

Enantioselective Total Synthesis of Macfarlandin C, a Spongian Diterpenoid Harboring a Concave-Substituted *cis*-Dioxabicyclo[3.3.0]octanone Fragment

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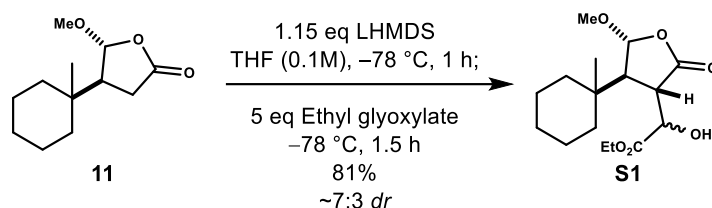
Materials and Methods:

Unless stated otherwise, reactions were conducted in oven-dried glassware under an atmosphere of argon. Tetrahydrofuran (THF), 1,2-dimethoxyethane (DME), dimethylformamide (DMF), toluene, dichloromethane (CH_2Cl_2), methanol (MeOH) and triethylamine were dried by passage through activated alumina. Commercial solutions of ethyl glyoxylate were distilled over P_2O_5 immediately prior to use. All other commercial reagents were used as received unless otherwise noted. Reaction temperatures were controlled using a temperature modulator, and unless stated otherwise, reactions were performed at rt (rt, approximately 23 °C). Thin-layer chromatography (TLC) was conducted with silica gel 60 F254 pre-coated plates, (0.25 mm) and visualized by exposure to UV light (254 nm) or by p-anisaldehyde, ceric ammonium molybdate, and potassium permanganate staining (KMnO_4). Silica gel 60 (particle size 0.040–0.063 mm) was used for flash column chromatography. ^1H NMR spectra were recorded at 500 or 600 MHz and are reported relative to deuterated solvent signals. Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. ^{13}C NMR spectra were recorded at 125 or 150 MHz. Data for ^{13}C NMR spectra are reported in terms of chemical shift. IR spectra were recorded on a ThermoFisher Nicolet iS5 FT-IR spectrometer with an iD7 ATR accessory and are reported in terms of frequency of absorption (cm^{-1}). High-resolution mass spectra were obtained from the UC Irvine Mass Spectrometry Facility with a Micromass LCT spectrometer. Optical rotation readings were obtained using JASCO P-1010 polarimeter. Kessil KSH150B LED Grow Light 150, Blue (34 W blue LED lamps) were purchased from <http://www.amazon.com>. Enantiomeric excess for compounds **22** and **26** were determined by HPLC analysis using an enantioselective column.

Abbreviations commonly used are: IPA (isopropyl alcohol), Hex (hexanes), DMAP (4-dimethylaminopyridine); For others, see: JOC Standard Abbreviations and Acronyms: http://pubs.acs.org/paragonplus/submission/jocea/jocea_abbreviations.pdf.

Experimental Procedures

Preparation of the Concave-Substituted *cis*-2,8-Dioxabicyclo[3.3.0]octanone Model System



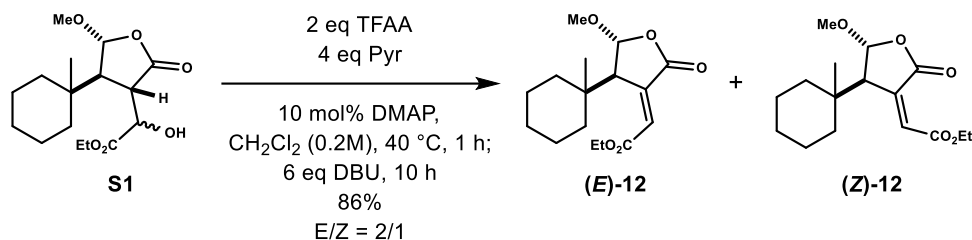
Preparation of Alcohol S1: A flame dried 250 mL round-bottom flask was charged with lactone **11**^{1,2} (1.37 g, 6.44 mmol) and THF (64 mL, 0.1 M). The solution was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of LHMDS (7.3 mL, 7.3 mmol, 1.15 eq, 1 M in THF) was added dropwise. The reaction was maintained at $-78\text{ }^{\circ}\text{C}$ for 1 h. During the enolate formation, ethyl glyoxylate (50 wt% in toluene) was distilled over P_2O_5 under argon (10–15 min at $110\text{ }^{\circ}\text{C}$ then warm to $140\text{ }^{\circ}\text{C}$ over 10 min then warm to $200\text{ }^{\circ}\text{C}$); the yellow distillate was used immediately. Freshly distilled ethyl glyoxylate (6.4 mL, 32 mmol, 5 eq) was added, the reaction mixture was maintained at $-78\text{ }^{\circ}\text{C}$ for 1.5 h, and then subsequently quenched by the addition of H_2O (50 mL) and allowed to warm to rt. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were then washed with brine (40 mL) and dried over MgSO_4 . The organic layer was filtered and concentrated to an orange oil. The residue was purified by column chromatography (SiO_2 , 20:1→4:1 Hex/EtOAc) to afford alcohol **S1** (1.64 g, 5.22 mmol, 81%) as a colorless oil and as a $\sim 7:3$ mixture of alcohol epimers. $R_f = 0.3$ (4:1 Hex/EtOAc, visualized with KMnO_4).

^1H NMR (600 MHz, CDCl_3): δ 5.23 (d, $J = 1.2$ Hz, 0.3H, minor), 5.17 (d, $J = 3.0$ Hz, 0.7H, major), 4.66 (dd, $J = 3.0, 8.9$, 0.3H, minor), 4.39–4.25 (m, 2.4H, major and minor), 4.18–4.10 (m, 0.3H, minor), 3.52 (s, 0.9H, minor), 3.51 (s, 2.1H, major), 3.48–3.44 (m, 0.3H, minor), 3.25 (d, $J = 4.1$ Hz, 0.7H, major), 3.08 (dd, $J = 3.0, 6.5$ Hz, 0.7H, major), 3.07 (app t, $J = 3.4$ Hz, 0.3H, minor), 2.40 (dd, $J = 3.1, 6.2$ Hz, 0.7H, major), 2.15–2.11 (m, 0.3H, minor), 1.64–1.51 (m, 3H), 1.50–1.41 (m, 2H), 1.38–1.21 (m, 5H), 1.35 (t, $J = 7.0$ Hz, 2.1H, major), 1.31 (t, $J = 7.1$ Hz, 0.9H, minor), 0.93 (s, 2.1H, major), 0.84 (s, 0.9H, minor)

^{13}C NMR (150 MHz, CDCl_3): δ (Major) 174.6, 172.4, 105.9, 70.5, 62.6, 57.2, 45.8, 35.6, 35.4, 34.4, 31.6, 25.9, 21.4, 21.3, 20.3, 14.0, (Minor) 176.1, 172.3, 105.3, 70.7, 62.0, 56.8, 45.4, 34.9, 34.6, 33.9, 29.7, 25.9, 21.37, 21.33, 19.5, 14.0

IR (thin film) 3475, 2927, 2852, 1773, 1737, 1446, 1371, 1263, 1220, 1184, 1121

HRMS (ESI) calculated for $[\text{C}_{16}\text{H}_{26}\text{O}_6\text{Na}]^+$ ($\text{M}+\text{Na}$) 337.1627, observed 337.1614



Preparation of Alkenes 12: A 100 mL round-bottom flask was charged with alcohol **S1** (1.63 g, 5.2 mmol), DMAP (63 mg, 0.52 mmol, 10 mol%), and CH_2Cl_2 (25 mL, 0.2 M). After sequential addition of pyridine (1.67 mL, 20.8 mmol, 4 eq) and trifluoroacetic anhydride (1.4 mL, 10 mmol, 2 eq), the reaction mixture was maintained at 40 °C for 1 h when complete consumption of the starting material was observed by TLC analysis. The reaction was cooled to rt and DBU (4.6 mL, 31 mmol, 6 eq) was added via syringe. The mixture was stirred at rt for 1 h and then quenched by the addition of H_2O (20 mL). The layers were separated and the aqueous layer was washed with CH_2Cl_2 (2 x 20 mL). The combined organic layers were then washed with brine (30 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure to a brown oil. This residue was purified by flash column chromatography (SiO_2 , 20:1 \rightarrow 10:1 Hex/EtOAc) to afford (*E*)-**12** (865 mg, 2.91 mmol, 56%) and (*Z*)-**12** (459 mg, 1.56 mmol, 30%) as colorless oils. $R_f = 0.60$ and 0.45 (4:1 Hex/EtOAc), respectively.

12: (*E*)-Alkene

$^1\text{H NMR}$ (600 MHz, CDCl_3): δ 6.90 (d, $J = 1.6$ Hz, 1H), 5.39 (s, 1H), 4.31-4.19 (m, 2H), 3.51 (d, $J = 1.6$ Hz, 1H), 3.48 (s, 3H), 1.66-1.59 (m, 1H), 1.56-1.50 (m, 2H), 1.49-1.35 (m, 3H), 1.32 (t, $J = 7.1$ Hz, 3H), 1.29-1.18 (m, 3H), 1.15-1.06 (m, 1H), 0.94 (s, 3H)

$^{13}\text{C NMR}$ (150 MHz, CDCl_3): δ 170.4, 165.2, 141.2, 127.9, 104.9, 61.2, 56.47, 55.7, 38.0, 35.0, 34.2, 25.8, 21.6, 21.5, 19.6, 14.1

IR (thin film) 2927, 2851, 1776, 1724, 1465, 1446, 1372, 1353, 1255, 1206, 1113, 1065, 1024, 999, 929, 786, 673

HRMS (ESI) calculated for $[\text{C}_{16}\text{H}_{24}\text{NaO}_5]^+$ (M) 319.1521, observed 319.1533

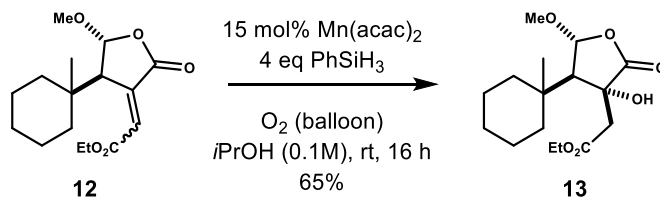
12: (*Z*)-Alkene

$^1\text{H NMR}$ (600 MHz, CDCl_3): δ 6.27 (d, $J = 1.6$ Hz, 1H), 5.27 (s, 1H), 4.31 (q, $J = 7.2$ Hz, 2H), 3.48 (s, 3H), 2.69 (s, 1H), 1.60-1.37 (m, 8H), 1.34 (t, $J = 7.2$ Hz, 3H), 1.31-1.22 (m, 2H), 0.87 (s, 3H)

$^{13}\text{C NMR}$ (150 MHz, CDCl_3): δ 167.1, 165.1, 133.0, 130.6, 104.1, 61.7, 56.5, 55.5, 35.7, 35.2, 34.6, 25.9, 21.44, 21.40, 20.5, 14.0

IR (thin film) 2927, 2851, 1772, 1732, 1465, 1446, 1367, 1328, 1219, 1176, 1090, 1025, 942, 674

HRMS (ESI) calculated for $[\text{C}_{16}\text{H}_{24}\text{NaO}_5]^+$ (M) 319.1521, observed 319.1533



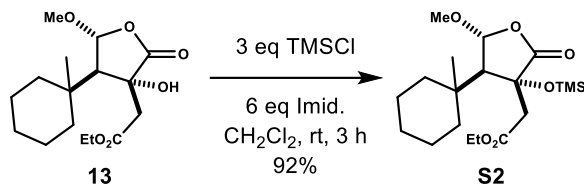
Preparation of Alcohol 14: A 25 mL round-bottom flask was charged with alkenes **12** (169 mg, 0.57 mmol) and *i*PrOH (6 mL, 0.1 M). The mixture was sparged with O₂ for 5 min. Then Mn(acac)₂ (23.5 mg, 0.092 mmol, 15 mol%) and PhSiH₃ (0.28 mL, 2.26 mmol, 4 eq) were added. The mixture was gently warmed with a heat gun until the reaction turned yellow in color and started to bubble. The reaction was then allowed to cool to rt and stirred at rt for 24 h. The reaction was then concentrated under reduced pressure and purified by flash column chromatography (SiO₂, 10:1→4:1 Hex/EtOAc) to afford alcohol **13** (116 mg, 65%) as a colorless oil that solidifies over time. R_f = 0.3 (9:1 Hex/EtOAc, visualized with KMnO₄). X-ray quality crystals were obtained by slow evaporation from chloroform.

¹H NMR (600 MHz, CDCl₃): δ 5.31 (d, *J* = 7.3 Hz, 1H), 4.68 (s, 1H), 4.26-4.16 (m, 2H), 3.57 (s, 3H), 2.98 (d, *J* = 15.1 Hz, 1H), 2.68 (d, *J* = 15.0 Hz, 1H), 2.48 (d, *J* = 7.4 Hz, 1H), 1.70-1.64 (m, 1H), 1.63-1.57 (m, 1H), 1.55-1.48 (m, 2H), 1.48-1.38 (m, 5H), 1.32-1.24 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.09 (s, 3H)

¹³C NMR (150 MHz, CDCl₃): δ 175.1, 170.5, 104.4, 77.0, 61.7, 58.2, 57.5, 39.2, 38.2, 36.3, 34.4, 25.8, 22.3, 21.4, 21.3, 14.0

IR (thin film) 3448, 2930, 2854, 1782, 1735, 1448, 1392, 1373, 1298, 1216, 1175, 1135, 1044, 922

HRMS (ESI) calculated for [C₁₆H₂₇O₆]⁺ (M) 315.1808, observed 315.1811



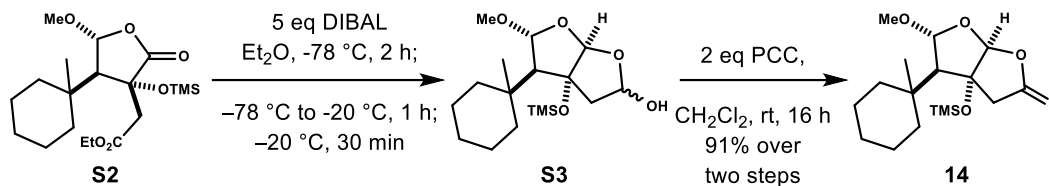
Preparation of TMS-protected Alcohol S2: A 10 mL round-bottom flask was charged with alcohol **13** (113 mg, 0.358 mmol) and CH_2Cl_2 (3 mL, 0.1 M). Imidazole (148 mg, 2.17 mmol, 6 eq) was added, followed by freshly distilled TMSCl (0.14 mL, 1.1 mmol, 3 eq). The reaction was then stirred at rt for 3 h, at which time TLC analysis indicated consumption of starting material. The reaction was quenched by the addition of H_2O (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The organic layers were then dried over MgSO_4 , filtered, and concentrated to afford lactone **S2** (127 mg, 92%) as a pale-yellow oil that was used without further purification. $R_f = 0.66$ (4:1 Hex/EtOAc, visualized with KMnO_4).

$^1\text{H NMR}$ (600 MHz, C_6D_6): δ 5.32 (d, $J = 7.7$ Hz, 1H), 3.93 (dq, $J = 7.1, 11.0$ Hz, 1H), 3.79 (dq, $J = 7.1, 11.0$ Hz, 1H), 3.13 (s, 3H), 3.10 (d, $J = 16.4$ Hz, 1H), 2.93 (d, $J = 16.4$ Hz, 1H), 2.58 (d, $J = 7.7$ Hz, 1H), 1.67-1.58 (m, 1H), 1.55-1.43 (m, 3H), 1.43-1.30 (m, 4H), 1.30-1.25 (m, 1H), 1.24-1.14 (m, 1H), 0.93 (s, 3H), 0.91 (t, $J = 7.1$ Hz, 3H), 0.33 (s, 9H)

$^{13}\text{C NMR}$ (150 MHz, C_6D_6): δ 174.3, 169.0, 104.2, 79.7, 61.5, 60.4, 56.6, 42.9, 38.0, 36.5, 34.3, 25.9, 21.8, 21.6, 21.4, 13.6, 1.6

IR (thin film) 2925, 2850, 1780, 1739, 1373, 1339, 1248, 1132, 954, 844

HRMS (ESI) calculated for $[\text{C}_{19}\text{H}_{34}\text{NaO}_6\text{Si}]^+$ (M)⁺ 409.2022, observed 409.2013



Preparation of Dioxabicyclo[3.3.0]octan-3-one 14: A 10 mL round-bottom flask was charged with lactone **S2** (19 mg, 0.05 mmol) and Et₂O (1.5 mL, 0.03 M). The mixture was cooled to $-78\text{ }^\circ\text{C}$ and DIBAL (0.25 mL, 0.25 mmol, 5 eq, 1 M in Hexanes) was added. The reaction was then stirred at $-78\text{ }^\circ\text{C}$ for 2 h and then allowed to warm passively over an hour to $-20\text{ }^\circ\text{C}$. The reaction was stirred at $-20\text{ }^\circ\text{C}$ for 30 min and then quenched by the addition of an aqueous solution of saturated with Rochelle's salt (2 mL) and saturated aqueous NaHCO₃ (2 mL). The mixture was then vigorously stirred for 30 min. The reaction mixture was then extracted with Et₂O (3 x 10 mL). The organic extracts were then dried over MgSO₄, filtered and concentrated to afford lactols **S3** as a colorless oil.

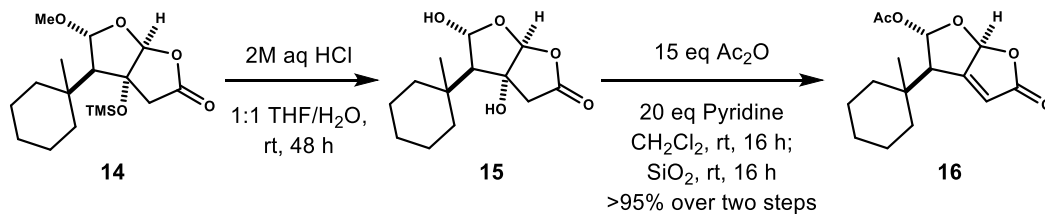
A 10 mL round-bottom flask was charged with the crude lactols **S3** and CH₂Cl₂ (1.5 mL, 0.03 M). PCC (22 mg, 0.10 mmol, 2 eq) was added and the reaction mixture was stirred at rt for 16 h. Celite (2 g) was added to the reaction mixture followed by dilution with 10 mL of 4:1 hexane/EtOAc. The mixture was then filtered through a SiO₂ plug with 4:1 hexane/EtOAc (30 mL). The filtrate was concentrated to afford dioxabicyclo[3.3.0]octanone **14** (16 mg, 91% over two steps) as a colorless oil: $R_f = 0.35$ (9:1 hexanes/EtOAc, visualized with KMnO₄). This material was taken on without further purification, as the TMS-protecting group was quite labile. A small sample was purified by flash column chromatography for characterization purposes.

¹H NMR (600 MHz, C₆D₆): δ 5.71 (s, 1H), 4.55 (d, $J = 6.4$ Hz, 1H), 3.16 (s, 3H), 2.63 (d, $J = 17.4$ Hz, 1H), 2.43 (d, $J = 6.3$ Hz, 1H), 2.28 (d, $J = 17.4$ Hz, 1H), 1.53-1.03 (m, 10H), 0.70 (s, 3H), 0.01 (s, 9H)

¹³C NMR (150 MHz, C₆D₆): δ 174.2, 106.8, 105.0, 85.3, 55.4, 39.0, 37.4, 37.0, 34.2, 25.9, 21.6, 21.3, 1.2

IR (thin film) 2924, 2850, 1803, 1254, 1162, 1129, 1111, 1054, 1031, 946, 913, 844

HRMS (ESI) calculated for [C₁₇H₃₀NaO₅Si]⁺ (M) 365.1760, observed 365.1761



Preparation of Dioxabicyclo[3.3.0]oct-4-en-3-one 16: A 10 mL round-bottom flask was charged with lactone **14** (12 mg, 0.035 mmol) and THF (1 mL, 0.03 M). Aqueous HCl (1 mL, 4 M aqueous, 110 eq) was added, and the reaction mixture was allowed to stir at rt for 48 h. The reaction was then diluted with H₂O (10 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were then dried over MgSO₄, filtered and concentrated to afford lactol **15** as colorless oil.

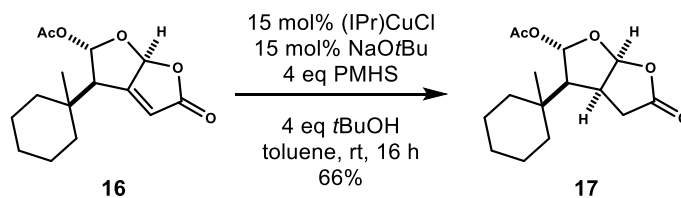
A 10 mL round-bottom flask was charged with the crude lactol **15**, DMAP (1.5 mg, 0.012 mmol, 35 mol%) and CH₂Cl₂ (2 mL, 0.01 M). Then freshly distilled pyridine (60 μL, 0.75 mmol, 20 eq) was added followed by Ac₂O (50 μL, 0.53 mmol, 15 eq). The reaction mixture was then stirred at rt for 24 h. The reaction was quenched by the addition of H₂O (10 mL) and extracted with CH₂Cl₂ (3 x 5 mL). The combined organic layers were dried over MgSO₄ and filtered. SiO₂ (2 g) was added to the filtrate and the mixture was concentrated to give a colorless solid, which was allowed to sit at rt under vacuum for 16 h. The material was then purified by column chromatography (SiO₂, 4:1 Hex/EtOAc) to afford butenolide **16** (10 mg, >95%) as a colorless oil. R_f = 0.26 (4:1 Hex/EtOAc, visualized with KMnO₄).

¹H NMR (600 MHz, CDCl₃): δ 6.48 (d, *J* = 3.9 Hz, 1H), 6.16 (s, 1H), 5.97 (d, *J* = 2.1 Hz, 1H), 3.25-3.21 (m, 1H), 2.13 (s, 3H), 1.54-1.48 (m, 4H), 1.47-1.35 (m, 3H), 1.34-1.27 (m, 3H), 1.01 (s, 3H)

¹³C NMR (150 MHz, CDCl₃): δ 171.0, 169.3, 167.5, 115.4, 104.1, 100.5, 53.7, 36.2, 36.1, 34.3, 25.9, 21.5, 21.3, 21.2, 20.7

IR (thin film) 2925, 2851, 1790, 1749, 1660, 1446, 1368, 1215, 1164, 1133, 1043, 987, 973, 944, 863

HRMS (ESI) calculated for [C₁₅H₂₀NaO₅]⁺ (M+Na) 303.1208, observed 303.1214



Preparation of Dioxabicyclo[3.3.0]octan-3-one **17:** A 5 mL round-bottom flask was charged with (*i*Pr)CuCl (2.3 mg, 0.0047 mmol, 15 mol%), NaOtBu (0.05 mL, 0.1 M in toluene, 15 mol%), and toluene (0.5 mL). PMHS (7 μ L, 0.1 mmol, 4 eq) was added as a solution in toluene (0.1 mL). The reaction mixture was then stirred for 5 min. Then a solution of butenolide **16** (8.1 mg, 0.029 mmol) and *t*BuOH (11 μ L, 0.12 mmol, 4 eq) in toluene (0.5 mL) was added to the reaction. The mixture was then stirred at rt for 16 h. The reaction was quenched by the addition of H₂O (5 mL) and allowed to stir for 5 min. The mixture was then extracted with EtOAc (3 x 5 mL). The organic layers were dried over MgSO₄, filtered, and concentrated to a colorless solid. This material was purified by flash column chromatography (SiO₂, 4:1 Hexanes/EtOAc) to afford lactone **17** (5.3 mg, 66%) as a colorless solid. R_f = 0.36 (4:1 Hexanes/EtOAc, visualized with KMnO₄)

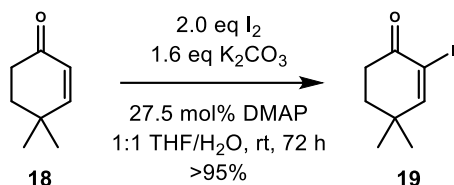
¹H NMR (600 MHz, CDCl₃): δ 6.41 (d, J = 7.1 Hz, 1H), 6.04 (d, J = 4.0 Hz, 1H), 3.07 (dddd, J = 4.4, 6.4, 9.2, 10.2 Hz, 1H), 2.72 (dd, J = 10.2, 17.5 Hz, 1H), 2.55 (dd, J = 9.1, 17.6 Hz, 1H), 2.57-2.53 (m, 1H), 2.09 (s, 3H), 1.56-1.51 (m, 2H), 1.51-1.43 (m, 3H), 1.37-1.31 (m, 3H), 1.29-1.21 (m, 2H), 1.03 (s, 3H)

¹³C NMR (150 MHz, CDCl₃): δ 175.5, 169.9, 105.1, 96.7, 54.1, 41.3, 38.0, 37.4, 34.0, 29.7, 25.8, 22.7, 21.7, 21.3, 21.2

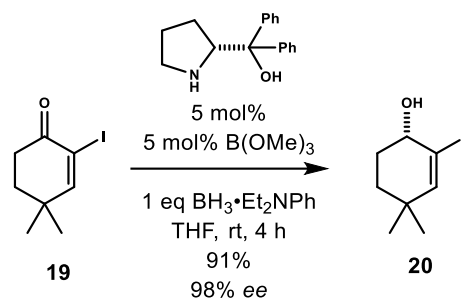
IR (thin film) 2925, 2851, 1795, 1749, 1376, 1228, 1163, 1016, 984, 939, 865

HRMS (ESI) calculated for [C₁₅H₂₂O₅Na]⁺ (M+Na) 305.1365, observed 305.1375

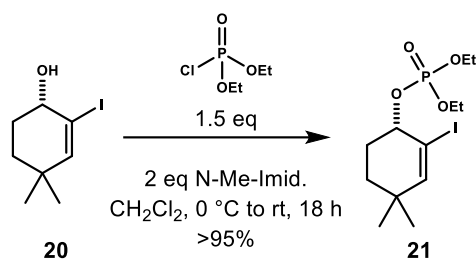
Preparation of (-)-Macfarlandin C



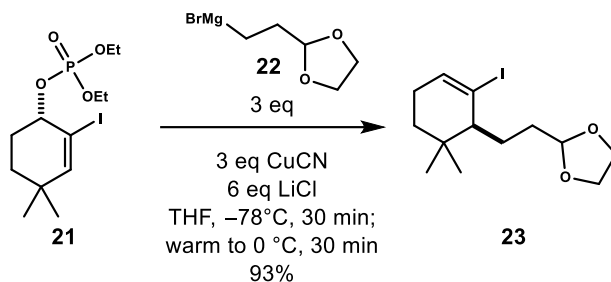
Preparation of 2-iodo-4,4-dimethylcyclohex-2-en-1-one (19):³ To a solution of 4,4-dimethylcyclohex-2-ene-1-one (**18**) (18 mL, 140 mmol) in 1:1 THF/H₂O (680 mL, 0.2 M) at rt was sequentially added K₂CO₃ (23 g, 160 mmol, 1.2 eq), I₂ (52 g, 205 mmol, 1.5 eq) and DMAP (3.3 g, 27 mmol, 20 mol%). The purple heterogeneous solution was stirred vigorously for 48 h at rt. After this time, additional K₂CO₃ (7.6 g, 55 mmol, 0.4 eq), I₂ (17 g, 68 mmol, 0.5 eq), and DMAP (1.3 g, 10 mmol, 7.5 mol %) were added sequentially. After stirring for an additional 24 h at rt, Et₂O (500 mL) was added and the biphasic mixture was transferred to a separatory funnel. The organic layer was separated, washed with saturated aqueous Na₂S₂O₃ solution (3 x 300 mL) and brine (2 x 300 mL), and then dried over Na₂SO₄. The drying agent was removed by filtration and the filtrate concentrated to provide a viscous yellow oil. The crude product was loaded onto a short plug of silica gel and was quickly eluted into a single round-bottom flask using Et₂O (1.5 L). Removal of the solvent under reduced pressure gave iodoenone **19** (34.2 g, 136 mmol, >95%) as an orange oil that solidified upon storage at -20 °C. Spectral data acquired for the compound matched those previously reported.³



Preparation of (*S*)-2-iodo-4,4-dimethylcyclohex-2-en-1-ol (20**):**⁵ To a solution of *D*-diphenylprolinol (250 mg, 1.0 mmol, 5 mol %) in THF (21 mL) under argon at rt was added B(OMe)₃ (110 μL, 1.0 mmol, 5 mol%) under argon. The resulting colorless solution was maintained at rt for 1h. After this time, BH₃·Et₂NPh (3.56 mL, 20.0 mmol, 1 eq) was added via syringe. A solution of enone **19** (5.00 g, 20.0 mmol) in THF (21 mL, ~1 M) was then added over 1 h using a syringe pump. After the addition was complete, the homogenous solution was maintained at rt for an additional 3 h. Methanol (10 mL) was then added and the reaction mixture was concentrated under reduced pressure. The residue was diluted with Et₂O (200 mL) and washed with saturated aqueous Na₂CO₃ (3 x 150 mL), saturated aqueous KHSO₄ (3 x 150 mL) and brine (3 x 150 mL). The organic layer was dried over MgSO₄, filtered and concentrated to provide a crude residue that was purified by flash column chromatography (SiO₂, 4:1 Hex/EtOAc) to afford alcohol **20** (4.58 g, 18.2 mmol, 91%) as a colorless oil. Characterization data for **20** matched those previously reported. Analysis by HPLC confirmed that the compound was obtained in 98% *ee*: OD-H column, 215 nm, 2% IPA/*n*-hexane, 0.3 mL/min: t_R 26.5 min (major), 32.6 min (minor). [α]^{26.7}_D -39.8, [α]^{26.7}₅₇₇ -42.0, [α]^{26.7}₅₄₆ -49.3, [α]^{26.7}₄₃₅ -92.2, [α]^{26.7}₄₀₅ -117 (*c* = 1.28, CHCl₃). The *R*-enantiomer of **20** was previously prepared by Overman and Knochel.^{4,5}

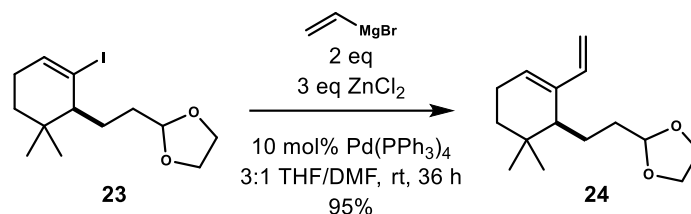


Preparation of (S)-diethyl (2-iodo-4,4-dimethylcyclohex-2-en-1-yl) phosphate (21):⁵ To a solution of alcohol **20** (4.58 g, 18.2 mmol) in CH_2Cl_2 (48 mL, ~0.4 M) at 0 °C was added sequentially *N*-methylimidazole (2.9 mL, 36 mmol, 2 eq) and diethyl chlorophosphate (3.9 mL, 27 mmol, 1.5 eq). The mixture was allowed to warm to rt and maintained at this temperature for 18 h. Brine (50 mL) was added and the biphasic mixture was transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried over Na_2SO_4 , filtered, and concentrated. The residue was purified by flash column chromatography (SiO_2 , 3:1 \rightarrow 1:1 Hex/EtOAc) to provide phosphate **21** (6.78 g, 17.5 mmol, >95%) as a colorless oil. Spectral data acquired for the compound matched those previously reported for the enantiomer.⁵ $[\alpha]_{\text{D}}^{26.7} -27.2$, $[\alpha]_{577}^{26.7} -29.8$, $[\alpha]_{546}^{26.7} -34.1$, $[\alpha]_{435}^{26.7} -63.8$, $[\alpha]_{405}^{26.7} -79.6$ ($c = 1.10$, CHCl_3).



Preparation of (S)-2-(2-(2-iodo-6,6-dimethylcyclohex-2-en-1-yl)ethyl)-1,3-dioxolane (23):⁵ A solution of 2-(2-bromoethyl)-1,3-dioxolane (6.96 g, 38.7 mmol, 3 eq) and 1,2-dibromoethane (0.7 mL, 8 mmol, 0.65 eq) in THF (25 mL) was added to a suspension of Mg turnings (2.82 g, 116 mmol, 9 eq) in THF (55 mL). The mixture was briefly warmed with the heat gun for 10 sec, and was then stirred for 2 h at rt. The resulting black suspension of Grignard reagent **22** was then transferred via cannula to a round-bottom flask containing a stir bar under argon. The mixture was cooled to -78°C and a homogenous solution of CuCN (3.46 g, 38.7 mmol, 3 eq) and LiCl (3.28 g, 77.3 mmol, 6 eq) in THF (40 mL) was added via syringe. After stirring vigorously for 15 min at -78°C , a solution of phosphate **21** (5.00 g, 12.8 mmol) in THF (25 mL) was added. The resulting suspension was stirred for 30 min at -78°C and then was allowed to warm to 0°C while stirring for an additional 30 min. Saturated aqueous NH_4Cl solution (150 mL) was added and the biphasic mixture was transferred to a separatory funnel. The aqueous layer was extracted with Et_2O (3 x 200 mL) and the combined organic layers were washed with brine (2 x 300 mL), dried over MgSO_4 , filtered and concentrated. The residue was purified by flash column chromatography (SiO_2 , 20:1 Hex/ EtOAc) to afford vinyl iodide **23** (4.03 g, 11.9 mmol, 93%) as a colorless oil. Spectral data acquired for the compound matched those previously reported for the enantiomer.⁵ $[\alpha]^{24.9}_{\text{D}} -59.2$, $[\alpha]^{24.9}_{577} -62.6$, $[\alpha]^{25.0}_{546} -70.5$, $[\alpha]^{25.1}_{435} -126.5$, $[\alpha]^{25.1}_{405} -156$ ($c = 1.02$, CHCl_3).

Analysis of a comparable sample ($[\alpha]^{26.7}_{\text{D}} -58.5$) by HPLC confirmed that the enantiomeric purity of this sample was 99% ee: AD column, 215 nm, 0.5% IPA/n-hexane, 0.15 mL/min. t_{R} : 36.5 min (major), 39.0 min (minor).



