Total Syntheses of the Squalene-Derived Halogenated Polyethers *ent*-Dioxepandehydrothyrsiferol and Armatol A via Bromonium- and Lewis Acid-Initiated Epoxide-Opening Cascades

Supporting Information[1]

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[1] Part of this work has been reported in the Supporting Information of a previous communication: Tanuwidjaja, J.; Ng, S.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2009**, *131*, 12084.

I. Experimental Section

General Experimental Methods: Unless otherwise noted, all reactions were performed under an oxygen-free atmosphere of argon with rigid exclusion of moisture from reagents and glassware. Teflon stir bars were oven or flame-dried prior to use. Except where noted, all solvents and triethylamine used in the reactions were purified via an SG Water USA solvent column system. 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) (≥ 99%) was purchased from Aldrich Chemical Company and was used without further purification. Nitromethane was dried at 90 °C overnight with CaH_2 before being distilled into and stored in an airtight Schlenk tube. 4Å MS were activated by flame drying under high vacuum three times (with cooling in between) immediately before use. HN(*i*-Pr)$_2$, hexamethylphosphoramide (HMPA), and 1,3-dimethyltetrahydropyrimin-2(1*H*)-one (DMPU) were distilled from CaH_2 before use. BF_3•OEt_2 and Ti(O*i*-Pr)$_4$ were distilled from CaH_2 before use. EtOH was distilled from 4Å MS before use. Solvents for the Suzuki cross-coupling reaction were rigorously degassed through freeze-pump-thaw cycles within a week before use and kept in an airtight Schlenck tube. Cs_2CO_3 used in the Suzuki cross-coupling reaction was pumped on under high vacuum overnight, kept and used inside a glovebox. 9-Borabicyclo[3.3.1]nonane (9-BBN) dimer was pumped on under high vacuum overnight, kept and used inside a glovebox. CuI and the CH_2Cl_2 adduct of $PdCl_2$(dppf) was purchased from Strem chemical company and kept and used inside a glovebox. Bis(cyclooctadienyl)nickel(0) (Ni(cod)$_2$) and tricyclopentylphosphine (Cyp$_3$P) were purchased from Strem Chemicals, Inc., stored under nitrogen atmosphere and used without further purification. Tetrabutylammonium acetate was pumped under vacuum overnight, kept and used inside a glovebox. Trimethylsulfonium iodide was azeotropically dried from toluene three times before use. SO_3•pyr and $(CH_3)_3N$•HCl was pumped on under high vacuum overnight before use. $NaIO_4$ adsorbed on SiO_2 was made as follows: 2.57 g of $NaIO_4$ was dissolved in 5 mL of H_2O at 70−80 °C. It was then poured into 10.0 g of silica. The resulting mixture was stirred well for 30 min until homogenous.[2] Shi ketone **36** was prepared from D-fructose according to the procedure of Vidal-Ferran and coworkers and was used without recrystallization.[3] *t*-BuOOH was purchased from Fluka as a ~5.5 M solution in decane stored over activated 4Å MS. MsCl was distilled from calcium hydride before use. [(Ph$_3$P)CuH]$_6$ was purchased from Fluka (brick red powder), pumped on under high vacuum overnight, kept and used inside a glovebox. *N*-Bromosuccinimide (NBS) was recrystallized from H_2O before use and kept at 0 °C in the absence of light. Br(coll)$_2ClO_4$ was prepared according to the previously reported procedure,[4] and kept at 0 °C in the absence of light.

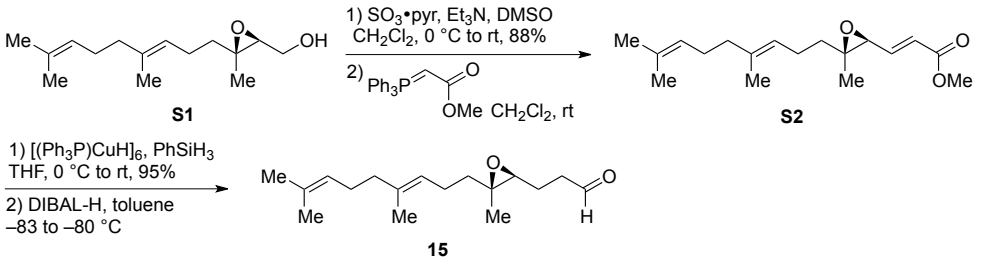
Analytical thin layer chromatography was performed using EM Science silica gel 60 F_{254} plates. The developed chromatogram was analyzed by UV lamp (254 nm) and Ceric Ammonium Molybdate (CAM) or ethanolic phosphomolybdic acid (PMA) solution. Liquid chromatography was performed using flash chromatography of the indicated solvent system on Silicycle Silica Gel (230-400 mesh). Alternatively, flash chromatography was also performed on the Biotage Isolera™ automated purification unit

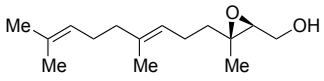
[2] Zhong, Y.-L.; Shing, T. K. M. *J. Org. Chem.* **1997**, *62*, 2622.

[3] Nieto, N.; Molas, P.; Benet-Buchholz, J.; Vidal-Ferran, A. *J. Org. Chem.* **2005**, *70*, 10143.

[4] (a) Neverov, A. A.; Brown, R. F. *J. Org. Chem.* **1998**, *63*, 5977. (b) Neverov, A. A.; Feng, H. X.; Hamilton, K.; Brown, R. S. *J. Org. Chem.* **2003**, *68*, 3802.

with SNAP columns.™ Analytical HPLC was performed on the column phase indicated on a Hewlett-Packard 1100 Series HPLC. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova-500 MHz, Bruker AVANCE-400 MHz, or Bruker AVANCE-600 MHz spectrometer in $CDCl_3$ or C_6D_6. Chemical shifts in ^{1}H NMR spectra are reported in part per million (ppm) on the δ scale from an internal standard of residual $CHCl_3$ in $CDCl_3$ (7.27 ppm) or residual C_6HD_5 in C_6D_6 (7.16 ppm). Data are reported as follows: chemical shift, multiplicity (app = apparent, br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in hertz (Hz), and integration. Chemical shifts of ^{13}C NMR spectra are reported in ppm from the central peak of $CDCl_3$ (77.23 ppm) or residual C_6D_6 (128.39 ppm) on the δ scale. ^{19}F NMR spectra were recorded on a Varian Inova-300 MHz or Bruker AVANCE-400 MHz spectrometer in C_6D_6 using either CF_3CH_2OH (at –77.8 ppm) or C_6F_6 (at –164.9 ppm) as a reference. Infrared (IR) spectra were recorded on a Perkin-Elmer 2000 FT-IR. High resolution mass spectra (HRMS) were obtained on a Bruker Daltonics APEXIV 4.7 Tesla Fourier Transform Ion Cyclotron Resonanace Mass Spectrometer by Li Li of the Massachusetts Institute of Technology Department of Chemistry Instrumentation Facility. Optical rotations were measured on a Jasco Model 1010 polarimeter at 589 nm.





L-(+)-Diethyltartrate (428 μL, 2.5 mmol, 12.5 mol %) and 4Å molecular sieves (2g, 0.1g/mmol) were placed in a 50 mL round bottom flask under a stream of argon. CH_2Cl_2 (20 mL) was added at room temperature, followed by Ti(O*i*-Pr)$_4$ (600 μL, 2 mmol, 10 mol %). The mixture was stirred vigorously at room temperature for 20 min. *tert*-Butylhydroperoxide (4.54 mL, ~25 mmol, 125 mol%, 5–6 M in decane) was added and the mixture was stirred 5 min at room temperature. The mixture was cooled in a CH_3CN / dry ice bath. The temperature was maintained below –40 °C. Farnesol (5.06 mL, 20 mmol, 100 mol %) was added and stirred in the CH_3CN / dry ice bath for 10 h. The mixture was placed in the freezer overnight. The next day citric acid monohydrate (420 mg, 2 mmol, 10 mol%) was dissolved in 1:1 acetone / diethylether (~5 mL) and the solution was added to the reaction mixture. The mixture was stirred vigorously for 20 min at room temperature. Celite was added to the mixture and stirred vigorously for 1 min. The slurry was filtered through a thick pad of celite and the celite was washed with Et_2O. The clear filtrate was washed with saturated $Na_2S_2O_3$ and then dried with $MgSO_4$. Column chromatography isolated 4.53 g of **S1** (95% yield). The enantiomeric excess was determined by HPLC of the benzoate to be 87%.

^{1}H NMR (400 MHz, $CDCl_3$):
δ 5.10 (m, 2H), 3.84 (ddd, *J* = 4.3, 7.5, 12.0 Hz, 1H), 3.70 (ddd, *J* = 4.9, 6.7, 11.8 Hz, 1H), 2.99 (dd, *J* = 4.3, 6.7 Hz, 1H), 2.16-1.94 (m, 6H), 1.71 (m, 1H), 1.69 (s, 3H), 1.614 (s, 3H), 1.608 (s, 3H), 1.48 (m, 1H), 1.32 (s, 3H).

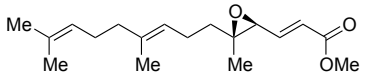
^{13}C NMR (125 MHz, $CDCl_3$):
δ 136.0, 131.6, 124.4, 123.3, 63.2, 61.6, 61.4, 39.8, 38.7, 26.8, 25.9, 23.8, 17.9, 17.0, 16.2.

IR (NaCl, thin film): 3422, 2919, 1456, 1384, 1033 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{15}H_{26}O_2$ $[M+Na]^+$: 261.1825, found 261.1830.

$[\alpha]^{20}_D$ = –4.2 (*c* = 1.9, $CHCl_3$).

Chiral HPLC analysis: Analysis was performed on the corresponding benzoate (BzCl, Et_3N, DMAP, CH_2Cl_2): (Chiralcel AD-H, hexanes:2-propanol, 99:1, 1.0 mL/min): t_R(2S,3S) = 7.3 min; t_R(2R,3R) = 8.1 min. The enantiomeric excess was determined to be 87%.



S2

Alcohol **S1** (1.57g, 6.59 mmol, 100 mol %) was dissolved in dichloromethane (50 mL). Triethylamine (4.60 mL, 32.9 mmol, 500 mol %) was then added at room temperature, followed by dimethylsulfoxide (12 mL). The mixture was cooled in an ice/water bath. SO_3•pyridine complex (2.64 g, 16.5 mmol, 250 mol %) was added in one portion. The wall of the flask was rinsed with 5 mL of dichloromethane. The reaction mixture was stirred in ice/water bath while slowly warming to rt for 5 h. The mixture was then diluted with diethylether, washed with saturated NH_4Cl and dried with $MgSO_4$. Column chromatography isolated 1.38 g of the intermediate aldehyde (88% yield).

The aldehyde was dissolved in dichloromethane (55 mL) at room temperature. (Methoxycarbonylmethylene)triphenylphosphorane (2.0 g, 11.68 mmol, 200 mol %) was added in one portion. The wall of the flask was rinsed with dichloromethane (5 mL). The mixture was stirred at room temperature overnight. The mixture was loaded directly to a silica column chromatography, which isolated 1.57 g of **S2** and its geometric isomer as a mixture (91% yield).

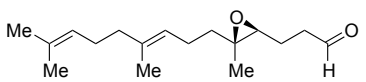
^{1}H NMR (400 MHz, $CDCl_3$):
δ 6.84 (dd, *J* = 6.4, 15.7 Hz, 1H), 6.10 (dd, *J* = 1.0, 15.7 Hz, 1H), 5.08 (m, 2H), 3.75 (s, 3H), 3.33 (dd, *J* = 0.8, 6.4 Hz, 1H), 2.20-1.90 (m, 6H), 1.74 (m, 1H), 1.68 (s, 3H), 1.60 (s, 6H), 1.55 (m, 1H), 1.28 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$):
δ 166.3, 143.4, 136.2, 131.7, 124.5, 124.3, 123.2, 64.4, 61.6, 51.9, 39.8, 38.6, 26.8, 25.9, 23.8, 17.9, 16.7, 16.2.

IR (NaCl, thin film): 2966, 2919, 2857, 1726, 1437, 1263, 1171 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{18}H_{28}O_3$ $[M+Na]^+$: 315.1931, found 315.1927.

$[\alpha]^{20}_D$ = +3.5 (*c* = 1.7, $CHCl_3$).



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Enoate **S2** (1.210 g, 4.138 mmol, 100 mol %) was placed in a 100 mL round bottom flask. The flask was evacuated under vacuum and back-filled with argon. Tetrahydrofuran (30 mL) was added at room temperature, followed by phenylsilane

(0.767 mL, 6.20 mmol, 150 mol %). The mixture was cooled in an ice/water bath. Triphenylphosphine-copper(I)-hydride-hexamer (161 mg, 0.0828 mmol, 2 mol %) was added in one portion. Rinse the wall of the flask with tetrahydrofuran (10 mL). Temperature gradually rose to room temperature. After a total of 2.5 h, TLC indicated that starting material was consumed. Still in the water bath, septum was removed and water (10 mL) was added. Bubbling occurred. The mixture was stirred in the water bath for 30 min. Celite was added while the mixture was vigorously stirring and the solid was filtered and rinsed with diethyl ether (200 mL). The filtrate was washed with saturated NH_4Cl. The organic fraction was dried with $MgSO_4$ and then filtered through a small plug of silica. Column chromatography isolated 1.2 g of the ester intermediate (98% yield).

The ester (966 mg, 3.28 mmol, 100 mol %) was dissolved in toluene (30 mL). The solution was cooled to –83 °C in a diethylether/dry ice bath. Stirred at –83 °C for 5 min. DIBAL-H solution (4.30 mL, 4.27 mmol, 130 mol %, 1 M in toluene) was diluted with toluene (16 mL) and added to the reaction mixture over 45 min. The temperature was kept below –80 °C throughout the reaction. After the addition completed the mixture was stirred below –80 °C for 1 h. Methanol (4 mL) was added, followed by saturated Rochelle's salt solution (30 mL). The cold bath was removed. The mixture was stirred for 1 h after the ice melted. The mixture was diluted with diethylether, washed with water and dried with $MgSO_4$. Column chromatography isolated 823 mg of **15** (94% yield).

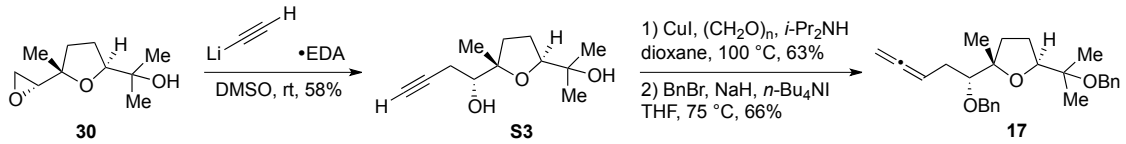
^{1}H NMR (400 MHz, $CDCl_3$):
δ 9.82 (t, *J* = 1.2 Hz, 1H), 5.08 (t, *J* = 5.5 Hz, 2H), 2.74 (dd, *J* = 5.1, 7.6 Hz, 1H), 2.62 (m, 2H), 2.10-1.85 (m, 7H), 1.82-1.60 (m, 2H), 1.67 (s, 3H), 1.60 (s, 3H), 1.59 (s, 3H), 1.43 (m, 1H). 1.27 (s, 3H).
^{1}H NMR (400 MHz, C_6H_6):
δ 9.24 (s, 1H), 5.24 (t, *J* = 6.8 Hz, 1H), 5.17 (t, *J* = 6.1 Hz, 1H), 2.49 (dd, *J* = 5.2, 7.5 Hz, 1H), 2.51-2.48 (m, 8H), 1.68 (s, 3H), 1.64-1.34 (m, 4H), 1.57 (s, 3H), 1.56 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$):
δ 201.2, 135.8, 131.6, 124.4, 123.6, 62.5, 61.5, 41.0, 39.9, 38.8, 26.8, 25.6, 23.9, 21.6, 17.8, 16.8, 16.2.
^{13}C NMR (100 MHz, C_6D_6):
δ 200.2, 135.8, 131.6, 125.2, 124.6, 62.3, 60.9, 41.2, 40.5, 39.3, 27.5, 26.2, 24.5, 22.1, 18.1, 17.0, 16.4.

HR-MS (ESI) *m/z* calcd for $C_{17}H_{28}O_2$ $[M+Na]^+$: 287.1982, found 287.1991.

IR (NaCl, thin film): 2966, 2924, 1726, 1451, 1385, 1108 cm^{-1}.

$[\alpha]^{20}_D$ = –10.4 (*c* = 3.2, CH_2Cl_2).
$[\alpha]^{20}_D$ = –11.4 (*c* = 4.2, $CHCl_3$).



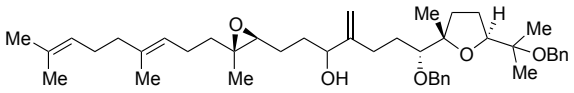
Epoxide **30** (1.22 g, 6.55 mmol, 100 mol%, 83:17 dr) was placed in a round bottom flask and the flask purged with argon. Lithium acetylide ethylene diamine complex (2.128 g, 19.7 mmol, 300 mol %, previously stored in a glove box) was quickly added to the epoxide. DMSO (13 mL) was added to the mixture. The reaction was exothermic. The mixture was stirred at rt for 18 h. Epoxide **30** was all consumed as judged by GCMS. The reaction mixture was cooled in an ice/water bath and quenched with water. The mixture was acidified to pH ~3 by 1M HCl, extracted with Et_2O, and dried with MgSO4. Column chromatography isolated 810 mg of the intermediate alkyne **S3** (58% yield).

CuI (359 mg, 1.884 mmol, 50 mol %), $(CH_2O)_n$ (283 mg, 9.42 mmol, 250 mol %), and *i*-Pr_2NH (1.06 mL, 7.536 mmol, 200 mol %) were placed in a pressure vessel and connected to an Ar line. Alkyne from the previous step (800 mg, 3.77 mmol, 100 mol %) in minimal Et_2O was added, followed by dioxane (8 mL). Et_2O was removed by bubbling nitrogen through the solution. The pressure vessel was purged with argon, then quickly sealed with a screw cap. The mixture was heated to 100 °C for 14 h. The mixture was cooled to rt. Solid was removed by filtration over celite and washed with Et_2O. Solvent was removed and redissolved in Et_2O and water was added. The mixture was acidified with 1 M HCl. Layers were separated and the aqueous layer was extracted again with Et_2O. The organic solution was washed with saturated $NaHCO_3$ and dried with $MgSO_4$. Column chromatography allowed separation of any minor diastereomer (hexane/ethyl acetate) to yield 542 mg of the allene intermediate (63% yield).

The allene intermediate (390 mg, 1.723 mmol, 100 mol%) was dissolved in THF (6.4 mL). Sodium hydride (92 mg, 3.844 mmol, 223 mol%) was added and the reaction was stirred at rt for 2 min. Benzyl bromide (0.457 mL, 3.844 mmol, 223 mol%) and *n*-Bu_4NI (473 mg, 1.281 mmol, 74 mol%) were added. The reaction was stirred at rt for 1 h and then 75 °C for 18 h. After the reaction mixture was cooled down to rt, it was poured into ice-cold water. This mixture was extracted with Et2O and dried with $MgSO_4$. Column chromatography isolated 142 mg of monobenzylether (27% yield) and 446 mg of dibenzylether **17** (66% yield).

^{1}H NMR (400 MHz, $CDCl_3$):
δ 7.40-7.10 (m, 10H), 5.22 (quintet, *J* = 7.2 Hz, 1H), 4.73 (dd, *J* = 11.6, 37.2 Hz, 2H), 4.66 (dd, *J* = 2.8, 6.4 Hz, 2H), 4.56 (t, *J* = 2.4 Hz, 2H), 3.98 (dd, *J* = 6.0, 9.6 Hz, 1H), 3.48 (dd, *J* = 3.2, 8.8 Hz, 1H), 2.33 (m, 1H), 2.15 (m, 2H), 1.87 (m, 2H), 1.60 (m, 1H), 1.27 (s, 3H), 1.23 (s, 3H), 1.19 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$):
δ 209.3, 140.4, 139.5, 128.44, 128.35, 127.9, 127.5, 127.2, 127.1, 88.0, 86.2, 86.15, 85.0, 76.6, 74.8, 74.5, 64.5, 33.4, 31.4, 27.6, 24.3, 22.5, 22.0.

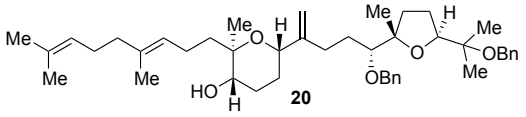


18

Ni(cod)$_2$ (309 mg, 1.12 mmol, 100 mol%) and Cyp$_3$P (315 μL, 1.12 mmol, 100 mol%) was placed into a flask in a glove box. The flask was sealed with a rubber septum and brought out of the glove box. Under argon, aldehyde **15** (594 mg, 2.25 mmol, 200 mol%) in THF (31 mL) was added to the catalyst mixture at room temperature to yield an orange-yellow solution. TBSH (269 μL, 1.69 mmol, 150 mol %) was added to the mixture. Allene **17** (440 mg, 1.12 mmol, 100 mol %) in THF (20 mL) was added to the reaction mixture over 3 h. After addition completed, the reaction mixture was stirred for 15 min. Volatiles were removed *in vacuo*. The crude was dissolved in Et$_2$O, washed with sat. NH$_4$Cl, and dried with MgSO$_4$. Column chromatography isolated an allylic ether in 67% yield. The silyl group was removed by TBAF in THF to yield epoxy-alcohol **18**.

^{1}H NMR (400 MHz, C_6D_6):
δ 7.42 (d, *J* = 7.8 Hz, 2H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 4H), 7.12 (t, *J* = 7.4 Hz, 2H), 5.21 (m, 2H), 5.14 (s, 0.5H), 5.10 (s, 0.5H), 4.88 (t, *J* = 11.3 Hz, 2H), 4.64 (s, 0.5H), 4.61 (s, 0.5H), 4.50 (dd, *J* = 11.9, 17.8 Hz, 2H), 4.08 (m, 0.5H), 4.00 (m, 0.5H), 3.96 (dd, *J* = 5.6, 9.6 Hz, 1.5H), 3.41 (d, *J* = 8.5 Hz, 1H), 2.67 (m, 1H), 2.35-1.38 (m, 20H), 1.68 (s, 3H), 1.57 (s, 6H), 1.25-1.12 (m, 12H).

^{13}C NMR (100 MHz, C_6D_6):
δ 152.8, 152.7, 141.2, 140.4, 140.4, 135.7, 131.6, 128.9, 128.8, 128.3, 128.2, 127.9, 127.6, 127.5, 125.2, 124.7, 109.9, 87.0, 87.0, 87.0, 85.5, 85.4, 76.6, 75.4, 75.2, 75.0, 74.8, 64.9, 63.7, 63.5, 61.1, 60.9, 40.5, 39.6, 39.5, 33.9, 33.7, 33.4, 33.3, 30.9, 30.90, 29.6, 29.4, 27.8, 27.5, 26.3, 25.9, 25.8, 24.8, 24.7, 24.55, 24.53, 23.0, 22.1, 22.0, 18.1, 17.19, 17.16, 16.4.



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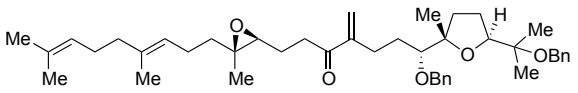
^{1}H NMR (500 MHz, C_6D_6):
δ 7.46 (d, *J* = 7.0 Hz, 2H), 7.40 (d, *J* = 7.4 Hz, 2H), 7.23 (m, 4H), 7.12 (t, *J* = 7.0 Hz, 2H), 5.25 (m, 2H), 5.18 (s, 1H), 4.93 (s, 1H), 4.90 (d, *J* = 11.8 Hz, 1H), 4.67 (d, *J* = 11.6 Hz, 1H), 4.51 (q, *J* = 11.9 Hz, 1H), 3.98 (dd, *J* = 5.8, 9.9 Hz, 1H), 3.94 (d, *J* = 8.4 Hz, 1H), 3.43 (dd, *J* = 2.8, 9.2 Hz, 1H), 3.18 (s, 1H), 2.55 (m, 1H), 2.35-1.40 (m, 19H), 1.69 (s, 3H), 1.61 (s, 3H), 1.58 (s, 3H), 1.25 (s, 3H), 1.23 (s, 3H), 1.21 (s, 3H), 1.20 (s, 3H).

^{13}C NMR (125 MHz, C_6D_6):
δ 151.3, 141.3, 140.6, 135.5, 131.7, 128.9, 128.8, 127.8, 127.6, 127.5, 125.3, 125.5, 110.0, 87.1, 87.0, 85.5, 77.3, 76.5, 75.1, 73.1, 69.4, 64.9, 40.6, 34.4, 33.7, 31.2, 29.9, 27.8, 27.6, 27.5, 26.3, 24.9, 24.3, 23.3, 23.2, 22.4, 22.0, 18.1, 16.5.

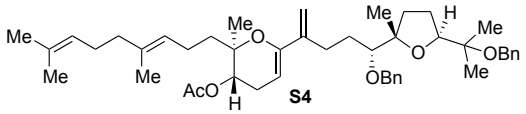


22

Epoxy-alcohol **18** (20.0 mg, 0.0297 mmol, 100 mol %), triethylamine (17 μL, 400 mol %), DMSO (21 μL, 1000 mol %) were dissolved in CH_2Cl_2 and cooled in an ice / water bath. SO_3•pyr (9.5 mg, 200 mol%) was added in one portion. The cold bath was allowed to be warmed gradually to rt. The mixture was stirred for 3 d. The mixture was diluted in CH_2Cl_2, washed with water, and dried with $MgSO_4$. Column chromatography isolated 8 mg of **22** (40% yield).

^{1}H NMR (400 MHz, C_6D_6):
δ 7.44 (d, *J* = 7.0 Hz, 2H), 7.40 (d, *J* = 7.0 Hz, 2H), 7.23 (q, *J* = 7.3 Hz, 4H), 7.12 (m, 2H), 5.55 (s, 1H), 5.33 (s, 1H), 5.22 (m, 2H), 4.88 (d, *J* = 11.6 Hz, 1H), 4.63 (d, *J* = 11.7 Hz, 1H), 4.50 (q, *J* = 11.9 Hz, 2H), 3.96 (dd, *J* = 5.8, 9.8 Hz, 1H), 3.37 (dd, *J* = 2.9, 9.1 Hz, 1H), 2.68 (dd, *J* = 4.6, 7.9 Hz, 1H), 2.57 (m, 3H), 2.12 (m, 7H), 1.96 (m, 1H), 1.86-1.52 (m, 7H), 1.67 (s, 3H), 1.57 (s, 6H), 1.45 (m, 2H), 1.21 (s, 3H), 1.19 (s, 3H), 1.17 (s, 3H), 1.14 (s, 3H).

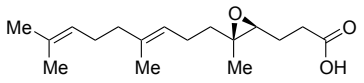
^{13}C NMR (100 MHz, C_6D_6):
δ 200.2, 149.5, 141.3, 140.5, 135.7, 131.6, 128.9, 127.9, 127.6, 127.5, 125.2, 124.7, 123.9, 86.9, 85.4, 76.5, 74.9, 64.9, 62.7, 61.0, 40.5, 39.5, 35.2, 33.7, 31.6, 29.2, 27.8, 27.5, 26.2, 24.7, 24.5, 24.3, 23.1, 22.1, 18.1, 17.2, 16.4.



S4

Enone **22** (~5 mg) was dissolved in CH_2Cl_2 (1.5 mL). Amberlyst 15 (2 mg) was added at rt. After stirring for 5 h, most enone **22** was consumed. Solid $NaHCO_3$ was added and the mixture was stirred 2h. The mixture was filtered through a cotton plug and concentrated. Column chromatography separated enone **22** from the cyclization product. The cyclization product was dissolved in CH_2Cl_2. Ac_2O, Et_3N and DMAP was added. The mixture was stirred 3 h at rt. After aqueous workup, column chromatography isolated the acetate **S4**. Comparison of NMR spectra of the acetate and the alcohol suggested that cyclization of enone **22** in Amberlyst 15 yielded a dihydropyran and not a dihydrofuran.

^{1}H NMR (500 MHz, C_6D_6):
δ 7.43 (d, *J* = 7.4 Hz, 2H), 7.40 (d, *J* = 7.7 Hz, 2H), 7.22 (m, 4H), 7.11 (m, 2H), 5.79 (s, 1H), 5.23 (t, *J* = 6.9 Hz, 2H), 5.12 (t, *J* = 5.9 Hz, 1H), 5.02 (s, 1H), 4.90 (m, 2H), 4.63 (d, *J* = 11.7 Hz, 1H), 4.50 (q, *J* = 11.7 Hz, 2H), 3.98 (dd, *J* = 5.7, 9.8 Hz, 1H), 3.40 (m, 1H), 2.61 (m, 1H), 2.43 (m, 1H), 2.33 (m, 2H), 2.27-1.97 (m, 7H), 1.74 (m, 6H), 1.68 (s, 3H), 1.62 (s, 6H), 1.56 (s, 3H), 1.36 (m, 1H), 1.26 (s, 3H), 1.22 (s, 3H), 1.20 (s, 3H), 1.15 (s, 3H).



26

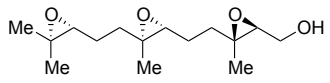
Aldehyde **15** (600 mg, 2.27 mmol, 100 mol %) was dissolved in 2-methyl-2-butene (60 mL, ~25 mL/mmol of aldehyde) at room temperature in a 250 mL Erlenmeyer flask. *tert*-Butyl alcohol (60 mL) and water (30 mL) were added. $NaH_2PO_4 \bullet H_2O$ (1.252 g, 9.076 mmol, 400 mol%) was added and the mixture was stirred vigorously at rt for 5 min until the mixture became homogeneous. Sodium chlorite (1.23 g, 13.6 mmol, 600 mol %) was added in one portion. The mixture was stirred vigorously at rt for 1 h. The mixture was poured into 5% aqueous NaH_2PO_4 solution (200 mL) and extracted twice with diethylether (100 mL then 150 mL). The organic fraction was dried with $MgSO_4$. NMR of the crude reaction mixture showed the desired acid **26**. The crude mixture was used directly in the next step.

^{1}H NMR (400 MHz, C_6D_6):
δ 5.23 (t, *J* = 6.7 Hz, 1H), 5.16 (t, *J* = 7.1 Hz, 1H), 2.59 (t, *J* = 6.7 Hz, 1H), 2.4-2.0 (m, 9H), 1.69 (s, 3H), 1.60 (m, 1H), 1.58 (s, 3H), 1.56 (s, 3H), 1.40 (m, 1H), 1.08 (s, 3H).

^{13}C NMR (100 MHz, C_6D_6):
δ 179.0, 135.8, 131.6, 125.2, 124.6, 62.2, 61.0, 40.5, 39.3, 31.5, 27.5, 26.2, 24.7, 24.5, 18.1, 17.0, 16.4.

HR-MS (ESI) *m/z* calcd for $C_{17}H_{28}O_3$ $[M+Na]^+$: 303.1931, found 303.1929.

$[\alpha]^{20}_D = -8.4$ (*c* = 3.0, CH_2Cl_2).



33

Alcohol **S1** (1.19 g, 5.00 mmol, 100 mol %), *n*-Bu_4NHSO_4 (0.679 g, 2.00 mmol, 40 mol %) and (–)-Shi ketone **36** (2.38 g, 10.0 mmol, 200 mol %) were placed into an 1 L Erlenmeyer flask. 1:2 CH_3CN:DMM (200 mL) was added at room temperature. The mixture was cooled in an ice/water bath. Buffer solution (100 mL, 0.05 M $Na_2B_4O_7 \bullet 10H_2O$, in $4x10^{-4}$ M Na_2EDTA solution) was added. K_2CO_3 solution (170 mL, 0.89 M in water) and oxone solution (24.9 g Oxone dissolved in $4x10^{-4}$ M Na_2EDTA solution to 170 mL) were added simultaneously over 45 min. After the addition completed the mixture was stirred for 10 min. The mixture was diluted with water to dissolve all solid. The mixture was extracted twice with dichloromethane (500 mL then 300 mL). The dichloromethane extract was dried with $MgSO_4$. The same procedure was performed three times. The combined crude was purified by column chromatography to yield 3.57 g of **33** (88% yield, average of three runs).

