Supporting Information

Synthetic studies towards volvalerenol A: Access of fully functionalized cycloheptane framework in asymmetric fashion through the exploitation of C_2-symmetry

Rajkumar Sahoo, Saubhik Ghosh, Suman Bhatta, Santu Bisui and Samik Nanda*

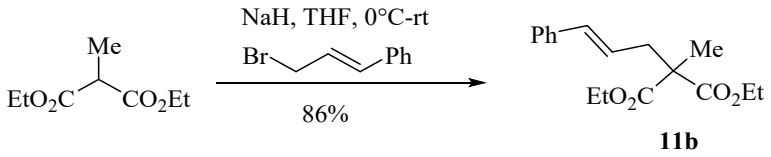
Department of Chemistry, Indian Institute of Technology Kharagpur, Kharagpur, 721302, India

snanda@chem.iitkgp.ac.in

Materials and methods: All oxygen and/or moisture-sensitive reactions were carried out under an N_2 atmosphere in glassware that had been flame-dried under vacuum (ca. 0.5 Torr) and purged with N_2 before use. Unless otherwise stated, materials were obtained from commercial suppliers and used without further purification. THF and diethyl ether were distilled from sodium benzophenone ketyl. Dichloromethane (DCM), DMSO, DMF and hexane were distilled from calcium hydride. Reactions were stirred magnetically using Teflon-coated magnetic stirring bars. Teflon-coated magnetic stirring bars and syringe needles were dried in an oven at 120 °C for at least 12 h prior to use then cooled in a desiccator's cabinet over dry calcium chloride. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates with UV light, ethanolic anisaldehyde, and phosphomolybdic acid/heat as developing agents. Silica gel 100-200 mesh was used for column chromatography. Yields refer to chromatographically and spectroscopically homogeneous materials unless otherwise stated. NMR spectra were recorded on 600, 500, 400 and 200 MHz spectrometers at 25 °C in $CDCl_3$ using TMS as the internal standard. Chemical shifts are shown in δ. ^{13}C NMR spectra were recorded with a complete proton decoupling environment. The chemical shift value is listed as δ_H and δ_C for ^1H and ^{13}C, respectively. Coupling constants (*J*) are reported in hertz (Hz) and the resonance multiplicity abbreviations used are s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; m, multiplet; comp, overlapping multiplets of magnetically non-equivalent protons. Optical rotations were measured on Anton

Paar digital polarimeter and Mass spectrometric analysis was performed in the CRF, IIT-Kharagpur (TOF analyzer).

Diethyl 2-cinnamyl-2-methylmalonate (11b)



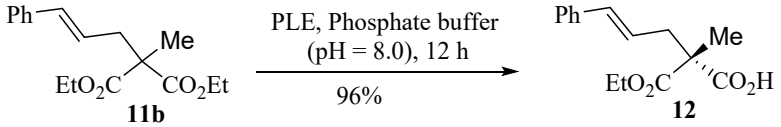
11b

To a stirred solution of diethyl methylmalonate (20 g, 0.114 mol) in THF (300 mL) at 0 °C was added NaH (60%; 5.44 g, 0.136 mol) in portions. The mixture was then warmed to room temperature and stirred for 1 hour. *E*-cinnamyl bromide (37.24 g, 0.136 mol) was next added to the reaction solution. The reaction solution was stirred at room temperature for 4h and then cooled to 0 °C. The reaction mixture was then quenched with saturated NH_4Cl solution (80 mL) carefully. The product was extracted with diethyl ether (4 × 200 mL), and the extracts were washed with brine (2 × 200 mL) and dried over Na_2SO_4. The solution was then filtered and the solvent was evaporated in vacuo. Purification by flash chromatography (10% EtOAc in hexanes) afforded diethyl 2-cinnamyl-2-methylmalonate **11b** (28.51 g, 86% yield) as a light yellow liquid.

R_f = 0.85 (10% EtOAc in hexane).

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.44 – 7.02 (m, 5H), 6.46 (d, *J* = 15.7 Hz, 1H), 6.13 (dd, *J* = 15.3, 7.8 Hz, 1H), 4.21 (q, *J*= 7.1 Hz, 4H), 2.86 – 2.54 (m, 2H), 1.45 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 6H).; ^{13}C NMR (50 MHz, $CDCl_3$) δ 172.1, 137.3, 134.1, 128.6, 127.5, 126.3, 124.5, 61.4, 54.0, 39.5, 20.1, 14.2; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{17}H_{23}O_4$ = 291.1596, found = 291.1598.

(*R*,*E*)-2-(ethoxycarbonyl)-2-methyl-5-phenylpent-4-enoic acid (12)



11b **12**

To a suspension of the diester **11b** (28.0 g, 0.096 mmol) in phosphate buffer (pH 8.0; 2.1 L) was added PLE (crude acetone powder of pig liver) and the reaction mixture was stirred at 30 ºC in an incubator shaker (180 rpm). The disappearance of compound **11b** was measured by TLC analysis, and the solution was made acidic with 2.0 M HCl to pH = 3.0. The aqueous layer was extracted with EtOAc (1.5 L × 2) and thoroughly washed with brine. The organic extract was then dried over Na_2SO_4, filtered and evaporated under a vacuum. The crude residue was

then purified by flash chromatography (hexane/ethyl acetate=4/1) to afford **12** (24.21 g, 96%, 96% ee) as a colorless liquid.

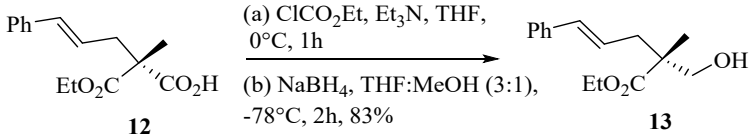
R_f = 0.25 (20% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 5.2 (*c* = 1.0 MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.22 (m, 5H), 6.51 (d, *J* = 15.7 Hz, 1H), 6.15 (m, *J* = 15.4, 7.5 Hz, 1H), 4.25 (m, *J* = 10.7, 6.7, 3.7 Hz, 2H), 2.83 (ddd, *J* = 42.7, 14.0, 7.5 Hz, 2H), 1.52 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 172.0, 137.1, 134.5, 128.6, 127.6, 126.4, 123.9, 61.9, 54.0, 39.6, 20.2, 14.2.

HRMS (ESI) *m/z*: calcd for $C_{15}H_{18}O_4Na$ $[M+Na]^+$:285.1103, Found:285.1105.

(*R*,*E*)-ethyl 2-(hydroxymethyl)-2-methyl-5-phenylpent-4-enoate (13)



Triethylamine (9.6 mL, 0.1 mol) was added at 0^{o}C to a stirred solution of monoester **12** (24.0 g, 0.0914 mol) in THF (300 mL), and then Ethyl chloroformate (13.9 mL, 0.1 mol) was introduced dropwise at the same temperature. The reaction solution was then allowed to stir for 1 hour, and then the reaction mixture was filtered and the precipitate was washed with cold THF. The filtrate was then cooled to –78 ^{o}C and $NaBH_4$ (3.78 g, 0.10 mol) was introduced to the reaction flask portionwise. Methanol (100 mL) was then added dropwise through a syringe over 30 min. The reaction solution was then kept at the same temperature for 2h, after that the cooling bath was removed and 10% HCl solution was added slowly until no residual $NaBH_4$ remained. Evaporation of THF under vacuum afforded a gummy residue. Which was then extracted with CH_2Cl_2 (3 ×100 mL) and thoroughly washed with brine. The organic solvent was dried with Na_2SO_4. Filtration and evaporation under vacuum afforded the crude alcohol which was purified with coolumn chromatography on silica gel (ethyl acetate/petroleum ether 1:6) furnished the colourless liquid **13** (18.8 g, 83%).

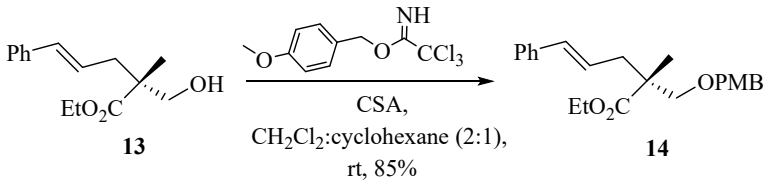
R_f = 0.50 (20% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 15.4 (*c* = 1.0 MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 4H), 7.23 (t, *J* = 7.3 Hz, 1H), 6.47 (d, *J* = 15.8 Hz, 1H), 6.19 (dd, *J* = 15.6, 7.7 Hz, 1H), 4.20 (m, *J* = 10.8, 6.9, 3.7 Hz, 2H), 3.75 (d, *J* = 11.2 Hz, 1H), 3.63 (d, *J* = 11.2 Hz, 1H), 3.04 – 2.77 (m, 1H), 2.58 – 2.46 (m, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.25 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 176.6, 137.3, 133.4, 128.5, 127.3, 126.1, 124.9, 67.8, 60.8, 48.2, 39.0, 19.5, 14.2.

HRMS (ESI) *m/z*: calcd for $C_{15}H_{20}O_3$ $[M+H]^+$:249.1491, Found:249.1495.

(*R*,*E*)-ethyl 2-(((4-methoxybenzyl)oxy)methyl)-2-methyl-5-phenylpent-4-enoate (14)



4-Methoxybenzyl alcohol (17.43 mL, 0.14 mol) was added to a suspension of NaH (0.672 g, 0.028 mmol) in Et_2O (150 mL) at room temperature. After 30 min, the mixture was cooled to 0 °C and Cl_3CCN (16.8 mL, 0.168 mol) was added. The mixture was allowed to warm to room temperature. After 4 hours, the solvent was evaporated. Hexane (150 mL) and MeOH (3.0 mL) were added and the solution was swirled heavily, the mixture was then filtered through celite and the solvent was evaporated to afford the crude trichloroacetimidate. To this solution was added CH_2Cl_2 (74 mL) and cyclohexane 220 mL, the alcohol **13** (18.5 g, 0.074 mol) and CSA (1.7g, 0.0074 mol) at room temperature. After 18 hours, saturated aqueous $NaHCO_3$ (15 mL) was added and the mixture was extracted with Et_2O (3 × 100 mL). The organic layers were washed with water and purified by column chromatography on silica, eluting with petrol–EtOAc (9:1), to furnish the ester **14** (22.6 g, 85%) as an oil.

R_f = 0.80 (20% EtOAc in hexane).

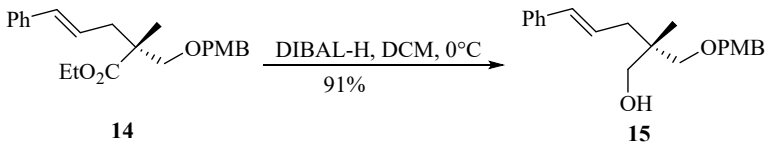
$[\alpha]_D^{30}$ = + 10.8 (*c* = 1.0 MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 14.0, 6.3 Hz, 7H), 6.90 (t, *J* = 7.8 Hz, 3H), 6.41 (d, *J* = 15.7 Hz, 1H), 4.48 (s, 3H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 3.51 (q, *J* = 8.8 Hz, 2H), 2.57 (dd, *J* = 13.6, 7.5 Hz, 1H), 2.47 (dd, *J* = 13.6, 7.7 Hz, 1H), 1.32 – 1.21 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.7, 159.4, 137.6, 133.4, 129.6, 129.3, 128.7, 127.3, 126.32, 125.7, 113.9, 74.6, 73.1, 60.7, 55.4, 47.6, 39.0, 20.3, 14.5.

HRMS (ESI) *m/z*: calcd for $C_{23}H_{29}O_4$ $[M+H]^+$:369.2066, Found:369.2072.

(*S*,*E*)-2-(((4-methoxybenzyl)oxy)methyl)-2-methyl-5-phenylpent-4-en-1-ol (15)



Under argon atmosphere, to a stirred solution of **14** (22.6 g, 0.061 mol) in dry CH_2Cl_2 (150 mL) at –78°C was added dropwise a 1.0 M solution of DIBAL-H in toluene (120 mL, 0.12 mol) over 30 min and was stirred at the same temperature for 3 hours. The reaction solution was then quenched by slow addition of saturated solution of potassium sodium tartrate (15.0 mL), followed by addition of distilled water. The organic solution was then extracted with ether and

washed with brine. The organic extract was then dried with Na_2SO_4 and evaporated under vacuum. The crude alcohol was then purified by flash column chromatography (10% ethyl acetate / n-hexane) to afford **15** as a colorless liquid (18.1 g, 91%).

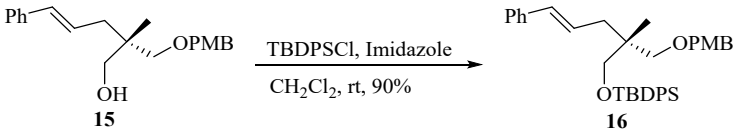
R_f = 0.25 (10% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 6.4 (*c* = 1.0 MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.1 Hz, 2H), 7.30 – 7.26 (m, 2H), 7.23 (t, *J* = 6.6 Hz, 1H), 6.91 (d, *J* = 8.3 Hz, 2H), 6.42 (d, *J* = 15.7 Hz, 1H), 6.20 (m, *J* = 15.5, 7.6 Hz, 1H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 3.83 (s, 3H), 3.55 (q, *J* = 10.9 Hz, 2H), 3.40 (d, *J* = 8.9 Hz, 1H), 3.36 (d, *J* = 8.9 Hz, 1H), 2.35 (dd, *J* = 13.3, 8.0 Hz, 1H), 2.29 (dd, *J* = 13.5, 7.6 Hz, 1H), 1.29 (s, 1H), 0.89 (s, 2H).^{13}C NMR (151 MHz, $CDCl_3$) δ 159.3, 137.6, 132.8, 130.0, 129.3, 128.5, 127.0, 126.1, 126.0, 113.8, 77.3, 73.2, 70.5, 55.2, 39.7, 37.9, 19.1.

HRMS (ESI) *m/z*: calcd for $C_{21}H_{27}O_3$ $[M+H]^+$: 327.1960, Found:327.1968.

(*R,E*)-*tert*-butyl((2-(((4-methoxybenzyl)oxy)methyl)-2-methyl-5-phenylpent-4-en-1-yl)oxy)diphenylsilane (16)



To a solution of alcohol **15** (18.1 g, 0.055 mol) in CH_2Cl_2 (160.0 mL) were added imidazole (4.08 g, 0.060 mol) and TBDPS-Cl (15.117 g, 14.3 mL, 0.055 mol). After stirring the solution at room temperature for 16 hours, the mixture was poured into water (50.0 mL). After separation of the organic layer, the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Evaporation of the solvent and column chromatography of the crude mixture (petroleum ether/EtOAc (4:1)) afforded compound **16** (28.2 g, 90 %) as a colourless oil.

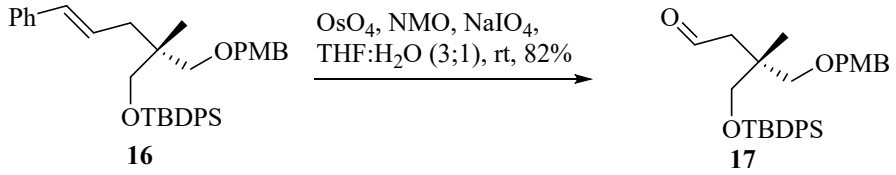
R_f = 0.80 (20% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 13.2 (*c* = 0.8 MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 6.7 Hz, 4H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.32 (dd, *J* = 12.8, 7.7 Hz, 4H), 7.26 (d, *J* = 8.0 Hz, 4H), 7.22 (d, *J* = 6.8 Hz, 1H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.39 (d, *J* = 15.7 Hz, 1H), 6.16 (dt, *J* = 15.3, 7.5 Hz, 1H), 4.46 (s, 2H), 3.82 (s, 3H), 3.53 (s, 2H), 3.35 (t, *J* = 6.5 Hz, 2H), 2.27 (d, *J* = 7.3 Hz, 2H), 1.09 (s, 9H), 0.95 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 137.9, 135.8, 133.9, 132.6, 131.1, 129.6, 129.1, 128.5, 127.7, 126.9, 126.1, 113.8, 74.1, 73.0, 67.8, 55.4, 41.0, 38.1, 27.0, 19.6, 19.5.

HRMS (ESI) *m/z*: calcd for $C_{37}H_{44}O_3NaSi$ $[M+Na]^+$:587.2957, Found:587.2956.

(*R*)-4-((*tert*-butyldiphenylsilyl)oxy)-3-(((4-methoxybenzyl)oxy)methyl)-3-methylbutanal (17)



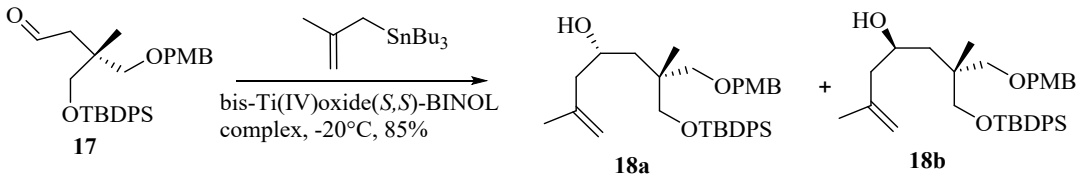
To a solution of compound **16** (28.2 g, 0.05 mol) in mixture of water and THF (1:3, 120 mL), 100 mL of 0.05M solution of OsO_4 in toluene and 8.79 g of NMO were added sequentially. The solution was then stirred for 5 minutes during which time the mixture became dark brown (due to osmate ester formation). While the temperature of the stirred mixture was maintained at 24-26° C, a total of 15.975 g. of finely powdered $NaIO_4$ was added in portions over a period of 30 minutes. The dark slurry was then stirred for an additional 1.5 hours. The reaction mixture (pale yellow in colour) was extracted thoroughly with EtOAc (about 200 mL). The solution was filtered through a pad of anhydrous Na_2SO_4.The organic solvent was then evaporated to furnish the crude aldehyde, which was immediately purified by flash column chromatography (10% ethyl acetate / n-hexane) to afford **17** as a colourless oil (20.1 g, 82%).

R_f = 0.75 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.83 (t, J = 2.8 Hz, 1H), 7.79 – 7.70 (d, 2H), 7.70 – 7.59 (d, 2H), 7.41 (q, J = 8.2 Hz, 6H), 7.22 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 4.43 (s, 2H), 3.82 (s, 3H), 3.78 – 3.70 (m, 1H), 3.64 – 3.51 (m, 2H), 3.47 (d, J = 8.9 Hz, 1H), 3.36 (d, J = 8.9 Hz, 1H), 2.49 – 2.31 (m, 2H), 1.10 (d, J = 7.5 Hz, 12H).^{13}C NMR (101 MHz, $CDCl_3$) δ 202.8, 159.1, 135.6, 135.3, 134.8, 133.2, 130.4, 129.6, 129.1, 127.7, 113.7, 74.1, 72.9, 68.3, 55.2, 49.2, 40.8, 26.6, 20.2, 19.3, 19.0.

HRMS (ESI) *m/z*: calcd for $C_{30}H_{38}O_4NaSi$ $[M+Na]^+$:513.2437, Found:513.2419.

(4*S*,6*R*)-7-((*tert*-butyldiphenylsilyl)oxy)-6-(((4-methoxybenzyl)oxy)methyl)-2,6-dimethylhept-1-en-4-ol (18a)



Dried $Ti(O^iPr)_4$ (0.12 mL, 0.4 mmol) was added under argon at 0°C to a stirred solution of $TiCl_4$ (0.16 mL in DCM, 0.16 mmol) in CH_2Cl_2 (2.0 mL). The solution was allowed to warm to room temperature. After 1 hour, silver(I)oxide (72 mg, 0.31 mmol) was added at room

temperature, and the whole mixture was stirred for 5 hours in absence of direct light. The mixture was diluted with CH_2Cl_2(1 mL), and treated with (*S*)-BINOL (0.134g, 0.47 mmol) at room temperature for 2 hours to furnish chiral bis-Ti(IV)oxide (*S,S*) **19** in CH_2Cl_2 solvent.

Compound bis-Ti(IV)oxide (*S,S*) **19** (0.39 mmol), generated in situ in CH_2Cl_2 (2.0 mL), was cooled to –15˚C, and treated sequentially at –15˚C with aldehyde **17** (1.91 g, 3.9 mmol) in 15.0 mL DCM and allyltributyltin (1.5 mL, 4.6 mmol). The mixture was allowed to warm to 0˚C and stirred for 4 hours. The reaction mixture was quenched with saturated $NaHCO_3$, and extracted with ether. The organic extracts were dried over Na_2SO_4. Evaporation of solvents and purification of the residue by column chromatography on silica gel (EtOAc/hexane 1:10 as eluent) gave **18a** and **18b** (4:1) as a colorless oil (1.59 g, 85% yield).

R_f = 0.50 (20% EtOAc in hexane).
$[\alpha]_D^{30}$ = + 24.2 (*c* = 1.0 MeOH).
^{1}H NMR of **18a** (600 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.9, 1.2 Hz, 4H), 7.44 (dt, *J* = 35.7, 7.3 Hz, 6H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 8.6 Hz, 2H), 4.83 (d, *J* = 37.5 Hz, 2H), 4.51 (dd, *J* = 24.5, 11.5 Hz, 2H), 4.00 (dt, *J* = 23.1, 11.4 Hz, 1H), 3.84 (s, 3H), 3.53 (d, *J* = 9.5 Hz, 2H), 3.44 (dd, *J* = 24.3, 9.3 Hz, 2H), 2.32 (dd, *J* = 13.6, 7.1 Hz, 1H), 2.11 (dd, *J* = 13.6, 6.3 Hz, 1H), 1.80 (s, 3H), 1.55 (d, *J* = 14.7 Hz, 1H), 1.51 – 1.39 (m, 1H), 1.11 (s, 9H), 1.04 (s, 3H).
^{13}C NMR of **18a** (151 MHz, $CDCl_3$) δ 159.3, 143.2, 135.7, 133.4, 133.4, 129.7, 129.4, 127.71, 127.7, 113.8, 112.8, 74.8, 73.2, 70.2, 65.3, 55.2, 47.1, 43.4, 39.7, 26.9, 22.6, 19.5.
HRMS (ESI) *m/z*: calcd for $C_{34}H_{47}O_4Si$ $[M+H]^+$:547.3244, Found:547.3229.
The absolute configuration at the newly generated stereocenter after methallylation reaction of **18a** was assigned by Mosher ester derivatization of alcohol **18a** by treating with (*R*)-(+)-α-methoxy-α-trifluoromethyl)phenylacetic acid (*R*-MTPA) and (*S*)-(+)-α-methoxy-α-trifluoromethyl)phenylacetic acid (*S*-MTPA) respectively, under Yamaguchi condition using 2,4,6-trichloro benzoyl chloride, DMAP and Et_3N.[1]

The ^{1}H NMR spectra of both the MTPA esters of **18a** were analysed, which showed a positive chemical shift difference [$\Delta\delta = (\delta_S - \delta_R) \times 10^3$] for protons on C_1 (figure 1), while protons on C_3 showed negative chemical shift differences, which is indicative of C_2 bearing an *S*-configuration. Therefore, the absolute configuration of C_2 was assigned as *S* in compound **18a**.

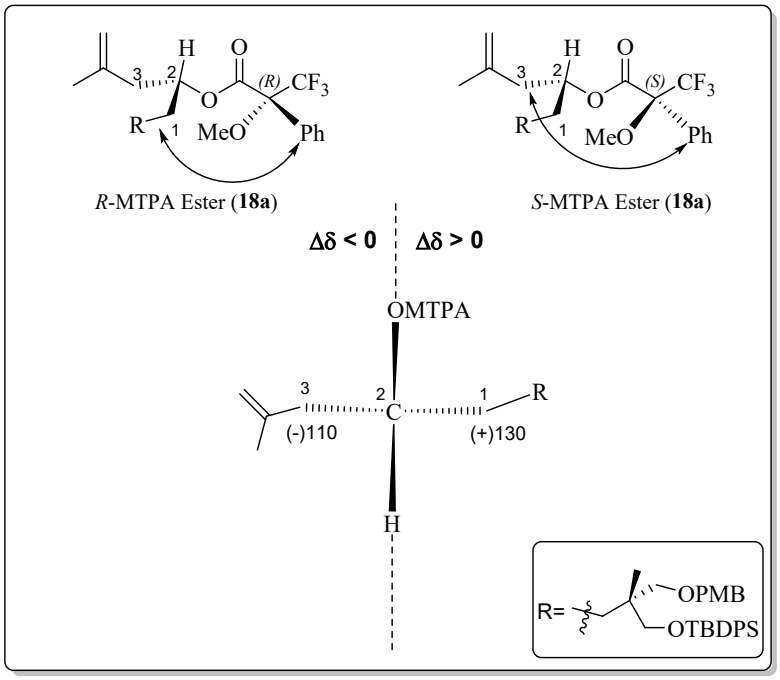
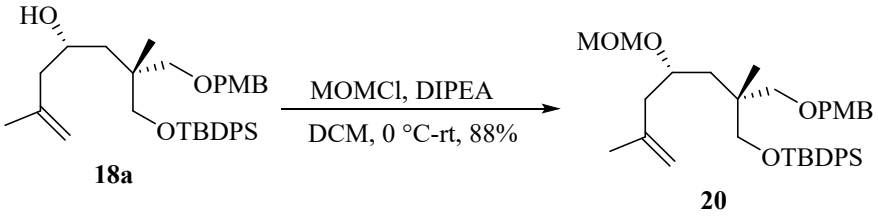


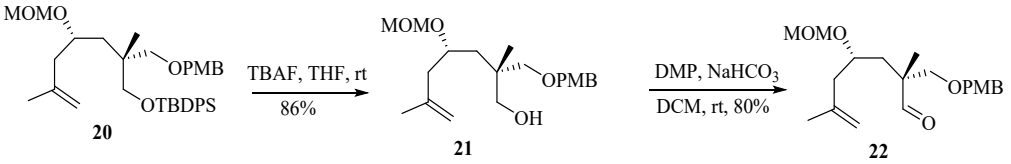
Figure-1: $(\Delta\delta) = (\delta_S - \delta_R) \times 10^3$ for (*S*)-and (*R*)-MTPA ester of alcohol **18a**.

(5*S*,7*R*)-7-(((4-methoxybenzyl)oxy)methyl)-7,11,11-trimethyl-5-(2-methylallyl)-10,10-diphenyl-2,4,9-trioxa-10-siladodecane (20)



To a stirred solution of alcohol **18a** (1.49 g, 2.8 mmol) and DIPEA (1.54 g, 2.0 mL, 11.95 mmol) in dichloromethane (12.0 mL) was added MOM-Cl (0.6 g, 4 mmol) dropwise at 0 °C. The mixture was warmed to room temperature and stirred for 6 hours. The reaction was then quenched with saturated aqueous NH_4Cl solution (12.0 mL) and extracted with ethyl acetate (20.0 mL). The organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give the desired product. The crude product was then purified by flash column chromatography (silica gel, 10% ethyl acetate/hexanes) to afford compound **20** (1.45 g, 88%) as a colorless oil. It was immediately used for the next step.

(2*R*,4*S*)-2-(((4-methoxybenzyl)oxy)methyl)-4-(methoxymethoxy)-2,6-dimethylhept-6-enal (22)



Step 1:

TBAF (2.95 mL of a 1 M solution in THF) was added to a solution of the silyl ether **20** (1.45 g, 2.45 mmol) in THF (7.3 mL) and stirred for 12 hours. The reaction mixture was then quenched with NH_4Cl solution (5.0 mL). The organic layer was separated and the aqueous layer was extracted with ether (2 × 5.0 mL). The combined organic extracts were dried (Na_2SO_4), evaporated under reduced pressure and purified by column chromatography on silica gel to furnish the corresponding alcohol **21** (0.78 g, 86 %) as an oil.

$[\alpha]_D^{30}$ = + 22.48 (*c* = 1.0 MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 4.80 (s, 1H), 4.75 (s, 1H), 4.73 – 4.64 (m, 2H), 4.44 (s, 2H), 3.98 – 3.93 (m, 1H), 3.83 (s, 3H), 3.56 (d, *J* = 8 Hz, 1H), 3.43 (d, *J* = 8 Hz, 1H), 3.39 (s, 3H), 3.35 (s, 2H), 2.47 (dd, *J* = 13.8, 4.9 Hz, 1H), 2.13 (dd, *J* = 13.8, 8.1 Hz, 1H), 1.74 (s, 3H), 1.55 (d, *J* = 8.5 Hz, 1H), 1.43 (d, *J* = 7.7 Hz, 1H), 0.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 142.5, 130.3, 129.1, 113.7, 113.1, 95.7, 73.8, 73.1, 69.7, 56.2, 55.2, 44.5, 39.3, 38.8, 29.7, 22.6, 21.2.

HRMS (ESI) *m/z*: calcd for $C_{20}H_{33}O_5$ $[M+H]^+$:353.2328, Found:353.2333.

Step 2:

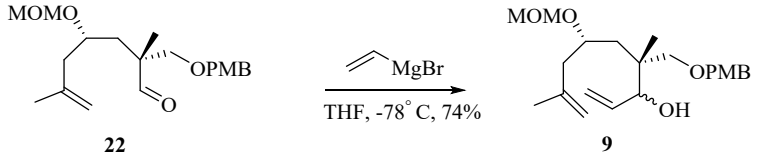
To a solution of alcohol **21** (0.75 g, 2.2 mmol) in CH_2Cl_2 (8.8 mL) was subjected to the oxidation reaction with DMP, by following the same reaction procedure as described earlier to afford aldehyde **22** (0.72 g, 80%).

R_f = 0.75 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 7.20 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 4.74 (d, *J* = 26.0 Hz, 2H), 4.56 (d, *J* = 7.1 Hz, 1H), 4.46 (d, *J* = 11.0 Hz, 1H), 4.40 (s, 3H), 3.80 (d, *J* = 1.4 Hz, 3H), 3.77 – 3.67 (m, 1H), 3.43 (d, *J* = 9.1 Hz, 1H), 3.31 (s, 3H), 3.26 (d, *J* = 9.0 Hz, 1H), 2.49 (dd, *J* = 13.6, 3.7 Hz, 1H), 2.09 (dd, *J* = 13.5, 8.9 Hz, 1H), 1.94 (dd, *J* = 14.6, 10.7 Hz, 1H), 1.68 (d, *J* = 20.6 Hz, 4H), 1.54 (d, *J* = 14.7 Hz, 1H), 1.10 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.87, 159.3, 142.2, 130.1, 129.2, 113.9, 113.4, 96.2, 74.8, 73.1, 73.0,

56.3, 55.4, 49.3, 43.9, 39.1, 22.8, 15.5. HRMS (ESI) *m/z*: calcd for $C_{20}H_{31}O_5$ $[M+H]^+$:351.2171, Found:351.2177.

(4*R*,6*S*)-4-(((4-methoxybenzyl)oxy)methyl)-6-(methoxymethoxy)-4,8-dimethylnona-1,8-dien-3-ol (9)



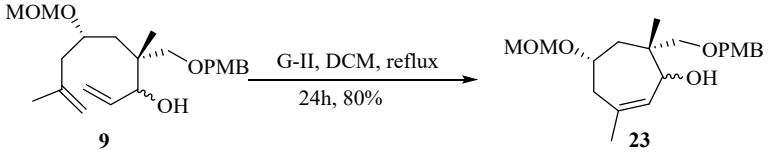
Vinylmagnesium bromide (1.0 M in THF, 2.48 mL, 2.48 mmol) was added dropwise to a solution of aldehyde **22** (0.72 g, 2.0 mmol) in dry THF (5.2 mL) at 0 °C. After stirring for 10 min the reaction mixture was allowed to warm to room temperature and was stirred for 4 hours. The reaction was then quenched by addition of saturated NH_4Cl (5.0 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (5.0 mL), dried over Na_2SO_4, and concentrated under vacuum to afford the crude product. The crude alcohol was then purified through silica-gel chromatography to furnish pure alcohol **9** (diastereomeric mixture) as yellow oil, yield (0.65 g, 74%).

R_f = 0.4 (20% EtOAc in hexane).

mp 85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.18 (m, 2H), 6.87 (d, *J* = 7.7 Hz, 2H), 5.94 – 5.85 (m, 1H), 5.26 (d, *J* = 17.1 Hz, 1H), 5.17 (d, *J* = 10.3 Hz, 1H), 4.71 (ddd, *J* = 33.5, 17.2, 8.5 Hz, 4H), 4.39 (s, 3H), 4.08 – 3.97 (m, 2H), 3.81 (s, 3H), 3.61 (d, *J* = 6.2 Hz, 1H), 3.45 (d, *J* = 8.8 Hz, 1H), 3.38 (s, 3H), 3.23 (d, *J* = 8.8 Hz, 1H), 2.48 – 2.34 (m, 1H), 2.13 (dd, *J* = 13.7, 7.5 Hz, 2H), 1.72 (s, 3H), 1.65 (d, *J* = 8.9 Hz, 1H), 1.42 (dd, *J* = 14.8, 8.4 Hz, 1H), 0.94 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 142.4, 137.4, 130.2, 129.4, 129.3, 116.3, 113.9, 113.9, 113.4, 95.7, 78.3, 76.8, 75.9, 73.6, 73.2, 56.4, 55.4, 44.6, 41.0, 39.2, 29.8, 22.8, 19.1.

HRMS (ESI) *m/z*: calcd for $C_{22}H_{34}O_5Na$ $[M+Na]^+$:401.2304, Found: 401.2309.

(5*S*,7*R*)-7-(((4-methoxybenzyl)oxy)methyl)-5-(methoxymethoxy)-3,7-dimethylcyclohept-2-en-1-ol (23)



Argon stream was bubbled for 30 min through a stirred solution of alcohols **9** (0.66 g, 1.74 mmol) in CH_2Cl_2 (3.5 mL) and Grubbs catalyst (2nd generation, 45.0 mg, 0.055 mmol) was added. The reaction mixture was stirred at 40˚C for 24 hours and then evaporated. Flash

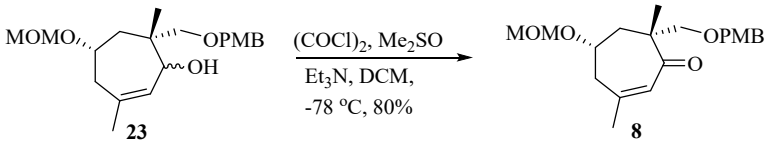
chromatography of the residue over silica gel, using 1:5 Et_2O-hexane, gave **23** (diastereomeric mixture, 0.47 g, 80 %) which was used directly in the next step without any further purification.

R_f = 0.30 (10% EtOAc in hexane). A small portion of crude diastereomeric mixture of **23** (20 mg) was purified through chromatography and the NMR data was recorded for the major diastereomer (less polar in TLC).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.3 Hz, 2H), 6.90 (d, *J* = 8.3 Hz, 2H), 5.35 – 5.24 (m, 1H), 4.69 – 4.57 (m, 2H), 4.53 – 4.38 (m, 3H), 3.82 (s, 3H), 3.59 – 3.48 (m, 1H), 3.36 (d, *J* = 4.4 Hz, 4H), 3.27 (d, *J* = 9.0 Hz, 1H), 2.29 (t, *J* = 12.5 Hz, 1H), 2.16 (d, *J* = 13.8 Hz, 1H), 1.79 (s, 3H), 1.74 (s, 1H), 1.73 – 1.69 (m, 1H), 0.93 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 131.5, 131.3, 129.8, 129.2, 113.8, 94.5, 79.3, 77.0, 74.6, 73.1, 69.9, 55.2, 45.6, 41.5, 40.3, 25.6, 15.6.

HRMS (ESI) *m/z*: calcd for $C_{20}H_{31}O_5$ $[M+H]^+$:351.2171, Found:351.2176.

(5*S*,7*R*)-7-(((4-methoxybenzyl)oxy)methyl)-5-(methoxymethoxy)-3,7-dimethylcyclohept-2-en-1-one (8)



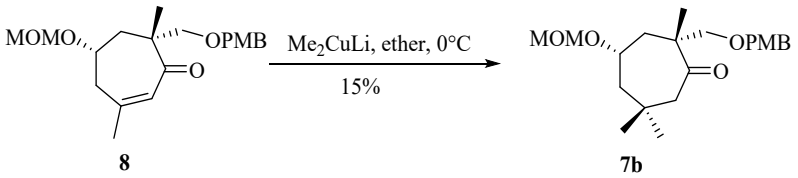
To a solution of alcohol **23** (200 mg, 0.57mmol) in CH_2Cl_2 (4.5 mL) was subjected to the Swern oxidation reaction, by following the standard reported reaction procedure [2] to afford product ketone, which was purified by SiO_2 column chromatography (typically 10% EtOAc-hexanes) to yield ketone **8** (168 mg, 80%).

R_f = 0.5 (10% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 5.2 (*c* = 1.0 MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 – 7.21 (m, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 5.87 (s, 1H), 4.65 (d, *J* = 6.7 Hz, 1H), 4.58 (d, *J* = 6.7 Hz, 1H), 4.54 – 4.35 (m, 2H), 4.05 (t, *J* = 9.2 Hz, 1H), 3.82 (s, 2H), 3.69 (d, *J* = 8.9 Hz, 1H), 3.44 (d, *J* = 9.0 Hz, 1H), 3.33 (s, 2H), 2.65 (d, *J* = 18.1 Hz, 1H), 2.41 (dd, *J* = 18.2, 9.5 Hz, 1H), 2.27 (d, *J* = 14.3 Hz, 1H), 1.92 (s, 2H), 1.86 – 1.77 (m, 1H), 1.12 (s, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.0, 159.0, 148.4, 130.4, 129.2, 127.7, 113.6, 94.7, 75.2, 73.1, 71.5, 55.3, 55.2, 49.9, 44.1, 40.7, 29.7, 24.6. HRMS (ESI) *m/z*: calcd for $C_{20}H_{28}O_5Na$ $[M+Na]^+$:371.1834, Found:371.1840.

