

Supporting Information

Total Synthesis of the *Cephalotaxus* Norditerpenoids (\pm)-Cephanolides A–D

Maximilian Haider, Goh Sennari, Alina Eggert, Richmond Sarpong*

Department of Chemistry, University of California, Berkeley, CA 94720, United States

Corresponding Author

*rsarpong@berkeley.edu (R.S.).

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1. General Considerations

1-1. Solvents and Reagents

Unless noted below, commercial reagents were purchased from Sigma Aldrich, Acros Organics, Chem-Impex, Combi-blocks, TCI, Chemshuttle and/or Alfa Aesar, and used without additional purification. Solvents were purchased from Fisher Scientific, Acros Organics, Alfa Aesar, and Sigma Aldrich. Tetrahydrofuran (THF), and triethylamine (Et_3N) were sparged with argon and dried by passing through alumina columns using argon in a Glass Contour solvent purification system. Dichloromethane (DCM) was freshly distilled over calcium hydride under N_2 atmosphere prior to each use. Toluene (PhMe) was distilled over calcium hydride under N_2 atmosphere, degassed *via* freeze-pump-thaw (3 cycles), and stored over 4 Å molecular sieves in a Schlenk flask under N_2 . 1,4-Dioxane was purchased in AcroSeal bottling (99.5%, anhydrous, stabilized, over 4 Å molecular sieves) and sparged with N_2 prior to use.

1-2. Experimental Procedures

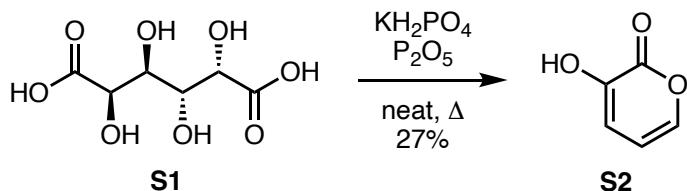
Unless otherwise noted in the experimental procedures, reactions were carried out in flame- or oven-dried glassware under a positive pressure of N_2 in anhydrous solvents using standard Schlenk techniques. Reaction temperatures above room temperature (22–23 °C) were controlled by an IKA® temperature modulator and monitored using liquid-in-glass thermometers. Reaction progress was monitored by thin-layer chromatography (TLC) on Merck Aluminum-backed silica gel coated TLC plates (60 Å, F254 indicator). TLC plates were visualized by exposure to ultraviolet light (254 nm), and/or stained by submersion in aqueous potassium permanganate solution (KMnO_4) or *p*-anisaldehyde stain and were developed by heating with a heat gun. Organic solutions were concentrated under reduced pressure on an IKA RV 3 temperature-controlled rotary evaporator equipped with a dry ice/isopropanol condenser. Flash column chromatography was performed with either glass columns using Silicycle silica gel (40–63 µm particle size) or with a Yamazen Smart Flash EPCLC W-Prep 2XY (dual channel) automated flash chromatography system on prefilled, premium, universal columns using ACS grade solvents. All yields refer to chromatographically and spectroscopically (^1H and ^{13}C NMR) pure material.

1-3. Analytical Instrumentation

^1H NMR and ^{13}C NMR data were recorded on Bruker AVQ-400, AVB-400, DRX-500, AV-600 and AV-700 spectrometers using CDCl_3 or CD_3OD as solvents, typically at 20–23 °C. Chemical shifts (δ) are reported in ppm relative to the residual solvent signal (δ 7.26 for ^1H NMR, δ 77.16 for ^{13}C NMR in CDCl_3 and δ 3.31 for ^1H NMR, δ 49.00 for ^{13}C NMR in CD_3OD). Data for ^1H and ^{13}C spectroscopy are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent), coupling constant (Hz), integration. Melting points were determined using a MEL-TEMP™ apparatus and are uncorrected. High-resolution mass spectra (HRMS) were obtained from the Mass Spectral Facility at the University of California, Berkeley, on a Finnigan/Thermo LTQ-FT instrument (ESI). Data acquisition and processing were performed using the XcaliburTM software.

2. Experimental Procedures and Characterization Data

3-Hydroxy pyranone S2



3-Hydroxy pyranone **S2** was prepared according to a literature procedure.¹

Mucic acid (**S1**) (100 g, 480 mmol, 1 equiv) was thoroughly mixed with KH₂PO₄ (100 g, 730 mmol, 1.5 equiv) and P₂O₅ (60 g, 210 mmol, 0.4 equiv) and ground in a mortar before transferring the heterogenous mixture into a 500 mL one-necked round-bottomed flask. A three-necked 500 mL round-bottomed flask was connected using a U-shaped glass tube. To the three-necked flask, an open reflux condenser was attached and the residual joint was sealed with a glass stopper. The three-necked 500 mL round-bottomed flask was immersed into a Dewar flask filled with dry ice (**Note: only solid dry ice was used to avoid flammable convection liquids**). The mixture in the single-necked round-bottomed flask was carefully pyrolyzed with a bunsen flame (by heating from top to bottom) resulting in yellow steam collecting in the condensation flask. After the evolution of yellow steam had ceased (typically 1 h), the apparatus was left to cool to room temperature, before the brown/yellow solid residue in the one-necked 500 mL flask was dissolved in 500 mL of Et₂O and the acidity adjusted to pH ~6 (as judged using pH-paper) with 1 M KOH. The resulting solution was subjected to continuous liquid/liquid extraction using a Kutscher-Steudl apparatus (containing 1000 mL of Et₂O in the extraction flask) for 24 h. After this time, the ethereal solution was dried with MgSO₄, filtered and the product **S2** was obtained after evaporation of the solvent (14.7g, 131 mmol, 27% yield) as a yellow solid.

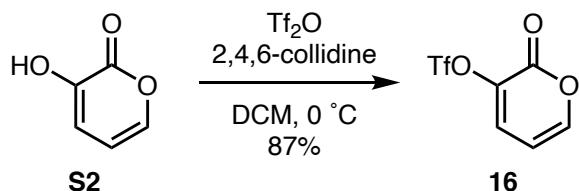
Rf-value: 0.22 (PhMe:EtOAc = 5:1; KMnO₄)

¹H NMR (400 MHz, CDCl₃): δ 7.15 (dd, *J* = 5.2, 1.7 Hz, 1H), 6.68 (dd, *J* = 7.1, 1.7 Hz, 1H), 6.51 (br-s, 1H), 6.21 (dd, *J* = 7.1, 5.2 Hz, 1H).

*NMR data were identical to those reported in the literature.

1) Profitt, J. A.; Jones, T.; Watt, D. S. *Synth. Comm.* **1975**, 5, 457–460.

Pyranone 3-triflate **16**



Pyranone 3-triflate **16** was prepared according to a literature procedure.²

3-Hydroxypyranone **S2** (10 g, 89.2 mmol) was dissolved in 250 mL of dry DCM and the resulting solution was cooled to 0°C before 2,4,6-collidine (13 mL, 98.1 mmol, 1.1 equiv) was added, followed by the dropwise addition of Tf_2O (15.8 mL, 93.7 mmol, 1.05 equiv). After full consumption of the starting material (as judged by TLC analysis; 50 min), the reactives in the reaction mixture were quenched with 250 mL of 2 M HCl and the resulting solution was extracted with DCM (3×200 mL), washed once with 2 M HCl (500 mL) and once with brine (500 mL) before being dried over Na_2SO_4 , filtered to provide a filtrate from which the volatiles were removed by rotary evaporation. The resulting dark blue solid concentrate was purified by passing it through a short plug of SiO_2 with 100% PhMe (2 L). Evaporation of the solvent furnished pyranone 3-triflate **16** (19.2 g, 78.6 mmol, 87% yield) as a yellow solid.

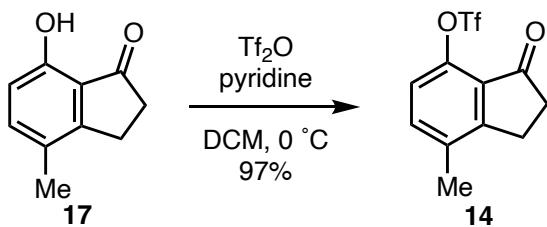
Rf-value: 0.41 (PhMe:EtOAc = 5:1; KMnO_4)

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.52 (dd, $J = 5.1, 1.8$ Hz, 1H), 7.36 (dd, $J = 7.2, 1.8$ Hz, 1H), 6.32 (dd, $J = 7.2, 5.2$ Hz, 1H).

*NMR data were identical to those reported in the literature.

2) Frébault, F.; Oliveira, M. T.; Wöstefeld, E.; Maulide, N. *J. Org. Chem.* **2010**, *75*, 7962–7965.

Indanone 7-triflate 14



In a 1 L flask under N_2 atmosphere, 7-hydroxy-4-methyl-1-indanone **17** (10 g, 61.7 mmol, 1 equiv) was dissolved in 300 mL of dry DCM and cooled to $0\text{ }^\circ\text{C}$. Pyridine (11.6 mL, 142 mmol, 2.3 equiv) was added followed by the dropwise addition of Tf_2O (11.4 mL, 67.8 mmol, 1.1 equiv). The mixture was stirred at $0\text{ }^\circ\text{C}$ until complete consumption of the starting material (1 h as judged by TLC) and the reactives were quenched by the addition of 300 mL of 2 M HCl. After extraction of the resulting mixture with DCM (3×100 mL), the combined organic phase was washed once with 2 M HCl (100 mL) and once with brine (50 mL) before drying over Na_2SO_4 , filtered, and concentrated by rotary evaporation. The crude black solid residue was purified by passing through a short silica plug eluting with PhMe. After concentration of the collected fractions, indanone 7-triflate **14** (17.5 g, 59.5 mmol, 97% yield) was obtained as a slightly yellow solid.

Rf-value: 0.26 (PhMe:EtOAc = 5:1; *p*-anisaldehyde)

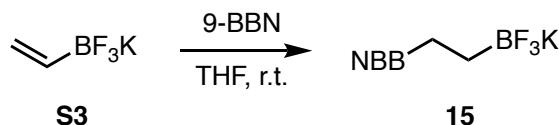
HRMS (m/z): ESI [M] calculated for $\text{C}_{11}\text{H}_9\text{O}_4\text{SF}_3$ $[\text{M}]^+$: 294.0174, found $[\text{M}]^+$: 294.0175.

Melting Point: 83–84 °C

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ 7.44 (d, $J = 8.1$ Hz, 1H), 7.09 (d, $J = 8.1$ Hz, 1H), 3.08 – 3.02 (m, 2H), 2.80 – 2.74 (m, 2H), 2.38 (s, 3H).

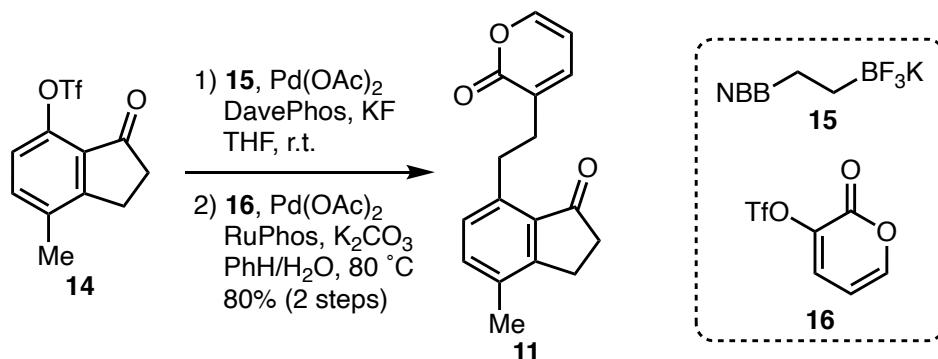
$^{13}\text{C NMR}$ (101 MHz, CDCl_3): δ 202.7, 156.4, 143.3, 136.9, 136.2, 128.7, 120.2, 118.8 (q, $J = 320.7$ Hz), 36.6, 24.9, 17.6.

Preparation of the borane reagent (**15**)



Potassium vinyltrifluoroborate (**S3**) (1.47 g, 11.0 mmol, 1.1 equiv) was weighed into a 25 mL μ wave-vial and placed under N_2 atmosphere. The vial was evacuated and backfilled with N_2 three times before 9-BBN (0.5 M solution in THF, 22.0 mL, 11.0 mmol, 1.1 equiv) was added. The mixture was stirred at room temperature for 3 h. This mixture was transferred to the coupling reaction *via* cannula.

Indanone 7-ethylpyranone **11**



Indanone 7-triflate **14** (2.94 g, 10.0 mmol, 1 equiv) was weighed into a 100 mL Schlenk flask and $Pd(OAc)_2$ (44.9 mg, 200 μ mol, 2 mol%), DavePhos (157 mg, 400 μ mol, 4 mol%) and KF (1.92 g, 33.0 mmol, 3.3 equiv) were added sequentially. The flask was placed under N_2 atmosphere following evacuation and backfilling with N_2 (x 3) before 22 mL of dry THF was added. The resulting orange suspension was subjected to three freeze-pump-thaw cycles. The 0.5 M solution of previously prepared borane **15** (see above) was added *via* a transfer-canula, at which point the solution turned dark brown. The mixture was stirred under N_2 atmosphere for 48 h resulting in a beige suspension. 500 mL of Et_2O was added and the suspension was stirred for an additional 15 min before the solids (**18** and KF) were removed by vacuum filtration. The beige solid residue was washed twice with Et_2O (100 mL) and dried under vacuum, yielding 7.80 g of a beige solid mixture and KF. This solid mixture was used in the next reaction without further purification.

The crude solid mixture was added to a 250 mL pressure flask containing pyranone 3-triflate **16** (4.88 g, 20.0 mmol, 2 equiv), $Pd(OAc)_2$ (112 mg, 500 μ mol, 5 mol%), RuPhos (560 mg, 1.20 mmol, 12 mol%) and K_2CO_3 (4.15 g, 30.0 mmol, 3 equiv) and $PhMe/H_2O$ (5:1 v/v, 150 mL) mixture was added. The pressure tube was sealed under N_2 atmosphere and immersed in an 80 °C preheated oil bath. After 48 h, the resulting mixture was allowed to cool to room temperature and 125 mL of water was added, followed by extraction with $EtOAc$ (4 x 150 mL). The combined organic phase was washed with brine

(100 mL), dried over MgSO₄ and concentrated by rotary evaporation. The crude concentrate was purified by flash column chromatography (PhMe/EtOAc = 12:1 to 10:1) yielding indanone 7-ethylpyranone **11** (2.15 g, 8.01 mmol, 80% yield over 2 steps) as an off-white solid.

Rf-value: 0.28 (PhMe:EtOAc = 5:1; *p*-anisaldehyde)

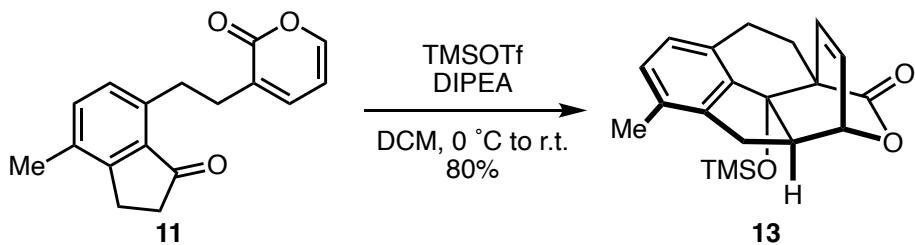
HRMS (m/z): ESI [M] calculated for C₁₇H₁₆O₃+Na [M+Na]⁺: 291.0992, found [M+Na]⁺: 291.0993.

Melting Point: 120–122 °C

¹H NMR (500 MHz, CDCl₃): δ 7.36 (dd, *J* = 5.1, 2.1 Hz, 1H), 7.25 (d, *J* = 7.5, Hz, 1H), 7.14 (app ddt, *J* = 6.5, 2.1, 1.1 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.12 (dd, *J* = 6.5, 5.1 Hz, 1H), 3.27 – 3.21 (m, 2H), 2.98 – 2.93 (m, 2H), 2.73 – 2.67 (m, 2H), 2.67 – 2.63 (m, 2H), 2.29 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 208.2, 163.0, 155.3, 149.4, 139.0, 138.8, 134.8, 133.71, 133.69, 129.8, 128.7, 106.4, 36.8, 31.8, 29.9, 24.4, 17.5.

Pentacyclic olefin 13



Indanone 7-ethylpyranone **11** (3.73 g, 13.9 mmol, 1 equiv) was dissolved in 140 mL of dry DCM. DIPEA (5.34 mL, 30.6 mmol, 2.2 equiv) was added, at which point the mixture turns a deep yellow color. The yellow solution was cooled to 0 °C and TMSOTf (5.28 mL, 29.2 mmol, 2.1 equiv) was added dropwise. Upon completion of addition, the resulting dark red solution was stirred for an additional 5 min at 0 °C before being allowed to warm to room temperature and then stirred for an additional 25 h. After full conversion of the starting material (as judged by TLC), the mixture was cooled to 0 °C and the reagents quenched by dropwise addition of sat. aq. NaHCO₃ solution (50 mL) and extracted with DCM (3 x 150 mL), washed once with brine (50 mL), dried over Na₂SO₄, filtered, and concentrated by rotary evaporation to give a dark red solid residue. The crude product was purified by filtration over a short plug of SiO₂ (eluted with DCM) and after concentration of the eluents, pentacyclic olefin **13** (3.77 g, 11.1 mmol, 80% yield) was obtained as a yellow solid (**Note: the product is somewhat unstable under flash chromatography conditions, resulting in 50 to 60% yields of pure 13 as a white solid.**). A simple SiO₂-plug filtration delivers essentially pure product (compare attached ¹H-NMR in Section 4).

Rf-value: 0.65 (PhMe:EtOAc = 5:1; *p*-anisaldehyde)

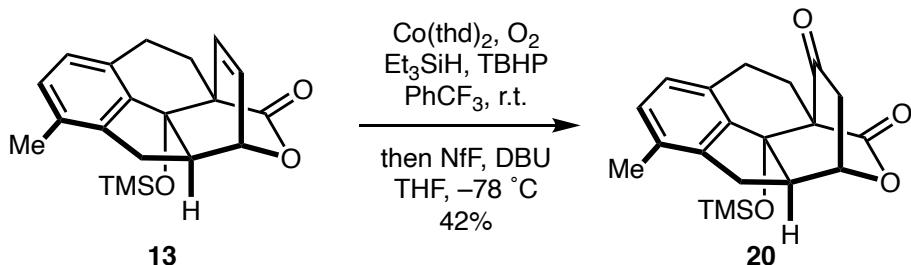
HRMS (m/z): ESI [M] calculated for C₂₀H₂₄O₃Si+Na [M+Na]⁺: 363.1387, found [M+Na]⁺: 363.1388.

Melting Point: 139–141 °C

¹H NMR (400 MHz, CDCl₃): δ 7.00 (d, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 7.5 Hz, 1H), 6.07 (dd, *J* = 7.6, 4.8 Hz, 1H), 5.48 (dd, *J* = 7.6, 2.0 Hz, 1H), 5.22 (app td, *J* = 4.9, 2.0 Hz, 1H), 3.32 (dd, *J* = 17.2, 9.2 Hz, 1H), 3.17 – 3.06 (m, 2H), 2.87 (ddd, *J* = 14.7, 10.8, 4.5 Hz, 1H), 2.76 (ddd, *J* = 16.9, 9.5, 4.5 Hz, 1H), 2.17 (s, 3H), 2.14 – 1.99 (m, 2H), –0.13 (s, 9H).

¹³C NMR (101 MHz, CDCl₃): δ 173.3, 142.1, 140.8, 137.2, 132.5, 131.4, 130.9, 128.1, 126.4, 85.4, 77.3, 54.5, 50.4, 32.4, 23.4, 20.7, 18.3, 1.0 (3C).

Pentacyclic ketone 20



Pentacyclic olefin **13** (1.35 g, 3.97 mmol, 1 equiv) and $\text{Co}(\text{thd})_2$ (169 mg, 397 μmol , 10 mol%) were placed in a 250 mL one-necked flask equipped with a septum and the flask was placed under O_2 atmosphere. 40 mL of an O_2 -saturated solution of PhCF_3 (sparged with O_2 for at least 1 h) was added, followed by the sequential addition of Et_3SiH (1.39 mL, 8.73 mmol, 2.2 equiv) and TBHP (5–6 M in decane; 40 μL , 200 μmol , 5 mol%). Upon addition of TBHP , the purple mixture instantly turned green and stirring was continued for 16 h at room temperature. The solution was diluted with 200 mL of dry THF and NfF (860 μL , 4.76 mmol, 1.2 equiv) were added and the solution stirred continued for 10 min before being cooled to -78°C . DBU (590 μL , 3.97 mmol, 1 equiv) was added dropwise (**Note: The resulting product, ketone 20, is unstable in the presence of DBU**) and the mixture was stirred at -78°C for 25 min with constant TLC-monitoring. Upon complete consumption of the intermediate TES-peroxide (as judged by TLC), the solution was quenched by the addition of sat. aq. NaHCO_3 solution (100 mL) and extracted with EtOAc (3 x 250 mL), washed with brine (500 mL), dried over MgSO_4 , filtered and the solvents were removed by rotary evaporation. Flash column chromatography (hexanes/EtOAc = 20:1 to 4:1) furnished pentacyclic ketone **20** (594 mg, 1.67 mmol, 42% yield) as a white solid.

Rf-value: 0.40 (PhMe:EtOAc = 5:1; *p*-anisaldehyde)

HRMS (m/z): ESI [M] calculated for $\text{C}_{20}\text{H}_{24}\text{O}_4\text{Si}+\text{Na}^+$: 379.1336, found $[\text{M}+\text{Na}]^+$: 379.1336.

Melting Point: 132–134 $^\circ\text{C}$

$^1\text{H NMR}$ (700 MHz, CDCl_3): δ 7.05 (d, J = 7.5 Hz, 1H), 6.91 (d, J = 7.5 Hz, 1H), 5.07 (ddd, J = 5.3, 4.3, 1.2 Hz, 1H), 3.48 (dd, J = 17.5, 9.1 Hz, 1H), 3.26 (ddt, J = 9.3, 5.2, 2.1 Hz, 1H), 2.97 – 2.91 (m, 1H), 2.85 (ddd, J = 16.8, 9.6, 4.3 Hz, 1H), 2.50 (ddd, J = 13.6, 10.9, 4.4 Hz, 1H), 2.45 – 2.38 (m, 3H), 2.20 (s, 3H), 1.94 (dd, J = 19.4, 1.2 Hz, 1H), –0.11 (s, 9H).

$^{13}\text{C NMR}$ (176 MHz, CDCl_3): δ 199.8, 167.9, 139.5, 137.9, 134.2, 132.3, 131.9, 127.3, 84.1, 75.7, 68.7, 48.8, 35.4, 31.5, 23.4, 18.4, 15.3, 1.0 (3C).

Preparation of the reagents for olefination

The following reagents were prepared according to the reported procedures with slight modifications.^{3,4}

1 M solution of Ti(O*i*-Pr)₂Cl₂:

In a 25 mL microwave vial under N₂ atmosphere, TiCl₄ (1.64 mL, 15.0 mmol, 1 equiv) and 15 mL of dry DCM were combined. Subsequently, Ti(O*i*-Pr)₄ (4.26 mL, 15.0 mmol, 1 equiv) was added dropwise. The mixture was stirred for 30 min at room temperature. The colorless homogenous solution was stored in a -20 °C freezer. (Note: Ti(O*i*-Pr)₂Cl₂ crystallizes in the freezer and should be warmed to ambient temperature before use).

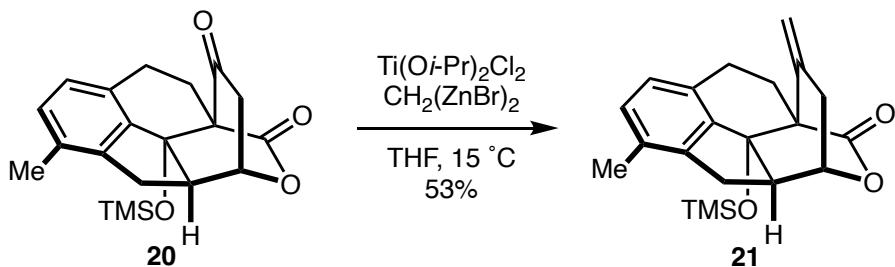
0.5 M Bis(bromozincio)methane CH₂(ZnBr)₂:

In a 25 mL microwave vial under N₂ atmosphere, Zn dust (3.27 g, 50.0 mmol, 2.5 equiv) and PbCl₂ (5.6 mg, 20.0 µmol, 0.1 mol%) were suspended in 4 mL of dry THF. TMSCl (130 µL, 1.00 mmol, 2 mol% per mol of Zn) was added *via* microliter syringe followed by 140 µL of dibromomethane. The Zn was activated by sonication in an ultrasonic bath at 25 °C for 30 min. Then 16 mL of dry THF was added, followed by the dropwise addition of dibromomethane (1.40 mL, 20.0 mmol, 1 equiv). Sonication of this mixture at 25 °C for 1 h provided the active reagent as a grey/white suspension. The reagent can be stored in a -20 °C freezer for at least 4 weeks without losing activity.

3) Barnych, B.; Vatèle, J. M. *Synlett* **2011**, 2, 1912–1916.

4) Matsubara, S.; Oshima, K. *Proc. Jpn. Acad., Ser. B, Phys. Biol. Sci.* **2003**, 79, 71–77.

Exo-olefin 21



Pentacyclic ketone **20** (640.7 mg, 1.80 mmol, 1 equiv) was dissolved in 36 mL of dry THF under N_2 atmosphere and the resulting solution was cooled to 15°C . A 1.0 M $\text{Ti}(\text{O}-\text{i-Pr})_2\text{Cl}_2$ solution in DCM (4.49 mL, 4.49 mmol, 2.5 equiv; prepared as described above) was added, followed by an assumed 0.5 M solution of $\text{CH}_2(\text{ZnBr})_2$ in THF (10.8 mL, 5.39 mmol, 3 equiv; prepared as described above) were added dropwise *via* syringe pump (1 mL/min). The dispersion assumes a chocolate brown color and bubbles slightly upon $\text{CH}_2(\text{ZnBr})_2$ addition. After 4.5 h, the excess Zn species was precipitated by dilution with 250 mL of Et_2O . The solids were removed by filtration over a Celite-plug followed by washing the solid residue with 250 mL of Et_2O . The combined ethereal filtrate was carefully quenched by the addition of ice followed by 2 M HCl (the biphasic mixture should be colorless and transparent). The mixture was extracted with Et_2O (3 x 250 mL) and washed with 2 M HCl (250 mL), H_2O (2 x 250 mL) and brine (250 mL) before being dried over MgSO_4 , filtered and the volatiles evaporated. Column chromatography (PE/EE = 20:1 to 3:1) yielded *exo*-olefin **21** (340.9 mg, 0.96 mmol, 53% yield) as a white solid.

Rf-value: 0.12 (hexanes: EtOAc = 10:1; *p*-anisaldehyde)

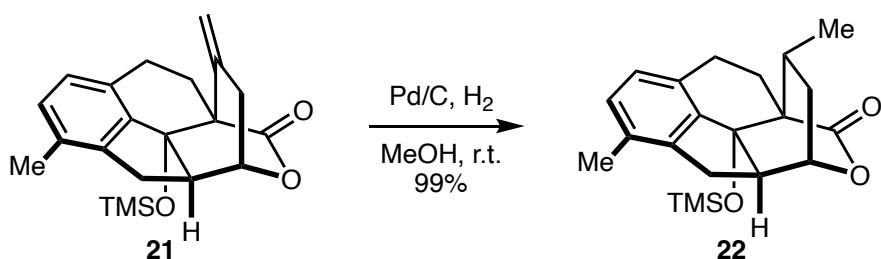
HRMS (m/z): ESI [M] calculated for $\text{C}_{21}\text{H}_{26}\text{O}_3\text{Si}+\text{Na} [\text{M}+\text{Na}]^+$: 377.1543, found $[\text{M}+\text{Na}]^+$: 377.1543.

Melting Point: 120–121 °C

$^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.01 (d, $J = 7.5$ Hz, 1H), 6.84 (d, $J = 7.5$ Hz, 1H), 4.82 (app t, $J = 4.7$ Hz, 1H), 4.67 (app t, $J = 2.5$ Hz, 1H), 4.56 (app t, $J = 2.1$ Hz, 1H), 3.35 (dd, $J = 17.4, 9.3$ Hz, 1H), 3.07 – 2.97 (m, 2H), 2.82 – 2.67 (m, 2H), 2.48 (ddq, $J = 17.8, 4.5, 2.2$ Hz, 1H), 2.40 (dd, $J = 17.4, 2.7$ Hz, 1H), 2.21 (s, 3H), 2.11 (ddd, $J = 13.8, 9.5, 2.2$ Hz, 1H), 2.06 (app d, $J = 17.4$ Hz, 1H), –0.13 (s, 9H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 172.7, 140.1, 139.2, 138.8, 133.4, 131.4, 131.1, 126.4, 112.4, 85.2, 77.3, 55.9, 49.0, 31.2, 28.3, 23.4, 18.4, 17.4, 1.1 (3C).

(exo)-Methyl pentacycle **22**



Exo-olefin **21** (60.0 mg, 0.17 mmol, 1 equiv) was dissolved in 17 mL of HPLC-grade MeOH and purged with H₂ while sonicating for 30 min. Meanwhile, Pd/C (198 mg, 0.19 mmol, 1.1 equiv) was weighed into a 25 mL μ wave-vial and capped with a Biotage μ wave-seal. The vial was placed under H₂ atmosphere by evacuating once and backfilling with H₂. After purging, the MeOH solution was transferred to the vial containing Pd/C using a syringe. H₂ was bubbled through the dispersion for one minute, before stirring under positive H₂-pressure (balloon) was continued for 45 minutes. The Pd/C was removed by filtration through Celite and the residue was washed with DCM/MeOH (10:1, 20 mL). The filtrate was evaporated to yield *(exo)*-methyl pentacycle **22** (59.7 mg, 0.17 mmol, 99% yield) as a white solid.

Rf-value: 0.53 (hexanes:EtOAc = 3:1; *p*-anisaldehyde)

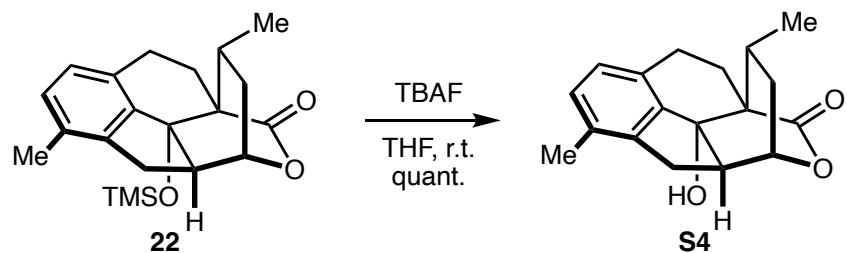
HRMS (m/z): ESI [M] calculated for C₂₁H₂₈O₃Si+Na [M+Na]⁺: 379.1700, found [M+Na]⁺: 379.1698.

Melting Point: 125–127 °C

¹H NMR (600 MHz, CDCl₃) δ 7.07 (d, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 4.72 (app td, *J* = 4.9, 1.1 Hz, 1H), 3.32 (dd, *J* = 17.5, 9.4 Hz, 1H), 2.99 (dd, *J* = 17.5, 10.1 Hz, 1H), 2.95 (dddd, *J* = 9.4, 4.9, 2.9, 1.9 Hz, 1H), 2.64 (ddd, *J* = 13.8, 10.1, 7.1 Hz, 1H), 2.60 – 2.53 (m, 1H), 2.40 (dd, *J* = 17.4, 2.9 Hz, 1H), 2.24 (s, 3H), 1.92 (ddd, *J* = 13.8, 8.9, 1.9 Hz, 1H), 1.60 (ddd, *J* = 14.5, 10.2, 1.1 Hz, 1H), 1.27 (app tdt, *J* = 14.5, 4.7, 1.9 Hz, 1H), 0.94 (dq, *J* = 10.2, 7.1, 4.7 Hz, 1H), 0.83 (d, *J* = 7.1 Hz, 3H), –0.17 (s, 9H).

¹³C NMR (151 MHz, CDCl₃) δ 174.8, 140.4, 139.6, 133.3, 131.6, 131.0, 126.4, 84.8, 78.3, 51.8, 48.8, 30.8, 28.7, 28.7, 22.8, 19.6, 18.3, 17.2, 1.0 (3C).

Pentacyclic alcohol S4



To a solution of (*exo*)-methyl pentacycle **22** (22.0 mg, 61.70 µmol, 1 equiv) in dry THF (1.23 mL) was added TBAF (1.0 M solution in THF, 0.12 mL, 0.123 mmol, 2 equiv). After stirring for 10 min at room temperature, to the reaction mixture was added sat. aq. NH₄Cl (20 mL) and extracted with EtOAc (20 mL). The organic phase was dried over Na₂SO₄ and the solvents were evaporated. The crude residue was purified by preparative TLC (hexanes/EtOAc = 1:1), yielding pentacyclic alcohol **S4** (17.5 mg, 61.54 µmol, quant.) as a white solid.

Rf-value: 0.35 (hexanes:EtOAc = 1:1; *p*-anisaldehyde)

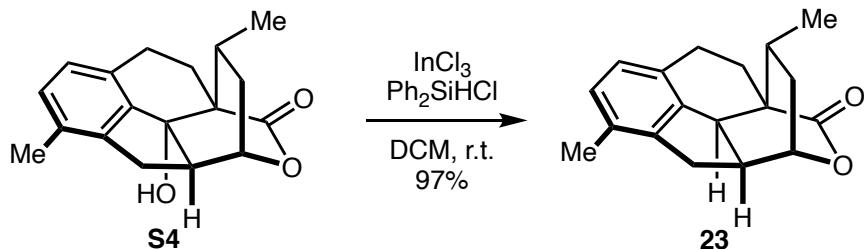
HRMS (m/z): ESI [M] calculated for C₁₈H₂₀O₃+Na [M+Na]⁺: 307.1305, found [M+Na]⁺: 307.1305.

Melting Point: 203–205 °C

¹H NMR (600 MHz, CDCl₃) δ 7.08 (d, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 4.75 (app td, *J* = 4.8, 1.1 Hz, 1H), 3.39 (dd, *J* = 17.4, 9.3 Hz, 1H), 3.09 (dd, *J* = 16.9, 10.0 Hz, 1H), 2.98 (dddd, *J* = 9.5, 4.9, 2.9, 1.9 Hz, 1H), 2.68 – 2.58 (m, 2H), 2.44 (dd, *J* = 17.4, 2.9 Hz, 1H), 2.24 (s, 3H), 2.02 – 1.96 (m, 1H), 1.63 (ddd, *J* = 14.5, 10.2, 1.1 Hz, 1H), 1.32 (app dt, *J* = 14.5, 4.7, 1.9 Hz, 1H), 0.98 (dq, *J* = 11.2, 7.0, 4.5 Hz, 1H), 0.85 (d, *J* = 7.0 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 174.9, 140.5, 140.0, 132.4, 132.1, 131.3, 126.8, 83.0, 78.7, 51.0, 49.1, 31.0, 29.7, 28.8, 22.7, 19.6, 18.5, 17.2.

Deoxygenated pentacycle 23



A dry 2 mL vial was charged with pentacyclic alcohol **S4** (12.0 mg, 42.20 μmol , 1 equiv) and transferred to a glovebox. After addition of InCl_3 (1.9 mg, 8.44 μmol , 20 mol%), the vial was sealed with a septa cap and removed from the glovebox. To the vial was added dry DCM (0.84 mL) and Ph_2SiHCl (18 μL , 84.40 μmol , 2 equiv) and the reaction mixture was stirred for 24 h at room temperature. After complete consumption of the siloxy intermediate (as judged by TLC), the mixture was quenched by adding sat. aq. NaHCO_3 (15 mL) and extracted with EtOAc (15 mL). The organic phase was dried over Na_2SO_4 and concentrated. The crude residue was purified by preparative TLC (hexanes/EtOAc = 4:1), yielding deoxygenated pentacycle **23** (11.0 mg, 40.99 μmol , 97%) as a white solid.