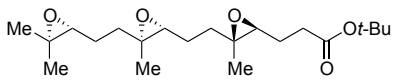
^{1}H NMR (400 MHz, $CDCl_3$):
δ 3.82-3.62 (m, 2H), 2.97 (t, *J* = 5.8 Hz, 1H), 2.75 (dd, *J* = 3.7, 7.7 Hz, 1H), 2.69 (t, *J* = 6.0 Hz, 1H), 2.62 (m, 1H), 1.96-1.48 (m, 8H), 1.30 (s, 3H), 1.291 (s, 3H), 1.289 (s, 3H), 1.25 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$):
δ 64.0, 63.2, 63.0, 61.0, 60.9, 60.8, 58.7, 36.2, 35.2, 25.0, 24.7, 24.6, 18.8. 16.9, 16.5.

IR (NaCl, thin film): 3442, 2964, 1457, 1386, 1035 cm^{-1}.

HRMS-ESI *m/z* calcd for $C_{15}H_{26}O_4$ $[M+Na]^+$: 293.172, found 293.173.

$[\alpha]^{20}_D$ = +26.2 (*c* = 2.1, $CHCl_3$).



31

Triphenylphosphine (5.83 g, 22.2 mmol, 120 mol %) and imidazole (3.03 g, 44.5 mmol, 240 mol %) were dissolved in 150 mL dichloromethane. The solution was stirred under argon and cooled in an ice/water bath. Iodine (5.64 g, 22.2 mmol, 120 mol %) was added in one portion. Once all iodine was dissolved, alcohol **33** (5.01 g, 18.5 mmol, 100 mol %) in 15 mL of dichloromethane was added. The reaction mixture was stirred in the ice/water bath for 30 min. The ice/water bath was removed and the mixture was stirred at rt for 30 min. The mixture was diluted to 200 mL and washed with 2:1 saturated $Na_2S_2O_3$/brine (200 mL). The aqueous layer was extracted again with CH_2Cl_2 (100 mL). The organic solution was dried with $MgSO_4$. The solution was concentrated to ~20 mL, diluted with 1:1 CH_2Cl_2/hexane, and loaded directly to a silica column that was packed with 1:1 CH_2Cl_2/hexane. Column chromatography isolated 6.1 g of the intermediate iodide (87% yield).

Diisopropylamine (7.53 mL, 53.7 mmol, 335 mmol%) was dissolved in 200 mL THF under argon. The solution was cooled to –78 °C and *n*-BuLi (19.9 mL, 49.7 mmol, 2.5 M in hexane, 310 mol %) was added in one portion. The mixture was stirred at –78 °C for 1.5 h. *tert*-Butylacetate (6.92 mL, 51.3 mmol, 320 mol %) was added. The reaction mixture was stirred for another 1.5 h at –78 °C. Iodide from the previous step (6.10 g, 16.0 mmol, 100 mol %) in THF (20 mL) was added to the reaction mixture. After 10 min at –78 °C, HMPA (8.02 mL, 0.5 mL/mmol iodide) was added. The mixture was stirred for 35 min at –78 °C and quenched with saturated NH_4Cl. The reaction was removed from the cold bath and allowed to warm to rt. The mixture was diluted with Et_2O, washed with saturated NH_4Cl, and dried with $MgSO_4$. Column chromatography isolated 5.25 g of ester **31** (88% yield).

^{1}H NMR (400 MHz, C_6D_6):
δ 2.64 (dd, *J* = 5.5, 7.1 Hz, 1H), 2.70-2.45 (m, 2H), 2.35-2.20 (m, 2H), 1.85-1.62 (m, 3H), 1.58-1.42 (m, 7H), 1.37 (s, 9H), 1.14 (s, 3H), 1.09 (s, 3H), 1.08 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (100 MHz, C_6D_6):
δ 172.3, 80.2, 63.7, 62.7, 62.6, 60.5, 60.0, 57.9, 36.3, 35.9, 32.9, 28.4, 25.4, 25.3, 25.1, 19.1, 17.2, 16.9.

IR (NaCl, thin film): 2965, 1728, 1462, 1367, 1153 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{21}H_{36}O_5$ $[M+Na]^+$: 391.2455, found 391.2465.

$[\alpha]^{20}_D$ = +4.3 (*c* = 5.6, CH_2Cl_2).

*X-Ray Crystallographic Data for Tricycle **34**:*

The structure is saved on MIT's Reciprocal Net server as sample 07089. It has also been deposited to the Cambridge Crystallographic Data Centre with submission number 931730. All thermal ellipsoid images were generated using Ortep-3 for Windows v. 2.02. all displacement ellipsoids are scaled to 50% probability.

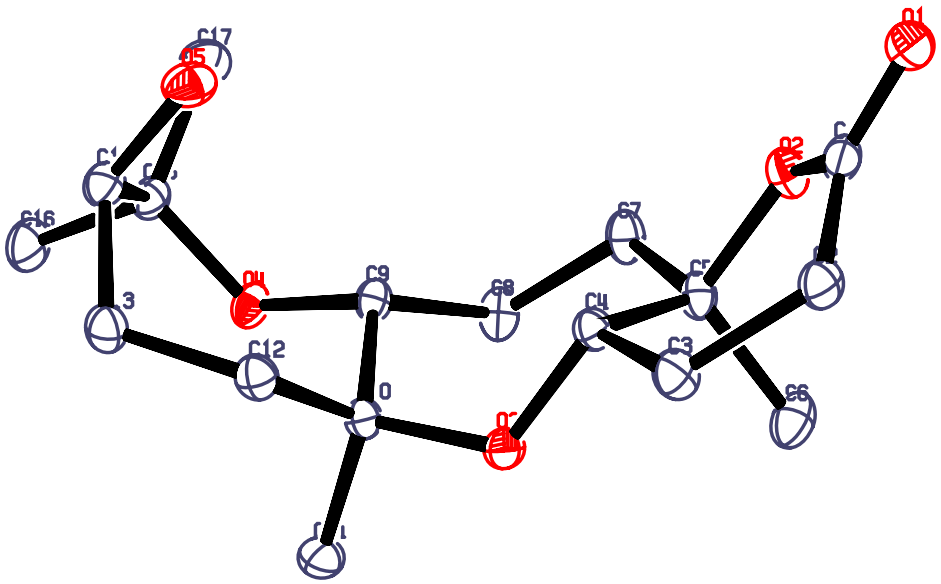


Table 1. Crystal data and structure refinement for 07089.

Identification code	07089	
Empirical formula	C17 H28 O5	
Formula weight	312.39	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 9.2319(3) Å	a= 90°.
	b = 11.1178(3) Å	b= 90°.
	c = 16.0469(5) Å	g = 90°.
Volume	1647.03(9) $Å^3$	
Z	4	
Density (calculated)	1.260 Mg/m^3	
Absorption coefficient	0.091 mm^{-1}	
F(000)	680	
Crystal size	0.50 x 0.35 x 0.30 mm^3	
Theta range for data collection	2.23 to 29.57°.	
Index ranges	-12<=h<=12, -15<=k<=15, -22<=l<=22	
Reflections collected	36736	
Independent reflections	2614 [R(int) = 0.0259]	
Completeness to theta = 29.57°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9732 and 0.9558	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2614 / 1 / 206	
Goodness-of-fit on F^2	1.031	
Final R indices [I>2sigma(I)]	R1 = 0.0302, wR2 = 0.0807	
R indices (all data)	R1 = 0.0312, wR2 = 0.0822	
Absolute structure parameter	?	
Largest diff. peak and hole	0.333 and -0.160 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 07089. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	-138(1)	6898(1)	1964(1)	24(1)
O(2)	2094(1)	6297(1)	2169(1)	19(1)
O(3)	4002(1)	3700(1)	1243(1)	17(1)
O(4)	7307(1)	5175(1)	496(1)	16(1)
O(5)	4984(1)	6087(1)	-917(1)	21(1)
C(1)	714(1)	6063(1)	1963(1)	18(1)
C(2)	285(1)	4792(1)	1761(1)	19(1)
C(3)	1473(1)	4016(1)	1357(1)	19(1)
C(4)	2950(1)	4630(1)	1324(1)	15(1)
C(5)	3231(1)	5360(1)	2122(1)	16(1)
C(6)	3171(1)	4584(1)	2904(1)	23(1)
C(7)	4615(1)	6123(1)	2087(1)	19(1)
C(8)	5992(1)	5490(1)	1787(1)	19(1)
C(9)	5891(1)	5158(1)	861(1)	14(1)
C(10)	5239(1)	3903(1)	702(1)	15(1)
C(11)	6289(1)	2903(1)	939(1)	21(1)
C(12)	4765(1)	3779(1)	-210(1)	17(1)
C(13)	5912(1)	4087(1)	-870(1)	19(1)
C(14)	6309(1)	5423(1)	-938(1)	17(1)
C(15)	7432(1)	5832(1)	-276(1)	16(1)
C(16)	8949(1)	5509(1)	-582(1)	24(1)
C(17)	7336(2)	7184(1)	-108(1)	23(1)

Table 3. Bond lengths [Å] and angles [°] for 07089.

O(1)-C(1)	1.2164(16)
O(2)-C(1)	1.3414(15)
O(2)-C(5)	1.4799(14)
O(3)-C(4)	1.4251(14)
O(3)-C(10)	1.4523(13)
O(4)-C(9)	1.4322(13)
O(4)-C(15)	1.4418(14)
O(5)-C(14)	1.4287(15)
C(1)-C(2)	1.5027(18)
C(2)-C(3)	1.5389(17)
C(3)-C(4)	1.5262(16)
C(4)-C(5)	1.5386(16)
C(5)-C(6)	1.5243(17)
C(5)-C(7)	1.5347(17)
C(7)-C(8)	1.5314(17)
C(8)-C(9)	1.5342(15)
C(9)-C(10)	1.5408(16)
C(10)-C(11)	1.5223(17)
C(10)-C(12)	1.5334(16)
C(12)-C(13)	1.5370(17)
C(13)-C(14)	1.5336(17)
C(14)-C(15)	1.5526(16)
C(15)-C(16)	1.5275(17)
C(15)-C(17)	1.5293(17)

C(1)-O(2)-C(5)	121.67(10)
C(4)-O(3)-C(10)	118.51(9)
C(9)-O(4)-C(15)	115.50(9)
O(1)-C(1)-O(2)	117.78(12)
O(1)-C(1)-C(2)	123.19(12)
O(2)-C(1)-C(2)	119.01(11)
C(1)-C(2)-C(3)	115.51(10)
C(4)-C(3)-C(2)	113.59(10)
O(3)-C(4)-C(3)	106.72(9)

O(3)-C(4)-C(5)	110.09(9)
C(3)-C(4)-C(5)	110.96(9)
O(2)-C(5)-C(6)	109.33(9)
O(2)-C(5)-C(7)	101.74(10)
C(6)-C(5)-C(7)	111.90(10)
O(2)-C(5)-C(4)	107.08(9)
C(6)-C(5)-C(4)	112.37(10)
C(7)-C(5)-C(4)	113.68(9)
C(8)-C(7)-C(5)	116.65(11)
C(7)-C(8)-C(9)	111.42(10)
O(4)-C(9)-C(8)	109.74(9)
O(4)-C(9)-C(10)	107.52(9)
C(8)-C(9)-C(10)	113.68(9)
O(3)-C(10)-C(11)	103.75(9)
O(3)-C(10)-C(12)	109.41(9)
C(11)-C(10)-C(12)	110.76(10)
O(3)-C(10)-C(9)	110.44(9)
C(11)-C(10)-C(9)	111.77(10)
C(12)-C(10)-C(9)	110.51(9)
C(10)-C(12)-C(13)	116.17(10)
C(14)-C(13)-C(12)	115.40(10)
O(5)-C(14)-C(13)	107.13(10)
O(5)-C(14)-C(15)	113.85(10)
C(13)-C(14)-C(15)	113.23(10)
O(4)-C(15)-C(16)	103.31(9)
O(4)-C(15)-C(17)	110.02(10)
C(16)-C(15)-C(17)	109.93(11)
O(4)-C(15)-C(14)	112.69(9)
C(16)-C(15)-C(14)	108.87(10)
C(17)-C(15)-C(14)	111.69(10)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for 07089. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	21(1)	25(1)	26(1)	6(1)	5(1)	5(1)
O(2)	15(1)	21(1)	21(1)	-3(1)	3(1)	1(1)
O(3)	13(1)	17(1)	21(1)	4(1)	4(1)	1(1)
O(4)	11(1)	22(1)	15(1)	3(1)	1(1)	-1(1)
O(5)	18(1)	22(1)	24(1)	6(1)	-3(1)	2(1)
C(1)	16(1)	22(1)	15(1)	3(1)	4(1)	1(1)
C(2)	13(1)	22(1)	21(1)	2(1)	2(1)	0(1)
C(3)	13(1)	20(1)	24(1)	-1(1)	2(1)	-2(1)
C(4)	13(1)	16(1)	16(1)	0(1)	1(1)	0(1)
C(5)	12(1)	21(1)	15(1)	-2(1)	1(1)	1(1)
C(6)	17(1)	34(1)	17(1)	5(1)	0(1)	1(1)
C(7)	16(1)	25(1)	17(1)	-6(1)	2(1)	-3(1)
C(8)	13(1)	28(1)	15(1)	-3(1)	-1(1)	-2(1)
C(9)	11(1)	18(1)	14(1)	0(1)	1(1)	-1(1)
C(10)	12(1)	16(1)	16(1)	1(1)	2(1)	1(1)
C(11)	18(1)	19(1)	25(1)	5(1)	3(1)	5(1)
C(12)	17(1)	16(1)	18(1)	-2(1)	0(1)	-1(1)
C(13)	20(1)	19(1)	16(1)	-3(1)	1(1)	-1(1)
C(14)	17(1)	20(1)	15(1)	1(1)	0(1)	0(1)
C(15)	14(1)	19(1)	16(1)	2(1)	2(1)	-1(1)
C(16)	16(1)	32(1)	25(1)	4(1)	6(1)	1(1)
C(17)	22(1)	19(1)	28(1)	1(1)	1(1)	-5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 07089.

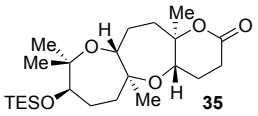
	x	y	z	U(eq)
H(5)	5030(20)	6705(14)	-1211(11)	26
H(2A)	-559	4816	1381	23
H(2B)	-31	4395	2283	23
H(3A)	1565	3256	1674	23
H(3B)	1171	3809	783	23
H(4)	2997	5173	828	18
H(6A)	3320	5090	3396	34
H(6B)	3933	3971	2878	34
H(6C)	2223	4191	2940	34
H(7A)	4432	6818	1716	23
H(7B)	4800	6446	2652	23
H(8A)	6146	4751	2119	22
H(8B)	6835	6025	1875	22
H(9)	5277	5771	572	17
H(11A)	6597	3010	1518	31
H(11B)	7137	2934	572	31
H(11C)	5807	2123	878	31
H(12A)	3915	4307	-300	20
H(12B)	4443	2941	-302	20
H(13A)	6804	3628	-743	22
H(13B)	5556	3812	-1420	22
H(14)	6754	5551	-1499	21
H(16A)	9659	5701	-148	36
H(16B)	9170	5972	-1086	36
H(16C)	8992	4648	-709	36
H(17A)	6399	7371	149	34
H(17B)	7428	7624	-634	34
H(17C)	8118	7424	270	34

Table 6. Hydrogen bonds for 07089 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(5)-H(5)...O(1)#1	0.834(14)	1.974(15)	2.8025(13)	171.6(19)

Symmetry transformations used to generate equivalent atoms:

#1 x+1/2,-y+3/2,-z



35

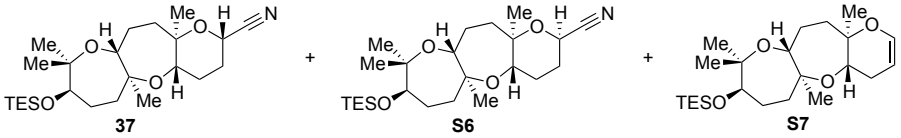
Alcohol **34** solution in CH_2Cl_2 (~3-5 mL) from the previous step and imidazole (3.00 g, 44.07 mmol) were dissolved in DMF (20 mL) and fitted with a condenser. The reaction setup was purged with argon. Chlorotriethylsilane (3.00 mL, 17.9 mmol) was added to the reaction mixture at rt. The mixture was heated for 16 h at 45 °C and then quenched with MeOH (3 mL). The mixture was stirred for 45 min at 45 °C. The mixture was cooled to rt. The mixture was diluted with Et_2O, washed with saturated NH_4Cl and dried with $MgSO_4$. Column chromatography isolated 1.53 g of silyl ether **35** (25% from ester **31**).

^{1}H NMR (400 MHz, C_6D_6):
δ 4.18 (d, *J* = 9.1 Hz, 1H), 3.74 (dd, *J* = 5.0, 11.9 Hz, 1H), 3.55 (d, *J* = 6.7 Hz, 1H), 2.35-2.10 (m, 3H), 2.85-1.25 (m, 9H), 1.26 (s, 3H), 1.18 (s, 3H), 1.16 (s, 3H), 0.96 (s, 3H); 0.93 (t, *J* = 8.0 Hz, 9H), 0.47 (q, J = 7.9 Hz, 6H).

^{13}C NMR (100 MHz, C_6D_6):
168.0, 84.6, 80.3, 78.7, 78.0, 76.3, 69.3, 42.5, 32.0, 29.8, 28.9, 28.7, 26.6, 25.7, 23.6, 20.9, 20.7, 7.6, 5.5.

IR (NaCl, thin film): 2952, 1740, 1380, 1267, 1083, 738 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{23}H_{42}O_5Si$ $[M+Na]^+$: 449.2694, found 449.2698.



37 **S6** **S7**

Lactone **35** (1.50 g, 3.52 mmol, 100 mol %) was dissolved in toluene (50 mL) and cooled to –78 °C under argon. DIBAL-H (5.27 mL, 5.27 mmol, 1 M in toluene) was diluted in toluene (15 mL) and the diluted DIBAL-H solution was added to the lactone solution over 40 min. After addition completed the reaction was stirred an extra 5 min. The reaction mixture was quenched with methanol (5.3 mL) and the mixture was stirred 10 min. The cold solution was poured into saturated Rochelle's salt solution (200 mL), diluted with Et_2O (100 mL), and stirred vigorously for 1 h. Layers were separated and the aqueous layer was extracted with diethylether. The organic mixture was dried with $MgSO_4$ and concentrated. The crude hemiacetal was used directly.

The crude hemiacetal was dissolved in dichloromethane (35 mL) and cooled to –12 °C under argon. Trimethylsilylcyanide (2.200 mL, 17.6 mmol, 500 mol %) was added, followed by BF_3•OEt_2 (0.67 mL, 5.27 mmol, 150 mol %). The mixture was stirred 45 min and the temperature gradually rose to –5 °C. The reaction was quenched with 1:1:1 CH_2Cl_2/MeOH/Et_3N (35 mL) and stirred 15 min at –5 °C. The mixture was diluted with

Et_2O, washed with saturated $NaHCO_3$, and dried with $MgSO_4$. Column chromatography isolated 600 mg of **37** (39%), 190 mg of its diastereomer **S6** (12%), and 420 mg of cyclic enol ether **S7** (29%). Relative configurations of **37** and **S6** were determined by nOe data.

Characterization data for tricycle **37**:

^{1}H NMR (400 MHz, C_6D_6):
δ 4.18 (d, *J* = 10.2 Hz, 1H), 4.00 (d, *J* = 4.5 Hz, 1H), 3.56 (d, *J* = 6.8 Hz, 1H), 3.40 (dd, *J* = 4.5, 11.6 Hz, 1H), 2.16 (dt, *J* = 2.8, 13.2 Hz, 1H), 2.00-1.70 (m, 3H), 1.61 (s, 3H), 1.70-1.31 (m, 8H), 1.30 (s, 3H), 1.18 (s, 3H), 0.97 (s, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.50 (q, *J* = 7.8 Hz, 6H).

^{13}C NMR (100 MHz, C_6D_6):
δ 120.7, 80.8, 80.2, 78.5, 78.1, 76.4, 71.2, 59.6, 42.8, 32.3, 29.8, 29.1, 28.8, 26.6, 25.1, 23.6, 21.0, 18.3, 7.6, 5.4.

IR (NaCl, thin film): 2950, 1458, 1379, 1233, 1100, 729 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{24}H_{43}NO_4Si$ $[M+Na]^+$: 460.2854, found 460.2860.

$[\alpha]^{20}_D$ = +12.9 (*c* = 3.1, CH_2Cl_2).

Characterization data for tricycle **S6**:

^{1}H NMR (400 MHz, C_6D_6):
δ 4.21 (d, *J* = 10.0 Hz, 1H), 3.59 (dd, *J* = 2.4, 12.1 Hz, 1H), 3.56 (d, *J* = 6.8 Hz, 1H), 2.18 (dt, *J* = 2.7, 12.8 Hz, 1H), 1.84 (m, 1H), 1.72-1.38 (m, 8H), 1.32 (m, 1H), 1.30 (s, 3H), 1.21 (s, 3H), 1.17 (m, 1H), 0.98 (s, 3H), 0.96 (t, *J* = 7.9 Hz, 1H), 0.90 (s, 3H), 0.49 (q, *J* = 8.0 Hz, 6H).

^{13}C NMR (100 MHz, C_6D_6):
δ 119.2, 80.1, 79.7, 78.6, 78.0, 76.3, 70.2, 59.6, 42.1, 32.2, 31.1, 29.2, 28.8, 27.6, 26.6, 23.6, 21.0, 15.7, 7.6, 5.5.

IR (NaCl, thin film): 2951, 2877, 1458, 1380, 1244, 1094, 738 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{24}H_{43}NO_4Si$ $[M+Na]^+$: 460.2854, found 460.2867.

$[\alpha]^{20}_D$ = –7.0 (*c* = 3.3, CH_2Cl_2).

Characterization data for tricycle **S7**:

^{1}H NMR (400 MHz, C_6D_6):
δ 6.23 (d, *J* = 6.1 Hz, 1H), 4.46 (dt, *J* = 2.4, 5.4 Hz, 1H), 4.30 (d, *J* = 9.9 Hz, 1H), 3.95 (dd, *J* = 6.7, 9.4 Hz, 1H), 3.60 (d, *J* = 6.9 Hz, 1H), 2.36 (dt, *J* = 3.0, 13.1 Hz, 1H), 2.30-1.80 (m, 5H), 1.68 (dt, *J* = 2.7, 14.4 Hz, 1H), 1.60 (m, 2H), 1.41 (m, 1H), 1.40 (s, 3H),

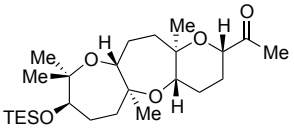
1.30 (s, 3H), 1.24 (s, 3H), 1.01 (s, 3H), 0.97 (t, J = 7.9 Hz, 9H), 0.50 (q, J = 7.9 Hz, 6H).

^{13}C NMR (100 MHz, C_6D_6):
δ 141.7, 97.5, 79.8, 78.7, 78.6, 78.2, 77.2, 68.6, 42.5, 31.9, 29.2, 28.8, 27.8, 26.7, 23.8, 21.2, 17.8, 7.6, 5.5.

IR (NaCl, thin film): 2952, 1656, 1445, 1380, 1248, 1081, 1045, 737 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{23}H_{42}O_4Si$ $[M+Na]^+$: 433.3745, found 433.2755.

$[\alpha]^{20}_D$ = +9.4 (c = 3.1, CH_2Cl_2).



38

$Ni(acac)_2$ (9 mg, 0.0338 mmol, 37 mol %) was dissolved in toluene (0.9 mL, saturated with N_2) and cooled to –15 °C. Methylmagnesium bromide (200 μL, 0.274 mmol, 300 mol %, 1.4 M in 3:1 THF/toluene) was added and stirred 5 min. The mixture turned from green to black. Nitrile **37** (40 mg, 0.0915 mmol, 100 mol %, >95:5 dr) was dissolved in toluene (1.3 mL) and added to the catalyst mixture. The mixture was stirred 30 min and temperature slowly warmed to –8 °C. The mixture was cooled in an ice/water bath, poured into ice-cold HCl solution (4 mL, 0.5 M), and rinsed with Et_2O. The mixture was stirred vigorously for 15 min. The mixture was diluted with Et_2O, washed with saturated NH_4Cl, and dried with $MgSO_4$. Column chromatography isolated 21.0 mg of **38** (50% yield, 93:7 dr)

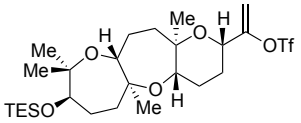
^{1}H NMR (400 MHz, C_6D_6):
δ 4.36 (d, J = 9.9 Hz, 1H), 3.71 (dd, J = 2.4, 6.3 Hz, 1H), 3.68 (m, 1H), 3.65 (d, J = 6.6 Hz, 1H), 2.45-2.25 (m, 2H), 2.06 (s, 3H), 2.12-1.82 (m, 4H), 1.75-1.55 (m, 5H), 1.45 (m, 1H), 1.41 (s, 3H), 1.29 (s, 3H), 1.20 (s, 3H), 1.06 (t, J = 8.1 Hz, 12H), 0.59 (q, J = 7.9 Hz, 6H).

^{13}C NMR (100 MHz, C_6D_6):
δ 209.6, 79.9, 79.6, 78.5, 78.2, 76.7, 76.1, 71.8, 43.1, 32.2, 29.6, 28.8, 26.7, 26.4, 25.3, 24.5, 23.7, 21.1, 18.7, 7.7, 5.5.

IR (NaCl, thin film): 2952, 1719, 1457, 1379, 1243, 1101, 729 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{25}H_{46}O_5Si$ $[M+Na]^+$: 477.3007, found 477.3004.

$[\alpha]^{20}_D$ = –9.18 (c = 4.7, CH_2Cl_2).



39

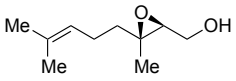
Comins' reagent (40 mg, 0.102 mmol, 115 mol %) was dissolved in THF (0.5 mL) and cooled to –78 °C. LHMDS (0.90 mL, 0.18 mmol, 200 mol%, 0.2 M in THF, freshly prepared) was added to the Comins' reagent solution. After stirring for 2 min at –78 °C, ketone **38** (40.0 mg, 0.884 mmol, 100 mol %) in THF (1 mL) was added. More THF (0.5 mL) was used to rinse the wall of the flask. The mixture was stirred 2.5 h at –78 °C and then at 0 °C for 30 min. The crude was diluted with Et_2O and washed with saturated $NaHCO_3$ and then twice with 1M NaOH. The crude was dried with $MgSO_4$ and concentrated. NMR of the crude indicated the presence of the alkenyl triflate **39** and HMDS. The crude was used directly in the next step.

^{1}H NMR (400 MHz, C_6D_6):
δ 4.77 (dd, *J* = 1.1, 4.0 Hz, 1H), 4.54 (dd, *J* = 1.5, 3.9 Hz, 1H), 4.34 (m, 1H), 4.24 (d, *J* = 10.2 Hz, 1H), 3.66 (dd, *J* = 5.0, 11.2 Hz, 1H), 3.57 (m, 1H), 2.25 (t, *J* = 13.1 Hz, 1H), 1.99-1.15 (m, 11H), 1.41 (s, 3H), 1.33 (s, 3H), 1.30 (s, 3H), 1.20 (s, 3H), 1.00 (t, *J* = 8.0 Hz, 9H), 0.53 (q, *J* = 7.8 Hz, 6H).

^{13}C NMR (100 MHz, C_6D_6):
δ 157.7, 104.9, 80.2, 79.6, 78.6, 78.1, 76.5, 71.2, 68.2, 67.8, 42.0, 32.5, 29.4, 28.8, 26.7, 26.1, 24.4, 23.6, 21.1, 19.3, 7.7, 5.5.

^{19}F NMR (376 MHz, C_6D_6):
δ –76.32 (s, 3F). (Referenced with CF_3CH_2OH at –77.8 ppm).

HR-MS (ESI) *m/z* calcd for $C_{26}H_{45}F_3O_7SSi$ $[M+Na]^+$: 609.2500, found 609.2491.



S8

L-(+)-Diethyltartrate (5.55 mL, 32.4 mmol, 12.5 mol %) and 4Å molecular sieves (26 g, 0.1 g/mmol alkene) were placed in a 500 mL Erlenmeyer flask under a stream of argon. Dichloromethane (260 mL) was added at room temperature, followed by Ti(O*i*-Pr)$_4$ (7.7 mL, 25.9 mmol, 10 mol %). The mixture was stirred vigorously at room temperature for 20 min. *tert*-Butylhydroperoxide (59.0 mL, ~324 mmol, 125 mol %, 5–6 M in decane) was added and the mixture was stirred 10 min at room temperature. The mixture was cooled in a CH_3CN/dry ice bath. The temperature was maintained below –40 °C. Geraniol (45.5 mL, 259 mmol, 100 mol%) was added and stirred in the CH_3CN/dry ice bath for 10 h. The mixture was placed in the freezer overnight. The next day citric acid monohydrate (5.44 g, 25.9 mmol, 10 mol %) was dissolved in 1:1 acetone / diethylether (just enough to dissolve all citric acid monohydrate) and the solution was added to the reaction mixture. The mixture was stirred vigorously for 1 h at room temperature. Celite was added to the mixture and stirred vigorously for 1 min. The slurry

was filtered through a thick pad of celite and the celite was washed with Et_2O. The mixture was concentrated andsaturated $Na_2S_2O_3$ (400 mL) was added to the ether solution. White solid precipitated, which was filtered with the aid of celite and silica gel to give a clear solution. Layers were separated. Aqueous layer was extracted again with Et_2O. Combined organic solution was washed again with saturated $Na_2S_2O_3$ and then dried with $MgSO_4$. The organic solution was concentrated to ~400 mL. Sodium hydroxide solution in brine (32.4 mL, this solution was prepared from 30 g NaOH, 5 g NaCl and 90 mL H_2O) was added and the mixture was stirred vigorously in an ice / water bath for 45 min. The aqueous layer was separated and the organic layer was dried with $MgSO_4$. The organic solution was concentrated and vacuum distillation removed low boiling materials and isolated 42 g of epoxide **S8** (95% yield). The crude was used directly.
The enantiomeric excess was determined by HPLC of the benzoate to be 84.5%.

^{1}H NMR (500 MHz, C_6D_6):
δ 5.05 (t, *J* = 7.2 Hz, 1H), 3.79 (dd, *J* = 4.1, 12.2 Hz, 1H), 3.64 (dd, *J* = 6.9, 12.2 Hz, 1H), 2.96 (dd, *J* = 4.12, 6.9 Hz, 1H), 2.70 (bs, 1H), 2.06 (m, 2H), 1.66 (s, 3H), 1.64 (m, 1H), 1.58 (s, 3H), 1.44 (m, 1H), 1.27 (s, 3H).

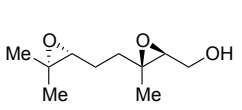
^{13}C NMR (125 MHz, C_6D_6):
δ 132.3, 123.4, 63.4, 61.5, 61.4, 38.6, 25.8, 23.8, 17.8, 16.9.

IR (NaCl, thin film): 3419, 2926, 1452, 1384, 1033 cm^{-1}.

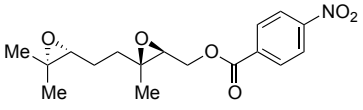
HR-MS (ESI) *m/z* calcd for $C_{10}H_{18}O_2$ $[M+Na]^+$: 193.1199, found 193.1203.

$[\alpha]^{20}_D$ = –4.7 (*c* = 10.0, $CHCl_3$).

Chiral HPLC analysis: Analysis was performed on the corresponding benzoate of the epoxide alcohol (BzCl, Et_3N, CH_2Cl_2): Chiralcel AD-H, hexanes:2-propanol, 99:1, 1.0 mL/min. The retention times for the two enantiomers were 8.9 and 9.5 min.



32



S9

Alcohol **S8** (5.53 g, 32.5 mmol, 100 mol %), *n*-Bu_4NHSO_4 (441 mg, 1.30 mmol, 4 mol %), and (–)-Shi ketone **36** (2.32 g, 9.75 mmol, 30 mol %) were placed in a 2 L bottle with a big stir bar. 0.05 M $Na_2B_4O_7$•$10H_2O$ in $4x10^{-4}$ M EDTA (325 mL, 10 mL/mmol alkene) added, followed by a 1:2 mixture of CH_3CN/DMM (488 mL). This mixture was cooled in an ice/water bath and stirred vigorously. Oxone (27.6 g, 44.9 mmol, 138 mol %) in $4x10^{-4}$ M EDTA (214 mL, to make a 0.21 M Oxone solution) and aqueous K_2CO_3 solution (0.89 M, same volume as the Oxone solution) were added to the reaction mixture simultaneously over ~30 min. Once the addition was completed the reaction mixture was stirred for another 15 min and quenched with water. The mixture was extracted with CH_2Cl_2 (1.5 L), dried with $MgSO_4$, and column chromatography isolated 5.02 g of epoxy-

alcohol **32** (83% yield).

