Supporting Information for

Substitution dependent stereoselective construction of bicyclic lactones and its application to the total synthesis of Pyranopyran, Tetraketide and Polyrhacitide A

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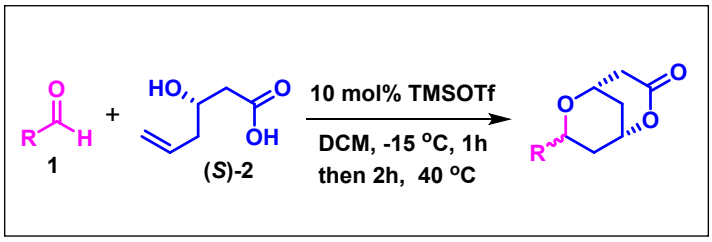
B. Sridhar



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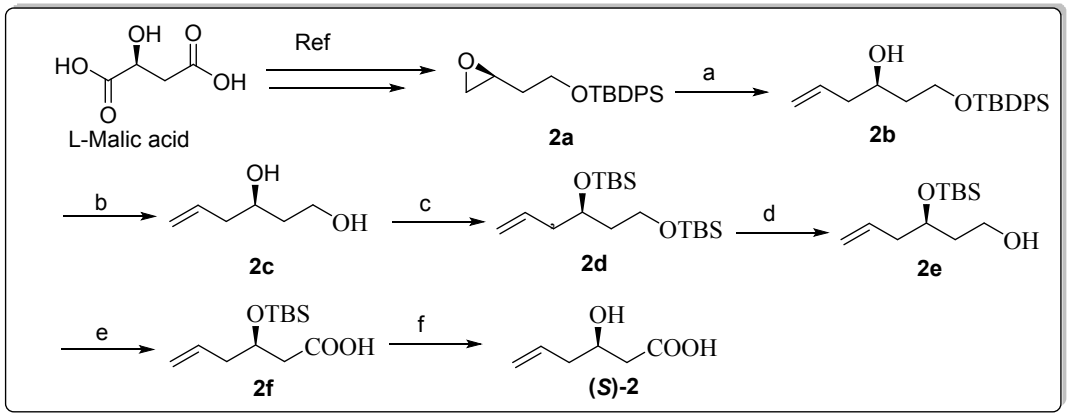
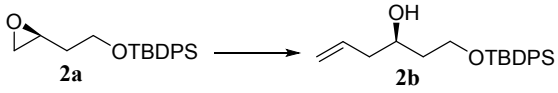
1. Preparation of starting materials (2a-(*S*)-2)



Scheme 1. Preparation of (**2a-(*S*)-2)**

Reagents & conditions: (a) Vinyl bromide, Mg, $(CH_2)_2Br_2$, CuCN, 88%; (b) TBAF, THF, 0 °C to rt, 3h, 70%; (c) TBSCl, imidazole, CH_2Cl_2, DMAP, 0 °C to rt, 3h, 90%; (d) CSA, CH_2Cl_2:MeOH (4:1), 0 °C, 1h, 70%; (e) TEMPO, BAIB, CH_3CN:H_2O (1:1), 0 °C to rt, 3h, 85%; (h) TBAF, THF, 0 °C to rt, 3h, 80%.

(*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)hex-5-en-3-ol (2b):

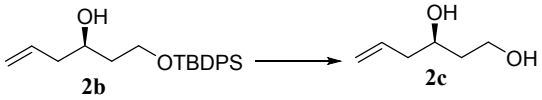


To a suspension of magnesium metal (1.72 g, 74..60 mmol) in dry THF (35 mL) at room temperature were sequentially added 1,2-dibromoethane (3 drops) and a freshly prepared vinyl bromide (3.5 mL, 49.07 mmol) in a dropwise manner. After generation of Grignard reagent, the stirring was continued for 1h at room temperature. The reaction mixture was cooled to -20 °C and then CuCN (109 mg, 5 mol%) was added. After stirring the reaction mixture for 0.5h, the colour of the reagent was turned to a brown. The mixture was then cooled to –78 °C and a solution of epoxide (**2a**) (8.0 g, 24.54 mmol) in dry THF (60 mL) was added. The resulting mixture was stirred at –40 °C for 4h. After completion as indicated by TLC, the mixture was quenched at 0 °C with sat. NH_4Cl solution (100 mL) and extracted with EtOAc (2 x100 mL). The combined organic extracts were washed with water (2 x 60 mL), brine solution (2 x 60 mL) and

dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, 12% EtOAc/hexane) to afford homoallylic alcohol **2b** (6.12 g, 88 %)) as a clear oil.

$[\alpha]_D^{20}$ + 26.4 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.71 – 7.66 (m, 4H), 7.46 – 7.36 (m, 6H), 5.85 (ddt, *J* = 17.3, 10.2, 7.1 Hz, 1H), 5.14 – 5.06 (m, 2H), 3.94 – 4.0 (m, 1H), 3.91 – 3.80 (m, 2H), 3.24 (s, 1H), 2.30 – 2.21 (m, 2H), 1.79 – 1.63 (m, 2H), 1.08 – 0.99 (m, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 135.4, 134.8, 132.9, 129.7, 127.6, 117.2, 70.5, 63.0, 41.9, 38.0, 26.8, 26.7, 18.9 ppm; IR (KBr) υ 3048, 2927, 2856, 1467, 1427, 1108, 824, 793, 704, 613 cm^{-1}; MS (ESI): *m/z* 377 [M+Na]; HRMS (ESI) Calcd for $C_{22}H_{30}O_2Si$: 377.19073 (M+Na); found 377.19178.

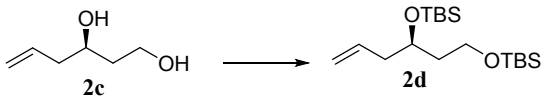
(*R*)-Hex-5-ene-1,3-diol (2c):



To a solution of silyl ether **2b** (6.0 g, 16.90 mmol) in dry THF (15 mL) was added TBAF (33.67 mL, 1M solution in THF, 33.8 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 4h. After completion as indicated by TLC, the reaction mixture was quenched with aqueous NH_4Cl solution (10 mL) and extracted with EtOAc (3x10 mL). The combined organic extracts were washed with water (2 x 60 mL), brine solution (2 x 60 mL) and dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography utilizing ethyl acetate and hexane (6:4) as a mobile phase to obtain the diol **2c** (2.8 g, 70 %).

$[\alpha]_D^{20}$ + 22.5 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.80 (ddt, *J* = 17.3, 10.2, 7.1 Hz, 1H), 5.20– 5.10 (m, 2H), 3.98 – 3.78 (m, 3H), 2.51 (s, 1H), 2.36 – 2.19 (m, 2H), 1.81 – 1.64 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 134.5, 117.8, 70.5, 61.0, 42.2, 37.7 ppm; IR (KBr) υ 3448, 2927, 2866, 1468, 1427, 1118, 826, 793, 744, 655 cm^{-1}; MS (ESI): *m/z* 117 $[M+H]^+$.

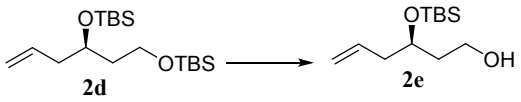
(*R*)-5-Allyl-2,2,3,3,9,9,10,10-octamethyl-4,8-dioxa-3,9-disilylundecane (2d):



To a 0 ºC cooled solution of the diol **2c** (2.7 g, 23.27 mmol) in CH_2Cl_2 (35 mL) were added imidazole (3.16 mL, 46.55 mmol), TBDMSCl (4.4 g, 27.93 mmol) and DMAP (73 mg, 0.59 mmol). The resulting mixture was stirred at 0 ºC for 3 h. After completion, the mixture was quenched with NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2x40 mL). The combined organic extracts were washed with water (30 mL), brine solution (30 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude product was purified by silica gel column chromatography (1% ethyl acetate/hexane) as a mobile phase to obtain the compound **2d** (2.55 g, 90%) as a colorless liquid.

$[\alpha]_D^{20}$ - 58.3 (*c* 2.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.77 (ddt, *J* = 17.7, 10.7, 7.2 Hz, 1H), 5.02 –4.96 (m, 2H), 3.87 – 3.79 (m, 1H), 3.66 – 3.59 (m, 2H), 2.26 – 2.12 (m, 2H), 1.65 – 1.56 (m, 2H), 0.86 (s, 18H), 0.05 (s, 6H), 0.04 (s, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 141.7, 135.1, 128.4, 128.2, 125.9, 116.8, 68.9, 59.8, 42.2, 39.9, 38.0, 26.0, 25.9, 18.3, 18.1, -4.2, -4.6, -5.3 ppm; IR(KBr) υ 3077, 2954, 2931, 2892, 2858, 1639, 1468, 1253, 1096, 1039, 835 cm^{-1}; MS (ESI): *m/z* 345 $[M+H]^+$; HRMS (ESI) Calcd. for $C_{18}H_{40}O_2NaSi_2$: 345.26304 (M+Na); found 345.26313.

(*R*)-3-((*tert*-Butyldimethylsilyl)oxy)hex-5-en-1-ol (2e):

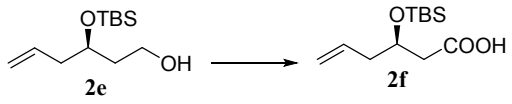


To a solution of bis-TBS ether **2d** (6.4 g, 18.60 mmol) in dry CH_2Cl_2/MeOH (4:1, 60 mL), CSA (90 mg, 0.9 mmol) was added at 0 ºC under N_2 atmosphere and stirred for 1.5 h at the same temperature. After completion, the mixture was quenched with triethylamine, extracted with EtOAc, washed with brine solution, and dried over anhydrous Na_2SO_4. Removal of the solvent followed by purification on silica gel column chromatography (SiO_2, 35 to 40% EtOAc in petroleum ether) gave the primary alcohol **2e** (2.99 g, 70 %) as a colorless liquid.

$[\alpha]_D^{20}$ - 62.4 (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.75 (ddt, *J* = 17.7, 10.7, 7.2 Hz, 1H), 5.10 – 5.02 (m, 2H), 4.00 – 3.94 (m, 1H), 3.86 – 3.79 (m, 1H), 3.75 – 3.68 (m, 1H), 2.34 (s, 1H), 2.33 –2.28 (m, 2H), 1.85 – 1.77 (m, 1H), 1.72 – 1.64 (m, 1H), 0.90 (s, 9H), δ 0.10 (d, *J* = 6.5 Hz, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 134.5, 117.1, 70.9, 59.8, 41.5, 37.9, 25.8, 17.9, -4.5, -

4.9 ppm; IR (KBr) υ 3077, 2954, 2931, 2892, 2858, 1639, 1468, 1253, 1096, 1039, 835 cm^{-1}; MS (ESI): *m/z* 231 $[M+H]^+$; HRMS (ESI) Calcd for $C_{12}H_{27}O_2Si$: 231.18742 $(M+H)^+$; found 231.18758.

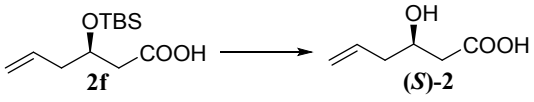
(*R*)-3-((*tert*-Butyldimethylsilyl)oxy)hex-5-enoic acid (2f):



To a solution of alcohol **2e** (2.80 g, 11.47 mmol) in acetonitrile/water (50 mL, 1:1 ratio) were added BAIB (7.39 g, 22.95 mmol) and TEMPO (0.35 g, 2.29 mmol) sequentially and stirred it for 4h at room temperature. The resulting precipitate was filtered through a small pad of celite and concentrated in *vacuo*. The residue was diluted with ethyl acetate followed by 50 mL aqueous solution of $Na_2S_2O_7$ and stirred for another 10 min. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3x50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated to dryness under *vacuo*. The residue was purified by silica gel chromatography (SiO_2, 25% EtOAc in petroleum ether) to give the acid **2f** (2.52 g, 85 %) as a viscous liquid.

$[\alpha]_D^{20}$ - 44.4 (*c* 1.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 5.78 (ddt, *J* = 17.6, 10.4, 7.2 Hz, 1H), 5.14 5.04 (m, 2H), 4.24 – 4.14 (m, 1H), 2.53 – 2.46 (m, 2H), 2.34 2.27 (m, 2H), 0.88 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.9, 133.8, 118.0, 68.8, 42.0, 25.7, 18.0, -4.5, - 5.0 ppm. IR (KBr) υ 3404, 3077, 2926, 2855, 1718, 1644, 1404, 1176, 1054, 995, 920 cm^{-1}; MS (ESI): *m/z* 245 $[M+H]^+$; HRMS (ESI) Calcd for $C_{12}H_{25}O_3Si$: 245.15675 $(M+H)^+$; found 245.15726.

(*R*)-3-Hydroxyhex-5-enoic acid (*S*)-2:

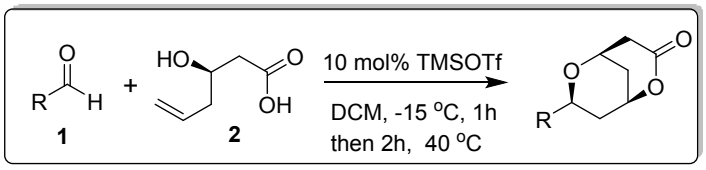


To a solution of silyl ether **2f** (2.4 g , 9.83 mmol) in dry THF (25 mL), was added TBAF (1M in THF, 14.6 mL, 14.75 mmol) at 0 °C. After 15 min of stirring, the mixture was stirred at room temperature for another 4 h. After completion, the reaction (TLC) was cooled and quenched with

sat. NH_4Cl solution and extracted with EtOAc (3x100 mL), The combined organic extracts were washed with brine solution (2 x 20 mL) and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (SiO_2, 10% MeOH/$CHCl_3$) to afford the hydroxy acid (*S*)-**2** (1.02 g , 80%) as a viscous liquid.

$[\alpha]_D^{20}$ = -124.2 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 5.81 (ddd, *J* = 15.0, 11.8, 6.4 Hz, 1H), 5.15 (dd, *J* = 9.6, 6.6 Hz, 2H), 4.16 – 4.09 (m, 1H), 2.61 – 2.43 (m, 2H), 2.37 – 2.24 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.7, 133.6, 118.4, 67.4, 40.8, 40.5, 18.5 ppm; IR (KBr) υ 3404, 3077, 2926, 2855, 1718, 1644, 1404, 1176, 1054, 995, 920 cm^{-1}; MS (ESI): *m/z* 129 $[M-H]^+$131 $[M+H]^+$, 153 $[M+Na]^+$, HRMS (ESI) Calcd for $C_7H_{14}O_2Na$: 153.08860 (M +Na); found 153.08826.

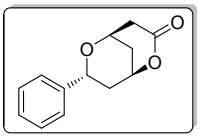
2. Experimental procedure for bicyclic lactones (3 & 4):



To a stirred solution of aldehyde (1, 1.1 mmol) and hydroxy acid (2, 1.0 mmol), in DCM (4 mL), TMSOTf (10 mol%) was added at -15 °C and the temperature was slowly raised to 40 °C. The resulting mixture was allowed to stir for a specified time (see Table 1 & 2). After complete conversion, as indicated by TLC, the mixture was diluted with water and extracted with dichloromethane (2x10 mL). The combined organic layers were dried over anhydrous Na_2SO_4. Removal of the solvent followed by purification on silica gel (Merck, 60-120 mesh, ethyl acetate-hexane, 3:7) column chromatography afforded the pure bicyclic lactone (Table 1 & 2).

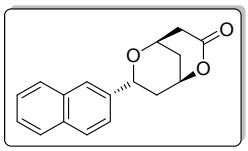
3. Characterization data of bicyclic lactones (3a-n)

(1*R*,5*R*,7*R*)-7-Phenyl-2,6-dioxabicyclo[3.3.1]nonan-3-one (3a):



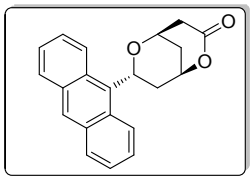
Solid. m. p. 140-142 ^{o}C purified by column chromatography (22 % ethyl acetate/hexane); $[\alpha]_D^{22}$ - 8.28 (*c* 0.88, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.44 – 7.31 (m, 5H), 5.04- 4.96 (s, 1H), 4.87 (dd, *J* = 11.7, 2.8 Hz, 1H), 4.58 – 4.52 (m, 1H), 2.95 (dt, *J* = 19.3, 12.3 Hz, 1H), 2.31 (d, *J* = 13.8 Hz, 1H), 2.20 (dd, *J* = 13.8, 1.9 Hz, 1H), 2.04 (d, *J* = 12.1 Hz, 1H), 1.85 (ddd, *J* = 14.1, 10.8, 2.1 Hz, 1H) ppm; **^{13}C-** NMR (75 MHz, $CDCl_3$) δ 169.7, 140.7, 128.5, 128.0, 125.8, 73.1, 68.2, 66.4, 38.9, 36.4, 29.5 Ppm; IR (neat, KBr) υ 2928, 2856, 1738, 1509, 1257, 1215, 1162, 1038, 916, 837, 761 cm^{-1}; MS (ESI): *m/z* 219 $(M+H)^+$, 241 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{13}H_{14}O_3Na$: 241.08352 (M + Na)+; found 241.08335.

(1*R*,5*R*,7*R*)-7-(Naphthalen-2-yl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3b):



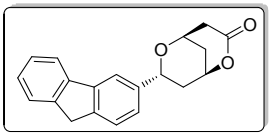
Solid. m. p. 152-154 ^{o}C purified by column chromatography (20% ethyl acetate/hexane); $[\alpha]_D^{22}$ - 10.4 (*c* 0.38, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 -7.80 (m, 4H) 7.50 -7.44 (m, 3H), 5.02 (dd, *J* = 5.1, 3.1 Hz, 1H), 4.64 - 4.58 (s, 1H), 3.07 (d, *J* = 19.4 Hz, 1H), 2.92 (dd, *J* = 19.3,5. 2 Hz, 1H), 2.37 (d, *J* = 13.0 Hz, 1H), 2.22 (d, *J* = 13.9 Hz, 1H), 2.06 (d, *J* = 13.8 Hz, 1H), 1.0 (dd, *J* = 19.1, 6.9 Hz, 1H) ppm; **^{13}C** NMR (125 MHz, $CDCl_3$) δ 169.6, 138.1, 133.2, 133.0, 128.3, 127.8, 127.6, 126.2, 126.0, 124.6, 123.6, 73.1, 68.3, 66.4, 38.9, 36.4, 29.5 ppm; IR (KBr) υ 3443, 3055, 2957, 2924, 2854, 1730, 1385, 1364, 1268, 1217, 1075, 816, 751 cm^{-1}; ESI-MS: *m/z* 269 $(M+H)^+$, $(M+NH_4)^+$, 291 $(M+Na)^+$; HRMS (ESI) Calcd for $C_{17}H_{17}O_3$: 269.09917 $(M+H)^+$; found 269.09860.

(1*R*,5*R*,7*R*)-7-(Anthracen-9-yl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3c):



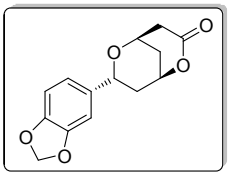
Solid. m. p. 214-216 ^{o}C purified by column chromatography (16 % ethyl acetate/hexane); $[\alpha]_D^{22}$ - 24.8 (*c* 0.23, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (s, 2H), 8.01 (d, *J* = 8.3 Hz, 2H), 7.57 – 7.42 (m, 5H), 6.41 (dd, *J* = 12.3, 3.2 Hz, 1H), 5.16 (s, 1H), 4.78 (s, 1H), 3.19 (d, *J* = 19.4 Hz, 1H), 3.01 (dd, *J* = 19.4, 5.3 Hz, 1H), 2.78 – 2.69 (m, 1H), 2.57 (d, *J* = 14.1 Hz, 1H), 2.35 (d, *J* = 14.7 Hz, 1H), 2.27 – 2.20 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 131.6, 129.8, 129.5, 129.3, 129.0, 126.2, 124.8, 73.6, 67.1, 65.3, 36.4, 36.2, 29.6 ppm; IR (KBr) υ 3449, 2923, 2853, 1733, 1460, 1262, 1159, 1065, 732 cm^{-1}; MS (ESI): *m/z* 319 $(M+H)^+$; HRMS (ESI) Calcd. for $C_{21}H_{19}O_3$: 319.13287$(M+H)^+$; found 319.13331.

(1*R*,5*R*,7*R*)-7-(9*H*-Fluoren-3-yl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3d):



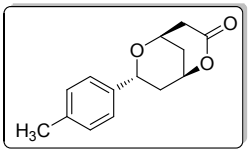
Solid. m. p. 183-185 ^{o}C purified by column chromatography (20 % ethyl acetate/hexane); $[\alpha]_D^{22}$ - 6.7 (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (t, *J* = 7.7 Hz, 2H), 7.54 (dd, *J* = 16.4, 9.0 Hz, 2H), 7.41 – 7.28 (m, 3), 5.01 (d, *J* = 1.8 Hz, 1H), 4.93 (dd, *J* = 11.7, 2.8 Hz, 1H), 4.60 – 4.56 (m, 1H), 3.90 (s, 2H), 3.06 (d, *J* = 19.4 Hz, 1H), 2.90 (dd, *J* = 19.3, 5.4 Hz, 1H), 2.34 (d, *J* = 12.3 Hz, 1H), 2.24 – 2.18 (m, 1H), 2.08 – 2.02 (m, 1H), 1.95 (ddd, *J* = 14.0, 11.9, 2.0 Hz, 1H) ppm; **^{13}**C NMR (125 MHz, $CDCl_3$) δ 169.8, 143.6, 143.3, 141.6, 141.2, 139.2, 126.7, 126.6, 125.0, 124.6, 122.5, 119.9, 119.8, 73.1, 68.5, 66.4, 39.0, 36.8, 36.4, 29.5 ppm; IR (KBr) υ 3424, 2924, 2852, 1722, 1335, 1221, 1156, 1071, 1001, 822, 767, 734, 585 cm^{-1}; MS (ESI): *m/z* 307 $(M+H)^+$ 324 $(M+NH_4)^+$, 329 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{20}H_{19}O_3$: 307.13287 $(M+H)^+$; found 307.13234.

(1*R*,5*R*,7*R*)-7-(Benzo[*d*][1,3]dioxol-5-yl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3e):



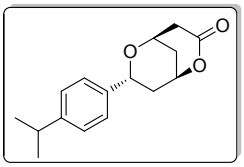
Solid. m. p. 170-172 ^{o}C purified by column chromatography (22 % ethyl acetate/hexane); $[\alpha]_D^{22}$ - 12.6 (*c* 0.96, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.87 (d, *J* = 5.3 Hz, 1H), 6.82 – 6.76, (m, 2H), 5.96 (s,2H), 4.98 (d, *J* = 1.5 Hz, 1H), 4.75 (dd, *J* = 11.7, 2.8 Hz, 1H), 4.52 (s, 1H), 3.01(d, *J* = 19.3 Hz, 1H), 2.87 (dd, *J* = 19.3, 5.3 Hz, 1H), 2.24 (dd, *J* = 14.2, 1.8 Hz, 1H), 2.18 – 2.12 (m, 1H), 2.04 – 1.97 (m, 1H), 1.88 – 1.81 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6,147.8, 147.2, 134.6, 119.4, 108.2, 106.5, 101.1, 73.1, 68.1, 66.4, 39.0, 36.4, 29.5 ppm; IR (neat, KBr) υ 2925, 1718, 1498, 1445, 1393, 1345, 1248, 1194, 1071, 1037, 934, 816 cm^{-1}; MS (ESI): *m/z* 263$(M+H)^+$, 280 $(M+NH_4)^+$, 285 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{14}H_{14}O_5Na$: 285.07334 (M+Na)+; found 285.07291.

(1*R*,5*R*,7*R*)-7-(*p*-Tolyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3f):



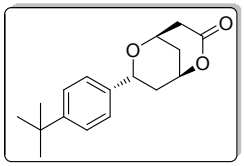
Solid. m. p. 149-151 ^{o}C purified by column chromatography (20 % ethyl acetate/hexane); $[\alpha]_D^{22}$ + 14.5 (*c* 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (d, 2H, *J*= 8.0 Hz), 7.16 (d, *J*= 8.0 Hz, 2H), 4.97 (d, *J*=2.0 Hz, 1H), 4.81 (dd, *J*=3.0, 11.8 Hz, 1H), 4.57 -4.52 (m, 1H), 2.87 (dd, *J*=5.4, 19.3 Hz, 1H), 2.26 (ddt, *J*=2.6, 3.4, 14.2 Hz, 1H), 2.16 (ddt, *J*=2.1, 4.2, 13.8 Hz, 1H), 2.01 (ddt, *J*=2.0, 4.1, 13.8 Hz, 1H), 1.87 (ddd, *J*=2.2, 11.8, 14.2 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 137.6, 129.2, 125.8, 73.1, 68.1, 66.4, 38.8, 36.4, 29.5, 21.1 ppm; IR (neat, KBr) υ 3420, 2924, 2855, 1717, 1515, 1385, 1335, 1212, 1154, 1077, 1037, 996, 799 cm^{-1}; MS (ESI): *m/z* 232 $(M+H)^+$, 250 $(M+NH_4)^+$, 255 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{14}H_{17}O_3$: 233.11722 $(M + H)^+$; found 233.11722.

(1*R*,5*R*,7*R*)-7-(4-Isopropylphenyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3g):



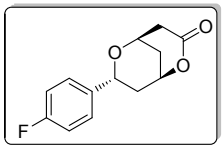
Solid. m. p. 130-132 ^{o}C purified by column chromatography (20 % ethyl acetate/hexane); $[\alpha]_D^{22}$ + 32.9 (*c* 0.46, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (d, *J* = 9.3 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 4.99 (dt, *J* = 5.9, 2.0 Hz, 1H), 4.82 (dd, *J* = 11.8, 2.9 Hz, 1H), 4.53 (s, 1H), 3.02 (d, *J* = 19.3 Hz, 1H), 2.89 (ddd, *J* = 17.3, 11.9, 6.1 Hz, 2H), 2.28 (ddd, *J* = 14.2, 5.4, 3.1 Hz, 1H), 2.17 (ddt, *J* = 13.8, 4.1, 2.0 Hz, 1H), 2.06 – 1.98 (m, 1H), 1.90 (ddd, *J* = 14.1, 11.8, 2.1 Hz, 1H), 1.23 (d, *J* = 6.9 Hz, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 148.8, 138.0, 126.6, 126.0, 73.2, 68.2, 66.4, 38.7, 36.5, 33.8, 29.6, 24.0 ppm; IR (KBr) υ 2924, 2854, 1705, 1461, 1261, 1079, 1018, 799, 710 cm^{-1}; MS (ESI): *m/z* 261 $(M+H)^+$, 268 $(M+NH_4)^+$, 283 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{16}H_{20}O_3Na$: 283.13047 $(M+H)^+$; found 283.13033.

(1*R*,5*R*,7*R*)-7-(4-(*tert*-Butyl)phenyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3h):



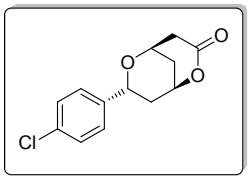
Solid. m. p. 194-196 ^{o}C purified by column chromatography (22% ethyl acetate/hexane); $[\alpha]_D^{22}$ + 65.3 (*c* 0.27, $CHCl_3$); ^{1}H- NMR (500 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 5.00 (d, *J* = 1.9 Hz, 1H), 4.82 (dd, *J* = 11.8, 2.8 Hz, 1H), 4.53 (s, 1H), 3.02 (d, *J* = 9.3 Hz, 1H), 2.87 (dd, *J* = 19.3, 5.4 Hz, 1H), 2.28 (d, *J* = 14.1 Hz, 1H), 2.21 – 2.14 (m, 1H), 2.07 – 1.98 (m, 1H), 1.91 (ddd, *J* = 14.0, 11.9, 2.0 Hz, 1H), 1.31 (d, *J* = 7.7 Hz, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 151.1, 137.5, 125.7, 125.5, 73.2, 68.1, 66.4, 38.7, 36.5, 34.5, 31.3, 29.6 ppm; IR (KBr) υ 3429, 2960, 2927, 2860, 1747, 1340, 1216, 1161, 1075, 1004, 827 cm^{-1}; MS (ESI): *m/z* 275 $(M+H)^+$, 292 $(M+NH_4)^+$, 297 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{17}H_{23}O_3$: 275.16417 $(M+H)^+$; found 275.16360.

(1*R*,5*R*,7*R*)-7-(4-Fluorophenyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3i):



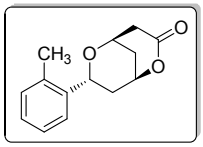
Solid. m. p. 157-159 ^{o}C purified by column chromatography (20% ethyl acetate/hexane); $[\alpha]_D^{22}$ - 10.3 (*c* 0.3, $CHCl_3$), ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (d, *J* = 8.2 Hz, 2H), 7.04 (d, *J* = 8.3 Hz, 2H), 5.01 – 4.96 (m, 1H), 4.83 (dd, *J* = 11.8, 2.9 Hz, 1H), 4.55 (s, 1H), 3.02 (d, *J* = 19.4 Hz, 1H), 2.89 (dd, *J* = 19.4, 5.3 Hz, 1H), 2.31 – 2.24 (m, 1H), 2.20 – 2.13 (m, 1H), 2.07 – 2.00 (m, 1H), 1.84 (ddd, *J* = 13.8, 11.6, 2.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 162.2(d, $^1J_{CF}$ = 246.1 Hz), 136.5 (d, $^4J_{CF}$ = 2.7 Hz), 127.4 (d, $^3J_{CF}$ = 8.2 Hz), 115.3 (d, $^2J_{CF}$ = 20.9 Hz), 72.9, 67.6, 66.4, 38.9, 36.3, 29.4 ppm; IR (KBr) υ 3447, 2924, 2853, 1730, 1511, 1339,1222, 1157, 1074, 1001, 830, 771 cm^{-1}; MS (ESI):*m/z* 237 $(M+H)^+$, 259 $(M+Na)^+$; HRMS (ESI) Calcd for $C_{13}H_{14}O_3F$: 237.09215 $(M+H)^+$; found 237.09189.

(1*R*,5*R*,7*R*)-7-(4-Chlorophenyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3j):



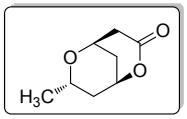
Solid. m. p. 145-147 ^{o}C purified by column chromatography (22 % ethyl acetate/hexane); $[\alpha]_D^{22}$ - 7.28 (*c* 0.88, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.25 (m, 5H), 4.98 (s, 1H), 4.82 (dd, *J* = 11.7, 2.3 Hz, 1H), 4.55 (s, 1H), 3.01 (d, *J* = 19.3 Hz, 1H), 2.88 (dd, *J* = 19.3, 5.3 Hz, 1H), 2.27 (d, *J* = 14.1 Hz, 1H), 2.16 (d, *J* = 14.2 Hz, 1H), 2.03 (d, *J* = 13.3 Hz, 2H), 1.85 – 1.77 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 139.3, 133.7, 128.7, 127.1, 72.9, 67.6, 66.5, 39.1, 36.4, 29.5 ppm; IR (neat, KBr) υ 2940, 2866, 1663, 1549, 1257, 1168, 1038, 916, 837 cm^{-1}; MS (ESI): *m/z* 253 $(M+H)^+$, 275 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{13}H_{13}O_3ClNa$: 275.04454 $(M + Na)^+$; found 275.04444.

(1*R*,5*R*,7*R*)-7-(o-Tolyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3k):



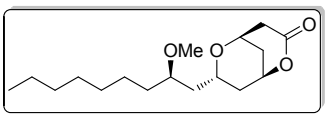
Solid. m. p. 167-169 ^{o}C purified by column chromatography (22% ethyl acetate/hexane); $[\alpha]_D^{22}$ - 11.7 (*c* 0.27, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 – 7.44 (m, 1H), 7.25 – 7.12 (m, 3H), 5.05 (dd, *J* = 11.7, 2.7 Hz, 1H), 5.02 – 4.98 (m, 1H), 4.58 – 45.2 (m, 1H), 3.08 – 2.84 (m, 2H), 2.34 (s, 3H), 2.29 – 2.14 (m, 2H), 2.07 – 1.99 (m, 1H), 1.88 (ddd, *J* = 14.0, 11.8, 2.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 138.5, 134.6, 130.5, 127.8, 126.4, 125.5, 73.2, 66.6, 65.0, 37.2, 36.4, 29.6, 18.9 ppm; IR (KBr) υ 2924, 2853, 1728, 1460, 1383, 1267, 1217, 1075, 1002, 758 cm^{-1}; MS (ESI): *m/z* 232 $(M+H)^+$, 250 $(M+NH_4)^+$; HRMS (ESI) Calcd. for $C_{14}H_{17}O_3N$: 233.11749 $(M + H)^+$; found 233.11722.

(1*S*,5*R*,7*S*)-7-Methyl-2,6-dioxabicyclo[3.3.1]nonan-3-one (3l):



Solid. m. p. 96-98 ^{o}C ^{o}C purified by column chromatography (22 % ethyl acetate/hexane); $[\alpha]_D^{22}$ - 56.2 (*c* 0.8, $CHCl_3$) ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.94 – 4.89 (m, 1H), 4.45 (dd, *J* = 5.3, 2.5 Hz, 1H), 3.93 – 3.85 (m, 1H), 2.86 (ddt, *J* = 18.1, 2.5, 0.8 Hz, 1H), 2.56 – 2.50 (m, 1H), 2.32–2.26 (m, 1H), 2.14 (ddd, *J* = 15.6, 7.8, 5.0 Hz, 1H), 1.93 – 1.85 (m, 2H), 1.19 (d, *J* = 6.2 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2, 72.5, 64.6, 64.0, 40.8, 39.4, 25.9, 21.6 ppm ; IR(KBr) υ 3444, 2925, 2855, 1725, 1504, 1457, 1381, 1252, 1223, 1118, 1066, 1023, 767 cm^{-1}; MS (ESI): *m/z* 155 $(M-H)^+$, 157 $(M+H)^+$; HRMS (ESI) Calcd. for $C_8H_{13}O_3$: 157.8592 $(M+H)^+$; found 157. 08611.

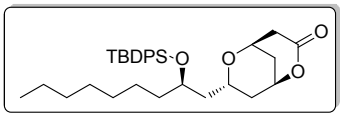
(1*S*,5*R*,7*S*)-7-((*R*)-2-Methoxynonyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3m):



Colorless liquid purified by column chromatography (18% ethyl acetate/hexane); $[\alpha]_D^{22}$ - 31.4 (*c* 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.85 (s, 1H), 4.36 (s, 1H), 3.79 (dd, *J* = 10, 5.2 Hz, 1H), 3.22 (s, 3H), 2.77 (d, *J* = 18.0 Hz, 1H), 2.44 (dd, *J* = 17.9, 2.0 Hz, 1H), 2.25(d, *J* = 13.3 Hz, 1H), 2.12 – 2.02 (m, 1H), 1.92 – 1.78 (m, 2H), 1.72 (dd, *J* = 13.8, 6.9 Hz, 1H), 1.48 – 1.35 (m,

2H), 1.27-1.16 (m, 9H), 0.82 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2, 77.3, 72.5, 64.8, 64.5, 56.0, 40.8, 39.6, 38.0, 33.2, 31.7, 29.6, 29.2, 26.0, 25.0, 22.5, 14.0 ppm; IR (KBr) υ 2926, 2855, 1735, 1461, 1383, 1275, 1216, 1074, 1039 cm^{-1}; MS (ESI): *m/z* 299 (M+H), 321(M+Na)$^+$; HRMS (ESI) Calcd. for $C_{17}H_{31}O$: 299.22169 (M+H)$^+$; found 299.22123.