Rf-value: 0.52 (hexanes:EtOAc = 3:1; *p*-anisaldehyde)

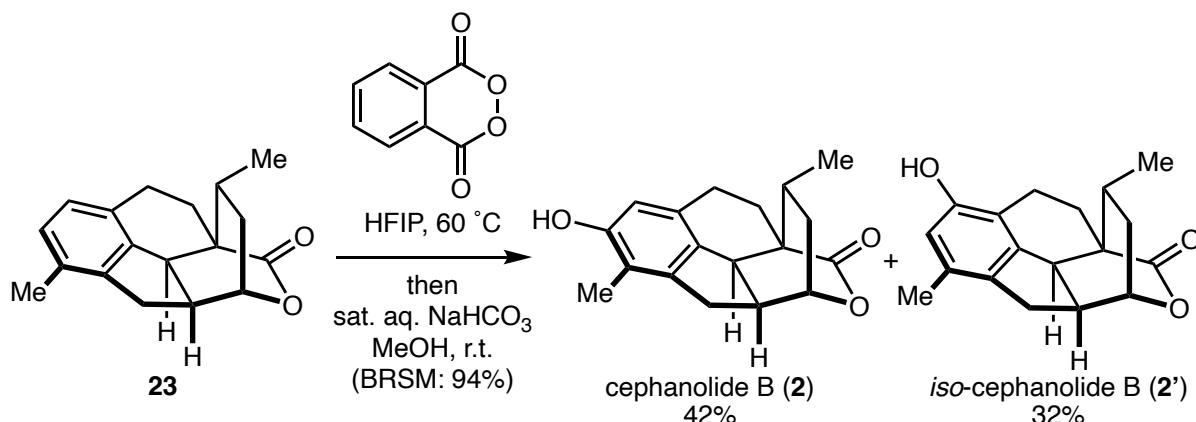
HRMS (m/z): ESI [M] calculated for $\text{C}_{18}\text{H}_{20}\text{O}_2+\text{Na} [\text{M}+\text{Na}]^+$: 291.1356, found $[\text{M}+\text{Na}]^+$: 291.1359.

Melting Point: 103–105 °C

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 6.98 (d, $J = 7.5$ Hz, 1H), 6.90 (d, $J = 7.5$ Hz, 1H), 4.68 – 4.65 (m, 1H), 3.31 – 3.22 (m, 2H), 3.15 (dd, $J = 12.2, 9.8, 4.6, 2.2$ Hz, 1H), 3.01 (app dt, $J = 17.8, 6.4$ Hz, 1H), 2.67 – 2.60 (m, 1H), 2.60 – 2.55 (m, 1H), 2.24 (s, 3H), 2.15 – 2.10 (m, 2H), 1.70 (ddd, $J = 14.4, 10.3, 1.0$ Hz, 1H), 1.28 (app dtd, $J = 14.5, 4.7, 1.8$ Hz, 1H), 1.20 – 1.12 (m, 1H), 0.81 (d, $J = 7.1$ Hz, 3H).

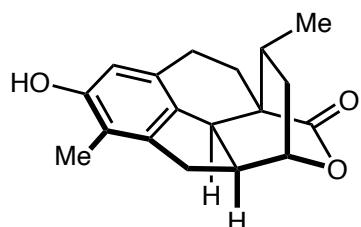
$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 177.1, 140.2, 140.0, 132.1, 131.8, 129.1, 125.8, 79.2, 48.0, 45.7, 39.3, 32.9, 28.8, 26.7, 24.0, 23.1, 19.5, 18.8.

Cephanolide B (2)



To a solution of deoxygenated pentacycle **23** (8.0 mg, 29.81 µmol, 1 equiv) in HFIP (0.60 mL) was added phthaloyl peroxide⁵ (6.4 mg, 38.75 µmol, 1.3 equiv). After the reaction mixture was stirred for 24 h at 60 °C, sat. aq. NaHCO₃ (0.30 mL) and HPLC-grade MeOH (0.30 mL) were added. The resulting suspension was stirred for 30 min at room temperature. After the completion of the ester hydrolysis (as judged by TLC), H₂O (15 mL) was added, and the resulting mixture was extracted with EtOAc (15 mL) and washed with brine (15 mL). The organic phase was dried over Na₂SO₄ and the solvents were evaporated. The crude residue was purified by preparative TLC (PhH/EtOAc = 15:1 x 3), yielding cephanolide B (**2**) (3.6 mg, 12.66 µmol, 42%) as a white solid and *iso*-cephanolide B (**2'**) (2.7 mg, 9.50 µmol, 32%) as a white solid, along with recovered starting material **23** (1.6 mg, 5.96 µmol, 20%).

Cephanolide B;



Rf-value: 0.50 (PhH:EtOAc = 5:1; *p*-anisaldehyde)

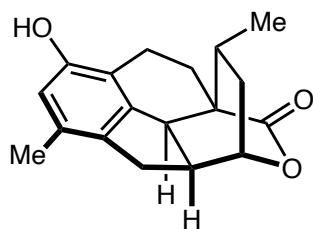
HRMS (m/z): ESI [M] calculated for C₁₈H₂₀O₃+Na [M+Na]⁺: 307.1305, found [M+Na]⁺: 307.1308.

Melting Point: 209–211 °C

¹H NMR (500 MHz, CDCl₃) δ 6.47 (s, 1H), 4.67 – 4.63 (m, overlapped, 2H), 3.24 (dd, *J* = 15.0, 9.6 Hz, 1H), 3.23 (d, *J* = 9.6 Hz, 1H), 3.14 (app ddt, *J* = 17.0, 9.6, 2.2 Hz, 1H), 2.97 (dd, *J* = 17.4, 9.4 Hz, 1H), 2.61 – 2.52 (m, 2H), 2.13 (s, 3H), 2.12 – 2.00 (m, 2H), 1.70 (ddd, *J* = 14.4, 10.3, 1.0 Hz, 1H), 1.32 – 1.26 (m, 1H), 1.18 (dq, *J* = 10.1, 7.1, 3.5 Hz, 1H), 0.81 (d, *J* = 7.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 177.2, 154.3, 141.9, 132.7, 132.3, 117.7, 112.8, 79.2, 47.5, 45.9, 39.7, 33.0, 28.8, 26.5, 24.1, 23.1, 19.5, 12.3.

Iso-cephanolide B;



Rf-value: 0.49 (PhH:EtOAc = 5:1; *p*-anisaldehyde)

HRMS (m/z): ESI [M] calculated for C₁₈H₂₀O₃+Na [M+Na]⁺: 307.1305, found [M+Na]⁺: 307.1305.

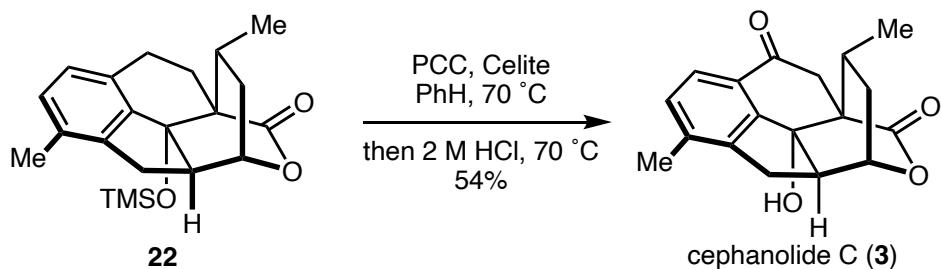
Melting Point: 251–255 °C

¹H NMR (500 MHz, CDCl₃) δ 6.49 (s, 1H), 4.66 (app t, *J* = 4.3 Hz, 1H), 4.57 (s, 1H), 3.25 (d, *J* = 10.0 Hz, 1H), 3.21 – 3.10 (m, 2H), 2.82 (dd, *J* = 17.7, 9.6 Hz, 1H), 2.62 (app dt, *J* = 17.7, 8.7 Hz, 1H), 2.49 (dd, *J* = 15.4, 2.2 Hz, 1H), 2.22 (ddd, *J* = 15.4, 9.7, 1.6 Hz, 1H), 2.18 (s, 3H), 2.09 (ddd, *J* = 14.4, 9.7, 8.5 Hz, 1H), 1.73 (dd, *J* = 15.0, 11.5 Hz, 1H), 1.35 – 1.27 (m, 2H), 0.83 (d, *J* = 7.0 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 177.0, 152.4, 141.6, 133.3, 132.4, 117.1, 115.9, 79.2, 47.9, 45.2, 39.7, 32.0, 28.7, 26.3, 23.2, 19.5, 19.1, 18.8.

5) Yuan, C.; Liang, Y.; Hernandez, T.; Berriochoa, A.; Houk, K. N.; Siegel, D. *Nature* **2013**, *499*, 192–196.

Cephanolide C (3)



To a solution of (*exo*)-methyl pentacycle **22** (10.0 mg, 28.05 µmol, 1 equiv) in dry PhH (0.93 mL) was added PCC (30.2 mg, 0.140 mmol, 5 equiv) and Celite (140 mg) in one portion and the mixture was heated to 70 °C. After stirring for 12 h at 70 °C, the reaction mixture was cooled down to room temperature, then THF (1.00 mL) and 2 M HCl (1.00 mL) were added. After stirring for 24 h at 70 °C, the mixture was cooled down to room temperature and filtered through a short pad of Celite (washed with EtOAc). The biphasic mixture was diluted with EtOAc (15 mL) and washed with H₂O (20 mL) and brine (20 mL). The organic phase was dried over MgSO₄, filtered and concentrated. Purification using preparative TLC (hexanes/EtOAc = 1:2) yielded cephalolide C (**3**) (4.5 mg, 15.08 µmol, 54%) as a white solid.

Rf-value: 0.18 (hexanes/EtOAc = 1:1; p-anisaldehyde)

HRMS (m/z): ESI [M] calculated for C₁₈H₁₈O₄+Na [M+Na]⁺: 321.1097, found [M+Na]⁺: 321.1096.

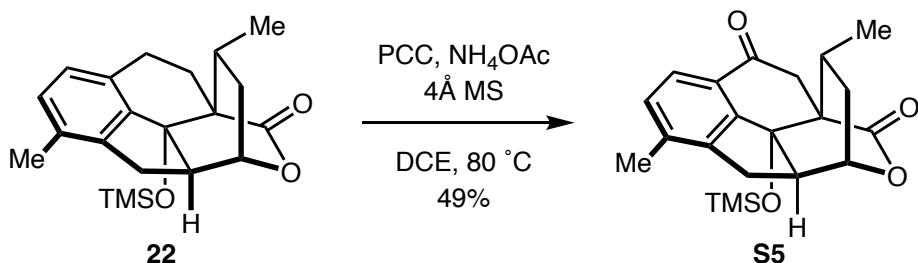
Melting Point: >260°C (*The highest temperature of the graduation of our thermometer is 260 °C. The thermometer showed roughly 265 °C when the compound melted, which is identical to the literature.⁶)

¹H NMR (500 MHz, CD₃OD) δ 7.55 (d, *J* = 7.7 Hz, 1H), 7.33 (d, *J* = 7.7 Hz, 1H), 4.90 (app td, *J* = 4.7, 1.2 Hz, 1H), 3.47 (dd, *J* = 17.6, 9.3 Hz, 1H), 3.43 (dd, *J* = 18.5, 1.8 Hz, 1H), 3.01 (dddd, *J* = 9.3, 4.7, 3.1, 1.8 Hz, 1H), 2.71 (dd, *J* = 17.6, 3.1 Hz, 1H), 2.61 (d, *J* = 18.5 Hz, 1H), 2.38 (s, 3H), 1.86 (ddd, *J* = 14.8, 10.2, 1.2 Hz, 1H), 1.37 (app ttd, *J* = 14.8, 4.7, 1.9 Hz, 1H), 1.21 (dq, *J* = 10.2, 7.0, 4.7 Hz, 1H), 0.83 (d, *J* = 7.0 Hz, 3H).

¹³C NMR (126 MHz, CD₃OD) δ 198.3, 175.9, 147.2, 143.5, 142.3, 132.6, 129.2, 125.7, 82.7, 80.7, 54.8, 49.7, 37.3, 32.0, 31.4, 29.7, 19.5, 19.2.

6) Xu, L.; Wang, C.; Gao, Z.; Zhao, Y.-M. *J. Am. Chem. Soc.* **2018**, *140*, 5653–5658.

Benzylidic ketone S5



To a solution of (*exo*)-methyl pentacycle **22** (25.0 mg, 70.12 μmol, 1 equiv) and 4 Å MS (250 mg) in dry DCE (2.34 mL) was added NH₄OAc (32.4 mg, 0.421 mmol, 6 equiv) and PCC (64.6 mg, 0.351 mmol, 5 equiv). The reaction mixture was stirred for 24 h at 80 °C, before being cooled down to room temperature. The resulting suspension was filtrated through a short pad of silica (eluted with hexanes/EtOAc = 1:1) and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexanes/EtOAc = 10:1), yielding benzylic ketone **S5** (12.7 mg, 34.28 μmol, 49%) as a white solid.

Rf-value: 0.55 (hexanes:EtOAc = 1:1; *p*-anisaldehyde)

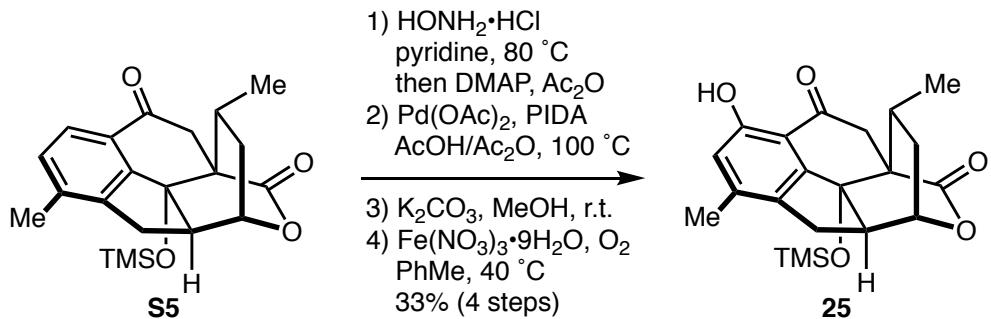
HRMS (m/z): ESI [M] calculated for C₂₁H₂₆O₄Si+Na [M+Na]⁺: 393.1493, found [M+Na]⁺: 393.1492.

Melting Point: 128–130 °C

¹H NMR (500 MHz, CDCl₃) δ 7.60 (d, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 4.82 (app td, *J* = 4.9, 1.1 Hz, 1H), 3.48 (d, *J* = 18.6 Hz, 1H), 3.42 (dd, *J* = 17.6, 9.5 Hz, 1H), 3.07 (dd, *J* = 9.5, 4.9, 3.1, 1.8 Hz, 1H), 2.69 (d, *J* = 18.6 Hz, 1H), 2.57 (dd, *J* = 17.6, 3.1 Hz, 1H), 2.36 (s, 3H), 1.73 (ddd, *J* = 14.6, 10.2, 1.1 Hz, 1H), 1.41 (app dt, *J* = 14.7, 4.7, 1.8 Hz, 1H), 1.19 (dq, *J* = 10.2, 7.0, 4.7 Hz, 1H), 0.87 (d, *J* = 7.0 Hz, 3H), -0.18 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 196.5, 172.8, 144.6, 141.5, 140.6, 132.1, 128.9, 125.2, 84.6, 78.5, 54.6, 48.3, 36.7, 31.4, 29.8, 29.0, 19.7, 19.4, 1.2 (3C).

(*ortho*)-Hydroxy ketone 25



To a solid mixture of benzylic ketone **S5** (10.0 mg, 26.99 μmol , 1 equiv) and $\text{HONH}_2 \cdot \text{HCl}$ (7.5 mg, 0.108 mmol, 4 equiv) was added dry pyridine (0.90 mL). The reaction mixture was stirred for 15 h at 80 °C, and then cooled down to room temperature. To the mixture was added DMAP (ca. 0.3 mg, 2.70 μmol , 10 mol%) and Ac_2O (25.5 μL , 0.270 mmol, 10 equiv). After stirring for 2 h at room temperature, the reaction mixture was concentrated *in vacuo*. The crude mixture was diluted with EtOAc (15 mL) and washed with H_2O (15 mL), 1 M HCl (15 mL), and brine (15 mL). The organic phase was dried over Na_2SO_4 and concentrated. This crude material was used in the next reaction without further purification.

A 2 mL vial was charged with the crude material, $\text{Pd}(\text{OAc})_2$ (1.8 mg, 8.10 μmol , 30 mol%) and PIDA (17.4 mg, 53.98 mmol, 2 equiv), and $\text{AcOH}/\text{Ac}_2\text{O}$ (10:1 v/v, 0.90 mL) were added. The reaction mixture was stirred for 4 h at 100 °C, then cooled down to room temperature, and concentrated *in vacuo*. This crude material was used in the next reaction without further purification.

To the crude mixture was added K_2CO_3 (37.3 mg, 0.270 mmol, 10 equiv) and HPLC-grade MeOH (0.90 mL). After stirring for 30 min at room temperature, the mixture was quenched with sat. aq. NH_4Cl (15 mL) and extracted with EtOAc (2 x 15 mL). The combined organic phase was dried over Na_2SO_4 and concentrated. This crude material was used in the next reaction without further purification.

A 2 mL vial was charged with the crude material and $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (1.1 mg, 2.70 μmol , 10 mol%), evacuated and backfilled with O_2 . To this vial was added PhMe (0.90 mL) and the reaction mixture was stirred for 3 h at 40 °C under O_2 (balloon) atmosphere. After cooling down to room temperature, the mixture was filtered through a short plug of SiO_2 (eluted with hexanes/EtOAc = 1:1) and the filtrate was concentrated *in vacuo*. The residue was purified by preparative TLC (hexanes/EtOAc = 2:1), yielding hydroxy ketone **25** (3.4 mg, 8.80 μmol , 33% over 4 steps) as a white amorphous solid.

**Oxime intermediates seem to be unstable under usual operations for purification so that was used immediately without purification.*

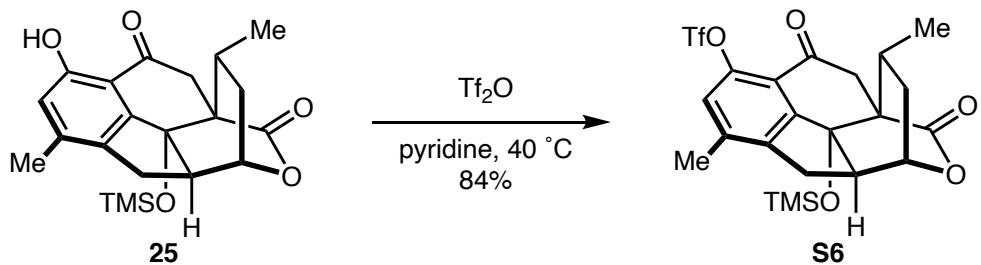
Rf-value: 0.43 (hexanes:EtOAc = 2:1; *p*-anisaldehyde)

HRMS (m/z): ESI [M] calculated for $\text{C}_{21}\text{H}_{26}\text{O}_5\text{Si} + \text{Na}$ $[\text{M}+\text{Na}]^+$: 409.1442, found $[\text{M}+\text{Na}]^+$: 409.1442.

¹H NMR (500 MHz, CD₂Cl₂) δ 10.30 (s, 1H), 6.78 (s, 1H), 4.81 (app td, *J* = 4.9, 1.1 Hz, 1H), 3.52 (d, *J* = 18.4 Hz, 1H), 3.31 (dd, *J* = 16.9, 9.2 Hz, 1H), 3.04 (dddd, *J* = 9.2, 4.9, 2.9, 1.7 Hz, 1H), 2.70 (d, *J* = 18.4 Hz, 1H), 2.47 (dd, *J* = 16.9, 2.9 Hz, 1H), 2.30 (d, *J* = 0.7 Hz, 3H), 1.79 (ddd, *J* = 14.7, 10.3, 1.3 Hz, 1H), 1.42 (app dtd, *J* = 14.7, 4.9, 1.7 Hz, 1H), 1.38 – 1.30 (m, 1H), 0.90 (d, *J* = 7.0 Hz, 3H), –0.13 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 201.2, 172.5, 160.0, 145.6, 144.3, 131.3, 120.1, 112.8, 84.4, 78.5, 54.9, 48.6, 36.7, 31.0, 29.5, 29.0, 19.9, 19.7, 1.2 (3C).

Keto-triflate S6



To a solution of hydroxy ketone **25** (3.0 mg, 7.76 µmol, 1 equiv) in dry pyridine (0.39 mL) was added Tf₂O (3.9 µL, 23.28 mmol, 3 equiv) at 0 °C. After stirring for 12 h at 40 °C, to the reaction mixture was added sat. aq. NaHCO₃ (15 mL) and extracted with EtOAc (15 mL). The organic phase was washed with 1 M HCl (15 mL) and brine (15 mL), dried over Na₂SO₄ and the solvents were evaporated. The crude residue was purified by preparative TLC (hexanes/EtOAc = 1:1), yielding keto-triflate **S6** (3.4 mg, 6.56 µmol, 84%) as a white amorphous solid.

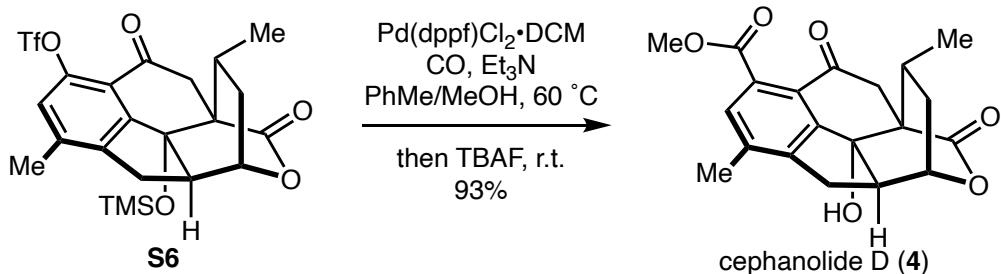
Rf-value: 0.40 (hexanes:EtOAc = 1:1; *p*-anisaldehyde)

HRMS (m/z): ESI [M] calculated for C₂₂H₂₅O₇SF₃Si+Na [M+Na]⁺: 541.0935, found [M+Na]⁺: 541.0932.

¹H NMR (500 MHz, CDCl₃) δ 7.09 (s, 1H), 4.83 (app t, *J* = 4.8 Hz, 1H), 3.48 (dd, *J* = 17.8, 8.6 Hz, 1H), 3.43 (dd, *J* = 19.0, 10.2 Hz, 1H), 3.15 – 3.09 (m, 1H), 2.74 (d, *J* = 19.0 Hz, 1H), 2.60 (dd, *J* = 17.8, 3.0 Hz, 1H), 2.40 (s, 3H), 1.77 (dd, *J* = 14.8, 10.2 Hz, 1H), 1.49 – 1.43 (m, 1H), 1.27 – 1.17 (m, 1H), 0.90 (d, *J* = 7.0 Hz, 3H), –0.13 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 192.8, 171.9, 146.8, 145.6, 143.8, 140.7, 125.5, 120.9, 118.9 (q, *J* = 320.8 Hz), 84.3, 78.0, 54.0, 48.3, 36.9, 31.1, 29.9, 28.9, 19.57, 19.55, 1.2 (3C).

Cephanolide D (4)



A 1 mL vial was charged with keto-triflate **S6** (3.3 mg, 6.36 μ mol, 1 equiv) and Pd(dppf)Cl₂•DCM (1.6 mg, 1.91 μ mol, 30 mol%), evacuated and backfilled with CO. To this vial was added Et₃N (2.7 μ L, 19.09 μ mol, 3 equiv) and PhMe/MeOH (1:1 v/v, 0.64 mL, sparged with CO for 10 min before use) and the reaction mixture was stirred for 24 h at 60 °C under CO (balloon) atmosphere. After cooling down to room temperature, to the mixture was added TBAF (1 M in THF, 63.6 μ L, 63.64 μ mol, 10 equiv) and stirred for 30 h. To the reaction mixture was added sat. aq. NH₄Cl (20 mL) and extracted with EtOAc (2 x 20 mL). The combined organic phase was dried over Na₂SO₄ and the solvents were evaporated. The crude residue was purified by preparative TLC (hexanes/EtOAc = 1:2), yielding cephanolide D (**4**) (2.1 mg, 5.89 μ mol, 93%) as a white amorphous solid.

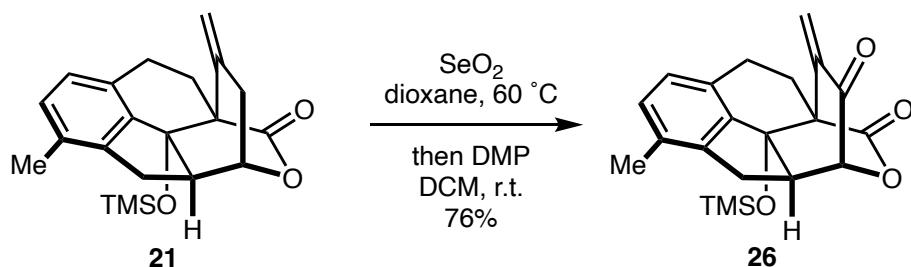
Rf-value: 0.38 (hexanes:EtOAc = 1:2; *p*-anisaldehyde)

HRMS (m/z): ESI [M] calculated for C₂₀H₂₀O₆+Na [M+Na]⁺: 379.1152, found [M+Na]⁺: 379.1151.

¹H NMR (600 MHz, CD₂Cl₂) δ 7.30 (s, 1H), 4.87 (app t, *J* = 4.6 Hz, 1H), 3.92 (s, 3H), 3.54 (d, *J* = 18.6 Hz, 1H), 3.51 (br-d, *J* = 17.6 Hz, 1H), 3.11 (br-s, 1H), 2.74 (d, *J* = 18.6 Hz, 1H), 2.61 (br-d, *J* = 17.6 Hz, 1H), 2.36 (s, 3H), 1.76 (dd, *J* = 14.7, 10.2 Hz, 1H), 1.47 (dt, *J* = 14.7, 4.6 Hz, 1H), 1.33 (m, 1H), 0.92 (d, *J* = 7.0 Hz, 3H).

¹³C NMR (151 MHz, CD₂Cl₂) δ 194.0, 172.5, 169.3, 145.3, 142.2, 141.7, 132.0, 131.2, 125.2, 82.5, 78.5, 53.16, 53.14, 48.9, 36.7, 31.5, 30.6, 28.8, 19.6, 19.3.

Enone 26



Exo-olefin **21** (28.3 mg, 79.83 μmol , 1 equiv) and SeO_2 (88.6 mg, 0.798 mmol, 10 equiv) were dissolved in dry dioxane (1.60 mL) and heated to 60 $^\circ\text{C}$ and held at this temperature for 15 h. After cooling the reaction mixture to room temperature, Dess-Martin periododinane (101.5 mg, 0.239 mmol, 3 equiv) in wet DCM (1.6 mL) was added and stirring was continued for 24 h. The mixture was quenched with sat. aq. NaHCO_3 (5 mL) and sat. aq. Na_2SO_3 (5 mL) and extracted with DCM (3 x 20 mL), washed with brine (20 mL), dried over MgSO_4 , filtered and the solvents evaporated in vacuo. Flash chromatography (hexanes/EtOAc = 4:1 to 1:1) yielded enone **26** (22.2 mg, 60.24 μmol , 76% yield) as a white solid.

Rf-value: 0.63 (PhMe:EtOAc = 5:1; *p*-anisaldehyde)

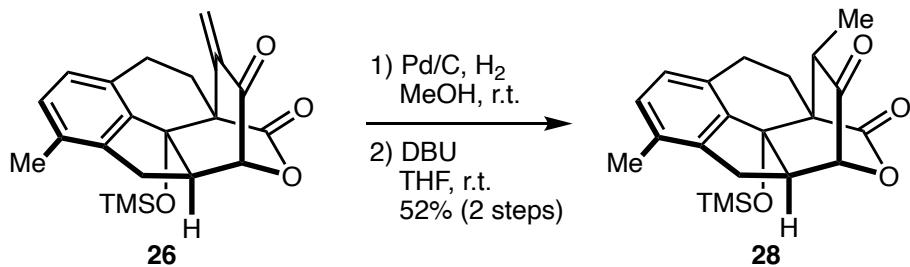
HRMS (m/z): ESI [M] calculated for $\text{C}_{21}\text{H}_{24}\text{O}_4\text{Si}+\text{Na}$ $[\text{M}+\text{Na}]^+$: 391.1336, found $[\text{M}+\text{Na}]^+$: 391.1336.

Melting Point: 126–128 $^\circ\text{C}$

$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.00 (d, J = 7.5 Hz, 1H), 6.85 (d, J = 7.5 Hz, 1H), 5.81 (s, 1H), 5.16 (s, 1H), 4.77 (d, J = 5.5 Hz, 1H), 3.38 (dd, J = 17.0, 9.5 Hz, 1H), 3.32 (ddd, J = 9.5, 5.5, 2.4 Hz, 1H), 3.08 (dd, J = 17.4, 11.3 Hz, 1H), 2.86 (ddd, J = 14.5, 11.3, 5.1 Hz, 1H), 2.72 (ddd, J = 17.4, 9.8, 5.1 Hz, 1H), 2.38 (dd, J = 17.0, 2.4 Hz, 1H), 2.19 (ddd, J = 14.5, 9.8, 2.4 Hz, 1H), 2.15 (s, 3H), -0.10 (s, 9H).

$^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 191.7, 169.9, 139.1, 138.9, 137.2, 132.5, 132.2, 131.8, 126.9, 122.8, 85.4, 83.2, 56.4, 49.6, 30.1, 23.0, 18.4, 17.6, 1.0 (3C).

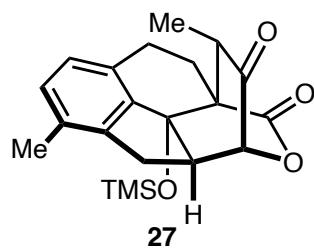
α -(*exo*)-Methyl ketone 28



A 10 mL vial was charged with Pd/C (5.7 mg, 5.43 µmol, 0.1 equiv), evacuated once and backfilled with H₂ before enone **26** (20.0 mg, 54.27 µmol, 1 equiv) in 5.43 mL of HPLC-grade MeOH was added. The mixture was sparged with H₂ for 1 min and then stirred under H₂ (balloon) for 15 h at room temperature. The Pd/C was removed by filtration through a short plug of silica (eluted with DCM/MeOH = 1:1). The filtrate was concentrated using a rotary evaporator, yielding 19.1 mg of crude α-(*endo*)-methyl ketone **27** as a slightly yellow oil. This crude material was used for the next reaction without further purification.

A 2 mL vial was charged with crude **27** and placed under N₂ atmosphere before 1 mL of dry THF was added followed by the addition of DBU (10 µL, 5.43 µmol, 1 equiv) and the mixture was stirred at room temperature for 1 h. The mixture was quenched by the addition of sat. aq. NH₄Cl (5 mL) and extracted with Et₂O (3 x 20 mL). The combined organic phase was washed with H₂O (20 mL) and brine (20 mL), and concentrated. The crude material was purified by flash chromatography (hexanes/EtOAc = 20:1 to 10:1), yielding α -(*exo*)-methyl ketone **28** (10.5 mg, 28.34 µmol, 52% yield over 2 steps) as a white solid.

α -(*endo*)-Methyl ketone 27 (crude*); *further purification to obtain an analytically pure material resulted in partial isomerization of the α -Me group

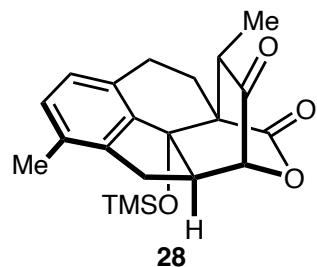


Rf-value: 0.30 (hexanes:EtOAc = 5:1; *p*-anisaldehyde)

¹H NMR (600 MHz, CDCl₃) δ 7.07 (d, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 7.5 Hz, 1H), 4.73 (d, *J* = 5.7 Hz, 1H), 3.36 – 3.27 (m, 2H), 3.09 (ddd, *J* = 16.3, 11.3, 3.9 Hz, 1H), 2.87 (ddd, *J* = 14.6, 11.3, 3.2 Hz, 1H), 2.72 (ddd, *J* = 16.3, 9.8, 3.2 Hz, 1H), 2.44 – 2.39 (m, 1H), 2.32 (q, *J* = 7.3 Hz, 1H), 2.19 (s, 3H), 1.77 (ddd, *J* = 14.6, 9.8, 4.0 Hz, 1H), -0.11 (d, *J* = 7.3 Hz, 3H), -0.11 (s, 9H).

¹³C NMR (151 MHz, CDCl₃) δ 207.5, 173.4, 139.2, 138.7, 134.6, 132.8, 132.2, 126.8, 84.1, 84.0, 53.4, 49.8, 45.5, 29.9, 24.1, 20.1, 18.3, 8.9, 1.2 (3C).

a-(exo)-Methyl ketone **28**:



Rf-value: 0.50 (hexanes:EtOAc = 4:1; *p*-anisaldehyde)

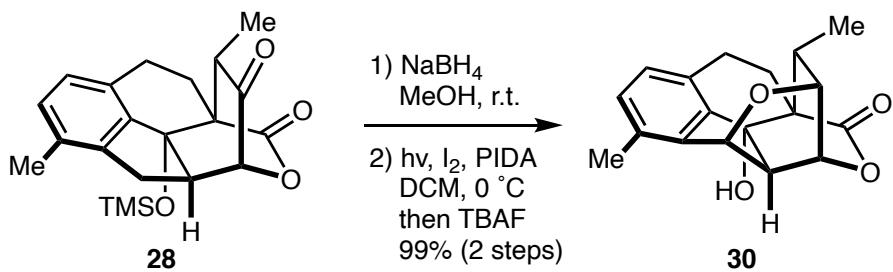
HRMS (m/z): ESI [M] calculated for C₂₁H₂₆O₄Si+Na [M+Na]⁺: 393.1493, found [M+Na]⁺: 393.1492.

Melting Point: 136–137 °C

¹H NMR (500 MHz, CDCl₃) δ 7.07 (d, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 4.63 (d, *J* = 5.7 Hz, 1H), 3.36 (dd, *J* = 17.4, 9.6 Hz, 1H), 3.26 (ddd, *J* = 9.6, 5.7, 2.9 Hz, 1H), 3.08 – 3.00 (m, 1H), 2.72 – 2.56 (m, 2H), 2.36 (dd, *J* = 17.4, 2.9 Hz, 1H), 2.18 (s, 3H), 1.90 (ddd, *J* = 13.9, 9.1, 2.5 Hz, 1H), 1.19 (dq, *J* = 8.5, 7.6 Hz, 1H), 1.02 (d, *J* = 7.6 Hz, 3H), –0.13 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 207.0, 172.0, 140.0, 138.2, 132.7, 132.5, 132.0, 127.1, 84.8, 84.3, 54.0, 49.5, 42.4, 30.0, 22.8, 18.4, 17.5, 12.9, 1.1 (3C).

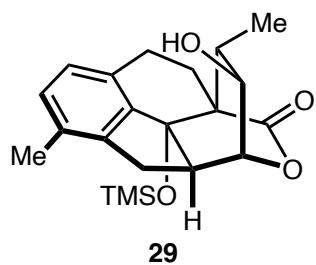
Hexacyclic alcohol 30



To a solution of α -(*exo*)-methyl ketone **28** (14.0 mg, 37.78 μ mol, 1 equiv) in dry MeOH (0.76 mL) was added NaBH₄ (2.1 mg, 56.68 mmol, 1.5 equiv). After stirring at room temperature for 30 min, the mixture was quenched by addition of acetone (0.1 mL) and sat. aq. NaHCO₃ (15 mL) was added. The resulting solution was extracted with EtOAc (15 mL) and the organic phase was dried over Na₂SO₄ and the solvents were evaporated, yielding 16.0 mg of crude alcohol **29** as a pale yellow oil. This crude material was used in the next reaction without further purification.

To a solution of crude alcohol **29** in dry DCM (0.76 mL) was added I₂ (9.6 mg, 37.78 µmol, 1 equiv) and PIDA (26.8 mg, 83.12 µmol, 2.2 equiv). The mixture was irradiated using a 90 W sunlamp at 0 °C using an ice-water Dewar bath for 1 h. After the complete consumption of the starting material (as judged by TLC), the reaction mixture was allowed to warm up to room temperature and TBAF (1.0 M solution in THF, 0.19 mL, 0.189 mmol, 5 equiv) was added. After being stirred an additional 3 h, the mixture was quenched with sat. aq. Na₂S₂O₃ (5 mL) and sat. aq. NaHCO₃ (5 mL) was added. The resulting solution was extracted with EtOAc (15 mL) and the organic phase was dried over Na₂SO₄ and the solvents were evaporated. The crude residue was purified by preparative TLC (hexanes/EtOAc = 1:2), yielding hexacyclic alcohol **30** (11.2 mg, 37.54 µmol, 99% over 2 steps) as a white solid.

