

# **Supporting Information for**

## **Total Synthesis of Potential Anti-tumor Agent, (-)-Dictyostatin**

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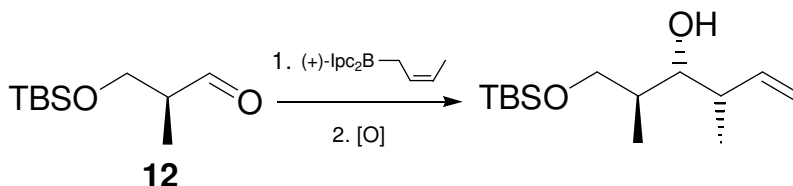
### **Contents (100 pages):**

1. Experimental procedures and product characterization data (pp S2 – S27).
2.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra (pp S28-S100).

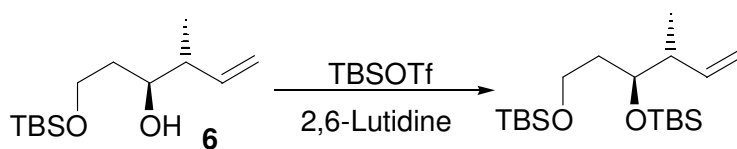
### **General Experimental Procedures.**

$^1\text{H}$  and  $^{13}\text{C}$  spectra were recorded at 25 °C on Varian Inova spectrometers at the indicated frequencies using  $\text{CDCl}_3$  as the solvent unless otherwise mentioned. All dry reactions were performed in a flame dried glassware under a dry  $\text{N}_2$  atmosphere. All dry solvents were distilled before used. All flash chromatography was performed using standard grade silica gel (Sorbant Technologies, particle size: 40-63  $\mu\text{m}$ , 230 X 400 mesh).

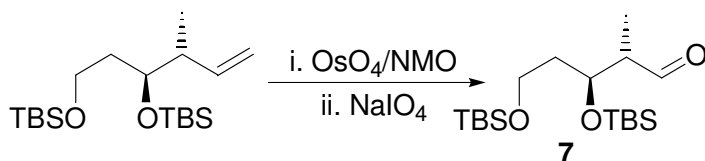
### General Procedure for pinane-based crotylboration:



To a  $-78^{\circ}\text{C}$  solution of *t*-BuOK (1.0M in THF, 191 mL, 191 mmol) in THF (300 mL), was added via cannula, *cis*-2-Butene (35 mL, 367.5 mmol). After 5 minutes, a  $-78^{\circ}\text{C}$  cooled solution of *n*-BuLi (2.5M in Hexanes, 76.4 mL, 191 mmol) in THF (100 mL) was added dropwise via cannula. The reaction mixture was warmed to  $-55^{\circ}\text{C}$ , stirred there for 45 minutes and again cooled to  $-78^{\circ}\text{C}$ . A  $-40^{\circ}\text{C}$  cooled solution of (+)-Ipc<sub>2</sub>BOMe (70 g, 220.5 mmol) in THF (200 mL) was added dropwise, via cannula and the reaction mixture was stirred for 1 h. BF<sub>3</sub>·Et<sub>2</sub>O (31.4 mL, 250 mmol) was added dropwise followed by the dropwise addition of a  $-78^{\circ}\text{C}$  cooled solution of aldehyde **12** (30 g, 147 mmol) in THF (100 mL) via cannula. The reaction mixture was stirred at  $-78^{\circ}\text{C}$  for 4 h and then oxidized by a slow addition of 3M NaOH solution (88.2 mL, 264.6 mmol) and H<sub>2</sub>O<sub>2</sub> (30% solution, 88 mL, 264.6 mmol) at  $-78^{\circ}\text{C}$ , warming to rt and then refluxing for 4 h. Layers were separated and the aqueous layer was extracted with ether (3 x 200 mL). Combined organic layers were washed with brine (100 mL), dried over MgSO<sub>4</sub> and concentrated in *vacuo*. The crude product was purified by flash column chromatography (2:98::EtOAc:Hexanes) to give homoallylic alcohol (33.7 g, 129.6 mmol, 88%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 5.95-5.83 (m, 1H), 5.15-5.09 (m, 2H), 3.98-3.82 (m, 2H), 3.77-3.72 (m, 1H), 3.24 (brs, 1H), 2.36-2.24 (m, 1H), 1.73-1.66 (m, 2H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.96 (s, 9H), 0.13 (s, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 140.7, 115.1, 74.9, 62.7, 43.9, 35.6, 25.9, 25.8, 18.1, 15.8, -5.4; EI-MS: 189 (M-C<sub>4</sub>H<sub>7</sub>)<sup>+</sup>; CI-MS: 245 (M+H)<sup>+</sup>, 189 [(M+H-C<sub>4</sub>H<sub>8</sub>)<sup>+</sup>, 100%].

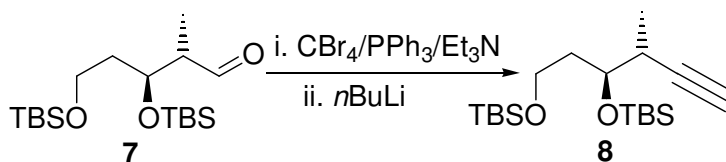


To a  $-78\text{ }^{\circ}\text{C}$  solution of **6** (4.1 g, 16.8 mmol) in  $\text{CH}_2\text{Cl}_2$  (80 mL), was added 2,6-Lutidine (3.81 mL, 32.78 mmol) dropwise followed by the addition of TBSOTf (15.4 mL, 67.2 mmol). Reaction mixture was stirred at  $-78\text{ }^{\circ}\text{C}$  for 1 h, quenched with satd.  $\text{NaHCO}_3$  (25 mL) and warmed to rt. Layers were separated and the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 50 mL). Organic layers were combined, washed with brine (50 mL), dried over  $\text{MgSO}_4$ , and concentrated in *vacuo*. The crude product was purified by flash column chromatography (3:97::EtOAc:Hexanes) to furnish TBS ether (5.4 g, 15.12 mmol, 90%) as colorless oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 5.91-5.80 (m, 1H), 5.11-5.04 (m, 2H), 3.86 (dt,  $J = 6.0\text{ Hz}, 3.3\text{ Hz}$ , 1H), 3.79-3.66 (m, 2H), 2.43-2.35 (m, 1H), 1.71-1.63 (m, 2H), 1.09 (d,  $J = 6.9\text{ Hz}$ , 3H), 0.92-0.94 (m, 18H), 0.14-0.11 (m, 12H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 140.9, 114.4, 72.3, 60.2, 43.3, 36.3, 26.0, 25.7, 18.2, 14.7, -2.8, -4.4, -5.2; EI-MS: 303 ( $\text{M}-\text{C}_4\text{H}_7$ ) $^+$ ; 359 ( $\text{M}+\text{H}$ ) $^+$ .



**3,5-Bis-(tert-butyl-dimethyl-silyloxy)-2-methyl-pentanal, 7:** To a solution of the intermediate alkene (4.75 g, 13.25 mmol) in *t*-BuOH and water (56 mL and 14 mL), was added NMO (50% by wt. In water, 4.12 mL, 19.89 mmol) and  $\text{OsO}_4$  (100 mg, 0.3977 mmol) and reaction mixture was stirred at rt for 12 h before it was quenched with addition of granular sodium bisulfite (500 mg). After stirring for 15 min, reaction mixture was filtered and filtrate was concentrated in *vacuo*. Residue was diluted with EtOAc (150 mL) and brine (50 mL). Layers were separated and the aqueous layer was extracted with EtOAc (3 x 50 mL). Combined organic layers were dried over  $\text{MgSO}_4$  and concentrated

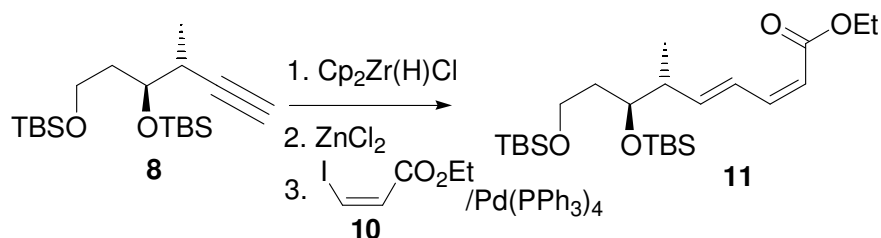
in *vacuo*. The crude diol was taken in acetone and water (56 mL and 14 mL) and solid sodium meta periodate (5.7 g, 26.51 mmol) was added. The white suspension was stirred at rt for 1 h before it was filtered and filtrate was concentrated in *vacuo*. The residue was diluted with Et<sub>2</sub>O (150 mL) and water (50 mL). Layers were separated and aqueous layer was extracted with Et<sub>2</sub>O (3 x 50 mL). Organic layers were combined, dried over MgSO<sub>4</sub> and concentrated in *vacuo*. The crude product was purified by flash column chromatography (10:90::EtOAc:Hexanes) to yield aldehyde **7** (3.4 g, 9.54 mmol, 72%, from 6a) as colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 9.80 (d, *J* = 2.4 Hz, 1H), 4.24-4.19 (m, 1H), 3.74 (t, *J* = 5.7 Hz, 2H), 2.66-2.57 (m, 1H), 1.90-1.66 (m, 2H), 1.17 (d, *J* = 6.9 Hz, 3H), 0.95 (s, 9H), 0.94 (s, 9H), 0.14-0.10 (m, 12H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 204.9, 70.4, 59.1, 51.6, 37.7, 25.9, 25.8, 10.2, -4.3, -4.7, -5.3.



**4,6-Bis-(tert-butyl-dimethyl-silyloxy)-3-methyl-hex-1-yne, 8:** A solution of **7** (150 mg, 0.41 mmol) and Et<sub>3</sub>N (0.18 mL, 1.24 mmol) was taken in 1.0 mL CH<sub>2</sub>Cl<sub>2</sub> and cooled to 0 °C. In a separate flask, CBr<sub>4</sub> (317 mg, 0.95 mmol) solution in 2.0 mL CH<sub>2</sub>Cl<sub>2</sub> was cooled to 0 °C and PPh<sub>3</sub> (502 mg, 1.91 mmol) was added. This solution was added, dropwise via cannula, to the aldehyde solution. After stirring at 0 °C for 45 minutes, half of the solvent was evaporated in *vacuo* and crude residue was filtered on a short pad of silica gel (2% EtOAc/Hexanes) to give dibromide (192 mg, 0.37 mmol), which was taken in 4.0 mL THF and cooled to -78 °C. *n*-BuLi (2.5M in Hexanes, 0.6 mL, 1.48 mmol) was added dropwise. The reaction mixture was stirred at -78 °C for 2 h, before it was quenched with 2.0 mL water and warmed to rt. Layers were separated and aqueous later was extracted with Et<sub>2</sub>O (3 x 25 mL). Combined organic layers were washed with brine (25 mL), dried over MgSO<sub>4</sub> and concentrated in *vacuo*. The crude product was purified by flash column chromatography (2:98::EtOAc:Hexanes) to furnish alkyne **8** (124 mg, 0.35 mmol, 85% from **7**), as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 3.98-3.93 (m, 1H), 3.80-3.67 (m, 2H), 2.72-2.63 (m, 1H), 2.10 (d, *J* = 2.1 Hz, 1H), 2.00-1.90 (m, 1H), 1.74-1.63 (m, 1H), 1.22 (d, *J* = 6.9 Hz, 3H), 0.95 (s, 18H), 0.13-0.11 (s, 12H); <sup>13</sup>C NMR (75 MHz,

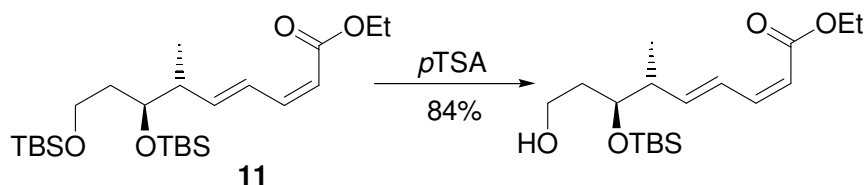


CDCl<sub>3</sub>)  $\delta$  (ppm): 86.3, 70.8, 69.7, 60.0, 35.9, 32.0, 25.9, 25.8, 18.3, 18.1, 14.7, -4.5, -4.6, -5.2; EI-MS: 303 (M-C<sub>4</sub>H<sub>5</sub>)<sup>+</sup>, CI-MS: 357 (M+H)<sup>+</sup>.



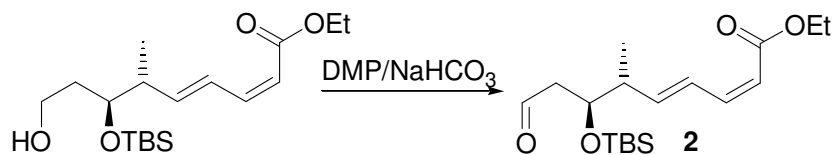
**7,9-Bis-(tert-butyl-dimethyl-silyloxy)-6-methyl-nona-2,4-dienoic acid ethyl ester, 11:**

To a suspension of Cp<sub>2</sub>Zr(H)Cl (90 mg, 0.3275 mmol) in 1.0 mL THF, was added dropwise a solution of **8** (100 mg, 0.28 mmol) dropwise. The clear solution was stirred at rt for 45 minutes and then THF (0.5 mL) solution of anhydrous ZnCl<sub>2</sub> (51 mg, 0.37 mmol) was added dropwise. After 5 minutes, a THF (0.5 mL) solution of **10** and Pd catalyst was added dropwise. After stirring at rt for 1 h, solvent was removed, diluted with 50 mL of 10% ether/pentane, filtered and concentrated in *vacuo*. The crude product was purified with flash column chromatography (3:97::EtOAc:Hexanes) to provide *E,Z*-diene ester **11** (75 mg, 0.16 mmol, 70% from **8**) as a colorless oil.



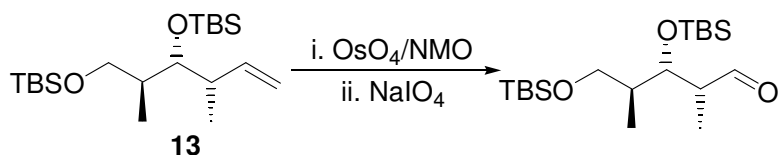
To a solution of **11** (80 mg, 0.17 mmol) in 1.5 mL MeOH at 0 °C, was added *p*TSA (3.2 mg, 0.017 mmol) and the reaction mixture was stirred at rt for 1.5 h before it was quenched with 0.5 mL Et<sub>3</sub>N. The solvent was evaporated in *vacuo* and the crude product was purified via a flash column chromatography (20:80::EtOAc:Hexanes) to furnish the intermediate 1° alcohol (50.4 mg, 0.15 mmol, 84%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 7.37 (dd, *J* = 15.4 Hz, 11.4 Hz, 1H), 6.53 (t, *J* = 11.3 Hz, 1H), 5.99 (dd, *J* = 15.4 Hz, 7.7 Hz, 1H), 5.58 (d, *J* = 11.3 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.88-3.82 (m, 1H), 3.75-3.67 (m, 2H), 2.59-2.49 (m, 1H), 1.86 (s, 1H), 1.73-1.58 (m,

2H), 1.29 (t,  $J = 7.1$  Hz, 3H), 1.06 (d,  $J = 6.9$  Hz, 3H), 0.89 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 166.4, 146.7, 145.0, 126.8, 116.1, 73.6, 59.9, 59.8, 42.6, 35.5, 25.7, 17.9, 14.6, 14.2, -4.4, -4.6; ESI: 365.13 ( $\text{M}+\text{Na}$ ) $^+$ .



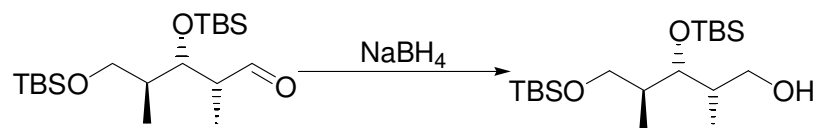
**7-(tert-Butyl-dimethyl-silyloxy)-6-methyl-9-oxo-nona-2,4-dienoic acid ethyl ester, 2:**

To a suspension of DMP reagent (699 mg, 1.65 mmol) and  $\text{NaHCO}_3$  (345 mg, 4.11 mmol) in  $\text{CH}_2\text{Cl}_2$  (6.0 mL) at 0  $^\circ\text{C}$ , was added a  $\text{CH}_2\text{Cl}_2$  (4.0 mL) solution of the intermediate alcohol (470 mg, 1.37 mmol) and the reaction mixture was stirred at 0  $^\circ\text{C}$  for 1 h before the solvent was partially evaporated in *vacuo*. The crude product was purified via a flash column chromatography (15:85::EtOAc:Hexanes) to yield aldehyde **2** (440 mg, 1.29 mmol, 94%) as a yellow oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 9.77 (s, 1H), 7.38 (dd,  $J = 15.3$  Hz, 11.2 Hz, 1H), 6.53 (t,  $J = 11.2$  Hz, 1H), 5.96 (dd,  $J = 16.3$  Hz, 7.9 Hz, 1H), 5.61 (d,  $J = 11.3$  Hz, 1H), 4.24-4.14 (m, 3H), 2.59-2.40 (m, 3H), 1.29 (t,  $J = 7.0$  Hz, 3H), 1.09 (d,  $J = 6.9$  Hz, 3H), 0.87 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 201.5, 166.3, 145.2, 144.6, 127.5, 116.7, 70.8, 59.8, 48.1, 43.2, 25.7, 17.9, 14.8, 14.2, -4.6, -4.6; EI-MS: 295 ( $\text{M}-\text{OC}_2\text{H}_5$ ) $^+$ ; CI-MS: 341 ( $\text{M}+\text{H}$ ) $^+$ ; 297 [ $(\text{M}+\text{H})-\text{OC}_2\text{H}_4$ ] $^+$ .

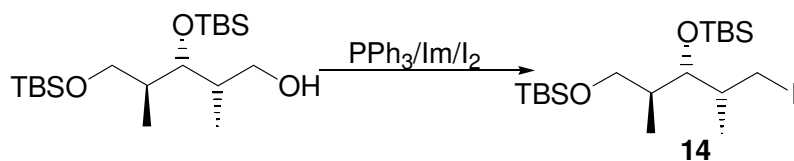


To a solution of **13** (12.4 g, 33.29 mmol) in *t*-BuOH and water (135 mL and 34 mL), was added NMO (50% by wt. In water, 10.3 mL, 49.94 mmol) and  $\text{OsO}_4$  (170 mg, 0.67 mmol) and reaction mixture was stirred at rt for 12 h before it was quenched with addition of granular sodium bisulfite (1 g). After stirring for 15 min, reaction mixture was filtered and filtrate was concentrated in *vacuo*. Residue was diluted with EtOAc (250 mL)

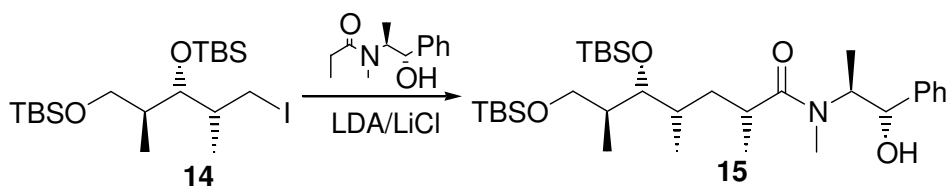
and brine (100 mL). Layers were separated and aqueous layer was extracted with EtOAc (3 x 100 mL). Combined organic layers were dried over MgSO<sub>4</sub> and concentrated in *vacuo*. The crude diol was taken in acetone and water (135 mL and 34 mL) and solid sodium meta periodate (14.2 g, 66.58 mmol) was added. The white suspension was stirred at rt for 1 h before it was filtered and filtrate was concentrated in *vacuo*. The residue was diluted with Et<sub>2</sub>O (200 mL) and water (75 mL). Layers were separated and aqueous layer was extracted with Et<sub>2</sub>O (3 x 75 mL). Organic layers were combined, dried over MgSO<sub>4</sub> and concentrated in *vacuo*. The crude product was purified by flash column chromatography (10:90::EtOAc:Hexanes) to yield the intermediate aldehyde (9.4 g, 25.1 mmol, 75%, from **13**) as colorless oil.



To a 0 °C cooled solution of the intermediate aldehyde (9.4 g, 25.1 mmol) in 100 mL EtOH, was added NaBH<sub>4</sub>, reaction mixture was warmed to rt and stirred for 45 minutes before the solvent was evaporated and residue was diluted with Et<sub>2</sub>O (200 mL) and water (100 mL). Layers were separated and the aqueous layer was extracted with Et<sub>2</sub>O (3 x 75 mL). Combined organic layer was washed with brine (100 mL), dried over MgSO<sub>4</sub> and concentrated in *vacuo*. The crude product was purified with flash column chromatography (15:85::EtOAc:Hexanes) to give the intermediate alcohol (9.35 g, 24.8 mmol, 99%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 3.83-3.80 (m, 1H), 3.76-3.71 (m, 1H), 3.64-3.46 (m, 3H), 2.27 (brs, 1H), 2.01-1.88 (m, 2H), 0.96-0.95 (m, 21H), 0.93 (d, *J* = 7.5 Hz, 3H), 0.12 (s, 6H), 0.10 (s, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 74.2, 66.5, 65.6, 40.0, 38.6, 26.0, 25.9, 18.3, 14.1, 11.9, -4.0, -4.2, -5.2, -5.3; EI-MS: 73 [Si(CH<sub>3</sub>)<sub>3</sub><sup>+</sup>, 100%]; CI-MS: 377 (M+H)<sup>+</sup>.

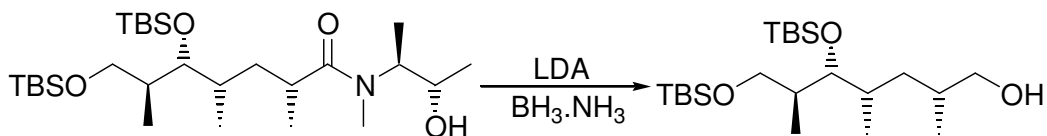


**1,3-Bis-(tert-butyl-dimethyl-silyloxy)-5-iodo-2,4-dimethyl-pentane, 14:** To a stirred solution of  $\text{PPh}_3$  (976 mg, 3.72 mmol) and Im (362 mg, 5.31 mmol) in THF (5 mL) and  $\text{CH}_3\text{CN}$  at rt, was added  $\text{I}_2$  (944 mg, 3.72 mmol). After 10 minutes, a THF (5 mL) solution of the intermediate alcohol (1.0 g, 2.66 mmol) was added dropwise. After stirring at rt for 1 h, solvent was removed in *vacuo*, residue was dissolved in minimum amount of  $\text{CH}_2\text{Cl}_2$ , diluted with *n*-Pentane (25 mL) and filtered. The filtrate was concentrated and the above sequence was repeated thrice. Solvent was removed in *vacuo*, diluted with  $\text{Et}_2\text{O}$  (50 mL) and washed with satd.  $\text{NaHCO}_3$  (20 mL), aq.  $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$  (by dissolving 1 g of  $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$  in 20 mL water) and brine (20 mL). The organic layer was dried over  $\text{MgSO}_4$  and concentrated in *vacuo*. The crude product was purified by flash column chromatography (2:98::EtOAc:Hexanes) to obtain iodide **14** (1.18 g, 2.42 mmol, 91%) as a colorless oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 3.77 (dd,  $J = 6.3$  Hz, 3 Hz, 1H), 3.74-3.69 (m, 1H), 3.49 (dd,  $J = 9.9$  Hz, 6.3 Hz, 1H), 3.31-3.17 (m, 2H), 2.07-1.95 (m, 1H), 1.91-1.78 (m, 1H), 1.06 (d,  $J = 6.9$  Hz, 3H), 0.96-0.93 (m, 21H), 0.14 (s, 6H), 0.10 (s, 6H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 75.7, 65.1, 40.3, 39.5, 26.1, 26.0, 18.5, 18.3, 15.0, 14.8, 14.3, -3.6, -3.9, -5.2, -5.3; ESI: 487.88 ( $\text{M}+\text{H}$ ) $^+$



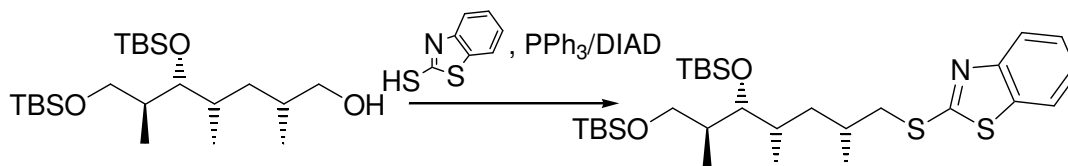
**5,7-Bis-(tert-butyl-dimethyl-silyloxy)-2,4,6-trimethyl-heptanoic acid (2-hydroxy-1-methyl-propyl)-methyl-amide, 15:** To a suspension of dry  $\text{LiCl}$  (1.22 g, 28.7 mmol) in 10.0 mL THF, was added diisopropylamine (1.23 mL, 8.81 mmol) and cooled to  $-78^\circ\text{C}$  before  $n\text{BuLi}$  (2.5M, 3.28 mL, 8.2 mmol) was added dropwise. The reaction was warmed to  $0^\circ\text{C}$ , stirred for 30 min, again cooled to  $-78^\circ\text{C}$  and a solution of amide (951 mg, 4.3 mmol) in 10 mL THF was added dropwise. The reaction mixture was stirred at  $-78^\circ\text{C}$  for

1 h and then warmed to rt and stirred there for 10 min before it was cooled to 0 °C. A solution of **14** (1.0 g, 2.05 mmol) in 3.0 mL THF was then added dropwise, reaction was warmed to rt and stirred there for 32 h. Reaction was quenched with satd. NaHCO<sub>3</sub> (25 mL), layers were separated and the aqueous layer was extracted with EtOAc (4 x 25 mL). Combined organic layers were dried over MgSO<sub>4</sub>, solvent was evaporated in *vacuo* and the crude product was purified with flash column chromatography (25:75::EtOAc:Hexanes) to furnish amide **15** (1.11 g, 1.91 mmol, 93%) as white solid. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 7.42-7.28 (M, 5H), 4.66 (d, *J* = 7.8 Hz, 1H), 4.47 (brs, 1H), 3.78-3.73 (m, 1H), 3.53-3.41 (m, 2H), 2.91 (s, 3H), 2.81-2.70 (m, 1H), 1.84-1.75 (m, 2H), 1.67-1.59 (m, 1H), 1.36-1.27 (m, 1H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.13 (d, *J* = 6.3 Hz, 3H), 0.97-0.93 (m, 21H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.10-0.09 (m, 12H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 179.0, 142.7, 128.3, 127.5, 126.2, 65.7, 40.6, 39.9, 34.2, 33.2, 26.2, 26.0, 18.5, 18.3, 14.5, 14.3, 13.5, -3.5, -3.8, -5.1, -5.2.

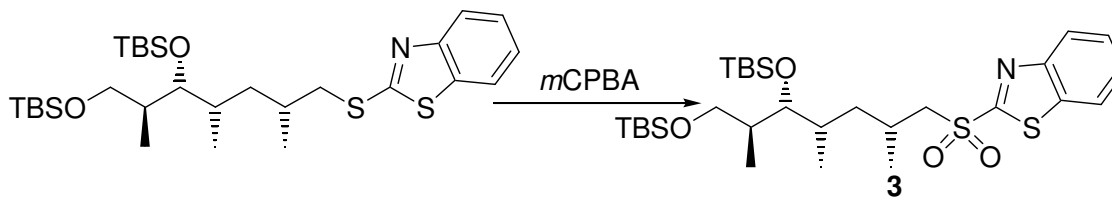


To a -78 °C cooled solution of diisopropylamine (1.17 mL, 8.33 mmol) in 5.0 mL THF, was added *n*-BuLi (2.5M in Hexanes, 3.03 mL, 7.57 mmol) dropwise before the mixture was warmed to 0 °C and stirred there for 30 min. Solid BH<sub>3</sub>.NH<sub>3</sub> (266 mg, 7.76 mmol) was added to the reaction mixture, which was stirred at 0 °C for 15 min, at rt for 30 min and again cooled to 0 °C. Solution of **15** (1.1 g, 1.89 mmol) in 10.0 mL THF was then added dropwise, the reaction mixture was warmed to rt and then stirred there for 18 h before it was quenched with brine (25 mL). Layers were separated and the aqueous layer was extracted with Et<sub>2</sub>O (3 x 25 mL). Combined organic layers were dried over MgSO<sub>4</sub> and solvent was evaporated in *vacuo*. The crude product was purified by flash column chromatography (8:92::EtOAc:Hexanes) to yield alcohol the intermediate alcohol (722 mg, 1.72 mmol, 91%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 3.74-3.69 (m, 1H), 3.60-3.53 (m, 2H), 3.45 (dd, *J* = 9.9 Hz, 6.9 Hz, 1H), 3.41-3.35 (m, 1H), 1.98 (brs, 1H), 1.88-1.68 (m, 4H), 1.48-1.39 (m, 1H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.95-0.94 (m,

21H), 0.91 (d,  $J = 6.6$  Hz, 3H), 0.09-0.08 (m, 12H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 76.3, 67.9, 65.7, 40.5, 38.6, 33.1, 32.9, 26.2, 25.9, 18.4, 18.3, 17.6, 14.9, 14.4, -3.7, -3.9, -5.2, -5.3; EI-MS: 301 ( $\text{M}-\text{C}_4\text{H}_9$ ) $^+$ ; CI-MS: 419 ( $\text{M}+\text{H}$ ) $^+$ .



To a stirred solution of the intermediate alcohol (200 mg, 0.48 mmol) in 4.0 mL THF,  $\text{PPh}_3$  (175 mg, 0.67 mmol) and 2-mercaptobenzothiazole (104 mg, 0.62 mmol) were added at rt. The reaction mixture was then cooled to 0  $^\circ\text{C}$  before DIAD (0.15 mL, 0.76 mmol) was added dropwise. The reaction was warmed to rt and stirred there for 2 h. Solvent was removed and the crude product was purified with flash column chromatography (1:99::EtOAc:Hexanes) to give the intermediate sulfide (270 mg, 0.48 mmol, 100%) as colorless oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.91 (d,  $J = 8.4$  Hz, 1H), 7.78 (d,  $J = 7.8$  Hz, 1H), 7.47-7.42 (m, 1H), 7.34-7.29 (m, 1H), 3.81-3.72 (m, 1H), 3.66-3.55 (m, 2H), 3.52-3.46 (m, 1H), 3.16-3.09 (m, 1H), 2.14-2.07 (m, 1H), 1.94-1.84 (m, 2H), 1.63-1.51 (m, 1H), 1.33-1.24 (m, 1H), 1.15 (d,  $J = 6.6$  Hz, 3H), 0.99-0.96 (m, 24H), 0.15-0.10 (m, 12H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 167.5, 153.3, 135.2, 125.9, 124.1, 121.4, 120.9, 76.4, 65.6, 42.0, 40.7, 40.4, 33.0, 30.9, 26.3, 26.0, 20.3, 18.5, 18.3, 14.7, 14.4, -3.6, -3.9, -5.2, -5.3; ESI: 568.85 ( $\text{M}+\text{H}$ ) $^+$ , 590.02 ( $\text{M}+\text{Na}$ ) $^+$ .

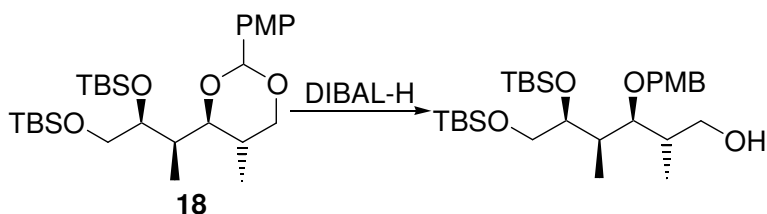


### 2-[5,7-Bis-(tert-butyl-dimethyl-silyloxy)-2,4,6-trimethyl-heptane-1-sulfonyl]

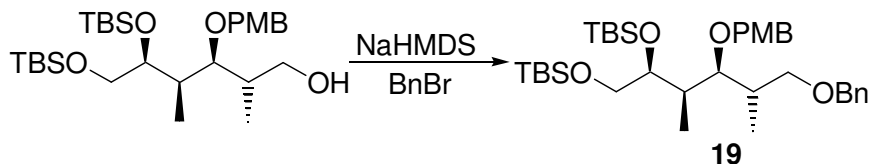
**benzothiazole, 3:** To a stirred solution of intermediate (260 mg, 0.46 mmol) in  $\text{CH}_2\text{Cl}_2$ , was added  $\text{NaHCO}_3$  (115 mg, 1.37 mmol) and *m*CPBA (205 mg, 1.19 mmol) at rt and stirred for 8 h. Then another 0.91 mmol of *m*CPBA and 1.37 mmol of  $\text{NaHCO}_3$  were

added and the reaction was further stirred for another 8 h before it was filtered and stirred with satd.  $\text{NaHCO}_3$  (10 mL) for 15 min. Layers were separated, the aqueous layer was extracted with  $\text{Et}_2\text{O}$  (3 x 25 mL), combined organic layers were dried over  $\text{MgSO}_4$  and solvent was removed in *vacuo*. The crude product was purified by flash column chromatography (6:94::EtOAc:Hexanes) to furnish sulfone **3** (255 mg, 0.43 mmol, 93%) as colorless oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.20 (d,  $J = 7.5$  Hz, 1H), 8.01 (d,  $J = 7.4$  Hz, 1H), 7.67-7.56 (m, 2H), 3.64-3.58 (m, 2H), 3.44-3.35 (m, 2H), 3.23 (dd,  $J = 14.4$  Hz, 9.6 Hz, 1H), 2.40-2.29 (m, 1H), 1.83-1.69 (m, 2H), 1.44-1.35 (m, 1H), 1.29-1.22 (m, 1H), 1.19 (d,  $J = 6.5$  Hz, 3H), 0.87-0.85 (m, 21H), 0.73 (d,  $J = 6.7$  Hz, 3H), 0.023-0.02 (m, 12H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 166.7, 152.7, 136.8, 128.0, 127.6, 125.4, 122.4, 65.5, 60.4, 42.6, 40.4, 33.0, 26.4, 26.1, 21.0, 18.4, 18.3, 14.4, 14.0, -3.7, -4.0, -5.2, -5.3; ESI: 622.16 ( $\text{M}+\text{Na}$ ) $^+$ .

**4-[2,3-Bis-(tert-butyl-dimethyl-silyloxy)-1-methyl-propyl]-2-(4-methoxy-phenyl)-5-methyl-[1,3]diOxane, **18**:** To a stirred solution of **17** (6.8 g, 16.7 mmol) in dry toluene (100 mL), was added anhydrous MgSO<sub>4</sub> (17 g), *p*-anisaldehyde (3.8 mL, 33.44 mmol) and PPTS (430 mg, 1.67 mmol) and the mixture was stirred at 80 °C for 3 d before it was cooled to rt, filtered and solvent was evaporated in *vacuo*. The crude product was purified with flash column chromatography (7:93::EtOAc:Hexanes) to provide acetal **18** (8.3 g, 15.8 mmol, 95%) as light yellow solid. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 7.50 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 5.55 (s, 1H), 4.21 (dd, *J* = 11.1 Hz, 4.8 Hz, 1H), 3.89-3.84 (m, 6H), 3.78-3.72 (m, 1H), 3.64-3.57 (m, 1H), 2.18-2.08 (m, 2H), 1.14 (d, *J* = 7.5 Hz, 3H), 1.04 (s, 9H), 1.01 (s, 9H), 0.85 (d, *J* = 6.3 Hz, 3H), 0.22-0.17 (m, 12H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 159.6, 131.5, 127.1, 113.3, 100.4, 81.4, 76.5, 73.3, 65.7, 55.1, 37.9, 30.5, 26.0, 25.9, 18.4, 18.1, 12.3, 10.1, -4.1, -4.8, -5.2, -5.4; ESI: 547.15 (M+Na)<sup>+</sup>.



