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Supporting Information

for

Chiral bifunctional sulfide-catalyzed enantioselective bromolactonizations of α- and β-substituted 5-hexenoic acids

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Experimental procedures, characterization data, copies of NMR spectra, and copies of HPLC charts

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General information

^{1}H and ^{13}C NMR spectra were measured on a JEOL JNM-ECZ 400R NMR instrument (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR). Tetramethylsilane (TMS) served as the internal standard (0 ppm) for ^{1}H NMR, and $CDCl_3$ served as the internal standard (77.0 ppm) for ^{13}C NMR. The following abbreviations were used to express the multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet. High-resolution mass spectra (HRMS) were measured on a JEOL JMS-700N. Infrared spectra (IR) were measured on a JASCO FT/IR-4200 spectrometer. Optical rotations were measured on a JASCO P-2100 polarimeter. High-performance liquid chromatography (HPLC) was performed on Shimadzu LC-20AT and SPD-20A instruments using Daicel Chiralpak AS-3, IB-3, IC-3, IE-3, IG-3 columns (4.6 mm × 250 mm). All reactions were monitored by thin-layer chromatography using Merck precoated TLC plates (silica gel 60GF-254, 0.25 mm), with visualization by the use of UV lamp (254 nm) or dyes. The products were purified by flash column chromatography on silica gel.

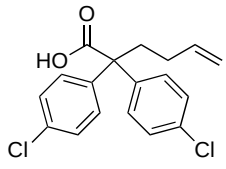
Experimental section

Synthesis of catalysts.

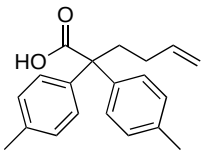
BINOL-derived chiral sulfide catalysts (*S*)-**1a**,[S1] (*S*)-**1b**,[S2] (*S*)-**1c**,[S3] (*S*)-**1d**,[S4] (*S*)-**1e**,[S2] (*S*)-**1f**,[S2] (*S*)-**1g**,[S4] (*S*)-**4**,[S1] (*S*)-**5**,[S5] and (*S*)-**6**[S1] were prepared according to the literature method.

Preparation of substrates.

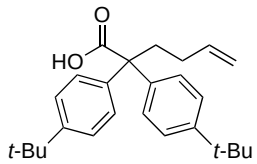
Substrates **2a**, **2e**, **2f**, **2g**, **2h**, **2i**, **2j**, and **2o** are known and commercially available compounds. Substrates **2b**,[S6] **2c**,[S6] **2d**,[S6] **2k**,[S7] **2l**,[S7] **2m**[S7] and **2n**[S7] were prepared according to the literature procedures.



2b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.8 Hz, 4H), 7.22 (d, *J* = 8.8 Hz, 4H), 5.79–5.69 (m, 1H), 4.99–4.93 (m, 2H), 2.42–2.28 (m, 2H), 1.82–1.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.9, 140.3, 137.5, 133.3, 130.3, 128.3, 115.1, 59.2, 36.9, 29.4; IR (neat): 3076, 2977, 2958, 2936, 1698, 1492, 1095, 1013, 905, 820, 729 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{16}Cl_2O_2$: 334.0527 ([M]$^+$), found 334.0527.

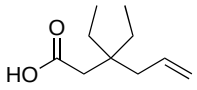


2c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dt, *J* = 8.4, 2.0 Hz, 4H), 7.10 (d, *J* = 8.0 Hz, 4H), 5.80–5.70 (m, 1H), 4.98–4.88 (m, 2H), 2.42–2.38 (m, 2H), 2.33 (s, 6H), 1.83–1.77 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.2, 139.3, 138.3, 136.5, 128.8, 128.6, 114.5, 59.4, 37.0, 29.6, 20.9; IR (neat): 3064, 2923, 2871, 1696, 1510, 1260, 907, 811, 732 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{22}O_2$: 294.1620 ([M]$^+$), found 294.1620.

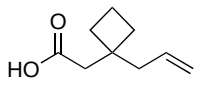


2d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (dt, *J* = 8.8, 2.0 Hz, 4H), 7.22 (dt, *J* = 8.4, 2.0 Hz, 4H), 5.82–5.72 (m, 1H), 5.00–4.89 (m, 2H), 2.44–2.40 (m, 2H), 1.85–1.80 (m, 2H), 1.31 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.0, 149.6, 139.0, 138.4, 128.6, 124.8, 114.4, 59.3, 37.0, 34.4, 31.3, 29.5; IR (neat): 3076, 2962, 2904, 2869, 1697, 1269, 908,

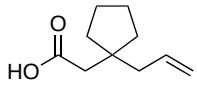
826, 733 cm^{-1}; HRMS (FAB) calcd for $C_{26}H_{35}O_2$: 379.2637 ($[M+H]^+$), found 379.2638.



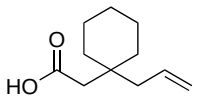
2k: ^1H NMR (400 MHz, $CDCl_3$) δ 5.86–5.75 (m, 1H), 5.11–5.06 (m, 2H), 2.24 (s, 2H), 2.12 (d, *J* = 7.5 Hz, 2H), 1.39 (q, *J* = 7.5 Hz, 4H) , 0.84 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.2, 134.3, 117.8, 40.1, 39.9, 38.9, 28.2, 7.5; IR (neat): 3075, 2968, 2926, 2883, 1703, 1458, 1408, 1297, 1217, 914 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{18}O_2$: 170.1307 ($[M]^+$), found 170.1307.



2l: ^1H NMR (400 MHz, $CDCl_3$) δ 5.85–5.75 (m, 1H), 5.12–5.07 (m, 2H), 2.47 (s, 2H), 2.34 (dt, *J* = 7.2, 1.2 Hz, 2H), 1.99–1.86 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.0, 134.5, 117.7, 42.91, 42.89, 39.7, 31.1, 15.2; IR (neat): 3077, 2978, 2933, 2859, 1702, 1408, 1274, 915 cm^{-1}; HRMS (EI) calcd for $C_9H_{14}O_2$: 154.0994 ($[M]^+$), found 154.0994.



2m: ^1H NMR (400 MHz, $CDCl_3$) δ 5.88–5.78 (m, 1H), 5.10–5.05 (m, 2H), 2.35 (s, 2H), 2.22 (d, *J* = 7.5 Hz, 2H), 1.66–1.53 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.4, 135.2, 117.7, 44.3, 42.8, 42.5, 37.1, 24.2; IR (neat): 3076, 2952, 2869, 1702, 1442, 1407, 1291, 1224, 995, 914 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{16}O_2$: 168.1150 ($[M]^+$), found 168.1150.

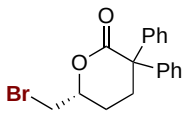


2n: ^1H NMR (400 MHz, $CDCl_3$) δ 5.89−5.79 (m, 1H), 5.11–5.05 (m, 2H), 2.31 (s, 2H), 2.22 (d, *J* = 7.5 Hz, 2H), 1.56–1.35 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.3, 134.2, 118.0, 41.7, 41.6, 36.1, 35.4, 26.0, 21.5; IR (neat): 3074, 2925, 2853, 1700, 1455, 1407, 1294, 1210, 913 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{18}O_2$: 182.1307 ($[M]^+$), found 182.1307.

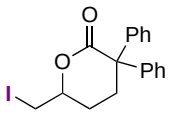
General procedure for asymmetric bromolactonizations (Scheme 4).

In a manner similar to our previous report,[S8] a solution of substrate **2** (0.10 mmol) and catalyst (*S*)-**1g** (6.0 mg, 0.010 mmol, 10 mol %) in CH_2Cl_2 (1.5 mL)-toluene (0.5 mL) was cooled to –78 °C. After stirring for 10 min at –78 °C, *N*-bromophthalimide (NBP) (27.1 mg, 0.12 mmol, 1.2 equiv) was added to the cooled reaction solution. The

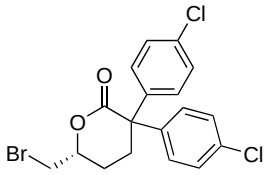
reaction mixture was stirred for 24 h at –78 °C. After 24 h, the reaction mixture was quenched with saturated aqueous Na_2SO_3 (3 mL) at –78 °C and stirred for 10 min at –78 °C. The quenched reaction mixture was diluted with CH_2Cl_2 (2 mL) and H_2O (2 mL), and the solution was warmed to room temperature. The organic materials were extracted with CH_2Cl_2 for three times (5 mL × 3). The combined extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel to give product **3**. The enantioselectivities of the isolated products **3** were determined by HPLC analysis on a chiral stationary phase.



3a: $[\alpha]^{26}_D$ –23.4 (*c* = 1.0, $CHCl_3$, 89:11 er); HPLC analysis: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm; retention time: 22.2 min (major) and 25.6 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.24 (m, 8H), 7.18–7.15 (m, 2H), 4.54–4.47 (m, 1H), 3.49 (dd, *J* = 10.7, 4.3 Hz, 1H), 3.43 (dd, *J* = 10.6, 6.3 Hz, 1H), 2.81–2.74 (m, 1H), 2.69–2.63 (m, 1H), 2.11–2.03 (m, 1H), 1.94–1.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 142.1, 141.1, 128.6, 128.4, 128.11, 128.09, 127.6, 127.3, 77.9, 56.8, 34.0, 31.6, 24.1; IR (neat): 3060, 3026, 2963, 2932, 1736, 1496, 1446, 1263, 1164, 1144, 1121, 1109, 1063, 751, 698 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{17}BrO_2$: 344.0412 ([M]$^+$), found 344.0411.

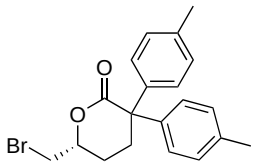


Iodolactonization Product: HPLC analysis: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm; retention time: 23.6 min and 27.7 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.22 (m, 8H), 7.19–7.15 (m, 2H), 4.32–4.26 (m, 1H), 3.32 (ddd, *J* = 10.4, 4.2, 1.6 Hz, 1H), 3.24 (dd, *J* = 10.4, 6.7 Hz, 1H), 2.80–2.73 (m, 1H), 2.67–2.61 (m, 1H), 2.17–2.08 (m, 1H), 1.84–1.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 142.0, 141.2, 128.5, 128.4, 128.14, 128.08, 127.5, 127.3, 78.1, 56.6, 31.8, 25.9, 7.7; IR (neat): 3059, 3031, 2958, 2937, 1733, 1496, 1446, 1258, 1156, 1137, 1121, 1108, 1052, 751, 698 cm^{-1}; HRMS (FAB) calcd for $C_{18}H_{18}IO_2$: 393.0351 ([M+H]$^+$), found 393.0351.

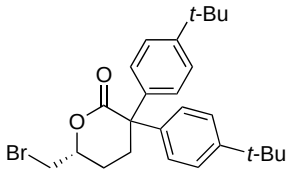


3b: $[\alpha]^{25}_D$ –10.4 (*c* = 1.0, $CHCl_3$, 86:14 er); HPLC analysis: Daicel Chiralpak IC-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm; retention time: 19.9 min (minor) and 22.8 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 4H), 7.16 (dt, *J* = 8.9,

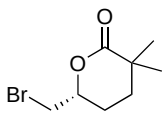
2.2 Hz, 2H), 7.10 (dt, J = 8.9, 2.2 Hz, 2H), 4.57–4.51 (m, 1H), 3.49 (dd, J = 10.8, 4.4 Hz, 1H), 3.46 (dd, J = 10.8, 5.8 Hz, 1H), 2.76–2.69 (m, 1H), 2.63–2.57 (m, 1H), 2.09–2.02 (m, 1H), 1.93–1.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 140.3, 139.6, 133.8, 133.6, 129.49, 129.48, 128.8, 128.7, 78.3, 55.9, 33.9, 31.7, 24.0; IR (neat): 2963, 1732, 1492, 1248, 1164, 1145, 1128, 1095, 1012, 820, 734 cm^{-1}; HRMS (FAB) calcd for $C_{18}H_{16}BrCl_2O_2$: 412.9711 ([M+H]$^+$), found 412.9711.



3c: $[\alpha]^{26}_D$ –20.7 (c = 1.0, $CHCl_3$, 89:11 er); HPLC analysis: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm; retention time: 28.8 min (major) and 33.9 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17–7.11 (m, 6H), 7.03 (dt, J = 8.4, 2.0 Hz, 2H), 4.51–4.45 (m, 1H), 3.47 (dd, J = 10.7, 4.3 Hz, 1H), 3.41 (dd, J = 10.7, 6.2 Hz, 1H), 2.77–2.70 (m, 1H), 2.64–2.58 (m, 1H), 2.34 (s, 3H), 2.33 (s, 3H), 2.08–2.01 (m, 1H), 1.93–1.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 139.3, 138.1, 137.3, 136.9, 129.3, 129.0, 127.93, 127.87, 77.7, 56.1, 34.1, 31.5, 24.2, 21.0, 20.9; IR (neat): 3024, 2961, 2922, 1733, 1512, 1249, 1160, 1143, 1134, 1104, 1062, 810, 731 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{21}BrO_2$: 372.0725 ([M]$^+$), found 372.0719.

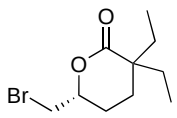


3d: $[\alpha]^{19}_D$ –13.2 (c = 1.0, $CHCl_3$, 80:20 er); HPLC analysis: Daicel Chiralpak IE-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 254 nm; retention time: 24.3 min (major) and 29.5 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dt, J = 8.4, 2.2 Hz, 2H), 7.32 (dt, J = 8.4, 2.2 Hz, 2H), 7.16 (dt, J = 8.4, 2.2 Hz, 2H), 7.06 (dt, J = 8.8, 2.2 Hz, 2H), 4.51–4.45 (m, 1H), 3.49 (dd, J = 10.7, 4.3 Hz, 1H), 3.42 (dd, J = 10.5, 6.4 Hz, 1H), 2.76–2.69 (m, 1H), 2.65–2.58 (m, 1H), 2.11–2.04 (m, 1H), 1.93–1.84 (m, 1H), 1.31 (s, 9H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 150.3, 149.9, 139.2, 138.0, 127.7, 127.6, 125.5, 125.2, 77.8, 56.1, 34.43, 34.38, 34.0, 31.8, 31.3, 24.2; IR (neat): 2962, 2903, 2868, 1734, 1509, 1463, 1363, 1268, 1164, 1138, 1108, 911, 827, 735 cm^{-1}; HRMS (FAB) calcd for $C_{26}H_{34}BrO_2$: 457.1742 ([M+H]$^+$), found 457.1742.

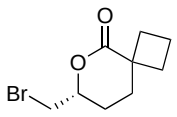


3e: $[\alpha]^{26}_D$ +5.2 (c = 1.1, $CHCl_3$, 69:31 er); HPLC analysis: Daicel Chiralpak IC-3, hexane/2-propanol = 3:1, flow rate = 0.5 mL/min, 214 nm; retention time: 19.6 min (major) and 23.4 min (minor). ^{1}H NMR (400 MHz,

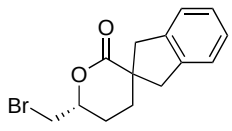
$CDCl_3$) δ 4.54–4.48 (m, 1H), 3.53 (dd, *J* = 10.8, 4.4 Hz, 1H), 3.50 (dd, *J* = 10.6, 5.8 Hz, 1H), 2.05–1.89 (m, 2H), 1.86–1.71 (m, 2H), 1.32 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 79.1, 37.9, 34.3, 33.7, 27.6, 27.4, 24.2; IR (neat): 2966, 2871, 1729, 1387, 1287, 1146, 1121, 1016, 749 cm^{-1}; HRMS (EI) calcd for $C_8H_{13}BrO_2$: 220.0099 ($[M]^+$), found 220.0097.



3f: $[\alpha]^{23}_D$ +4.1 (*c* = 0.91, $CHCl_3$, 79:21 er); HPLC analysis: Daicel Chiralpak IC-3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, 214 nm; retention time: 24.4 min (major) and 28.2 min (minor). ^1H NMR (400 MHz, $CDCl_3$) δ 4.49–4.40 (m, 1H), 3.52 (dd, *J* = 10.9, 4.0 Hz, 1H), 3.46 (dd, *J* = 10.6, 6.3 Hz, 1H), 2.10–1.99 (m, 1H), 1.89–1.72 (m, 5H), 1.68–1.58 (m, 1H), 1.53–1.46 (m, 1H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 78.7, 45.7, 34.1, 31.8, 31.0, 27.3, 24.8, 8.7, 8.6; IR (neat): 2964, 2925, 1723, 1461, 1249, 1139, 1116, 1034, 948 cm^{-1}; HRMS (FAB) calcd for $C_{10}H_{18}BrO_2$: 249.0490 ($[M+H]^+$), found 249.0490.

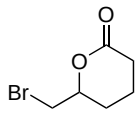


3g: $[\alpha]^{25}_D$ +5.6 (*c* = 1.1, $CHCl_3$, 72:28 er); HPLC analysis: Daicel Chiralpak IC-3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, 254 nm; retention time: 40.4 min (major) and 50.4 min (minor). ^1H NMR (400 MHz, $CDCl_3$) δ 4.47–4.41 (m, 1H), 3.50 (dd, *J* = 10.7, 4.3 Hz, 1H), 3.44 (dd, *J* = 10.7, 6.2 Hz, 1H), 2.73–2.65 (m, 1H), 2.59–2.51 (m, 1H), 2.16–1.70 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 78.0, 42.6, 34.0, 32.3, 31.0, 30.5, 24.4, 15.5; IR (neat): 2928, 2855, 1732, 1306, 1151, 1113, 1090, 1012 cm^{-1}; HRMS (EI) calcd for $C_9H_{13}BrO_2$: 232.0099 ($[M]^+$), found 232.0099.

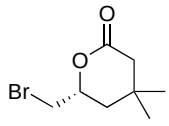


3h: $[\alpha]^{25}_D$ +28.4 (*c* = 1.3, $CHCl_3$, 80:20 er); HPLC analysis: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm; retention time: 22.2 min (major) and 23.7 min (minor). ^1H NMR (400 MHz, $CDCl_3$) δ 7.22–7.16 (m, 4H), 4.65–4.59 (m, 1H), 3.79 (d, *J* = 15.8 Hz, 1H), 3.60–3.53 (m, 2H), 3.48 (d, *J* = 15.8 Hz, 1H), 3.05 (d, *J* = 15.8 Hz, 1H), 2.89 (d, *J* = 15.8 Hz, 1H), 2.13–1.86 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 140.7, 139.5, 127.0, 126.8, 124.6, 124.5, 78.7, 48.7, 45.6, 45.2, 34.3, 31.6, 24.6; IR (neat): 2937, 1731, 1302, 1228, 1150, 1101, 1071, 989, 913, 747 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{15}BrO_2$:

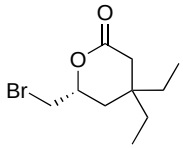
294.0255 ([M]$^+$), found 294.0255.



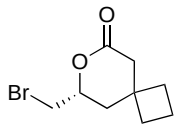
3i:[S9] HPLC analysis: Daicel Chiralpak IE-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm; retention time: 34.0 min (major) and 37.1 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.54–4.48 (m, 1H), 3.54 (ddd, *J* = 10.7, 4.5, 0.8 Hz, 1H), 3.48 (dd, *J* = 10.7, 6.2 Hz, 1H), 2.67–2.59 (m, 1H), 2.53–2.44 (m, 1H), 2.18–2.10 (m, 1H), 2.04–1.83 (m, 2H), 1.77–1.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 78.6, 33.7, 29.4, 26.3, 18.1; IR (neat): 1736, 1234, 1041 cm^{-1}; HRMS (EI) calcd for $C_6H_9BrO_2$: 191.9786 ([M]$^+$), found 191.9788.



3j:[S10] [α]$^{21}_D$ +3.0 (*c* = 1.2, $CHCl_3$, 84:16 er); HPLC analysis: Daicel Chiralpak IE-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm; retention time: 25.0 min (major) and 27.2 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.62–4.55 (m, 1H), 3.54 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.51 (dd, *J* = 10.8, 5.6 Hz, 1H), 2.40 (dd, *J* = 16.8, 2.2 Hz, 1H), 2.26 (d, *J* = 16.9 Hz, 1H), 1.87 (ddd, *J* = 14.0, 4.0, 2.0 Hz, 1H), 1.62 (dd, *J* = 14.0, 11.9 Hz, 1H), 1.12 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 75.8, 43.6, 40.1, 34.4, 30.7, 29.8, 26.9; IR (neat): 2960, 1739, 1371, 1238, 1198, 1054, 1044 cm^{-1}; HRMS (EI) calcd for $C_8H_{13}BrO_2$: 220.0099 ([M]$^+$), found 220.0099.

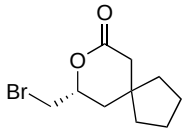


3k: [α]$^{19}_D$ –11.2 (*c* = 1.1, $CHCl_3$, 89:11 er); HPLC analysis: Daicel Chiralpak IG-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm; retention time: 22.1 min (major) and 24.1 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.51–4.45 (m, 1H), 3.53 (dd, *J* = 10.6, 4.7 Hz, 1H), 3.47 (dd, *J* = 10.6, 6.1 Hz, 1H), 2.37 (dd, *J* = 16.5, 1.4 Hz, 1H), 2.26 (d, *J* = 16.2 Hz, 1H), 1.94 (ddd, *J* = 14.2, 3.3, 1.3 Hz, 1H), 1.53–1.35 (m, 5H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.85 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 75.4, 40.2, 36.4, 35.3, 33.9, 31.7, 29.2, 7.6, 7.3; IR (neat): 2965, 2927, 1748, 1457, 1248, 1218, 1053 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{17}BrO_2$: 248.0412 ([M]$^+$), found 248.0415.

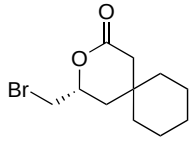


3l: [α]$^{20}_D$ +9.7 (*c* = 1.4, $CHCl_3$, 81:19 er); HPLC analysis: Daicel Chiralpak IE-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm; retention time: 30.2 min (major) and 31.8 min (minor). ^{1}H NMR (400

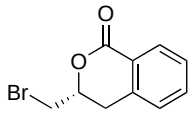
MHz, $CDCl_3$) δ 4.53–4.46 (m, 1H), 3.54 (dd, *J* = 10.8, 4.4 Hz, 1H), 3.51 (dd, *J* = 10.8, 6.0 Hz, 1H), 2.80 (dd, *J* = 17.5, 2.2 Hz, 1H), 2.43 (d, *J* = 17.6 Hz, 1H), 2.18 (ddd, *J* = 13.7, 3.5, 2.2 Hz, 1H), 2.02–1.87 (m, 6H), 1.75 (dd, *J* = 13.7, 11.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 75.5, 42.3, 38.4, 36.4, 34.2, 33.1, 31.9, 14.9; IR (neat): 2950, 1739, 1236, 1195, 1123, 1036, 913, 741 cm^{-1}; HRMS (EI) calcd for $C_9H_{14}BrO_2$: 233.0177 ($[M+H]^+$), found 233.0175.



3m: $[\alpha]^{21}_D$ +5.1 (*c* = 1.2, $CHCl_3$, 82:18 er); HPLC analysis: Daicel Chiralpak IG-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm; retention time: 25.5 min (major) and 27.7 min (minor). ^1H NMR (400 MHz, $CDCl_3$) δ 4.59–4.53 (m, 1H), 3.54 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.51 (dd, *J* = 10.8, 5.6 Hz, 1H), 2.52 (dd, *J* = 17.2, 2.1 Hz, 1H), 2.31 (d, *J* = 17.2 Hz, 1H), 1.91 (ddd, *J* = 13.6, 3.6, 2.2 Hz, 1H), 1.79–1.63 (m, 5H), 1.61–1.48 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 76.5, 41.9, 40.54, 40.52, 38.6, 36.9, 34.5, 24.1, 23.5; IR (neat): 2952, 2864, 1733, 1245, 1099, 1056, 1041 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{15}BrO_2$: 246.0255 ($[M]^+$), found 246.0255.



3n: $[\alpha]^{19}_D$ –9.8 (*c* = 0.95, $CHCl_3$, 85:15 er); HPLC analysis: Daicel Chiralpak IG-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm; retention time: 26.9 min (major) and 29.8 min (minor). ^1H NMR (400 MHz, $CDCl_3$) δ 4.56–4.50 (m, 1H), 3.53 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.49 (dd, *J* = 10.8, 6.0 Hz, 1H), 2.49 (dd, *J* = 16.7, 1.4 Hz, 1H), 2.26 (d, *J* = 16.5 Hz, 1H), 2.08–2.03 (m, 1H), 1.53–1.33 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 75.2, 41.9, 39.4, 37.8, 35.7, 34.2, 32.7, 25.6, 21.6, 21.3; IR (neat): 2927, 2853, 1741, 1243, 1202, 1102, 1052, 1035, 913, 739 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{17}BrO_2$: 260.0412 ($[M]^+$), found 260.0412.



3o:[S11] $[\alpha]^{19}_D$ +34.7 (*c* = 0.83, $CHCl_3$, 67:33 er), $[\alpha]^{21}_D$ +29.1 (*c* = 1.4, CH_2Cl_2, 67:33 er); HPLC analysis: Daicel Chiralpak AS-3, hexane/2-propanol = 1:1, flow rate = 0.5 mL/min, 254 nm; retention time: 18.7 min (major) and 26.2 min (minor). ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.58 (td, *J* = 7.4, 1.4 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 7.5 Hz, 1H), 4.78–4.72 (m, 1H), 3.69 (dd, *J* = 10.7, 4.6 Hz, 1H), 3.60 (dd, *J* = 10.7, 7.1 Hz, 1H), 3.24–3.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 137.8, 134.1, 130.4, 128.0, 127.7,

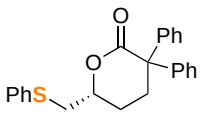
124.5, 76.7, 32.4, 31.5; IR (neat): 1727, 1278, 1242, 1120, 1085, 1032, 913, 741 cm^{-1}; HRMS (EI) calcd for $C_{10}H_9BrO_2$: 239.9786 ($[M]^+$), found 239.9786.

Asymmetric bromolactonization of 2a on a larger scale (Scheme 5).

In a manner similar to our previous report,[S8] a solution of substrate **2a** (266 mg, 1.0 mmol) and catalyst (*S*)-**1g** (60.1 mg, 0.10 mmol, 10 mol %) in CH_2Cl_2 (15 mL)-toluene (5 mL) was cooled to –78 °C. After stirring for 10 min at –78 °C, *N*-bromophthalimide (NBP) (271 mg, 1.2 mmol) was added to the cooled reaction solution. The reaction mixture was stirred for 24 h at –78 °C. After 24 h, the reaction mixture was quenched with saturated aqueous Na_2SO_3 (30 mL) at –78 °C and stirred for 10 min at –78 °C. The quenched reaction mixture was diluted with CH_2Cl_2 (20 mL) and H_2O (20 mL), and the mixture was warmed to room temperature. The organic materials were extracted with CH_2Cl_2 for three times (20 mL × 3). The combined extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/ethyl acetate = 40:1–3:1) to give product **3a** in 91% yield (314 mg, 0.91 mmol). The enantioselectivity of isolated product **3a** was determined by HPLC analysis on a chiral stationary phase (Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm).

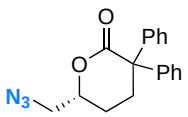
Transformations of 3a (Scheme 5).

In a manner similar to our previous report,[S8] to a solution of **3a** (34.5 mg, 0.10 mmol) in CH_3CN (1 mL) was added K_2CO_3 (41.5 mg, 0.30 mmol) and thiophenol (33.1 mg, 0.30 mmol). The reaction mixture was warmed to 75 °C and stirred for 3 h at 75 °C. After 3 h, the reaction mixture was cooled to 0 °C and quenched with saturated aqueous NH_4Cl (5 mL). After evaporation to remove CH_3CN, the organic materials were extracted with ethyl acetate for three times (5 mL × 3). The combined extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/ethyl acetate = 40:1–3:1 as eluent) to give product **7** in 95% yield (35.6 mg, 0.095 mmol).



7: $[\alpha]^{20}_{D}$ –19.6 (*c* = 1.1, $CHCl_3$, 89:11 er); HPLC analysis: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm; retention time: 37.9 min (major) and 39.5 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.24 (m, 10H), 7.22–7.15 (m, 5H), 4.46–4.39 (m, 1H), 3.32 (dd, *J* = 13.7, 4.6 Hz, 1H), 2.95 (dd, *J* = 13.7, 8.2 Hz, 1H), 2.74–2.59 (m, 2H), 2.18–2.05 (m, 1H), 1.83–1.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 142.3, 141.5, 134.9, 129.9, 129.1, 128.4, 128.3, 128.11, 128.06, 127.4, 127.2, 126.7, 78.5, 56.9, 39.0, 31.9, 24.6; IR (neat): 3059, 2960, 2926, 1733, 1496, 1445, 1255, 1166, 1120, 1091, 1054, 745 cm^{-1}; HRMS (EI) calcd for $C_{24}H_{22}O_2S$: 374.1341 ($[M]^+$), found 374.1341.

