

Supporting information for

**Stereocontrolled access to isoprostanes via a bicyclo[3.3.0]octene framework**

Camille Oger, Yasmin Brinkmann, Samira Bouazzaoui, Thierry Durand, Jean-Marie Galano\*

*Institut des Biomolécules Max Mousseron, IBMM, UMR CNRS 5247, Université Montpellier I,  
Université Montpellier II, Faculté de Pharmacie, 15. Av. Ch. Flahault, F-34093 Montpellier  
cedex 05, France*

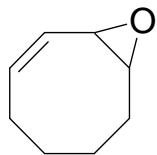
Jgalano@univ-montp1.fr

- Preparative procedures and characterisation data for **4,6-8, 10-21**, and **1** and *epi-1*.
- Copies of  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **4, 6-8, 11-21** and **1** and *epi-1*.

### **General Details**

All reactions requiring anhydrous conditions were conducted in oven-dried glassware with magnetic stirring under an atmosphere of nitrogen, unless mentioned otherwise. Syringes and needles for the transfer of reagents were dried at 120 °C and allowed to cool in a desiccators over  $\text{P}_2\text{O}_5$  before use. THF and  $\text{Et}_2\text{O}$  were distilled from benzophenone ketyl;  $\text{CH}_2\text{Cl}_2$  from  $\text{CaH}_2$ . Other solvents and reagents were used as obtained from supplier, unless otherwise noted.

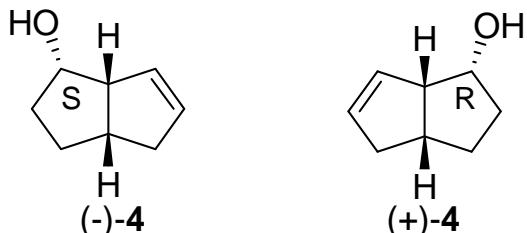
Air was dried by passing through  $\text{CaCl}_2$ . Reactions were monitored by TLC, using plates pre-coated Silica Gel 60 (Merck). Visualization of reaction components was achieved with 254 nm, and treatment with acidic *p*-anisaldehyde stain, followed by gentle heating. Organic layers were dried using  $\text{MgSO}_4$  unless otherwise stated. Column chromatography was carried out on Kieselgel 60 (40–63 µm). Petroleum ether refers to the fraction of petroleum boiling between 30 °C and 40 °C. Infrared spectra were obtained using a Perkin-Elmer Spectrum One spectrophotometer. They were reported as wavenumber ( $\text{cm}^{-1}$ ) of significant peaks. Electrospray mass spectra (MS) were obtained by ionisation methods using a Finnegan LQC advantage spectrometer. Melting points were recorded on a Stuart SMP3 block, and are uncorrected. Unless otherwise stated,  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded at 303K with a Bruker AMX 300 spectrometer or at 305K with a Bruker AV400 spectrometer, in  $\text{CDCl}_3$ : the peak due to residual  $\text{CDCl}_3$  was used as the internal reference (fixed at 7.24 ppm). The  $^1\text{H}$  NMR spectra are reported as follows: chemical shift in parts per million (multiplicity, coupling constant(s)  $J$  (Hz), relative integral, assignment) where multiplicity is defined as: br = broad, m = multiplet, AB = AB doublet, s = singlet, d = doublet, t = triplet, or combination thereof. Selected  $^{13}\text{C}$  NMR spectra were conducted using a  $J$  modulated sequence and the central peak of the  $\text{CDCl}_3$  triplet was used as an internal reference (77.00 ppm). The assignments of NMR spectra were assisted by homonuclear ( $^1\text{H}-^1\text{H}$ ) and heteronuclear ( $^1\text{H}-^{13}\text{C}$ ) correlation spectroscopy (COSY45, HMQC, HMBC).



### 3,4-Epoxycyclooctene

Peracetic acid (40% in acetic acid; 100 mL, 0.61 mol, 1.33 equiv) was added dropwise to a mechanically stirred solution of cycloocta-1,3-diene **9** (57 mL, 0.46 mol, 1.0 equiv) and Na<sub>2</sub>CO<sub>3</sub> (200 g, 1.88 mol, 4.08 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (750 mL) at 0 °C. The reaction mixture was slowly allowed to warm up to room temperature over a period of 2 h, and then filtered and washed with CH<sub>2</sub>Cl<sub>2</sub> (2 × 150 mL). The organic phase was washed with saturated aq. NaHCO<sub>3</sub> until neutral pH, the layers were separated and the aqueous one extracted with CH<sub>2</sub>Cl<sub>2</sub> (100 mL). The organic extracts were then washed with brine (100 mL), dried and evaporated to give the corresponding monoepoxide as a yellow oil (56.7 g, 92%) which was used in the next step without further purification; *R*<sub>f</sub>(50% Et<sub>2</sub>O : petroleum ether) 0.60; δ<sub>H</sub>(300 MHz, CDCl<sub>3</sub>): 5.81-5.75 (m, 1H), 5.59 (d, *J*=11.2 Hz, 1H), 3.50-3.40 (br dd, 1H), 3.13-3.08 (m, 1H), 2.37-2.26 (m, 1H), 2.11-1.95 (m, 2H), 1.85-1.57 (m, 3H), 1.49-1.34 (m, 2H).

### Bicyclo[3.3.0]oct-7-en-endo-2-ol (*S*)-4 and (*R*)-4



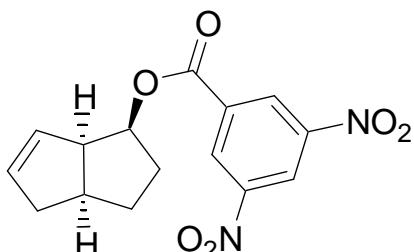
To a 2-litre 3 neck round bottom flask equipped with an electronic thermometer and a condenser; *n*BuLi (10 M in hexanes, 100 mL, 1.00 mol) was slowly added, with a canula; to a solution of *N,N*-diethylamine (104.7 mL, 1.00 mol) in anhydrous Et<sub>2</sub>O (650 mL) at 0 °C. After addition the reaction is left to stir for 1 h at 0 °C, then an external heater solution (water bath is generally used) is step up at 30 °C and the condenser equipped with a CaCl<sub>2</sub> moisture trap only. At this temperature, previously synthesized 3,4-epoxycyclooctene (56.7 g, ~0.46 mmol) dissolved in Et<sub>2</sub>O (100 mL) was added dropwise at a rate that a small exotherm is kept constant. (**Attention:** the CH-insertion reaction takes place almost immediately at this temperature. After a few mls of dropping addition, the external bath can be removed and temperature is kept at around 30 °C by its own exothermicity. Adding the epoxide at room temperature, then heat up to 30 °C caused extremely fast reaction and build-up of high risk of over-pressure). After addition, the reaction is allowed to reach room temperature, and then cooled to 0 °C. Aqueous HCl (~500 mL, 5 M) was added with vigorous

stirring until an acidic pH was reached (first 100 mL are exothermic). The aqueous and organic layers were separated. The aqueous layer was extracted with Et<sub>2</sub>O (2 x 200 mL) and the combined organic phases were washed with saturated NaHCO<sub>3</sub> (200 mL), brine (100 mL), dried and concentrated to leave a residue which is distilled (20 mmHg, ~82 °C) to yield approx. (42 g, 72 %, 2 steps) of bicyclo[3.3.0]oct-7-en-endo-2-ol (**4**): *R*<sub>f</sub> (50% Et<sub>2</sub>O/petroleum ether) 0.29;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3351, 2941, 2866, 2845, 1618, 1447, 1363, 1333, 1299, 1212, 1172, 1084, 1063, 1111;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>): 5.87-5.82 (m, 1H), 5.61-5.57 (m, 1H), 4.19 (q, *J*=5.4 Hz, 1H), 3.27-3.19 (m, 1H), 2.73-2.57 (m, 2H), 2.12-1.99 (m, 1H), 1.86-1.75 (m, 1H), 1.71-1.52 (m, 2H), 1.42-1.32 (m, 2H),  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>): 134.4, 127.6, 74.7, 55.9, 41.5, 39.6, 34.9, 31.0; HRMS (ESI) calculated for C<sub>8</sub>H<sub>13</sub>O [M+H]<sup>+</sup> 125.0984, found 125.0966.

### Enzymatic Resolution:

To a solution of the racemic alcohol **4** (20 g, 16.14 mmol, 1.0 equiv) in 325 mL of Et<sub>2</sub>O were successively added succinic anhydride (16.17 g, 16.16 mmol, 1.0 equiv) and the *Amano AK* lipase (1.01g). The suspension was stirred with the rotavapor for 15 h. After 50% conversion, the suspension was filtered and washed with Et<sub>2</sub>O. The filtrate was extracted with a 2 M solution of Na<sub>2</sub>CO<sub>3</sub> (2 x 100 mL) and the layers separated. The aqueous layer (containing compound **10**) was extracted with Et<sub>2</sub>O (3 x 150 mL) and the combined organic layers were washed with a 10% solution of NaCl/Na<sub>2</sub>CO<sub>3</sub> 1/1 (150 mL), dried, filtered and the solvent removed under reduced pressure. The (*S*)-**4** alcohol was obtained as a yellow oil (9.60 g, 48%, ee > 98%);  $[\alpha]_D^{20} = -136$  (c 1.02 10<sup>-2</sup>, CHCl<sub>3</sub>). NaOH pellets were added to the aqueous layer (containing compound **10**) at 10 °C until basic pH and stirred for 1 h. Et<sub>2</sub>O (200 mL) was added, and the layers were separated and the aqueous one extracted three times with Et<sub>2</sub>O (150 mL). The combined organic layers were dried, filtered and the solvent removed under reduced pressure. The (*R*)-**4** alcohol was obtained as a yellow oil (9.46 g, 47%, ee > 98 %);  $[\alpha]_D^{20} = +144$  (c 1.02 10<sup>-2</sup>, CHCl<sub>3</sub>)

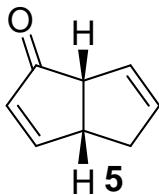
### Dinitroderivative synthesis:



To a solution of the alcohol **4** (201 mg, 1.62 mmol, 1.0 equiv) in 5 mL of anhydrous pyridine at 0 °C, was added the 3,5-dinitrobenzoyl chloride (1.0 g, 4.34 mmol, 2.7 equiv). After 1 h at 0 °C, the

reaction was warmed to rt during the night. Et<sub>2</sub>O (20 mL) was added and the layers separated. The aqueous layer was extracted with Et<sub>2</sub>O (3 x 10 mL). The combined organic layers were washed with a HCl solution (1 M, 3 x 10 mL), a solution of saturated NaHCO<sub>3</sub> (3 x 10 mL), 10 mL of brine, then dried and the solvents removed under reduced pressure. The dinitroderivatives was obtained as a white powder (360 mg, 70%),  $\nu_{\text{max}}$  cm<sup>-1</sup> 3085, 2951, 1717, 1629, 1540, 1460, 1288, 1172, 1080, 1007;  $\delta_{\text{H}}$ (300 MHz) 9.21 (t,  $J=2.1$  Hz, 1H), 9.11 (d,  $J=2.1$  Hz, 2H), 5.86-5.77 (m, 1H), 5.52-5.40 (m, 2H), 3.55 (m, 1H), 2.95-2.65 (m, 2H), 2.25-2.10 (td,  $J=16.8$  and 2.8 Hz, 1H), 2.10-1.80 (m, 3H), 1.64-1.54 (m, 1H); HPLC analysis of dinitroderivative for ee determination: (HPLC Perkin Helmer serie 200, Chiral column Chiralcel OD 0.46 cm x 25 cm, Diode Array Detector ( $\lambda=254$  nm)). Flow: 0.7 mL/min; derivative from (S)-(-)-4: tr= 29.2 min, derivative from (R)-(+)4: tr= 26.8 min.

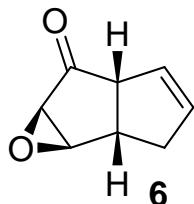
## 5



To a 2-neck round bottomed flask (500 mL) equipped with a mechanic stirrer and a DrySyn® heating block, alcohol (-)-4 (8.0 g, 64.5 mmol) was added followed by DMSO (80 mL, A.C.S. reagent) and IBX in three portions (53.8 g, 0.194 mol). The digital probe of the DrySyn® heating block was set-up at 90 °C, and the flask covered with aluminum foil. The reaction was allowed to proceed for 14 h and a pale brown solution resulted. The resulting mixture was filtered and the resulting white cake was rinsed DMSO (60 mL) until the filtrate remains colorless (note: the white cake, approx. 35 g, was recycled into IBX by oxone oxydation). To the filtrate was added a cold solution of saturated NaCl (200 mL), and Et<sub>2</sub>O (200 mL) and the mixture mechanically stirred for 15 min. The layers were then separated, and the aqueous extracted with Et<sub>2</sub>O (3 x 100 mL). The combined organic layers were filtered, and then a 10% solution of NaHCO<sub>3</sub> (100 mL) and a 10% solution of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (100 mL) were added to the combined organic layers. After 1 h, the layers were separated and the aqueous layer extracted with Et<sub>2</sub>O (2 x 100 mL). The combined organic layers were dried, filtered, and concentrated to give an oily residue (5.6 g). <sup>1</sup>H NMR revealed the complete conversion into enone (-)-(5) with up to 5 to 10 % of ketone [ $R_f$  (50% Et<sub>2</sub>O/petroleum ether) 0.51] resulting from an incomplete oxidation. No chromatographic purification was required at this stage for the next reaction. For characterization and yield determination, purification by column chromatography on silica with petroleum ether-Et<sub>2</sub>O (8-2) as eluents gave (-)-5 (5.3 g, 65%);  $[\alpha]_D^{23} = -564$  (c. 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>);  $R_f$  (50% Et<sub>2</sub>O/petroleum ether) 0.37,  $\nu_{\text{max}}$  cm<sup>-1</sup> 3059, 2918, 2853, 1696, 1583, 1178, 694;  $\delta_{\text{H}}$ (300 MHz)  $\delta=7.49$  (dd,  $J=5.6$  and 2.6 Hz, 1H), 6.01 (dd,  $J=5.6$  and 1.8 Hz, 1H), 5.67-5.62 (m, 2H), 3.56-3.53 (m, 1H), 3.44-3.41 (m, 1H), 2.66 (br ddd,  $J=17.4$ , 11.1 and 2.4 Hz,

1H), 2.2- (dm,  $J=17.0$  Hz, 1H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>) : 209.5, 166.5, 131.5, 130.8, 128.3, 58.0, 43.5, 35.4; HRMS (ESI) calculated for C<sub>8</sub>H<sub>9</sub>O [M+H]<sup>+</sup> 121.0653, found 121.0641.

## 6

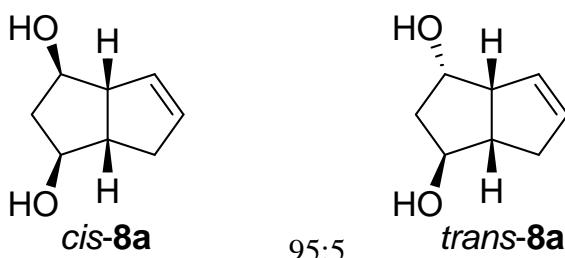


To a solution of the *tert*-butyl hydroperoxide (70 wt. % in water, 600  $\mu$ L, 4.19 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) was added water (3 mL). The layers were separated and the organic one dried over MgSO<sub>4</sub>, filtered, and washed with dry CH<sub>2</sub>Cl<sub>2</sub> until 10 mL of solvent were obtained. To this solution was added enone (*-*)-5 (500 mg, 4.17 mmol, 1.0 equiv). DBU (100  $\mu$ L, 0.668 mmol, 0.16 equiv) was added slowly (over 5 min). After 16 h at rt, the solution was extracted with HCl solution (1 M, 5 mL). The organic layer was washed with a solution of Na<sub>2</sub>SO<sub>3</sub> (500 mg / 10 mL H<sub>2</sub>O), brine then dried, filtered and the solvents evaporated under reduced pressure. This reaction can be scale-up to 1 g of enone 5. We are routinely preparing multigram quantity of **6** by running 5 reactions overnight (crude **5** is divided in 5 fractions) with only one work-up as shown above.

Remaining saturated ketone (from IBX oxidation) coelute with epoxide **6**. No chromatographic purification was required at this stage for the next reaction because subsequent reduction step will ease up the chromatographic separation of unwanted intermediates.

For characterization and yield determination purification by column chromatography on silica with petroleum ether-Et<sub>2</sub>O (7-3) as eluents gave (*-*)-**6** in 82 % yield;  $[\alpha]_D^{23} = -378$  (c. 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>);  $R_f$  (50% Et<sub>2</sub>O/petroleum ether) 0.49;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3058, 2925, 2855, 1734, 1615, 1448, 1368, 1173, 836;  $\delta_{\text{H}}$ (300 MHz) 5.79-5.75 (m, 1H), 5.59-5.56 (m, 1H), 3.67 (br s, 1H), 3.36 (d,  $J=2.7$  Hz, 1H), 3.34 (m, 1H), 3.28-3.21 (m, 1H), 2.74-2.61 (ddq,  $J=17.6$ , 10.2 and 2.3 Hz, 1H), 2.31 (dm,  $J=17.5$  Hz, 1H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>) : 207.8, 132.6, 126.6, 60.9, 56.4, 56.0, 40.0, 34.1; HRMS (ESI) calculated for C<sub>8</sub>H<sub>9</sub>O<sub>2</sub> [M+H]<sup>+</sup> 137.0603, found 137.0607.

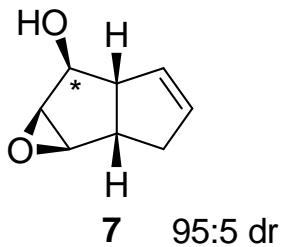
## 8a



To a solution of epoxide (*-*)-**6** (4.2 g, 30.9 mmol, 1.0 equiv) in THF (200 ml) at -80 °C, was added dropwise a solution of LiAlH<sub>4</sub> (1 M in THF, 58.3 mL, 58.3 mmol, 7.6 equiv per hydride). The temperature was allowed reach 0 °C and the reaction quenched with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>•5H<sub>2</sub>O (25 g) added by portion. After 30 min, the precipitate was filtered and the cake washed with AcOEt. The filtrate was dried, evaporated under reduced pressure, and the crude residue purified by column chromatography on silica with petroleum ether-Et<sub>2</sub>O (2:8) then 100% Et<sub>2</sub>O as eluents to give *cis*-**8a** (2.99 g; 71%) and *trans*-**8a** (0.16 g; 4%).

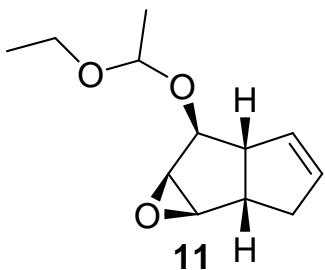
To be noted: if reduction is performed on crude material (no column chromatography from 1,3-COD) reduced by products coming from saturated ketone and remaining enone **5** (as well as some other alcohols or by-products) are easily removed by column chromatography; thanks to their lower polarities than diols **8**; *cis*-**8a**  $[\alpha]_D^{23} = -35.5$  (*c.* 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>);  $R_f$  (100% Et<sub>2</sub>O) 0.25;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3351, 2921, 1431, 1178, 1067, 953, 692;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>) 5.56-5.48 (m, 2H), 4.04 (m, 2H), 3.38-3.33 (m, 1H), 3.05-2.98 (m, 2H, OH), 2.93-2.85 (m, 1H), 2.68 (br dd, *J*=17.5 and 10.3 Hz, 1H), 1.96 (br dm, *J*=17.6 Hz, 1H), 1.82 (br dm, *J*=14.3 Hz, 1H), 1.65 (dt, *J*=14.3 and 4.3 Hz, 1H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>): 130.8, 130.5, 81.3, 77.7, 60.3, 48.9, 39.2, 38.0; HRMS (EI) calculated for C<sub>8</sub>H<sub>13</sub>O<sub>2</sub> [M+H]<sup>+</sup> 141.0916, found: 141.0921.

*trans*-**8a**;  $R_f$  (100 % Et<sub>2</sub>O) 0.13;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3341, 2921, 1441, 1330, 1082, 1059, 996;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>) 5.67 (br dd, *J*=5.6 and 1.9 Hz, 1H), 5.57 (br dd, *J*=5.6 and 2.2 Hz, 1H), 4.46-4.39 (m, 1H), 3.83 (br s, 1H), 3.77-3.65 (br m, OH), 3.30 (br s, 1H), 2.64-2.55 (m, 1H), 2.50-2.44 (m, 1H), 2.05 (br d, *J*=16.9 Hz, 1H), 1.75 (br dt, *J*=12.2 and 4.2 Hz, 1H), 1.53 (ddd, *J*= 13.0, 8.6 and 4.6 Hz, 1H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>): 132.0, 128.6, 77.8, 72.9, 53.6, 48.5, 41.2, 38.8.

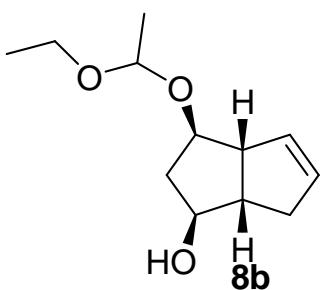


Epoxide **6** (1.9 g, 13.9 mmol, 1.0 equiv) was dissolved in THF (80 mL). The resulting solution was cooled to -78 °C and LiAlH<sub>4</sub> (1 M in THF, 6 mL, 6.0 mmol, 2.3 equiv per hydride) was added dropwise at the same temperature. After 20 min the reaction was quenched by adding a solution of NaOH (1 M). The reaction mixture was warmed up to room temperature and a solution of Na/K tartrate (1 M) was added to allow a better phase separation. After stirring for 2 h at room temperature, layers were separated and the aqueous one was extracted with Et<sub>2</sub>O (2 x 30 mL). The combined organic layers were washed with brine, dried, filtered and the solvent was evaporated

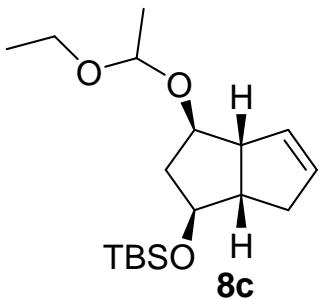
under reduced pressure. Crude compounds **7** were obtained as colourless oil (1.9 g, dr: 95/5).  $R_f$  (50% Et<sub>2</sub>O/petroleum ether) 0.43;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3389, 3049, 2931, 2848, 1616, 1397, 1063, 856, 705;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>):  $\delta$ : 5.76-5.73 (m, 1H), 5.65-5.61 (m, 1H), 3.94 (br dd,  $J=7.5$  Hz, 1H,), 3.63 (t,  $J=2.3$  Hz, 1H), 3.41 (d,  $J=2.4$ , 1H), 3.10 (ddd,  $J=10.0$ , 8.0 and 5.4 Hz, 1H), 2.75 (m, 1H), 2.48 (ddm,  $J=17.2$  and 9.0 Hz, 1H), 2.16 (dm,  $J=17.2$  Hz, 1H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>):  $\delta$  131.4, 129.8, 78.8, 62.5, 62.2, 58.1, 43.6, 34.2; HRMS (EI) calculated for C<sub>8</sub>H<sub>11</sub>O<sub>2</sub> [M+H]<sup>+</sup> 139.0759, found: 139.0743.



Crude compounds **7** (1.9 g, 13.7 mmol, 1.0 equiv) and a catalytic amount of PPTS were dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (30 mL) at room temperature. Ethoxyvinylether (30 mL) was added dropwise at the same temperature. After completion of the reaction (TLC, 3 h), solid NaHCO<sub>3</sub> (excess) was added, followed by a saturated solution of NaHCO<sub>3</sub>. Layers were separated and the aqueous one was extracted three times with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were washed with brine, dried, filtered and the solvent was eliminated under reduced pressure. Crude **11** was purified by flash chromatography (cyclohexane/AcOEt: 9.5/0.5) to remove *endo*-**11** byproduct, using deactivated silica gel (treated with a 1% solution of NEt<sub>3</sub> prior use). Exo-**11** was obtained as colourless oil (2.48 g, 80% (2 steps));  $R_f$  (40% Et<sub>2</sub>O/petroleum ether) 0.48;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3049, 2978, 2933, 1446, 1392, 1337, 1131, 1095, 1057, 943, 862, 724;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>) 5.84-5.77 (m, 1H), 5.68-5.64 (m, 1H), 4.89 (q,  $J=5.3$  Hz, 1H), 4.84 (dia q,  $J=5.4$  Hz, 1H), 3.94 (m,  $J=4.5$  Hz, 1H), 3.78-3.48 (ABX3 systems of *dias*, 2H), 3.62 (d,  $J=2.4$  Hz, 1H), 3.40 (t,  $J=2.7$  Hz, 1H), 3.18-3.10 (m, 1H), 2.83 (m, 1H), 2.51 (ddm,  $J=17.2$  and 10.0, 1H), 2.24-2.12 (m, 1H), 1.39 (2x d,  $J=5.4$  Hz, 3H), 1.22 (t,  $J=7.2$  Hz, 3H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>) 131.9, 129.9, 99.0, 98.7, 82.0, 81.2, 61.3, 60.5, 60.2, 60.19, 59.9, 59.6, 54.5, 54.2, 43.6, 43.5, 33.9, 33.8, 20.1, 19.96, 15.12.

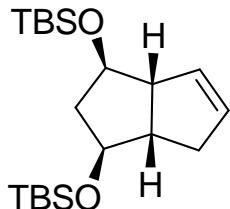


Compound **11** (2.48 g, 11.8 mmol, 1.0 equiv) was dissolved in Et<sub>2</sub>O (80 mL). The resulting solution was cooled to –78 °C and LiAlH<sub>4</sub> (1 M in Et<sub>2</sub>O, 11.8 mL, 4.0 equiv per hydride) was added dropwise to the reaction mixture. The reaction mixture was allowed to reach room temperature and was stirred overnight. Then, the reaction mixture was cooled to 0 °C and hydrolysed with NaOH (1 M). For a better phase separation a Na/K tartrate solution (1 M) was added and the resulting solution was stirred for 2 h. Layers were separated and the aqueous one was extracted Et<sub>2</sub>O (2 x 30 mL). The combined organic layers were washed with brine, dried, filtered and the solvent was evaporated under reduced pressure yielding crude alcohol **8b** (2.39 g, colourless oil). *R*<sub>f</sub> (40% Et<sub>2</sub>O/petroleum ether) 0.32;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3430, 3049, 2976, 2932, 1446, 1377, 1337, 1055, 980, 875, 695;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>) δ 5.59-5.55 (m, 1H), 5.52-5.45 (m, 1H), 4.76 (2 x q, *J*=5.3 Hz, 1H), 4.05-4.01 (m, 1H), 3.88 (br dd, *J*=10.3 Hz and 4.1 Hz, 1H), 3.62 (ABX<sub>3</sub> systems of *dias*, 1H), 3.48 (ABX<sub>3</sub> systems of *dias*, 1H), 3.43-3.33 (m, 1H), 3.16 and 3.05 (2 x d, 1H, *J*=10.5 and 10.6 Hz, 1H), 2.92-2.84 (bs, 1H, OH), 2.68 (ddm, *J*=17.6 and 10.2 Hz, 1H), 1.99 (dm, *J*=17.6 Hz, 1H), 1.89-1.81 ((m, 1H), 1.74-1.59 (m, 1H), 1.30 (2 x d, *J*=5.3, 3H), 1.19 (2 x t, *J*=7.1 Hz, 3H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>) 131.0, 130.5, 98.6, 80.8, 60.4, 57.8, 57.1, 49.3, 38.4, 38.1, 20.5, 15.2; HRMS (EI): calculated for C<sub>12</sub>H<sub>21</sub>O<sub>3</sub> [M+H]<sup>+</sup> 213.1491, found: 213.1469.



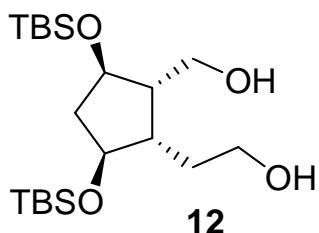
Crude alcohol **8b** above (2.39 g, 11.3 mmol, 1.0 equiv), imidazole (3.05 g, 44.8 mmol, 4.0 equiv) and a catalytic amount of DMAP were dissolved in DMF (8 mL) followed by addition of a solution of *tert*-butyldimethylsilyl chloride (2.54 g, 17.0 mmol, 1.5 equiv) in DMF (10 mL). The resulting reaction mixture was stirred at room temperature overnight. The solution was then cooled to 0 °C, H<sub>2</sub>O was added, followed by a saturated solution of NaHCO<sub>3</sub>. Phases were separated and the aqueous layer was extracted three times with Et<sub>2</sub>O. The combined organic layers were washed three times with H<sub>2</sub>O, and with brine. The organic layers were dried, filtered and the solvent was eliminated under reduced pressure affording crude **8c**. Purification by flash chromatography (cyclohexane/AcOEt: 9.5/0.5) with deactivated silica gel (treated with a 1% solution of NEt<sub>3</sub> prior use) afforded pure **8c** as a colourless oil (3.08 g, 80%, 2 steps); *R*<sub>f</sub> (40% Et<sub>2</sub>O/petroleum ether) 0.83;  $\nu_{\text{max}}$  cm<sup>-1</sup> 2930, 2898, 172, 1376, 1251, 1040, 1084, 937, 835, 773, 695;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>): 5.72-5.65 (m, 1H), 5.61-5.56 (m, 1H), 4.78-4.69 (m, 1H), 3.83-3.75 (m, 1H), 3.71-3.59 (m, 2H), 3.54-

3.42 (m, 1H), 3.18-3.07 (m, 1H), 2.67-2.45 (m, 2H), 2.18 (dm,  $J=16.6$  Hz, 1H), 2.14-2.03 (m, 1H), 1.78-1.63 (m, 1H), 1.31 (2 x d,  $J=5.4$  Hz, 3H), 1.20 (2 x t,  $J=7.1$  Hz, 3H), 0.88 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>) 132.7, 132.6, 129.8, 129.6, 98.7, 98.5, 79.0, 78.5, 78.2, 60.1, 59.7, 56.8, 56.5, 48.7, 42.8, 41.8, 37.2, 37.0, 25.8, 20.4, 20.3, 15.2, -3.1, -4.6, -4.7.



To the diol **8a** (2.06 g, 14.7 mmol, 1.0 equiv) in dry DMF (20 mL) at 0 °C, were added successively, the imidazole (5.3 g, 77.85 mmol, 5.3 equiv) and *tert*-butyldimethylsilyl chloride (6.05 g, 40.1 mmol, 2.7 equiv) by portion, then the reaction was allowed to reach room temperature. After 1.5 h, water (50 mL) and Et<sub>2</sub>O (50 mL) were added, and the layers were separated. The aqueous layer was extracted with Et<sub>2</sub>O (2 x 100 mL). The combined organic layers were washed with water (5 x 100 mL), brine (50 mL), dried, filtered and the solvents evaporated under reduced pressure. The crude material was left a night under high vacuum to recover 5.58 g of the protected bis-TBS diol of **8a** (rdt >100%; excess of residual silanol by-product);  $R_f$  (100% Et<sub>2</sub>O) 0.81;  $\nu_{\text{max}}$  cm<sup>-1</sup> 2955, 2929, 2989, 2857, 1472, 1463, 1375, 1361, 1250, 1189, 1095, 1066, 1006;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>): 5.69-5.65 (m, 1H), 5.57-5.53 (m, 1H), 3.84-3.78 (m, 1H); 3.67-3.60 (m, 1H), 3.05-2.97 (m, 1H), 2.66-2.57 (m, 1H), 2.54, 2.43 (m, 1H), 2.19-2.10 (br d,  $J=16.8$  Hz), 2.04-1.96 (m, 1H), 1.71-1.61 (m, 1H), 0.87 (s, 9H), 0.86 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); HRMS (ESI) calculated for C<sub>20</sub>H<sub>41</sub>O<sub>2</sub>Si<sub>2</sub> [M+H]<sup>+</sup> 369.2631, found 369.2645.

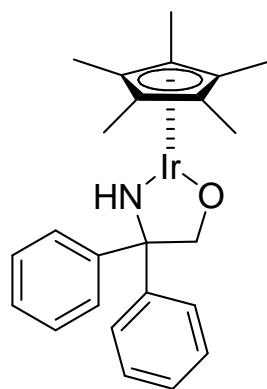
## 12



Bis-TBS diol of **8a** above (14.7 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub>/MeOH (5/1) (72 mL) at -80 °C, was left under a stream of ozone. After 1.5 h a blue coloration indicating of an excess of ozone, the reaction is flushed under nitrogen, then NaBH<sub>4</sub> (5.56 g, 147 mmol, 10.0 equiv) was added. The

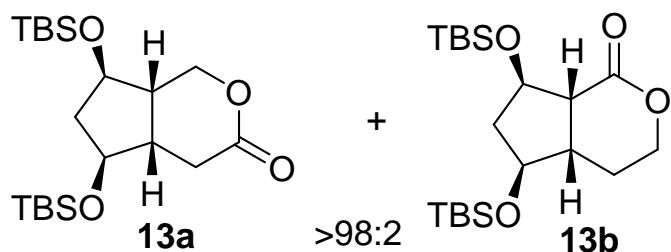
mixture was then allowed to rise room temperature and water (30 mL) was added. The layers were separated and the aqueous one extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 50 mL). The combined organic layers were washed with brine (30 mL), dried, filtered and the solvents removed under reduced pressure. The diol **12** was obtained as a white solid (4.44 g, 75%, 2 steps from **8a**) and used as such for the next step.  $[\alpha]_D^{23} = +3.4$  (*c.* 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>);  $R_f$  (100% Et<sub>2</sub>O) 0.41; mp 104.0-104.6 °C;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3265, 2953, 2929, 2857, 1472, 1370, 1251, 1079, 1054, 1034, 1006;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>): 4.01-3.96 (m, 1H), 3.86-3.80 (m, 1H), 3.76-3.63 (m, 3H), 3.59-3.54 (m, 1H), 2.33-2.24 (m, 1H), 2.21-2.15 (m, 2H), 1.76-1.65 (m, 1H), 1.57-1.45 (m, 3H), 0.87 (s, 9H), 0.86 (s, 9H), 0.04 (s, 6H), 0.03 (s, 6H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>) 76.8, 74.1, 62.3, 62.1, 51.1, 45.2, 44.3, 31.0, 25.8, 17.9, -4.12, -4.43, -4.70, -4.78; HRMS (ESI) calculated for C<sub>20</sub>H<sub>45</sub>O<sub>4</sub>Si<sub>2</sub> [M+H]<sup>+</sup> 405.2778, found 405.2844.

### Iridium catalyst



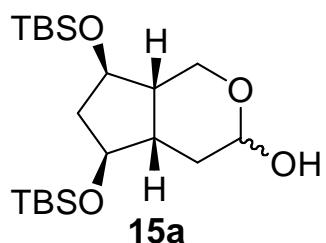
To a solution of [Cp\*IrCl<sub>2</sub>]<sub>2</sub> (100 mg, 0.126 mmol, 1.0 equiv) and 2,2-diphenyl glycinol (53 mg, 0.252 mmol, 2.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (2.5 mL) was added a solution of KOH (200 mg, 3.5 mmol, 28.0 equiv) in distilled water (2.5 mL). After stirring for 30 min at room temperature, the layers were separated and the aqueous one extracted CH<sub>2</sub>Cl<sub>2</sub> (2.5 mL). The combined organic layers were dried over CaH<sub>2</sub>. Evaporation of solvent gave a red solid (132 mg, 93%) which is used without further purification.