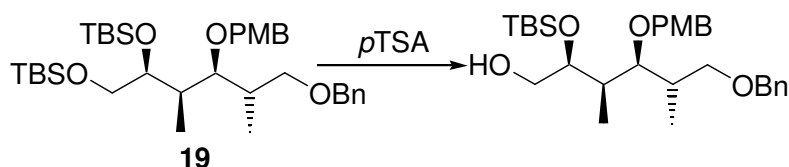
To a  $-78\text{ }^{\circ}\text{C}$  cooled solution of **18** (1g, 1.9 mmol) in  $\text{CH}_2\text{Cl}_2$  (16.0 mL), was added DIBAL-H (1.4 mL, 7.6 mmol) dropwise. After stirring at  $-78\text{ }^{\circ}\text{C}$  for 15 min, the reaction was warmed to  $0\text{ }^{\circ}\text{C}$  and stirred there for 2 h. Reaction was quenched with very slow addition of 3M NaOH solution, until hydrogen evolution stops. Mixture was warmed to rt, layers were separated and the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 30 mL). Combined organic layers were washed with brine (25 mL), dried over  $\text{MgSO}_4$  and solvent was evaporated under *vacuo*. The crude product was purified by flash column chromatography (15:85::EtOAc:Hexanes) to furnish the intermediate primary alcohol (900 mg, 1.71 mmol, 90%) as a colorless oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.32 (d,  $J = 8.4$  Hz, 2H), 6.92 (d,  $J = 8.1$  Hz, 2H), 4.62-4.54 (m, 2H), 3.90-3.85 (m, 4H), 3.77-3.72 (m, 1H), 3.66-3.50 (m, 4H), 2.75 (brs, 1H), 2.20-2.10 (m, 1H), 2.04-1.96 (m, 1H), 1.17 (d,  $J = 7.8$  Hz, 3H), 1.07 (d,  $J = 7.2$  Hz, 3H), 0.97 (s, 9H), 0.94 (s, 9H), 0.14-0.10 (m, 12H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 159.1, 130.4, 129.2, 113.7, 85.3, 75.0, 74.0, 65.4, 64.9, 55.1, 39.0, 36.8, 25.9, 18.2, 18.1, 15.5, 9.6, -3.9, -4.8, -5.4, -5.5; ESI: 549.07 ( $\text{M}+\text{Na}$ ) $^{+}$ .



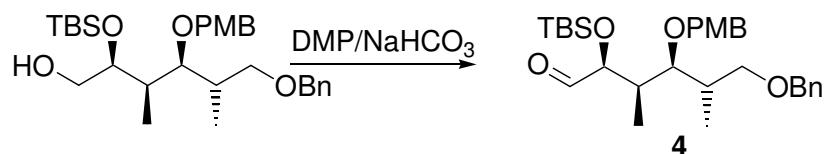
**5,6-Bis-(tert-butyl-dimethyl-silyloxy)-3-(4-methoxy-benzyloxy)-2,4-dimethyl-hexan-1-benzyl ether, 19:** To a  $0\text{ }^{\circ}\text{C}$  cooled solution of intermediate alcohol (3.5 g, 6.65 mmol) and BnBr (1.18 mL, 9.98 mmol) in THF/DMF (2:1; 30 mL, 15 mL), was added NaHMDS (1.0M in THF, 9.31 mL, 9.31 mmol) dropwise before the reaction was warmed to rt and stirred there for 2 h. Reaction was quenched with satd.  $\text{NaHCO}_3$  solution (25



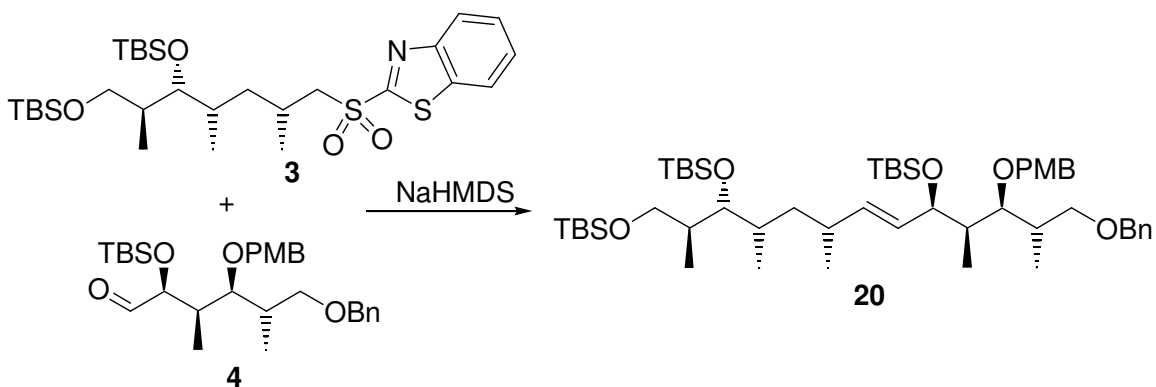
mL) and diluted with water (25 mL). Layers were separated and the aqueous layer was extracted with Et<sub>2</sub>O (3 x 30 mL). Combined organic layers were washed with brine (30 mL), dried over MgSO<sub>4</sub> and the solvent was evaporated in *vacuo*. The crude product was purified with flash column chromatography (5:95::EtOAc:Hexanes) to obtain benzyl ether **19** (4.01 g, 6.5 mmol, 98%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 7.49-7.37 (m, 5H), 7.34 (d, *J* = 8.7 Hz, 2H), 6.96 (d, *J* = 8.1 Hz, 2H), 4.68-4.56 (m, 4H), 3.90 (s, 3H), 3.87-3.83 (m, 1H), 3.75-3.57 (m, 5H), 2.28-2.20 (m, 1H), 2.18-2.08 (m, 1H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.09 (d, *J* = 7.2 Hz, 3H), 1.04 (s, 9H), 1.00 (s, 9H), 0.20-0.19 (m, 6H), 0.15 (s, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 158.9, 138.8, 131.3, 128.9, 128.2, 127.4, 127.3, 113.6, 81.7, 74.8, 74.1, 73.0, 72.3, 65.7, 55.2, 38.5, 36.7, 25.9, 18.3, 18.1, 15.7, 9.7 -3.9, -4.7, -5.3, -5.4; ESI: 639.10 (M+Na)<sup>+</sup>.



To a 0°C cooled solution of **19** (1.1 g, 1.78 mmol) in 15 mL MeOH at 0 °C, was added *p*TSA (17 mg, 0.09 mmol) and the reaction mixture was stirred at 0 °C for 1 h and rt for 6 h before it was quenched with 1.0 mL Et<sub>3</sub>N. Solvent was evaporated in *vacuo* and the crude product was purified via a flash column chromatography (20:80::EtOAc:Hexanes) to furnish the intermediate primary alcohol (571 mg, 1.14 mmol, 64%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 7.44-7.36 (m, 5H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 2H), 4.60-4.47 (m, 4H), 3.86 (s, 3H), 3.77-3.52 (m, 6H), 2.24-2.14 (m, 1H), 2.10-2.02 (m, 1H), 1.13 (d, *J* = 7.2 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 3H), 1.01 (s, 9H), 0.17-0.16 (m, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 158.9, 138.5, 130.9, 129.1, 128.2, 127.5, 127.3, 113.6, 79.8, 74.7, 73.2, 72.9, 72.4, 64.2, 55.1, 37.8, 36.8, 25.8, 18.0, 15.0, 10.4, -4.4, -4.6; ESI: 525.21 (M+Na)<sup>+</sup>.

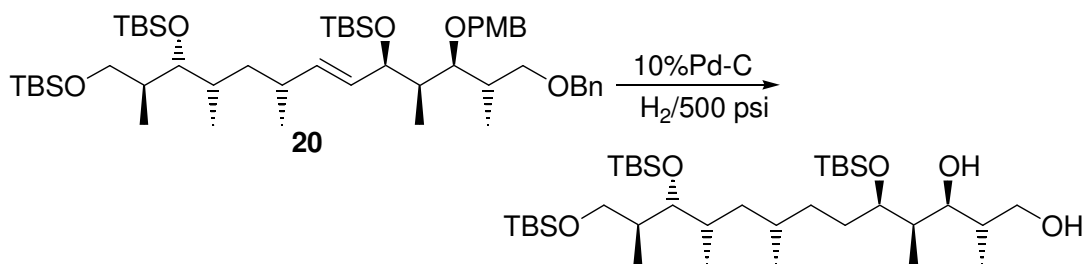


**6-Benzyloxy-2-(tert-butyl-dimethyl-silyloxy)-4-(4-methoxy-benzyloxy)-3,5-dimethyl-hexanal, 4:** To a 0 °C cooled stirred suspension of DMP reagent (1.82 g, 4.3 mmol) and NaHCO<sub>3</sub> (902 mg, 10.74 mmol) in 20.0 mL CH<sub>2</sub>Cl<sub>2</sub>, was added CH<sub>2</sub>Cl<sub>2</sub> (10.0 mL) solution of the intermediate alcohol (1.8 g, 3.58 mmol) dropwise. The reaction mixture was stirred at rt for 1 h before the solvent was partially removed in *vacuo* and the crude product was purified by flash column chromatography (10:90::EtOAc:Hexanes) to obtain aldehyde **4** (1.72 g, 3.44 mmol, 96%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 9.62 (d, *J* = 1.2 Hz, 1H), 7.4-7.32 (m, 5H), 7.26 (d, *J* = 8.7 Hz, 2H), 6.93 (d, *J* = 8.1 Hz, 2H), 4.59 (s, 2H), 4.49 (AB quartet, 2H), 4.05 (dd, *J* = 6.6 Hz, 0.9 Hz, 1H), 3.86 (s, 3H), 3.74 (dd, *J* = 8.1 Hz, 3.6 Hz, 1H), 3.69-3.57 (m, 2H), 2.35-2.24 (m, 1H), 2.22-2.09 (m, 1H), 1.15 (d, *J* = 7.5 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.04 (s, 9H), 0.19 (s, 3H), 0.15 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 201.9, 158.8, 138.5, 130.8, 128.9, 128.2, 127.3, 113.5, 79.3, 78.2, 72.9, 72.8, 72.2, 55.1, 40.5, 36.4, 25.7, 18.1, 15.0, 9.7, -4.5, -5.2; ESI: 523.09 (M+Na)<sup>+</sup>.



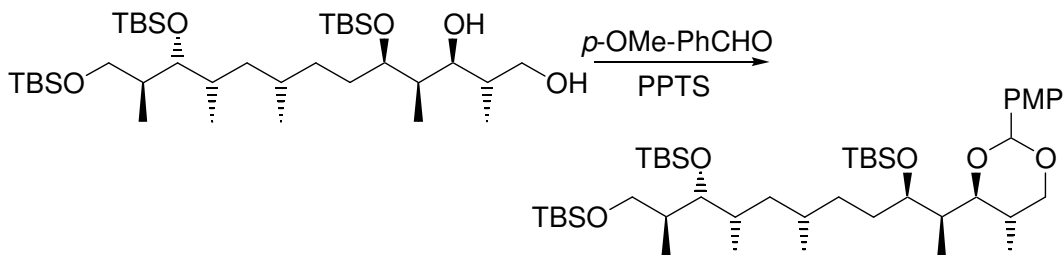
**5,11,13-Tris-(tert-butyl-dimethyl-silanyloxy)-3-(4-methoxy-benzyloxy)-2,4,8,10,12-pentamethyl-tridec-6-en-1-benzyl ether, 20:** To -60 °C cooled stirred solution of **3** (2.03 g, 3.37 mmol) in 20.0 mL DMF, was added NaHMDS (0.6M in toluene, 7.77 mL, 4.66 mmol) dropwise. The reaction mixture was stirred at -60 °C for 1.5 h and then DMF

(15.0 mL) solution of **4** (1.3 g, 2.29 mmol) was added dropwise. After stirring at -60°C for 1 h, reaction was warmed to rt and stirred there for 12 h before it was quenched with water (25 mL). Layers were separated, aqueous layer was extracted with Et<sub>2</sub>O (3 x 30 mL), combined organic layers were washed with brine (30 mL), dried over MgSO<sub>4</sub> and solvent was removed in *vacuo*. The crude product was purified with flash column chromatography (5:95::EtOAc:Hexanes) to furnish alkene **20** (1.90 g, 2.0 mmol, 80%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 7.34-7.27 (m, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 6.86 (d, 8.6 Hz, 2H), 5.36 (dd, *J* = 15.5 Hz, 7.1 Hz, 1H), 5.25 (dd, *J* = 15.5 Hz, 7.7 Hz, 1H), 4.49-4.40 (m, 4H), 4.01 (t, *J* = 7.0 Hz, 1H), 3.81 (s, 3H), 3.67 (dd, *J* = 9.8 Hz, 4.7 Hz, 1H), 3.58 (dd, *J* = 8.9 Hz, 3.8 Hz, 1H), 3.49-3.36 (m, 2H), 2.28-2.22 (m, 1H), 2.20-2.01 (m, 1H), 1.80-1.69 (m, 2H), 1.68-1.61 (m, 1H), 1.31-1.15 (m, 2H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.90-0.86 (m, 30H), 0.81 (d, *J* = 6.6 Hz, 3H), 0.048-0.01 (m, 18H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 158.9, 138.8, 137.7, 131.6, 131.5, 128.8, 128.2, 127.4, 127.3, 113.6, 81.0, 77.1, 75.8, 73.7, 72.9, 72.5, 65.6, 55.2, 42.9, 42.2, 40.5, 37.1, 34.1, 33.2, 26.2, 25.9, 22.0, 18.5, 18.2, 15.5, 14.4, 13.4, 10.3, -3.5, -3.6, -3.8, -4.7, -5.2, -5.3; ESI: 907.65 (M+Na)<sup>+</sup>.

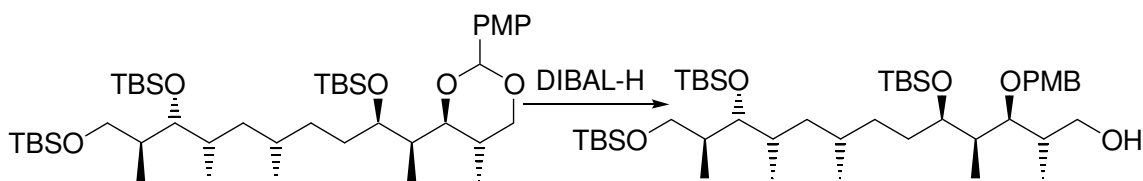


To a stirred solution of **20** (1.1 g, 1.24 mmol) in 50.0 mL cyclohexane, was added 10% Pd-C (330 mg, 30 wt%) and the reaction was stirred under 500 psi hydrogenic pressure for 1 d. pressure was released and reaction mixture was filtered over short pad of celite. The filtrate was concentrated and the crude product was purified by flash column chromatography (20:80::EtOAc:Hexanes) to provide 820 mg diol (820 mg, 1.21 mmol, 98%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 3.89-3.82 (m, 1H), 3.70-3.57 (m, 4H), 3.49 (dd, *J* = 6.5 Hz, 2.0 Hz, 1H), 3.40 (dd, *J* = 9.6 Hz, 7.0 Hz, 1H), 1.95-1.61 (m, 5H), 1.50-1.35 (m, 2H), 1.40-1.15 (m, 2H), 1.12-1.06 (m 1H), 0.89 (m, 36H), 0.82 (d, *J* = 6.7 Hz,

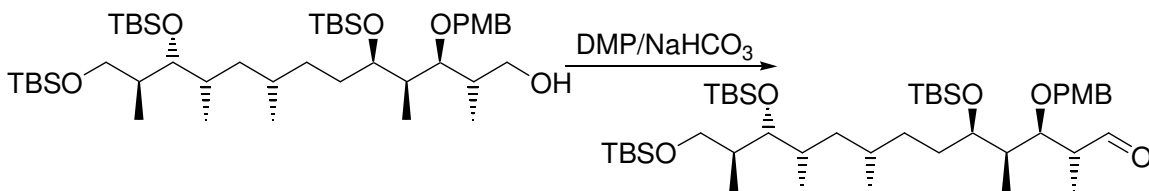
3H), 0.75 (d,  $J = 6.8$  Hz, 3H), 0.12-0.02 (m, 18H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 82.7, 79.3, 76.4, 69.0, 65.6, 42.8, 40.5, 37.5, 36.1, 32.8, 32.2, 32.0, 30.2, 26.1, 25.9, 25.8, 20.0, 18.4, 18.2, 17.9, 14.5, 14.4, 13.6, 4.6, -3.4, -3.7, -3.9, -4.5, -5.2, -5.3; ESI: 699.35 ( $\text{M}+\text{Na}$ ) $^+$ , 677.04 ( $\text{M}+\text{H}$ ) $^+$ .



To a stirred solution of diol (450 mg, 0.66 mmol) in dry toluene (7.0 mL), was added anhydrous  $\text{MgSO}_4$  (600 mg),  $p$ -anisaldehyde (0.16 mL, 1.33 mmol) and PPTS (17 mg, 0.066 mmol) and the mixture was stirred at 80  $^\circ\text{C}$  for 3 d before it was cooled to rt, filtered and solvent was evaporated in *vacuo*. The crude product was purified with flash column chromatography (7:93::EtOAc:Hexanes) to provide the intermediate acetal (513 mg, 0.65 mmol, 99%) as thick yellow oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.38 (d,  $J = 8.6$  Hz, 2H), 6.88 (d,  $J = 8.6$  Hz, 2H), 5.43 (s, 1H), 4.11 (dd,  $J = 11.1$  Hz, 4.5 Hz, 1H), 3.80 (s, 3H), 3.68-3.59 (m, 3H), 3.53-3.46 (m, 2H), 3.38 (dd,  $J = 9.7$  Hz, 7.4 Hz, 1H), 2.12-1.86 (m, 2H), 1.80-1.62 (m, 3H), 1.50-1.33 (m, 3H), 1.29-1.20 (m, 1H), 1.12-1.05 (m, 1H), 1.00 (d,  $J = 7.0$  Hz, 3H), 0.90-0.89 (m, 30H), 0.85 (d,  $J = 7.0$  Hz, 3H), 0.82 (d,  $J = 6.7$  Hz, 3H), 0.73 (d,  $J = 6.7$  Hz, 3H), 0.05-0.03 (m, 18H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 159.6, 131.6, 127.1, 113.3, 100.4, 81.9, 76.4, 74.9, 73.3, 65.6, 55.2, 43.2, 40.7, 38.7, 32.4, 31.4, 31.0, 30.7, 30.5, 26.2, 25.9, 20.0, 18.5, 18.2, 18.0, 14.3, 14.2, 12.3, 10.6, -3.6, -3.8, -4.2, -4.3, -5.2, -5.3; ESI: 817.74 ( $\text{M}+\text{Na}$ ) $^+$ .

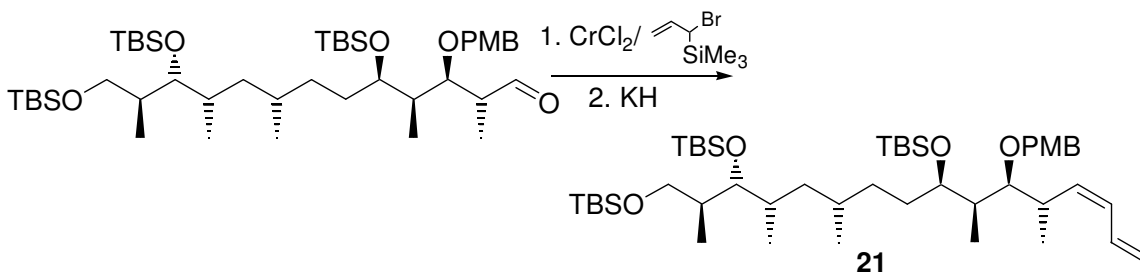


To a  $-78\text{ }^{\circ}\text{C}$  cooled solution of acetal (72 mg, 0.091 mmol) in  $\text{CH}_2\text{Cl}_2$  (1.0 mL), was added DIBAL-H (0.162 mL, 0.91 mmol) dropwise. After stirring at  $-78\text{ }^{\circ}\text{C}$  for 15 min, the reaction was warmed to  $-45\text{ }^{\circ}\text{C}$  and stirred there for 12 h. Reaction was quenched with very slow addition of 3M NaOH solution, until hydrogen evolution stops. Mixture was warmed to rt, layers were separated and the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 10 mL). Combined organic layers were washed with brine (10 mL), dried over  $\text{MgSO}_4$  and solvent was evaporated under *vacuo*. The crude product was purified by flash column chromatography (15:85::EtOAc:Hexanes) to furnish the intermediate primary alcohol (68 mg, 0.086 mmol, 95%) as a colorless oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.26 (d,  $J = 8.4$  Hz, 2H), 6.87 (d,  $J = 8.5$  Hz, 2H), 4.45 (s, 2H), 3.83-3.76 (m, 4H), 3.74-3.55 (m, 3H), 3.49-3.36 (m, 3H), 2.00-1.83 (m, 2H), 1.80-1.72 (m, 1H), 1.69-1.51 (m, 5H), 1.48-1.21 (m, 3H), 1.10 (d,  $J = 7.0$  Hz, 3H), 1.00 (d,  $J = 6.7$  Hz, 3H), 0.85 (d,  $J = 6.3$  Hz, 3H), 0.82 (d,  $J = 6.7$  Hz, 3H), 0.06-0.03 (m, 18H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 159.2, 130.4, 129.2, 113.8, 85.7, 76.4, 75.2, 73.7, 65.6, 65.1, 55.1, 42.9, 40.6, 40.5, 36.9, 32.5, 32.0, 31.8, 30.4, 26.1, 25.9, 20.1, 18.4, 18.2, 18.1, 15.7, 14.3, 14.2, 10.0, -3.7, -3.8, -3.9, -4.4, -5.3, -5.4; ESI: 819.46 ( $\text{M}+\text{Na}$ ) $^{+}$ .



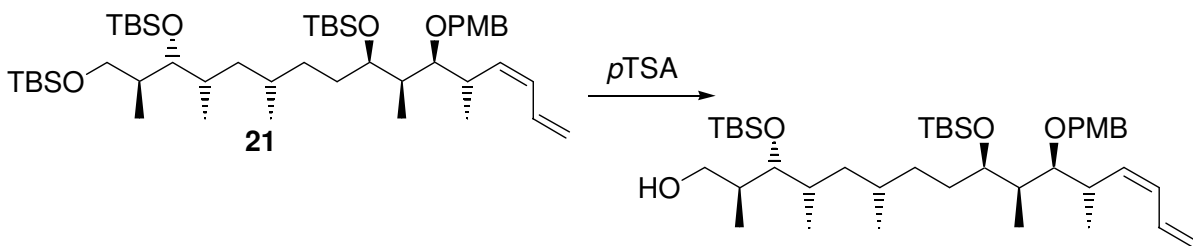
To a  $0\text{ }^{\circ}\text{C}$  cooled stirred suspension of  $\text{CH}_2\text{Cl}_2$  reagent (79 mg, 0.16 mmol) and  $\text{NaHCO}_3$  (32 mg, 0.38 mmol) in 0.5 mL  $\text{CH}_2\text{Cl}_2$ , was added  $\text{CH}_2\text{Cl}_2$  (1.0 mL) solution of alcohol (100 mg, 0.125 mmol) dropwise. The reaction mixture was stirred at  $0\text{ }^{\circ}\text{C}$  for 1.5 h before the solvent was partially removed in *vacuo* and the crude product was purified by flash column chromatography (10:90::EtOAc:Hexanes) to obtain the intermediate aldehyde (96

mg, 0.121 mmol, 97%) as a colorless oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 9.88 (d,  $J = 2.1$  Hz, 1H), 7.31 (d,  $J = 8.7$  Hz, 2H), 6.94 (d,  $J = 9.0$  Hz, 2H), 4.56 (s, 2H), 3.87 (s, 3H), 3.80-3.71 (m, 3H), 3.56-3.44 (m, 2H), 2.91-2.82 (m, 1H), 2.00-1.66 (m, 5H), 1.51-1.37 (m, 3H), 1.35-1.27 (m, 2H), 1.22 (d,  $J = 6.9$  Hz, 3H), 1.07 (d,  $J = 7.2$  Hz, 3H), 0.98-0.97 (m, 30H), 0.92 (d,  $J = 6.3$  Hz, 3H), 0.89 (d,  $J = 6.6$  Hz, 3H), 0.14-0.10 (m, 18H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 204.8, 159.2, 130.5, 129.2, 113.8, 81.9, 76.5, 74.3, 73.8, 65.9, 65.7, 55.3, 49.4, 43.0, 41.0, 40.7, 32.6, 32.1, 31.6, 30.4, 26.2, 26.0, 20.1, 18.5, 18.3, 18.2, 15.3, 14.3, 12.0, 10.4, -3.6, -3.7, -4.2, -5.1, -5.2; ESI: 817.70 ( $\text{M}+\text{Na}$ ) $^+$ .

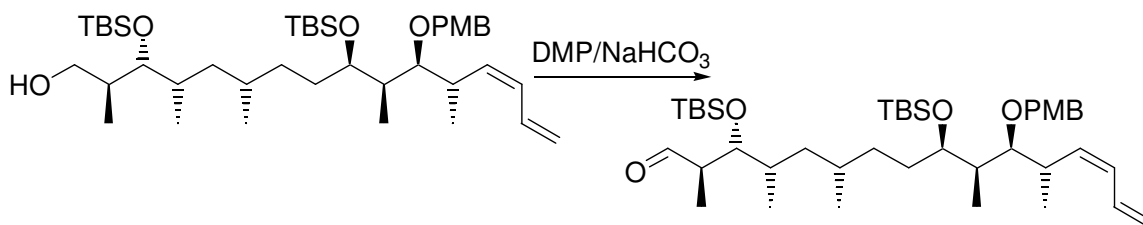


**1-Methoxy-4-{2-methyl-1-[2,8,10-tris-(tert-butyl-dimethyl-silyloxy)-1,5,7,9-tetramethyl-decyl]-hexa-3,5-dienyloxymethyl}-benzene, 21:** To a 0 °C cooled suspension of  $\text{CrCl}_2$  (155 mg, 1.26 mmol) in THF (1.5 mL), was added a THF (1.5 mL) solution of the intermediate aldehyde (100 mg, 0.126 mmol) and allylsilane reagent (122 mg, 0.63 mmol), the reaction was warmed to rt and the purple suspension was stirred there for 20 h before it was quenched with pH-7 buffer (4.0 mL). Layers were separated and the aqueous layer was extracted with EtOAc (4 x 25 mL). Combined organic layers were washed with brine (25 mL), dried over  $\text{MgSO}_4$  and concentrated in *vacuo*. The crude product was dissolved in THF (1.5 mL) and was added to a KH (51 mg, 1.26 mmol) suspension in THF (1.5 mL) at 0°C. After stirring at 0°C for 2.5 h, the reaction was quenched with slow addition of ice cold water until the hydrogen evolution stops. Reaction was warmed to rt, diluted with  $\text{Et}_2\text{O}$  (10 mL), layers were separated and aqueous layer was extracted with  $\text{Et}_2\text{O}$  (3 x 15 mL). Combined organic layers were washed with brine (15 mL), dried over  $\text{MgSO}_4$  and solvent was removed in *vacuo*. The crude product was purified with flash column chromatography (2:98::EtOAc:Hexanes) to furnish the diene **21** (98 mg, 0.12 mmol, 95%) as a colorless oil.  $^1\text{H}$  NMR (300 MHz,

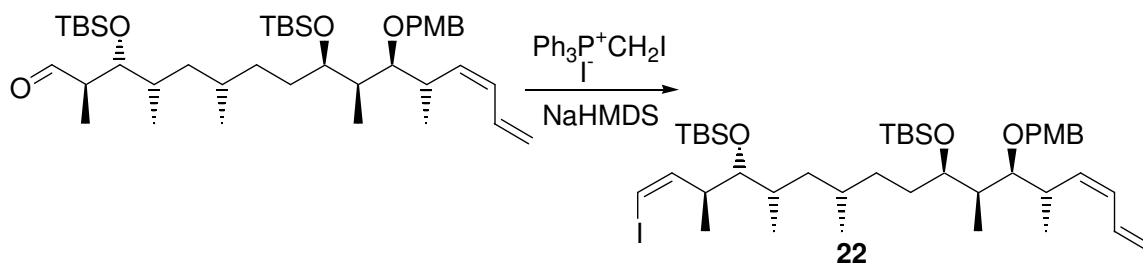
CDCl<sub>3</sub>)  $\delta$  (ppm): 7.29 (d,  $J$  = 8.4 Hz, 2H), 6.88 (d,  $J$  = 8.4 Hz, 2H), 5.58 (ddd,  $J$  = 16.8 Hz, 10.9 Hz, 10.5 Hz, 1H), 6.01 (t,  $J$  = 10.9 Hz, 1H), 5.58 (t,  $J$  = 10.5 Hz, 1H), 5.20 (d,  $J$  = 16.8, Hz, 1H), 5.10 (d, 10.3 Hz, 1H), 4.53 (AB quartet, 2H), 3.81 (s, 3H), 3.69-3.61 (m, 2H), 3.47-3.31 (m, 3H), 2.12-2.94 (m, 1H), 1.89-1.51 (m, 4H), 1.50-1.62 (m, 3H), 1.61-1.23 (m, 4H), 1.11 (d,  $J$  = 6.7 Hz, 3H), 0.97-0.87 (m, 33H), 0.09-0.03 (m, 18H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 158.9, 134.5, 132.3, 131.3, 129.1, 128.9, 117.2, 113.6, 84.4, 75.0, 72.7, 65.7, 55.2, 43.0, 40.6, 40.4, 35.1, 32.5, 32.4, 31.7, 30.2, 26.2, 25.9, 20.0, 18.8, 18.5, 18.2, 18.1, 14.3, 14.2, 9.1, -3.5, -3.7, -3.8, -4.5, -5.2; ESI: 841.71 (M+Na)<sup>+</sup>.



To a 0 °C cooled solution of **21** (2.13 g, 2.61 mmol) in 17.0 mL MeOH and 9.0 mL CH<sub>2</sub>Cl<sub>2</sub> at 0 °C, was added *p*TSA (50 mg, 0.26 mmol) and the reaction mixture was stirred at 0 °C for 1.5 h before it was quenched with 2.0 mL Et<sub>3</sub>N. Solvent was evaporated in *vacuo* and the crude product was purified via a flash column chromatography (20:80::EtOAc:Hexanes) to furnish the primary alcohol (1.54 g, 2.19 mmol, 84%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 7.28 (d,  $J$  = 8.4 Hz, 2H), 6.86 (d,  $J$  = 8.5 Hz, 2H), 6.58 (ddd,  $J$  = 16.8 Hz, 10.7 Hz, 10.5 Hz, 1H), 6.00 (t, 11.1 Hz, 1H), 5.58 (t,  $J$  = 10.4 Hz, 1H), 5.18 (d,  $J$  = 16.5 Hz, 1H), 5.09 (d,  $J$  = 10.3 Hz, 1H), 4.52 (AB quartet, 2H), 3.80 (s, 3H), 3.64-3.56 (m, 3H), 3.45-3.42 (m, 1H), 3.33 (dd,  $J$  = 7.7 Hz, 2.7 Hz, 1H), 3.15-2.91 (m, 1H), 1.89-1.78 (m, 1H), 1.71-1.50 (m, 5H), 1.48-1.31 (m, 5H), 1.10 (d,  $J$  = 6.7 Hz, 3H), 0.95-0.81 (m, 39H), 0.11-0.07 (m, 12H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 158.9, 134.5, 132.3, 131.2, 129.1, 128.8, 117.2, 113.6, 84.3, 80.8, 75.0, 72.6, 66.0, 55.2, 41.8, 40.4, 38.2, 35.1, 34.8, 32.3, 31.3, 30.3, 26.1, 25.9, 20.3, 18.8, 18.3, 18.1, 16.0, 14.9, 9.1, -3.5, -3.7, -3.9, -4.5; ESI: 727.54 (M+Na)<sup>+</sup>.



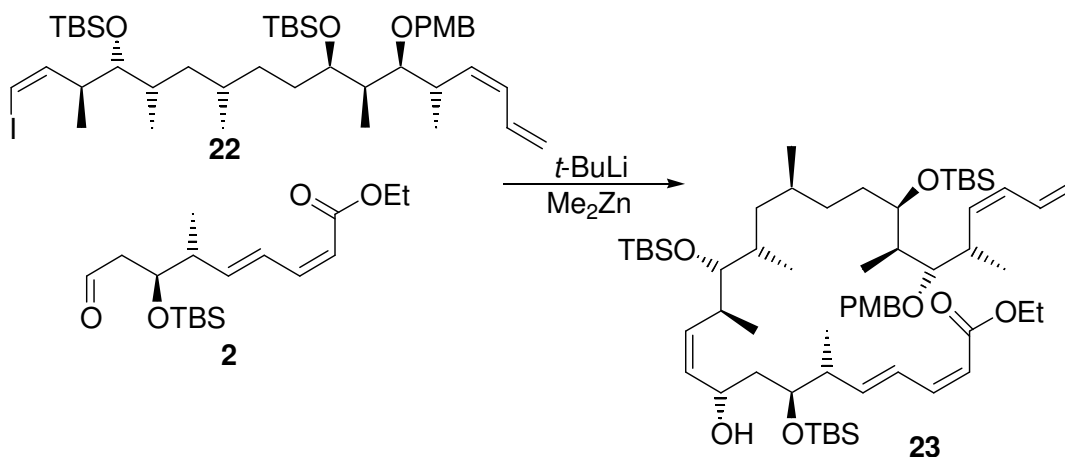
To a 0 °C cooled stirred suspension of DMP reagent (488 mg, 1.15 mmol) and NaHCO<sub>3</sub> (161 mg, 1.9 mmol) in 2.5 mL CH<sub>2</sub>Cl<sub>2</sub>, was added CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL) solution of the alcohol (450 mg, 0.64 mmol) dropwise. The reaction mixture was stirred at 0 °C for 1 h before the solvent was partially removed in *vacuo* and the crude product was purified by flash column chromatography (8:92::EtOAc:Hexanes) to obtain the intermediate aldehyde (421 mg, 0.6 mmol, 94%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 9.76 (d, *J* = 2.6 Hz, 1H), 7.28 (d, *J* 8.4 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.58 (ddd, *J* = 16.6 Hz, 10.7 Hz, 10.4 Hz, 1H), 5.99 (t, *J* = 11.0 Hz, 1H), 5.58 (t, *J* = 10.6 Hz, 1H), 5.17 (d, *J* = 16.9 Hz, 1H), 5.09 (d, *J* = 10.0 Hz, 1H), 4.52 (AB quartet, 2H), 3.80 (s, 3H), 3.72-3.69 (m, 1H), 3.64-3.57 (m, 1H), 3.33 (dd, *J* = 7.9 Hz, 3.0 Hz, 1H), 2.92-3.09 (m, 1H), 2.48-2.60 (m, 1H), 1.78-1.51 (m, 4H), 1.46-1.31 (m, 5H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.05 (d, *J* = 7.1 Hz, 3H), 0.94 (d, *J* = 7.1 Hz, 3H), 0.92 (s, 9H), 0.88 (s, 9H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.81 (d, *J* = 6.6 Hz, 3H), 0.08-0.03 (m, 12H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 204.8, 158.9, 134.5, 132.2, 131.2, 129.0, 128.8, 117.1, 113.6, 84.3, 77.9, 75.0, 72.5, 55.1, 50.3, 41.3, 40.4, 35.0, 34.5, 32.3, 31.1, 30.2, 25.9, 20.2, 18.7, 18.2, -3.6, -3.8, -4.1, -4.5; ESI: 725.59 (M+Na)<sup>+</sup>.



