

Toward the Total Synthesis of Maoecrystal V: Establishment of Contiguous Quaternary Stereocenters

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Supporting Information

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General Experimental Details

Unless otherwise specified, all reactions were carried out under an inert N₂ atmosphere in oven-dried glassware. Flash column chromatography was performed using the analytical grade solvents indicated and Merck silica gel (40-63 µm, 60 Å) as the stationary phase. Reactions and chromatography fractions were monitored with Merck silica gel 60 F₂₅₄ glass plates and visualized using a 254 nm UV lamp and/or by treatment with a suitable dip followed by heating: potassium permanganate and ceric ammonium molybdate. Tetrahydrofuran (THF), and diethyl ether (Et₂O) were distilled from sodium benzophenone ketyl. Diisopropylamine was distilled from and stored over CaH₂. *n*-Butyllithium (*n*-BuLi) was titrated with diphenylacetic acid prior to use. All other solvents, as well as starting materials and reagents were used without further purification from commercial sources.

Unless otherwise specified, proton (¹H) and carbon (¹³C) spectra were recorded at 18 °C in base filtered CDCl₃ on Varian Mercury spectrometers operating at 300 Hz, 400 MHz and 600 MHz for proton nuclei (75 MHz, 100 MHz and

150 MHz for carbon nuclei). For ^1H NMR spectra signals arising from residual protio-forms of the solvent were used as the internal standards. ^1H NMR data are recorded as follows: chemicals shift (δ) [multiplicity, coupling constant(s) J (Hz), relative integral] where multiplicity is defined as: s=singlet; d=doublet; t=triplet; q=quartet; m=multiplet br=broad or combinations of the above. The residual CHCl_3 peak (δ 7.26) was used as reference for ^1H NMR spectra. The central peak (δ 77.16) of the CDCl_3 'triplet' was used as reference for proton-decoupled ^{13}C NMR spectra.

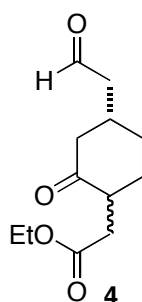
Low- and high-resolution electrospray (ESI) mass spectra were obtained on a Varian MAT 711 MS instrument operating in either positive or negative ionization modes. Fast atom bombardment (FAB) mass spectra were measured on a VG ProSpec Mass Spectrometer.

Melting points were measured on a Büchi melting point B-540 system and are uncorrected.

X-ray analysis measurements of **7** were made on a Bruker APEX¹ CCD area detector with graphite monochromated Mo- K_α radiation ($\lambda = 0.71069 \text{ \AA}$). The data collections for **14** and **17** were performed on an Oxford Diffraction Xcalibur diffractometer at 173 K using graphite monochromated Mo- K_α -radiation ($\lambda = 0.71073 \text{ \AA}$).

Experimental Procedures

Aldehydes 4



Ozone was bubbled into a mixture of **3** (26.5 g, 118 mmol), NaHCO_3 (0.33g, 4 mmol), CH_2Cl_2 (200 mL) and MeOH (200 mL) at -78°C until a blue color developed. Excess ozone was then removed by bubbling N_2 through the mixture. Me_2S (14.5 mL, 12.2 g, 197 mmol) was added and the mixture was left to stir overnight at rt. The mixture was then concentrated *in vacuo* and purified by flash

column chromatography (hexanes/EtOAc = 2/1) to give 25.3 g (112 mmol, 94 %) of **4** as a colorless oil.

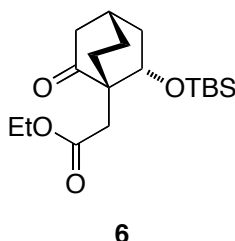
TLC: R_f = 0.22 (hexanes/EtOAc = 2/1) [KMnO₄]

¹H-NMR (400 MHz, CDCl₃): δ = 1.21 (t, ³*J* = 7.1 Hz, 3H), 1.35-2.92 (m, 12H), 4.08 (q, ³*J* = 7.1 Hz, 2H), 9.68-9.72 (m, 1H).

¹³C-NMR (100 MHz, CDCl₃, only shifts of major diastereomer are listed): δ = 14.2, 31.6, 32.2, 34.1, 34.4, 46.4, 47.5, 50.4, 60.5, 172.4, 200.5, 208.9.

HRMS (FAB+): calcd for C₁₂H₁₈O₄Na [(M+Na)⁺]: 249.1097, found: 249.1098

t-Butyldimethylsilyloxybicyclo[2.2.2]octanone **6**

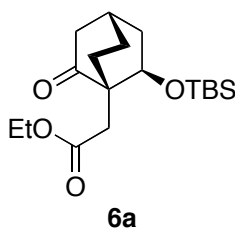


A mixture of **4** (6.27 g, 27.7 mmol), 2 N HCl aq (5.54 mL, 11.1 mmol), and acetone (105 mL) was heated at reflux for 10 min. After cooling, NaHCO₃ (0.931 g, 11.1 mmol) and water (2.5 mL) were added and the mixture was concentrated *in vacuo*. The residue was extracted with ethyl ether (3 × 40 mL), washed with saturated NaHCO₃ aq (10 mL) and brine (20 mL), dried over MgSO₄, filtered, and concentrated *in vacuo* to give a mixture of diastereomers **5** and **5a** (3.54 g, 15.6 mmol, 56%), which was carried on without further purification.

A solution of the hydroxybicyclo[2.2.2]octanones **5** and **5a** obtained above (3.76 g, 16.6 mmol), *t*-butyldimethylsilyl chloride (3.0 g, 19.9 mmol) and imidazole (1.70 g, 24.9 mmol) in DMF (20 mL) was stirred overnight at rt. The mixture was poured into water (200 mL) and extracted with ethyl ether (3 × 100 mL). The organic phase was washed with 2 N HCl aq (100 mL), water (3 × 80 mL), and brine (100 mL), dried over MgSO₄, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (hexanes/EtOAc = 19/1) to give 3.65 g **6** (10.7 mmol, 65%) as well as 0.50 g **6a** (1.46 mmol, 9%), both as colorless oils. 0.46 g (2.05 mmol, 12%) of the starting materials **5** and **5a** could be reisolated.

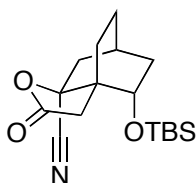
6:

TLC:	$R_f = 0.55$ (hexanes/EtOAc = 5/1) [KMnO ₄]
¹ H-NMR	(400 MHz, CDCl ₃): $\delta = 0.02$ (s, 3H), 0.04 (s, 3H), 0.82 (s, 9H), 1.24 (t, $^3J = 7.1$ Hz, 3H), 1.48-1.57 (m, 1H), 1.60-1.74 (m, 3H), 1.86 (ddd, $^2J = 13.9$ Hz, $^3J = 11.3$, 7.1 Hz, 1H), 2.09 (ddt, $^2J = 13.9$ Hz, $^3J = 8.2$, 2.2 Hz, 1H), 2.17-2.24 (m, 2H), 2.31-2.38 (m, 1H), 2.51 (d, $^2J = 16.0$ Hz, 1H), 2.61 (d, $^2J = 16.0$ Hz, 1H), 4.10 (q, $^3J = 7.1$ Hz, 2H), 4.33 (d, $^3J = 7.9$ Hz, 1H).
¹³ C-NMR	(100 MHz, CDCl ₃): $\delta = -5.1$, -4.1, 14.4, 17.9, 24.0, 25.3, 25.8, 27.5, 33.9, 37.6, 44.0, 50.9, 60.2, 70.2, 172.5, 212.8.
HRMS	(FAB+): calcd for C ₁₈ H ₃₂ O ₄ SiNa [(M+Na) ⁺]: 363.1962, found: 363.1963

6a:

TLC:	$R_f = 0.50$ (hexanes/EtOAc = 5/1) [KMnO ₄]
¹ H-NMR	(400 MHz, CDCl ₃ , observed): $\delta = 0.00$ (s, 3H), 0.06 (s, 3H), 0.90 (s, 9H), 1.25 (t, $^3J = 7.1$ Hz, 3H), 1.52-1.65 (m, 3H), 1.76-1.87 (m, 1H), 2.04-2.25 (m, 5H), 2.32 (d, $^2J = 16.7$ Hz, 1H), 2.43 (d, $^2J = 16.7$ Hz, 1H), 4.10 (q, $^3J = 7.1$ Hz, 2H), 4.34 (d, $^3J = 8.2$ Hz, 1H).
¹³ C-NMR	(100 MHz, CDCl ₃): $\delta = -5.0$, -4.1, 14.3, 18.0, 22.8, 24.9, 25.9, 27.5, 34.8, 38.6, 43.9, 52.2, 60.1, 67.4, 172.0, 212.8.
HRMS	(FAB+): calcd for C ₁₈ H ₃₂ O ₄ SiNa [(M+Na) ⁺]: 363.1962, found: 363.1963

Lactone **7**



7

To a solution of **6** (6.92 g, 20.3 mmol) in 100 mL toluene at 0 °C was added a 1 M solution of diethylaluminium cyanide in toluene (26.5 mL, 26.5 mmol). The reaction mixture was stirred at 0 °C for 3 h, then warmed to rt. After 9 h, the reaction mixture was poured into a mixture of 3 M NaOH aq (400 mL) and 200 mL ice and the aqueous phase was extracted with CH₂Cl₂ (3 × 500 mL). The combined organic phases were washed with brine (500 mL), dried over MgSO₄, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography (hexanes/EtOAc = 9/1) affording 5.47 g (17.0 mmol, 84%) of **7** as a white, crystalline solid.

TLC: R_f = 0.16 (hexanes/EtOAc = 9/1) [KMnO₄]

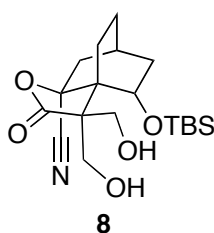
m.p.: 130 °C

¹H-NMR (400 MHz, CDCl₃): δ = 0.07 (s, 3H), 0.09 (s, 3H), 0.93 (s, 9H), 1.38 (ddd, ² J = 13.7 Hz, ³ J = 10.8, 1.3 Hz, 1H), 1.46-1.55 (m, 1H), 1.56-1.64 (m, 1H), 1.76 (ddd, ² J = 13.7 Hz, ³ J = 10.7, 8.0 Hz, 1H), 1.80 (dd, ² J = 14.0 Hz, ³ J = 6.7 Hz, 1H), 1.91 (d, ² J = 14.3 Hz, 1H), 2.03 (virt. q, J \approx 4.9 Hz, 1H), 2.04 (d, ² J = 16.7 Hz, 1H), 2.21 (dddd, ² J = 14.0 Hz, ³ J = 9.1, 4.9 Hz, ⁴ J = 2.0 Hz, 1H), 2.58 (ddd, ² J = 14.3 Hz, ³ J = 4.9 Hz, ⁴ J = 2.2 Hz, 1H), 3.08 (d, ² J = 16.7 Hz, 1H), 3.98 (dd, ³ J = 6.7 Hz, 9.1 Hz, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ = -5.1, -4.3, 18.1, 24.6, 25.1, 25.7, 25.8, 35.1, 37.0, 37.2, 47.5, 67.4, 76.6, 119.8, 174.6.

HRMS (FAB⁺): calcd for C₁₇H₂₇O₃NSiNa [(M+Na)⁺]: 344.1652, found: 344.1661

Diol 8



A LDA solution was prepared by dissolving diisopropylamine (1.35 mL, 0.97 g, 9.59 mmol) in THF (4 mL) at $-78\text{ }^{\circ}\text{C}$ and adding a 2.39 M solution of *n*-butyllithium in hexanes (3.65 mL, 8.71 mmol) dropwise. After stirring at $-78\text{ }^{\circ}\text{C}$ for 30 min the reaction mixture was warmed to $0\text{ }^{\circ}\text{C}$ for 10 min and cooled to $-78\text{ }^{\circ}\text{C}$ again. To a solution of **7** (400 mg, 1.24 mmol) in THF (40 mL) was added gradually the prepared LDA solution at $-78\text{ }^{\circ}\text{C}$. After addition was completed, stirring was continued for 30 min and the temperature was then raised to $-40\text{ }^{\circ}\text{C}$ for 30 min. A stream of formaldehyde gas, generated by thermolysis ($160\text{ }^{\circ}\text{C}$) of paraformaldehyde was introduced through a cannula in a stream of N_2 for 10 min. The reaction mixture was quenched by addition of saturated NH_4Cl aq (4 mL) and extracted with EtOAc ($3 \times 20\text{ mL}$). The combined organic phases were filtered through celite and washed with EtOAc. After removing the solvent *in vacuo*, the residue was purified by flash column chromatography (hexanes/EtOAc = 5/1 \rightarrow 1/1) to give 232 mg **8** (0.61 mmol, 49%) as a white, crystalline solid.

TLC: $R_f = 0.14$ (hexanes/EtOAc = 2/1) [KMnO_4]

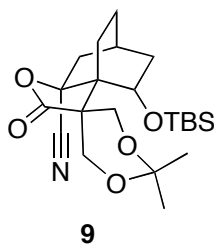
m.p.: $164\text{ }^{\circ}\text{C}$

$^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta = 0.19$ (s, 3H), 0.20 (s, 3H), 0.97 (s, 9H), 1.47 - 1.64 (m, 3H), 1.89 - 1.96 (m, 2H), 2.04 - 2.14 (m, 2H), 2.28 (dddd, $^2J = 13.8\text{ Hz}$, $^3J = 8.9, 5.0\text{ Hz}$, $^4J = 1.9\text{ Hz}$, 1H), 2.68 (ddd, $^2J = 14.2\text{ Hz}$, $^3J = 5.4\text{ Hz}$, $^4J = 2.2\text{ Hz}$, 1H), 2.96 (dd, $^3J = 9.1, 3.5\text{ Hz}$, 1H), 3.40 (dd, $^3J = 8.4, 5.7\text{ Hz}$, 1H), 3.85 (dd, $^2J = 12.1\text{ Hz}$, $^3J = 9.1\text{ Hz}$, 1H), 4.15 (dd, $^2J = 12.3\text{ Hz}$, $^3J = 8.4\text{ Hz}$, 1H), 4.22 (dd, $^2J = 12.1\text{ Hz}$, $^3J = 3.5\text{ Hz}$, 1H), 4.49 (dd, $^3J = 8.9, 7.3\text{ Hz}$, 1H), 4.67 (dd, $^2J = 12.3\text{ Hz}$, $^3J = 5.7\text{ Hz}$, 1H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = -3.6, -3.5, 18.6, 23.9, 24.3, 24.6, 26.0, 38.2, 38.9, 51.2, 56.0, 64.0, 64.7, 71.3, 73.9, 121.4, 174.9$.

HRMS (FAB+): calcd for $\text{C}_{19}\text{H}_{31}\text{O}_5\text{NSiNa}$ $[(\text{M}+\text{Na})^+]$: 404.1864, found: 404.1863

Acetal **9**



Diol **8** (52.0 mg, 136 μ mol) was dissolved in DMF (2 mL) and 2,2-dimethoxypropane (0.85 mL, 0.71 g, 6.81 mmol) and p-toluenesulfonic acid (0.51 mg, 2.72 μ mol) were added. After stirring the resulting solution at rt for 48 h, pyridine (0.1 mL) and water (15 mL) were added and the mixture was extracted with EtOAc (3×20 mL). The combined organic phases were dried over MgSO_4 , filtered, and the solvent was removed *in vacuo*. Purification of the residue by flash column chromatography (hexanes/EtOAc = 3/1) afforded 24.7 mg **9** (58.9 μ mol, 43%) as a white solid.

TLC: R_f = 0.38 (hexanes/EtOAc = 2/1) [KMnO_4]

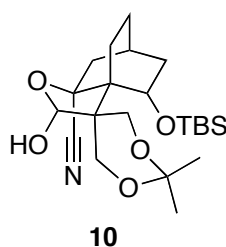
m.p.: 201 $^\circ\text{C}$

^1H -NMR (400 MHz, CDCl_3): δ = 0.14 (s, 3H), 0.18 (s, 3H), 0.95 (s, 9H), 1.34-1.58 (m, 10H), 1.83 (dddd, 2J = 13.7 Hz, 3J = 6.4, 2.6 Hz, 4J = 1.4 Hz, 1H), 1.89 (d, 2J = 14.3 Hz, 1H), 1.97-2.07 (m, 1H), 2.26 (dddd, 2J = 13.7 Hz, 3J = 9.0, 4.8 Hz, 4J = 2.1 Hz, 1H), 2.65 (ddd, 2J = 14.3 Hz, 3J = 5.3 Hz, 4J = 1.5 Hz, 1H), 3.86 (d, 2J = 3.6 Hz, 2H), 4.19 (d, 2J = 12.3 Hz, 1H), 4.25 (dd, 3J = 9.8, 6.4 Hz, 1H), 4.98 (d, 2J = 12.3 Hz, 1H).

^{13}C -NMR (100 MHz, CDCl_3): δ = -4.4, -3.5, 18.1, 22.2, 22.6, 23.8, 24.5, 25.1, 26.0, 38.9, 39.3, 49.5, 50.3, 60.1, 60.6, 68.9, 73.0, 99.5, 121.2, 175.7.

HRMS (FAB $^+$): calcd for $\text{C}_{22}\text{H}_{35}\text{O}_5\text{NSi}$ $[(\text{M}+\text{H})^+]$: 422.2354, found: 422.2358

Lactol **10**



To a solution of **9** (35 mg, 0.083 mmol) in DCM (2 mL) at $-78\text{ }^{\circ}\text{C}$ was added dropwise a 1.0 M solution of DIBAH in DCM. After stirring for 30 min at this temperature, the reaction was quenched by addition of water (5 mL) and extracted with EtOAc ($3 \times 5\text{ mL}$). The combined organic phases were washed with 0.5 M aqueous HCl (5 mL), then brine, dried over Na_2SO_4 , filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography (hexanes/EtOAc = 2/1) affording 35 mg (0.083 mmol, 99%) of **10** as a white, crystalline solid.

TLC: $R_f = 0.31$ (hexanes/EtOAc = 2/1) [CAM]

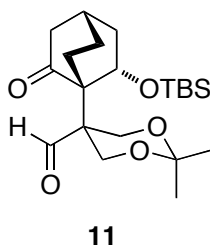
m.p.: $181\text{ }^{\circ}\text{C}$

$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 0.12$ (s, 3H), 0.17 (s, 3H), 0.95 (s, 9H), 1.18 - 1.24 (m, 2H), 1.37 (s, 3H), 1.46 (s, 3H), 1.49 - 1.56 (m, 1H), 1.64 - 1.71 (m, 1H), 1.81 - 1.91 (m, 2H), 1.93 - 2.05 (m, 1H), 2.07 - 2.17 (m, 1H), 2.45 - 2.55 (m, 1H), 3.64 (d, $J = 3.0$, 1H), 3.83 (d, $J = 11.2$, 1H), 4.02 - 4.11 (m, 2H), 4.33 (dd, $J = 3.2, 12.9$, 1H), 4.61 (d, $J = 12.9$, 1H), 5.83 (d, $J = 3.0$, 1H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = -4.3, -3.5, 18.1, 18.6, 21.8, 24.4, 24.8, 26.0, 29.5, 39.2, 40.4, 48.4, 50.1, 61.8, 65.1, 70.1, 75.1, 97.8, 103.3, 123.4$.

HRMS (ESI $^-$): calcd for $\text{C}_{23}\text{H}_{38}\text{NO}_7\text{Si}$ [(M+HCOO) $^-$]: 468.2418, found: 468.2413.

Keto Aldehyde **11**



To a solution of **10** (50 mg, 0.118 mmol) in EtOH (2 mL) at rt was added 2 M aqueous NaOH and the reaction was stirred for 30 min. This mixture was extracted with EtOAc (3 × 5 mL) and the combined organic phases were washed with water (10 mL), then brine, dried over Na₂SO₄, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography (hexanes/EtOAc = 5/1) affording 45 mg (0.114 mmol, 96%) of **11** as a colourless oil.

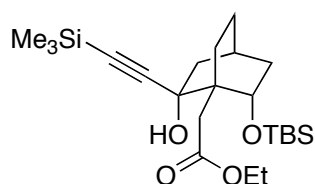
TLC: R_f = 0.72 (hexanes/EtOAc = 2/1) [CAM]

¹H-NMR (300 MHz, CDCl₃): δ = 0.13 (s, 3H), 0.14 (s, 3H), 0.80 (s, 9H), 1.30 (s, 3H), 1.35 (s, 3H), 1.35-1.50 (m, 1H), 1.60-1.77 (m, 3H), 2.01-2.15 (m, 3H), 2.17-2.22 (m, 1H), 2.31-2.40 (m, 1H), 3.94-4.04 (m, 2H), 4.16-4.28 (m, 3H), 9.89 (s, 1H).

