

Total Synthesis of *ent*-Dioxepandehydrothrysiferol via a Bromonium-Initiated Epoxide-Opening Cascade

Supporting Information

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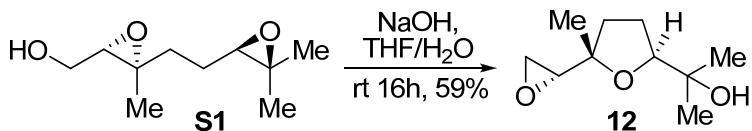
General Experimental Methods.

Unless otherwise noted, all reactions were performed under an oxygen-free atmosphere of argon with rigid exclusion of moisture from reagents and glassware. Teflon stir bars were oven or flame-dried prior to use. Unless otherwise noted, all solvents and triethylamine used in the reactions were purified via an SG Water USA solvent column system. Benzene was distilled from calcium hydride prior to use. Diisopropylamine was distilled from calcium hydride before use. Shi ketone **5** was prepared from D-fructose according to the procedure of Vidal-Ferran and coworkers and was used without recrystallization.^{S2} Trimethylsulfonium iodide was azeotropically dried from toluene three times before use. SO₃•pyr was pumped on under high vacuum overnight before use. Solvents for the Suzuki cross-coupling reaction were rigorously degassed (FPT) within a week before use and kept in an airtight Schlenck tube. Cs₂CO₃ used in the Suzuki cross-coupling reaction was pumped on under high vacuum overnight, kept and used inside a glovebox. 9-Borabicyclo[3.3.1]nonane dimer was pumped on under high vacuum overnight, kept and used inside a glovebox. The CH₂Cl₂ adduct of PdCl₂(dpff) was purchased from Strem® Chemical Company and kept and used inside a glovebox. *t*-BuOOH was purchased from Fluka® as a ~5.5 M solution in decane stored over activated 4Å MS. MsCl was distilled from calcium hydride before use. [(Ph₃P)CuH]₆ was purchased from Fluka® (brick red powder), pumped on under high vacuum overnight, kept and used inside a glovebox. 4Å MS used in the Sharpless asymmetric epoxidations or the bromonium-initiated epoxide-opening cascades were activated by flame drying under high vacuum three times (with cooling in between) immediately before use. For the bromonium-initiated epoxide-opening cascades, we found no significant differences in isolated yields whether the sieves were activated this way or by heating it at 180 °C for two days. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) (\geq 99%) was purchased from Aldrich® Chemical Company and was used without further purification. *N*-Bromosuccinimide (NBS) was recrystallized from H₂O before use and kept at 0 °C in the absence of light.

Analytical thin layer chromatography was performed using EM Science silica gel 60 F₂₅₄ plates.

The developed chromatogram was analyzed by UV lamp (254 nm) and ethanolic phosphomolybdic acid (PMA). Liquid chromatography was performed using flash chromatography of the indicated solvent system on Silicycle Silica Gel (230-400 mesh). ¹H and ¹³C NMR spectra were recorded on a Varian Inova-500 MHz spectrometer, a Bruker AVANCE-400 MHz spectrometer, or Bruker AVANCE-600 MHz spectrometer in CDCl₃ or C₆D₆. Chemical shifts in ¹H NMR spectra are reported in part per million (ppm) on the δ scale from an internal standard of residual CHCl₃ in CDCl₃ (7.27 ppm) or residual C₆HD₅ in C₆D₆ (7.16 ppm). Data are reported as follows: chemical shift, multiplicity (app = apparent, br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in hertz (Hz), and integration. Chemical shifts of ¹³C NMR spectra are reported in ppm from the central peak of CDCl₃ (77.23 ppm) or residual C₆D₆ (128.39 ppm) on the δ scale. Infrared (IR) spectra were recorded on a Perkin-Elmer 2000 FT-IR. High resolution mass spectra (HRMS) were obtained on a Bruker Daltonics APEXIV 4.7 Tesla Fourier Transform Ion Cyclotron Resonance Mass Spectrometer by Li Li of the Massachusetts Institute of Technology Department of Chemistry Instrumentation Facility.

Syntheses of and characterization of intermediates towards *ent*-1:



Epoxy furan 12: To a vigorously stirring solution of diepoxide **S1**^{S3} (2.51 g, 13.5 mmol, 100 mol%) in THF (6 mL) was added slowly a 0.5 M aqueous solution of NaOH (27 mL, 100 mol%) over 2 minutes. The mixture was stirred for 16 h at rt. It was then diluted with Et₂O (350 mL) and the layers were separated. The aqueous layer was extracted with 50 mL of Et₂O. The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (50% EtOAc in hexanes) isolated 1.50 g (7.97 mmol, 59%) of epoxy furan **12** as a colorless oil.

Characterization for diepoxide **S1:**

¹H NMR (600 MHz, C₆D₆)

δ 3.73 (ddd, *J* = 11.9, 6.5, 5.6 Hz, 1H), 3.64-3.60 (m, 1H), 2.91 (t, *J* = 5.8 Hz, 1H), 2.80 (td, *J* = 5.5, 1.8 Hz, 1H), 2.38 (dd, *J* = 7.9, 3.6 Hz, 1H), 1.65-1.61 (m, 1H), 1.41-1.33 (m, 1H), 1.29-1.24 (m, 1H), 1.09 (s, 3H), 1.04 (s, 3H), 0.98 (s, 3H).

¹³C NMR (125 MHz, C₆D₆)

δ 64.2, 63.4, 61.5, 60.4, 58.4, 36.8, 25.4, 25.1, 19.0, 16.8.

HR-MS (ESI) *m/z* calcd for C₁₀H₁₈O₃ [M+Na]⁺: 209.1148, found 209.1149.

IR (thin film, NaCl): 3424, 2964, 1458, 1380, 1032 cm⁻¹.

[α]_D²⁰ = +39.7 (c = 3.20, CHCl₃).

Characterization for epoxy furan **12:**

¹H NMR (400 MHz, C₆D₆)

δ 3.64–3.60 (m, 1H), 2.78 (dd, *J* = 4.1, 2.6 Hz, 1H), 2.25 (dd, *J* = 5.1, 4.1 Hz, 1H), 2.12 (dd, *J* = 5.1, 2.7

Hz, 1H), 1.98 (br s, 1H), 1.78-1.65 (m, 1H), 1.55-1.47 (m, 2H), 1.22 (s, 3H), 1.19-1.14 (m, 1H), 1.03 (s, 3H), 1.01 (s, 3H).

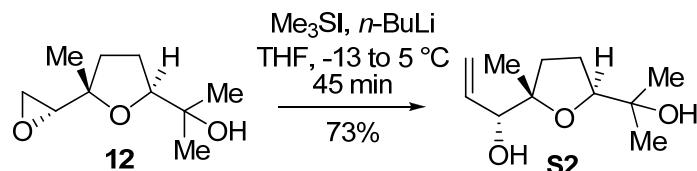
¹³C NMR (100 MHz, C₆D₆)

δ 87.2, 82.0, 70.6, 57.2, 43.4, 32.7, 28.1, 26.6, 25.2, 24.4.

HR-MS (ESI) m/z calcd for C₁₀H₁₈O₃ [M+Na]⁺: 209.1148, found 209.1155.

IR (thin film, NaCl): 3474, 2976, 2874, 1465, 1373, 1055, 897 cm⁻¹.

[α]_D²⁰ = +2.08 (c = 2.40, CHCl₃).



Allylic alcohol S2: To trimethylsulfonium iodide (547 mg, 2.68 mmol, 500 mol%) under an argon atmosphere was added THF (5 mL). The reaction mixture was cooled to -13 °C and a 2.5 M solution of *n*-BuLi in hexanes (1.03 mL, 2.58 mmol, 480 mol%) was added dropwise. The reaction was stirred for 45 min while warming to 0 °C. Epoxy furan **12** (98.3 mg, 0.5285 mmol, 100 mol%) in 1 mL of THF was added at 0 °C dropwise using a syringe. The reaction mixture was stirred another 45 min while warming to 5 °C. The reaction mixture was then diluted with Et₂O (5 mL) and quenched with 2 mL of satd. aq. NaHCO₃ at 5 °C. After warming to rt, it was further diluted with Et₂O to a total volume of 50 mL. It was then washed with 50 mL of satd. aq. NaHCO₃. The aqueous layer was extracted with Et₂O (3 x 5 mL). The combined organic layer was dried over MgSO₄, filtered, and concentrated. Column chromatography (50% EtOAc in hexanes) isolated 77.2 mg of allylic alcohol **S2** (0.385 mmol, 73%) as a colorless oil.

¹H NMR (500 MHz, C₆D₆)

δ 5.77 (ddd, *J* = 16.5, 10.7, 5.6, Hz, 1H), 5.40 (d, *J* = 17.5 Hz, 1H), 5.10 (d, *J* = 10.5 Hz, 1H), 3.98 (d, *J* = 5.0 Hz, 1H), 3.47 (dd, *J* = 10.5, 5.5 Hz, 1H), 2.21 (br s, 1H), 1.99 (ddd, *J* = 12.2, 12.2, 7.7 Hz, 1H), 1.87 (br s, 1H).

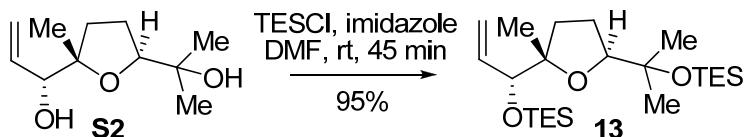
¹³C NMR (125 MHz, C₆D₆)

δ 137.5, 116.7, 88.4, 85.9, 78.2, 70.5, 32.3, 28.2, 26.7, 24.8, 24.4.

HR-MS (ESI) *m/z* calcd for C₁₁H₂₀O₃ [M+Na]⁺: 223.1305, found 223.1313.

IR (thin film, NaCl): 3421, 2974, 1653, 1457, 1375, 1056 cm⁻¹.

[α]_D²² = -2.8 (c = 1.73, CHCl₃).



TES ether 13: To allylic alcohol **S2** (29.7 mg, 0.1483 mmol, 100 mol%) and imidazole (70.7 mg, 1.04 mmol, 700 mol%) under an argon atmosphere was added anhydrous DMF (0.5 mL). After the imidazole had been dissolved, TESCl (87.1 μL, 0.519 mmol, 350 mol%) was added. The reaction was stirred for 45 min at rt. The reaction mixture was then diluted with Et₂O to a total volume of 50 mL and washed with satd. aq. NaCl (50 mL). The aqueous layer was extracted with Et₂O (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (2.5% EtOAc in hexanes) isolated TES ether **13** as a colorless oil.

¹H NMR (600 MHz, C₆D₆)

δ 5.92 (ddd, *J* = 16.9, 10.4, 6.2 Hz, 1H), 5.27 (app dt, *J* = 17.2, 1.7 Hz, 1H), 5.07 (ddd, *J* = 10.5, 2.2, 1.2 Hz, 1H), 4.12 (d, *J* = 6.1 Hz, 1H), 3.89 (dd, *J* = 8.9, 6.3 Hz, 1H), 2.18 (ddd, *J* = 18.0, 9.6, 8.4 Hz, 1H),

1.93-1.83 (m, 2H), 1.47 (ddd, J = 12.0, 8.2, 3.7 Hz, 1H), 1.28 (s, 3H), 1.26 (s, 3H), 1.20 (s, 3H), 1.06 (t, J = 8.0 Hz, 9H), 1.06 (t, J = 8.0 Hz, 9H), 0.71-0.64 (m, 12H).

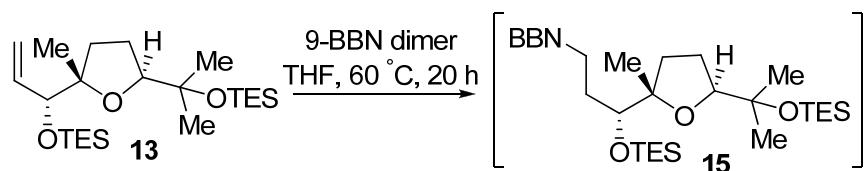
^{13}C NMR (100 MHz, C_6D_6)

δ 139.7, 116.0, 88.5, 86.1, 80.1, 75.0, 33.6, 28.6, 27.4, 25.9, 24.4, 7.8, 7.6, 7.6, 5.9.

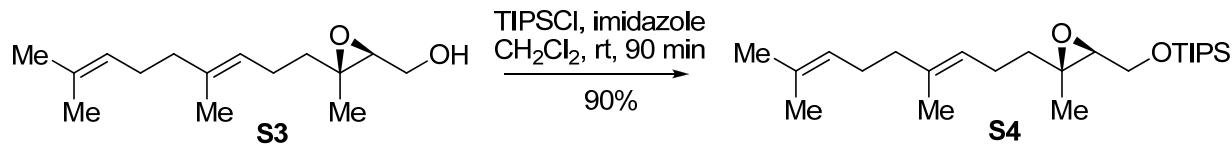
HR-MS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{48}\text{O}_3\text{Si}_2 [\text{M}+\text{Na}]^+$: 451.3034, found 451.3044.

IR (thin film, NaCl): 2955, 2877, 1653, 1458, 1239, 1172, 1096, 1039 cm^{-1} .

$[\alpha]^{22}_{\text{D}} = +6.1$ (c = 0.74, CHCl_3).



Alkylboron 15: To 9-borabicyclo[3.3.1]nonane dimer (6.45 mg, 0.0265 mmol, 118 mol%) in a Schlenck tube under an argon atmosphere was added TES ether **13** (9.6 mg, 0.0224 mmol, 100 mol%) in 1 mL of degassed (FPT) THF. The tube was closed and the reaction mixture was heated at 60 °C for 20 h. The alkylboron solution of **15** was used immediately in the cross-coupling step.



TIPS ether S4: Epoxy alcohol **S3**^{S4} (27.65 g, 116 mmol, 100 mol%) and imidazole (23.7 g, 348 mmol, 300 mol%) was purged with argon and CH_2Cl_2 (250 mL) was added under an argon atmosphere. The reaction mixture was stirred to dissolve all the imidazole. TIPSCl (38.5 mL, 174 mmol, 150 mol%, used

as received) was added in one portion at rt. The reaction mixture was stirred for 90 min at rt. The reaction mixture was diluted with Et₂O (300 mL), washed with brine (300 mL) and then H₂O (2 x 300 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. Column chromatography (2.5% EtOAc in hexanes) isolated 41.3 g (105 mmol, 90%) of TIPS ether **S4** as a colorless oil.

¹H NMR (500 MHz, C₆D₆)

δ 5.23–5.16 (m, 2H), 3.80 (dd, *J* = 11.4, 5.4 Hz, 2H), 3.00 (t, *J* = 5.4 Hz, 1H), 2.17–2.03 (m, 6H), 1.68 (s, 3H), 1.64–1.58 (m, 1H), 1.56 (s, 3H), 1.55 (s, 3H), 1.48–1.42 (m, 1H) 1.16 (s, 3H), 1.11–1.09 (m, 21H).

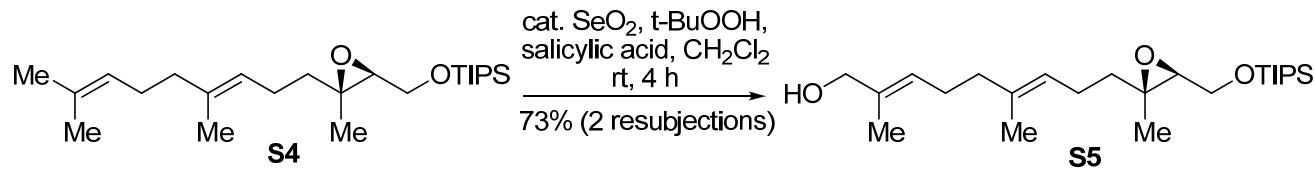
¹³C NMR (100 MHz, C₆D₆)

δ 135.8, 131.6, 125.2, 124.6, 63.5, 63.4, 60.1, 40.5, 39.3, 27.5, 26.2, 24.5, 18.6, 18.1, 17.3, 16.3, 12.7.

HR-MS (ESI) *m/z* calcd for C₂₄H₄₆O₂Si [M+Na]⁺: 417.3159, found 417.3166.

IR (thin film, NaCl): 2943, 2867, 1653, 1457, 1384, 1247, 1128, 1093, 1067, 883, 683 cm⁻¹.

[α]_D²² = -6.8 (*c* = 0.48, CHCl₃).



Allylic alcohol S5: TIPS ether **S4** (21.7 g, 55.0 mmol, 100 mol%) and salicylic acid (759 mg, 5.50 mmol, 10 mol%) were sparged with argon and CH₂Cl₂ (218 mL) was added under an argon atmosphere. t-BuOOH (11.5 mL, 63.2 mmol, 115 mol%) and then SeO₂ (305 mg, 2.75 mmol, 5 mol%) were added at rt. The reaction mixture was stirred for 5 h at rt and then diluted with CH₂Cl₂ (300 mL) and washed with a 1:1 mixture of satd. aq. NaCl and satd. aq. Na₂S₂O₃ (2 x 500 mL of mixture). The organic layer was

dried over MgSO₄, filtered, and concentrated. The starting material was separated from the product by column chromatography (a gradient of 0 to 25% EtOAc in hexanes). The starting material was resubjected to the reaction conditions two more times with amounts of reagents scaled accordingly to isolate a total of 16.6 g (40.3 mmol, 73%) of allylic alcohol **S5** as a colorless oil (obtained as a 3:1 mixture of *E/Z* isomers).

¹H NMR (500 MHz, C₆D₆)

δ 5.40 (t, J = 6.9 Hz, 1H), 5.20 (d, J = 7.2 Hz, 1H), 3.88-3.79 (m, 4H), 3.02 (t, J = 5.2 Hz, 1H), 2.16-2.03 (m, 6H), 1.62-1.56 (m, 1H), 1.57 (s, 3H), 1.55 (s, 3H), 1.52-1.46 (m, 1H), 1.16 (s, 3H), 1.13-1.10 (m, 21H).

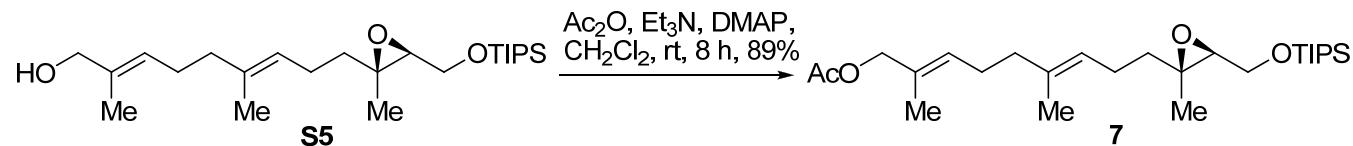
¹³C NMR (125 MHz, C₆D₆)

δ 135.9, 135.4, 125.3, 124.8, 69.0, 63.4, 63.4, 60.3, 40.1, 39.1, 26.7, 24.4, 18.6, 17.1, 16.3, 14.1, 12.7.

HR-MS (ESI) m/z calcd for C₂₄H₄₆O₄Si [M+Na]⁺: 449.3058, found 449.3055.

IR (thin film, NaCl): 2943, 2866, 1653, 1457, 1385, 1127, 1093, 1067, 883 cm⁻¹.

$[\alpha]^{22}_D$ = -7.7 (c = 2.48, CHCl₃) (as a 3:1 mixture of *E/Z* diastereomers).



Allylic acetate 7: To allylic alcohol **S5** (32.4 g, 79.0 mmol, 100 mol%) under an argon atmosphere was added CH₂Cl₂ (700 mL). Et₃N (33.0 mL, 237 mmol, 300 mol%) was added followed by Ac₂O (11.2 mL, 118 mmol, 150 mol%, used as received). DMAP (96.5 mg, 0.790 mmol, 1 mol%, used as received) was added while the reaction was stirring. The reaction mixture was stirred for 8 h at rt. It was then washed

with satd. aq. NaHCO_3 (800 mL). The aqueous layer was extracted once with CH_2Cl_2 (700 mL). The combined organic layers were dried over MgSO_4 , filtered, and concentrated. Column chromatography (2.5% EtOAc in hexanes) isolated 31.7 g (70.0 mmol, 89%) of allylic acetate **7** as a colorless oil (as a 3:1 mixture of *E/Z* isomers).

^1H NMR (500 MHz, C_6D_6)

δ 5.41 (t, $J = 7.1$ Hz, 1H), 5.14 (t, $J = 7.0$ Hz, 1H), 4.48 (s, 2H), 3.81 (dd, $J = 11.1, 5.5$ Hz, 2H), 3.01 (t, $J = 5.3$ Hz, 1H), 2.13-1.95 (m, 6H), 1.71 (s, 3H), 1.63-1.57 (m, 1H), 1.55 (s, 3H), 1.50 (s, 3H), 1.49-1.43 (m, 1H), 1.16 (s, 3H), 1.12-1.09 (m, 21H).

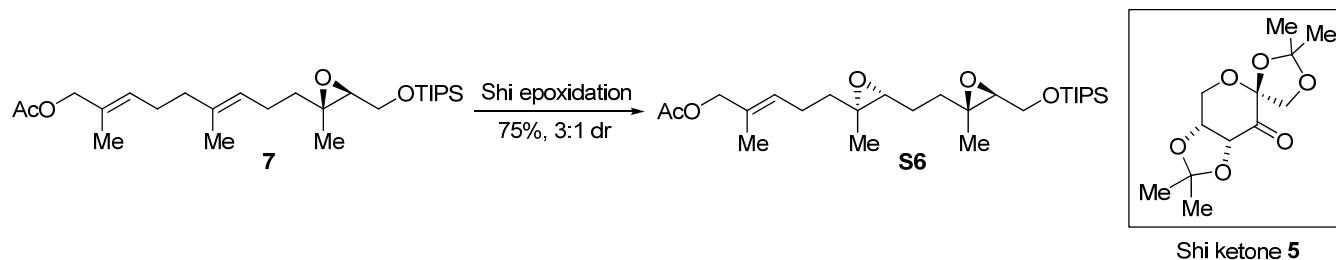
^{13}C NMR (125 MHz, C_6D_6)

δ 170.2, 135.2, 131.0, 129.6, 124.9, 70.4, 63.5, 63.4, 60.1, 39.7, 39.2, 27.0, 24.4, 20.9, 18.5, 17.3, 16.2, 14.3, 12.6.

HR-MS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{48}\text{O}_4\text{Si} [\text{M}+\text{Na}]^+$: 475.3214, found 475.3235.

IR (thin film, NaCl): 2943, 2867, 1741, 1463, 1384, 1240, 1094, 1067, 883 cm^{-1} .

$[\alpha]^{22}_D = -6.1$ ($c = 5.06$, CHCl_3) (as a 3:1 mixture of *E/Z* diastereomers).



See also ref. S5

Diepoxide S6: To a solution of allylic acetate **7** (6.74 g, 14.9 mmol, 100 mol%) in 2:1 v/v DMM/MeCN (309 mL) was added a 0.05 M solution of $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$ in 4×10^{-4} Na_2EDTA (155 mL), $n\text{Bu}_4\text{HSO}_4$ (1.05 g, 3.09 mmol, 20 mol%), and Shi ketone (4.00 g, 14.9 mmol, 100 mol %). This biphasic mixture was stirred vigorously at 0 °C for 10 min. To this mixture was added, simultaneously over 30 min via

syringe pump, a solution of Oxone® (8.50 g, 15.5 mmol, 105 mol%, freshly prepared) in 75.0 mL of 4×10^{-4} M Na₂EDTA solution and a 0.89 M solution of aq. K₂CO₃ (75.0 mL, 65.7 mmol, 440 mol%). Upon completion of addition, the reaction mixture was immediately diluted with Et₂O (200 mL) and washed with H₂O (300 mL). The aqueous layer was extracted with Et₂O (2 x 150 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (10% EtOAc in hexanes) isolated 5.25 g (11.2 mmol, 75%) of diepoxyde **S6** as a colorless oil (as a 3:1 mixture of *R*, *S* and *S*, *S* diastereomers). This procedure was repeated several times on a similar scale and the product was combined and carried on to the subsequent steps.

¹H NMR (600 MHz, C₆D₆)

δ 5.33 (t, *J* = 7.3 Hz, 1H), 4.44 (d, *J* = 2.1 Hz, 2H), 3.81 (dd, *J* = 5.3, 1.1 Hz, 1H), 2.97 (t, *J* = 5.3 Hz, 1H), 2.51 (t, *J* = 5.8 Hz, 1H), 2.03-1.98 (m, 2H), 1.73 (s, 3H), 1.57-1.48 (m, 8H), 1.39-1.34 (ddd, *J* = 16.5, 9.5, 7.0 Hz, 1H), 1.12 (s, 3H), 1.10 (s, 3H), 1.09-1.07 (m, 21H).

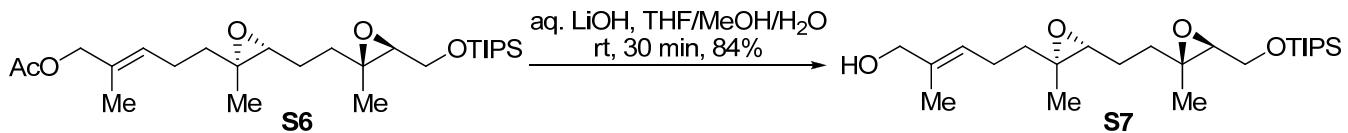
¹³C NMR (100 MHz, C₆D₆)

δ 170.3, 131.3, 129.2, 70.3, 63.7, 63.5, 63.0, 60.1, 59.8, 38.8, 36.2, 25.3, 24.1, 20.9, 18.6, 17.1, 17.0, 14.2, 12.7.

HR-MS (ESI) *m/z* calcd for C₂₆H₄₈O₅Si [M+Na]⁺: 491.3163, found 491.3182.

IR (thin film, NaCl): 2943, 2867, 1741, 1457, 1384, 1231, 1092, 1067, 883 cm⁻¹.

[α]_D²² = -6.5 (*c* = 2.23, CHCl₃).



Allylic alcohol S7: To diepoxide **S6** (23.2 g, 49.4 mmol, 100 mol%) was added a 1.5:3.5 v/v THF/MeOH (1000 mL, solvents used without drying). The reaction mixture was put in a water bath at 22 °C. A 0.5 M solution of aq. LiOH (198 mL, 98.8 mmol, 200 mol%) was added over 10 min. The reaction mixture was stirred at rt for 30 min. It was then concentrated to a volume of 400 mL and diluted with Et₂O (600 mL) and washed with satd. aq. NaCl (1000 mL). The aqueous layer was extracted with Et₂O (3 x 200 mL), dried over MgSO₄, filtered, and concentrated. Column chromatography (20% EtOAc in hexanes) isolated 17.7 g (41.5 mmol, 84%) of allylic alcohol **S7** as a colorless oil.

¹H NMR (500 MHz, C₆D₆)

δ 5.36 (t, *J* = 7.3 Hz, 1H), 3.92-3.78 (m, 4H), 3.00 (t, *J* = 5.3 Hz, 1H), 2.58 (t, *J* = 4.9, 1H), 2.11-2.05 (m, 2H), 1.63-1.41 (m, 6H), 1.57 (s, 3H), 1.13-1.09 (m, 27H).

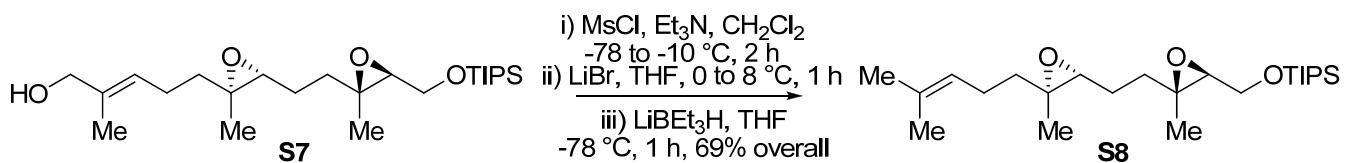
¹³C NMR (125 MHz, C₆D₆)

δ 136.1, 124.9, 68.8, 63.8, 63.5, 63.1, 60.4, 60.0, 39.1, 36.1, 25.3, 24.1, 18.6, 17.1, 17.0, 14.0, 12.6.

HR-MS (ESI) *m/z* calcd for C₂₄H₄₆O₄Si [M+Na]⁺: 449.3058, found 449.3065.

IR (thin film, NaCl): 3446, 2943, 2866, 1457, 1386, 1010, 1095, 883 cm⁻¹.

[*α*]_D²² = -1.8 (*c* = 1.33, CHCl₃).



Diepoxide S8: Allylic alcohol **S7** (2.95 g, 6.91 mmol, 100 mol%) and Et_3N (1.45 mL, 10.4 mmol, 150 mol%) in CH_2Cl_2 (63 mL) was cooled to $-78 \text{ }^\circ\text{C}$ under an argon atmosphere. MsCl (0.62 mL, 7.95 mmol, 115 mol%) in CH_2Cl_2 (9 mL) was added via syringe over 2 min. The reaction mixture was stirred for 1 h at $-78 \text{ }^\circ\text{C}$ and then $-10 \text{ }^\circ\text{C}$ for another 1 h. It was then further warmed to 0 $^\circ\text{C}$ and stirred another 1.5 h. LiBr (1.5 g, 17.3 mmol, 250 mol%) in THF (19 mL) was added over 5 min. The reaction mixture was let warm to 8 $^\circ\text{C}$ over 1 h. It was then diluted with Et_2O (400 mL) and washed with satd. aq. NaCl (400 mL). The organic layer was dried over MgSO_4 , filtered, and concentrated. The residue was taken up in CH_2Cl_2 (200 mL), filtered through celite, and rinsed with CH_2Cl_2 to a total volume of about 400 mL. It was re-concentrated to give the intermediate allylic bromide as a brown oil, which was pumped on under high vacuum for three hours to remove any residual water. The crude residue was then dissolved in dry THF (103 mL) and cooled to $-78 \text{ }^\circ\text{C}$ under an argon atmosphere. A 1.0 M solution of LiBEt_3H in THF (12.2 mL, 12.2 mmol, 200 mol%) was added over 15 min. The reaction was stirred for 1 h at $-78 \text{ }^\circ\text{C}$. It was then quenched by dropwise addition of H_2O (10 mL) at $-78 \text{ }^\circ\text{C}$. The reaction mixture was warmed to rt whereupon it was further diluted with Et_2O and H_2O (200 mL each). The organic layer was further washed with satd. aq. NaCl (200 mL). The combined aqueous layers were extracted with Et_2O (2 x 100 mL). The combined organic layers were dried over MgSO_4 , filtered, and concentrated. Column chromatography (10% EtOAc in hexanes) isolated 1.93 g (4.70 mmol, 69% from **S7**) of diepoxide **S8** as a colorless oil.

^1H NMR (500 MHz, C_6D_6)

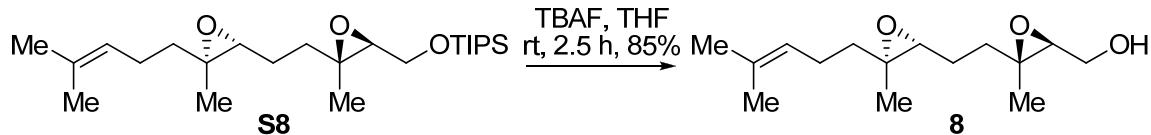
δ 5.11 (t, $J = 6.6 \text{ Hz}$, 1H), 3.80 (d, $J = 5.0 \text{ Hz}$, 2H), 2.95 (t, $J = 5.5 \text{ Hz}$, 1H), 2.53 (m, 1H), 2.11-2.03 (m,

2H), 1.64 (s, 3H), 1.63-1.38 (m, 6H), 1.52 (s, 3H), 1.16-1.04 (m, 27H).

¹³C NMR (125 MHz, C₆D₆)

δ 131.8, 124.9, 63.7, 63.5, 63.0, 60.3, 59.8, 39.5, 36.2, 26.2, 25.4, 24.6, 18.6, 18.0, 17.2, 17.0, 12.7.

HRMS (ESI) m/z calcd for C₂₄H₄₆O₃Si [M+Na]⁺: 433.3108, found 433.3117.



Diepoxy alcohol 8: To diepoxyide **S8** (5.96 g, 14.5 mmol, 100 mol%) in THF (140 mL) under an argon atmosphere at rt was added a 1 M TBAF solution in THF (42.0 mL, 42.0 mmol, 290 mol%). The reaction mixture was stirred for 2.5 h at rt. The THF was removed by rotary evaporator and the residue was redissolved in Et₂O (300 mL). It was then washed with 300 mL satd. aq. NaCl. The aqueous layer was extracted with Et₂O (1 x 100 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (50% EtOAc in hexanes) isolated 3.15 g (12.3 mmol, 85%) of diepoxy alcohol **8** as a colorless oil.

¹H NMR (600 MHz, C₆D₆)

δ 5.10 (t, *J* = 7.2 Hz, 1H), 3.72 (dd, *J* = 11.7, 4.93 Hz, 1H), 3.58 (dd, *J* = 11.7, 6.4 Hz, 1H), 2.88 (dd, *J* = 6.5, 5.4 Hz, 1H), 2.47 (dd, *J* = 7.9, 3.8 Hz, 1H), 2.06-1.97 (m, 2H), 1.69-1.62 (m, 4H), 1.55-1.50 (m, 4H), 1.43-1.25 (m, 4H), 1.10 (s, 3H), 1.03 (s, 3H).

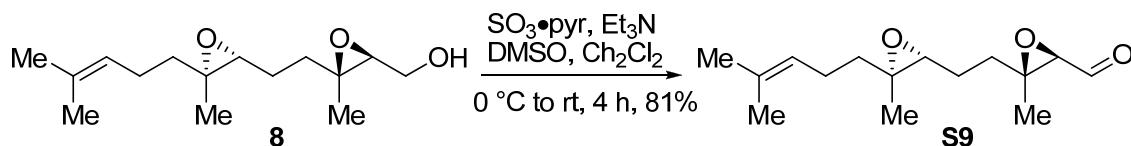
¹³C NMR (100 MHz, C₆D₆)

δ 132.0, 124.6, 63.5, 63.3, 61.4, 60.9, 60.4, 39.3, 36.8, 26.2, 25.3, 24.5, 18.0, 17.0, 16.8.

HR-MS (ESI) m/z calcd for C₁₅H₂₆O₃ [M+Na]⁺: 277.1774, found 277.1786.

IR (thin film, NaCl): 3432, 2966, 2927, 1457, 1386, 1037, 867 cm⁻¹.

$[\alpha]^{22}_D = +18.1$ ($c = 0.82$, CHCl₃).



Aldehyde S9: To diepoxy alcohol **8** (1.50 g, 5.88 mmol, 100 mol%) in CH₂Cl₂ under an argon atmosphere was added Et₃N (2.45 mL, 17.6 mmol, 300 mol%) and DMSO (5.88 mL, 82.8 mmol, 1400 mol%). The reaction mixture was cooled to 0 °C and SO₃•pyr (1.88 g, 11.8 mmol, 200 mol%) was added in one portion. The reaction mixture was stirred for 4 h while warming to rt. It was then diluted with Et₂O (200 mL) and washed with satd. aq. NH₄Cl (200 mL). The aqueous layer was extracted with Et₂O (2 x 100 mL) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (25% EtOAc in hexanes) isolated 1.21 g (4.76 mmol, 81%) of aldehyde **S9** as a colorless oil.

¹H NMR (500 MHz, C₆D₆)

δ 9.14 (dd, $J = 4.8, 0.7$ Hz, 1H), 5.13 (t, $J = 7.1$ Hz, 1H), 2.82 (d, $J = 4.8$ Hz, 1H), 2.42-2.40 (m, 1H), 2.10-2.02 (m, 2H), 1.65 (s, 3H), 1.63-1.57 (m, 1H), 1.54 (s, 3H), 1.47-1.24 (m, 5H), 1.05 (s, 3H), 0.94 (s, 3H).

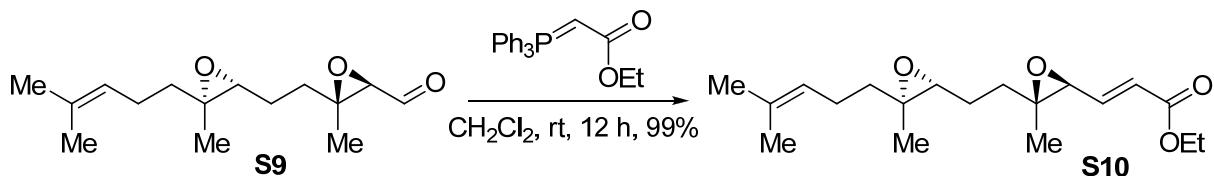
¹³C NMR (100 MHz, C₆D₆)

δ 198.6, 132.0, 124.7, 63.8, 63.6, 62.6, 60.4, 39.4, 35.6, 26.2, 24.8, 24.6, 18.0, 17.1, 17.0.

HR-MS (ESI) m/z calcd for C₁₅H₂₄O₃ [M+H]⁺: 253.1798, found 253.1807.

IR (thin film, NaCl): 2967, 2927, 1723, 1457, 1386, 1073 cm⁻¹.

$[\alpha]^{22}_D = +66.9$ ($c = 1.20$, CHCl₃).



Enoate S10: To aldehyde **S9** in CH_2Cl_2 under an argon atmosphere was added (carbethoxymethylene)triphenylphosphorane (6.5 g, 18.7 mmol, 150 mol%). The reaction mixture was stirred at rt for 4 h. The solvent was removed using a rotary evaporator and the residue was applied directly to flash column chromatography using 15% EtOAc in hexanes as the eluent. Enoate **S10** was obtained as a colorless oil (4.01 g, 12.5 mmol, 99%).

$^1\text{H NMR}$ (600 MHz, C_6D_6)

δ 6.98 (dd, $J = 15.7, 6.2$ Hz, 1H), 6.18 (dd, $J = 15.6, 1.04$ Hz, 1H), 5.15 (t, $J = 7.2$ Hz, 1H), 4.00 (qd, $J = 7.2, 1.5$ Hz, 2H), 2.97 (dd, $J = 6.2, 0.8$ Hz, 1H), 2.50 (t, $J = 6.2$ Hz, 1H), 2.11-2.03 (m, 2H), 1.65 (s, 3H), 1.64-1.59 (m, 1H), 1.54 (s, 3H), 1.49-1.39 (m, 5H), 1.10 (s, 3H), 0.96 (t, $J = 7.2$ Hz, 3H), 0.95 (s, 3H).

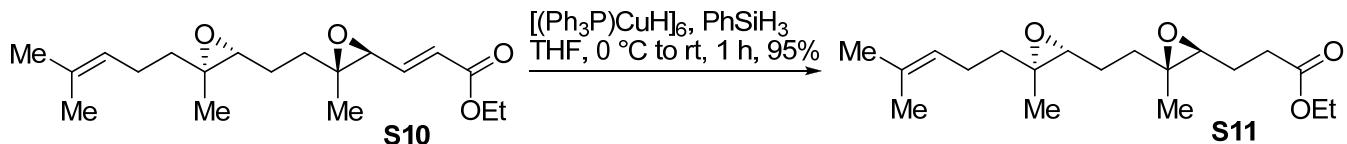
$^{13}\text{C NMR}$ (100 MHz, C_6D_6)

δ 165.7, 143.5, 132.0, 125.5, 124.8, 63.8, 62.9, 61.7, 60.7, 60.4, 39.4, 36.0, 26.2, 25.3, 24.6, 18.0, 17.1, 16.6, 14.6.

HR-MS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{24}\text{O}_3 [\text{M}+\text{Na}]^+$: 345.2036, found 345.2039.

IR (thin film, NaCl): 2967, 2928, 1718, 1653, 1457, 1262, 1177 cm^{-1} .

$[\alpha]_{\text{D}}^{22} = +18.9$ ($c = 0.67$, CHCl_3).



Ester S11: To enoate **S10** in THF (125 mL) under an argon atmosphere was added PhSiH₃ (3.1 mL, 24.8 mmol, 200 mol%) and the reaction mixture was cooled to 0 °C. [(Ph₃P)CuH]₆ (740 mg, 0.377 mmol, 3 mol%) was added in one portion. The reaction mixture was stirred for 1 h at 0 °C. It was then opened to air and H₂O (50 mL) was added at 0 °C. The quenched reaction mixture was stirred vigorously for 30 min at 0 °C. It was then filtered through celite, using Et₂O (250 mL) as the eluent. The biphasic filtrate was separated and the organic layer was washed with satd. aq. NH₄Cl (250 mL). The aqueous layer was extracted with Et₂O (2 x 100 mL). The combined organic layers were dried over MgSO₄, filtered through a bed of silica, and concentrated. Column chromatography (10% EtOAc in hexanes) isolated 3.82 g (11.8 mmol, 95%) of ester **S11** as a colorless oil.

¹H NMR (600 MHz, C₆D₆)

δ 5.13 (t, *J* = 7.2 Hz, 1H), 3.94 (q, *J* = 7.1 Hz, 2H), 2.64 (app t, *J* = 6.2 Hz, 1H), 2.54-2.53 (m, 1H), 2.32-2.22 (m, 2H), 2.13-2.02 (m, 2H), 1.82-1.69 (m, 2H), 1.65 (s, 3H), 1.63-1.59 (m, 1H), 1.53 (s, 3H), 1.51-1.41 (m, 5H), 1.12 (s, 3H), 1.07 (s, 3H), 0.95 (t, *J* = 7.2 Hz, 3H).

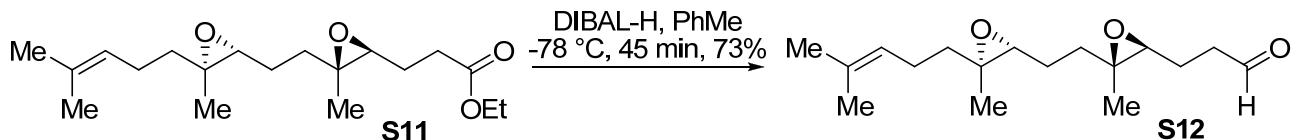
¹³C NMR (100 MHz, C₆D₆)

δ 172.8, 131.9, 124.8, 63.1, 62.5, 60.6, 60.6, 60.3, 39.5, 36.4, 31.6, 26.2, 25.5, 25.0, 24.6, 18.0, 17.0, 16.9, 14.6.

HR-MS (ESI) *m/z* calcd for C₁₉H₃₂O₄[M+Na]⁺: 347.2193, found 347.2192.

IR (thin film, NaCl): 2967, 2929, 1734, 1457, 1134 cm⁻¹.

[\alpha]_D²² = -4.6 (*c* = 2.01, CDCl₃).



Aldehyde S12: To ester **S11** (3.82 g, 11.8 mmol, 100 mol%) in toluene (105 mL) at $-78\text{ }^{\circ}\text{C}$ was added a 0.2 M solution of DIBAL-H in toluene (54.7 mL, 11.8 mmol, 100 mol%) slowly over 45 min using a syringe pump. After addition was completed the reaction mixture was immediately quenched with addition of MeOH (15 mL) at $-78\text{ }^{\circ}\text{C}$. It was further diluted with 105 mL of satd. aq. sodium potassium tartrate (Rochelle's salt) solution. The reaction mixture was warmed to rt while stirring rigorously for 30 min. It was then diluted with Et₂O (300 mL) and washed with satd. aq. NaCl (300 mL). The aqueous layer was extracted with Et₂O (2 x 100 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (20% EtOAc in hexanes) isolated 2.43 g (8.66 mmol, 73%) of aldehyde **S12** as a colorless oil.

¹H NMR (600 MHz, C₆D₆)

δ 9.28 (s, 1H), 5.14 (t, $J = 7.1$ Hz, 1H), 2.53-2.50 (m, 2H), 2.11-1.92 (m, 4H), 1.65 (s, 3H), 1.64-1.41 (m, 11H), 1.12 (s, 3H), 1.03 (s, 3H).

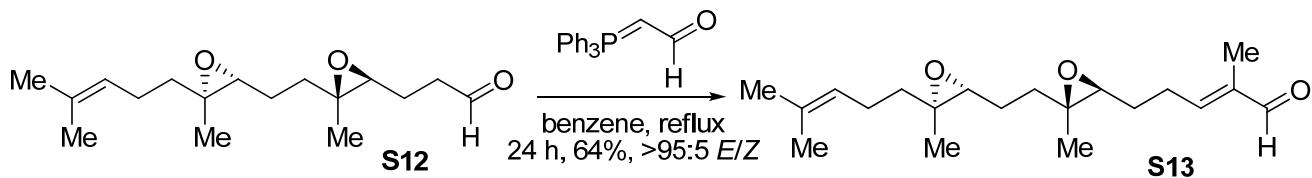
¹³C NMR (100 MHz, C₆D₆)

δ 200.1, 131.9, 124.8, 63.1, 62.5, 60.6, 60.3, 41.1, 39.5, 36.5, 26.2, 25.5, 24.6, 22.1, 18.0, 17.0, 16.8.

HR-MS (ESI) m/z calcd for C₁₇H₂₈O₃ [M+Na]⁺: 303.1931, found 303.1936.

IR (thin film, NaCl): 2966, 2928, 1725, 1700, 1653, 1559, 1457, 1386, cm⁻¹.

$[\alpha]^{22}_{\text{D}}$ = +5.9 ($c = 2.46$, CHCl₃).



Enal S13: A mixture of aldehyde **S12** (95.0 mg, 0.339 mmol, 100 mol%) and 2-(triphenylphosphoranylidene)propionaldehyde (140 mg, 0.440 mmol, 130 mol%) in benzene (2.5 mL) was refluxed for 24 h. The reaction mixture was then cooled to rt and the solvent removed using a rotary evaporator. The residue was applied directly to flash column chromatography using 20% EtOAc in hexanes as the eluent. Enal **S13** was obtained as a colorless oil (69.3 mg, 0.216 mmol, 64%).

¹H NMR (600 MHz, C₆D₆)

δ 9.29 (s, 1H), 5.89 (t, $J = 7.4$ Hz, 1H), 5.13 (t, $J = 7.2$ Hz, 1H), 2.56-2.54 (m, 1H), 2.46 (t, $J = 6.2$ Hz, 1H), 2.14-2.01 (m, 4H), 1.65 (s, 3H), 1.63 (s, 3H), 1.62-1.41 (m, 9H), 1.36-1.32 (m, 2H), 1.14 (s, 3H), 1.06 (s, 3H).

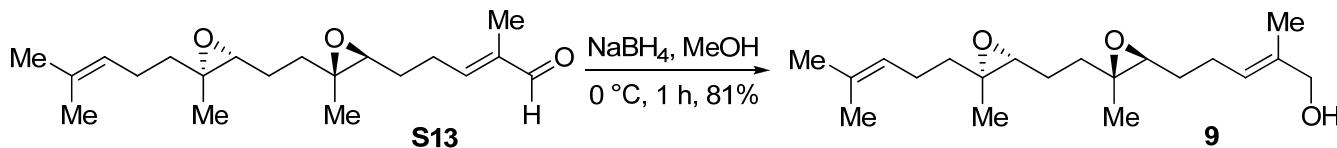
¹³C NMR (100 MHz, C₆D₆)

δ 194.2, 152.1, 140.3, 132.0, 124.7, 63.2, 62.9, 60.3, 60.3, 39.5, 36.6, 28.2, 26.4, 26.2, 25.5, 24.6, 18.0, 17.1, 16.9, 9.5.

HR-MS (ESI) m/z calcd for C₂₀H₃₂O₃ [M+Na]⁺ : 343.2244, found 343.2249.

IR (thin film, NaCl): 2965, 2927, 1686, 1653, 1457, 1385 cm⁻¹.

$[\alpha]^{22}_D = -4.0$ ($c = 0.86$, CHCl₃).



Allylic alcohol 9: To enal **S13** (38.6 mg, 0.120 mmol, 100 mol%) in MeOH (1 mL) at 0 °C was added NaBH₄ (12.1 mg, 0.32 mmol, 270 mol%). The reaction mixture was stirred at 0 °C for 1 h. It was then diluted with Et₂O (30 mL) and washed with 30 mL of satd. aq. NaHCO₃. The aqueous layer was extracted with Et₂O (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (40% EtOAc in hexanes) isolated 31.3 mg (0.0972 mmol, 81%) of allylic alcohol **9** as a colorless oil.

¹H NMR (500 MHz, C₆D₆)

δ 5.39 (t, *J* = 7.2 Hz, 1H), 5.13 (t, *J* = 7.1 Hz, 1H), 3.83 (br s, 2H), 2.63 (t, *J* = 5.9 Hz, 1H), 2.58 (t, *J* = 5.1 Hz, 1H), 2.14-2.06 (m, 4H), 1.65 (s, 3H), 1.63-1.60 (m, 1H), 1.58-1.54 (m, 6H), 1.53 (s, 3H), 1.52-1.41 (m, 4H), 1.13 (s, 3H), 1.12 (s, 3H).

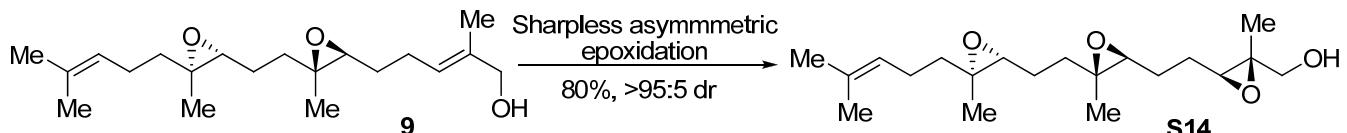
¹³C NMR (100 MHz, C₆D₆)

δ 136.5, 131.9, 124.8, 124.5, 68.7, 63.4, 63.3, 60.6, 60.3, 39.5, 36.5, 29.4, 26.2, 25.5, 25.3, 24.6, 18.0, 17.0, 14.0.

HR-MS (ESI) *m/z* calcd for C₂₀H₃₄O₃ [M+Na]⁺: 345.2400, found 345.2402.

IR (thin film, NaCl): 3447, 2964, 2922, 1653, 1559, 1457, 1387 cm⁻¹.

[α]_D²² = -6.2 (*c* = 1.24, CHCl₃).



Triepoxy alcohol S14: 82 mg of 4Å MS was activated according to the procedure given in the General Experimental Methods. To this 2 mL of CH₂Cl₂ was added under an argon atmosphere. The reaction mixture was cooled to –20 °C. L-(+)-DET (9.35 µL, 0.0546 mmol, 12.5 mol%) followed by Ti(O*i*-Pr)₄ (12.9 µL, 0.0437 mmol, 10 mol%) were added sequentially. The reaction mixture was cooled further to –48 °C and *t*-BuOOH (0.10 mL, 0.546 mmol, 125 mol%) was added. The reaction mixture was stirred at this temperature for 30 min. allylic alcohol **9** (141 mg, 0.437 mmol, 100 mol%) was then added in 0.5 mL CH₂Cl₂. The reaction mixture was stirred at –48 °C for 1 h. It was then quenched at the same temperature by the addition of ice-cold 40% NaOH solution in brine, made from 60 mg of NaOH and 7.5 mg of NaCl dissolved in 0.15 mL H₂O. The quenched reaction mixture was stirred at 0 °C for 30 min. It was then filtered through celite, eluted with 50 mL of Et₂O, and washed with satd. aq. Na₂S₂O₃ (50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. Column chromatography (50:49:1 hexanes:EtOAc:Et₃N) isolated 118 mg (0.350 mmol, 80%) of triepoxy alcohol **S14** as a colorless oil with a 95:5 dr.

¹H NMR (500 MHz, C₆D₆)

δ 5.14 (t, J = 7.2 Hz, 1H), 3.34 (d, J = 2.4 Hz, 1H), 3.33 (s, 1H), 2.89 (dd, J = 6.9, 5.4 Hz, 1H), 2.61-2.56 (m, 2H), 2.13-2.07 (m, 2H), 1.66 (s, 3H), 1.64-1.37 (m, 10H), 1.54 (s, 3H), 1.14 (s, 3H), 1.08 (s, 3H), 1.04 (s, 3H).

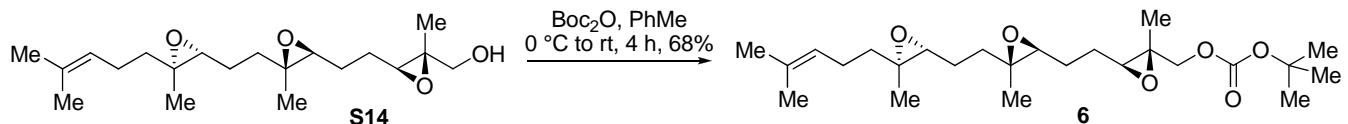
¹³C NMR (125 MHz, C₆D₆)

δ 131.9, 124.8, 66.5, 63.2, 63.0, 61.0, 60.5, 60.4, 59.8, 39.5, 36.5, 26.5, 26.2, 26.1, 25.5, 24.6, 18.0, 17.0
, 16.9, 14.6.

HR-MS (ESI) m/z calcd for $C_{20}H_{34}O_4 [M+Na]^+$: 361.2349, found 361.2354.

IR (thin film, NaCl): 3447, 2964, 2926, 1472, 1457, 1437, 1386, 1073, 1042 cm^{-1} .

$[\alpha]^{22}_D = -13.6$ ($c = 0.30$, CHCl_3).



Carbonate #: Triepoxy alcohol **S14** (724 mg, 2.14 mmol, 100 mol%) in toluene (6.6 mL) was cooled to 0 °C under an argon atmosphere. 1-Methylimidazole (0.230 mL, 2.89 mmol, 135 mol%) followed by Boc_2O (0.660 mL, 2.89 mmol, 135 mol%) were added dropwise. The reaction mixture was stirred for 5 h while warming to rt. The solvent was then removed using a rotary evaporator and the residue applied directly to flash column chromatography using a slow gradient of 90:9:1 to 30:69:1 hexanes: Et_2O : Et_3N as the eluent. Carbonate **6** was isolated as a colorless oil (636 mg, 1.46 mmol, 68%).

^1H NMR (500 MHz, C_6D_6)

δ 5.14 (t, $J = 7.1$ Hz, 1H), 4.07 (d, $J = 11.5$ Hz, 1H), 3.94 (d, $J = 11.5$ Hz, 1H), 2.72 (dd, $J = 6.6, 5.3$ Hz, 1H), 2.59-2.56 (m, 2H), 2.13-2.07 (m, 2H), 1.66 (s, 3H), 1.64-1.60 (m, 1H), 1.57-1.36 (m, 13H), 1.34 (s, 9H), 1.15 (s, 3H), 1.12 (s, 3H), 1.07 (s, 3H).

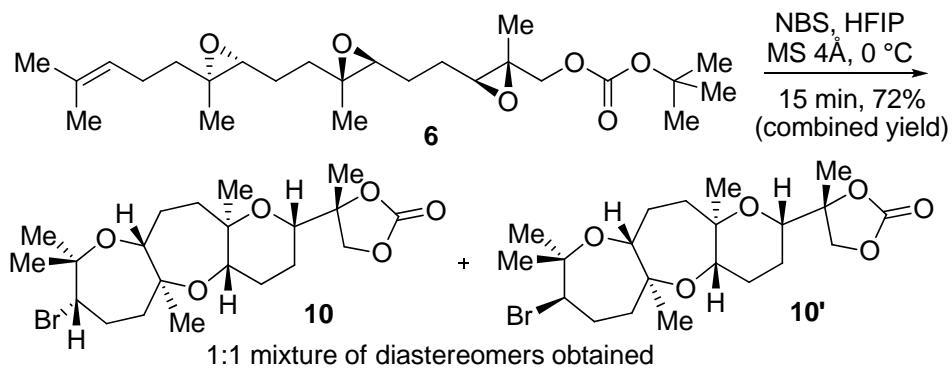
^{13}C NMR (125 MHz, C_6D_6)

δ 154.3, 131.9, 124.8, 81.9, 71.4, 63.2, 62.7, 60.8, 60.3 (2C), 58.6, 39.5, 36.4, 28.0, 26.4, 26.2, 25.9, 25.5, 24.6, 18.0, 17.1, 16.9, 14.7.

HR-MS (ESI) m/z calcd for $C_{25}H_{42}O_6 [M+Na]^+$: 461.2874, found 461.2870.

IR (thin film, NaCl): 2967, 2926, 1741, 1457, 1284, 1253, 1163 cm^{-1} .

$[\alpha]^{22}_D = -13.7$ ($c = 0.33$, CHCl_3).



Tetracycle 10 and 10': 760 mg of 4 \AA MS was activated according to the procedure given in the General experimental methods. To this was added carbonate **6** (91.9 mg, 0.2095 mmol, 100 mol%) in 7.60 mL of 1,1,1,3,3-hexafluoro-2-propanol (HFIP) under an argon atmosphere. The reaction mixture was cooled to 0 °C and *N*-bromosuccinimide (NBS) (122 mg, 0.684 mmol, 300 mol%) was added in one portion with rigorous stirring. The reaction mixture was kept out of light. After 15 min it was diluted with Et_2O and filtered through celite, using 30 mL of Et_2O as the eluent. The solvent was removed using a rotary evaporator and the residue was redissolved in 20 mL of Et_2O . It was then washed with a 1:1 mixture of satd. aq. $\text{Na}_2\text{S}_2\text{O}_3:\text{NaCl}$ (20 mL total). The aqueous layer was extracted with Et_2O (2 x 10 mL). The combined organic layers were dried over MgSO_4 , filtered, and concentrated. Column chromatography (50% EtOAc in hexanes) isolated the following as white amorphous solids: tetracycle **10** (31.6 mg, 0.0685 mmol, 33%), **10'** (31.2 mg, 0.0676 mmol, 33%) and ~1:1 mixture of the two (5.8 mg, 0.0126 mmol, 6%).

Characterization for tetracycle 10:

^1H NMR (500 MHz, C_6D_6)

δ 4.02 (d, $J = 8.2$ Hz, 1H), 3.99 (dd, $J = 10.5, 2.0$ Hz, 1H), 3.60 (dd, $J = 11.9, 4.6$ Hz, 1H), 3.37 (dd, $J = 12.0, 5.4$ Hz, 1H), 3.29 (d, $J = 10.8$, 1H), 3.27 (d, $J = 8.2$ Hz, 1H), 2.04-1.92 (m, 2H), 1.72-1.66 (m, 1H),

1.53-1.47 (m, 2H), 1.43-1.32 (m, 8H), 1.28-1.22 (m, 4H), 1.12 (s, 3H), 1.08 (s, 3H), 1.04-1.00 (m, 1H), 0.81 (s, 3H).

¹³C NMR (125 MHz, C₆D₆)

δ 154.7, 83.3, 79.6, 78.6, 78.0, 76.2, 71.3, 70.7, 69.5, 60.1, 40.9, 38.9, 32.2, 29.1, 26.0, 24.9, 23.9, 23.2, 21.1, 20.7, 19.9.

HR-MS (ESI) m/z calcd for C₂₁H₃₃BrO₆ [M+Na]⁺: 483.1353, found 483.1369.

IR (thin film, NaCl): 2938, 1793, 1457, 1382, 1094, 1070 cm⁻¹.

[α]_D²² = -26.1 (c = 0.20, CHCl₃).

Characterization for tetracycle 10':

¹H NMR (500 MHz, C₆D₆)

δ 4.21 (dd, J = 10.3, 1.1 Hz, 1H), 4.07 (dd, J = 5.4, 2.6 Hz, 1H), 3.89 (d, J = 8.1 Hz, 1H), 3.76 (app t, J = 8.4 Hz, 1H), 3.53 (dd, J = 11.9, 4.7 Hz, 1H), 3.18 (d, J = 8.1 Hz, 1H), 2.45 (ddd, J = 14.5, 10.9, 4.7 Hz, 1H), 1.78-1.62 (m, 4H), 1.53-1.43 (m, 5H), 1.32 (s, 3H), 1.22 (s, 3H), 1.13 (s, 3H), 1.07-1.00 (m, 1H), 1.91-0.84 (m, 4H), 0.65 (s, 3H).

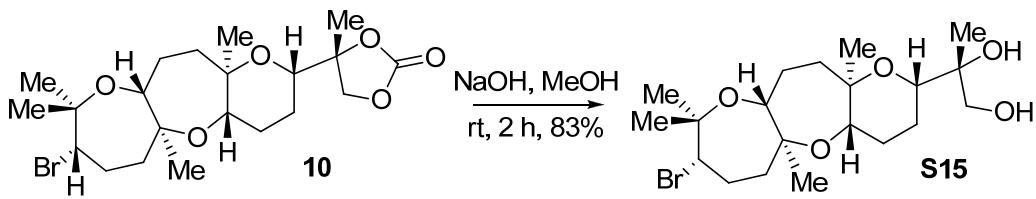
¹³C NMR (125 MHz, C₆D₆)

δ 154.8, 83.5, 80.2, 78.6, 76.8, 76.1, 71.0, 70.9, 70.1, 67.1, 39.1, 36.0, 29.9, 29.5, 28.7, 28.6, 24.1, 23.4, 21.6, 20.9, 20.3.

HR-MS (ESI) m/z calcd for C₂₁H₃₃BrO₆ [M+Na]⁺: 483.1353, found 483.1359.

IR (thin film, NaCl): 2978, 2938, 1802, 1457, 1381, 1284, 1250, 1181, 1156, 1094 cm⁻¹.

[α]_D²² = -5.6 (c = 6.69, CHCl₃).



Diol S15: To a vigorously stirring suspension of tetracycle **10** (33.1 mg, 0.0717 mmol, 100 mol%) in MeOH (1.6 mL) at rt was added NaOH (44 mg, 1.10 mmol, 1500 mol%) in one portion. The reaction was stirred vigorously at rt for 2 h. It was then quenched by the addition of solid NH₄Cl (35 mg). After stirring vigorously at rt for 10 min the reaction mixture was filtered through celite and eluted with 50 mL of Et₂O. The solvent was removed using a rotary evaporator and the residue was applied to flash column chromatography using 50% EtOAc in hexanes as the eluent. Diol **S15** was isolated as a white amorphous solid (25.8 mg, 0.0595 mmol, 83%).

¹H NMR (500 MHz, C₆D₆)

δ 3.74–3.66 (m, 3H), 3.39–3.35 (m, 2H), 3.14 (d, *J* = 10.8 Hz, 1H), 2.59 (br s, 1H), 2.21 (br s, 1H), 1.99–1.85 (m, 2H), 1.75–1.67 (m, 1H), 1.60–1.48 (m, 5H), 1.35 (s, 3H), 1.34–1.29 (m, 3H), 1.23–1.19 (m, 1H), 1.13 (s, 3H), 1.11 (s, 3H), 1.10 (s, 3H), 1.06 (s, 3H).

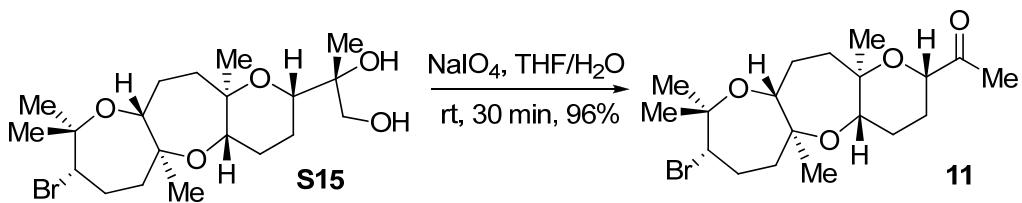
¹³C NMR (125 MHz, C₆D₆)

δ 79.5, 78.6, 78.0, 76.2, 73.6, 73.4, 69.8, 67.9, 60.2, 40.8, 38.8, 32.2, 29.4, 26.1, 24.8, 24.3, 23.7, 21.1, 21.0, 20.8.

HR-MS (ESI) *m/z* calcd for C₂₀H₃₅BrO₅ [M+Na]⁺: 457.1560, found 457.1575.

IR (thin film, NaCl): 3447, 2918, 2850, 1457, 1382, 1216, 1139, 1110, 1083, 1057, 759 cm⁻¹.

[α]_D²² = -34.4 (*c* = 0.24, CHCl₃).