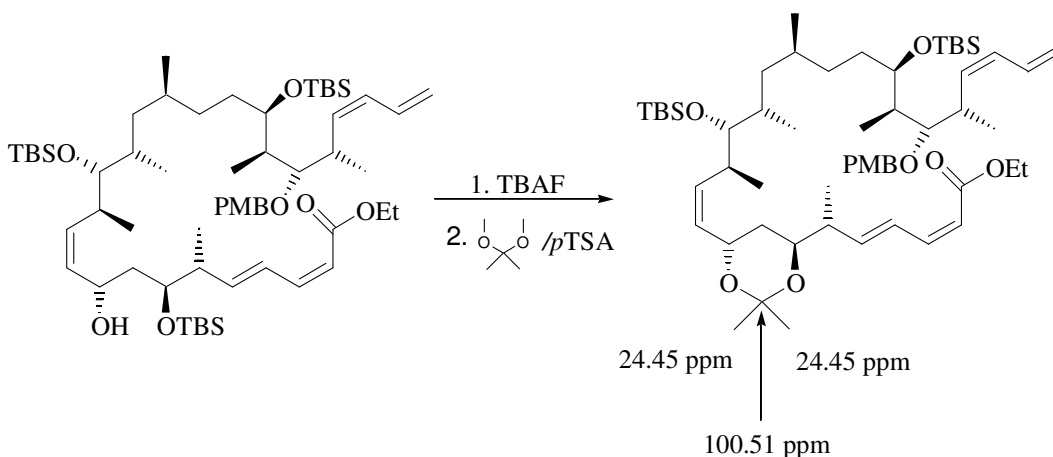
**1-{1-[2,8-Bis-(tert-butyl-dimethyl-silyloxy)-11-iodo-1,5,7,9-tetramethyl-undec-10-enyl]-2-methyl-hexa-3,5-dienyloxymethyl}-4-methoxy-benzene, 22:** To a suspension of the Wittig salt (170 mg, 0.32 mmol) in 1.5 mL THF at rt, was added dropwise



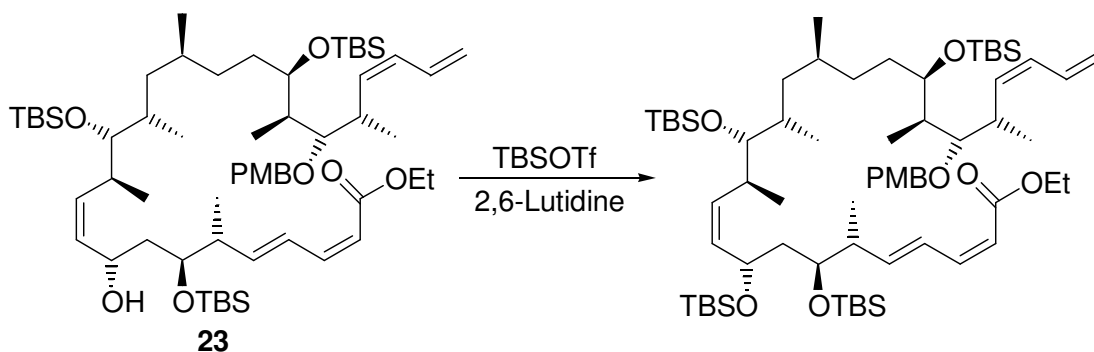
NaHMDS (0.6M in toluene, 0.47 mL, 0.285 mmol) and the dark red solution was stirred at rt for 15 min before it was cooled to -78 °C. HMPA (0.1 mL, 0.57 mmol) was added followed by dropwise addition of THF (1.0 mL) solution of the aldehyde (50mg, 0.071 mmol). After stirring at -78 °C for 10 min, reaction mixture was warmed to rt and stirred there for 1 h before it was quenched with satd. NH<sub>4</sub>Cl (5.0 mL) solution. The solid was filtered off, filtrate was diluted with Et<sub>2</sub>O (10.0 mL) and the layers were separated. The aqueous layer was extracted with Et<sub>2</sub>O (3 x 10 mL), combined organic layers were washed with brine (15 mL), dried over MgSO<sub>4</sub> and solvent was removed in *vacuo*. The crude product was purified with flash column chromatography (2:98::EtOAc:Hexanes) to provide the vinyl iodide **22** (44 mg, 0.053 mmol, 75%) as a light yellow oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 7.29 (d, *J* = 7.9 Hz, 2H), 6.88 (d, *J* = 8.0 Hz, 2H), 5.59 (ddd, *J* = 16.7 Hz, 10.6 Hz, 10.5 Hz, 1H), 6.26 (t, *J* = 8.1 Hz, 1H), 6.12 (d, *J* = 7.23 Hz, 1H), 6.01 (t, *J* = 10.9 Hz, 1H), 5.90 (t, *J* = 10.4 Hz, 1H), 5.19 (d, *J* = 16.7 Hz, 1H), 5.10 (d, *J* = 9.9 Hz, 1H), 4.53 (AB quartet, 2H), 3.81 (s, 3H), 3.63-3.58 (m, 1H), 3.47-3.43 (m, 1H), 3.36-3.30 (m, 1H), 3.05-3.92 (m, 1H), 2.72-3.62 (m, 1H), 1.69-1.51 (m, 2H), 1.39-1.17 (m, 7H), 1.11 (d, *J* = 6.4 Hz, 3H), 0.98 (d, *J* = 7.8 Hz, 3H), 0.91-0.83 (m, 27H), 0.81 (d, *J* = 6.9 Hz, 3H), 0.08-0.05 (m, 12H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 159.0, 144.2, 134.6, 132.3, 131.4, 129.1, 128.9, 117.2, 113.7, 84.5, 81.2, 79.2, 76.6, 75.1, 72.6, 55.3, 43.3, 41.4, 40.4, 35.3, 35.1, 32.4, 31.2, 30.4, 30.3, 26.2, 26.0, 20.4, 18.9, 18.4, 18.2, 17.8, 15.9, 9.2, -3.4, -3.5, -3.6, -4.4.



**(2Z,4E,6R,7S,9S,10Z,12S,13R,14S,16S,19R,20R,21S,22S,23Z)-9-Hydroxy-21-(4-methoxy-benzyloxy)-7,13,19-tris(*tert*-butyl-dimethylsilyloxy)-6,12,14,16,20,22-hexamethyl-hexacos-2,4,10,23,25-pentaenoic acid ethyl ester, 23:** To a -78 °C cooled solution of *t*-BuLi (1.7M in pentane, 0.235 mL, 0.399 mmol) in 0.3 mL Et<sub>2</sub>O, was added a Et<sub>2</sub>O (0.6 mL) solution of vinyl iodide **22** (150 mg, 0.181 mmol). After stirring at -78 °C for 1.5 h, dimethylzinc (2.0M in toluene, 0.145 mL, 0.29 mmol) was added dropwise and the reaction mixture was further stirred at -78 °C for 15 min before a Et<sub>2</sub>O (0.8 mL) solution of aldehyde **2** (62 mg, 0.18 mmol) was added dropwise. After stirring for 1 h at -78 °C, the reaction was quenched with water (3.0 mL), warmed to rt and diluted with Et<sub>2</sub>O (5.0 mL). Layers were separated, the aqueous layer was extracted with Et<sub>2</sub>O (3 x 15 mL), combined organic layers were washed with brine, dried over MgSO<sub>4</sub> and solvent was removed in *vacuo*. The crude product was purified by flash column chromatography (10:90::EtOAc:Hexanes) to furnish the *Z*-allyl alcohol **23** (66 mg, 0.063 mmol, 80% based on recovered aldehyde **2**) as a light yellow oil. Aldehyde **2** (35 mg, 0.103 mmol, 57%) was recovered. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.45 (dd, *J* = 15.6, 11.7 Hz, 1H), 7.34 (m, 2H), 6.92 (m, 2H), 6.63 (ddd, *J* = 16.8, 10.5, 10.5 Hz, 1H), 6.59 (t, *J* = 11.7 Hz, 1H), 6.05 (m, 2H), 5.64 (d, *J* = 11.1 Hz, 1H), 5.63 (t, *J* = 10.3 Hz, 1H), 5.53 (t, *J* = 10.5 Hz, 1H), 5.38 (dd, *J* = 11.0, 8.2 Hz, 1H), 5.23 (d, *J* = 16.5 Hz, 1H), 5.15 (d, *J* = 10.0 Hz, 1H), 4.68 (m, 1H), 4.58 (AB quartet, 2H), 4.24 (q, *J* = 7.2 Hz), 3.99 (m, 1H), 3.86 (s, 3H), 3.67 (m, 1H), 3.38 (m, 2H), 3.04 (m, 1H), 2.68 (m, 2H), 2.25 (brs, 1H), 1.61 (m, 4H), 1.32 (m, 7H), 1.16 (d, *J* = 6.6 Hz, 3H), 1.11 (d, *J* = 6.3 Hz, 3H), 0.98 (s, 9H), 0.96 (s, 9H), 0.94 (s, 9H), 0.85 (d, *J* = 6.3 Hz, 3H), 0.131 (m, 18H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 166.5, 159.0, 147.1, 145.2, 135.7, 134.5, 132.3, 131.4, 129.1, 128.9, 126.9, 117.3, 116.2, 113.7, 84.4, 79.6, 75.1, 72.7, 64.7, 59.9, 55.3, 42.8, 42.0, 40.4, 40.0, 36.3, 35.1, 34.1, 32.5, 31.5, 30.3, 26.3, 26.0, 25.9, 20.2, 19.8, 18.8, 18.5, 18.2, 18.1, 14.7, 14.5, 14.3, 9.2, -3.1, -3.7, -3.6, -4.4; LRMS (ESI) calcd for C<sub>60</sub>H<sub>108</sub>O<sub>8</sub>Si<sub>3</sub>Na 1063.72 (M+Na)<sup>+</sup>, found 1063.67.

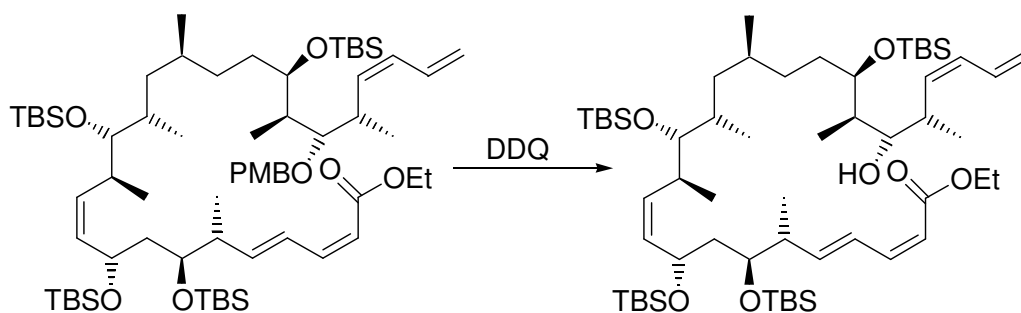


**Confirmation of the stereochemistry of **23** using Rychnovsky's rule:** **23** was converted to the 1,3-diol and the acetonide using TBAF and 2,2-dimethoxypropane/*p*TSA, respectively. The tertiary carbon of the acetonide was observed at  $\delta$  100.51 ppm and the methyl carbons at  $\delta$  24.45 ppm in the  $^{13}\text{C}$  spectrum. Selective deprotection of the TBS ether at C7 was possible since it has a neighboring carbon with an *anti*-methyl group, whereas the TBS ethers at C13 and C19 have *syn*-methyl groups on adjacent carbons.



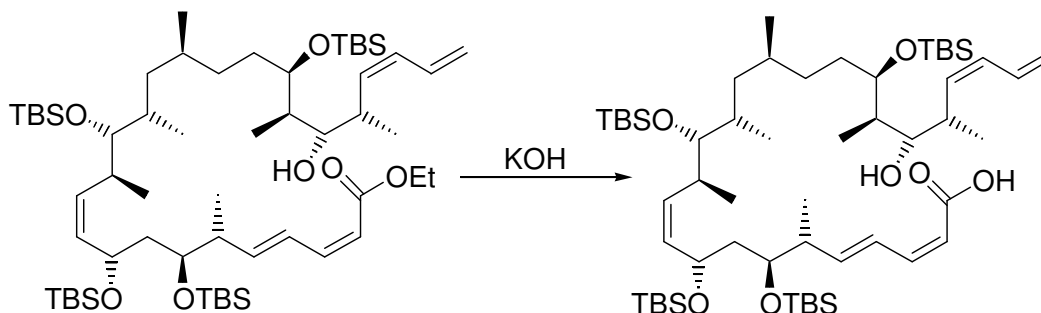
To a  $-78\text{ }^\circ\text{C}$  cooled solution of **23** (35 mg, 0.034 mmol) in 0.25 mL  $\text{CH}_2\text{Cl}_2$ , was added 2,6-Lutidine (0.015 mL, 0.135 mmol) followed by the addition of TBSOTf (0.015 mL, 0.067 mmol). After stirring at  $-78\text{ }^\circ\text{C}$  for 30 min, the reaction was quenched with dropwise addition of satd.  $\text{NaHCO}_3$  (1.5 mL) and warmed to rt. The mixture was diluted with 10.0 mL DCM, layers were separated and the aqueous layer was extracted with

CH<sub>2</sub>Cl<sub>2</sub> (3 x 10mL). Combined organic layers were washed with brine (10.0 mL), dried over MgSO<sub>4</sub> and solvent was removed in *vacuo*. The crude product was purified with flash column chromatography (8:92::EtOAc:Hexane) to obtain the TBS ether (37.7 mg, 0.033 mmol, 99%) as a colorless oil.



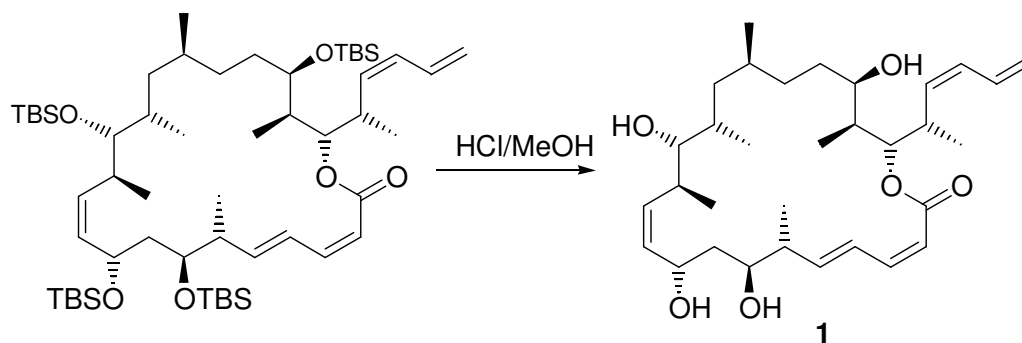
To a 0 °C cooled solution of the PMB ether (12 mg, 0.0104 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.3 mL) and pH-7 buffer (0.03 mL), was added DDQ (3.2 mg, 0.0135 mmol) and the reaction was stirred at 0 °C for 1 h before it was quenched with satd. NaHCO<sub>3</sub> (5.0 mL) and diluted with 10.0 mL CH<sub>2</sub>Cl<sub>2</sub>. Layers were separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 15 mL). Combined organic layers were washed brine (15.0 mL), dried over MgSO<sub>4</sub> and concentrated in *vacuo*. The crude product was purified by flash column chromatography (5:95::EtOAc:Hexanes) to provide the intermediate secondary alcohol (9.6 mg, 0.008 mmol, 90%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 7.44 (dd, *J* = 15.0 Hz, 11.1 Hz, 1H), 6.70 (ddd, *J* = 16.5 Hz, 10.5 Hz, 10.2 Hz, 1H), 6.59 (t, *J* = 11.7 Hz, 1H), 6.15 (t, *J* = 11.1 Hz, 1H), 6.04 (dd, *J* = 15.3 Hz, 6.3 Hz, 1H), 5.64 (d, *J* = 11.1 Hz, 1H), 5.51-5.42 (m, 2H), 5.36-5.24 (m, 2H), 5.18 (d, *J* = 10.5 Hz, 1H), 4.59-4.56 (m, 1H), 4.25 (q, *J* = 6.9 Hz, 2H), 4.02-3.98 (m, 1H), 3.83-3.79 (m, 1H), 3.54-3.51 (m, 1H), 3.43-3.40 (m, 1H), 2.94-2.81 (m, 1H), 2.71-2.49 (m, 2H), 2.44 (brs, 1H), 2.61-2.82 (m, 4H), 1.52-1.46 (m, 6H), 1.36 (t, *J* = 7.8 Hz, 3H), 1.09 (d, *J* = 7.2 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.96-0.87 (m, 51H), 0.16-0.08 (m, 24H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 166.5, 147.1, 145.3, 135.4, 132.6, 132.3, 129.9, 126.8, 117.7, 116.0, 79.9, 77.8, 72.1, 66.5, 59.8, 43.5, 42.3, 41.5, 37.6, 36.1, 35.6, 35.0, 32.1, 31.5,

30.6, 29.7, 26.3, 26.0, 20.4, 19.5, 18.5, 18.1, 17.7, 15.3, 14.3, 13.2, 6.8, -2.9, -3.3, -3.6, -4.1, -4.3; LRMS (ESI) calcd for  $C_{58}H_{114}O_7Si_4Na$  1057.66 ( $M+Na$ )<sup>+</sup>, found 1057.66.

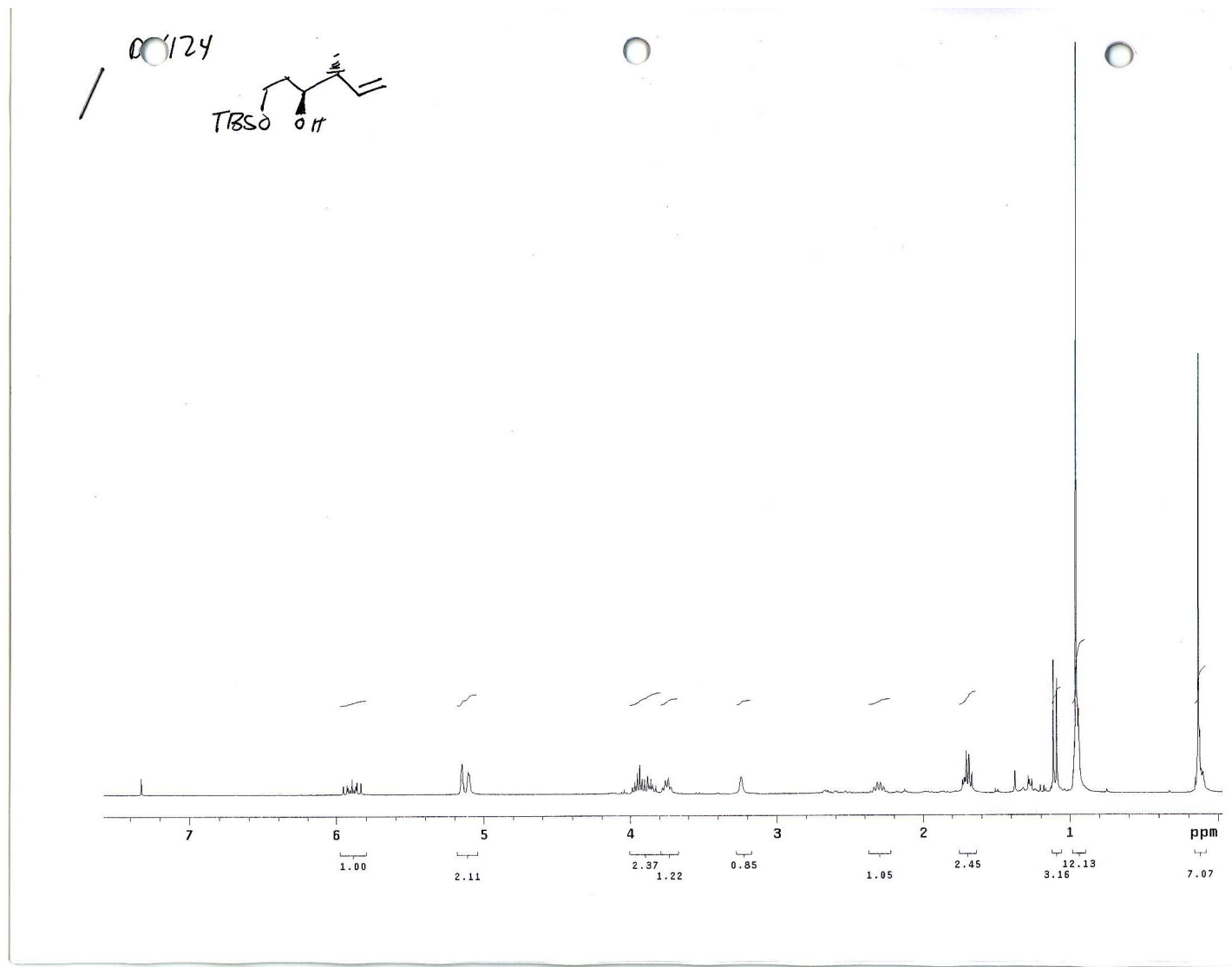


To a stirred solution of the intermediate ester (22 mg, 0.02127 mmol) in THF (1.1 mL) and EtOH (2.6 mL), was added KOH (1N solution in water, 0.21 mL, 0.21 mmol) and the reaction was refluxed (bath temp. 52 °C) for 1 d before it was cooled and the solvent was removed in *vacuo*. The residue was diluted with Et<sub>2</sub>O (10.0 mL) and satd. NH<sub>4</sub>Cl solution (5.0 mL), layers were separated and aqueous layer was extracted with Et<sub>2</sub>O (3 x 10 mL). Organic layers were combined, dried over MgSO<sub>4</sub> and the solvent was removed in *vacuo*. The crude product was purified by flash column chromatography (20:80::EtOAc:Hexanes) to provide the seco acid (21.2 mg, 0.021 mmol, 99%) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 7.41 (dd, *J* = 15.3 Hz, 11.7 Hz, 1H), 6.69 (t, *J* = 11.1 Hz, 1H), 6.76-6.62 (m, 1H), 6.16 (t, *J* = 10.5 Hz, 1H), 6.10 (dd, *J* = 15.9 Hz, 7.2 Hz, 1H), 1.67 (d, *J* = 11.1 Hz, 1H), 5.51-5.43 (m, 2H), 5.35-5.25 (m, 2H), 5.18 (d, *J* = 10.5 Hz, 1H), 4.62-4.55 (m, 1H), 4.01-3.99 (m, 1H), 3.83-3.79 (m, 1H), 3.57-3.53 (m, 1H), 3.43-3.42 (m, 1H), 2.91-2.84 (m, 1H), 2.64-2.58 (m, 2H), 1.81-1.1.62 (m, 4H), 1.59-1.22 (m, 7H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 1.02 (d, *J* = 6.3 Hz, 3H), 0.98-0.89 (m, 51H), 0.17-0.09 (m, 24H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ (ppm): 170.6, 148.3, 147.4, 135.3, 132.7, 132.3, 130.0, 126.9, 117.8, 115.0, 79.9, 77.7, 72.0, 66.4, 43.5, 42.6, 41.5, 37.7, 36.0, 35.7, 34.9, 32.1, 31.5, 30.6, 30.3, 29.7, 26.3, 26.0, 20.4, 19.4, 18.5, 18.1, 17.7, 15.3, 13.5, 6.9, -2.9, -3.3, -3.6, -4.1, -4.3; LRMS (ESI) calcd for  $C_{56}H_{110}O_7Si_4Na$  1029.72 ( $M+Na$ )<sup>+</sup>, found 1029.40.

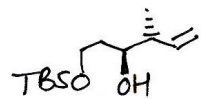




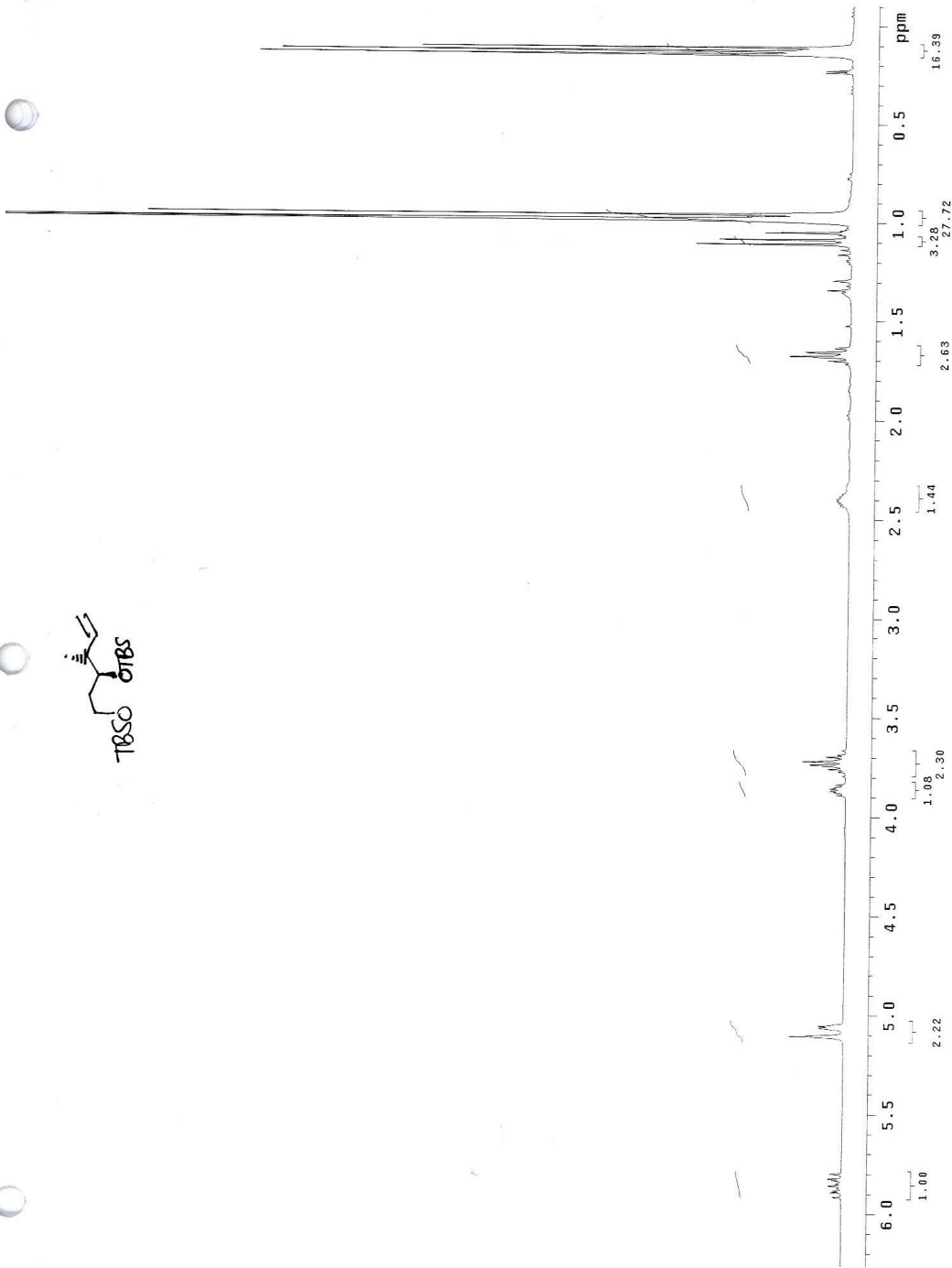
**8(*S*),10(*S*),14(*R*),20(*R*)-Tetrahydroxy-7(*R*),13(*S*),15(*S*),17(*S*),21(*S*)-pentamethyl-22(*S*)-(1(*S*)-methylpenta-2,4-dienyl)oxacyclodocosa-3,5,11-trien-2-one, 1:** To a 0 °C cooled solution of the macrolactone in (4.8 mg, 0.0048 mmol) in 0.5 mL THF, was added HCl (3N in MeOH, 1.1 mL). The reaction mixture was warmed to rt and stirred there for 12 h before it was diluted with water (4.0 mL) and Et<sub>2</sub>O (4.0 mL). Layers were separated and the aqueous layer was extracted with Et<sub>2</sub>O (4 x 4.0 mL). Combined organic layers were dried over MgSO<sub>4</sub> and the solvent was removed in *vacuo*. The crude product was purified flash column chromatography (30:70::<sup>i</sup>PrOH:Hexanes) to obtain (-)-Dictyostatin, **1** (1.5 mg, 0.0028 mmol, 58%) as a white solid. <sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>OD) δ 7.17 (dd, *J* = 15.5, 11.2 Hz, 1H), 6.67 (dt, *J* = 10.3, 16.3 Hz, 1H), 6.61 (t, *J* = 11.2 Hz, 1H), 6.14 (dd, *J* = 15.6, 6.6 Hz, 1H), 6.02 (t, *J* = 11.0 Hz, 1H), 5.52 (d, *J* = 11.3 Hz, 1H), 5.51 (t, *J* = 9.7 Hz, 1H), 5.33 (m, 2H), 5.21 (d, *J* = 16.9 Hz, 1H), 5.10 (m, 2H), 4.61 (m, 1H), 4.02 (m, 1H), 3.33 (m, 1H), 3.13 (m, 1H), 3.06 (dd, *J* = 8.1, 2.7 Hz, 1H), 2.72 (m, 1H), 2.57 (m, 1H), 1.84 (m, 2H), 1.59 (m, 1H), 1.55 (m, 1H), 1.46 (m, 1H), 1.39 (m, 1H), 1.21 (m, 1H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.06 (m, 1H), 1.08 (d, *J* = 6.9 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.7 Hz), 0.91 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 3H), 0.87 (m, 1H), 0.66 (m, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ (ppm): 166.5, 144.9, 143.4, 133.4, 133.0, 131.9, 129.8, 129.6, 127.0, 117.1, 116.5, 78.9, 72.2, 68.8, 64.0, 63.3, 42.2, 40.8, 39.3, 39.0, 34.3, 34.2, 33.8, 31.2, 29.7, 29.3, 20.3, 17.9, 16.6, 14.7, 12.1, 8.9; LRMS (ESI) calcd for C<sub>32</sub>H<sub>52</sub>O<sub>6</sub>Na 555.37 (M+Na)<sup>+</sup>, found 555.25.

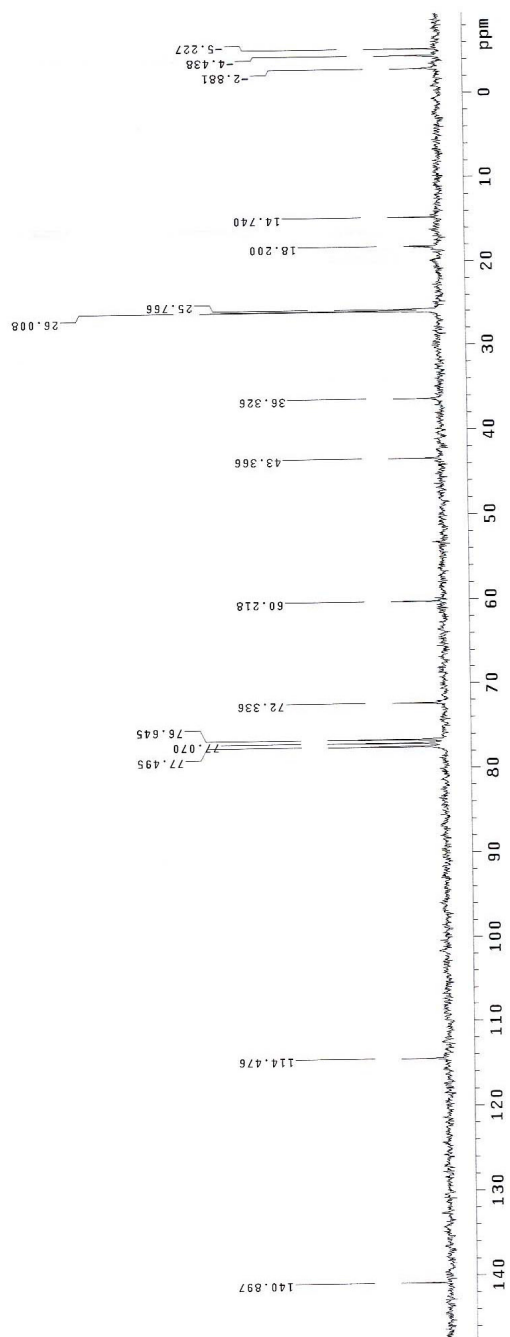
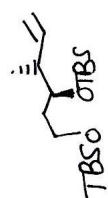
300 MHz  $^1\text{H}$  NMR of compound **6** in  $\text{CDCl}_3$