¹³C-NMR (75 MHz, CDCl₃, observed): δ = -4.3, -3.0, 17.9, 22.2, 25.0, 26.0, 26.8, 38.2, 44.9, 51.2, 57.6, 60.9, 61.9, 70.9, 98.4, 204.6, 212.7.

HRMS (ESI⁺): calcd for C₂₁H₃₆O₅SiNa [(M+Na)⁺]: 419.2230, found: 419.2223

Alcohol 13



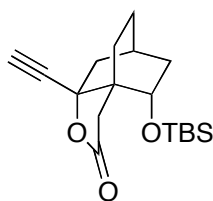
13

A solution of (trimethylsilyl)acetylene (0.395 mL, 2.77 mmol) in THF (5 mL) was treated at -78 °C with a 1.5 M solution of *n*-butyllithium in hexanes (1.76 mL, 2.64 mmol). After stirring for 30 min at this temperature, this solution was added dropwise to a solution of **6** (0.45 g, 1.32 mmol) in THF (15 mL) at -78 °C and left to stir for 20 min at this temperature. The reaction was warmed to rt and then quenched by addition of saturated NH₄Cl aq (10 mL) and extracted with Et₂O (3 × 20 mL). The combined organic phases were washed with brine (20 mL), dried over Na₂SO₄, filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography (hexanes/EtOAc = 20/1) affording 0.436 g (0.994 mmol, 75%) of **13** as a colourless oil.

TLC: R_f = 0.74 (hexanes/EtOAc = 10/1) [CAM]

$^1\text{H-NMR}$	(400 MHz, CDCl_3): δ = 0.08 (s, 3H), 0.09 (s, 3H), 0.15 (s, 9H), 0.87 (s, 9H), 1.24 (t, J = 7.1, 3H), 1.33-1.40 (m, 1H), 1.42-1.50 (m, 1H), 1.53-1.62 (m, 2H), 1.69-1.77 (m, 1H), 1.78-1.83 (m, 1H), 1.89-2.00 (m, 2H), 2.51-2.31 (m, 1H), 2.60 (d, J = 15.2, 1H), 2.90 (d, J = 15.2, 1H), 4.17-4.00 (m, 2H), 4.50 (dd, J = 2.0, 9.0, 1H), 4.85 (s, 1H).
$^{13}\text{C-NMR}$	(100 MHz, CDCl_3): δ = -5.2, -4.4, 0.0, 14.4, 17.7, 23.8, 24.6, 25.2, 25.8, 35.3, 38.1, 41.0, 47.1, 60.0, 71.4, 72.9, 87.5, 108.8, 172.9.
HRMS	(ESI+): calcd for $\text{C}_{23}\text{H}_{42}\text{O}_4\text{Si}_2\text{Na}$ $[(\text{M}+\text{Na})^+]$: 461.2519, found: 461.2515

Lactone **14**

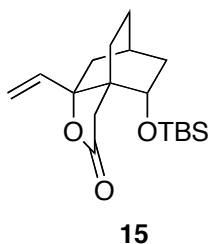


14

NaH (159 mg, 60% in mineral oil, 3.98 mmol) was suspended in a solution of **13** (436 mg, 0.994 mmol) in THF (20 mL) and the reaction was stirred for 3 h at 40 °C. After cooling to rt, the reaction mixture was poured into 1 M HCl (5 mL) and ice, then extracted with Et_2O (3×20 mL). The combined organic phases were washed with brine (20 mL), dried over Na_2SO_4 , filtered, and evaporated *in vacuo*. The crude product was purified by flash column chromatography (hexanes/ EtOAc = 10/1) affording 0.262 g (0.817 mmol, 82%) of **15** as a white, crystalline solid.

TLC:	R_f = 0.47 (hexanes/ EtOAc = 5/1) [CAM]
m.p.:	150 °C
$^1\text{H-NMR}$	(400 MHz, CDCl_3): δ = 0.05 (s, 3H), 0.06 (s, 3H), 0.88 (s, 9H), 1.35-1.48 (m, 2H), 1.58-1.68 (m, 1H), 1.88-2.08 (m, 4H), 2.13-2.22 (m, 2H), 2.32-2.38 (m, 1H), 2.57-2.62 (m, 2H), 3.82 (s, 1H).
$^{13}\text{C-NMR}$	(100 MHz, CDCl_3): δ = -4.9, -4.6, 17.8, 23.9, 25.7, 25.8, 37.7, 38.0, 39.2, 44.3, 73.7, 73.9, 81.0, 84.9, 176.0.
HRMS	(ESI+): calcd for $\text{C}_{18}\text{H}_{29}\text{O}_3\text{Si}$ $[(\text{M}+\text{H})^+]$: 321.1881 found: 321.1882

Lactone **15**



A solution of **14** (190 mg, 0.539 mmol) in pyridine (10 mL) was vigorously stirred in hydrogen with 6.3 mg (0.059 mg) of a 5% palladium-on-calcium carbonate catalyst, poisoned with 3.5% lead at atmospheric pressure and rt. After 30 min, the catalyst was removed and the solvent was evaporated *in vacuo*. The residue was purified by flash column chromatography (hexanes/EtOAc = 10/1) to give 183 mg (0.567 mmol, 96 %) of **15** as a white, crystalline solid.

TLC: R_f = 0.48 (hexanes/EtOAc = 5/1) [CAM]

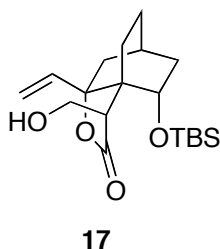
m.p.: 131 °C

¹H-NMR (600 MHz, CDCl₃): δ = 0.07 (s, 6H), 0.90 (s, 9H), 1.36 (ddd, J = 6.9, 10.7, 13.4, 1H), 1.46-1.52 (m, 1H), 1.65-1.77 (m, 3H), 1.91-2.11 (m, 5H), 2.34 (d, J = 16.2, 1H), 3.77 (d, J = 8.9, 1H), 5.15 (d, J = 0.9, 10.8, 1H), 5.32 (dd, J = 0.9, 16.9, 1H), 6.03 (dd, J = 10.8, 16.9, 1H).

¹³C-NMR (150 MHz, CDCl₃): δ = -4.9, -4.6, 17.8, 24.4, 24.7, 25.8, 25.9, 35.6, 36.7, 40.3, 43.4, 74.6, 85.7, 114.3, 140.5, 176.9.

HRMS (ESI⁺): calcd for C₁₈H₃₄O₃NSi [(M+NH₄)⁺]: 340.2308, found: 340.2303

Alcohol **17**



A LDA solution was prepared by dissolving diisopropylamine (0.67 mL, 0.477 g, 4.71 mmol) in THF (2 mL) at -78 °C and adding a 2.34 M solution of *n*-butyllithium in hexanes (1.99 mL, 4.65 mmol) dropwise. After stirring at -78 °C for 30 min the reaction mixture was warmed to 0 °C for 10 min and cooled to -78 °C again. To a

solution of **15** (100 mg, 0.31 mmol) in THF (3 mL) was added gradually the prepared LDA solution at $-78\text{ }^{\circ}\text{C}$. After addition was completed, stirring was continued for 30 min and the temperature was then raised to $-40\text{ }^{\circ}\text{C}$ for 30 min. A stream of formaldehyde gas, generated by thermolysis ($160\text{ }^{\circ}\text{C}$) of paraformaldehyde was introduced through a cannula in a stream of N_2 for 10 min. The reaction mixture was quenched by addition of saturated NH_4Cl aq (4 mL) and extracted with EtOAc ($3 \times 20\text{ mL}$). The combined organic phases were filtered through celite and washed with EtOAc. After removing the solvent *in vacuo*, the residue was purified by flash column chromatography (hexanes/EtOAc = 2/1) to give 101 mg **17** (0.29 mmol, 92%) as a white, crystalline solid.

TLC: $R_f = 0.25$ (hexanes/EtOAc = 2/1) [CAM]

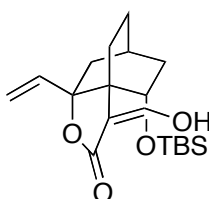
m.p.: $169\text{ }^{\circ}\text{C}$

$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 0.06$ (s, 6H), 0.88 (s, 9H), 1.30-1.40 (m, 1H), 1.45-1.60 (m, 1H), 1.62-1.75 (m, 3H), 1.82-2.00 (m, 3H), 2.08-2.17 (m, 1H), 2.34-2.47 (m, 2H), 3.66-3.79 (m, 2H), 3.83-3.93 (m, 1H), 5.11 (d, $J=10.8$, 1H), 5.31 (d, $J=16.9$, 1H), 6.12 (dd, $J=10.9$, 16.9, 1H).

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = -5.0$, -4.4 , 17.7, 21.2, 24.3, 25.5, 25.8, 36.6, 39.8, 44.9, 50.1, 61.3, 76.1, 86.0, 114.5, 142.8, 178.6.

HRMS (ESI $^-$): calcd for $\text{C}_{19}\text{H}_{32}\text{O}_4\text{SiCl}$ $[(\text{M}+\text{Cl})^-]$: 387.1758, found: 387.1863

Dicarbonyl **18**



18

To a solution of **17** (130 mg, 0.37 mmol) in CH_2Cl_2 (5 mL) at $0\text{ }^{\circ}\text{C}$ was added NaHCO_3 (43 mg, 0.517 mmol), then DMP (219 mg, 0.517 mmol) and the mixture was left to stir at rt for 2 h. The reaction was quenched by addition of conc. Na_2SO_3 aq : sat. NaHCO_3 aq : water = 5 mL : 5 mL : 5 mL and stirred vigorously for 20 min. After extracting the aqueous phase with EtOAc ($3 \times 20\text{ mL}$), the combined organic phases were washed with brine (30 mL), dried over Na_2SO_4 , filtered, and

evaporated *in vacuo*. The residue was purified by flash column chromatography (hexanes/EtOAc = 10/1) to give **18** (116 mg, 0.331 mmol, 90%) as a colorless oil.

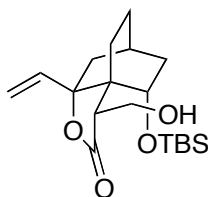
TLC: R_f = 0.65 (hexanes/EtOAc = 2/1) [CAM]

$^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = -0.08-0.12 (m, 6H), 0.81-0.94 (m, 9H), 1.16-2.19 (m, 12H), 3.03 (s, 1H), 4.17-4.20 (m, 1H), 5.10-5.38 (m, 2H), 5.92-6.08 (m, 1H), 9.99 (s, 1H).

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3 , mixture of enol and aldehyde): δ = -5.2, -4.8, -4.1, -3.9, 17.7, 17.8, 22.4, 23.7, 24.0, 24.8, 25.5, 25.7, 25.8, 25.9, 26.0, 29.9, 36.2, 39.3, 40.2, 45.8, 47.8, 54.2, 69.2, 84.6, 86.6, 108.6, 114.9, 115.3, 139.9, 140.4, 152.6, 173.6, 176.4, 199.4.

HRMS (ESI $^-$): calcd for $\text{C}_{19}\text{H}_{29}\text{O}_4\text{Si}$ [(M-H) $^-$]: 349.1841, found: 363.1836

Hydroxymethyl lactone **19**



19

Sodium borohydride (32 mg, 0.855 mmol) was added to a solution of **18** (100 mg, 0.285 mmol) in EtOH (2 mL) at 0 °C and the mixture was left to stir at rt for 1 h. The reaction was quenched by neutralization with 0.5 M HCl and extracted with EtOAc. The combined organic phases were washed with brine, dried over Na_2SO_4 , filtered, and evaporated *in vacuo*. Purification of the residue by flash column chromatography (hexanes/EtOAc = 2/1) yielded **19** (92 mg, 0.261 mmol, 92%) as a colorless oil.

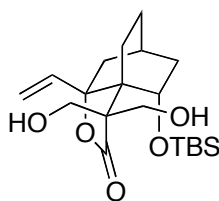
TLC: R_f = 0.28 (hexanes/EtOAc = 2/1) [CAM]

$^1\text{H-NMR}$ (600 MHz, CDCl_3): δ = 0.09 (s, 3H), 0.11 (s, 3H), 0.91 (s, 9H), 1.38-1.44 (m, 1H), 1.46-1.52 (m, 1H), 1.63-1.77 (m, 3H), 1.87-1.93 (m, 1H), 1.96-2.02 (m, 2H), 2.11-2.14 (m, 1H), 2.69 (dd, J =6.0, 8.8, 1H), 3.66 (dd, J =6.0, 10.9, 1H), 3.92 (d, J =8.2, 1H), 4.08 (dd, J =8.8, 10.9, 1H), 5.18 (dd, J =0.9, 10.8, 1H), 5.34 (dd, J =0.9, 16.9, 1H), 6.03 (dd, J =10.9, 16.9, 1H).

$^{13}\text{C-NMR}$ (150 MHz, CDCl_3): δ = -4.0, -3.4, 18.0, 24.2, 24.3, 25.3, 26.0, 35.6, 39.4, 45.7, 46.5, 58.7, 70.3, 85.0, 114.8, 139.8, 179.1.

HRMS (ESI+): calcd for $C_{19}H_{32}O_4SiNa$ $[(M+Na)^+]$: 375.1968, found: 375.1962

Diol 16



16

A LDA solution was prepared by dissolving diisopropylamine (0.23 mL, 0.165 g, 1.63 mmol) in THF (1.5 mL) at $-78\text{ }^{\circ}\text{C}$ and adding a 2.34 M solution of *n*-butyllithium in hexanes (1.58 mL, 6.76 mmol) dropwise. After stirring at $-78\text{ }^{\circ}\text{C}$ for 30 min the reaction mixture was warmed to $0\text{ }^{\circ}\text{C}$ for 10 min and cooled to $-78\text{ }^{\circ}\text{C}$ again. To a solution of **19** (40 mg, 0.113 mmol) in THF (1.5 mL) was added gradually the prepared LDA solution at $-78\text{ }^{\circ}\text{C}$. After addition was completed, stirring was continued for 20 min and the temperature was then raised to $-40\text{ }^{\circ}\text{C}$ for 20 min. A stream of formaldehyde gas, generated by thermolysis ($160\text{ }^{\circ}\text{C}$) of paraformaldehyde was introduced through a cannula in a stream of N_2 for 10 min. The reaction mixture was quenched by addition of saturated NH_4Cl aq (2 mL) and extracted with EtOAc ($3 \times 20\text{ mL}$). The combined organic phases were filtered through celite and washed with EtOAc. After removing the solvent *in vacuo*, the residue was purified by flash column chromatography (hexanes/EtOAc = 1/1) to give 28 mg **16** (0.073 mmol, 65%) as a colorless oil.

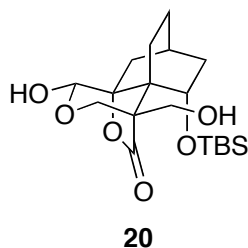
TLC: $R_f = 0.15$ (hexanes/EtOAc = 2/1) [CAM]

$^1\text{H-NMR}$ (400 MHz, $CDCl_3$): $\delta = 0.09\text{--}0.16$ (m, 6H), 0.91 (s, 9H), 1.23–1.55 (m, 4H), 1.65–2.00 (m, 6H), 2.25–2.30 (m, 1H), 2.52 (s br, 1H), 3.09 (s br, 1H), 3.91–3.97 (m, 1H), 4.02–4.06 (m, 1H), 4.11–4.14 (m, 1H), 4.15–4.21 (m, 1H), 4.23–4.28 (m, 1H), 5.11 (dd, $J=1.1, 10.9$, 1H), 5.35 (dd, $J=1.1, 17.0$, 1H), 6.33 (dd, $J=10.9, 16.9$, 1H).

$^{13}\text{C-NMR}$ (100 MHz, $CDCl_3$): $\delta = -4.2, -2.7, 18.2, 20.6, 24.5, 24.6, 26.1, 37.3, 38.7, 48.6, 51.6, 62.7, 63.5, 70.9, 85.4, 113.6, 144.1, 179.8$.

HRMS (ESI+): calcd for $C_{20}H_{34}O_5SiNa$ $[(M+Na)^+]$: 405.2073, found: 405.2067

Lactol/Lactone **20**



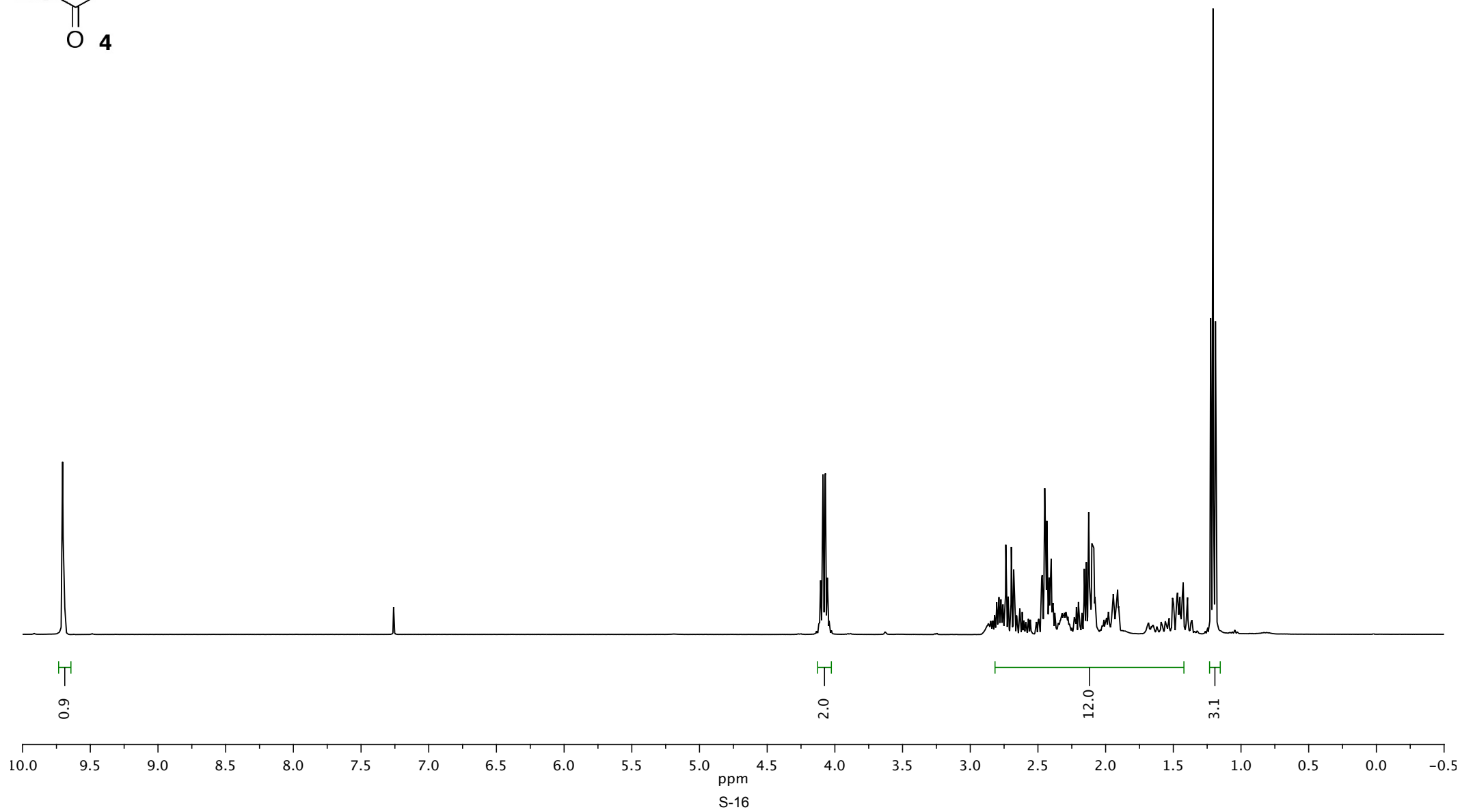
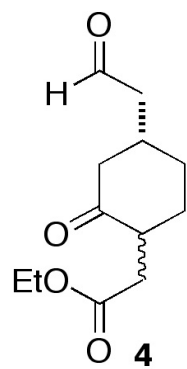
Ozone was bubbled into a mixture of **16** (30 mg, 0.078 mmol), NaHCO₃ (6.6 mg, 0.078 mmol), CH₂Cl₂ (1 mL) and MeOH (1 mL) for 10 min. Excess ozone was then removed by bubbling N₂ through the mixture. Me₂S (0.02 mL, 20 mg, 0.314 mmol) was added and the mixture was left to stir overnight at rt. The mixture was then concentrated *in vacuo* and purified by flash column chromatography (hexanes/EtOAc = 2/1) to give 14 mg (0.036 mmol, 46 %) of **20** as a colorless oil.