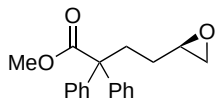
In a manner similar to our previous report,[S8] to a solution of **3a** (34.5 mg, 0.10 mmol) in *N*,*N*-dimethylformamide (2 mL) was added sodium azide (19.5 mg, 0.30 mmol). The reaction mixture was warmed to 100 °C and stirred for 24 h at 100 °C. After 24 h, the reaction mixture was cooled to 0 °C and quenched with H_2O (20 mL). The organic materials were extracted with ethyl acetate for three times (5 mL × 3). The combined extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/ethyl acetate = 40:1–3:1 as eluent) to give product **8** in 96% yield (29.5 mg, 0.096 mmol).



8: $[\alpha]^{23}_{D}$ –74.3 (*c* = 1.2, $CHCl_3$, 89:11 er); HPLC analysis: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm; retention time: 22.1 min (major) and 25.4 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.24 (m, 8H), 7.17–7.14 (m, 2H), 4.45–4.39 (m, 1H), 3.48 (dd, *J* = 13.2, 4.2 Hz, 1H), 3.35 (dd, *J* = 13.2, 4.9 Hz, 1H), 2.81–2.74 (m, 1H), 2.70–2.63 (m, 1H), 1.95–1.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 142.2, 140.9, 128.6, 128.4, 128.1, 127.6, 127.3, 77.8, 56.8, 54.4, 31.6, 22.6; IR (neat): 3059, 2955, 2937, 2099, 1732, 1496, 1446, 1287, 1257, 1172, 1122, 1100, 752, 698 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{17}N_3O_2$: 307.1321 ($[M]^+$), found 307.1321.

In a manner similar to our previous report,[S8] to a solution of **3a** (34.5 mg, 0.10 mmol) in MeOH (1 mL) was added K_2CO_3 (27.6 mg, 0.20 mmol) at room temperature.

The reaction mixture was stirred for 48 h at room temperature. After 48 h, the reaction mixture was quenched with H_2O (10 mL). The organic materials were extracted with ethyl acetate for three times (5 mL × 3). The combined extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/ethyl acetate = 20:1–3:1 as eluent) to give product **9** in 73% yield (21.6 mg, 0.073 mmol).



9: $[\alpha]^{22}_D$ +2.6 (*c* = 0.99, $CHCl_3$, 89:11 er); HPLC analysis: Daicel Chiralpak IB-3, hexane/2-propanol = 20:1, flow rate = 0.5 mL/min, 254 nm; retention time: 12.7 min (major) and 15.0 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.22 (m, 10H), 3.69 (s, 3H), 2.88–2.83 (m, 1H), 2.70 (dd, *J* = 4.8, 4.1 Hz, 1H), 2.59 (ddd, *J* = 13.2, 11.2, 5.2 Hz, 1H), 2.48 (ddd, *J* = 13.2, 11.2, 5.2 Hz, 1H), 2.38 (dd, *J* = 4.8, 2.8 Hz, 1H), 1.39–1.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 142.5, 142.4, 128.82, 128.80, 128.0, 126.93, 126.89, 59.9, 52.4, 52.3, 47.0, 34.2, 28.5; IR (neat): 3057, 2950, 1729, 1496, 1445, 1224, 731, 700 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{20}O_3$: 296.1412 ($[M]^+$), found 296.1412.

Determination of the absolute configuration of products.

Absolute stereochemistry of bromolactonization product **3o** was confirmed by comparison with reported data.[S11]

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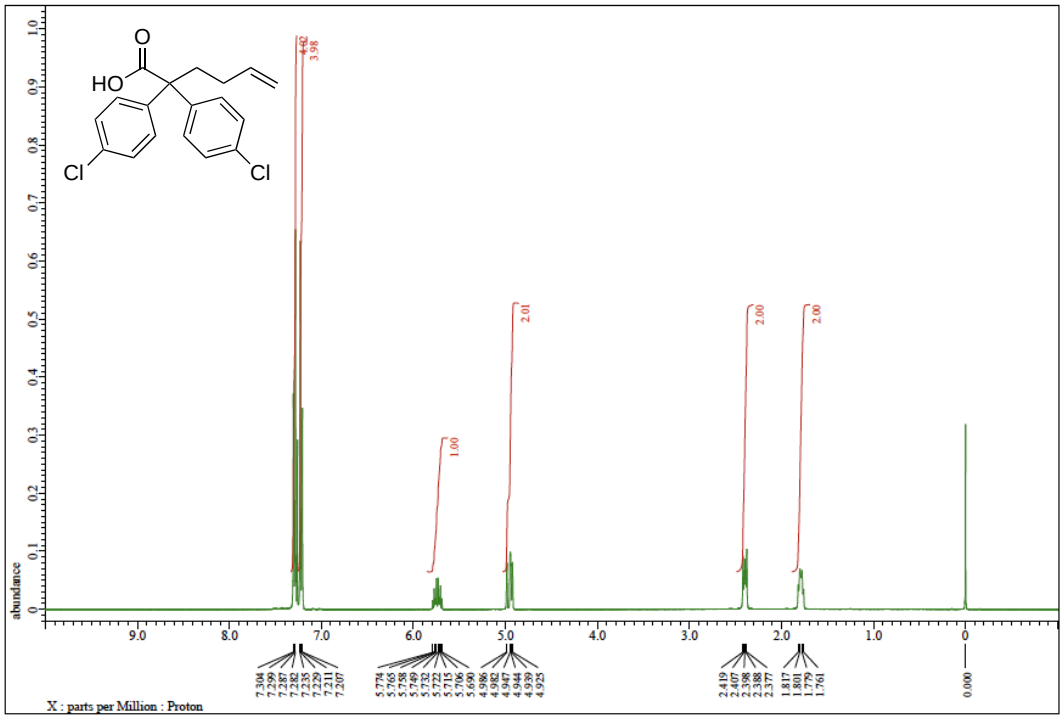
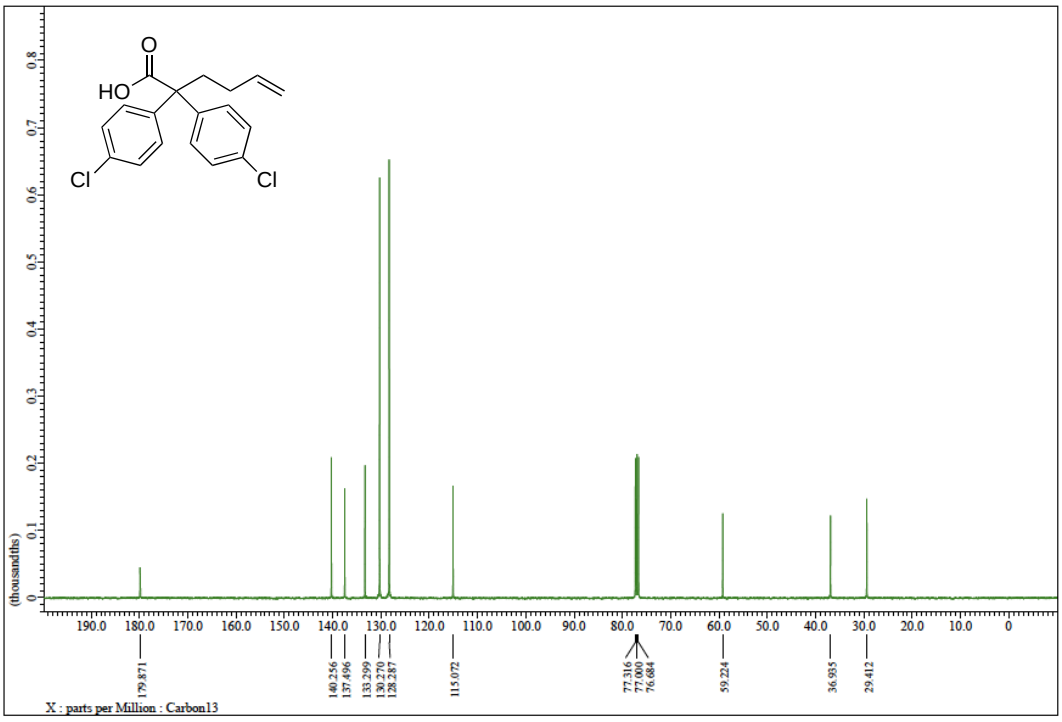
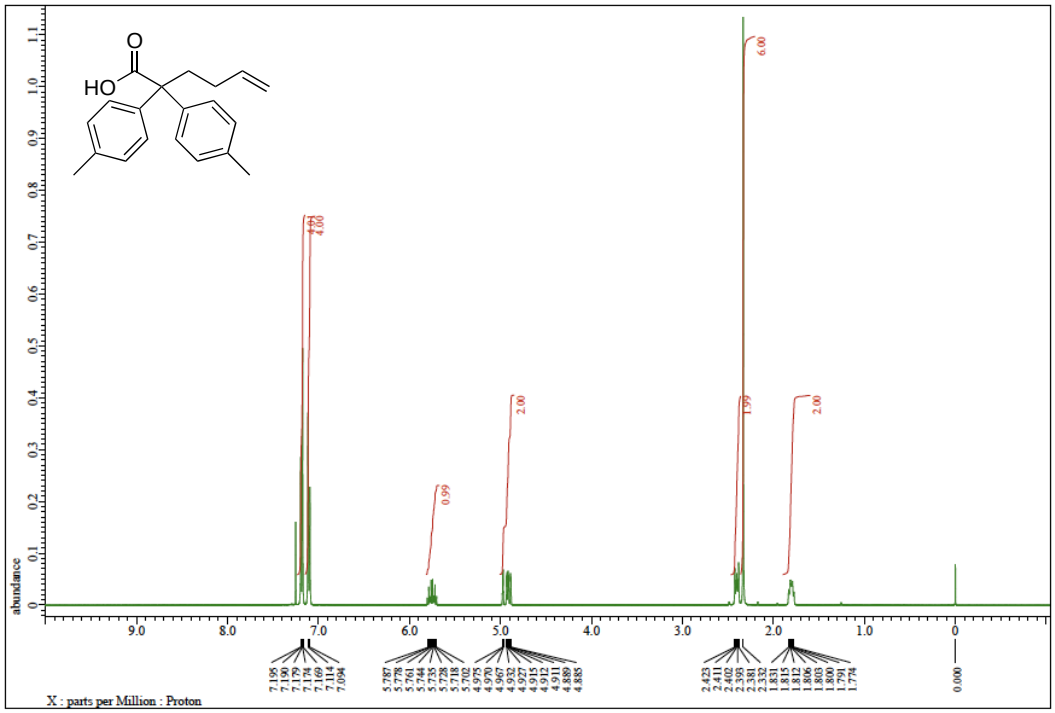
NMR Charts