(2*R*,4*S*)-2-(((4-methoxybenzyl)oxy)methyl)-4-(methoxymethoxy)-2,6,6-trimethylcycloheptan-1-one (7b)



8 **7b**

Anhydrous copper (I) bromide dimethyl sulphide complex (185 mg, 0.9 mmol) was added to a cooled solution of methyl lithium (3.0 M, 0.3 mL, 0.9 mmol) in ether. The mixture was stirred in an inert atmosphere for 5 min and a solution of enone **8** (158 mg, 0.45 mmol) in ether was added dropwise keeping the temperature below –5 °C. After the addition of ketone was completed, the reaction mixture was stirred for 1 hour and carefully neutralized with saturated aqueous NH_4Cl solution. Traditional workup for Grignard reactions gave crude material that was separated on a silica gel column, eluting with a petroleum ether/ ethyl acetate mixture. The cycloheptanone **7b** (32 mg, 0.09 mmol, 15%) was obtained as a colorless oil.

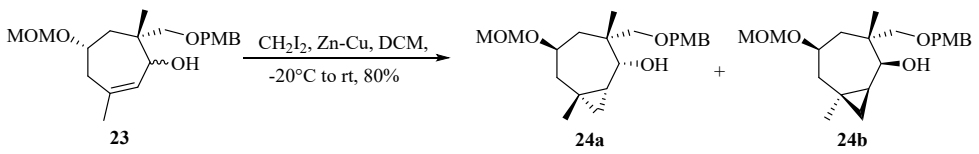
R_f = 0.6 (10% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 12.3 (*c* = 1.0 MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 4.64 (s, 2H), 4.43 – 4.33 (m, 2H), 3.83 (s, 3H), 3.68 (t, *J* = 10.8 Hz, 1H), 3.39 (d, *J* = 8.5 Hz, 1H), 3.37 (s, 3H), 3.20 (d, *J* = 8.4 Hz, 1H), 2.93 (d, *J* = 11.4 Hz, 1H), 2.45 (dd, *J* = 14.3, 10.7 Hz, 1H), 2.16 (d, *J* = 13.1 Hz, 1H), 1.88 (d, *J* = 14.5 Hz, 1H), 1.76 (d, *J* = 14.4 Hz, 1H), 1.63 (d, *J* = 11.4 Hz, 1H), 1.11 (s, 3H), 1.07 (s, 3H), 0.90 (s, 3H).;^{13}C NMR (151 MHz, $CDCl_3$) δ 212.6, 159.0, 130.6, 129.0, 113.6, 95.2, 74.2, 73.3, 73.1, 55.3, 55.2, 50.9, 39.2, 37.5, 31.4, 24.0, 18.3, 16.9.

HRMS (ESI) *m/z*: calc'd for $C_{21}H_{33}O_5$ $[M+H]^+$; calcd:365.2328, Found:365.2342.

(3*R*,5*R*)-3-(((4-methoxybenzyl)oxy)methyl)-5-(methoxymethoxy)-3,7-dimethylbicyclo[5.1.0]octan-2-ol (24a/24b)



23 **24a** **24b**

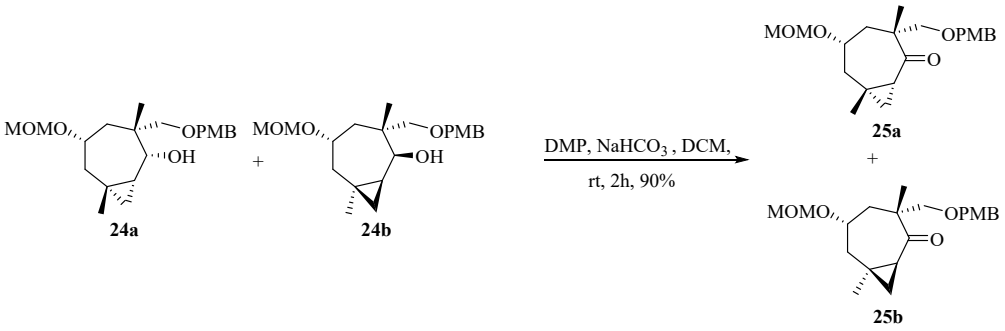
To a solution of diiodomethane (2.06 g, 7.74 mmol) in dried CH_2Cl_2 (5.2 mL) was added Et_2Zn (1.0 M in hexane, 3.85 mL, 3.85 mmol) slowly at −20 °C. The reaction mixture was allowed to stir at −20 °C for 0.5h. Then alcohol **23** (0.45 g, 1.284 mmol) in CH_2Cl_2 (0.5 mL) was added to the reaction mixture at −20 °C. After stirring at −20 °C for 0.5 hour, the reaction mixture

was allowed to warm to room temperature and further stirred at room temperature for 4 hours. Diluted aqueous NH_4Cl solution (5 mL) was added to quench the reaction, the reaction mixture was filtered through celite and extracted with CH_2Cl_2 (2 × 15 mL). The combined organic layers were dried with $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc:hexane = 1 : 4) to afford the title alcohols **24a** and **24b** as light yellow oil (0.364 g, 80%). The mixture of alcohols **24a** and **24b** (approximately 1:1 as indicated by NMR analysis) was taken directly for the next step without any further purification.

R_f = 0.3 (10% EtOAc in hexane).

^{1}H NMR of mixture of **24a** and **24b** (400 MHz, $CDCl_3$) δ 7.31 – 7.21 (m, 2H), 6.89 (dd, J = 8.5, 2.5 Hz, 2H), 4.72 – 4.57 (m, 2H), 4.53 – 4.40 (m, 2H), 4.13 (dd, J = 44.5, 5.2 Hz, 1H), 3.96 – 3.89 (m, 1H), 3.82 (s, 3H), 3.42 – 3.22 (m, 5H), 2.25 – 1.98 (m, 2H), 1.44 (dd, J = 13.7, 8.8 Hz, 1H), 1.33 – 1.21 (m, 2H), 1.16 – 0.94 (m, 7H), 0.73 – 0.56 (m, 1H), 0.37 (ddd, J = 30.6, 8.9, 3.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 159.0, 131.0, 129.6, 129.2, 129.0, 113.8, 113.6, 94.4, 94.1, 82.9, 77.2, 74.5, 74.0, 73.3, 72.9, 72.6, 71.3, 55.3, 55.15, 55.13, 41.4, 41.2, 39.9, 38.8, 38.4, 27.8, 26.8, 25.5, 25.4, 19.2, 17.7, 16.8, 14.8.

(3*R*,5*R*)-3-(((4-methoxybenzyl)oxy)methyl)-5-(methoxymethoxy)-3,7-dimethylbicyclo[5.1.0]octan-2-one (25a/25b)



The mixture of alcohols **24a** and **24b** (0.364 g, 1.01 mmol) in CH_2Cl_2 (4.0 mL) was subjected to DMP oxidation under the same reaction procedure as described earlier. The product ketones were now purified by SiO_2 column chromatography (typically 10% EtOAc-hexanes) to afford mixture of ketones **25a** and **25b** (0.32 g, 90%). The ketones being diastereomer are separable through column chromatography, and **25a** (160 mg, less polar in TLC plate) and **25b** (160 mg, more polar in TLC plate) was obtained. We did not confirm the absolute configuration of **25a** and **25b** at this stage as finally cyclopropane ring will be cleaved and both will lead to compound **28** in next step.

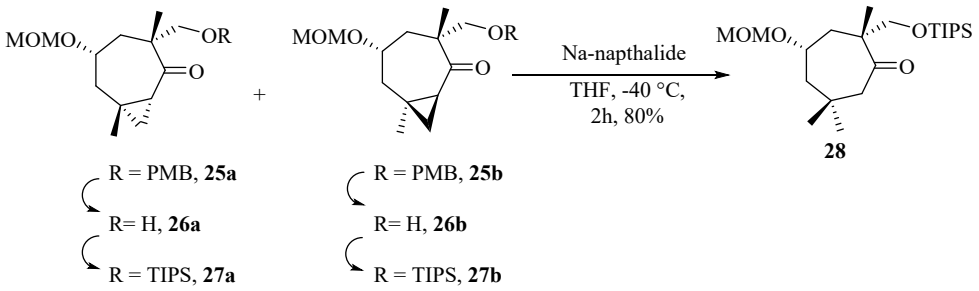
R_f = 0.4 (10% EtOAc in hexane).

^{1}H NMR of ketone isomer **25a**, having high R_f in TLC plate (600 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 4.70 – 4.61 (m, 2H), 4.49 – 4.39 (m, 2H), 3.92 (dtd, *J* = 9.9, 4.8, 1.8 Hz, 1H), 3.82 (s, 3H), 3.47 (d, *J* = 8.7 Hz, 2H), 3.41 (d, *J* = 8.7 Hz, 2H), 3.39 (s, 5H), 2.70 (dd, *J* = 13.7, 10.3 Hz, 1H), 2.22 (d, *J* = 15.7 Hz, 1H), 1.91 (ddd, *J* = 7.2, 5.4, 1.3 Hz, 1H), 1.72 (dd, *J* = 13.7, 4.9 Hz, 1H), 1.29 (s, 3H), 1.02 (s, 3H), 0.81 (d, *J* = 4.6 Hz, 1H), 0.79 (d, *J* = 4.6 Hz, 1H), 0.69 (t, *J* = 5.2 Hz, 1H), 0.63 (dd, *J* = 8.1, 5.0 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 213.7, 159.1, 130.1, 128.9, 113.7, 95.1, 78.1, 73.9, 73.0, 55.3, 55.2, 51.2, 38.9, 37.8, 33.8, 24.0, 19.5, 18.8, 16.6.

$[\alpha]_D^{30}$ = + 35.2 (*c* = 1.0 MeOH).

HRMS (ESI) *m/z*: calcd for $C_{21}H_{31}O_5$ $[M+H]^+$:363.2171, Found:363.2177.

(2*R*,4*S*)-4-(methoxymethoxy)-2,6,6-trimethyl-2-(((triisopropylsilyl)oxy)methyl) cycloheptanone (28)



Step 1: Ketone **25a** (less polar diastereomer obtained in previous step) (0.32 g, 0.88 mmol) was taken in water (1.0 mL), dichloromethane (3.5 mL) and phosphate buffer (pH-7.0) 0.4 mL at 0° C. The reaction solution was then treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (300 mg, 1.32 mmol). The resulting mixture was stirred for 5 hours and then filtered through anhydrous Na_2SO_4. The filtrate was washed with saturated sodium bicarbonate (5.0 mL) and dried over anhydrous Na_2SO_4. The solution was filtered and concentrated in vacuo to give the crude product. The crude residue was then purified by silica gel column chromatography (5:1 hexane:ethyl acetate), to furnish alcohol **26a** (0.191 g, 86%). Under the same reaction condition ketone **25b** (more polar diastereomer) was also converted to **26b** in almost similar yield.

R_f = 0.2 (20% EtOAc in hexane)

^{1}H NMR of **26a** (400 MHz, $CDCl_3$) δ 4.75 – 4.62 (m, 2H), 3.95 (bs, 1H), 3.88 (d, *J* = 5.5 Hz, 1H), 3.83 (dd, *J* = 11.4, 6.0 Hz, 1H), 3.72 – 3.66 (m, 1H), 3.41 (s, 3H), 2.48 (dd, *J* = 13.7, 10.0 Hz, 1H), 2.28 – 2.21 (m, 1H), 1.91 – 1.85 (m, 1H), 1.83 – 1.78 (m, 1H), 1.72 – 1.68 (m, 1H),

1.32 (s, 3H), 1.06 (s, 3H), 0.79 – 0.76 (m, 1H), 0.75 – 0.69 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.9, 95.1, 73.7, 70.5, 55.4, 52.1, 38.6, 38.1, 33.8, 25.8, 24.3, 19.2, 19.1.

$[\alpha]_D^{30}$ = + 24.2 (*c* = 1.0 MeOH).

HRMS (ESI) *m/z*: calcd for $C_{13}H_{23}O_4$ $[M+H]^+$:243.1596, Found:243.1588.

Step 2: To a dry flask were added alcohols **26a** (0.191 g, 0.79 mmol) and CH_2Cl_2 (1.0 mL) and the mixture cooled to 0 °C. Then imidazole (80.6 mg, 1.185 mmol) and DMAP (5 mol%) was added followed by TIPS-Cl (0.22 mL, 0.948 mmol). The reaction solution was stirred for 5 hours at room temperature. The reaction mixture was poured into a separatory funnel containing H_2O and CH_2Cl_2. The phases were separated and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic phases were washed with brine and dried over $MgSO_4$. The organic solvent was evaporated in vacuo. Flash chromatography of the crude extract (5% EtOAc in petroleum ether) afforded the compound **27a** as a colorless oil, yield 0.263 g, 92%. Under the same reaction condition alcohol **26b** was also converted to **27b** in almost similar yield.

R_f = 0.6 (10% EtOAc in hexane).

^{1}H NMR of **27a** (400 MHz, $CDCl_3$) δ 4.65 (dt, *J* = 12.9, 6.5 Hz, 2H), 3.91 (dd, *J* = 10.0, 4.7 Hz, 1H), 3.71 (d, *J* = 9.1 Hz, 1H), 3.61 (d, *J* = 9.1 Hz, 1H), 3.38 (s, 3H), 2.91 – 2.78 (m, 1H), 2.21 (d, *J* = 15.7 Hz, 1H), 1.90 (t, *J* = 6.6 Hz, 1H), 1.71 (dd, *J* = 13.7, 4.9 Hz, 1H), 1.29 (s, 3H), 1.05 (d, *J* = 4.7 Hz, 20H), 0.94 (s, 3H), 0.89 (s, 1H), 0.76 (dd, *J* = 15.7, 4.5 Hz, 1H), 0.62 (d, *J* = 6.8 Hz, 2H).; ^{13}C NMR (101 MHz, DMSO) δ 214.8, 95.3, 74.5, 72.6, 55.3, 52.2, 38.4, 37.9, 34.3, 23.7, 19.1, 18.6, 18.0, 16.4, 11.8.

$[\alpha]_D^{30}$ = + 11.6 (*c* = 1.0 MeOH).

HRMS (ESI) *m/z*: calcd for $C_{22}H_{43}O_4Si$ $[M+H]^+$:399.2931, Found:399.2937.

Step 3: To a suspension of freshly prepared Na-wire (2.18 mmol, 50 mg), naphthalene (2.18 mmol, 2.8 mg) in THF (2.8 mL) was slowly added. The solution becomes green after 30 min, then a solution of the compound **27a** (0.263 g, 0.726 mmol) in THF (0.8 mL) at -40 °C was added to it. Stirring was continued for 12 hours. The resulting mixture was then quenched with addition of saturated NH_4Cl solution (10 ml) and extracted with diethyl ether (2 × 50 ml). The organic layer was dried over anhydrous Na_2SO_4. Evaporation and purification through chromatography afforded ketone **28** (0.21 g, 80%). Under the same reaction condition alcohol ketone **27b** was also converted to **28** in almost similar yield.

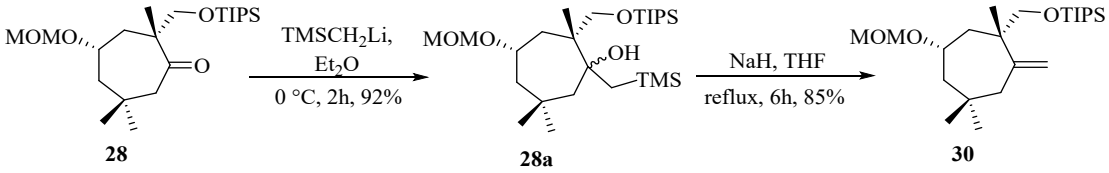
R_f = 0.5 (10% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 15.2 (*c* = 1.0 MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.74 – 4.59 (m, 2H), 3.70 (dd, *J* = 10.7, 5.3 Hz, 2H), 3.44 (d, *J* = 8.9 Hz, 1H), 3.39 (d, *J* = 8.5 Hz, 3H), 2.95 (d, *J* = 11.3 Hz, 1H), 2.52 (dd, *J* = 14.2, 10.7 Hz, 1H), 2.15 (dd, *J* = 11.3, 1.6 Hz, 1H), 1.95 – 1.85 (m, 1H), 1.75 (d, *J* = 14.3 Hz, 1H), 1.71 – 1.59 (m, 2H), 1.06 (dd, *J* = 13.1, 2.8 Hz, 27H), 0.89 (s, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 215.7, 94.2, 73.2, 70.5, 56.1, 55.2, 50.9, 50.5, 41.6, 34.0, 32.0, 26.6, 19.4, 17.9, 17.7, 11.8.

HRMS (ESI) *m/z*: calcd for $C_{22}H_{45}O_4Si$ $[M+H]^+$:401.3087, Found:401.308.

Triisopropyl(((1*S*,6*S*)-6-(methoxymethoxy)-1,4,4-trimethyl-2-methylenecycloheptyl)-methoxy)silane (30):



28 **28a** **30**

Step 1:

To a stirred solution of ketone **28** (0.21 g, 0.58 mmol) in ether (2.4 mL) was added dropwise $TMSCH_2Li$ (1 M in pentane, 1.16 mL, 1.16 mmol) at 0 ºC, and the mixture was stirred for 20 min at 0 ºC. The reaction solution was then quenched with saturated NH_4Cl aqueous solution, and extracted with EtOAc three times. The combined organic layers were washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The resulting residue was purified by column chromatography (hexane-EtOAc, 10:1) to afford **28a** (0.26 g, 92%) as a colorless oil, which was immediately used for the next step.

Step 2:

To a stirred suspension of NaH (55% in mineral oil, 44.8 mg, 1.07 mmol) in THF (1.0 mL) was added dropwise a solution of **28a** (0.26 g, 0.533 mmol) in THF (2.0 mL) at 0 ºC under Ar atmosphere, and the mixture was stirred for 6 hours at reflux. The reaction mixture was quenched with THF/MeOH (10:1) at 0 ºC, and extracted with Et_2O three times. The combined organic layers were washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The resulting residue was purified by column chromatography (hexane-AcOEt, 1:1) to afford **30** (0.18 g, 85%) as a colorless oil.

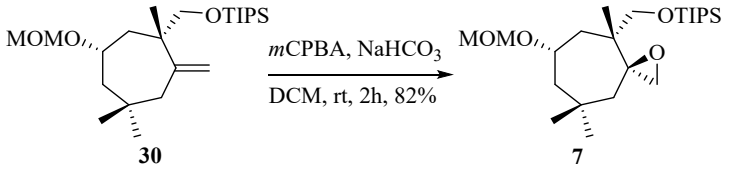
R_f = 0.6 (10% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 18.3 (*c* = 1.0 MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.93 (s, 1H), 4.81 (s, 1H), 4.69 – 4.57 (m, 2H), 3.59 – 3.49 (m, 1H), 3.47–3.42 (m, 2H), 3.37 (s, 3H), 2.34 (d, *J* = 13.1 Hz, 1H), 1.98 – 1.84 (m, 2H), 1.74 (dd, *J* = 18.4, 7.9 Hz, 2H), 1.45 – 1.35 (m, 1H), 1.21 (s, 3H), 1.15 – 1.06 (21H, due to TIPS group), 1.01 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.2, 114.5, 93.9, 74.2, 70.8, 55.0, 50.8, 47.6, 44.5, 42.3, 33.7, 31.4, 26.8, 23.1, 18.1, 12.0.

HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{23}H_{47}O_3Si$ = 399.3294, found = 399.3292

Triisopropyl(((3*S*,4*R*,6*S*)-6-(methoxymethoxy)-4,8,8-trimethyl-1-oxaspiro[2.6]nonan-4-yl)methoxy)silane (7)



30 **7**

To a solution of *m*CPBA (88.2 mg, 0.51 mmol) and sodium bicarbonate (0.178 g, 2.13 mmol) in methylene chloride (2.0 mL), a solution of **30** (0.17g, 0.43 mmol) in methylene chloride (1.0 mL) was added drop by drop, maintaining the reaction mixture at 5-10°C with a water bath. During the addition, sodium *m*-chlorobenzoate began to crystallize, indicating that the reaction was proceeding. After completion of the addition, stirring was continued at the same temperature. After the reaction was complete, the mixture was treated with 10% aqueous Na_2SO_3 solution (1.0 mL) and stirred for 30 min at room temperature to remove the excess of peracid. Water (1.0 mL) was added, and the methylene chloride phase was separated and washed with 2.0 mL of 5% aqueous sodium carbonate. The two aqueous washings were extracted with methylene chloride, and the organic solutions were combined and dried over anhydrous $MgSO_4$. Evaporation of the solvent under vacuum gave an oily residue that was purified by column chromatography through silica gel using a mixture of hexane and ethyl acetate (10:1) as eluent, yielding a colorless oil of the epoxide **7** (0.16 g, 82%).

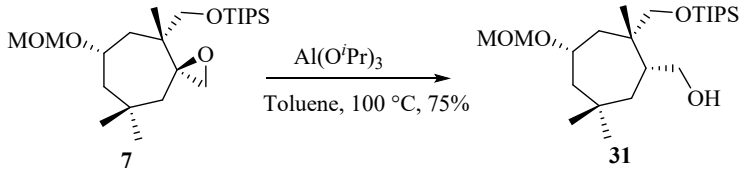
R_f = 0.20 (10% EtOAc in hexane).

$[\alpha]_D^{30}$ = − 11.48 (*c* = 1.0 MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.63 (s, 2H), 3.73 – 3.7 (m, 2H), 3.37 (m, 1H), 3.36 (s, 3H), 2.91 (m, 1H), 2.59 (s, 1H), 2.44 (d, *J* = 13.1 Hz, 1H), 2.14 (m, 1H), 1.77 – 1.74 (m, 3H), 1.54-1.5 (m, 1H), 1.15 – 1.06 (21H; due to TIPS group), 1.01 (s, 6H), 0.88 (s, 3H).; ^{13}C NMR (151 MHz, $CDCl_3$) δ 93.8, 70.3, 69.9, 60.8, 55.0, 52.4, 50.7, 46.6, 43.6, 38.9, 34.0, 32.1, 28.6, 20.8, 18.1, 12.0.

HRMS (ESI) *m/z*: calcd for $C_{23}H_{47}O_4Si$ $[M+H]^+$:414.3244, Found:415.3252.

((1*R*,2*S*,4*S*)-4-(methoxymethoxy)-2,6,6-trimethyl-2-(((triisopropylsilyl)oxy)methyl)cycloheptyl)methanol (31)



7 31

A solution of Al(O^{i}Pr)$_3$ (freshly distilled, 0.48 g, 1.158 mmol) in dry toluene (1.0 mL) was added through syringe to a stirred solution of epoxide **7** (0.16 g, 0.386 mmol) in dry toluene (2.0 mL) under a nitrogen atmosphere. The resulting mixture was then refluxed for 72 hours, and after that, it was extracted with ether. The organic extract was washed with water, dried over sodium sulphate, and evaporated. The residue was purified by column chromatography through silica gel using a mixture of hexane and ethyl acetate (10:1), yielding a colorless oil of the alcohol **31** (0.12 g, 75%).

R_f = 0.2 (10% EtOAc in hexane).

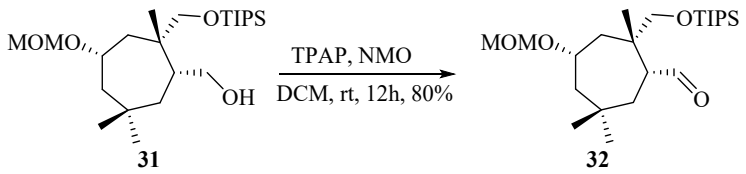
$[\alpha]_D^{30}$ = + 31.2 (*c* = 0.8 MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.63 (s, 2H), 3.75 – 3.67 (m, 2H), 3.563.5 (m, 2H), 3.4 (m, 1H), 3.38 (s, 3H), 1.7-1.55 (m, 10H), 1.09 (18H, due to –TIPS group), 1.01 (s, 3H), 0.99 (s, 3H), 0.83 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 93.80, 69.96, 68.9, 65.3, 55.07, 51.1, 46.66, 42.6, 39.6, 37.9, 34.3, 26.3, 24.5, 18.06, 18.03, 11.9.

HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{23}H_{49}O_4Si$ = 417.3400, found = 417.3392

(1*R*,2*S*,4*S*)-4-(methoxymethoxy)-2,6,6-trimethyl-2-(((triisopropylsilyl)oxy)methyl)cycloheptane-1-carbaldehyde (32)



31 32

To a solution of alcohol **31** (0.12 g, 0.3 mmol) in CH_2Cl_2 (1.2 mL) was sequentially added TPAP (tetra-^{n}propylammonium perruthenate; 15 mg, 0.03 mmol) and NMO (0.3 mmol, 35 mg) and the reaction solution was stirred at room temperature for 12 hours. After that time the

reaction solution was filtered through a pad of celite and the organic solvent was evaporated to afford the crude aldehyde **32**, which was purified by SiO_2 column chromatography (100 mg, 80%).

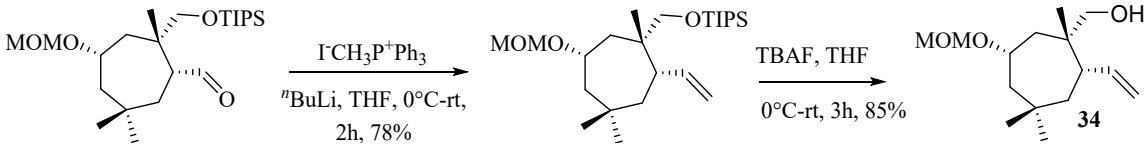
R_f = 0.5 (10% EtOAc in hexane).

$[\alpha]_D^{30}$ = − 19.4 (*c* = 0.6 MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (d, *J* = 2.7 Hz, 1H), 4.64 – 4.58 (m, 2H), 3.70 (d, *J* = 9.6 Hz, 1H), 3.47 (d, *J* = 9.7 Hz, 1H), 3.36 (s, 3H), 2.63 (dd, *J* = 9.0, 2.7 Hz, 1H), 1.84 (t, *J* = 12.1 Hz, 1H), 1.69 (d, *J* = 14.4 Hz, 2H), 1.59 – 1.36 (m, 5H), 1.17 – 1.10 (m, 3H), 1.09 – 1.04 (m, 22H), 1.00 (s, 3H), 0.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.1, 93.8, 71.4, 69.2, 55.1, 50.3, 48.4, 48.1, 40.2, 34.1, 31.1, 30.2, 30.1, 18.5, 18.0, 11.9.

HRMS (ESI) *m/z*: calcd for $C_{23}H_{47}O_4Si$ $[M+H]^+$:415.3244, Found:415.3232.

((1*S*,2*S*,6*S*)-6-(methoxymethoxy)-1,4,4-trimethyl-2-vinylcycloheptyl)methanol (34)



Step 1: To a suspension of methyltriphenylphosphonium bromide (128 mg, 0.36 mmol) in THF (10.0 mL) was added dropwise ^{n}BuLi (1.6 M) in hexane (0.25 mL, 0.36 mmol) at –78 °C. After stirring for 10 min at 0 °C, the mixture was cooled again to –78 °C and aldehyde **32** (100 mg, 0.24 mmol) in THF (7.0 mL) was added. The reaction mixture was stirred for 2 hours at 0 °C and then quenched with saturated NH_4Cl (10 mL) solution. The two layers were separated and the aqueous phase was extracted with Et_2O (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by flash chromatography (Et_2O/PE, 1:20) to furnish **33** as colourless oil (77 mg, 0.187 mmol, 78%), which was immediately used in the next step.

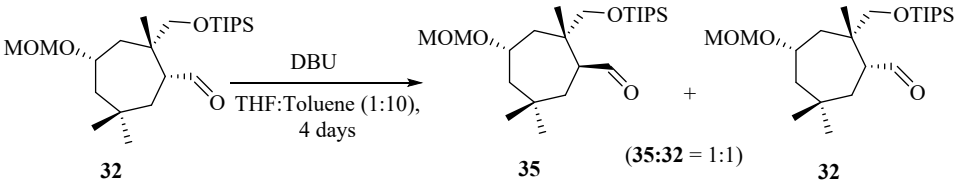
Step 2: TBAF (0.22 mL of a 1 M solution in THF) was added to a solution of the silyl ether **33** (77 mg, 0.187 mmol) in THF (1.5 mL) and then stirred for 3 hours. The reaction mixture was then quenched with saturated NH_4Cl solution (2.0 mL). The organic layer was then separated and the aqueous layer was extracted with ether (2 × 20 mL). The combined organic extracts were dried (Na_2SO_4), evaporated under reduced pressure and purified by column chromatography on silica gel to furnish the alcohol **34** (40 mg, 0.158 mmol, 85 %) as an oil.

R_f = 0.3 (10% EtOAc in hexane).

$[\alpha]_D^{30} = -4.8$ (c = 1.0 MeOH).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.90 – 5.77 (m, 1H), 5.06 – 4.92 (m, 2H), 4.64 (m, 2H), 3.76 (dd, J = 14.4, 5.3 Hz, 1H), 3.58 – 3.46 (m, 2H), 3.4 (s, 3H), 3.02 (m, 1H), 2.06 (m, 1H), 1.88 – 1.6 (m, 5H), 1.01 (s, 3H), 0.99 (s, 3H), 0.98 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.4, 114.1, 93.8, 69.4, 69.1, 55.1, 50.5, 46.4, 44.7, 42.5, 38.3, 34.4, 31.3, 26.2, 23.7. HRMS (ESI) *m/z*: calcd for $C_{15}H_{29}O_3$ $[M+H]^+$:257.2117, Found:257.2126.

(1*S*,2*S*,4*S*)-4-(methoxymethoxy)-2,6,6-trimethyl-2-(((triisopropylsilyl)oxy)methyl)-cycloheptanecarbaldehyde (mixture 32 and 35)



To a solution of aldehyde **32** (220 mg, 0.53 mmol) in THF:toluene (1:10, 3.0 mL) at room temperature was added DBU (0.1 mL, 0.03 mmol). The mixture was stirred at room temperature for 4 days. After that time no further improvement of diastereomeric excess was observed. The organic layer was separated and the aqueous layer was extracted with ether (2 × 10 mL). The solvent was removed with a rotary evaporator to afford 210 mg (90%) of a mixture of aldehydes **32** and **35** (ratio 1:1 by NMR analysis). Both the epimer was separated by flash chromatography on silica gel (yield of **35** = 110 mg, 1:50 EtOAc/hexane).

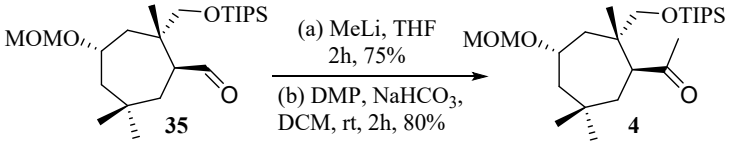
R_f = 0.5 (10% EtOAc in hexane).

$[\alpha]_D^{30} = +23.2$ (c = 0.5 MeOH).

^{1}H NMR of **35** (400 MHz, $CDCl_3$) δ 9.76 (d, J = 2.5 Hz, 1H), 4.61 (q, J = 6.9 Hz, 2H), 3.69 (t, J = 9.0 Hz, 2H), 3.47 (d, J = 9.7 Hz, 1H), 3.36 (s, 3H), 2.63 (d, J = 9.4 Hz, 1H), 1.92 – 1.66 (m, 3H), 1.61 – 1.30 (m, 5H), 1.05 (24 H), 0.95 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.1, 93.8, 71.4, 69.2, 55.1, 50.3, 48.4, 48.1, 40.2, 34.1, 31.1, 30.2, 30.1, 18.5, 18.0, 11.9.

HRMS (ESI) *m/z*: calcd for $C_{23}H_{47}O_4Si$ $[M+H]^+$:415.3244, Found:415.3252

1-((1*S*,2*S*,4*S*)-4-(methoxymethoxy)-2,6,6-trimethyl-2-(((triisopropylsilyl)oxy)methyl)-cycloheptyl)ethanone (4)



Step 1: To a solution of the aldehyde **35** (100 mg, 0.48 mmol) in ether (2.0 mL) was added MeLi (3.0 M in Et_2O; 0.24 mL, 0.72 mmol) at 0 °C under argon atmosphere. After stirring at room temperature for 1 hour, saturated $NaHCO_3$ solution was added and the mixture was extracted with EtOAc. The organic layer was washed with brine, and then dried over $MgSO_4$, and concentrated in vacuo. The residue was then purified by flash column chromatography (n-hexane:EtOAc = 10:1→5:1) to corresponding alcohol (76 mg, 75% yield), R_f = 0.3 (10% EtOAc in hexane).

Step 2: To a solution of alcohol obtained in the previous step (76 mg, 0.36 mmol) in CH_2Cl_2 (2.0 mL) was subjected to DMP oxidation by following the same reaction procedure as described earlier to afford the product ketone which was then purified by SiO_2 column chromatography (typically 10% EtOAc-hexane) to furnish ketone **4** (52 mg, 0.28 mmol, 80%).

R_f = 0.5 (10% EtOAc in hexane).

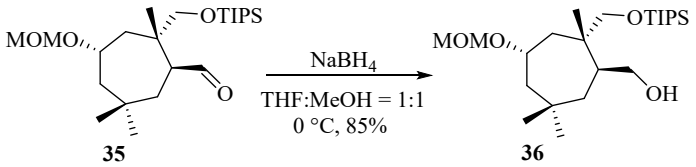
$[\alpha]_D^{30}$ = + 16.62 (*c* = 0.7 MeOH).

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.52 (q, *J* = 6.8 Hz, 2H), 3.54 (d, *J* = 9.5 Hz, 2H), 3.27 (s, 3H), 3.21 (d, *J* = 9.5 Hz, 1H), 2.76 (d, *J* = 9.3 Hz, 1H), 2.1 (s, 3H), 1.87 – 1.77 (m, 1H), 1.64 – 1.50 (m, 3H), 1.44 (dd, *J* = 14.0, 10.3 Hz, 2H), 1.35 (m, 3H, due to –TIPS group), 1.02–0.97 (24 H, 18H due to –TIPS group), 0.95 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 211.4, 93.9, 71.2, 69.5, 55.0, 49.2, 48.2, 48.1, 39.9, 37.2, 30.8, 30.6, 30.6, 30.5, 18.0, 17.8, 12.0.

HRMS (ESI) *m/z*: calcd for $C_{24}H_{49}O_4Si$ $[M+H]^+$:429.3400, Found:429.3408.

((1*S*,2*S*,4*S*)-4-(methoxymethoxy)-2,6,6-trimethyl-2-(((triisopropylsilyl)oxy)methyl)cycloheptyl)methanol (36)



35 **36**

To a stirred solution of aldehyde **35** (143 mg, 0.36 mmol) in 3.0 mL of THF:MeOH (1:1) was added $NaBH_4$ (12 mg, 0.44 mmol) at 0 °C, and the reaction mixture was stirred at the same temperature for 1 hour. The reaction mixture was then quenched with addition of saturated aqueous NH_4Cl solution (3.0 mL), and the aqueous layer was extracted with CH_2Cl_2 (5 mL × 3). The combined organic layer was washed with brine (10 mL), dried over Na_2SO_4, filtered,

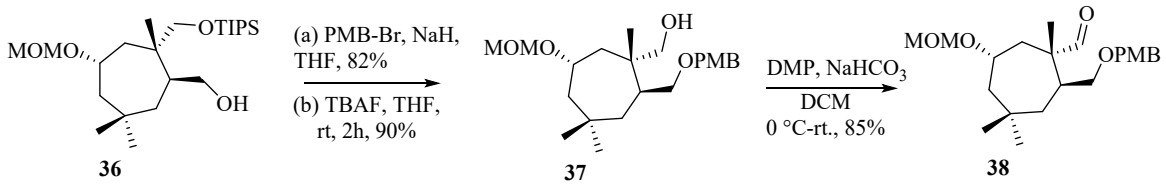
and concentrated under reduced pressure. The residue was then purified by flash silica gel column chromatography (hexane/ethyl acetate = 5/1) to afford **36** (122 mg, 85%) as a colorless oil (R_f= 0.2 (10% EtOAc in hexane), which was used for the next step.

$[\alpha]_D^{30}$ = + 22.6 (*c* = 0.6 MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.64 – 4.57 (m, 2H), 3.74 – 3.66 (m, 2H), 3.63 – 3.45 (m, 2H), 3.36 (s, 3H), 3.28 (dd, *J* = 10.8, 6.5 Hz, 1H), 1.84 – 1.70 (m, 2H), 1.64 (d, *J* = 13.8 Hz, 1H), 1.56 – 1.48 (m, 2H), 1.43 (q, *J* = 5.5 Hz, 2H), 1.17 – 1.12 (m, 3H), 1.10 (d, *J* = 5.4 Hz, 18H), 1.00 (s, 3H), 0.96 (s, 3H), 0.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 93.8, 72.0, 70.0, 65.3, 55.0, 48.8, 47.7, 40.2, 39.3, 38.5, 31.1, 30.2, 30.1, 18.0, 12.0.

HRMS (ESI) *m/z*: calcd for $C_{23}H_{49}O_4Si$ $[M+H]^+$:417.3400, Found:417.3392.