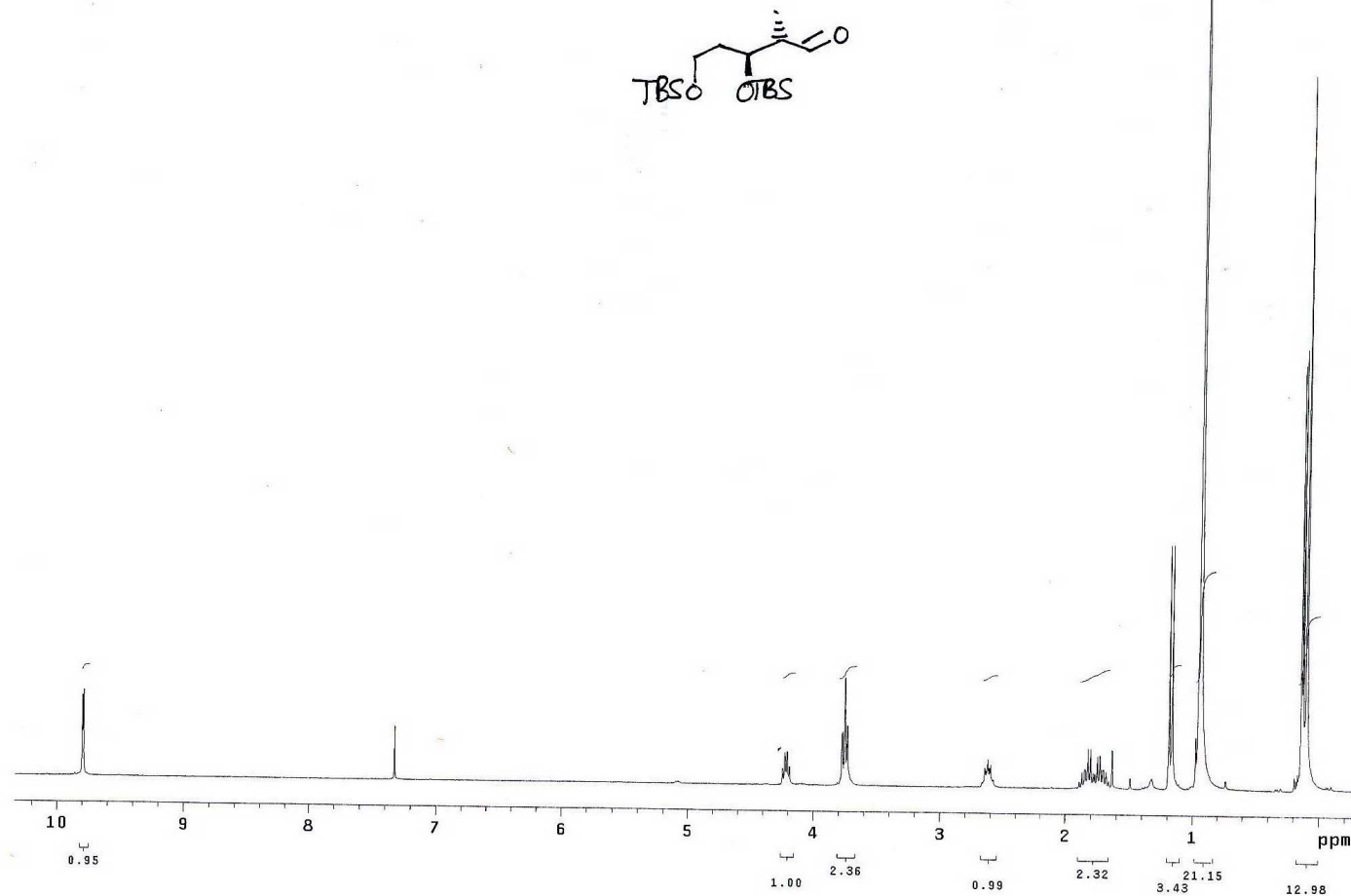


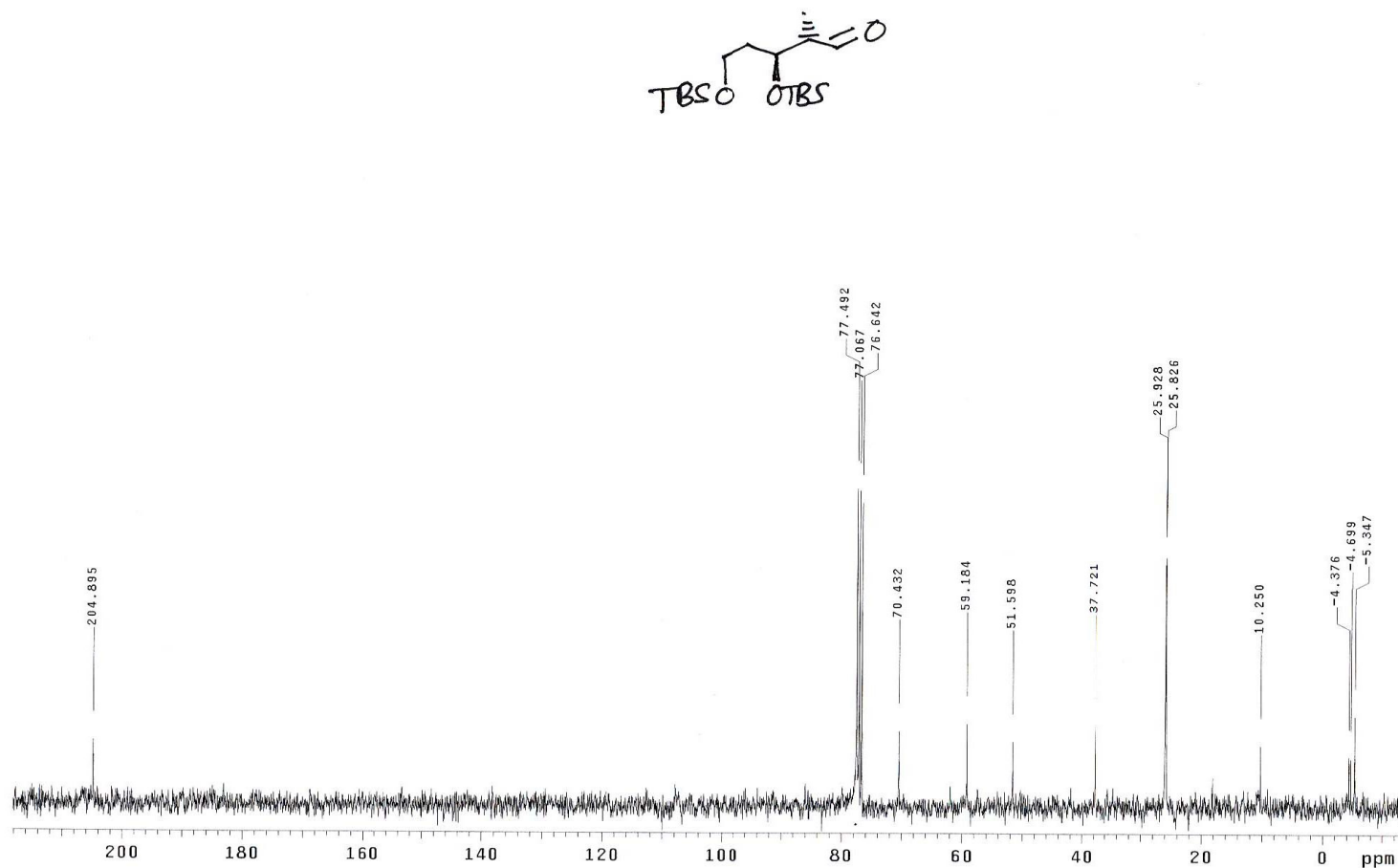


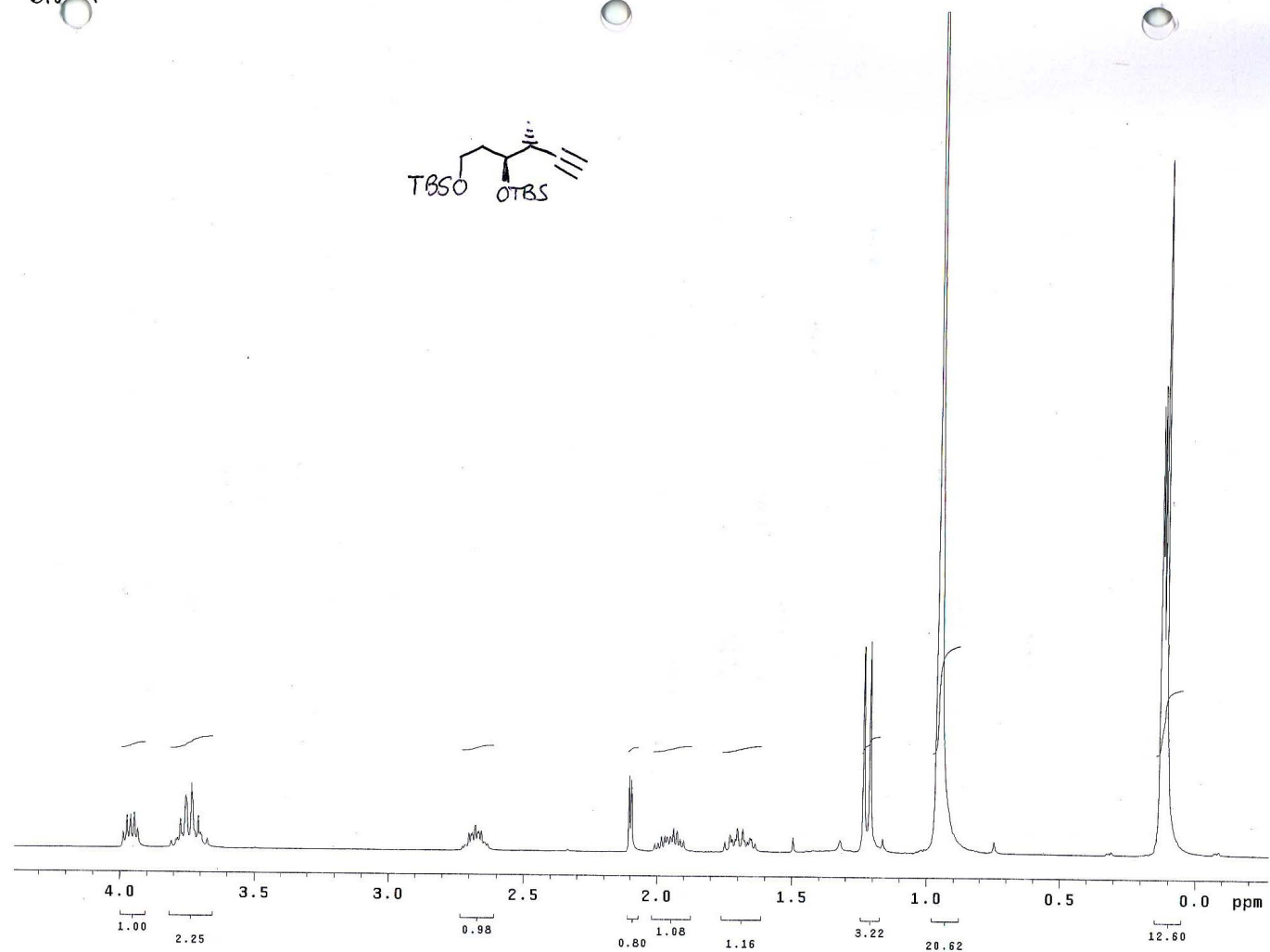
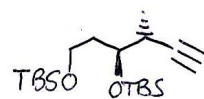
75 MHz  $^{13}\text{C}$  NMR of compound **6** in  $\text{CDCl}_3$



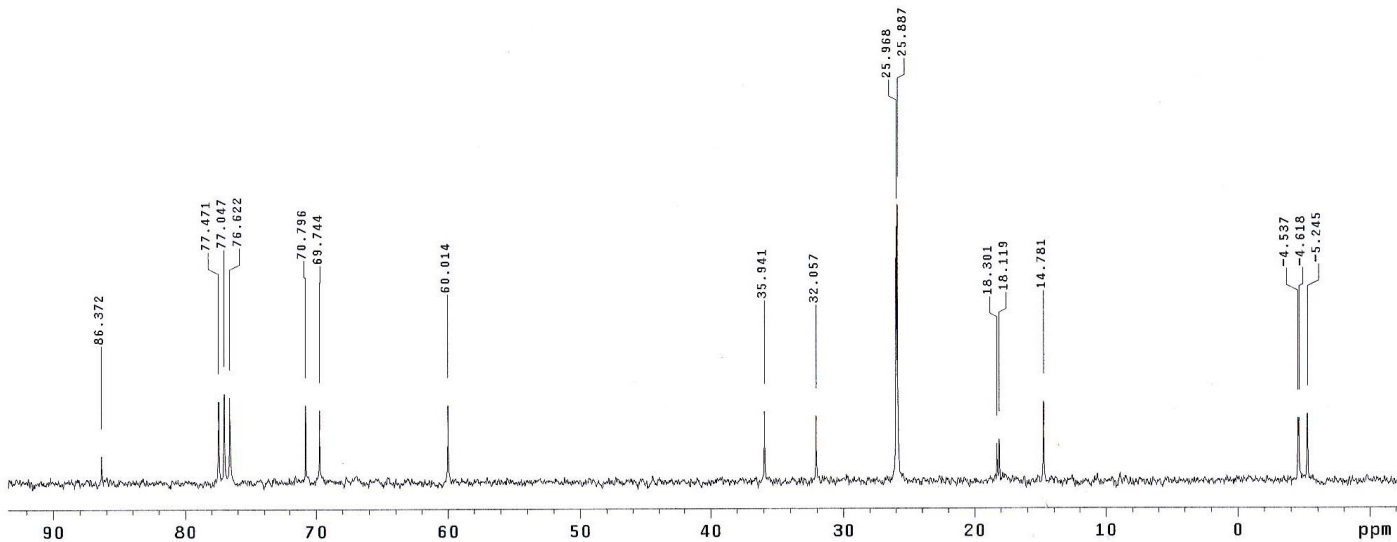


300 MHz <sup>1</sup>H NMR of compound 7 in CDCl<sub>3</sub>

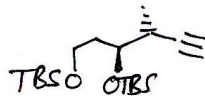
75 MHz <sup>13</sup>C NMR of compound 7 in CDCl<sub>3</sub>

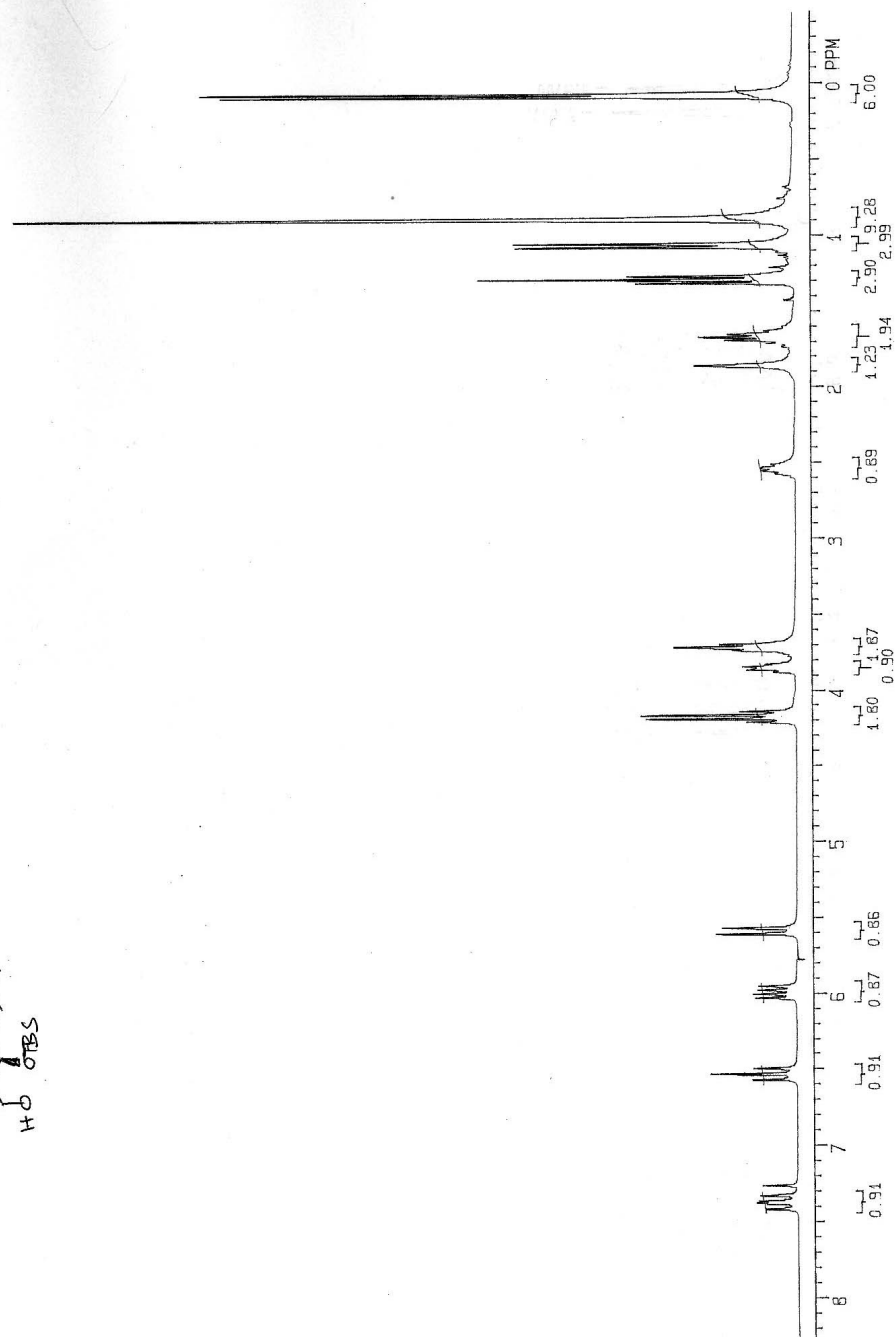
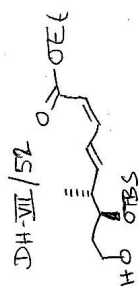


300 MHz  $^1\text{H}$  NMR of compound **8** in  $\text{CDCl}_3$

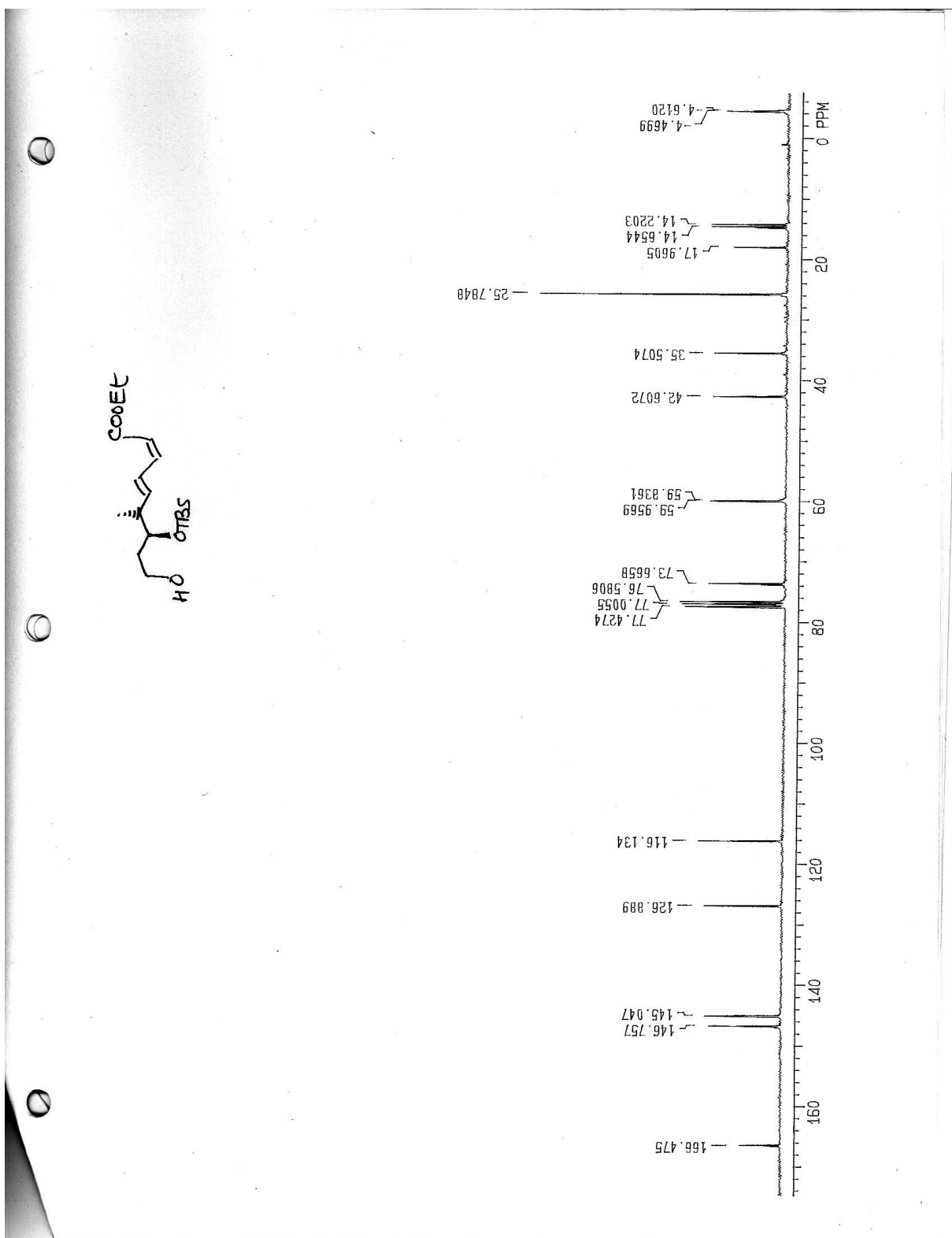


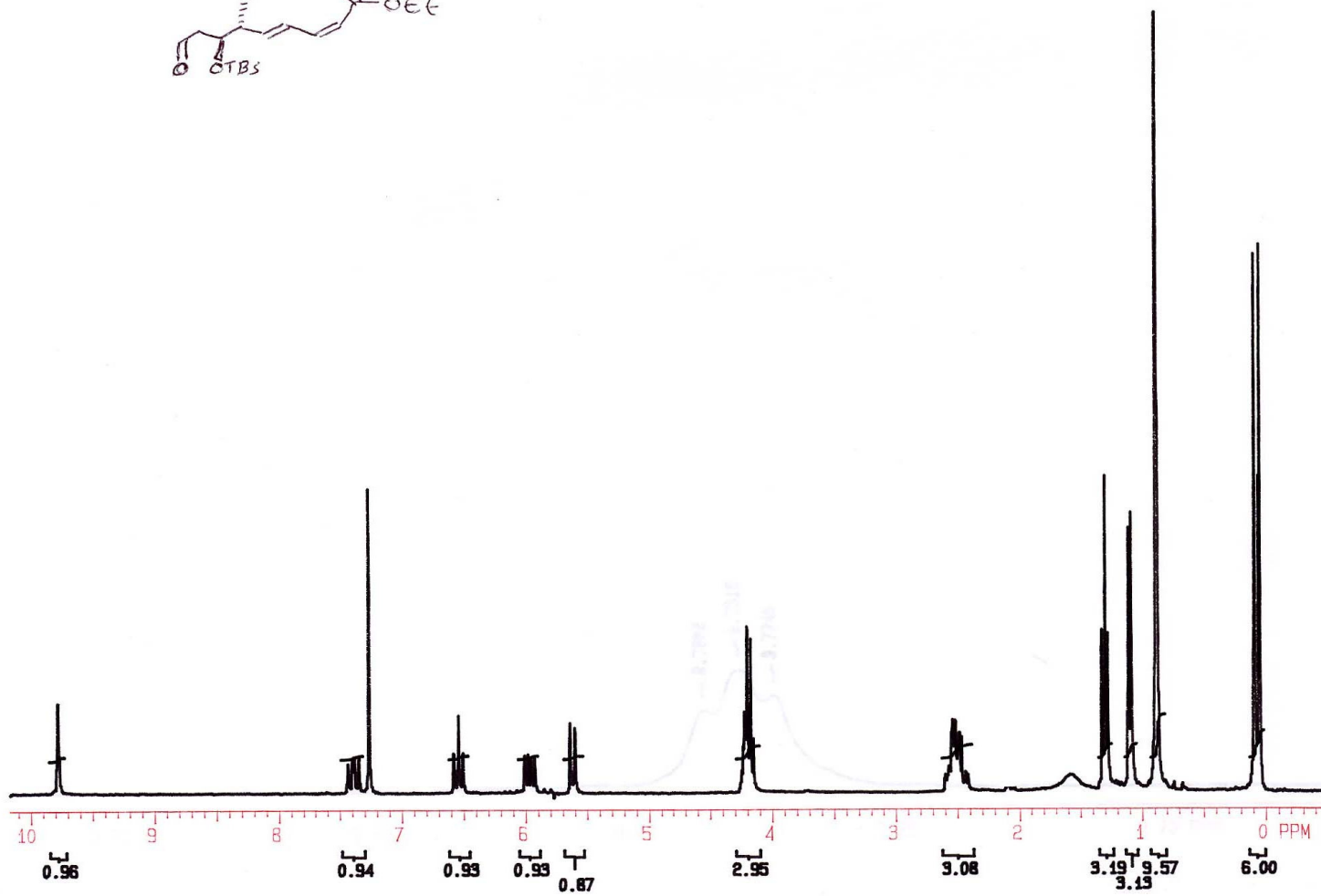
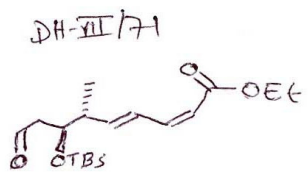
75 MHz  $^{13}\text{C}$  NMR of compound **8** in  $\text{CDCl}_3$



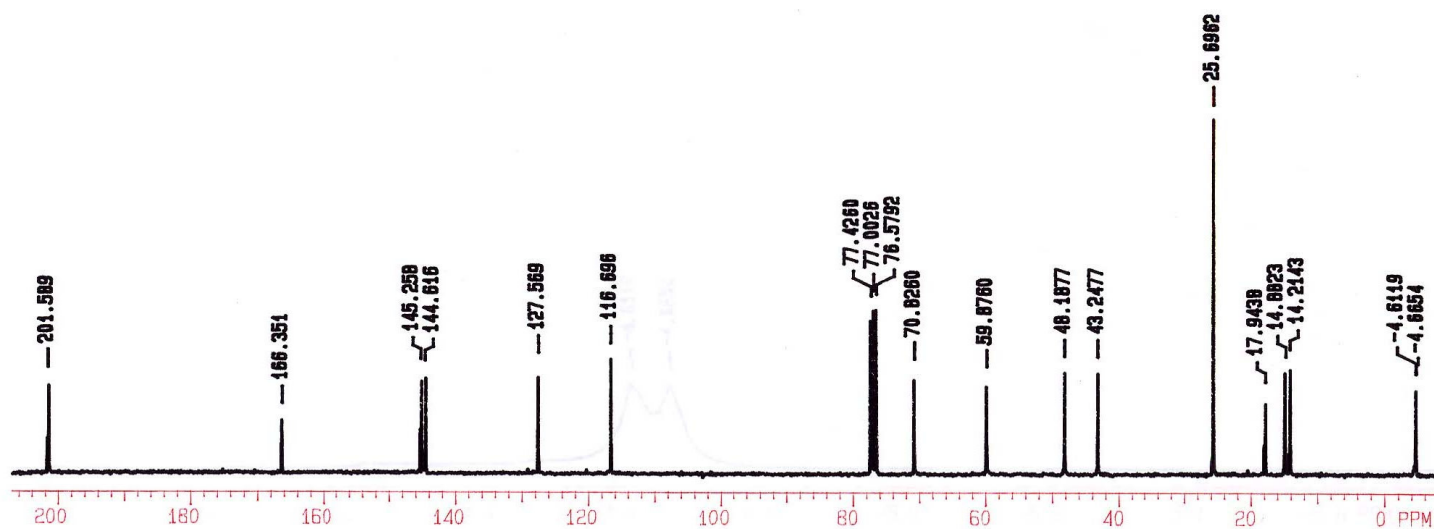
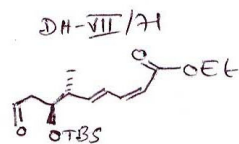




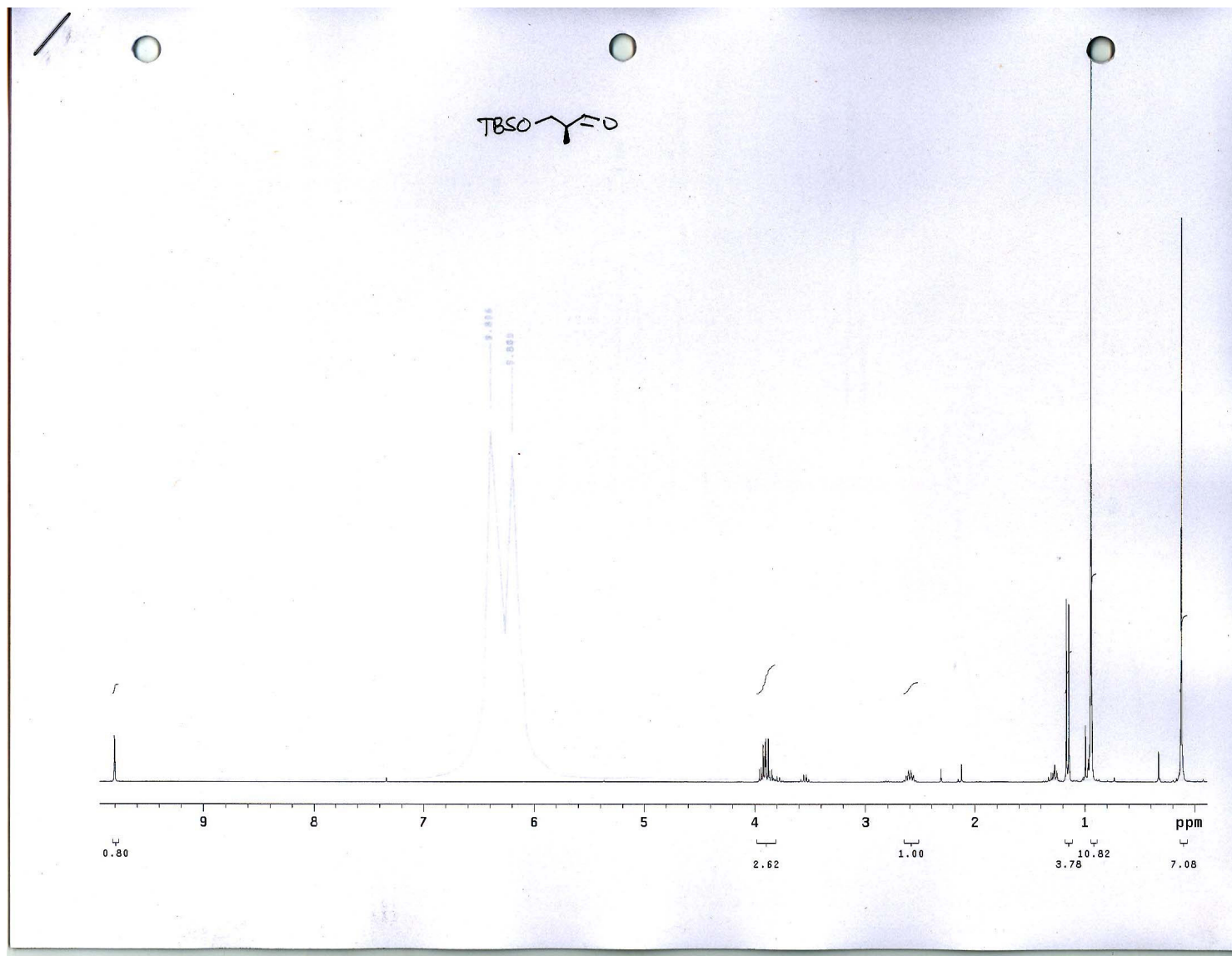


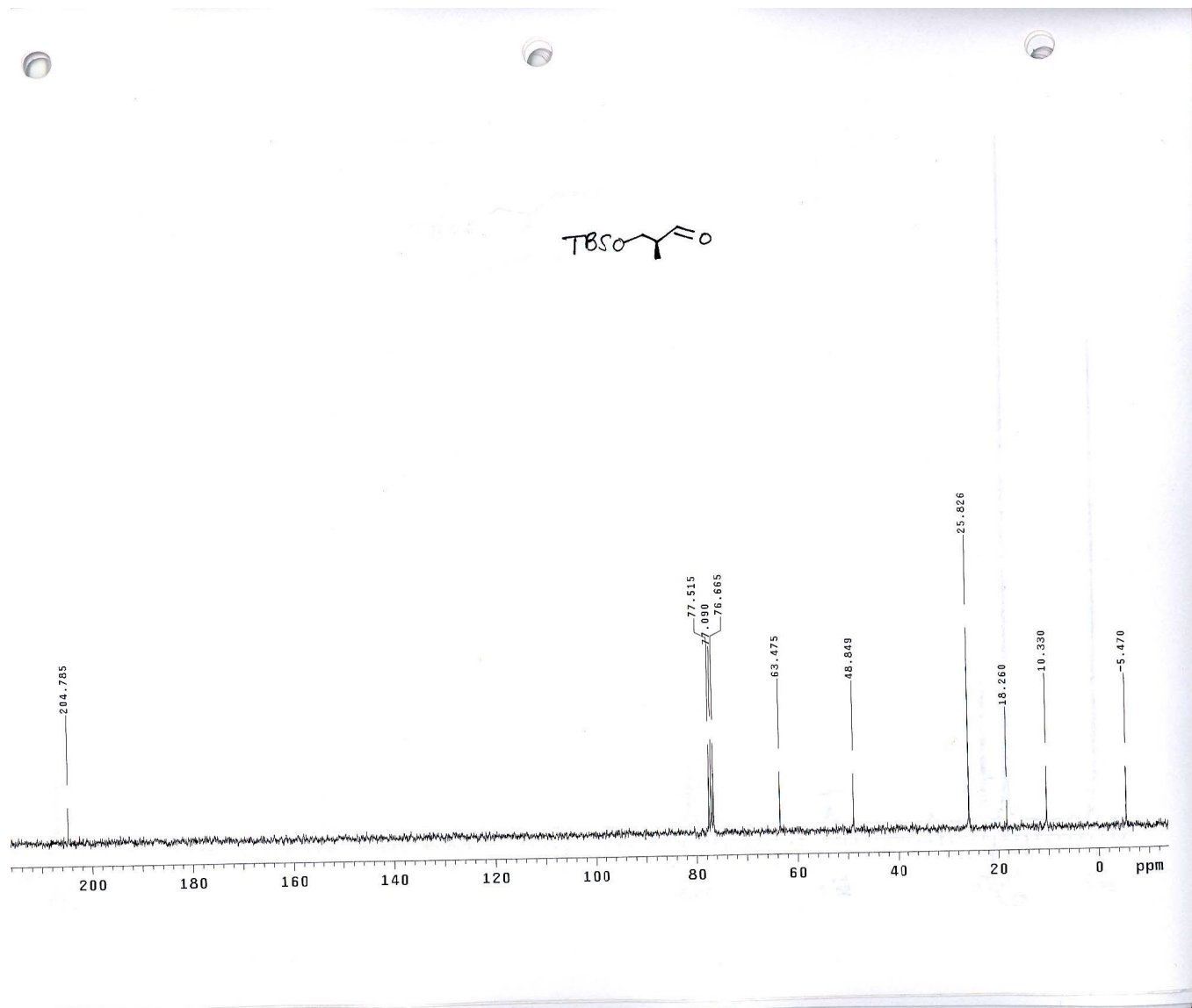


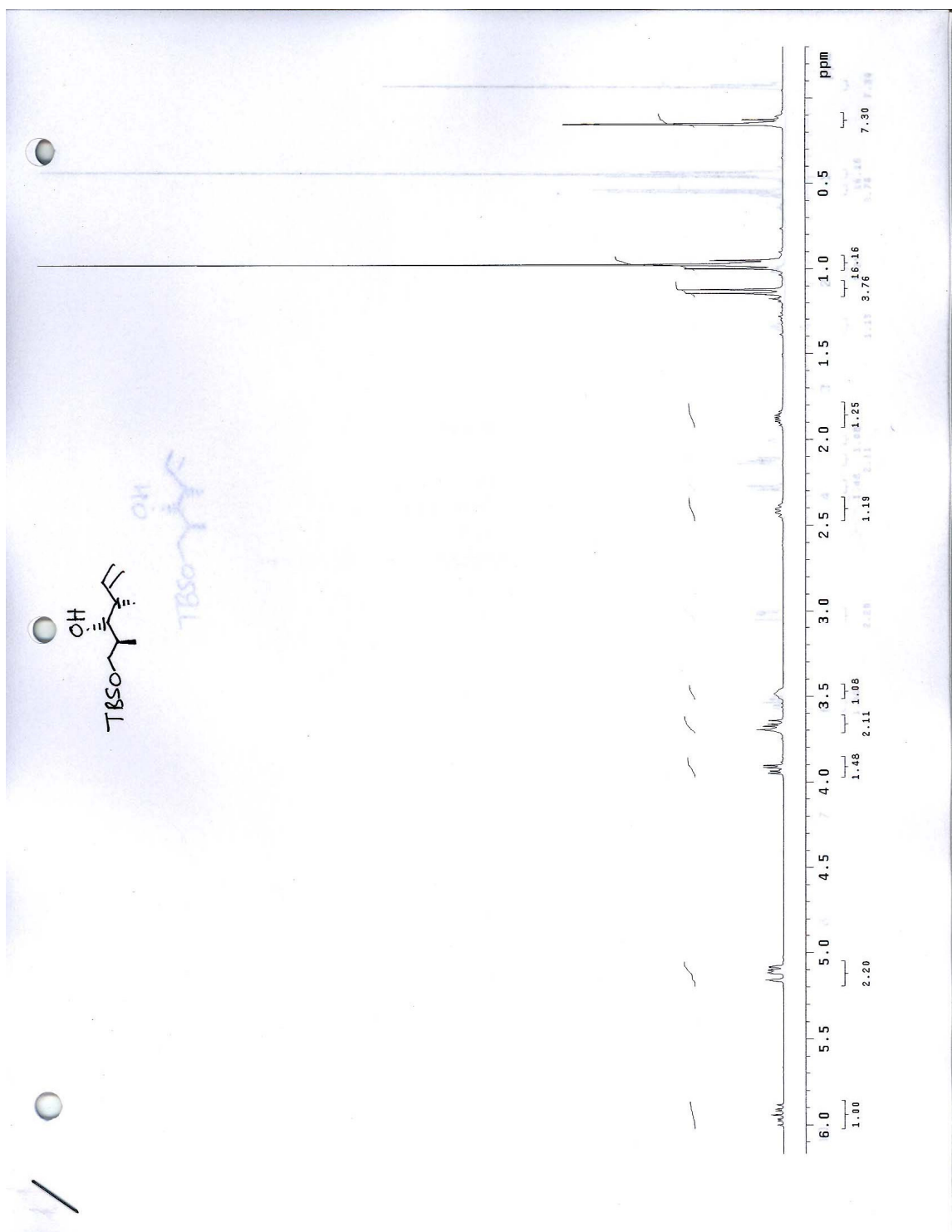
300 MHz  $^1\text{H}$  NMR of compound **2** in  $\text{CDCl}_3$