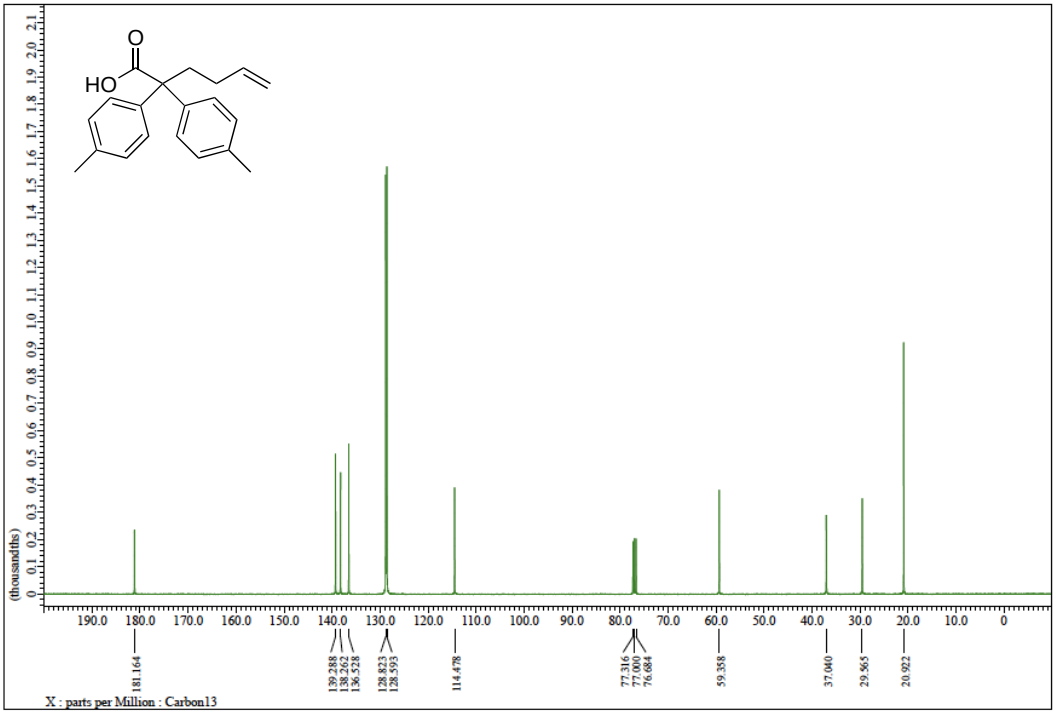
2b: ^{1}H and ^{13}C NMR



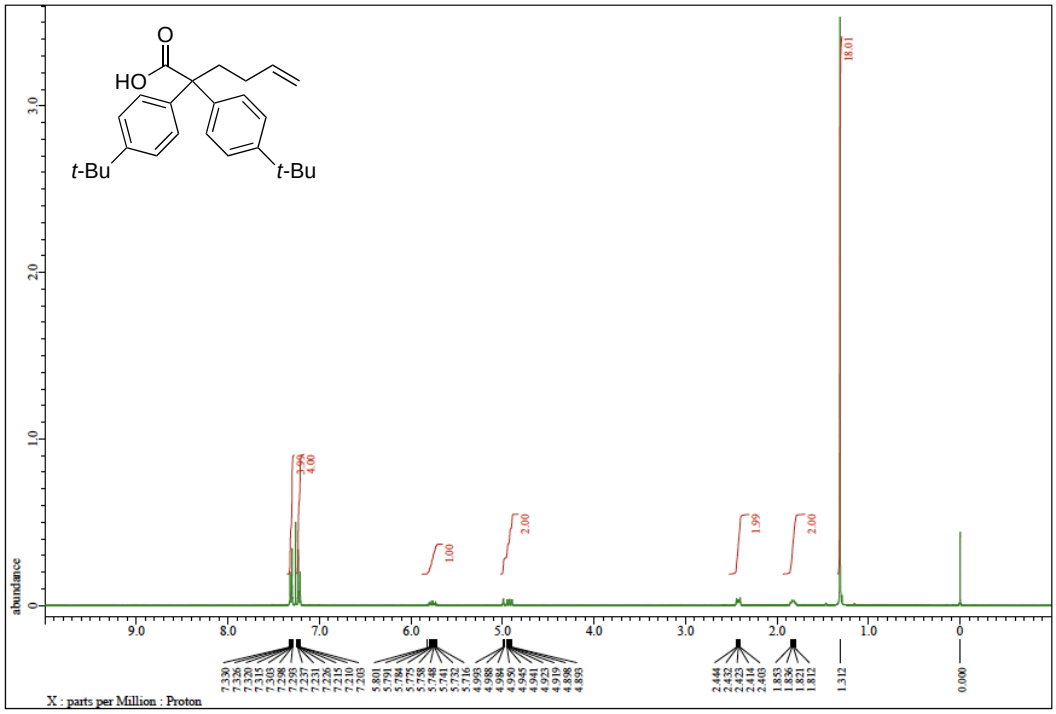


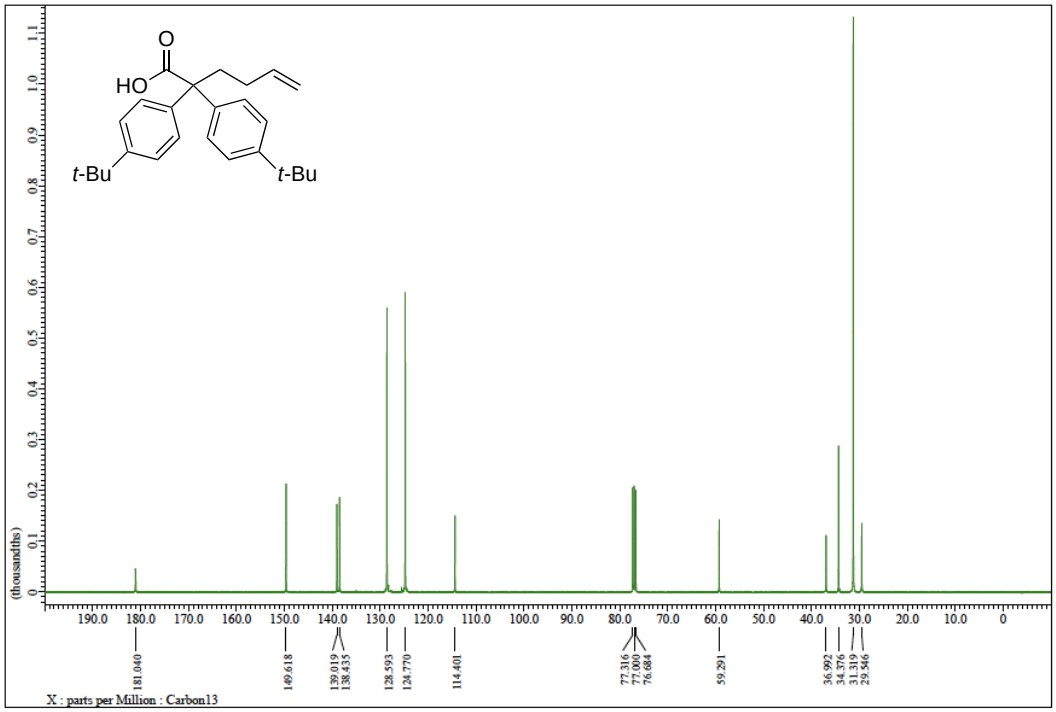
2c: ^{1}H and ^{13}C NMR



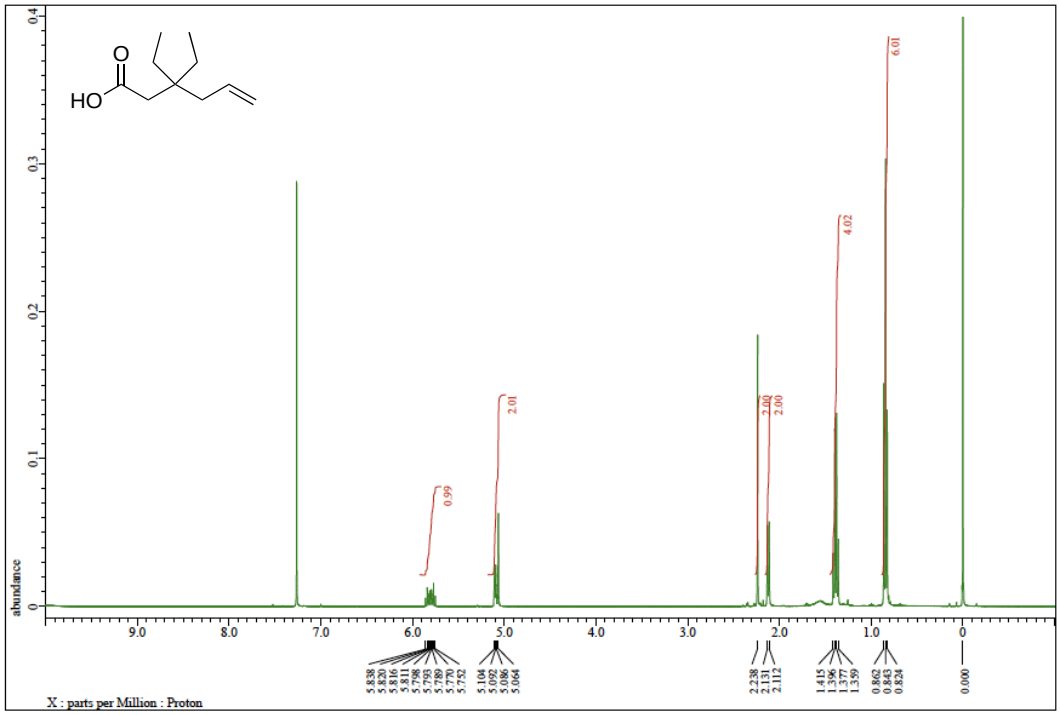


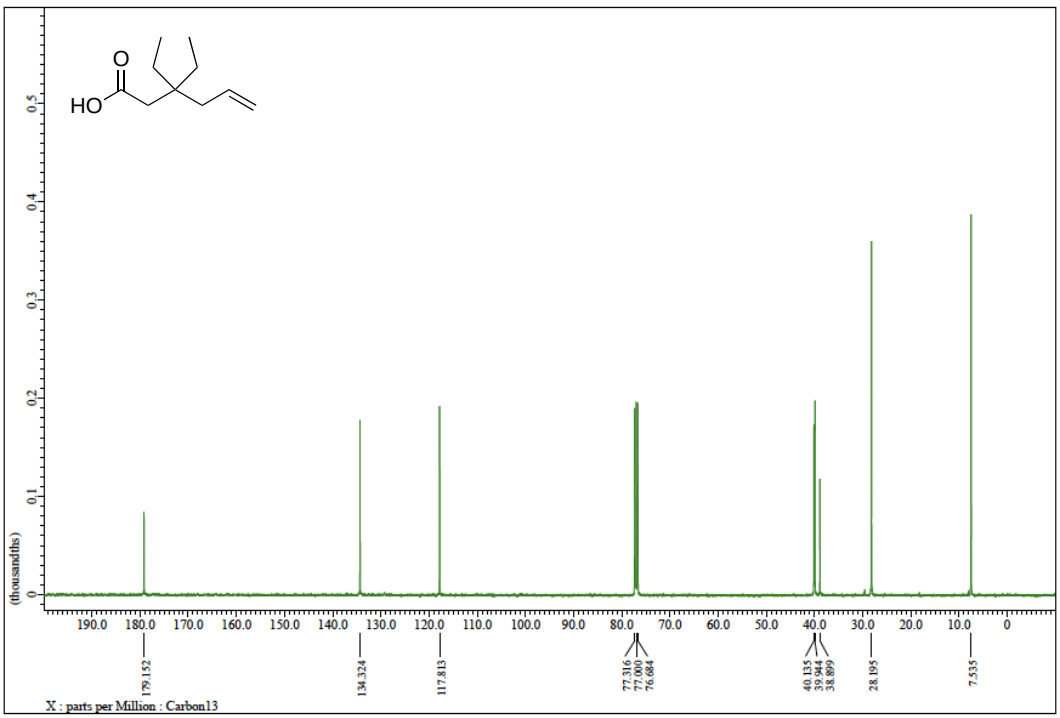
2d: ^{1}H and ^{13}C NMR



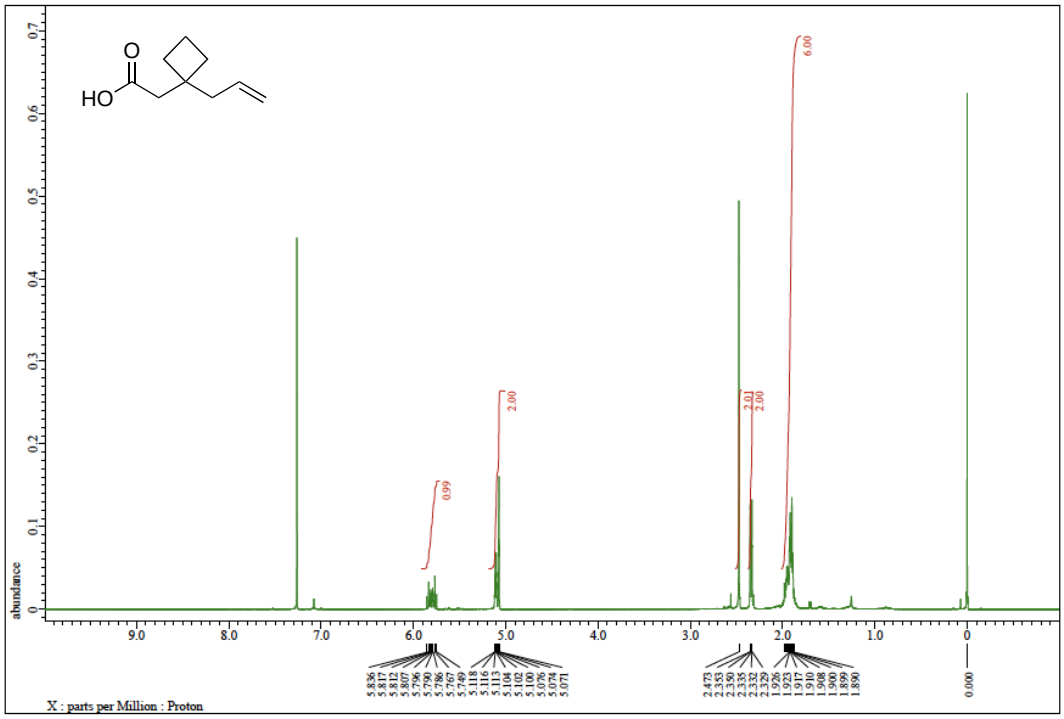


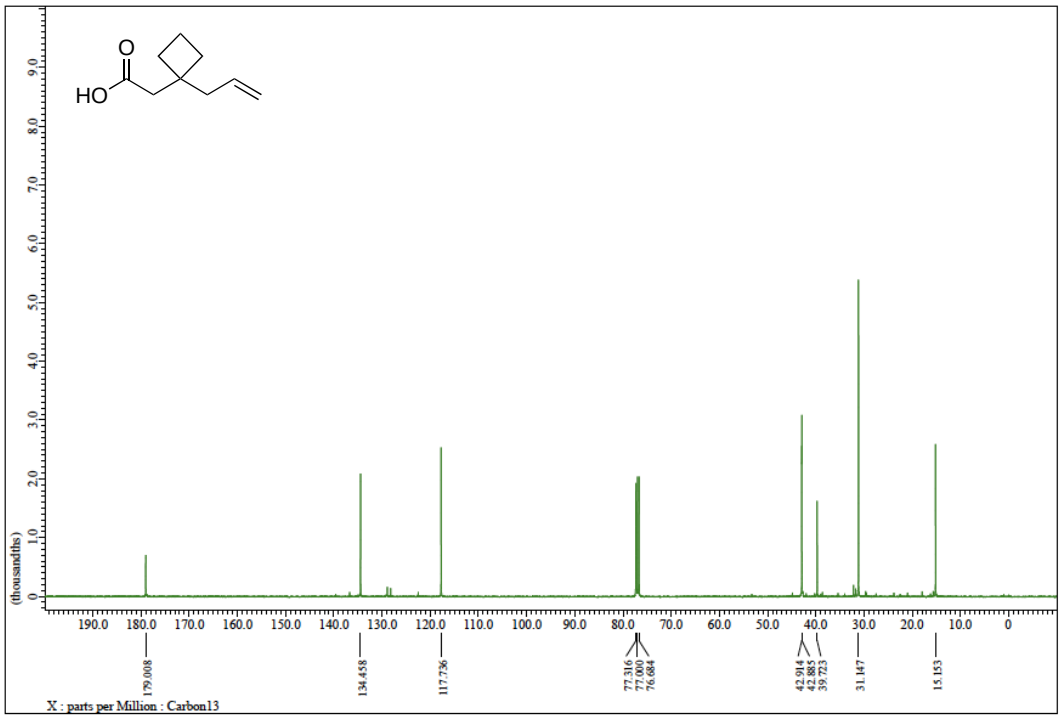
2k: ^{1}H and ^{13}C NMR



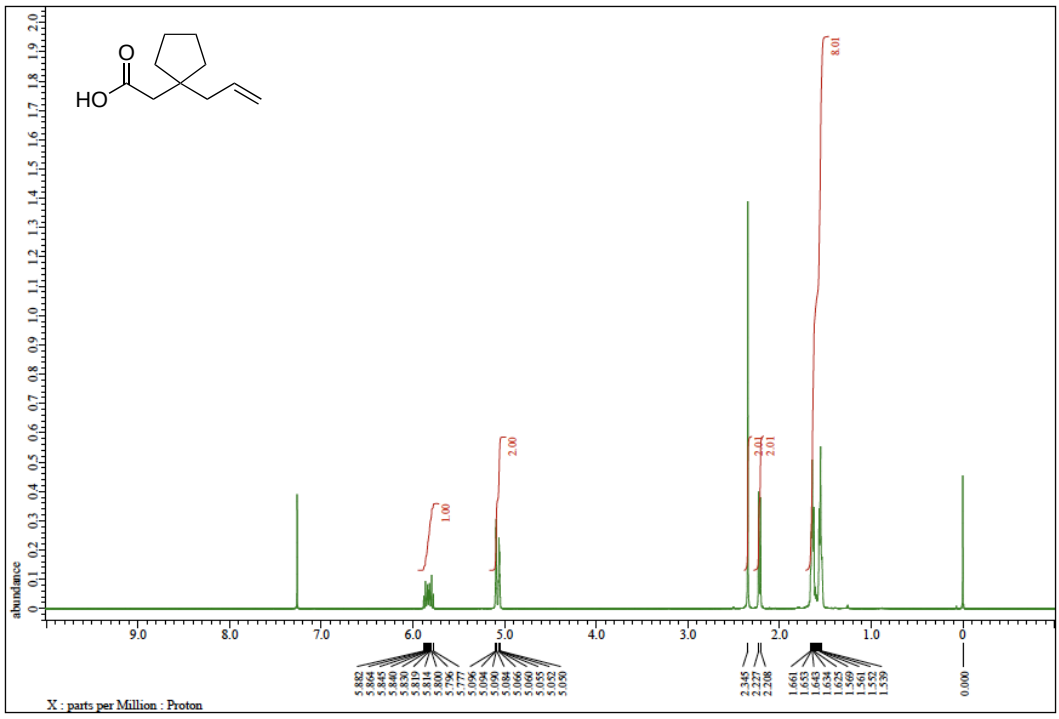


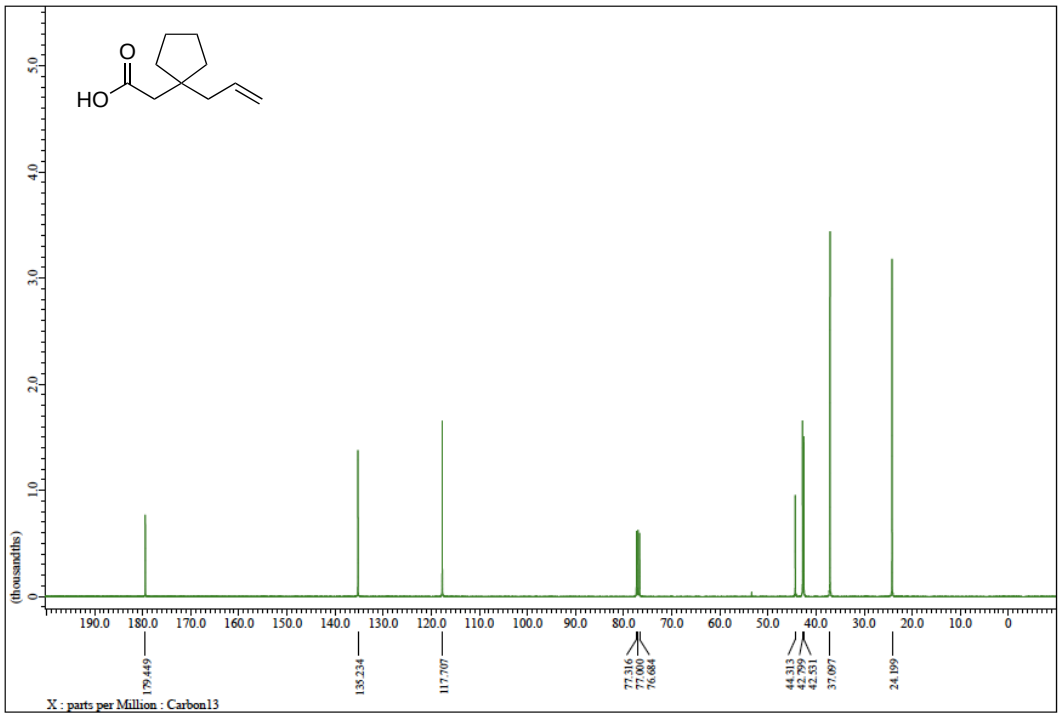
2l: ^{1}H and ^{13}C NMR



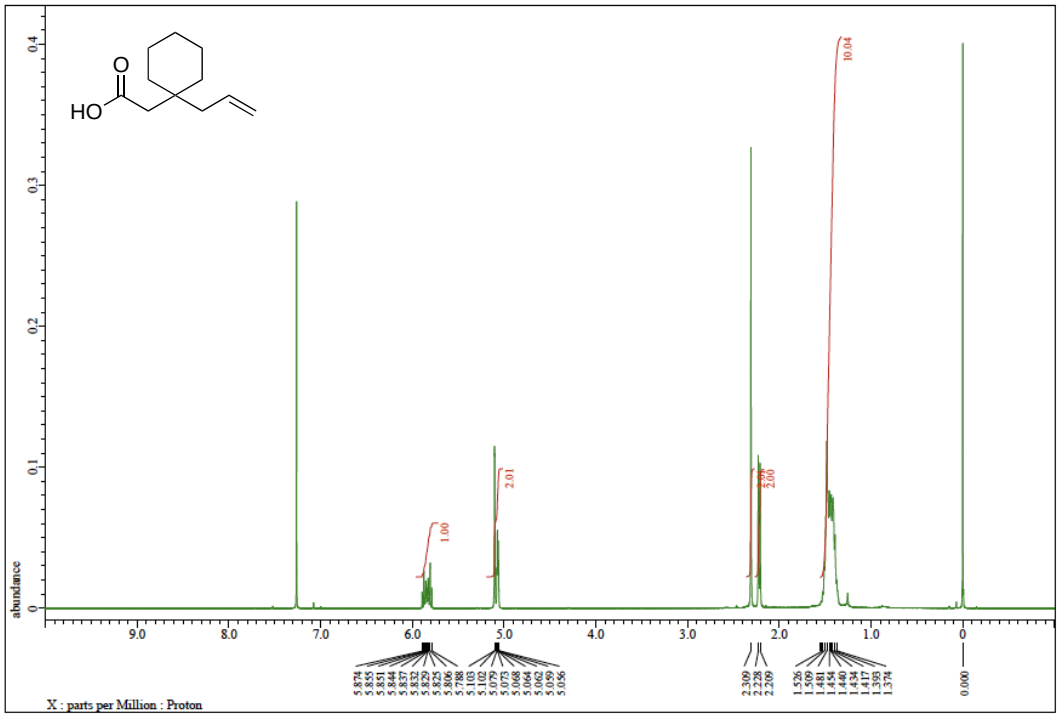


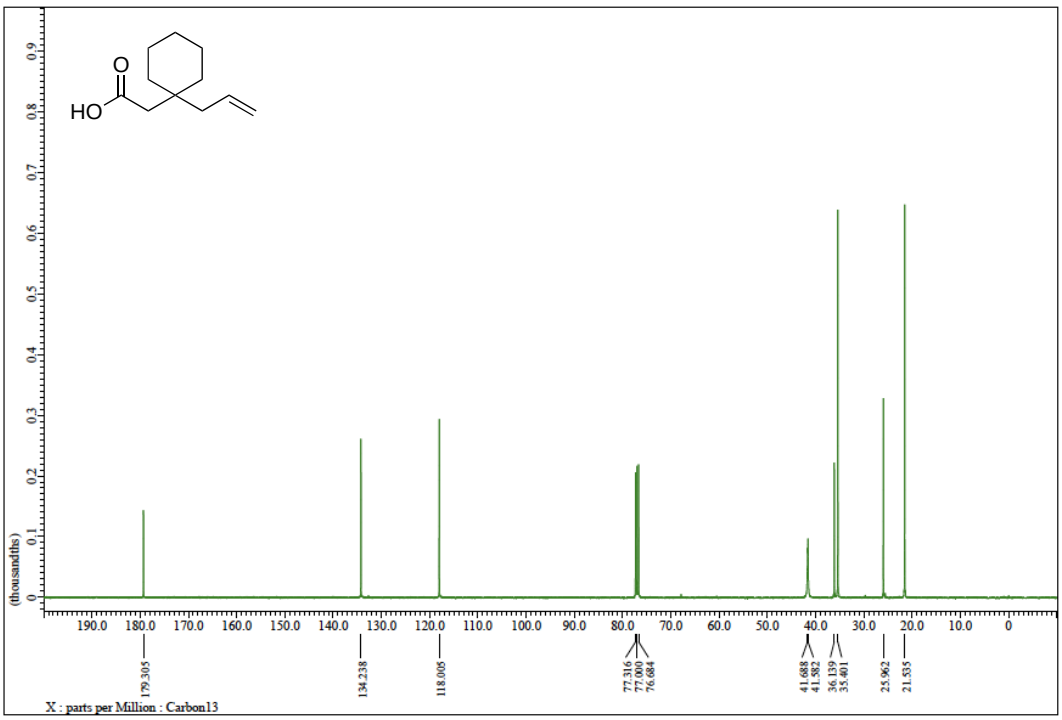
2m: ^{1}H and ^{13}C NMR



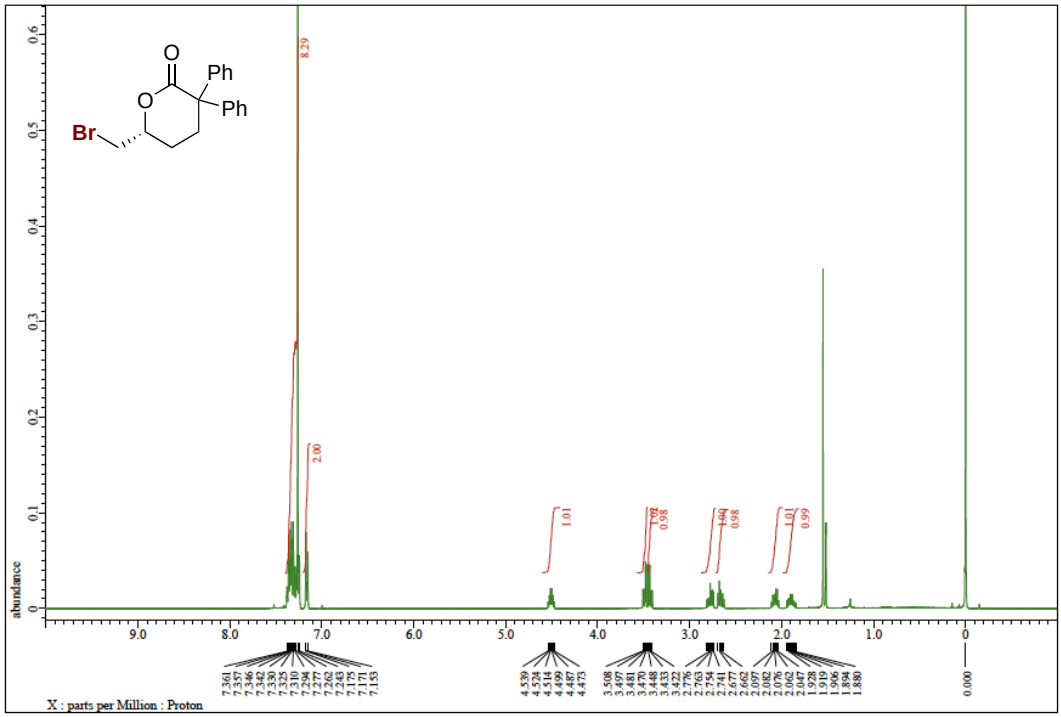


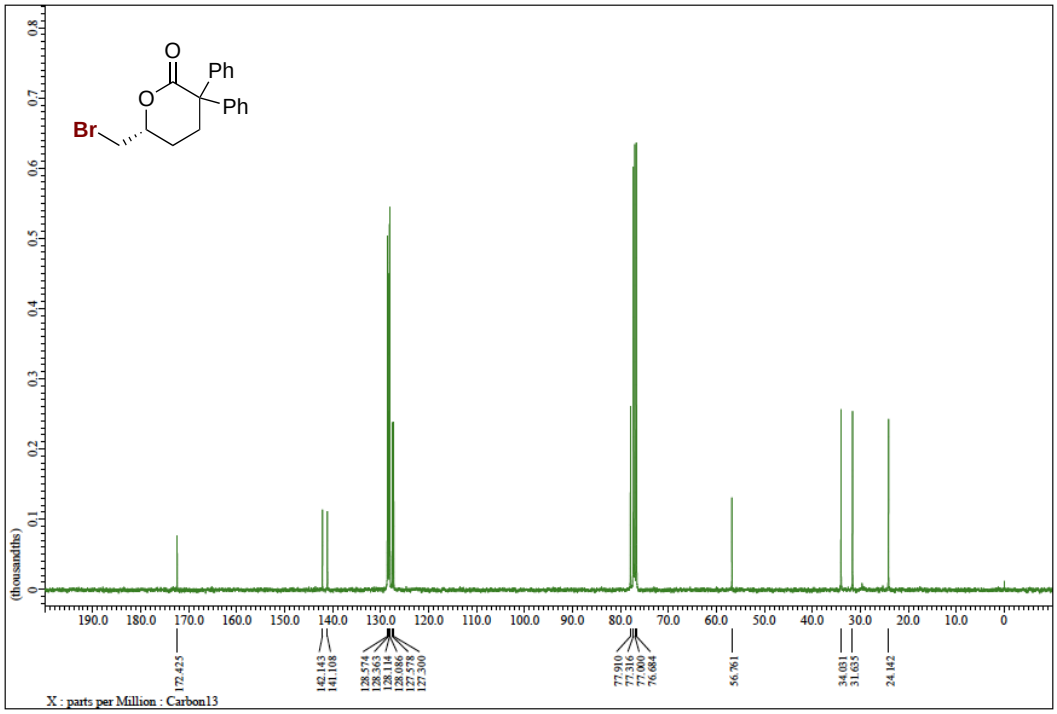
2n: ^{1}H and ^{13}C NMR



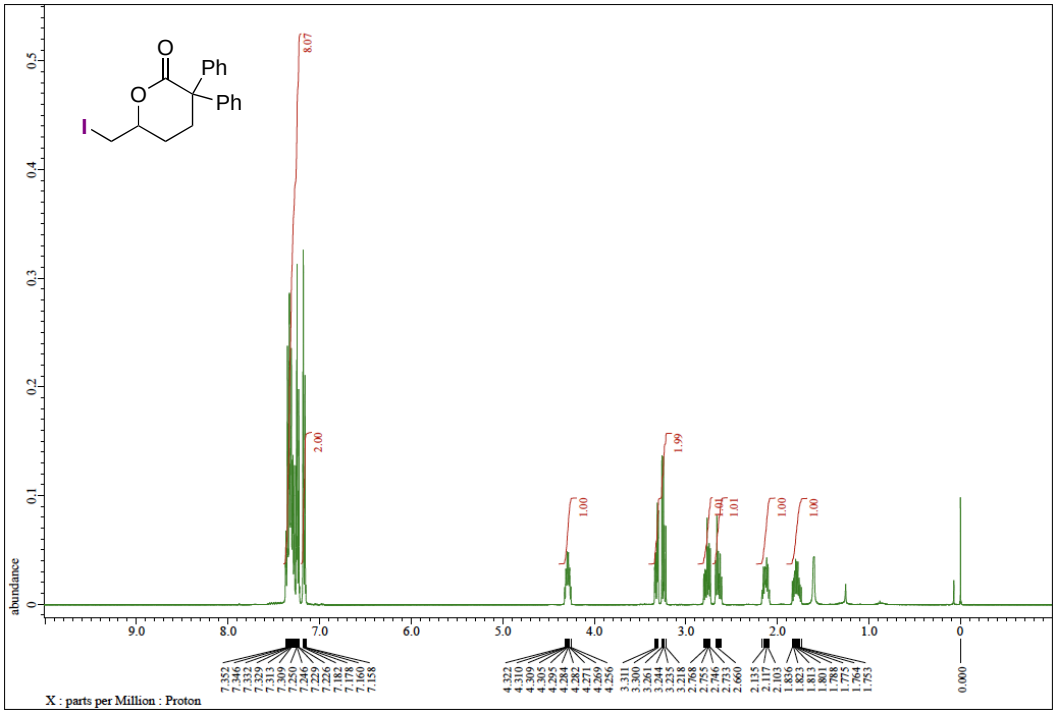


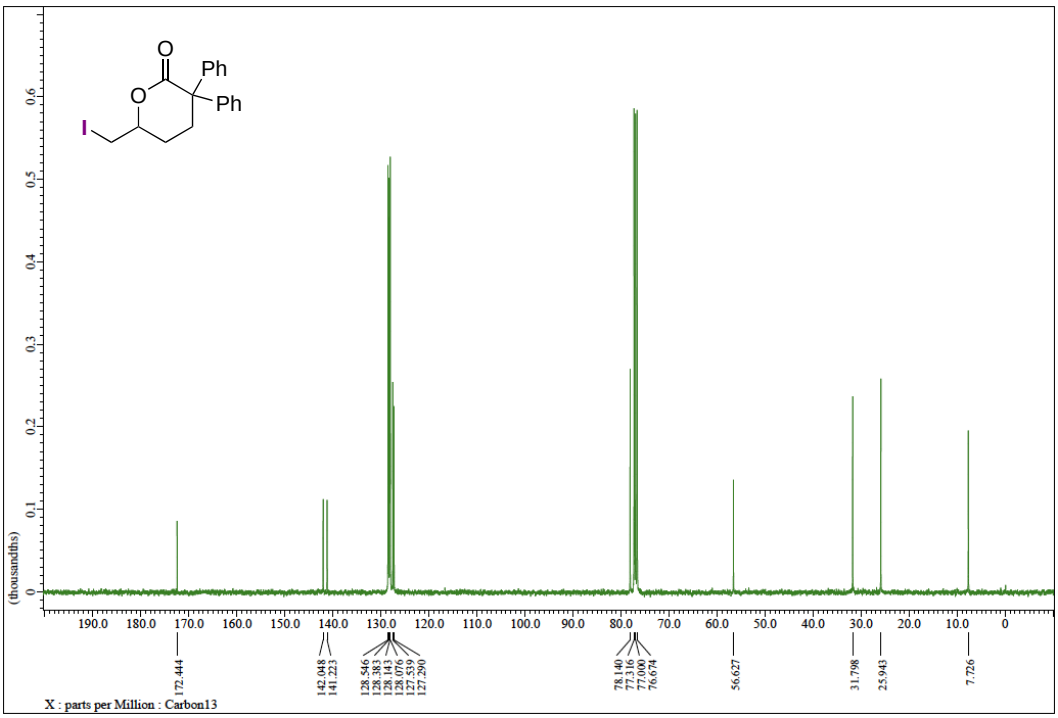
3a: ^{1}H and ^{13}C NMR



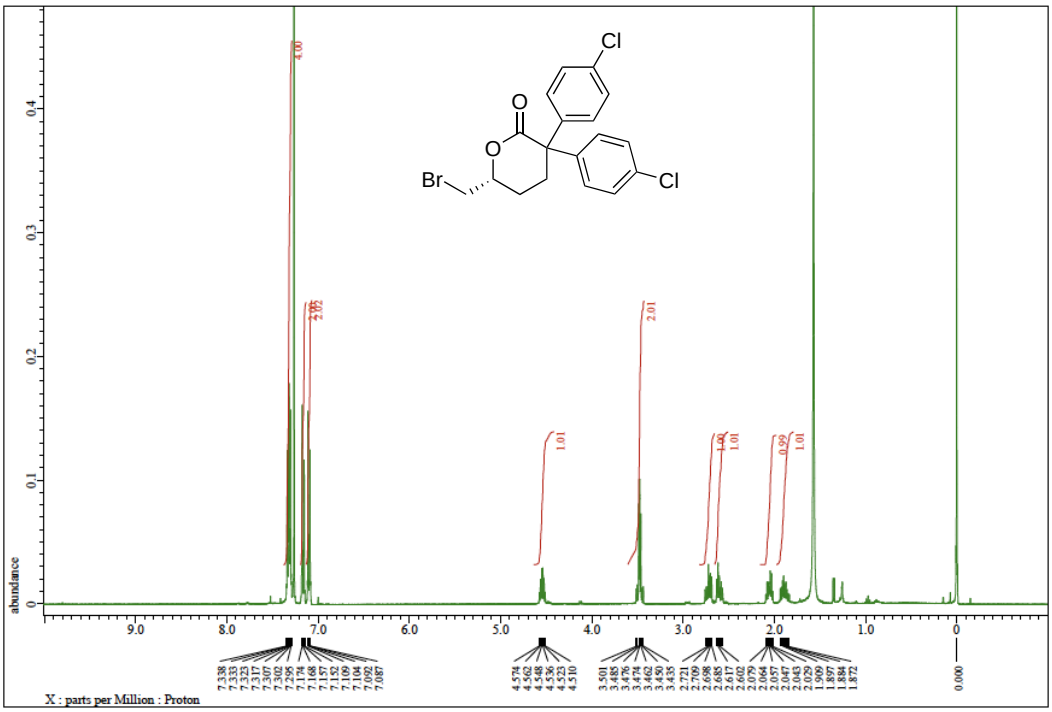


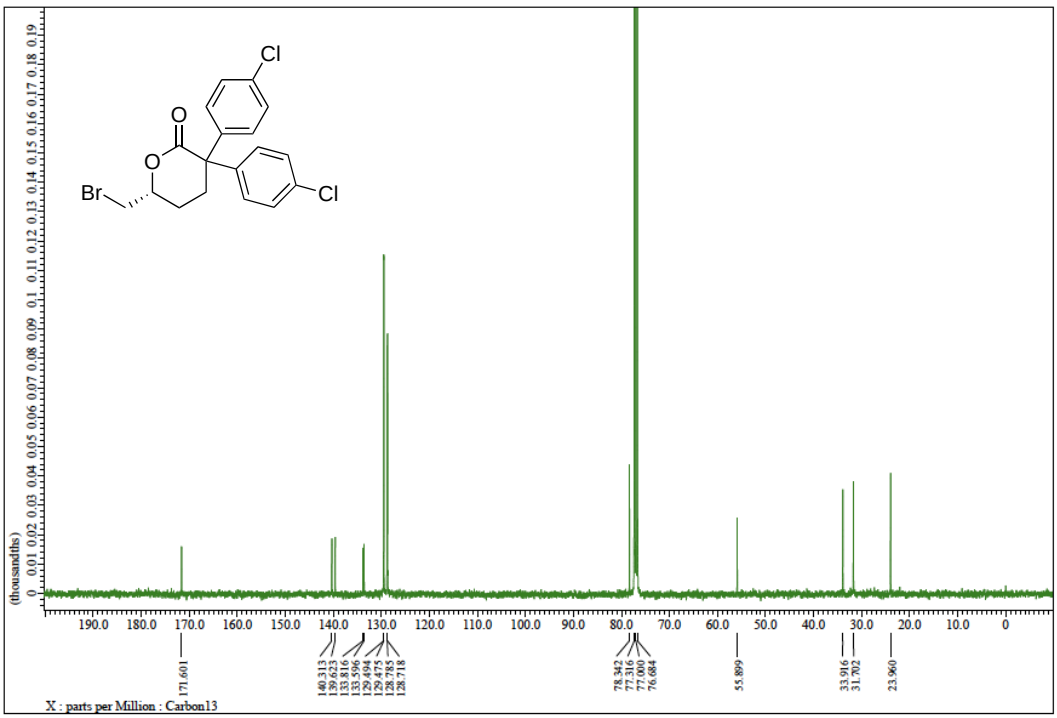
Iodolactonization Product: ^{1}H and ^{13}C NMR