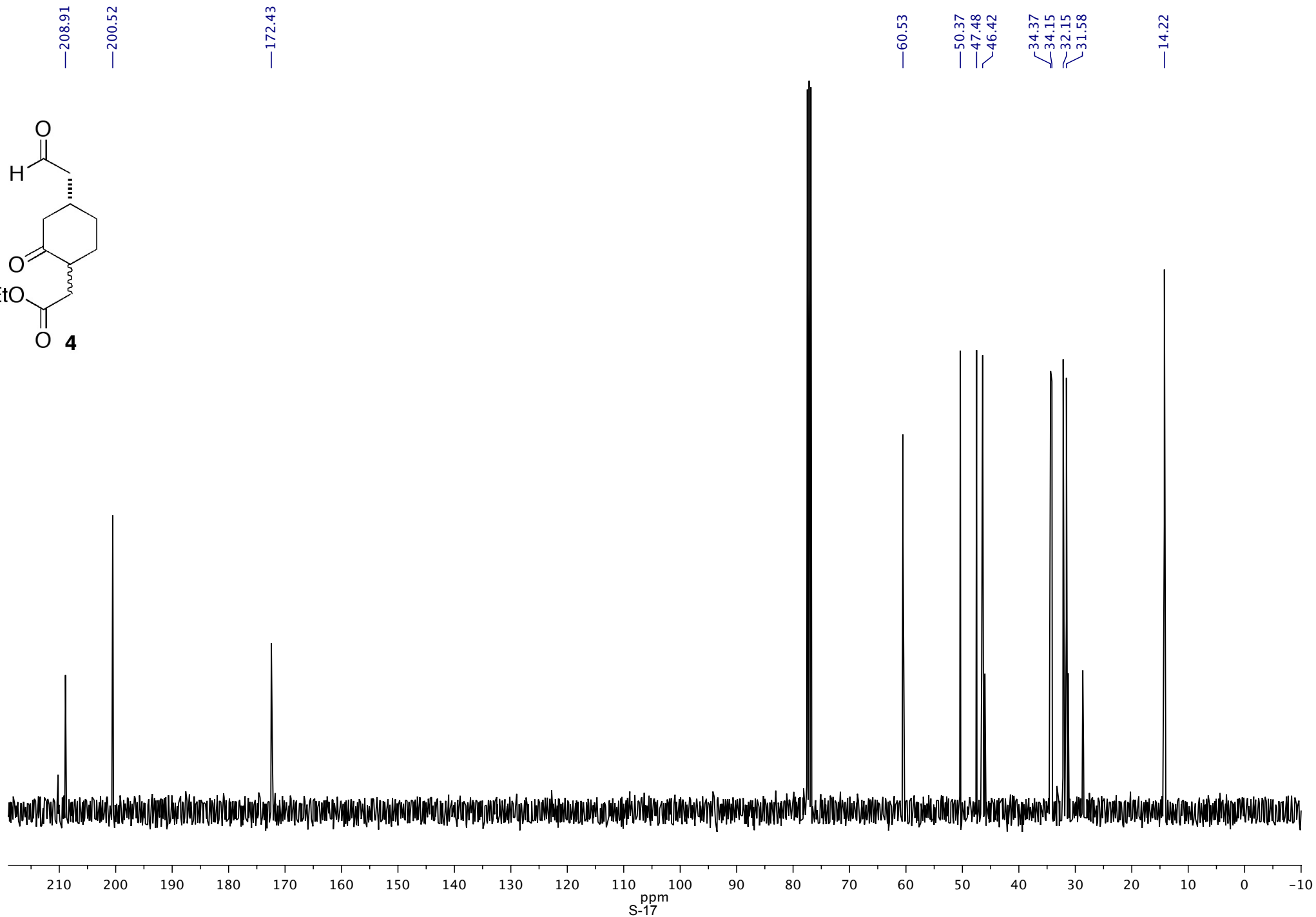
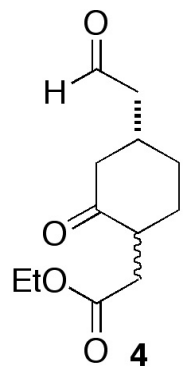
TLC: R_f = 0.11 (hexanes/EtOAc = 2/1) [CAM]

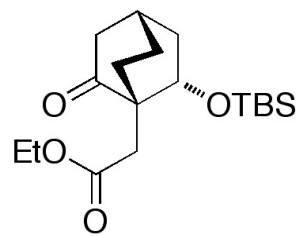
¹H-NMR (400 MHz, CDCl₃): δ = 0.10 (s, 3H), 0.11 (s, 3H), 0.92 (s, 9H), 1.15-1.28 (m, 1H), 1.47-1.61 (m, 2H), 1.64-1.74 (m, 1H), 1.83-1.88 (m, 1H), 1.95-2.10 (m, 3H), 2.14-2.21 (m, 1H), 2.59-2.69 (m, 1H), 2.76 (d, J =12.8, 1H), 3.50-3.57 (m, 1H), 3.97 (d, J =7.3, 1H), 4.03-4.10 (m, 2H), 4.19 (d, J =11.2, 1H), 4.83 (d, J =12.7, 1H).

¹³C-NMR (100 MHz, CDCl₃): δ = -4.1, -3.7, 18.0, 19.6, 23.8, 24.8, 26.0, 31.0, 39.3, 45.1, 48.2, 59.1, 64.4, 70.0, 83.9, 94.0, 178.8.

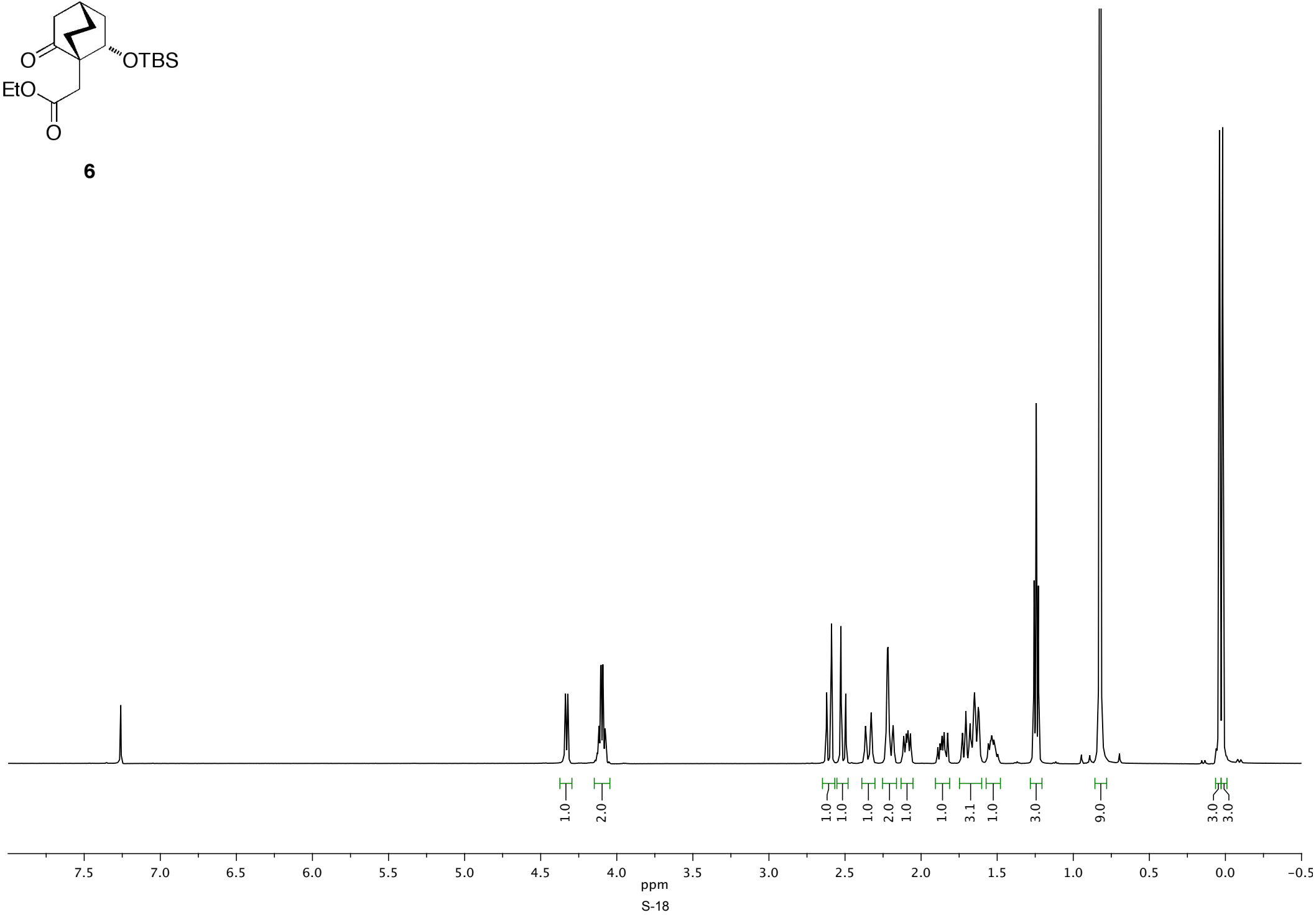
HRMS (ESI⁺): calcd for C₁₉H₃₃O₆SiNa [(M+H)⁺]: 385.2041, found: 385.2042.

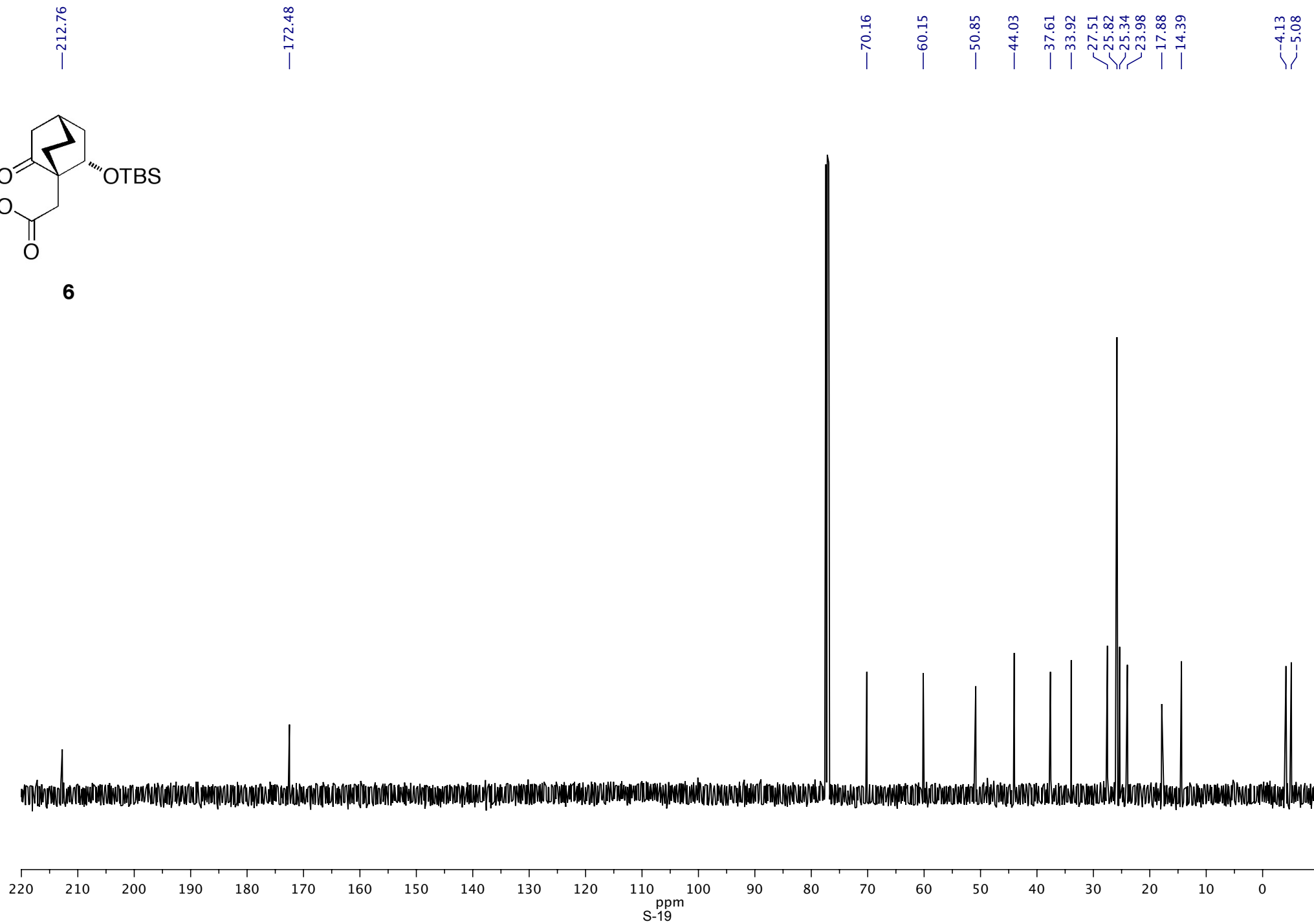
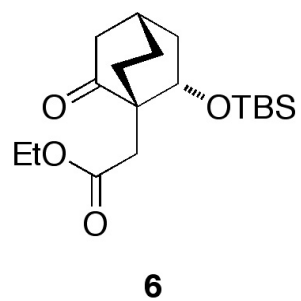


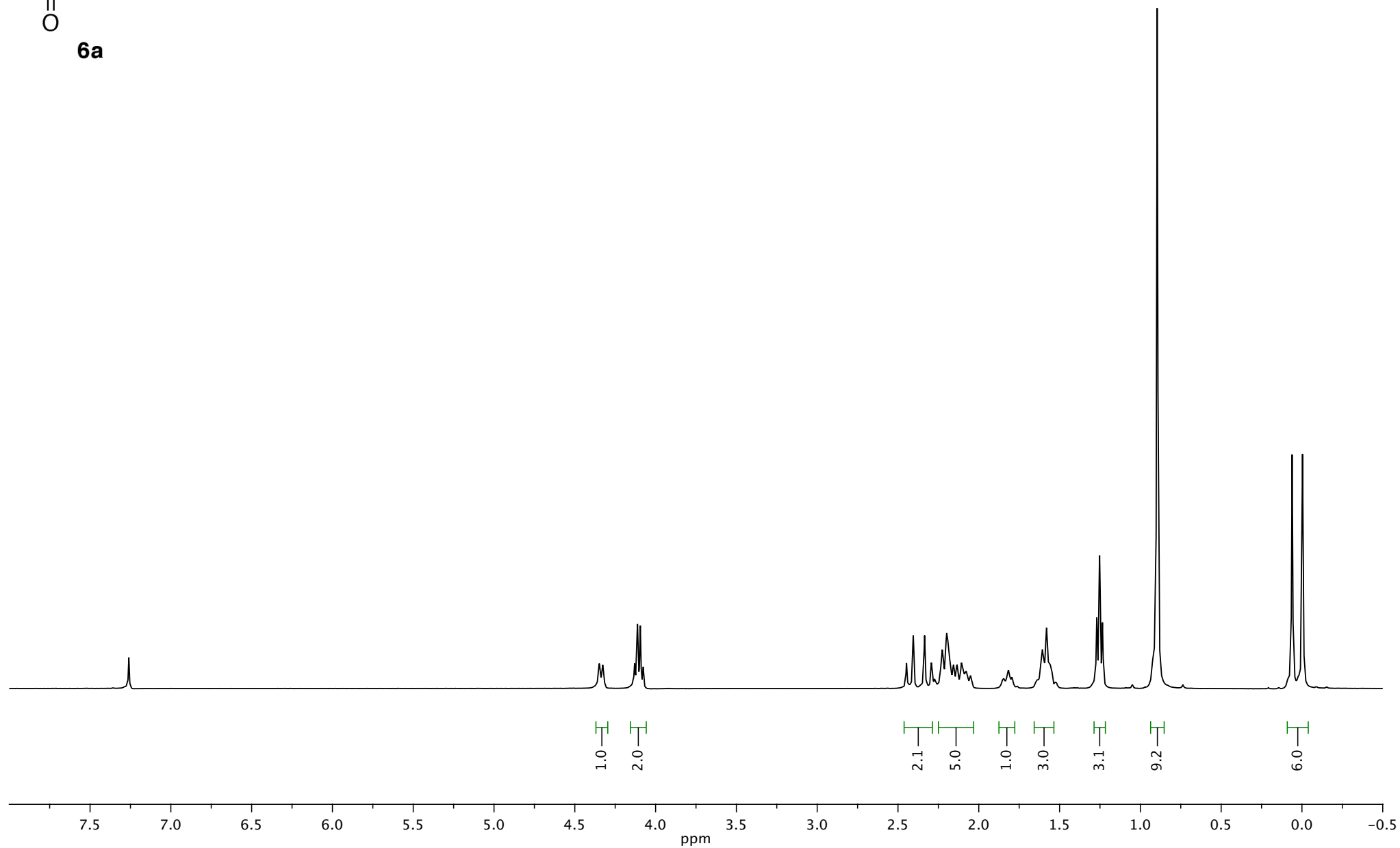
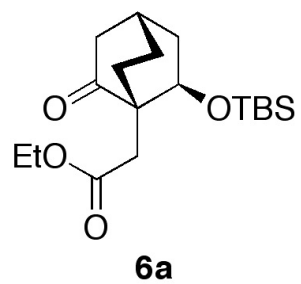


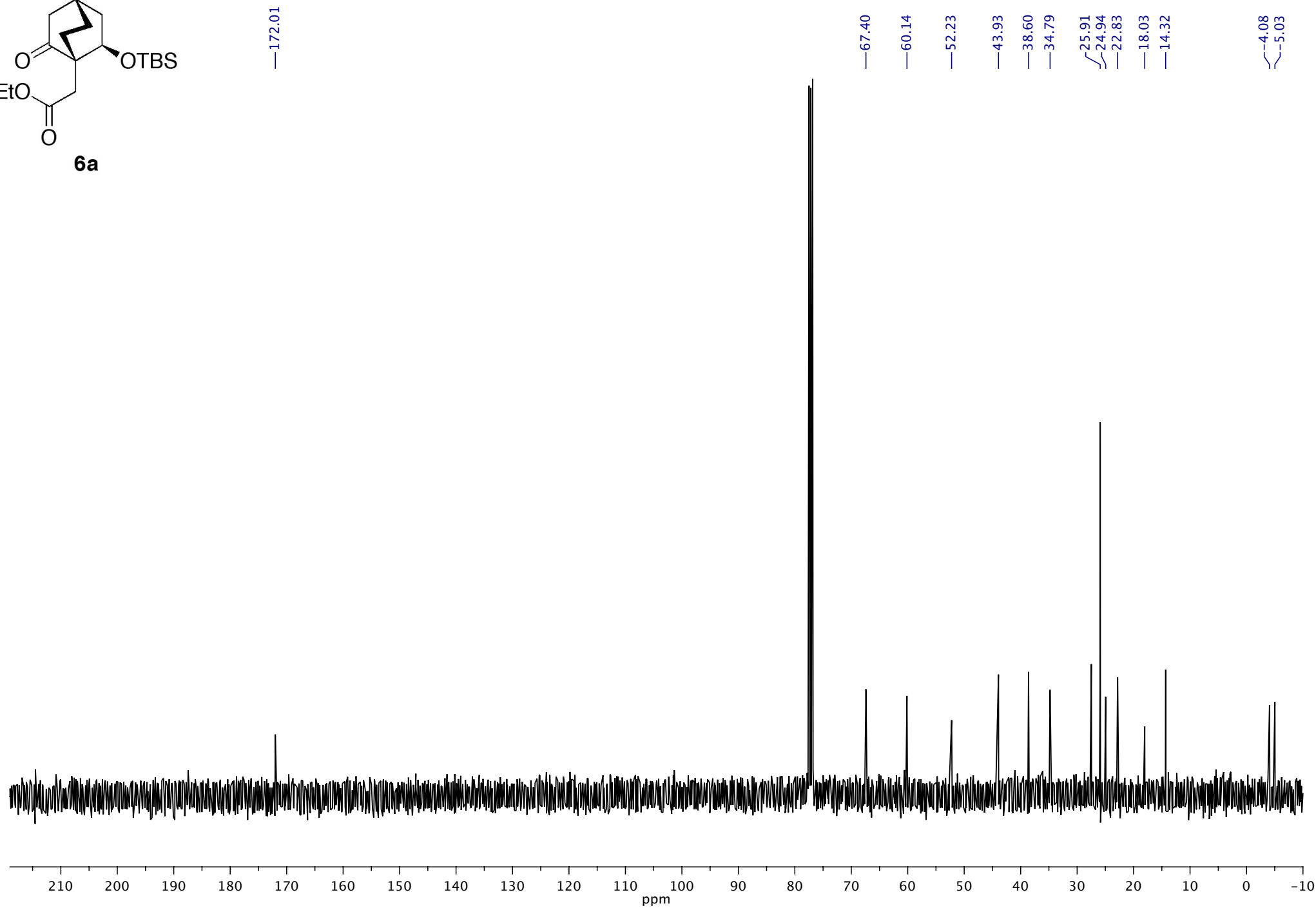
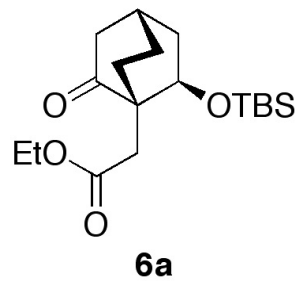