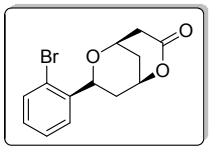
(1*S*,5*R*,7*R*)-7-((*R*)-2-((*tert*-Butyldiphenylsilyl)oxy)nonyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (3n):



Colorless liquid purified by column chromatography (10 % ethyl acetate/hexane); $[\alpha]_D^{22}$ = - 10.5 (*c* 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 – 7.62 (m, 4H), 7.45-734 (m, 6H), 4.68 (s, 1H), 4.29 (d, J = 2.4 Hz, 1H), 3.79 – 3.68 (m, 2H), 2.76 – 2.70 (m, 1H), 2.43 (dd, J = 18.0, 2.4 Hz, 1H), 2.05 (dd, J = 14.1, 4.7 Hz, 1H), 1.79 – 1.70 (m, 2H), 1.60 (dd, J = 12.8, 8.2 Hz, 2H), 1.45 (dt, J = 13.5, 10.9 Hz, 2H), 1.31 - 1.09 (m, 9H), 1.05 (s, 9H), 0.87 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2, 135.8, 135.7, 134.2, 129.5, 127.4, 72.4, 70.0, 64.7, 64.3, 42.7, 40.7, 37.8, 37.0, 31.6, 29.4, 29.1, 27.0, 25.7, 24.6, 22.5, 19.3, 14.0 ppm; IR (KBr) υ 2924, 2853, 1728, 1460, 1383, 1267, 1217, 1075, 1002, 758 cm^{-1}; MS (ESI): *m/z* 523 (M+H)$^+$, 540 (M+NH_4)$^+$, 545 (M+Na)$^+$; HRMS (ESI) Calcd. for $C_{32}H_{47}O_4NaSi$: 545.30576 (M+Na)$^+$; found 545.30535.

4. Characterization data of bicyclic lactones (4a-e):

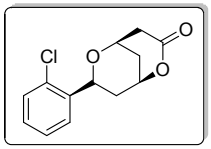
(1*R*,5*R*,7*S*)-7-(2-Bromophenyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (4a):



Solid. m. p. 151-153 ^{o}C purified by column chromatography (20 % ethyl acetate/hexane); $[\alpha]_D^{22}$ - 123.4 (*c* 0.16, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57 – 7.47 (m, 2H), 7.33 (dd, J =16, 8.9 Hz, 1H), 7.14 (td, J = 7.8, 1.6 Hz, 1H), 5.09 (dd, J = 11.1, 4.7 Hz, 1H), 5.06 – 5.00 (m, 1H), 4.68 – 4.62 (m, 1H), 3.03 (d, J = 18 Hz, 1H), 2.65 (ddd, J = 11.6, 10.2, 3.7 Hz, 2H), 2.59– 2.49 (m, 1H), 2.02 (ddd, J = 14.7, 11.2 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 140.6, 132.3, 129.1, 128.0, 127.6, 121.2, 72.3, 69.0, 65.4, 40.8, 38.9, 25.8 ppm; IR (KBr) υ 3432, 2975, 2926,

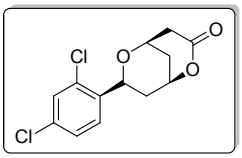
1728, 1470, 1385, 1274, 1216, 1162, 1078, 1046, 755, 718, 587 cm^{-1}; MS (ESI): *m/z* 297(M^+); HRMS (ESI) Calcd. for $C_{13}H_{14}O_3Br$: 297.01230 $(M+H)^+$; found 297.01208.

(1*R*,5*R*,7*S*)-7-(2-Chlorophenyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (4b):



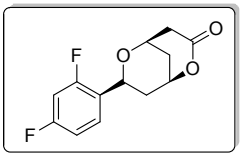
Solid. m. p. 172-174 ^oC purified by column chromatography (22 % ethyl acetate/hexane); $[\alpha]_D^{22}$-2.2 (*c* 0.168, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, *J* = 7.4 Hz, 1H), 7.26 (ddd, *J* = 15.1, 13.8, 6.9 Hz, 4H), 5.15 (dd, *J* = 11.3, 4.8 Hz, 1H), 5.04 (s, 1H), 4.65 (d, *J* = 2.7 Hz, 1H), 3.04 (d, *J* = 17.9 Hz, 1H), 2.70 – 2.50 (m, 3H), 2.12 – 1.96 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 139.1, 131.2, 129.1, 128.7, 127.4, 127.3, 72.4, 66.7, 65.4, 41.0, 38.9, 29.9 ppm; IR (KBr) υ 3448, 2924, 2854, 1733, 1463, 1383, 1275, 1077, 1050, 755 cm^{-1}; MS (ESI): *m/z* 253 $(M+H)^+$, 275 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{13}H_{14}O_3Cl$: 253.06260 $(M+H)^+$; found 253.06260.

(1*R*,5*R*,7*S*)-7-(2,4-Dichlorophenyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (4c):



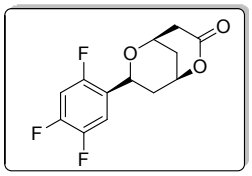
Solid. m. p. 173-175 ^oC purified by column chromatography (22 % ethyl acetate/hexane); $[\alpha]_D^{22}$ + 21.56 (*c* 0.87, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 2.1 Hz, 1H), 7.30 – 7.27 (m, 1H), 5.08 (dd, *J* = 11.2, 4.9 Hz, 1H), 5.05 – 5.01 (m, 1H), 4.65 (dd, *J* = 5.2, 2.4 Hz, 1H), 3.02 (dtd, *J* = 18.0, 2.6, 0.9 Hz, 1H), 2.68 – 2.58 (m, 2H), 2.57 – 2.50 (m, 1H), 2.08 – 1.95 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 137.8, 133.8, 131.7, 128.9, 128.3, 127.8, 72.2, 66.4, 65.5, 40.8, 38.9, 25.9 ppm; IR (KBr) υ 3429, 3097, 2971, 2930, 1727, 1588, 1472, 1382, 1274, 1213, 1161, 1079, 1045, 964, 834, 766 cm^{-1}; MS (ESI): *m/z* 286 $(M+H)^+$, 309 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{13}H_{13}O_3Cl_2$: 287.02363 $(M+H)^+$; found 287.02374.

(1*R*,5*R*,7*S*)-7-(2,4-Difluorophenyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (4d):



Solid. m. p. 172-174 ^{o}C purified by column chromatography (22% ethyl acetate/hexane); $[\alpha]_D^{22}$- 1.07 (*c* 0.48, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 – 7.42 (m, 1H), 6.90 (td, *J* = 8.2, 1.6 Hz, 1H), 6.80 – 6.74 (m, 1H), 5.07 – 5.00 (m, 2H), 4.65 – 4.61 (m, 1H), 2.99 (d, *J* = 18.1 Hz, 1H), 2.62 (dd, *J* = 18.0, 2.70 Hz, 1H), 2.54 – 2.43 (m, 2H), 2.16 (dd, *J* = 15.4, 11.1 Hz, 1H), 2.07– 2.01 (dd, *J* = 14.4, 4.7 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 168.7, 163.3 (d, $^1J_{CF}$ = 248.6 Hz), 163.2 (d, $^1J_{CF}$ = 248.8 Hz), 160.3 (d, $^1J_{CF}$ = 248.0 Hz), 160.2, ($^1J_{CF}$ = 248.0 Hz), 128.4 (d, $^3J_{CF}$ = 9.1 Hz), 128.3 (d, $^3J_{CF}$ = 8.9 Hz), 124.4 (d, $^4J_{CF}$ =3.6 Hz), 124.3, d, $^4J_{CF}$ =3.6 Hz), 111.7 (d,$^2J_{CF}$ = 21.0 Hz), 111.6 (d, $^2J_{CF}$ = 20.8 Hz), 103.7 (d, $^2J_{CF}$ = 25.4 Hz), 03.7, (d, $^2J_{CF}$ = 26.3 Hz), 72.2, 65.4, 63.2, 40.9, 39.5, 25.8 ppm; IR (KBr) υ 3451, 2925, 2854, 1733, 1618, 1503, 1383, 1274, 1218, 1139, 1076, 1048, 964, 849, 771 cm^{-1}; MS (ESI): *m/z* 255 $(M+H)^+$, 277 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{13}H_{12}O_3F_2$: 255.08270 $(M + H)^+$; found 255.08273.

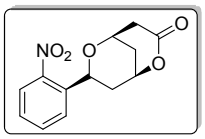
(1*R*,5*R*,7*S*)-7-(2,4,5-Trifluorophenyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (4e):



Solid. m. p. 160-162 ^{o}C purified by column chromatography (22% ethyl acetate/hexane); $[\alpha]_D^{22}$ - 98.3 (*c* 1.68, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (ddd, *J* = 10.6, 8.9, 6.7 Hz, 1H), 6.89 (td, *J* = 9.8, 6.4 Hz, 1H), 5.05 – 4.97 (m, 2H), 4.64 (dd, *J* = 5.0, 2.2 Hz, 1H), 3.00 (dt, *J* = 18.1, 2.1 Hz, 1H), 2.63 (dd, *J* = 18.1, 2.7 Hz, 1H), 2.51 (ddd, *J* = 14.5, 6.6, 1.2 Hz, 2H), 2.07 (ddd, *J* = 14.7, 12.9, 7.8 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 154.1 (d, $^1J_{CF}$ = 244.6 Hz), 154.0 (d, $^1J_{CF}$ = 244.6, Hz), 153.3 (d, $^1J_{CF}$ = 244.3 Hz), 153.1, ($^1J_{CF}$ = 244.3 Hz), 149.2 (d, $^1J_{CF}$ = 250.6 Hz), 149.1 (d, $^1J_{CF}$ = 250.6 Hz), 147.0 (d, $^1J_{CF}$ = 245.2 Hz), 146.9 (d, $^1J_{CF}$ = 245.2 Hz), 146.3 (d,$^1J_{CF}$ = 246.0 Hz), 146.2 (d, $^1J_{CF}$ = 244.3 Hz), 125.3 (d, $^4J_{CF}$ = 3.6 Hz), 125.25, (d, $^4J_{CF}$ = 4.5 Hz), 125.2 (d, $^4J_{CF}$ = 4.5 Hz), 125.1 (d, $^4J_{CF}$ = 4.5 Hz), 115.3 (d, $^3J_{CF}$ = 5.5 Hz), 115.1, (d, $^3J_{CF}$ = 5.5 Hz), 105.2 (d, $^2J_{CF}$ = 27.2 Hz), 105.1, (d, $^2J_{CF}$ = 27.2 Hz), 72.0, 65.4, 63.1, 40.7, 39.4, 25.7 ppm; IR (KBr) υ 3434, 2927, 1728, 1633, 1514, 1217, 1080, 893 cm^{-1}; MS (ESI): *m/z* 273

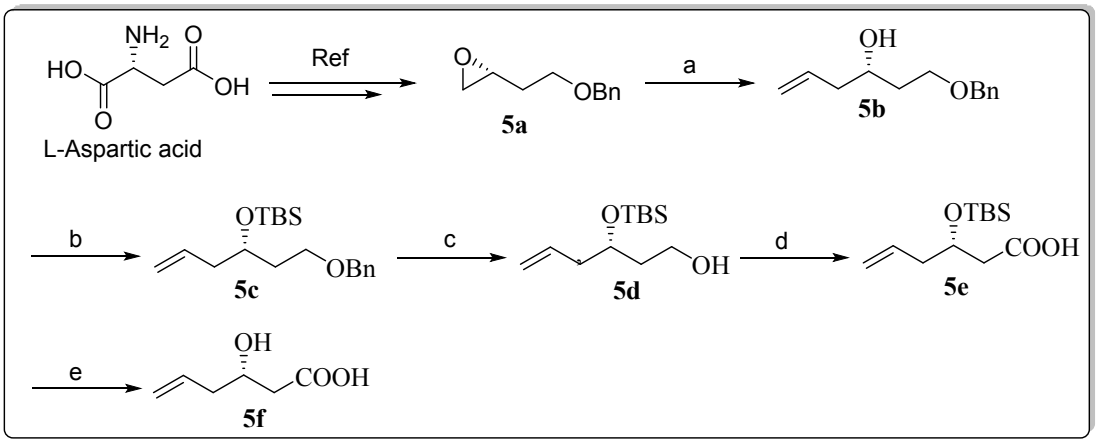
$(M+H)^+$, 295 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{13}H_{12}O_3F_3$: 273.07331 $(M+H)^+$; found 273.07364.

(1*R*,5*R*,7*S*)-7-(2-Nitrophenyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (4f):



Solid. m. p. 159-161 °C purified by column chromatography (30% ethyl acetate/hexane); $[\alpha]_D^{22}$ + 44.6 (*c* 1.2, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.85 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.73 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.62 – 7.57 (m, 1H), 7.40 – 7.34 (m, 1H), 5.25 (dt, *J* = 10.4, 5.2 Hz, 1H), 5.02 – 4.96 (m, 1H), 4.55 (dd, *J* = 5.2, 2.3 Hz, 1H), 2.98 – 2.91 (m, 1H), 2.71 (ddd, *J* = 15.5, 7.9, 4.9 Hz, 1H), 2.56 (dd, *J* = 18.0, 2.6 Hz, 1H), 2.49 – 2.43 (m, 1H), 2.13 – 2.05 (m, 1H), 1.98 (dd, *J* = 14.5, 4.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 168.7, 147.4, 137.0, 134.0, 72.3, 65.9, 65.6, 40.8, 39.8, 26.0 ppm; IR (neat, KBr) υ 3437, 3079, 2923, 1737, 1604, 1519, 1351, 1219, 1150, 1074, 1037, 848, 751 cm^{-1}; MS (ESI): *m/z* 264 $(M+H)^+$, 281 $(M+NH_4)^+$, 286 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{13}H_{14}O_5N$: 264.08665$(M + H)^+$; found 264.08612.

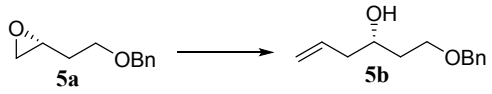
5. Preparation of starting materials (5a- *ent*-2)



Scheme 2. Preparation of **5 (a-*ent*-2)**

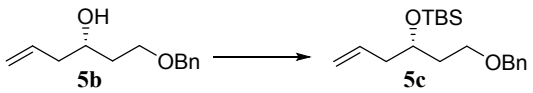
Reagents & conditions: (a) Vinyl bromide, Mg, $(CH_2)_2Br_2$, CuCN, 90%; (b) TBSCl, imidazole, CH_2Cl_2, DMAP, 0 ^oC to rt, 3h 92 %; (c) Li, naphthalene, - 20 ^oC THF, 1h, 80% (d) (i) DMP, CH_2Cl_2, 2h, 80%; (ii) $NaClO_2$, NaH_2PO_4, t-BuOH:H_2O (3:1), 2-methyl-2-butene, 0 ^oC to rt, 85%; (e) TBAF, THF, 0 ^oC to rt, 3h, 84%.

(*S*)-1-(Benzyloxy)hex-5-en-3-ol (5b):



To a suspension of magnesium (1.14 g, 47.19 mmol) in dry THF (35 mL) at room temperature were sequentially added 1,2-dibromoethane (2 drops) and a freshly prepared vinyl bromide (2.24 mL, 31.46 mmol) in a drop wise manner. After generation of Grignard reagent, CuCN (70 mg, 5 mol%) was added at -20 ^oC and stirred for 0.5 h. The color of the reaction mixture turned to dark brown. Then the mixture was cooled to –78 ^oC and a solution of epoxide **5a** (2.8 g, 15.73 mmol) in THF (10 mL) was added and the mixture was stirred at –40 ^oC for 4 h. After completion, the reaction mixture was quenched with sat. ammonium chloride solution (100 mL) and diluted with ethyl acetate (200 mL). The combined organic layers were washed with brine solution (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography (SiO_2,15% EtOAc/hexane) afforded the **5b** (2.91 g, 90 %) as a colorless liquid. $[\alpha]_D^{20}$ - 2.0 (*c* 1.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.38-7.26 (m, 5H), 5.88 -5.78 (m, 1H), 5.14-5.07 (m, 2H), 4.52 (s, 2H), 3.91-3.84 (m, 1H), 3.75 -3.62 (m, 2H), 2.90 (s, 1H), 2.27-2.23 (m, 2H), 1.79 - 1.71 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.7, 134.6, 128.1, 127.3, 117.1, 73.0, 69.5, 68.2, 41.6, 35.6 ppm; IR (KBr) υ 3440, 3069, 3030, 2919, 2862, 1640, 1495, 1364, 1206, 1096, 1026, 914, 738 cm^{-1}; MS (ESI): *m/z* 207 $[M+H]^+$, 229 $[M+Na]^+$; HRMS (ESI) Calcd. for $C_{13}H_{19}O_2$: 207.13796 $(M+H)^+$; found 207.13738.

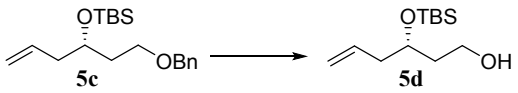
(*S*)-((1-(Benzyloxy)hex-5-en-3-yl)oxy)(tert-butyl)dimethylsilane (5c):



To a 0 ºC cooled solution of alcohol **5b** (2.8 g, 8.75 mmol) in CH_2Cl_2 (35 mL) were added imidazole (1.19 mL, 17.5 mmol), TBDMSCl (2.058 g, 13.12 mmol) and DMAP (73 mg, 0.59 mmol). The mixture was allowed to stir for 3h at room temperature. After completion of the reaction as monitored by TLC, the mixture was quenched with sat. NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2x40 mL). The combined organic extracts were washed with brine solution (30 mL), dried over Na_2SO_4 and concentrated in *vacuo*. The crude product was purified by silica gel column chromatography (SiO_2, 5% EtOAc/hexane) to afford the TBS ether **5e** (4.0 g, 92%) as a colorless liquid.

$[\alpha]_D^{20}$ + 10.2 (*c* 1, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.35 – 7.23 (m, 5H), 5.86 – 5.76 (m, 1H), 5.05 –5.0 (m, 2H), 4.52 – 4.42 (m, 2H), 3.90 (ddd, *J* = 10.7, 7.7, 5.2 Hz, 1H), 3.55 – 3.50 (m, 2H), 2.28 – 2.17 (m, 2H), 1.84 – 1.64 (m, 2H), 0.88 (s, 9H), 0.04 (d, *J* = 6.5, Hz, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 138.5, 134.8, 128.2, 127.5, 127.4, 116.9, 72.8, 68.8, 66.8, 42.2, 36.7, 25.8, 18.0, - 4.4, - 4.8 ppm; IR (KBr) υ 3426, 2921, 2851, 1735, 1460, 1217, 1017 cm^{-1}; MS (ESI): *m/z* 343 $[M+Na]^+$; HRMS (ESI) Calcd. for $C_{19}H_{32}O_2SiNa$: 343.20678 $(M+Na)^+$; found 343.20698**.**

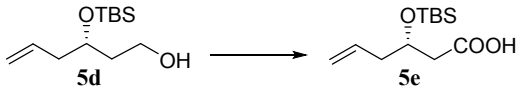
(*S*)-3-((*tert*-Butyldimethylsilyl)oxy)hex-5-en-1-ol (5d):



To a stirred solution of naphthalene (10.57 g, 5 eq. 82.60 mmol) in dry THF (100 mL) was added Lithium metal (0.35 g, 3 eq. 49.56 mmol) at room temperature under N_2 atmosphere. The mixture was stirred for 2h at same the temperature. The color of the reaction mixture turns to dark green due to the formation of lithium naphthalenide. After being stirred for 2 h at rt, the reaction mixture cooled to -20 ºC and then a solution of benzyl ether **5c** (3.8 g, 16.52 mmol) in dry THF (25 mL) was added. After 20 min of stirring at -20 ºC, the complete consumption of staring material (as monitored by TLC) was observed. Then the reaction mixture was quenched with saturated NH_4Cl solution (35 mL) and extracted with EtOAc (2x100 mL). Evaporation of the solvent followed by purification on silica gel column chromatography (SiO_2, 30 % EtOAc/hexane) afforded the pure alcohol **5d** (2.18 g, 80 %) as a colorless liquid.

$[\alpha]_D^{20}$ - 56.3 (*c* 2.8, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 5.75 (ddt, *J* = 17.7, 10.7, 7.2 Hz, 1H), 5.10– 5.02 (m, 2H), 4.00 – 3.94 (m, 1H), 3.86 – 3.79 (m, 1H), 3.75 – 3.68 (m, 1H), 2.34 (s, 1H), 2.33 – 2.28 (m, 2H), 1.85 – 1.77 (m, 1H), 1.72 – 1.64 (m, 1H), 0.90 (s, 9H), 0.10 (d, *J* = 6.5 Hz, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 134.5, 117.1, 70.9, 59.8, 41.5, 37.9, 25.8, 17.9, -4.5, - 4.9 ppm; IR (KBr) υ 3381, 3077, 2954, 2931, 2889, 2857, 1641, 1486, 1363, 1254, 1070, 912, 836, 775 cm^{-1}; MS (ESI): 231 $[M+H]^+$; HRMS (ESI) Calcd. for $C_{12}H_{27}O_2Si$: 231.18742 $(M+H)^+$; found 231.18758.

(*S*)-3-((tert-Butyldimethylsilyl)oxy)hex-5-enoic acid (5e):

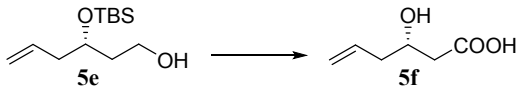


To a stirred solution of alcohol **5d** (2.0 g, 8.69 mmol) in anhydrous CH_2Cl_2 (10 mL) was added Dess-Martin periodinane (3.70 g, 8.69 mmol) at 0 °C under N_2 atmosphere and stirred for 2 h at room temperature. Then the reaction mixture was quenched with sat. $NaHCO_3$ (15 mL), and sat. $Na_2S_2O_3$ (15 mL) solutions and extracted with EtOAc (2 x 250 mL). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4 and concentrated under *vacuo* to give the crude aldehyde (2.1 g). The obtained aldehyde was used in the next step without further purification.

To a stirred solution of aldehyde (2.10 g, 9.21 mmol) in *tert*-butyl alcohol (25 mL), were added 2-methyl-2-butene (11.0 mL, 0.77 g, 11.05 mmol, 1 M solution in THF) and a clear solution of NaH_2PO_4 (2.76 g, 23.02 mmol) and a solution of sodium chlorite (1.24 g, 13.81 mmol) in water (15 mL) at 0 °C. It was then allowed to stir for another 3.5 h at room temperature. The reaction mixture was diluted with water (25 mL). The organic solvent was removed under reduced pressure and the aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layers were washed with brine solution (2 x 50 mL), and dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (SiO_2, 25%, EtOAc/hexane) to afford pure acid **5e** (1.81 g, 85 % over two step) as a colorless liquid.

$[\alpha]_D^{20}$ + 44.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.78 (ddt, *J* = 17.6, 10.4, 7.2 Hz, 1H), 5.10 – 5.06 (m, 2H), 4.22 – 4.14 (m, 1H), 2.54 – 2.41 (m, 2H), 2.32 – 2.22 (m, 2H), 0.86 (s, 9H), 0.090 (s, 3H), 0.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.9, 133.8, 118.0, 68.8, 42.0, 25.7, 18.0, -4.5, - 5.0 ppm; ^{13}C NMR (125 MHz, $CDCl_3$) : *δ* 177.9, 133.8, 118.0, 68.8, 42.0, 25.7, 18.0, -4.5 ppm; IR (KBr) υ 3078, 2955, 2930, 2857, 1713, 1434, 1254, 1091, 918, 834, 776 cm^{-1}; MS (ESI): *m/z* 245 $[M+H]^+$; HRMS (ESI) Calcd. for $C_{12}H_{25}O_3Si$: 245.15675 $(M+H)^+$; found 245.15726.

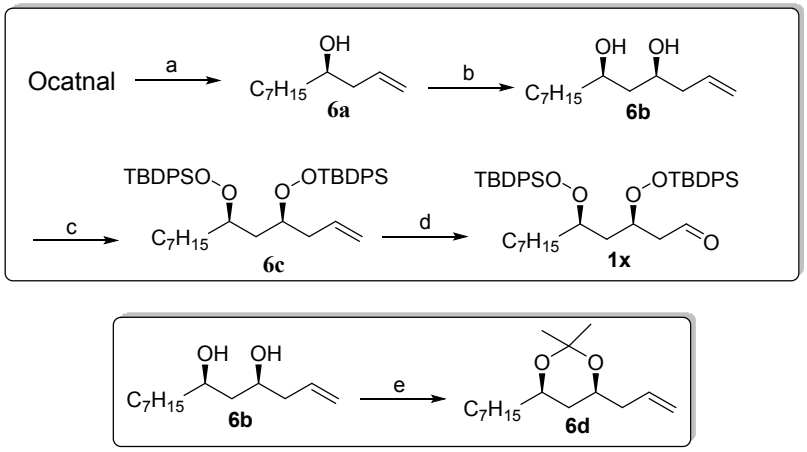
(*S*)-3-((*tert*-Butyldimethylsilyl)oxy)hex-5-enoic acid (*ent*-2):



To a solution of silyl ether **5e** (1.5 g, 6.14 mmol) in dry THF (5 mL), TBAF (1M in THF, 9 mL, 9.2 mmol) was added at 0 °C. After 15 min, the reaction mixture was brought to room temperature and stirred for another 4 h. After completion (as monitored by TLC), the reaction mixture was cooled and quenched with sat. ammonium chloride solution and extracted with EtOAc (3x20 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel chromatography utilizing 8% MeOH/$CHCl_3$ as a mobile phase to give hydroxy acid **5f** (0.671 g, 84%) as a colorless oil.

$[\alpha]_D^{20}$ -112.2 (*c* 0.42, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.81 (ddd, *J* = 14.9, 11.5, 6.2 Hz, 1H), 5.15 (dd, *J* = 9.8, 6.6 Hz, 2H), 4.16 – 4.09 (m, 1H), 2.58 – 2.41 (m, 2H), 2.35 – 2.25 (m, 2H) ppm; ^{13}CNMR (125 MHz, $CDCl_3$): δ 176.7, 133.6, 118.4, 67.4, 40.8, 40.5, 18.5 ppm; IR (KBr) υ 3404, 3077, 2926, 2855, 1718, 1644, 1404, 1176, 1054, 995, 920 cm^{-1}; MS (ESI): *m/z* $[M+H]^+$; 153 $[M+Na]^+$, HRMS (ESI) Calcd. for $C_7H_{14}O_2Na$: 153.08860 $(M+Na)^+$; found, 153.08826.

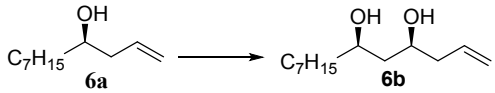
6. Experimental procedure for 6a-d,7,8



Scheme 2. Synthetic procedure for **6 (a-d)**:

Reagents and conditions: **(**a) (*S*)–BINOL, 4 ÅMS, $Ti(O^iPr)_4$, allyltributyltin, CH_2Cl_2, −78 0 °C to −20 °C, 36 h, 75%; (b) (i) O_3, CH_2Cl_2, TPP, -78 °C to rt, 0.5h ; (ii) $AllylSiMe_3$, $SnCl_4$, CH_2Cl_2, -78 °C, 75%; (c) TBDPSCl, imidazole, CH_2Cl_2, DMAP, 0 °C to rt, 3h, 82%; (d) O_3, CH_2Cl_2, TPP, -78 °C to rt, 30 min; (e) DMP, CSA (cat), CH_2Cl_2, 0 °C-rt, 2h, 85%.

(4*S*,6*R*)-Tridec-1-ene-4,6-diol (6b):



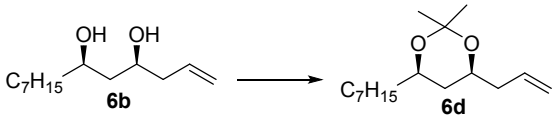
To a solution of alcohol **6a** (0.50 g, 2.94 mmol) in CH_2Cl_2 (10 mL) at -78 °C, ozone was bubbled till the solution turned into blue. Then the reaction mixture was quenched with DMS (1.14 ml, 14.70) at room temperature. After 4h, the solvent was removed and the residue was diluted with 50% EtOAc in hexane (50 mL) and filtered through a Celite. The filtrate was concentrated and the crude aldehyde was used in the next step without purification.

A brown colored solution of $SnCl_4$ (0.42 ml, 3.52 mmol) and allyltrimethylsilane (0.56 ml, 3.52 mml) in dry CH_2Cl_2 under argon atmosphere at room temperature was added to a solution of β-hydroxy aldehyde in dry CH_2Cl_2 at -78 °C. The mixture was allowed to stir at this temperature for 1h. The reaction was quenched with MeOH (10 mL), sat. NH_4Cl solution (20 mL and extracted with CH_2Cl_2 (3 x 50 mL) . The combined organic layers were washed with brine solution (2 x 50 mL), dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The

residue was purified by silica gel chromatography utilizing 12% EtOAc/hexane as a mobile phase to give the 1,3-diol **6b** (0.377 mg, 75%) as a colorless oil.

$[\alpha]_D^{22}$ + 2.7 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 5.89 – 5.74 (m, 1H), 5.19 – 5.05 (m, 2H), 4.08 – 3.87 (m, 2H), 2.68 (s, 2H), 2.37 – 2.17 (m, 2H), 1.72 – 1.15 (m, 14H), δ 0.88 (t, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.7, 117.6, 68.9, 68.0, 41.9, 37.3, 31.7, 29.5, 29.2, 25.7, 22.5, 14.0 ppm; IR (KBr) υ 3361, 3077, 2927, 2855, 1710, 1641, 1462, 1130, 1072, 995, 914, 830, 722 cm^{-1}; MS (ESI): *m/z* 237 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{13}H_{26}O_2Na$: 237.18250 $(M+Na)^+$; found 237.18247.

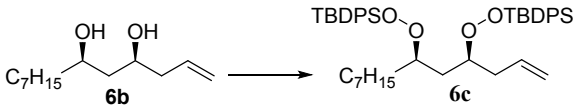
(4*S*,6*R*)-4-Allyl-6-heptyl-2,2-dimethyl-1,3-dioxane (6d):



To an ice cooled solution of 1,3-diol **6b** (0.05 g, 0.23 mmol) in dry CH_2Cl_2 (5 mL) was added 2,2-DMP (0.75 mL, 5.8 mmol) and CSA (cat.) at 0 ^oC under N_2 atmosphere and stirred for 2h at room temperature. After completion of the reaction, the mixture was quenched with sat. $NaHCO_3$ solution at room temperature. The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined CH_2Cl_2 layers were dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The residue was purified by silica gel chromatography using 2.5% EtOAc/petroleum ether to yield the acetonide **6d** (0.050 g, 85 %) as an oily liquid.

$[\alpha]_D^{22}$ + 14.6 (*c* 1.5 $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 5.91 – 5.73 (m, 1H), 5.16 – 5.02 (m, 2H), 3.94 – 3.70 (m, 2H), 2.38 – 2.10 (m, 2H), 1.70 – 1.17 (m, 20H), 0.89 (t, *J* = 6.7 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.2, 116.9, 98.3, 68.9, 68.7, 40.9, 36.4, 31.8, 30.2, 29.5, 29.2, 24.9, 22.6, 19.8, 14.1 ppm; IR (KBr) υ 3417, 2924, 2853, 1715, 1607, 1511, 1461,1381, 1257, 1217, 915, 837, 760 cm^{-1}; MS (ESI): *m/z* 277 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{16}H_{30}O_2Na$: 277.21434 $(M+H)^+$; found 277.21433.

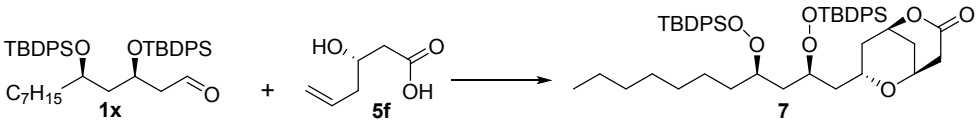
(6*S*,8*R*)-6-Allyl-8-heptyl-2,2,12,12-tetramethyl-3,3,11,11-tetraphenyl-4,5,9,10-tetraoxa-3,11-disilatridecane (6c):



To an ice-bath cooled solution of 1,3-diol **6b** (0.250 g, 1.16 mmol) in dry CH_2Cl_2 (5 ml) were added sequentially at 0 ^oC imidazole (0.317 g, 4.67 mmol), TBDPSCl (0.75 ml, 2.92 mmol) and a catalytic amount of DMAP (100 mg) under N_2 atmosphere. After being stirred for 4 h at room temperature, the reaction mixture was quenched with saturated NH_4Cl solution (20 mL) and extracted with CH_2Cl_2 (2 x 20 mL). The organic extracts were dried over Na_2SO_4 and concentrated in *vacuo*. Purification by column chromatography gave the pure disilyl ether **6c** (0.6608 g, 82 % yield) as a clear oil. R_f = 0.7 (SiO_2, 2% EtOAc in hexane).

$[\alpha]_D^{22}$ = -16.6 (*c* = 6.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 – 7.54 (m, 10H), 7.43 – 7.23 (m, 14H), 5.68 – 5.58 (m, 1H), 4.93 – 4.64 (m, 2H), 3.91 (dt, *J* = 12.5, 6.4 Hz, 1H), 3.80 (dt, *J* = 12.5, 6.3 Hz, 1H), 2.07 – 2.00 (m, 1H), 1.92 – 1.84 (m, 1H), 1.76 – 1.59 (m, 2H), 1.28 – 1.04 (m, 6H), 1.03 – 0.90 (m, 24H), 0.85 (t, *J* = 5.6 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.9, 134.7, 134.4, 134.2, 129.5, 129.4, 129.3, 127.4, 127.3, 117.0, 70.6, 70.2, 42.8, 40.8, 36.7, 31.8, 29.4, 29.1, 27.1, 24.3, 22.6, 19.3, 14.1 ppm; IR (KBr) υ 3361, 3077, 2927, 2855, 1710, 1641, 1462, 1130, 1072, 995, 914, 830, 722 cm^{-1}; MS (ESI): *m/z* 714 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{45}H_{62}O_2NaSi_2$: 714.42588 $(M+Na)^+$; found 714.42172.

(1*R*,5*S*,7*S*)-7-((2*S*,4*R*)-2,4-Bis((tert-butyldiphenylsilyl)peroxy)undecyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (7):



To a solution of olefin (0.175 g, 0.2530 mmol) in acetone/water mixture (4:1) (10 mL) were added NMO (0.1483 g, 1.26 mmol) and OsO_4 (0.04 M, 0.6 mL, 0.0050 mmol) sequentially at 0 ^oC. After being stirred for 24 h at the room temperature, the reaction was quenched with 10 mL of sat.$NaHSO_3$ solution at 0 ^oC. The acetone was removed under reduced pressure and the aqueous mixture was extracted with ethyl acetate (3 x 40 mL). The combined organic layers were washed with brine solution (30 mL), dried over anhydrous Na_2SO_4, concentrated under reduced pressure. The resuting diol was obtained as a, mixture of diastereomers, which were

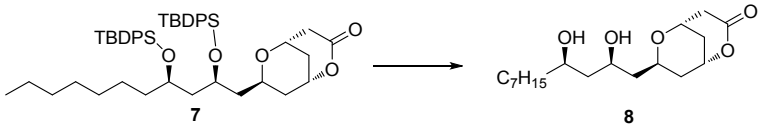
purified by silica gel column chromatography (40% ethyl acetate in hexane) to give the racemic diol **(** (0.1652 g) .