Ketone 11: To a vigorously stirring solution of diol **S15** (27.9 mg, 0.0641 mmol, 100 mol%) in THF/H₂O (1:1 v/v, 3.4 mL total) was added NaIO₄ (30.8 mg, 0.144 mmol, 225 mol%) in one portion. After stirring vigorously at rt for 15 min, the THF was removed using a rotary evaporator and the reaction mixture was diluted with Et₂O (15 mL) and washed with brine (10 mL). The aqueous layer was extracted with Et₂O (3 x 5 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (15% EtOAc in hexanes) isolated 24.8 mg (0.0615 mmol, 96%) of ketone **11** as a white solid.

¹H NMR (500 MHz, C₆D₆)

δ 3.69 (dd, *J* = 11.0, 1.6 Hz, 1H), 3.60 (dd, *J* = 6.6, 1.9 Hz, 1H), 3.12-3.08 (m, 2H), 2.39-2.34 (m, 1H), 2.02 (s, 3H), 1.96-1.85 (m, 2H), 1.80-1.65 (m, 3H), 1.56-1.42 (m, 3H), 1.36-1.30 (m, 4H), 1.27-1.83 (m, 2H), 1.12 (s, 3H), 1.09 (s, 3H), 1.02 (s, 3H).

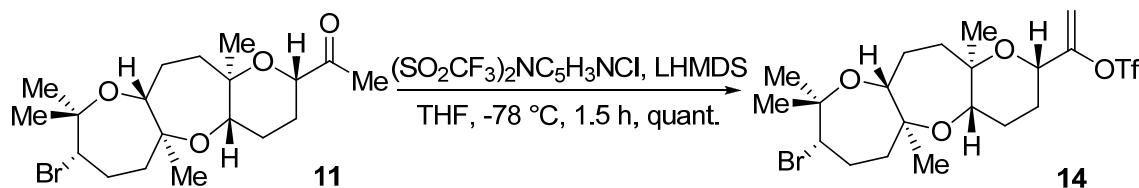
¹³C NMR (100 MHz, C₆D₆)

δ 209.5, 79.3, 79.2, 78.0, 76.5, 76.2, 71.5, 60.2, 42.5, 40.1, 32.2, 28.9, 26.5, 26.0, 25.0, 25.0, 24.0, 21.2, 18.3, 7.4, 7.4, 7.0, 5.7.

HR-MS (ESI) *m/z* calcd for C₁₉H₃₁BrO₄[M+Na]⁺: 425.1298, found 425.1306.

IR (thin film, NaCl): 2948, 1711, 1457, 1110, 1064 cm⁻¹.

[α]_D²² = -30.9 (*c* = 0.84, CHCl₃).



Alkenyl triflate 14: *N*-(5-Chloro-2-pyridyl)bis(trifluoromethanesulfonimide) (7.89 mg, 0.0201 mmol, 150 mol%) was dissolved in 0.3 mL of THF at rt under an argon atmosphere. After the reaction mixture was cooled to $-78\text{ }^{\circ}\text{C}$ a 1.0 M solution of LHMDS in THF (30.0 μL , 0.030 mmol, 150 mol%) was added in one portion. Ketone **11** (5.4 mg, 0.0134 mmol, 100 mol%) was then added in 0.3 mL THF dropwise via cannula transfer. The reaction mixture was stirred at to $-78\text{ }^{\circ}\text{C}$ for 1.5 h. It was then quenched at $-78\text{ }^{\circ}\text{C}$ by the dropwise addition of 0.5 mL of H_2O . The quenched reaction mixture was brought to rt and diluted with 15 mL of Et_2O . It was then washed with 15 mL of satd. aq. NaCl . The aqueous layer was extracted with Et_2O (2 x 7 mL). The combined organic layers were dried over MgSO_4 , filtered, and concentrated. Column chromatography (95:4:1 hexanes: EtOAc : Et_3N) isolated 8.0 mg (quant.) of alkenyl triflate **14** as a white solid.

^1H NMR (500 MHz, C_6D_6)

δ 4.77 (dd, $J = 4.1, 1.3\text{ Hz}$, 1H), 4.47 (dd, $J = 4.0, 1.7\text{ Hz}$, 1H), 4.33-4.32 (m, 1H), 3.71 (dd, $J = 10.9, 1.6\text{ Hz}$, 1H), 3.09 (d, $J = 10.8\text{ Hz}$, 1H), 3.08 (d, $J = 10.9\text{ Hz}$, 1H), 2.00-1.87 (m, 2H), 1.77-1.65 (m, 2H), 1.56-1.50 (m, 1H), 1.48-1.39 (m, 3H), 1.34 (s, 3H), 1.32-1.25 (m, 3H), 1.20-1.16 (m, 4H), 1.12 (s, 3H), 1.09 (s, 3H).

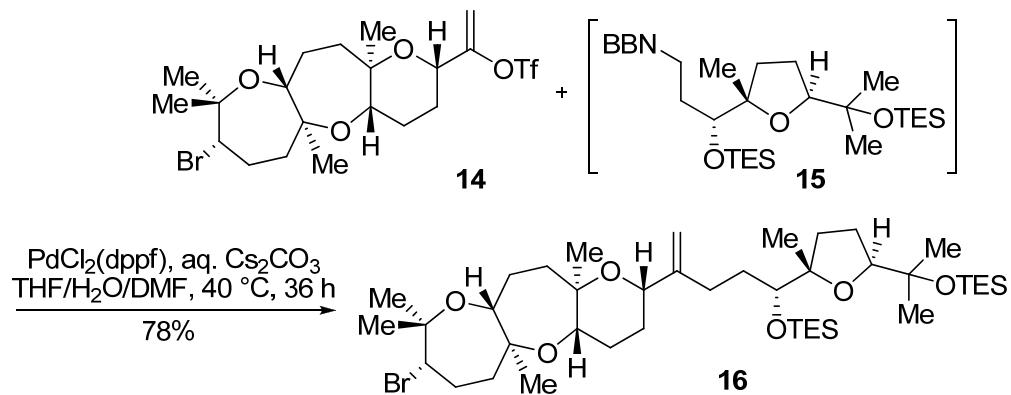
^{13}C NMR (100 MHz, C_6D_6)

δ 157.7, 105.1, 79.4, 79.2, 78.0, 76.4, 71.3, 68.1, 60.1, 41.9, 40.4, 32.2, 28.8, 26.2, 26.0, 24.8, 24.2, 21.2, 18.9.

HR-MS (ESI) m/z calcd for $\text{C}_{20}\text{H}_{30}\text{BrF}_3\text{O}_6\text{S} [\text{M}+\text{Na}]^+$: 557.0791, found 557.0798.

IR (thin film, NaCl): 2920, 1653, 1559, 1406, 1215 cm⁻¹.

$[\alpha]^{22}_D = -16.3$ ($c = 0.22$, CHCl₃).



TES ether #: The solution of alkylboron **15** (see S7) was cooled to rt. To it was added a solution of Cs_2CO_3 (15 mg, 0.046 mmol, 300 mol%) in 46 μL of degassed H₂O (FPT). The reaction mixture was stirred at rt for 20 min to completely quench the excess 9-BBN dimer.^{S6} Alkenyl triflate **14** (8.2 mg, 0.0153 mmol, 100 mol%) in 0.4 mL degassed (FPT) THF was added, followed by 0.15 mL (0.00153 mmol, 10 mol%) of a stock solution of $\text{PdCl}_2(\text{dppf})$, made by dissolving 5.0 mg of $\text{PdCl}_2(\text{dppf})$ in 0.6 mL of degassed (FPT) DMF. The Schlenk tube was closed and the reaction mixture was heated at 40 °C for 36 h. It was then cooled to rt, diluted with 10 mL of Et₂O, and washed with 0.5 M aq. HCl. The aqueous layer was extracted with Et₂O (3 x 3 mL). The combined organic layers were washed with satd. aq. NaHCO₃ (20 mL) and the aqueous layer extracted with Et₂O (2 x 5 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (5% EtOAc in hexanes) isolated 9.7 mg of TES ether **16** (0.0119 mmol, 78%) as a white amorphous solid.

¹H NMR (500 MHz, CDCl₃)

δ 4.95 (s, 1H), 4.86 (s, 1H), 4.18 (dd, $J = 10.2, 2.0$ Hz, 1H), 4.12 (t, $J = 5.4$ Hz, 1H), 3.63 (dd, $J = 9.2, 6.2$ Hz, 1H), 3.57–3.49 (m, 3H), 2.33 (ddd, $J = 15.8, 12.3, 4.8$ Hz, 1H), 2.21–2.08 (m, 3H), 2.07–2.00 (m, 1H), 1.99–1.94 (m, 1H), 1.90–1.63 (m, 9H), 1.57–1.43 (m, 5H), 1.37 (s, 3H), 1.35 (s, 3H), 1.26 (s,

3H), 1.18 (s, 3H), 1.17 (s, 3H), 1.13 (s, 3H), 1.08 (s, 3H), 0.97 (t, $J = 7.9$ Hz, 9H), 0.95 (t, $J = 7.9$ Hz, 9H), 0.63 (t, $J = 7.8$ Hz, 6H), 0.58 (t, $J = 7.8$ Hz, 6H).

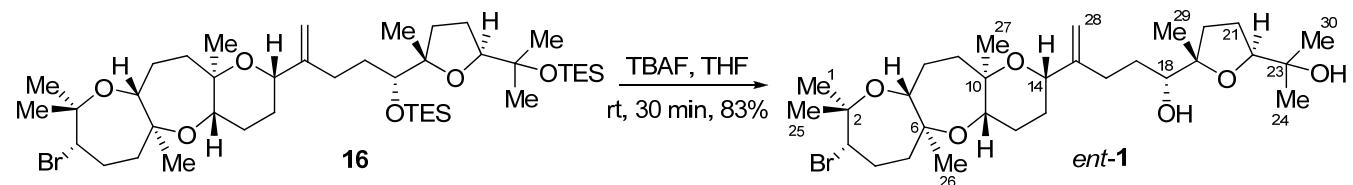
^{13}C NMR (100 MHz, CDCl_3)

δ 151.72, 109.2, 87.3, 86.0, 79.1, 78.1, 78.0, 76.2, 74.3, 71.5, 70.2, 59.7, 41.2, 40.3, 34.5, 32.6, 31.8, 30.6, 28.6, 28.1, 27.0, 26.6, 25.7, 25.6, 24.7, 24.5, 22.8, 20.8, 19.2, 7.4, 7.4, 7.0, 5.7.

HR-MS (ESI) m/z calcd for $\text{C}_{42}\text{H}_{79}\text{BrO}_6\text{Si}_2 [\text{M}+\text{Na}]^+$: 839.4495, found 839.4473.

IR (thin film, NaCl): 2953, 2875, 1457, 1379, 1237, 1172, 1137, 1096, 1041, 1010, 742 cm^{-1} .

$[\alpha]^{22}_{\text{D}} = -26.4$ ($c = 0.27$, CHCl_3).



Ent-1: To TES ether **16** (8.6 mg, 0.0105 mmol, 100 mol%) in THF (0.7 mL) was added a 1 M solution of TBAF in THF (53 μL , 0.053 mmol, 500 mol%). The reaction mixture was stirred for 30 min at rt. It was then diluted with Et_2O (8 mL) and washed with satd. aq. NaCl (8 mL). The aqueous layer was extracted with Et_2O (3 x 3 mL). The combined organic layers were dried over MgSO_4 , filtered, and concentrated. Column chromatography (35% EtOAc in hexanes) isolated 5.1 mg (8.7 μmol , 83%) of **ent-1** as a white amorphous solid.

HR-MS (ESI) m/z calcd for $\text{C}_{30}\text{H}_{51}\text{BrO}_6 [\text{M}+\text{Na}]^+$: 609.2761, found 609.2741.

IR (thin film, NaCl): 3447, 2921, 2851, 1717, 1700, 1653, 1647, 1457, 1378, 1086 cm^{-1} .

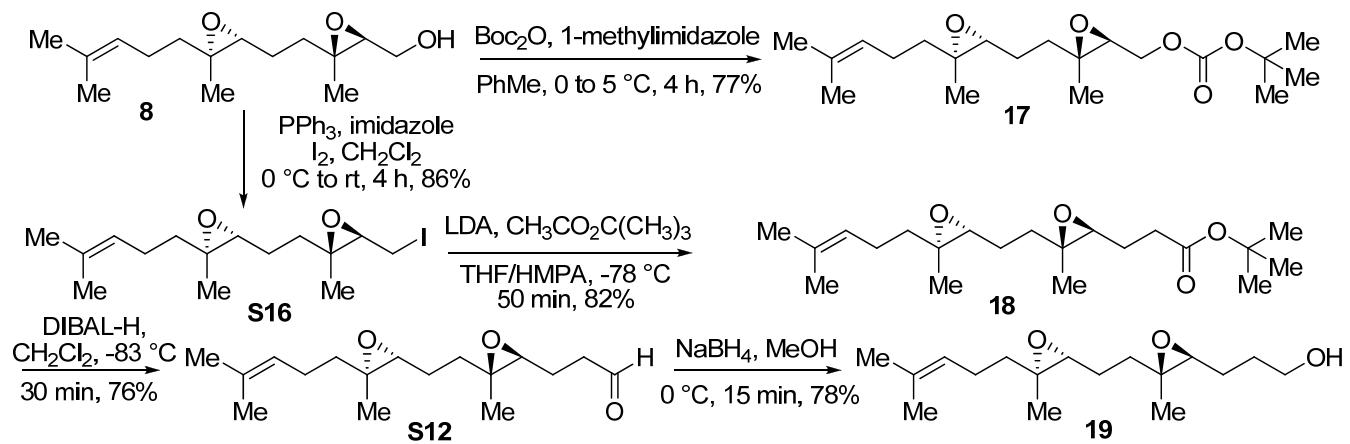
$[\alpha]^{22}_{\text{D}} = -26$ ($c = 0.050$, CHCl_3); lit. value^{2c}: $[\alpha]^{25}_{\text{D}} = +39$ ($c = 0.07$, CHCl_3).

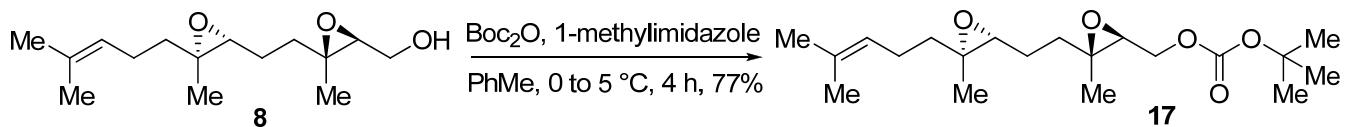
Comparison of our assignments for *ent*-1 with reported data for **1^{s1}:**

Assignment	Fernandez's report (¹³ C, 100 MHz, CDCl ₃)	This work (¹³ C, 100 MHz, CDCl ₃)	Fernandez's report (¹ H, 500 MHz, CDCl ₃)	This work (¹ H, 500 MHz, CDCl ₃)
C1	24.6	24.8	1.32 (s, 3H)	1.35 (s, 3H)
C2	77.8	78.0	—	—
C3	59.5	59.7	4.16 (dd, <i>J</i> = 2.0, 10.2 Hz, 1H)	4.19 (dd, <i>J</i> = 2.1, 10.2 Hz, 1H)
C4	31.6	31.8	2.10/2.20	2.10-2.22 (m, 2H)
C5	40.1	40.3	1.60/1.76	1.62/1.76
C6	78.9	79.1	—	—
C7	76.0	76.2	3.53 (dd, <i>J</i> = 1.0, 10.3 Hz, 1H)	3.56 (app d, <i>J</i> = 10.4 Hz, 1H)
C8	28.4	28.6	1.43/1.83	1.45/1.84
C9	41.1	41.3	1.50/1.69	1.54-1.57 (m, 1H)/1.71
C10	78.0	78.3	—	—
C11	71.2	71.5	3.49 (dd, <i>J</i> = 5.1, 11.5 Hz, 1H)	3.52 (dd, <i>J</i> = 5.1, 11.5 Hz, 1H)
C12	24.3	24.5	1.51/1.73	1.54/1.74
C13	26.8	26.9	1.84/2.04	1.83/2.06
C14	70.2	70.4	4.10 (dd, <i>J</i> = 5.5, 5.7 Hz, 1H)	4.13 (app t, <i>J</i> = 5.5 Hz, 1H)
C15	150.5	150.7	—	—
C16	29.8	30.0	2.23/2.44	2.25 (m, 1H) /2.47 (ddd, <i>J</i> = 4.7, 8.9, 14.4 Hz, 1H)
C17	30.0	30.2	1.40/1.63	1.42-1.50 (m, 1H)/1.63
C18	76.1	76.3	3.50 (dd, <i>J</i> = 1.7, 9.9 Hz, 1H)	3.53 (dd, <i>J</i> = 1.6, 9.9 Hz, 1H)
C19	86.1	86.3	—	—
C20	31.6	31.8	1.81/2.10	1.84/2.11

C21	26.6	26.8	1.57/1.86	1.58/1.86
C22	87.6	87.8	3.73 (dd, $J = 5.8, 10.2$ Hz, 1H)	3.76 (dd, $J = 5.8, 10.2$ Hz, 1H)
C23	70.5	70.7	—	—
C24	24.0	24.2	1.11 (s, 3H)	1.14 (s, 3H)
C25	25.4	25.6	1.34 (s, 3H)	1.37 (s, 3H)
C26	20.6	20.8	1.10 (s, 3H)	1.13 (s, 3H)
C27	19.0	19.2	1.15 (s, 3H)	1.19 (s, 3H)
C28	109.8	110.0	4.86/4.98 (bs/bs)	4.89/5.01 (bs/bs)
C29	23.8	24.0	1.12 (s, 3H)	1.15 (s, 3H)
C30	27.7	28.0	1.20 (s, 3H)	1.23 (s, 3H)
OH-18			2.35 (s, 1H)	2.39 (br s, 1H)

Scheme S1. Syntheses of the Diepoxide Model Substrates





Carbonate 17: To alcohol **8** (31.5 mg, 0.124 mmol, 100 mol%) in toluene (0.5 mL) at rt was added 1-methylimidazole (13.3 μ L, 0.167 mmol, 135 mol%) under an argon atmosphere. The reaction mixture was cooled to 0 °C and Boc_2O (0.040 mL, 0.167 mmol, 135 mol%) was added dropwise. The reaction mixture was stirred for 2 h at 0 to 5 °C. It was then brought back to 0 °C and another portion of 1-methylimidazole (13.3 μ L, 0.167 mmol, 135 mol%) and Boc_2O (0.040 mL, 0.167 mmol, 135 mol%) was added. The reaction mixture was stirred for another 2 h at 0 to 5 °C. The solvent was then removed using a rotary evaporator and the residue applied directly to flash column chromatography using a slow gradient of 90:9:1 to 80:19:1 hexanes:EtOAc:Et₃N as the eluent. Carbonate **17** was isolated as a colorless oil (33.7 mg, 0.0955 mmol, 77%).

¹H NMR (600 MHz, C₆D₆)

δ 5.13 (t, J = 7.1 Hz, 1H), 4.19 (dd, J = 11.9, 4.6 Hz, 1H), 4.09 (dd, J = 11.9, 6.4 Hz, 1H), 2.92 (dd, J = 6.3, 4.8 Hz, 1H), 2.49-2.47 (m, 1H), 2.12-2.03 (m, 2H), 1.65 (s, 3H), 1.63-1.58 (m, 1H), 1.53 (s, 3H), 1.46-1.36 (m, 5H), 1.34 (s, 9H), 1.08 (s, 3H), 0.99 (s, 3H).

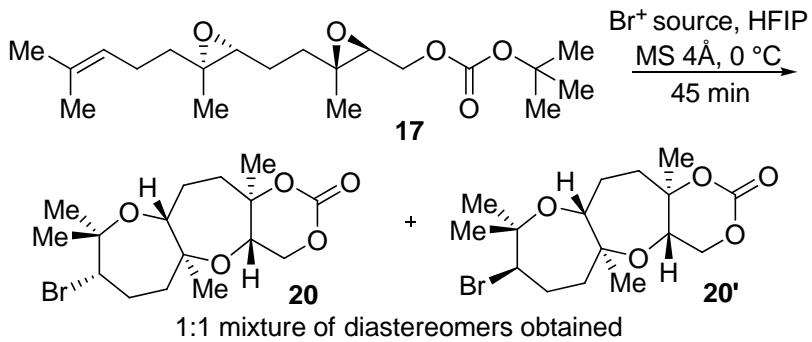
¹³C NMR (100 MHz, C₆D₆)

δ 154.4, 131.9, 124.9, 82.0, 66.3, 62.9, 60.3, 60.1, 60.0, 39.4, 35.8, 28.0, 26.2, 25.1, 24.6, 18.3, 18.0, 17.0.

HR-MS (ESI) m/z calcd for C₂₀H₃₄O₅ [M+Na]⁺: 377.2298, found 377.2300.

IR (thin film, NaCl): 2969, 2930, 1742, 1457, 1370, 1279, 1256, 1164 cm⁻¹.

$[\alpha]^{22}_{\text{D}}$ = -4.7 (c = 0.23, CHCl₃).



Tricycles 20 and 20' (using NBS as the Br⁺ source): 90 mg of 4Å MS was activated according to the procedure given in the General Experimental Methods. To this was added carbonate **17** (9.6 mg, 0.0271 mmol, 100 mol%, as a 4:1 mixture of diastereomers) in 1 mL of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) under an argon atmosphere. The reaction mixture was cooled to 0 °C and *N*-bromosuccinimide (NBS) (16.1 mg, 0.0846 mmol, 300 mol%) was added in one portion with rigorous stirring. The reaction mixture was kept out of light. After 45 min at 0 °C it was diluted with Et₂O and filtered through celite, using 15 mL of Et₂O as the eluent. The solvent was removed using a rotary evaporator and the residue was redissolved in 15 mL of Et₂O. It was then washed with a 1:1 mixture of satd. aq. Na₂S₂O₃:NaCl (15 mL total). The aqueous layer was extracted with Et₂O (2 x 7 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (20% EtOAc in hexanes) isolated tetracycles **20** and **20'** (6.7 mg, 0.0178 mmol, 66%) together as white amorphous solids. Repeated flash chromatography using this solvent system separated the two diastereomers for characterization purposes.

Tricycles 20 and 20' (using Br(coll)₂ClO₄ as the Br⁺ source): The same procedure was followed with 10.0 mg (0.0282 mmol, 100 mol%) of carbonate **17**, 84.7 mg of 4Å MS, 1 mL of HFIP, and 36.1 mg (0.0846 mmol, 300 mol%) of Br(coll)₂ClO₄. Column chromatography (80:19:1 hexanes:EtOAc:Et₃N) isolated tetracycles **20** and **20'** together (6.9 mg, 0.0183 mmol, 65%) as white amorphous solids.

Characterization for tricycle 20:

¹H NMR (500 MHz, C₆D₆)

δ 3.85 (dd, J = 7.7, 4.6 Hz, 1H), 3.62 (dd, J = 10.8, 6.6 Hz, 1H), 3.55 (t, J = 10.5 Hz, 1H), 3.00 (dd, J = 10.4, 6.7 Hz, 1H), 2.83(app d, J = 10.2 Hz, 1H), 1.84-1.80 (m, 2H), 1.52 (ddd, J = 13.1, 5.2, 2.1 Hz, 1H), 1.45-1.37 (m, 1H), 1.30-1.25 (m, 4H), 1.17-1.13 (m, 4H), 0.98 (td, J = 13.2, 3.8 Hz, 1H), 0.89-0.83 (m, 7H).

¹³C NMR (100 MHz, C₆D₆)

δ 146.9, 82.5, 79.8, 77.9, 75.3, 66.3, 63.5, 58.7, 39.7, 39.1, 31.4, 27.5, 25.3, 24.4, 20.2, 18.7.

HR-MS (ESI) m/z calcd for C₁₆H₂₅BrO₅ [M+Na]⁺: 399.0778, found 399.0789.

IR (thin film, NaCl): 2927, 2853, 1751, 1734, 1457, 1384, 1253, 1230 cm⁻¹.

$[\alpha]^{22}_D = -21.7$ (c = 0.22, CHCl₃).

Characterization for tricycle 20':

¹H NMR (500 MHz, C₆D₆)

δ 3.95–3.92 (m, 2H), 3.69-3.56 (m, 3H), 2.12-2.06 (m, 1H), 1.58-1.55 (m, 1H), 1.53-1.47 (m, 4H), 1.26-1.22 (m, 1H), 1.20 (s, 3H), 1.17-1.13 (m, 1H), 1.00 (s, 3H), 0.94 (s, 3H), 0.83 (s, 3H).

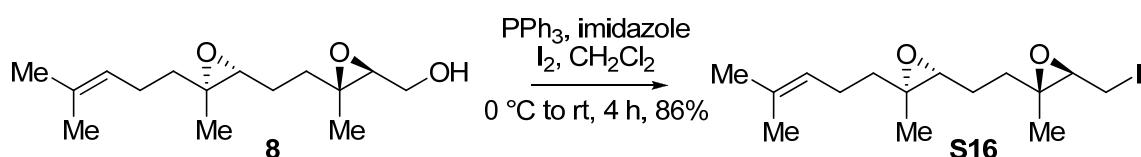
¹³C NMR (100 MHz, C₆D₆)

δ 147.1, 82.8, 80.8, 77.0, 75.8, 66.9, 65.7, 65.0, 40.4, 35.1, 29.7, 28.4, 28.3, 28.2, 21.2, 19.1.

HR-MS (ESI) m/z calcd for C₁₆H₂₅BrO₅ [M+Na]⁺: 399.0778, found 399.0778.

IR (thin film, NaCl): 2979, 2929, 1751, 1457, 1229, 1115, 1096 cm⁻¹.

$[\alpha]^{22}_D = -16.3$ (c = 0.45, CHCl₃).



Iodide S16: PPh₃ (357 mg, 1.36 mmol, 115 mol%) and imidazole (161 mg, 2.36 mmol, 200 mol%) was dissolved in CH₂Cl₂ (11.6 mL) under an argon atmosphere. The reaction mixture was cooled to 0 °C and iodine (330 mg, 1.3 mmol, 110 mol%) was added in one portion, forming a yellow suspension. The reaction mixture was stirred at 0 °C for 15 min before alcohol **8** was added in 6.6 mL of CH₂Cl₂. The reaction mixture was stirred for 1 h at 0 °C and then for 3 h at rt. It was then diluted with Et₂O (50 mL), washed with a 2:1 (v/v) mixture of satd. aq. Na₂S₂O₃/satd. aq. NaCl (100 mL total). The aqueous layer was extracted with Et₂O (2 x 50 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (10% EtOAc in hexanes) isolated 368 mg (1.01 mmol, 86%) of iodide **S16** as a colorless oil.

¹H NMR (500 MHz, C₆D₆)

δ 5.13 (t, *J* = 7.1 Hz, 1H), 2.84–2.75 (m, 2H), 2.58–2.50 (m, 2H), 2.12–2.04 (m, 2H), 1.65 (s, 3H), 1.54 (s, 3H), 1.49–1.42 (m, 4H), 1.16–1.13 (m, 1H), 1.11 (s, 3H), 0.98–0.95 (m, 1H), 0.91 (s, 3H).

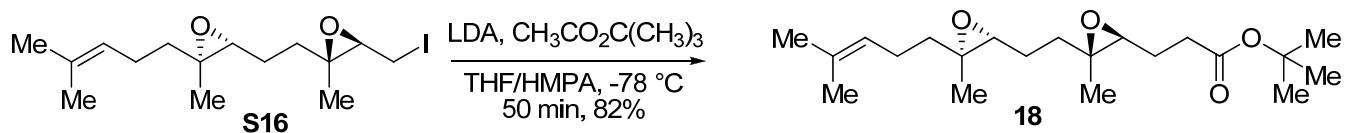
¹³C NMR (100 MHz, C₆D₆)

δ 131.9, 124.8, 63.5, 62.8, 62.8, 62.6, 60.4, 39.5, 35.8, 26.2, 25.4, 24.7, 18.0, 17.0, 15.9.

HR-MS (ESI) *m/z* calcd for C₁₅H₂₅IO₂ [M+Na]⁺: 387.0791, found 387.0789.

IR (thin film, NaCl): 2964, 2925, 1457, 1385, 1074 cm⁻¹.

[α]²²_D = +32.3 (*c* = 0.41, CHCl₃).



Tert-Butylester 18: To a solution of *i*-Pr₂NH (0.37 mL, 2.621 mmol, 310 mol%) in THF (9 mL) at -50 °C under an argon atmosphere was added a 2.5 M solution of *n*-BuLi in hexanes (1.0 mL, 2.53 mmol, 300 mol%). The reaction mixture was cooled to -78 °C and stirred for 30 min. *t*-BuOAc (353 µL, 2.621 mmol, 310 mol%) was added and the reaction mixture was stirred at -78 °C for another 45 min. Iodide **S16** (308 mg, 0.856 mmol, 100 mol%) in 6 mL of THF was added. The reaction mixture was stirred for 10 min, whereupon HMPA (423 µL, 2.43 mmol, 287 mol%) was added in one portion. After stirring for further 40 min at -78 °C, the reaction mixture was quenched at this temperature by the addition of satd. aq. NH₄Cl (5 mL). After warming to rt, the quenched reaction mixture was further diluted with Et₂O (50 mL) and washed with satd. aq. NH₄Cl (2 x 25 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. Column chromatography (10% EtOAc in hexanes) isolated 245 mg (0.693 mmol, 82%) of *tert*-butylester **18** as a colorless oil.

¹H NMR (500 MHz, C₆D₆)

δ 5.13 (t, *J* = 7.2 Hz, 1H), 2.64 (dd, *J* = 7.0, 5.5 Hz 1H), 2.54-2.52 (m, 1H), 2.29-2.25 (m, 2H), 2.11-2.05 (m, 2H), 1.83-1.68 (m, 2H), 1.65 (s, 3H), 1.63-1.59 (m, 1H), 1.53 (s, 3H), 1.50-1.49 (m, 3H), 1.46-1.40 (m, 1H), 1.39 (s, 3H), 1.15-1.14 (m, 1H), 1.11 (s, 3H), 1.06 (s, 3H).

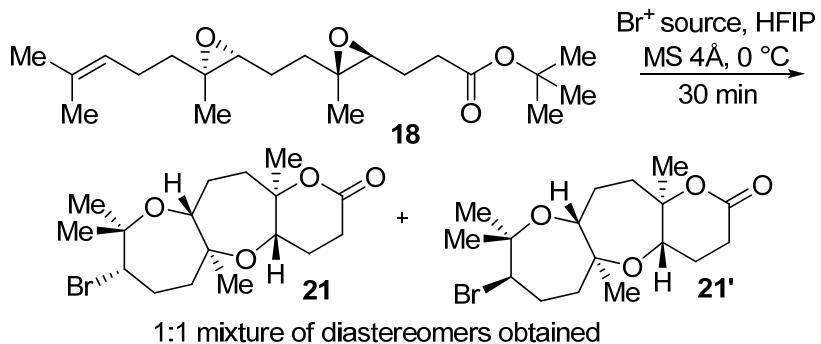
¹³C NMR (100 MHz, C₆D₆)

δ 172.3, 131.8, 124.9, 80.2, 63.1, 62.6, 60.5, 60.3, 39.5, 36.4, 32.9, 28.4, 26.2, 25.5, 25.1, 24.6, 18.0, 17.0, 16.9.

HR-MS (ESI) *m/z* calcd for C₂₁H₃₆O₄[M+Na]⁺: 375.2506, found 375.2505.

IR (thin film, NaCl): 2968, 2929, 1733, 1457, 1367, 1258, 1154 cm⁻¹.

[α]_D²² = -10.9 (*c* = 0.17, CHCl₃).



Tricycles 21 and 21' (using NBS as the Br⁺ source): 100 mg of 4Å MS was activated according to the procedure given in the General Experimental Methods. To this was added *tert*-butylester **18** (11.0 mg, 0.0312 mmol, 100 mol%, as a 4:1 mixture of diastereomers) in 1 mL of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) under an argon atmosphere. The reaction mixture was cooled to 0 °C and *N*-bromosuccinimide (NBS) (16.7 mg, 0.0936 mmol, 300 mol%) was added in one portion with rigorous stirring. The reaction mixture was kept out of light. After 30 min at 0 °C it was diluted with Et₂O and filtered through celite, using 20 mL of Et₂O as the eluent. The solvent was removed using a rotary evaporator and the residue was redissolved in 10 mL of Et₂O. It was then washed with a 1:1 mixture of satd. aq. Na₂S₂O₃:NaCl (10 mL total). The aqueous layer was extracted with Et₂O (2 x 5 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (50% Et₂O in hexanes) isolated tetracycles **21** and **21'** together (9.1 mg, 0.0228 mmol, 73%) as white amorphous solids. Repeated flash chromatography using this solvent system separated the two diastereomers for characterization purposes.

Tricycles 21 and 21' (using Br(coll)₂ClO₄ as the Br⁺ source): The same procedure was followed with 10.1 mg (0.0287 mmol, 100 mol%) of *tert*-butylester **18**, 100 mg of 4Å MS, 1 mL of HFIP, and 36.2 mg (0.0860 mmol, 300 mol%) of Br(coll)₂ClO₄. Column chromatography (50:49:1 hexanes:Et₂O:Et₃N) isolated tetracycles **21** and **21'** together (6.9 mg, 0.0175 mmol, 61%) as white amorphous solids.

Characterization of tricycle **21**:

^1H NMR (400 MHz, C_6D_6)

δ 3.84–3.81 (m, 1H), 3.04 (app dd, J = 11.6, 5.1 Hz, 1H), 2.97 (app d, J = 10.3 Hz, 1H), 2.27–2.22 (m, 2H), 1.93–1.87 (m, 2H), 1.69 (ddd, J = 13.4, 5.3, 1.9 Hz, 1H), 1.59–1.53 (m, 1H), 150–1.36 (m, 3H), 1.33 (s, 3H), 1.28–1.20 (m, 2H), 1.16–1.13 (m, 4H), 1.05 (s, 3H), 1.02 (s, 3H).

^{13}C NMR (100 MHz, C_6D_6)

δ 168.2, 84.0, 79.5, 78.2, 76.2, 68.6, 59.6, 41.7, 39.7, 32.0, 29.2, 28.2, 25.8, 25.3, 25.0, 21.0, 20.5.

HR-MS (ESI) m/z calcd for $\text{C}_{17}\text{H}_{27}\text{BrO}_4 [\text{M}+\text{Na}]^+$: 397.0985, found 397.0997.

IR (thin film, NaCl): 2937, 1727, 1382, 1272, 1142, 1083, 1073 cm^{-1} .

$[\alpha]_{\text{D}}^{22} = -20.9$ (c = 0.35, CHCl_3).

Characterization for tricycle **21'**:

^1H NMR (400 MHz, C_6D_6)

δ 4.10–4.08 (m, 1H), 4.02–4.00 (m, 1H), 3.61 (dd, J = 11.8, 5.1 Hz, 1H), 2.35–2.28 (m, 1H), 2.18 (ddd, J = 18.2, 7.2, 1.9 Hz, 1H), 1.99 (ddd, J = 20.0, 12.0, 7.9 Hz, 1H), 1.76 (dd, J = 10.8, 5.3 Hz, 1H), 1.67–1.58 (m, 3H), 1.57–1.47 (m, 1H), 1.38–1.30 (m, 4H), 1.26 (s, 3H), 1.14 (s, 3H), 1.11 (s, 3H), 0.87 (s, 3H).

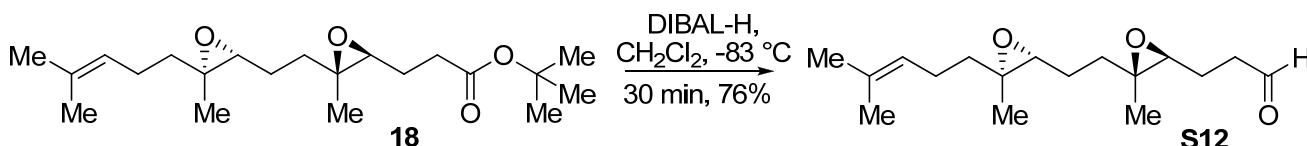
^{13}C NMR (100 MHz, C_6D_6)

δ 168.13, 84.2, 80.1, 76.9, 76.1, 69.5, 66.6, 42.0, 35.2, 29.7, 29.4, 28.7, 28.6, 28.4, 25.6, 21.5, 20.6.

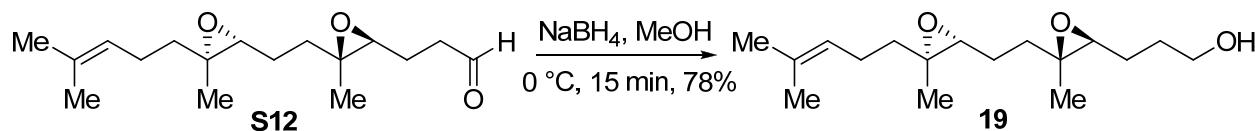
HR-MS (ESI) m/z calcd for $\text{C}_{17}\text{H}_{27}\text{BrO}_4 [\text{M}+\text{Na}]^+$: 397.0985, found 397.0981.

IR (thin film, NaCl): 2935, 1732, 1718, 1457, 1083 cm^{-1} .

$[\alpha]_{\text{D}}^{22} = -15.2$ (c = 0.42, CHCl_3).



Aldehyde S12: To *tert*-butylester **18** (100 mg, 0.284 mmol, 100 mol%) in CH_2Cl_2 (4.6 mL) at -83°C was added a 0.2 M solution of DIBAL-H in toluene (1.53 mL, 0.33 mmol, 115 mol%) slowly over 30 min using a syringe pump. After addition was completed the reaction mixture was immediately quenched with addition of MeOH (1 mL) at -83°C . It was further diluted with 25 mL of satd. aq. sodium potassium tartrate (Rochelle's salt) solution. The reaction mixture was warmed to rt while stirring rigorously for 30 min. The layers were separated and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried over MgSO_4 , filtered, and concentrated. Column chromatography (20% EtOAc in hexanes) isolated 60.3 mg (0.215 mmol, 76%) of aldehyde **S12** as a colorless oil (see S18 for characterization).



¹H NMR (500 MHz, C₆D₆)

δ 5.14 (t, *J* = 7.1, Hz, 1H), 3.40 (d, *J* = 4.2, Hz, 1H), 2.61–2.59 (m, 1H), 2.57–2.55 (m, 1H), 2.15–2.04 (m, 2H), 1.65 (s, 3H), 1.64–1.60 (m, 1H), 1.54–1.43 (m, 11H), 1.15–1.12 (m, 4H), 1.09 (s, 3H).

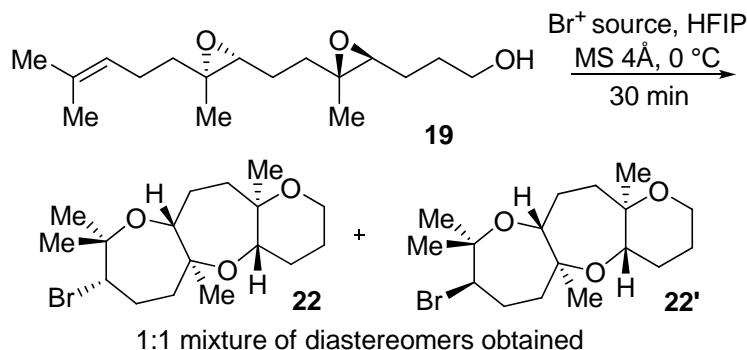
¹³C NMR (125 MHz, C₆D₆)

δ 131.9, 124.8, 63.6, 63.3, 62.6, 60.5, 60.4, 39.5, 36.6, 30.4, 26.2, 26.2, 25.5, 24.6, 18.0, 17.0, 16.9.

HR-MS (ESI) *m/z* calcd for C₁₇H₃₀O₃ [M+Na]⁺ : 305.2087, found 305.2096.

IR (thin film, NaCl): 2921, 2859, 1473, 1457, 1437, 1387, cm⁻¹.

[α]_D²² = -2.3 (c = 0.25, CHCl₃).



Tricycles 22 and 22' (using NBS as the Br⁺ source): 100 mg of 4Å MS was activated according to the procedure given in the General Experimental Methods. To this was added alcohol **19** (11.2 mg, 0.0397 mmol, 100 mol%, as a 4:1 mixture of diastereomers) in 1 mL of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) under an argon atmosphere. The reaction mixture was cooled to 0 °C and *N*-bromosuccinimide (NBS) (21.2 mg, 0.0936 mmol, 300 mol%) was added in one portion with rigorous stirring. The reaction mixture was kept out of light. After 30 min at 0 °C it was diluted with Et₂O and filtered through celite, using 20 mL of Et₂O as the eluent. The solvent was removed using a rotary evaporator and the residue was redissolved in 10 mL of Et₂O. It was then washed with a 1:1 mixture of satd. aq. Na₂S₂O₃:NaCl (10:1 v/v). The final yield is 11.2 mg (30% yield).

mL total). The aqueous layer was extracted with Et₂O (2 x 5 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Column chromatography (5% EtOAc in CH₂Cl₂) isolated tetracycles **22** and **22'** together (8.3 mg, 0.0230 mmol, 58%) as white amorphous solids. Repeated flash chromatography using this solvent system separated the two diastereomers for characterization purposes.

Tricycles 22 and 22' (using Br(coll)₂ClO₄ as the Br⁺ source): The same procedure was followed with 9.5 mg (0.0336 mmol, 100 mol%) of alcohol **19**, 100 mg of 4Å MS, 1 mL of HFIP, and 42.6 mg (0.101 mmol, 300 mol%) of Br(coll)₂ClO₄. Column chromatography (95:4:1 CH₂Cl₂:EtOAc:Et₃N) isolated tetracycles **22** and **22'** together (6.3 mg, 0.0175 mmol, 52%) as white amorphous solids.

Characterization for tricycle **22**:

¹H NMR (400 MHz, C₆D₆)

δ 3.66 (dd, *J* = 10.9, 1.5 Hz, 1H), 3.49 (app dd, *J* = 11.0, 4.2 Hz, 1H), 3.31 (td, *J* = 12.0, 2.0 Hz, 1H), 3.18-3.13 (m, 2H), 2.01-1.83 (m, 2H), 1.74 (ddd, *J* = 13.5, 5.4, 2.4 Hz, 1H), 1.67-1.44 (m, 5H), 1.40-1.35 (m, 4H), 1.32-1.23 (m, 3H), 1.16 (s, 3H), 1.14 (s, 3H), 1.11 (s, 3H).

¹³C NMR (100 MHz, C₆D₆)

δ 79.0, 77.9, 77.2, 76.6, 71.5, 60.3 (2 carbons), 42.5, 40.2, 32.2, 29.0, 28.6, 26.9, 26.0, 24.9, 21.3, 15.9.

HR-MS (ESI) *m/z* calcd for C₁₇H₂₉BrO₃ [M+Na]⁺: 383.1192, found 383.1208.

IR (thin film, NaCl): 2919, 2862, 1457, 1374, 1141, 1089, 1066 cm⁻¹.

[α]_D²² = -19.6 (c = 0.21, CHCl₃).

Characterization for tricycle **22'**:

¹H NMR (400 MHz, C₆D₆)

δ 4.29 (dd, J = 10.3, 0.9 Hz, 1H), 4.05 (dd, J = 6.1, 2.1 Hz 1H), 3.61 (dd, J = 10.9, 5.2 Hz, 1H), 3.47-3.43 (m, 1H), 3.33-3.26 (m, 1H), 2.53 (ddd, J = 14.5, 11.7, 4.0 Hz, 1H), 2.02-1.92 (m, 1H), 1.84-1.81 (m, 2H), 1.69-1.63 (m, 2H), 1.54-1.46 (m, 4H), 1.39-1.35 (m, 1H), 1.30 (s, 3H), 1.27 (s, 3H), 1.21 (s, 3H), 0.89 (s, 3H).

^{13}C NMR (100 MHz, C_6D_6)

δ 79.6, 77.3, 76.7, 76.6, 72.3, 66.8, 60.4, 43.0, 35.5, 29.9, 29.3, 28.8, 28.7, 28.6, 26.8, 21.8, 16.0

HR-MS (ESI) m/z calcd for $\text{C}_{17}\text{H}_{29}\text{BrO}_3$ [$\text{M}+\text{Na}]^+$: 383.1192, found 383.1209.

IR (thin film, NaCl): 2934, 2858, 1452, 1377, 1223, 1122, 1091, 1080, 1063 cm^{-1} .

$[\alpha]^{22}_{\text{D}} = -16.7$ ($c = 0.24$, CHCl_3).

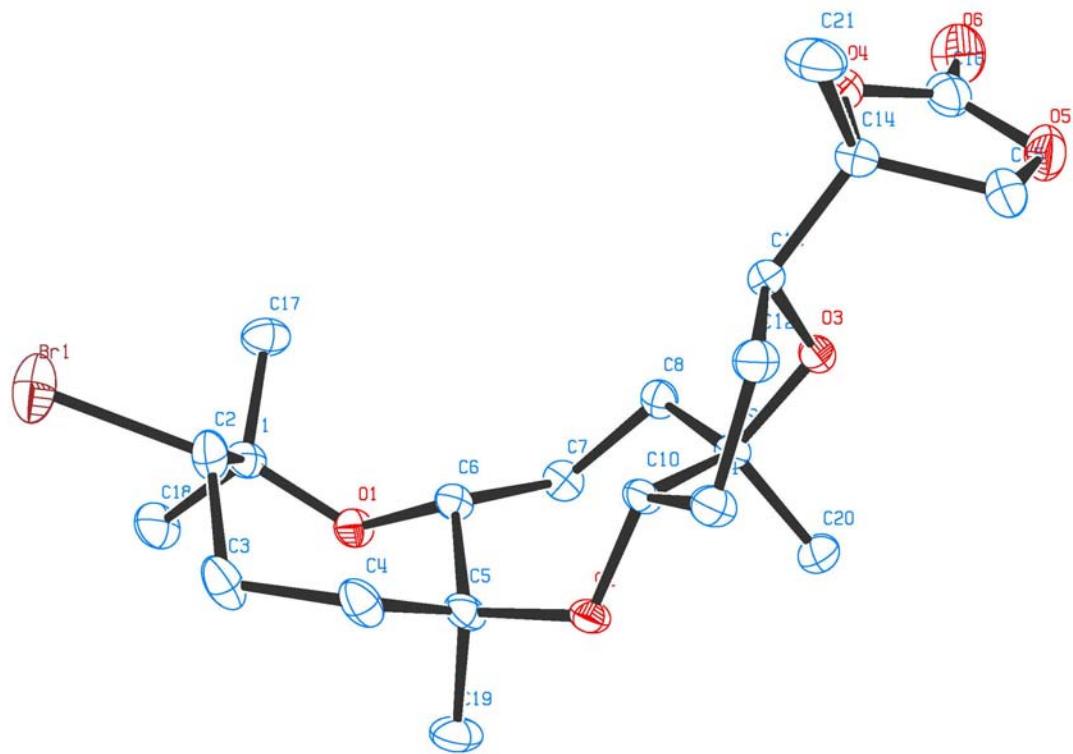
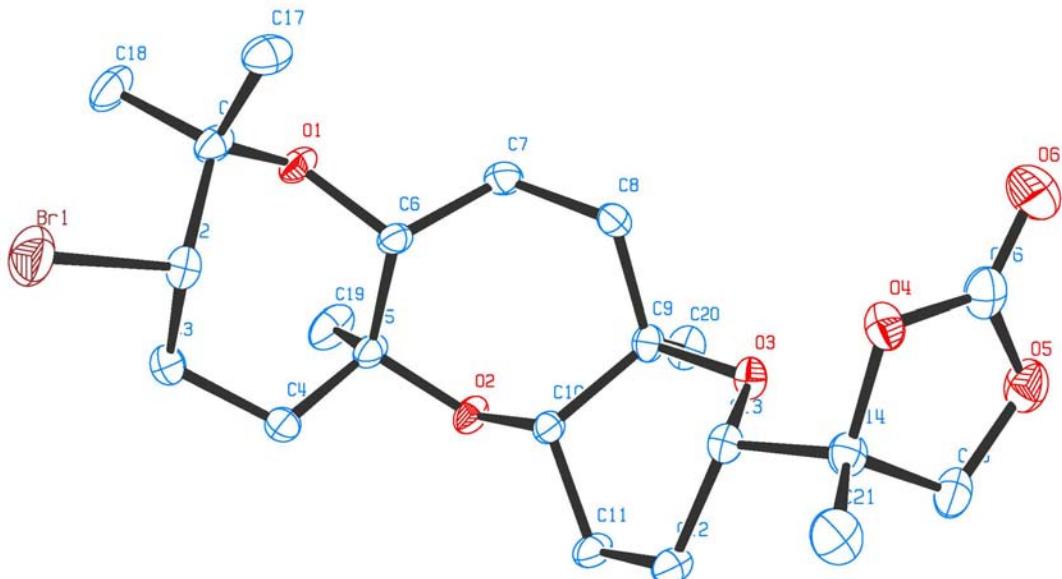


Table S1. Crystal data and structure refinement for tetracycle 10.

Identification code	08351	
Empirical formula	C21 H33 Br O6	
Formula weight	461.38	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 10.5972(11) Å	α= 90°.
	b = 13.1485(13) Å	β= 90°.
	c = 16.0477(16) Å	γ = 90°.
Volume	2236.0(4) Å ³	
Z	4	
Density (calculated)	1.371 Mg/m ³	
Absorption coefficient	1.871 mm ⁻¹	
F(000)	968	
Crystal size	0.33 x 0.30 x 0.20 mm ³	
Theta range for data collection	2.00 to 30.03°.	
Index ranges	-14<=h<=14, -18<=k<=18, -22<=l<=22	
Reflections collected	60558	
Independent reflections	6525 [R(int) = 0.0439]	
Completeness to theta = 30.03°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7060 and 0.5773	

Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	6525 / 0 / 258
Goodness-of-fit on F ²	1.043
Final R indices [I>2sigma(I)]	R1 = 0.0326, wR2 = 0.0817
R indices (all data)	R1 = 0.0390, wR2 = 0.0844
Absolute structure parameter	0.007(5)
Largest diff. peak and hole	0.769 and -0.274 e. \AA^{-3}

Table S2. Atomic coordinates (x 10⁴) and equivalent isotropic displacement parameters (Å²x 10³)

for 08351. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	1338(1)	6278(1)	1917(1)	40(1)
O(1)	5276(1)	6355(1)	2178(1)	20(1)
O(2)	6620(1)	6350(1)	68(1)	20(1)
O(3)	7609(1)	3722(1)	-328(1)	18(1)
O(4)	6819(1)	1685(1)	-287(1)	22(1)
O(5)	8640(1)	1583(1)	-972(1)	30(1)
O(6)	8408(2)	783(1)	254(1)	38(1)
C(1)	3982(2)	6155(1)	2416(1)	20(1)
C(2)	3150(2)	6253(2)	1616(1)	24(1)
C(3)	3478(2)	7166(1)	1061(1)	27(1)
C(4)	4502(2)	6914(1)	413(1)	24(1)
C(5)	5824(2)	6678(1)	749(1)	19(1)
C(6)	5741(2)	5854(1)	1437(1)	17(1)
C(7)	6986(2)	5311(1)	1636(1)	20(1)
C(8)	7249(2)	4396(1)	1060(1)	18(1)
C(9)	7522(2)	4661(1)	149(1)	17(1)
C(10)	6450(2)	5327(1)	-209(1)	16(1)
C(11)	6422(2)	5264(1)	-1154(1)	20(1)
C(12)	6074(2)	4165(1)	-1400(1)	20(1)

C(13)	6442(2)	3422(1)	-704(1)	17(1)
C(14)	6621(2)	2333(1)	-1021(1)	20(1)
C(15)	7855(2)	2185(1)	-1512(1)	26(1)
C(16)	7986(2)	1308(2)	-283(1)	25(1)
C(17)	3881(2)	5088(1)	2792(1)	25(1)
C(18)	3696(2)	6959(1)	3069(1)	29(1)
C(19)	6475(2)	7648(1)	1063(1)	30(1)
C(20)	8822(2)	5159(1)	50(1)	23(1)
C(21)	5453(2)	1950(1)	-1472(1)	30(1)

Table S3. Bond lengths [\AA] and angles [$^\circ$] for 08351.

Br(1)-C(2)	1.9811(17)
O(1)-C(6)	1.4449(19)
O(1)-C(1)	1.449(2)
O(2)-C(10)	1.4270(18)
O(2)-C(5)	1.4464(19)
O(3)-C(13)	1.4318(19)
O(3)-C(9)	1.4559(19)
O(4)-C(16)	1.332(2)
O(4)-C(14)	1.468(2)
O(5)-C(16)	1.355(2)
O(5)-C(15)	1.439(2)
O(6)-C(16)	1.191(2)
C(1)-C(18)	1.519(2)
C(1)-C(17)	1.530(2)
C(1)-C(2)	1.563(3)
C(2)-C(3)	1.535(3)
C(2)-H(2)	1.0000
C(3)-C(4)	1.540(2)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.533(3)
C(4)-H(4A)	0.9900

C(4)-H(4B)	0.9900
C(5)-C(19)	1.534(2)
C(5)-C(6)	1.551(2)
C(6)-C(7)	1.533(2)
C(6)-H(6)	1.0000
C(7)-C(8)	1.542(2)
C(7)-H(7A)	0.9900
C(7)-H(7B)	0.9900
C(8)-C(9)	1.532(2)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(20)	1.534(2)
C(9)-C(10)	1.544(2)
C(10)-C(11)	1.520(2)
C(10)-H(10)	1.0000
C(11)-C(12)	1.543(2)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-C(13)	1.534(2)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.532(2)
C(13)-H(13)	1.0000
C(14)-C(21)	1.520(2)

C(14)-C(15) 1.539(2)

C(15)-H(15A) 0.9900

C(15)-H(15B) 0.9900

C(17)-H(17A) 0.9800

C(17)-H(17B) 0.9800

C(17)-H(17C) 0.9800

C(18)-H(18A) 0.9800

C(18)-H(18B) 0.9800

C(18)-H(18C) 0.9800

C(19)-H(19A) 0.9800

C(19)-H(19B) 0.9800

C(19)-H(19C) 0.9800

C(20)-H(20A) 0.9800

C(20)-H(20B) 0.9800

C(20)-H(20C) 0.9800

C(21)-H(21A) 0.9800

C(21)-H(21B) 0.9800

C(21)-H(21C) 0.9800

C(6)-O(1)-C(1) 117.18(12)

C(10)-O(2)-C(5) 116.30(12)

C(13)-O(3)-C(9) 113.55(12)

C(16)-O(4)-C(14) 110.70(14)

C(16)-O(5)-C(15) 110.08(14)

O(1)-C(1)-C(18)	104.14(14)
O(1)-C(1)-C(17)	109.68(14)
C(18)-C(1)-C(17)	110.58(14)
O(1)-C(1)-C(2)	107.57(12)
C(18)-C(1)-C(2)	113.44(15)
C(17)-C(1)-C(2)	111.11(14)
C(3)-C(2)-C(1)	114.44(15)
C(3)-C(2)-Br(1)	110.35(12)
C(1)-C(2)-Br(1)	110.29(11)
C(3)-C(2)-H(2)	107.1
C(1)-C(2)-H(2)	107.1
Br(1)-C(2)-H(2)	107.1
C(2)-C(3)-C(4)	112.49(14)
C(2)-C(3)-H(3A)	109.1
C(4)-C(3)-H(3A)	109.1
C(2)-C(3)-H(3B)	109.1
C(4)-C(3)-H(3B)	109.1
H(3A)-C(3)-H(3B)	107.8
C(5)-C(4)-C(3)	116.77(14)
C(5)-C(4)-H(4A)	108.1
C(3)-C(4)-H(4A)	108.1
C(5)-C(4)-H(4B)	108.1
C(3)-C(4)-H(4B)	108.1
H(4A)-C(4)-H(4B)	107.3

O(2)-C(5)-C(4)	109.13(13)
O(2)-C(5)-C(19)	103.60(14)
C(4)-C(5)-C(19)	110.99(15)
O(2)-C(5)-C(6)	111.25(13)
C(4)-C(5)-C(6)	109.87(14)
C(19)-C(5)-C(6)	111.85(14)
O(1)-C(6)-C(7)	109.50(13)
O(1)-C(6)-C(5)	106.63(12)
C(7)-C(6)-C(5)	115.14(14)
O(1)-C(6)-H(6)	108.5
C(7)-C(6)-H(6)	108.5
C(5)-C(6)-H(6)	108.5
C(6)-C(7)-C(8)	113.17(13)
C(6)-C(7)-H(7A)	108.9
C(8)-C(7)-H(7A)	108.9
C(6)-C(7)-H(7B)	108.9
C(8)-C(7)-H(7B)	108.9
H(7A)-C(7)-H(7B)	107.8
C(9)-C(8)-C(7)	115.42(13)
C(9)-C(8)-H(8A)	108.4
C(7)-C(8)-H(8A)	108.4
C(9)-C(8)-H(8B)	108.4
C(7)-C(8)-H(8B)	108.4
H(8A)-C(8)-H(8B)	107.5

O(3)-C(9)-C(8)	108.73(12)
O(3)-C(9)-C(20)	104.50(13)
C(8)-C(9)-C(20)	111.43(14)
O(3)-C(9)-C(10)	109.42(13)
C(8)-C(9)-C(10)	110.17(13)
C(20)-C(9)-C(10)	112.37(13)
O(2)-C(10)-C(11)	111.38(12)
O(2)-C(10)-C(9)	109.02(13)
C(11)-C(10)-C(9)	110.76(14)
O(2)-C(10)-H(10)	108.5
C(11)-C(10)-H(10)	108.5
C(9)-C(10)-H(10)	108.5
C(10)-C(11)-C(12)	108.18(13)
C(10)-C(11)-H(11A)	110.1
C(12)-C(11)-H(11A)	110.1
C(10)-C(11)-H(11B)	110.1
C(12)-C(11)-H(11B)	110.1
H(11A)-C(11)-H(11B)	108.4
C(13)-C(12)-C(11)	110.38(13)
C(13)-C(12)-H(12A)	109.6
C(11)-C(12)-H(12A)	109.6
C(13)-C(12)-H(12B)	109.6
C(11)-C(12)-H(12B)	109.6
H(12A)-C(12)-H(12B)	108.1

O(3)-C(13)-C(14)	106.86(13)
O(3)-C(13)-C(12)	110.58(13)
C(14)-C(13)-C(12)	112.57(13)
O(3)-C(13)-H(13)	108.9
C(14)-C(13)-H(13)	108.9
C(12)-C(13)-H(13)	108.9
O(4)-C(14)-C(21)	107.85(14)
O(4)-C(14)-C(13)	107.06(13)
C(21)-C(14)-C(13)	111.55(15)
O(4)-C(14)-C(15)	102.47(14)
C(21)-C(14)-C(15)	113.96(15)
C(13)-C(14)-C(15)	113.17(14)
O(5)-C(15)-C(14)	104.59(14)
O(5)-C(15)-H(15A)	110.8
C(14)-C(15)-H(15A)	110.8
O(5)-C(15)-H(15B)	110.8
C(14)-C(15)-H(15B)	110.8
H(15A)-C(15)-H(15B)	108.9
O(6)-C(16)-O(4)	124.65(18)
O(6)-C(16)-O(5)	123.59(17)
O(4)-C(16)-O(5)	111.75(16)
C(1)-C(17)-H(17A)	109.5
C(1)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5

C(1)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(1)-C(18)-H(18A)	109.5
C(1)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(1)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(5)-C(19)-H(19A)	109.5
C(5)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(5)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(9)-C(20)-H(20A)	109.5
C(9)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(9)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(14)-C(21)-H(21A)	109.5
C(14)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5

C(14)-C(21)-H(21C) 109.5

H(21A)-C(21)-H(21C) 109.5

H(21B)-C(21)-H(21C) 109.5

Symmetry transformations used to generate equivalent atoms:

Table S4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for 08351. The anisotropicdisplacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
Br(1)	25(1)	56(1)	38(1)	-7(1)	6(1)	7(1)
O(1)	26(1)	19(1)	14(1)	-4(1)	4(1)	-1(1)
O(2)	28(1)	12(1)	18(1)	-1(1)	7(1)	-2(1)
O(3)	16(1)	16(1)	23(1)	-3(1)	1(1)	0(1)
O(4)	21(1)	18(1)	28(1)	2(1)	2(1)	2(1)
O(5)	21(1)	36(1)	33(1)	-5(1)	4(1)	4(1)
O(6)	31(1)	41(1)	41(1)	4(1)	-6(1)	10(1)
C(1)	27(1)	17(1)	16(1)	-3(1)	4(1)	-1(1)
C(2)	22(1)	27(1)	23(1)	-2(1)	4(1)	6(1)
C(3)	35(1)	24(1)	23(1)	2(1)	2(1)	14(1)
C(4)	34(1)	20(1)	18(1)	4(1)	3(1)	10(1)
C(5)	29(1)	14(1)	15(1)	-1(1)	4(1)	2(1)
C(6)	22(1)	16(1)	12(1)	-1(1)	0(1)	0(1)
C(7)	22(1)	22(1)	16(1)	-1(1)	-3(1)	0(1)
C(8)	17(1)	18(1)	18(1)	2(1)	-1(1)	3(1)
C(9)	17(1)	14(1)	19(1)	-2(1)	1(1)	-1(1)
C(10)	22(1)	12(1)	14(1)	0(1)	2(1)	1(1)
C(11)	30(1)	17(1)	14(1)	1(1)	3(1)	-1(1)
C(12)	24(1)	20(1)	15(1)	0(1)	1(1)	-2(1)

C(13)	16(1)	15(1)	19(1)	-1(1)	2(1)	-2(1)
C(14)	22(1)	16(1)	23(1)	-1(1)	1(1)	-1(1)
C(15)	29(1)	22(1)	27(1)	-4(1)	7(1)	2(1)
C(16)	22(1)	24(1)	30(1)	-8(1)	-3(1)	-1(1)
C(17)	34(1)	22(1)	20(1)	2(1)	2(1)	-5(1)
C(18)	41(1)	26(1)	21(1)	-7(1)	11(1)	2(1)
C(19)	47(1)	16(1)	26(1)	-5(1)	10(1)	-8(1)
C(20)	20(1)	22(1)	28(1)	-3(1)	3(1)	-5(1)
C(21)	31(1)	21(1)	37(1)	-4(1)	-7(1)	-5(1)

Table S5. Hydrogen coordinates (x 10⁴) and isotropic displacement parameters (Å²x 10³)

for 08351.

	x	y	z	U(eq)
H(2)	3294	5626	1276	28
H(3A)	3775	7733	1416	33
H(3B)	2706	7396	768	33
H(4A)	4213	6321	85	29
H(4B)	4571	7496	24	29
H(6)	5108	5332	1261	20
H(7A)	6963	5072	2221	24
H(7B)	7688	5804	1585	24
H(8A)	7979	4016	1286	22
H(8B)	6509	3936	1078	22
H(10)	5628	5070	12	19
H(11A)	7258	5445	-1385	25
H(11B)	5789	5745	-1379	25
H(12A)	5155	4119	-1505	24
H(12B)	6519	3977	-1921	24
H(13)	5766	3425	-269	20
H(15A)	7694	1826	-2044	31
H(15B)	8256	2849	-1634	31

H(17A)	4156	4584	2380	38
H(17B)	3003	4954	2949	38
H(17C)	4419	5044	3287	38
H(18A)	4332	6926	3512	44
H(18B)	2858	6835	3306	44
H(18C)	3715	7634	2810	44
H(19A)	7315	7478	1276	44
H(19B)	5970	7951	1510	44
H(19C)	6554	8134	603	44
H(20A)	9482	4653	159	35
H(20B)	8903	5721	448	35
H(20C)	8913	5420	-519	35
H(21A)	5531	1217	-1570	45
H(21B)	5370	2303	-2007	45
H(21C)	4704	2083	-1130	45

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^{S1} Manriquez, C. P.; Souto, M. L.; Gavin, J. A.; Norte, M.; Fernandez, J. J. *Tetrahedron* **2001**, *57*, 3117.

^{S2} Nieto, N.; Molas, P.; Benet-Buchholz, J.; Vidal-Ferran, A. *J. Org. Chem.* **2005**, *70*, 10143.