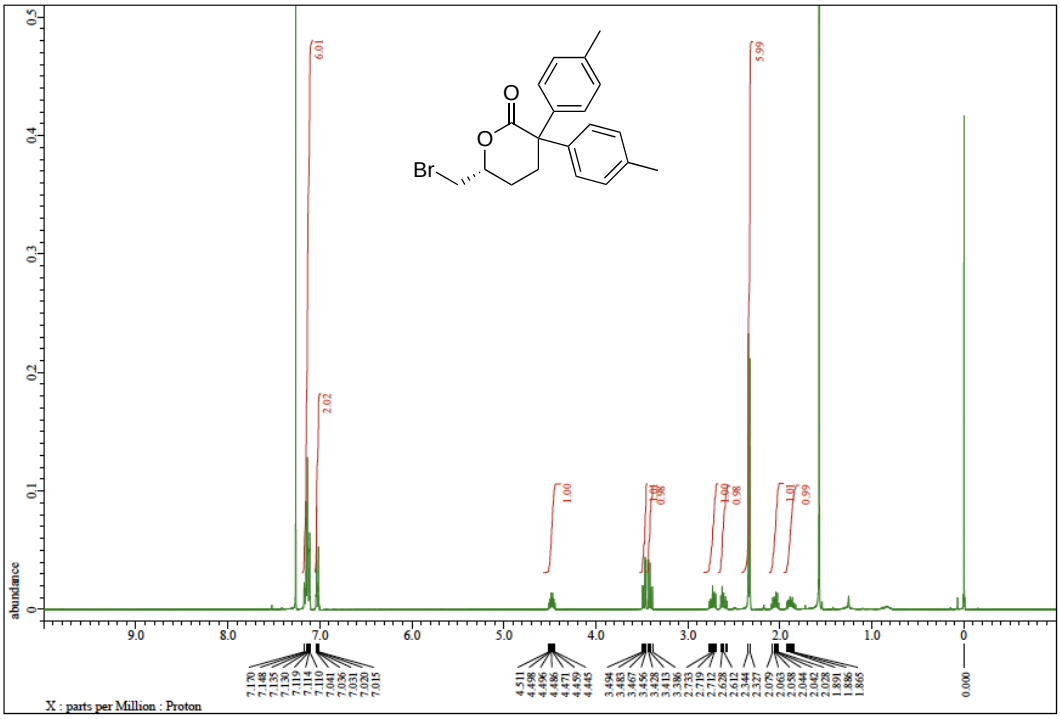


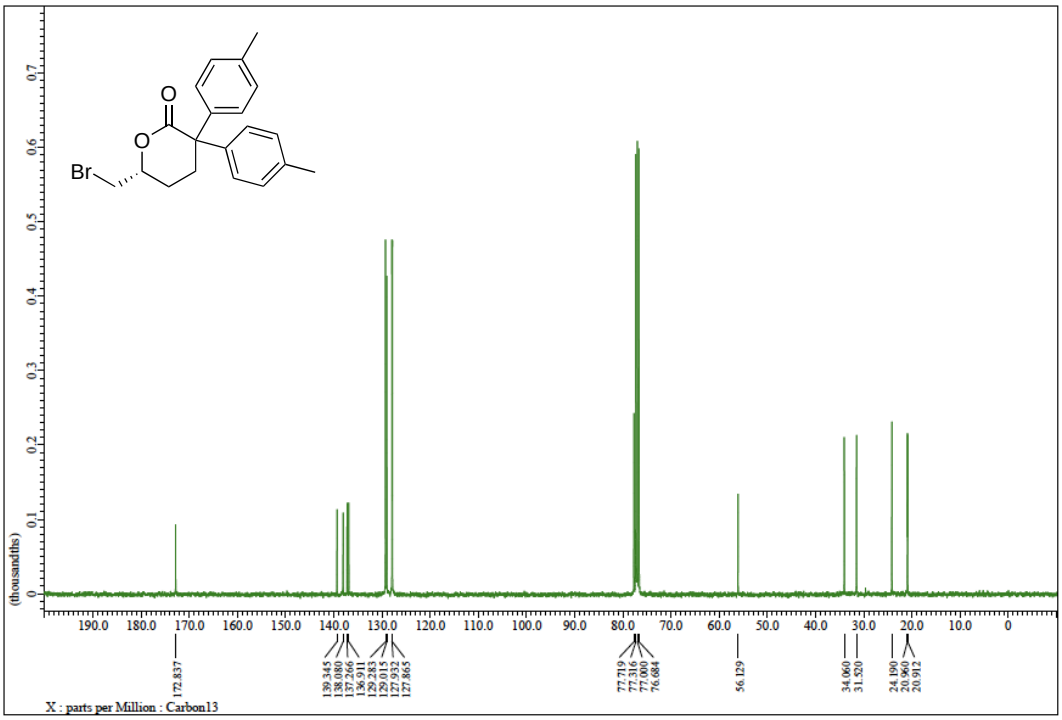
3b: ^{1}H and ^{13}C NMR



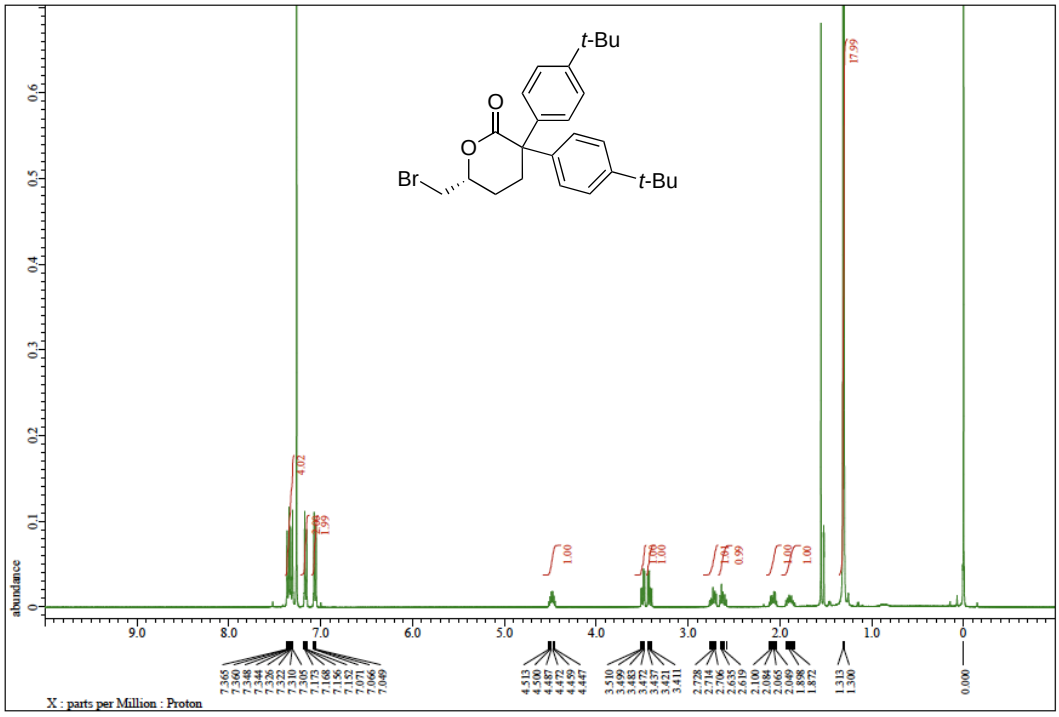


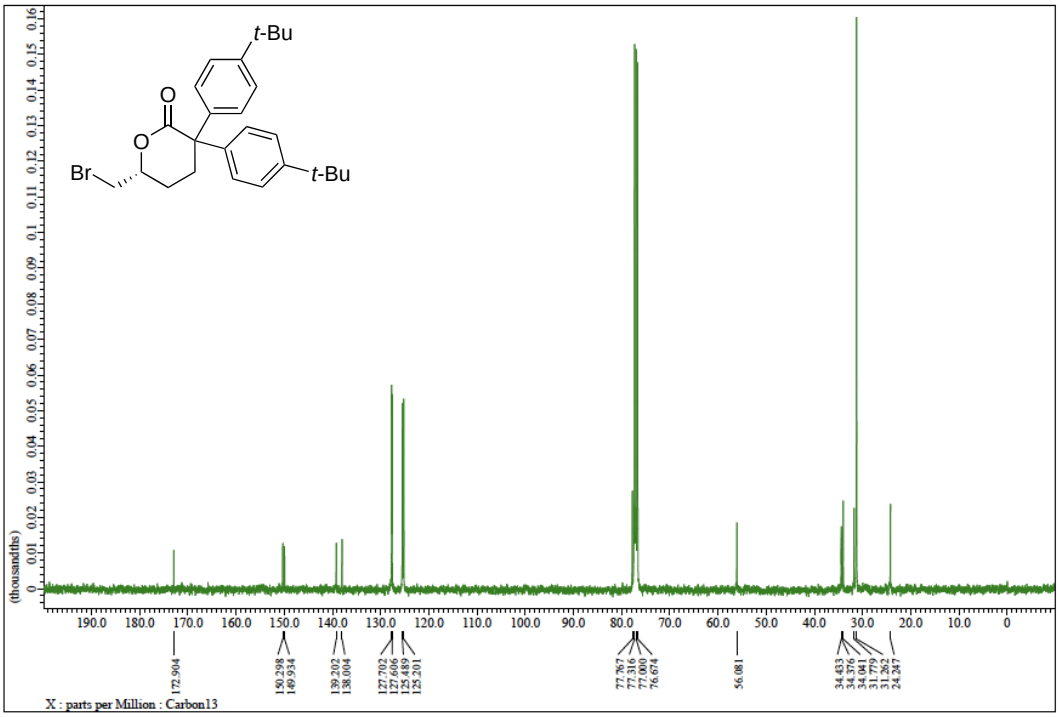
3c: ^{1}H and ^{13}C NMR



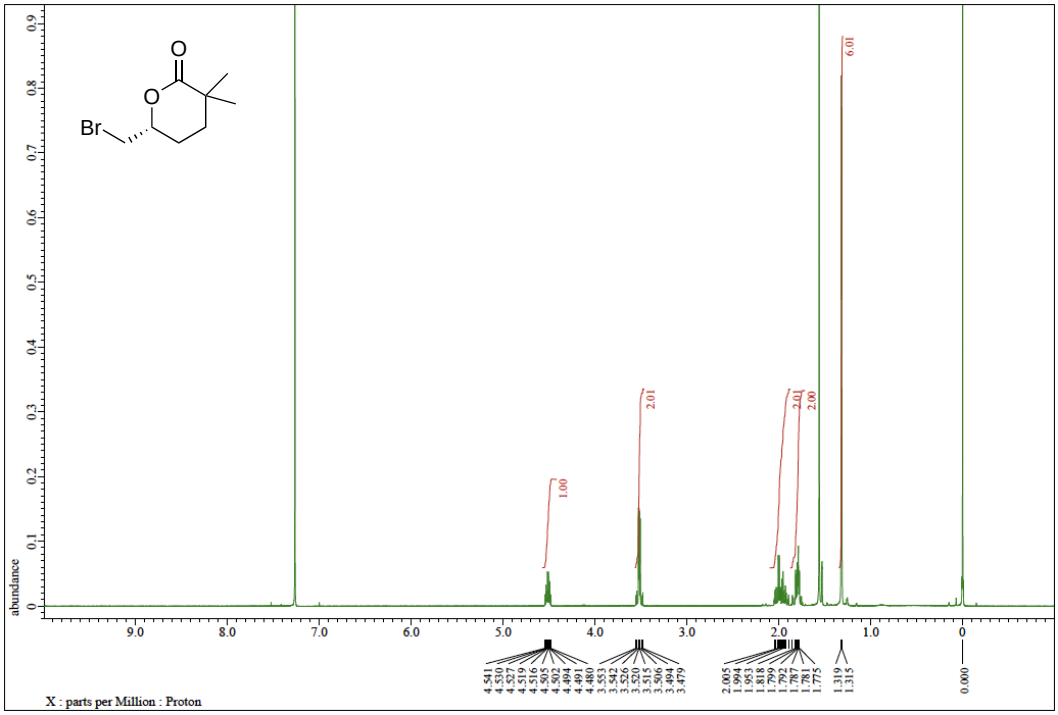


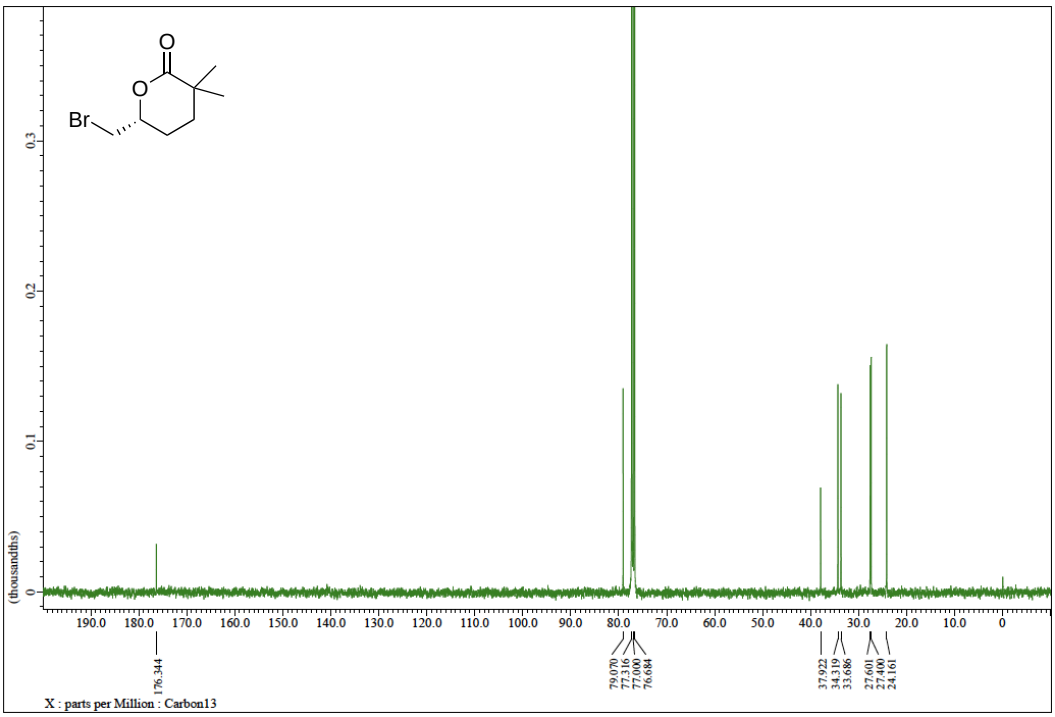
3d: ^{1}H and ^{13}C NMR



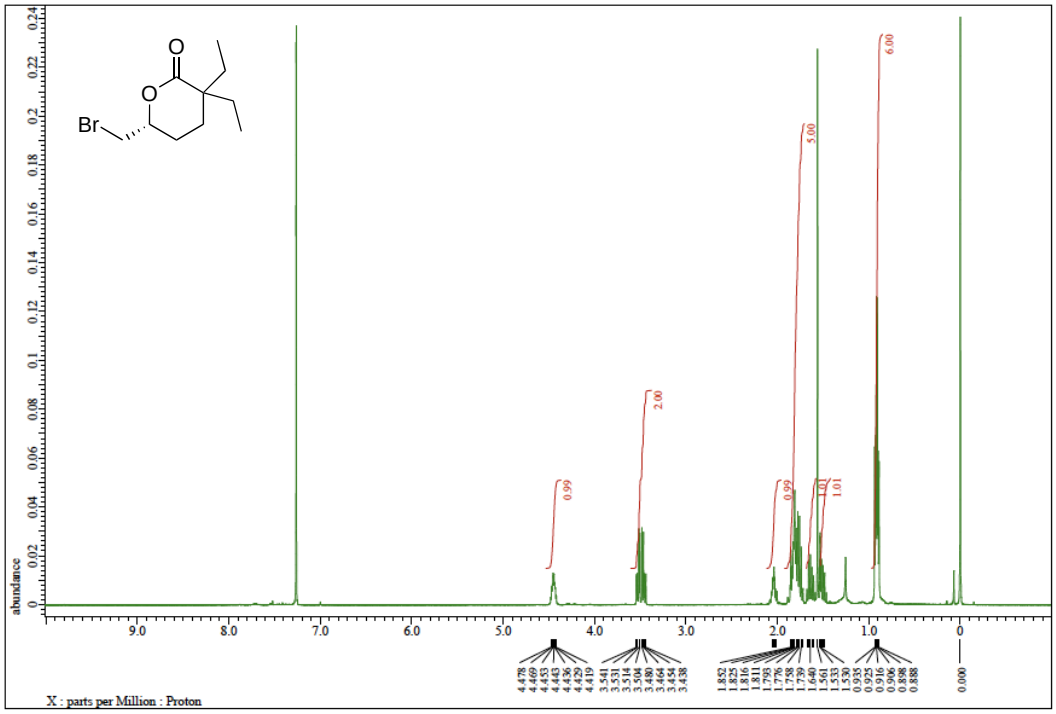


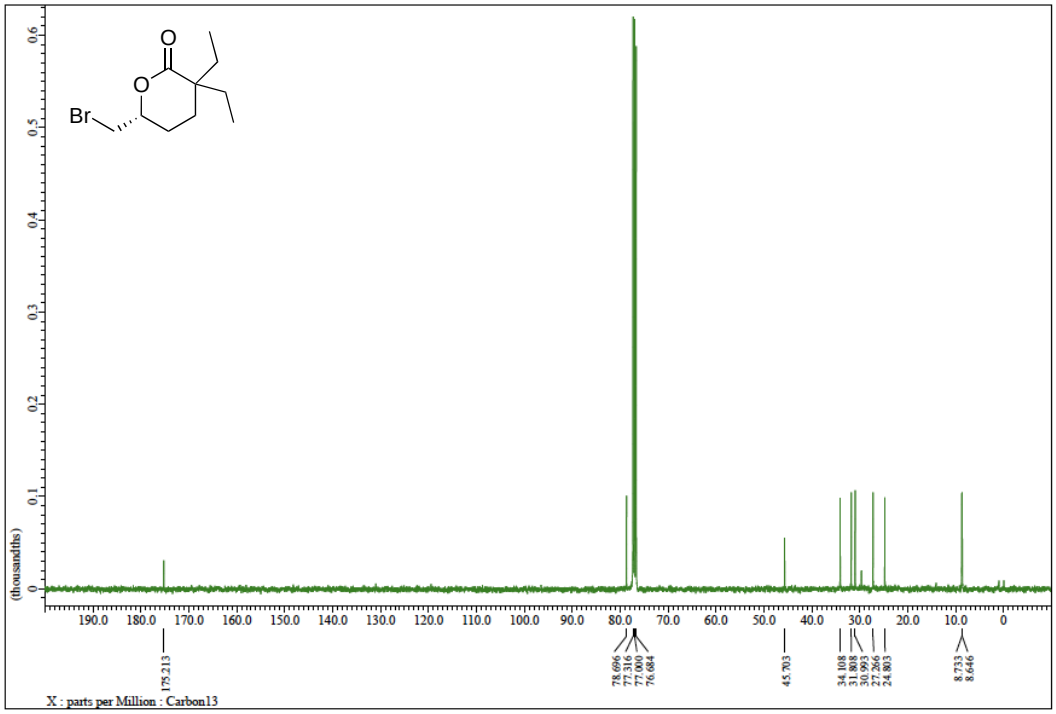
3e: ^{1}H and ^{13}C NMR



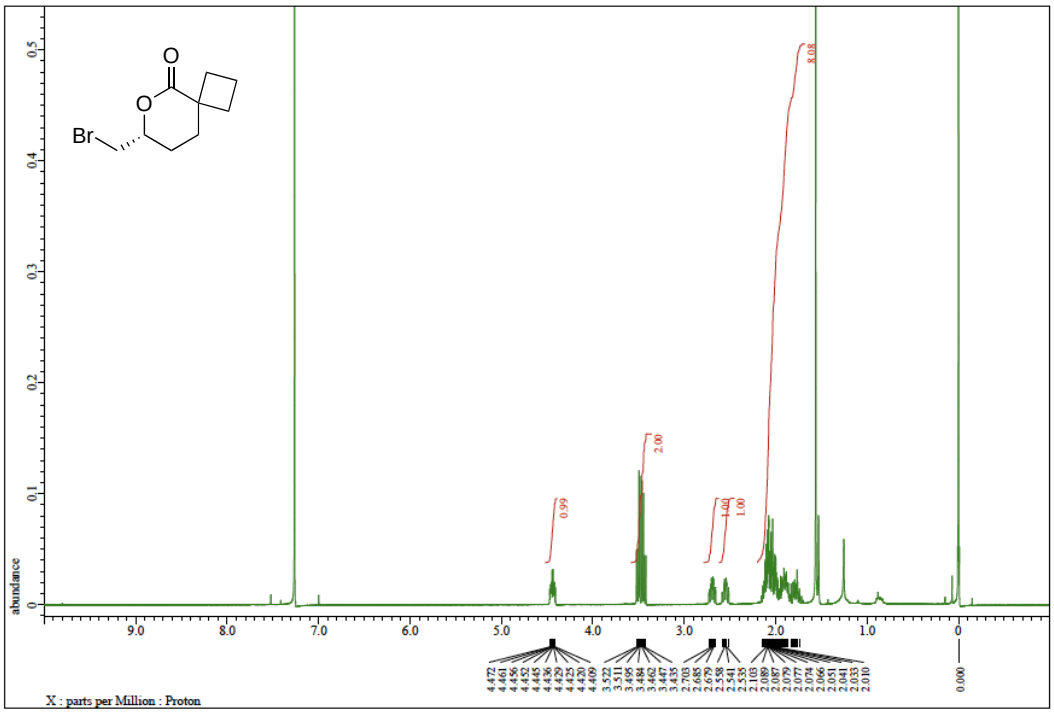


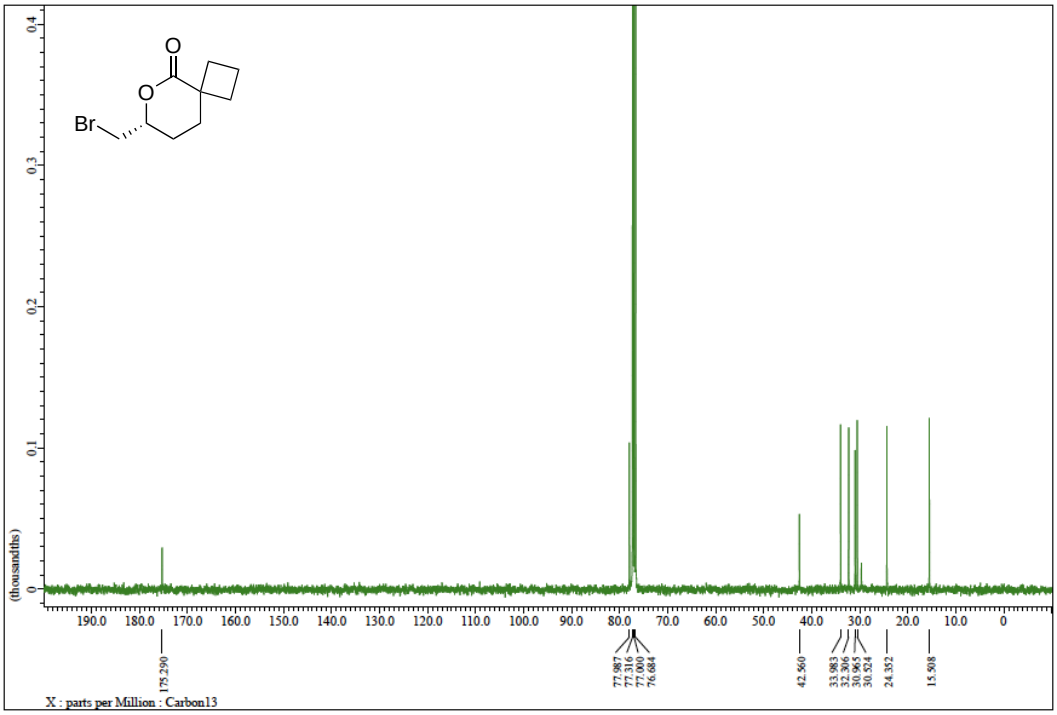
3f: ^{1}H and ^{13}C NMR



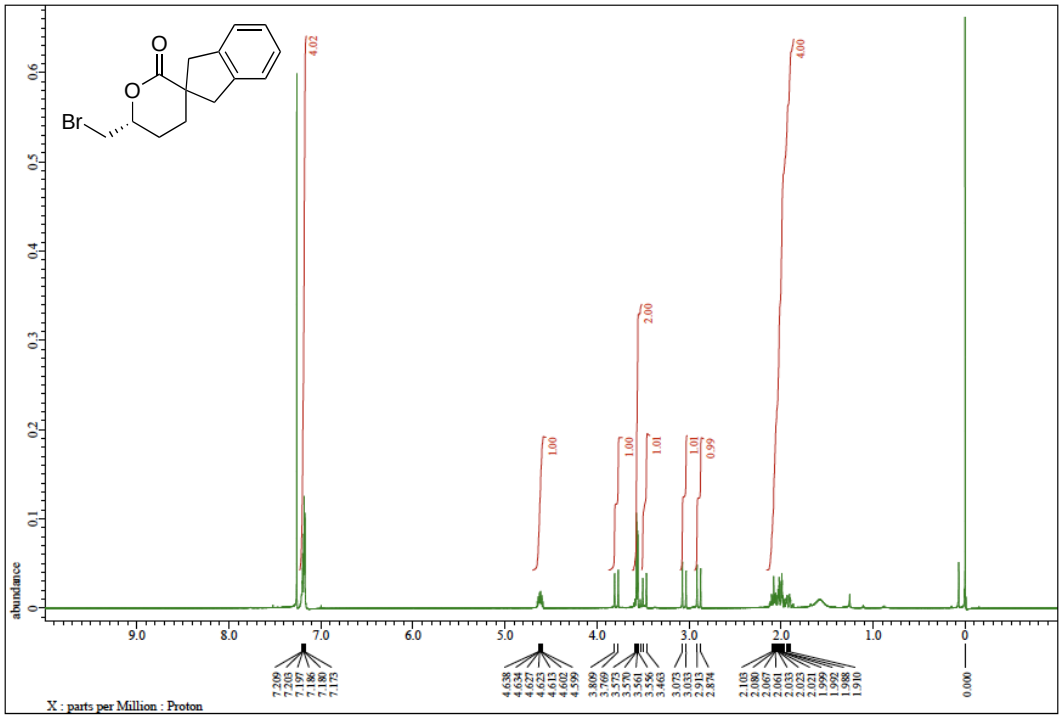


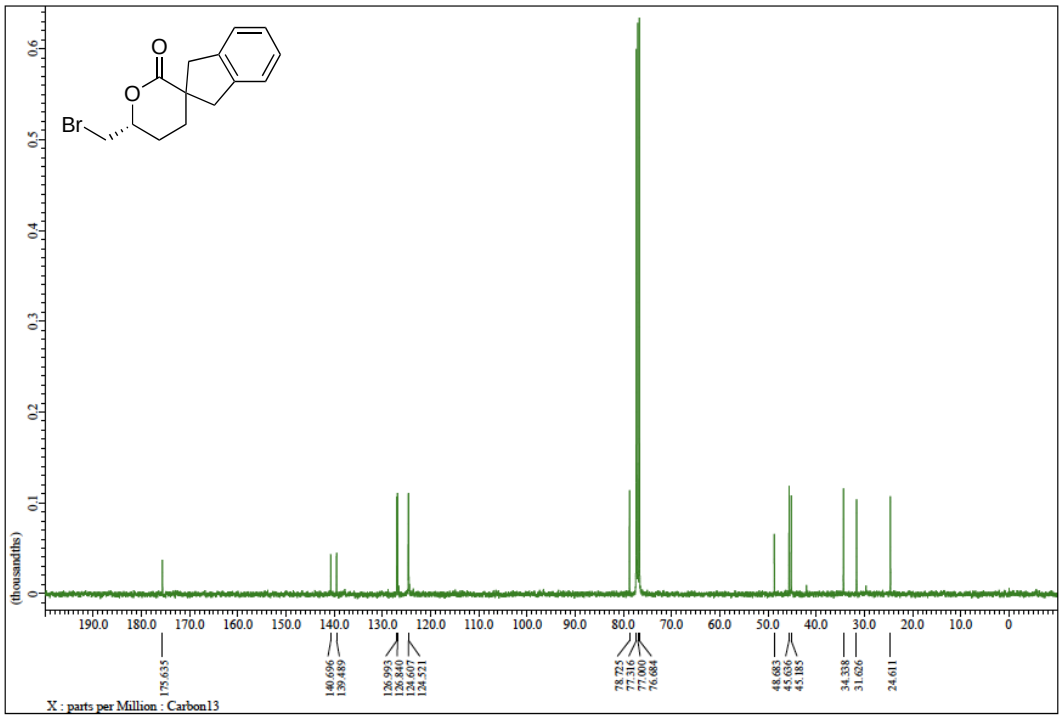
3g: ^{1}H and ^{13}C NMR



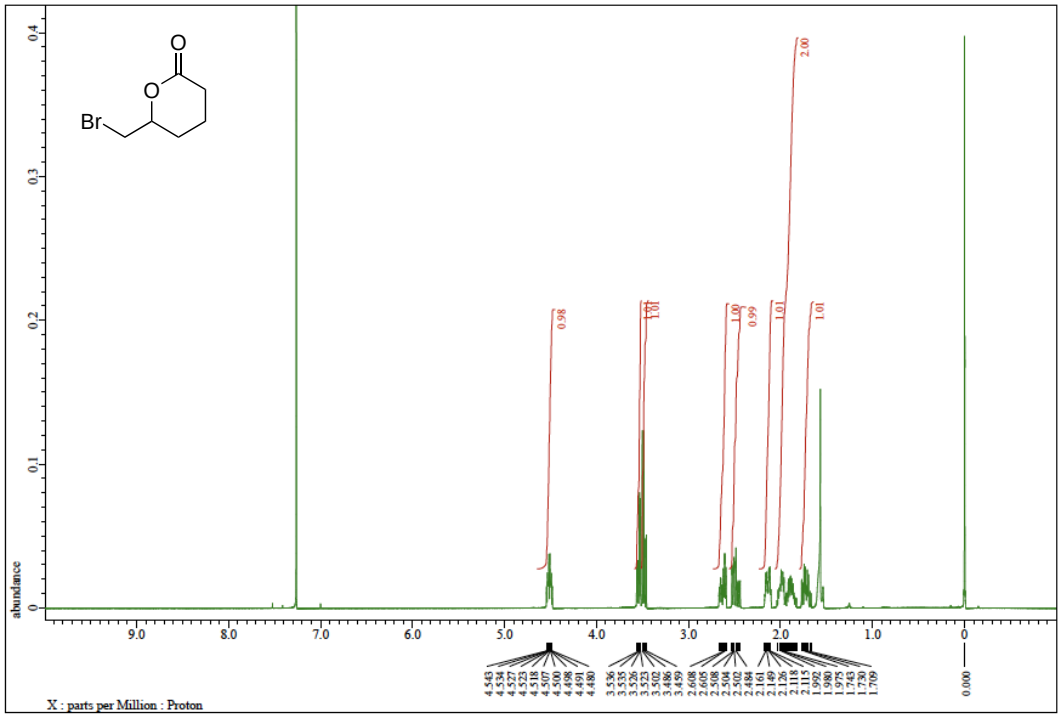


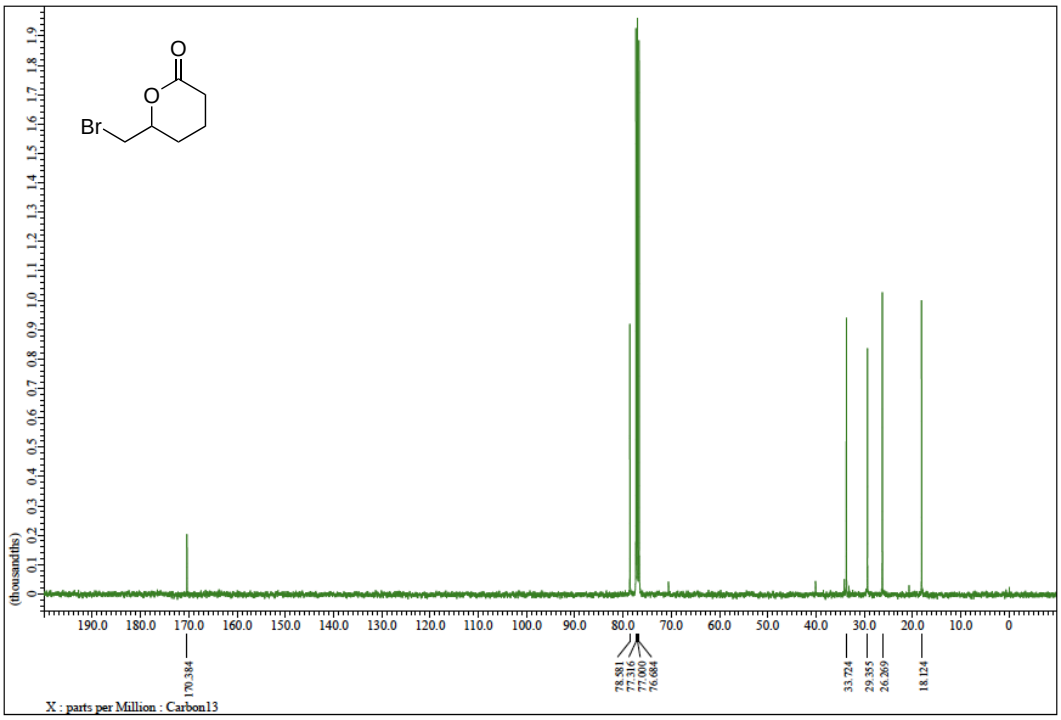
3h: ^{1}H and ^{13}C NMR



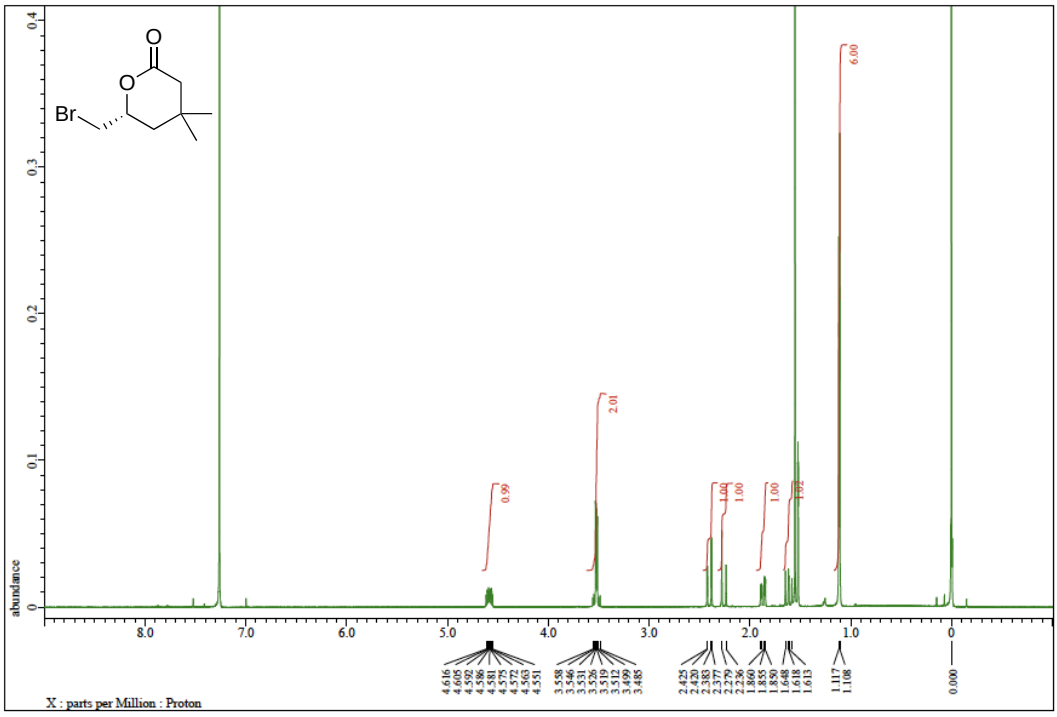


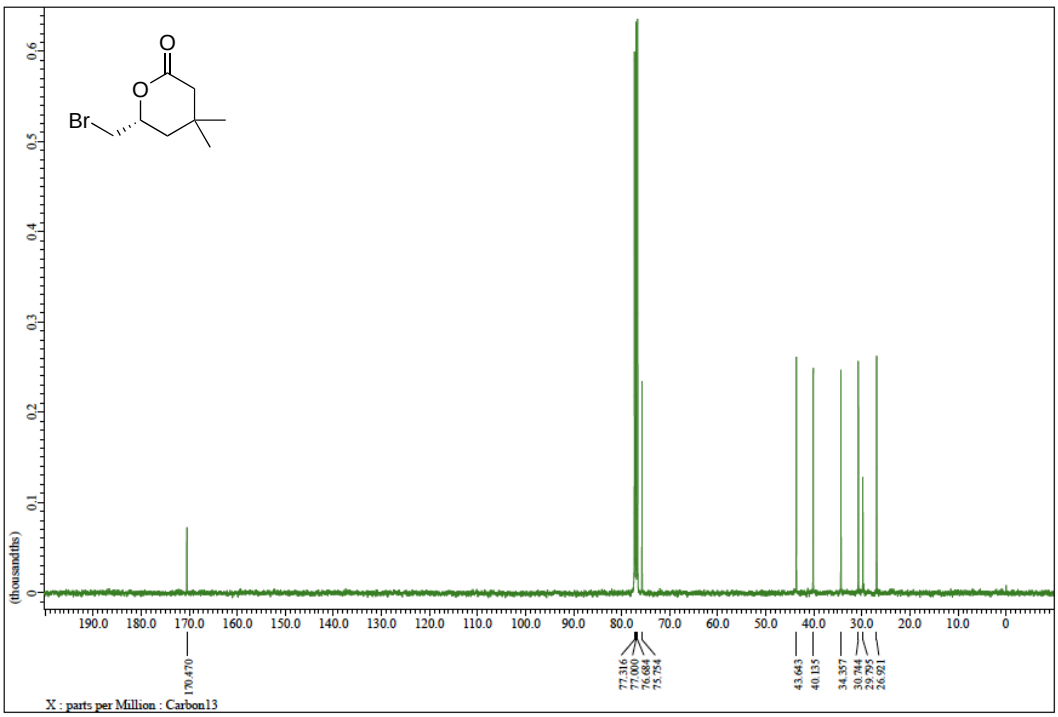
3i: ^{1}H and ^{13}C NMR



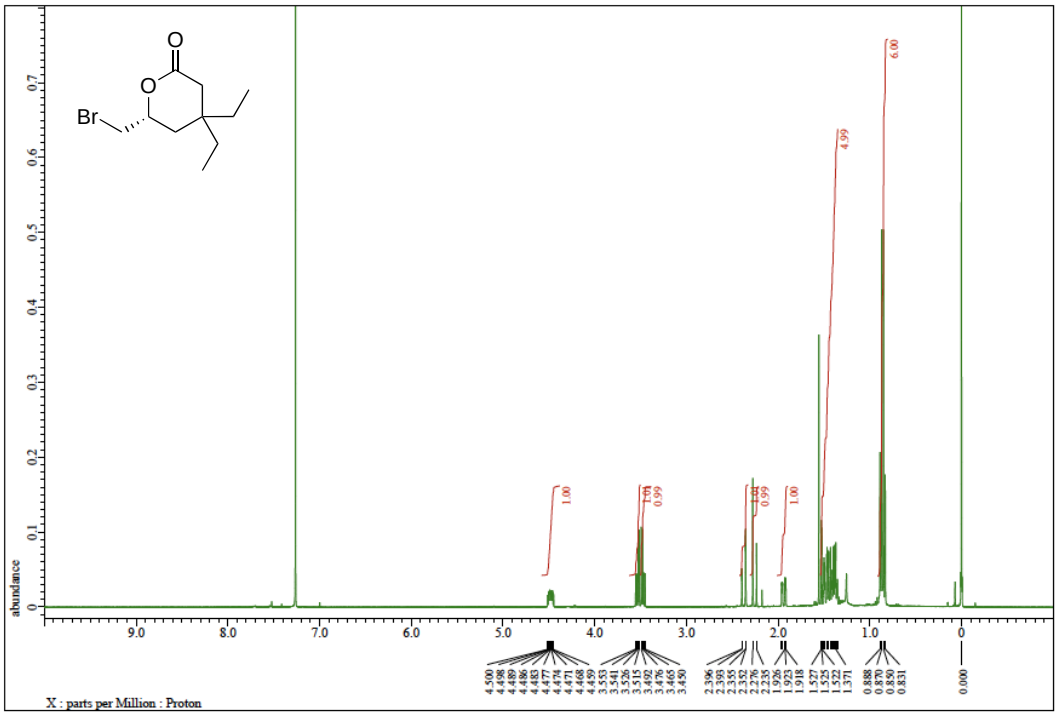


