Electronic Supplementary Information (ESI)

Synthetic studies toward *anti*-influenza agent (-)-oseltamivir free base and (-)-methyl 3-*epi*-shikimate

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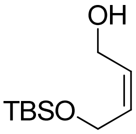
1. General information:

Solvents were purified and dried by standard procedures before use. Optical rotations were measured using sodium D line on a JASCO-181 digital polarimeter. ^{1}H NMR and ^{13}C NMR spectra were recorded on Brucker AC-200 spectrometer unless mentioned otherwise. Elemental analysis was carried out on a Carlo Erba CHNS-O analyzer. IR spectra were recorded on a Perkin-Elmer model 683 B and absorption is expressed in cm^{-1}. Purification was done using column chromatography (230-400 mesh).

2. Experimental section

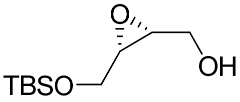
2.1. (*Z*)-4-(*tert*-Butyldimethylsilyloxy)but-2-en-1-ol (5)



To a solution of alcohol **4** (20.0 g, 227.27 mmol) in dry CH_2Cl_2 (700 mL) at 0 ^{o}C was added imidazole (23.21 g, 340.91 mmol) and *tert*-butyldimethylsilyl chloride (37.68 g, 250.0 mmol). The reaction mixture was then stirred at 0 ^{o}C for 6 h. After completion of reaction (monitored by TLC), it was diluted with CH_2Cl_2, washed with water, brine and dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure gave the crude product which was then purified by column chromatography with petroleum ether/EtOAc (9:1 v/v) to give **5** as a colorless liquid.

Yield: 73%; colorless liquid; **IR** ($CHCl_3$): 777, 837, 1033, 1088, 1255, 1471, 2857, 2929, 3354 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.04 (s, 6H), 0.86 (s, 9H), 2.2 (brs, 1H), 4.17-4.26 (m, 4H), 5.57-5.61 (m, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ -5.3, 18.3, 25.9, 58.6, 59.5, 130.1, 131.1; **Anal.** Calcd for $C_{10}H_{22}O_2Si$ requires C, 59.35; H, 10.96; Found: C, 59.38; H, 10.99%.

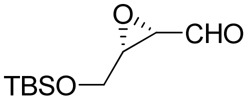
2.2. ((2*R*,3*S*)-3-((*tert*-Butyldimethylsilyloxy)methyl)oxiran-2-yl)methanol [(+)-6]



To a stirred suspension of powdered 4 Å molecular sieves (10.0 g) in dry CH_2Cl_2 (700 mL), titanium tetraisopropoxide (5.6 g, 20 mol %) was added under nitrogen atmosphere. The reaction mixture was cooled to -10 ºC and (+)-diethyl tartrate (4.4 g, 30 mol %) added and stirred for 10 min. To the above solution, *tert*-butyl hydroperoxide 5-6 molar solution in decane (35.2 mL, 2 equiv.) was added and stirred at -10 ºC for further 30 min, after which allylic alcohol **5** (20 g, 98.83 mmol) dissolved in dry CH_2Cl_2 (150 mL) was added and stirred at -10 ºC for 12 h. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with 1M NaOH (25 mL) with further stirring for 1 h at -10 ºC. The organic layer was then separated, washed with brine solution, dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude compound was purified by column chromatography using petroleum ether/EtOAc (7:3 v/v) to afford the allylic alcohol **(+)-6** as a colorless liquid.

Yield: 93%; colorless liquid; $[\alpha]_D^{25}$ +11.7 (*c* 2.0, $CHCl_3$); **IR** ($CHCl_3$): 777, 837, 1047, 1257, 1472, 2858, 2955, 3441 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.04 (s, 6H), 0.86 (s, 9H), 2.9 (brs, 1H), 3.13-3.20 (m, 2H), 3.65-3.73 (m, 4H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ -5.3, -5.4, 18.6, 25.8, 56.2, 56.5, 60.6, 61.6; **Anal.** Calcd for $C_{10}H_{22}O_3Si$ requires C, 55.00; H, 10.15; Found: C, 55.07; H, 10.18%.

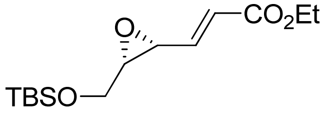
2.3. (2*S*,3*S*)-3-((*tert*-Butyldimethylsilyloxy)methyl)oxirane-2-carbaldehyde [(-)-7]



To a solution of alcohol **(+)-6** (15.0 g) in dry CH_2Cl_2 was added in one portion bis-acetoxy iodobenzene (24.34, 75.6 mmol) and TEMPO (1.07 g, 6.9 mmol). The reaction mixture was then allowed to stir at 25 ^oC for 1 h. After completion of reaction (monitored by TLC), the reaction mixture was quenched by addition of saturated solution of aq. ammoniumthiosulphate. The organic layer was separated, washed with brine and subjected to column chromatographic purification with petroleum ether/EtOAc (9:1 v/v) to afford the epoxy aldehyde **(-)-7**.

Yield: 95%; yellow liquid; $[\alpha]_D^{25}$ -41.7 (*c* 3.0, $CHCl_3$); **IR** ($CHCl_3$): 778, 838, 1099, 1256, 1472, 1720, 2858, 2930 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.08 (s, 6H), 0.89 (s, 9H), 3.34-3.44 (m, 2H), 3.90-4.09 (m, 2H), 9.47 (d, *J* = 4.2 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ -5.5, 18.2, 25.7, 57.4, 59.8, 60.1, 197.4; **Anal.** Calcd for $C_{10}H_{20}O_3Si$ requires C, 55.52; H, 9.32; Found: C, 55.60; H, 9.43%.

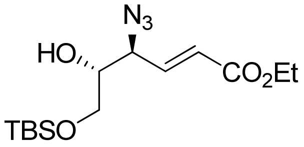
2.4. (*E*)-Ethyl3-((2*R*,3*S*)-3-((*tert*-butyldimethylsilyloxy)methyl)oxiran-2-yl)acrylate (8)



To a solution of aldehyde **(-)-7** (10.0 g, 46 mmol) in dry CH_2Cl_2 (250 mL) at 25 °C was added $Ph_3P=CHCO_2Et$ (24.0 g, 70.0 mmol) and the reaction mixture was stirred for 2 h. After completion of reaction (monitored by TLC), solvent was distilled off under reduced pressure and the crude mass on column chromatographic purification with petroleum ether/EtOAc (9:1 v/v) gave the α,β- unsaturated ester **8** as a slightly yellow colored liquid.

Yield: 92%; yellow liquid; $[\alpha]_D^{25}$ -13.7 (*c* 2.0, $CHCl_3$); **IR** ($CHCl_3$): 778, 838, 1035, 1260, 1722, 2858, 2930 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.07 (d, *J* = 6.4 Hz, 6H), 0.90 (s, 9H), 1.30 (t, d, *J* = 7.1 Hz, 3H), 3.32-3.35 (m, 1H), 3.56-3.58 (m, 1H), 3.70-3.78 (m, 2H), 4.20 (q, *J* = 7.1, 14.2 Hz, 2H), 6.11 (d, *J* = 15.8 Hz, 1H), 6.77-6.82 (m, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ -5.3, 14.2, 18.2, 25.8, 54.7, 59.2, 60.5, 60.9, 125.3, 141.3, 156.2; **Anal.** Calcd for $C_{14}H_{26}O_4Si$ requires C, 58.70; H, 9.15; Found: C, 58.78; H, 9.13%.

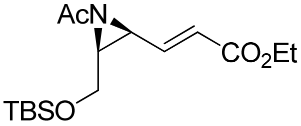
2.5. (4*S*,5*R*,*E*)-Ethyl 4-azido-6-(*tert*-butyldimethylsilyloxy)-5-hydroxyhex-2-enoate (9)



To a solution of epoxy ester **8** (9 g, 31.44 mmol) in DMF/EtOH/ H_2O (80:80:20 mL) were added NH_4Cl (10.2 g, 189 mmol) and NaN_3 (12.6 g, 189 mmol) at 0 °C. The mixture was then stirred at 25 °C for 10 h. After completion of reaction (monitored by TLC), EtOH was removed by rotary evaporation. The remaining solution was extracted with EtOAc (100 mL x 3). The combined organic layers were washed with brine (20 mL x 3) and dried (Na_2SO_4). After evaporation of the solvent, the residue was purified using coulumn chromatography with petroleum ether/EtOAc (7:3 v/v) to give the α,β- azido alcohol **9** as yellow colored liquid.

Yield: 85%; yellow liquid; $[\alpha]_D^{25}$ +15.1 (*c* 1.2.0, $CHCl_3$); **IR** ($CHCl_3$): 668, 765, 835, 1110, 1250, 1515, 1585, 1610, 1740, 2106, 2955, 3320 **cm**$^{-1}$; ^{1}**H NMR** (200 MHz, $CDCl_3$): δ 0.09 (s, 6H), 0.91 (s, 9H), 1.31 (t, d, *J* = 7.1 Hz, 3H), 2.46 (br.s, 1H), 3.60-3.73 (m, 3H), 4.17-4.28 (m, 3H), 6.07 (d, *J* = 15.7 Hz, 1H), 6.82-6.93 (m, 1H); ^{13}**C NMR** (50 MHz, $CDCl_3$): δ -5.4, 14.2, 18.2, 25.8, 60.7, 63.2, 64.2, 73.3, 124.8, 141.2, 165.4; **Anal.** Calcd for $C_{14}H_{27}N_3O_4Si$ requires C, 51.04; H, 8.26; N, 12.75; Found: C, 51.10; H, 8.23, N, 12.89%.

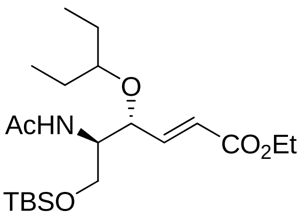
2.6. (*E*)-Ethyl 3-((2*S*,3*S*)-1-acetyl-3-((*tert*-butyldimethylsilyloxy)methyl)aziridin-2-yl)acrylate (10)



To a solution of azido alcohol **9** (5 g, 15.18 mmol) in toluene (30 mL) was added triphenylphosphine (4.38 g, 16.70 mmol) and the reaction mixture was refluxed for 3 h. After removal of the solvent under reduced pressure, diethylether (10 mL) was added, and the mixture cooled with ice-bath. The precipitated triphenylphosphine oxide was removed by filtration and the filtrate evaporated. This procedure was repeated to remove any traces of triphenylphosphine oxide. The residue obtained was then dissolved in dry CH_2Cl_2 cooled at 0 °C. To this solution was added Et_3N (3.10 g, 30.36 mmol), DMAP (5 mg) and acetic anhydride (2.32, 22.77 mmol) and the mixture stirred at 25 °C for further 45 minutes. After completion of reaction (monitored by TLC), the reaction mixture was quenched by addition of H_2O. The Organic layer was separated, washed with brine, dried (Na_2SO_4) and subjected to column chromatographic purification with petroleum ether/EtOAc (7:3 v/v) to afford the acetamide **10.**

Yield: 81%; yellow liquid; $[\alpha]_D^{25}$ +60.0 (*c* 2.0, $CHCl_3$); **IR** ($CHCl_3$): 973, 1187, 1256, 1356, 1472, 1643, 1715, 2858, 2930 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.05 (d, *J* = 2.1 Hz, 6H), 0.89 (s, 9H), 1.30 (t, *J* = 7.1 Hz, 3H), 2.15 (s, 3H), 2.82-2.91 (m, 1H), 3.15-3.22 (m, 1H), 3.56-3.80 (m, 2H), 4.15 (q, *J* = 7.2, 14.3 Hz, 2H), 6.09 (d, *J* = 15.7 Hz, 1H), 6.72-6.83 (m, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ -5.4, 14.2, 18.2, 23.1, 25.8, 39.8, 44.2, 60.5, 60.9, 125.2, 141.0, 165.3, 182.0; **Anal.** Calcd for $C_{16}H_{29}NO_4Si$ requires C, 58.68; H, 8.93; N, 4.28; Found: C, 58.73; H, 8.86, N, 4.35%.

2.7. (4*R*,5*R*,*E*)-Ethyl 5-acetamido-6-(*tert*-butyldimethylsilyloxy)-4-(pentan-3-yloxy)hex-2-enoate (11)

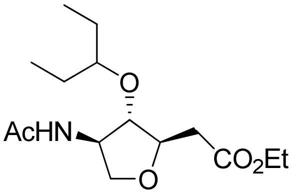


To a well stirred solution of acetamide **10** (4.00 g, 17.21 mmol) in 3-pentanol (30 mL), a solution of $BF_3 \cdot Et_2O$ in 3-pentanol was added at -10 °C, followed by stirring at this temperature for additional 30 minutes. After the completion of reaction (monitored by TLC), it was quenched with a saturated aq. solution of K_2CO_3. The organic layer is then washed with H_2O, brine and dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure gave crude product which on chromatographic separation with petroleum ether/EtOAc (6:4 v/v) gave title compound **11** as a light yellow colored liquid.

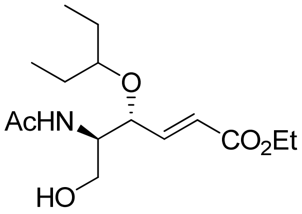
Yield: 75%; yellow liquid; $[\alpha]_D^{25}$ +23.6 (*c* 2.0, $CHCl_3$); **IR** ($CHCl_3$): 768, 838, 1199, 1345, 1472, 1645, 1720, 2959, 2930, 3320 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 0.06 (d, *J* = 3.3 Hz, 6H), 0.85-0.92 (m, 15H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.42-1.60 (m, 4H), 1.98 (s, 3H), 3.22-3.33 (m, 1H), 3.47-3.56 (m, 1H), 3.67-3.74 (m, 1H), 3.96-4.04 (m, 1H), 4.14 (q, *J* = 7.1, 14.3 Hz, 2H), 4.34-4.37 (m, 1H), 5.77 (d, *J* = 8.7 Hz, 1H), 5.94 (d, *J* = 15.8 Hz, 1H), 6.79 (m, 1H); **^{13}C NMR** (50 MHz, CDCl$_3$): δ -5.5, -5.3, 9.2, 9.3, 14.3, 18.1, 23.3, 25.2, 25.8, 26.1, 53.6, 60.3, 73.2, 80.6, 122.4, 146.8, 165.8, 169.6; **Anal.** Calcd for $C_{21}H_{41}NO_5Si$ requires C, 60.68; H, 9.94; N, 3.37; Found: C, 60.76; H, 10.06, N, 3.35%.

2.8. Ethyl 2-((2*R*,3*S*,4*R*)-4-acetamido-3-(pentan-3-yloxy)tetrahydrofuran-2-yl)acetate (12) and (4*R*,5*R*,*E*)-Ethyl 5-acetamido-6-hydroxy-4-(pentan-3-yloxy)hex-2-enoate (13)

To a well stirred solution of silyl ether **11** (200 mg, 0.48 mmol) was added 1 M solution of tetrabutylammonium fluoride (1 mL, 1 mmol) at 0 °C. The reaction mixture was stirred at this temperature for 2 h after which the solvent was removed under reduced pressure and the residue was subjected to column chromatography with petroleum ether/EtOAc (5:5 v/v) to afford furan derivative 12 as major product (65%) and free alcohol 13 as minor product (17%).

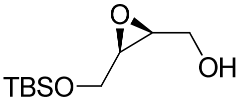


Compound 12; Yield: 65%; thick liquid; $[\alpha]_D^{25}$ +41.7 (*c* 2.0, CHCl$_3$); **IR** (CHCl$_3$): 1085, 1218, 1231, 1346, 1373, 1545, 1643, 1710, 2978, 3320, 3416 cm-1; **^{1}H NMR** (200 MHz, CDCl$_3$): 0.82-0.97 (m, 6H), 1.29 (t, *J* = 8.0 Hz, 3H), 1.45-1.54 (m, 4H), 2.00 (s, 3H), 2.60-2.87 (m, 2H), 3.36-3.52 (m, 1H), 3.81-3.92 (m, 3H), 4.12-4.29 (m, 3H), 6.55 (d, *J* = 6.5, Hz, 1H); **^{13}C NMR** (50 MHz, CDCl$_3$): δ 9.0, 9.9, 14.0, 23.0, 25.4, 26.2, 37.4, 56.3, 60.6, 72.3, 80.5, 81.3, 85.5, 169.4, 171.0; **Anal.** Calcd for $C_{15}H_{27}NO_5$ requires C, 59.78; H, 9.03; N, 4.65; Found: C, 59.83; H, 9.08, N, 4.70%.



Compound 13; Yield: 17%; thick liquid; $[\alpha]_D^{25}$ +34.8 (*c* 2.0, $CHCl_3$); **IR** ($CHCl_3$): 1165, 1274, 1266, 1306, 1455, 1485, 1659, 1710, 2968, 3311, 3377 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): 0.89 (t, *J* = 7.5 Hz, 6H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.43-1.57 (m, 4H), 2.01 (s, 3H), 2.59-2.76 (m, 1H), 3.25-3.34 (m, 1H), 3.58-3.78 (m, 2H), 3.94-4.04 (m, 1H), 4.18 (q, *J* = 7.1, 14.3 Hz, 2H), 4.32-4.36 (m, 1H), 5.98-6.14 (m, 2H), 6.77-6.88 (m, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 9.1, 9.7, 14.3, 23.3, 24.9, 26.2, 54.5, 60.6, 62.3, 74.8, 80.5, 123.2, 145.9, 165.8, 170.6; **Anal.** Calcd for $C_{15}H_{27}NO_5$ requires C, 59.78; H, 9.03; N, 4.65; Found: C, 59.91; H, 9.16, N, 4.79%.

2.9. ((2*S*,3*R*)-3-((*tert*-Butyldimethylsilyloxy)methyl)oxiran-2-yl)methanol [(-)-6]

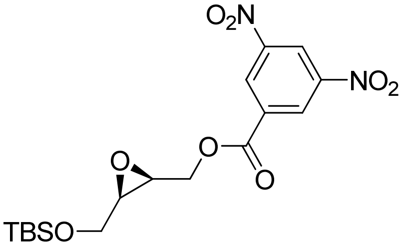


To a stirred suspension of powdered 4 Å molecular sieves (10.0 g) in dry CH_2Cl_2 (700 mL), titanium tetraisopropoxide (5.6 g, 20 mol %) was added under nitrogen atmosphere. The reaction mixture was cooled to -10 ºC and (+)-diethyl tartrate (4.4 g, 30 mol %) added and stirred for 10 min. To the above solution, *tert*-butyl hydroperoxide 5-6 molar solution in decane (35.2 mL, 2 equiv.) was added and stirred at -10 ºC for further 30 min, after which allylic alcohol **5** (20 g, 98.83 mmol) dissolved in dry CH_2Cl_2 (150 mL) was added and stirred at -10 ºC for 12 h. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with 1M NaOH (25 mL) with further stirring for 1 h at -10 ºC. The organic layer was then separated, washed with brine solution, dried over anhyd. Na_2SO_4 and concentrated under reduced pressure.

The crude compound was purified by column chromatography using petroleum ether/EtOAc (7:3 v/v) to afford the allylic alcohol **(-)-6** as a colorless liquid.

Yield: 93%; colorless liquid; $[\alpha]_D^{25}$ -11.1 (*c* 2.0, $CHCl_3$)

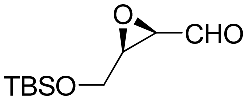
3,5-Dinitrobenzoate of alcohol (-)-6:



To a stirred solution of 3,5-dinitro benzoylchloride (230 mg, 1 mmol) in dry CH_2Cl_2 was added Et_3N (303 mg, 3 mmol) at 0 °C. To the cooled solution was added epoxy alcohol (218.4 mg, 1 mmol) in CH_2Cl_2 and DMAP (2 mg). The reaction is then stirred at 25 °C for further 2 h. After completion of the reaction (monitored by TLC), the reaction mixture is diluted with CH_2Cl_2 and quenched with H_2O. The organic layer is further washed with brine, dried (Na_2SO_4) and evaporated under vaccum. The crude product is then purified by column chromatography using petroleum ether/EtOAc (7:3 v/v) to afford the title compound as a pale yellow liquid.

Yield: 96%; yellow liquid; $[\alpha]_D^{25}$ -8.8 (*c* 3.0, $CHCl_3$); 97% ee HPLC analysis: Column: Chiracel OD-H (4.6X250 nm), mobile phase: hexane/isopropyl alcohol (80/20), flow rate: 0.5 mL/min, retention time: 46.24 min (-)-isomer, 58.29 min (+)-isomer; **IR** ($CHCl_3$): 721, 888, 1099, 1276, 1462, 1737, 2857, 2929, 3103 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.21 (s, 6H), 0.92 (s, 9H), 3.26-3.29, (m, 1H), 3.24-3.44 (m, 1H), 3.88-3.91 (m, 2H), 4.46-4.51 (m, 1H), 4.75-4.78 (m, 1H), 9.19 (s, 2H), 9.24 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ -5.3, 18.3, 25.8, 53.2, 56.3, 61.0, 65.2, 122.5, 129.5, 133.3, 148.7, 162.2; **Anal.** Calcd for $C_{17}H_{24}N_2O_8Si$ requires C, 49.50; H, 5.86; N, 6.79; Found: C, 49.53; H, 5.88; N, 6.80%.