### **13a and 13b**

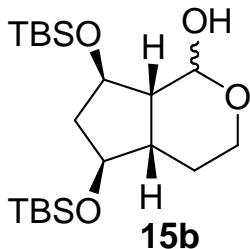


A mixture of Ir complex (11 mg, 0.07 mmol, 0.8 mol %) and diol **12** (1.0 g, 2.48 mmol, 1.0 equiv) in 9 mL of butanone freshly distilled and degassed was heated at reflux for 16 h. The resulting solution was then removed under reduced pressure, and the residue was purified on a small path of silica (to remove Ir catalyst) (petroleum ether/Et<sub>2</sub>O, 9/1) to give the lactones **13a** and **13b** (920 mg, 92%) as a white solid; *R*<sub>f</sub> (100% Et<sub>2</sub>O) 0.43; mp 108.4 °C;  $\nu_{\text{max}}$  cm<sup>-1</sup> 2954, 2930, 2857, 1748, 1472, 1387, 1361, 1251, 1084, 1036, 1006;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>): 4.18 (d, *J*=3.2 Hz, 2H), 3.99-3.91 (m, 1H), 3.64-3.57 (m, 1H), 2.54-2.44 (m, 3H), 2.36-2.27 (m, 1H), 2.08-2.00 (m, 1H), 1.62 (q, *J*=11 Hz, 1H) 0.86 (s, 18H), 0.04-0.03 (m, 12H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>): 172.8, 76.5, 71.4, 67.7, 44.4, 43.2, 41.7, 32.3, 25.6, 17.8, -4.5, -4.6,-4.9; HRMS (ESI) calculated for C<sub>20</sub>H<sub>41</sub>O<sub>4</sub>Si<sub>2</sub> [M+H]<sup>+</sup> 401.2571, found 401.2543.

### **15a**

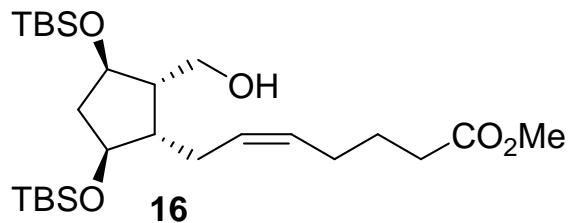


To a mixture of the lactones above **13a** and **13b** (920 mg, 2.30 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) at -78 °C, was slowly added DIBAL-H (1 M in toluene, 3.45 mL, 3.45 mmol, 1.5 equiv). After 30 min at the same temperature, the reaction was quenched by adding a solution of NH<sub>4</sub>Cl. The reaction mixture was warmed up to room temperature and a solution of Na/K tartrate (1 M) was added. After stirring for 1 h, the layers were separated and the aqueous one was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 40 mL). The combined organic layers were washed with brine, dried and the solvent was removed under reduced pressure. The crude material was purified by column chromatography on silica with dichloromethane to give lactol **15a** (820 mg, 89%) as colourless oil;  $[\alpha]_D^{23} = -38.4$  (*c.* 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>); *R*<sub>f</sub> (83% CH<sub>2</sub>Cl<sub>2</sub>/EtOAc) 0.55;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3385, 2953, 2929, 2886, 2857, 1472, 1462, 1388, 1360, 1251, 1108, 1067, 1018; 829, 771;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>): 5.16-5.13 (m, 0.46H), 4.69-4.63 (m, 0.54), 4.22-4.09 (m, 1H), 4.06 (dd epi 1, *J*=11.8 and 3.9 Hz, 0.46H), 3.97 (dd epi 2, *J*=12.1 and 1.5 Hz, 0.56H), 3.84-3.76 (m, 1H), 3.68 (dd, *J*=12.1 and 3.0 Hz, 0.56H), 3.53 (dd, *J*=11.8 and 2.7 Hz, 0.46H), 2.88 (d, *J*=5.3 Hz, 0.56H, OH), 2.52 (br d, 0.46H, OH), 2.45-2.30 (m, 1H), 2.29-2.21 (m, 0.46H), 2.10-1.99 (m, 1.63H), 1.64-1.50 (m, 1.5H), 1.42-1.33 (m, 0.51), 1.02-0.92 (m, 0.60), 0.86 (s, 18H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 6H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>): 95.2, 91.2, 76.3, 75.8, 63.7, 58.6, 44.3 , 44.2 (2x), 44.1, 44.0, 39.5, 32.8, 29.6, 25.8, 18.0, -4.5, -4.8 (3x); HRMS (ESI) calculated for C<sub>20</sub>H<sub>43</sub>O<sub>4</sub>Si<sub>2</sub> [M+H]<sup>+</sup> 403.2700, found 403.2672.



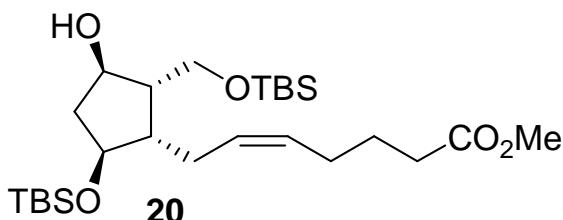
Lactol **15b**;  $[\alpha]_D^{23} = -18.4$  (*c.* 0.5 10<sup>-2</sup>, CHCl<sub>3</sub>);  $R_f$  (83% CH<sub>2</sub>Cl<sub>2</sub>/EtOAc) 0.60; mp 99.4 °C;  $\nu_{\max}$  cm<sup>-1</sup> 3400, 2952, 2930, 2887, 2857, 1472, 1462, 1388, 1361, 1254, 1113, 1072, 1035; 836, 774;  $\delta_H$ (300 MHz, CDCl<sub>3</sub>): 5.02 (br m, 0.6H), 4.90 (dd, *J*=8.0 and 2.8 Hz, 0.4H), (4.56, q, *J*=8.0 Hz, 0.4H), 4.17 (br q, *J*=7.8 Hz, 0.6H), 3.97-3.89 (m, 1H), 3.85-3.79 (m, 1H), 3.50 (dt epi 1, *J*=11.3 and 4.1 Hz, 0.6H), 3.40 (td, epi 2, *J*=11.7 and 2.6 Hz), 2.53-2.35 (m, 2H), 2.26-2.10 (m, 1H), 2.07-1.98 (m, 0.4H), 1.59-1.35 (m, 3H), 1.26-1.04 (m, 1H), 0.87-0.86 (3 singulets, 18H), 0.09-0.01 (5 singulets, 12H);  $\delta_C$ (75 MHz, CDCl<sub>3</sub>): 95.9, 92.8, 76.0, 71.6, 63.7, 58.4, 49.3, 47.4, 44.8, 44.4, 44.2, 41.2, 25.8, 25.7, 25.1, 25.0, -3.7, -4.5, -4.7, -4.9.

## 16

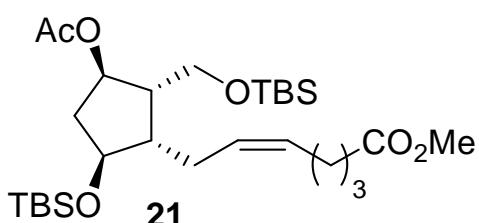


A solution of (4-carboxybutyl)triphenylphosphonium bromide (3.54 g, 8.0 mmol) in degassed THF (15 mL) was treated at 0 °C with a solution of potassium tert-butoxide (1M in THF, 16 mL, 16.0 mmol). After the mixture was stirred for 30 min at this temperature, a solution of the lactol **15a** (800 mg, 2.0 mmol) in THF (10 mL) was added via canula. The resulting mixture was then stirred at 0 °C for 1 h, quenched with addition of saturated aqueous NH<sub>4</sub>Cl solution, diluted with water, adjusted to pH 3 with 1 N HCl, and then extracted with EtOAc. The combined organic extracts were washed with brine, dried, filtered, and concentrated in vacuo. To the crude material was added a solution of Et<sub>2</sub>O/MeOH (5/1) (10 mL) and TMSCHN<sub>2</sub> (1 M in Et<sub>2</sub>O) was added until no bubbling is observed (N<sub>2</sub> formation). The crude material was purified by column chromatography on silica with dichloromethane-EtOAc (99-1) to give alcohol **16** (650 mg, 65%) as colorless oil (the first approx. 100 mg were discarded, because we believed them to be contaminated with some *E* isomer). A more polar compound is also obtained in 12% yield (120 mg) and was identified as compound **20** (see below); **16**  $[\alpha]_D^{23} = -0.8$  (*c.* 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>);  $R_f$  (90% CH<sub>2</sub>Cl<sub>2</sub>/EtOAc) 0.49;  $\nu_{\max}$  cm<sup>-1</sup> 3468, 2954,

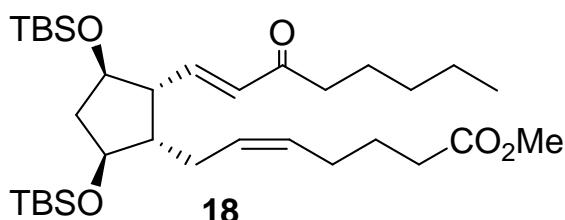
2929, 2887, 2857, 1741, 1472, 1361, 1252, 1065, 836, 774;  $\delta_{\text{H}}$ (300 MHz,  $\text{CDCl}_3$ ): 5.45-5.31 (m, 2H), 4.03 (br q,  $J=6.6$  Hz, 1H), 3.79 (br q,  $J=5.4$  Hz, 1H), 3.73-3.61 (m, 2H), 3.65 (s, 3H), 2.34-2.24 (m, 4H), 2.11-1.86 (m, 5H), 1.77 (br s, OH, 1H), 1.73-1.62 (m, 2H), 1.65 (dt,  $J=13.4$  and 6.0 Hz, 1H), 0.86 (s, 9H), 0.85 (s, 9H), 0.04 (s, 6H), 0.00 (s, 6H);  $\delta_{\text{C}}$ (75 MHz,  $\text{CDCl}_3$ ): 174.1, 129.7, 129.5, 75.7, 74.8, 62.5, 51.5, 50.2, 48.2, 44.5, 33.4, 26.7, 25.8 (+ hidden  $\text{CH}_2$ ), 24.7, 17.9, -4.3, -4.4, -4.7, -4.8; HRMS (ESI) calculated for  $\text{C}_{26}\text{H}_{53}\text{O}_5\text{Si}_2$  [ $\text{M}+\text{H}]^+$  501.3432, found 501.3418.



$R_f$  (90%  $\text{CH}_2\text{Cl}_2/\text{EtOAc}$ ) 0.36;  $\nu_{\text{max}}$   $\text{cm}^{-1}$  3428, 2953, 2929, 2896, 2857, 1742, 1472, 1361, 1252, 1093, 836, 774;  $\delta_{\text{H}}$ (300 MHz,  $\text{CDCl}_3$ ): 5.41-5.29 (m, 2H), 4.08-4.02 (m, 1H), 3.90 (br q,  $J=4.6$  Hz, 1H), 3.74-3.58 (m, 2H), 3.63 (s, 3H), 2.31-2.17 (m, 4H), 2.14-1.93 (m, 5H), 1.71-1.61 (m, 2H), 1.53 (dt,  $J=13.7$ , 4.6 Hz, 1H), 0.86 (s, 9H), 0.84 (s, 9H), 0.02 (s, 6H), 0.00 (s, 6H);  $\delta_{\text{C}}$ (75 MHz,  $\text{CDCl}_3$ ): 173.9, 129.8, 129.4, 76.9, 75.8, 62.9, 51.4, 50.6, 49.1, 43.3, 33.5, 26.8, 25.8, 25.8 ( $\text{CH}_2$ ), 24.8, 18.1, 17.9, -4.6, -4.7, -5.5; HRMS (ESI) calculated for  $\text{C}_{26}\text{H}_{53}\text{O}_5\text{Si}_2$  [ $\text{M}+\text{H}]^+$  501.3432, found 501.3414..



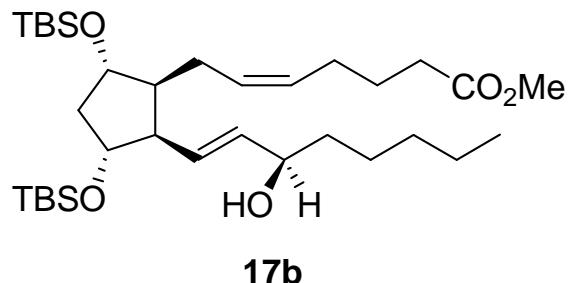
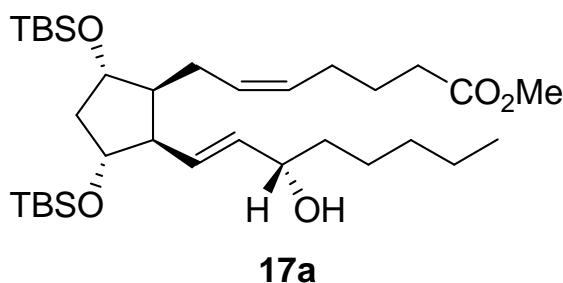
The silyl migration was confirmed by acetylation of the free alcohol of **20** to give compound **21**.  $^1\text{H}$  NMR showed a chemical shift of one hydrogen confirming a free secondary alcohol for compound **20** (see  $^1\text{H}$  NMR spectra provided).



To a solution of the alcohol **16** (600 mg, 1.2 mmol, 1.0 equiv) in  $\text{CH}_2\text{Cl}_2$  (30 mL) was added dropwise the Dess-Martin periodinane (6.0 mL, 0.3 M. in  $\text{CH}_2\text{Cl}_2$ , 1.8 mmol, 1.5 equiv). After 1 h at room temperature, a 10% solution of  $\text{NaHCO}_3$  (50 mL) and 10% solution of  $\text{Na}_2\text{S}_2\text{O}_3$  (50 mL) were added. The layers were separated and the aqueous one were extracted with  $\text{CH}_2\text{Cl}_2$  (20 mL). The

combined organic layers were washed brine, dried, filtered and the solvent removed under reduced pressure. The aldehyde was used as such for the next reaction. To a solution of NaH (60% in oil, 120 mg, 3.00 mmol, 2.5 equiv) in THF (30 mL) was added dimethyl-2-oxoheptyl phosphonate (994 mg, 3.60 mmol, 3.0 equiv) at room temperature. After 30 min., the aldehyde in THF (10 mL) was transferred via canula to the reaction mixture. After 1 h, water (20 mL) and Et<sub>2</sub>O (40 mL) were added, the layers separated and the aqueous one extracted once with 20 mL of Et<sub>2</sub>O. The combined organic layers were extracted with brine, dried, filtered and the solvent removed under reduced pressure. For characterization, purification by column chromatography on silica with dichloromethane as eluent gave enone **18** (585 mg, 82%, 2 steps) as an oil;  $[\alpha]_D^{23} = +1.4$  (*c.* 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>);  $R_f$  (90% cyclohexane /EtOAc) 0.49;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3029, 2918, 2853, 1730, 1700, 1583, 1446, 1334, 1179,  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>): 6.63 (dd, *J*=15.7 and 9.9 Hz, 1H), 6.13 (d, *J*=15.7 Hz, 1H), 5.38-5.27 (m, 2H), 3.97 (ddd, *J*=7.1 and 5.2 Hz, 1H), 3.83 (br ddd, *J*=5.7 Hz, 1H), 3.63 (s, 3H), 2.82-2.74 (m, 1H), 2.47 (t, *J*=7.3 Hz, 2H), 2.35 (dt, *J*=7.1 Hz, 1H), 2.26 (d, *J*=7.4 Hz, 2H), 2.16-1.95 (m, 4H), 1.91-1.82 (m, 1H), 1.69-1.52 (m, 5H), 1.33-1.23 (m ,4H), 0.89-0.82 (m, 3H), 0.85 (s, 3H), 0.83 (s, 3H), 0.01 (s, 6H), -0.02 (s, 3H), -0.03 (s, 3H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>): 200.1, 173.9, 145.3, 131.4, 129.6, 129.0, 75.6, 75.4, 52.7, 51.4, 50.8, 44.3, 40.8, 33.4, 31.5, 26.8, 26.4, 25.8, 24.7, 23.9, 22.4, 17.9, 13.9, -4.5, -4.6, -4.7, -4.8.

### 17a and 17b

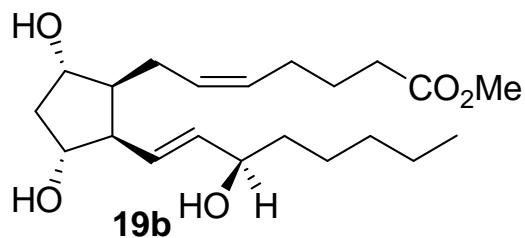
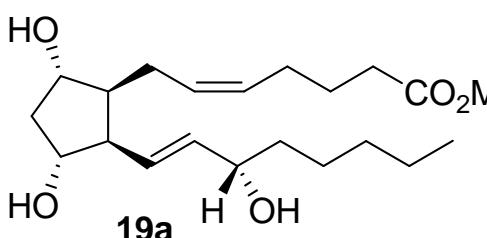


To a solution of the enone **18** (500 mg, 0.84 mmol, 1.00 equiv) in 10 mL of MeOH, was added the cerium chloryde heptahydrate (319 mg, 0.85 mmol, 1.01 equiv). The mixture was cooled at 0 °C and NaBH<sub>4</sub> was added (33.4 mg, 0.211 mmol, 1.05 equiv). After 10 min, the reaction was quenched with 12 mL of water and 25 mL of Et<sub>2</sub>O were added. The layers were separated and the aqueous one extracted three times with Et<sub>2</sub>O (20 mL). The combined organic layers were washed with brine, dried, filtered and the solvent removed under reduce pressure. The crude was purified by column chromatography on silica with dichloromethane-up to 1% EtOAc to give the alcohol **17a** (206 mg, 41%) and **17b** (226 mg, 45%) as a colourless oil; **17a**  $[\alpha]_D^{23} = +13.8$  (*c.* 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>);  $R_f$  (95% CH<sub>2</sub>Cl<sub>2</sub> /EtOAc) 0.59;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3480 , 2954, 2929, 2857, 1742, 1462, 1250, 1105, 1063;  $\delta_{\text{H}}$ (300

MHz, CDCl<sub>3</sub>): 5.50 (dd, *J*=15.4 and 5.8 Hz, 1H), 5.46 (m, 3H), 4.09-4.01 (m, 1H), 3.90 (dt, *J*=6.9 and 4.8 Hz), 3.78 (m, 1H), 3.64 (s, 3H), 2.65-2.57 (m, 1H), 2.35-2.26 (m, 3H), 2.08-1.98 (m, 4H), 1.93-1.82 (m, 1H), 1.70-1.61 (m, 2H), 1.51-1.38 (m, 3H), 1.27 (br s, 6H), 0.86-0.85 (m, 3H), 0.86 (s, 9H), 0.85 (s, 9H), 0.01 (s, 6H), 0.00 (s, 6H); δ<sub>C</sub>(75 MHz, CDCl<sub>3</sub>): 174.1, 135.4, 129.7, 129.4, 128.9, 76.1, 75.9, 72.7, 52.4, 51.4, 50.2, 44.2, 37.4, 33.5, 31.8, 26.7, 26.3, 25.8, 25.1, 24.8, 22.6, 18.0 (2x), 14.0, -4.4, -4.6, -4.8.

**17b** [α]<sub>D</sub><sup>23</sup> = +10.0 (*c.* 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>); *R*<sub>f</sub> (95% CH<sub>2</sub>Cl<sub>2</sub>/EtOAc) 0.54; ν<sub>max</sub> cm<sup>-1</sup> 3480, 2954, 2928, 2857, 1741, 1462, 1250, 1107, 1064 δ<sub>H</sub>(300 MHz, CDCl<sub>3</sub>): 5.50 (dd, *J*=16.4 and 6.3 Hz, 1H), 5.40 (dd, *J*=16.4 and 9.0 Hz, 1H), 5.37-5.27 (m, 2H), 4.06-4.00 (m, 1H), 3.88 (dt, *J*=7.0 and 4.6 Hz, 1H), 3.81-3.75 (m, 1H), 3.64 (s, 3H), 2.64-2.58 (m, 1H), 2.35-2.26 (m, 3H), 2.14-1.86 (m, 5H), 1.70-1.60 (m, 3H), 1.53-1.47 (m, 2H), 1.28 (br s, 6H), 0.90-0.84 (m, 2H), 0.86 and 0.84 (2 x s, 18H), 0.01 (s, 6H), -0.01 (2 x s, 6H); δ<sub>C</sub>(75 MHz, CDCl<sub>3</sub>): 174.2, 135.6, 129.9, 129.8, 128.9, 76.2, 75.8, 73.0, 52.4, 51.5, 50.2, 44.3, 37.4, 33.4, 31.8, 26.7, 26.2, 25.8, 25.1, 24.8, 22.6, 18.0 (2x), 14.0, -4.4, -4.6.

### **19a** and **19b**



To a solution of the silylated ether **17a** (200 mg, 0.34 mmol, 1.0 eq.) was added TBAF (1 M in THF, 2.72 mL, 2.72 mmol, 8.0 eq, 4.0 equiv per TBS). After 2 h, CaCO<sub>3</sub> (906 mg, 1.03 mmol, 27 equiv), the Dowex 50W resina (2.8 g) and 2 mL of MeOH were added. After 1 h, the precipitate was filtered over a pad of Celite, washed with EtOAc and the solvent evaporated over reduced pressure to give triol **19a** (112 mg, 91%) after column chromatography on silica with EtOAc as eluent. The same transformation was performed with **17b** to give triol **19b** in a similar yield.

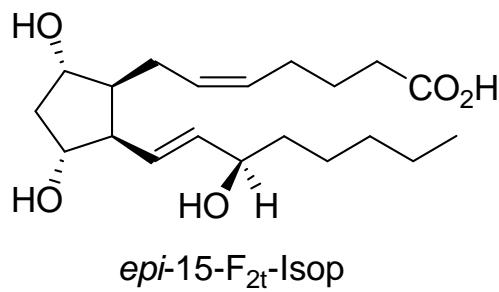
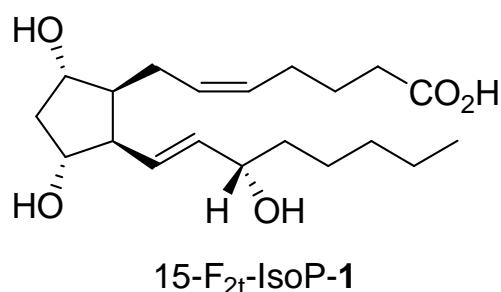
A crude mixture of **17a** and **17b** (starting from 320 mg of enone **18**) obtained from Luche reduction was desilylated following the same procedure, and a purification by column chromatography on silica with EtOAc gave the triol **19a** (73 mg, 37%, 2 steps) and triol **17b** (81 mg, 41%, 2 steps) as easily separable compounds. To be noted: compound **17a** is less polar than **17b**, but **19a** is more polar than **19b**.

**19b**, [α]<sub>D</sub><sup>23</sup> = -13.4 (*c.* 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>); *R*<sub>f</sub> (100% EtOAc) 0.20; ν<sub>max</sub> cm<sup>-1</sup> 3354, 2928, 2858, 1721, 1436, 1246, 1169, 972; δ<sub>H</sub>(300 MHz, CDCl<sub>3</sub>): 5.58 (dd, *J*=15.4 and 6.3 Hz, 1H), 5.48-5.34 (m, 3H),

4.11-3.94 (m, 3H), 3.65 (s, 3H), 2.80-2.73 (m, 1H), 2.46-2.36 (m, 1H), 2.30 (t,  $J=7.1$  Hz, 2H), 2.20-2.21 (m, 1H), 2.08-1.99 (m, 4H), 1.71-1.60 (m, 4H), 1.55-1.42 (m, 2H), 1.28 (br s, 6H), 0.86 (br t; 3H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>): 174.3, 135.9, 129.6, 129.3, 128.4, 76.0, 75.9, 72.5, 52.9, 51.5, 50.6, 42.3, 37.2, 33.3, 31.7, 26.6, 25.1, 24.6; 22.5, 13.9; HRMS (ESI) calculated for C<sub>21</sub>H<sub>34</sub>O<sub>5</sub> [M+H]<sup>+</sup> 369.2641, found 369.2650.

**19a**;  $[\alpha]_D^{23} = -5.5$  (c. 1.0 10<sup>-2</sup>, CHCl<sub>3</sub>);  $R_f$  (100% EtOAc) 0.14;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3356, 2927, 2857, 1722, 1436, 1245, 1171; ): 5.56 (dd,  $J=15.3$  and 6.5 Hz, 1H), 5.48-5.34 (m, 3H), 4.08-3.92 (m, 3H), 3.65 (s, 3H), 2.79-2.72 (m, 1H), 2.47-2.37 (m, 1H), 2.29 (t,  $J=7.3$  Hz, 2H), 2.19-1.97 (m, 4H + 3 OH), 1.71-1.59 (m, 4H), 1.57-1.40 (m, 4H), 1.27 (br s, 6H), 0.86 (br t; 3H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>): 174.2, 136.2, 129.6, 129.2, 76.0, 73.0, 53.1, 51.5, 50.7, 42.2, 37.1, 33.3, 31.7, 26.6, 25.1, 24.7, 22.6, 13.9; HRMS (ESI) calculated for C<sub>21</sub>H<sub>34</sub>O<sub>5</sub> [M+H]<sup>+</sup> 369.2641, found 369.2640.

### 15-F<sub>2t</sub>-IsoP 1 and epi-15-F<sub>2t</sub>-IsoP



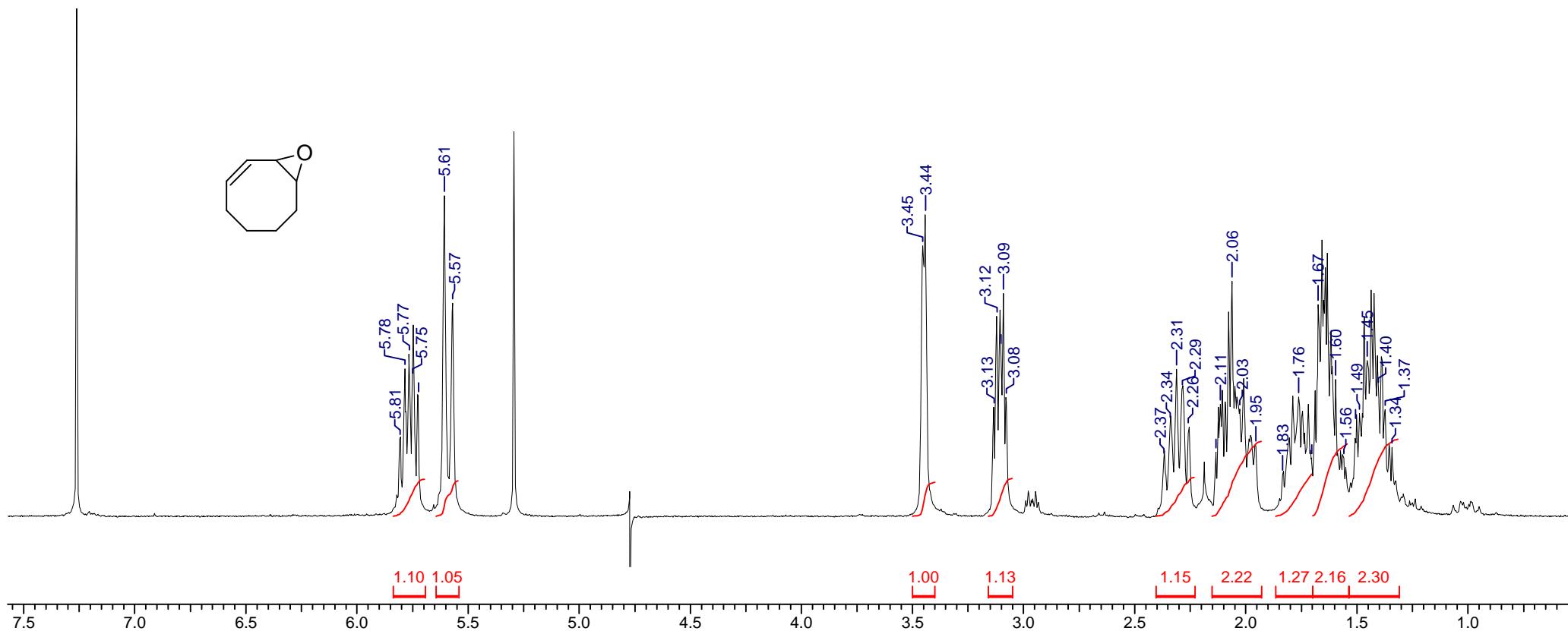
To a solution of the triol methyl ester **19a** (62 mg, 0.168 mmol, 1.0 equiv) in 2 mL of THF/H<sub>2</sub>O (1/1) was added LiOH·H<sub>2</sub>O (42 mg, 1.01 mmol, 6.0 equiv). After 3 h at rt, the solution was cooled at 0 °C and a HCl solution (1 M) was added until a acidic pH. The layers were separated and the aqueous one extracted with AcOEt (3 x 5 mL). The combined organic layers were dried, filtered and the solvents evaporated. The crude was purified by column chromatography on silica (AcOEt/MeOH, 9/1) to give 15-F<sub>2t</sub>-IsoP **1** as an oil (46.5 mg, 78%).

The same transformation was performed with **19b** (55 mg) to give *epi*-15-F<sub>2t</sub>-IsoP (42.9 mg, 81%) in a similar yield.

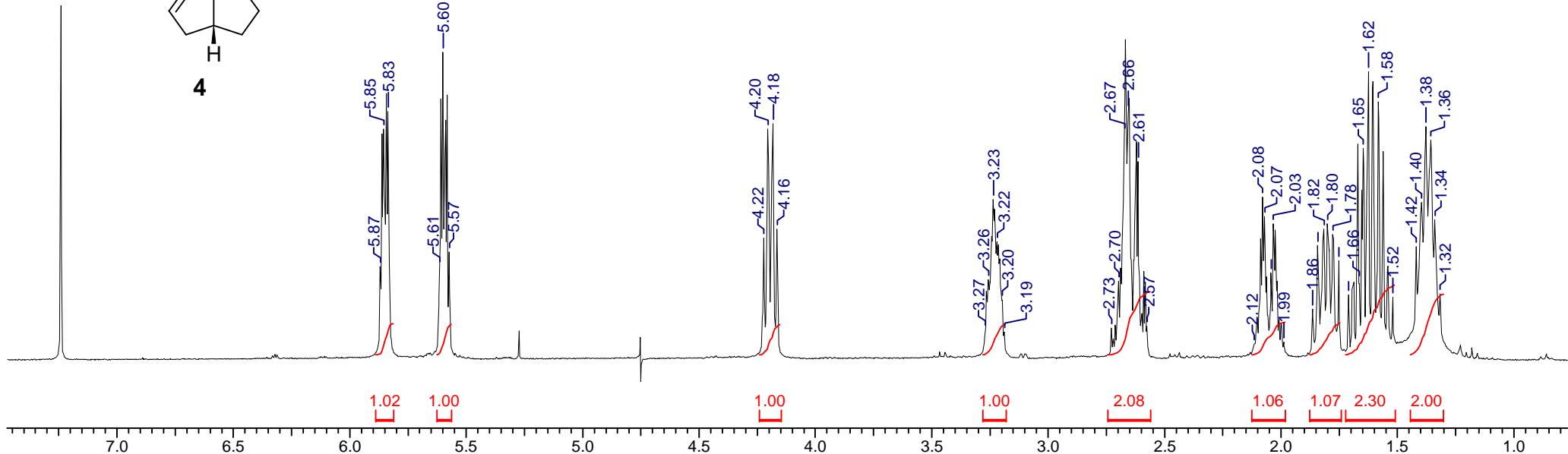
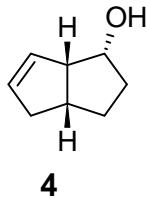
15-F<sub>2t</sub>-IsoP **1**;  $[\alpha]_D^{23} = +13.1$  (c. 1.0 10<sup>-2</sup>, MeOH);  $R_f$  (90% EtOAc/MeOH) 0.22;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3329, 2928, 2858, 1705, 1551, 1405, 1379, 1240, 1058, 1014, 970, 909, 730;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>): 5.57 (dd,  $J=15.4$  and 6.0 Hz, 1H), 5.50-5.35 (m, 3H), 4.08 (q,  $J=6.1$  Hz), 4.05-4.00 (m, 1H), 3.9-3.94 (m, 1H), 2.80-2.73 (m, 1H), 2.49-2.39 (m, 1H), 2.81 (t,  $J=6.5$  Hz, 2H), 2.17-1.95 (m, 5H), 1.65 (t,  $J=6.7$  Hz, 3H), 1.52-1.45 (m, 2H), 1.27 (br s, 6H), 0.86 (t,  $J=6.5$  Hz, 3H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>): 177.1, 135.4, 129.7, 129.3, 129.2, 76.0, 75.9, 72.9, 53.0, 50.6, 42.1, 37.0, 32.7, 31.6, 26.6, 26.2, 25.1, 24.3, 22.5, 13.9; HRMS (ESI) calculated for C<sub>20</sub>H<sub>34</sub>O<sub>5</sub>Na [M+Na]<sup>+</sup> 377.2304, found 377.2299.

*epi*-15-F<sub>2t</sub>-IsoP,  $[\alpha]_D^{23} = +1.4$  (*c.* 1.0 10<sup>-2</sup>, MeOH);  $R_f$  (90% EtOAc/MeOH) 0.27;  $\nu_{\text{max}}$  cm<sup>-1</sup> 3362, 2931, 1708, 1435, 1407, 1237, 1066, 972;  $\delta_{\text{H}}$ (300 MHz, CDCl<sub>3</sub>): 5.56 (dd, *J*=15.4 and 6.4 Hz, 1H), 5.51-5.36 (m, 3H), 4.09 (q, *J*=6.3 Hz, 1H), 3.99 (m, 2H); 2.80-2.73 (m, 1H), 2.47-2.37 (m, 1H), 2.30 (t, *J*=6.5 Hz, 2H), 2.20-2.03 (m, 4H), 1.98-1.87 (m, 1H), 1.70-1.59 (m, 3H), 1.54-1.46 (m, 2H); 1.27 (br s, 6H), 0.86 (t, *J*=6.7 Hz, 3H);  $\delta_{\text{C}}$ (75 MHz, CDCl<sub>3</sub>): 177.0, 135.4, 129.8, 129.5, 129.1, 76.2 (2x), 72.9, 53.3, 50.7, 42.2, 37.1, 32.7, 31.7, 26.7, 26.3, 25.1, 24.3, 22.6, 14.0; HRMS (ESI) calculated for C<sub>20</sub>H<sub>34</sub>O<sub>5</sub>Na [M+Na]<sup>+</sup> 377.2304, found 377.2306.