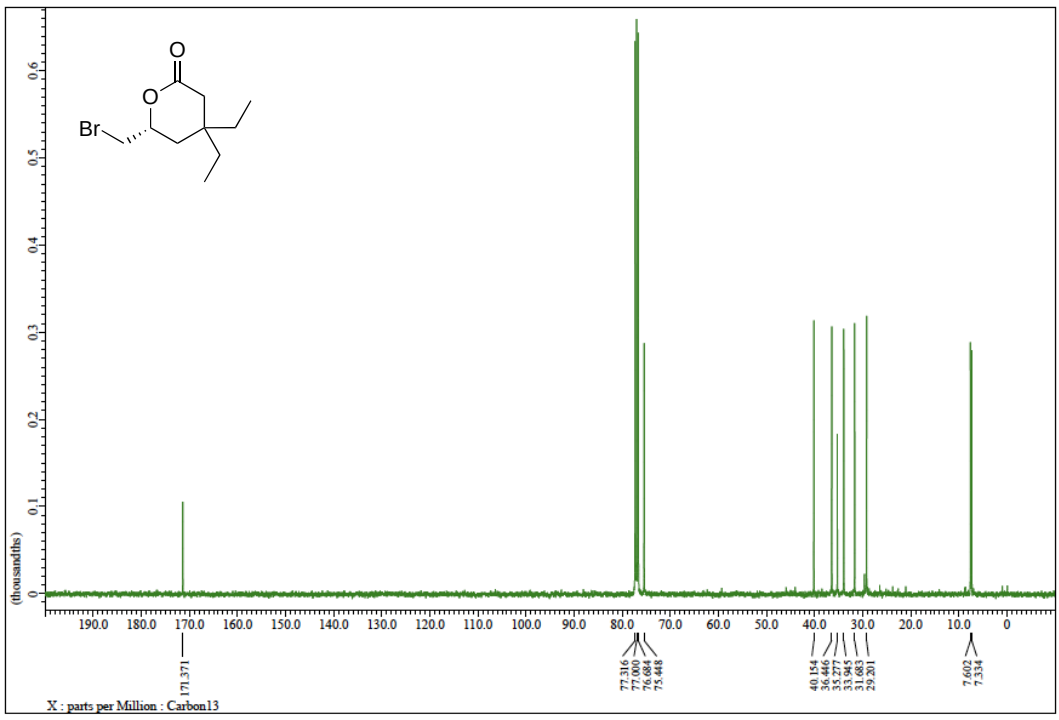
3j: ^{1}H and ^{13}C NMR



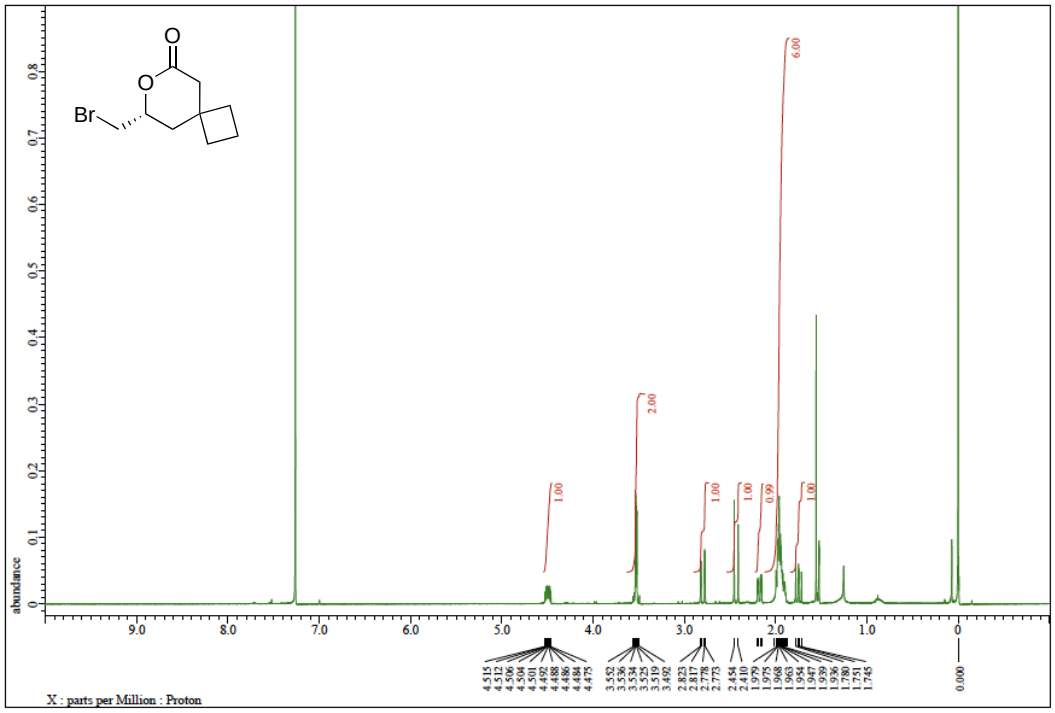


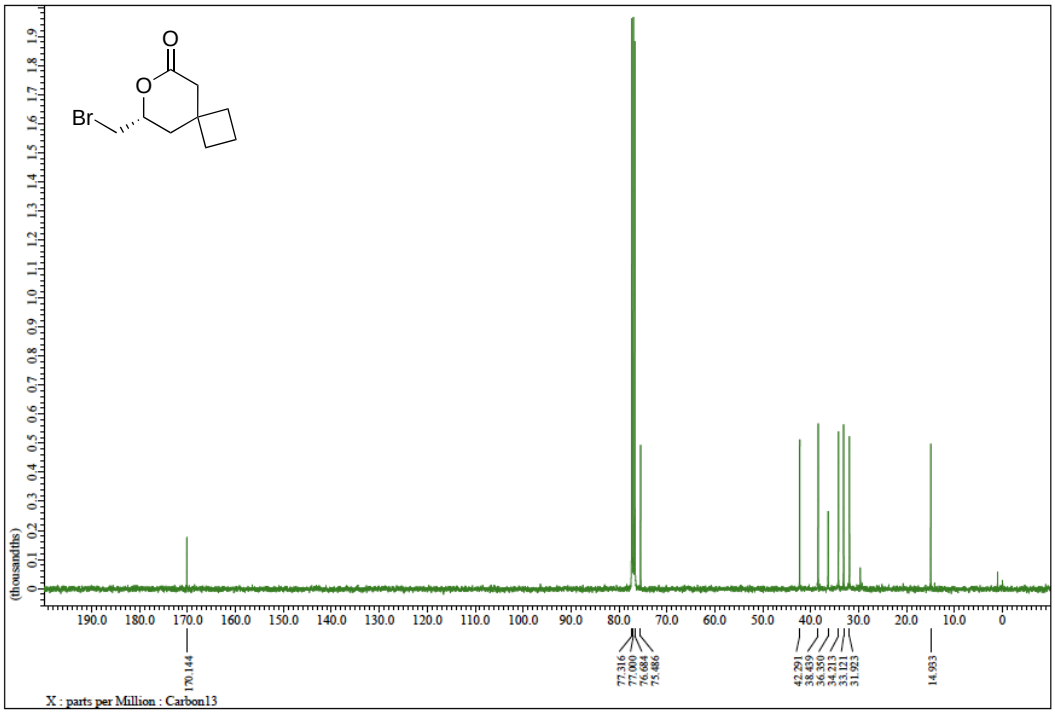
3k: ^{1}H and ^{13}C NMR



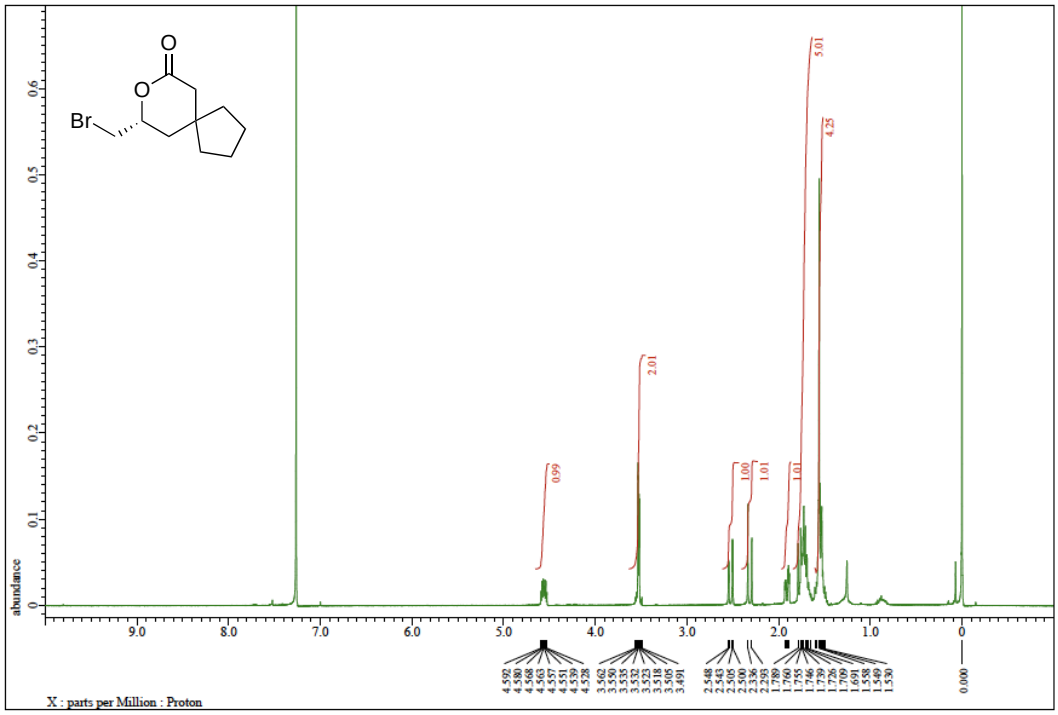


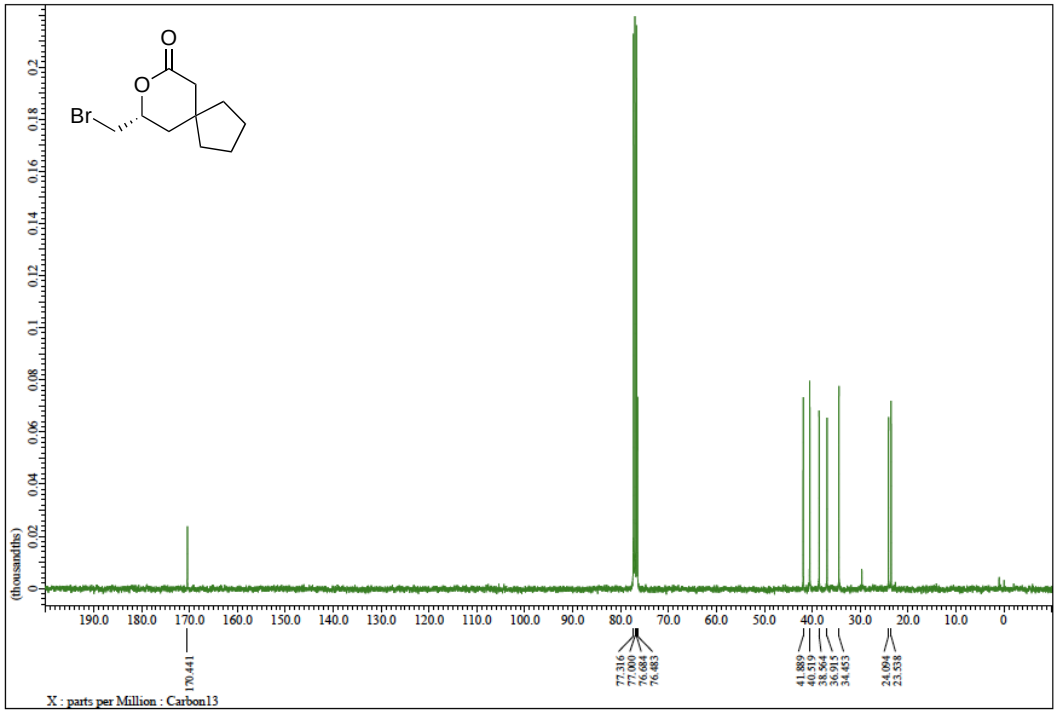
3l: ^{1}H and ^{13}C NMR



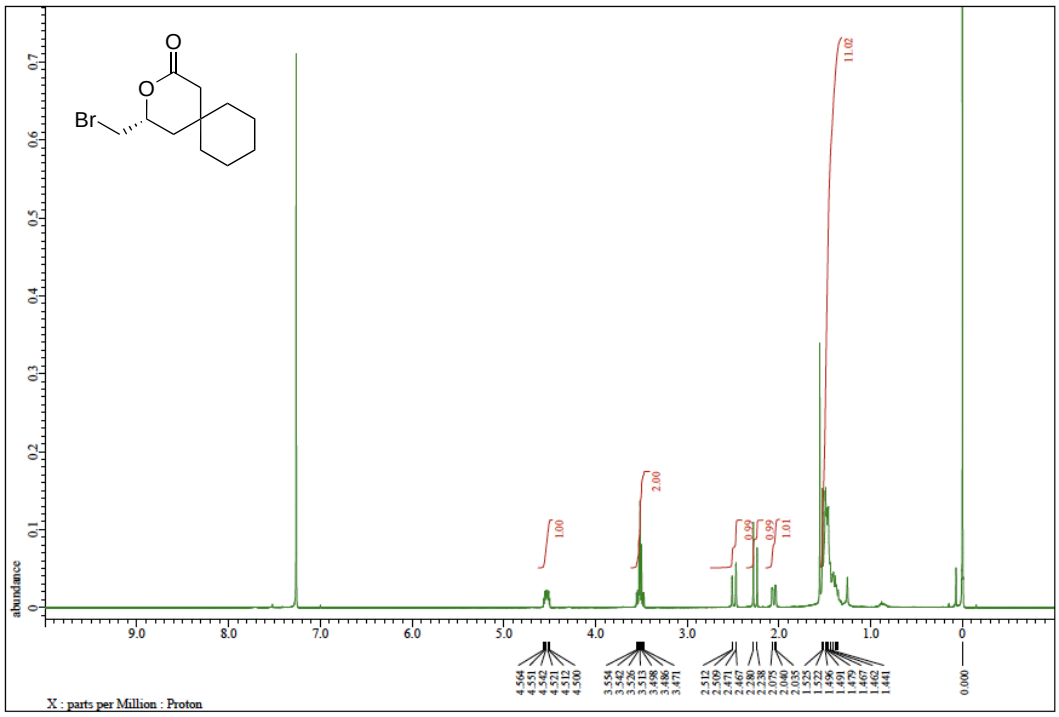


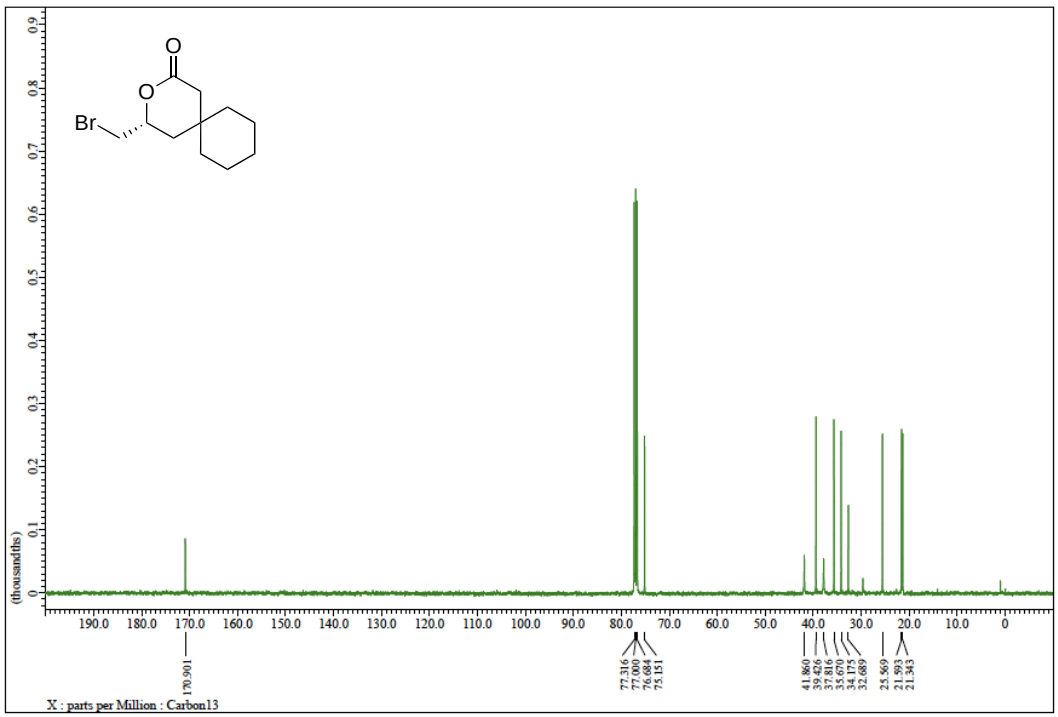
3m: ^{1}H and ^{13}C NMR



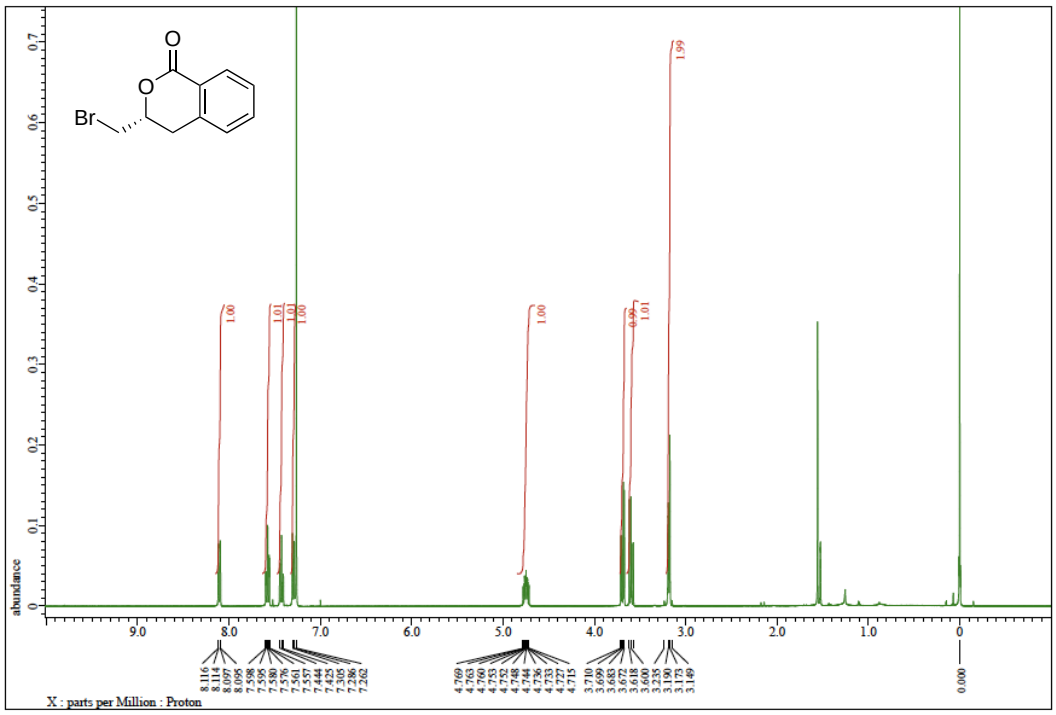


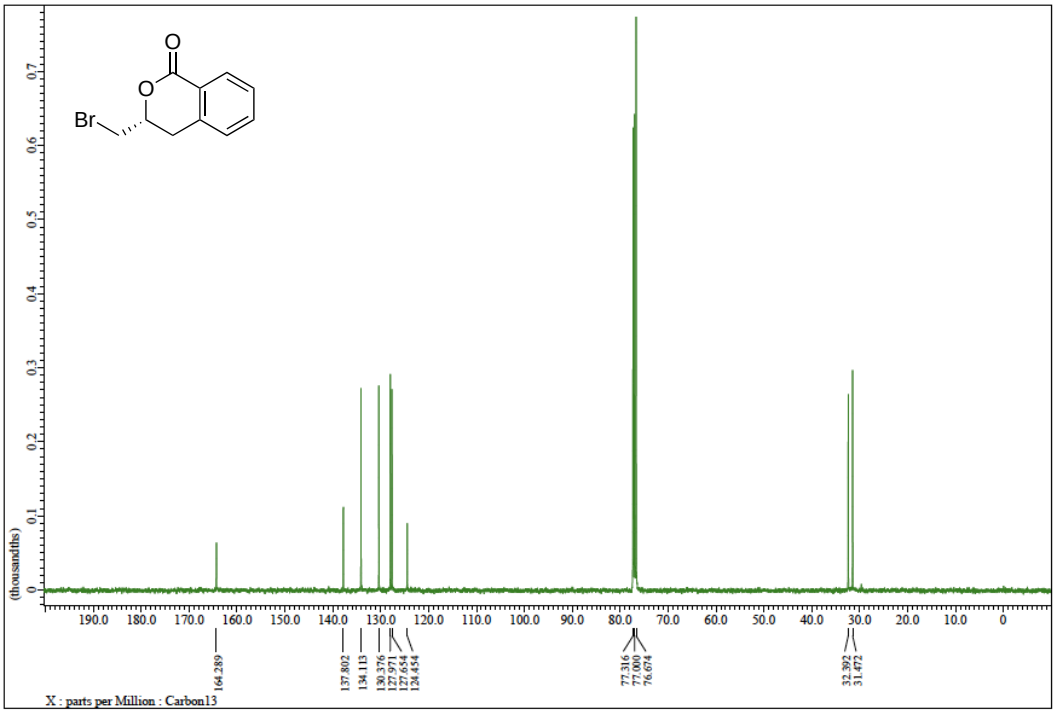
3n: ^{1}H and ^{13}C NMR



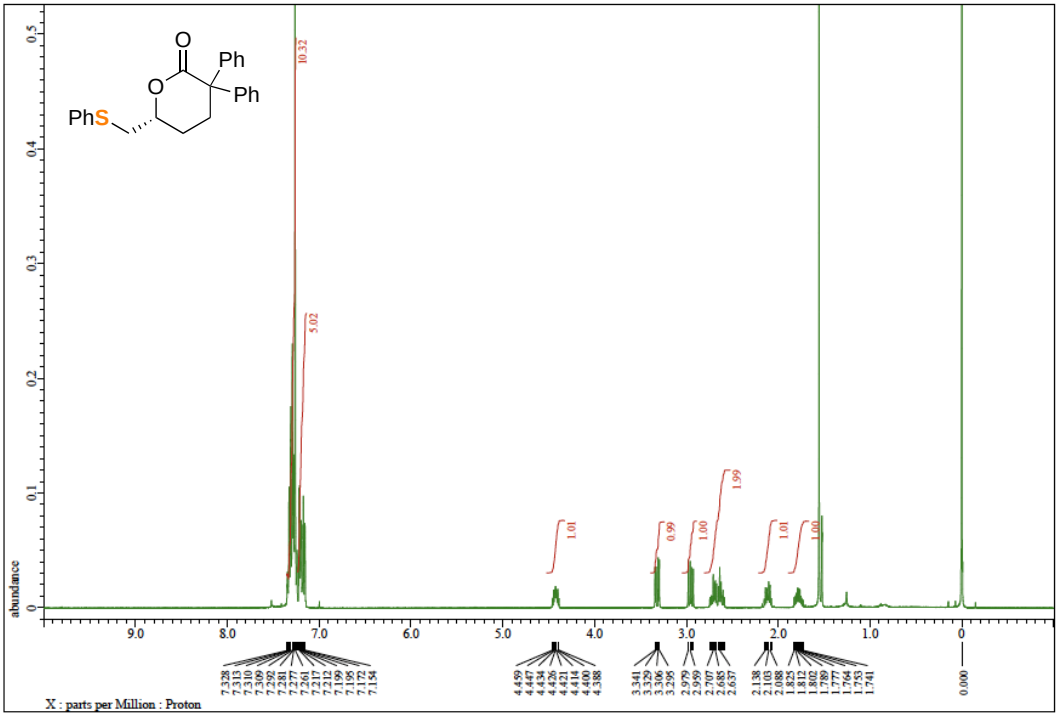


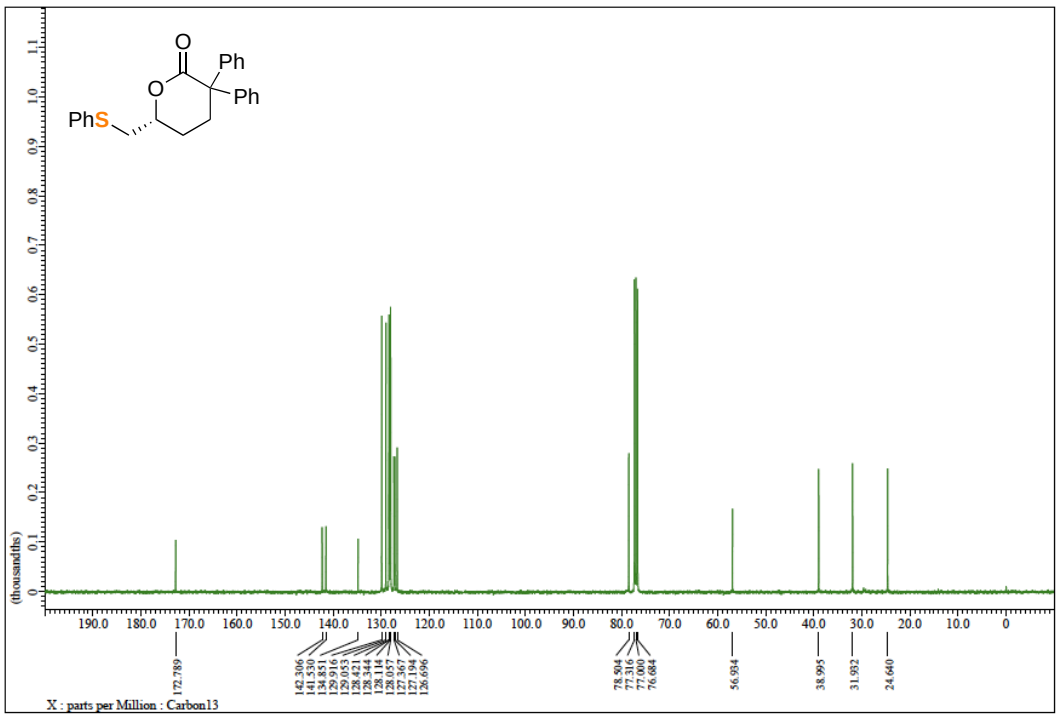
3o: ^{1}H and ^{13}C NMR



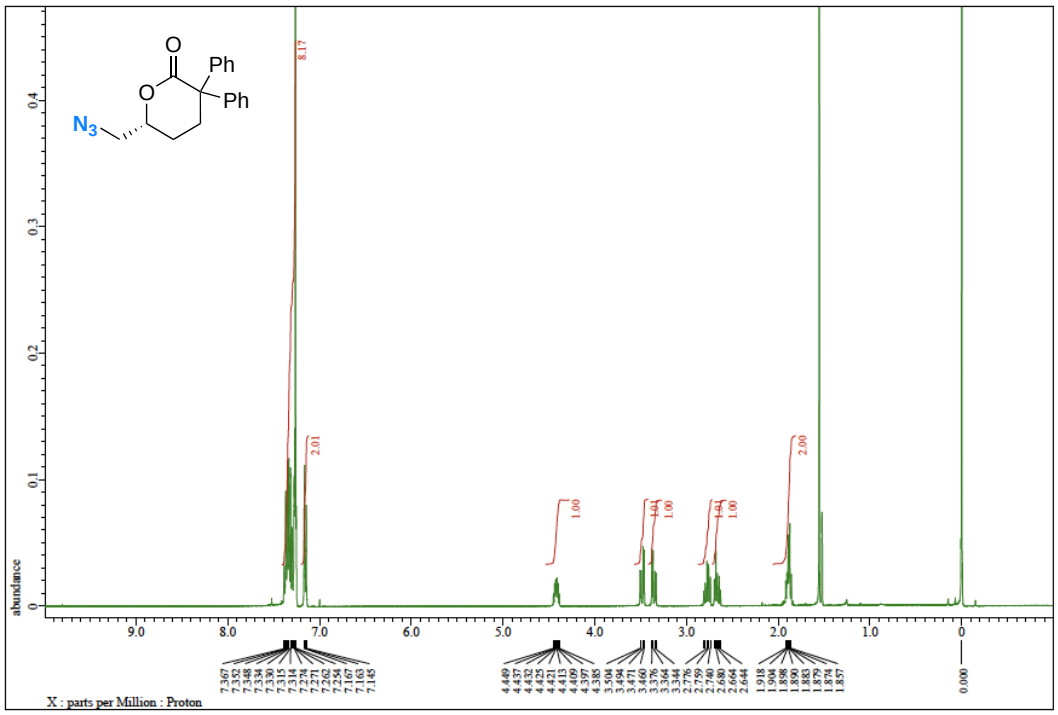


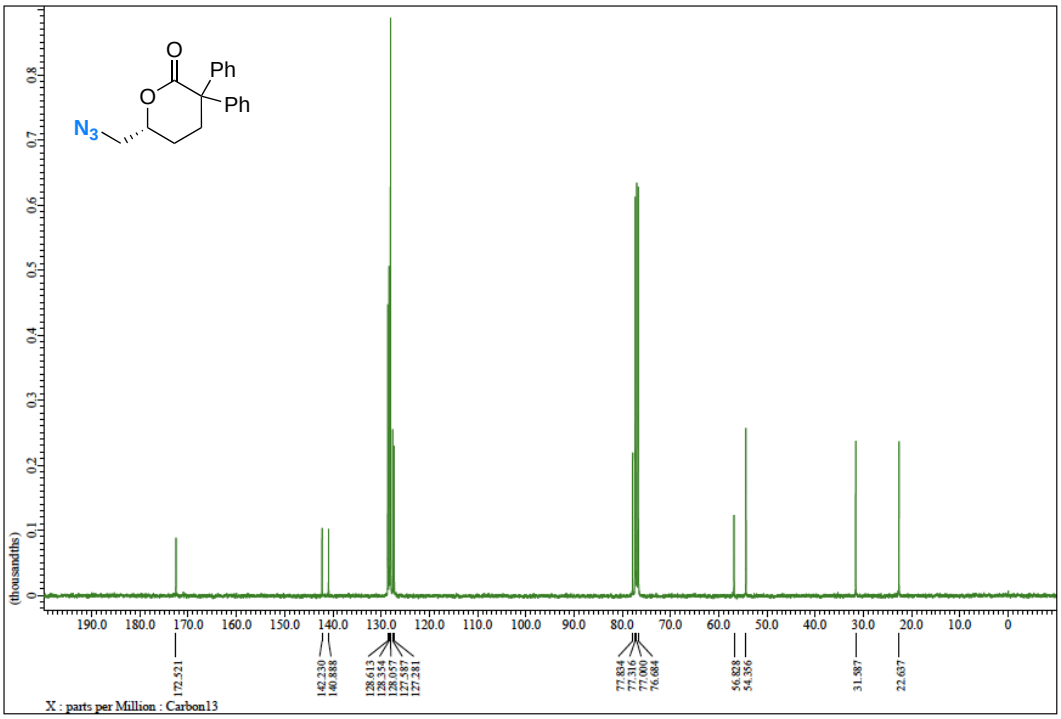
7: ^{1}H and ^{13}C NMR



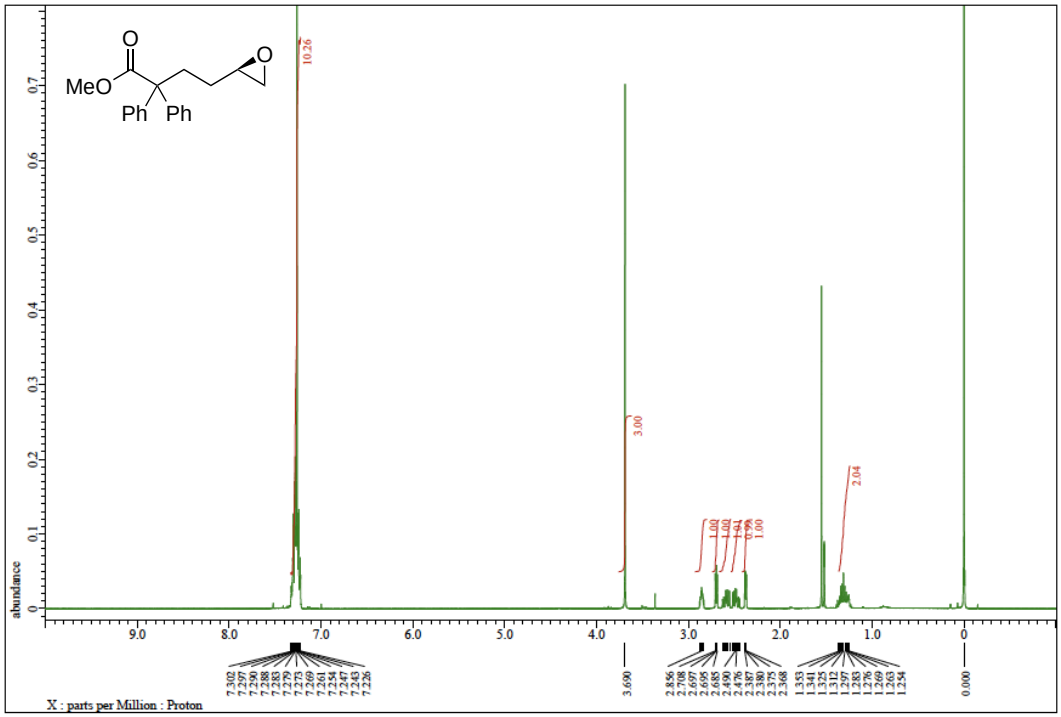


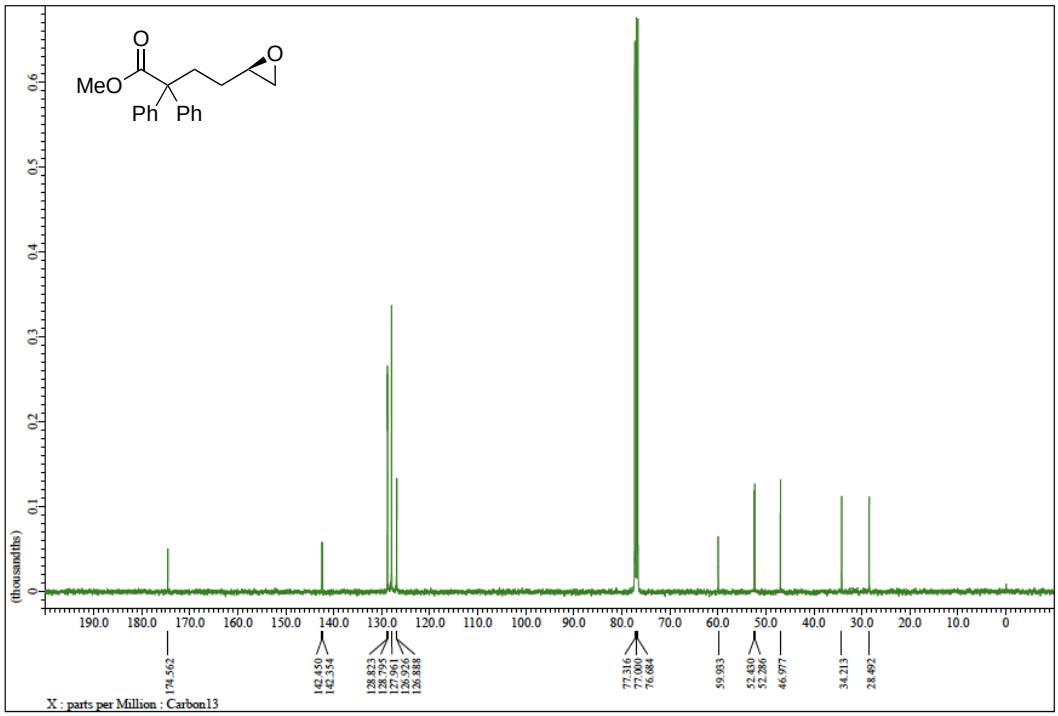
8: ^{1}H and ^{13}C NMR





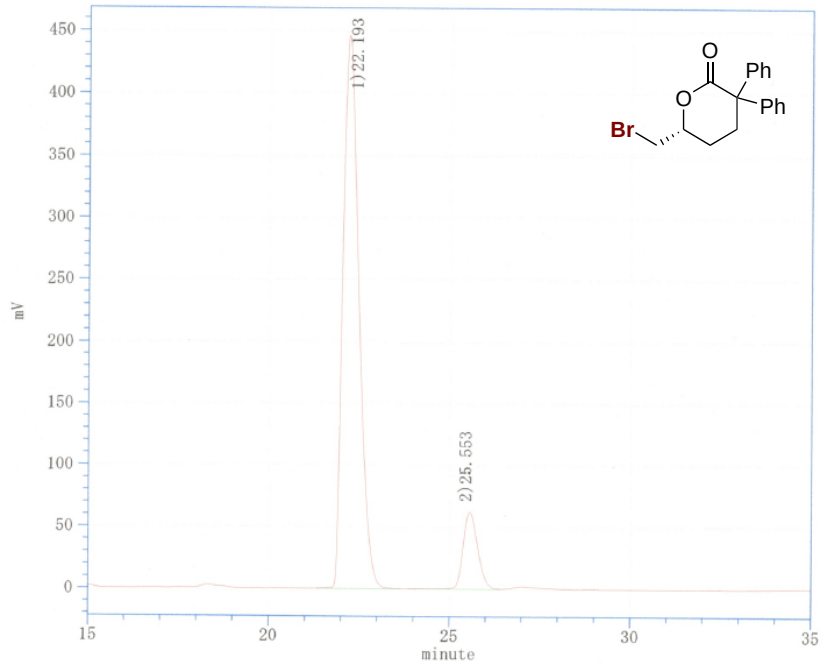
9: ^{1}H and ^{13}C NMR



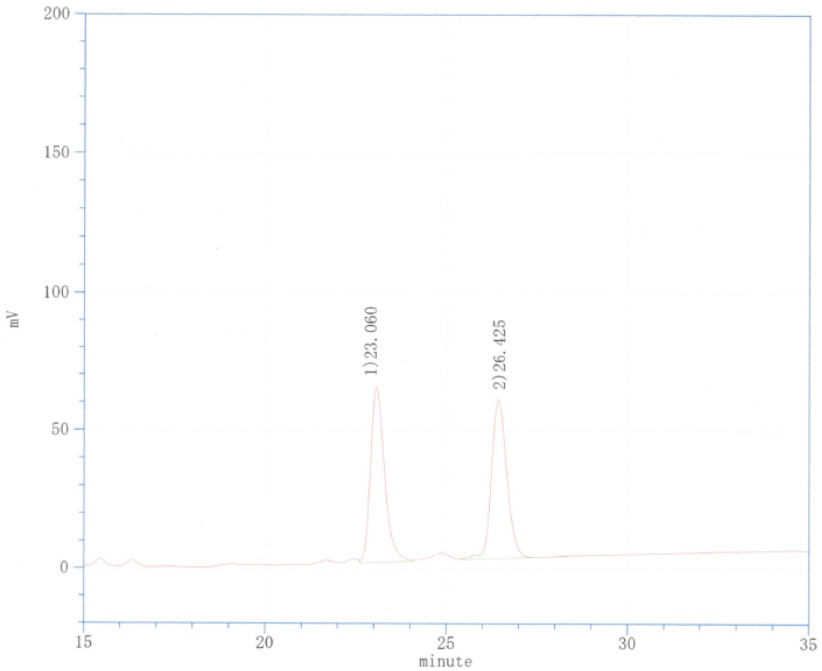