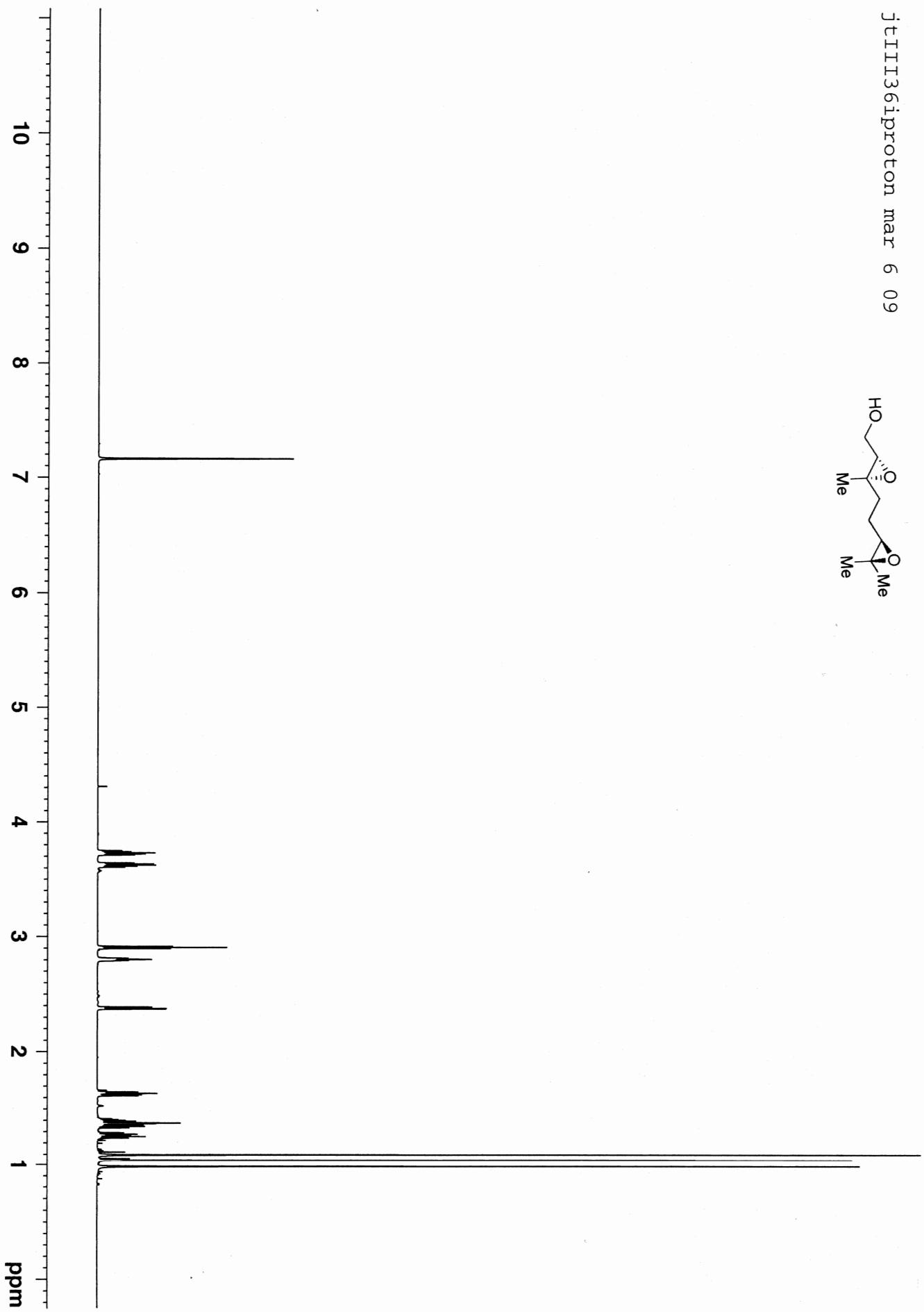
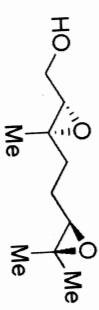
^{S3} For the synthesis of diepoxide **S1** see: McDonald, F. E.; Bravo, F.; Wang, X.; Wei, X.; Togano, M.; Rodriguez, J. R.; Do, B.; Neiwert, W. A.; Hardcastle, K. I. *J. Org. Chem.* **2002**, *67*, 2515.

^{S4} Epoxy alcohol **S3** was prepared according to the procedure reported in the following paper: Uyanik, M.; Ishibashi, H.; Ishihara, K.; Yamamoto, H. *Org. Lett.* **2005**, *7*, 1601. The *ee* was determined to be 82% (91:9 er). Epoxy alcohol # was protected with a benzyl group (BnBr, NaH, THF) and compared to the corresponding racemate obtained by VO(acac)₂ epoxidation of farnesol and then putting on the same protecting group. Chiral Analytical HPLC analysis was performed on a Hewlett-Packard 1100 Series HPLC equipped with a variable wavelength detector and Chiraldak AD-H column (hexanes:2-propanol, 99:1, 1.0 mL/min): t_R(2*S*, 3*S*) = 6.649 min, t_R(2*R*, 3*R*) = 6.024 min.

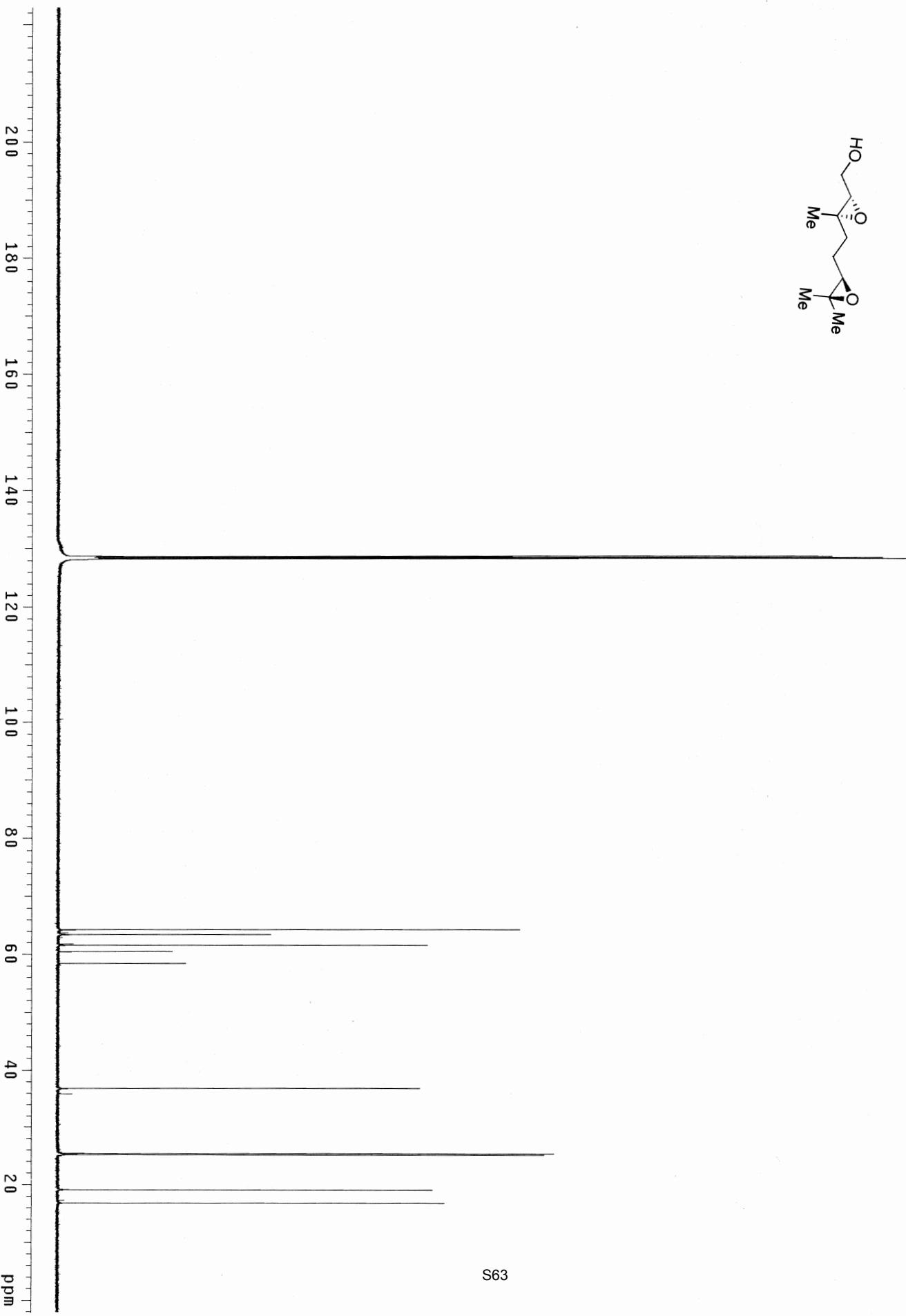
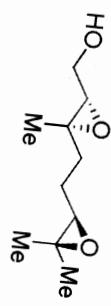
^{S5} Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224.

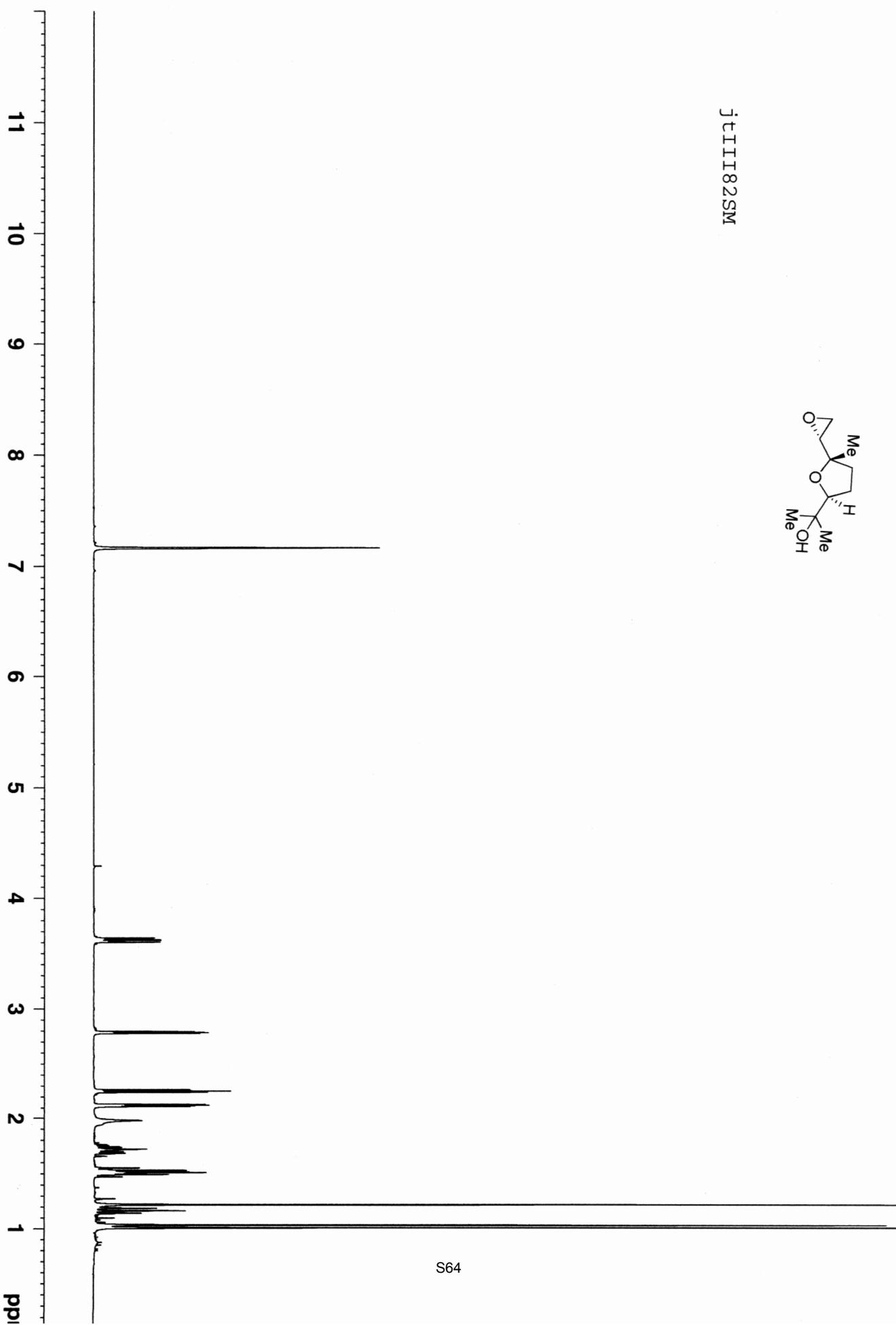
^{S6} (a) Potuzak, J. S.; Tan, D. S. *Tetrahedron Lett.* **2004**, *45*, 1797. b) Tsukano, C.; Sasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 14294. c) Sasaki, M.; Fuwa, H.; Inoue, M.; Tachibana, K. *Tetrahedron Lett.* **1998**, *39*, 9027.

jttIII36iproton mar 6 09



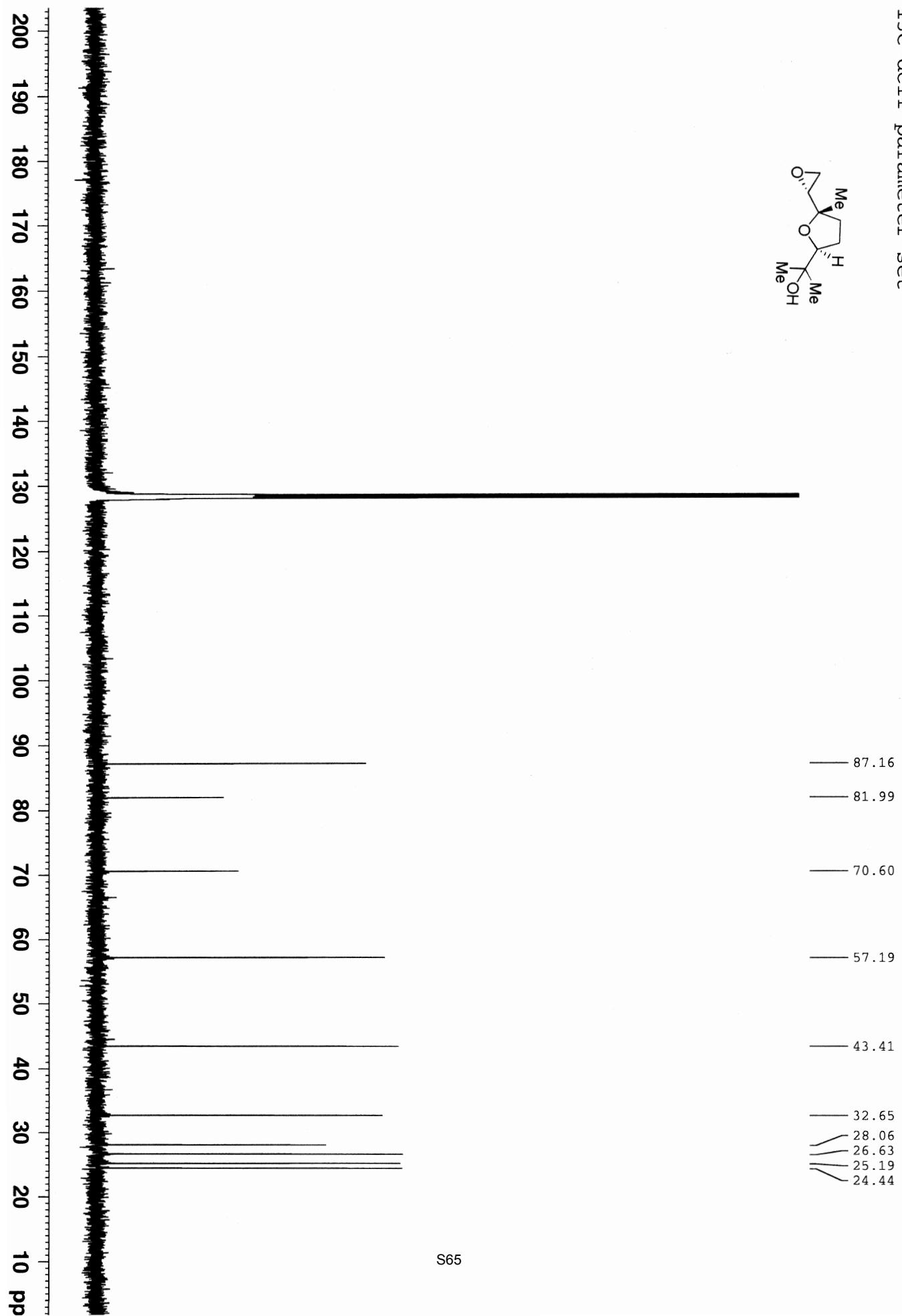
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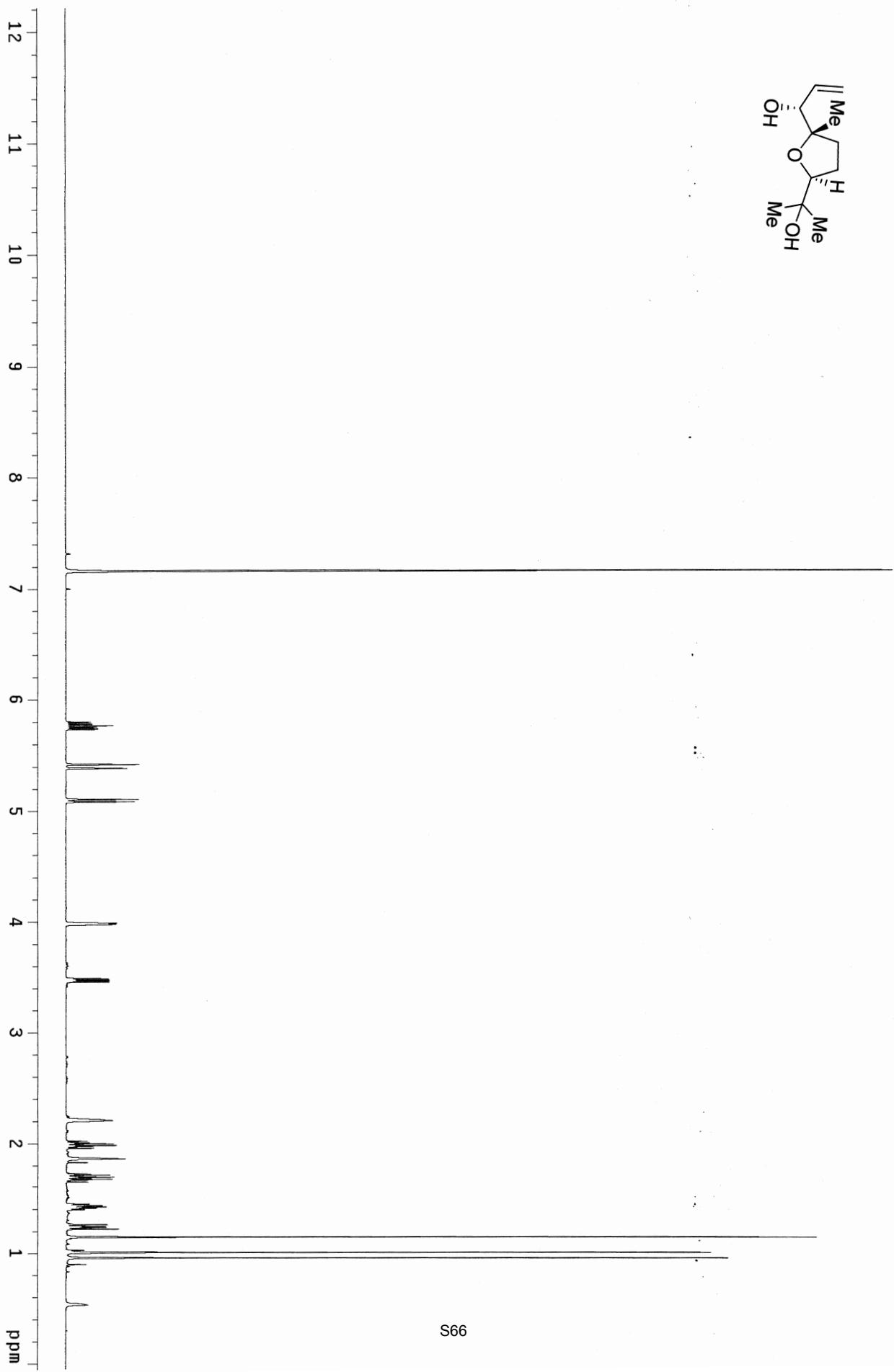
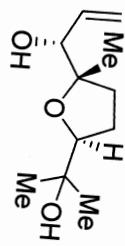


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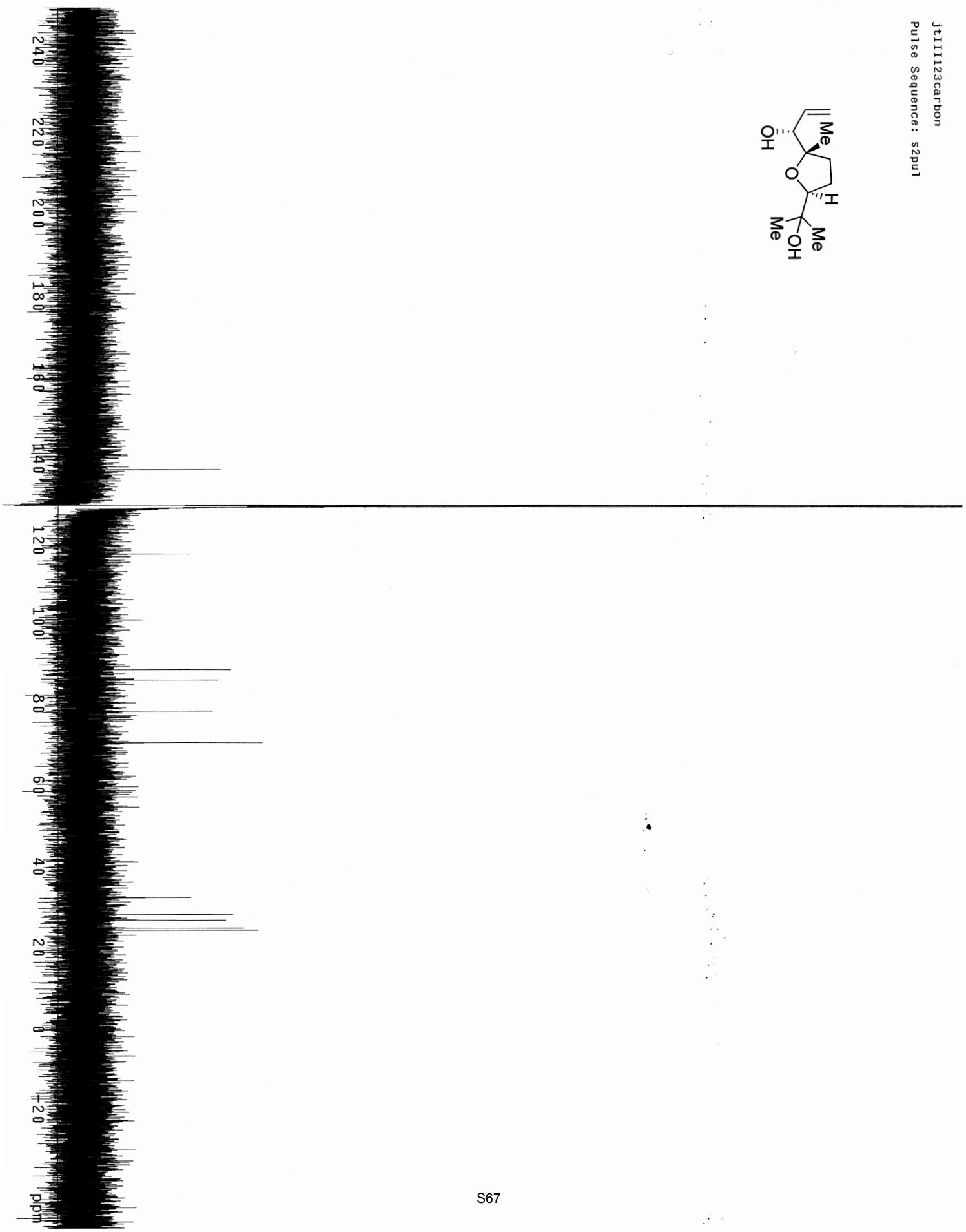
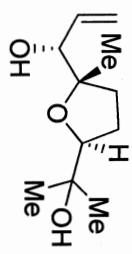
¹³C-dcif parameter set

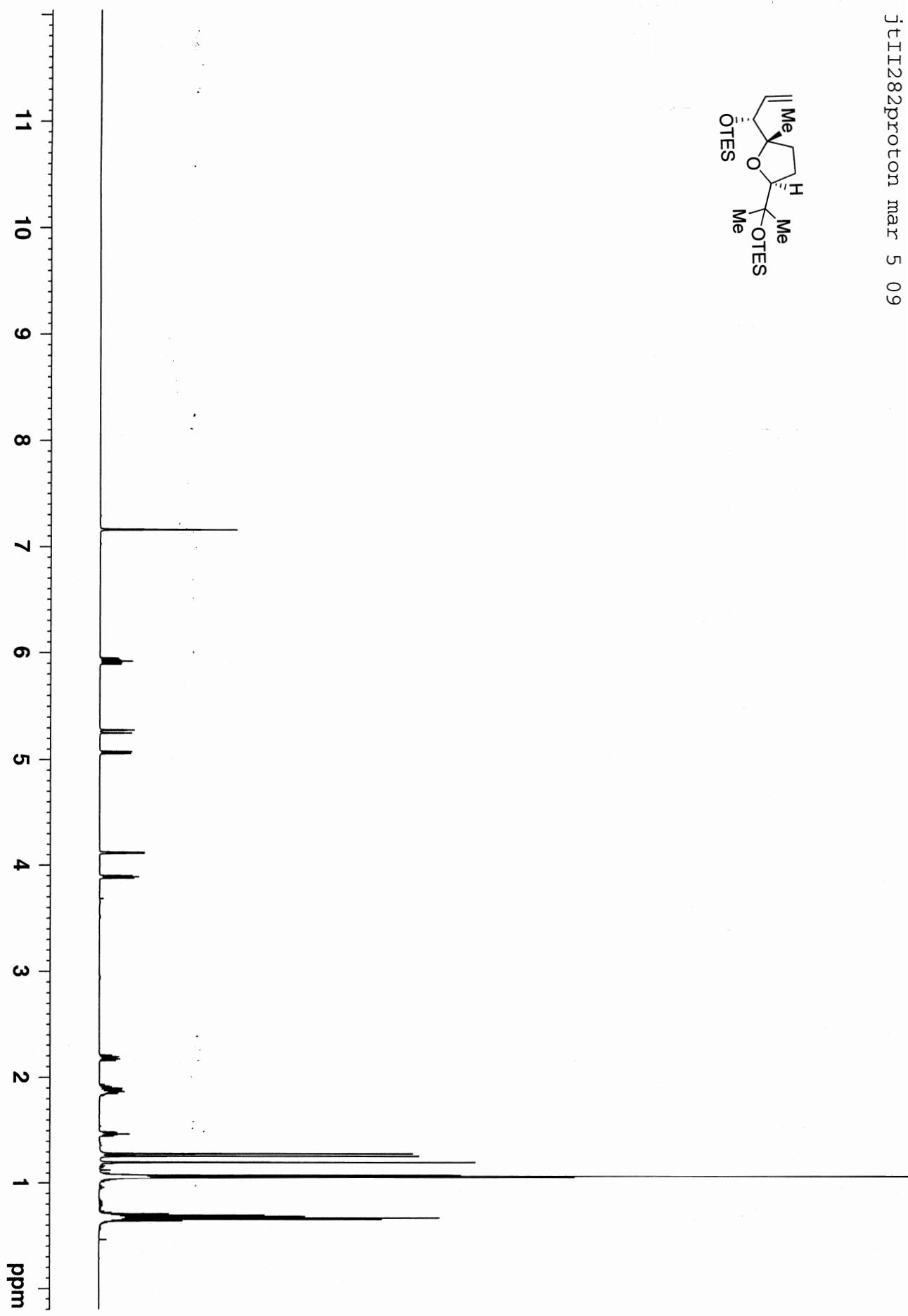


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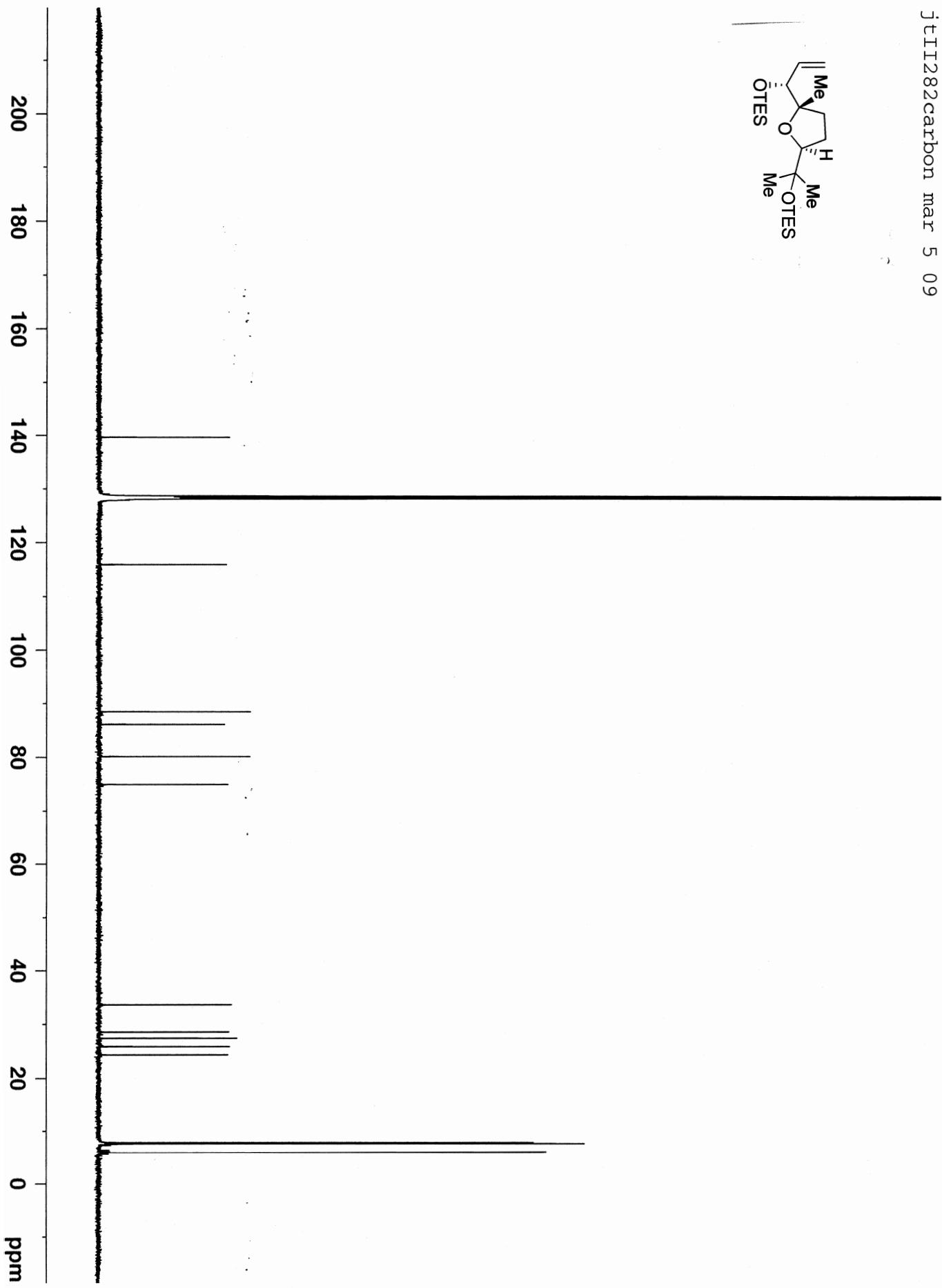
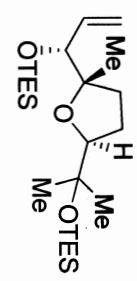


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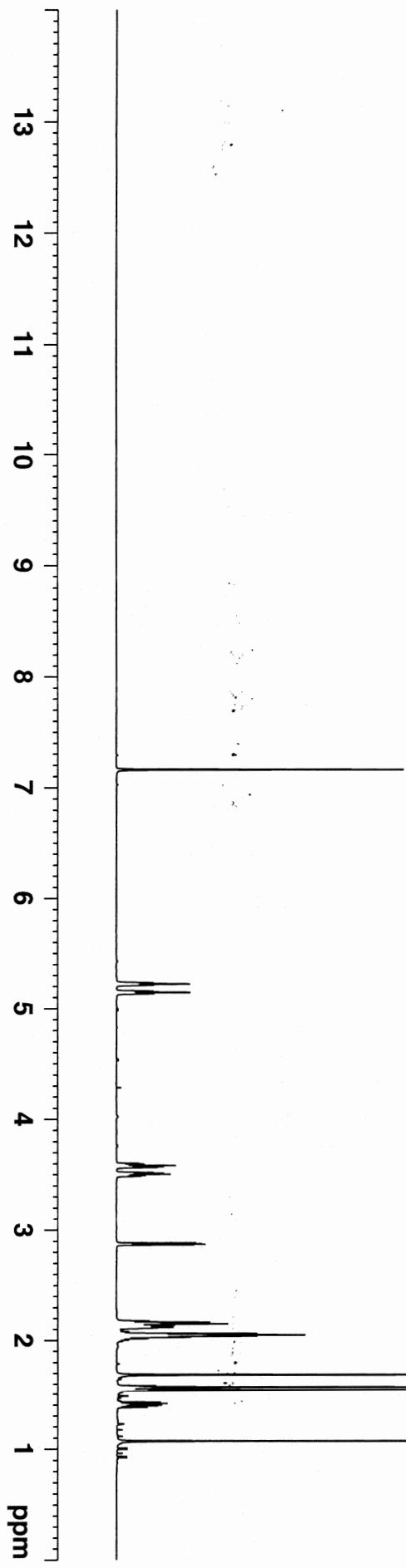
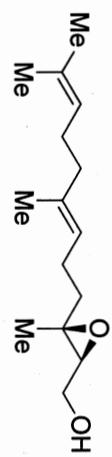




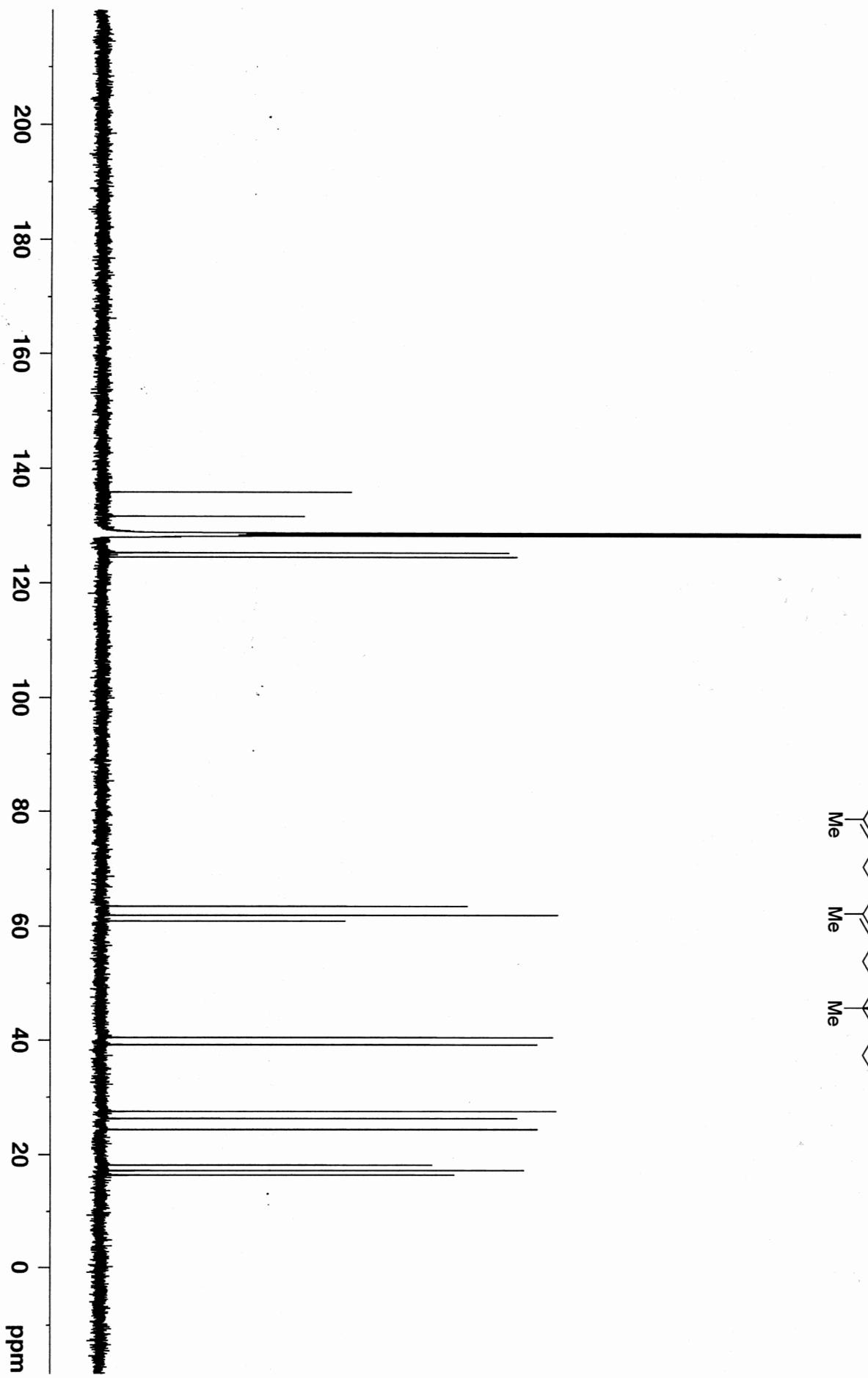
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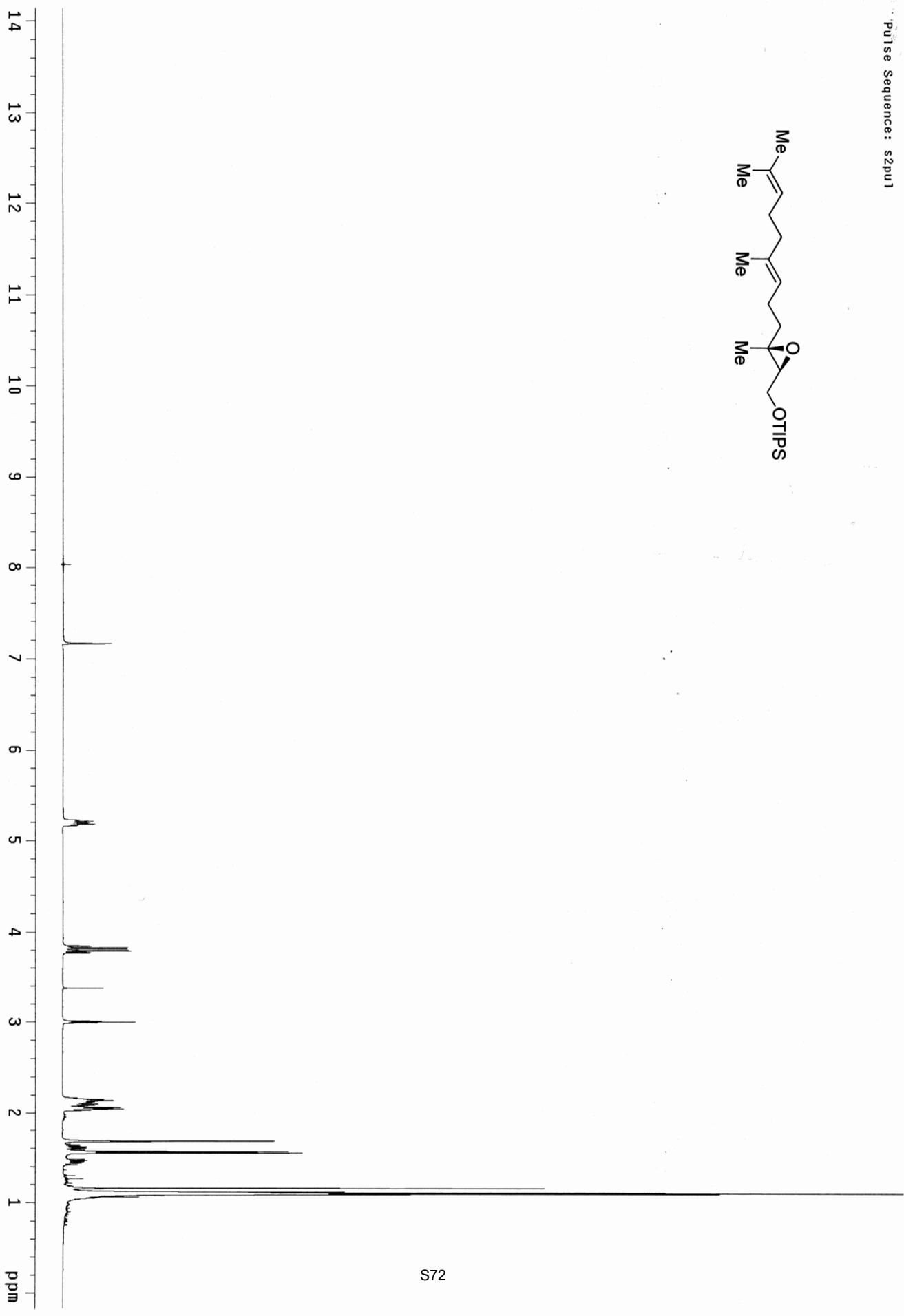


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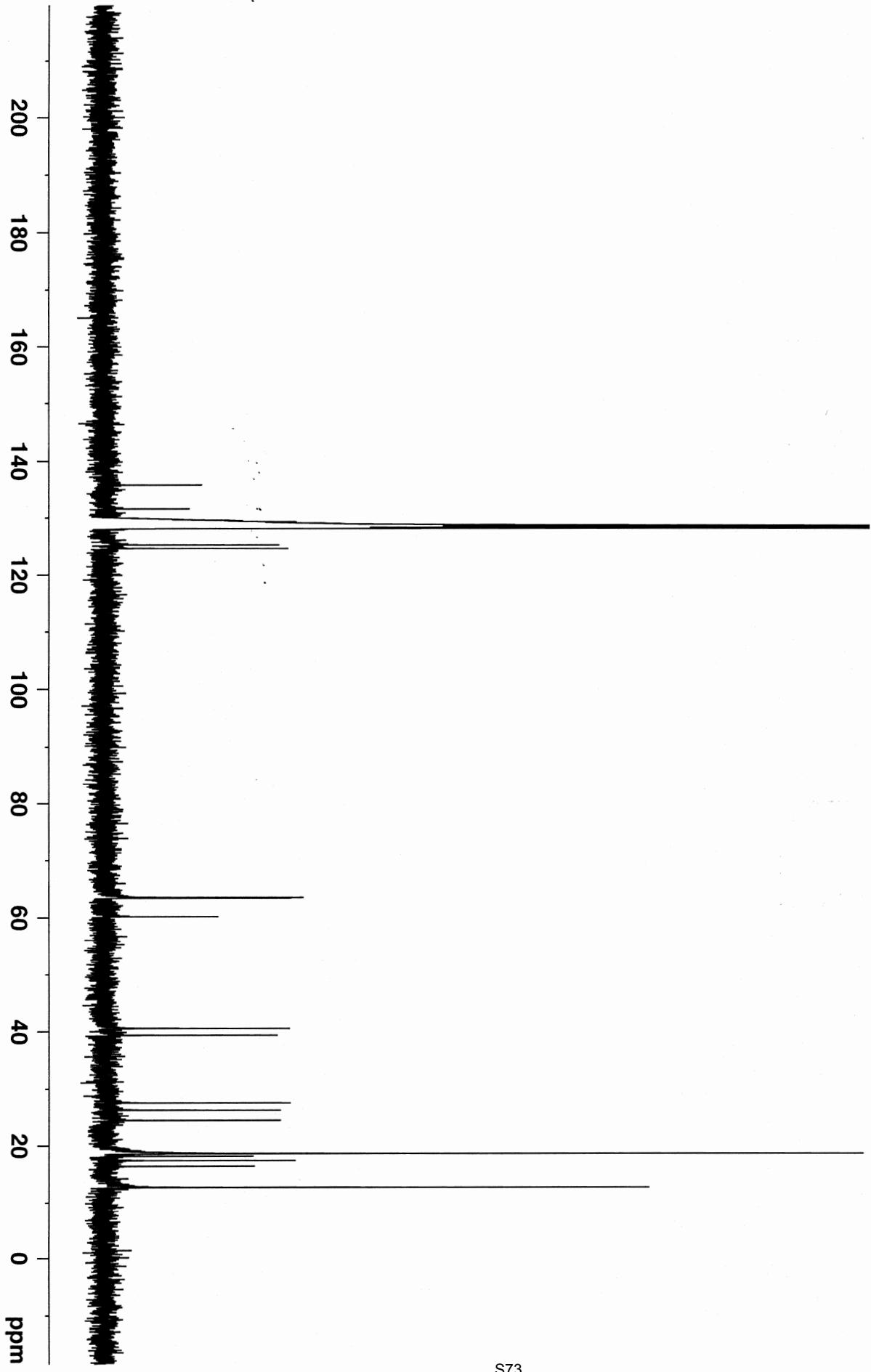
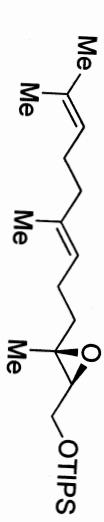


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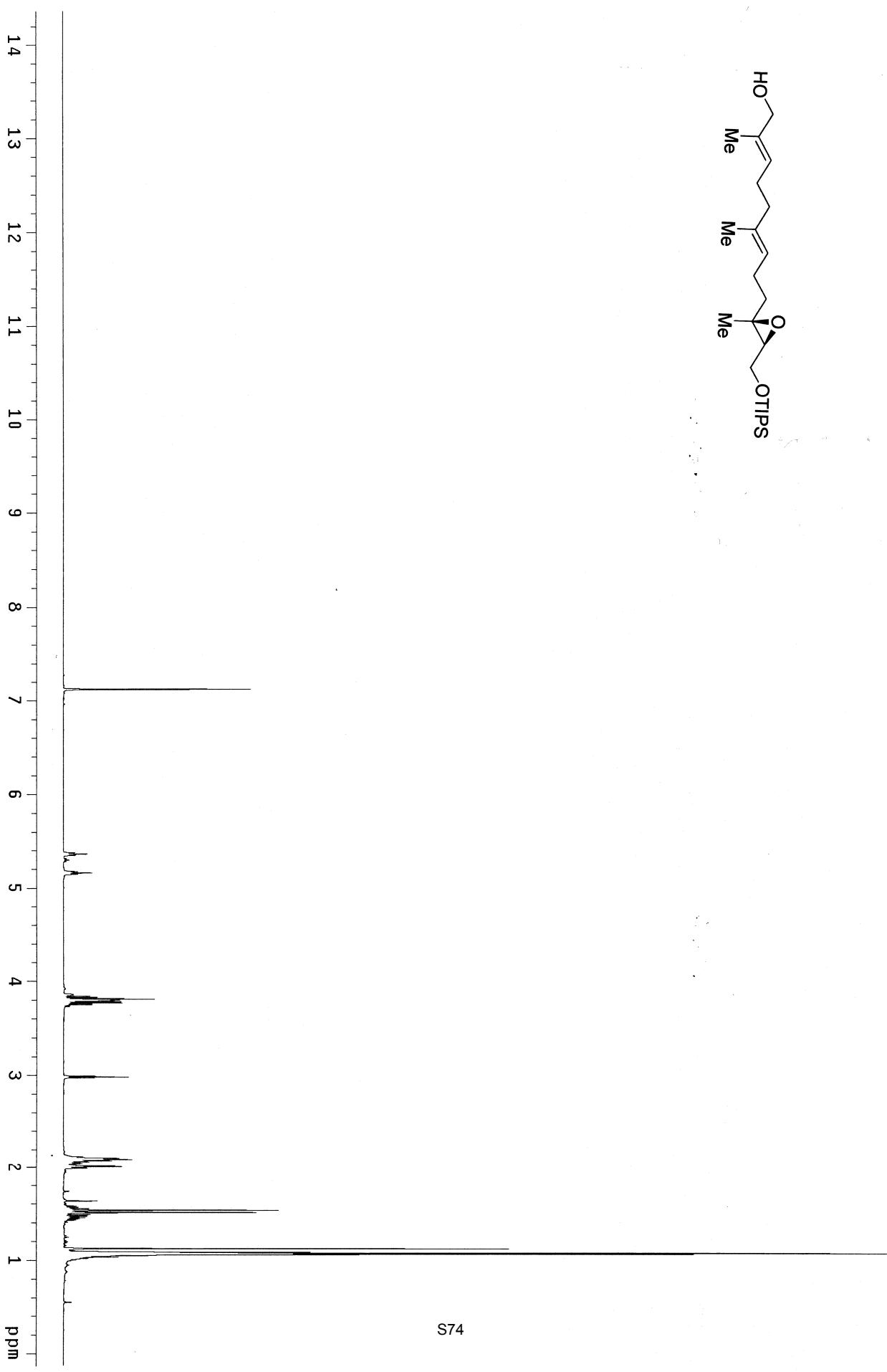
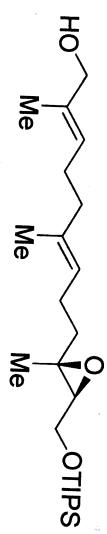




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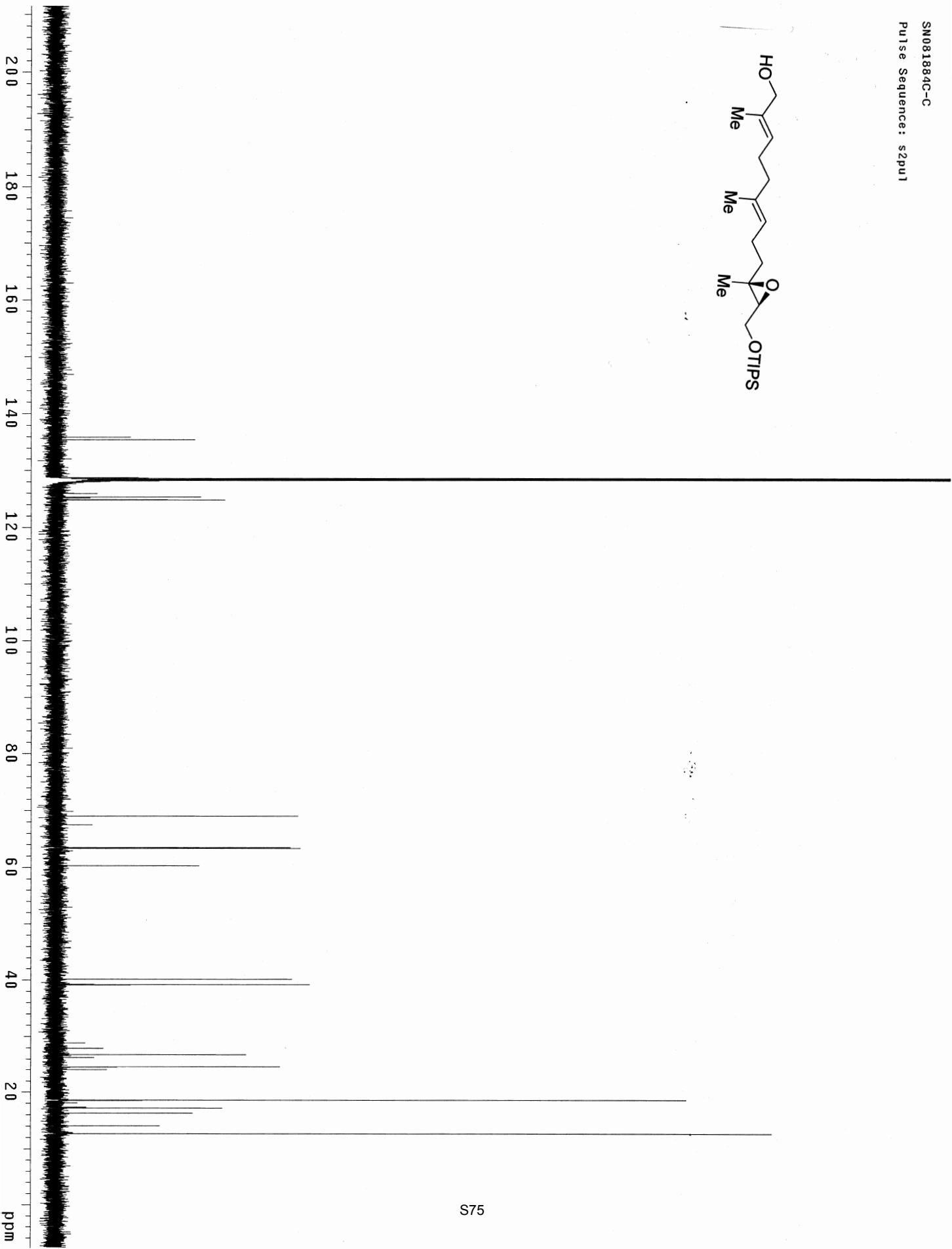
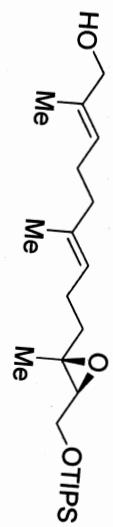


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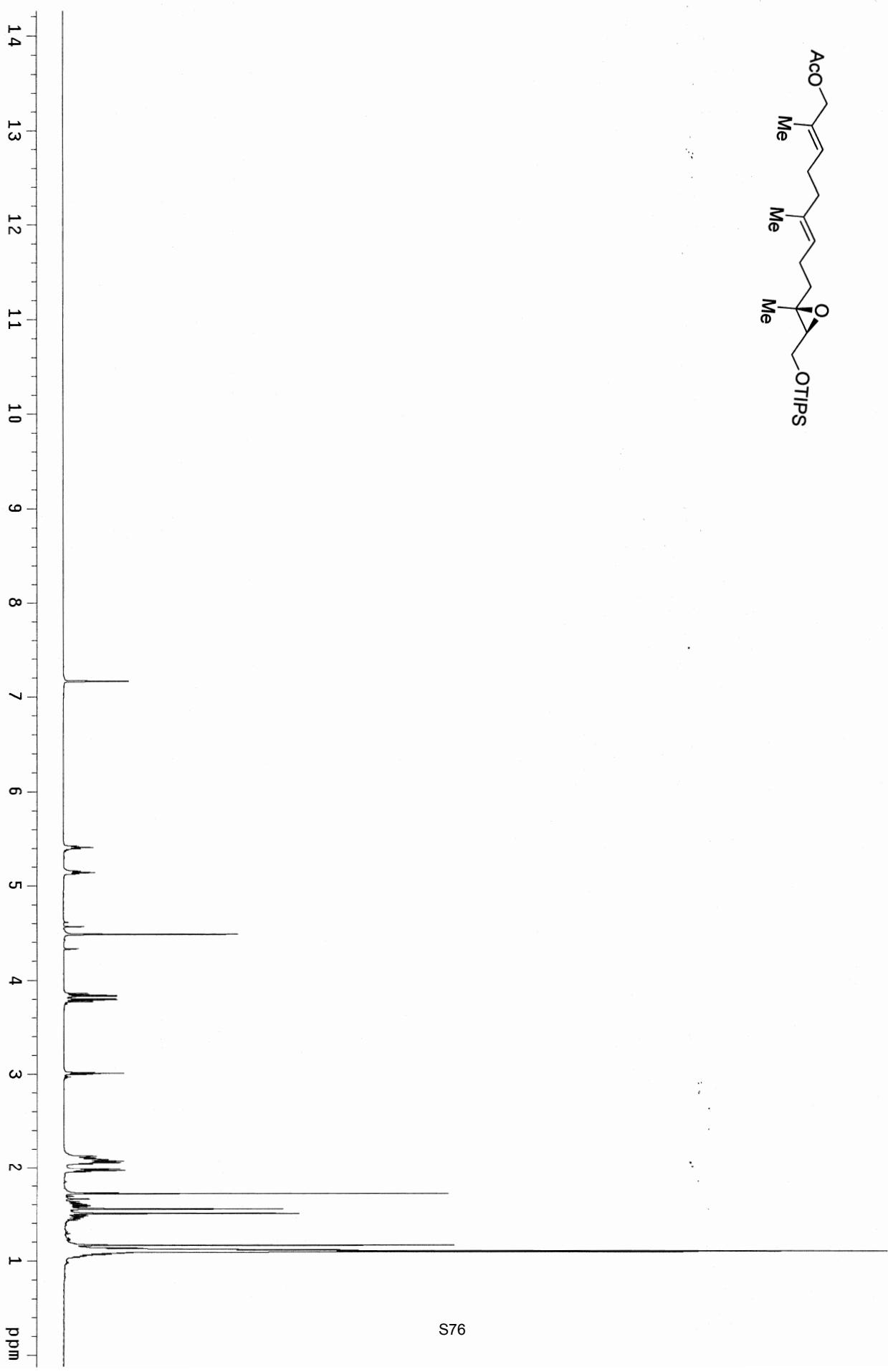
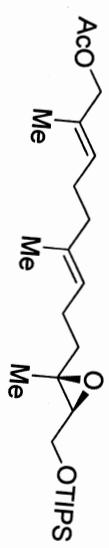
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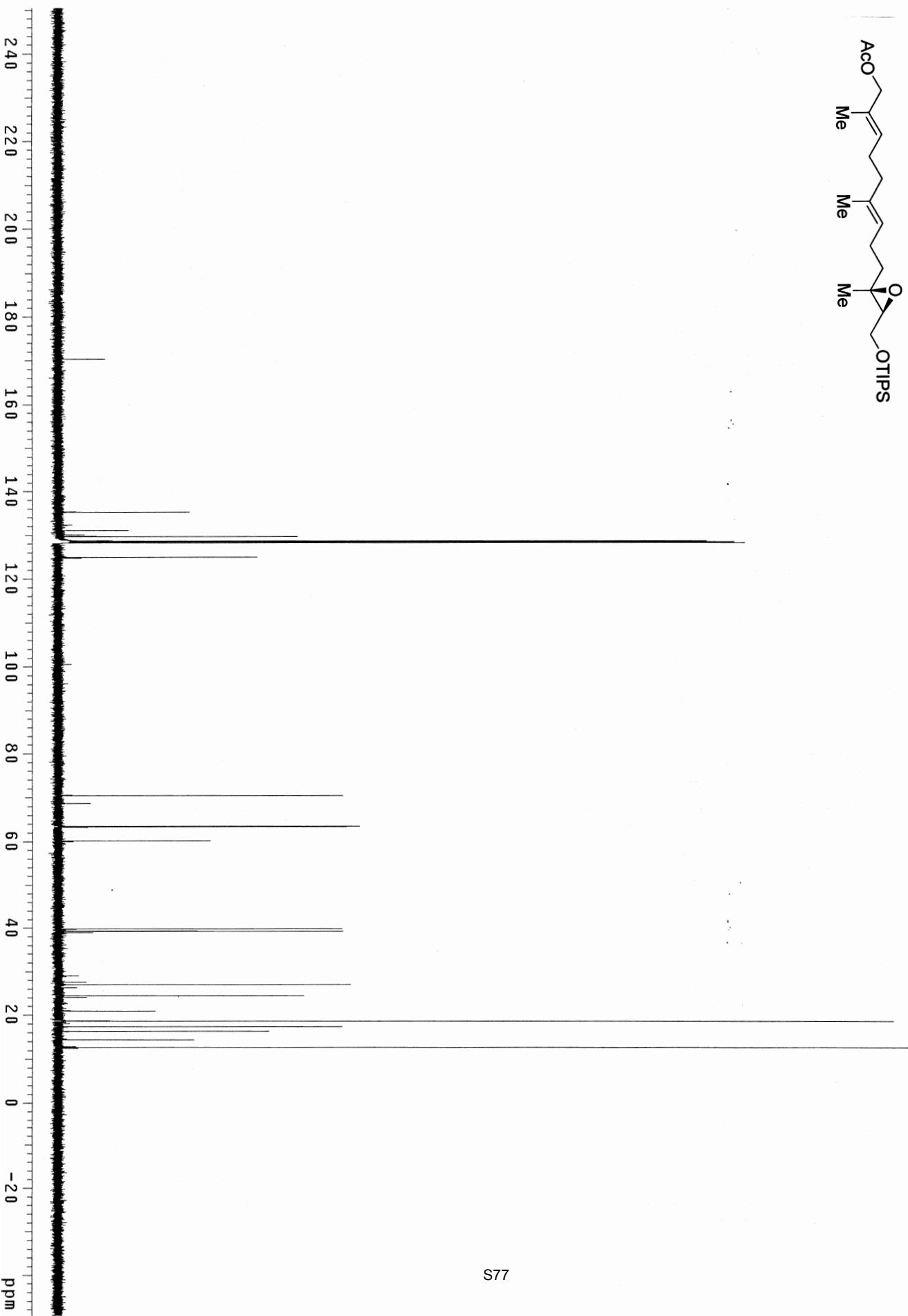
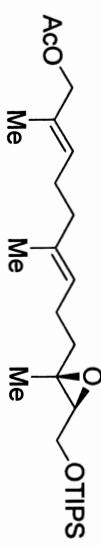
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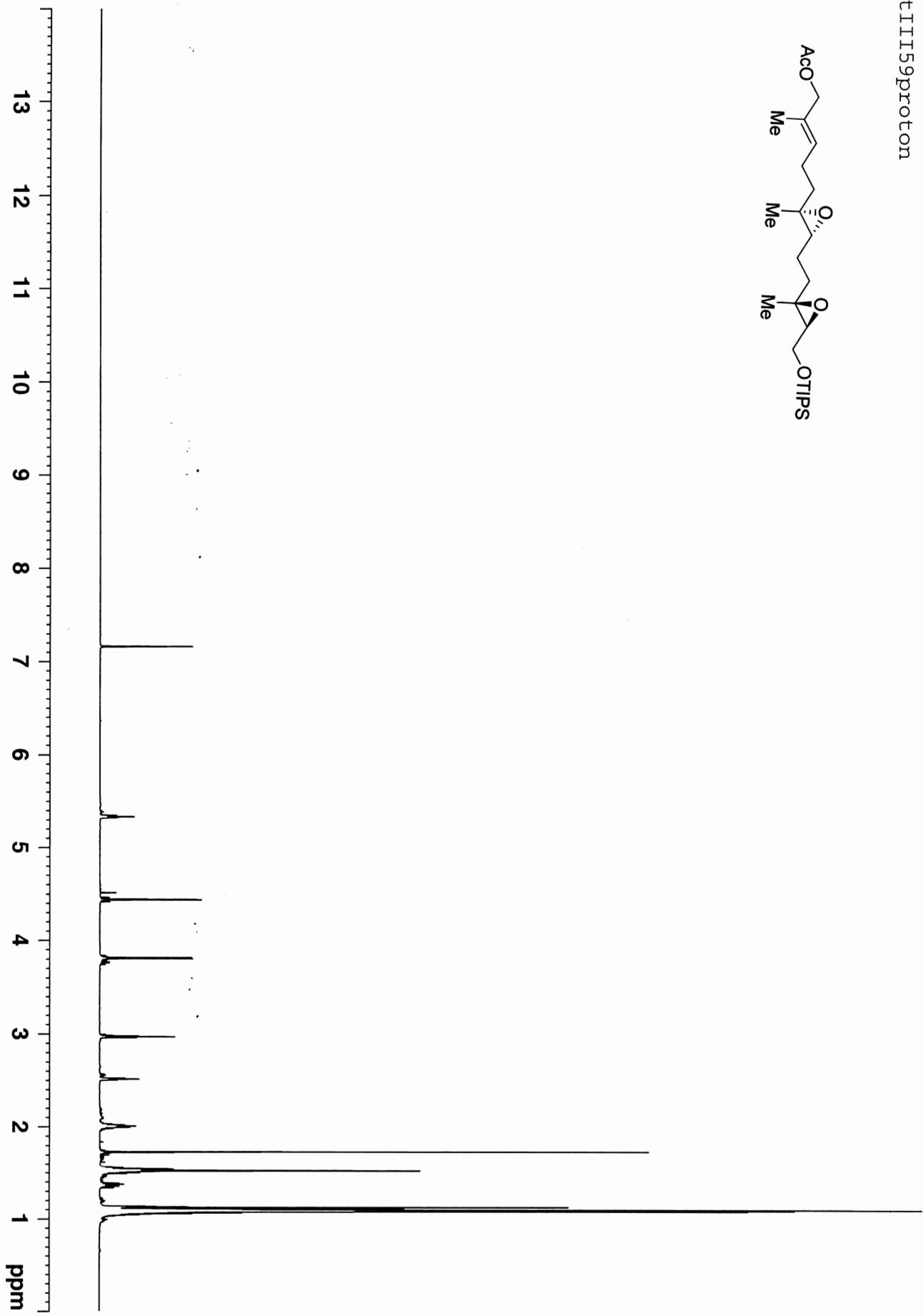
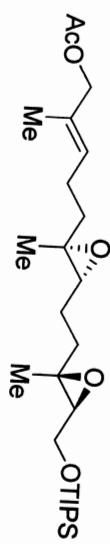