A solution of the above diol (0.1652g, 0.2281 mmol) in THF/water (4:1, 8 mL) was treated with $NaIO_4$ (0.14 g, 1.14 mmol) at 0 ºC. After completion of the reaction (as monitored by TLC), the acetone was removed under reduced pressure and the crude mixture was diluted with water and extracted with ethyl acetate (3 x 10 mL) and washed with $NaHCO_3$ (5 mL) followed water (10 mL) and brine solution (10 mL). Removal of the solvent followed by purification by column chromatograph (SiO_2, 10% EtOAc in petroleum ether) gave the aldehyde (0.1389 g) as a colorless oil.

To a stirred solution of homoallylic alcohol (***ent*-2**) (0.025 g, 0.1923 mmol), aldehyde (**1x**) (0.1330, 0.1923 mmol) and 4 Å molecular sieves (0.5 g) in dry CH_2Cl_2 (5 mL) at - 20 ^oC was added a solution of TMSOTf (0.034 mL, 0.1923 mmol) in dry CH_2Cl_2 (1 mL) under N_2 atmosphere. The mixture was allowed to stir at 40 °C for 2h. After complete consumption of homoallylic alcohol, the reaction was quenched with 2 mL of sat. solution of $NaHCO_3$. The mixture was then diluted with 10 mL water at room temperature and stirred for 10 min. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic fractions were washed with brine solution (3 x 20 mL) and dried over anhydrous Na_2SO_4. Removal of the solvent followed by purification on silica gel column chromatograph (10% EtOAc in petroleum ether eluent) to give the bicyclic lactone (**7**) (0.077 g, 50%) as a colorless oil.

$[\alpha]_D^{20}$ = + 6.64 (*c* 0.25, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 – 7.59 (m, 8H), 7.43 – 7.31 (m, 12H) 4.78 – 4.71 (m, 1H), 4.34 – 4.27 (m, 1H), 3.84 (d, *J* = 2.8 Hz, 1H), 3.72 – 3.59 (m, 2H), 2.62 (d, *J* = 18.0 Hz, 1H), 2.38 – 2.30 (m, 2H), 1.85 – 1.78 (m, 2H), 1.67 – 1.52 (m, 4H), 1.37 – 1.20 (m, 12H), 1.04 – 0.94 (m, 18H), 0.85 (t, *J* = 6.7 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 169.2, 136.0, 135.9, 134.8, 134.5, 1343.9, 129.5, 129.4, 129.3, 129.2, 127.5, 127.4, 127.2, 72.6, 70.7, 67.9, 64.1, 63.9, 44.8, 43.2, 40.8, 38.5, 37.0, 31.7, 29.6, 29.3, 29.1, 27.1, 27.0, 25.8, 24.4, 22.6, 19.3, 14.1 ppm; IR (KBr) υ 3447, 3071, 2929, 2856, 1743, 1639, 1466, 1428, 1383, 1260, 1108, 1071, 820, 737, 703 cm^{-1}; MS (ESI): *m/z* 827$(M+Na)^+$; HRMS (ESI) Calcd. for $C_{50}H_{68}O_5NaSi_2$: 827.44975 $(M+Na)^+$; found 827.44869.

(1*R*,5*S*,7*R*)-7-((2*R*,4*R*)-2,4-Dihydroxyundecyl)-2,6-dioxabicyclo[3.3.1]nonan-3-one (8):

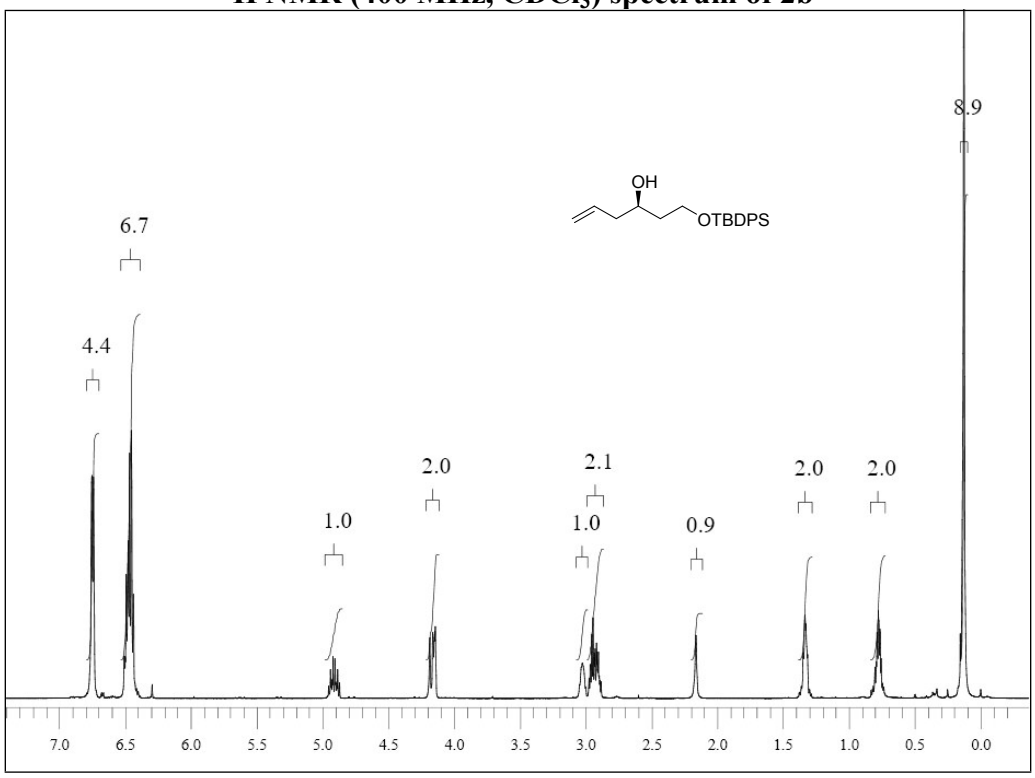


To a stirred solution of **7** (0.07 g, 0.08 mmol) in dry THF (3 mL) in a polypropylene vial was added HF/py (48% aqueous solution, 0.018 mL, 0.44 mmol, 5 equiv) dropwise at 0 °C. The mixture was stirred for 12h at room temperature. After completion of the reaction (as monitored by TLC), it was cautiously poured into sat. $NaHCO_3$ solution (5 mL) and stirred for 30 min. The layers were separated and the aqueous layer was extracted with $CHCl_3$ (3 × 15). The combined organic layers were washed with brine solution (5 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (SiO_2, 80% EtOAc in petroleum ether) to give the polyracitide A (**8**, 0.017 g, 60%) as a white solid.

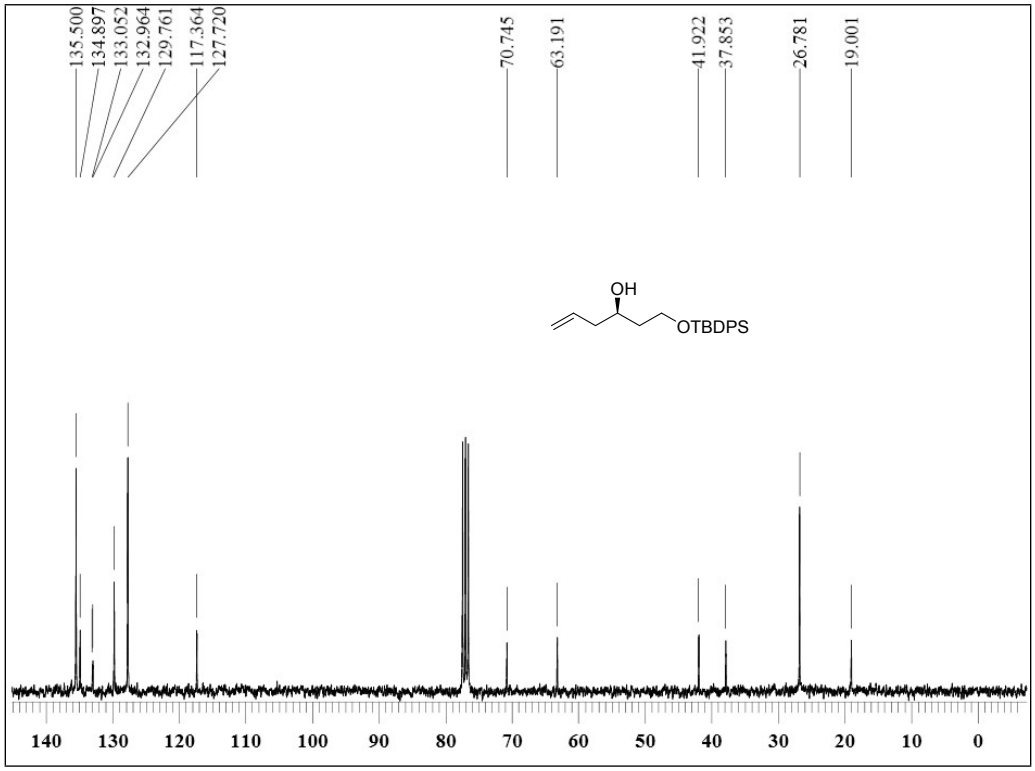
$[\alpha]_D^{22}$ = + 3.8 (*c* = 0.2 MeOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.92 – 4.86 (m, 1H), 4.45 – 4.39 (m, 1H), 4.07 (dddd, *J* = 14.7, 12.5, 8.1, 7.8 Hz, 2H), 3.88 – 3.80 (m, 1H), 2.84 – 2.79 (m, 2H), 2.04 (dd, *J* = 7.7, 5.4 Hz, 2H), 1.75 – 1.50 (m, 4H), 1.36 – 1.18 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 169.2, 72.7, 72.5, 72.1, 66.9, 66.8, 43.3, 42.8, 37.8, 37.2, 36.4, 31.8, 29.7, 29.6, 29.3, 25.4, 22.6, 14.1 ppm; IR (KBr) υ 3422, 2922, 2853, 1733, 1631, 1380, 1012, 775 cm^{-1}; MS (ESI): *m/z* 351 $(M+Na)^+$; HRMS (ESI) Calcd. for $C_{18}H_{32}O_5Na$: 351.21680 $(M+H)^+$; found 351.21668.

7. Copies of NMR spectra of all compounds

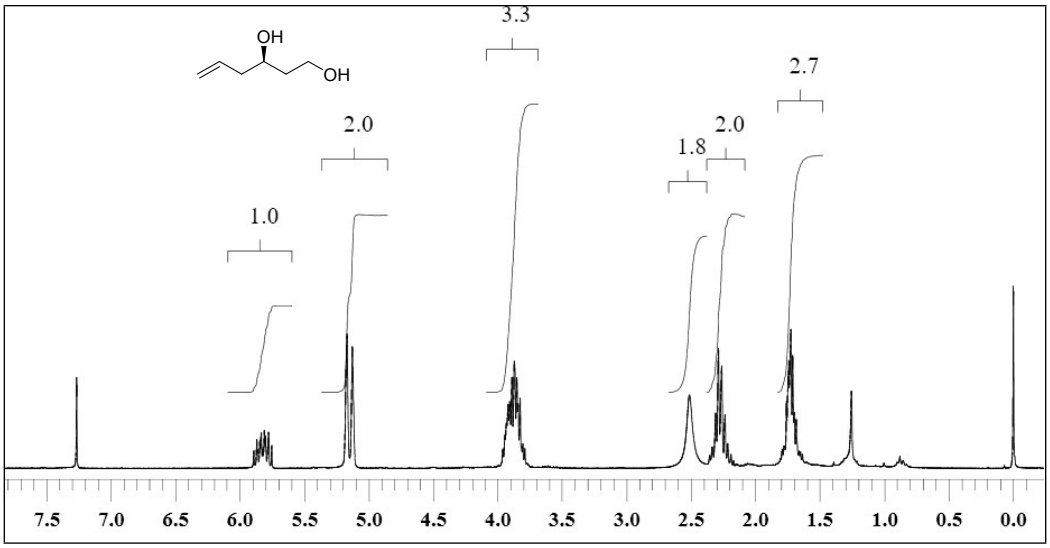
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2b



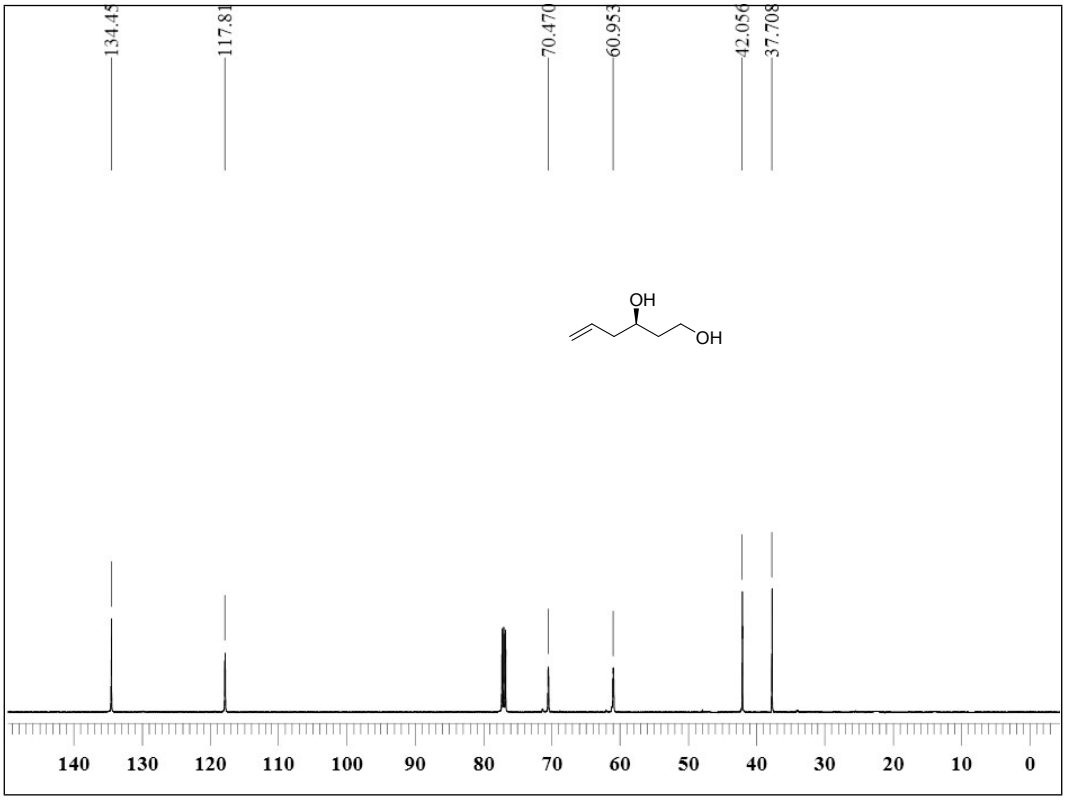
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 2b



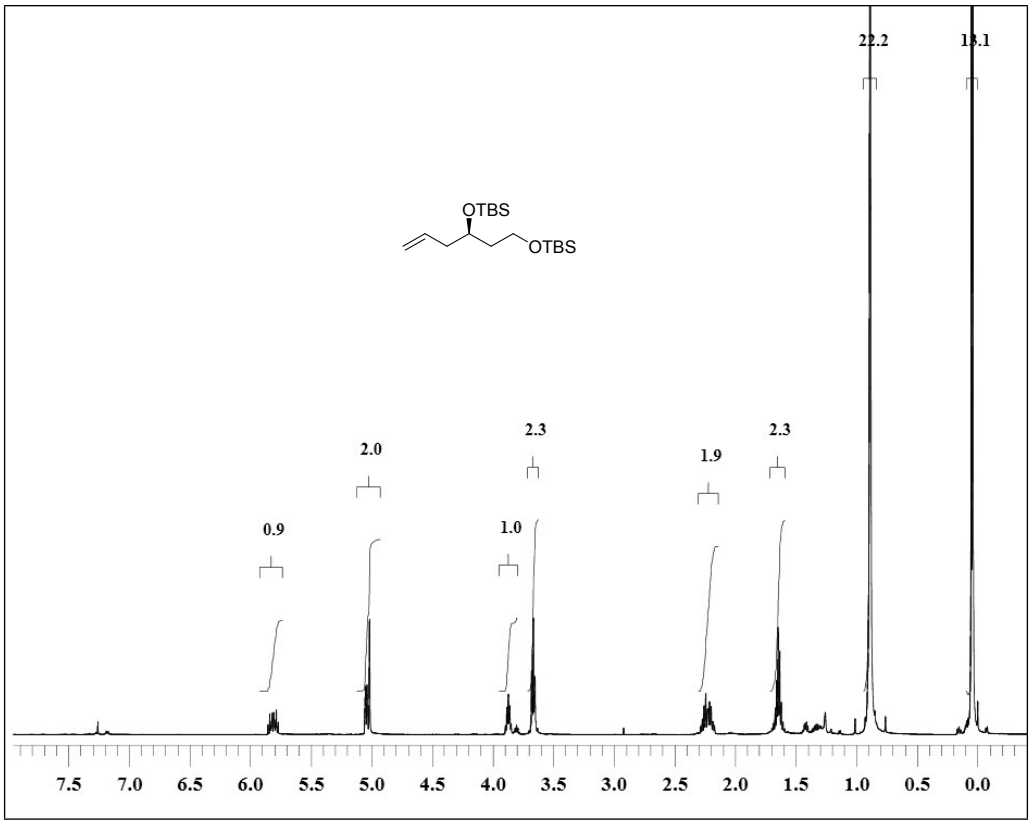
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 2c



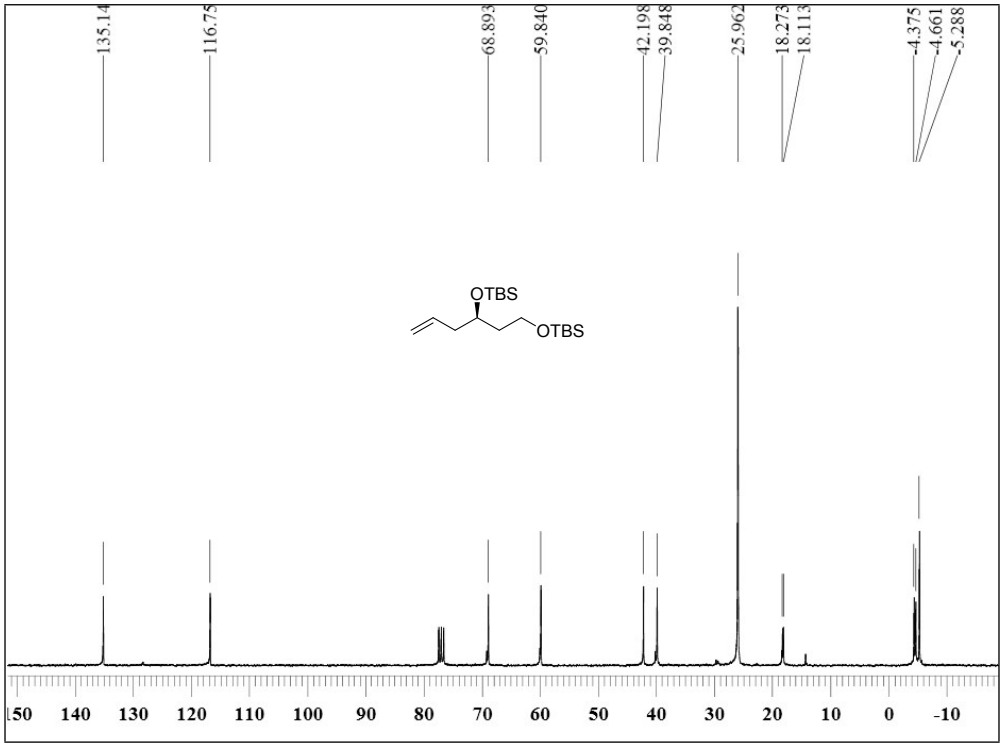
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 2c



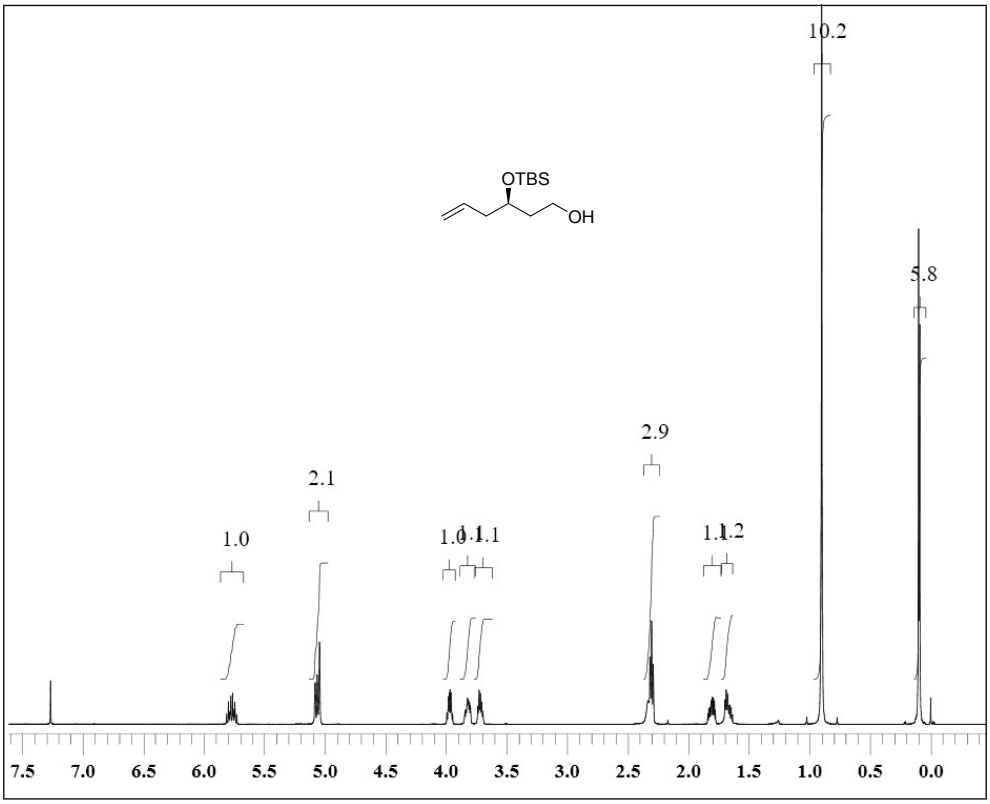
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 2d



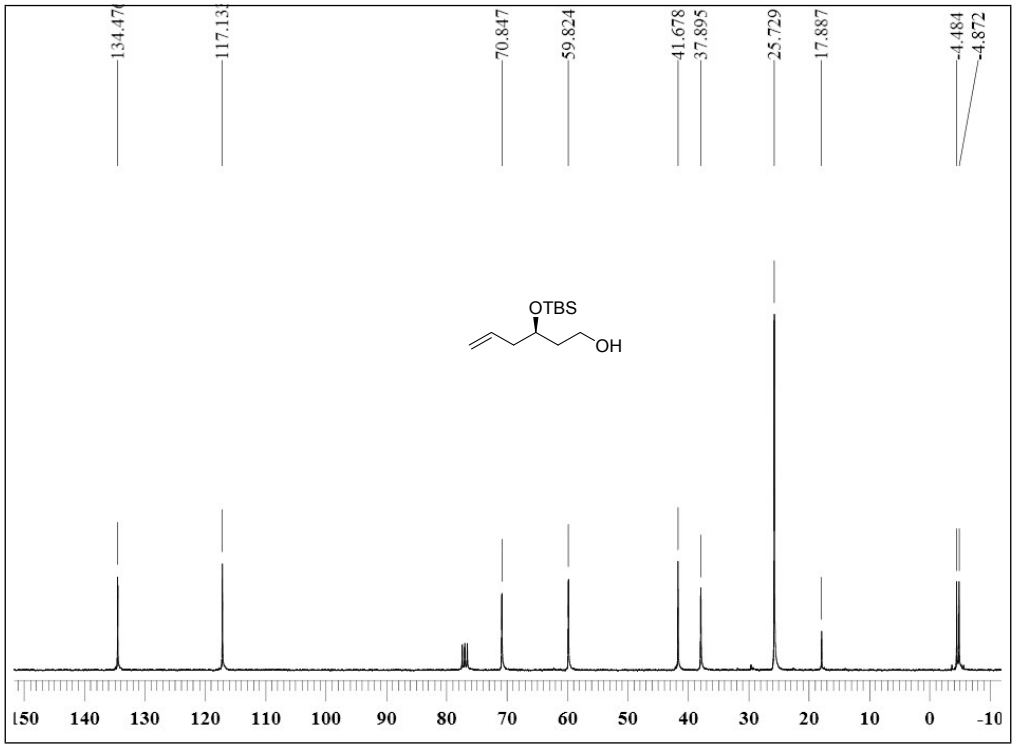
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 2d



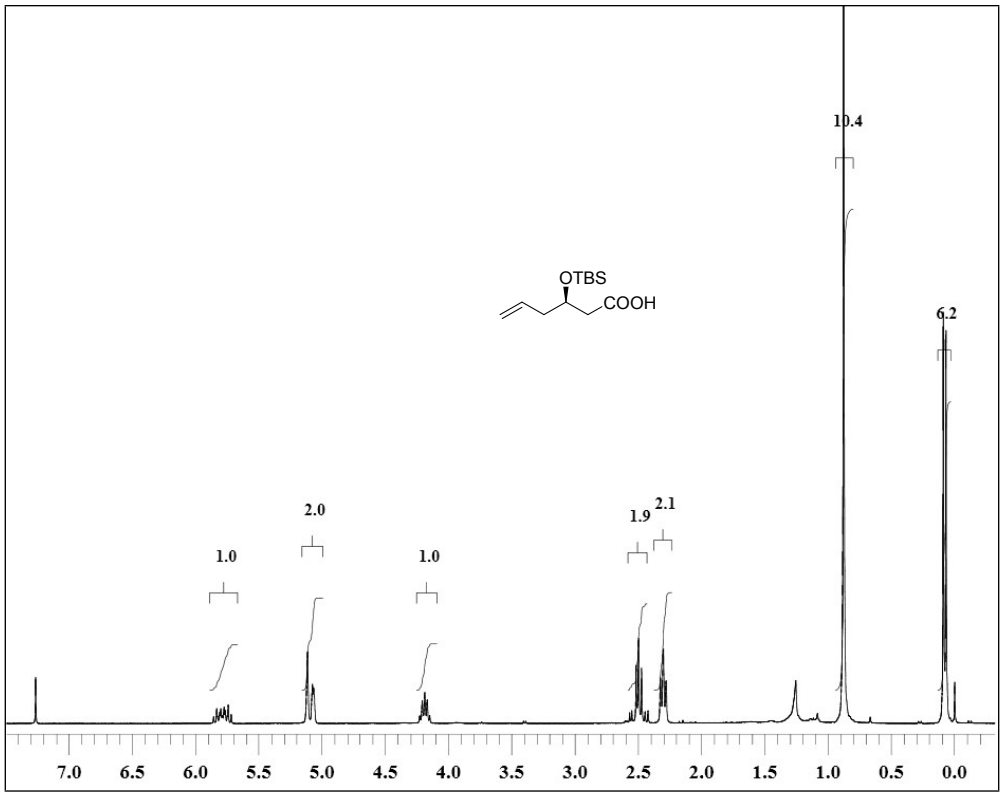
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 2e



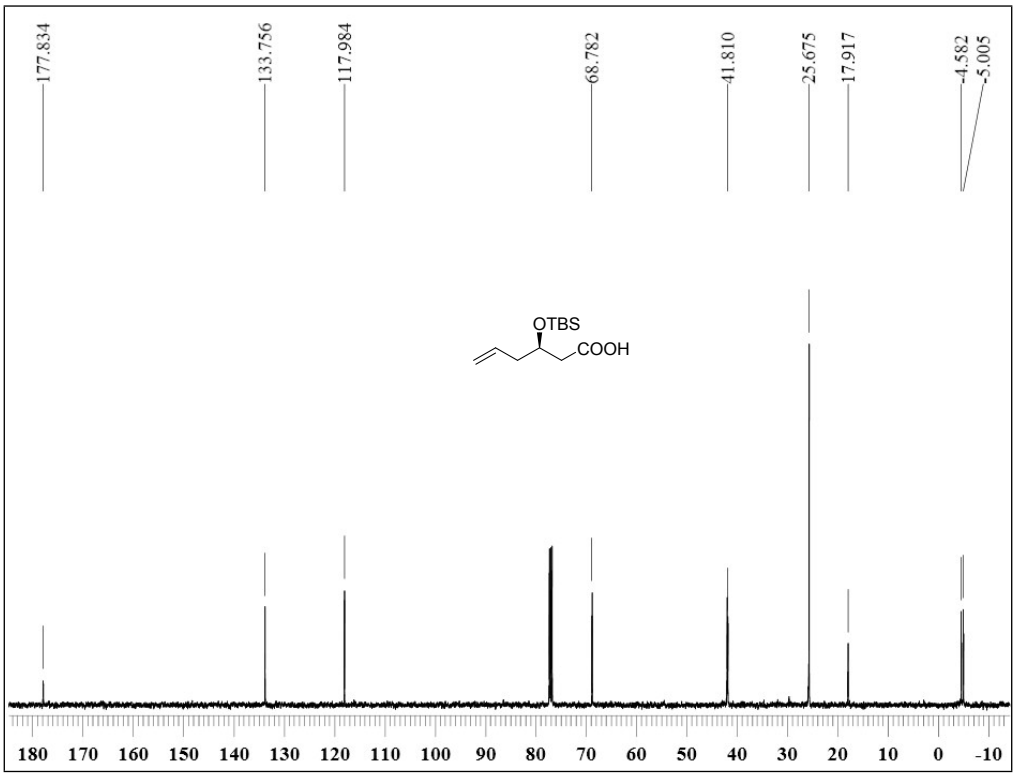
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 2e



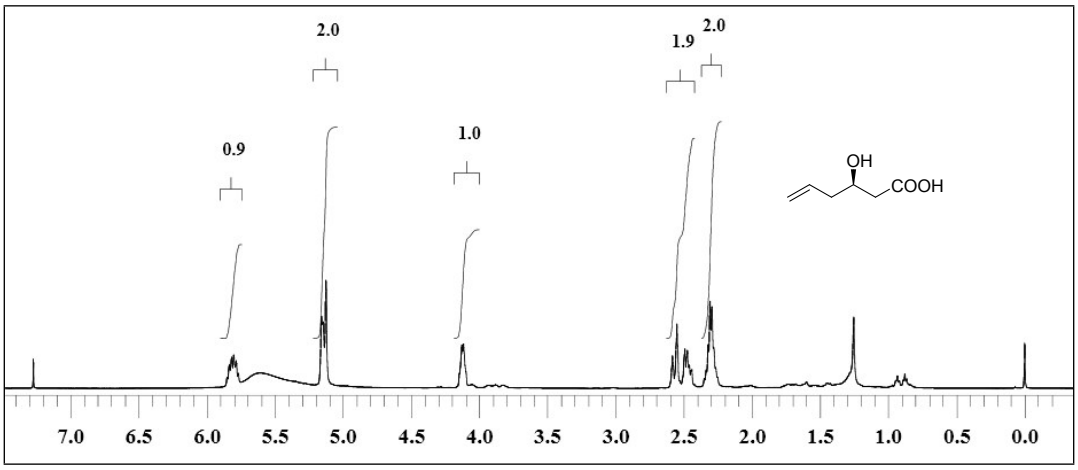
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 2f



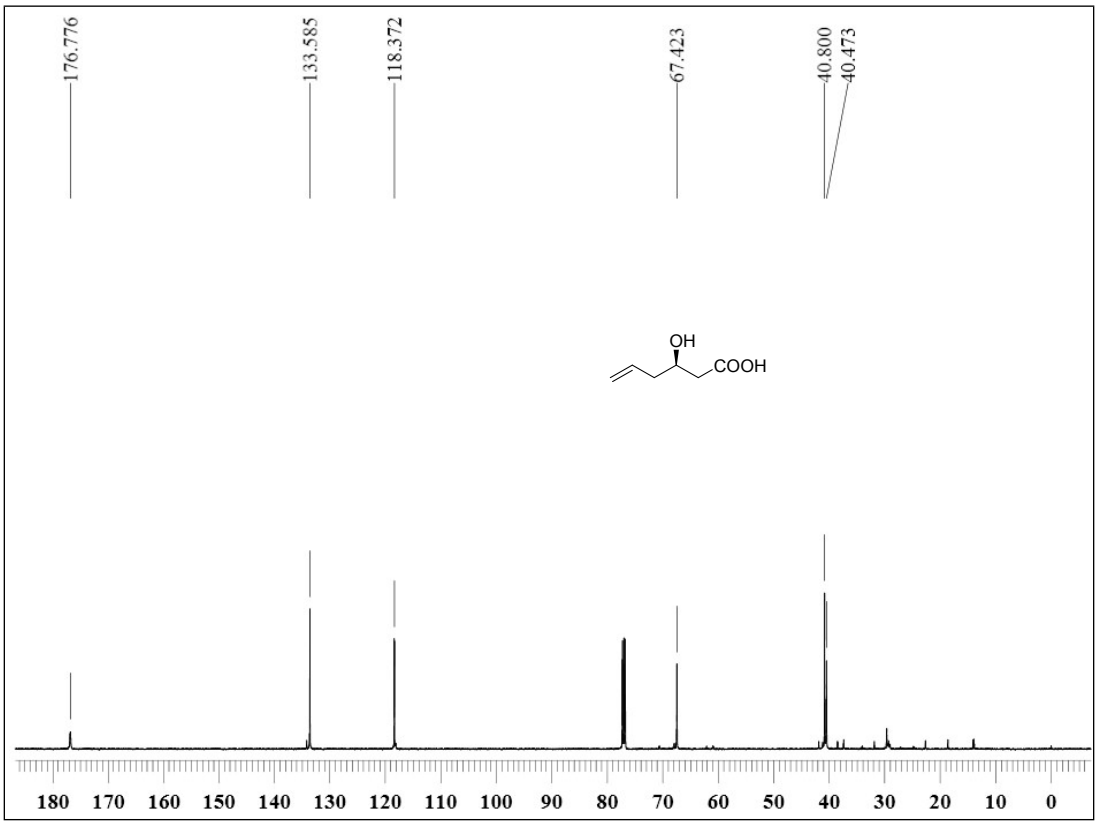
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 2f



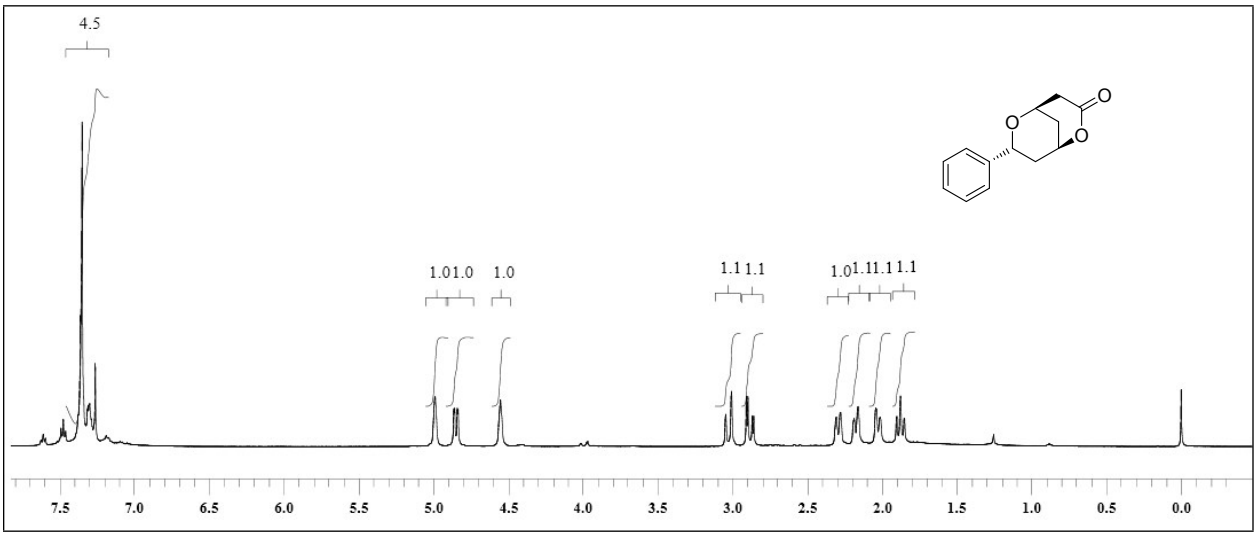
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of (*S*)-2



