Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supplementary Information

Diastereoselective One Pot Wittig Olefination - Michael Addition and Olefin Cross Metathesis Strategy for Total Synthesis of Cytotoxic Natural Product (+)-Varitriol and its Higher Analogues

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EXPERIMENTAL PROTOCOL FOR ANTI-CANCER SCREENING

The 96-well plate colorimetric assay using sulforhodamine-B (SRB) stain [1] was used to test the molecules on a panel of human cell lines representing various tumor types. The cell lines were procured from American Type Culture Collection (ATCC, Rockville, MD, USA). The main advantage of the *in vitro* assay is that it gives reproducible dose response curve over a concentration range matching the *in vivo* effective dose of the drug. The assay relies on the ability of the SRB to bind to protein components of the cells that have been fixed to culture plate by trichloroacetic acid (TCA). As the binding of SRB is stoichiometric, amount of SRB extracted from stained cells is directly proportional to the cell mass. Stock solutions of the samples were prepared in DMSO and their serial dilutions were screened against selected cancer cell lines. Percentage of cell growth inhibition in presence of the test sample was calculated as follows:

$$\textbf{\% of cells killed} = 100 - \left[\frac{(\text{mean OD}_{\text{test}})}{(\text{mean OD}_{\text{control}})} \times 100 \right]$$

The half maximal inhibitory concentrations (IC_{50}) were calculated using Graph Prism software.

Reference:

1. Skehan P, Storeng R, Scudiero D, Monks A, McMahon J, Vistica D, Warren JT, Bodesch H, Kenney S, Boyd MR. New colorimetric cytotoxicity assay for anticancer-drug screening. *Journal of the National Cancer Institute*. **82:** 1107-1112 (1990).

EXPERIMENTAL SECTION

General

Organic solvents were dried by standard methods. NMR spectra of the synthesized compounds were recorded on Bruker Avance DPX 200FT, Bruker Robotics, and Bruker DRX 300 Spectrometers at 200, 300 MHz (^{1}H) and 50, 75 MHz (^{13}C) respectively. Experiments were recorded in $CDCl_3$ and CD_3OD at 25 °C. Chemical shifts are given on the δ scale and are referenced to the TMS at 0.00 ppm for proton and 0.00 ppm for carbon. Reference $CDCl_3$ for ^{13}C NMR appeared at 77.4 ppm. Using ESI mode mass spectra were recorded on a 6520 Accurate Mass Q-TOF LC/MS high resolution spectrometer at 70 eV and IR spectra on Perkin–Elmer 881 and FTIR-8210 PC Shimadzu Spectrophotometers. Optical rotations were determined on an Autopol III polarimeter using a 1 dm cell at 28 °C in chloroform as the solvents; concentrations mentioned are in g/100 mL. The Auto System XL GC spectrum was recorded on Parkin Elmer Instrument on OB-1 column (10 feet) within temperature range 50 ^{o}C to 200 ^{o}C with a temperature rising rate 4 ^{o}C/min. and hold time 3 min. Analytical TLC was performed using 2.5 × 5 cm plates coated with a 0.25 mm thickness of silica gel (60F-254), and visualization was accomplished with $CeSO_4$ (1% in 2 N H_2SO_4) followed by charring over hot plate. Silica gel (100-200 and 230-400 mesh) was used for column chromatography. All the products were characterized by ^{1}H, ^{13}C, IR, ESI-MS spectroscopy. Low-temperature reactions were performed by using immersion cooler with ethanol as the cooling agent. Grubbs' second generation catalyst was purchased from Sigma-Aldrich Co.

General procedure for preparation of Compound 10

D-ribose (10 g, 66.2 mmol) and 2,2-dimethoxypropane (12.2 mL, 99.3 mmol) were taken in dry acetone (50 mL) and the mixture was cooled to 0 °C. The catalytic amount of *p*-toluenesulfonic acid (1.5 g) was added to the mixture and it was stirred for 2 h at 0 °C. After completion of the reaction, the reaction mixture was quenched with Et_3N and the mixture was evaporated under reduced pressure to give an oily residue. Water (80 ml) was added to it and extracted with EtOAc (3 × 60 mL). The combined organic layer was washed once with water, dried over Na_2SO_4 and evaporated under reduced pressure to obtain a residue. Column chromatographic purification of the residue yielded compound 2,3-*O*-isopropylidine D-ribose, **10**[18] as an oil (11.31 g, 59.60 mmol, 90%).

General procedure for preparation of lactol 8

To a stirred solution of MeMgI (82.1 mL, 246.3 mmol)], 2,3-O-isopropylidene-D-ribofuranose **10** (5.2 g, 27.37 mmol) in ether (15 mL) was added at −50 °C and the stirring was continued for 6h at this temperature. The reaction mixture was then slowly warmed to rt and stirred for another 12 h. Afterward it was quenched with saturated aqueous NH_4Cl (25 mL) and extracted with EtOAc (5 × 50 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude triol **9** was used for next step without further purification.

To the above obtained crude triol **9** dissolved in THF/H_2O (10:1, 50 mL) was added $NaIO_4$ (7.72 g, 36 mmol) at 0 °C and stirred for 5 h without further cooling. The reaction mixture was quenched with saturated $Na_2S_2O_3$ (30 mL) and extracted with EtOAc (2 × 50 mL). Combined organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give a residue which after column chromatographic purification afforded lactol **8**[12,19] (3.05g, 17.52 mmol, 64% over two steps) as pale yellow liquid.

Compound 7

To a solution of lactol **8** (304 mg, 1 mmol) in acetonitrile (5 mL), $Ph_3P{=}CHCO_2Me$ (500mg, 1.5 mmol) was added and the reaction mixture was allowed to stir under reflux (110 ^oC) for 2 hours. After completion of the Wittig olefination (TLC control), the reaction mixture was cooled to room temperature, K_2CO_3 (276 mg, 2 mmol) was added to it and left for stirring at this temperature. After 4h, water (10 ml) was added to the reaction mixture and was extracted with EtOAc (3 × 15 mL). The combined organic layer was evaporated under reduced pressure to get an oily residue which after column chromatographic purification afforded compound **7** (327 mg, 0.91 mmol, 91% from **8**) as a colorless oil.

Eluent for column chromatography: EtOAc/Hexane (1/11, v/v); $[\alpha]_D^{28}$ +2.5 (*c* 1.76, $CHCl_3$); R_f = 0.75 (1/4, EtOAc/Hexane); IR (neat, cm^{-1}): 2982, 2932, 2364, 1740, 1375, 1244; ^1H NMR (300 MHz, $CDCl_3$) δ 1.19(d, J = 6.4, 3H), 1.24 (s, 3H), 1.44 (s, 3H), 2.47-2.63 (m, 2H), 3.60 (s, 3H), 3.81-3.90 (m, 1H), 4.07-4.13 (m, 1H), 4.17-4.21 (m, 1H), 4.41 (dd, J = 4.7, 6.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1 (CH_3), 25.7 (CH_3), 27.5 (CH_3), 38.4(CH_2), 51.8 (CH), 80.3 (CH), 80.5 (CH), 84.8(CH), 86.3 (CH), 115.0 (qC), 170.9 (C=O); DART–HRMS: m/z $[M+H]^+$ Calcd for $C_{11}H_{19}O_5$ 231.1232, found 231.1230.

Compound 6

The ester **7** (500 mg, 2.17 mmol) was dissolved in dry THF (10 mL) and cooled to 0 °C. To the cooled solution was added $LiAlH_4$ (124 mg, 3.26 mmol) in 3 portions over a time period of about 5 min. The resulting reaction mixture was allowed to stir at 0 °C for 1h and then left for stirring for another 1h without cooling. After completion of the reaction, excess $LiAlH_4$ was quenched by adding EtOAc. The reaction mixture was then passed through a short silica gel bed and

washed with EtOAc (3 × 10 mL). The combined organic layer was evaporated under reduced pressure and purified by column chromatography to afford compound **6** (400 mg, 1.97 mmol, 91%).

Eluent for column chromatography: EtOAc/Hexane (1/6, v/v); $[\alpha]_D^{28}$ +7.0 (*c* 0. 896, $CHCl_3$); R_f = 0.33 (1/4, EtOAc/Hexane); IR (neat, cm^{-1}): 3423, 2980, 2931, 2361, 1378, 1214; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26(d, *J* = 6.4, 3H), 1.28 (s, 3H), 1.48 (s, 3H), 1.75-1.91 (m, 2H), 2.61 (brm, 1H), 3.71-3.75 (m, 2H), 3.86-3.91 (m, 2H), 4.21 (dd, *J* = 5.0, 7.0, 1H), 4.33-4.37 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.3 (CH_3), 25.8 (CH_3), 27.6 (CH_3), 36.1 (CH_2), 60.7 (CH_2), 80.6 (CH), 83.5 (CH), 85.4 (CH), 86.3 (CH), 115.4 (qC); DART–HRMS: m/z $[M+H]^+$ Calcd for $C_{10}H_{19}O_4$ 203.1283, found 203.1281.

Compound 5

To a stirred solution of alcohol **6** (650 mg, 3.21 mmol) in dry DCM (10 mL) at 0 °C Et_3N (1.3 mL, 9.3 mmol) was added. TsCl (1.23 g, 6.4 mmol) was added to the reaction mixture portion wise and the stirring was continued for one hour at the same temperature and afterward for 3 hours without cooling. After completion of the reaction, a saturated aqueous solution of NH_4Cl (15 mL) was added and the resulting solution was extracted with CH_2Cl_2 (4 × 20 mL). The combined organic phase was dried over Na_2SO_4 and the solvent was removed under reduced pressure. Column chromatographic purification of the residue furnished **5** as an oil (1.1 g, 3.09 mmol, 96%).

Eluent for column chromatography: EtOAc/Hexane (1/9, v/v); $[\alpha]_D^{28}$ +6.4 (*c* 1.00, $CHCl_3$); R_f = 0.44 (1/4, EtOAc/Hexane); IR (neat, cm^{-1}): 2982, 2931, 2369, 2339, 1599, 1458, 1363; ^1H NMR (300 MHz, $CDCl_3$) δ 1.19(d, *J* = 6.4, 3H), 1.27 (s, 3H), 1.47 (s, 3H), 1.80-1.87 (m, 1H),

1.98-2.05 (m, 1H), 2.42 (s, 3H), 3.71-3.80 (m, 2H), 4.08-4.19 (m, 3H), 4.26-4.30 (m, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1 (CH_3), 21.9 (CH_3), 25.8 (CH_3), 27.6 (CH_3), 33.2 (CH_2), 67.5 (CH_2), 80.40 (CH), 80.43 (CH), 85.3 (CH), 86.4 (CH), 115.4 (qC), 128.3 (2 × Ar-CH), 130.1 (2 × Ar-CH), 133.4 (Ar-qC), 145.0 (Ar-qC); DART–HRMS: m/z $[M+H]^+$ Calcd for $C_{17}H_{25}O_6S$ 357.1372, found 357.1378.

Compound 4

The tosylate **5** (500 mg, 1.4 mmol) was dissolved in dry THF (30 mL) and cooled to –30 °C. To the cooled solution was added ^{t}BuOK (400 mg, 3.6 mmol) portionwise over a time period of about 2h. The resulting reaction mixture was allowed to stir at this temperature for another 4h and then left for stirring for overnight without cooling. After completion of the reaction, the rection mixture was quenched by adding aqueous NH_4Cl solution (20 ml) and was extracted with DCM (3 × 20 mL). The combined organic phase was evaporated under reduced pressure and purified by column chromatography to afford compound **4** (219 mg, 1.19 mmol, 85%). Here all the workup, purification and evapouration of column fractions were done bellow 30 ^{o}C.

Eluent for column chromatography: EtOAc/Hexane (1/13, v/v); $[\alpha]_D^{28}$ +5.1 (c 0.345, $CHCl_3$); R_f = 0.45(1/4, EtOAc/Hexane); IR (neat, cm^{-1}): 2981, 2931, 2365, 1376, 1218; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29-1.31(m, 6H), 1.52 (s, 3H), 3.93-4.01(m, 1H), 4.22-4.29 (m, 2H), 4.42 (dd, J = 5.1, 6.8 Hz, 1H), 5.19 (d, J = 10.4 Hz, 1H), 5.35 (d, J = 17.2 Hz, 1H), 5.82-5.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.3 (CH_3), 25.8 (CH_3), 27.7 (CH_3), 80.5 (CH), 85.3 (CH), 85.7 (CH), 86.5 (CH), 115.2 (qC), 117.5 (CH_2), 136.4 (CH); DART–HRMS: m/z $[M+H]^+$ Calcd for $C_{10}H_{17}O_3$ 185.1178, found 185.1160.

Compound 2

Under argon atmosphere Grubbs' second generation catalyst (28 mg, 0.0335 mmol) was added to a 50 mL oven dried two necked round bottomed flask fitted with a reflux condenser and septum. Dry CH_2Cl_2 (2 mL) was added to the flask through a syringe and the solution was kept for stirring. Vinylic furanoside **4** (100 mg, 0.54 mmol) and the alkene **3** (180 mg, 1.1 mmol) in DCM (2 mL each) were added in succession through a syringe to the reaction mixture. The septum was replaced with a glass stopper while the stirring was continued. The solution was refluxed for 32h. After completion of the reaction, the organic solvent was evaporated under reduced pressure to give a black residue which was purified by column chromatography to give compound **2** as oil (108 mg, 0.337 mmol, 62.4% from alkene **4**).

Eluent for column chromatography: EtOAc/Hexane (1/3, v/v); $[\alpha]_D^{28}$ +17.1 (*c* 0.375, $CHCl_3$); R_f = 0.42 (1/3, EtOAc/Hexane); IR (neat, cm^{-1}): 3457, 2931, 2371, 1580, 1219; ^1H NMR (300 MHz, $CDCl_3$) δ 1.36-1.38 (m, 6H), 1.59 (s, 3H), 2.30 (brm, 1H, OH), 3.87 (s, 3H), 4.02-4.10 (m, 1H), 4.35 (dd, *J* = 4.7, 6.9 Hz, 1H), 4.44-4.48 (m, 1H), 4.54-4.58 (m, 1H), 4.80 (s, 2H), 6.17 (dd, *J* = 6.6, 15.8 Hz,1H), 6.83 (d, *J* = 8.0 Hz, 1H), 7.05-7.11 (m, 2H), 7.22-7.28 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.4 (CH_3), 25.9 (CH_3), 27.7 (CH_3), 56.0 (CH), 57.1 (CH_2), 80.7 (CH), 85.2 (CH), 85.9 (CH), 86.6 (CH), 110.1 (CH), 115.4 (qC), 119.7 (CH), 126.8 (Ar-qC), 129.2 (Ar-CH), 129.8 (Ar-CH), 131.1 (Ar-CH), 137.7 (Ar-qC), 158.4 (Ar-qC); DART–HRMS: m/z $[M]^+$ Calcd for $C_{18}H_{24}O_5$ 320.1624, found 320.1609.

Compound 1

A solution of compound **2** (80 mg, 0.25 mmol) in THF (5 mL) was stirred with 1M HCl (5 mL) for 4 hours at room temperature. After completion of the reaction, EtOAc (10 ml) was added to it and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined

organic layer was then washed with water, dried over Na_2SO_4 and concentrated under reduced pressure to give a residue which was purified by column chromatography to obtain (+)-varitriol (**1**) as a semisolid (63 mg, 0.225 mmol, 90%).

Eluent for column chromatography: EtOAc/Hexane (3/1, v/v); $[\alpha]_D^{28}$ +13.9 (*c* 0.52, CH_3OH) {Ref. 4. $[\alpha]_D^{28}$ + 18.5 (*c* 2.30, CH_3OH)}; R_f= 0.52 (EtOAc); IR (KBr, cm^{-1}): 3366, 2926, 2366, 1583, 1356, 1219; ^1H NMR (300 MHz, $CDCl_3$ + CD_3OD) δ 1.31 (d, *J* = 6.3 Hz, 3H), 2.34 (brm, 3H, 3OH), 3.67 (t, *J* = 5.54, 1H), 3.84-3.91 (m, 5H), 4.29 (t, *J* = 6.44, 1H), 4.76 (dd, *J* = 11.8, 32.0 Hz, 2H), 6.09 (dd, *J* = 7.0, 15.7 Hz,1H), 6.81 (d, *J* = 8.1 Hz, 1H), 6.99-7.10 (m, 2H), 7.20-7.28 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ + CD_3OD) δ 19.4 (CH_3), 56.0 (CH), 56.2 (CH_2), 75.5 (CH), 76.3 (CH), 80.2 (CH), 84.4 (CH), 110.2 (CH), 119.5 (CH), 126.3 (Ar-qC), 129.4 (CH), 129.8 (CH), 131.5 (CH), 138.0 (Ar-qC), 158.3 (Ar-qC); DART–HRMS: m/z $[M]^+$ Calcd for $C_{15}H_{20}O_5$ 280.1311, found 280.1297.

General procedure for preparation of Compound 24

To the precooled (0 °C) solution of 2,3-*O*-isopropylidine -D-ribose **10** (10.31 g, 54.28 mmol) in dry DCM (40 mL) was added imidazole (5.54 g, 81.4 mmol). TBDMSCl (9.00 g, 59.71 mmol) was then added to the reaction mixture and stirring was continued for 2 hours. After completion of the reaction, a saturated aqueous solution of NH_4Cl (15 mL) was added and the resulting solution was extracted with dichloromethane (4 × 20 mL). The combined organic phase was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography to furnish **24**[18] (14.87 g, 48.85 mmol, 90 %) as a colorless oil.

Compound 23

To a solution of the hemiacetal **24** (305 mg, 1 mmol) in acetonitrile (5 mL), $Ph_3P{=}CHCO_2Me$ (500mg, 1.5 mmol) was added and the reaction mixture was allowed to stir under reflux (110 ^oC) for 2 hours. After completion of the wittig olefination, the reaction mixture was cooled to room temperature, K_2CO_3 (276 mg, 2 mmol) was added to it and left for stirring at this temperature. After 4h, water (10 ml) was added to the reaction mixture to extract with EtOAc (3 × 15 mL). The combined organic layer was evaporated under reduced pressure to get an oily residue which after column chromatographic purification afforded compound **23** (312 mg, 0.87 mmol, 87% from **24**) as a colorless oil.

Eluent for column chromatography: EtOAc/Hexane (1/15, v/v); $[\alpha]_D^{25}$ –17.9 (*c* 1.135, $CHCl_3$); R_f = 0.64 (1/4, EtOAc/Hexane); IR (neat, cm^{-1}): 2936, 2365, 1740, 1465, 1378, 1218; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.89 (brs, 9H), 1.33 (s, 3H), 1.52 (s, 3H), 2.61-2.64 (m, 2H), 3.68-3.69 (m, 5H), 4.06 (dd, *J* = 3.25, 6.51Hz, 1H), 4.28-4.34 (m, 1H), 4.41 (dd, *J* = 4.50, 6.24 Hz, 1H), 4.65 (dd, *J* = 3.05, 6.37 Hz, 1H); ^{13}C (75 MHz, $CDCl_3$) δ –5.1 (CH_3), –5.0 (CH_3), 18.7 (qC), 25.9 (CH_3), 26.3 (3 × CH_3), 27.8 (CH_3), 39.0 (CH_2), 52.1 (CH_3), 64.2 (CH_2), 81.6 (CH), 82.4 (CH), 85.0 (CH), 85.3 (CH), 114.2 (qC), 171.5 (C=O); IR (neat, cm-^{1}): 3021, 2936, 2365, 1740, 1650, 1218; ESI–HRMS: m/z $[M]^+$ Calcd for $C_{17}H_{32}O_6Si$ 360.1963, found 360.1956.

Compound 22

The ester **23** (500 mg, 1.39 mmol) was dissolved in dry THF (10 mL) and cooled to 0 °C. To the cooled solution was added $LiAlH_4$ (80 mg, 2.1 mmol) in 3 portions over a time period of about 5 min. The resulting reaction mixture was allowed to stir at 0 °C for 1h and then left for stirring for another 1h without cooling. After completion of the reaction, excess $LiAlH_4$ was quenched by adding EtOAc. The reaction mixture was then passed through a short silica gel bed

and washed with EtOAc (3 × 10 mL). The combined organic layer was evaporated under reduced pressure and purified by column chromatography to afford compound **22** (400 mg, 1.20 mmol, 87%).

Eluent for column chromatography: EtOAc/Hexane (1/4, v/v); $[\alpha]_D^{28}$ –15.9 (*c* 0.71, $CHCl_3$); R_f = 0.33 (1/3, EtOAc/Hexane); IR (neat, cm^{-1}): 3452, 2935, 2862, 2360, 1518, 1464, 1217; ^1H NMR (300 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.88 (brs, 9H), 1.32 (s, 3H), 1.51 (s, 3H), 1.75-1.94 (m, 2H), 2.50 (brm, 1H, OH), 3.71 (d, *J* = 3.67, 2H), 3.75 (t, *J* = 5.5 Hz, 2H), 3.98-4.04 (m, 2H), 4.32-4.36(m,1H), 4.61 (dd, *J* = 3.5, 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –5.1 (CH_3), –5.0 (CH_3), 18.7 (qC), 25.9 (CH_3), 26.2 (3 × CH_3), 27.8 (CH_3), 35.8 (CH_2), 60.9 (CH_2), 63.7 (CH_2), 81.9 (CH), 84.4 (CH), 84.8(CH), 85.1 (CH), 114.5 (qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{16}H_{32}O_5Si$ 332.2019, found 332.2030.

Compound 21

To a stirred solution of alcohol **22** (500 mg, 1.5 mmol) in dry DCM (20 mL) at 0 °C Et_3N (0.6 mL, 4.3 mmol) was added. TsCl (575 mg, 3 mmol) was then added to the reaction mixture portion wise and the stirring was continued first for one hour at the same temperature and then for 3 hours without cooling. After completion of the reaction, a saturated aqueous solution of NH_4Cl (15 mL) was added and the resulting solution was extracted with CH_2Cl_2 (4 × 20 mL). The combined organic phase was dried over Na_2SO_4 and the solvent was removed under reduced pressure. Column chromatographic purification of the residue furnished **21** as an oil (635 mg, 1.3 mmol, 87%).

Eluent for column chromatography: EtOAc/Hexane (1/5, v/v); $[\alpha]_D^{28}$ –27.8 (*c* 0.83, $CHCl_3$); R_f = 0.42(1/3, EtOAc/Hexane); IR (neat, cm^{-1}): 2933, 2362, 1643, 1365, 1217; ^1H NMR (300 MHz,

$CDCl_3$) δ 0.02 (s, 3H), 0.03 (s, 3H), 0.87 (brs, 9H), 1.31 (s, 3H), 1.49 (s, 3H), 1.86-1.91 (m, 1H), 1.98-2.03 (m, 1H), 2.44 (s, 3H), 3.65 (d, J = 2.7, 2H), 3.83-3.89 (m, 1H), 3.93 (dd, J = 3.3, 6.7 Hz, 1H), 4.11-4.17 (m, 2H), 4.24-4.27 (m, 1H), 4.60 (dd, J = 3.4, 6.5 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 8.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –5.1 (CH_3), –5.0 (CH_3), 18.6 (qC), 21.9 (CH_3), 25.8 (CH_3), 26.2 (3 × CH_3), 27.8 (CH_3), 33.4 (CH_2), 63.8 (CH_2), 67.8 (CH_2), 81.0 (CH), 82.1 (CH), 84.9 (CH), 85.2 (CH), 114.3 (qC), 128.3 (2 × Ar-CH), 130.1 (2 × Ar-CH), 133.4 (Ar-qC), 145.0 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{23}H_{38}O_7SSi$ 486.2102, found 486.2095.

Compound 20

The tosylate **21** (500 mg, 1.03 mmol) was dissolved in dry THF (10 mL) and cooled to –20 °C. To this cooled solution was added $LiAlH_4$ (78 mg, 2.06 mmol) in 3 portions over a time period of about 15 min. The resulting reaction mixture was stirred at –20 °C for about 1h then the reaction mixture was allowed to stir for another one hour without further cooling. After completion of the reaction, excess $LiAlH_4$ was quenched with EtOAc at 0 °C. The reaction mixture was then passed through a short silica gel bed and washed with EtOAc (3 × 15 mL). The combined organic layer was evaporated under reduced pressure to obtain an oily residue which on column chromatographic purification yielded compound **20** (235 mg, 0.74 mmol, 72%).

Eluent for column chromatography: EtOAc/Hexane (1/9, v/v); $[\alpha]_D^{28}$ –5.8 (c 1.18, $CHCl_3$); R_f= 0.54 (1/4, EtOAc/Hexane); IR (neat, cm^{-1}): 2935, 2864, 2366, 1465, 1378, 1218; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.02 (s, 3H), 0.03 (s, 3H), 0.86 (brs, 9H), 0.93 (t, J = 7.4, 3H), 1.30 (s, 3H), 1.49 (s, 3H), 1.51-1.61 (m, 2H), 3.67 (d, J = 2.7, 2H), 3.72-3.78 (m, 1H), 3.93 (dd, J = 3.8, 7.6 Hz, 1H), 4.23 (dd, J = 4.9, 6.7 Hz, 1H), 4.57 (dd, J = 3.7, 6.7 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ

–5.1 (CH_3), –5.0 (CH_3), 10.1 (CH_3), 18.7 (qC), 25.9 (CH_3), 26.2 (3 × CH_3), 27.1 (CH_2), 27.8 (CH_3), 64.0 (CH_2), 82.2 (CH), 84.6 (CH), 85.2 (CH), 86.1 (CH), 114.1 (qC); ESI–HRMS: m/z $[M+Na-H]^+$ Calcd for $C_{16}H_{31}O_4SiNa$ 338.1884, found 338.1884.

Compound 19

To a stirred solution of silyl ether **20** (500 mg, 1.58 mmol) in THF (10 mL) was added TBAF (1.8 mL, 1M solution in THF) at 0 °C and left for stirring at room temperature. After 2 h, saturated aqueous solution of NH_4Cl (15 mL) was added to the reaction mixture and it was extracted with EtOAc (3 × 15 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to give a residue which on column purification afforded compound **19** (287 mg, 1.42 mmol, 90%) as a colorless oil.

Eluent for column chromatography: EtOAc/Hexane (1/5, v/v); $[\alpha]_D^{28}$ + 7.2 (*c* 1.12, $CHCl_3$); R_f = 0.4 (1/4, EtOAc/Hexane); IR (neat, cm^{-1}): 3460, 2973, 2935, 2879, 2366, 1460, 1379, 1216; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J = 7.4 Hz, 3H), 1.27 (s, 3H), 1.47 (s, 3H), 1.54-1.59 (m, 2H), 2.64 (brs, 1h, OH), 3.58-3.61 (m, 1H), 3.70-3.74 (m, 2H), 3.87-3.89 (m, 1H), 4.21-4.24 (m, 1H), 4.49-4.53 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.0 (CH_3), 25.7 (CH_3), 26.7 (CH_2), 27.6 (CH_3), 62.9 (CH_2), 81.7 (CH), 84.4 (CH), 84.9 (CH), 86.0 (CH), 114.8 (qC); ESI–HRMS: m/z $[M+Na-H]^+$ Calcd for $C_{10}H_{17}O_4Na$ 224.1019, found 224.1035.

Compound 16

A solution of CH_3CN (10 mL) containing alcohol **19** (500 mg, 2.47 mmol) and IBX (2.77 g, 9.9 mmol) in a 100 mL round bottom flask was refluxed for 1 h with cold water circulation. The reaction mixture was then cooled to 0 °C and diluted with ether. After 1h, the reaction mixture was filtered through a celite bed and the filtrate was concentrated under reduced pressure to

obtain an oil **18** (485 mg) which was immediately used for the next step without further purification.

Methyl triphenylphosphonium bromide (3.03g, 8.3 mmol) and ^{t}BuOK (683 mg, 6.1 mmol) were taken in a flame dried two necked round bottomed flask and cooled to –20 °C. Dry THF (25 mL) was added to the reaction mixture under nitrogen atmosphere and it was stirred for 1 h without further cooling. The reaction mixture was then again cooled to –20 °C and the aldehyde **18** in THF (3 mL) was added to the mixture drop wise. The reaction mixture was allowed to warm to 0 °C and the stirring was continued for another 2h. After completion of the reaction, saturated aqueous NH_4Cl was added to the reaction mixture and was extracted with EtOAc (3 × 20 mL). The combined organic layer was washed twice with brine, dried over Na_2SO_4 and concentrated in vacuo to give a residue. Column Chromatographic purification of the residue yielded compound **16** as an oil (310 mg, 1.56 mmol, 63% for two steps). Here the work-up, purification and evaporation of column fractions were done bellow 30 ^{o}C.

Eluent for column chromatography: EtOAc/Hexane (1/49, v/v); $[\alpha]_D^{28}$ + 10.0 (*c* 0.23, $CHCl_3$); R_f = 0.9 (1/40, EtOAc/Hexane); IR (neat, cm^{-1}): 2983, 2933, 2877, 2364, 1460, 1378, 1216; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (t, *J* = 7.4 Hz, 3H), 1.33 (s, 3H), 1.54 (s, 3H), 1.60-1.66 (m, 2H), 3.78-3.82 (m, 1H), 4.25 (dd, *J* = 5.00, 6.1, 1H), 4.31-4.42 (m, 2H), 5.18-5.22 (m, 1H), 5.37 (dt, *J* = 1.3, 17.3 Hz, 1H), 5.83-5.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2 (CH_3), 25.8 (CH_3), 26.9 (CH_2), 27.7 (CH_3), 85.1 (CH), 85.2 (CH), 85.5 (CH), 85.8 (CH), 115.1 (qC), 117.6 (CH_2), 136.4 (CH); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{11}H_{18}O_3$ 198.1250, found 198.1254.

Compound 14

To a precooled solution of **13** (100 mg, 0.67 mmol) in DMF (5 mL) was added anhydrous NaH (48 mg, 2 mmol), methyl iodide (0.16 mL, 2.68 mmol) and the resulting mixture was allowed to stir for 2h at 0 ^{o}C and then at rt. After 2 h the reaction mixture was quenched by adding MeOH and the resulting solution was concentrated under reduced pressure to a residue that was dissolved in ethyl acetate (15 mL) and washed with water. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to an oil which was purified by column chromatography to give **14** (105 mg, 0.58 mmol, 88%) as a colorless oil.

Eluent for column chromatography: EtOAc/Hexane (1/10, v/v); R_f = 0.5 (2/7, EtOAc/Hexane); IR (neat, cm–1): 3011, 2929, 2368, 1646, 1577, 1467, 1262; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.38 (s, 3H), 3.81 (s, 3H), 4.58 (s, 2H), 5.33 (dd, J = 1.2, 11.0 Hz, 1H), 5.68 (dd, J = 1.2, 17.4 Hz, 1H), 6.80 (d, J = 7.9, 2H), 7.03-7.27 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.2 (CH_3), 58.4 (CH_3), 65.0 (CH), 110.3 (CH), 116.9 (CH_2), 118.6 (CH), 123.7 (Ar-qC), 129.5 (CH), 134.8 (CH), 140.2 (Ar-qC), 158.5 (Ar-qC); ESI–HRMS: m/z [M]+ Calcd for $C_{11}H_{14}O_2$ 178.0988, found 178.0979.

Compound 15a

Under argon atmosphere Grubbs' second generation catalyst (28 mg, 0.0335 mmol) was added to a 50 mL oven dried two necked round bottomed flask fitted with a reflux condenser and septum. Dry CH_2Cl_2 (2 mL) was then added to the flask through a syringe and the solution was kept for stirring. Vinylic furanoside **16** (100 mg, 0.5 mmol) and the alkene **3** (164 mg, 1 mmol) in DCM (2 mL each) were added in succession through a syringe to the reaction mixture. The septum was replaced with a glass stopper and the stirring was continued. The solution was refluxed for 12h. After completion of the reaction, the organic solvent was evaporated under reduced pressure to give a black residue which was purified by column chromatography to give compound **15a** as a semi-solid (117 mg, 0.35 mmol, 70%).

Eluent for column chromatography: EtOAc/Hexane (1/10, v/v); $[\alpha]_D^{28}$ + 36.9 (*c* 0.13, $CHCl_3$); R_f = 0.52 (1/9, EtOAc/Hexane); IR (neat, cm^{-1}): 3452, 3009, 2930, 2367, 1579, 1466, 1218; ^1H NMR (300 MHz, $CDCl_3$) δ 1.03 (t, *J* = 7.4 Hz, 3H), 1.36 (s, 3H), 1.58 (s, 3H), 1.62-1.74 (m, 3H), 3.84-3.91 (m, 4H), 4.37-4.53 (m, 3H), 4.79 (s, 3H), 6.14 (dd, *J* = 6.4, 15.8 Hz, 1H), 6.82 (d, *J* = 8.1 Hz,1H), 7.03-7.09 (m, 2H), 7.20-7.26 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2 (CH_3), 25.9 (CH_3), 27.0 (CH_2), 27.8 (CH_3), 56.0 (CH), 57.2 (CH_2), 85.1 (CH), 85.2 (CH), 85.8 (CH), 85.9 (CH), 110.1 (CH), 115.3 (qC), 119.7 (CH), 126.8 (Ar-qC), 129.2 (CH), 129.7 (CH), 131.2 (CH), 137.7 (Ar-qC), 158.5 (Ar-qC); ESI–HRMS: m/z $[M+Na-H]^+$ Calcd for $C_{19}H_{25}O_5Na$ 356.1594, found 356.1597.

Compounds **15b-j** were synthesized by following the same procedure as adopted for compound **15a**. The respective equivalents of alkenes and time are given in **Table1**.

Compound 15c

Eluent for column chromatography: EtOAc/Hexane (1/10, v/v); $[\alpha]_D^{28}$ + 46.4 (*c* 0.79, $CHCl_3$); R_f = 0.50 (1/8, EtOAc/Hexane); IR (neat, cm^{-1}): 3022, 2934, 2365, 1469, 1218; ^1H NMR (300 MHz, $CDCl_3$) δ 1.02 (t, *J* = 7.4 Hz, 3H), 1.35 (s, 3H), 1.43 (t, *J* = 6.9 Hz, 3H), 1.57 (s, 3H), 1.61-1.71 (m, 2H), 3.81 (s, 3H), 3.84-3.89 (m, 1H), 4.05 (dd, *J* = 6.9, 13.9 Hz, 2H), 4.37-4.41 (m, 1H), 4.45-4.53 (m, 2H), 6.23 (dd, *J* = 6.6, 16.1 Hz, 1H), 6.79 (d, *J* = 7.2 Hz,1H), 6.93-7.07 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 10.2 (CH_3), 15.2 (CH_3), 25.8 (CH_3), 27.0 (CH_2), 27.7 (CH_3), 61.1 (CH), 64.5 (CH_2), 85.2 (CH), 85.4 (CH), 85.8 (CH), 85.9 (CH), 113.2 (CH), 115.0 (qC), 118.6 (CH), 124.1 (CH), 127.3 (CH), 128.7 (CH), 130.9 (Ar-qC), 147.5 (Ar-qC), 152.6 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{20}H_{28}O_5$ 348.1931, found 348.1923.

Compound 15d

Eluent for column chromatography: EtOAc/Hexane (1/10, v/v); $[\alpha]_D^{28}$ + 39.4 (c 0.49, $CHCl_3$); R_f = 0.54 (1/8, EtOAc/Hexane); IR (neat, cm–1): 2973, 2927, 2358, 2334, 1577, 1463, 1265, 1213; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (t, J = 7.4 Hz, 3H), 1.35-1.45 (m, 9H), 1.58 (s, 3H), 1.64-1.71 (m, 2H), 3.87-3.88 (m, 1H), 3.99-4.08 (m, 4H), 4.37-4.41 (m, 1H), 4.47-4.51 (m, 2H), 6.23 (dd, J = 6.4, 16.1 Hz, 1H), 6.78 (dd, J = 1.1, 8.0 Hz, 1H), 6.92-6.98 (m, 1H), 7.02-7.08 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2 (CH_3), 15.3 (CH_3), 16.0 (CH_3), 25.9 (CH_3), 27.1 (CH_2), 27.8 (CH_3), 64.6 (CH_2), 69.4 (CH_2), 85.3 (CH), 85.4 (CH), 85.9 (CH), 85.94 (CH), 113.3 (CH), 115.0 (qC), 118.6 (CH), 124.0 (CH), 127.6 (CH), 128.5 (CH), 131.3 (Ar-qC), 146.7 (Ar-qC), 152.7 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{21}H_{30}O_5$ 362.2088, found 362.2083.

Compound 15f

Eluent for column chromatography: EtOAc/Hexane (1/12, v/v); $[\alpha]_D^{28}$ + 51.2 (*c* 1.06, $CHCl_3$); R_f= 0.74 (1/9, EtOAc/Hexane); IR (neat, cm^{-1}): 2975, 2934, 2367, 1459, 1377, 1217; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (t, *J* = 7.4 Hz, 3H), 1.37 (s, 3H), 1.60 (s, 3H), 1.64-1.76 (m, 2H), 3.91 (dd, *J* = 6.5, 10.9 Hz, 1H), 4.40-4.43 (m, 1H), 4.48-4.54 (m, 2H), 6.24 (dd, *J* = 5.8, 15.8 Hz, 1H), 7.08-7.17 (m, 2H), 7.39 (dd, *J* = 7.8, 21.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2 (CH_3), 25.8 (CH_3), 27.0 (CH_2), 27.7 (CH_3), 30.0 (Grease), 84.7 (CH), 85.2 (CH), 85.6 (CH), 86.0 (CH), 115.2 (qC), 125.5 (CH), 127.4 (CH), 128.6 (CH), 129.7 (CH), 131.8 (CH), 133.7 (Ar-qC), 137.4 (2 × Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{17}H_{20}Cl_2O_3$ 342.0784, found 342.0791.

Compound 15h

Eluent for column chromatography: EtOAc/Hexane (1/15, v/v); $[\alpha]_D^{28}$ + 42.8 (*c* 0.97, $CHCl_3$); R_f= 0.62 (1/12, EtOAc/Hexane); IR (neat, cm^{-1}): 2932, 2362, 1377, 1218; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (t, *J* = 7.4 Hz, 3H), 1.38 (s, 3H), 1.61 (s, 3H), 1.66-1.78 (m, 2H), 3.92 (dd, *J* = 6.7,

11.1 Hz, 1H), 4.41-4.45 (m, 1H), 4.56-4.58 (m, 2H), 6.24-6.31 (m, 1H), 7.40-7.53 (m, 4H), 7.60 (dd, J = 6.9, 1H), 7.76-7.85 (m, 2H), 8.10-8.13 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2 (CH_3), 25.9 (CH_3), 27.0 (CH_2), 27.8 (CH_3), 85.2 (CH), 85.3 (CH), 85.85 (CH), 85.9 (CH), 115.2 (qC), 124.2 (CH), 124.3 (CH), 125.9 (CH), 126.1 (CH), 126.4 (CH), 128.5 (CH), 128.8 (CH), 129.8 (CH), 130.9 (CH), 131.5 (Ar-qC), 133.9 (Ar-qC), 134.6 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{21}H_{24}O_3$ 324.1720, found 324.1711.

Compound 15j

Eluent for column chromatography: EtOAc/Hexane (1/11, v/v); $[\alpha]_D^{28}$ + 17.1 (c 0.34, $CHCl_3$); R_f = 0.44 (1/9, EtOAc/Hexane); IR (neat, cm^{-1}): 2926, 2856, 2368, 1462, 1216; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85-0.90 (m, 3H), 0.99 (t, J = 7.4 Hz, 3H), 1.25 (m, 22H), 1.33 (s, 3H), 1.54 (s, 3H), 1.60-1.67 (m, 2H), 2.04 (dd, J = 6.5, 13.3 Hz, 2H), 3.73-3.79 (m, 1H), 4.19 (dd, J = 5.2, 7.0 Hz, 1H), 4.30-4.39 (m, 2H), 5.47 (dd, J = 7.5, 15.6 Hz, 1H), 5.77-5.85 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2 (CH_3), 14.5 (CH_3), 23.1 (CH_2), 25.9 (CH_3), 26.9 (CH_2), 27.8 (CH_3), 29.3 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 29.9 (CH_2), 29.96 (CH_2), 30.0 (CH_2), 30.0-30.1 (3 × CH_2), 32.3 (CH_2), 32.7 (CH_2), 85.3 (2 × CH), 85.6 (CH), 85.8 (CH), 115.2 (qC), 127.9 (CH), 135.7 (CH); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{21}H_{16}O_7$ 380.0891, found 380.0919.

Compound 1a

A solution of compound **15a** (100 mg, 0.3 mmol) in THF (5 mL) was stirred with 2M HCl (10 mL) for 8 hours at room temperature. After completion of the reaction, EtOAc (10 ml) was added to it and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic layer was then washed with water, dried over Na_2SO_4 and concentrated under reduced

pressure to give a residue which was purified by column chromatography to obtain varitriol analogue (**1a**) as a colorless oil (70 mg, 0.238 mmol, 79%).