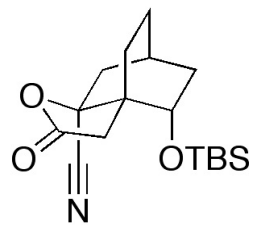
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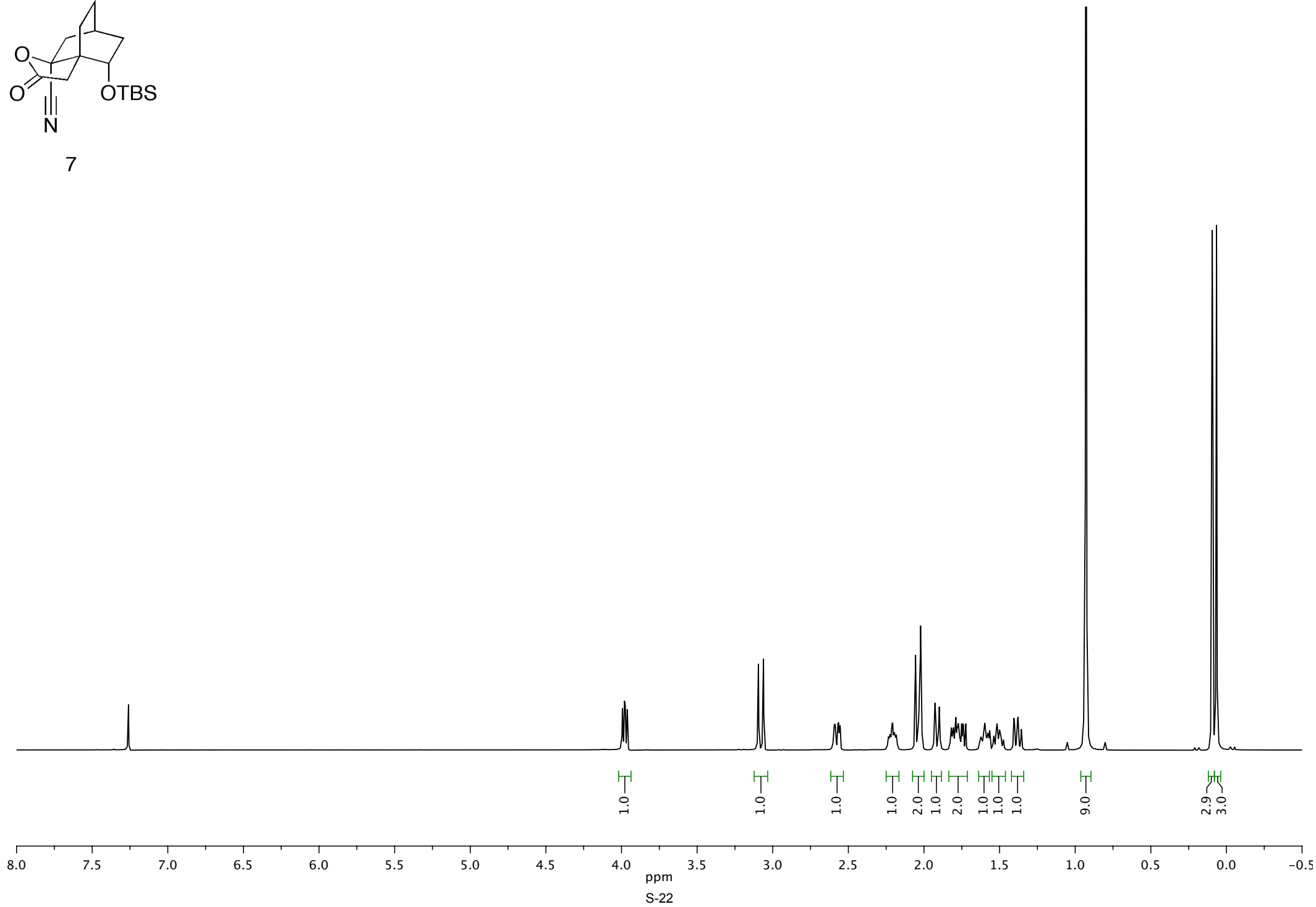


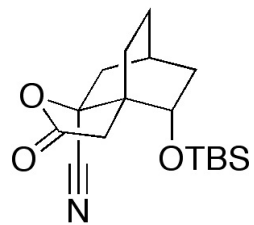




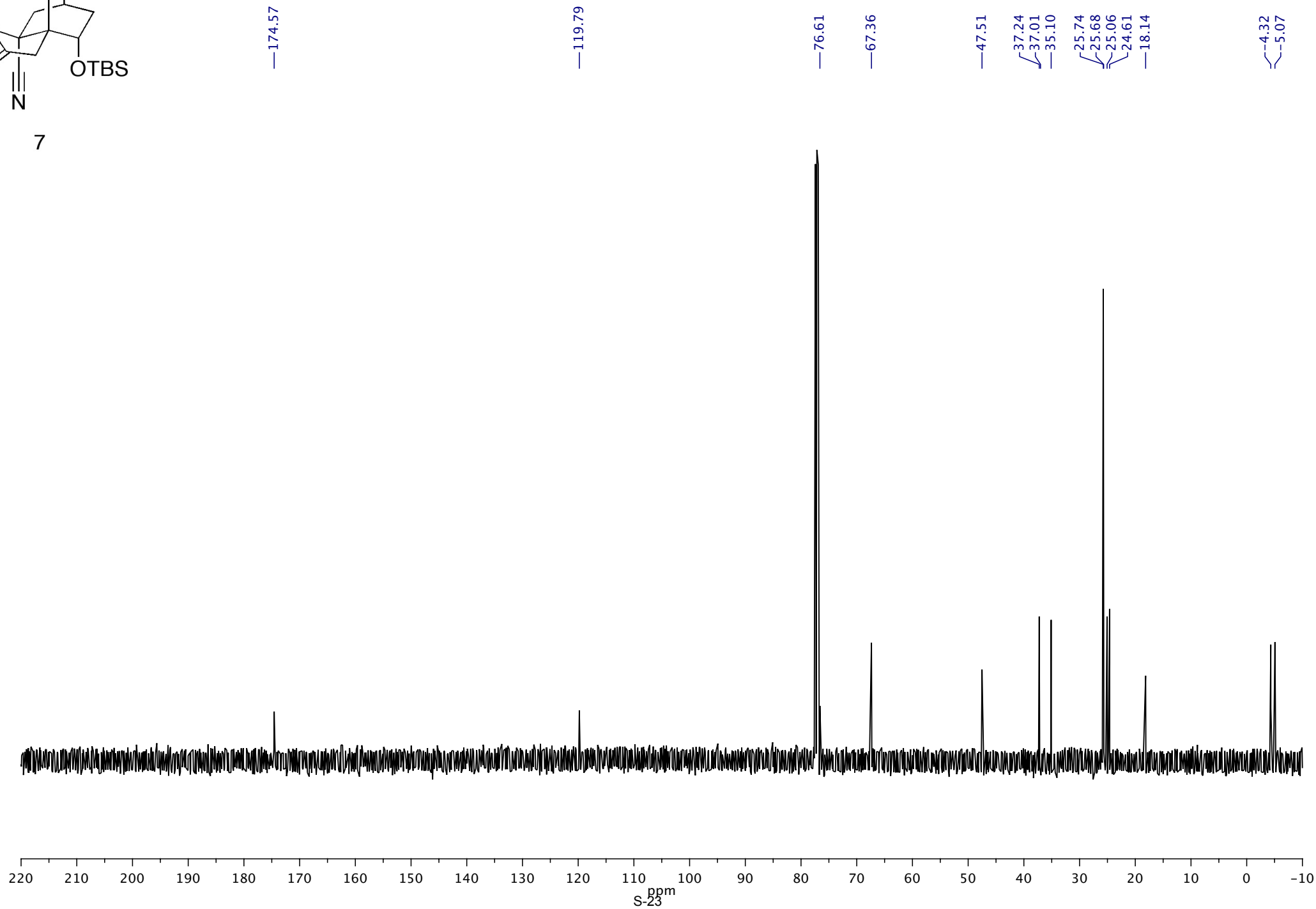


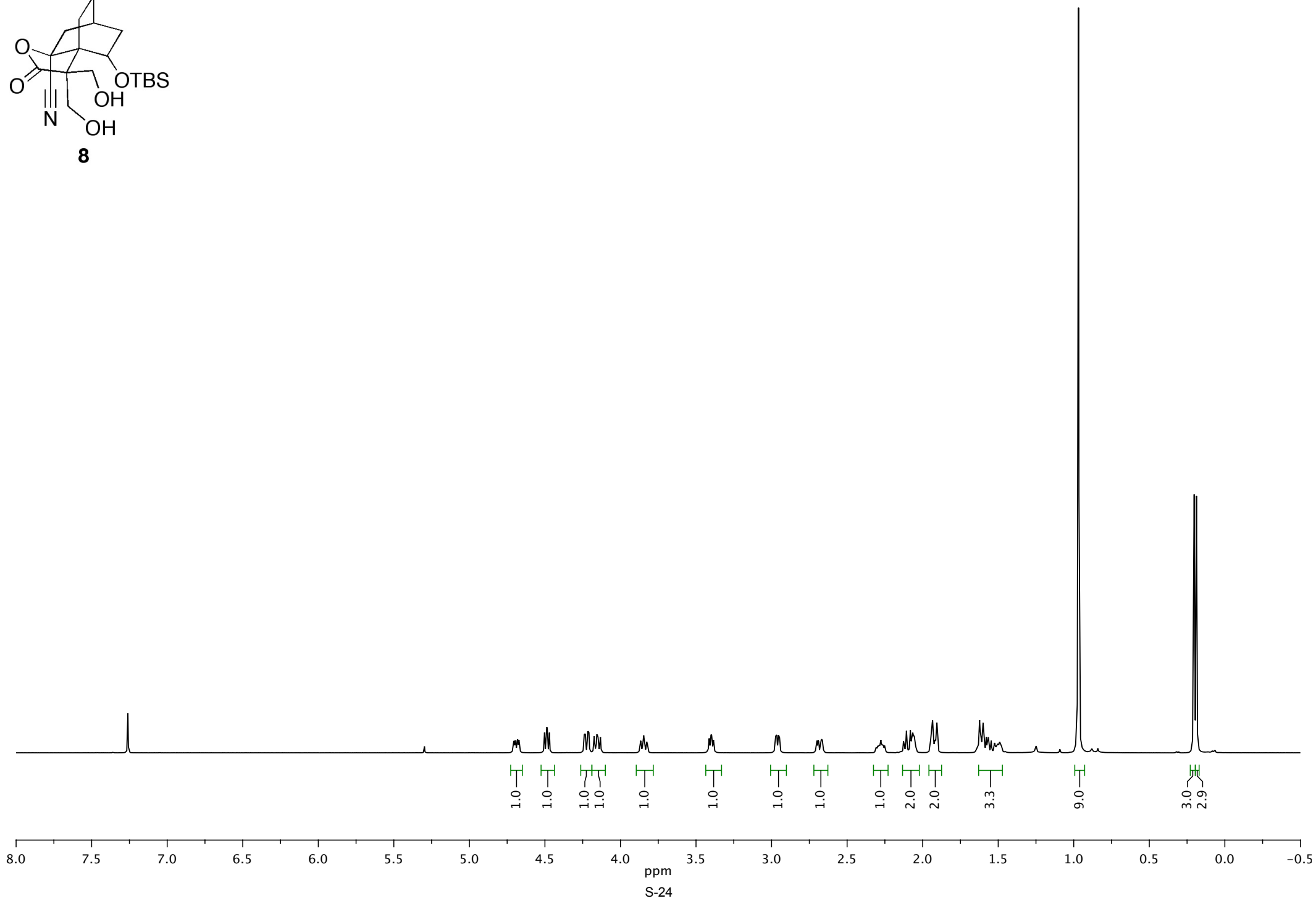
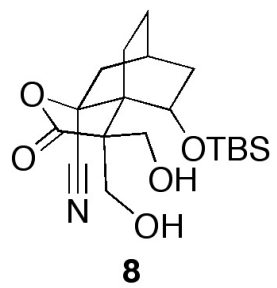
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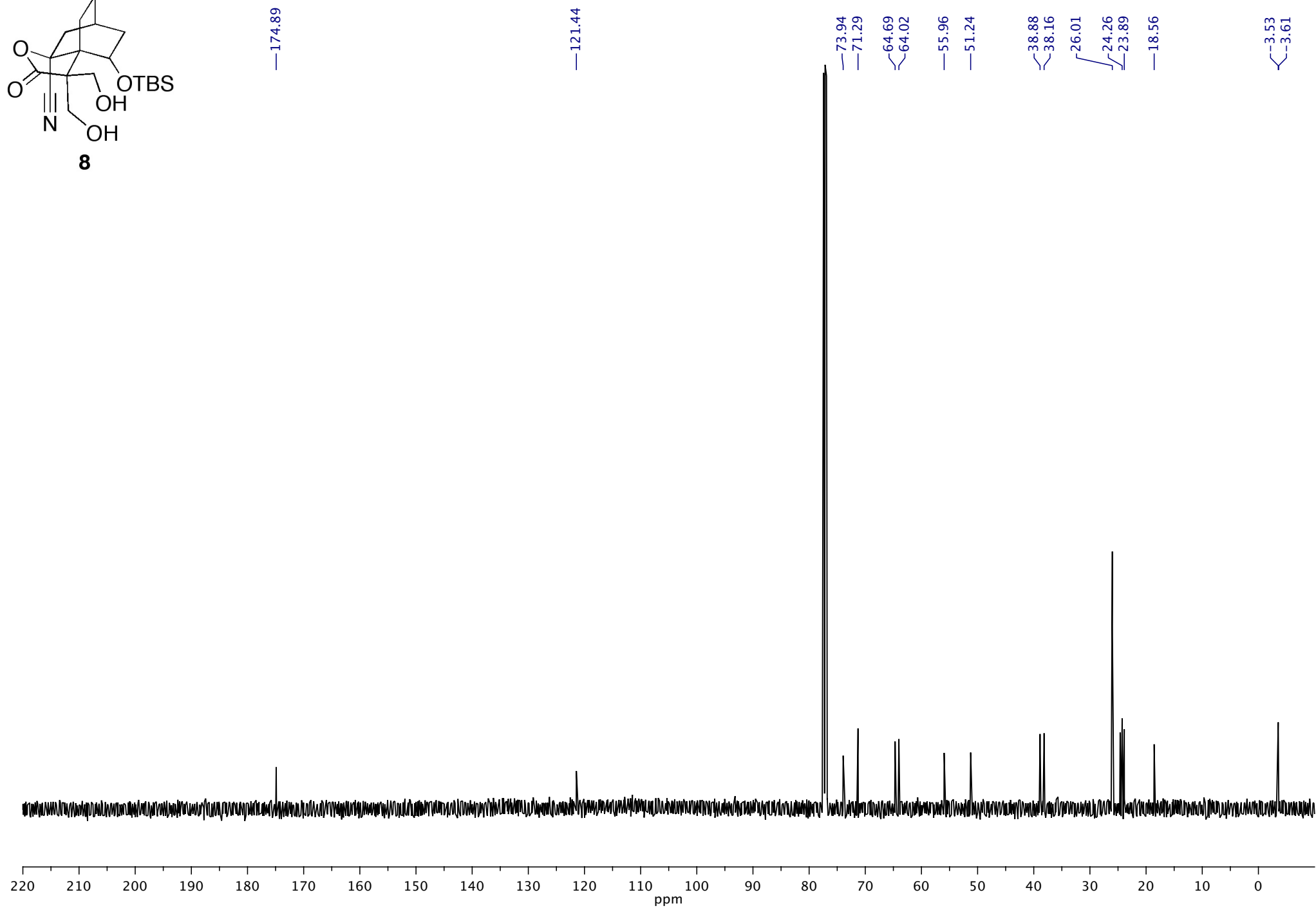
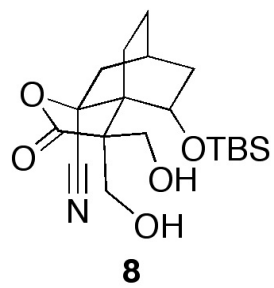


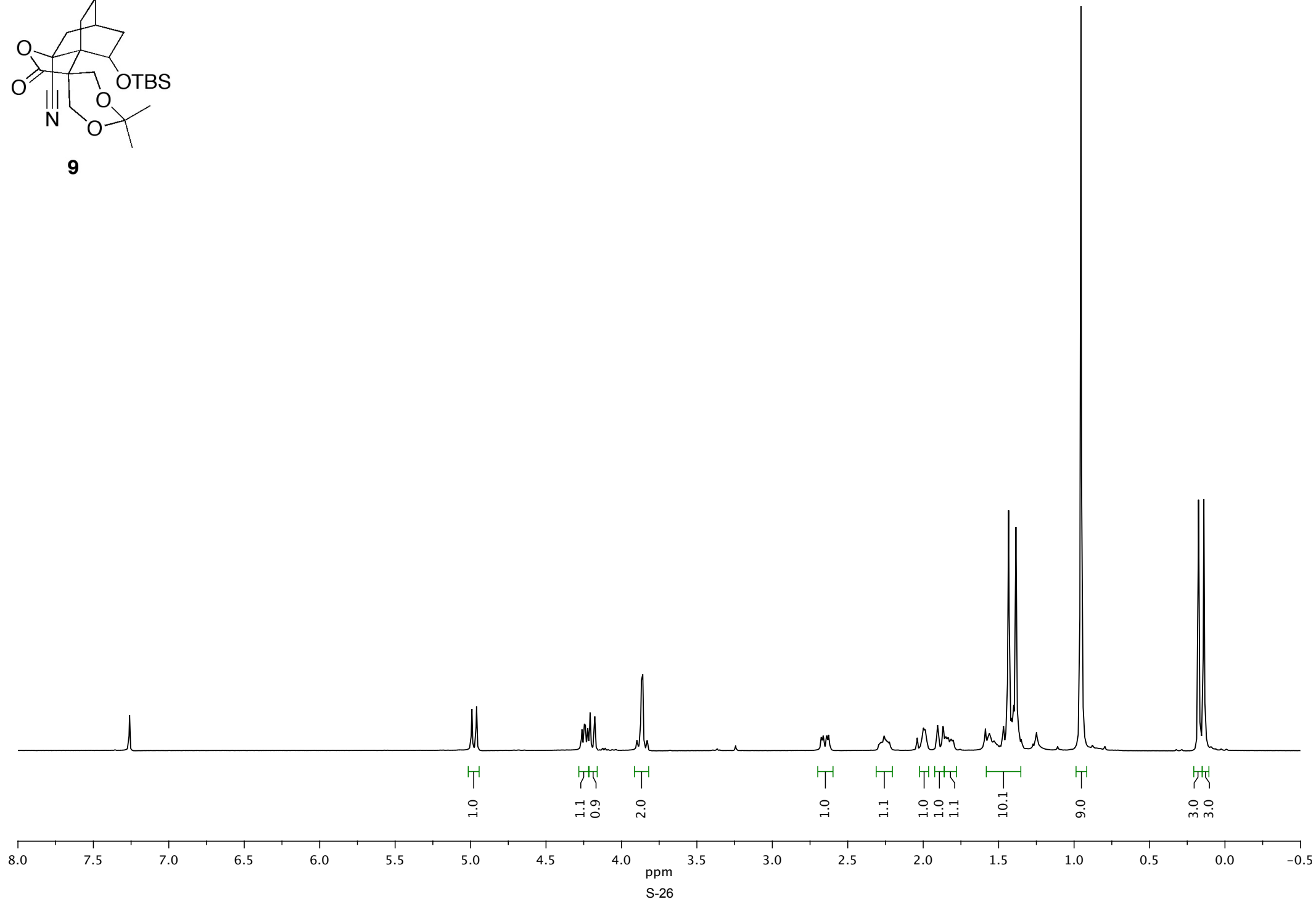
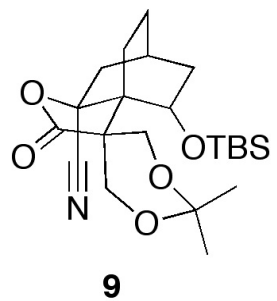