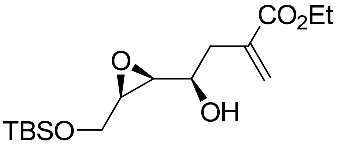
2.10. (2*R*,3*R*)-3-((*tert*-Butyldimethylsilyloxy)methyl)oxirane-2-carbaldehyde [(+)-7]



To a solution of alcohol **(+)-6** (15.0 g) in dry CH_2Cl_2 was added in one portion bis-acetoxy iodobenzene (24.34, 75.6 mmol) and TEMPO (1.07 g, 6.9 mmol). The reaction mixture was then allowed to stir at 25 °C for 1 h. After completion of reaction (monitored by TLC), the reaction mixture was quenched by addition of saturated solution of aq. ammoniumthiosulphate. The Organic layer was separated, washed with brine and subjected to column chromatographic purification with petroleum ether/EtOAc (9:1 v/v) to afford the epoxy aldehyde **(+)-7**.

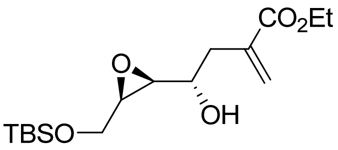
Yield: 95%; yellow liquid; $[\alpha]_D^{25}$ +43.0 (*c* 3.0, $CHCl_3$).

2.11. (*R*)-Ethyl 4-((2*S*,3*R*)-3-((*tert*-butyldimethylsilyloxy)methyl)oxiran-2-yl)-4-hydroxy-2-methylenebutanoate (14)



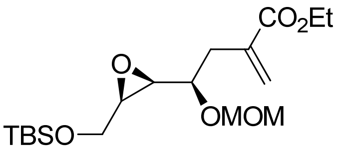
To a pre-cooled (0 °C), well stirred mixture of **(-)-6** (4 g, 18.51 mmol), Zn dust (3 g, 45 mmol) and ethyl 2-(bromoester)acrylate (8 g, 41 mmol) in 80 mL of THF was added a saturated solution of NH_4Cl (8 mL). The mixture was stirred for 10 h at ambient temperature until the aldehyde was totally consumed (monitored by TLC). The mixture was filtered and the precipitate was thoroughly washed with THF (3 x 10 mL). THF was then removed under vaccum and the remaining solution extracted with EtOAc. The organic layer is then washed with brine and dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure gave crude product which on chromatographic separation with petroleum ether/EtOAc (7:3 v/v) gave title compound *syn*-epoxy alcohol **14** along with minor amount of its corresponding diastereomer as a yellow colored liquid in 4:1 ratio.

Yield: 64%; yellow liquid; $[\alpha]_D^{25}$ -19.2 (*c* 2.0, $CHCl_3$); 98% ee HPLC analysis: Column: Chiracel OJ-H (4.6X250 nm), mobile phase: hexane/isopropyl alcohol (90/10), flow rate: 0.5 mL/min, retention time: 15.747 min (+)-isomer, 17.517 min (-)-isomer; **IR** ($CHCl_3$): 778, 838, 1097, 1256, 1472, 1715, 2857, 2956, 3471 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.10 (d, *J* = 3.3 Hz, 6H), 0.91 (s, 9H), 1.32 (t, *J* = 7.0 Hz, 3H), 2.58 (dd, *J* = 7.8, 14.1 Hz, 1H), 2.74 (dd, *J* = 3.8, 14.1 Hz, 1H), 2.91 (m, 1H), 3.12 (m, 1H), 3.18 (brs, 1H), 3.61 (m, 1H), 3.78 (dd, *J* = 5.8, 11.8 Hz, 1H), 3.90 (dd, *J* = 5.8, 11.5 Hz, 1H), 4.24 (q, *J* = 7.3, 14.3 Hz, 2H), 5.76 (s, 1H), 6.29 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ -5.4, -5.3, 14.1, 18.2, 25.8, 37.8, 56.1, 58.2, 60.9, 61.9, 69.0, 127.9, 136.5, 167.6; **Anal.** Calcd for $C_{16}H_{30}O_5Si$: C, 58.15; H, 9.15; Found: C, 58.20; H, 9.12%.



Yield: 16%; yellow liquid; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.08 (d, *J* = 3.0 Hz, 6H), 0.90 (s, 9H), 1.32 (t, *J* = 7.2 Hz, 3H), 2.54-2.60 (m, 2H), 2.99 (dd, *J* = 4.2, 7.3 Hz, 1H), 3.14 (dd, *J* = 4.7, 10.5 Hz, 1H), 3.68-3.81 (m, 2H), 4.20 (q, *J* = 7.1, 14.3 Hz, 2H), 5.72 (s, 1H), 6.27 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ -5.3, -5.2, 14.2, 18.3, 25.9, 37.1, 57.7, 59.8, 60.9, 61.7, 68.7, 128.1, 136.2, 166.9.

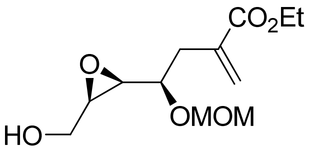
2.12. (*R*)-Ethyl 4-((2*S*,3*R*)-3-((*tert*-butyldimethylsilyloxy)methyl)oxiran-2-yl)-4-(methoxymethoxy)-2-methylenebutanoate (15)



To a solution of compound **14** (3 g, 9.9 mmol) in dry CH_2Cl_2 (50 mL) was added DIPEA (1.3 g, 29.7 mmol), followed by addition of MOMCl (1 mL, 19.8 mmol) at 0 °C. The mixture was stirred for 10 h and H_2O (10 mL) was added to quench the reaction. The aqueous layer was extracted with CH_2Cl_2 (30 mL x 3). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by chromatography (petroleum ether/ EtOAc = 9/1) to give MOM protected compound **15** as a colorless oil.

Yield: 90%; colorless liquid; $[\alpha]_D^{25}$ +2.9 (*c* 1.0, $CHCl_3$); **IR** ($CHCl_3$): 778, 838, 1150, 1257, 1716, 2857, 2955 cm^{-1}; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.08 (d, *J* = 2.9 Hz, 6H), 0.90 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H), 2.53-2.57 (m, 2H), 2.96-3.09 (m, 2H), 3.32 (s, 3H), 3.62-3.87 (m, 3H), 4.16 (q, *J* = 7.2, 14.4 Hz, 2 H), 4.56 (dd, *J* = 6.7 Hz, 1H), 4.84 (dd, *J* = 6.8 Hz, 1H), 5.68 (s, 1H), 6.25 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ -5.4, -5.2, 14.2, 18.3, 25.9, 35.4, 55.5, 55.6, 59.1, 60.7, 61.8, 73.3, 95.3, 127.7, 136.2, 166.4; **Anal.** Calcd for $C_{18}H_{34}O_6Si$: C, 57.72; H, 9.15; Found: C, 57.78; H, 9.12%.

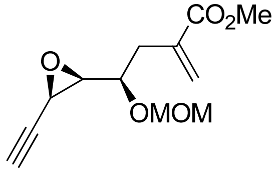
2.13. (*R*)-Ethyl 4-((2*S*,3*R*)-3-(hydroxymethyl)oxiran-2-yl)-4-(methoxymethoxy)-2-methylenebutanoate (16)



To a well stirred solution of silyl ether **15** (1.1 g, 2.94 mmol) was added 1 M solution of tetrabutylammonium fluoride (6.2 mL, 5.87 mmol) at 0 °C. The reaction mixture was stirred at this temperature for 2 h after which the solvent was removed under reduced pressure and the residue was subjected to column chromatography with petroleum ether/EtOAc (6:4 v/v) to afford free alcohol **16** oily liquid.

Yield: 88%; colorless liquid; $[\alpha]_D^{25}$ +4.1 (*c* 0.6, $CHCl_3$); **IR** ($CHCl_3$, cm^{-1}): 919, 1048, 1305, 1410, 1632, 1716, 2983.3, 3453; **^{1}H NMR** (200 MHz, $CDCl_3$): 1.22 (t, *J* = 7.1 Hz, 3H), 2.44 (dd, *J* = 9.0, 14.0 Hz, 1H), 2.68 (dd, *J* = 3.4, 13.6 Hz, 1H), 2.83 (m, 1H), 3.09 (m, 1H), 3.24 (brs, 1H), 3.30 (s, 3H), 3.55 (m, 2H), 3.79 (m, 1H), 4.11 (q, *J* = 7.1, 13.3 Hz, 2H), 4.52 (d, *J* = 7.2 Hz, 1H), 4.66 (d, *J* = 7.2 Hz, 1H), 5.59 (s, 1H), 6.16 (s, 1H); ^{13}**C NMR** (50 MHz, CDCl$_3$): δ 14.2, 36.5, 55.4, 56.1, 57.8, 59.9, 60.7, 72.6, 96.0, 127.7, 136.4, 166.7; **Anal.** Calcd for $C_{12}H_{20}O_6$ requires C, 55.37; H, 7.74; Found: C, 55.43; H, 7.90%.

2.14. (*R*)-Methyl 4-((2*S*,3*R*)-3-ethynyloxiran-2-yl)-4-(methoxymethoxy)-2-methylenebutanoate (19)



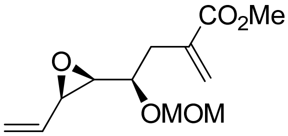
To a solution of epoxy alcohol **16** (1.4 g, 4 mmol) in DMSO (5 mL) in a round-bottomed flask was added IBX (1.68 g, 6 mmol) in one portion and the reaction mixture was stirred

for 1 h at ambient temperature. The reaction mixture was quenched with diethylether (5 mL), H_2O (0.5 mL) and filtered through a pad of celite. The residue was repeatedly washed with diethyl ether. The filtrate was then washe with H_2O, brine, dried ($Na_2SO_{4)}$ and concentrated to give the crude aldehyde **17**, which was pure enough and used in the next step without further purification. To a solution of crude aldehyde **17** and K_2CO_3 (900 mg, 8 mmol) in 20 mL dry MeOH are added diethyl-1-diazo-2-oxopropylphosphonate (1.26 g, 6 mmol) and stirring is continued until the reaction is complete as indicated by TLC (2 h). The reaction mixture is diluted with diethylether (100 mL), washed with an aq. solution of $NaHCO_3$ and dried over Na_2SO_4. Evaporation of solvent yielded analytically pure terminal alkyne **19**.

Yield: 82%; colorless liquid; $[\alpha]_D^{25}$ -9.4 (*c* 0.5, CHCl$_3$); **IR** (CHCl$_3$, cm^{-1}): 818, 1149, 1304, 1441, 1514, 1632, 1721, 2116, 2924; ^{1}**H NMR** (200 MHz, CDCl$_3$): 2.45 (d, *J* = 1.6 Hz, 1H), 2.61 (dd, *J* = 7.4, 14.3 Hz, 1H), 2.79 (dd, *J* = 5.4, 15.3 Hz, 1H), 2.98 (dd, *J* = 3.7, 8.1 Hz, 1H), 3.34 (s, 3H), 3.48-3.51 (m, 1H), (3.77 (s, 3H), 3.80 (m, 1H), 4.63 (d, *J* = 6.7 Hz, 1H), 4.71 (d, *J* =

6.8 Hz, 1H), 5.72 (d, *J* = 1.0 Hz, 1H), 6.27 (d, *J* = 1.3 Hz, 1H); **^{13}C NMR** (50 MHz, CDCl$_3$): δ 35.4, 45.2, 51.8, 55.7, 58.5, 73.6, 75.1, 78.2, 95.7, 127.7, 136.2, 167.4; **Anal.** Calcd for $C_{12}H_{16}O_5$ requires C, 59.99; H, 6.71; O, 33.30; Found: C, 60.02; H, 6.78%.

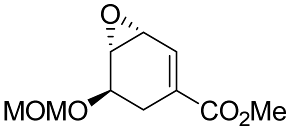
2.15. (*R*)-Methyl 4-(methoxymethoxy)-2-methylene-4-((2S,3R)-3-vinyloxiran-2-yl)butanoate (20)



To a solution of **19** (240 mg, 1 mmol) in 5 mL of ethyl acetate/pyridine/1-octene (10:1:1) was added Lindlar's catalyst (12.0 mg). The reaction mixture was stirred for 6 h under a balloon of H_2 at room temperature and filtered through a celite pad. The filtrate was concentrated and the residue was purified by silica gel column chromatography using petroleum ether/EtOAc (7:3 v/v) as eluent to give olefin **20**.

Yield: 95%; colorless liquid; $[\alpha]_D^{25}$ -5.4 (*c* 0.5, CHCl$_3$); **IR** (CHCl$_3$, cm^{-1}): 878, 1169, 1204, 1341, 1514, 1711, 2924, 3034; **^{1}H NMR** (200 MHz, CDCl$_3$): 2.51 (d, *J* = 7.0 Hz, 2H), 3.05-3.11 (m, 1H), 3.34 (s, 3H), 3.38-3.41 (m, 1H), 3.67-3.74 (m, 1H), 3.76 (s, 3H), 4.58 (d, *J* = 6.7 Hz, 1H), 4.86 (d, *J* = 6.8 Hz, 1H), 5.33 (m, 1H), 5.52 (d, *J* = 1.7 Hz, 1H), 5.67-5.71 (m, 2H), 6.23 (d, *J* = 1.3 Hz, 1H); **^{13}C NMR** (50 MHz, CDCl$_3$): δ 36.1, 51.8, 55.3, 57.4, 59.3, 71.1, 94.9, 120.5, 127.7, 132.1, 136.4, 167.1; **Anal.** Calcd for $C_{12}H_{18}O_5$ requires C, 59.49; H, 7.49; Found: C, 59.71; H, 7.61%.

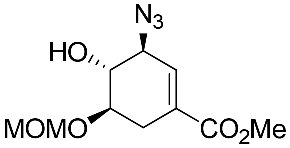
2.16. (1*R*,5*R*,6*S*)-Methyl 5-(methoxymethoxy)-7-oxabicyclo[4.1.0]hept-2-ene-3-carboxylate (3)



A mixture of diene **20** (400 mg, 1.65 mmol) and Grubbs' second-generation catalyst (70 mg, 5 mol%) in dry CH_2Cl_2 (50 mL) was stirred under reflux for 14 h. The reaction mixture was evaporated and then purified on silica gel chromatography by eluting with petroleum ether/ EtOAc (7:3 v/v) to afford **21** (0.16 g, 82%) as gum.

Yield: 90%; thick liquid; $[\alpha]_D^{25}$ -32.7 (*c* 0.5, $CHCl_3$); **IR** ($CHCl_3$, cm^{-1}): 1091, 1139, 1235, 1387, 1497, 1579, 1719, 2986; **^{1}H NMR** (200 MHz, $CDCl_3$): 2.13-2.28 (m, 1H), 2.83 (m, 1H), 3.45 (s, 3H), 3.47 (m, 1H), 3.66 (m, 1H), 3.76 (s, 3H), 4.03 (m, 1H), 4.79 (s, 2H), 6.99 (t, *J* = 3.4 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 26.5, 46.5, 51.9, 55.0, 55.4, 69.3, 95.9, 128.3, 131.1, 167.5; **Anal.** Calcd for $C_{10}H_{14}O_5$ requires C, 56.07; H, 6.59; Found: C, 56.01; H, 6.53%.

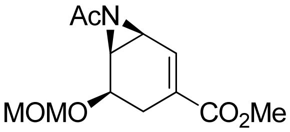
2.17. (3*S*,4*R*,5*R*)-Methyl 3-azido-4-hydroxy-5-(methoxymethoxy)cyclohex-1-enecarboxylate (21)



To a solution of cyclic epoxy ester **3** (107 mg, 0.5 mmol) in DMF/EtOH/ H_2O (1:1:0.5 mL) were added NH_4Cl (160.5 g, 3 mmol) and NaN_3 (197.4 g, 3 mmol) at 0 °C. The mixture was then stirred at 25 °C for 10 h. After completion of reaction (monitored by TLC), EtOH was removed by rotary evaporation. The remaining solution was extracted with EtOAc (100 mL x 3). The combined organic layers were washed with, brine (20 mL x 6) and dried (Na_2SO_4). After evaporation of the solvent, the residue was purified by chromatography (petroleum ether/ EtOAc (6/4 v/v).

Yield: 83%; yellow liquid; $[\alpha]_D^{25}$ +17.3 (*c* 0.7, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): 1073, 1176, 1235, 1365, 1448, 1489, 1561, 1714, 2106, 2994, 3345; ^{1}H NMR (200 MHz, $CDCl_3$): 2.17-2.34 (m, 1H), 2.89-3.00 (m, 1H), 3.45 (s, 3H), 3.63-3.67 (m, 2H), 3.77 (s, 3H), 4.10 (m, 1H), 4.77 (s, 2H), 6.59 (t, *J* = 2.5 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 30.5, 52.1, 55.8, 63.3, 74.5, 77.8, 96.7, 129.8, 134.3, 165.7; Anal. Calcd for $C_{10}H_{15}N_3O_5$ requires C, 46.69; H, 5.88; N, 16.33; Found: C, 46.61; H, 5.85; N, 16.38%.

2.18. (1*S*,5*R*,6*S*)-Methyl 7-acetyl-5-(methoxymethoxy)-7-azabicyclo[4.1.0]hept-2-ene-3-carboxylate (22)

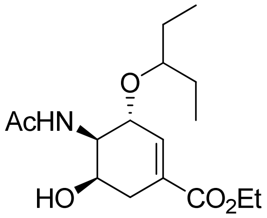


To a solution of azido alcohol **20** (150 mg, 0.58 mmol) in toluene (5 mL) was added triphenylphosphine (152 mg, 0.58 mmol) and the reaction mixture was refluxed for 3 h. After removal of the solvent under reduced pressure, diethylether (1 mL) was added, and the mixture cooled with ice-bath. The precipitated triphenylphosphine oxide was removed by filtration and the filtrate evaporated. This procedure was repeated to remove any traces of triphenylphosphine oxide. The residue obtained was then dissolved in dry CH_2Cl_2 cooled at 0 °C. To this solution was added Et_3N (175.74 mg, 1.74 mmol), DMAP (5 mg) and acetic anhydride (118.32 mg, 1.16 mmol) and the mixture stirred at 25 °C for further 45 minutes. After completion of reaction (monitored by TLC), the reaction mixture was quenched by addition of H_2O. The Organic layer was separated, washed with brine, dried (Na_2SO_4) and subjected to column chromatographic purification with petroleum ether/ EtOAc (7:3 v/v) to afford the cyclic acetamide **22**.

Yield: 81%; colorless liquid; $[\alpha]_D^{25}$ -57.8 (*c* 0.5, $CHCl_3$); **IR** ($CHCl_3$, cm^{-1}): 1073, 1195, 1255, 1324, 1369, 1448, 1708, 1732, 2987, 3115; **^{1}H NMR** (200 MHz, $CDCl_3$): 2.10 (s, 3H), 2.20-2.27

(m, 1H), 2.86-2.96 (m, 2H), 3.16 (m, 1H), 3.36 (s, 3H), 3.76 (s, 3H), 4.41-4.46 (m, 1H), 5.61-5.73 (m, 2H), 7.11 (t, *J* = 1.9 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.1, 23.8, 46.4, 51.9, 55.0, 55.4, 69.3, 95.9, 133.2, 148.3, 166.2, 184.9; **Anal.** Calcd for $C_{12}H_{17}NO_5$ requires C, 56.46; H, 6.71; N, 5.49; Found: C, 56.51; H, 6.85; N, 5.48%.

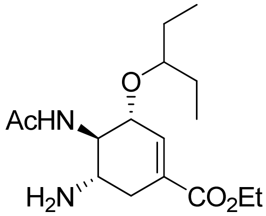
2.19. (3*R*,4*R*,5*R*)-Ethyl 4-acetamido-5-hydroxy-3-(pentan-3-yloxy)cyclohex-1-enecarboxylate (23)



To a well stirred solution of cyclic acetamide **22** (160 mg, 0.64 mmol) in 3-pentanol (10 mL), a solution of 1.5 equiv. $BF_3{\cdot}Et_2O$ (0.96 mmol) in 3-pentanol (2 mL) was added at -10 °C, followed by stirring at this temperature for additional 30 minutes. After the completion of reaction (monitored by TLC), it was quenched with a saturated aq. solution of K_2CO_3. The organic layer is then washed with H_2O, brine and dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure gave crude amino alcohol product of sufficient purity as a gum, which could be used for further reaction. To a well stirred solution of crude amino alcohol in EtOH (10 mL), a 2 N solution of HCl (2 mL) was added. The reaction was stirred for an additional 12 h at 25 °C. After the completion of reaction (monitored by TLC), the reaction mixture was quenched by adding aqueous K_2CO_3. The reaction mixture is then partitioned between EtOAc and brine. The organic layer is further washed with brine, dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure gave crude product which on chromatographic purification with petroleum ether/ EtOAc (3:7 v/v) gave title compound **23** as white solid.