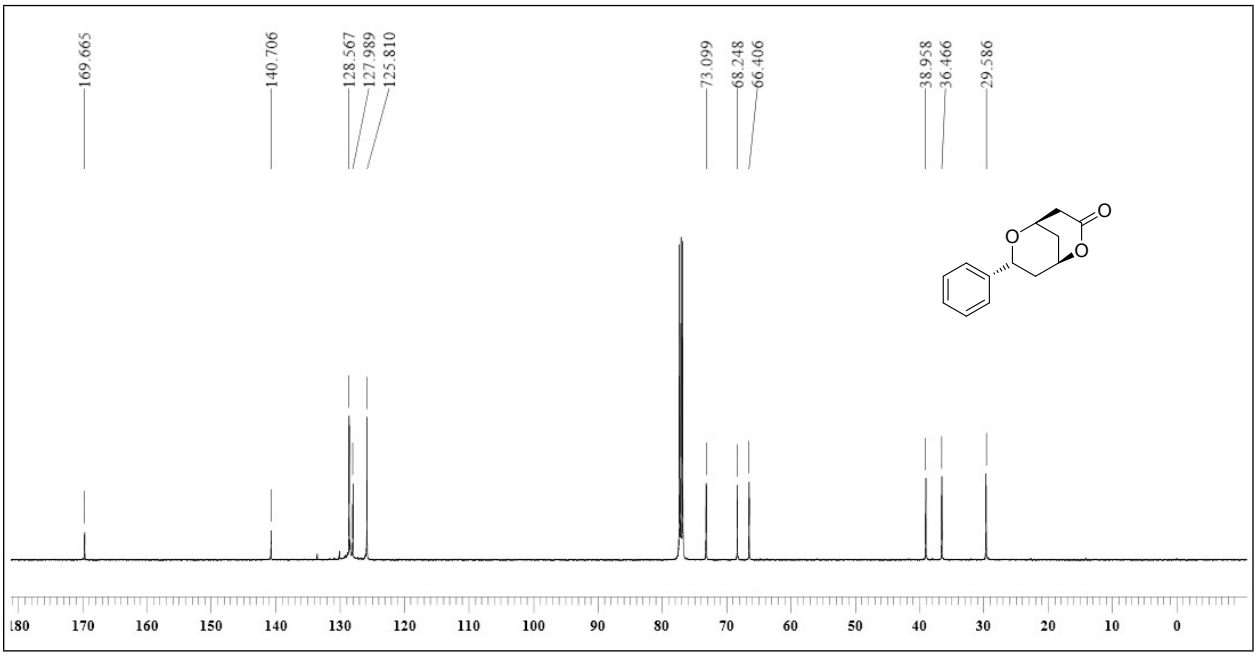
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of (*S*)-2



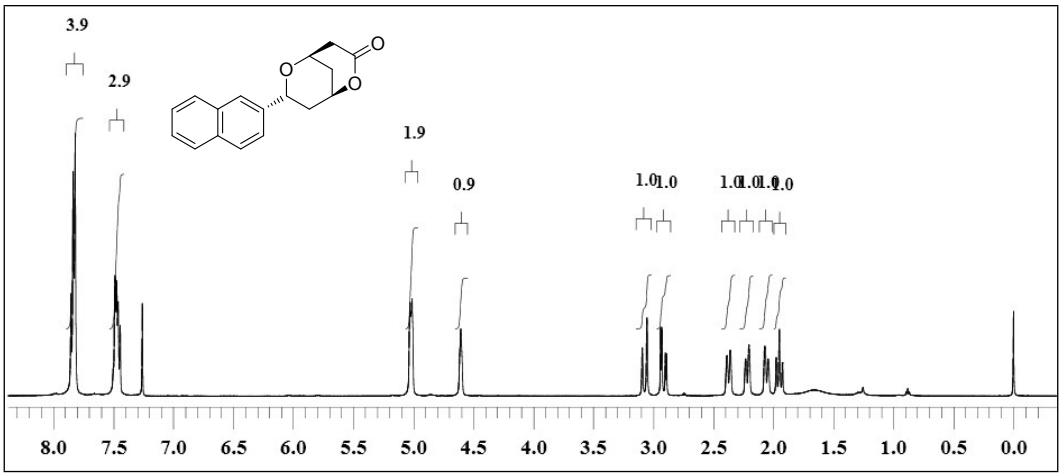
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3a



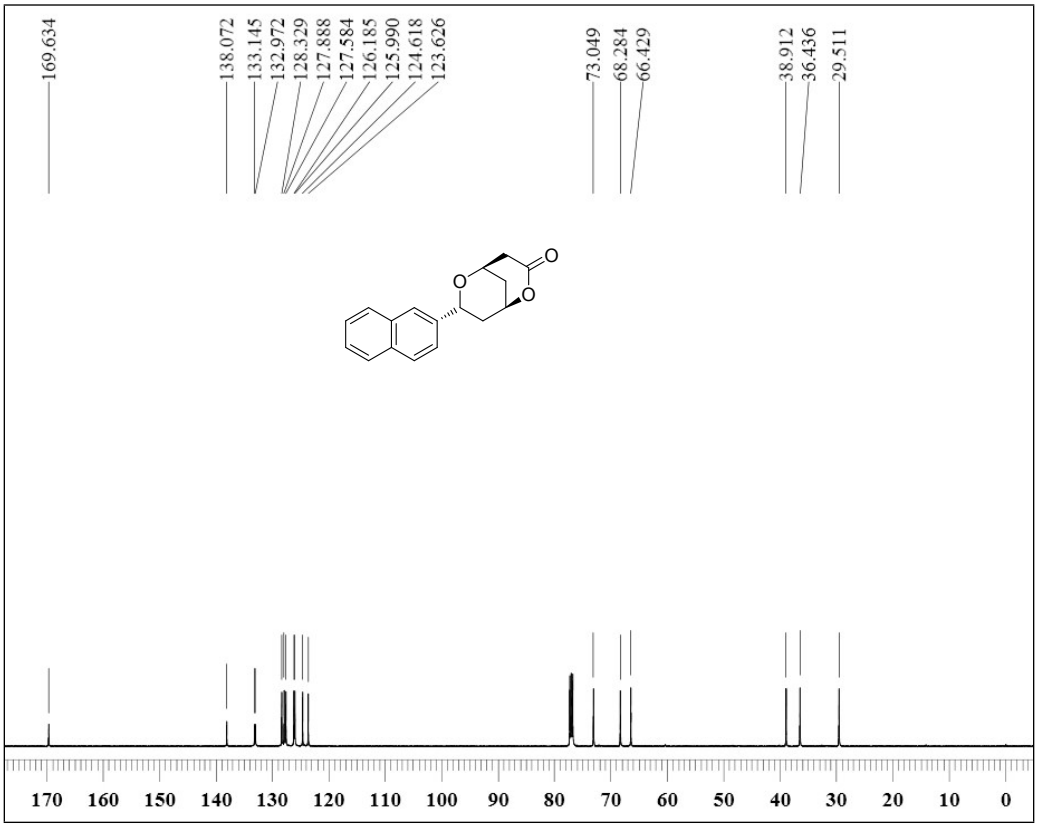
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3a



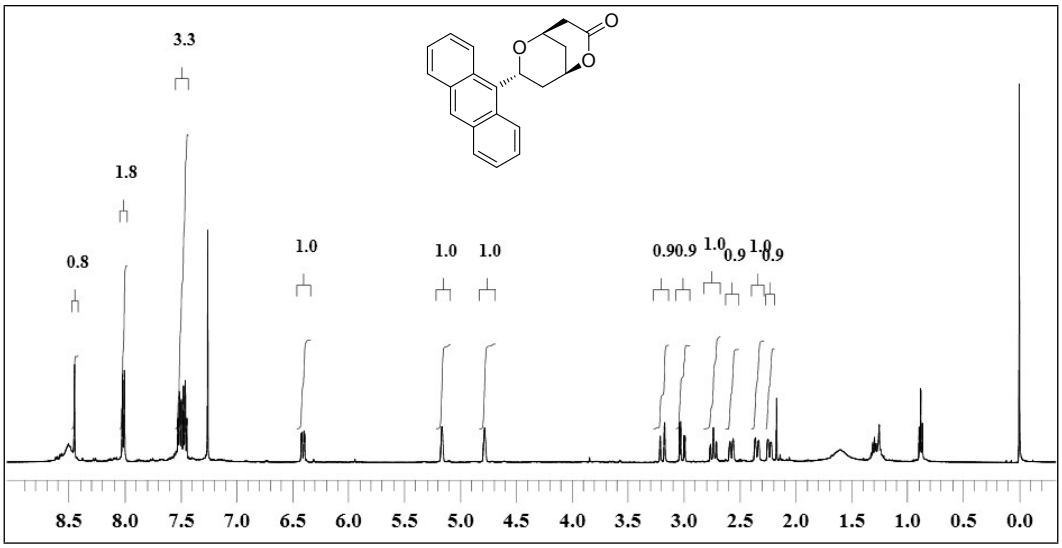
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3b (Table 1)



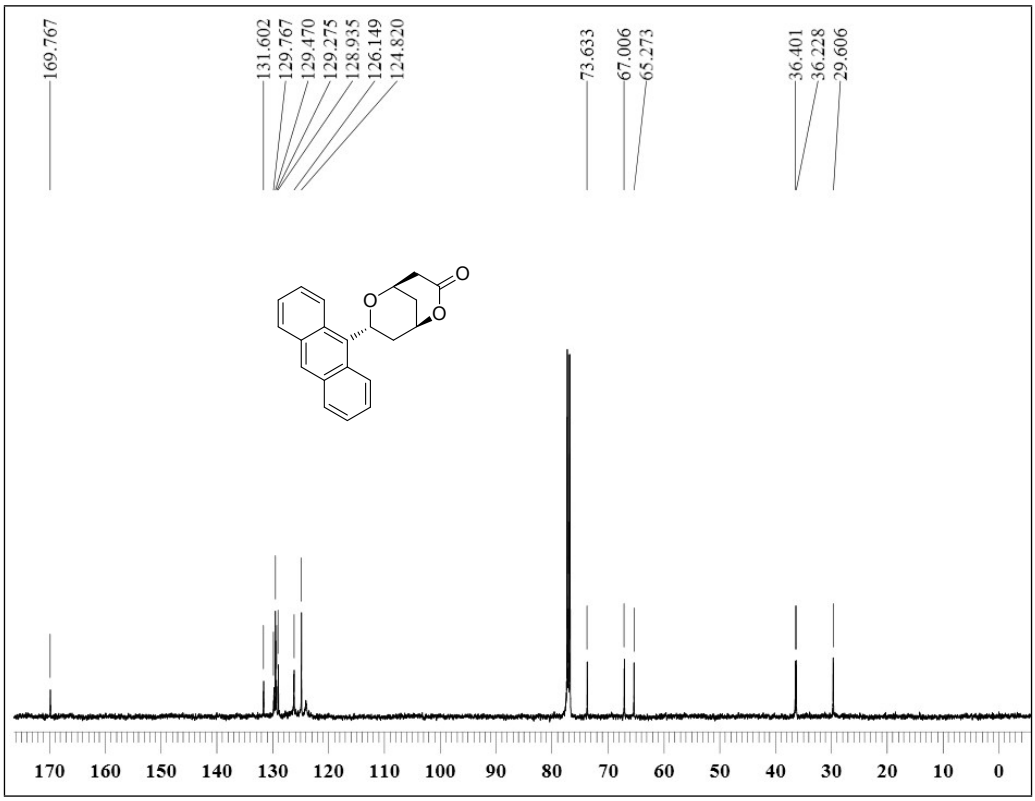
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3b (Table 1)



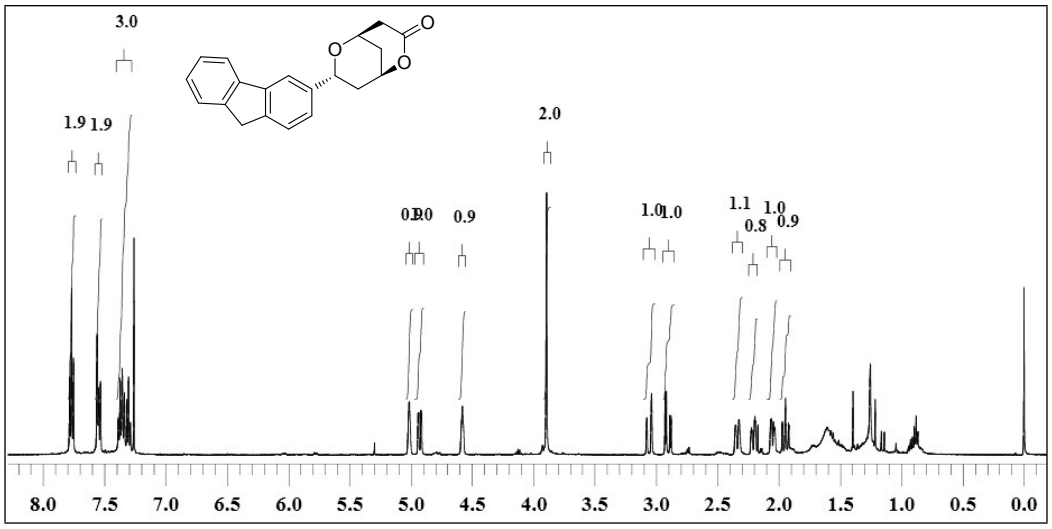
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3c (Table 1)



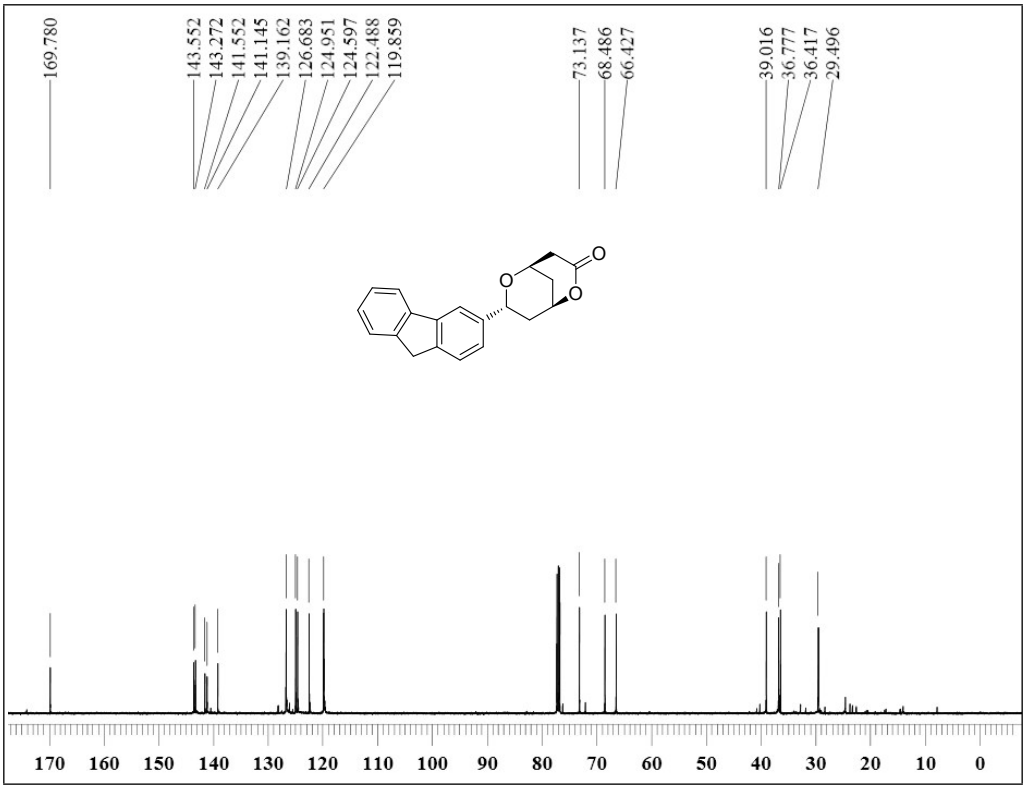
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3c (Table 1)



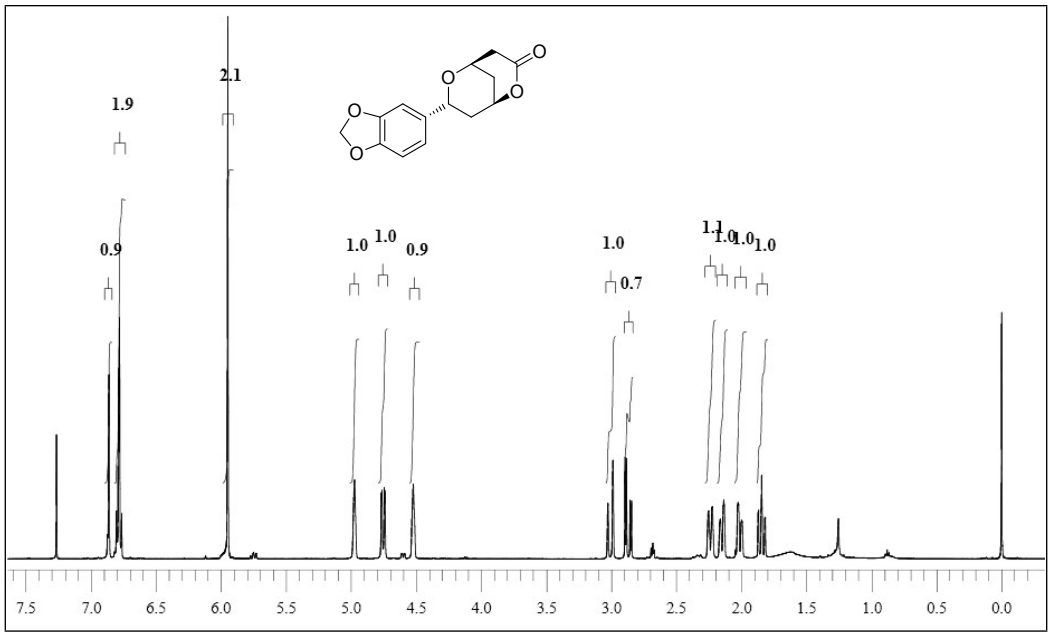
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3d (Table 1)



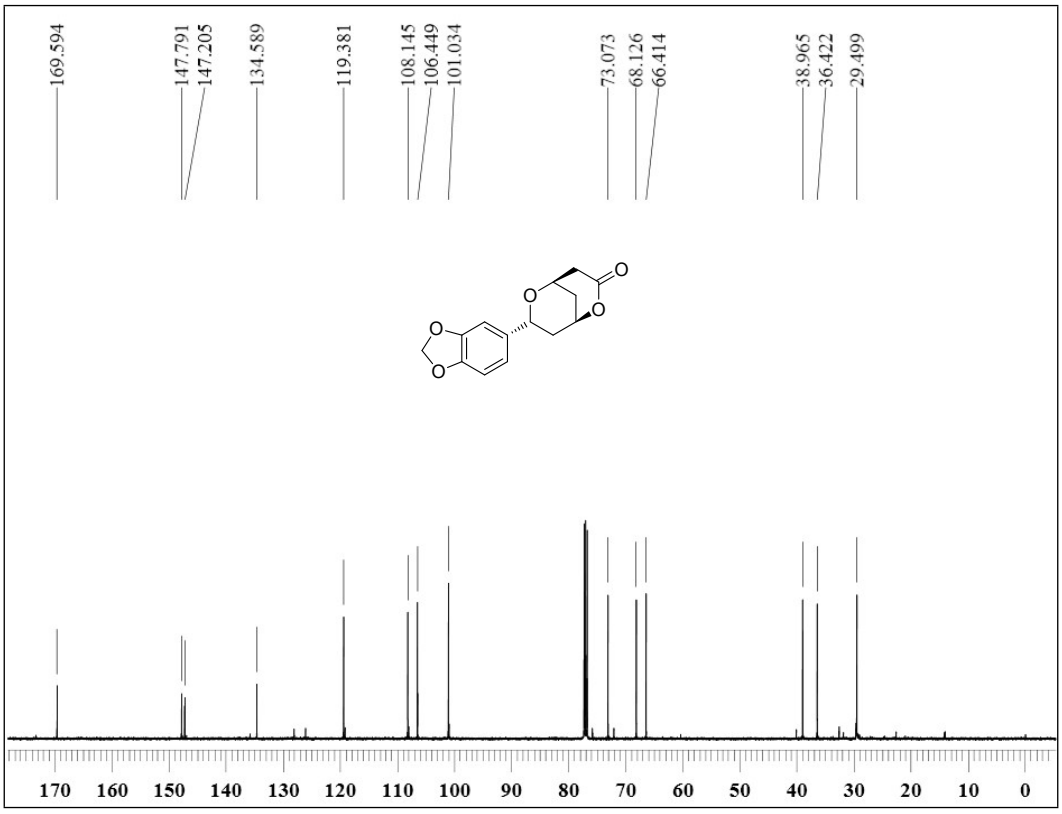
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3d (Table 1)



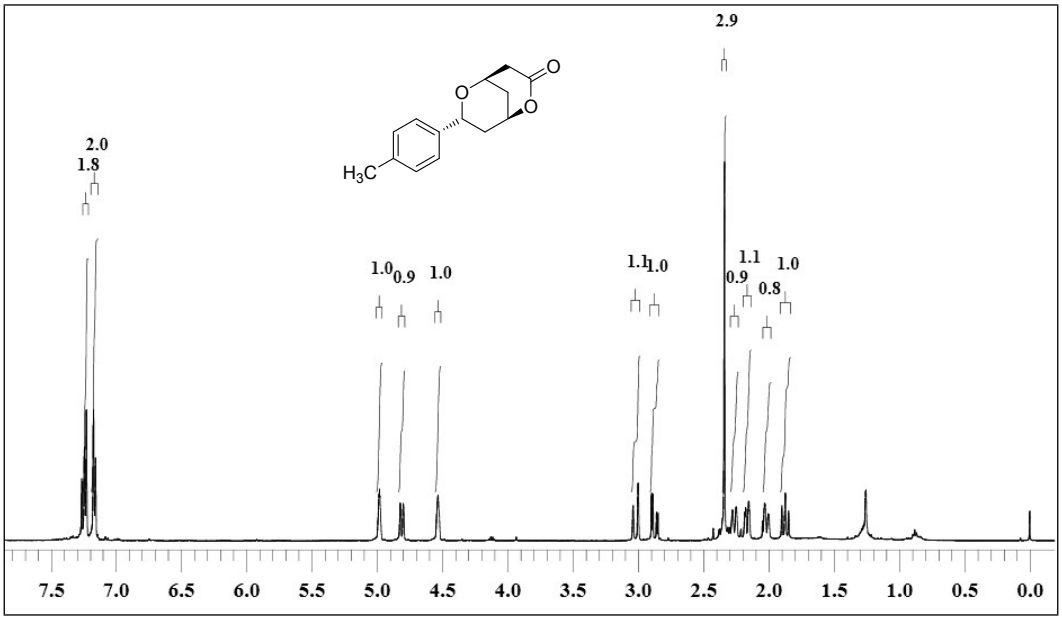
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3e (Table 1)



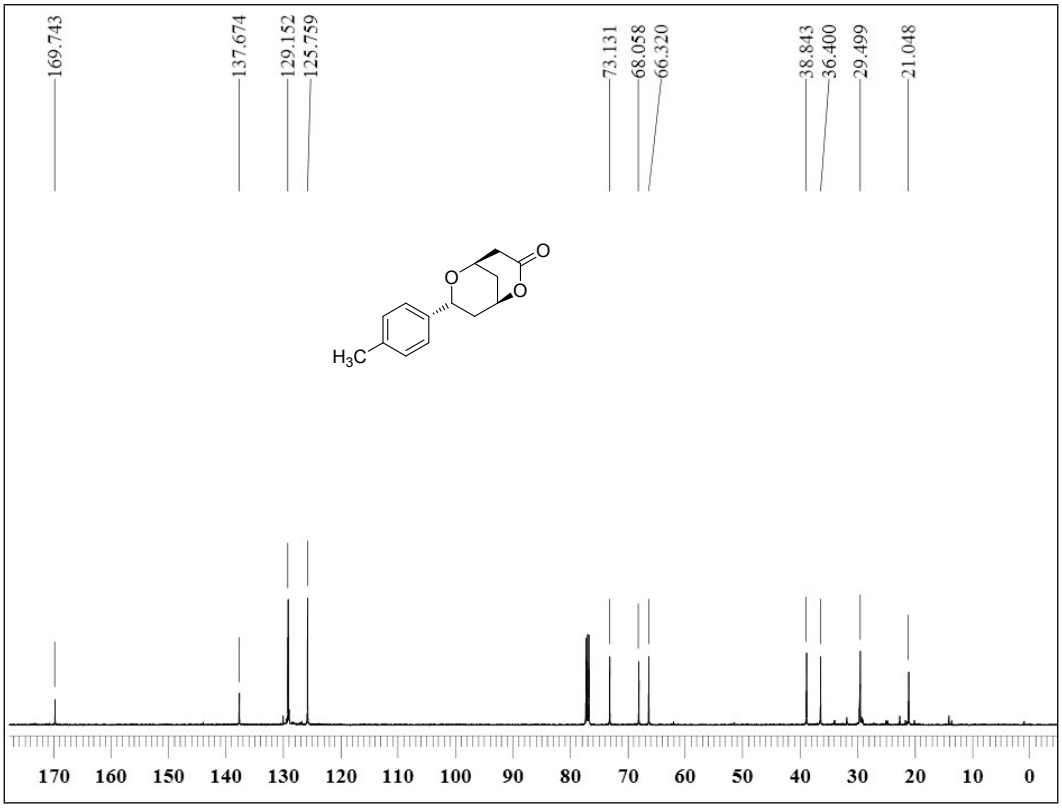
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3e (Table 1)



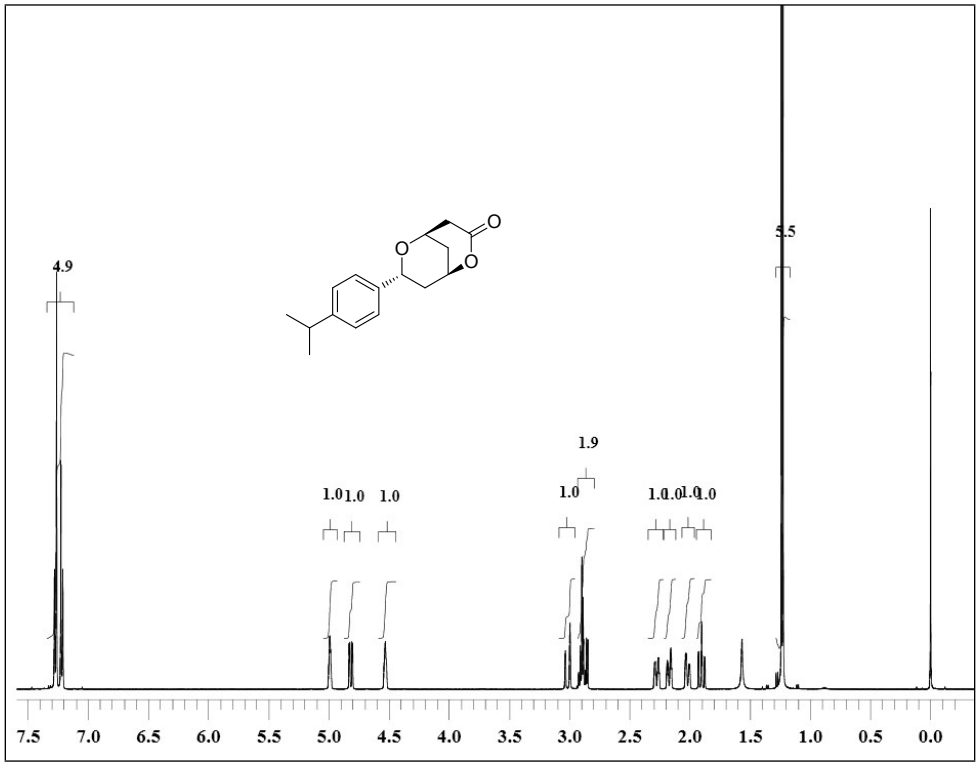
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3f (Table 1)



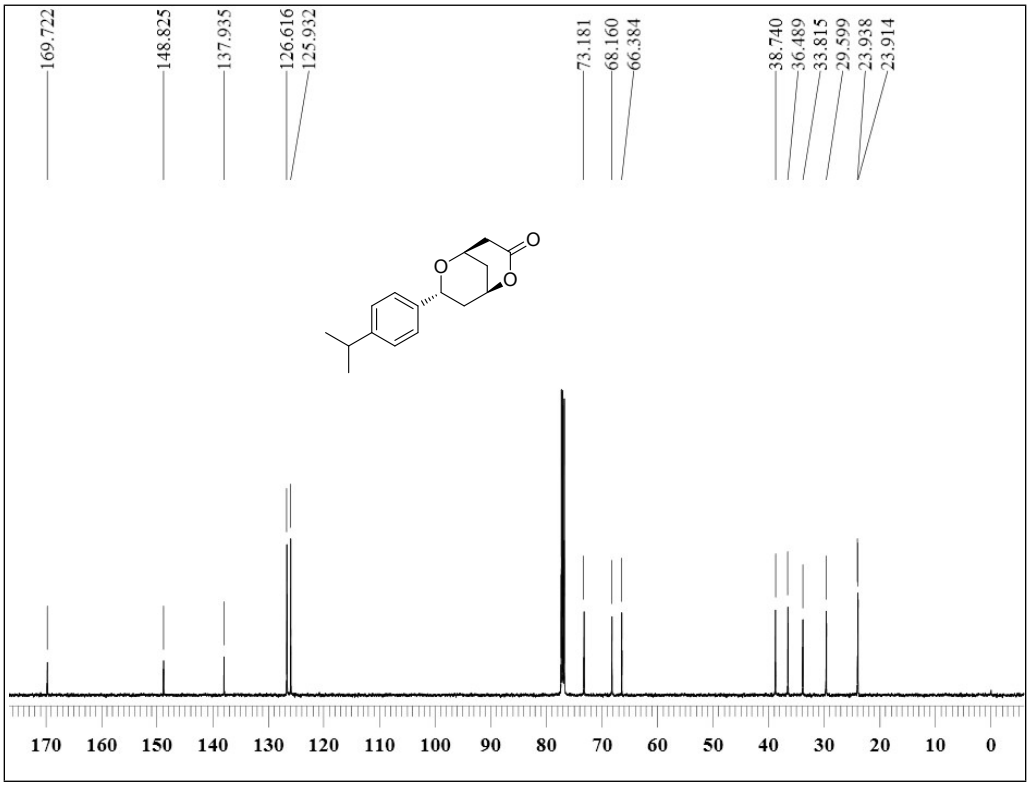
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3f (Table 1)



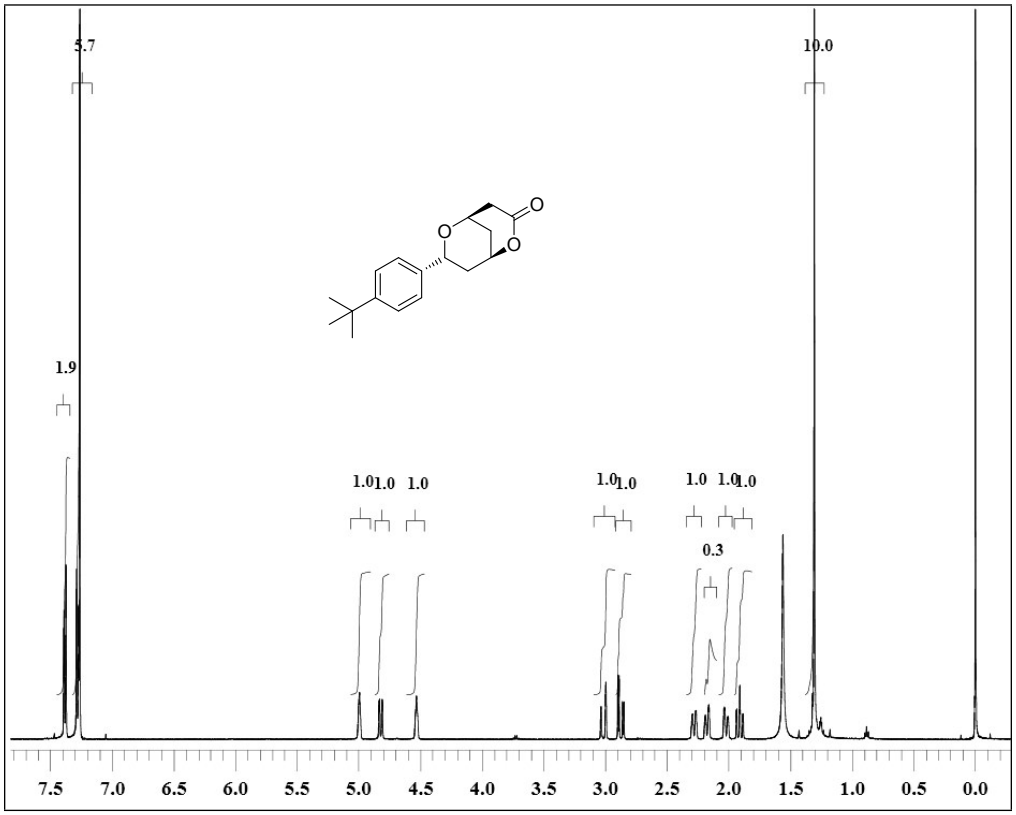
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3g (Table 1)



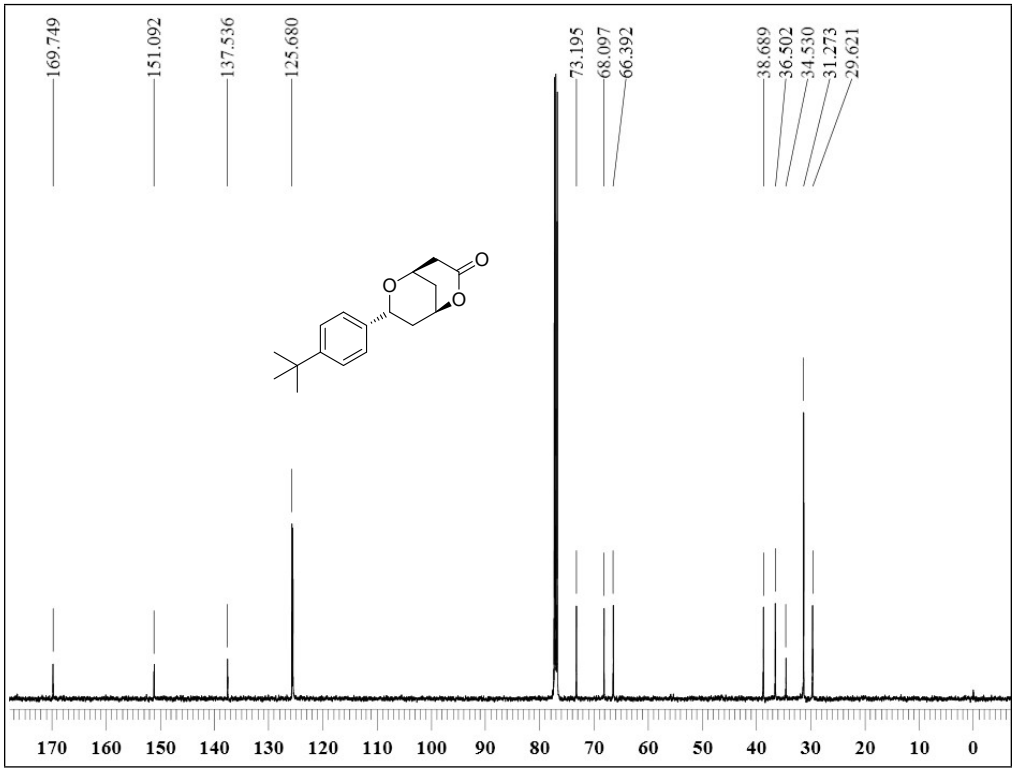
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3g (Table 1)