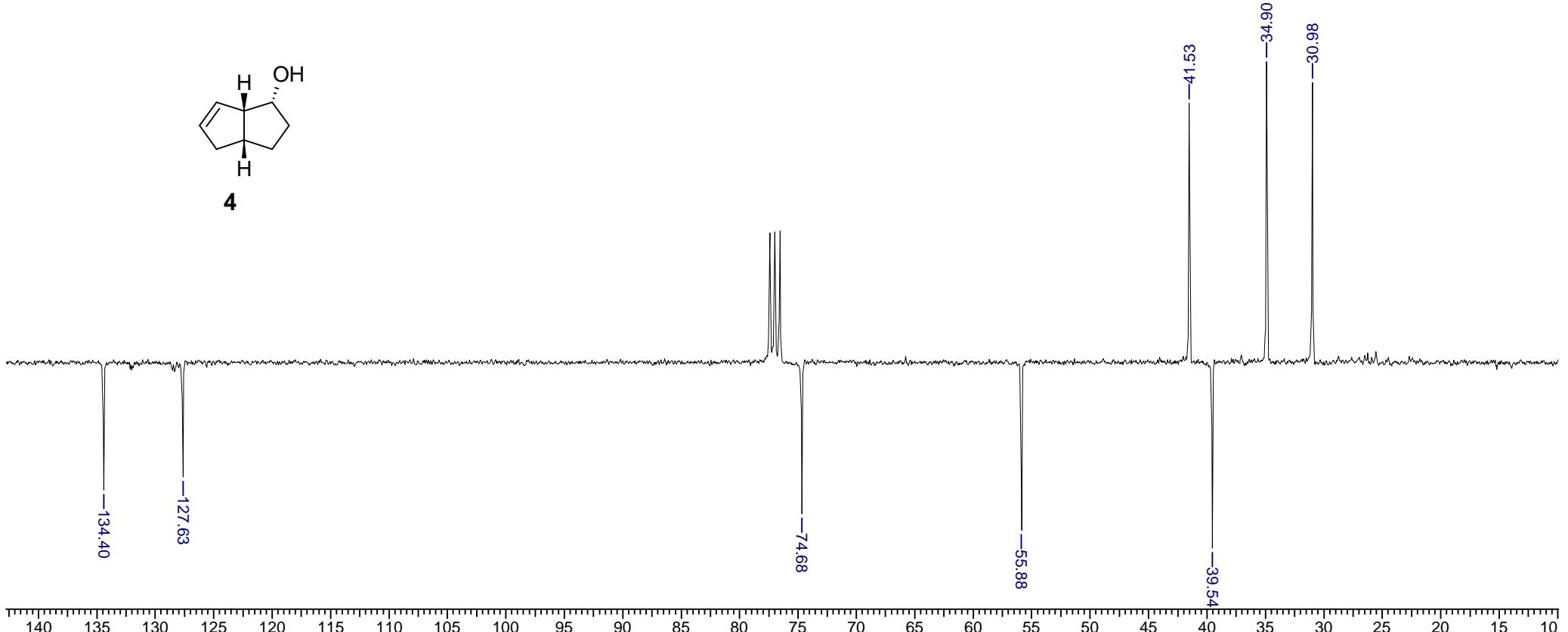
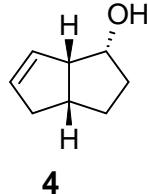
Acquisition Time (sec)	10.3547	Comment	1H sur CO1-131 brut		Date	03/09/2008 15:48:44	
Frequency (MHz)	300.13	Nucleus	1H	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	3164.56



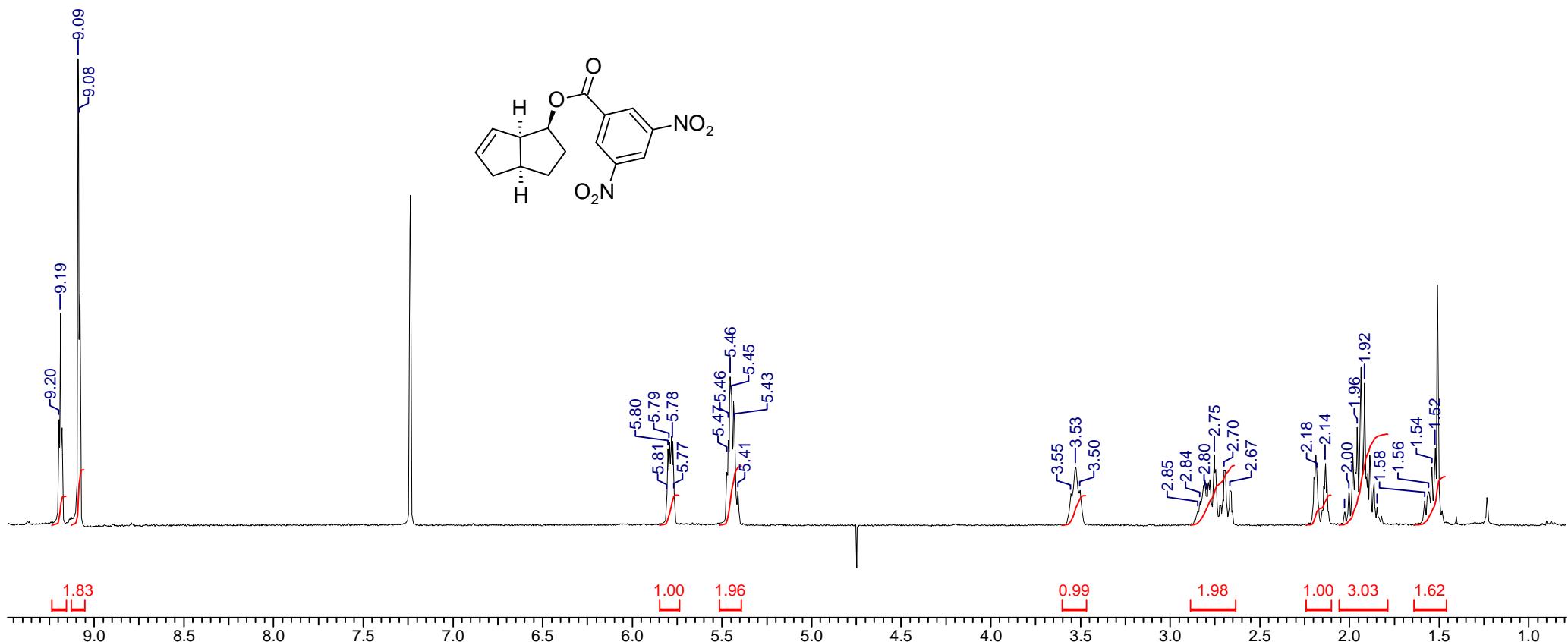
<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	1H sur CO1-146 pur F2		<b>Date</b>	04/09/2008 10:58:26	
<b>Frequency (MHz)</b>	300.13	<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768
<b>Temperature (grad C)</b>	0.000			<b>Sweep Width (Hz)</b>	3164.56		



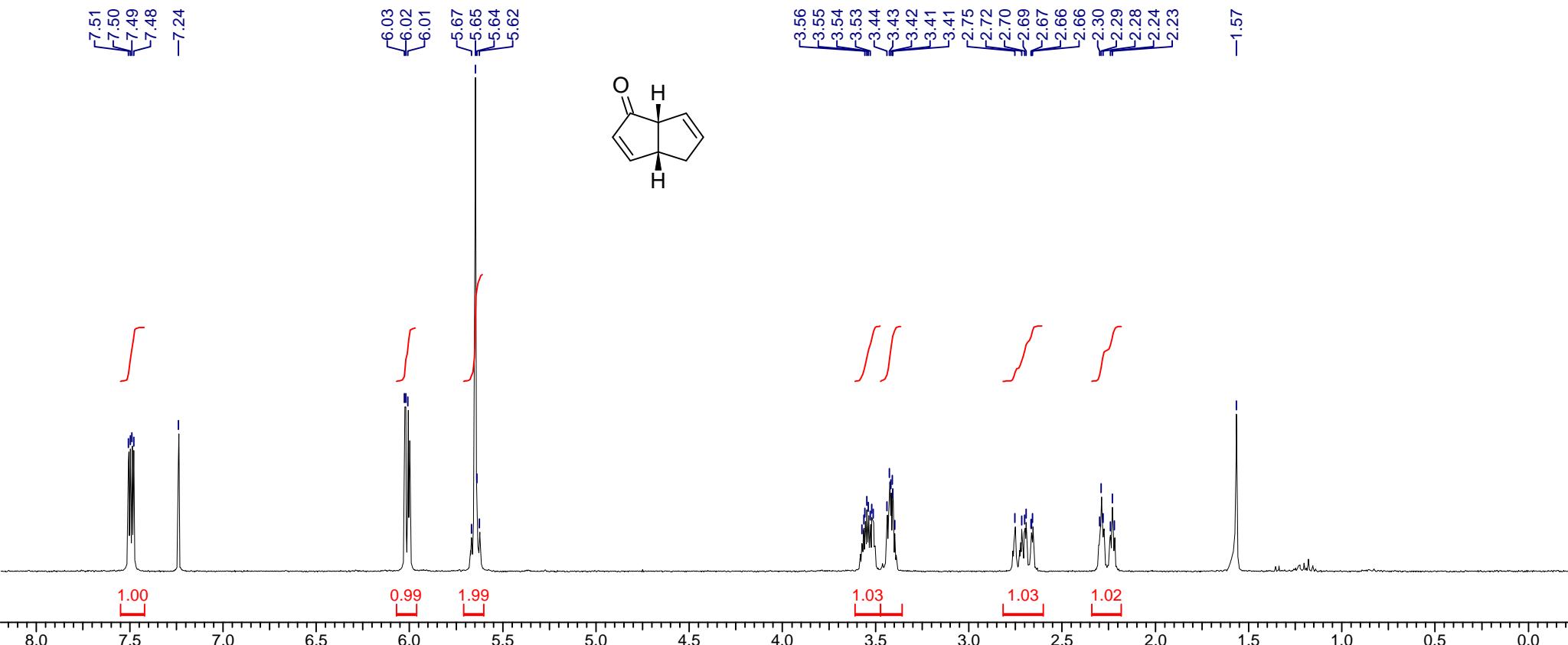
Acquisition Time (sec)	1.7695	Comment	Jmod sur CO1-90F1		Date	04/09/2008 11:05:42	
Frequency (MHz)	75.47	Nucleus	13C	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	18518.52



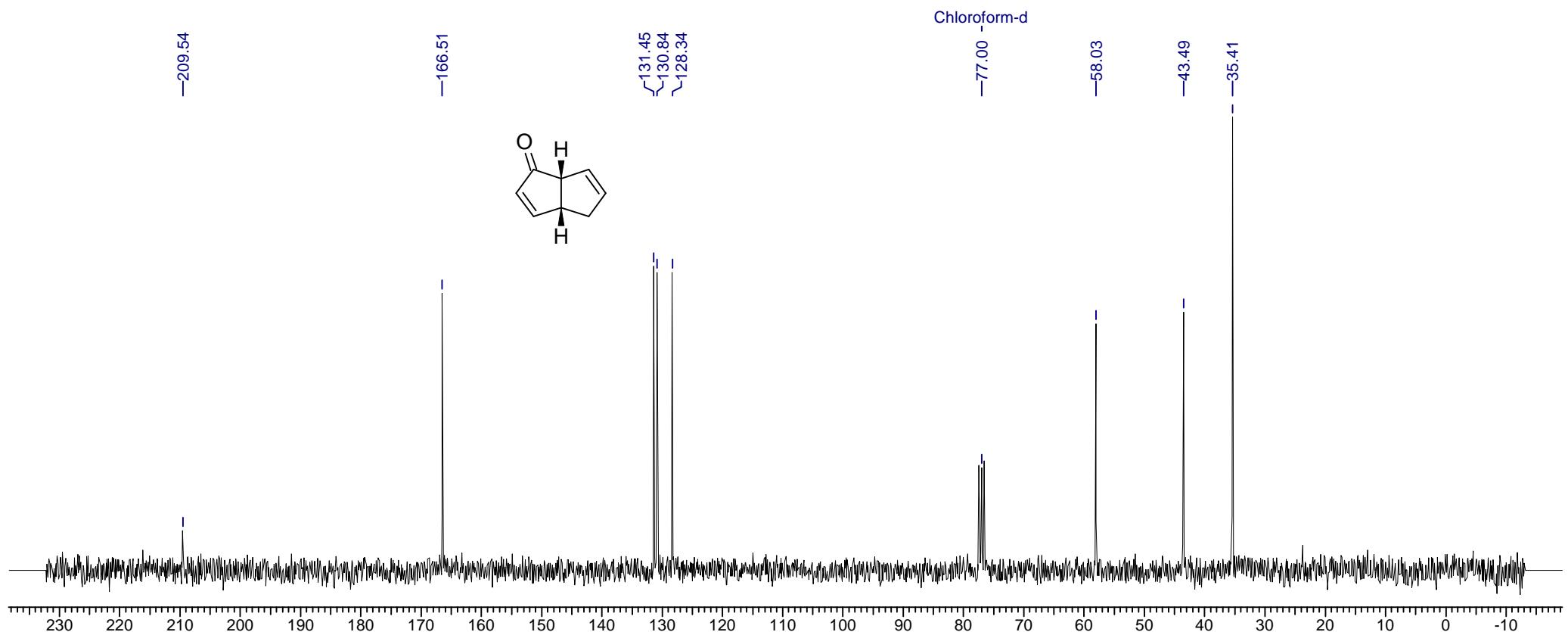
Acquisition Time (sec)	10.3547	Comment	1H sur CO1-109 pur		Date	03/09/2008 15:48:38	
Frequency (MHz)	300.13	Nucleus	1H	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	3164.56



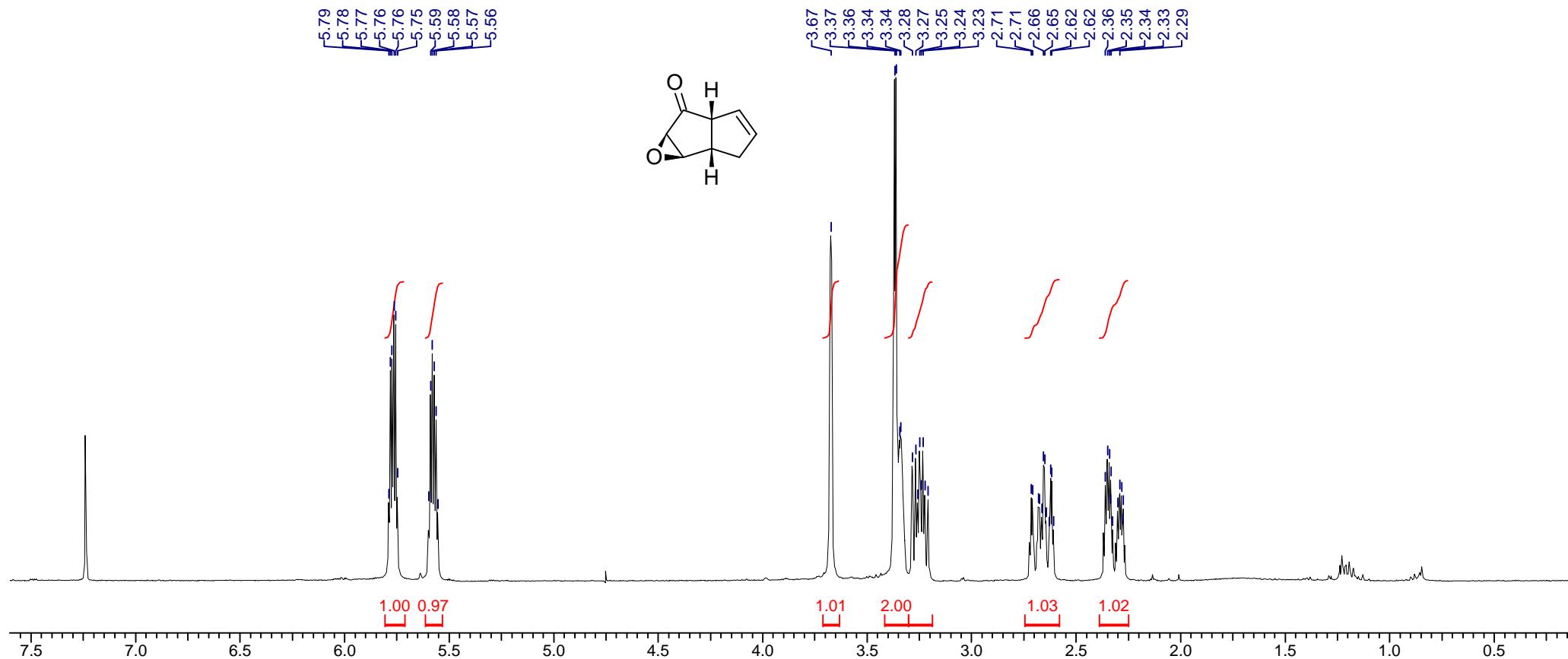
<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	enantiopure enone from minus alcool		<b>Date</b>	23/07/2008 15:16:26	
<b>Frequency (MHz)</b>	300.13	<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768
<b>Temperature (grad C)</b>	0.000					<b>Sweep Width (Hz)</b>	3164.56



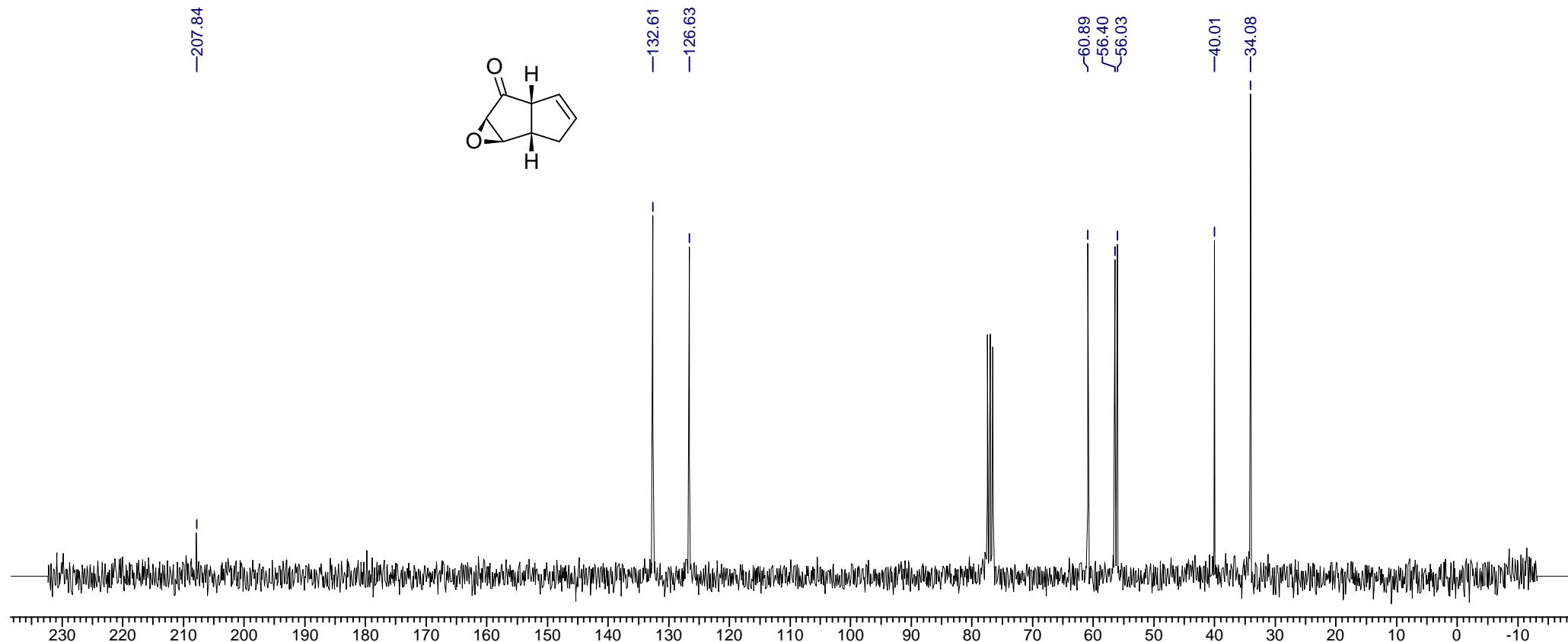
<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	colonne IBX oxidation		<b>Date</b>	23/07/2008 13:44:36	
<b>Frequency (MHz)</b>	75.47	<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768
<b>Temperature (grad C)</b>	0.000					<b>Sweep Width (Hz)</b>	18518.52



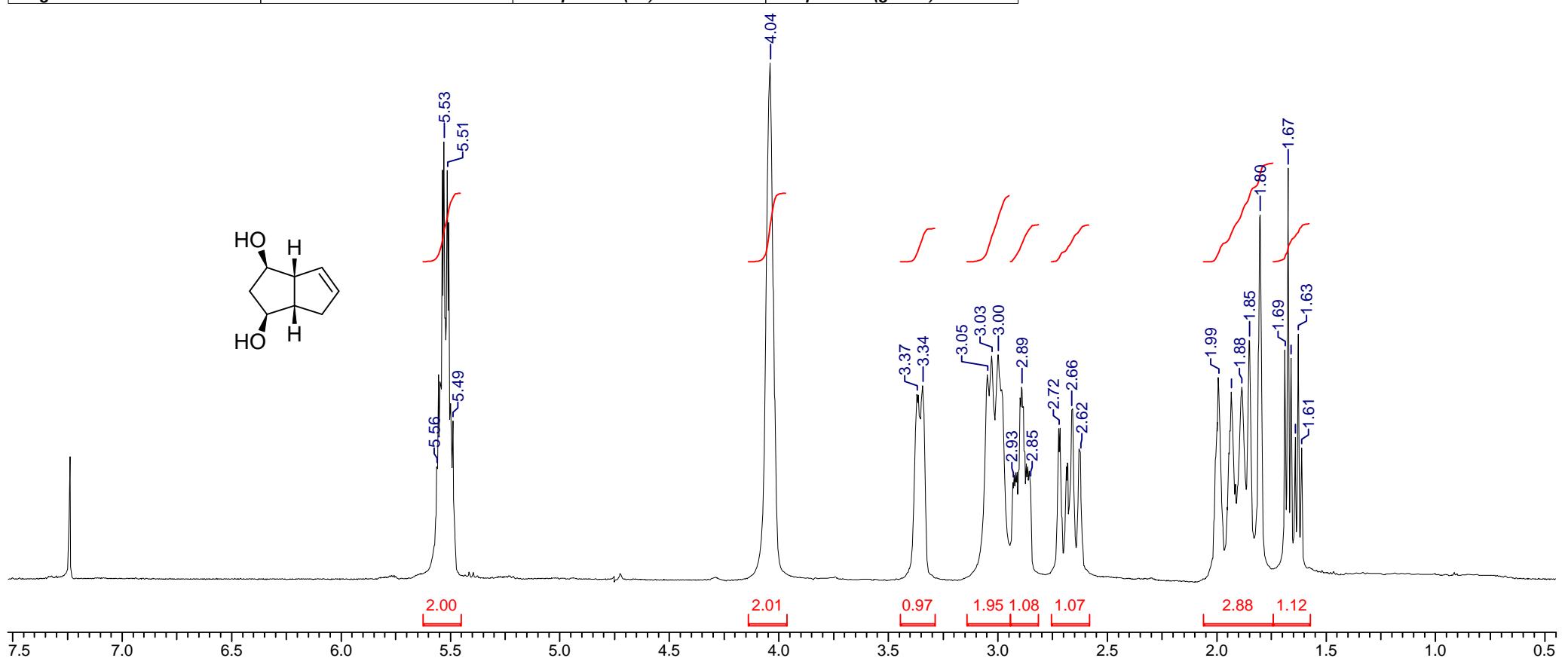
Acquisition Time (sec)	10.3547	Comment	jmg280 3 1	Date	23/07/2008 14:30:04	Frequency (MHz)	300.13		
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C)	0.000



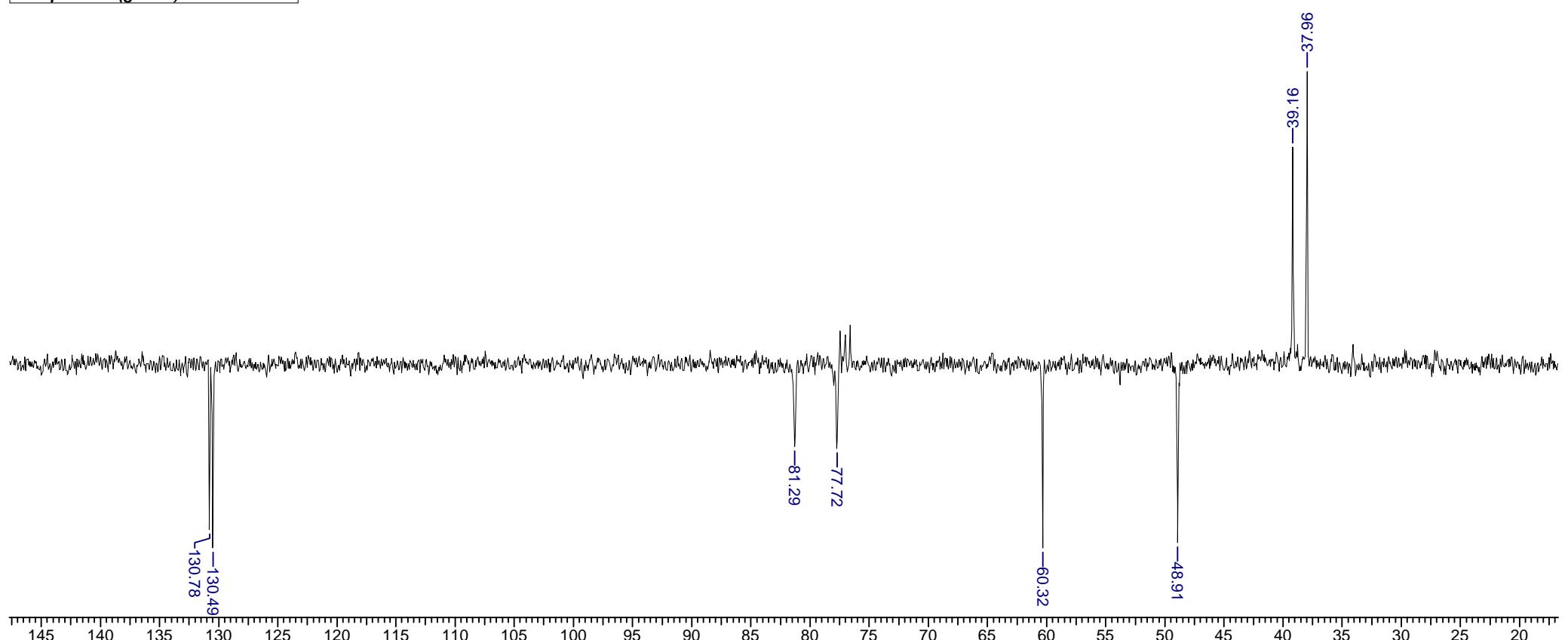
<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	fraction 3 epoxydattion		<b>Date</b>	23/07/2008	15:57:42
<b>Frequency (MHz)</b>	75.47	<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768
<b>Temperature (grad C)</b>	0.000					<b>Sweep Width (Hz)</b>	18518.52



Acquisition Time (sec)	10.3547	Comment	pure diol	Date	23/07/2008 15:16:18	Frequency (MHz)	300.13	Nucleus	1H
Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C)	0.000		

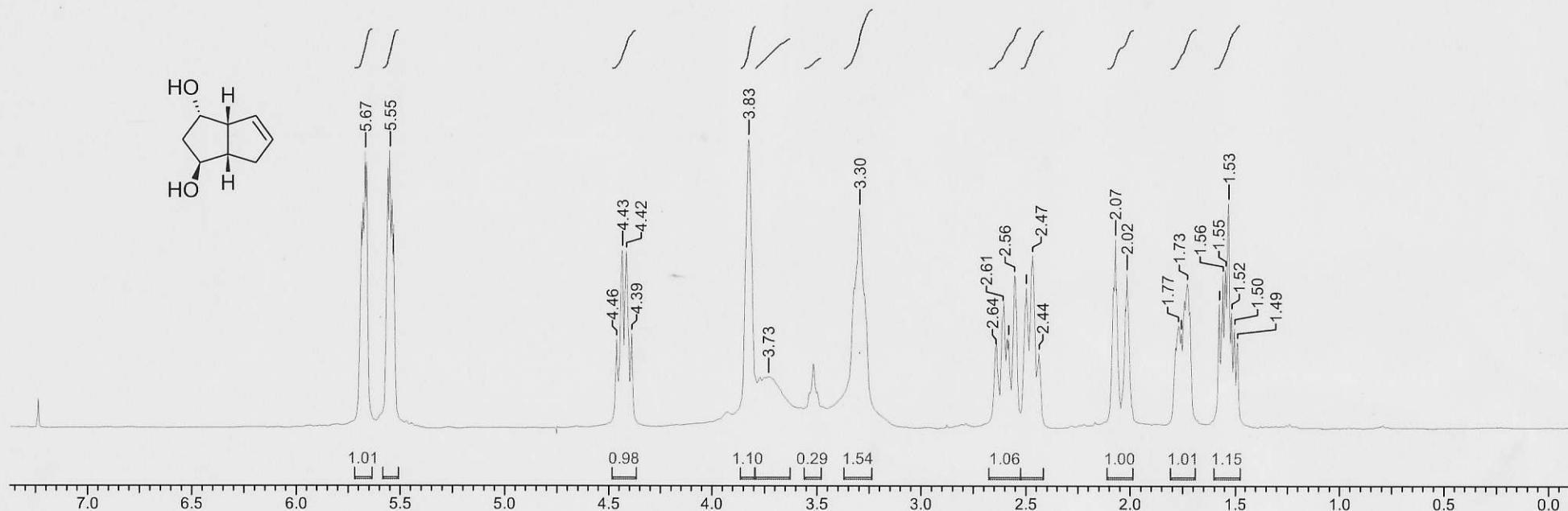


Acquisition Time (sec)	1.7695	Comment	LiAlH4 reduction de ketoepoxide de -78 at -25C		Date	23/07/2008 17:37:02	
Frequency (MHz)	75.47	Nucleus	13C	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	18518.52



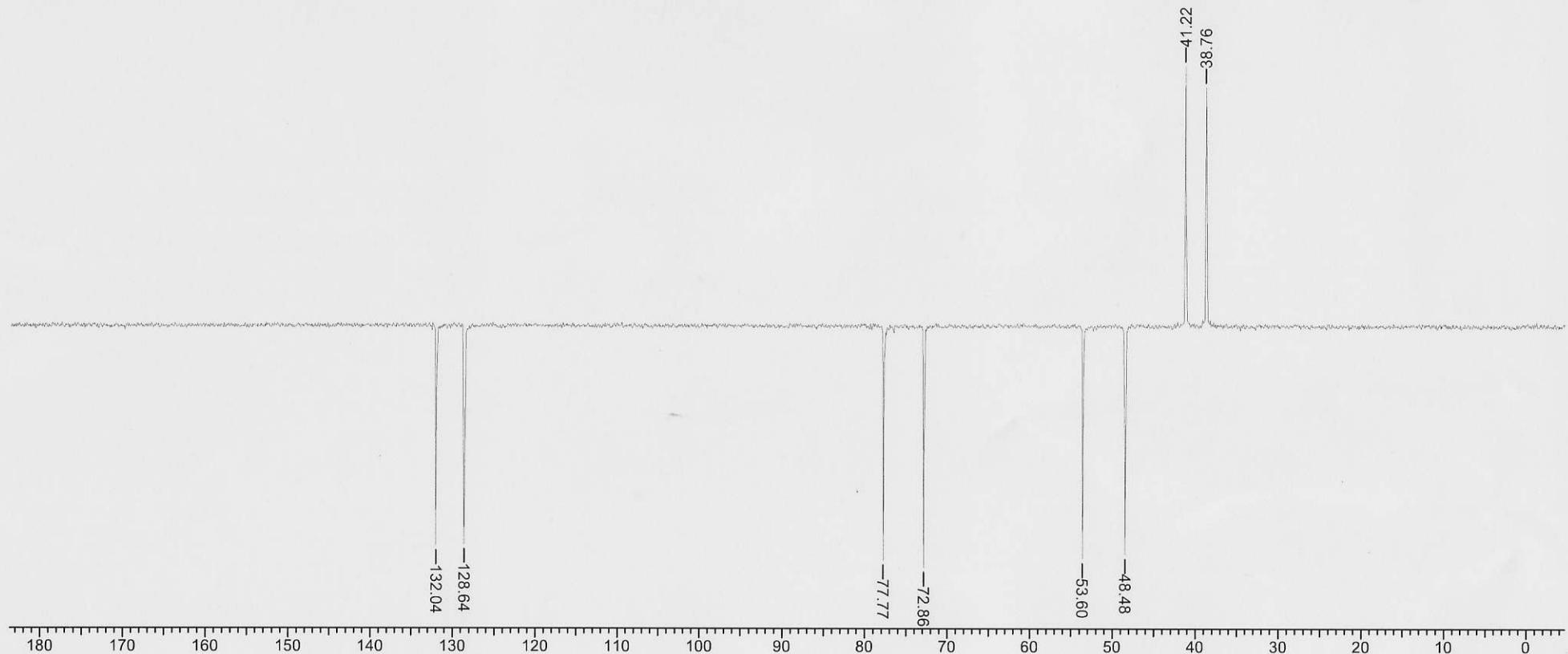
2 Sep 2008

Acquisition Time (sec)	10.3547	Comment	jmg284 1 1	Date	23/07/2008 14:31:42	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56 Temperature (grad C) 0.000



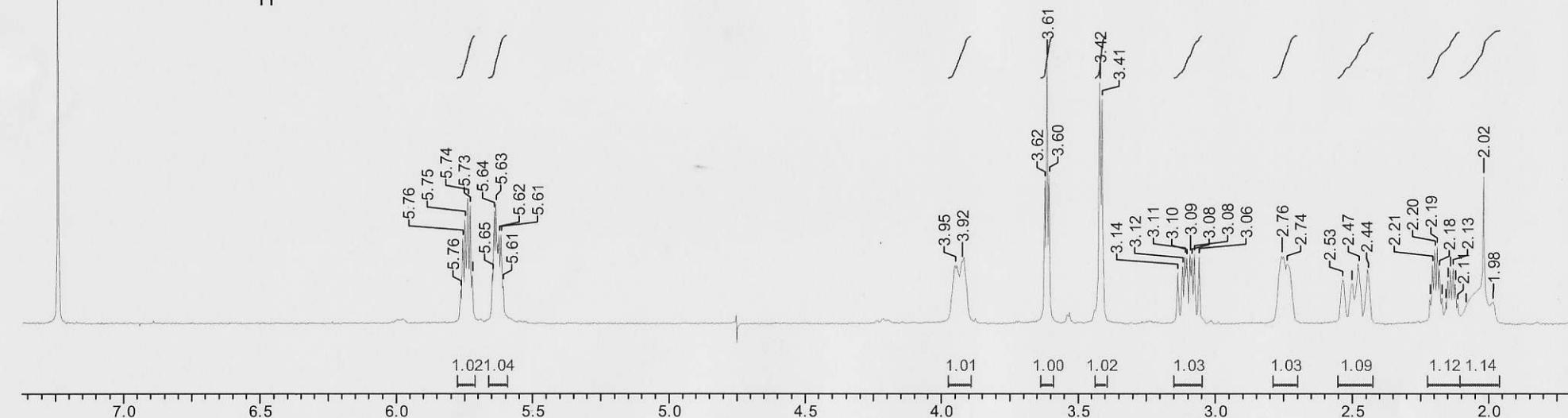
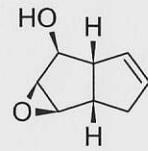
2 Sep 2008

Acquisition Time (sec)	1.7695	Comment	jmg284 3 1	Date	23/07/2008 14:31:50	Frequency (MHz)	75.47
Nucleus	13C	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	18518.52