Preparation of (S)-2-(2-(6,6-dimethyl-2-vinylcyclohex-2-en-1-yl)ethyl)-1,3-dioxolane (24): A solution of vinyl magnesium bromide (22.5 mL, 22.5 mmol, 2 eq, 1 M in THF) was added to a solution of ZnCl₂ (48 mL, 34 mmol, 3 eq, 0.7 M in THF) and THF (19 mL) at -78 °C. The suspension was then allowed to warm over 1.5 h to rt while stirring. A solution of iodide **23** (3.78 g, 11.2 mmol) and Pd(PPh₃)₄ (1.30 g, 1.12 mmol, 10 mol%) in THF (25 mL) and DMF (25 mL) was added slowly. The reaction mixture was allowed to stir at rt for 36 h, after which saturated aqueous NH₄Cl solution (100 mL) was added. The mixture was extracted with Et₂O (3 x 150 mL), and the organic layer was separated, washed with brine (2 x 200 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO₂, 30:1 → 15:1 Hex/EtOAc) to provide diene **24** (2.54 g, 10.7 mmol, 95%) as a colorless oil: $R_f = 0.61$ (9:1 Hex/EtOAc).

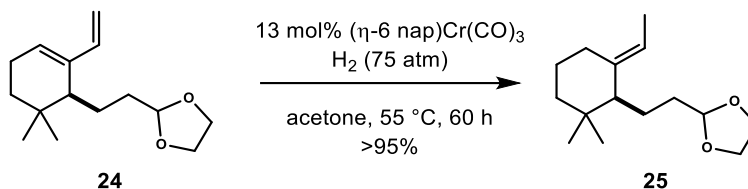
¹H NMR (500 MHz, CDCl₃) δ 6.29 (dd, $J = 17.7, 10.8$ Hz, 1H), 5.64-5.61 (m, 1H), 5.06 (d, $J = 17.7$ Hz, 1H), 4.88 (d, $J = 11.1$ Hz, 1H), 4.75 (t, $J = 4.8$ Hz, 1H), 3.98-3.91 (m, 2H), 3.84-3.79 (m, 2H), 2.15-2.10 (m, 2H), 1.96-1.92 (m, 1H), 1.76-1.69 (m, 2H), 1.66-1.57 (m, 2H), 1.42-1.34 (m, 1H), 1.18-1.12 (m, 1H), 1.00 (s, 3H), 0.85 (s, 3H)

¹³C NMR (125 MHz, CDCl₃) δ 140.5, 140.2, 127.9, 109.8, 105.1, 64.95, 64.92, 43.0, 34.7, 32.5, 20.5, 28.8, 27.0, 26.8, 23.7

IR (thin film) 2954, 2870, 1647, 1406, 1139, 1034, 893 cm⁻¹

HRMS (ESI) calculated for C₁₅H₂₈NO₂ (M + NH₄)⁺ 254.2120, observed 254.2129

Optical Rotation $[\alpha]^{22.4}_D -87.4$, $[\alpha]^{22.4}_{577} -93.7$, $[\alpha]^{22.4}_{546} -105$, $[\alpha]^{22.4}_{435} -183$, $[\alpha]^{22.4}_{405} -219$ ($c = 1.02$, CHCl₃)



Preparation of (*S,E*)-2-(2-(6-ethylidene-2,2-dimethylcyclohexyl)ethyl)-1,3-dioxolane (25**):** In a glove box under a N_2 atmosphere, a stainless steel Parr bomb containing a stir bar was charged with (η^6 -naphthalene)chromium tricarbonyl (560 mg, 2.1 mmol, 13 mol %), diene **24** (3.94 g, 16.7 mmol) and acetone (170 mL, 0.1 M, degassed in a Schlenk tube by three freeze-pump-thaw cycles prior to bringing into the glove box). The Parr bomb was sealed, removed from the glove box, and quickly purged with H_2 gas three times before being pressurized to 75 atm (~ 1100 psi) H_2 . The apparatus was then placed in a sand bath preheated to $55 \text{ }^\circ\text{C}$ and was maintained at this temperature while stirring for 60 h. The H_2 pressure was released and the reaction mixture was transferred to a round-bottom flask and concentrated. The crude residue was purified by flash column chromatography (SiO_2 , 50:1 Hex/EtOAc) to afford (*E*)-ethylidene acetal **25** (3.97 g, 16.6 mmol, $>95\%$) as a colorless oil: $R_f = 0.67$ (9:1 Hex/EtOAc).

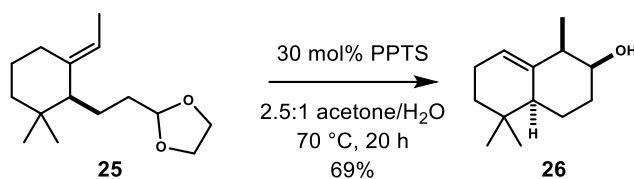
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 5.08 (q, $J = 6.4$ Hz, 1H), 4.82 (t, $J = 4.4$ Hz, 1H), 3.98-3.95 (m, 2H), 3.87-3.82 (m, 2H), 2.28-2.25 (m, 1H), 1.76-1.71 (m, 1H), 1.59 (dd, $J = 6.7, 1.0$ Hz, 3H), 1.56-1.34 (m, 8H), 1.19-1.14 (m, 1H), 0.87 (s, 3H), 0.85 (s, 3H)

$^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 138.9, 118.0, 105.2, 65.0, 64.9, 55.7, 35.6, 34.8, 32.8, 28.2, 28.0, 23.8, 22.9, 21.2, 12.8

IR (thin film) 2951, 2926, 2460, 1408, 1382, 1364, 1140, 1037, 955, 891, 907, 824 cm^{-1}

HRMS (CI) calculated for $\text{C}_{15}\text{H}_{26}\text{O}_2$ (M) $^+$ 238.1933, observed 238.1942

Optical Rotation $[\alpha]^{22.7}_{\text{D}} +32.8$, $[\alpha]^{22.7}_{577} +33.3$, $[\alpha]^{22.7}_{546} +38.2$, $[\alpha]^{22.7}_{435} +60.8$, $[\alpha]^{22.7}_{405} +74.5$ ($c = 0.96$, CHCl_3)



Preparation of (1R,2S,4aS)-1,5,5-trimethyl-1,2,3,4,4a,5,6,7-octahydronaphthalen-2-ol (26):

A round-bottom flask was charged with ethylidene acetal **25** (3.97 g, 16.6 mmol), acetone (150 mL, 0.1 M), and H₂O (57 mL, 220 eq). To the mixture was added pyridine *p*-toluenesulfonate (PPTS, 1.26 g, 5.01 mmol, 30 mol %), and the flask was placed in a sand bath pre-heated to 70 °C. The reaction was stirred at this temperature for 20 h, after which it was allowed to cool to rt. The mixture was diluted with H₂O (100 mL) and extracted with Et₂O (3 x 100 mL). The combined organic layers were washed with brine (2 x 100 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (SiO₂, 9:1 Hex/EtOAc) to afford alcohol **26** (2.23 g, 11.5 mmol, 69%) as a colorless oil which solidified upon storage at -20 °C: R_f = 0.40 (9:1 Hex/EtOAc).

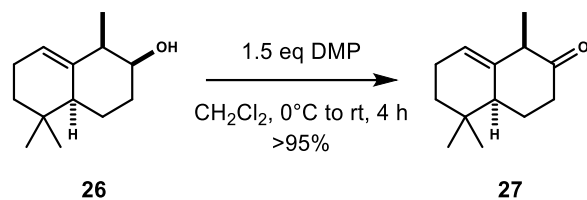
¹H NMR (600 MHz, CDCl₃) δ 5.38 (br s, 1H), 3.82-3.72 (m, 1H), 2.28-2.24 (m, 1H), 2.05-2.02 (m, 2H), 1.92 (dq, *J* = 13.7, 3.2 Hz, 1H), 1.69-1.65 (m, 1H), 1.60 (tdd, *J* = 2.4, 4.5, 13.6 Hz, 1H), 1.53-1.50 (m, 1H), 1.41-1.34 (m, 2H), 1.32 (qd, *J* = 4.0, 12.9 Hz, 1H), 1.17 (dt, *J* = 4.7, 13.0 Hz, 1H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 3H), 0.86 (s, 3H)

¹³C NMR (150 MHz, CDCl₃) δ 140.0, 119.6, 72.4, 49.1, 43.7, 33.9, 32.7, 31.4, 27.8, 27.0, 24.4, 23.0, 14.3

IR (thin film) 2911, 2867, 2360, 2340, 1452, 1382, 1363, 1186, 1093, 969, 940, 714 cm⁻¹

HRMS (CI) calculated for C₁₃H₂₂O (M)⁺ 194.1671, observed 194.1672

Optical Rotation [α]^{22.5}_D -84.8, [α]^{22.5}₅₇₇ -89.2, [α]^{22.5}₅₄₆ -101, [α]^{22.7}₄₃₅ -174, [α]^{22.7}₄₀₅ -208 (*c* = 1.14, CHCl₃)



Preparation of (1*R*,4*aS*)-1,5,5-trimethyl-3,4,4*a*,5,6,7-hexahydronaphthalen-2(1*H*)-one (27):

A round-bottom flask was charged with alcohol **26** (808 mg, 4.16 mmol) and CH_2Cl_2 (40 mL, 0.1 M) under argon. The solution was cooled to 0 °C and Dess-Martin periodinane (DMP, 2.11 g, 4.99 mmol, 1.2 eq)⁶ was added in one portion. The reaction mixture was then allowed to warm to rt and was maintained at this temperature for 2 h. TLC analysis indicated starting material was still present, so an additional portion of DMP (0.35 g, 0.82 mmol, 0.2 eq) was added. The reaction was stirred for an additional 2 h, after which TLC analysis indicated that the starting material was consumed. The reaction mixture was then diluted with Et_2O (40 mL) and the solution was flushed through a pad of Celite[®]. The pad of Celite[®] was washed with Et_2O (300 mL), and the filtrate was concentrated under reduced pressure. The oily solid residue was suspended in 9:1 Hex/EtOAc (20 mL) and flushed through a small plug of silica gel. The plug of silica gel was eluted with 9:1 Hex/EtOAc (300 mL), and the filtrate was concentrated to afford ketone **27** (777 mg, 4.04 mmol, >95%) as a colorless oil. β,γ -Unsaturated ketone **27** was prone to double bond isomerization upon storage at room temperature and was used immediately in the next step: $R_f = 0.48$ (9:1 Hex/EtOAc).

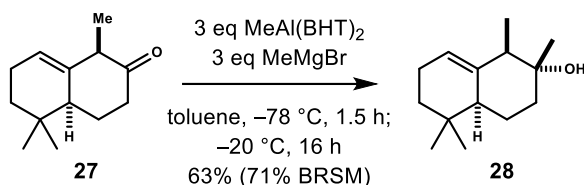
¹H NMR (600 MHz, CDCl_3) δ 5.41 (br s, 1H), 3.04-3.00 (m, 1H), 2.48 (ddd, $J = 3.5, 5.1, 14.5$ Hz, 1H), 2.41 (dddd, $J = 1.0, 6.2, 12.3, 14.6$ Hz, 1H), 2.11-2.04 (m, 2H), 2.04-1.98 (m, 2H), 1.48-1.42 (m, 1H), 1.41-1.36 (m, 1H), 1.23 (dt, $J = 5.1, 13.1$ Hz, 1H), 1.16 (d, $J = 6.6$ Hz, 3H), 1.00 (s, 3H), 0.92 (s, 3H)

¹³C NMR (125 MHz, CDCl_3) δ 210.9, 139.0, 118.5, 52.2, 48.0, 41.1, 32.9, 31.8, 28.1, 27.7, 26.5, 23.1, 10.5

IR (thin film) 2953, 2869, 1717, 1673, 1453, 1365, 1337, 1174, 953, 849 cm^{-1}

HRMS (EI) calculated for $\text{C}_{13}\text{H}_{20}\text{O}$ (M)⁺ 192.1514, observed 192.1519

Optical Rotation $[\alpha]^{22.5}_{\text{D}} -139$, $[\alpha]^{22.5}_{577} -148$, $[\alpha]^{22.5}_{546} -171$, $[\alpha]^{22.5}_{435} -333$, $[\alpha]^{22.5}_{405} -72.8$ ($c = 1.05$, CHCl_3)



Preparation of (1*R*,2*R*,4*aS*)-1,2,5,5-tetramethyl-1,2,3,4,4*a*,5,6,7-octahydronaphthalen-2-ol (28):⁷ A round-bottom flask was charged with 2,6-di-*tert*-butyl-4-methylphenol (5.34 g, 24.2 mmol, 6 eq) and toluene (40 mL) under argon. A solution of AlMe₃ (6.1 mL, 12 mmol, 3 eq, 2 M in toluene) was added slowly via syringe at rt and vigorous gas evolution was observed. The homogenous light-yellow solution was maintained at rt for 1 h, after which it was cooled to -78 °C. Ketone **27** (777 mg, 4.04 mmol) was added slowly as a solution in toluene (16 mL) and the resulting solution was maintained at -78 °C for 10 min. A solution of MeMgBr (4.0 mL, 12 mmol, 3 eq, 3.0 M in Et₂O) was added slowly, and the solution was maintained at -78 °C for 1.5 h. The reaction mixture was then allowed to slowly warm to -20 °C overnight (16 h). After this time, the solution was then allowed to warm to 0 °C over 20 min. The reaction mixture was then quenched with saturated aqueous NH₄Cl solution (40 mL) and the layers were separated. The aqueous layer was extracted with Et₂O (3 x 50 mL), and the combined organic layers were washed with brine (2 x 40 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO₂, 9:1 Hex/EtOAc) to afford alcohol **31** (532 mg, 2.55 mmol, 63%) as a colorless solid: R_f = 0.30 (9:1 Hex/EtOAc) and recovered ketone **30** (64.3 mg, 0.33 mmol, 8%).

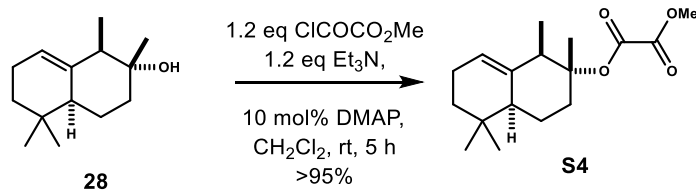
¹H NMR (500 MHz, CDCl₃) δ 5.35 (br s, 1H), 2.07-1.98 (m, 3H), 1.84 (dt, *J* = 3,7, 12.8 Hz, 1H), 1.76 (dq, *J* = 4.4, 13.3 Hz, 1H), 1.61-1.53 (m, 2H), 1.45-1.35 (br s, 1H), 1.35-1.29 (m, 1H), 1.20-1.15 (m, 1H), 1.11 (qd, *J* = 4.0, 13.1 Hz, 1H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.96 (s, 3H), 0.91 (s, 3H), 0.83 (s, 3H)

¹³C NMR (125 MHz, CDCl₃) δ 140.9, 117.8, 74.5, 48.9, 48.5, 42.8, 34.0, 31.4, 28.4, 26.0, 23.0, 20.2, 10.6

IR (thin film) 3307, 2947, 2922, 2845, 1454, 1374, 1126, 1001, 948 cm⁻¹

HRMS Several attempts to acquire HRMS data for alcohol **31** using ESI and CI ionization techniques were unsuccessful

Optical Rotation [α]^{22.4}_D -88.5, [α]^{22.4}₅₇₇ -91.6, [α]^{22.4}₅₄₆ -108.8, [α]^{22.4}₄₃₅ -180.6, [α]^{22.4}₄₀₅ -212.5 (*c* = 0.04, CHCl₃)



Preparation of Methyl Oxalate S4: A round-bottom flask was charged with alcohol **28** (558 mg, 2.67 mmol), DMAP (33 mg, 0.27 mmol, 10 mol %) and CH₂Cl₂ (14 mL, 0.2 M) under argon. After sequential addition of Et₃N (0.75 mL, 5.35 mmol, 2 eq) and methyl chlorooxacetate (0.49 mL, 5.3 mmol, 2 eq), the reaction was maintained at rt for 5 h, after which time TLC analysis indicated complete conversion. The reaction mixture was diluted with saturated aqueous NH₄Cl solution (20 mL) and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (3 x 20 mL), and the combined organic layers were washed with brine (2 x 20 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (SiO₂, 30:1 Hex/EtOAc) to afford methyl oxalate ester **S4** (773 mg, 2.62 mmol, >95%) as a colorless oil: R_f = 0.57 (9:1 Hex/EtOAc).

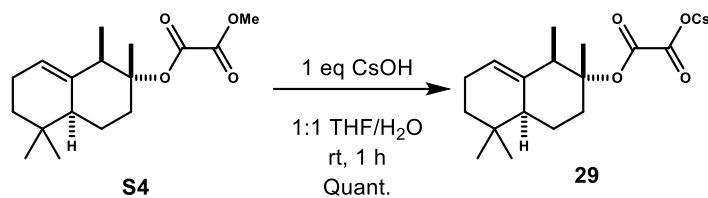
¹H NMR (500 MHz, CDCl₃) δ 5.43 (s, 1H), 3.86 (s, 3H), 2.65-2.55 (m, 2H), 2.03-1.98 (m, 2H), 1.89 (td, *J* = 13.2, 4.0 Hz, 1H), 1.83-1.77 (m, 1H), 1.64-1.57 (m, 1H), 1.33 (s, 3H), 1.32-1.28 (m, 1H), 1.23-1.16 (m, 1H), 1.16-1.07 (m, 1H), 1.05 (d, *J* = 7.1 Hz, 3H), 0.90 (s, 3H), 0.82 (s, 3H)

¹³C NMR (125 MHz, CDCl₃) δ 159.2, 156.8, 139.3, 119.7, 91.2, 53.4, 48.2, 46.1, 36.7, 34.0, 31.4, 28.4, 25.7, 25.4, 23.0, 17.3, 10.9

IR (thin film) 2951, 2919, 1772, 1741, 1200, 1168 cm⁻¹

HRMS (ESI) calculated for C₁₇H₂₆O₄Na (M + Na)⁺ 317.1729, observed 317.1732

Optical Rotation [α]^{22.4}_D -103, [α]^{22.4}₅₇₇ -101, [α]^{22.4}₅₄₆ -108, [α]^{22.4}₄₃₅ -187, [α]^{22.4}₄₀₅ -222 (*c* = 0.22, CHCl₃)



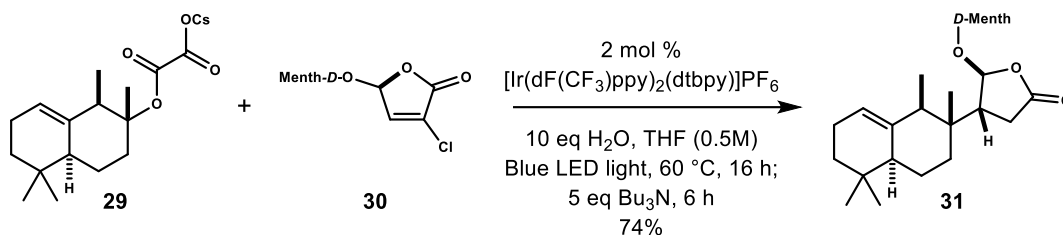
Preparation of Cesium Oxalate 29: A round-bottom flask was charged with methyl oxalate ester **S4** (379 mg, 1.29 mmol) and THF (2.6 mL). A solution of CsOH (1.29 mL, 1.29 mmol, 1 M in H₂O) was added slowly. The reaction was then stirred at rt for 1 h, after which TLC analysis indicated that starting material had been consumed. The reaction was then carefully concentrated under reduced pressure at 50 °C. The residue was then dried under vacuum overnight to produce cesium oxalate salt **29** (525 mg, 1.27 mmol, 99%) as a colorless powder.

¹H NMR (500 MHz, DMSO-*d*₆) δ 5.36 (br s, 1 H), 2.56-2.52 (m, 1H), 2.41-2.35 (m, 1H), 2.00-1.93 (m, 1H), 1.84 (td, *J* = 3.5, 13.6 Hz, 1H), 1.75-1.69 (m, 1H), 1.61-1.55 (m, 1H), 1.33-1.26 (m, 1H), 1.18-1.14 (m, 1H), 1.12 (s, 3H), 1.05 (qd, *J* = 3.8, 13.7 Hz, 1H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.88 (s, 3H), 0.80 (s, 3H)

¹³C NMR (125 MHz, DMSO-*d*₆) δ 167.5, 163.4, 139.8, 118.0, 83.7, 47.6, 45.3, 36.4, 33.6, 30.9, 28.1, 25.3, 24.8, 22.4, 17.5, 10.5

IR (thin film) 2943, 2907, 2866, 2843, 1705, 1689, 1644, 1605, 1381, 1221, 1089, 898, 780, 764, 749

HRMS (ESI) calculated for C₁₆H₂₃O₄ (M-Cs)⁻ 279.1596, observed 279.1602



Preparation of Lactone 31: Cesium oxalate **29** (414 mg, 1.00 mmol), chlorobutenolide **30** (274 mg, 1.00 mmol, 1 eq)^{1,2}, $[\text{Ir}(\text{dF}(\text{CF}_3)\text{ppy})_2(\text{dtbbpy})]\text{PF}_6$ (22.8 mg, 0.02 mmol, 2 mol %), H_2O (0.18 mL, 10 mmol, 10 eq), and THF (2 mL, 0.5 M) were divided equally into four 2-dram vials. The vials were then sparged with argon for 15 min. The vials were then placed in a photobox and irradiated with blue LEDs at 60 °C for 20 h. Then *n*- Bu_3N (0.30 mL, 1.3 mmol, 5 eq) was added to each vial and irradiation was continued for another 6 h. The reactions were then poured into a separatory funnel and diluted with H_2O (15 mL) and extracted with Et_2O (3 x 10 mL). The organics were then dried over MgSO_4 , filtered, and concentrated to an orange oil. The residue was then purified by flash column chromatography (SiO_2 , 30:1→20:1 Hex/ EtOAc) to afford lactone **31** (320 mg, 74%) as a colorless solid $R_f = 0.45$ (9:1 Hex/ EtOAc).

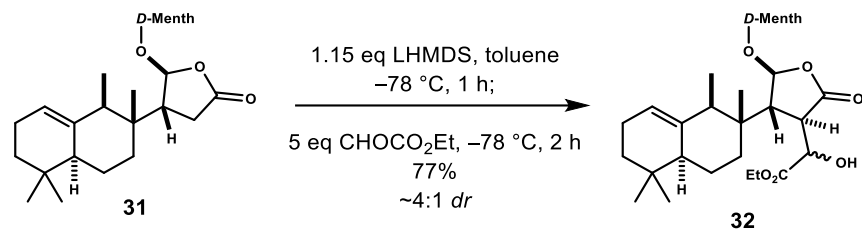
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 5.68 (d, $J = 1.3$ Hz, 1H), 5.33 (dd, $J = 2.2, 3.5$ Hz, 1H), 3.52 (dt, $J = 4.1, 10.5$ Hz, 1H), 2.72 (dd, $J = 9.8, 18.3$ Hz, 1H), 2.49 (ddd, $J = 1.3, 3.3, 10.1$ Hz, 1H), 2.36 (dd, $J = 3.5, 18.2$ Hz, 1H), 2.18-2.12 (m, 1H), 2.11-2.05 (m, 2H), 2.05-2.00 (m, 2H), 1.73-1.60 (m, 3H), 1.51-1.45 (m, 1H), 1.42 (dt, $J = 3.1, 12.6$ Hz, 1H), 1.40-1.33 (m, 2H), 1.28 (dt, $J = 3.8, 8.9$ Hz, 1H), 1.24-1.14 (m, 3H), 1.05-0.97 (m, 1H), 0.96 (d, $J = 7.0$ Hz, 3H), 0.94 (d, $J = 6.8$ Hz, 3H), 0.92-0.81 (m, 2H), 0.91 (s, 3H), 0.88 (d, $J = 7.1$ Hz, 3H), 0.84 (s, 3H), 0.79 (d, $J = 6.9$ Hz, 3H), 0.66 (s, 3H)

$^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 177.1, 140.6, 118.3, 101.0, 76.7, 49.1, 48.8, 47.9, 43.3, 39.7, 39.2, 34.3, 33.3, 32.4, 31.4, 31.3, 29.7, 28.0, 26.3, 25.4, 24.5, 23.1, 22.9, 22.3, 20.9, 17.3, 15.6, 11.1

IR (thin film) 2952, 2920, 2867, 1788, 1455, 1384, 1168, 1091, 1015, 970, 945

HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{46}\text{O}_3\text{Na}$ ($\text{M}+\text{Na}$)⁺ 453.3345, observed 453.3342

Optical Rotation $[\alpha]^{22.2}_{\text{D}} +27.4$, $[\alpha]^{22.3}_{577} +28.3$, $[\alpha]^{22.3}_{546} +29.0$, $[\alpha]^{22.4}_{435} +39.9$, $[\alpha]^{22.4}_{405} +46.5$ ($c = 0.75$, CHCl_3)



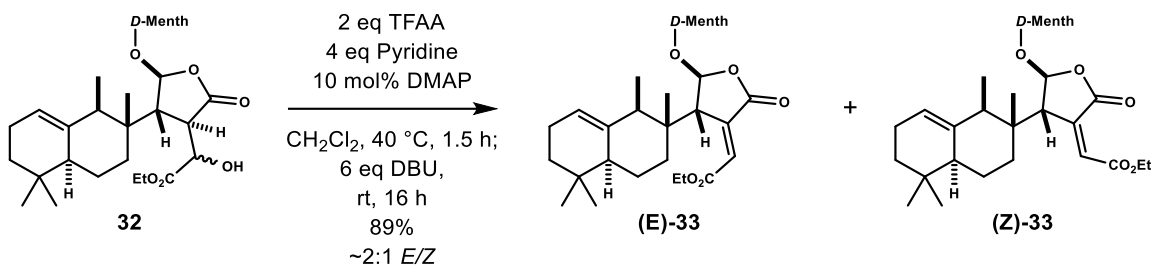
Preparation of Alcohols 32: A flame dried 100 mL round-bottom flask was charged with lactone **31** (712 mg, 1.65 mmol) and toluene (17 mL, 0.1 M). The solution was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of LHMDS (2.5 mL, 2.5 mmol, 1.5 eq, 1 M in THF) was added dropwise. The reaction was maintained at $-78\text{ }^{\circ}\text{C}$ for 1 h. During the enolate formation, ethyl glyoxylate (50 wt% in toluene) was distilled over P_2O_5 under argon (10–15 min at $110\text{ }^{\circ}\text{C}$, warm to $140\text{ }^{\circ}\text{C}$ over 10 min, and then warm to $200\text{ }^{\circ}\text{C}$); the obtained yellow distillate was used immediately. The freshly distilled ethyl glyoxylate (1.6 mL, 8.2 mmol, 5 eq) was added dropwise to the cold enolate solution. The reaction mixture was maintained at $-78\text{ }^{\circ}\text{C}$ for 2 h and then quenched by the addition of H_2O (20 mL) and allowed to warm to rt. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (40 mL) and dried over MgSO_4 . After filtration, concentration of the filtrate gave a yellow oil, which was purified immediately by flash column chromatography (SiO_2 , 20:1 \rightarrow 9:1 Hex/EtOAc)⁸ to afford alcohols **32** (678 mg, 77%) as a colorless oil and an inseparable ~4:1 mixture of alcohol epimers. $R_f = 0.3$ (9:1 Hex/EtOAc, visualized with KMnO_4).

$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 5.67 (m, 0.2H, minor), 5.66 (d, $J = 2.6$ Hz, 0.8H, major), 5.37-5.34 (m, 0.8H, major), 5.34-5.31 (m, 0.2H, minor), 4.66 (dd, $J = 3.7, 9.7$ Hz, 0.2H, minor), 4.40-4.30 (m, 1.6H, major), 4.30-4.25 (m, 0.2H, minor), 4.24 (dd, $J = 3.2, 4.4$ Hz, 0.8H, major), 4.14-4.05 (m, 0.2H, minor), 3.52 (dt, $J = 4.0, 10.8$ Hz, 1H), 3.27 (d, $J = 9.7$ Hz, 0.2H, minor), 3.23 (d, $J = 4.7$ Hz, 0.8H, major), 3.08 (dd, $J = 3.0, 6.0$ Hz, 0.8H, major), 2.84 (app t, $J = 3.3$ Hz, 0.2H, minor), 2.64 (dd, $J = 2.6, 6.0$ Hz, 0.8H, major), 2.39 (app d, $J = 2.8$ Hz, 0.2H, minor), 2.24-2.15 (m, 1H), 2.10-2.00 (m, 4H), 1.75-1.70 (m, 1H), 1.69-1.60 (m, 3H), 1.53-1.46 (m, 2H), 1.41-1.31 (m, 3.6H), 1.34 (t, $J = 7.1$ Hz, 2.4H, major), 1.31-1.12 (m, 4.4H), 1.29 (t, $J = 7.2$ Hz, 0.6H, minor), 0.99 (d, $J = 6.7$ Hz, 3H), 0.95-0.90 (m, 6H), 0.87 (d, $J = 7.1$ Hz, 3H), 0.85 (s, 2.4H, major), 0.83 (s, 0.6H, minor), 0.73 (s, 2.4H, major), 0.55 (s, 0.6H, minor)

$^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ (only major listed) 175.0, 172.5, 140.3, 118.6, 103.3, 100.2, 77.5, 71.2, 62.5, 51.2, 49.1, 47.9, 46.3, 43.2, 40.0, 39.5, 34.4, 33.3, 32.6, 31.5, 31.4, 28.0, 26.4, 25.0, 24.5, 23.0, 22.4, 21.0, 17.3, 15.5, 14.2, 11.3

IR (thin film) 3500, 2952, 2920, 2868, 1775, 1738, 1662, 1454, 1382, 1369, 1320, 1297, 1266, 1239, 1180, 1114, 1097, 945, 732

HRMS (ESI) calculated for $[\text{C}_{32}\text{H}_{52}\text{NaO}_6]^+$ (M) 555.3661, observed 555.3676



Preparation of Alkenes (*E*)-33 and (*Z*)-33: A 15 mL round-bottom flask containing a stir bar was charged with the mixture of alcohol epimers **32** (678 mg, 1.27 mmol), DMAP (19 mg, 0.15 mmol, ~10 mol %) and CH₂Cl₂ (13 mL, 0. M) under argon. After sequential addition of pyridine (0.42 mL, 5.2 mmol, 4 eq) and trifluoroacetic anhydride (0.36 mL, 2.6 mmol, 2 eq), the reaction mixture was maintained at 40 °C for 1.5 h at which time complete consumption of the starting material was observed by TLC analysis. After this time, DBU (1.1 mL, 7.7 mmol, 6 eq) was added by syringe and the reaction mixture was stirred at rt for 16 h. The reaction mixture was then quenched by the addition of H₂O (10 mL) and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (3 x 20 mL) and the combined organic layers were washed with 1 M HCl (10 mL), dried over MgSO₄, filtered, and concentrated under reduced pressure. The orange residue was purified by flash column chromatography (SiO₂, 1:0→30:1→20:1 Hex/EtOAc) to provide (*E*)-**33** (375 mg, 0.73 mmol, 57%) as a colorless foam: *R*_f = 0.65 (4:1 Hexanes/EtOAc, visualized with KMnO₄) and (*Z*)-**33** (206 mg, 0.40 mmol, 32%) as a colorless oil: *R*_f = 0.40 (4:1 Hexanes/EtOAc).

(*E*)-33

¹H NMR (600 MHz, CDCl₃) δ 6.84 (d, *J* = 1.7 Hz, 1H), 5.79 (s, 1H), 5.34 (bs, 1H), 4.27-4.19 (m, 2H), 3.82 (d, *J* = 1.6 Hz, 1H), 3.51 (dt, *J* = 4.2, 10.7 Hz, 1H), 2.28-2.24 (m, 1H), 2.06-2.01 (m, 3H), 1.94-1.89 (m, 1H), 1.67-1.58 (m, 4H), 1.50-1.47 (m, 1H), 1.40-1.28 (m, 4H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.22-1.13 (m, 4H), 1.03 (d, *J* = 7.0 Hz, 3H), 1.01-0.95 (m, 1H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.88 (s, 3H), 0.82 (d, *J* = 7.0 Hz, 3H), 0.80 (s, 3H), 0.72 (d, *J* = 6.9 Hz, 3H), 0.67 (s, 3H)

¹³C NMR (150 MHz, CDCl₃) δ 170.6, 165.4, 143.2, 140.4, 127.0, 118.6, 100.1, 77.1, 61.1, 51.8, 49.2, 47.5, 43.7, 43.6, 39.8, 34.3, 33.7, 33.4, 31.4, 31.3, 28.0, 26.2, 25.3, 24.2, 23.2, 22.9, 22.3, 20.8, 16.0, 15.6, 14.2, 11.4

IR (thin film) 2952, 2920, 2850, 1777, 1727, 1455, 1370, 1254, 1209, 1111, 1026, 918

HRMS (ESI) calculated for [C₃₂H₅₀NaO₅]⁺ (M) 537.3556, observed 537.3576

Optical Rotation [α]^{21.0}_D +0.7, [α]^{21.1}₅₇₇ +0.4, [α]^{21.3}₅₄₆ -0.8, [α]^{21.4}₄₃₅ -12.8, [α]^{21.3}₄₀₅ -20.9 (*c* = 1.0, CHCl₃)

(*Z*)-33

¹H NMR (600 MHz, CDCl₃) δ 6.28 (d, *J* = 1.6 Hz, 1H), 5.72 (s, 1H), 5.35 (bs, 1H), 4.33-4.22 (m, 2H), 3.55 (dt, *J* = 4.2, 10.7 Hz, 1H), 2.87 (d, *J* = 1.3 Hz, 1H), 2.21 (q, *J* = 6.6 Hz, 1H), 2.09-1.98 (m, 4H), 1.69-1.57 (m, 4H), 1.51-1.46 (m, 1H), 1.40-1.26 (m, 4H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.26-

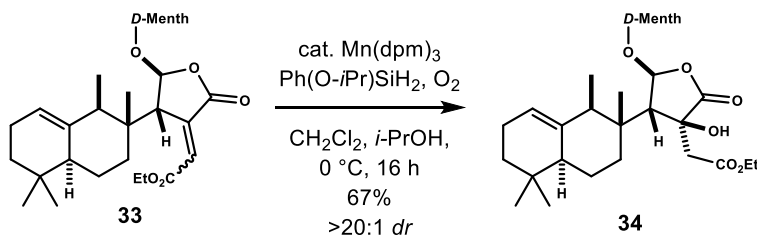
1.10 (m, 4H), 1.03-0.97 (m, 1H), 0.95 (d, $J = 7.0$ Hz, 3H), 0.93 (d, $J = 6.5$ Hz, 3H), 0.89 (s, 3H), 0.85 (d, $J = 7.1$ Hz, 3H), 0.82 (s, 3H), 0.81 (s, 3H), 0.76 (d, $J = 6.9$ Hz, 3H)

^{13}C NMR (150 MHz, CDCl_3) δ 167.3, 165.3, 140.3, 134.9, 129.7, 118.8, 98.6, 76.7, 61.5, 54.8, 49.1, 47.8, 43.3, 41.2, 39.7, 34.3, 33.42, 33.39, 31.41, 31.39, 28.0, 26.2, 25.4, 24.3, 23.2, 22.9, 22.3, 20.9, 16.6, 15.7, 13.9, 11.2

IR (thin film) 2954, 2922, 2867, 1775, 1733, 1667, 1455, 1367, 1325, 1241, 1180, 1087, 1029, 933

HRMS (ESI) calculated for $[\text{C}_{32}\text{H}_{50}\text{NaO}_5]^+$ (M) 537.3556, observed 537.3576

Optical Rotation $[\alpha]^{22.1}_{\text{D}} +27.3$, $[\alpha]^{22.1}_{577} +28.4$, $[\alpha]^{21.7}_{546} +30.9$, $[\alpha]^{21.7}_{435} +52.4$, $[\alpha]^{22.2}_{405} +64.2$
($c = 1.0$, CHCl_3)



Preparation of Tertiary Alcohol 34:⁹ A 50 mL round-bottom flask was charged with alkenes **33** (103 mg, 0.20 mmol) and Mn(dpm)_3 (12 mg, 0.02 mmol, 10 mol%) dissolved in 1:1 $\text{CH}_2\text{Cl}_2/i\text{PrOH}$ (20 mL, 0.01 M) at 0 °C. The system was then sparged with oxygen for 10 min. Then $\text{Ph(O-}i\text{Pr)SiH}_2$ (0.07 mL, 0.3898 mmol, ~2 eq) in CH_2Cl_2 (0.5 mL) was added via syringe pump over 1 h while sparging continued. The reaction was then allowed to slowly warm to rt overnight (16 h). The reaction mixture was then quenched with saturated $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL) and stirred for 10 min. The reaction mixture was then diluted with H_2O (30 mL) and extracted with EtOAc (3 x 20 mL). The organic layers were then dried over MgSO_4 , filtered, and concentrated to a brown oil. The residue was then purified by flash column chromatography (SiO_2 , 1:0→9:1→4:1 Hex/ EtOAc) to afford alcohol **34** (71.5 mg, 67%) as a colorless oil: $R_f = 0.3$ (9:1 Hex/ EtOAc , visualized with KMnO_4).