Eluent for column chromatography: EtOAc/Hexane (1/2, v/v); $[\alpha]_D^{28}$ –7.2 (*c* 0.77, $CHCl_3$); R_f= 0.34 (1/3, EtOAc/Hexane); IR (neat, cm^{-1}): 3347, 2923, 2364, 1571, 1461, 1253; ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.4 Hz, 3H), 1.43-1.50 (m, 2H), 3.59-3.63 (m, 4H), 3.72 (s, 3H), 4.16 (t, *J* = 6.5 Hz, 1H), 4.59 (d, *J* = 11.8 Hz, 1H), 4.71 (d, *J* = 11.8 Hz, 1H), 5.96 (dd, *J* = 7.0, 15.6 Hz,1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.91 (d, *J* = 15.7 Hz, 1H), 7.00 (d, *J* = 7.7 Hz, 1H), 7.12 (t, *J* = 7.9 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 10.2 (CH_3), 27.1 (CH_2), 55.9 (CH_2), 56.0 (CH), 74.7 (CH), 75.8 (CH), 83.5 (CH), 85.7 (CH), 110.2 (CH), 119.3 (CH), 126.2 (Ar-qC), 129.3 (CH), 129.8 (CH), 131.4 (CH), 138.0 (Ar-qC), 158.2 (Ar-qC); ESI–HRMS: m/z $[M+Na-H]^+$ Calcd for $C_{16}H_{21}O_5Na$ 316.1281, found 316.1272.

The other analogues **1b-j** were synthesized by following the same procedure as described above for **1a**. The respective strength of the HCl solution and time are given in **Table 2**.

Compound 1b

Eluent for column chromatography: EtOAc/Hexane (1/3, v/v); $[\alpha]_D^{28}$ + 2.4 (*c* 0.65, $CHCl_3$); R_f= 0.44 (1/3, EtOAc/Hexane); IR (neat, cm^{-1}): 3391, 2927, 2365, 1578, 1464, 1259; ^1H NMR (300 MHz, $CDCl_3$) δ 1.00 (t, *J* = 7.4 Hz, 3H), 1.60-1.64 (m, 2H), 3.21 (m, 1H, OH), 3.37 (s, 3H), 3.57 (m, 1H, OH), 3.74 (brm, 3H), 3.82 (s, 3H), 4.29 (t, *J* = 5.7 Hz, 1H), 4.59 (dd, *J* = 10.6, 17.4 Hz, 2H), 6.10 (dd, *J* = 6.9, 15.6 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 15.8 Hz,1H), 7.11-7.14 (m, 1H), 7.21-7.26 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3 (CH_3), 27.1 (CH_2), 56.2 (CH), 58.3 (CH), 65.0 (CH_2), 74.8 (CH), 76.0 (CH), 83.9 (CH), 85.6 (CH), 110.3 (CH), 119.0

(CH), 123.5 (Ar-qC), 129.7 (CH), 129.9 (CH), 130.9 (CH), 139.0 (Ar-qC), 158.6 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{17}H_{24}O_5$ 308.1618, found 308.1627.

Compound 1c

Eluent for column chromatography: EtOAc/Hexane (2/5, v/v); $[\alpha]_D^{28}$ + 18.8 (c 0.47, $CHCl_3$); R_f = 0.33 (1/3, EtOAc/Hexane); IR (neat, cm–1): 3435, 2928, 2358, 1602, 1466, 1263; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (t, J = 7.4 Hz, 3H), 1.46 (t, J = 6.9 Hz, 3H), 1.59-1.67 (m, 2H), 3.19-3.34 (brm, 2H, 2 OH), 3.72-3.87 (m, 6H), 4.05 (dd, J = 6.9, 13.9 Hz, 2H), 4.28-4.32 (m, 1H), 6.18 (dd, J = 7.2, 16.0 Hz, 1H), 6.79 (d, J = 8.0 Hz,1H), 6.93-7.07 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 10.2 (CH_3), 15.3 (CH_3), 27.1 (CH_2), 30.0 (Grease), 61.2 (CH), 64.6 (CH_2), 74.9 (CH), 76.0 (CH), 84.3 (CH), 85.6 (CH), 113.2 (CH), 118.7 (CH), 124.3 (CH), 127.3 (CH), 129.2 (CH), 130.9 (Ar-qC), 147.3 (Ar-qC), 152.6 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{17}H_{24}O_5$ 308.1618, found 308.1615.

Compound 1d

Eluent for column chromatography: EtOAc/Hexane (2/5, v/v); $[\alpha]_D^{28}$ + 15.1 (*c* 0.87, $CHCl_3$); R_f = 0.40 (1/2, EtOAc/Hexane); IR (neat, cm^{-1}): 3426, 2925, 2858, 2362, 1580, 1463, 1217; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (t, J = 7.4 Hz, 3H), 1.34-1.45 (m, 6H), 1.61-1.67 (m, 2H), 3.20 (m, 2H, 2OH), 3.74-3.84 (m, 3H), 3.98-4.07 (m, 4H), 4.30 (t, J = 5.9 Hz, 1H), 6.17 (dd, J = 7.0, 16.0 Hz, 1H), 6.78(d, J = 7.4 Hz, 1H), 6.92-7.07 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3 (CH_3), 15.3 (CH_3), 16.0 (CH_3), 27.1 (CH_2), 64.6 (CH_2), 69.5 (CH_2), 74.9 (CH), 76.1 (CH), 84.2 (CH), 85.5 (CH), 113.2 (CH), 118.5 (CH), 124.1 (CH), 127.5 (CH), 128.9 (CH), 131.2 (Ar-qC), 146.3 (Ar-qC), 152.7 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{18}H_{26}O_5$ 322.1775, found 322.1784.

Compound 1e

Eluent for column chromatography: EtOAc/Hexane (1/2, v/v); $[\alpha]_D^{28}$ + 15.7 (c 0.75, $CHCl_3$); R_f = 0.40 (1/2, EtOAc/Hexane); IR (neat, cm–1): 3395, 2930, 2368, 1462, 1220; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (t, J = 7.4 Hz, 3H), 1.61-1.66 (m, 2H), 3.04 (m, 2H, 2 OH), 3.71-3.76 (m, 1H), 3.84 (brm, 11H), 4.25-4.29 (m, 1H), 6.09 (dd, J = 7.2, 15.9 Hz, 1H), 6.62 (d, J = 8.7 Hz, 1H), 6.85-6.90 (m, 1H), 7.13-7.17 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3 (CH_3), 27.1 (CH_2), 56.4 (CH), 61.2 (CH), 61.5 (CH), 74.9 (CH), 76.1 (CH), 84.4(CH), 85.5 (CH), 108.1(CH), 121.6 (CH), 123.9 (Ar-qC), 127.1 (CH), 127.4 (CH), 142.6 (Ar-qC), 151.9 (Ar-qC), 153.7 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{17}H_{24}O_6$ 324.1567, found 324.1569.

Compound 1f

Eluent for column chromatography: EtOAc/Hexane (1/3, v/v); $[\alpha]_D^{28}$ + 29.0 (c 0.24, $CHCl_3$); R_f = 0.42 (1/3, EtOAc/Hexane); IR (neat, cm–1): 3448, 3022, 2927, 2361, 1568, 1419, 1218; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (t, J = 7.4 Hz, 3H), 1.65-1.73 (m, 2H), 3.03 (brm, 2H, 2 OH), 3.77-3.82 (m, 1H), 3.86-3.93 (m, 2H), 4.35 (t, J = 5.7Hz, 1H), 6.20 (dd, J = 6.5, 15.8 Hz, 1H), 7.07-7.16 (m, 2H), 7.33-7.44 (m,2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3 (CH_3), 27.1 (CH_2), 74.9 (CH), 76.1 (CH), 83.5 (CH), 85.8 (CH), 125.5 (CH), 127.5 (CH), 128.9 (CH), 129.8 (CH), 131.7 (Ar-qC), 131.9 (CH), 133.8 (Ar-qC), 137.3 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{14}H_{16}Cl_2O_3$ 302.0471, found 302.0466.

Compound 1g

Eluent for column chromatography: EtOAc/Hexane (1/2, v/v); $[\alpha]_D^{28}$ + 20.1 (c 0.39, $CHCl_3$); R_f = 0.46 (1/2, EtOAc/Hexane); IR (neat, cm–1): 3387, 2926, 2362, 1579, 1453, 1220; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (t, J = 7.4 Hz, 3H), 1.59-1.69 (m, 2H), 3.13-3.25 (m, 2H, 2 OH), 3.71-

3.77 (m, 1H), 3.81-3.89 (m, 2H), 4.24-4.28 (m, 1H), 5.96 (m, 2H), 6.39 (dd, J = 6.8, 16.0 Hz, 1H), 6.60-6.81 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3 (CH_3), 27.0 (CH_2), 53.8 (solvent peak, DCM), 74.9 (CH), 76.0 (CH), 84.1(CH), 85.6 (CH), 101.2 (CH_2), 108.0 (CH), 119.5 (Ar-qC), 121.4 (CH), 121.9 (CH), 127.2 (CH), 130.7 (CH), 145.2 (Ar-qC), 147.9 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{15}H_{18}O_5$ 278.1149, found 278.1149.

Compound 1h

Eluent for column chromatography: EtOAc/Hexane (1/3, v/v); $[\alpha]_D^{28}$ + 20.6 (c 0.80, $CHCl_3$); R_f = 0.50 (1/4, EtOAc/Hexane); IR (neat, cm–1): 3407, 2362, 1646, 1458, 1218; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (t, J = 7.4 Hz, 3H), 1.67-1.72 (m, 2H), 3.29 (brm, 2H, 2 OH), 3.82-3.99 (m, 3H), 4.46 (t, J = 6.3Hz, 1H), 6.25 (dd, J = 6.8, 15.6 Hz, 1H), 7.40-7.53 (m, 4H), 7.60-7.63 (m,1H), 7.78-7.87 (m, 2H), 8.11-8.14 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3 (CH_3), 27.1 (CH_2), 75.0 (CH), 76.2 (CH), 84.1 (CH), 85.6 (CH), 124.0 (CH), 124.3 (CH), 125.9 (CH), 126.1 (CH), 126.5 (CH), 128.5 (CH), 128.9 (CH), 130.0 (CH), 130.9 (CH), 131.5 (Ar-qC), 134.0 (Ar-qC), 134.4 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{18}H_{20}O_3$ 284.1407, found 284.1419.

Compound 1i

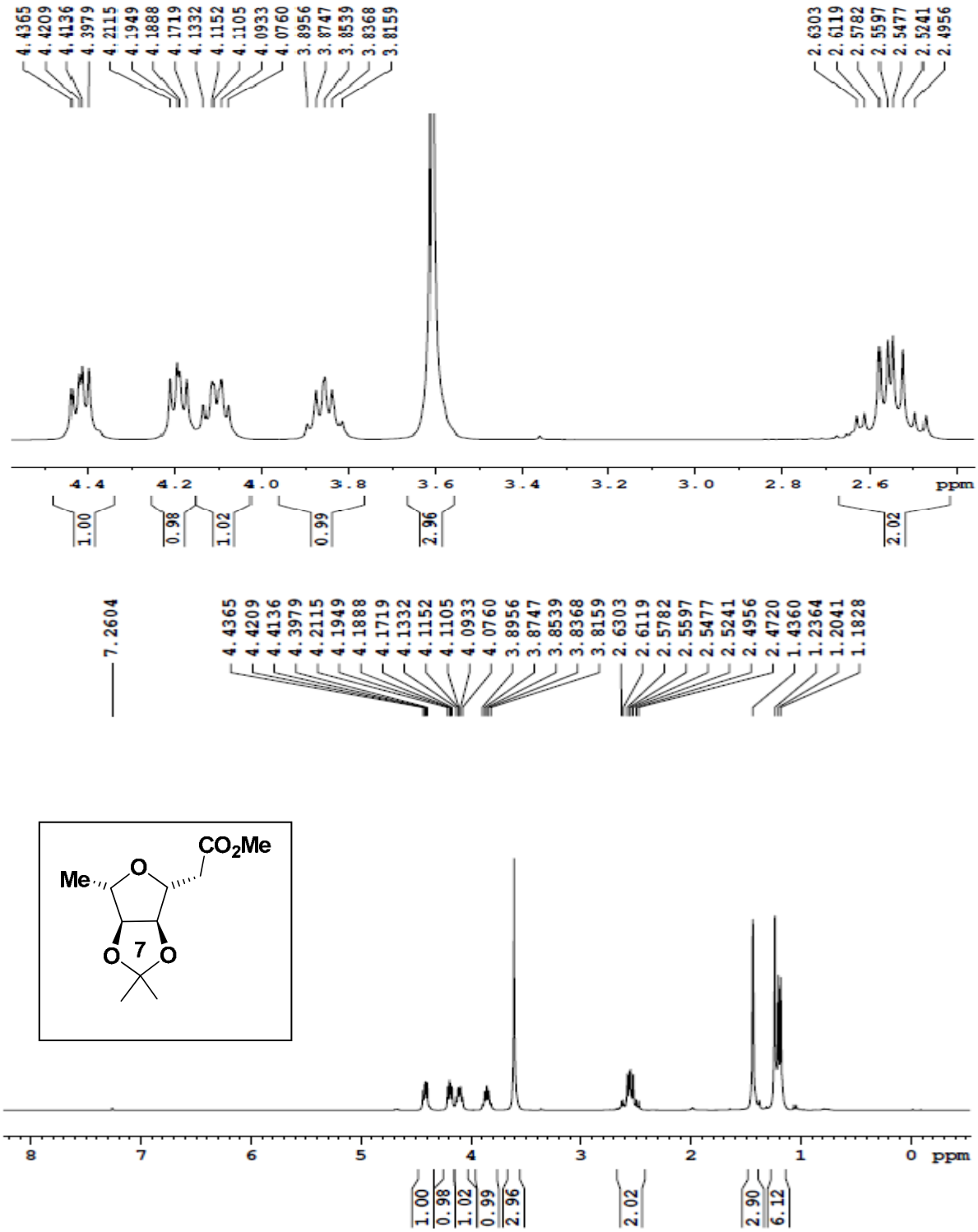
Eluent for column chromatography: EtOAc/Hexane (1/2, v/v); $[\alpha]_D^{28}$ + 13.7 (c 0.79, $CHCl_3$); R_f = 0.34 (1/3, EtOAc/Hexane); IR (neat, cm^{-1}): 3415, 3020, 2929, 2365, 1470, 1217; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (t, J = 7.4 Hz, 3H), 1.59-1.70 (m, 2H), 3.06-3.21 (brm, 2H, 2OH), 3.74-3.88 (m, 9H), 4.28-4.32 (m, 1H), 6.19 (dd, J = 7.0, 16.1 Hz, 1H), 6.79-6.82 (m, 1H), 6.97-7.10 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2 (CH_3), 27.1 (CH_2), 56.1 (CH), 61.3 (CH), 74.9 (CH), 76.0 (CH), 84.3 (CH), 85.6 (CH), 112.0 (CH), 118.7 (CH), 124.4 (CH), 127.2 (CH), 129.3

(CH), 130.9 (Ar-qC), 147.0 (Ar-qC), 153.0 (Ar-qC); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{16}H_{22}O_5$ 294.1462, found 294.1470.

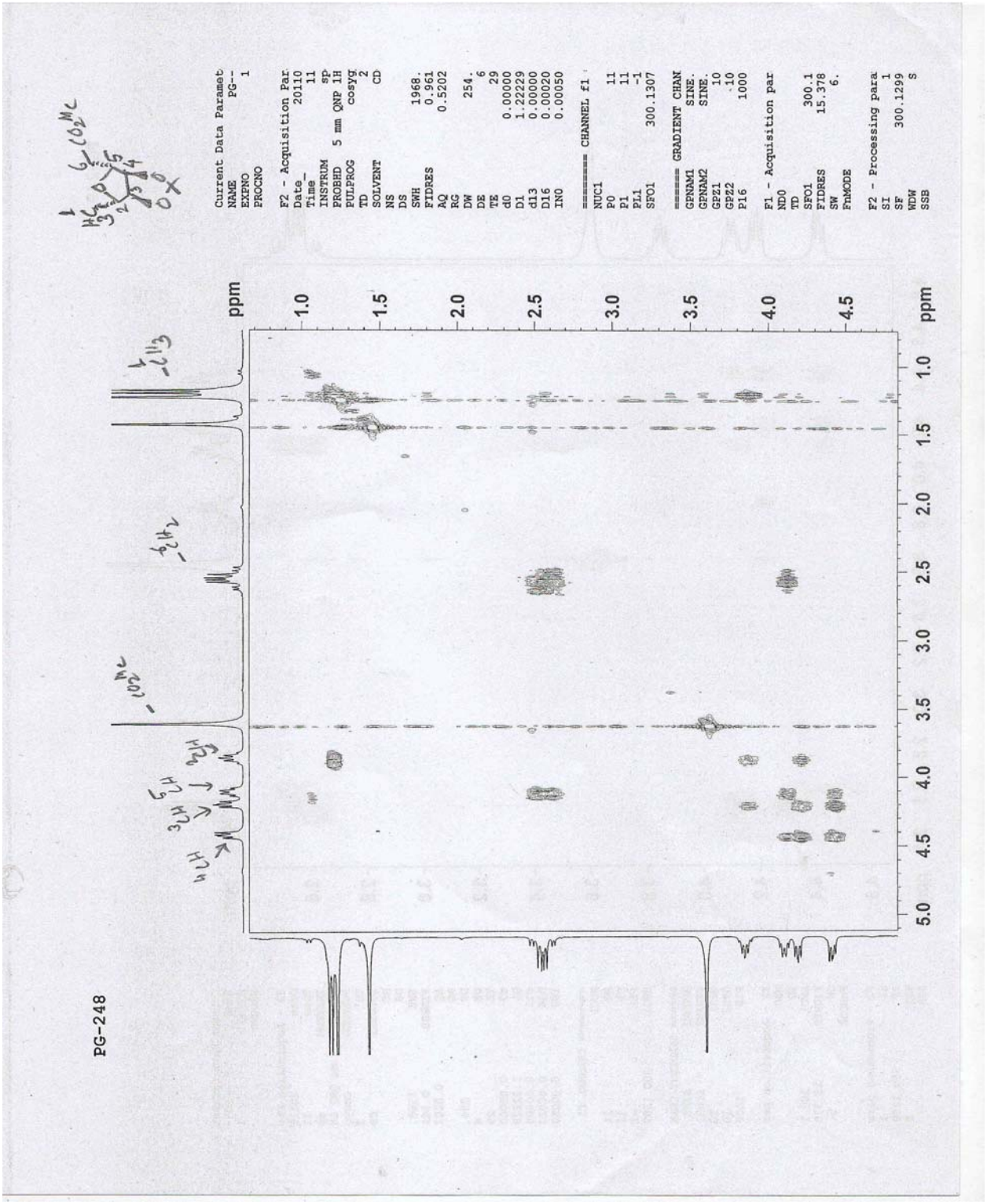
Compound 1j

Eluent for column chromatography: EtOAc/Hexane (1/3, v/v); $[\alpha]_D^{28}$ + 8.7 (*c* 0.39, $CHCl_3$); R_f= 0.46 (1/3, EtOAc/Hexane); IR (neat, cm^{-1}): 3399, 2924, 2363, 1644, 1219; ^1H NMR (300 MHz, $CDCl_3$) δ 0.85-0.90 (m, 3H), 1.00 (t, *J* = 7.4 Hz, 3H), 1.25-1.38 (m, 22H), 1.58-1.67 (m, 2H), 2.01-2.08 (m, 2H), 2.74 (brm, 2H, 2OH), 3.67 (dd, *J* = 6.1, 10.7 Hz, 1H), 3.74-3.80 (m, 2H), 4.02-4.07 (m, 1H), 5.44 (dd, *J* = 7.4, 15.3 Hz, 1H), 5.77-5.85 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3 (CH_3), 14.5 (CH_3), 23.1 (CH_2), 27.1 (CH_2), 29.4 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 29.9 (CH_2), 30.0 (CH_2), 30.1 (4 × CH_2), 32.3 (CH_2), 32.8 (CH_2), 74.9 (CH), 75.9 (CH), 84.2 (CH), 85.5 (CH), 128.0 (CH), 136.0 (CH); ESI–HRMS: m/z $[M]^+$ Calcd for $C_{21}H_{40}O_3$ 340.2972, found 340.2984.

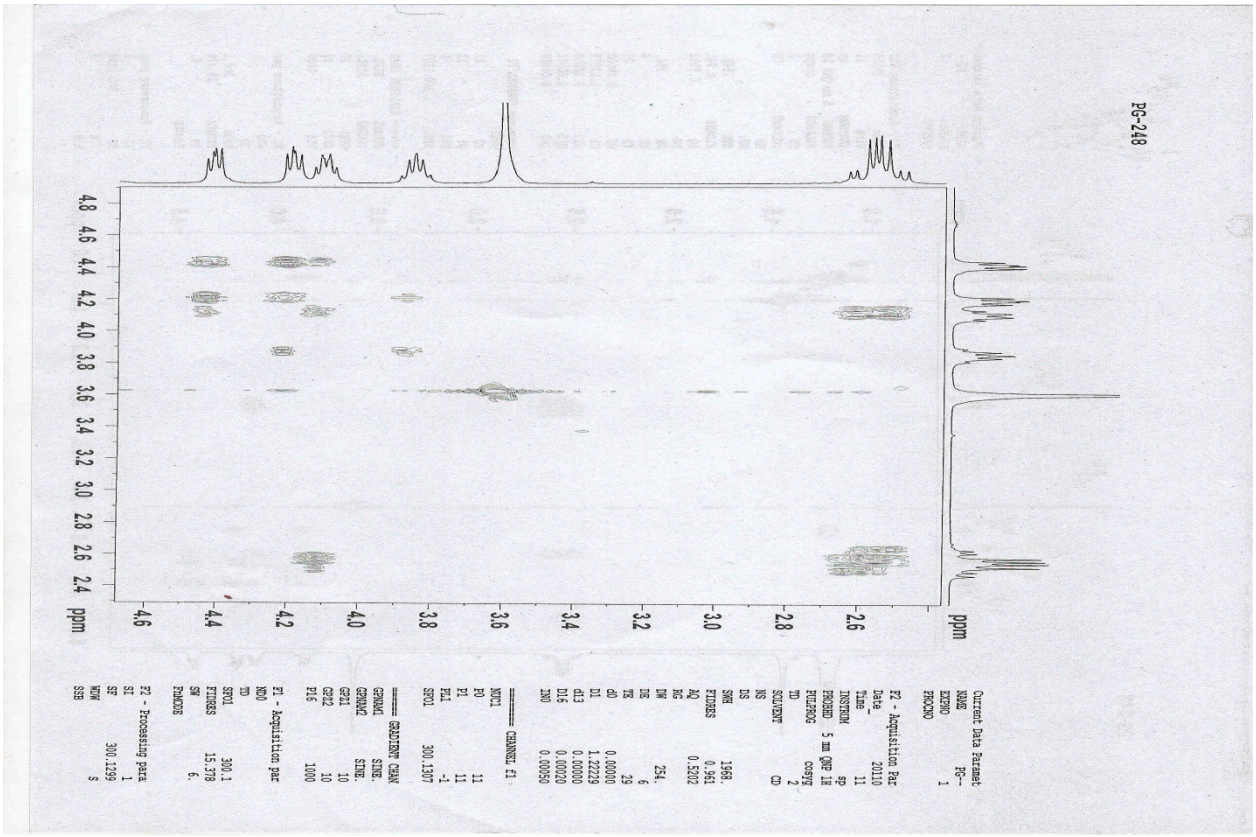
NMR spectra of the synthesized compounds



^{1}H spectrum of compound 7



^{1}H-^{1}H COSY spectrum of compound 7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4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6
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NUC1
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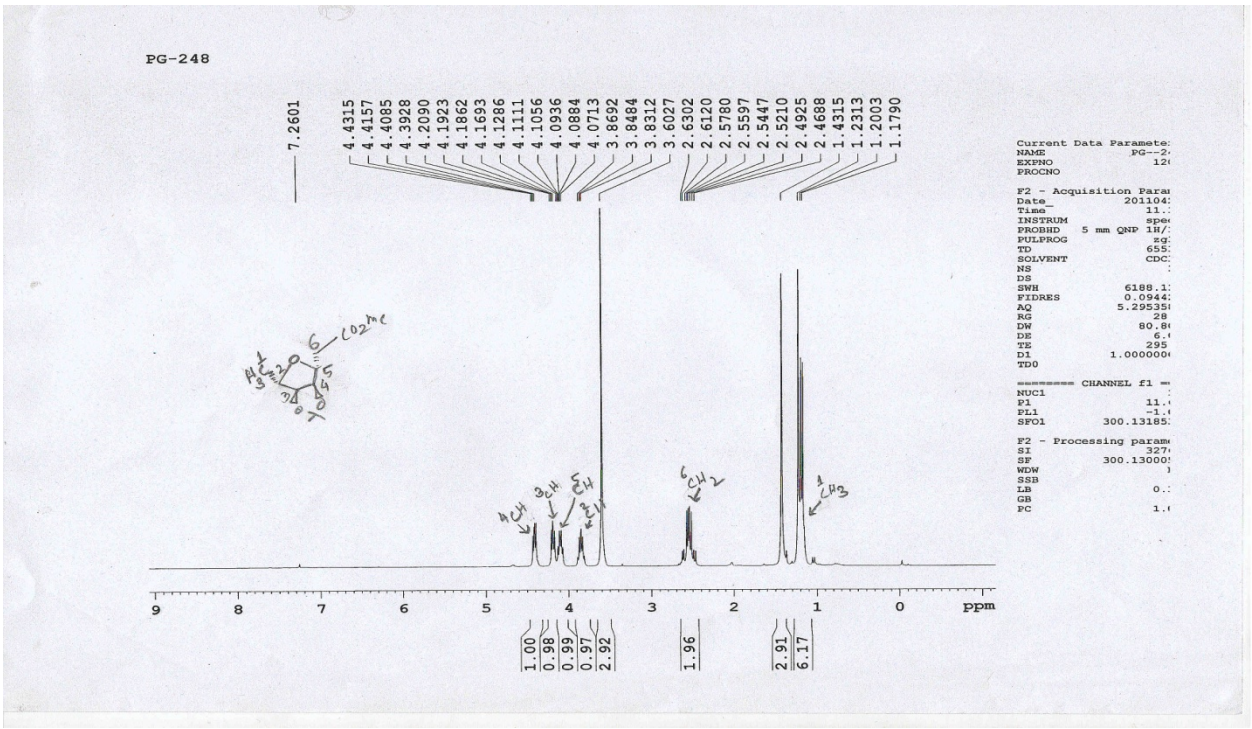
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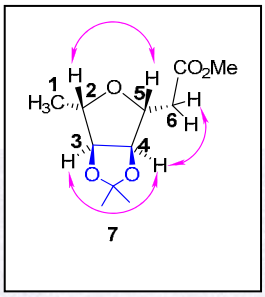
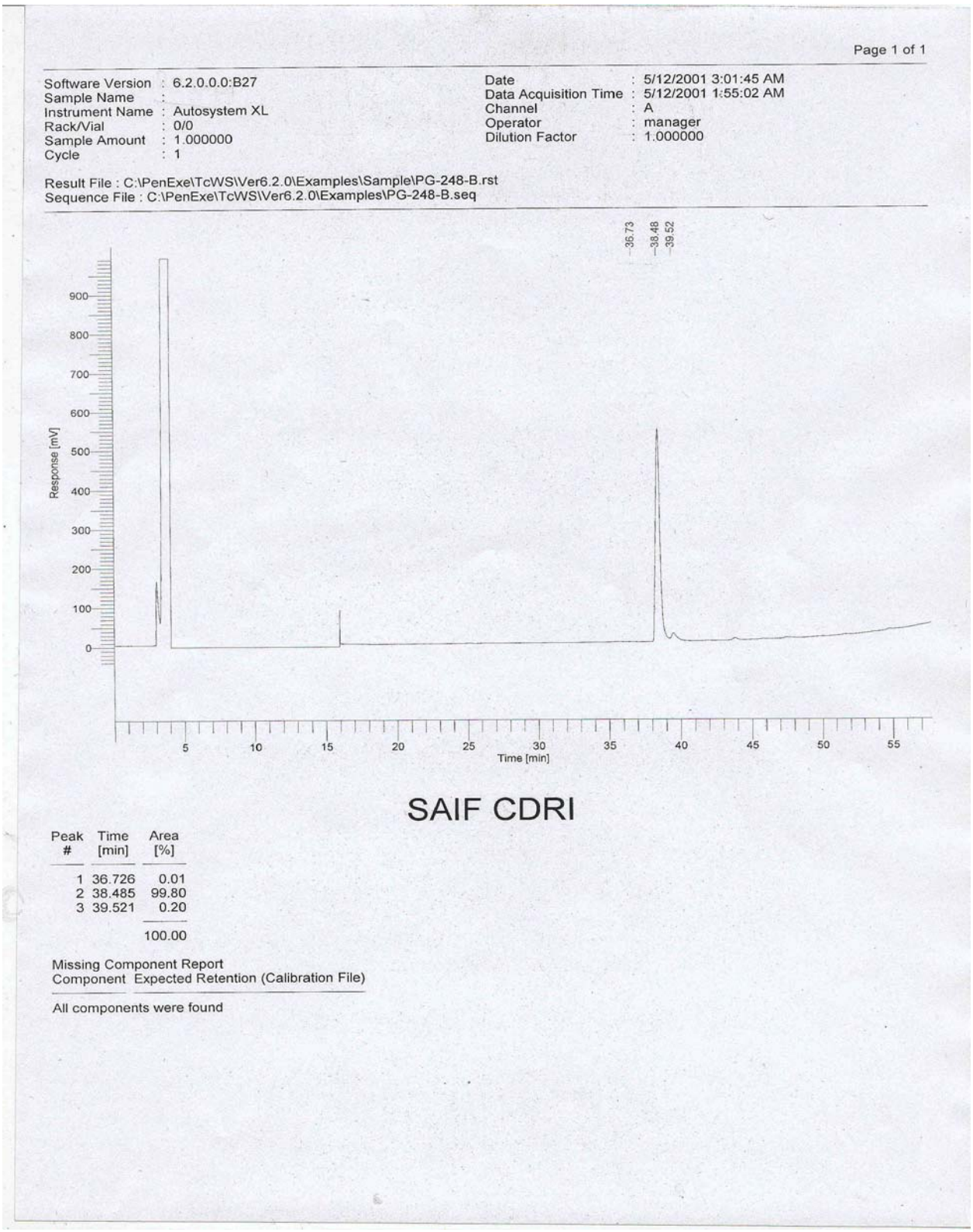


NOE spectrum of compound 7



Page 1 of 1

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Cycle	: 1		

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SAIF CDRI

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Missing Component Report
Component Expected Retention (Calibration File)

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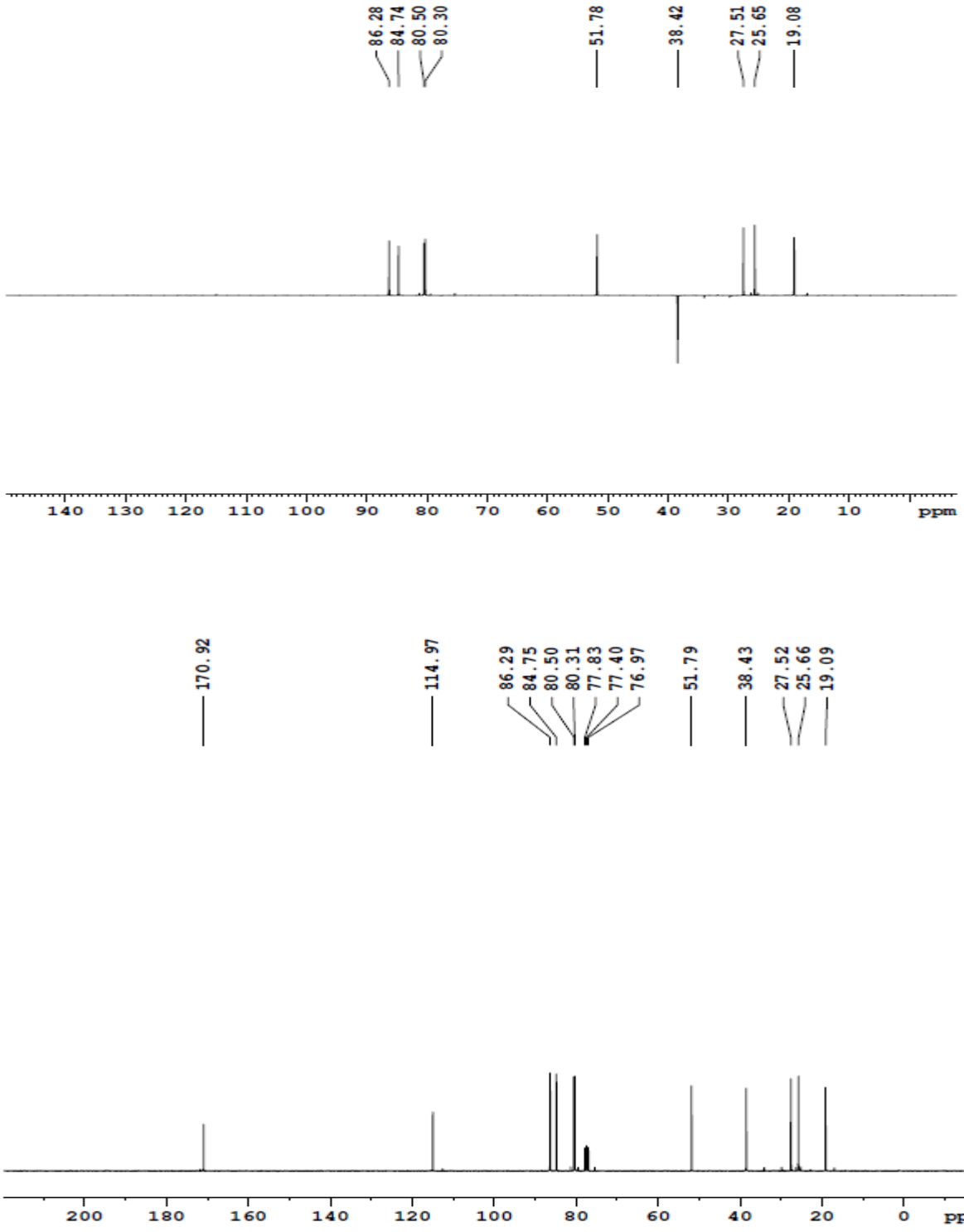
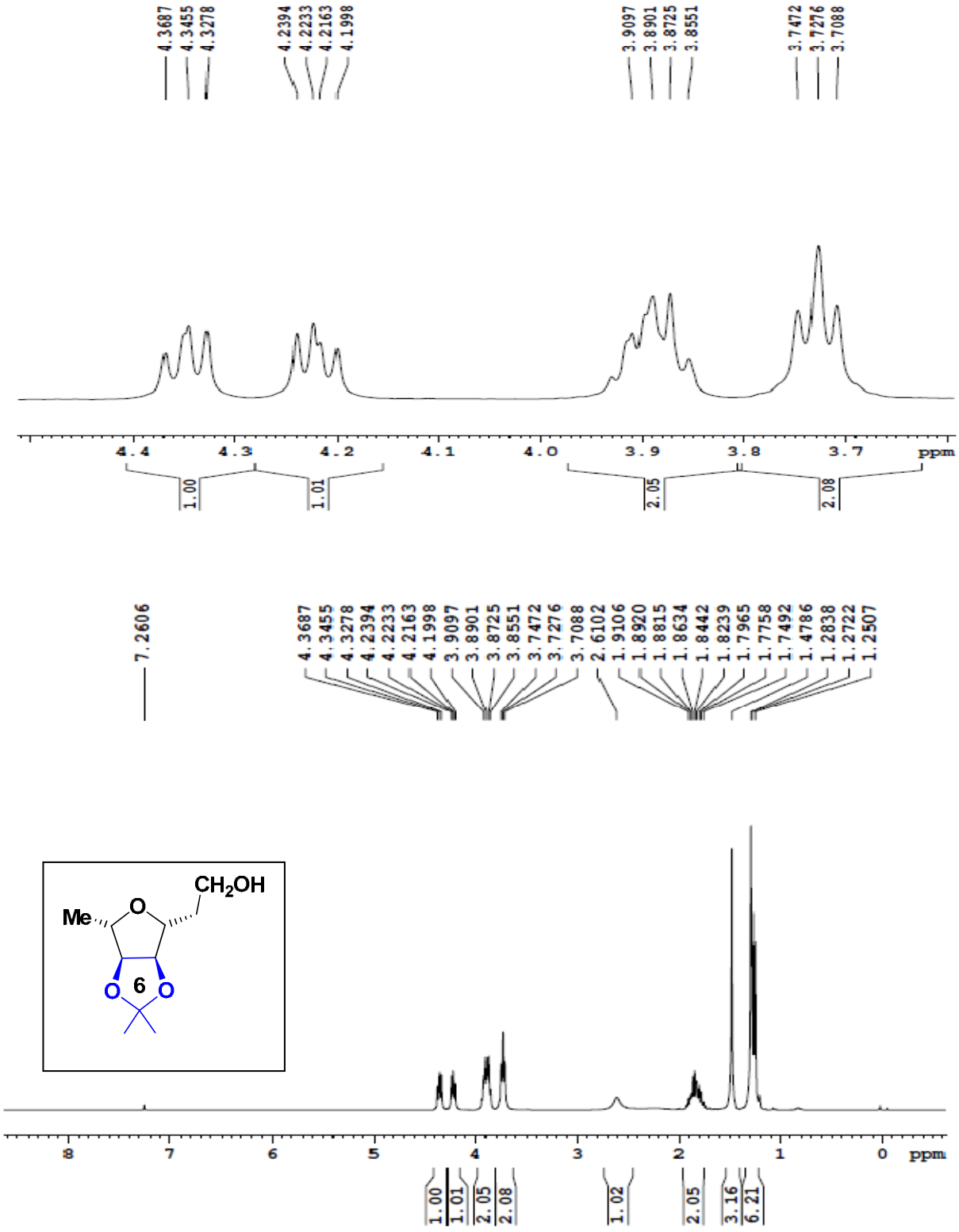
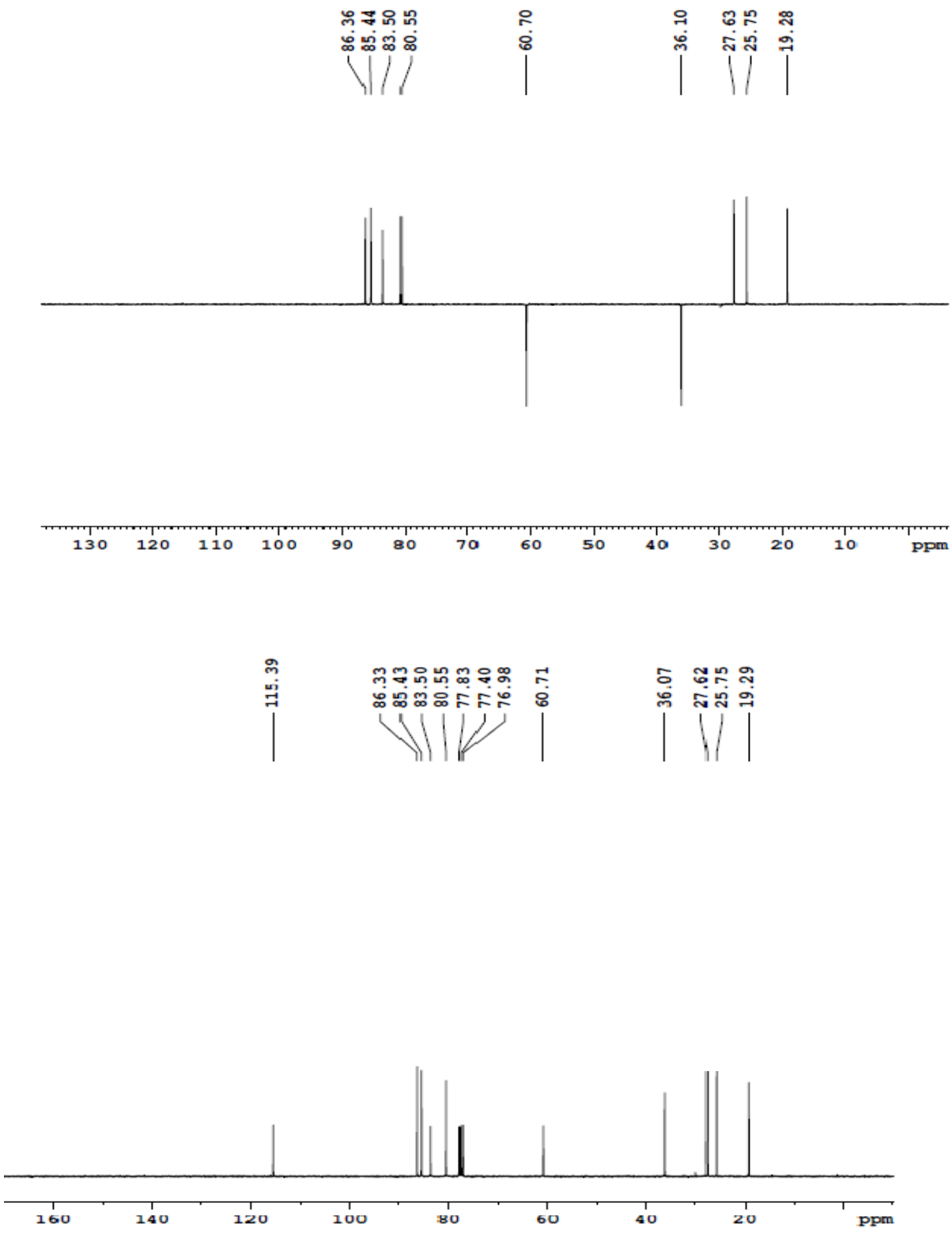
GC analysis for compound 7