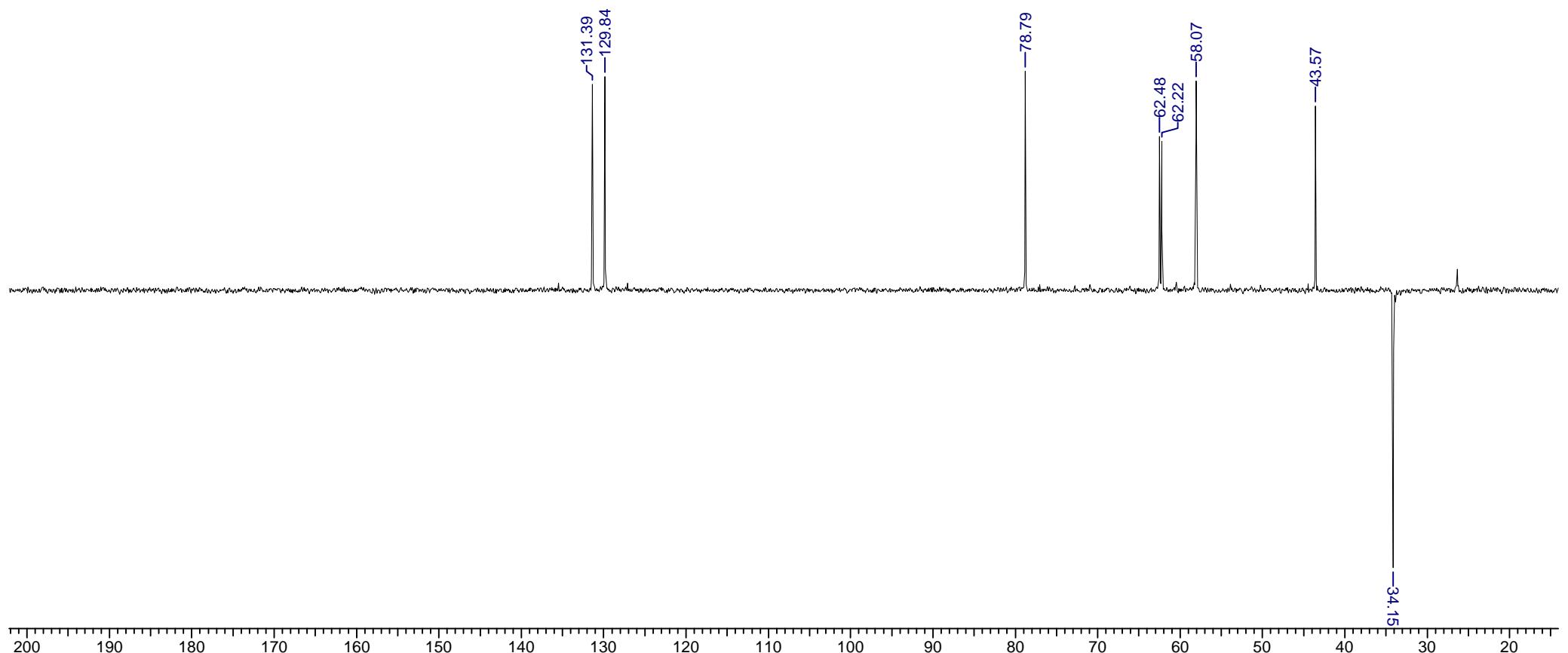


3 Sep 2008

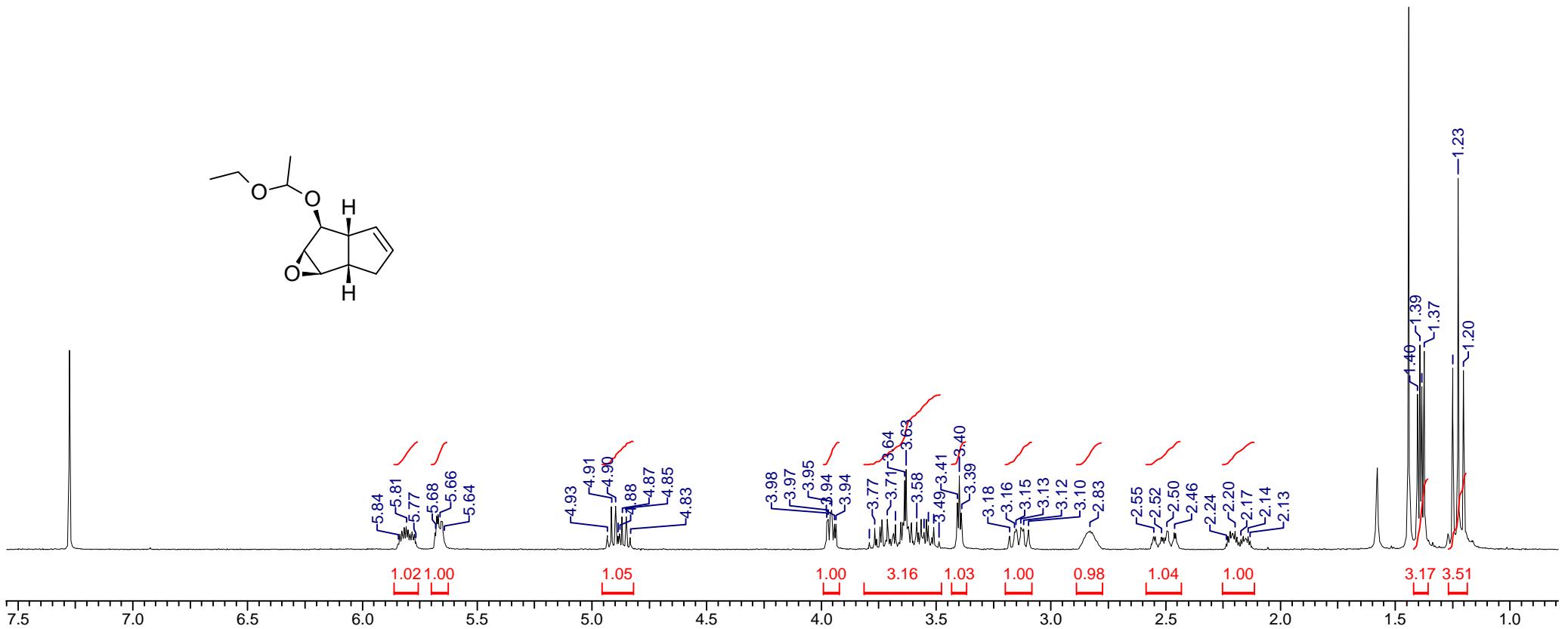
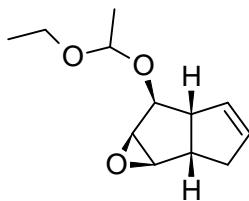
Acquisition Time (sec)	10.3547	Comment	LiAlH4 reduction at -78C only		Date	23/07/2008	14:46:22
Frequency (MHz)	300.13	Nucleus	1H	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	3164.56



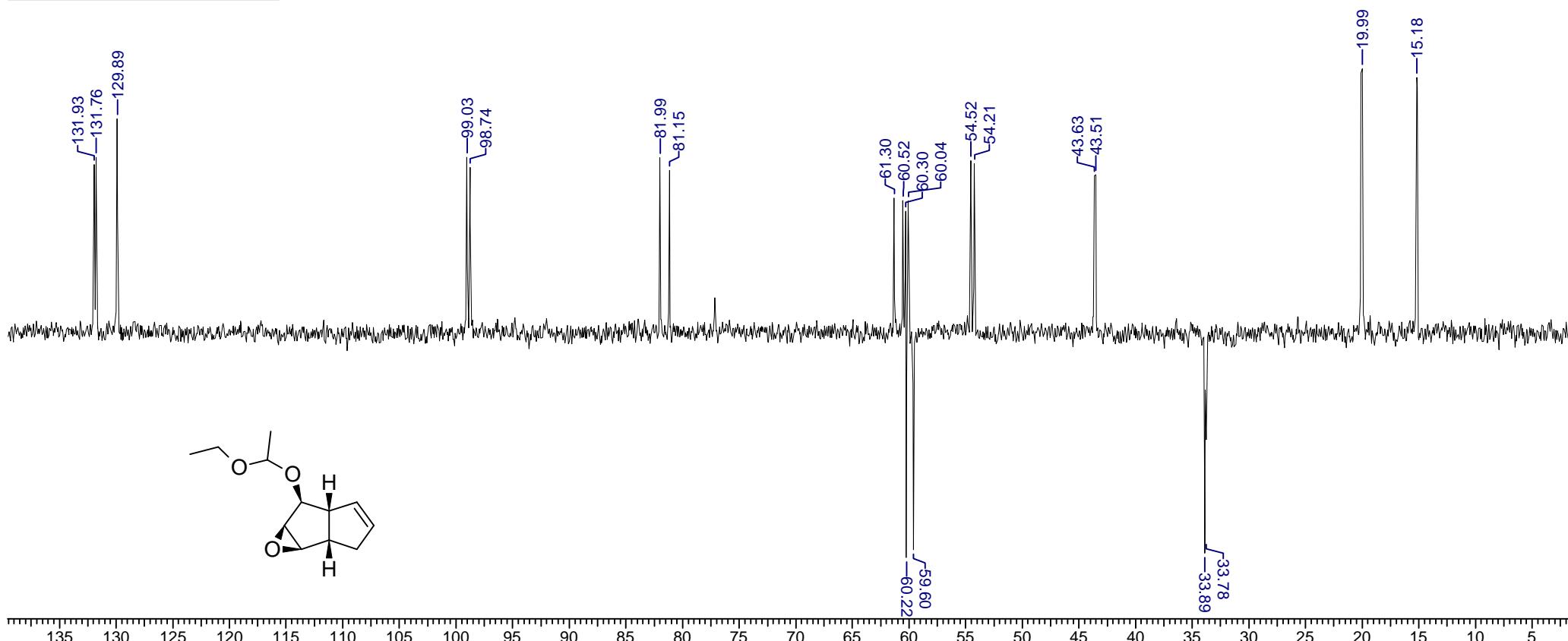
Acquisition Time (sec)	1.7695	Comment	13C sur	Date	03/09/2008 15:52:56	Frequency (MHz)	75.47	Nucleus	13C
Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	18518.52	Temperature (grad C)	0.000		



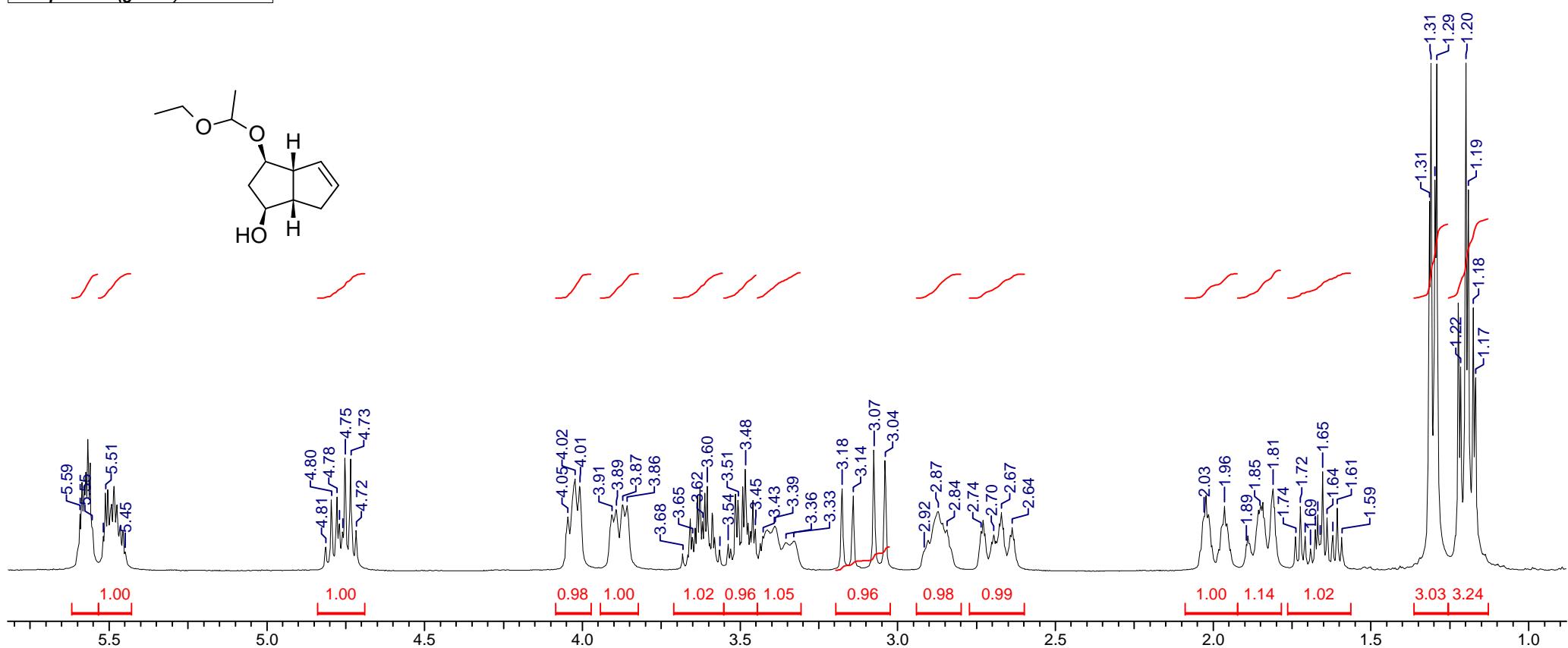
Acquisition Time (sec)	10.3547	Comment	1 H RMN sur yas072 exp3		Date	03/09/2008 15:53:46	
Frequency (MHz)	300.13	Nucleus	1H	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	3164.56



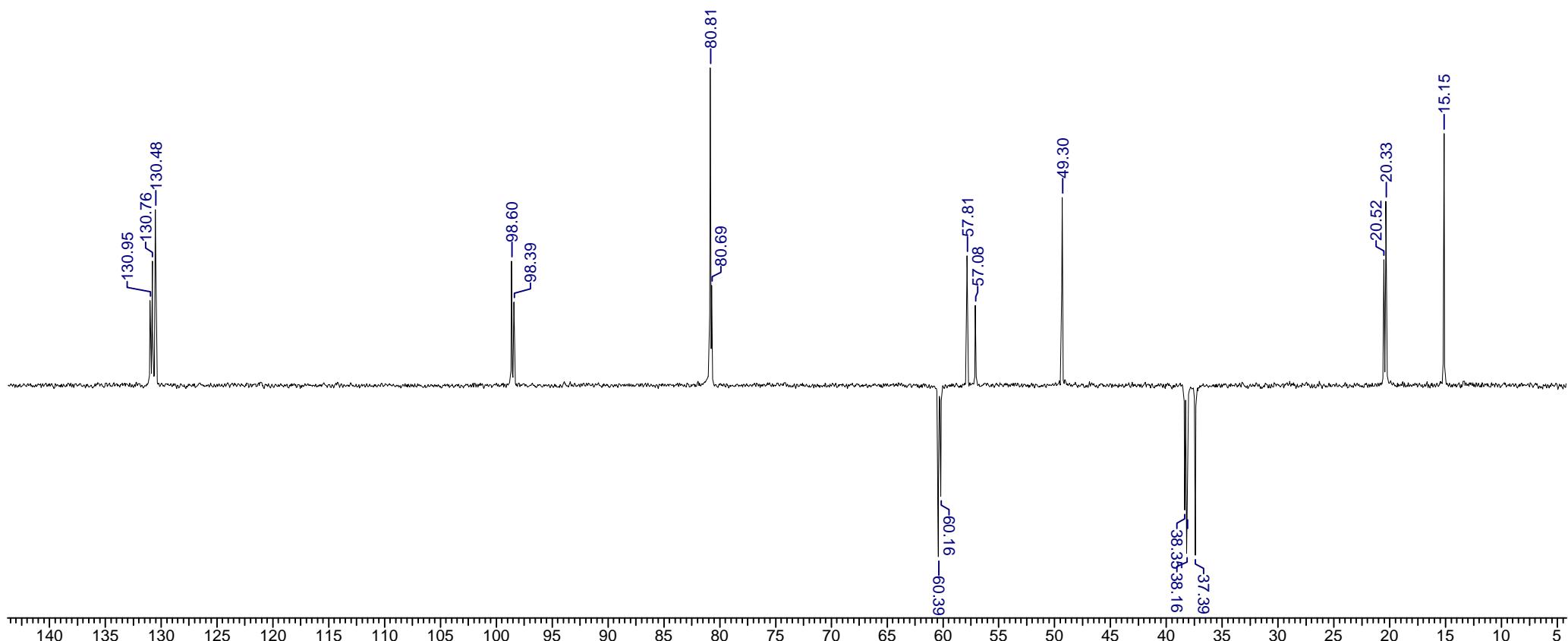
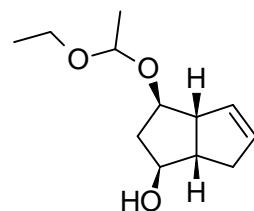
Acquisition Time (sec)	1.7695	Comment	Dept135 sur yas072 exp 9		Date	03/09/2008 15:54:12	
Frequency (MHz)	75.47	Nucleus	13C	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	18518.52



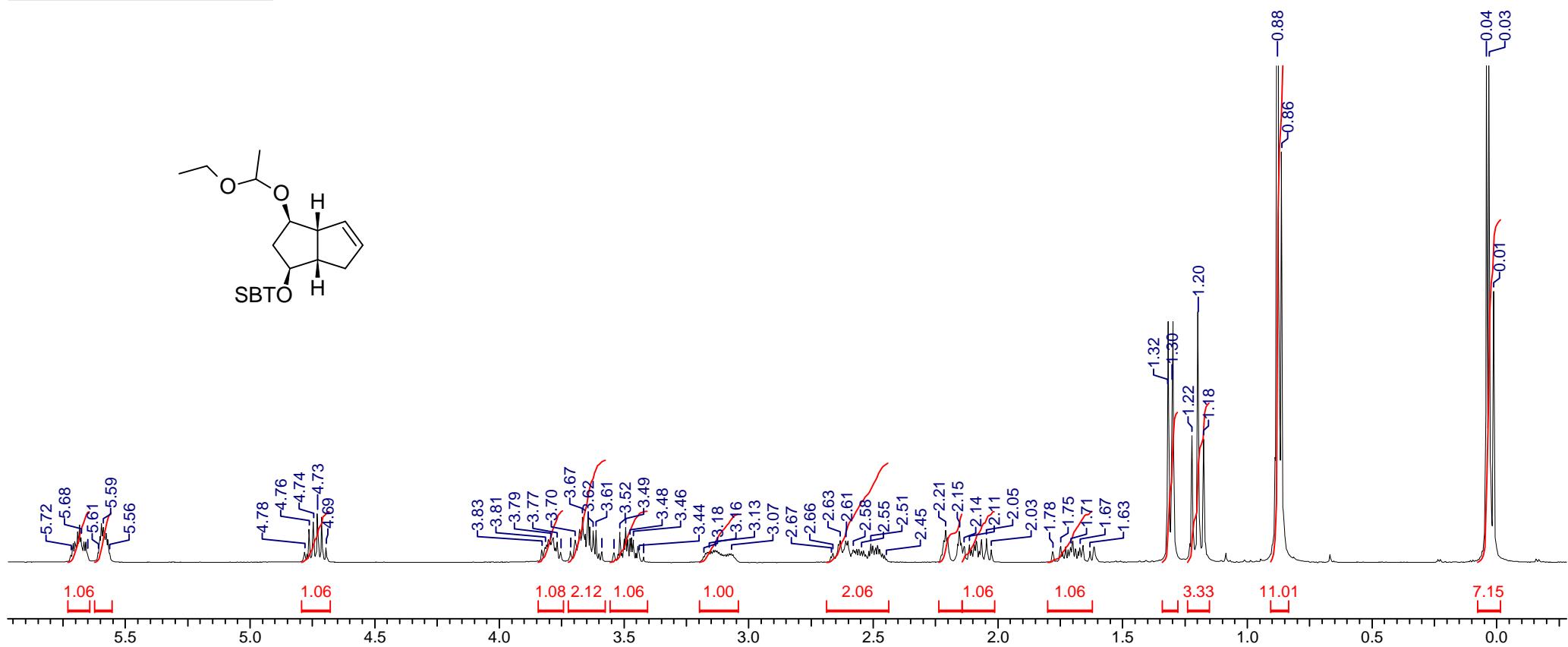
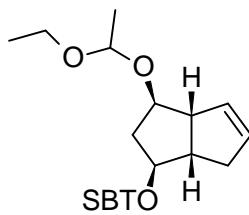
Acquisition Time (sec)	10.3547	Comment	1H sur yas073 exp1		Date	03/09/2008 15:54:34	
Frequency (MHz)	300.13	Nucleus	1H	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	3164.56



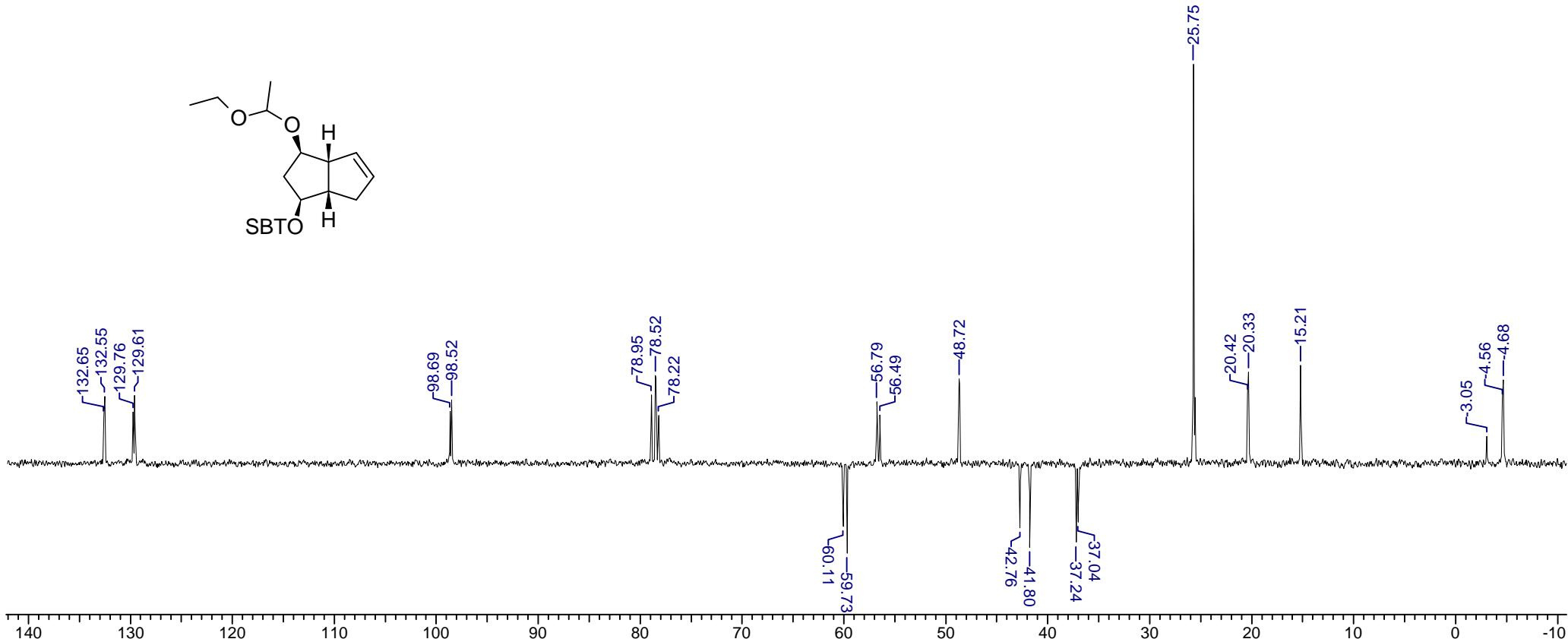
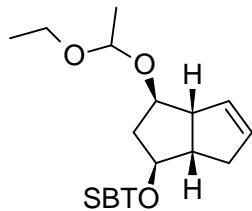
Acquisition Time (sec)	1.7695	Comment	Dept135 sur yas073 exp3		Date	03/09/2008	15:54:44
Frequency (MHz)	75.47	Nucleus	13C	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	18518.52



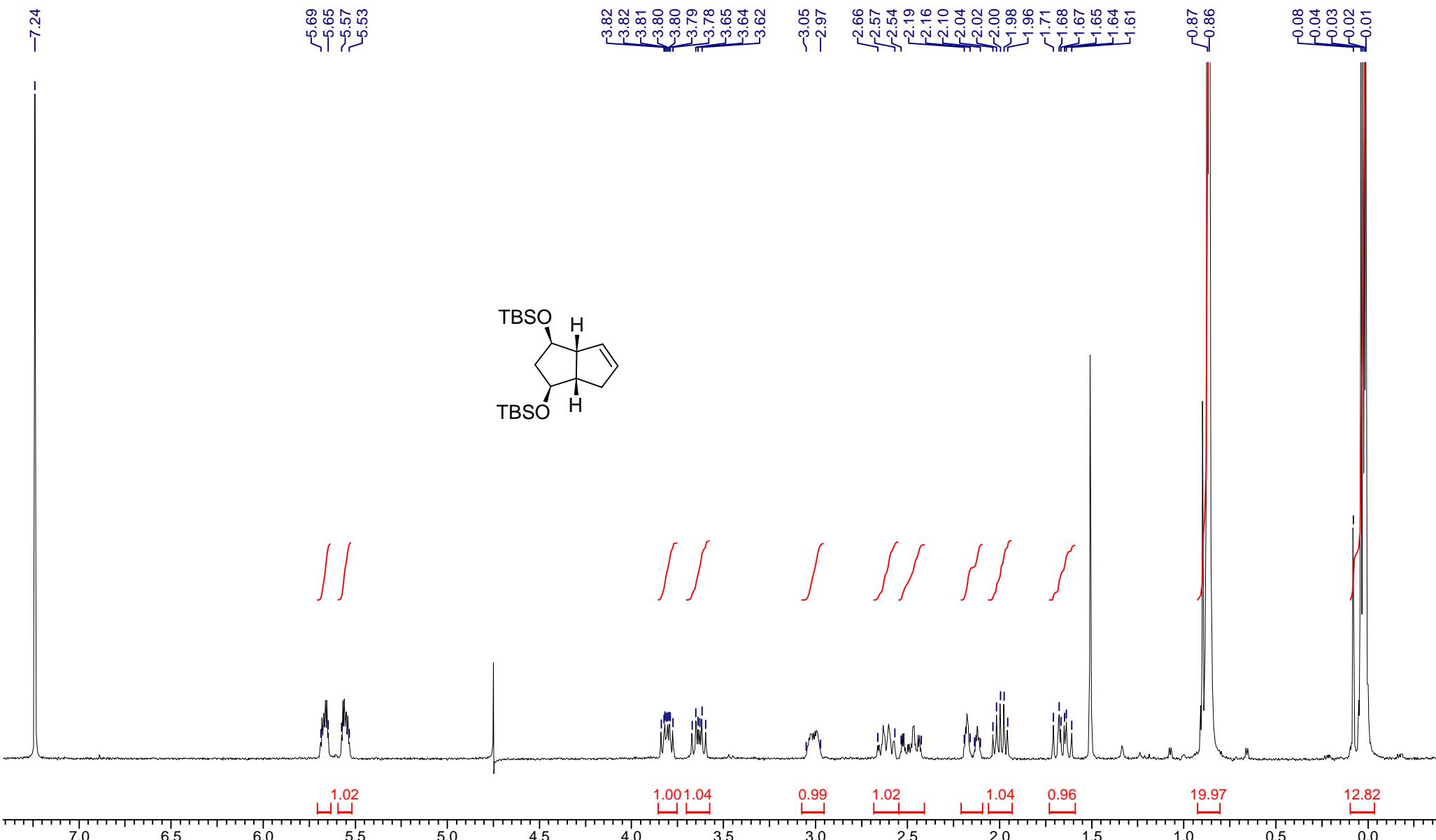
Acquisition Time (sec)	10.3547	Comment	1H sur yas079 exp6		Date	03/09/2008 15:55:18	
Frequency (MHz)	300.13	Nucleus	1H	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	3164.56

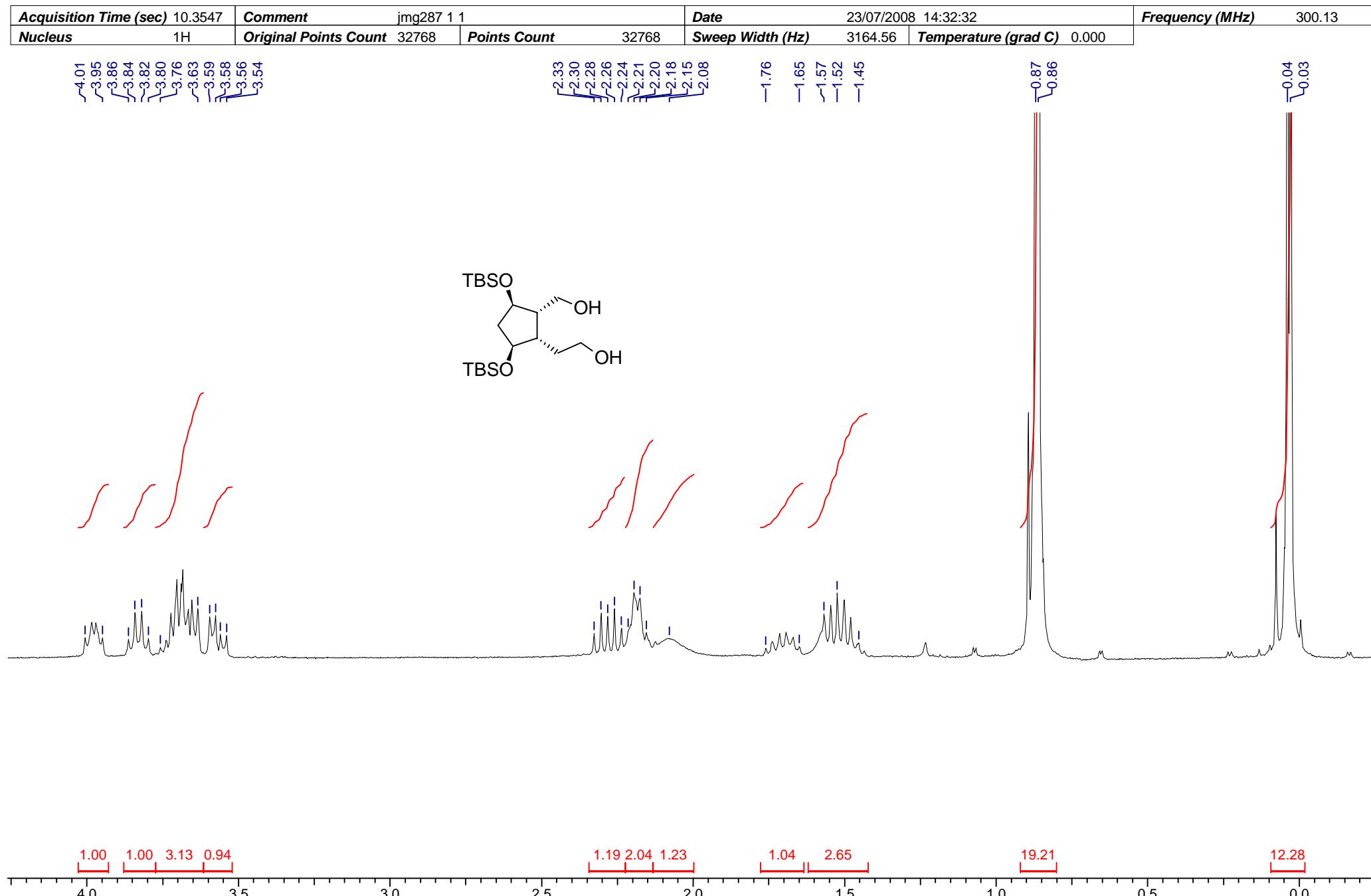


Acquisition Time (sec)	1.7695	Comment	13C DEPT sur Yas079 exp 9		Date	03/09/2008 15:55:32	
Frequency (MHz)	75.47	Nucleus	13C	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	18518.52

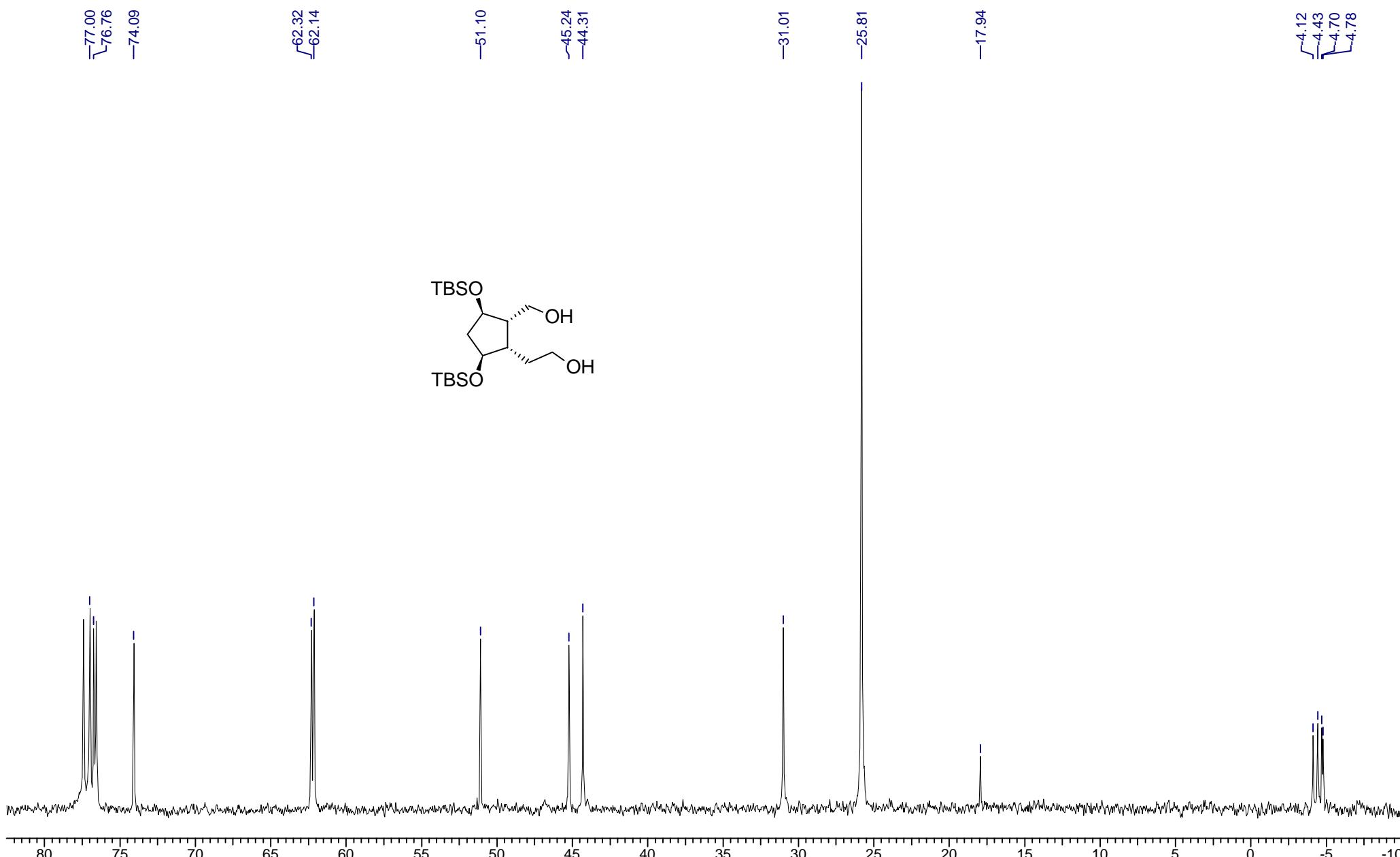


Acquisition Time (sec)	10.3547	Comment	crude TBS protection sur diol		Date	23/07/2008 14:32:22	
Frequency (MHz)	300.13	Nucleus	1H	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	3164.56