Yield: 64%; white solid; m.p. 129-131 °C {lit.[4a] m.p. 131.9-132.2 °C}; $[\alpha]_D^{25}$ -84.8 (*c* 1.0, EtOAc) {lit.[4a] $[\alpha]_D^{25}$ -104 (*c* 3, EtOAc)}; **IR** ($CHCl_3$, cm^{-1}): 1085, 1274, 1266, 1306, 1373, 1455, 1585, 1649, 1707, 2963, 3311, 3396 cm-1; **^{1}H NMR** (200 MHz, $CDCl_3$): 0.90 (t, *J* = 6.7 Hz, 6H), 1.25 (t, *J* = 7.9 Hz, 3H), 1.42 (m, 4H), 1.99 (s, 3H), 2.59 (m, 2H), 3.40 (m, 1H), 3.46 (s, 1H), 3.86 (m, 1H), 3.91 (t, *J* = 6.7 Hz, 1H), 4.15 (m, 3H), 4.41 (m, 1H), 5.78 (m, 1H), 6.84 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 9.7, 9.8, 14.2, 23.8, 26.1, 26.7, 31.9, 55.2, 61.1, 67.4, 72.9, 82.3, 129.4, 136.4, 166.8, 171.8; **Anal.** Calcd for $C_{16}H_{27}NO_5$ requires C, 59.46 requires C, 61.32; H, 8.68; N, 4.47; Found: C, 61.47; H, 8.71; N, 4.56%.

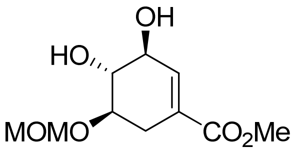
2.20 (-)-Oseltamivir free base



Compound **23** (312 mg, 1 mmol) and triethylamine (303 mg, 3 mmol) were dissolved in dry CH_2Cl_2 (15 mL), and the solution cooled to 0 °C. Methanesulfonyl chloride (229.2 mg, 2 mmol) was added, and then the resulting solution was stirred at 0 °C for 1 h. After TLC showed that the reaction was complete, more CH_2Cl_2 (20 mL) was added. The organic phase was washed with brine and then dried over anhydrous Na_2SO_4. After the solvent was removed under vaccum, the crude product was dissolved in DMF and NaN_3 (390 mg, 6 mmol) was added. The reaction mixture was then stirred at 80 °C for 3 h. After the completion of reaction (monitored by TLC), the reaction mixture is then partitioned between EtOAc and brine. The organic layer is further washed with brine, dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure gave crude product which on chromatographic purification with petroleum ether/EtOAc (4:6 v/v) gave the corresponding cyclic azide. The cyclic azide was then dissolved in EtOH and Lindlar's catalyst (20 mg) added. The reaction mixture was stirred for 6 h under a balloon of H_2 at room temperature and filtered through a celite pad. The filtrate was concentrated and the residue was purified by silica gel column chromatography using MeOH/EtOAc (5:5 v/v) as eluent to give (-)-oseltamivir free base.

Yield: 72%; $[\alpha]_D^{25}$ -37.8 (*c* 1, EtOH) {lit.[4a] $[\alpha]_D^{25}$ -49.2 (*c* 9.33, EtOH)}; **IR** ($CHCl_3$, cm^{-1}): 1068, 1127, 1255, 1374, 1456, 1568, 1644, 1714, 2977, 3289 cm-1; **^{1}H NMR** (200 MHz, $CDCl_3$): 0.90 (m, 6H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.42 (m, 4H), 2.03 (s, 3H), 2.23 (m, 1H), 2.76 (m, 1H), 3.30 (m, 1H), 3.46 (m, 1H), 4.15 (m, 3H), 5.78 (m, 1H), 6.79 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 10.1, 10.2, 14.8, 24.5, 26.3, 26.7, 34.3, 49.8, 59.5, 61.3, 75.7, 82.3, 129.9, 138.0, 167.1, 171.8; **Anal.** Calcd for $C_{16}H_{28}N_2O_4$ requires C, 61.51; H, 9.03; N, 8.97; Found: C, 61.47; H, 8.98; N, 8.88%.

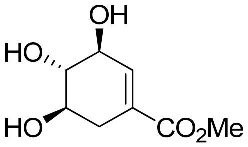
2.21. (3*R*,4*S*,5*R*)-Methyl 3,4-dihydroxy-5-(methoxymethoxy)cyclohex-1-enecarboxylate (24)



To a well stirred solution of compound **3** (107 mg, 0.5 mmol) in THF/H_2O (3:1), concentrated H_2SO_4 (5 drops) was added. The reaction was stirred for an additional 2 h at 25 °C. After the completion of reaction (monitored by TLC), the reaction mixture was diluted with excess of EtOAc. The organic layer is further washed with H_2O, brine, dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure gave crude product which on chromatographic purification with petroleum ether/EtOAc (2:8 v/v) gave title compound **22** as gum.

Yield: 96%; thick liquid; $[\alpha]_D^{25}$ -45.1 (*c* 0.5, EtOH); **IR** ($CHCl_3$, cm^{-1}): 1088, 1300, 1373, 1717, 2878, 2967, 3387, 3468; **^{1}H NMR** (200 MHz, $CDCl_3$): 2.57-2.68 (m, 2H), 3.42 (s, 3H), 3.59 (m, 1H), 3.63 (m, 1H), 3.66 (s, 3H), 3.7 (m, 1H), 4.05 (m, 1H), 4.41 (m, 1H), 4.72 (s, 2H), 6.83 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 30.9, 51.9, 55.8, 70.2, 77.6, 97.1, 127.9, 137.8, 166.6; **Anal.** Calcd for $C_{10}H_{16}O_6$ requires C, 51.72; H, 6.94; Found C, 51.82; H, 6.98.

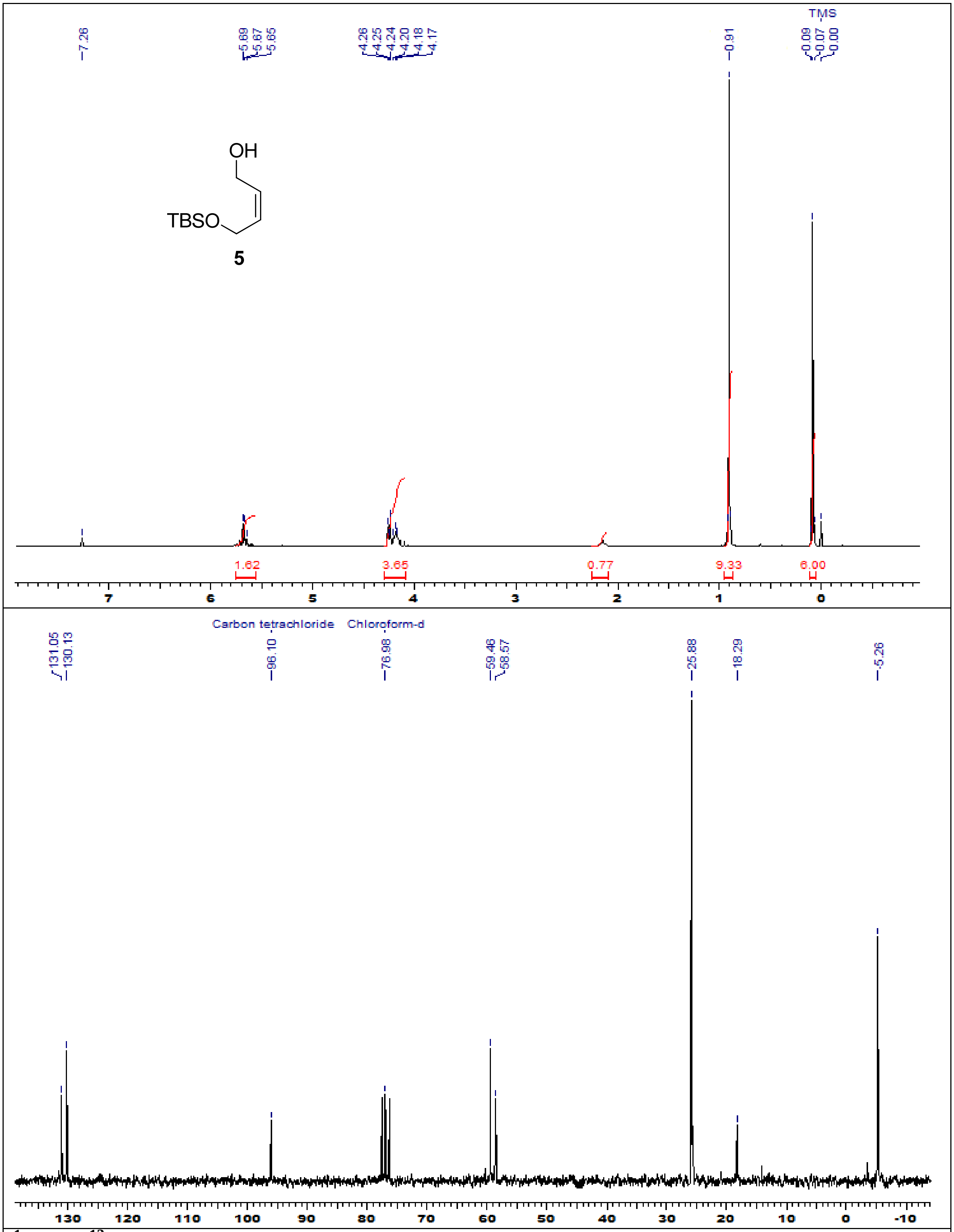
2.22. Methyl 3-*epi* shikimate (2)



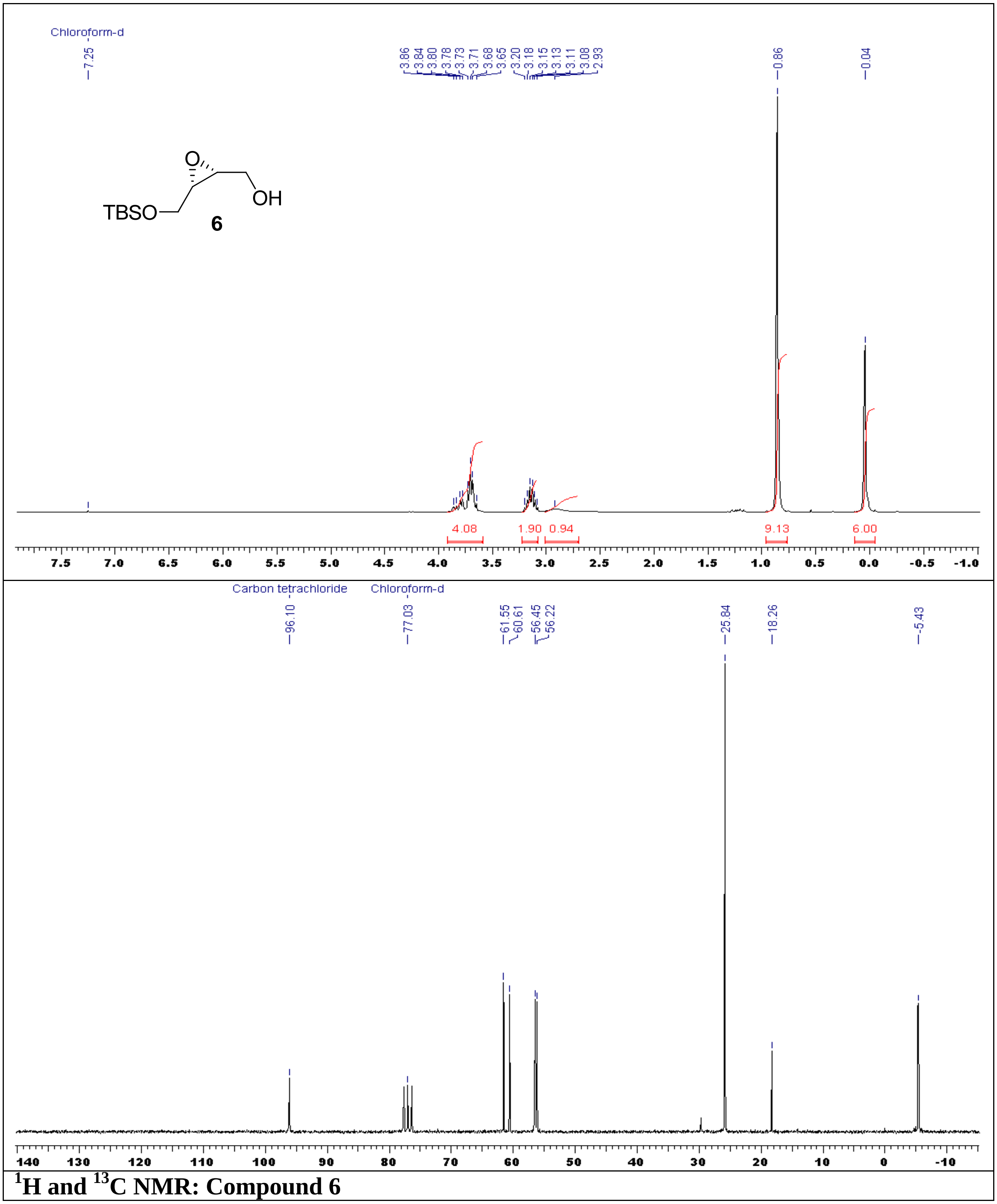
To a well stirred solution of compound **25** (95 mg, 0.5 mmol) in MeOH was added 2N solution of HCL. The reaction was stirred for an additional 6 h at 25 °C. After the completion of reaction (monitored by TLC), the reaction mixture was diluted with excess of EtOAc. The organic layer is further washed with H_2O, brine, dried over anhydrous Na_2SO_4. Removal of solvent under reduced pressure gave crude product which on chromatographic purification with MeOH/EtOAc (3:7 v/v) gave title compound **2** in 74% yield as colorless solid.

Yield: 74%; white solid; m.p. 131-133 °C {lit.[13] m.p. 132 °C}; $[\alpha]_D^{25}$ -13.1 (*c* 0.5, MeOH) {lit.[13] $[\alpha]_D^{25}$ -13.4 (*c* 0.5, MeOH)}; IR ($CHCl_3$, cm^{-1}): 1089, 1176, 1245, 1378, 1489, 1661, 1714, 2106, 2994, 3456; **^{1}H NMR** (200 MHz, D_2O): 2.23 (m, 1H), 2.81 (m, 1H), 3.47 (dd, *J* = 8.5, 10 Hz, 1H), 3.76 (s, 3H), 3.77 (m, 1H), 4.24 (m, 1H), 6.68 (m, 1H); **^{13}C NMR** (50 MHz, D_2O): 168.6, 138.4, 127.2, 76.4, 71.9, 68.6, 52.8, 31.7; **Anal.** Calcd for $C_8H_{12}O_5$ requires C, 51.06; H, 6.43; O, 42.51; Found C, 51.11; H, 6.54.