(endo)-Alcohol 29; an analytically pure sample was prepared for characterization purposes



Rf-value: 0.51 (hexanes:EtOAc = 1:1; *p*-anisaldehyde)

HRMS (m/z): ESI [M] calculated for C₂₁H₂₈O₄Si+Na [M+Na]⁺: 395.1649, found [M+Na]⁺: 395.1648.

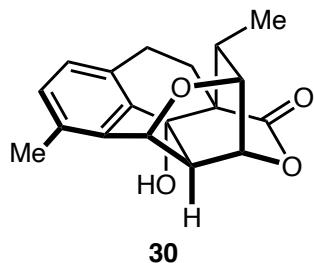
Melting Point: 163–165 °C

¹H NMR (500 MHz, CDCl₃) δ 7.08 (d, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 4.68 (dd, *J* = 4.8, 4.0 Hz, 1H), 3.61 (ddd, *J* = 5.5, 4.1, 1.5 Hz, 1H), 3.29 – 3.18 (m, 2H), 3.04 – 2.99 (m, 2H), 2.65 – 2.51 (m,

2H), 2.22 (s, 3H), 1.93 – 1.84 (m, 1H), 0.93 (d, J = 7.1 Hz, 3H), 0.78 (qd, J = 7.1, 5.3 Hz, 1H), –0.17 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 174.4, 142.2, 139.2, 133.0, 131.9, 131.3, 126.5, 84.9, 78.6, 75.4, 51.1, 48.3, 38.2, 30.0, 23.0, 18.4, 17.3, 17.1, 1.1 (3C).

Hexacyclic alcohol 30;



Rf-value: 0.45 (hexanes:EtOAc = 1:1; *p*-anisaldehyde)

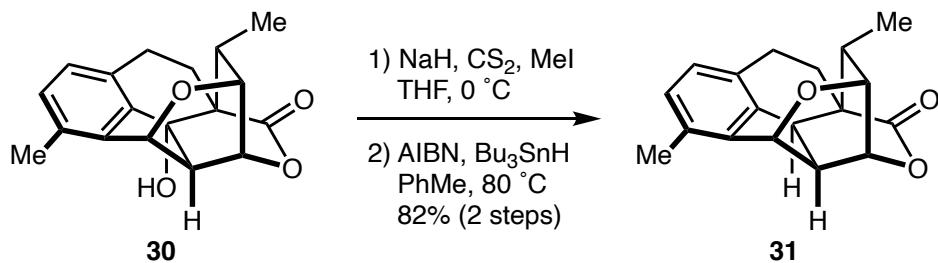
HRMS (m/z): ESI [M] calculated for C₁₈H₁₈O₄+Na [M+Na]⁺: 321.1097, found [M+Na]⁺: 321.1098.

Melting point: 185–187 °C

¹H NMR (500 MHz, CDCl₃) δ 7.14 (d, J = 7.4 Hz, 1H), 7.07 (d, J = 7.4 Hz, 1H), 5.57 (d, J = 5.0 Hz, 1H), 5.19 (app td, J = 5.8, 0.8 Hz, 1H), 3.77 (d, J = 5.6 Hz, 1H), 3.33 (t, J = 5.5 Hz, 1H), 3.25 (ddd, J = 15.1, 12.4, 8.6 Hz, 1H), 2.78 – 2.64 (m, 2H), 2.37 (s, 3H), 1.43 (app dt, J = 14.5, 8.3 Hz, 1H), 0.76 (d, J = 7.6 Hz, 3H), 0.46 (q, J = 7.6 Hz, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 172.3, 142.4, 141.5, 134.2, 133.0, 132.4, 128.7, 84.9, 80.8, 79.7, 78.6, 53.0, 52.7, 41.4, 25.5, 20.3, 17.8, 15.2.

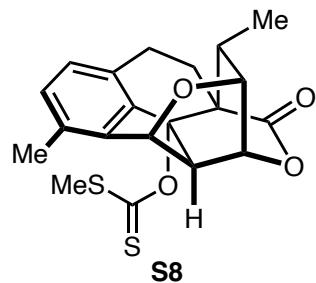
Deoxygenated hexacycle 31



To a solution of hexacyclic alcohol **30** (10.5 mg, 35.19 μmol , 1 equiv) in dry THF (1.17 mL) was added NaH (2.8 mg, 70.39 μmol , 2 equiv) at 0 $^\circ\text{C}$. After stirring for 10 min at 0 $^\circ\text{C}$, CS_2 (21 μL , 0.352 mmol, 10 equiv) and MeI (22 μL , 0.352 mmol, 10 equiv) were added sequentially (**Note: After addition of CS_2 , stirring without MeI results in decomposition; MeI should be added right after the addition of CS_2**). After stirring for 2 h at 0 $^\circ\text{C}$, the reaction mixture was quenched with sat. aq. NH_4Cl (15 mL) and extracted with EtOAc (15 mL). The organic phase was washed with H_2O (15 mL) and brine (15 mL), and dried over Na_2SO_4 . The organic solvents were evaporated, yielding 15.8 mg of crude xanthate **S8** as a pale yellow solid. This crude material was used in the next reaction without further purification.

To a solution of the crude xanthate **S8** in dry PhMe (1.17 mL) was added AIBN (1.2 mg, 7.04 μmol , 20 mol%) and Bu_3SnH (19 μL , 70.38 μmol , 2 equiv). The reaction mixture was stirred at 80 $^\circ\text{C}$ for 1 h and then cooled down to room temperature. The solution was filtrated through a short plug of silica containing 10% wt/wt K_2CO_3 and the filtrate was concentrated. The crude residue was purified by preparative TLC (hexanes/EtOAc = 2:1), yielding hexacycle **31** (8.1 mg, 28.69 μmol , 82% over 2 steps) as a white solid.

Xanthate S8; *an analytically pure sample was prepared for characterization purposes*



Rf-value: 0.44 (hexanes:EtOAc = 3:1; *p*-anisaldehyde)

HRMS (m/z): ESI [M] calculated for $\text{C}_{20}\text{H}_{20}\text{O}_4\text{S}_2+\text{Na} [\text{M}+\text{Na}]^+$: 411.0695, found $[\text{M}+\text{Na}]^+$: 411.0696.

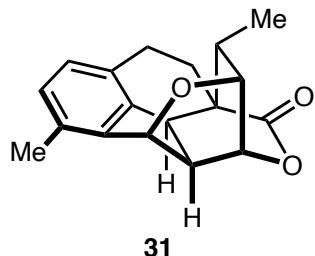
Melting point: 223–225 $^\circ\text{C}$

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.14 (d, $J = 7.5$ Hz, 1H), 7.01 (d, $J = 7.5$ Hz, 1H), 5.72 (d, $J = 5.2$ Hz, 1H), 5.24 – 5.20 (m, 1H), 4.49 (ddd, $J = 6.1, 5.2, 0.7$ Hz, 1H), 3.83 (d, $J = 5.5$ Hz, 1H), 2.99 – 2.90 (m,

1H), 2.84 – 2.77 (m, 1H), 2.73 – 2.67 (m, 1H), 2.44 (s, 3H), 2.38 (s, 3H), 1.47 (app dt, J = 14.4, 8.5 Hz, 1H), 0.80 (d, J = 7.6 Hz, 3H), 0.57 (q, J = 7.6 Hz, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 210.4, 170.9, 143.0, 139.9, 132.9, 132.7, 132.5, 127.9, 98.2, 81.3, 79.5, 78.4, 53.0, 48.0, 41.0, 25.9, 21.0, 19.2, 17.8, 15.0.

Deoxygenated hexacycle 31;



Rf-value: 0.42 (hexanes:EtOAc = 3:1; *p*-anisaldehyde)

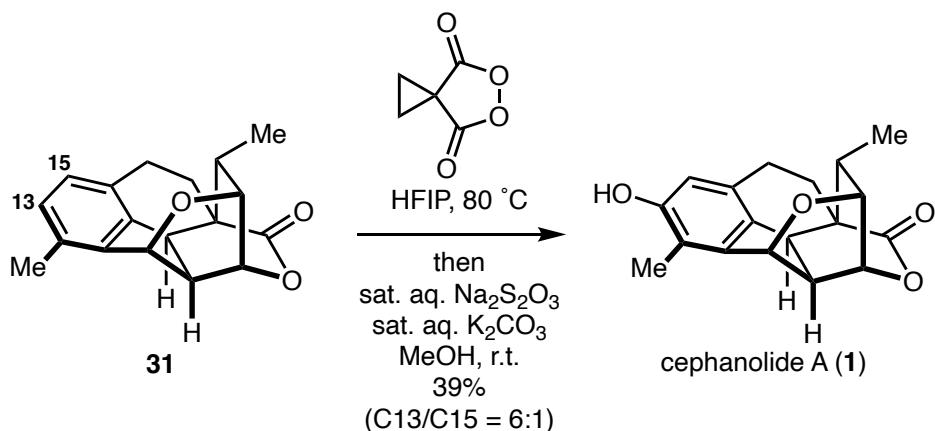
HRMS (m/z): ESI [M] calculated for C₁₈H₁₈O₃+Na [M+Na]⁺: 305.1148, found [M+Na]⁺: 305.1150.

Melting point: 198–199 °C

¹H NMR (500 MHz, CDCl₃) δ 7.08 (d, J = 7.5 Hz, 1H), 7.06 (d, J = 7.5 Hz, 1H), 5.59 (d, J = 5.0 Hz, 1H), 5.17 (app td, J = 5.9, 0.8 Hz, 1H), 3.80 (d, J = 5.7 Hz, 1H), 3.60 – 3.55 (m, 1H), 3.24 (d, J = 8.7 Hz, 1H), 2.86 – 2.71 (m, 2H), 2.65 (ddd, J = 14.6, 9.3, 1.3 Hz, 1H), 2.40 (s, 3H), 1.33 (ddd, J = 14.6, 9.6, 7.9 Hz, 1H), 0.73 (d, J = 6.9 Hz, 3H), 0.68 (dq, J = 6.9, 5.2 Hz, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 174.7, 143.2, 142.2, 133.5, 132.9, 130.5, 127.4, 84.0, 80.3, 79.2, 47.4, 46.8, 43.5, 40.6, 26.7, 23.3, 18.2, 15.1.

Cephanolide A (1)



To a solution of deoxygenated hexacycle **31** (14.3 mg, 51.36 μ mol, 1 equiv) in HFIP (1.02 mL) was added malonoyl peroxide⁷ (13.2 mg, 0.10 mmol, 2 equiv). After the reaction mixture was stirred for 48 h at 80 °C, sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$ (0.51 mL), sat. aq. K_2CO_3 (0.51 mL) and MeOH (0.30 mL) were added. The resulting suspension was stirred for 24 h at room temperature. After the complete hydrolysis of the ester intermediate (as judged by TLC), H_2O (15 mL) was added, and the resulting mixture was extracted with EtOAc (15 mL) and washed with brine (15 mL). The organic phase was dried over Na_2SO_4 and the solvents were evaporated. The crude residue was purified by preparative TLC (hexanes/EtOAc = 1:1), yielding cephanolide A (**1**) (5.9 mg, 19.78 μ mol, 39%, C13/C15 = 6:1) as a white solid.

The minor phenol constitutional isomer was removed by further preparative TLC (PhH/THF/EtOAc = 50:1:1 x 3) to afford analytically pure cephanolide A (**1**) as a white solid.

Rf-value: 0.36 (hexanes:EtOAc = 2:1; *p*-anisaldehyde)

HRMS (m/z): ESI [M] calculated for $\text{C}_{18}\text{H}_{18}\text{O}_4+\text{Na} [\text{M}+\text{Na}]^+$: 321.1097, found $[\text{M}+\text{Na}]^+$: 321.1098.

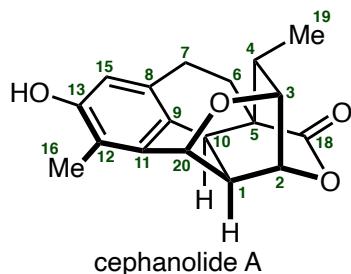
Melting point: 259–261 °C

$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 6.65 (s, 1H), 5.55 (d, J = 5.0 Hz, 1H), 5.15 (app t, J = 5.6 Hz, 1H), 4.71 (s, 1H), 3.79 (d, J = 5.6 Hz, 1H), 3.57 (app dt, J = 8.8, 5.6 Hz, 1H), 3.18 (d, J = 8.7 Hz, 1H), 2.83 – 2.75 (m, 1H), 2.67 (ddd, J = 14.9, 8.0, 1.2 Hz, 1H), 2.62 (ddd, J = 14.6, 9.5, 1.2 Hz, 1H), 2.28 (s, 3H), 1.33 (ddd, J = 14.6, 9.5, 8.0 Hz, 1H), 0.76 – 0.68 (m, 1H), 0.74 (d, J = 7.3 Hz, 3H).

$^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 174.7, 155.1, 144.0, 135.4, 134.5, 118.2, 114.9, 83.9, 80.3, 79.2, 47.7, 46.3, 43.8, 40.5, 26.8, 23.1, 15.1, 11.9.

7) Dragan, A.; Kubczyk, T. M.; Rowley, J. H.; Sproules, S.; Tomkinson, N. C. O. *Org. Lett.* **2015**, *17*, 2618–2621.

3. Spectral Data Comparison of Natural Products with Synthetic Cephalolides A–D

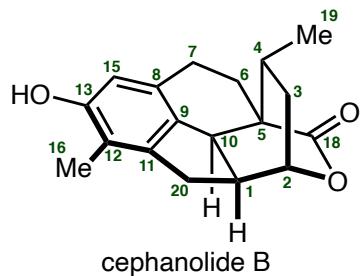


3-1. ^1H NMR of cephalolide A

Position	Natural (400 MHz) δ_{H} (J in Hz)	Gao (Ref. 8) (400 MHz) δ_{H} (J in Hz)	This work (600 MHz) δ_{H} (J in Hz)
1	3.61, ddd (8.7, 6.0, 5.0)	3.60, m	3.57, app dt (8.8, 5.6)
2	5.18, dd (6.0, 5.7)	5.17, t (5.8)	5.15, app t (5.6)
3	3.82, d (5.7)	3.81, d (5.8)	3.79, d (5.6)
4	0.75, m	0.75, m	0.72, m
6 α	2.64, ddd (14.5, 9.6, 1.2)	2.63, m	2.62, ddd (14.6, 9.5, 1.2)
6 β	1.35, ddd (14.5, 9.3, 8.0)	1.35, m	1.33, ddd (14.6, 9.5, 8.0)
7 α	2.82, ddd (14.9, 9.6, 9.3)	2.82, m	2.79, m
7 β	2.69, ddd (14.9, 8.0, 1.2)	2.69, m	2.67, ddd (14.9, 8.0, 1.2)
10	3.21, d (8.7)	3.20, d (8.7)	3.18, d (8.7)
15	6.66, s	6.66, s	6.65, s
16	2.30, s	2.30, s	2.28, s
19	0.75, d (7.3)	0.75, s	0.74, d (7.3)
20	5.57, d (5.0)	5.57, d (5.0)	5.55, d (5.0)
13-OH	4.83, brs	4.93, brs	4.71, s

3-2. ^{13}C NMR of cephalolide A

Position	Natural (125 MHz) δc	Gao (Ref. 8) (125 MHz) δc	This work (151 MHz) δc
1	43.8	43.8	43.8
2	80.3	80.1	80.3
3	79.1	79.2	79.2
4	40.5	40.5	40.5
5	47.6	47.7	47.7
6	23.1	23.1	23.1
7	26.8	26.8	26.8
8	134.4	134.4	134.5
9	135.3	135.2	135.4
10	46.3	46.3	46.3
11	144.0	144.0	144.0
12	118.2	118.3	118.2
13	155.1	155.3	155.1
15	114.9	114.9	114.9
16	11.9	11.9	11.9
18	174.8	175.0	174.7
19	15.1	15.1	15.1
20	83.9	84.0	83.9

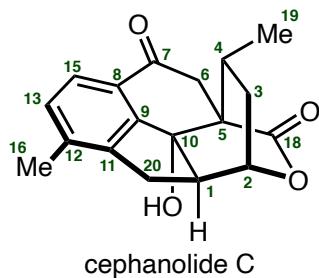


3-3. ^1H NMR of cephalolide B

Position	Natural (400 MHz) δ_{H} (J in Hz)	Zhao (Ref. 6) (600 MHz) δ_{H} (J in Hz)	This work (500 MHz) δ_{H} (J in Hz)
1	3.15, m	3.13, m	3.14, app ddt (17.0, 9.6, 2.2)
2	4.65, m	4.65, m	4.65, overlap
3 α	1.70, dd (14.4, 10.4)	1.70, dd (14.5, 10.3)	1.70, ddd (14.4, 10.3, 1.0)
3 β	1.28, ddd (14.4, 4.6, 1.8)	1.31 – 1.24, m	1.32 – 1.26, m
4	1.18, m	1.18, m	1.18, dqd (10.1, 7.1, 3.5)
6 α , β	2.12 – 2.05, m (2H)	2.11 – 1.98, m (2H)	2.12 – 2.00, m (2H)
7 α	2.96, dd (17.5, 9.0)	2.96, dd (17.4, 9.6)	2.97, dd (17.4, 9.3)
7 β	2.56, overlap	2.59 – 2.47, overlap	2.61 – 2.52, overlap
10	3.23, d (9.3)	3.24, dd (17.5, 9.7)	3.23, d (9.6)
15	6.46, s	6.48, s	6.47, s
16	2.13, s	2.13, s	2.13, s
19	0.81, d (7.1)	0.81, d (7.1)	0.81, d (7.1)
20 α	3.24, dd (15.0, 9.6)	3.24, dd (17.5, 9.7)	3.24, dd (15.0, 9.6)
20 β	2.56, overlap	2.59 – 2.47, overlap	2.61 – 2.52, overlap
13-OH		4.83, brs	4.65, overlap

3-4. ^{13}C NMR of cephalolide B

Position	Natural (125 MHz) δc	Zhao (Ref. 6) (151 MHz) δc	This work (126 MHz) δc
1	39.6	39.7	39.7
2	79.2	79.3	79.2
3	28.8	28.9	28.8
4	26.5	26.5	26.5
5	45.9	45.9	45.9
6	23.1	23.1	23.1
7	24.1	24.1	24.1
8	132.7	132.7	132.7
9	132.3	132.3	132.3
10	47.5	47.5	47.5
11	141.9	141.8	141.9
12	117.7	117.8	117.7
13	154.2	154.4	154.3
15	112.8	112.8	112.8
16	12.3	12.3	12.3
18	177.2	177.3	177.2
19	19.5	19.5	19.5
20	33.0	33.0	33.0

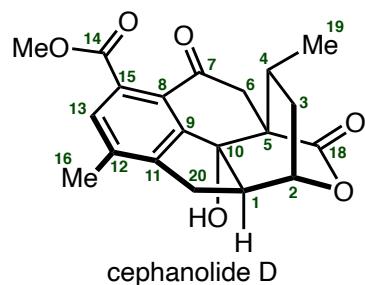


3-5. ^1H NMR of cephanolide C

Position	Natural (400 MHz) δ_{H} (J in Hz)	Zhao (Ref. 6) (600 MHz) δ_{H} (J in Hz)	This work (500 MHz) δ_{H} (J in Hz)
1	3.01, m	3.01, m	3.01, dddd (9.3, 4.7, 3.1, 1.8)
2	4.89, m	4.90 – 4.87, m	4.90, app td (4.7, 1.2)
3 α	1.85, dd (14.8, 10.2)	1.86, dd (14.8, 10.2)	1.86, ddd (14.8, 10.2, 1.2)
3 β	1.37, ddd (14.8, 4.7, 1.8)	1.37, m	1.37, app dtd (14.8, 4.7, 1.9)
4	1.20, m	1.20, m	1.21, dqd (10.2, 7.0, 4.7)
6 α	3.43, d (18.4)	3.43, dd (18.4, 1.7)	3.43, dd (18.5, 1.8)
6 β	2.61, d (18.4)	2.61, dd (18.5, 1.7)	2.61, d (18.5)
13	7.33, d (7.7)	7.33, d (7.7)	7.33, d (7.7)
15	7.55, d (7.7)	7.55, d (7.7)	7.55, d (7.7)
16	2.38, s	2.38, s	2.38, s
19	0.83, d (7.1)	0.83, dd (7.1, 1.7)	0.83, d (7.0)
20 α	3.48, dd (17.7, 9.6)	3.47, dd (17.6, 9.3)	3.47, dd (17.6, 9.3)
20 β	2.71, dd (17.7, 2.9)	2.72, dt (17.6, 2.2)	2.71, dd (17.6, 3.1)

3-6. ^{13}C NMR of cephalolide C

Position	Natural (125 MHz) δc	Zhao (Ref. 6) (151 MHz) δc	This work (126 MHz) δc
1	49.9	49.7	49.7
2	80.7	80.7	80.7
3	29.7	29.7	29.7
4	31.4	31.4	31.4
5	54.8	54.8	54.8
6	37.3	37.4	37.3
7	198.3	198.2	198.3
8	129.2	129.2	129.2
9	147.2	147.2	147.2
10	82.7	82.7	82.7
11	142.3	142.3	142.3
12	143.5	143.5	143.5
13	132.6	132.6	132.6
15	125.7	125.7	125.7
16	19.2	19.2	19.2
18	175.9	175.8	175.9
19	19.5	19.5	19.5
20	32.0	32.0	32.0



3-7. ^1H NMR of cephalolide D

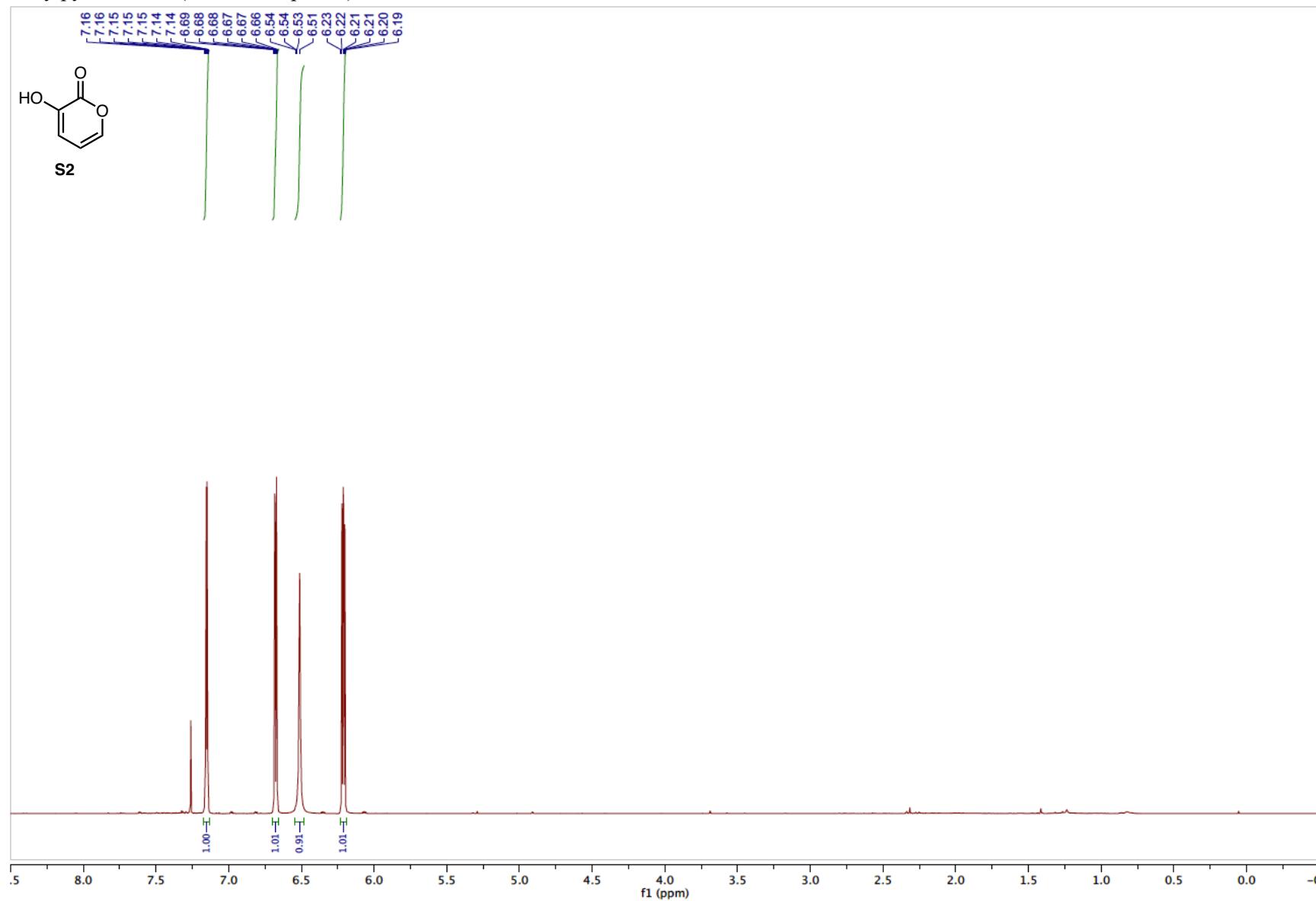
Position	Natural (400 MHz) δ_{H} (<i>J</i> in Hz)	This work (600 MHz) δ_{H} (<i>J</i> in Hz)
1	3.10, m	3.11, br-s
2	4.87, m	4.87, app t (4.6)
3 α	1.76, dd (14.7, 10.2)	1.76, dd (14.7, 10.2)
3 β	1.47, ddd (14.7, 4.6, 1.7)	1.47, dd (14.7, 4.6)
4	1.34, m	1.33, m
6 α	3.54, d (18.6)	3.54, d (18.6)
6 β	2.74, d (18.6)	2.74, d (18.6)
13	7.31, s	7.30, s
16	2.37, s	2.36, s
19	0.91, d (7.0)	0.92, d (7.0)
20 α	3.51, dd (17.8, 9.5)	3.51, br-d (17.6)
20 β	2.61, dd (17.8, 3.0)	2.61, br-d (17.6)
14-OMe	3.93, s	3.92, s

3-8. ^{13}C NMR of cephalolide D

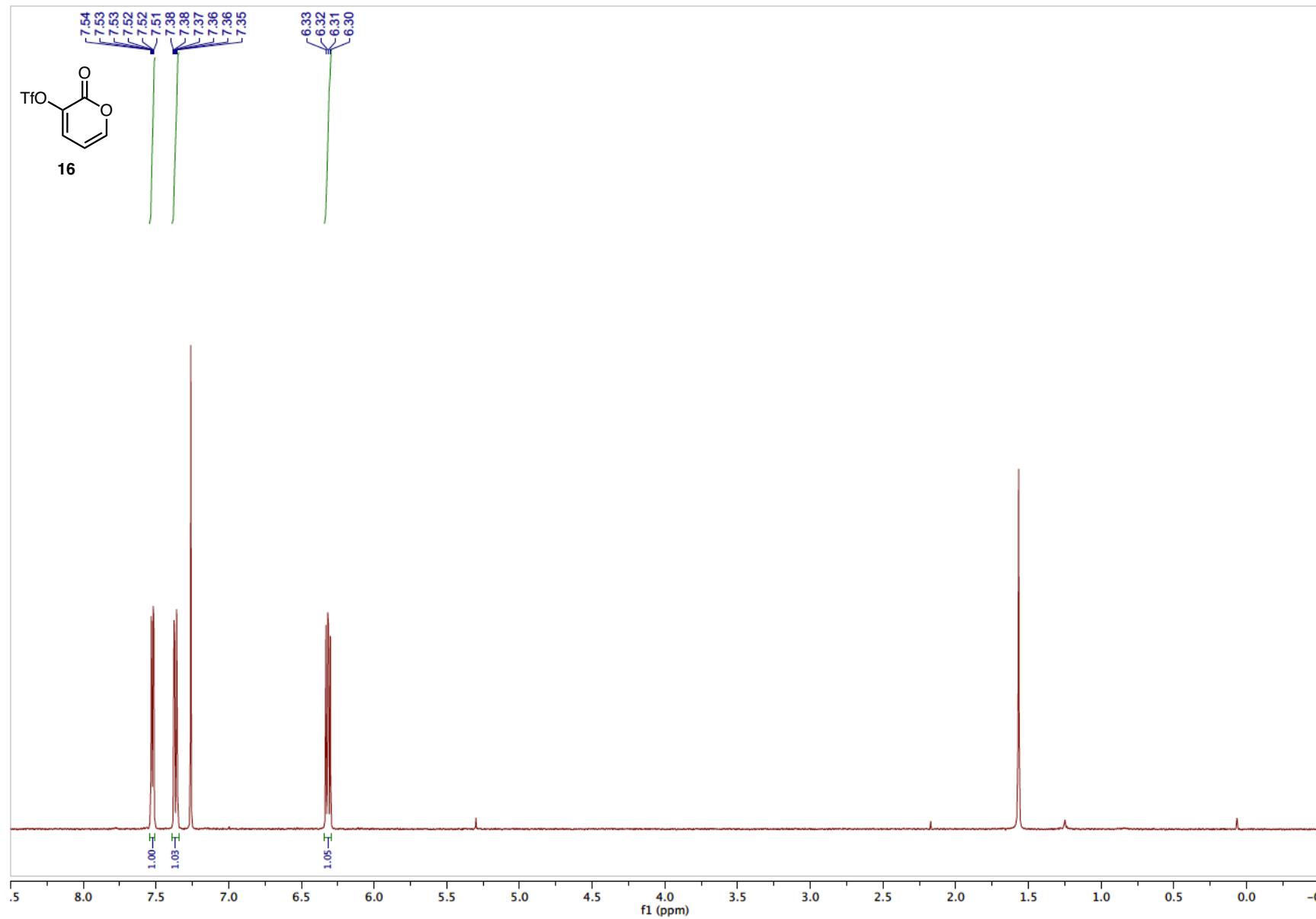
Position	Natural (125 MHz) δc	This work (151 MHz) δc
1	48.8	48.9
2	78.5	78.5
3	28.7	28.8
4	30.6	30.6
5	53.2	53.1
6	36.7	36.7
7	194.1	194.0
8	125.1	125.2
9	145.3	145.3
10	82.5	82.5
11	142.2	142.2
12	141.7	141.7
13	131.1	131.2
14	169.3	169.3
15	132.1	132.0
16	19.3	19.3
18	172.6	172.5
19	19.6	19.6
20	31.5	31.5
14-OMe	53.2	53.2

4. ^1H and ^{13}C NMR spectra

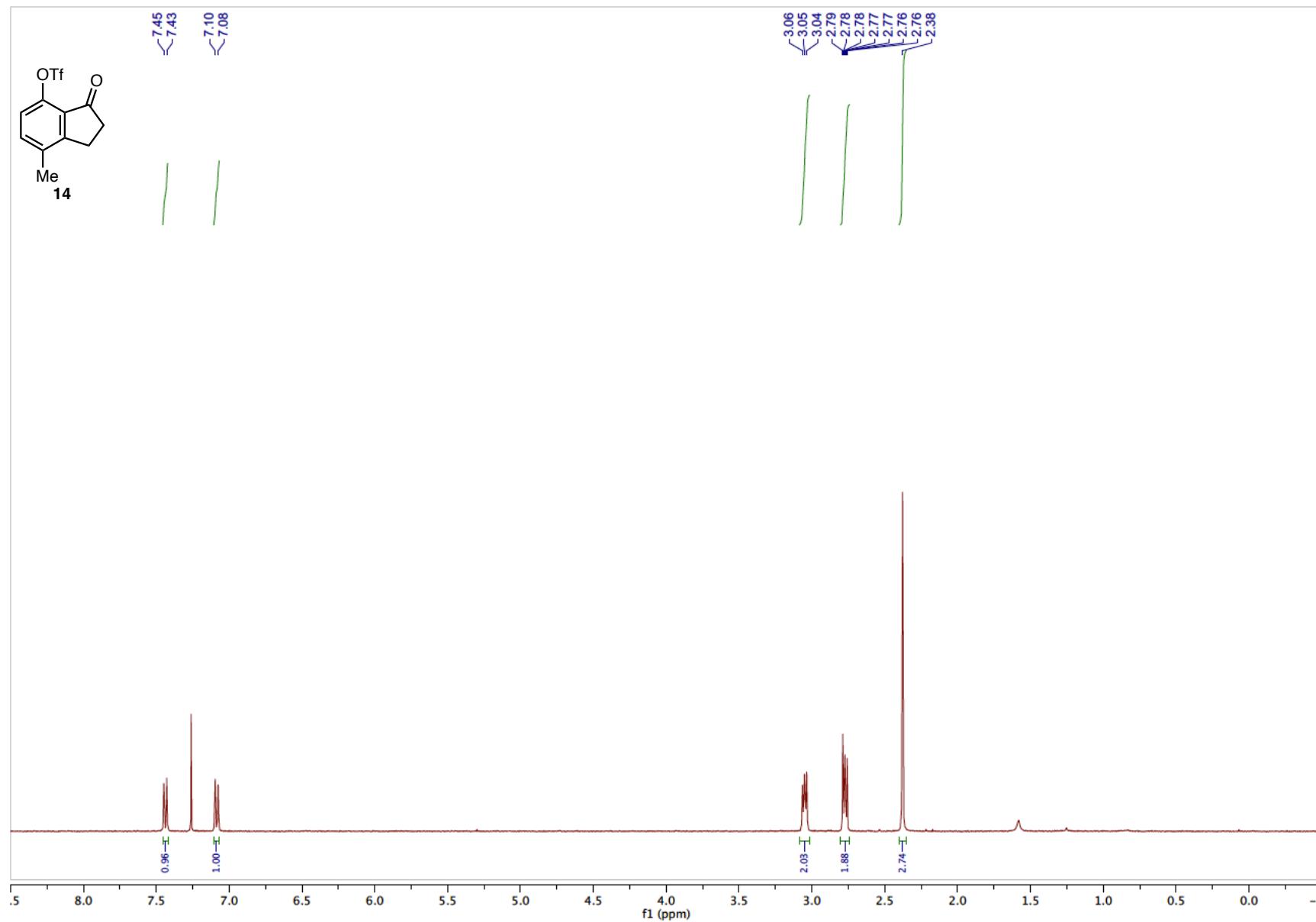
3-Hydroxy pyranone **S2** (known compound): ^1H NMR



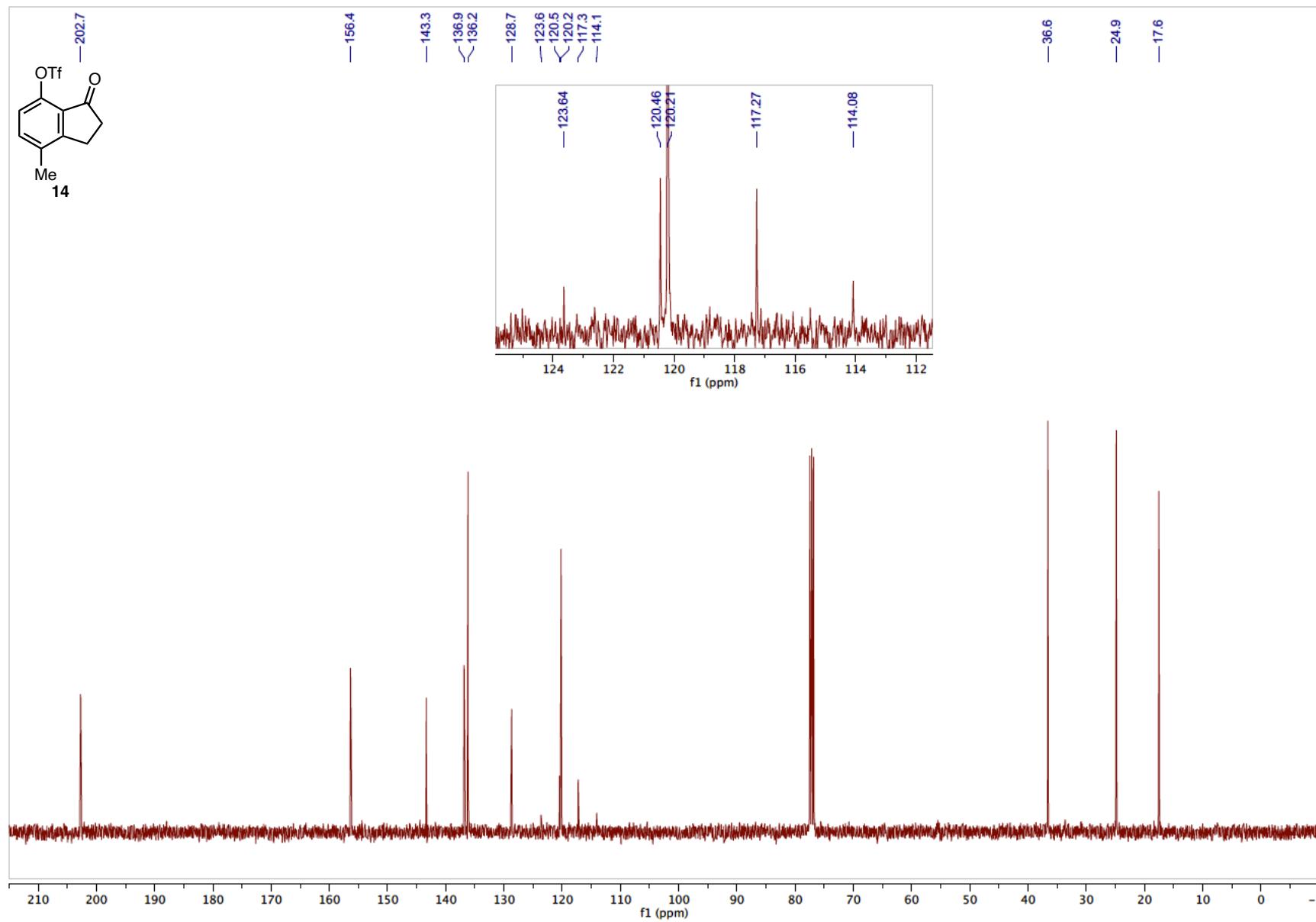
Pyranone 3-triflate **16** (known compound): ^1H NMR