To upgrade the enantio- and diastereoratio of epoxy-alcohol **32**, this intermediate was converted to a *p*-nitrobenzoate **S9** (*p*-NO_2BzCl, Et_3N, CH_2Cl_2, rt) and recrystallized to afford a pale yellow solid. Saponification of **S9** (1 M NaOH, 1:3 H_2O/THF, rt; extraction with Et_2O) returned epoxy-alcohol **32** with 95% *ee* and 95:5 dr.

^{1}H NMR (400 MHz, C_6D_6):
δ 3.77 (dd, *J* = 5.4, 11.7 Hz, 1H), 3.67 (dd, *J* = 6.2, 11.8 Hz, 1H), 2.99 (t, *J* = 5.8 Hz, 1H), 2.74 (dd, *J* = 4.1, 8.1 Hz, 1H), 2.65 (bs, 1H), 1.91 (m, 1H), 1.81 (m, 1H), 1.56 (m, 2H), 1.31 (s, 3H), 1.31 (s, 3H), 1.28 (s, 3H).

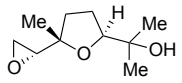
^{13}C NMR (100 MHz, C_6D_6):
δ 64.5, 63.0, 61.0, 60.9, 59.0, 36.3, 25.0, 24.9, 18.9, 16.6.

IR (NaCl, thin film): 3424, 2964, 1458, 1380, 1032 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{10}H_{18}O_3$ $[M+Na]^+$: 209.1148, found 209.1149.

$[\alpha]^{20}_D$ = +35.2 (*c* = 1.1, $CHCl_3$) before recrystallization from benzoate.
$[\alpha]^{20}_D$ = +39.7 (*c* = 3.2, $CHCl_3$) after recrystallization from benzoate.

Chiral HPLC analysis: Analysis was performed on the corresponding benzoate of **32** (BzCl, Et_3N, DMAP, DCM): Chiralcel AD-H, hexanes:2-propanol, 99:1, 1.3 mL/min. The retention times for the four possible diastereomers were 28.6, 30.4, 32.6, and 49.3 min. The retention time of the desired diastereomer was 30.4 min.



30

Epoxyalcohol **32** (2.51 g, 13.5 mmol, 100 mol %) was dissolved in THF (6 mL) in a 100 mL round bottom flask. The solution was stirred vigorously while NaOH solution (27 mL, 0.5 M, 100 mol %) was added at rt over 2 min. The mixture was stirred for 16 h. It was diluted with Et_2O (350 mL) and the layers were separated. The aqueous layer was extracted again with 50 mL Et_2O. The combined organic solution was dried with $MgSO_4$. Column chromatography isolated 1.50 g of epoxide **30** (59% yield).

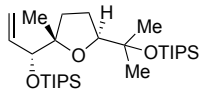
^{1}H NMR (400 MHz, C_6D_6):
δ 3.76 (t, *J* = 7.4 Hz, 1H), 3.01 (dd, *J* = 2.8, 4.1 Hz, 1H), 2.72 (t, *J* = 4.8 Hz, 1H), 2.56 (dd, *J* = 2.8, 5.0 Hz, 1H), 2.16 (bs, 1H), 1.82 (m, 3H), 1.60 (m, 1H), 1.25 (s, 3H), 1.20 (s, 3H), 1.11 (s, 3H).

^{13}C NMR (100 MHz, C_6D_6):
δ 86.9, 81.4, 70.8, 57.2, 44.0, 32.9, 27.6, 26.4, 24.4, 24.3.

IR (NaCl, thin film): 3474, 2976, 2874, 1465, 1373, 1055, 897 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{10}H_{18}O_3$ $[M+Na]^+$: 209.1148, found 209.1155.

$[\alpha]^{20}_D = +2.08$ (*c* = 2.4, $CHCl_3$).



40

Trimethylsulfonium iodide (102 mg, 0.5 mmol, 500 mol%) was mixed with THF (1 mL) and cooled in an ice / salt bath (–15 °C). *n*-Butyllithium (0.2 mL, 0.5 mmol, 500 mol%, 2.5 M in hexanes) was added. The reaction mixture was stirred 40 min and the temperature rose to –10 °C. Epoxide **30** (19 mg, 0.1 mmol, 100 mol%) in THF (1 mL) was added to the mixture. The mixture was stirred 3h and gradually warmed to rt. Triisopropylsilane (128 µL, 0.65 mmol, 650 mol%) was added and the mixture was stirred 4h at rt. The reaction was quenched with MeOH (0.2 mL) and stirred 5 min. The mixture was diluted with Et_2O, washed with saturated NH_4Cl, saturated $NaHCO_3$, and dried with $MgSO_4$. Column chromatography isolated mono-TIPS-ether. This intermediate was dissolved in DCM (2 mL). Triethylamine (100 µL) and TIPSOTf (100 µL) were added. The mixture was heated at 45 °C for 24 h. The mixture was quenched with MeOH (0.2 mL) and refluxed for 1h. The mixture was cooled to rt and diluted with Et_2O. The mixture was washed with water, saturated $NaHCO_3$, and dried with $MgSO_4$. Column chromatography isolated 33 mg of **40** (64% yield).

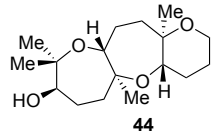
^{1}H NMR (400 MHz, C_6D_6):
δ 5.82 (ddd, *J* = 7.5, 10.4, 17.6 Hz, 1H), 5.16 (d, *J* = 9.7 Hz, 1H), 5.02 (d, *J* = 10.4 Hz, 1H), 4.24 (d, *J* = 7.4 Hz, 1H), 3.98 (dd, *J* = 6.6, 8.8 Hz, 1H), 2.28 (m, 1H), 1.93 (m, 2H), 1.45 (m, 1H), 1.35 (s, 3H), 1.29 (s, 3H), 1.19 (s, 3H), 1.18-1.12 (m, 42H).

^{13}C NMR (100 MHz, C_6D_6):
δ 140.0, 116.8, 88.5, 86.2, 81.1, 75.0, 33.2, 29.3, 27.6, 25.2, 24.8, 19.0, 18.9, 14.1, 13.6.

IR (NaCl, thin film): 2944, 2867, 1464, 1382, 1172, 1097, 1067, 882, 679 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{29}H_{60}O_3Si_2$ $[M+Na]^+$: 535.3973, found 535.3983.

$[\alpha]^{20}_D = -2.7$ (*c* = 4.5, CH_2Cl_2).



44

Enol ether **S7** (obtained as a side product of conversion of lactone **35** to nitrile **37**, 52.0 mg, 0.127 mmol, 100 mol %) and 10 wt% Pd/C (20.0 mg, 0.0188 mmol, 15 mol %) was evacuated under vacuum for a minute. A H_2 balloon was then attached and MeOH (1 mL) was added. The reaction mixture was stirred at rt for 7 h. It was then exposed to ambient atmosphere and filtered through a plug of silica and celite, eluting with CH_2Cl_2.

After removal of solvent, the crude residue was dissolved in THF (1.27 mL) and TBAF (1 M in THF, 0.317 mL, 0.317 mmol, 250 mol %) was added. The reaction mixture was stirred at rt for 13 h. It was then diluted with Et_2O (10 mL) and washed with 10 mL of H_2O. The aqueous layer was extracted with Et_2O (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography (10% to 50% EtOAc in hexanes) isolated alcohol **44** as a white amorphous solid (33.6 mg, 0.113 mmol, 89%).

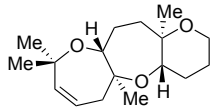
^{1}H NMR (600 MHz, $CDCl_3$)
δ 4.10 (d, *J* = 10.8 Hz, 1H), 3.80 (d, *J* = 6.6 Hz, 1H), 3.58-3.50 (m, 2H), 3.45 (dd, *J* = 11.4, 4.8 Hz, 1H), 2.20 (td, *J* = 13.2, 2.4 Hz, 1H), 1.90 (br s, 1H), 1.86-1.82 (m, 2H), 1.76 (td, *J* = 15.6, 1.8 Hz, 1H), 1.70 (ddd, *J* = 13.2, 5.4, 1.8 Hz, 1H), 1.67-1.61 (m, 3H), 1.56-1.49 (m, 2H), 1.42 (dt, *J* = 13.8, 3.6 Hz, 1H), 1.32 (dt, *J* = 13.2, 3.6 Hz, 1H), 1.29 (s, 3H), 1.18 (s, 3H), 1.16 (s, 3H), 1.10 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$)
δ 80.0, 78.5, 77.8, 77.2, 77.2, 71.4, 60.9, 42.5, 31.9, 29.4, 29.2, 28.6, 26.7, 26.2, 22.9, 20.8, 16.1.

HR-MS (ESI) *m/z* calcd for $C_{17}H_{30}O_4$ $[M+H]^+$: 299.2217, found 299.2205.

IR (thin film, NaCl): 3447, 2976, 2939, 2867, 1456, 1378, 1218, 1148, 1104, 1087, 1063, 921, 737 cm^{-1}.

$[\alpha]^{22}_D$ = +1.2 (*c* = 4.0, $CHCl_3$).



46

To alcohol **44** (31.8 mg, 0.106 mmol, 100 mol %) in CH_2Cl_2 at rt was added DMAP (19.0 mg, 0.155 mmol, 150 mol %) and pyr (0.21 mL, 2.54 mmol, 2400 mol %). The reaction mixture was cooled to –78 °C and then $ClCH_2SO_2Cl$ (64.5 mL, 0.636 mmol, 600 mol %) was added. The cold bath was removed and the reaction mixture was stirred at rt for 21 h. It was then diluted with EtOAc (20 mL) and washed with H_2O, satd. aq. $NaHCO_3$ solution, and brine (10 mL each). The organic layer was dried over $MgSO_4$, filtered, and concentrated. Column chromatography (25% EtOAc in hexanes) isolated the intermediate chloromesylate (27.8 mg, 0.0678 mmol, 64%) as a yellow oil.

The chloromesylate (21.9 mg, 0.0533 mmol, 100 mol %) was dissolved in DMPU (1 mL) at rt and and LiBr (26.2 mg, 0.302 mmol, 600 mol %) was added. The reaction mixture was heated to 60 °C for 36 h. It was then cooled to rt and diluted with EtOAc (10 mL). The organic layer was washed with H_2O and brine (5 mL each) and then dried over Na_2SO_4. Column chromatography (10% EtOAc in hexanes) isolated olefin **46** (10.0 mg, 0.0357 mmol, 67%) as a colorless solid.

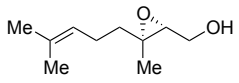
^{1}H NMR (500 MHz, $CDCl_3$)
δ 5.29 (d, *J* = 2.0 Hz, 2H), 3.83 (d, *J* = 10.0 Hz, 1H), 3.59-3.50 (m, 2H), 3.36 (dd, *J* = 11.5, 4.5 Hz, 1H), 2.48 (d, *J* = 17.5 Hz, 1H), 2.20 (ddd, *J* = 18.0, 3.5, 1.0 Hz, 1H), 2.00-1.91 (m, 1H), 1.76 (ddd, *J* = 13.5, 5.5, 2.5 Hz, 1H), 1.64-1.59 (m, 3H), 1.55-1.50 (m, 3H), 1.26 (s, 3H), 1.24 (s, 3H), 1.20 (s, 3H), 1.17 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$)
δ 135.9, 120.7, 79.5, 78.3, 76.7, 76.1, 72.1, 60.4, 42.2, 40.7, 31.0, 29.4, 28.0, 26.3, 25.7, 21.9, 15.4.

HR-MS (ESI) *m/z* calcd for $C_{17}H_{28}O_3$ $[M+H]^+$: 281.2111, found 281.2092.

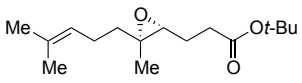
IR (thin film, NaCl): 2970, 2942, 2864, 1457, 1437, 1375, 1172, 1123, 1104, 1090, 1068 cm^{-1}.

$[\alpha]^{22}_D = -11.1$ (*c* = 0.42, $CHCl_3$).



S10

4Å MS (11.8 g, unactivated mass) was activated as described in the general experimental procedure. To this was added CH_2Cl_2 (118 mL) and the mixture was cooled to –45 °C. D-(–)-DIPT (3.08 mL, 14.7 mmol, 12.5 mol %) was added followed by Ti(O*i*-Pr)$_4$ (3.50 mL, 11.8 mmol, 10 mol %) and then *t*-BuOOH (26.7 mL, 147 mmol, 125 mol %). The catalyst mixture was stirred at –45 °C for 30 to 45 min. Geraniol (20.4 mL, 118 mmol, 100 mol %) was added dropwise. The reaction was stirred at –40 to –20 °C for 6 h. A quench solution was made by dissolving NaOH (16 g) and NaCl (2 g) in 36 mL of H_2O. After cooling to 0 °C, the reaction mixture was poured into this. The resulting mixture was stirrec vigorously at 0 °C for 30 min. It was then filtered through celite. The filtrate was washed with satd. aq. $Na_2S_2O_3$ solution and filtered through celite one more time. After separating off the aqueous layer, the organic layer was dried over $MgSO_4$, filtered, and concentrated. Epoxide **S10** was used in the next step crude, 76 mol % in decane).



50

PPh_3 (7.24 g, 27.6 mmol, 120 mol %) and imid (3.76 g, 55.2 mmol, 240 mol %) were dissolved in CH_2Cl_2 (185 mL) at rt. After cooling to 0 °C, I_2 (7.05 g, 27.6 mmol, 120 mol %) was added in one portion to give a yellow suspension. Epoxyalcohol **S10** (5.16 g, 23.0 mmol, 100 mol %) was added as a solution in 16 mL of CH_2Cl_2 via syringe. The reaction mixture was stirred at 0 °C for 30 min, then at rt for 2 h. It was then diluted with CH_2Cl_2 (100 mL) and washed with a 2:1 mixture of satd. aq. $Na_2S_2O_3$ solution/brine

(2 x 300 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated. Column chromatography (5% to 10% EtOAc in hexanes) gave the intermediate iodide (7.11 g, quant.).

i-Pr_2NH (12.0 mL, 85.1 mmol, 335 mol %) was dissolved in THF (310 mL) and cooled to –78 °C. *n*-BuLi (2.50 M in hexanes, 31.5 mmol, 78.7 mmol, 310 mol %) was added at this temperature and the resulting mixture was stirred at –78 °C for 90 min. *Tert*-butyl acetate (10.6 mL, 81.3 mmol, 320 mol %) was added and the resulting mixture was stirred at –78 °C for 90 min. Iodide from the previous step (7.11 g, 25.4 mmol, 100 mol %) was added in 10 mL of THF at –78 °C, followed by HMPA (12.7 mL). The reaction mixture was stirred at –78 °C for 15 min. It was then quenched at this temperature with satd. aq. NH_4Cl solution (200 mL) and warmed to rt. It was diluted with 100 mL of Et_2O and another 100 mL portion of satd. aq. NH_4Cl solution. After washing and separating, the organic layer was washed with H_2O (300 mL). The H_2O layer was extracted once with Et_2O (150 mL), The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography (10% to 20% EtOAc in hexanes) gave the ester **50** (4.86 g, 18.1 mmol, 71%) as a colorless oil.

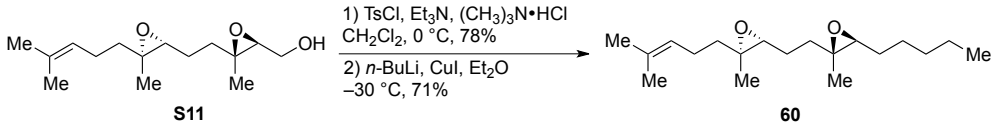
^{1}H NMR (600 MHz, $CDCl_3$)
δ 5.10 (app t, *J* = 7.2 Hz, 1H), 2.77 (dd, *J* = 6.0, 7.2 Hz, 1H), 2.44-2.34 (m, 2H), 2.12-2.07 (m, 2H), 1.89-1.76 (m, 2H), 1.70 (s, 3H), 1.69-1.67 (m, 2H), 1.63 (s, 3H), 1.47 (s, 9H), 1.29 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$)
δ 172.9, 132.6, 124.3, 81.1, 63.2, 61.7, 39.4, 33.0, 31.3, 28.8, 28.8, 26.4, 25.1, 24.5, 18.3, 17.2.

HR-MS (ESI) *m/z* calcd for $C_{16}H_{28}O_3$ $[M+H]^+$: 269.2111, found 269.2118.

IR (thin film, NaCl): 2977, 2930, 1732, 1457, 1367, 1257, 1154, 848 cm^{-1}.

$[\alpha]^{22}_D$ = +6.0 (*c* = 1.5, $CHCl_3$).



S11 **60**

Alcohol **S11** (1.17 g, 4.60 mmol, 100 mol %) and NMe_3•HCl (44.0 mg, 0.460 mmol, 10 mol %) were dissolved in CH_2Cl_2 (15 mL) and cooled to 0 °C.[5] Et_3N (1.90 mL, 13.8 mmol, 300 mol %) was then added to the reaction mixture. In a separate flask, TsCl (1.32 g, 6.90 mmol, 150 mol %) was dissolved in 10 mL of CH_2Cl_2 and the mixture was

[5] Y. Yoshida, Y. Sakakura, N. Aso, S. Okada, Y. Tanabe, *Tetrahedron* **1999**, *55*, 2183.

cannulated into the reaction mixture at 0 °C. The reaction mixture was stirred at 0 °C for 90 min. *N*,*N*-Dimethylethylenediamine (0.40 mL, 3.5 mmol, 75 mol %) was then added to quench the excess tosylating agent. After stirring at 0 °C for 15 min, the reaction mixture was diluted with Et_2O (150 mL) and washed with brine (100 mL) followed by H_2O (50 mL). The combined aqueous layers were extracted with Et_2O (2 x 70 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography (25% EtOAc in hexanes) isolated the intermediate tosylate (1.46 g, 3.57 mmol, 78%).

To CuI (1.10 g, 5.79 mmol, 120 mol %) in 50 mL of dry Et_2O at –30 °C under Ar was added *n*-BuLi (4.43 mL, 11.6 mmol, 240 mol %). The resulting mixture was stirred for 30 min at –30 °C, resulting in a violet suspension. The tosylate from the previous step (1.97 g, 4.82 mmol, 100 mol %) in 10 mL of dry Et_2O was added by cannula at –30 °C. The reaction mixture was stirred at –30 °C for 15 min. It was then opened to atmosphere and 100 mL of satd. aq. NH_4Cl was added. After stirring at rt for 30 min, the mixture was filtered through celite, eluting with 400 mL of Et_2O. The filtrate was washed with 400 mL of satd. aq. NH_4Cl and the aqueous layer was extracted with Et_2O (2 x 150 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography (20% EtOAc in hexanes) isolated diepoxide **60** (918 mg, 3.12 mmol, 65%) as a pale yellow oil.

^{1}H NMR (500 MHz, C_6D_6)
δ 5.14 (t, *J* = 7.0 Hz, 1H), 2.61-2.58 (m, 2H), 2.14-2.06 (m, 2H), 1.67-1.61 (m, 5H), 1.57 (s, 3H), 1.57 (s, 3H), 1.49-1.38 (m, 5H), 1.34 -1.28 (m, 2H), 1.27-1.21 (m, 5H), 1.15 (s, 3H), 1.12 (s, 3H), 0.87 (t, *J* = 7.0 Hz, 3H).

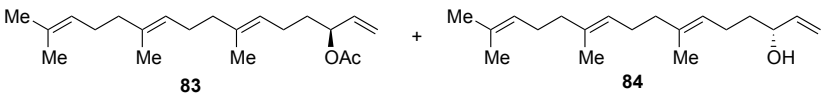
^{13}C NMR (100 MHz, C_6D_6)
δ 131.9, 124.9, 63.7, 63.2, 60.3, 59.9, 39.5, 36.5, 32.4, 29.5, 27.0, 26.2, 25.6, 24.6, 23.3, 18.0, 17.1, 17.0, 14.6.

HR-MS (ESI) *m*/*z* calcd for $C_{19}H_{34}O_2$ $[M+H]^+$: 295.2632, found 295.2636.

IR (thin film, NaCl): 2959, 2926, 2858, 1653, 1559, 1540, 1507, 1457, 1385 cm^{-1}.

$[\alpha]^{22}_D$ = –4.6 (*c* = 0.51, $CHCl_3$).

$[\alpha]^{22}_D$ = –31.0 (*c* = 0.29, $CHCl_3$).



83 **84**

Aldehyde **82** (5.85 g, 23.6 mmol)[6] was dissolved in 200 mL of THF in a 500 mL

[6] Coates, R. M.; Ley, D. A.; Cavender, P. L. *J. Org. Chem.* **1978**, *43*, 4915.

flame-dried round-bottomed flask equipped with a stir bar. The reaction mixture was cooled to –10 °C in acetone/dry ice bath and a solution of vinyl magnesium bromide in THF (50 mL, 1.0 M, 50 mmol) was added slowly over 5 min. The reaction was allowed to warm to room temperature over 1 h, then was quenched with saturated NH_4Cl and transferred into a separatory funnel. It was extracted 3x with Et_2O. After washing the combined organic layers with brine, it was dried over $MgSO_4$. Filtration and solvent removal *in vacuo* gave a crude residue, which was purified by column chromatography (5 to 10% EtOAc/hexanes) to give a racemic mixture of the intermediate allylic alcohol (4.73 g, 17.1 mmol, 73% yield) as a colorless oil.

To a 20 mL vial equipped with a stir bar was added the racemic alcohol (571 mg, 2.07 mmol) in 1 mL of Et_2O followed by vinyl acetate (950 μL, 10.3 mmol). Beads of Novozyme 435 enzyme (33 mg, Aldrich L4777 from Candida antartica) were added and the reaction was stirred for 2.5 h at room temperature and then 13.5 h at 4 °C in the fridge. The reaction was filtered through glass wool and washed with Et_2O (5x). The reaction was concentrated *in vacuo* and then purified by column chromatography (5 to 10% EtOAc/hexanes) to give **83** (264 mg, 0.827 mmol, 40% yield, 99% *ee*) and **84** (304 mg, 1.10 mmol, 53% yield, 80% *ee*). Resubjecting **84** to the reaction conditions for an additional 16.5 h provided this intermediate in 33% yield and 98% *ee*.

Characterization data for **83**:

^{1}H NMR (500 MHz, $CDCl_3$):
δ 5.78 (ddd, J = 17.1, 10.6, 6.5 Hz, 1H), 5.26-5.22 (m, 2H), 5.19-5.16 (m, 1H), 5.13-5.09 (m, 3H), 2.08 (s, 3H), 2.09-2.06 (m, 3H), 2.06-1.96 (m, 7H), 1.69 (d, J = 1.1 Hz, 3H), 1.68-1.62 (m, 2H), 1.61 (s, 3H), 1.60 (s, 3H), 1.59 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$):
δ 170.6, 136.7, 136.2, 135.2, 131.5, 124.6, 124.3, 123.3, 116.8, 74.7, 39.9, 39.9, 34.5, 27.0, 26.8, 25.9, 23.8, 21.5, 17.9, 16.2, 16.2.

$[\alpha]^{24}_D$ = –3.1 (c = 0.17, $CHCl_3$).

IR (NaCl, thin film): 2924, 1996, 1741, 1653, 1540, 1457, 1374, 1237 cm^{-1}.

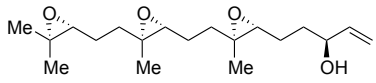
HR-MS (ESI) *m/z* calcd for $C_{21}H_{34}O_2$ $[M+Na]^+$: 341.2451, found 341.2455.

Chiral HPLC analysis: (Chiralcel OD, hexanes:2-propanol, 210 nm): t_R (R) = 10.9 min; t_R (S) = 11.4 min. The enantiomeric excess was determined to be 98%.

Data for **84**:

Chiral HPLC analysis: was performed on the benzonate derivative (BzCl, Et_3N, DMAP, CH_2Cl_2): (Chiralcel OBH, hexanes:2-propanol): t_R (S) = 7.5 min; t_R (R) = 8.4 min. The enantiomeric excess was determined to be 98%.

$[\alpha]^{24}_D$ = –3.4 (c = 1.3, $CHCl_3$).



14

To a 250 mL round-bottom flask equipped with a stir bar was added a solution of acetate **83** (260 mg, 0.817 mmol) in 37 mL of 2:1 DMM/CH_3CN and 25 mL of EDTA buffer. *n*-Bu_4NHSO_4 (34.7 mg, 0.102 mmol) was added and the reaction was vigorously stirred followed by the addition of Shi ketone **36** (155.4 mg, 0.602 mmol). A solution of Oxone (2.78 g, 4.52 mmol) in 20.5 mL of EDTA solution and a solution of 20.5 mL of 0.89 M K_2CO_3 were added dropwise side-by-side over 30 min. The reaction was allowed to stir for an additional 30 min before 100 mL of water was added and stirred for an additional 45 min. The reaction was extracted with CH_2Cl_2 (3x) and dried over Na_2SO_4. The reaction was filtered and concentrated *in vacuo* and subjected to column chromatography (20 to 50% EtOAc in hexanes) to provide the intermediate triepoxy ester (263 mg, 0.718 mmol, 88% yield, 3.5:1 dr).

To a 20 ml vial equipped with a stir bar was added triepoxy ester from the previous step (259 mg, 0.707 mmol) in 1.5 mL of THF and cooled to 0 °C. 750 μL of MeOH was added followed by dropwise addition of 750 μL of a 1 M LiOH solution (prepared from 30.9 mg of LiOH in 815 μL of H_2O). The reaction was stirred for 30 min at which time TLC showed complete consumption of the starting material. The reaction was quenched with saturated NH_4Cl and extracted with Et_2O (3x). The organic layers were combined and dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Column chromatography provided the colorless oil **14** (213 mg, 0.657 mmol, 93%).

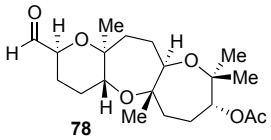
^{1}H NMR (500 MHz; $CDCl_3$):
δ 5.92-5.84 (m, 1H), 5.25 (d, J = 17.2 Hz, 1H), 5.13 (d, J = 10.4 Hz, 1H), 4.20-4.17 (m, 1H), 2.82-2.77 (m, 1H), 2.76-2.69 (m, 2H), 1.81-1.53 (m, 14H), 1.31 (s, 3H), 1.30 (s, 2H), 1.28 (s, 4H), 1.27 (s, 3H).

^{13}C NMR (125 MHz; $CDCl_3$):
δ 141.0, 115.1, 72.6, 64.2, 64.0, 63.3, 63.1, 62.8, 60.8, 35.8, 35.4, 33.9, 25.0, 25.0, 24.8, 24.6, 18.9, 16.9, 16.8.

$[\alpha]^{24}_D$ = +17.5 (c = 0.44, $CHCl_3$).

IR (NaCl, thin film): 3448, 2926, 1653, 1636, 1617, 1559, 1507, 1473, 1457, 1437, 1387, 1177 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{19}H_{32}O_4$ $[M+Na]^+$: 347.2198, found 347.2195.



78

To a 100 mL round-bottom flask equipped with a stir bar was added acetate **85** (324.6 mg, 0.886 mmol) in 44 mL of CH_2Cl_2. Sodium bicarbonate (20.2 mg, 0.240

mmol) and 8.9 mL of MeOH were added. The reaction was cooled to –78 °C and subjected to ozone until the reaction turned light blue (~10 min). Oxygen was bubbled through the solution for 2 min, followed by nitrogen for 1 min. The reaction was quenched by the addition of triphenylphosphine (257 mg, 0.978 mmol) and allowing the reaction to warm to room temperature for 1 h. The reaction was concentrated *in vacuo* and then loaded directly onto a silica gel column. The crude was purified by column chromatography (20% EtOAc in hexanes) to furnish aldehyde **78** (240 mg, 0.652 mmol, 65% yield) as a colorless oil.

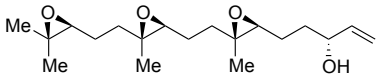
^{1}H NMR (500 MHz, $CDCl_3$):
δ 9.59 (s, 1H), 4.92 (d, *J* = 6.4 Hz, 1H), 3.92 (dd, *J* = 12.2, 3.0 Hz, 1H), 3.62 (dd, *J* = 10.4, 5.8 Hz, 1H), 3.46 (dd, *J* = 11.3, 2.4 Hz, 1H), 2.12 (s, 3H), 2.07-2.00 (m, 2H), 1.94-1.90 (m, 1H), 1.86 (dtd, *J* = 11.9, 5.8, 3.0 Hz, 2H), 1.82-1.76 (m, 1H), 1.73-1.68 (m, 3H), 1.54-1.45 (m, 3H), 1.28 (s, 2H), 1.26 (s, 3H), 1.17 (s, 3H), 1.15 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$):
δ 202.3, 170.2, 79.0, 78.6, 78.3, 78.1, 77.4, 75.0, 69.7, 40.3, 36.7, 29.1, 28.9, 27.0, 26.7, 23.2, 21.8, 21.3, 19.5, 16.4.

$[\alpha]^{24}_D$ = –4.6 (*c* = 0.4, $CHCl_3$).

IR (NaCl, thin film): 2938, 1996, 1739, 1653, 1559, 1540, 1457, 1379, 1241, 1097, 1071, 981, 893 cm^{-1}.

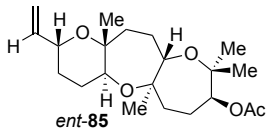
HR-MS (ESI) *m/z* calcd for $C_{20}H_{32}O_6$ $[M+Na]^+$: 391.2091, found 391.2086.



ent-**14**

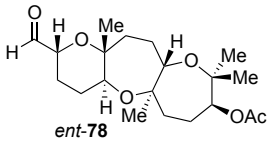
To a 250 mL round-bottom flask equipped with a stir bar was added a solution of allylic alcohol **84** (260 mg, 0.817 mmol) in 37 mL of 2:1 DMM/CH_3CN and 25 mL of EDTA buffer. *n*-Bu_4NHSO_4 (34.7 mg, 0.102 mmol) was added and the reaction was vigorously stirred followed by the addition of *ent*-Shi ketone *ent*-**36** (155 mg, 0.602 mmol).[7] A solution of Oxone (2.78 g, 4.52 mmol) in 20.5 mL of EDTA solution and a solution of 20.5 mL of 0.89 M K_2CO_3 were added dropwise side-by-side over 30 min. The reaction was allowed to stir for an additional 30 min before 100 mL of water was added and stirred for an additional 45 min. The reaction was extracted with CH_2Cl_2 (3x) and dried over Na_2SO_4. The reaction was filtered and concentrated *in vacuo* and subjected to column chromatography (20 to 50% EtOAc/hexanes) to provide a colorless oil of triepoxide *ent*-**14** (263 mg, 0.718 mmol, 61% yield, 3.5:1 dr).

[7] This reagent was prepared by Yutaka Ikeuchi from our group. The procedure will be reported in due course.



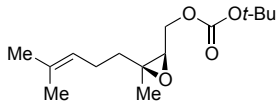
ent-**85**

An identical procedure as **85** was used to furnish the enantiomer from *ent*-**14** in 25% yield.



ent-**78**

An identical procedure as **78** was used to furnish the enantiomer from *ent*-**85** in 74% yield.



80

To a 1 L round-bottom flame-dried flask equipped with a stir bar was added 4 Å molecular sieves (1.01 g) and heated under vacuum for 15 min. CH_2Cl_2 (40 mL) was added and the flask was cooled with a CryoCool to –23 ºC. Titanium isopropoxide (0.62 mL, 2.1 mmol) and D-(–)-diethyl tartrate (0.49 mL, 2.8 mmol) were added and stirred for 30 min. A solution of *tert*-butyl hydrogen peroxide (5.5 M in decanes, 7.2 mL, 40 mol) was added and stirred for 30 min. Nerol (3.60 mL, 20.4 mmol) was added slowly over 15 min. The reaction was stirred at this temperature for 15 h. The reaction was quenched by adding of H_2O at 0 °C and stirring for 5 h. Added 74 mL of 22.1 g of NaOH in 72 mL of H_2O followed by saturating with NaCl. The reaction mixture was filtered through Celite. Extracted with CH_2Cl_2 (3x) and the organic layers were dried over Na_2SO_4, filtered, and the solvent was removed *in vacuo*. The crude oil was purified by column chromatography (20% EtOAc in hexanes) to provide the intermediate epoxyalcohol (3.05 g, 17.9 mmol, 88% yield) as a colorless oil.