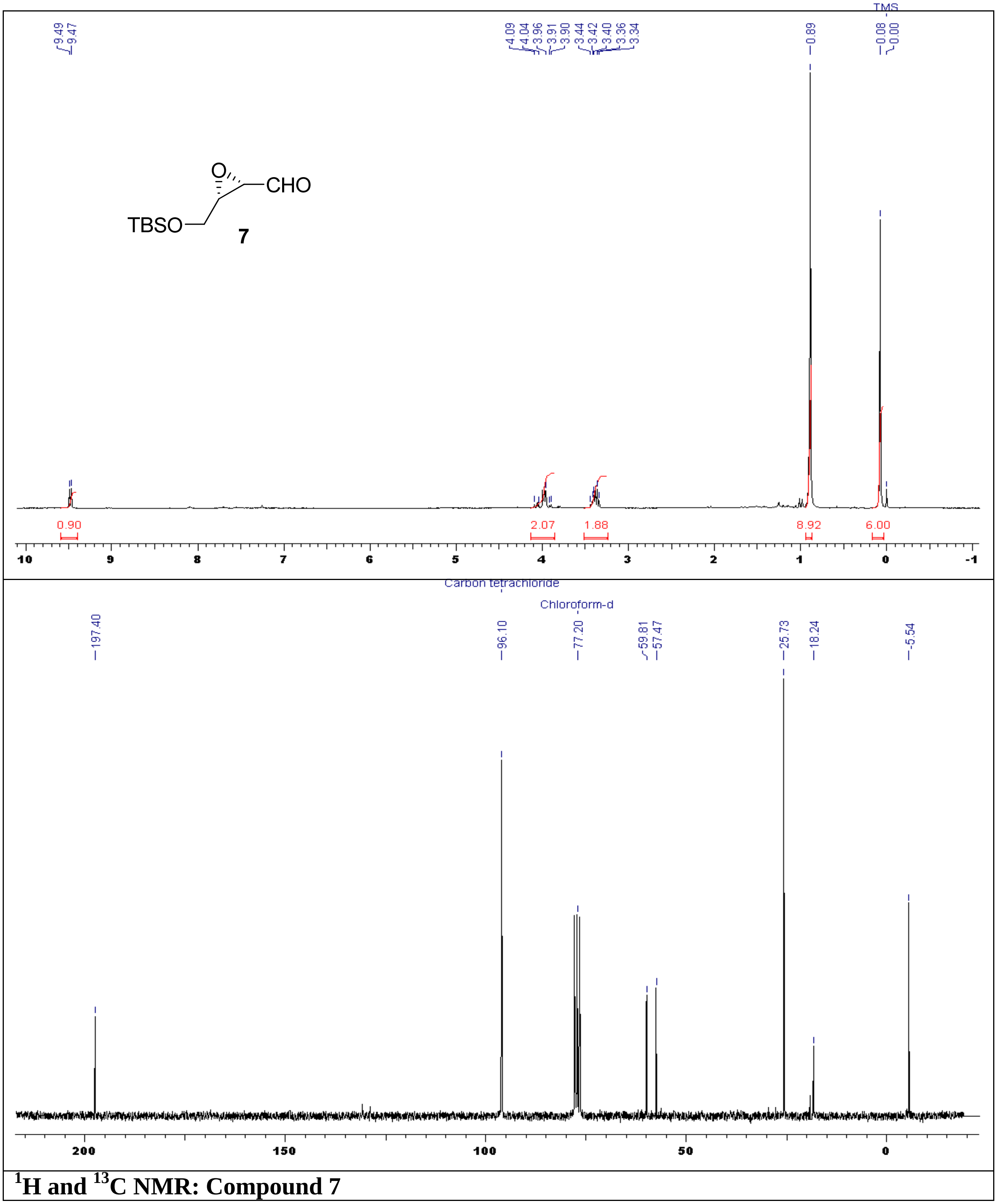
3. Spectral Data



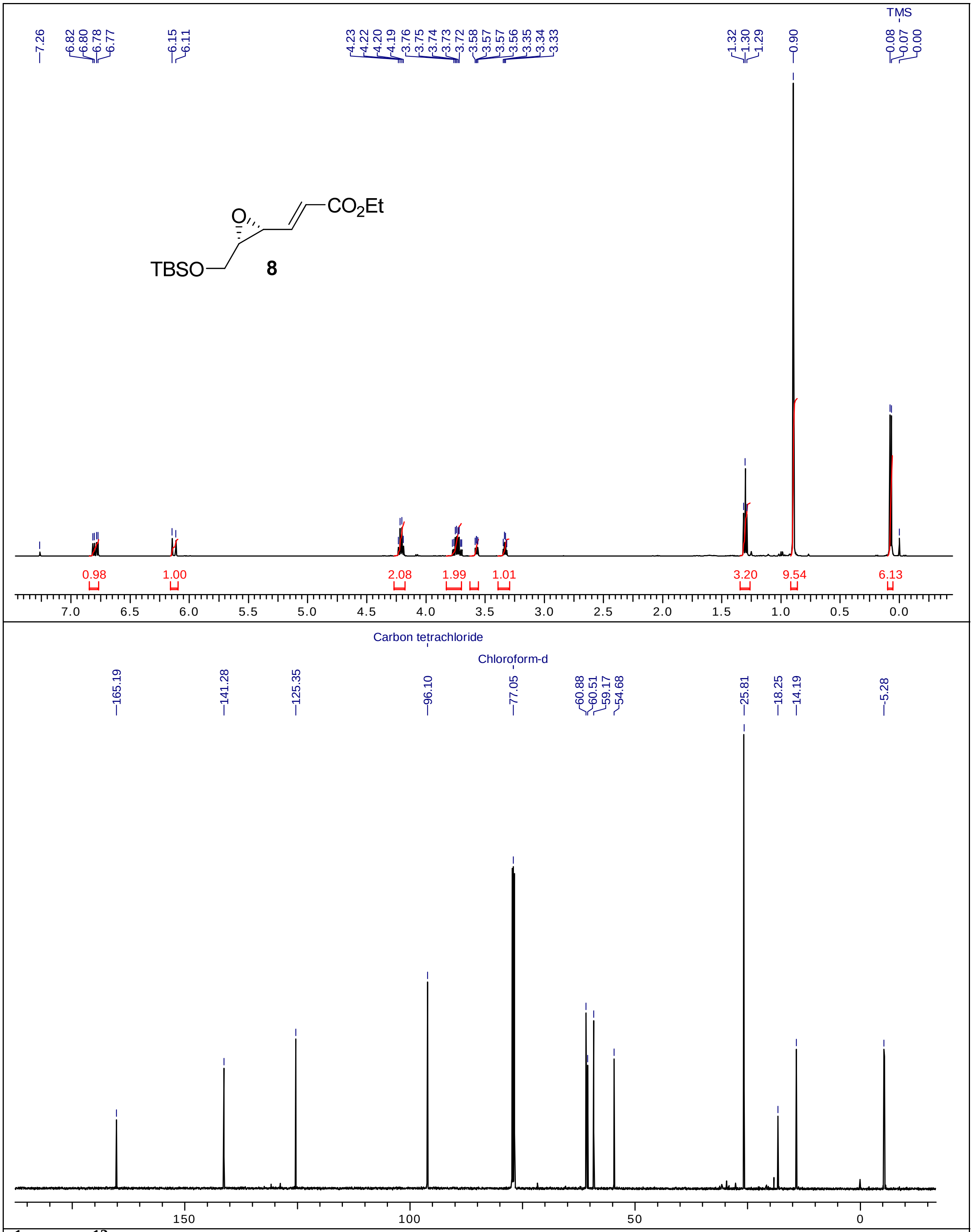
^{1}H and ^{13}C NMR: Compound 5



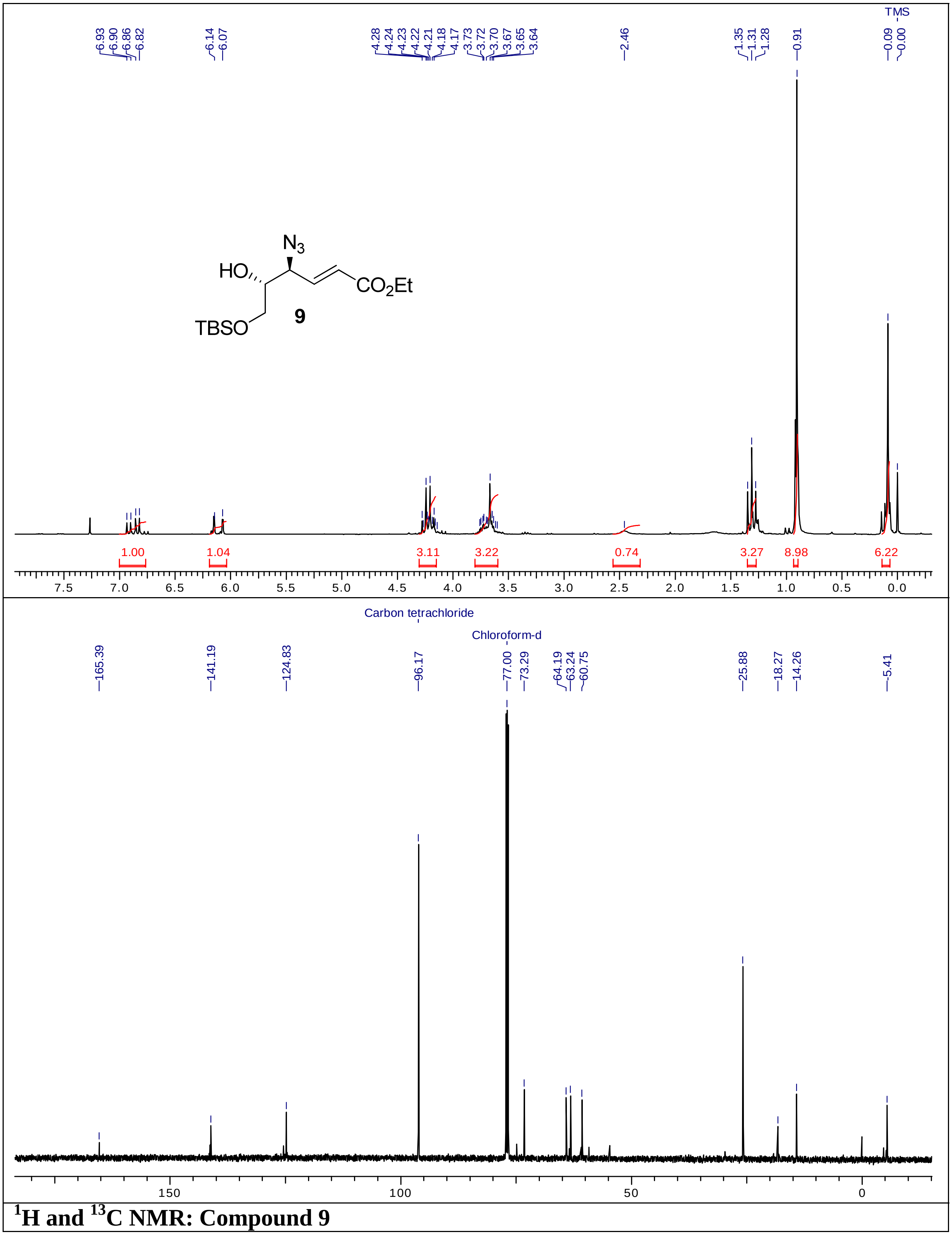
^{1}H and ^{13}C NMR: Compound 6



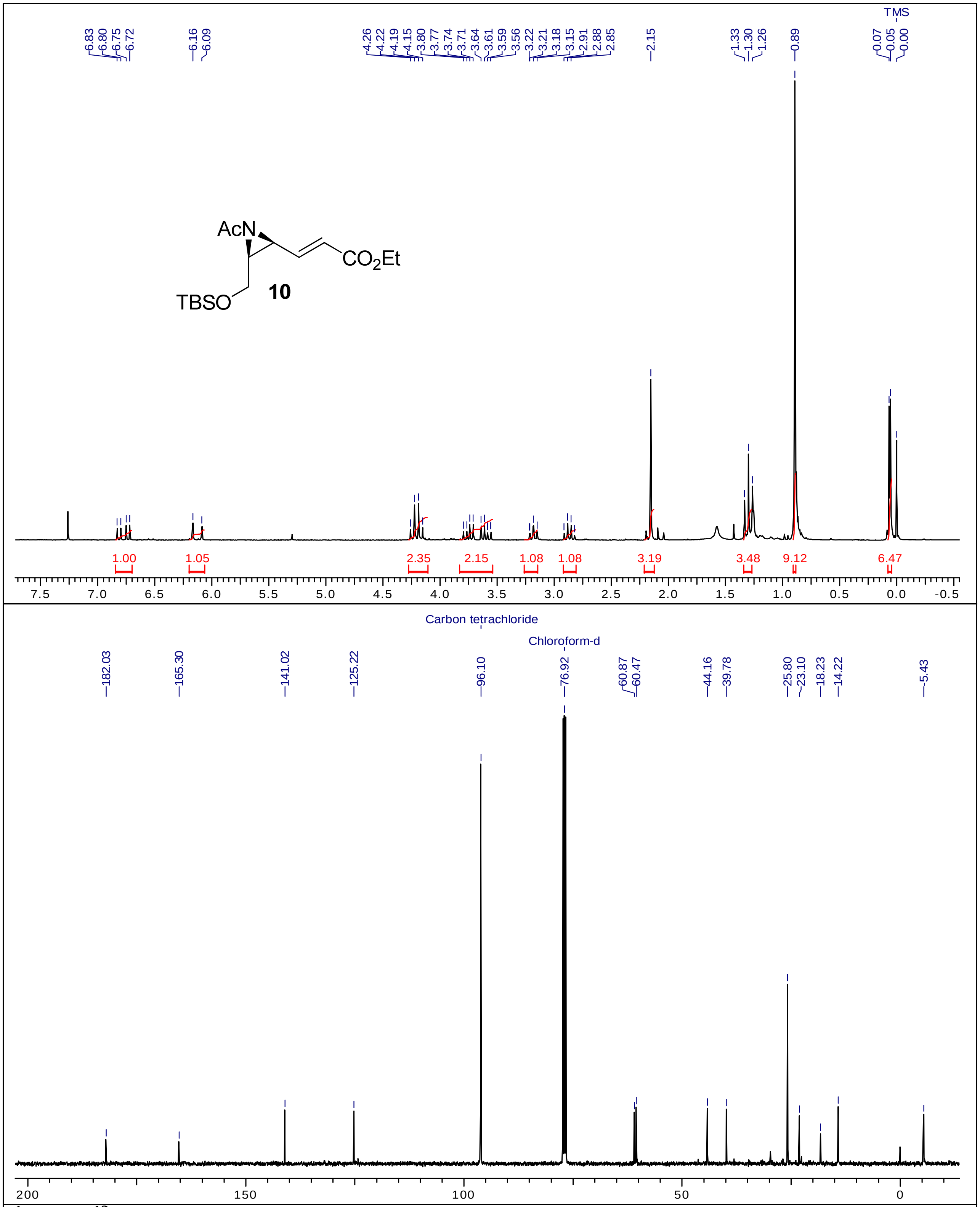
^{1}H and ^{13}C NMR: Compound 7



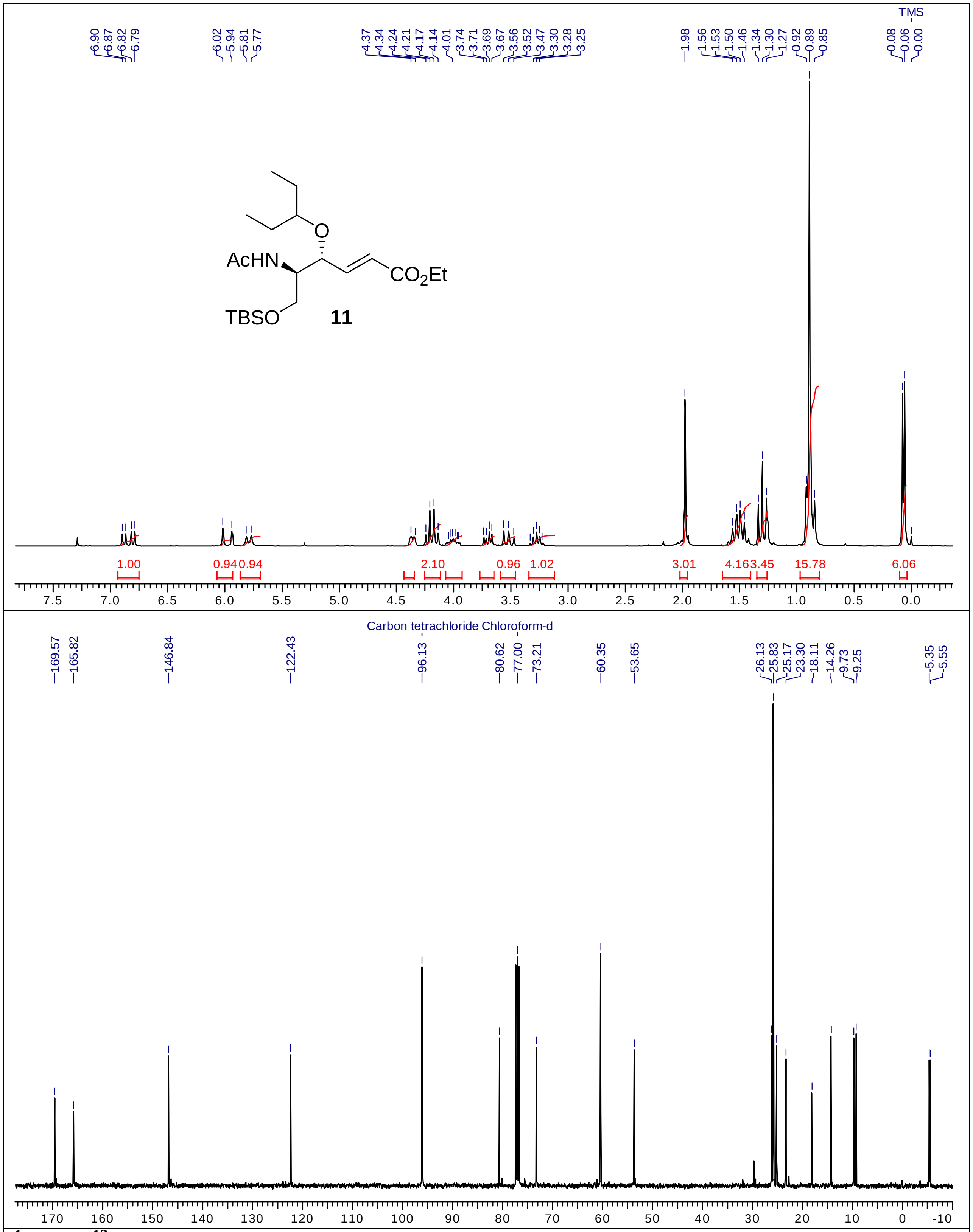
^{1}H and ^{13}C NMR: Compound 8



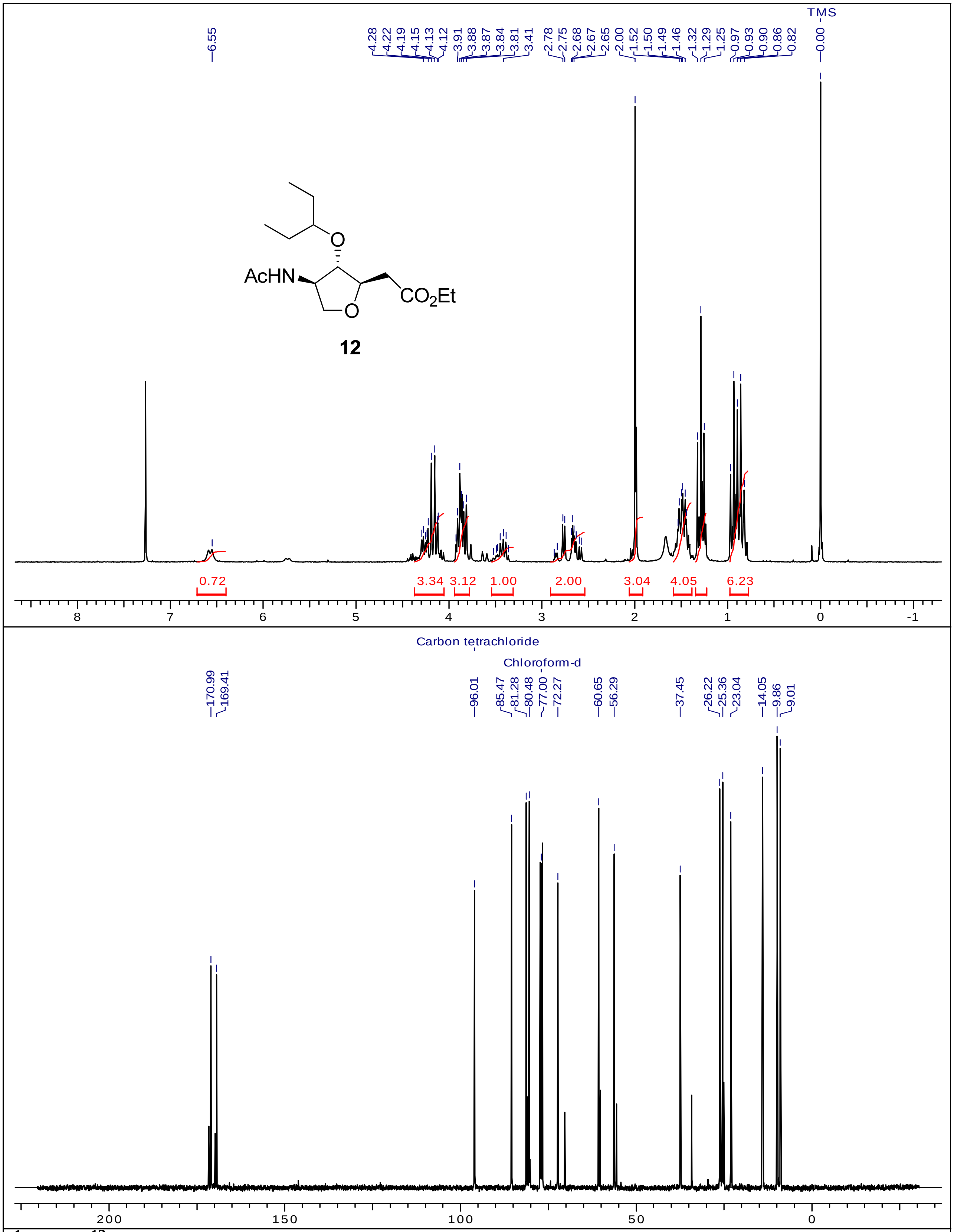
^{1}H and ^{13}C NMR: Compound 9



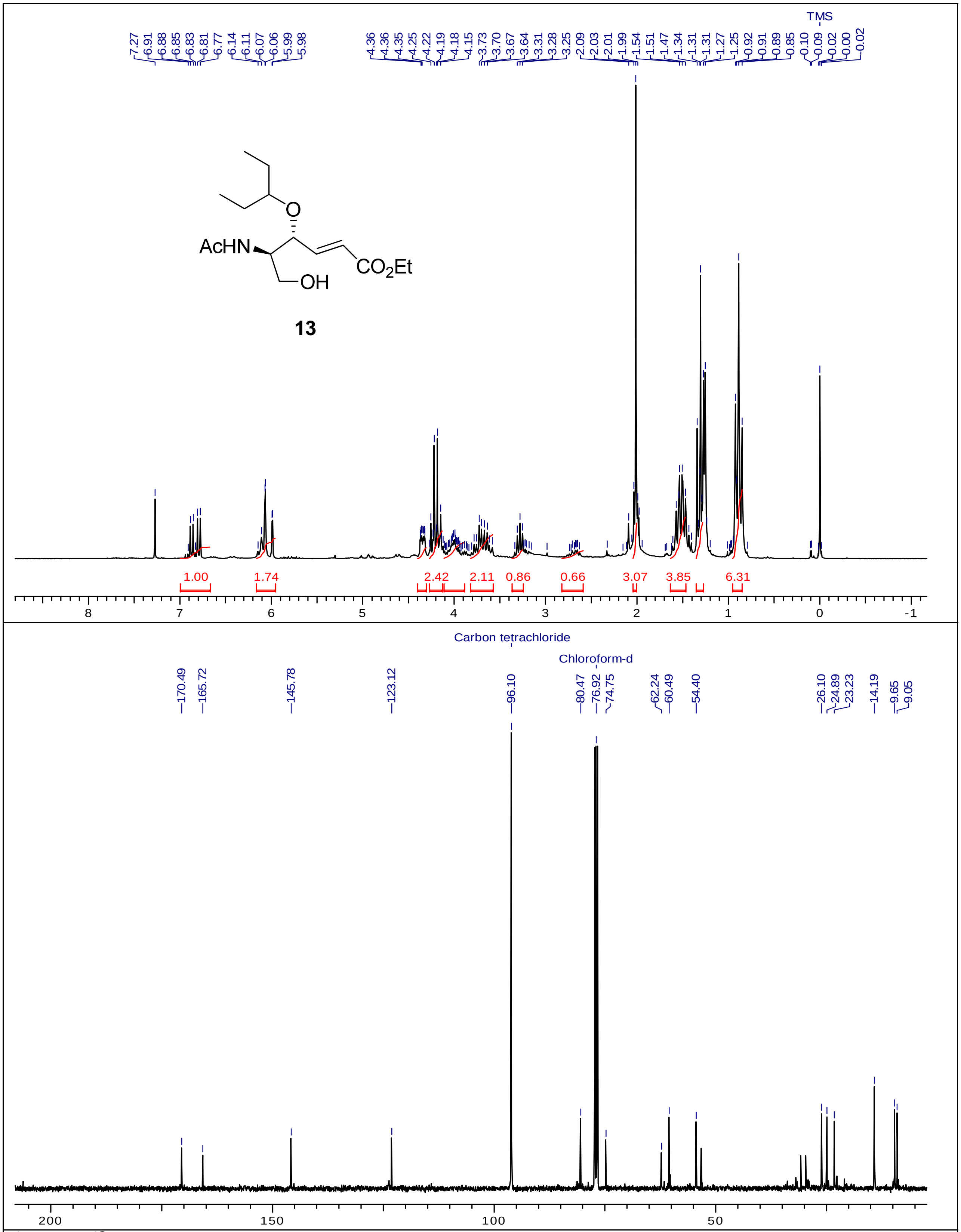
^{1}H and ^{13}C NMR: Compound 10



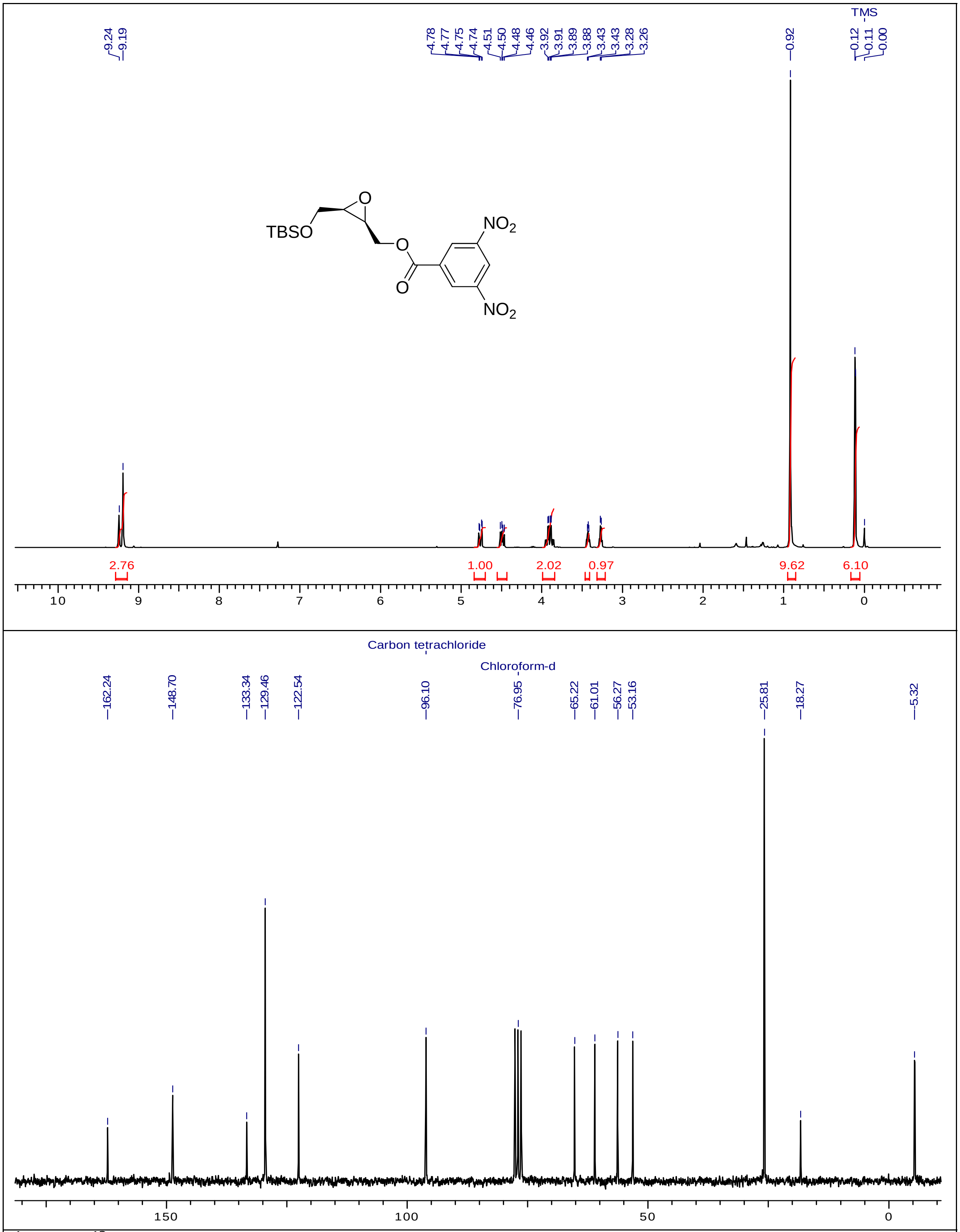
^{1}H and ^{13}C NMR: Compound 11



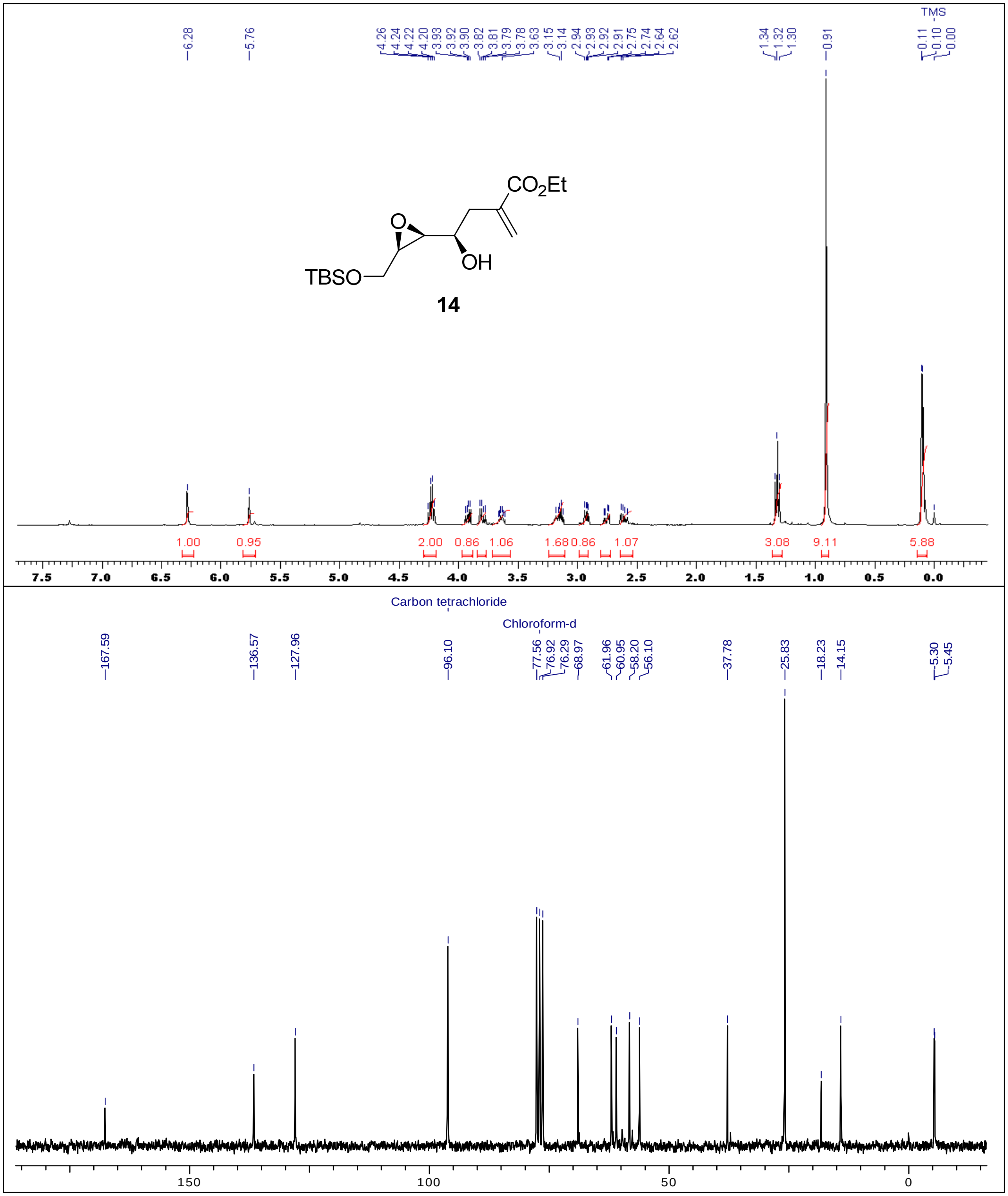
^{1}H and ^{13}C NMR: Compound 12



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