HPLC Charts

3a: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm

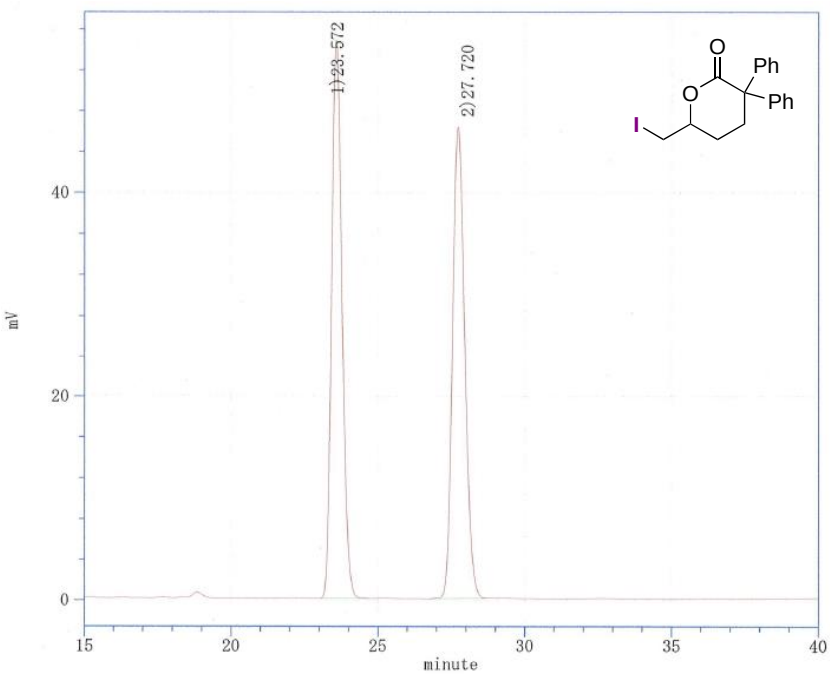


22.193	13707820	88.7739
25.553	1733448	11.2261

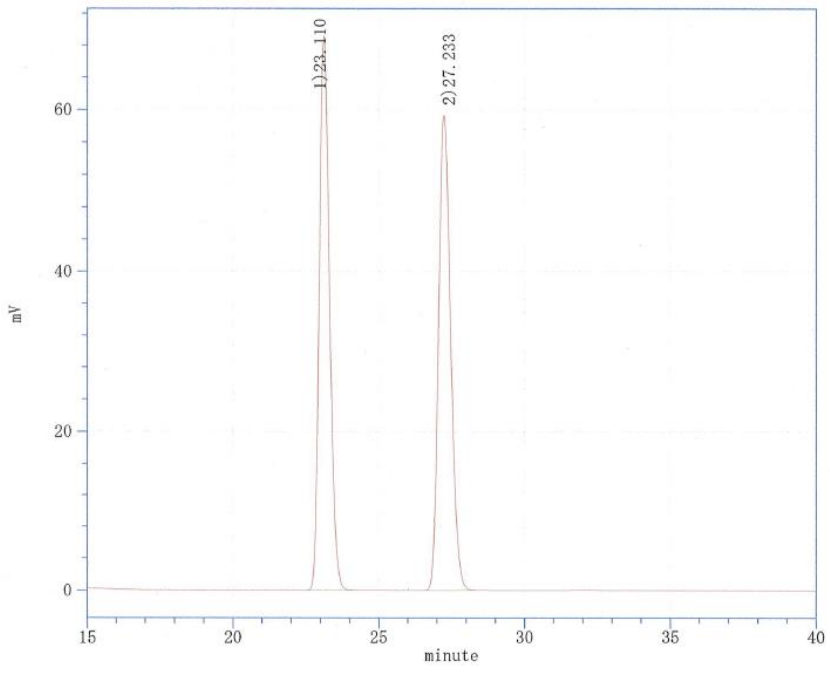


23.060	1710506	49.9263
26.425	1715558	50.0737

Iodolactonization Product: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm

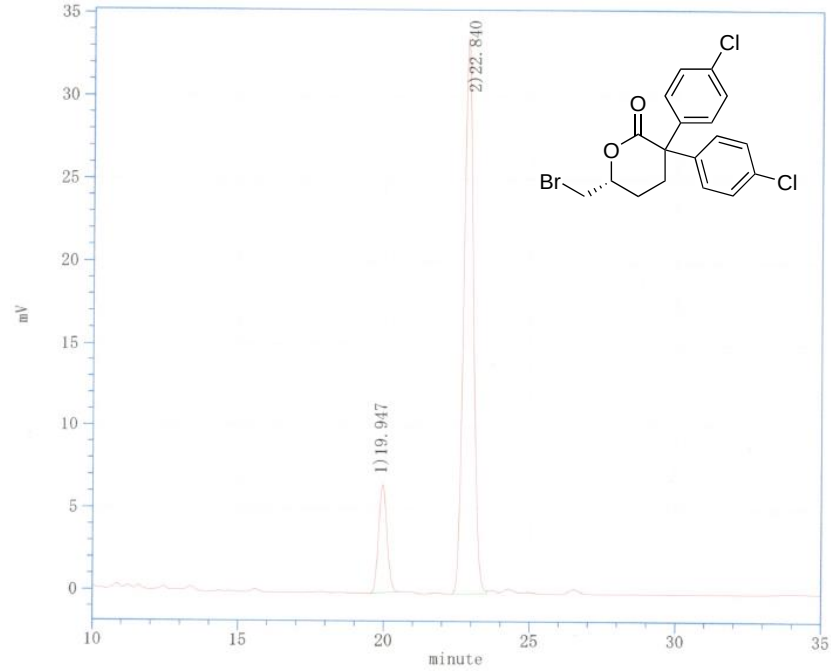


23.572	1347435	50.1752
27.720	1338025	49.8248

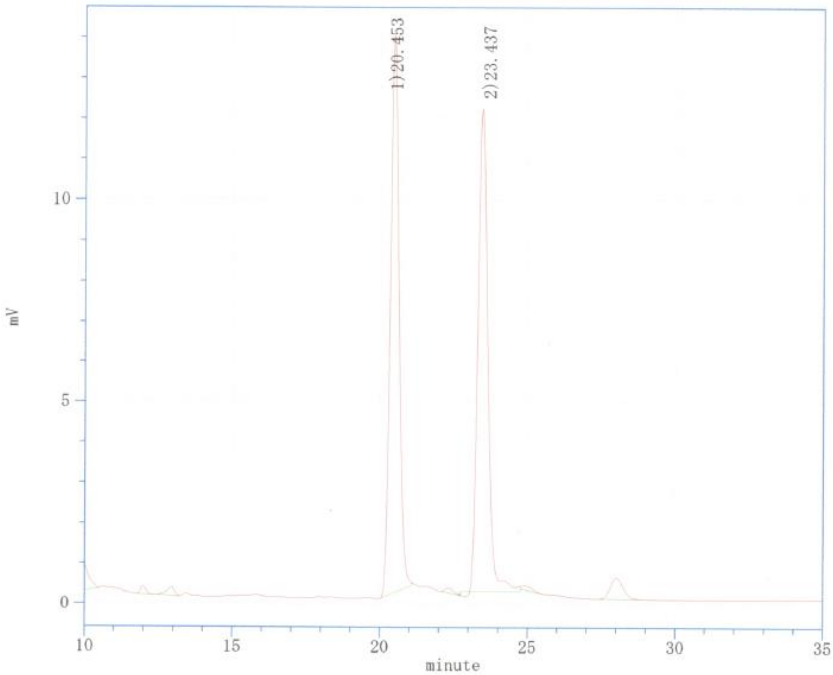


23.110	1708735	50.0166
27.233	1707603	49.9834

3b: Daicel Chiralpak IC-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm

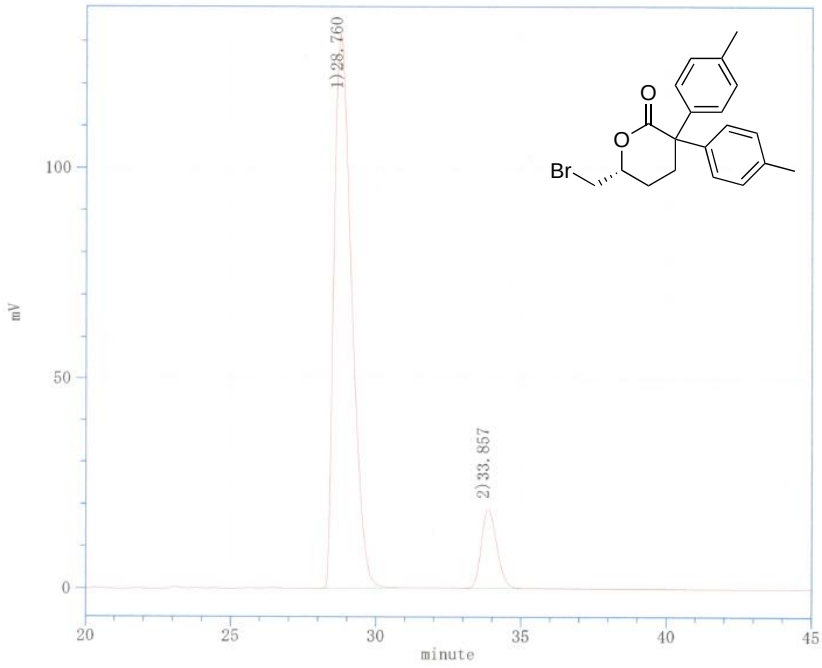


19.947	131440	14.4174
22.840	780238	85.5826

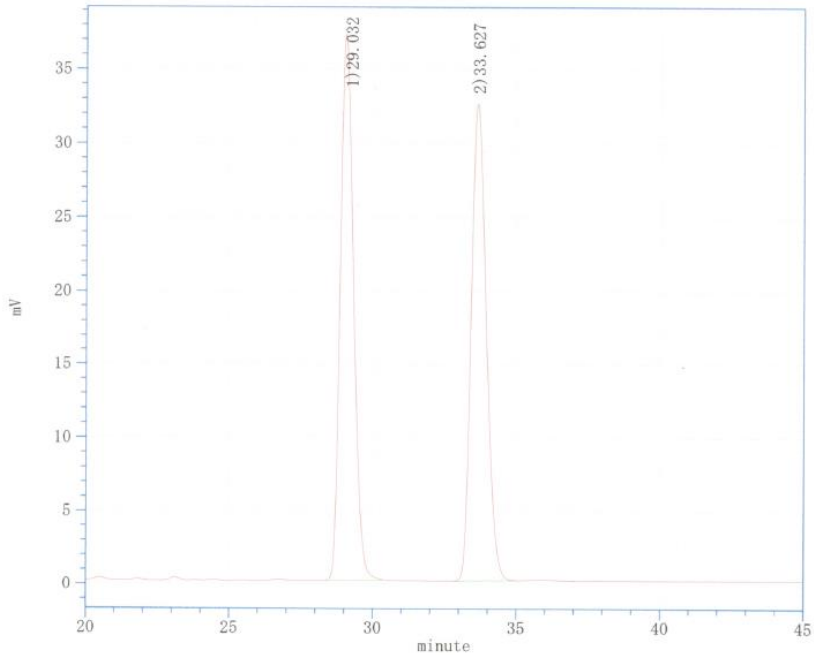


20.453	282650	50.1116
23.437	281391	49.8884

3c: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm

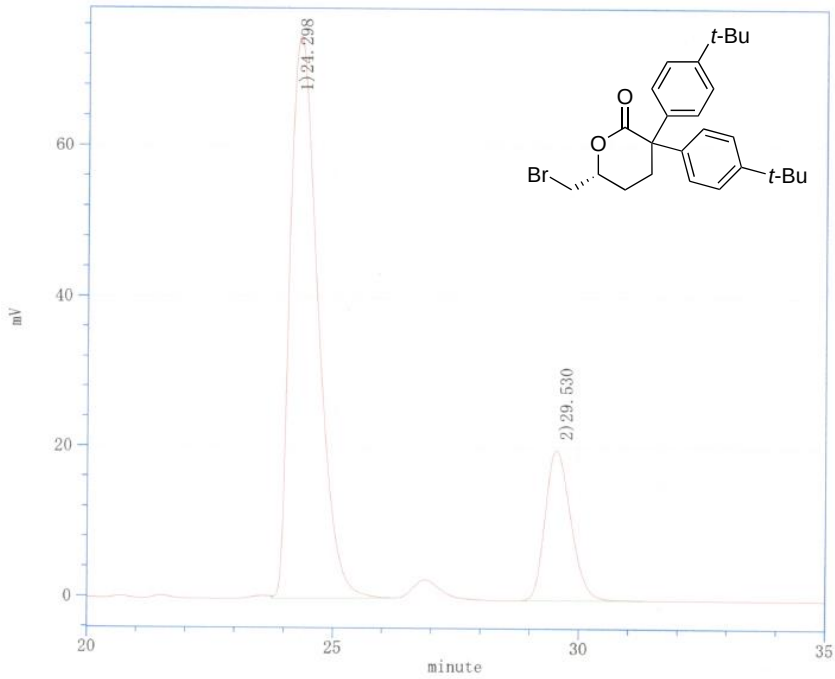


28.760	5572493	88.9717
33.857	690729	11.0283