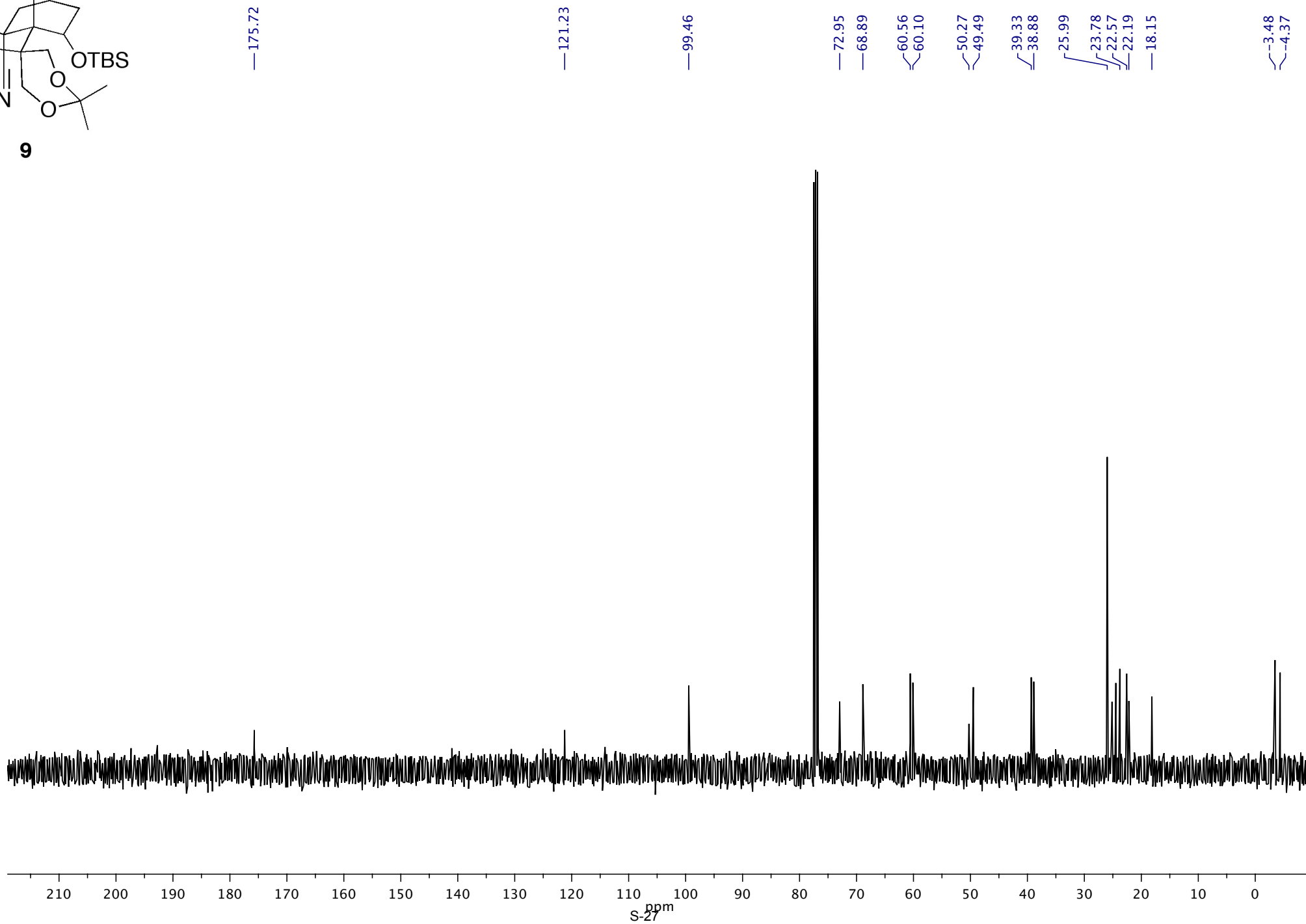
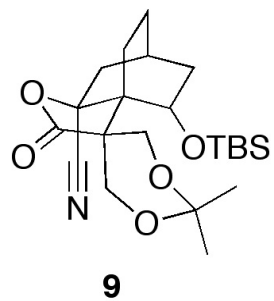
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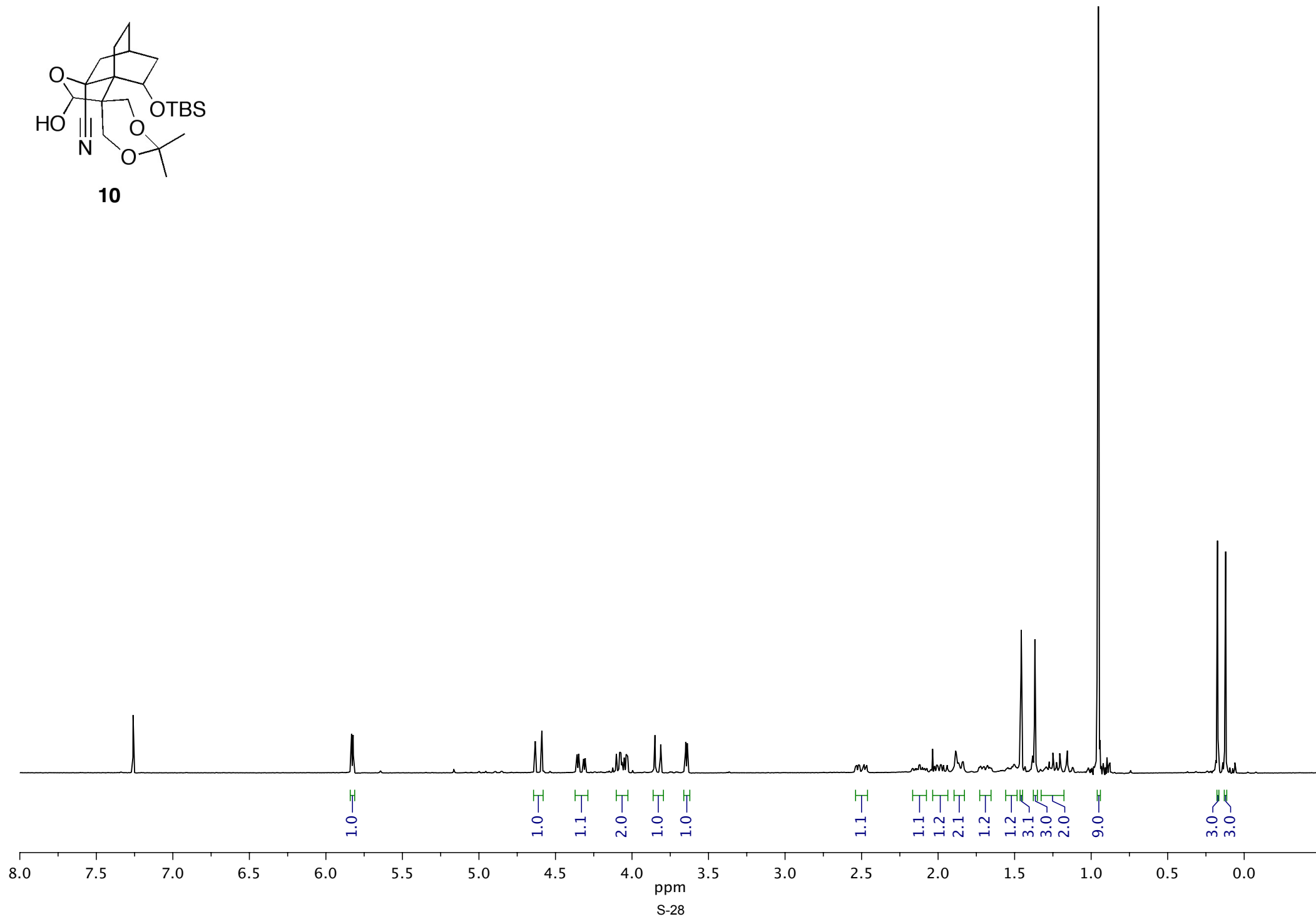
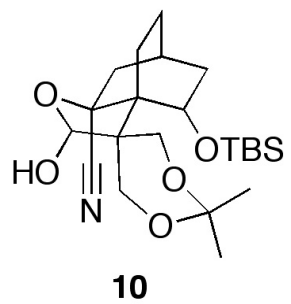


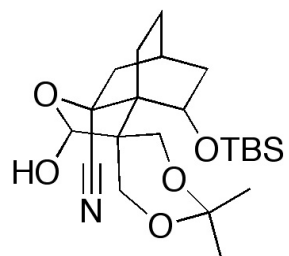




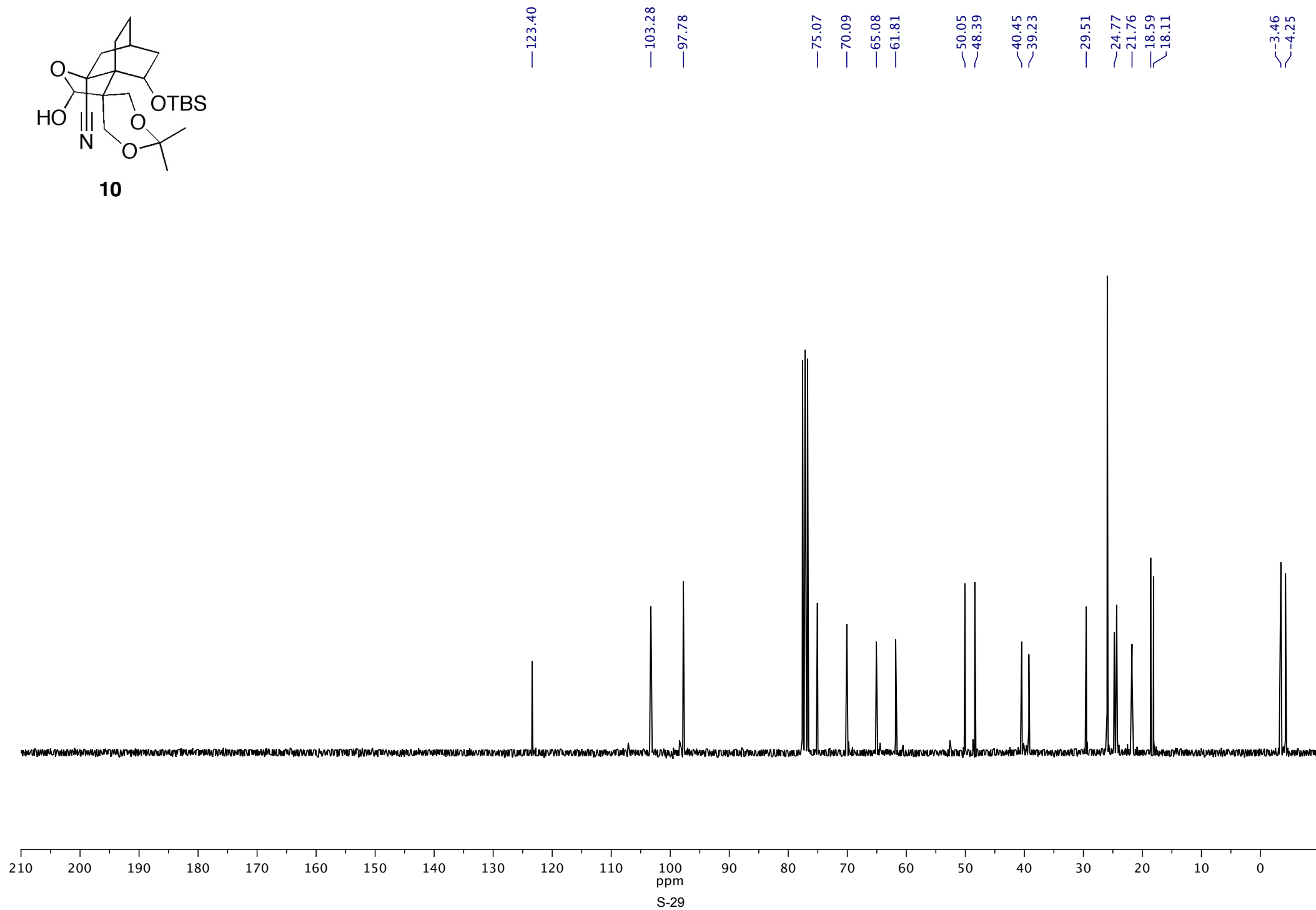


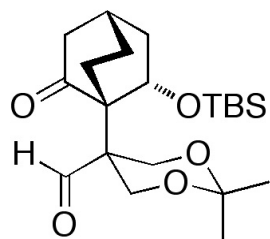




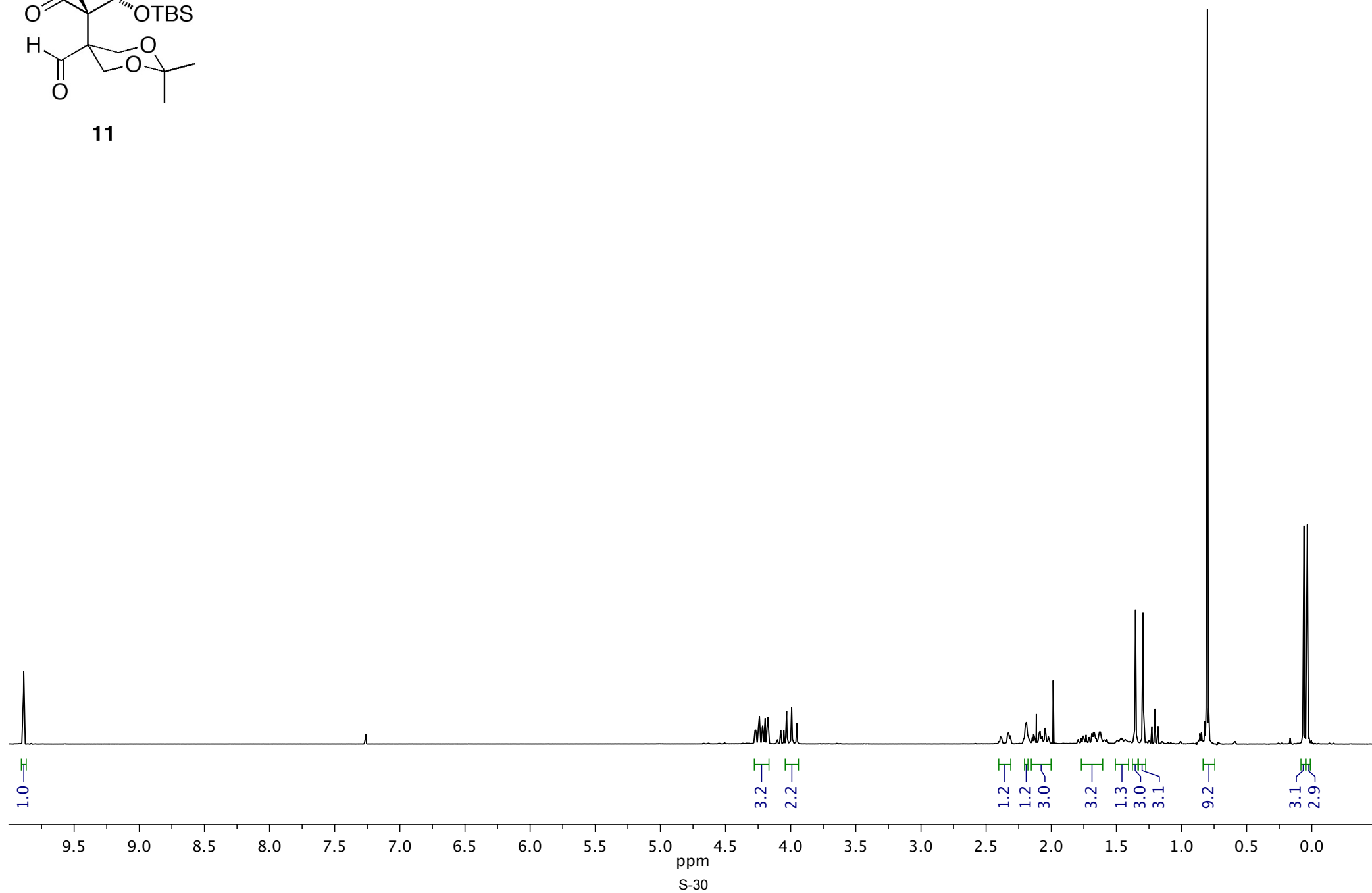


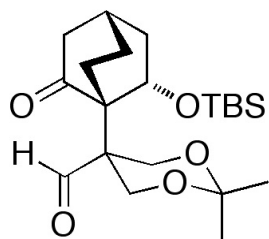
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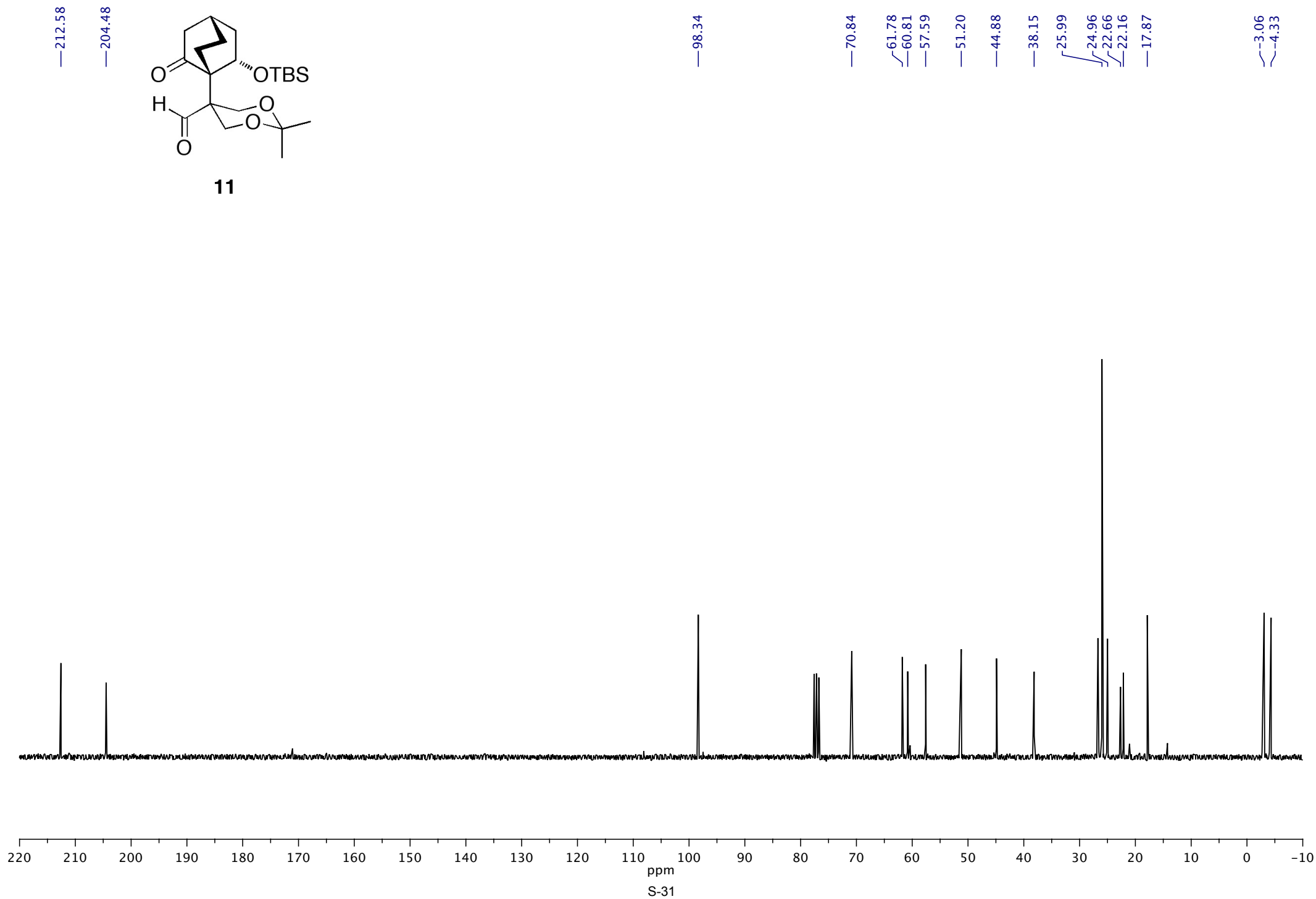