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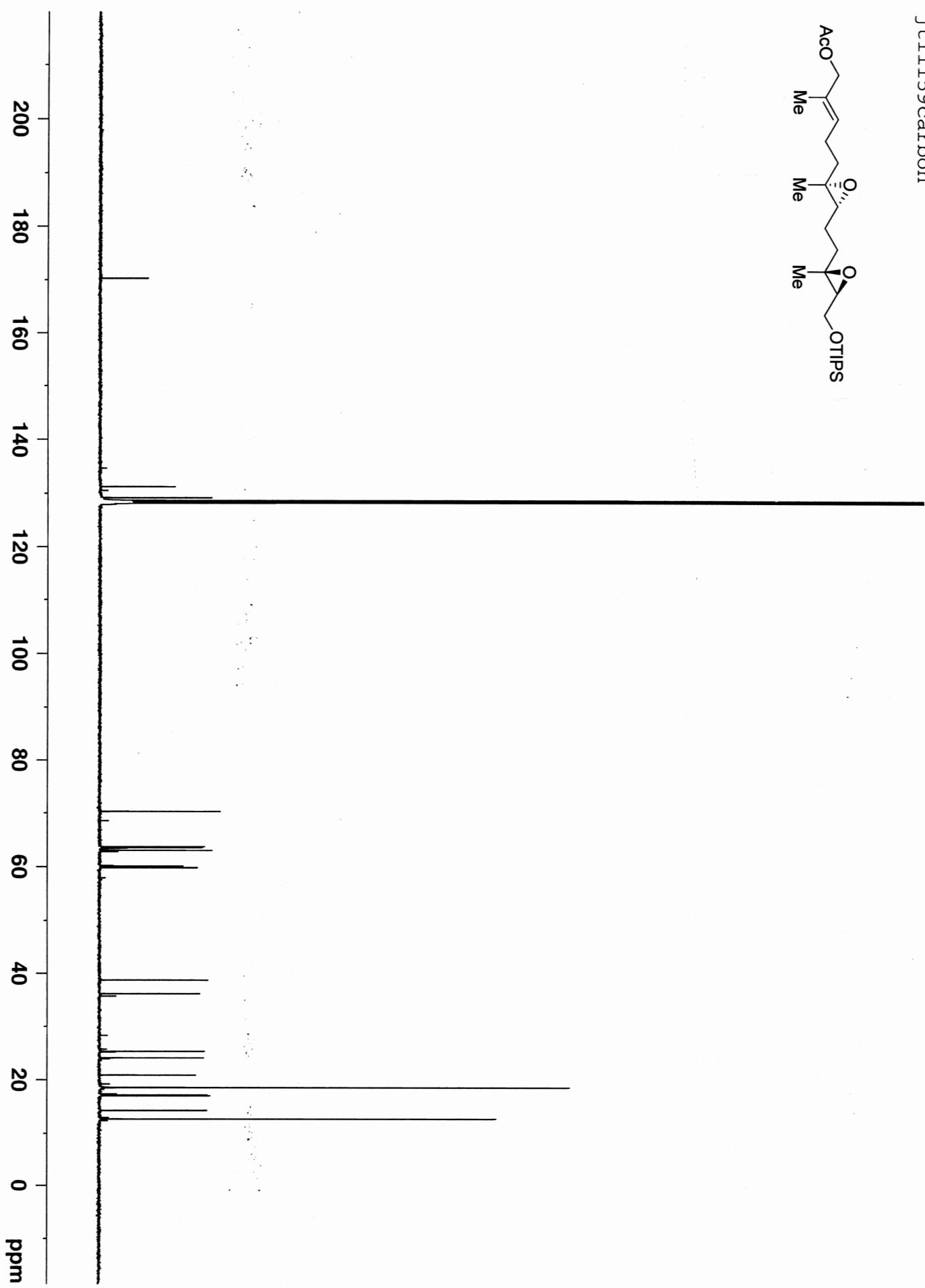
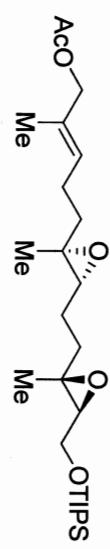
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β tIII59proton

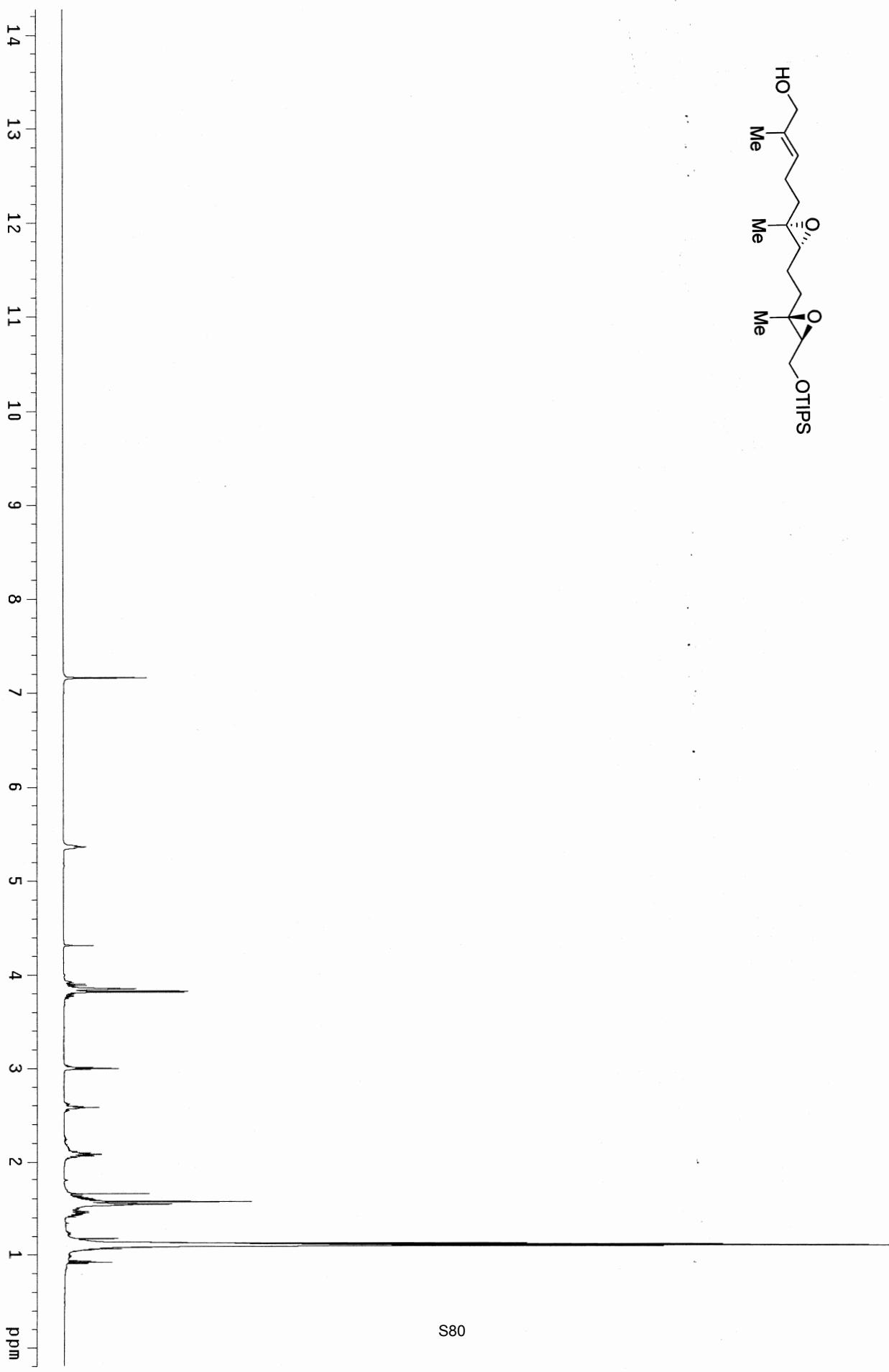
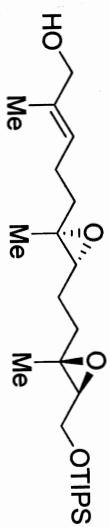


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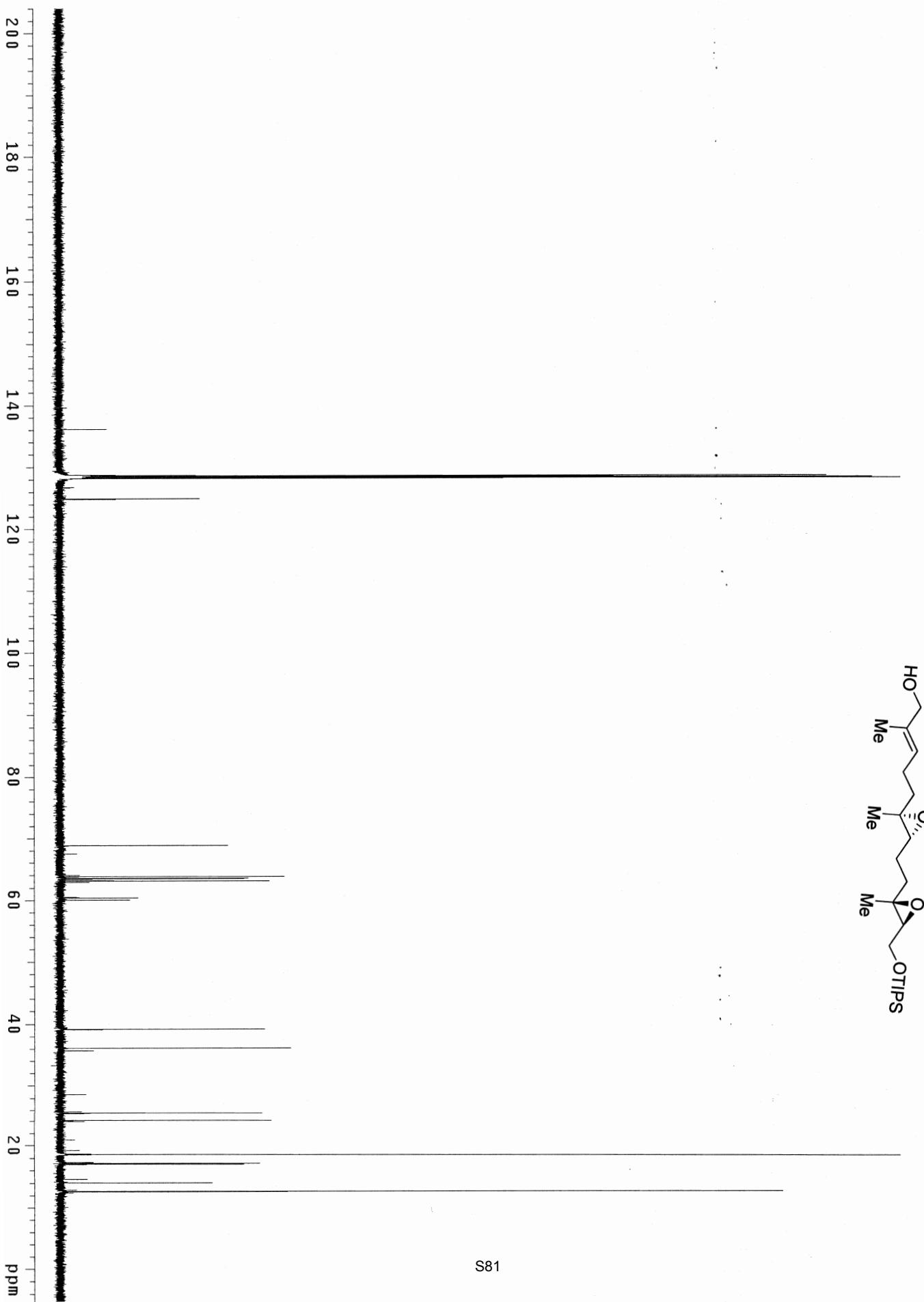


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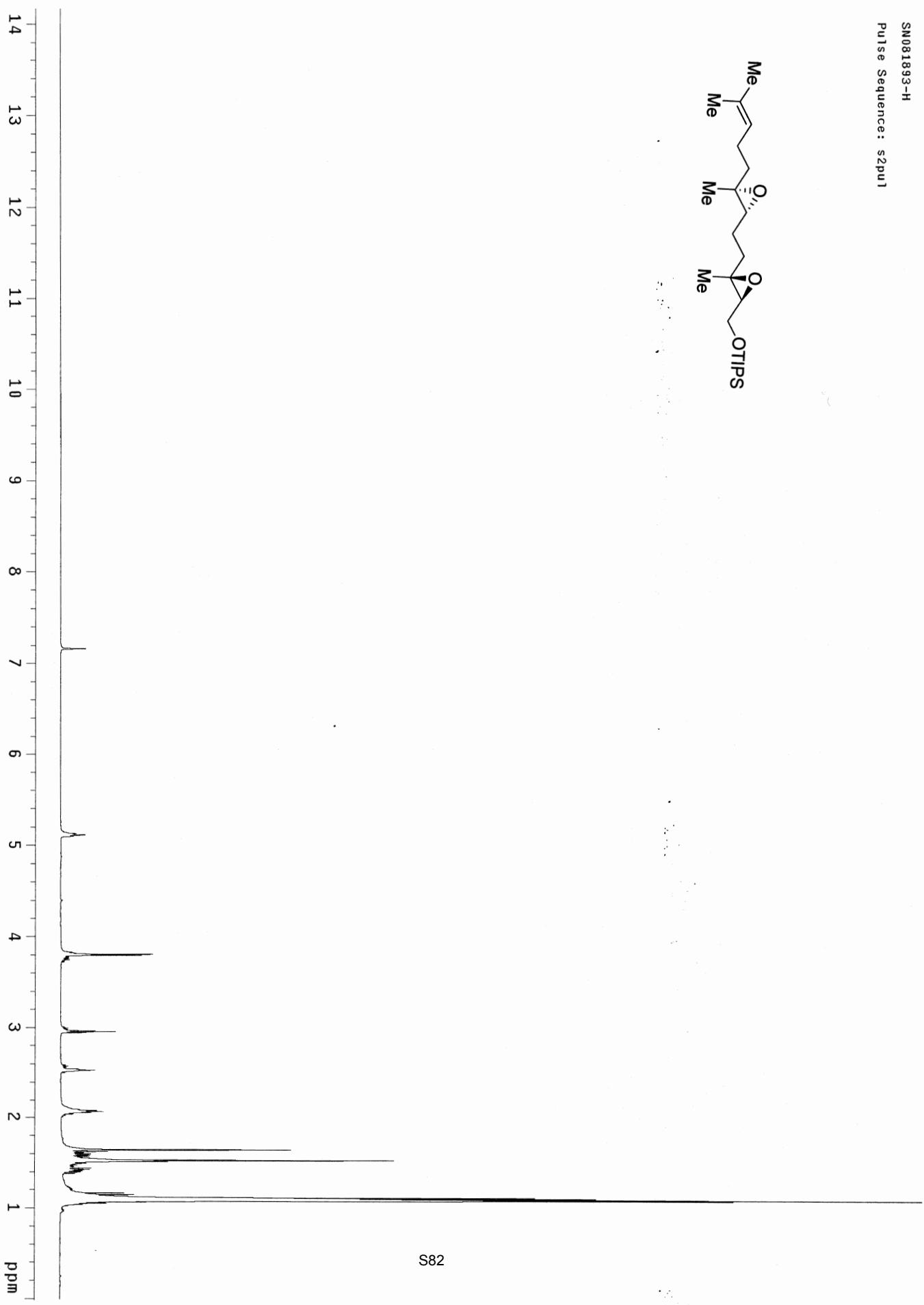
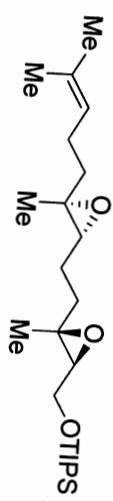


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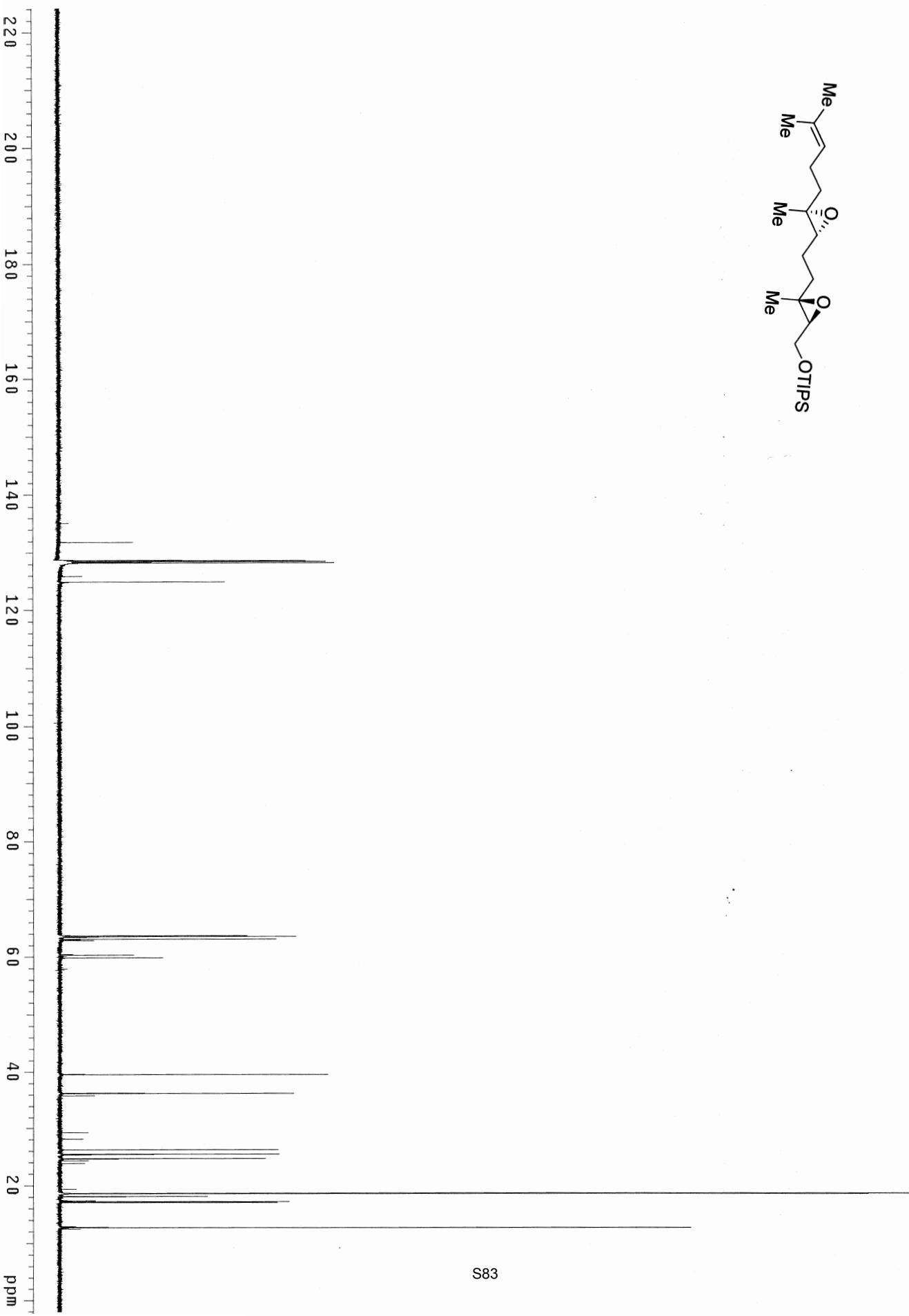
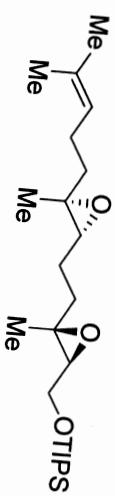
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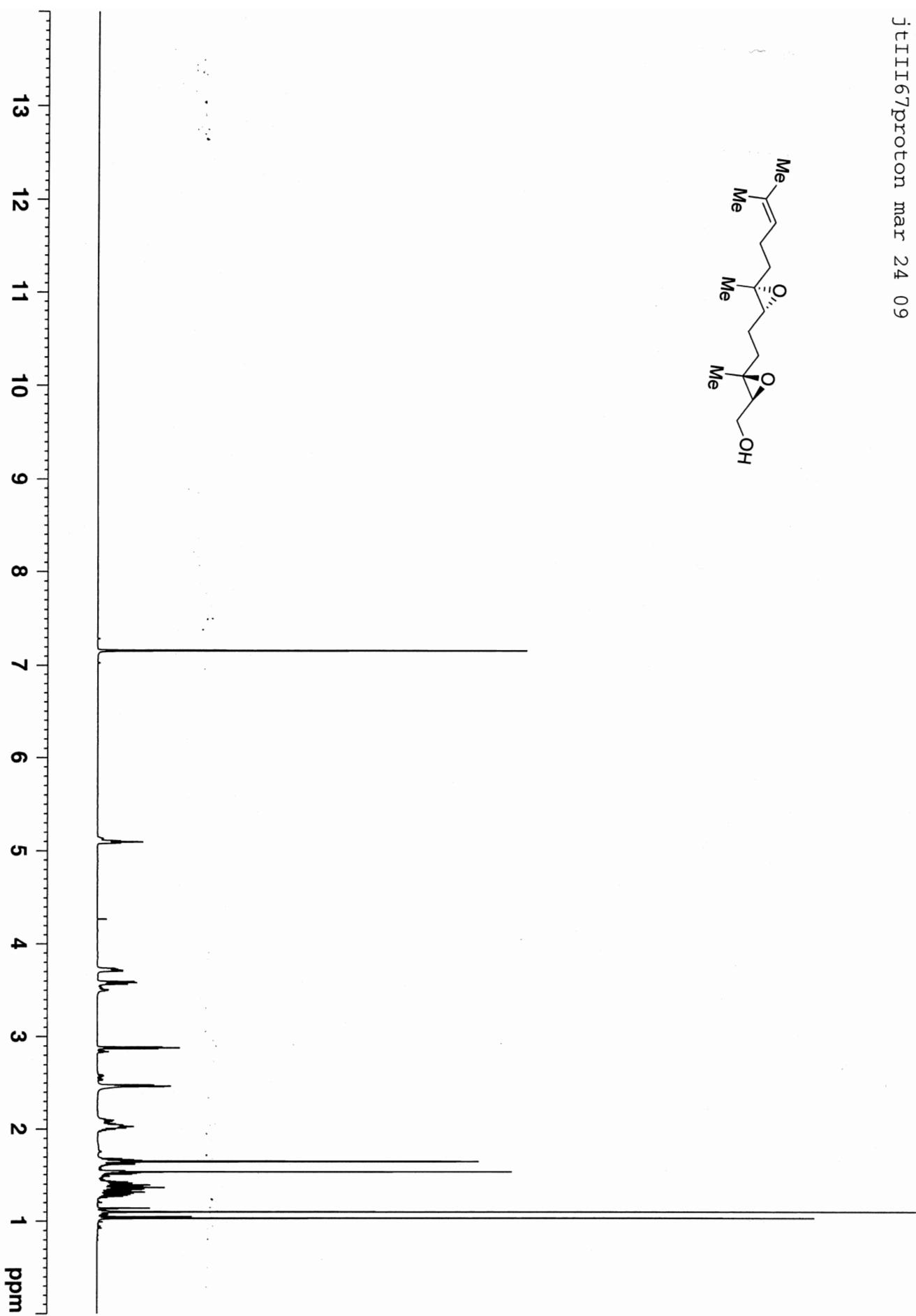
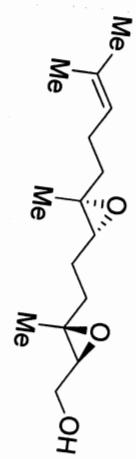


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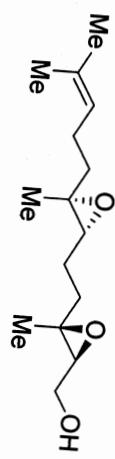
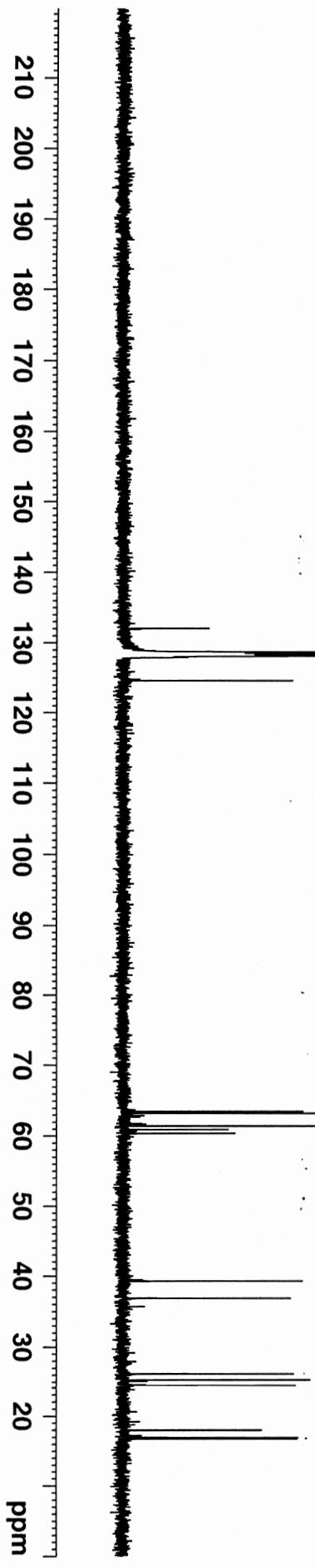
Pulse Sequence: s2pu1



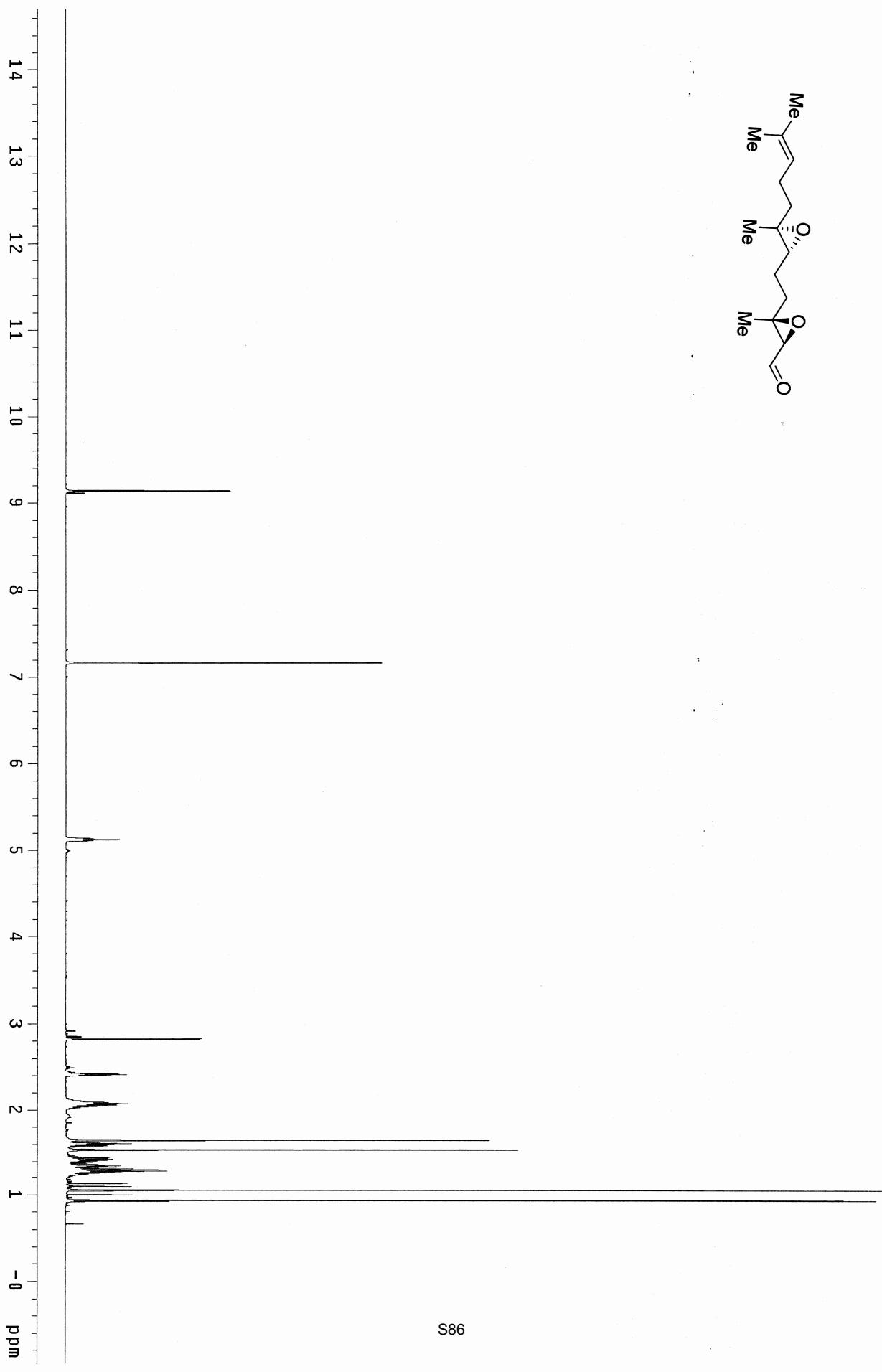
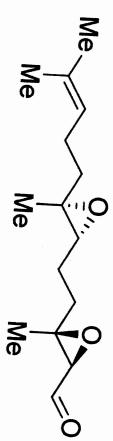
JtIII67 proton mar 24 09



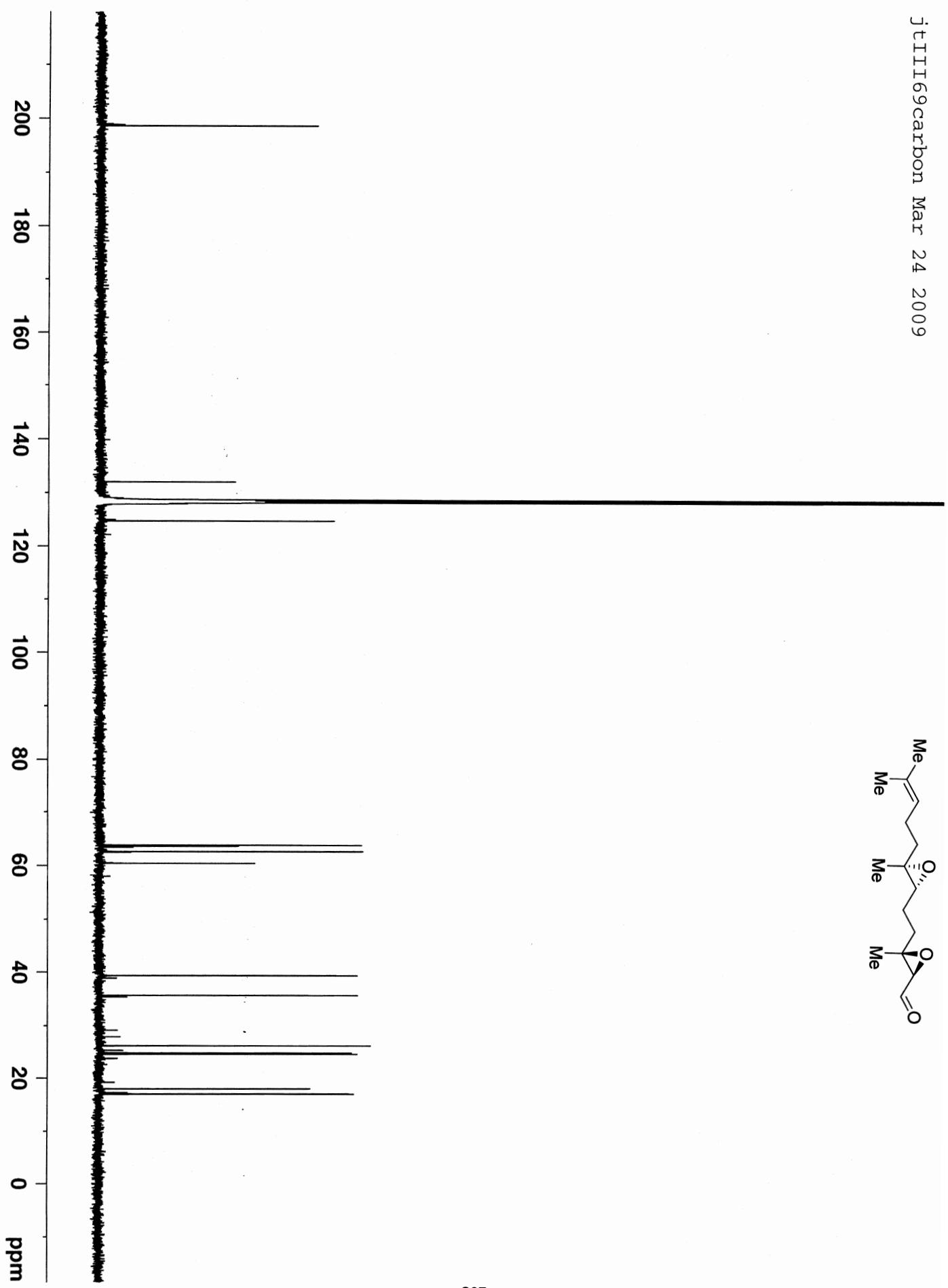
JtIII67carbon Mar 24 2009



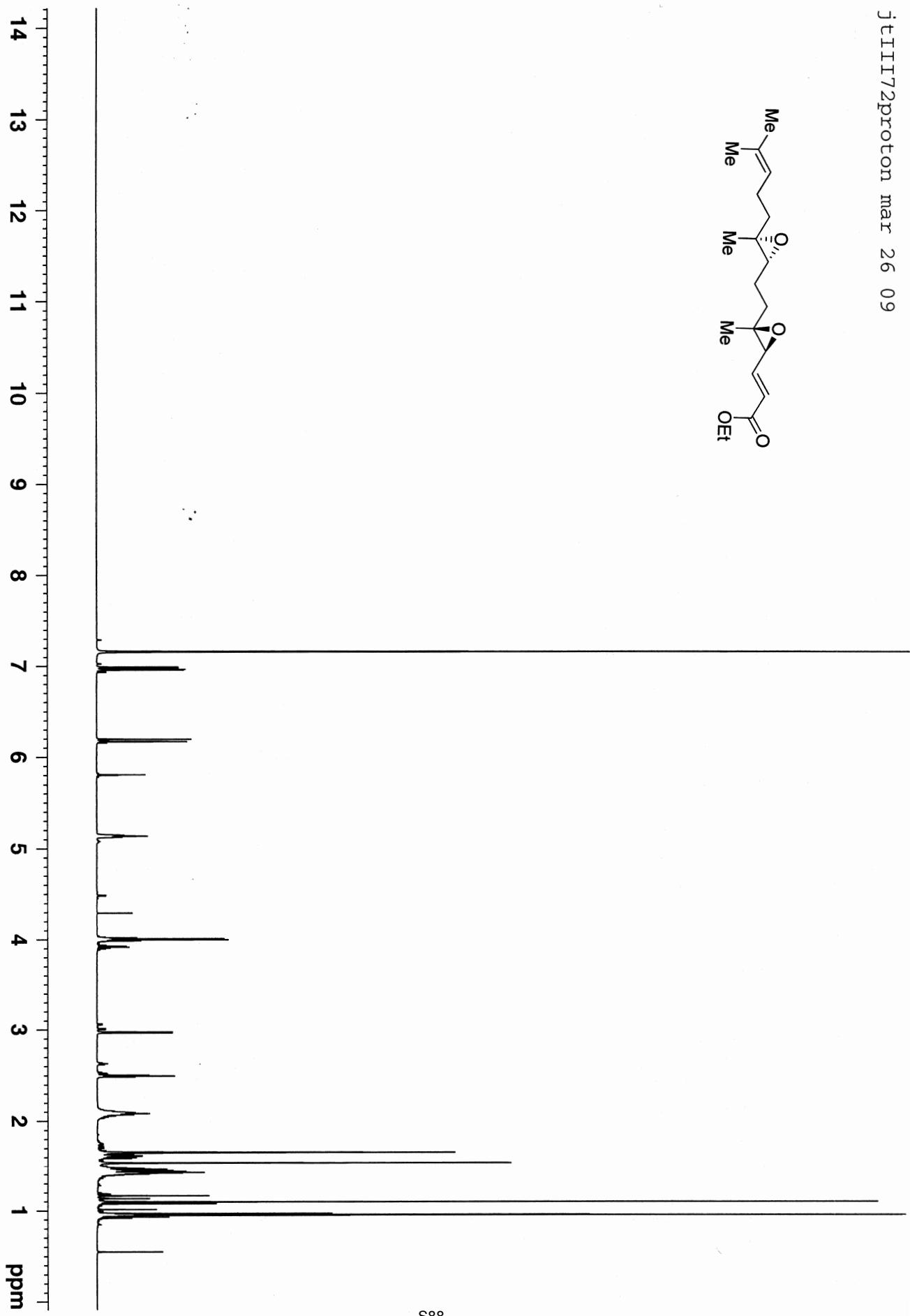
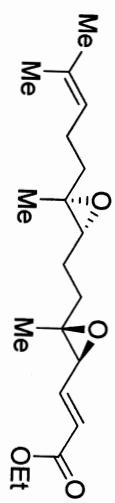
jT1163proton
Pulse Sequence: s2pul



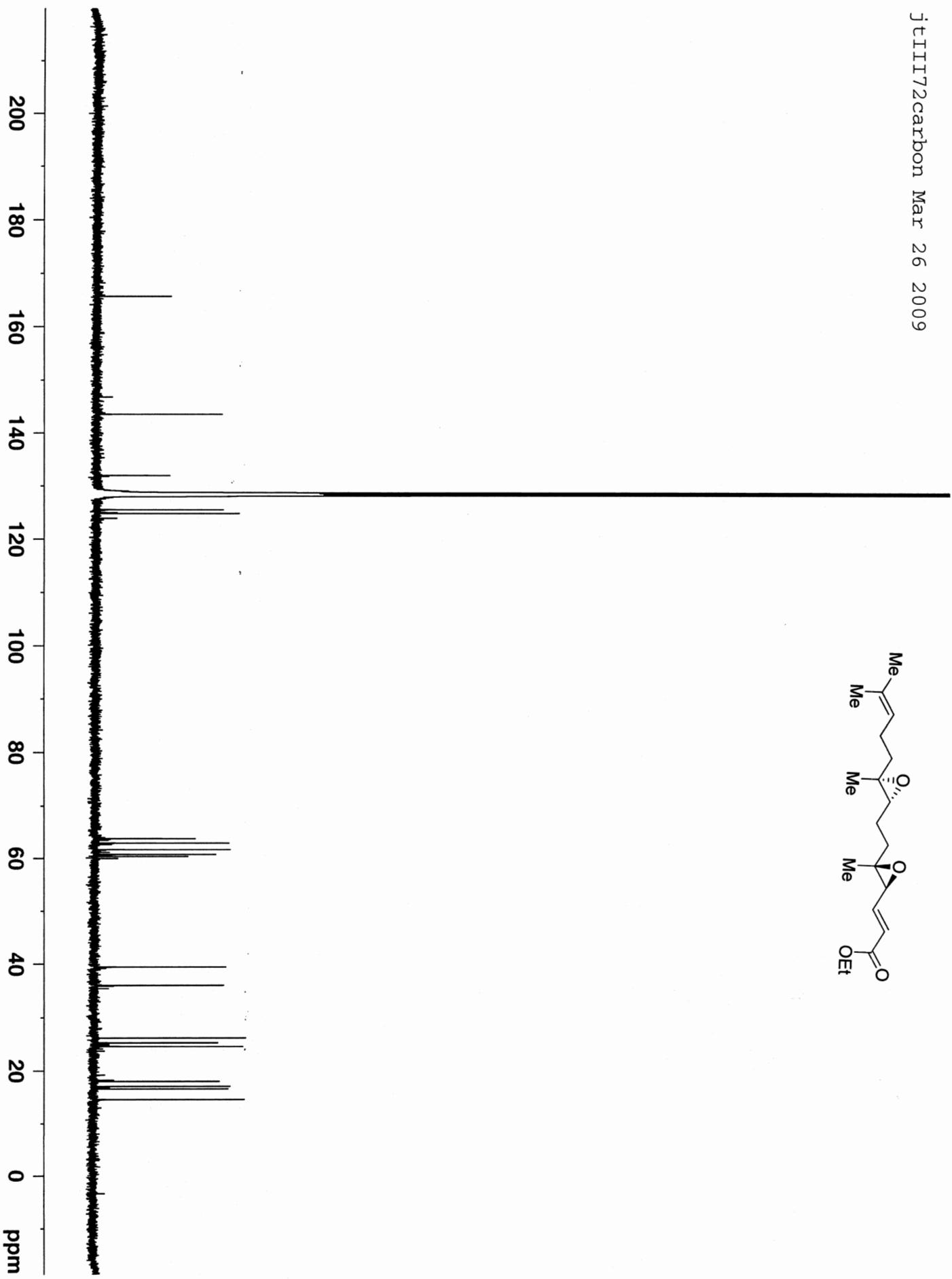
jttIIIGcarbon Mar 24 2009



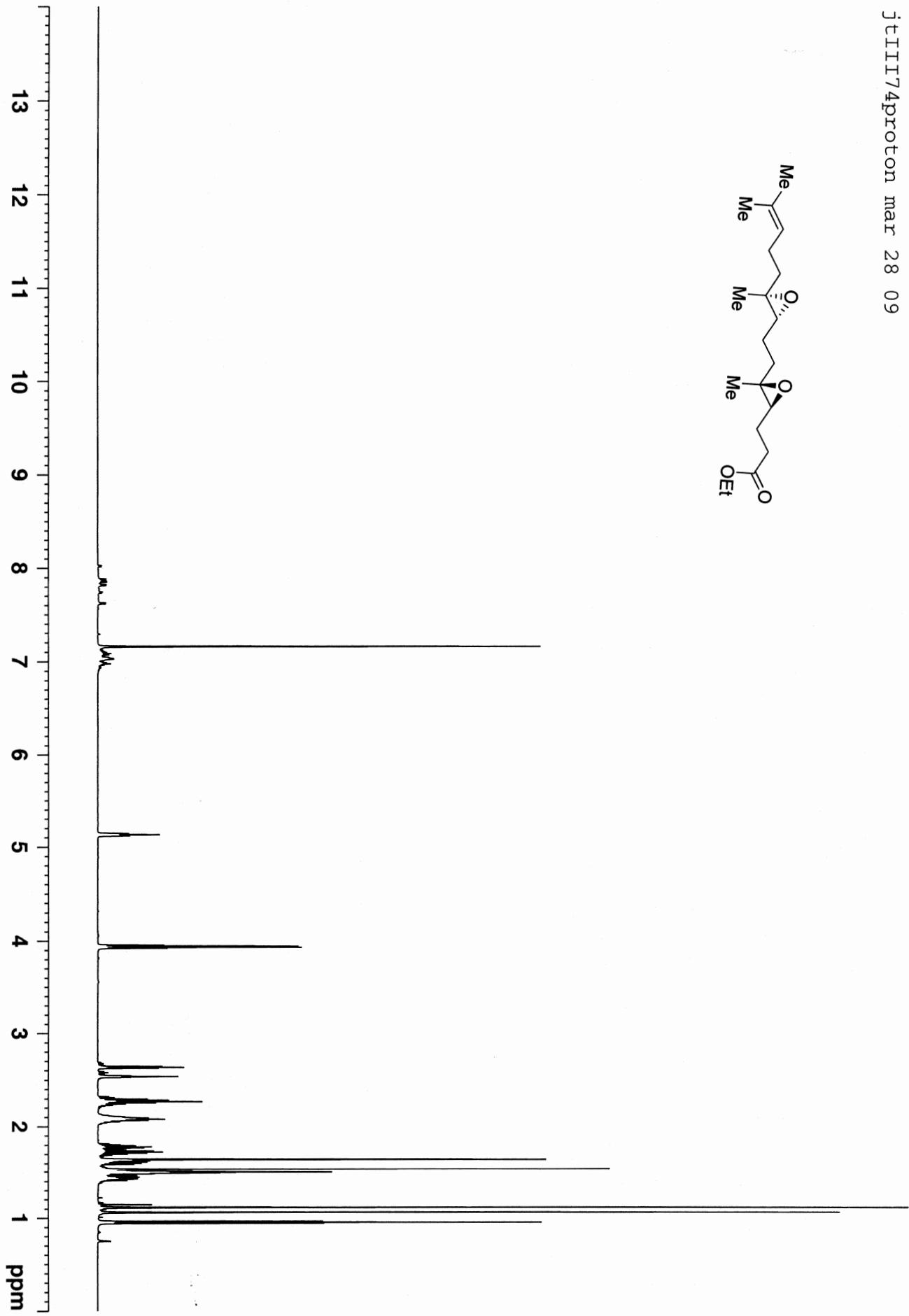
JtIII72proton mar 26 09



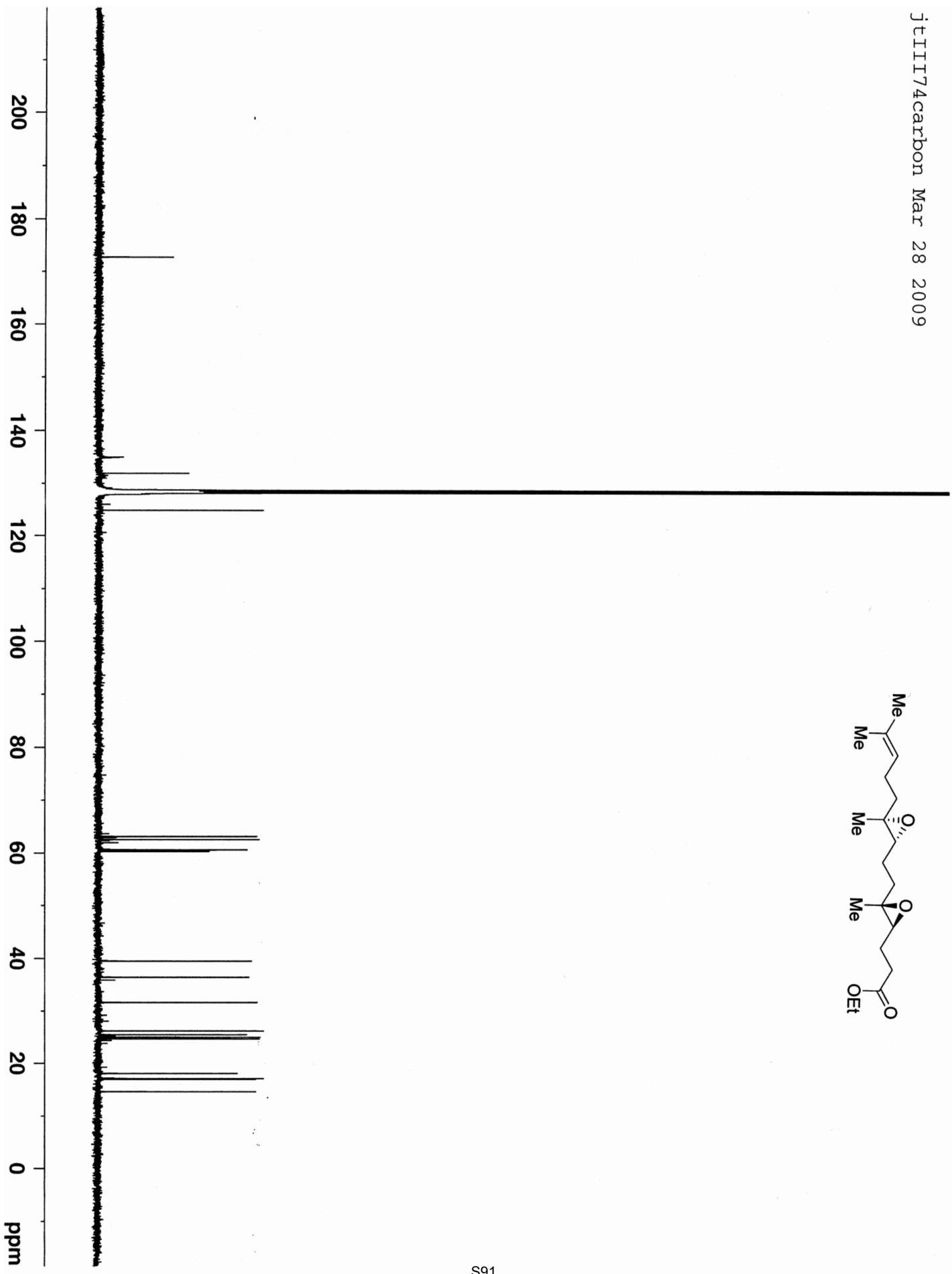
JtIII72carbon Mar 26 2009



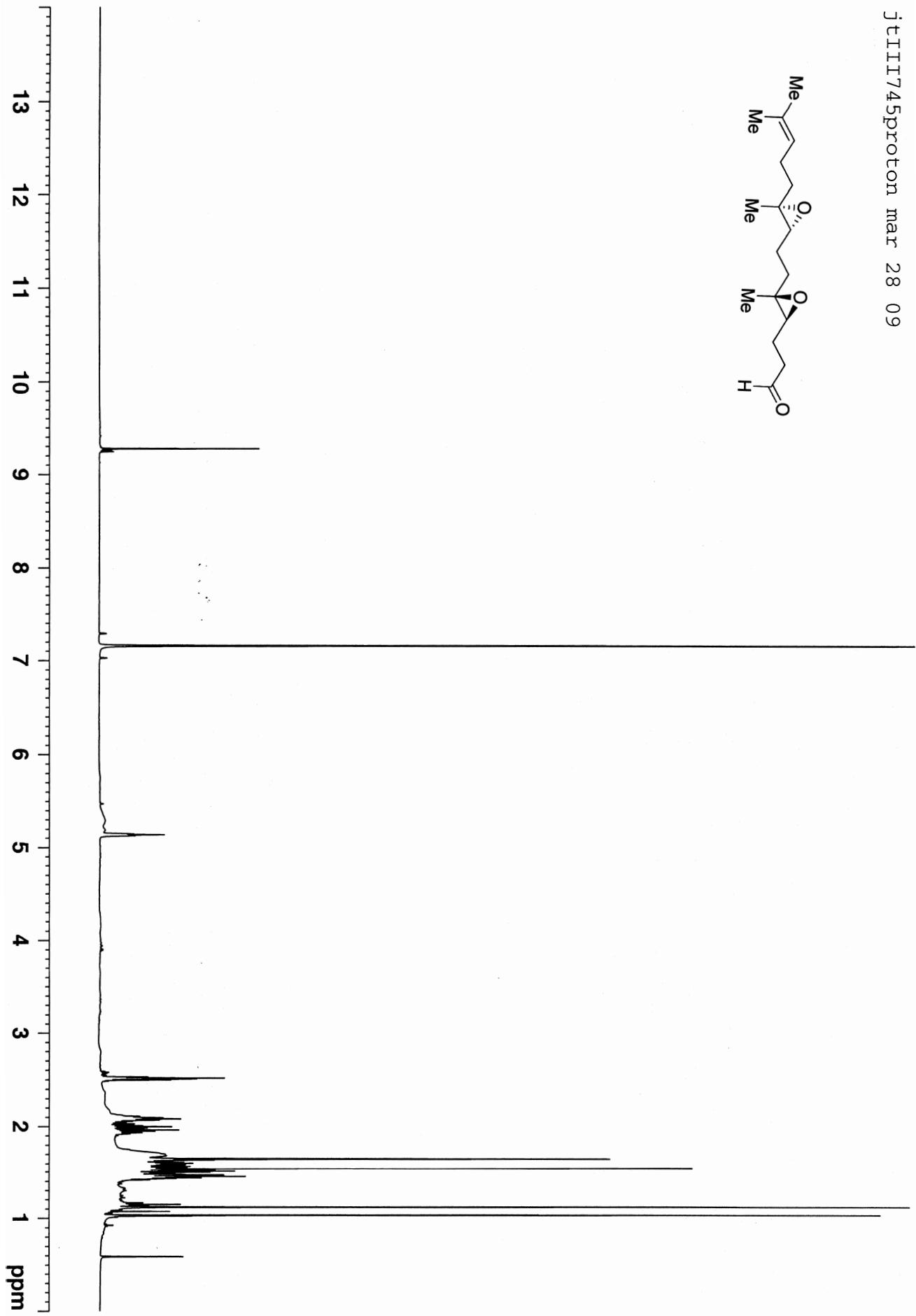
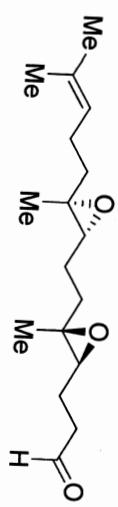
jtIII74proton mar 28 09



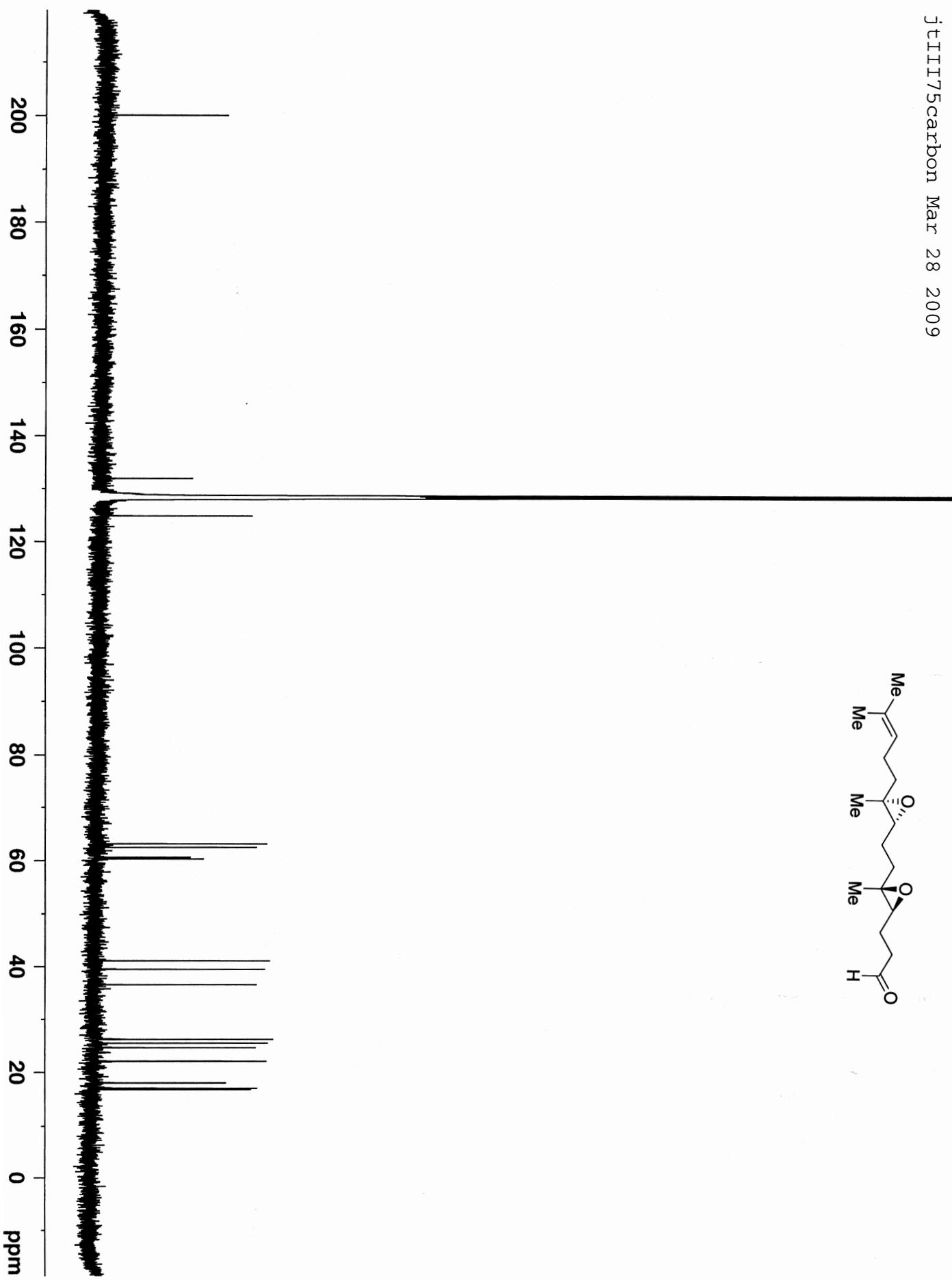
JtIII74carbon Mar 28 2009

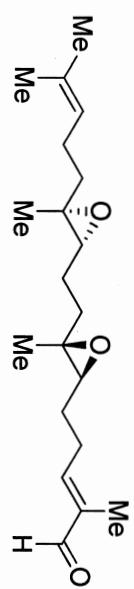
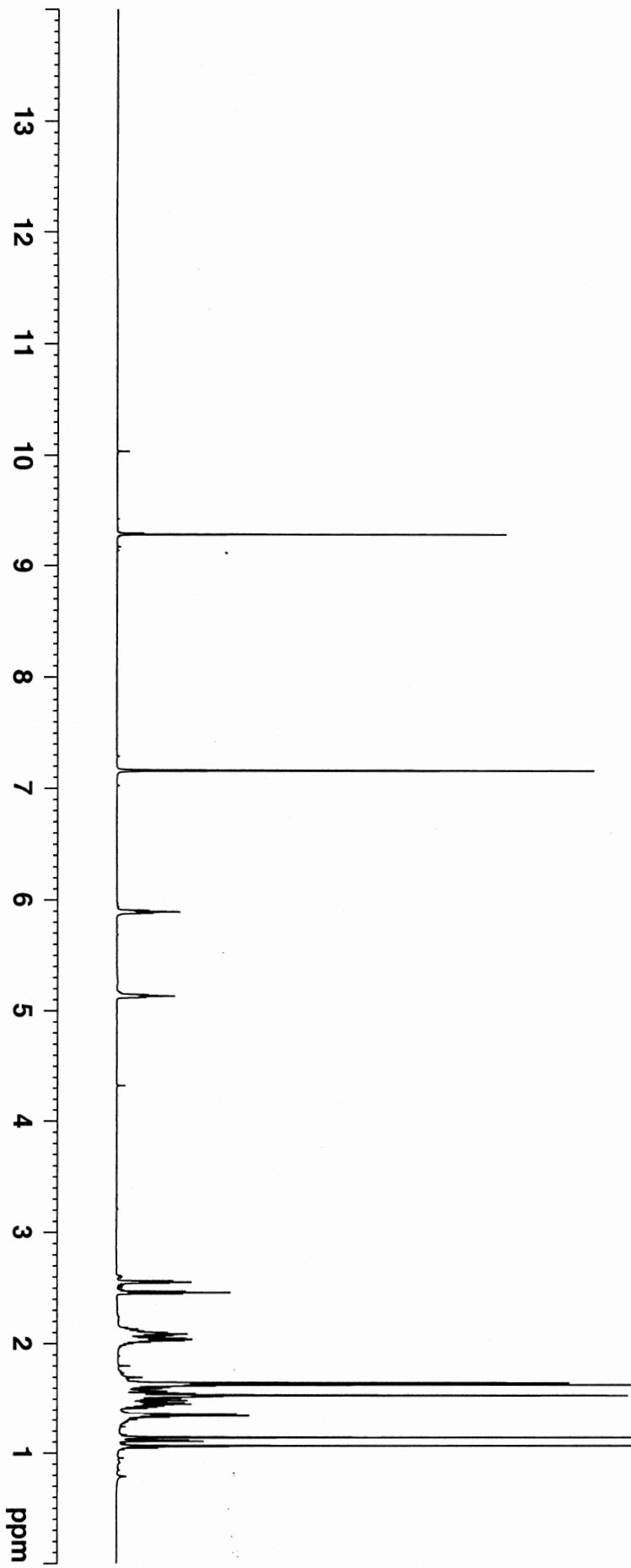


jtIII745proton mar 28 09

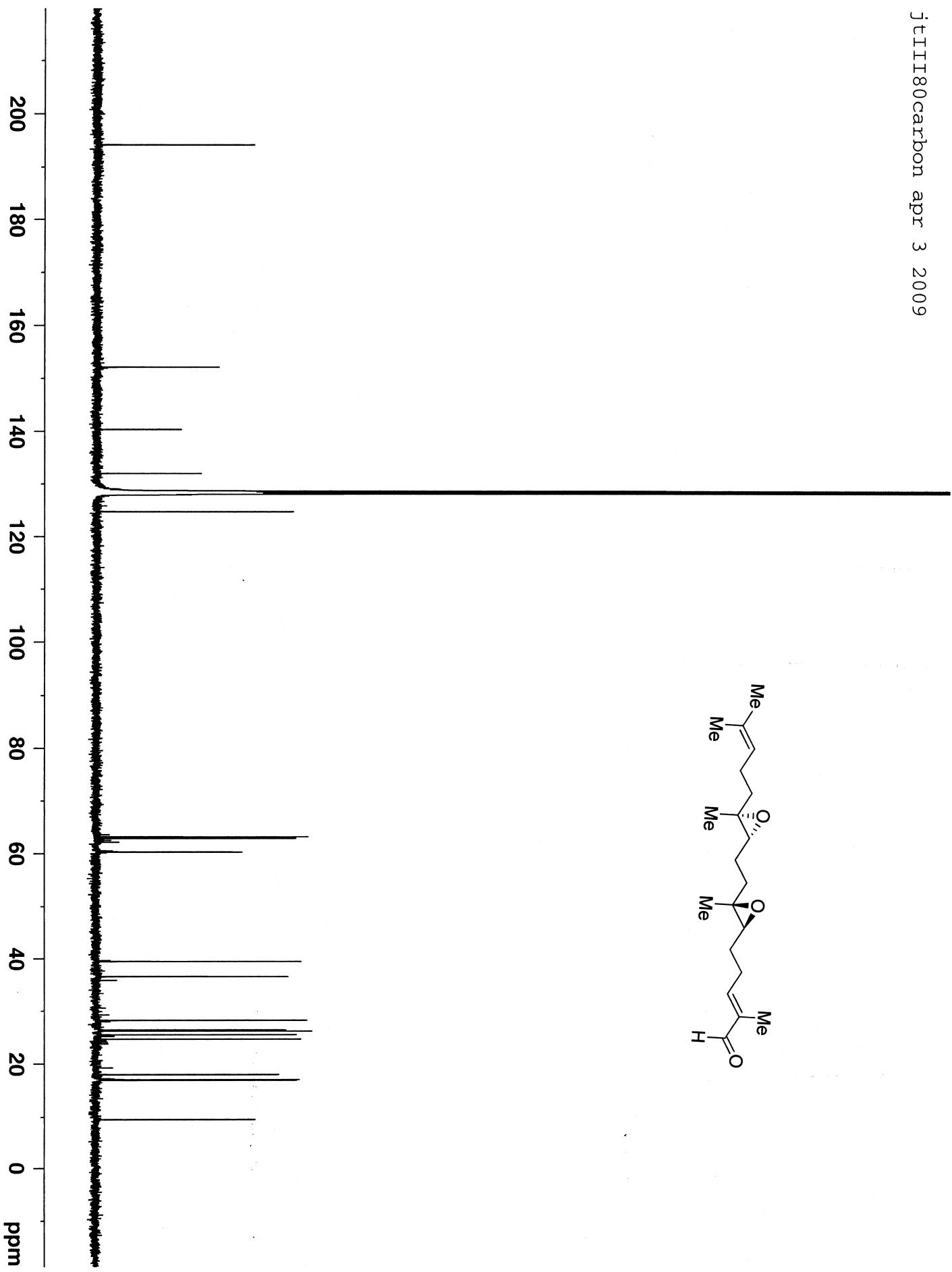


JtIII75carbon Mar 28 2009

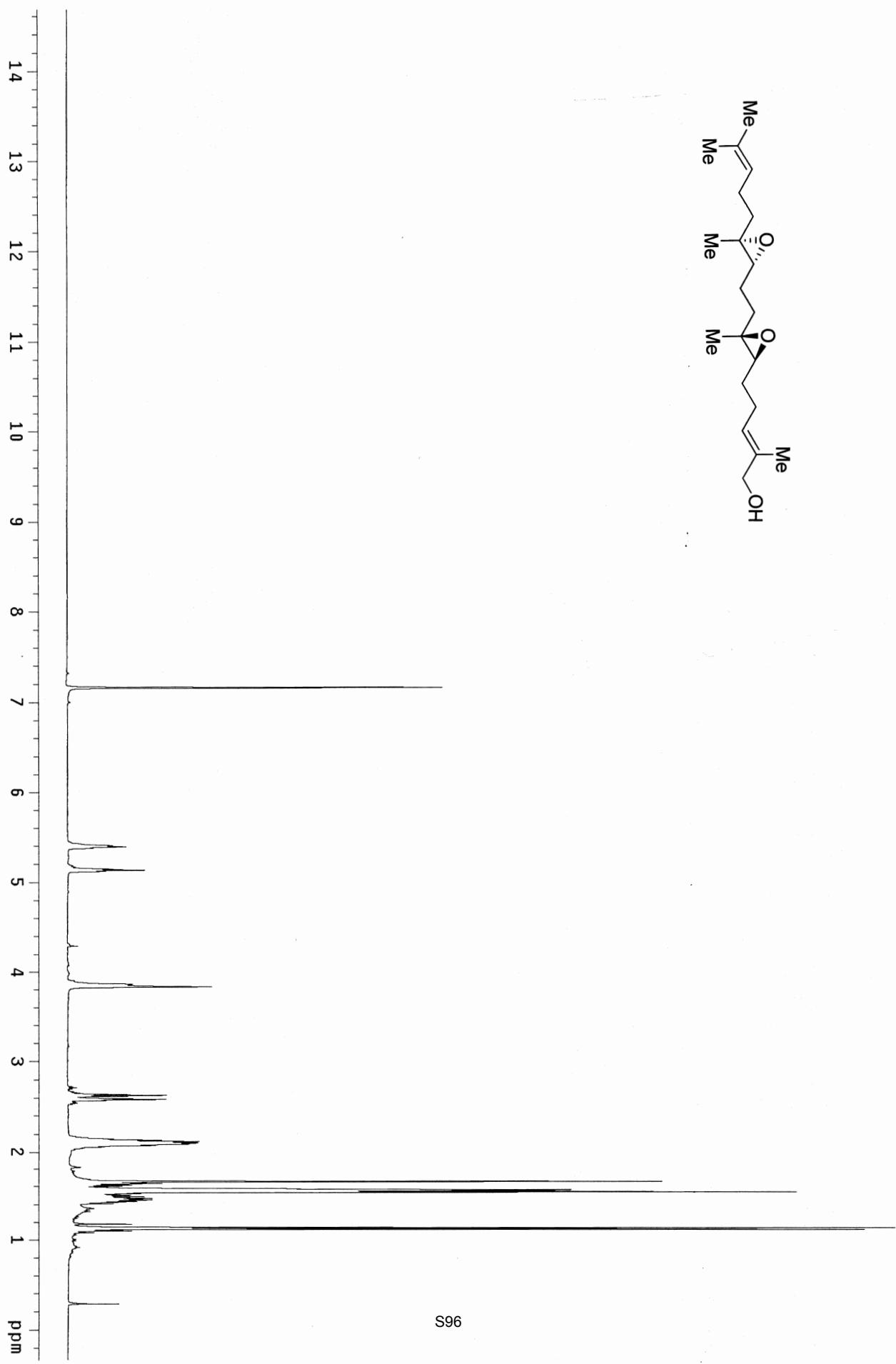
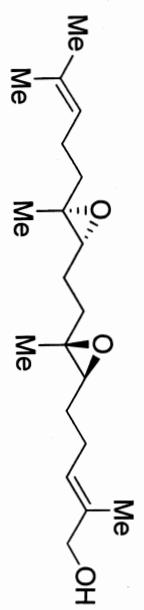