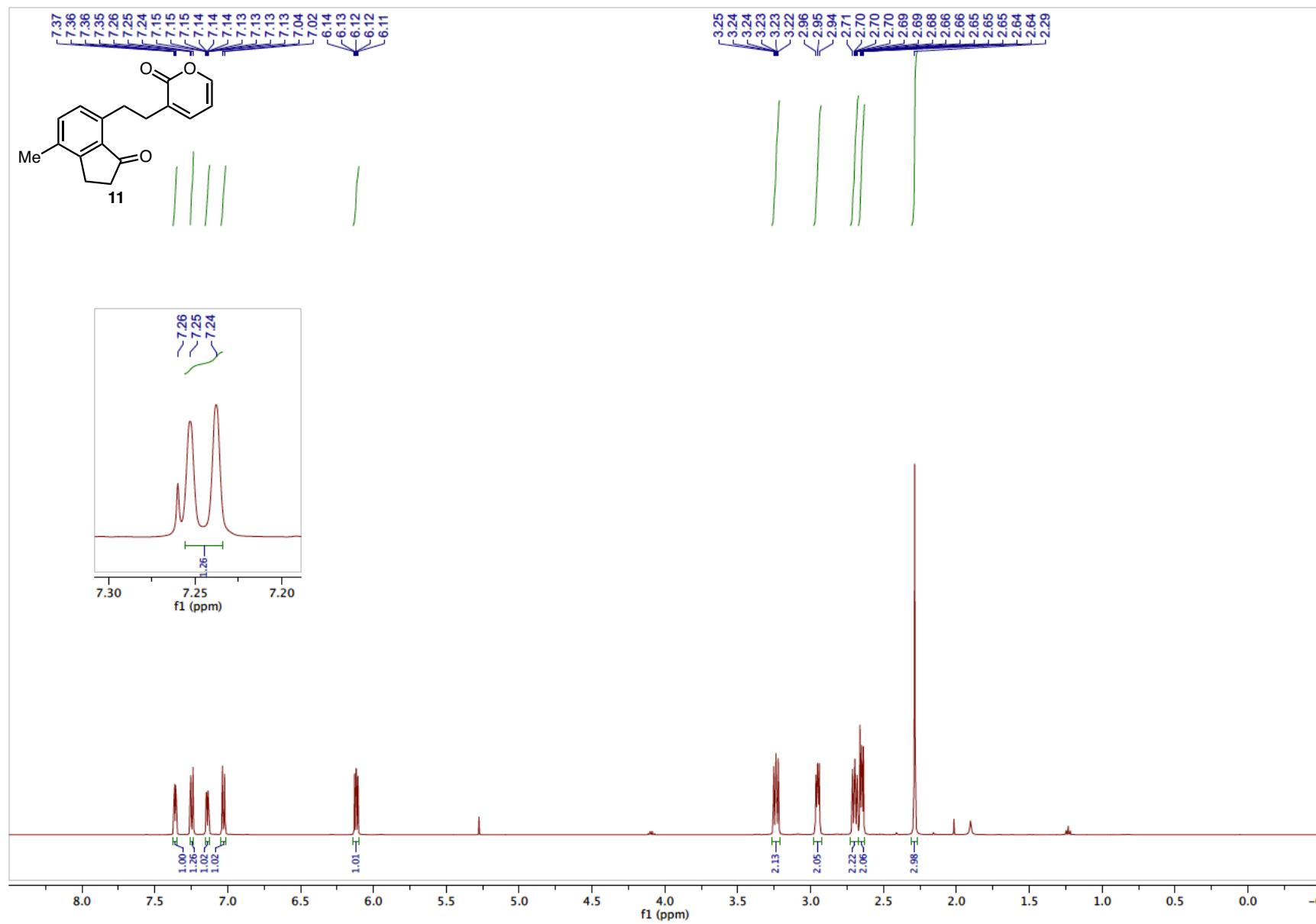
Indanone 7-triflate **14**: ^1H NMR



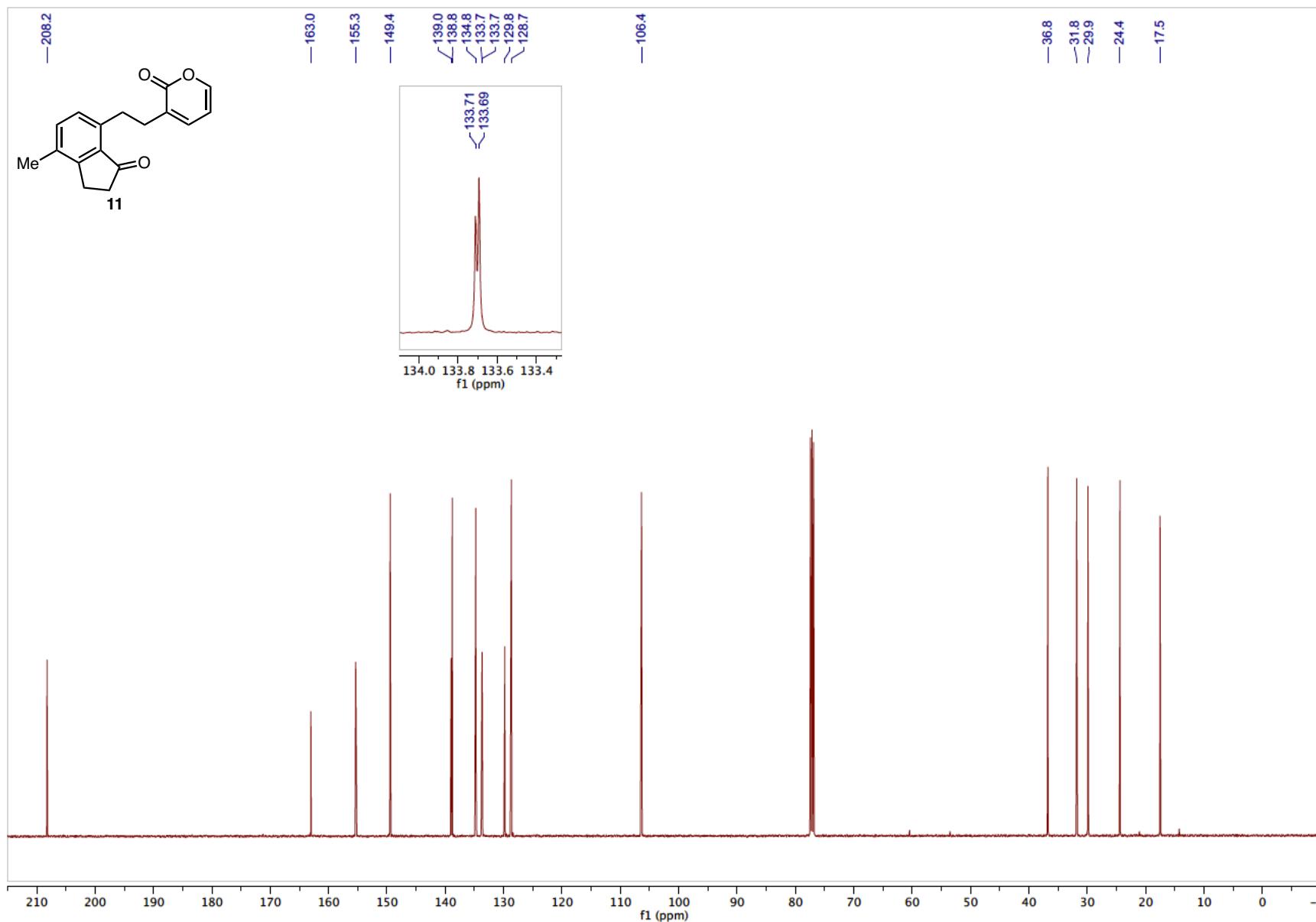
Indanone 7-triflate **14**: ^{13}C NMR



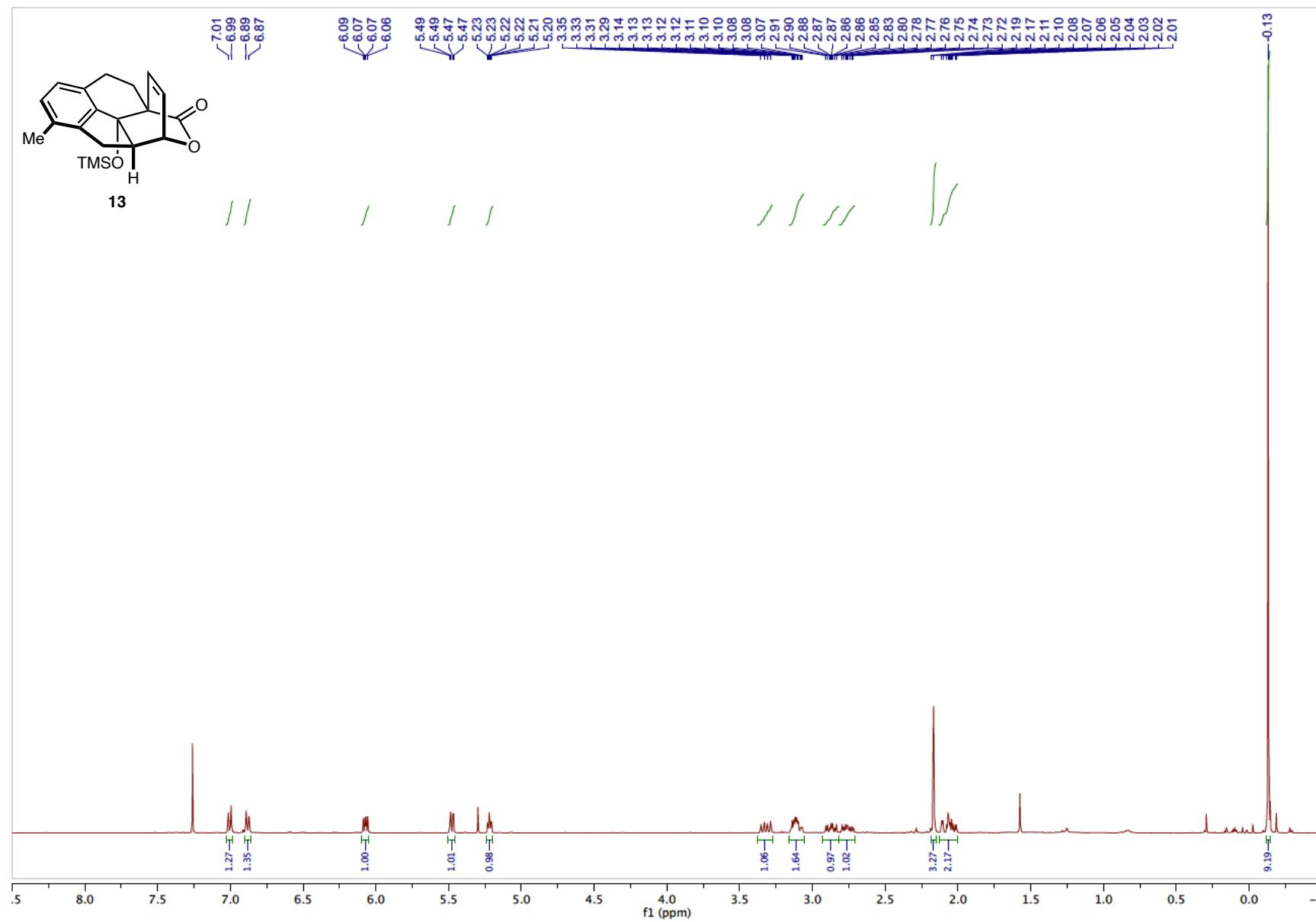
Indanone 7-ethylpyranone **11**: ^1H NMR



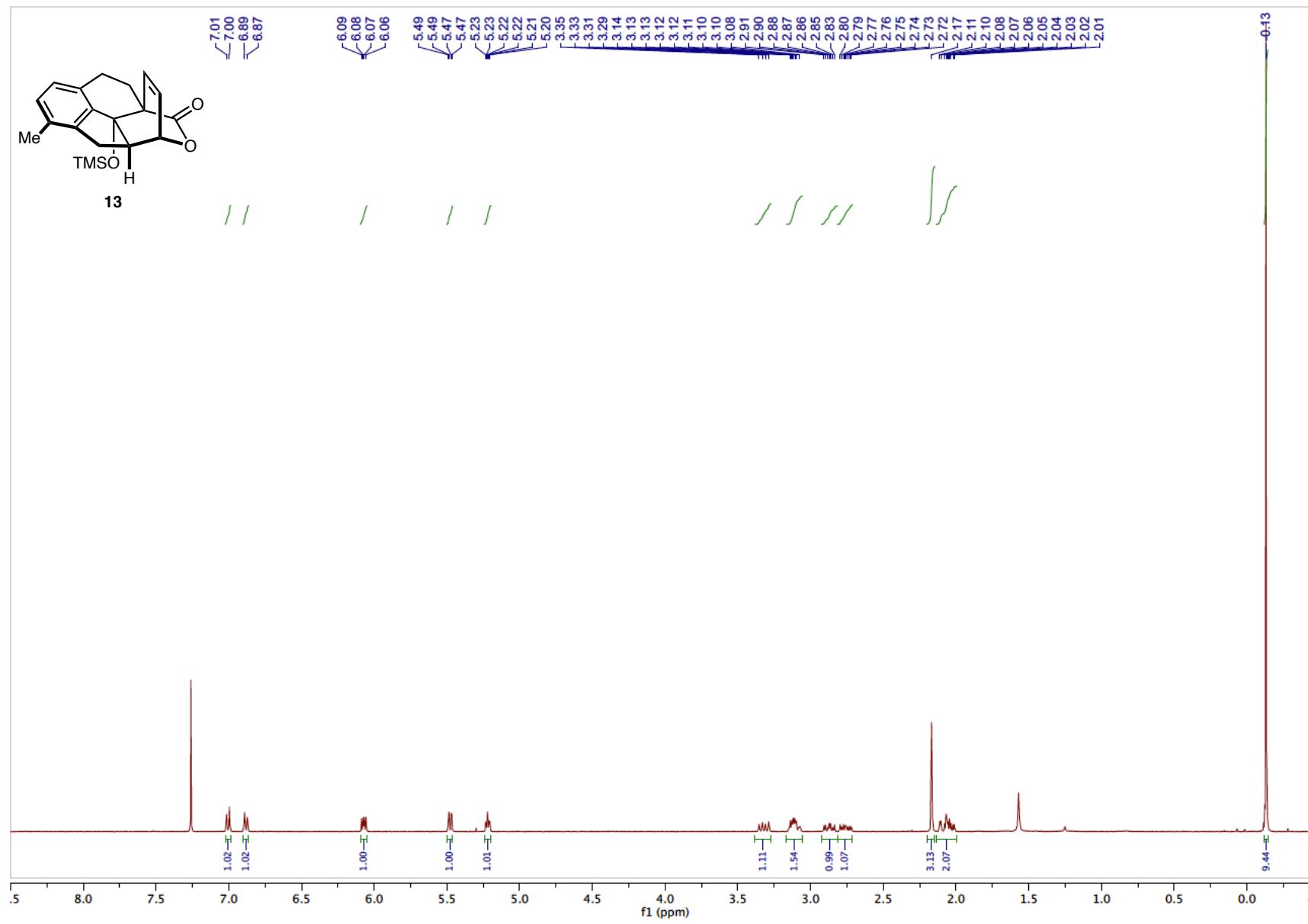
Indanone 7-ethylpyranone **11**: ^{13}C NMR



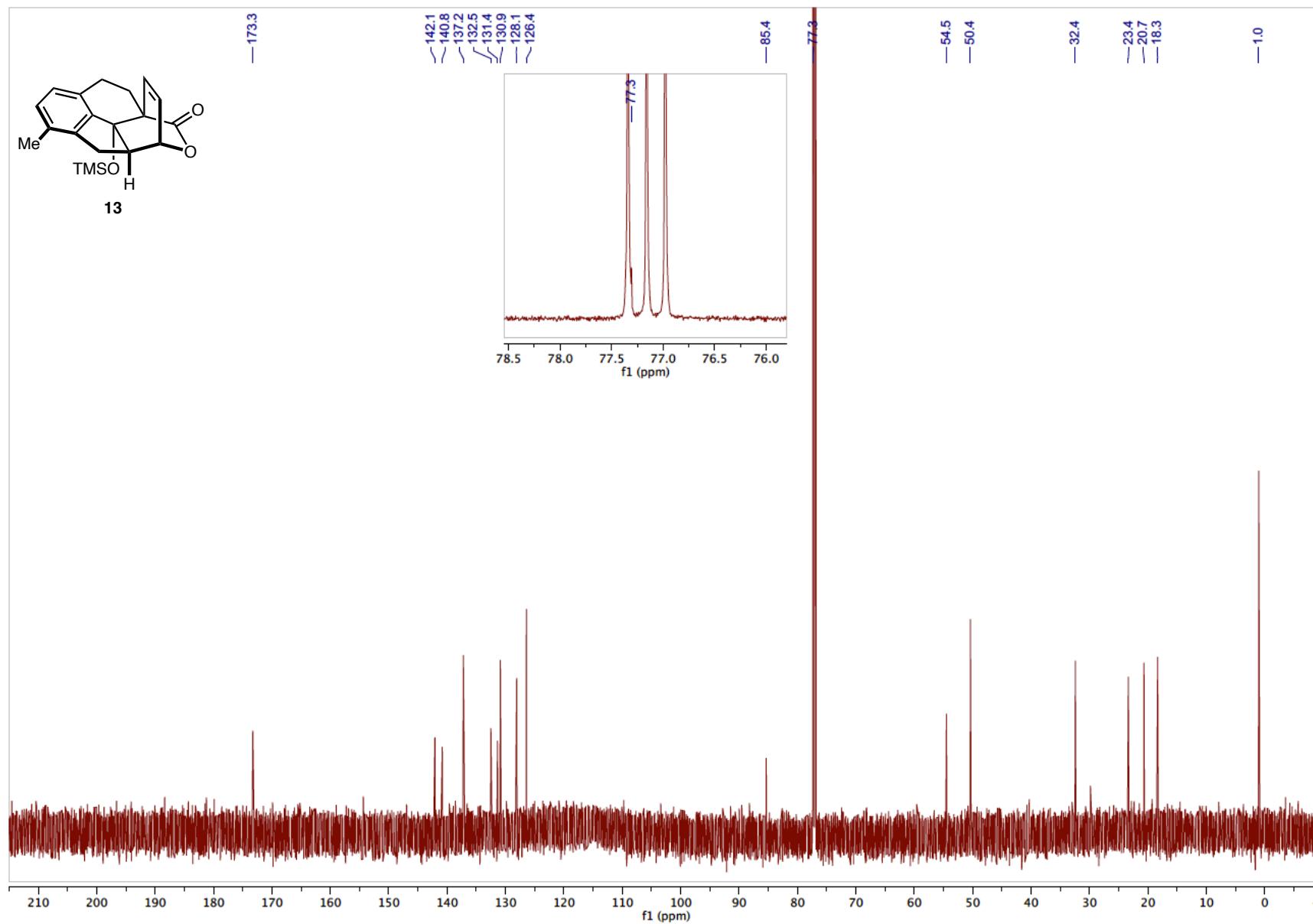
Pentacyclic olefin **13**: ^1H NMR (after a short plug of silica gel)



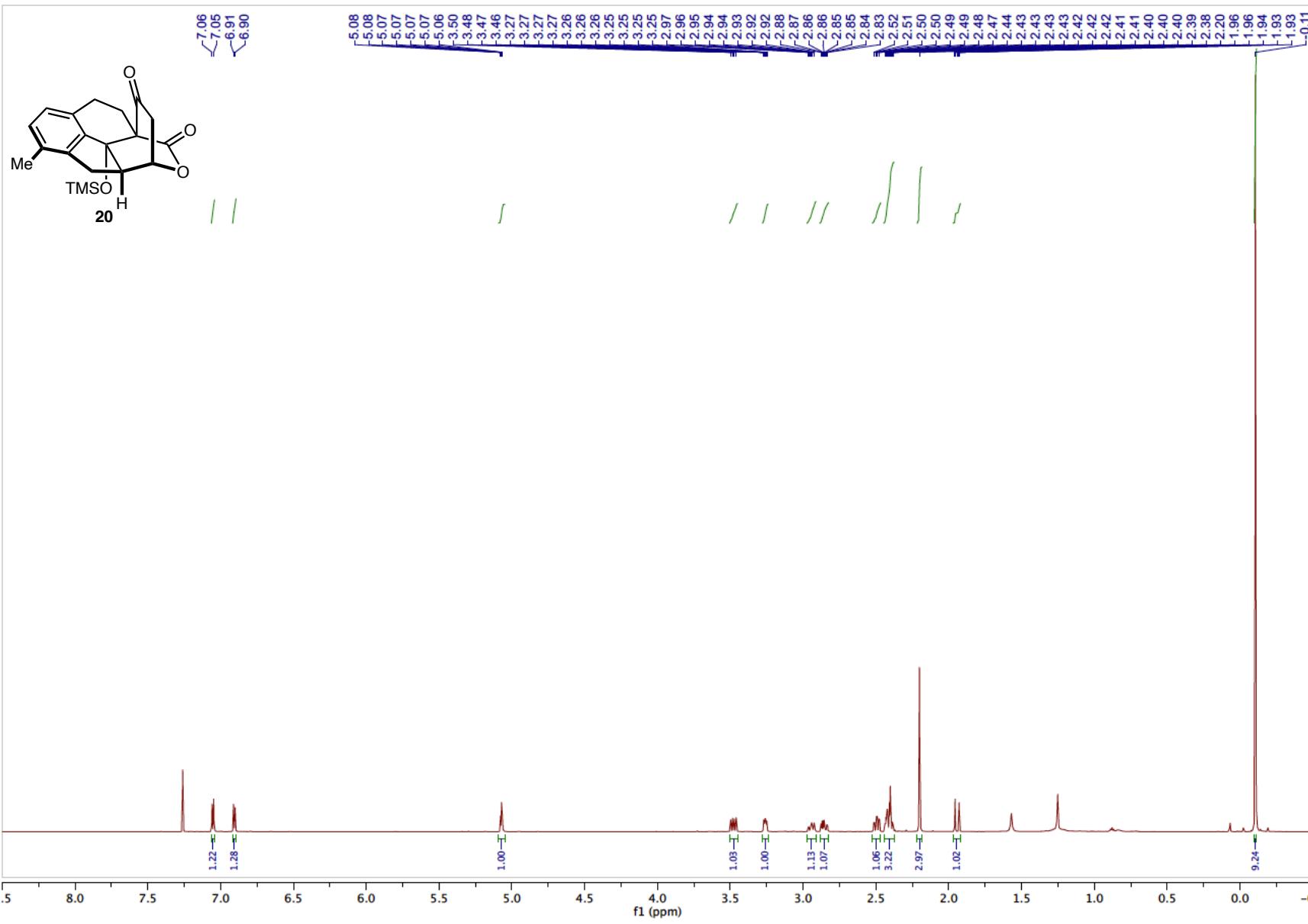
Pentacyclic olefin **13**: ^1H NMR (after silica gel column chromatography)