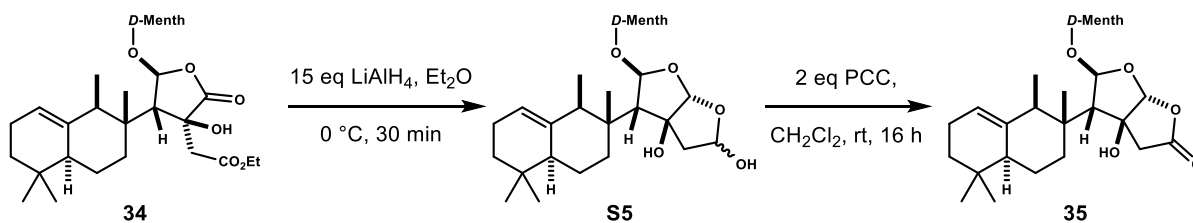
$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 5.78 (d, $J = 5.4$ Hz, 1H), 5.33 (broad s, 1H), 4.79 (s, 1H), 4.26-4.13 (m, 2H), 3.61 (dt, $J = 3.4, 10.4$ Hz, 1H), 2.89 (d, $J = 15.4$ Hz, 1H), 2.78 (d, $J = 15.4$ Hz, 1H), 2.69 (d, $J = 5.2$ Hz, 1H), 2.36-2.29 (m, 1H), 2.22-2.10 (m, 2H), 2.06-1.98 (m, 2H), 1.70-1.62 (m, 3H), 1.61-1.56 (m, 2H), 1.53-1.49 (m, 1H), 1.45-1.31 (m, 4H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.25-1.20 (m, 2H), 1.20-1.14 (m, 1H), 1.03-0.98 (m, 1H), 0.97-0.92 (m, 6H), 0.91 (s, 3H), 0.89 (s, 3H), 0.88 (d, $J = 6.7$ Hz, 3H), 0.83 (s, 3H), 0.79 (d, $J = 6.7$ Hz, 3H)

$^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 175.3, 170.9, 140.3, 118.9, 99.6, 78.3, 76.8, 61.5, 56.7, 49.4, 47.8, 44.8, 39.9, 39.5, 39.0, 34.7, 34.2, 33.3, 31.5, 31.3, 28.0, 26.2, 25.3, 24.7, 23.0, 22.9, 22.3, 21.0, 16.7, 15.7, 14.0, 11.6

IR (thin film) 3457, 2950, 2920, 2867, 1778, 1734, 1453, 1370, 1333, 1201, 1153, 1137, 1035, 919, 733

HRMS (ESI) calculated for $[\text{C}_{32}\text{H}_{52}\text{NaO}_6]^+$ (M+Na) 555.3661, observed 555.3665

Optical Rotation $[\alpha]^{22.3}_D +37.9$, $[\alpha]^{22.4}_{577} +39.5$, $[\alpha]^{22.5}_{546} +44.4$, $[\alpha]^{22.6}_{435} +68.2$, $[\alpha]^{22.6}_{405} +79.5$ ($c = 1.0$, CHCl_3)



Preparation of Dioxabicyclo[3.3.0]octan-3-one 35: A 10 mL round-bottom flask was charged with lactone **34** (14.2 mg, 0.0266 mmol), which was dissolved in Et₂O (5 mL, 0.005 M) and cooled to 0 °C. Solid LiAlH₄ (16 mg, 0.43 mmol, 15 eq) was added in one portion. The mixture was then allowed to stir at 0 °C for 30 min and then quenched by the Fieser method (0.02 mL of H₂O, then 0.02 mL of 15% aqueous NaOH, then 0.06 mL of H₂O). The mixture was then warmed to rt and stirred for 1 h or until the residual gray color of LiAlH₄ had been fully converted to colorless solids. Then MgSO₄ was added and the mixture was filtered. The filtered solids were washed with Et₂O (30 mL) and the filtrate was concentrated to afford **S5**, a mixture of lactol epimers, as a colorless foam, which was carried on without further purification.

A 10 mL round-bottom flask was charged with the crude lactols **S5** and dissolved in CH₂Cl₂ (5 mL, 0.005 M) at rt. PCC (12mg, 0.056 mmol, 2.1 eq) was then added to the reaction and the mixture was stirred at rt overnight (~16 h). Celite (100 mg) was then added to the reaction and the mixture was concentrated. The solids were then suspended in 4:1 hexanes/EtOAc (10 mL) and filtered through a SiO₂ plug, which was washed with 4:1 hexanes/EtOAc (30 mL). The filtrate was then concentrated to afford lactone **35** (9.4 mg, 72%) as a colorless oil, which was used without further purification: R_f = 0.3 (9:1 Hex/EtOAc, visualized with KMnO₄).

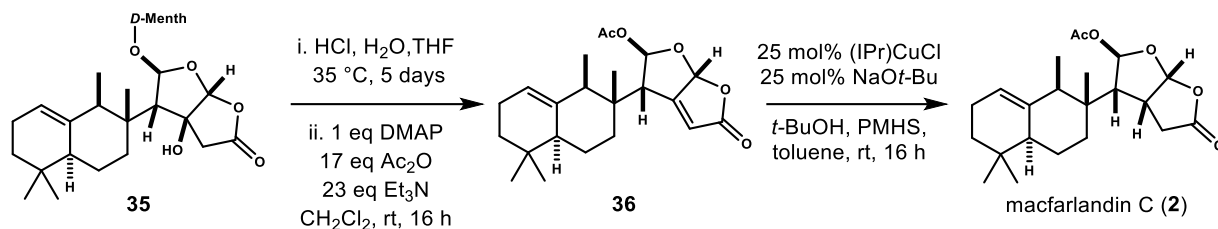
¹H NMR (600 MHz, CDCl₃) 5.61 (s, 1H), 5.46 (d, *J* = 5.8 Hz, 1H), 5.33-5.28 (m, 1H), 3.54 (dt, *J* = 3.9, 10.5 Hz, 1H), 3.09 (d, *J* = 17.5 Hz, 1H), 2.55 (d, *J* = 17.5 Hz, 1H), 2.55 (d, *J* = 5.9 Hz, 1H), 2.20-2.11 (m, 2H), 2.10-2.05 (m, 1H), 2.05-1.98 (m, 2H), 1.74-1.69 (m, 1H), 1.68-1.65 (m, 1H), 1.65-1.62 (m, 2H), 1.62-1.60 (m, 1H), 1.43 (s, 1H), 1.40-1.32 (m, 3H), 1.29-1.24 (m, 3H), 1.23-1.20 (m, 1H), 1.20-1.18 (m, 1H), 1.18-1.13 (m, 1H), 1.03-0.98 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 7.2 Hz, 3H), 0.89 (s, 3H), 0.88 (s, 3H), 0.84 (s, 3H), 0.82 (d, *J* = 6.9 Hz, 3H)

¹³C NMR (150 MHz, CDCl₃) δ 174.7, 140.4, 118.3, 108.8, 100.0, 83.6, 76.2, 58.4, 49.4, 47.9, 44.5, 40.0, 39.7, 38.6, 35.3, 34.4, 32.7, 31.4, 31.2, 27.7, 26.8, 25.7, 25.2, 23.2, 23.0, 22.3, 21.0, 18.0, 15.8, 11.6

IR (thin film) 3403, 2921, 2867, 1792, 1455, 1383, 1219, 1163, 1104, 1035, 924, 772

HRMS (ESI) calculated for [C₃₀H₄₈O₅Na]⁺ (M+Na) 511.3399, observed 511.3399

Optical Rotation [α]^{22.7}_D +23.7, [α]^{22.8}₅₇₇ +24.4, [α]^{22.8}₅₄₆ +24.4, [α]^{22.8}₄₃₅ +34.3, [α]^{22.8}₄₀₅ +39.7 (*c* = 0.6, CHCl₃)



Preparation of (–)-macfarlandin C (2): Aqueous HCl (4 M, 1.5 mL, 0.06 M overall) was added to a solution of acetal **35** (9.1 mg, 0.019 mmol) in THF (1.5 mL). The reaction was then warmed to 35 °C and stirred at this temperature for 5 days. The reaction was then cooled to rt and diluted with H₂O (5 mL) and extracted with EtOAc (3 x 5 mL). The combined organic extracts were dried over MgSO₄ and filtered. The filtrate was concentrated to afford the intermediate lactol alcohol as a pale-yellow oil, which was carried on without further purification.

The crude lactol alcohol was dissolved in CH₂Cl₂ (3 mL, 0.06 M) and DMAP (2.2 mg, 0.019 mmol, 1 eq) and Et₃N (0.06 mL, 0.4 mmol, 23 eq) were added, followed by Ac₂O (0.03 mL, 0.3 mmol, 17 eq). The reaction was then stirred at rt overnight (~16 h) and then quenched by the addition of H₂O (5 mL) and saturated aq. NaHCO₃ (5 mL). The mixture was then extracted with CH₂Cl₂ (3 x 5 mL) and the combined organic extracts were dried over MgSO₄. Filtration and concentration of the filtrate gave a yellowish solid. This residue was taken up in 4:1 hexanes/EtOAc (5 mL) and flushed through a SiO₂ plug (neutralized with 10 mL of 5% Et₃N in Hexanes) with 25 mL of 4:1 hexanes/EtOAc. The filtrate was then concentrated to afford butenolide **36** as a pale-yellow oil, which was used immediately without further purification.¹⁰

A flame-dried 10 mL flask was charged with (IPr)CuCl (2.2 mg, 0.0046 mmol, 25 mol%) and toluene (0.5 mL). To this solution, NaOtBu (2.3 μL, 2M in THF, 0.0046 mmol, 25 mol%) was added followed by PMHS (3.3 μL, 16.66M neat, 0.0558 mmol, 3 eq). The resulting yellow solution was stirred at rt for 5 min. Then crude butenolide **36** and *t*BuOH (3.5 μL, 0.0372 mmol, 2 eq) as a solution in toluene (1.5 mL, 0.01 M final concentration) were added to the reaction. The mixture was then stirred at rt overnight (~16 h). The reaction was then quenched with H₂O (5 mL) and vigorously stirred for 5 min. The mixture was then diluted with brine (5 mL) and poured into a separatory funnel. The mixture was extracted with EtOAc (3 x 10 mL). The organic layers were then dried over MgSO₄, filtered, and concentrated to a green oil. The residue was then purified by preparative TLC (SiO₂, 4:1 Hex/EtOAc) to afford (–)-macfarlandin C (**2**) (2.7 mg, 38% over three steps) as a colorless solid: R_f = 0.29 (4:1 Hex/EtOAc, visualized with KMnO₄).¹¹

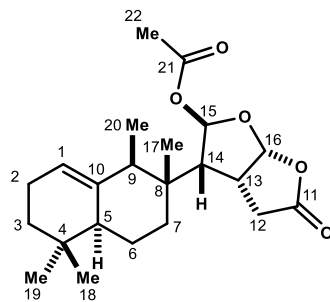
¹H NMR (600 MHz, CDCl₃) δ 6.53 (d, *J* = 7.3 Hz, 1H), 6.04 (d, *J* = 4.1 Hz, 1H), 5.31 (br. t, *J* = 3.7 Hz, 1H), 3.06-3.00 (m, 1H), 2.81 (app t, *J* = 6.8 Hz, 1H), 2.74 (dd, *J* = 10.4, 17.4 Hz, 1H), 2.55 (dd, *J* = 8.9, 17.4 Hz, 1H), 2.09 (s, 3H), 2.05-1.98 (m, 2H), 1.89 (bq, *J* = 7.0 Hz, 1H), 1.76-1.69 (m, 1H), 1.66-1.57 (m, 2H), 1.43-1.37 (m, 1H), 1.36-1.31 (m, 1H), 1.25-1.19 (m, 1H), 1.15 (dt, *J* = 4.8, 12.8 Hz, 1H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 3H), 0.84 (s, 3H), 0.82 (s, 3H)

¹³C NMR (150 MHz, CDCl₃) δ 175.4, 169.7, 140.3, 118.4, 104.8, 96.1, 51.7, 49.0, 44.4, 42.1, 39.7, 35.5, 32.6, 31.2, 30.2, 27.6, 26.8, 25.2, 23.0, 21.2, 18.9, 11.6

IR (thin film) 2921, 2851, 1799, 1750, 1455, 1375, 1225, 999

HRMS (ESI) calculated for $[\text{C}_{22}\text{H}_{32}\text{O}_5\text{Na}]^+$ ($\text{M}+\text{Na}$)⁺ 399.2148, observed 399.2159

Optical Rotation $[\alpha]^{21.0}_{\text{D}} -27.7$, $[\alpha]^{21.1}_{577} -29.5$, $[\alpha]^{21.2}_{546} -43.1$, $[\alpha]^{21.2}_{435} -112$, $[\alpha]^{21.3}_{405} -125$ ($c = 0.4$, CHCl_3); $[\alpha]_{\text{D}} -29.1$ ($c 0.75$, CHCl_3) is reported for the natural isolate.¹²



macfarlandin C

^1H (600 MHz) and ^{13}C (150 MHz) Solvent: CDCl_3

Atom	^1H Shift Exp.	^1H Shift Lit. ¹²	^{13}C Shift Exp.	^{13}C Shift Lit. ¹²
1	5.31 (br t, 4.0 Hz)	5.32 (br t, 4.0 Hz)	118.4	118.3
2	2.05-1.98 (m)	2.05 (m)	23.0	23.0
3a	1.36-1.31 (m, 1H)	1.36 (ddd, 13, 7.5, 6.9 Hz)	32.6	32.6
3b	1.15 (dt, 4.8, 12.8 Hz)	1.16 (dt, 4.6, 13.0 Hz)	32.6	32.6
4	NA	NA	31.2	31.2
5	1.43-1.37 (m)	Not Reported	49.0	49.0
6a	1.76-1.69 (m)	Not Reported	25.2	25.2
6b	1.25-1.19 (m)	Not Reported	25.2	25.2
7	1.66-1.57 (m, 2H)	Not Reported	35.5	35.4
8	NA	NA	39.7	39.6
9	1.89 (bq, 7.0 Hz)	1.90 (bq, 7.0 Hz)	44.4	44.4
10	NA	NA	140.3	140.2
11	NA	NA	175.4	175.3
12a	2.55 (dd, 8.9, 17.2 Hz)	2.56 (dd, 9.0, 17.3 Hz)	30.2	30.2
12b	2.74 (dd, 10.4, 17.2 Hz)	2.74, (dd, 10.4, 17.3 Hz)	30.2	30.2
13	3.06-3.00 (m)	3.04 (m)	42.1	42.1
14	2.81 (t, 6.7 Hz)	2.81 (t, 6.6 Hz)	51.7	51.7
15	6.53 (d, 7.3 Hz)	6.52 (d, 6.6 Hz)	104.8	104.8
16	6.04 (d, 4.4 Hz)	6.04 (d, 4.0 Hz)	96.1	96.0
17	0.82 (s)	0.82 (s)	18.9	18.9
18	0.84 (s)	0.84 (s)	26.8	26.8
19	0.87 (s)	Not Reported	27.6	27.6
20	1.00 (d, 6.8 Hz)	1.01 (d, 7.0 Hz)	11.6	11.6
21	NA	NA	169.7	169.7
22	2.09 (s)	2.10 (s)	21.2	21.1

ORTEP Image of Mukaiyama Hydration Product 13

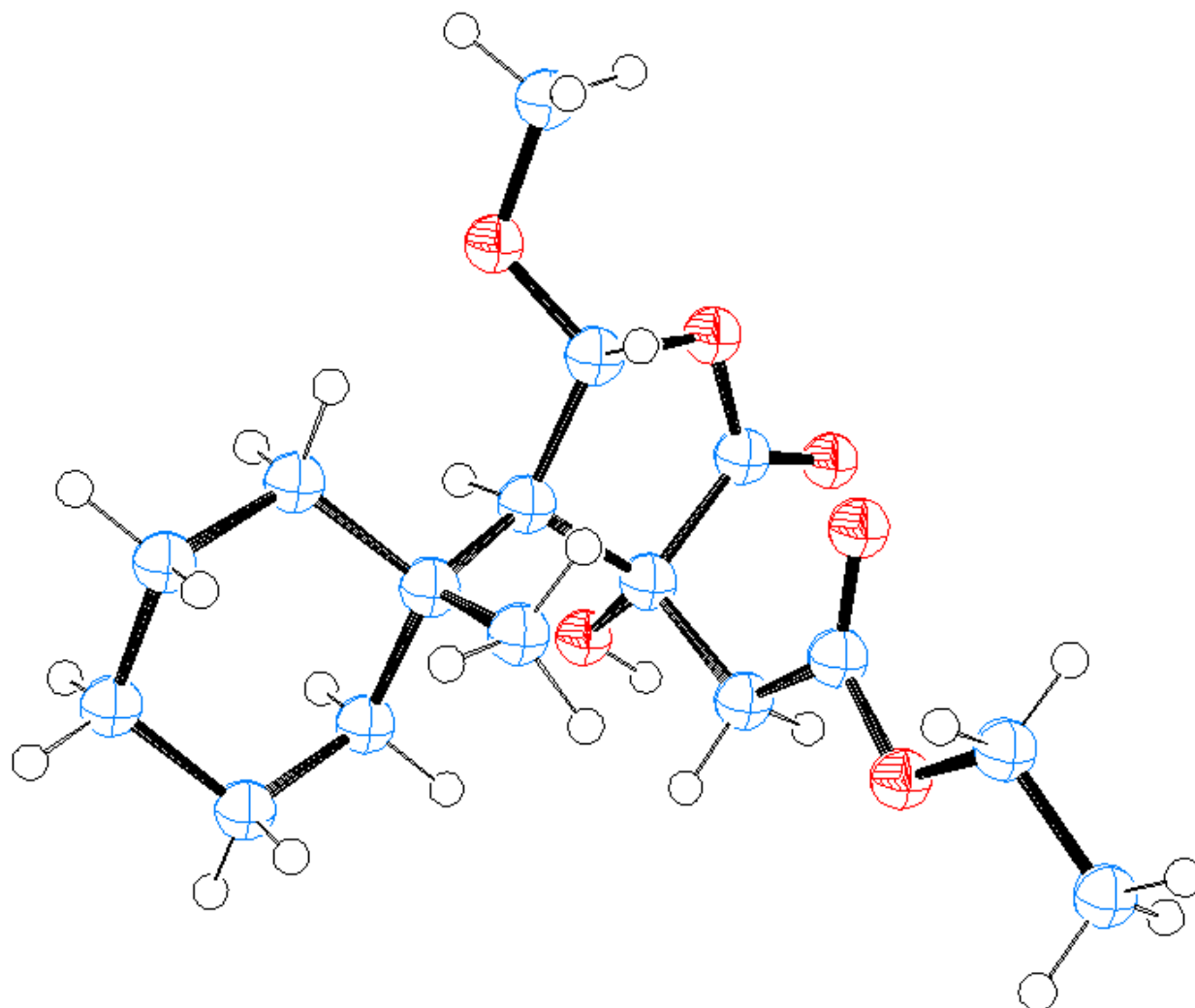
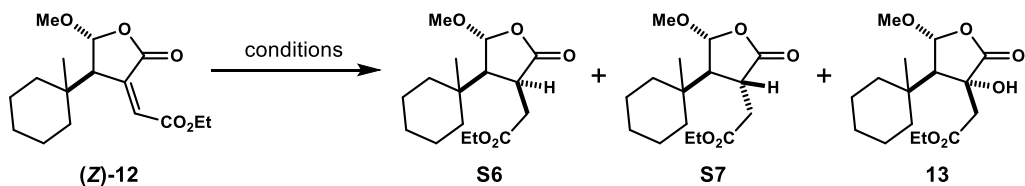


Table S1. Crystal data and structure refinement for Compound **13**.

Identification code	leo298	
Empirical formula	C ₁₆ H ₂₆ O ₆	
Formula weight	314.37	
Temperature	88(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	<i>P</i> $\bar{1}$	
Unit cell dimensions	$a = 9.0979(11)$ Å	$\alpha = 97.5790(15)^\circ$.
	$b = 9.8102(12)$ Å	$\beta = 99.4092(15)^\circ$.
	$c = 18.733(2)$ Å	$\gamma = 92.7169(16)^\circ$.
Volume	1631.0(3) Å ³	

Z	4
Density (calculated)	1.280 Mg/m ³
Absorption coefficient	0.097 mm ⁻¹
F(000)	680
Crystal color	colorless
Crystal size	0.551 x 0.388 x 0.329 mm ³
Theta range for data collection	2.099 to 29.010°
Index ranges	-11 ≤ <i>h</i> ≤ 12, -13 ≤ <i>k</i> ≤ 13, -25 ≤ <i>l</i> ≤ 25
Reflections collected	18926
Independent reflections	7953 [R(int) = 0.0243]
Completeness to theta = 25.500°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8621 and 0.7658
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	7953 / 0 / 605
Goodness-of-fit on F ²	1.036
Final R indices [I > 2σ(I) = 6267 data]	R1 = 0.0394, wR2 = 0.1029
R indices (all data, 0.73 Å)	R1 = 0.0526, wR2 = 0.1136
Largest diff. peak and hole	0.411 and -0.272 e.Å ⁻³

Table S2: Summary of Unsuccessful HAT Hydrogenation Conditions for the Conversion of **S1** to **S6/S7**

Conditions ^{9,3-16}	Yield ^{a,b}	<i>dr</i> (S6:S7) ^c
CoCl ₂ ·6H ₂ O (1 eq), NaBH ₄ (2 eq), EtOH (0.1 M), 0 °C, 3 h	27% (0%)	1:8
Co(acac) ₂ (1 eq), <i>t</i> -BuOOH (3 eq), Et ₃ SiH (10 eq), 1,4-cyclohexadiene (10 eq), <i>i</i> -PrOH (0.1 M), rt, 3 h	10% (8%)	1:2
Co(dpm) ₂ (10 mol%), PhSiH ₃ (3 eq), <i>t</i> -BuOOH (3 eq), PhCF ₃ (0.1 M), rt, 18 h	0% (50%)	–
Mn(dpm) ₃ (3 mol%), PhSiH ₃ (1.5 eq), CH ₂ Cl ₂ / <i>i</i> -PrOH (4:1, 0.1 M) rt, 18 h	80% (15%)	1:7
Mn(dpm) ₃ (10 mol%), PhSiH ₃ (3 eq), <i>t</i> -BuOOH (3 eq), <i>i</i> -PrOH (0.1 M), rt, 18 h	40% (12%)	1:1
Mn(dpm) ₃ (3 mol%), Ph(<i>Oi</i> -Pr)SiH ₂ (3 eq), <i>t</i> -BuOOH (3 eq), hexanes (0.1 M), rt, 18 h	24% (8%)	1:2

^aDetermined by ¹H NMR integration relative to an internal standard (1,2-dibromo-4,5-methylenedioxybenzene).

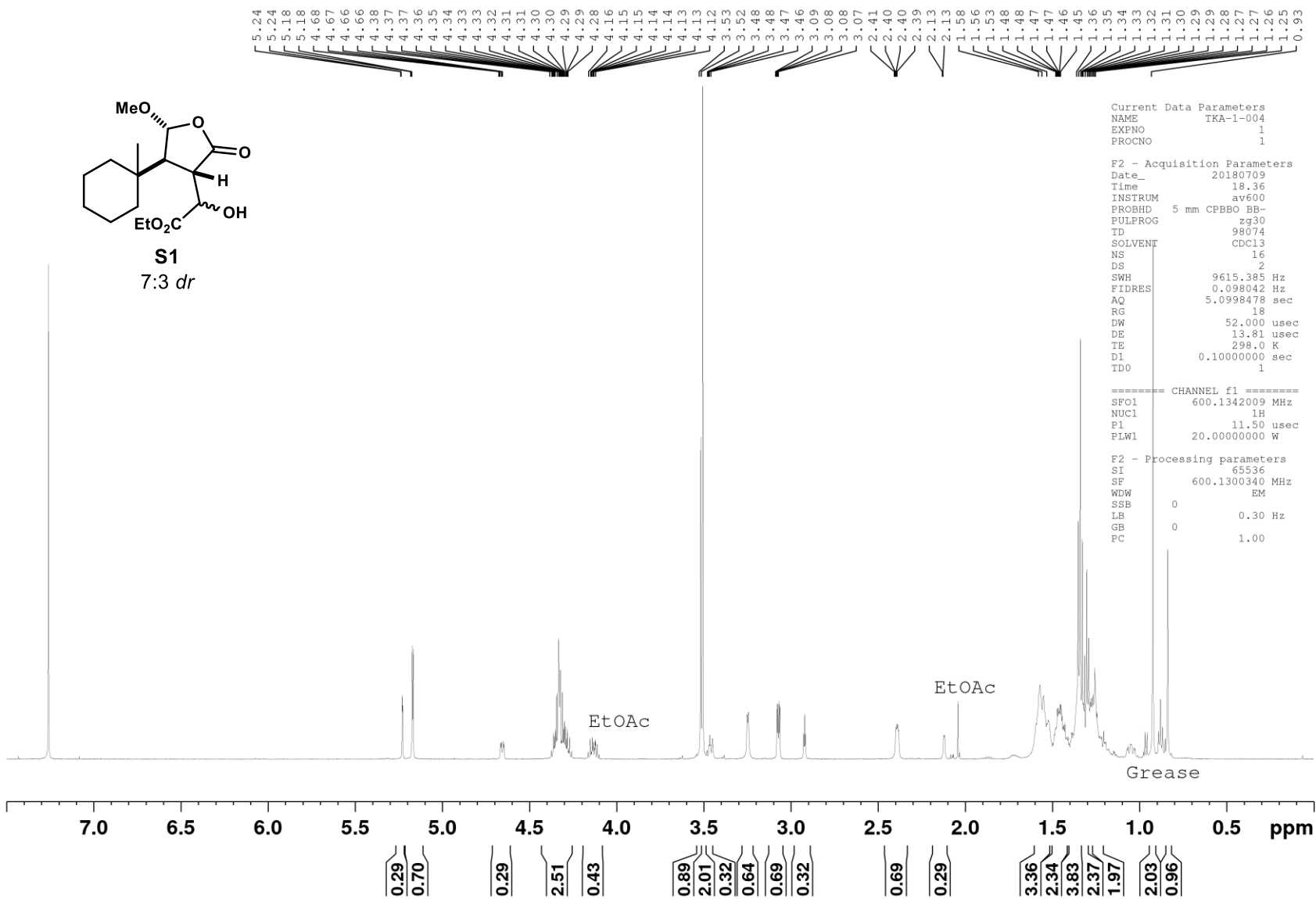
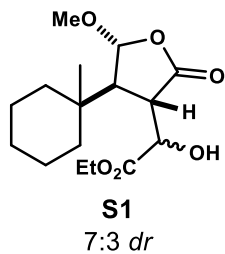
^bYield of hydration byproduct shown in parentheses, only one diastereomer observable by ¹H NMR

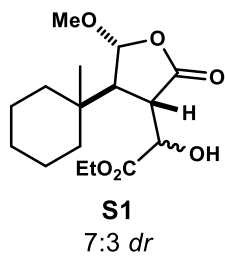
^cDiastereomeric ratio determined by comparing integrations of acetal proton

References:

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9. Obradors, C.; Martinez, R. M.; Shenvi, R. A. *J. Am. Chem. Soc.* **2016**, *138*, 4962 – 4971.
10. Butenolide **36** unstable when stored for extended periods of time; this instability is exacerbated by storage in chlorinated solvents or by dry loading on SiO₂ gel. The major observed decomposition product is a grease-like broad multiplet centered at 1.25 ppm in CDCl₃.
11. Macfarlandin C decomposes under mildly acidic conditions such as prolonged exposure to silica gel or CDCl₃, resulting in the growth of an inseparable decomposition product showing a diagnostic broad multiplet at 1.25 ppm (¹H NMR, CDCl₃) and peaks at 29.7, 29.4 and 14.1 ppm (¹³C NMR, CDCl₃).
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16. Magnus, P.; Waring, M.J.; Scott, D.A. *Tetrahedron Lett.* **2000**, *41*, 9731 – 9733.