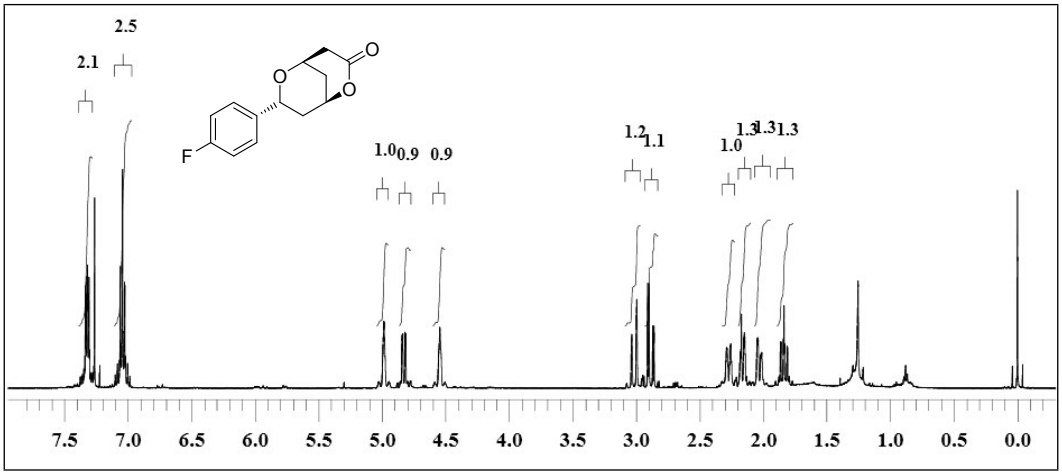
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3h (Table 1)



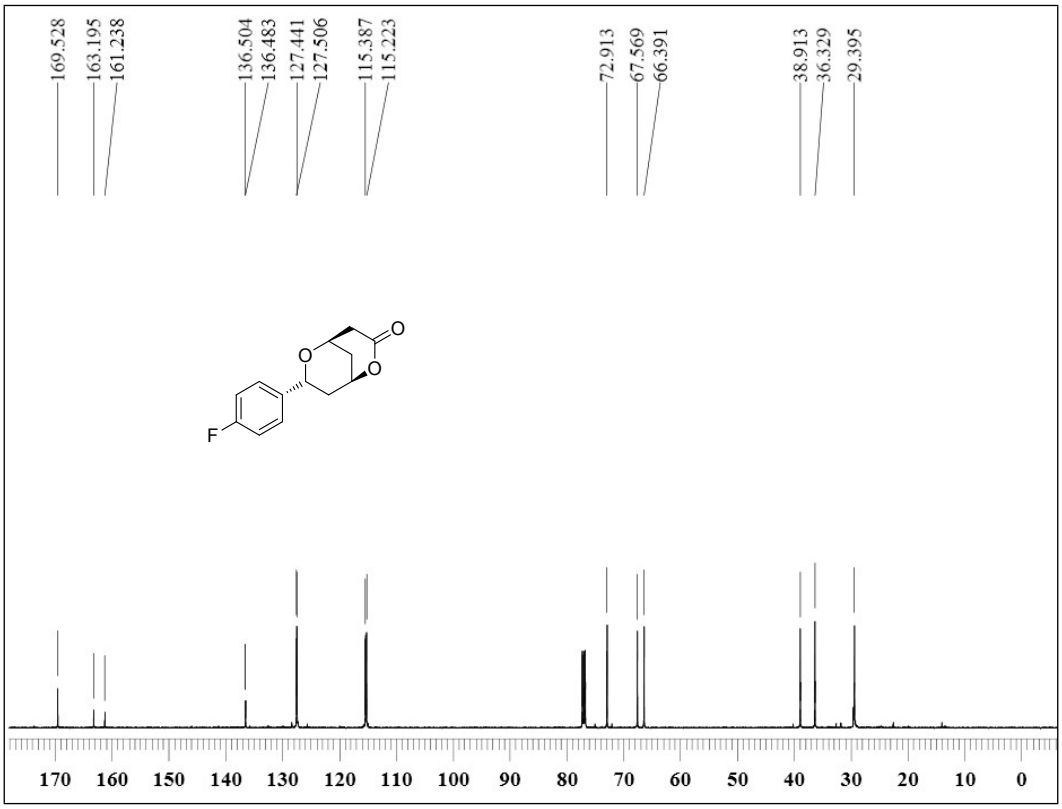
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3h (Table 1)



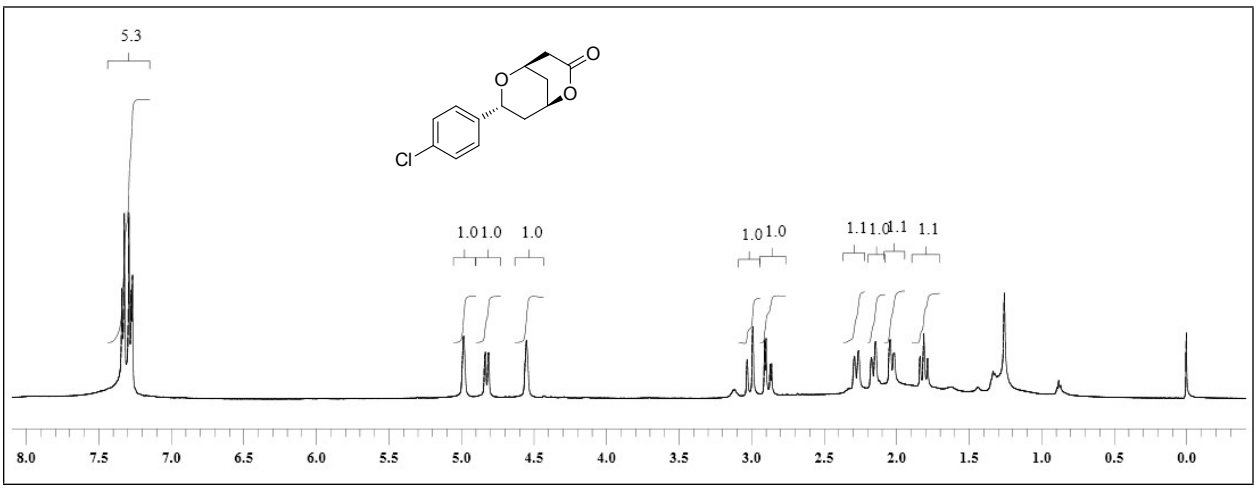
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 3i (Table 1)



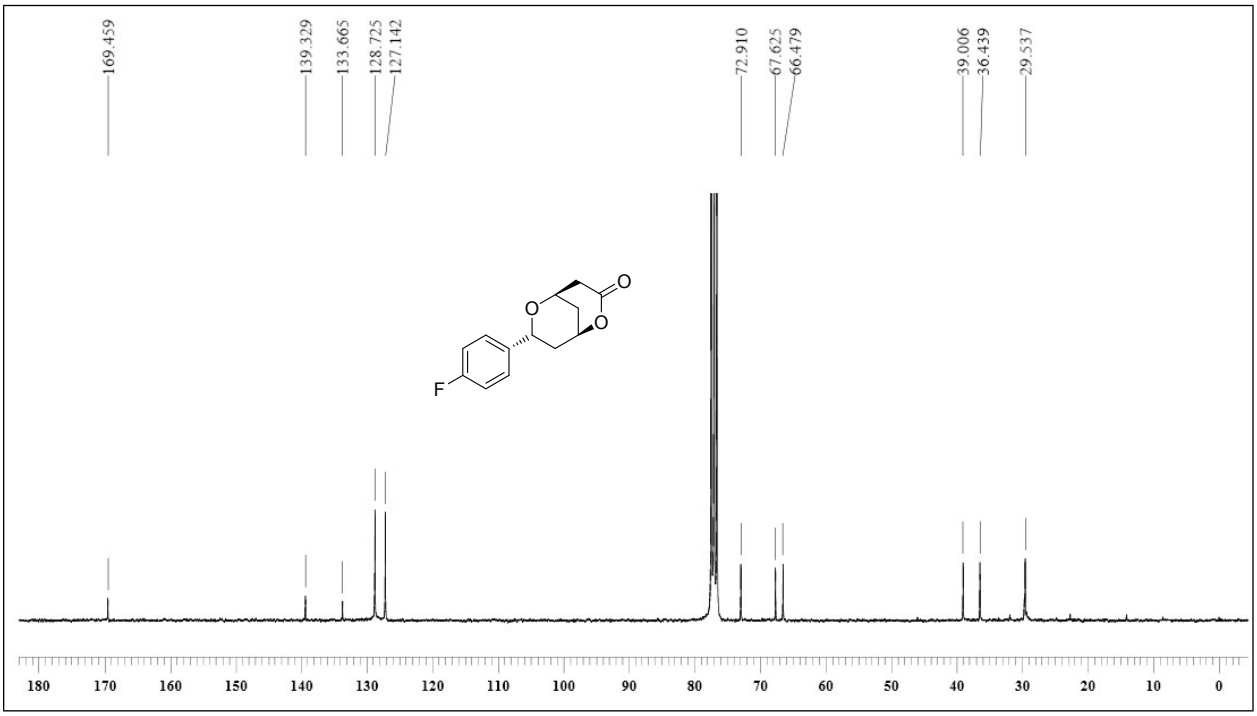
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3i (Table 1)



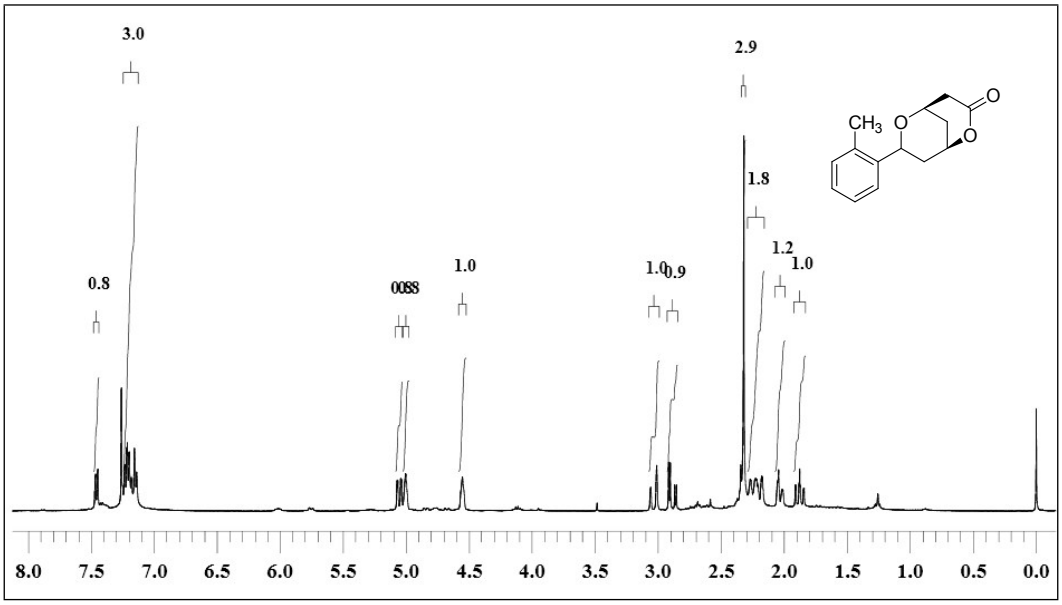
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3j



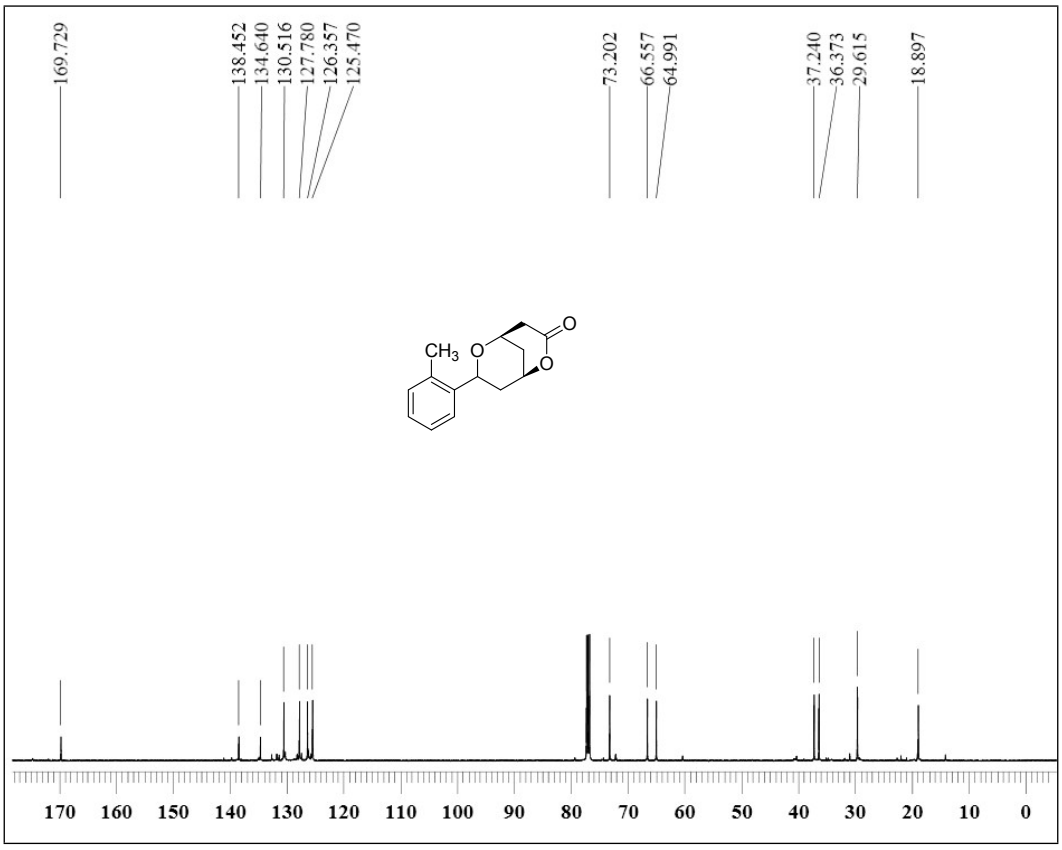
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3j



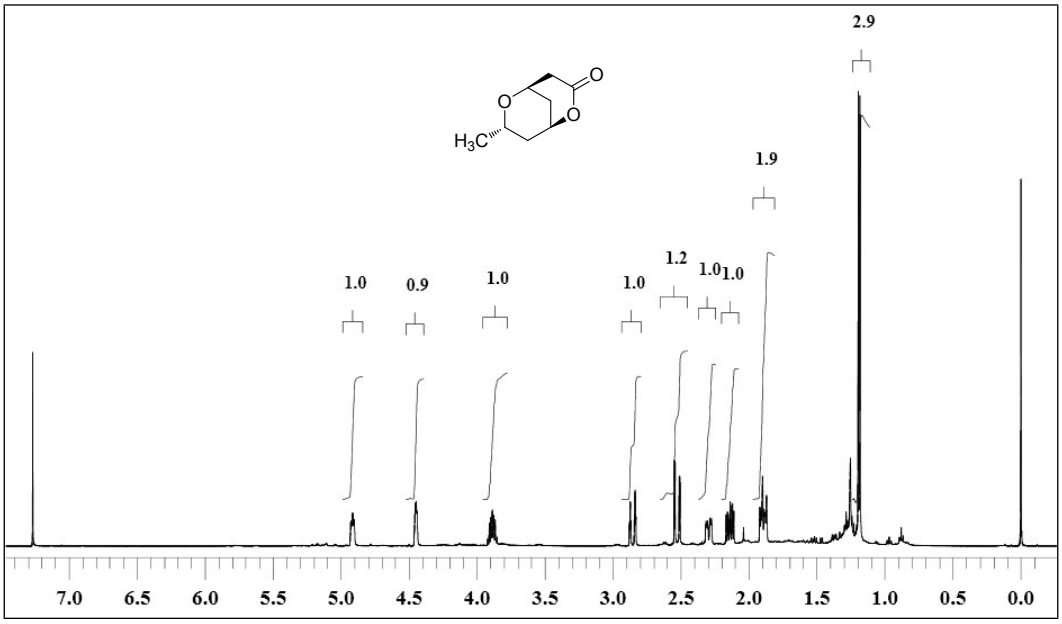
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 3k (Table 1)



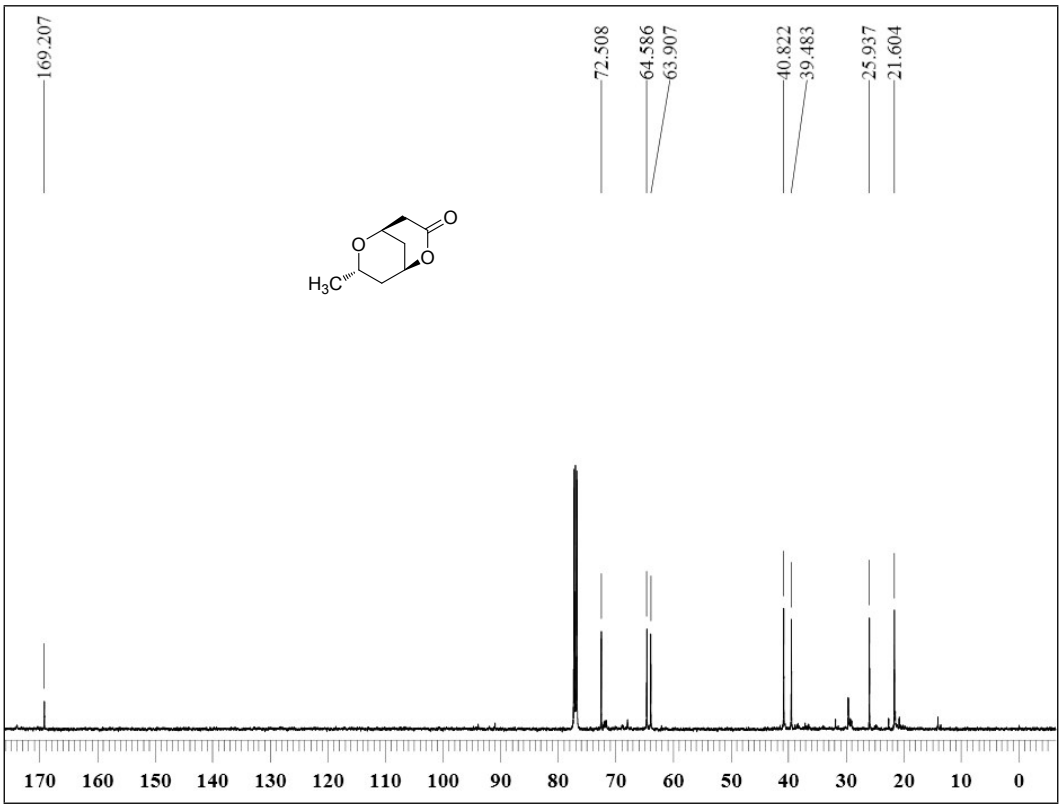
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3k (Table 1)



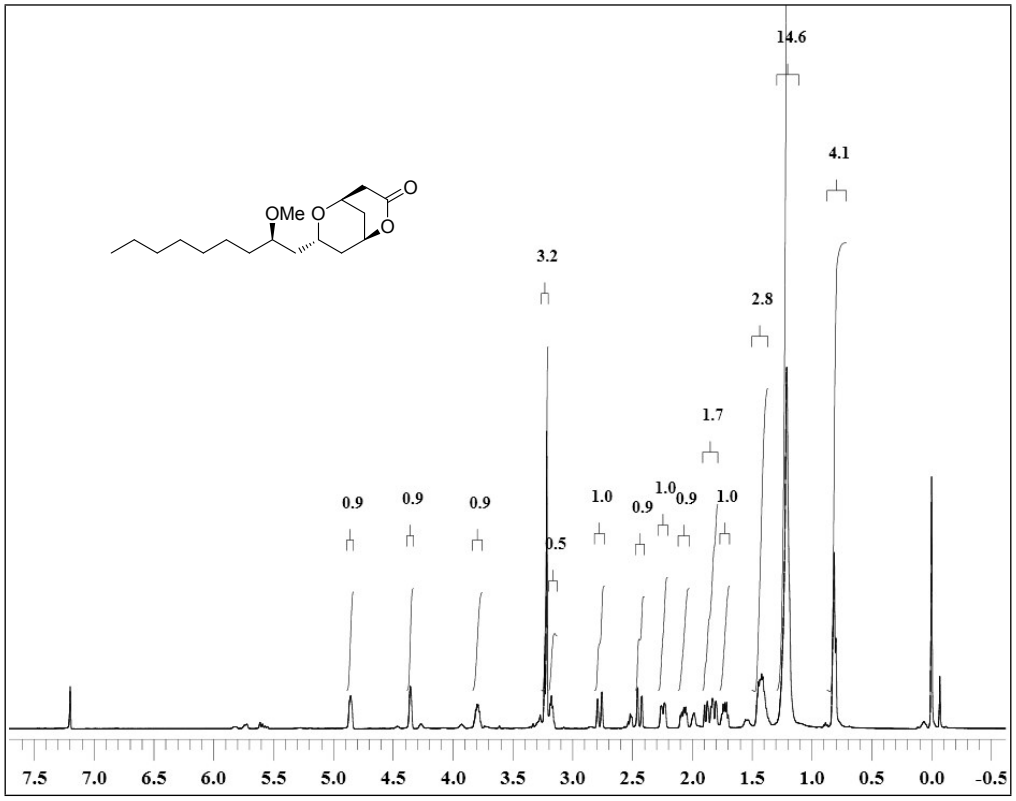
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3l (Table 1)



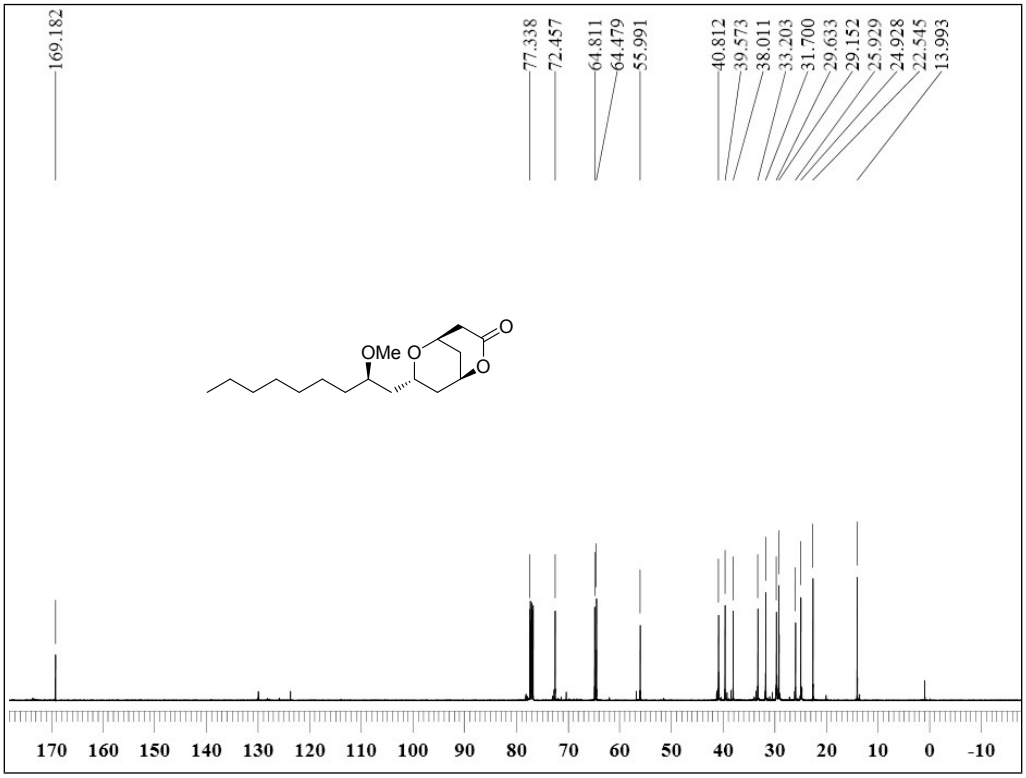
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 3l (Table 1)



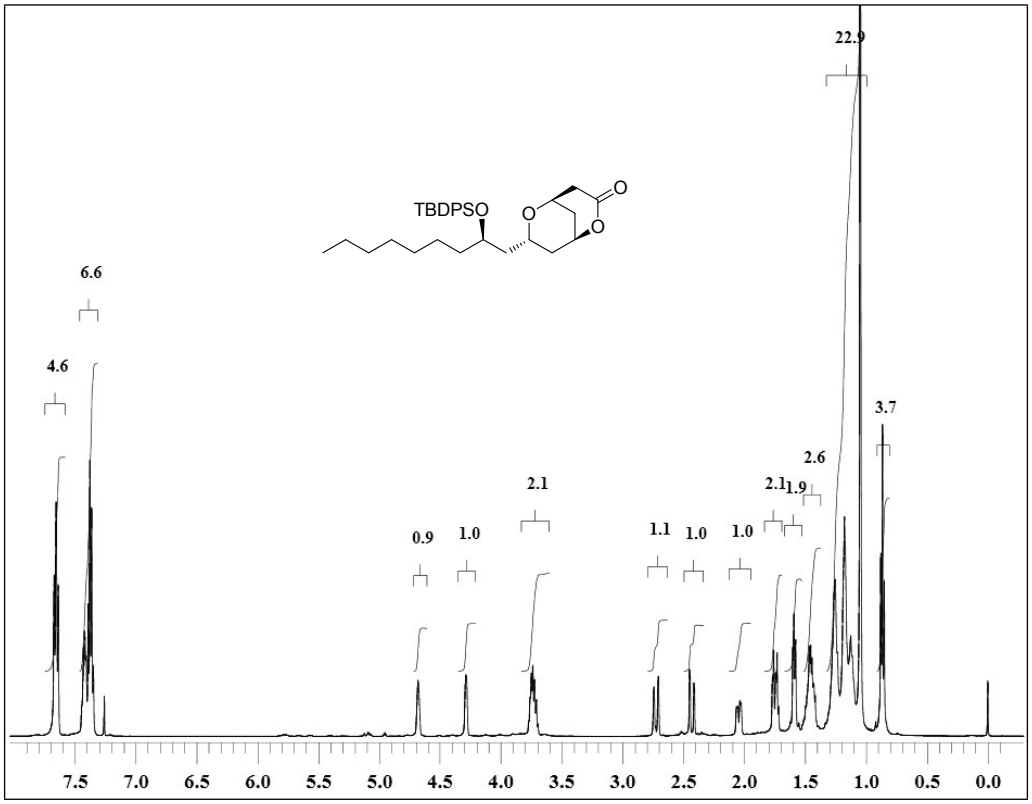
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3m (Table 1)



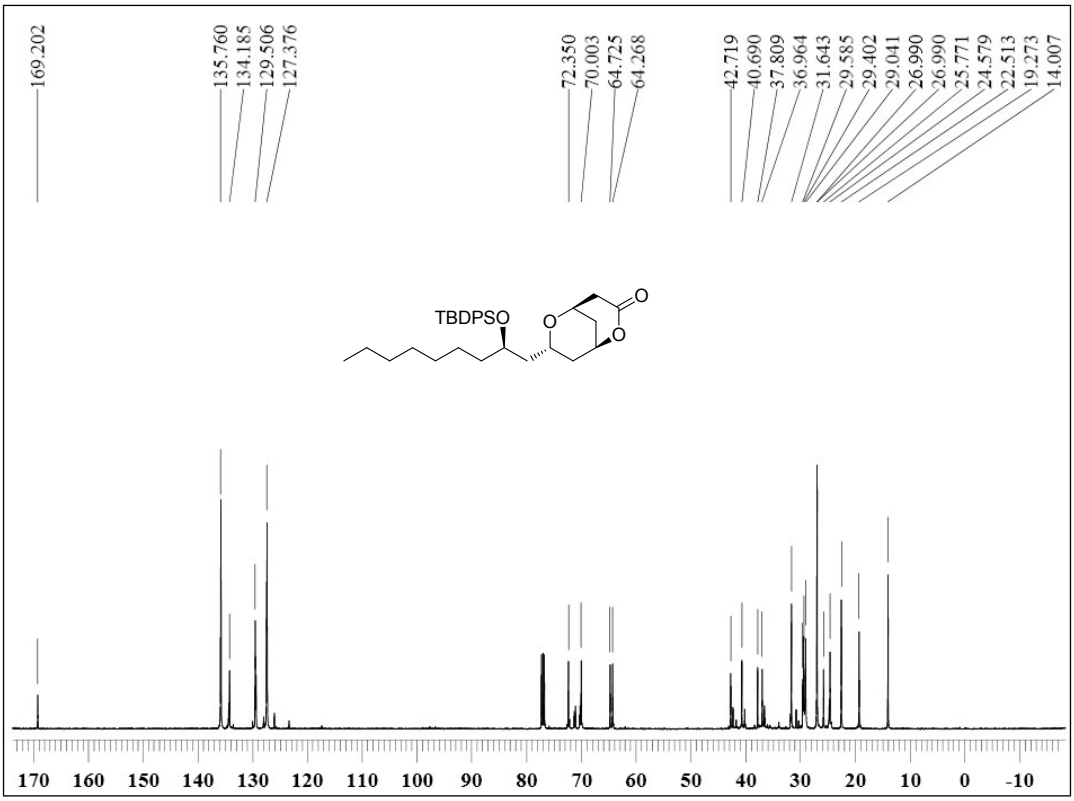
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3m (Table 1)



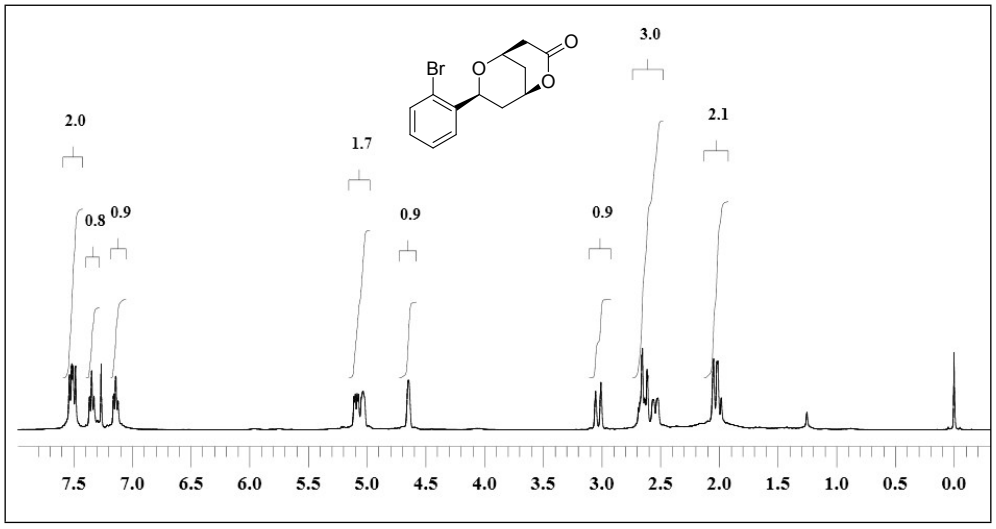
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3n (Table 1)



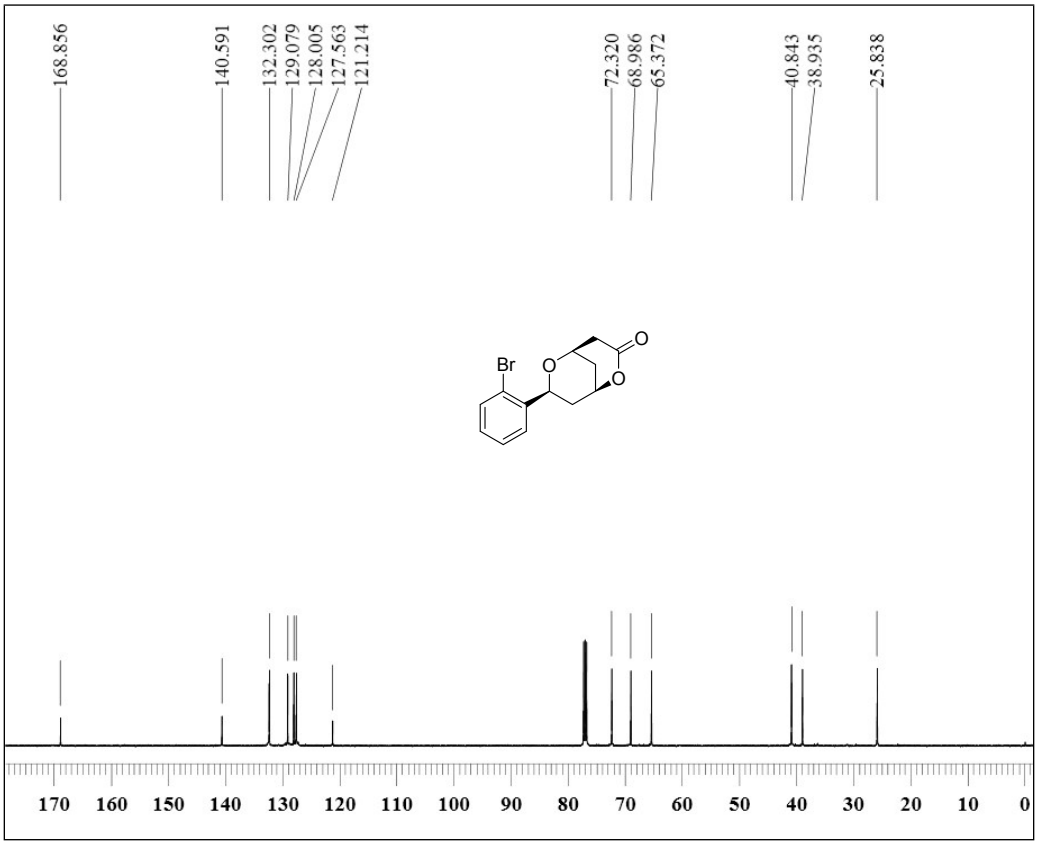
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3n (Table 1)