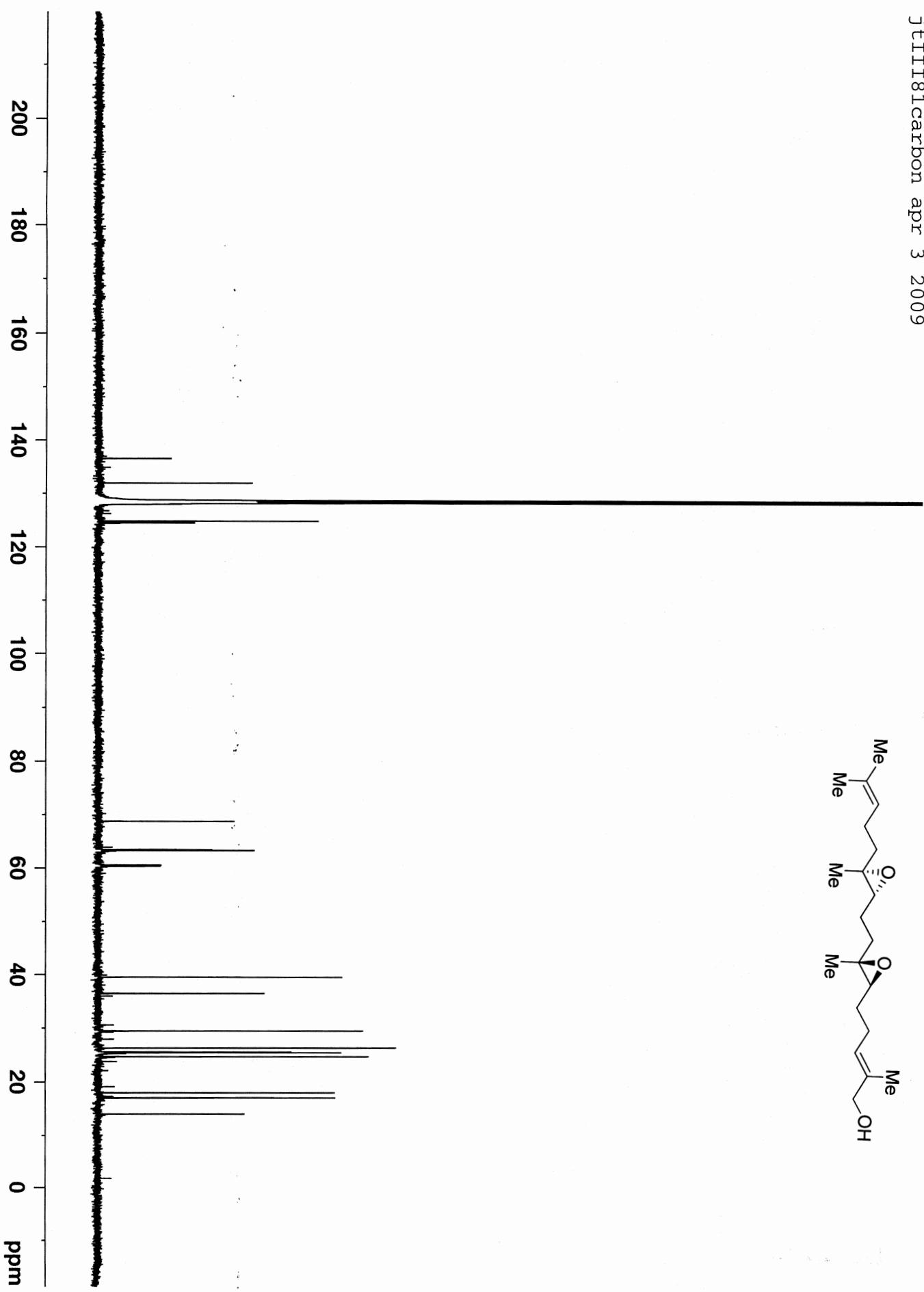
jtitIII8carbon apr 3 2009



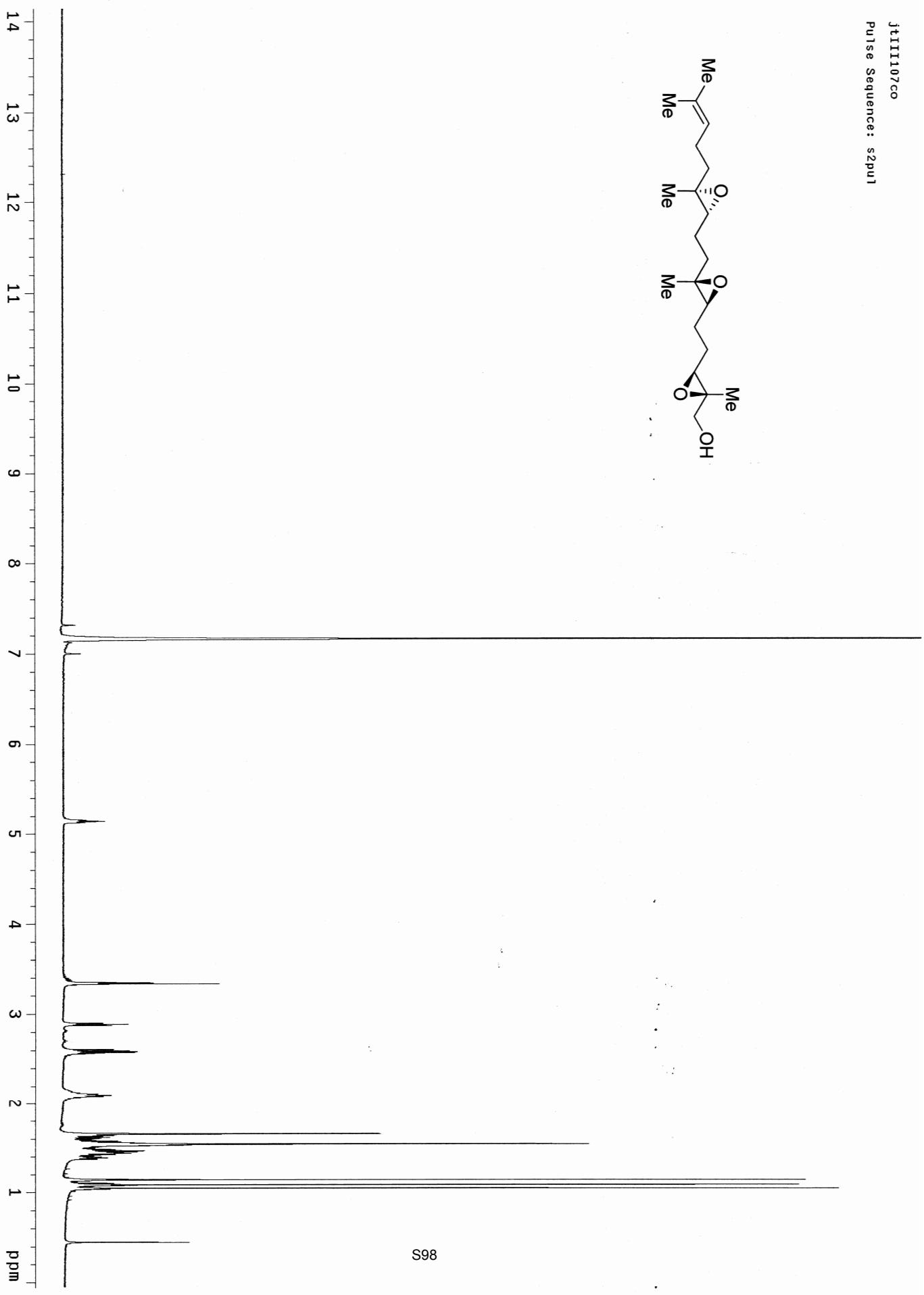
jt11181proton
Pulse Sequence: s2pul



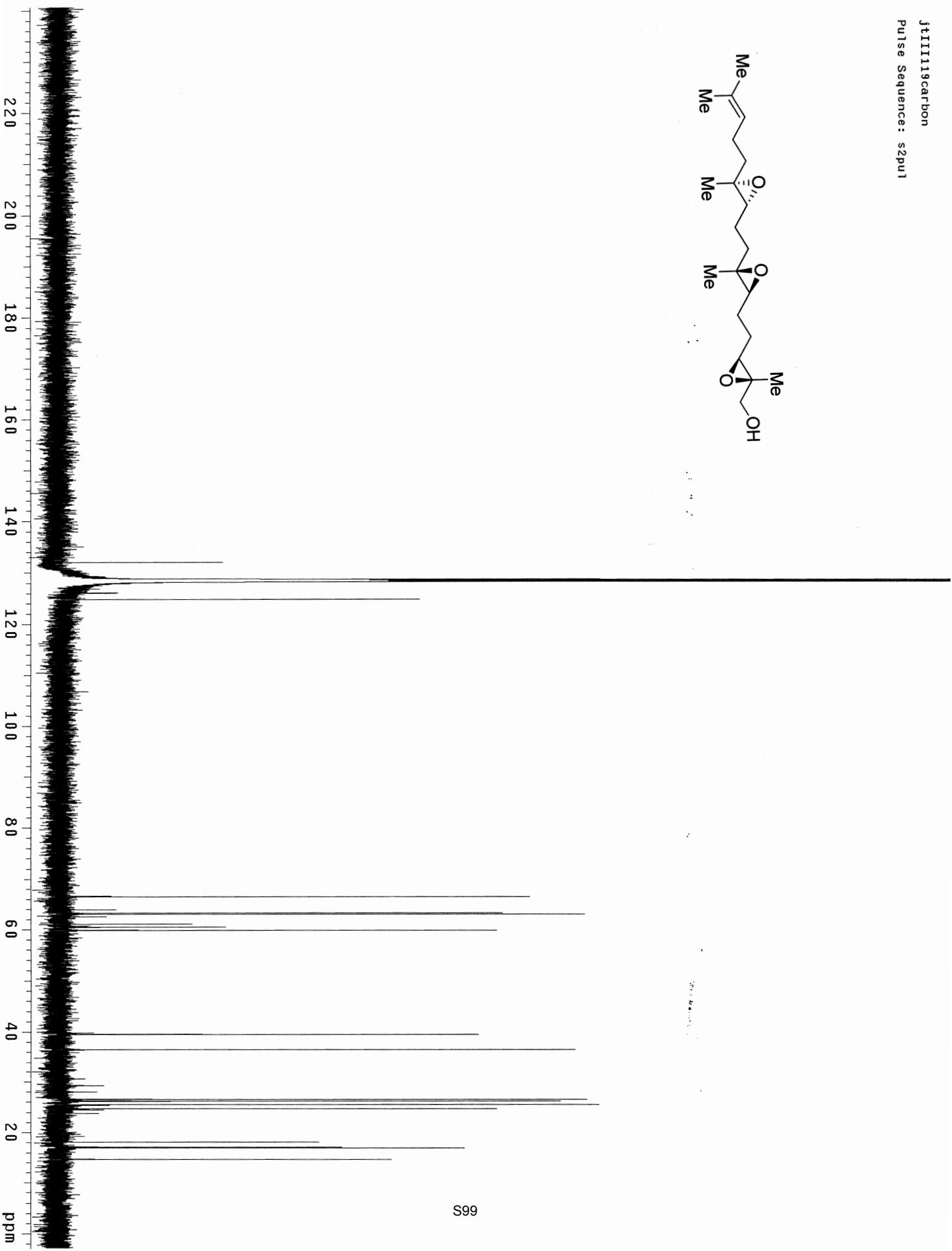
JtIII81carbon apr 3 2009



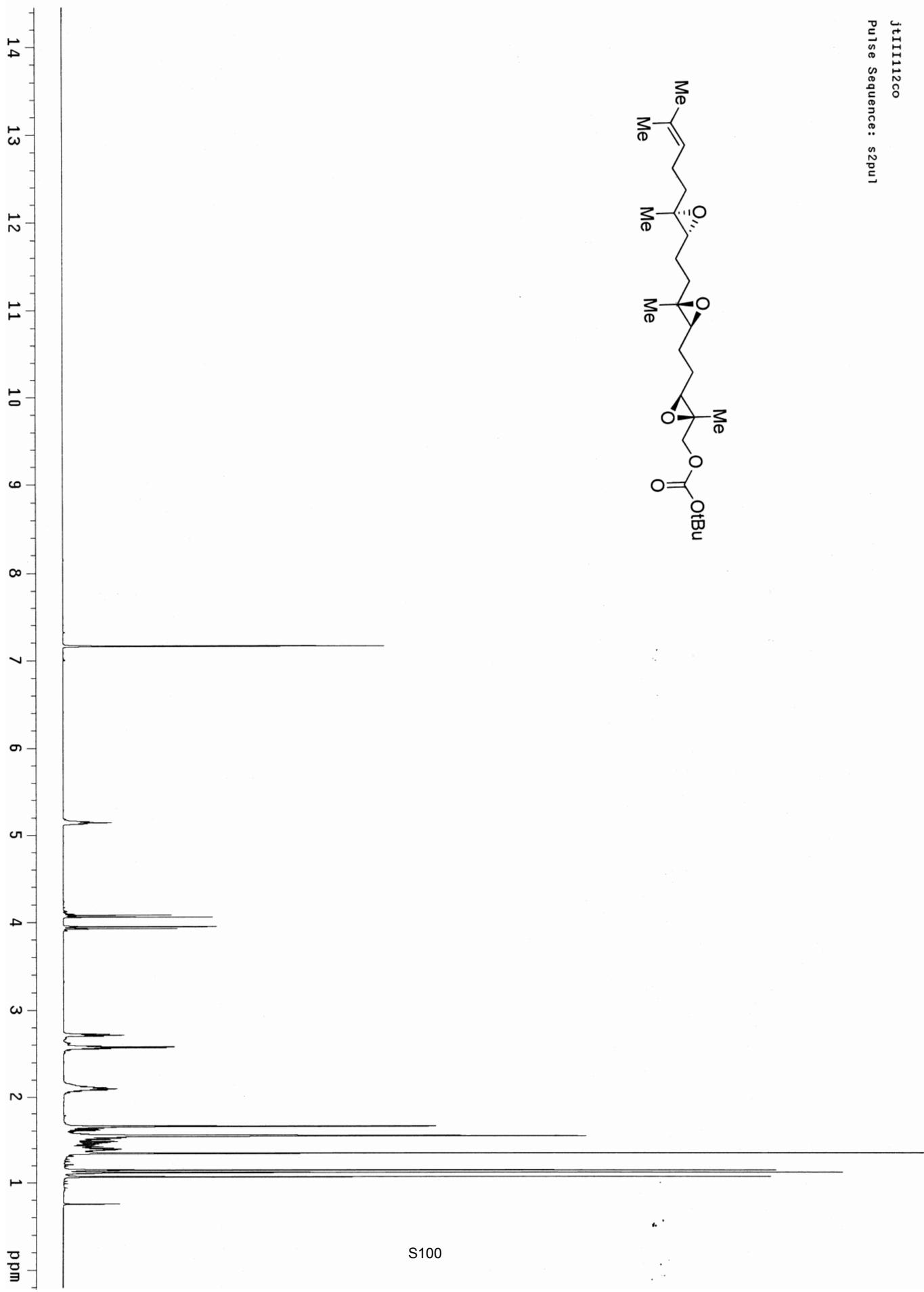
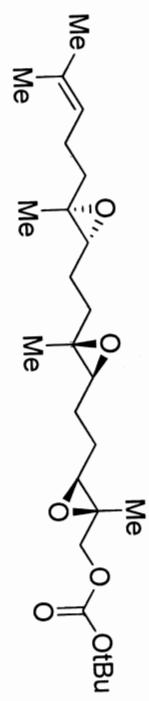
jt111107co
Pulse Sequence: s2pul



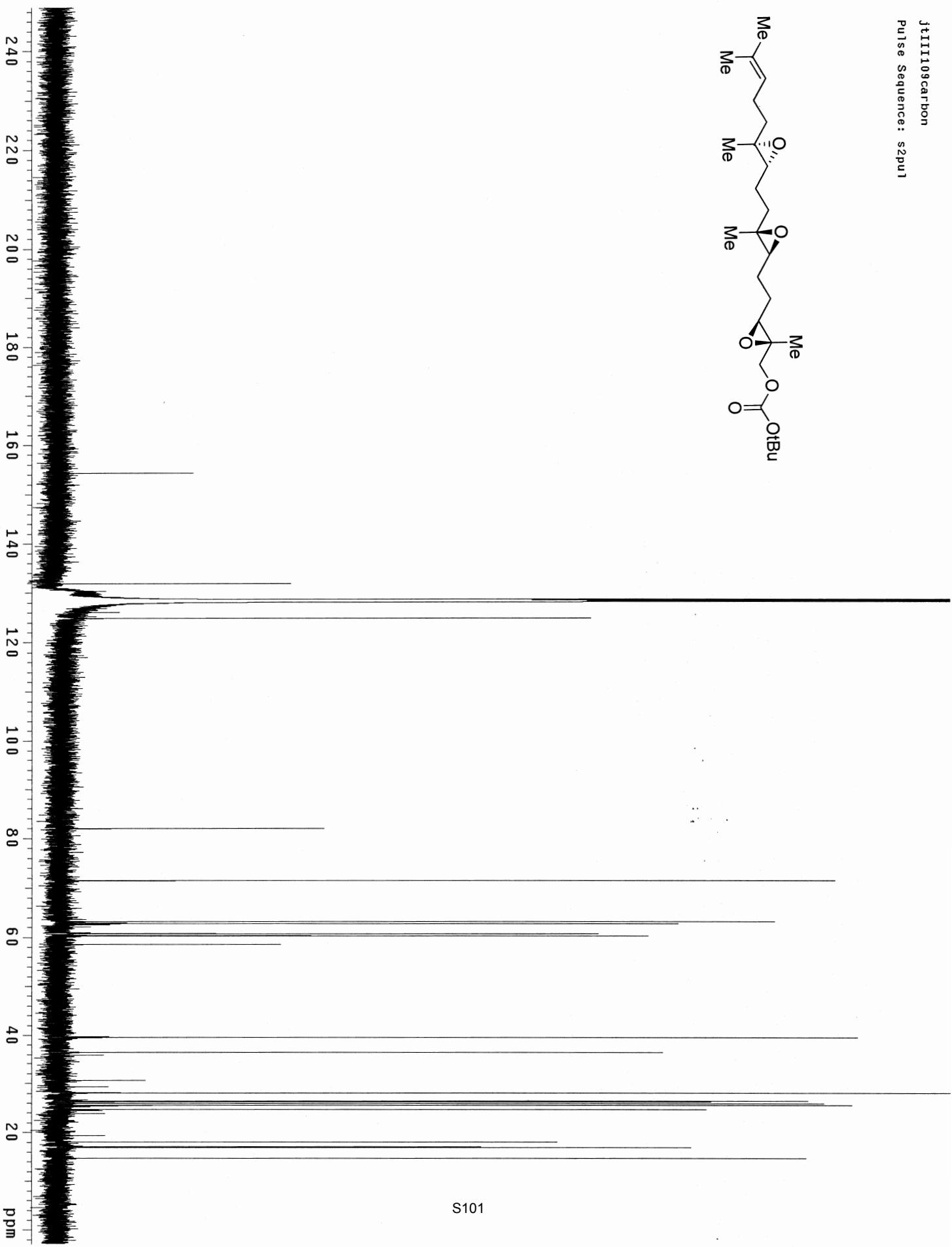
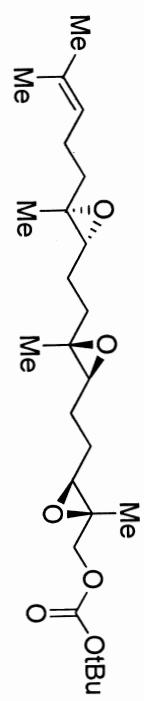
jt11119carbon
Pulse Sequence: s2pu1



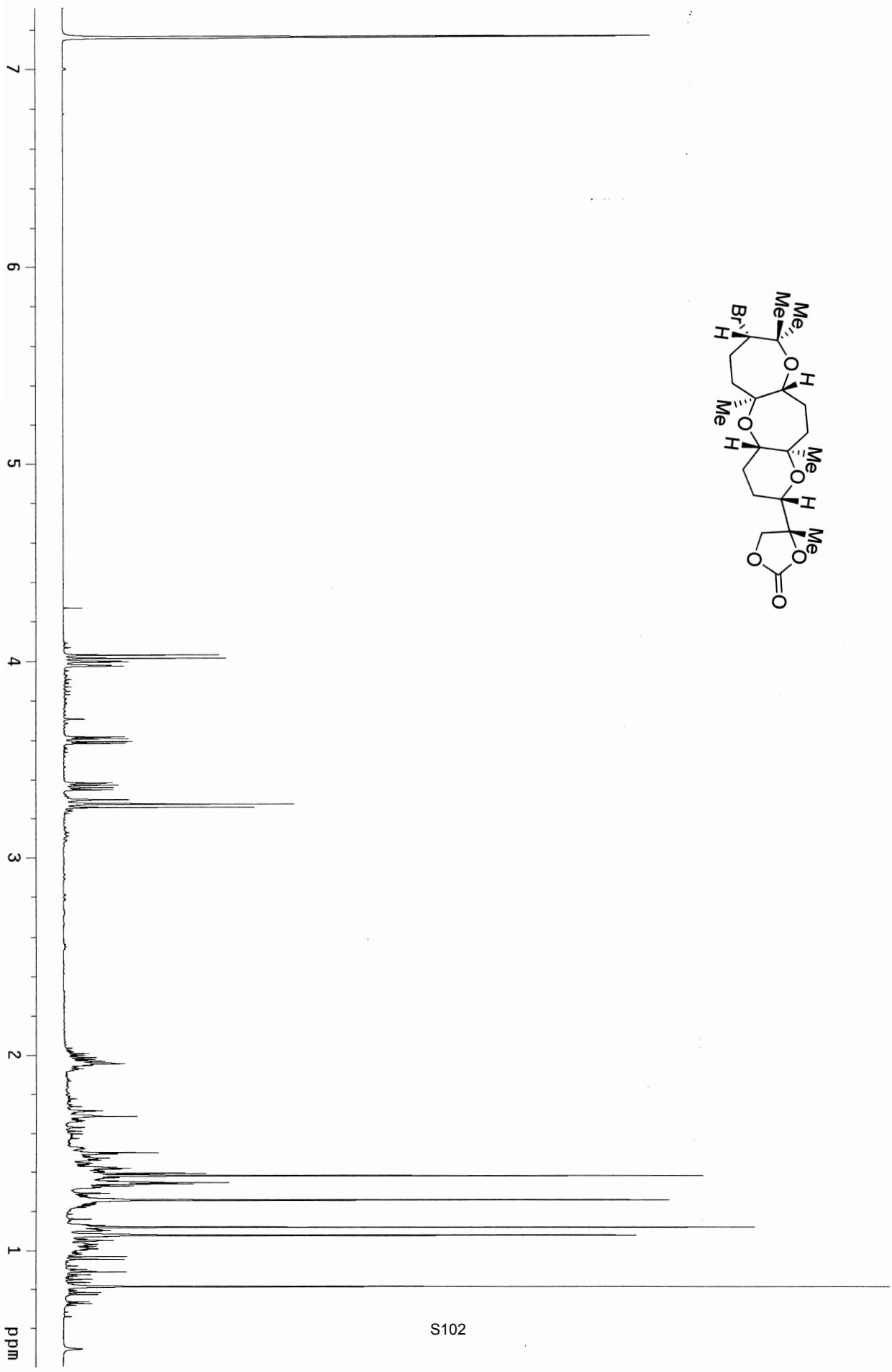
Pulse Sequence: s2pull



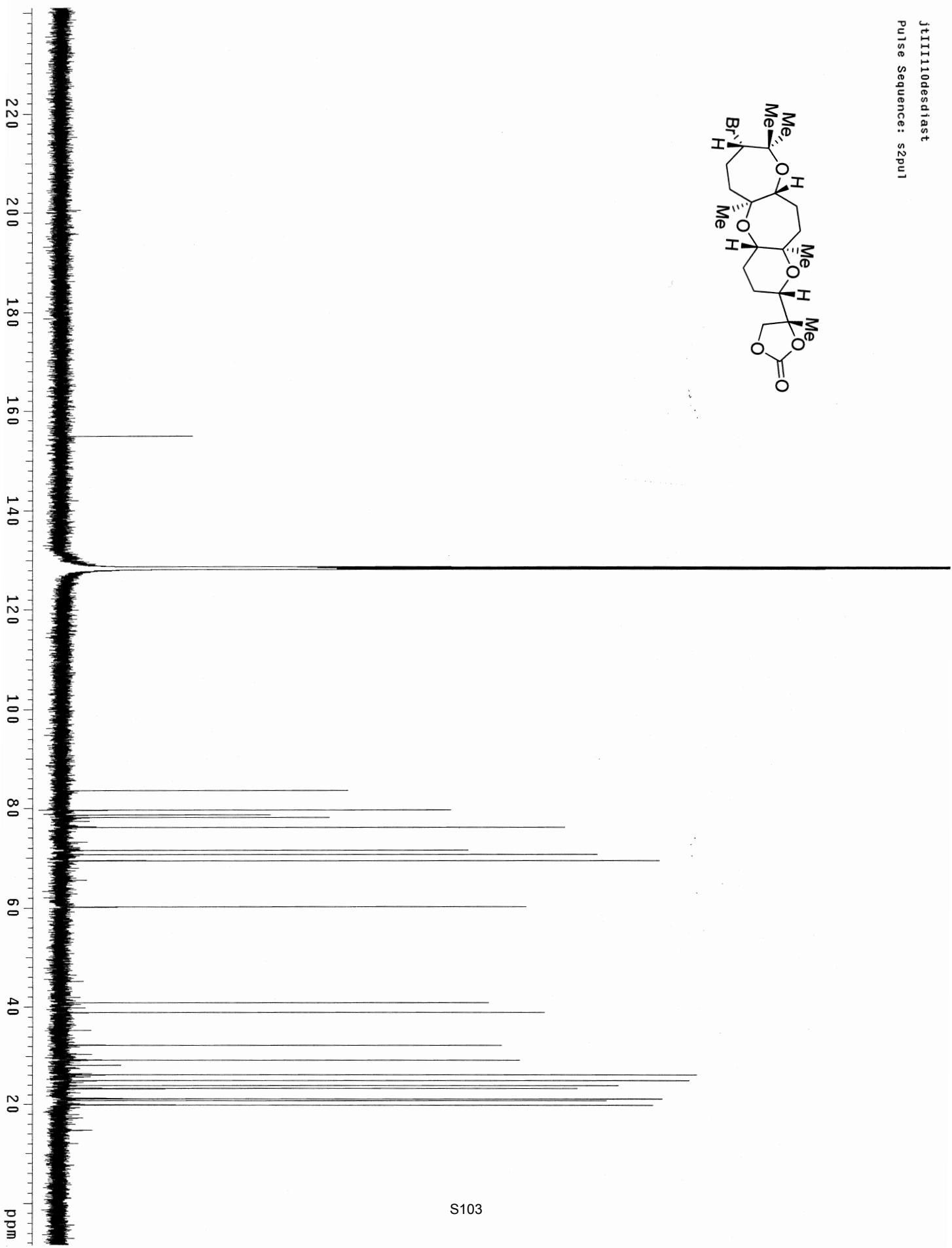
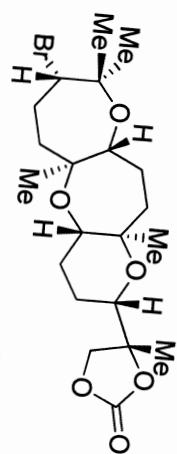
Jt111109carbon
Pulse Sequence: s2pul



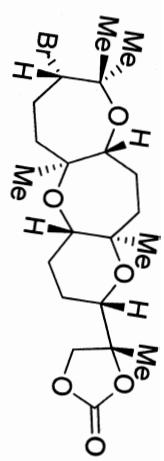
jt11110desdiast
Pulse Sequence: s2pul



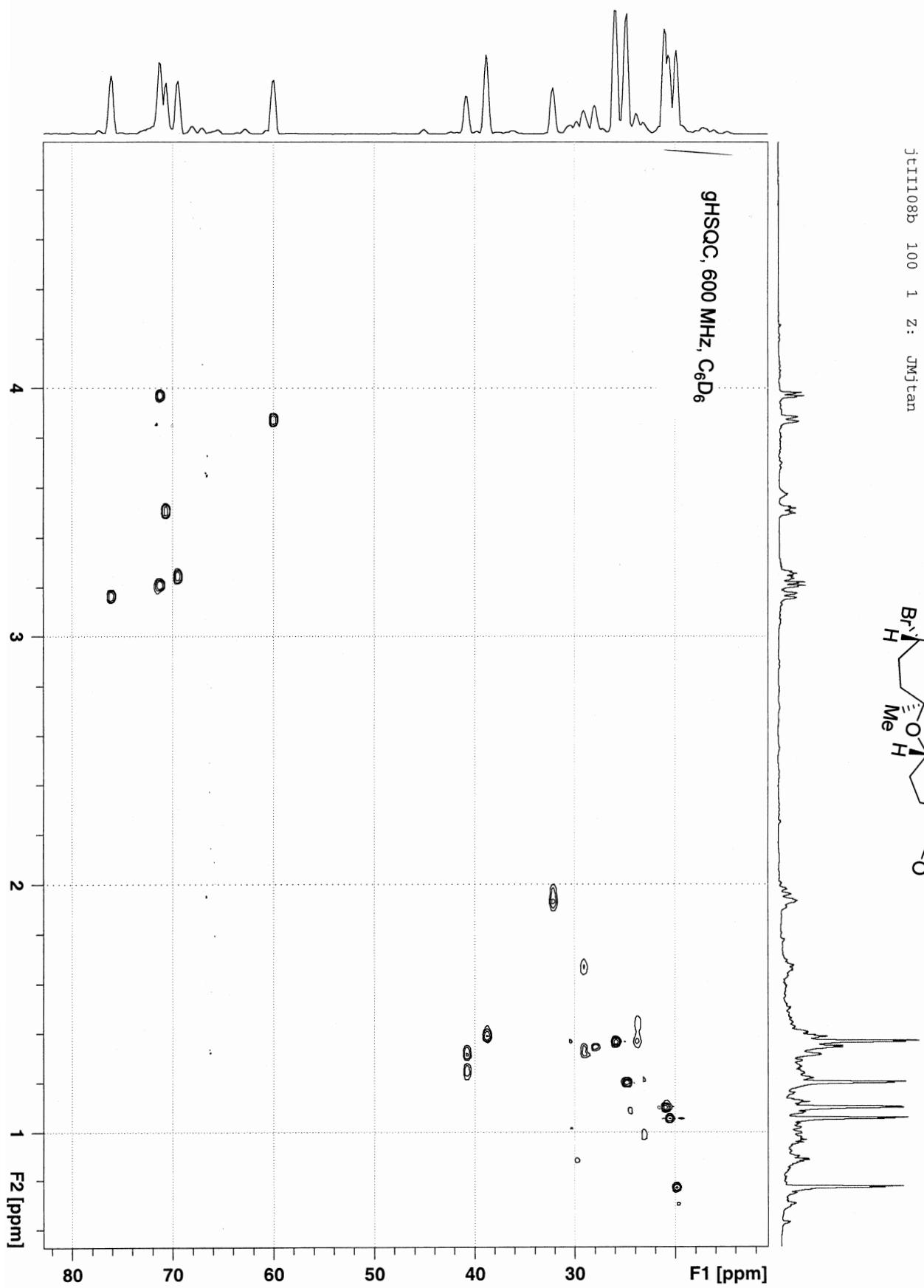
j111110desdiast
Pulse Sequence: s2pu1



jtiI108b 100 1 Z: JMjtan

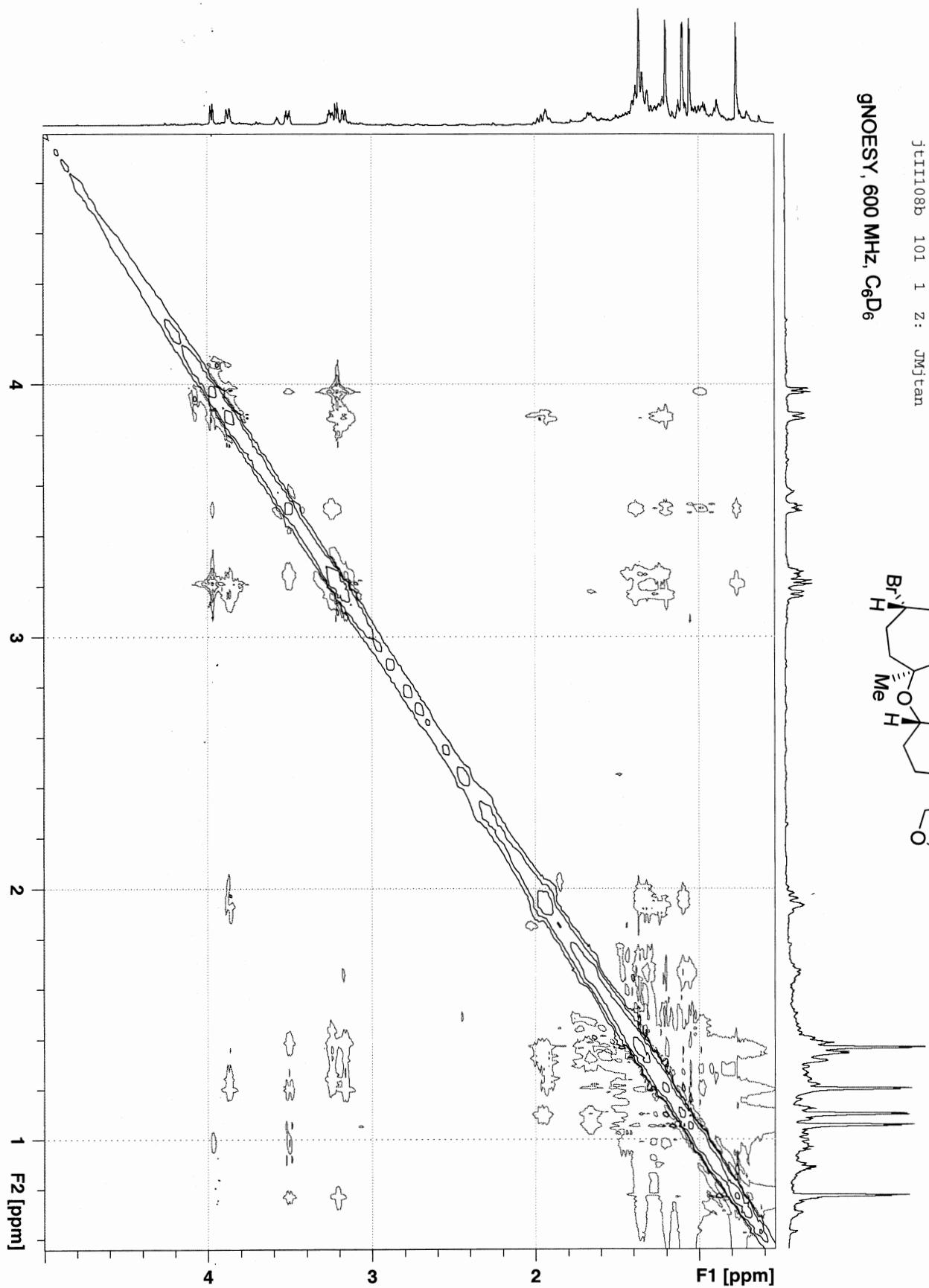
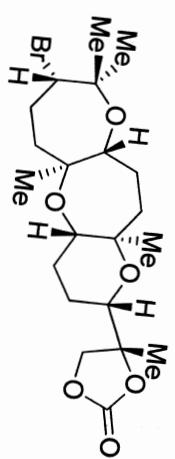


gHSQC, 600 MHz, C₆D₆



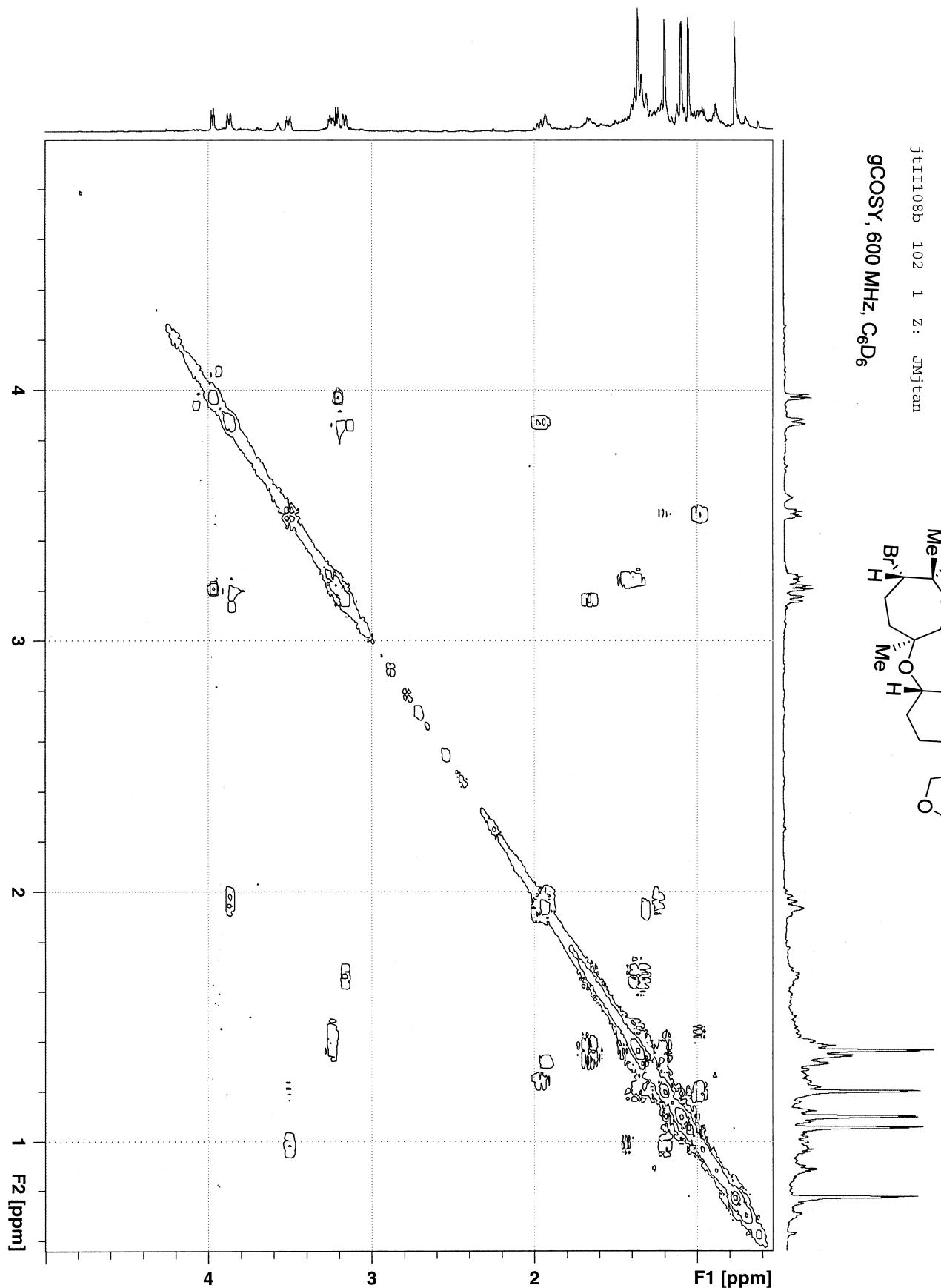
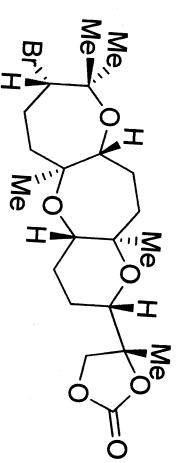
gNOESY, 600 MHz, C₆D₆

jtiI103b 101 1 Z: JMjtan

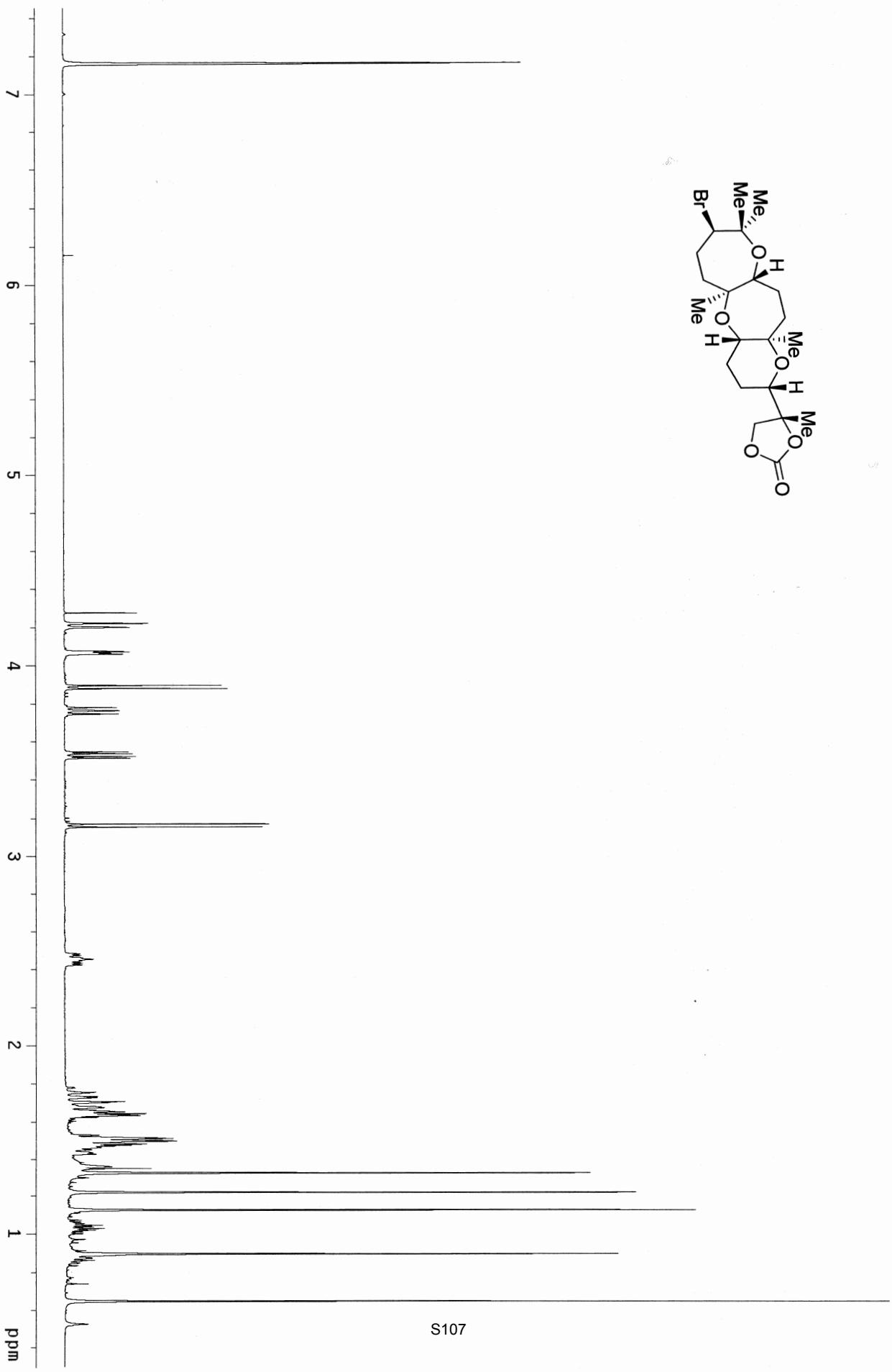


jT11I103b 102 1 Z: JMjtan

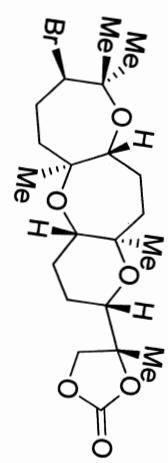
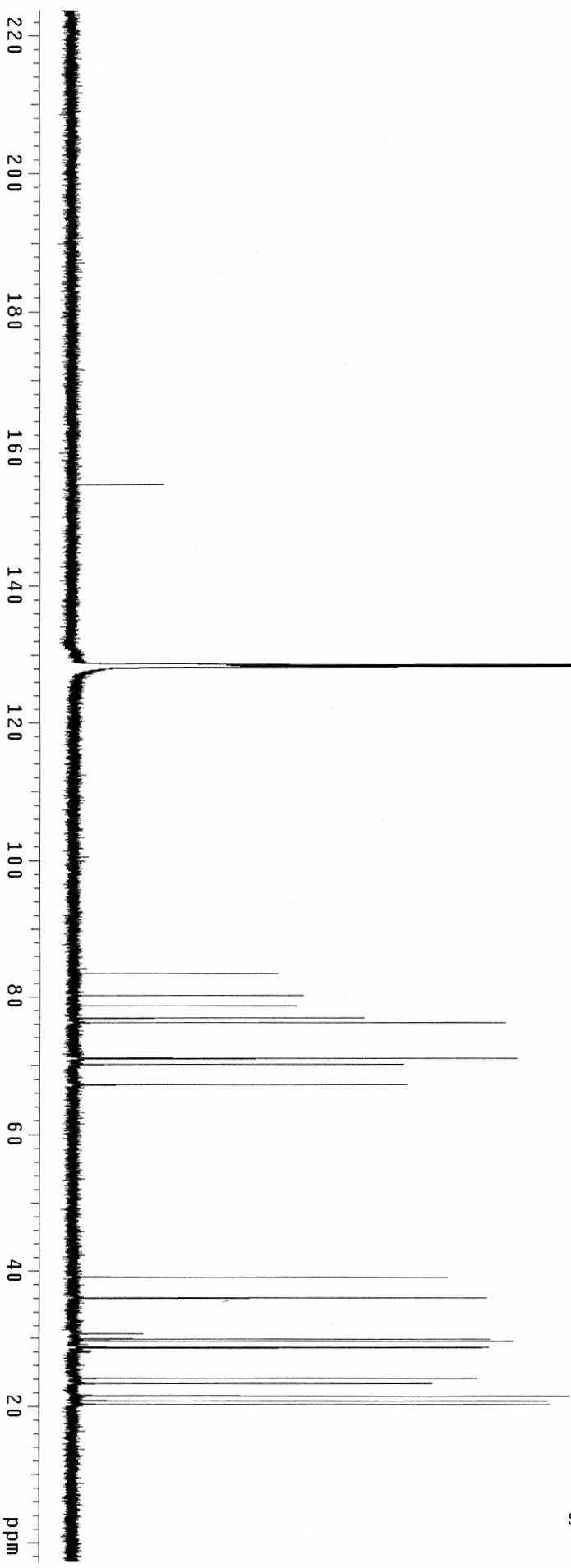
gCOSY, 600 MHz, C₆D₆



jt111113a
Pulse Sequence: s2pul



jt111113acarbon
Pulse Sequence: s2pul

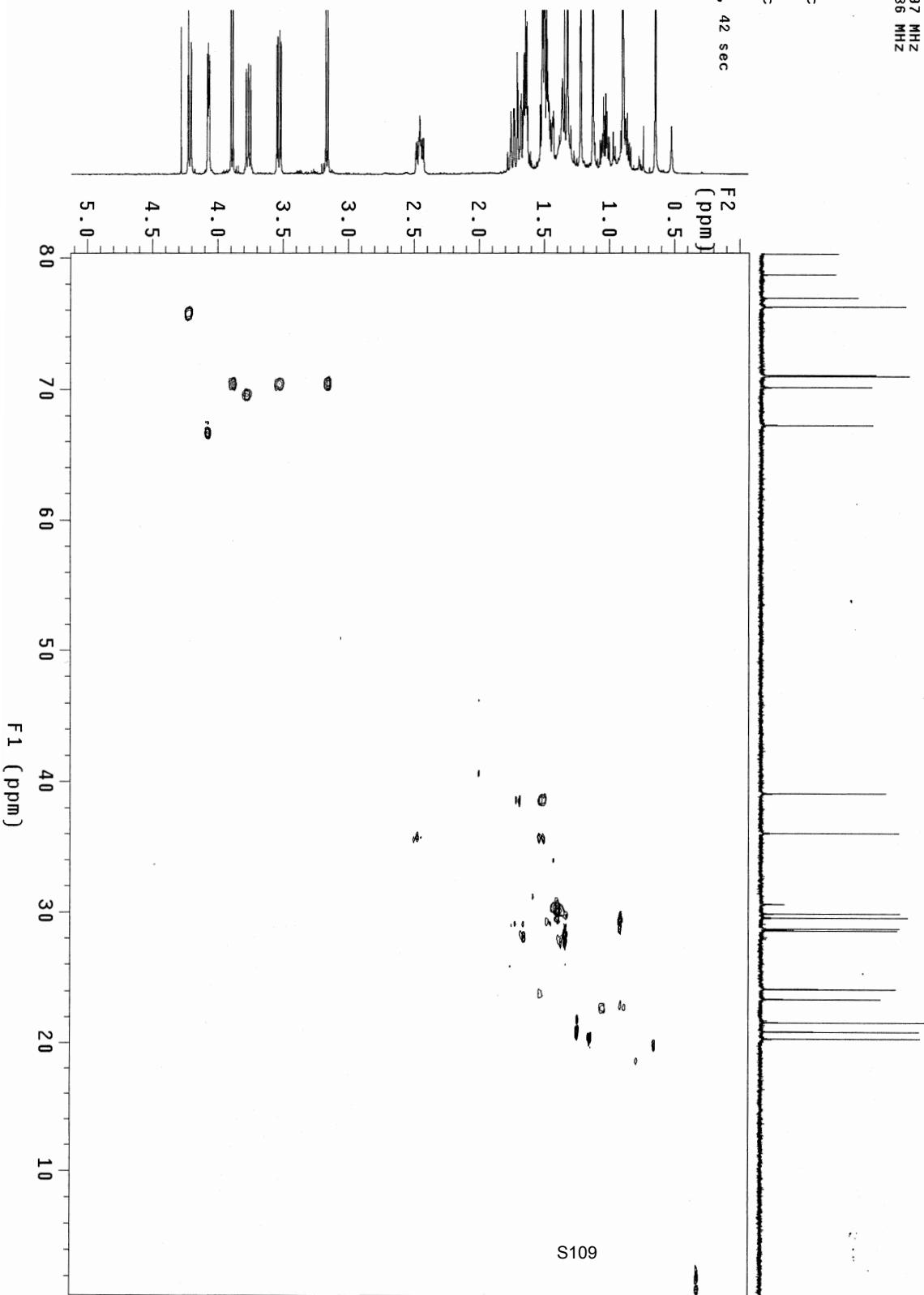
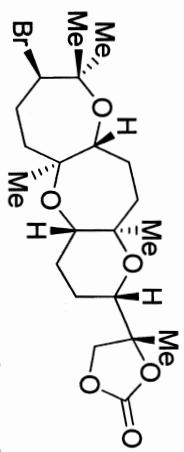


STANDARD PROTON PARAMETERS

Pulse Sequence: HSQC
 Solvent: Benzene
 Ambient temperature
 User: 1-14-87
 File: j111108ahHSQC
 INNOVA-500 "zippy"

Relax. delay 1.000 sec
 Acq. time 0.150 sec
 Width 4724.8 Hz
 2D Width 21990.1 Hz
 16 repetitions
 2×200 increments
 OBSERVE H1, 499.7417397 MHz
 DECOUPLE C13, 125.6711336 MHz
 Power 53 dB
 on during acquisition
 off during delay
 GARP-1 modulated

DATA PROCESSING
 Sq. sine bell 0.150 sec
 Shifted by -0.150 sec
 F1 DATA PROCESSING
 Sq. sine bell 0.023 sec
 Shifted by -0.023 sec
 FT size 2048 x 2048
 Total time 2 hr, 10 min, 42 sec



STANDARD PROTON PARAMETERS

Pulse Sequence: gHMQC
 Solvent: Benzene
 Ambient temperature

User: 1-4-87
 File: jtti108aq4HMQC
 INOVA-500 "zipipy"

Relax. delay 1.000 sec
 Acq. time 0.433 sec
 Width 4724.8 Hz
 2D Width 21990.1 Hz

64 repetitions
 512 increments

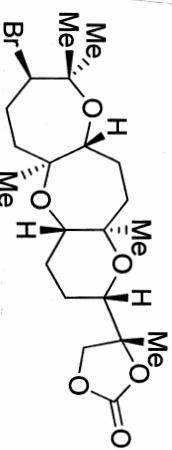
OBSERVE H1, 499.7417397 MHz
 DATA PROCESSING

Sine bell 0.217 sec
 F1 DATA PROCESSING

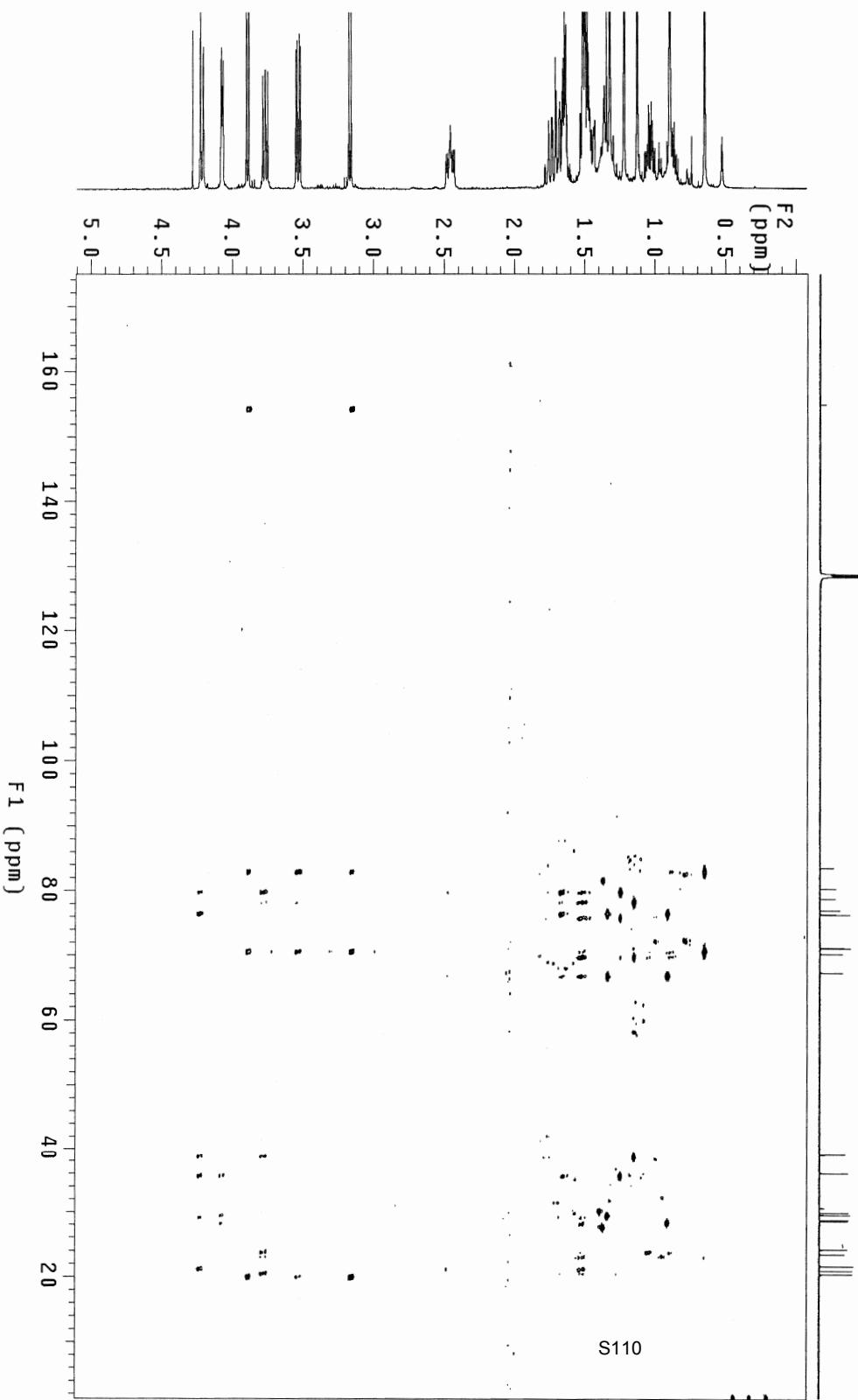
Sine bell 0.012 sec

FT size 4096 x 2048

Total time 13 hr, 58 min, 55 sec

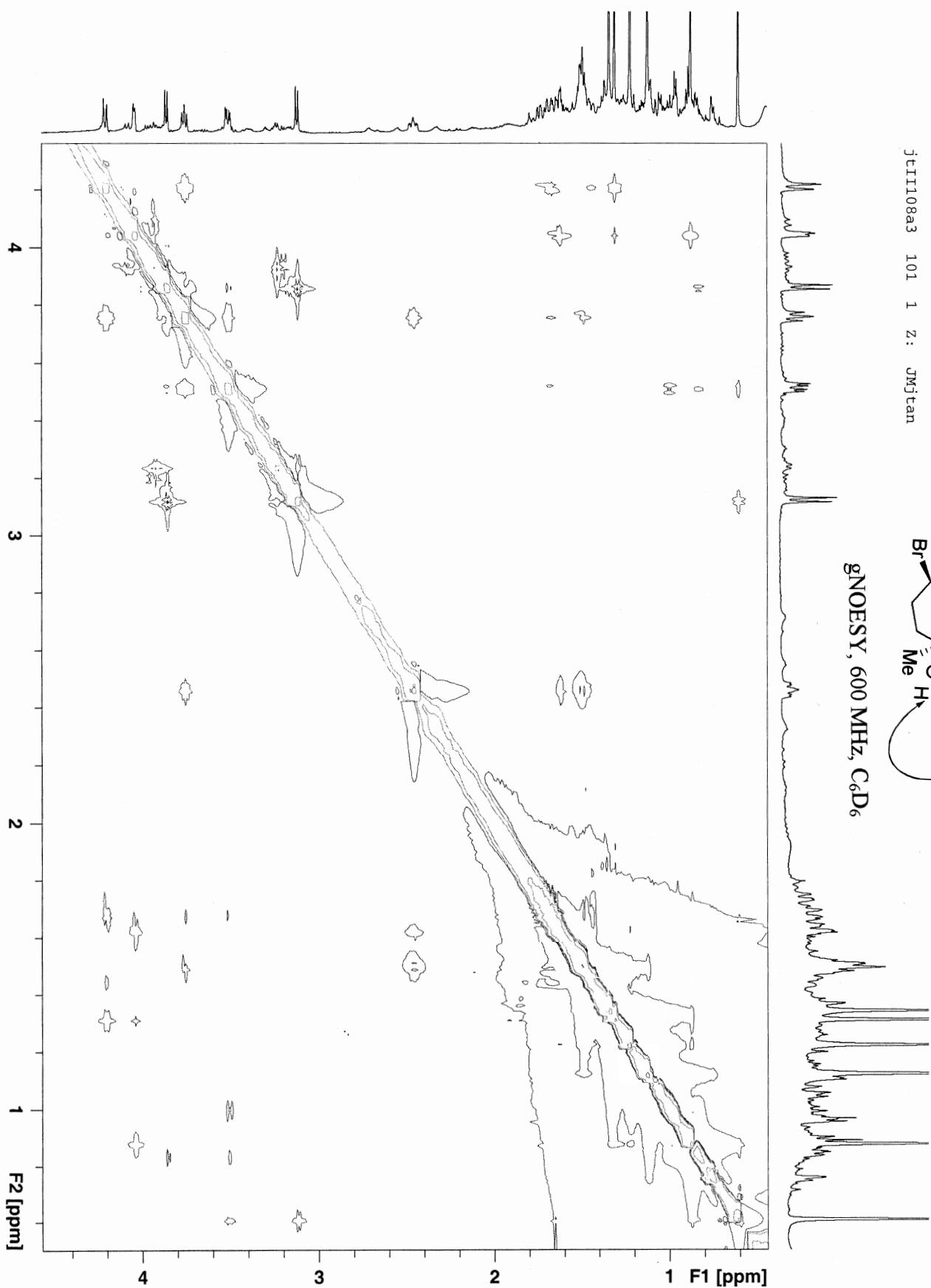
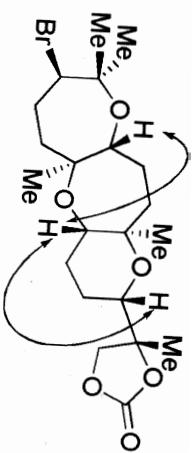


gHMQC, 500 MHz, C₆D₆



jtiI108a3 101 1 Z: JMjtan

gNOESY, 600 MHz, C₆D₆



STANDARD PROTON PARAMETERS

Pulse Sequence: gCOSY

Solvent: Benzene

Ambient temperature

File: JTI110Ba4gCOSY

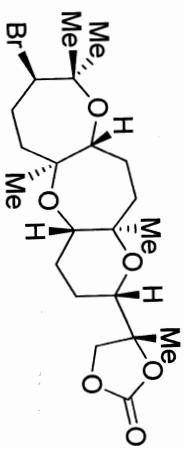
INOVA-500 "zippy"