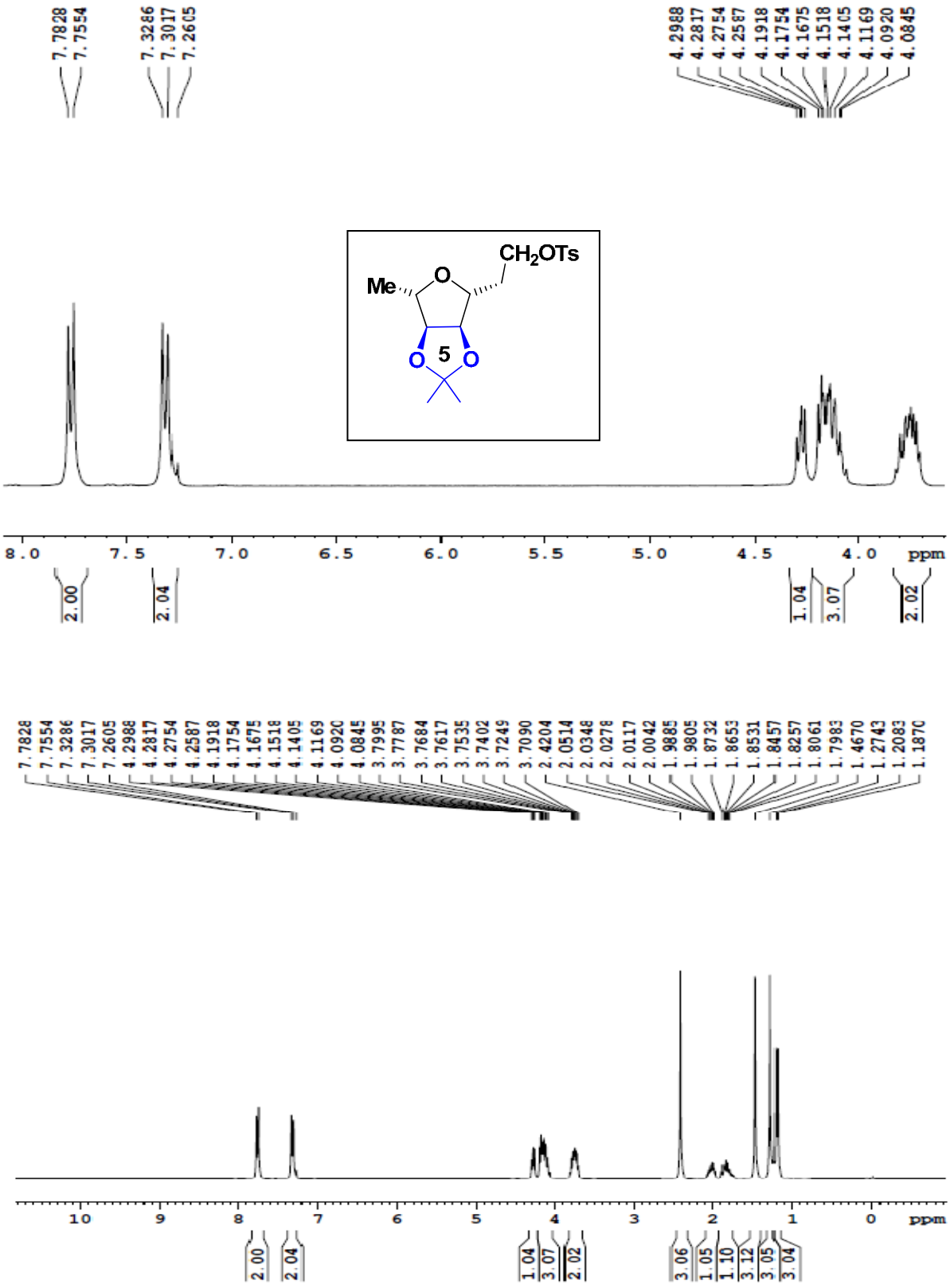
^{13}C spectrum of compound 7



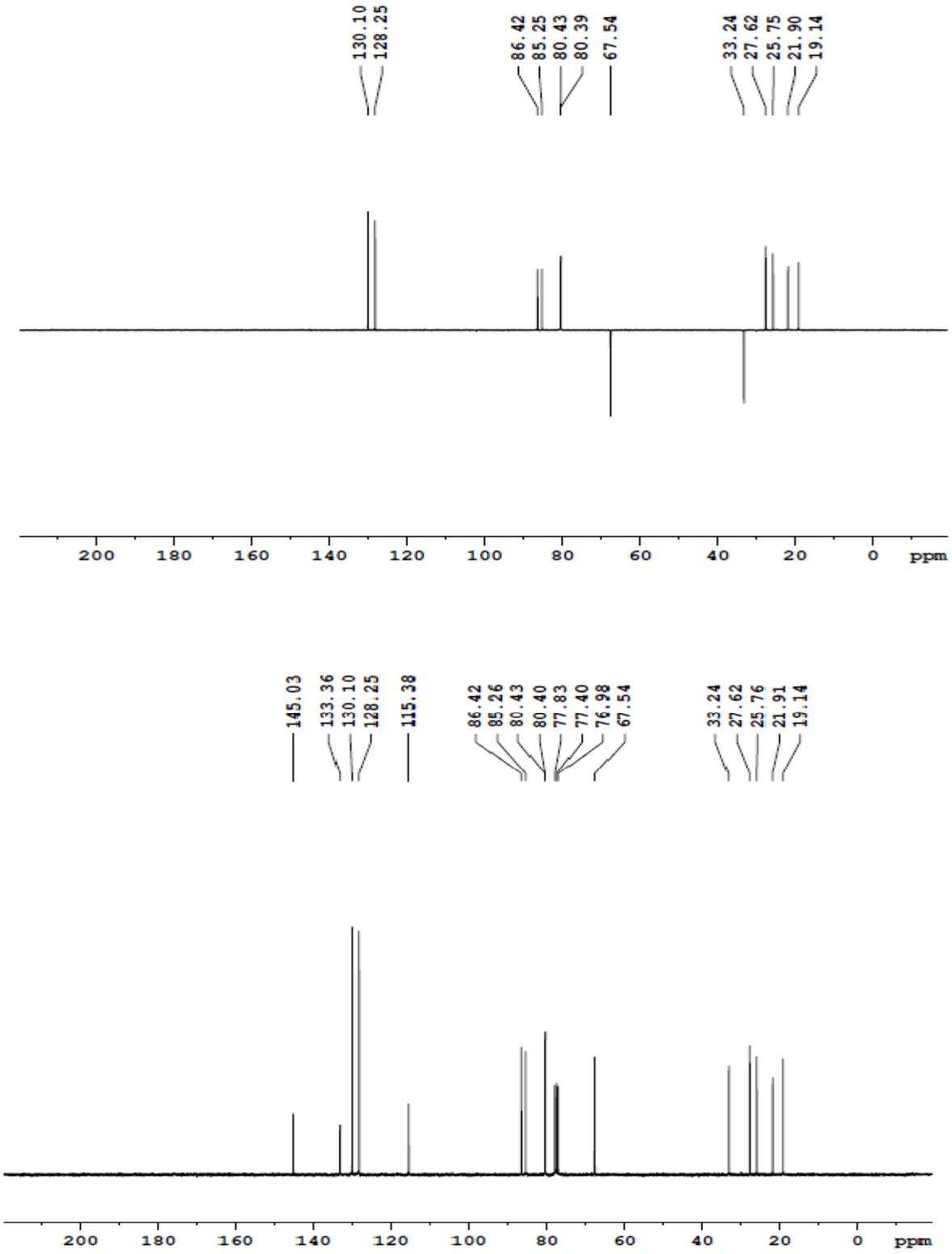
^{1}H spectrum of compound 6



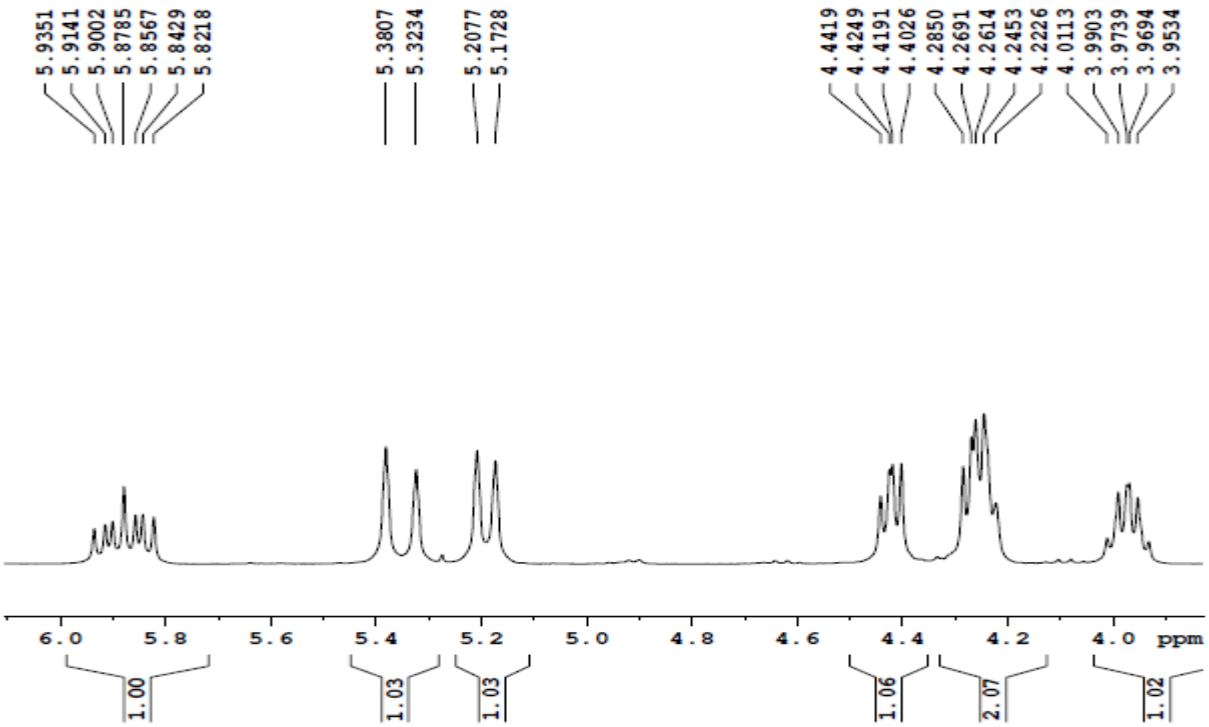
^{13}C spectrum of compound 6

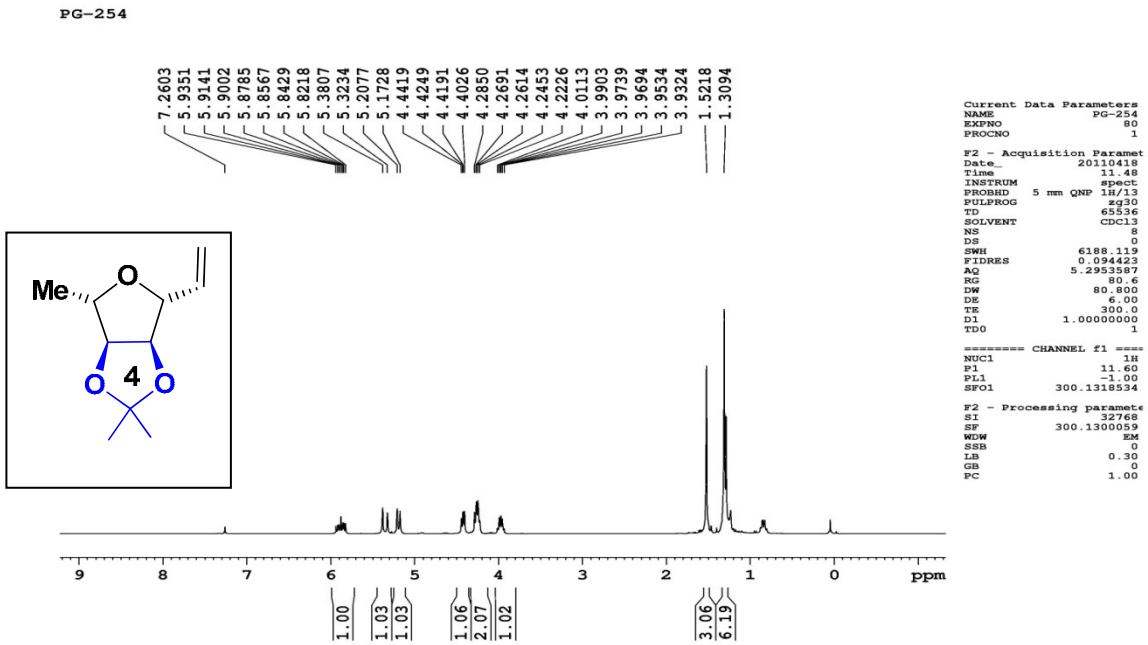


^{1}H spectrum of compound 5

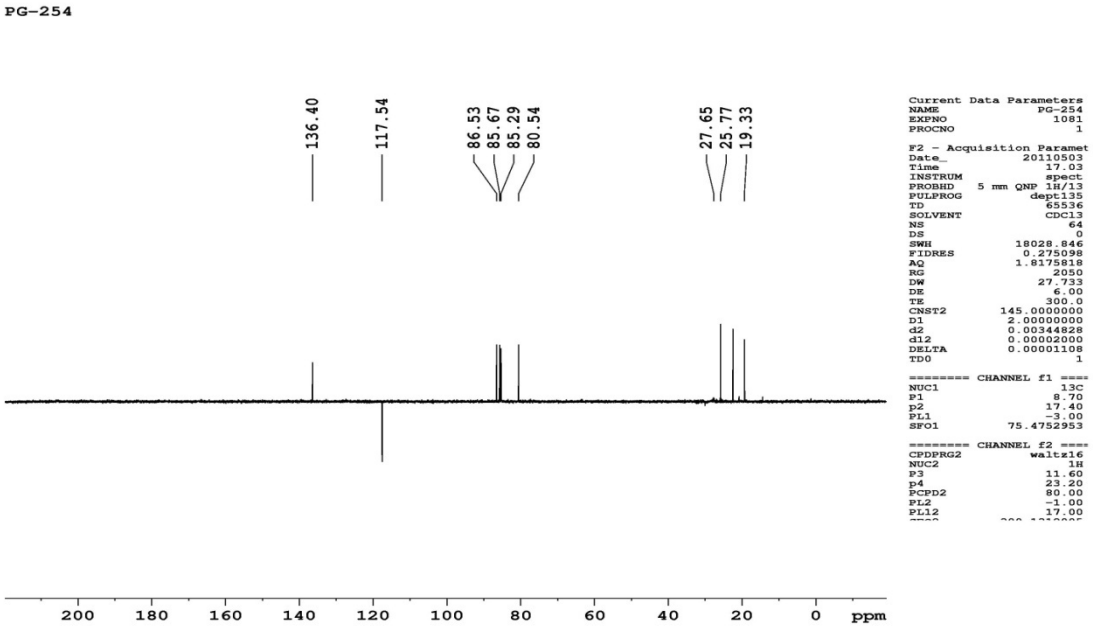


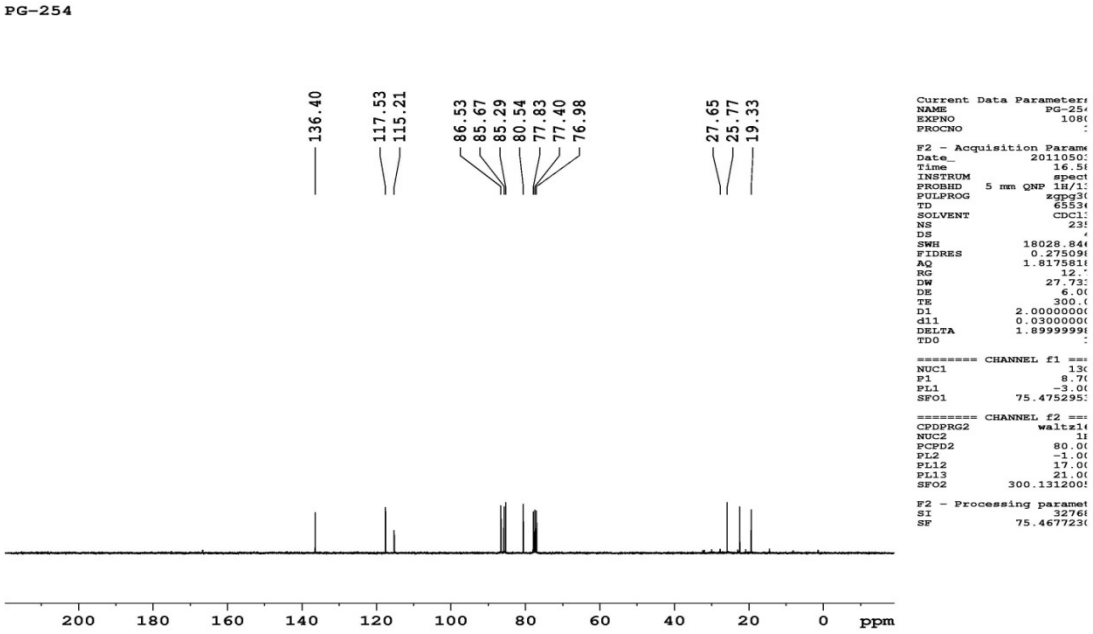
^{13}C spectrum of compound 5



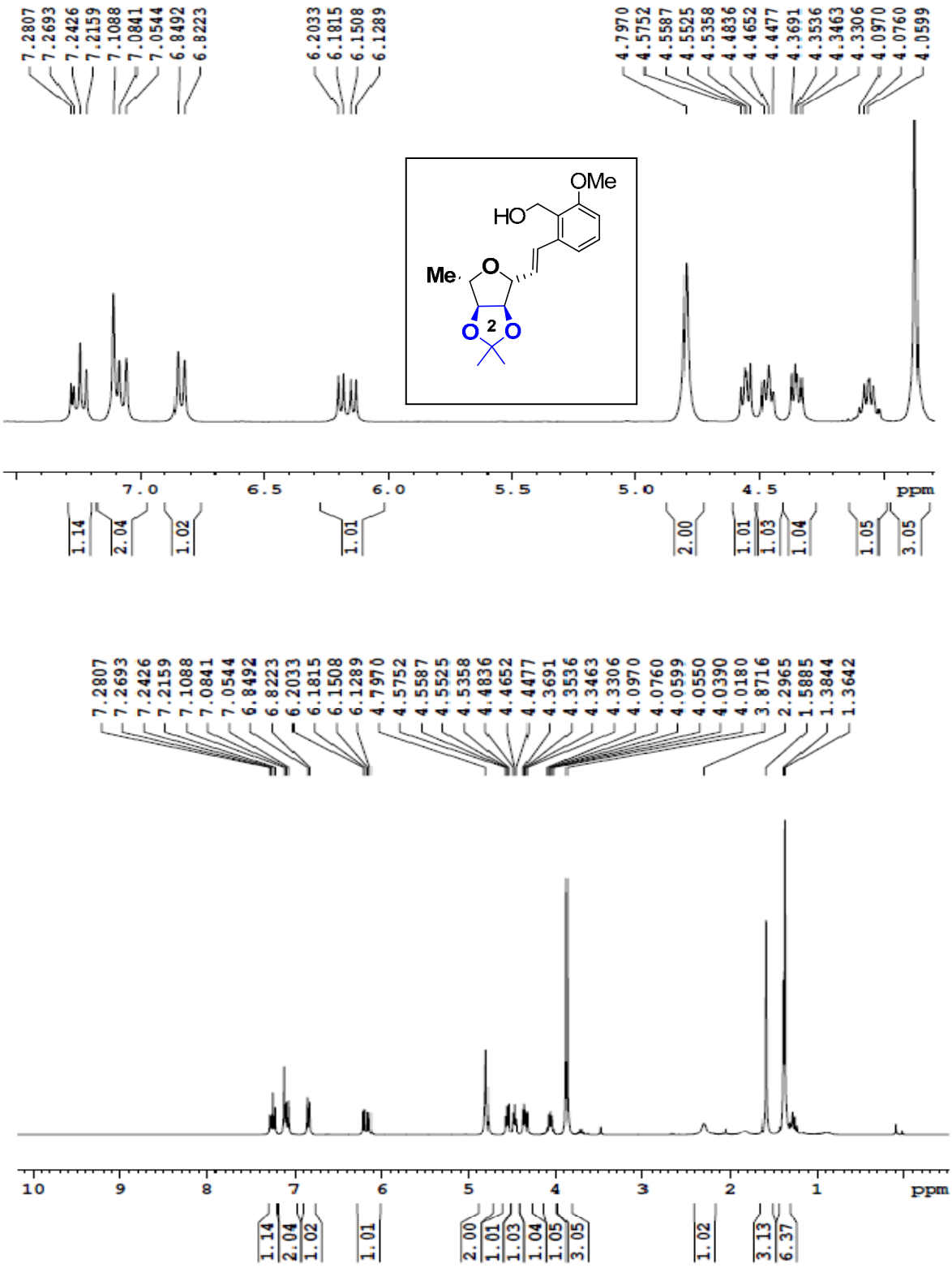


^{1}H spectrum of compound 4

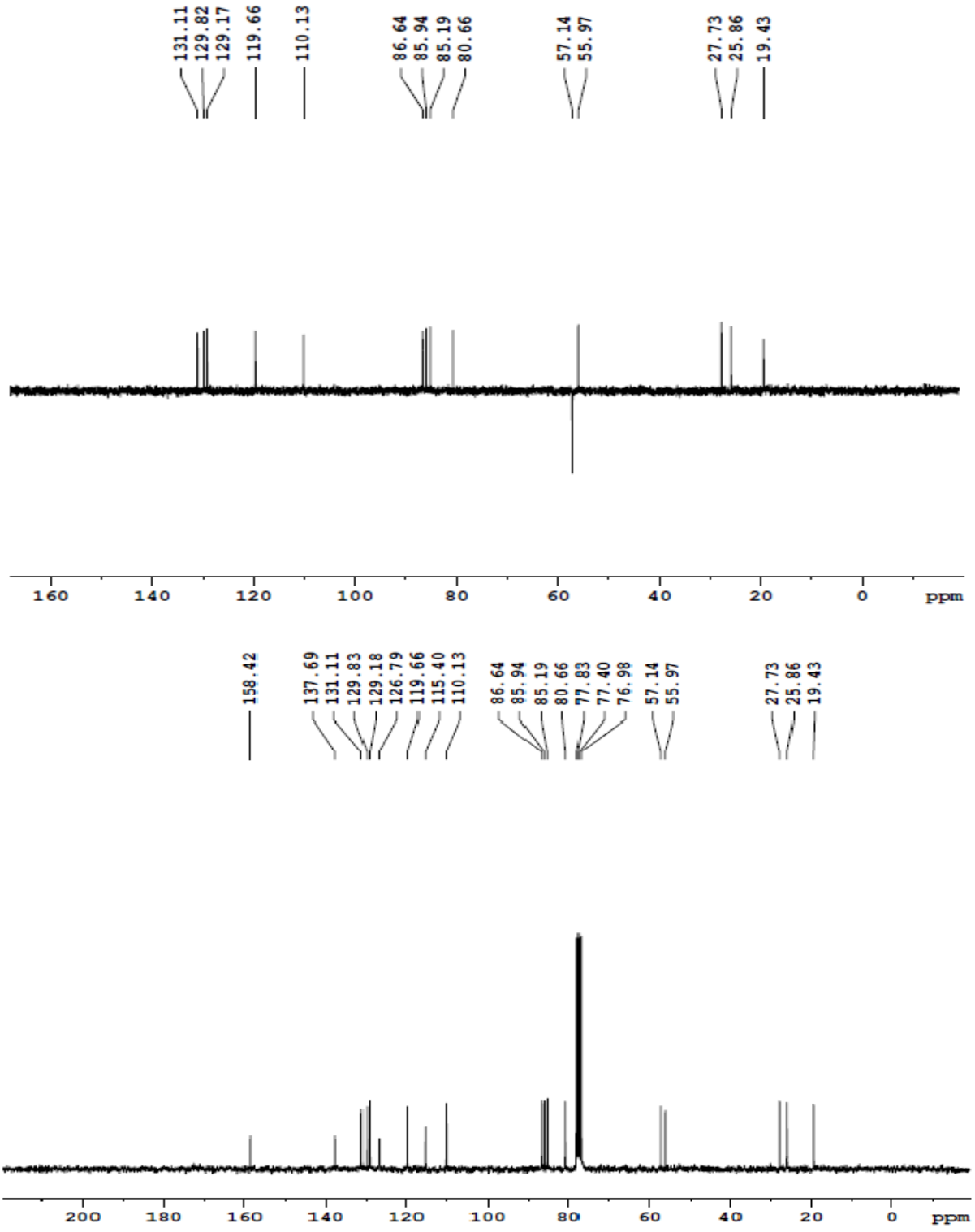




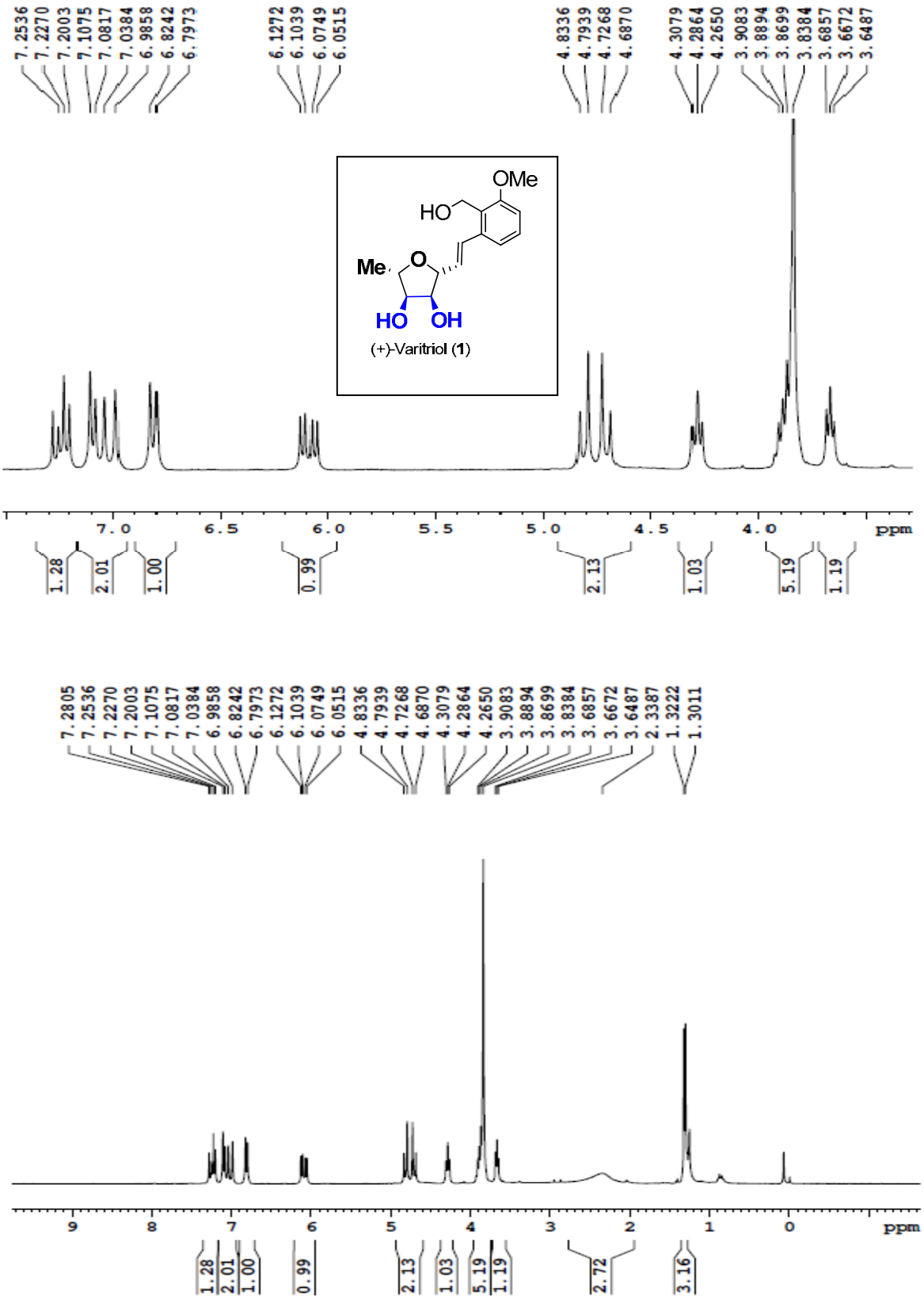
^{13}C spectrum of compound 4



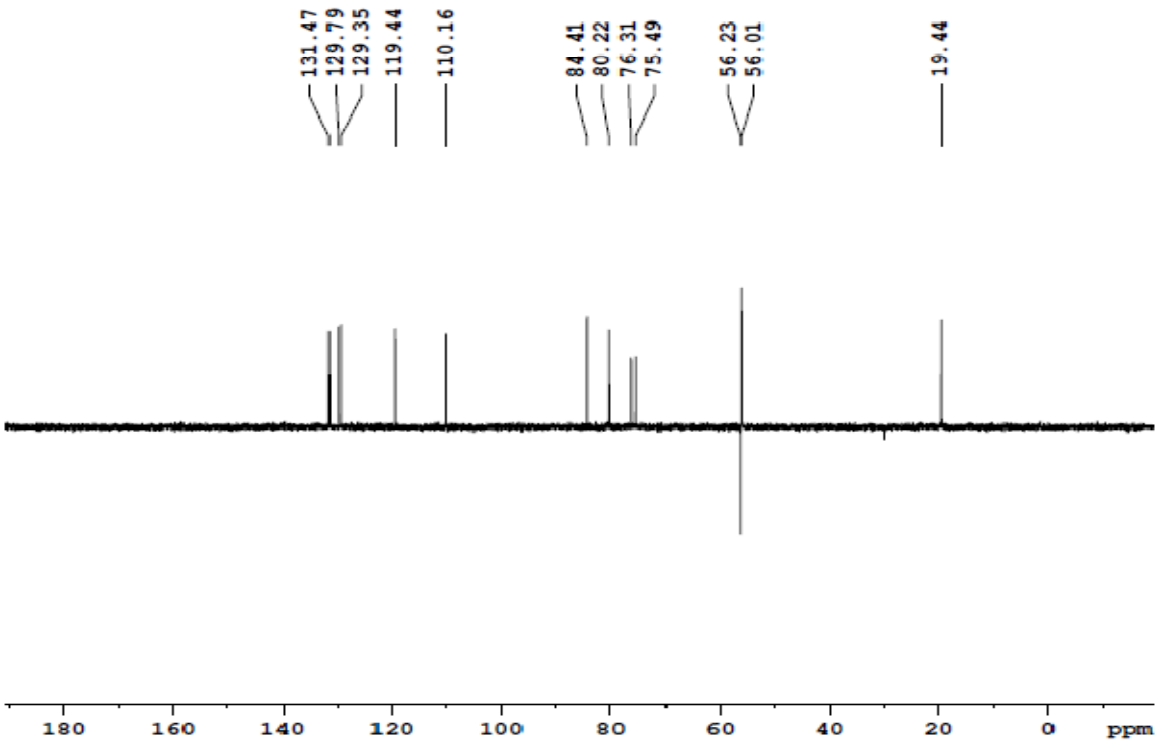
^{1}H spectrum of compound 2

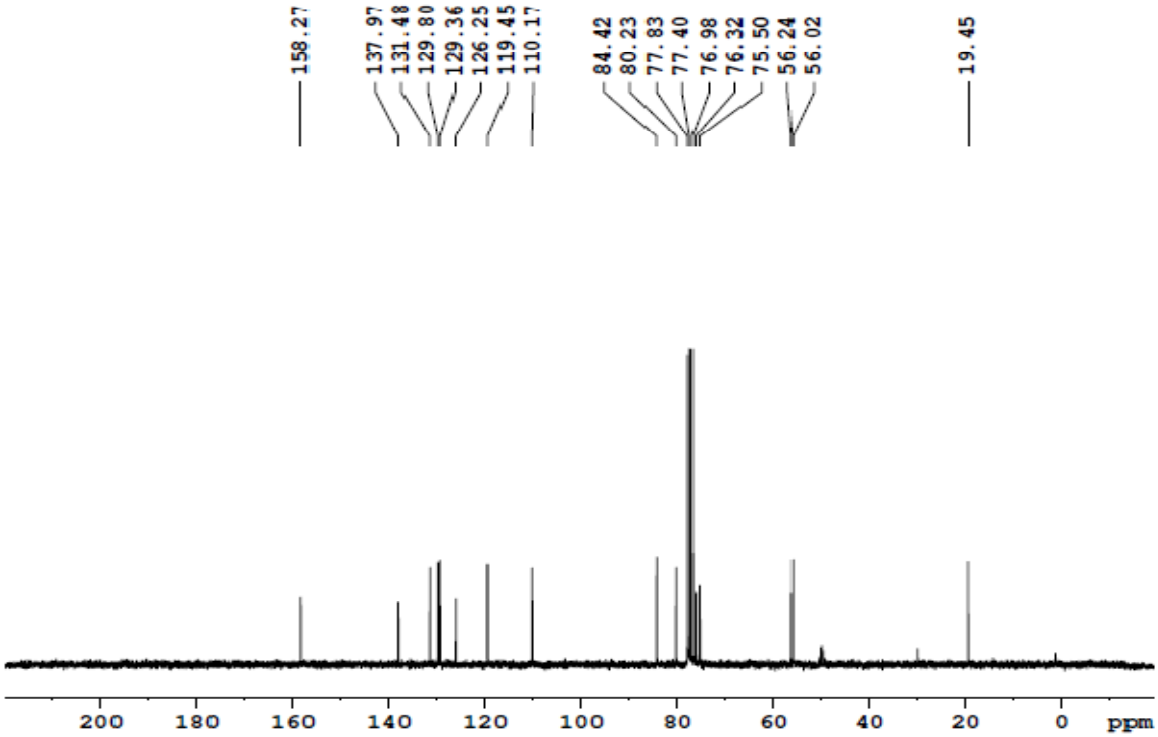


^{13}C spectrum of compound 2

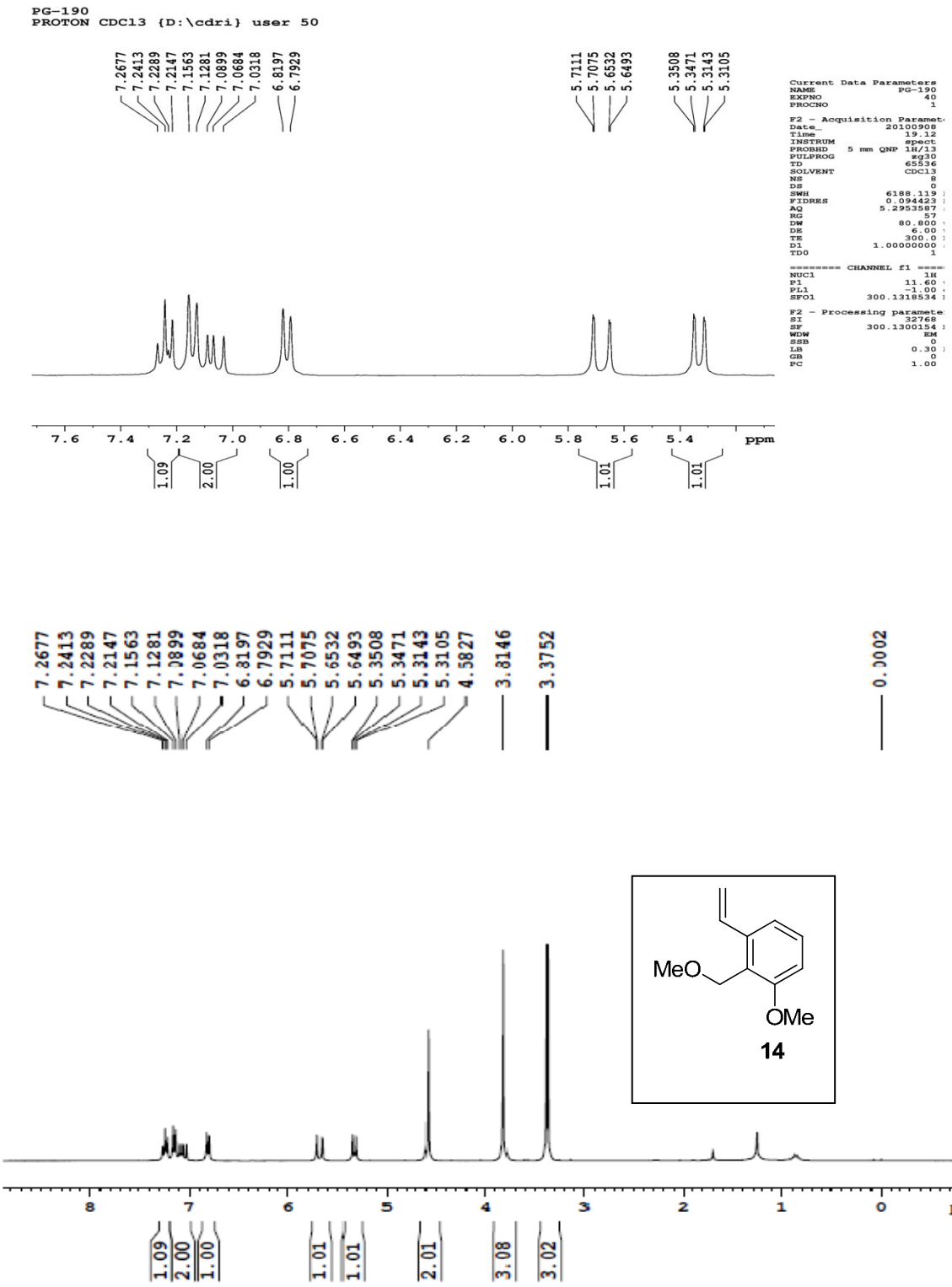


^{1}H spectrum of (+)-varitriol (1)

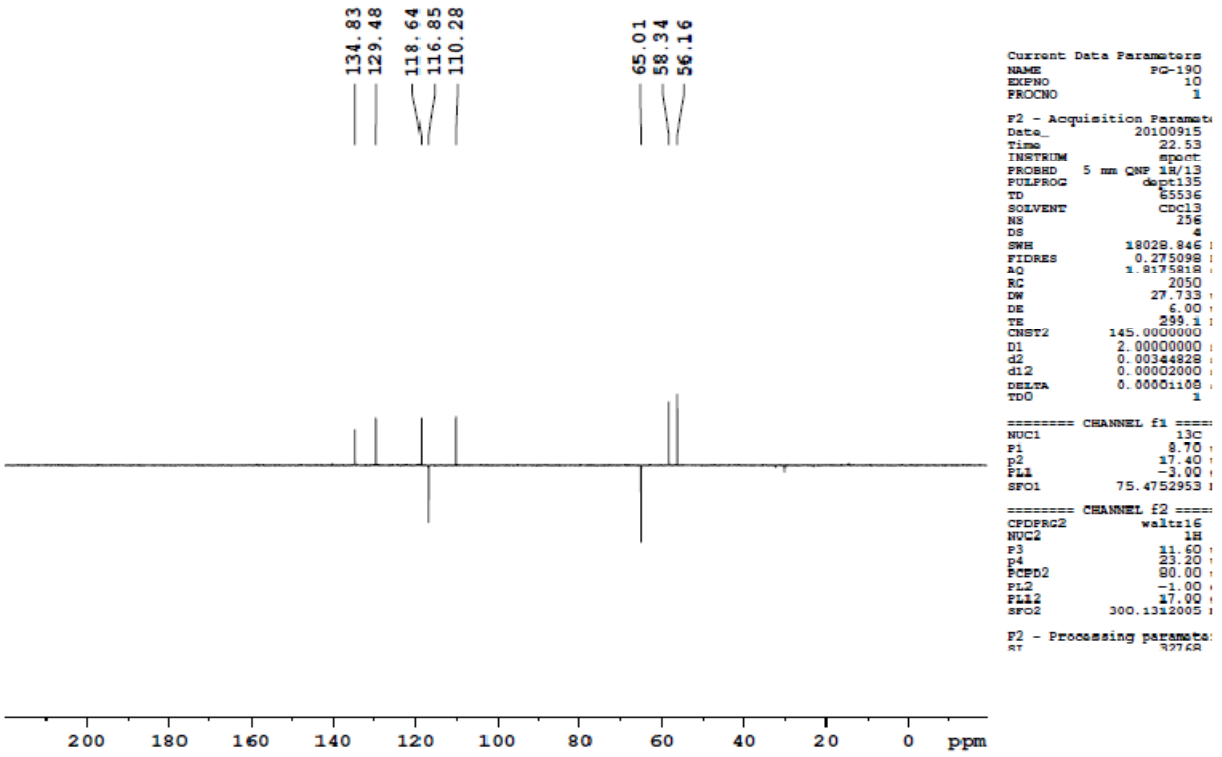


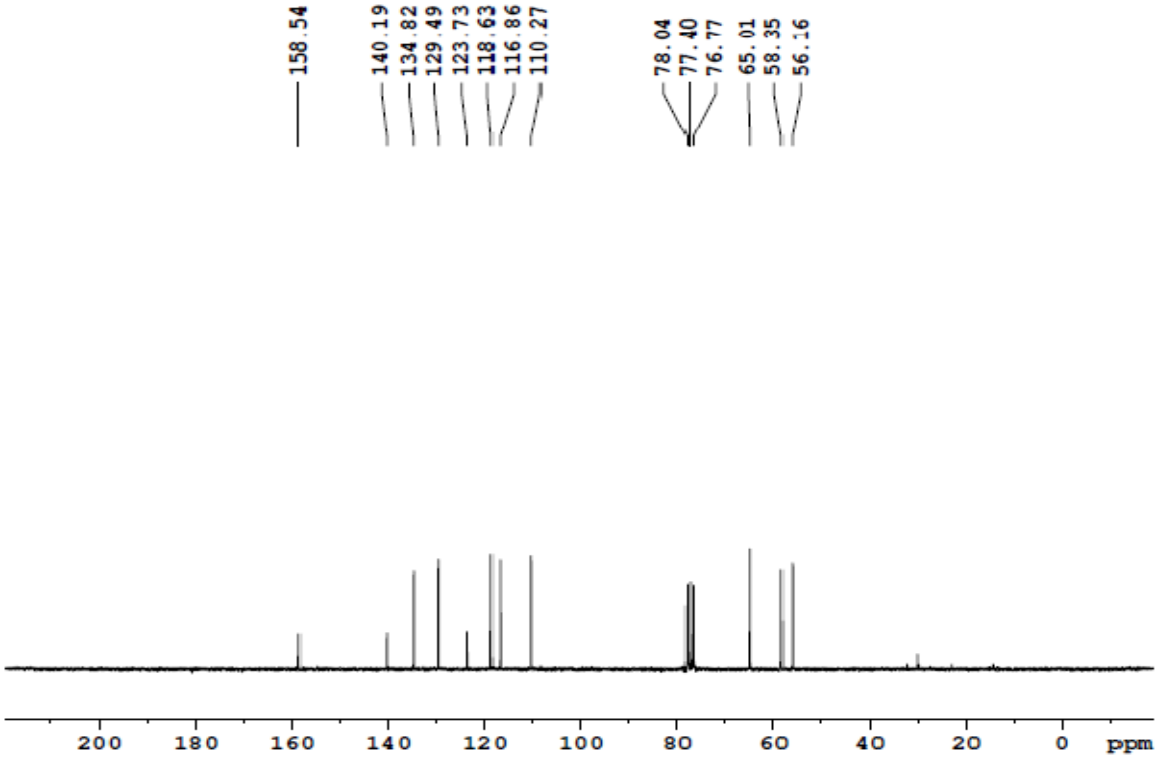


^{13}C spectrum of (+)-varitriol (1)