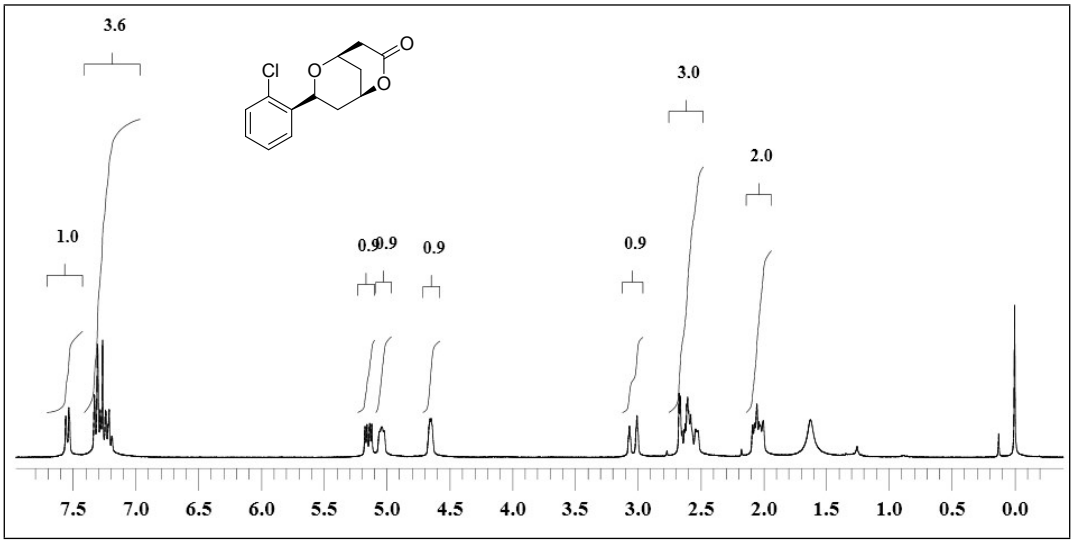
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 4a (Table 2)



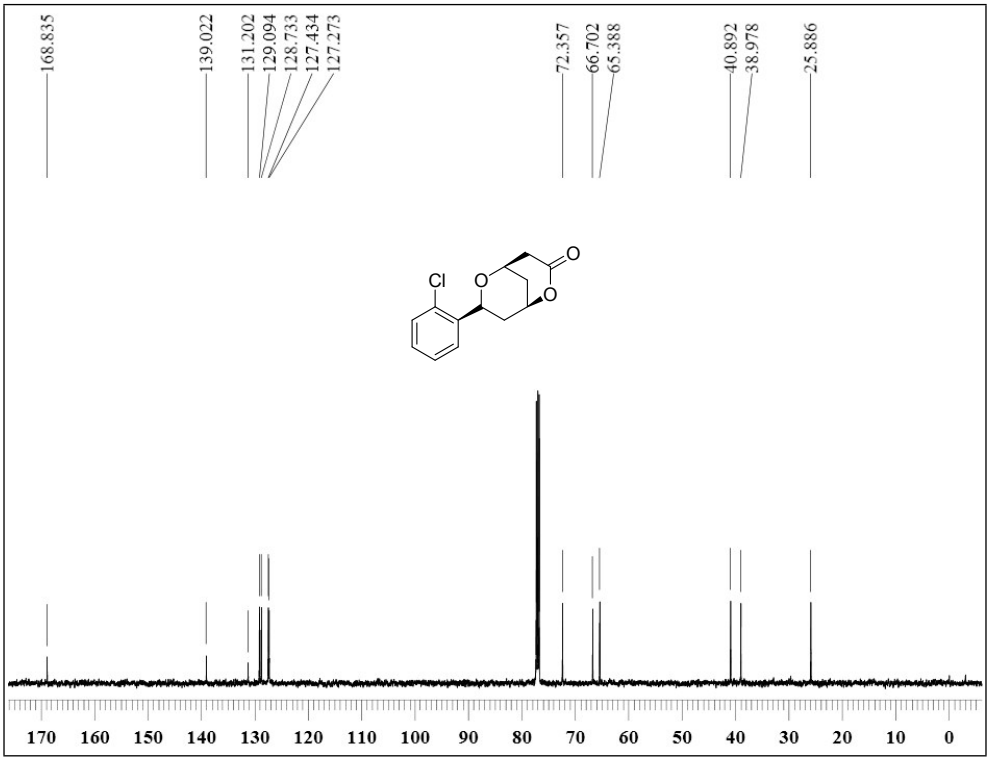
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4a (Table 2)



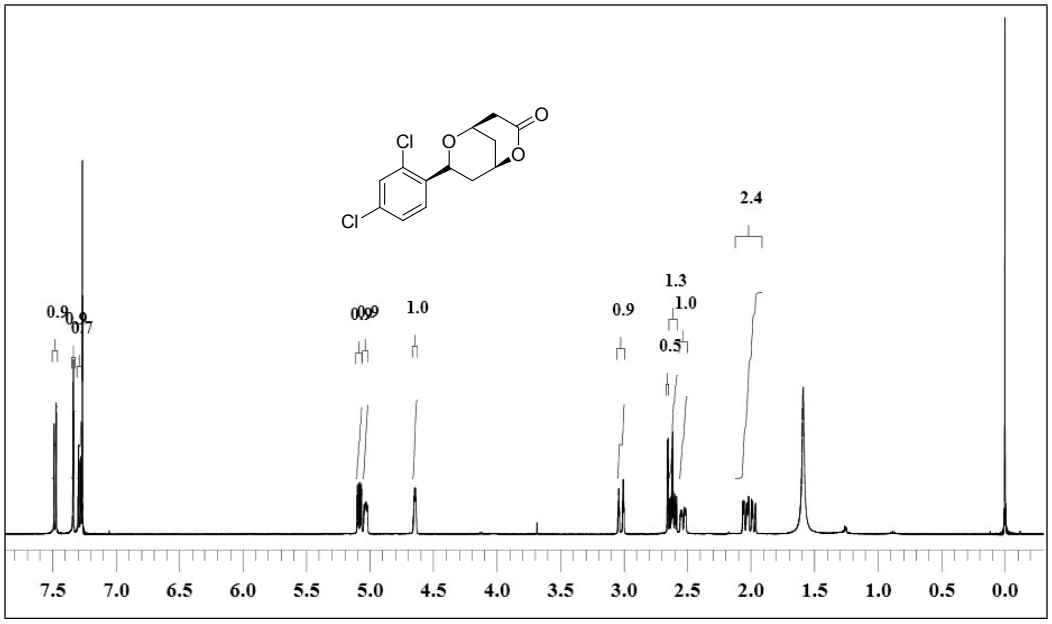
^{1}H NMR (300 MHz, $CDCl_3$) spectrum of 4b (Table 2)



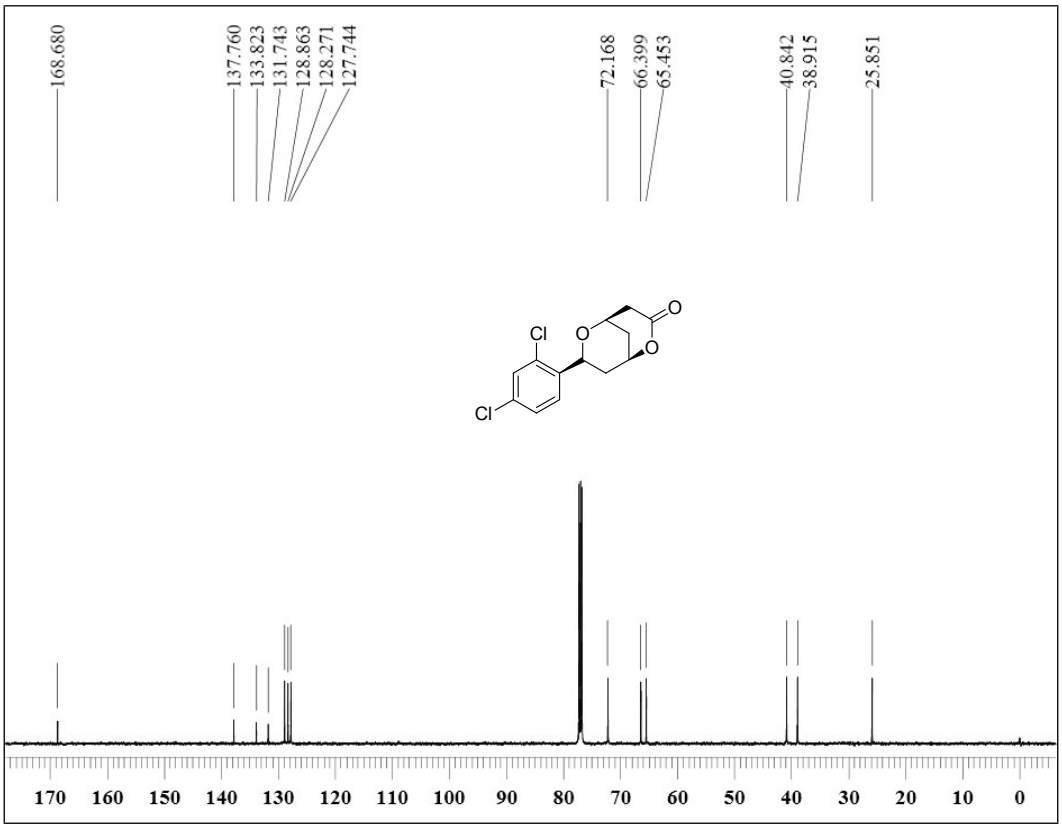
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4b (Table 2)



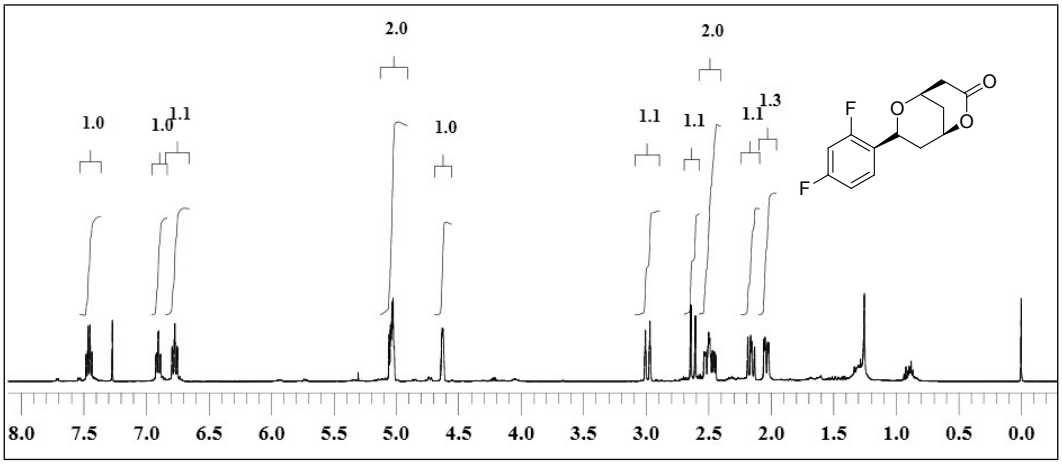
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 4c (Table 2)



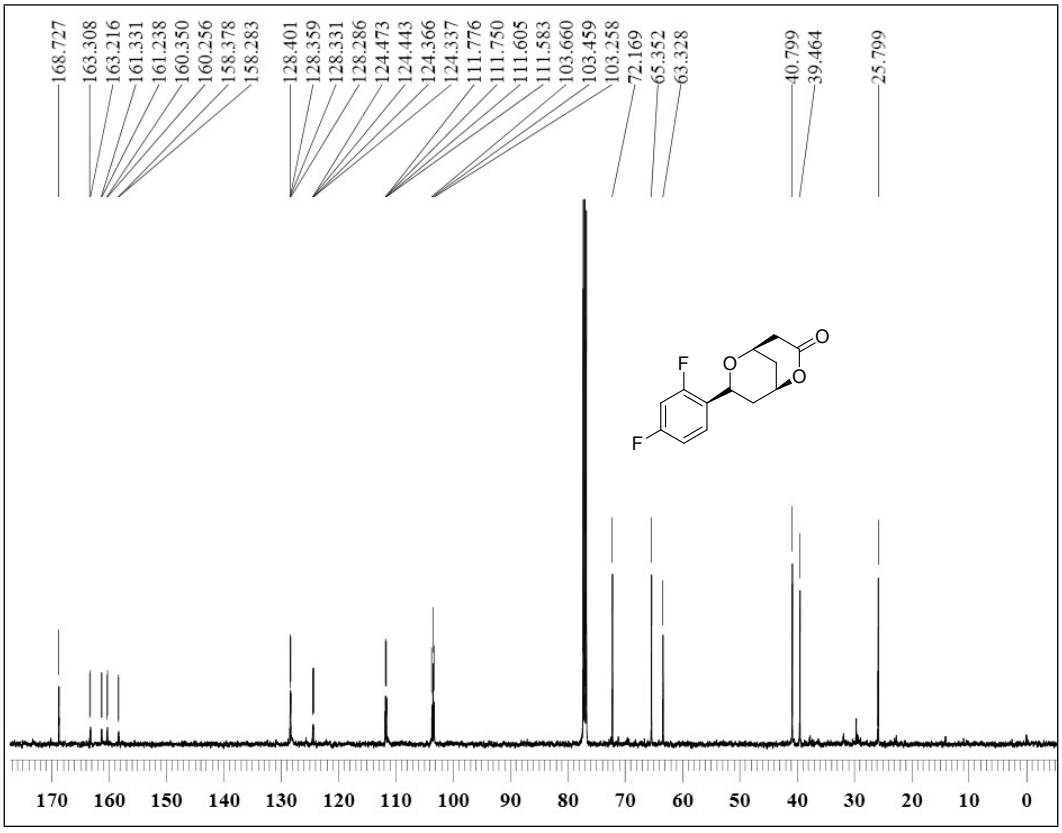
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 4c (Table 2)



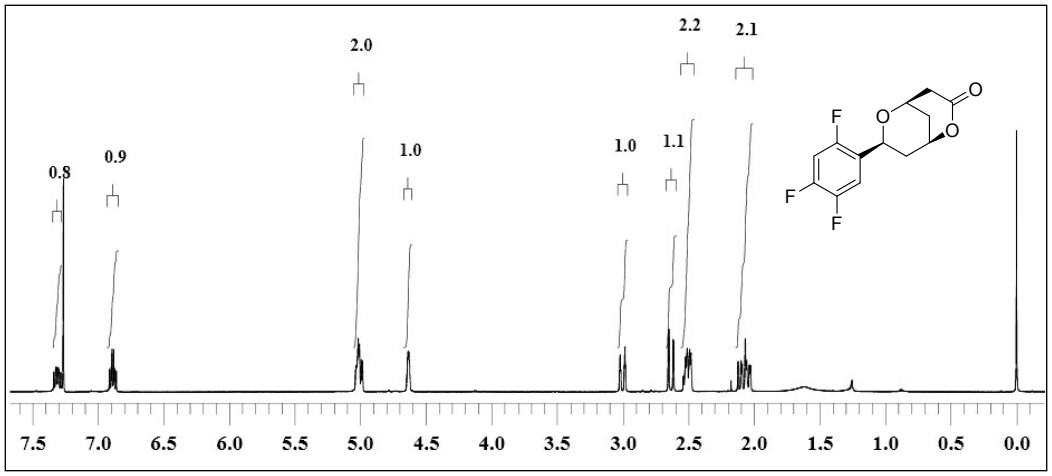
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4d (Table 2)



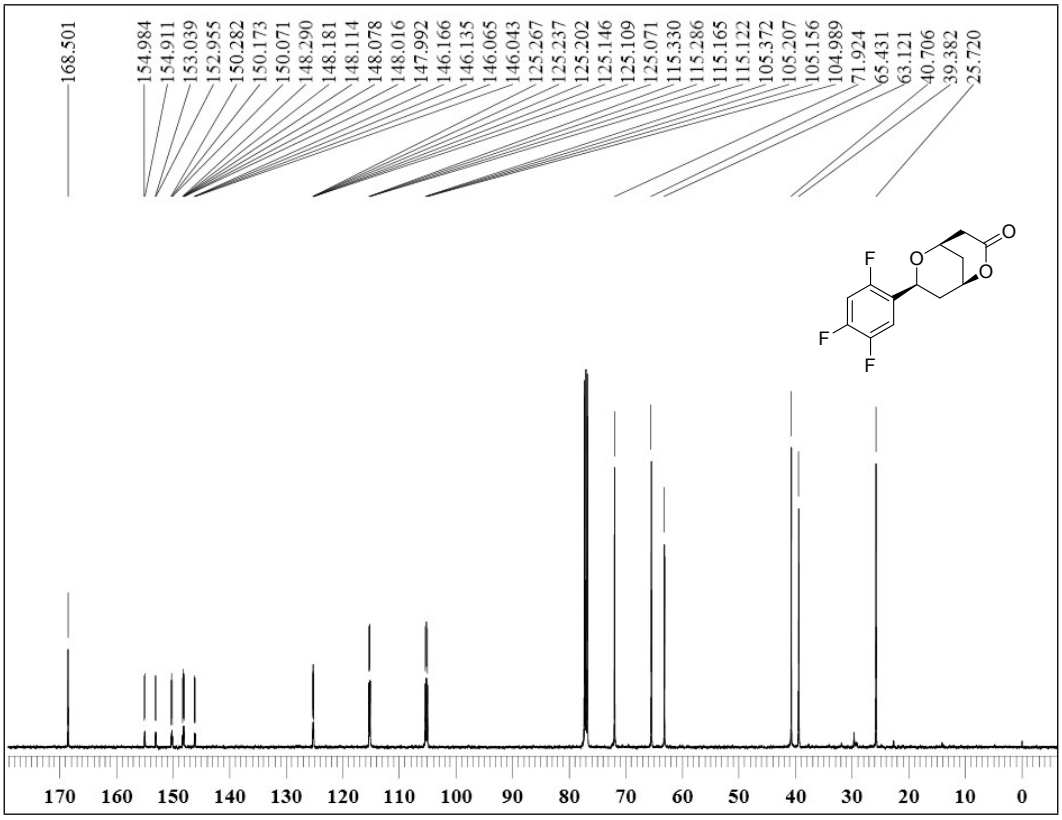
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4d (Table 2)



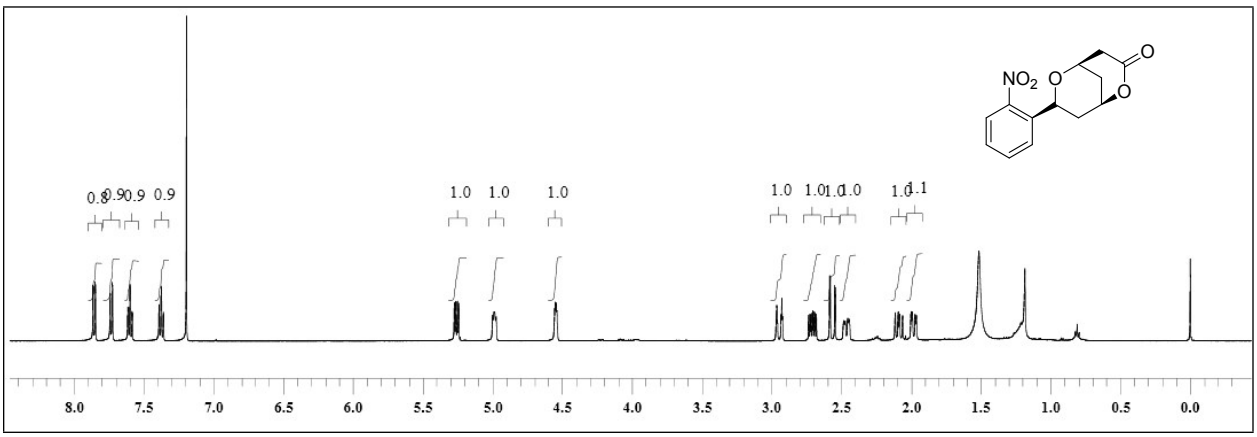
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 4e (Table 2)



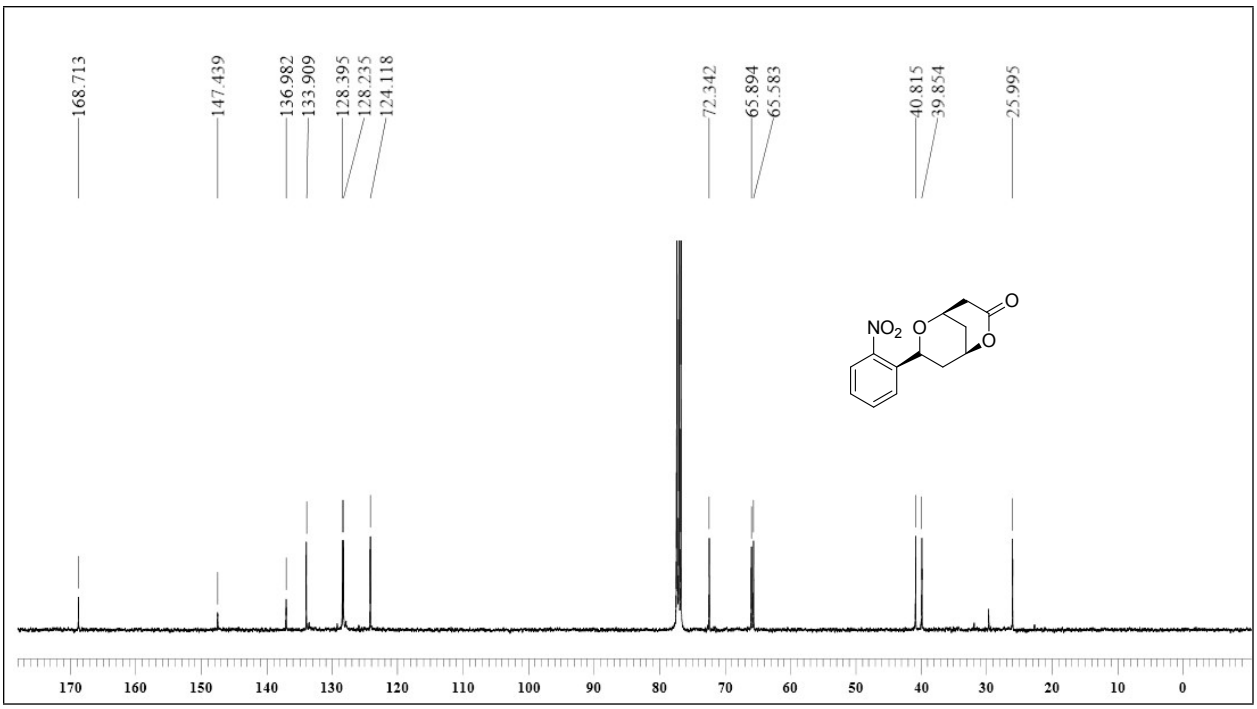
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 4e (Table 2)



^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 3h

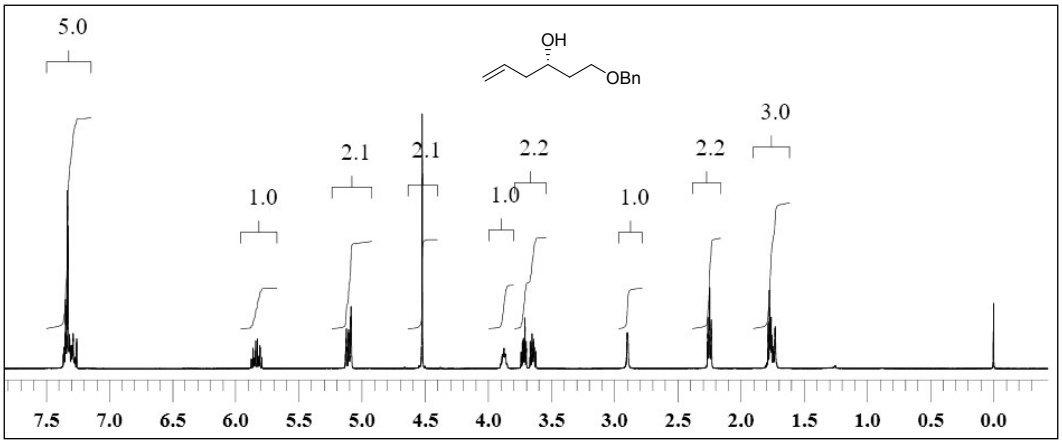


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 3h

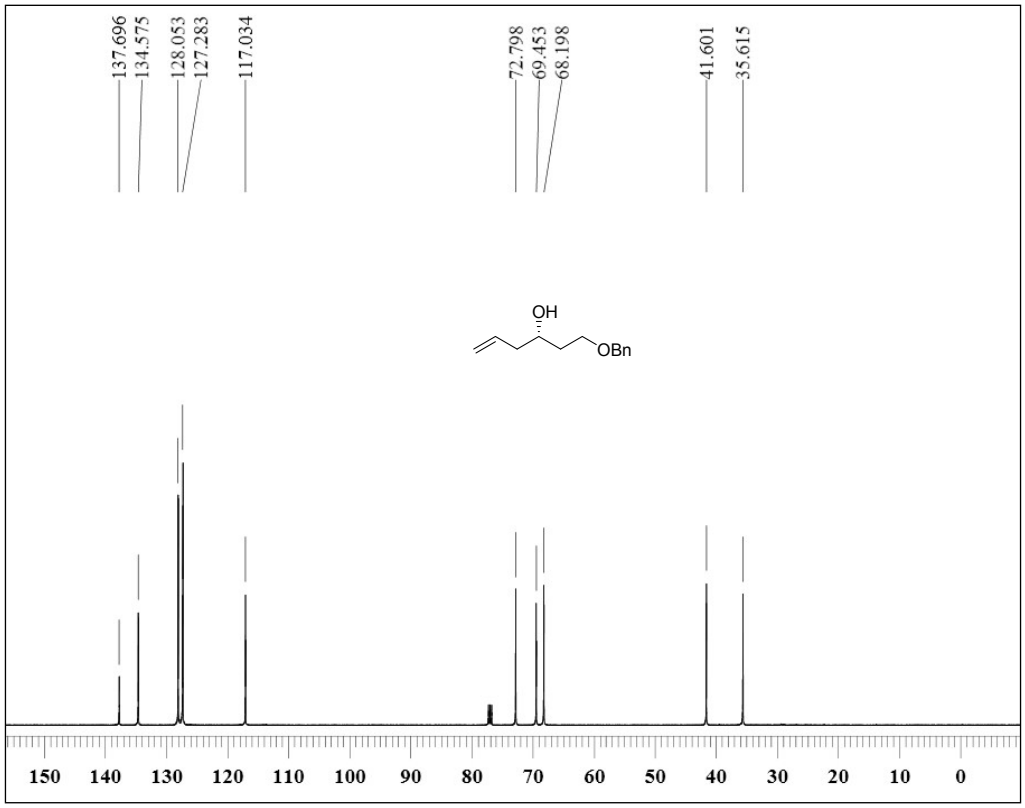


Copies of NMR spectra of products (5b-f)

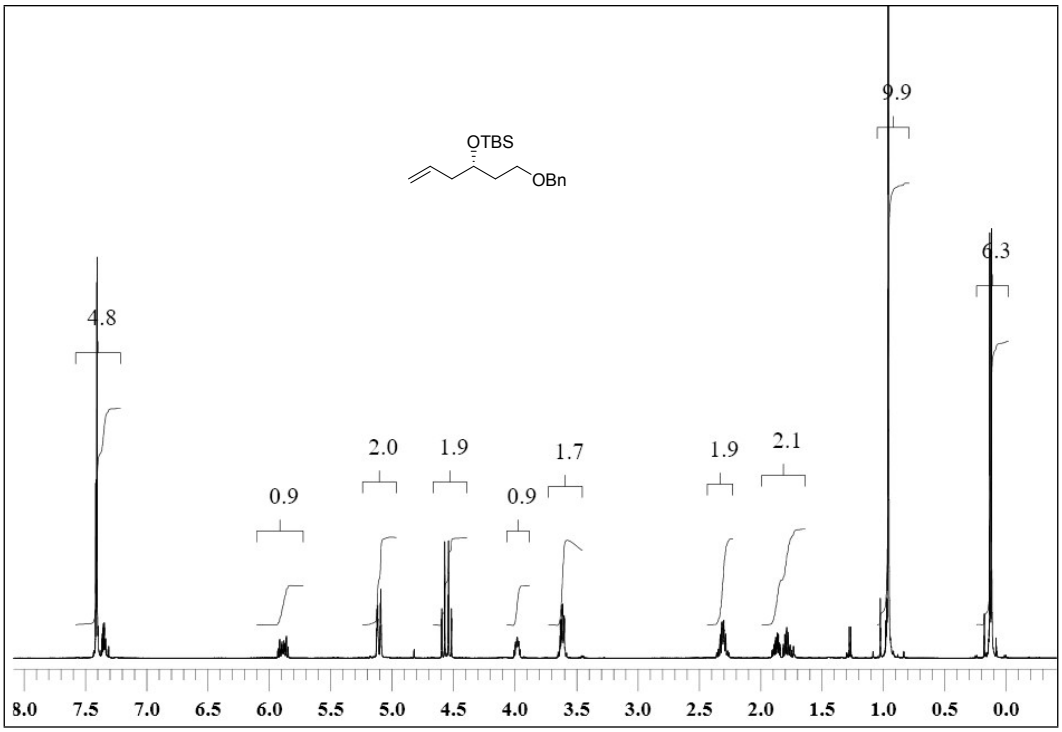
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 5b



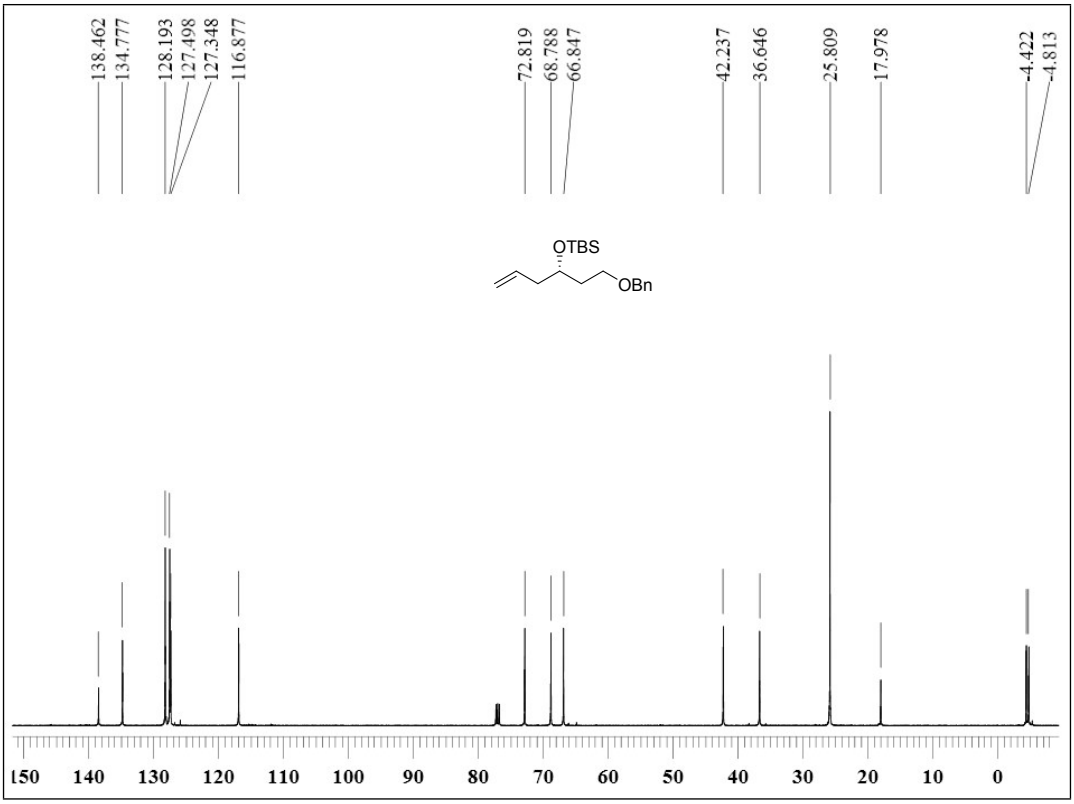
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 5b



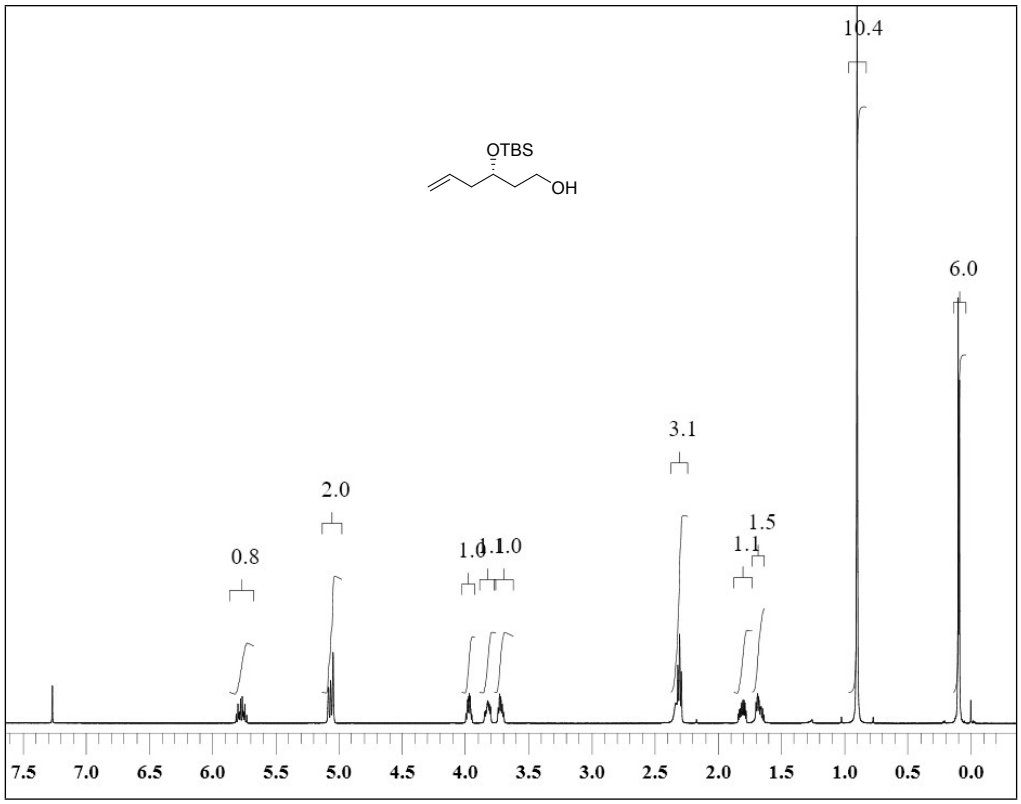
^{1}H NMR (500 MHz, $CDCl_3$) spectrum 5c