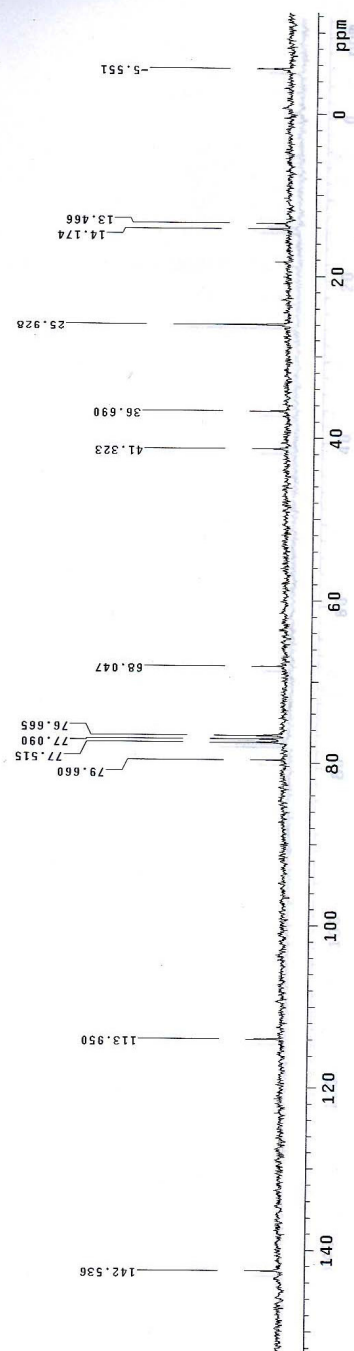


75 MHz <sup>13</sup>C NMR of compound 2 in CDCl<sub>3</sub>

300 MHz  $^1\text{H}$  NMR of compound **12** in  $\text{CDCl}_3$

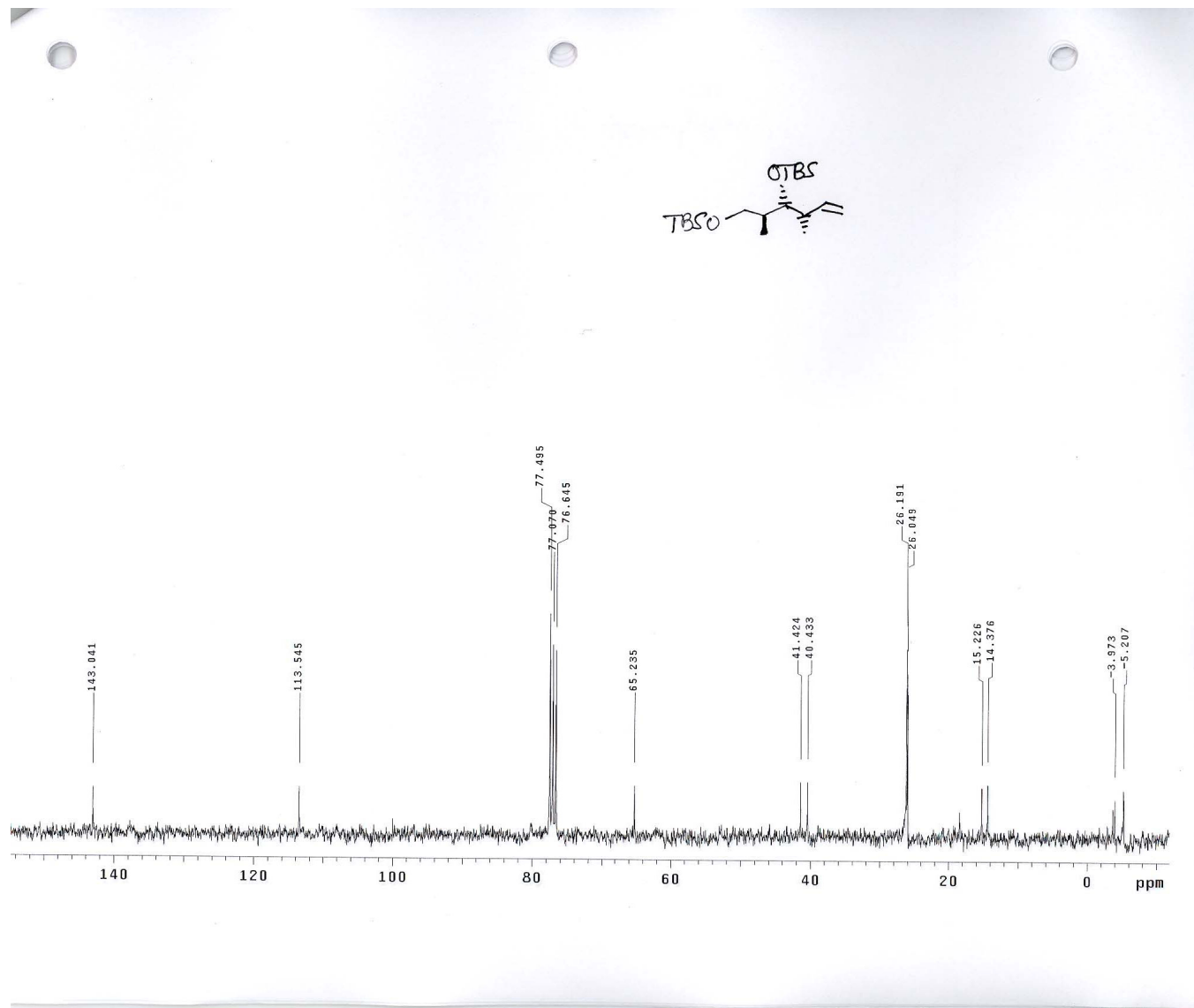
75 MHz <sup>13</sup>C NMR of compound **12** in CDCl<sub>3</sub>





300 MHz  $^1\text{H}$  NMR of compound **13** in  $\text{CDCl}_3$

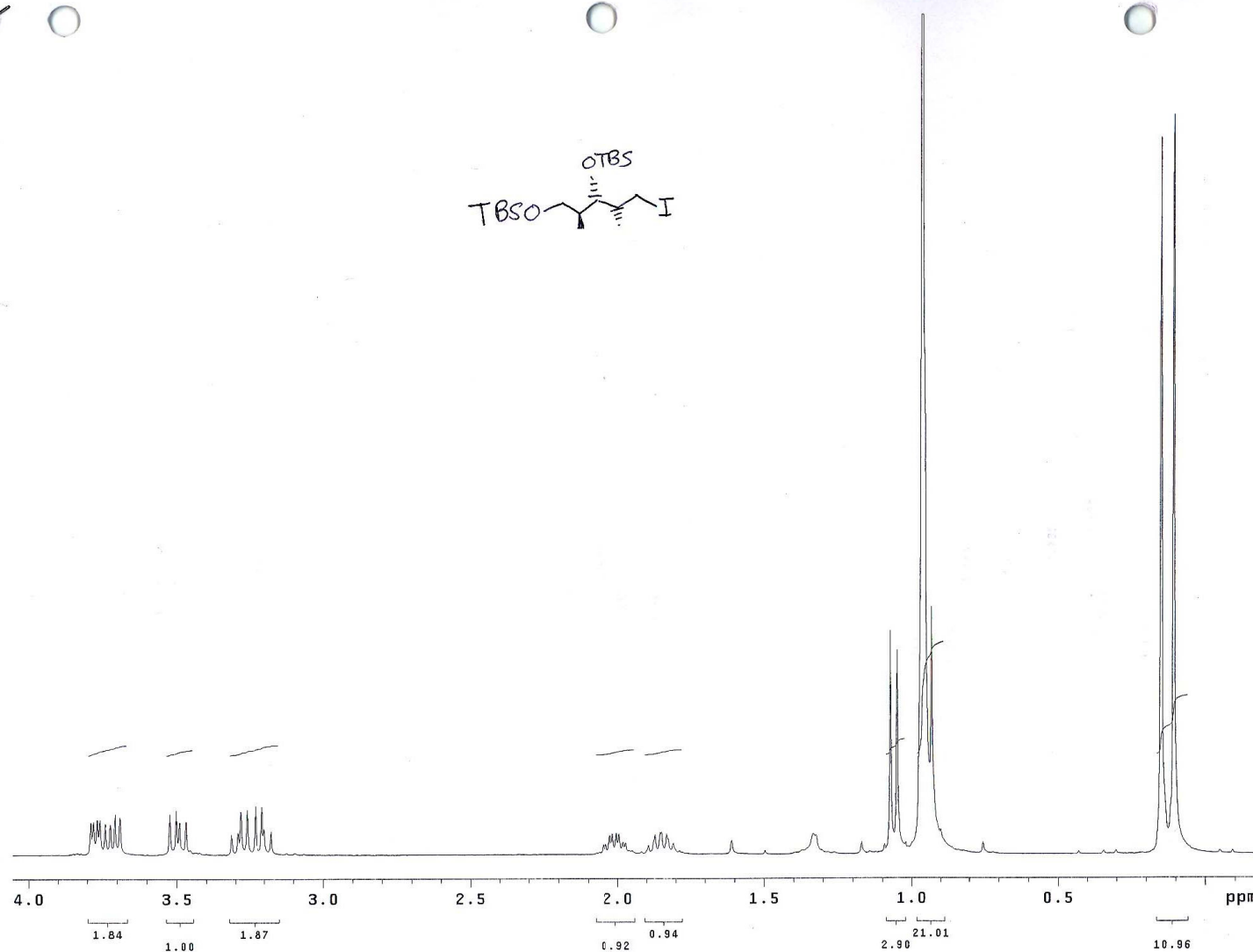




75 MHz <sup>13</sup>C NMR of compound **13** in CDCl<sub>3</sub>



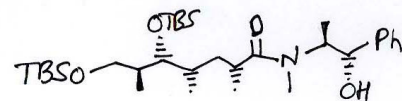




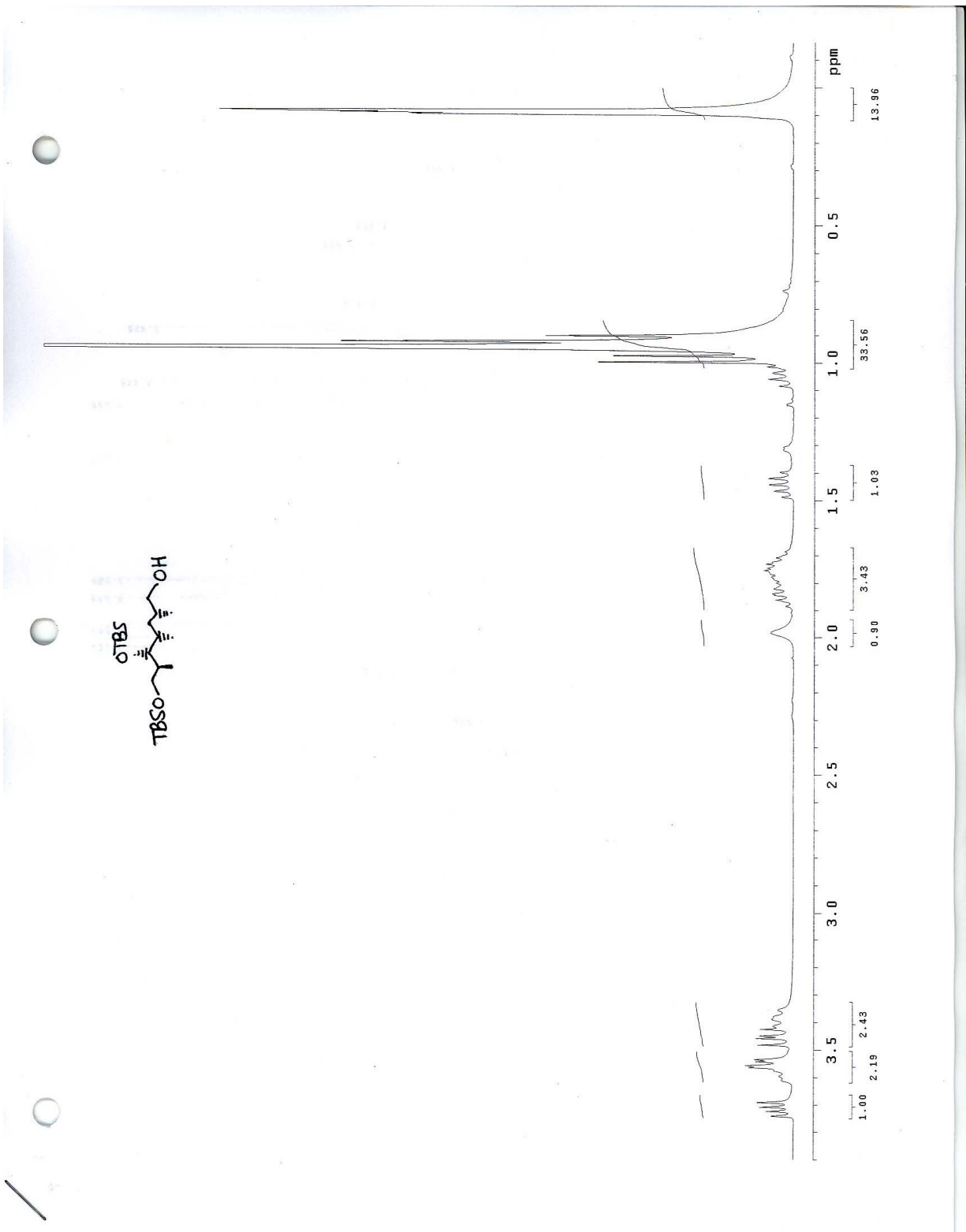
300 MHz  $^1\text{H}$  NMR of compound **14** in  $\text{CDCl}_3$

75 MHz  $^{13}\text{C}$  NMR of compound **14** in  $\text{CDCl}_3$

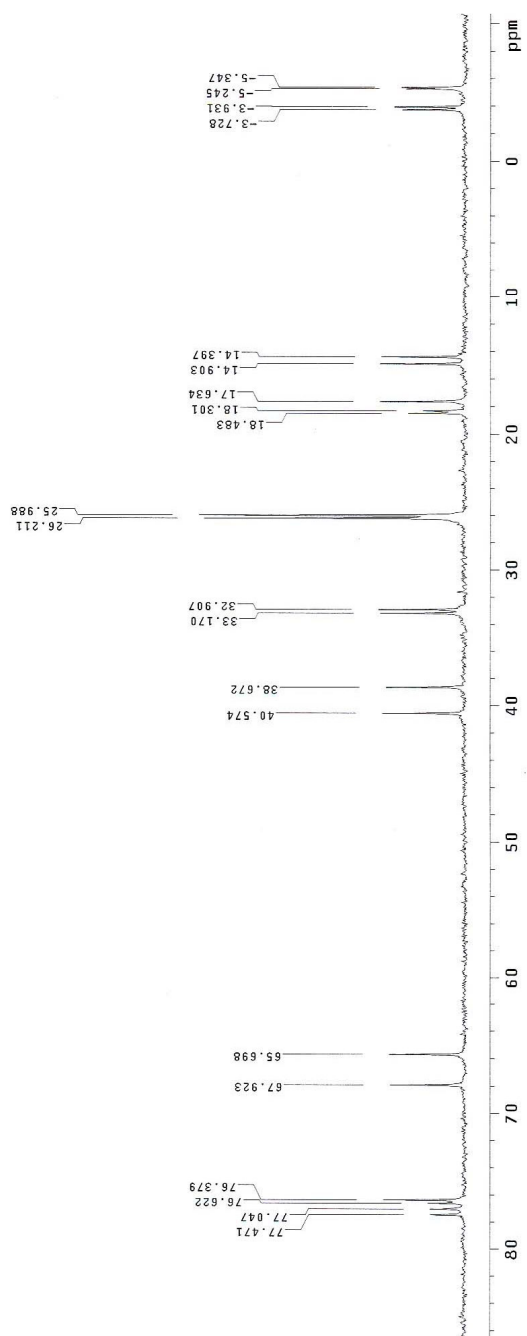
300 MHz  $^1\text{H}$  NMR of compound **15** in  $\text{CDCl}_3$



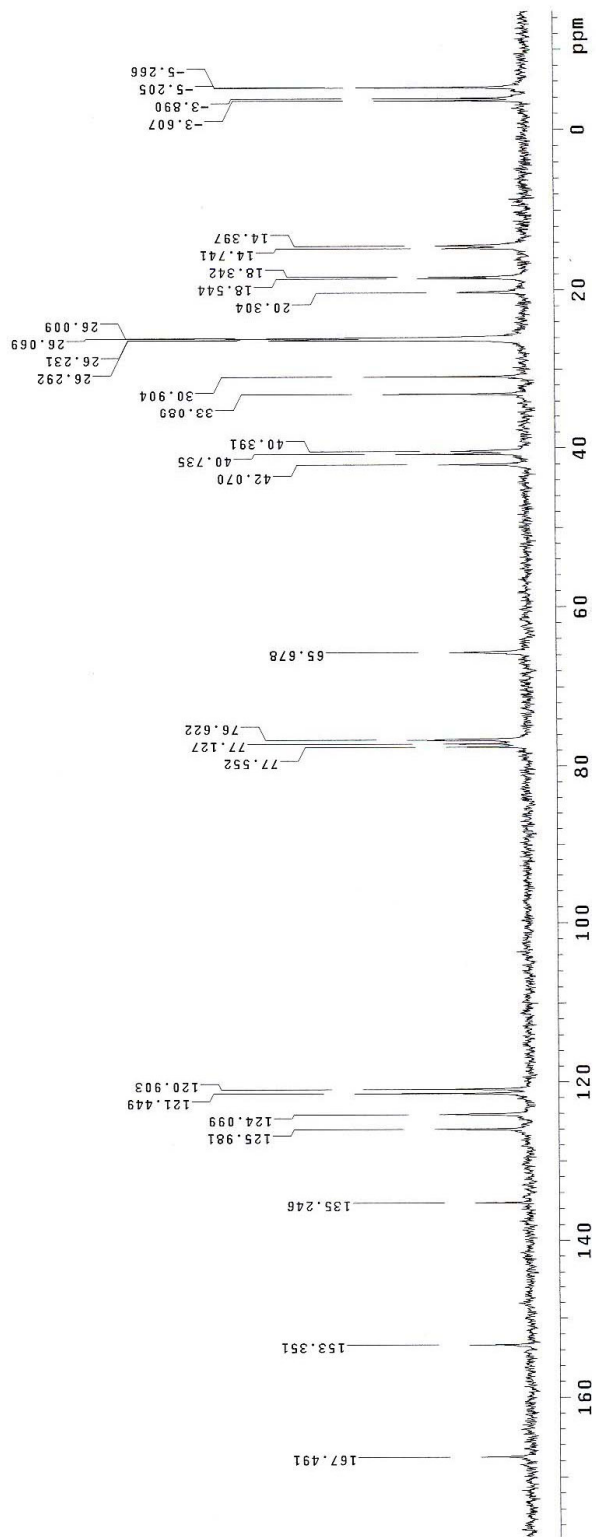
75 MHz  $^{13}\text{C}$  NMR of compound **15** in  $\text{CDCl}_3$

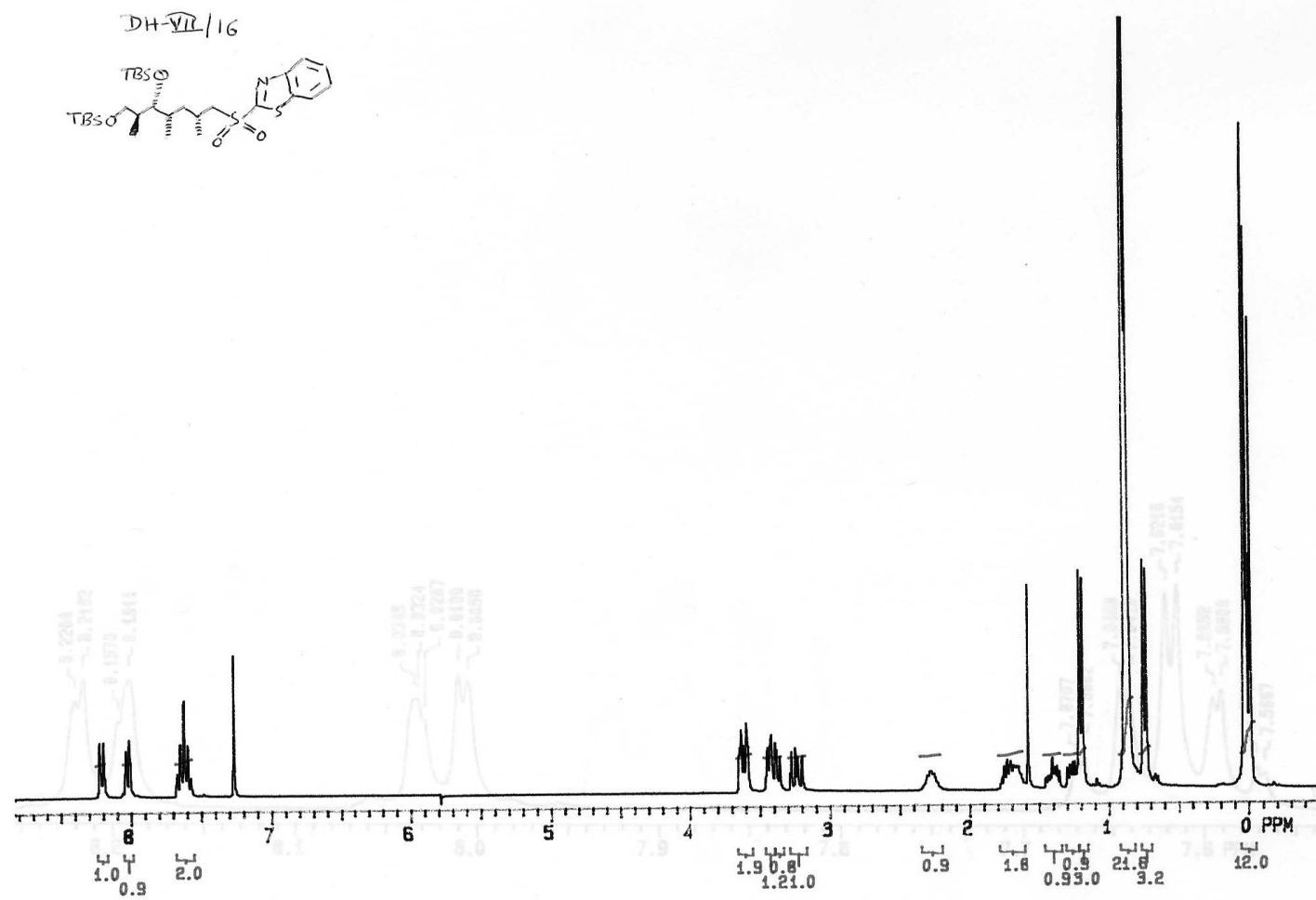


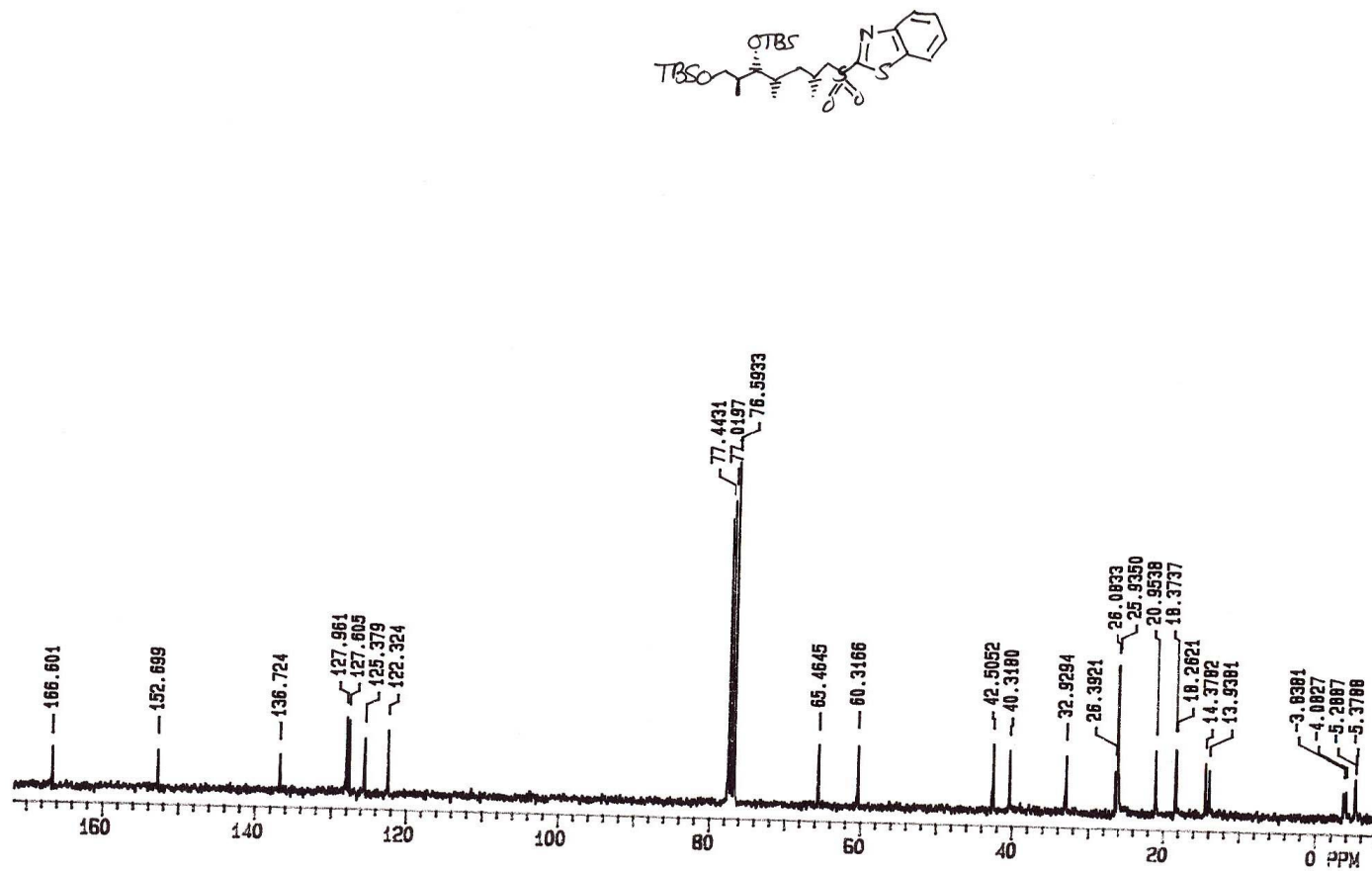




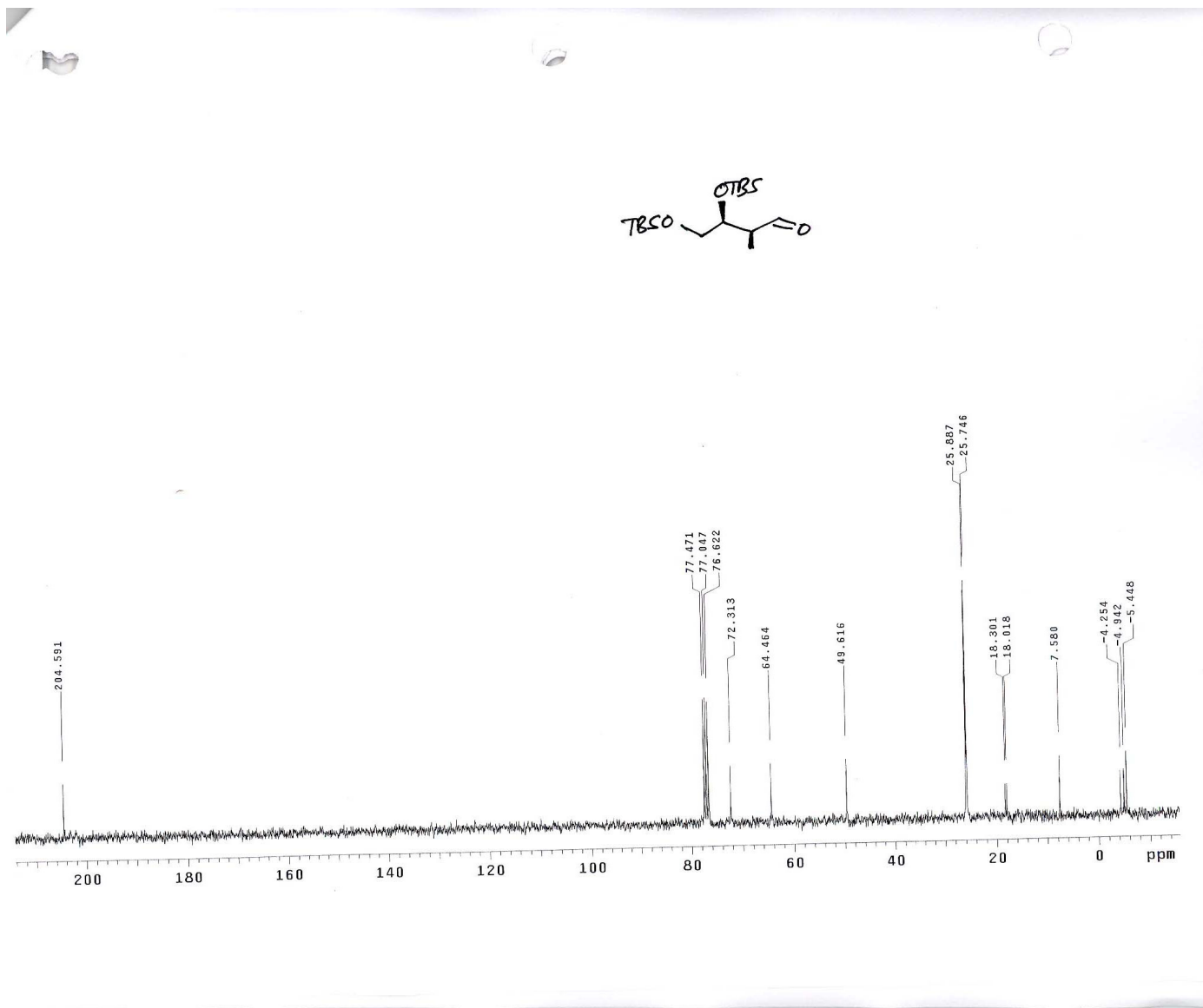




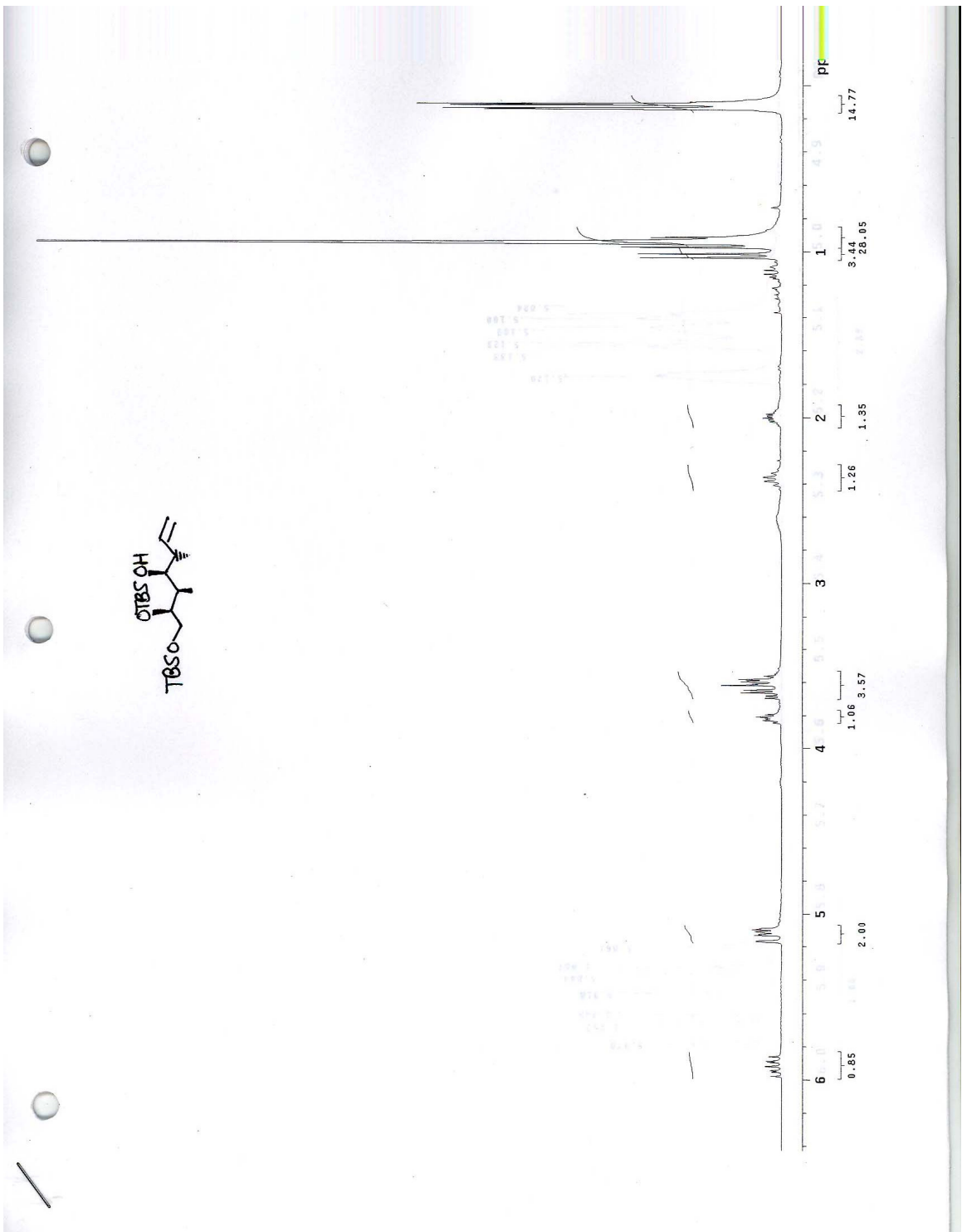
300 MHz  $^1\text{H}$  NMR of compound **3** in  $\text{CDCl}_3$