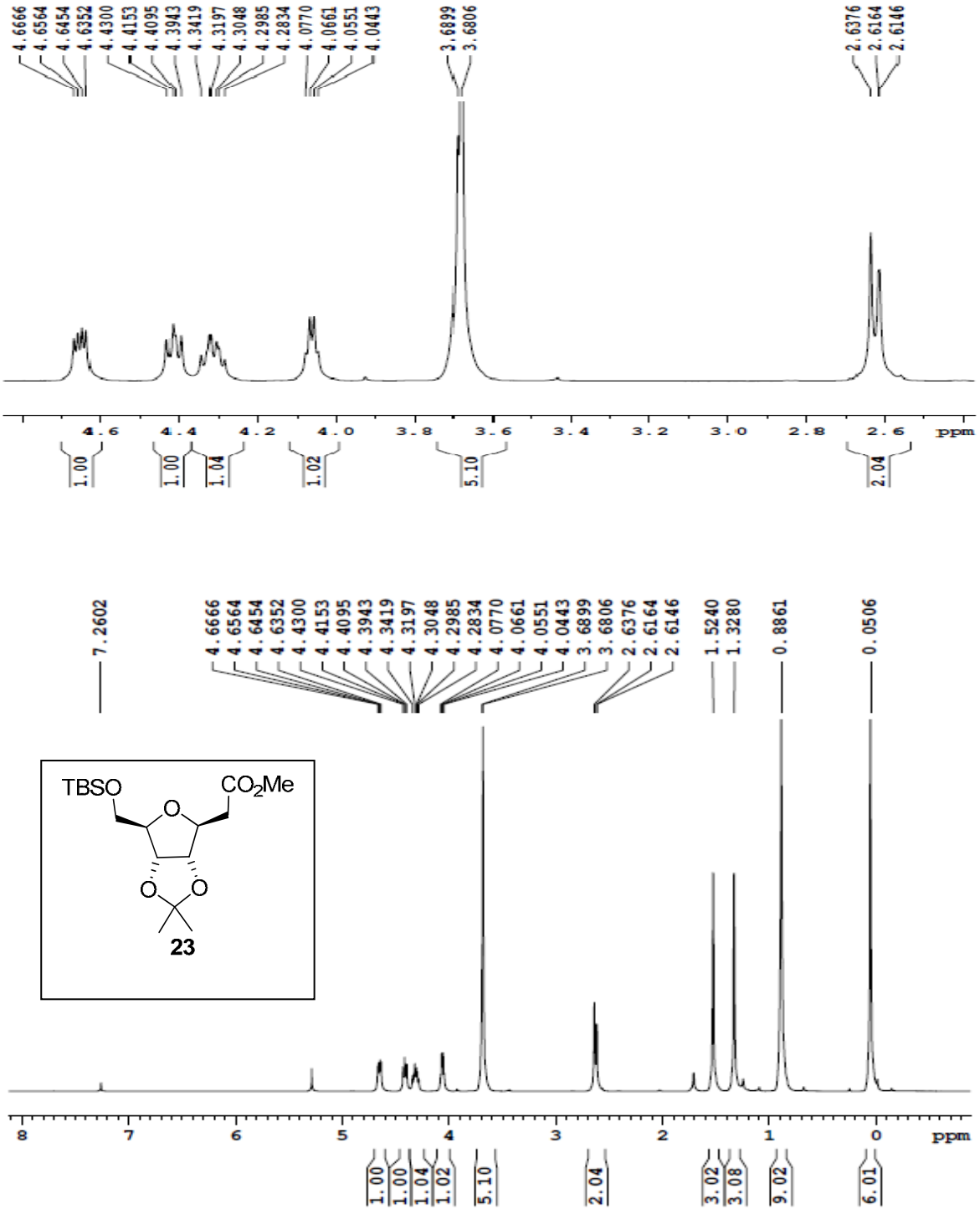


^{1}H spectrum of compound 14

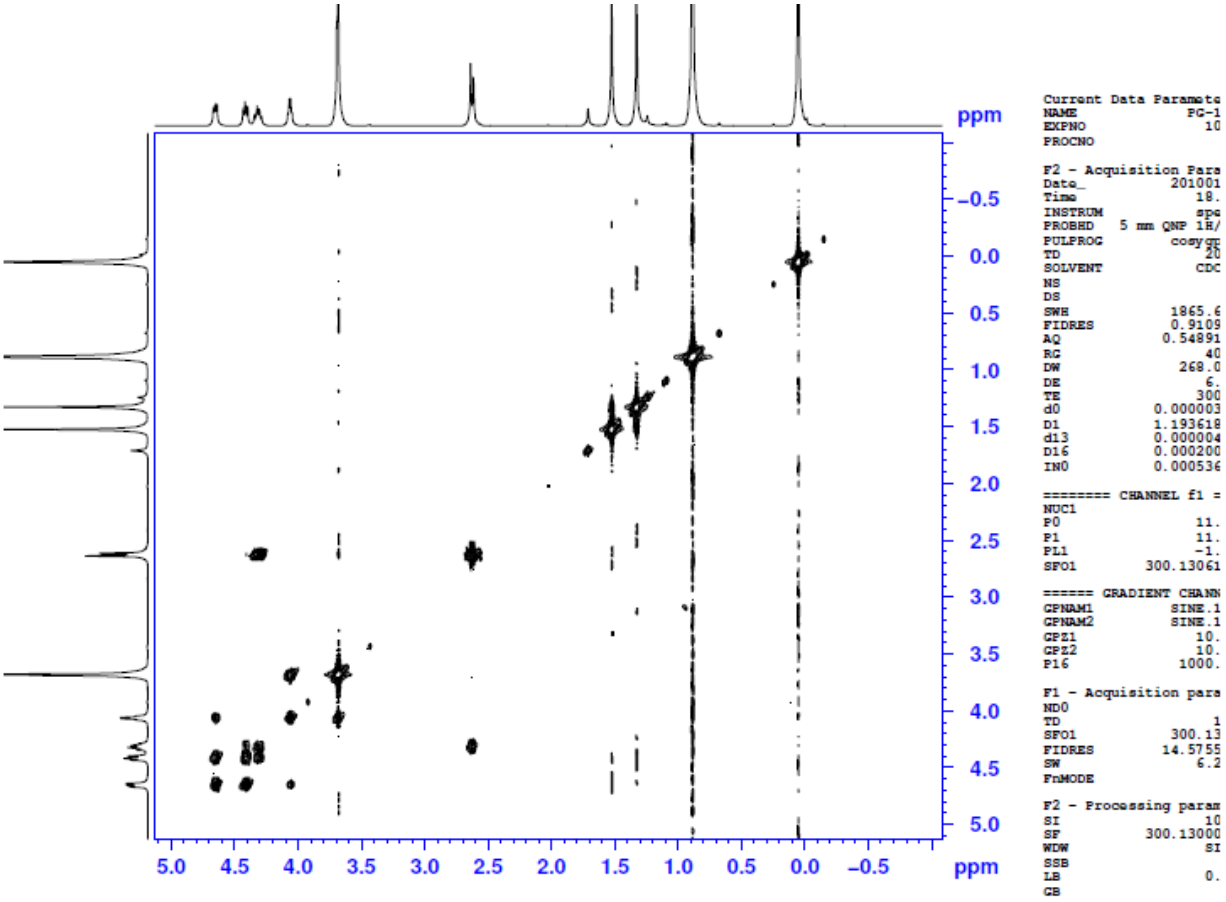




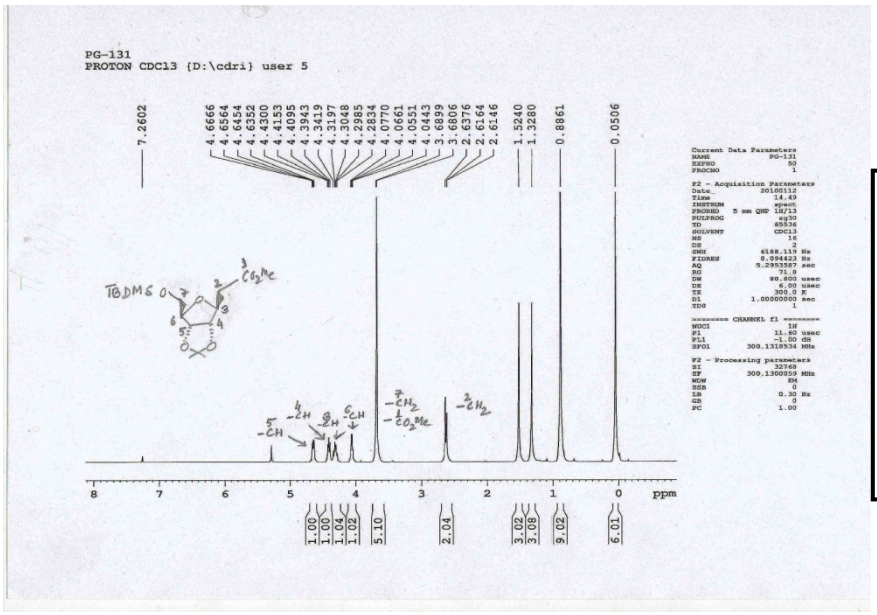
^{13}C spectrum of compound 14

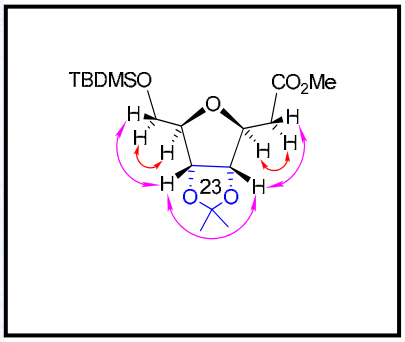


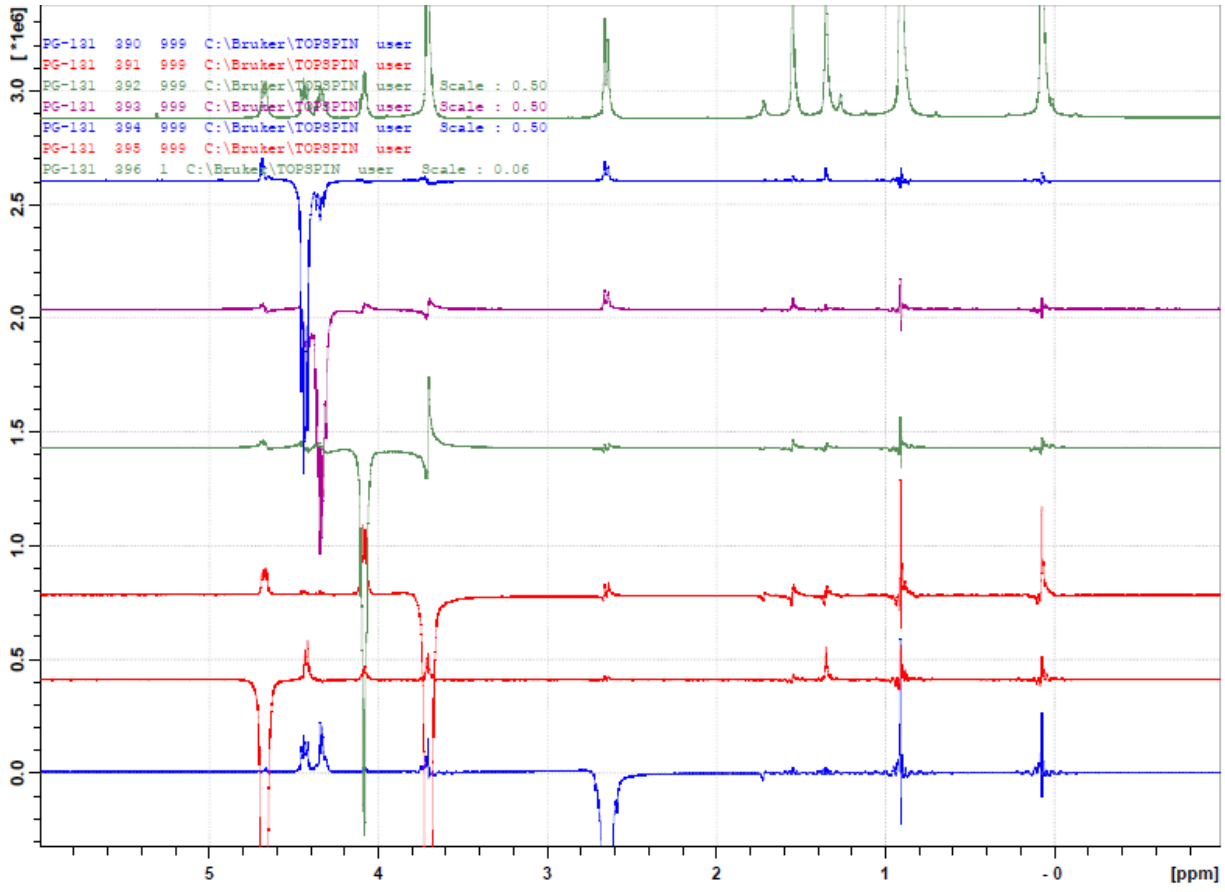
^{1}H spectrum of compound 23



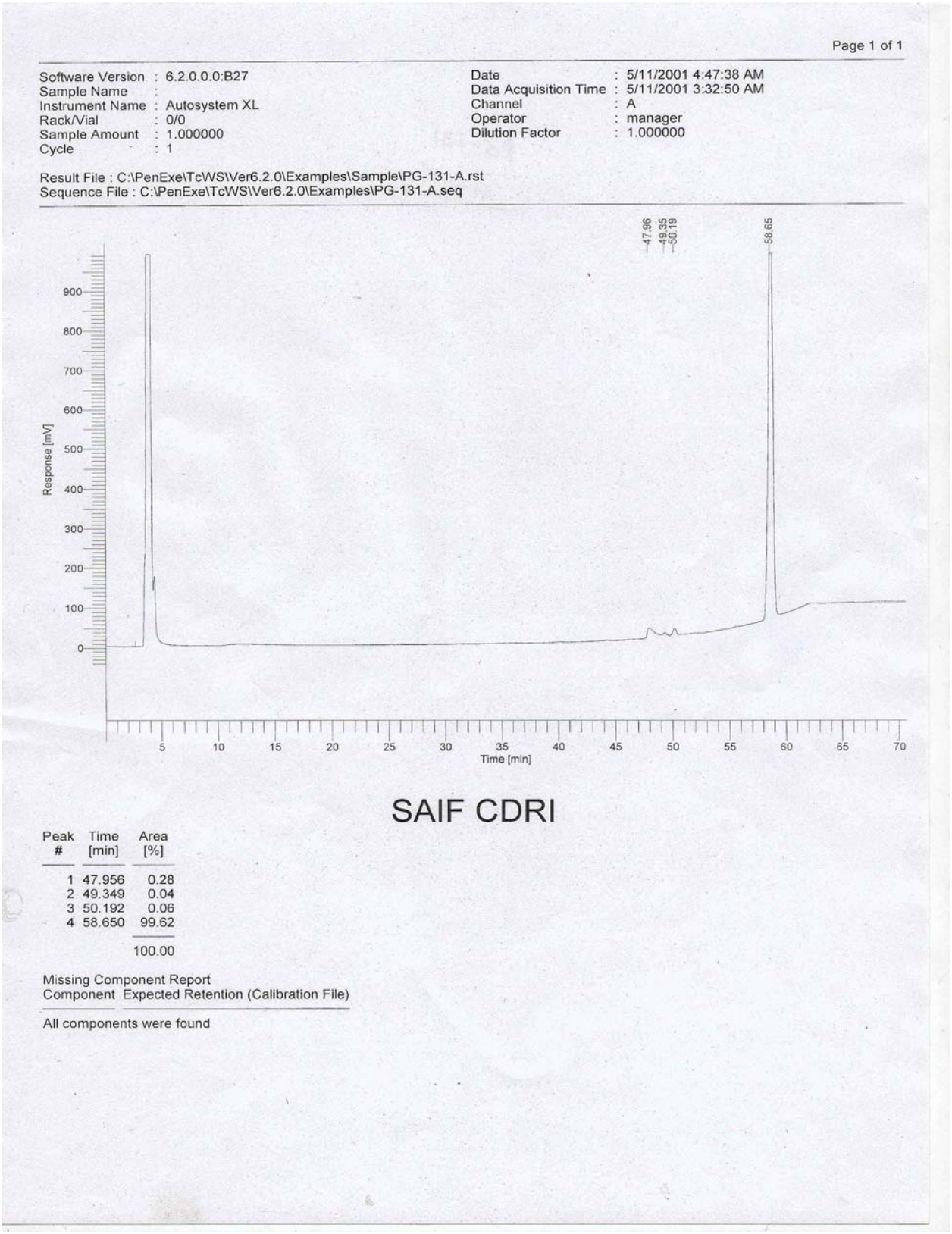
^{1}H-^{1}H COSY spectrum of compound 23







NOE spectrum of compound 23



Page 1 of 1

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SAIF CDRI

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Missing Component Report

Component	Expected Retention (Calibration File)

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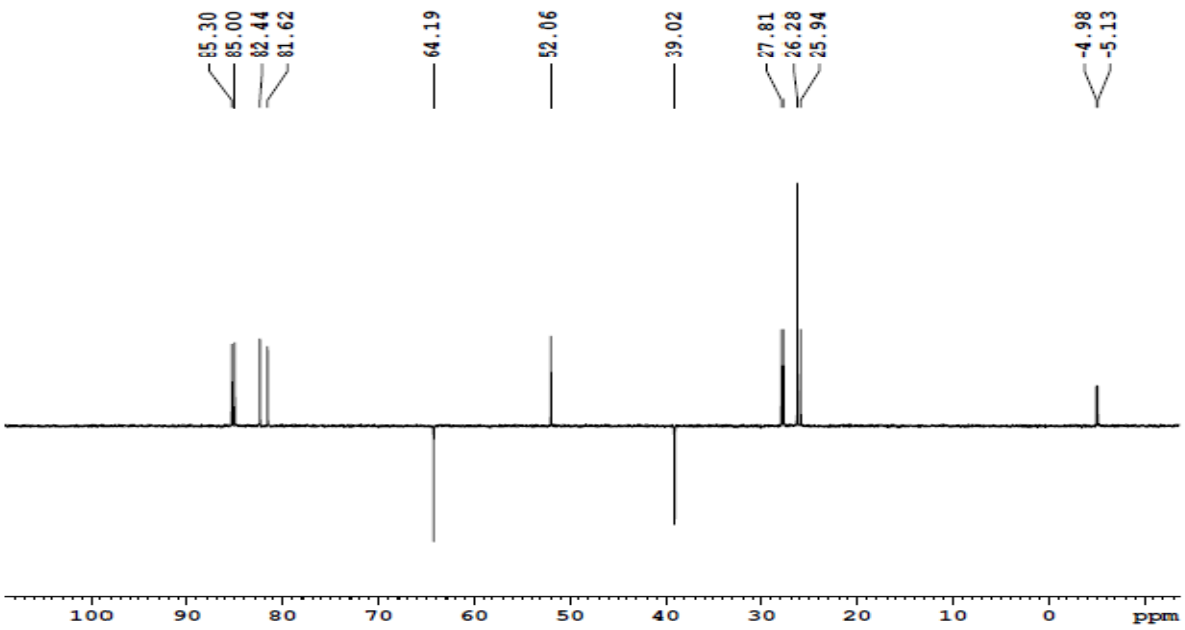
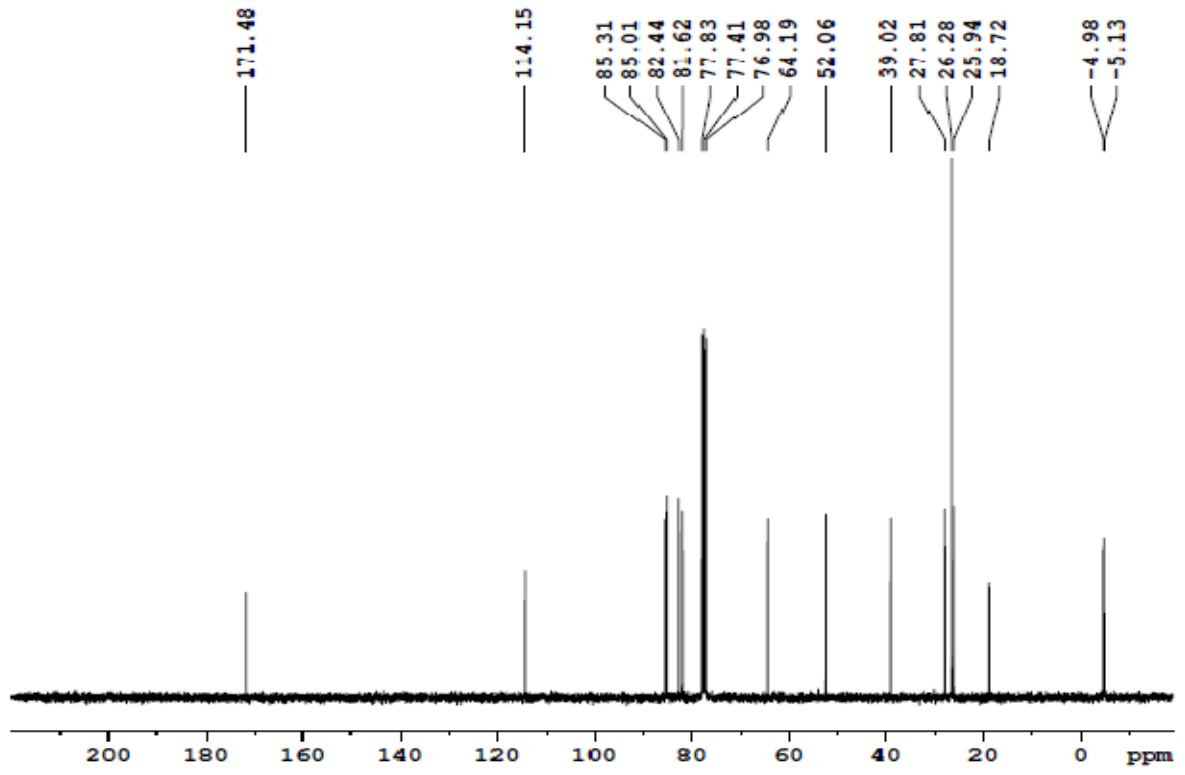
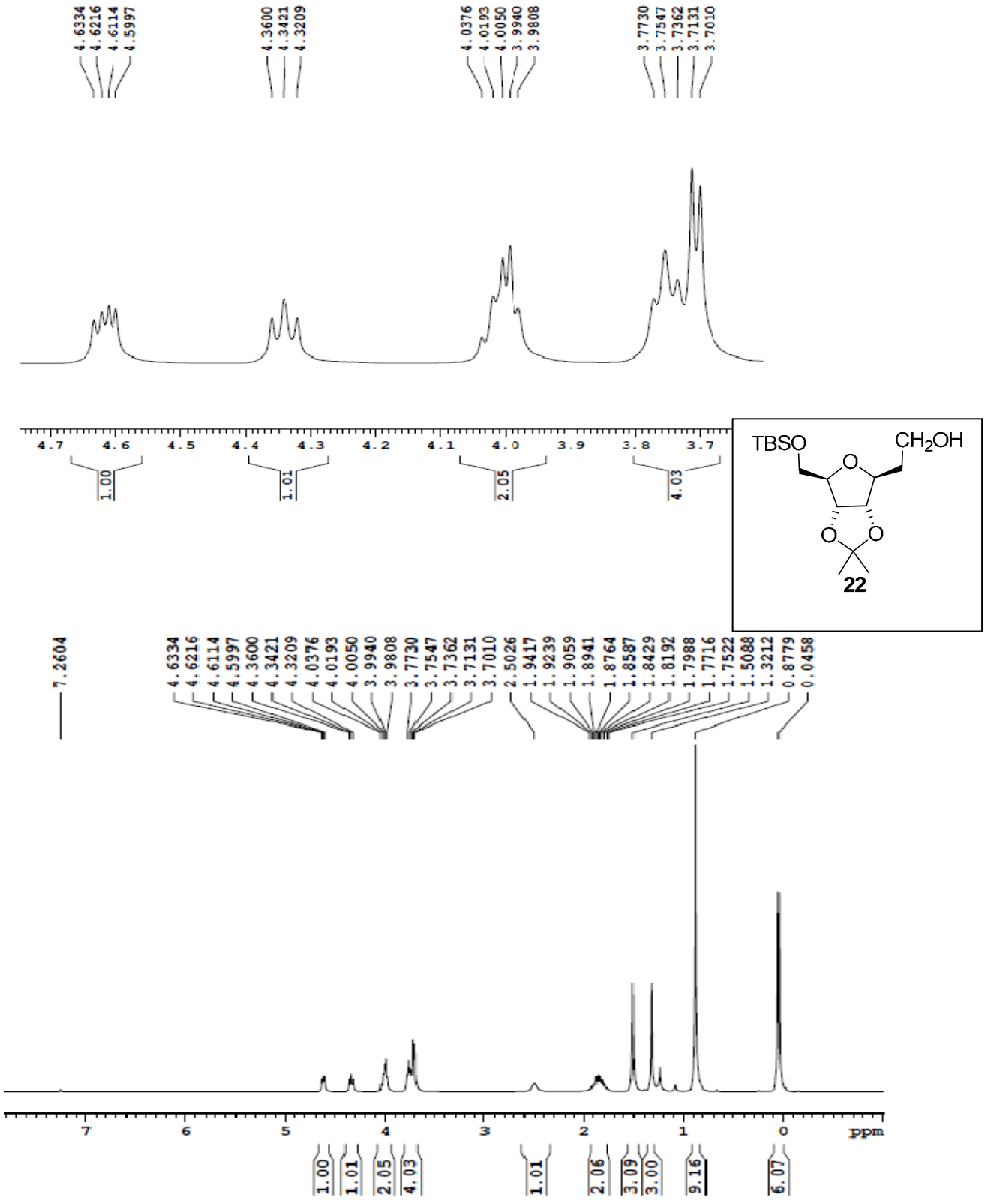
GC analysis for compound 23