To a 500 mL flame-dried round-bottom flask equipped with a stir bar was added epoxyalcohol from the previous step (6.7 g, 39 mmol) in toluene (130 mL). 1-methylimidazole (4.15 mL, 52.1 mmol) was added and the reaction was cooled to 0 °C. Liquid di-*tert*-butyl dicarbonate (9.72 g, 44.5 mmol) was added dropwise over 15 min and then stirred while warming to room temperature overnight. The reaction was poured into water and enough CH_2Cl_2 was added to separate into two layers. The aqueous layer was extracted with CH_2Cl_2 (3x) and then the organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude was purified by column chromatography (10% EtOAc in hexanes) to provide carbonate **80** (7.91 g, 29.3 mmol, 74% yield) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$):
5.11-5.08 (m, 1H), 4.24 (dd, J = 11.8, 4.7 Hz, 1H), 4.10 (dd, J = 11.8, 6.6 Hz, 1H), 3.02

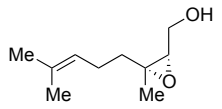
(dd, J = 6.6, 4.7 Hz, 1H), 2.14-2.10 (m, 2H), 1.70 (s, 3H), 1.67-1.64 (m, 1H), 1.63 (s, 3H), 1.50 (s, 9H), 1.49-1.48 (m, 1H), 1.35 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$):
153.5, 132.6, 123.4, 82.7, 65.7, 61.0, 60.9, 33.4, 27.9, 25.9, 24.3, 22.1, 17.8.

$[\alpha]^{24}_D$ = +5.8 (c = 0.26, $CHCl_3$).

IR (NaCl, thin film): 3584, 2981, 2925, 1744, 1457, 1369, 1278, 1255, 1163, 1094 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{15}H_{26}O_4$ $[M+Na]^+$: 293.1723, found 293.1727.



S12

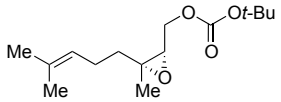
To a 1 L round-bottom flame-dried flask equipped with a stir bar was added 4 Å molecular sieves (9.00 g) and heated under vacuum for 15 min. CH_2Cl_2 (500 mL) was added and the flask was cooled with a CryoCool to –23 ºC. Titanium isopropoxide (19.0 mL, 64.8 mmol) and L-(+)-diethyl tartrate (14.0 mL, 81.8 mmol) were added and stirred for 30 min. A solution of *tert*-butyl hydrogen peroxide (5.5 M in decanes, 64 mL, 12 mol) was added and stirred for 30 min. Nerol (57.0 mL, 326 mmol) was added slowly over 49 min. The reaction was stirred at this temperature for 3 h. The reaction was quenched by adding 370 mL of H_2O at 0 °C and stirring for 5 h. Added 74 mL of 22.1 g of NaOH in 72 mL of H_2O followed by saturating with NaCl. The reaction mixture was filtered through Celite. Extracted with CH_2Cl_2 (3x) and the organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo* to furnish **S12** (40.1 g, 236 mmol). The reaction mixture was carried on directly to the enzymatic resolution.

To a 1 L flask with stir bar was loaded epoxyalcohol from the previous step (40.1 g, 236 mmol) in vinyl acetate (100 mL) and Et_2O (390 mL) and cooled to 0 °C in an ice bath. Amano lipase-PS (2.61 g) was added and stirred at 0 °C for 14 h. The reaction mixture was filtered through Celite (eluted with Et_2O) and the solvent was removed *in vacuo*. The reaction mixture was purified by column chromatography (10 to 20 to 30% EtOAc in hexanes) to provide the intermediate epoxyacetate (28.6g, 135 mmol, 41% from nerol) as a colorless oil.

$[\alpha]^{24}_D$ = –25.7 (c = 5.9, $CHCl_3$) {lit. $[\alpha]^{23}_D$ = –25.7 (c = 0.58, $CHCl_3$)}.

IR (NaCl, thin film): 2968, 2928, 2863, 1746, 1451, 1376, 1233, 1036, 887 cm^{-1}.

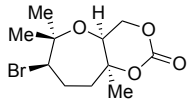
To a 1 L round-bottom flask equipped with a stir bar was added epoxyacetate from the previous step (28.6 g, 135 mmol) in 340 mL of MeOH. K_2CO_3 (1.88 g, 13.6 mmol) was added and stirred for 4 h. The solvent was removed *in vacuo*, and the crude product was redissolved in Et_2O. The resulting suspension was filtered through Celite and concentrated *in vacuo* to provide **S12** (22.7 g, 133 mmol, 99% yield), which was used without further purification.



ent-**80**

To a 1 L flame-dried round-bottom flask equipped with a stir bar was added epoxyalcohol **S12** (22.7 g, 133 mmol) in toluene (620 mL). 1-methylimidazole (14.0 mL, 176 mmol) was added and the reaction was cooled to 0 °C. Liquid di-*tert*-butyl dicarbonate (117 g, 537 mmol) was added dropwise over 15 min and then stirred while warming to room temperature overnight. The reaction was poured into 1 L of water and enough CH_2Cl_2 was added to separate into two layers. The aqueous layer was extracted with CH_2Cl_2 (3x) and then the organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude was purified by column chromatography (10% EtOAc in hexanes) to provide carbonate *ent*-**80** (27.7 g, 103 mmol, 77 % yield) as a colorless oil.

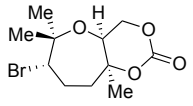
$[\alpha]^{24}_D = -9.6$ ($c = 4.6$, $CHCl_3$).



ent-**79**

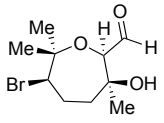
To a 2 L round-bottom flask equipped with a stir bar was added 4Å molecular sieves (104 g) followed by 2:1 mixture of Boc_2O and carbonate *ent*-**80** (13.9 g, 51.3 mmol) and 1 L of nitromethane. The reaction was cooled in an ice bath for 15 min with manual shaking. The reaction was covered with foil and $Br(coll)_2BF_4$ (51.6 g, 126 mmol) was added in one portion and the reaction was swirled in an ice bath for 15 min. The reaction was filtered through Celite and the solvent was removed *in vacuo* at 40 °C. The reaction turned dark brown and was dissolved in CH_2Cl_2 and 1:1 $Na_2S_2O_3$/NaCl solutions. The aqueous layer was extracted with CH_2Cl_2 (3x) and then washed with 1N HCl. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude solid was purified by column chromatography (25% to 75% EtOAc in hexanes) to furnish *ent*-**79** (3.30 g, 11.3 mmol, 22% yield) as a white solid and *ent*-**79'** for characterization purposes.

$[\alpha]^{24}_D = +33.6$ ($c = 0.66$, $CHCl_3$).



ent-**79'**

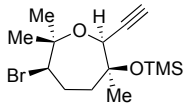
$[\alpha]^{24}_D = +19.1$ ($c = 1.1$, $CHCl_3$).



86

To a 200 mL round-bottom flask equipped with a stir bar was added *ent*-**79** (3.30 g, 11.3 mmol) in 115 mL of MeOH. NaOH (536 mg, 13.4 mmol) was added and the reaction was stirred for 2 h at room temperature. The reaction was concentrated *in vacuo* and then the remaining oil was redissolved in EtOAc. A saturated NH_4Cl solution was added and was extracted with EtOAc (3x) followed by extraction with CH_2Cl_2 (3x). The organic layers were combined and dried over Na_2SO_4, filtered, and concentrated *in vacuo* to provide the intermediate diol (2.8 g), which was used without further purification.

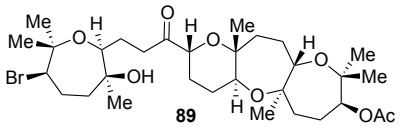
To a 25 mL round-bottom flask equipped with a stir bar was added SO_3•pyr (3.65 g, 23.0 mmol) in 12 mL of DMSO and stirred for 15 min. To a separate 250 mL round-bottomed flask equipped with a stir bar was added diol (3.06 g, 11.5 mmol) in 120 mL of CH_2Cl_2. Triethylamine (4.80 mL, 34.4 mmol) and 2 mL of DMSO was added and cooled to 0 °C. The SO_3•DMSO complex was added slowly and the reaction was stirred for 8 h while warming to room temperature. The reaction was poured into 100 mL of saturated NH_4Cl and extracted with CH_2Cl_2 (3x). The organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude oil was purified by the Biotage purification system to furnish aldehyde **86** (2.42 g, 9.13 mmol, 74% yield from *ent*-**79**) as a colorless oil.



77

To a 200 mL round-bottom flask equipped with a stir bar was added aldehyde **86** (1.64g, 6.18 mmol) and dissolved in 86 mL of MeOH. Potassium carbonate (1.99 g, 14.4 mmol) was added followed by dropwise addition of dimethyl-1-diazo-2 oxopropylphosphate (1.33 g, 6.90 mmol). The reaction was stirred for 16 h at room temperature, during which time the color the mixture changed from yellow to orange. 100 mL of Et_2O was added to the reaction, followed by 150 mL of saturated $NaHCO_3$. The aqueous layer was extracted with Et_2O (3x) and then dried over Na_2SO_4. The reaction was filtered and concentrated *in vacuo* to provide a milky light yellow solution. The crude residue was purified by the Biotage purification system to provide the intermediate alkyne (1.22 g, 4.65 mmol, 75% yield) was obtained a colorless oil.

To a 100 mL round-bottom flask equipped with a stir bar was added alkyne from the previous step (1.22 g, 4.65 mmol) and dissolved in 47 mL of CH_2Cl_2. The reaction was cooled to 0 °C and 2,6-lutidine (1.62 mL, 14.0 mmol) was added followed by dropwise addition of TMSOTf (1.26 mL, 7.00 mmol). The reaction was stirred for 1 h at this temperature and then quenched with 30 mL of saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3x) and the organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude oil was purified by column chromatography (2% to 5% EtOAc in hexanes) to provide alkyne **77** (1.21 g, 3.63 mmol, 78% yield) as a white solid.



89

To a 50 mL round-bottom flask equipped with a stir bar was added [$Cp_2Zr(H)Cl$] (387.2 mg, 1.50 mmol) and alkyne **77** (498 mg, 1.49 mmol) and placed under nitrogen in the dark. 15 mL of CH_2Cl_2 was added and stirred for 30 min at room temperature. The flask was then cooled to –78 °C and Me_2Zn (2.0 M in toluene, 780 μL, 1.56 mmol) was added dropwise. After stirring for 20 min, a solution of aldehyde *ent*-**78** (450 mg, 1.22 mmol) in 12.5 mL of CH_2Cl_2 was added and the reaction was allowed to slowly warm to room temperature overnight. A saturated solution of NH_4Cl was added and a white solid formed. The aqueous layer was extracted with CH_2Cl_2 (3x) and then the organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo* to provide a colorless oil. The crude was purified by column chromatography (5 to 50% EtOAc in hexanes) to provide the allylic alcohol intermediate (667 mg) as a colorless oil, which was used without further purification.

To a 25 mL round-bottom flask equipped with a stir bar was added allylic alcohol from the previous step (600.0 mg, 0.85 mmol) and 17 mL of EtOH. Palladium on carbon (235 mg, 10% by weight) was added and placed under vacuum. Hydrogen gas was added and the reaction was stirred at room temperature for 2 h. The solution was filtered through Celite (eluted with EtOAc) to remove the palladium. The crude reaction mixture was purified by the Biotage purification system to provide the saturated alcohol (402 mg, 0.634 mmol, 52% from *ent*-**78**) as a colorless oil.

To a 10 mL round-bottom flask equipped with a stir bar were added 4Å molecular sieves (360 mg) followed by alcohol from the previous step (383 mg, 0.604 mmol) in 3.5 mL of CH_2Cl_2. *N*-Methylmorpholine-*N*-oxide (230 mg, 1.96 mmol) was added and the reaction was cooled to 0 °C. Tetrapropylammonium perruthenate (30 mg, 0.085 mmol) was added and the reaction was allowed to warm to room temperature over 4 h. The crude reaction was filtered through Celite using a CH_2Cl_2 and EtOAc wash and concentrated *in vacuo*. The reaction was purified by the Biotage purification system to provide **89** (358.8 mg, 0.568 mmol, 90% yield) as a colorless oil.

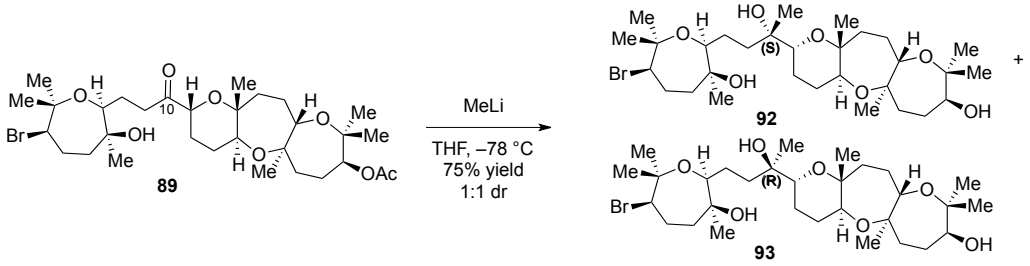
^{1}H NMR (400 MHz, $CDCl_3$):

δ 4.97 (d, J = 6.8 Hz, 1H), 3.67 (dd, J = 11.9, 2.9 Hz, 1H), 3.63-3.54 (m, 2H), 3.47 (d, J = 10.8 Hz, 1H), 2.98 (dd, J = 9.4, 3.7 Hz, 1H), 2.84 (s, 1H), 2.68-2.60 (m, 2H), 2.20-2.10 (m, 1H), 1.91-1.74 (m, 8H), 1.70 (s, 3H), 1.66-1.36 (m, 9H), 1.31 (s, 3H), 1.22 (s, 3H), 1.22 (s, 3H), 1.21 (s, 3H), 1.07 (s, 3H), 1.04 (s, 3H), 0.99 (s, 3H)

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

δ 210.5, 169.5, 79.3, 78.7, 78.6, 78.3, 78.0, 77.6, 75.8, 75.1, 72.3, 70.6, 59.6, 44.6, 41.1, 37.4, 34.8, 30.9, 29.7, 29.0, 28.7, 28.0, 26.0, 25.50, 25.5, 23.8, 23.6, 22.0, 20.8, 19.8, 16.8.

$[\alpha]^{24}_D$ = +17.4 (c = 1.6, $CHCl_3$).



To a 20 mL vial equipped with a stir bar were added ketone **89** (192 mg, 0.304 mmol) and 6 mL of THF and the reaction was cooled to –78 °C. MeLi (2.0 mL, 1.6 M in Et_2O, 3.2 mmol) was added dropwise and the reaction was stirred for 2.5 h. Saturated NH_4Cl was added and the reaction was allowed to warm to rt. The aqueous layer was extracted with Et_2O (3x), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by the Biotage purification system to provide clean alcohol **93** (56.2 mg, 0.0928 mmol, 31% yield) and the remaining material as a mixture of alcohol **92** and alcohol **93** (80.2 mg, 0.132 mmol, 44% yield).

Chatacterization data for **92**:

^{1}H NMR (400 MHz, C_6D_6):
δ 3.82 (dd, *J* = 11.4, 2.6 Hz, 1H), 3.66 (dd, *J* = 10.1, 6.1 Hz, 1H), 3.54 (d, *J* = 11.1 Hz, 1H), 3.28-3.23 (m, 2H), 2.94 (s, 1H), 2.76 (dd, *J* = 9.3, 3.1 Hz, 1H), 2.25-2.15 (m, 4H), 1.92-1.80 (m, 5H), 1.72-1.44 (m, 13H), 1.34 (s, 3H), 1.33 (s, 3H), 1.28 (s, 3H), 1.24 (s, 3H), 1.16 (s, 3H), 1.15 (s, 3H), 1.00 (s, 3H), 0.98 (s, 3H).

^{13}C NMR (100 MHz, C_6D_6):
δ 79.6, 78.2, 78.1, 78.0, 77.9, 76.7, 76.5, 76.3, 73.3, 72.4, 71.2, 59.8, 44.8, 41.1, 36.8, 34.7, 31.0, 30.0, 29.4, 28.4, 26.3, 26.1, 26.1, 25.6, 25.5, 24.4, 24.3, 22.1, 20.2, 17.1.

$[\alpha]^{24}_D = -15.0$ (*c* = 0.2, $CHCl_3$).

IR (NaCl, thin film): 3451, 2974, 2937, 1445, 1378, 1138, 1071, 801, 755 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{30}H_{53}BrO_7$ $[M+H]^+$: 605.3047, found 605.3035.

Chatacterization data for **93**:

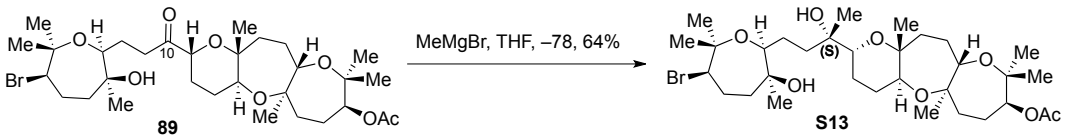
^{1}H NMR (400 MHz, C_6D_6):
δ 3.82 (dd, *J* = 11.4, 2.6 Hz, 1H), 3.62 (t, *J* = 8.1 Hz, 1H), 3.55 (d, *J* = 10.9 Hz, 1H), 3.27-3.15 (m, 2H), 2.94 (bs, 1H), 2.80 (dd, *J* = 8.1, 4.3 Hz, 1H), 2.31 (bs, 1H), 2.27-2.11 (m, 3H), 1.96-1.79 (m, 4H), 1.73-1.40 (m, 13H), 1.36 (s, 3H), 1.34 (s, 3H), 1.28 (s, 3H), 1.25 (s, 3H), 1.14 (s, 3H), 1.04 (s, 3H), 1.02 (s, 3H), 0.98 (s, 3H).

^{13}C NMR (100 MHz, C_6D_6):
δ 79.6, 78.1, 78.1, 77.9, 77.9, 76.7, 76.7, 75.4, 73.4, 72.4, 71.0, 59.8, 44.7, 41.0, 36.8, 36.8, 31.0, 30.0, 29.4, 28.4, 26.3, 26.1, 25.9, 25.7, 25.6, 24.6, 22.0, 21.7, 20.4, 17.1.

$[\alpha]^{24}_D = -22.1$ ($c = 0.5$, $CHCl_3$).

IR (NaCl, thin film): 3451, 2975, 2937, 1447, 1379, 1302, 1137, 1071, 1034, 995, 891, 754 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{30}H_{53}BrO_7$ $[M+H]^+$: 605.3047, found 605.3029.

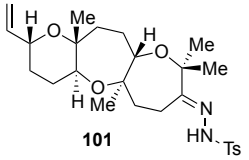


To a 20 mL vial with stir bar was added ketone **89** (11.7 mg, 18.5 mmol) in 1 mL of THF. The reaction was cooled to –78 °C and then a 3.0 M solution of methylmagnesium bromide in Et_2O (50 μL, 150 mmol) was added dropwise. The reaction was allowed to stir at this temperature for 1 h. The reaction was quenched with saturated NH_4Cl (1 mL) and then 5 mL of brine was added. The aqueous layer was extracted with Et_2O (5x) and then the organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude oil was purified by column chromatography to furnish starting material **89** (4.2 mg, 6.6 mmol) and acetate **S13** (7.70 mg, 11.9 mmol, 64% yield, 100% BRSM).

^{1}H NMR (500 MHz, $CDCl_3$):
δ 4.92 (d, J = 6.8 Hz, 1H), 3.91 (d, J = 11.1 Hz, 1H), 3.55 (dd, J = 10.5, 5.7 Hz, 1H), 3.46 (dd, J = 11.4, 2.5 Hz, 1H), 3.31-3.27 (m, 2H), 3.04 (s, 1H), 2.37 (s, 1H), 2.39-2.34 (m, 1H), 2.12 (s, 3H), 2.07-2.00 (m, 3H), 1.90-1.85 (m, 2H), 1.82-1.70 (m, 5H), 1.70-1.60 (m, 5H), 1.52-1.46 (m, 4H), 1.42 (s, 3H), 1.37 (s, 3H), 1.26 (s, 3H), 1.23 (s, 3H), 1.16 (s, 3H), 1.15 (s, 3H), 1.12 (s, 3H), 1.11 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$):
δ 170.3, 78.8, 78.6, 78.3, 78.0, 77.4, 77.4, 76.2, 75.7, 73.2, 72.4, 70.5, 59.4, 44.6, 40.7, 36.8, 33.6, 30.6, 29.1, 28.9, 27.6, 25.9, 25.7, 25.4, 25.2, 24.0, 23.8, 23.2, 21.8, 21.3, 20.1, 16.4.

HR-MS (ESI) *m/z* calcd for $C_{32}H_{55}BrO_8$ $[M+Na]^+$: 669.2973, found 669.2979.



To a 5 mL round-bottom flask equipped with a stir bar was added alcohol **100** (53.9 mg, 0.166 mmol) in 7.2 mL of CH_2Cl_2. Sodium bicarbonate (609 mg, 7.25 mmol) was added and the reaction was cooled to 0 °C. Dess-Martin periodinane (670.0 mg, 1.58 mmol) was added and the reaction was allowed to warm to room temperature and stir for 3 h. The reaction was quenched with a 1:1 solution of saturated $Na_2S_2O_3$ and $NaHCO_3$

and extracted with CH_2Cl_2 (3x). The organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude was purified by column chromatography (2 to 10% EtOAc in hexanes) to furnish the intermediate ketone (34.4 mg, 0.107 mmol, 64% yield) as colorless oil.

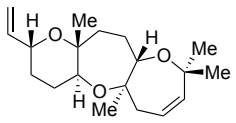
To a 5 mL round-bottom flask equipped with a stir bar was added ketone from the previous step (34.4 mg, 0.107 mmol) and tosyl hydrazide (37.8 mg, 0.203 mmol) in 1 mL of MeOH. The reaction was heated to 40 °C for 18 h. The reaction was cooled to room temperature and concentrated *in vacuo*. The crude white solid was purified by column chromatography (50 to 100% EtOAc in hexanes) to furnish hydrazone **101** (22.6 mg, 0.046 mmol, 43% yield).

^{1}H NMR (500 MHz, $CDCl_3$):
δ 7.84 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 0.6 Hz, 1H), 5.81-5.74 (m, 1H), 5.19 (d, *J* = 17.3 Hz, 1H), 5.08 (d, *J* = 10.4 Hz, 1H), 3.98-3.94 (m, 1H), 3.52 (dd, *J* = 11.3, 4.6 Hz, 1H), 2.87-2.76 (m, 1H), 2.44 (s, 3H), 2.24 (dd, *J* = 10.4, 3.3 Hz, 1H), 2.05-2.02 (m, 1H), 1.84 (t, J = 1.9 Hz, 1H), 1.72-1.65 (m, 2H), 1.65-1.52 (m, 4H), 1.49-1.31 (m, 3H), 1.23 (s, 3H), 1.22 (s, 3H), 1.15 (s, 3H), 1.11 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$):
δ 164.3, 144.3, 139.4, 129.7, 128.5, 128.3, 115.4, 80.6, 79.9, 77.6, 71.07, 70.90, 70.4, 40.5, 40.3, 32.0, 28.9, 27.5, 27.1, 22.9, 21.9, 20.7, 19.6, 15.9.

$[\alpha]^{24}_D = -14.5$ (*c* = 0.4, $CHCl_3$).

IR (NaCl, thin film): 3219, 2977, 2935, 1462, 1379, 1347, 1169, 1075, 1020 cm^{-1}.

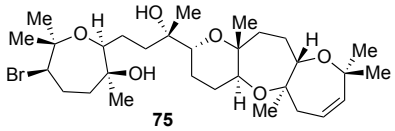


102

To a 1 mL Schlenk flask equipped with stir bar was added 95% sodium hydride in mineral oil (2.0 mg, 0.079 mmol) from a glovebox and transferred to a hood under nitrogen. A solution of hydrazone **101** (7.90 mg, 0.0161 mmol) in 500 μL of toluene was added and the flask was sealed and heated to 90 °C for 2.5 h. The flask was cooled and slowly quenched with saturated NH_4Cl. The aqueous layer was extracted with CH_2Cl_2 (3x) and the organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude reaction was purified by column chromatography (5% EtOAc in hexanes) to furnish oxepene **102** (0.80 mg, 0.0026 mmol, 16% yield).

^{1}H NMR (500 MHz, $CDCl_3$):
δ 5.84-5.77 (m, 1H), 5.47-5.42 (m, 1H), 5.38-5.35 (m, 1H), 5.24-5.19 (m, 1H), 5.10-5.06 (m, 1H), 4.02-3.97 (m, 1H), 3.73 (ddd, *J* = 11.4, 4.8, 2.8 Hz, 1H), 3.52-3.48 (m, 1H), 2.51-2.46 (m, 1H), 2.13-2.08 (m, 1H), 2.01-1.88 (m, 2H), 1.87-1.67 (m, 4H), 1.67-1.59 (m, 2H), 1.28 (s, 3H), 1.27 (s, 3H), 1.25 (s, 3H), 1.21 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$):
δ 139.7, 136.7, 122.1, 115.2, 78.0, 76.8, 73.8, 73.2, 70.6, 70.4, 42.3, 38.8, 32.3, 29.7, 27.64, 27.50, 26.2, 18.2, 17.8.



75

To a 500 μL sealed tube equipped with a stir bar was added sodium hydride (7.80 mg, 0.309 mmol, 95% in mineral oil) in the glove box and then transferred to the hood under nitrogen. The reaction was purged while a solution of hydrazone **104** (20.7 mg, 26.8 μmol) in 500 μL of THF was added by syringe. The reaction was sealed and heated to 100 °C for 3 h. The reaction turned brown and was then cooled to room temperature. H_2O was added to quench remaining sodium hydride, followed by addition of 1 mL of saturated NH_4Cl. The aqueous layer was extracted with Et_2O (5x) and then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Careful column chromatography (20 to 50% HPLC-grade EtOAc in hexanes) provided a small amount of analytically clean **75** (0.9 mg, 1.5 μmol, 6% yield) as colorless oil.

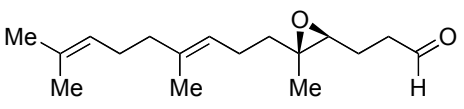
^{1}H NMR (600 MHz, C_6D_6):
δ 5.46 (dt, *J* = 11.8, 6.0 Hz, 1H), 5.21 (d, *J* = 11.5 Hz, 1H), 3.88 (dt, *J* = 11.4, 6.4 Hz, 1H), 3.53 (d, *J* = 11.2 Hz, 1H), 3.48 (dd, *J* = 11.5, 4.3 Hz, 1H), 3.28-3.24 (m, 1H), 2.92 (bs, 1H), 2.75 (dd, *J* = 9.1, 2.7 Hz, 1H), 2.61 (ddd, *J* = 15.5, 5.6, 1.7 Hz, 1H), 2.25-2.17 (m, 2H), 2.11 (bs, 1H), 1.99-1.96 (m, 1H), 1.93-1.85 (m, 2H), 1.86-1.68 (m, 5H), 1.67-1.58 (m, 2H), 1.58-1.54 (m, 1H), 1.54-1.44 (m, 4H), 1.46 (td, J = 7.9, 3.9 Hz, 1H), 1.33 (s, 3H), 1.30 (s, 3H), 1.25 (s, 3H), 1.24 (s, 3H), 1.18 (s, 3H), 1.12 (s, 3H), 1.10 (s, 3H), 1.01 (s, 3H), 0.95-0.90 (m, 1H).

^{13}C NMR (125 MHz, C_6D_6):
δ 137.1, 122.8, 78.3, 77.9, 77.8, 77.7, 76.9, 76.5, 75.8, 74.6, 73.2, 72.3, 59.8, 44.8, 42.6, 39.1, 34.6, 31.0, 29.9, 28.0, 28.0, 26.5, 26.2, 26.1, 25.6, 25.5, 24.4, 24.3, 18.5, 17.8.

$[\alpha]^{24}_D = -17.9$ (*c* = 0.05, $CHCl_3$).

IR (NaCl, thin film): 3428, 2926, 2852, 1726, 1464, 1377, 1262, 1139, 1084 cm^{-1}.