75 MHz  $^{13}\text{C}$  NMR of compound **3** in  $\text{CDCl}_3$

300 MHz  $^1\text{H}$  NMR of compound **16** in  $\text{CDCl}_3$

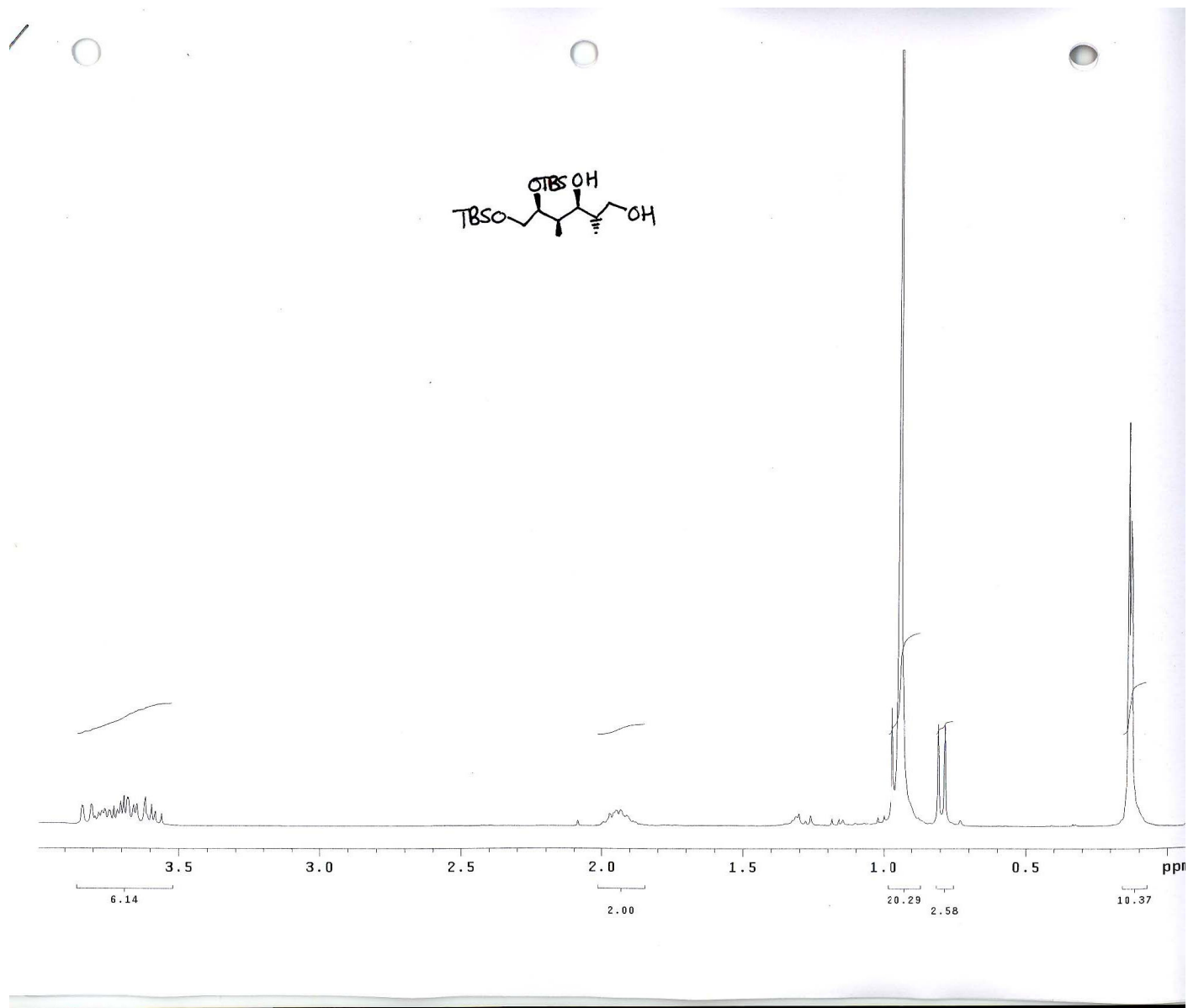


75 MHz <sup>13</sup>C NMR of compound **16** in CDCl<sub>3</sub>

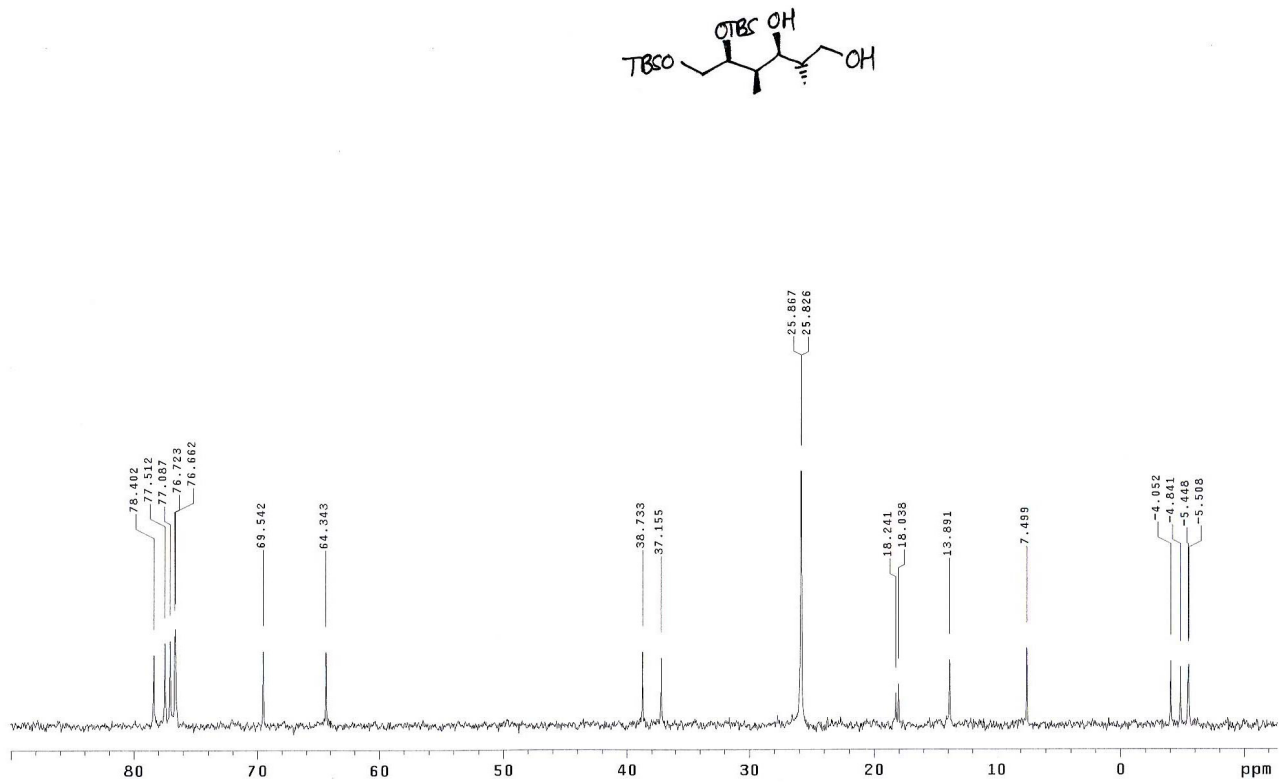




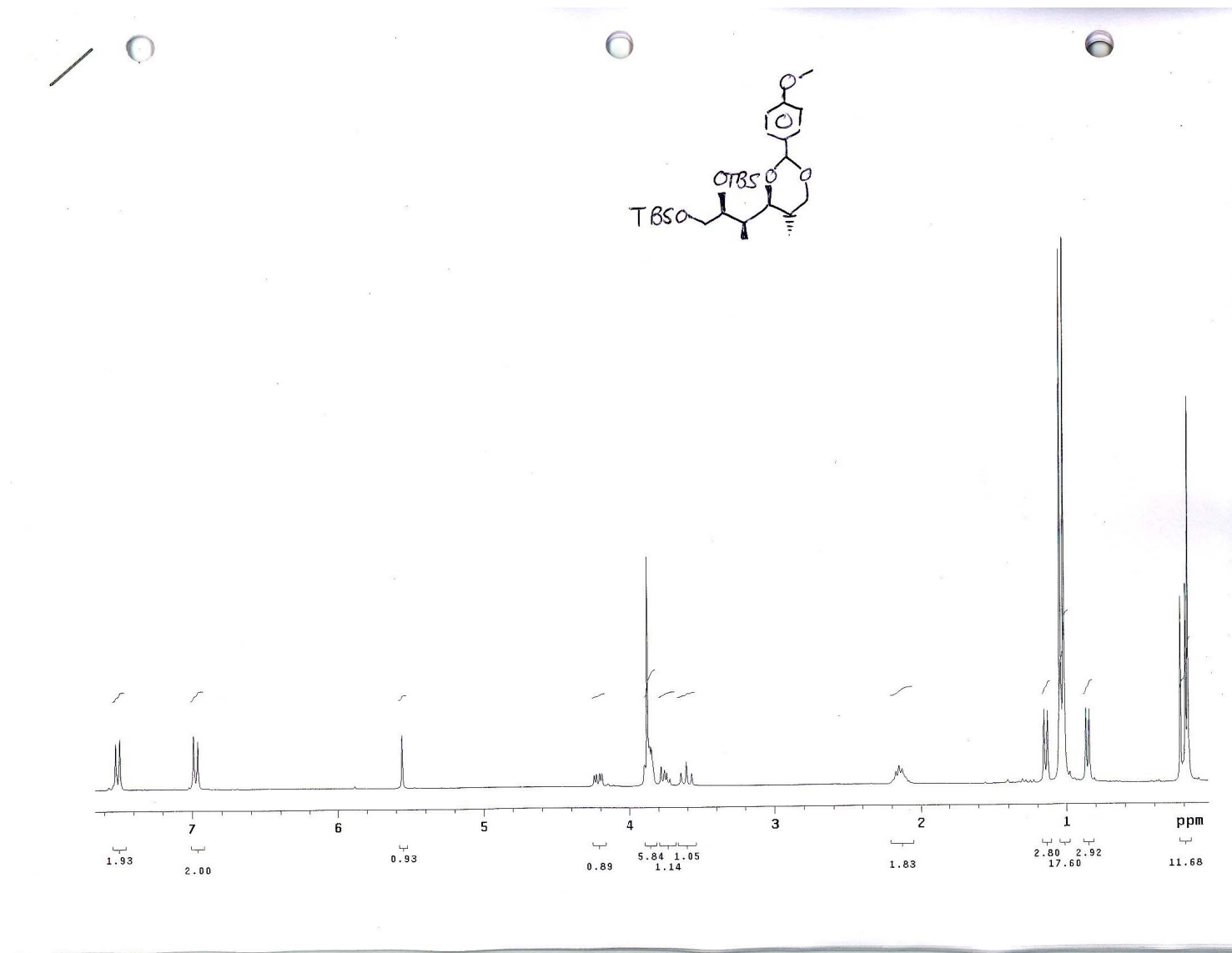




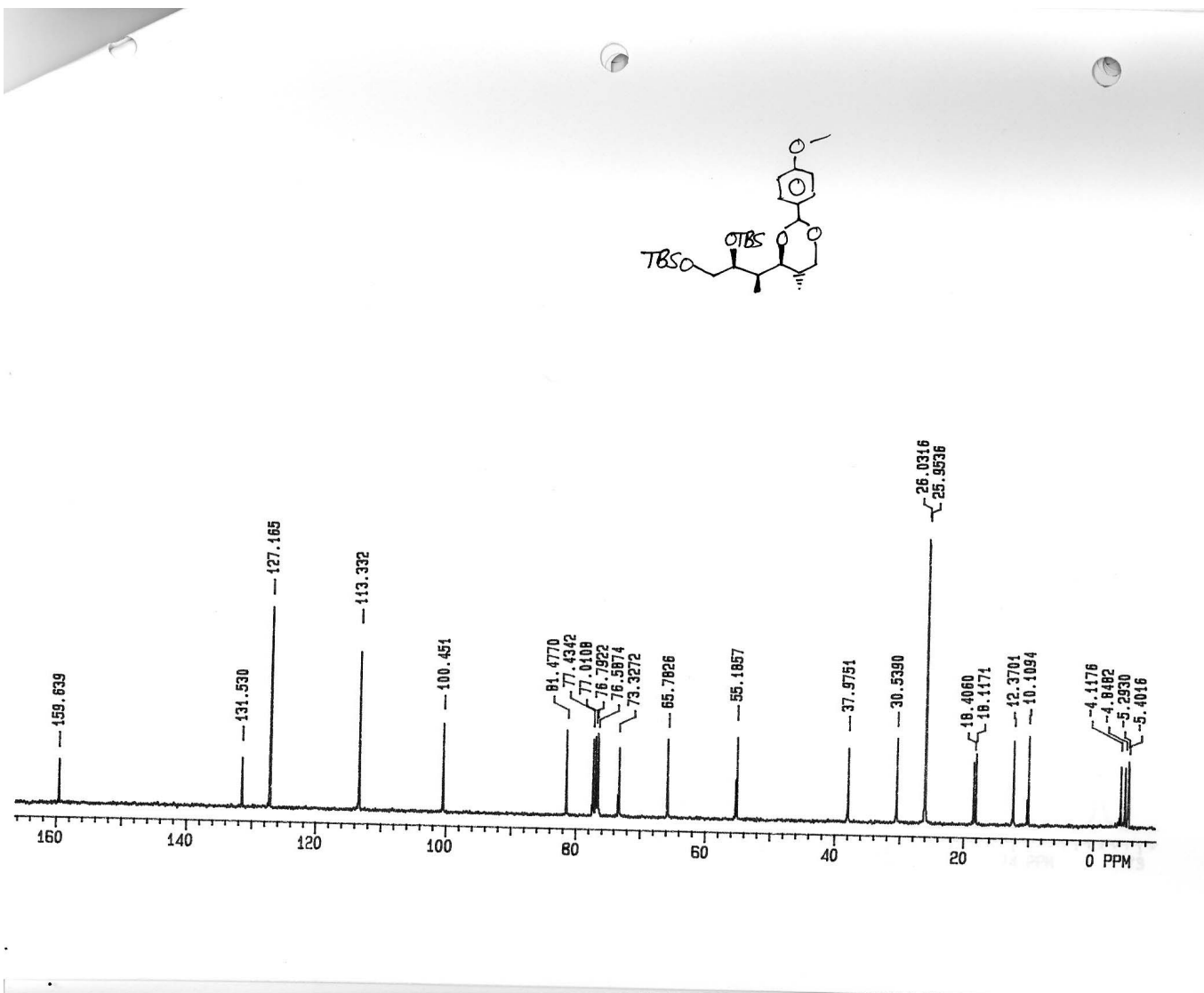
300 MHz  $^1\text{H}$  NMR of compound **17** in  $\text{CDCl}_3$



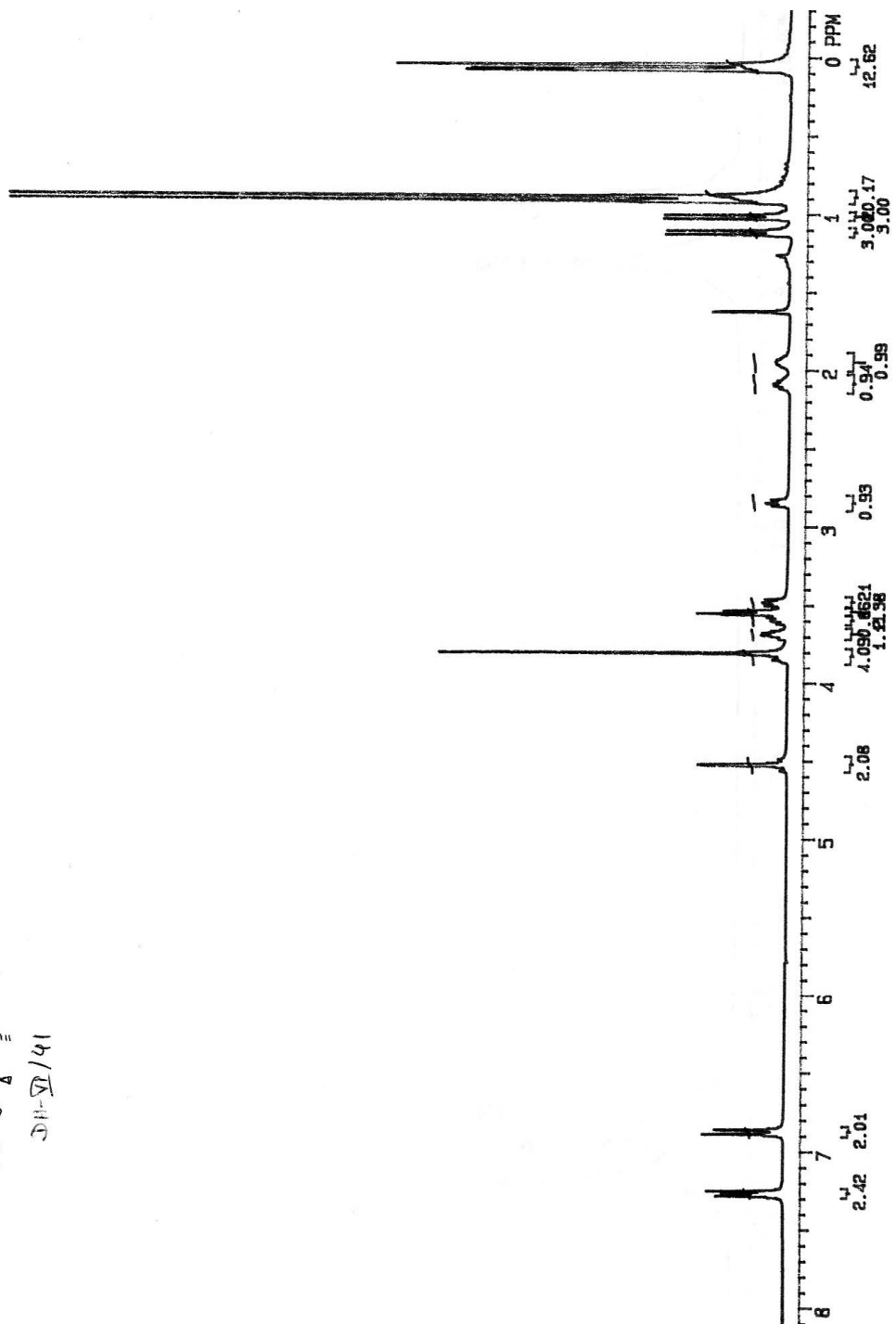
75 MHz <sup>13</sup>C NMR of compound **17** in CDCl<sub>3</sub>



300 MHz  $^1\text{H}$  NMR of compound **18** in  $\text{CDCl}_3$

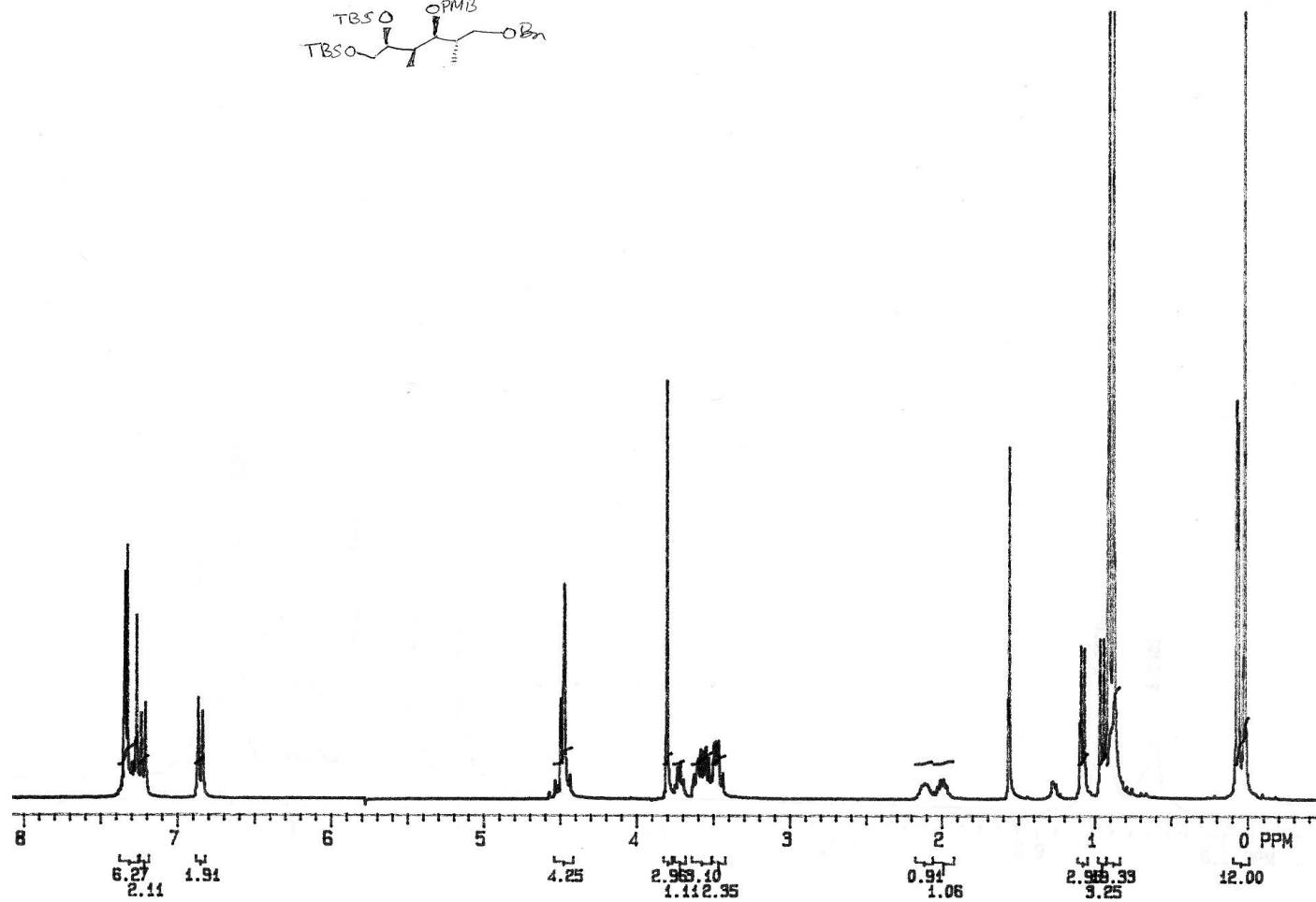


75 MHz  $^{13}\text{C}$  NMR of compound **18** in  $\text{CDCl}_3$



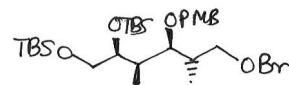


DH-VI/42

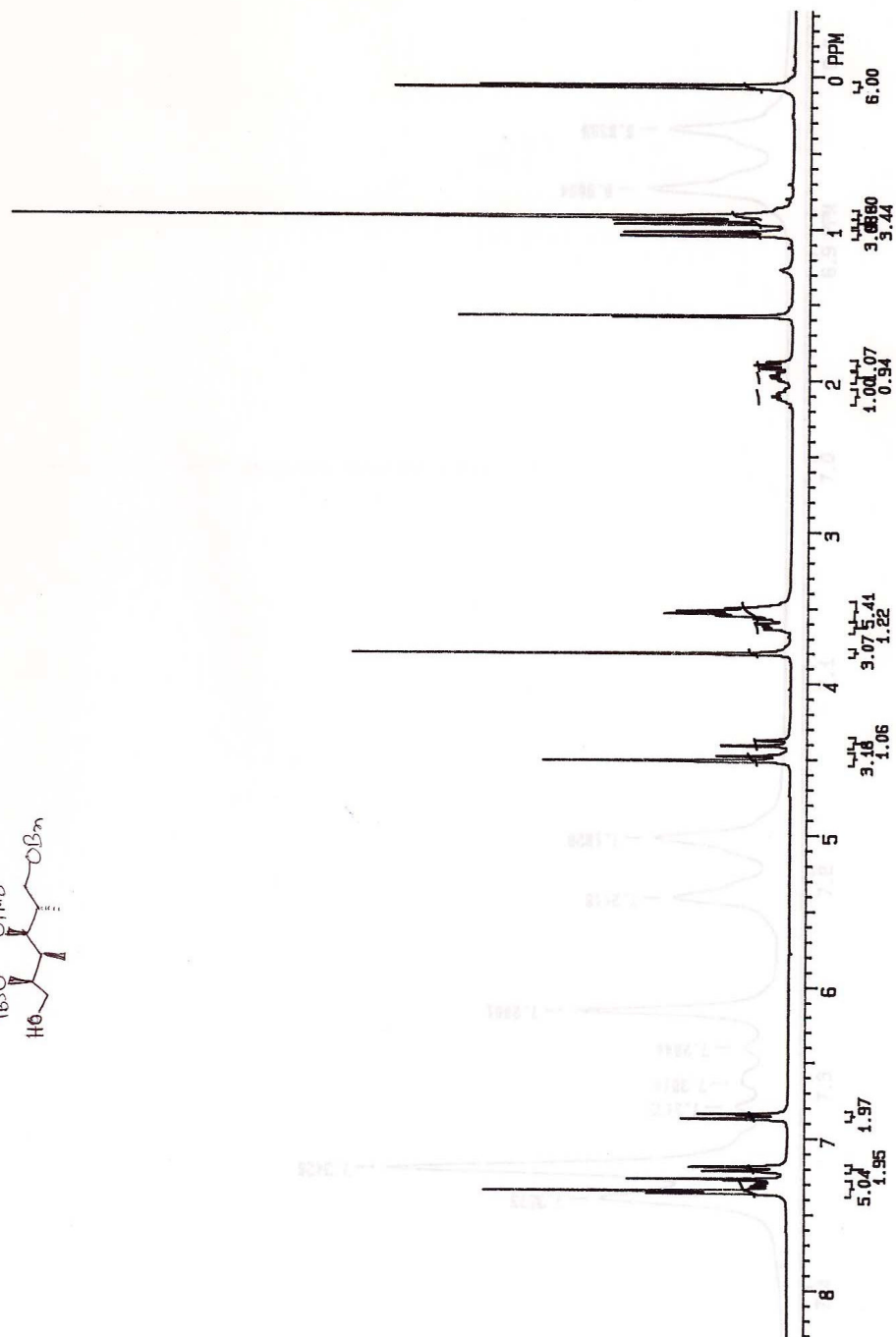
300 MHz  $^1\text{H}$  NMR of compound **19** in  $\text{CDCl}_3$

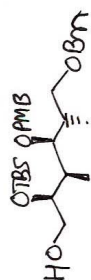


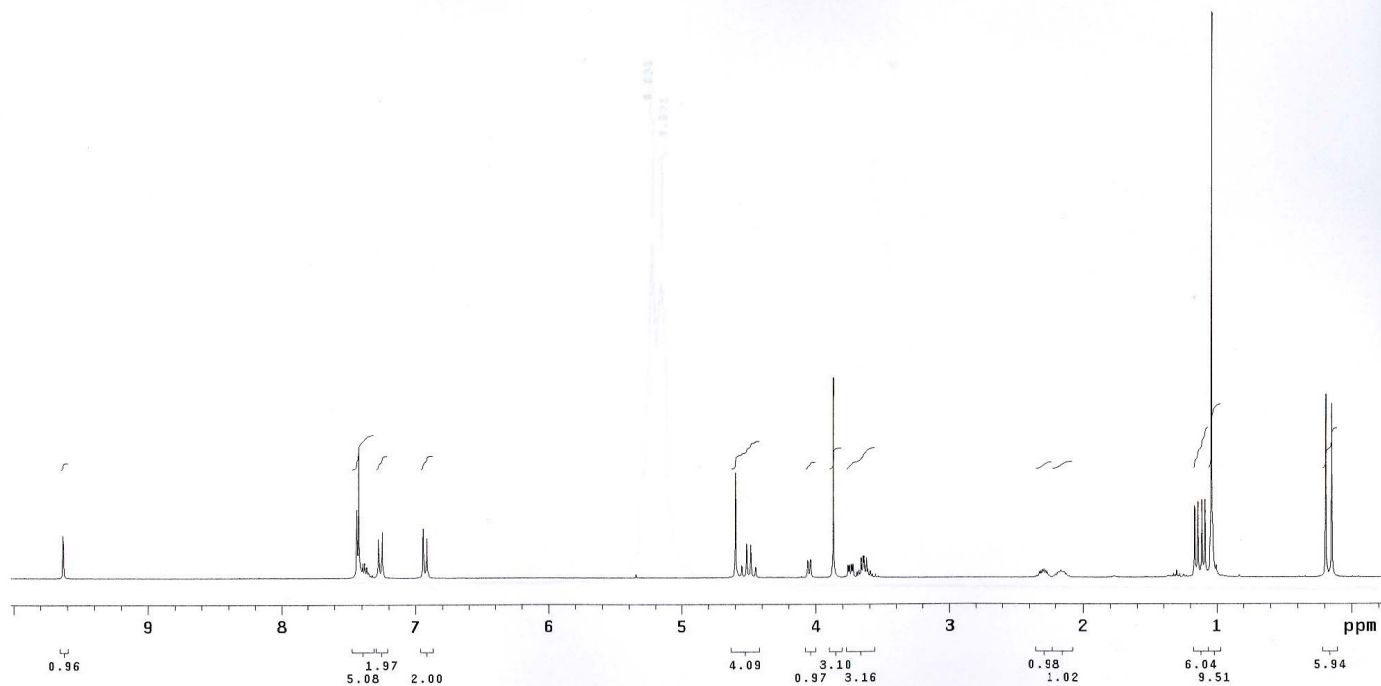
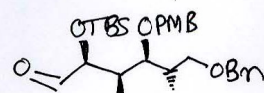
75 MHz  $^{13}\text{C}$  NMR of compound **19** in  $\text{CDCl}_3$



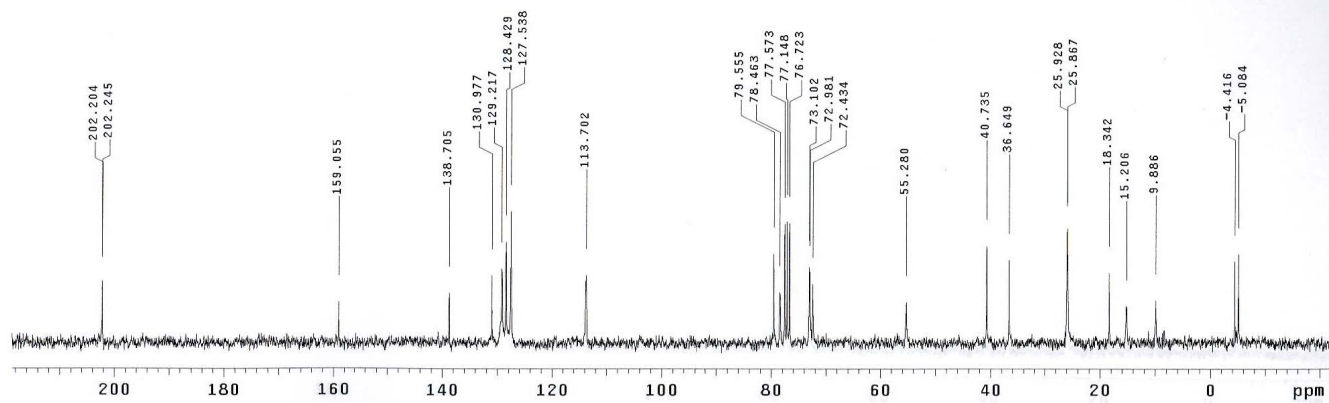
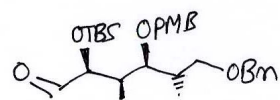
DH-VI/43



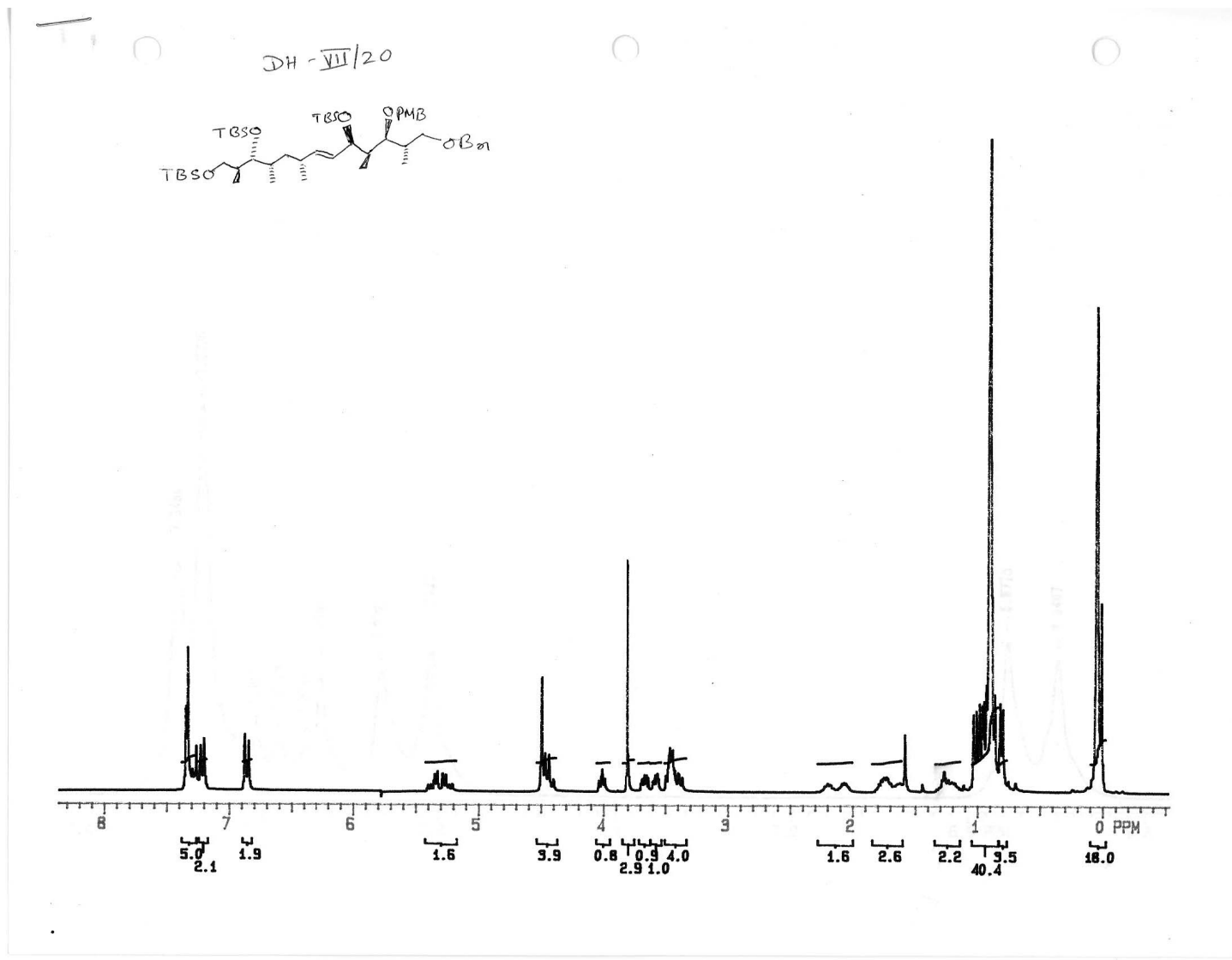




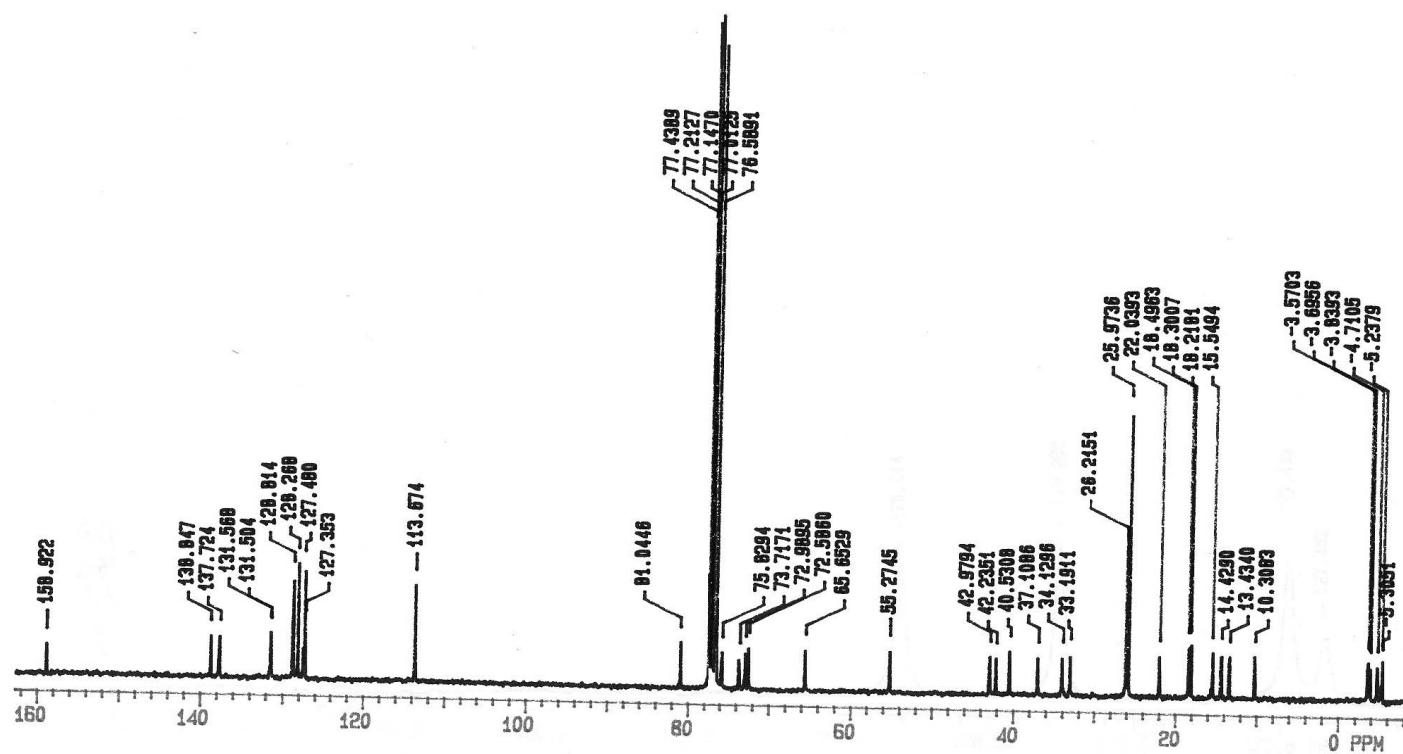
300 MHz  $^1\text{H}$  NMR of compound 4 in  $\text{CDCl}_3$