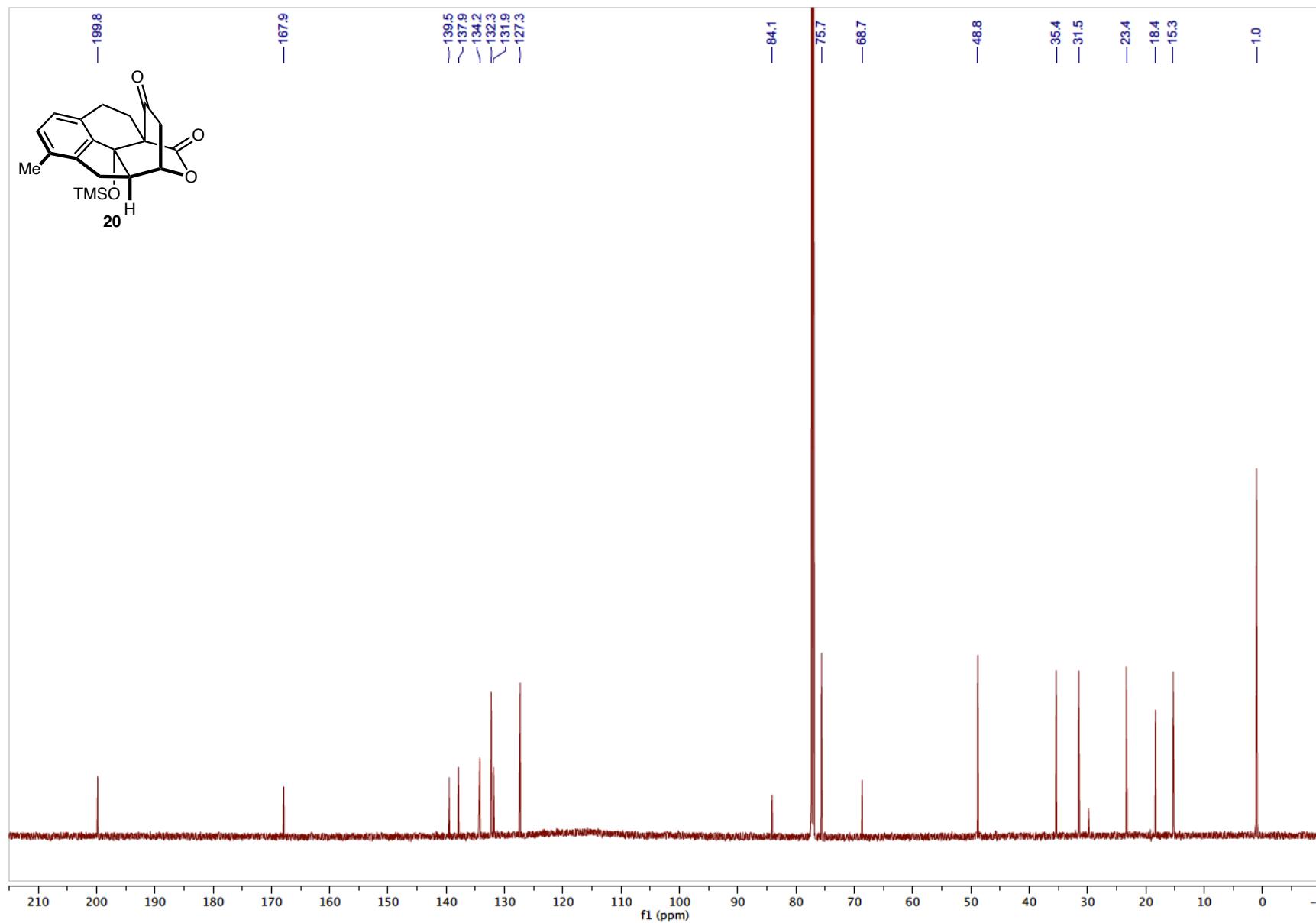
Pentacyclic olefin **13**: ^{13}C NMR



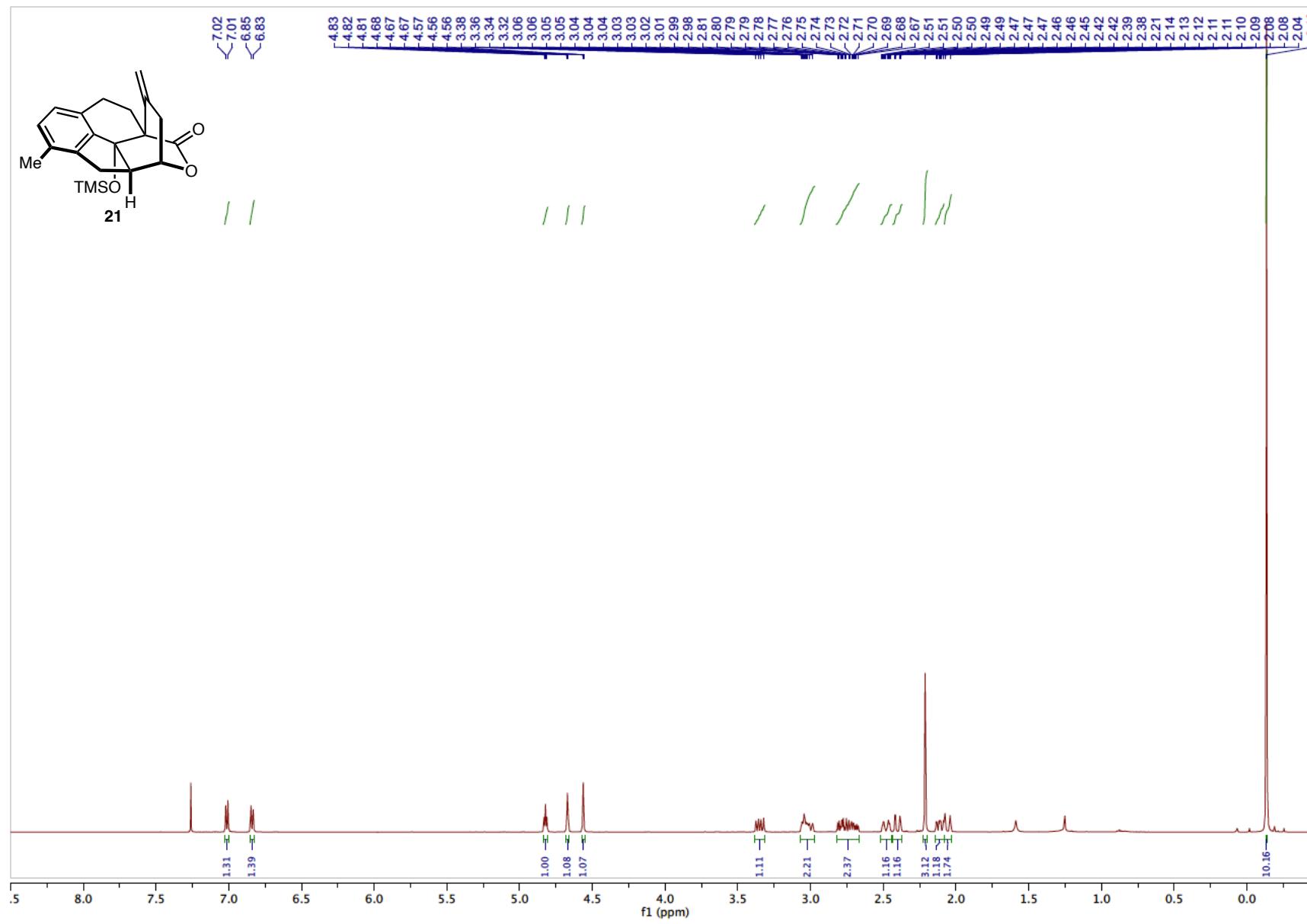
Pentacyclic ketone **20**: ^1H NMR



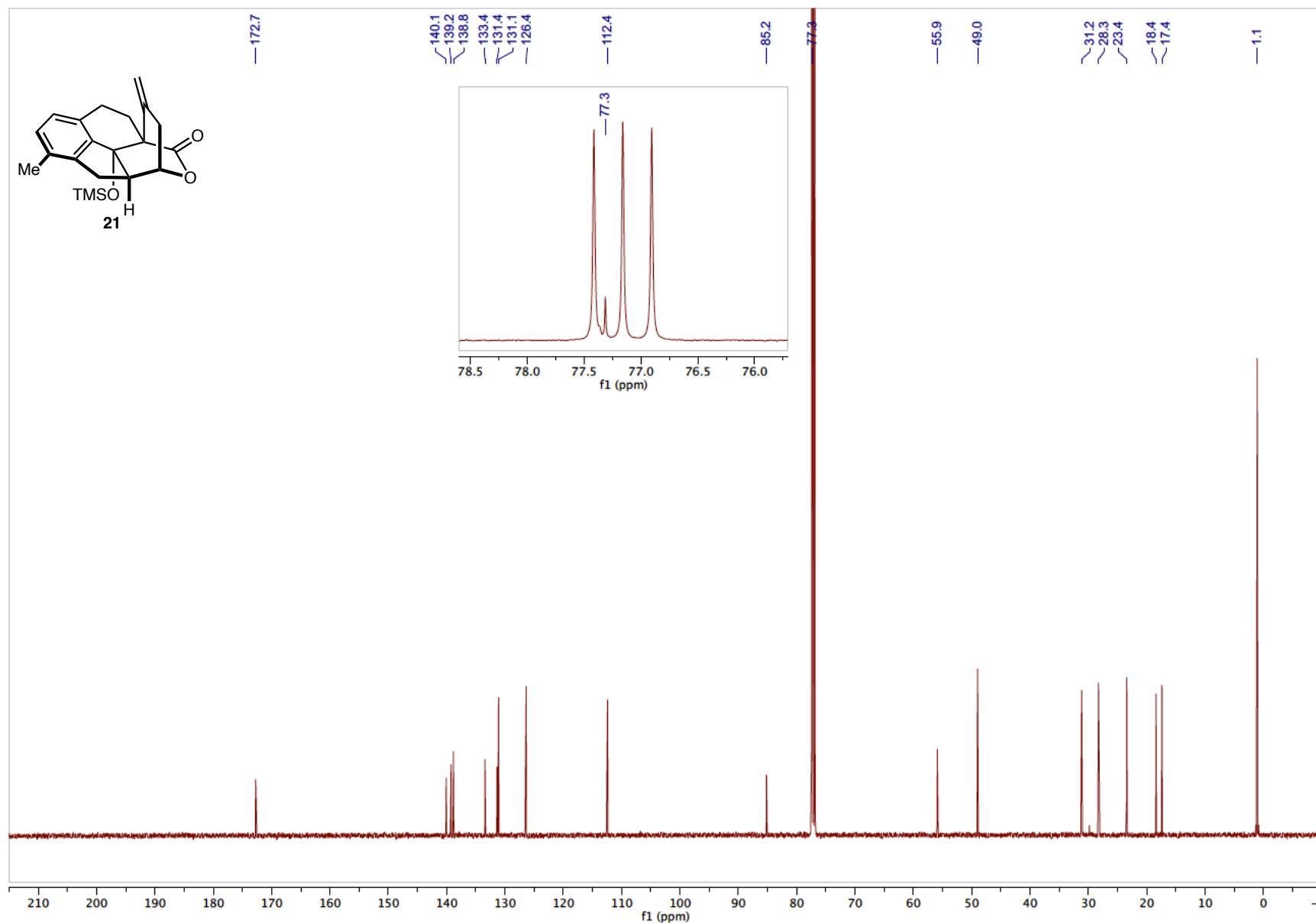
Pentacyclic ketone **20**: ^{13}C NMR



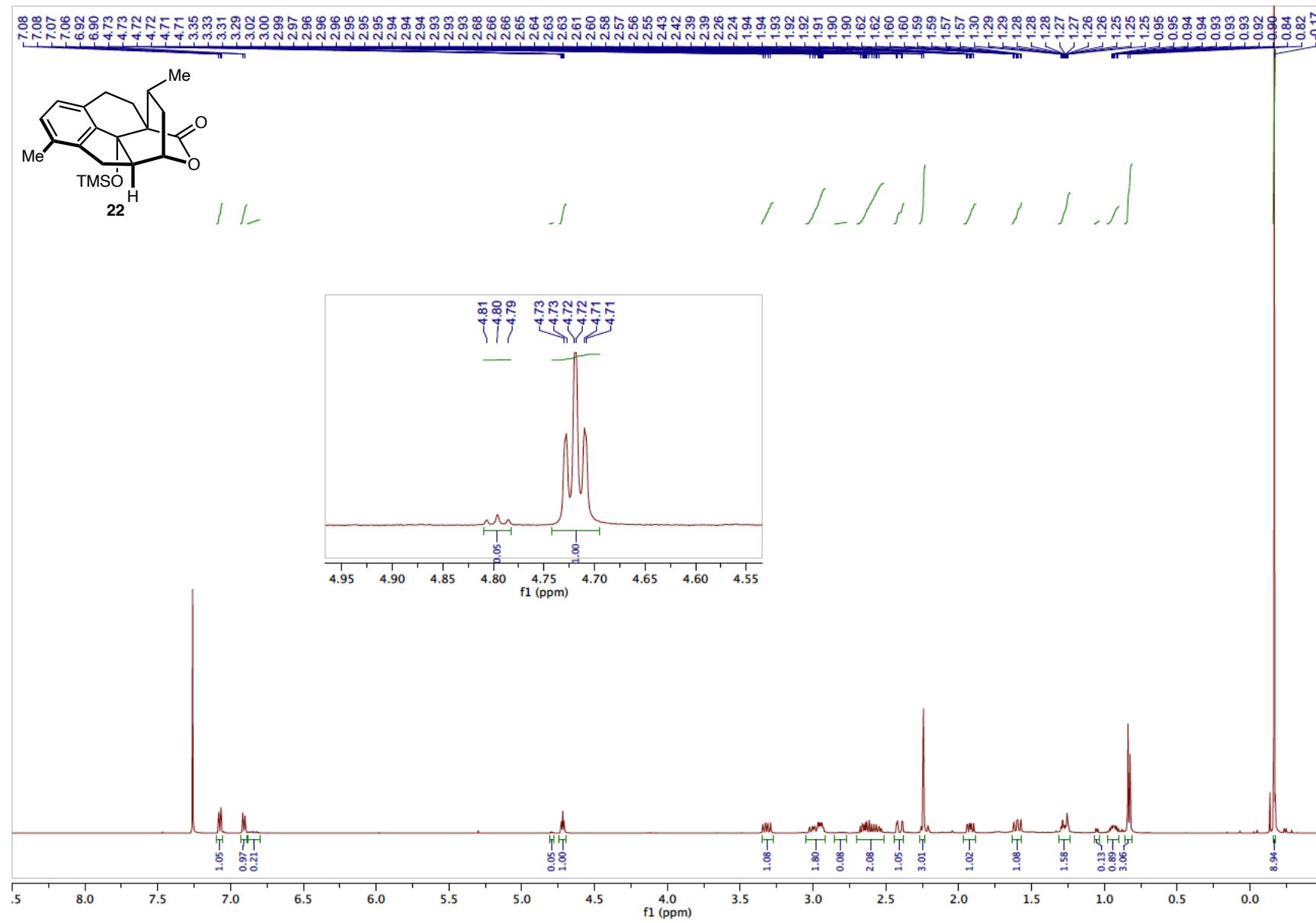
Exo-olefin **21**: ^1H NMR



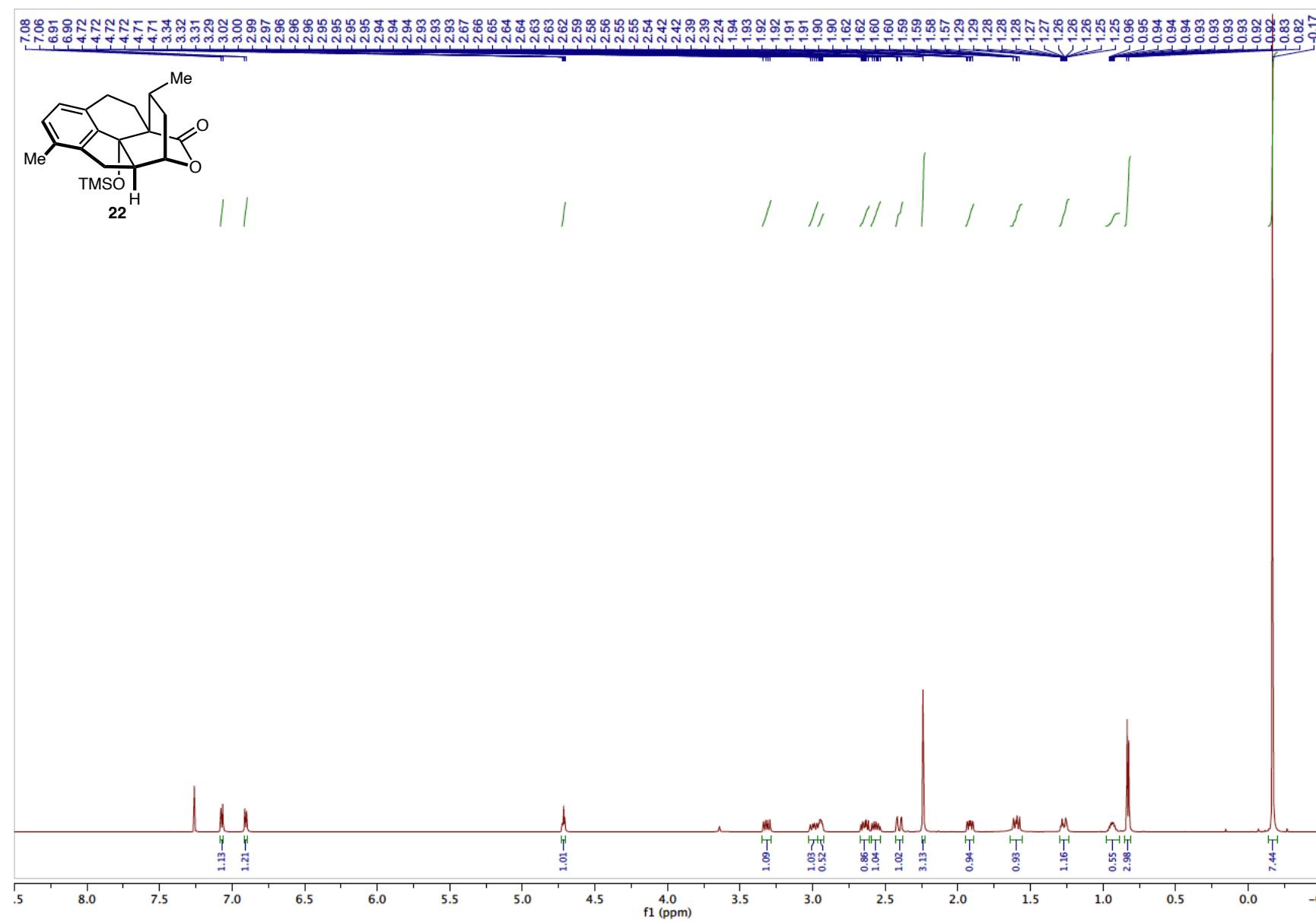
Exo-olefin **21**: ^{13}C NMR



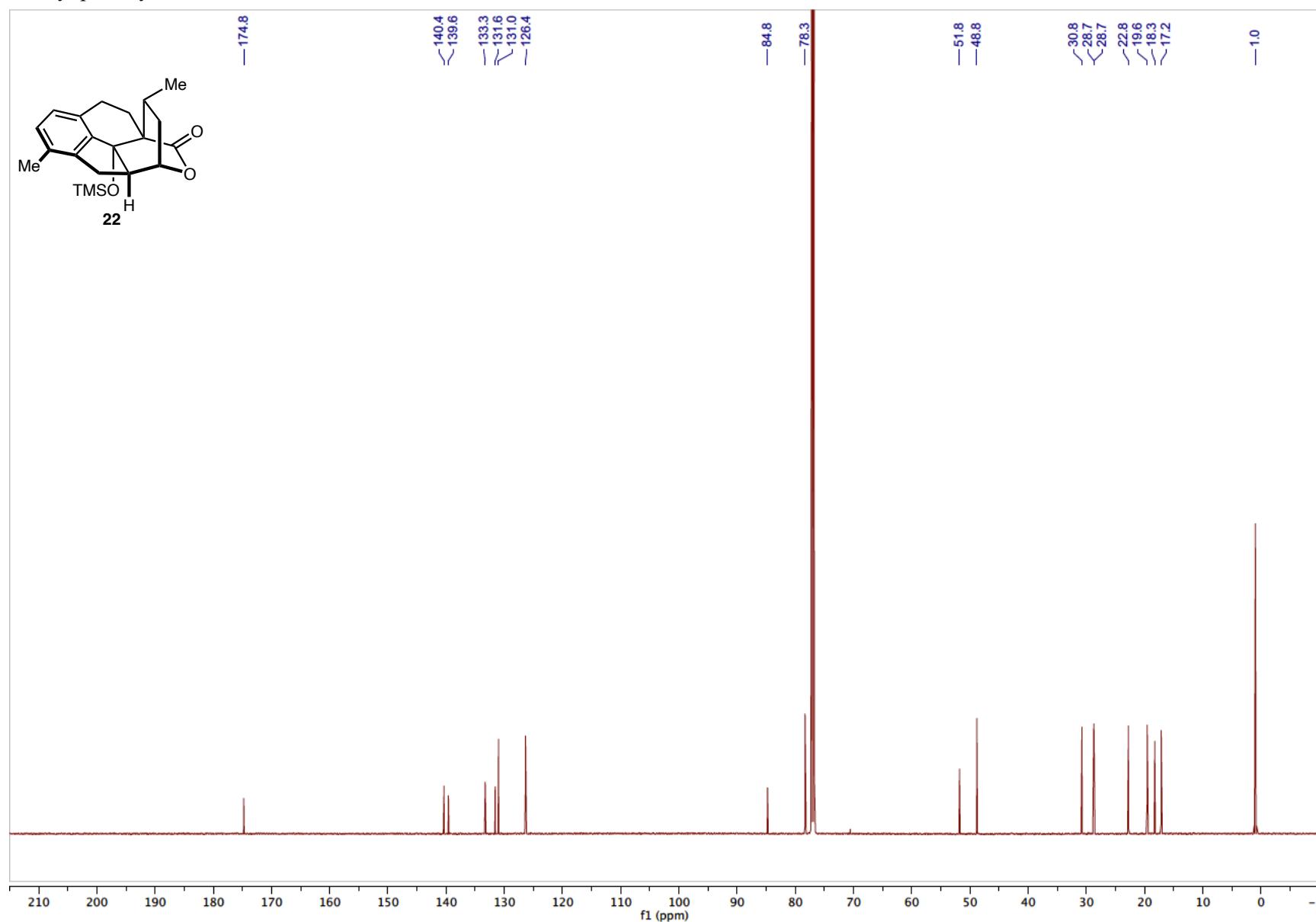
(*exo*)-Methyl pentacycle **22**: ^1H NMR (*d.r.* = >20:1)



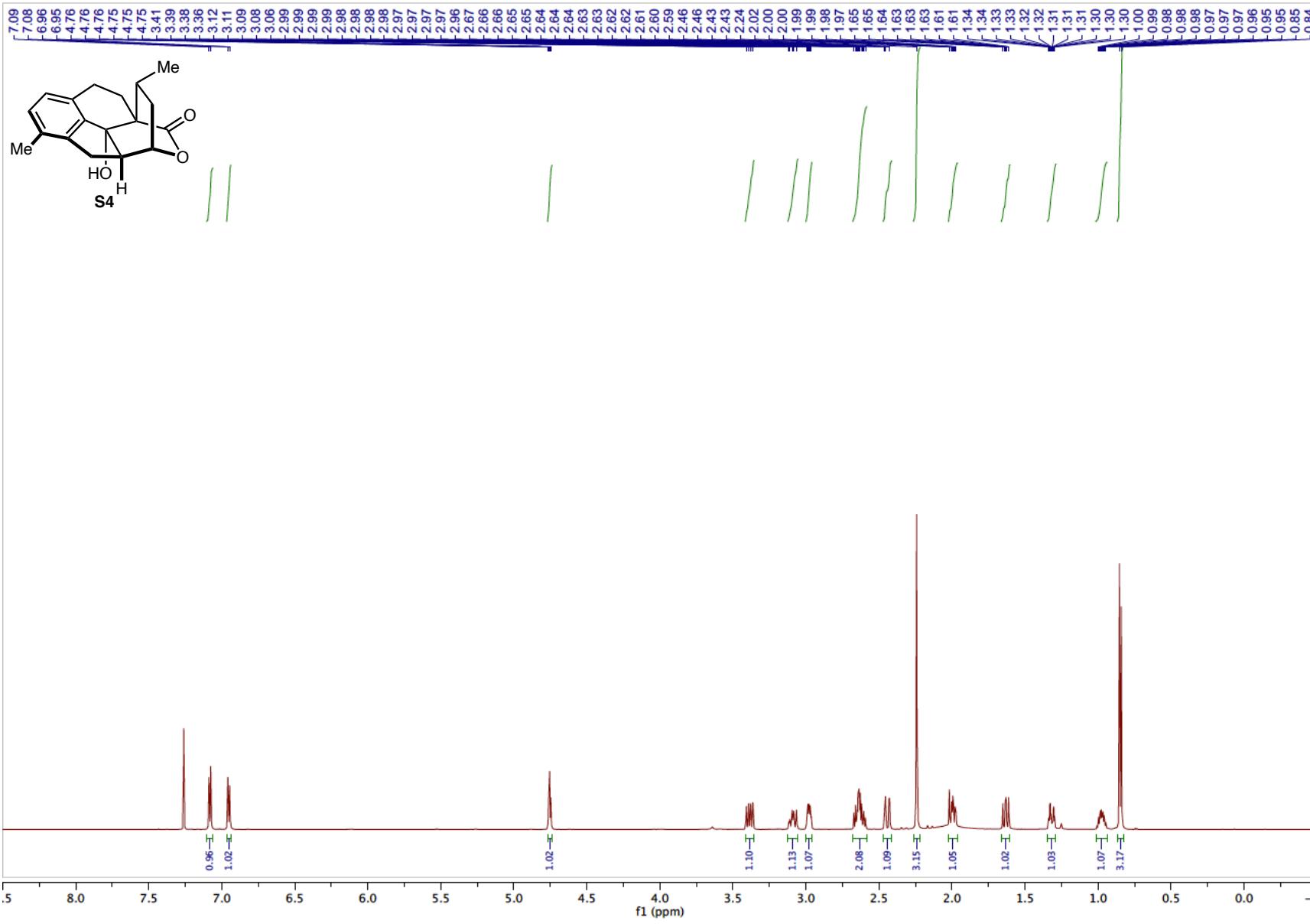
(*exo*)-Methyl pentacycle **22**: ^1H NMR (pure)



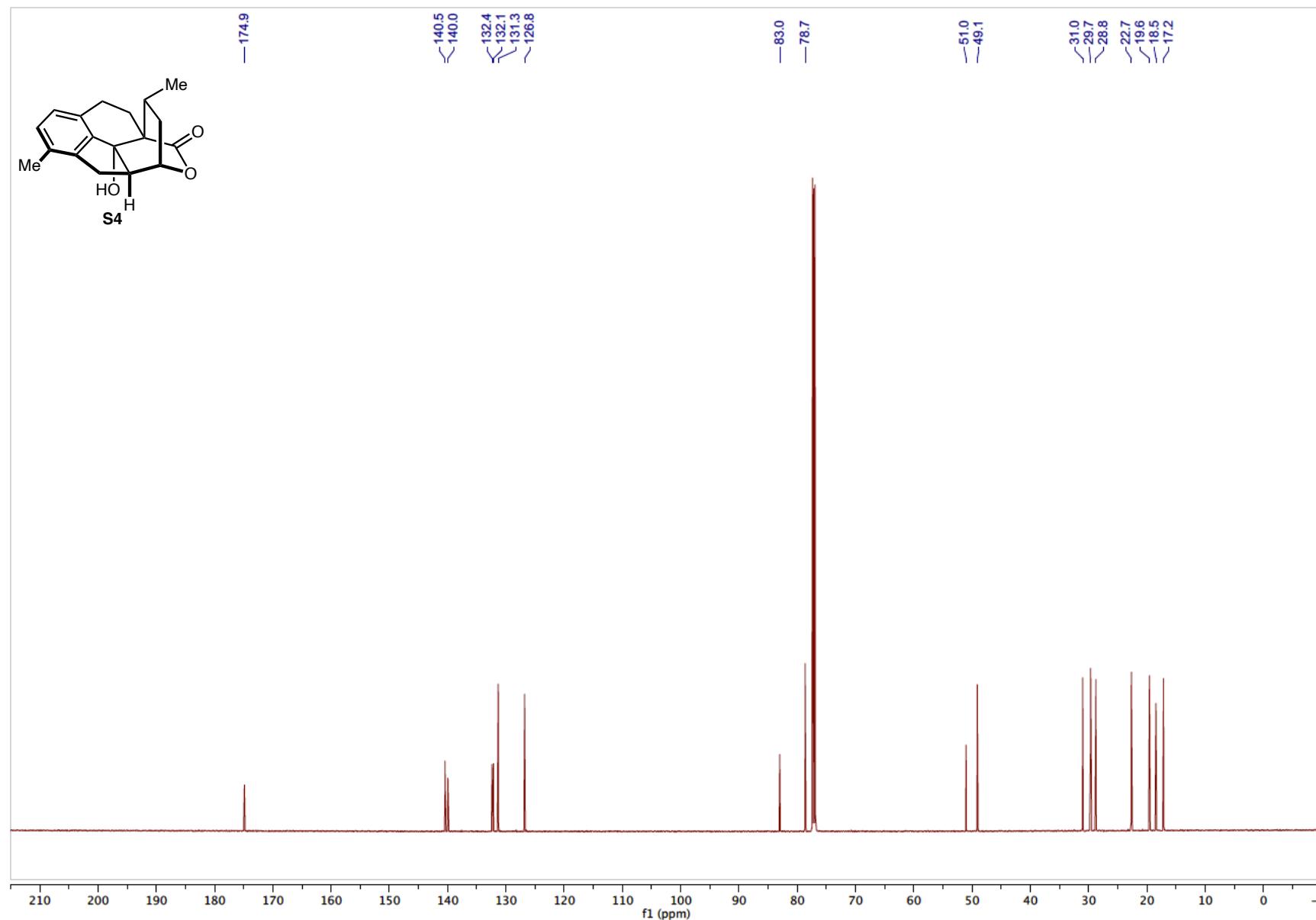
(*exo*)-Methyl pentacycle **22**: ^{13}C NMR



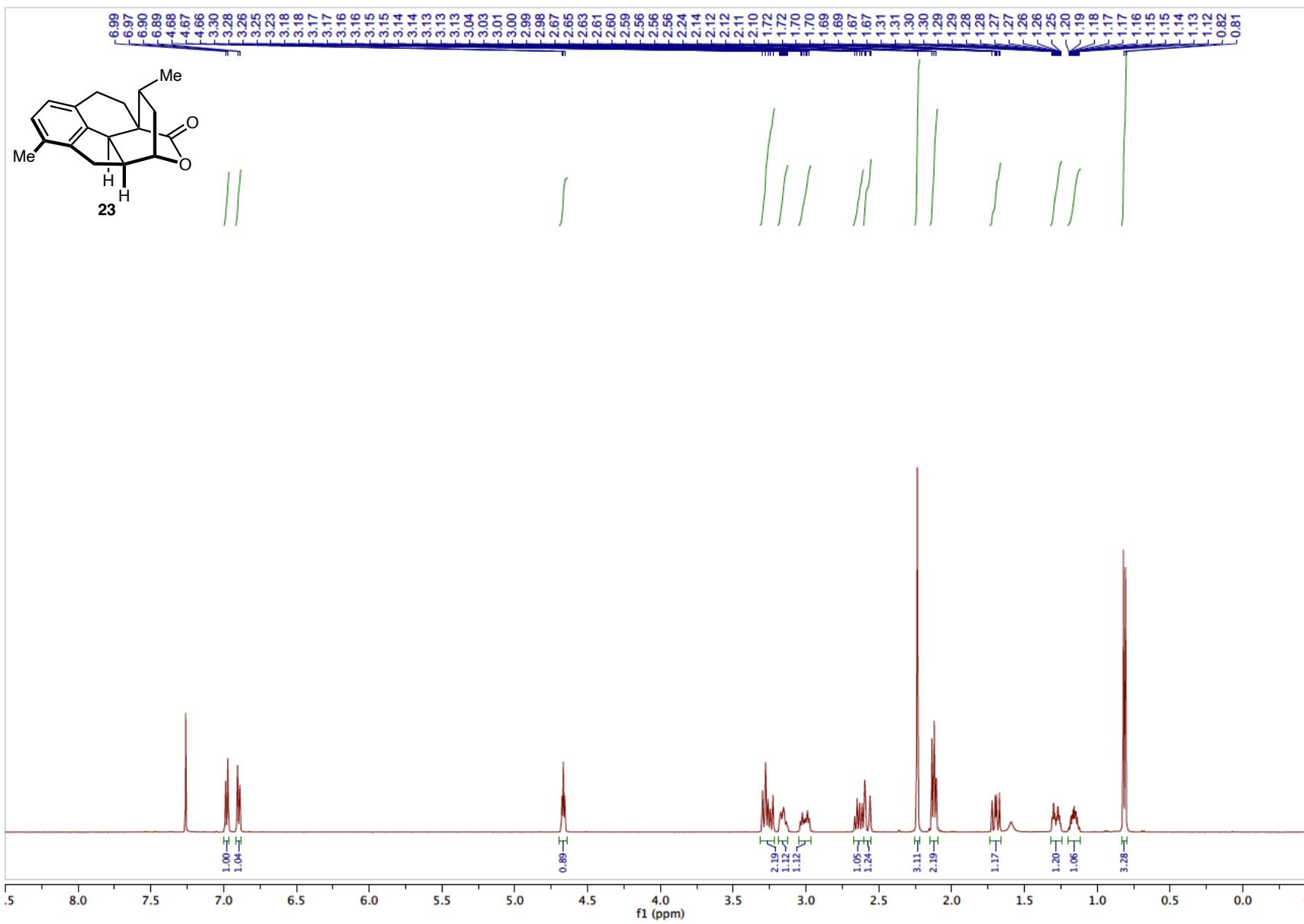
Pentacyclic alcohol S4: ^1H NMR



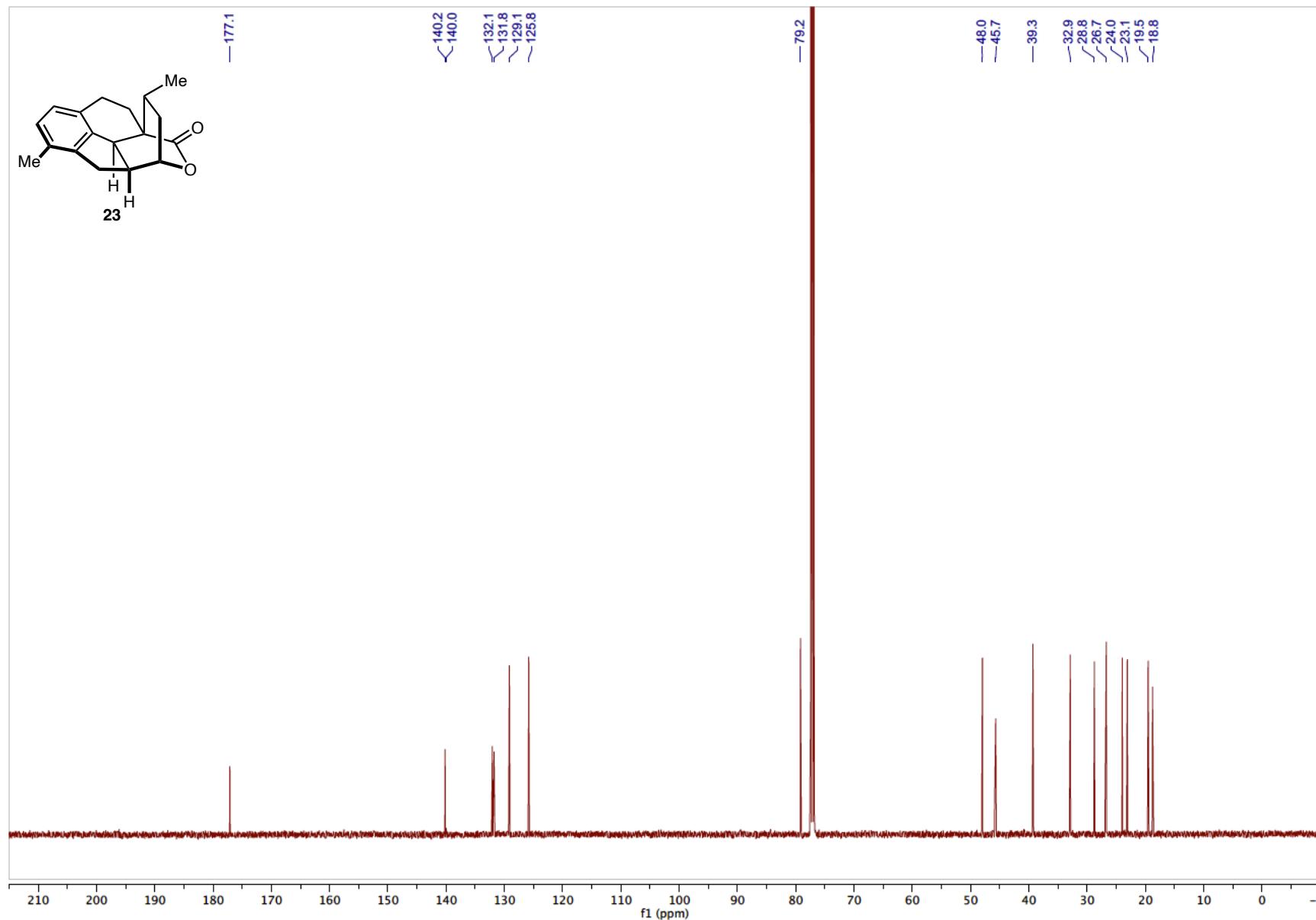
Pentacyclic alcohol S4: ^{13}C NMR



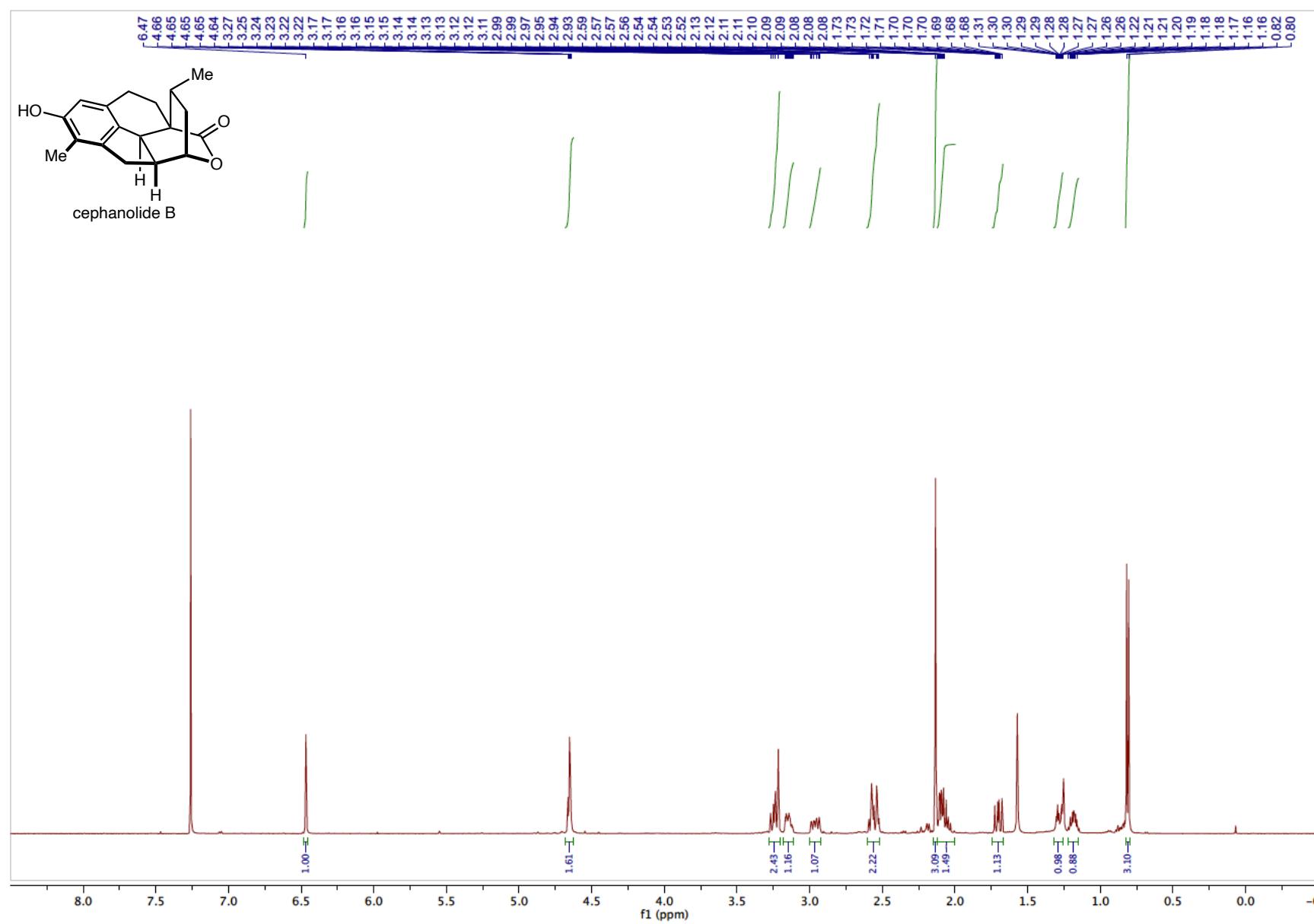
Deoxygenated pentacycle **23**: ^1H NMR



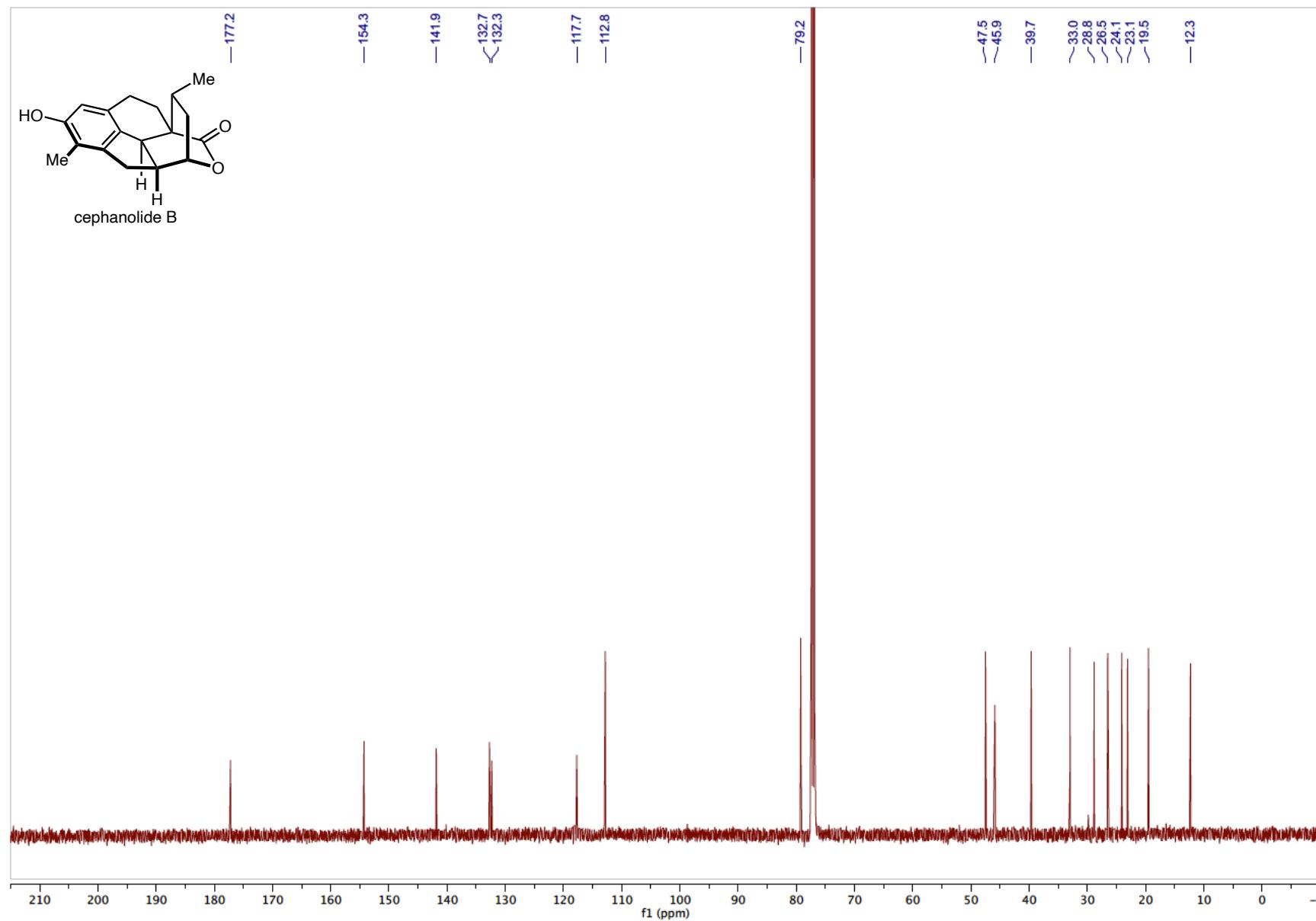
Deoxygenated pentacycle **23**: ^{13}C NMR