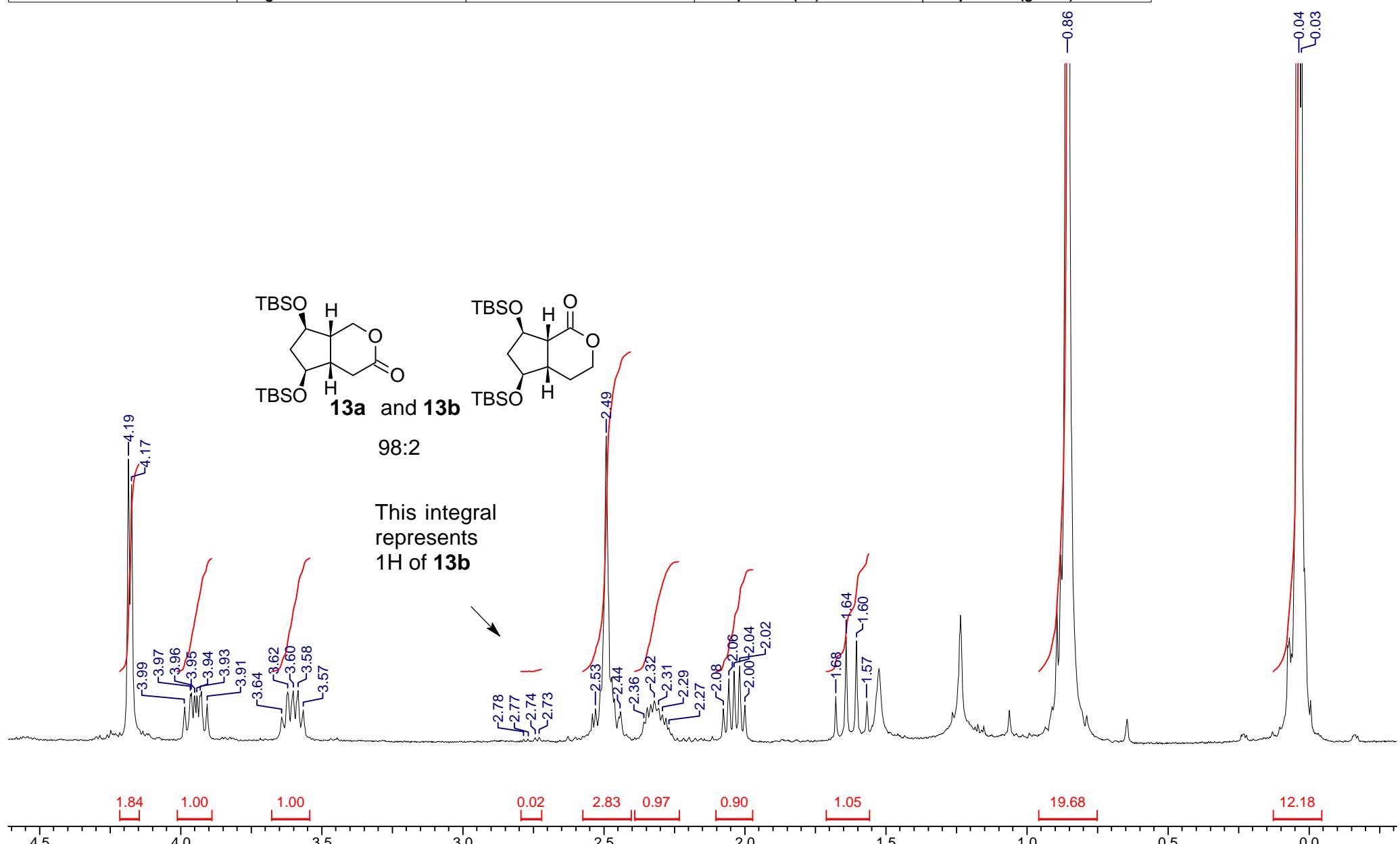




<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmg287 3 1		<b>Date</b>	23/07/2008 14:32:40	<b>Frequency (MHz)</b>	75.47	
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52	<b>Temperature (grad C)</b>	0.000

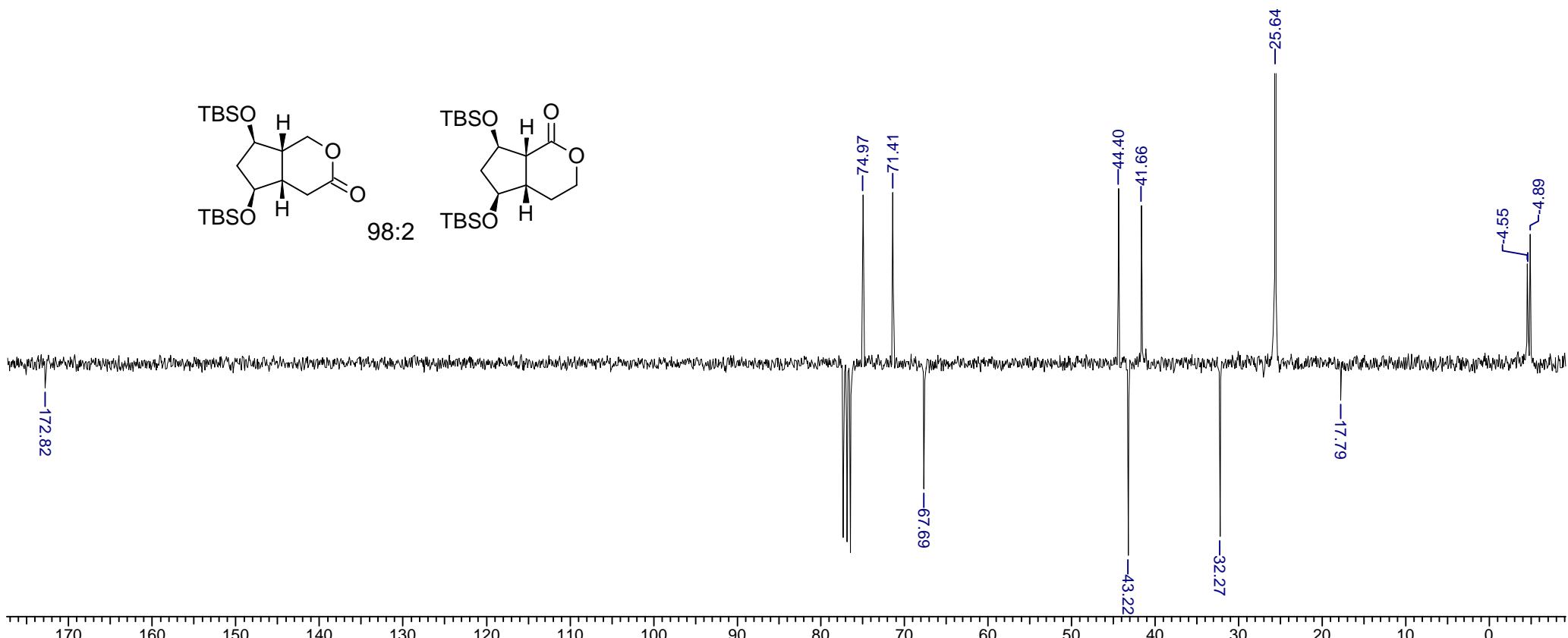


Acquisition Time (sec)	10.3547	Comment	jmg288 1 1	Date	23/07/2008 14:32:44	Frequency (MHz)	300.13		
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C)	0.000

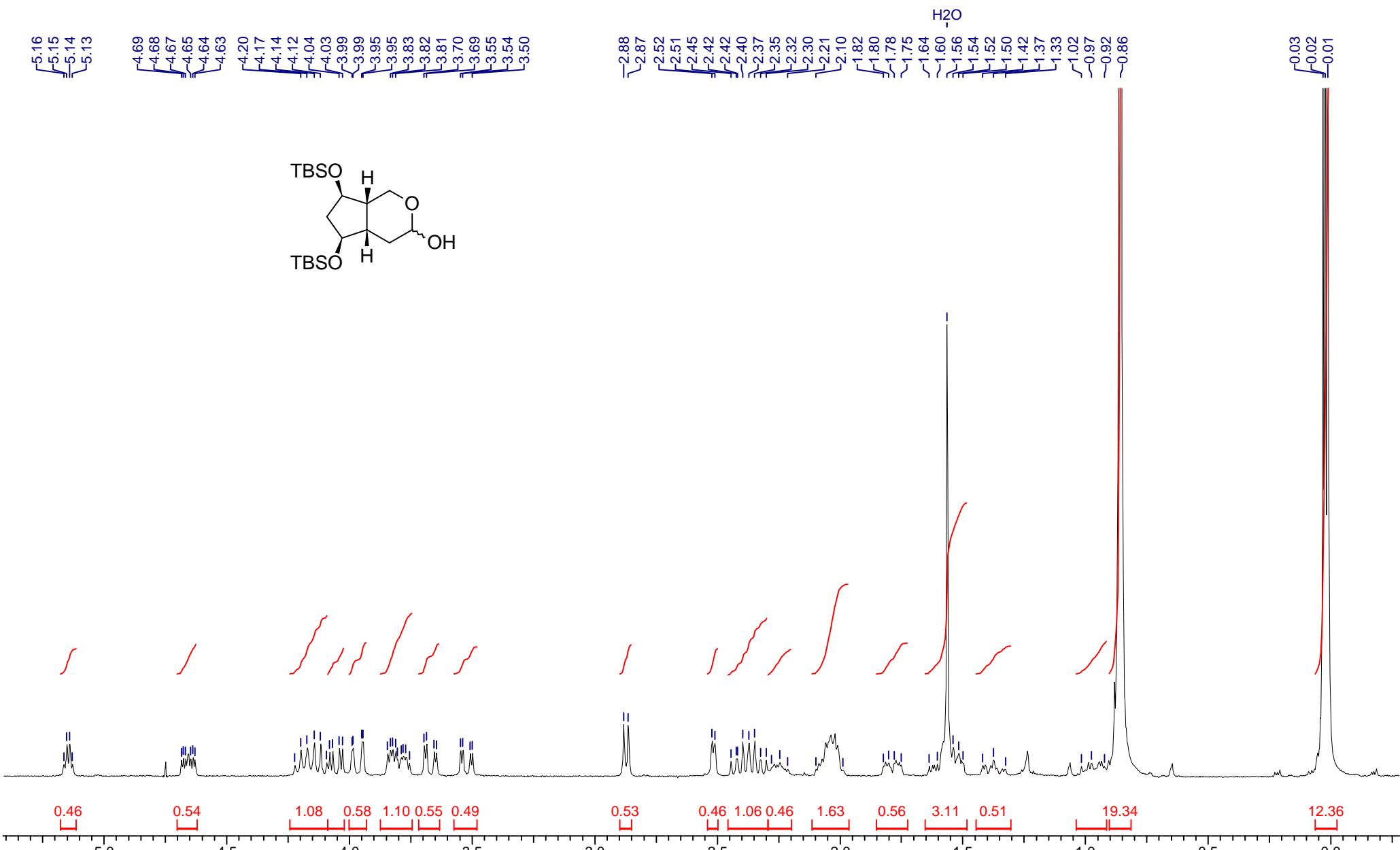


3 Sep 2008

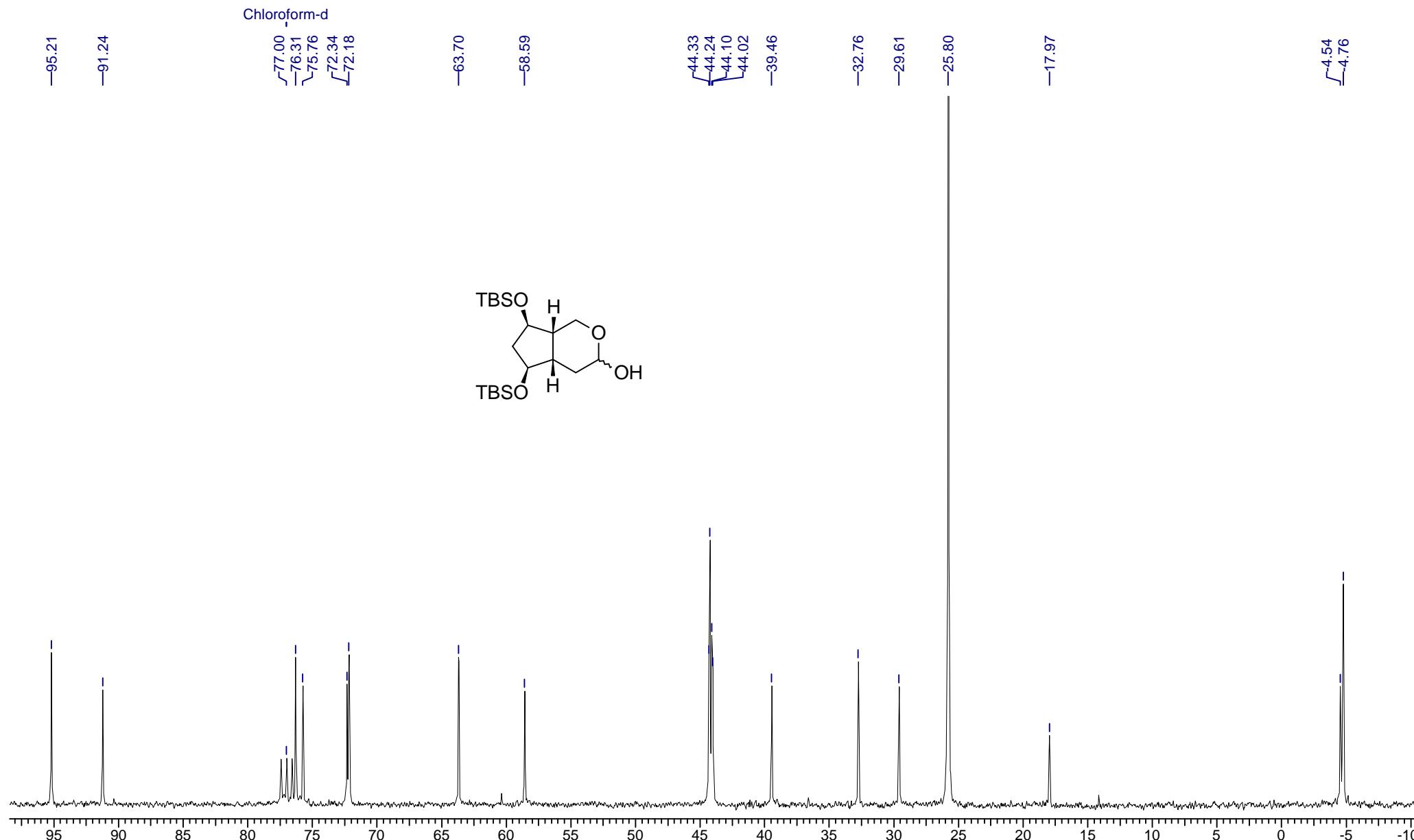
Acquisition Time (sec)	1.7695	Comment	Jmod sur CO1-45 pur		Date	03/09/2008	15:46:28
Frequency (MHz)	75.47	Nucleus	13C	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	18518.52

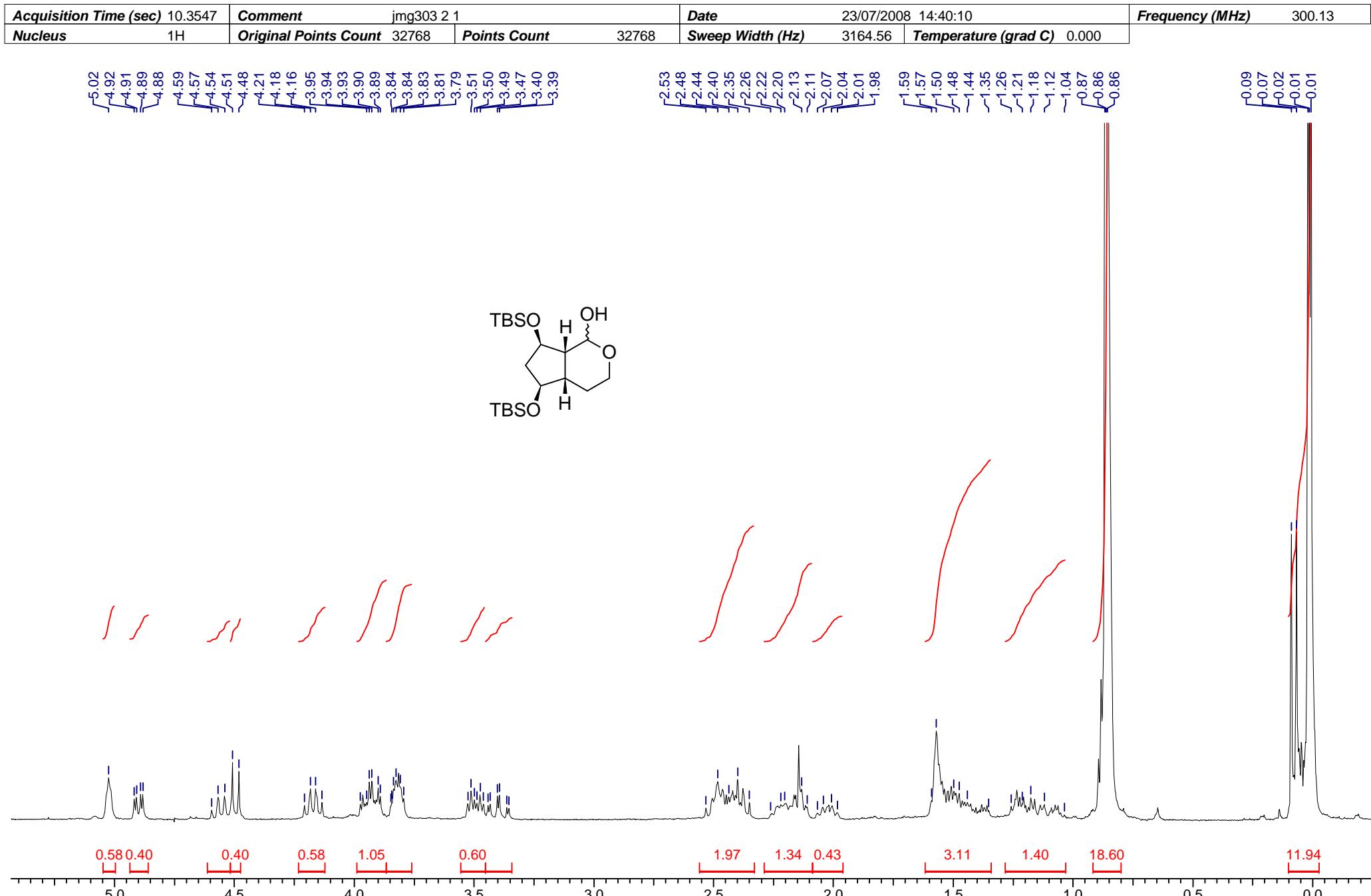


<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	1H sur	<b>Date</b>	23/07/2008	14:38:40	<b>Frequency (MHz)</b>	300.13	<b>Nucleus</b>	1H
<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000			



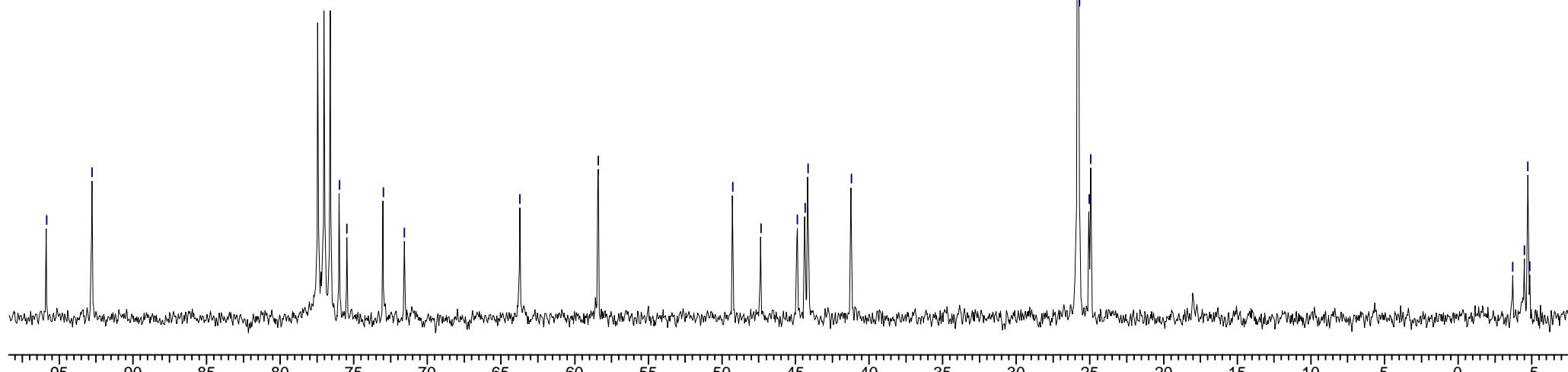
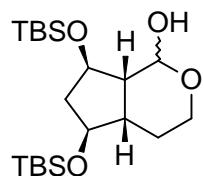
<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmg301 4 1		<b>Date</b>	23/07/2008 14:38:28	<b>Frequency (MHz)</b>	75.47	
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52	<b>Temperature (grad C)</b>	0.000



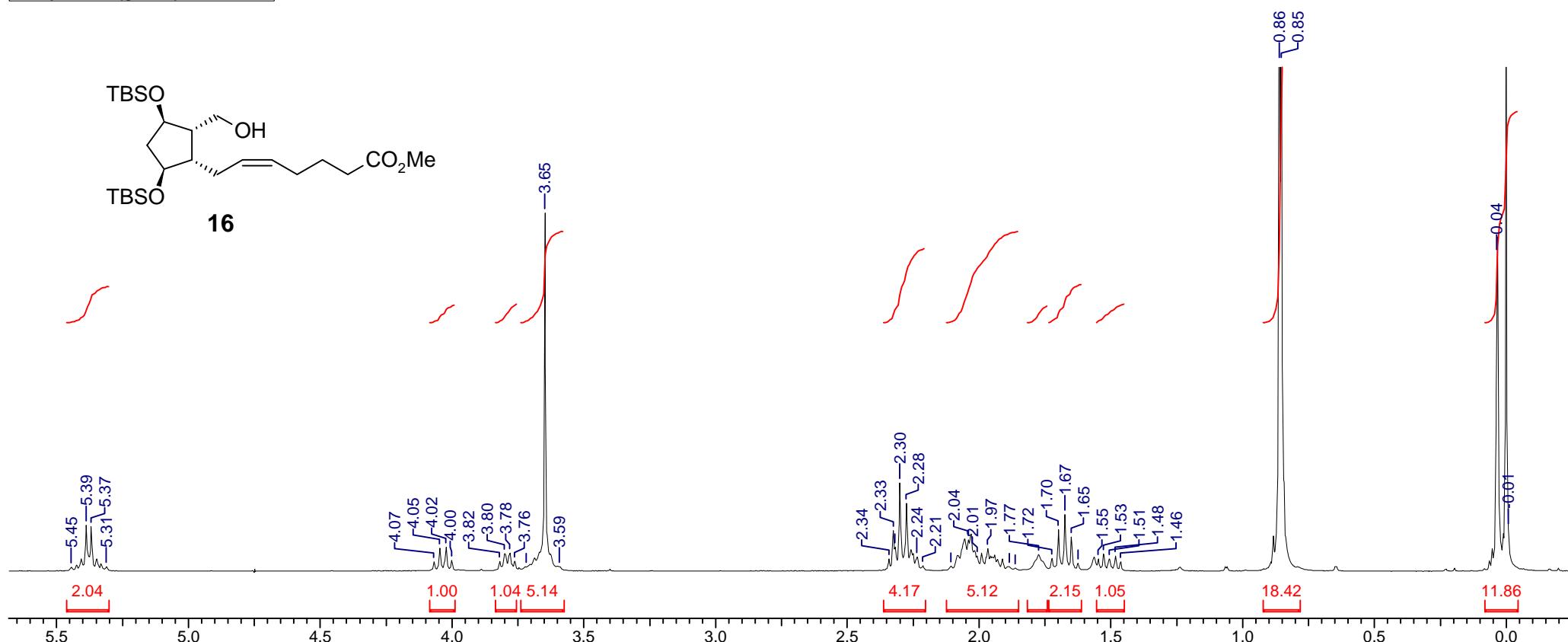


<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmg301 11 1	<b>Date</b>	23/07/2008 14:38:12	<b>Frequency (MHz)</b>	75.47
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52

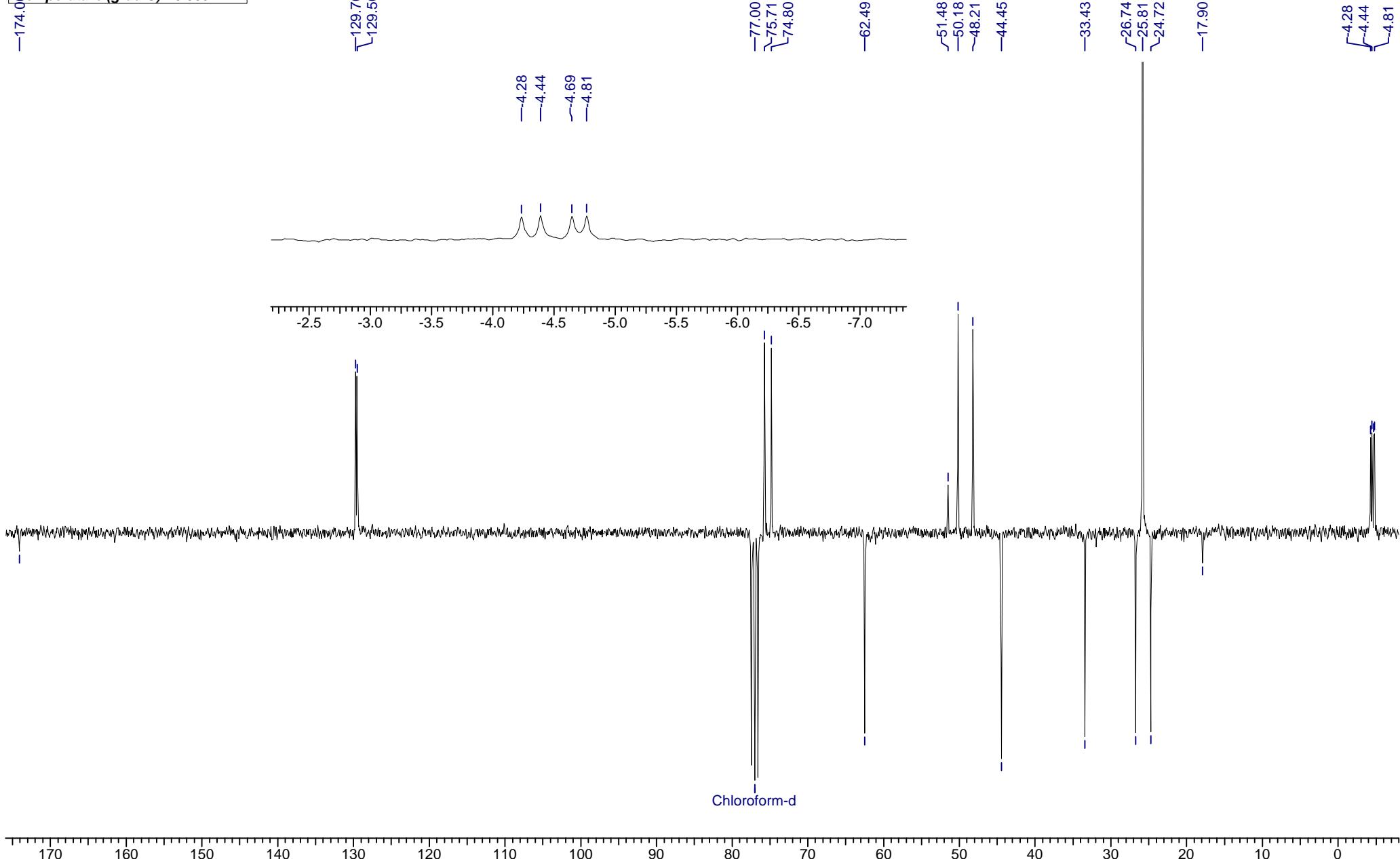
—95.87  
 —92.77  
 —75.98  
 —75.46  
 —73.00  
 —71.55  
 —63.72  
 —58.39  
 —49.27  
 —47.36  
 —44.87  
 —44.35  
 —44.15  
 —41.21  
 —25.81  
 —25.72  
 —25.05  
 —24.95  
 —3.69  
 —4.49  
 —4.72  
 —4.86



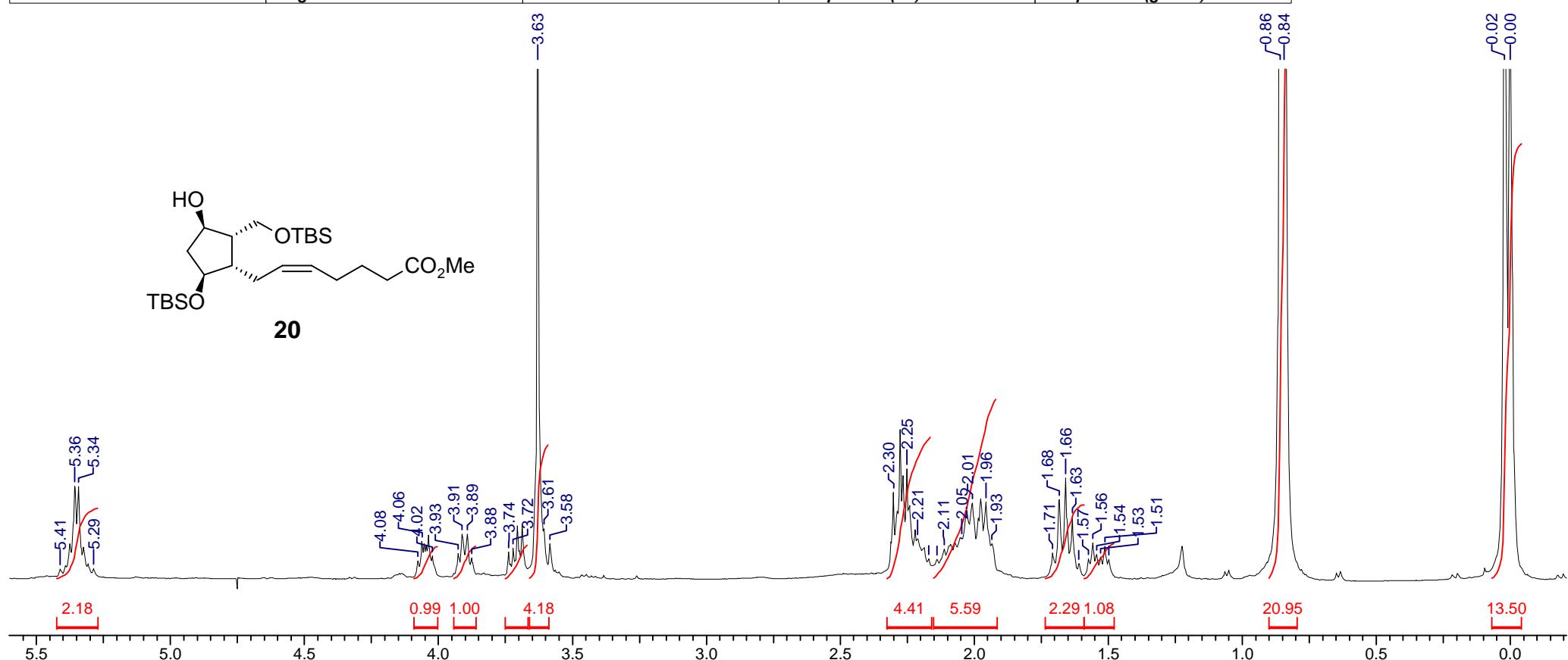
Acquisition Time (sec)	10.3547	Comment	1H sur idem_Rokach		Date	12/08/2008 16:17:28	
Frequency (MHz)	300.13	Nucleus	1H	Original Points Count	32768	Points Count	32768
Temperature (grad C)	0.000					Sweep Width (Hz)	3164.56



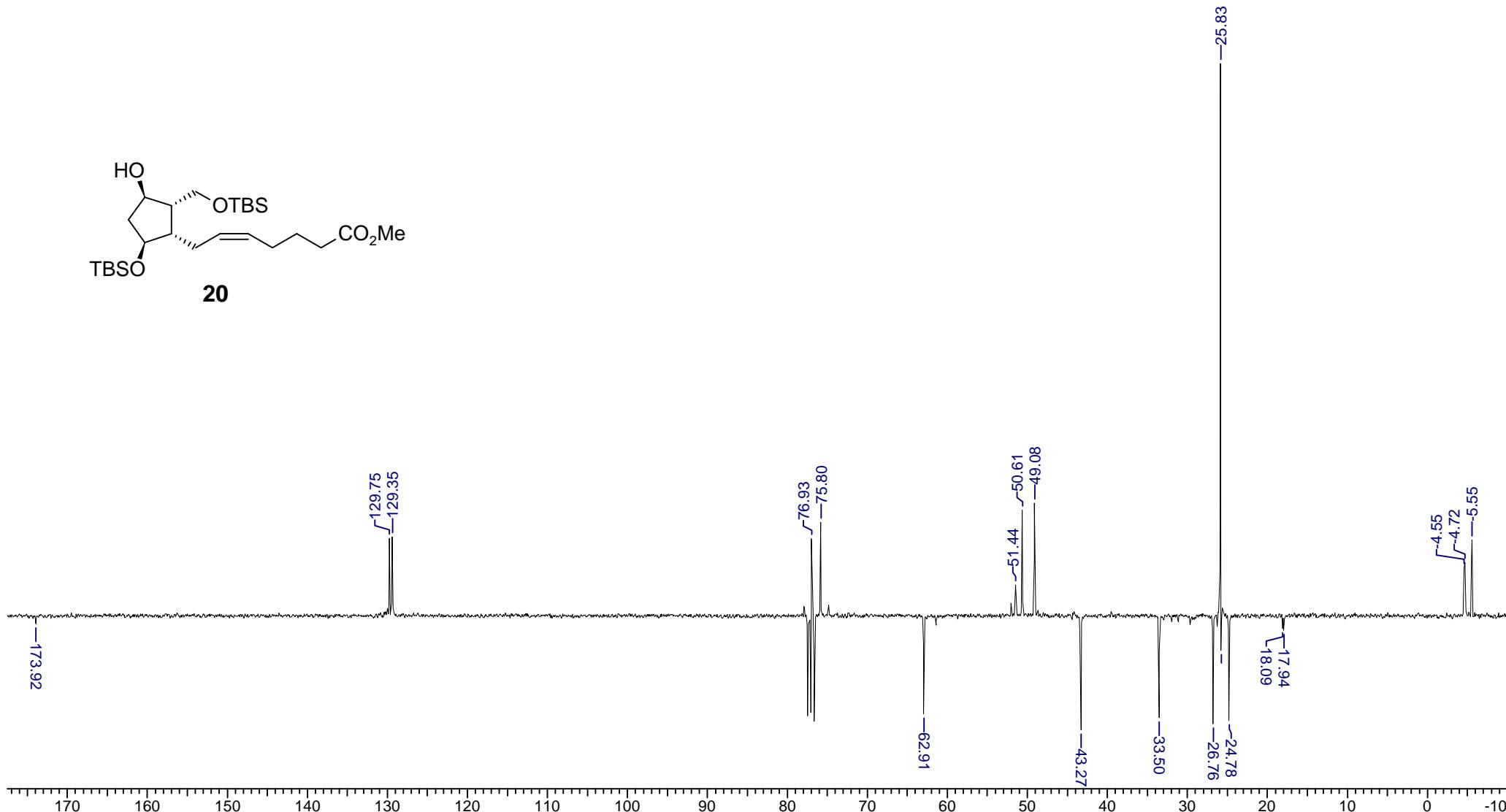
<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	Jmod sur idem <sub>R</sub> okach		<b>Date</b>	12/08/2008 16:17:00		
<b>Frequency (MHz)</b>	75.47	<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>
<b>Temperature (grad C)</b>	0.000							18518.52