(1*S*,2*S*,6*S*)-2-(((4-methoxybenzyl)oxy)methyl)-6-(methoxymethoxy)-1,4,4-trimethyl-cycloheptanecarbaldehyde (38)



Step 1a: At room temperature, to a suspension of NaH (34 mg, 1.4 mmol) in THF (5 mL) was added solution of compound **36** (122 mg, 0.3 mmol in 1.0 mL of THF). The reaction solution was stirred at room temperature for 30 min, and then the mixture was refluxed for 1 hour. After cooling to room temperature, to this solution was added 1-(bromomethyl)-4-methoxybenzene (90.0 mg, 0.45 mmol) slowly. The reaction solution was then stirred for 8 hours. The resulting solution was treated with water, and extracted with ethyl acetate. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford crude product that was purified by chromatography through a silica column to furnish pure **6** (125 mg, 82%).

Step 1b: To a solution of compound **6** (125 mg, 0.24 mmol) was subjected to the same reaction procedure as described earlier to afford the crude product (after removal of the –TIPS group), that was purified by SiO_2 column chromatography (typically 10% EtOAc-hexanes) to furnish alcohol **37** (78 mg, 90%).

R_f = 0.3 (20% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 31.4 (*c* = 1.2 MeOH).

^{1}H NMR of **37** (500 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 4.59 – 4.45 (m, 2H), 4.32 (s, 2H), 3.71 (s, 3H), 3.63 – 3.52 (m, 1H), 3.47 – 3.34 (m, 2H), 3.25 (s, 3H), 3.05 (dd, *J* = 9.5, 4.5 Hz, 2H), 1.95 (td, *J* = 9.2, 4.5 Hz, 1H), 1.76 – 1.64 (2, 1H), 1.53 – 1.45 (m, 2H), 1.38 – 1.25 (m, 2H), 0.86 (s, 6H), 0.65 (s, 3H).

^{13}C NMR of **37** (126 MHz, $CDCl_3$) δ 159.3, 129.9, 129.2, 113.8, 94.0, 73.8, 72.9, 71.2, 70.9, 55.2, 55.1, 47.1, 46.5, 39.5, 39.2, 36.3, 30.7, 30.7, 30.6, 18.2.

HRMS (ESI) *m/z*: calcd for $C_{22}H_{37}O_5$ $[M+H]^+$:381.2641, Found: 381.2654.

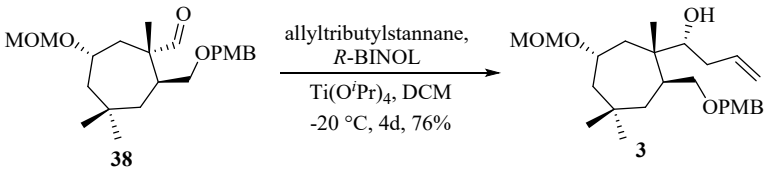
Step 2: To a solution of alcohol **37** (78 mg, 0.38 mmol) in CH_2Cl_2 (4.0 mL) was subjected to DMP oxidation by following the same reaction procedure as described earlier and the product was purified by SiO_2 column chromatography (typically 10% EtOAc-hexanes) to afford aldehyde **38** (68 mg, 85%). R_f = 0.6 (20% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 25.6 (*c* = 0.8 MeOH).

^{1}H NMR of **38** (500 MHz, $CDCl_3$) δ 9.34 (s, 1H), 7.12 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.50 (ABq, *J* = 15.0 Hz, 2H), 4.25 (ABq, *J* = 10.0 Hz, 2H), 3.77 (s, 3H), 3.70 – 3.60 (m, 1H), 3.25 (s, 3H), 3.10 (dd, *J* = 9.5, 6.1 Hz, 1H), 3.02 (t, *J* = 9.5 Hz, 1H), 2.31 (td, *J* = 9.4, 6.1 Hz, 1H), 1.58-1.3 (m, 6H), 0.96 (s, 3H), 0.93 (s, 3H), 0.90 (s, 3H).**;** ^{13}C NMR of **38** (126 MHz, $CDCl_3$) δ 203.8, 159.2, 129.9, 129.2, 113.7, 94.0, 72.7, 72.3, 69.9, 55.24, 55.20, 49.1, 48.1, 44.2, 38.0, 37.2, 31.8, 30.4, 29.8, 14.0.

HRMS (ESI) *m/z*: calcd for $C_{22}H_{35}O_5$ $[M+H]^+$:379.2484, Found:379.2481.

(*R*)-1-((1*S*,2*S*,6*S*)-2-(((4-methoxybenzyl)oxy)methyl)-6-(methoxymethoxy)-1,4,4-trimethylcycloheptyl)but-3-en-1-ol (3):



A mixture of (*R*)-(+)-1,1'-bi-2-naphthol (10.0 mg, 0.114 mmol), 1.0 M of $Ti(O^iPr)_4$ in CH_2CI_2 (1.0 mL, 0.114 mmol), and oven-dried powdered 4Å molecular sieves (200 mg) in CH_2Cl_2 (2 mL) was heated at reflux for 1 hour. The red-brown mixture was cooled to room temperature and aldehyde **38** (54 mg, 0.57mmol) was added. After being stirred for 10 min, the contents were cooled to –78 °C, and allyltri ^{n}butylstannane (55 mg, 0.2 mmol) was added. The reaction was stirred for 10 min and then placed in a –20 °C freezer for 96 hours. Saturated $NaHCO_3$ (2.0 mL) was added, and the contents were stirred for 1h and then poured over Na_2SO_4

and filtered through a plug of celite. The crude material was purified by flash chromatography, eluting with 20:1 hexanes/EtOAc to give **3** as a clear oil (42 mg, 76%).

R_f = 0.3 (20% EtOAc in hexane).

$[\alpha]_D^{30}$ = + 31.4 (*c* = 1.0 MeOH).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.6 Hz, 2H), 6.83 – 6.69 (d, *J* = 8.6 Hz, 2H), 5.83 (ddt, *J* = 17.1, 10.3, 6.8 Hz, 1H), 4.97 (dd, *J* = 9.2, 8.3 Hz, 2H), 4.51 (dd, *J* = 15.6, 6.8 Hz, 2H), 4.36 – 4.24 (m, 2H), 3.70 (s, 3H), 3.65 – 3.53 (m, 1H), 3.43 – 3.34 (m, 2H), 3.25 (s, 3H), 3.05 (dd, *J* = 9.6, 5.4 Hz, 1H), 2.24-2.0 (m, 4H), 1.64-1.44 (m, 5H), 0.86 (s, 6H), 0.71 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 137.6, 130.2, 129.2, 116.0, 113.8, 93.9, 76.0, 73.3, 72.6, 71.2, 55.26, 55.2, 46.1, 42.4, 41.8, 39.5, 36.8, 36.2, 30.7, 30.66, 30.60, 18.5.

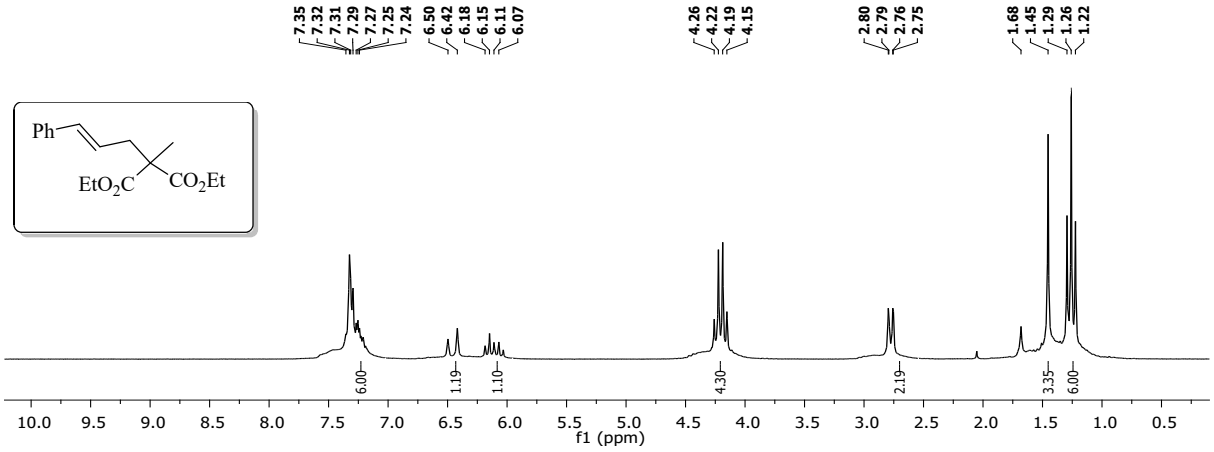
HRMS (ESI) *m/z*: calcd for $C_{25}H_{41}O_5$ $[M+H]^+$:421.2954, Found:421.2959.

References

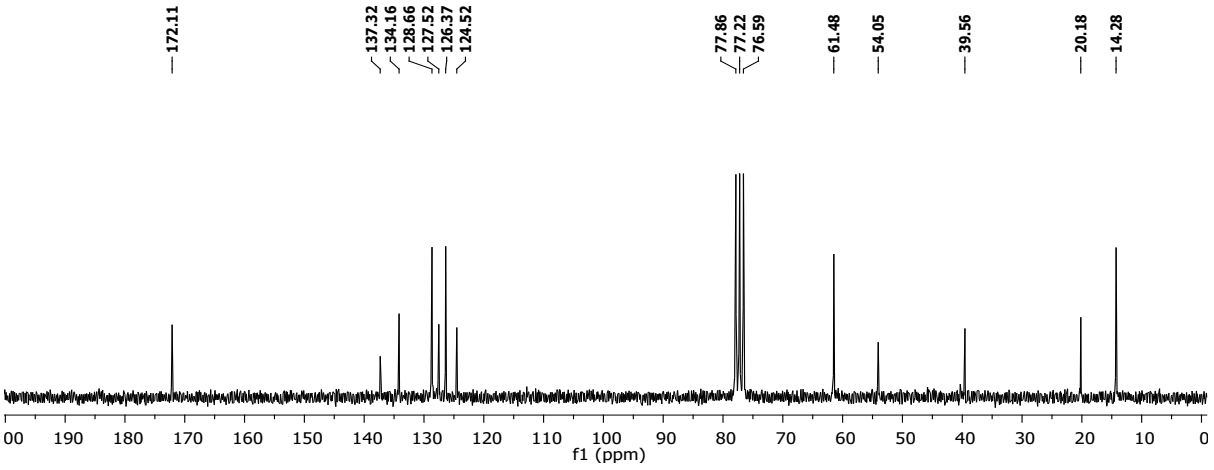
1. (a) T. R. Hoye, C. S. Jeffrey and F. Shao, Mosher Ester Analysis for the Determination of Absolute Configuration of Stereogenic (Chiral) Carbinol Carbons. *Nat. Protoc.*, **2007**, 2, 2451-2458. (b) D. P. Curran and B. A. Sui, "Shortcut" Mosher Ester Method to Assign Configurations of Stereocenters in Nearly Symmetric Environments. Fluorous Mixture Synthesis and Structure Assignment of Petrocortyne A. *J. Am. Chem. Soc.*, **2009**, 131, 5411-5413. (c) D. R. Kelly, A New Method for the Determination of the Absolute Stereochemistry of Aromatic and Heteroaromatic Alkanols Using Mosher's Esters. *Tetrahedron Asymmetry*., **1999**, 10, 2927-2934.

Spectral Data of the Synthesized Compounds

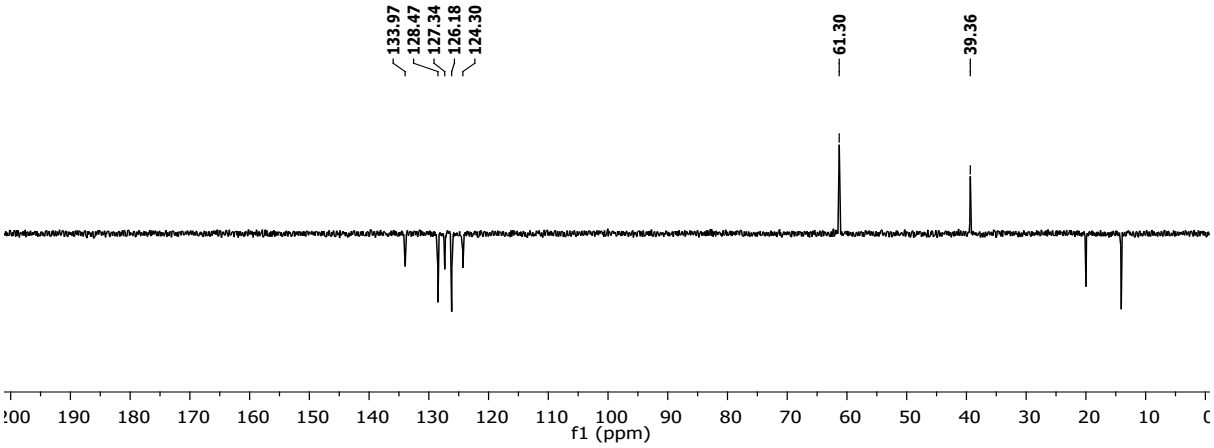
^{1}H-NMR of compound 11b ($CDCl_3$, 200 MHz)



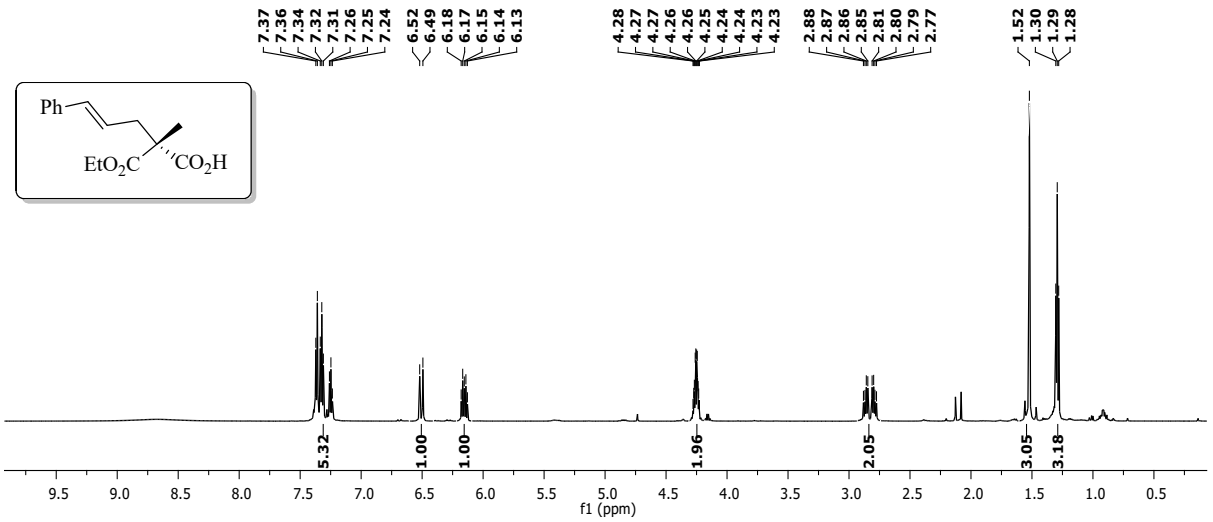
^{13}C-NMR of compound 11b ($CDCl_3$, 50MHz)



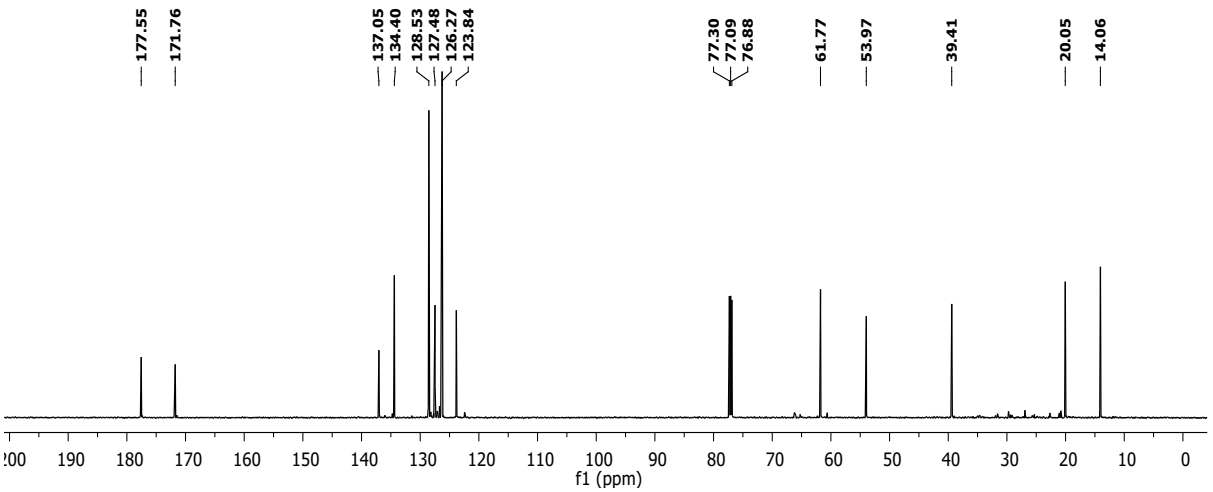
DEPT-135 NMR of compound 11b ($CDCl_3$, 50 MHz)



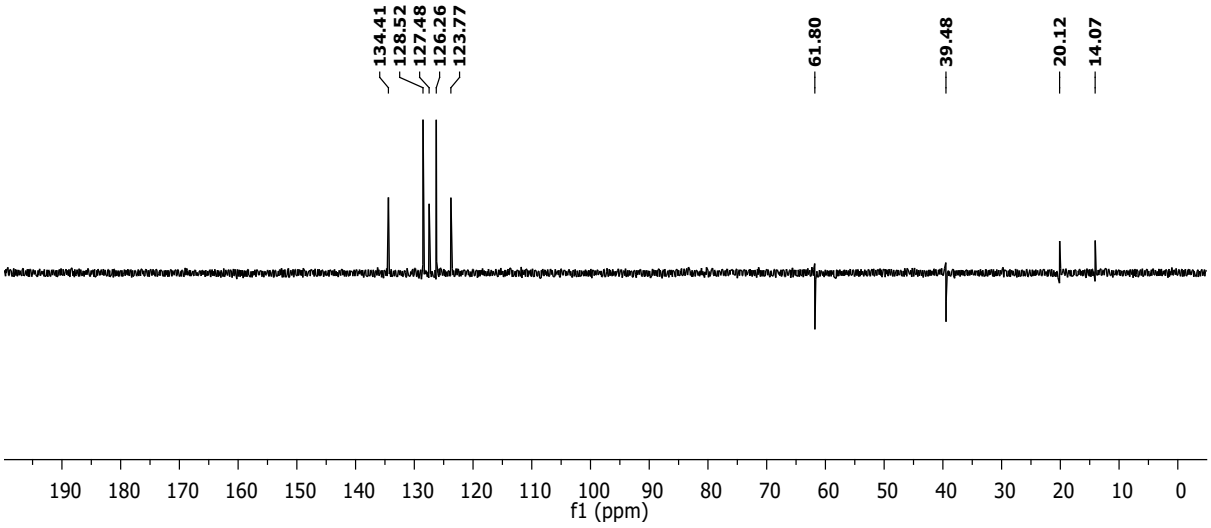
^{1}H-NMR of compound 12 ($CDCl_3$, 600MHz)



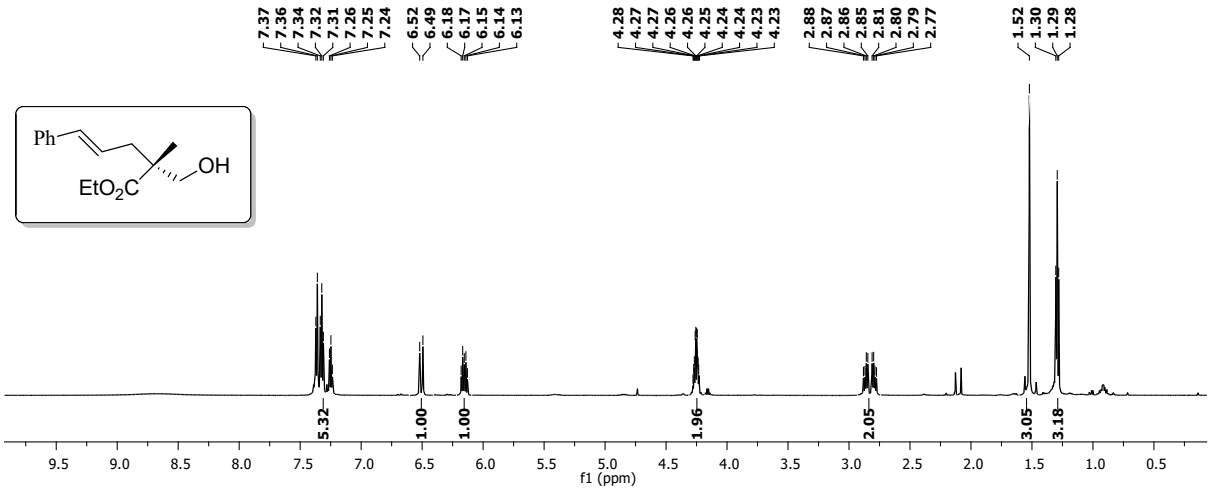
^{13}C-NMR of compound 12 ($CDCl_3$, 150MHz)



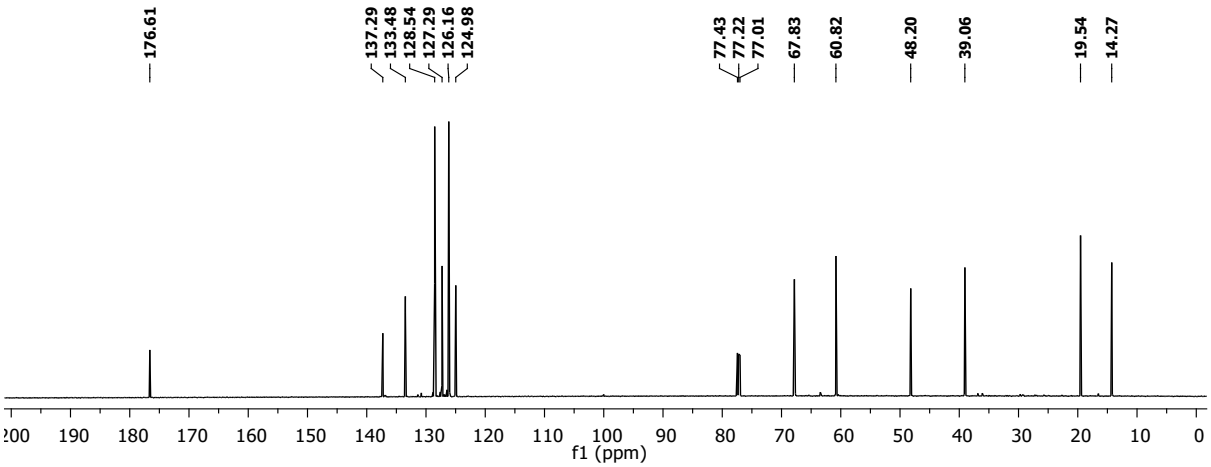
DEPT-135 NMR of compound 12 ($CDCl_3$, 150 MHz)



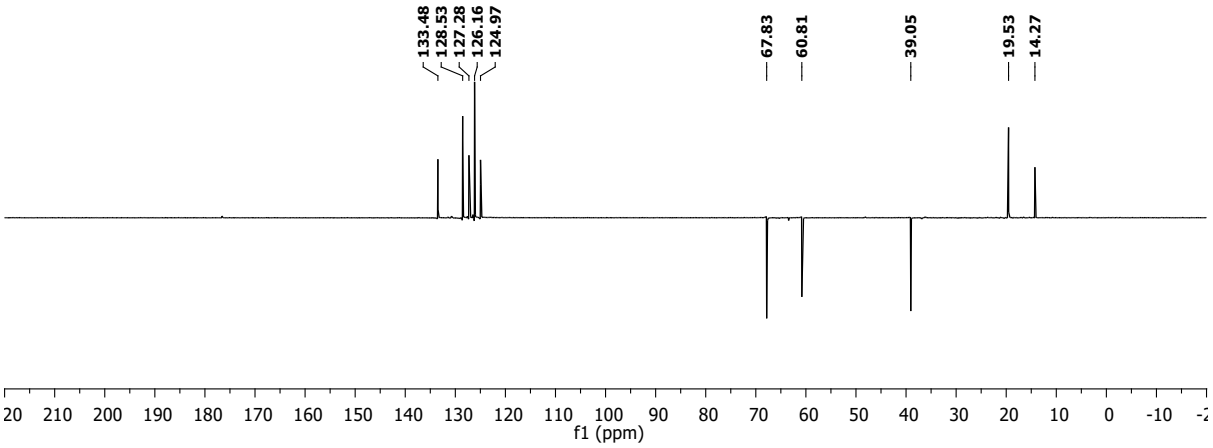
^{1}H-NMR of compound 13 ($CDCl_3$, 600MHz)



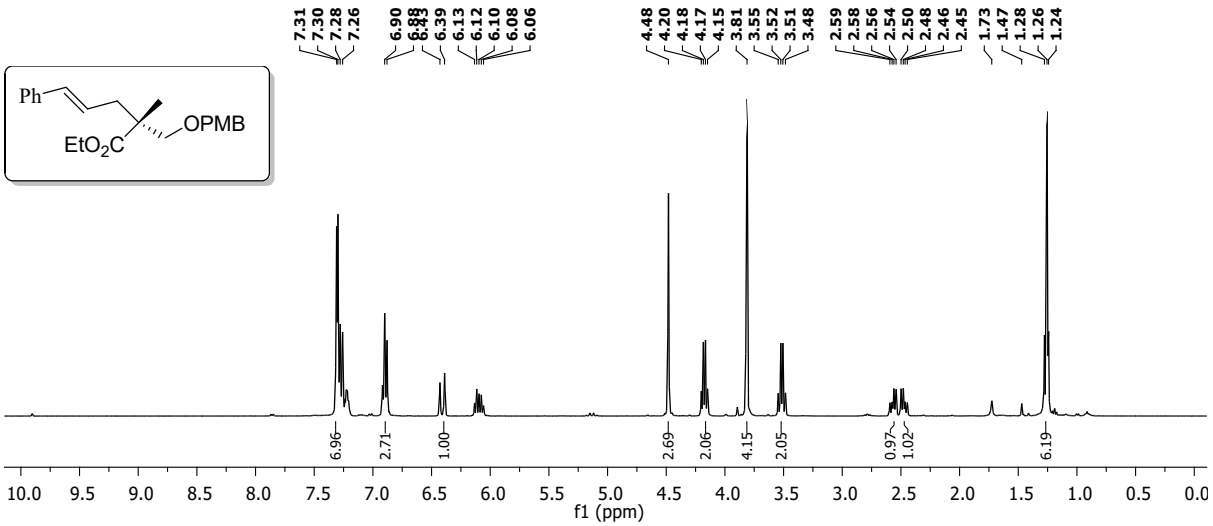
^{13}C-NMR of compound 13 ($CDCl_3$, 150 MHz)



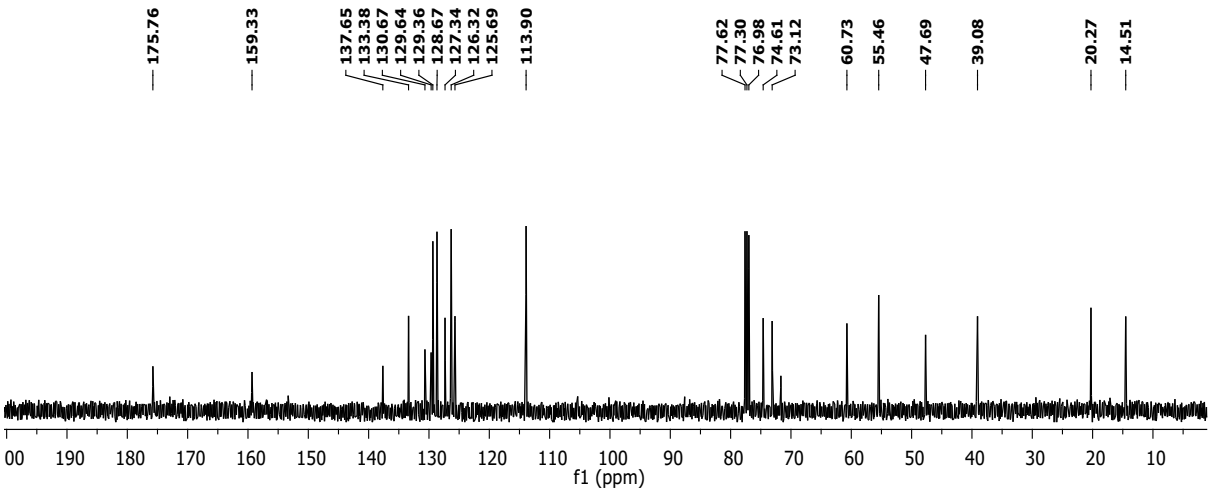
DEPT-135 NMR of compound 13 ($CDCl_3$, 150 MHz)



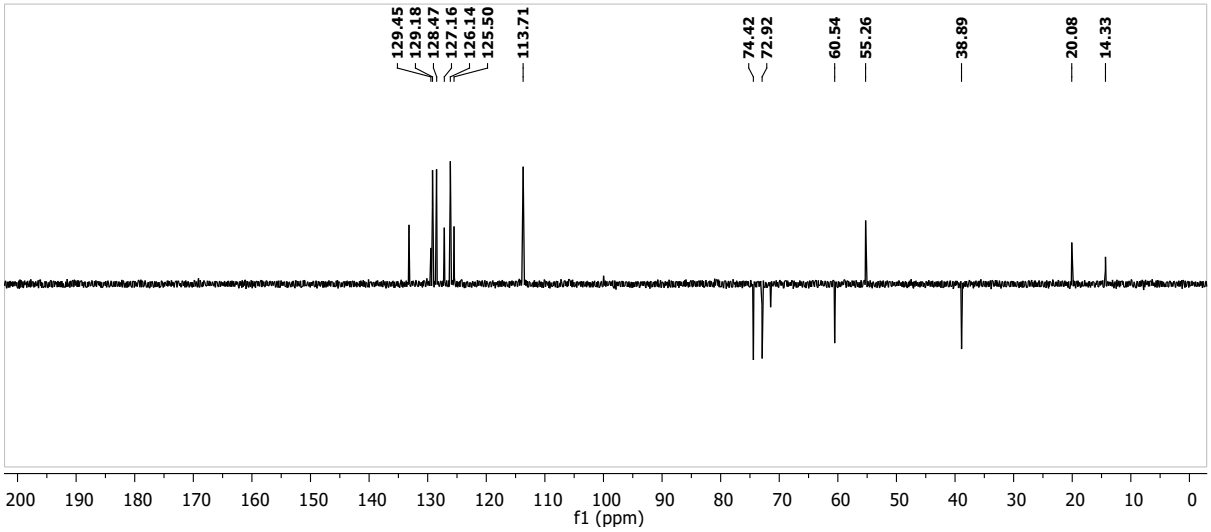
^{1}H-NMR of compound 14 ($CDCl_3$, 400MHz)



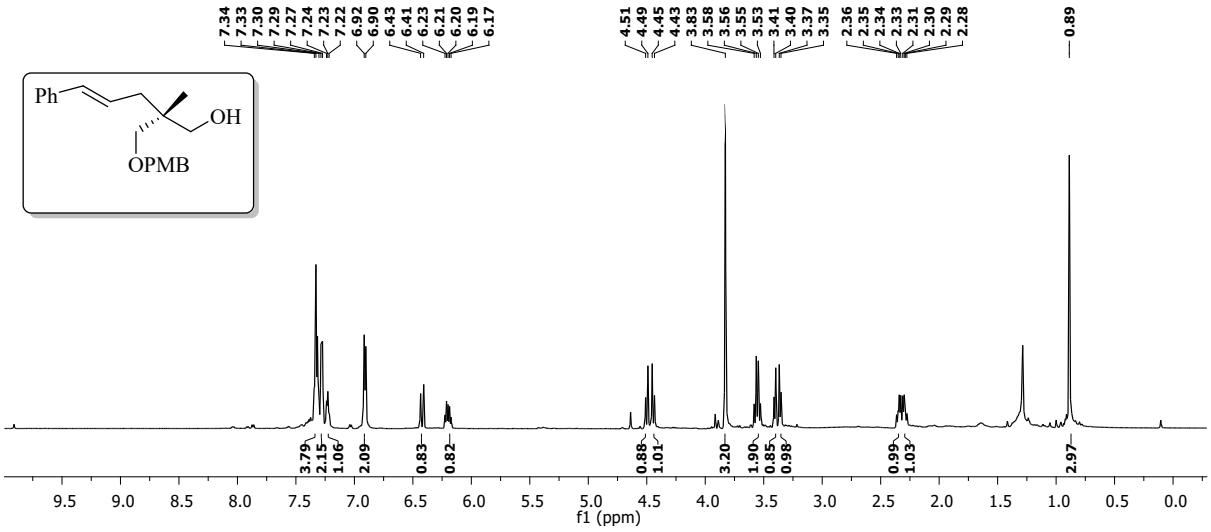
^{13}C-NMR of compound 14 ($CDCl_3$, 100MHz)



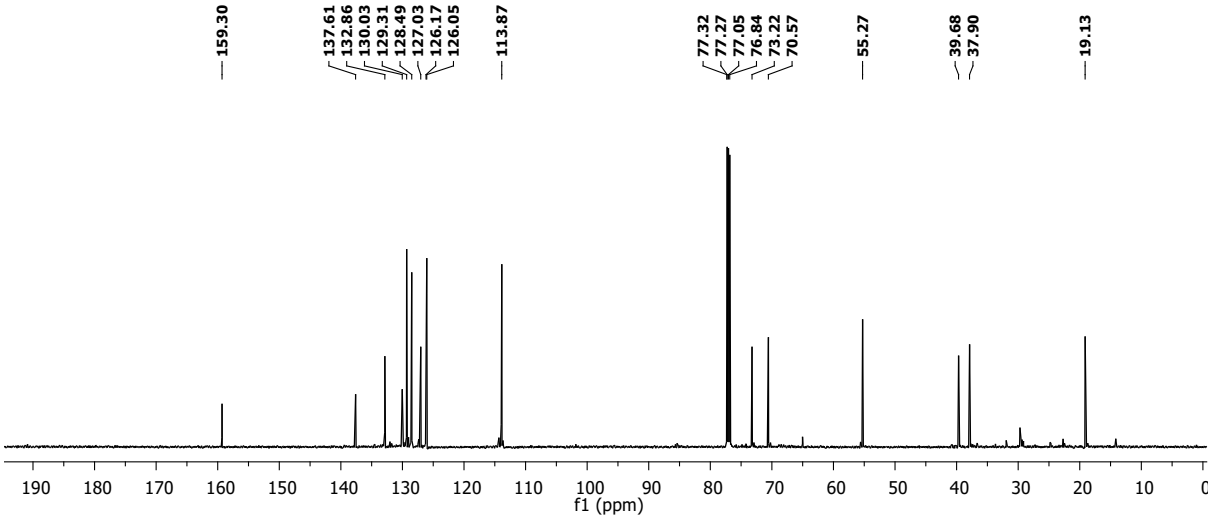
DEPT-135 NMR of compound 14 ($CDCl_3$, 100 MHz)



^{1}H-NMR of compound 15 ($CDCl_3$, 400MHz)



^{13}C-NMR of compound 15 ($CDCl_3$, 100MHz)



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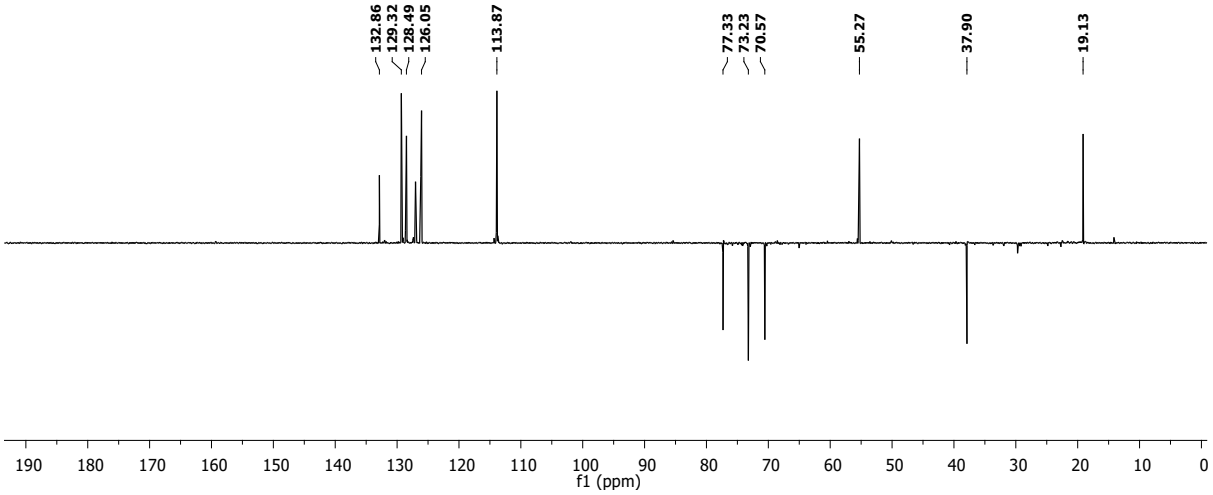
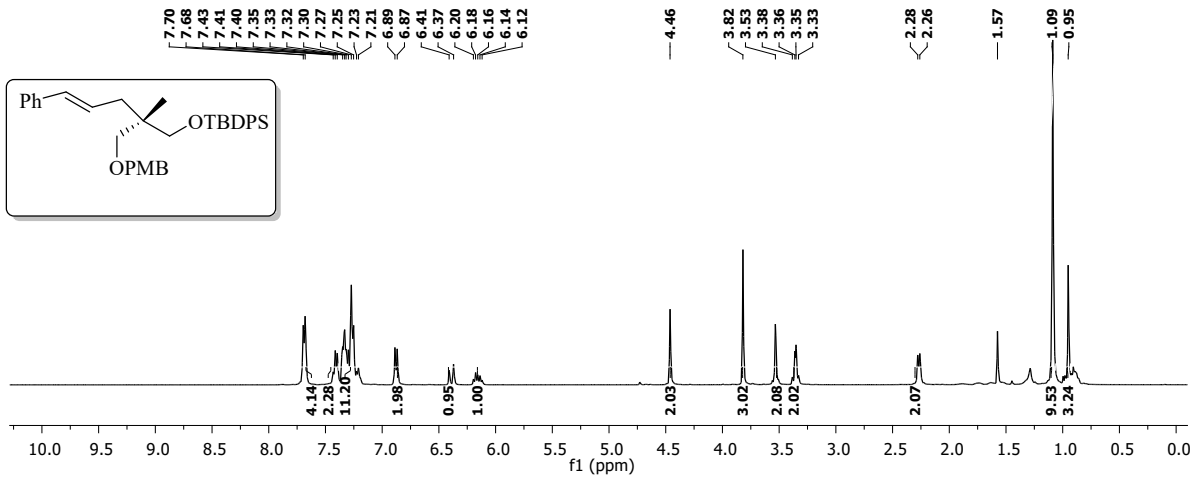