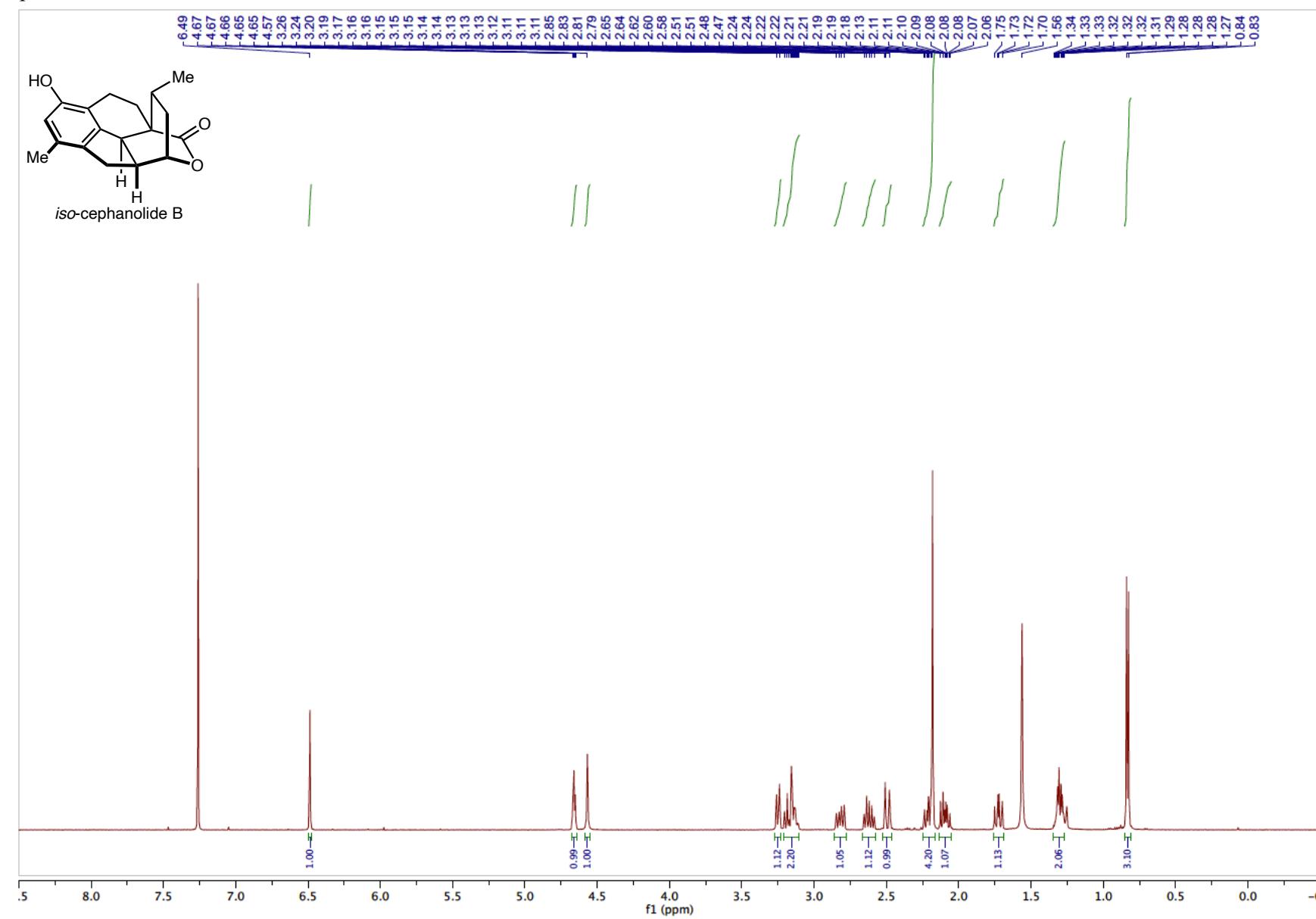
Cephalolide B: ^1H NMR



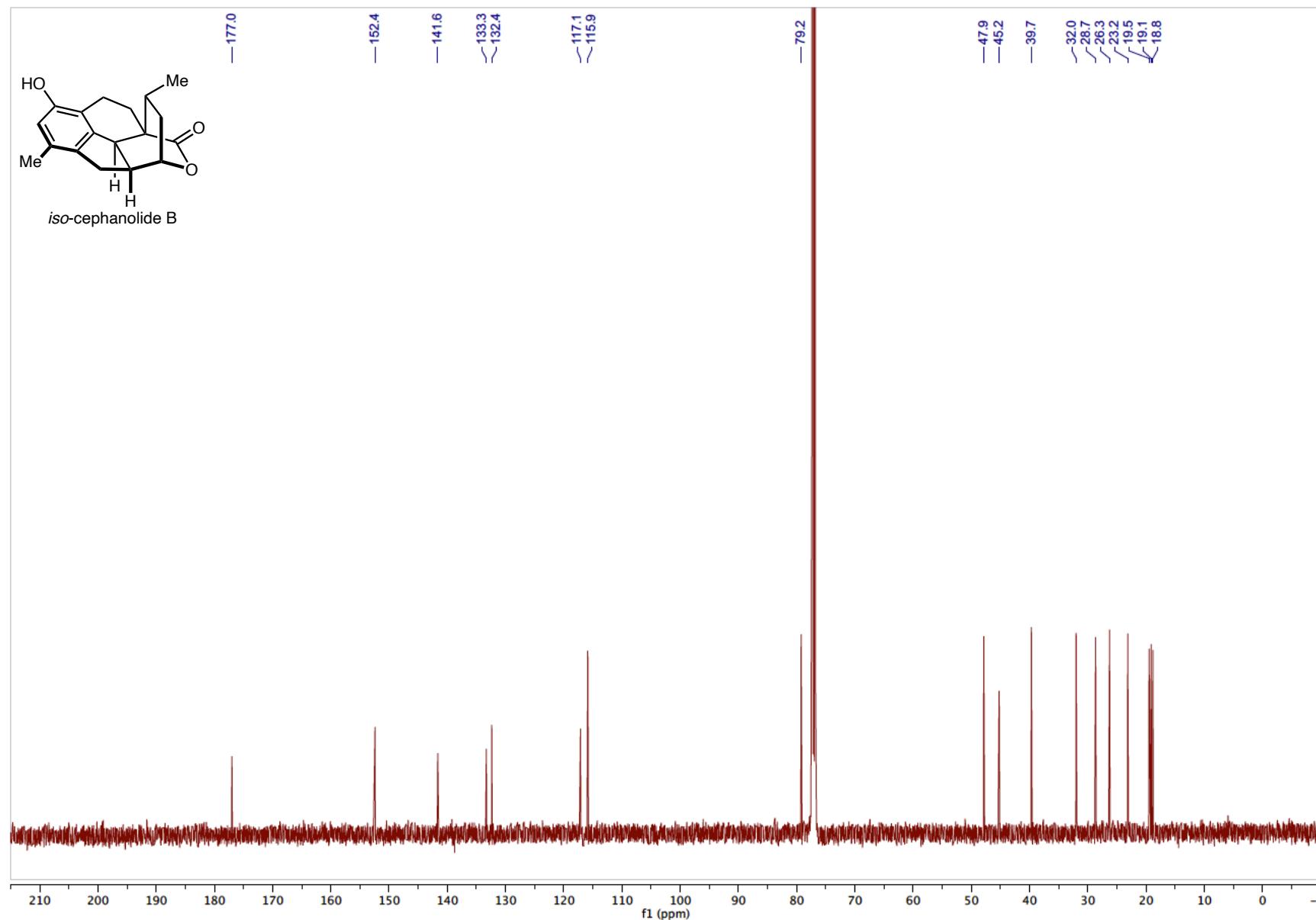
Cephanolide B: ^{13}C NMR



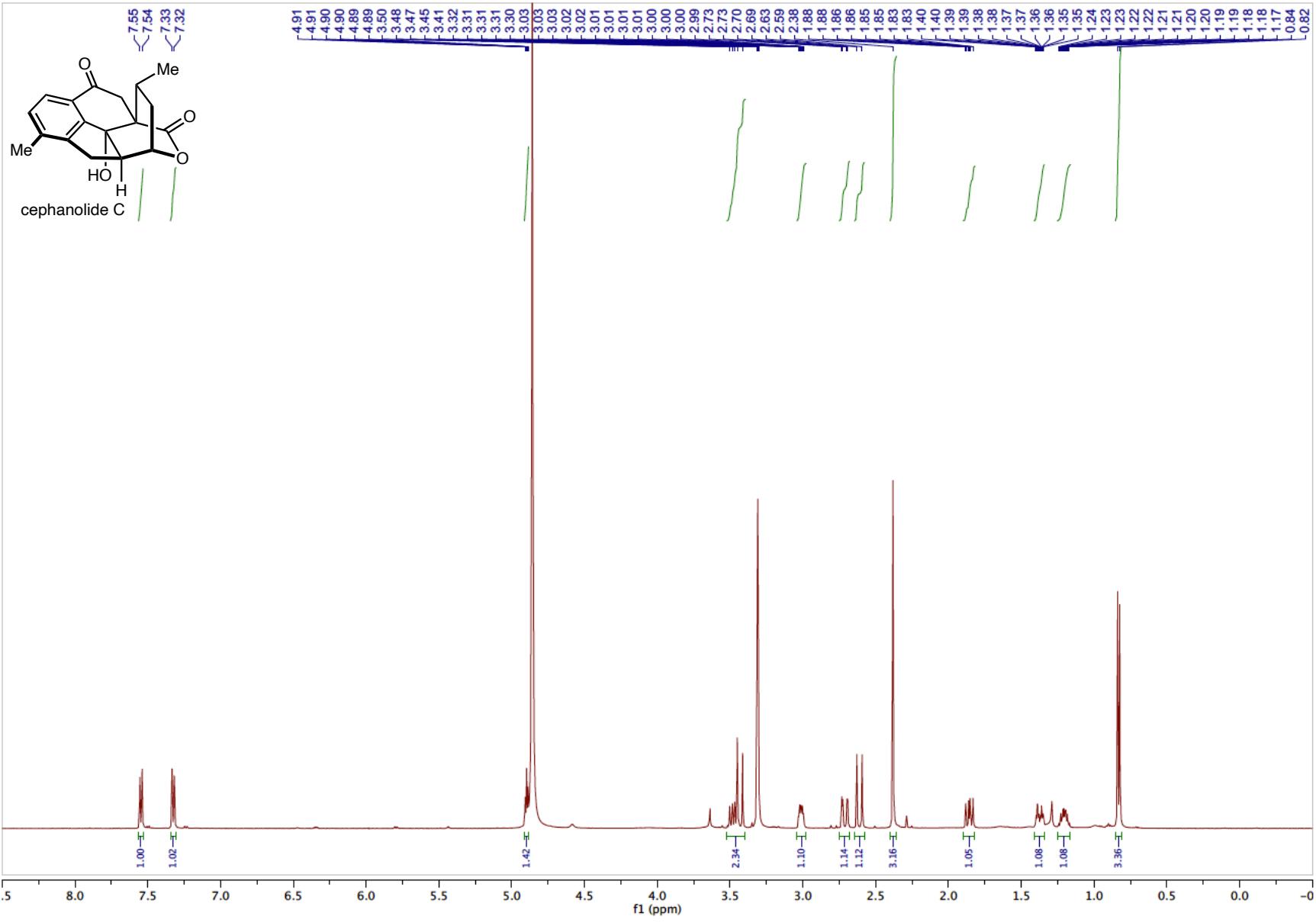
Iso-cephanolide B: ^1H NMR



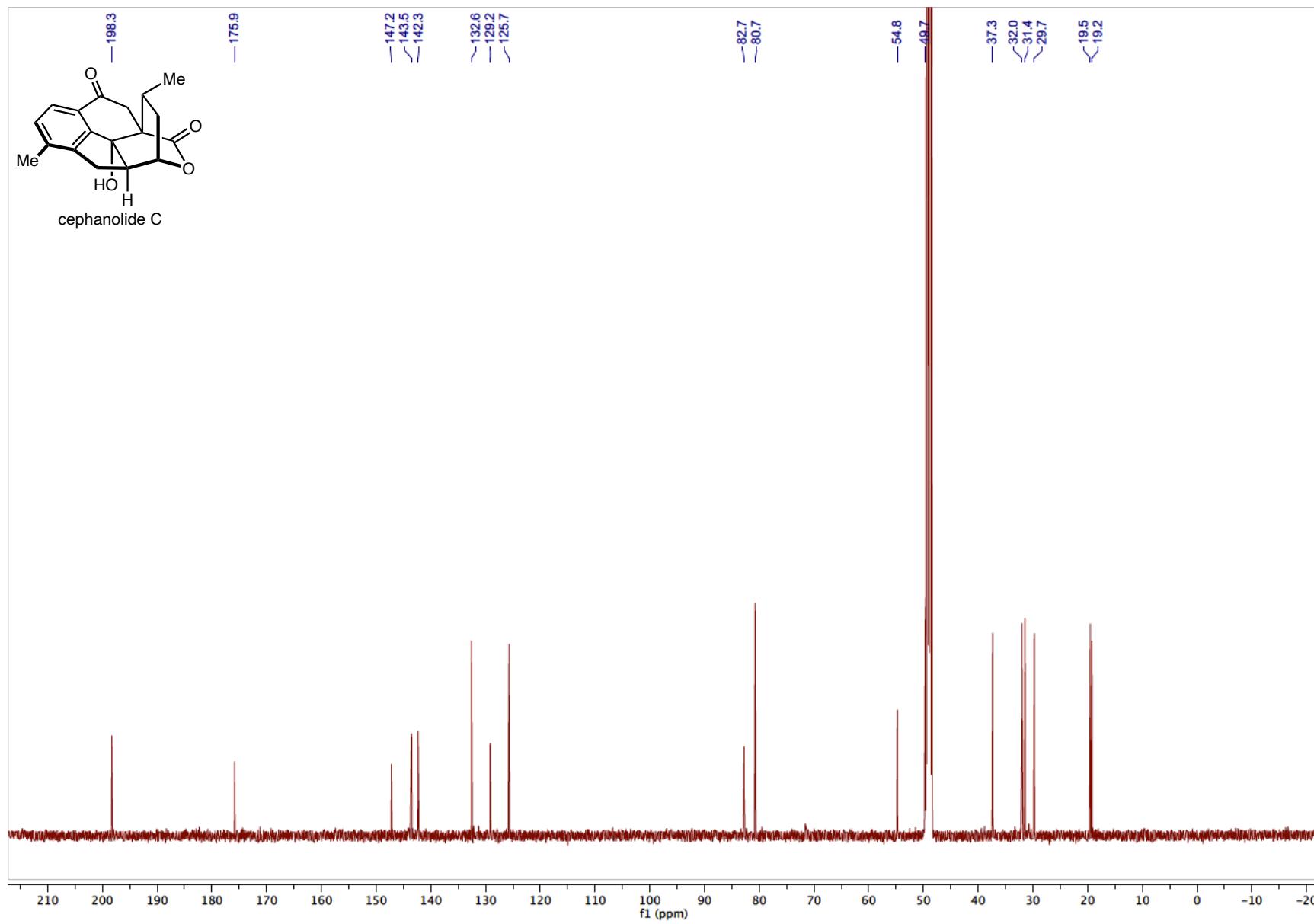
Iso-cephanolide B: ^{13}C NMR



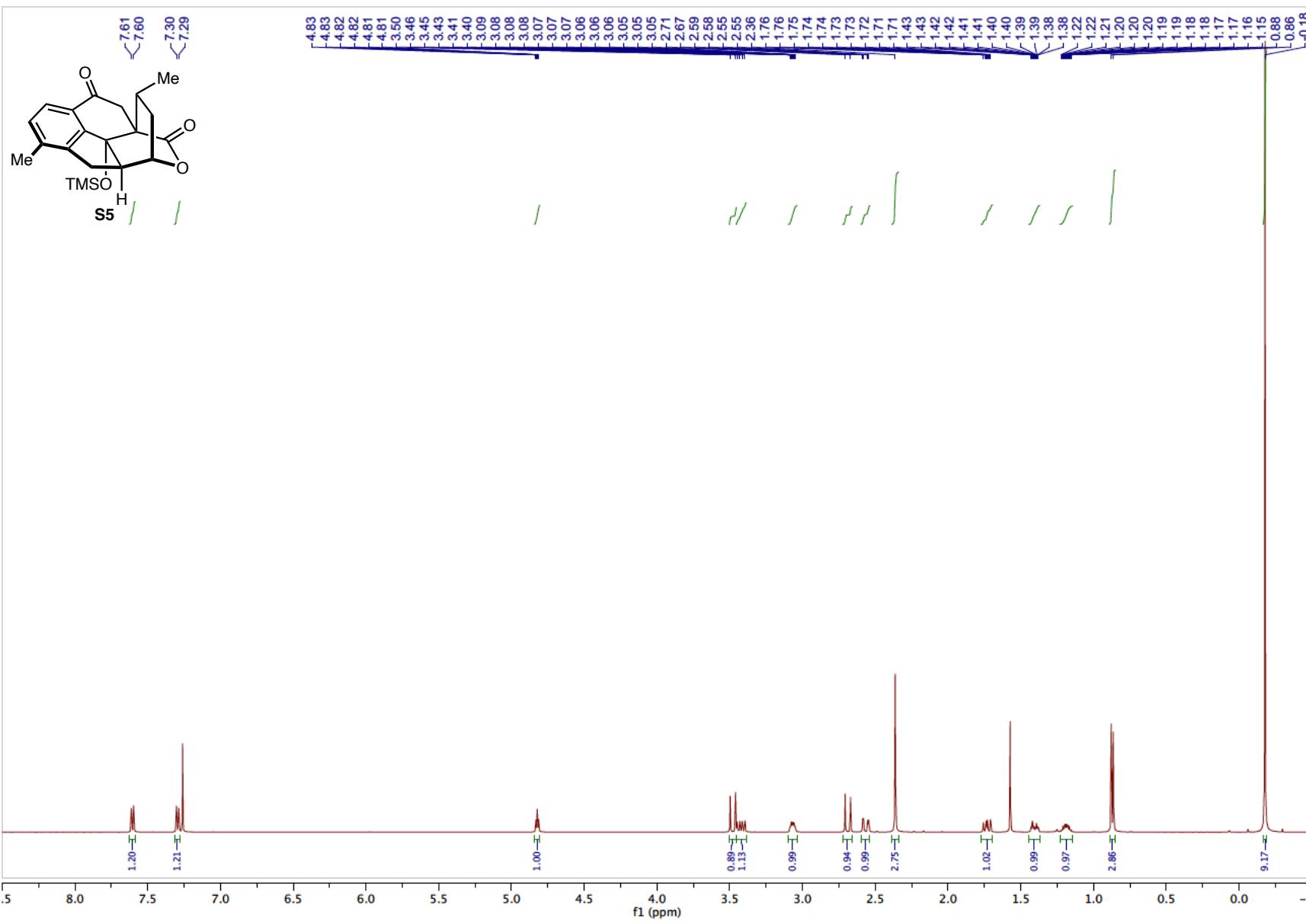
Cephalolide C: ^1H NMR



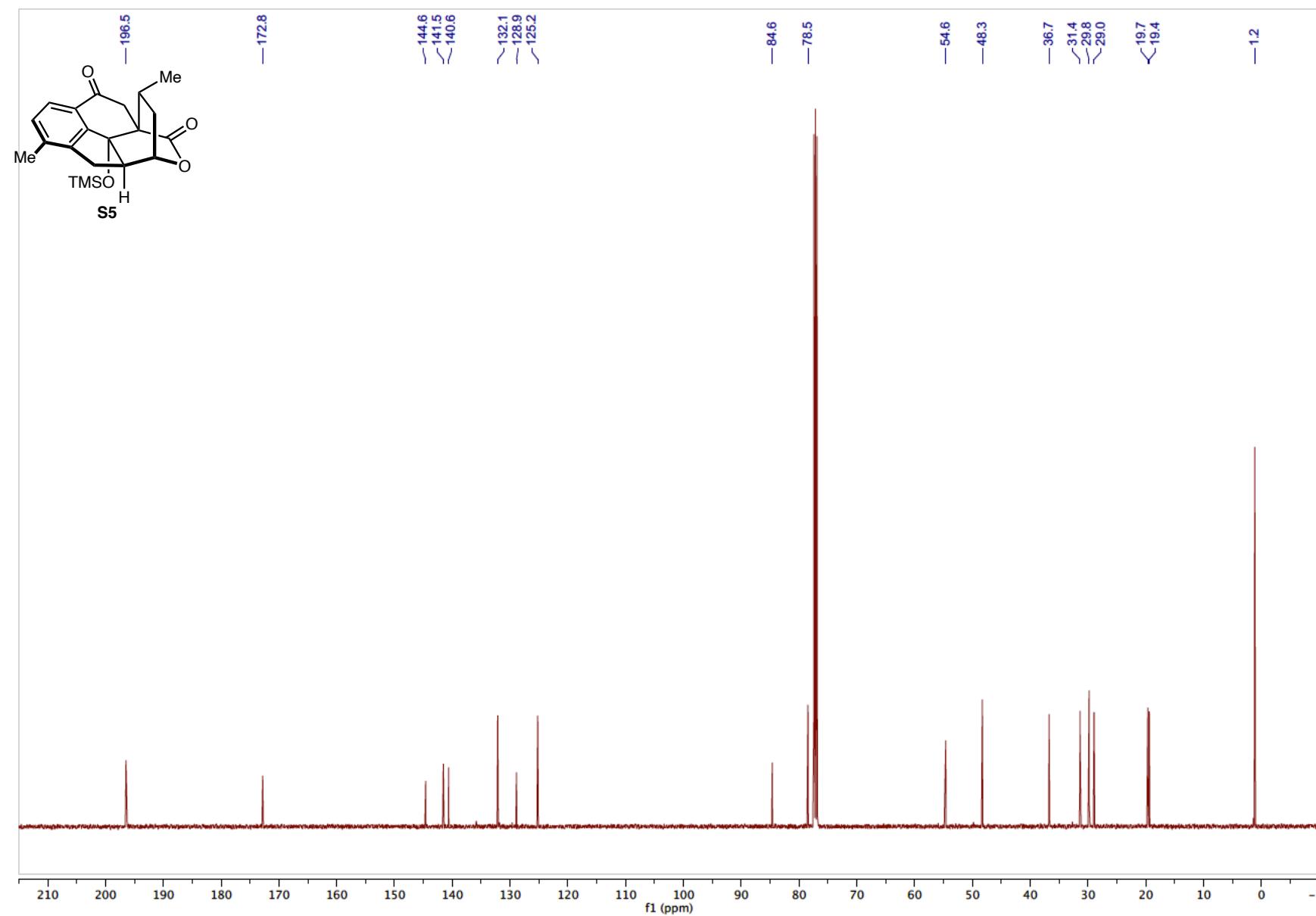
Cephalolide C: ^{13}C NMR



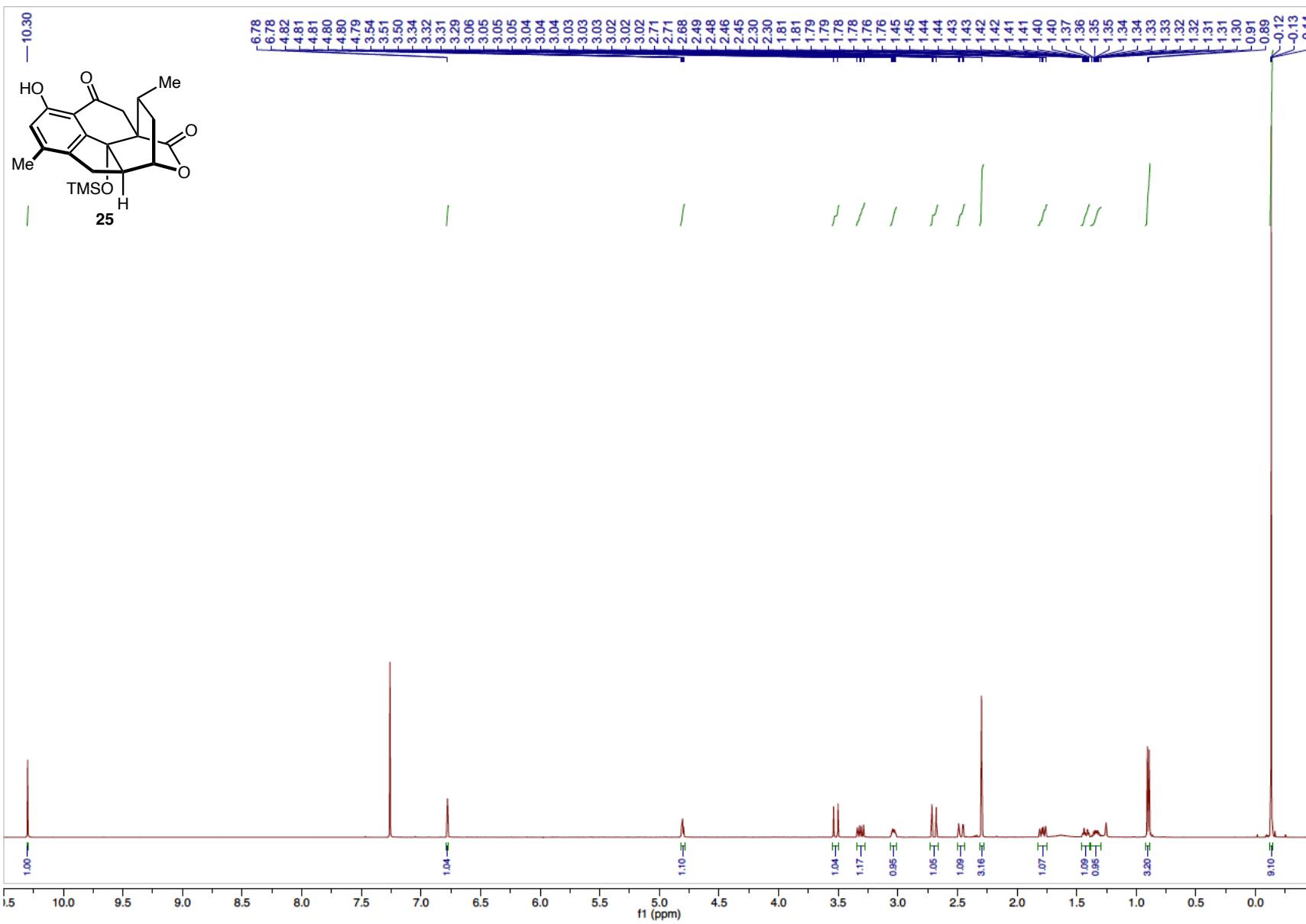
Benzylidene ketone S5: ^1H NMR



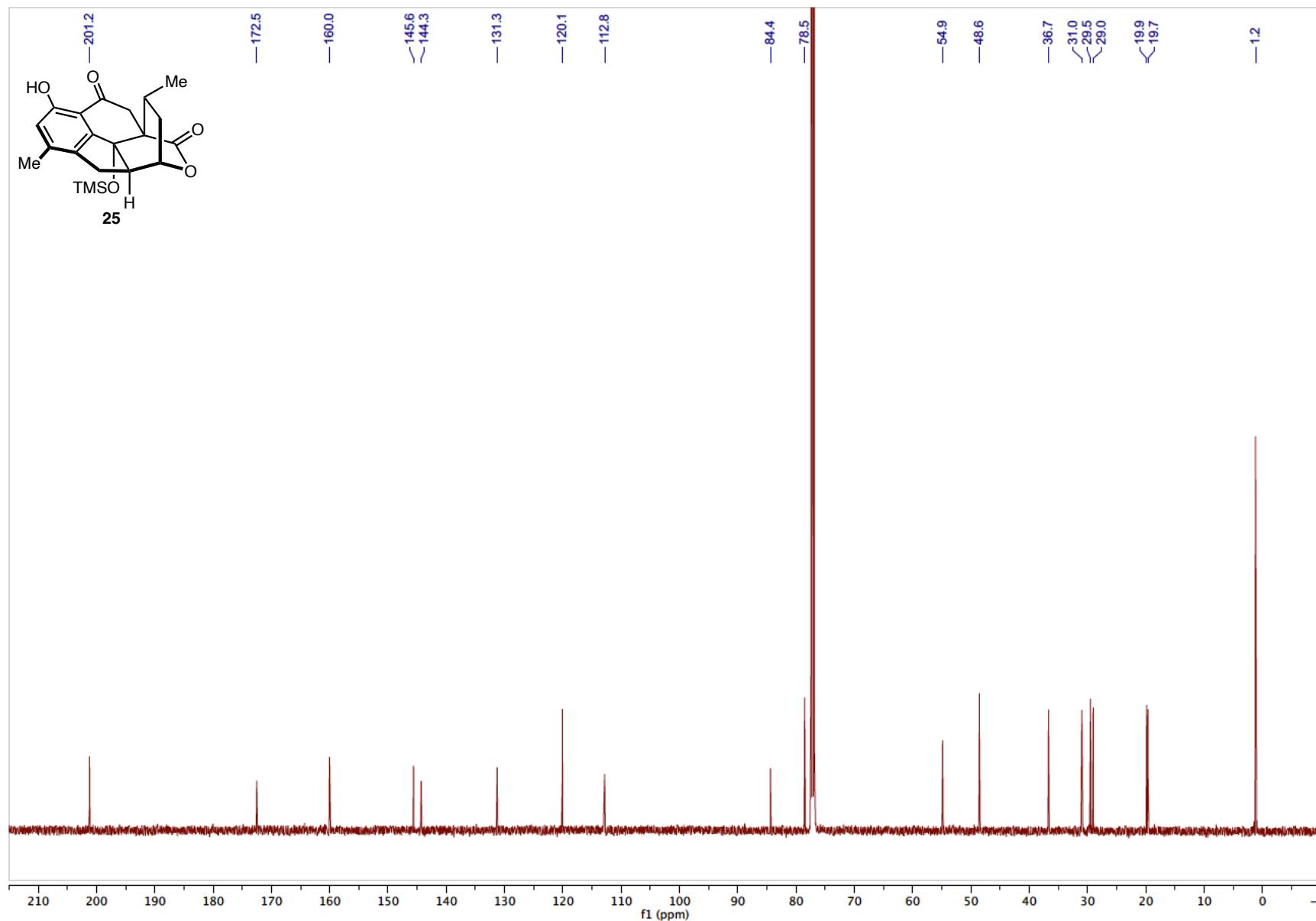
Benzyllic ketone S5: ^{13}C NMR



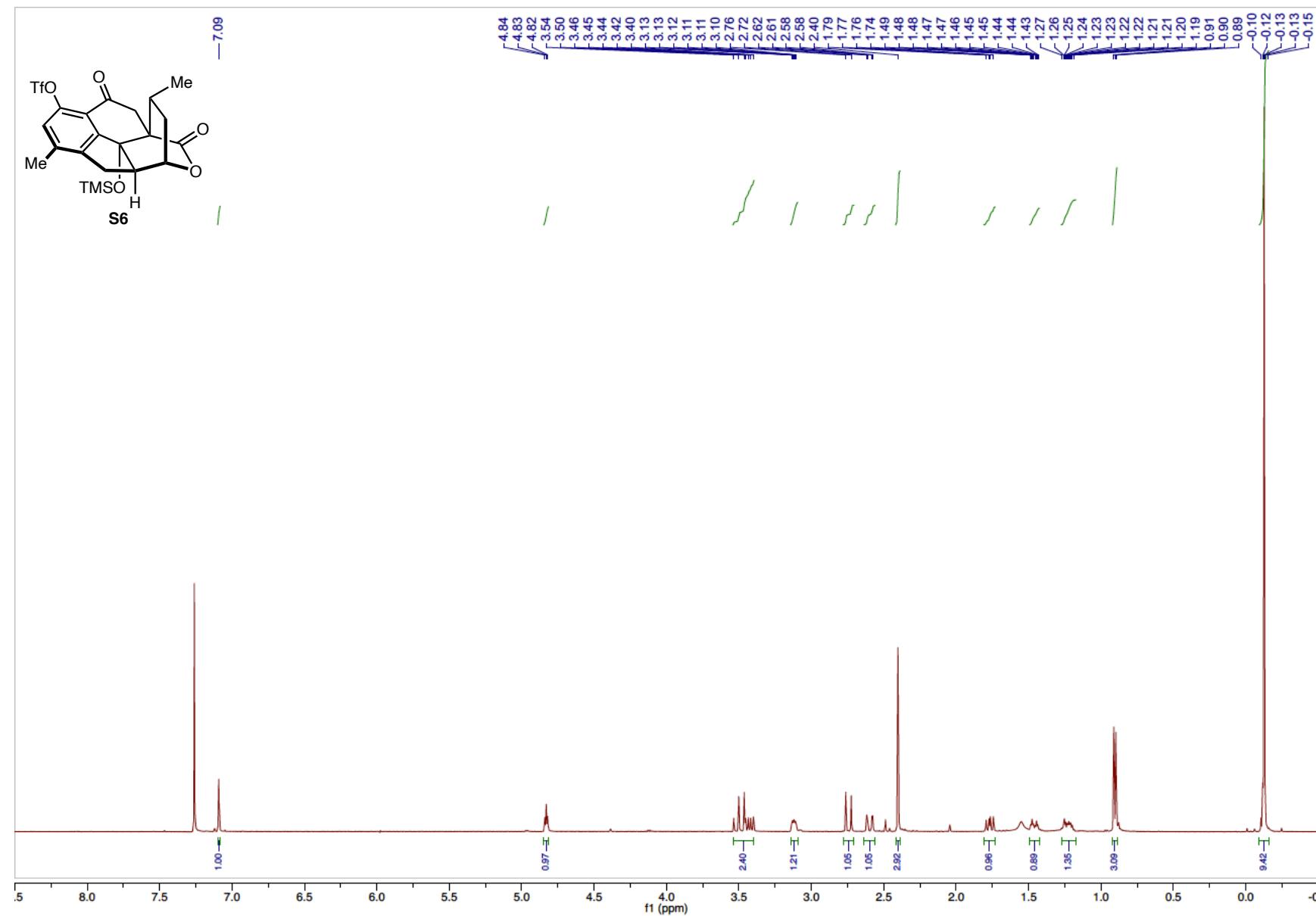
(*ortho*)-Hydroxy ketone **25**: ^1H NMR



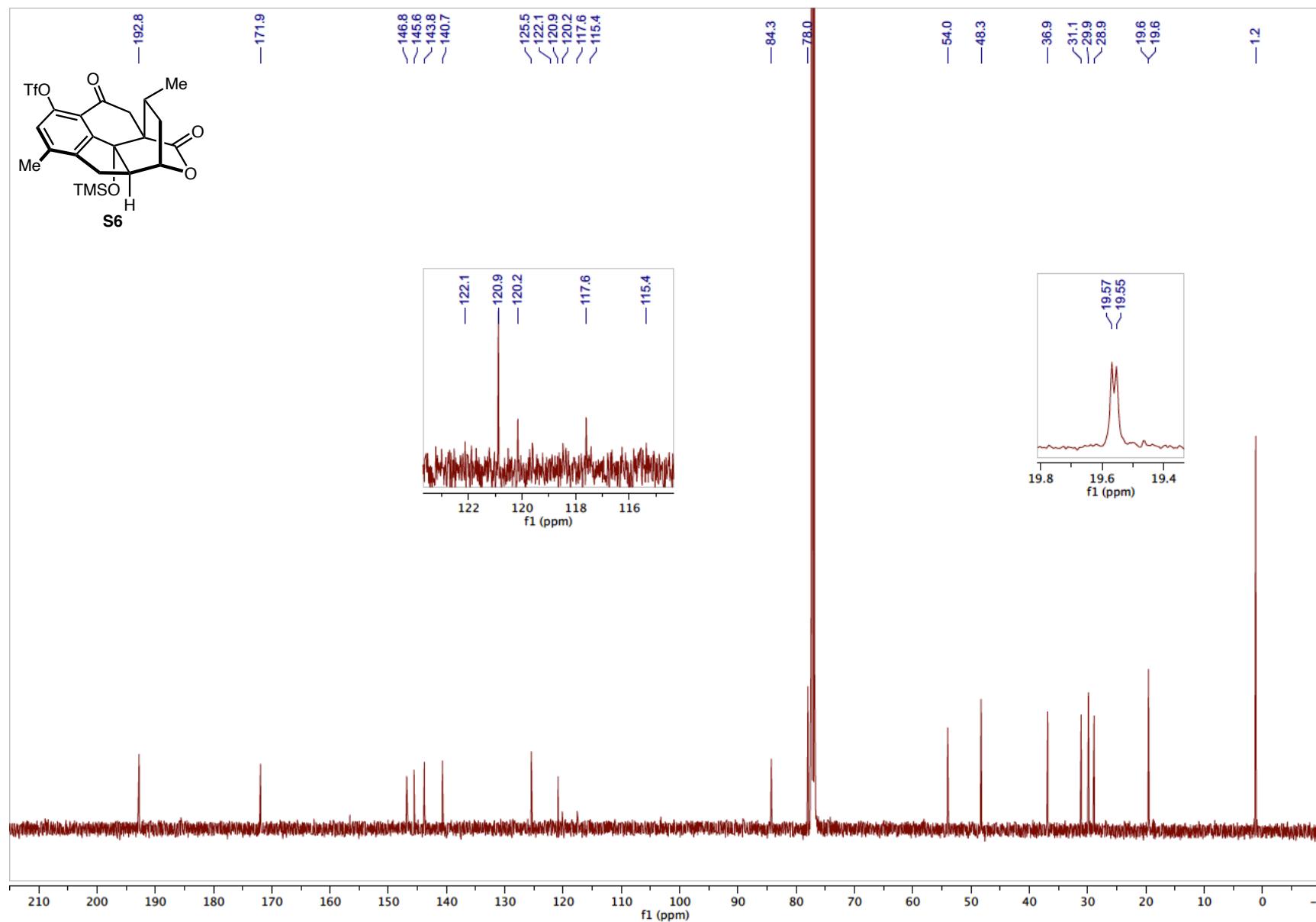
(*ortho*)-Hydroxy ketone **25**: ^{13}C NMR