Relax. delay 1.000 sec
Acq. time 0.217 sec
Width 4724.8 Hz
2D Width 4724.8 Hz
4 repetitions
512 increments

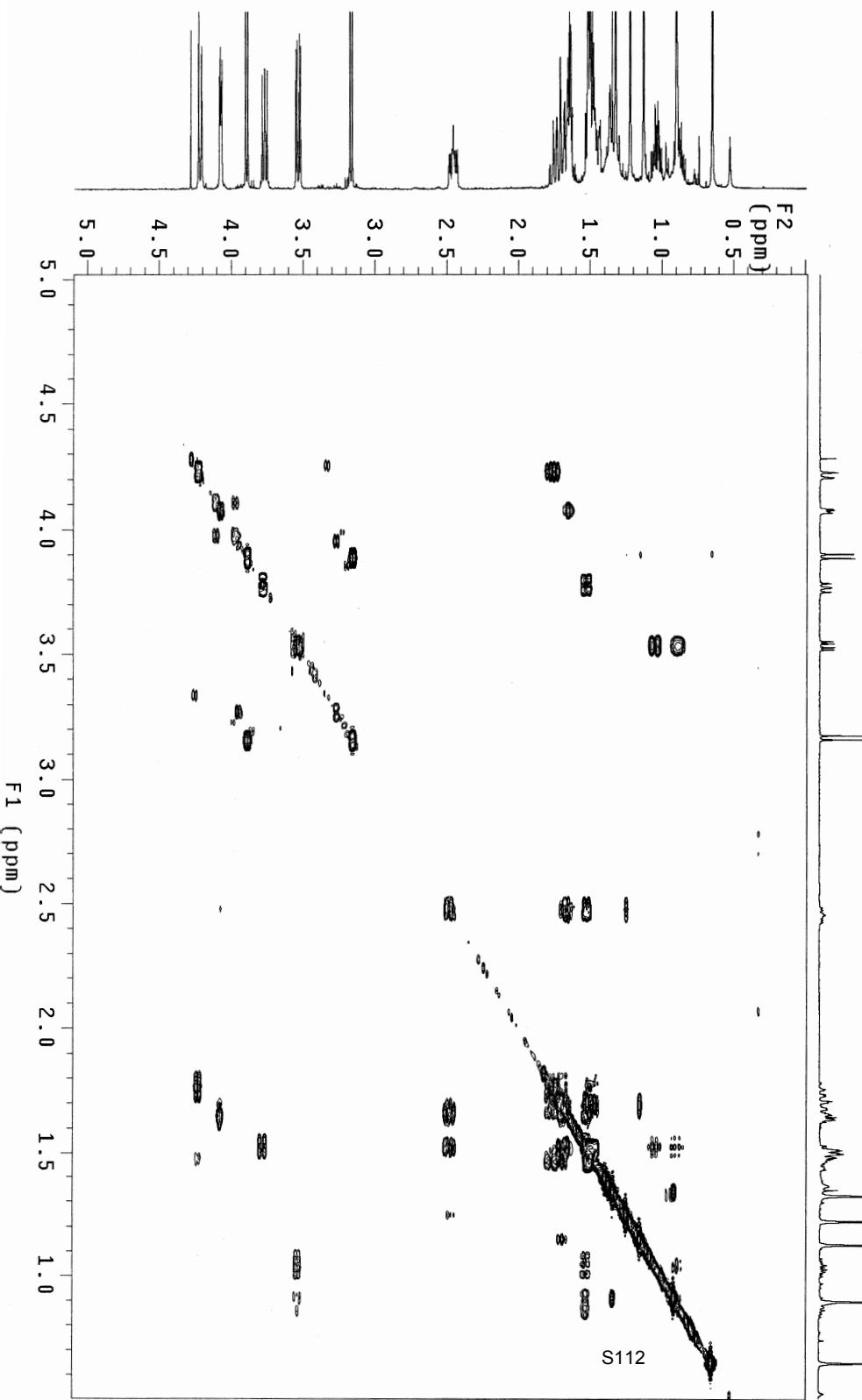
OBSERVE H1, 499.7417397 MHz
DATA PROCESSING
Sq. sine bell 0.109 sec

F1 DATA PROCESSING
Sq. sine bell 0.054 sec

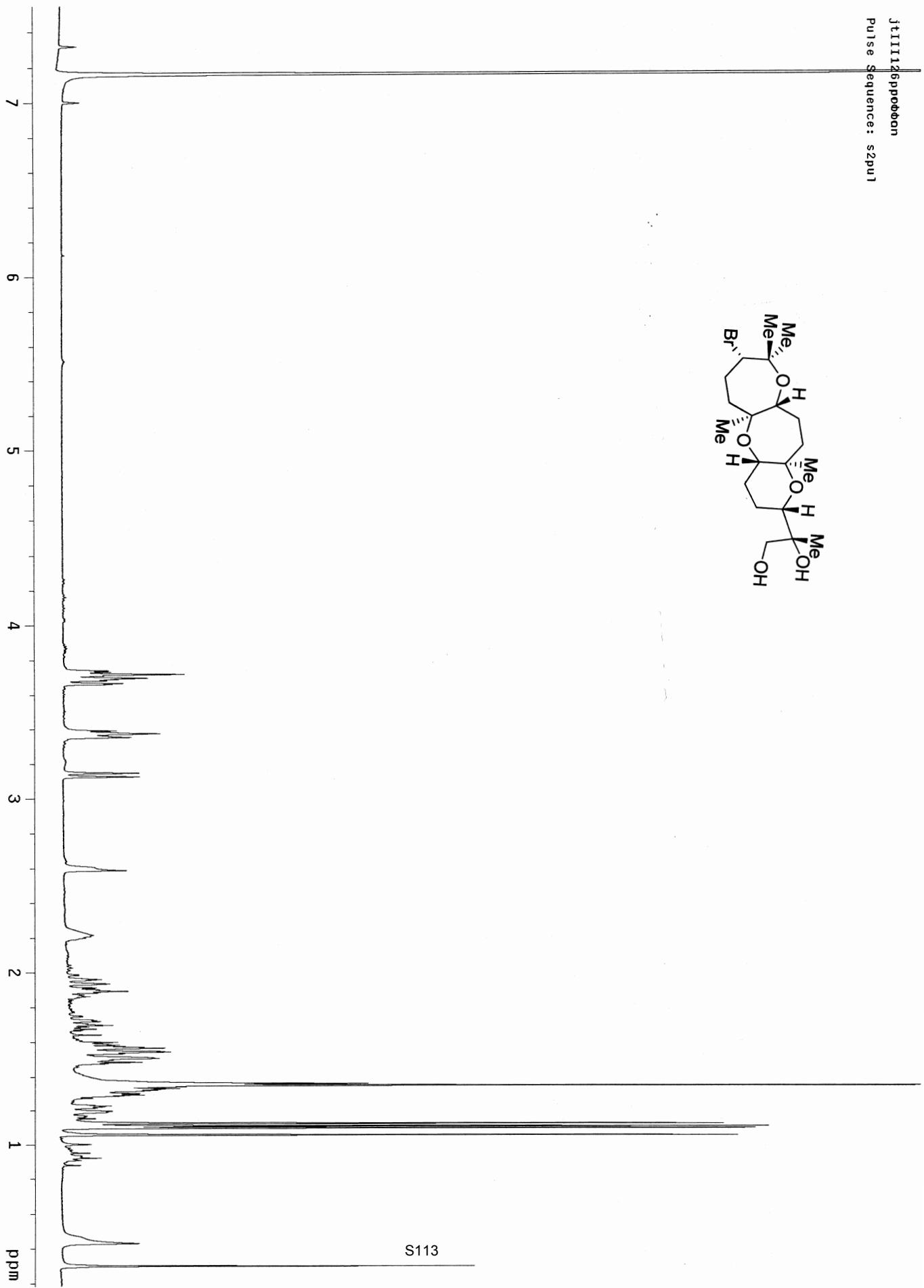
FT size 4096 x 4096
Total time 45 min, 7 sec



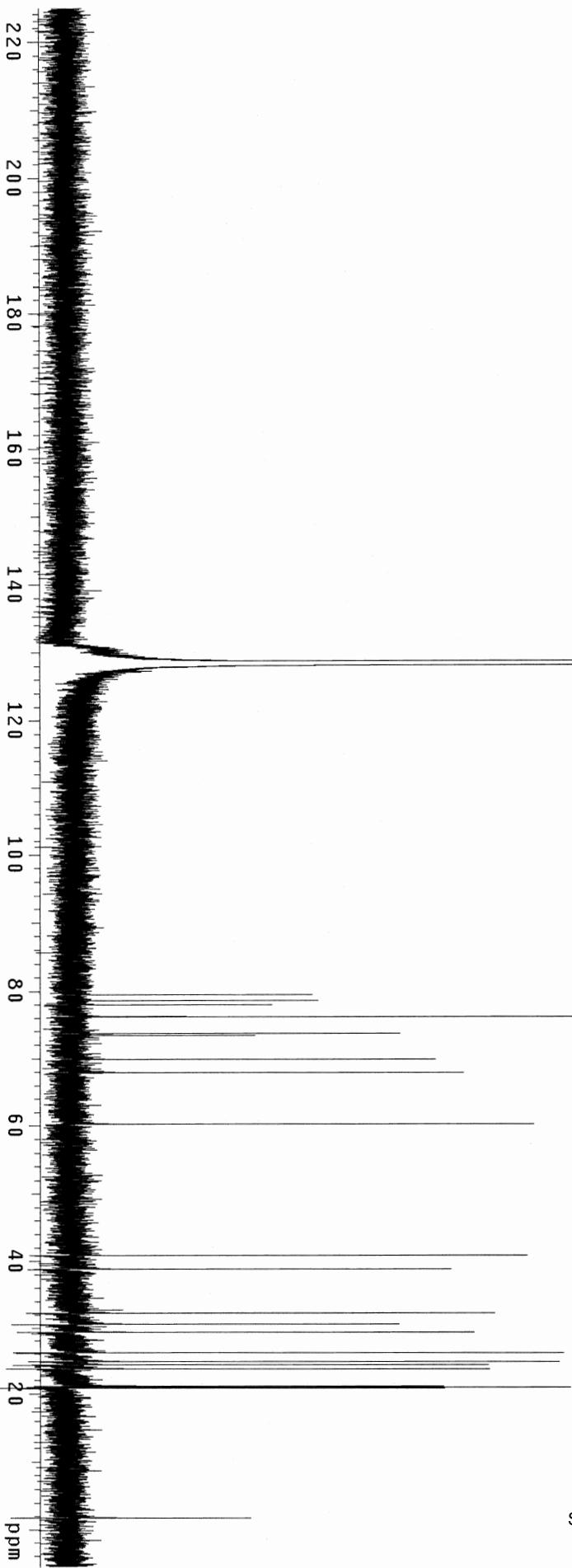
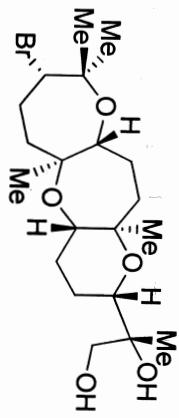
gCOSY, 500 MHz, C₆D₆



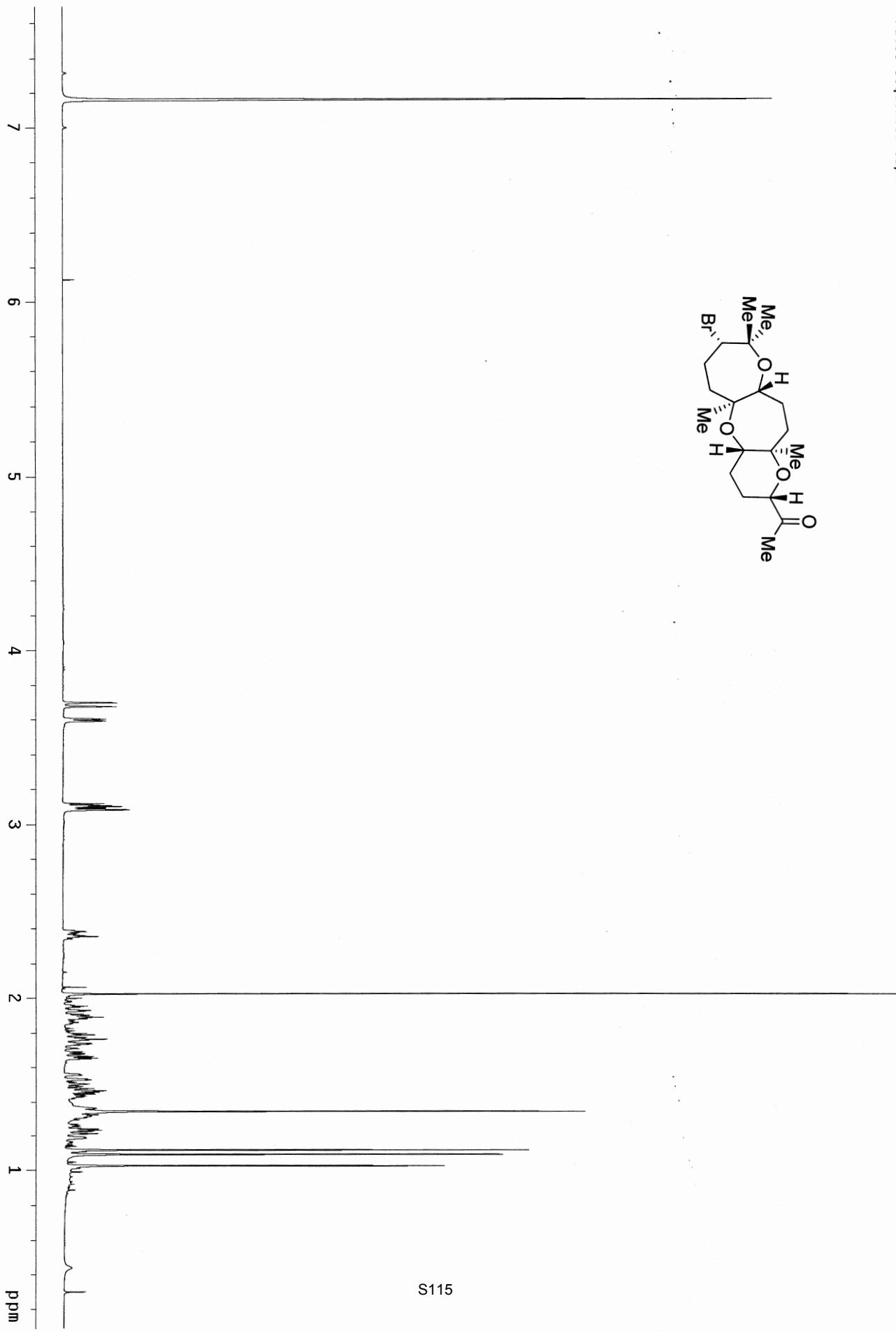
jt111126pp0000
Pulse Sequence: s2pul



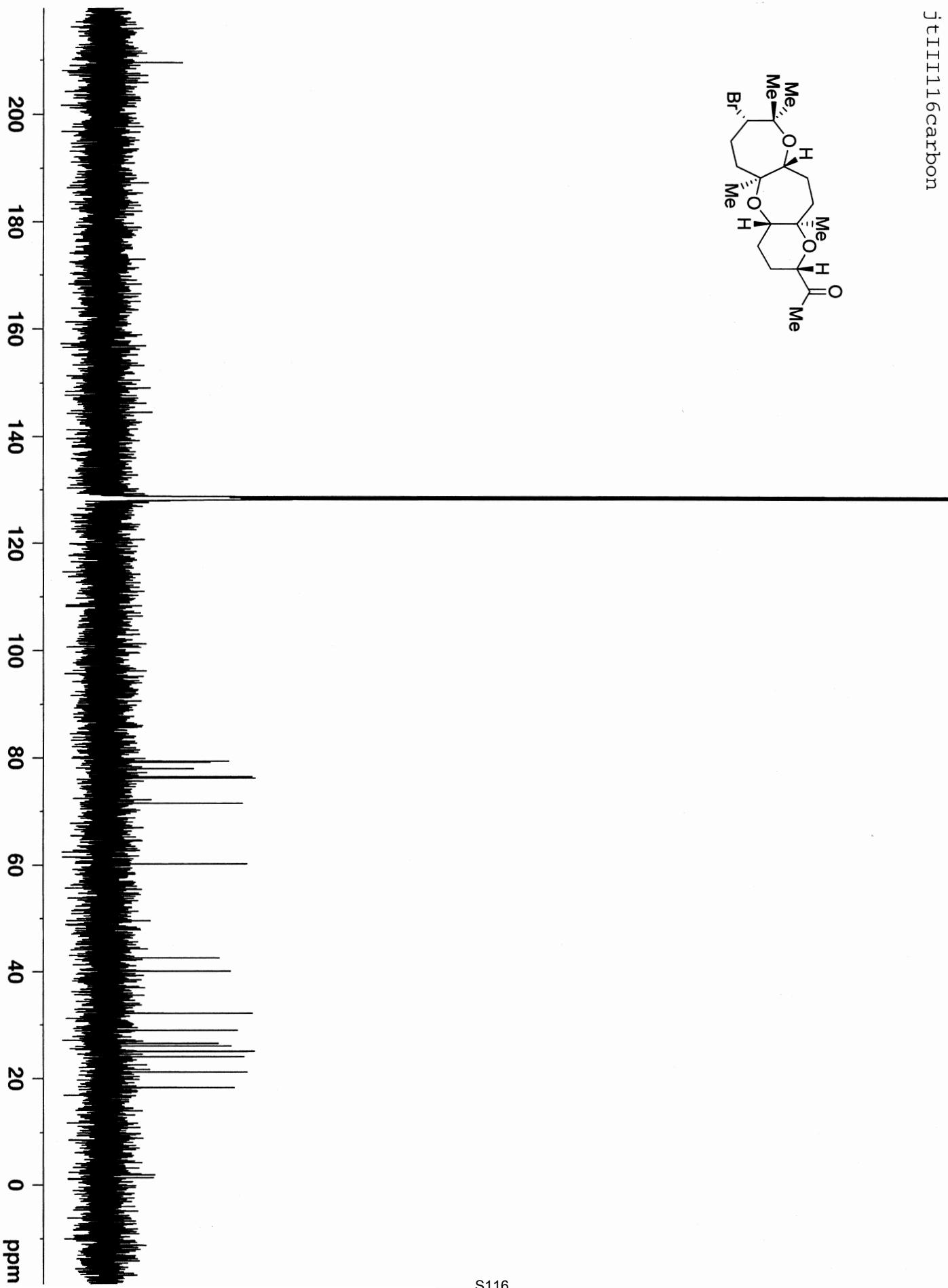
jt111126carbon
Pulse Sequence: s2pu1



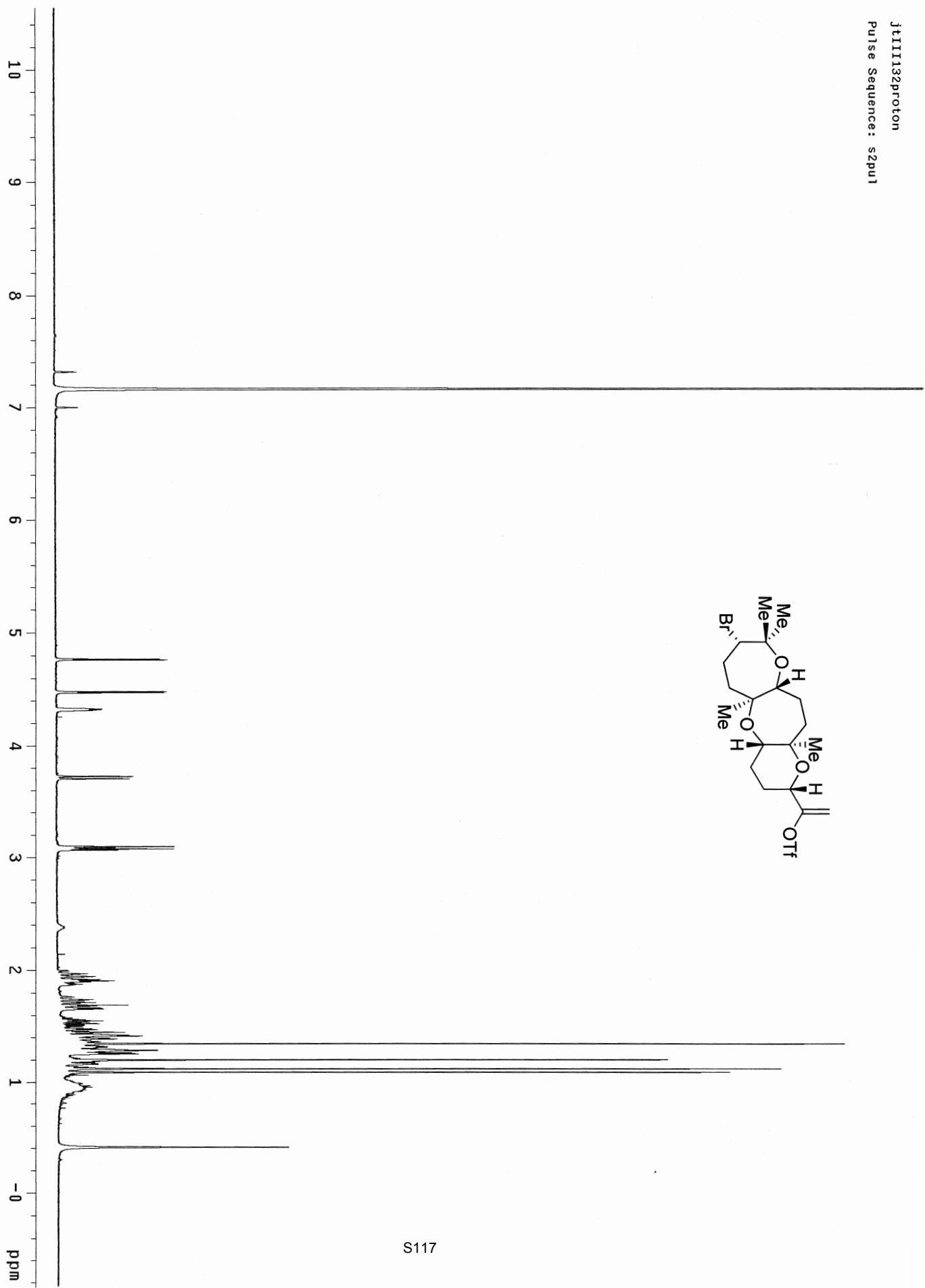
jt111127proton
Pulse Sequence: s2pu1

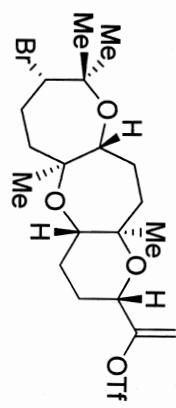
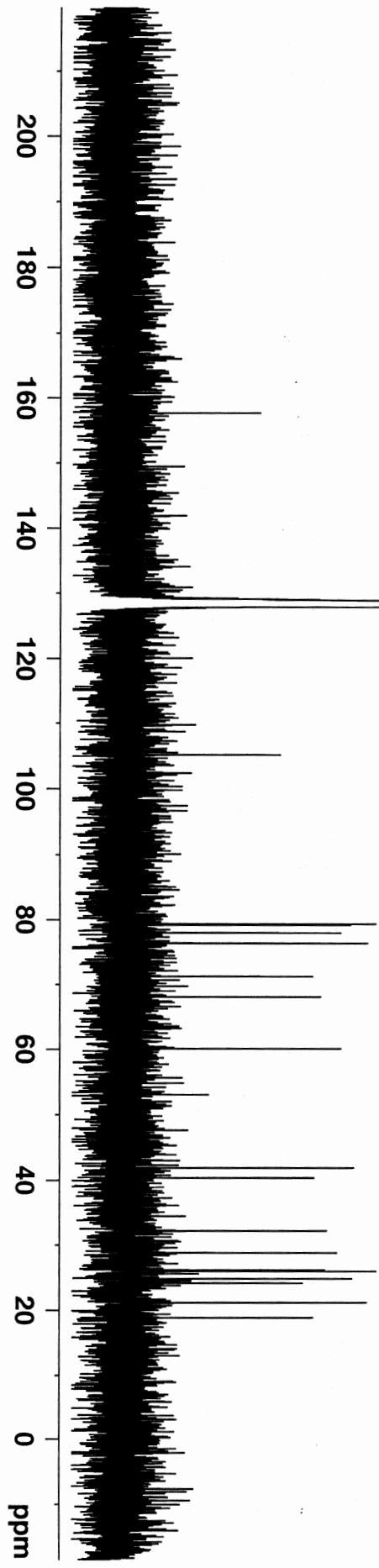


jttttttt16carbon



jtIII132proton
Pulse Sequence: s2pul

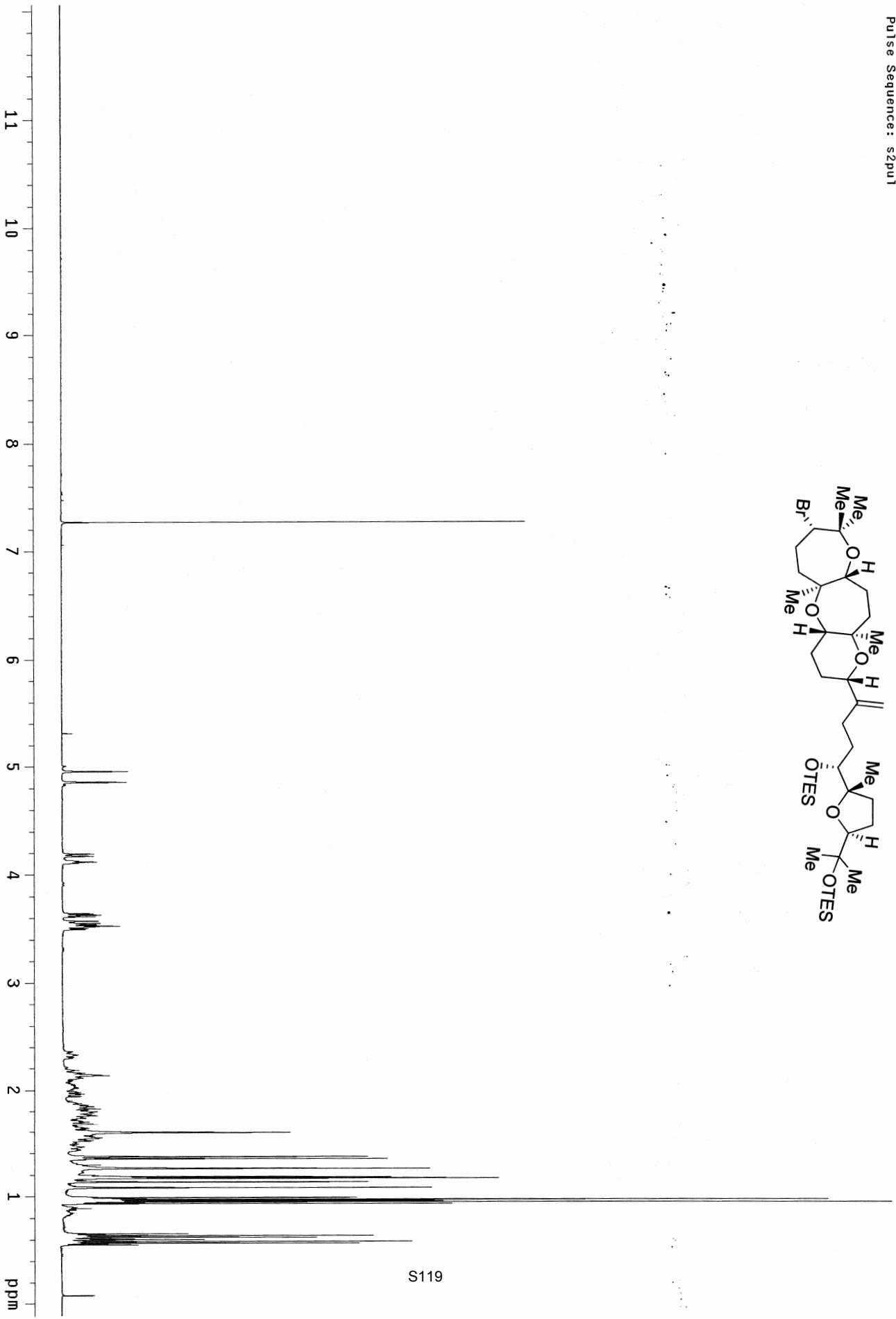




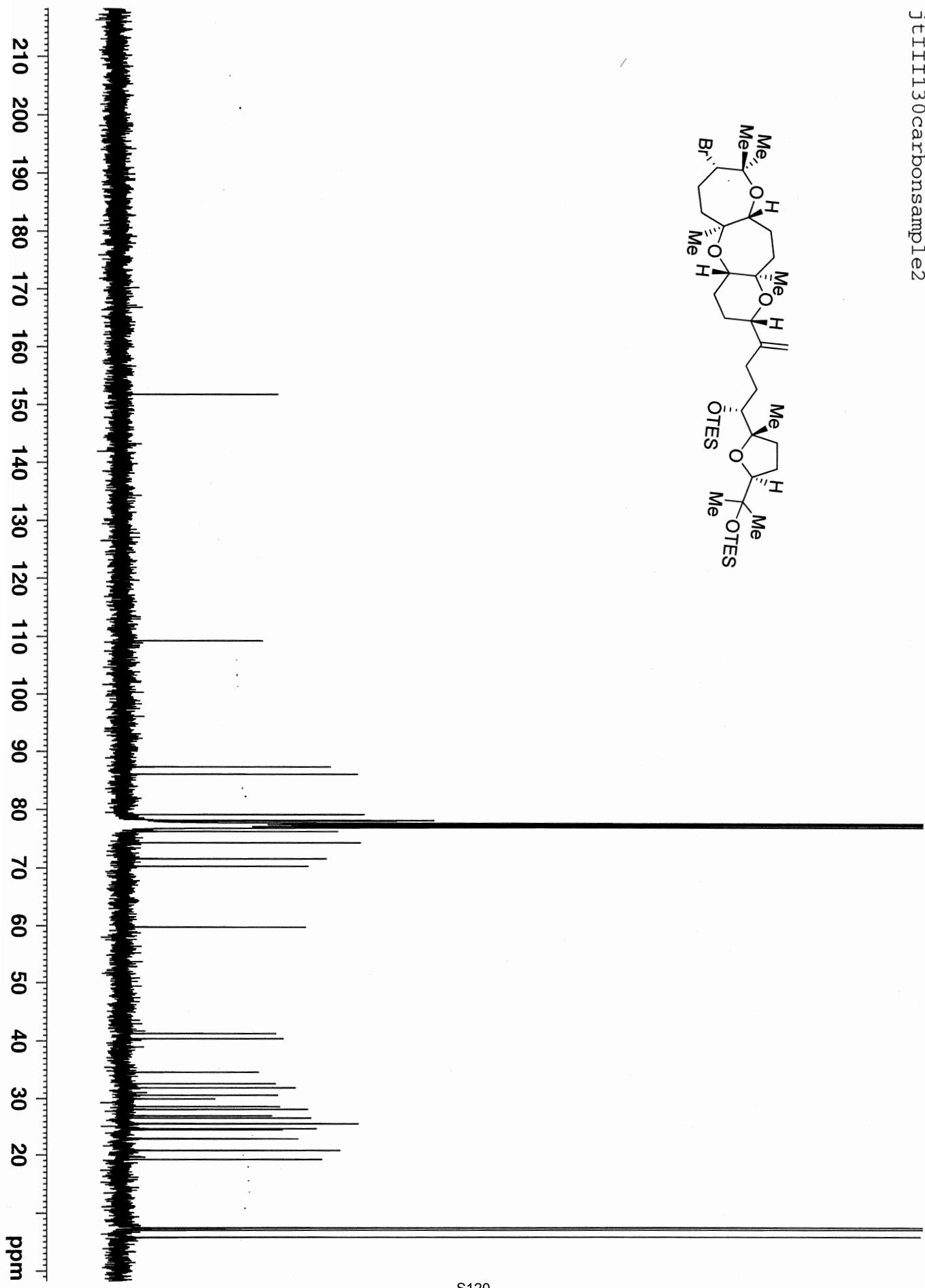
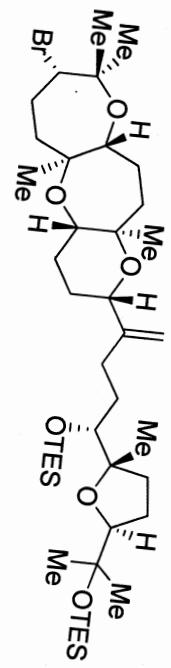
jt111117a

jT11130proton

Pulse Sequence: s2pul

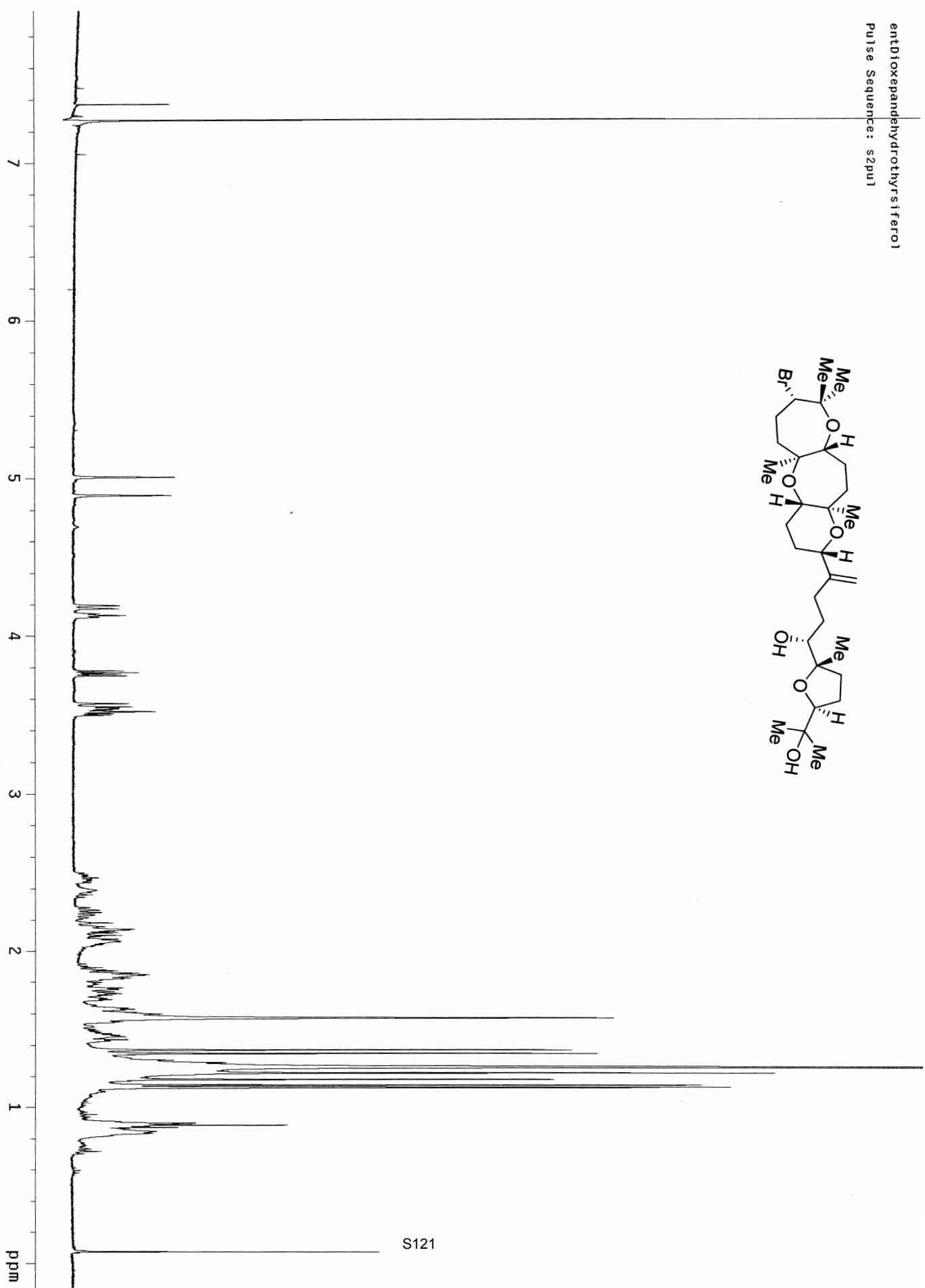
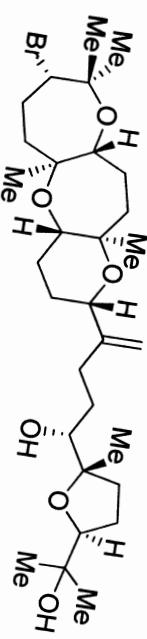


Jt111130carbonsample2



entDioxygenatedhydrothyristero1

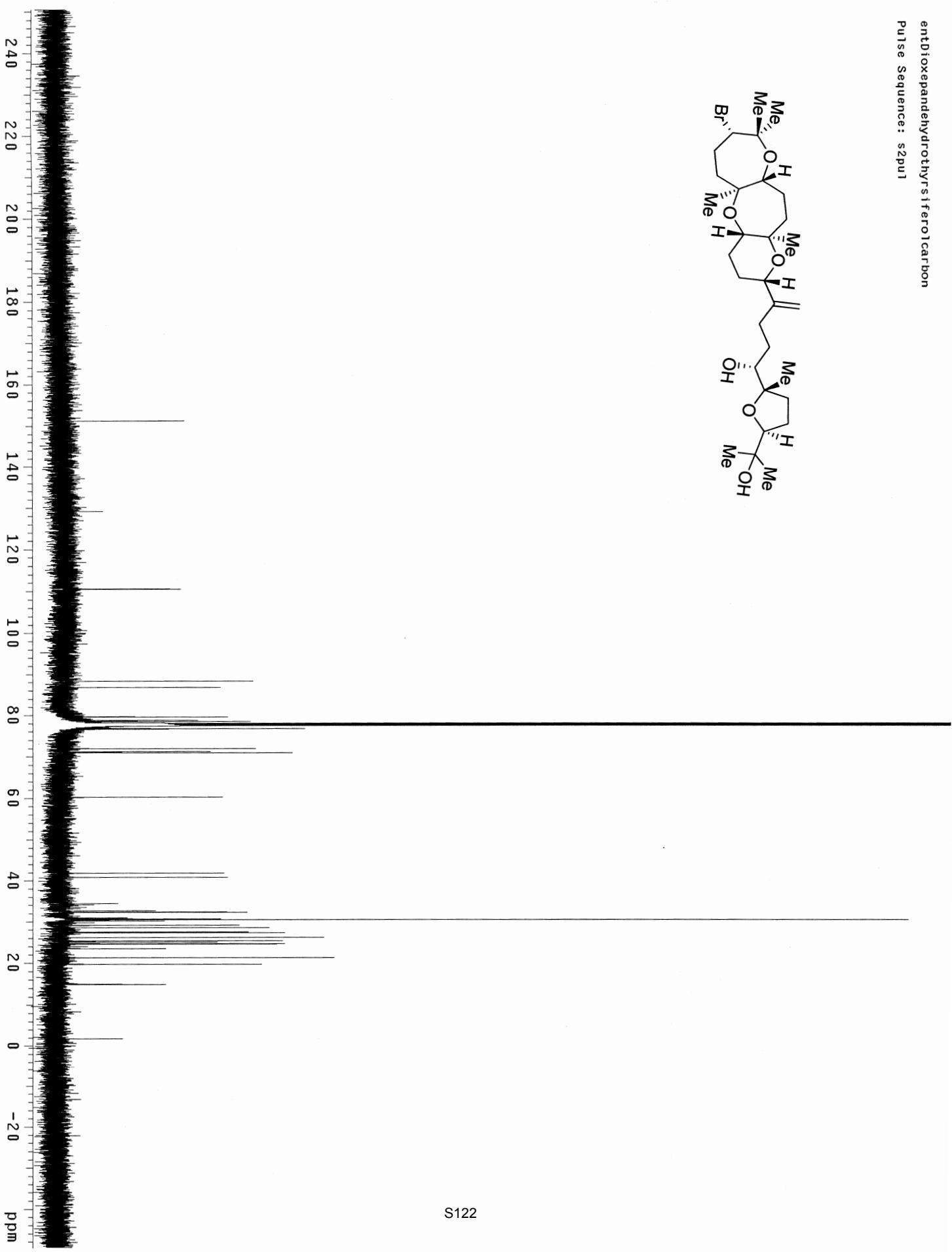
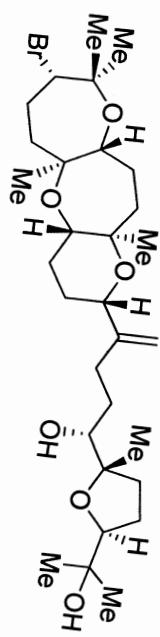
Pulse Sequence: s2pu1



S121

entDioxepandehydrothyrsiferolcarbon

Pulse Sequence: s2pul



entDioxepandehydrothysifero1gHSQC

Pulse Sequence: HSQC

Solvent: CDCl₃

Temp. 20.0 C / 293.1 K

User: 1-14-87

File: entDioxepandehydrothysifero1gHSQCproc

INOVA-500 "zippy"

Relax. delay 1.000 sec

Acq. time 0.150 sec

Width 4056.8 Hz

2D Width 20105.6 Hz

16 repetitions

2 x 512 increments

OBSERVE H1, 499.7417206 MHz

DECOUPLE C13, 125.6701797 MHz

Power 53 dB

on during acquisition

off during delay

GARP-1 modulated

DATA PROCESSING

Gauss apodization 0.058 sec

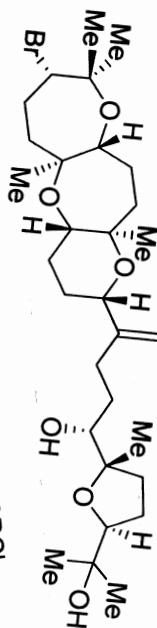
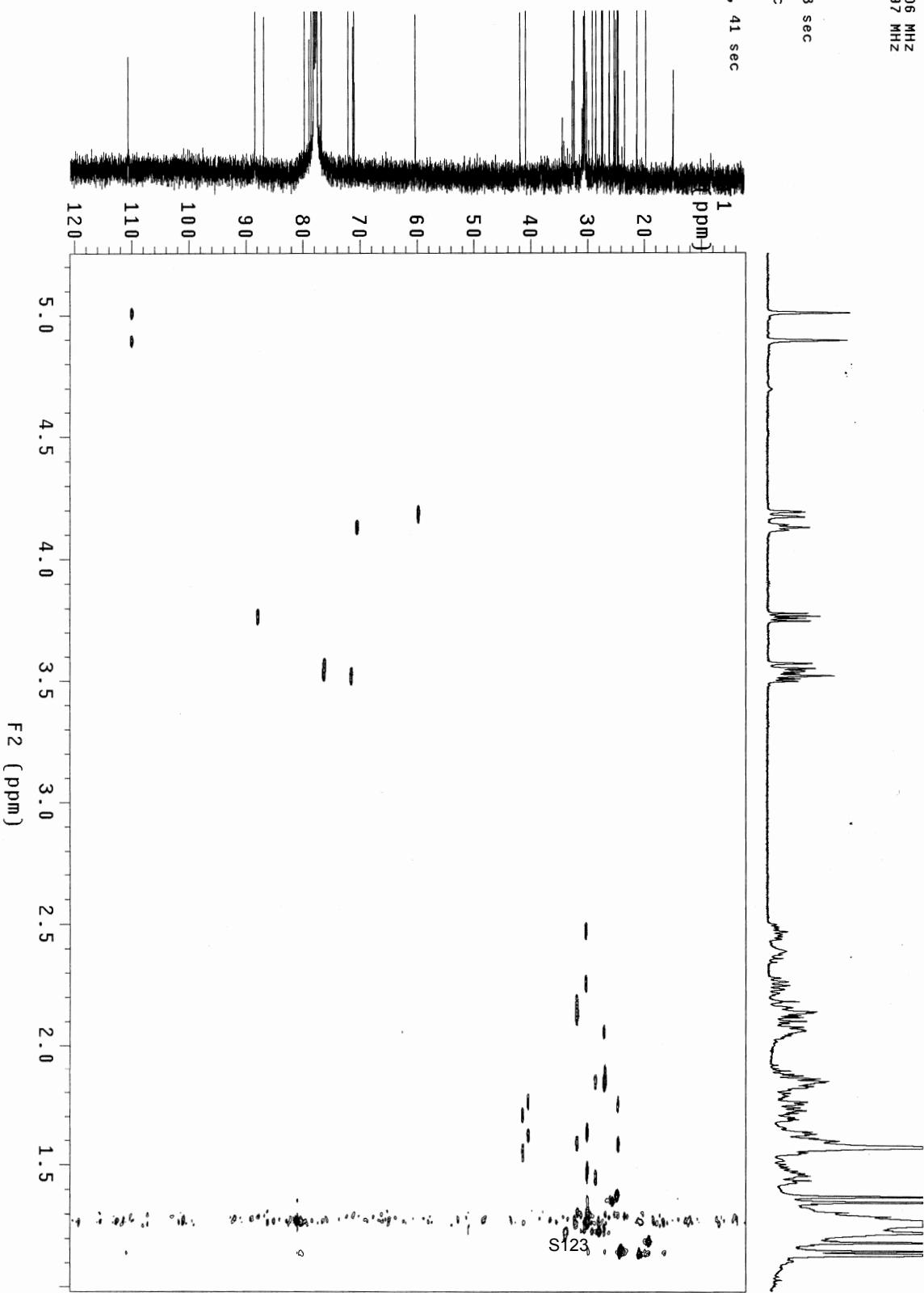
F1 DATA PROCESSING

Sq. sine bell 0.025 sec

Shifted by -0.025 sec

FT size 2048 x 2048

Total time 5 hr, 30 min, 41 sec



gHSQC, 500 MHz, CDCl₃

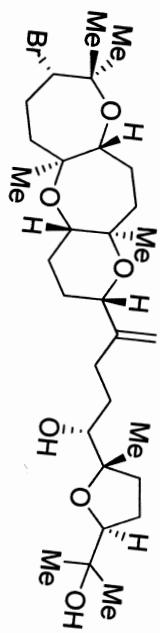
entDioxepandehydrothrysifero1gHSQC

Pulse Sequence: HSQC
 Solvent: CDCl₃
 Temp. 20.0 C / 293.1 K
 User: 1-14-87
 File: entDioxepandehydrothrysifero1gHSQCproc
 INOVA-500 "zippy"

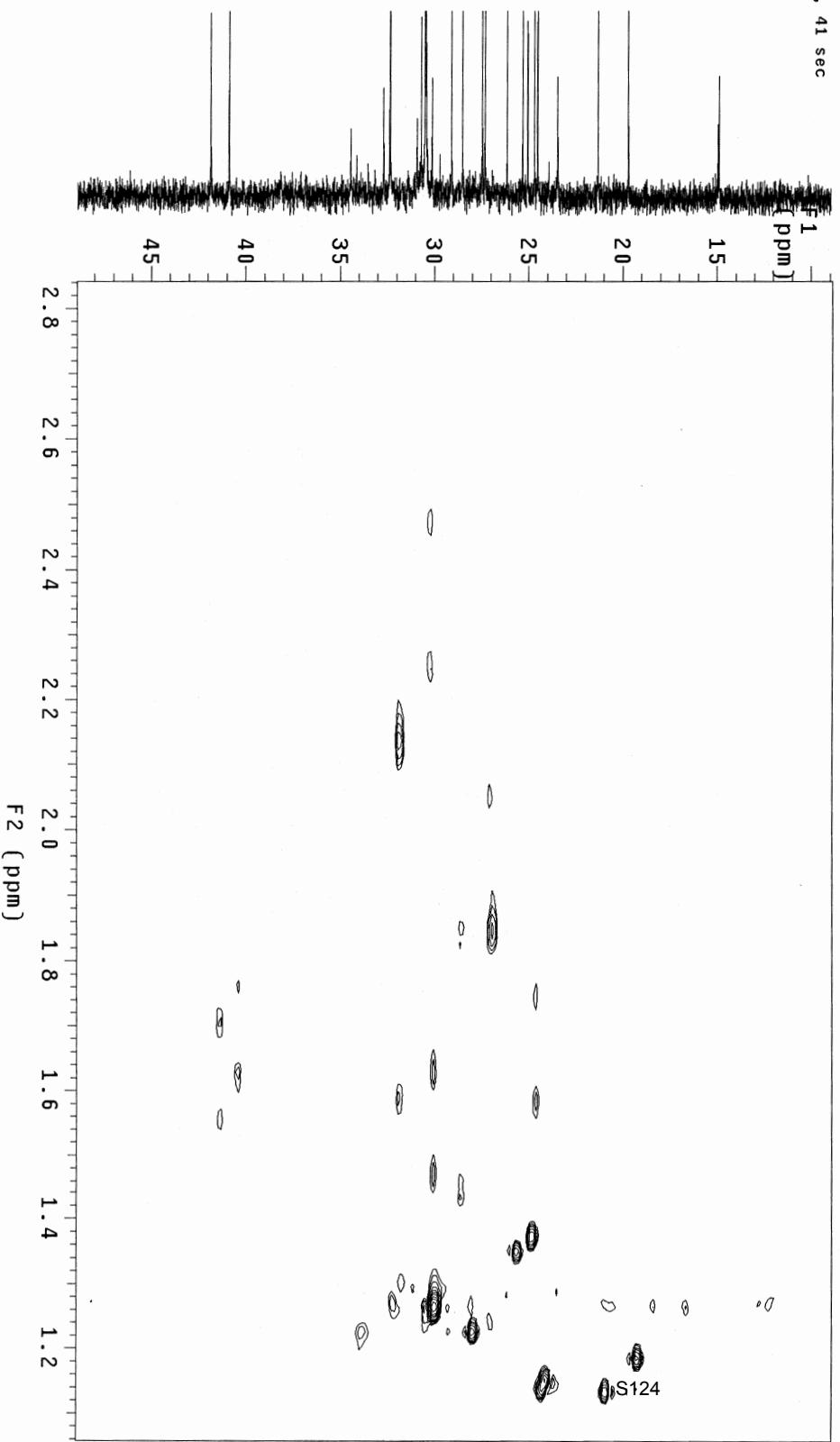
Relax. delay 1.000 sec
 Aq. time 0.150 sec
 Width 4056.8 Hz
 2D Width 20105.6 Hz

16 repetitions
 2 x 512 increments
 OBSERVE H1, 499.7417206 MHz
 DECOUPLE C13, 125.6701797 MHz
 Power 53 dB
 on during acquisition
 off during delay

GARP-1 modulated
 DATA PROCESSING
 Gaus apodization 0.058 sec
 F1 DATA PROCESSING
 Sq. sine bell 0.025 sec
 Shifted by -0.025 sec
 FT size 2048 x 2048
 Total time 5 hr, 30 min, 41 sec



gHSQC, 500 MHz, CDCl₃



entDioxepanhydrohydrisifero1gHMB

Pulse Sequence: gHMBC

Solvent: CDCl₃

Temp. 20.0 C / 293.1 K

User: 1-14-87

File: entDioxepanhydrohydrisifero1gHMBproc

INOVA-500 "zipper"

Relax. delay 0.695 sec

Acq. time 0.505 sec

Width 4056.8 Hz

2D Width 20105.6 Hz

64 repetitions

512 increments

OBSERVE H1 499.7417206 MHz

DATA PROCESSING

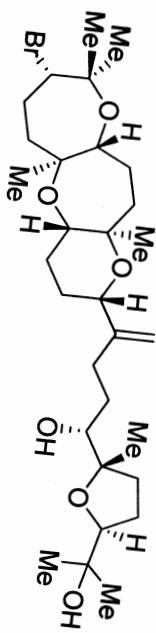
Sine bell 0.053 sec

F1 DATA PROCESSING

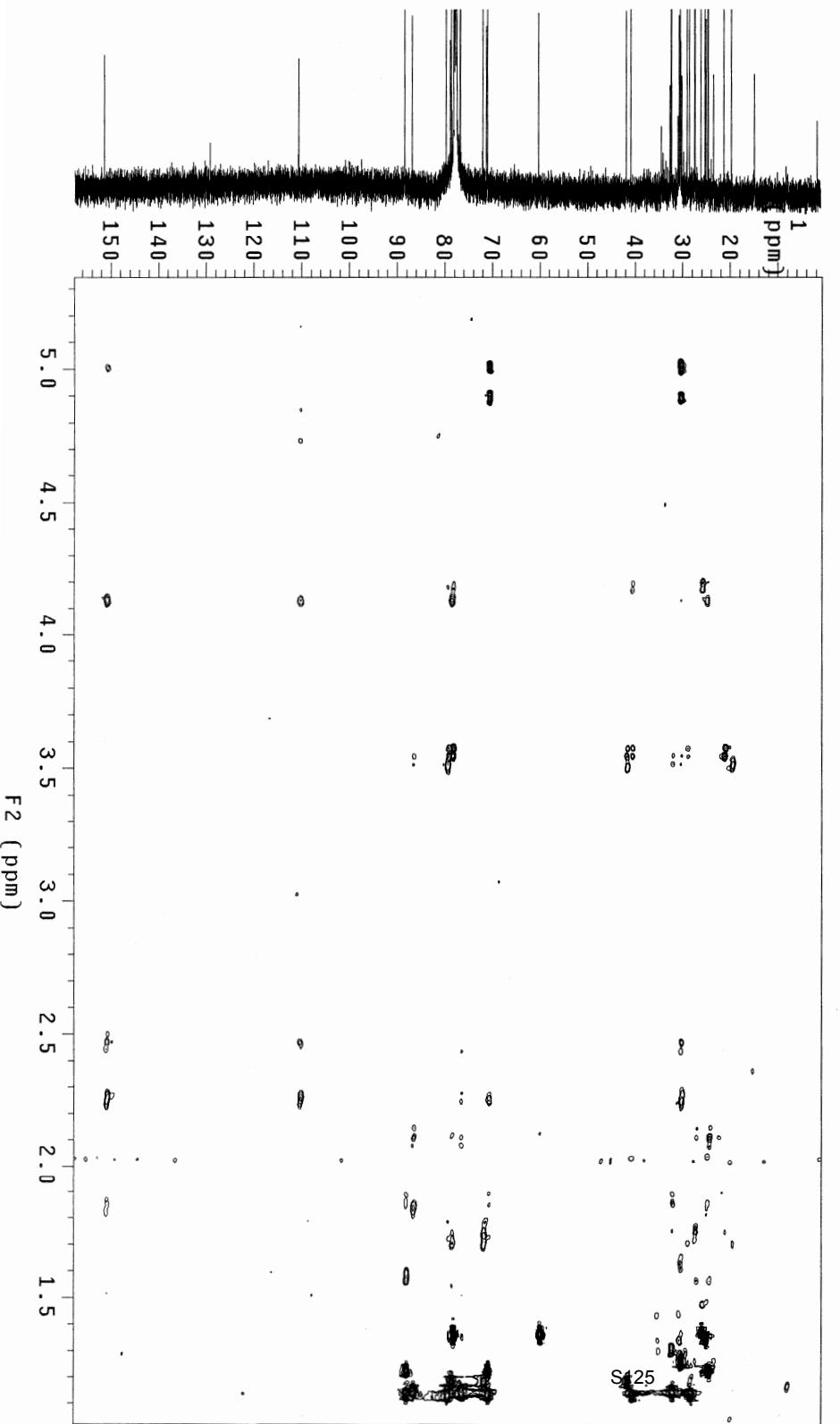
Sine bell 0.025 sec

FT size 4096 x 4096

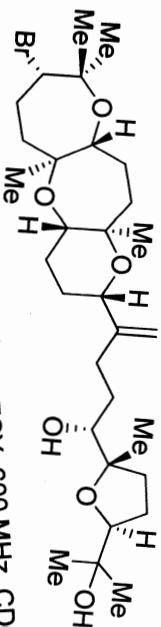
Total time 11 hr, 47 min, 38 sec



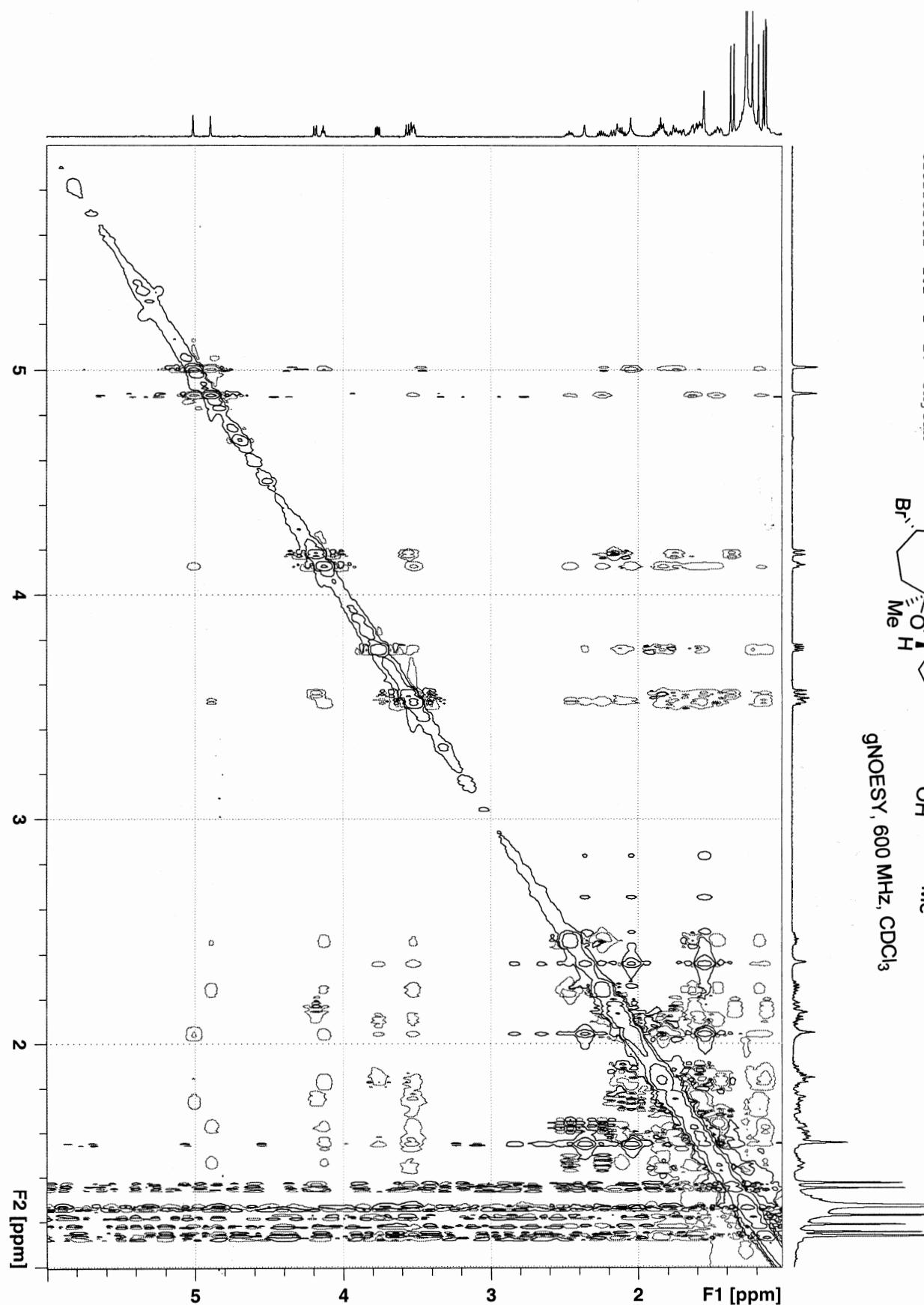
gHMBC, 500 MHz, CDCl₃



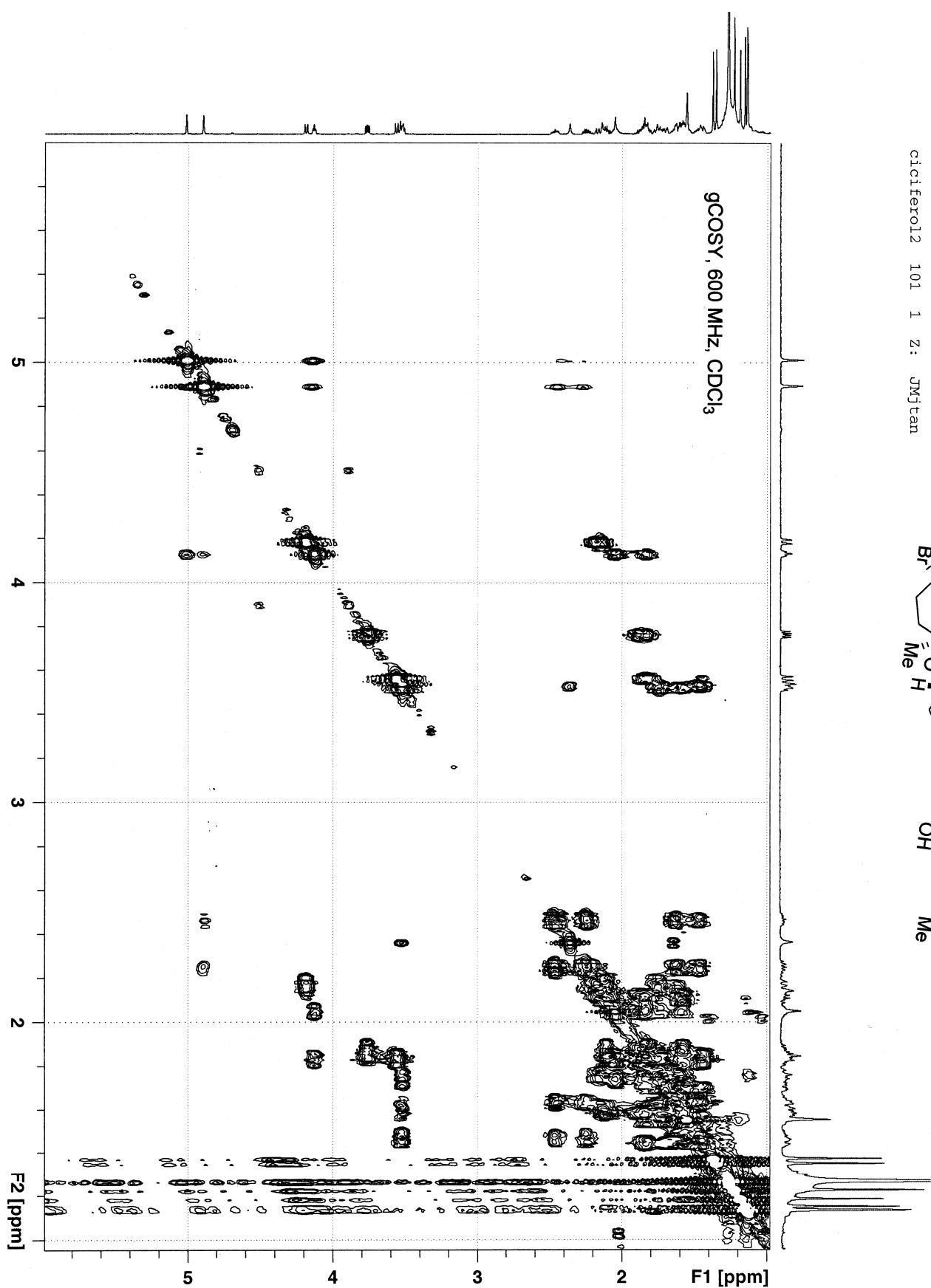
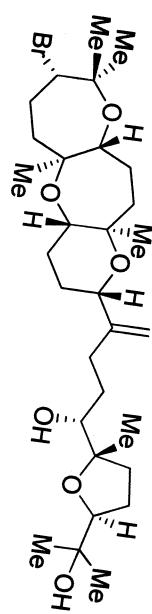
cicifero12 102 1 z: JMjtan