75 MHz  $^{13}\text{C}$  NMR of compound **4** in  $\text{CDCl}_3$



300 MHz  $^1\text{H}$  NMR of compound **20** in  $\text{CDCl}_3$

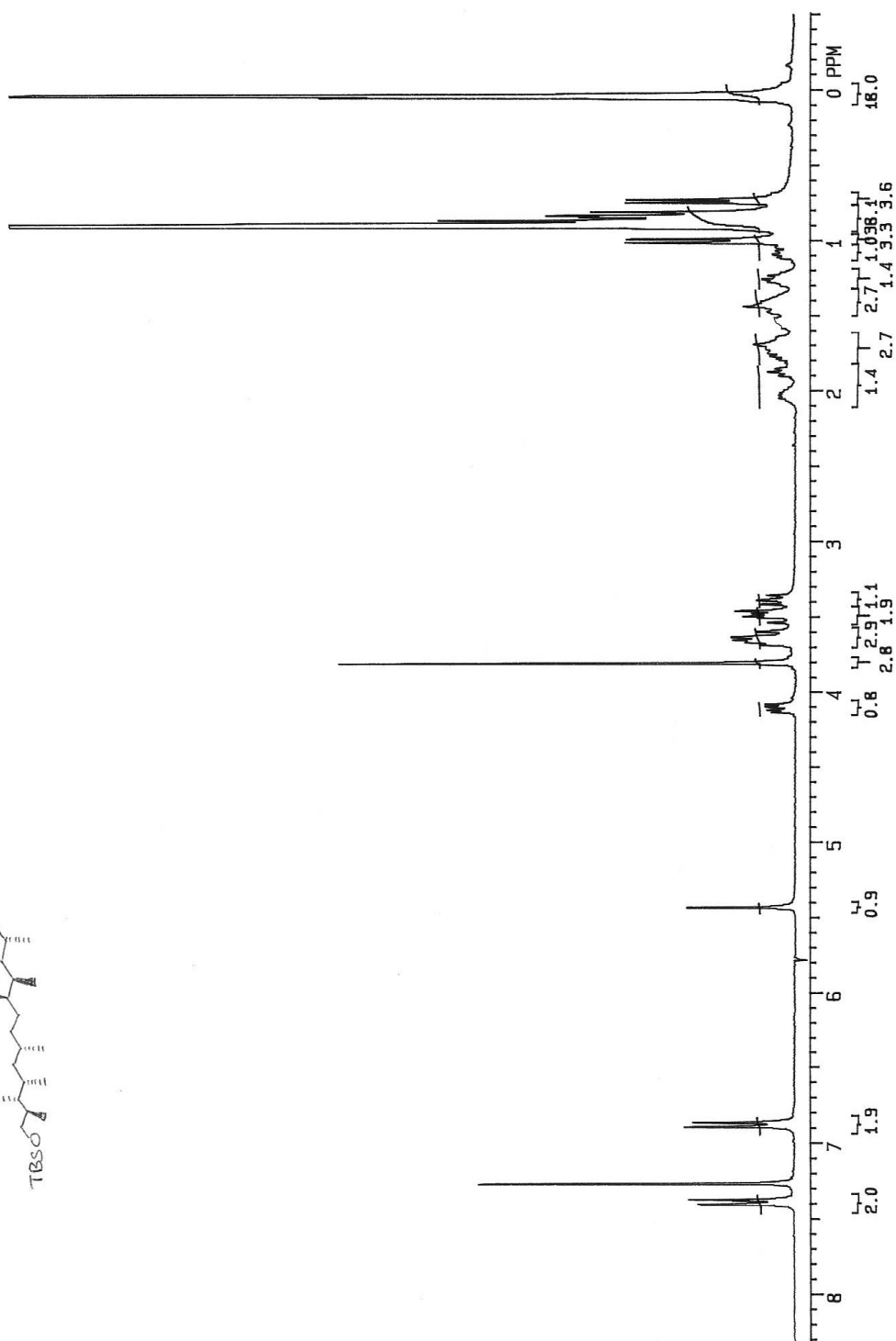
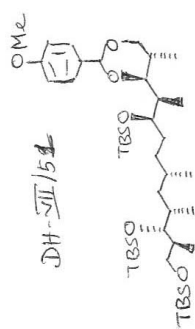


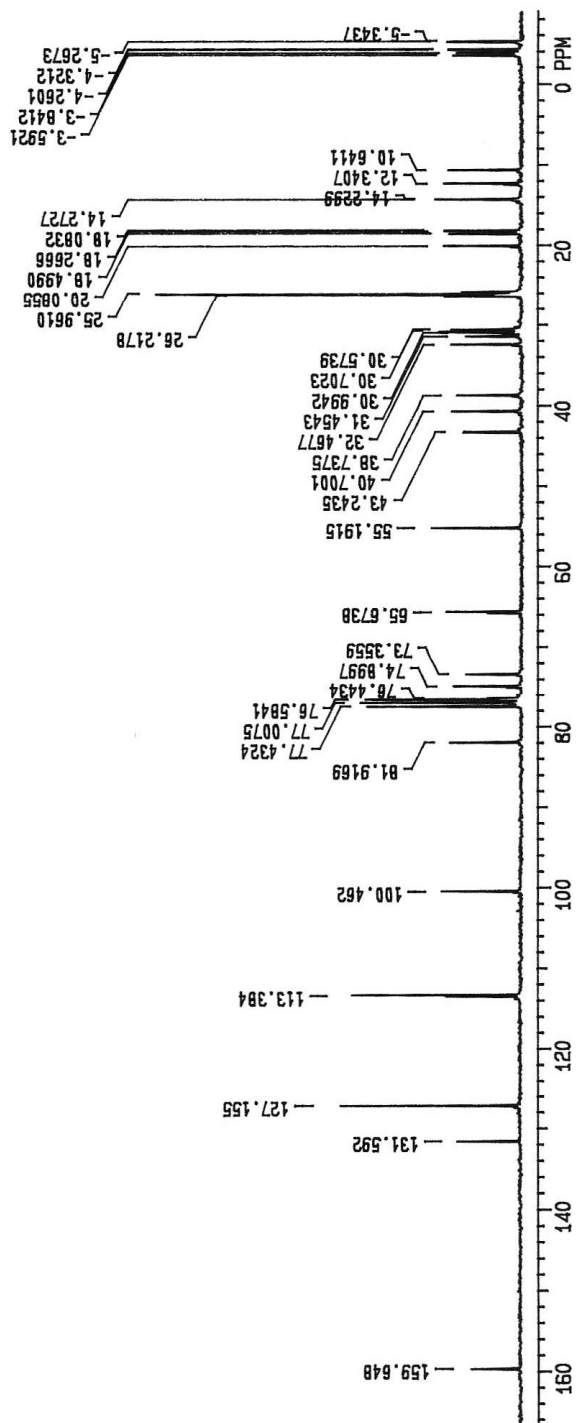
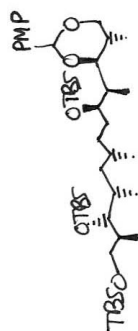
75 MHz  $^{13}\text{C}$  NMR of compound **20** in  $\text{CDCl}_3$

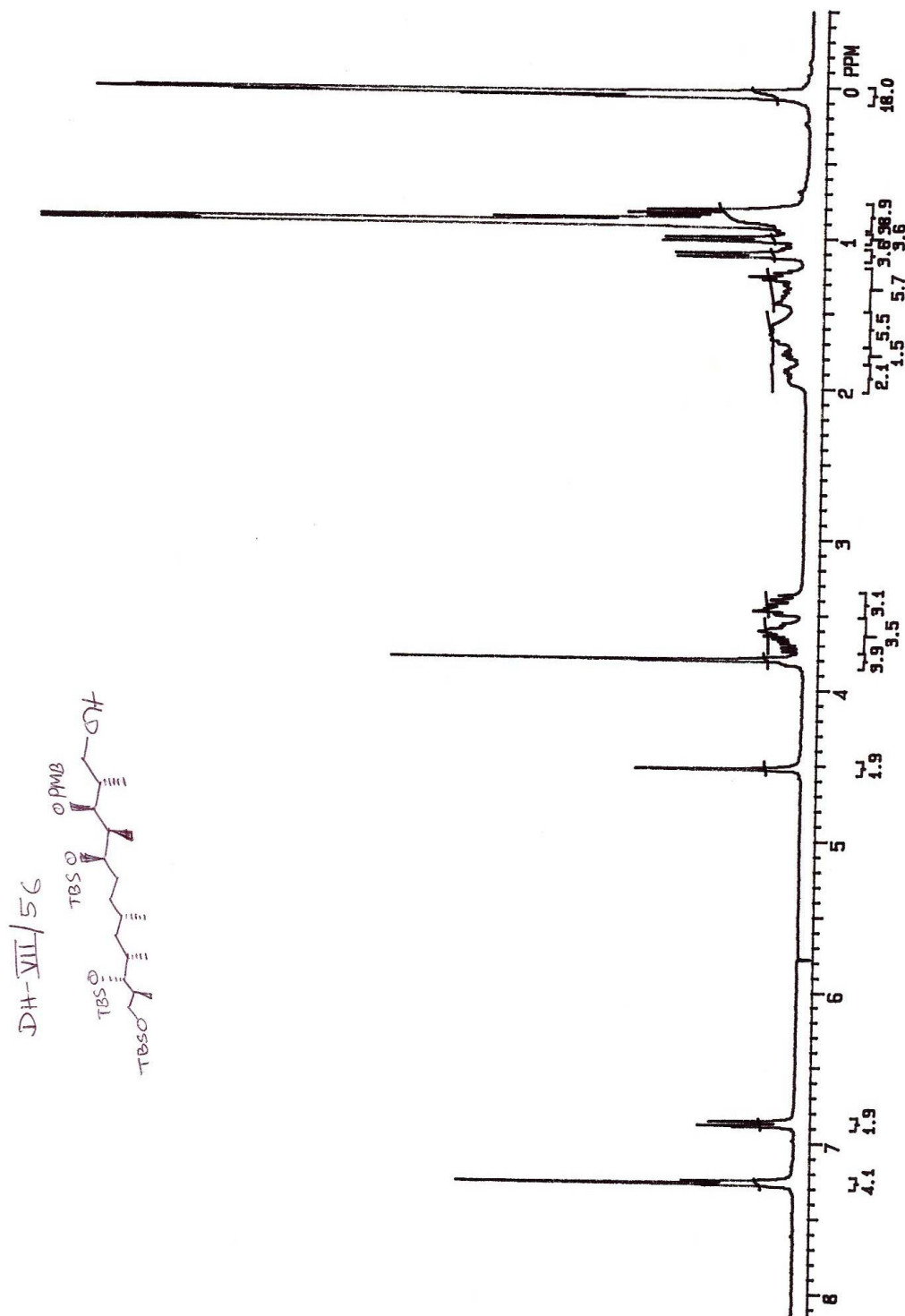




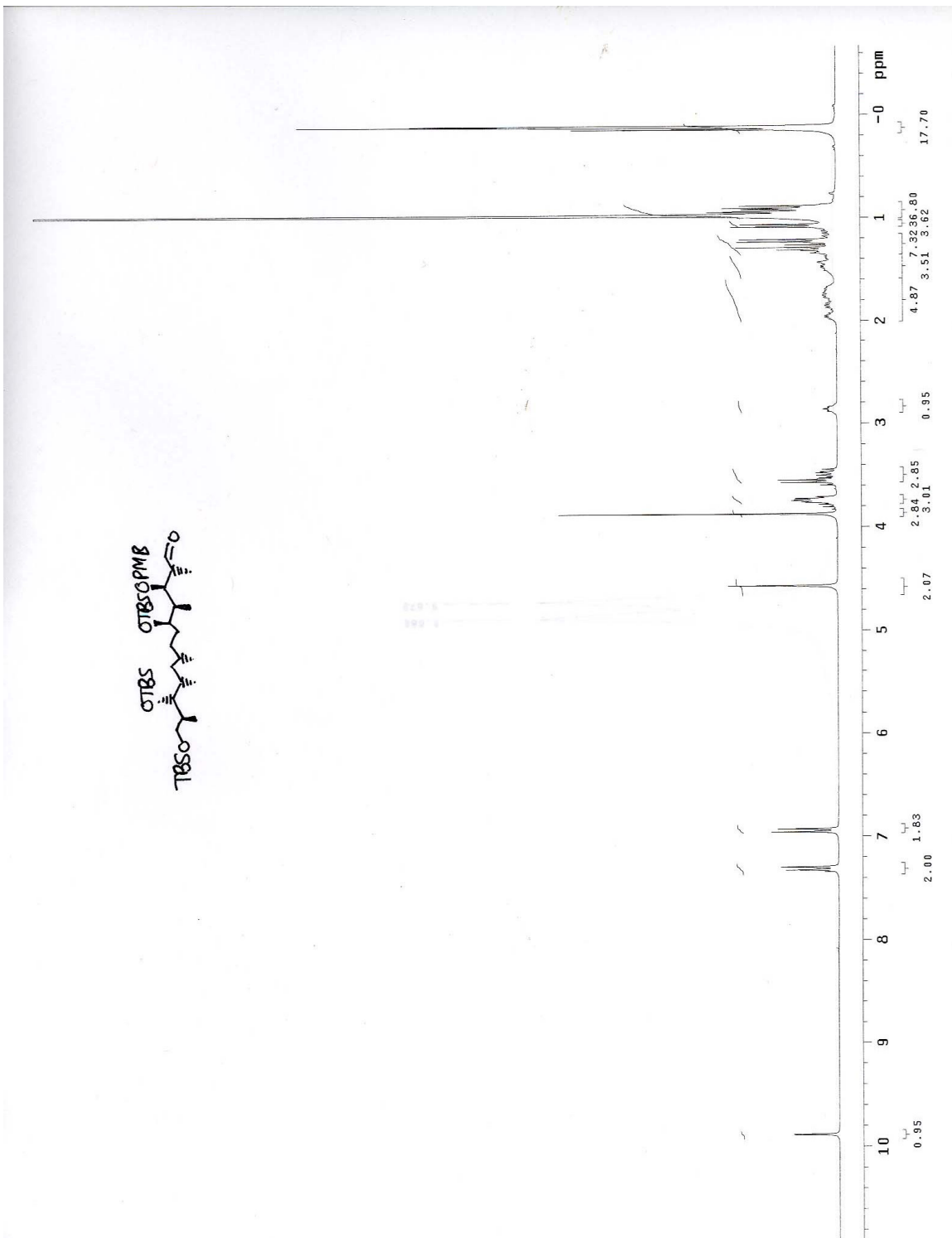


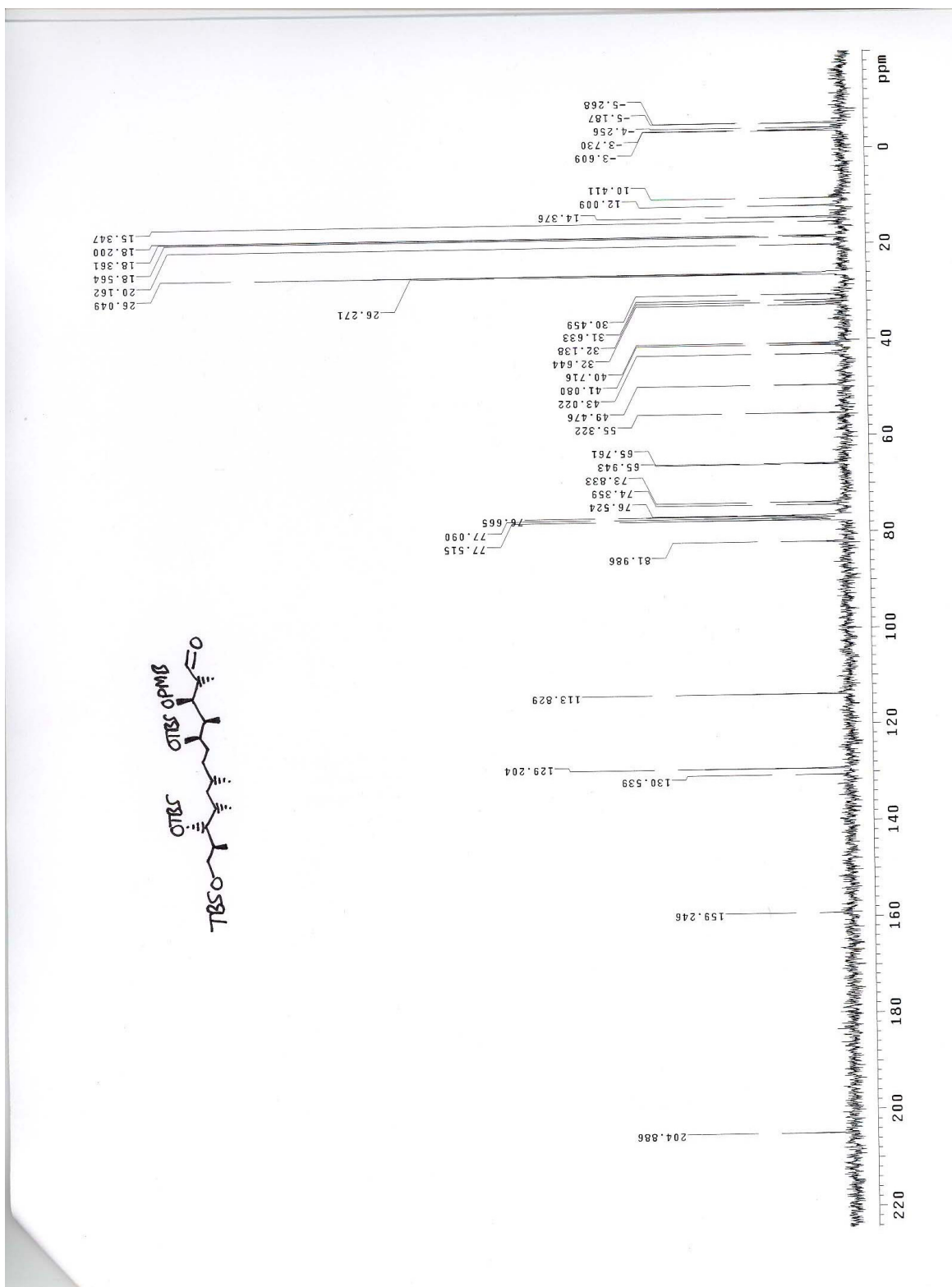




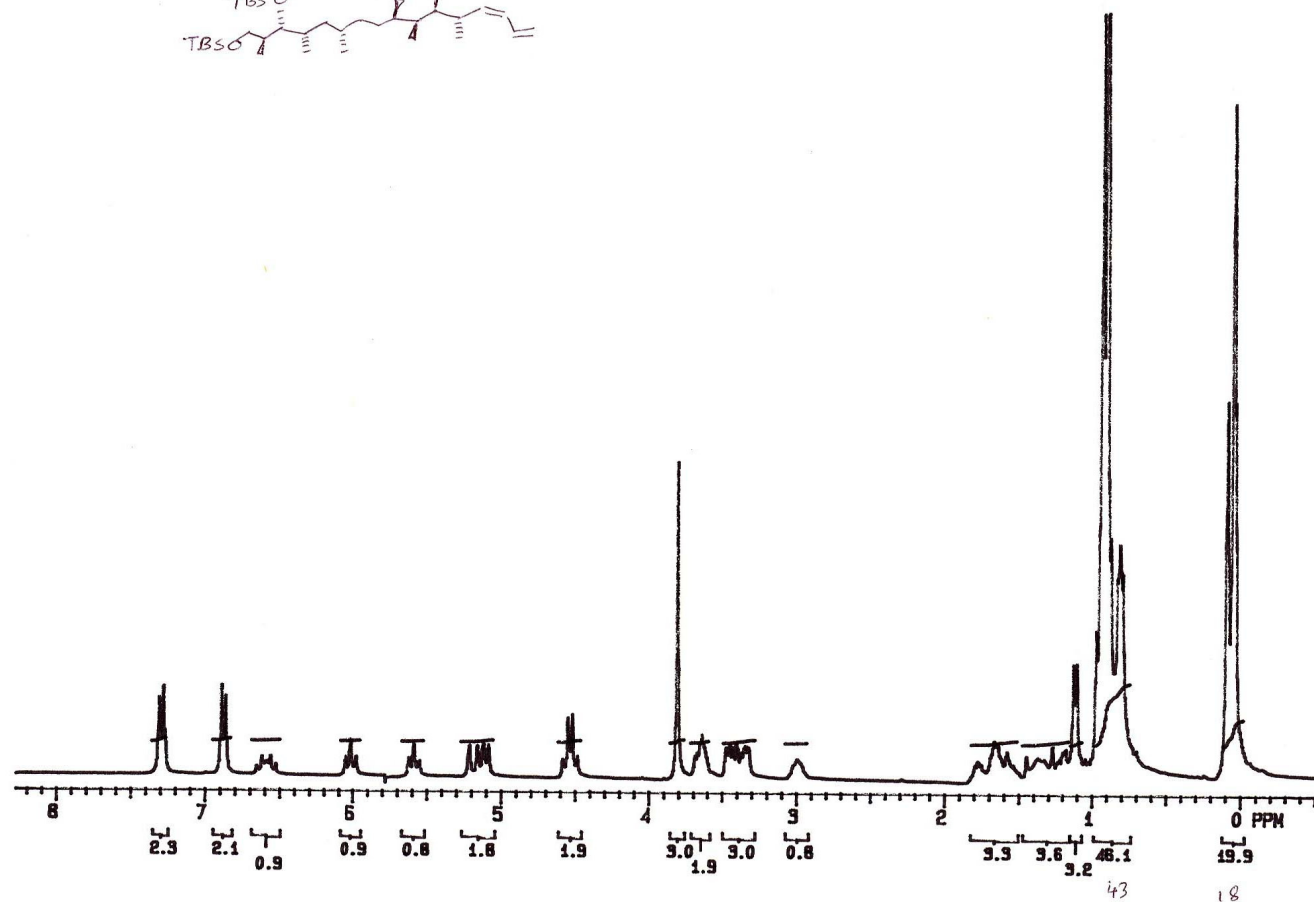
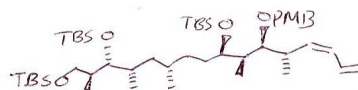








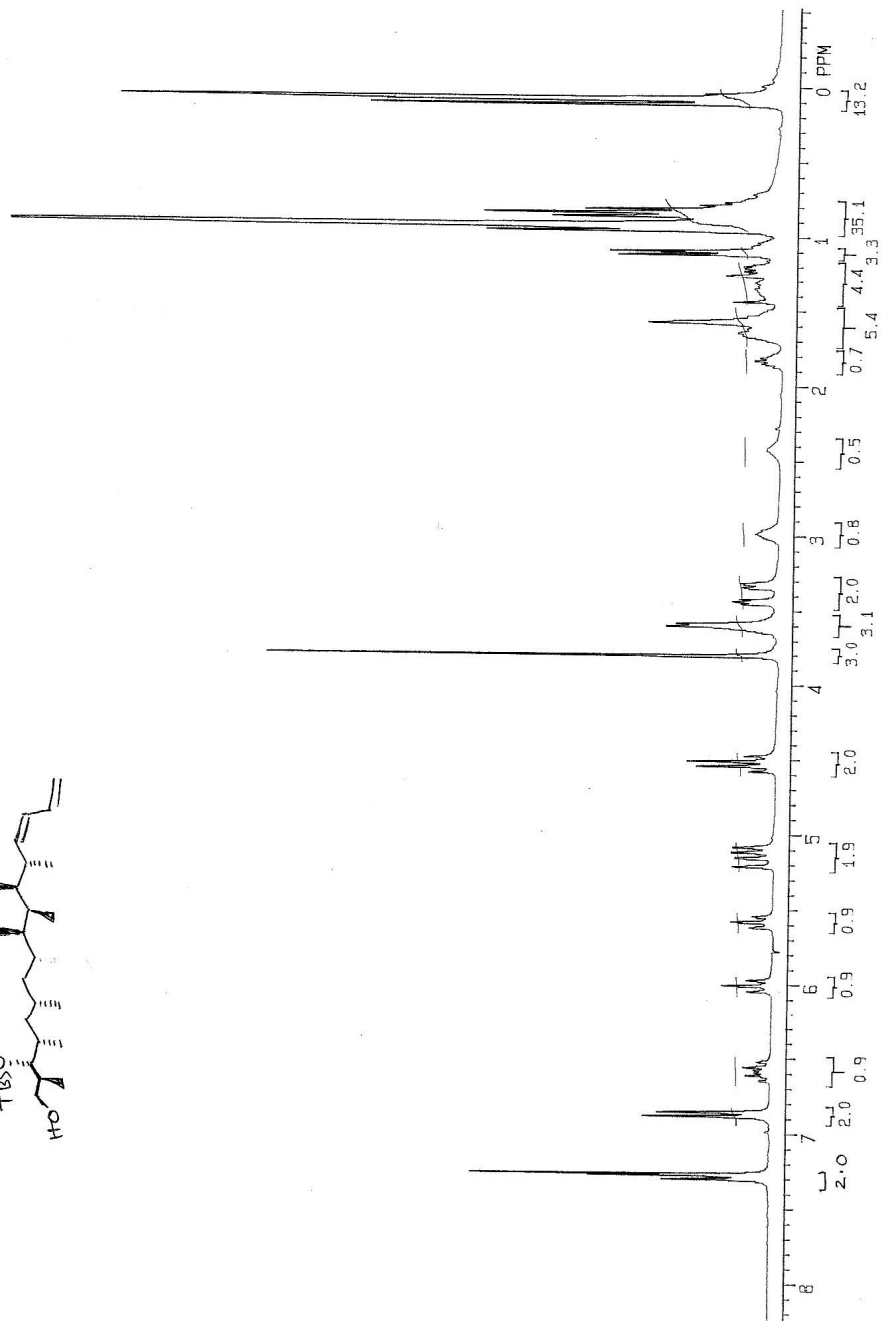
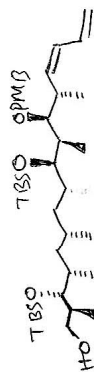
DH-VII/66

300 MHz  $^1\text{H}$  NMR of compound **21** in  $\text{CDCl}_3$

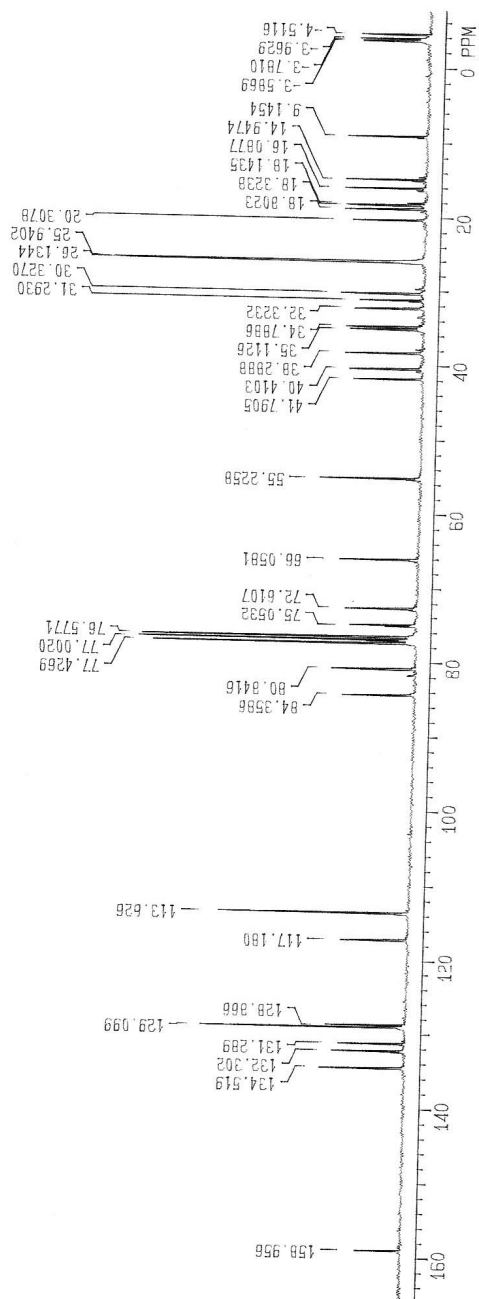
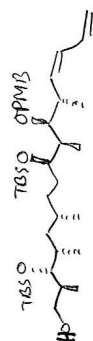


75 MHz  $^{13}\text{C}$  NMR of compound **21** in  $\text{CDCl}_3$

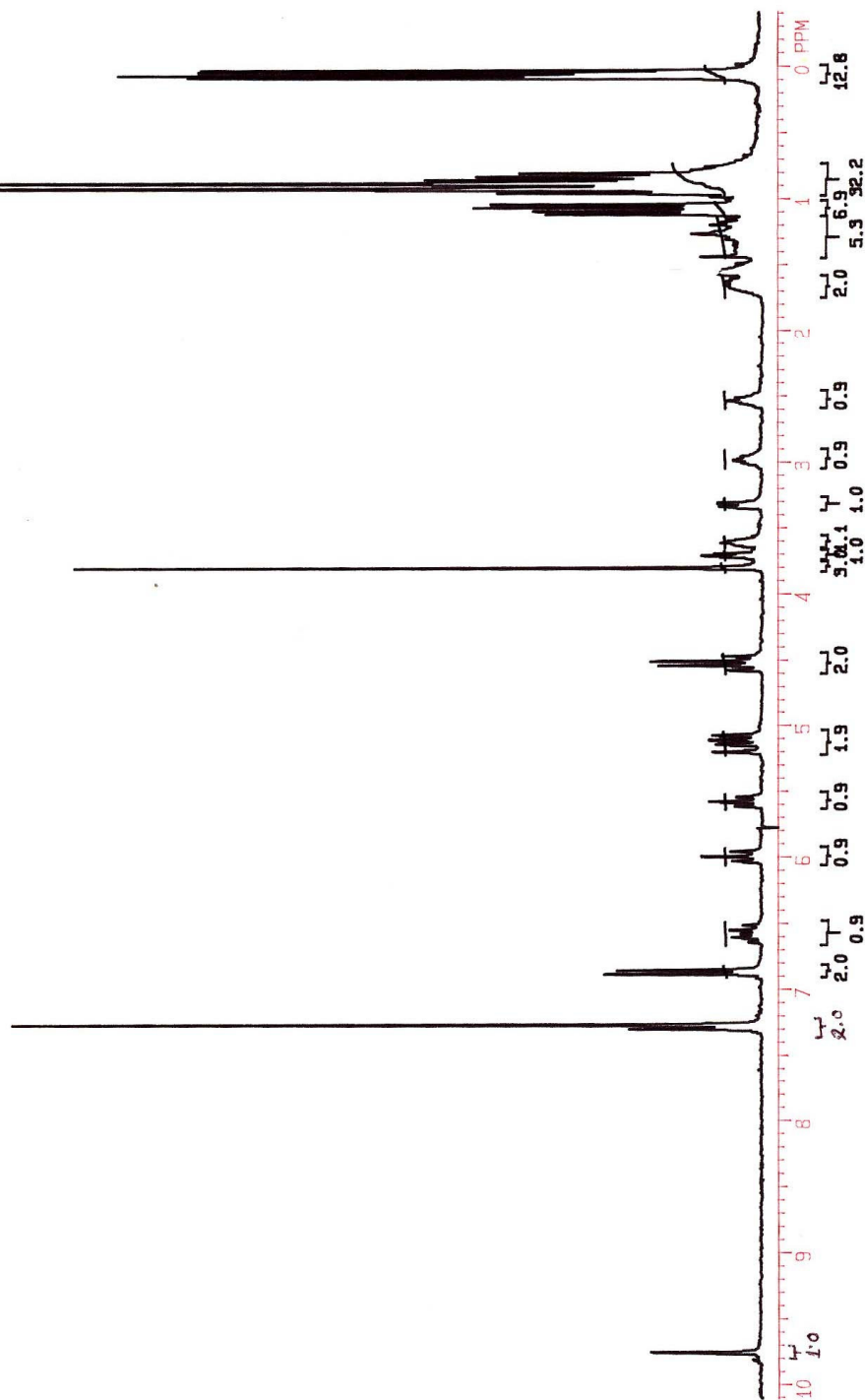
DM-571/68



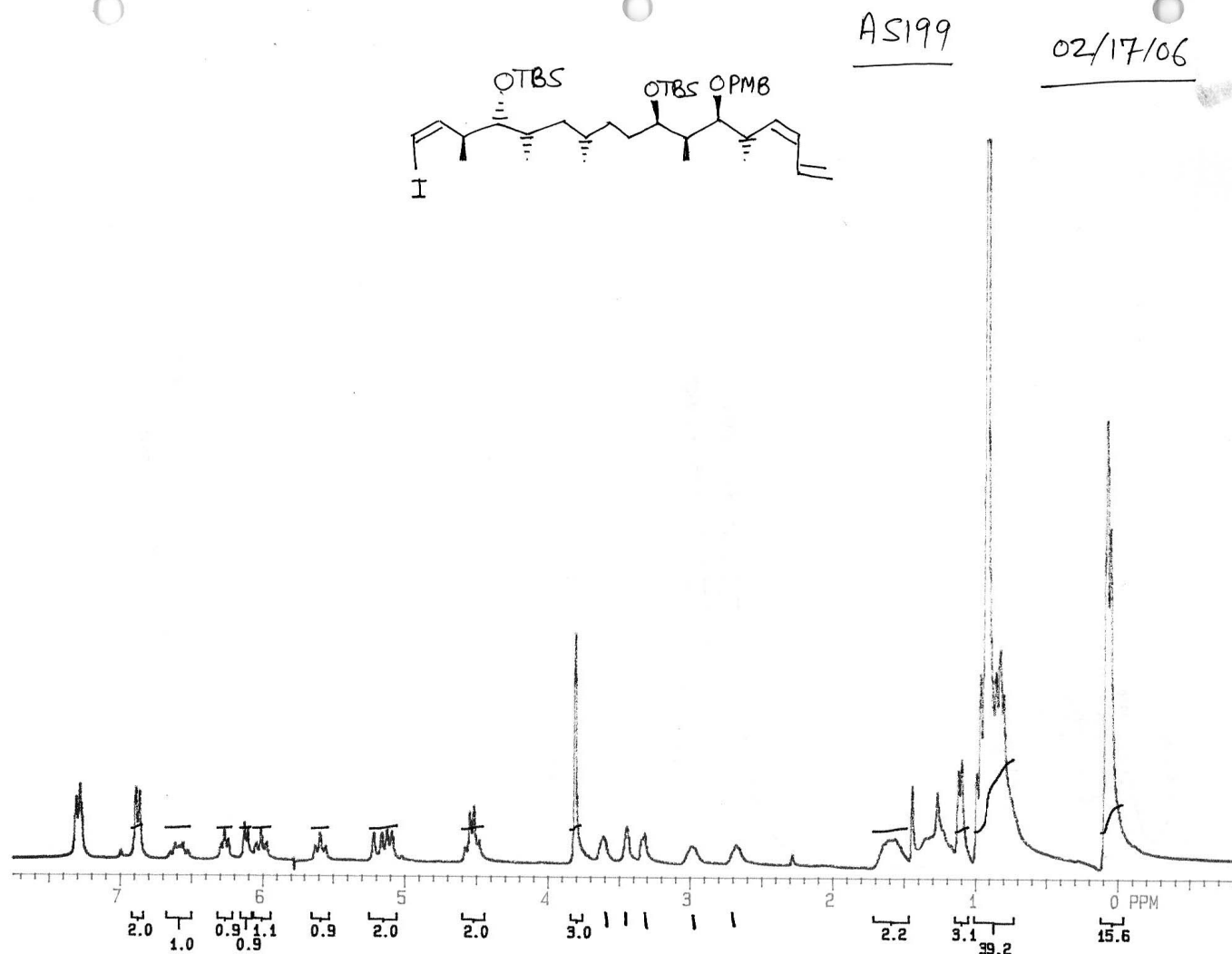
891 (V)-H-13C

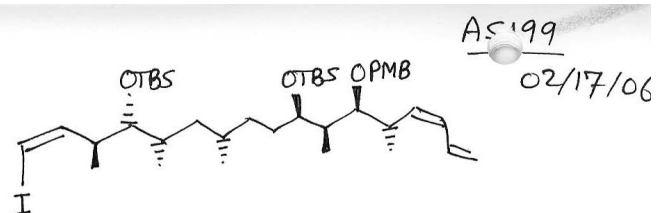
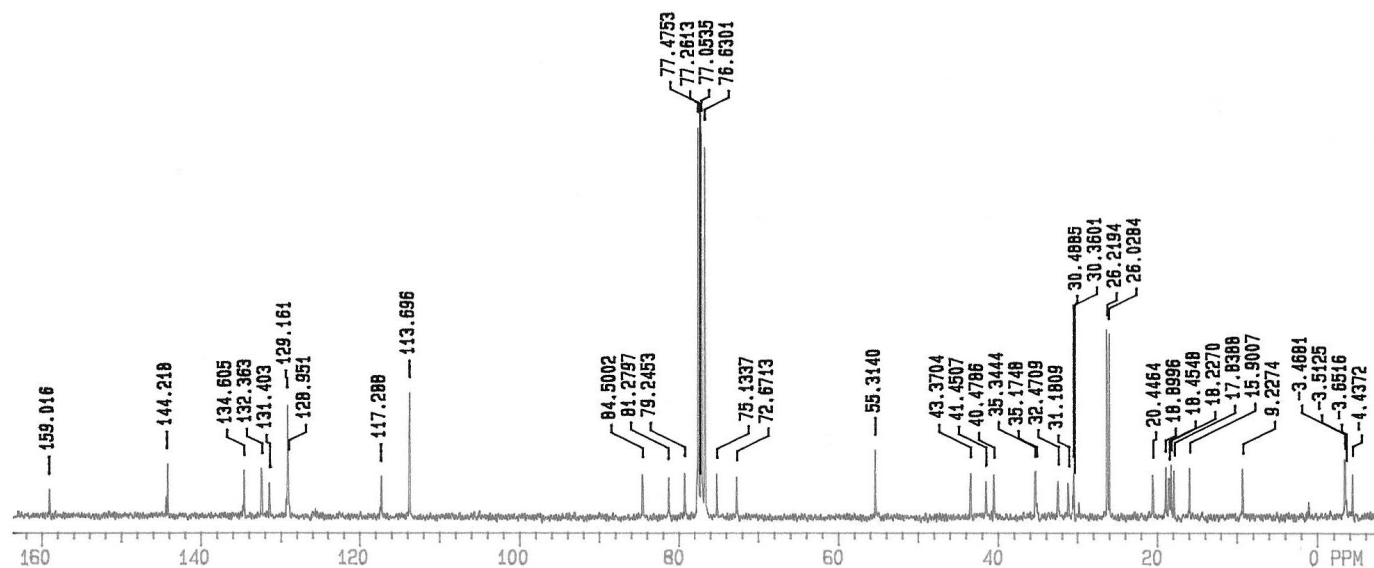