Spectral Data





176.20
174.64
172.41
172.35

105.97
105.37

70.77
70.58
62.63
62.05
57.26
56.87
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35.61
35.45
34.95
34.64
34.42
33.98
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21.34
21.32
20.30
19.52
14.08
14.06

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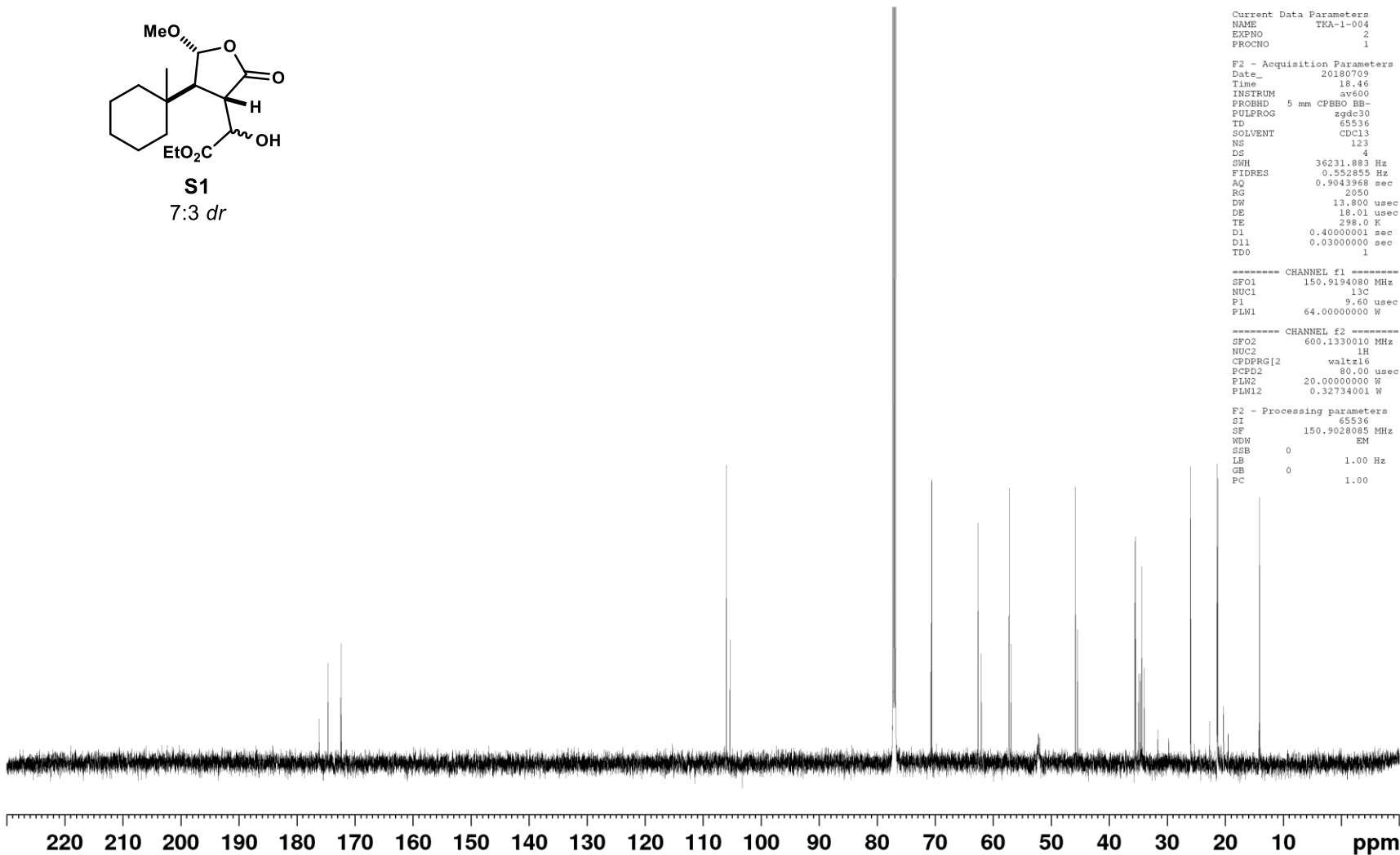
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PROCNO    1

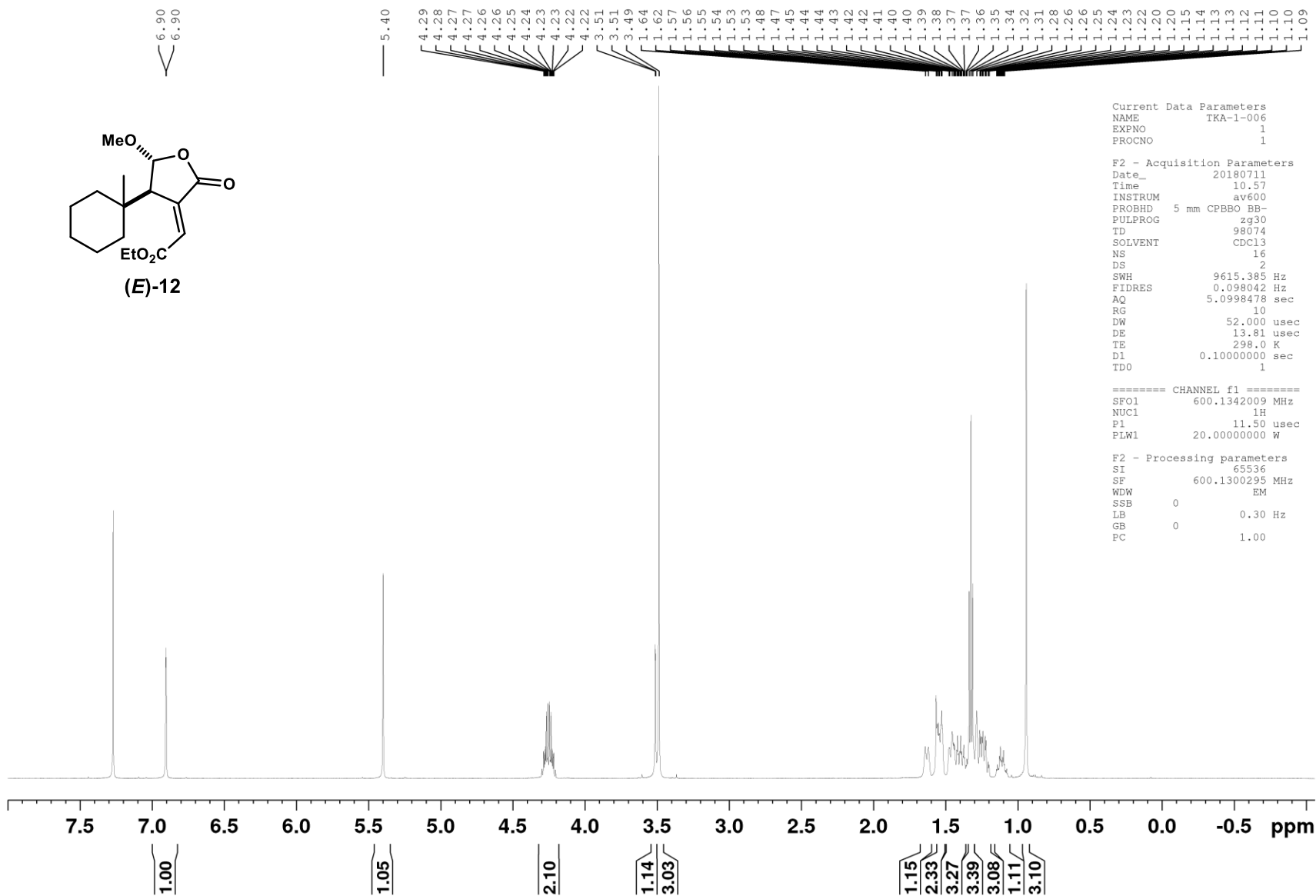
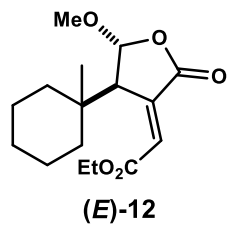
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NS         123
DS         4
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FIDRES     0.552855 Hz
AQ         0.9043968 sec
RG         2050
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DE         18.01 usec
TE         298.0 K
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D11        0.03000000 sec
TDO        1

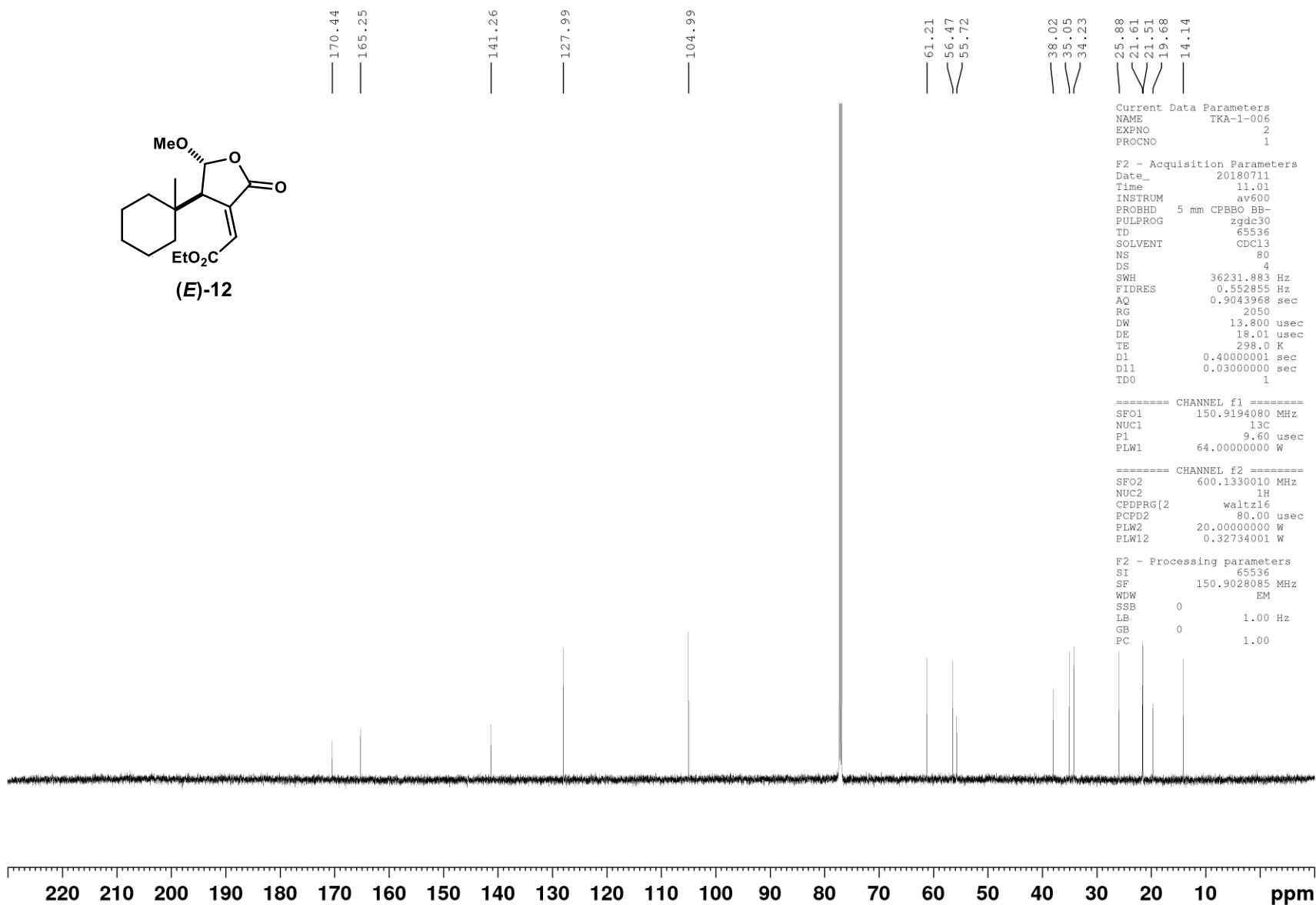
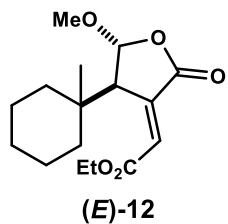
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NUC1       13C
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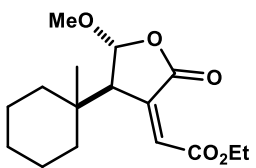
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PCPD2      80.00 usec
PLW2       20.00000000 W
PLW12      0.32734001 W

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SF         150.9028085 MHz
WDW        EM
SSB        0
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FC         1.00
  
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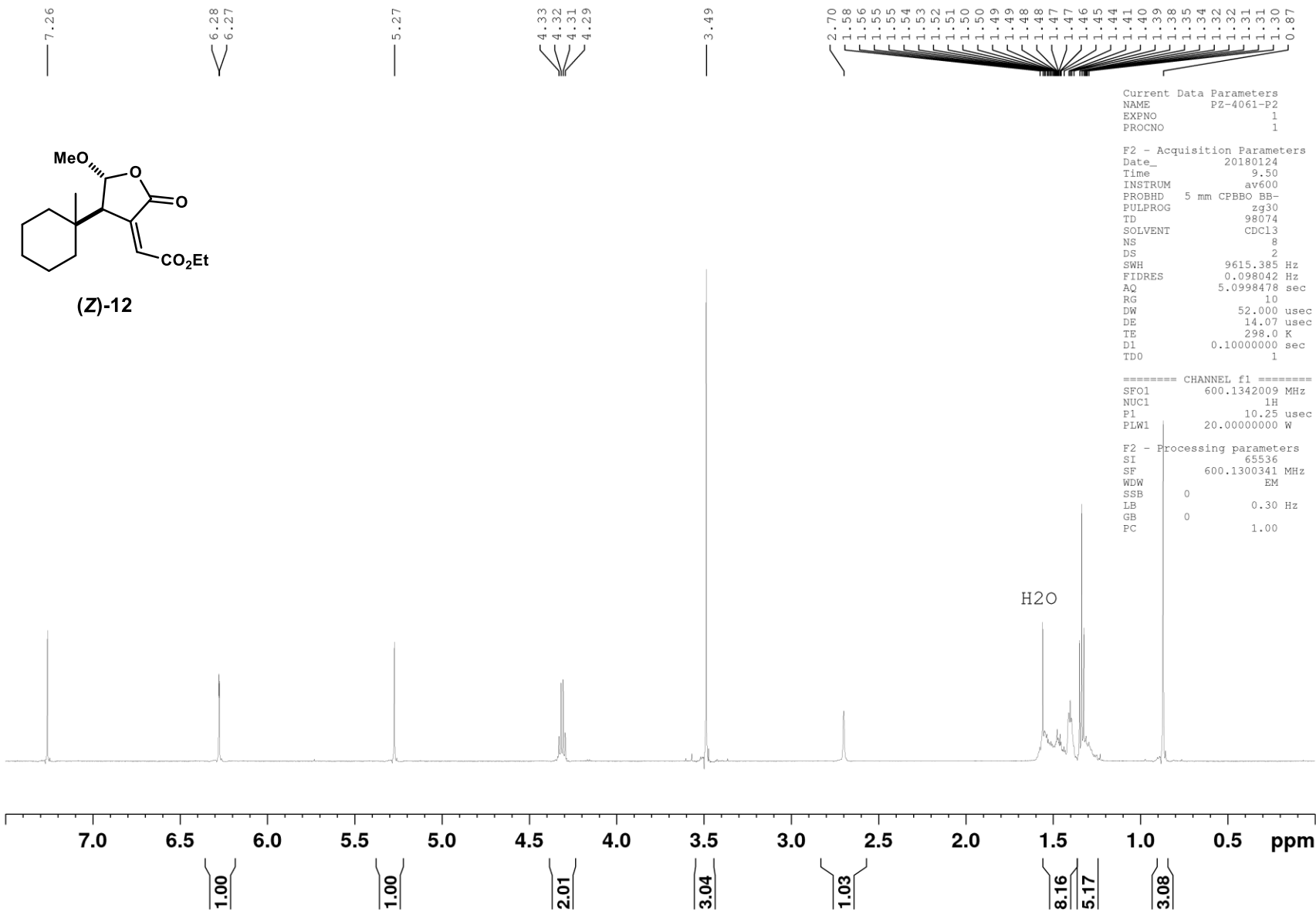


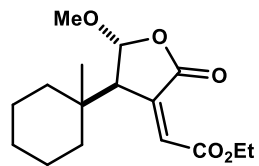




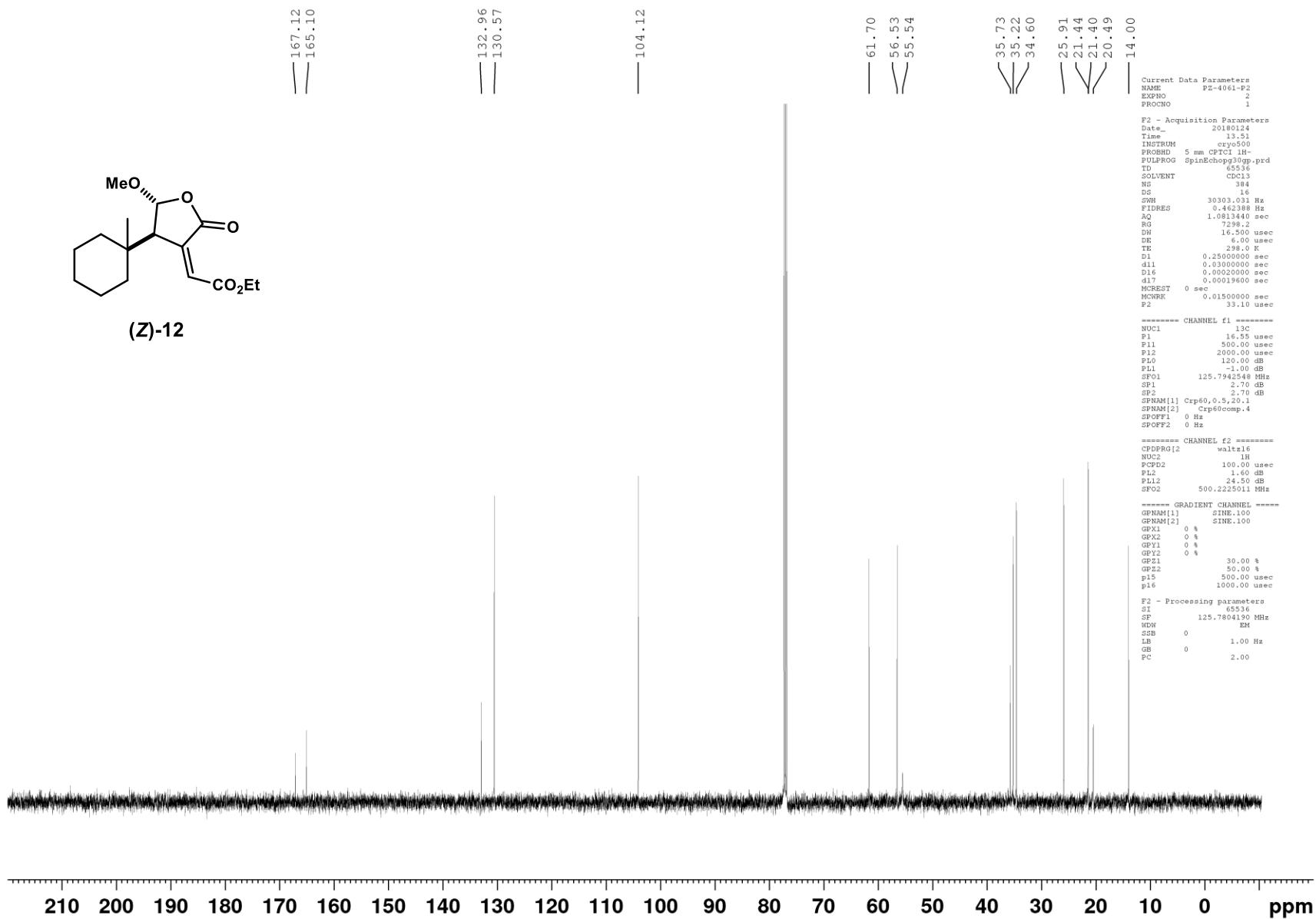


(Z)-12





(Z)-12



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EXPNO     2
PROCNO    1

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PULPROG   spinEchop30pp.prd
TD         65536
SOLVENT   CDCl3
NS         384
DS         16
SWH        30303.031 Hz
FIDRES     0.462388 Hz
AQ         1.0813440 sec
RG         7298.2
DM         16.500 usec
DE         6.00 usec
TE         298.0 K
D1         0.25000000 sec
d11        0.03000000 sec
D16        0.00020000 sec
d17        0.00018000 sec
MCREST     0 sec
MCNRK      0.01500000 sec
P2         33.10 usec

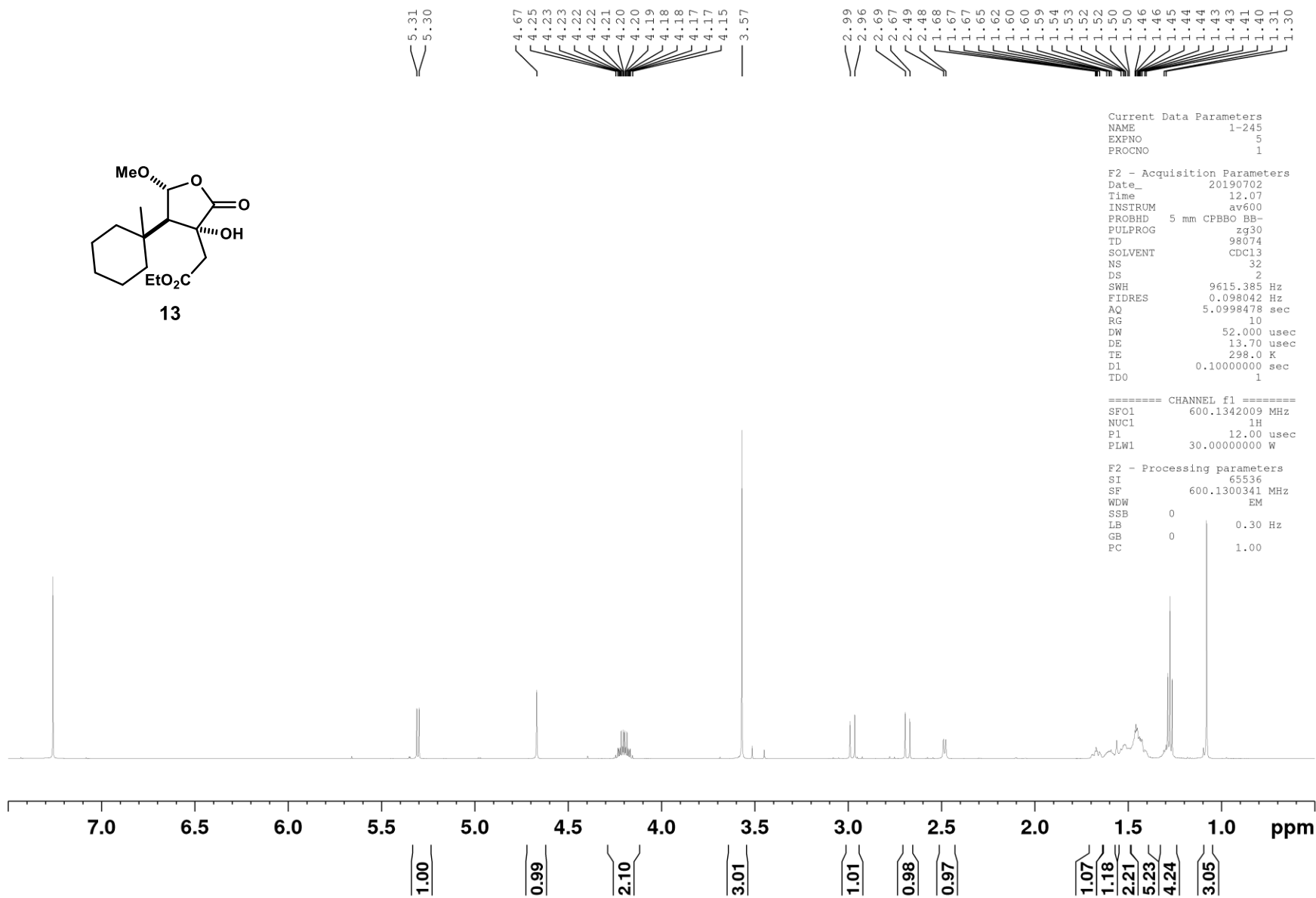
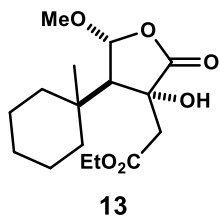
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PLO        120.00 dB
PL1        -1.00 dB
SFO1       125.7942548 MHz
SP1        2.70 dB
SP2        2.70 dB
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SPNAM[2]   Crp60comp.4
SPOFF1     0 Hz
SPOFF2     0 Hz

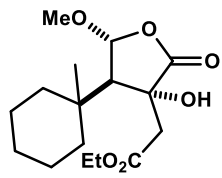
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CPDPRG2    waltz16
NUC2       1H
PCPD2      100.00 usec
PL2        1.60 dB
PL12       24.50 dB
SFO2       500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM[1]   SINE.100
GPNAM[2]   SINE.100
GPX1       0 %
GPX2       0 %
GPV1       0 %
GPV2       0 %
GPZ1       30.00 %
GPZ2       50.00 %
p15        500.00 usec
p16        1000.00 usec

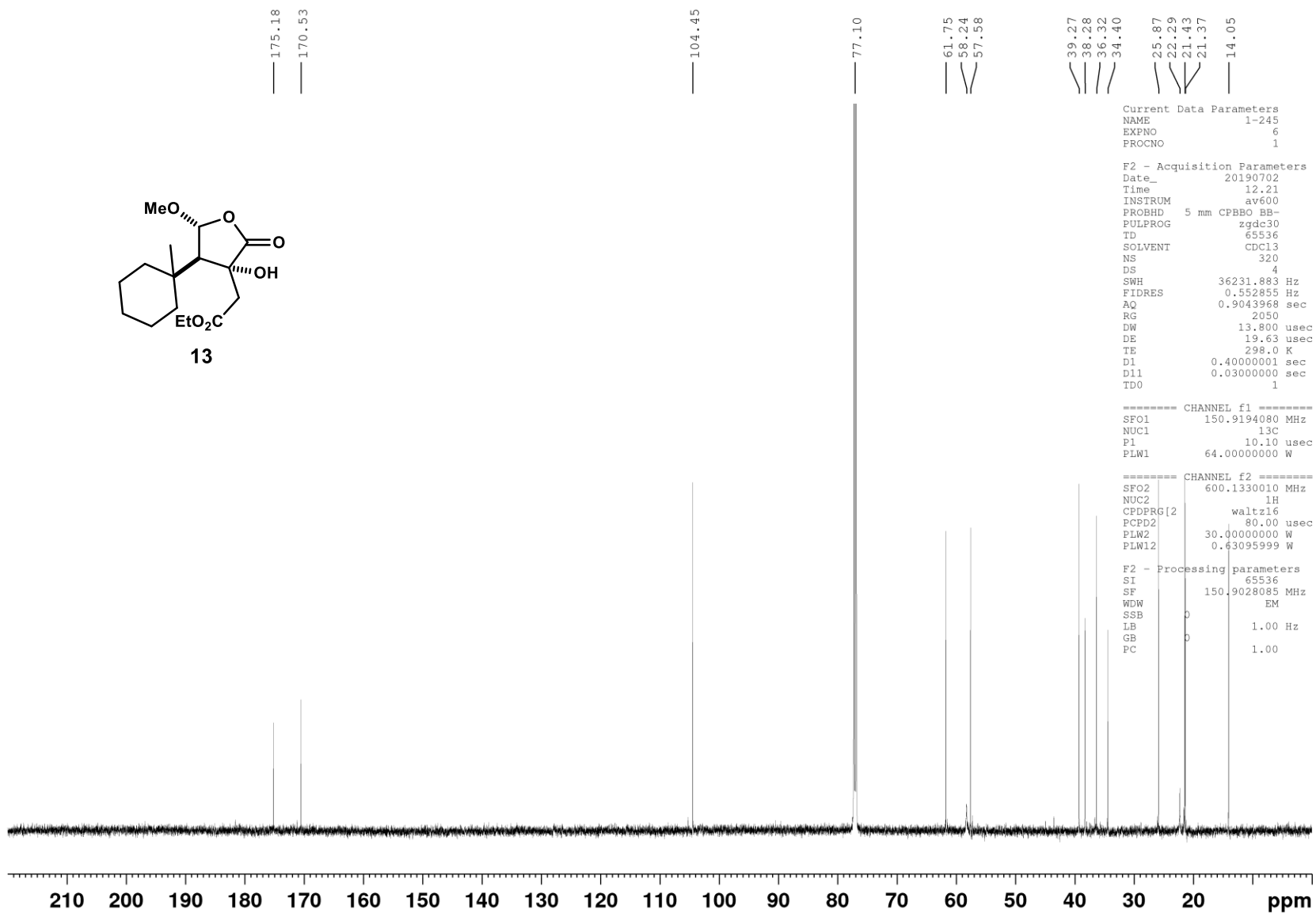
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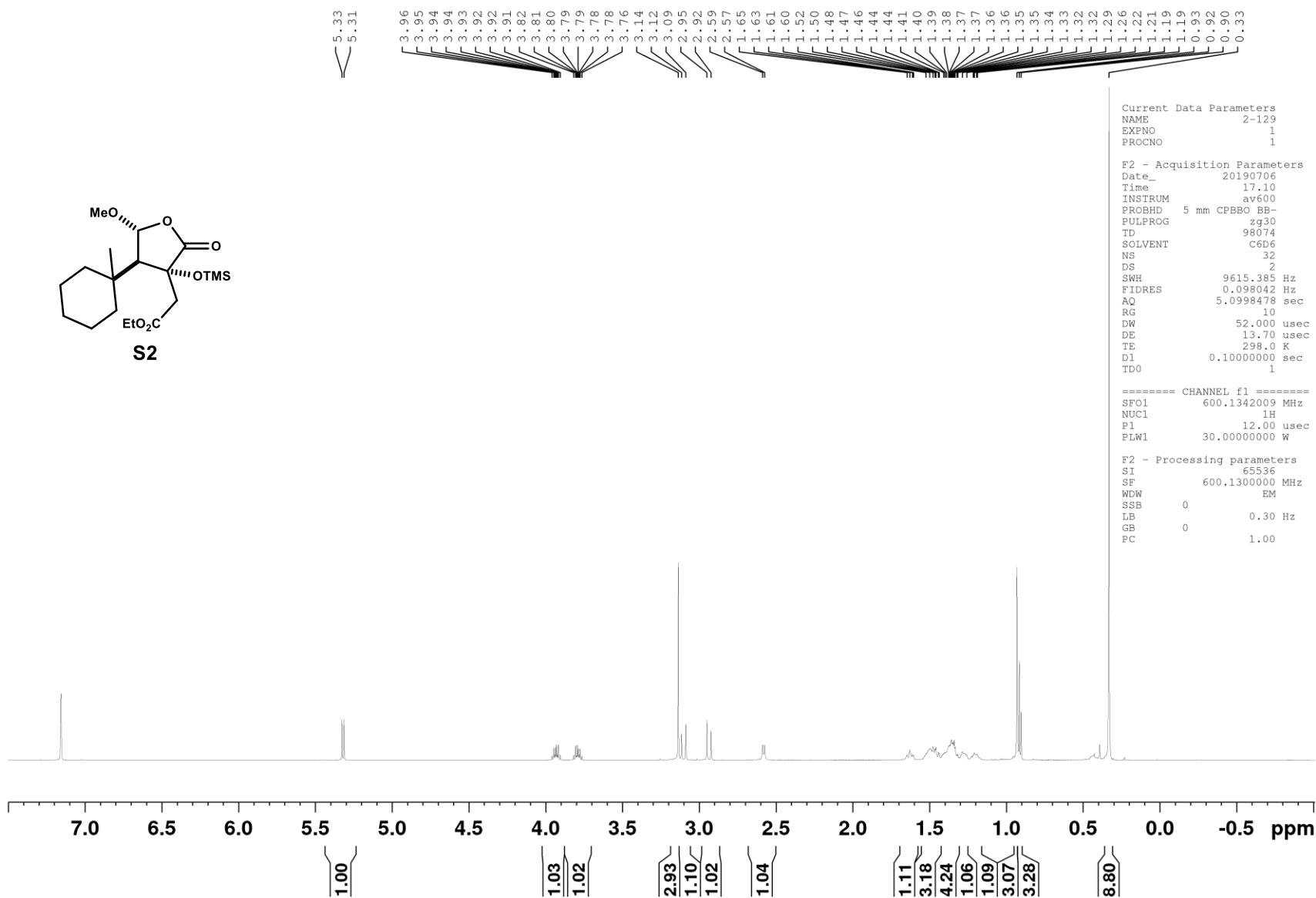
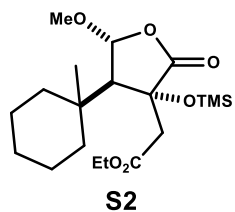
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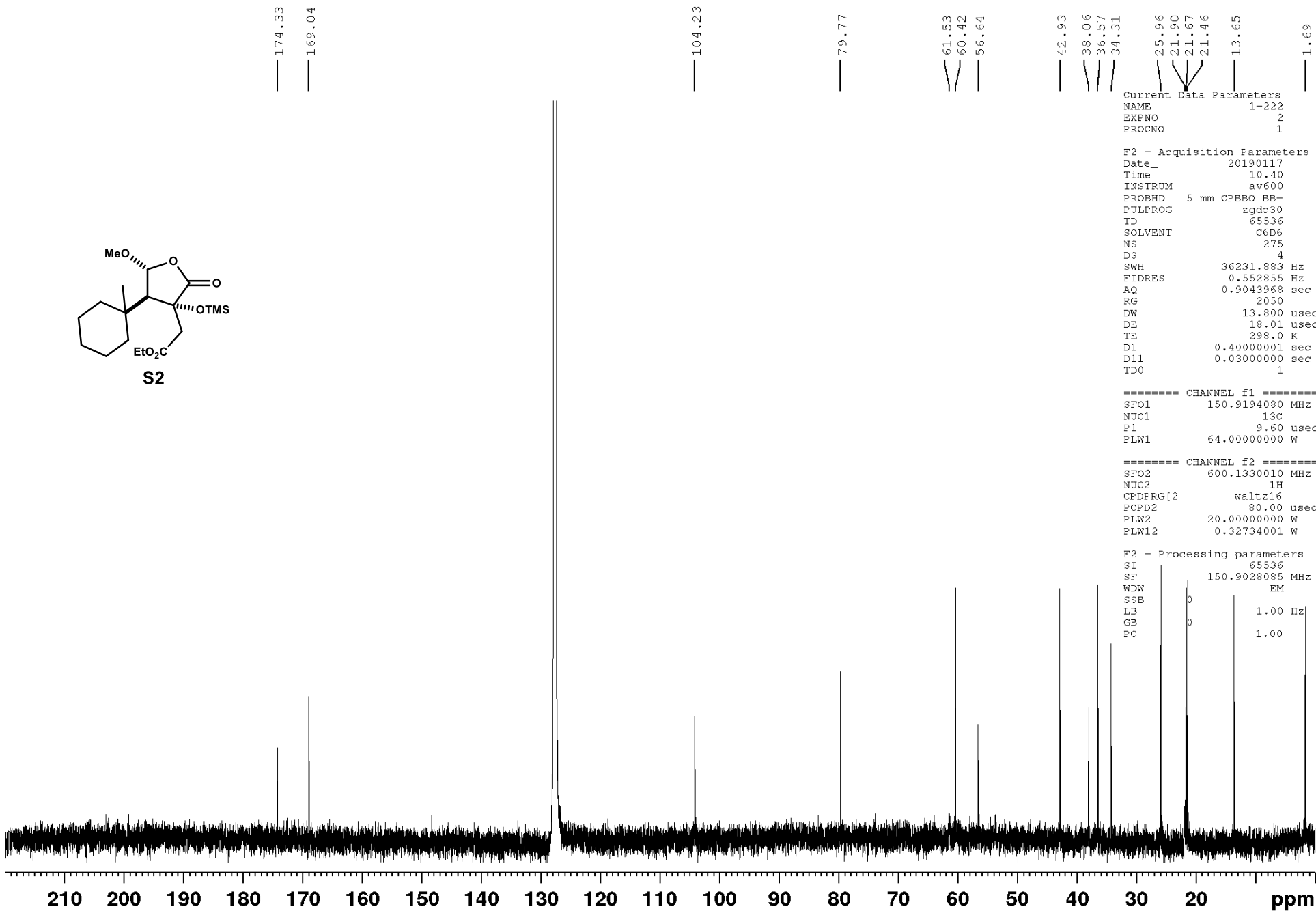
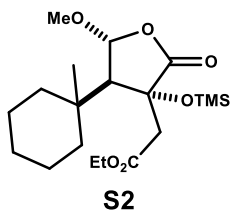




13







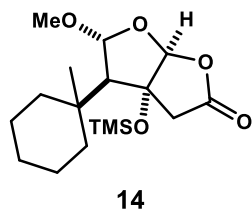
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 PROCNO 1

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 DS 4
 SWH 36231.883 Hz
 FIDRES 0.552855 Hz
 AQ 0.9043968 sec
 RG 2050
 DW 13.800 usec
 DE 18.01 usec
 TE 298.0 K
 D1 0.40000001 sec
 D11 0.03000000 sec
 TD0 1

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 NUC1 13C
 P1 9.60 usec
 PLW1 64.00000000 W

===== CHANNEL f2 =====
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 NUC2 1H
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 PCD2 80.00 usec
 PLW2 20.00000000 W
 PLW12 0.32734001 W

F2 - Processing parameters
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 SF 150.9028085 MHz
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 SSB 0
 LB 1.00 Hz
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 PC 1.00