^{1}H-NMR of compound 16 ($CDCl_3$, 400MHz)



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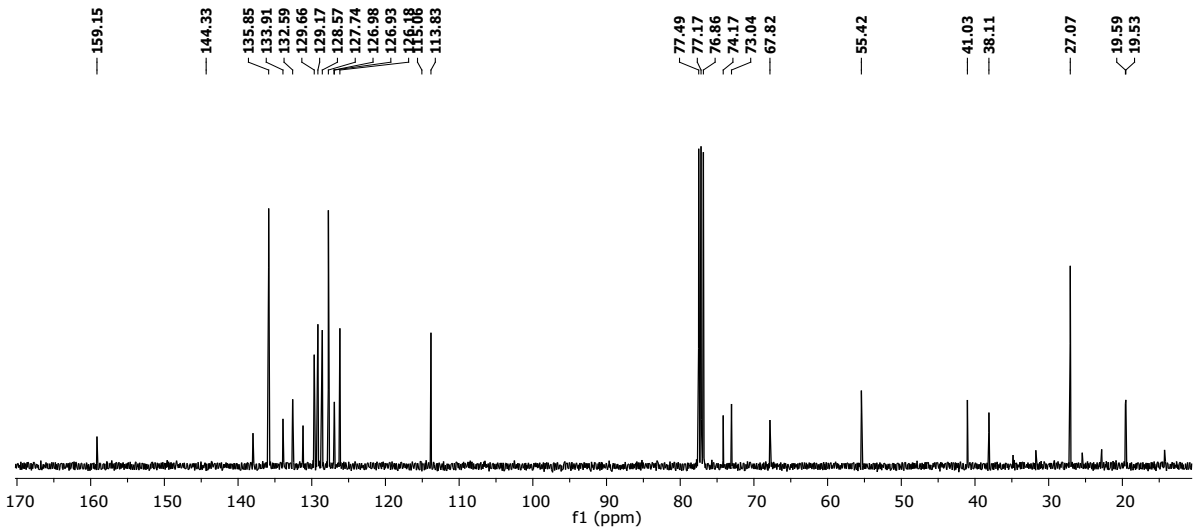

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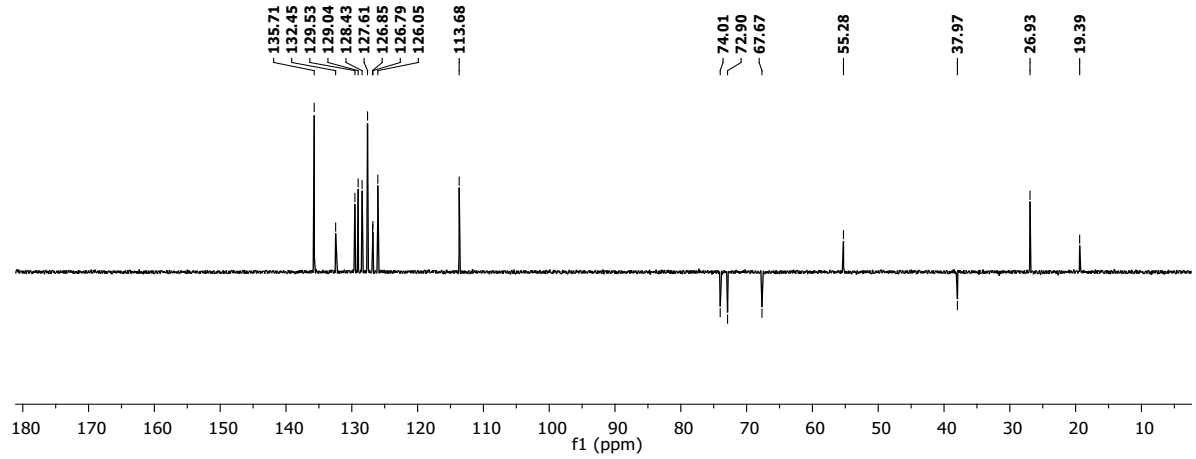

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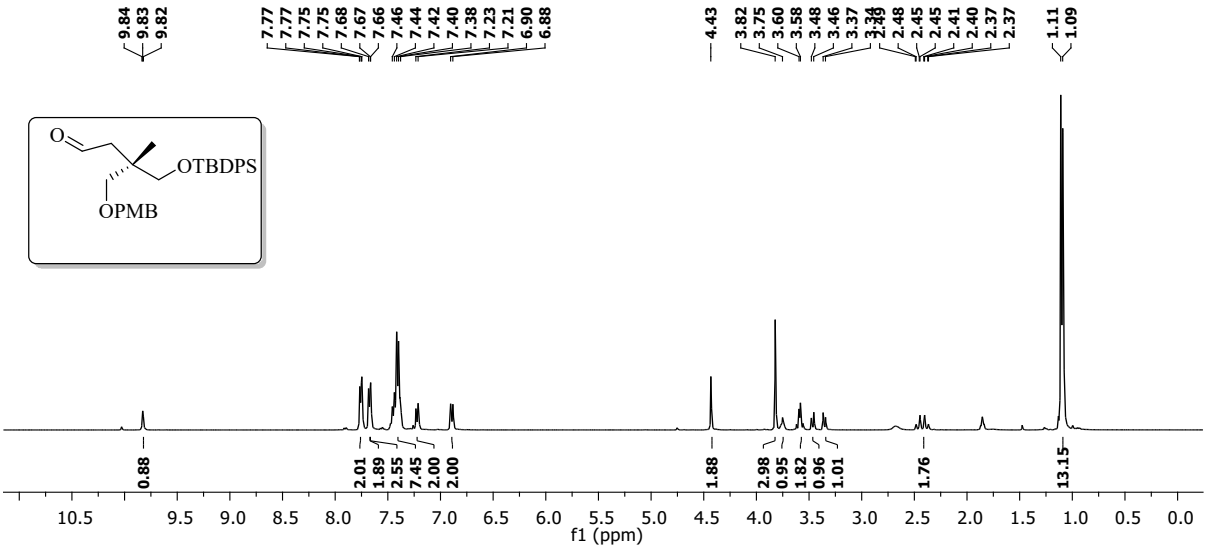
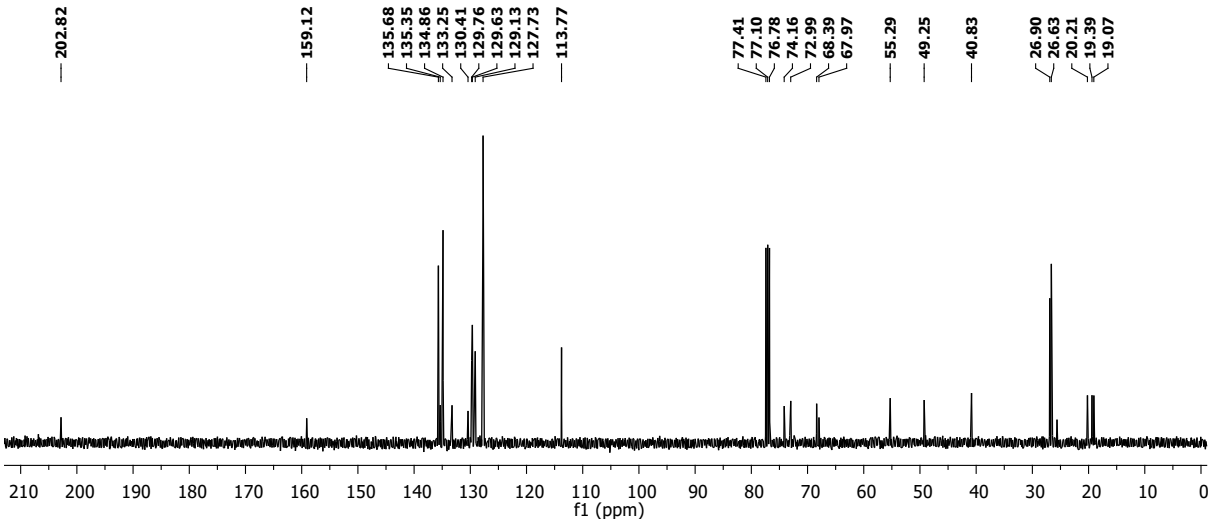
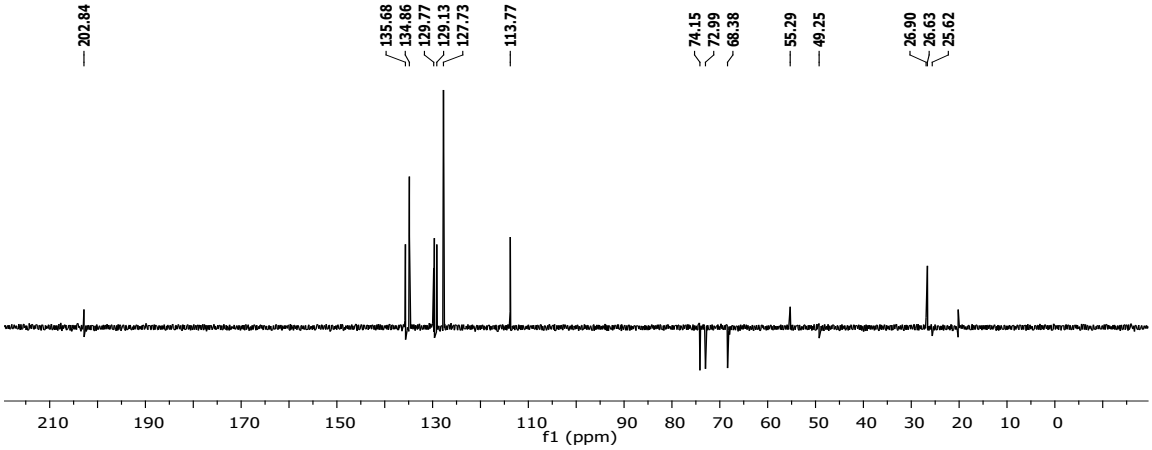


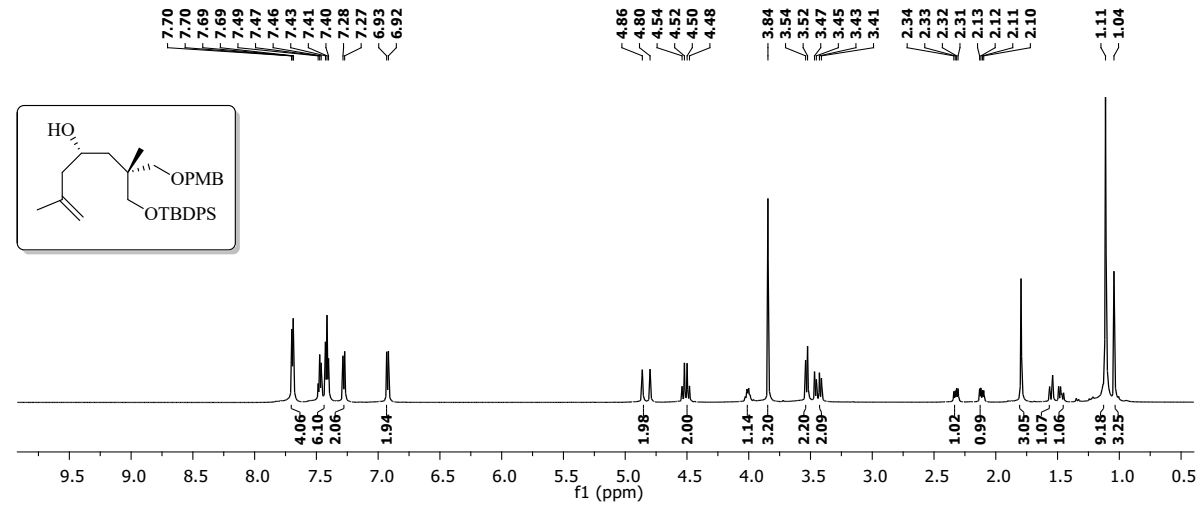
^{13}C-NMR of compound 17 ($CDCl_3$, 100MHz)



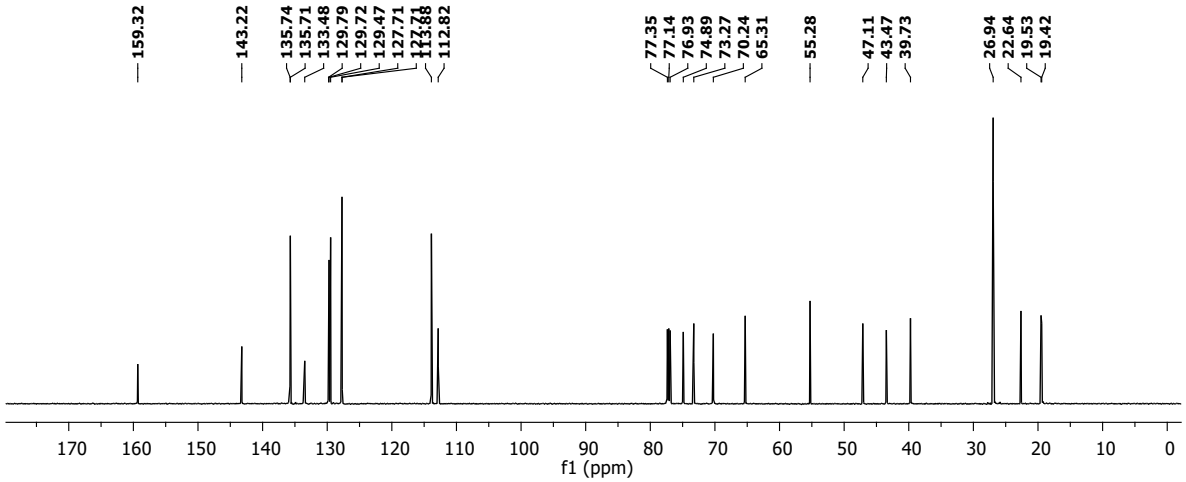
DEPT-135 NMR of compound 17 ($CDCl_3$, 100 MHz)



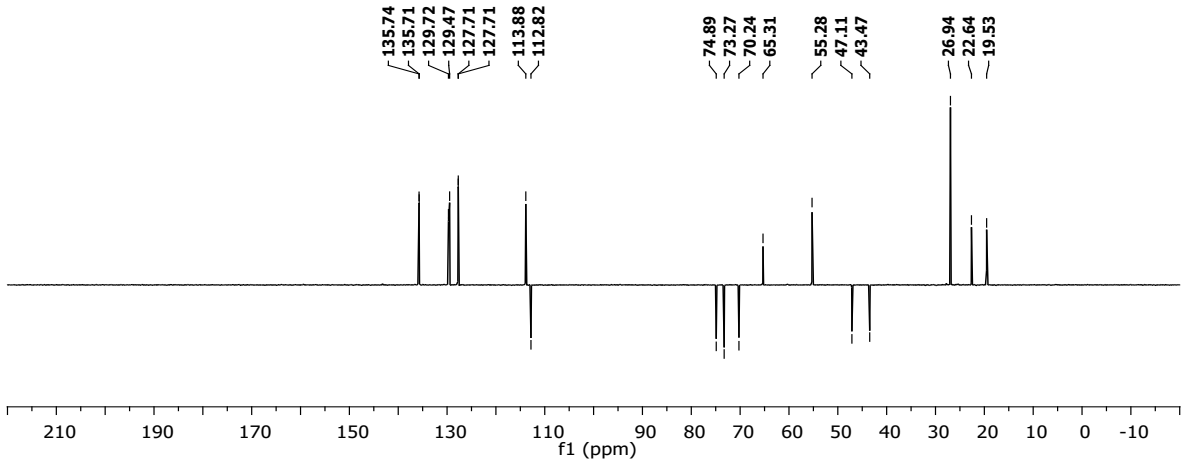
^{1}H-NMR of compound 18a ($CDCl_3$, 600MHz)



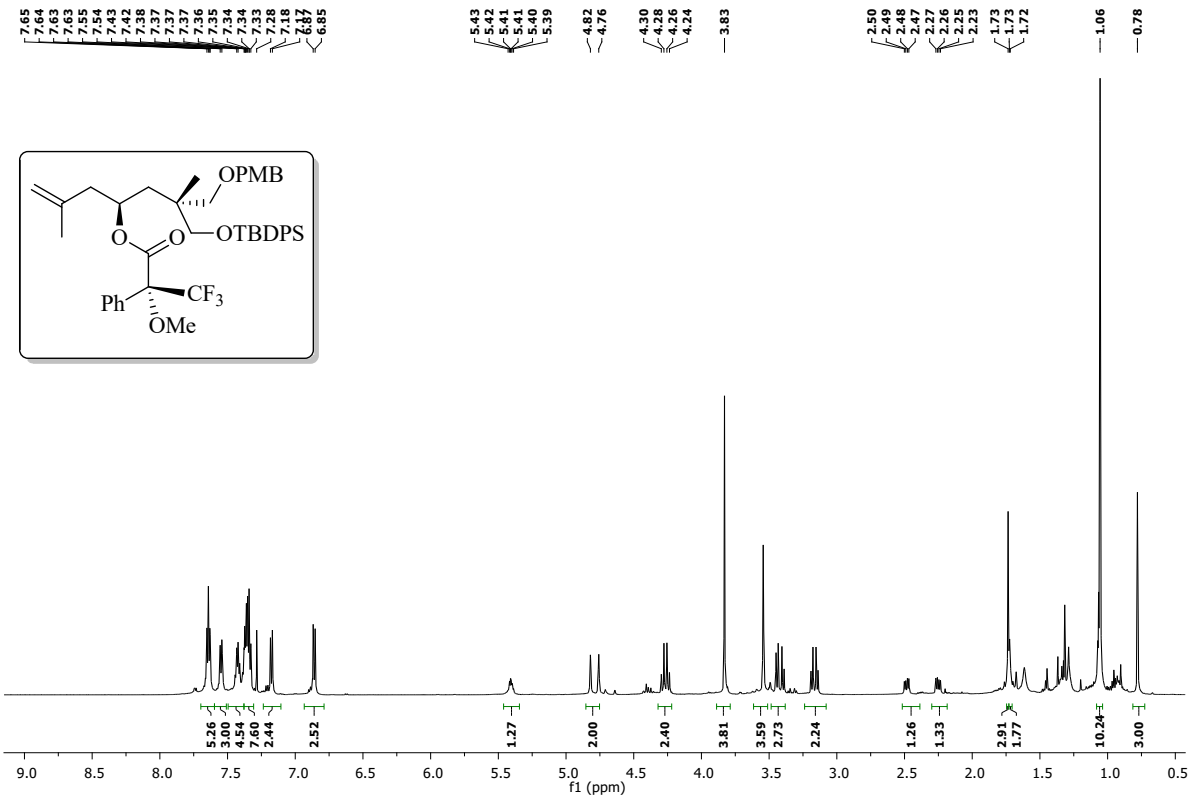
^{13}C-NMR of compound 18a ($CDCl_3$, 150MHz)



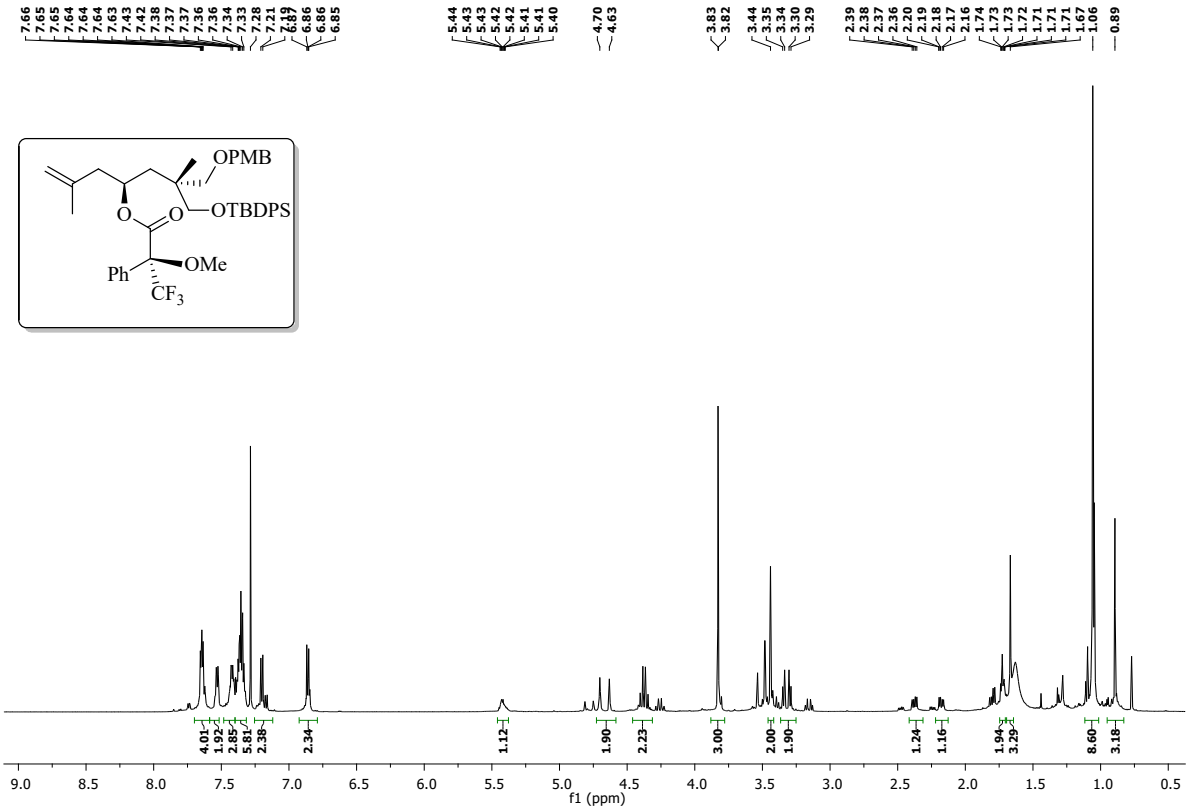
DEPT-135 NMR of compound 18a ($CDCl_3$, 150 MHz)



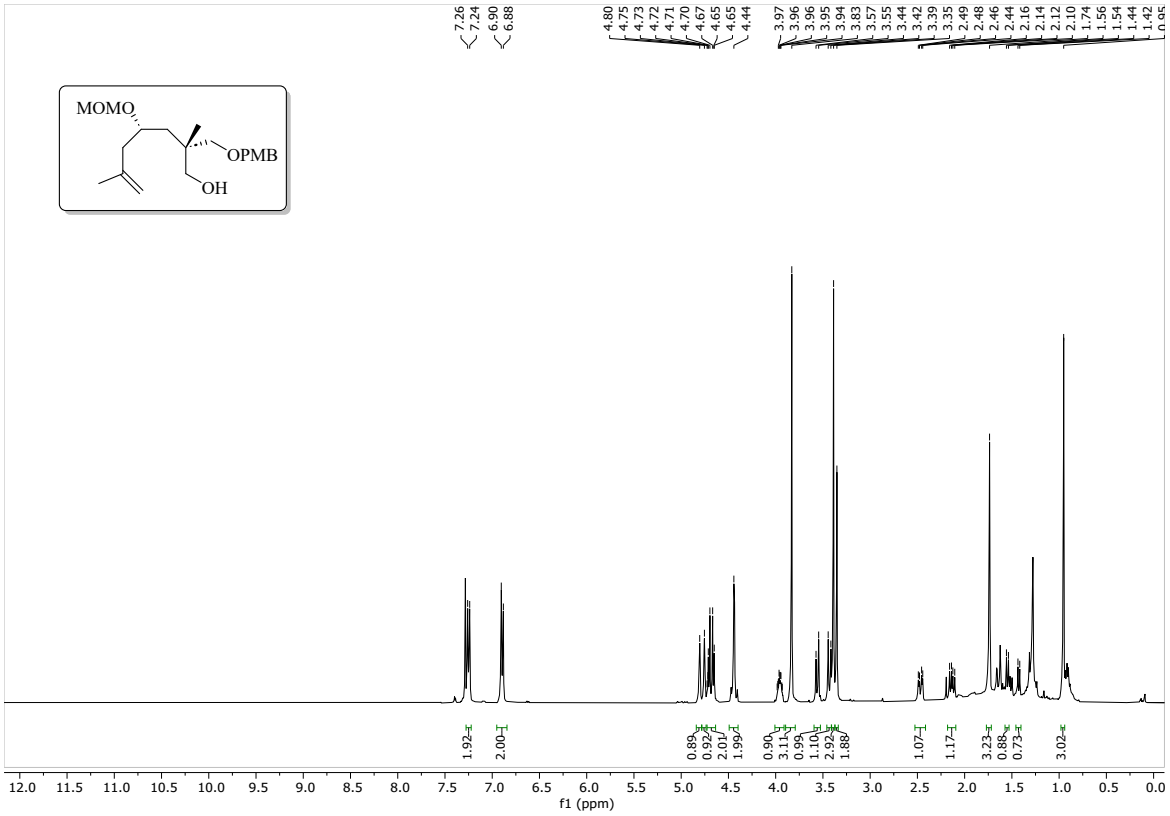
^{1}H-NMR of *R*-Mosher ester of 18a ($CDCl_3$, 600MHz)



^{1}H-NMR of *S*-Mosher ester of 18a ($CDCl_3$, 600MHz)



^{1}H-NMR of compound 21 ($CDCl_3$, 400MHz)



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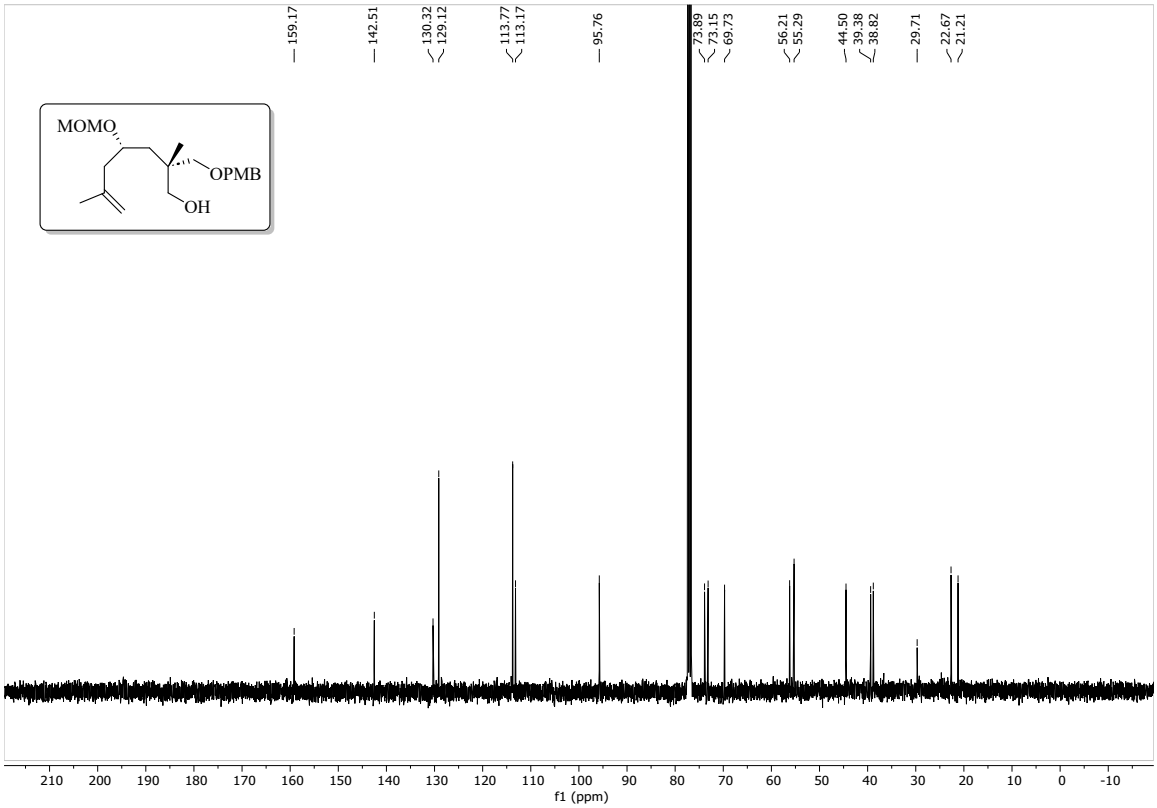
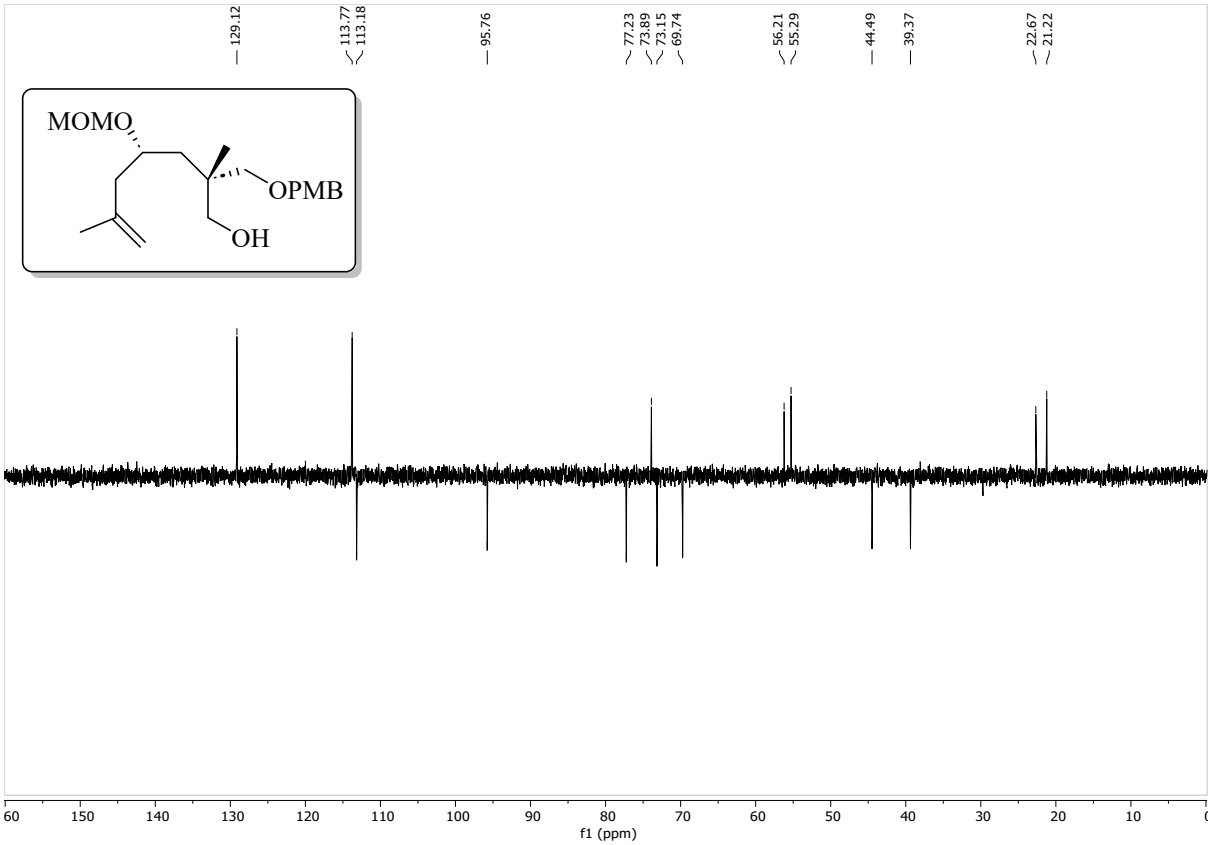
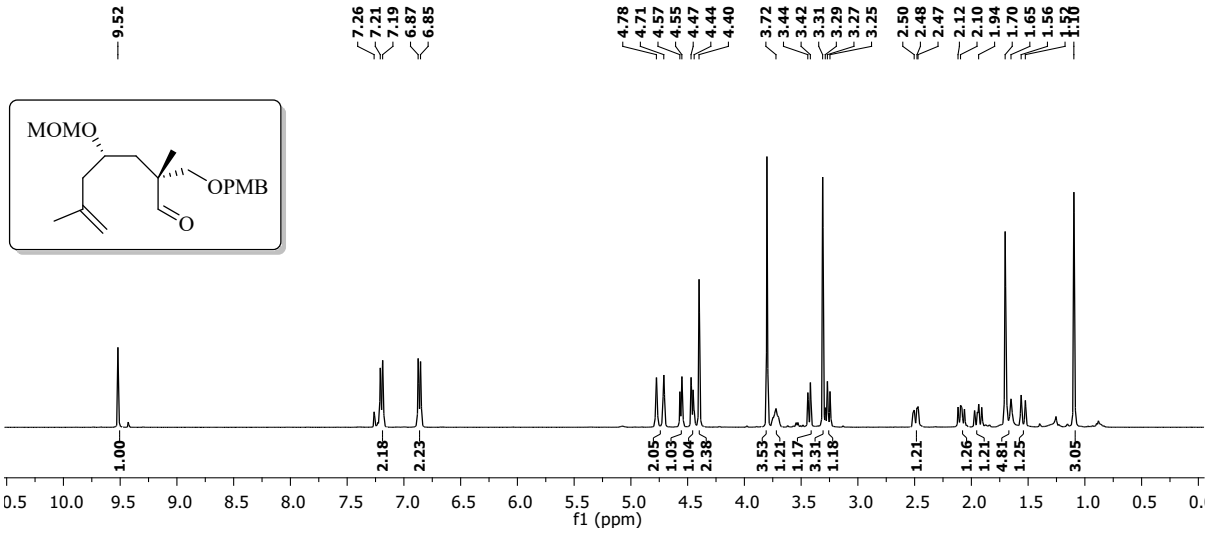


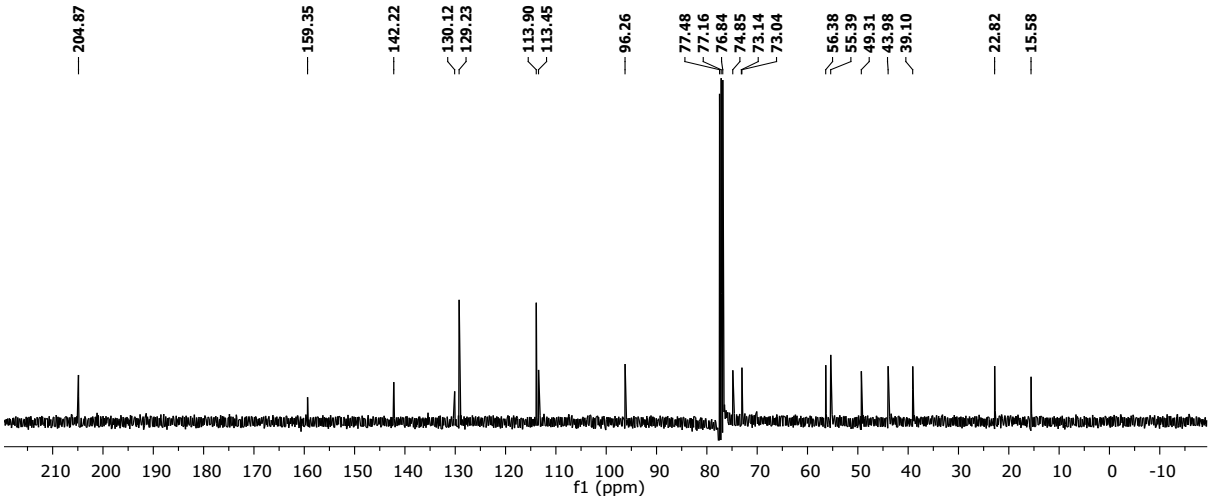
DEPT-135 NMR of compound 21 ($CDCl_3$, 100 MHz)