^{1}H and ^{13}C NMR: 3,5-dinitro benzoate of alcohol (-)-6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4.26
4.24
4.22
4.20
3.93
3.92
3.90
3.82
3.81
3.79
3.78
3.63
3.15
3.14
2.94
2.93
2.92
2.91
2.75
2.74
2.64
2.62
1.34
1.32
1.30
0.91
0.11
0.10
0.00
CO2Et
O
OH
TBSO
14
1.00
0.95
2.00
0.86
1.06
1.68
0.86
1.07
3.08
9.11
5.88
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Carbon tetrachloride
Chloroform-d
167.59
136.57
127.96
96.10
77.56
76.92
76.29
68.97
61.96
60.95
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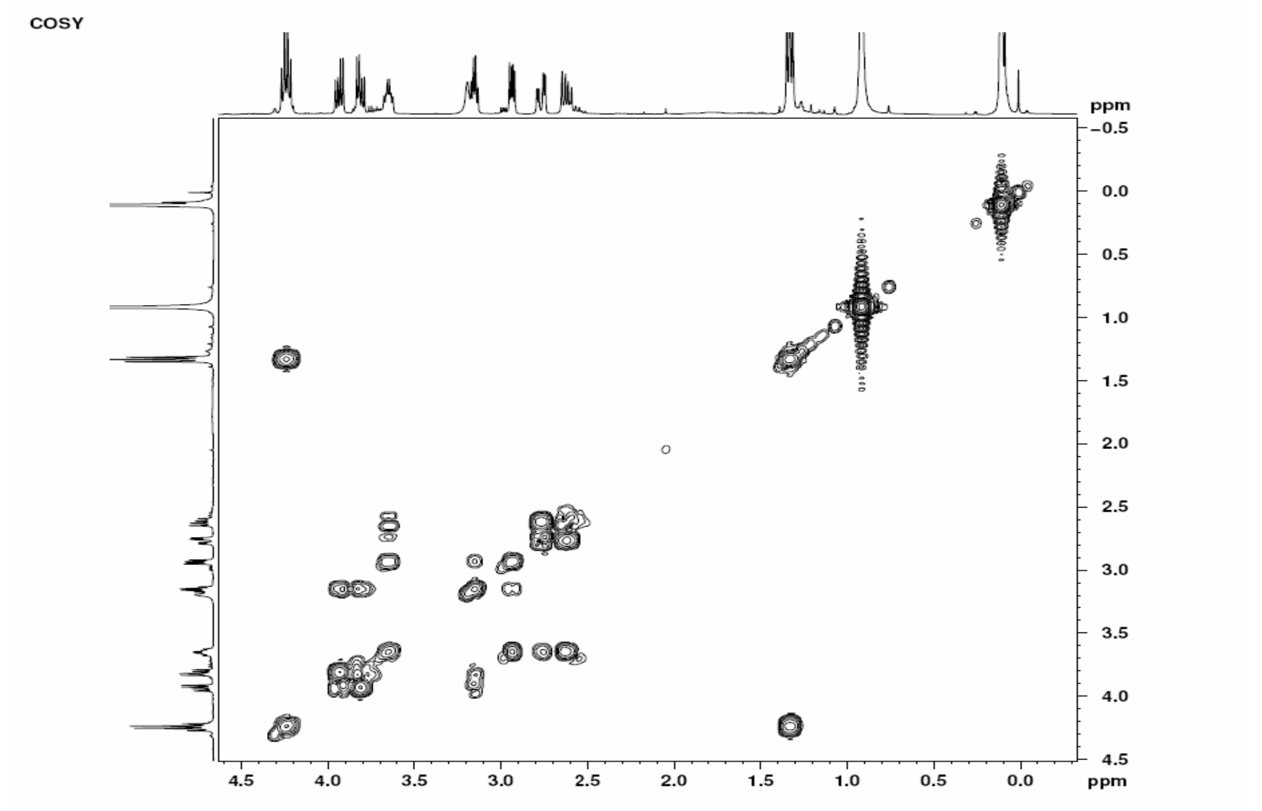
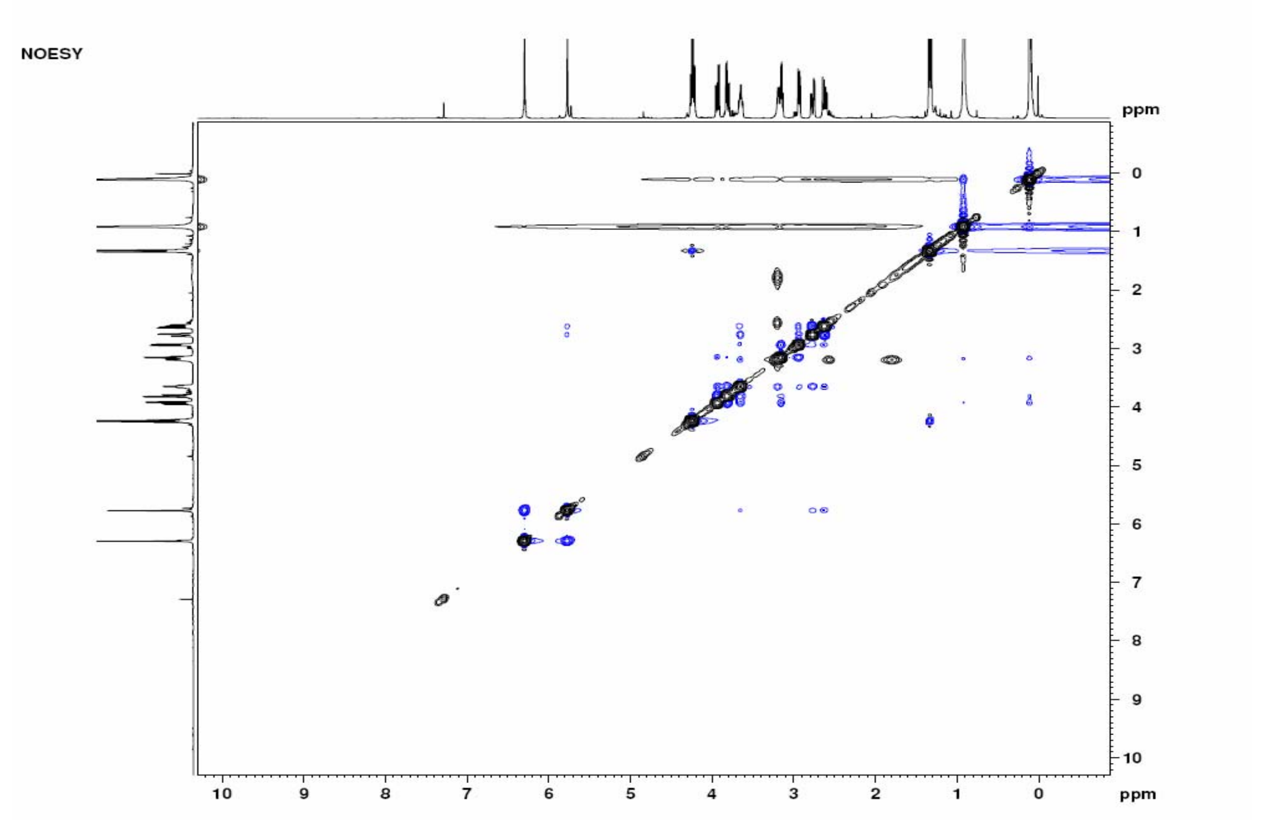
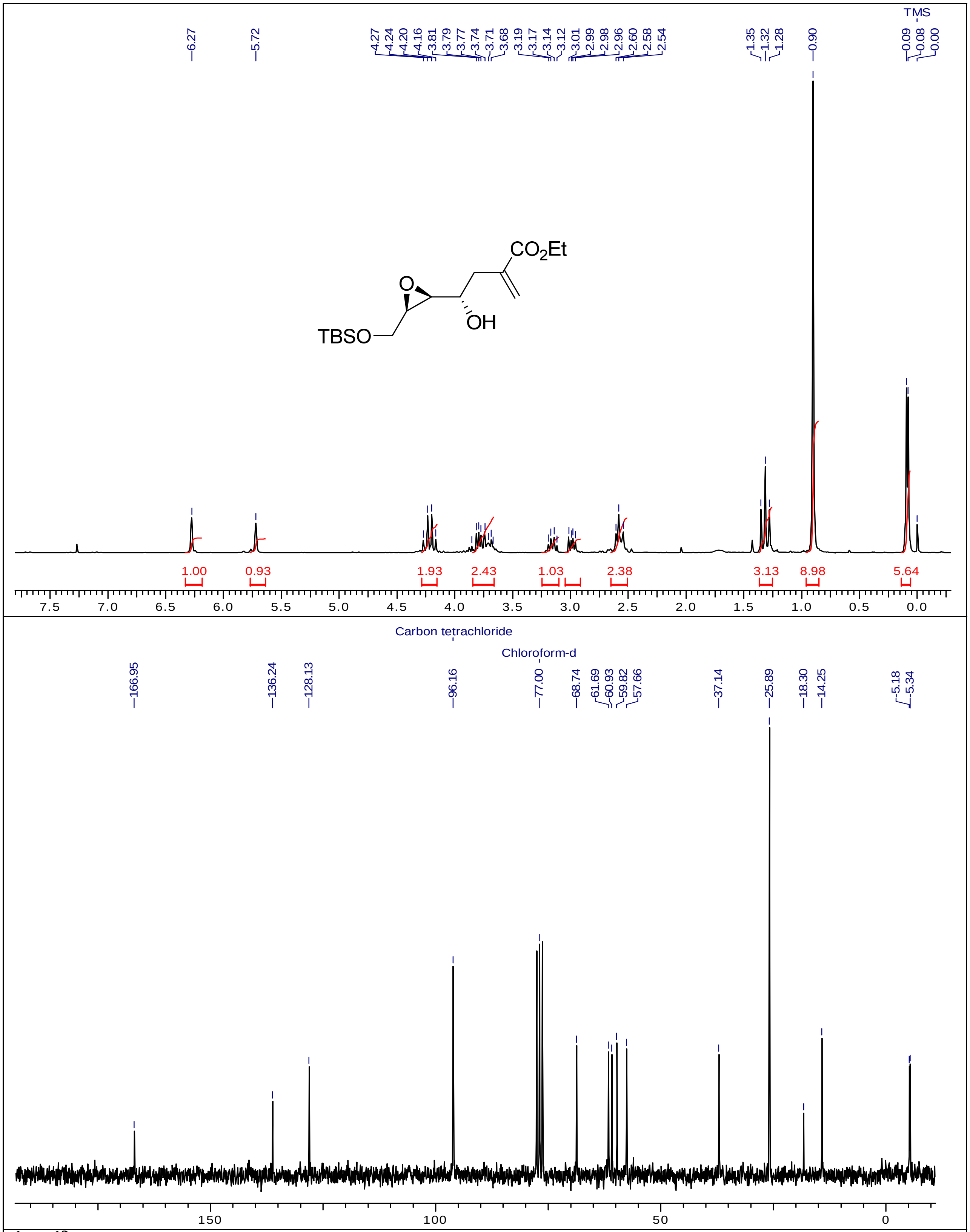
56.10
37.78
25.83
18.23
14.15
-5.30
-5.45
150
100
50
0