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5.71

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4.55
4.54

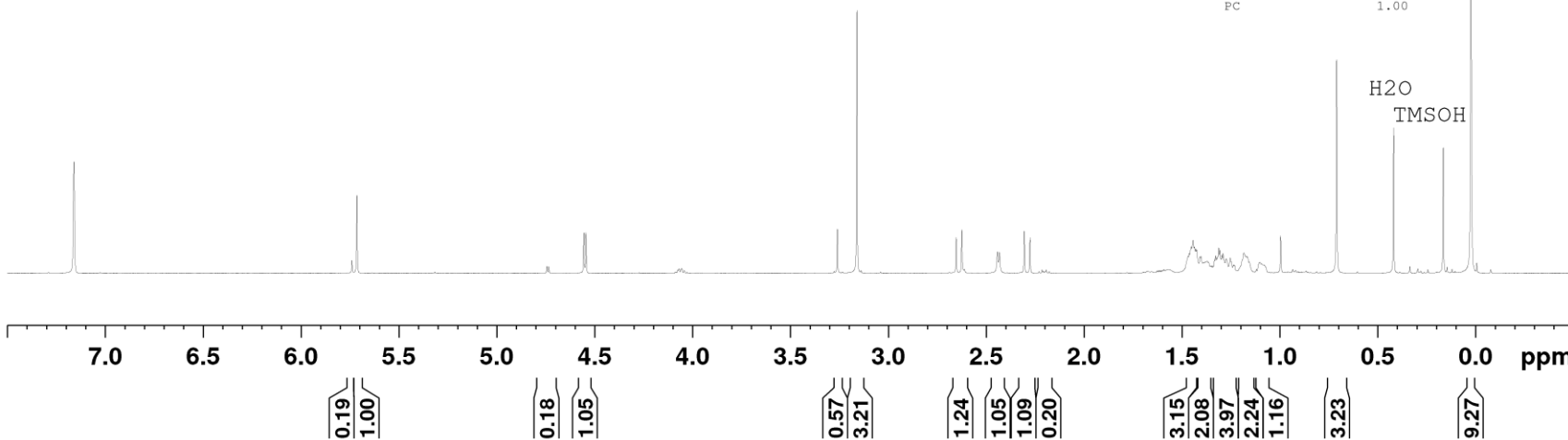
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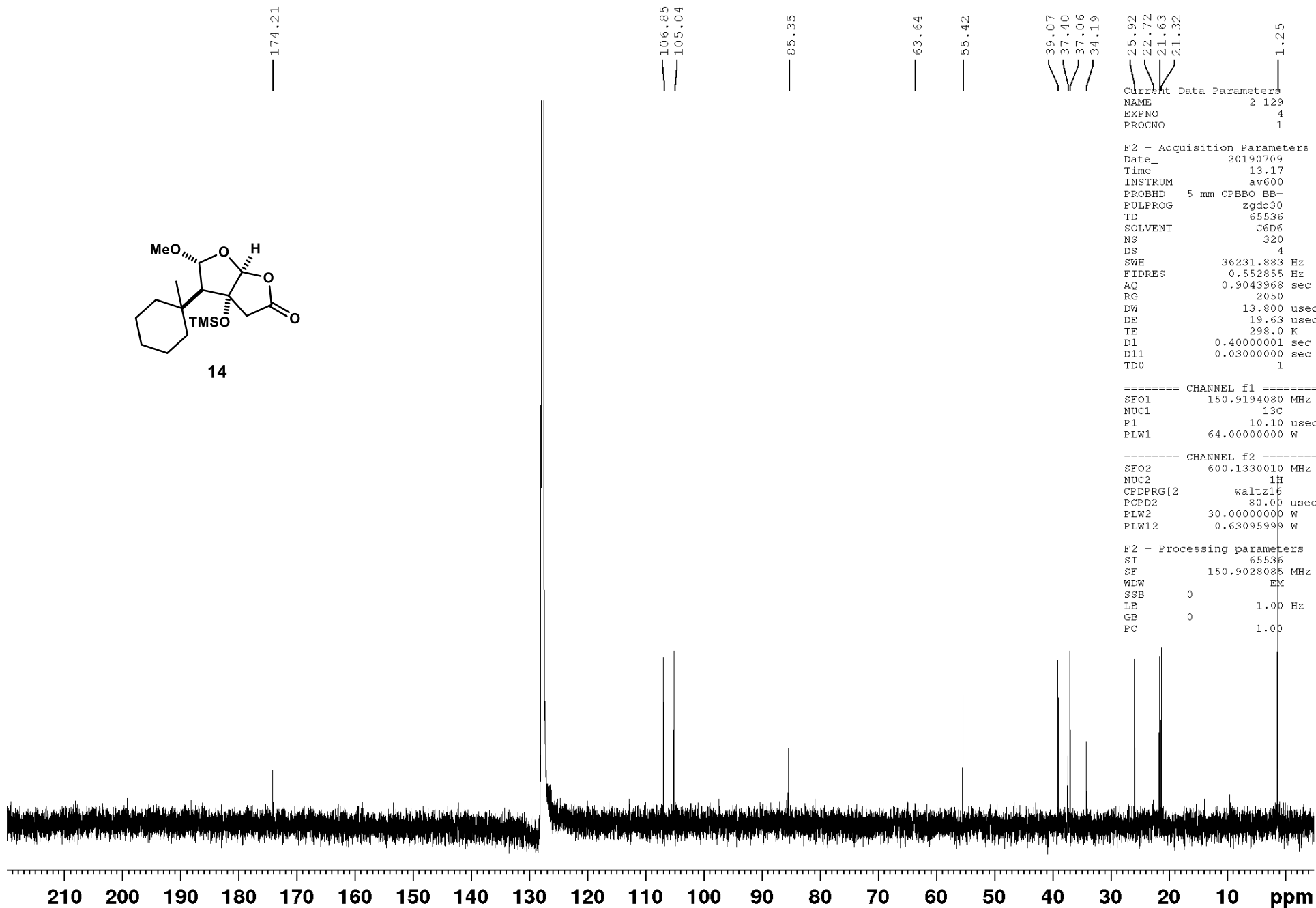
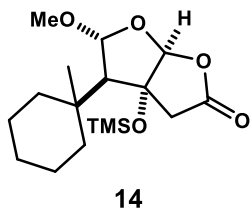
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TD 98074
SOLVENT C6D6
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DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 10
DW 52.000 usec
DE 13.70 usec
TE 298.0 K
D1 0.10000000 sec
TDO 1

===== CHANNEL f1 =====
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NUC1 1H
P1 12.00 usec
PLW1 30.00000000 W

F2 - Processing parameters
SI 65536
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SSB 0
LB 0.30 Hz
GB 0
PC 1.00





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Current Data Parameters
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EXPNO         4
PROCNO        1

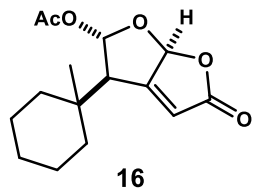
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DS            4
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FIDRES        0.552855 Hz
AQ            0.9043968 sec
RG            2050
DW            13.800 usec
DE            19.63 usec
TE            298.0 K
D1            0.40000001 sec
D11           0.03000000 sec
TD0           1

===== CHANNEL f1 =====
SFO1          150.9194080 MHz
NUC1           13C
P1             10.10 usec
PLW1           64.00000000 W

===== CHANNEL f2 =====
SFO2          600.1330010 MHz
NUC2            1H
CPDPRG[2]     waltz16
PCPD2         80.00 usec
PLW2          30.00000000 W
PLW12         0.63095999 W

F2 - Processing parameters
SI            65536
SF            150.9028085 MHz
WDW           EM
SSB           0
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GB            0
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```



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5.98
5.98

3.22

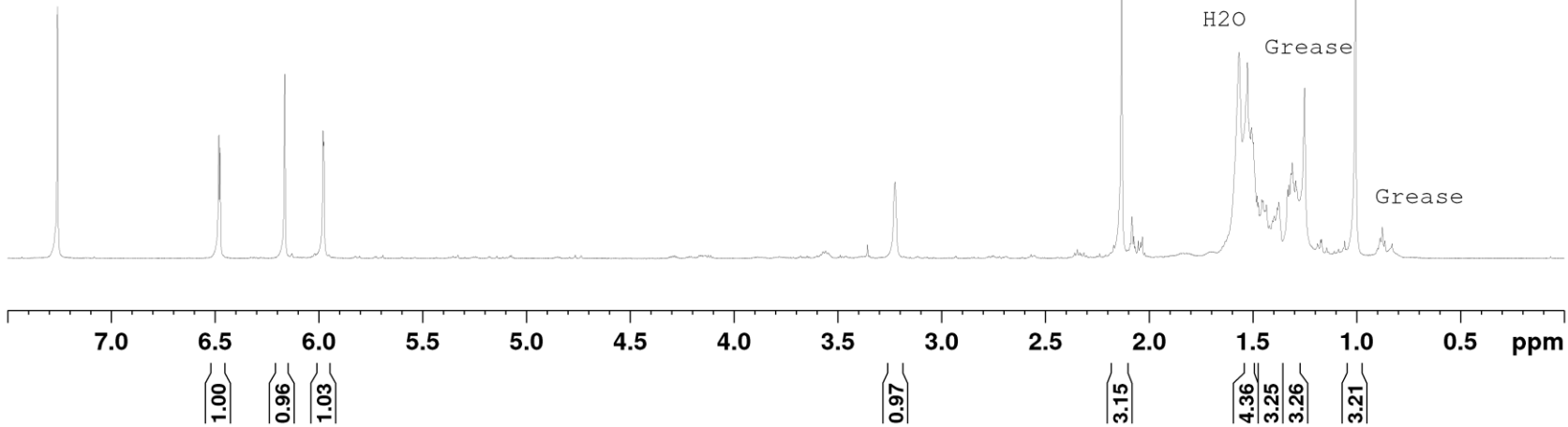
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1.33
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1.31
1.29
1.25
1.01

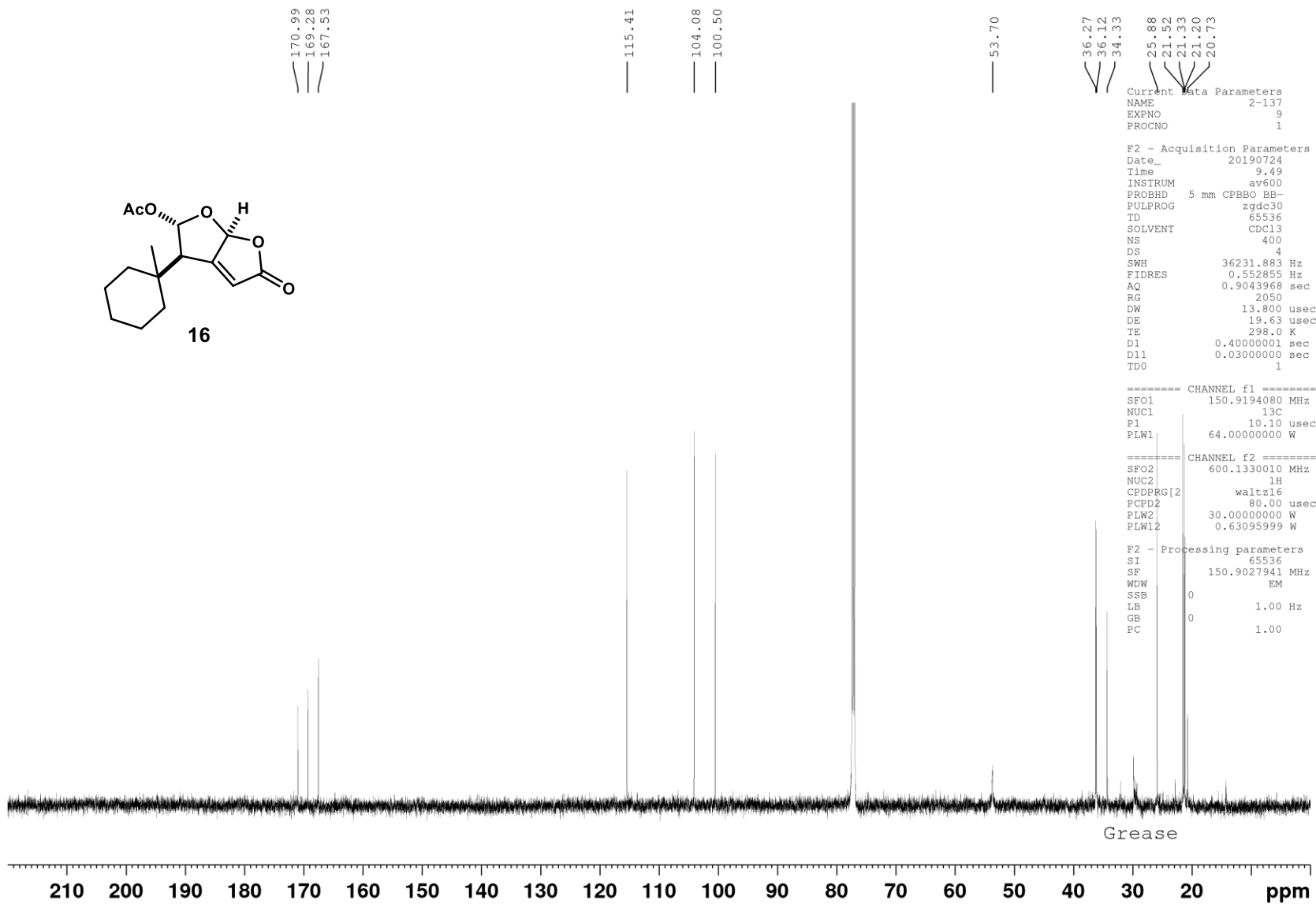
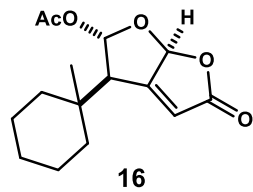
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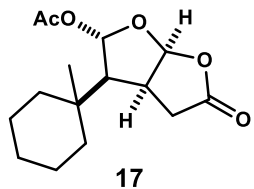
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TD            98074
SOLVENT       CDCl3
NS            32
DS            2
SWH           9615.385 Hz
FIDRES        0.098042 Hz
AQ            5.0998478 sec
RG            10
DW            52.000 usec
DE            13.70 usec
TE            298.0 K
D1            0.10000000 sec
TD0           1

===== CHANNEL f1 =====
SFO1          600.1342009 MHz
NUC1          1H
PI            12.00 usec
PLW1          30.00000000 W

F2 - Processing parameters
SI            65536
SF            600.1300364 MHz
WDW           EM
SSB           0
LB            0.30 Hz
GB            0
PC            1.00
```

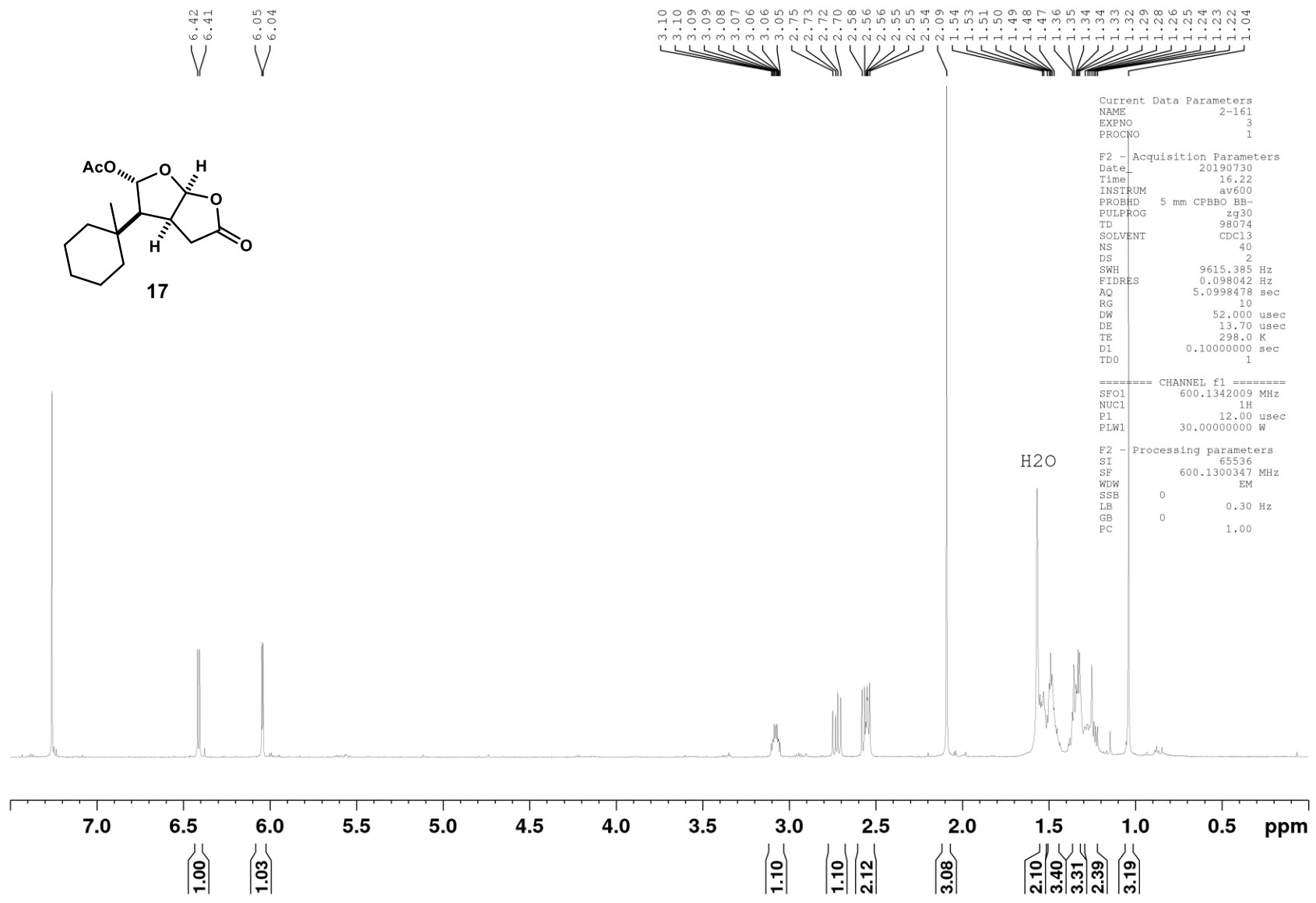


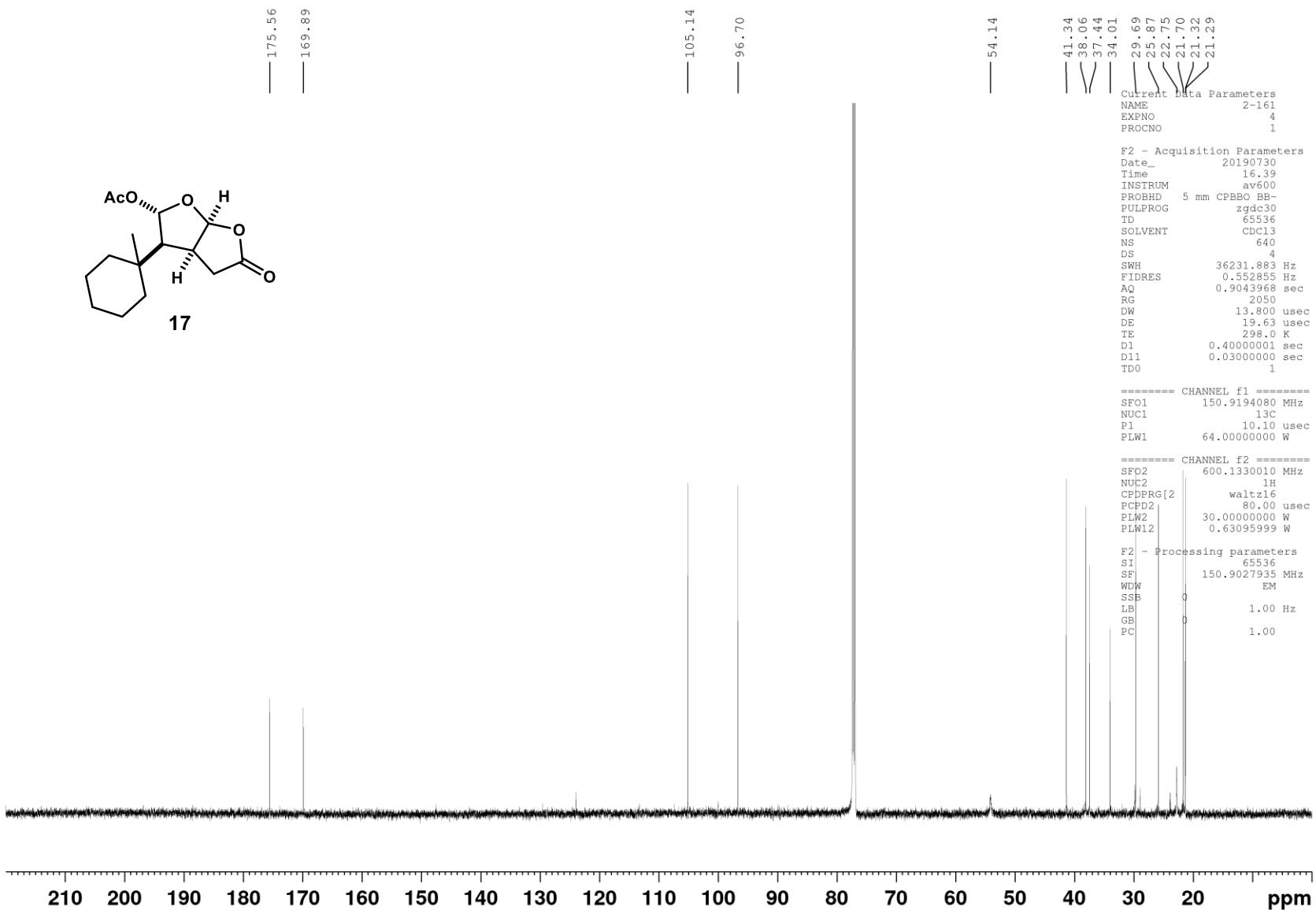
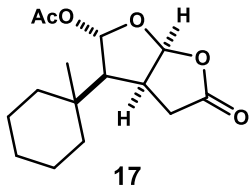


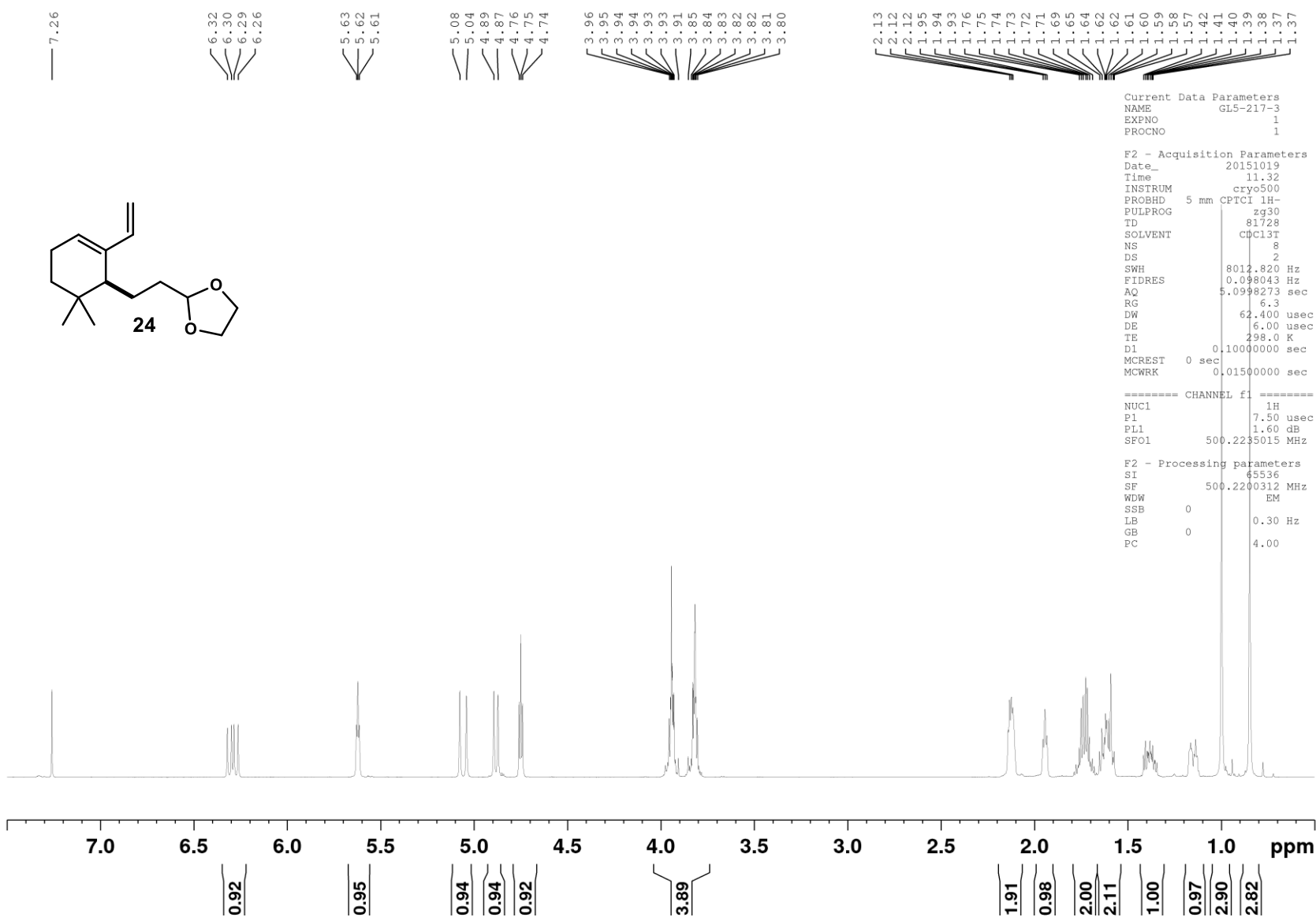


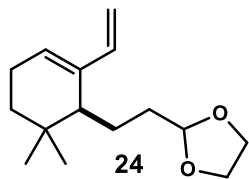
6.42
6.41

6.05
6.04









140.49
140.21

127.95

109.77
105.13

77.41
77.16
76.90

64.96
64.92

43.05

34.68
32.50
30.47
28.85
27.05
26.79
23.66

Current Data Parameters
NAME GLS-217-3
EXPNO 2
PROCNO 1

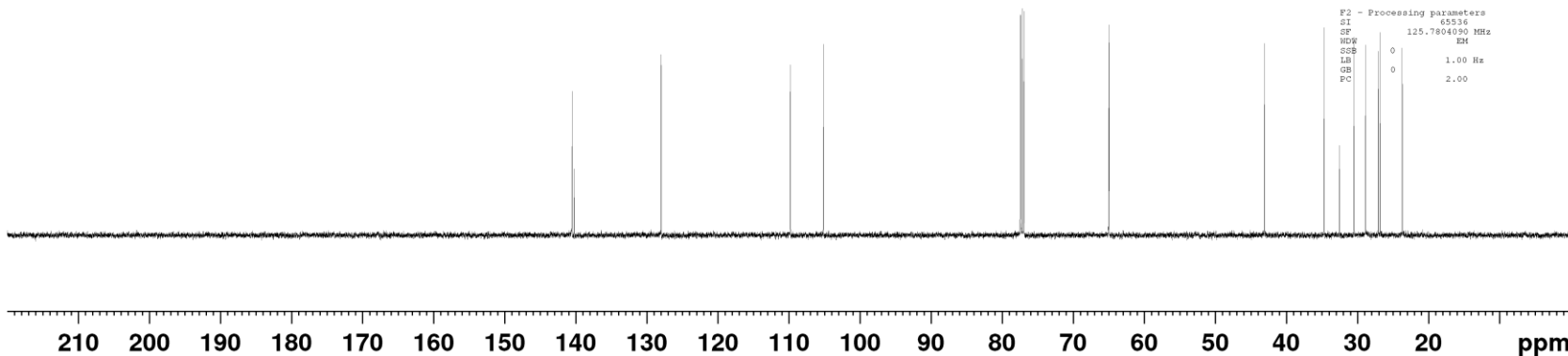
F2 - Acquisition Parameters
Date_ 20191019
Time 11:34
INSTRUM cryo500
PROBHD 5 mm CPXI 1H-
PULPROG SpinEcho30ppr.prd
TD 65536
SOLVENT CDCl3
NS 85
DS 16
SFO 30303.031 Hz
FIDRES 0.462388 Hz
AQ 1.0819440 sec
RG 10321.3
DM 16.500 usec
DE 6.00 usec
TE 298.0 K
DL 0.25000000 sec
dL1 0.03000000 sec
D16 0.00020000 sec
d17 0.00019600 sec
MCREST 0 sec
MCWRR 0.01500000 sec
F2 33.10 usec

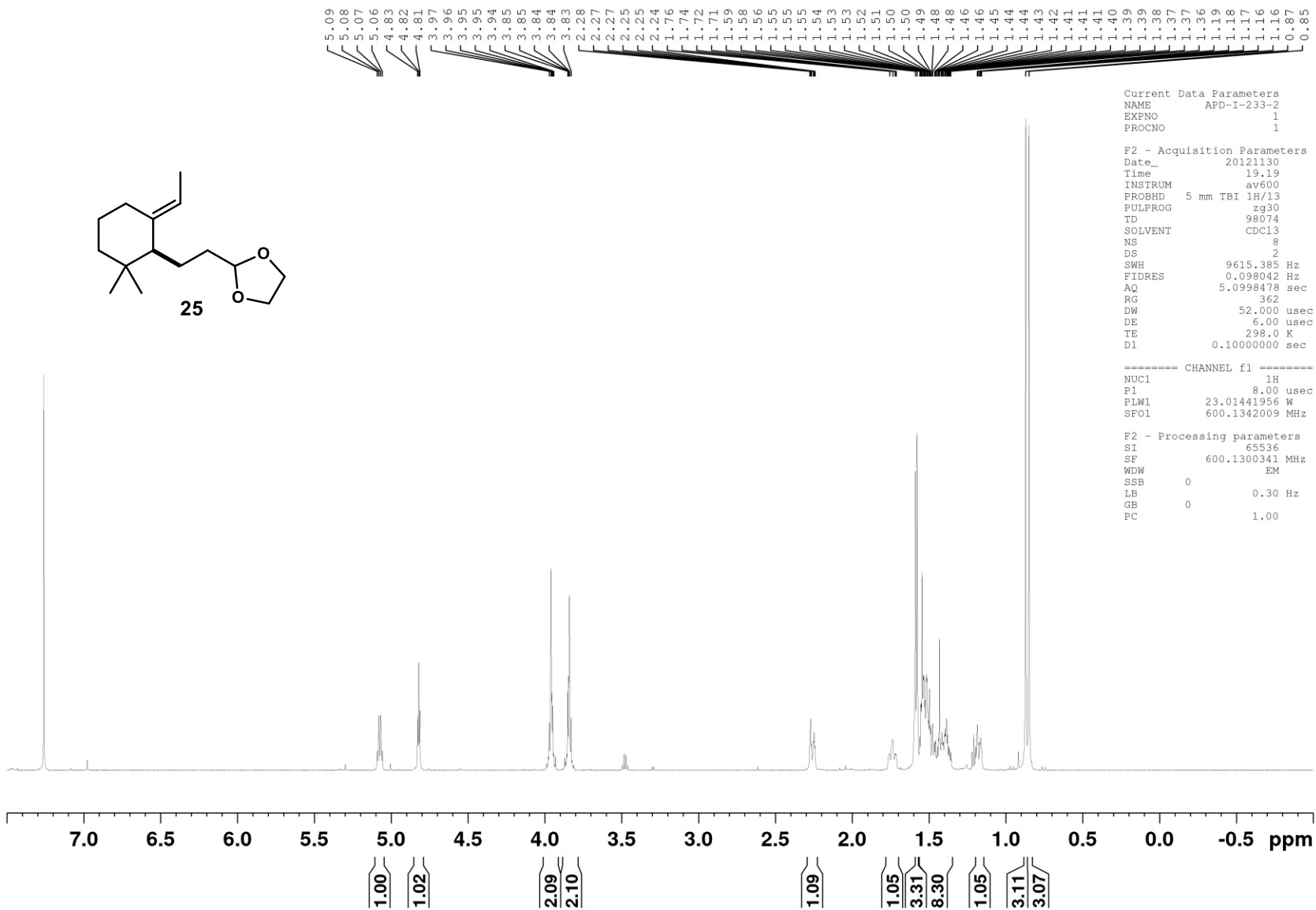
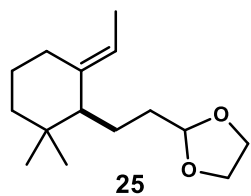
===== CHANNEL f1 =====
NUC1 13C
P1 16.55 usec
P11 500.00 usec
P12 2000.00 usec
PL0 120.00 dB
PL1 -1.00 dB
SFO1 125.7942548 MHz
SP1 2.70 dB
SP2 2.70 dB
SFOFF1 0 Hz
SFOFF2 0 Hz

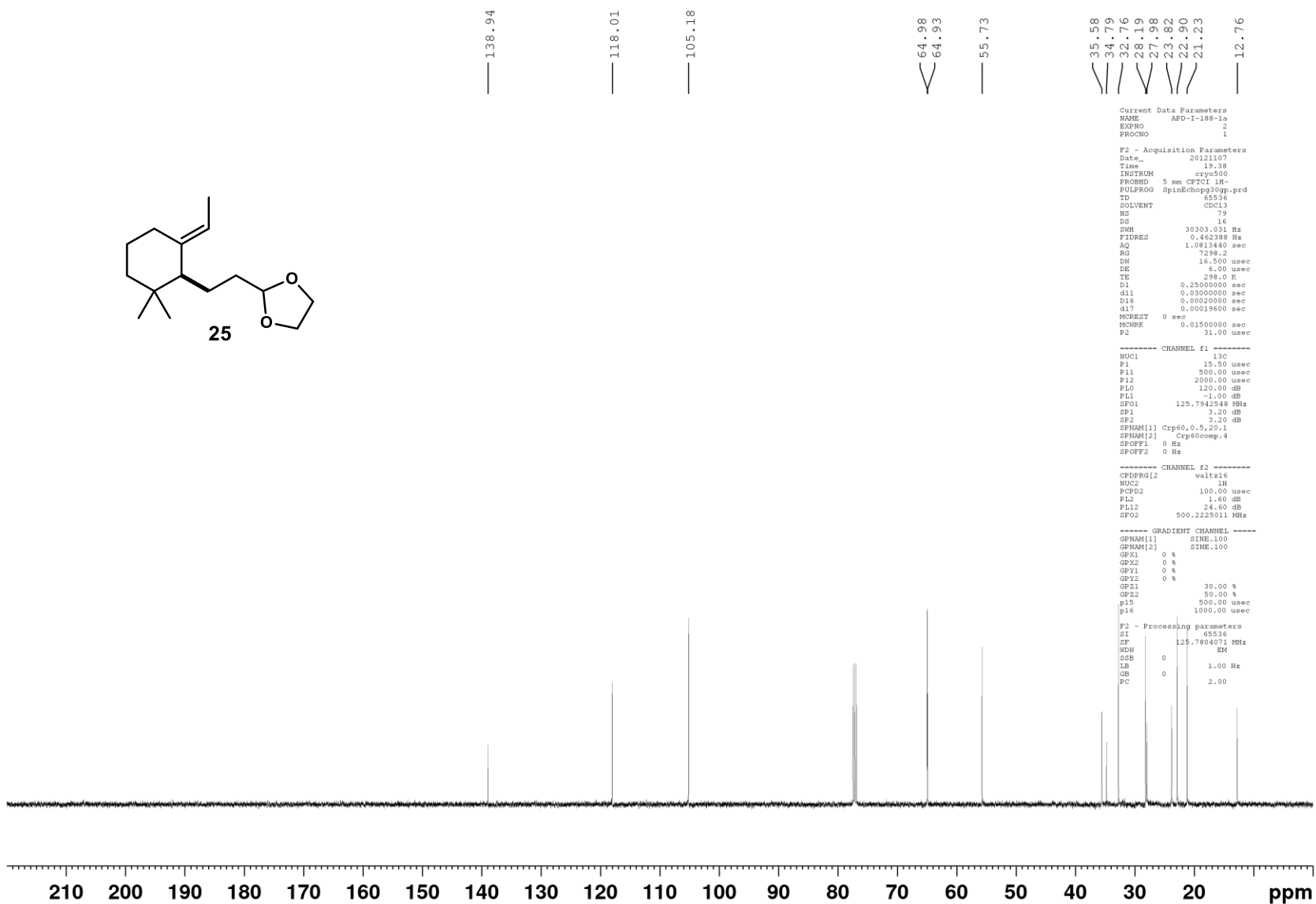
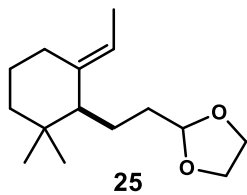
===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 1.60 dB
PL12 24.50 dB
SFO2 500.2225011 MHz

===== GRADIENT CHANNEL =====
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPX1 0 %
GPX2 0 %
GPY1 0 %
GPY2 0 %
GPZ1 30.00 %
GPZ2 50.00 %
p15 500.00 usec
p16 1000.00 usec

F2 - Processing parameters
SI 65536
SF 125.7804090 MHz
RG 0 EM
LB 1.00 Hz
GB 0
PC 2.00