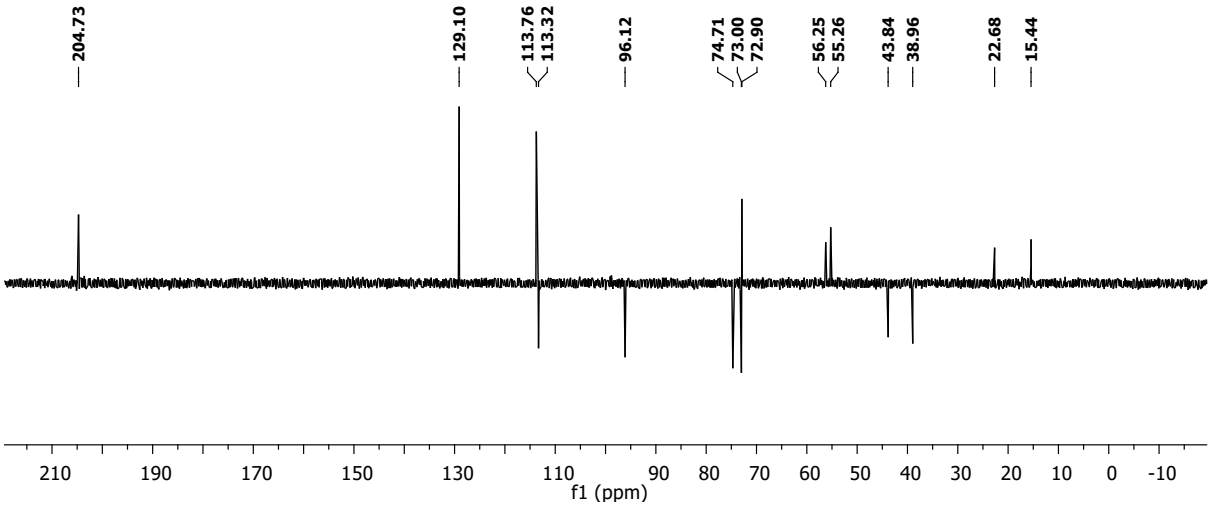
^{1}H-NMR of compound 22 ($CDCl_3$, 400MHz)



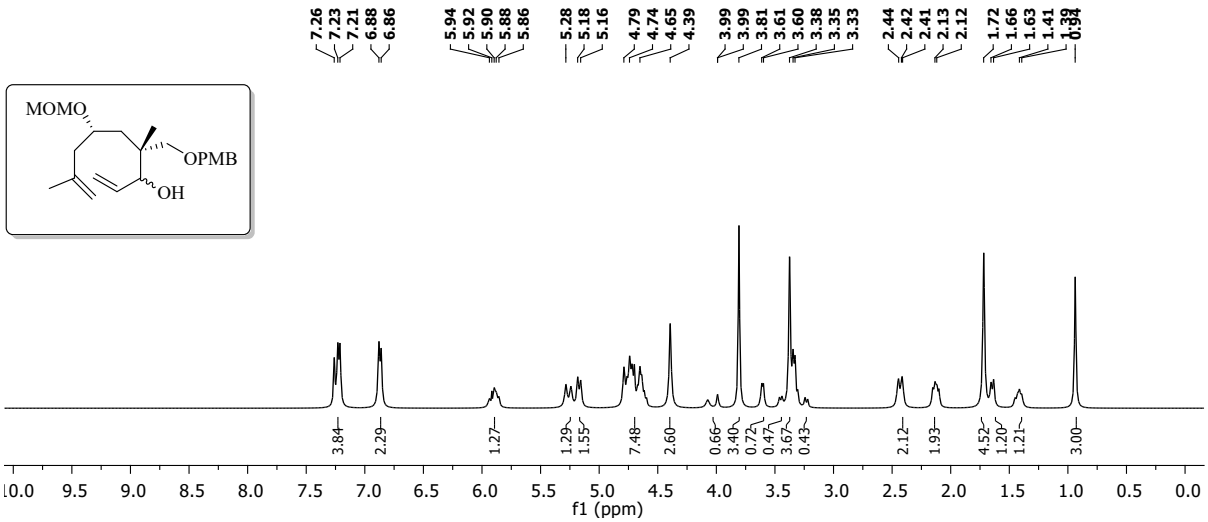
^{13}C-NMR of compound 22 ($CDCl_3$, 100MHz)



DEPT-135 NMR of compound 22 ($CDCl_3$, 100 MHz)



^{1}H-NMR of compound 9 ($CDCl_3$, 400MHz)



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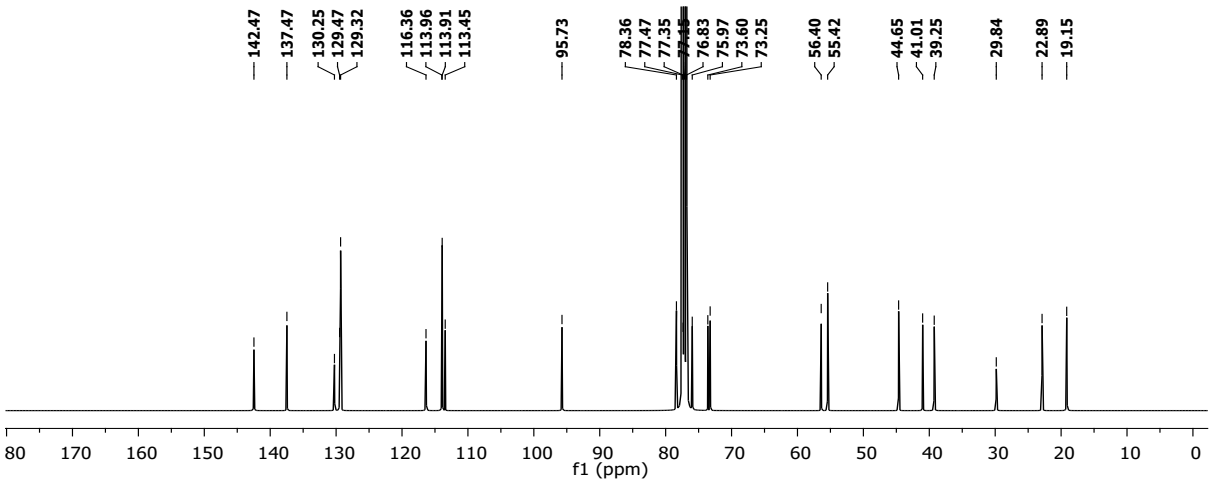
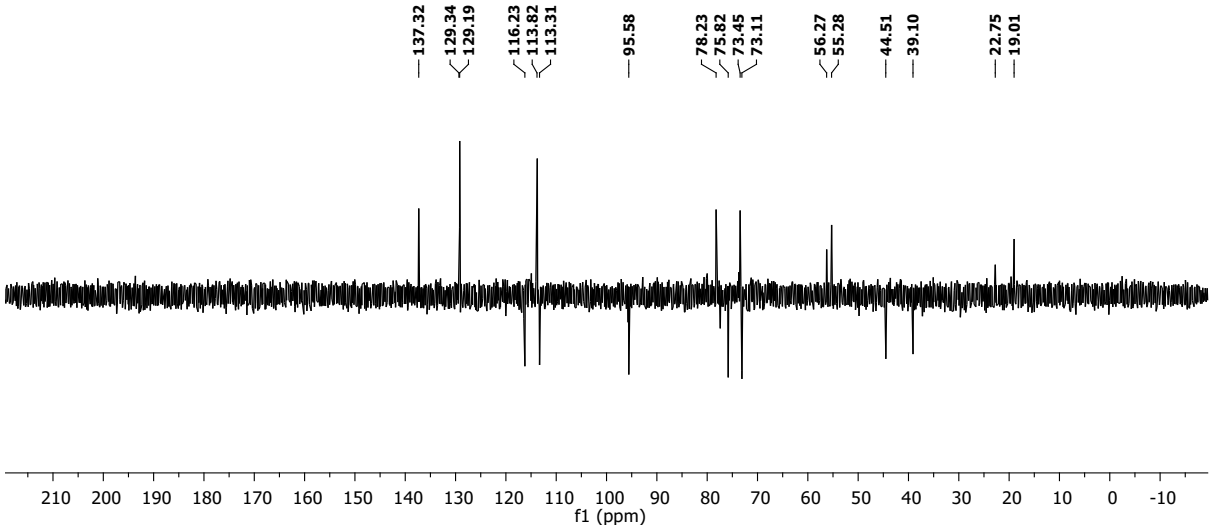
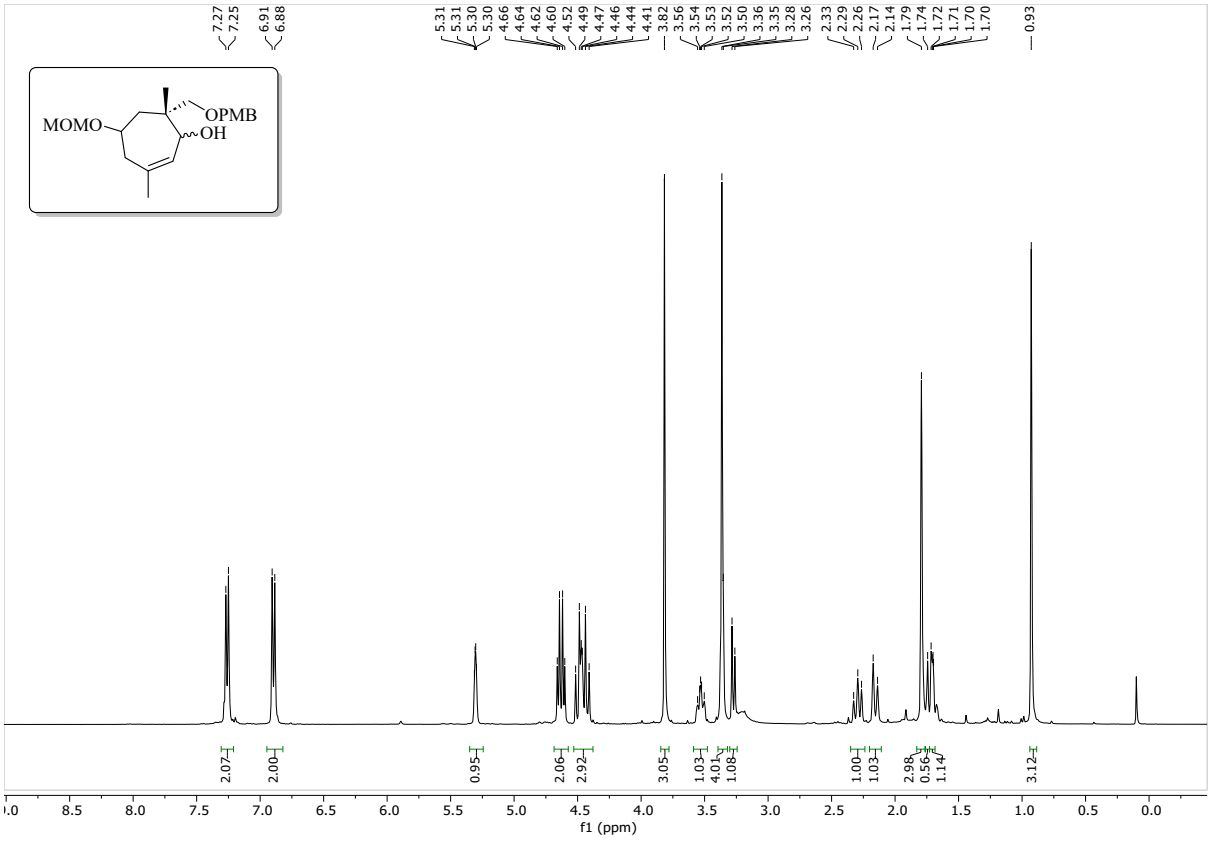


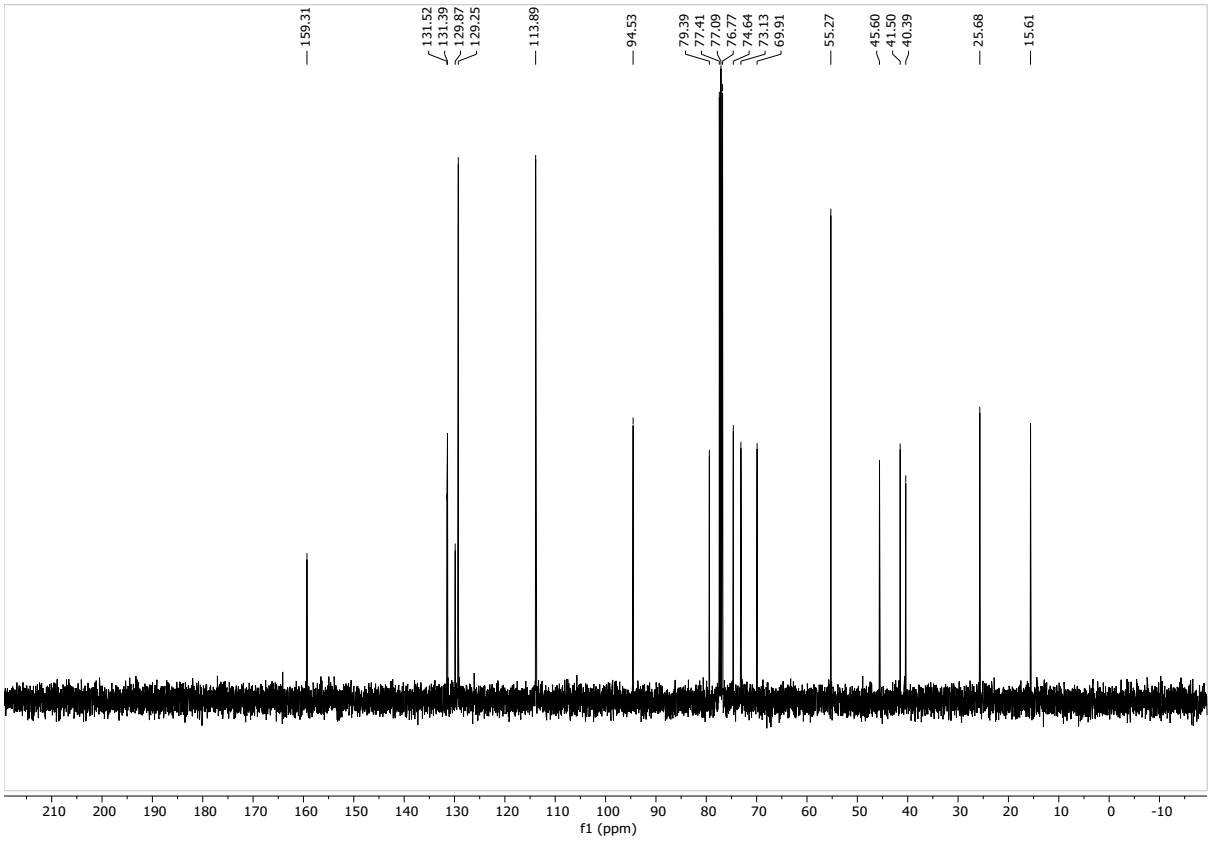
DEPT-135 NMR of compound 9 ($CDCl_3$, 100 MHz)



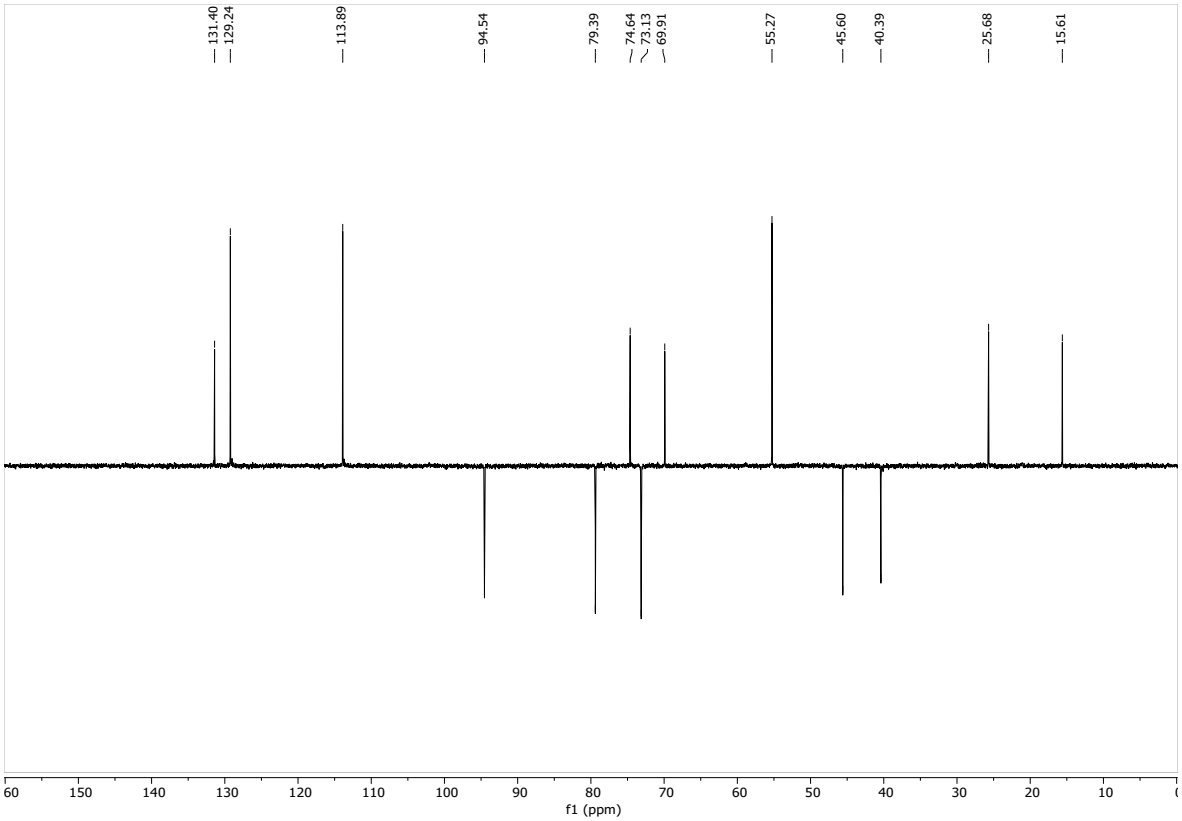
^{1}H-NMR of major diastereomer 23 (less polar in TLC; $CDCl_3$, 400 MHz)



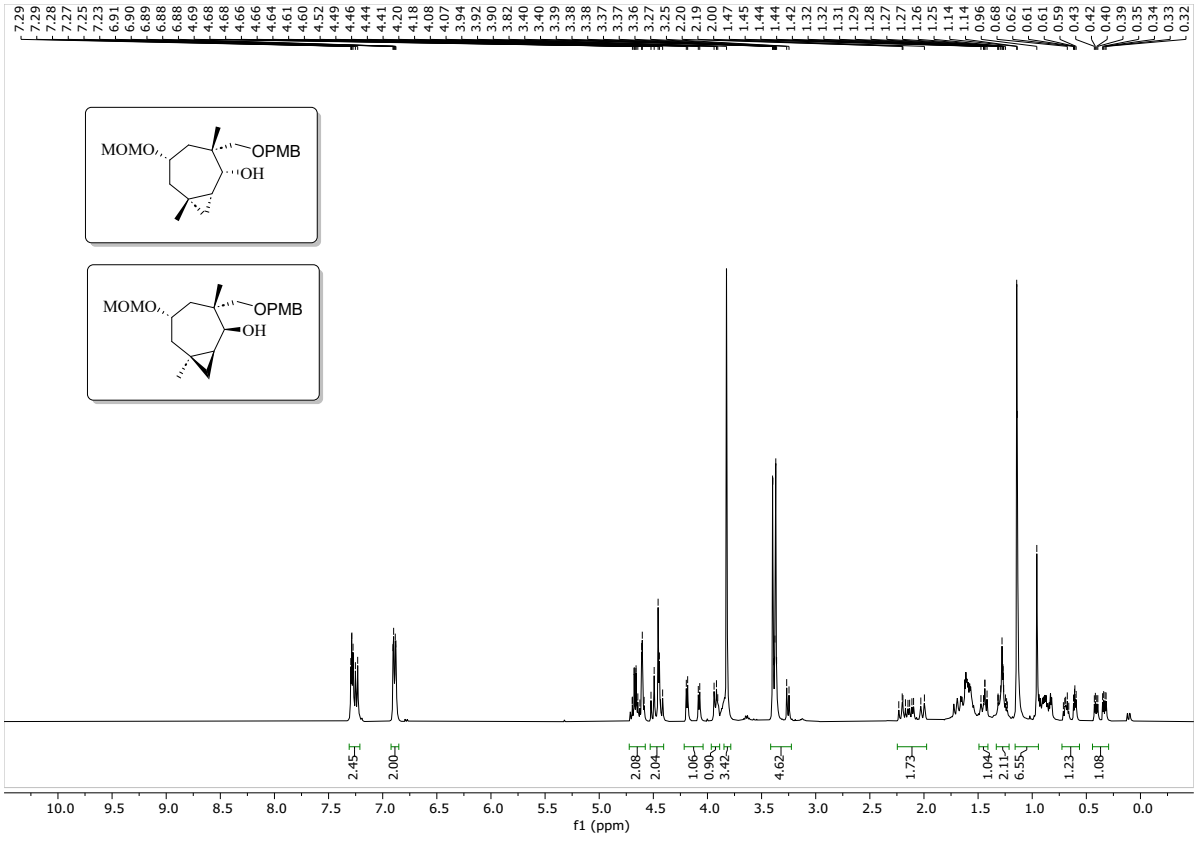
^{13}C-NMR of major diastereomer of 23 (less polar in TLC; $CDCl_3$, 150 MHz)



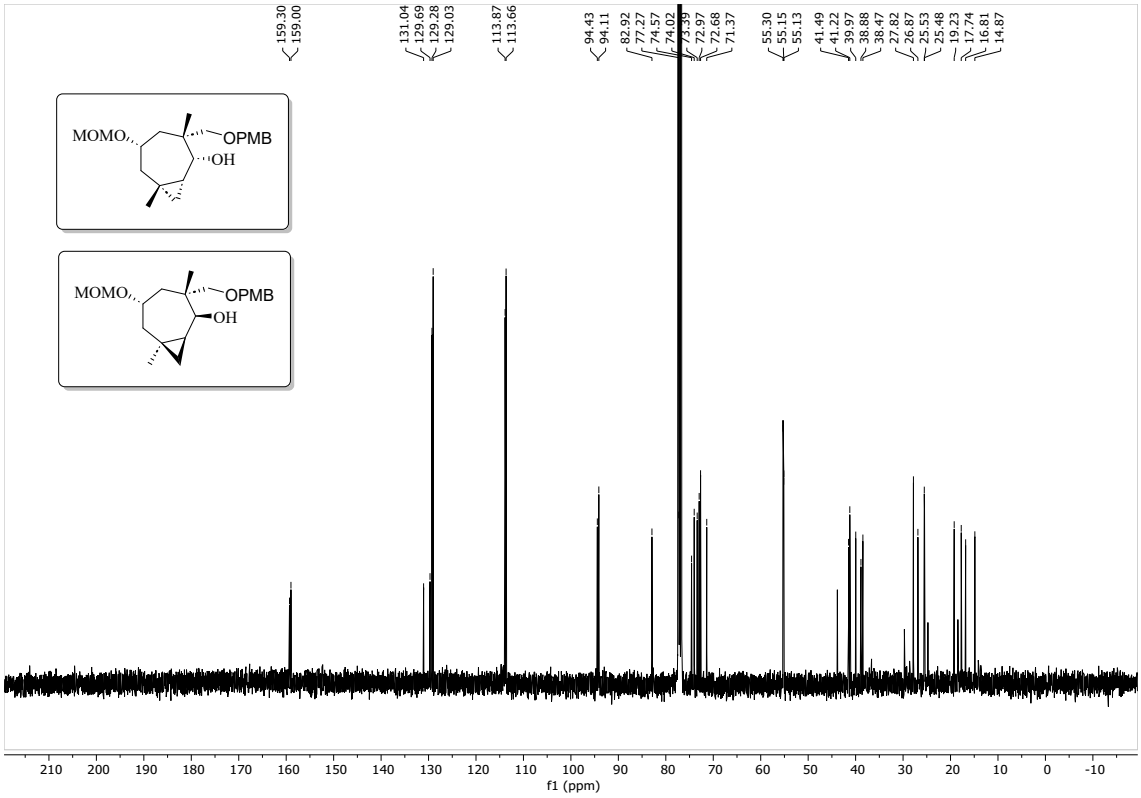
DEPT-135 NMR of major diastereomer of 23 (less polar in TLC; $CDCl_3$, 150 MHz)



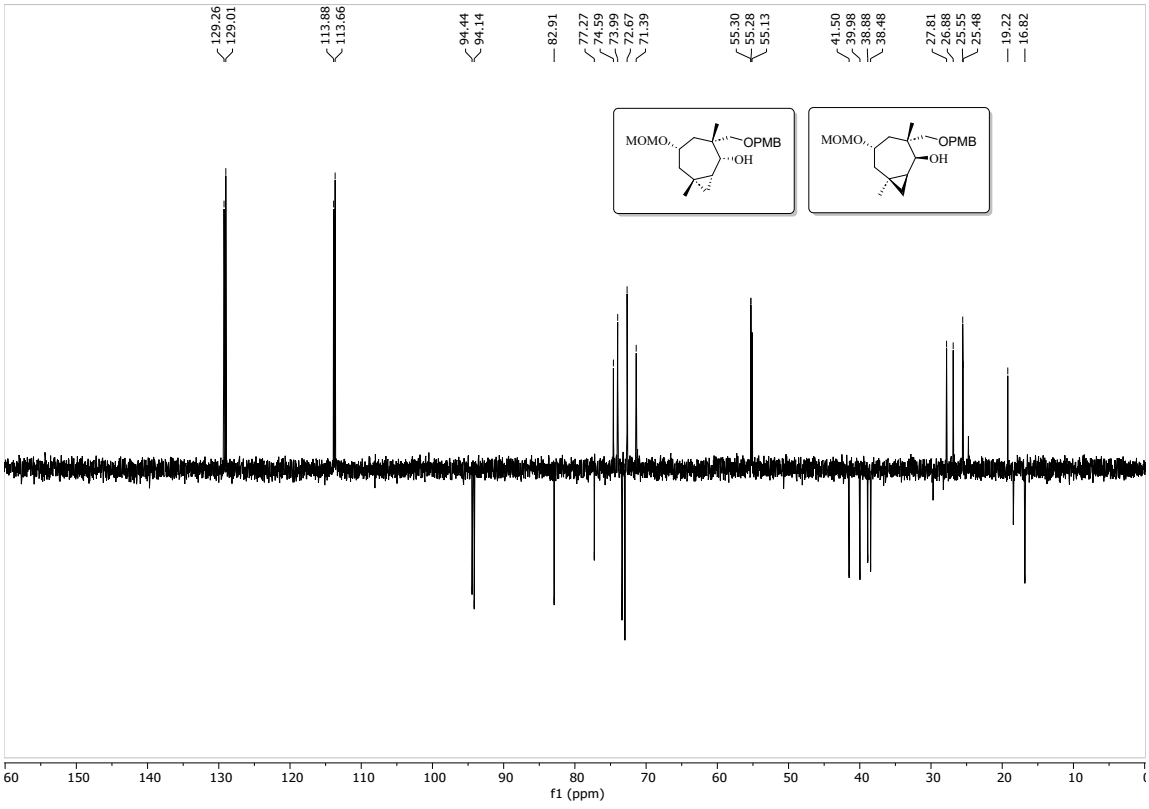
^{1}H-NMR of mixtures of 24a and 24b ($CDCl_3$, 400 MHz)



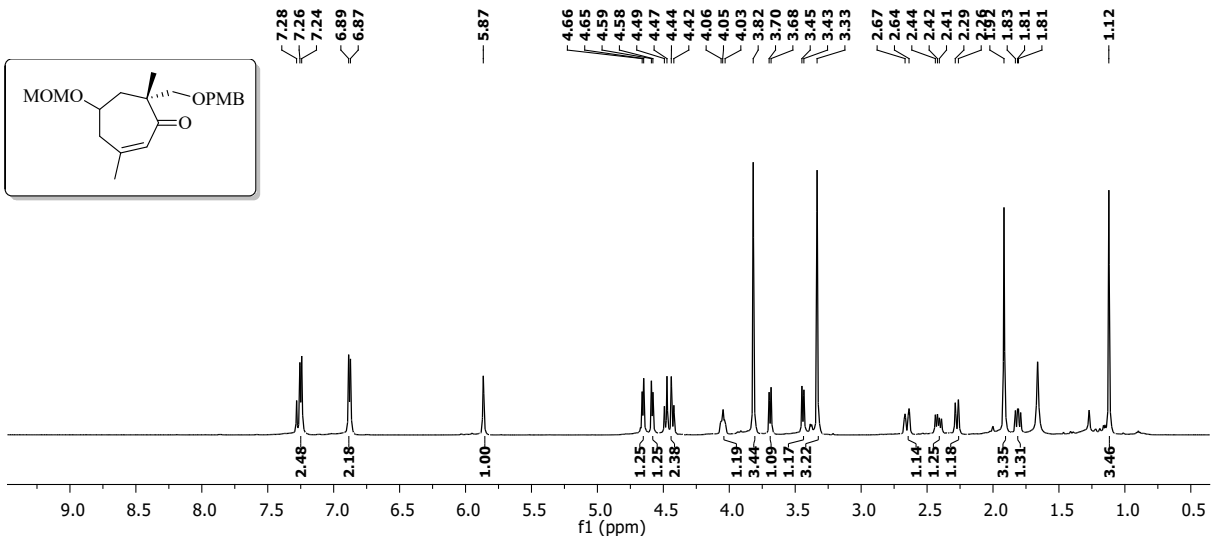
^{13}C-NMR of mixtures of 24a and 24b ($CDCl_3$, 100 MHz)



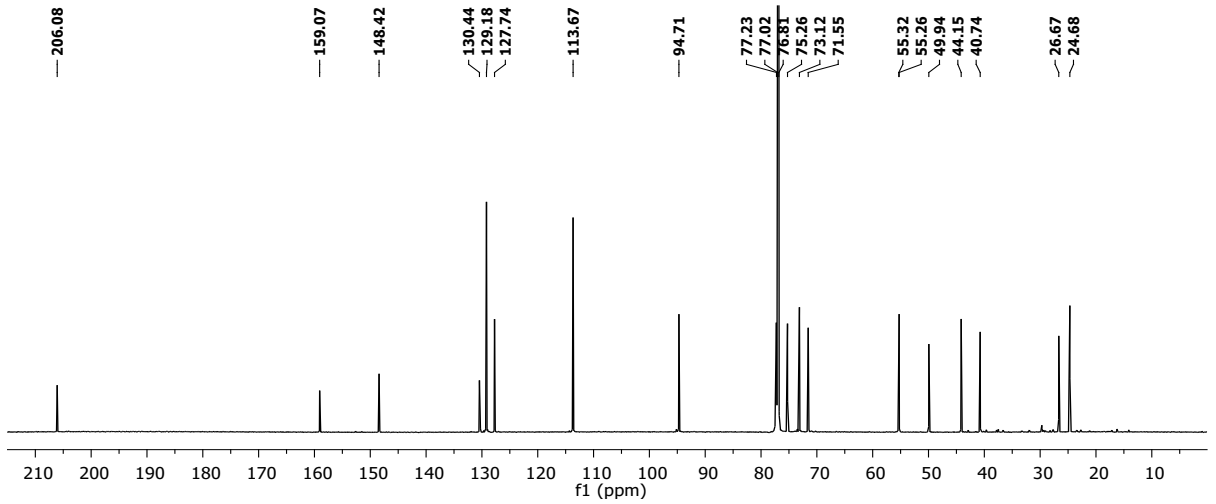
DEPT-135 NMR of mixtures of 24a and 24b ($CDCl_3$, 100 MHz)



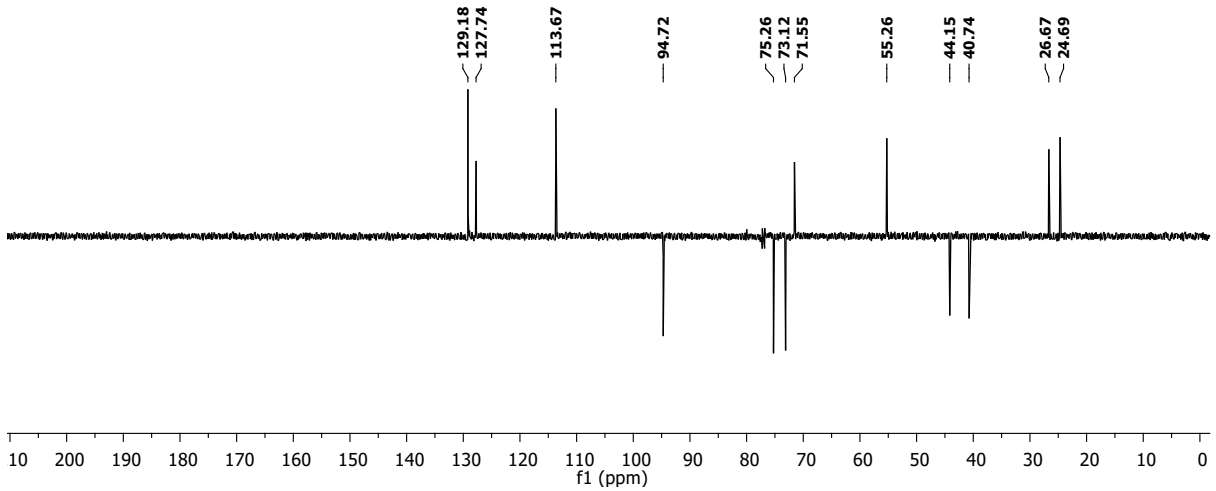
^{1}H-NMR of compound 8 ($CDCl_3$, 400MHz)



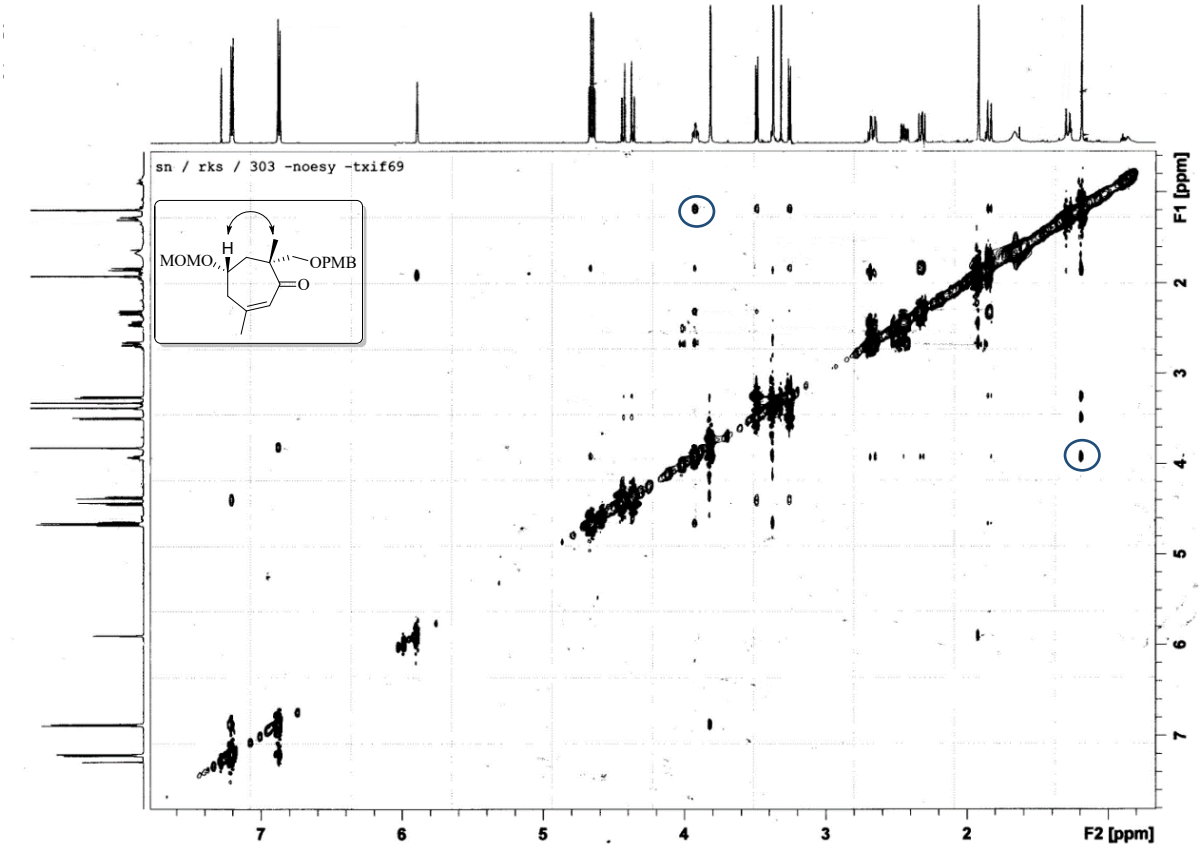
^{13}C-NMR of compound 8 ($CDCl_3$, 150MHz)



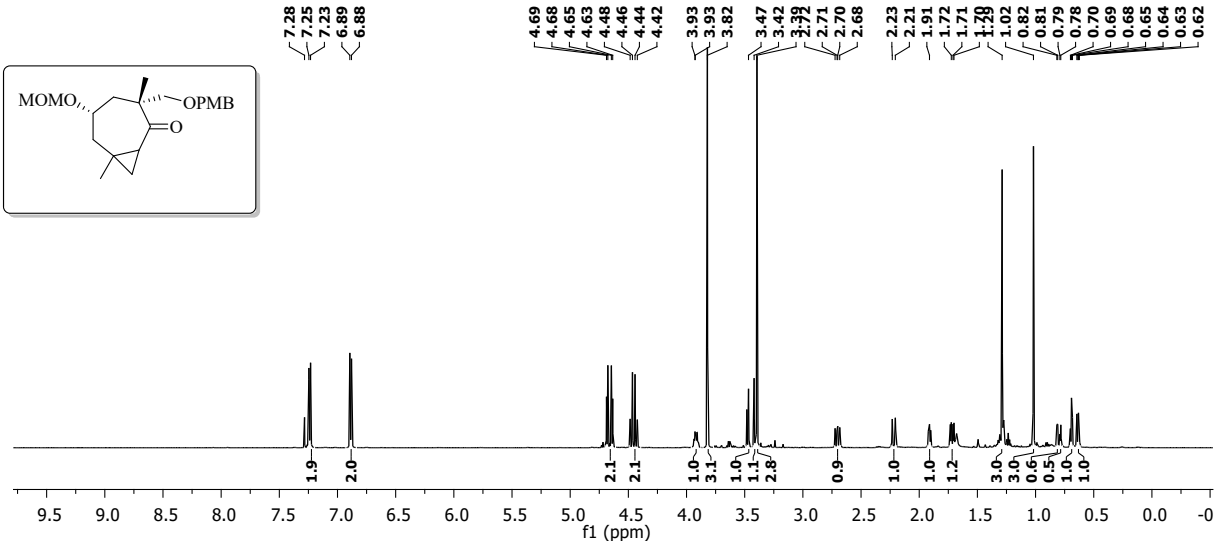
DEPT-135 NMR of compound 8 ($CDCl_3$, 150 MHz)