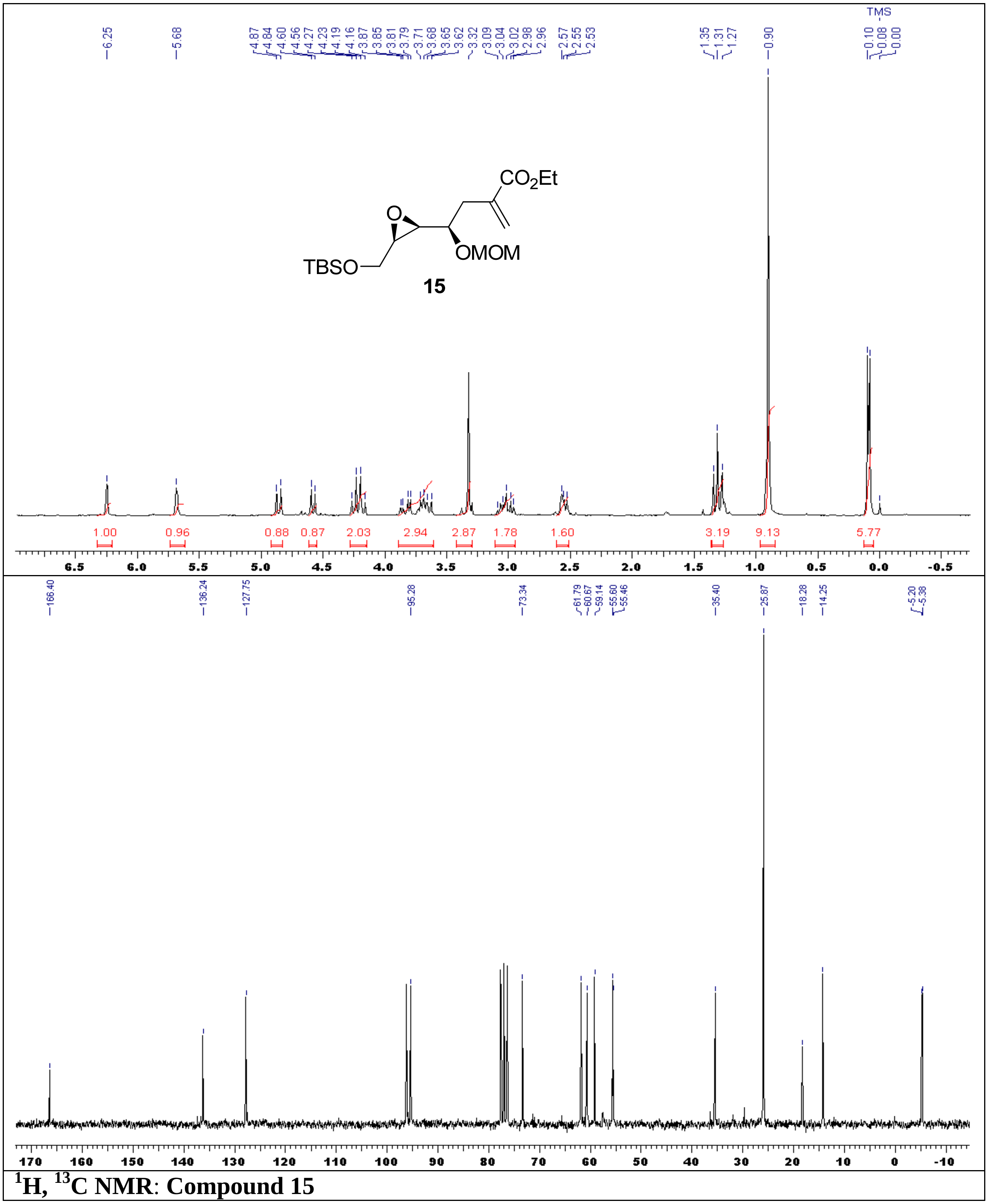




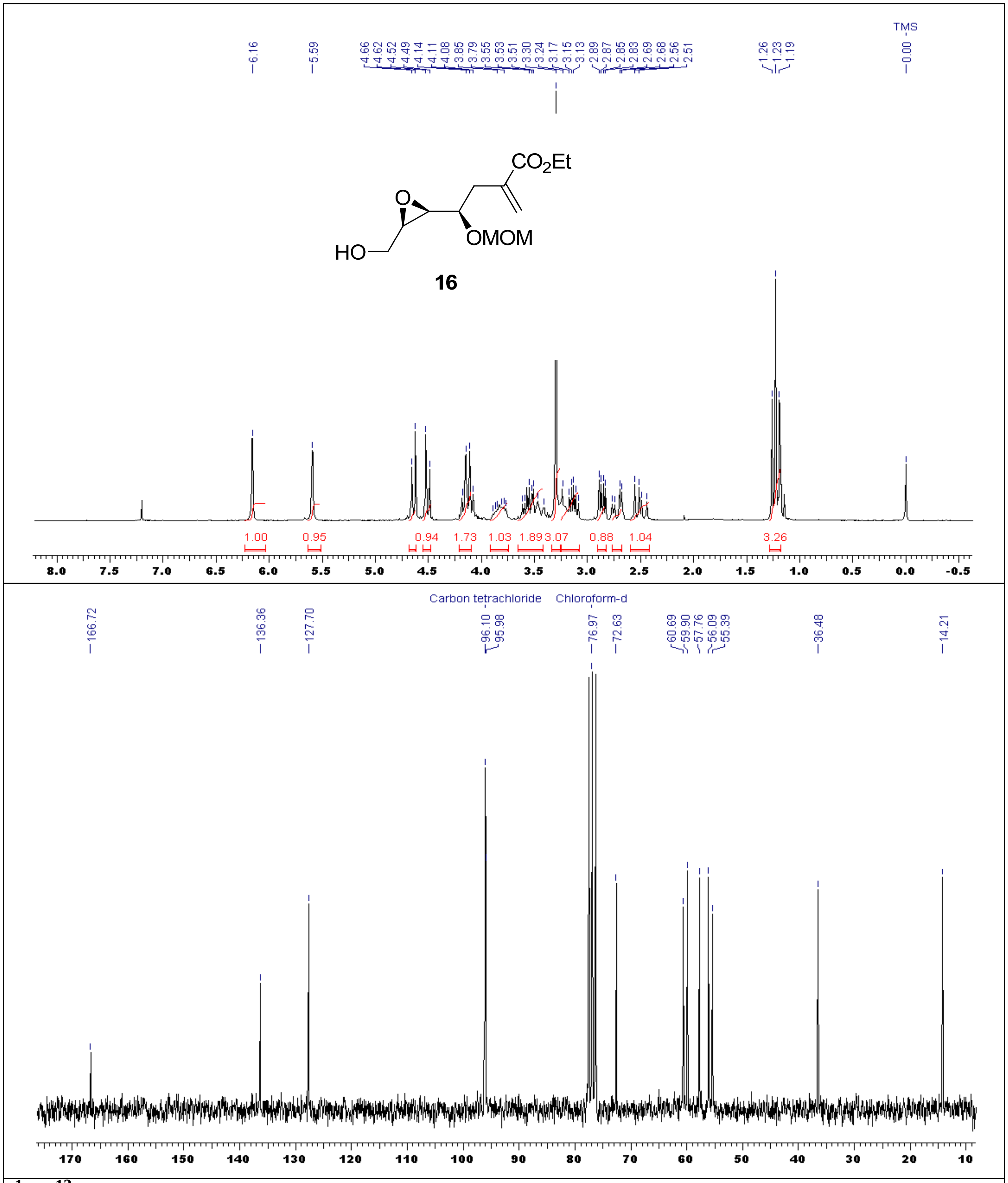
^{1}H, ^{13}C NMR, NOESY and COSY: Compound 14



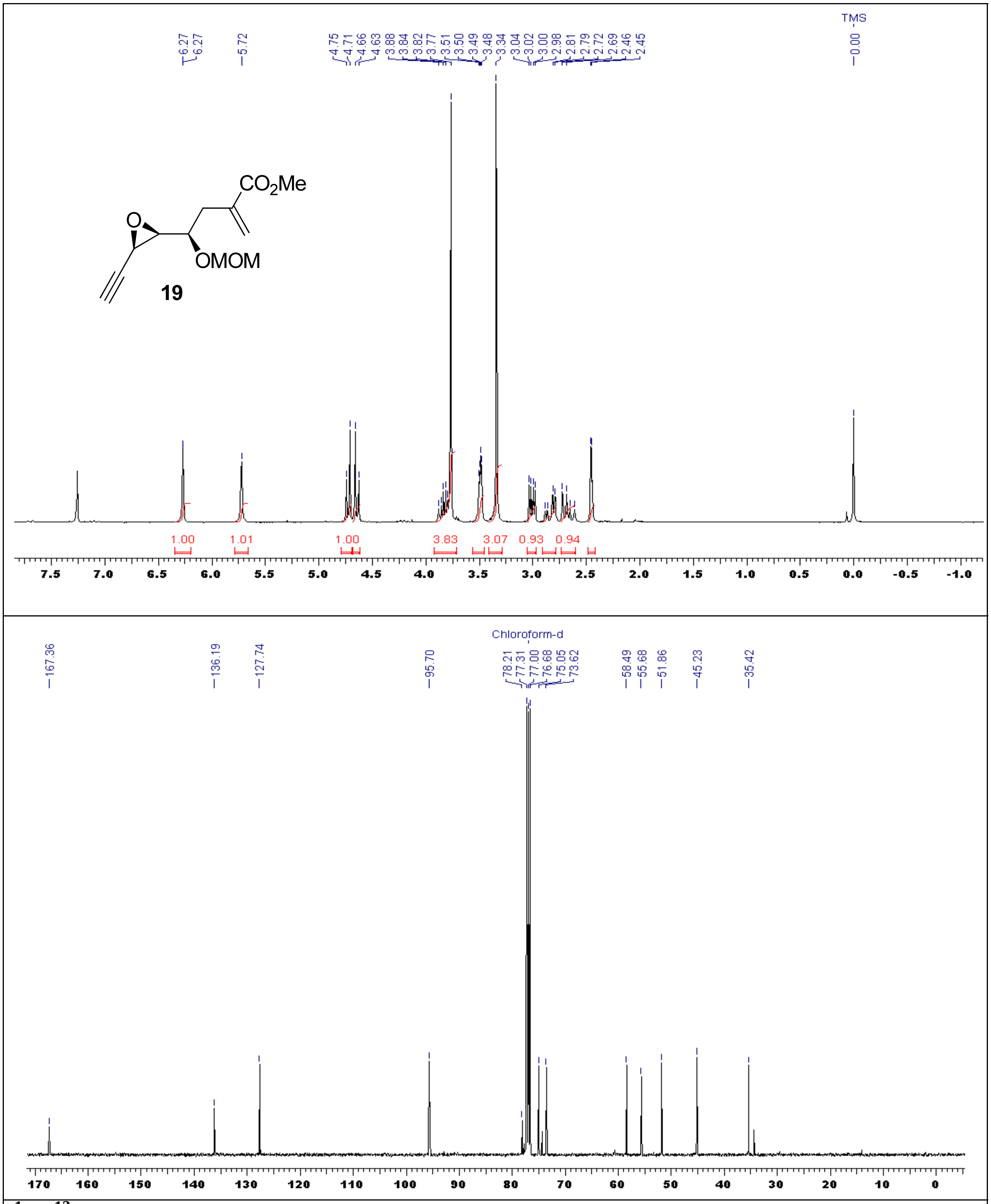
^{1}H, ^{13}C NMR: ***anti*-diastereomer of epoxy alcohol 14**



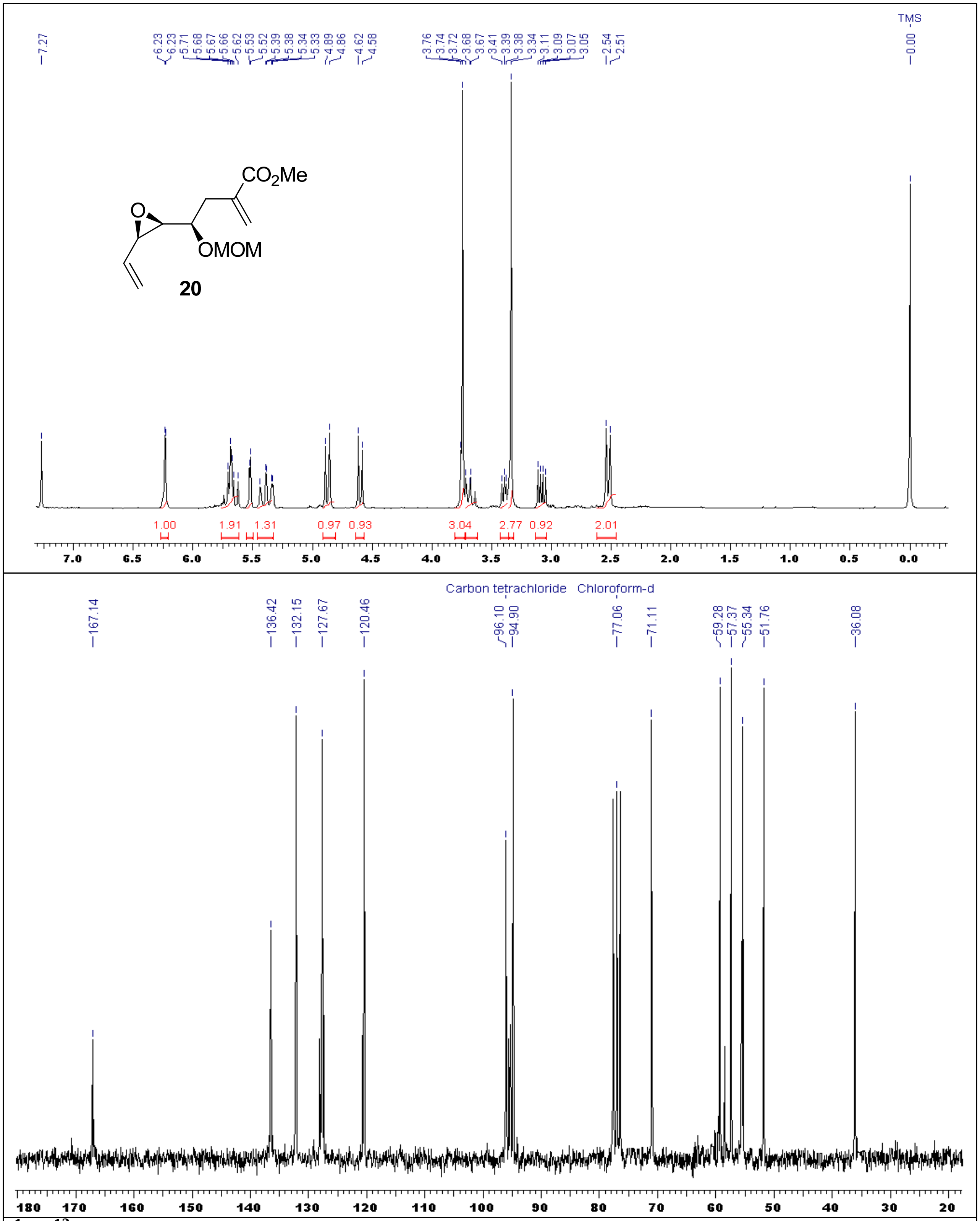
^{1}H, ^{13}C NMR: Compound 15



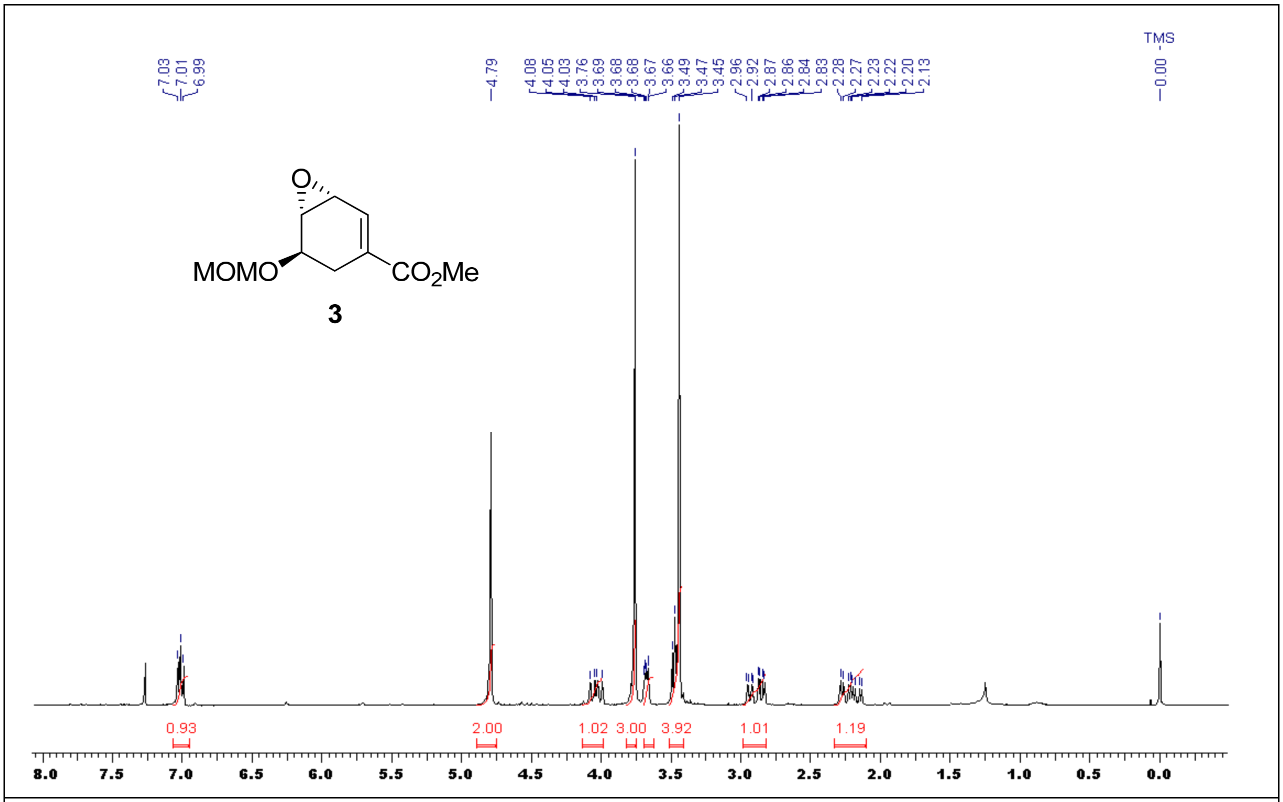
^{1}H, ^{13}C NMR: Compound 16



^{1}H, ^{13}C NMR: Compound 19



^{1}H, ^{13}C NMR: Compound 20


TMS
7.03
7.01
6.99
4.79
4.08
4.05
4.03
3.76
3.69
3.68
3.68
3.67
3.66
3.49
3.47
3.45
2.96
2.92
2.87
2.86
2.84
2.83
2.28
2.27
2.23
2.22
2.20
2.13
0.00
O
MOMO
CO2Me
3
0.93
2.00
1.02
3.00
3.92
1.01
1.19
8.0
7.5
7.0
6.5
6.0
5.5
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4.0
3.5
3.0
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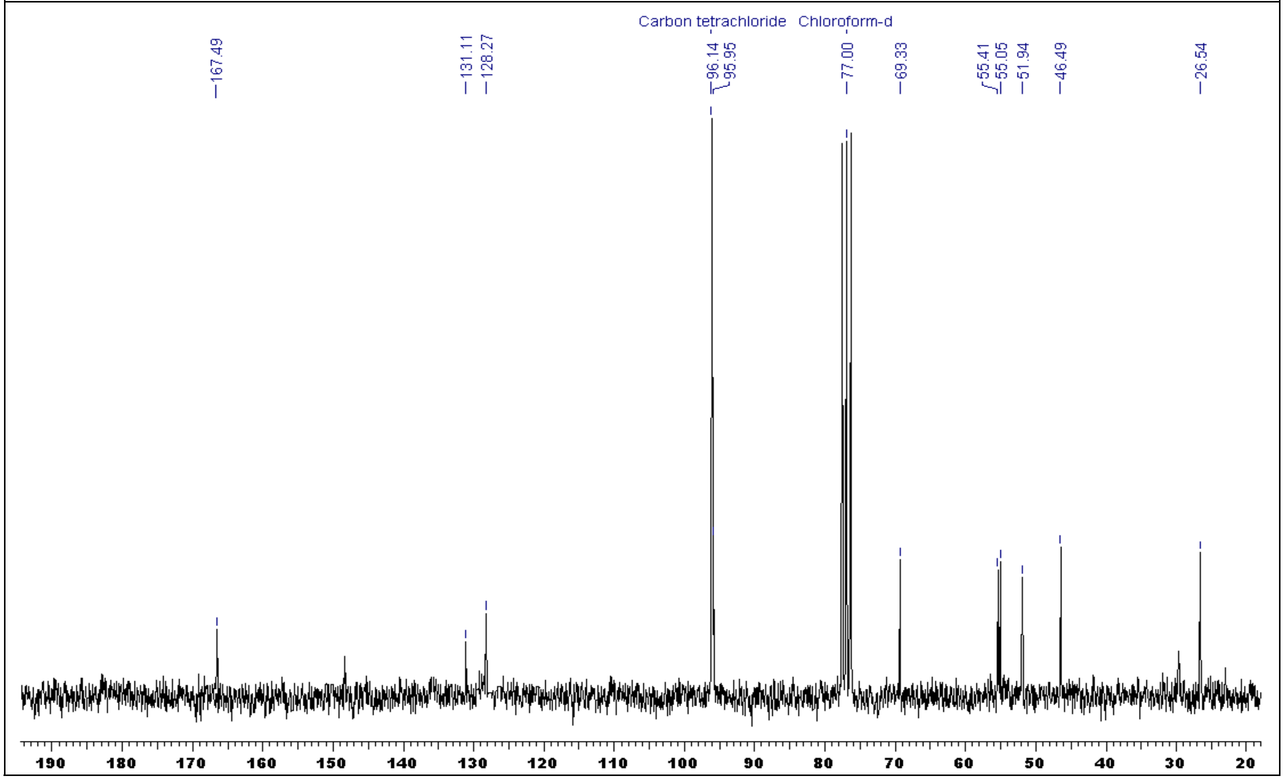
0.0