HR-MS (ESI) *m/z* calcd for $C_{30}H_{51}BrO_6$ $[M+Na]^+$: 609.2761 found 609.2770.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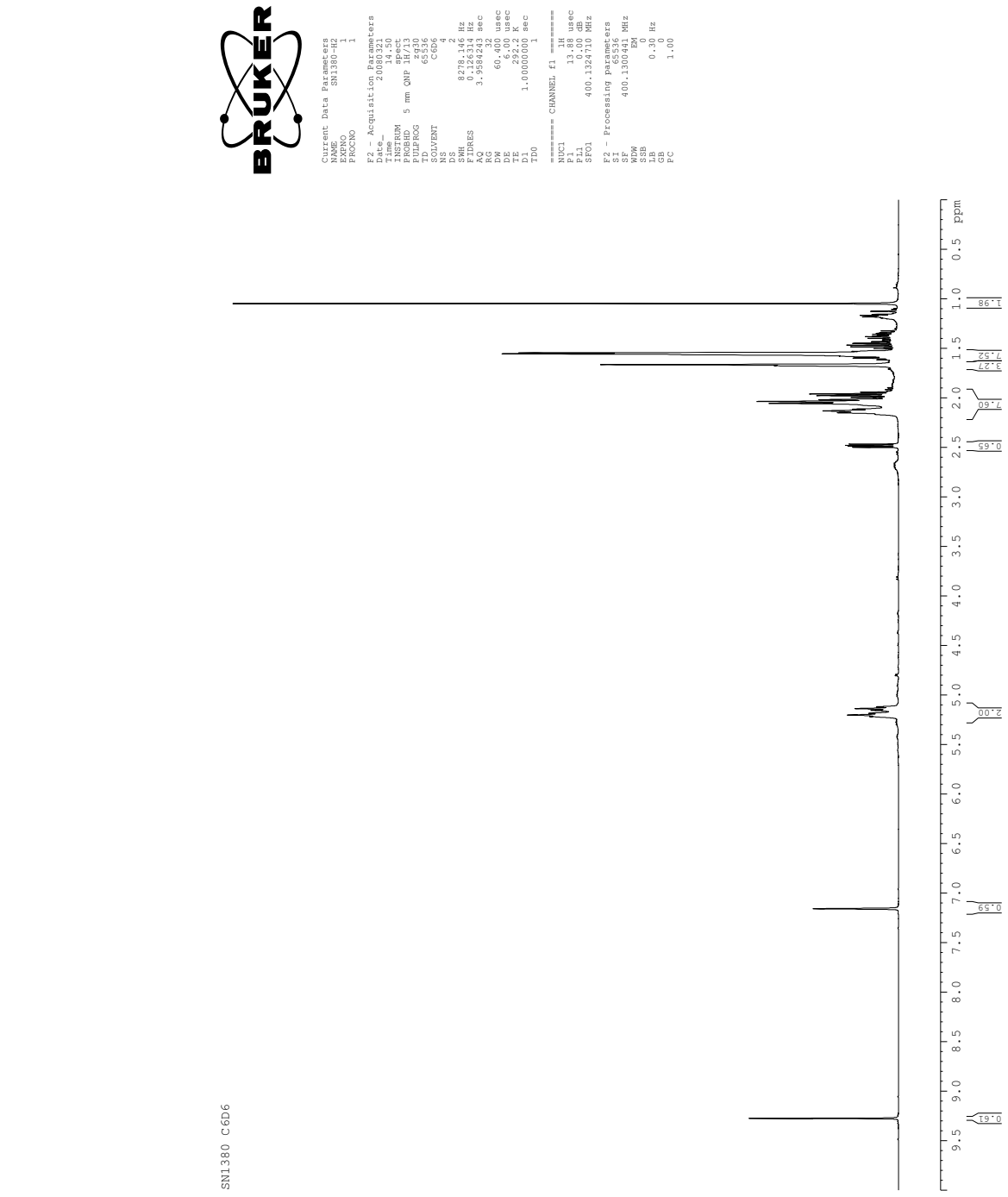
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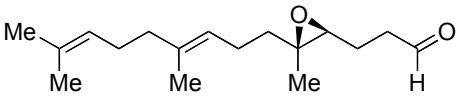
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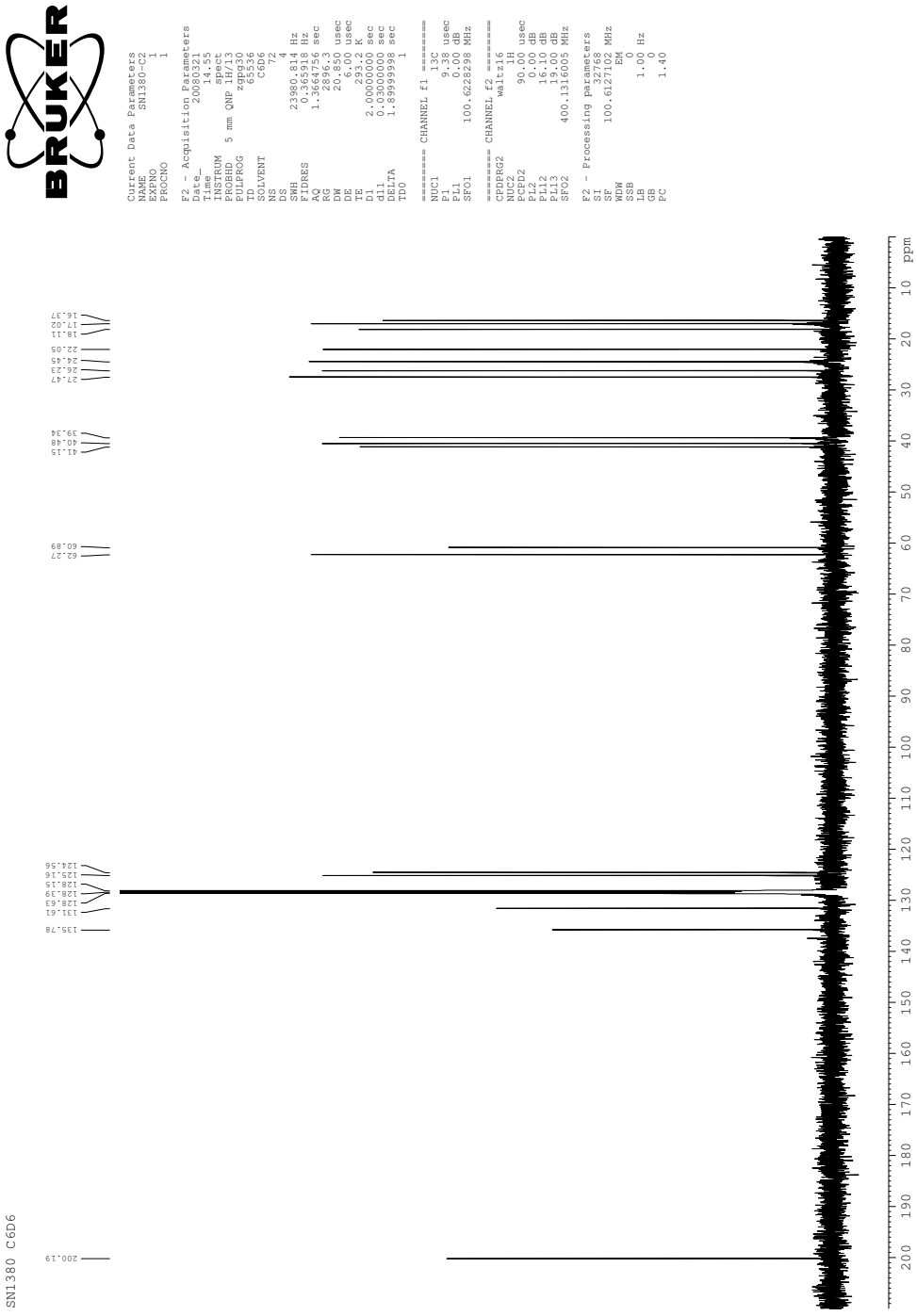
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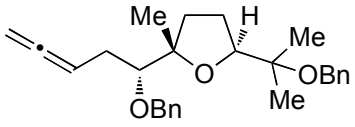

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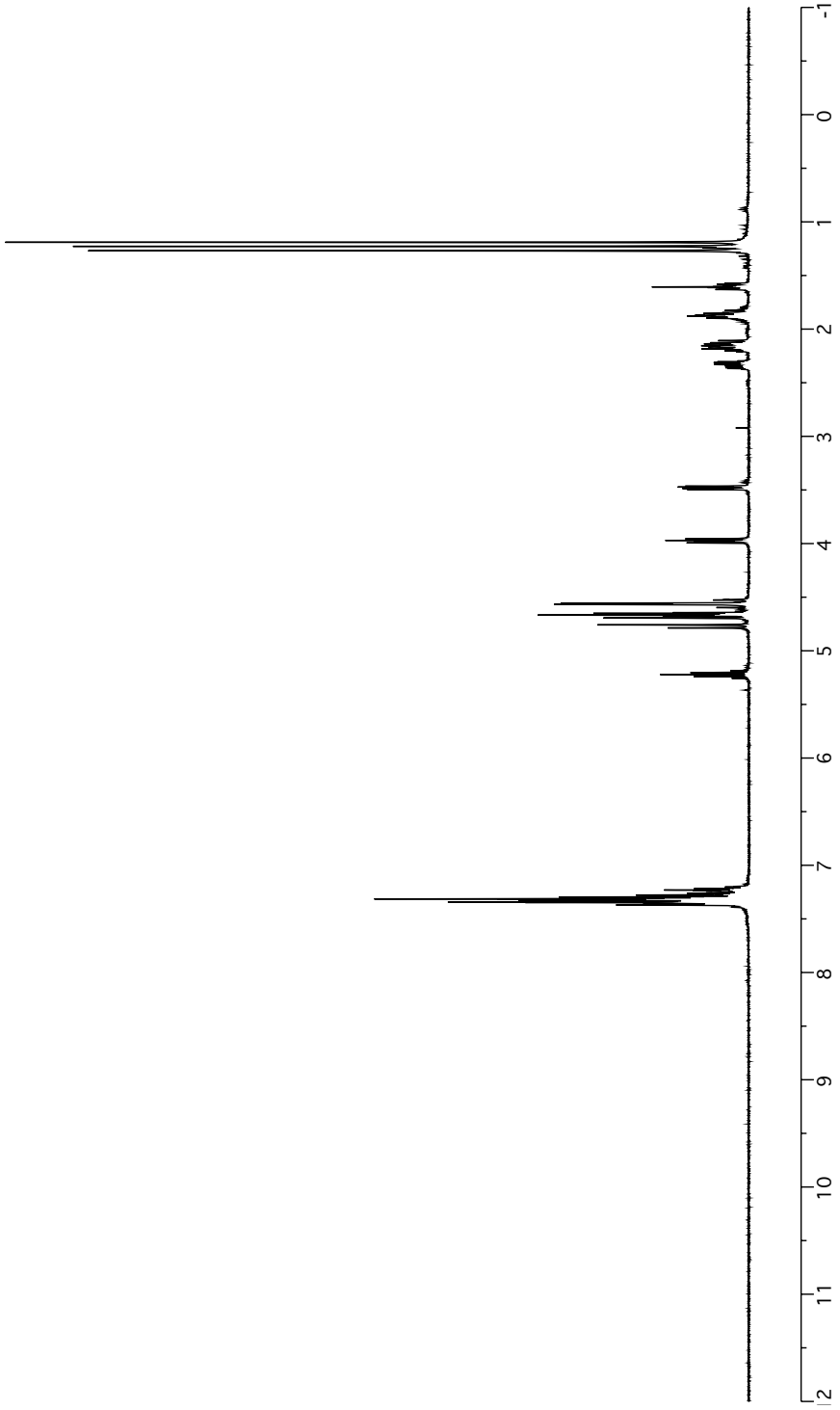

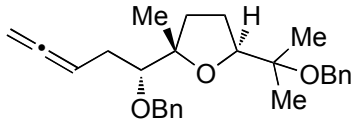

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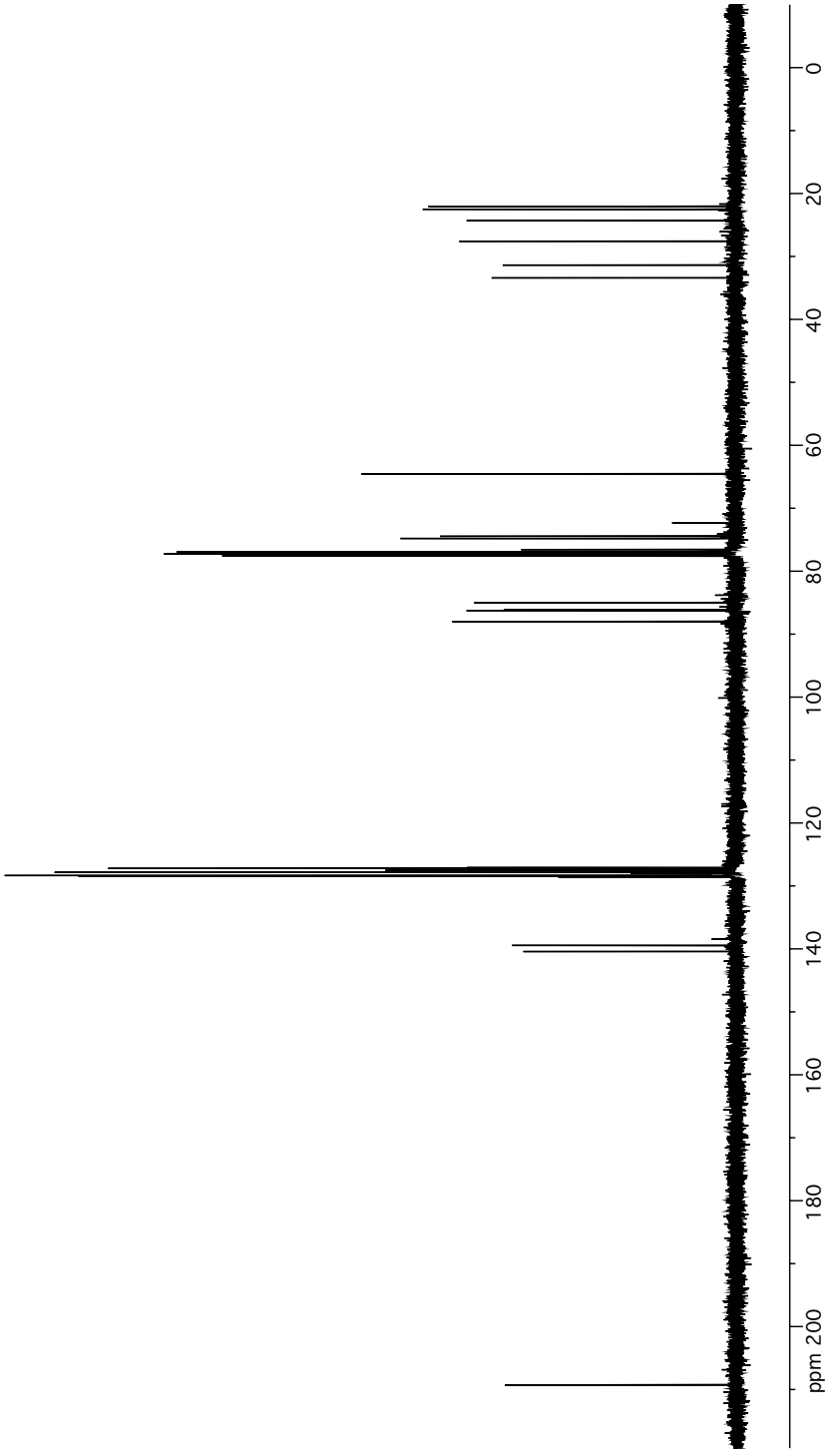

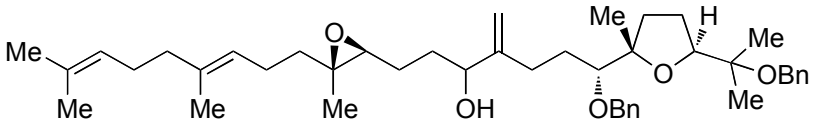

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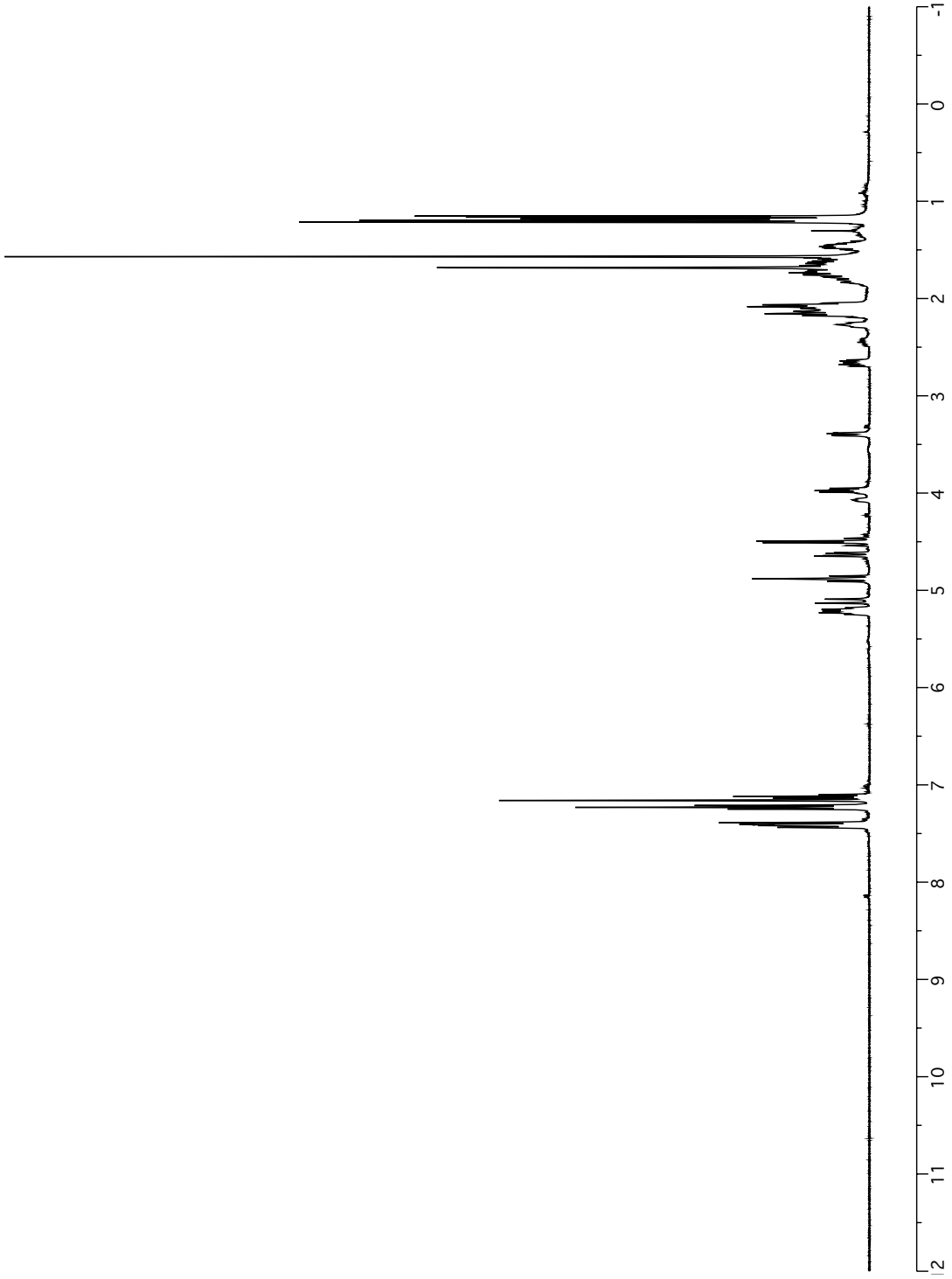

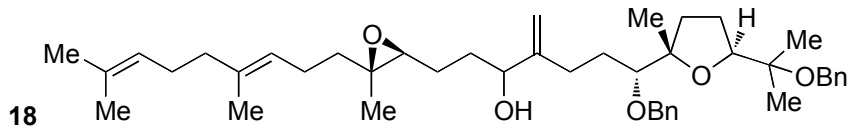
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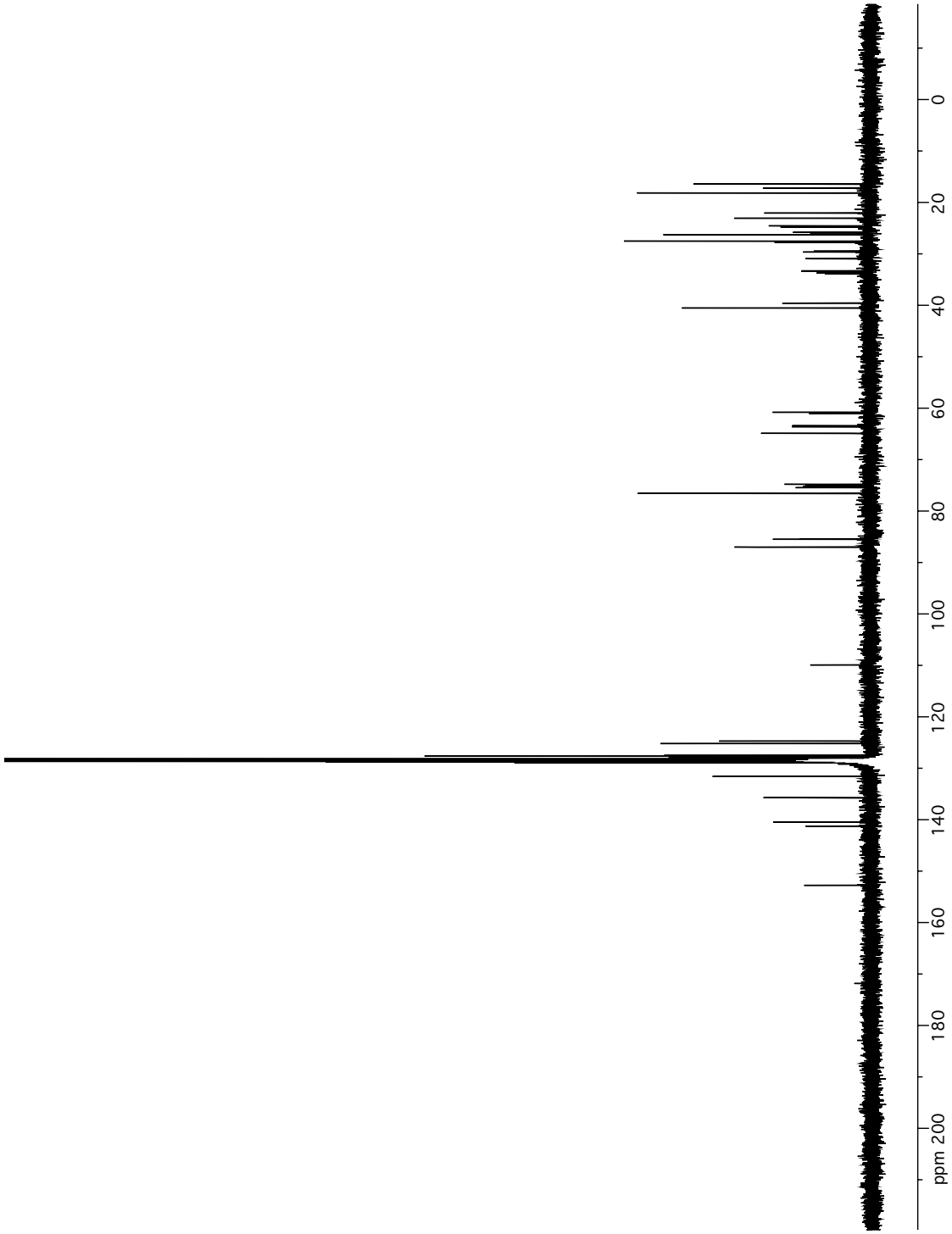
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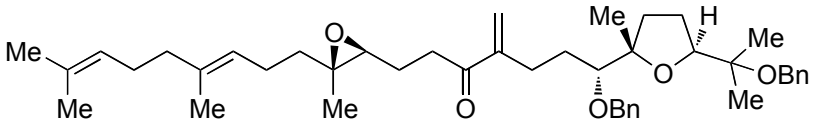

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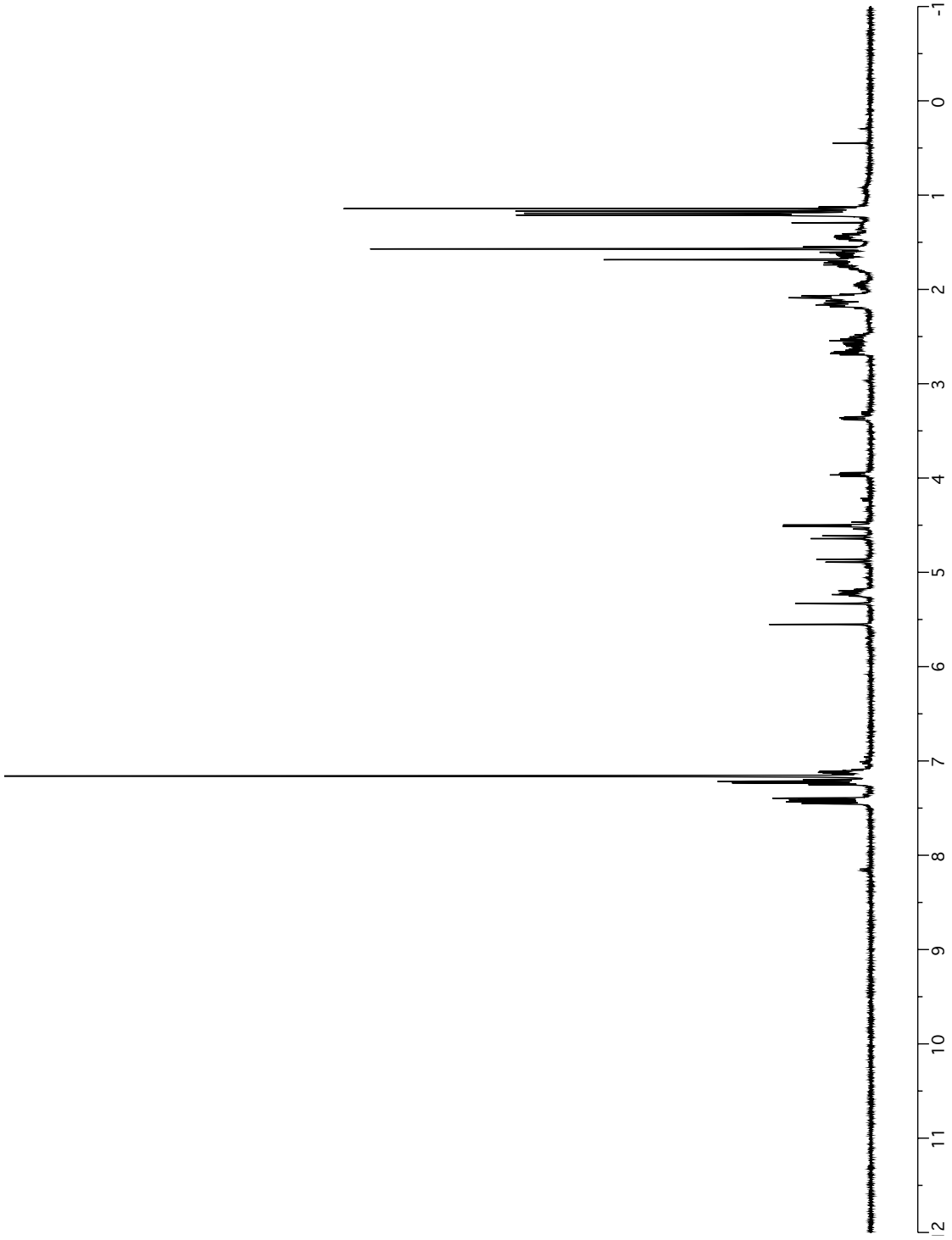

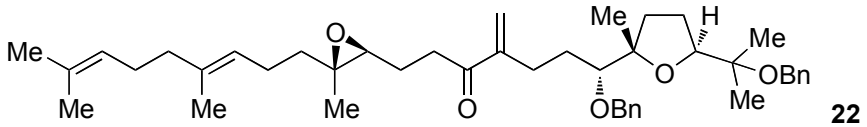
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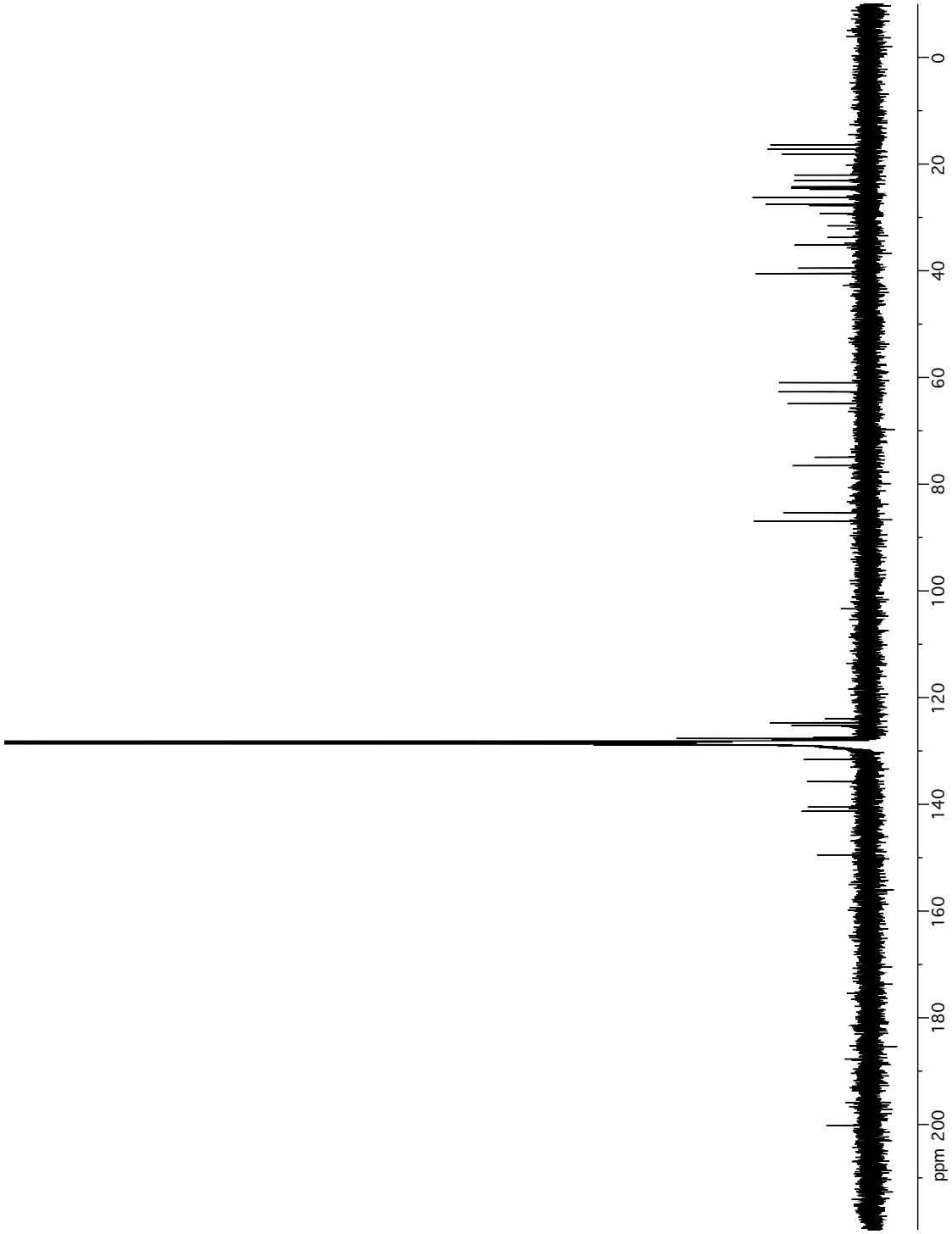
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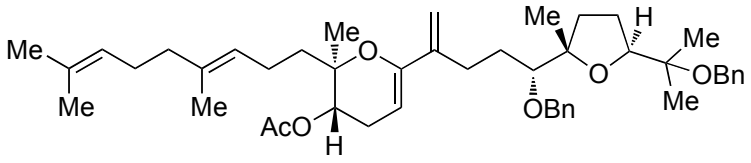
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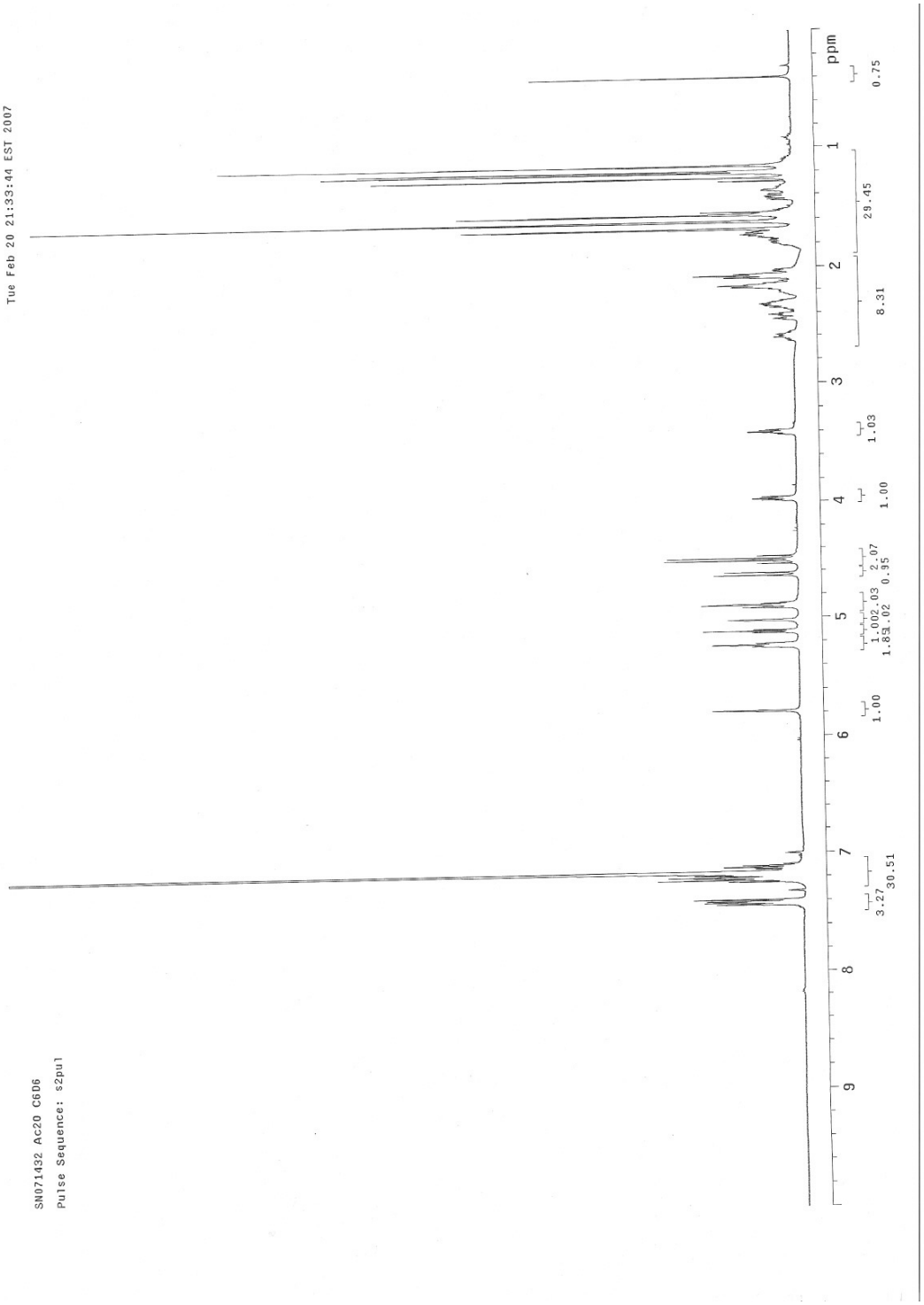
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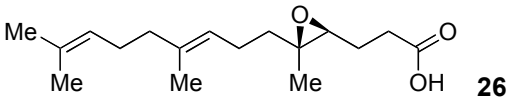
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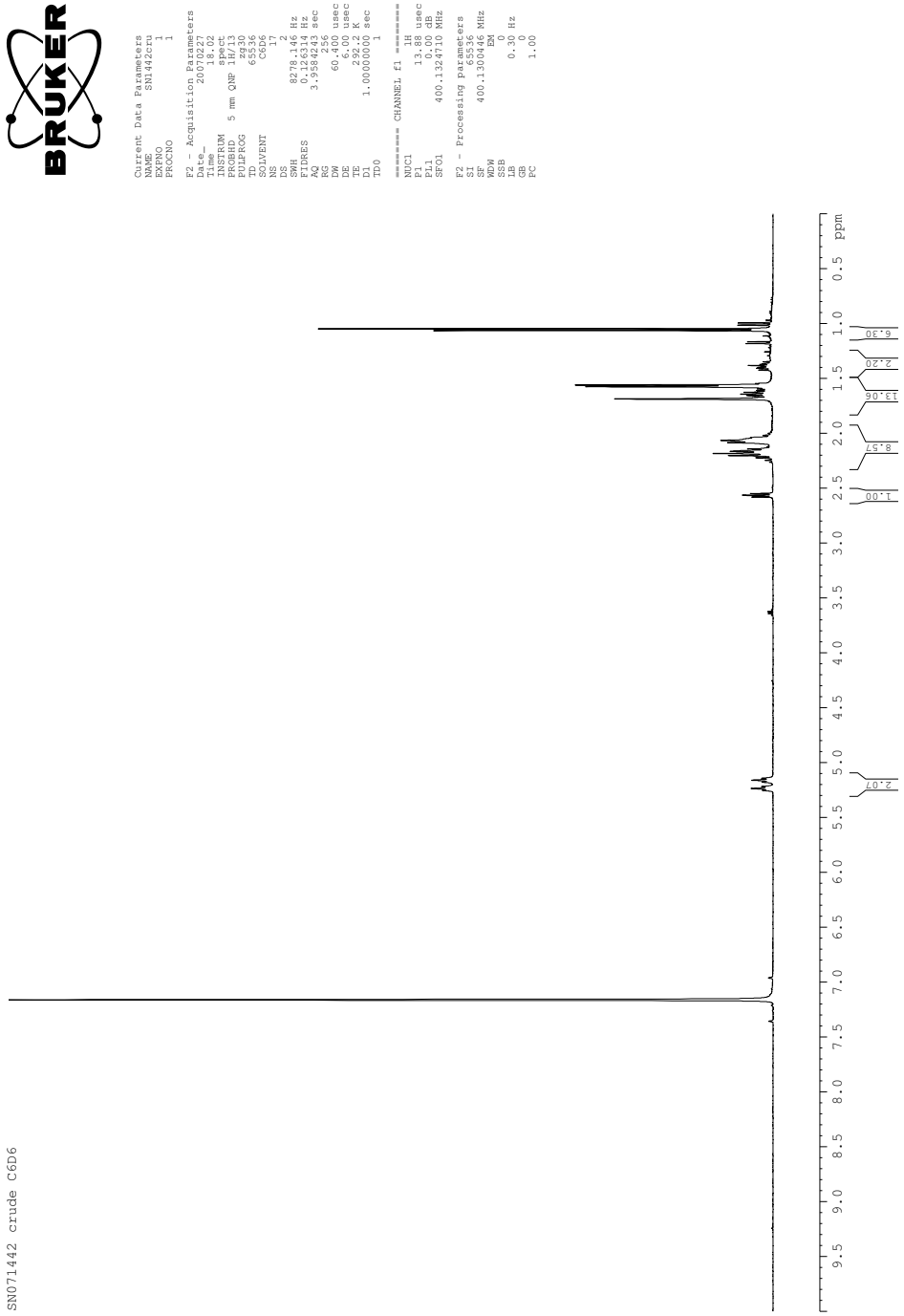
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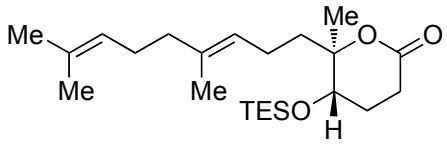