```

Current Data Parameters
NAME      APD-I-188-1a
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20121107
Time      19.38
INSTRUM   cryo500
PROBHD    5 mm CPTCI 1H-
PULPROG   spinEchoq30pp-prd
ID         65536
SOLVENT   CDCl3
NS         79
DS         16
SWH        30303.031 Hz
FIDRES     0.462388 Hz
AQ         1.0813440 sec
RG         7298.2
DW         14.500 usec
DE         6.00 usec
TE         298.0 K
D1         0.25000000 sec
d11        0.03000000 sec
D16        0.00200000 sec
d17        0.00019600 sec
MCRET     0 sec
MCHREK    0.01500000 sec
P2         31.00 usec

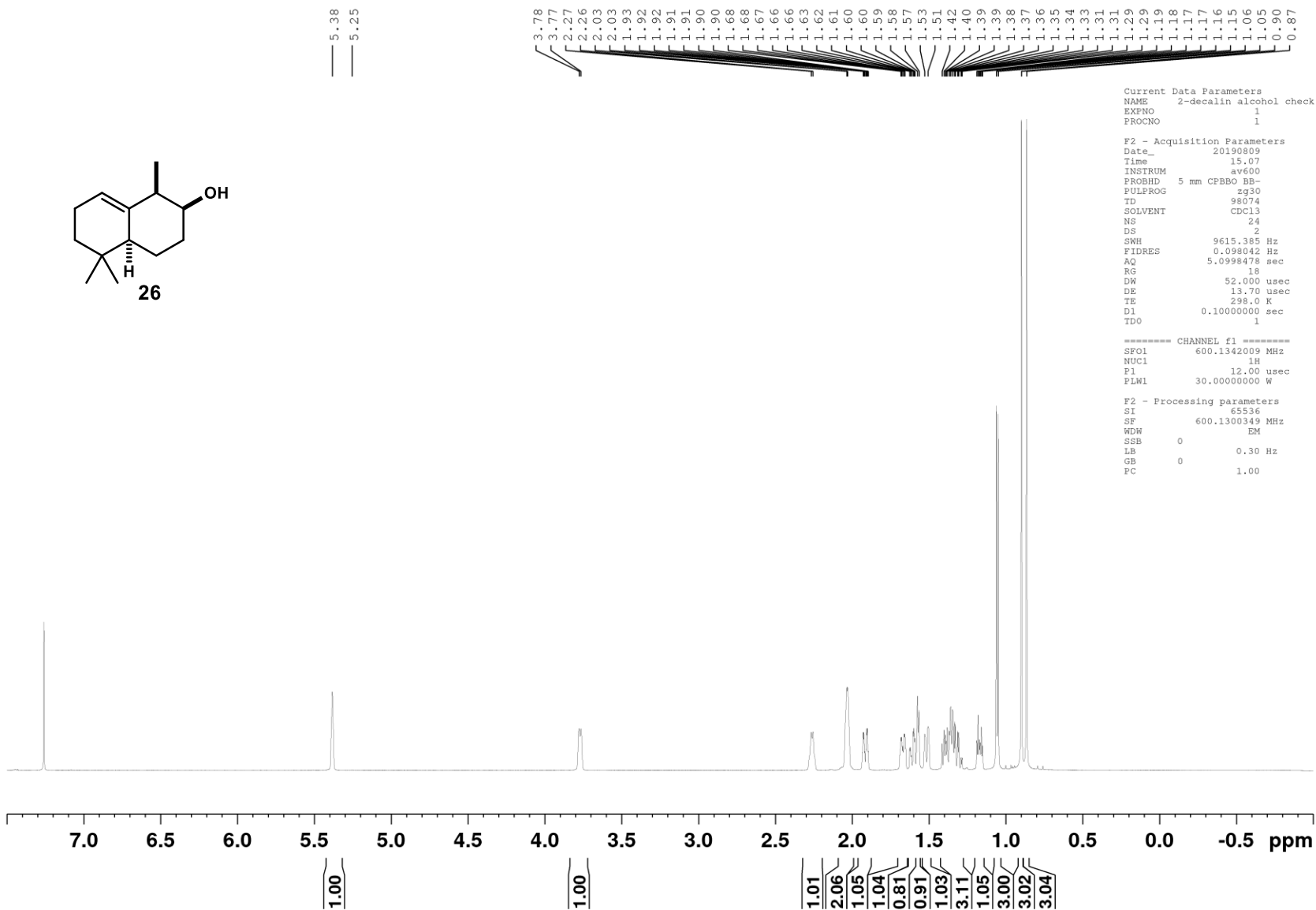
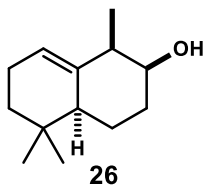
----- CHANNEL f1 -----
NUC1       13C
P1         15.50 usec
P11        500.00 usec
P12        2000.00 usec
PL0        120.00 dB
PL1        -1.00 dB
SFO1       125.7942548 MHz
SP1        3.20 dB
SP2        3.20 dB
SFOFF[1]   Crp60,0.5,30.1
SFOFF[2]   Crp60comp,4
SFOFF1     0 Hz
SFOFF2     0 Hz

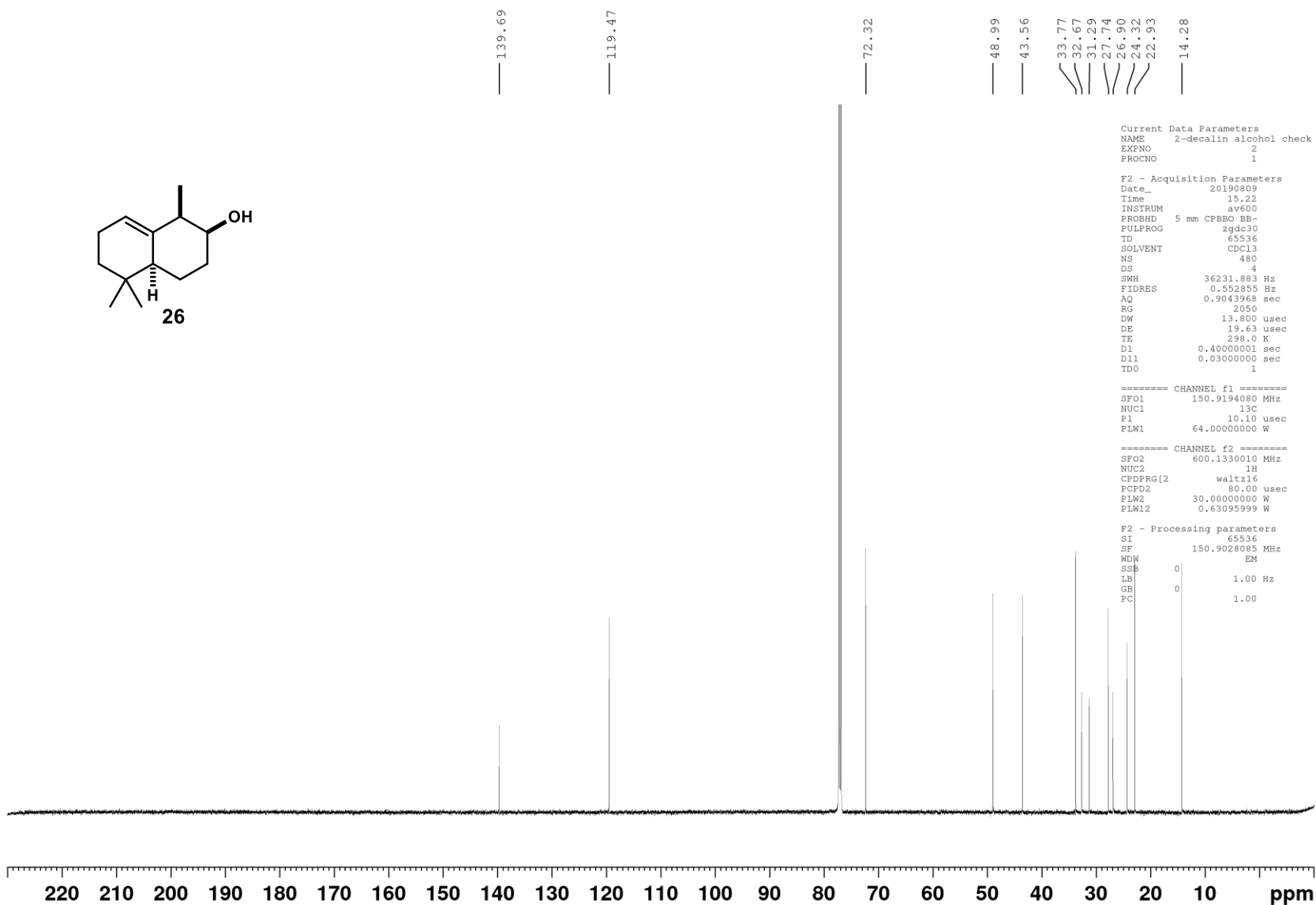
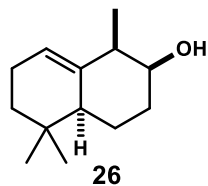
----- CHANNEL f2 -----
CPDPRG2    waltz16
NUC2       1H
PCPD2     100.00 usec
PL2        1.60 dB
PL12       24.60 dB
SFO2       500.225011 MHz

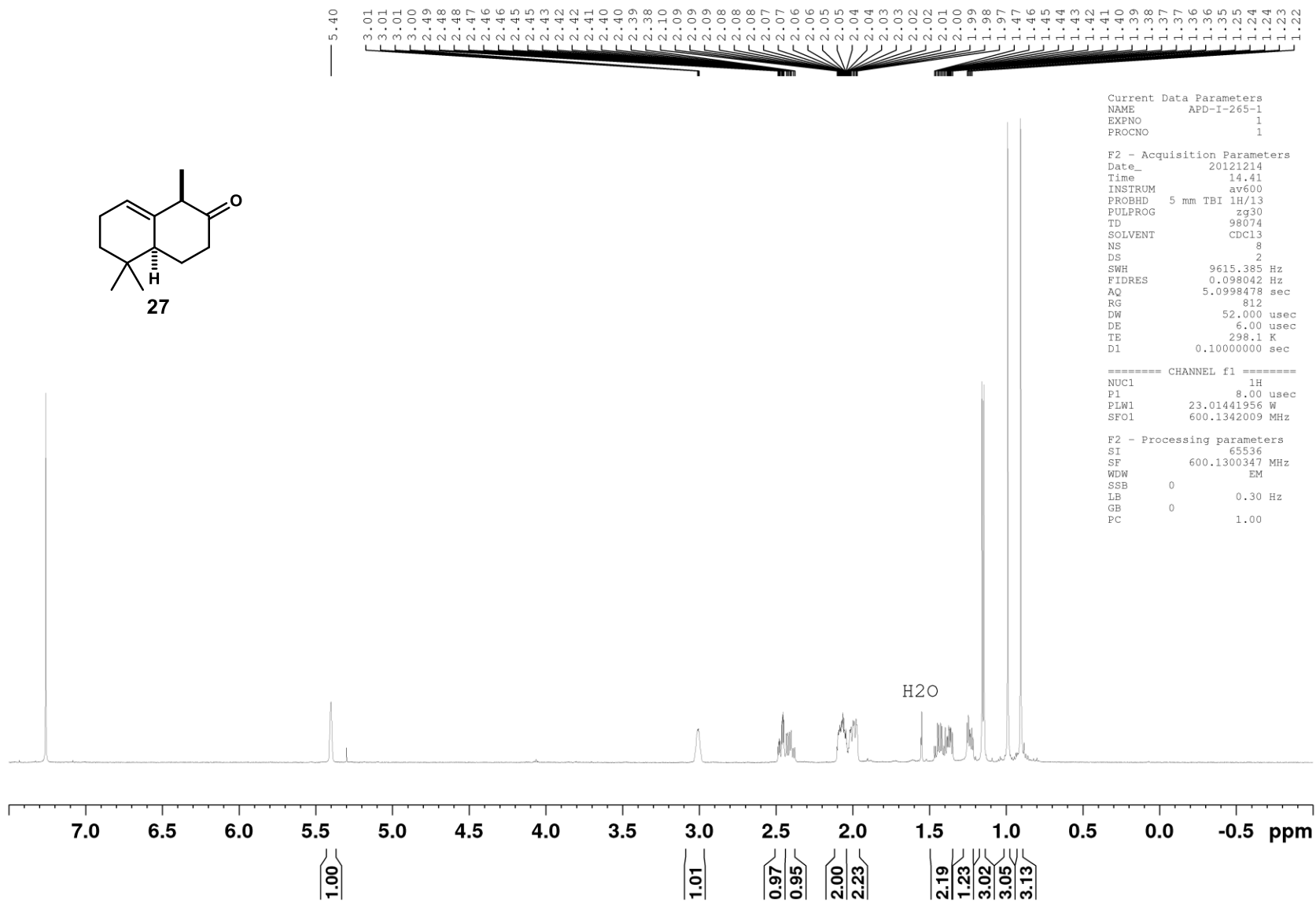
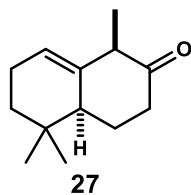
----- GRADIENT CHANNEL -----
GPNAM[1]   SINE.100
GPNAM[2]   SINE.100
GPX1       0 %
GPX2       0 %
GPY1       0 %
GPY2       0 %
GPZ1       30.00 %
GPZ2       50.00 %
p15        500.00 usec
p16        1000.00 usec

F2 - Processing parameters
SI         65536
SF         125.7804071 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         2.00

```







210.87

139.04

118.52

52.21

48.00

41.13

32.91

31.75

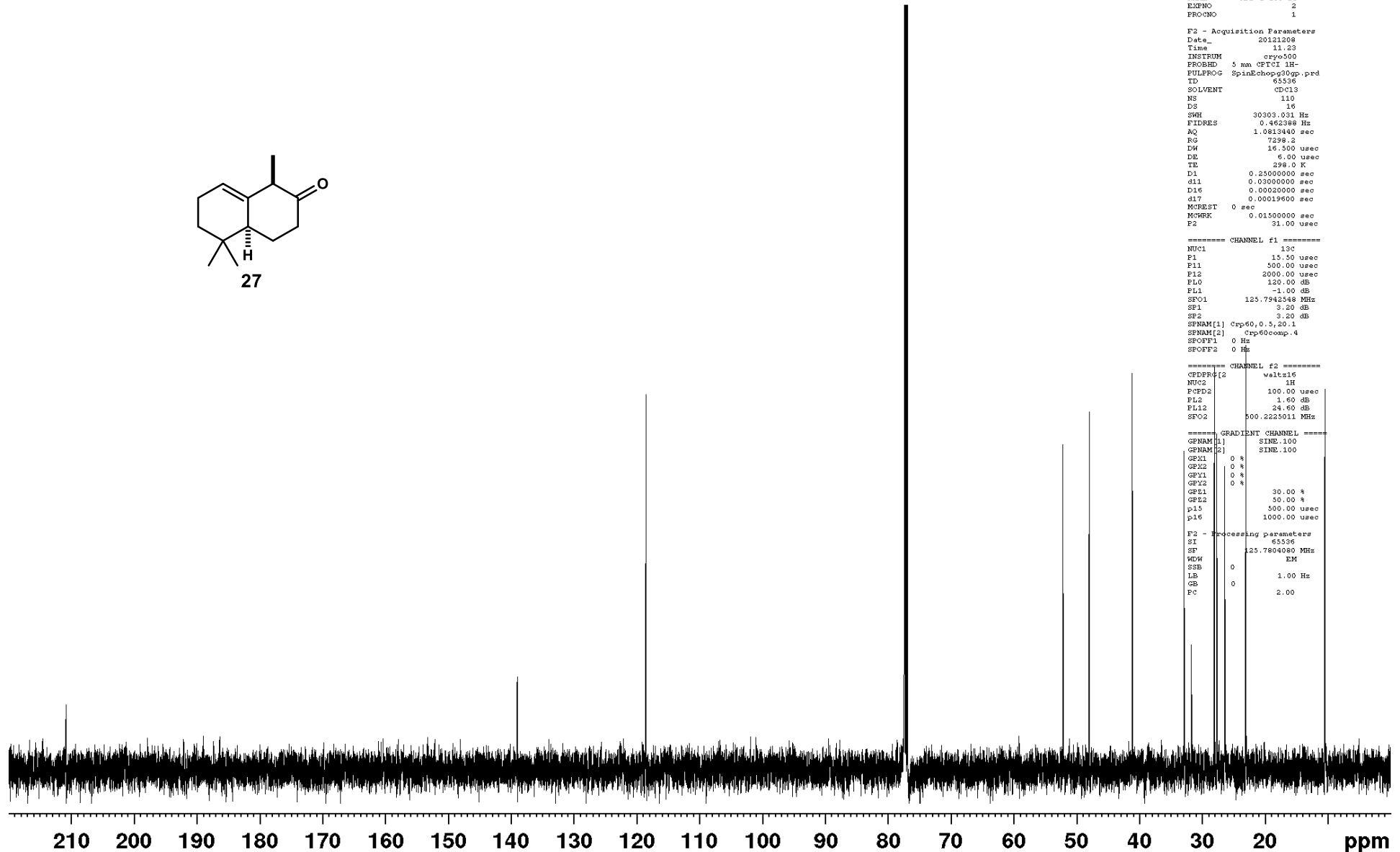
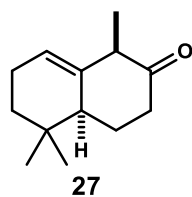
28.08

27.69

26.44

23.09

10.49



```

Current Data Parameters
NAME      APD-I-230-1a
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_     20121208
Time      11.23
INSTRUM   cryo500
PROBHD    5 mm CPXI 1H-
PULPROG   SpinEchoq30pp.prd
TD         65536
SOLVENT   CDCl3
NS         110
DS         16
SWH        30303.031 Hz
FIDRES     0.462368 Hz
AQ         1.0813440 sec
RG         7298.2
DM         16.500 usec
DE         6.00 usec
TE         298.0 K
D1         0.25000000 sec
d11        0.03000000 sec
D16        0.00200000 sec
d17        0.00019600 sec
MORST      0 sec
MORWK      0.01500000 sec
F2         31.00 usec

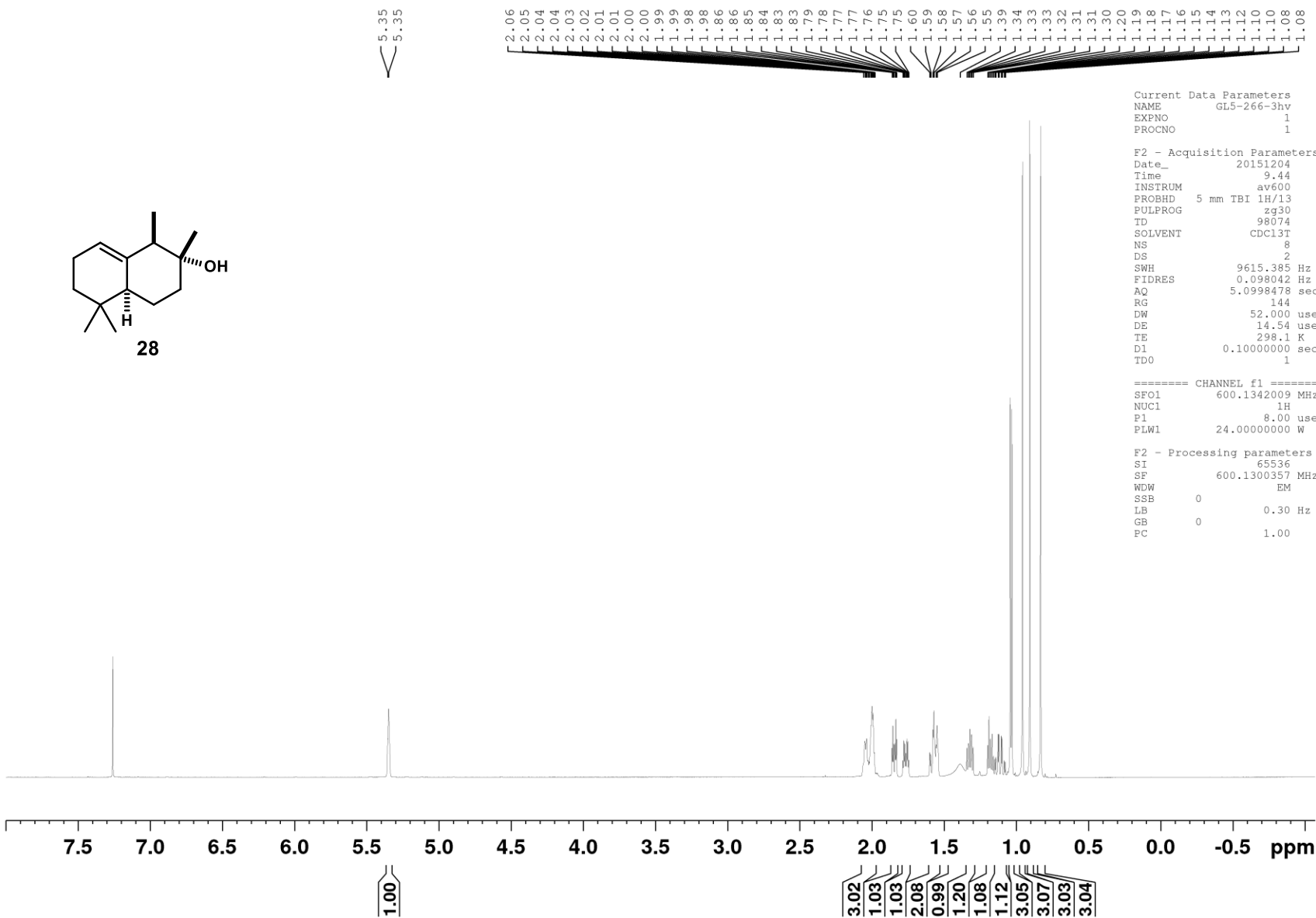
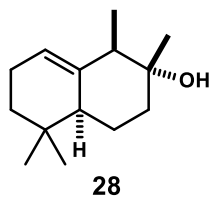
===== CHANNEL f1 =====
NUC1       13C
P1         15.50 usec
PL1        500.00 usec
PI2        2000.00 usec
PL0        120.00 dB
PL1        -1.00 dB
SFO1       125.7942548 MHz
SF1        3.20 dB
SF2        3.20 dB
SENAM[1]   Crp60,0.5,20.1
SENAM[2]   -Crp60comp.4
SFOFF1     0 Hz
SFOFF2     0 Hz

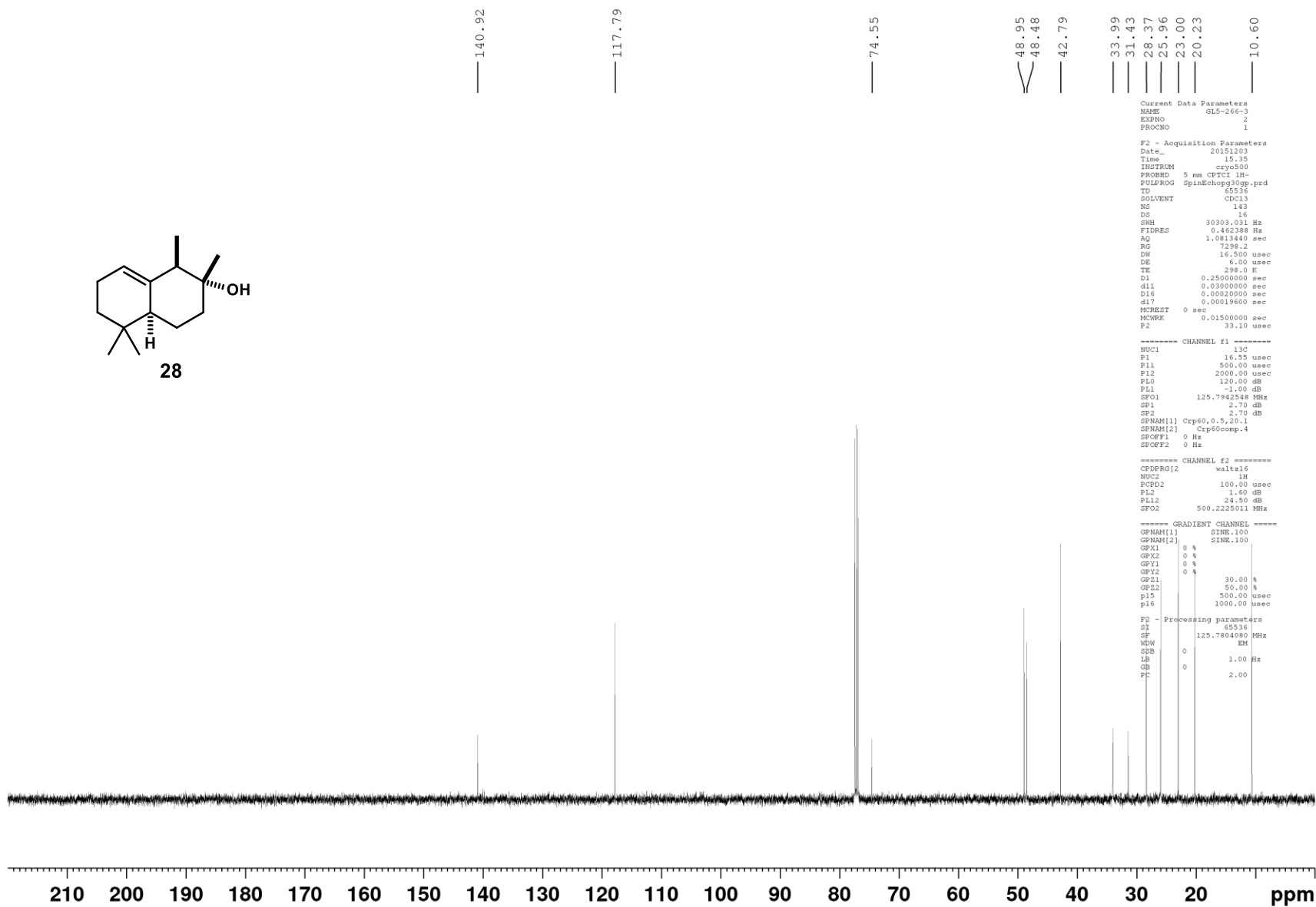
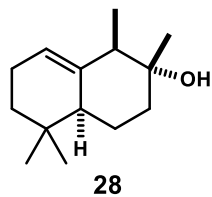
===== CHANNEL f2 =====
CPDPRG2    waltz16
NUC2       1H
PCPD2      100.00 usec
PI2        1.60 dB
PL12       24.60 dB
SFO2       500.2225011 MHz

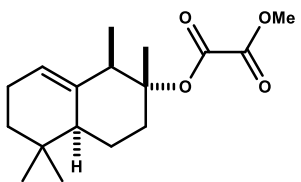
===== GRADIENT CHANNEL =====
GENAM[1]   SINE.100
GENAM[2]   SINE.100
GFX1       0 %
GFX2       0 %
GFX1       0 %
GFX2       0 %
GFX1       30.00 %
GFX2       50.00 %
p15        500.00 usec
p16        1000.00 usec

F2 - Processing parameters
SI         65536
SF         125.7804080 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         2.00

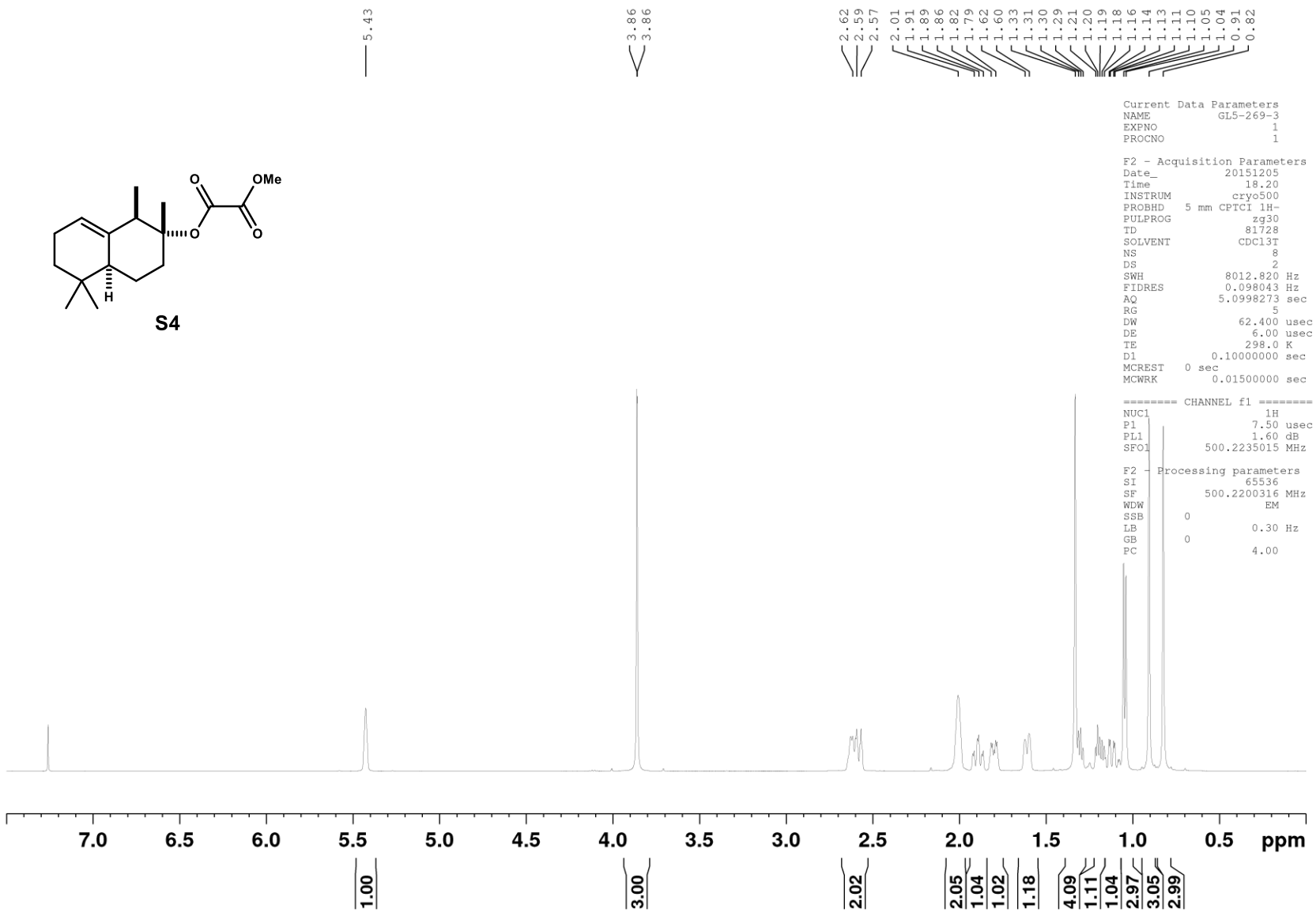
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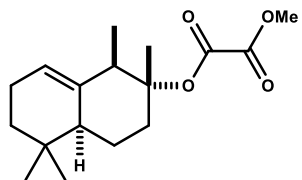