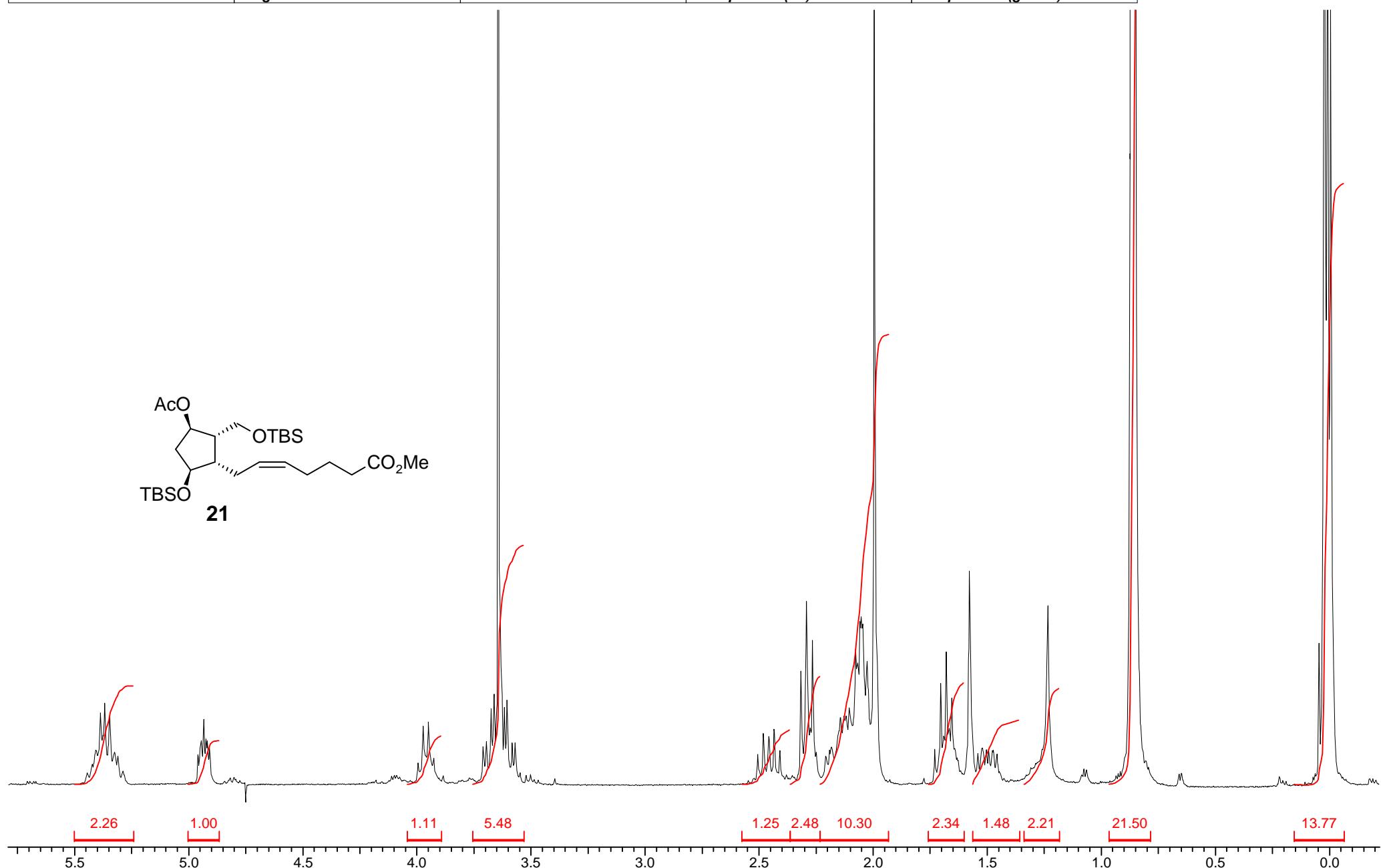
Acquisition Time (sec)	10.3547	Comment	jmg302 6 1	Date	23/07/2008 14:39:32	Frequency (MHz)	300.13		
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C)	0.000



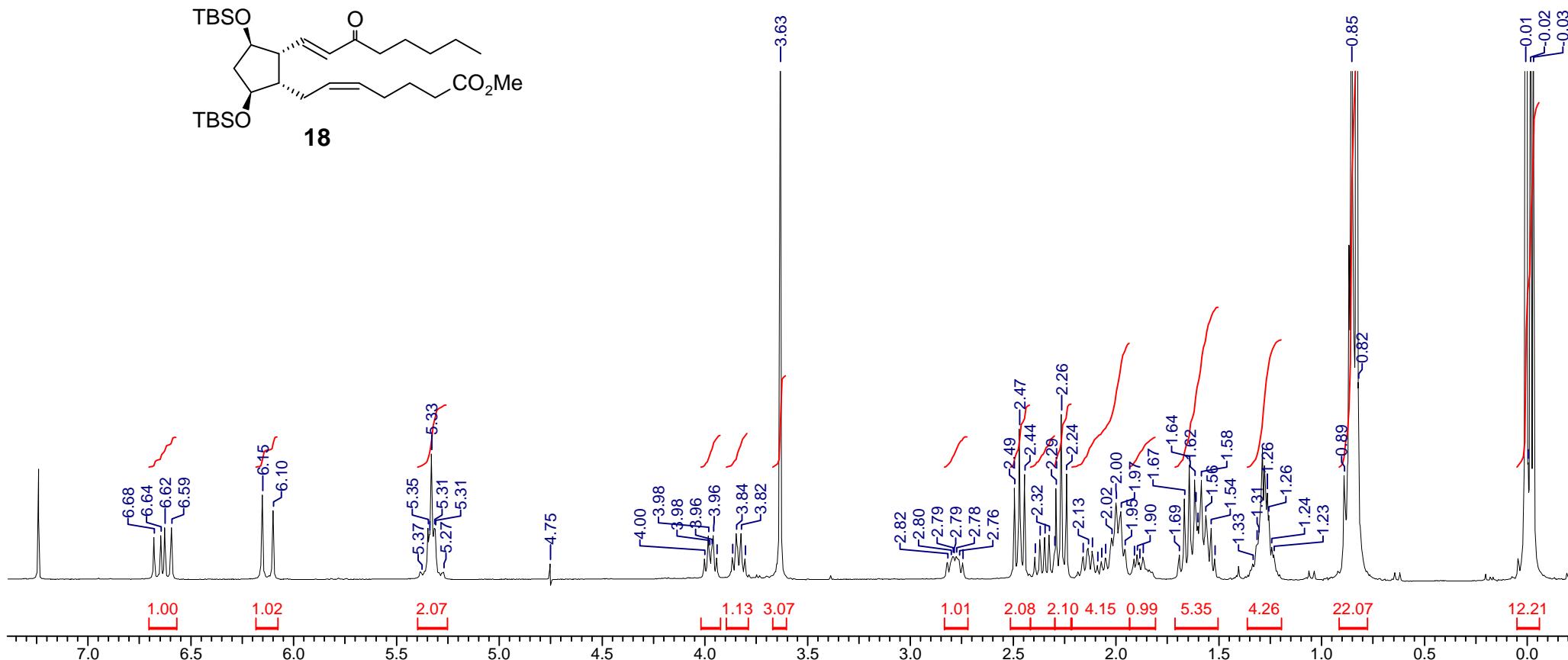
Acquisition Time (sec)	1.7695	Comment		Date	12/08/2008 16:21:56
Frequency (MHz)	75.47	Nucleus	13C	Original Points Count	32768
Temperature (grad C)	0.000			Points Count	32768



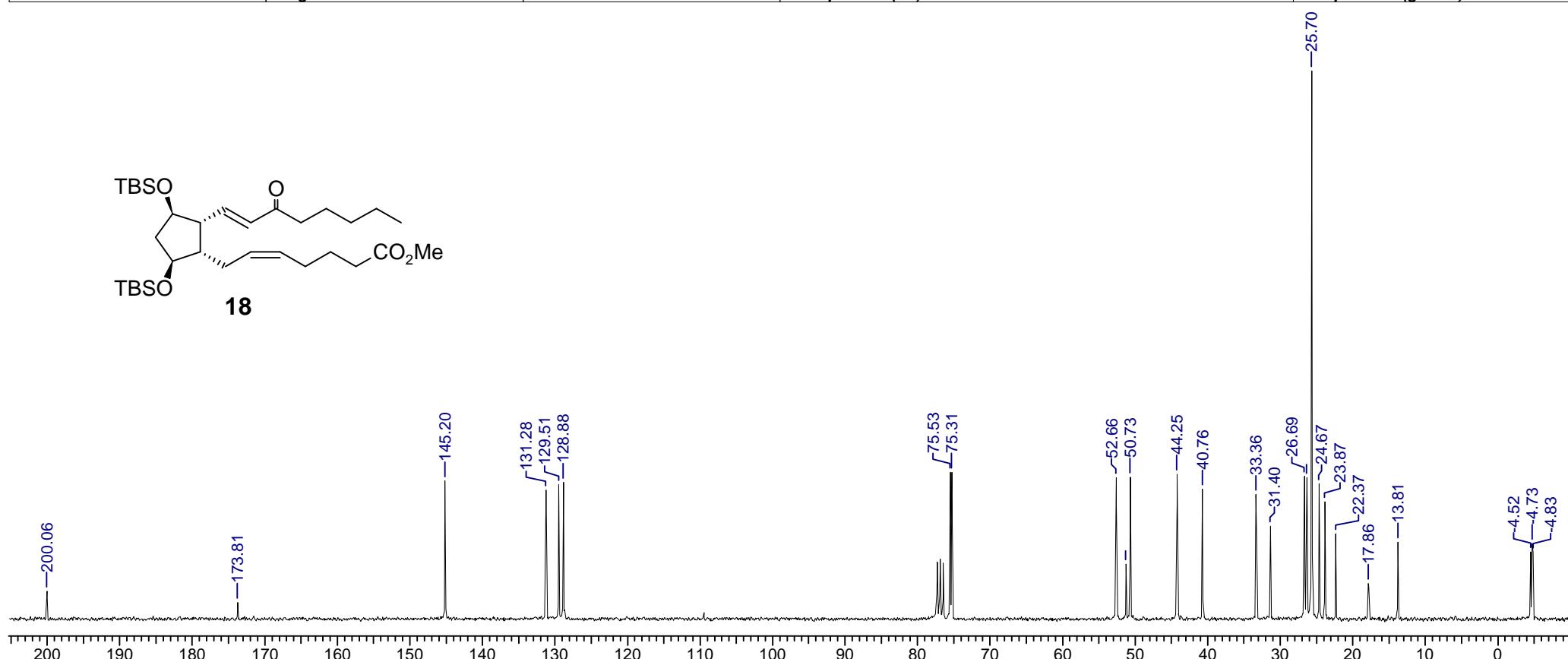
Acquisition Time (sec)	10.3547	Comment	jmg303 1 1	Date	23/07/2008 14:40:06	Frequency (MHz)	300.13		
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C)	0.000



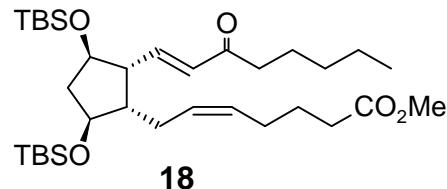
Acquisition Time (sec)	10.3547	Comment	jmg296 6 1	Date	23/07/2008 14:36:08	Frequency (MHz)	300.13		
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C)	0.000



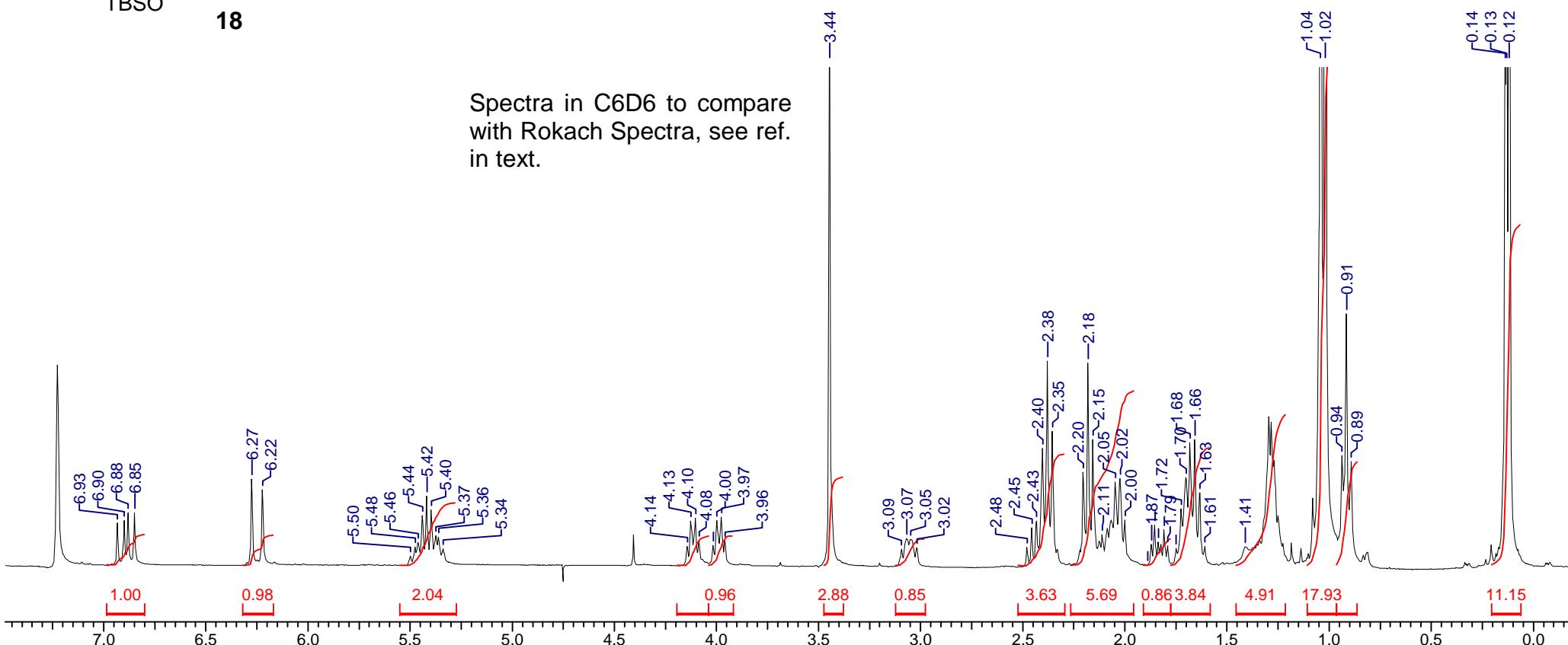
<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmg296 1 1	<b>Date</b>	23/07/2008 14:35:50	<b>Frequency (MHz)</b>	75.47
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52

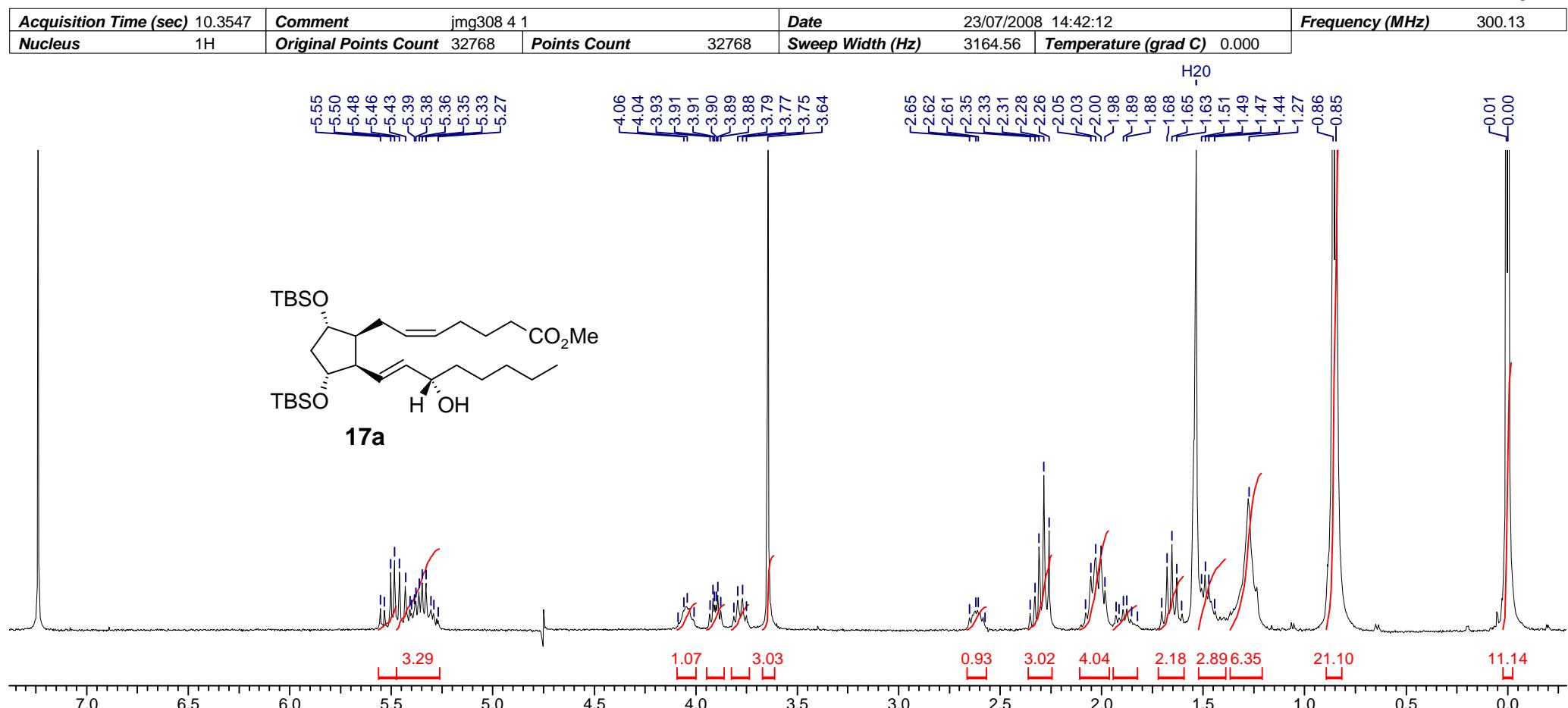


Acquisition Time (sec)	10.3547	Comment	jmg275 1 1 dngs C6D6	Date	23/07/2008 14:28:06		
Frequency (MHz)	300.13	Nucleus	1H	Original Points Count	32768		
Temperature (grad C)	0.000			Points Count	32768	Sweep Width (Hz)	3164.56

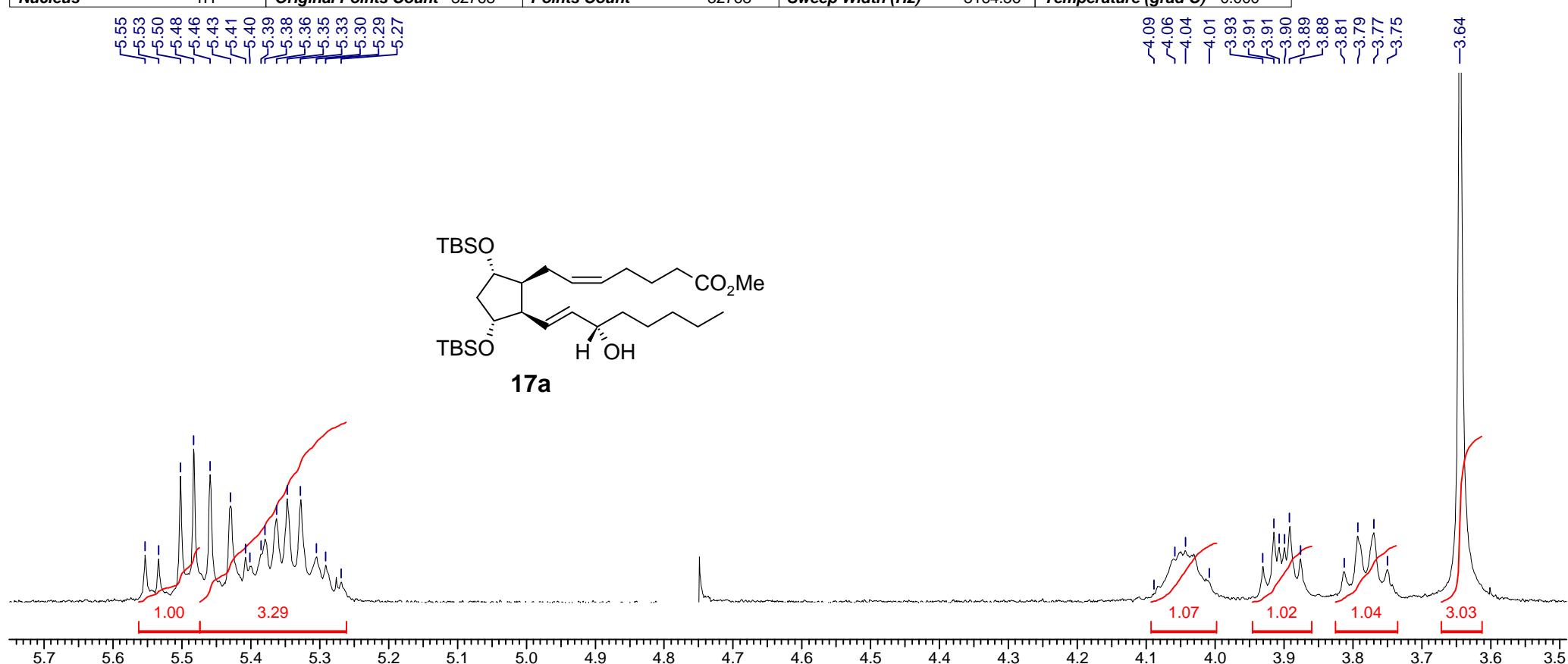


Spectra in C6D6 to compare with Rokach Spectra, see ref. in text.

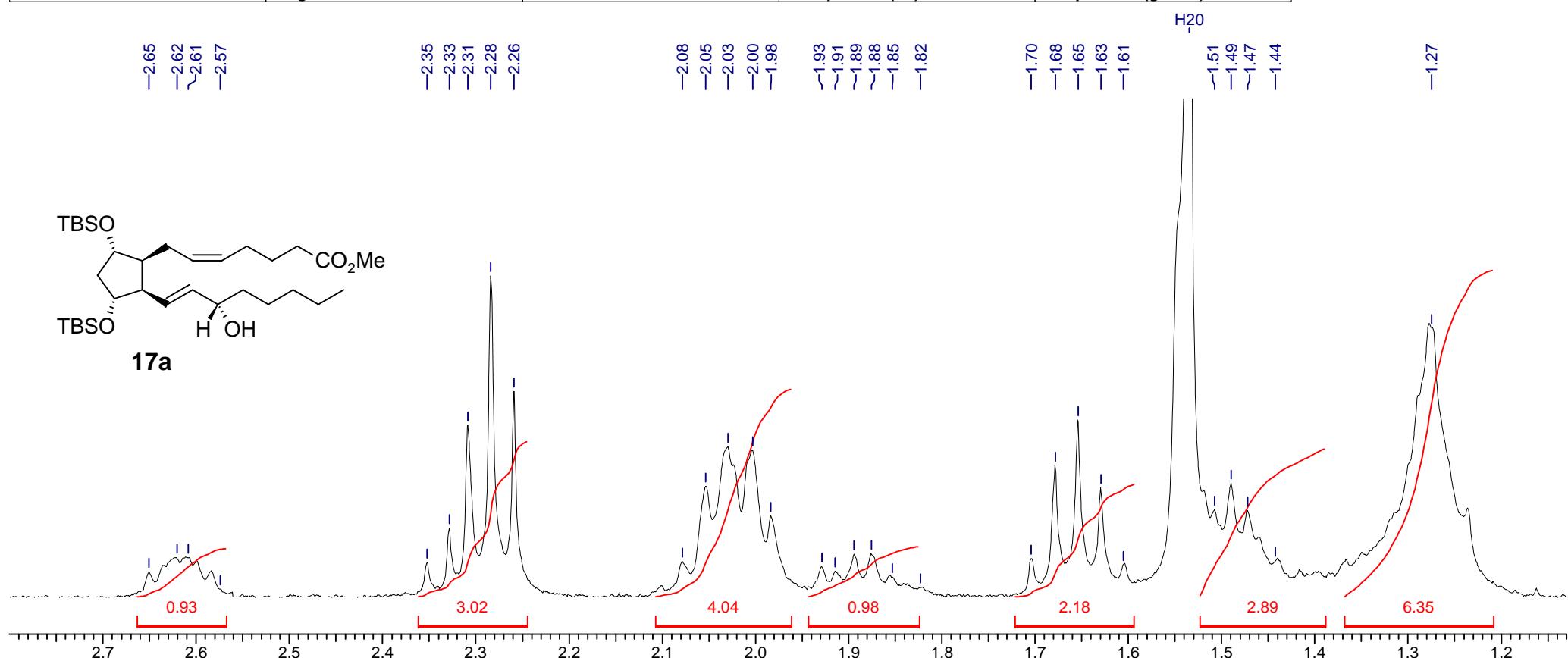




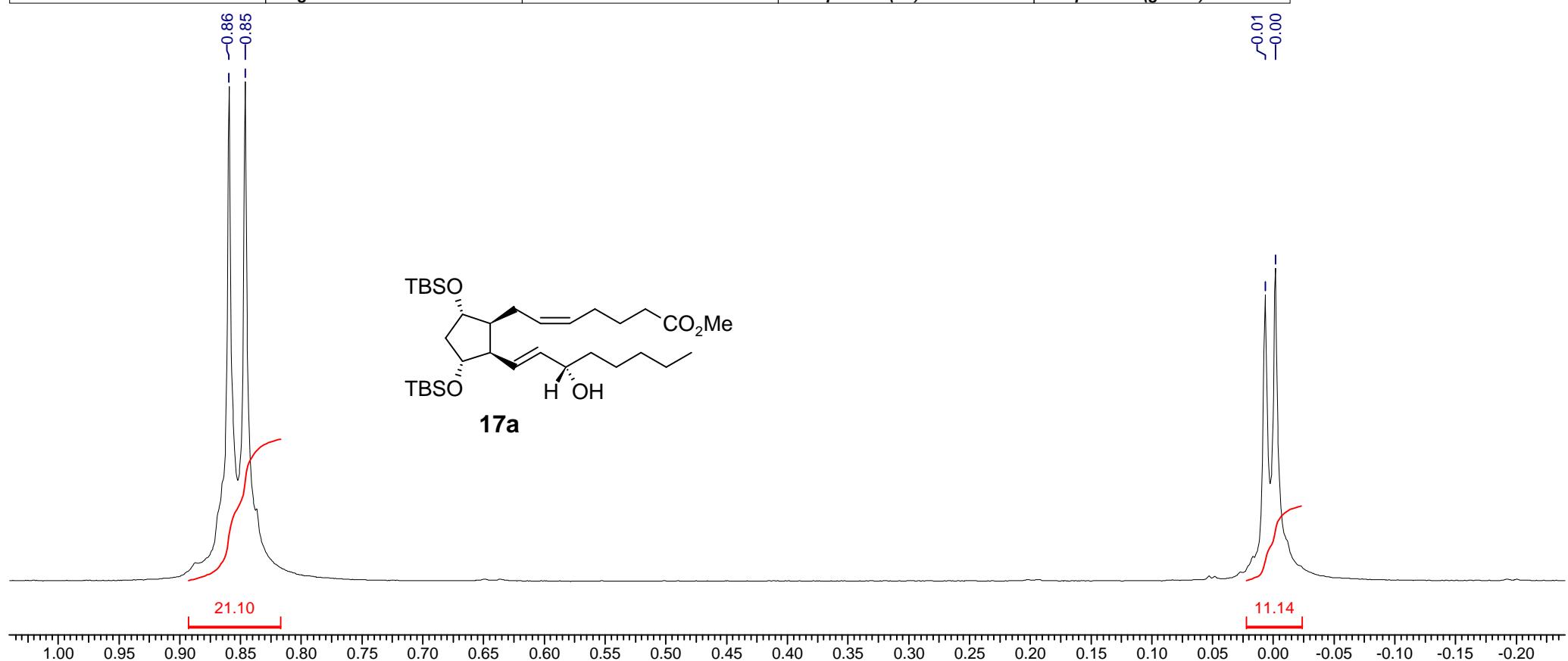
<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg308 4 1	<b>Date</b>	23/07/2008 14:42:12	<b>Frequency (MHz)</b>	300.13		
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000



<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg308 4 1	<b>Date</b>	23/07/2008 14:42:12	<b>Frequency (MHz)</b>	300.13		
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000



<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg308 4 1	<b>Date</b>	23/07/2008 14:42:12	<b>Frequency (MHz)</b>	300.13		
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000



<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmg308 5 1	<b>Date</b>	23/07/2008 14:42:18	<b>Frequency (MHz)</b>	75.47
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52

-174.10

Chloroform-d

-135.43  
 -129.65  
 -129.41  
 -128.89

77.00  
 76.08  
 75.85  
 -72.71

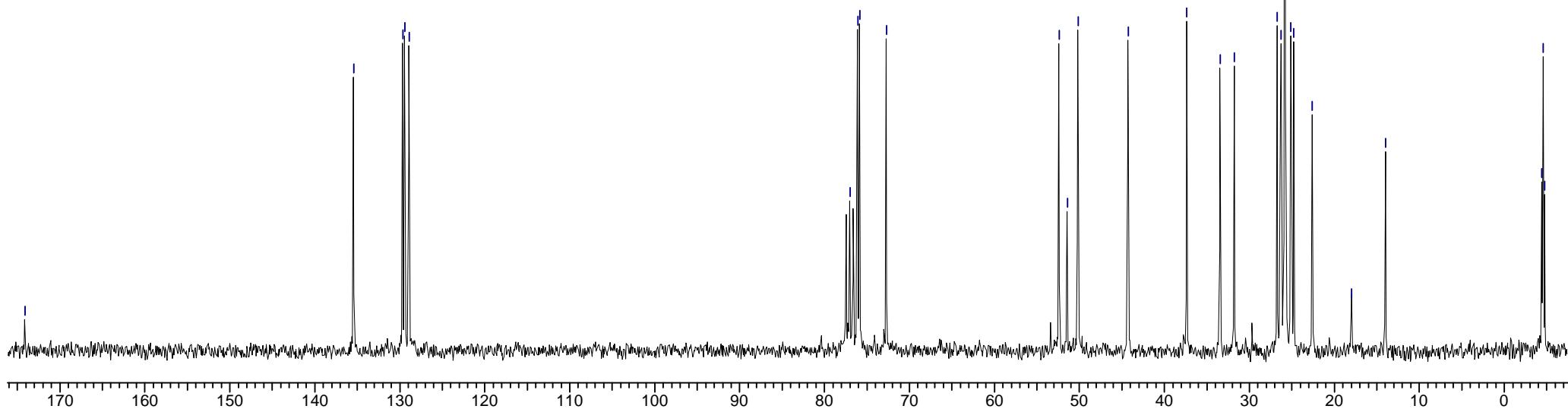
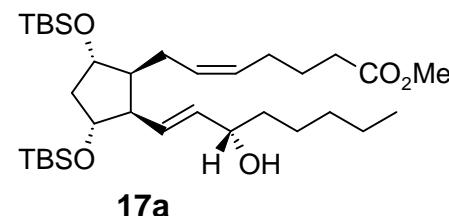
-52.39  
 -51.43  
 -50.15

-44.24  
 -37.37  
 -33.45  
 -31.77

-26.72  
 -26.27  
 -25.81  
 -25.12

-24.77  
 -22.59  
 -18.00  
 -13.98

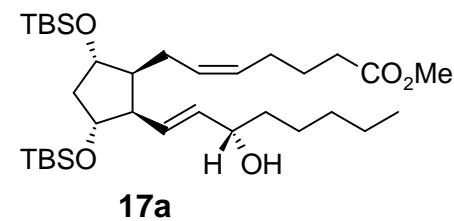
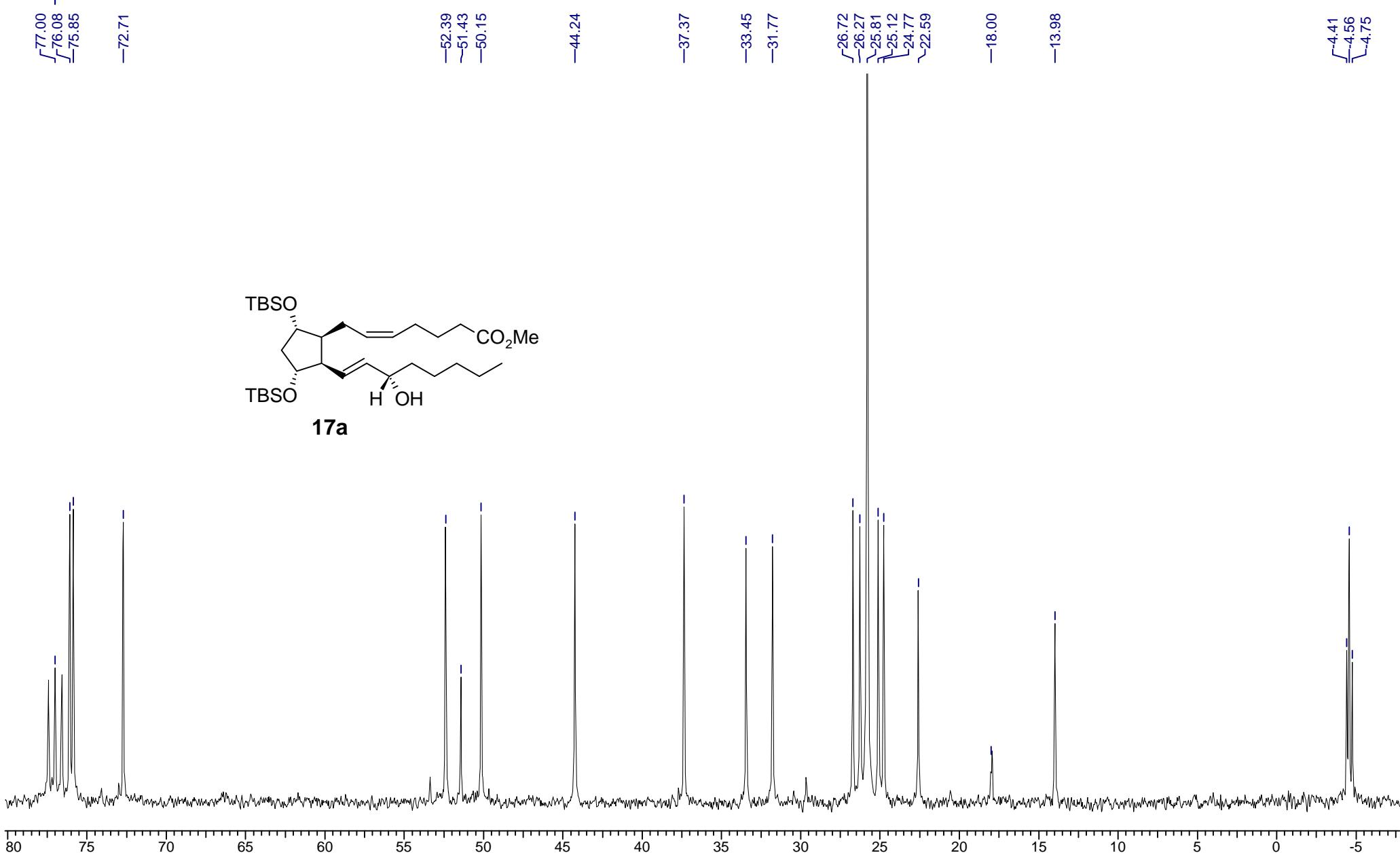
-4.41  
 -4.56