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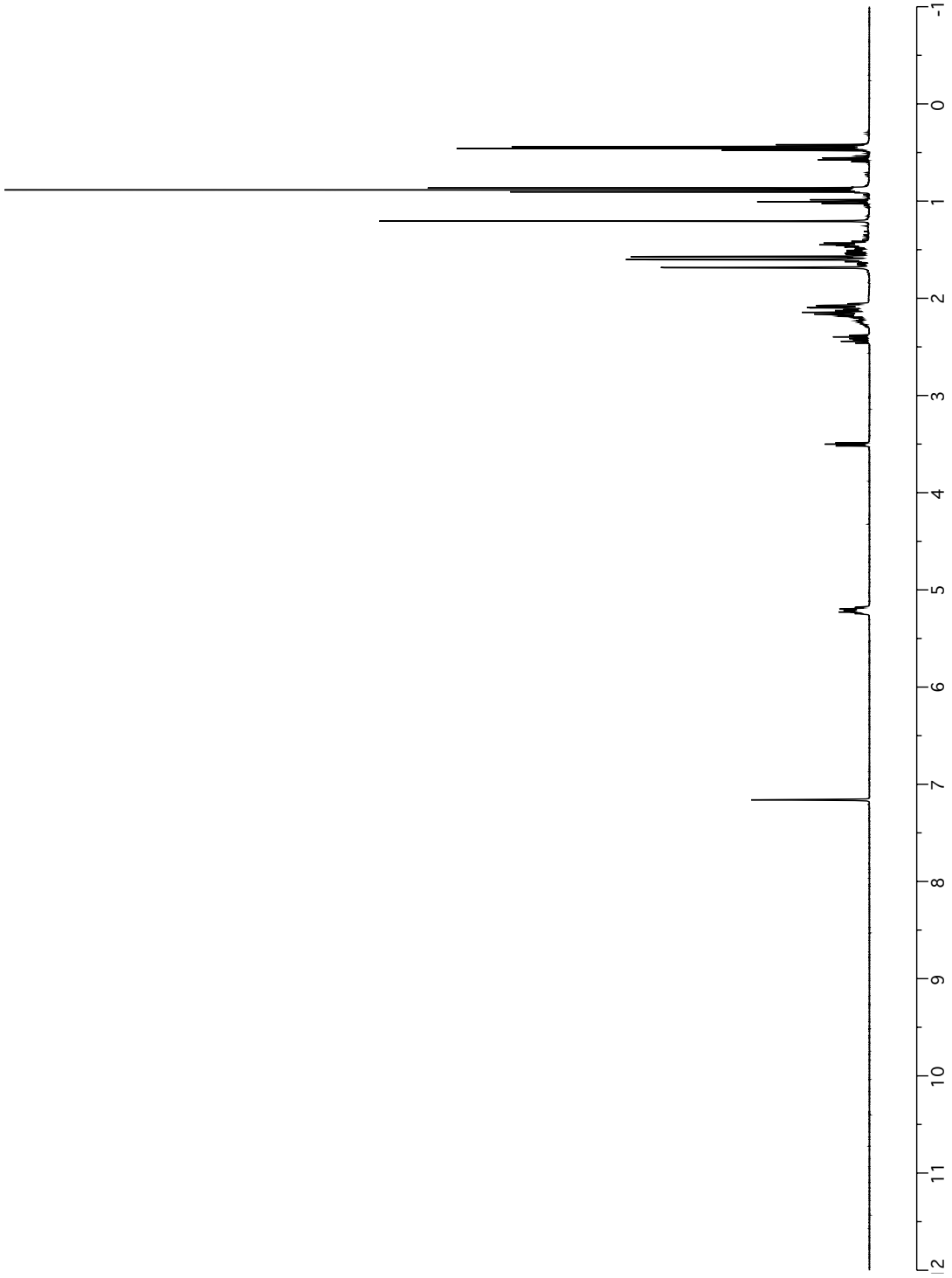

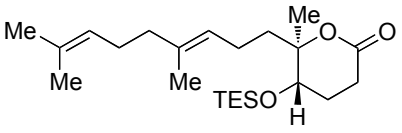

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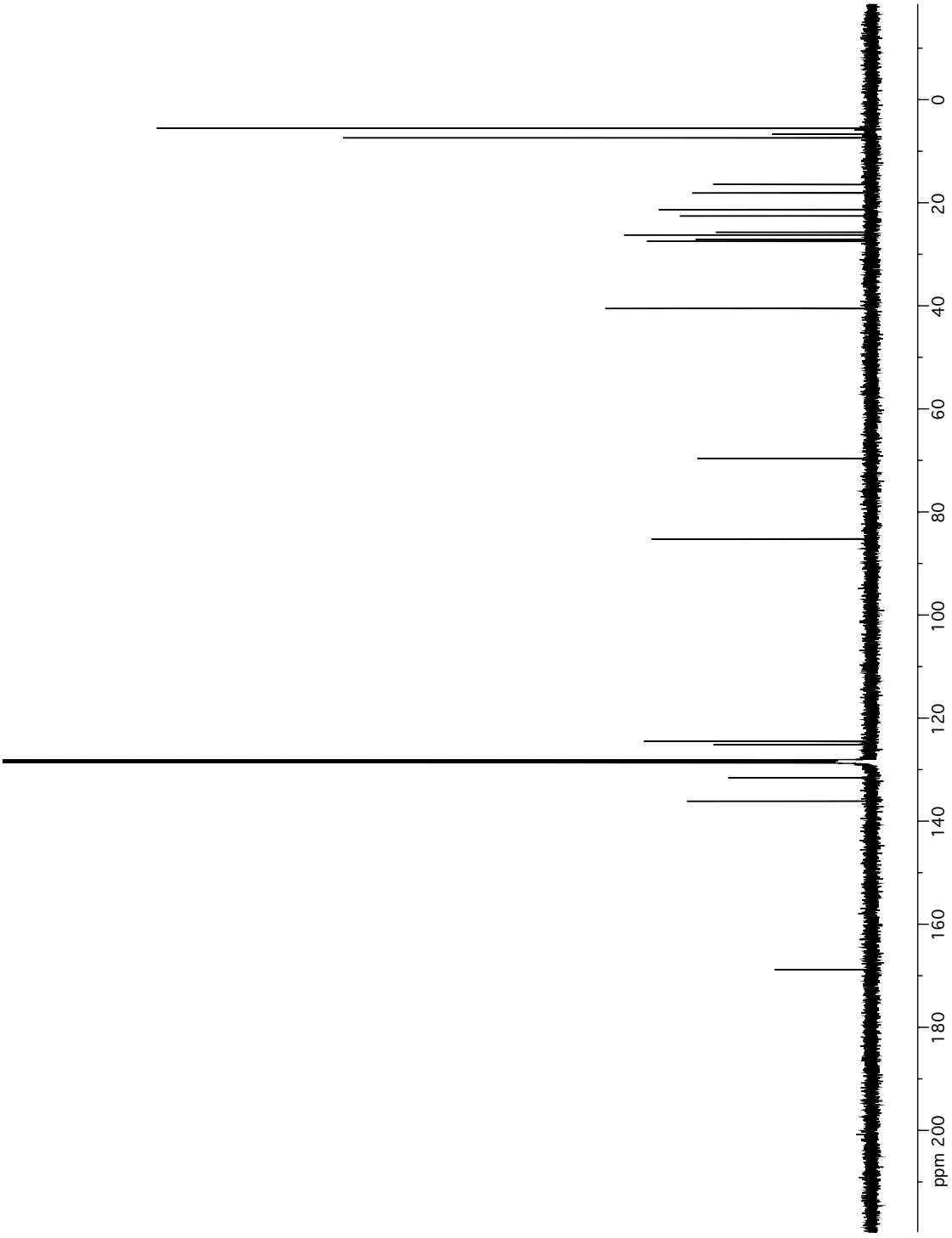

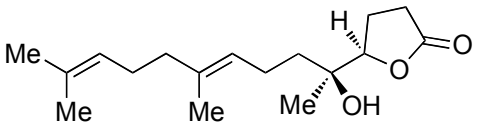

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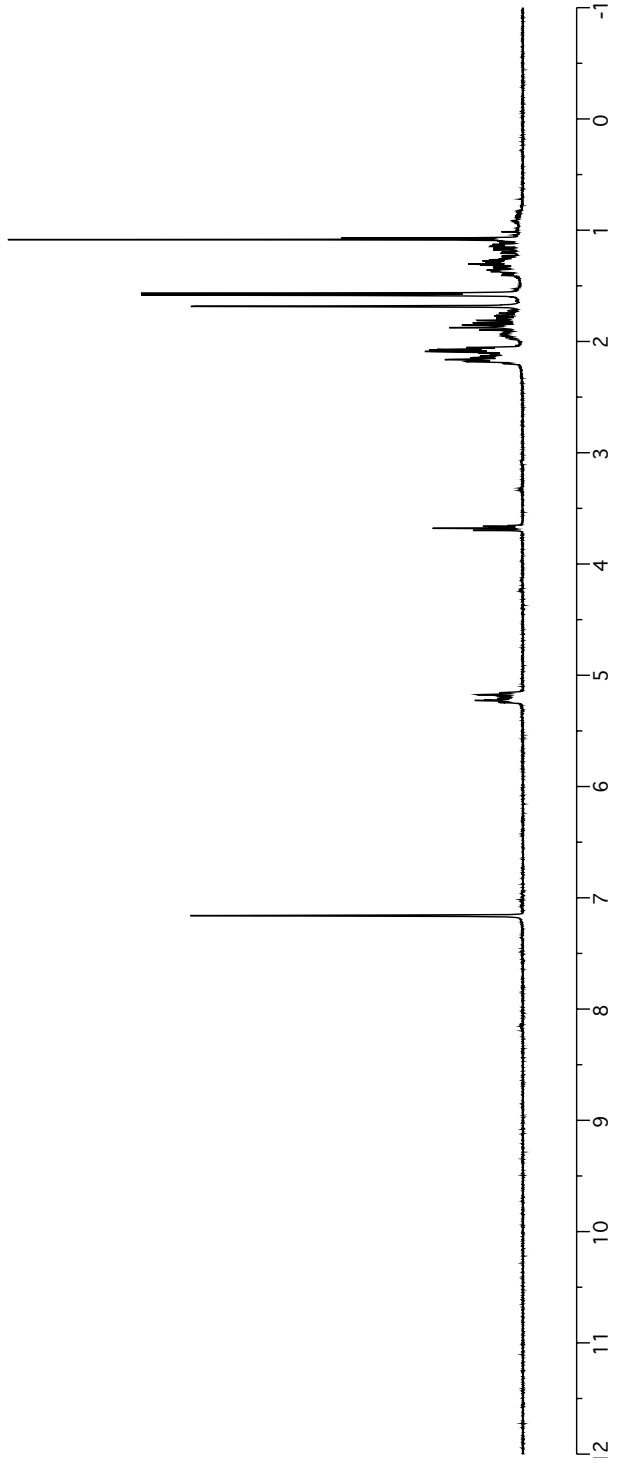

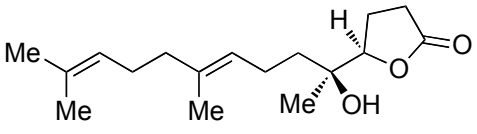

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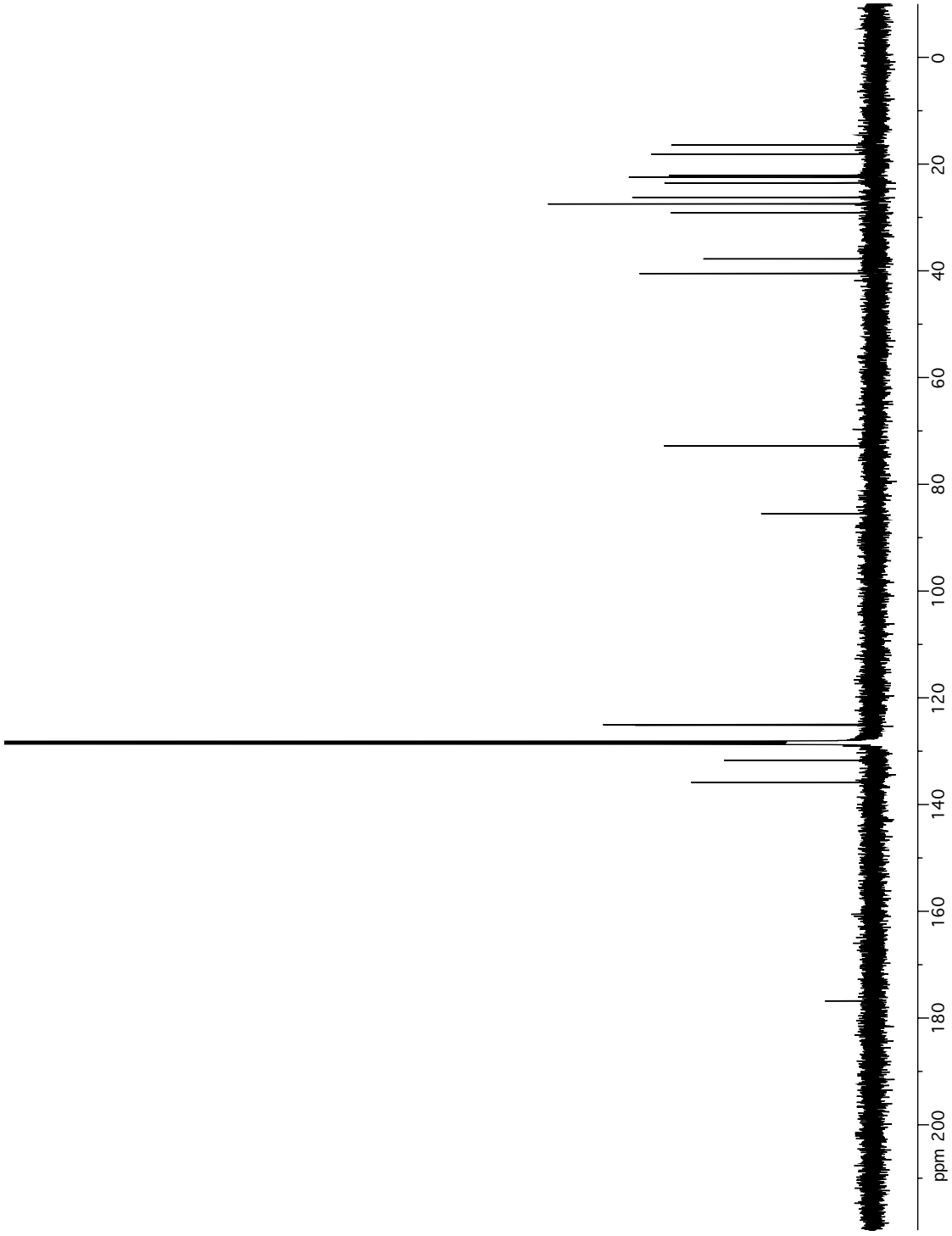

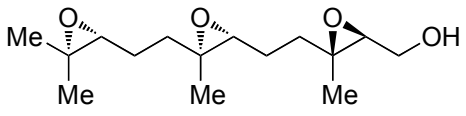

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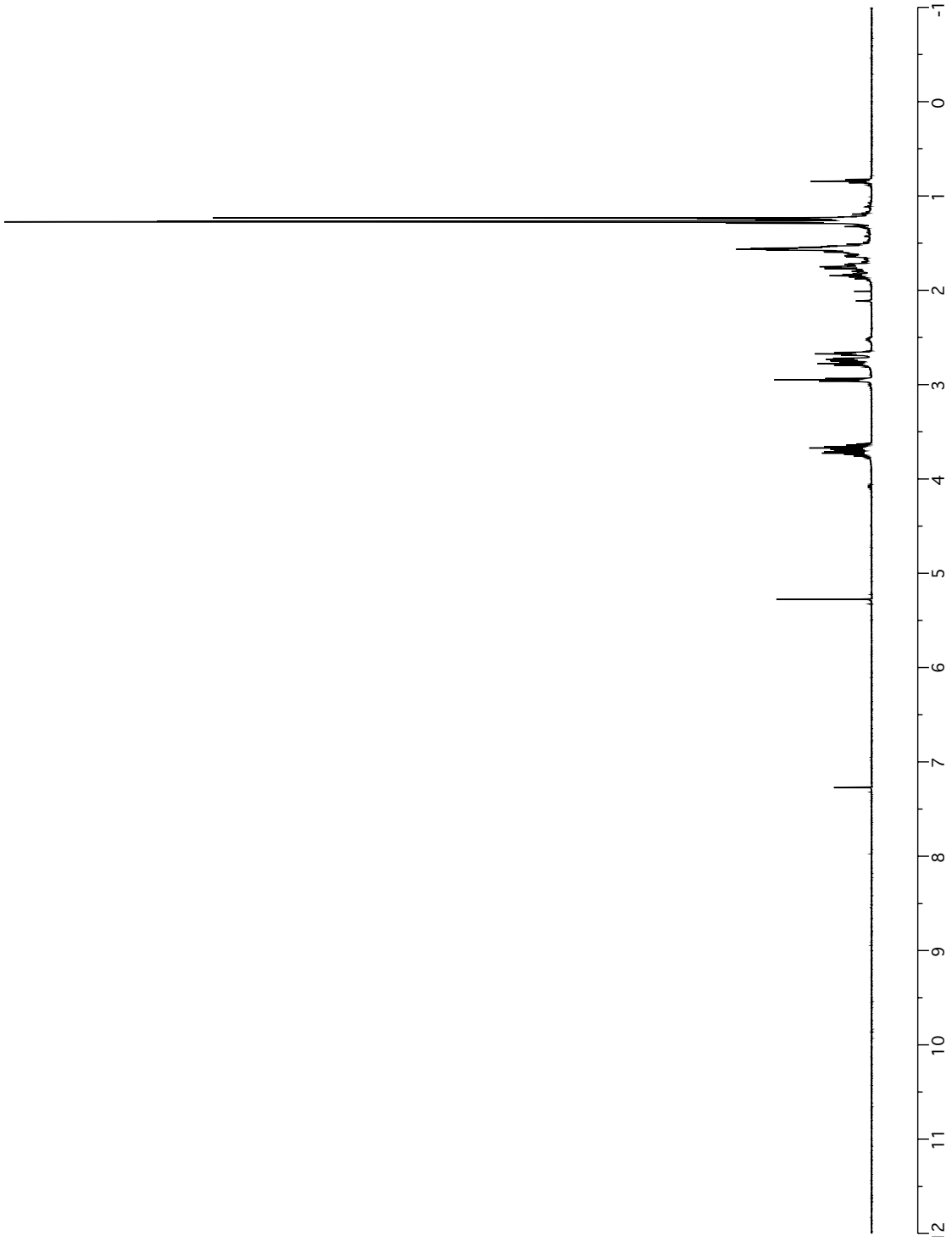

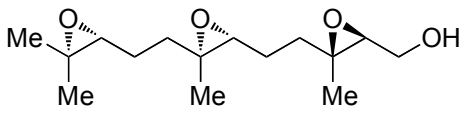

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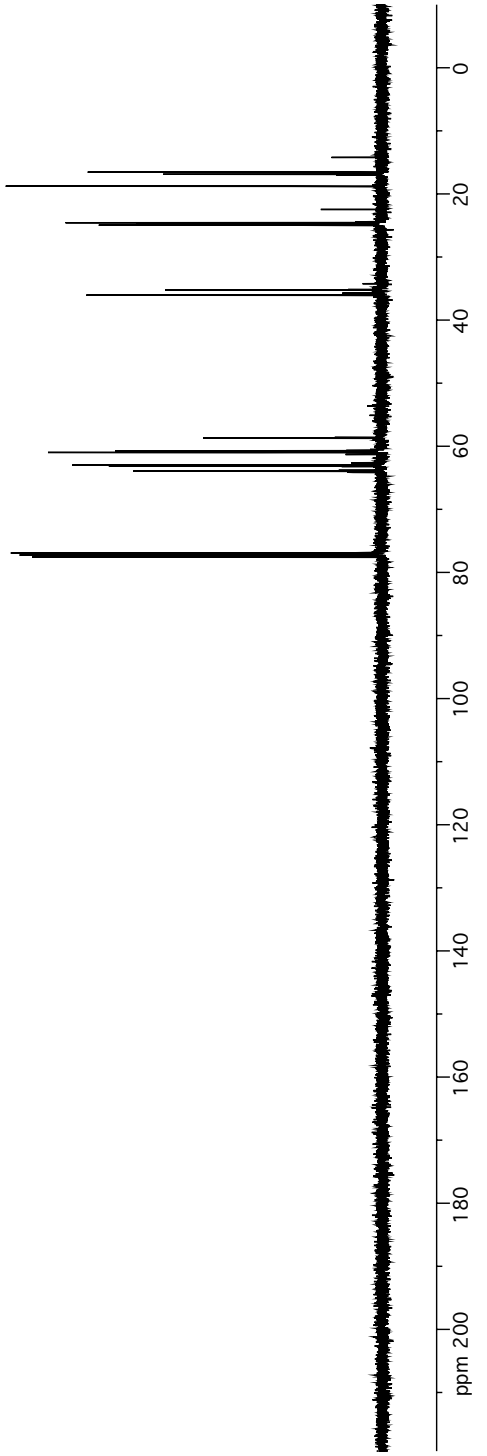

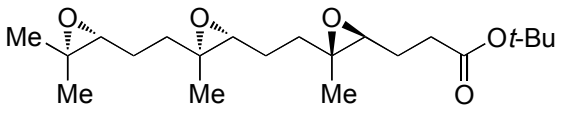

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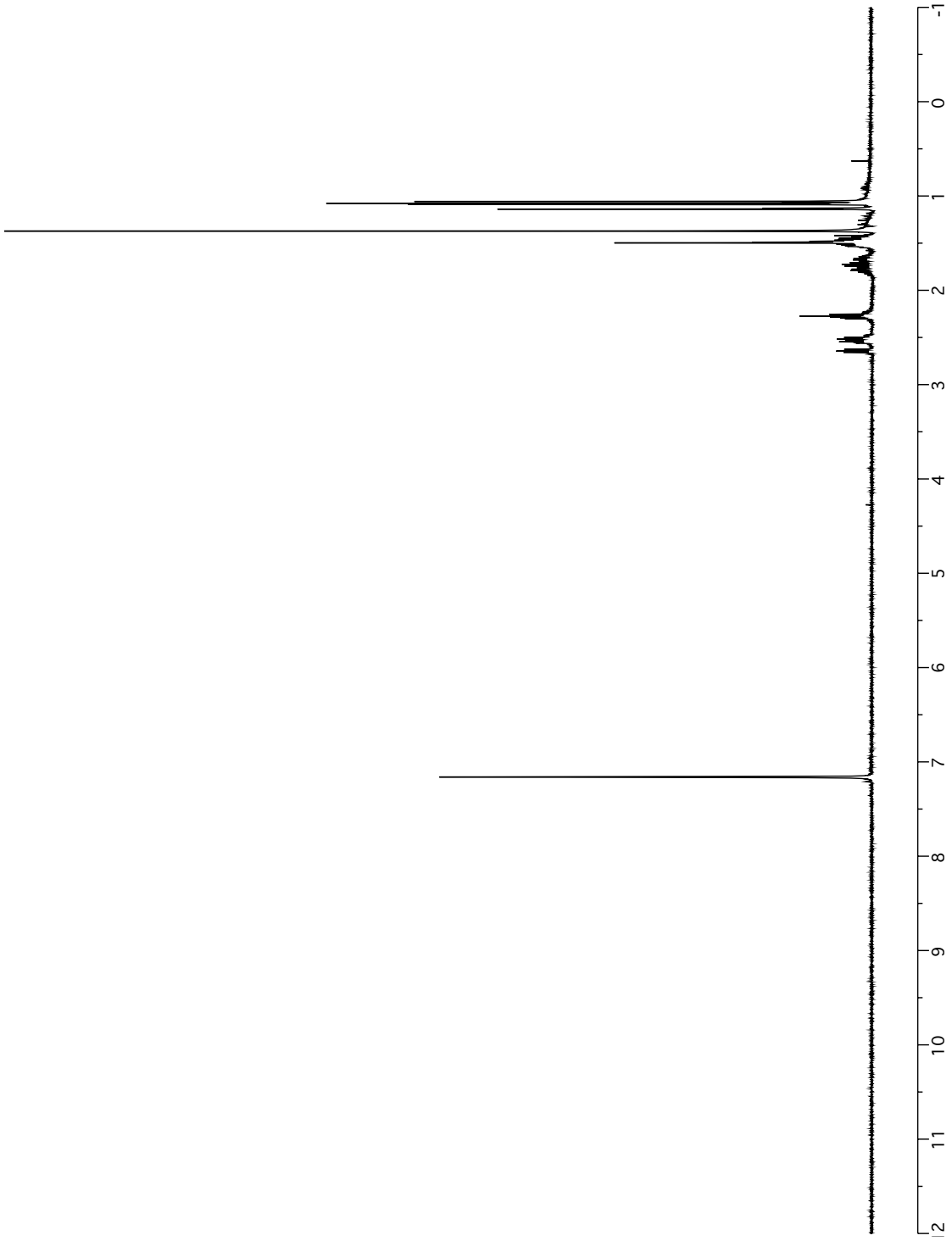

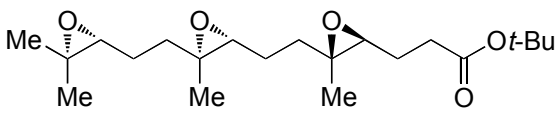

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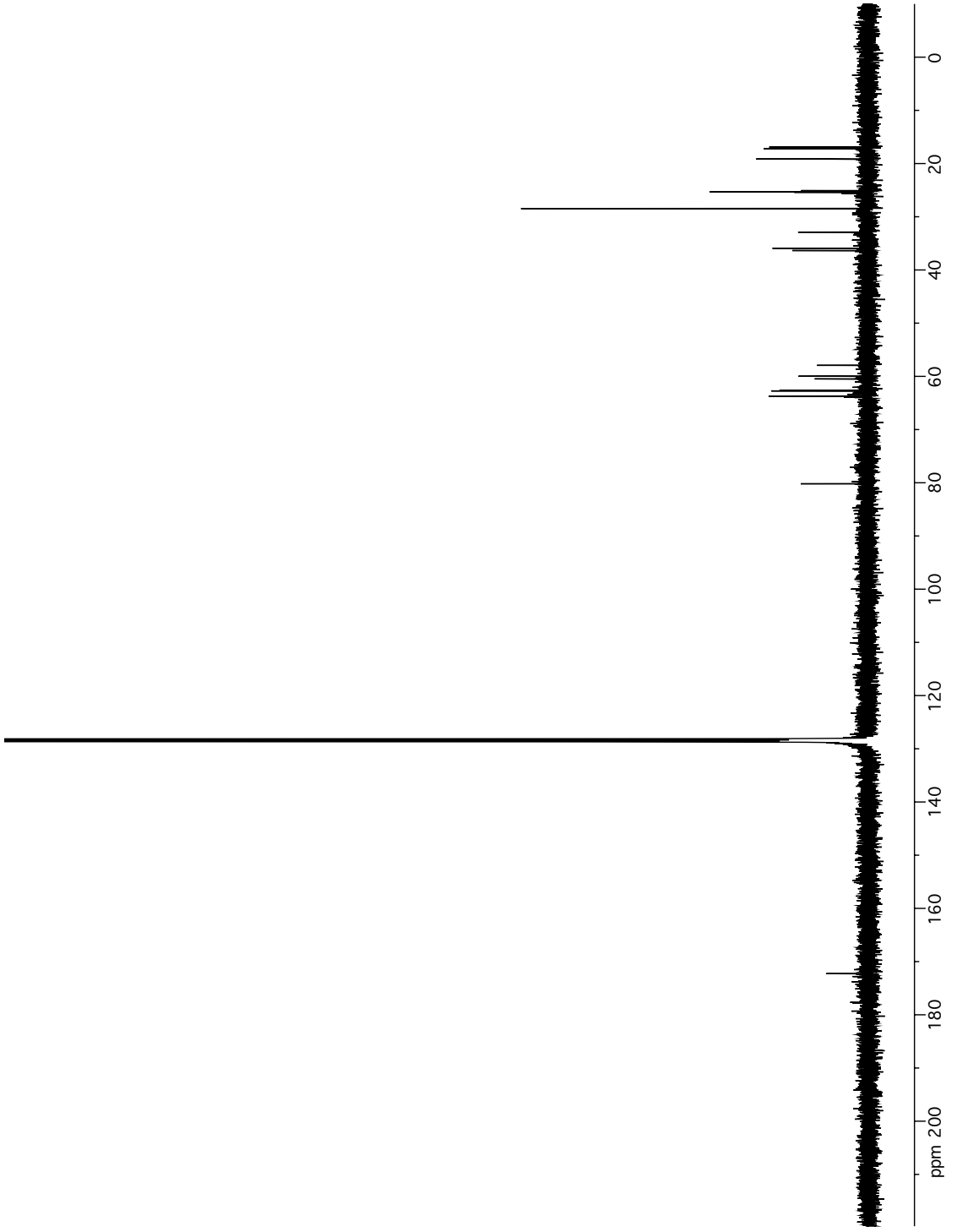