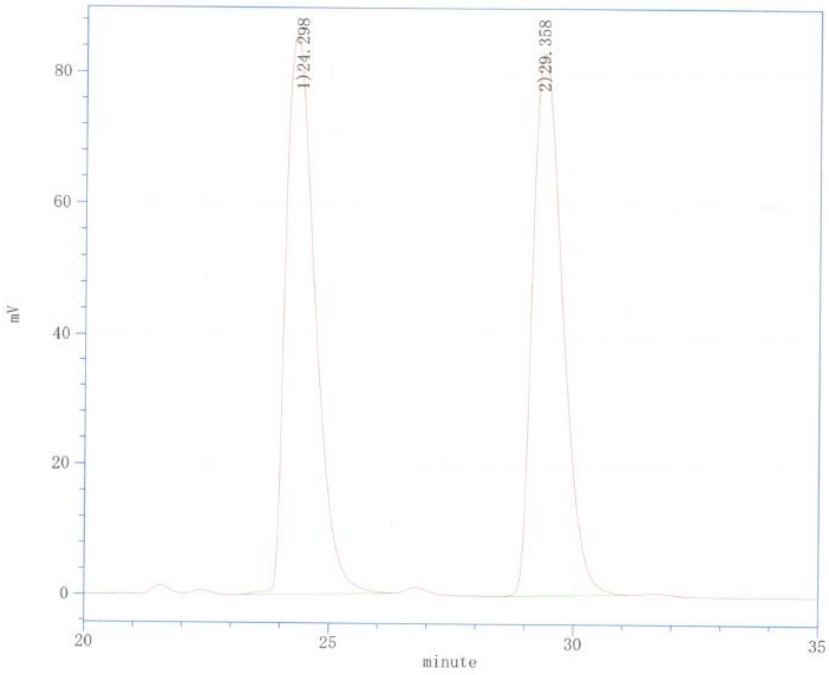


29.032	1194906	50.2229
33.627	1184301	49.7771

3d: Daicel Chiralpak IE-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 254 nm

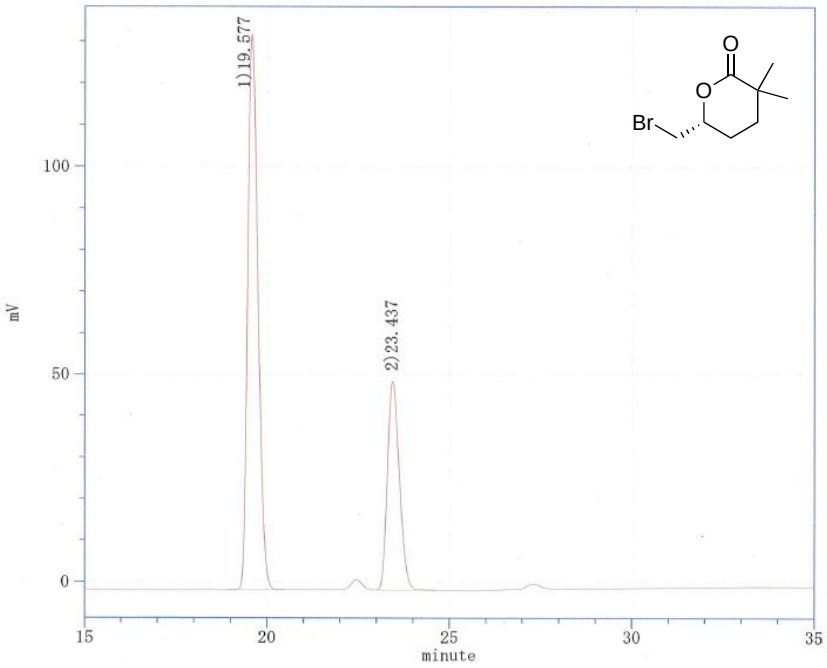


24.298	2943890	80.2351
29.530	725188	19.7649

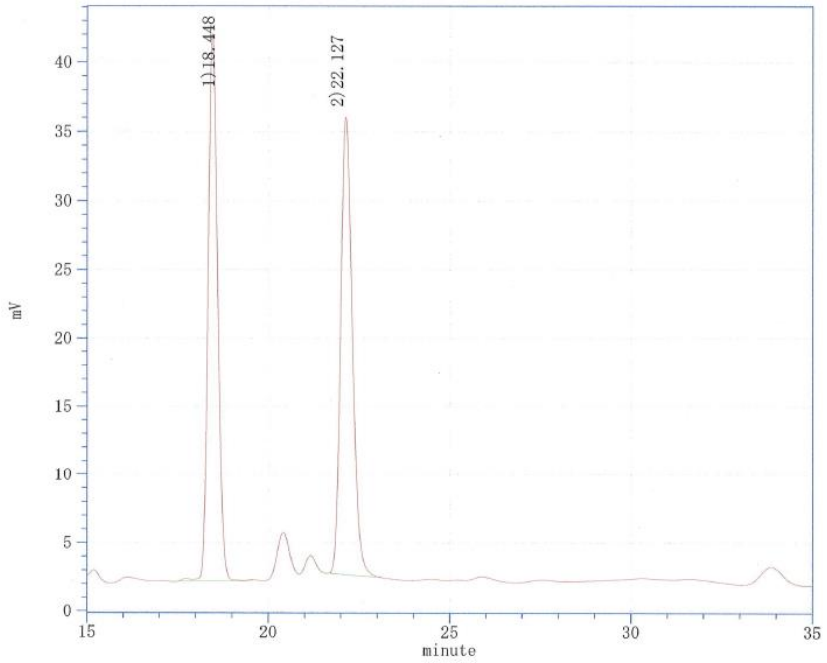


24.298	3571091	50.1734
29.358	3546407	49.8266

3e: Daicel Chiralpak IC-3, hexane/2-propanol = 3:1, flow rate = 0.5 mL/min, 214 nm

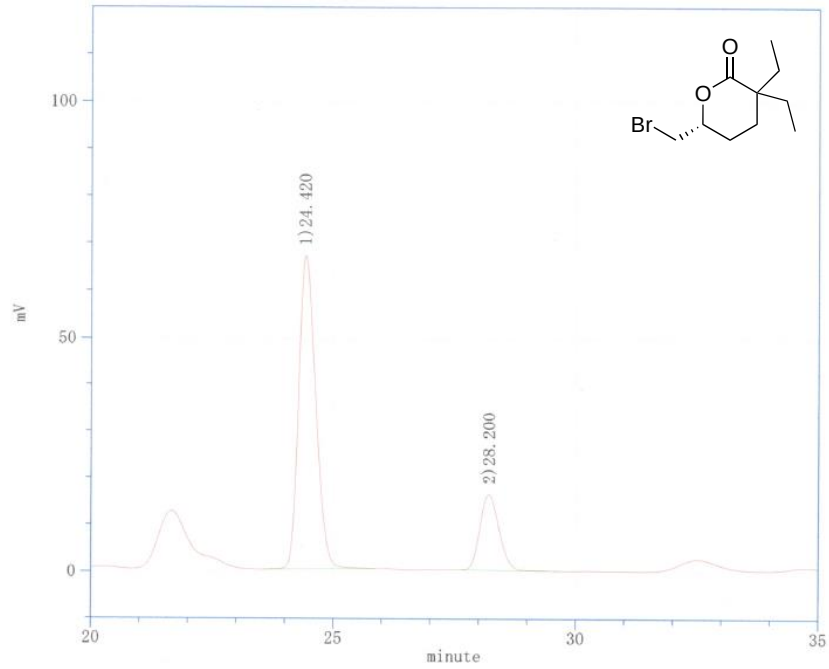


19.577	2607105	69.4690
23.437	1145798	30.5310

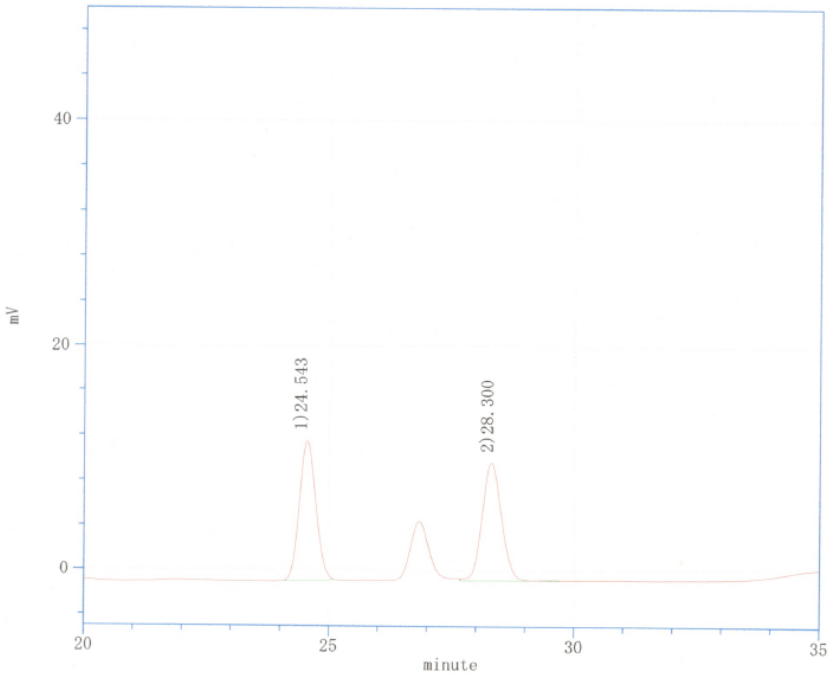


18.448	730965	49.5018
22.127	745678	50.4982

3f: Daicel Chiralpak IC-3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, 214 nm

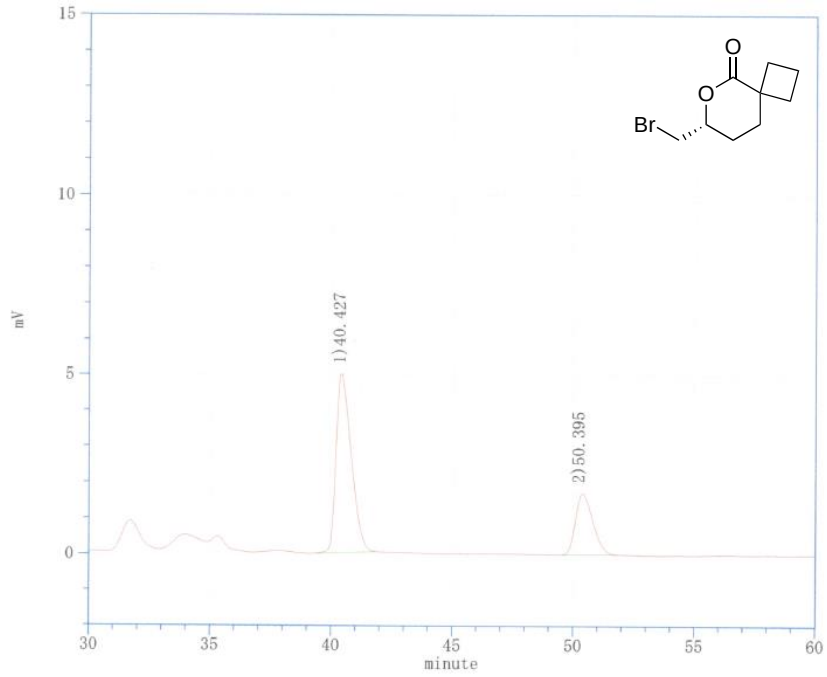


24.420	1637718	78.8689
28.200	438788	21.1311

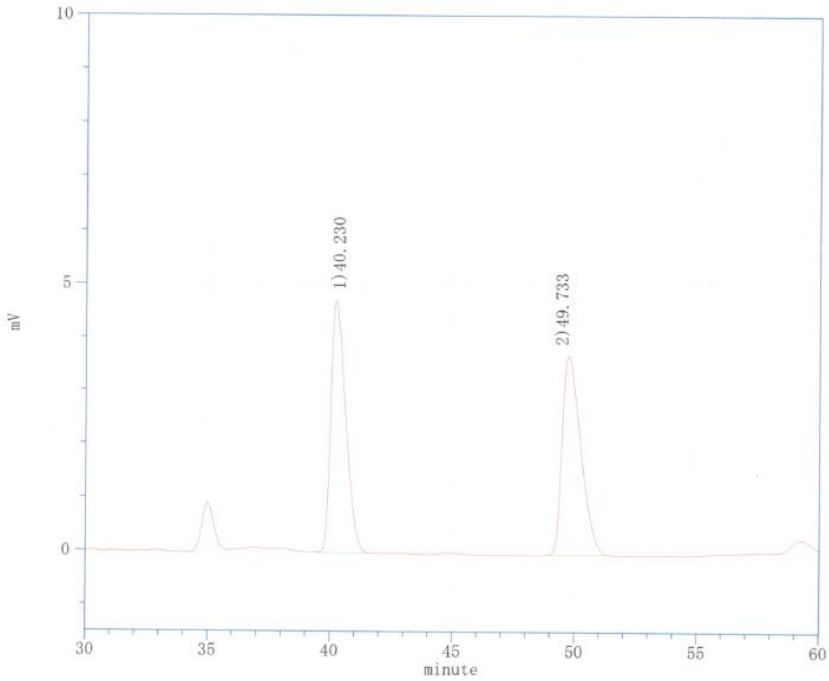


24.543	291307	50.1254
28.300	289849	49.8746

3g: Daicel Chiralpak IC-3, hexane/2-propanol = 10:1, flow rate = 0.5 mL/min, 254 nm