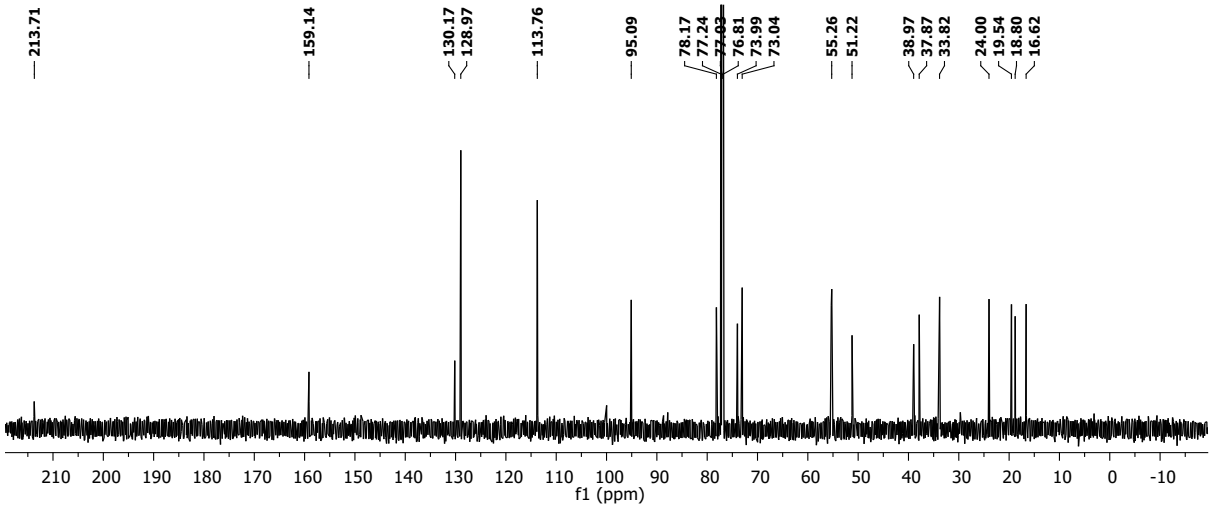
2-D NOESY spectrum of 8 ($CDCl_3$, 600MHz)



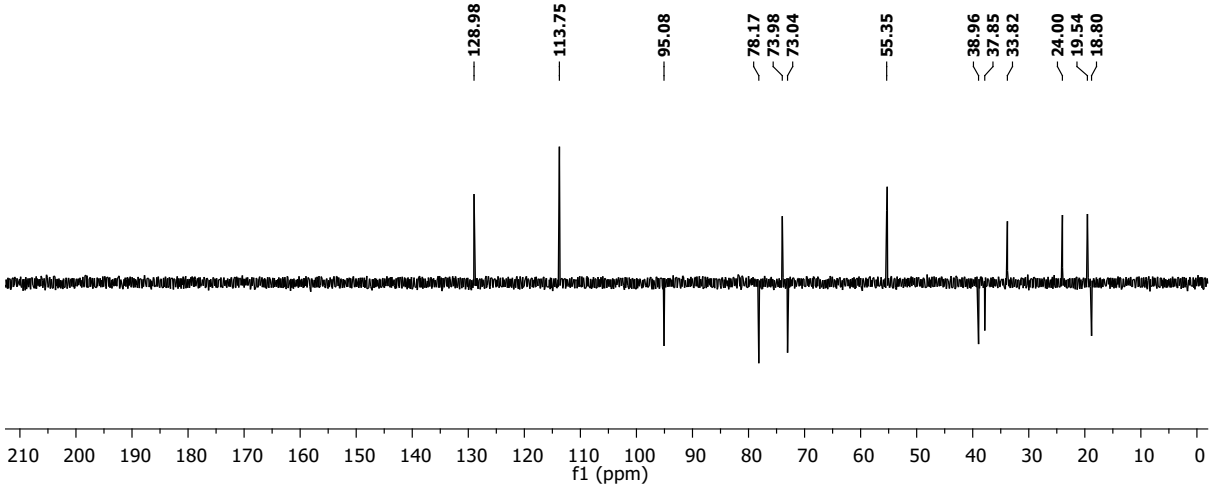
^{1}H-NMR of compound 25a ($CDCl_3$, 400MHz)



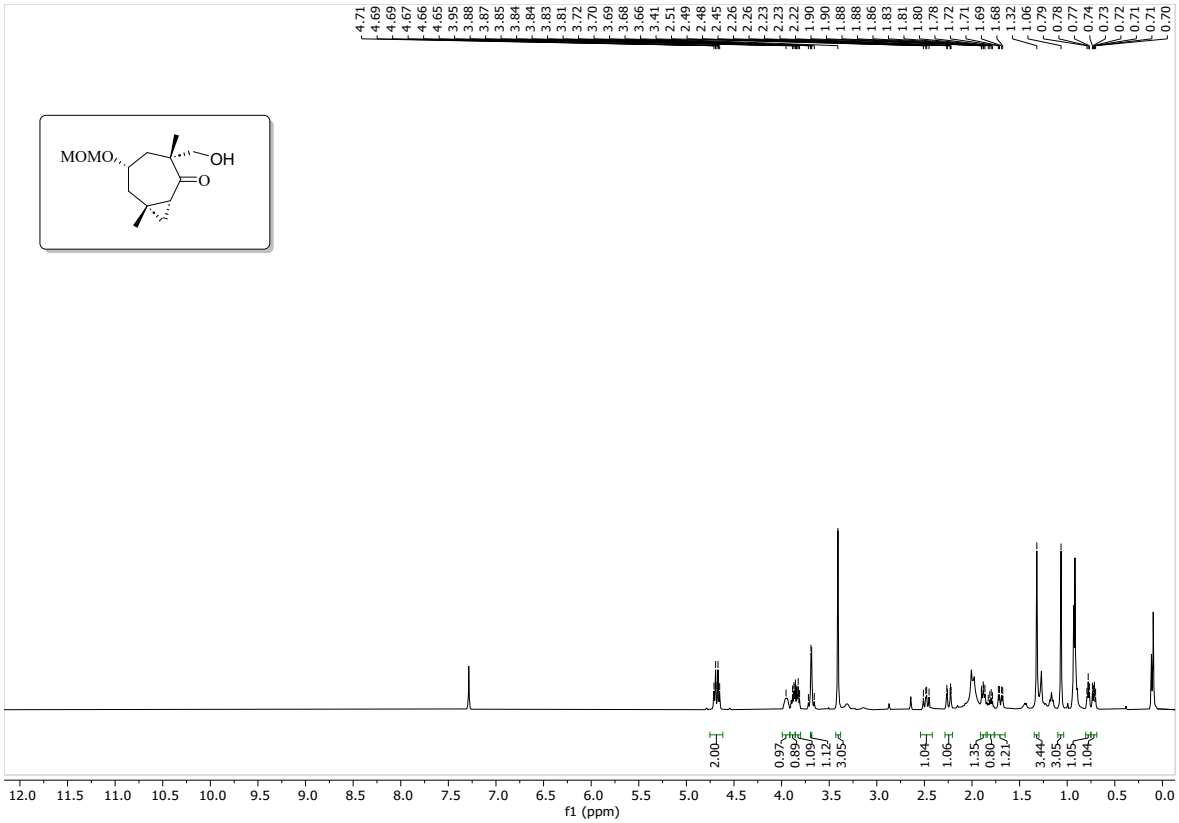
^{13}C-NMR of compound 25a ($CDCl_3$, 150MHz)



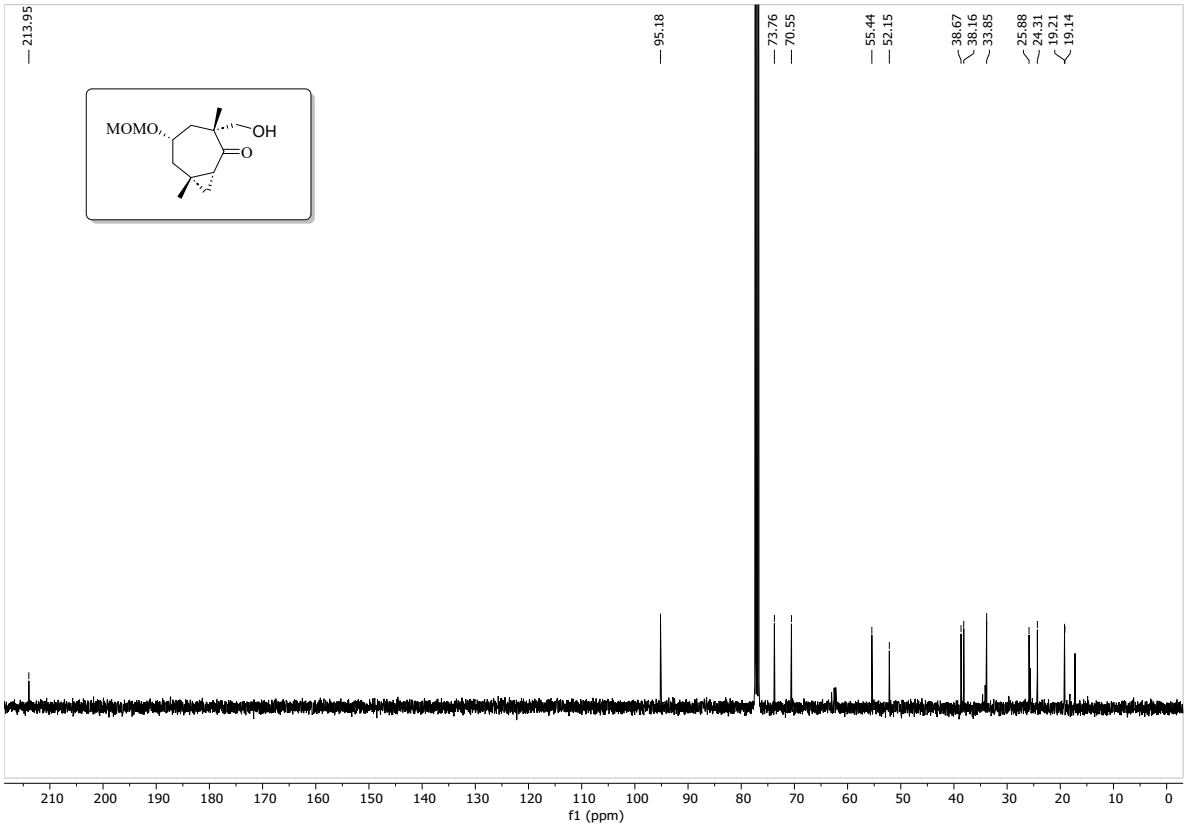
DEPT-135 NMR of compound 25a ($CDCl_3$, 150 MHz)



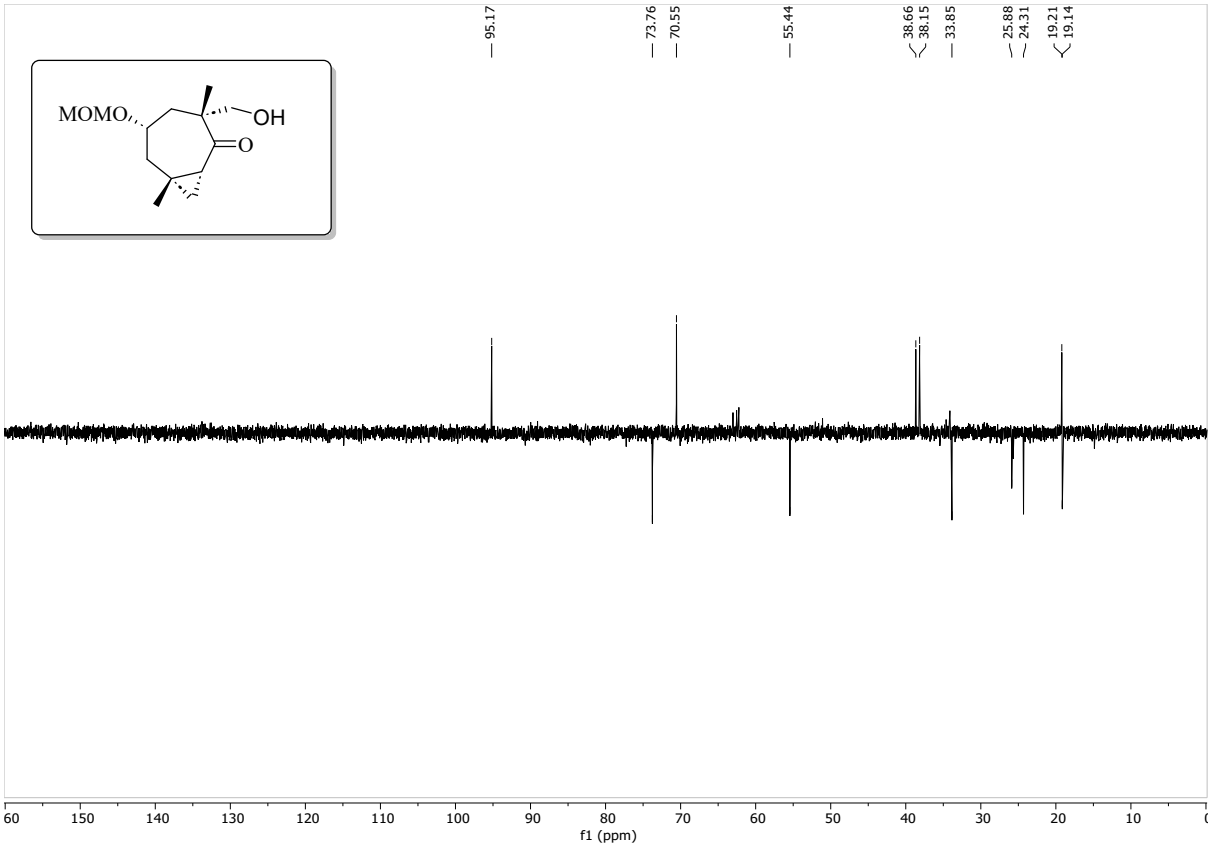
^{1}H-NMR of compound 26a ($CDCl_3$, 400MHz)



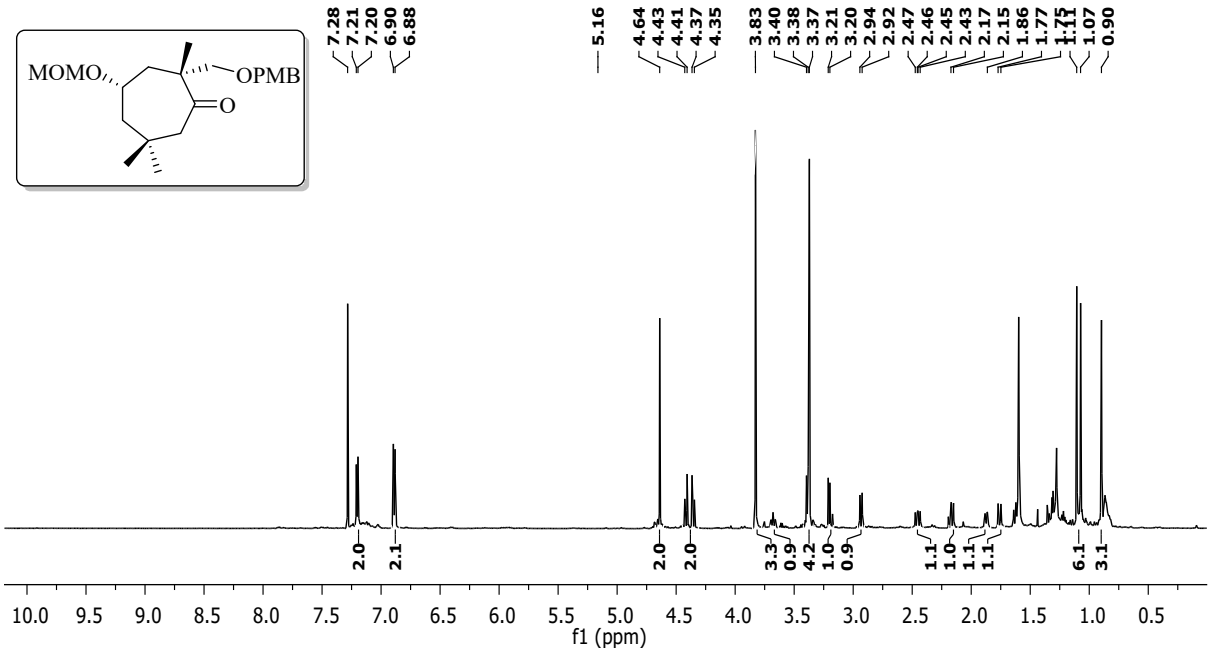
^{13}C-NMR of compound 26a ($CDCl_3$, 150MHz)



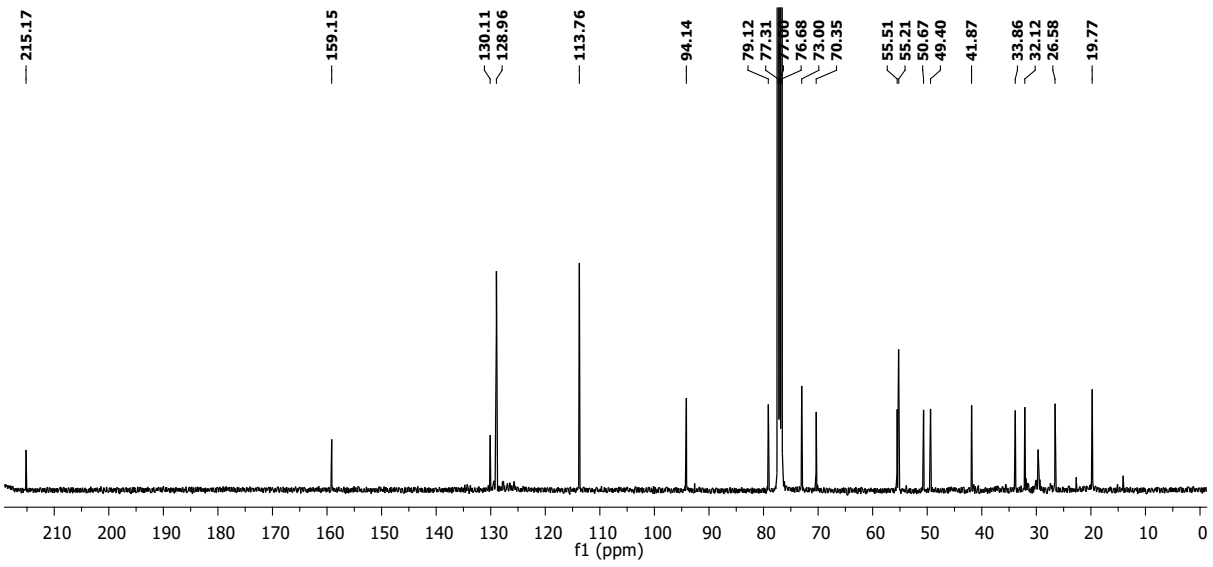
DEPT-135 NMR of compound 26a ($CDCl_3$, 150 MHz)



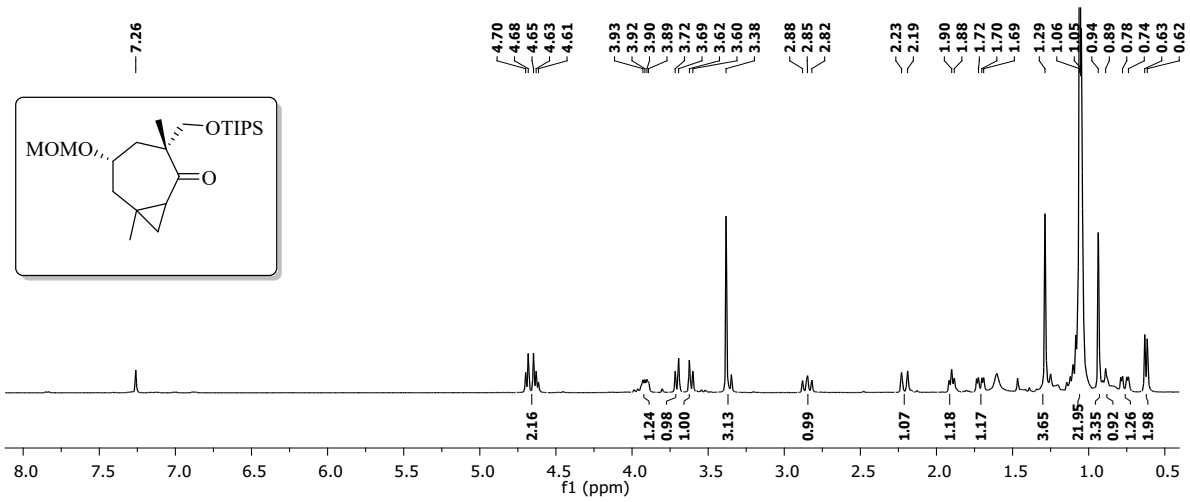
^{1}H-NMR of compound 7b ($CDCl_3$, 400MHz)



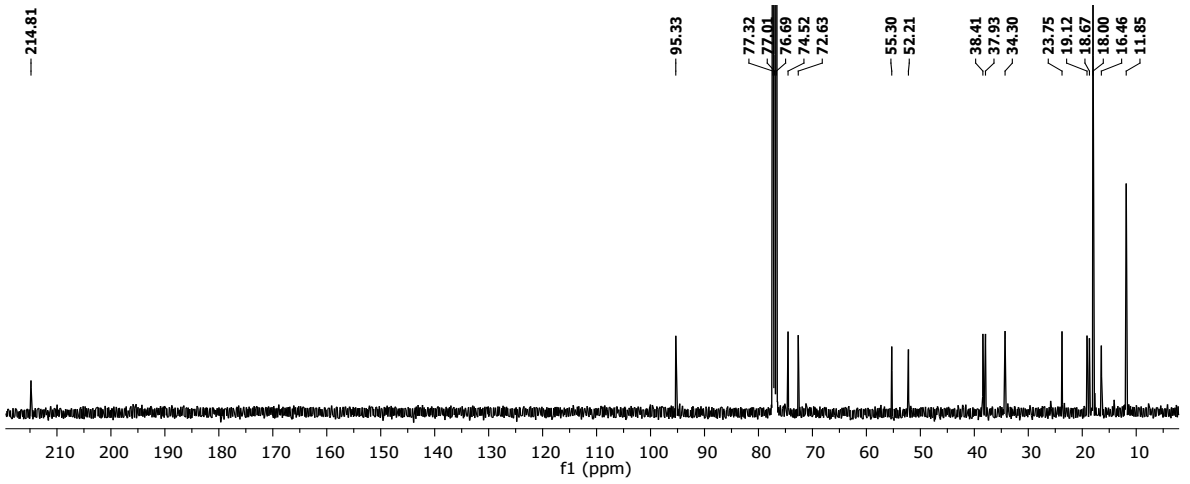
^{13}C-NMR of compound 7b ($CDCl_3$, 150MHz)



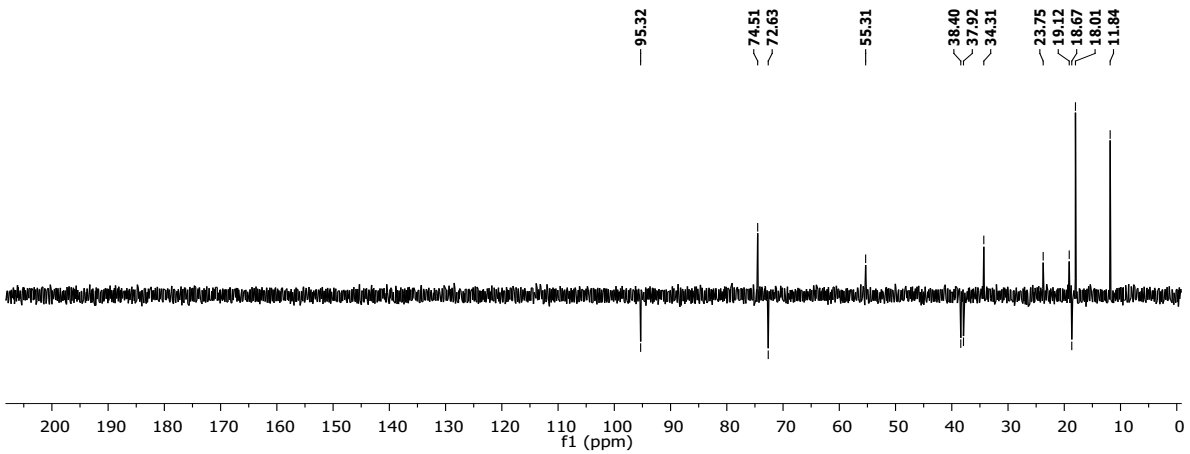
^{1}H-NMR of compound 27a ($CDCl_3$, 400MHz)



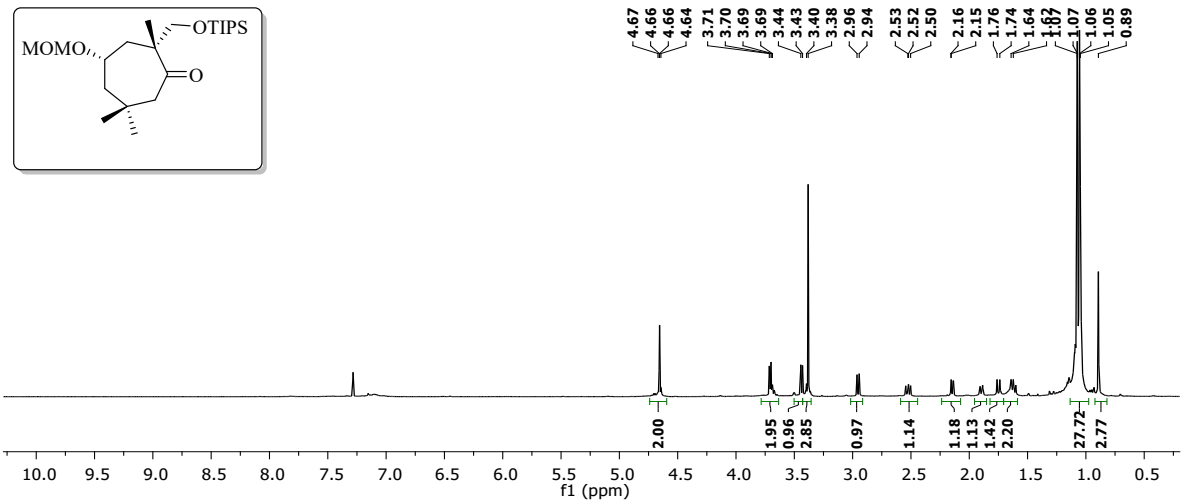
^{13}C-NMR of compound 27a ($CDCl_3$, 100MHz)



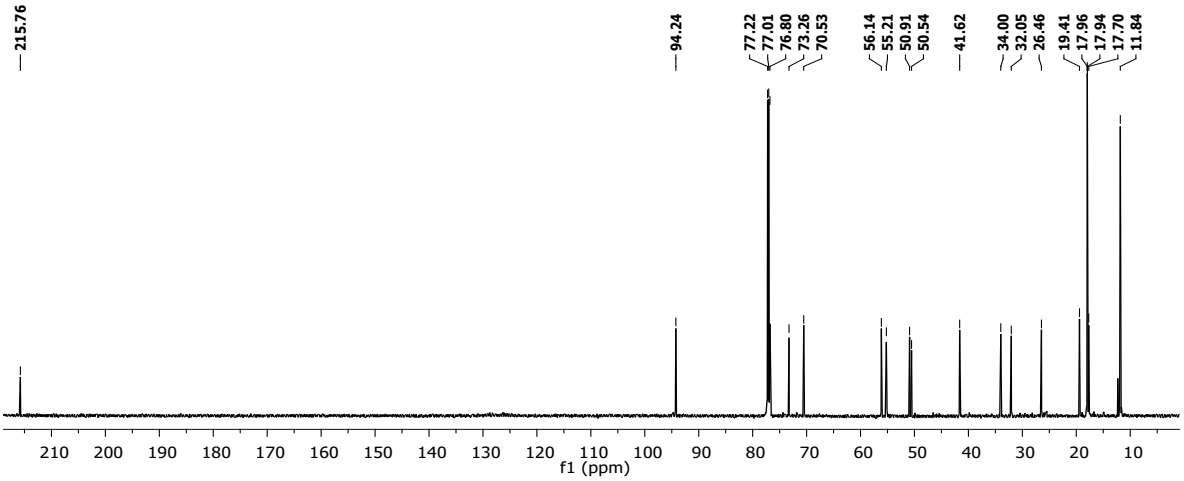
DEPT-135 NMR of compound 27a ($CDCl_3$, 100 MHz)



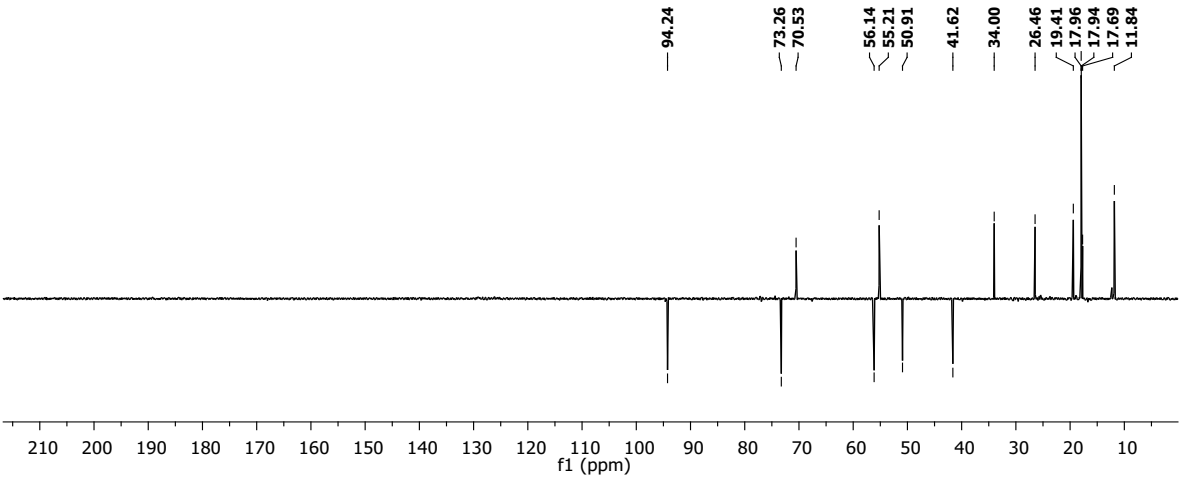
^{1}H-NMR of compound 28 ($CDCl_3$, 600MHz)



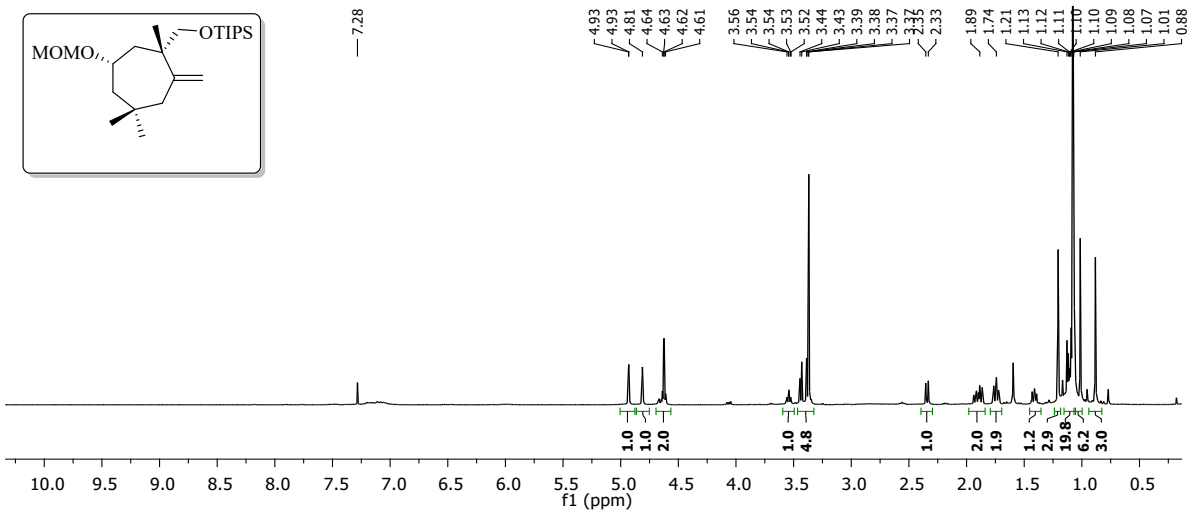
^{13}C-NMR of compound 28 ($CDCl_3$, 150MHz)



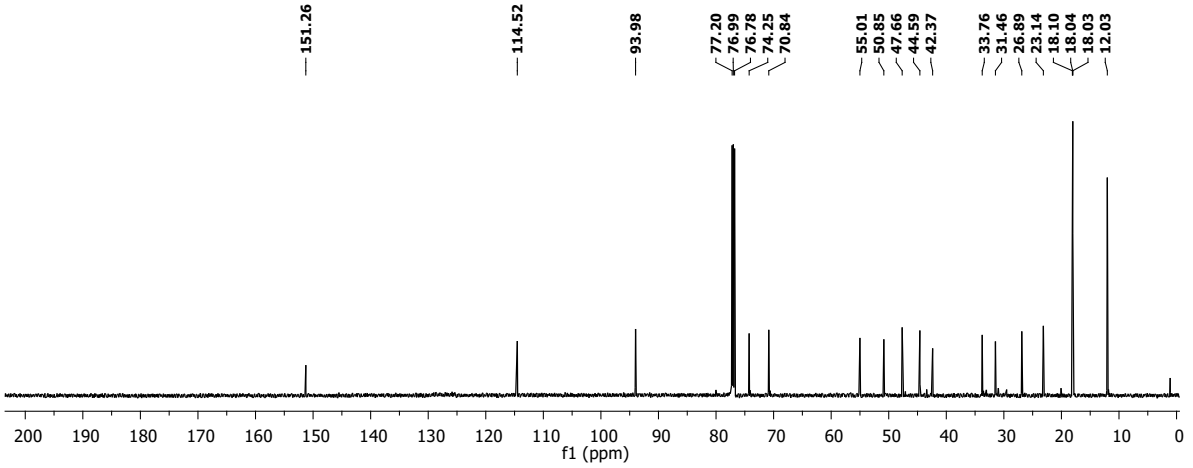
DEPT-135 NMR of compound 28 ($CDCl_3$, 150 MHz)



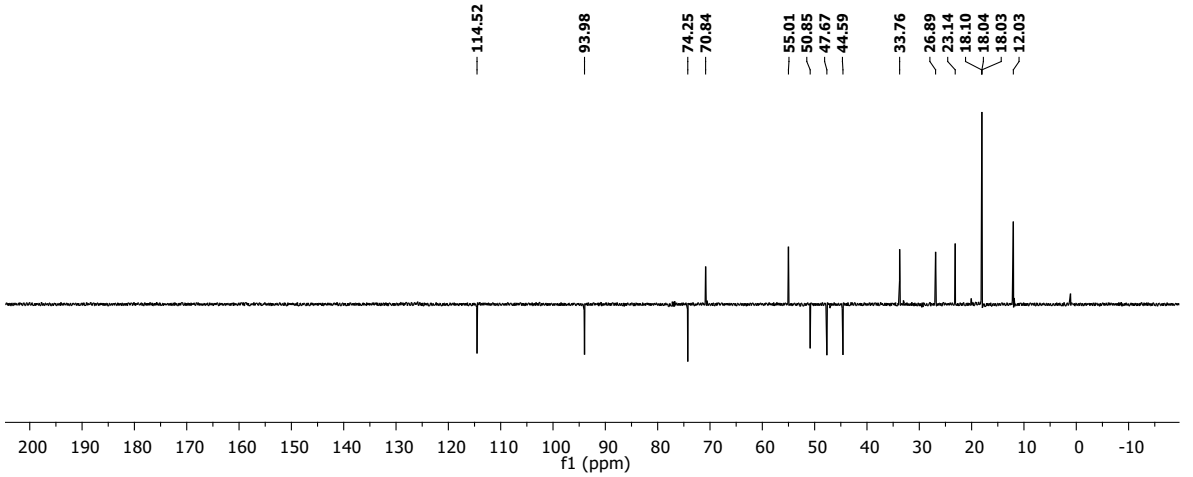
^{1}H-NMR of compound 30 ($CDCl_3$, 600MHz)