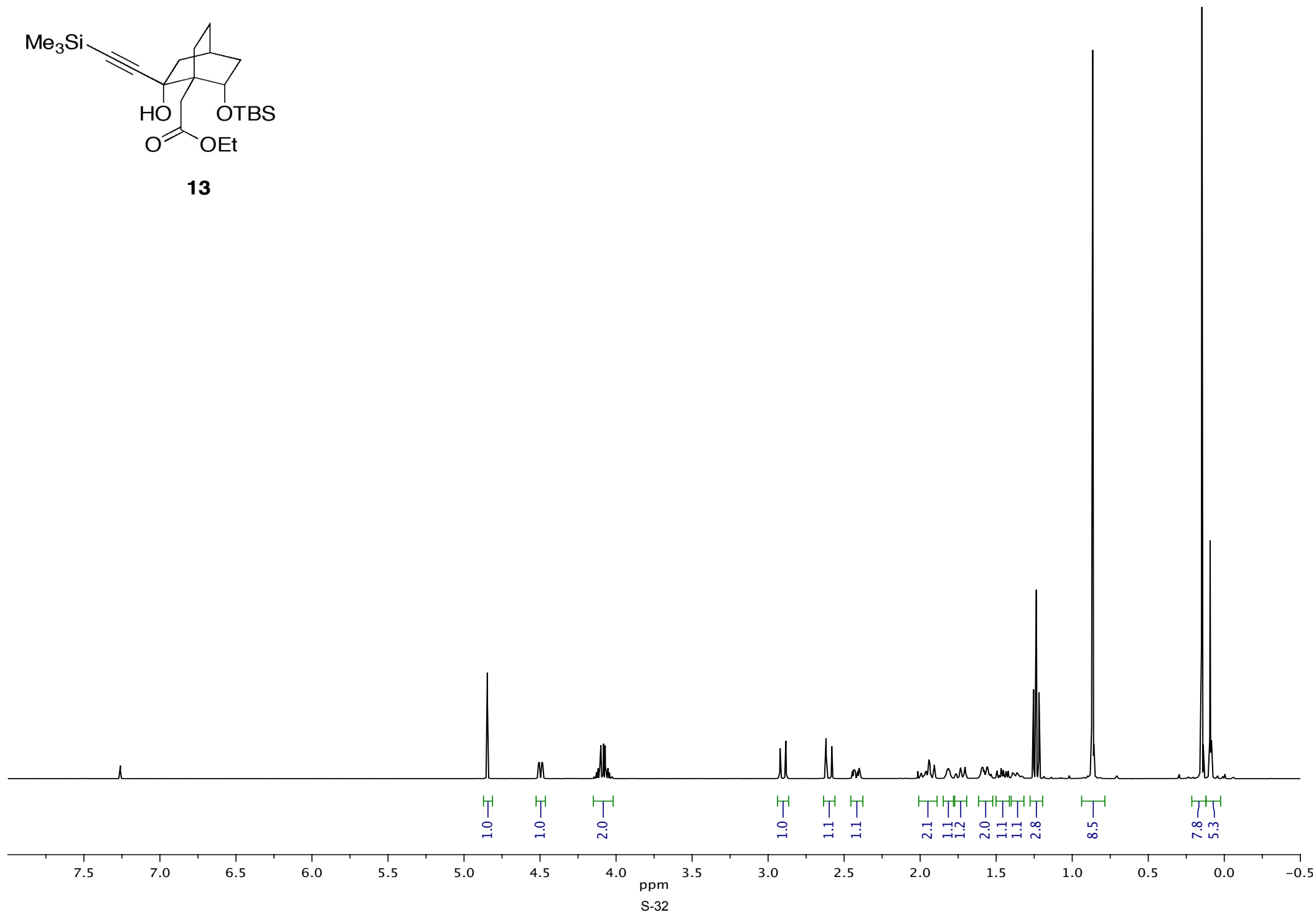
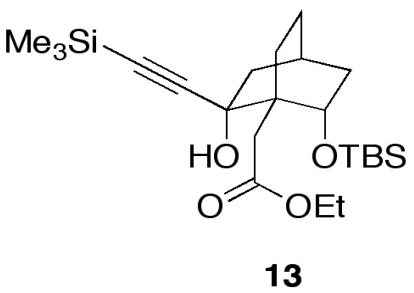
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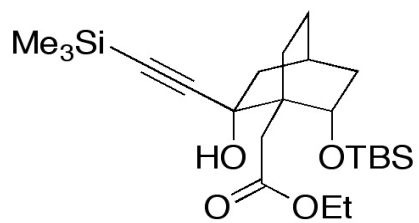




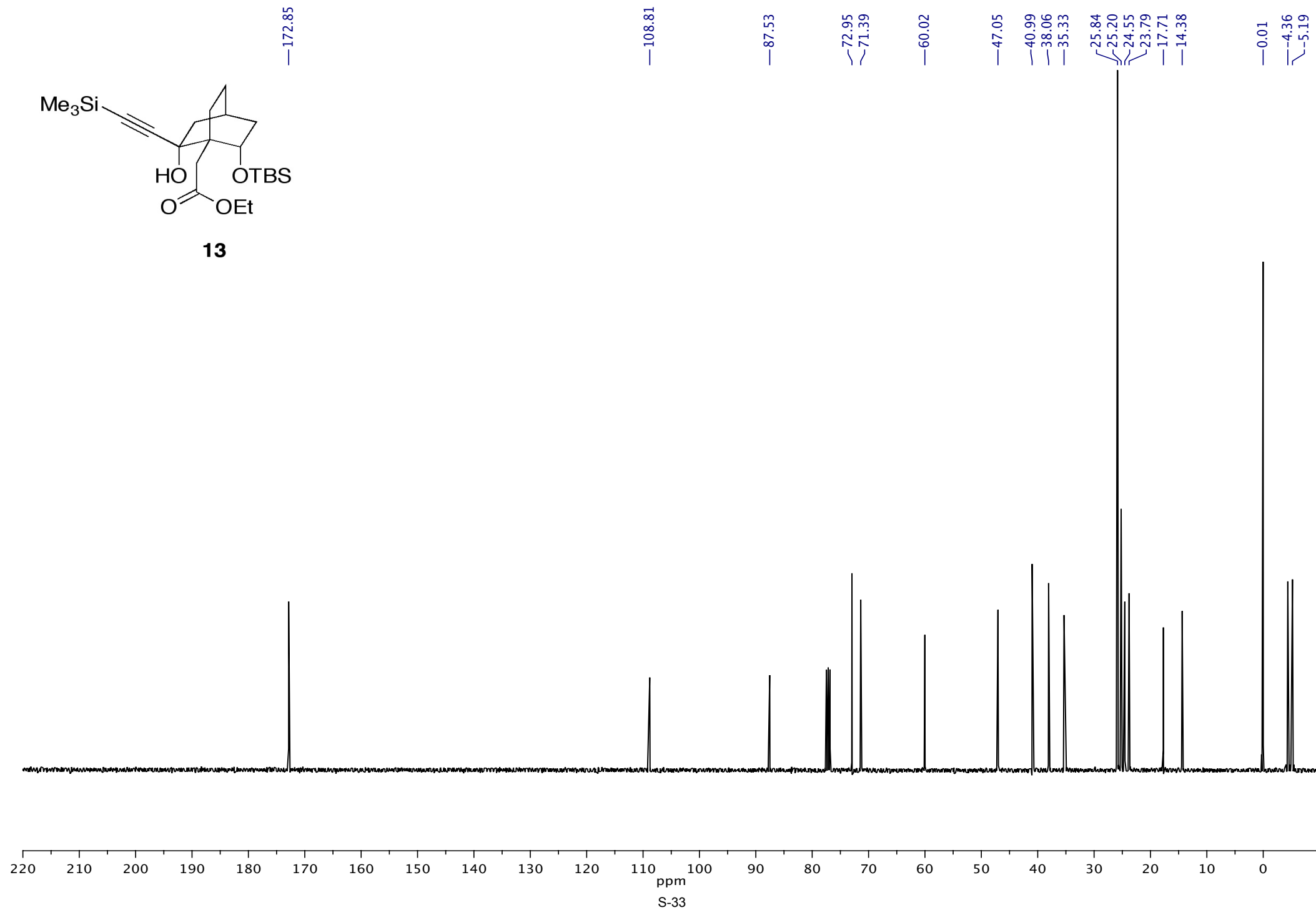
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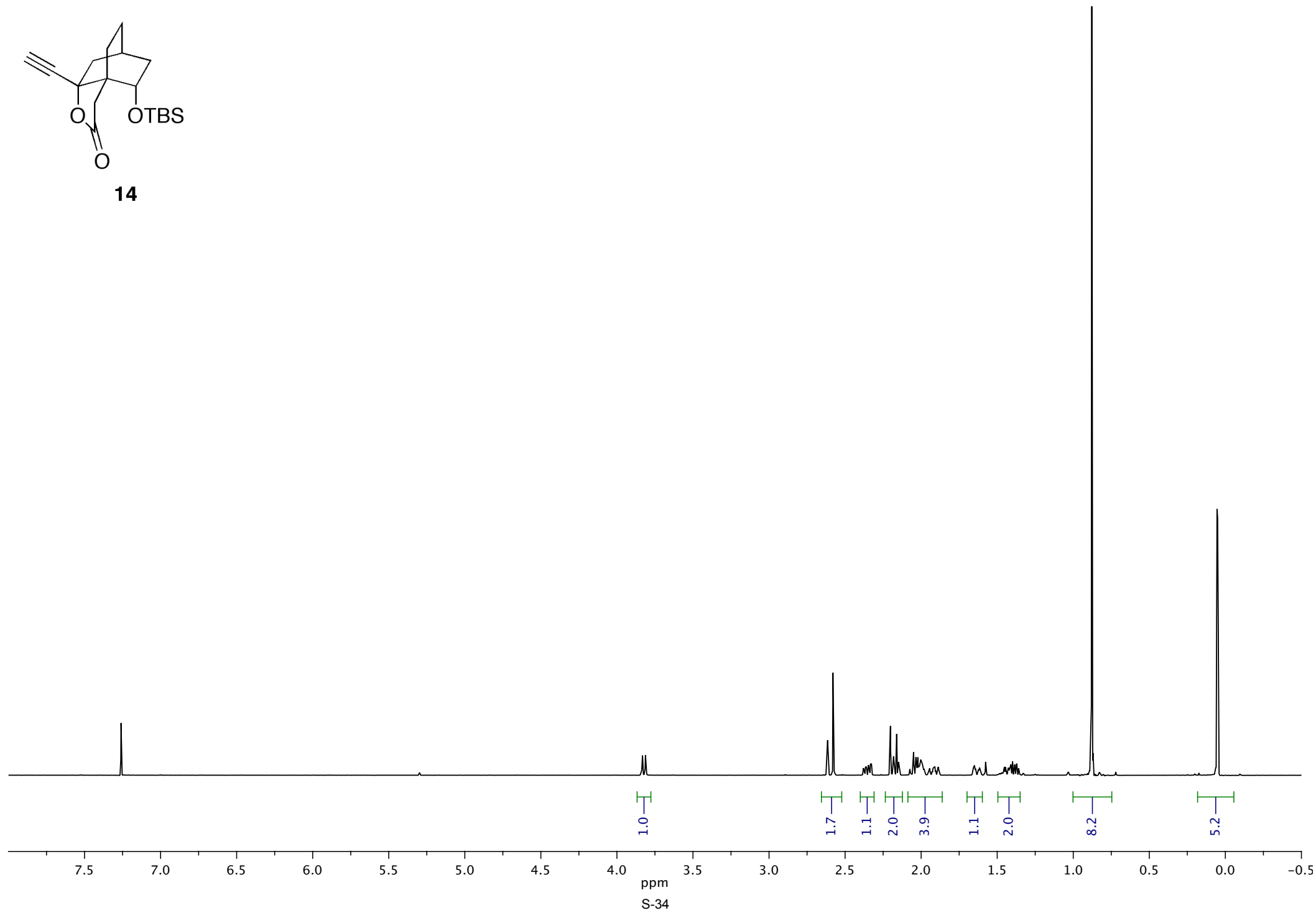
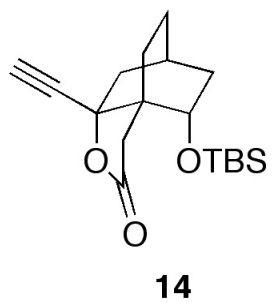


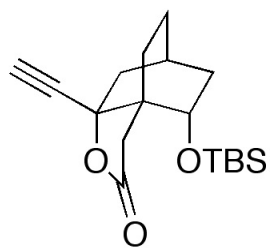




13







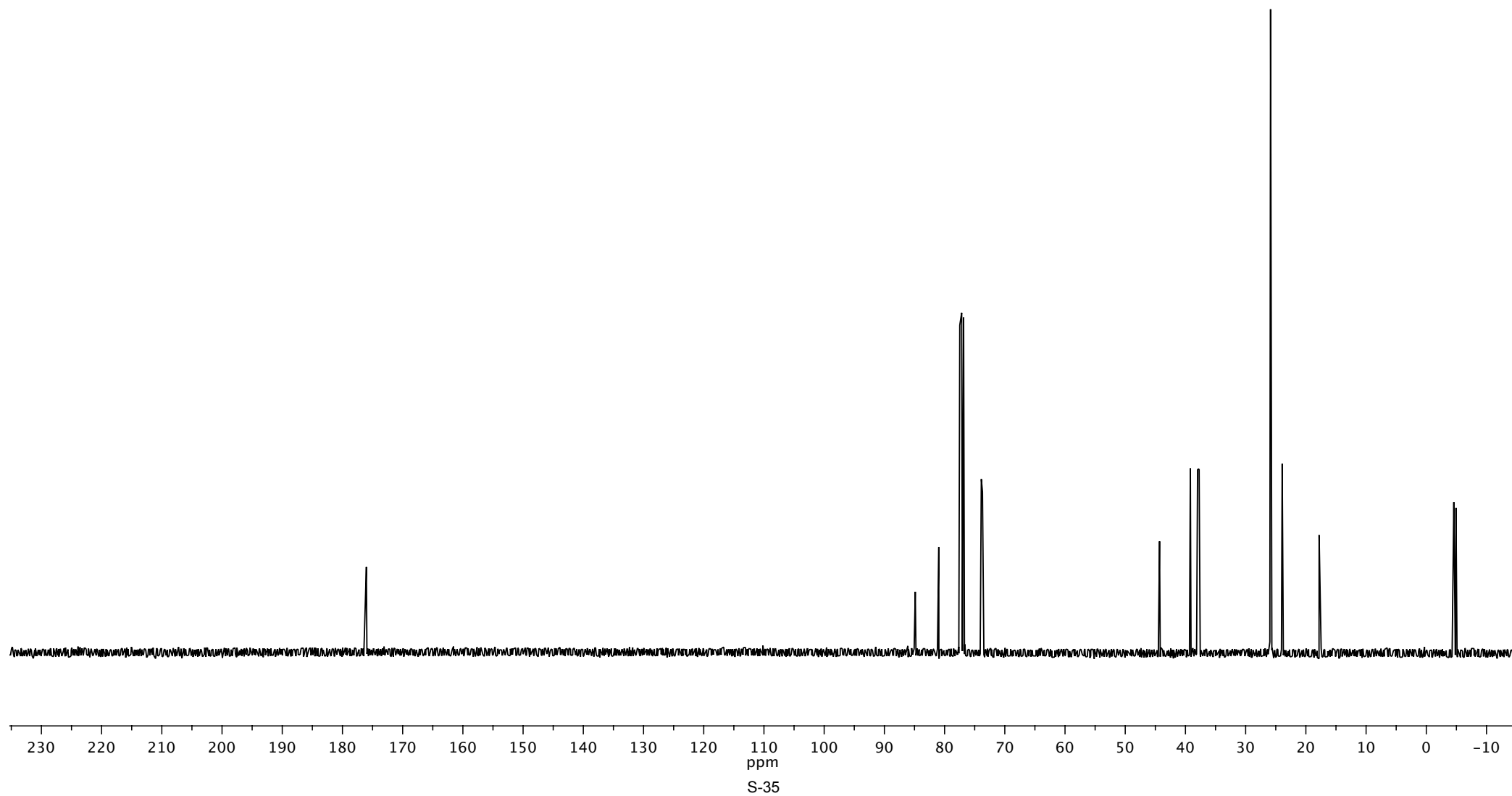
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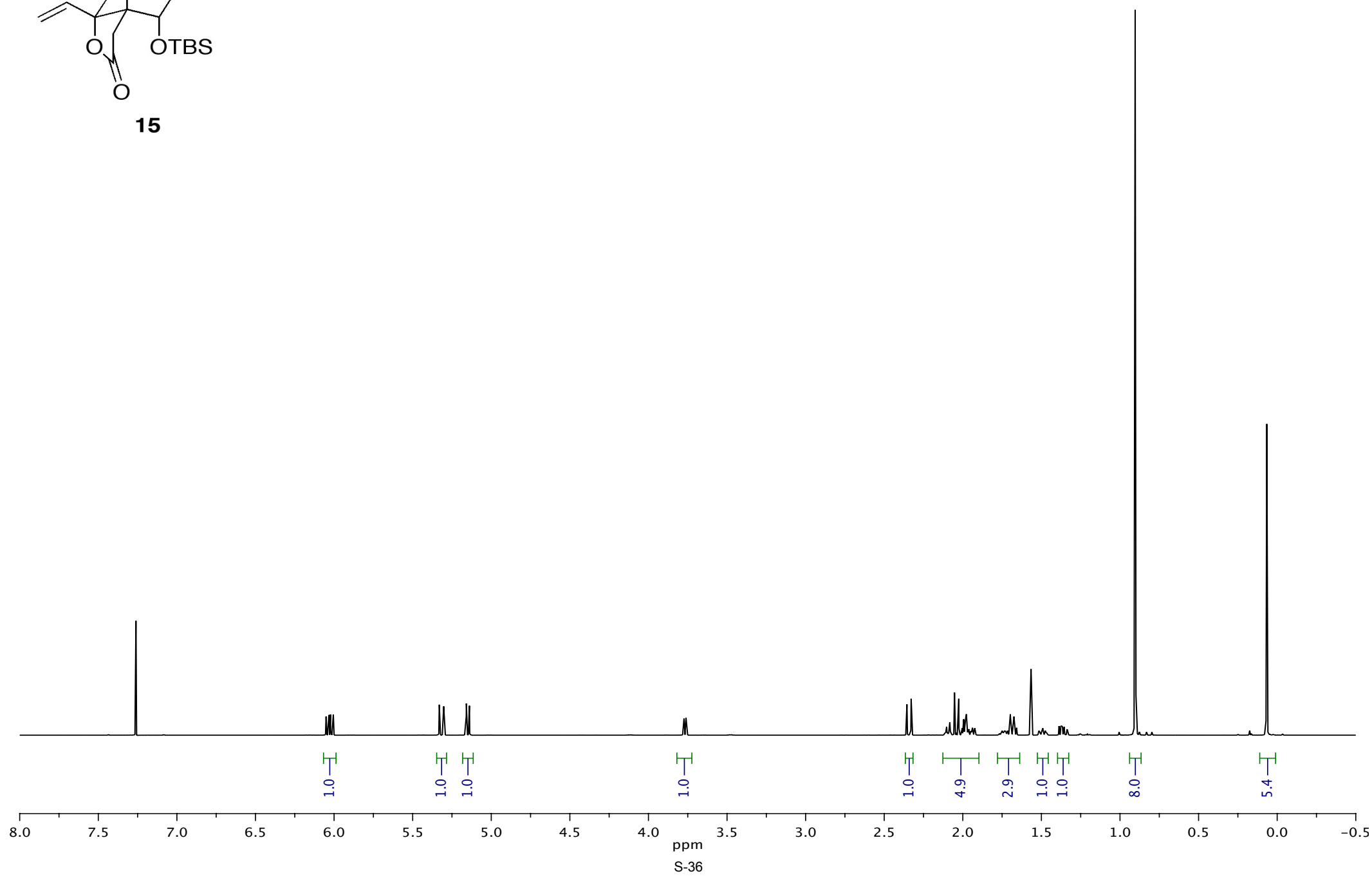
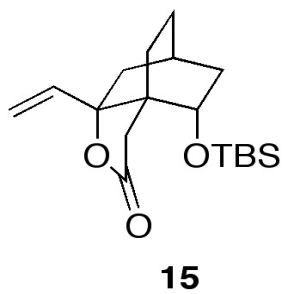
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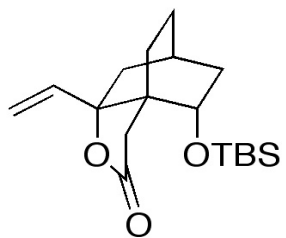
— 84.87
— 80.96
73.90
73.71