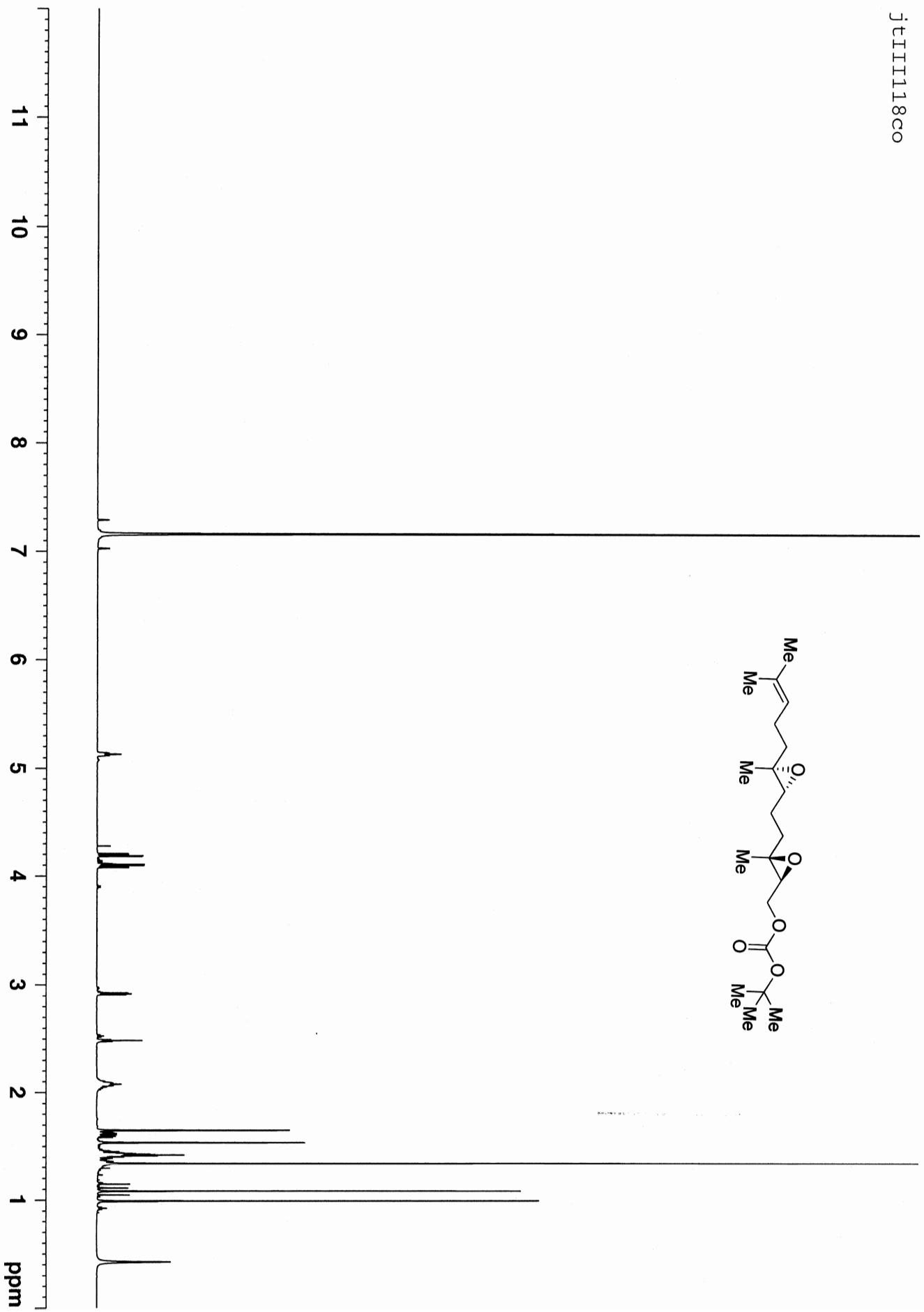
gNOESY, 600 MHz, CDCl₃



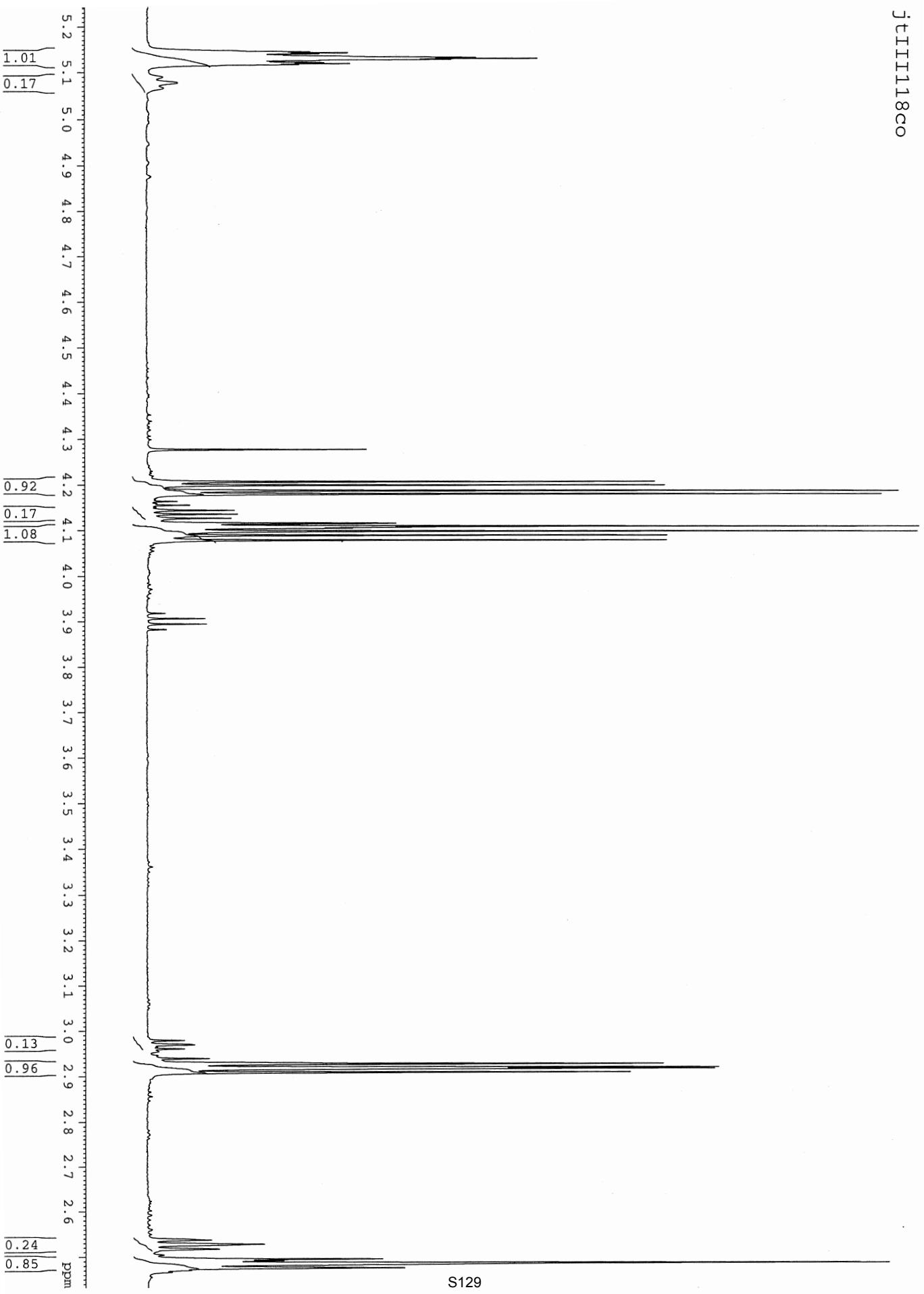
ciciferol2 101 1 Z: JMjtan



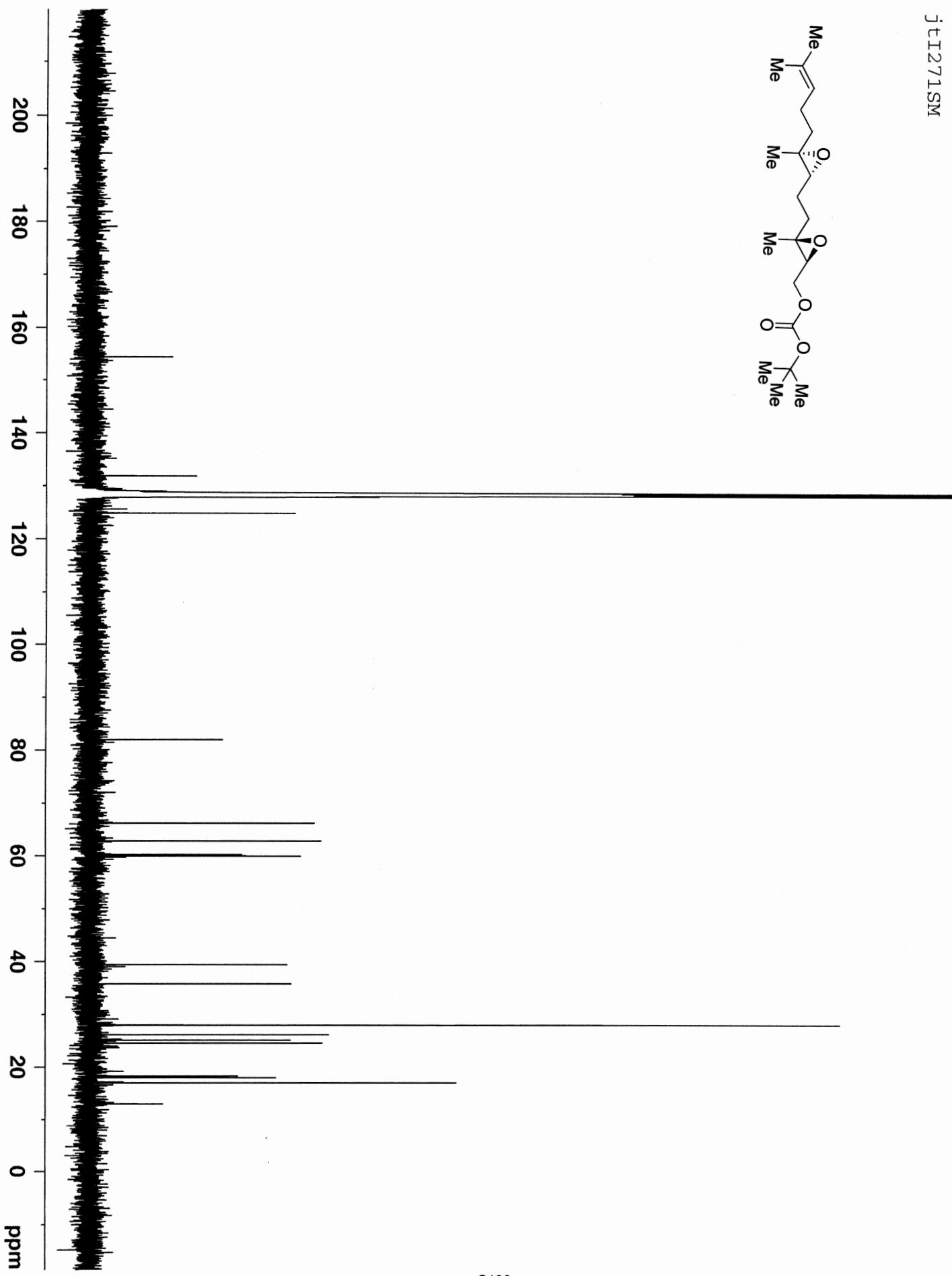
Jt111118co



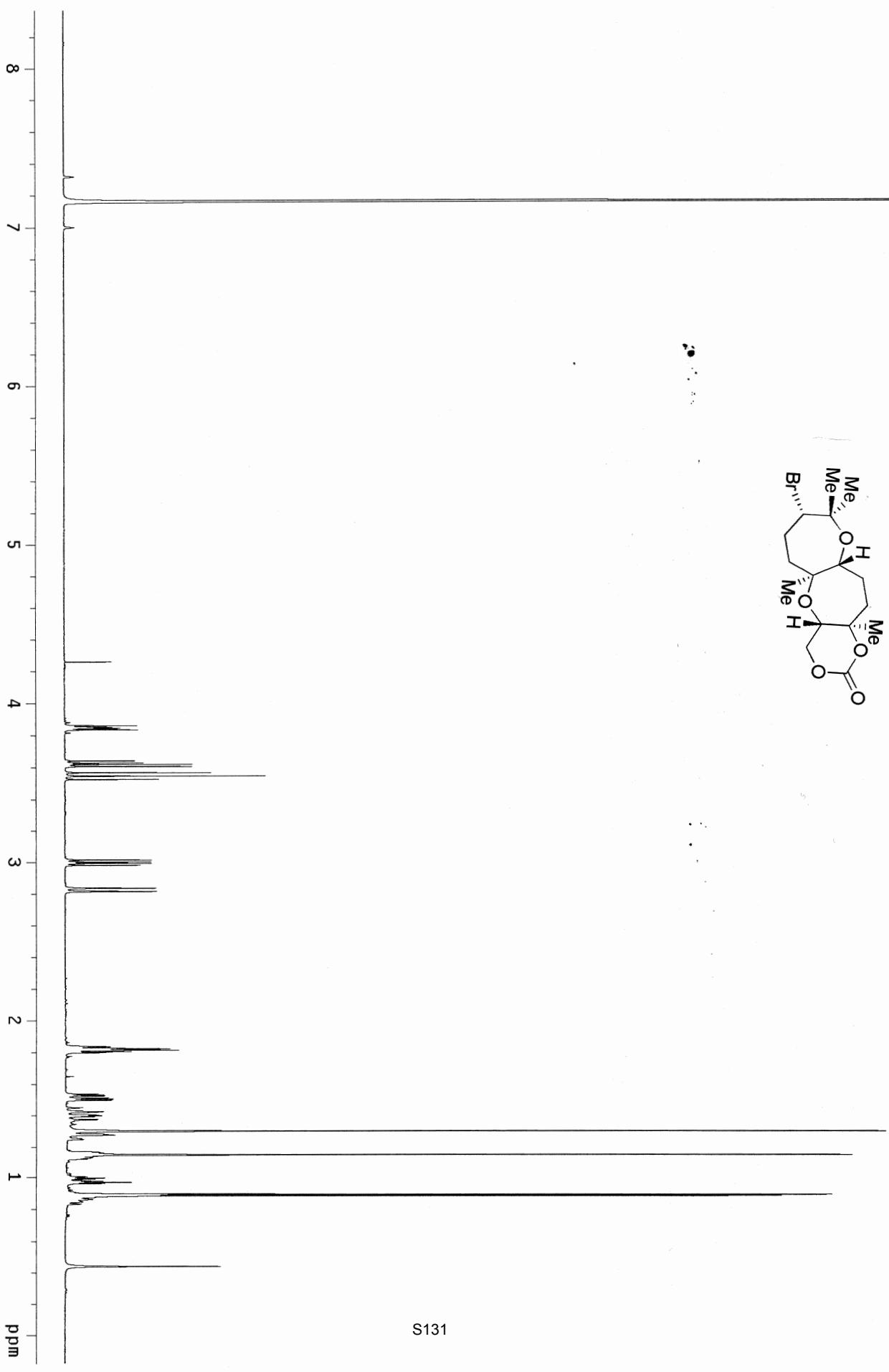
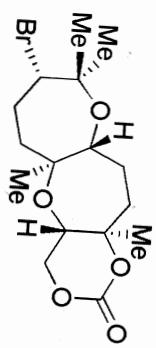
jtIIII118co



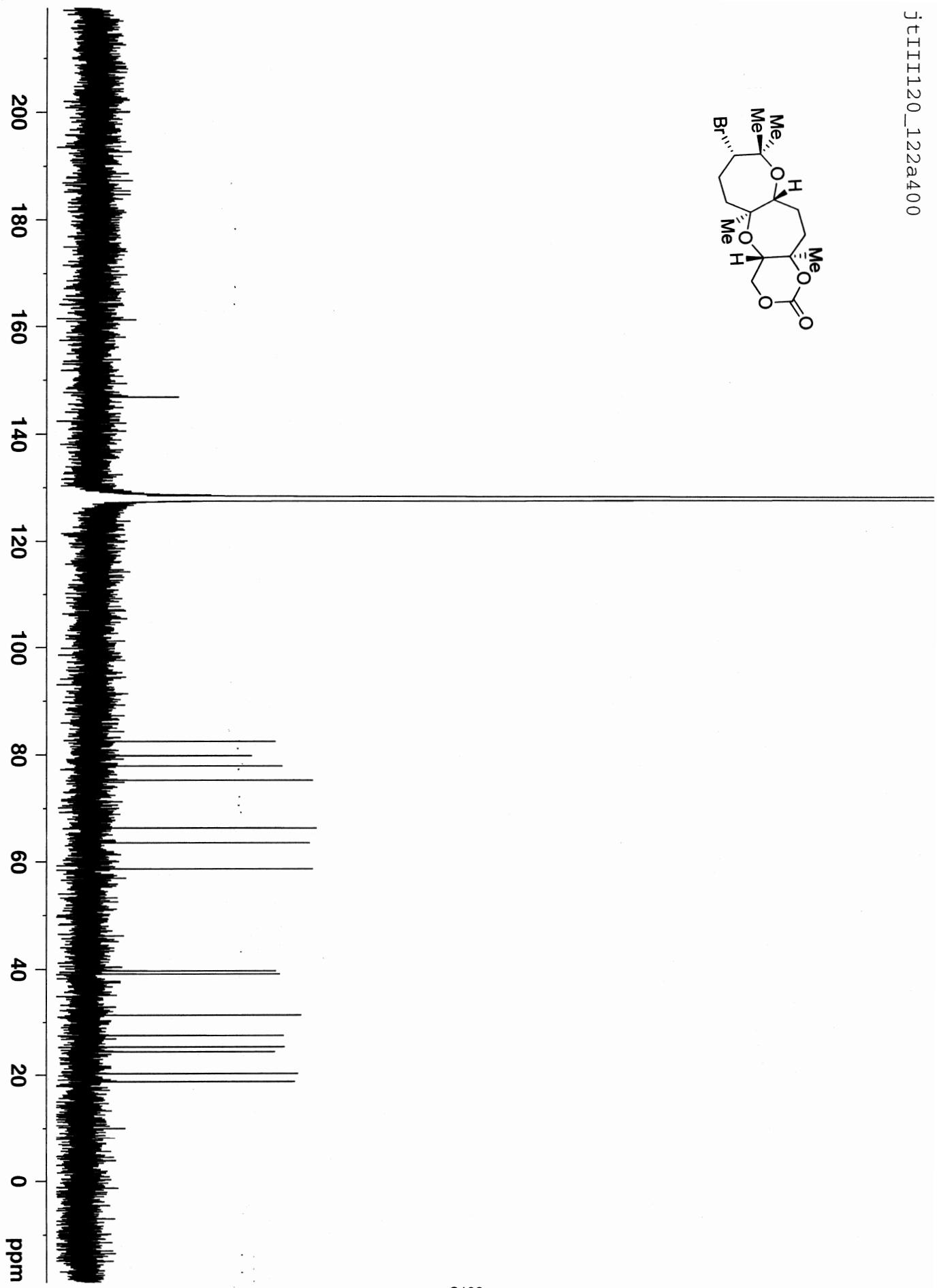
S129



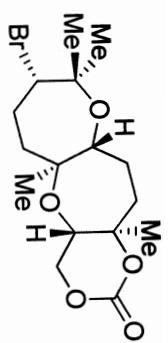
jt111120_122a
Pulse Sequence: s2pu1



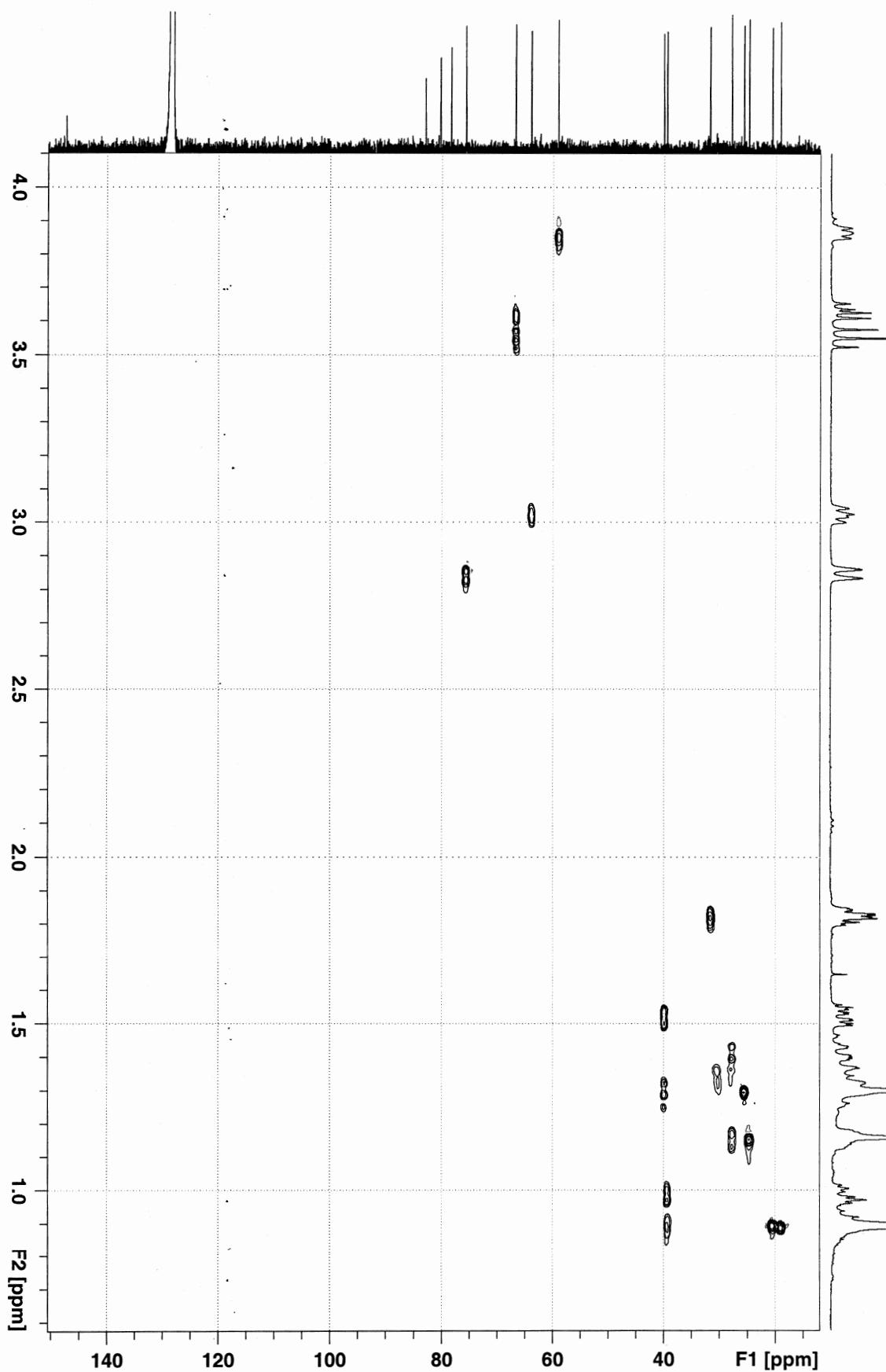
jt111120_122a400



jttIII120_122a 100 1 z: JMjtan

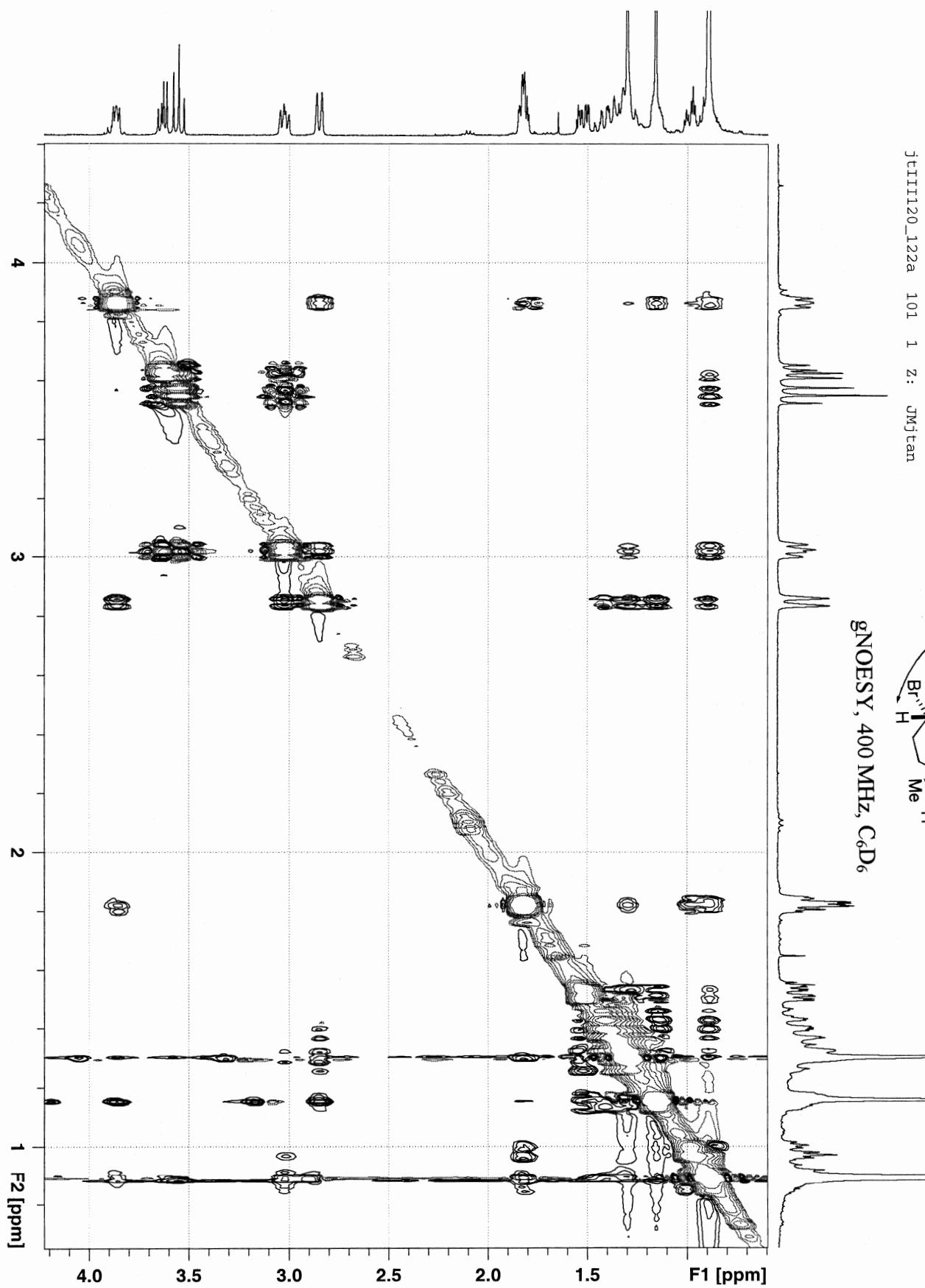
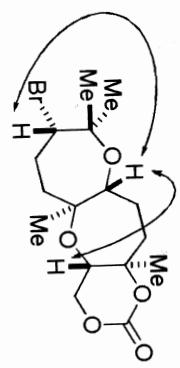


gHSQC, 400 MHz, C₆D₆



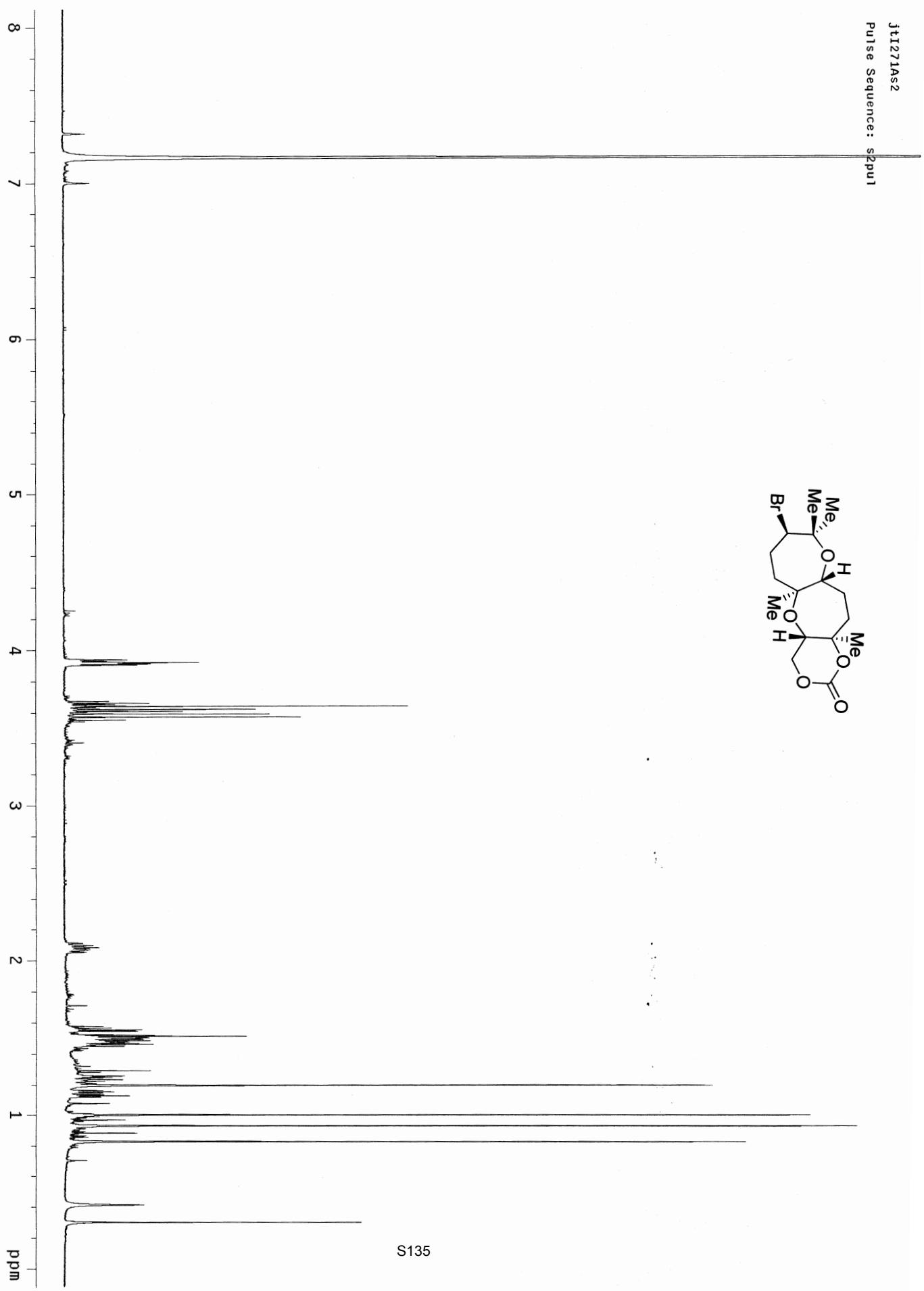
jt111120_122a 101 1 Z: JMjtan

gNOESY, 400 MHz, C₆D₆

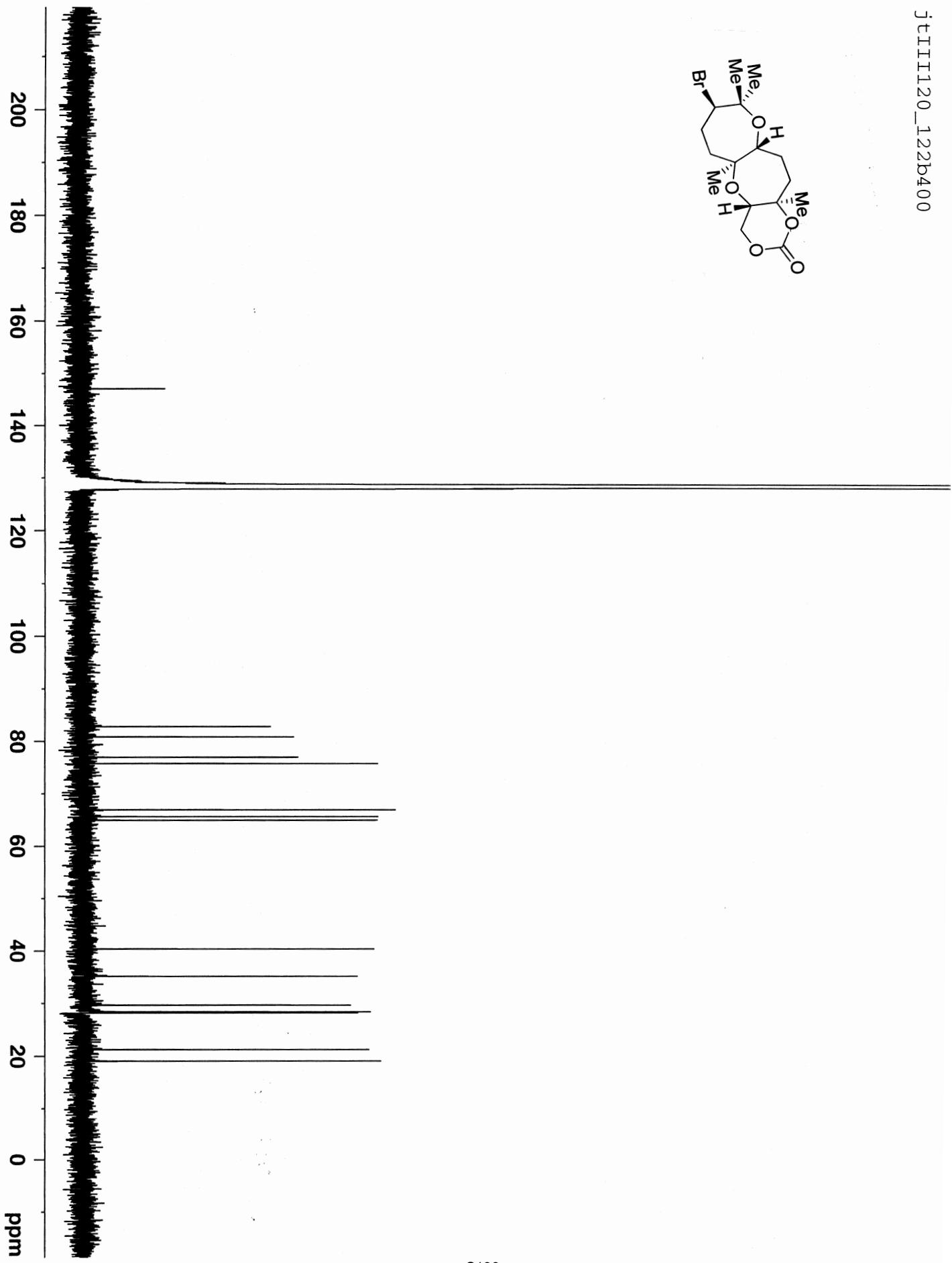


jtI27As2

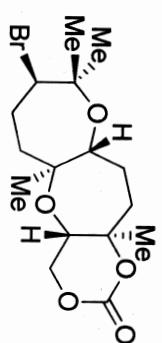
Pulse Sequence: s2pul



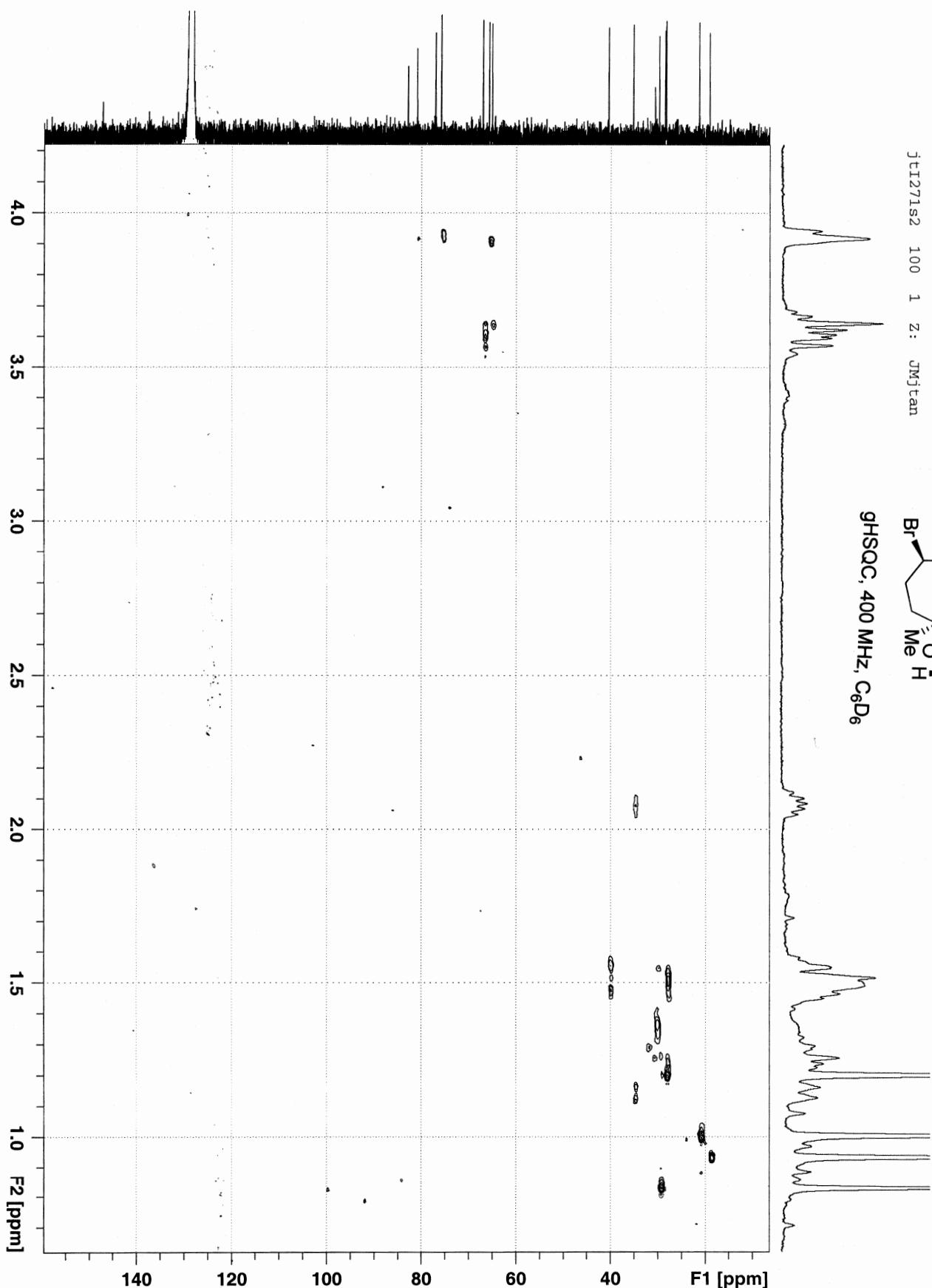
jttttt120_122b400



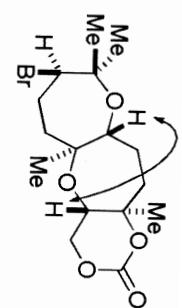
jt1271s2 100 1 Z: JMjtan



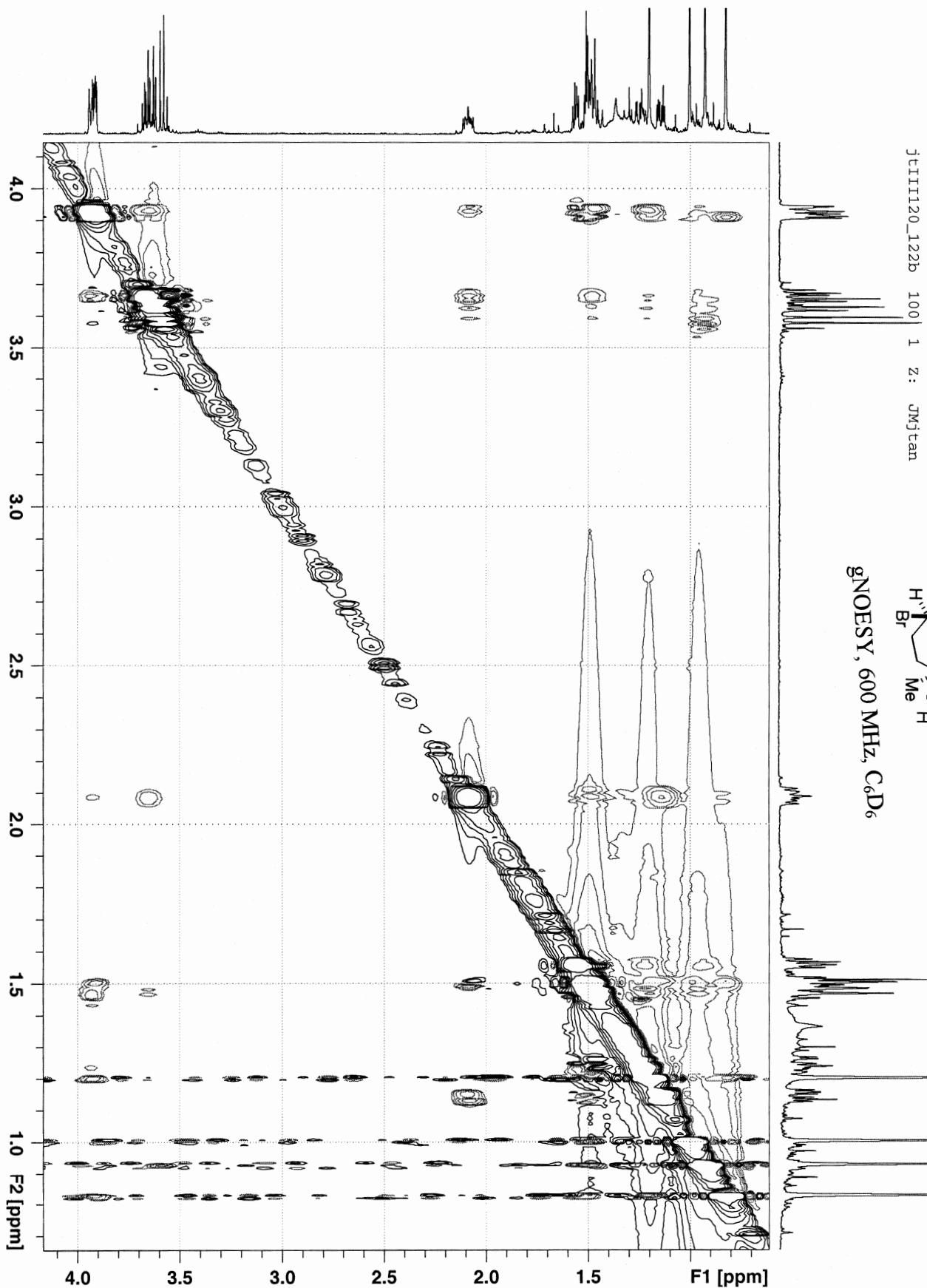
gHSQC, 400 MHz, C_6D_6



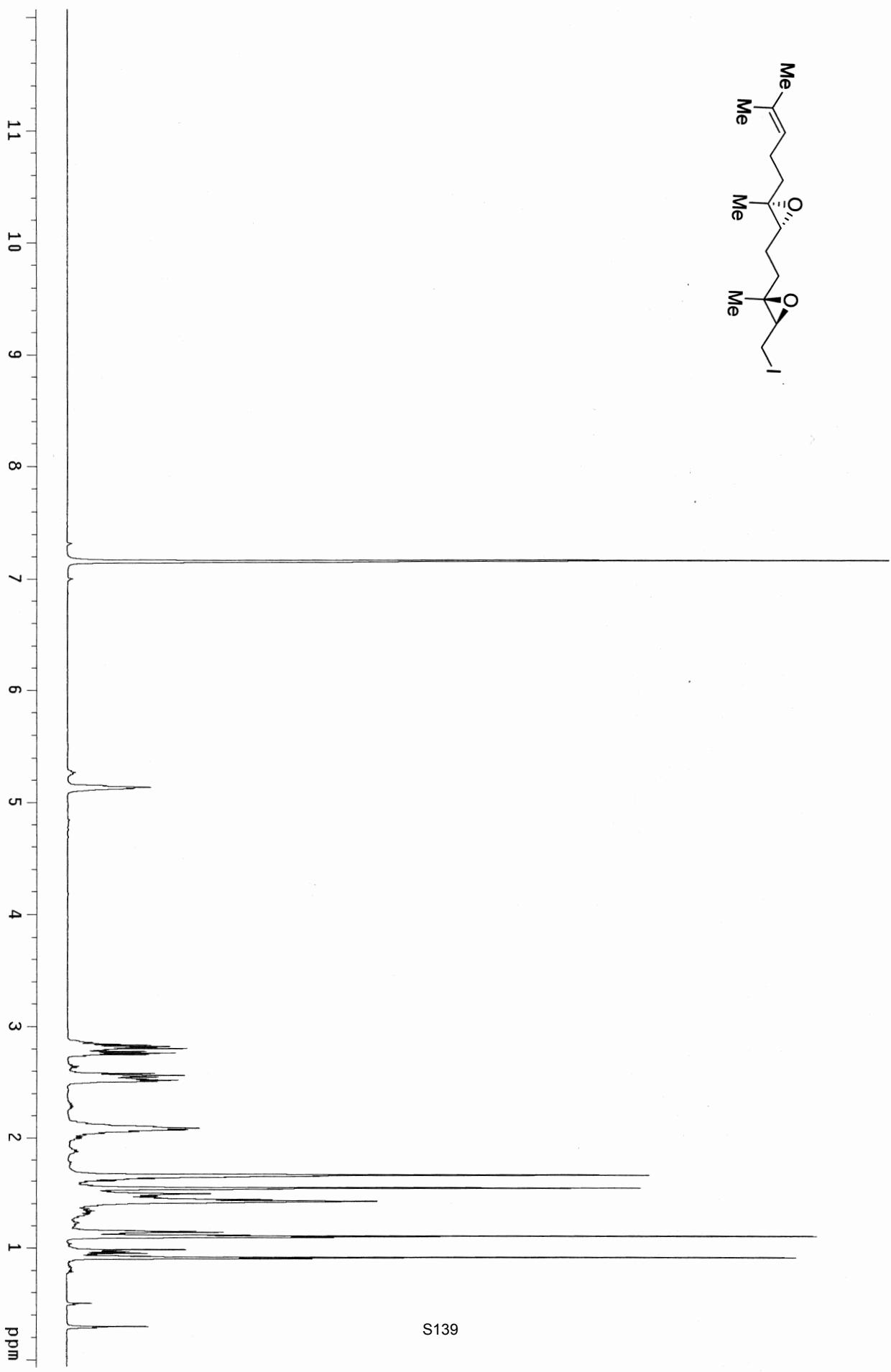
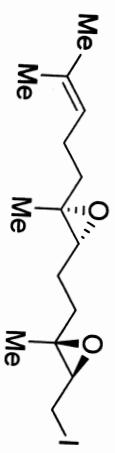
jttIII120_122b 100 1 Z: JMjtan

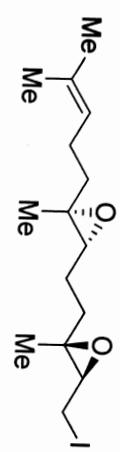
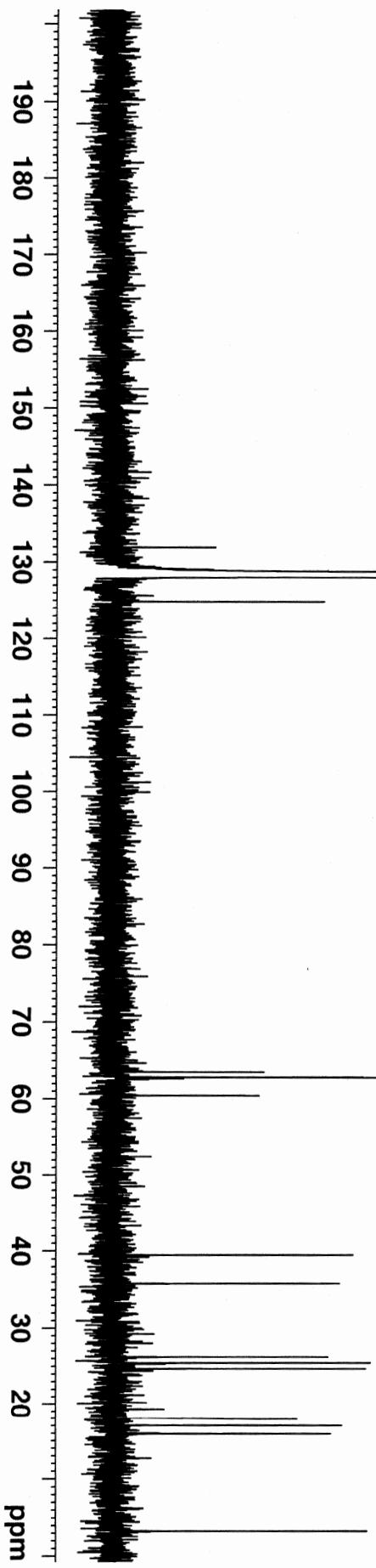


gNOESY, 600 MHz, C₆D₆

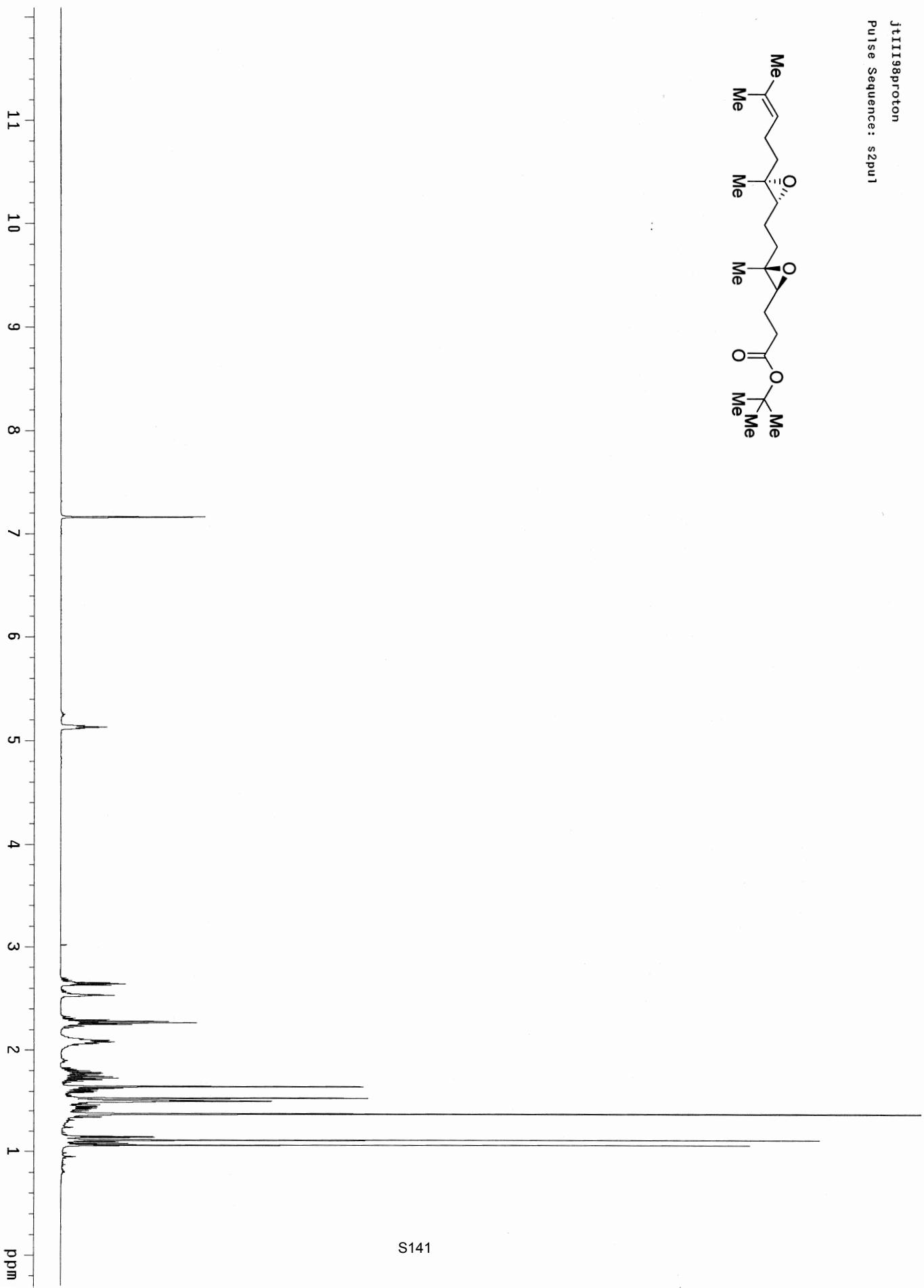
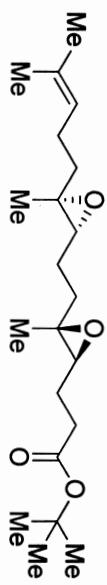


jt11197proton
Pulse Sequence: s2pul

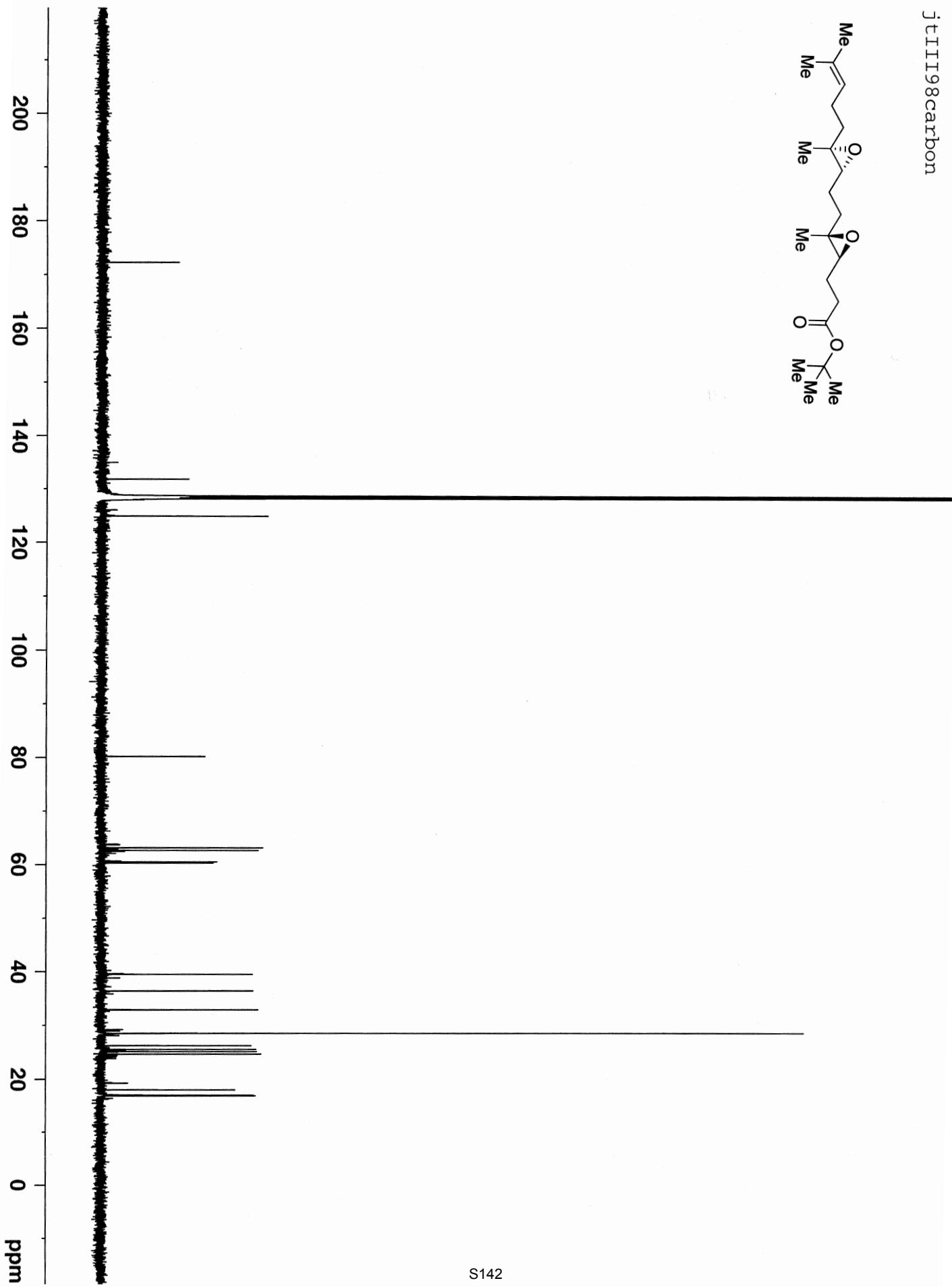




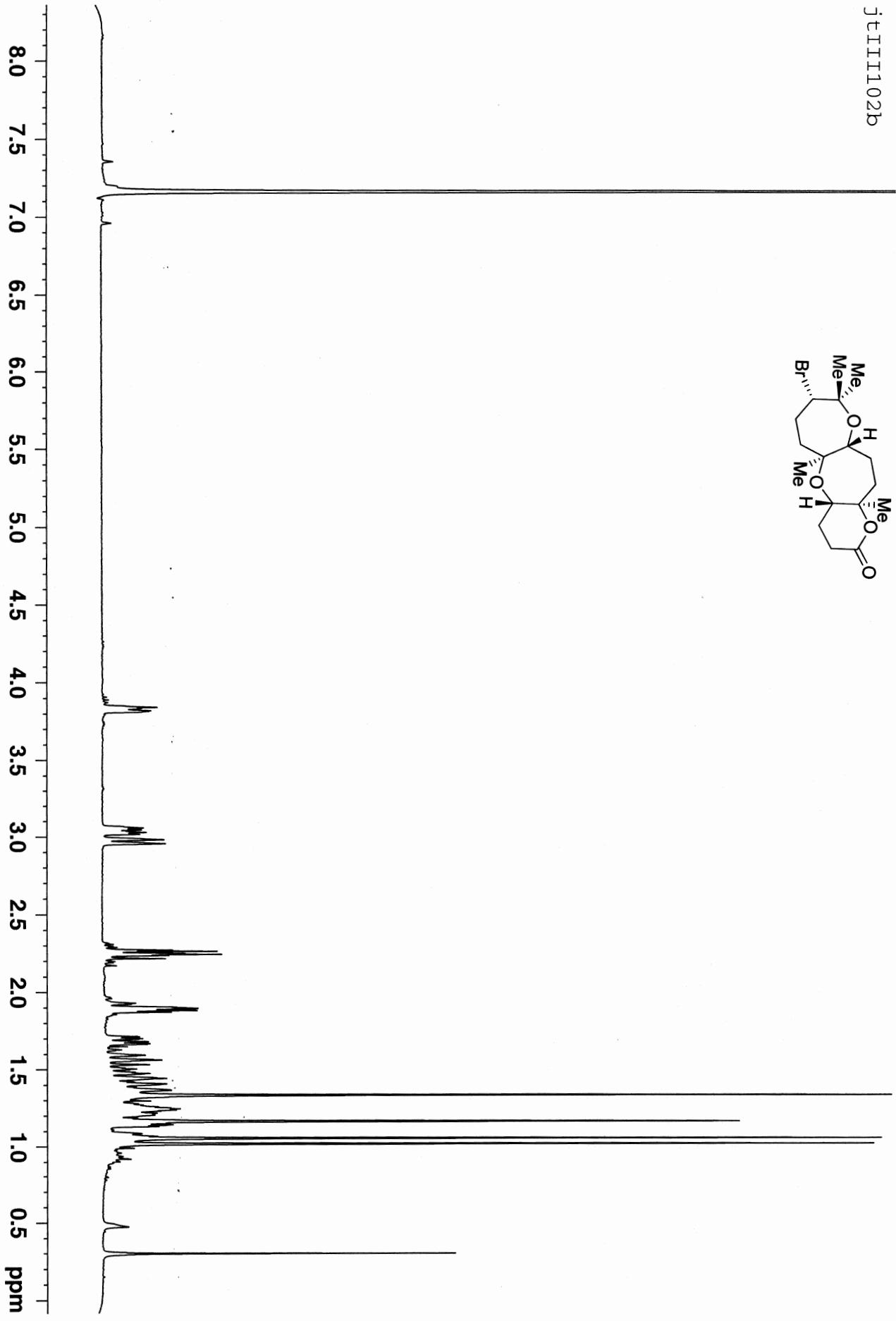
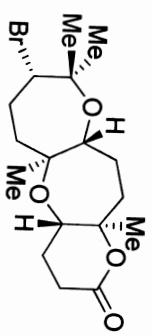
jt11198proton
Pulse Sequence: s2pu1



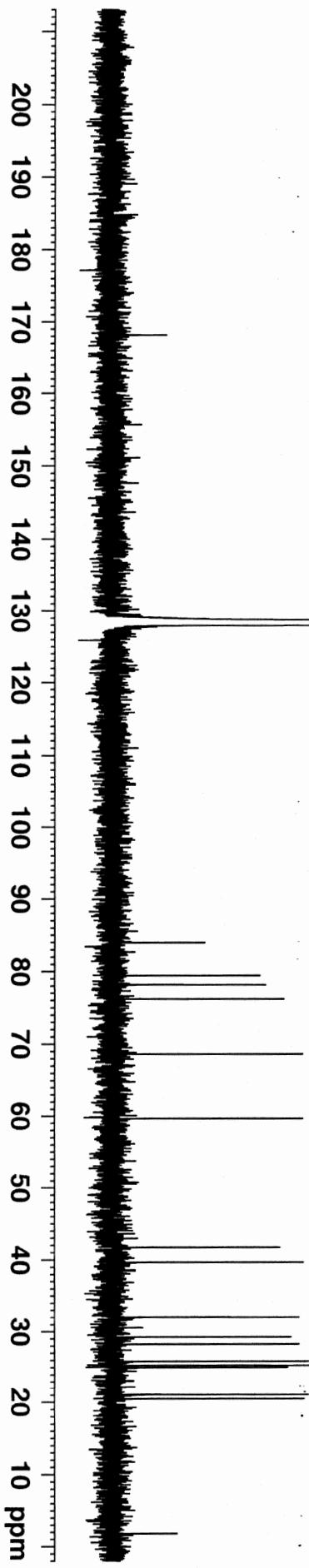
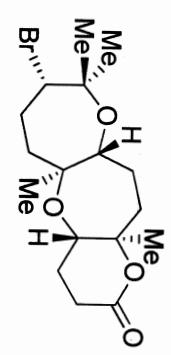
jtit98carbon