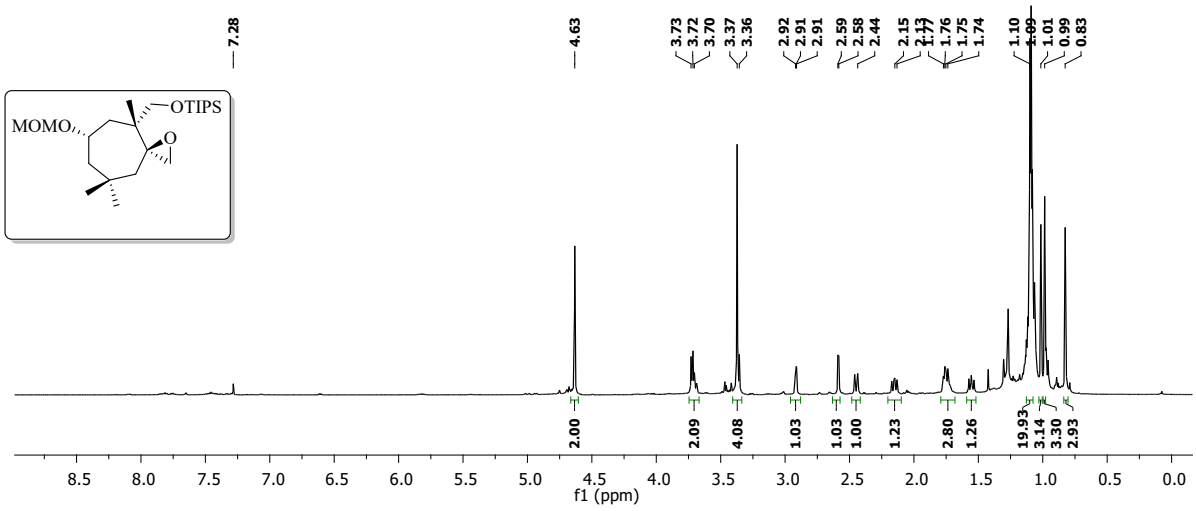
^{13}C-NMR of compound 30 ($CDCl_3$, 150MHz)



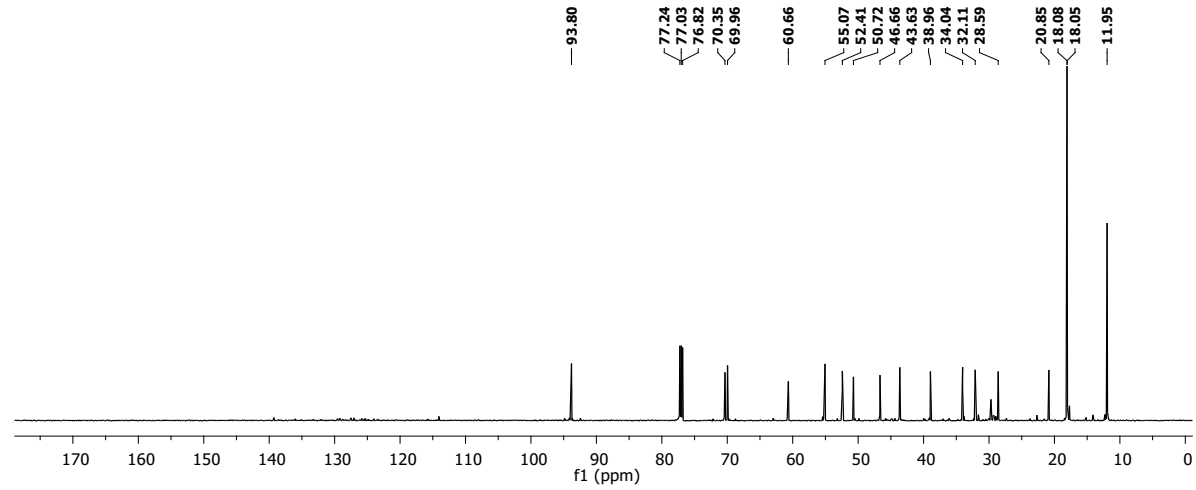
DEPT-135 NMR of compound 30 ($CDCl_3$, 150 MHz)



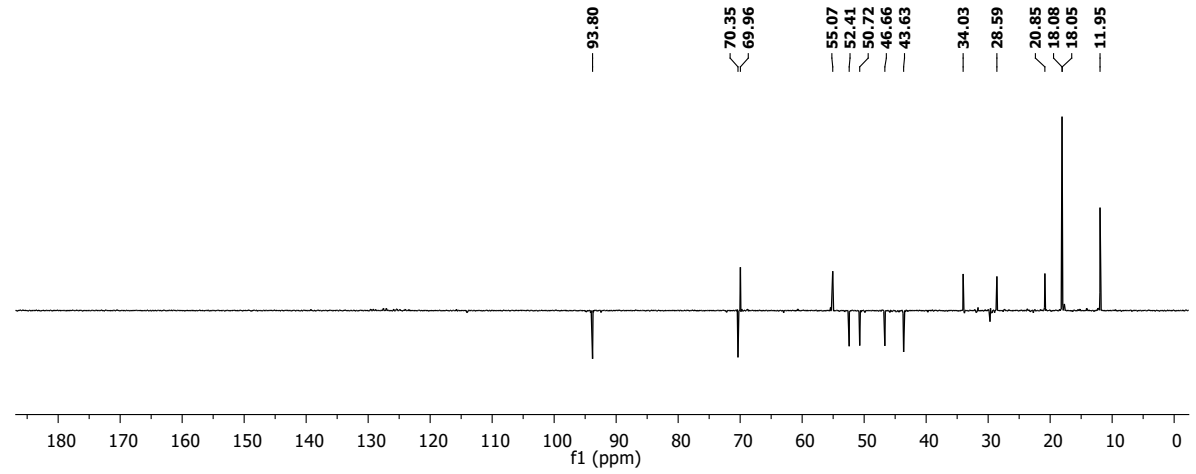
^{1}H-NMR of compound 7 ($CDCl_3$, 600MHz)



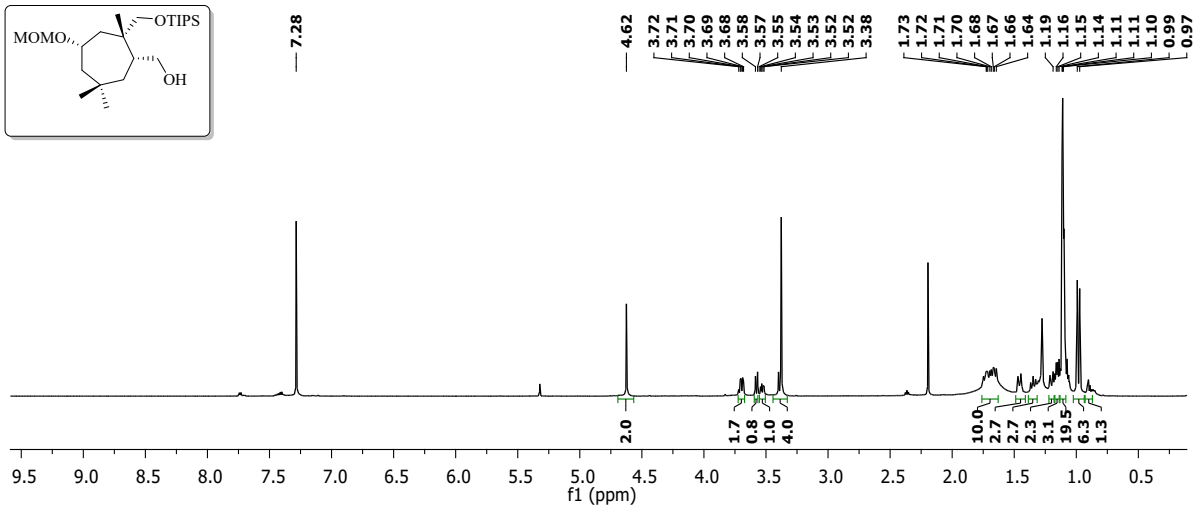
^{13}C-NMR of compound 7 ($CDCl_3$, 150MHz)



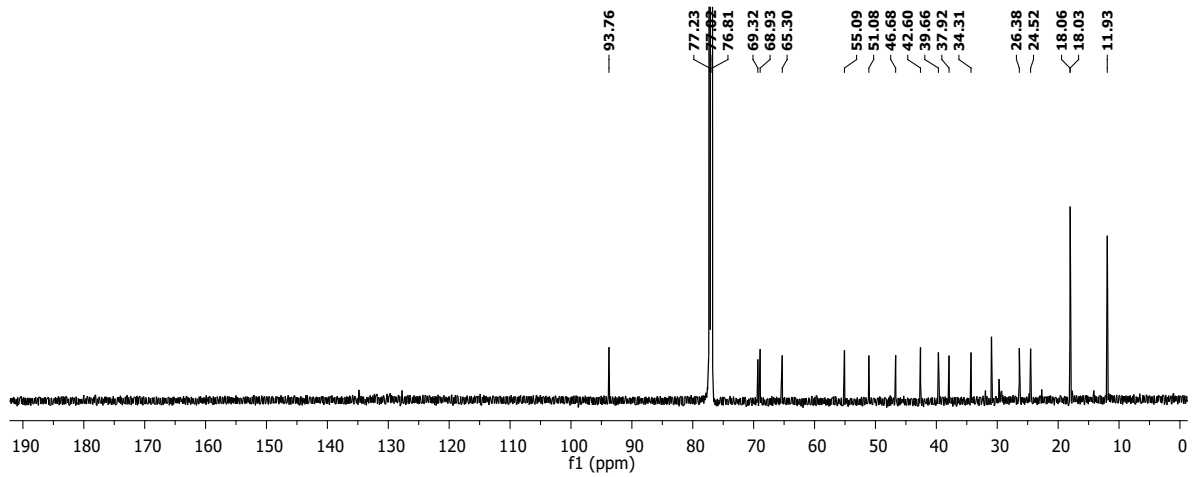
DEPT-135 NMR of compound 7 ($CDCl_3$, 150 MHz)



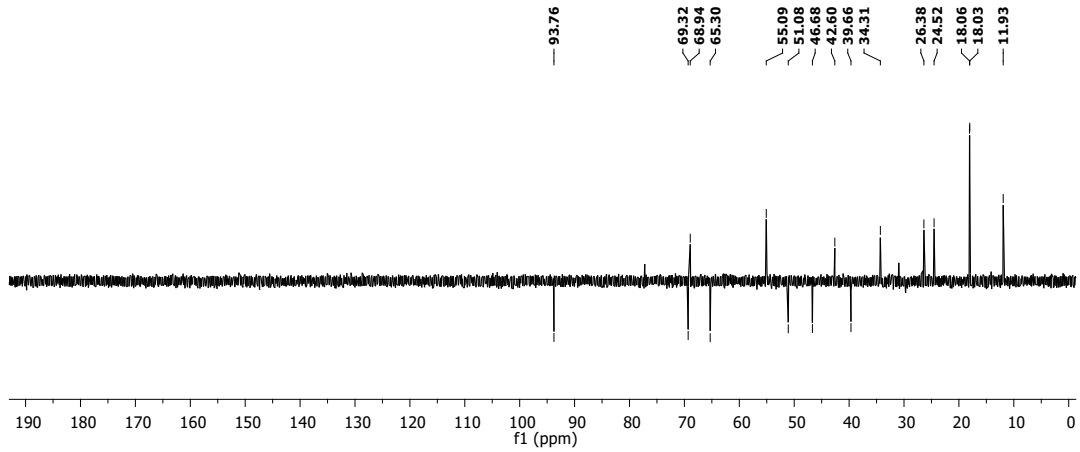
^{1}H-NMR of compound 31 ($CDCl_3$, 600MHz)



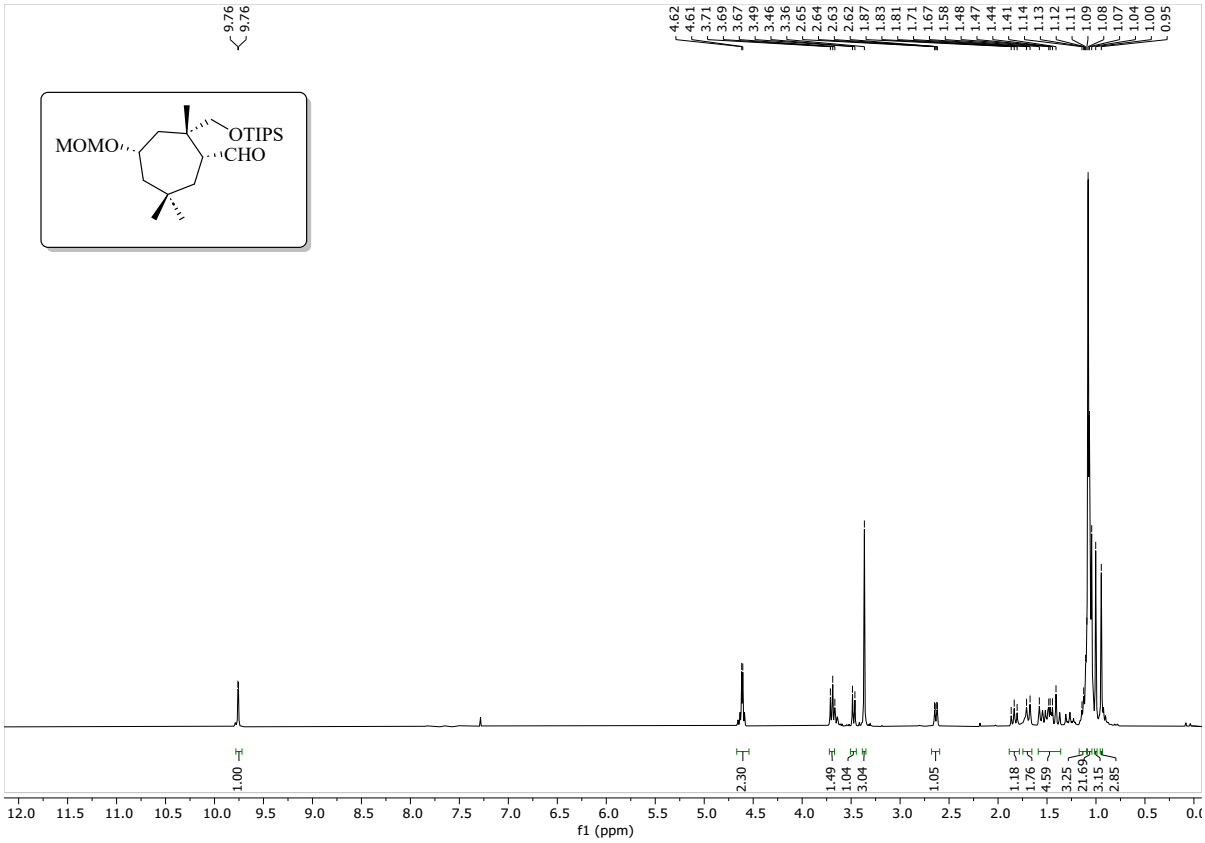
^{13}C-NMR of compound 31 ($CDCl_3$, 150MHz)



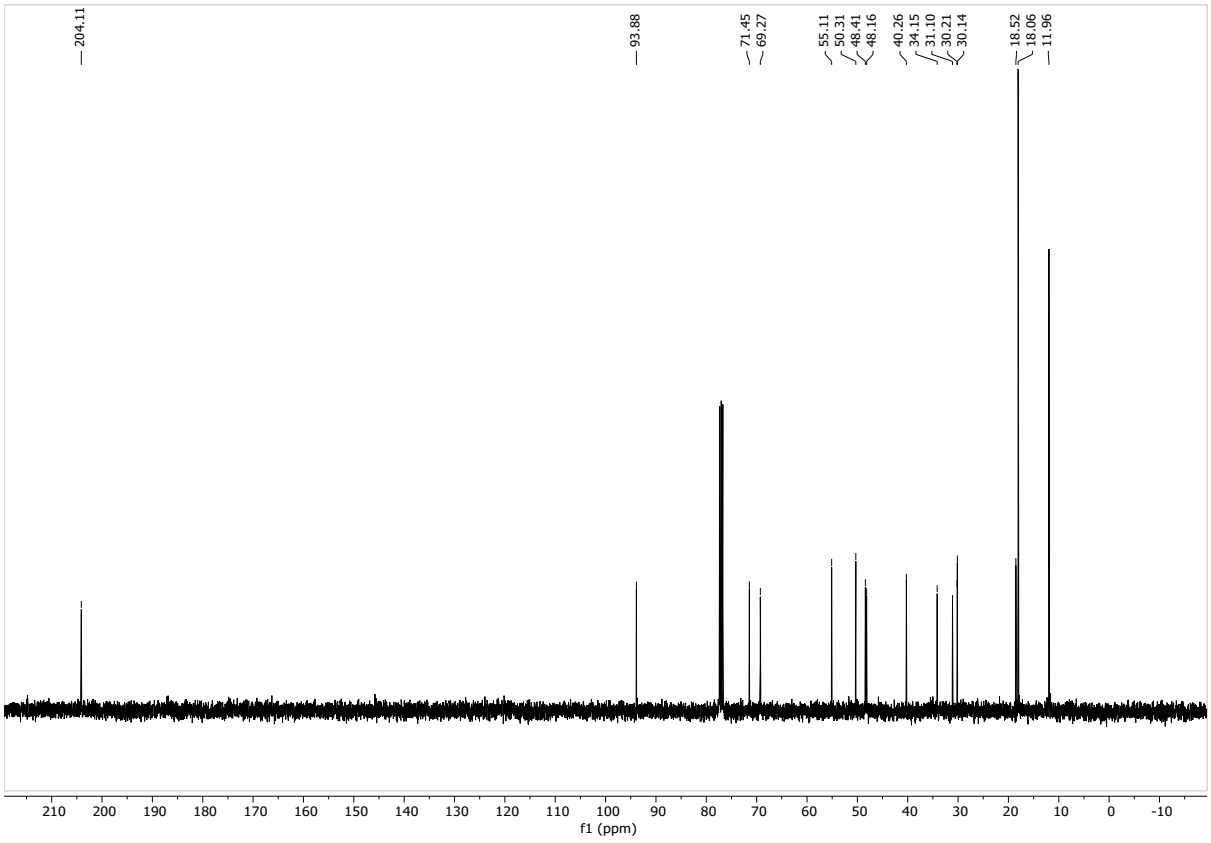
DEPT-135 NMR of compound 31 ($CDCl_3$, 150 MHz)



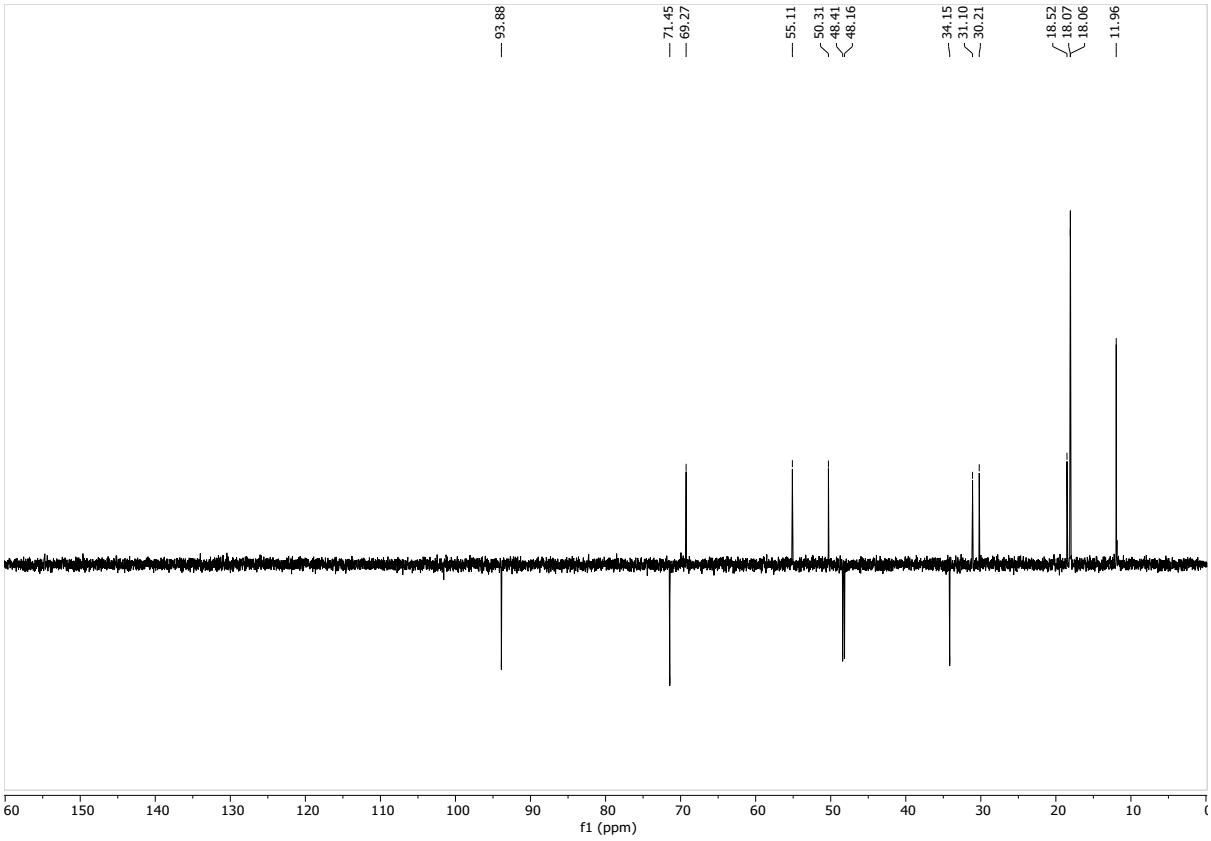
^{1}H-NMR of compound 32 ($CDCl_3$, 400MHz)



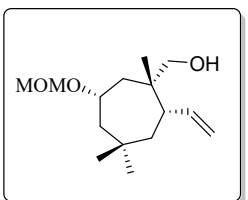
^{13}C-NMR of compound 32 ($CDCl_3$, 100MHz)

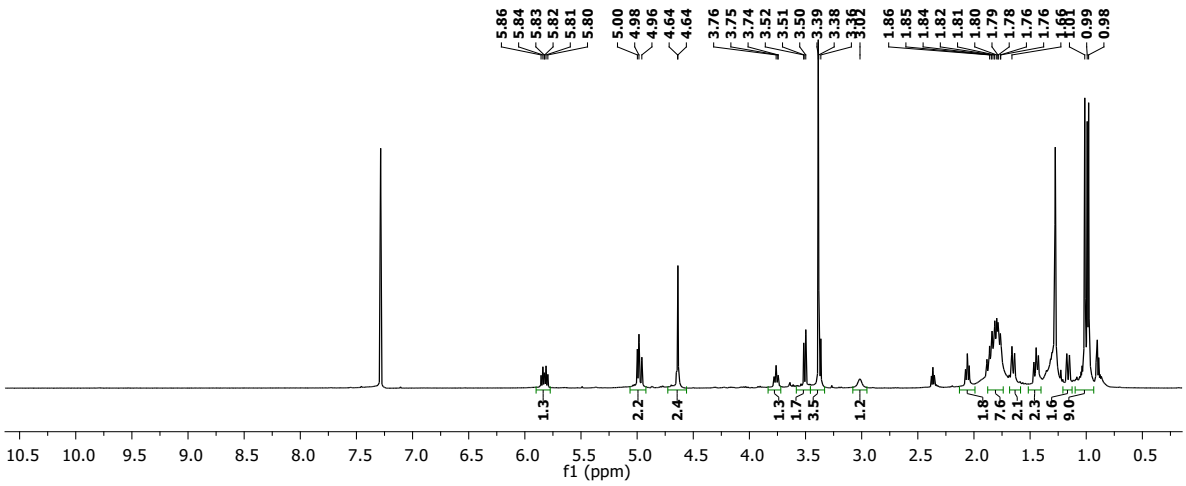


DEPT135-NMR of compound 32 ($CDCl_3$, 100MHz)

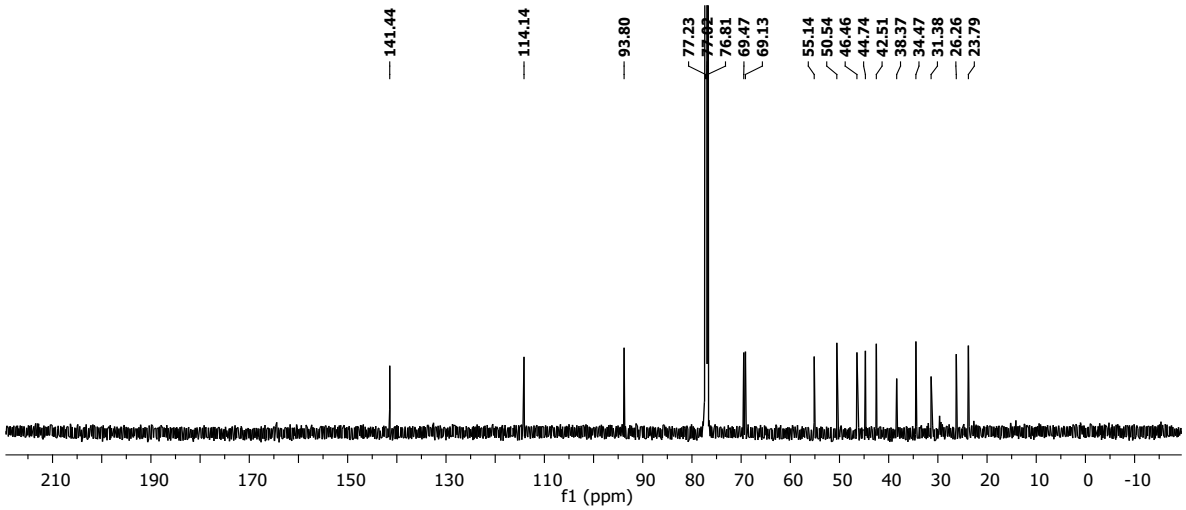


^{1}H-NMR of compound 34 ($CDCl_3$, 600MHz)

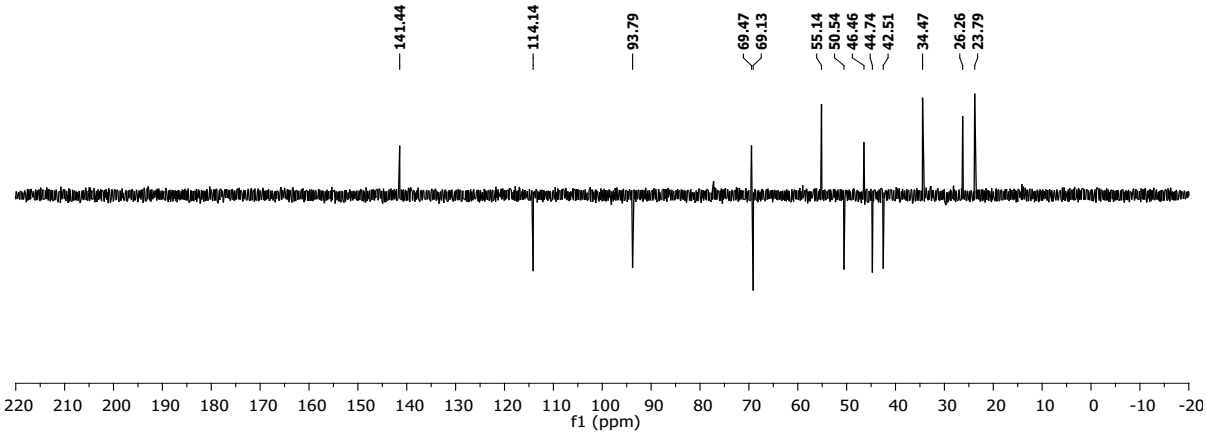




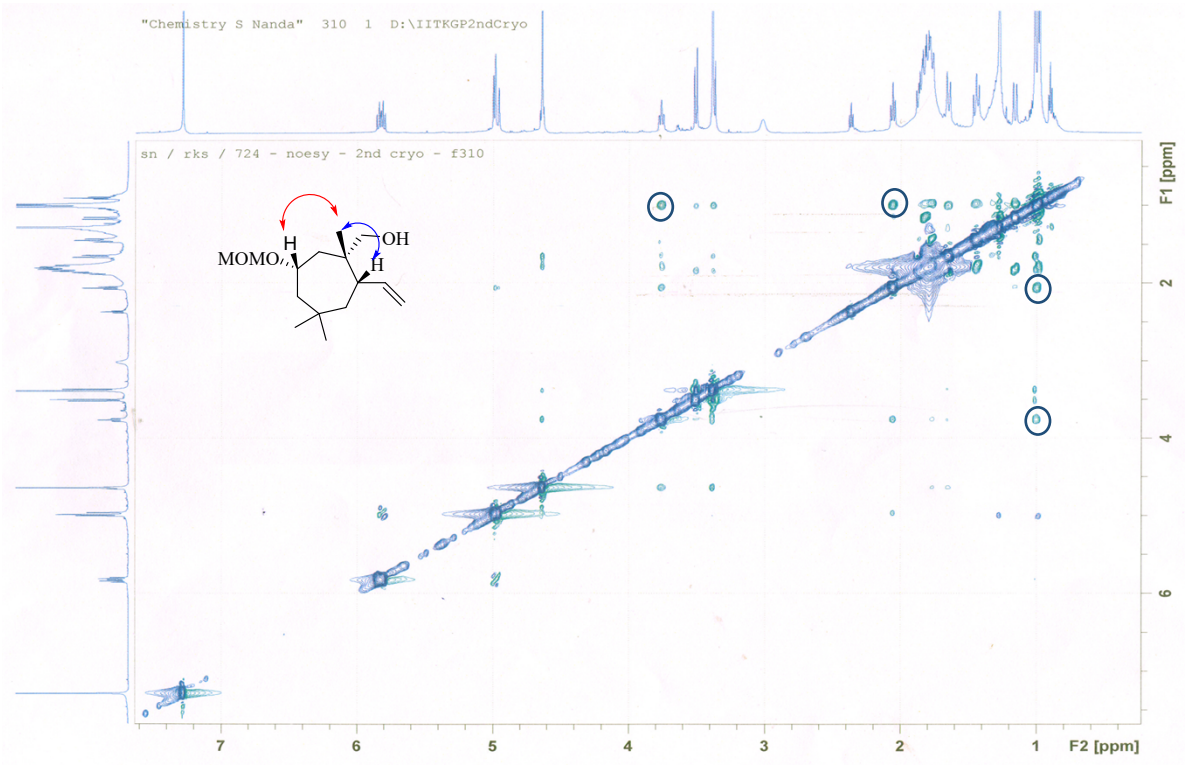
^{13}C-NMR of compound 34 ($CDCl_3$, 150MHz)



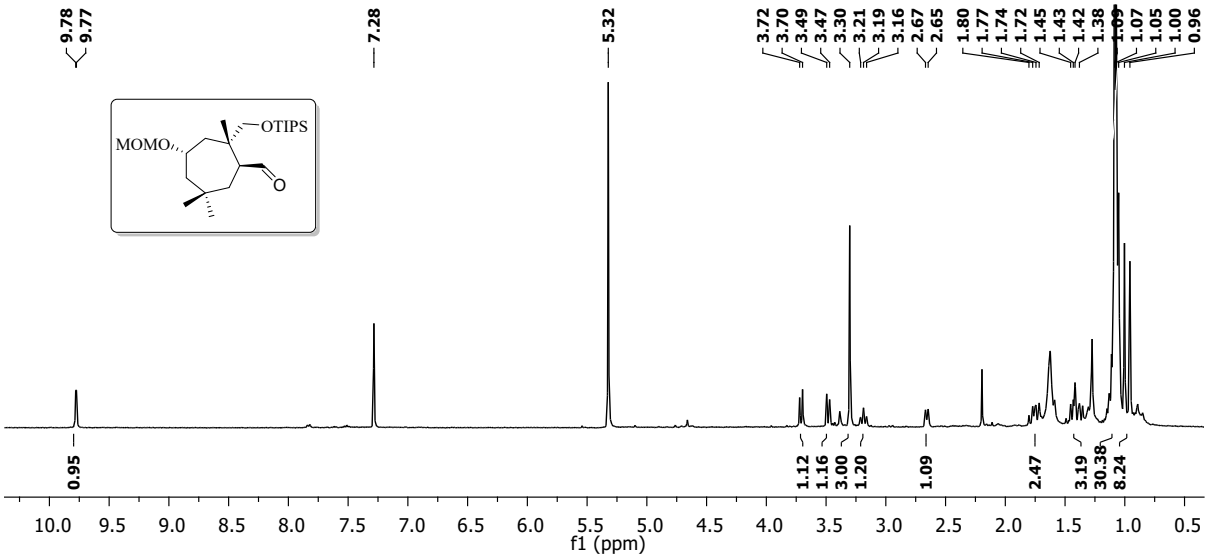
DEPT-135 NMR of compound 34 ($CDCl_3$, 150 MHz)



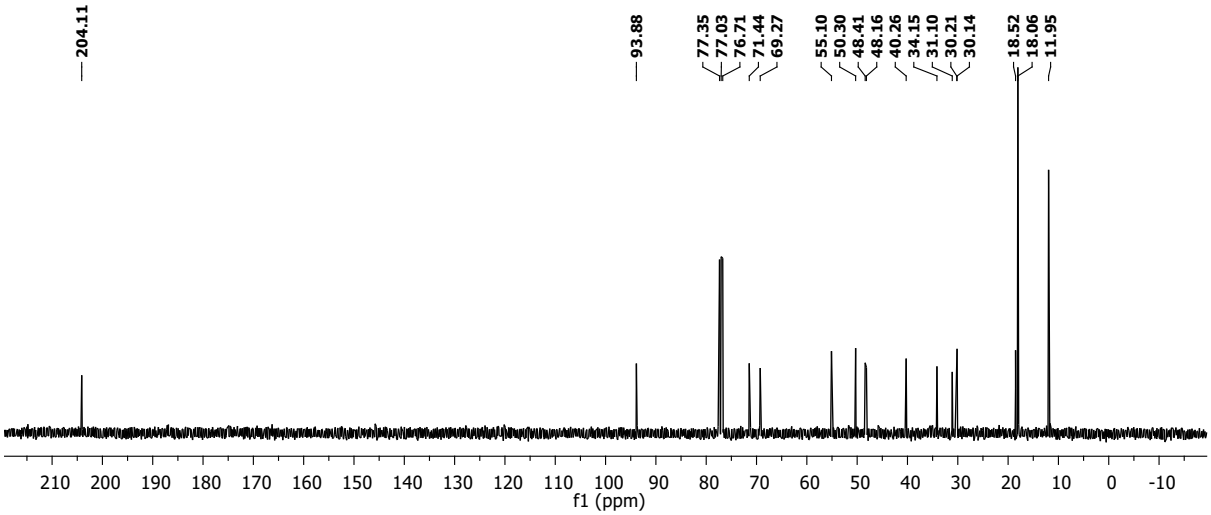
2-D NOESY spectrum of 34 ($CDCl_3$, 600Mz)



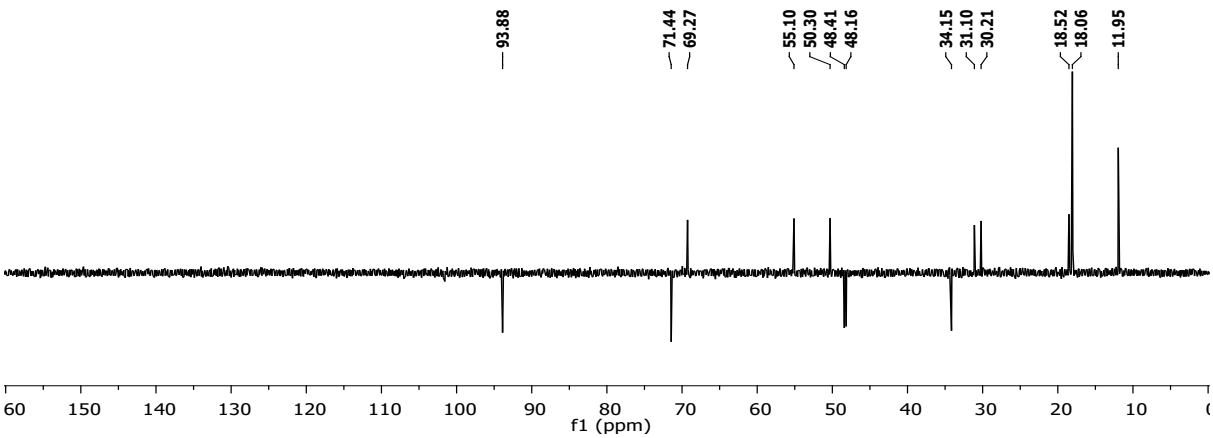
^{1}H-NMR of compound 35 ($CDCl_3$, 400MHz)



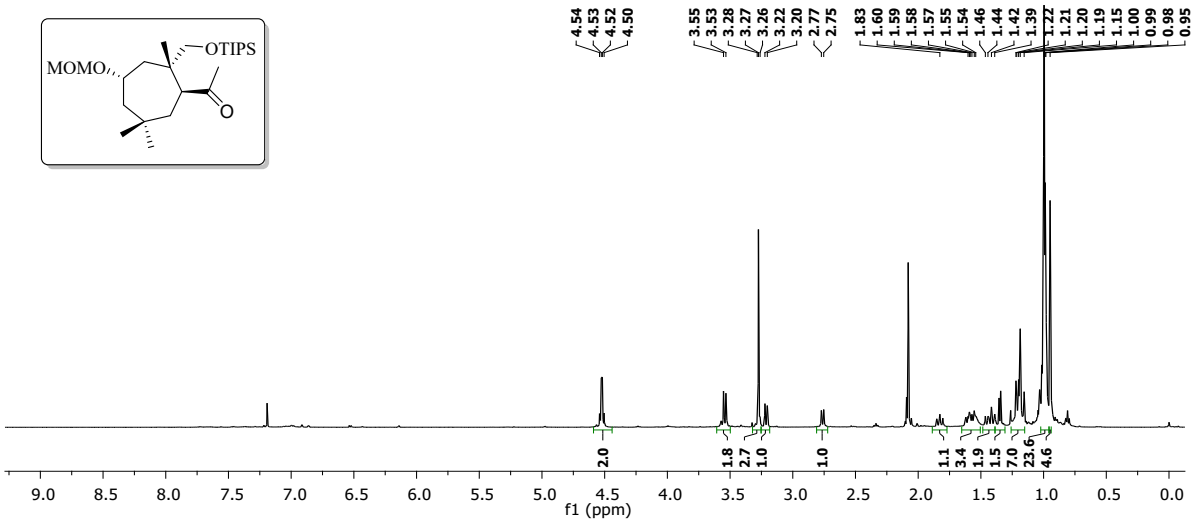
^{13}C-NMR of compound 35 ($CDCl_3$, 100MHz)