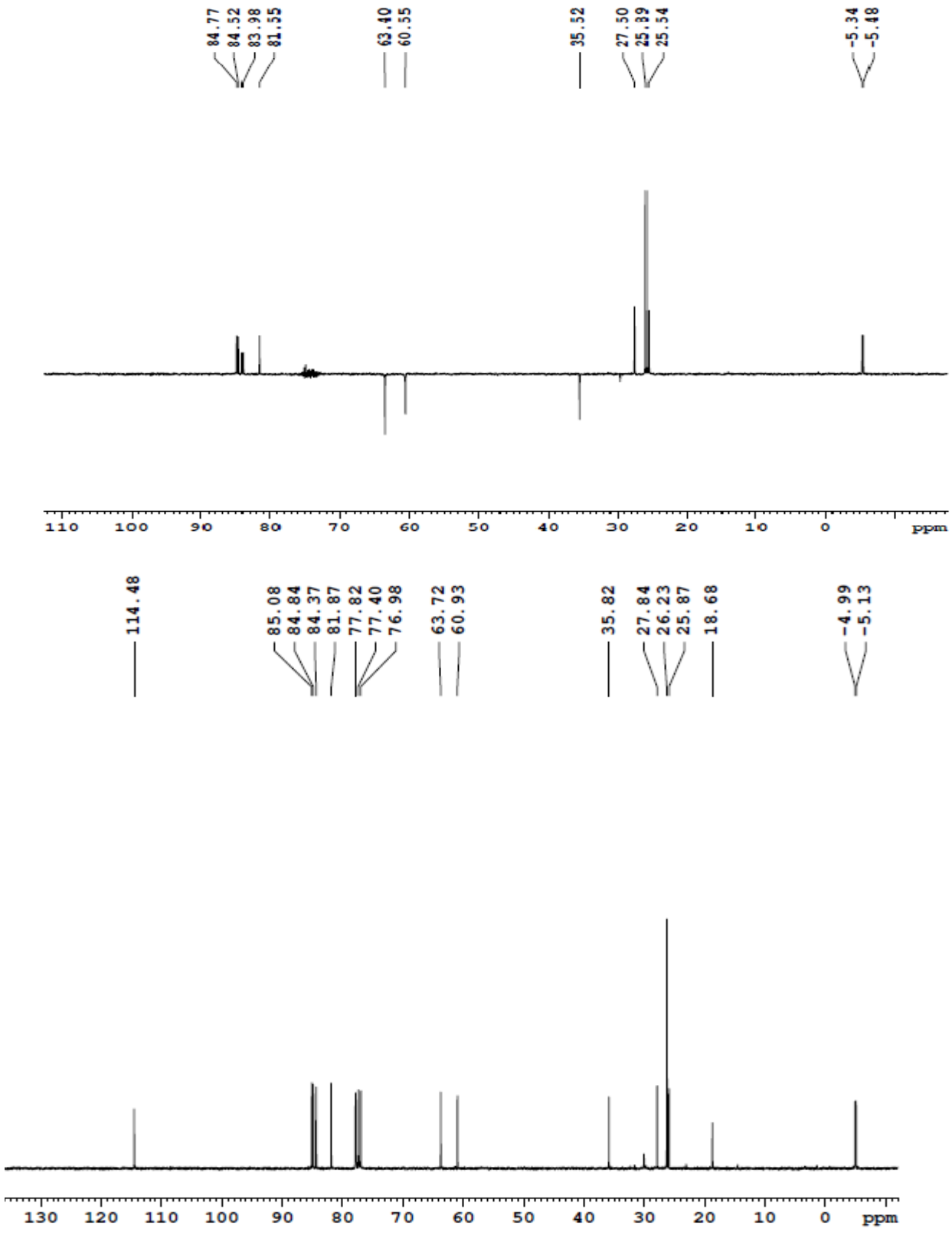




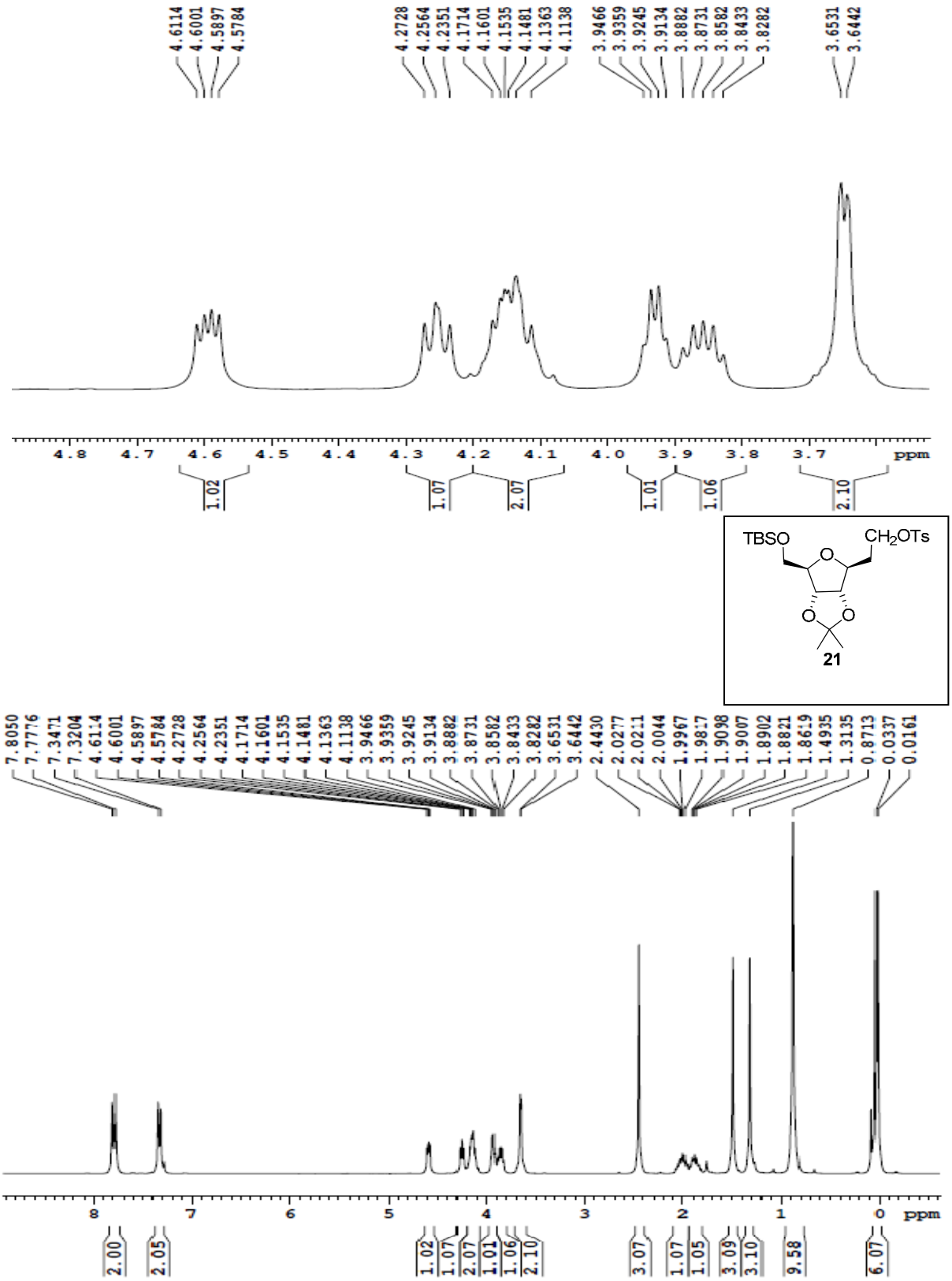
^{13}C spectrum of compound 23



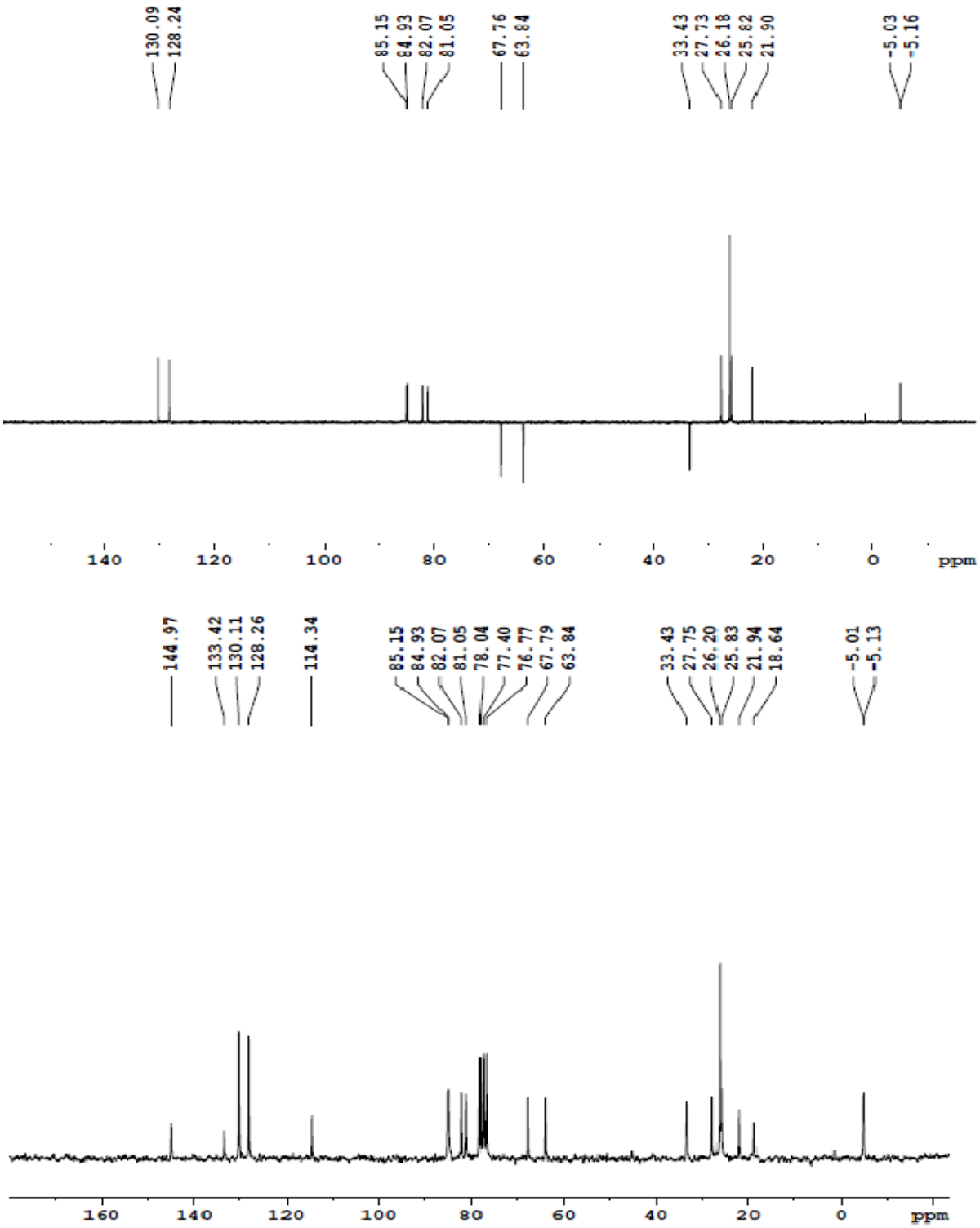
^{1}H spectrum of compound 22



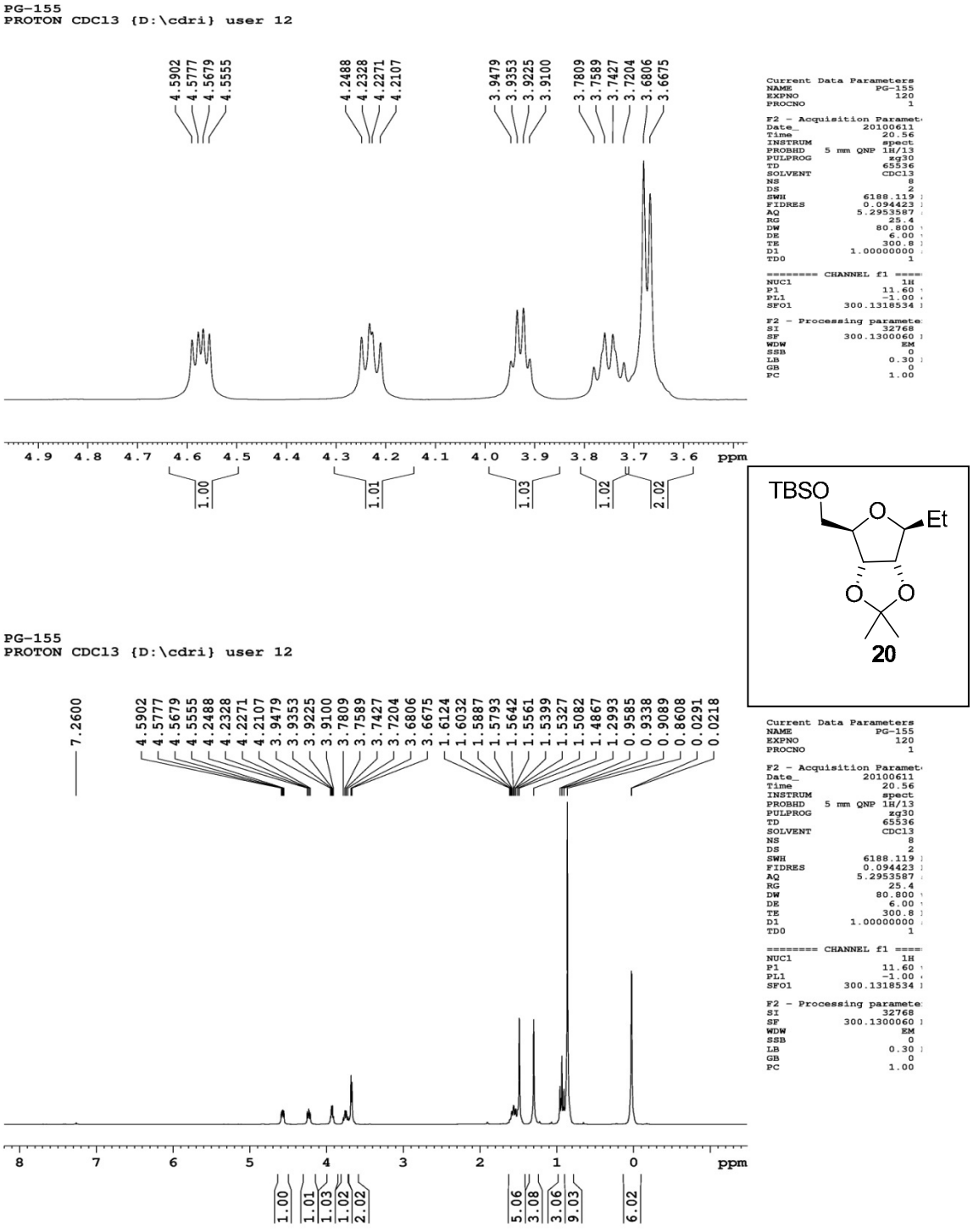
^{13}C spectrum of compound 22



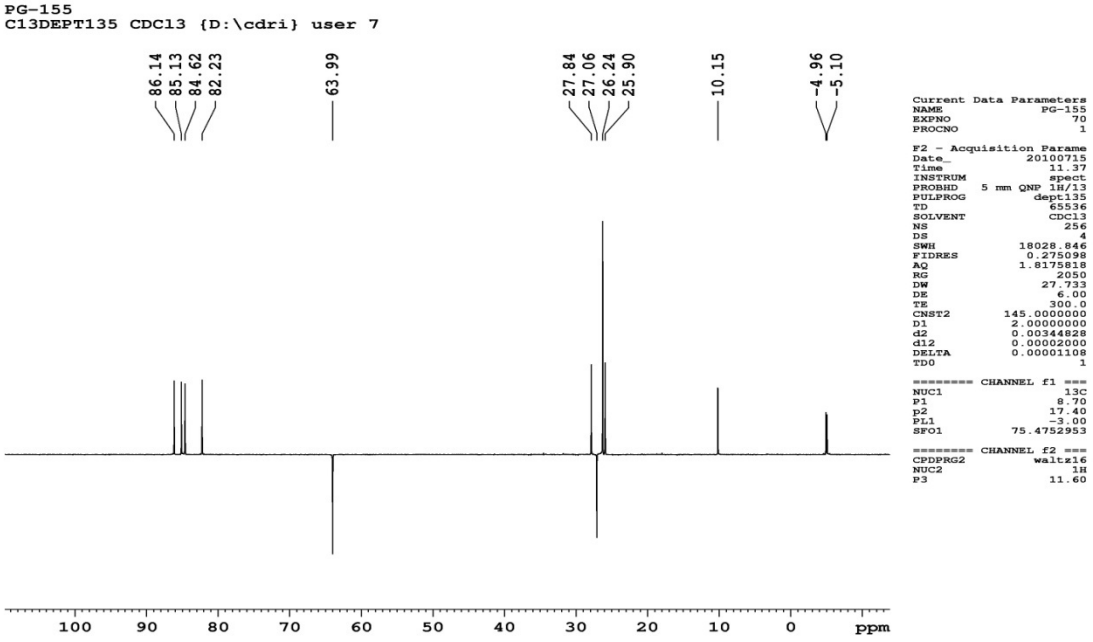
^{1}H spectrum of compound 21

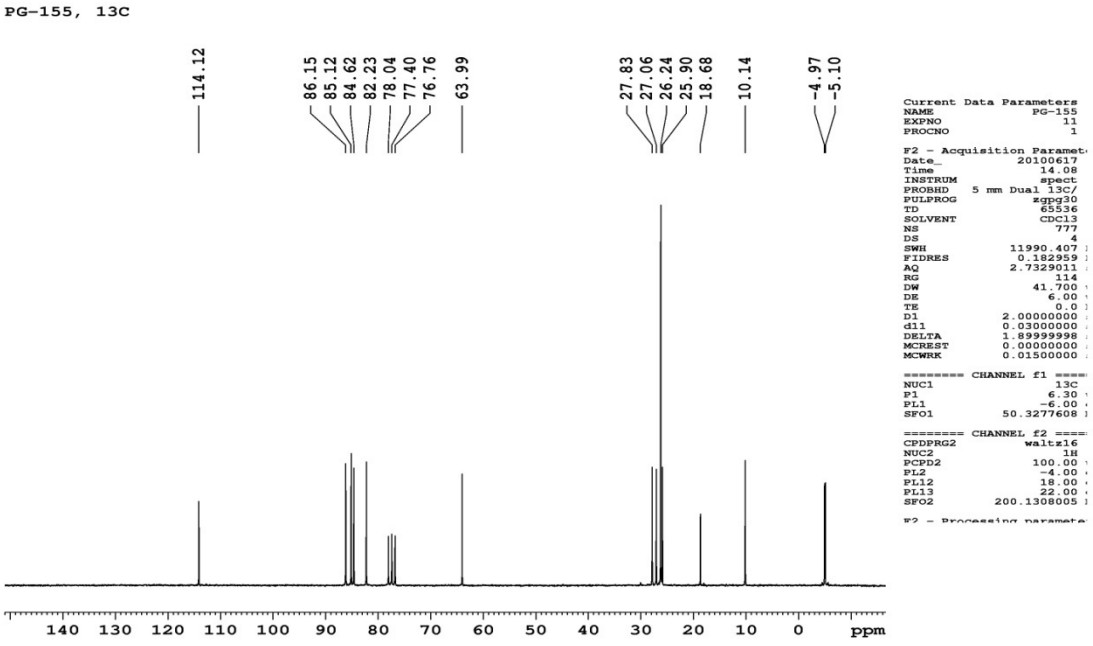


^{13}C spectrum of compound 21

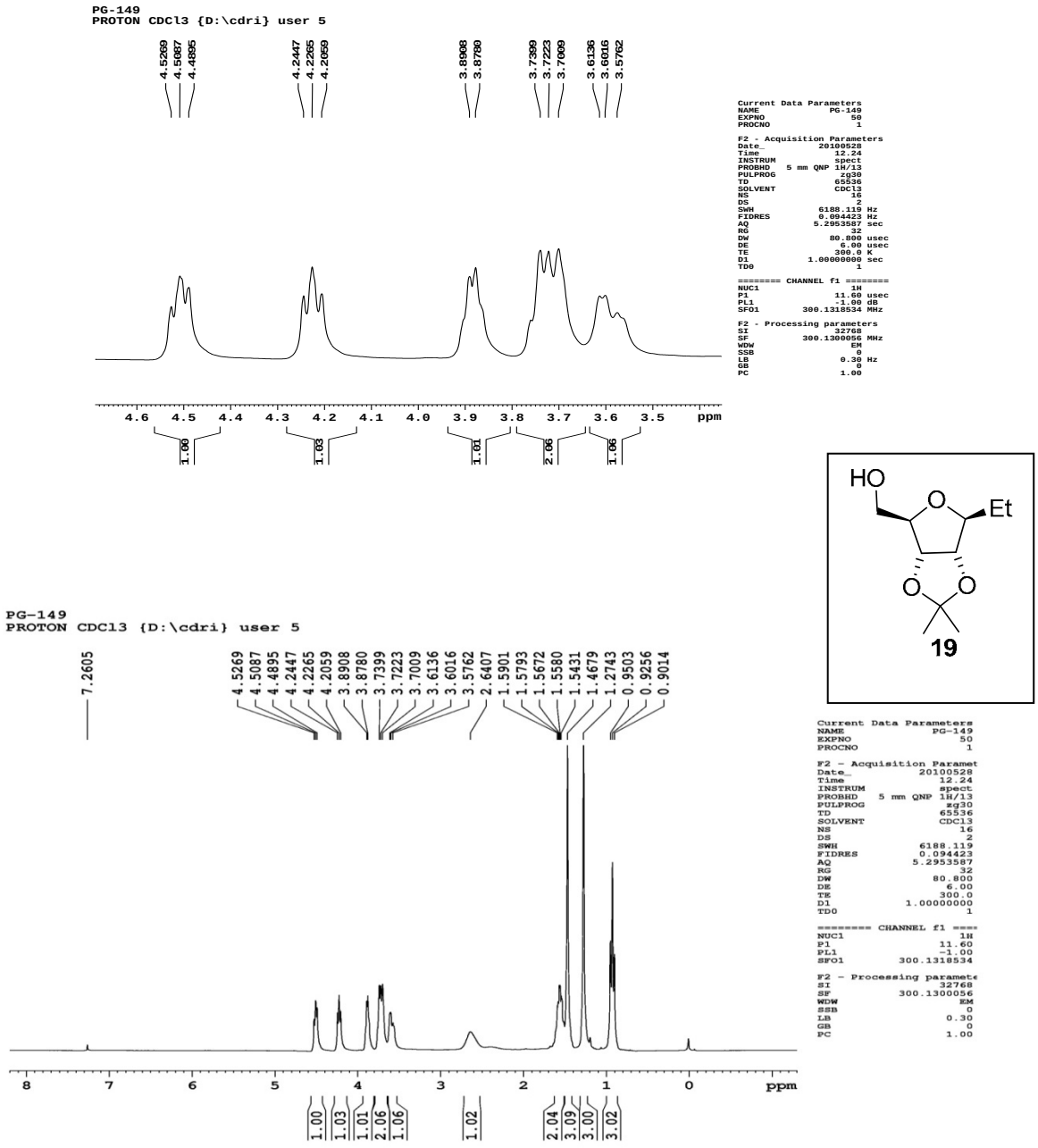


^{1}H spectrum of compound 20

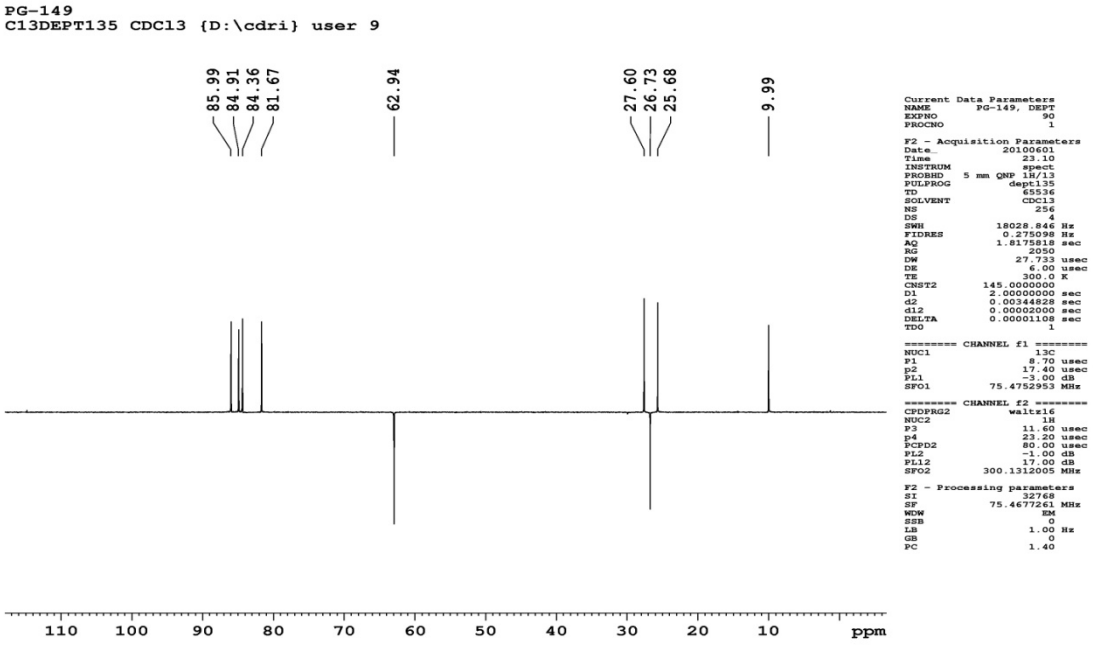


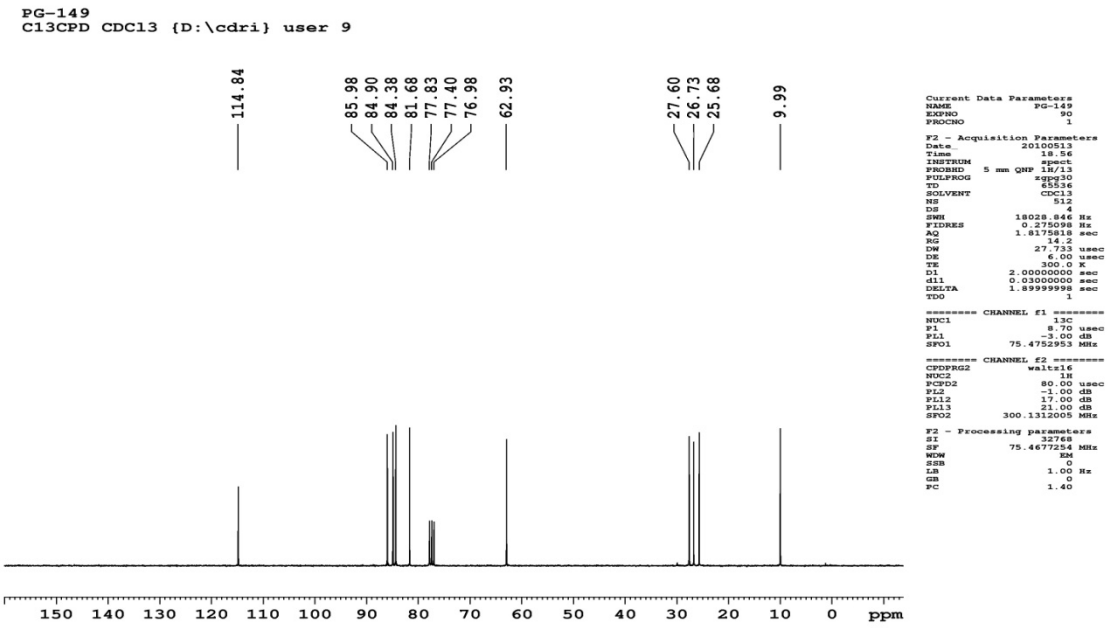


^{13}C spectrum of compound 20

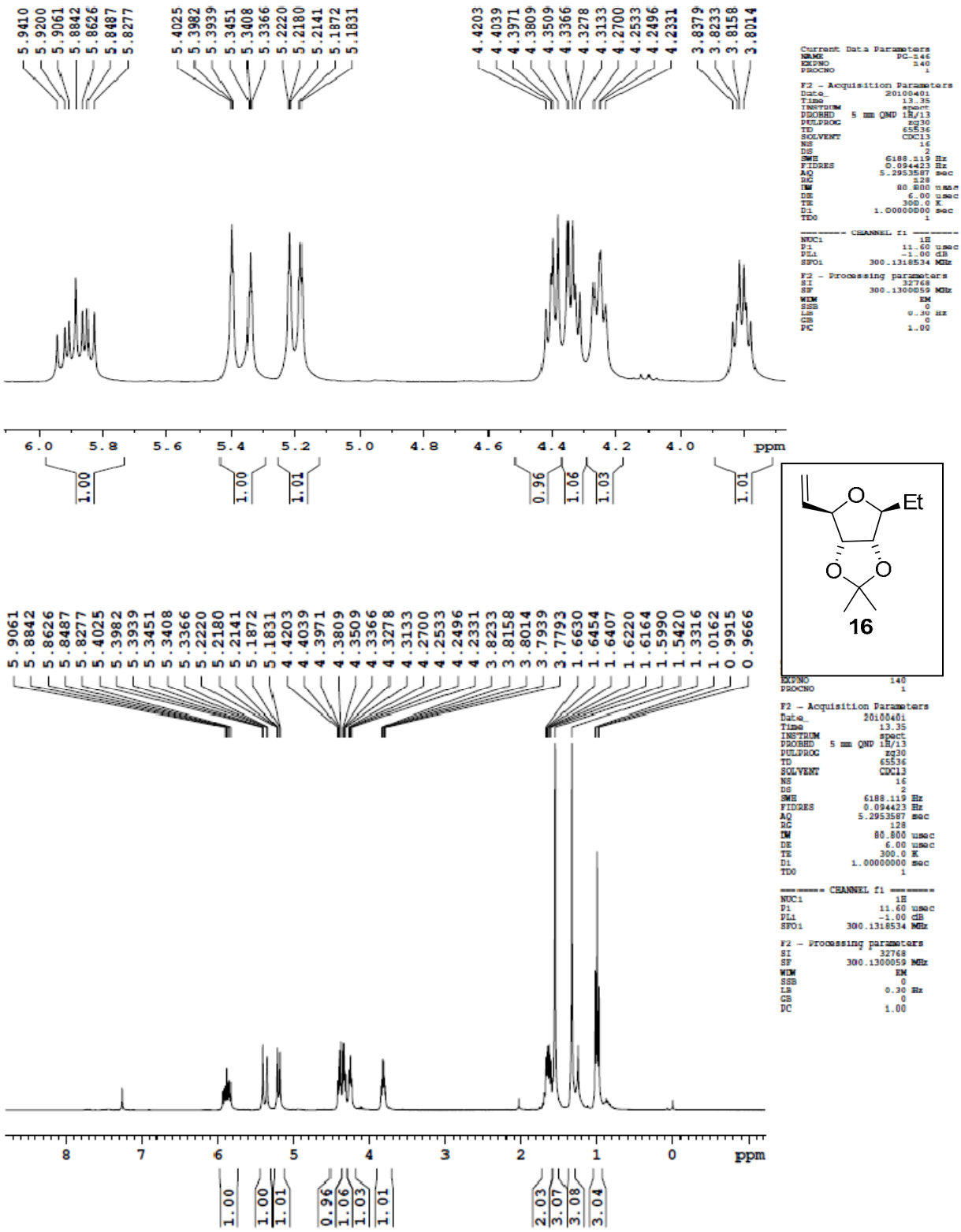


^{1}H spectrum of compound 19

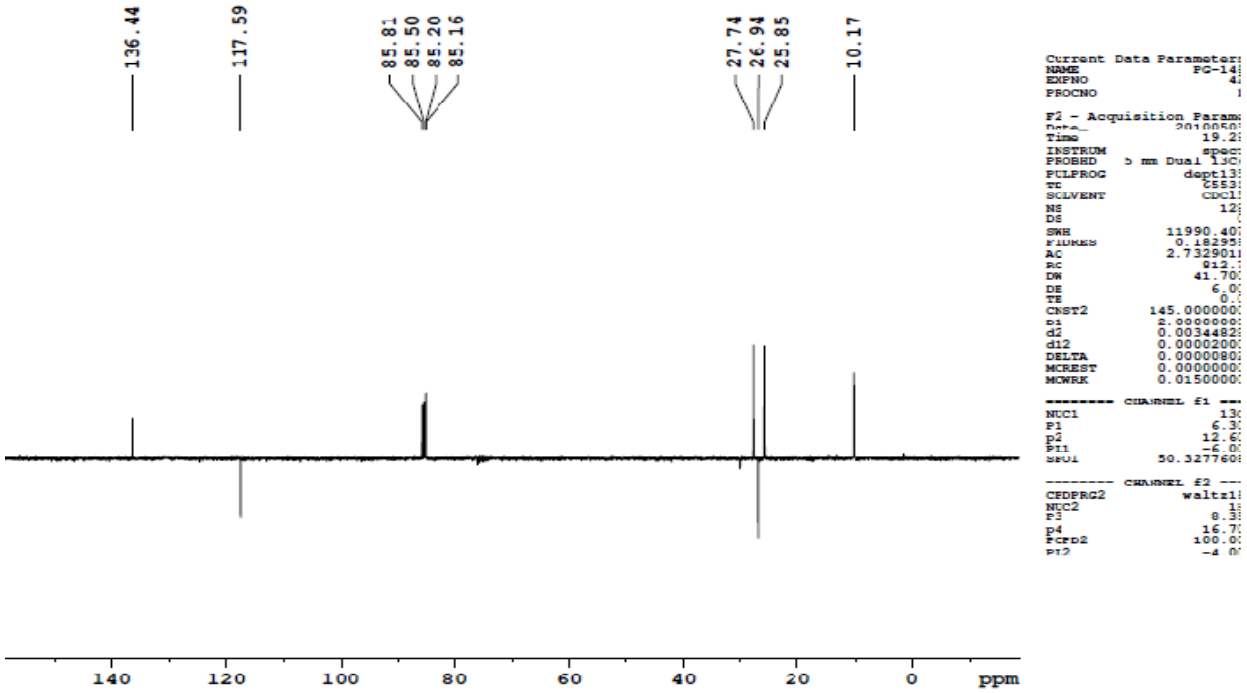


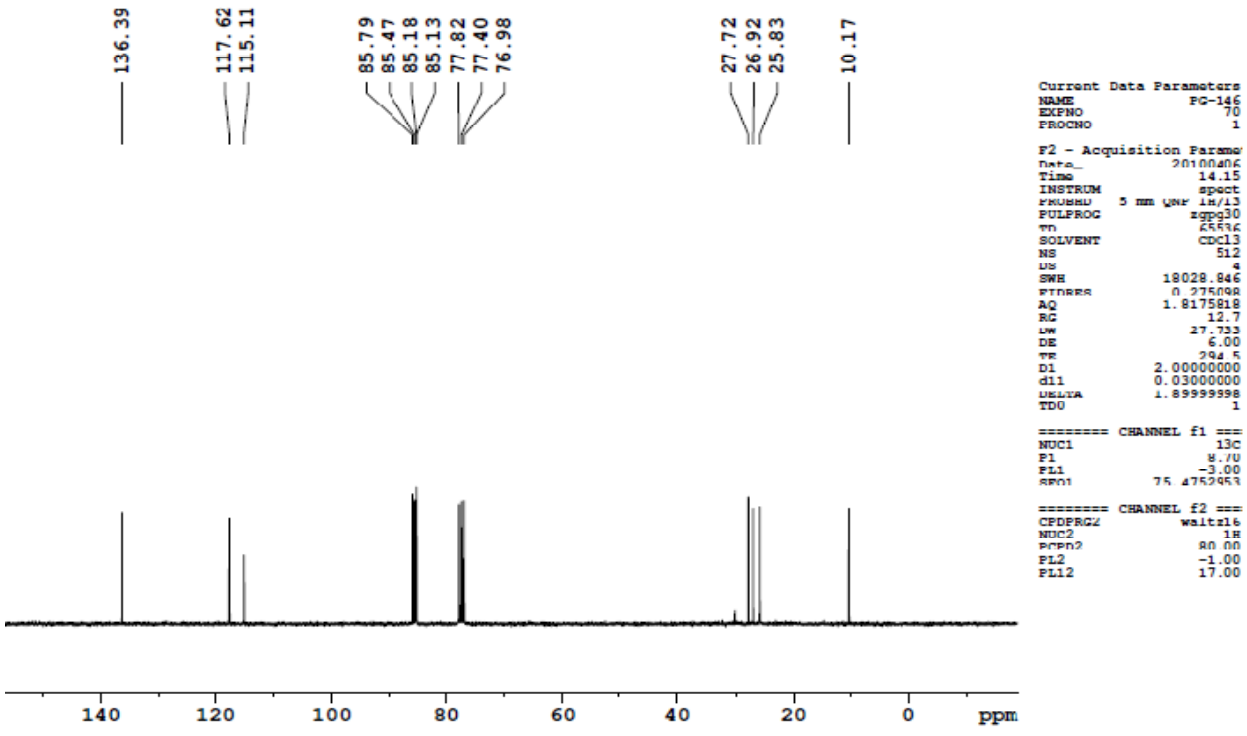


^{13}C spectrum of compound 19

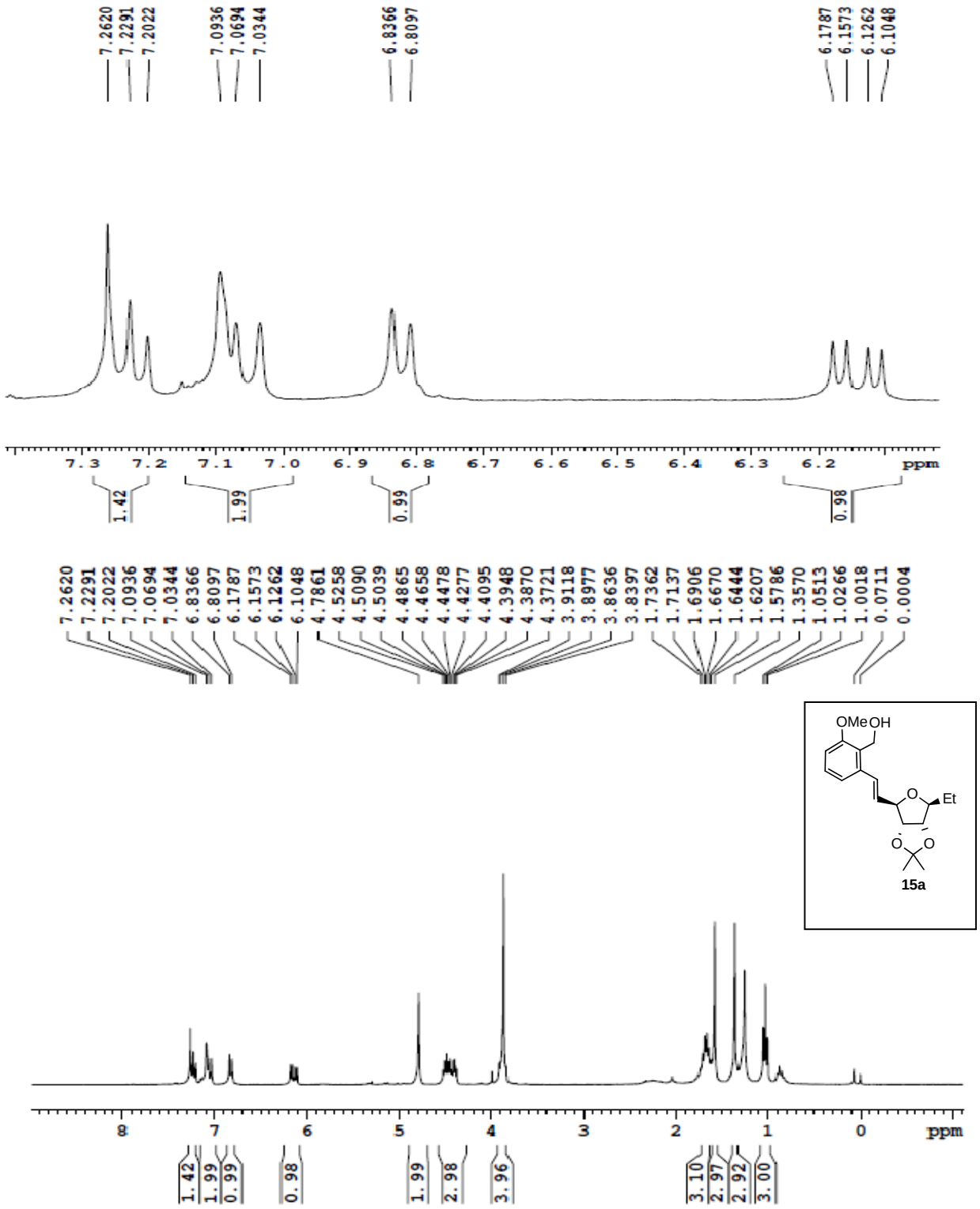


^{1}H spectrum of compound 16

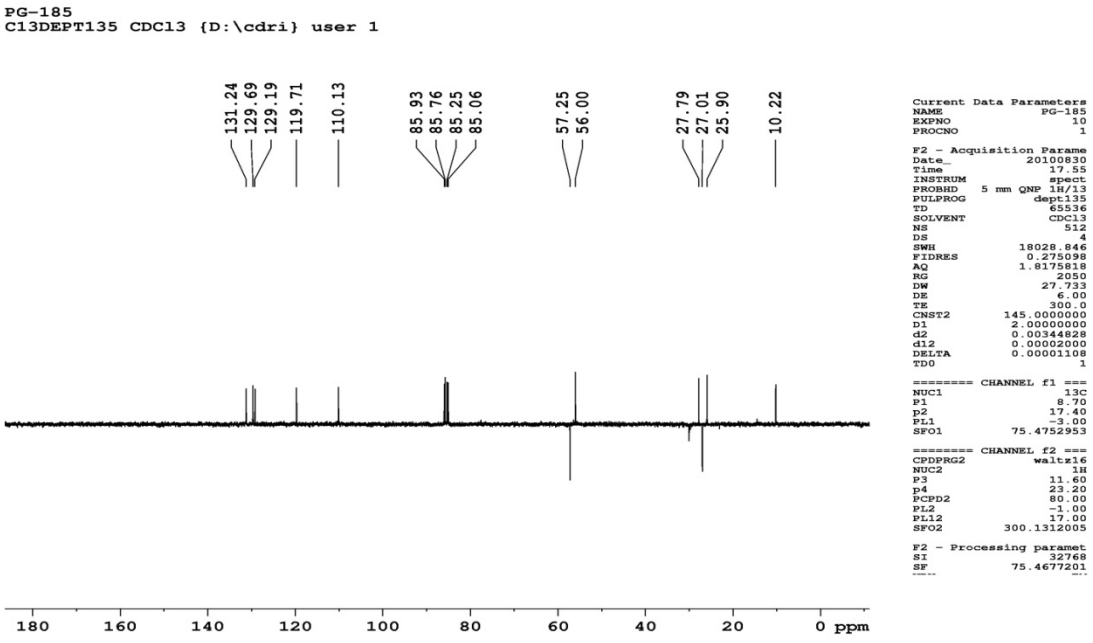


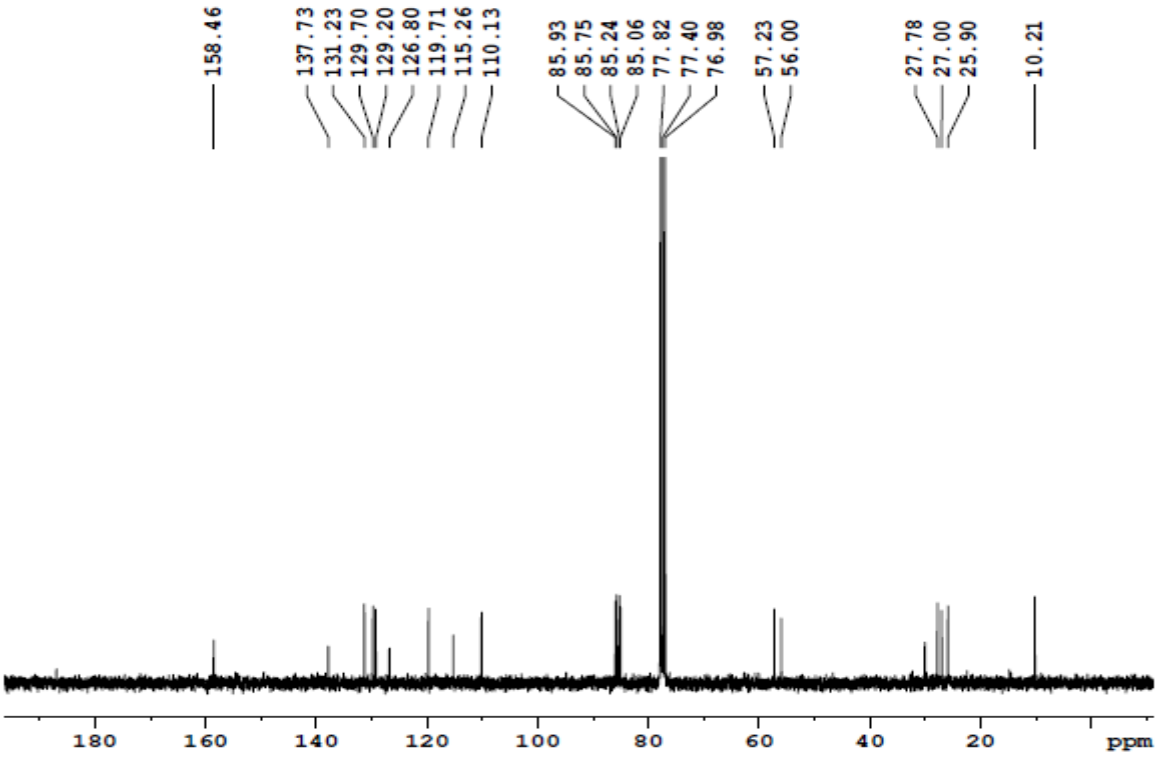


^{13}C spectrum of compound 16

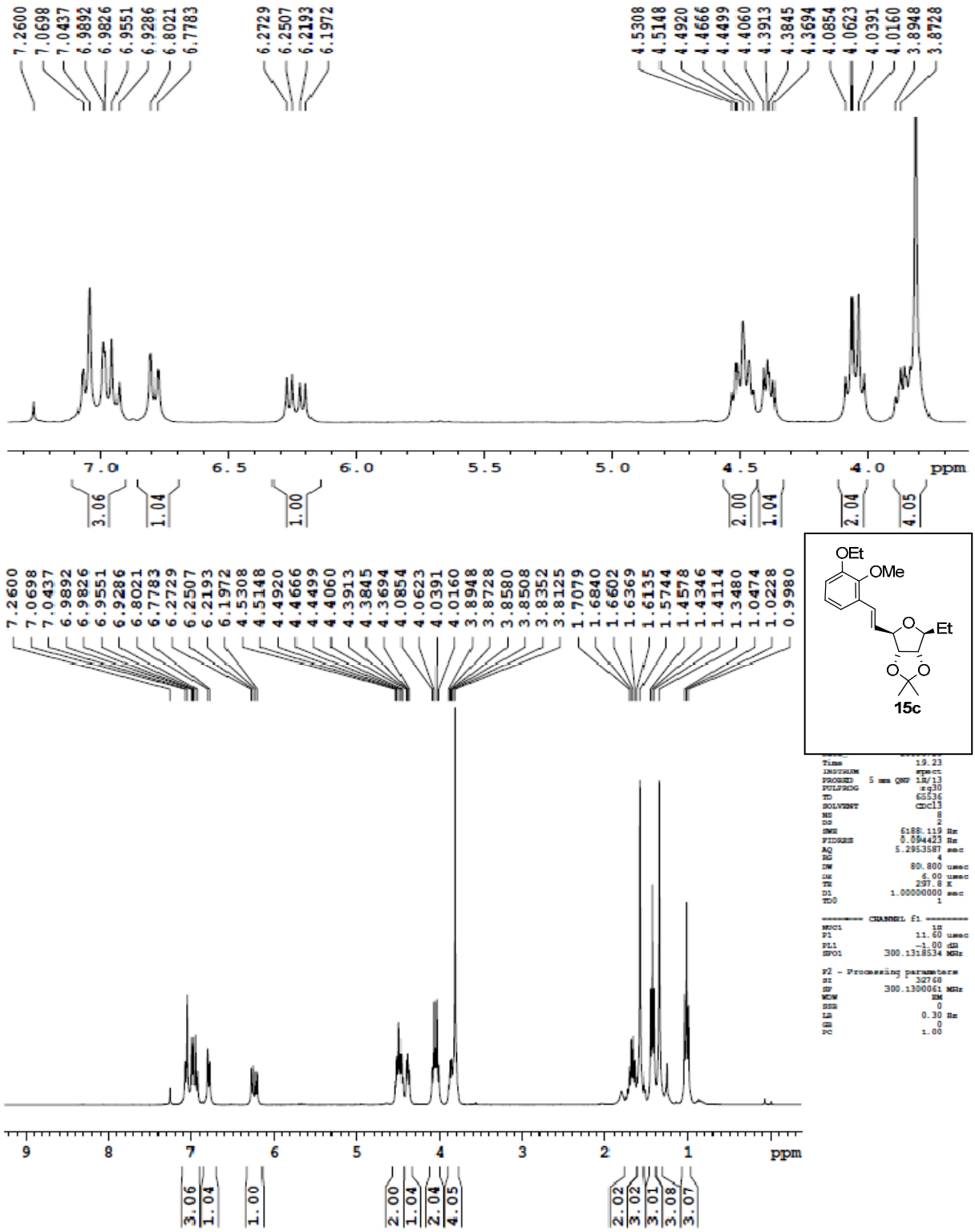


^{1}H spectrum of compound 15a

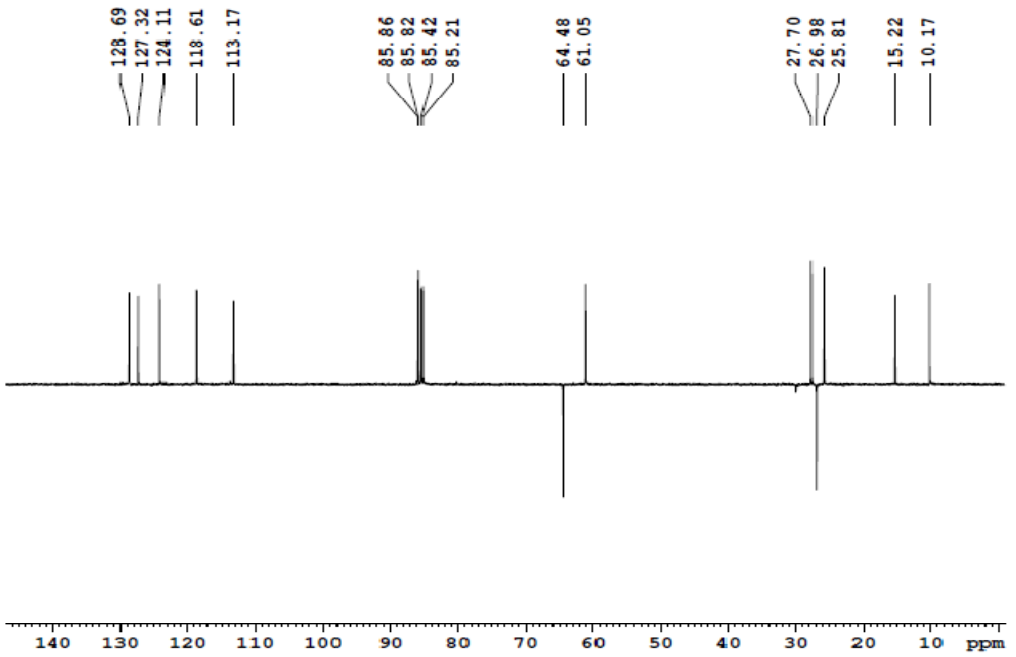


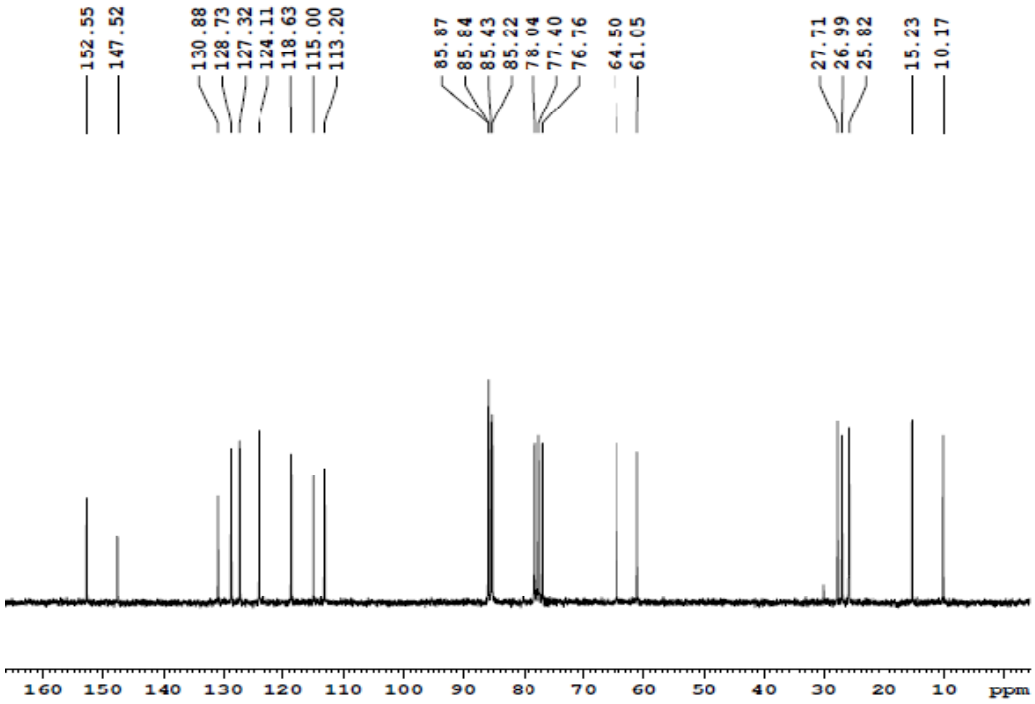


^{13}C spectrum of compound 15a



^{1}H spectrum of compound 15c





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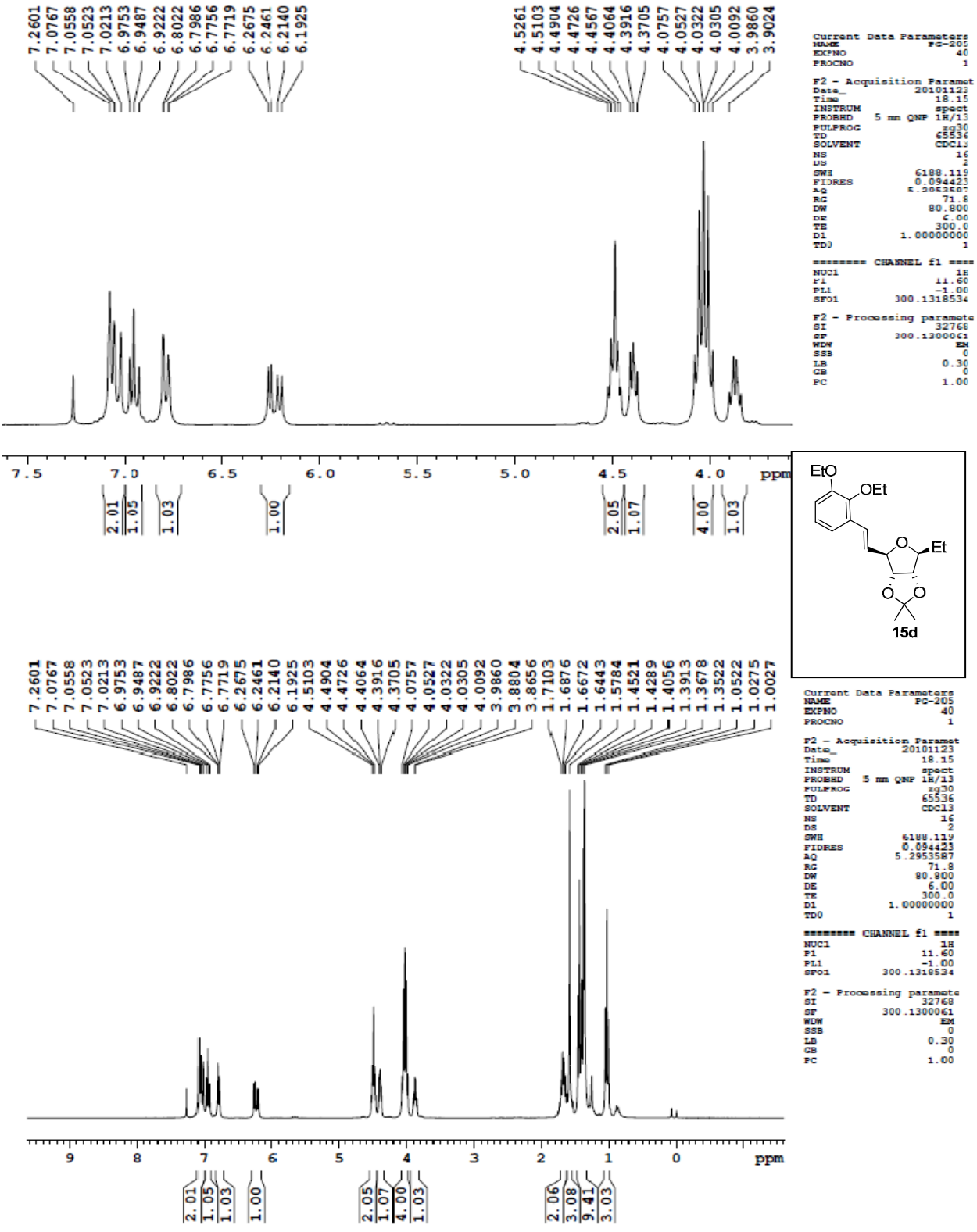
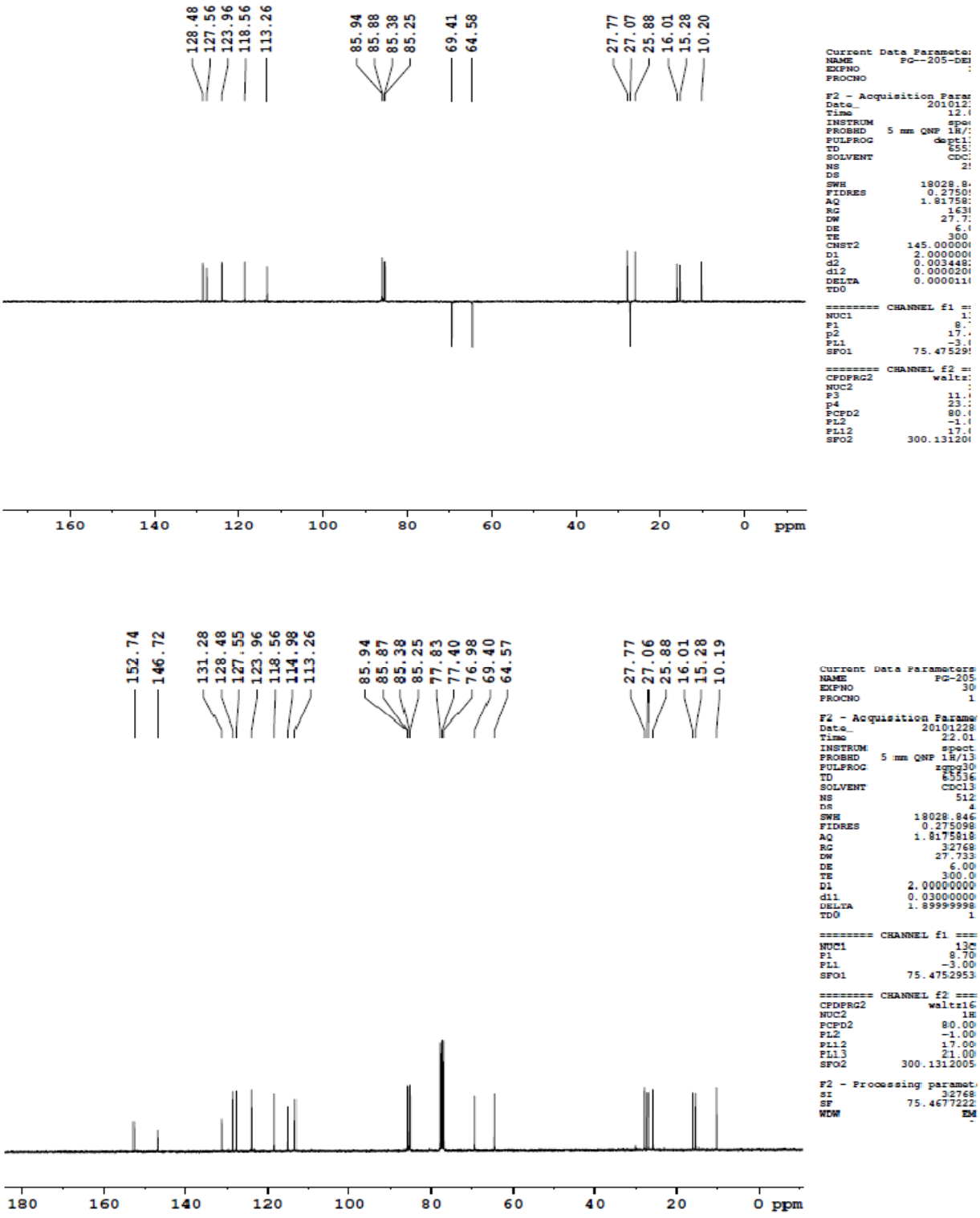
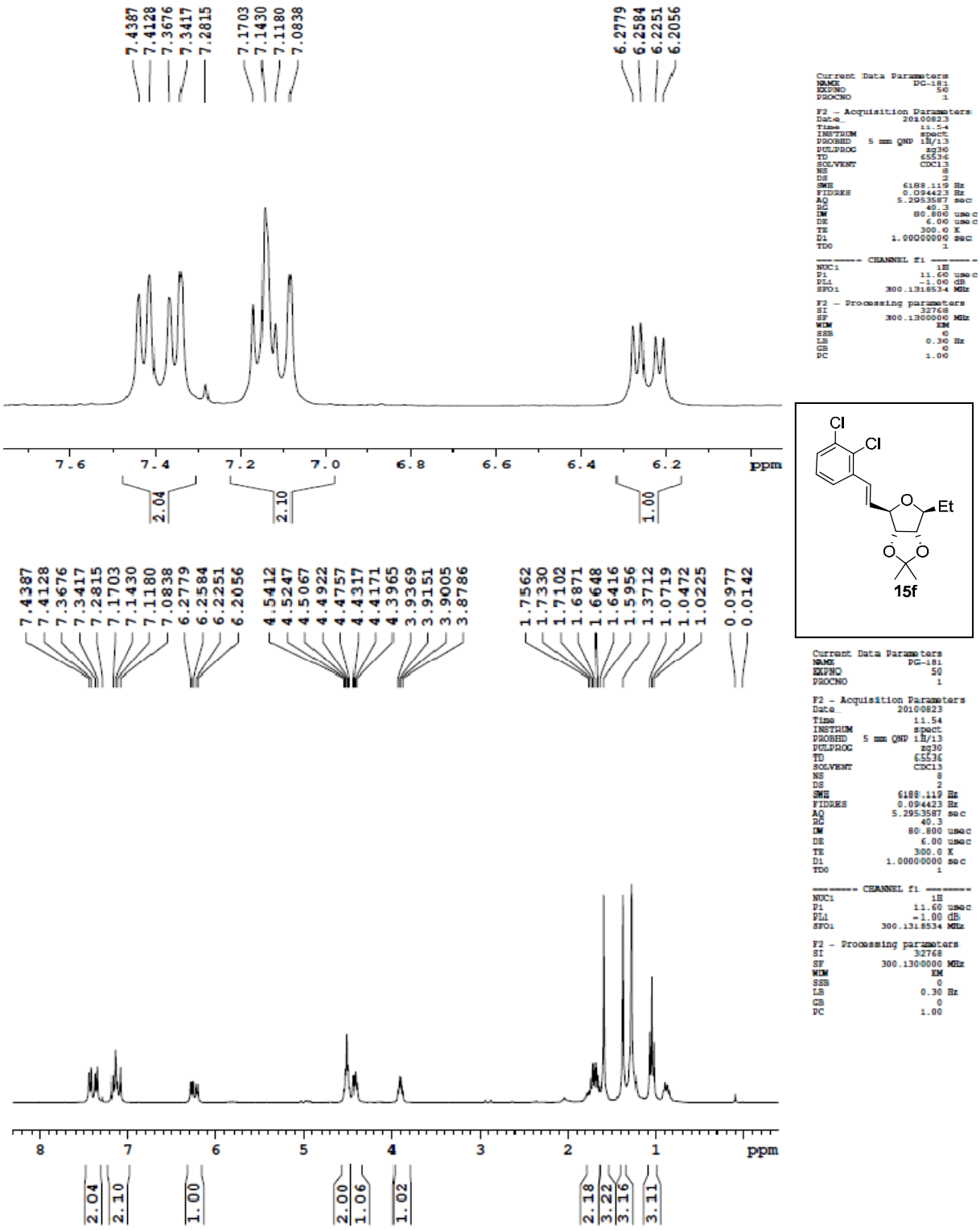


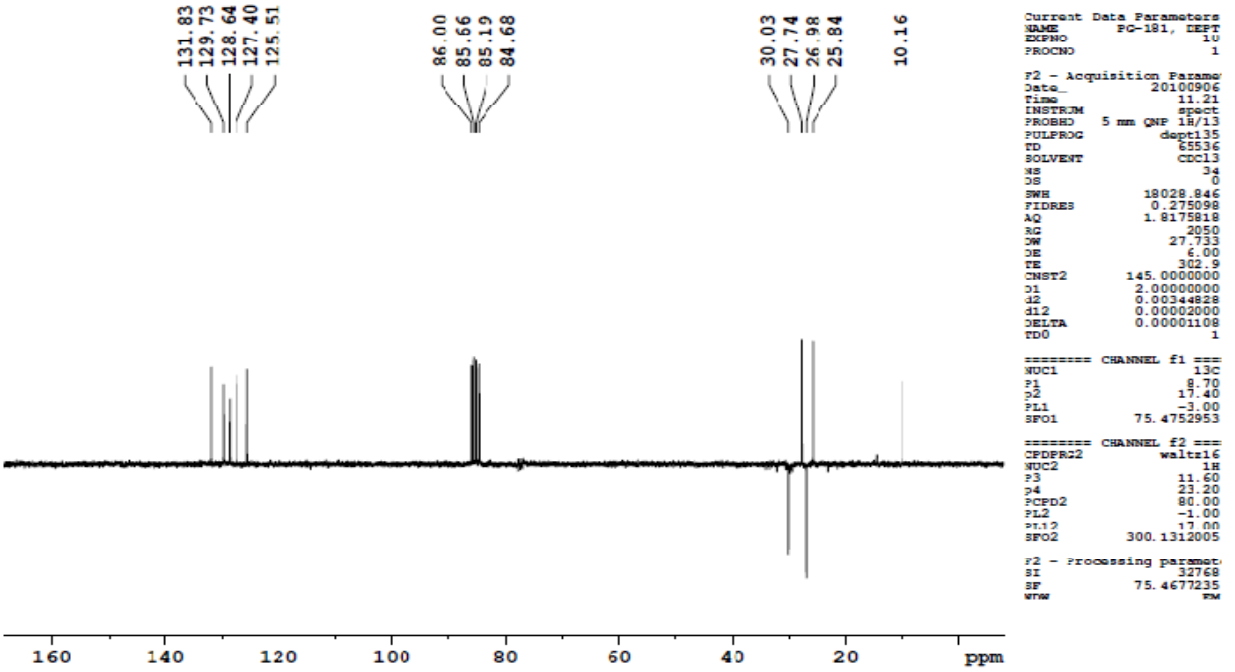
^{1}H spectrum of compound 15d