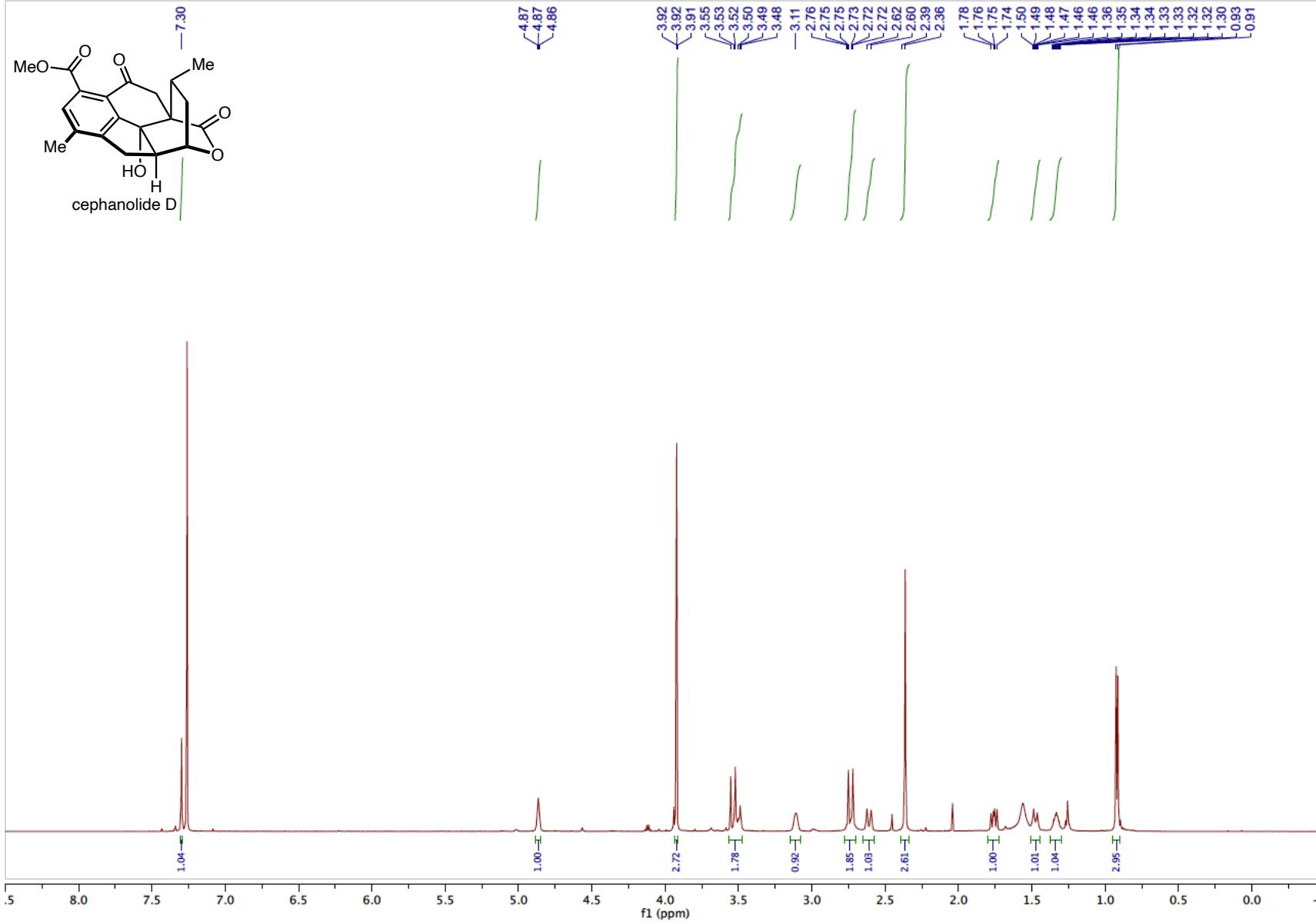
Keto-triflate **S6**: ^1H NMR



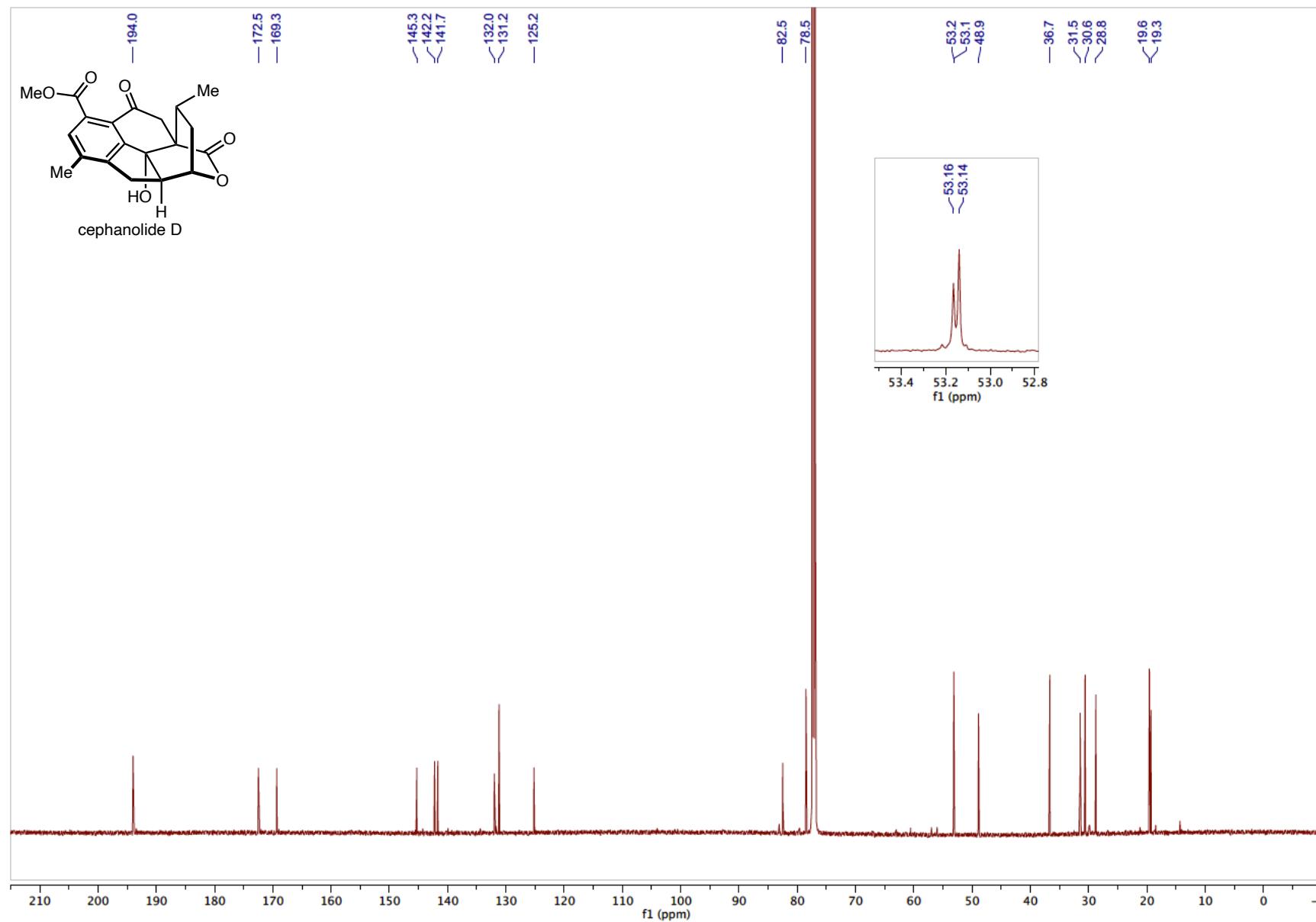
Keto-triflate **S6**: ^{13}C NMR



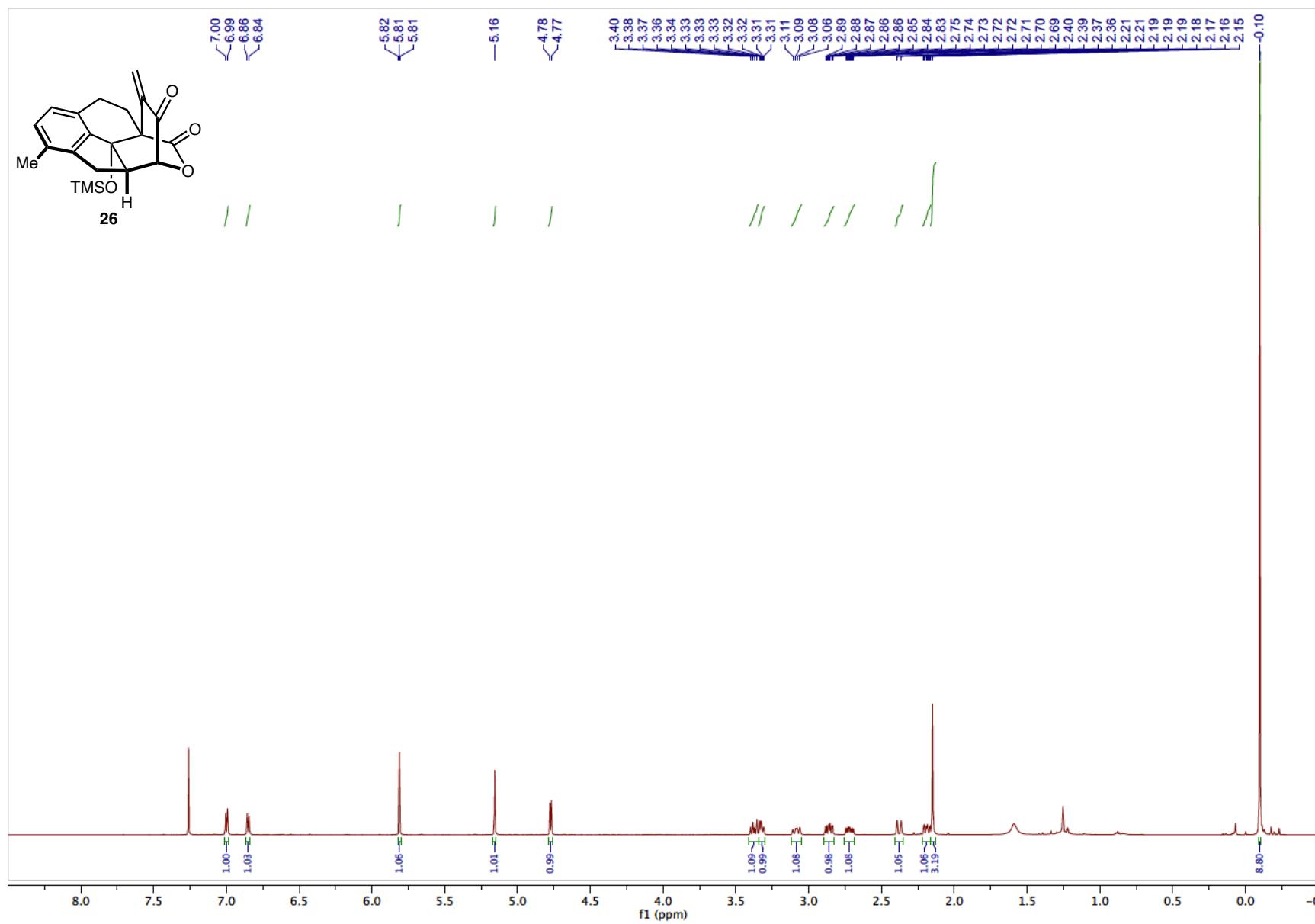
Cephalolide D: ^1H NMR



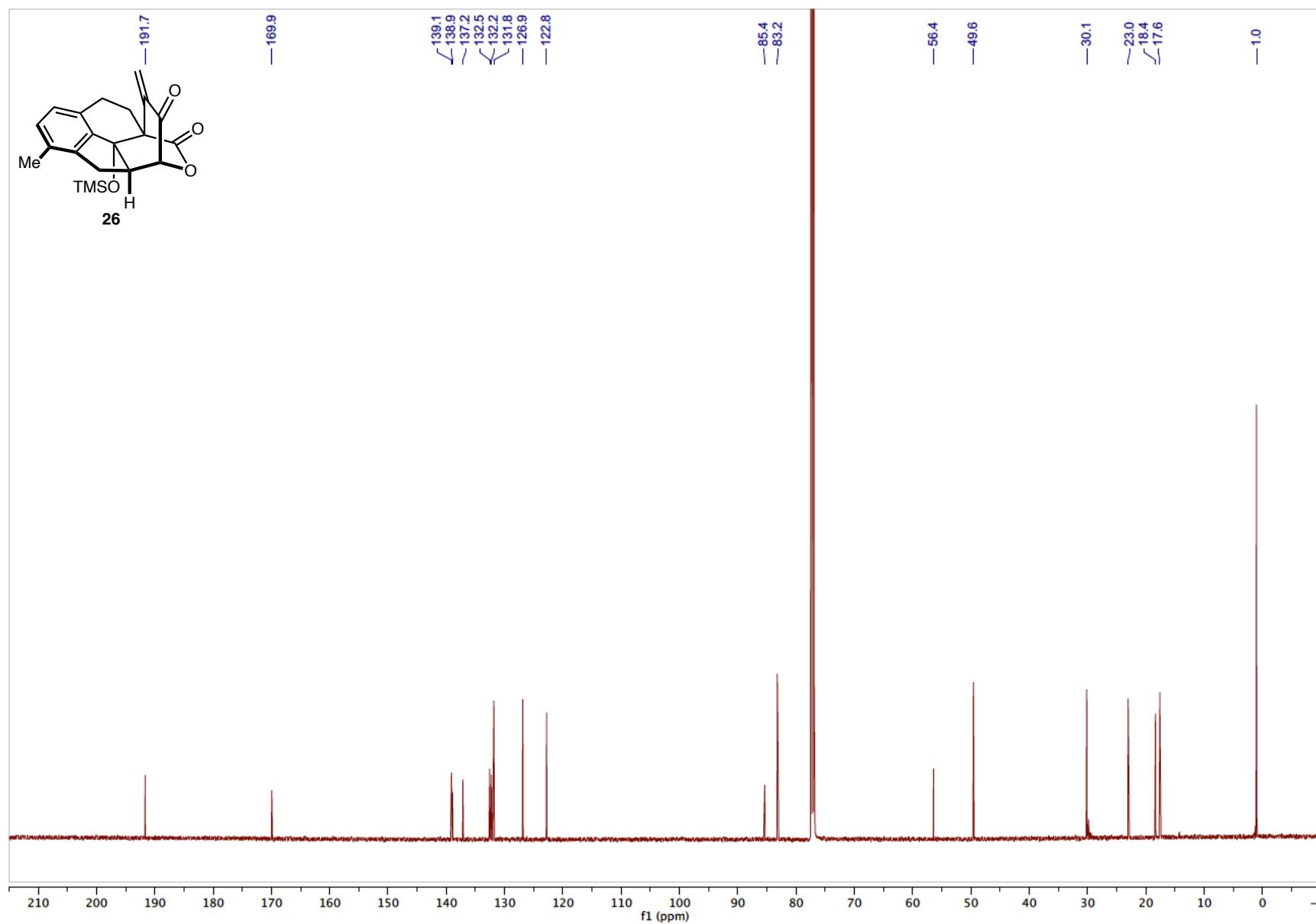
Cephanolide D: ^{13}C NMR



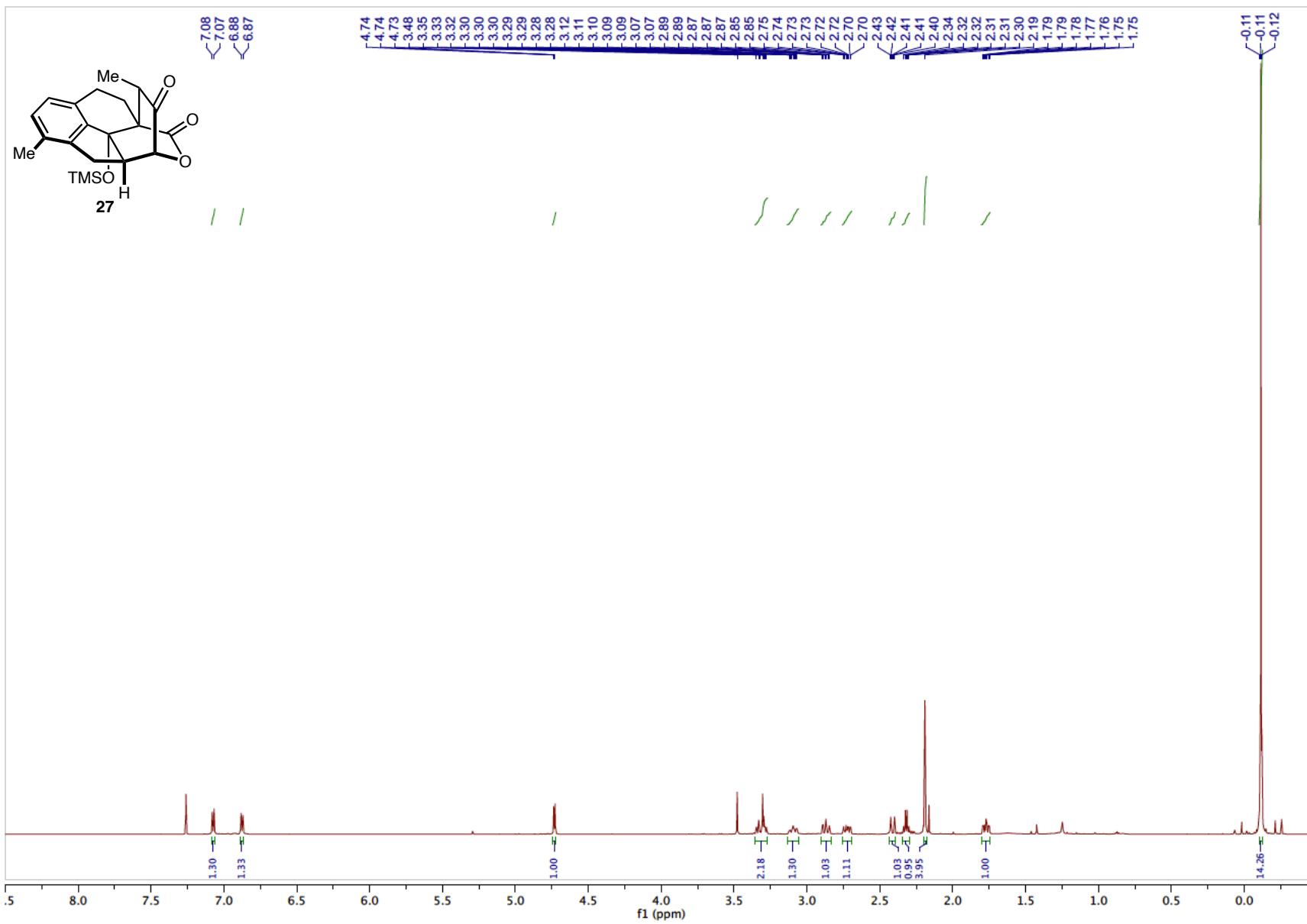
Enone **26**: ^1H NMR



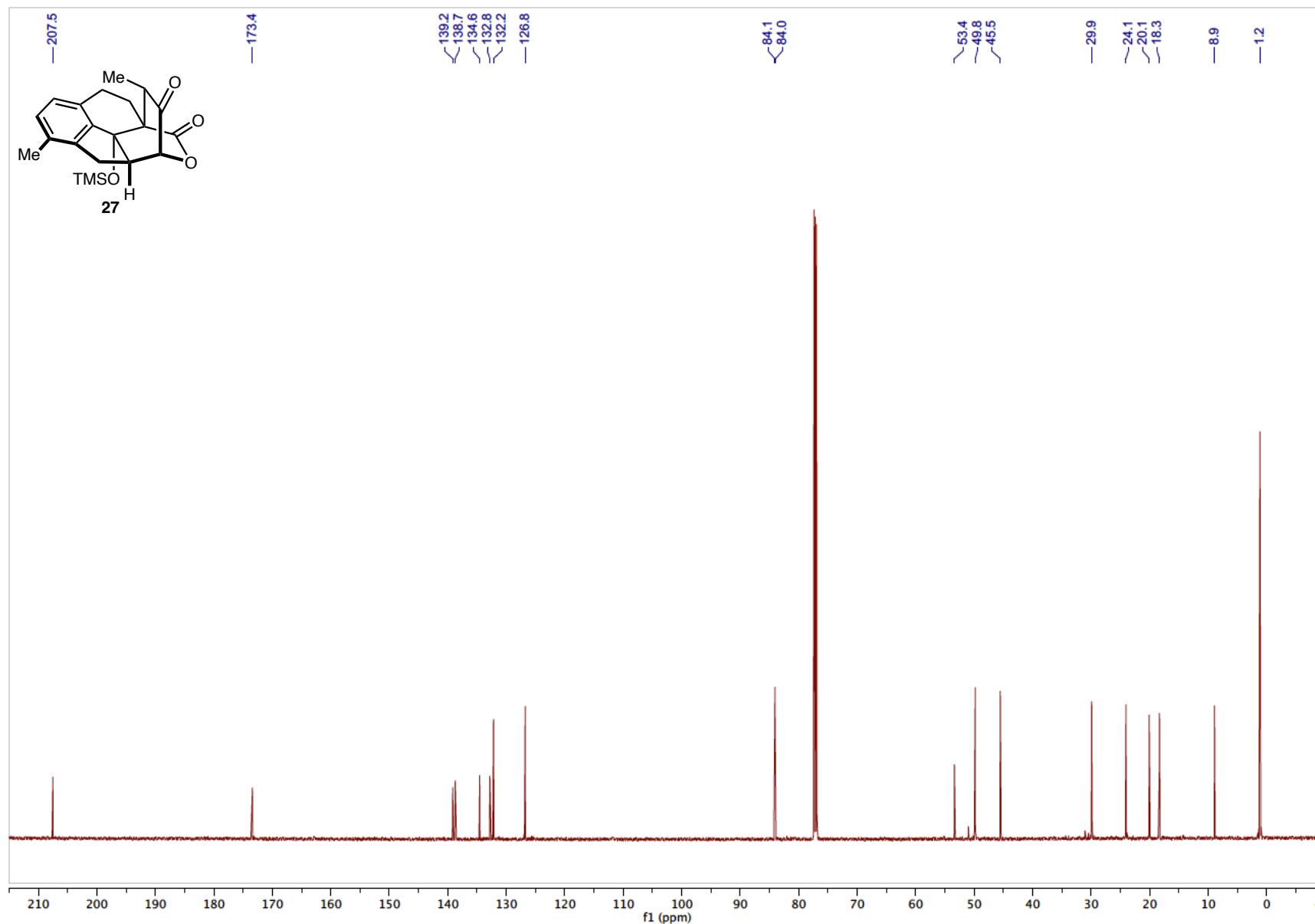
Enone **26**: ^{13}C NMR



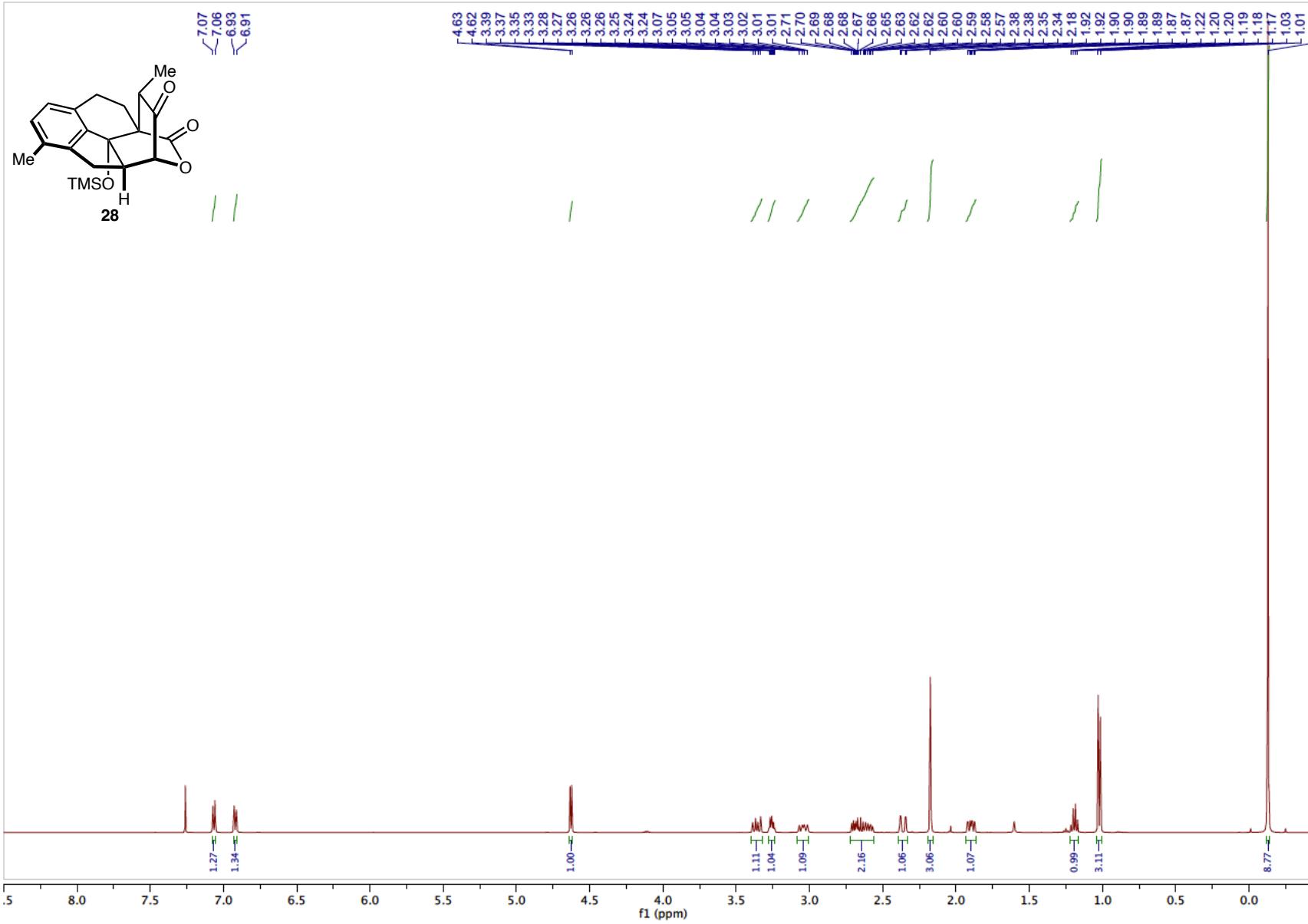
α -(*endo*)-Methyl ketone 27: ^1H NMR (crude)



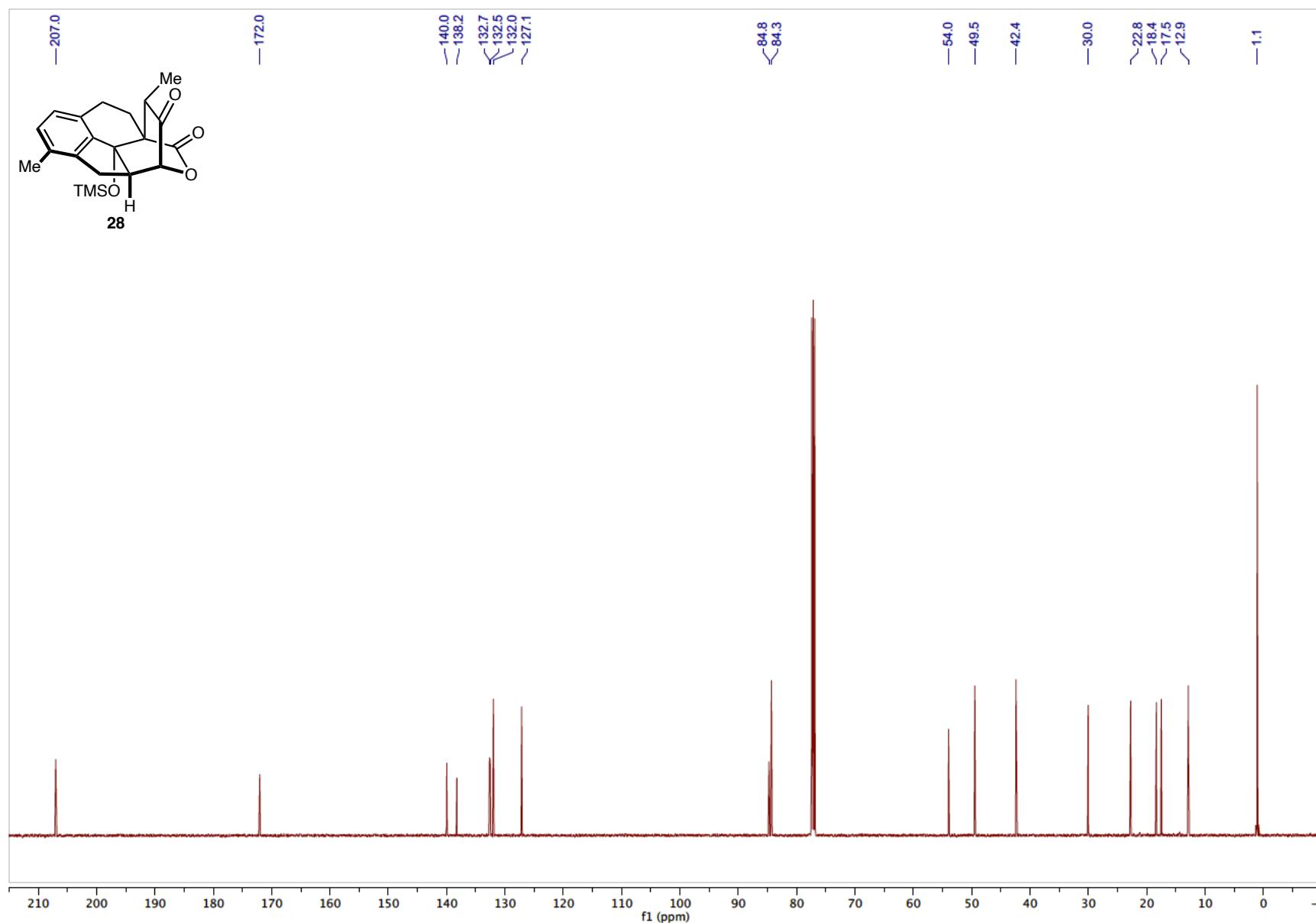
α -(*endo*)-Methyl ketone **27**: ^{13}C NMR (crude)



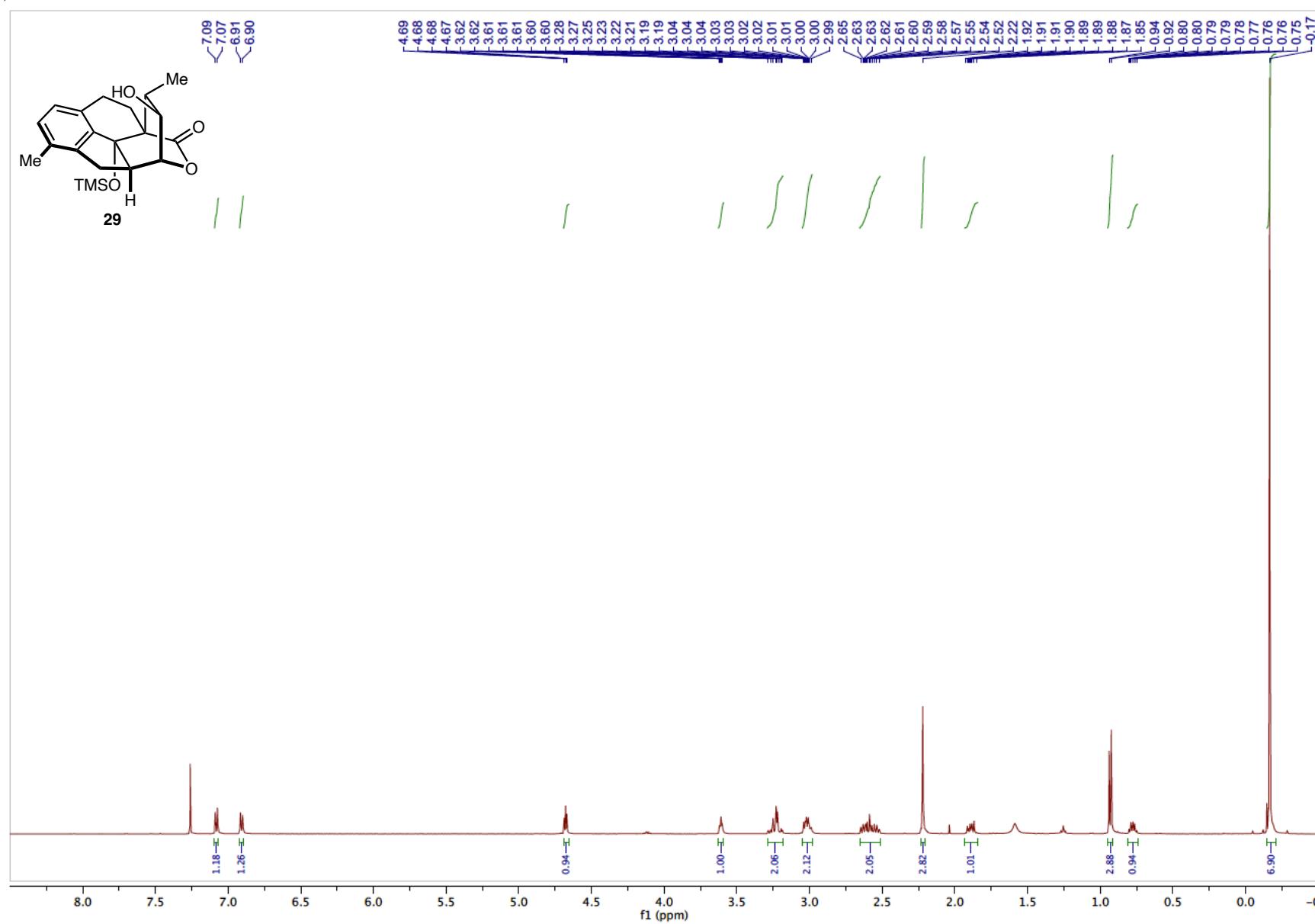
α -(*exo*)-Methyl ketone **28**: ^1H NMR



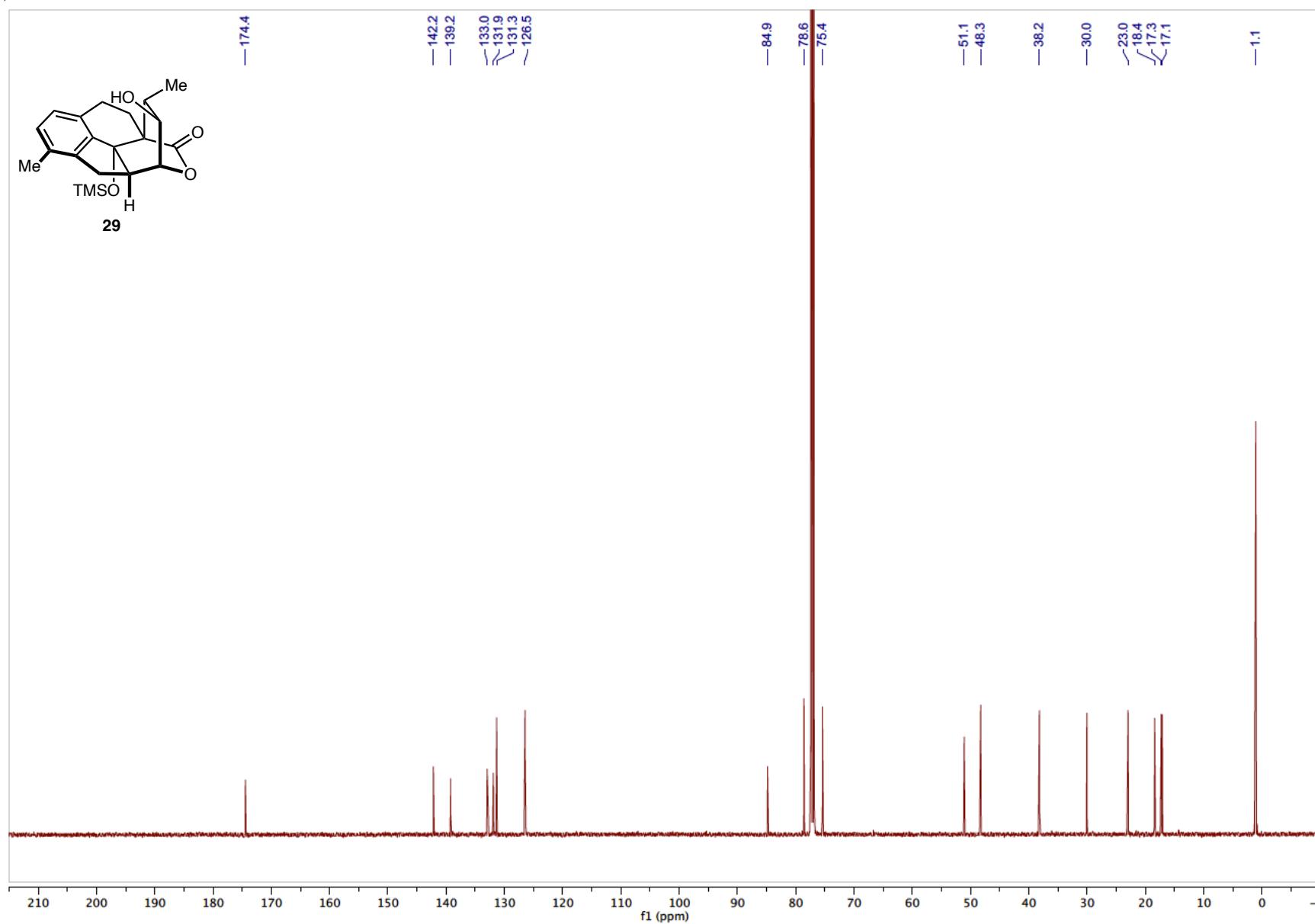
α -(*exo*)-Methyl ketone **28**: ^{13}C NMR