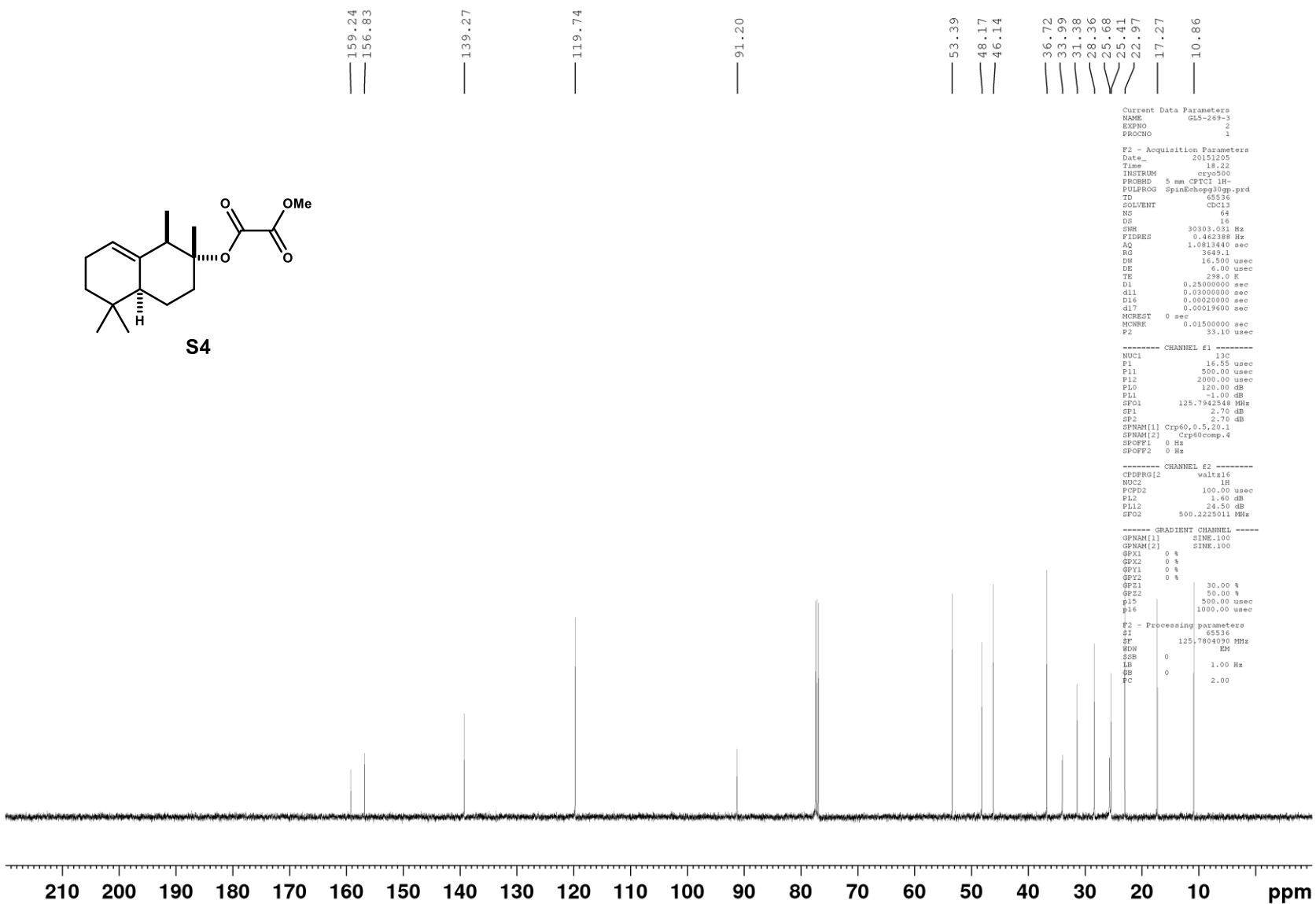


S4





S4



```

Current Data Parameters
NAME          GL5-269-3
EXPNO        2
PROCNO       1

F2 - Acquisition Parameters
Date_        20151205
Time         18.22
INSTRUM      crys500
PROBHD       5 mm CPTCI 1H-
PULPROG      SpinEcho30pp.prd
TD           65536
SOLVENT      CDCl3
NS           64
DS           16
SWH          30303.031 Hz
FIDRES       0.462388 Hz
AQ           1.0813440 sec
RG           3049.1
DW           16.500 usec
DE           6.00 usec
TE           298.0 K
D1           0.25000000 sec
d11          0.03000000 sec
D16          0.00020000 sec
d17          0.00019600 sec
MCRET       0 sec
MCHRT       0.01500000 sec
P2           33.10 usec

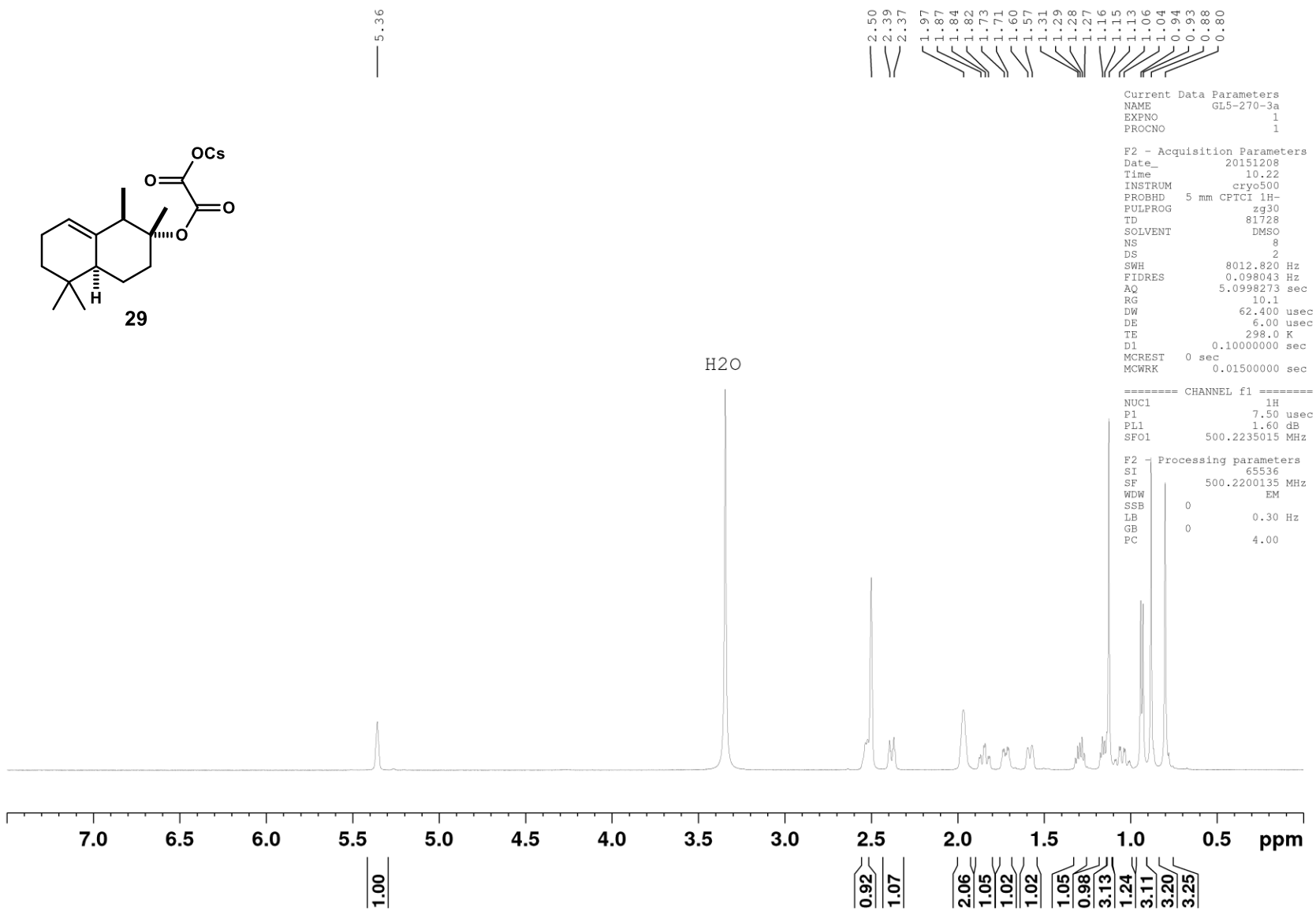
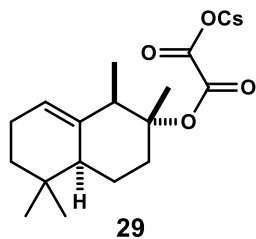
----- CHANNEL f1 -----
NUC1         13C
P1           16.55 usec
P11          500.00 usec
P12          2000.00 usec
PLO          150.00 dB
PL1          -1.00 dB
SFO1        125.7942348 MHz
SF1          2.70 dB
SF2          2.70 dB
SFO2        Ccp60,0.5,20.1
SF22        Ccp60comp.4
SFOFF1      0 Hz
SFOFF2      0 Hz

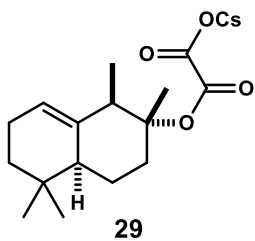
----- CHANNEL f2 -----
CPDPRG2     waltz16
NUC2         1H
PCPD2       100.00 usec
PL2         1.60 dB
PL12        24.50 dB
SFO2        500.2289011 MHz

----- GRADIENT CHANNEL -----
GPNAM[1]    SINE.100
GPNAM[2]    SINE.100
GFX1        0 %
GFX2        0 %
GFI1        0 %
GFI2        0 %
GPE1        30.00 %
GPE2        50.00 %
p15         500.00 usec
p16         1000.00 usec

F2 - Processing parameters
SI          65536
SF          125.7804090 MHz
WDW         EM
SSB         0
LB          1.00 Hz
GB          0
PC          2.00

```



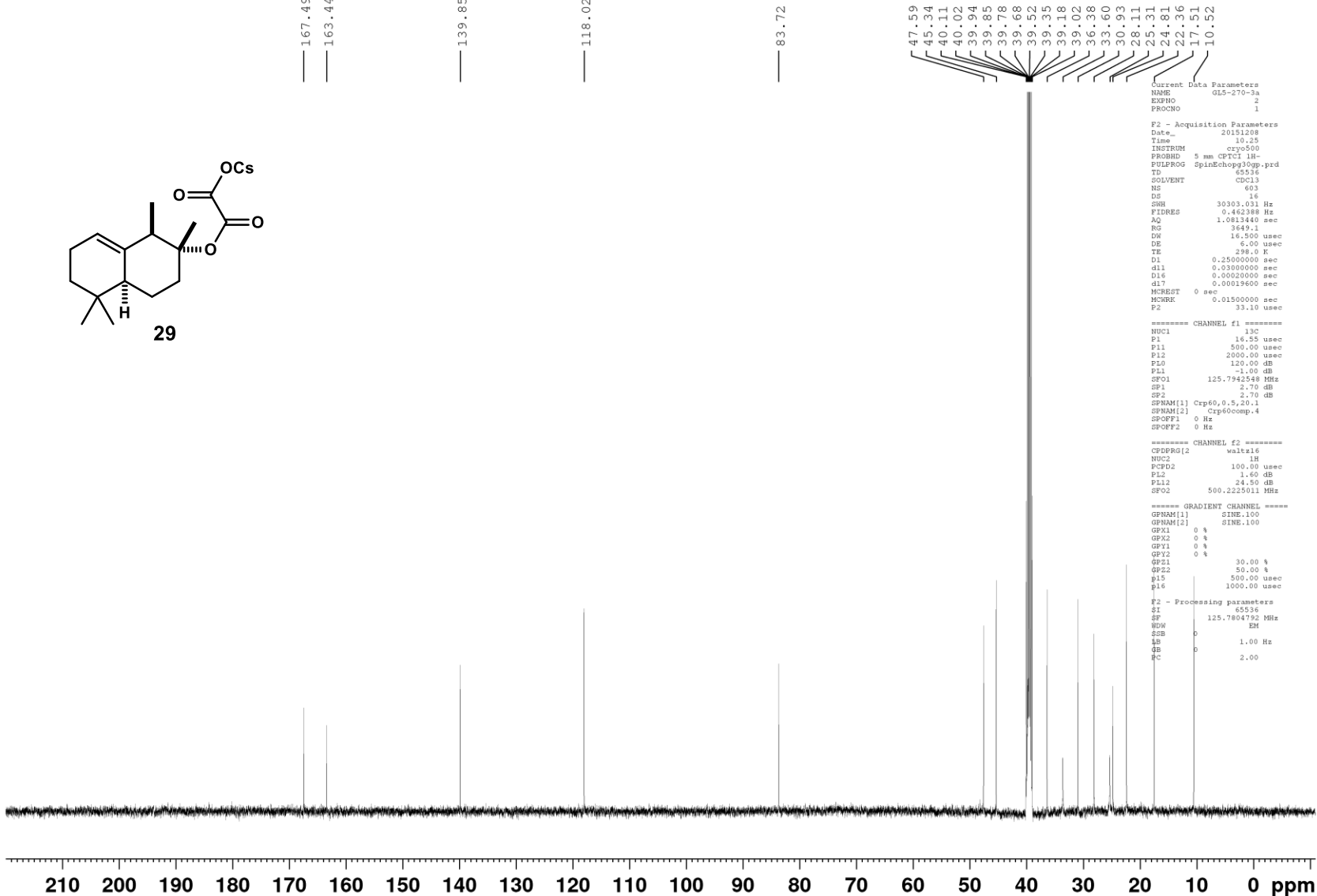


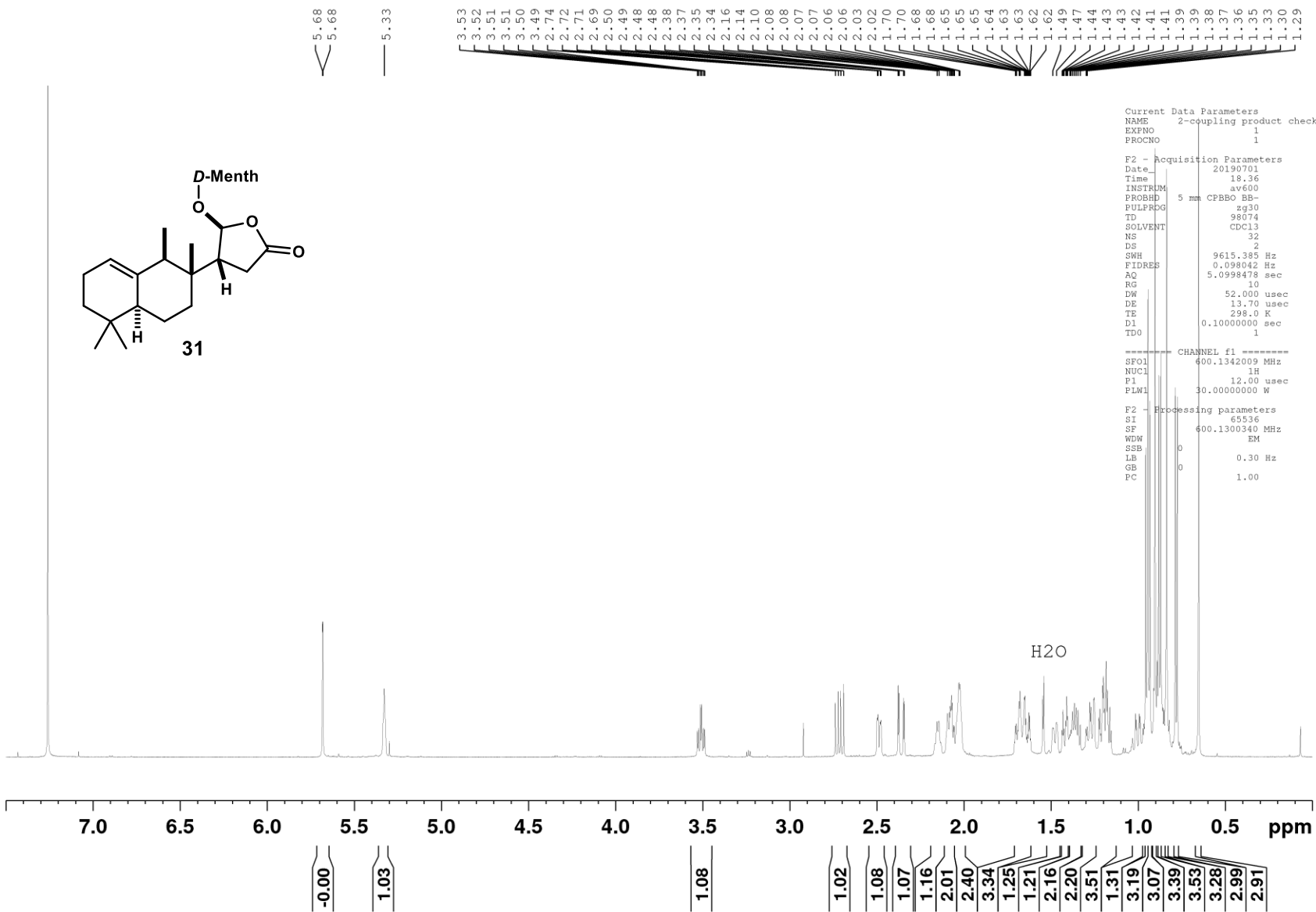
— 167.49
— 163.44

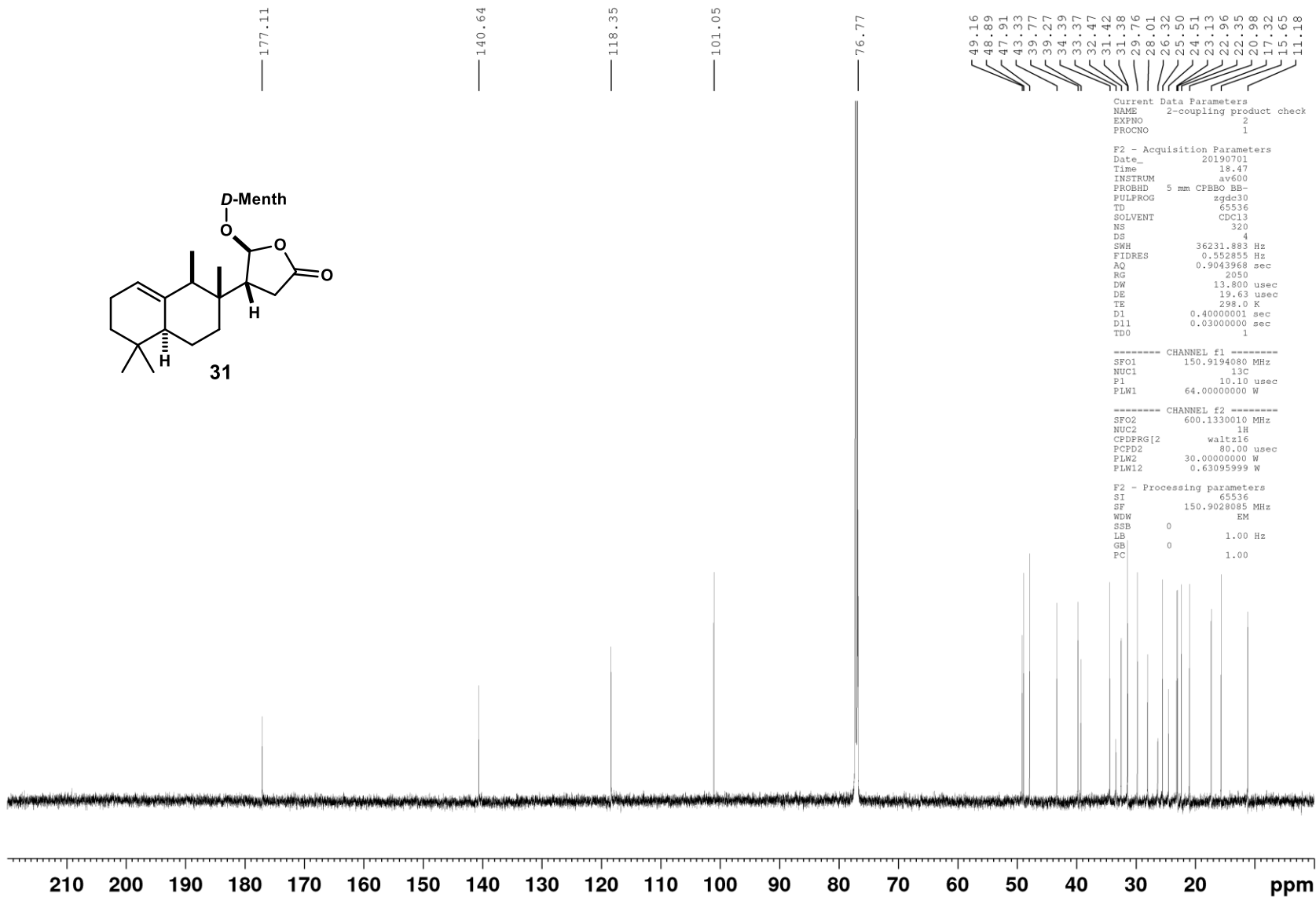
— 139.85

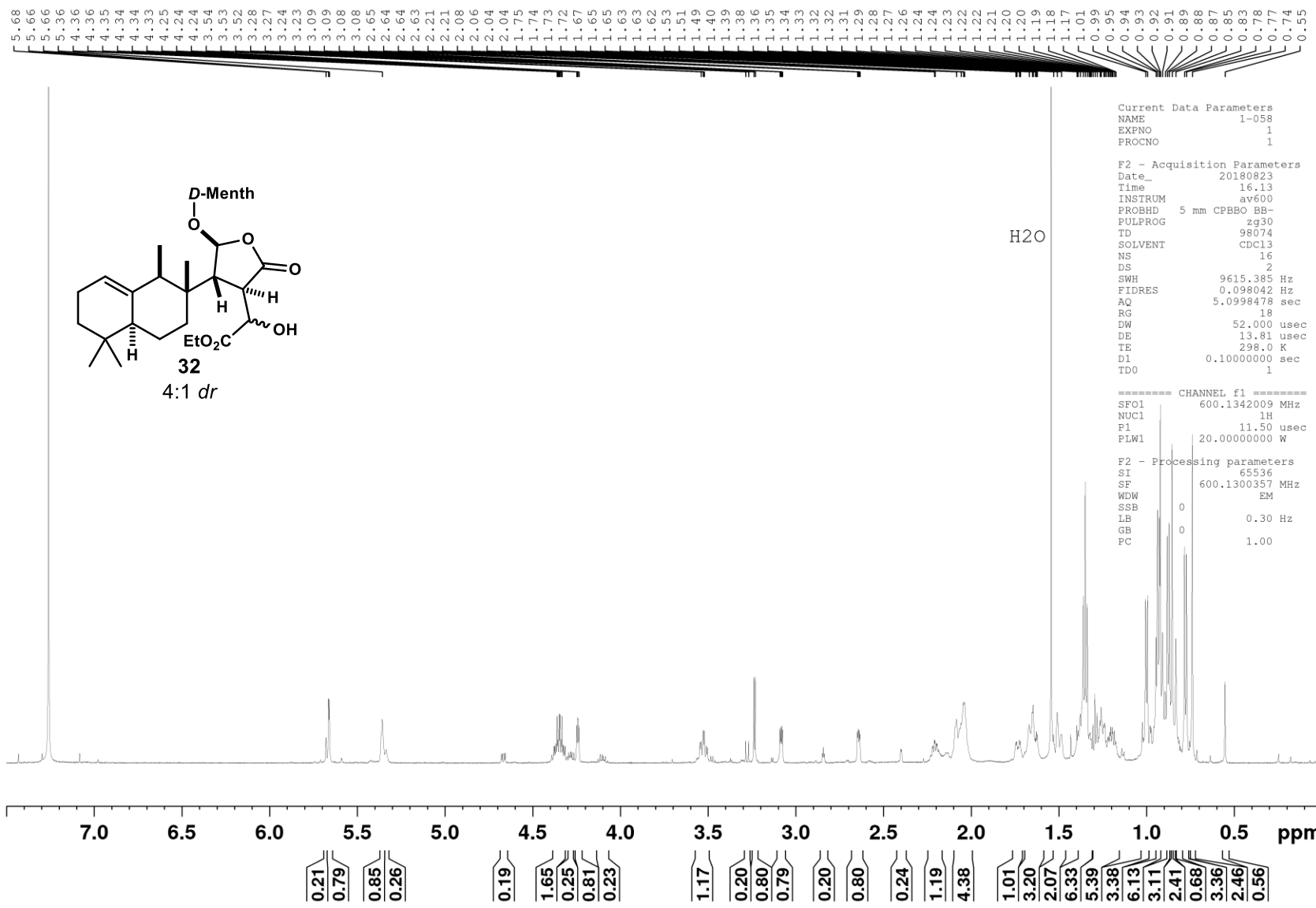
— 118.02

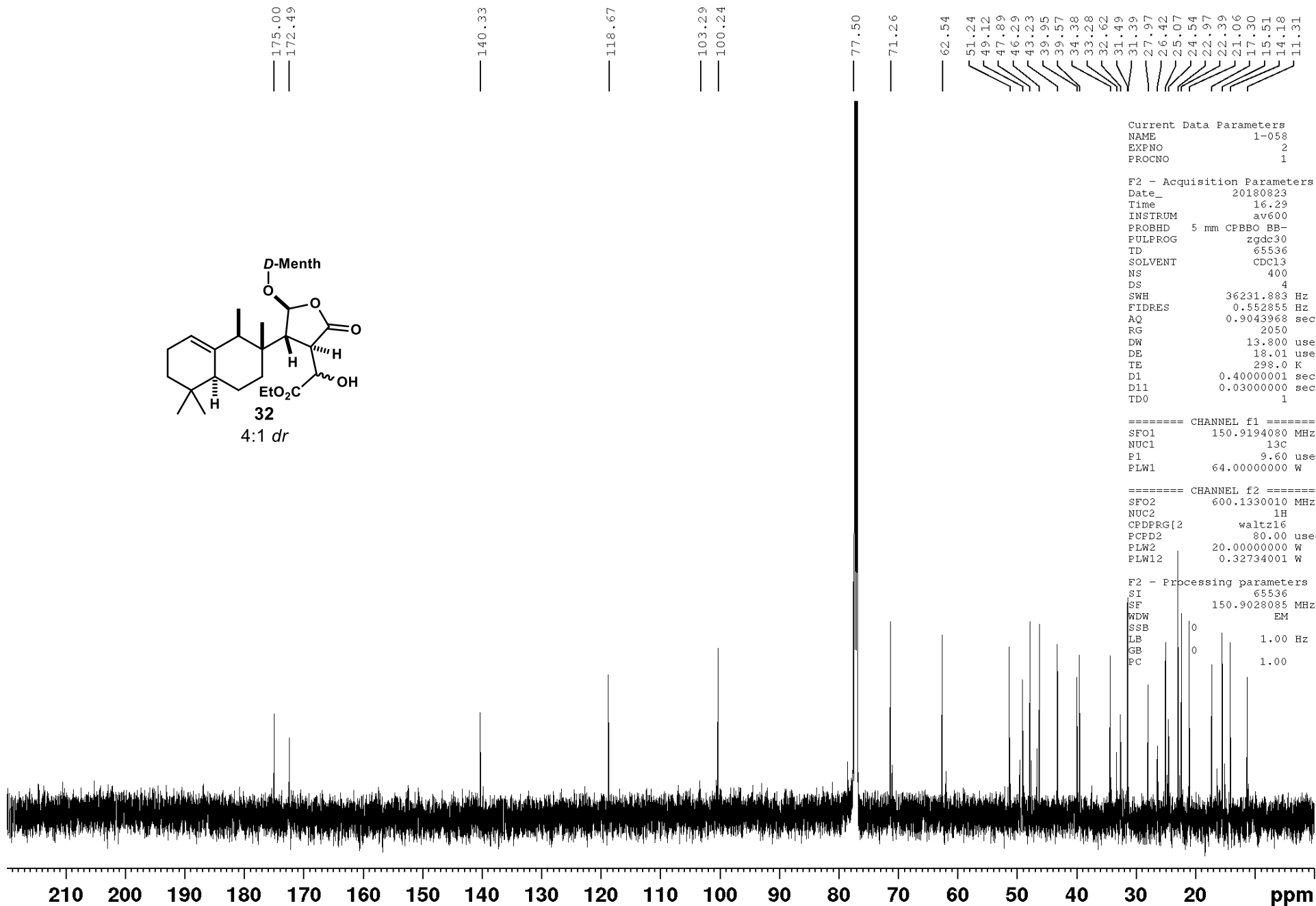
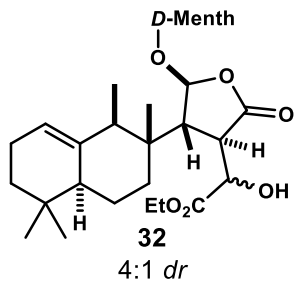
— 83.72











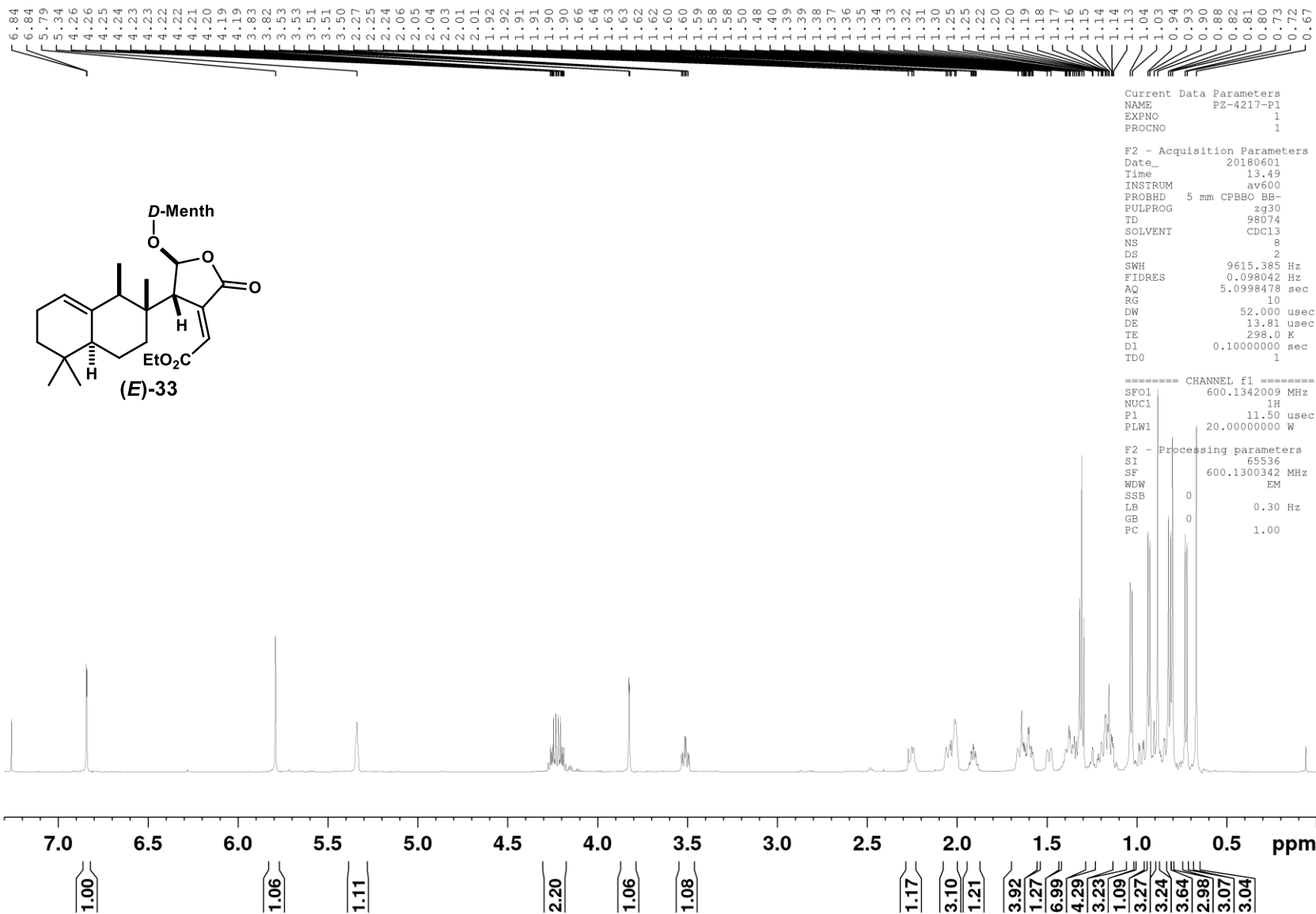
Current Data Parameters
NAME 1-058
EXPNO 2
PROCNO 1

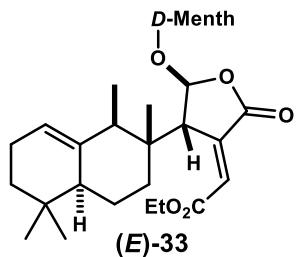
F2 - Acquisition Parameters
Date_ 20180823
Time 16.29
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 400
DS 4
SWH 36231.883 Hz
FIDRES 0.552855 Hz
AQ 0.9043968 sec
RG 2050
DW 13.800 usec
DE 18.01 usec
TE 298.0 K
D1 0.40000001 sec
D11 0.03000000 sec
TD0 1

==== CHANNEL f1 =====
SFO1 150.9194080 MHz
NUC1 13C
P1 9.60 usec
PLW1 64.00000000 W

==== CHANNEL f2 =====
SFO2 600.1330010 MHz
NUC2 1H
CPDPRG2 waltz16
PCPD2 80.00 usec
PLW2 20.00000000 W
PLW12 0.32734001 W

F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00





— 170.61
— 165.45

— 143.22
— 140.41

— 127.05
— 118.63

— 100.10

— 77.12

— 61.10
— 51.80
— 49.18
— 47.55
— 43.69
— 43.58
— 39.85
— 34.33
— 33.72
— 33.37
— 31.45
— 31.38
— 27.99
— 26.21
— 25.34
— 24.22
— 23.20
— 22.93
— 22.31
— 20.84
— 16.04
— 15.59
— 14.15
— 11.40