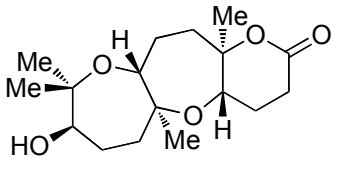

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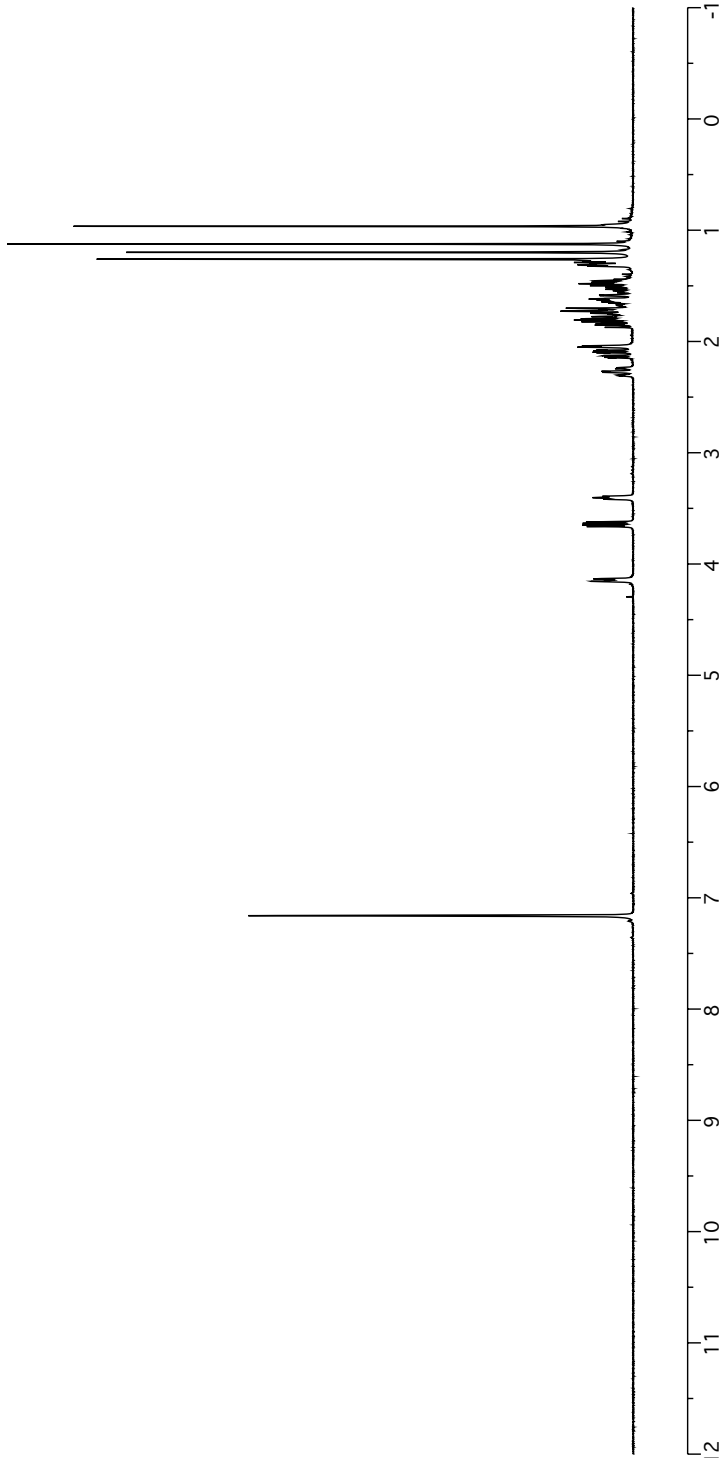

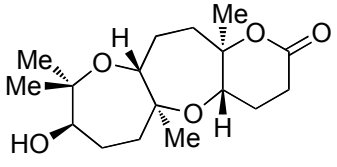

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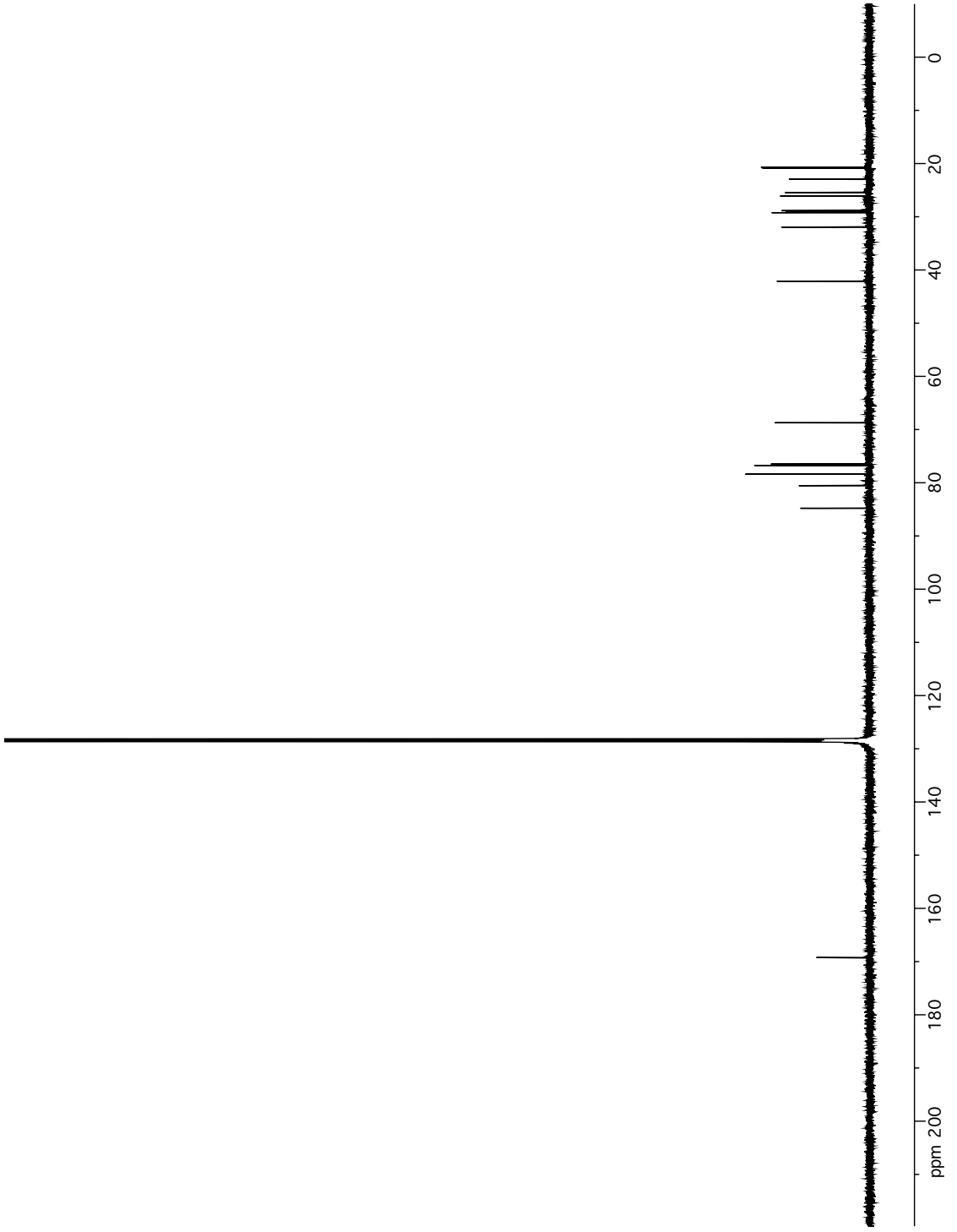

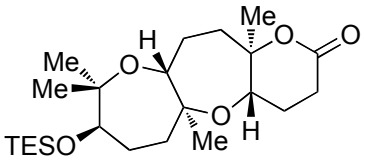

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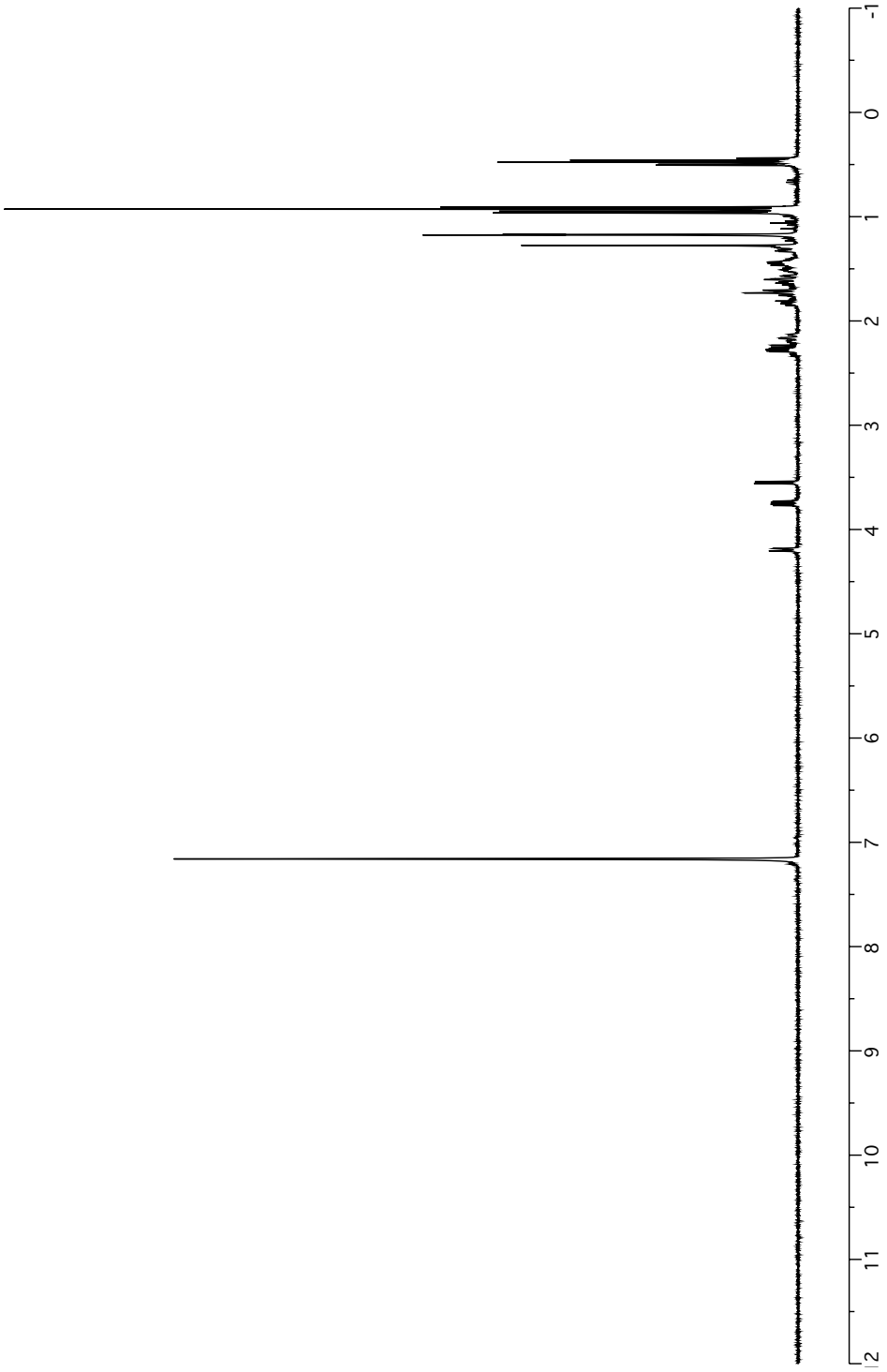

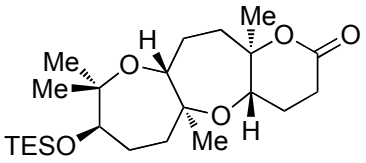

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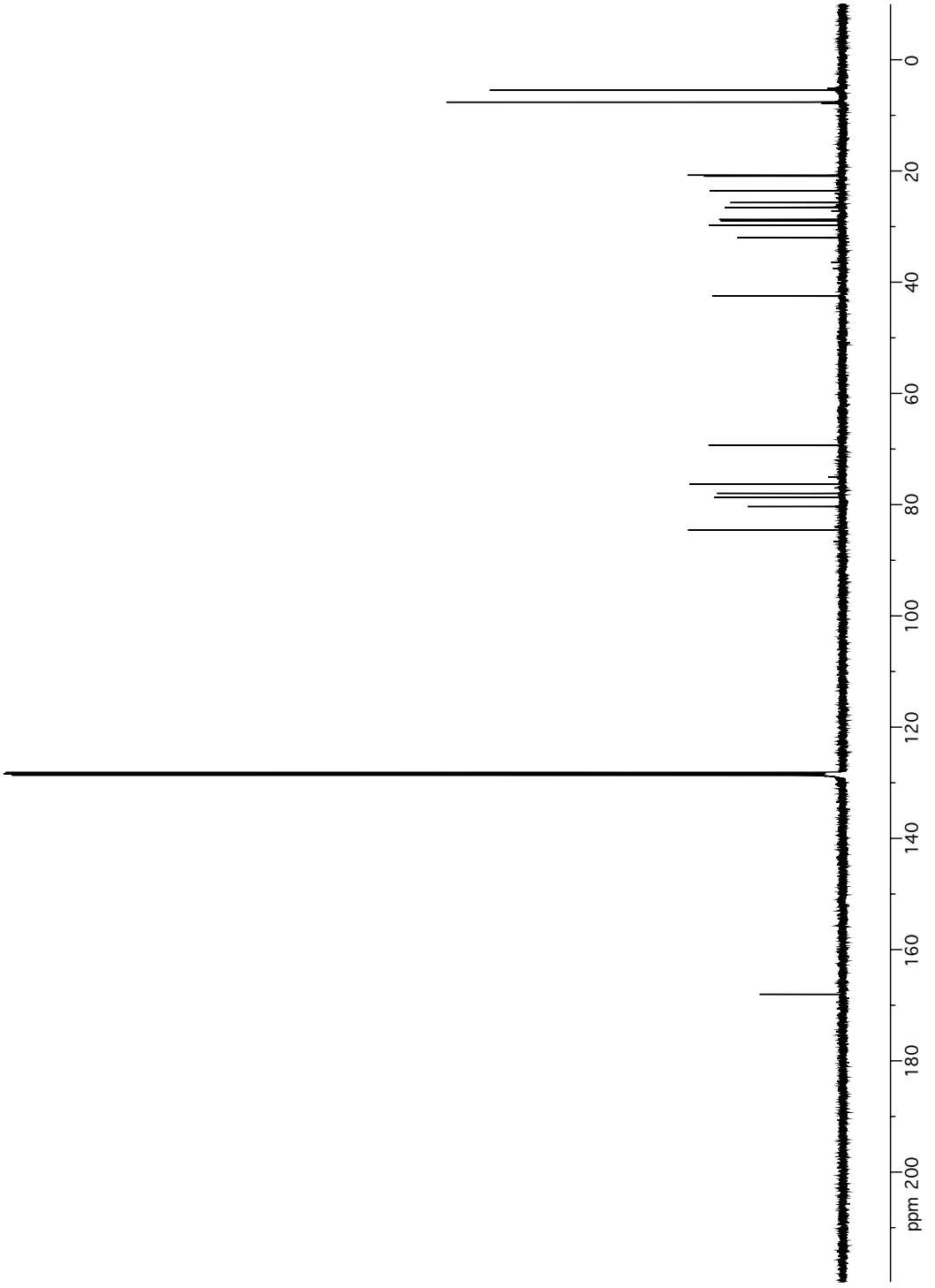

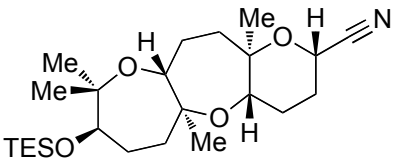

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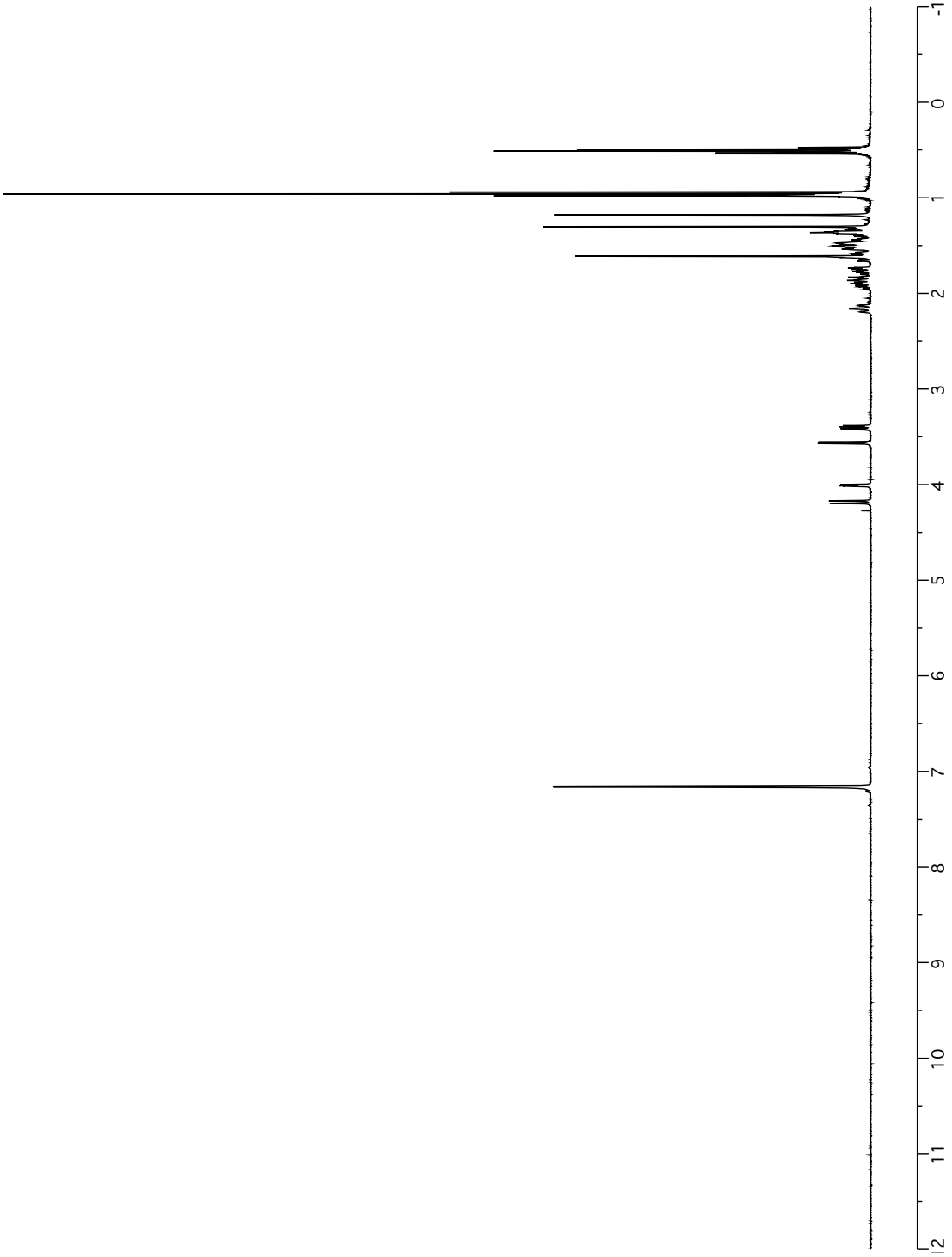

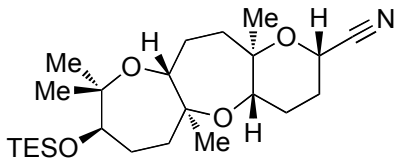

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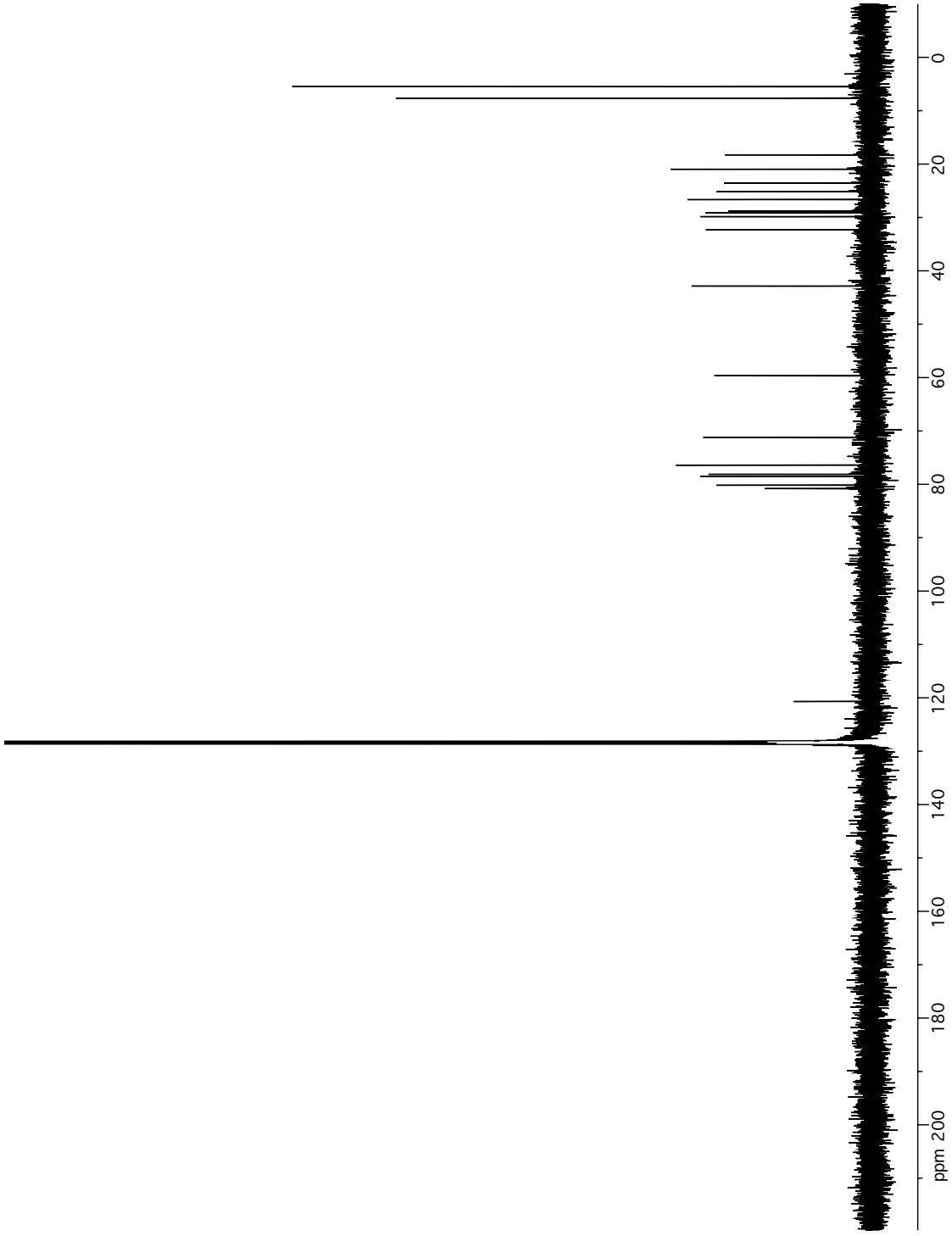

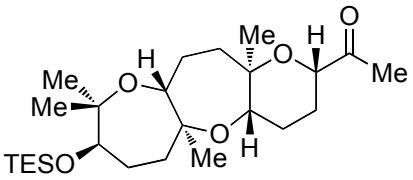

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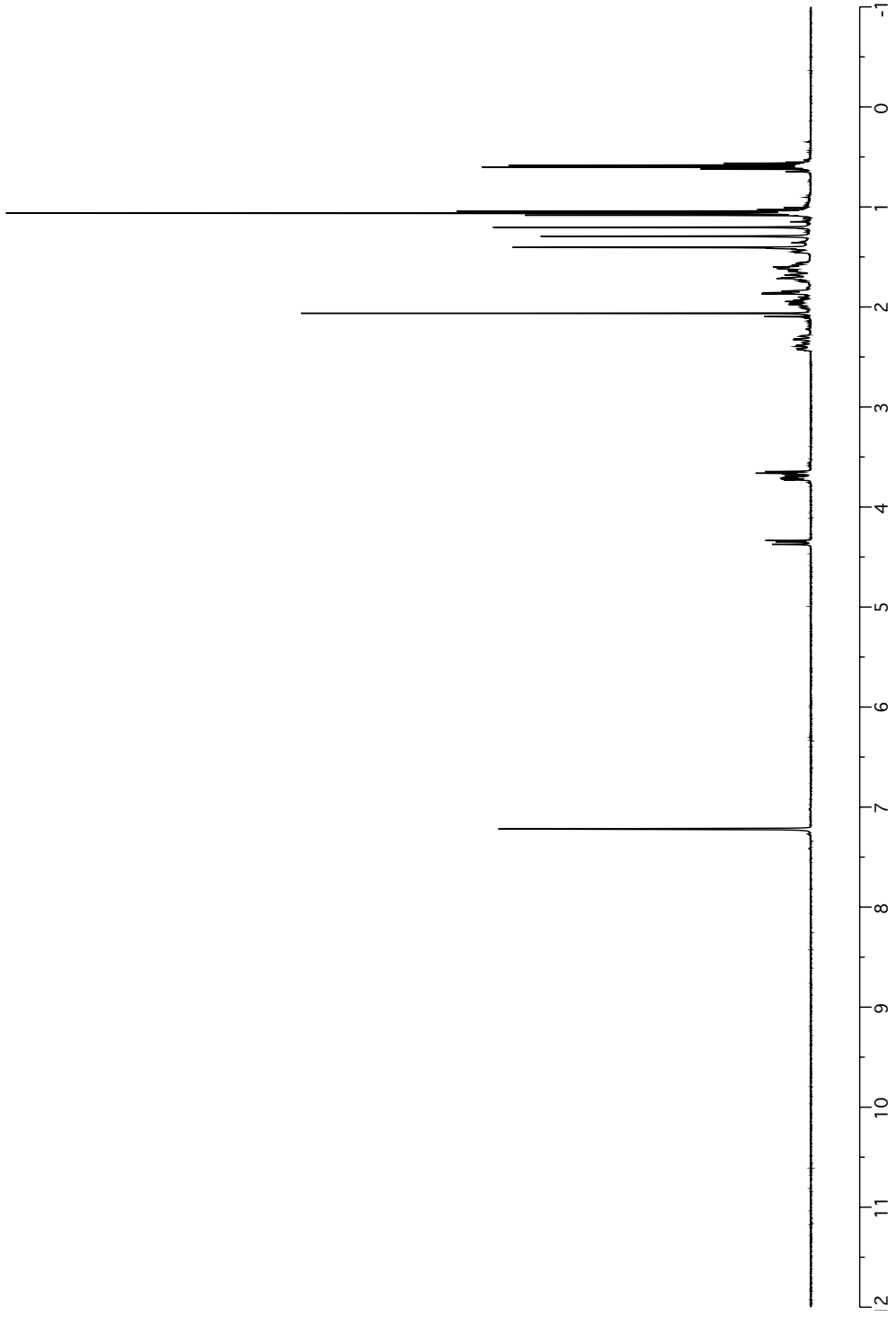

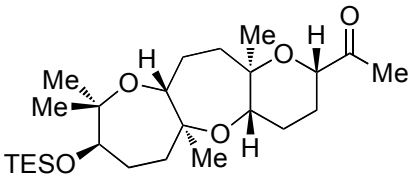
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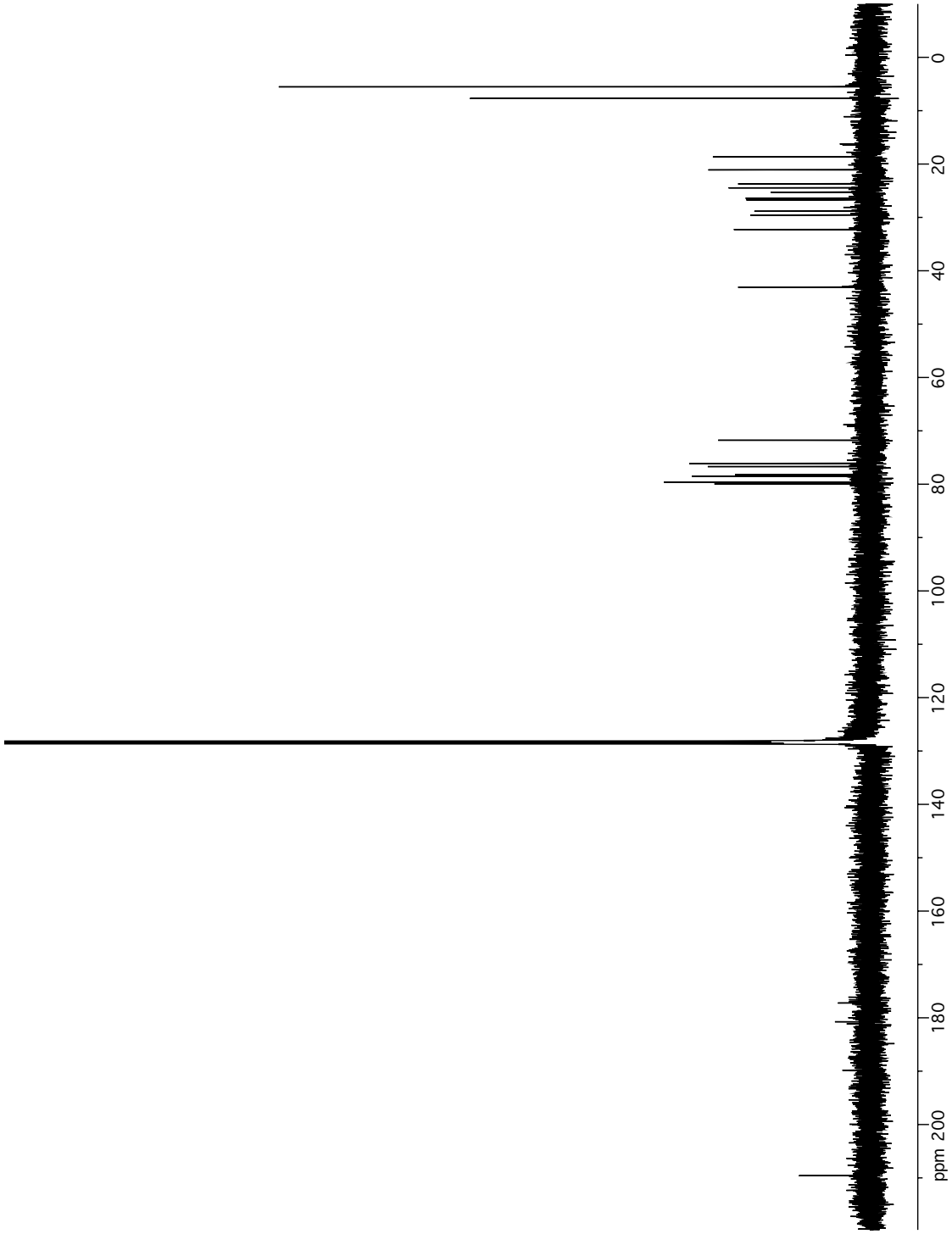
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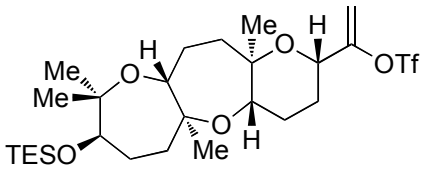