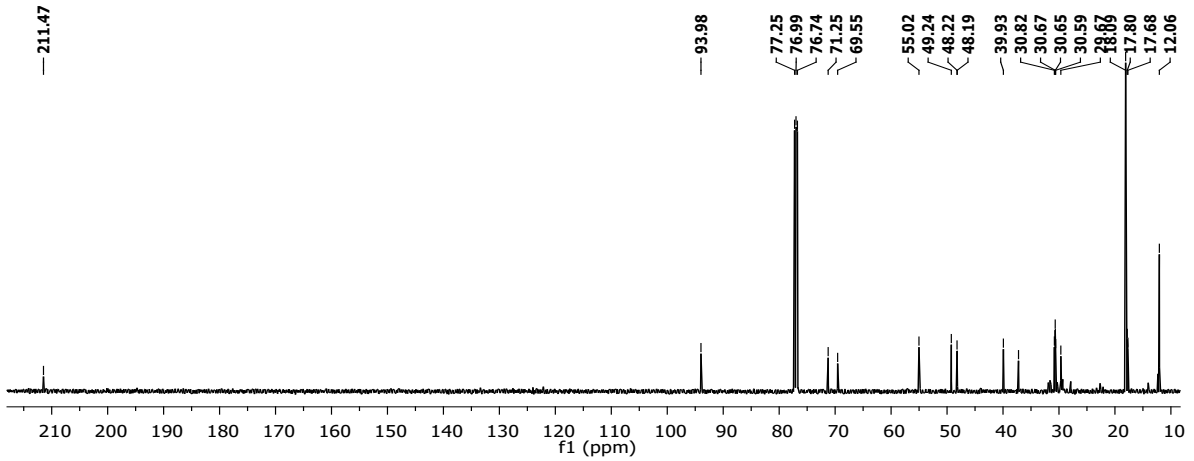
DEPT-135 NMR of compound 35 ($CDCl_3$, 100MHz)



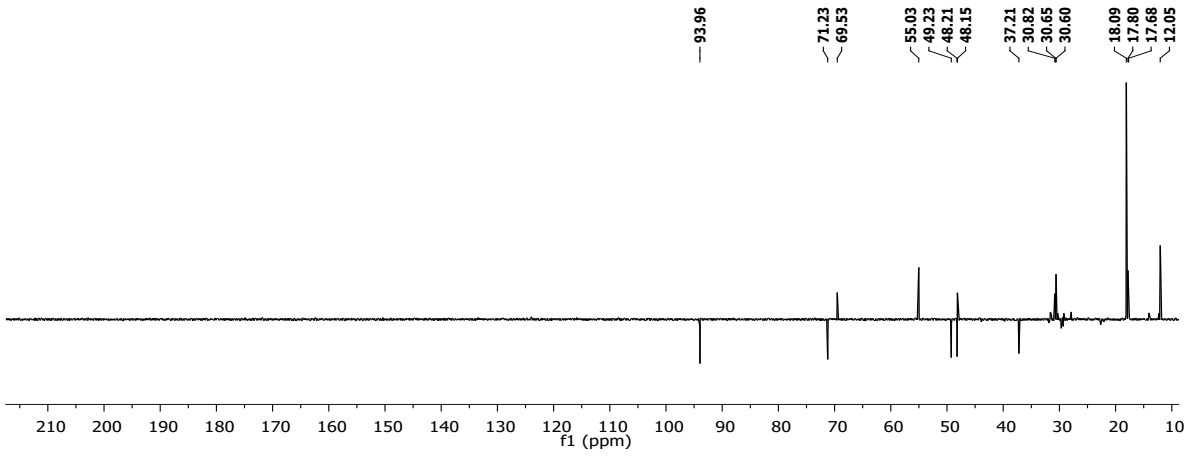
^{1}H-NMR of compound 4 ($CDCl_3$, 500MHz)



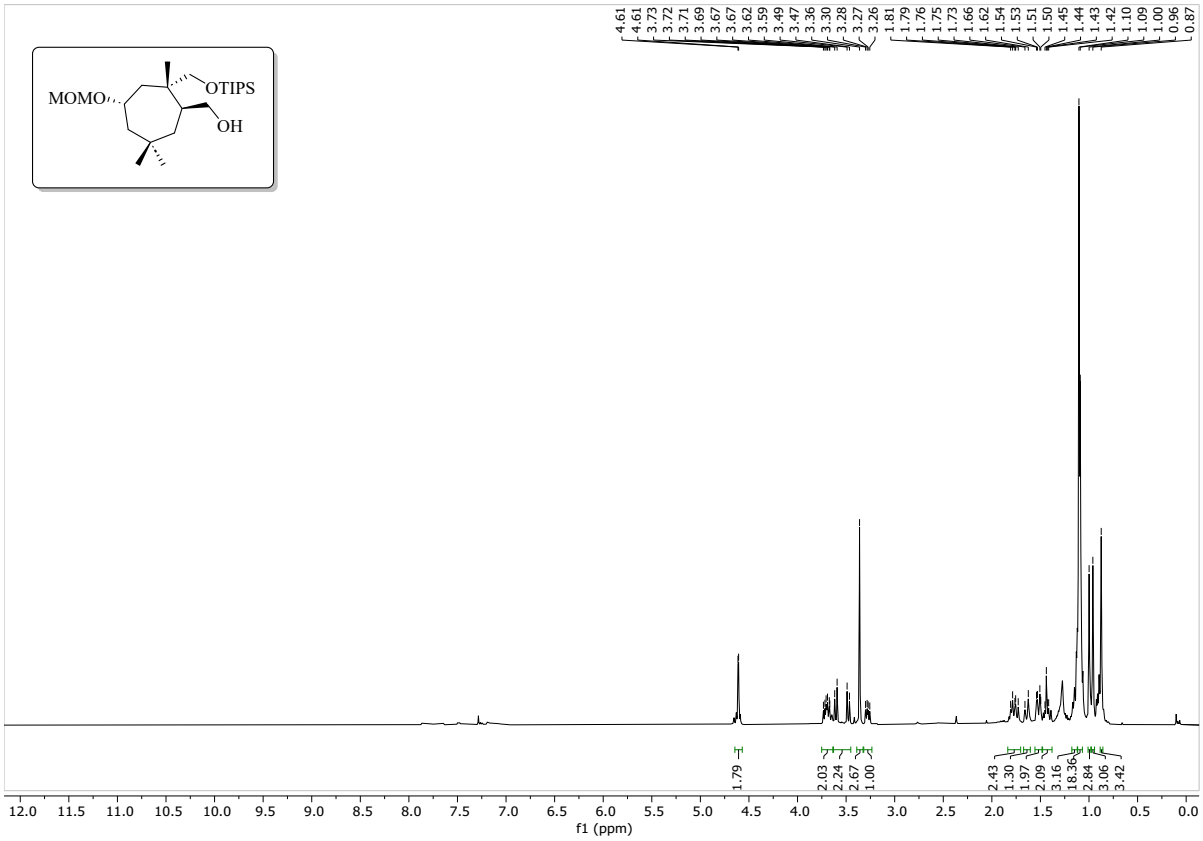
^{13}C-NMR of compound 4 ($CDCl_3$, 125MHz)



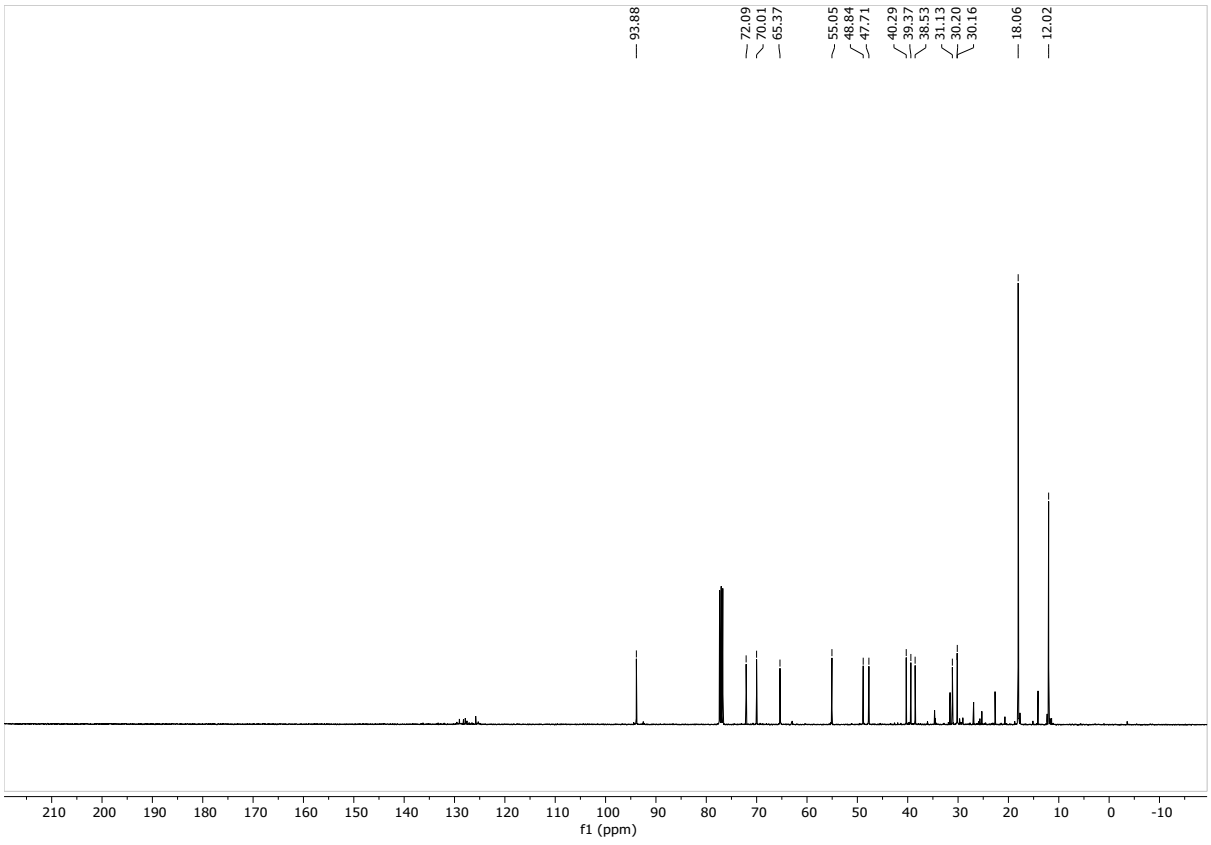
DEPT-135 NMR of compound 4 ($CDCl_3$, 125)



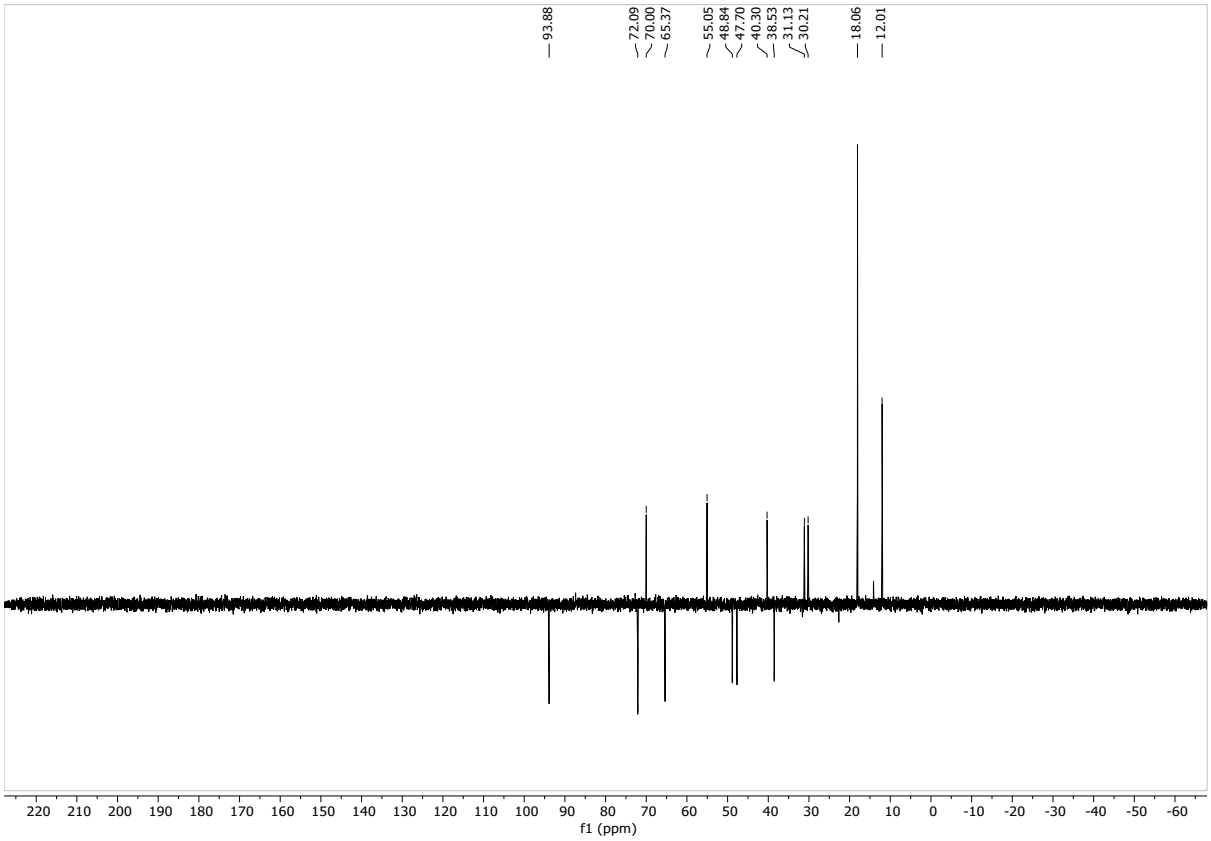
^{1}H-NMR of compound 36 ($CDCl_3$, 500MHz)



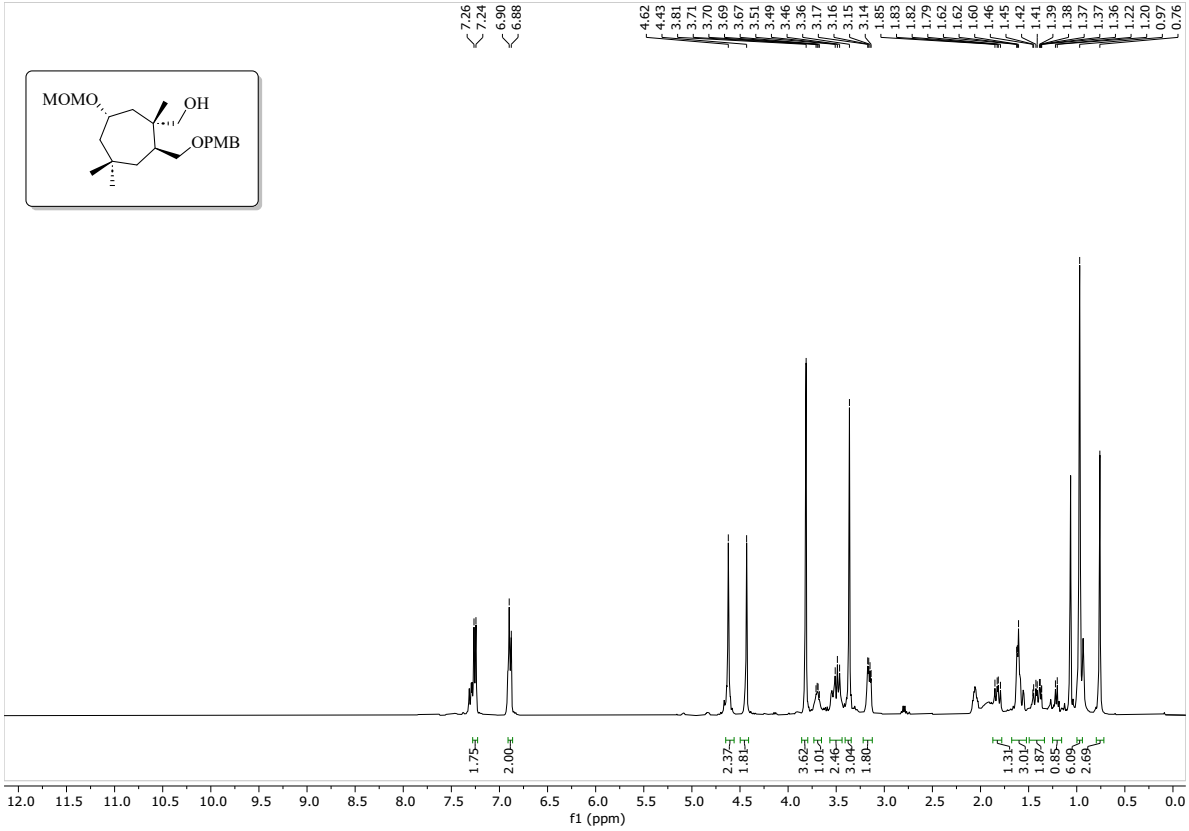
^{13}C-NMR of compound 36 ($CDCl_3$, 125 MHz)



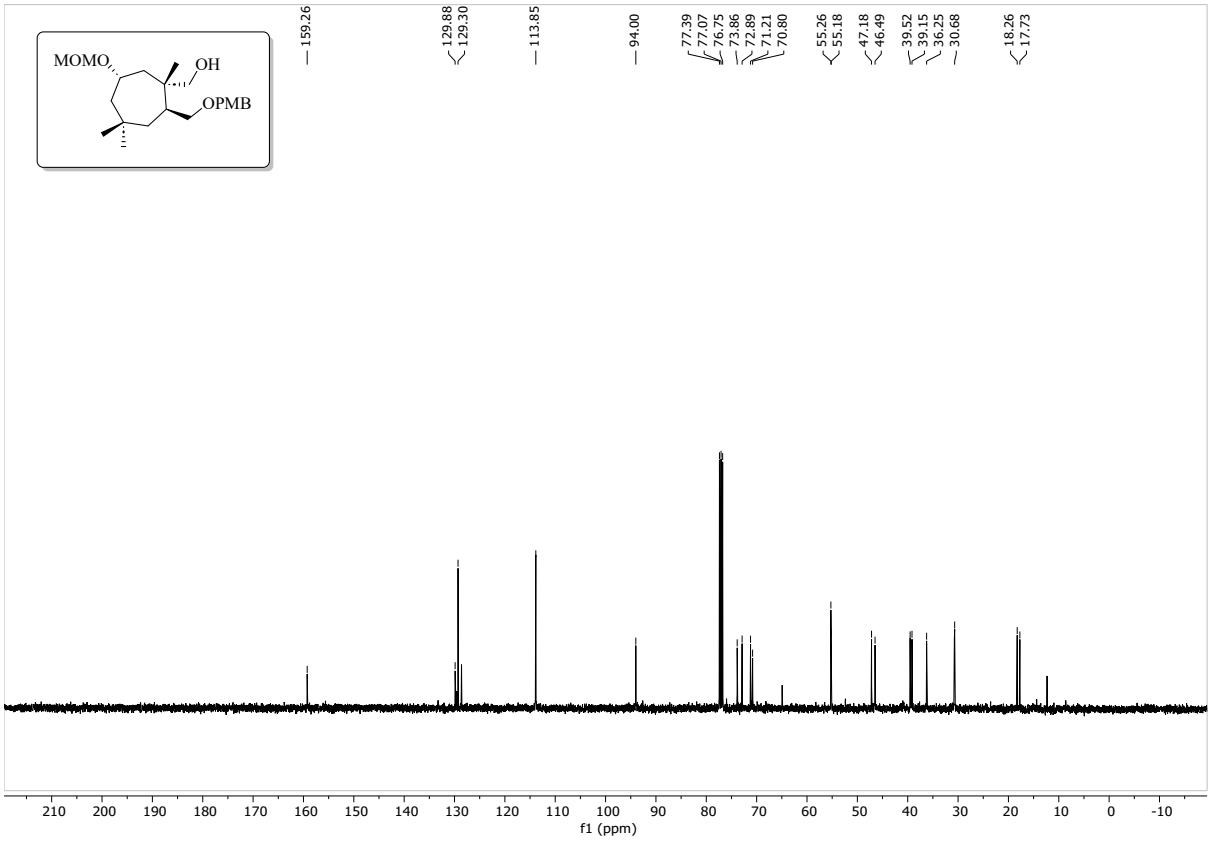
DEPT-135 NMR of compound 36 ($CDCl_3$, 125 MHz)



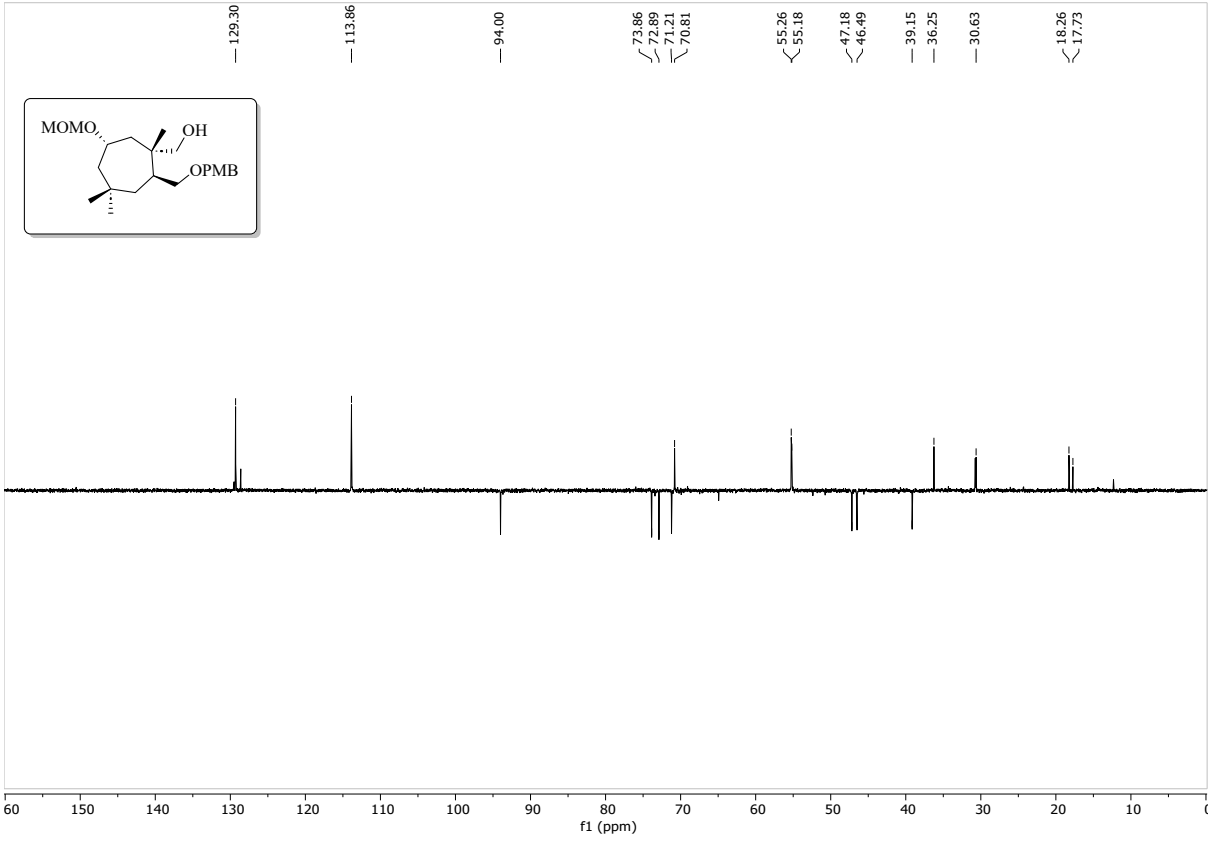
^{1}H-NMR of compound 37 ($CDCl_3$, 500MHz)



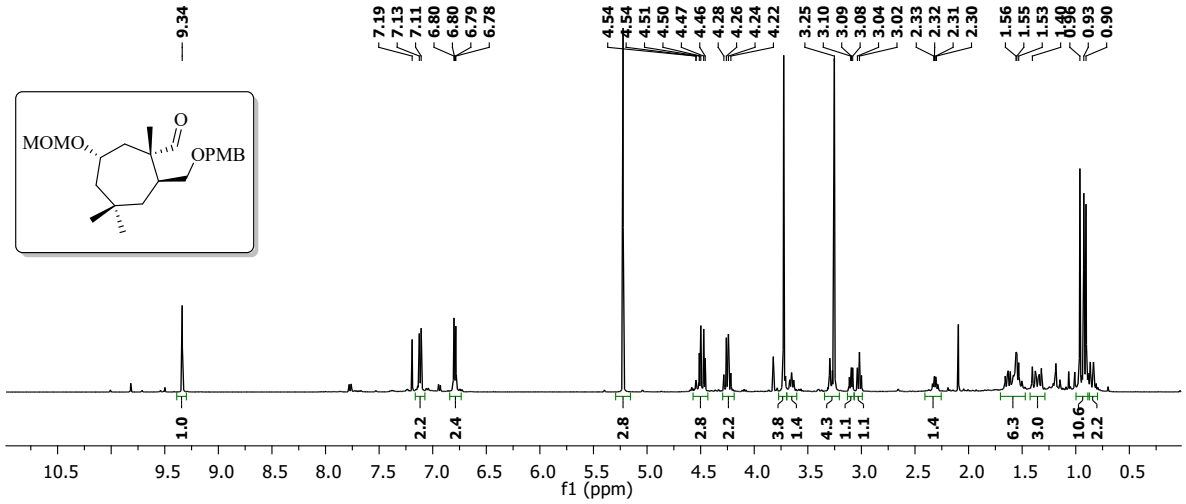
^{13}C-NMR of compound 37 ($CDCl_3$, 125MHz)



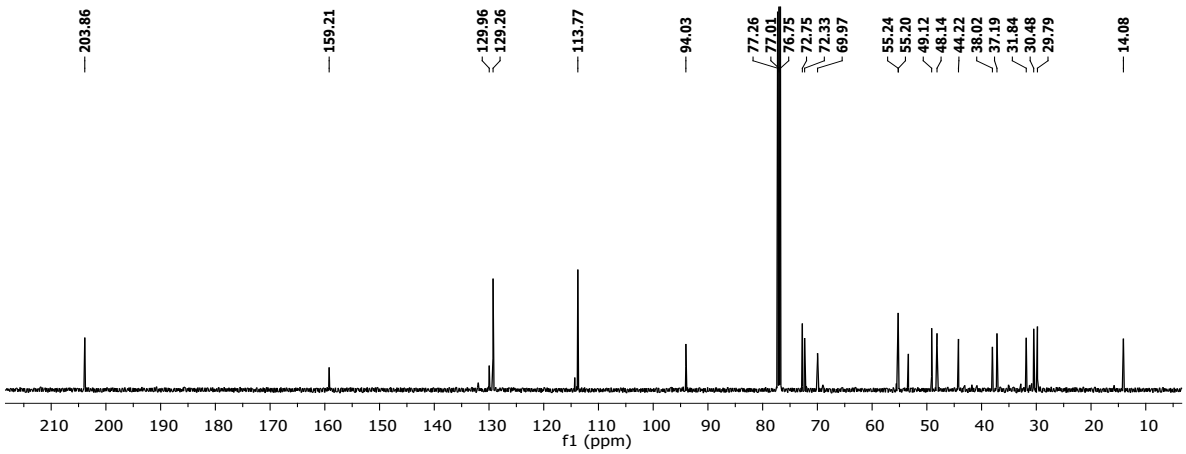
DEPT-NMR of compound 37 ($CDCl_3$, 125MHz)



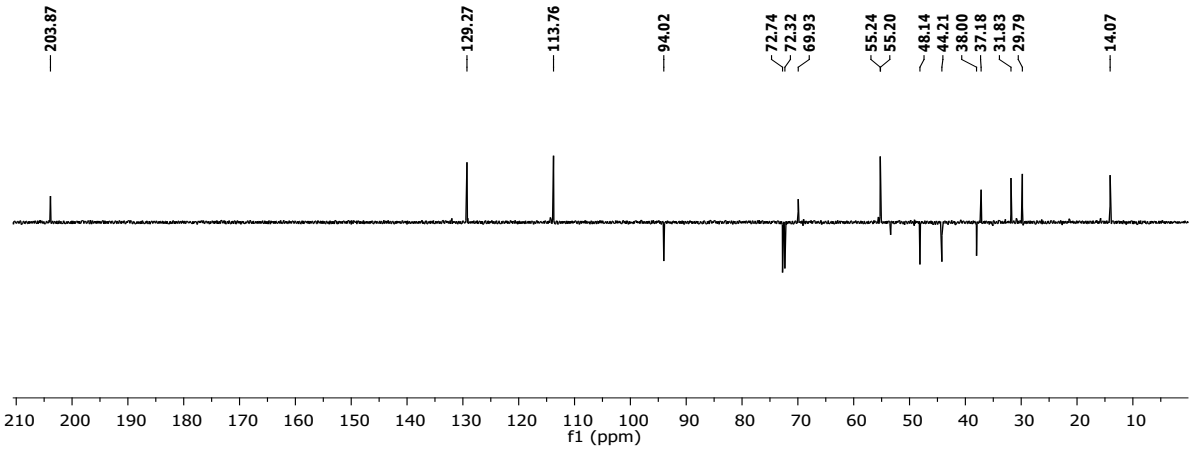
^{1}H-NMR of compound 38 ($CDCl_3$, 500MHz)



^{13}C-NMR of compound 38 ($CDCl_3$, 125MHz)

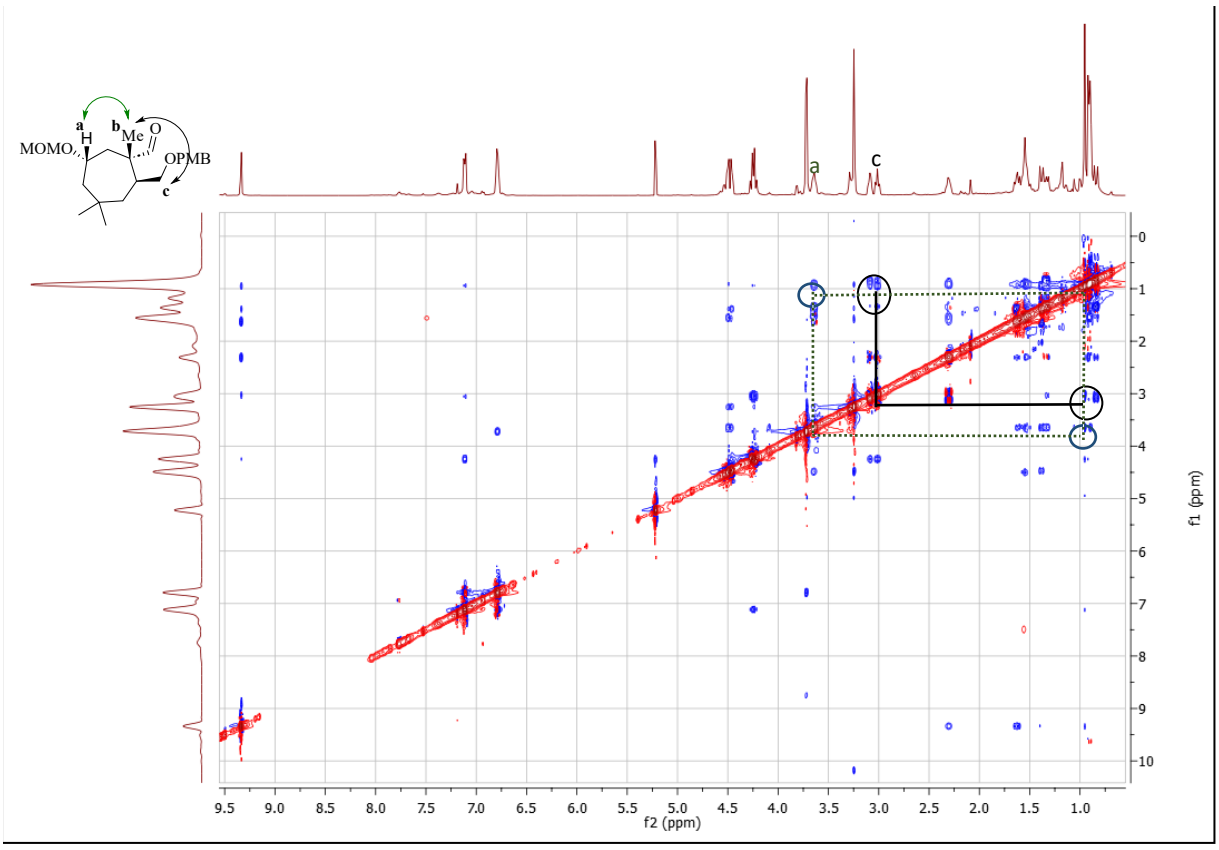


DEPT-135 NMR of compound 38 ($CDCl_3$, 125 MHz)

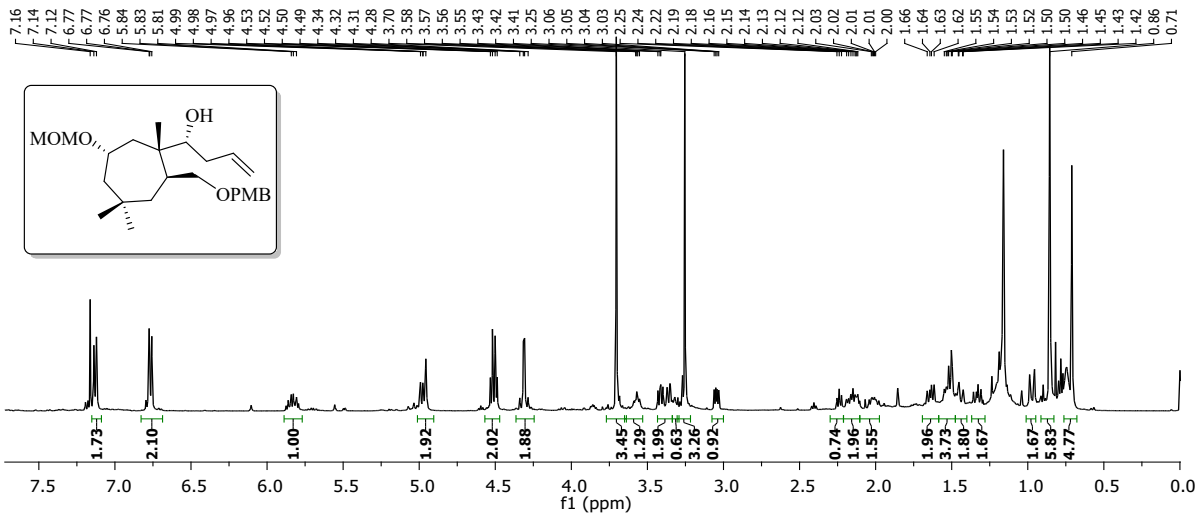


2-D NOESY spectrum of 38 ($CDCl_3$, 500Mz)

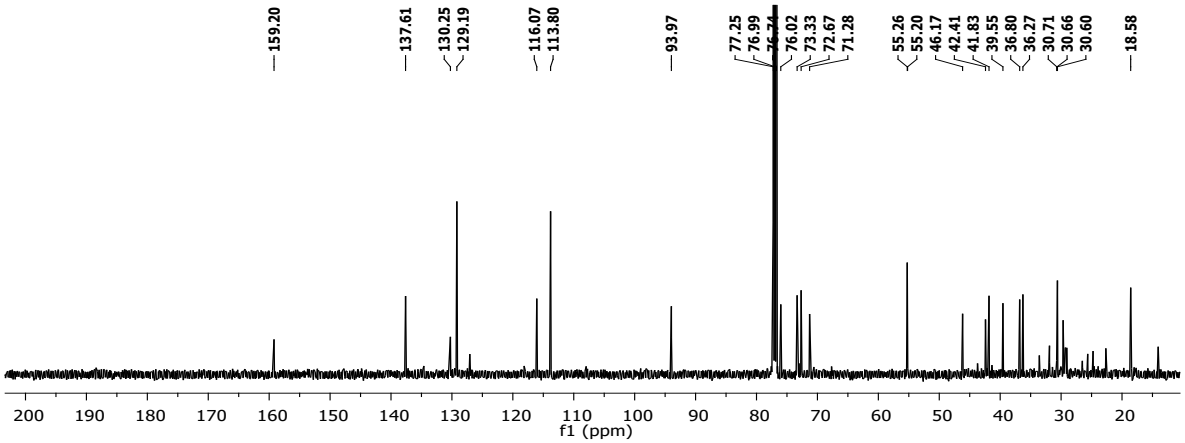
b



^{1}H-NMR of compound 3 ($CDCl_3$, 500MHz)



^{13}C-NMR of compound 3 ($CDCl_3$, 125MHz)



DEPT-135 NMR of compound 3 ($CDCl_3$, 125 MHz)