Carbon tetrachloride
Chloroform-d
167.49
131.11
128.27
96.14
95.95
77.00
69.33
55.41
55.05
51.94
46.49
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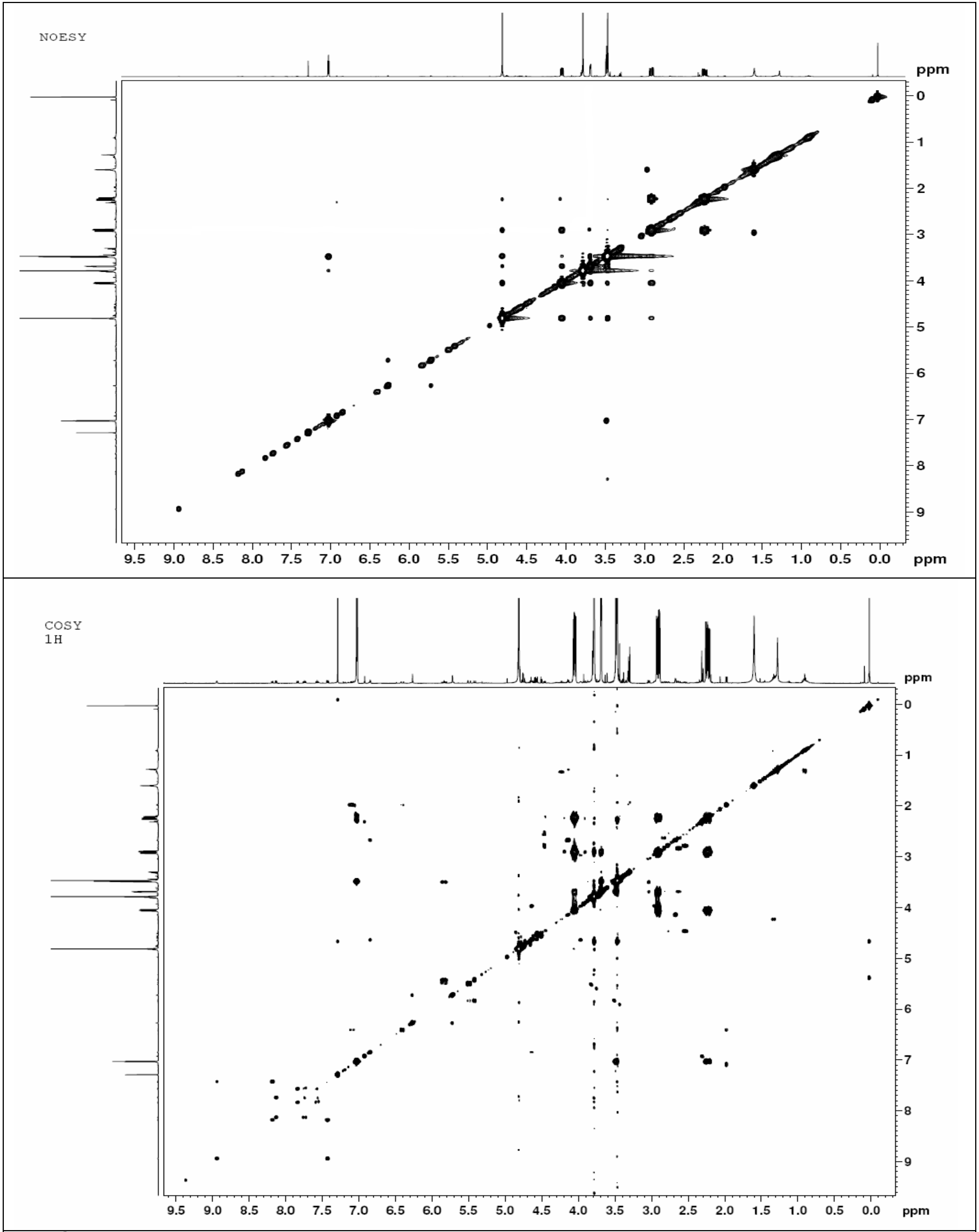
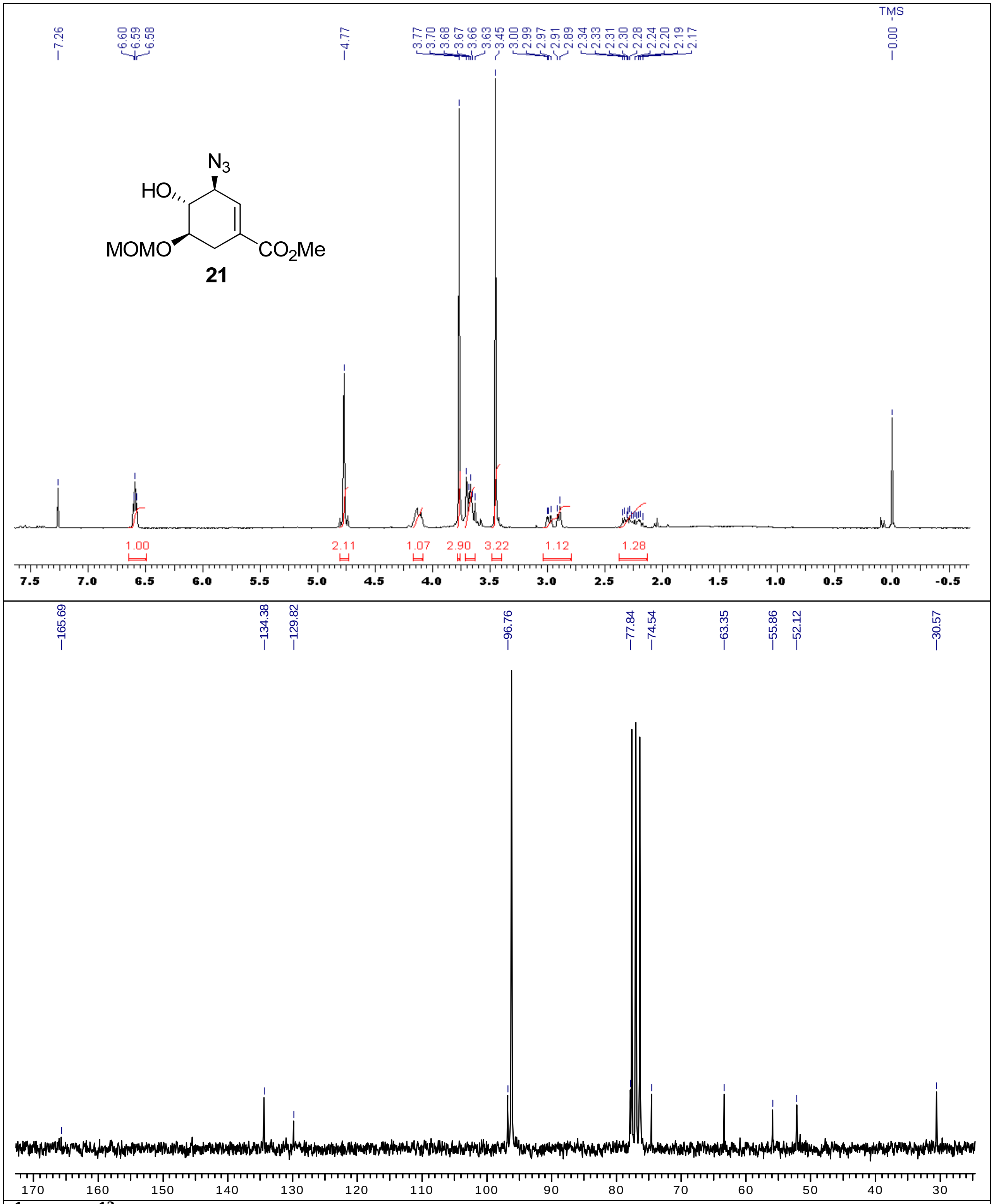
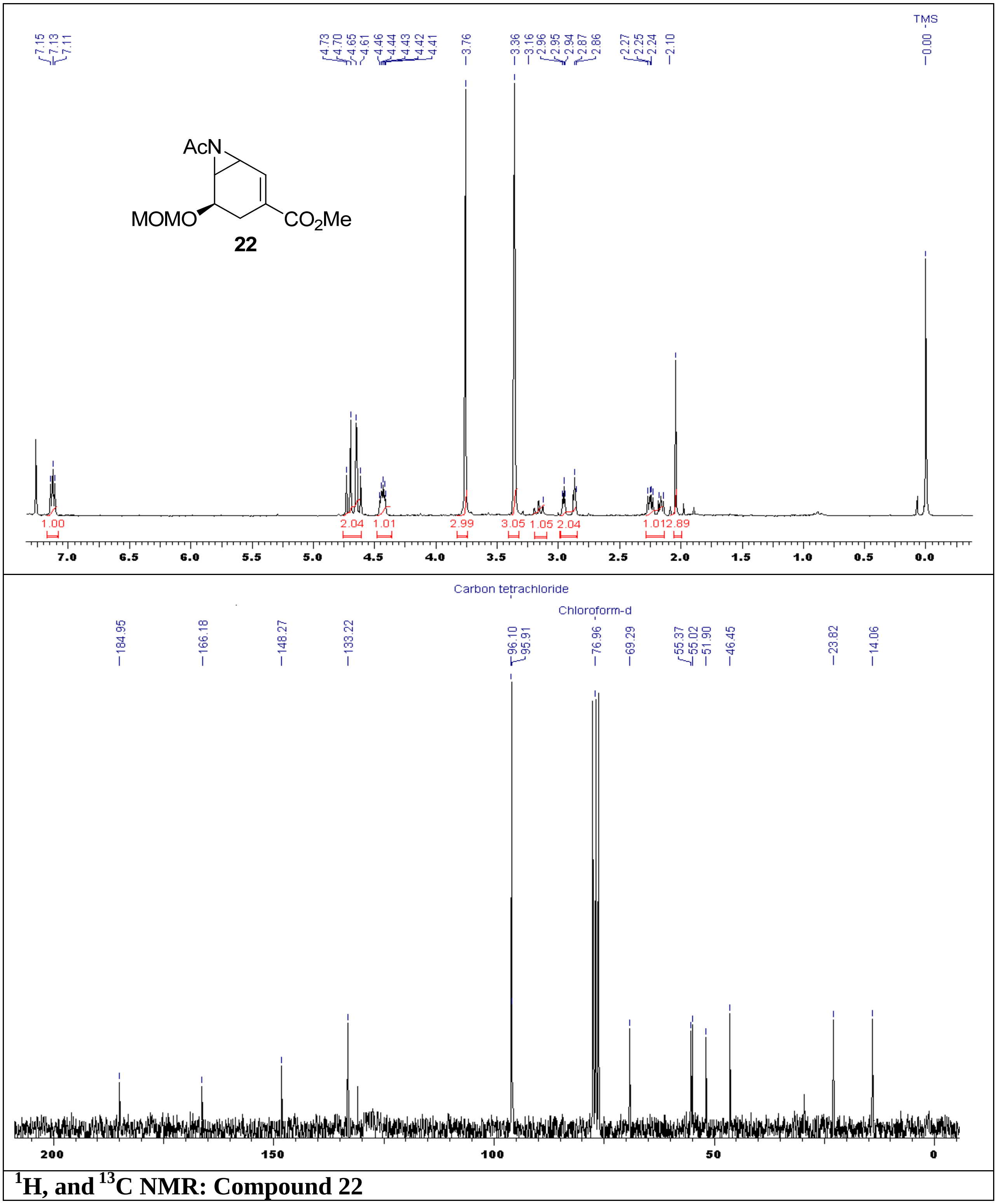
70
60
50
40
30
20



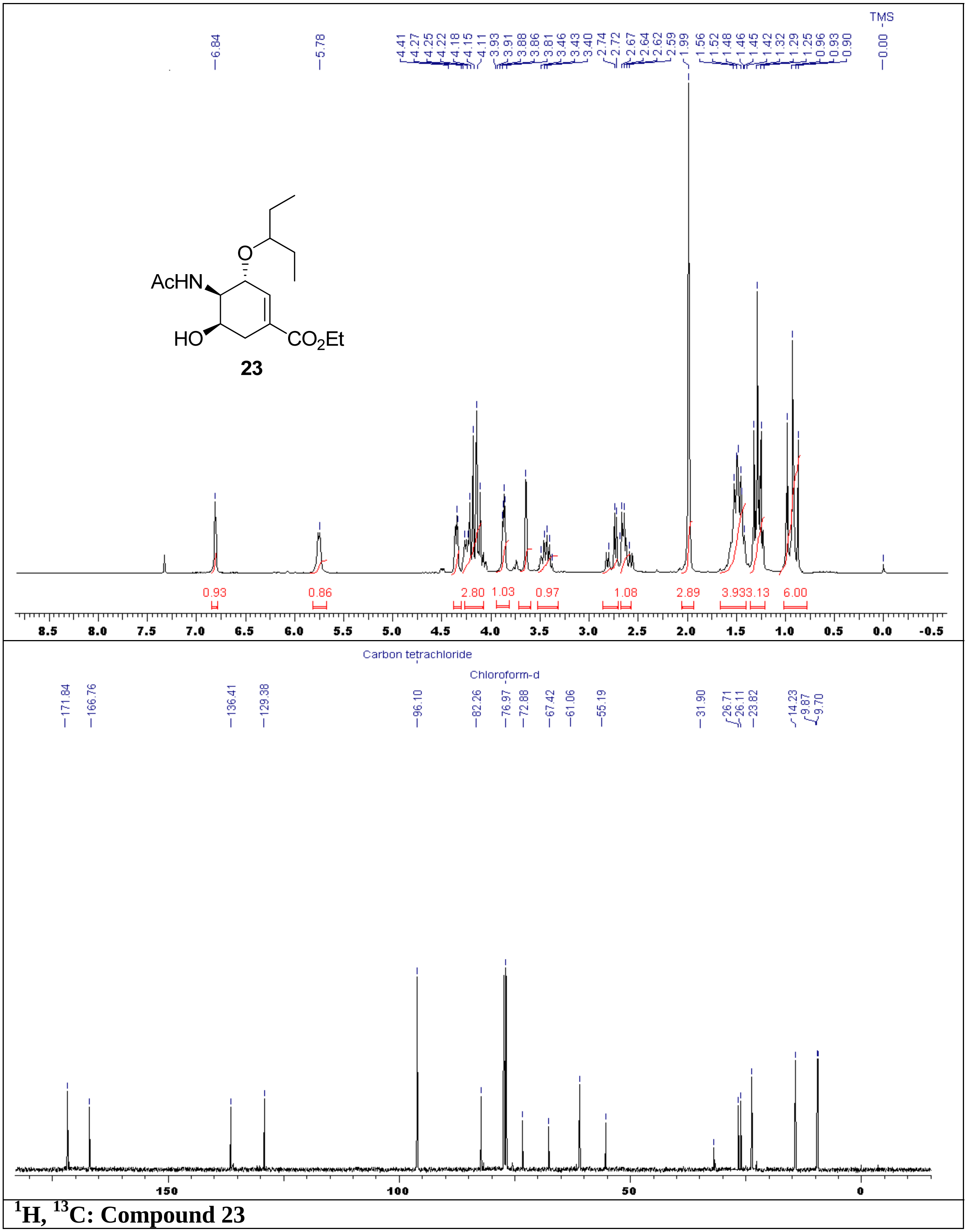
^{1}H, ^{13}C NMR, NOESY and COSY: Compound 3



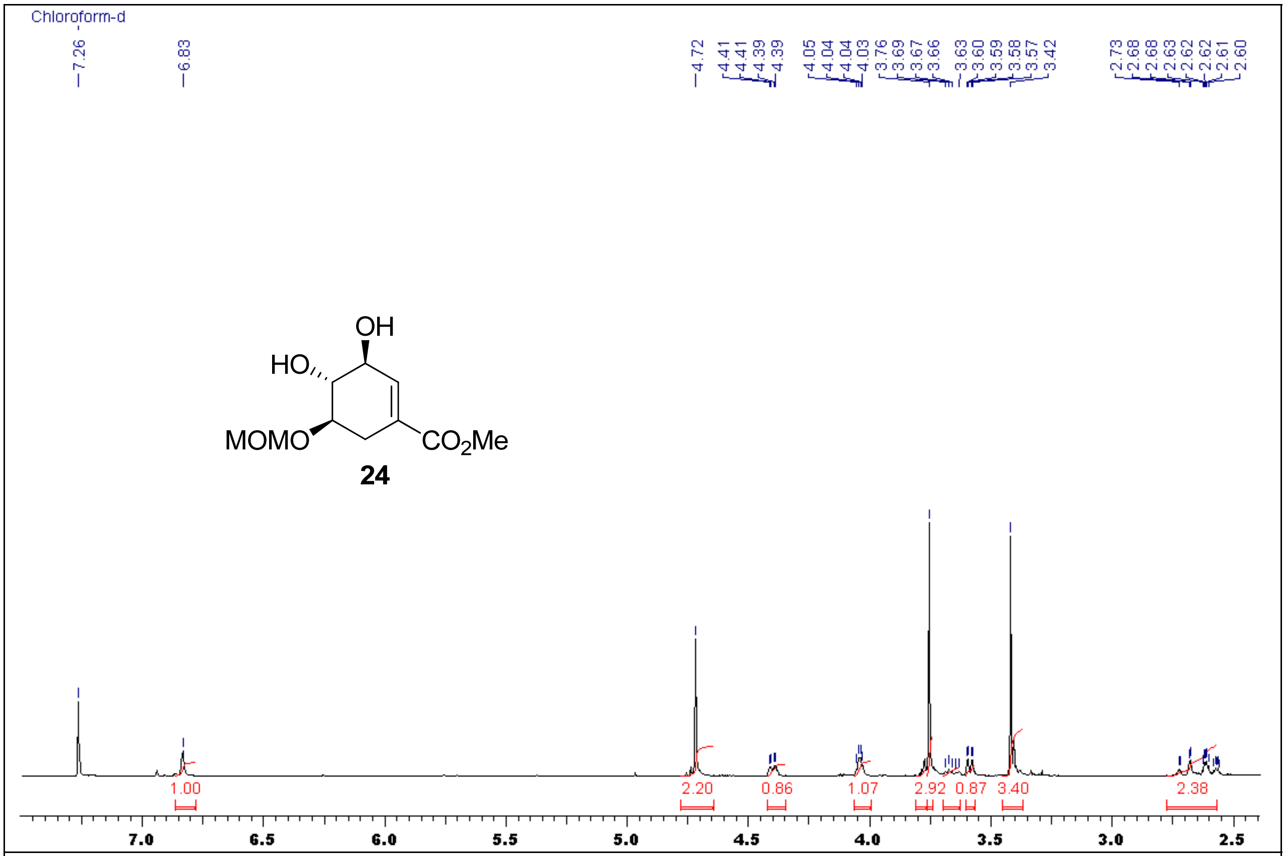
^{1}H, and ^{13}C NMR: Compound 21



^{1}H, and ^{13}C NMR: Compound 22



^{1}H, ^{13}C: Compound 23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6.83
4.72
4.41
4.41
4.39
4.39
4.05
4.04
4.04
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3.76
3.69
3.67
3.66
3.63
3.60
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3.58
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2.62
2.61
2.60
OH
HO
MOMO
CO_2Me
24
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2.20
0.86
1.07
2.92
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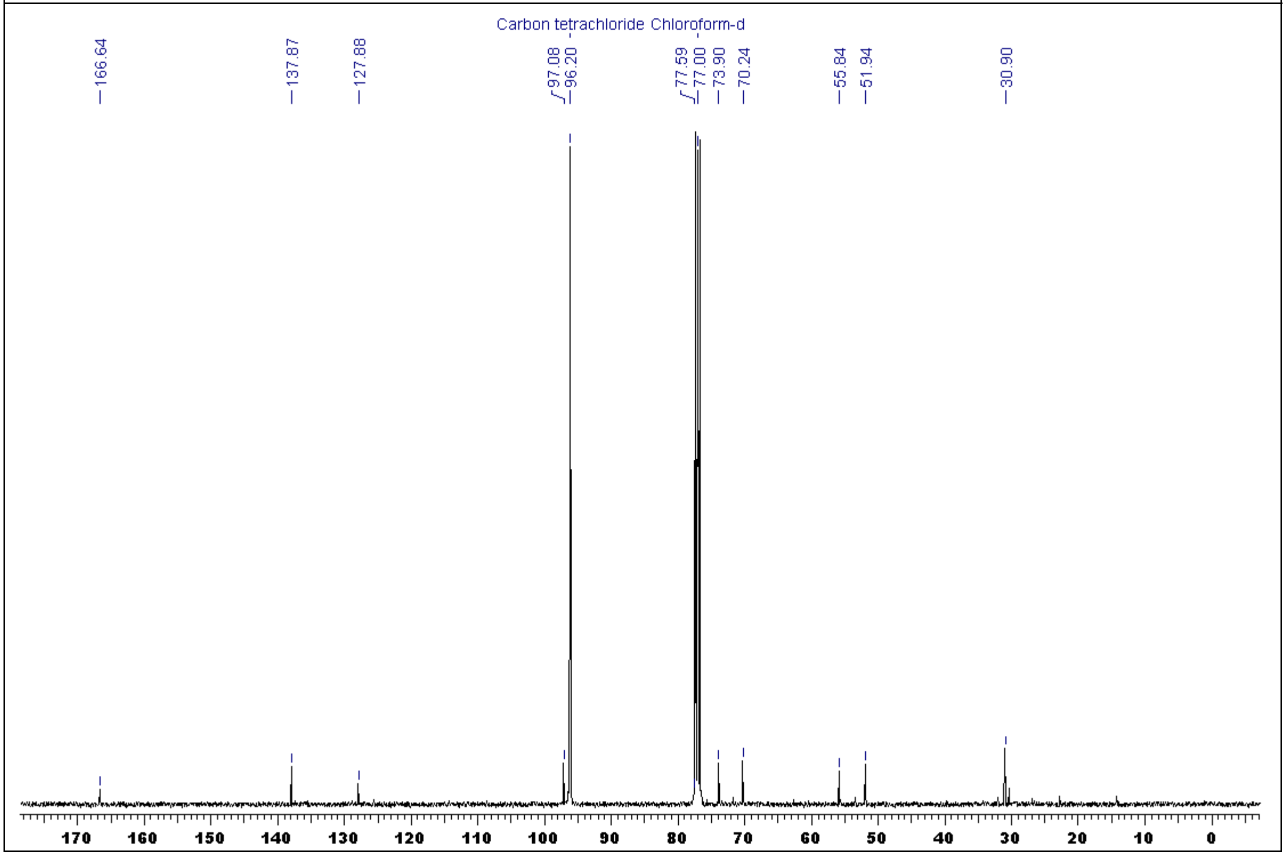
3.5
3.0
2.5