JtIII102b

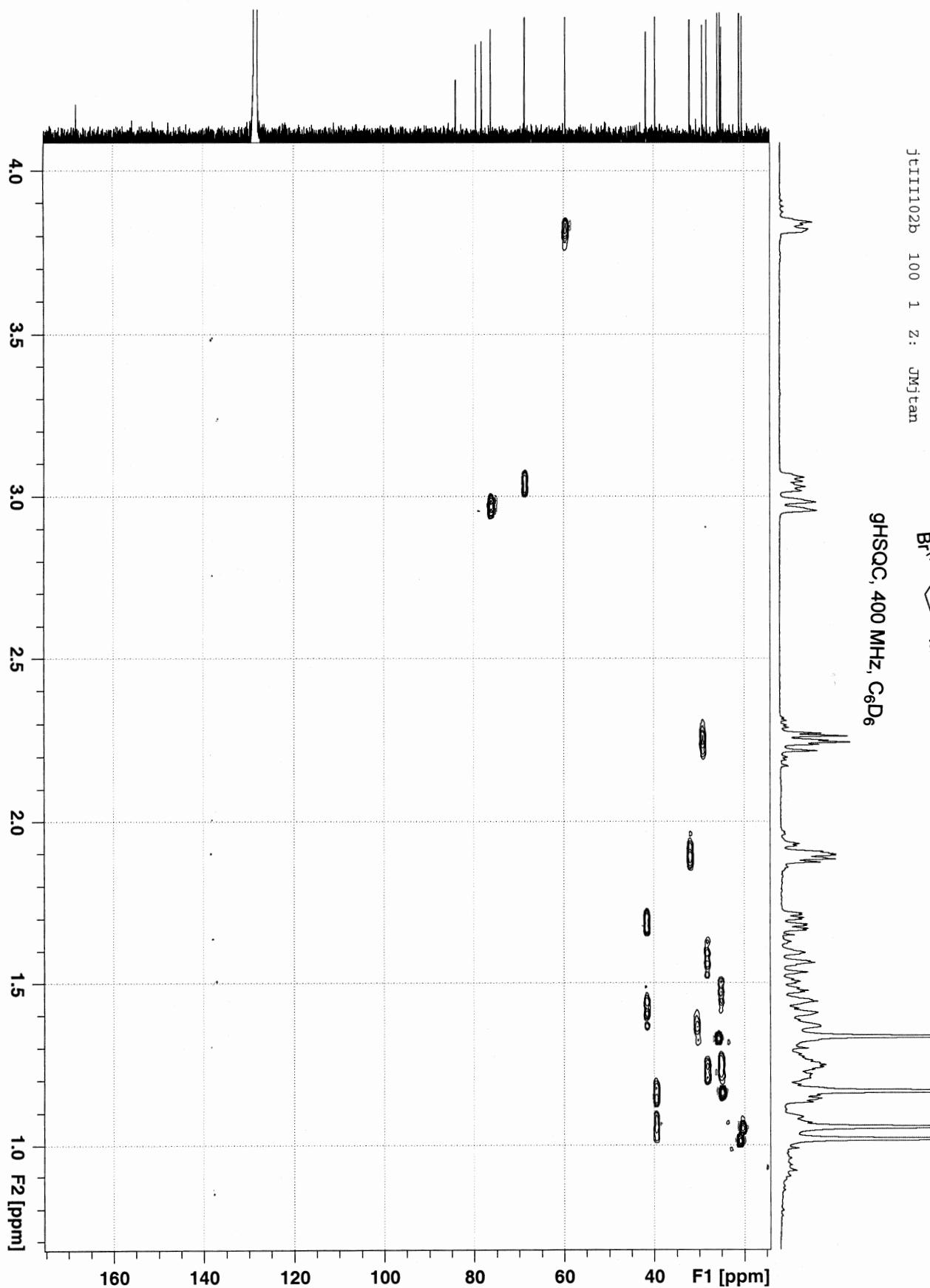
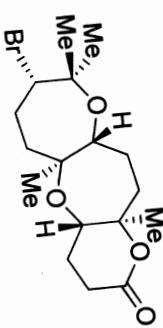


JtIII102b



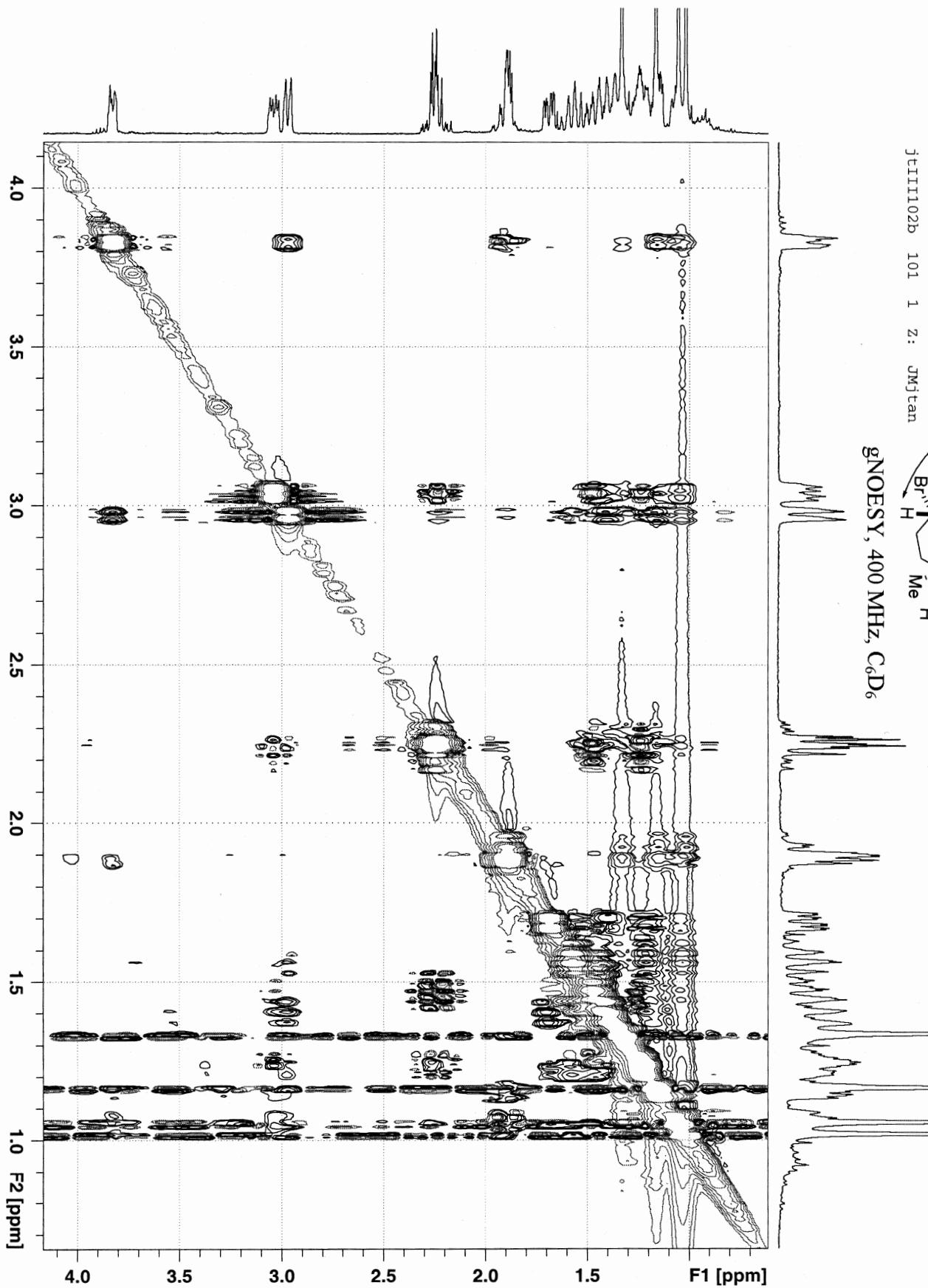
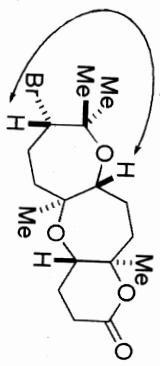
jTIII102b 100 1 Z: JMjtan

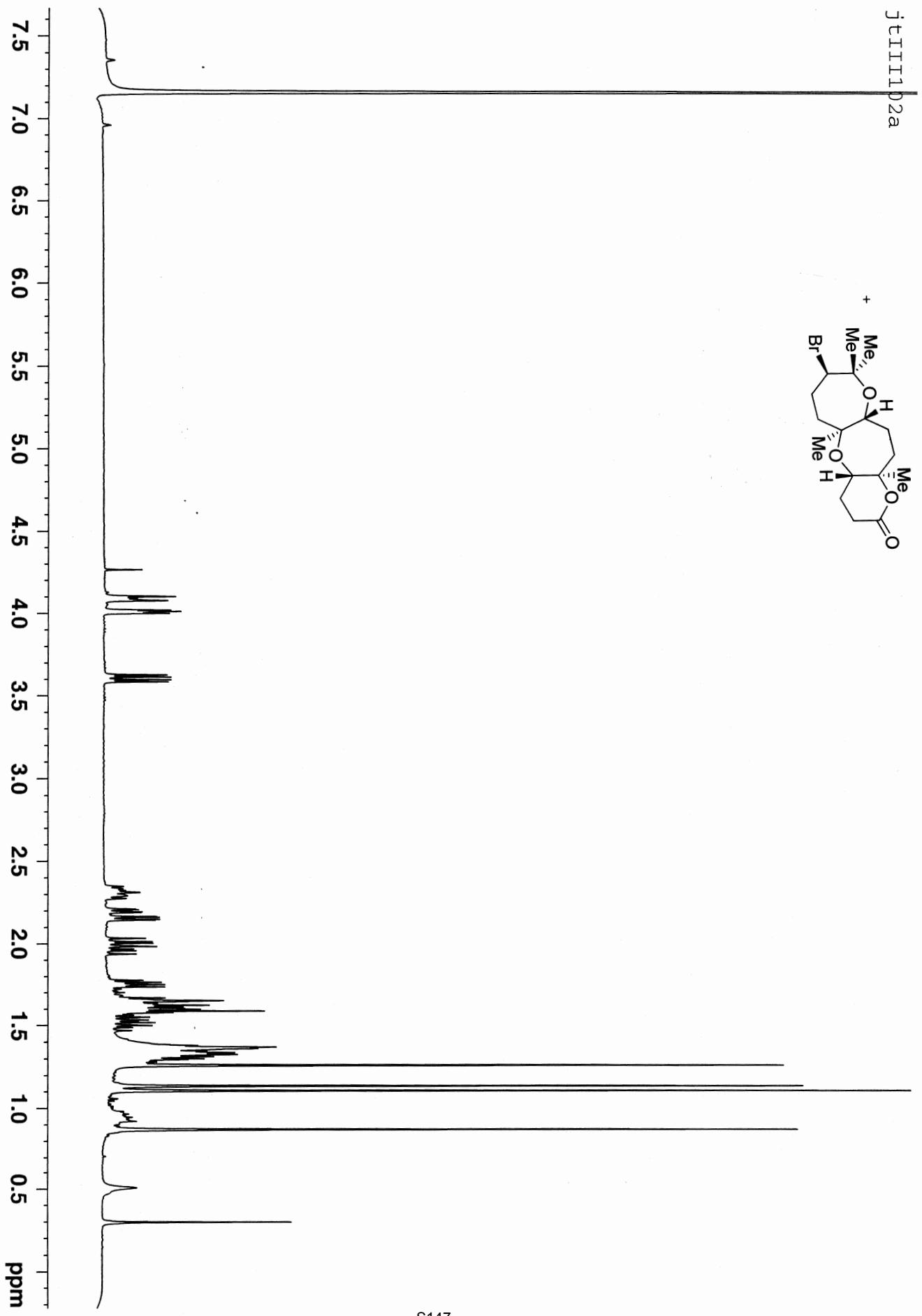
gHSQC, 400 MHz, C₆D₆



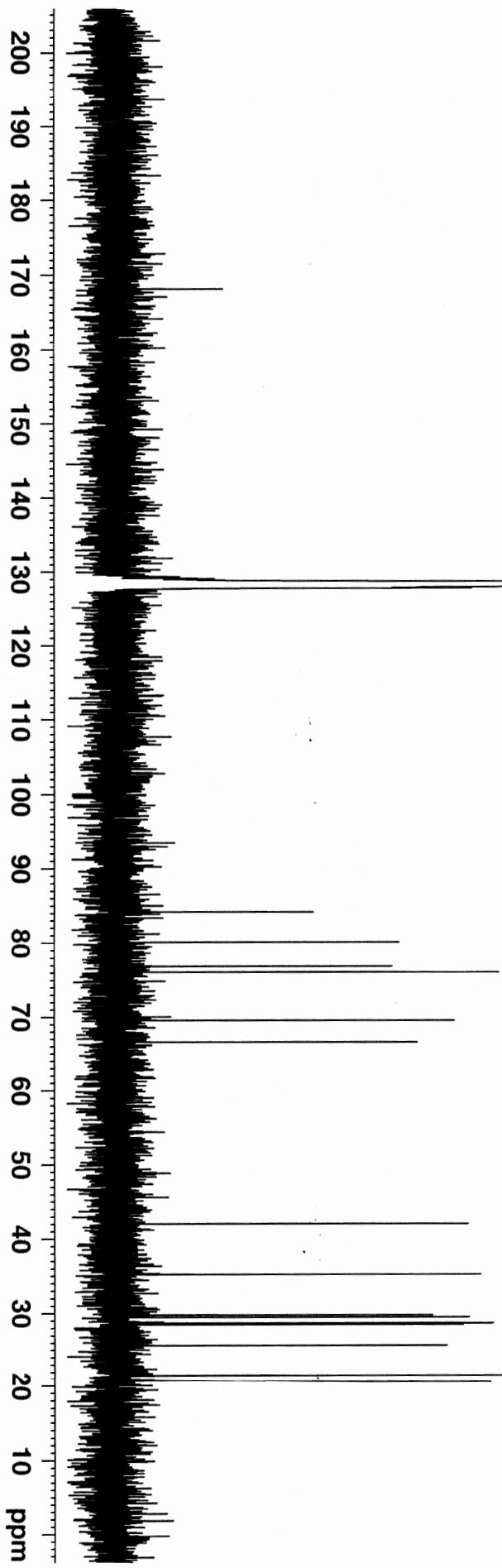
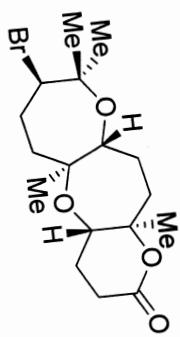
jtttt1102b 101 1 Z: JMjtan

gNOESY, 400 MHz, C₆D₆



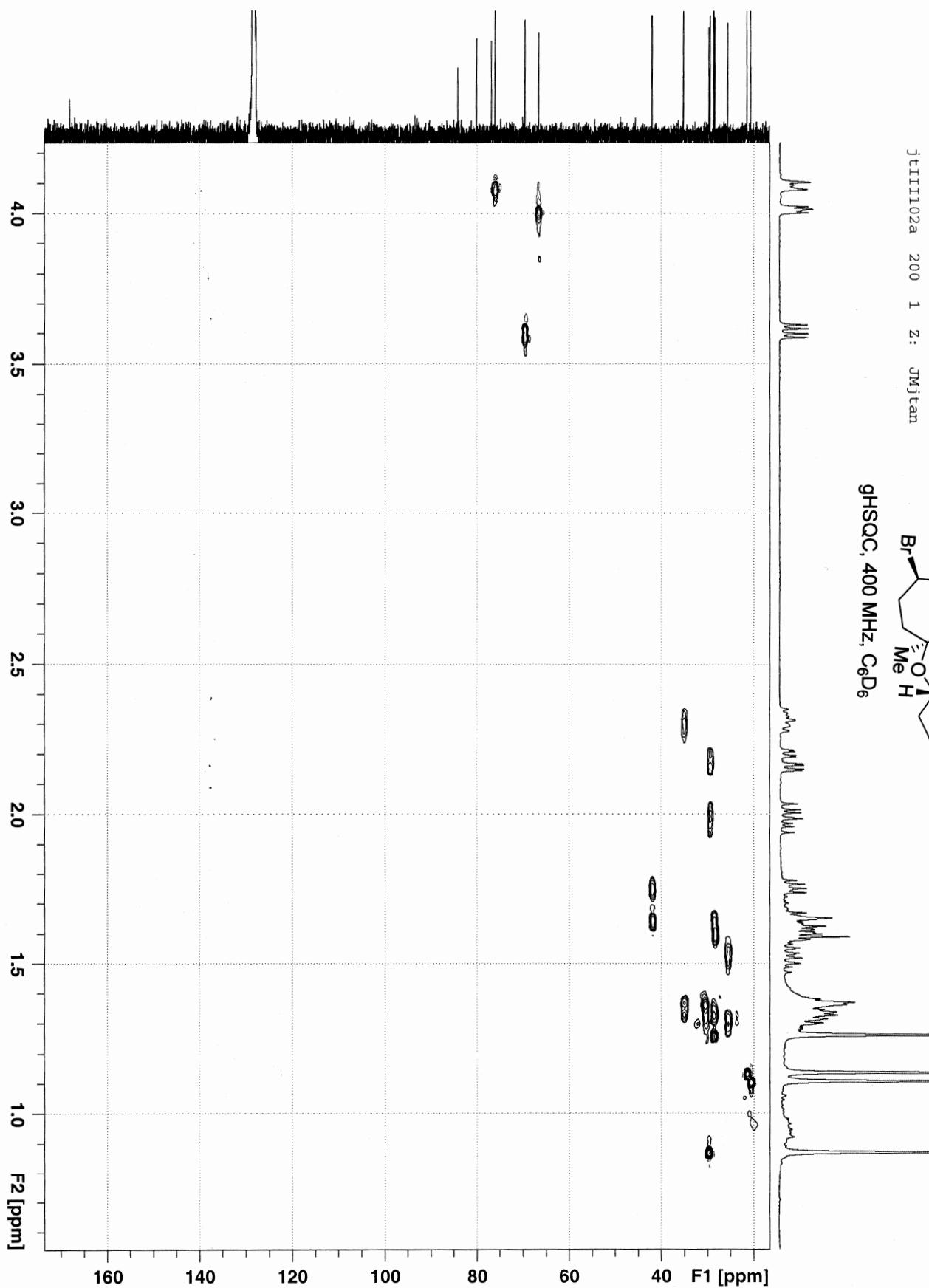
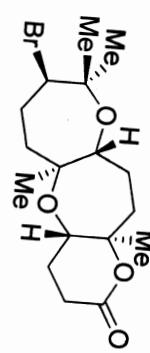


JtIII102a



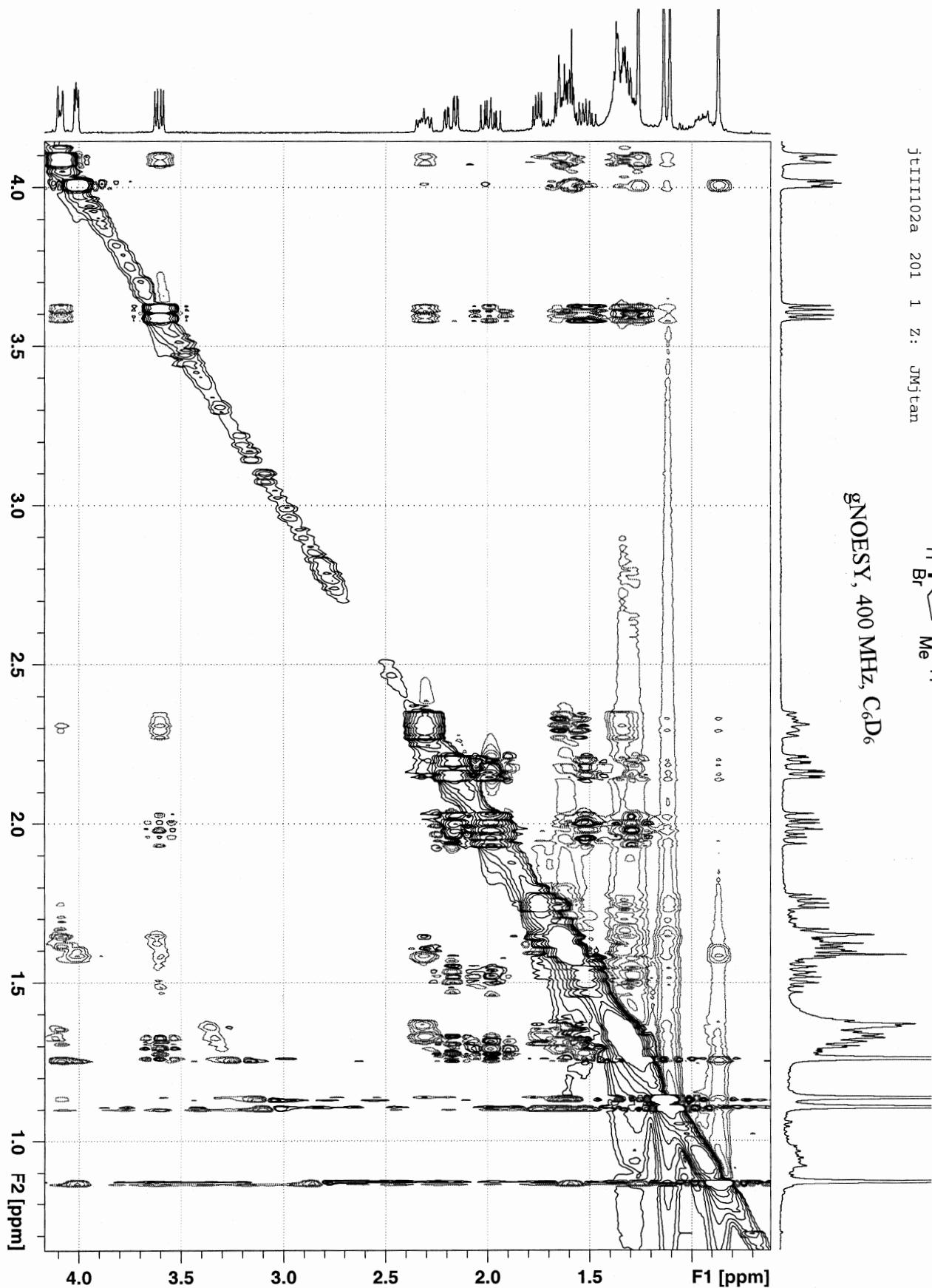
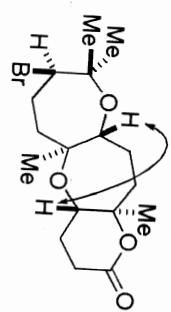
jt111102a 200 1 Z: Jmjtan

gHSQC, 400 MHz, C₆D₆

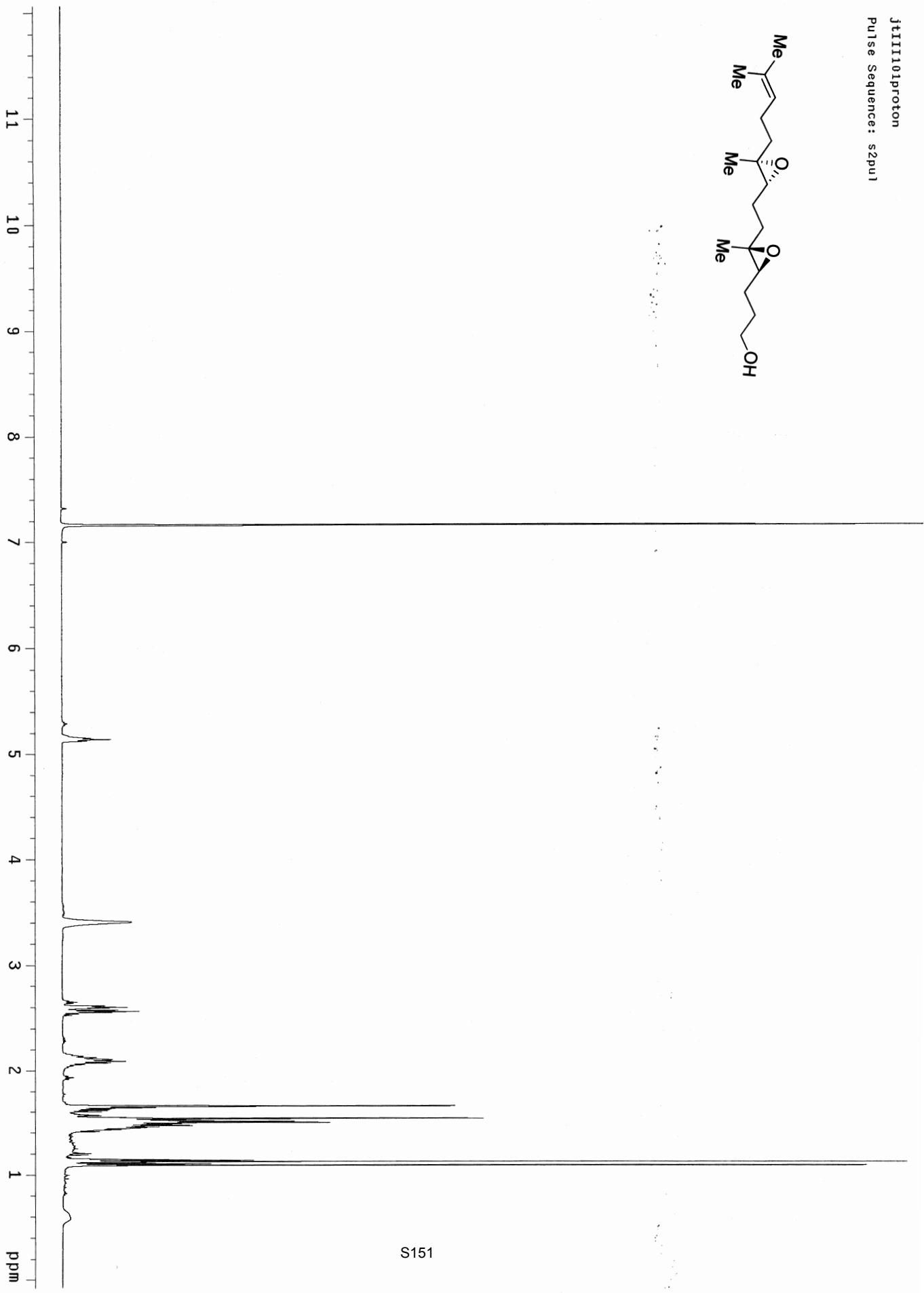


jtIII102a 201 1 Z: JMjtan

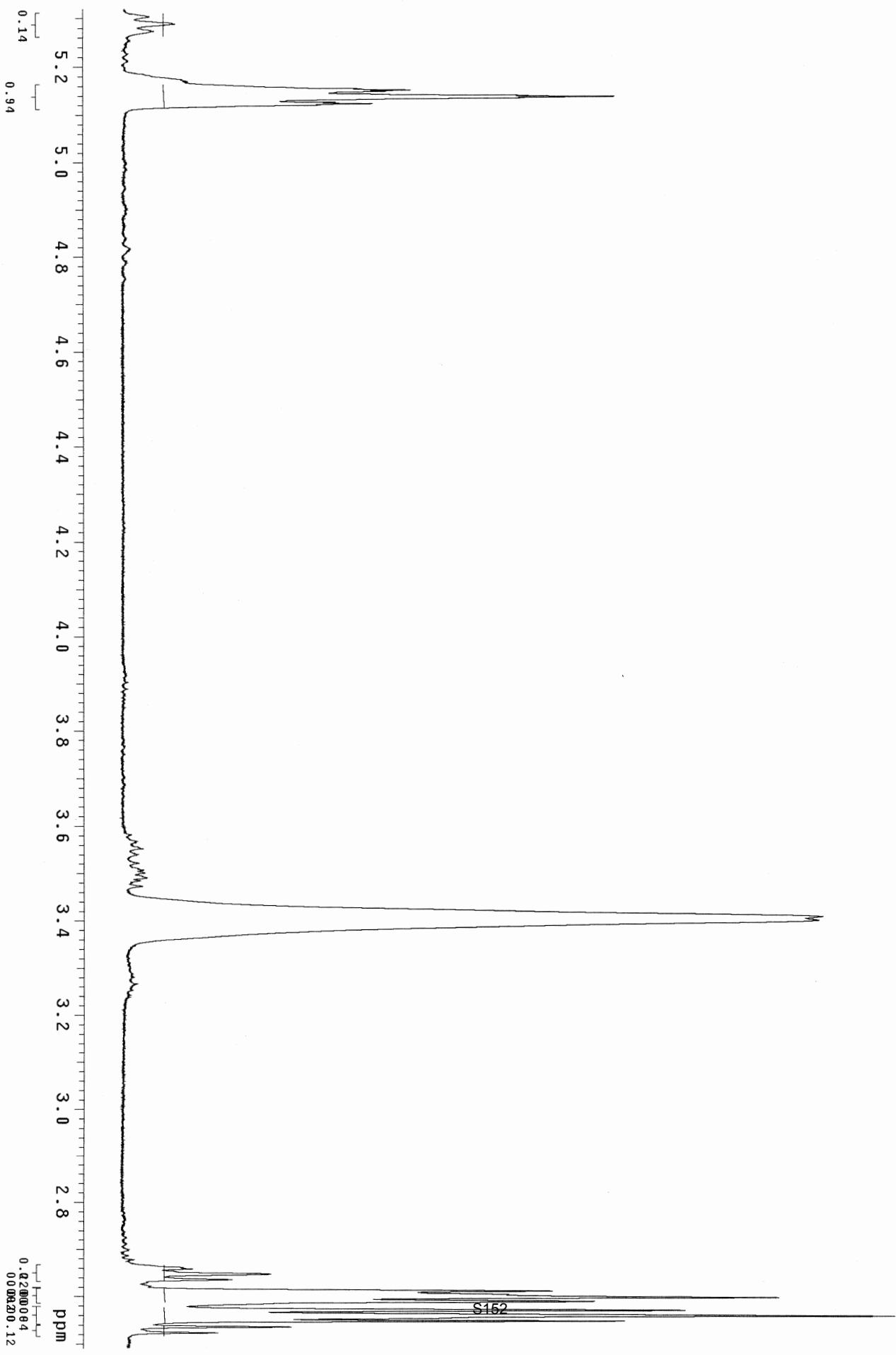
gNOESY, 400 MHz, C₆D₆



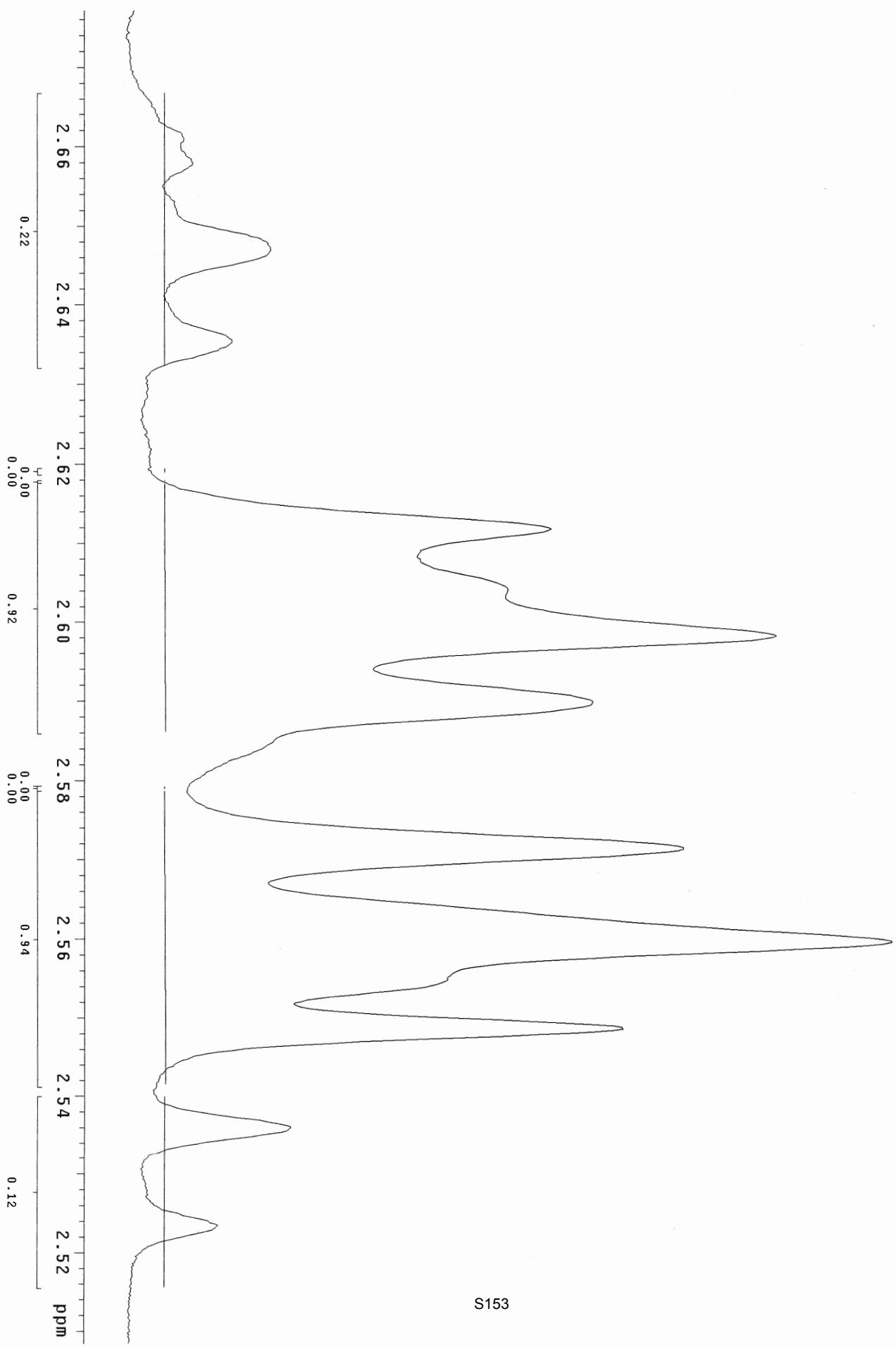
jt111101proton
Pulse Sequence: s2pul



jt111101proton
Pulse Sequence: s2pul



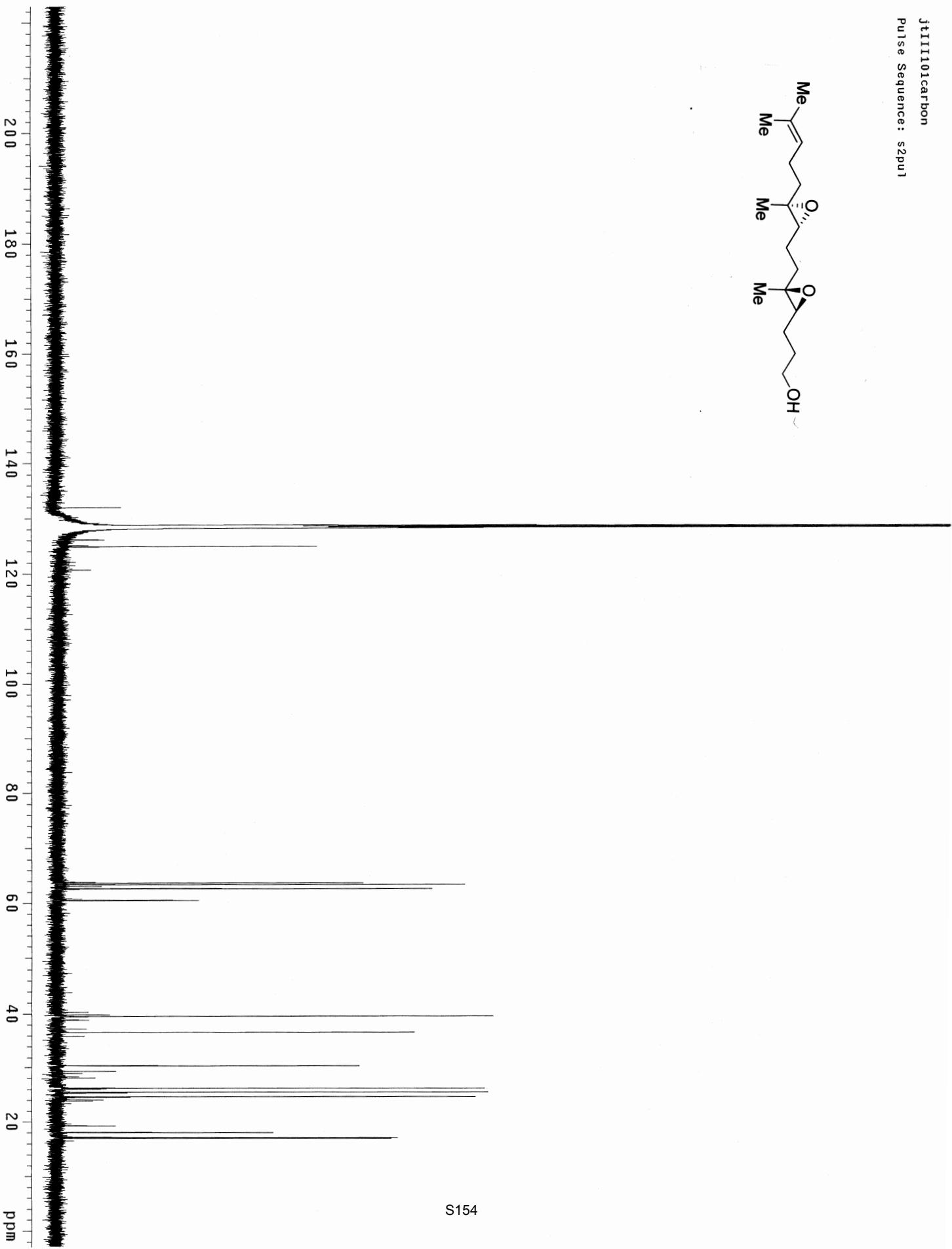
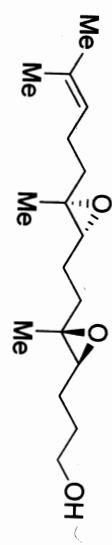
jt111101proton
Pulse Sequence: s2pul



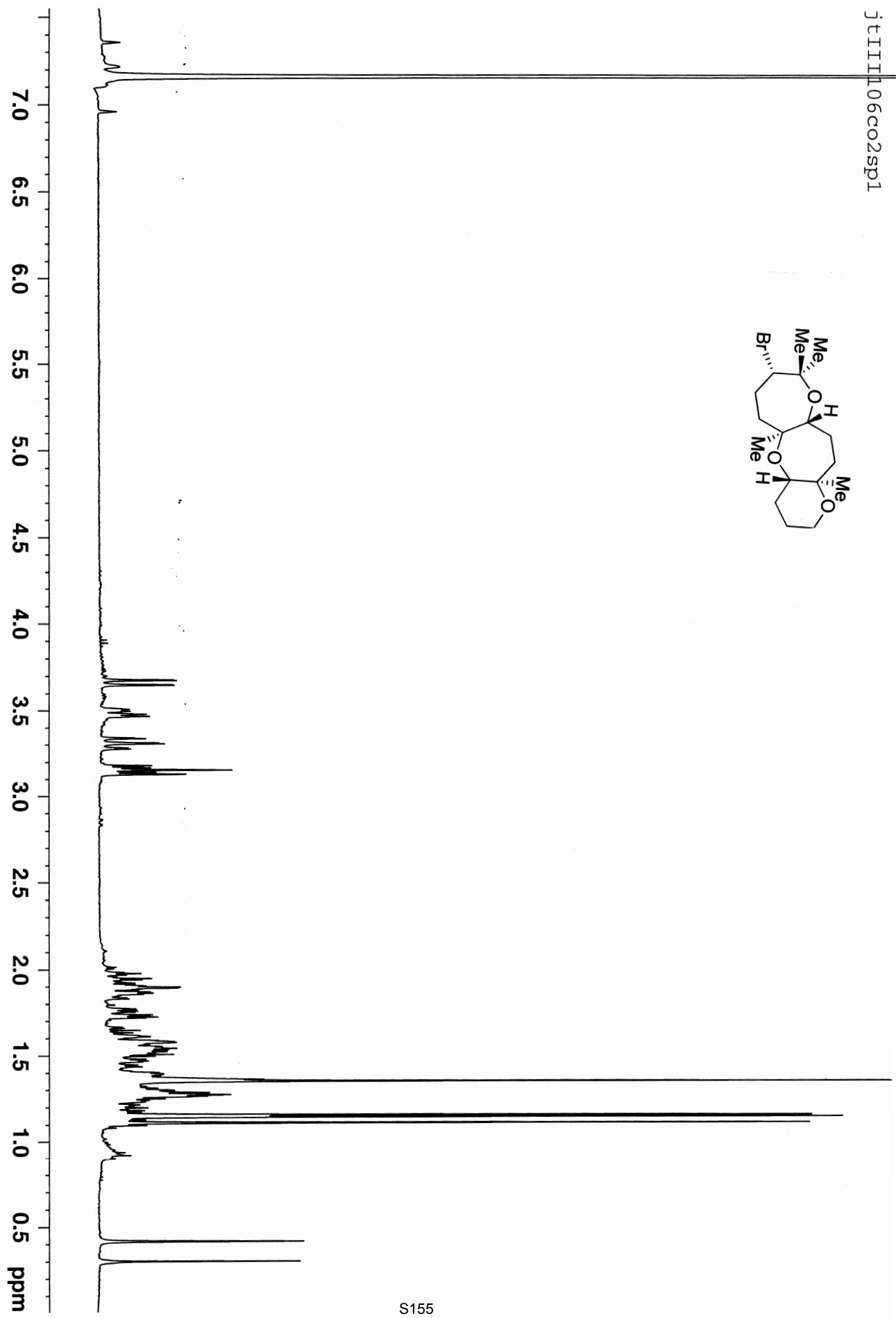
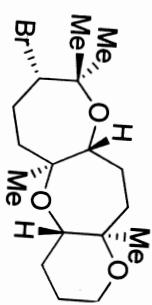
S153

jT111101carbon

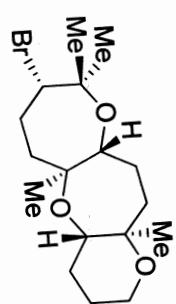
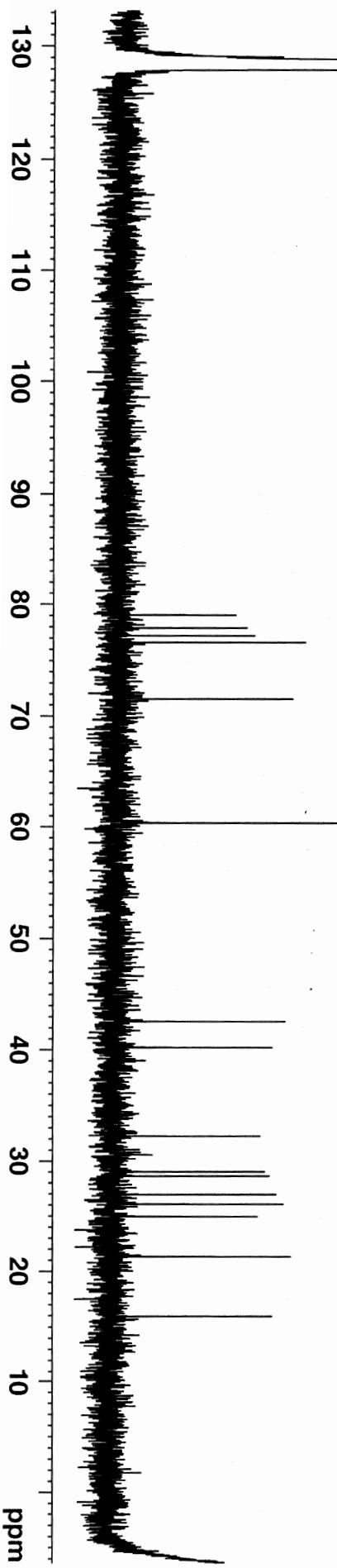
Pulse Sequence: s2pu1



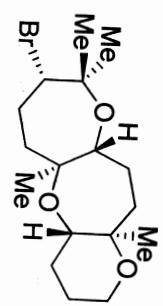
jtilt06co2spl



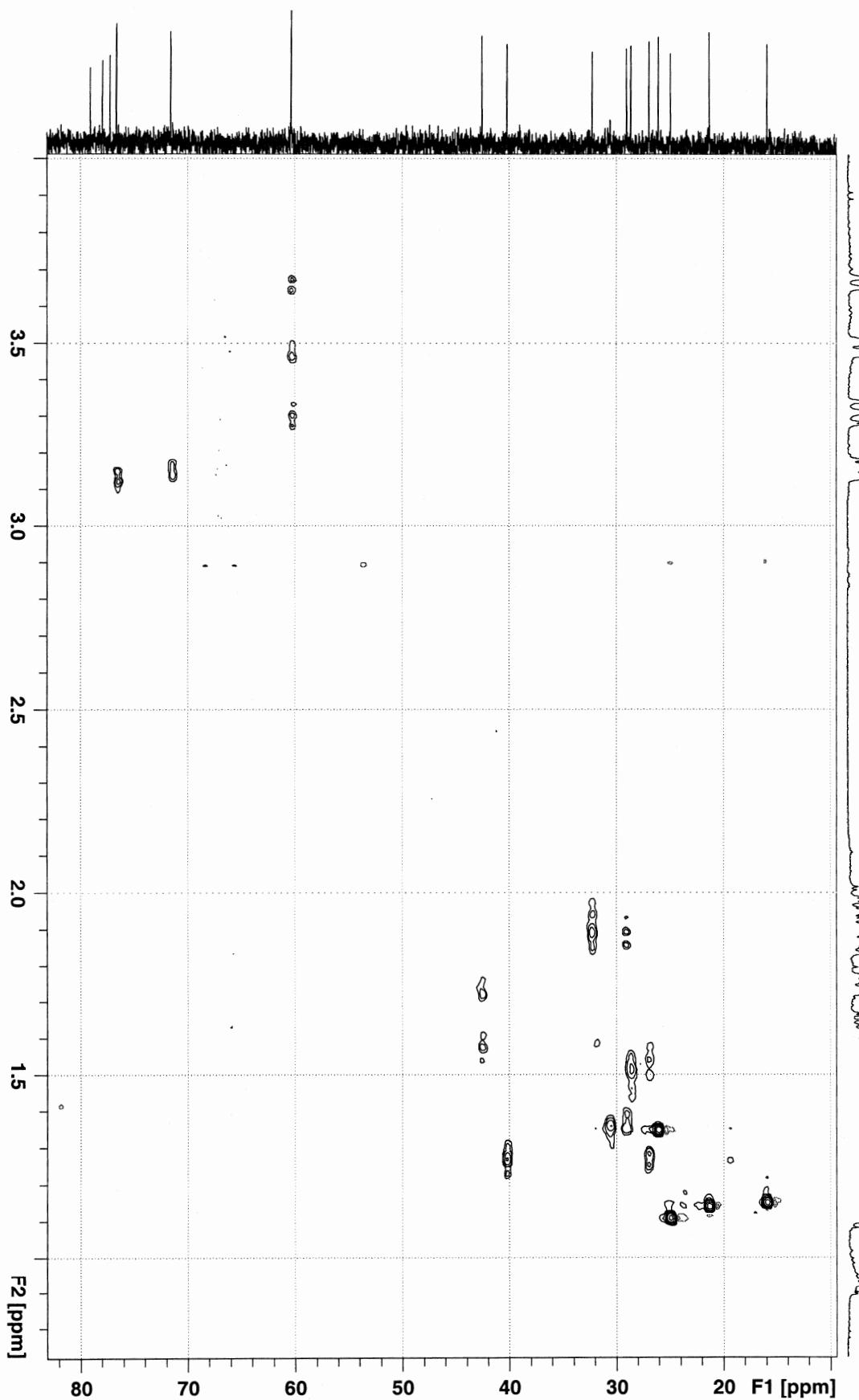
jt111106c02spl



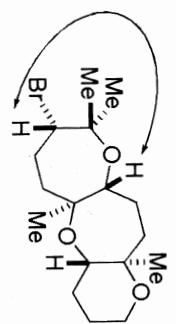
jtIII106co2sp1 100 1 Z: JMjtan



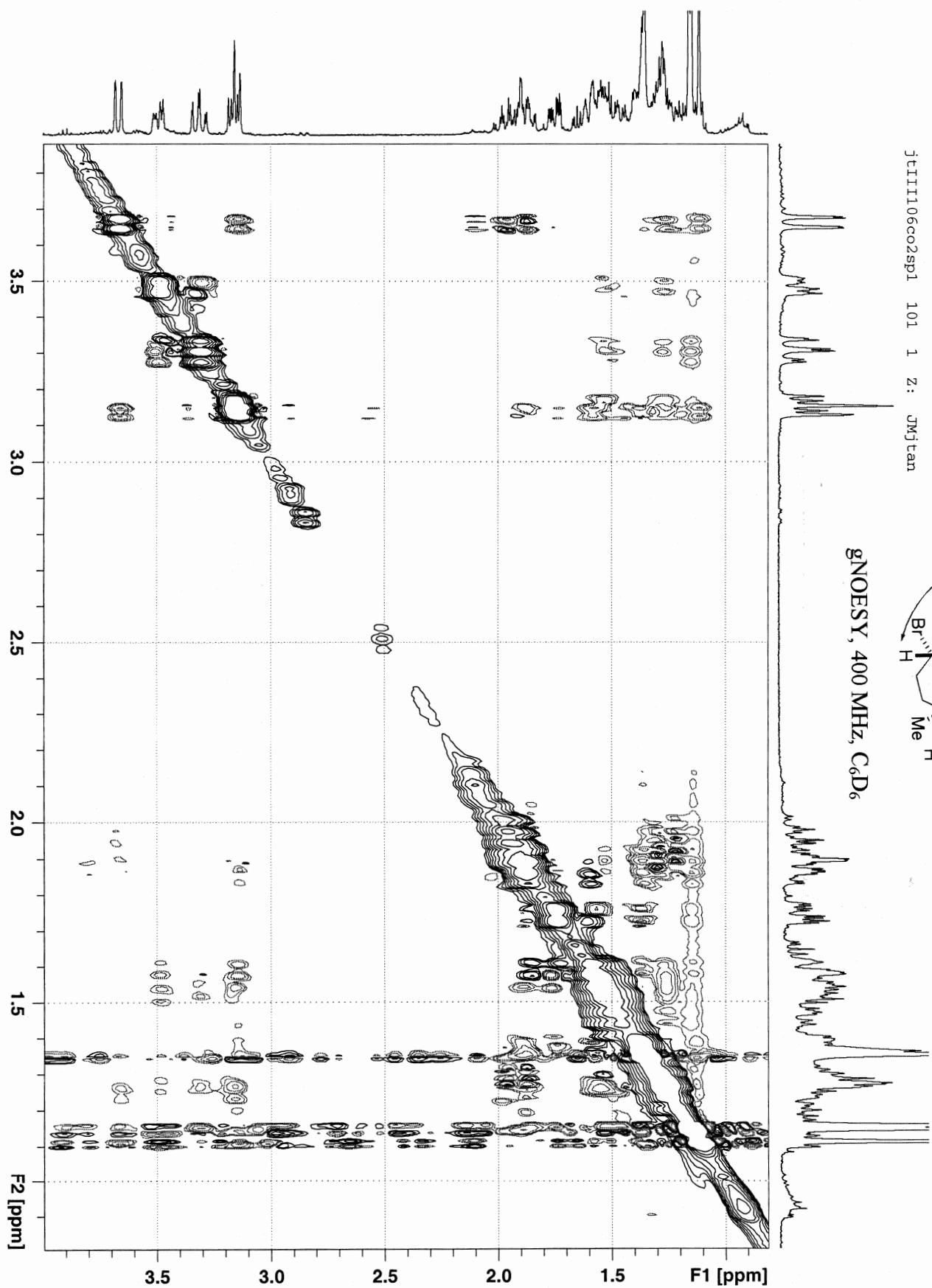
gHSQC, 400 MHz, C₆D₆



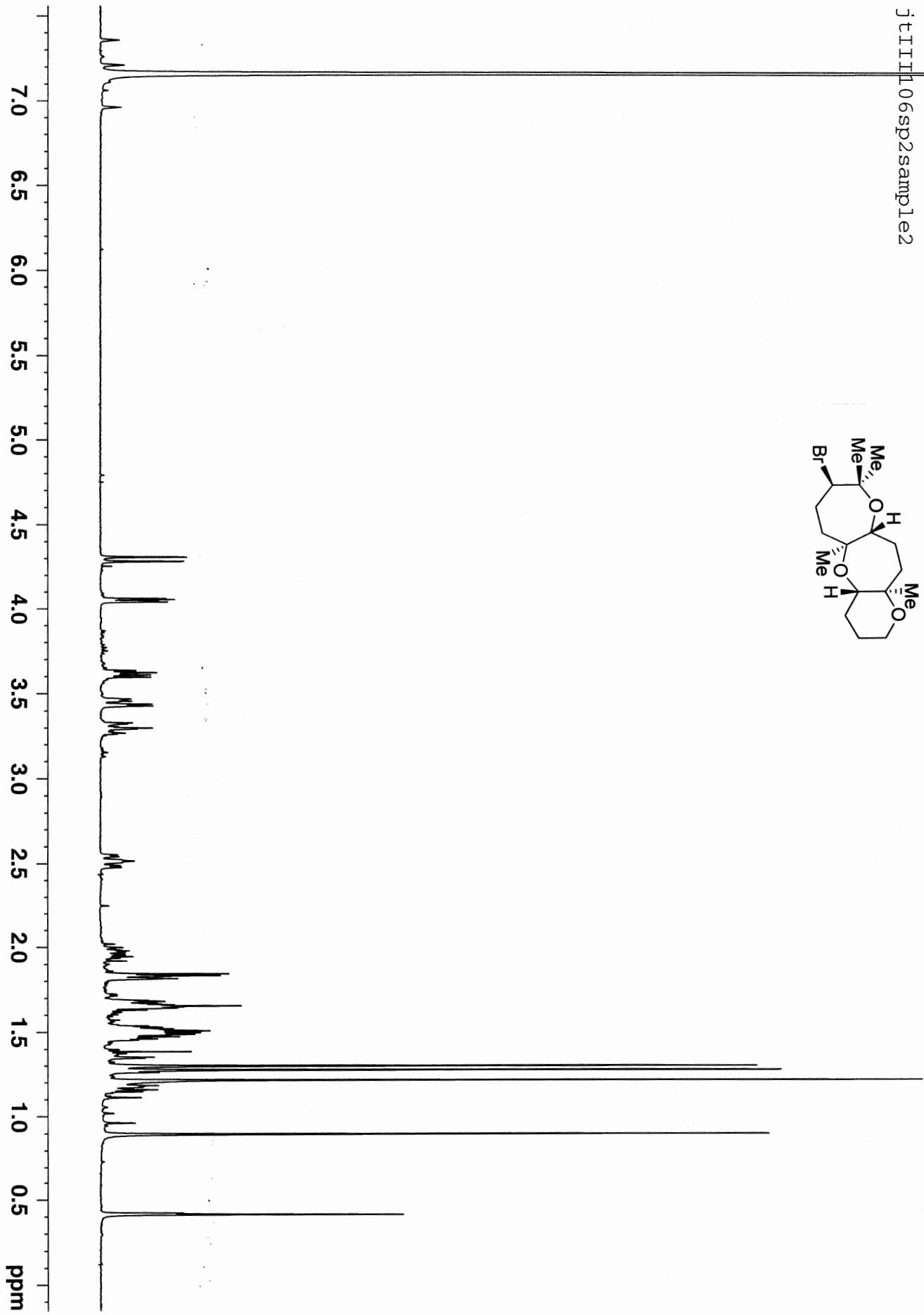
jttttttt106co2sp1 101 1 Z: JMjtan



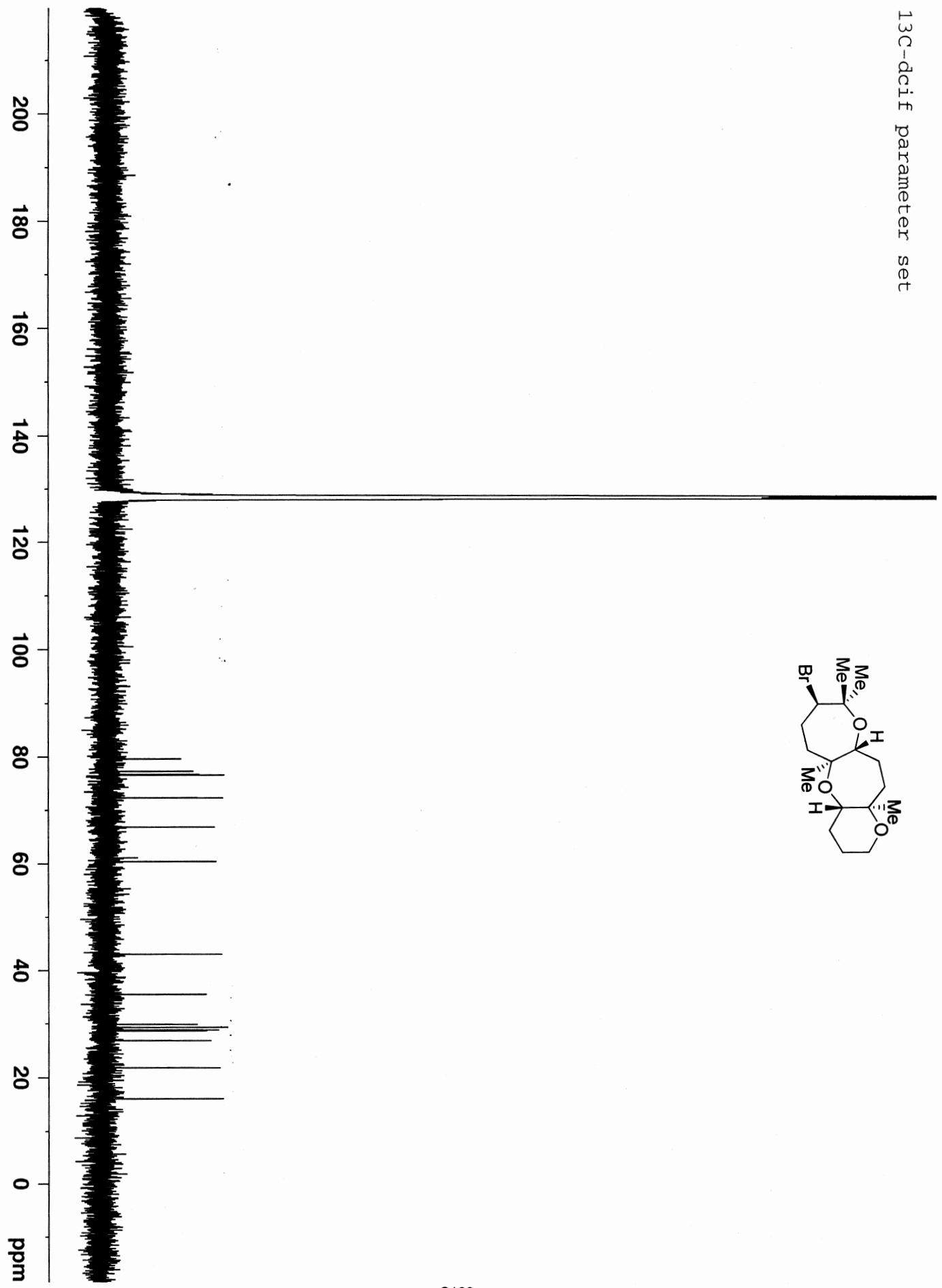
gNOESY, 400 MHz, C₆D₆



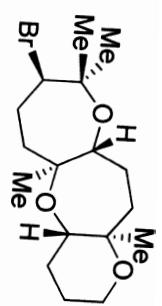
jtitlh06sp2sample



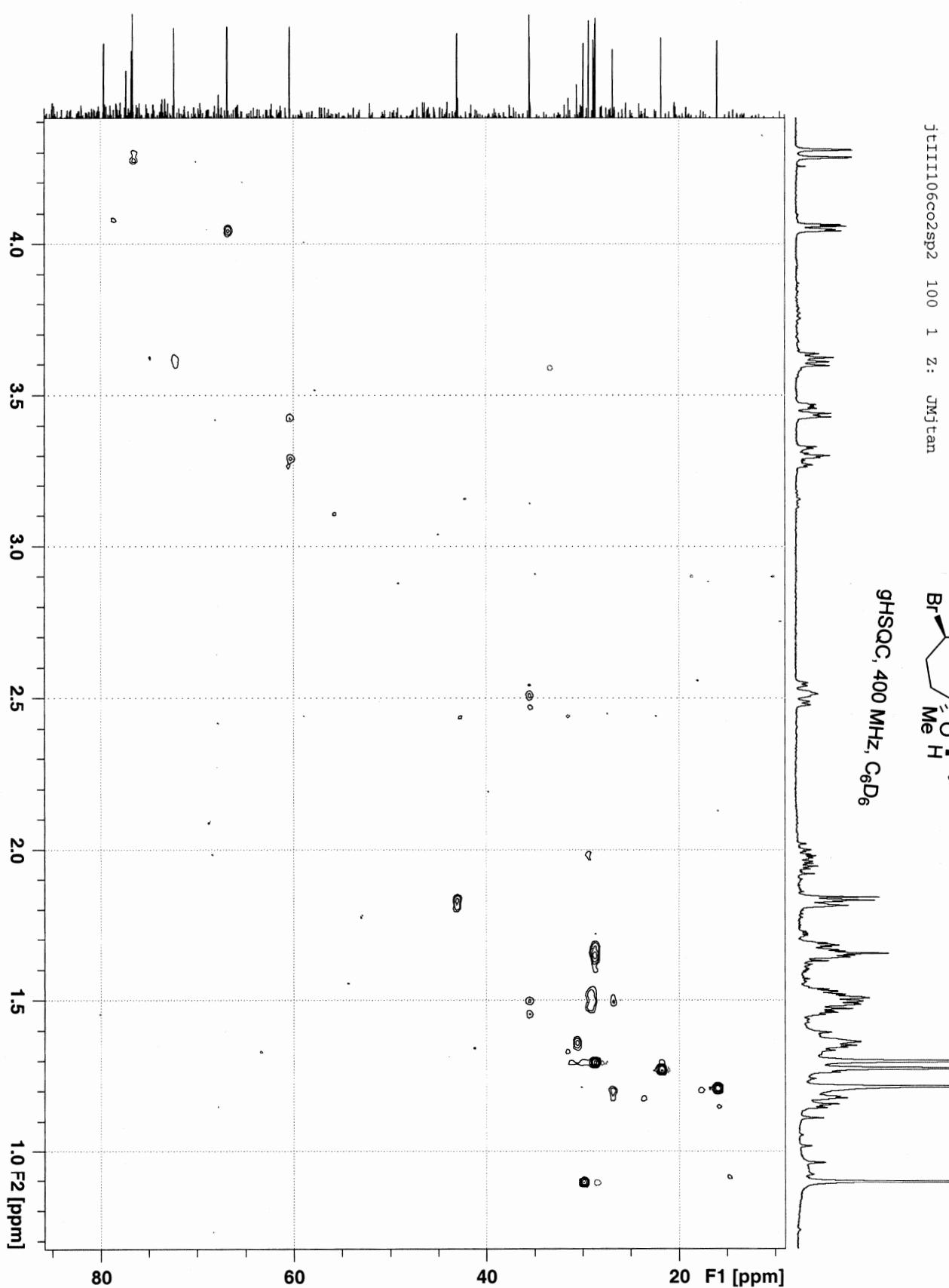
¹³C-dcif parameter set



jttttt106co2sp2 100 1 Z: JMjtan



gHSQC, 400 MHz, C₆D₆



jttttt106co2sp2 101 1 Z: JMjtan

gNOESY, 400 MHz, C₆D₆