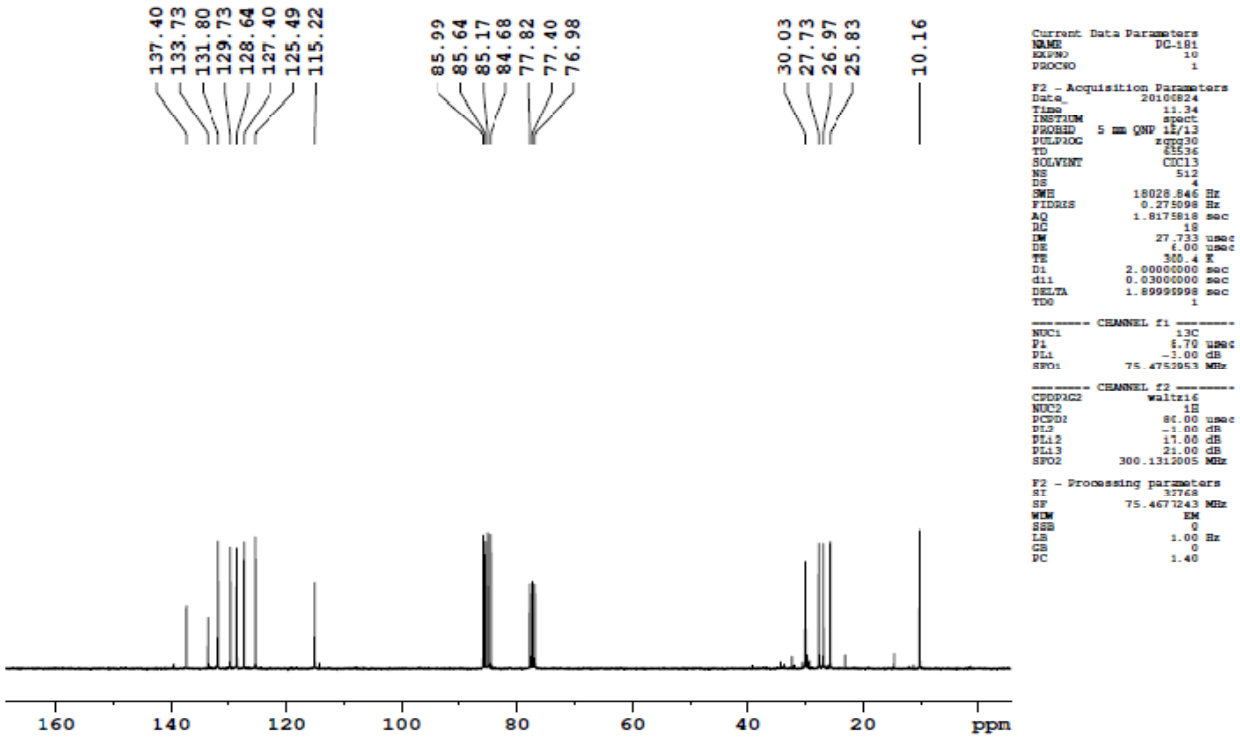


^{13}C spectrum of compound 15d



^{1}H spectrum of compound 15f





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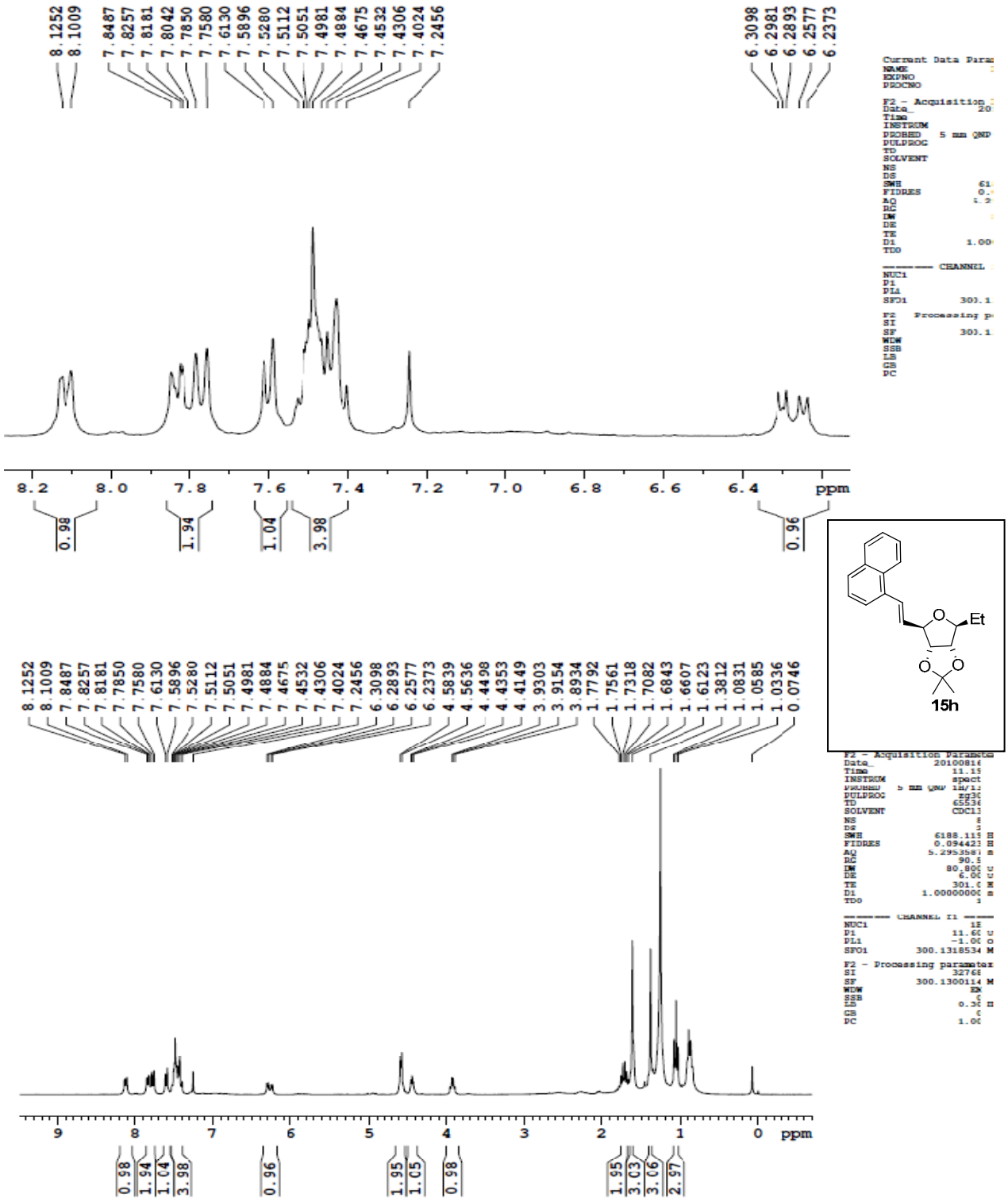
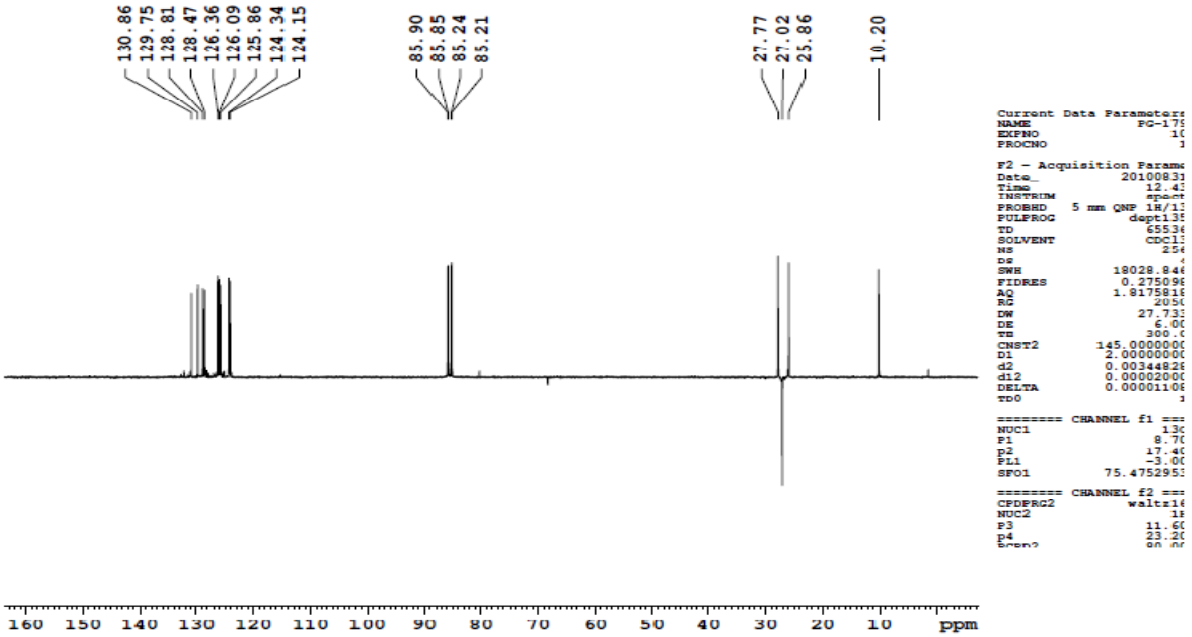
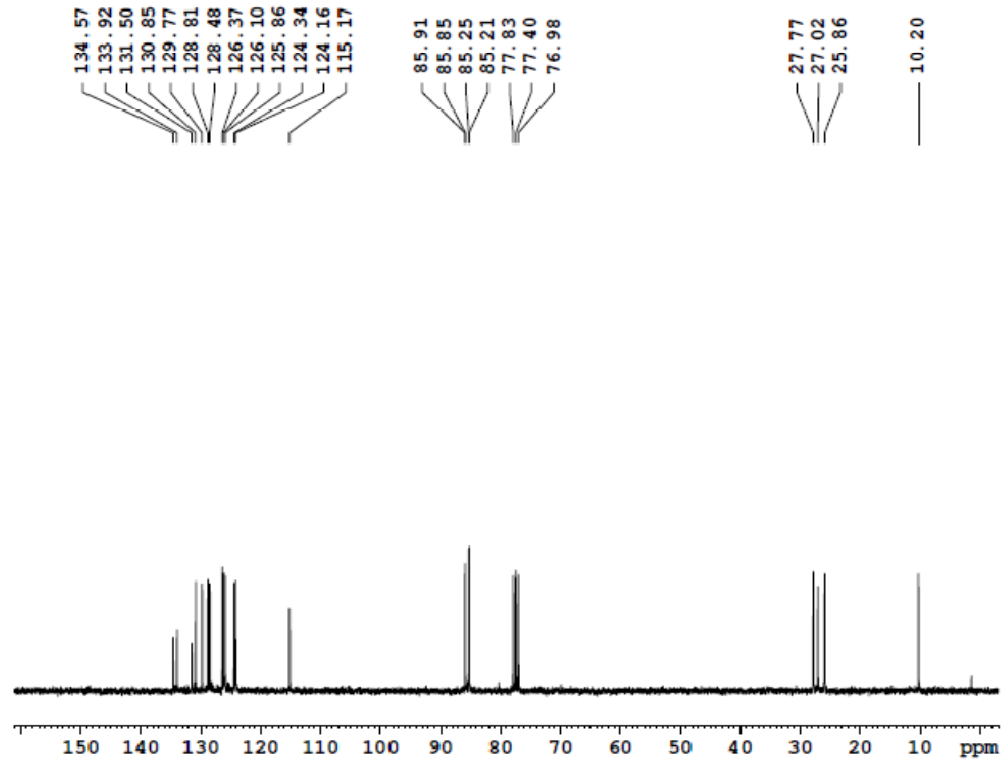


^{1}H spectrum of compound 15h





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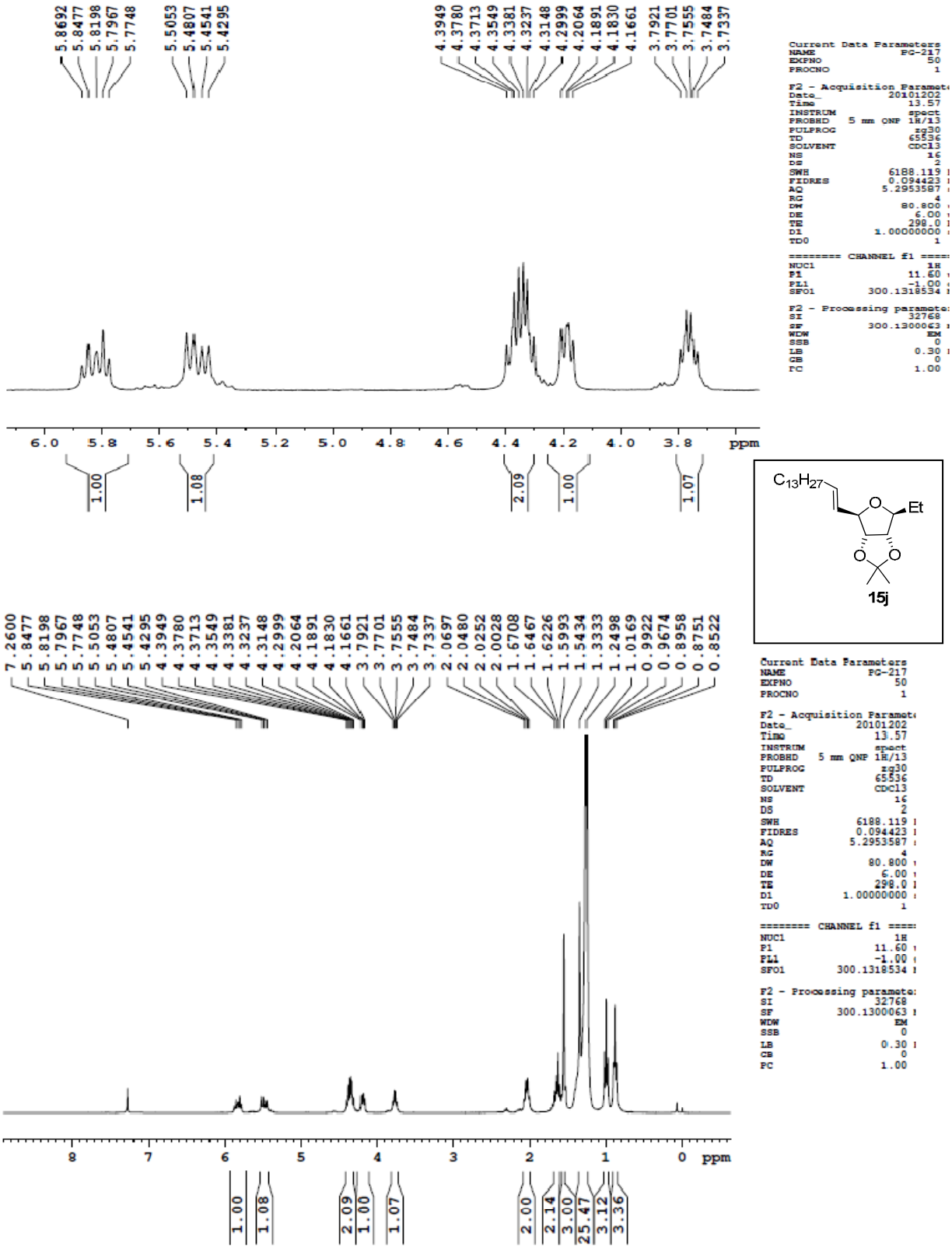
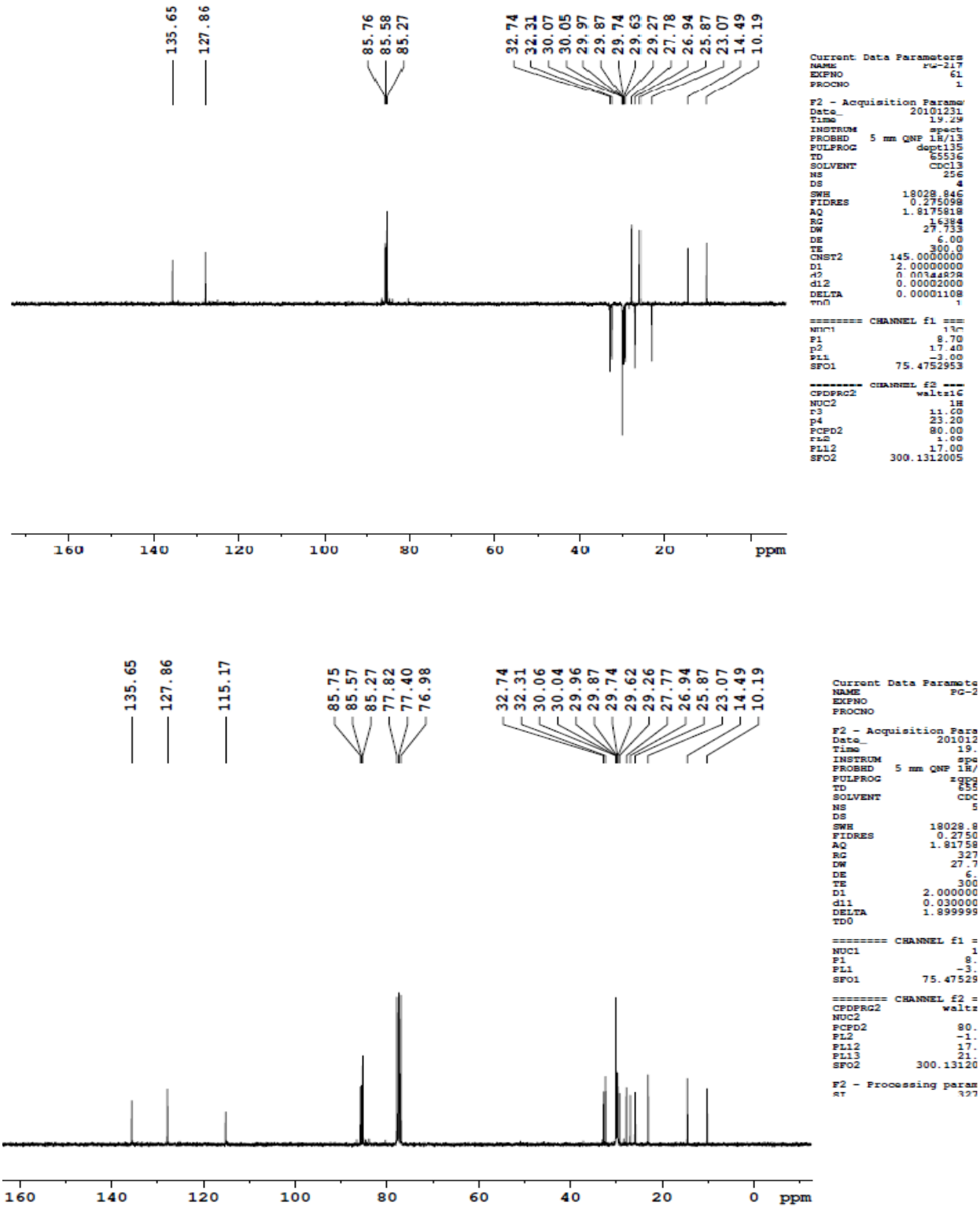
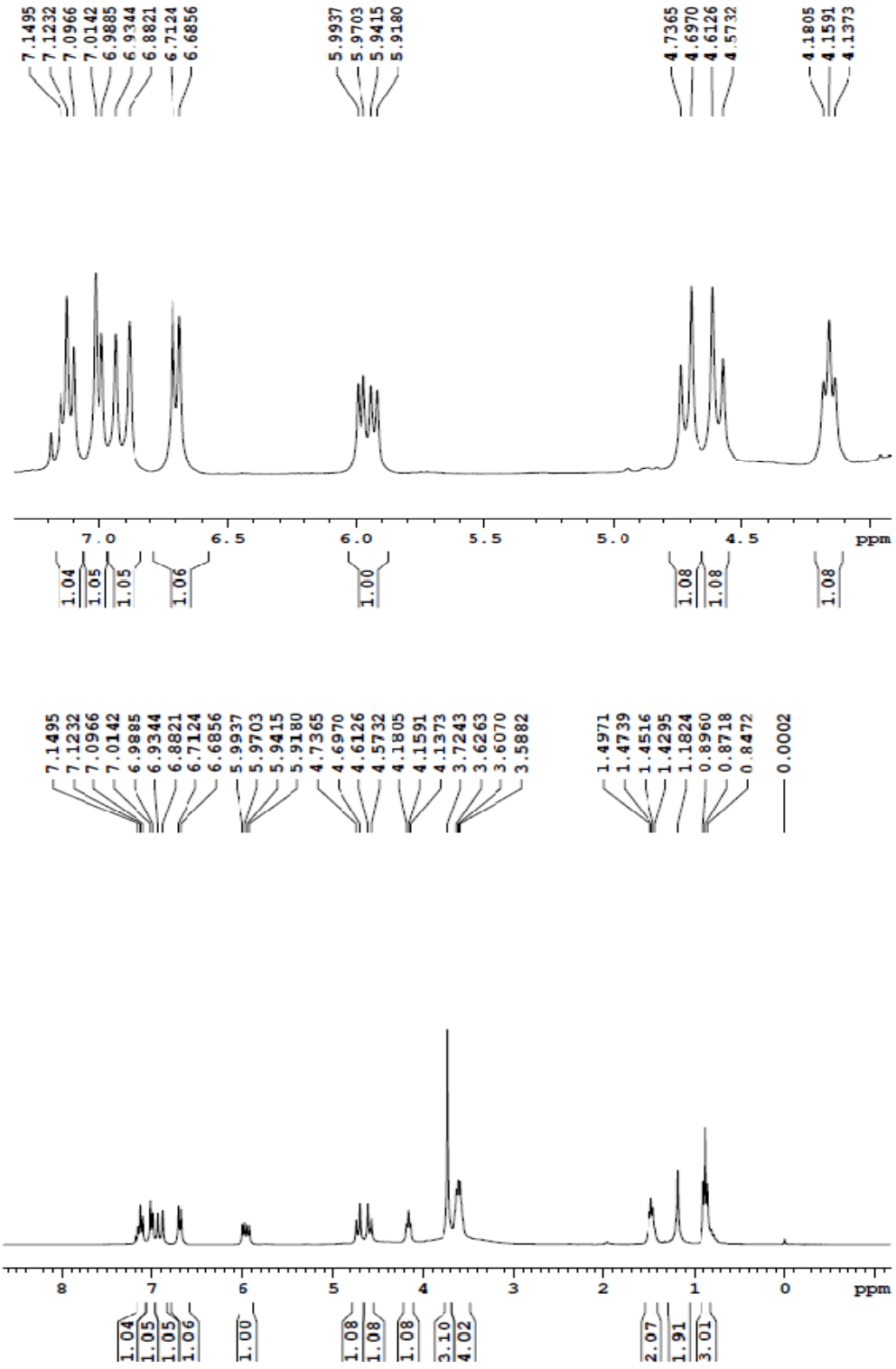


^{1}H spectrum of compound 15j



^{13}C spectrum of compound 15j

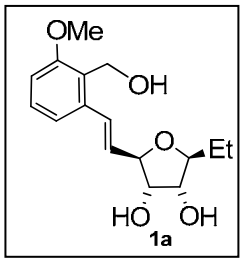


Current Data Parameters
NAME PG-187
EXPNO 20
PROCNO 1

F2 - Acquisition Parameters
Date_ 20100830
Time 11.13
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 6188.119 Hz
FIDRES 0.094423 Hz
AQ 5.2953587 sec
RG 57
DW 80.800 usec
DE 6.00 usec
TE 300.1 K
D1 1.00000000 sec
TD0 1

---------- CHANNEL f1 ----------
NUC1 1H
P1 11.60 usec
PL1 -1.00 dB
SFO1 300.1318534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300285 MHz
WDW EM
SSB 2
LB 0.30 Hz
GB 0
PC 1.00



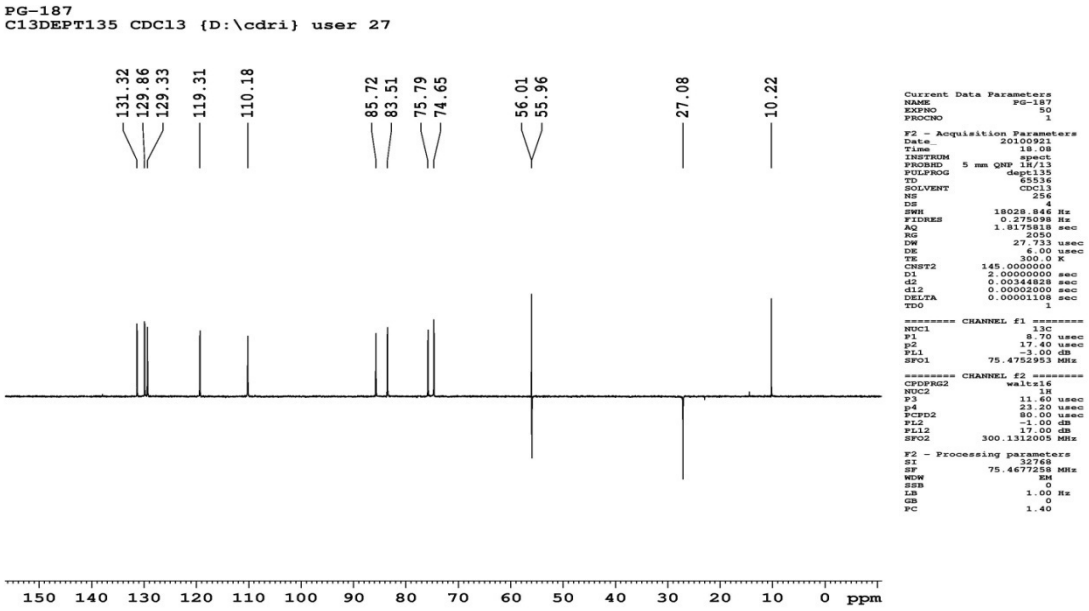
Current Data Parameters
NAME PG-187
EXPNO 20
PROCNO 1

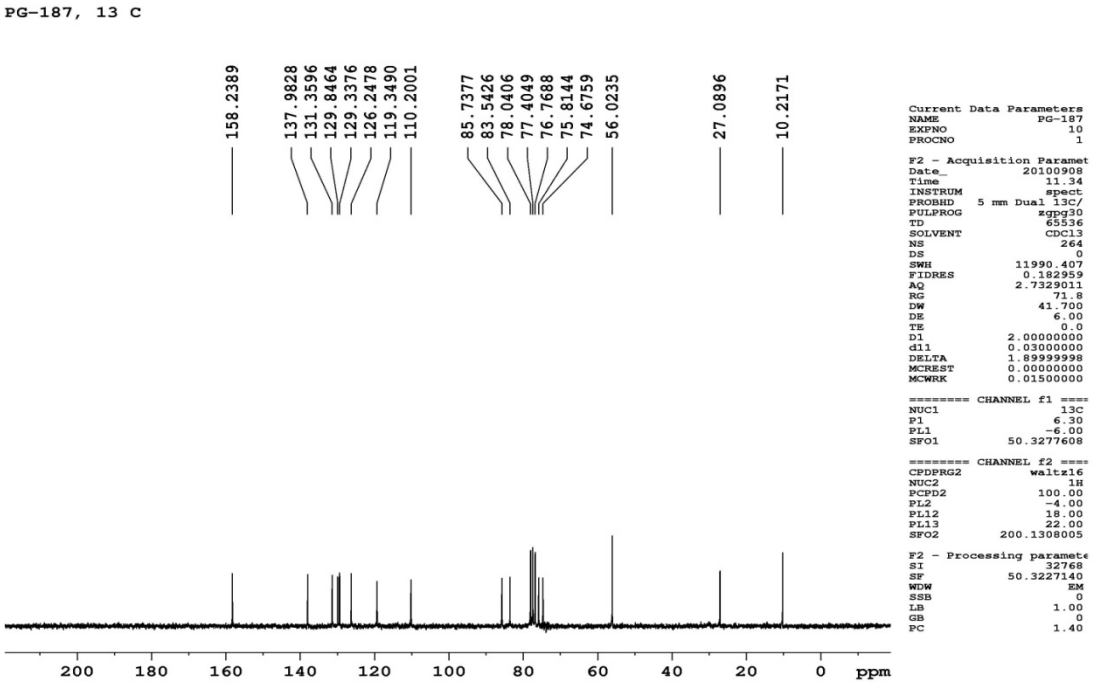
F2 - Acquisition Parameters
Date_ 20100830
Time 11.10
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 6188.119 Hz
FIDRES 0.094423 Hz
AQ 5.2953587 sec
RG 57
DW 80.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