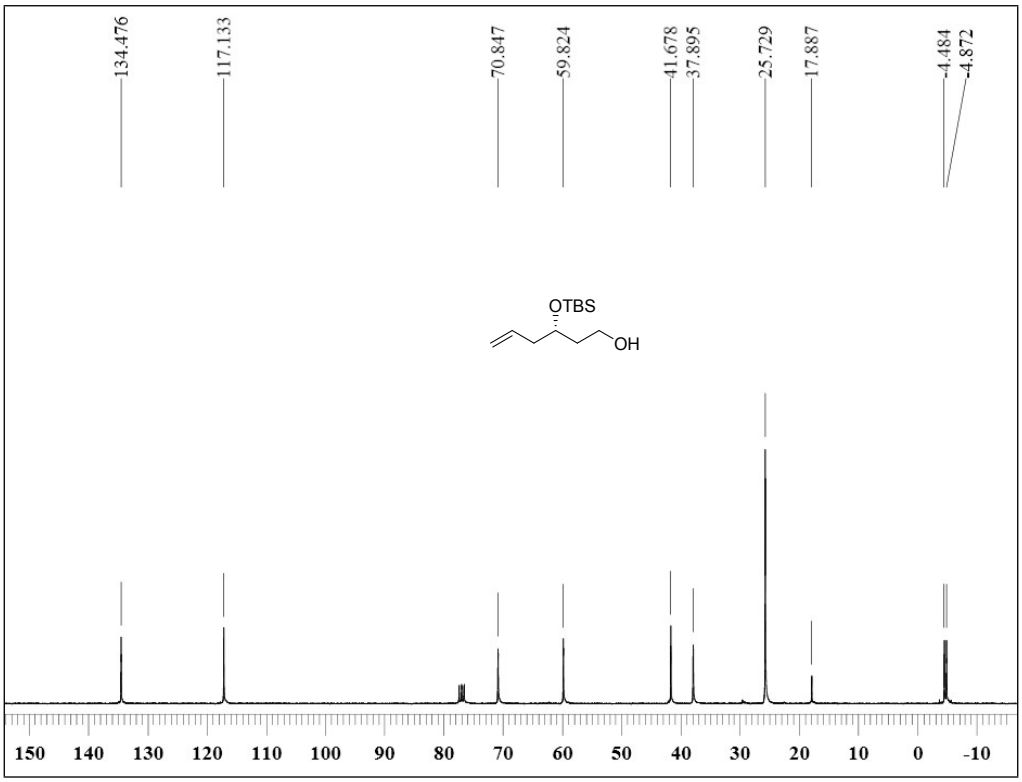
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 5c



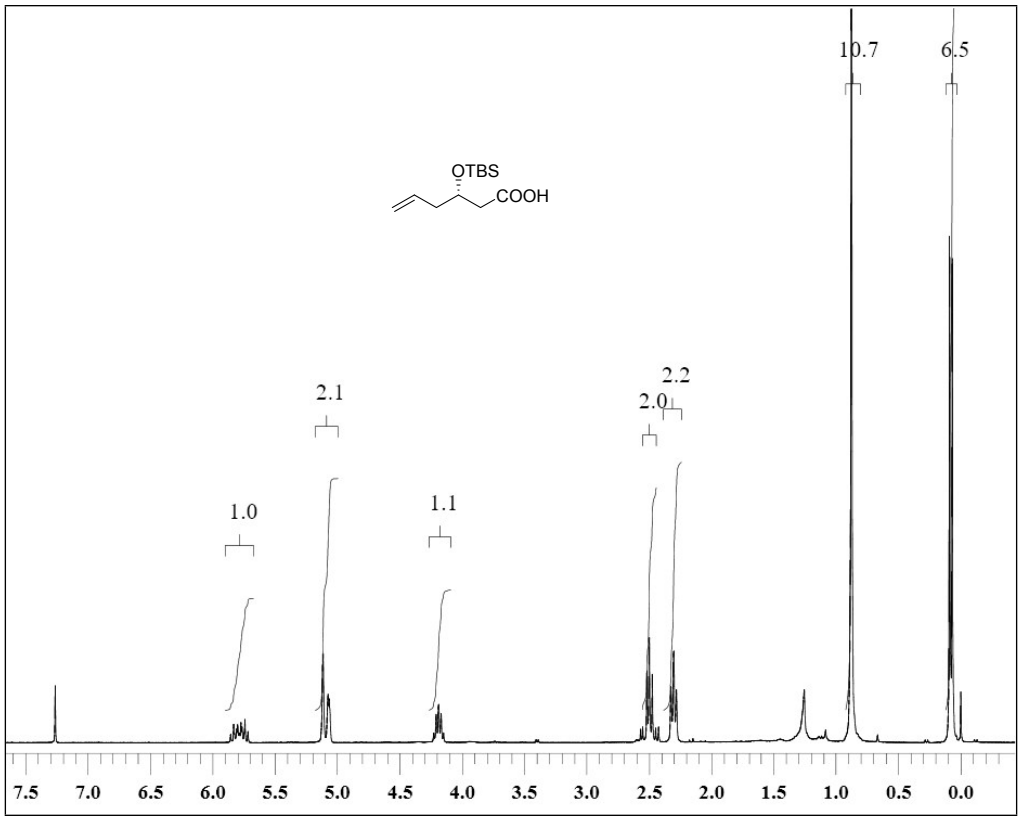
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 5d



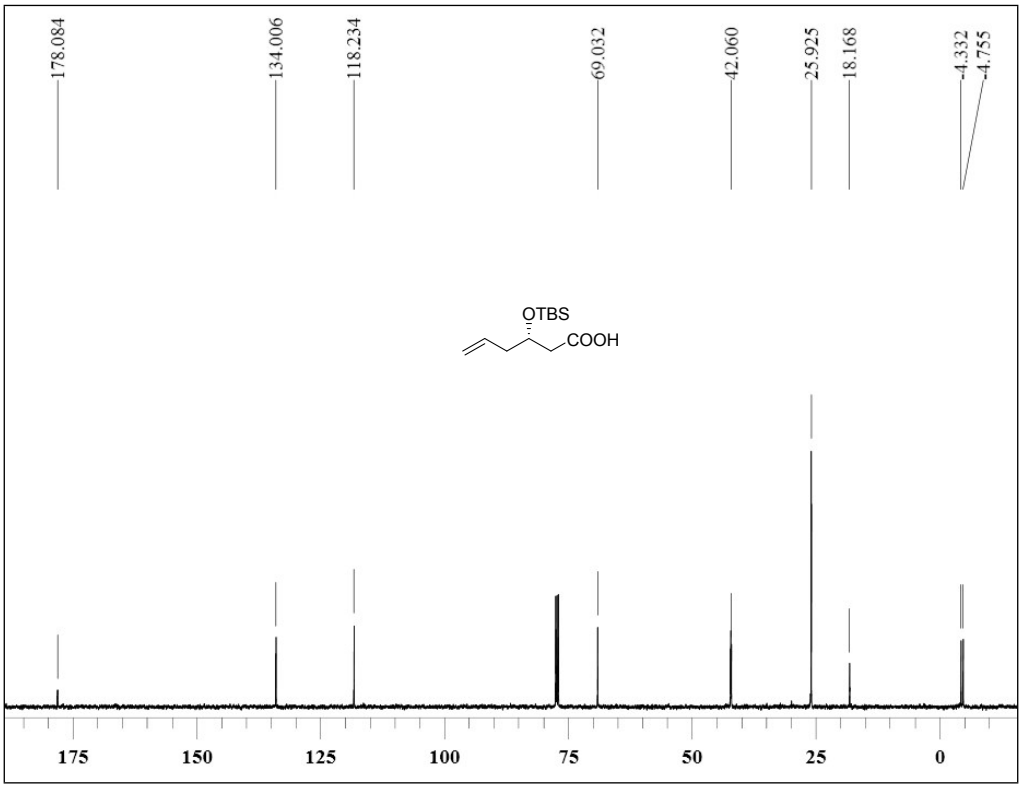
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 5d



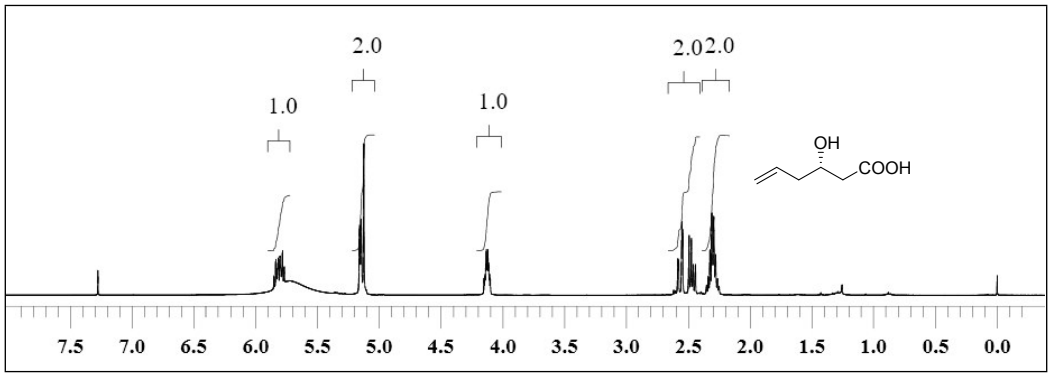
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 5e



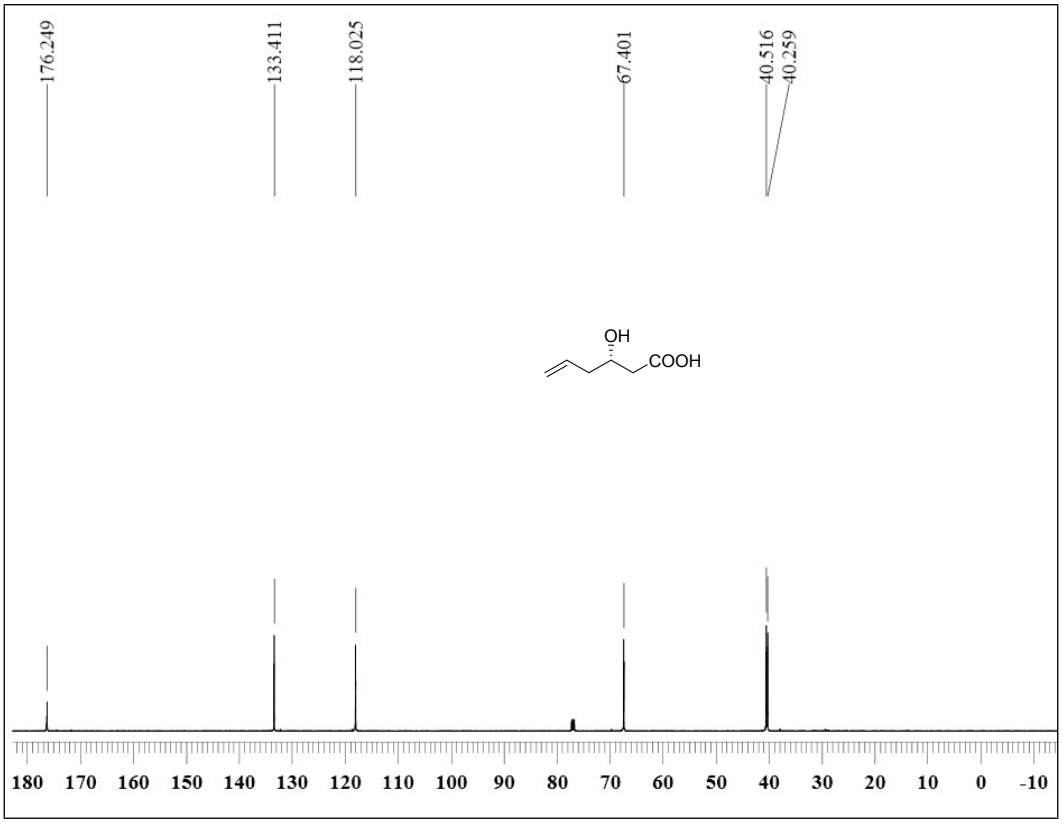
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 5e



^{1}H NMR (500 MHz, $CDCl_3$) spectrum of *ent*-2

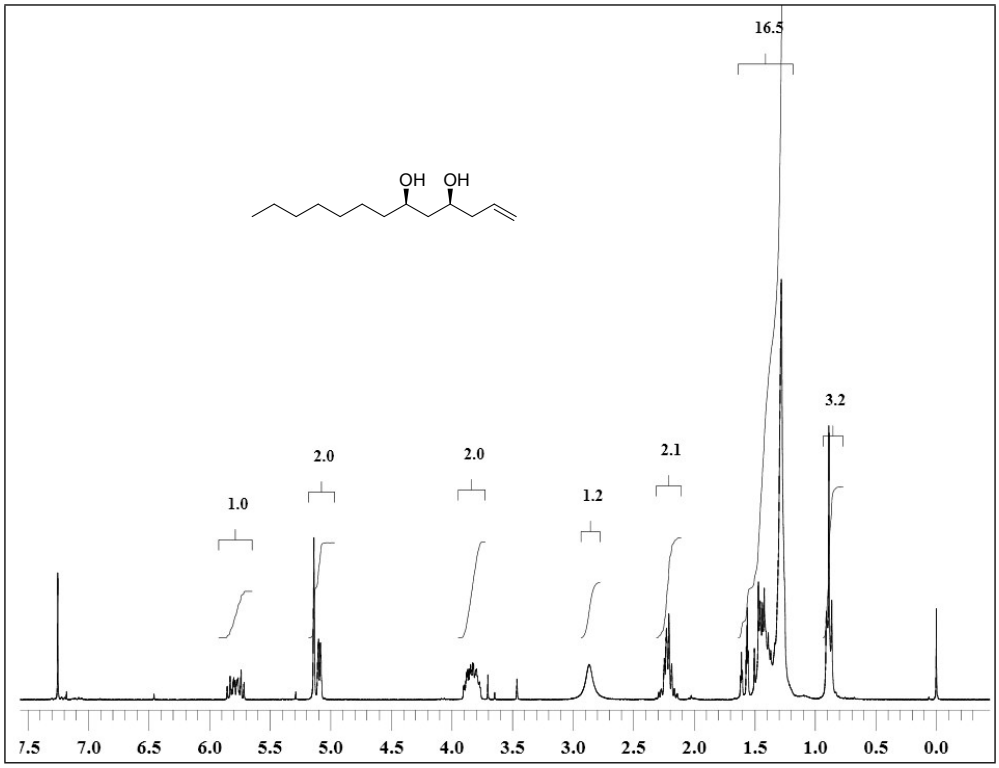


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of *ent*-2

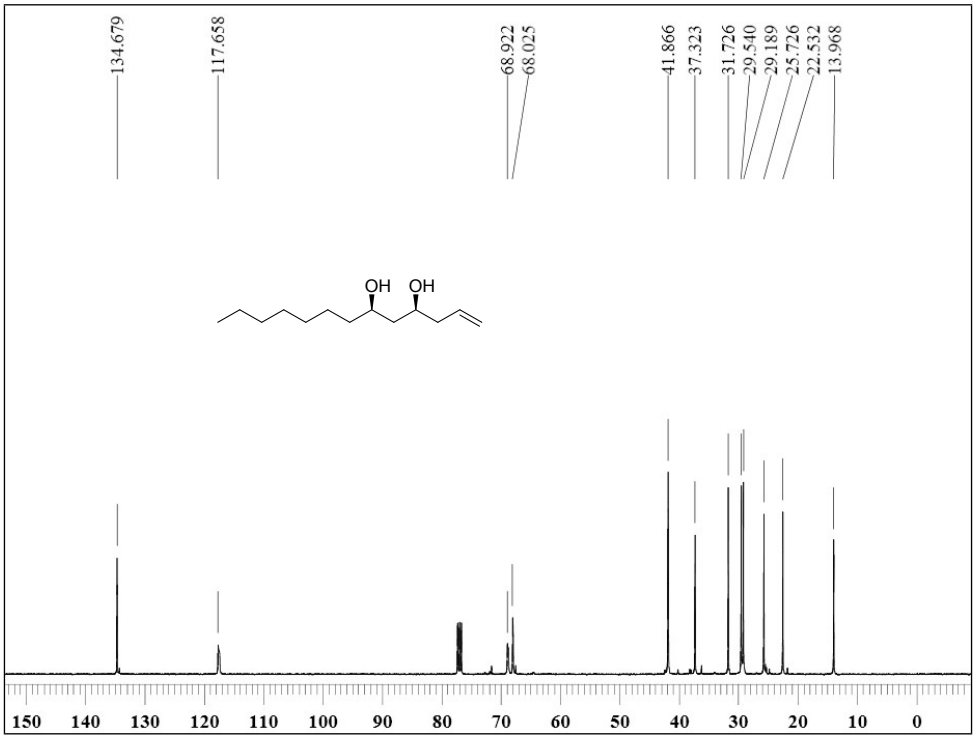


Copies of NMR spectra of products (6b-d), (7,8)

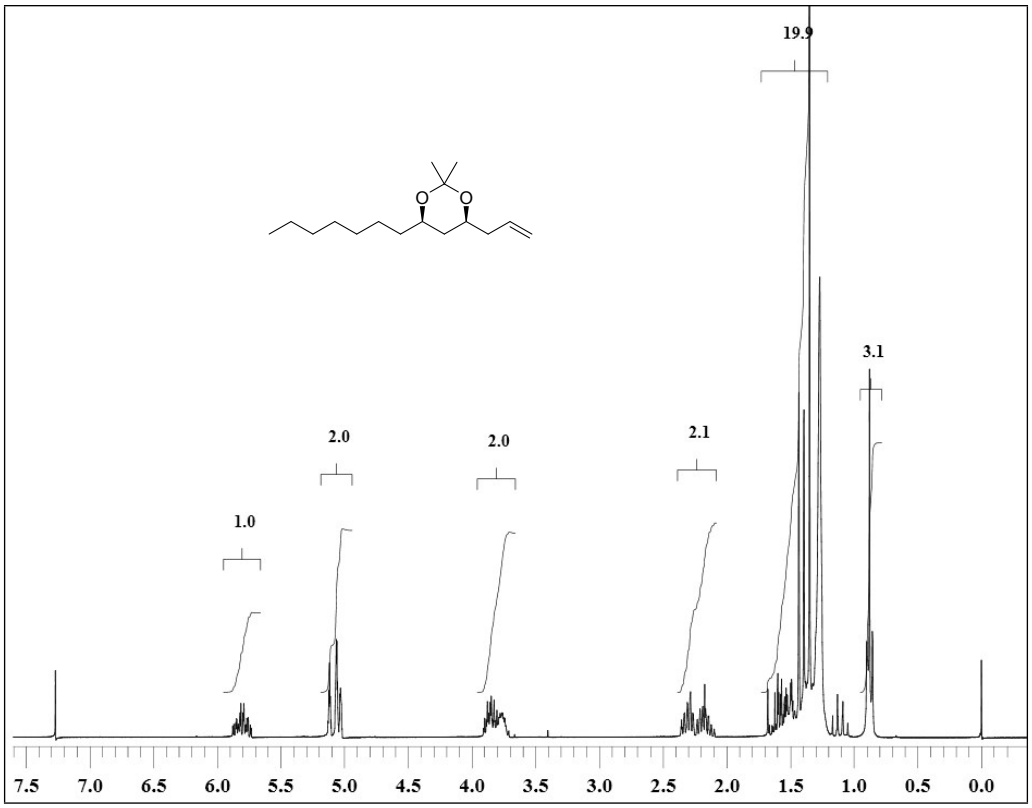
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 6b



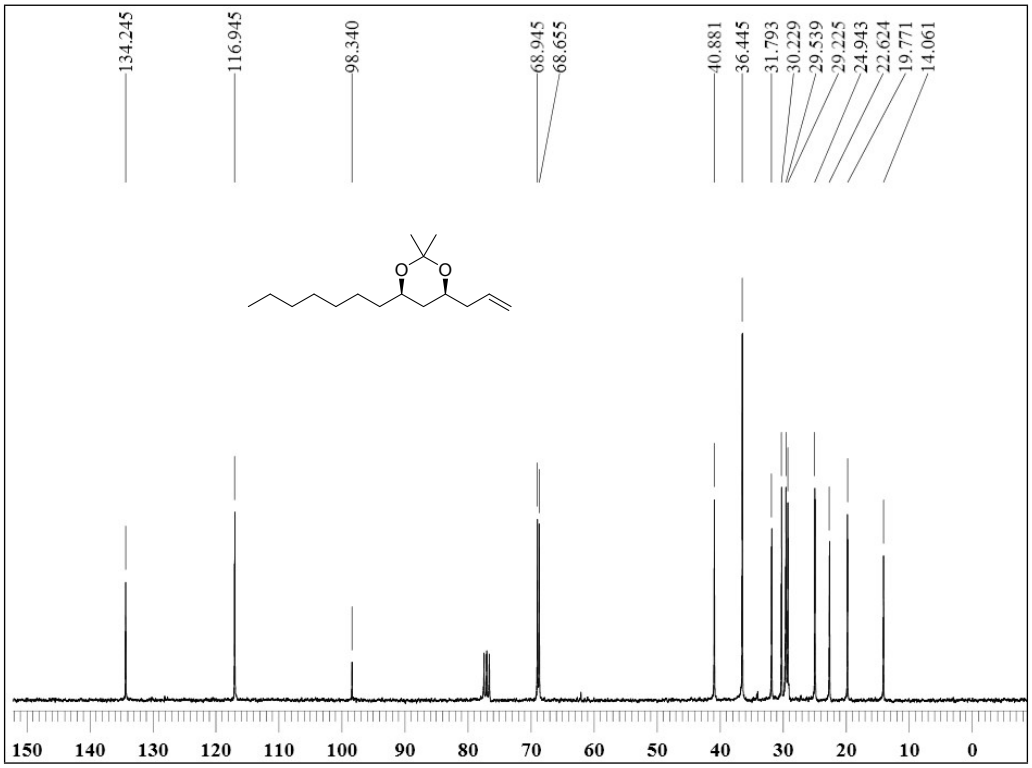
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 6b



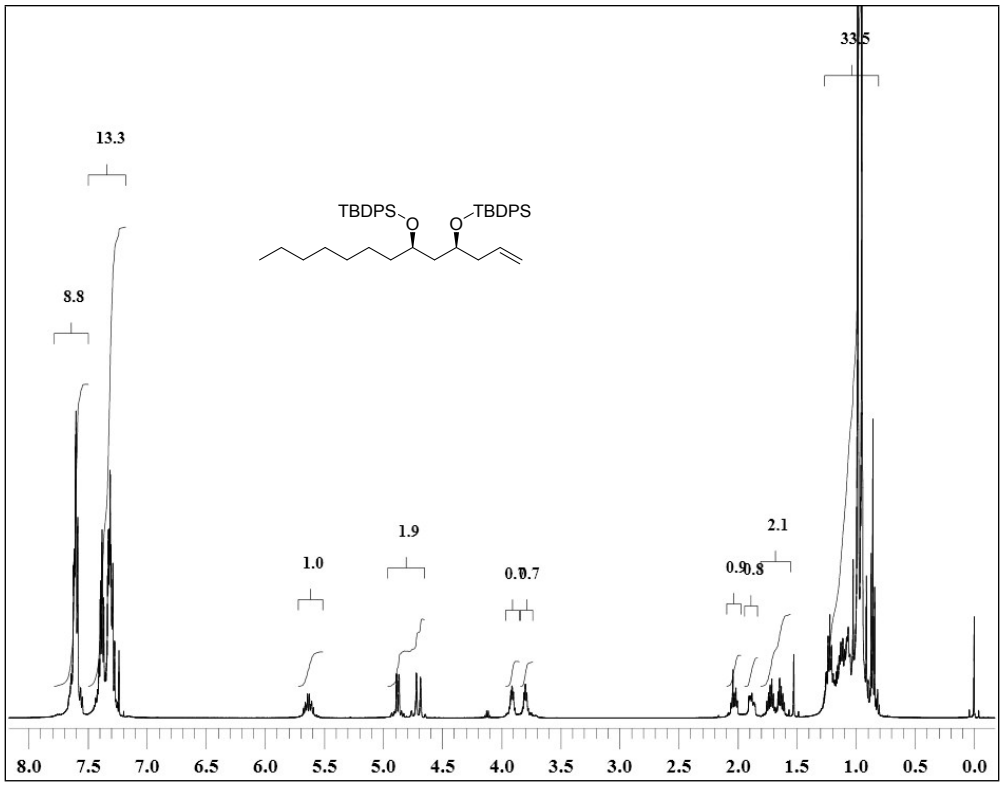
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 5d



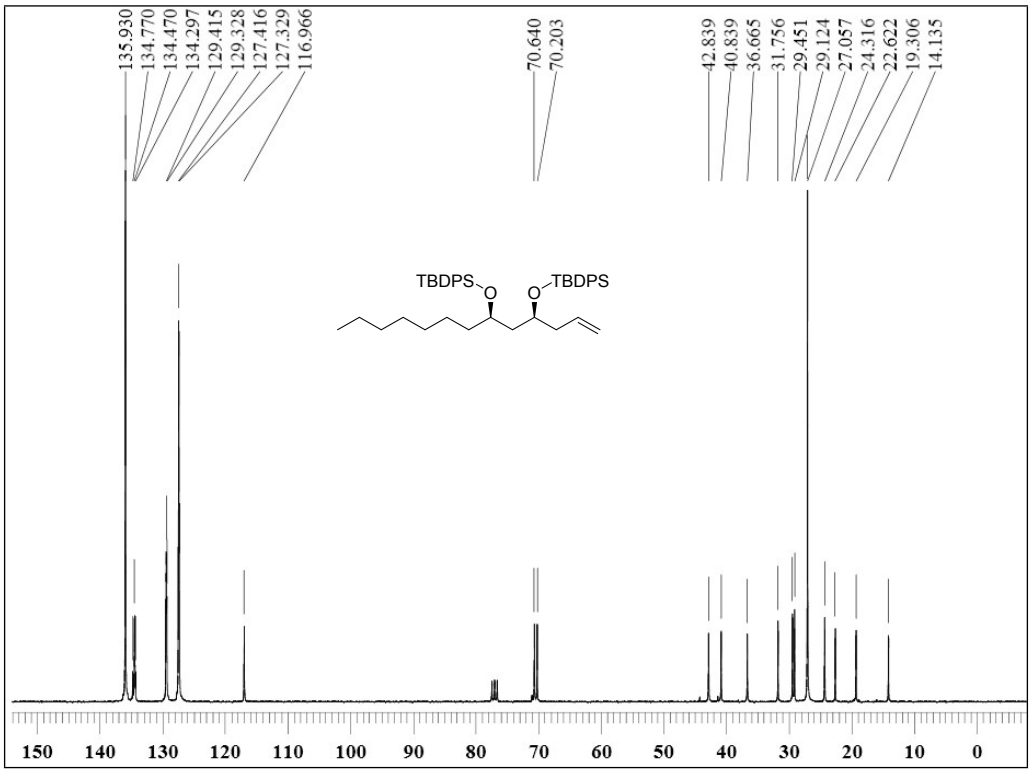
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 5d



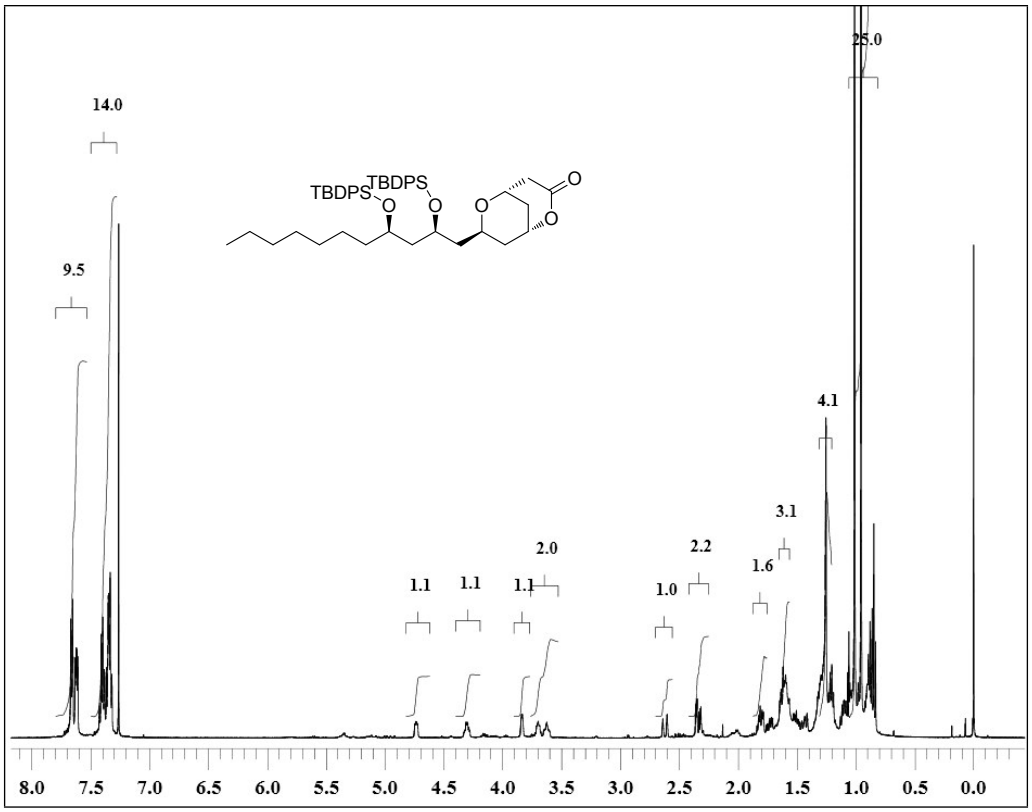
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 5c



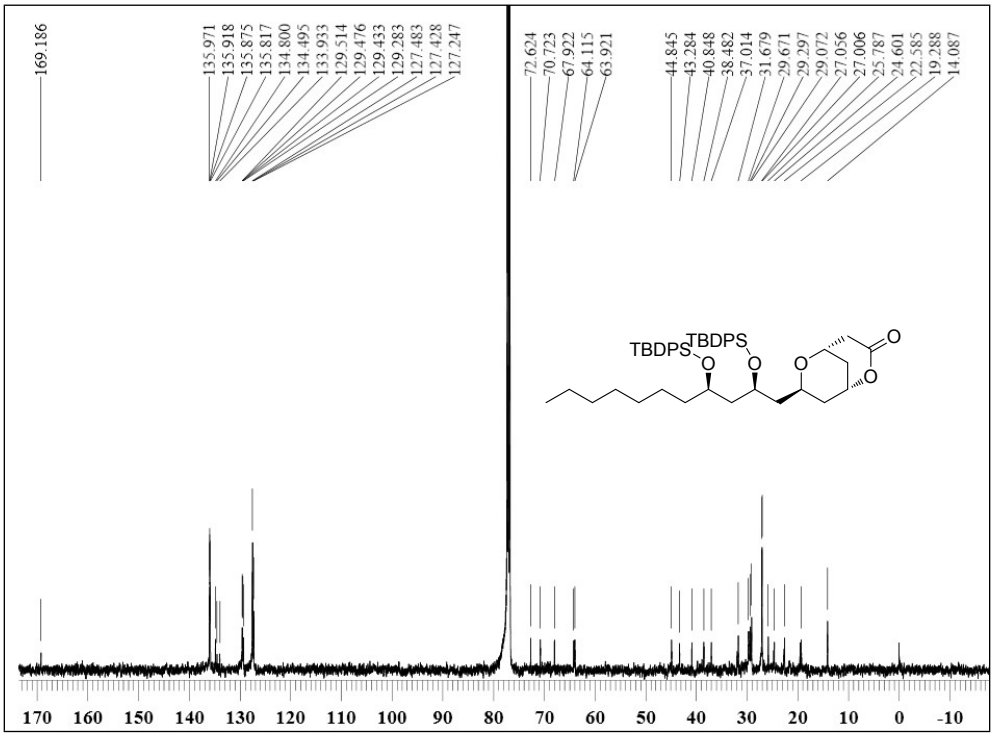
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 5c



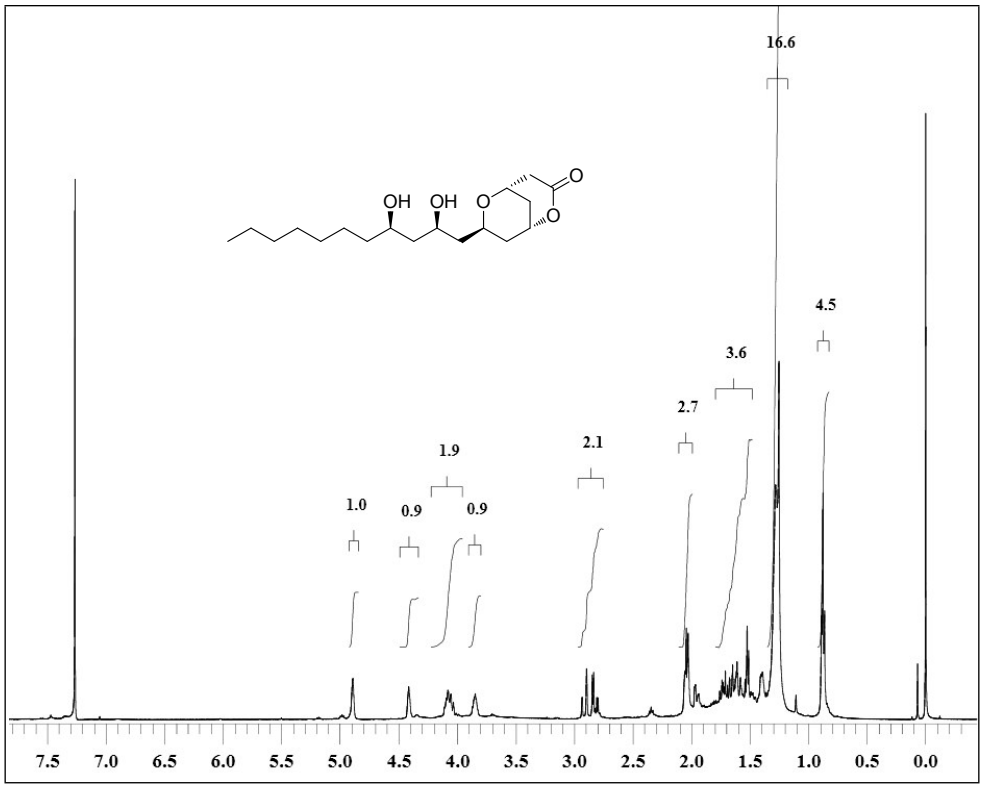
^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 7



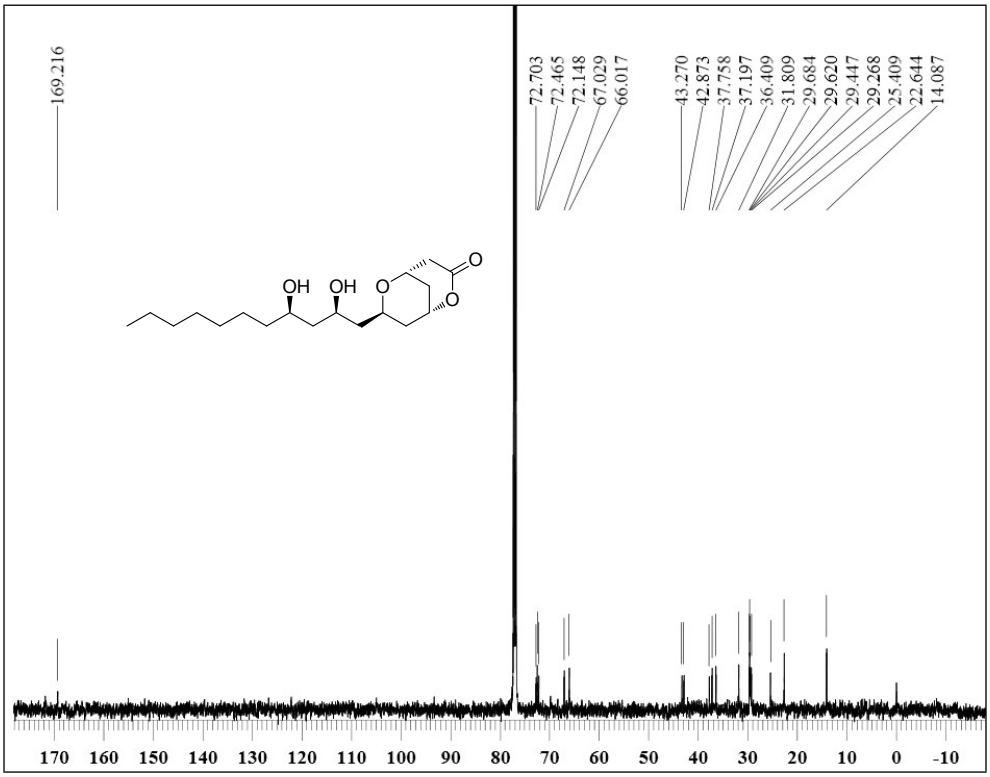
^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 7