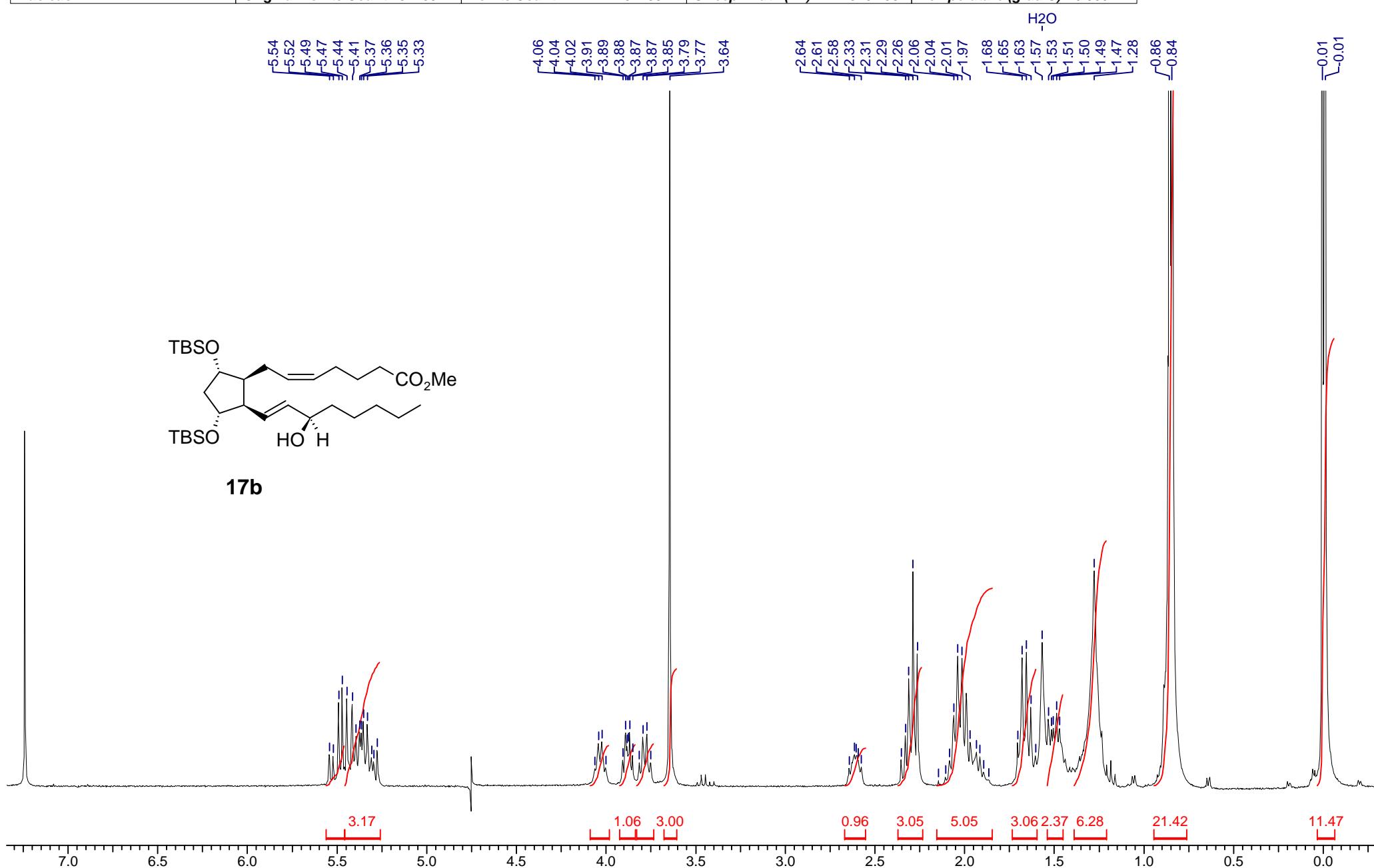
21 Aug 2008

<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmj308 5 1		<b>Date</b>	23/07/2008	14:42:18	<b>Frequency (MHz)</b>	75.47
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52	<b>Temperature (grad C)</b>	0.000

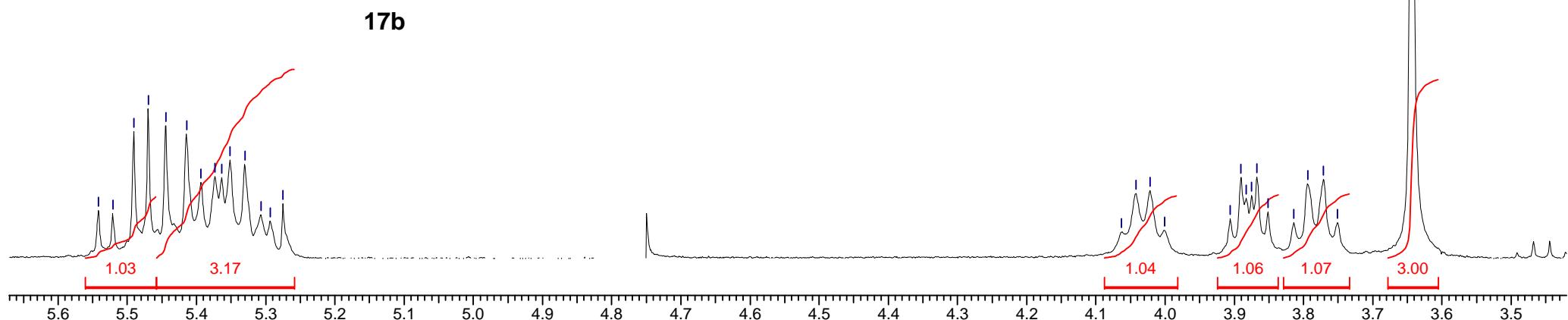
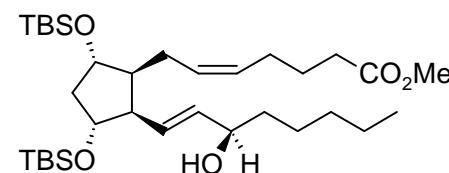
Chloroform-d



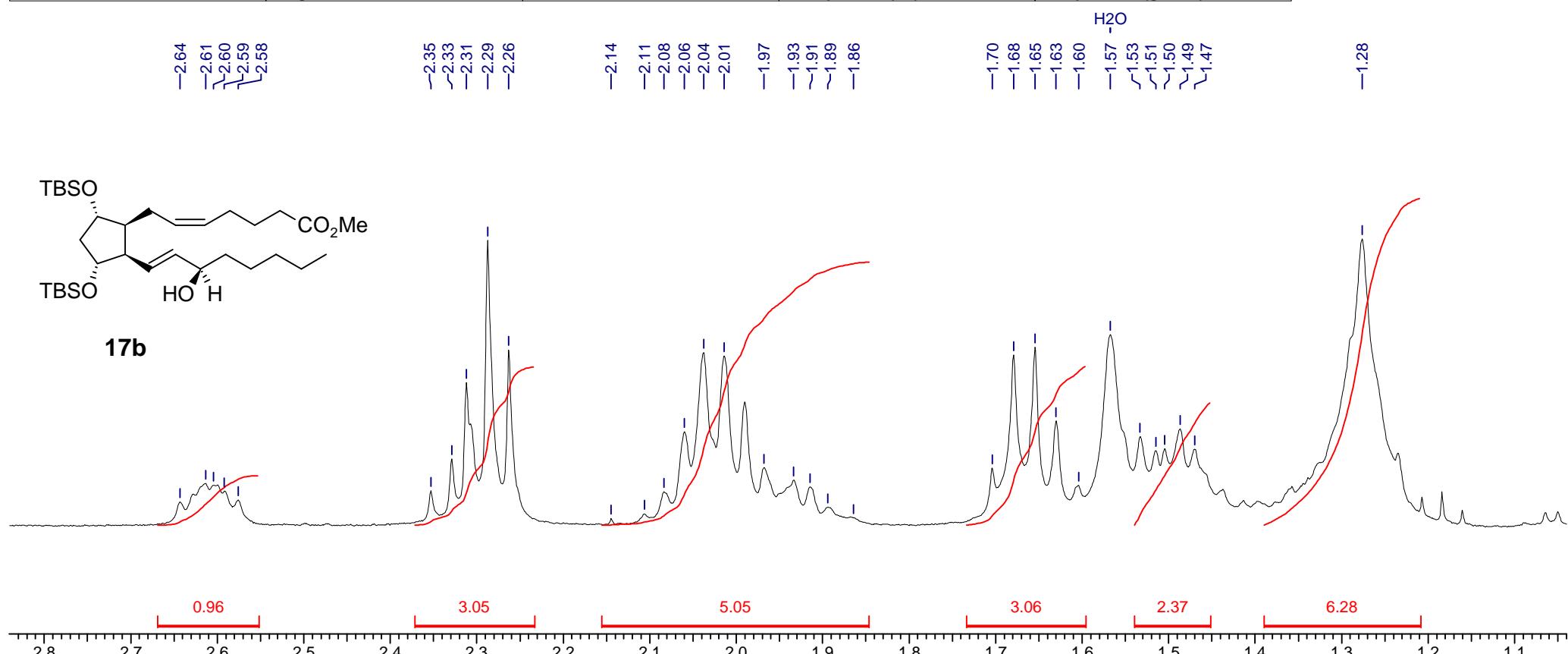
Acquisition Time (sec)	10.3547	Comment	jmg308 1 1	Date	23/07/2008 14:42:00	Frequency (MHz)	300.13		
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C)	0.000



Acquisition Time (sec)	10.3547	Comment	jmg308 1 1	Date	23/07/2008 14:42:00	Frequency (MHz)	300.13		
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C)	0.000

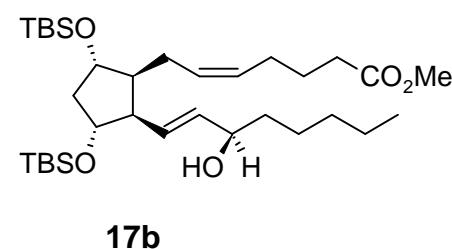
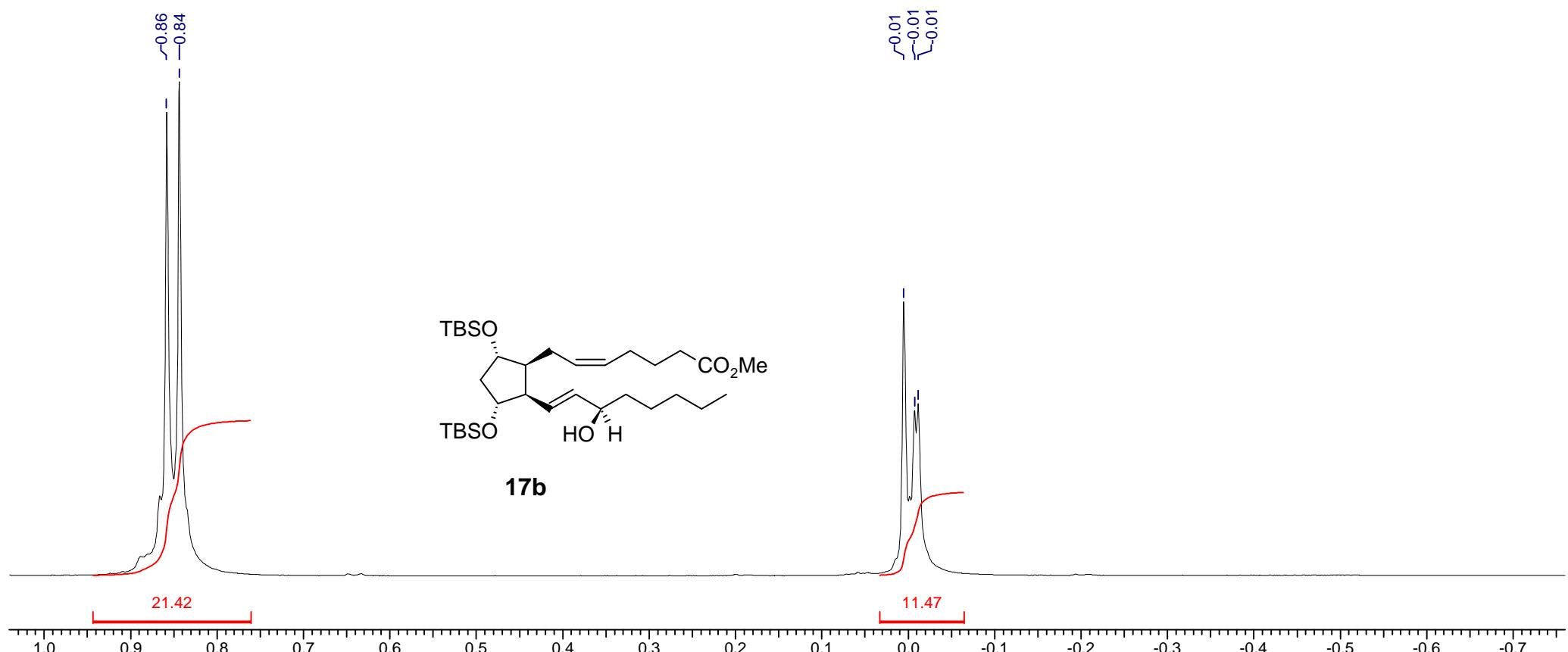


<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg308 1 1	<b>Date</b>	23/07/2008 14:42:00	<b>Frequency (MHz)</b>	300.13		
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000



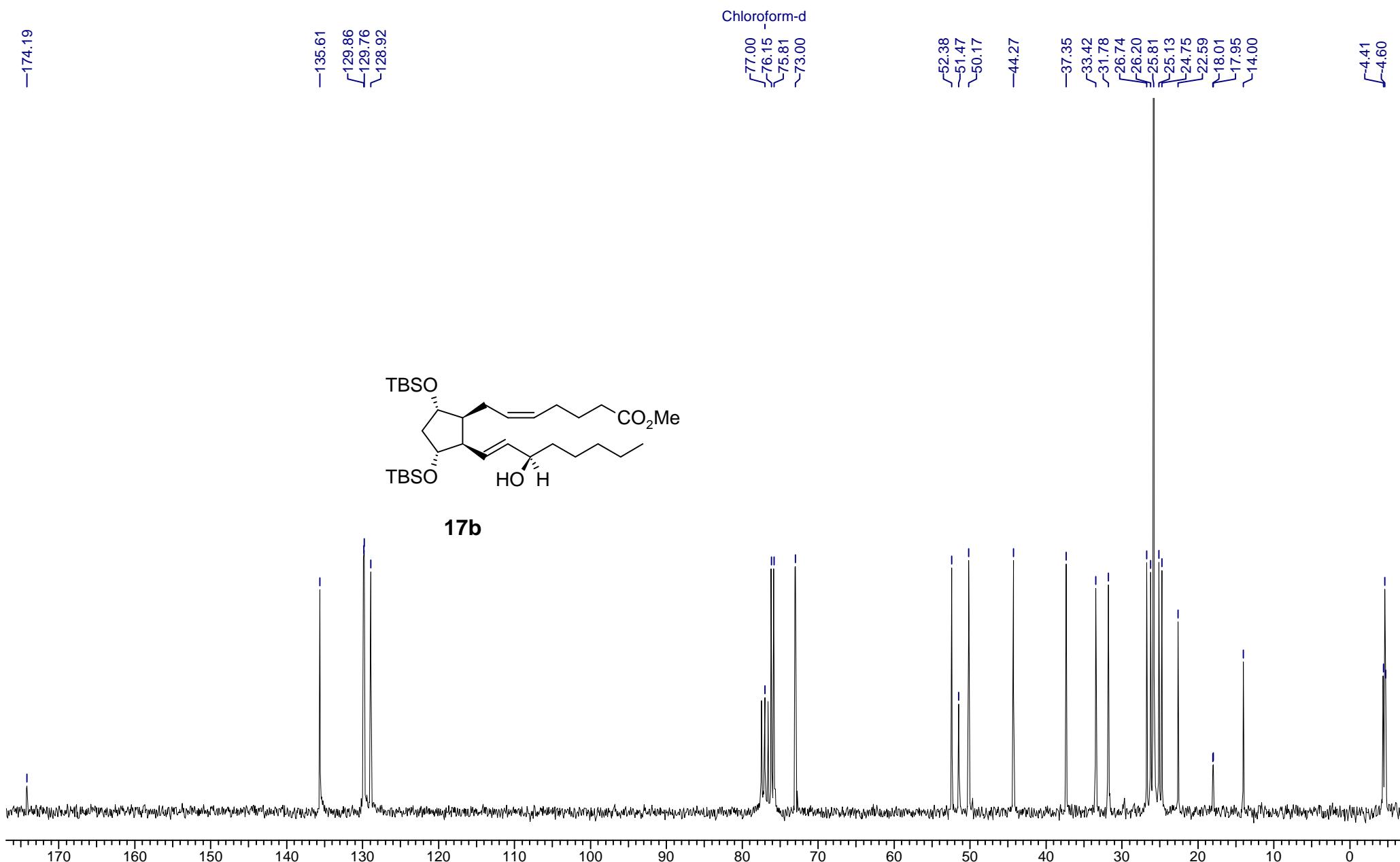
21 Aug 2008

<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg308 1 1		<b>Date</b>	23/07/2008 14:42:00		<b>Frequency (MHz)</b>	300.13
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000

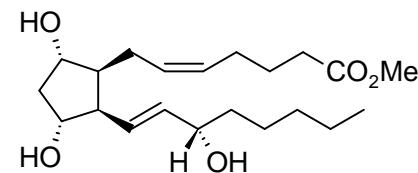
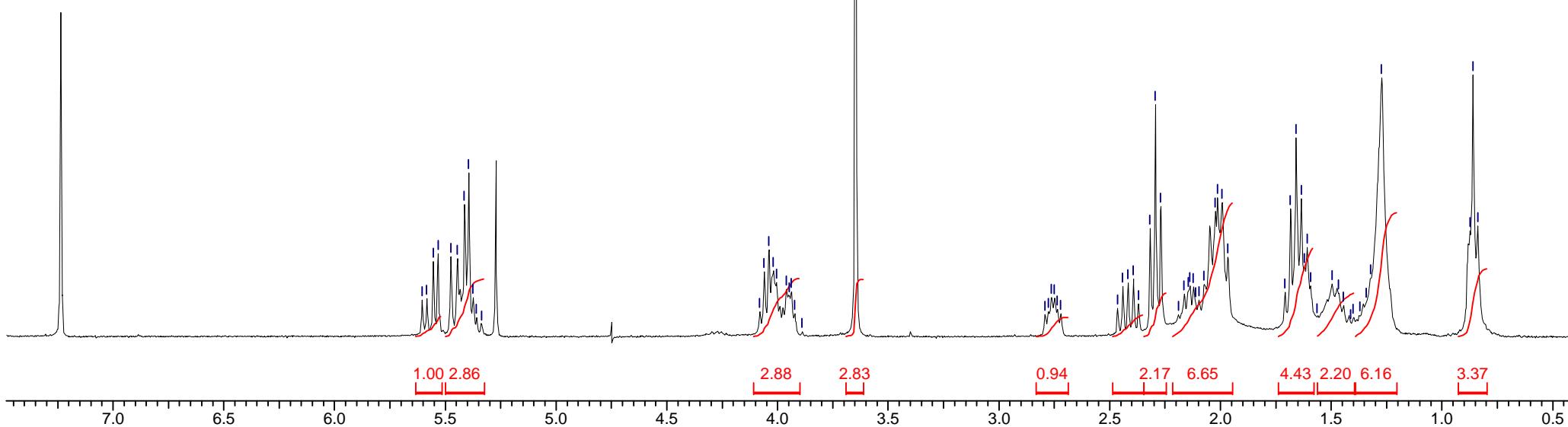


21 Aug 2008

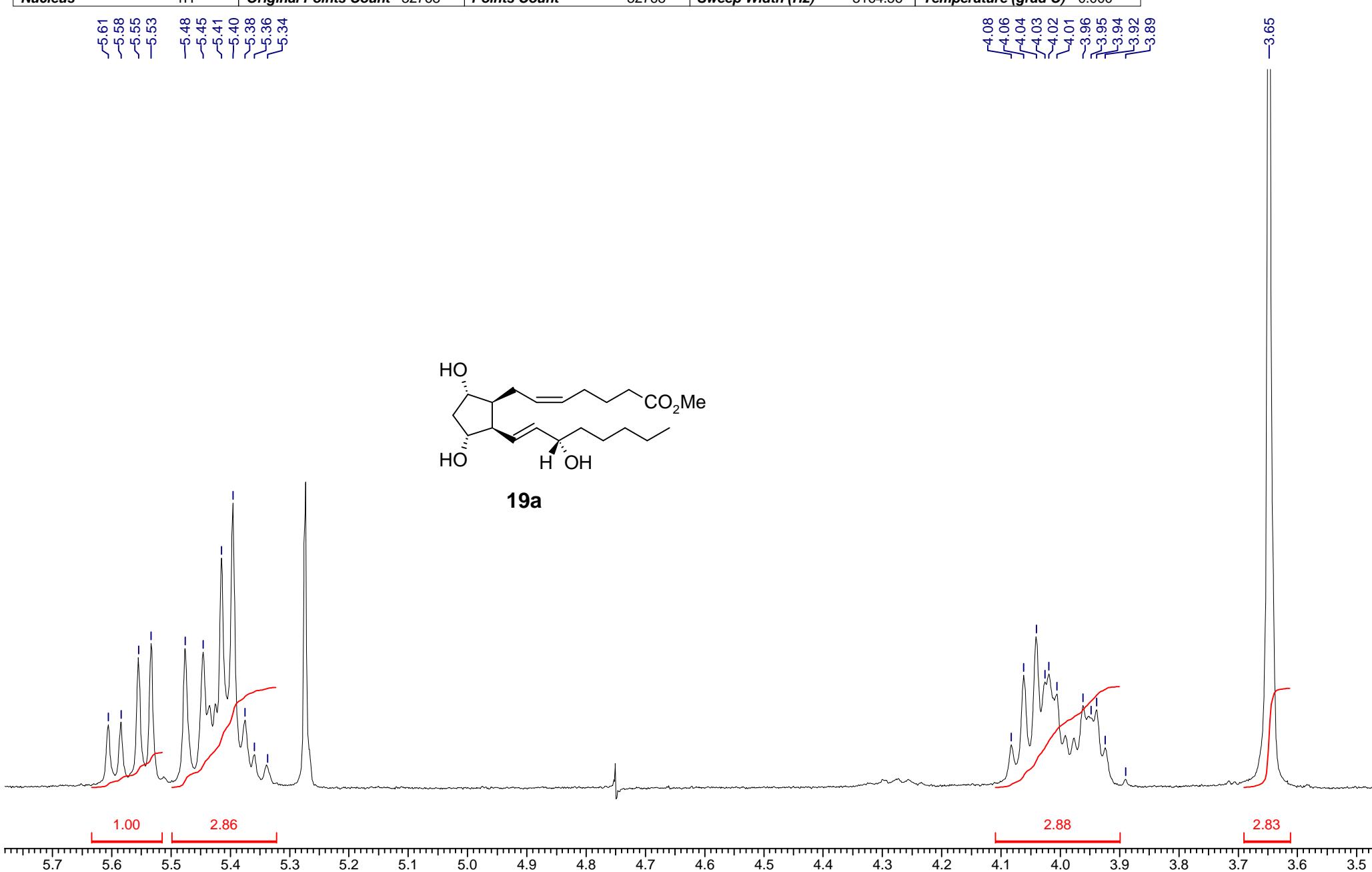
<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmg308 2 1		<b>Date</b>	23/07/2008 14:42:04	<b>Frequency (MHz)</b>	75.47	
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52	<b>Temperature (grad C)</b>	0.000



Acquisition Time (sec)	10.3547	Comment	jmg311 4 1	Date	23/07/2008 14:43:46	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56

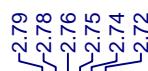
**19a**

<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg311 4 1	<b>Date</b>	23/07/2008 14:43:46	<b>Frequency (MHz)</b>	300.13		
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000



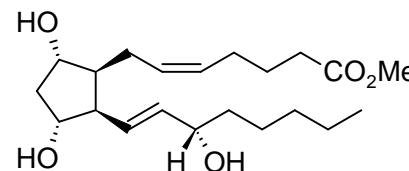
22 Aug 2008

<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg311 4 1		<b>Date</b>	23/07/2008 14:43:46		<b>Frequency (MHz)</b>	300.13
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000

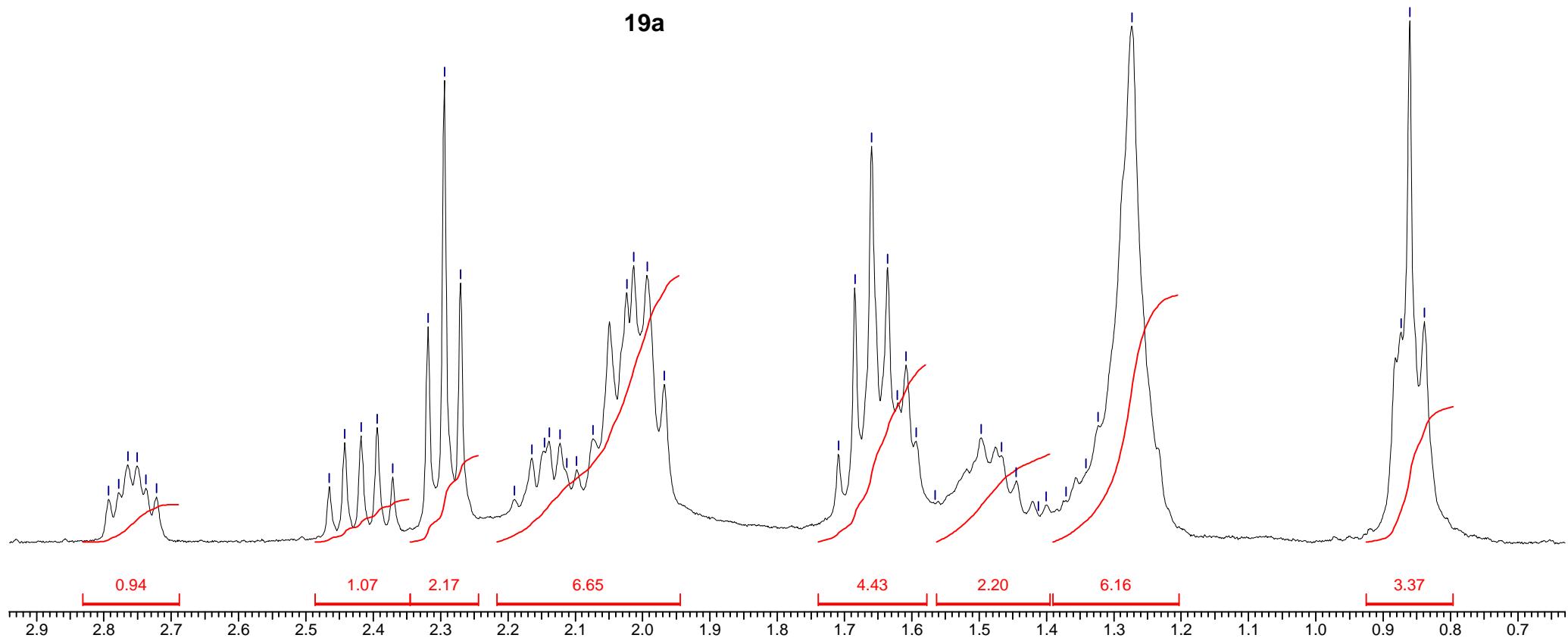


$\sqrt{1.71}$   $\sqrt{1.68}$   $\sqrt{1.66}$   $\sqrt{1.64}$   $\sqrt{1.62}$   $\sqrt{1.61}$   $\sqrt{1.59}$   $\sqrt{1.57}$   $\sqrt{1.50}$   $\sqrt{1.47}$   $\sqrt{1.44}$   $\sqrt{1.41}$   $\sqrt{1.40}$   $\sqrt{1.37}$   $\sqrt{1.34}$   $\sqrt{1.32}$

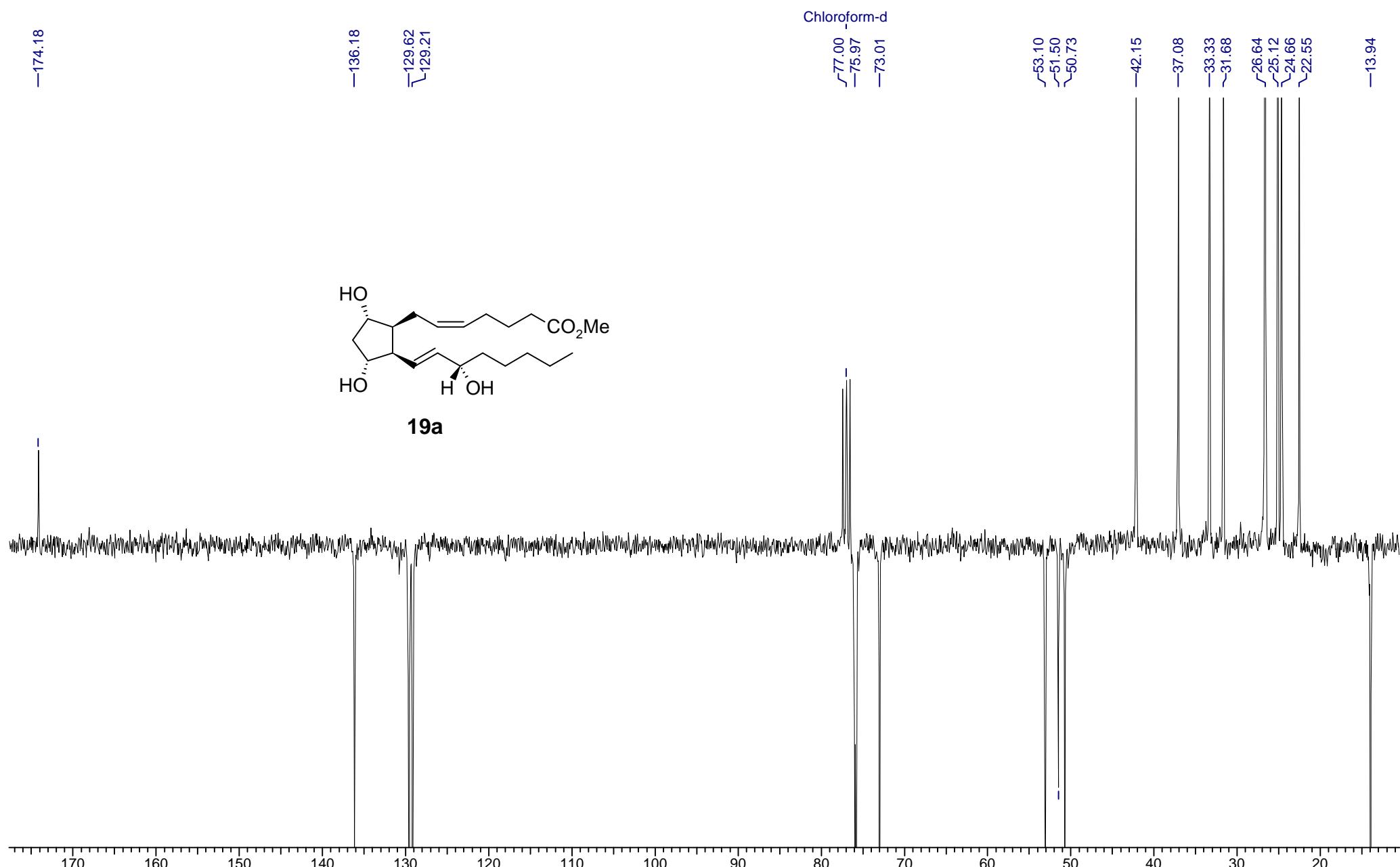
0.87  
0.86  
0.84



19a

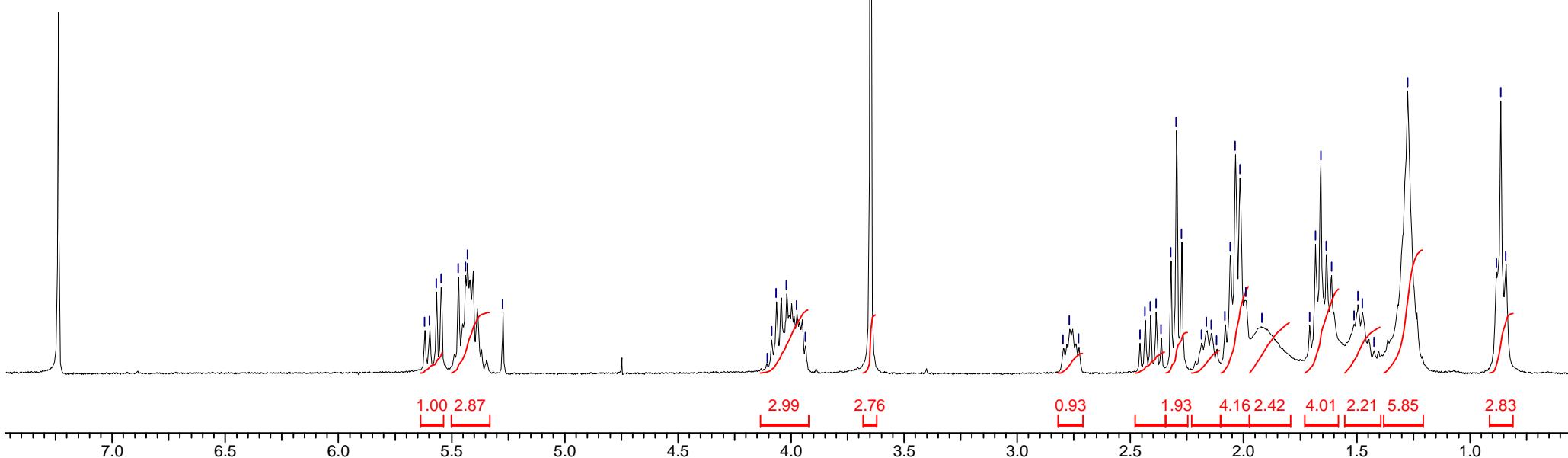
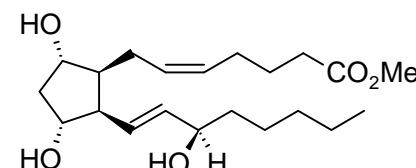
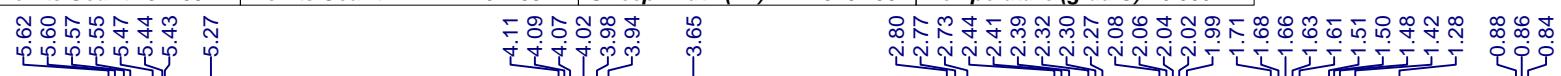