---------- CHANNEL f1 ----------
NUC1 1H
P1 11.60 usec
PL1 -1.00 dB
SFO1 300.1318534 MHz

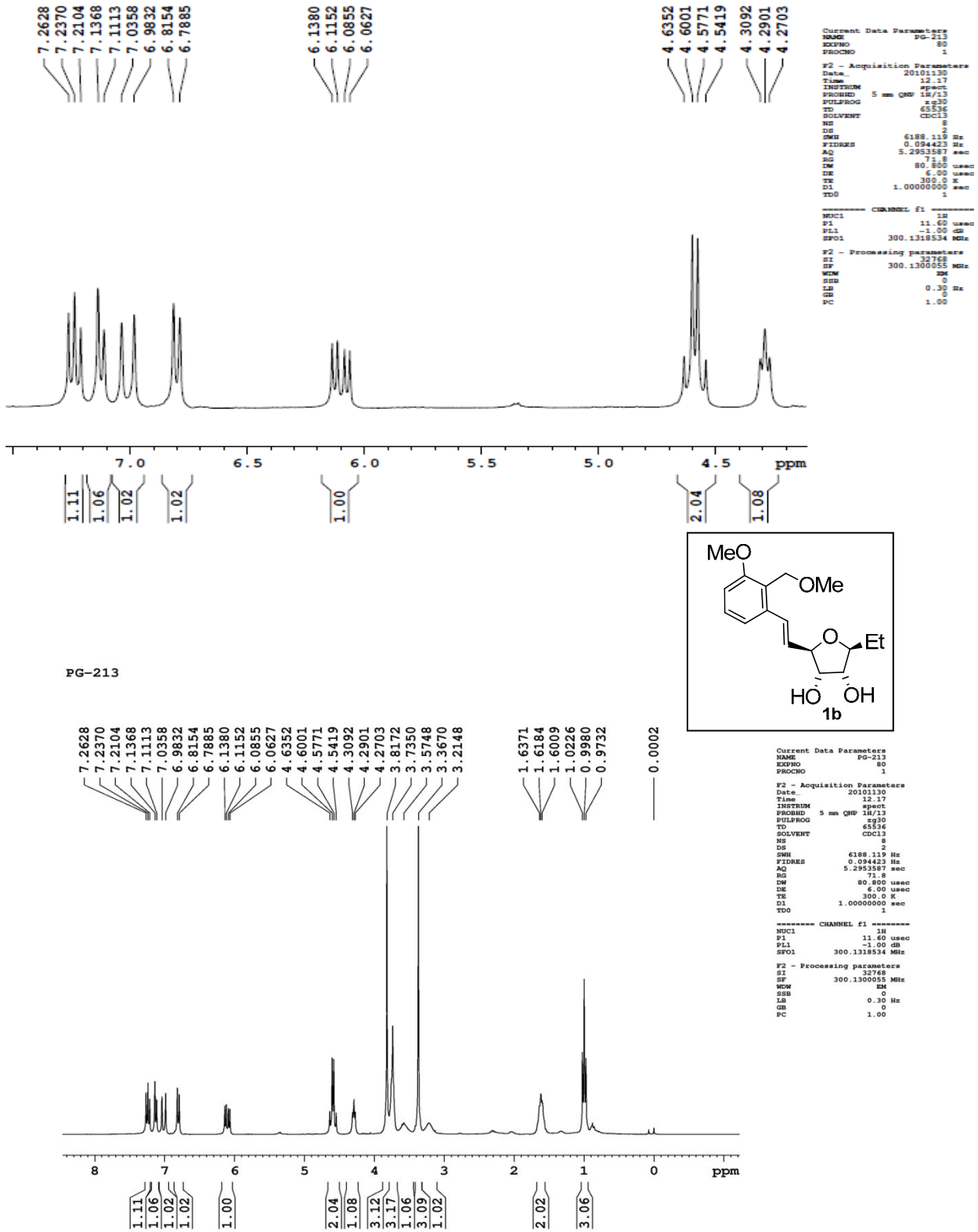
F2 - Processing parameters
SI 32768
SF 300.1300280 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