Carbon tetrachloride Chloroform-d
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137.87
127.88
97.08
96.20
77.59
77.00
73.90
70.24
55.84
51.94
30.90
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70
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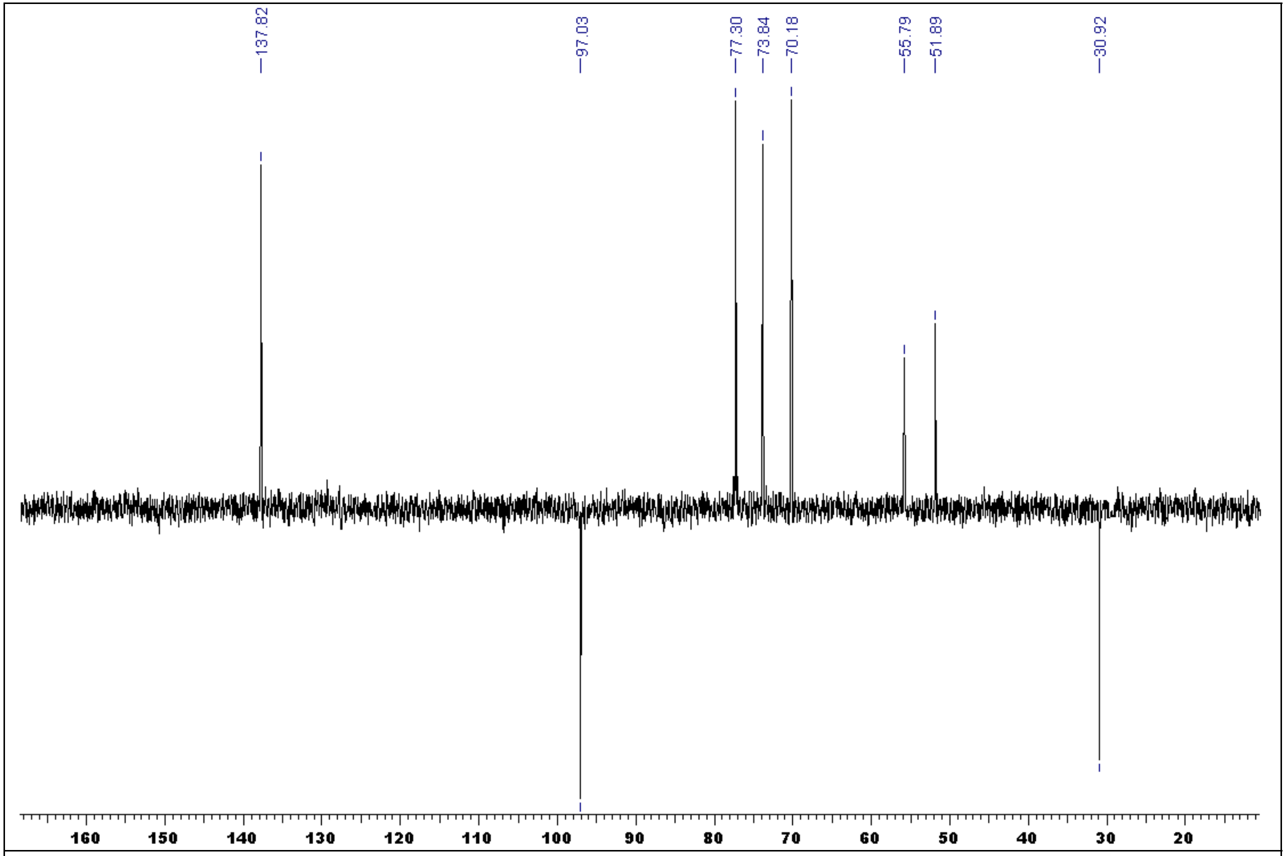
50
40
30
20
10
0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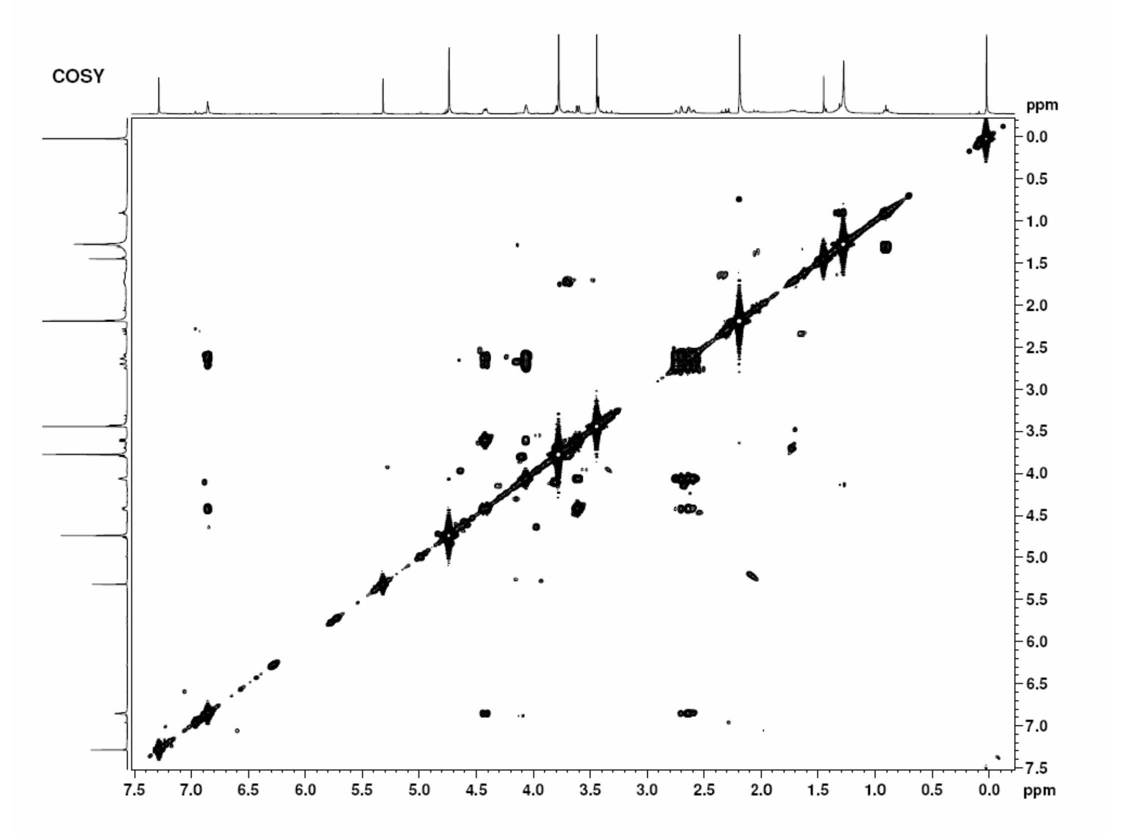
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4.5
5.0
5.5
6.0
6.5
7.0
7.5
7.5
7.0
6.5
6.0
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5.0
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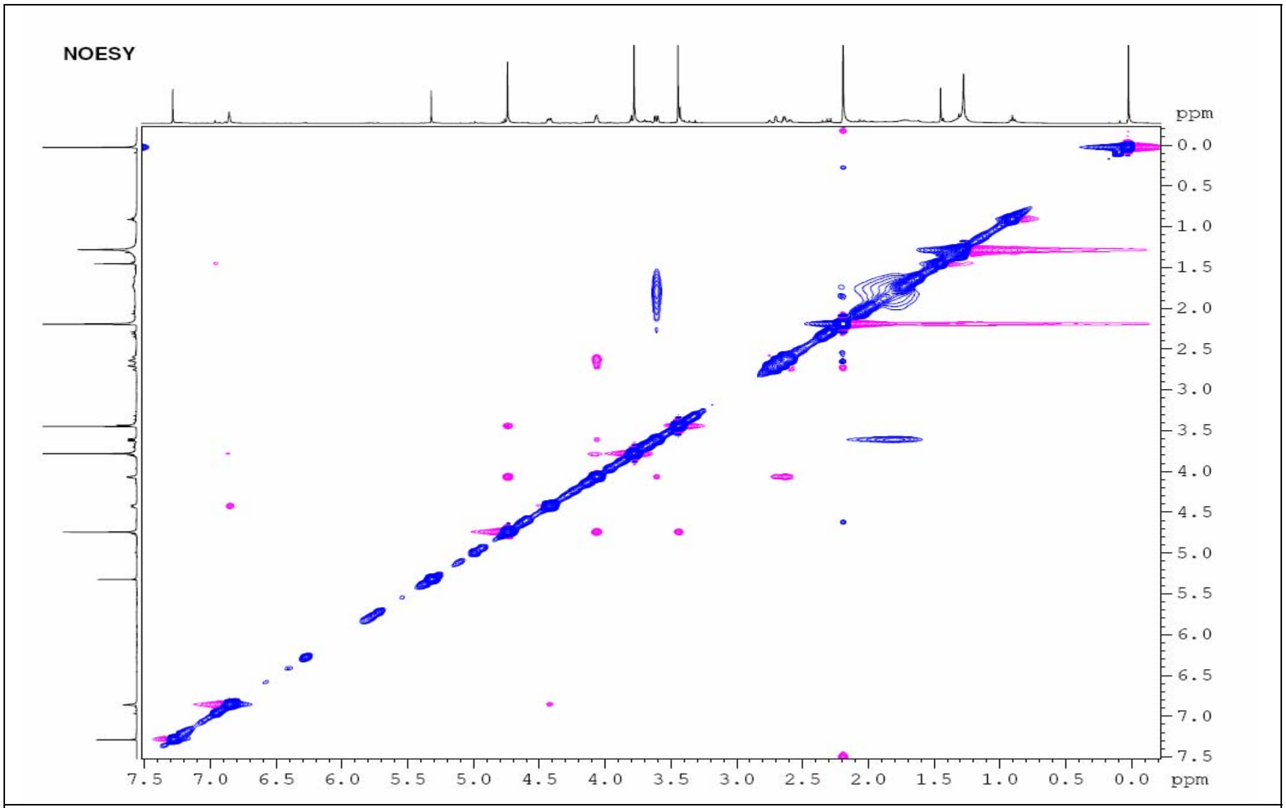
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


NOESY
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2.0
2.5
3.0
3.5
4.0
4.5
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5.5
6.0
6.5
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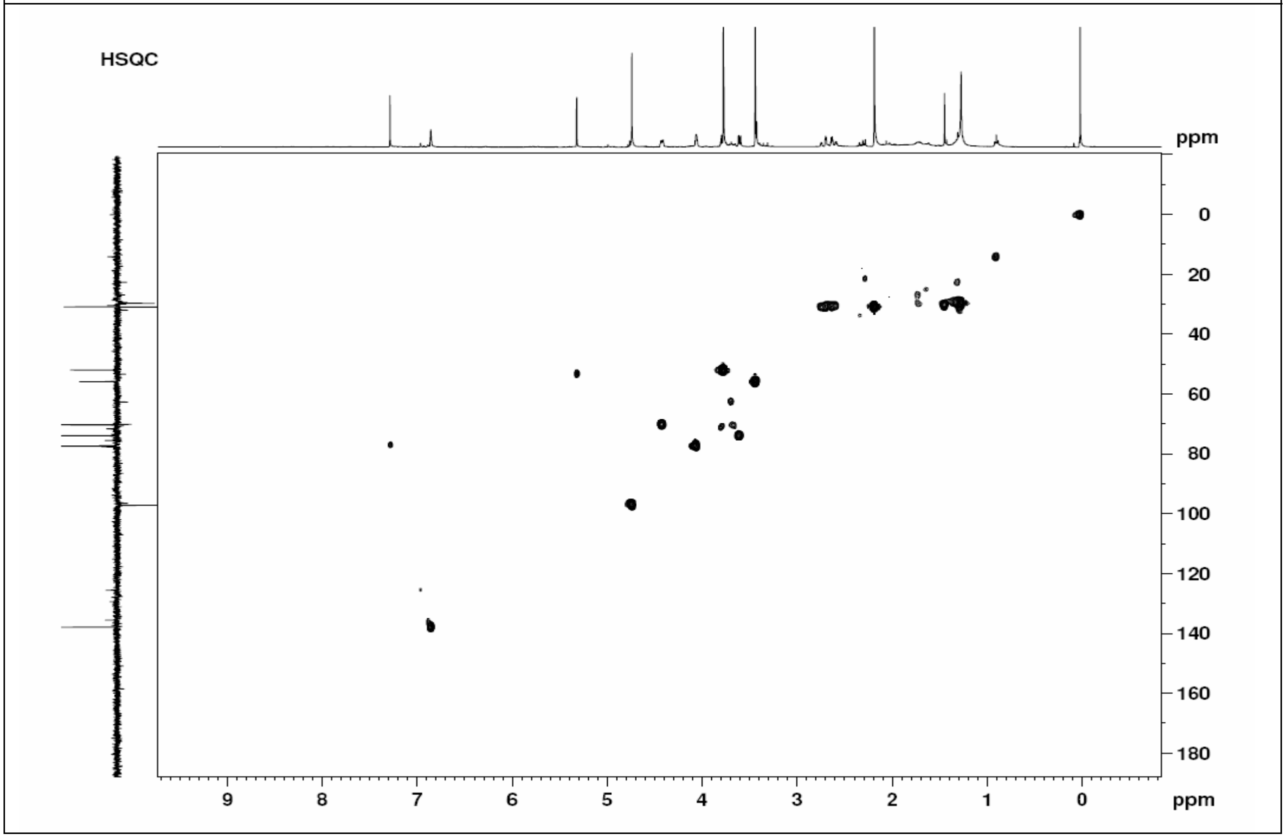
HSQC
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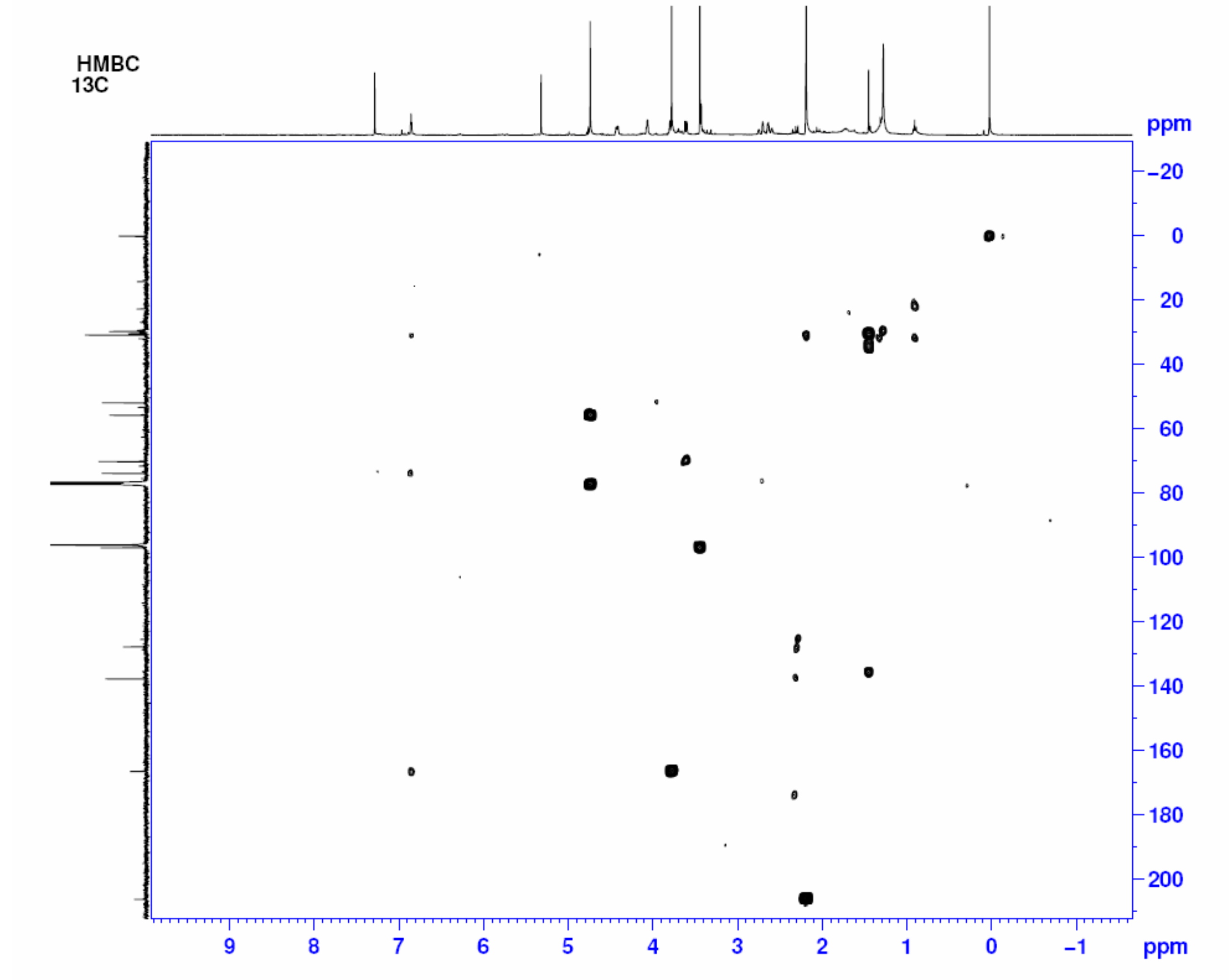
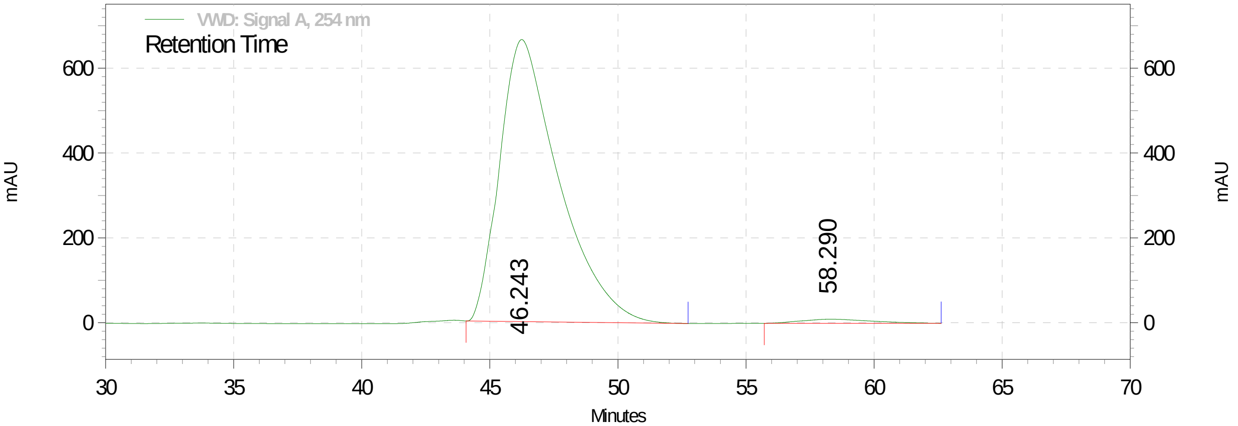


^{1}H, ^{13}-C, DEPT, COSY, NOESY, HSQC and HMBC: Compound 24

HPLC

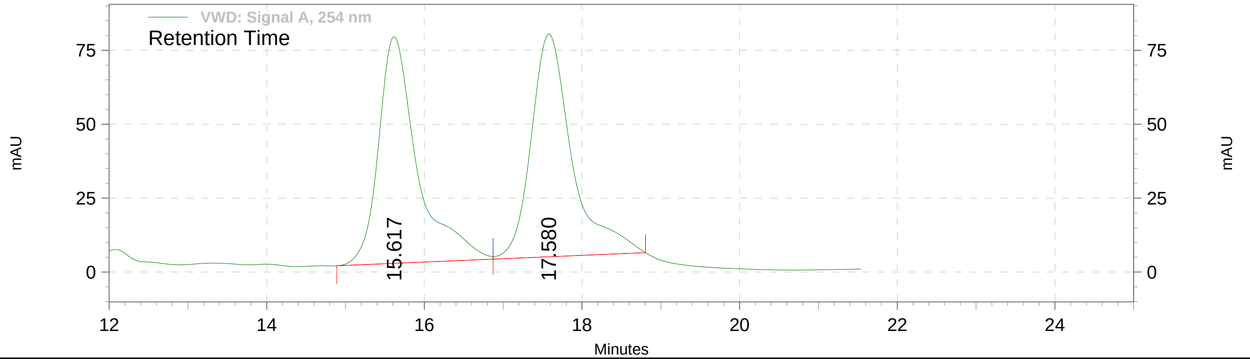


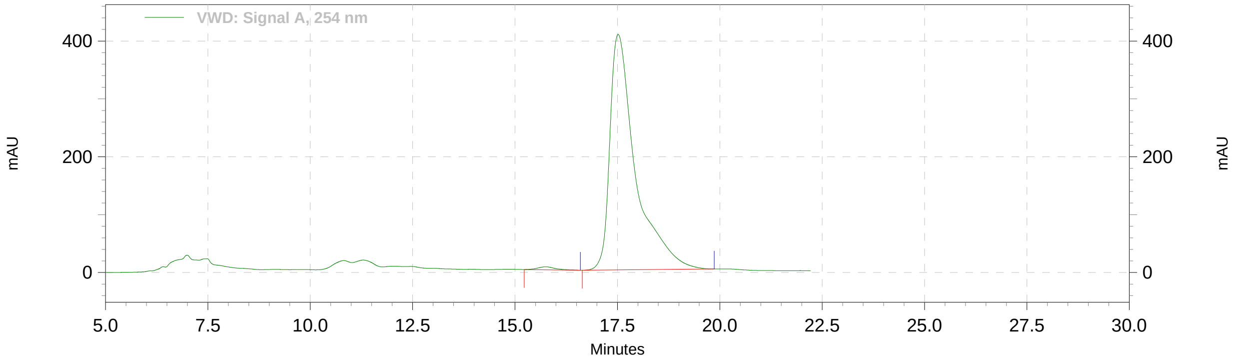
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
46.243	1792753436	98.31	11156727	98.56
58.290	30806312	1.69	162754	1.44
Totals	1823559748	100.00	11319481	100.00

Column :ODH (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(20:80)
Wavelength :254nm
Flow rate :0.5ml/min(25 bar)
Con. :1.5mg/ml
Inject Vol : 10uL

Chiral HPLC of 3,5-dinitro benzoate of epoxy alcohol (-)-6





VWD: Signal A, 254 nm Results

Retention Time	Area	Area %	Height	Height %
15.747	2578055	0.86	86067	1.24
17.517	297132318	99.14	6829082	98.76
Totals	299710373	100.00	6915149	100.00

Column :OJH
Mobile Phase :IPA:n-Hexane(10:90)
Wavelength :210nm
Flow rate :0.5ml/min (25 bar)
Con. :1.5mg/ml
Inject Vol : 10uL

HPLC of *syn*- epoxy alcohol 14