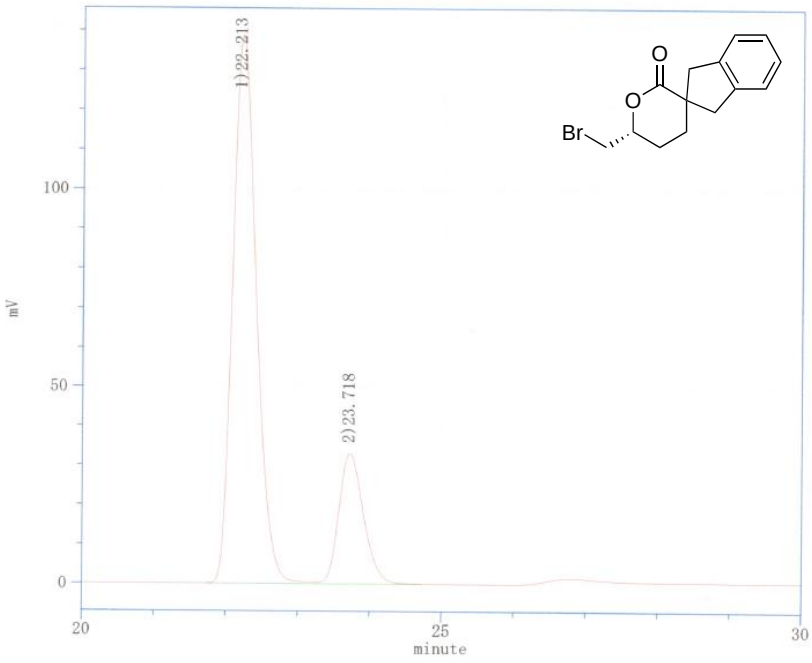


40.427	216031	71.7456
50.395	85076	28.2544

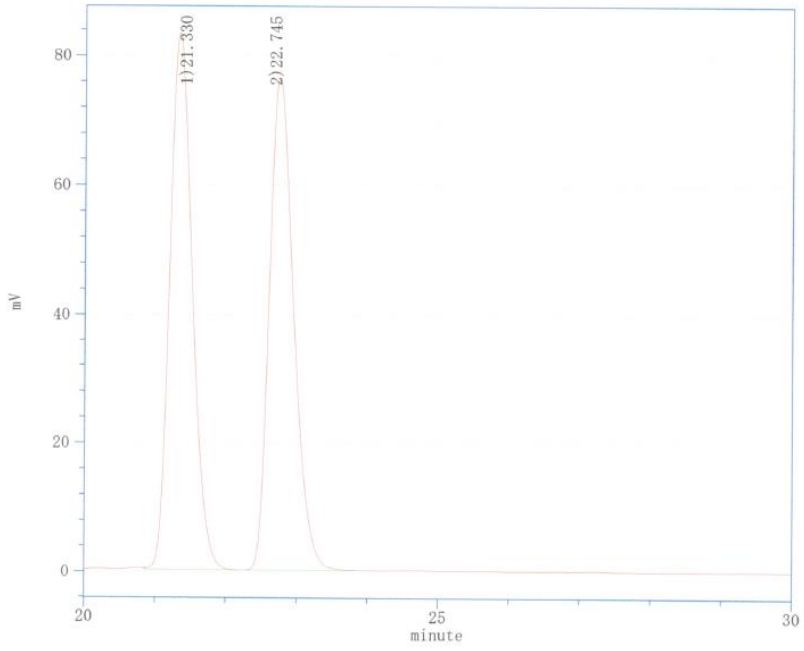


40.230	198440	50.0708
49.733	197879	49.9292

3h: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm

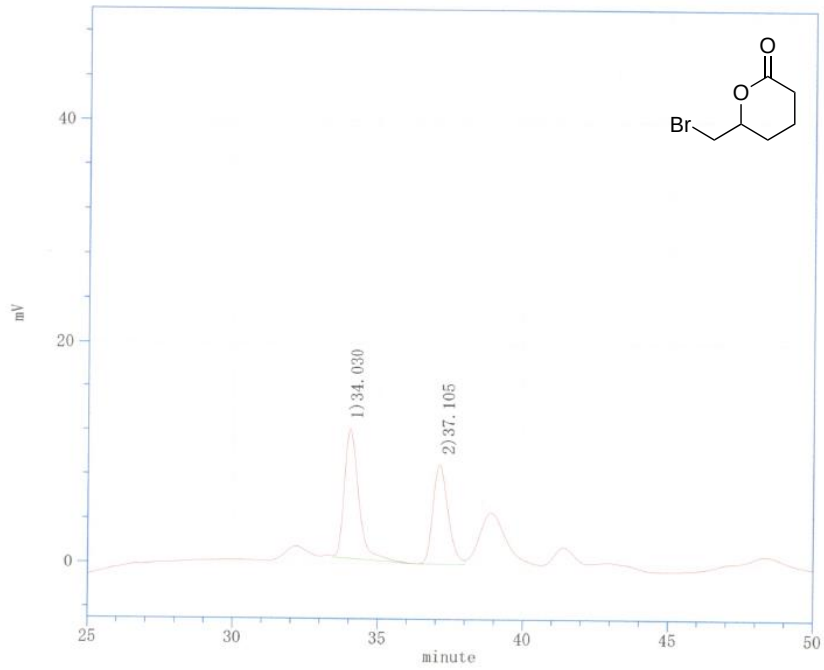


22.213	3143495	80.0602
23.718	782921	19.9398

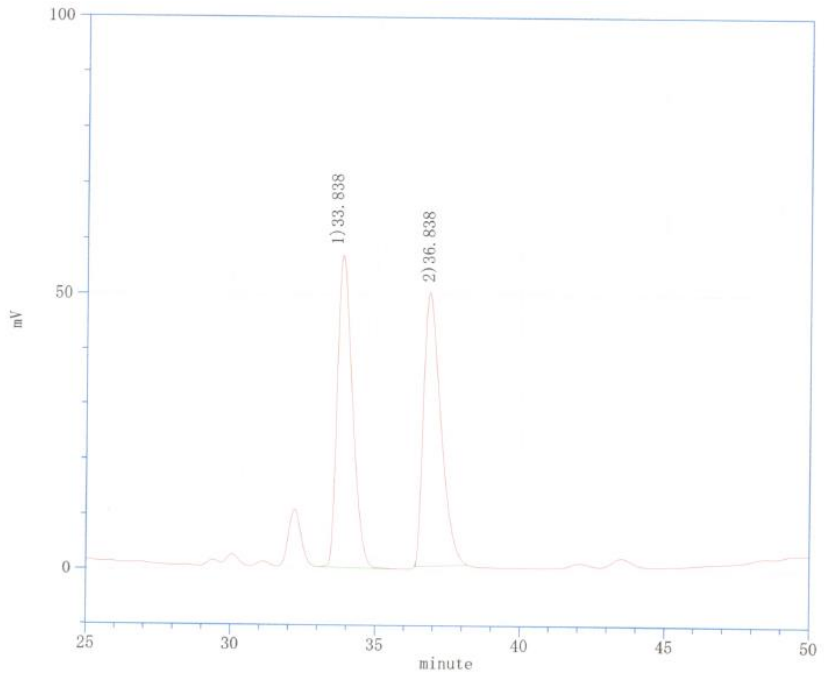


21.330	1834694	50.1959
22.745	1820371	49.8041

3i: Daicel Chiralpak IE-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm

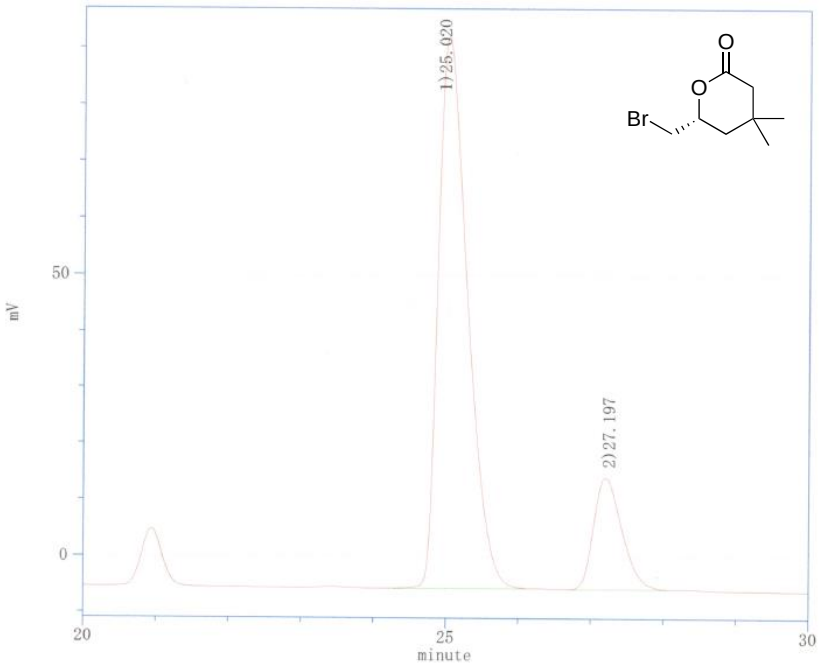


34.030	402636	55.4373
37.105	323655	44.5627

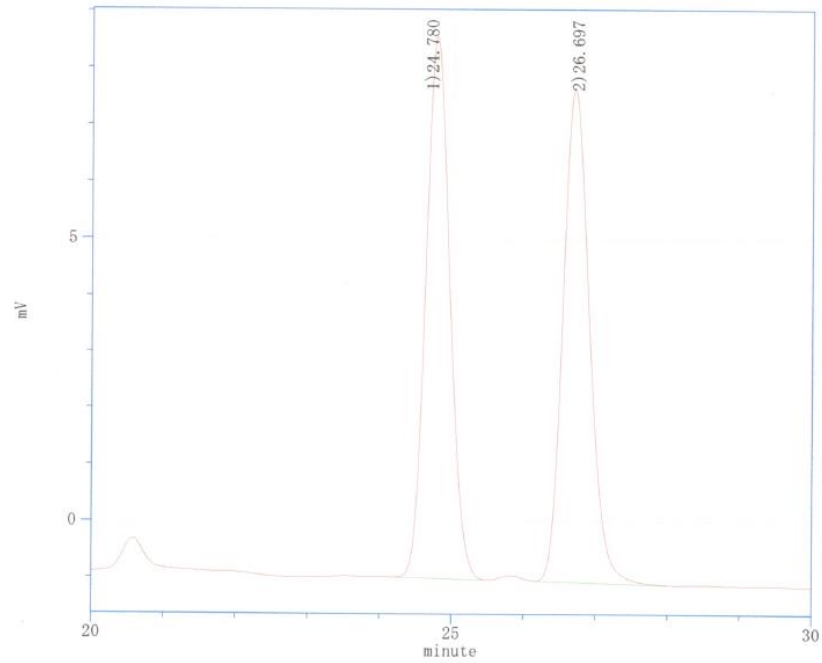


33.838	2062228	50.0371
36.838	2059173	49.9629

3j: Daicel Chiralpak IE-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm

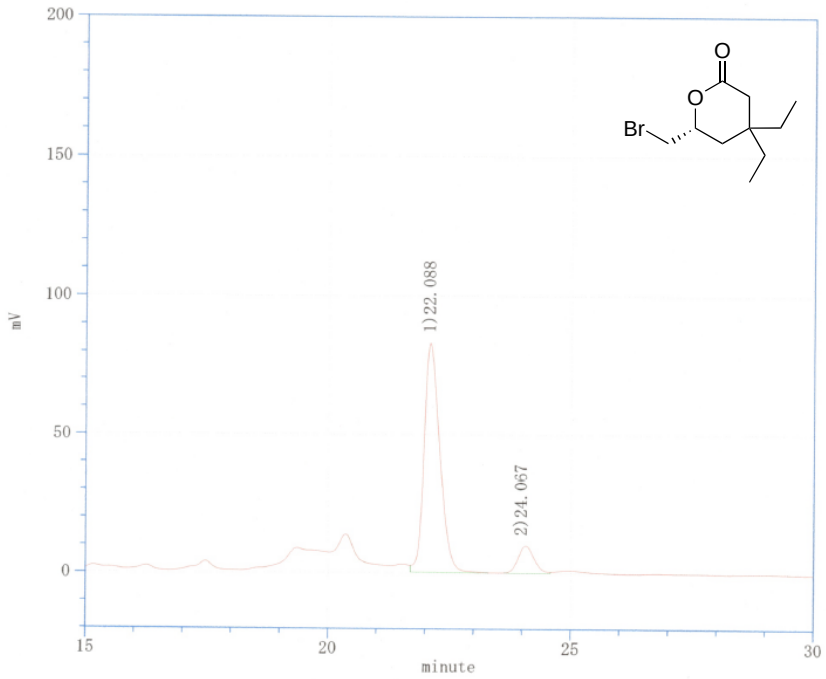


25.020	2727226	83.6594
27.197	532689	16.3406

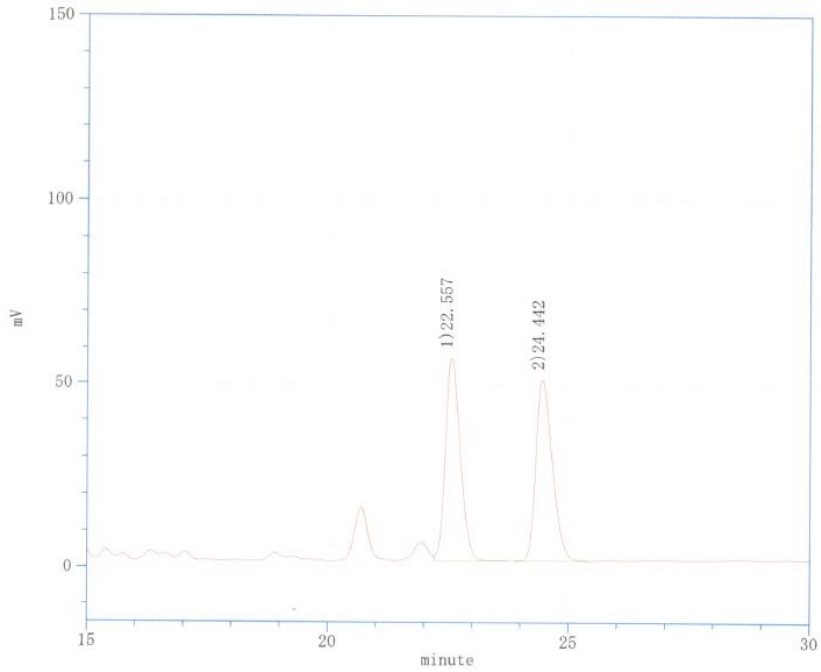


24.780	221420	49.8743
26.697	222536	50.1257

3k: Daicel Chiralpak IG-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm

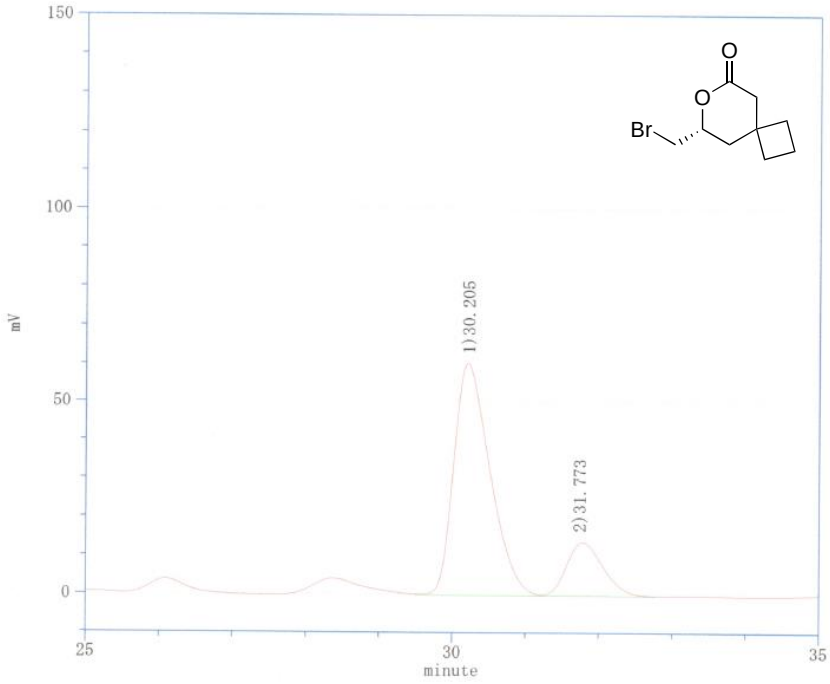


22.088	1861641	89.1916
24.067	225596	10.8084

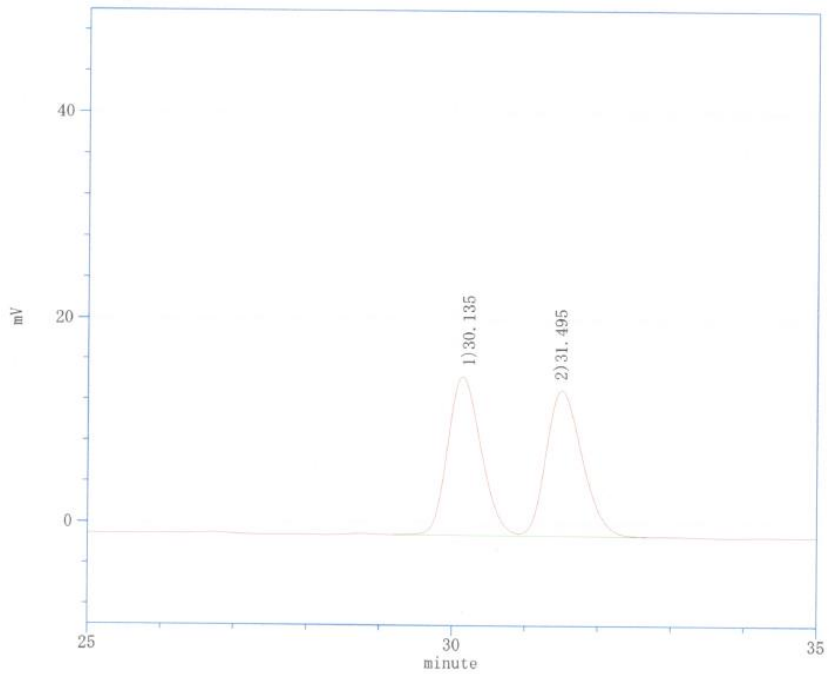


22.557	1182808	50.2473
24.442	1171165	49.7527

3l: Daicel Chiralpak IE-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm

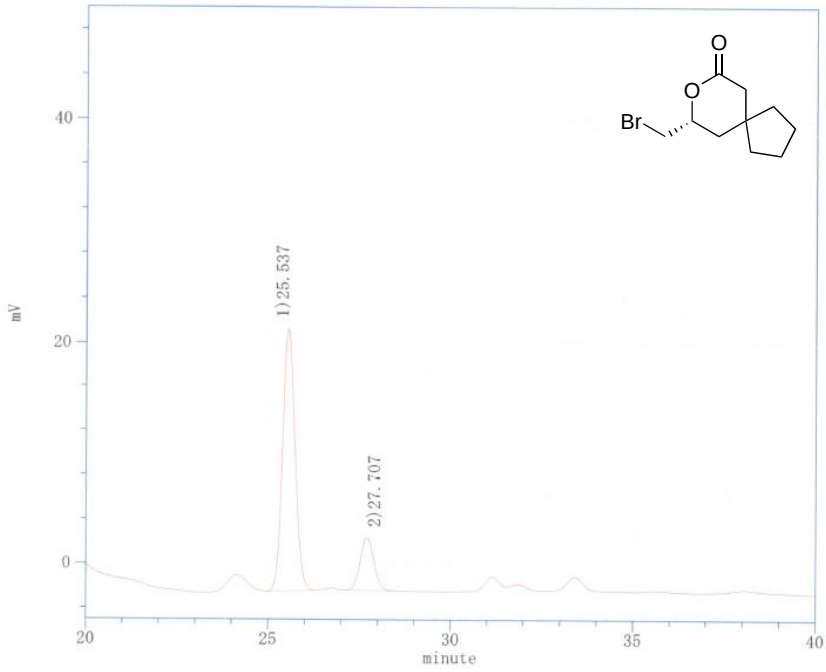


30.205	2065541	81.2117
31.773	477863	18.7883

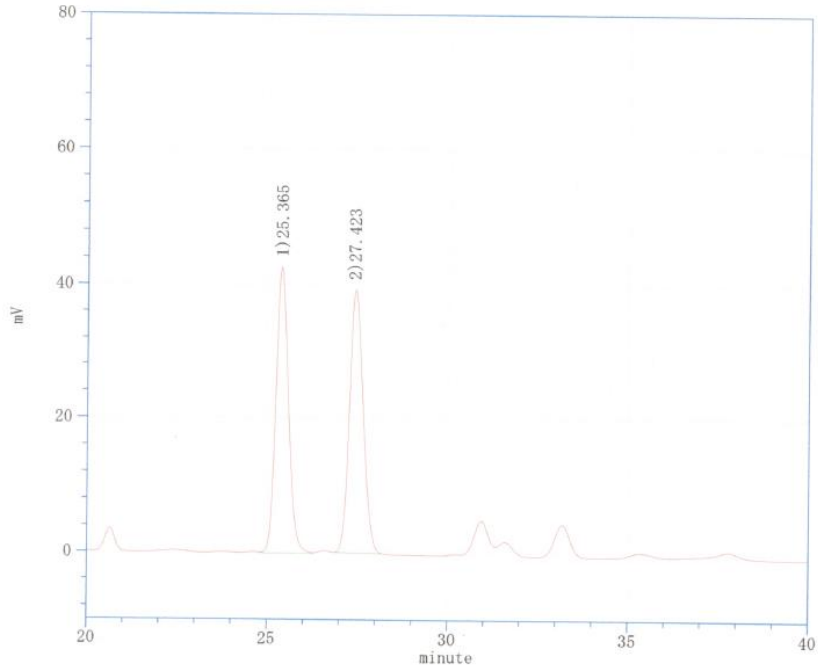


30.135	492944	50.1758
31.495	489489	49.8242

3m: Daicel Chiralpak IG-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm

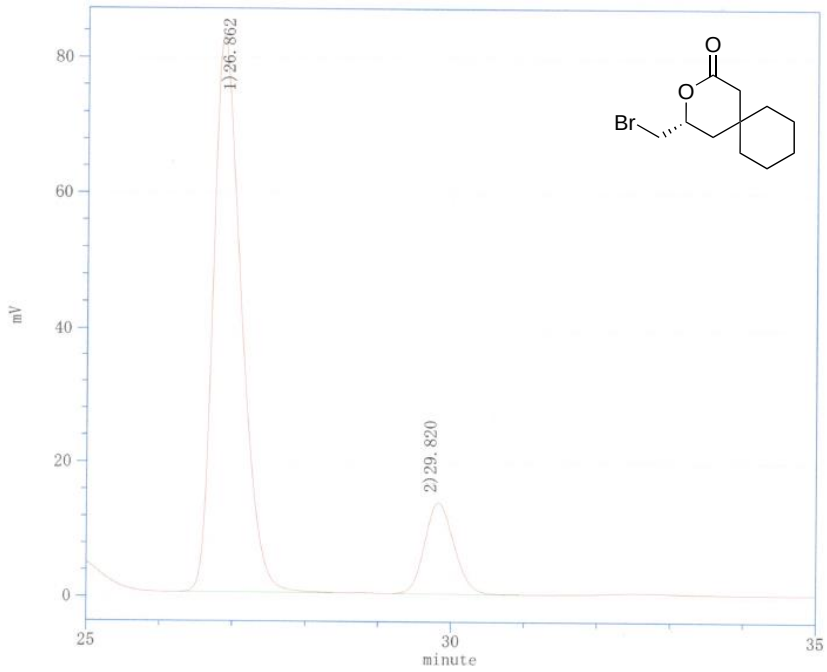


25.537	558927	81.8608
27.707	123850	18.1392

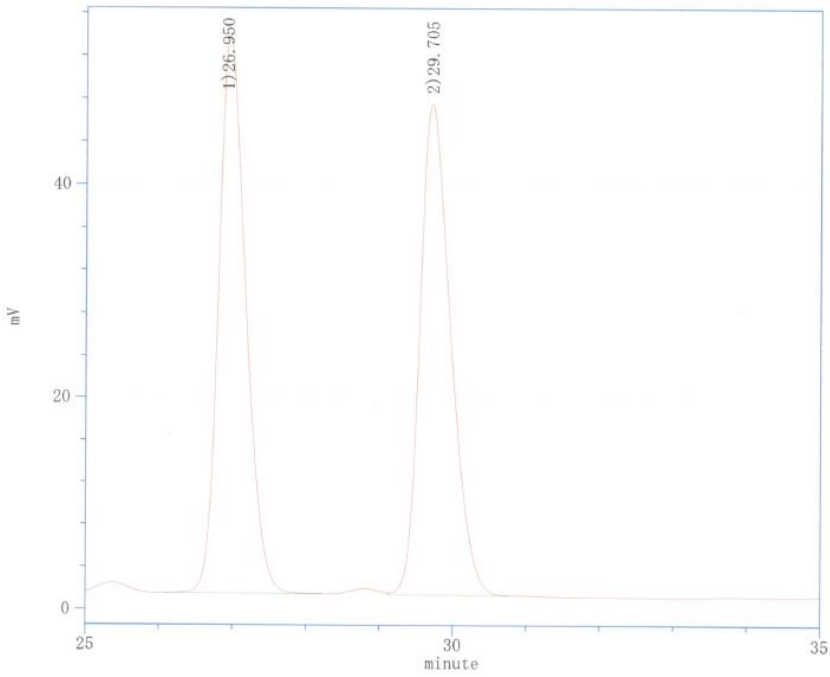


25.365	1027807	49.8744
27.423	1032984	50.1256

3n: Daicel Chiralpak IG-3, hexane/2-propanol = 5:1, flow rate = 0.5 mL/min, 214 nm

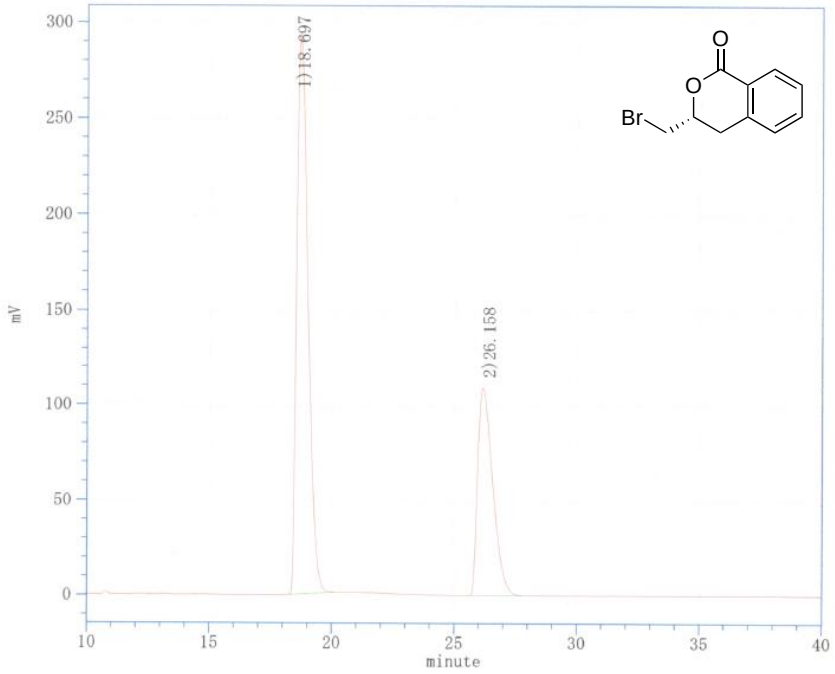


26.862	2203906	85.3009
29.820	379778	14.6991

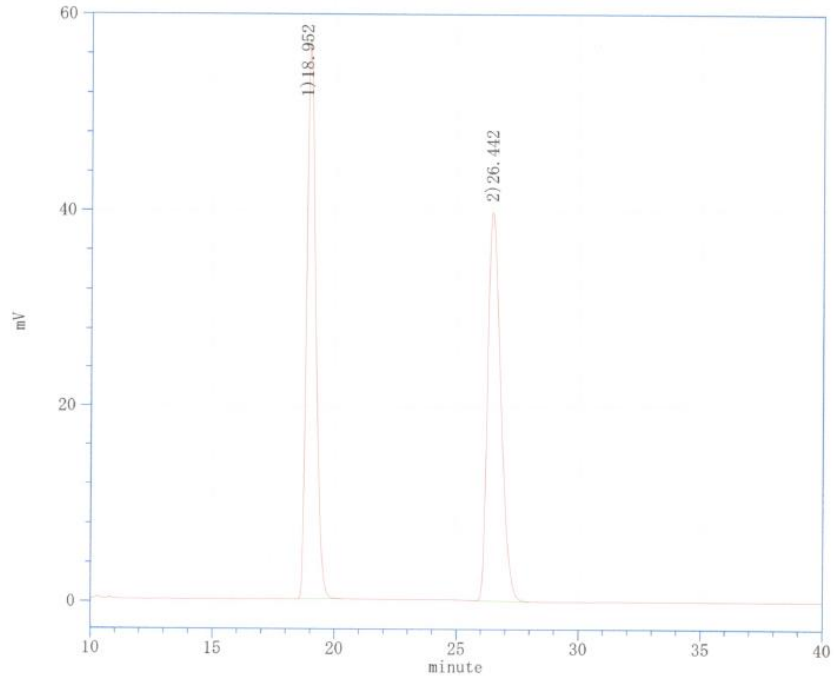


26.950	1351054	50.1754
29.705	1341609	49.8246

3o: Daicel Chiralpak AS-3, hexane/2-propanol = 1:1, flow rate = 0.5 mL/min, 254 nm

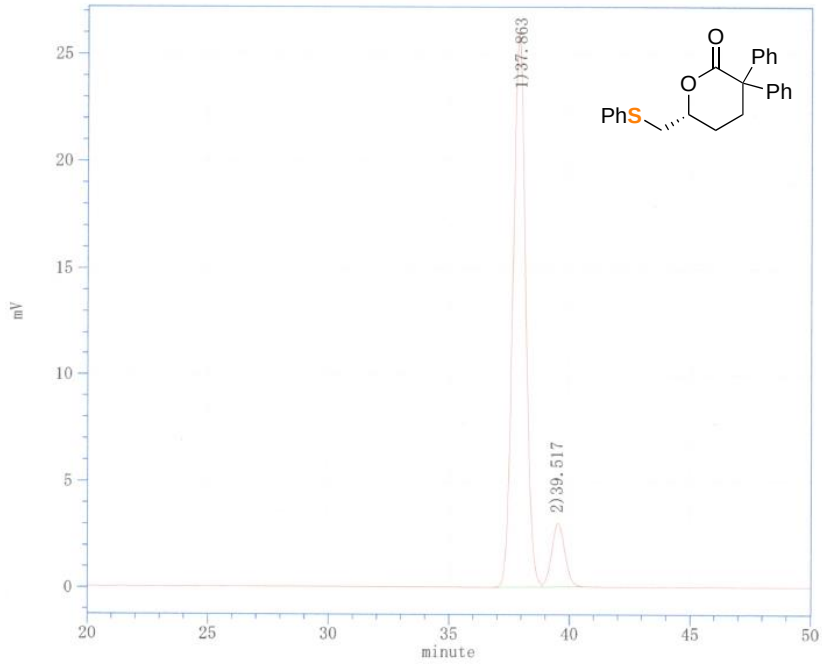


18.697	9408720	66.9825
26.158	4637818	33.0175

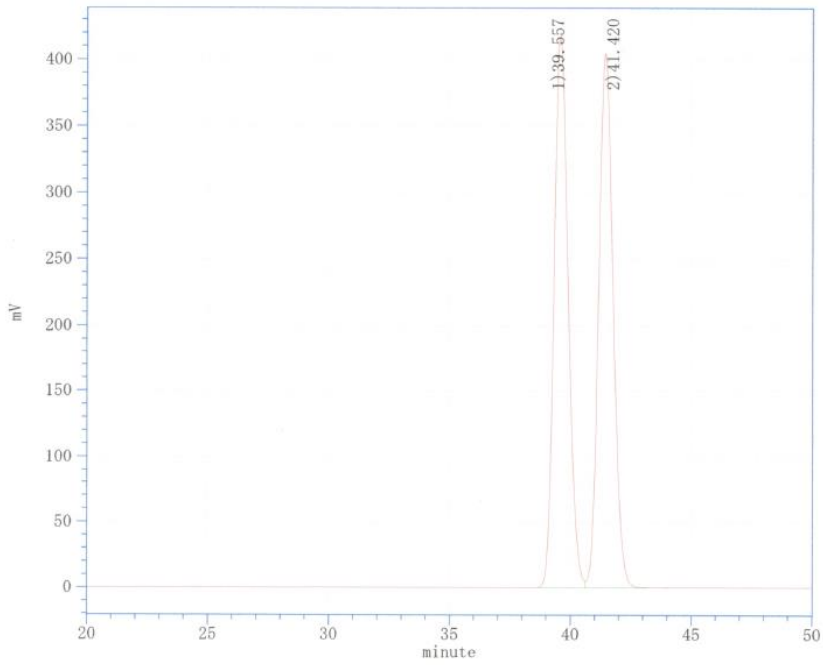


18.952	1485652	49.9527
26.442	1488468	50.0473

7: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm

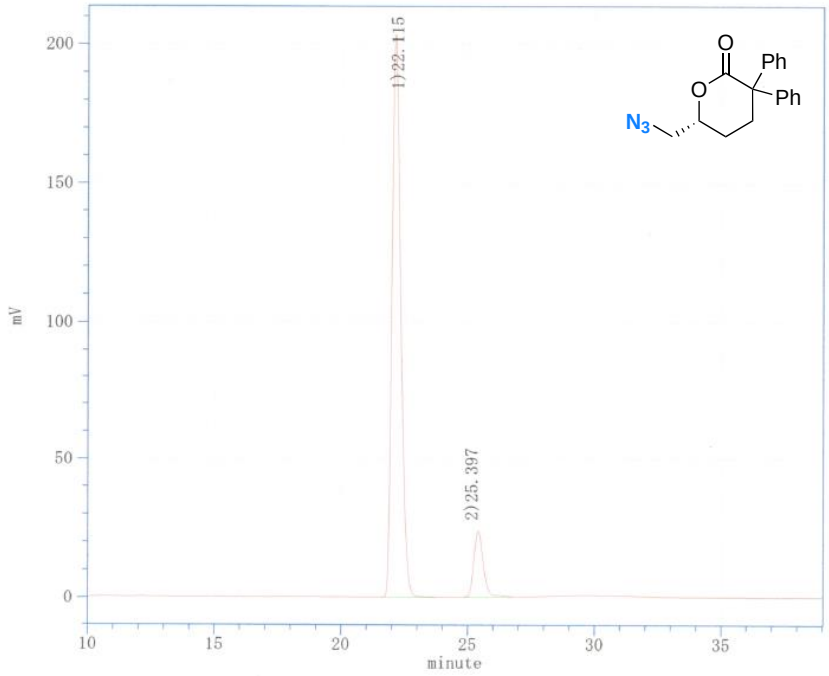


37.863	947658	89.2704
39.517	113901	10.7296

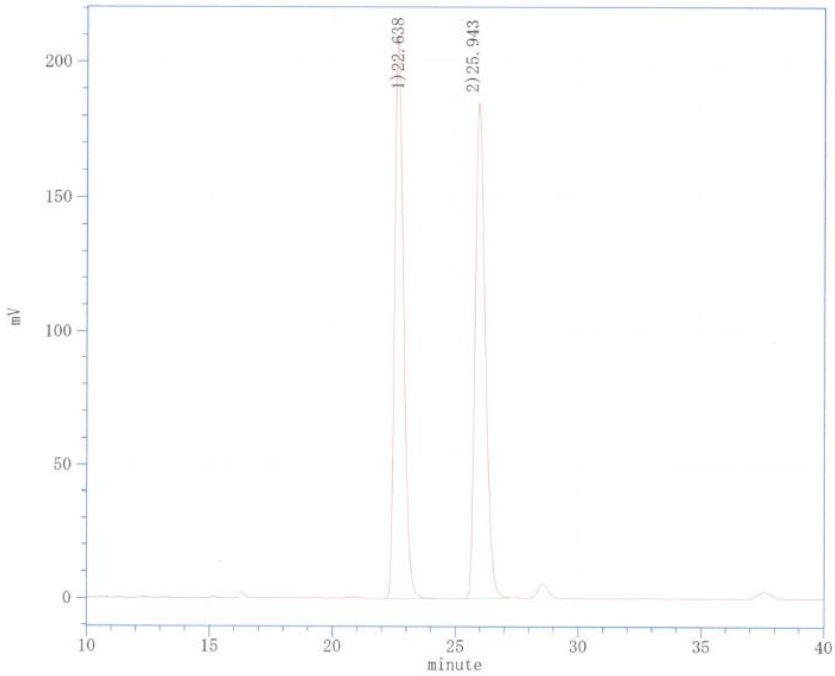


39.557	16994030	50.0661
41.420	16949160	49.9339

8: Daicel Chiralpak IE-3, hexane/2-propanol = 2:1, flow rate = 0.5 mL/min, 254 nm

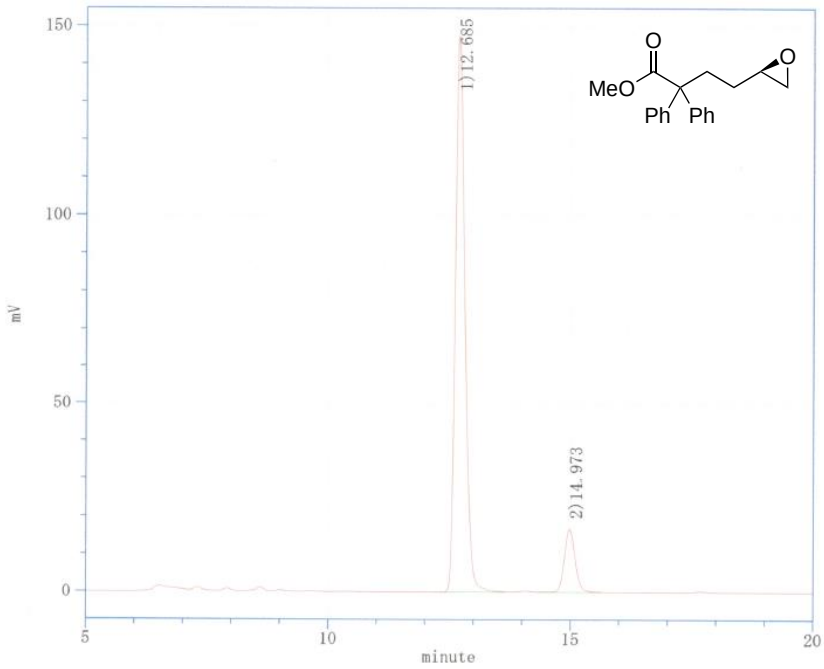


22.115	4903154	88.7473
25.397	621694	11.2527

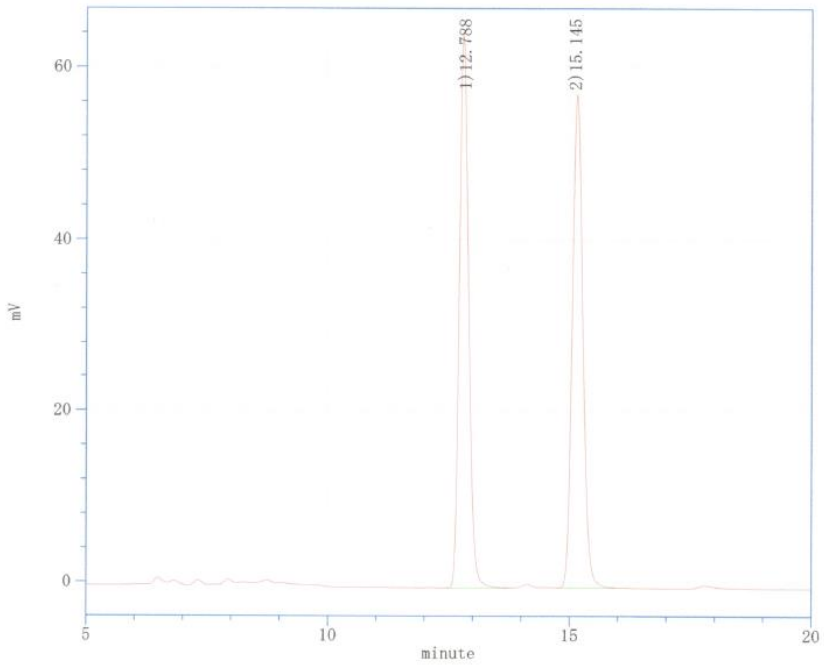


22.638	5332079	50.0280
25.943	5326117	49.9720

9: Daicel Chiralpak IB-3, hexane/2-propanol = 20:1, flow rate = 0.5 mL/min, 254 nm



12.685	2029262	88.8373
14.973	254984	11.1627



12.788	862647	49.7922
15.145	869846	50.2078