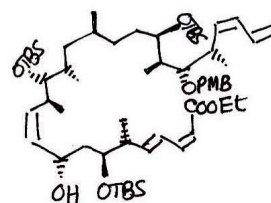
DH-VII/69



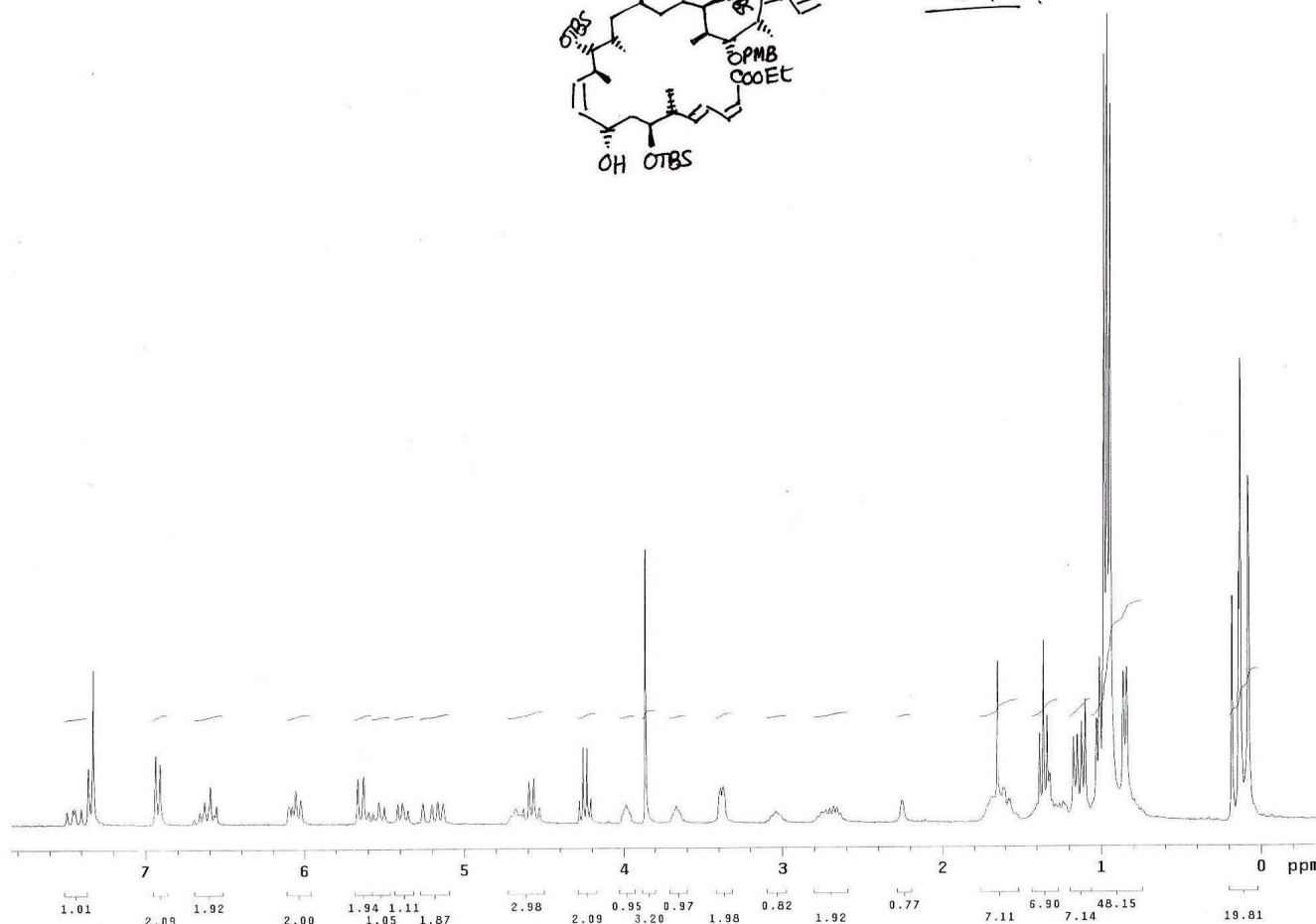


300 MHz  $^1\text{H}$  NMR of compound **22** in  $\text{CDCl}_3$

75 MHz  $^{13}\text{C}$  NMR of compound **22** in  $\text{CDCl}_3$

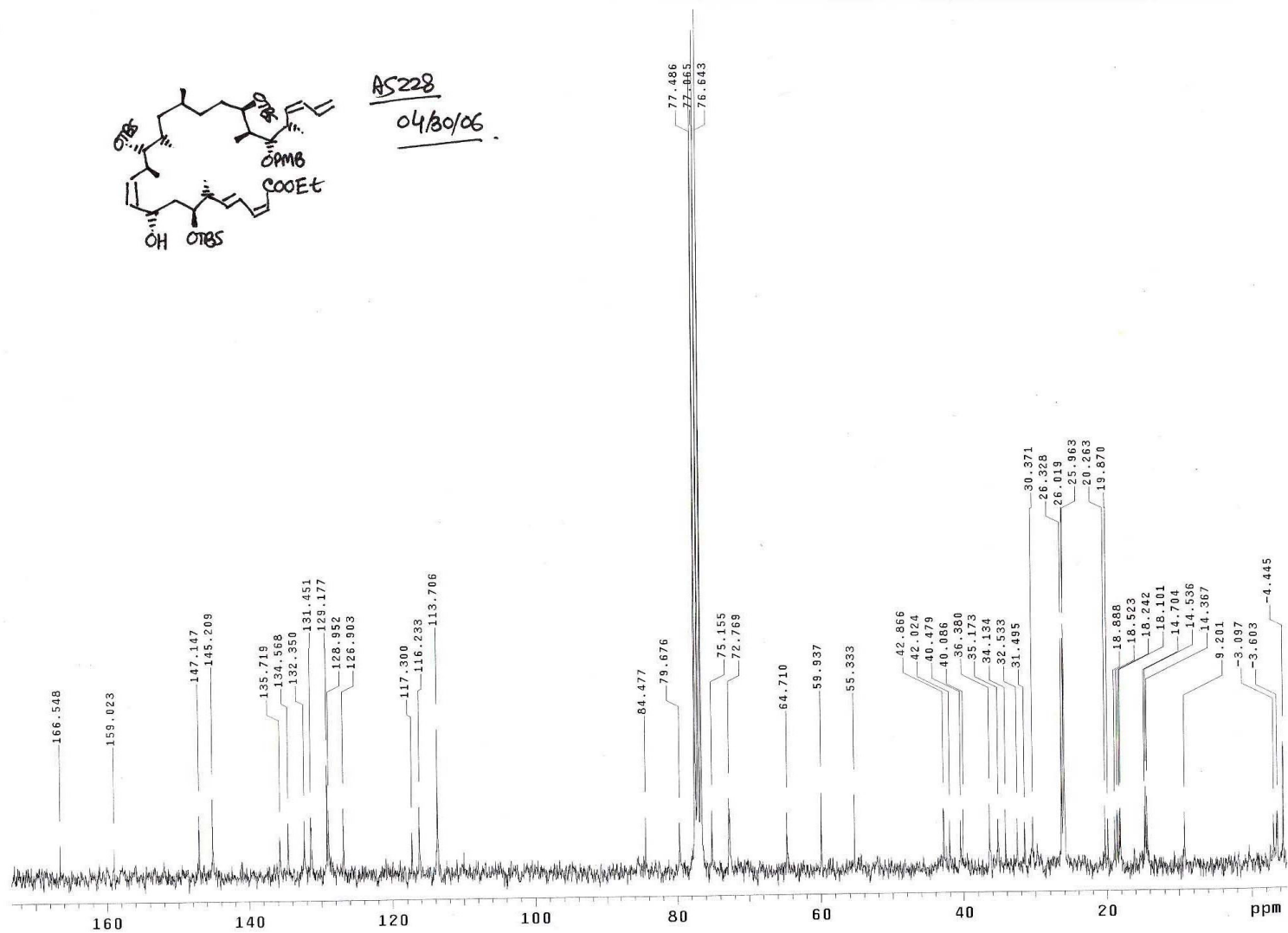


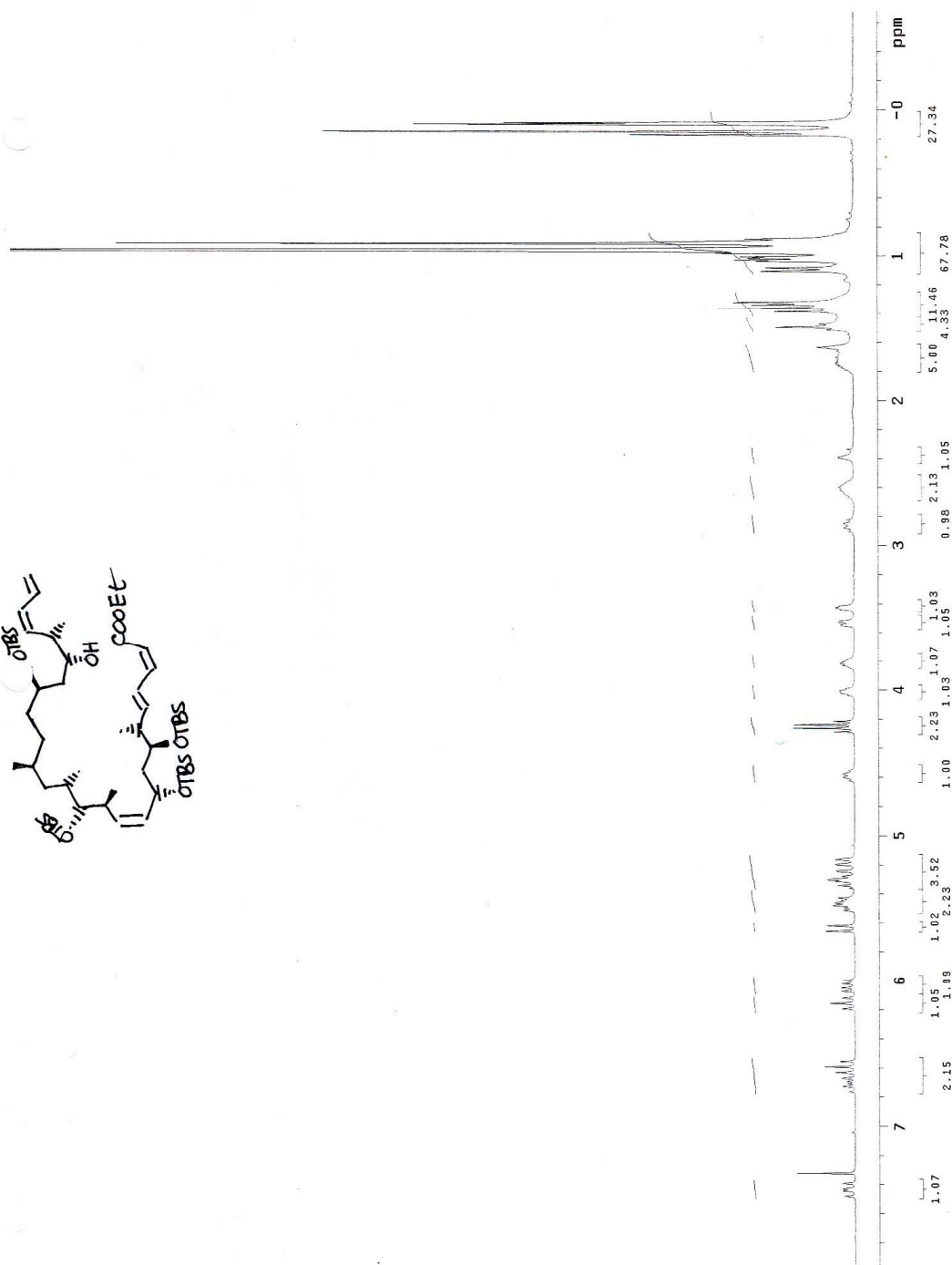
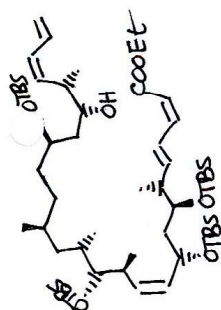
AS228  
04/30/06

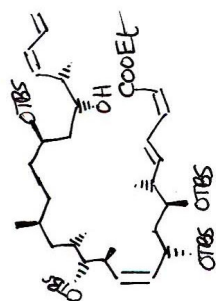
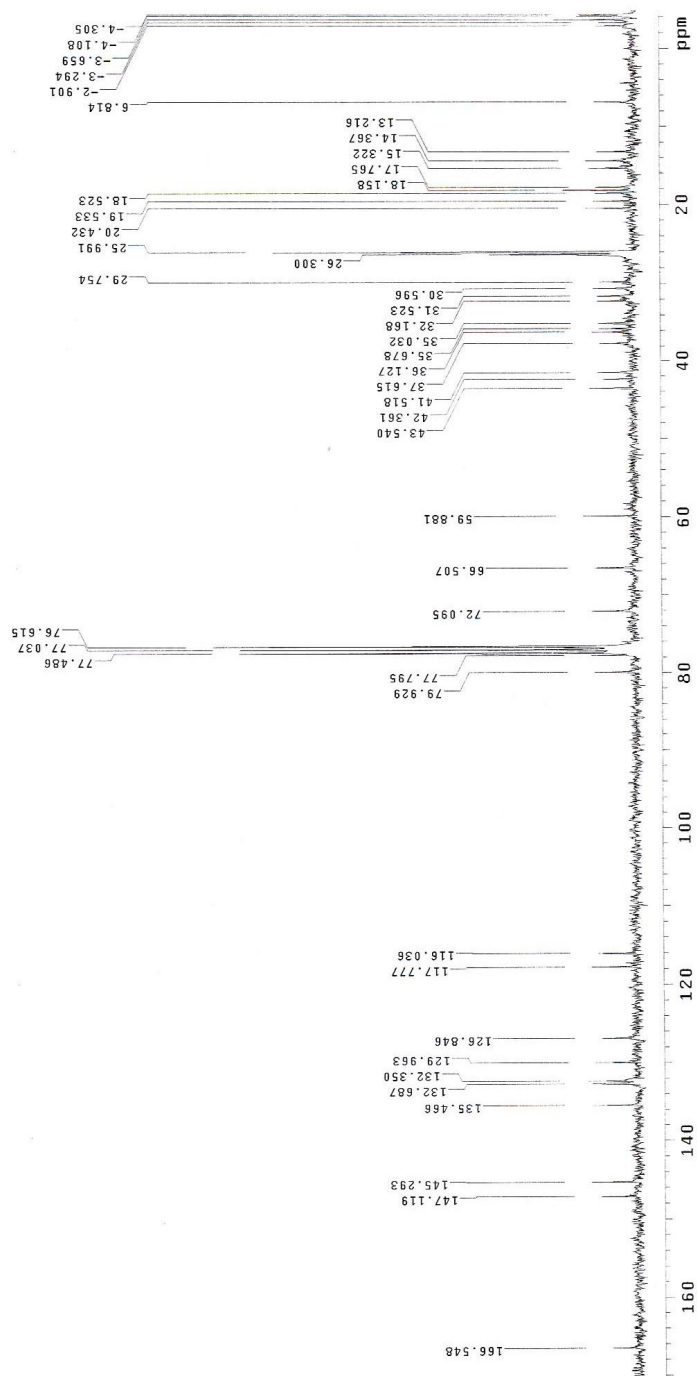


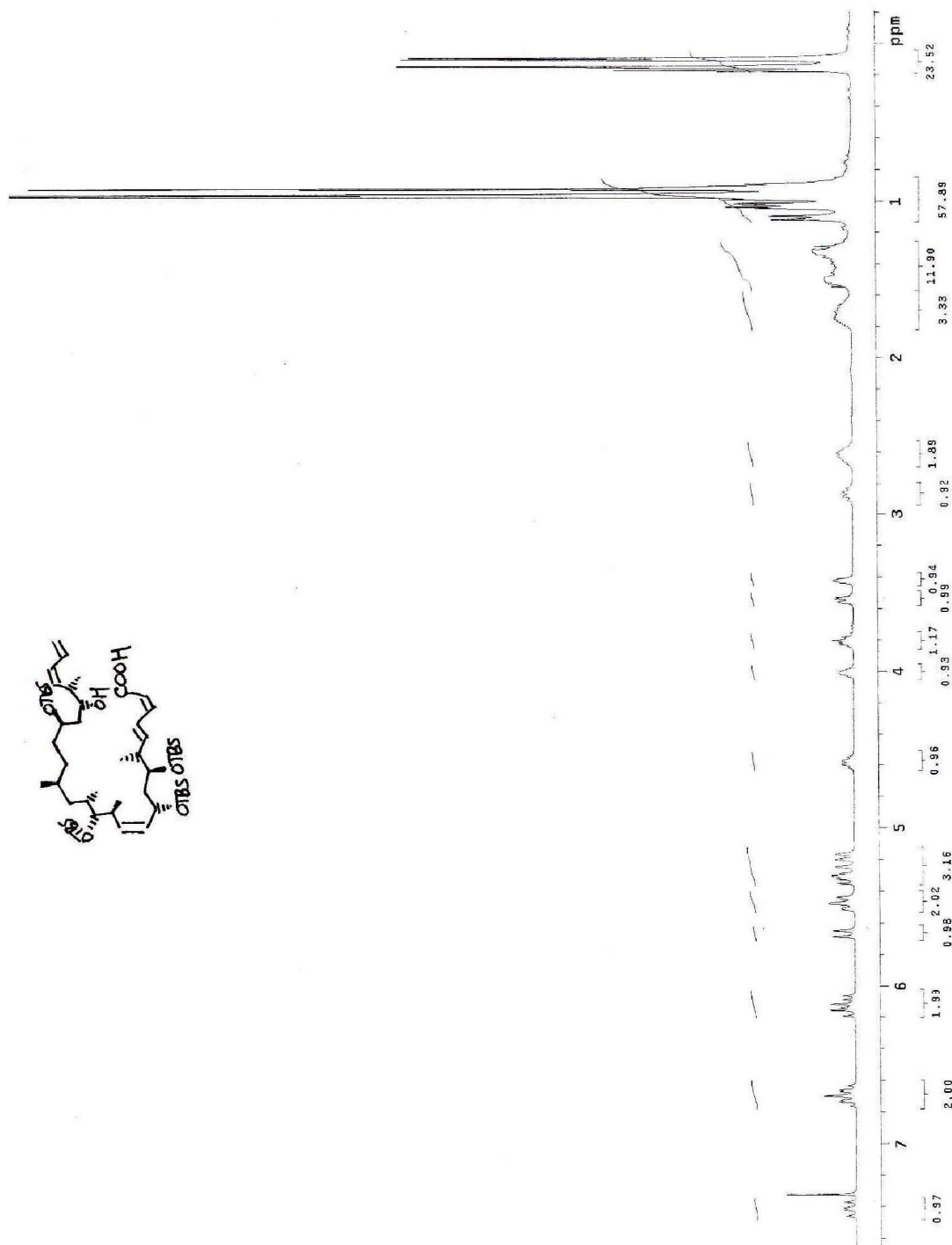
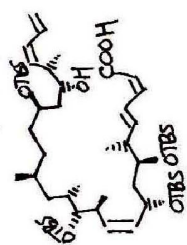
300 MHz <sup>1</sup>H NMR of compound **23** in CDCl<sub>3</sub>

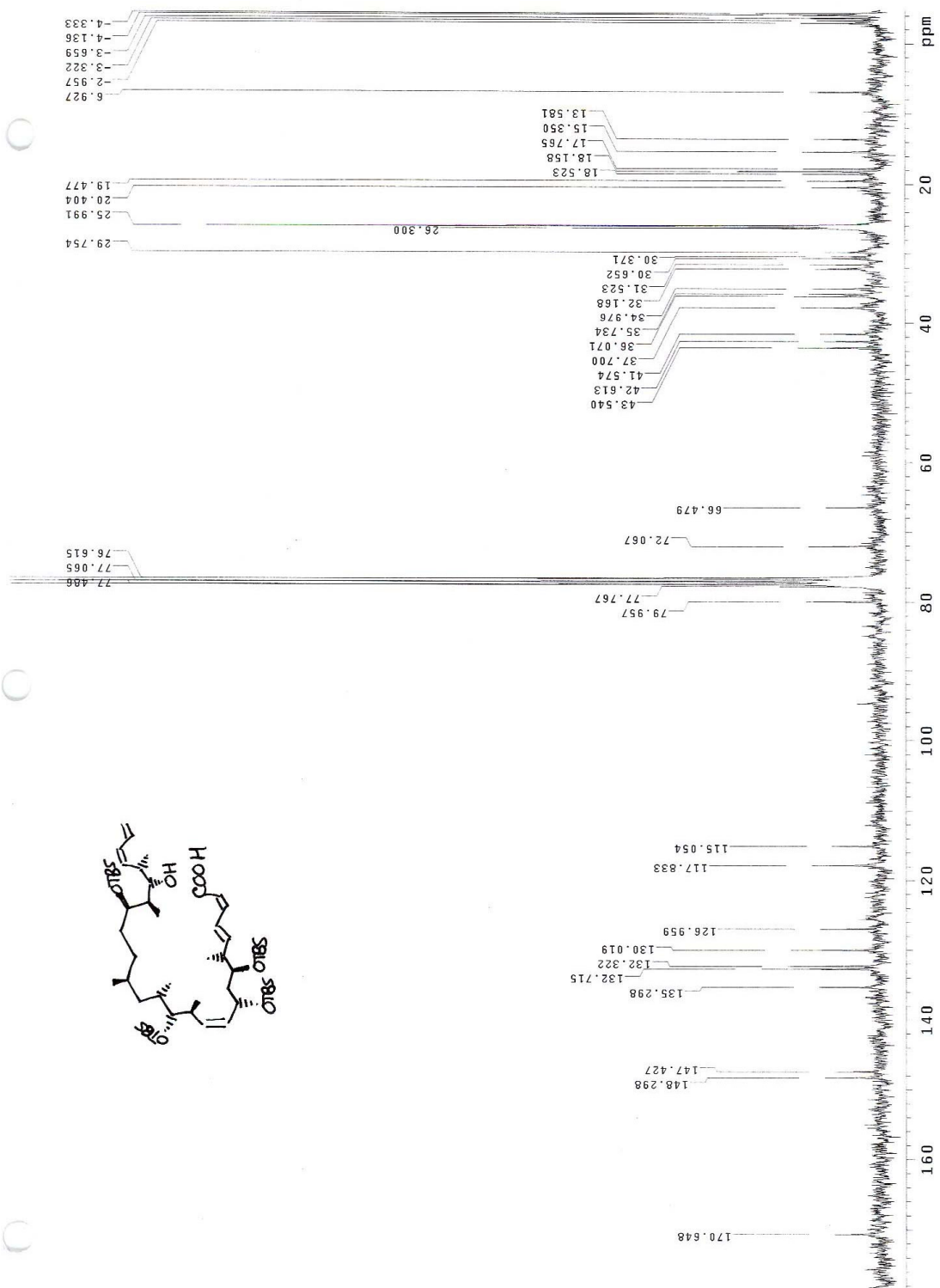


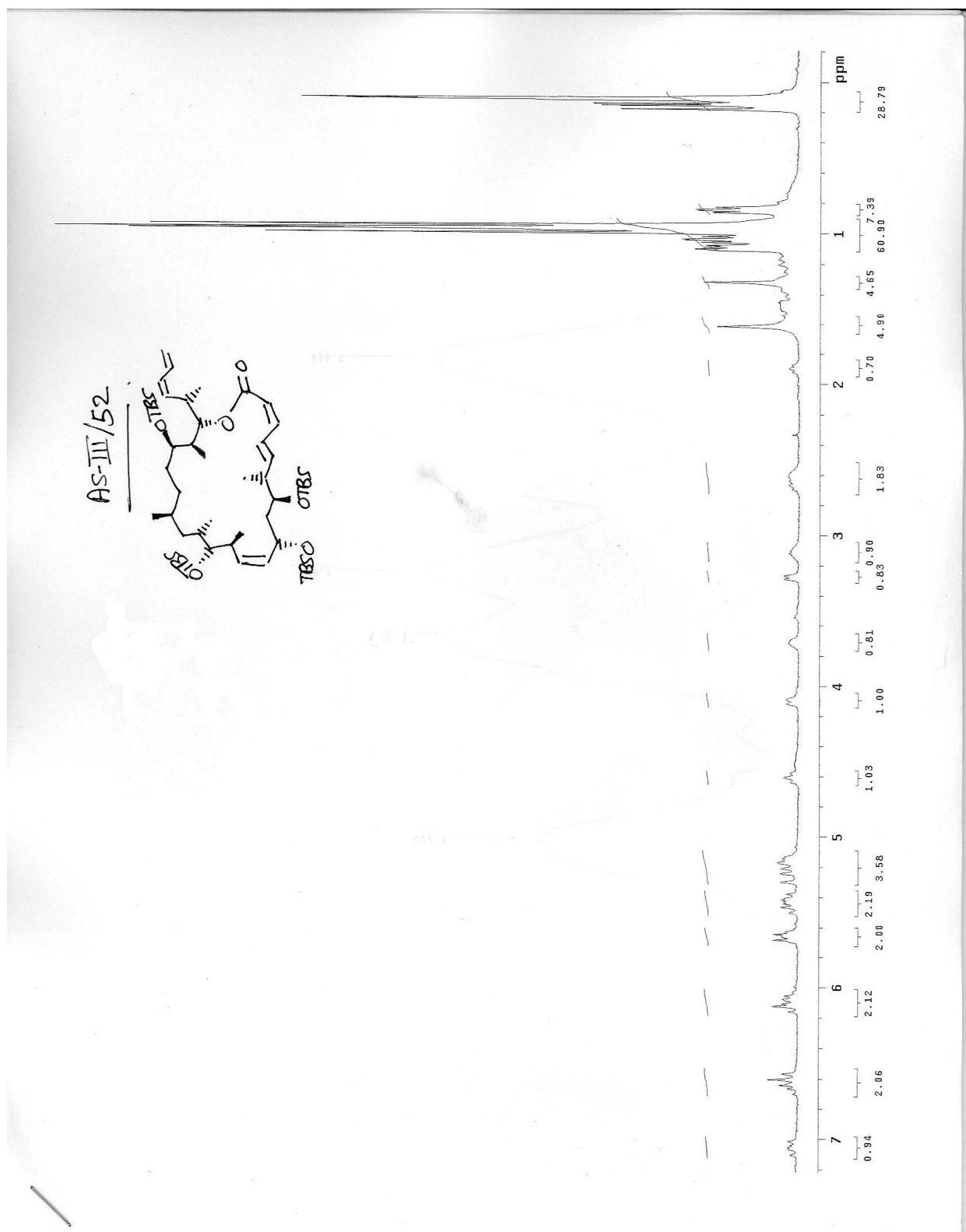
75 MHz <sup>13</sup>C NMR of compound **23** in CDCl<sub>3</sub>

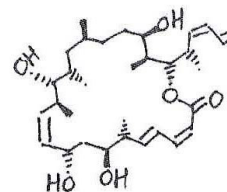




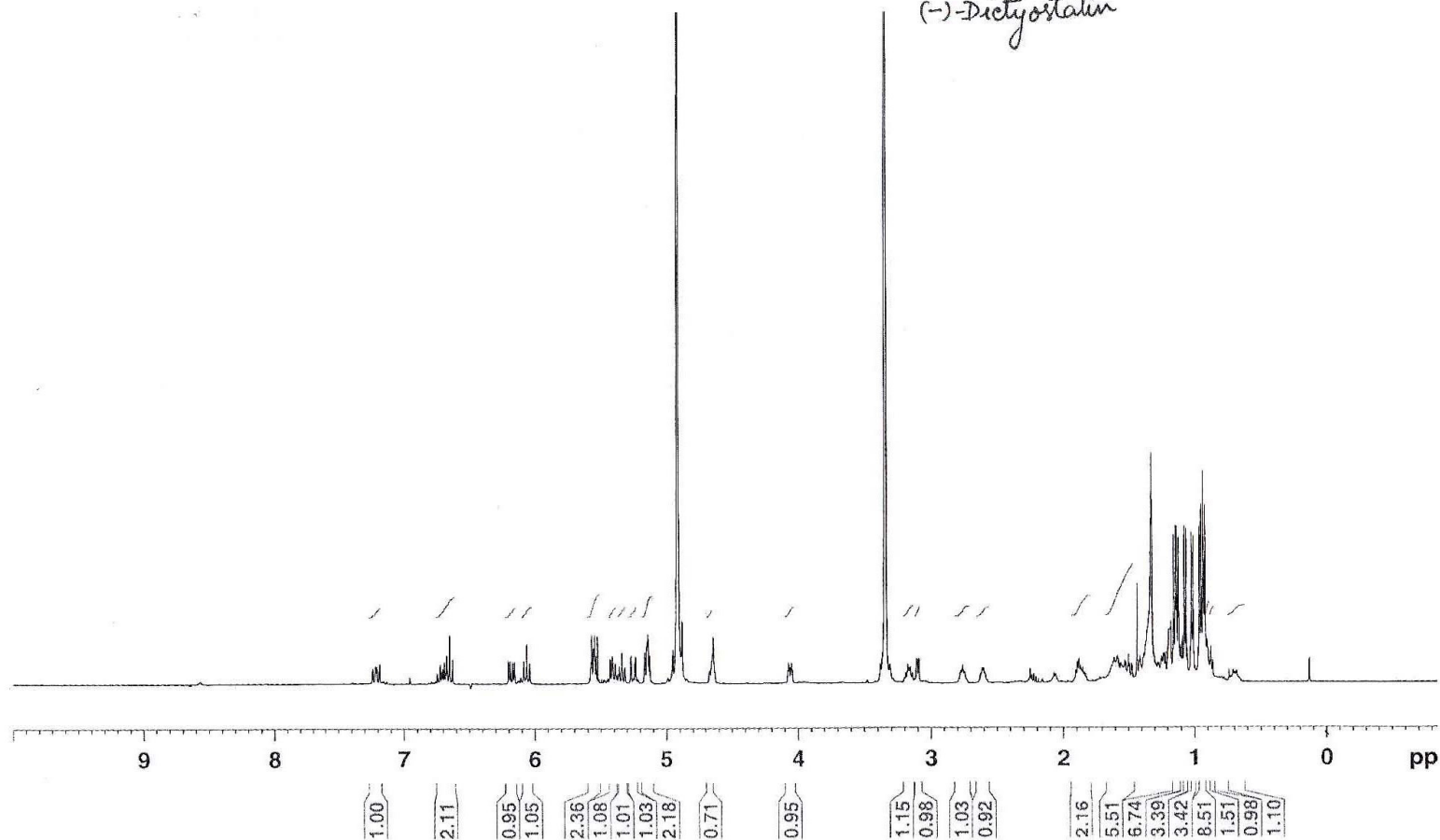




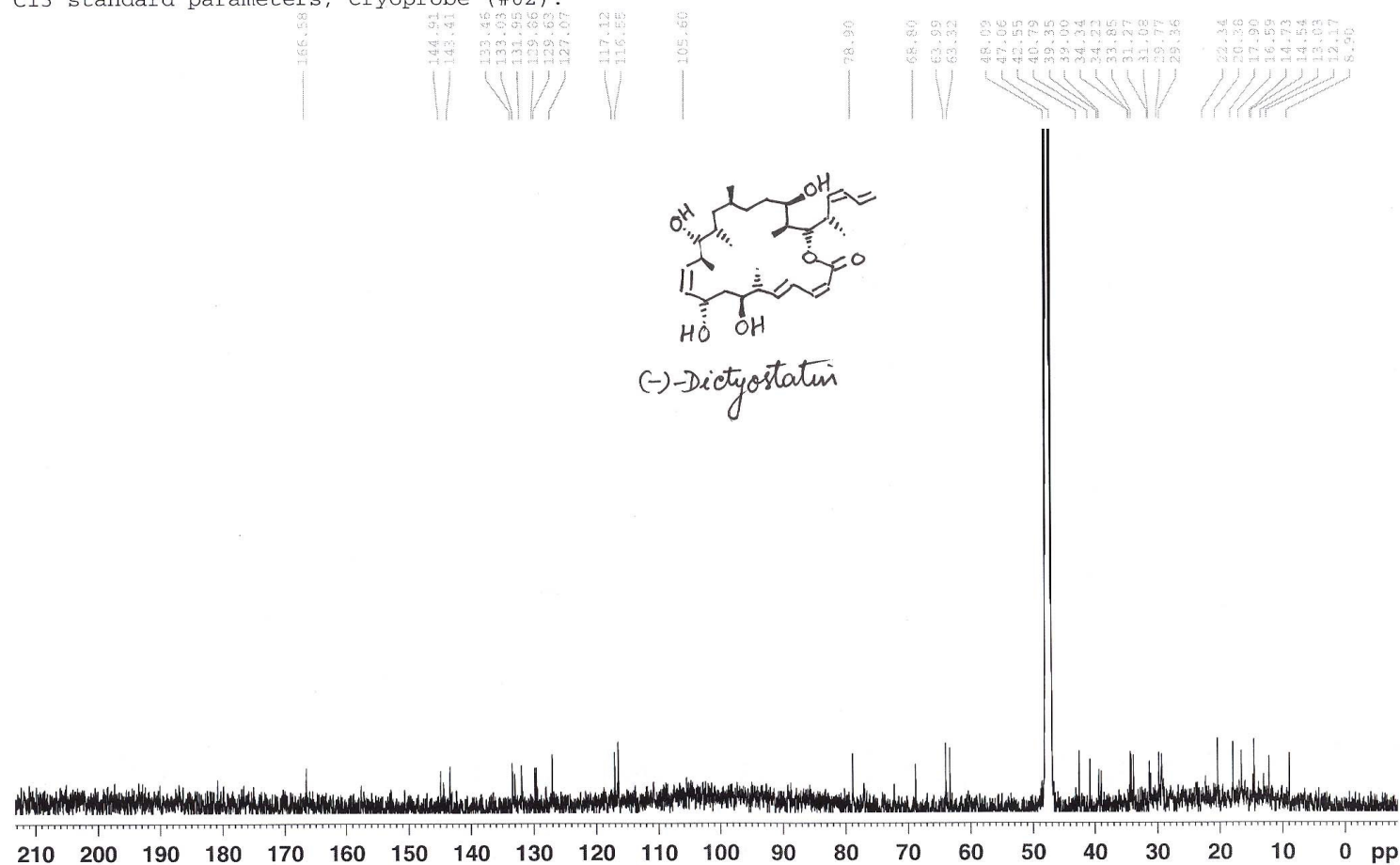




(-)-Dictyostatin

500 MHz <sup>1</sup>H NMR of compound **1** in CD<sub>3</sub>OD

C13 standard parameters, cryoprobe (#02).



125 MHz  $^{13}\text{C}$  NMR of compound **1** in  $\text{CD}_3\text{OD}$