^{1}H NMR (500 MHz, $CDCl_3$) spectrum of Polyracitide A (8)

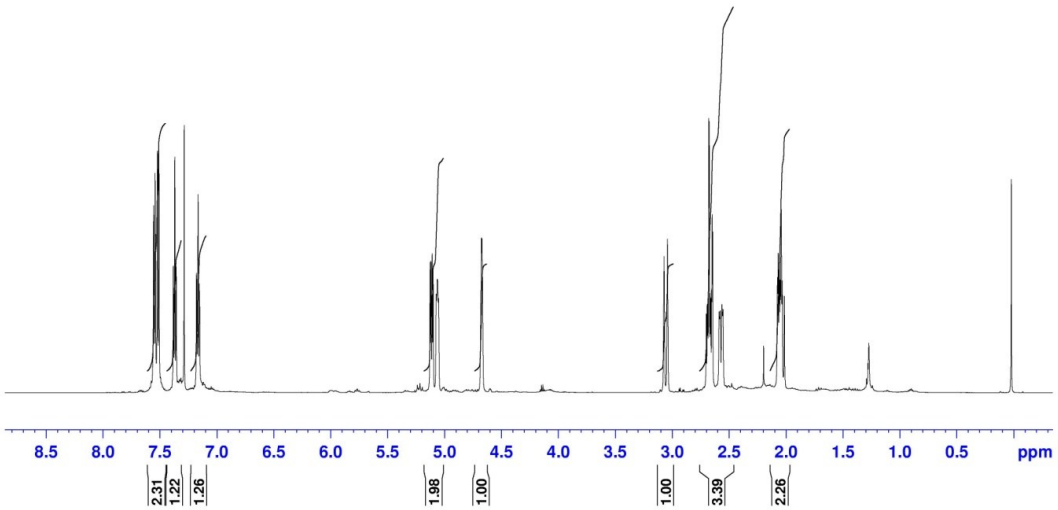


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of Polyracitide A (8)

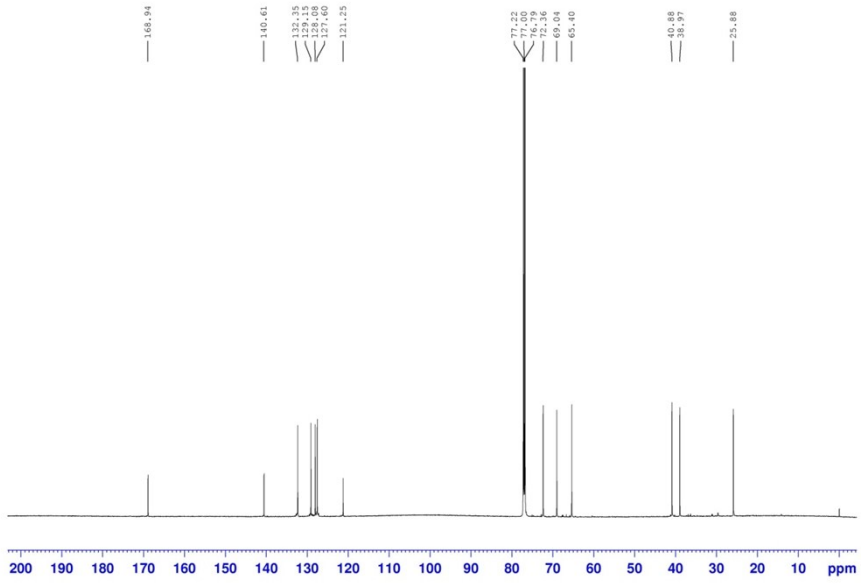


8. NMR experiments of 4a,3k,4b,4f

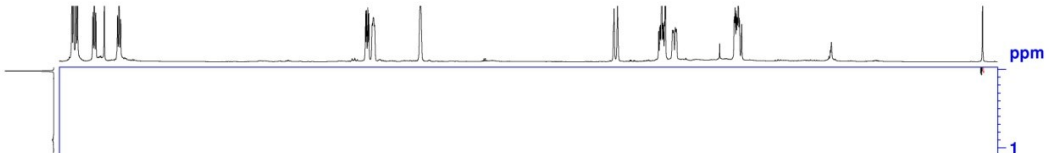
^{1}H NMR spectrum of 4a



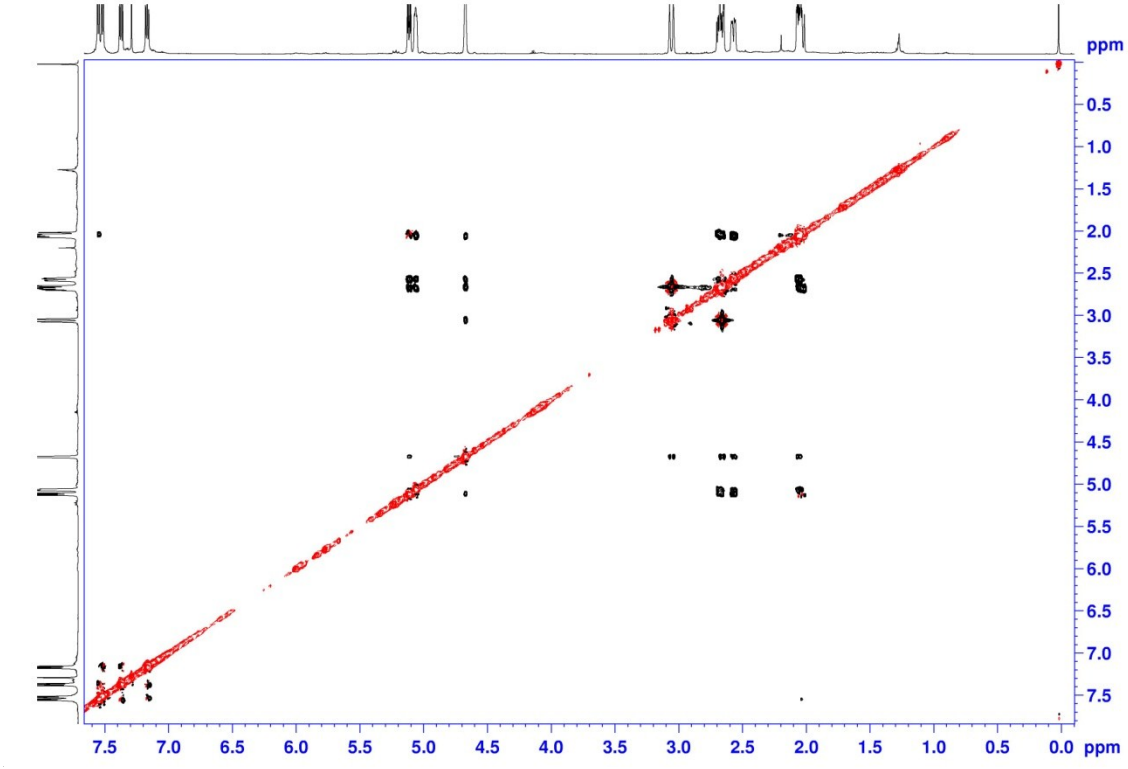
^{13}C NMR spectrum of 4a



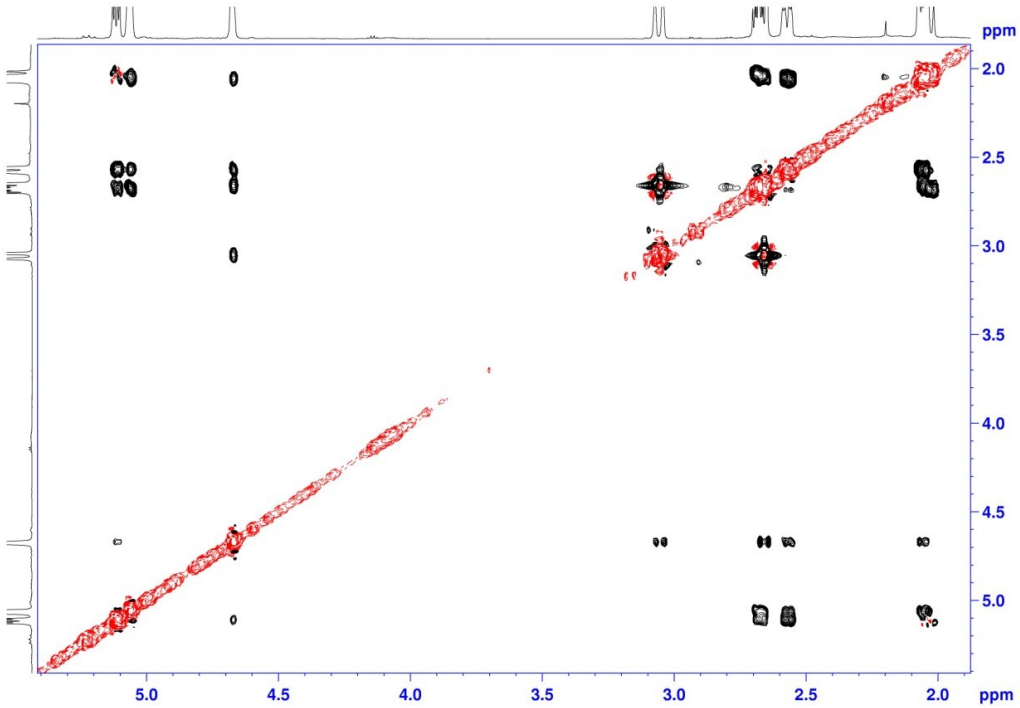
2D Double Quantum Coherence (COSY) spectrum of 4a



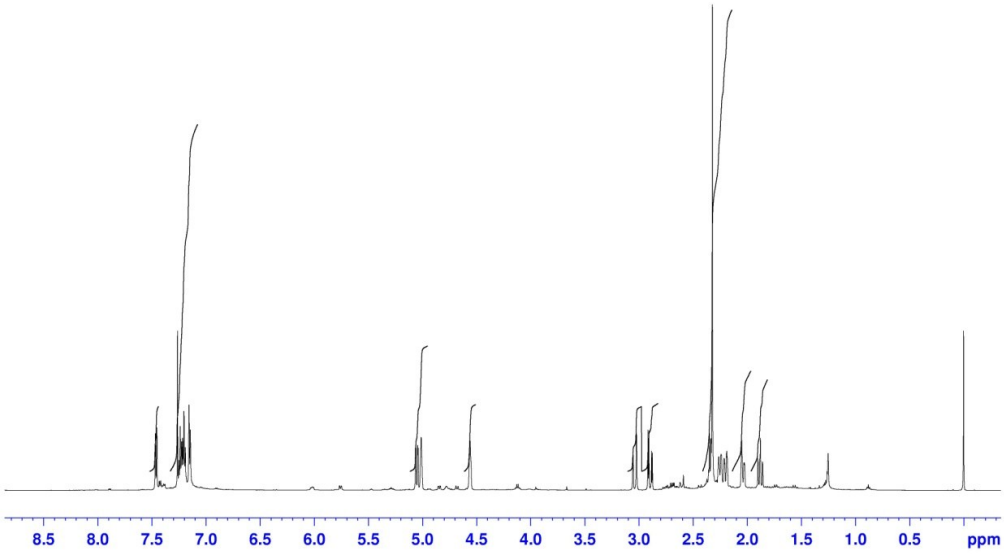
2D Nuclear Overhauser Effect (NOESY) spectrum of 4a



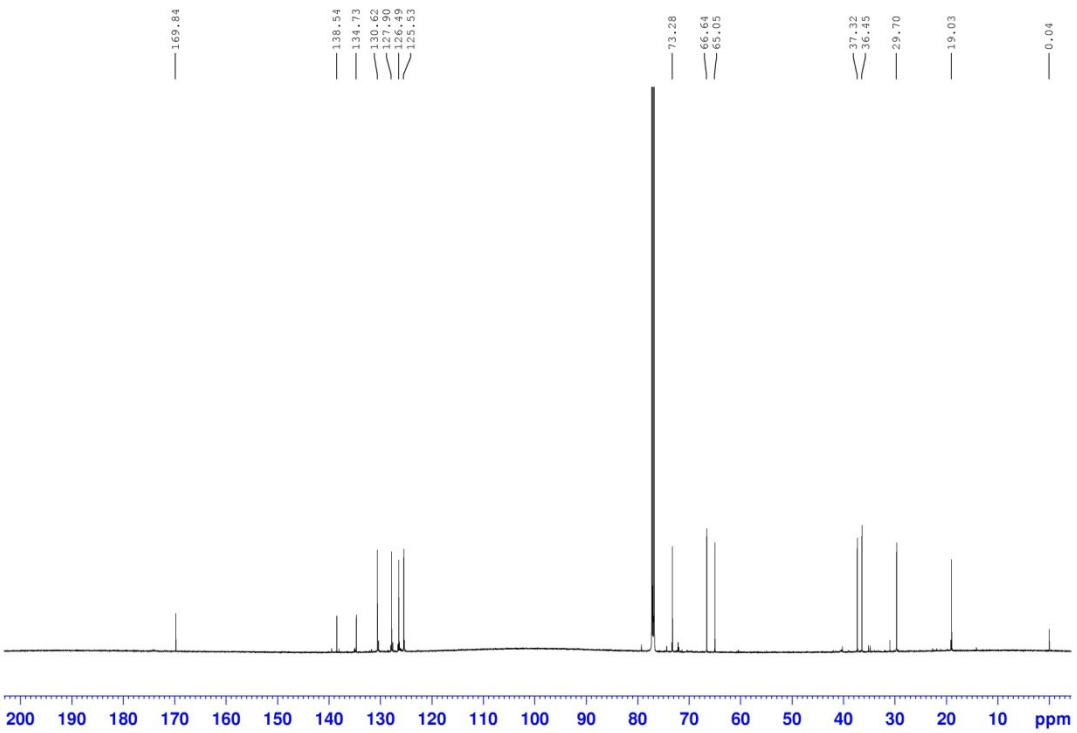
Expansion of 2D Nuclear Overhauser Effect (NOESY) spectrum of 4a



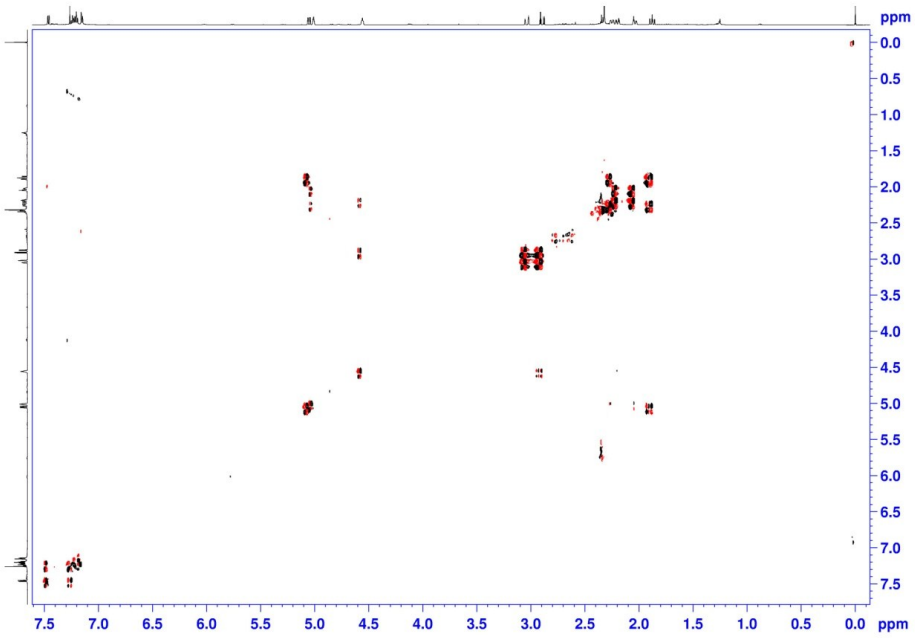
^{1}H NMR spectrum of 3k



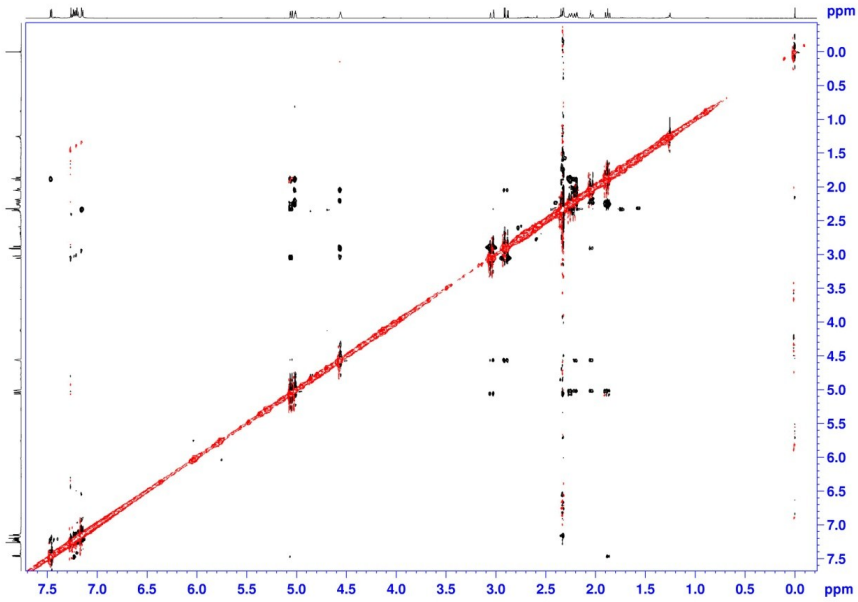
^{13}C NMR spectrum of 3k



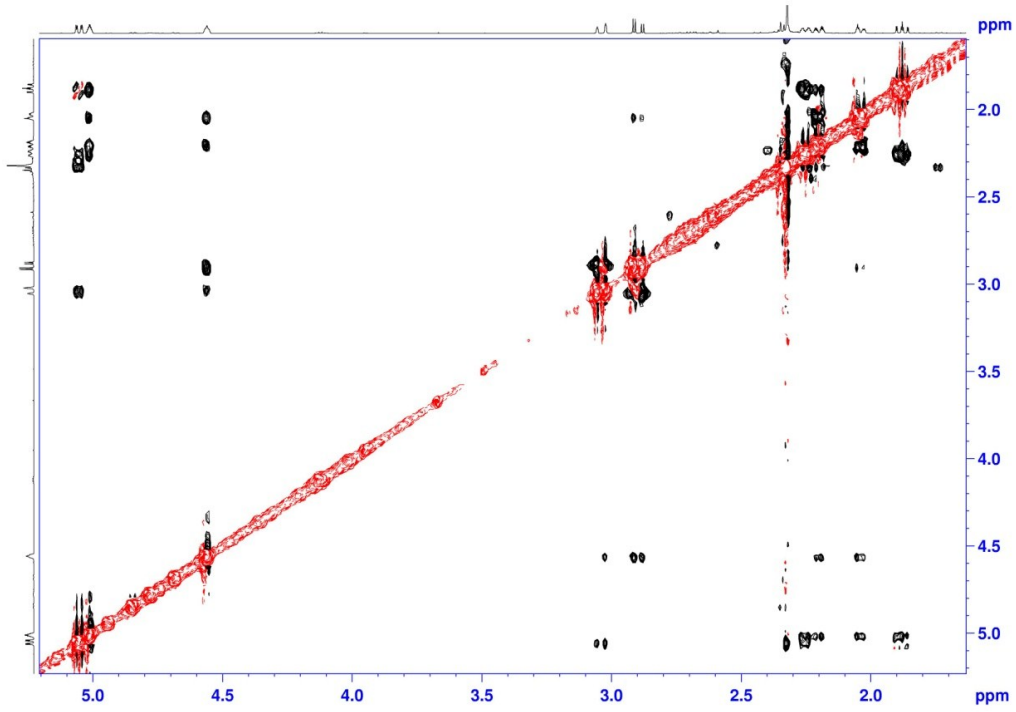
2D Double Quantum Coherence (COSY) spectrum of 3k



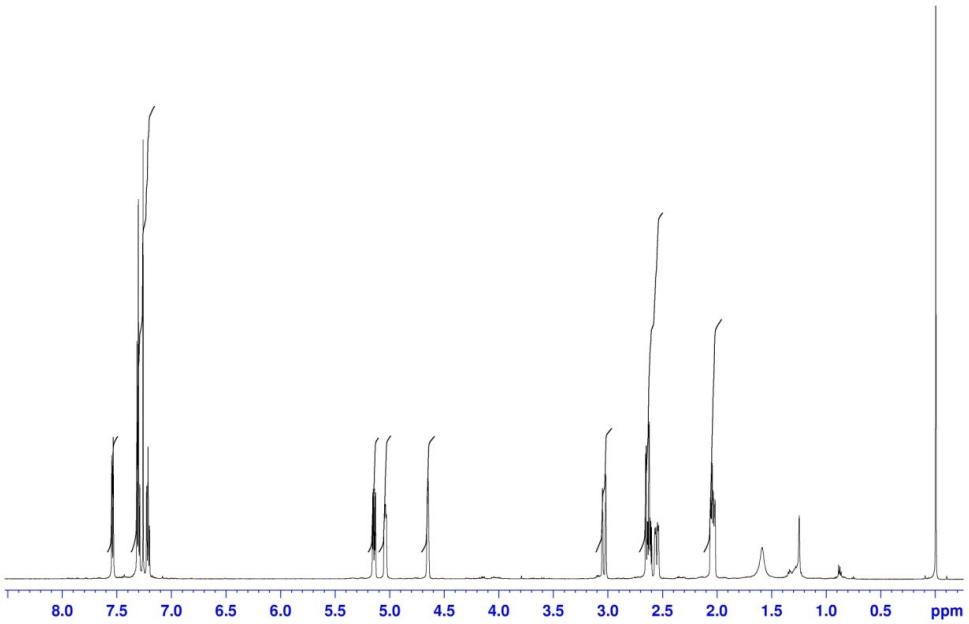
2D Nuclear Overhauser effect (NOESY) spectrum of 3k



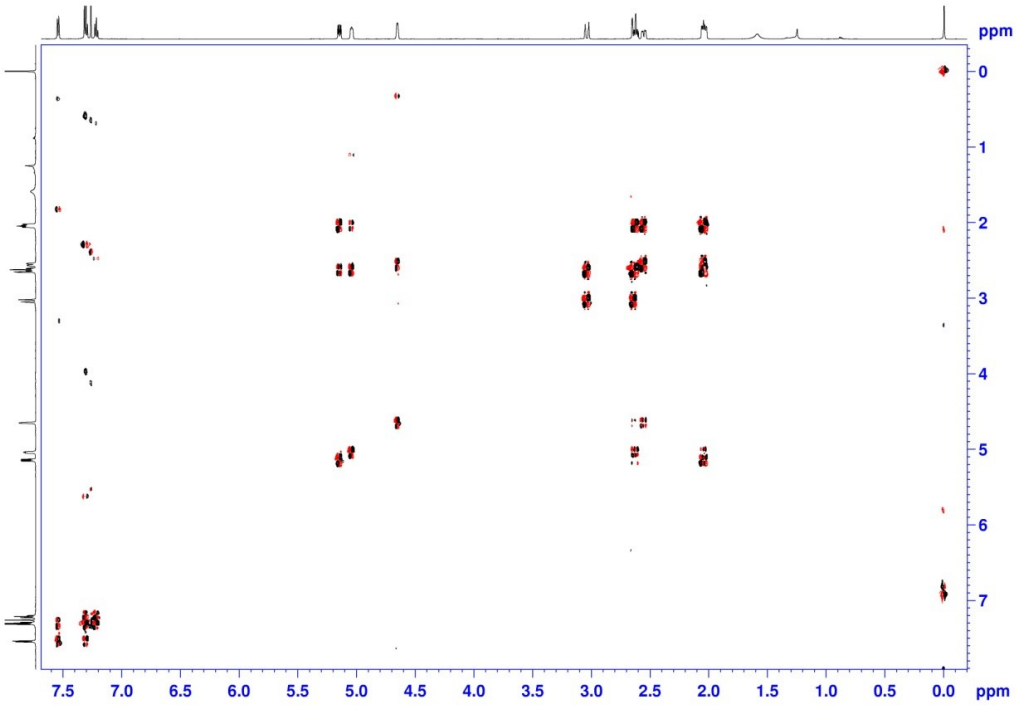
Expansion of 2D Nuclear Overhauser effect (NOESY) spectrum of 3k



^{1}H NMR spectrum of 4b



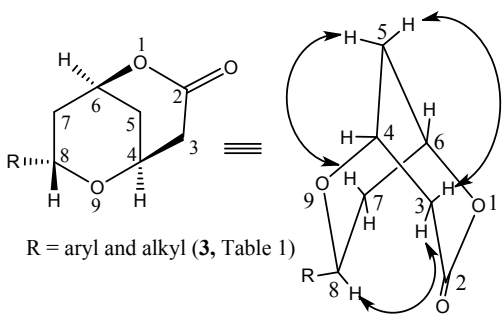
2D Double Quantum Coherence (COSY) spectrum of 4b



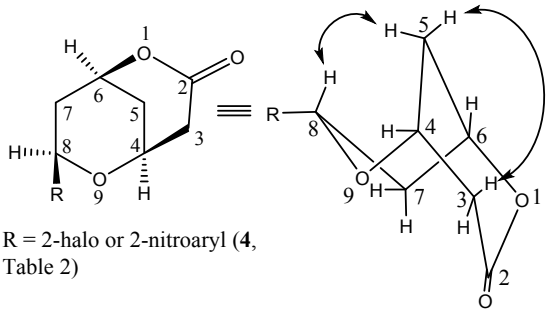
NOE studies of compounds 3-**4**

The absolute stereochemistry of the above compounds were determined by using 1D and 2D NMR experiments. For compounds a-d (left figure), the scalar couplings for H8 ($^3J_{H8\text{-}H7}$=3.0Hz, $^3J_{H8\text{-}H7'}$=11.5Hz), H3($^3J_{H3\text{-}H4}$=5.4Hz), H3'($^3J_{H3'\text{-}H4}$=1.5Hz) and H4 (all small couplings), H6(small couplings) along with the presence of nOe cross correlations between H7(ax)/H5, H8/H3(eq), H5'/H3(ax) suggest the structure adopts a bicyclononane conformation with both rings in $^5C_2$ and $^5C_8$ chair conformation as shown in the figure. For compounds e-g (right figure) the scalar couplings for H8 ($^3J_{H8\text{-}H7}$=5.0Hz, $^3J_{H8\text{-}H7'}$=11.5Hz), along with the nOe cross peaks between H8/H5, H4/H8, H5'/H3(ax) support the first ring of the bicyclononane in $^5C_2$ chair conformation where the second ring adopts a boat conformation with H5 and H8 being flagpole hydrogens as shown in figure x.

Figure x. Characteristic nOe cross peaks of product **3** and **4**

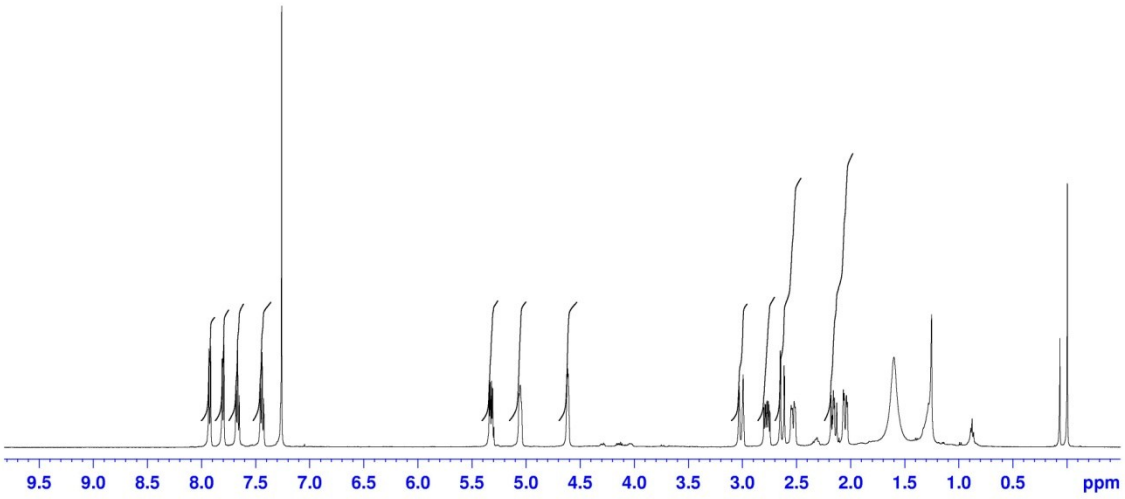


R = aryl and alkyl (**3,** Table 1)

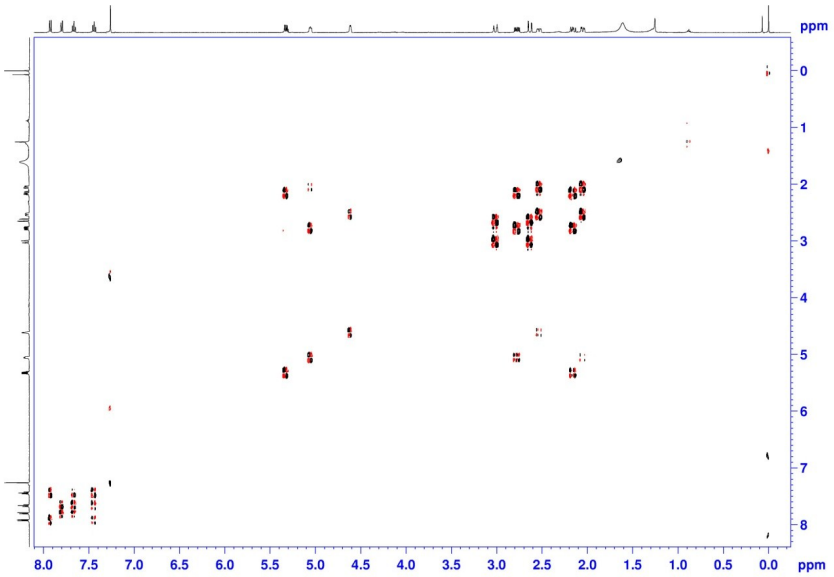


R = 2-halo or 2-nitroaryl (**4**, Table 2)

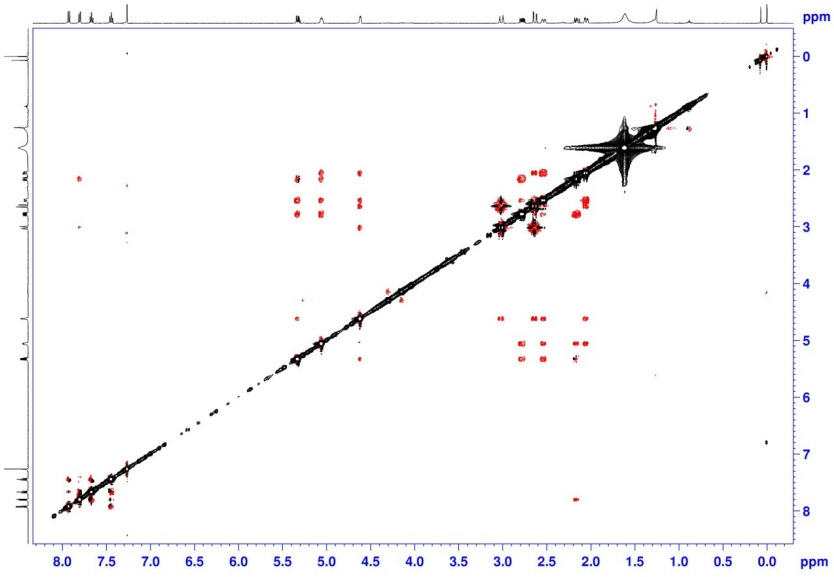
^{1}H NMR Spectrum of compound **4f**



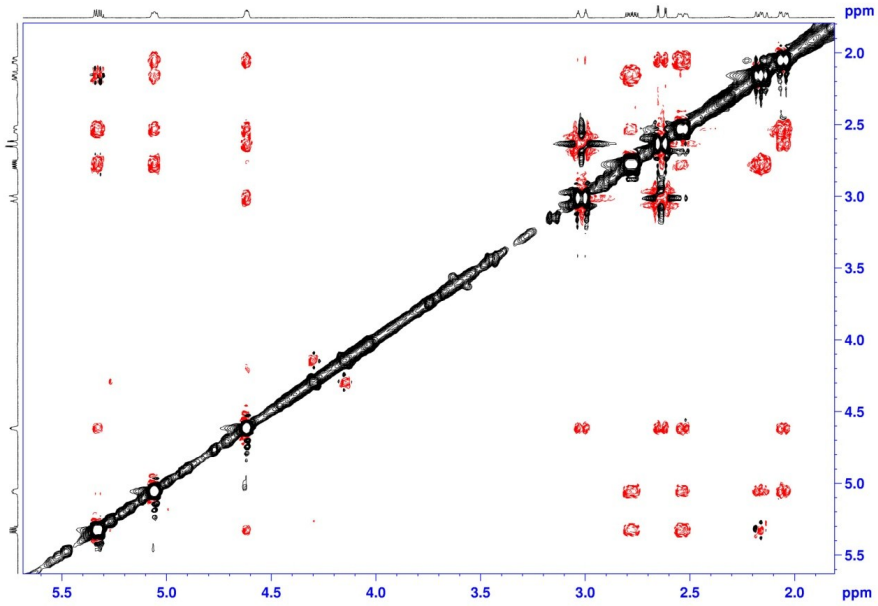
2D DQFCOSY (Double quantum coherence spectroscopy) spectrum of 4f



2D NOESY (Nuclear Overhauser effect spectroscopy) spectrum of compound **4f**



Expansion of 2D NOESY (Nuclear Overhauser effect spectroscopy) spectrum of compound 4f



9. X-ray crystallography of 4b

X-ray data for the compounds were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073Å) with ω-scan method [1]. Preliminary lattice parameters and orientation matrices were obtained from four sets of frames.

Integration and scaling of intensity data was accomplished using SAINT program [1]. The structure was solved by direct methods using SHELXS [2] and refinement was carried out by full-matrix least-squares technique using SHELXL [2]. Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å and U_{iso}(H) = 1.5U_{eq}(C) for methyl H or 1.2U_{eq}(c) for other H atoms]. The methyl groups were allowed to rotate but not to tip. The absolute configuration of the procured material was known in advance and was confirmed by unambiguous refinement of the absolute structure parameter (Flack & Bernardinelli, 2000).

Crystal Data for 4b: $C_{13}H_{13}O_3Cl$ (*M* =252.68): monoclinic, space group $P2_1$ (no. 4), *a* = 7.1086(14) Å, *b* = 6.9376(14) Å, *c* = 12.442(3) Å, *β* = 94.573(3)°, *V* = 611.7(2) Å^3, *Z* = 2, *T* = 294.15 K, μ(MoKα) = 0.305 mm^{-1}, *Dcalc* = 1.372 g/mm^3, 6788 reflections measured (3.284 ≤ 2Θ ≤ 56.766), 2841 unique (R_{int} = 0.0251) which were used in all calculations. The final R_1 was 0.0418 (I > 2σ(I)) and wR_2 was 0.1040 (all data). CCDC 1436533 contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

1. Bruker (2001). SAINT (Version 6.28a) & SMART (Version 5.625). Bruker AXS Inc., Madison, Wisconsin, USA.
2. Sheldrick G. M. (2015**)** Acta Crystallogr C71: 3-8.
3. Flack, H. D. & Bernardinelli, G. (2000). J. Appl. Cryst. 33, 1143–1148.

Figure Caption

Figure 1. A view of **4b**, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary radii.