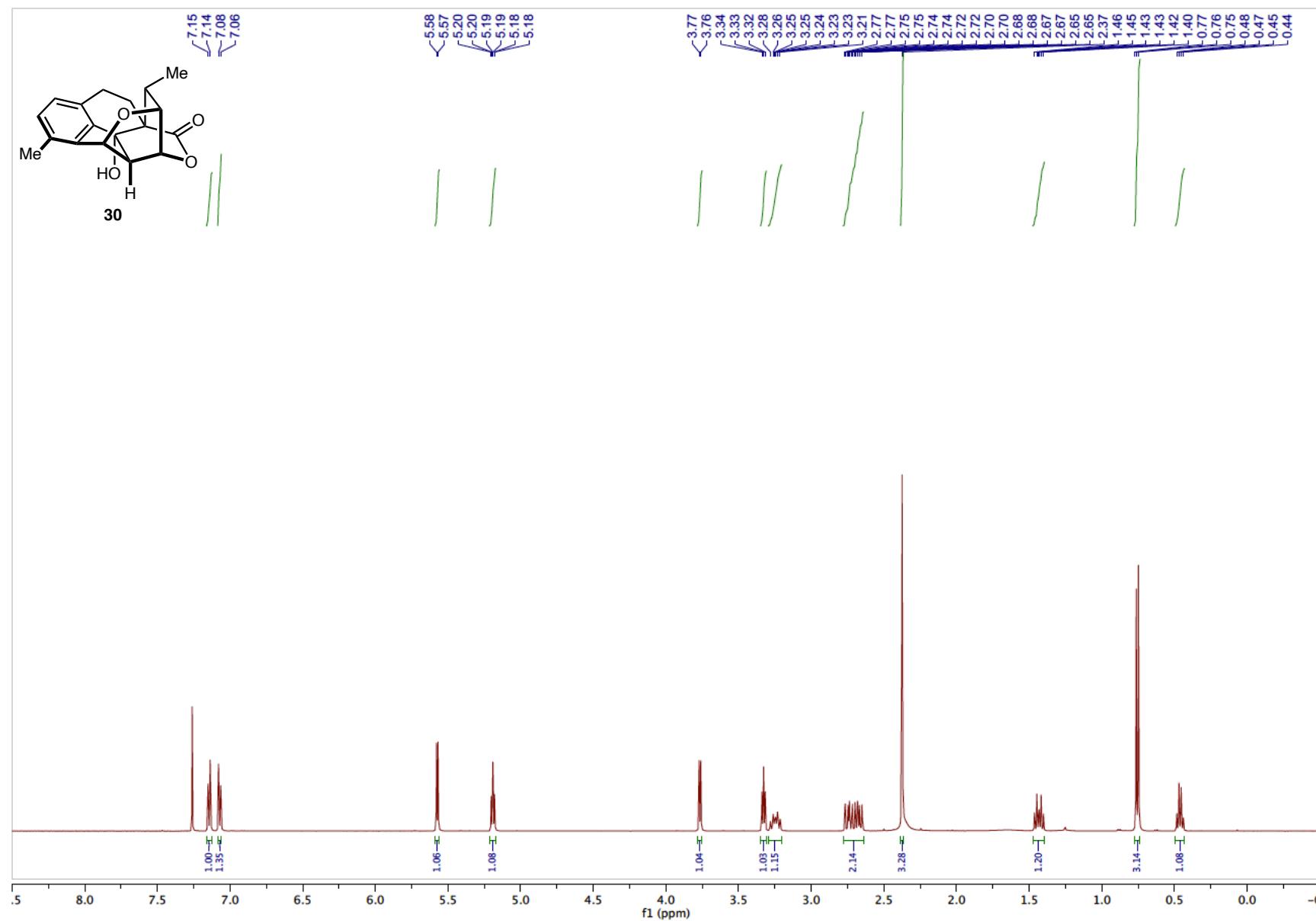
(*endo*)-Alcohol **29**: ^1H NMR



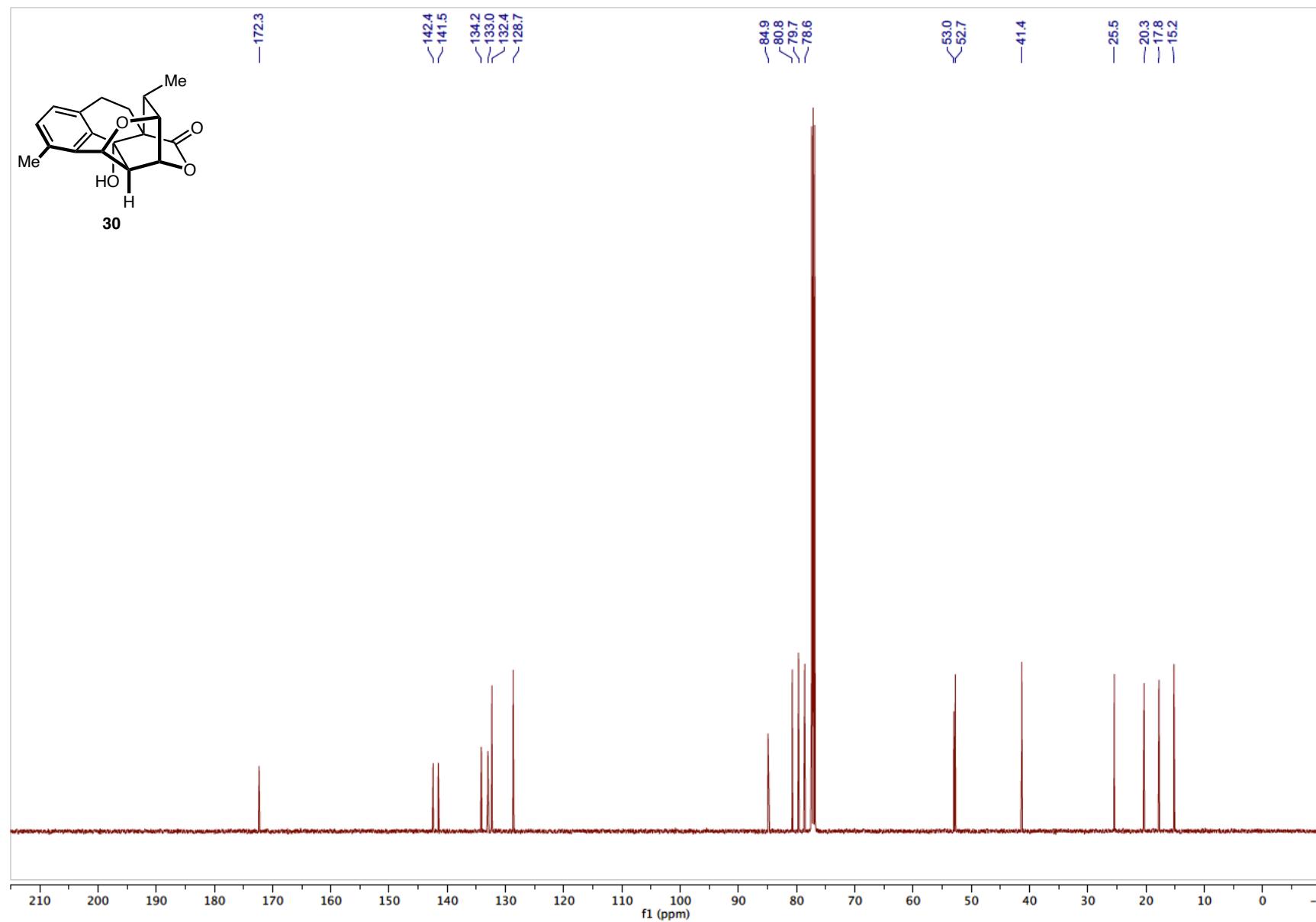
(*endo*)-Alcohol **29**: ^{13}C NMR



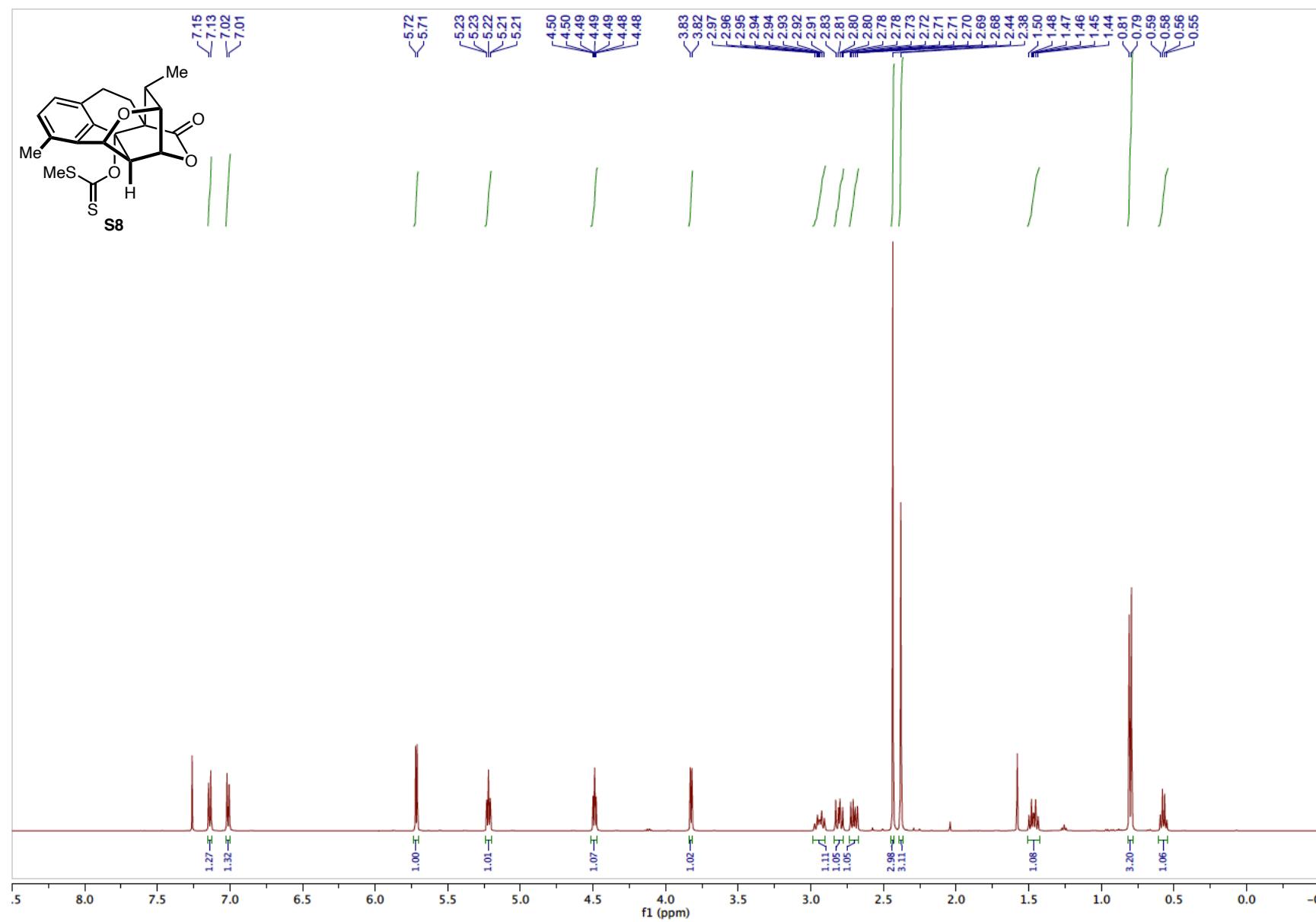
Hexacyclic alcohol **30**: ^1H NMR



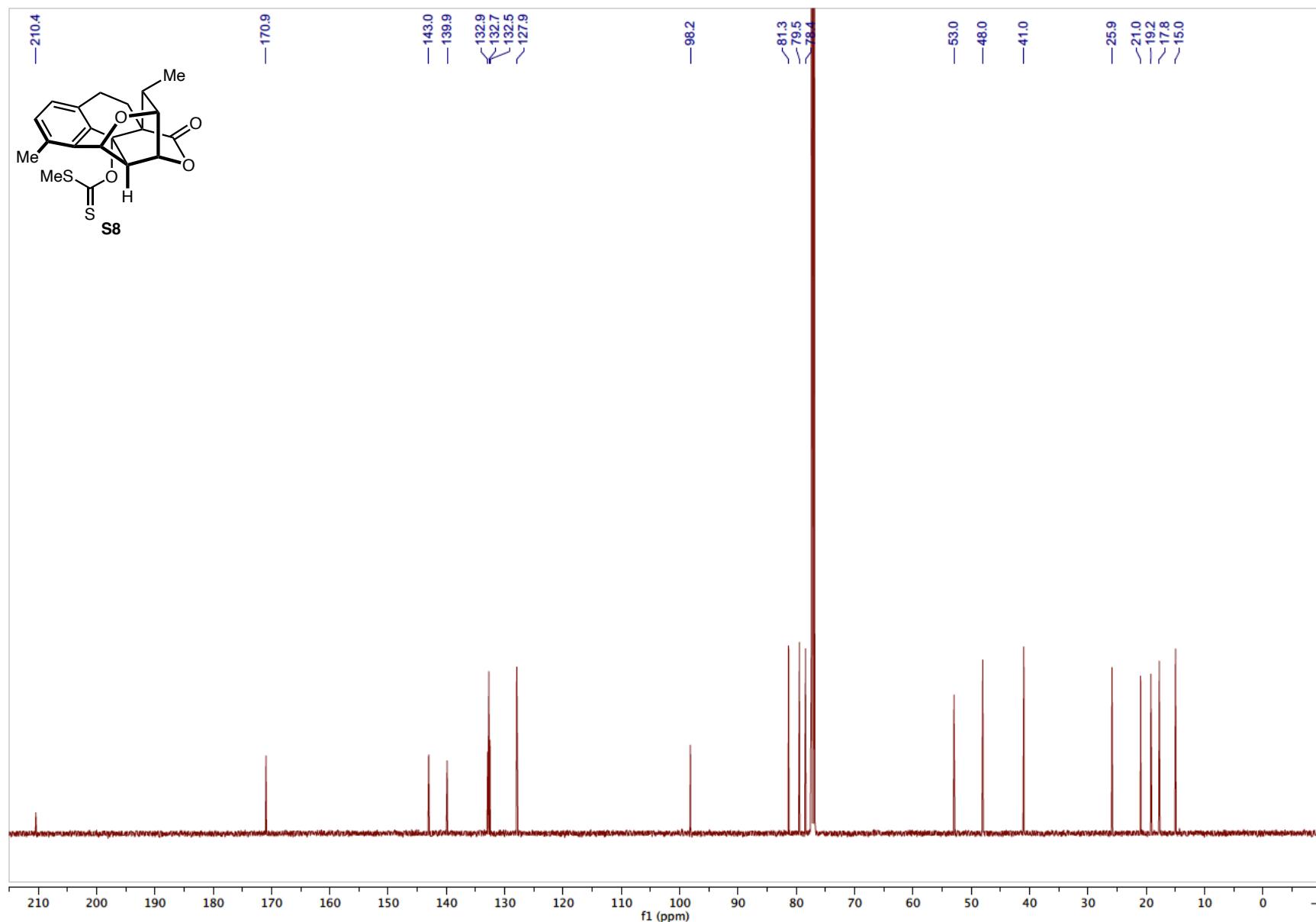
Hexacyclic alcohol **30**: ^{13}C NMR



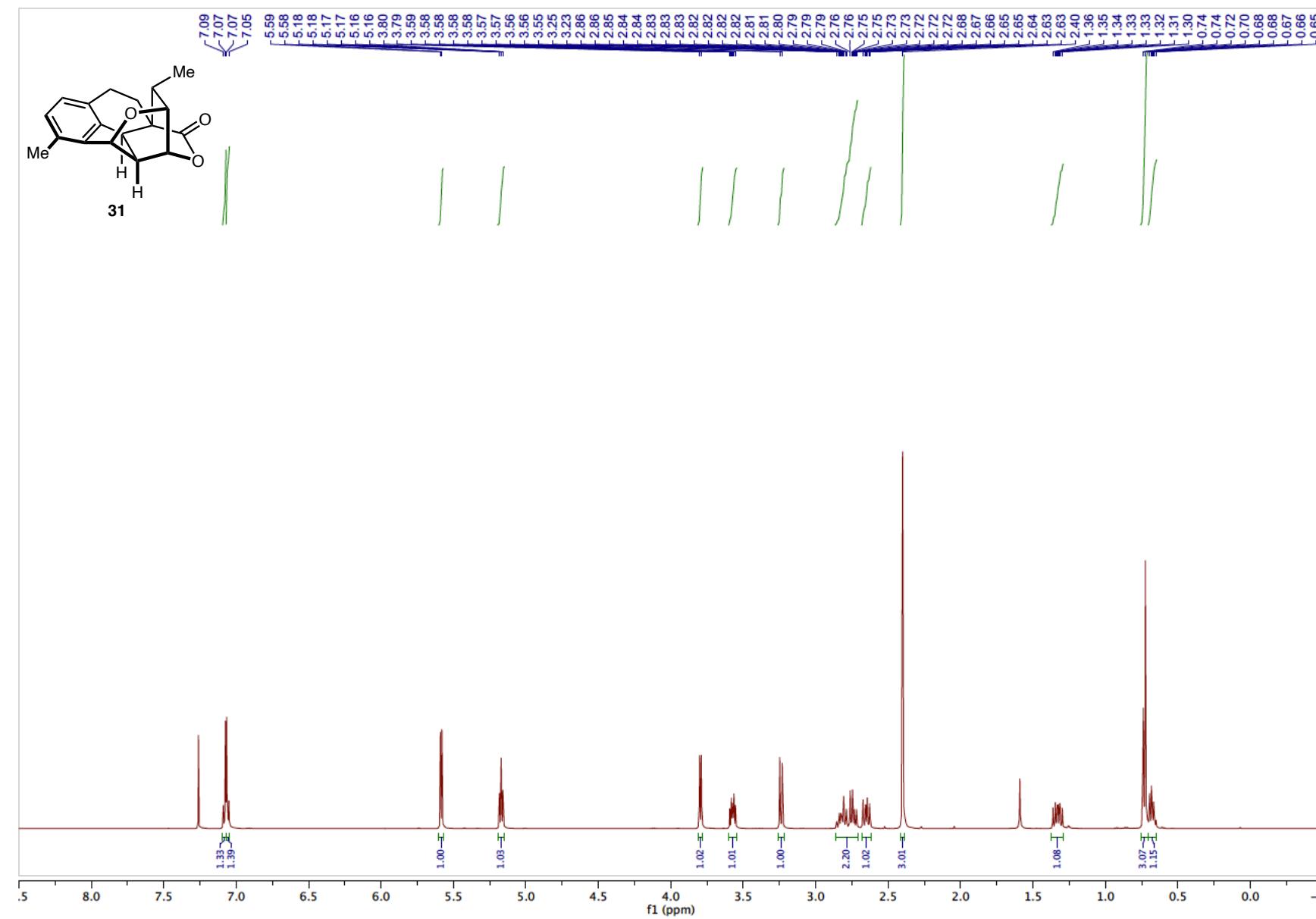
Xanthate S8: ^1H NMR



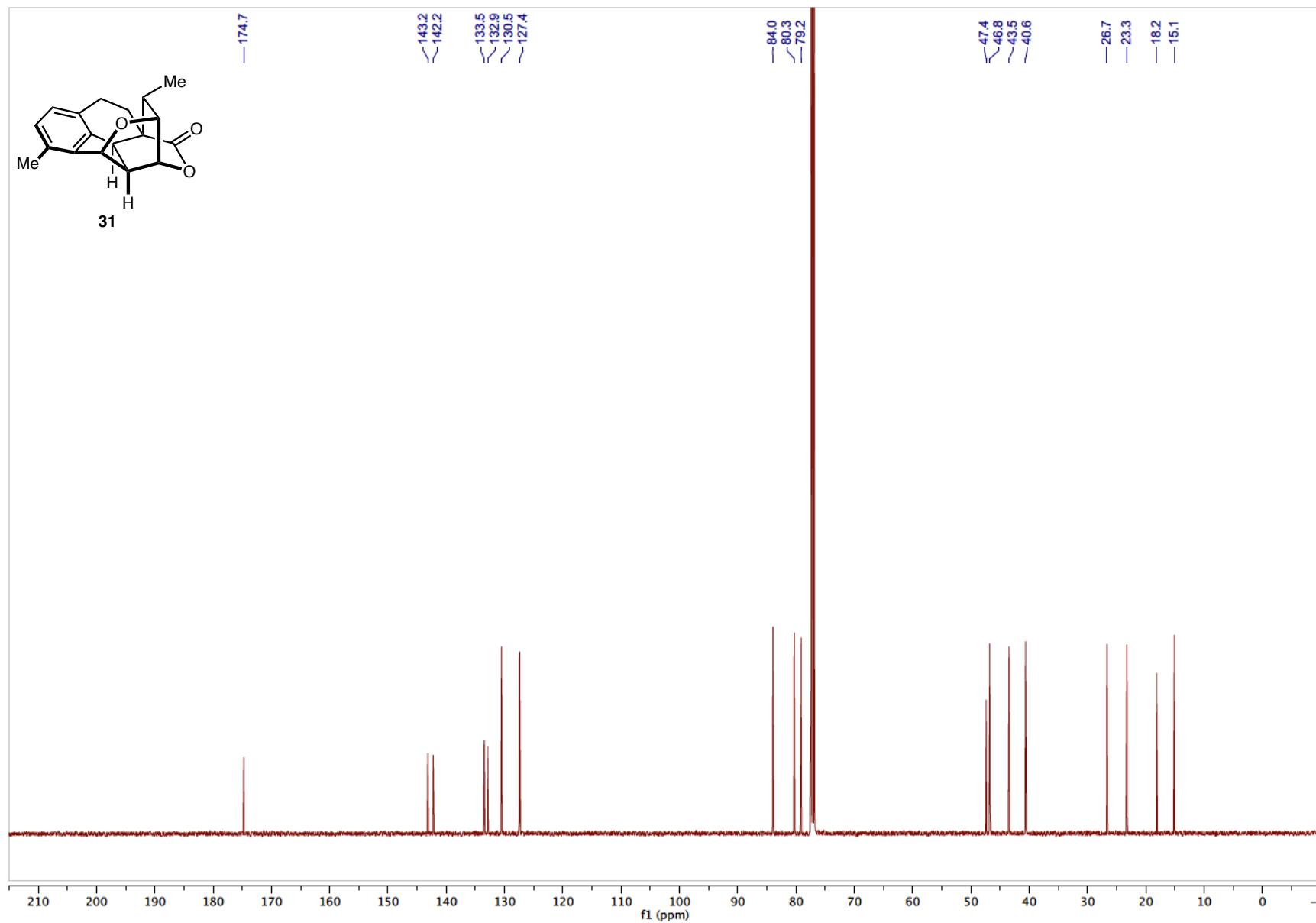
Xanthate S8: ^{13}C NMR



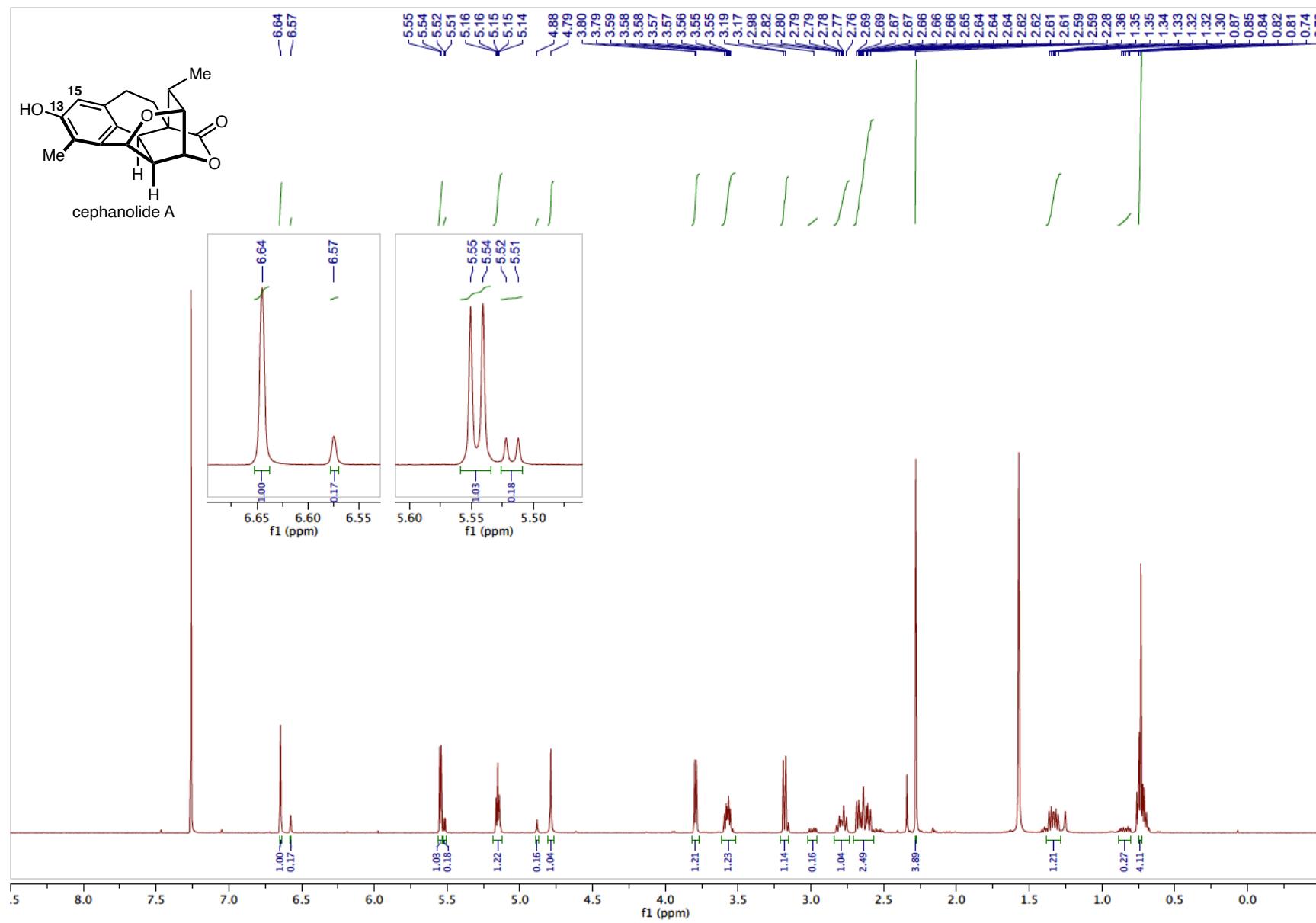
Deoxygenated hexacycle **31**: ^1H NMR



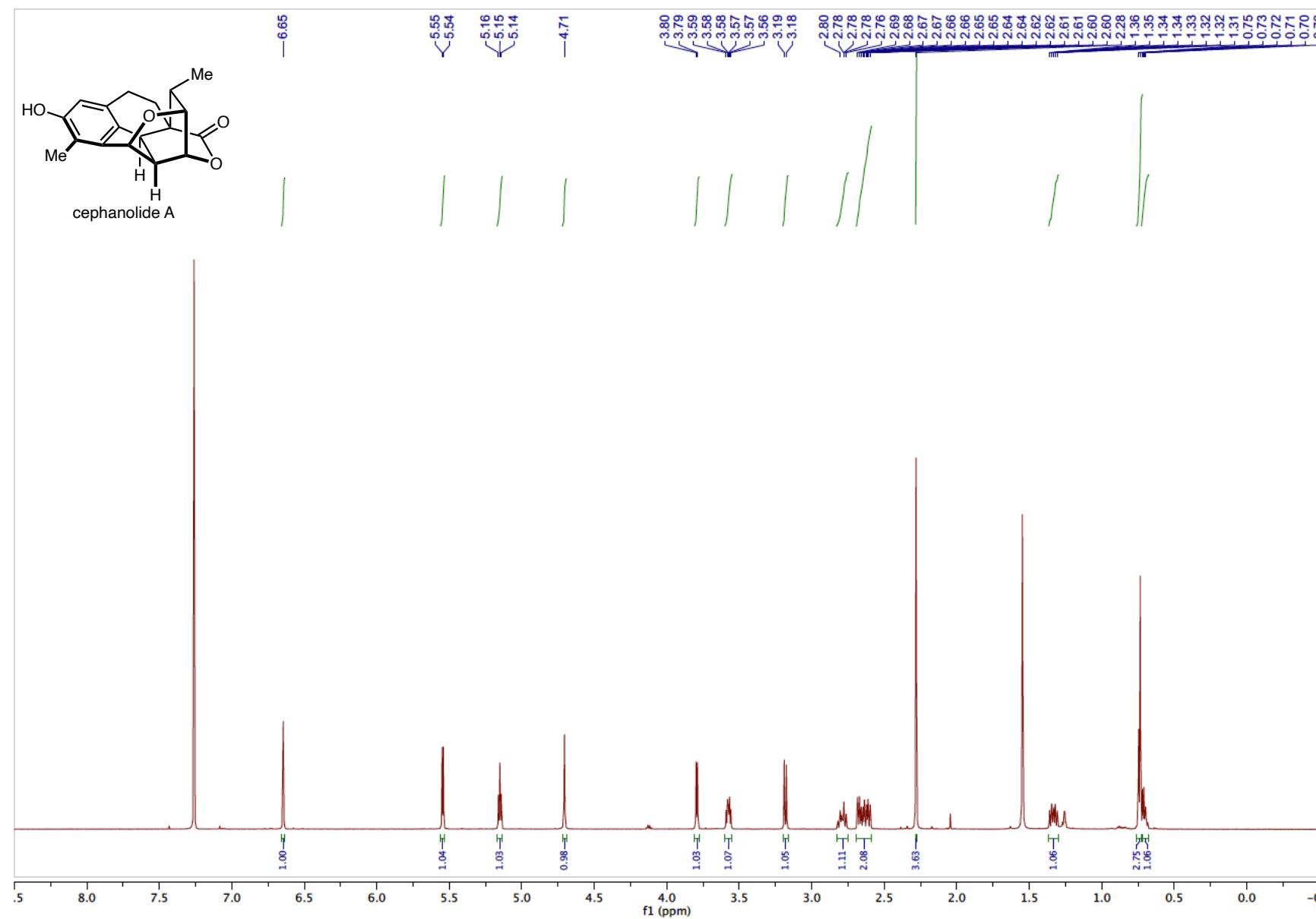
Deoxygenated hexacycle **31**: ^{13}C NMR



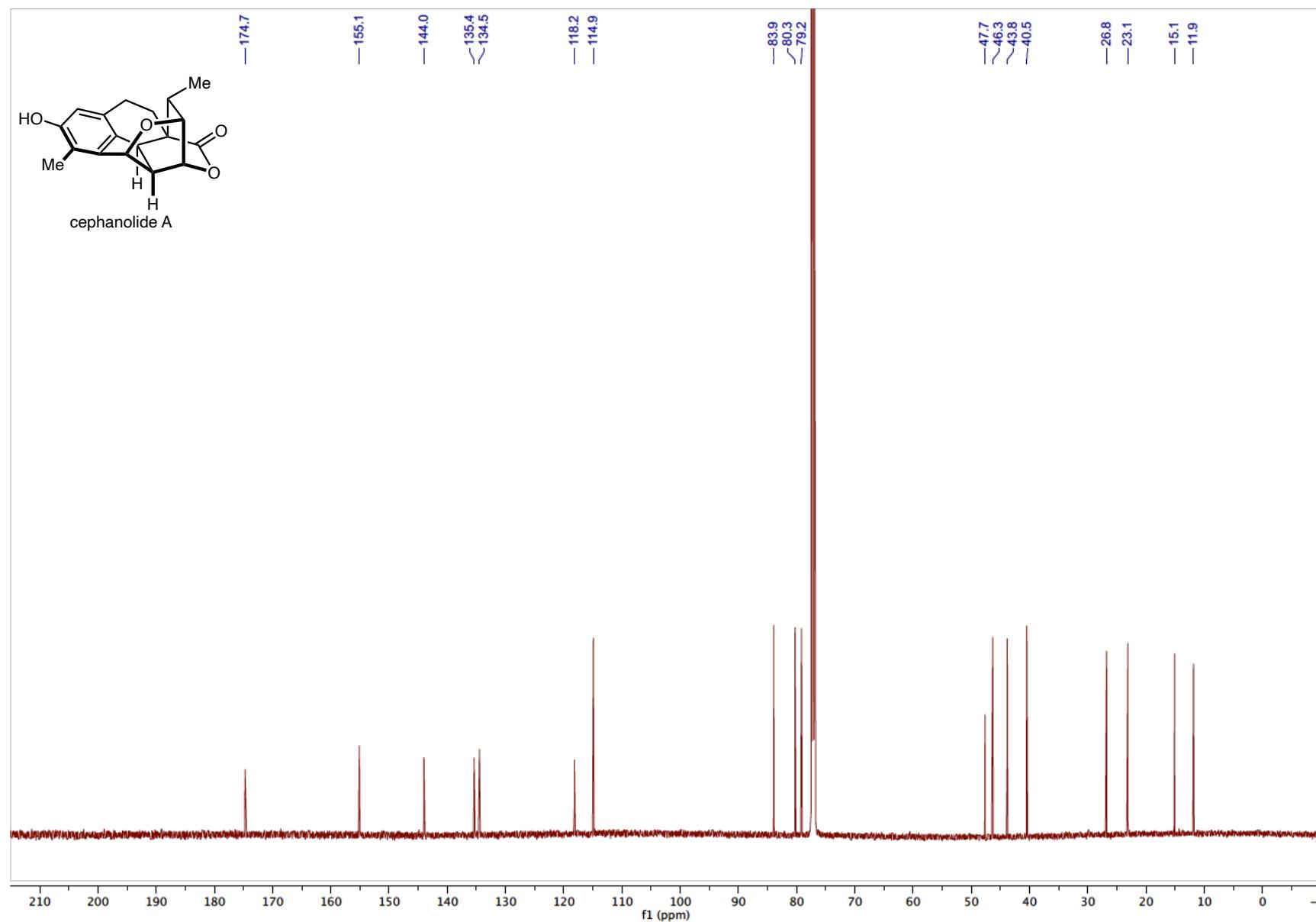
Cephanolide A: ^1H NMR (C13/C15 = 6:1)



Cephanolide A: ^1H NMR (pure)



Cephanolide A: ^{13}C NMR



5. References

- 1) Profitt, J. A.; Jones, T.; Watt, D. S. *Synth. Comm.* **1975**, *5*, 457–460.
- 2) Frébault, F.; Oliveira, M. T.; Wöstefeld, E.; Maulide, N. *J. Org. Chem.* **2010**, *75*, 7962–7965.
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- 4) Matsubara, S.; Oshima, K. *Proc. Jpn. Acad., Ser. B, Phys. Biol. Sci.* **2003**, *79*, 71–77.
- 5) Yuan, C.; Liang, Y.; Hernandez, T.; Berriochoa, A.; Houk, K. N.; Siegel, D. *Nature* **2013**, *499*, 192–196.
- 6) Xu, L.; Wang, C.; Gao, Z.; Zhao, Y.-M. *J. Am. Chem. Soc.* **2018**, *140*, 5653–5658.
- 7) Dragan, A.; Kubczyk, T. M.; Rowley, J. H.; Sproules, S.; Tomkinson, N. C. O. *Org. Lett.* **2015**, *17*, 2618–2621.
- 8) Zhang, H.; He, H.; Gao, S. Asymmetric Total Synthesis of Cephalolide A. *Angew. Chem. Int. Ed.* **2020**, Accepted Article. 10.1002/anie.202009562.