<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmg311 2 1	<b>Date</b>	23/07/2008 14:43:38	<b>Frequency (MHz)</b>	75.47
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52



22 Aug 2008

Acquisition Time (sec)	10.3547	Comment	jmg311 3 1	Date	23/07/2008 14:43:42	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56



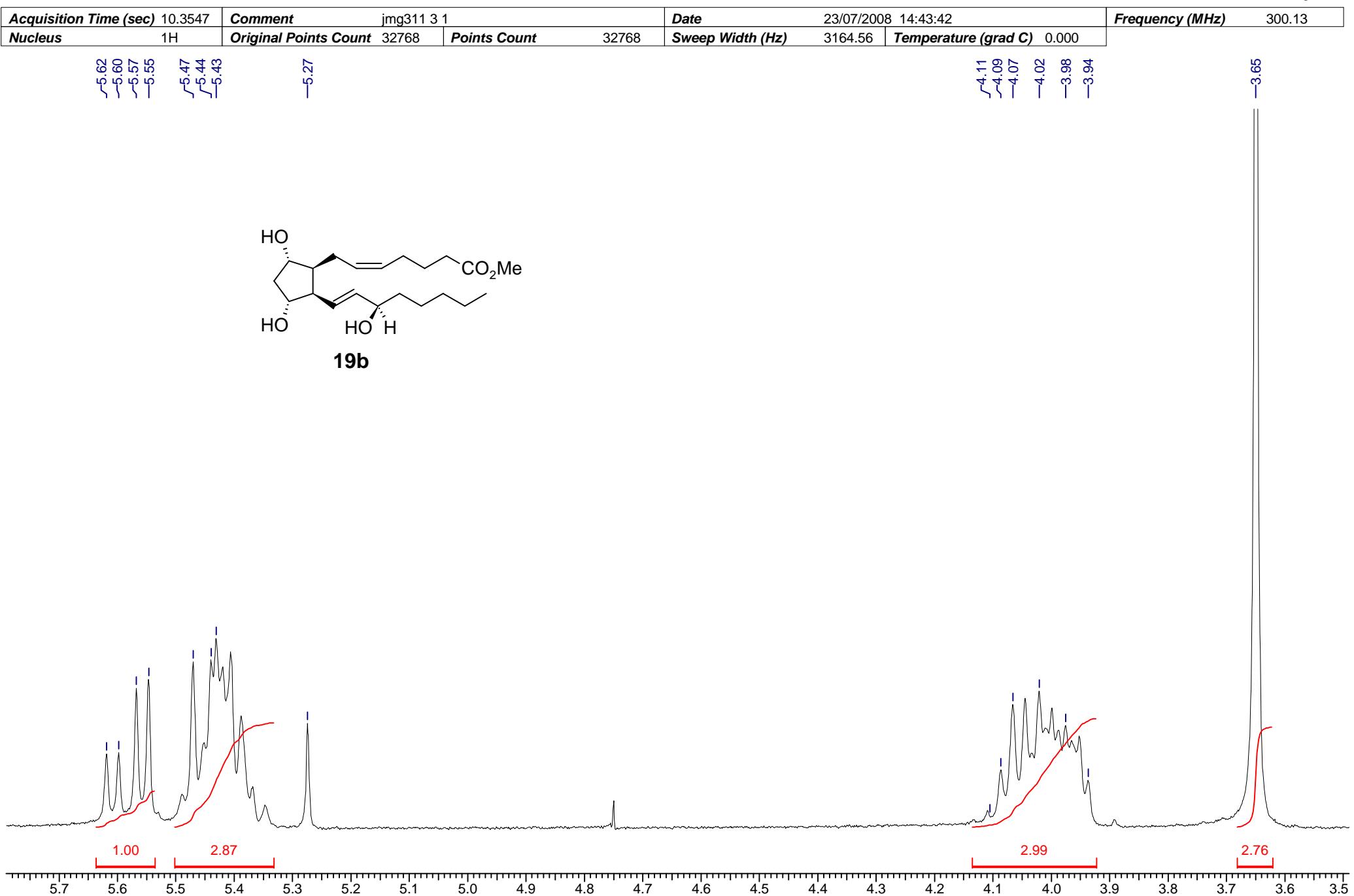
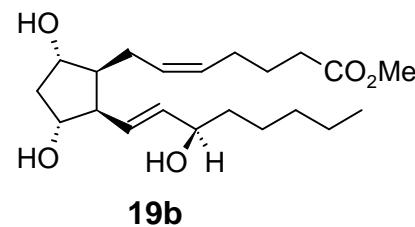
<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg311 3 1	<b>Date</b>	23/07/2008 14:43:42	<b>Frequency (MHz)</b>	300.13		
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000

$\sim$ 5.62  
 $\sim$ 5.60  
 $\sim$ 5.57  
 $\sim$ 5.55  
 $\sqrt{5.47}$   
 $\sqrt{5.44}$   
 $\sqrt{5.43}$

$\sim$ 5.27

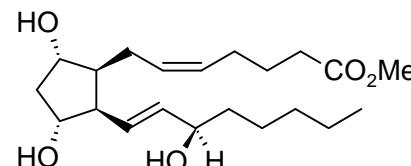
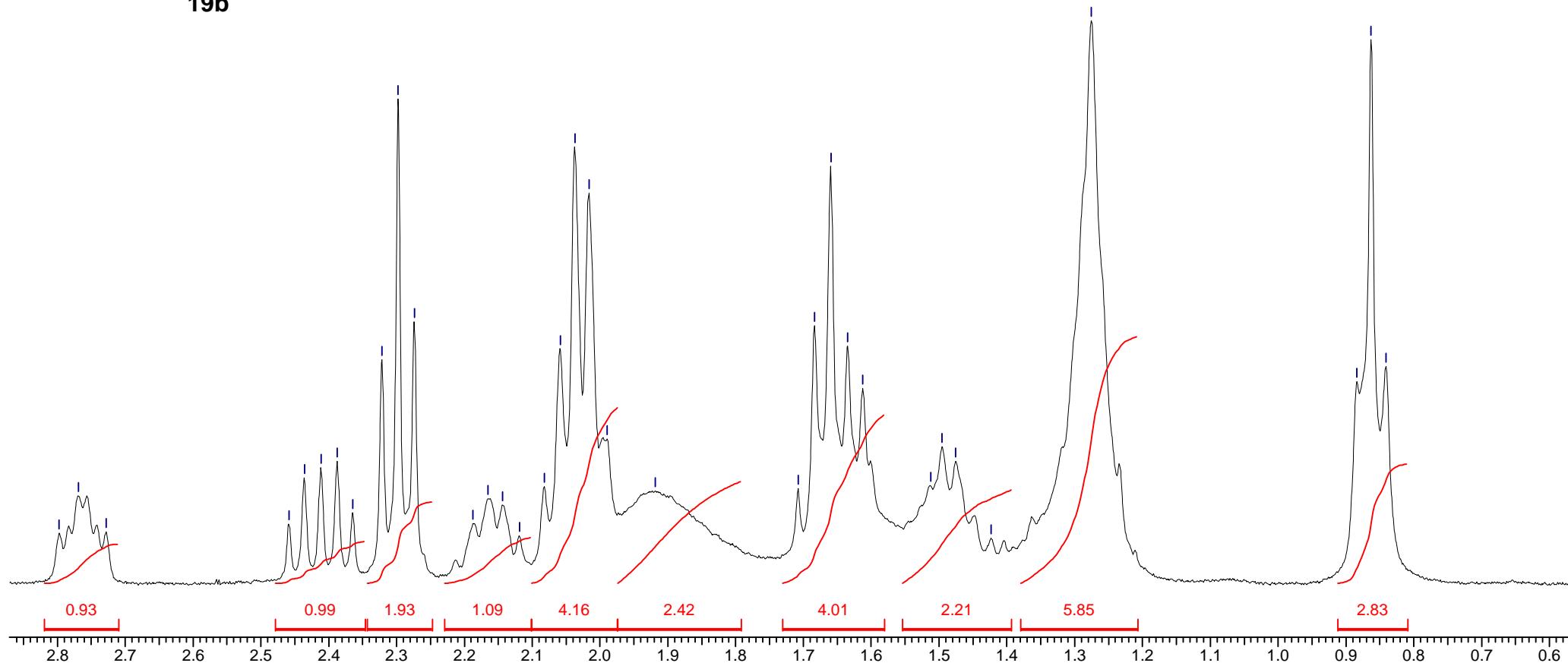
$\sqrt{4.11}$   
 $\sim$ 4.09  
 $\sim$ 4.07  
 $\sim$ 4.02  
 $\sim$ 3.98  
 $\sim$ 3.94

$\sim$ 3.65



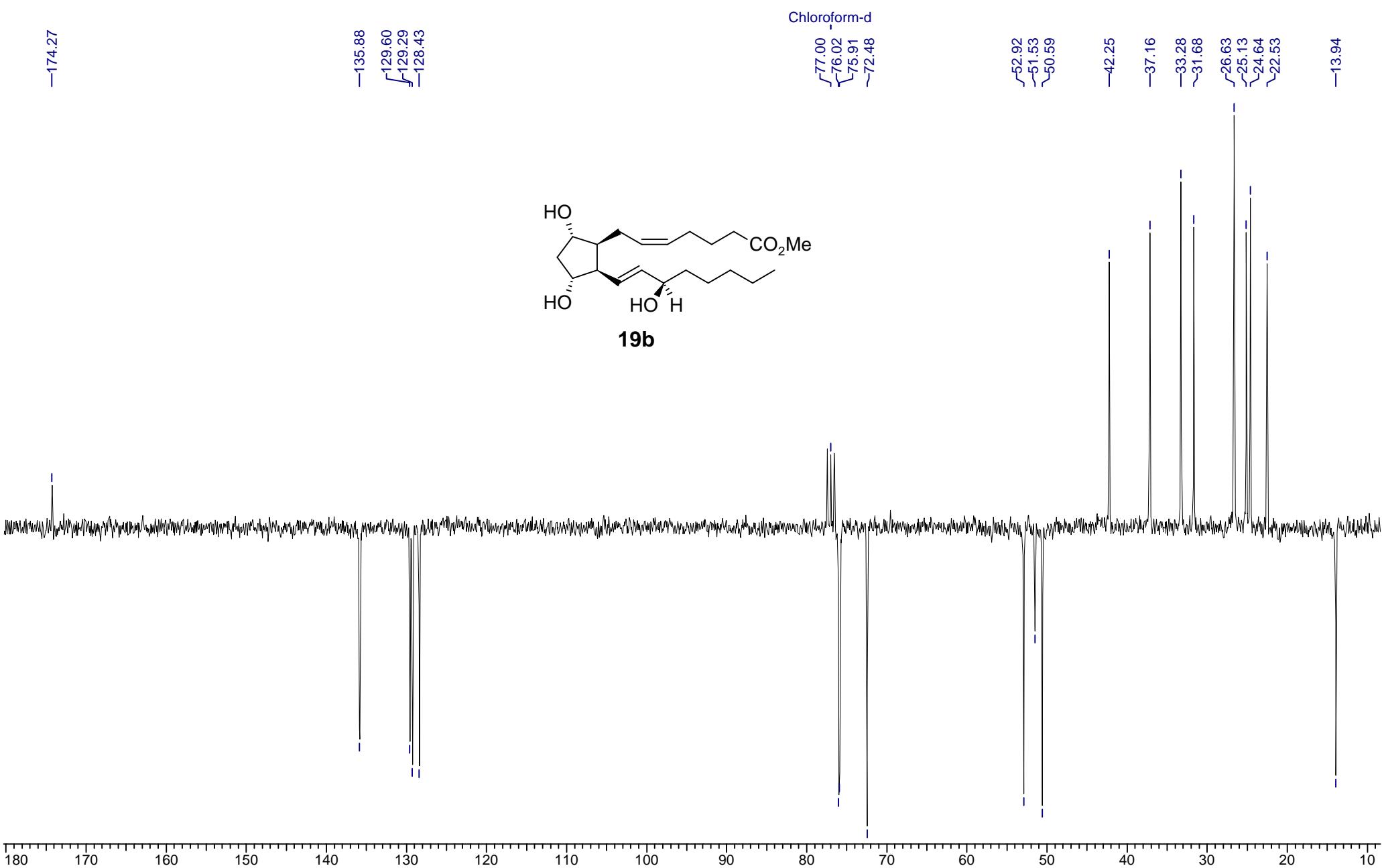
Acquisition Time (sec)	10.3547	Comment	jmg311 3 1	Date	23/07/2008 14:43:42	Frequency (MHz)	300.13	
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C) 0.000

-2.80  
-2.77      -2.46  
-2.44  
-2.41  
-2.39  
-2.36  
-2.30  
-2.27      -2.19  
-2.16  
-2.14  
-2.12  
-2.08  
-2.06  
-2.04  
-2.02  
-1.99  
-1.92      -1.71  
-1.68  
-1.66  
-1.63  
-1.61      -1.51  
-1.50  
-1.48  
-1.42      -1.28  
-0.88  
-0.86  
-0.84

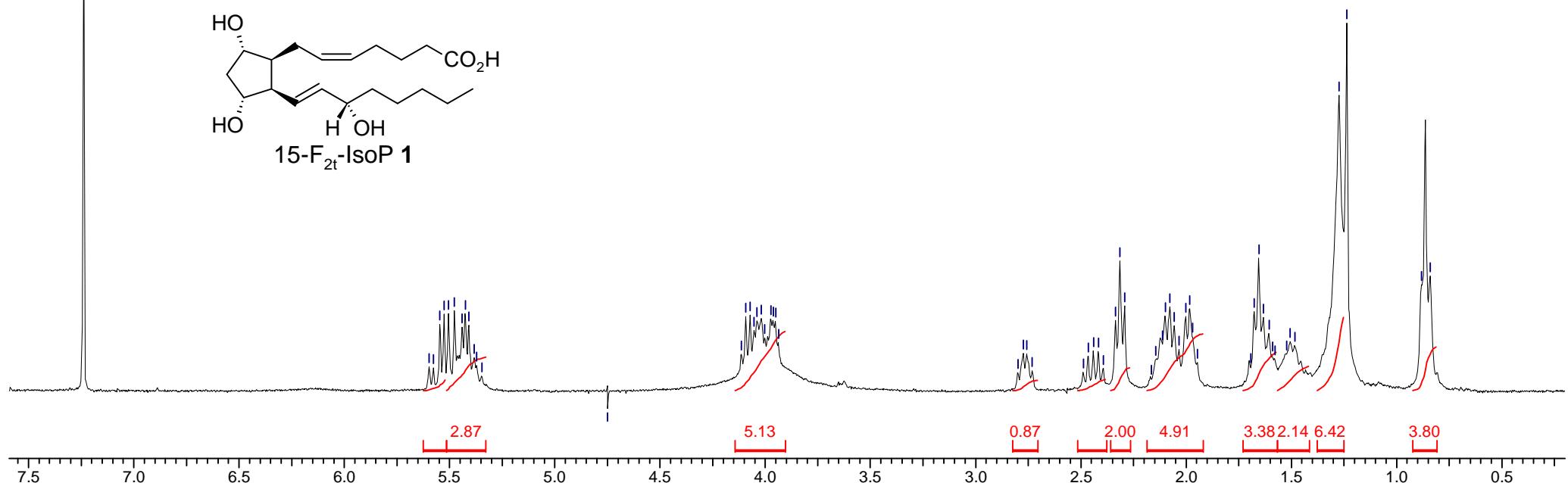
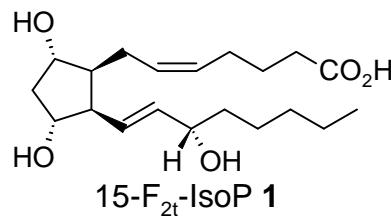
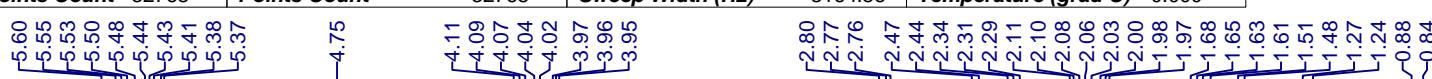
**19b**

22 Aug 2008

<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmg311 1 1	<b>Date</b>	23/07/2008 14:43:34	<b>Frequency (MHz)</b>	75.47
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52



Acquisition Time (sec)	10.3547	Comment	jmg312 10 1	Date	23/07/2008	20:10:38	Frequency (MHz)	300.13
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C) 0.000

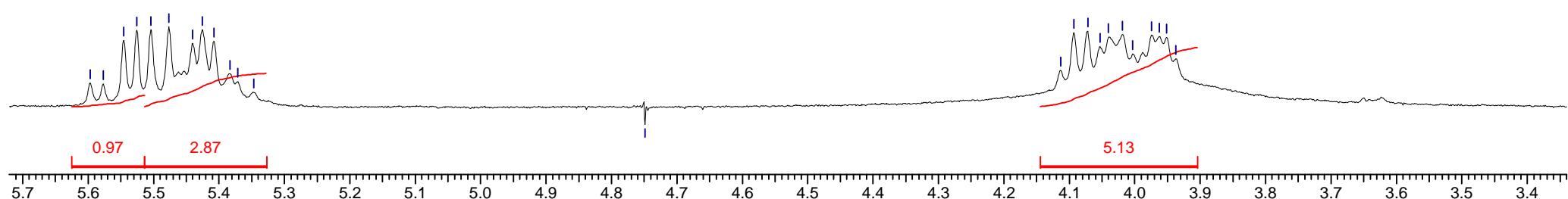
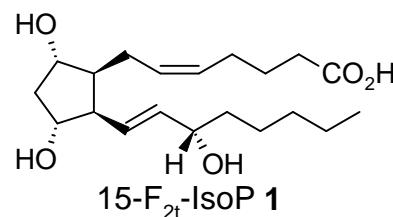


<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg312 10 1	<b>Date</b>	23/07/2008	20:10:38	<b>Frequency (MHz)</b>	300.13	
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000

~5.60  
 ~5.58  
 ~5.55  
 ~5.53  
 ~5.50  
 ~5.48  
 ~5.44  
 ~5.43  
 ~5.41  
 ~5.38  
 ~5.37  
 ~5.35

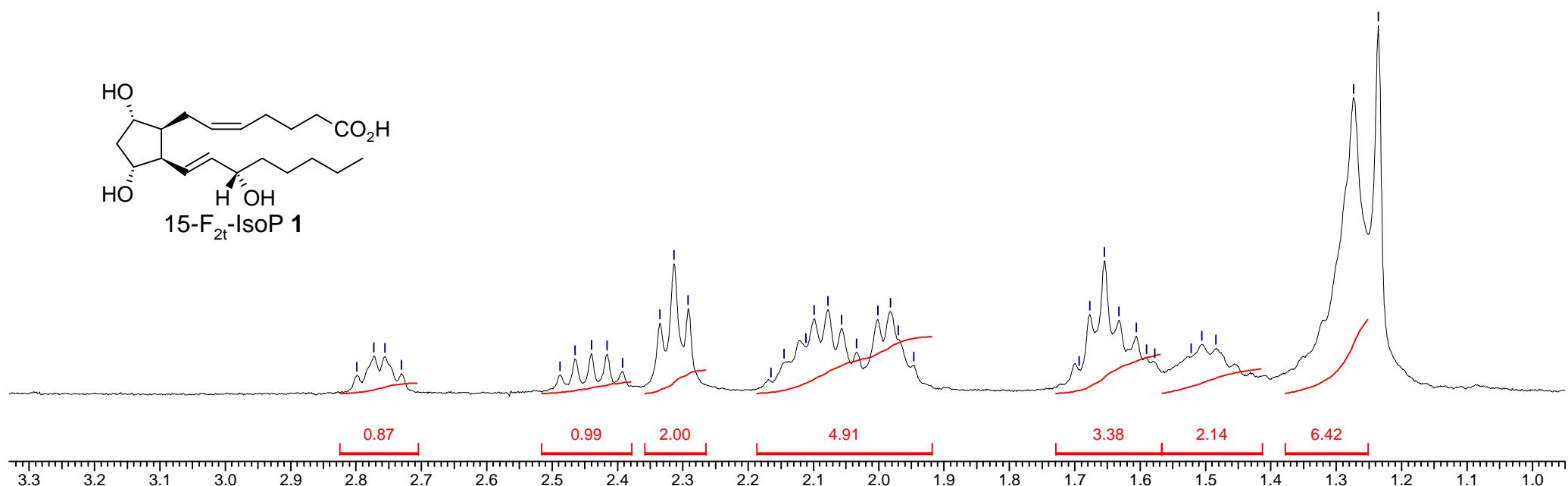
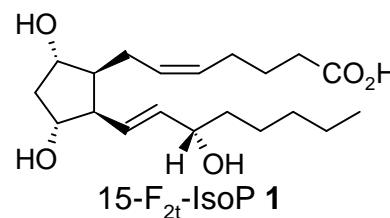
-4.75

4.11  
 4.09  
 4.07  
 4.05  
 4.04  
 4.02  
 4.00  
 3.97  
 3.96  
 3.95  
 3.94



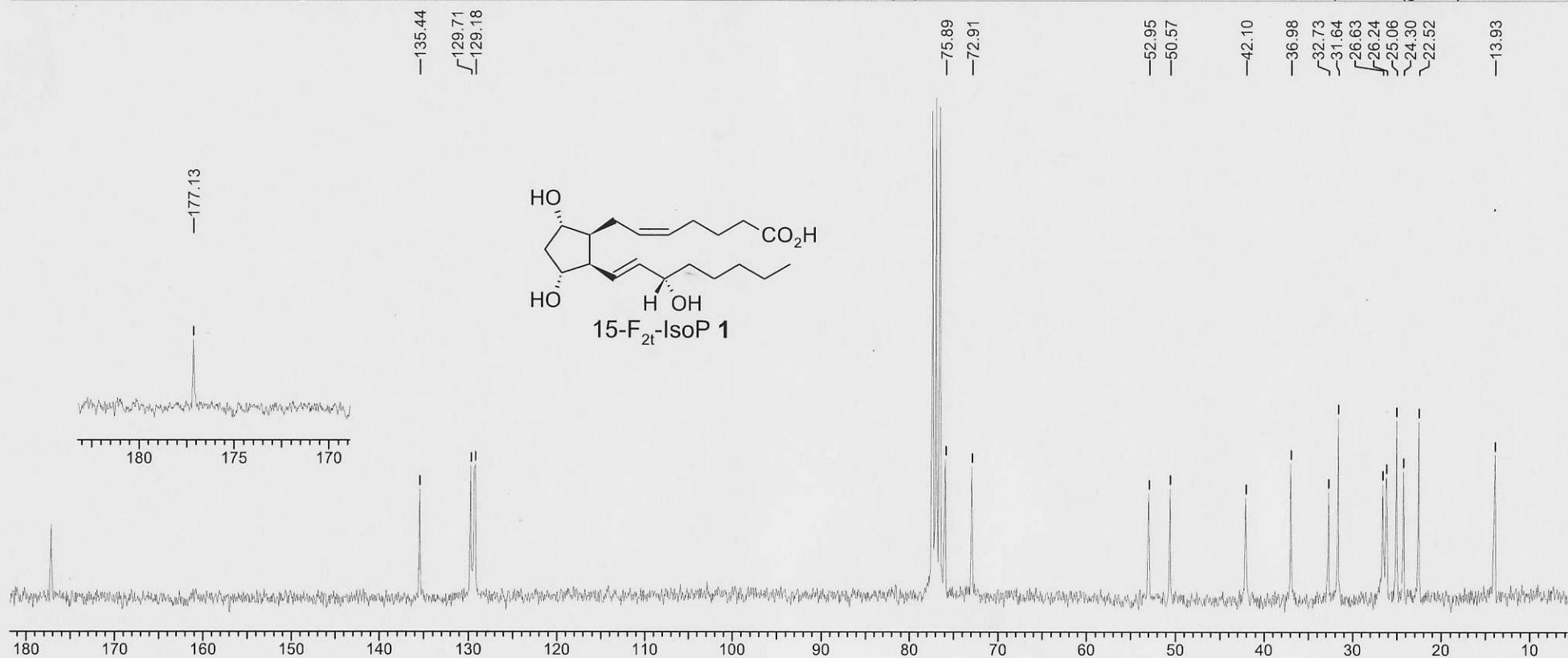
<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg312 10 1	<b>Date</b>	23/07/2008	20:10:38	<b>Frequency (MHz)</b>	300.13	
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000

-2.80  
 -2.77  
 -2.76  
 -2.73  
 -2.49  
 -2.47  
 -2.44  
 -2.42  
 -2.39  
 -2.34  
 -2.31  
 -2.29  
 -2.17  
 -2.14  
 -2.11  
 -2.10  
 -2.08  
 -2.06  
 -2.03  
 -2.00  
 -1.98  
 -1.97  
 -1.95  
 -1.69  
 -1.68  
 -1.65  
 -1.63  
 -1.61  
 -1.59  
 -1.58  
 -1.52  
 -1.51  
 -1.48  
 -1.27  
 -1.24



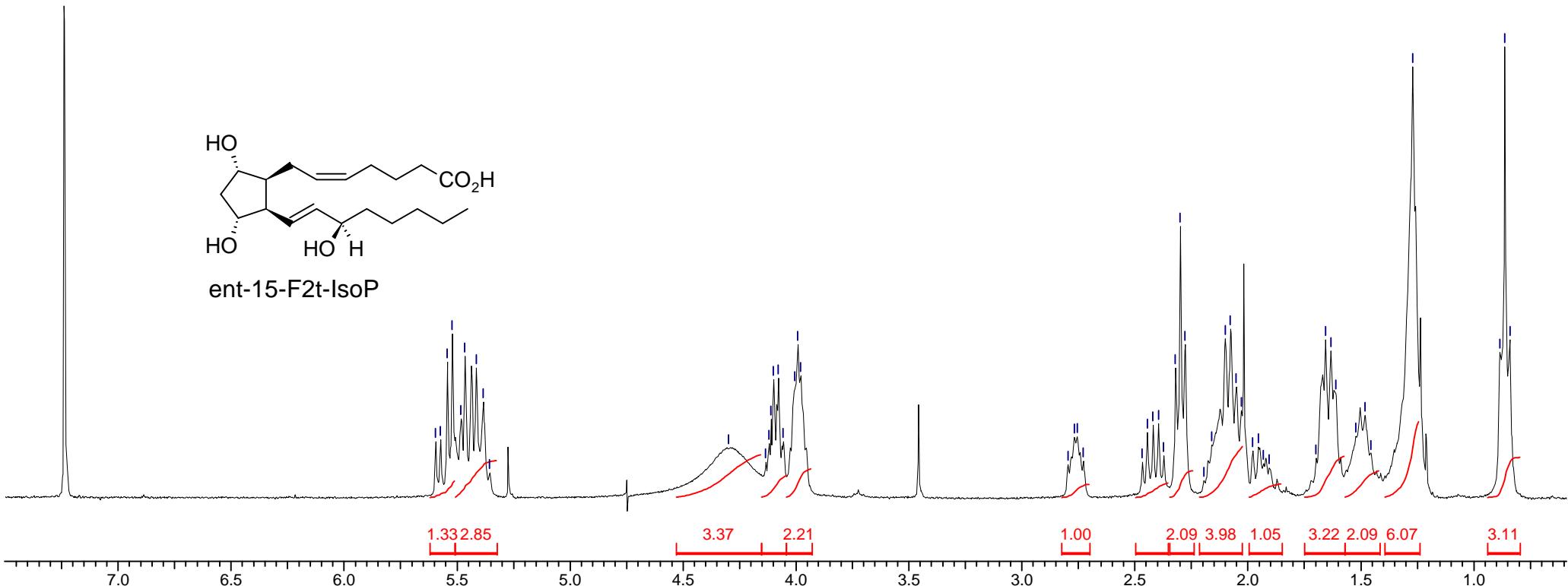
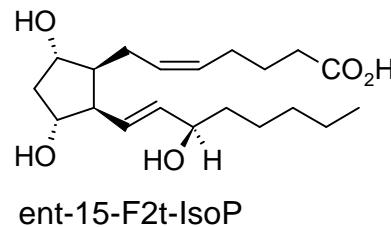
26 Aug 2008

<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmg312 2 1	<b>Date</b>	23/07/2008 20:10:50	<b>Frequency (MHz)</b>	75.47
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52



27 Aug 2008

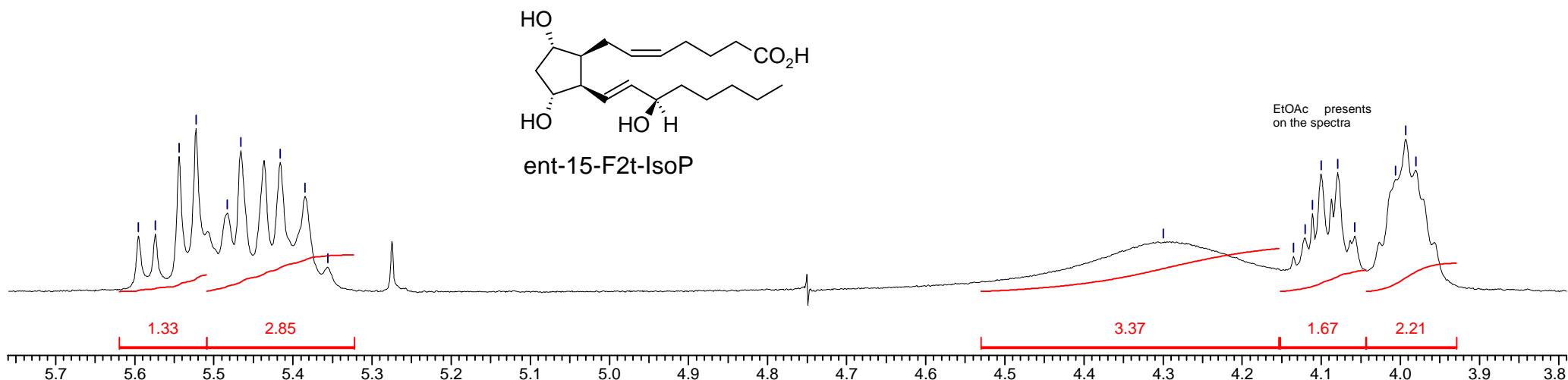
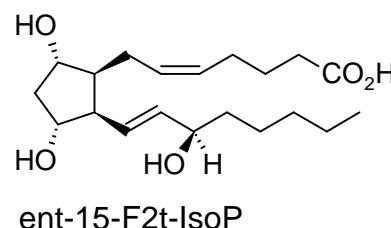
Acquisition Time (sec)	10.3547	Comment	jmg317 3 1	Date	23/07/2008 19:00:02	Frequency (MHz)	300.13		
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C)	0.000



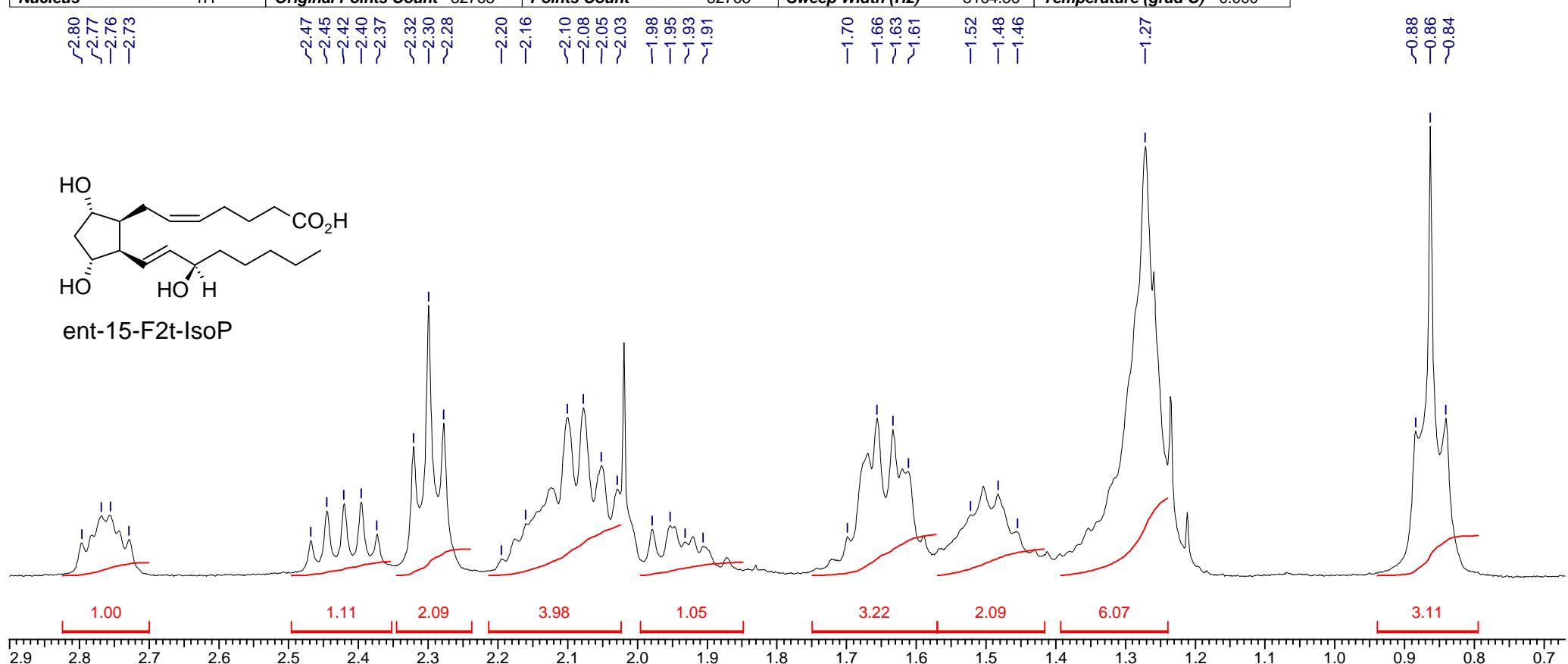
<b>Acquisition Time (sec)</b>	10.3547	<b>Comment</b>	jmg317 3 1	<b>Date</b>	23/07/2008 19:00:02	<b>Frequency (MHz)</b>	300.13		
<b>Nucleus</b>	1H	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	3164.56	<b>Temperature (grad C)</b>	0.000

-5.60  
 -5.57  
 -5.54  
 -5.52  
 -5.48  
 -5.47  
 -5.42  
 -5.38  
 -5.36

-4.30  
 -4.14  
 -4.12  
 -4.11  
 -4.10  
 -4.08  
 -4.06  
 -4.01  
 -3.99  
 -3.98



Acquisition Time (sec)	10.3547	Comment	jmg317 3 1	Date	23/07/2008 19:00:02	Frequency (MHz)	300.13	
Nucleus	1H	Original Points Count	32768	Points Count	32768	Sweep Width (Hz)	3164.56	Temperature (grad C) 0.000



27 Aug 2008

<b>Acquisition Time (sec)</b>	1.7695	<b>Comment</b>	jmg337 5 1	<b>Date</b>	23/07/2008 19:00:10	<b>Frequency (MHz)</b>	75.47
<b>Nucleus</b>	13C	<b>Original Points Count</b>	32768	<b>Points Count</b>	32768	<b>Sweep Width (Hz)</b>	18518.52