— 44.30
37.99
37.73
25.93
25.86
25.69
23.93
— 17.80

— 4.57
— 4.93







15

— 176.95

— 140.54

— 114.34

— 85.67

— 74.58

— 43.36

— 40.23

— 35.63

— 25.92

— 25.89

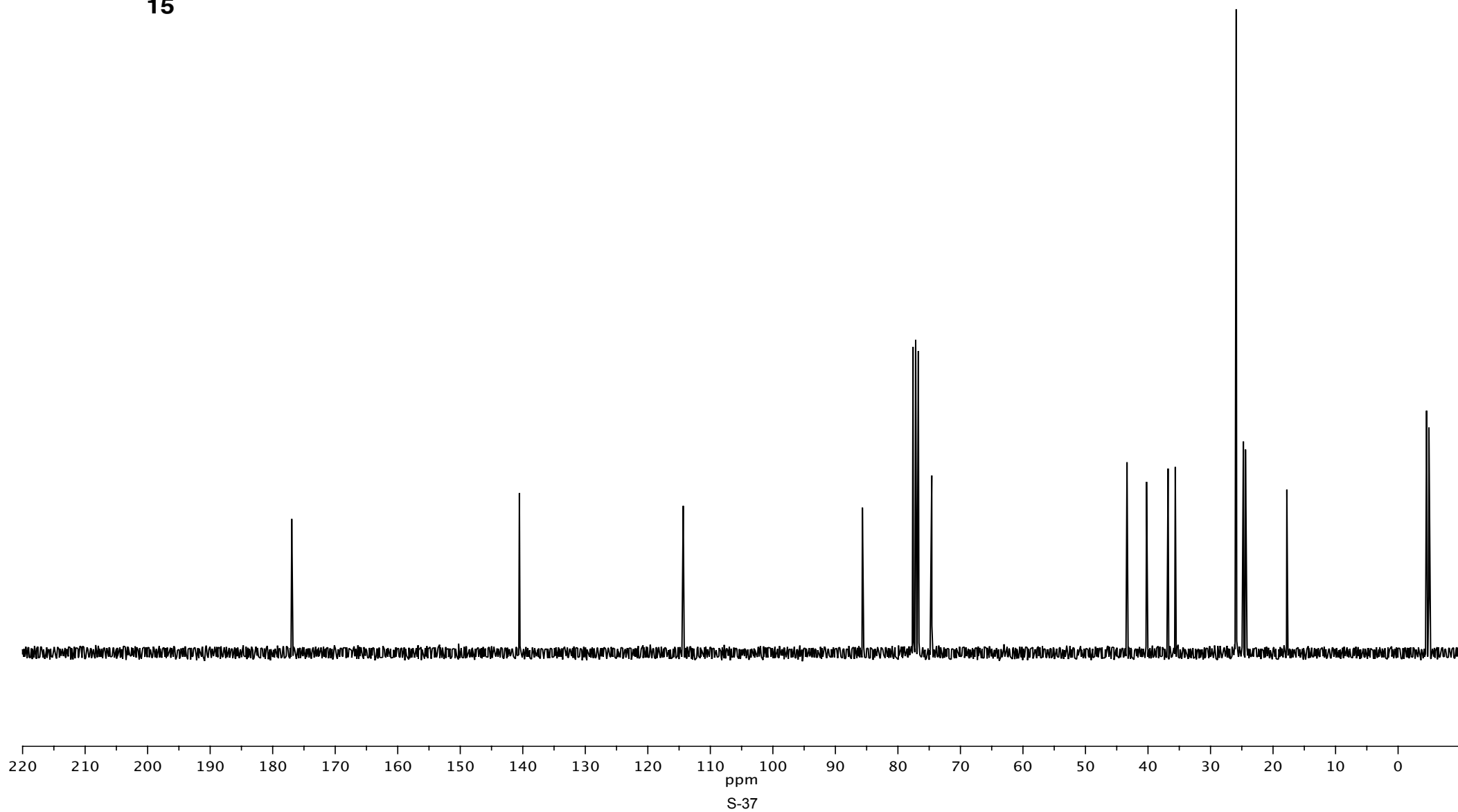
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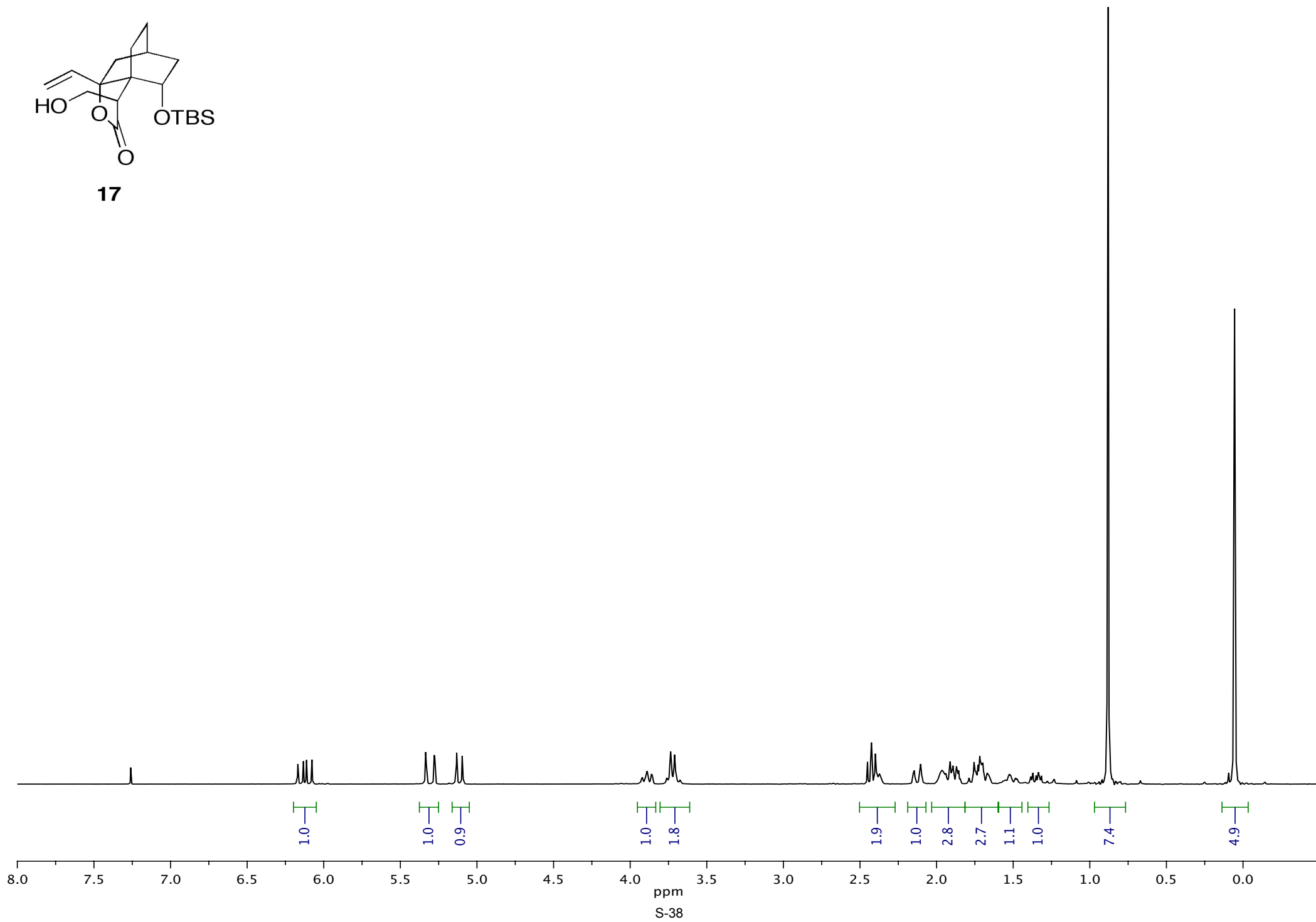
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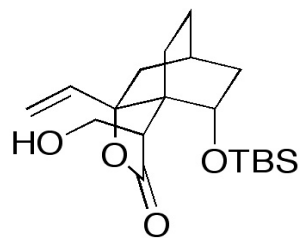
— 17.80

— 4.55

— 4.93







17

—178.61

—142.84

—114.53

—86.01

—76.10

—61.34

—50.09

—44.87

—39.84

—36.59

—25.81

—25.47

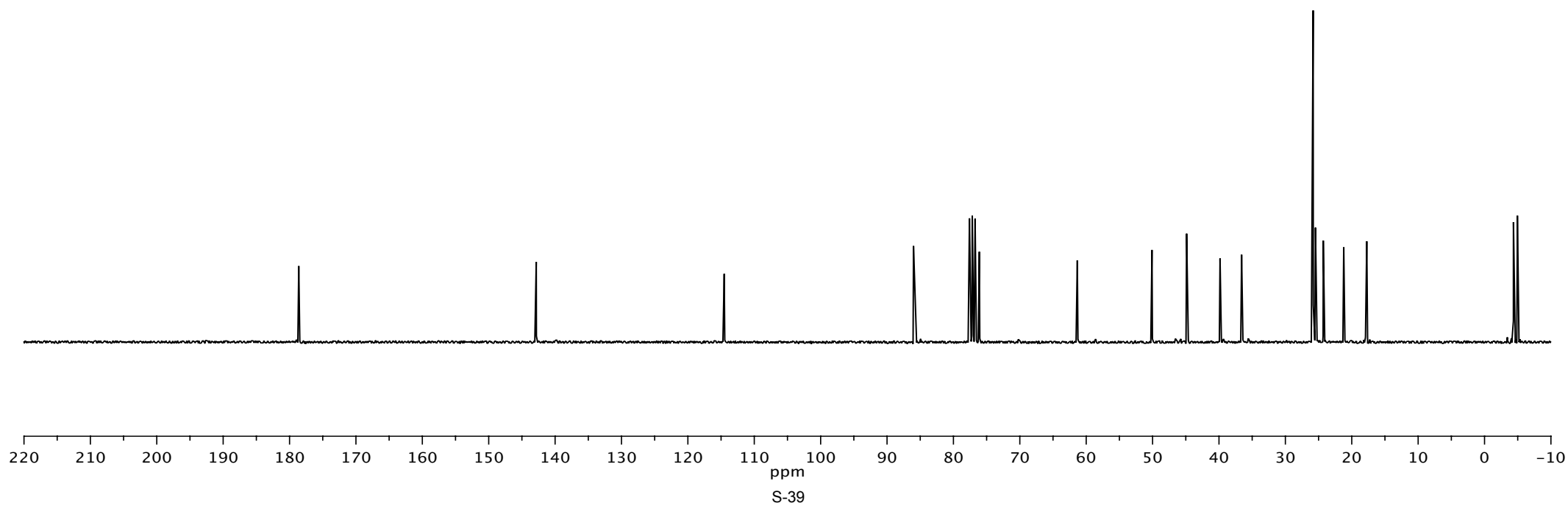
—24.29

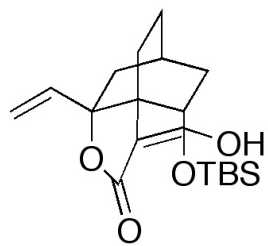
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—17.74

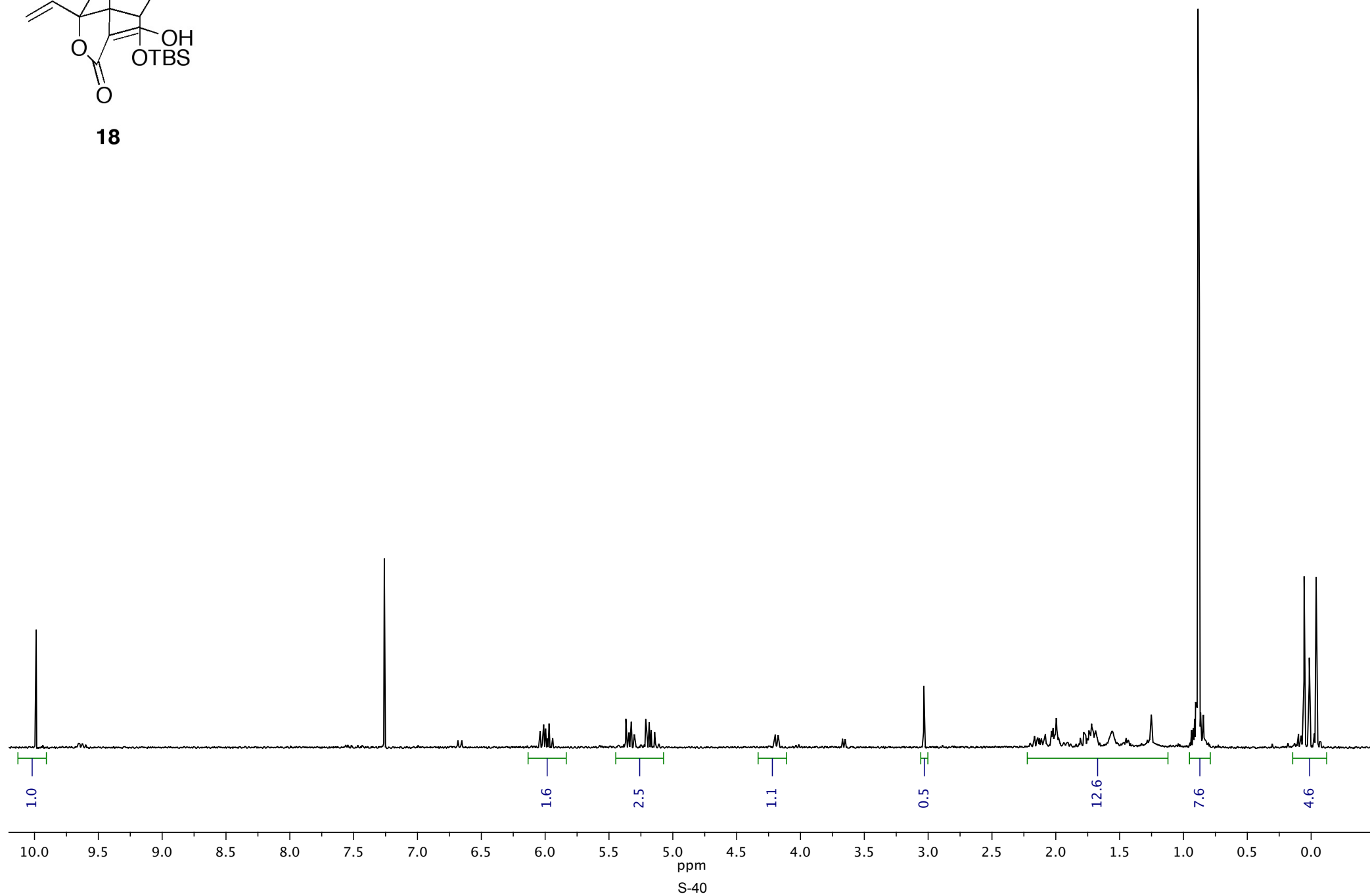
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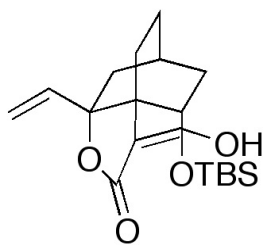
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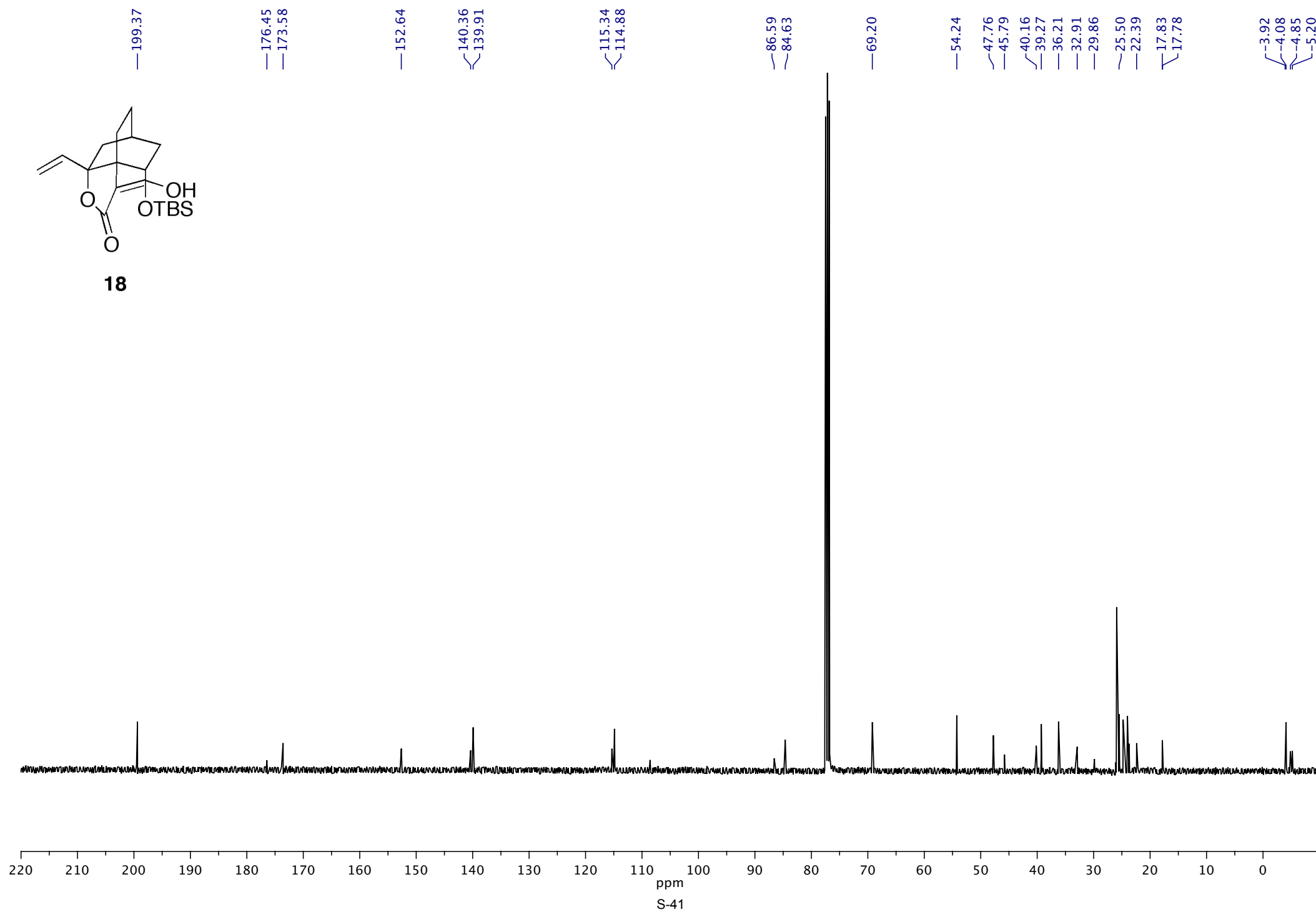