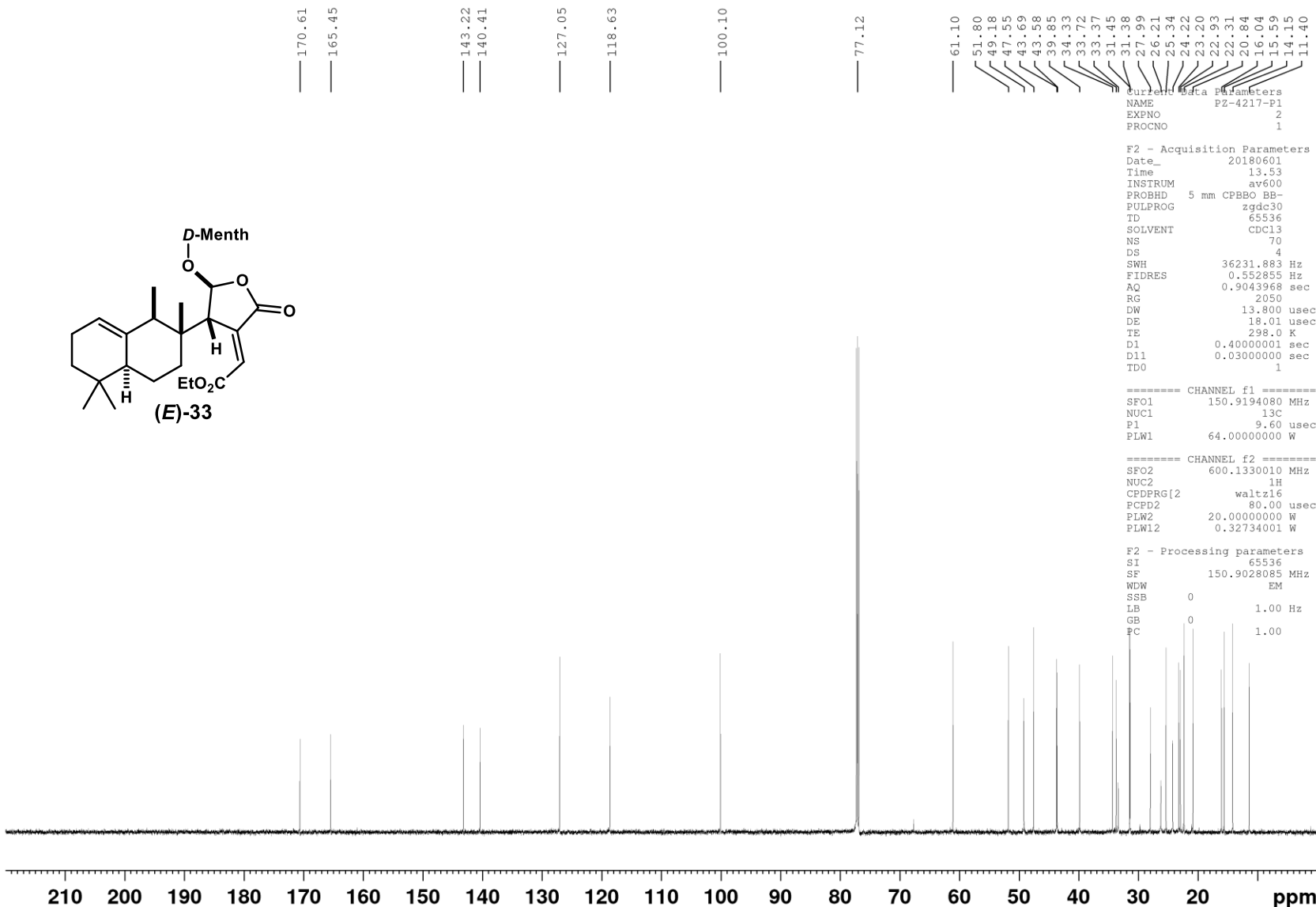
Current Data Parameters
 NAME PZ-4217-P1
 EXPNO 2
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20180601
 Time 13.53
 INSTRUM av600
 PROBHD 5 mm CPBBO BB-
 PULPROG zgdc30
 TD 65536
 SOLVENT CDCl3
 NS 70
 DS 4
 SWH 36231.883 Hz
 FIDRES 0.552855 Hz
 AQ 0.9043968 sec
 RG 2050
 DW 13.800 usec
 DE 18.01 usec
 TE 298.0 K
 D1 0.40000001 sec
 D11 0.03000000 sec
 TDO 1

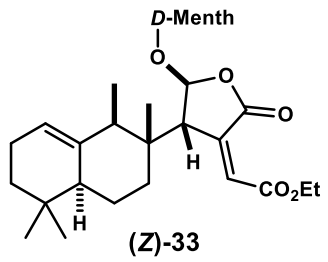
===== CHANNEL f1 =====
 SFO1 150.9194080 MHz
 NUC1 13C
 P1 9.60 usec
 PLW1 64.00000000 W

===== CHANNEL f2 =====
 SFO2 600.1330010 MHz
 NUC2 1H
 CPDPRG[2] waltz16
 PCPD2 80.00 usec
 PLW2 20.00000000 W
 PLW12 0.32734001 W

F2 - Processing parameters
 SI 65536
 SF 150.9028085 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.00



6.29
6.28
5.72
5.35
4.32
4.31
4.31
4.30
4.29
4.29
4.28
4.28
4.27
4.26
4.26
4.25
3.57
3.56
3.55
3.55
3.54
3.53
2.87
2.87
2.22
2.21
2.07
2.06
2.04
2.03
2.03
2.02
2.01
2.01
2.00
2.00
1.67
1.65
1.64
1.63
1.63
1.62
1.62
1.60
1.50
1.48
1.39
1.37
1.36
1.35
1.34
1.34
1.33
1.32
1.31
1.30
1.25
1.21
1.19
1.18
1.17
1.16
1.16
1.15
1.13
1.01
1.00
0.99
0.98
0.97
0.95
0.94
0.93
0.92
0.91
0.89
0.88
0.88
0.86
0.85
0.84
0.83
0.83
0.82
0.81
0.77
0.76

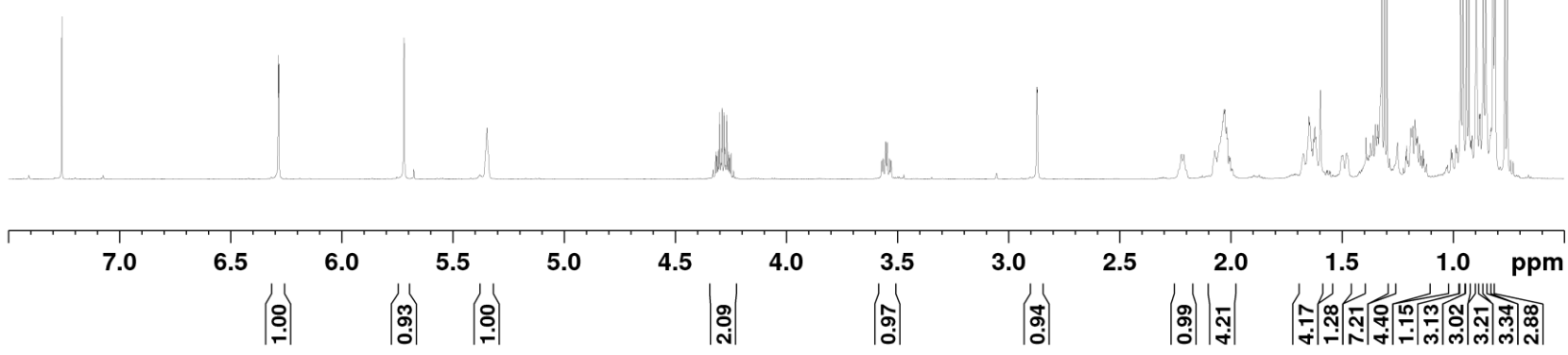


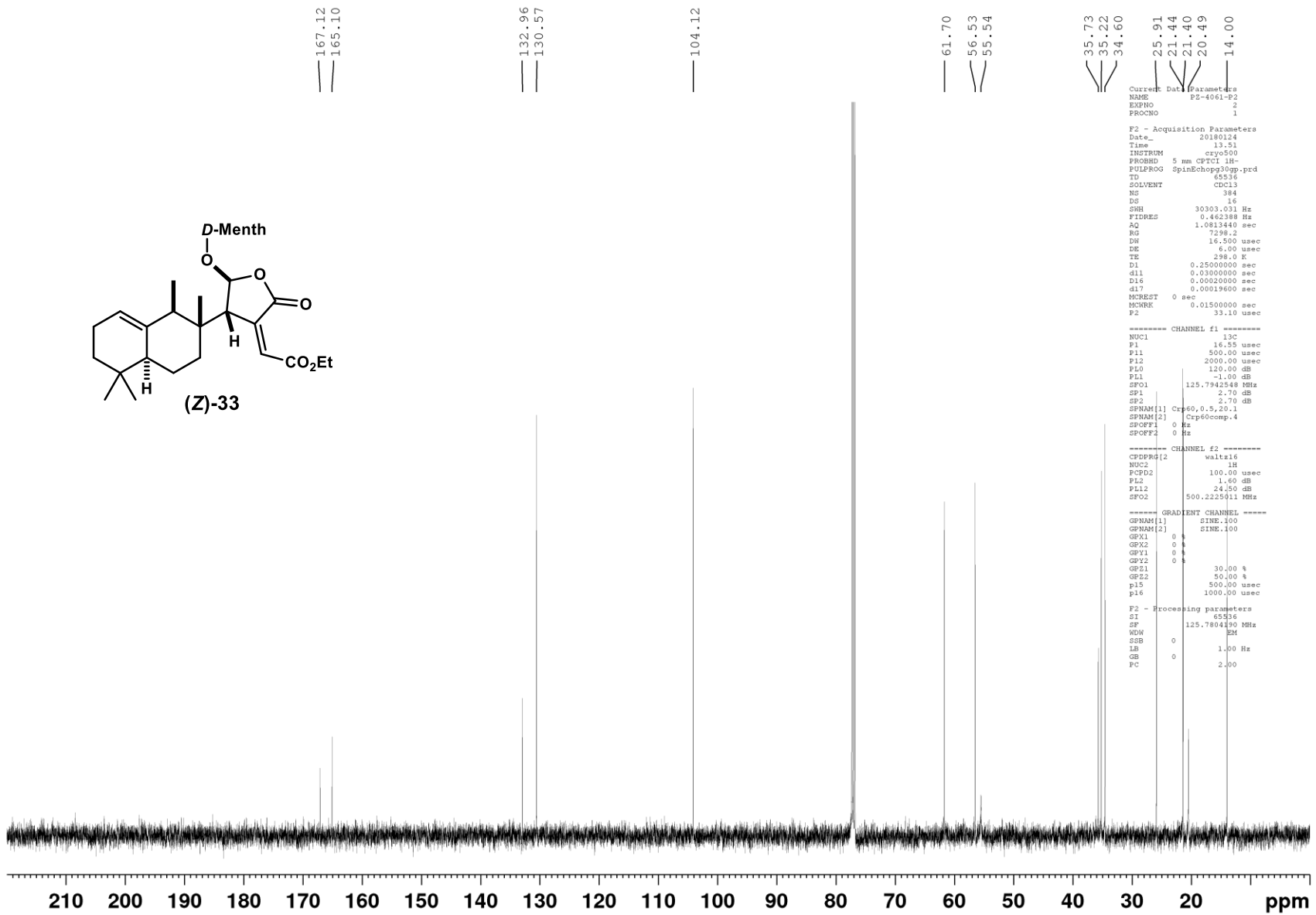
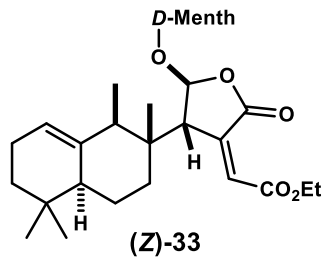
Current Data Parameters
 NAME PZ-4217-P2
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20180601
 Time 13.38
 INSTRUM av600
 PROBHD 5 mm CPBBO BB-
 PULPROG zg30
 TD 98074
 SOLVENT CDCl3
 NS 8
 DS 2
 SWH 9615.385 Hz
 FIDRES 0.098042 Hz
 AQ 5.0998478 sec
 RG 22.6
 DW 52.000 usec
 DE 13.81 usec
 TE 298.0 K
 D1 0.10000000 sec
 TD0 1

===== CHANNEL f1 =====
 SF01 600.1342009 MHz
 NUC1 1H
 P1 11.50 usec
 PLW1 20.00000000 W

F2 - Processing parameters
 SI 65536
 SF 600.1300343 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00





```

Current Date Parameters
NAME      F2-4061-F2
EXPNO    2
PROCNO    1

F2 - Acquisition Parameters
Date_     20180124
Time      13:51
INSTRUM   cryo500
PROBHD    5 mm CPCL1 1H-
PULPROG   SpinEchopg30pp-prd
TD         65536
SOLVENT   CDCl3
NS         384
DS         16
SWH        30303.031 Hz
FIDRES     0.462388 Hz
AQ         1.0813440 sec
RG         7298.2
DN         16.500 usec
DE         6.00 usec
TE         298.0 K
d11        0.25000000 sec
d111       0.03000000 sec
d16        0.00020000 sec
d17        0.00019600 sec
MCRET      0 sec
MCRNK      0.01500000 sec
F2         33.10 usec

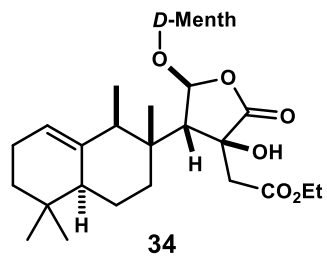
----- CHANNEL f1 -----
NUC1       13C
P1         16.55 usec
P11        500.00 usec
P12        2000.00 usec
PL0        120.00 dB
PL1        -1.00 dB
SFO1       125.7942548 MHz
SP1        2.70 dB
SP2        2.70 dB
SFOFF1[1] Crp60.0.5.20.1
SFOFF1[2] Crp60comp.4
SFOFF2     0 Hz
SFOFF3     0 Hz

----- CHANNEL f2 -----
CPDPRG[2] waltz16
NUC2       1H
PCPD2      100.00 usec
PL2        1.60 dB
PL12       24.50 dB
SFO2       500.2225011 MHz

----- GRADIENT CHANNEL -----
GRNAM[1]   SINE.100
GRNAM[2]   SINE.100
GPX1       0 %
GPX2       0 %
GPY1       0 %
GPY2       0 %
GRZ1       30.00 %
GRZ2       50.00 %
p15        500.00 usec
p16        1000.00 usec

F2 - Processing parameters
SI         65536
SF         125.7804490 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         2.00

```



5.79
5.78

5.34

4.79

4.22
4.20
4.19

3.62
3.61
3.60

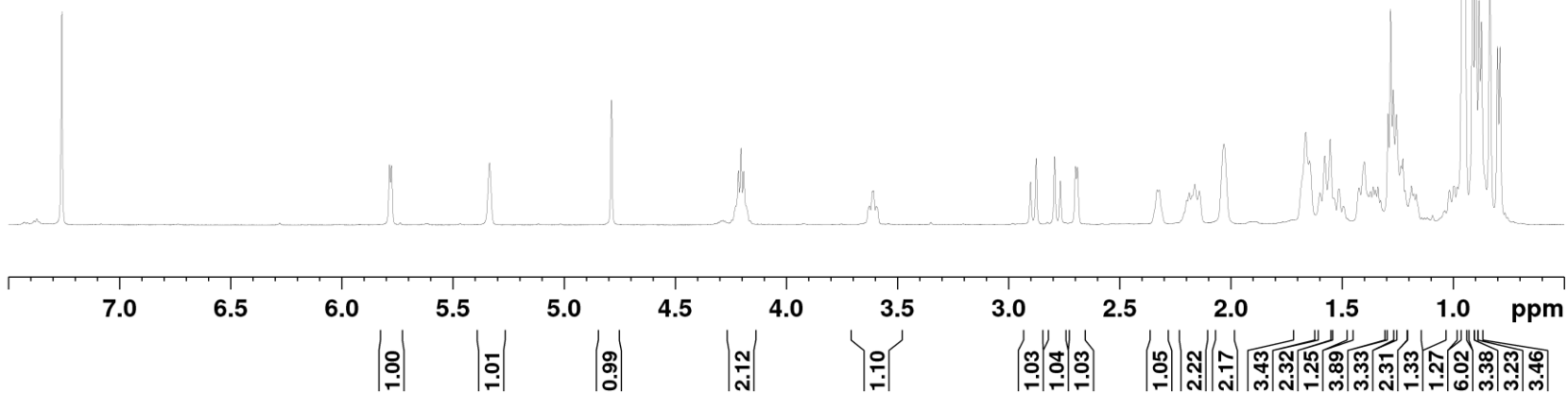
2.90
2.88
2.79
2.77
2.70
2.69
2.33
2.32
2.20
2.19
2.17
2.16
2.14
2.03
1.66
1.64
1.60
1.58
1.54
1.51
1.49
1.42
1.40
1.37
1.36
1.35
1.34
1.33
1.29
1.28
1.27
1.25
1.23
1.22
1.19

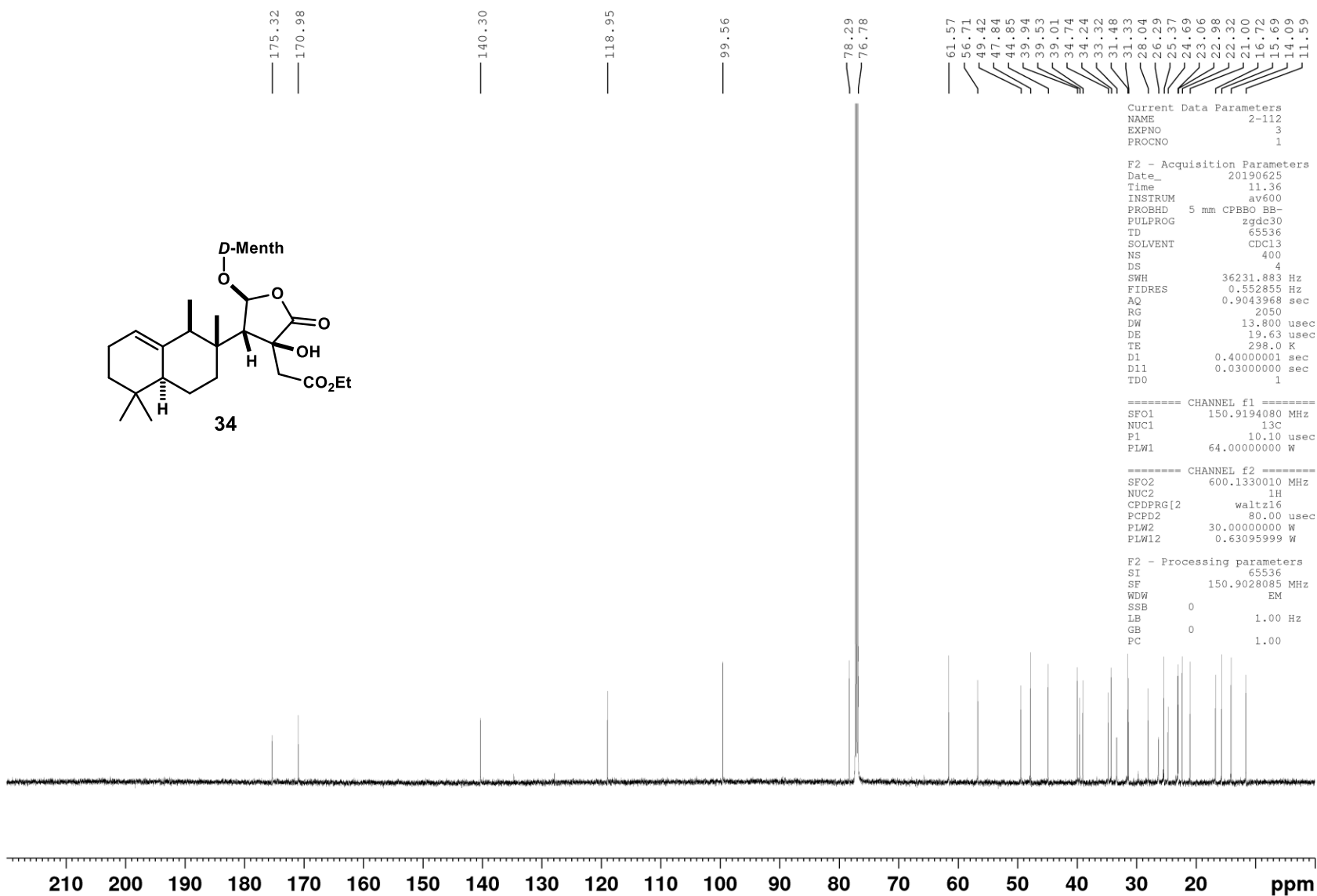
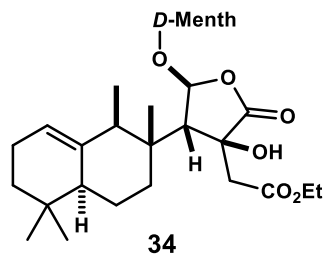
Current Data Parameters
NAME 2-112
EXPNO 2
PROCNO 1

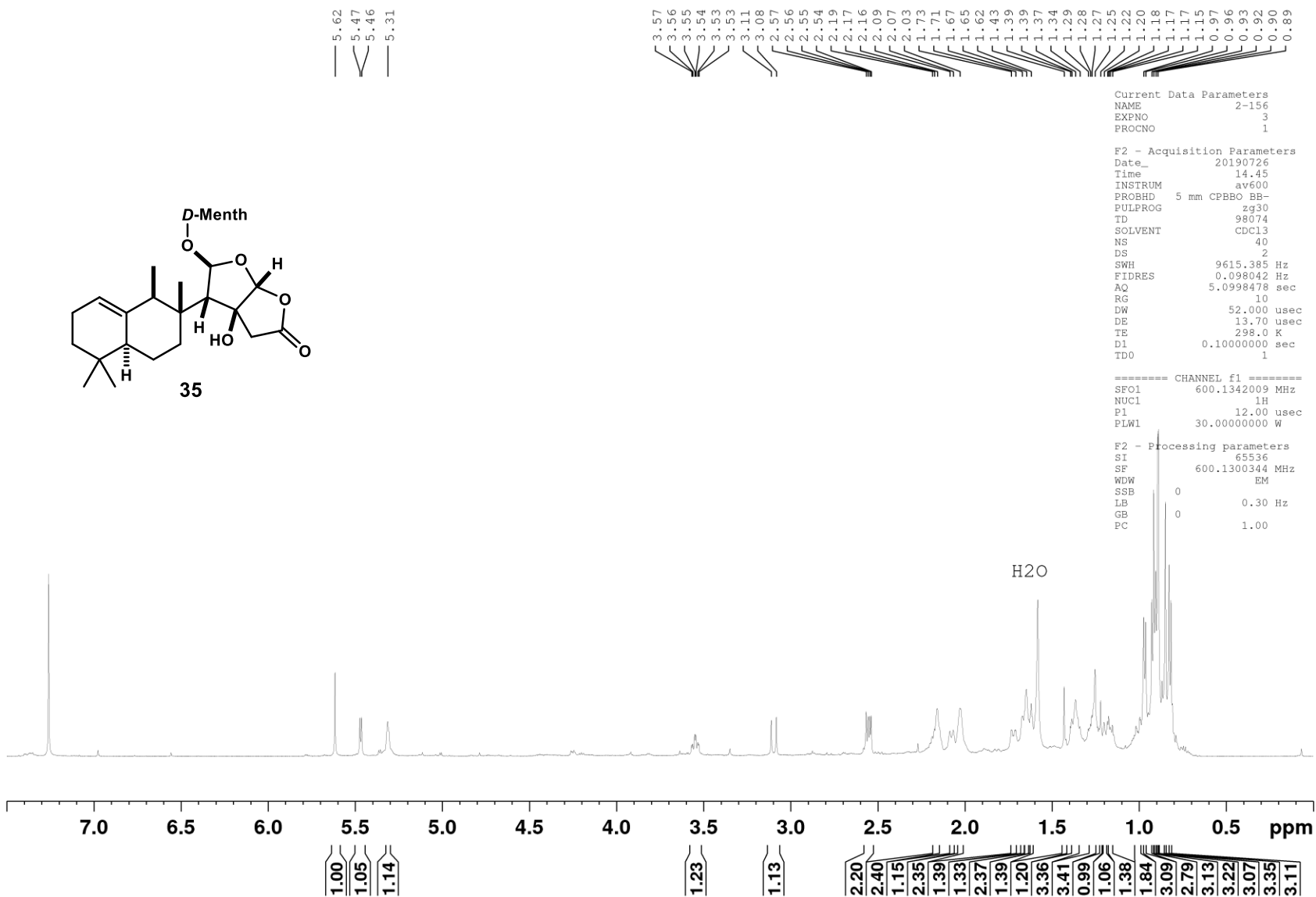
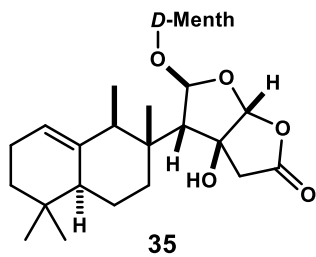
F2 - Acquisition Parameters
Date_ 20190625
Time 11.23
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zg30
TD 98074
SOLVENT CDC13
NS 48
DS 2
SWH 9615.385 Hz
FIDRES 0.098042 Hz
AQ 5.0998478 sec
RG 10
DW 52.000 usec
DE 13.70 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1

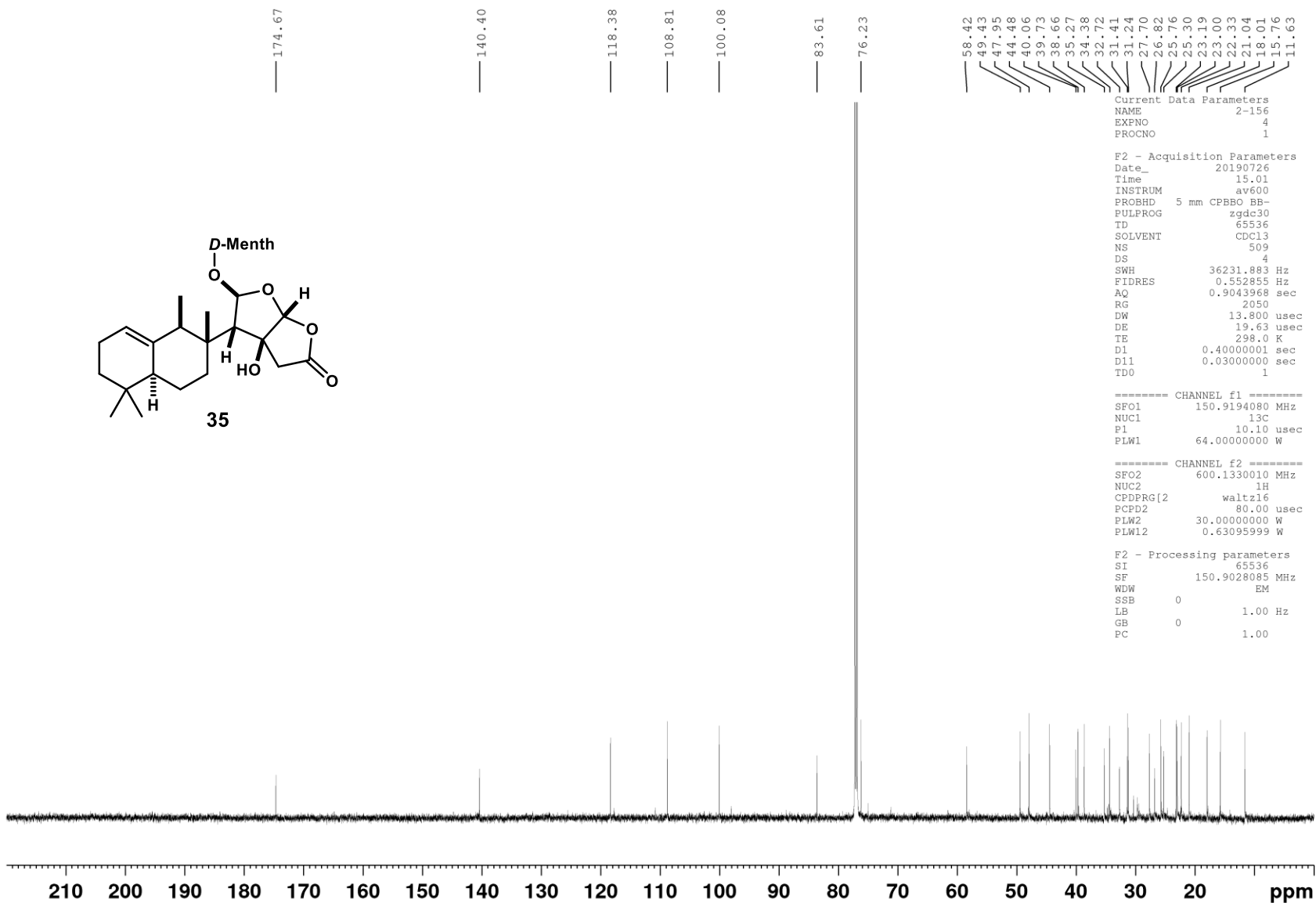
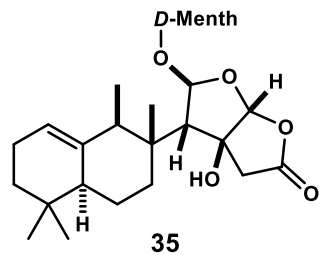
===== CHANNEL f1 =====
SF01 600.1342009 MHz
NUC1 1H
P1 12.00 usec
PLW1 30.00000000 W

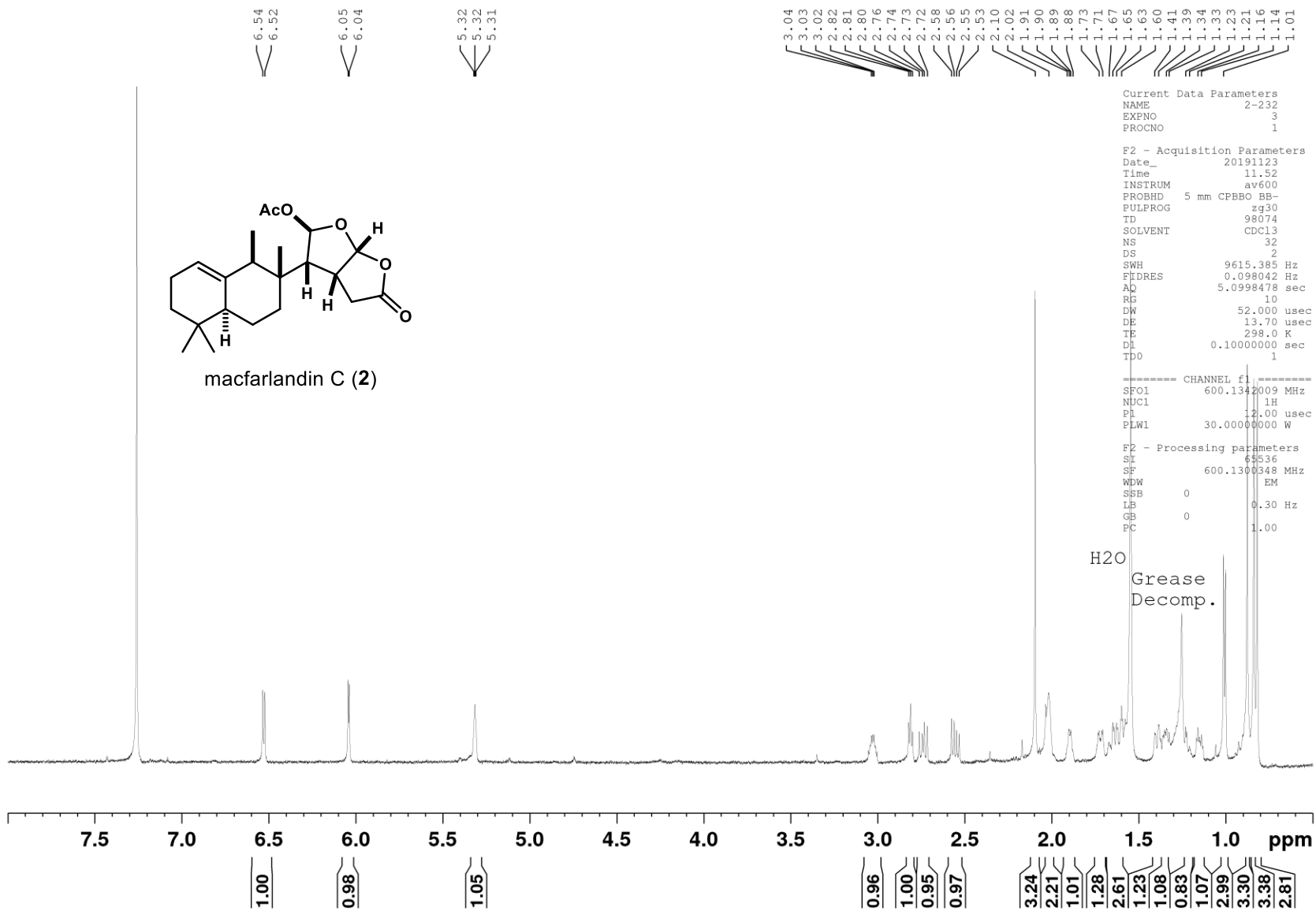
F2 - Processing parameters
SI 65536
SF 600.1300345 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

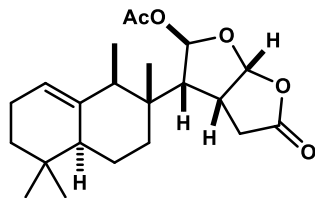












macfarlandin C (2)

— 175.39
— 169.77

— 140.29

— 118.43

— 104.81

— 96.11

— 51.76
— 49.02
— 44.48
— 42.17
— 39.69
— 35.47
— 32.64
— 31.23
— 30.22
— 27.64
— 26.80
— 25.19
— 22.99
— 21.17
— 18.92
— 11.57

Current Data Parameters
NAME 2-232
EXPNO 9
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191230
Time 23.05
INSTRUM av600
PROBHD 5 mm CPBBO BB-
PULPROG zgdc30
TD 65536
SOLVENT CDCl3
NS 30000
DS 4
SWH 36231.883 Hz
FIDRES 0.552855 Hz
AQ 0.9043968 sec
RG 2050
DW 13.800 usec
DE 19.63 usec
TE 298.0 K
D1 0.40000001 sec
D11 0.03000000 sec
TDO 1

===== CHANNEL f1 =====
SFO1 150.9194080 MHz
NUC1 13C
P1 10.10 usec
PLW1 64.00000000 W

===== CHANNEL f2 =====
SFO2 600.1330010 MHz
NUC2 1H
CPDPRG[2] waltz16
PCPD2 80.00 usec
PLW2 30.00000000 W
PLW12 0.63095999 W

F2 - Processing parameters
SI 65536
SF 150.9028085 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00