^{1}H spectrum of compound 1a

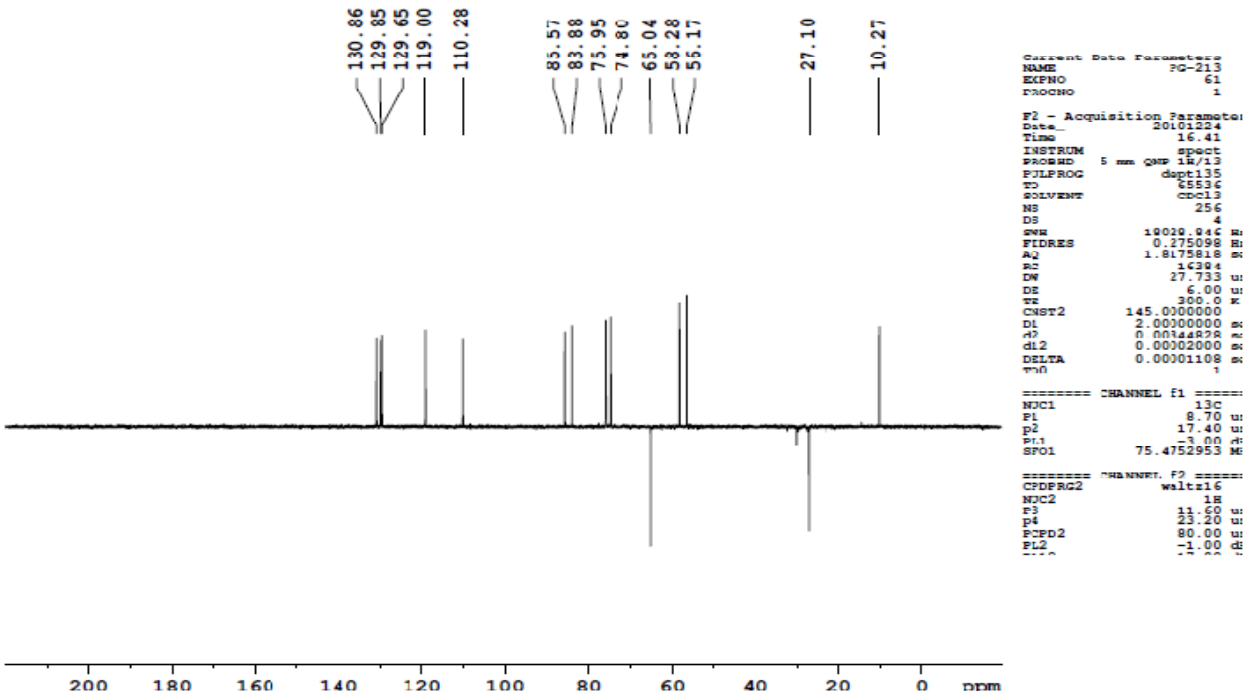


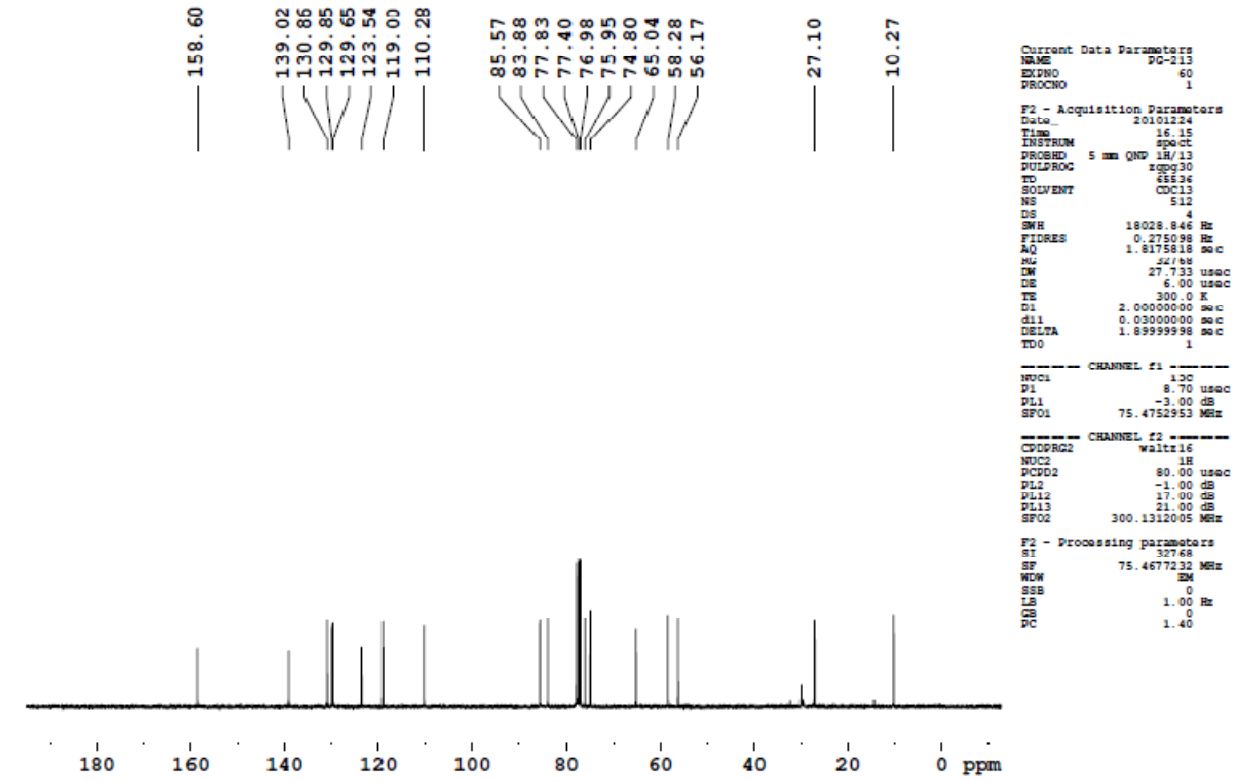


^{13}C spectrum of compound 1a

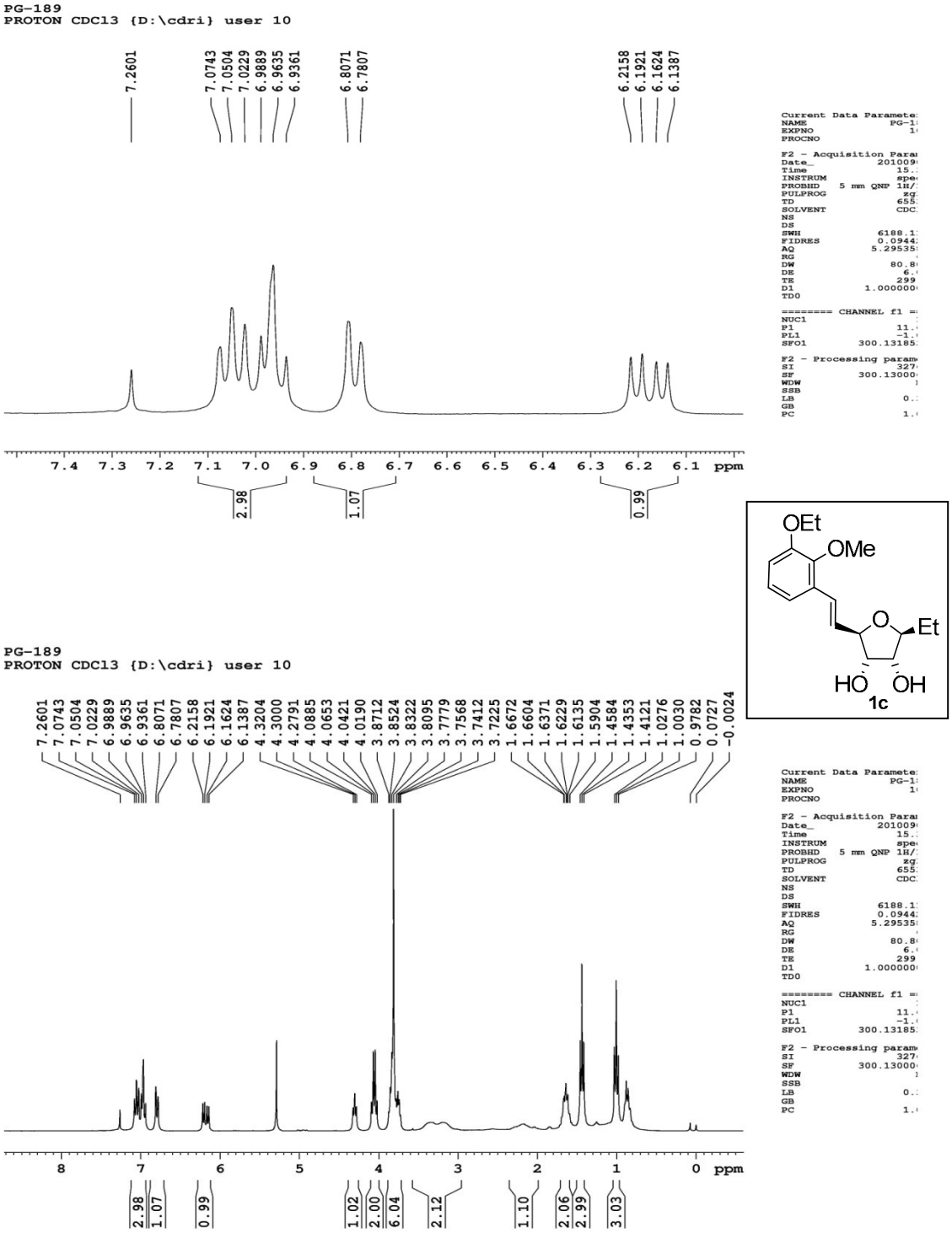


^{1}H spectrum of compound 1b

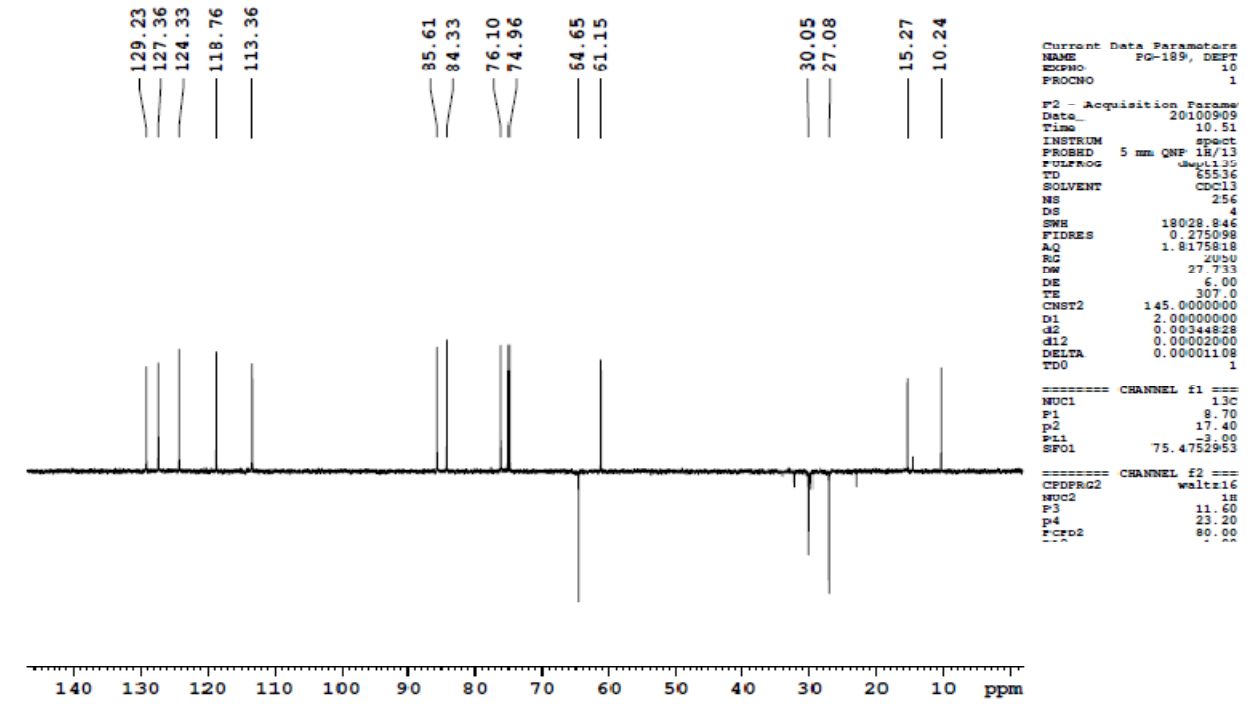


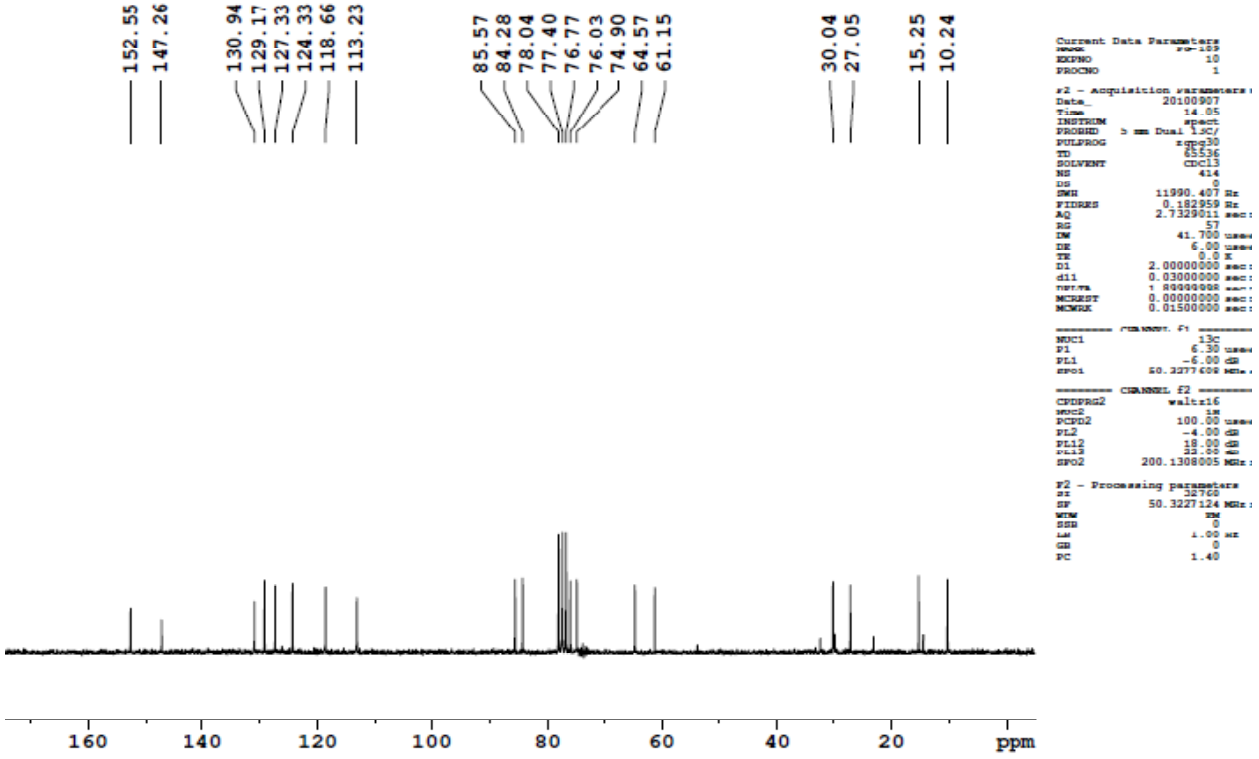


^{13}C spectrum of compound 1b

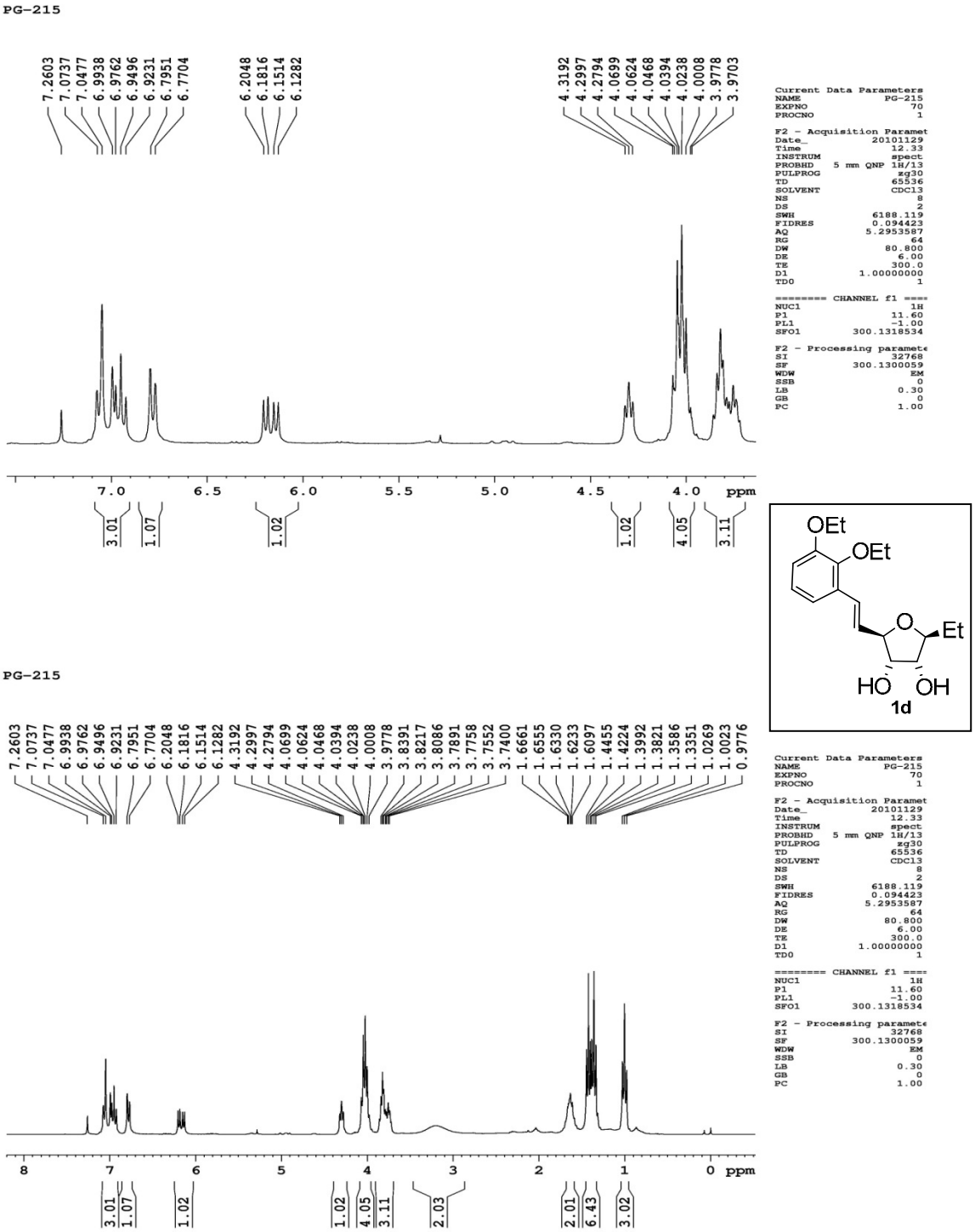


^{1}H spectrum of compound 1c

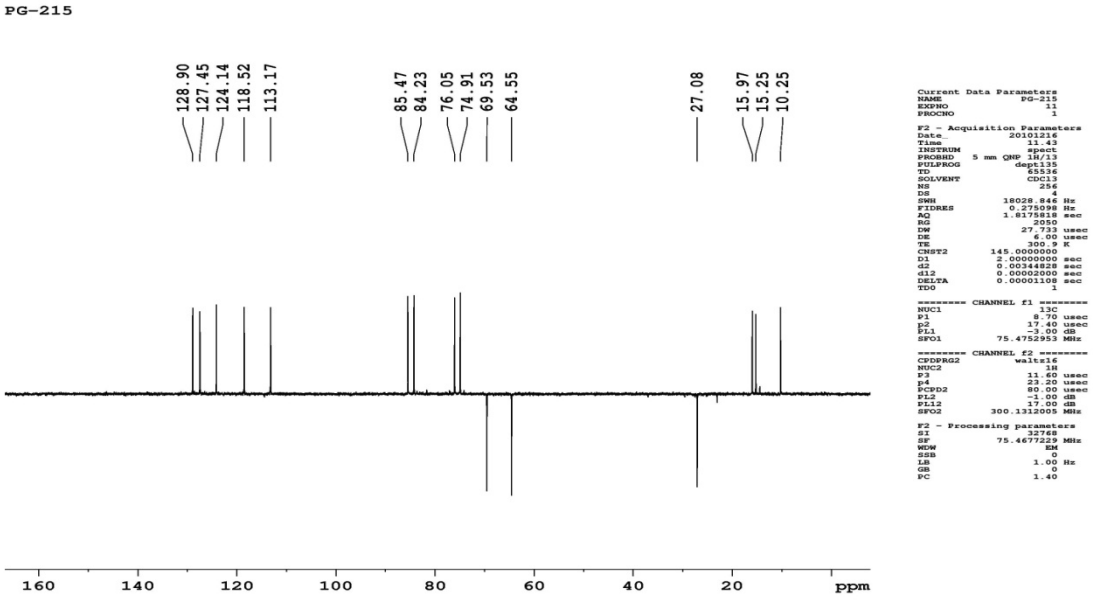


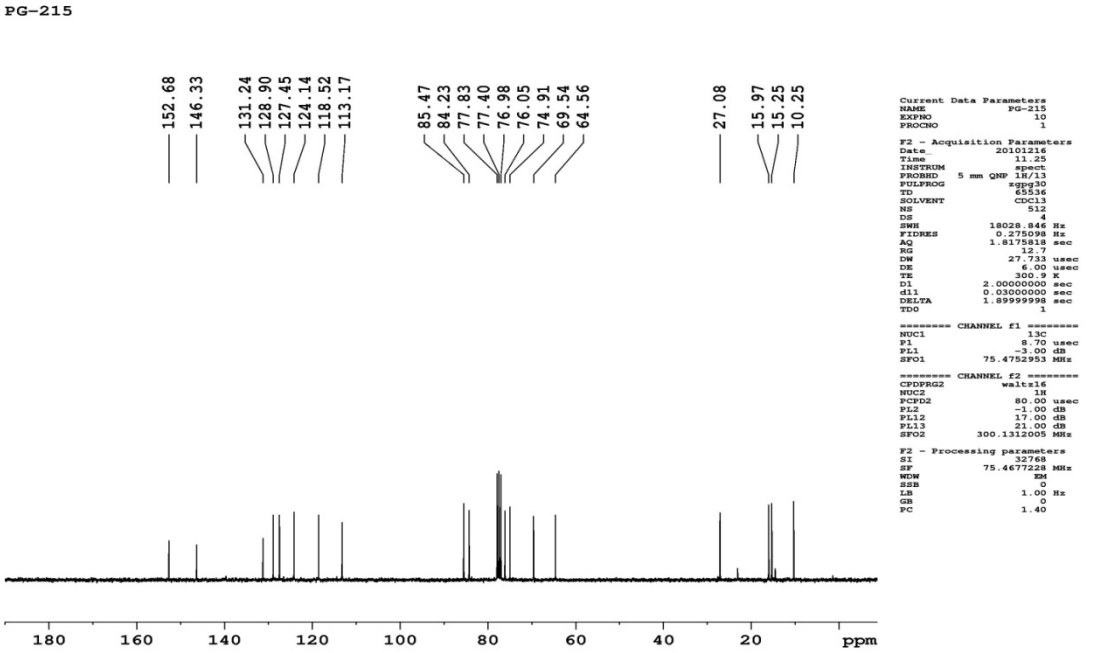


^{13}C spectrum of compound 1c

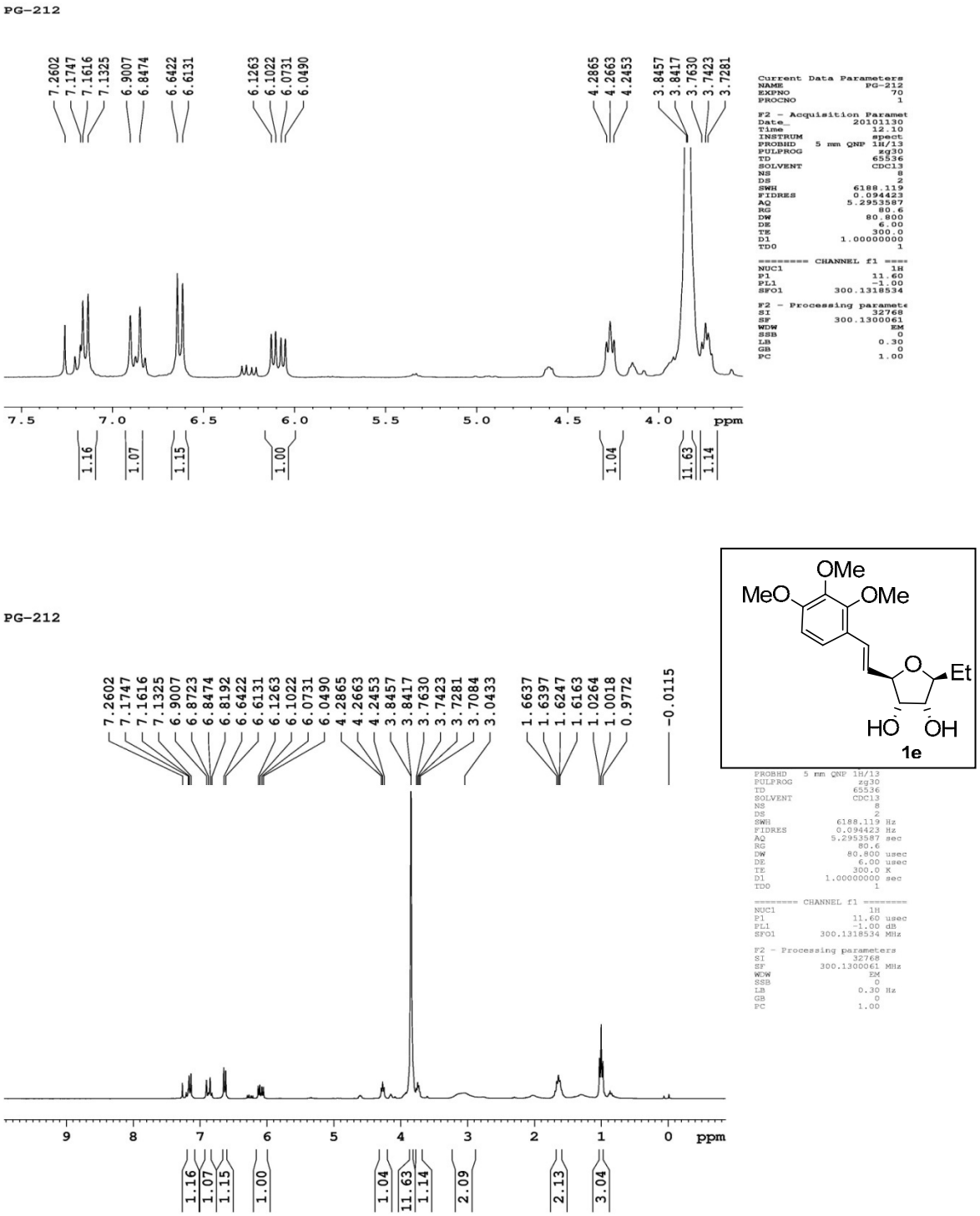


^{1}H spectrum of compound 1d

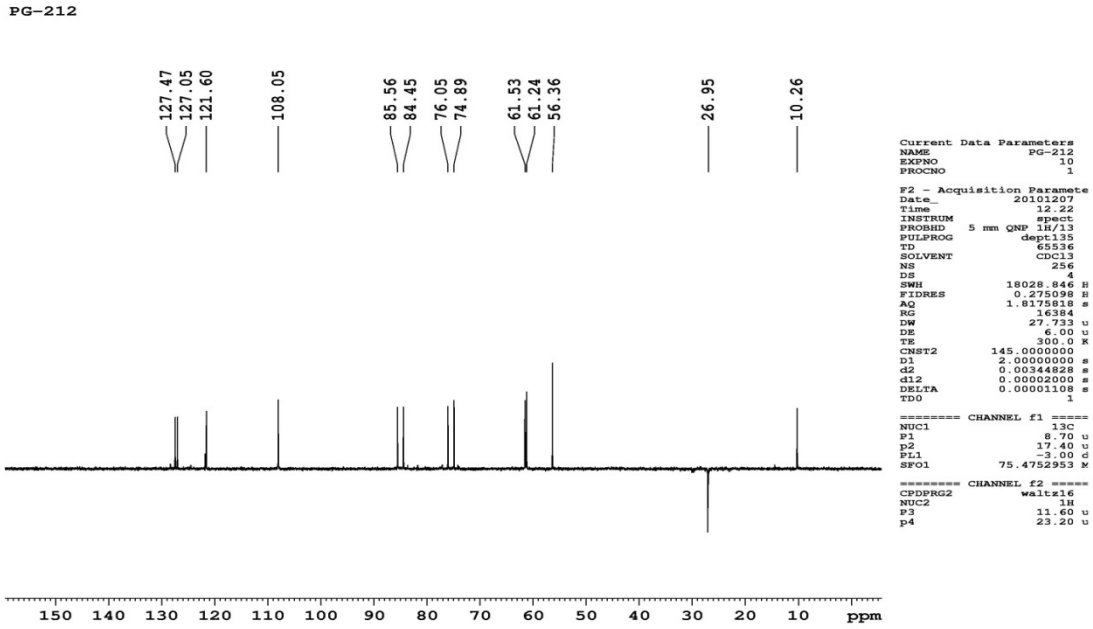


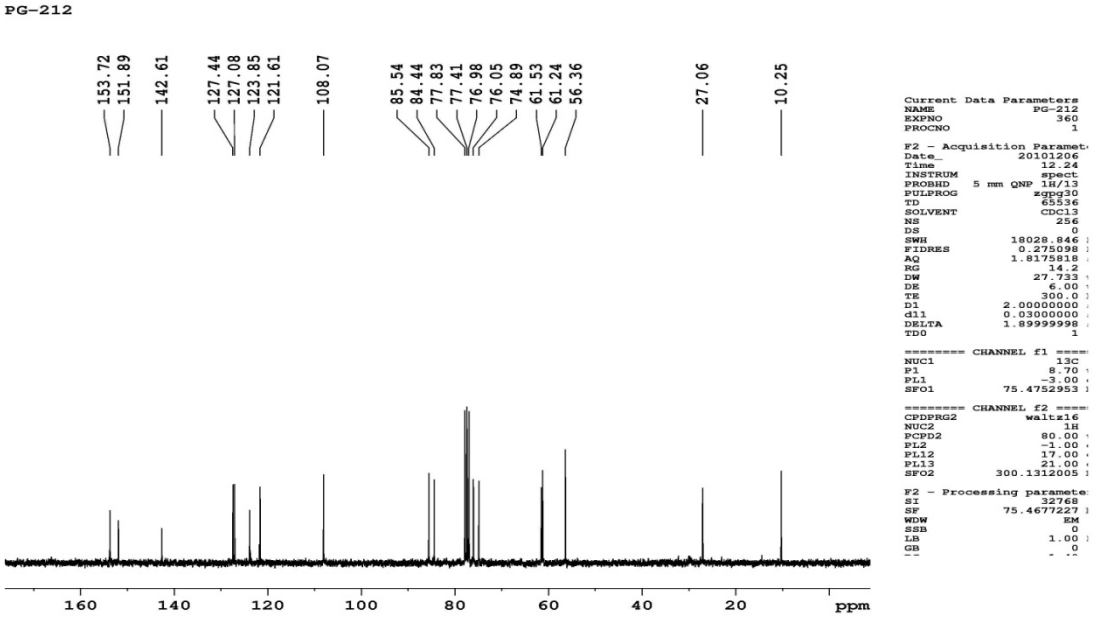


^{13}C spectrum of compound 1d

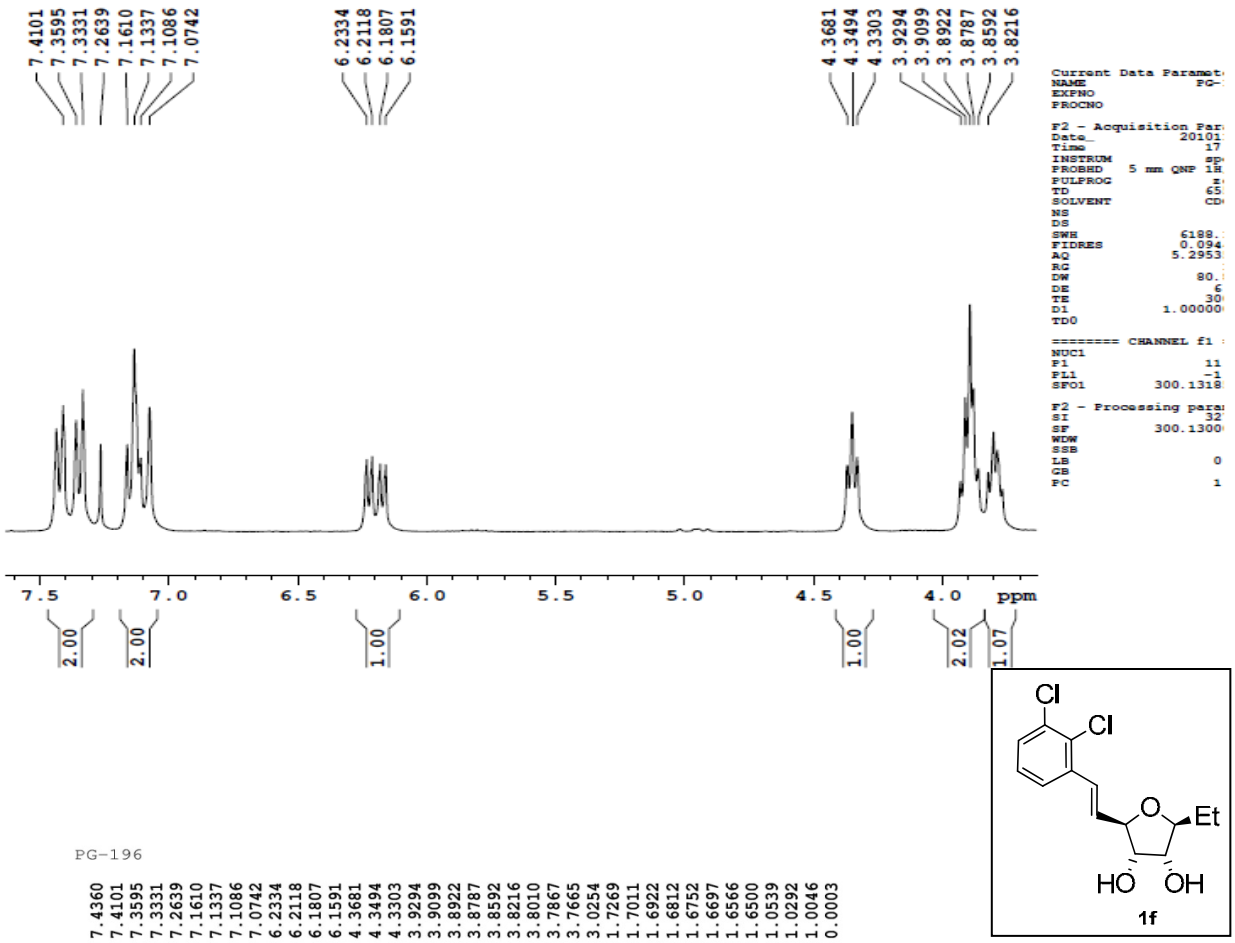


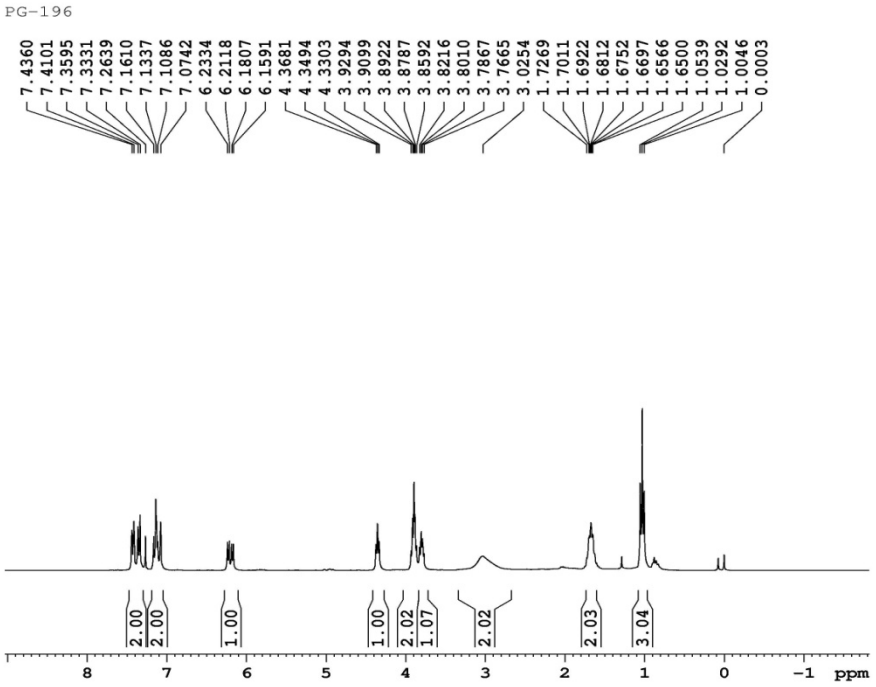
^{1}H spectrum of compound 1e



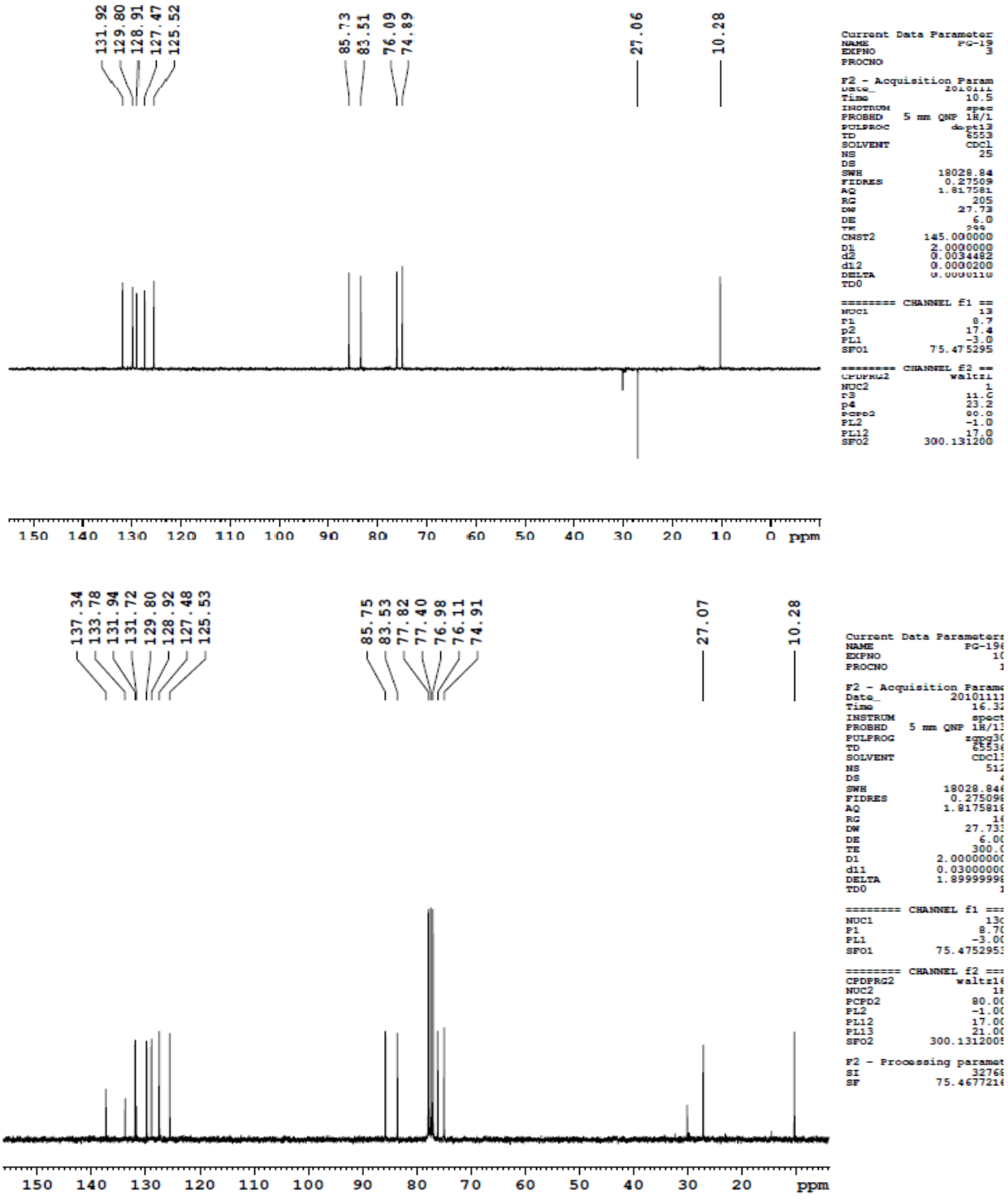


^{13}C spectrum of compound 1e

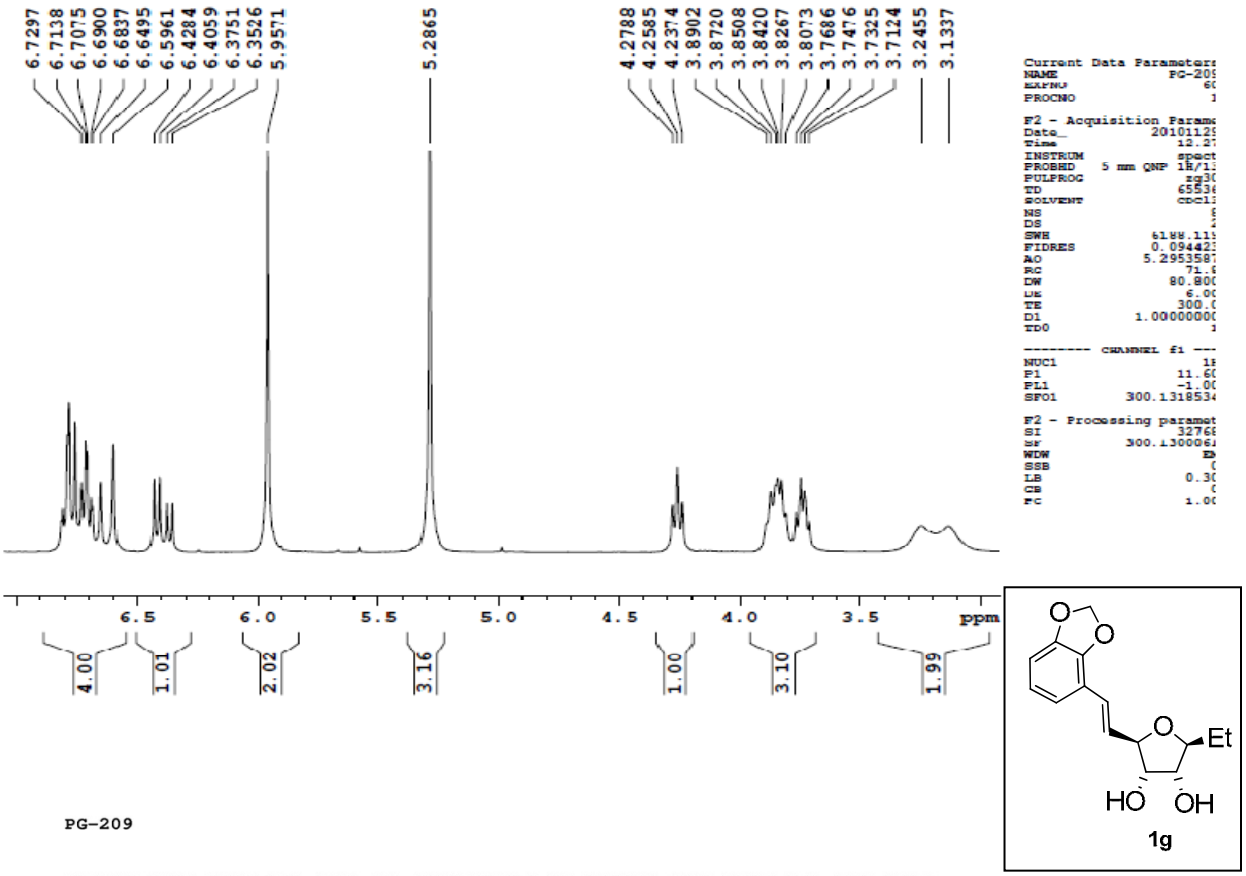




^{1}H spectrum of compound 1f



^{13}C spectrum of compound 1f



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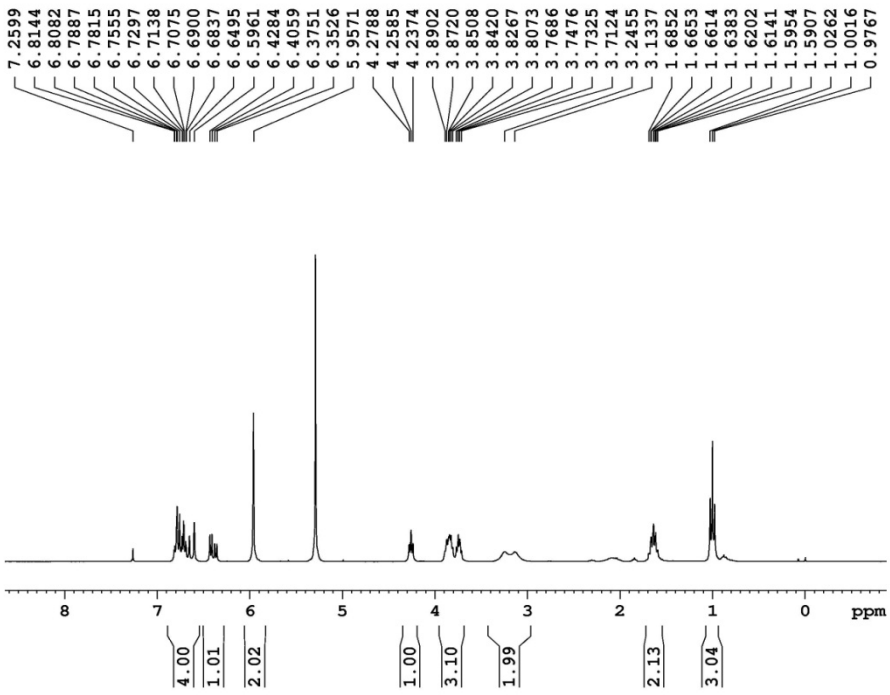
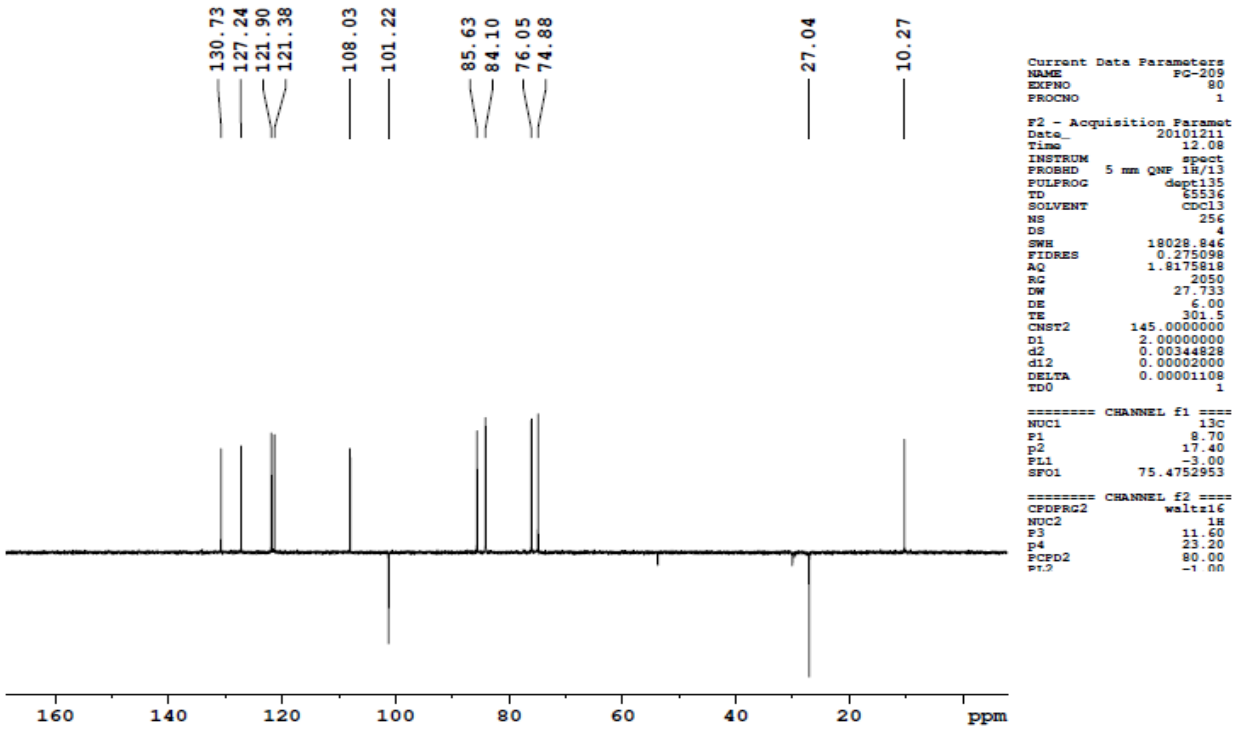
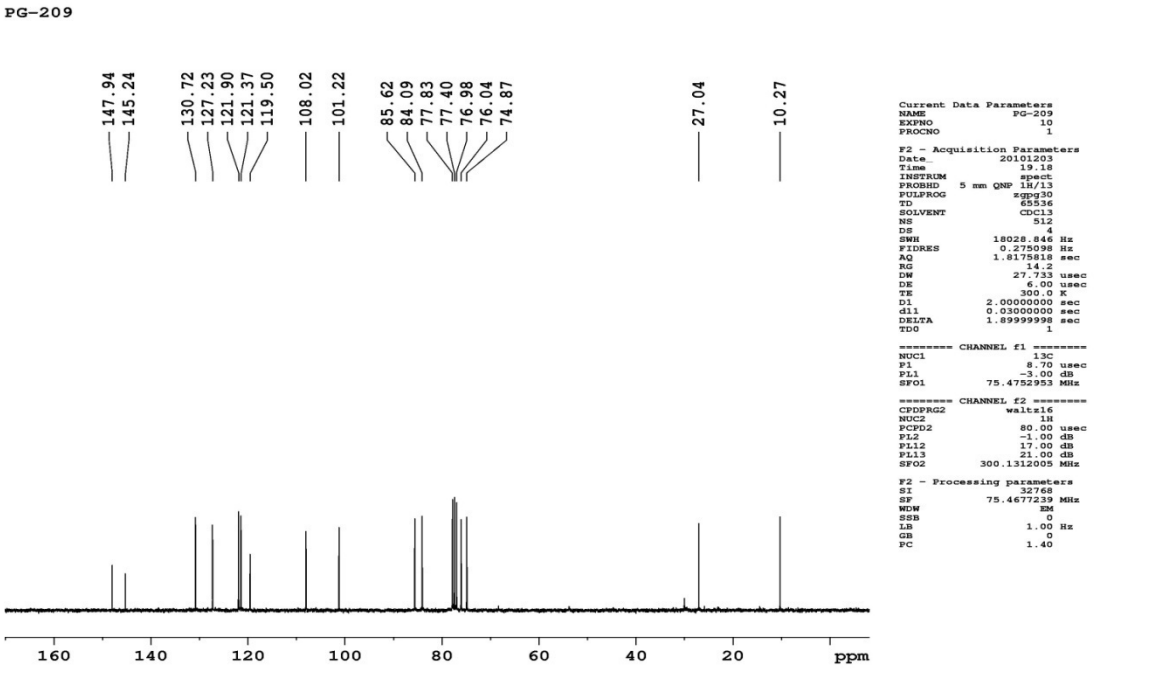
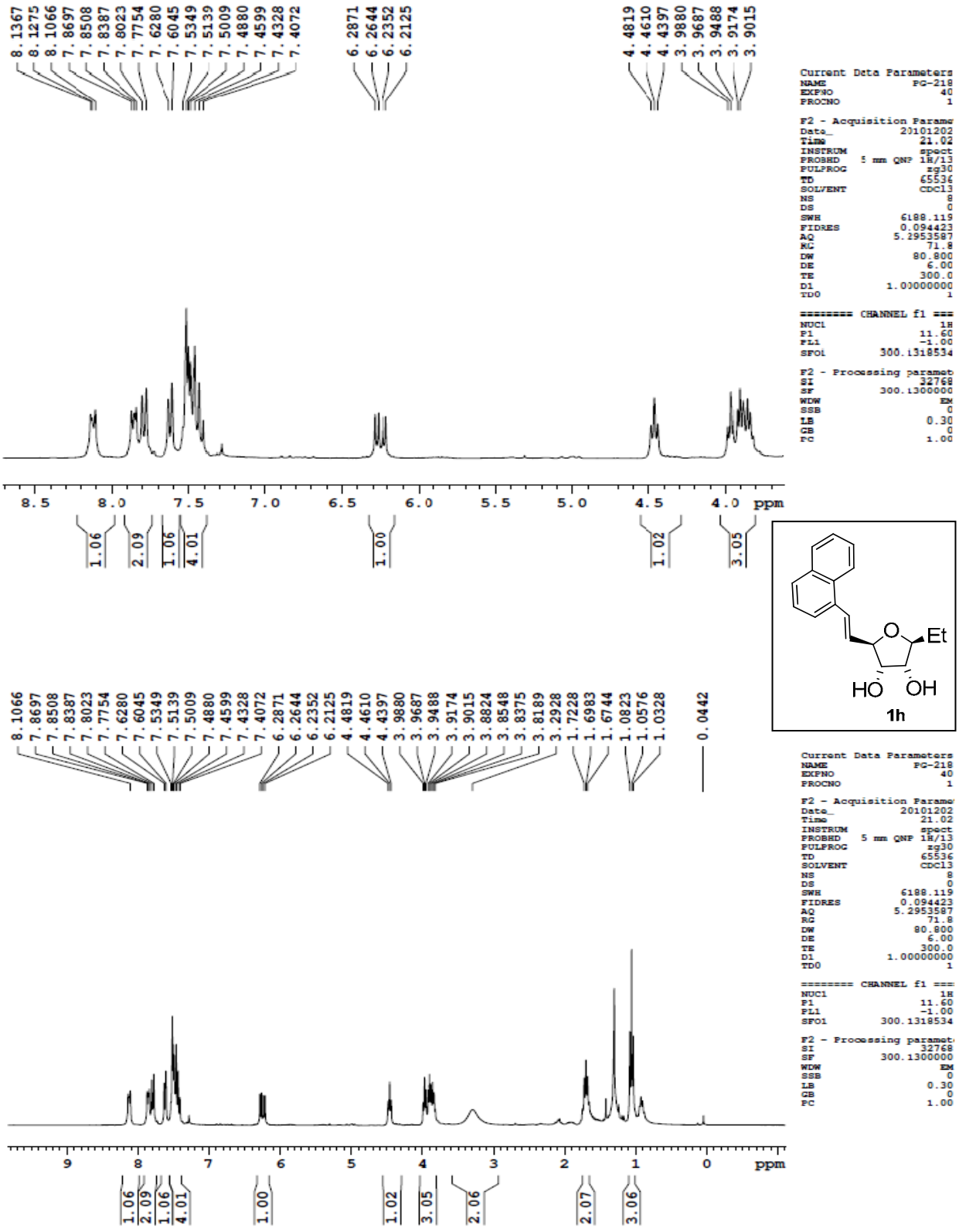


^{1}H spectrum of compound 1g

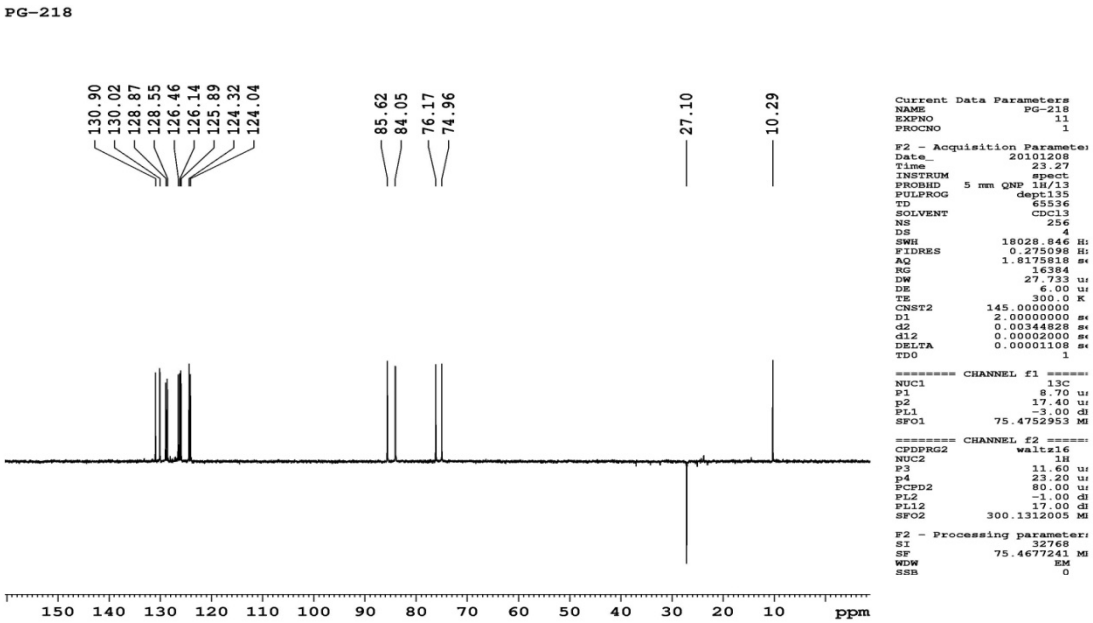


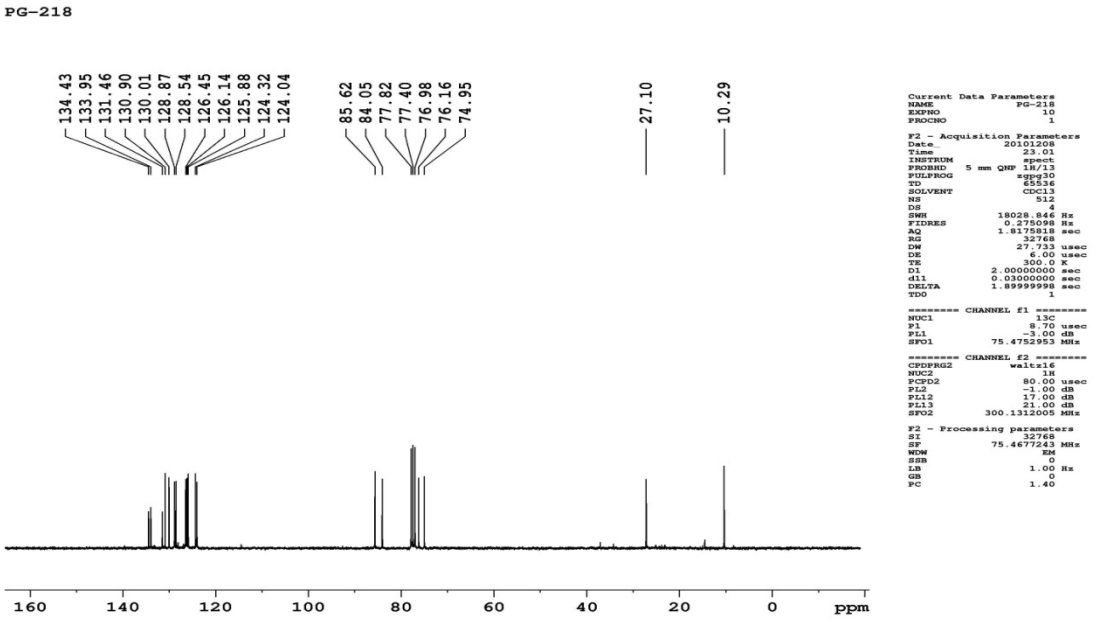


^{13}C spectrum of compound 1g

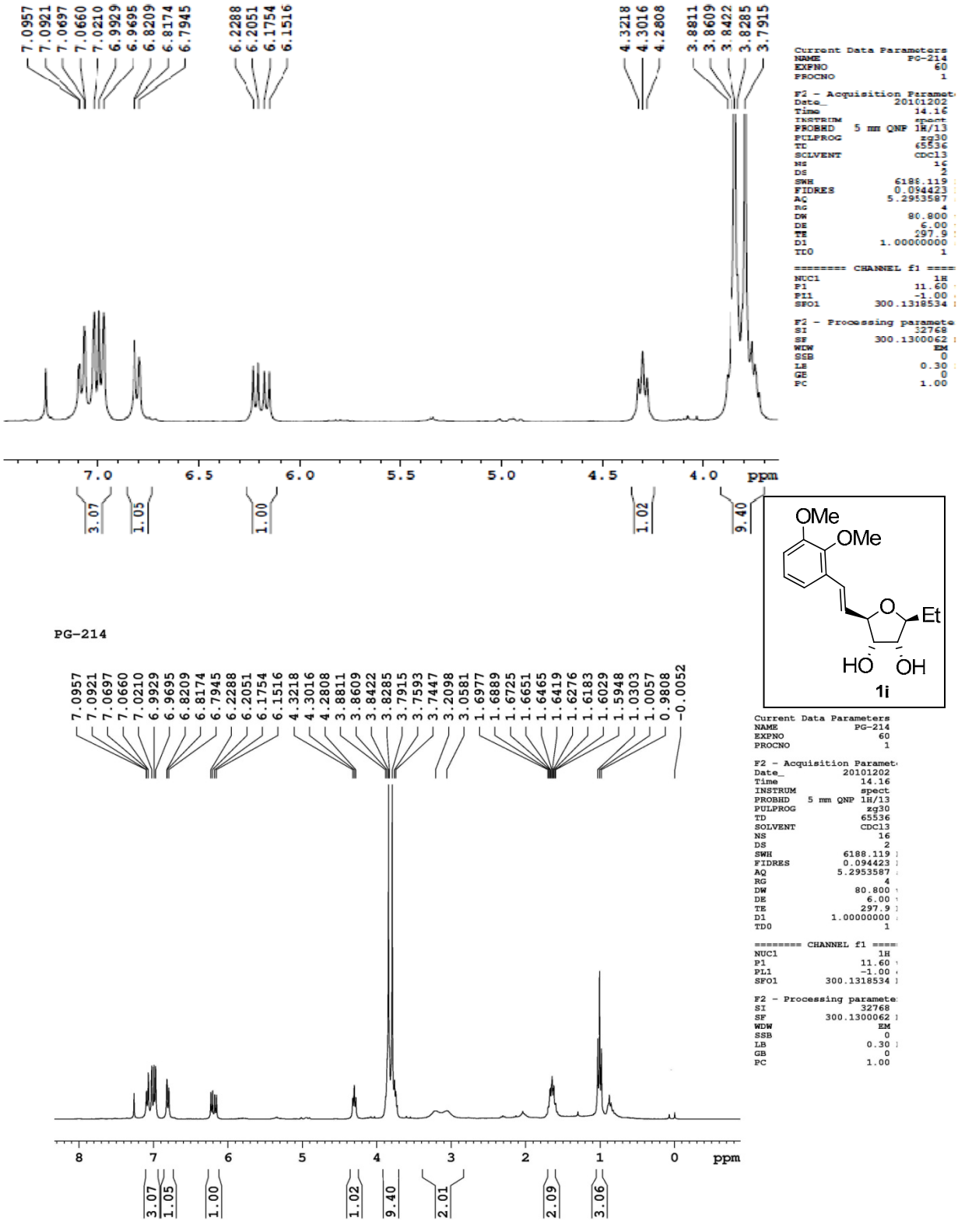


^{1}H spectrum of compound 1h

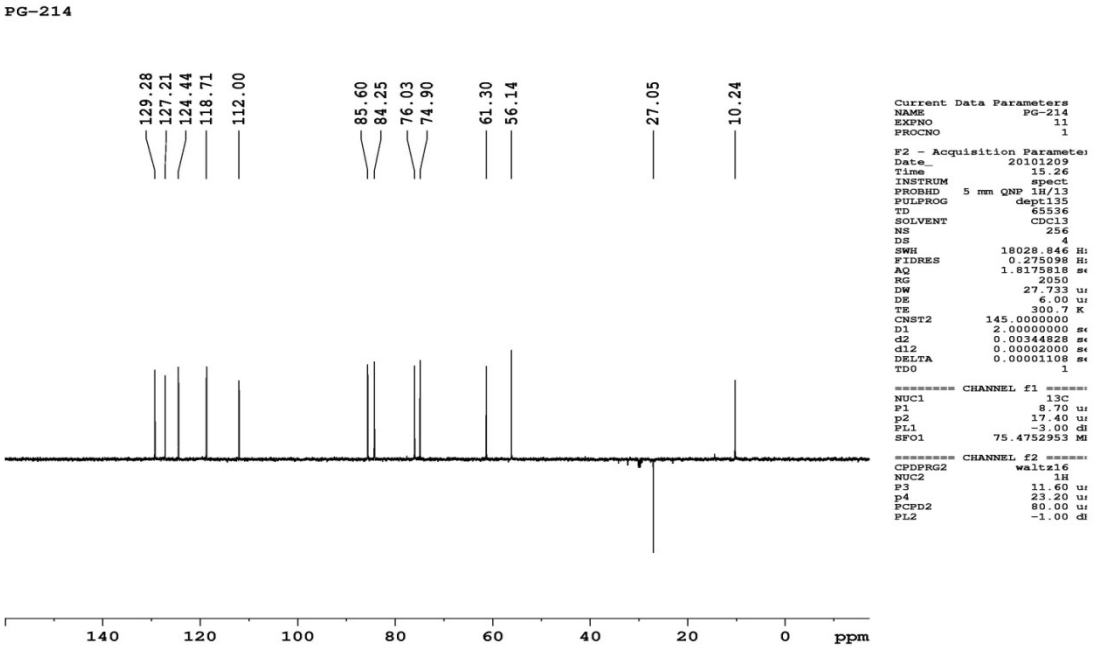


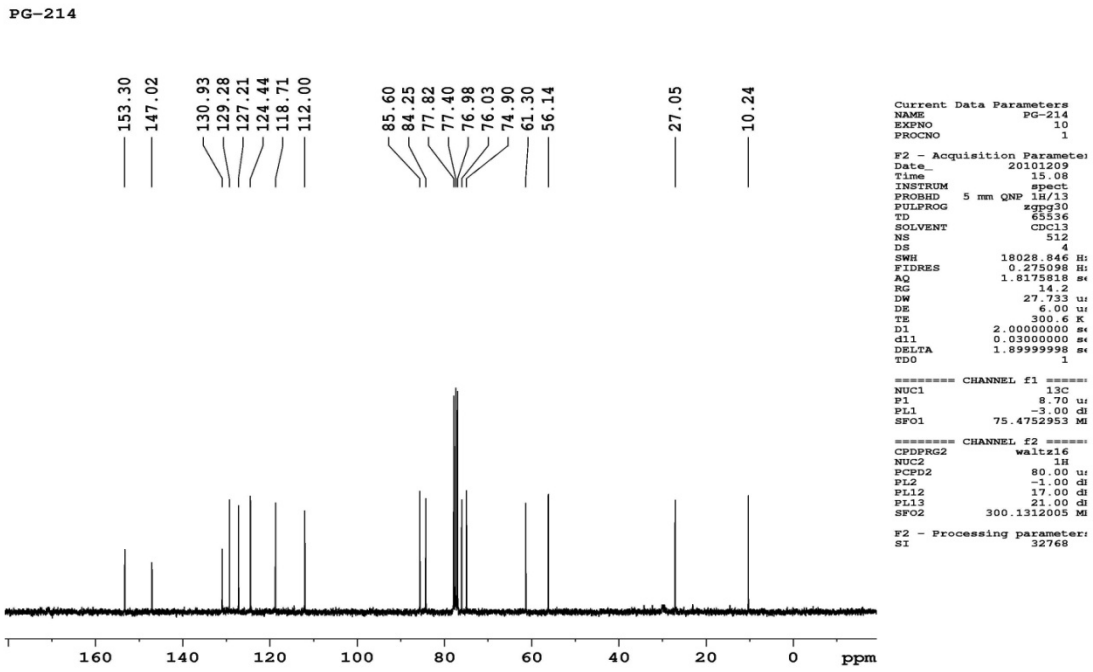


^{13}C spectrum of compound 1h

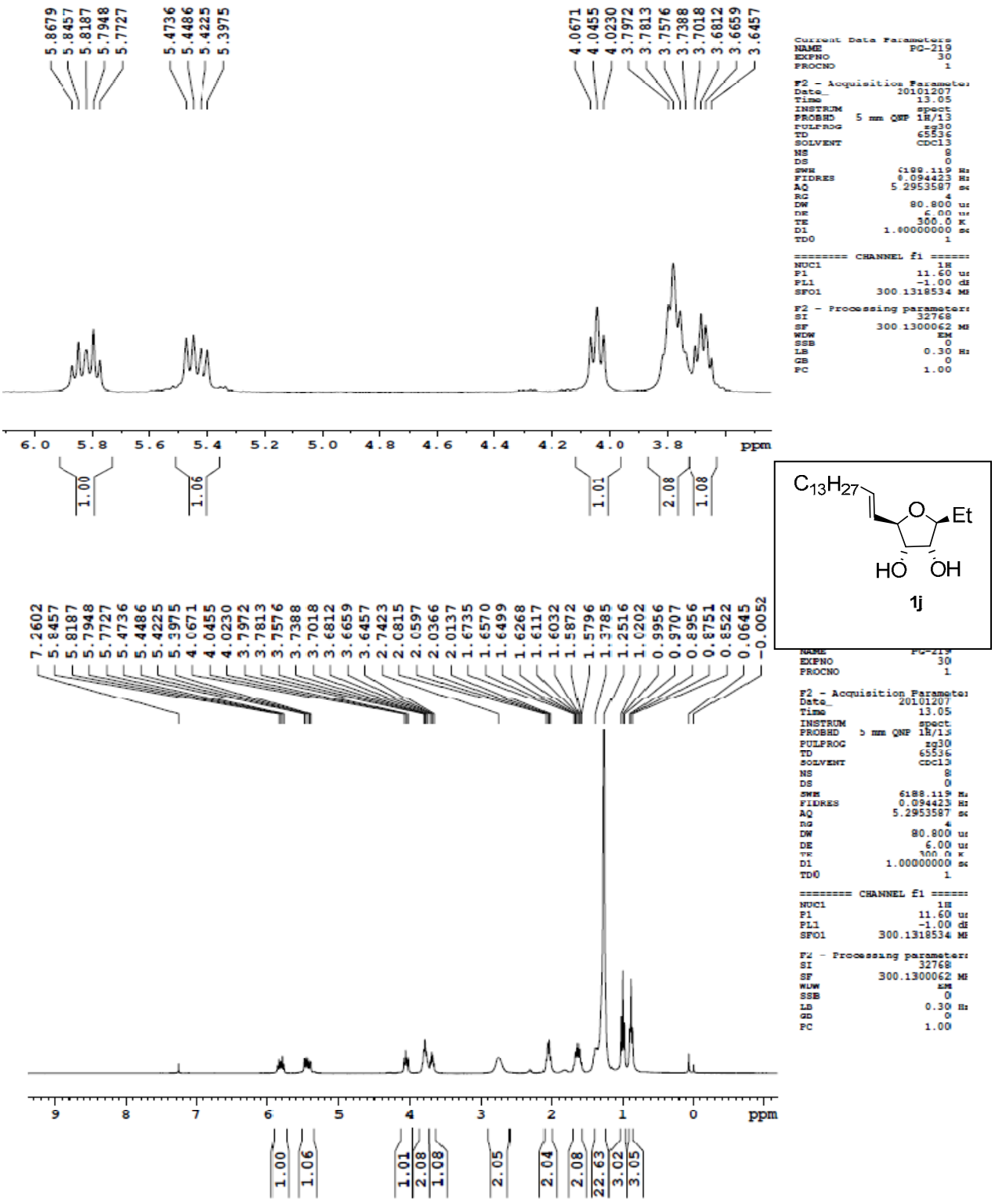


^{1}H spectrum of compound 1i

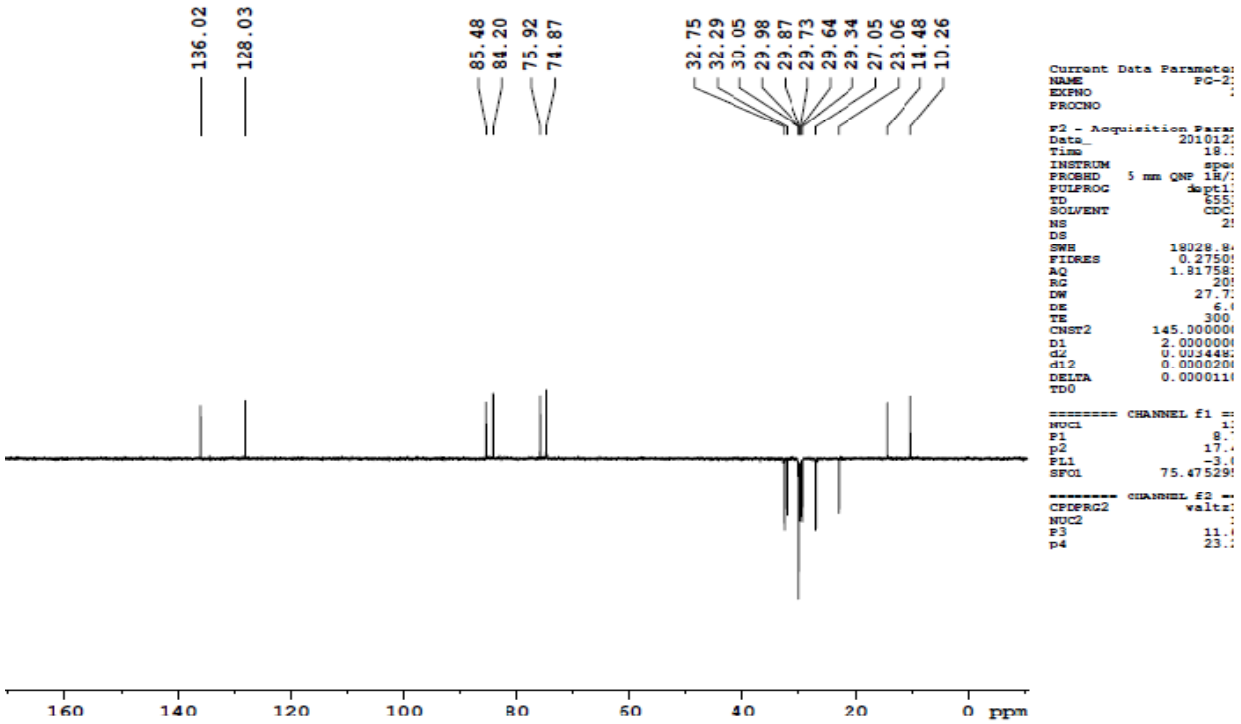


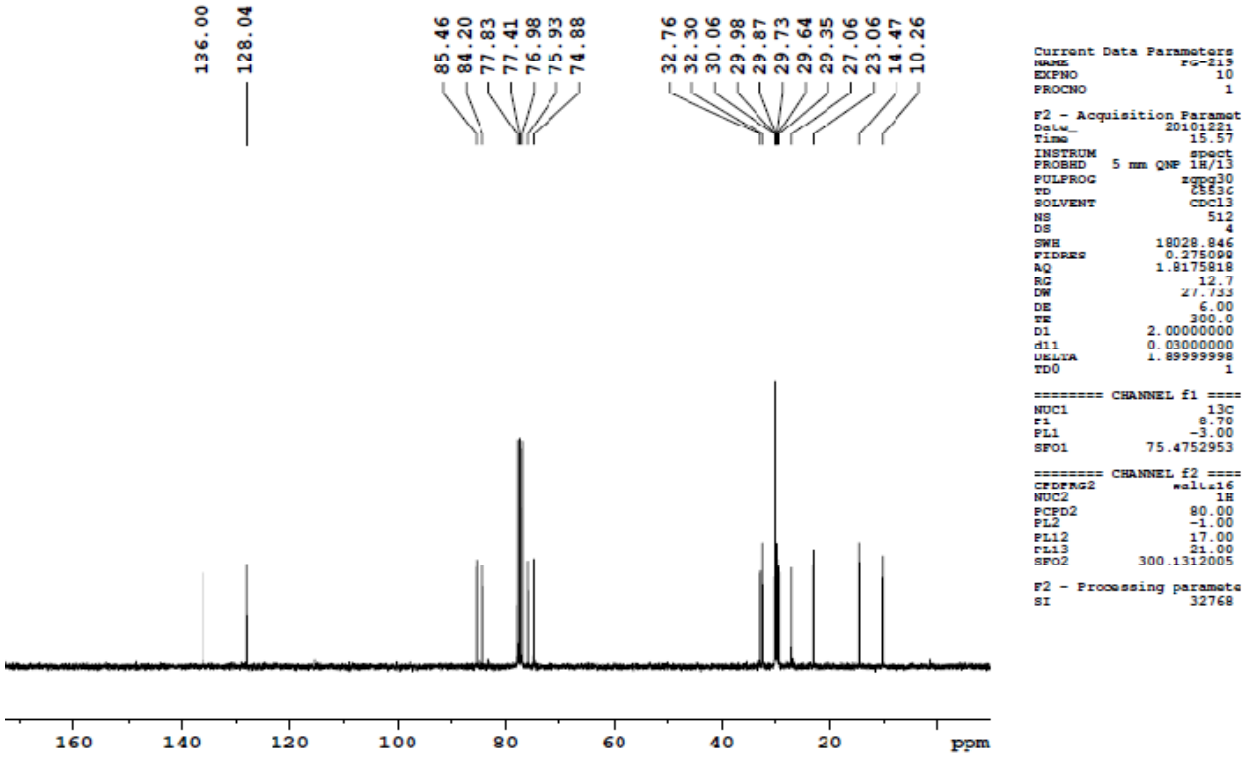


^{13}C spectrum of compound 1i



^{1}H spectrum of compound 1j





^{13}C spectrum of compound 1j