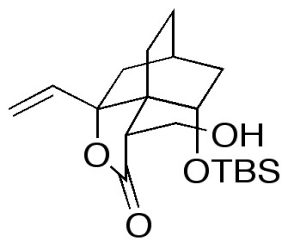
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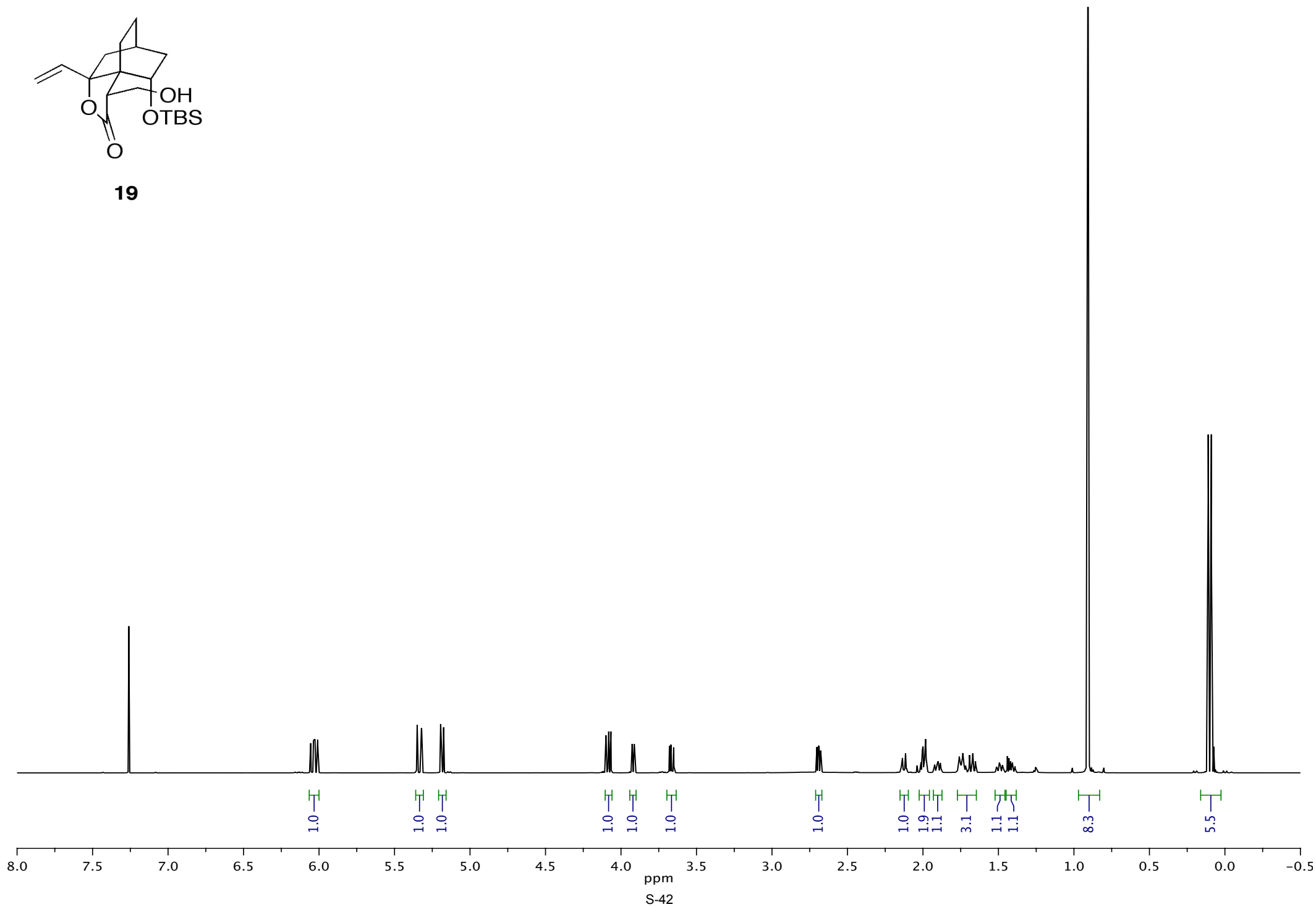


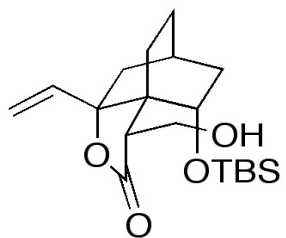
18





19





19

—179.11

—139.76

—114.78

—85.00

—70.32

—58.67

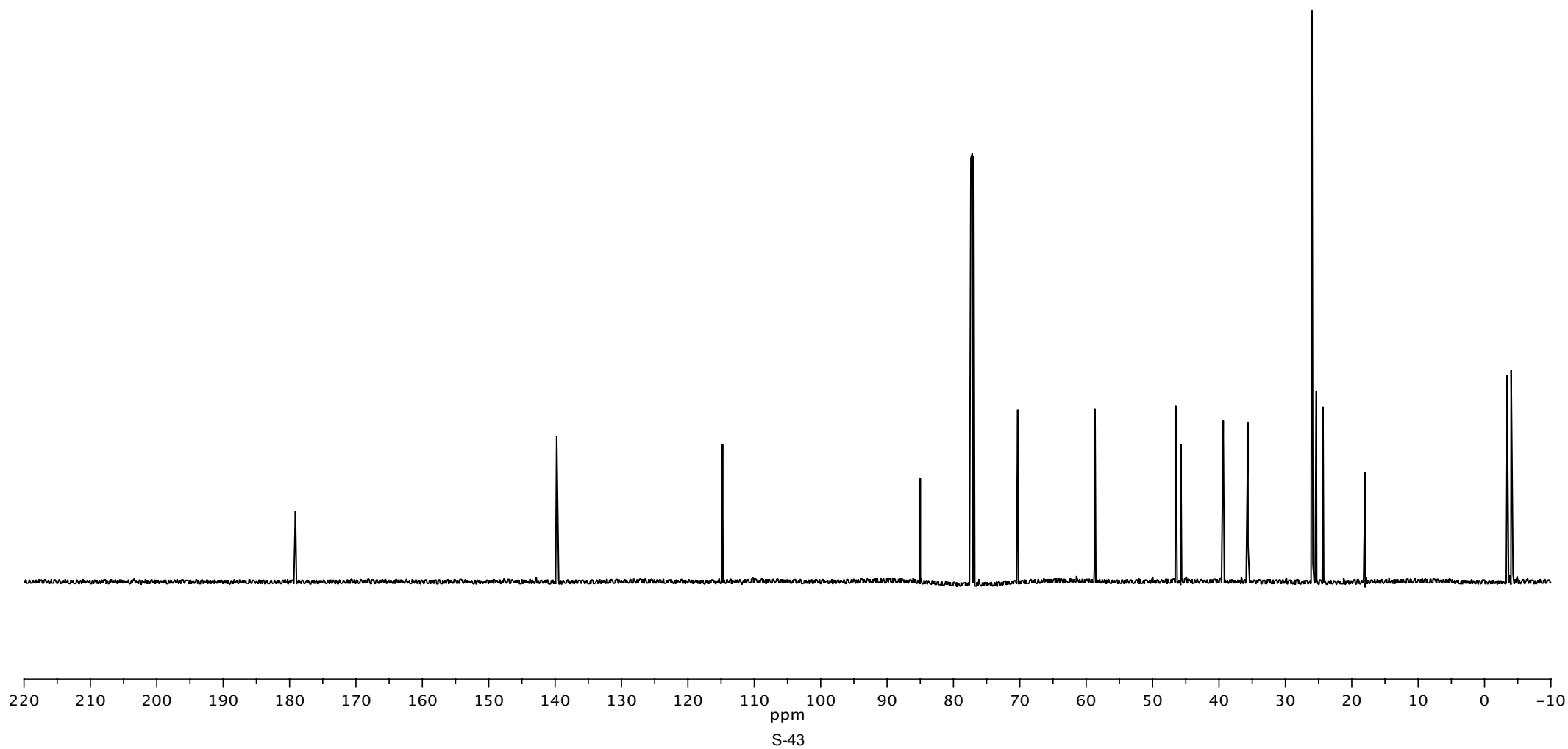
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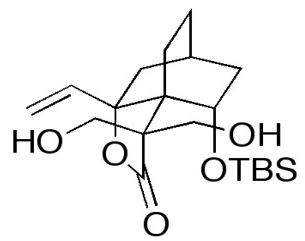
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—35.63

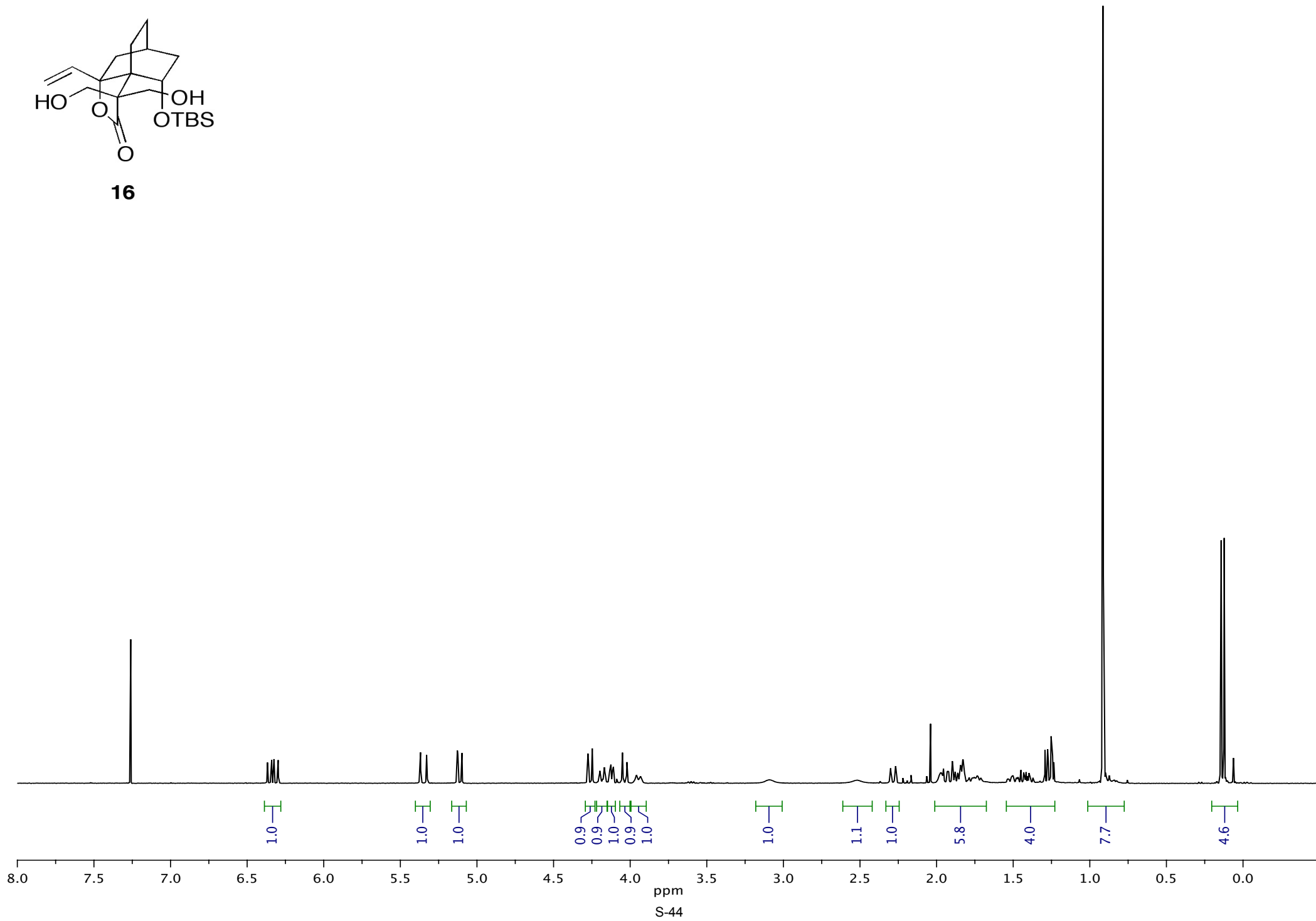
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—25.34
—24.33
—24.18
—17.99

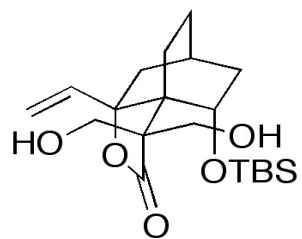
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—4.01



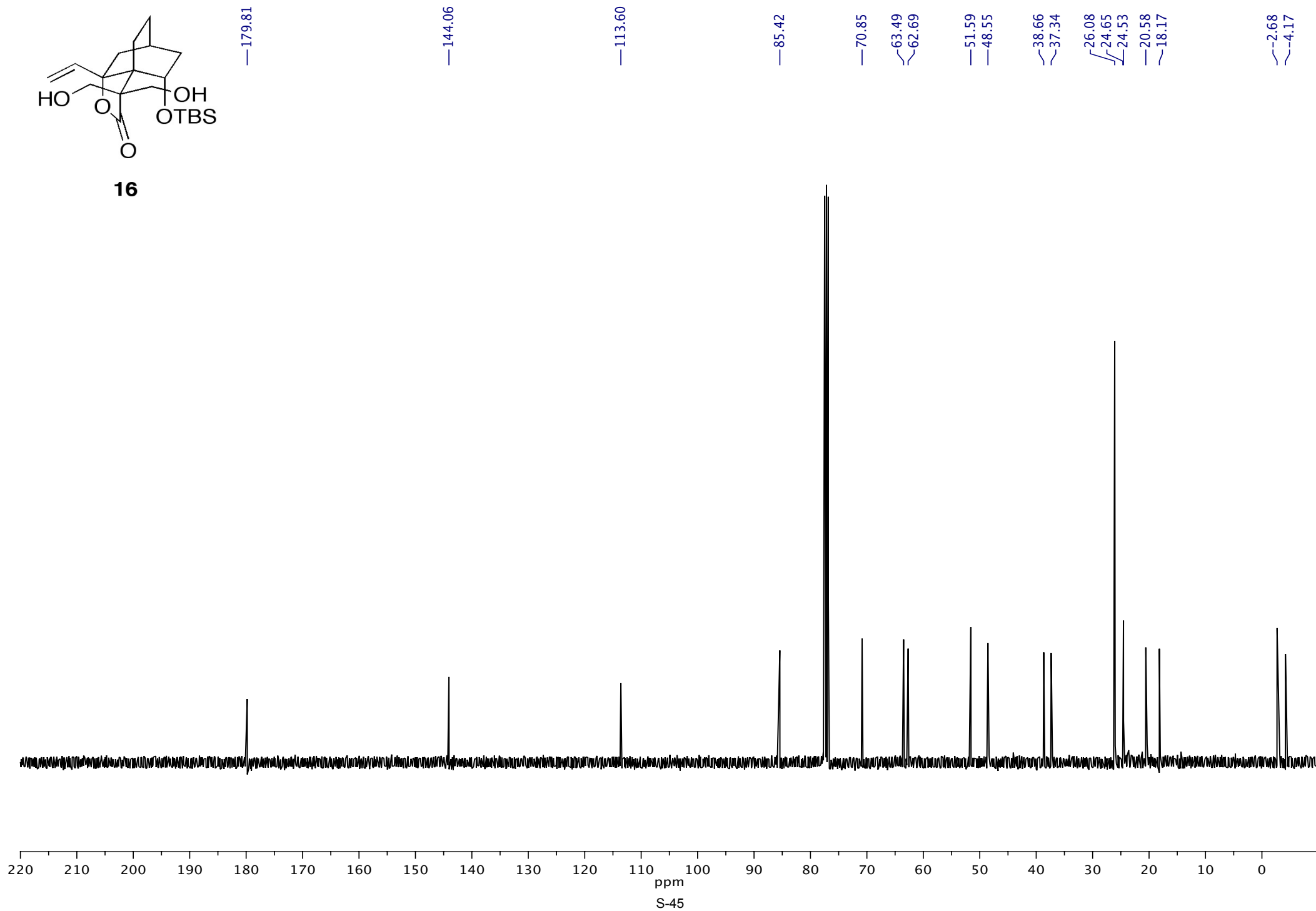


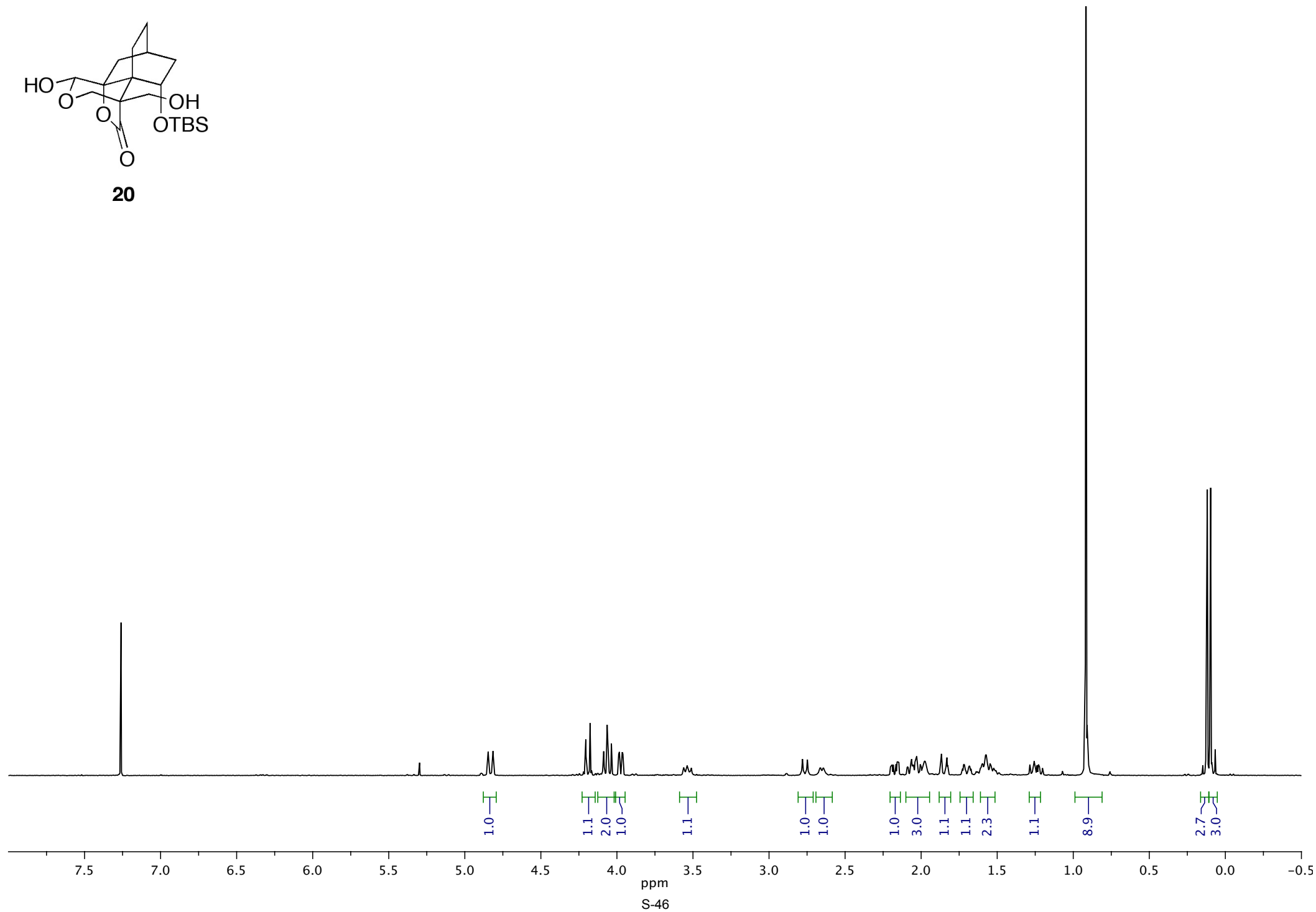
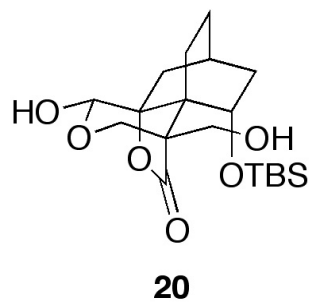
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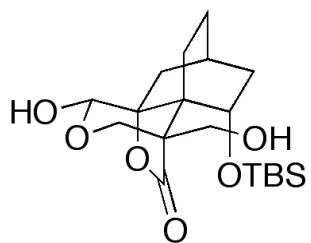




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20