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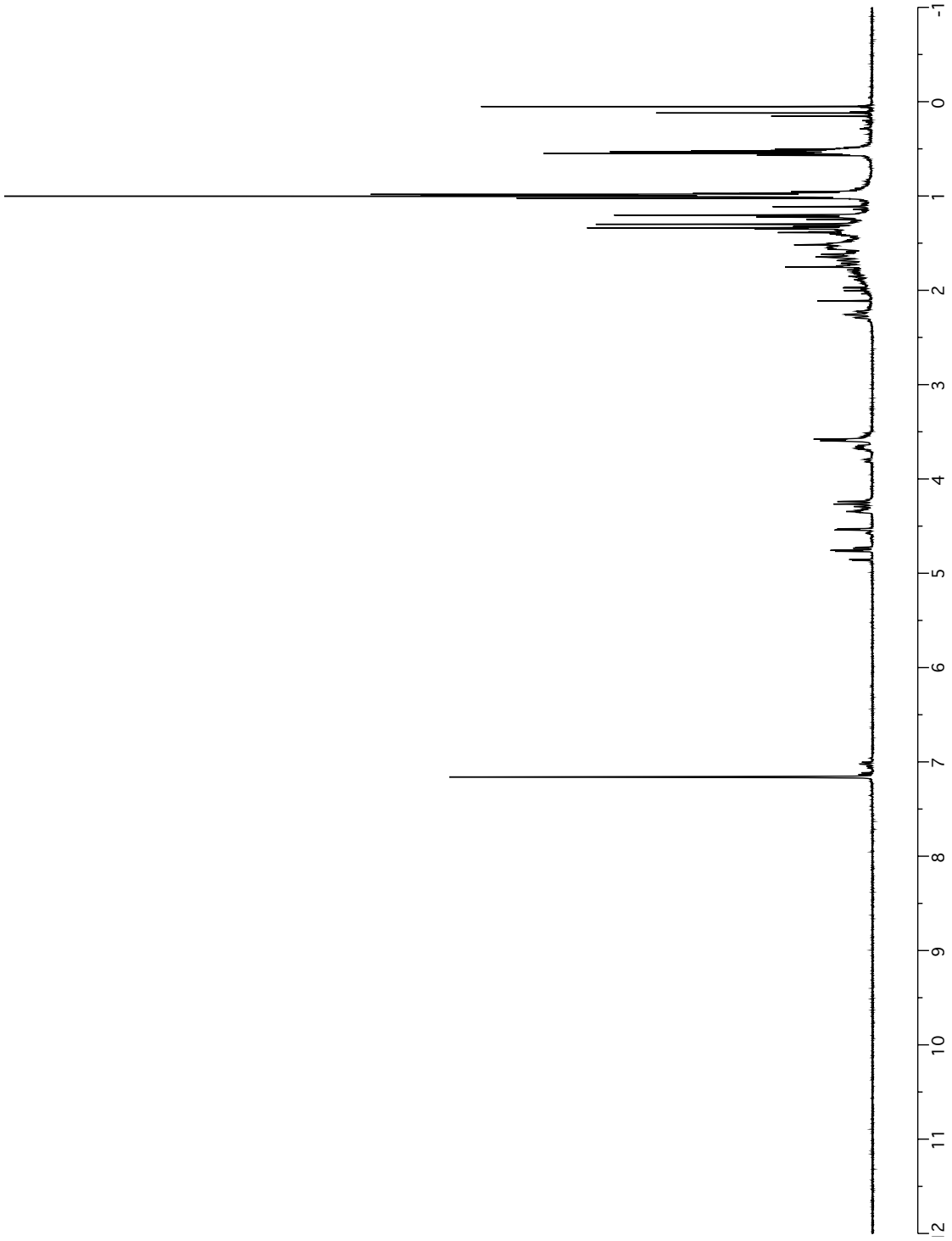

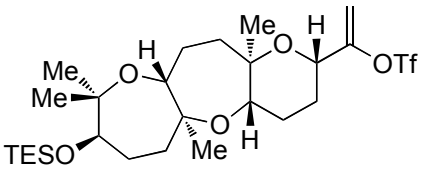

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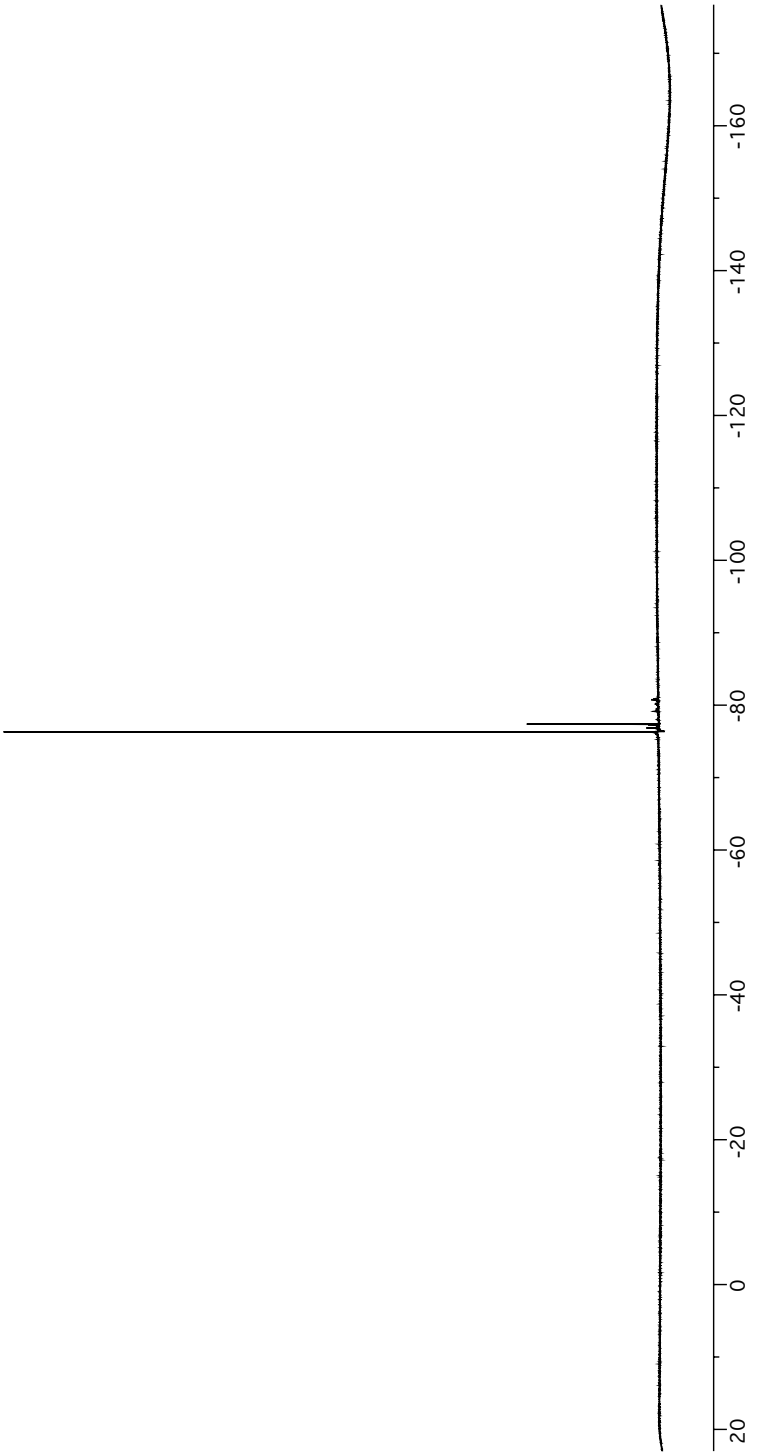

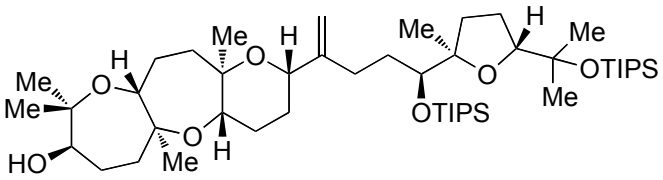

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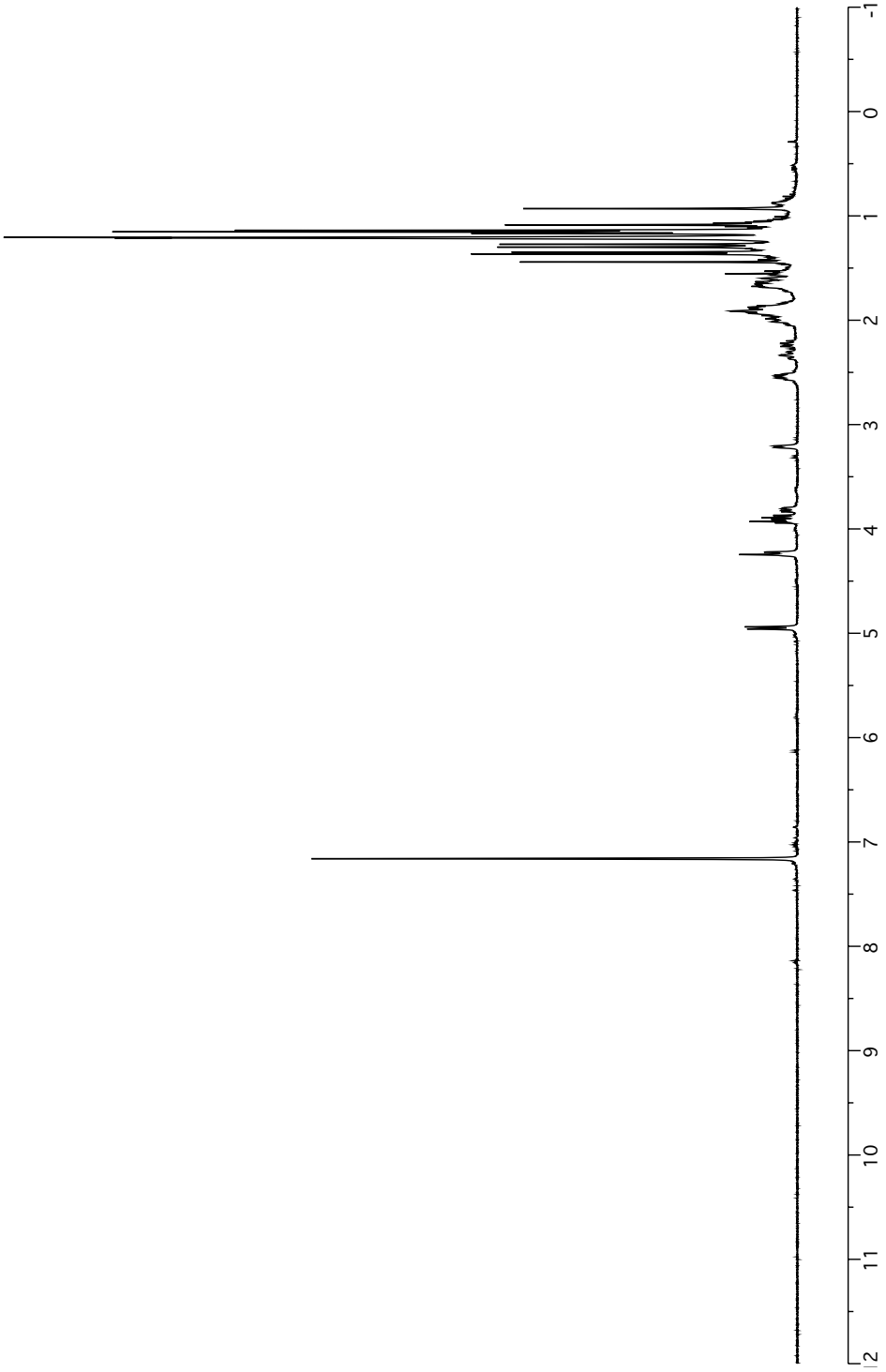

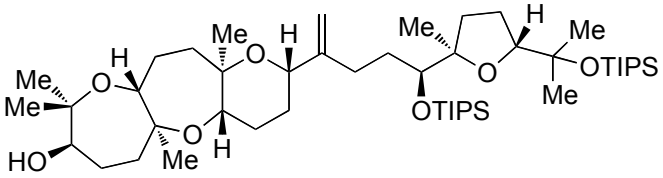
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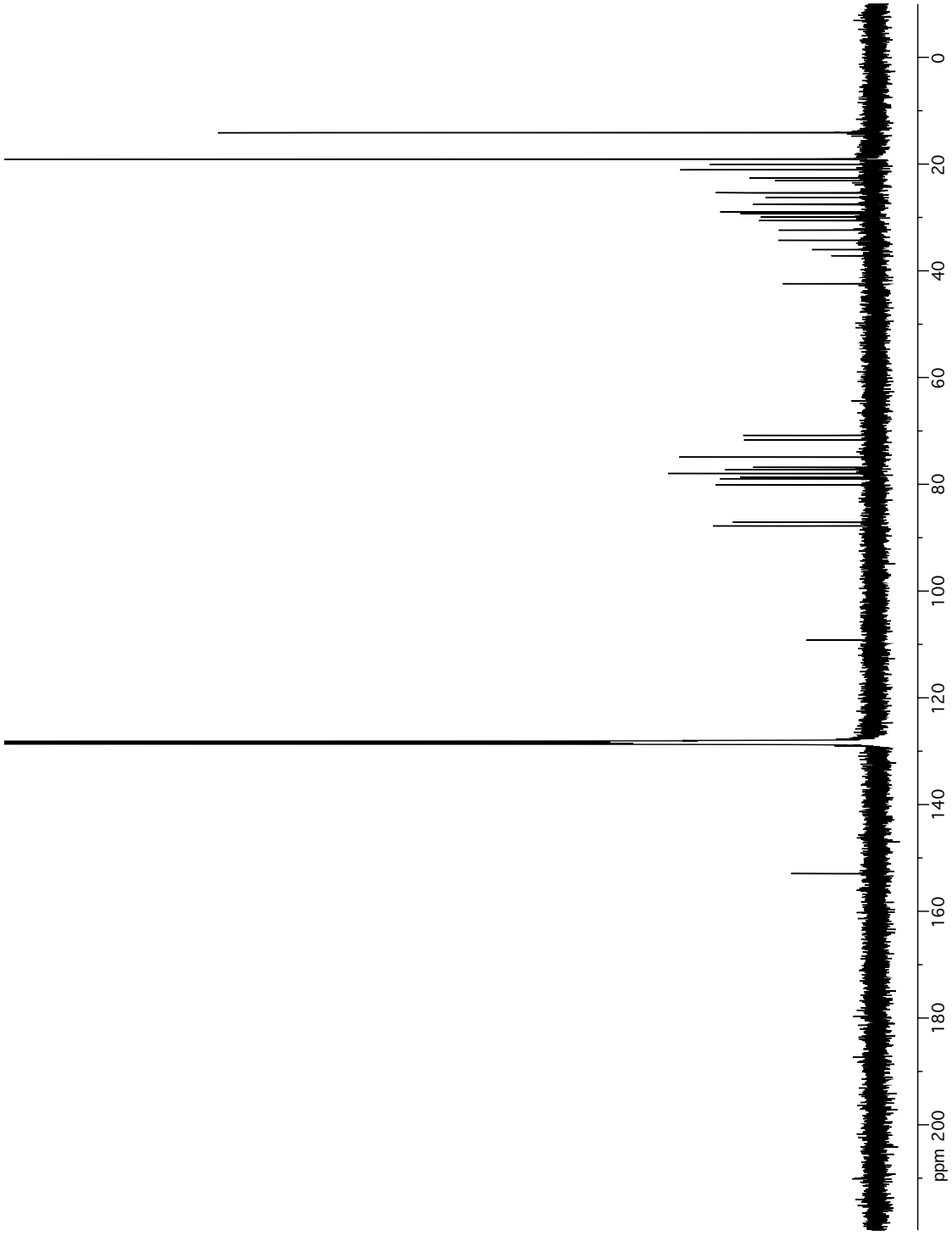
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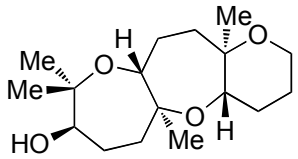

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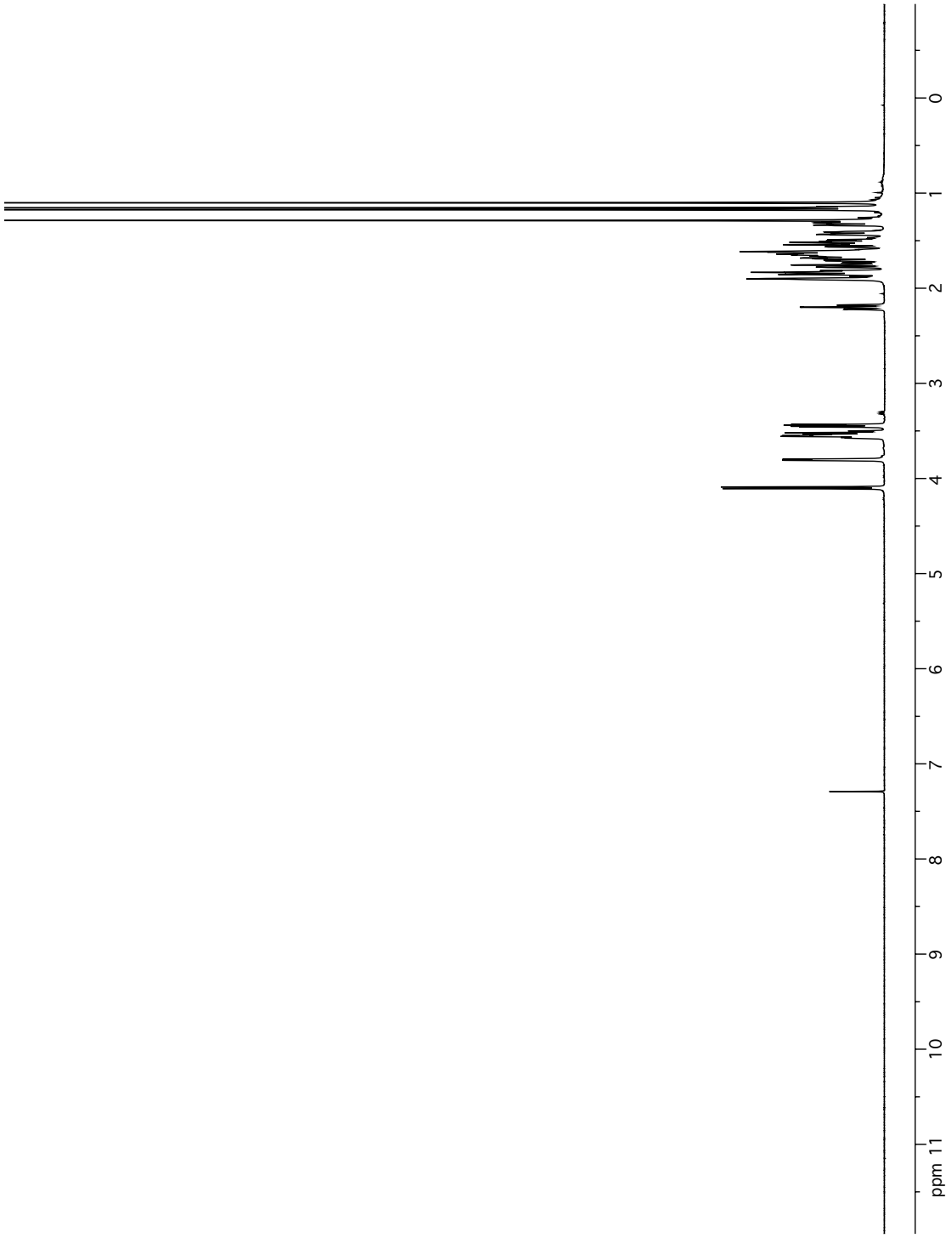

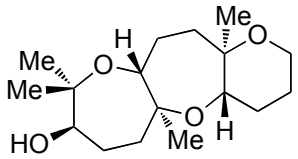

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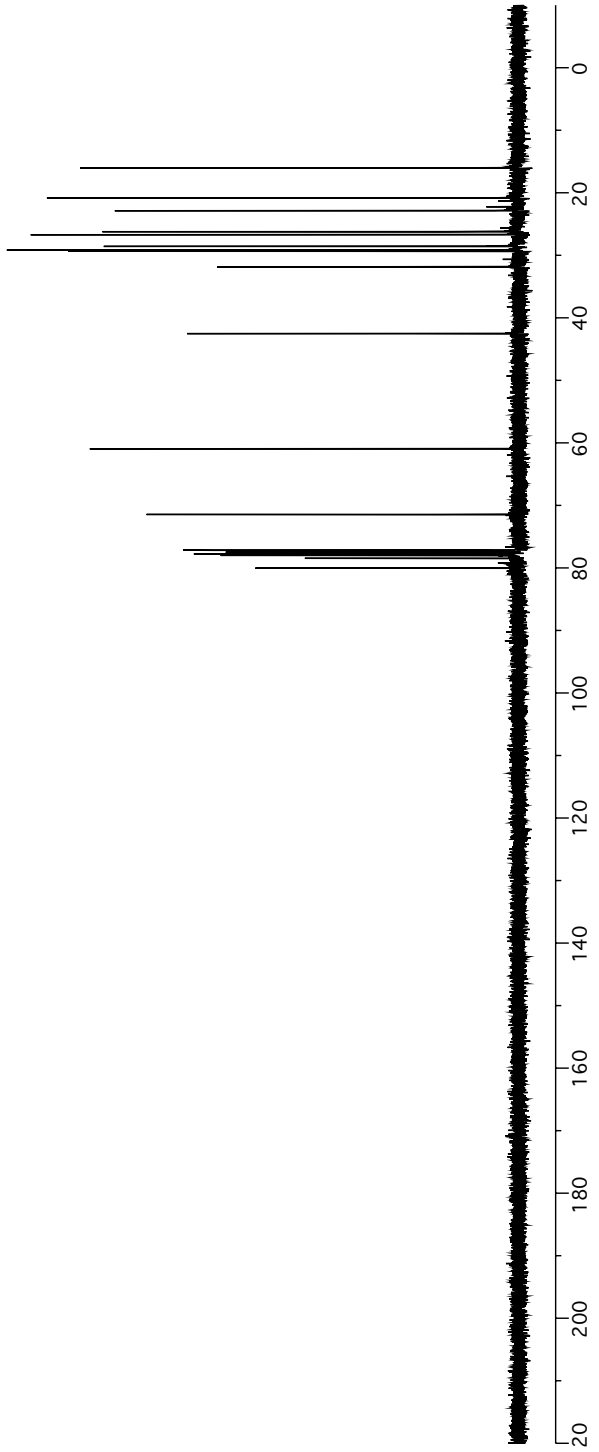

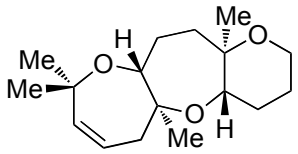

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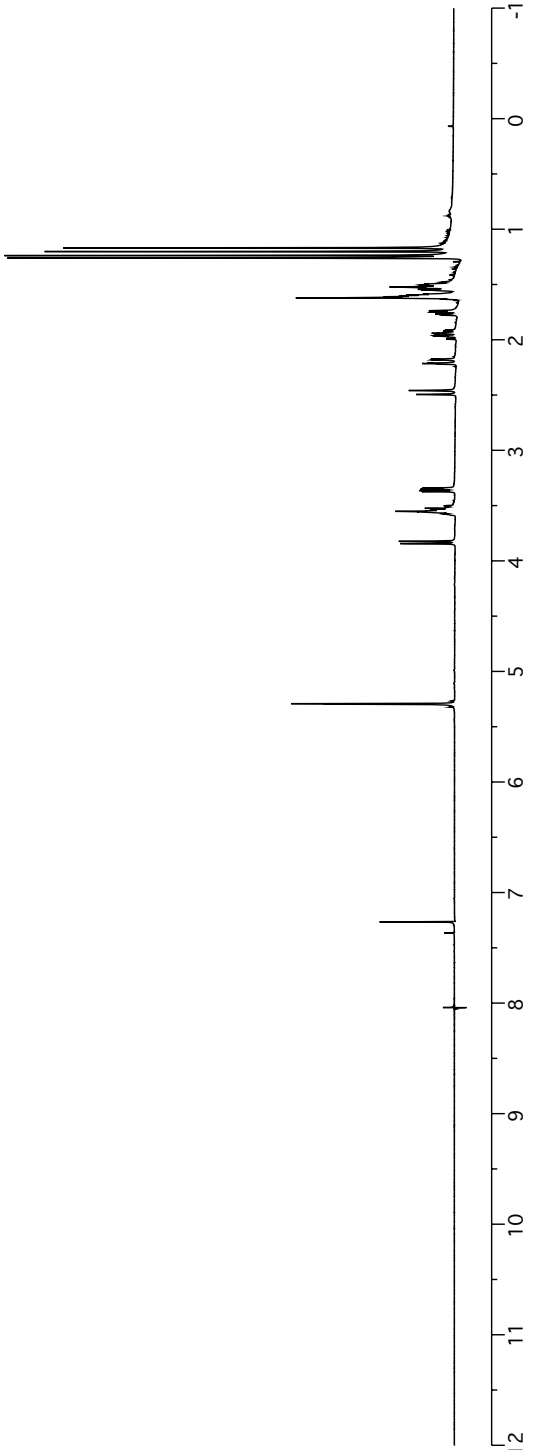

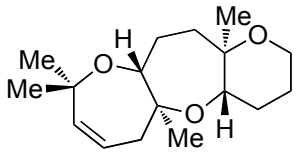

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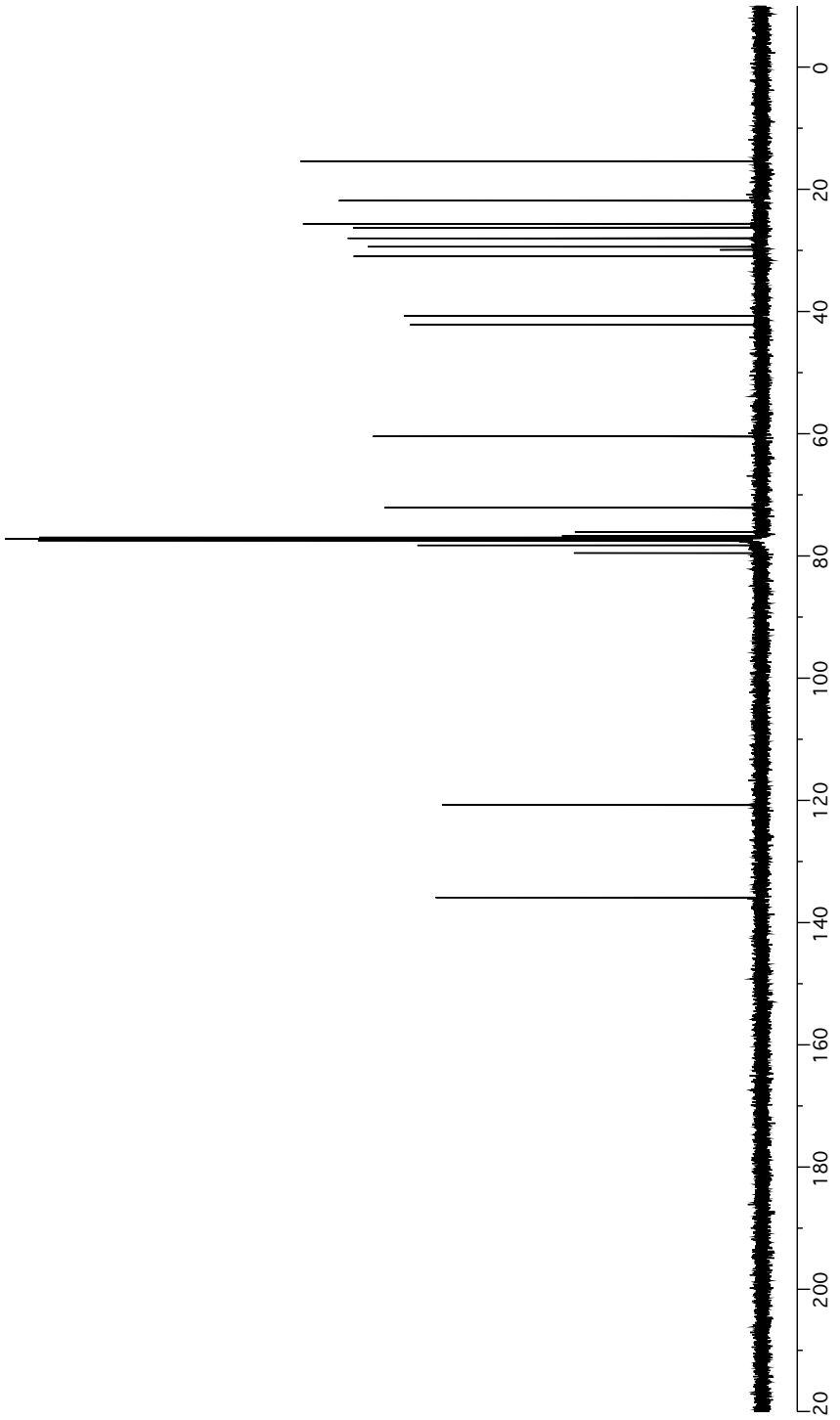

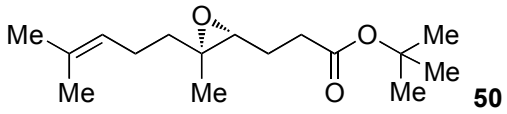

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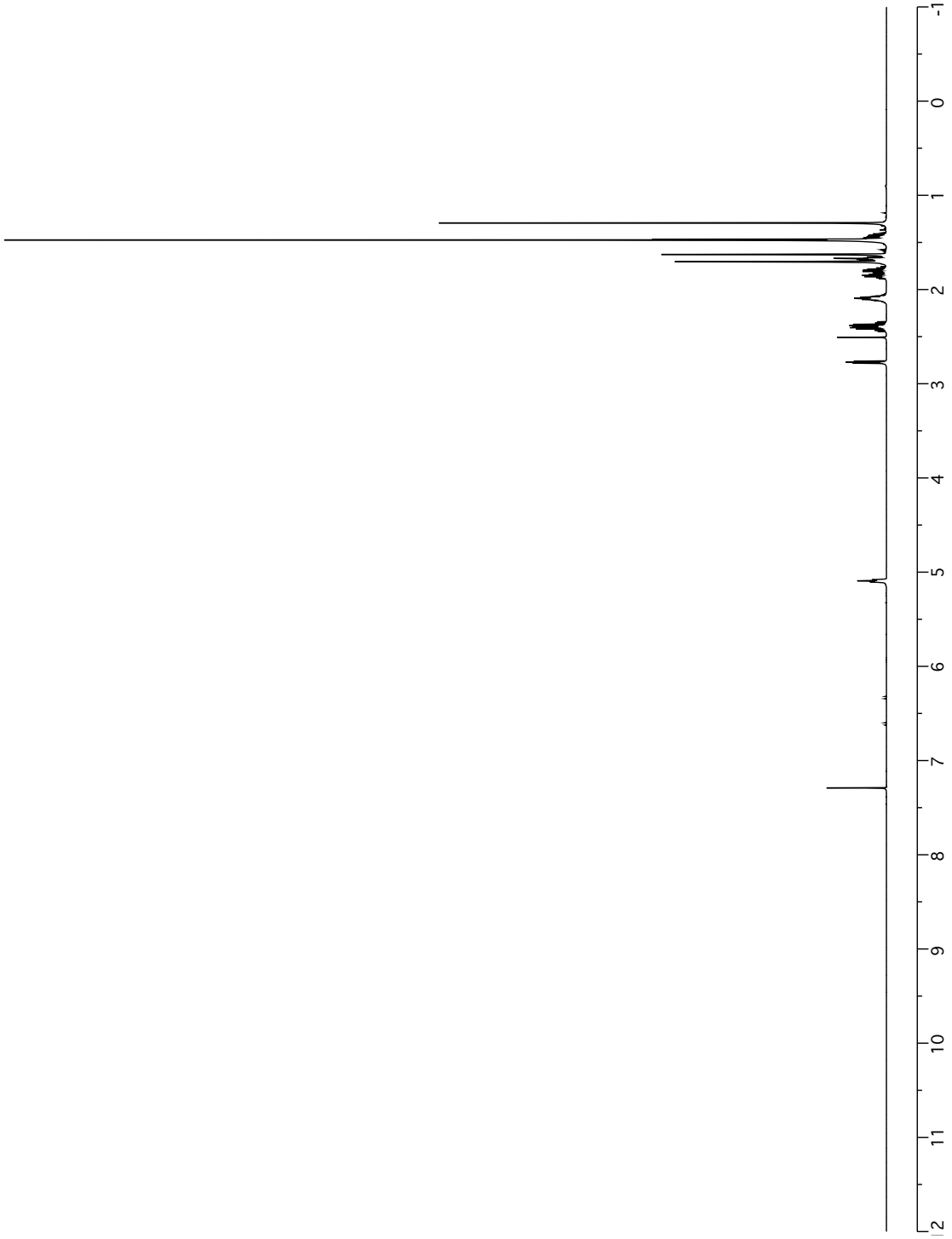

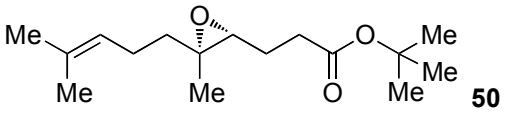

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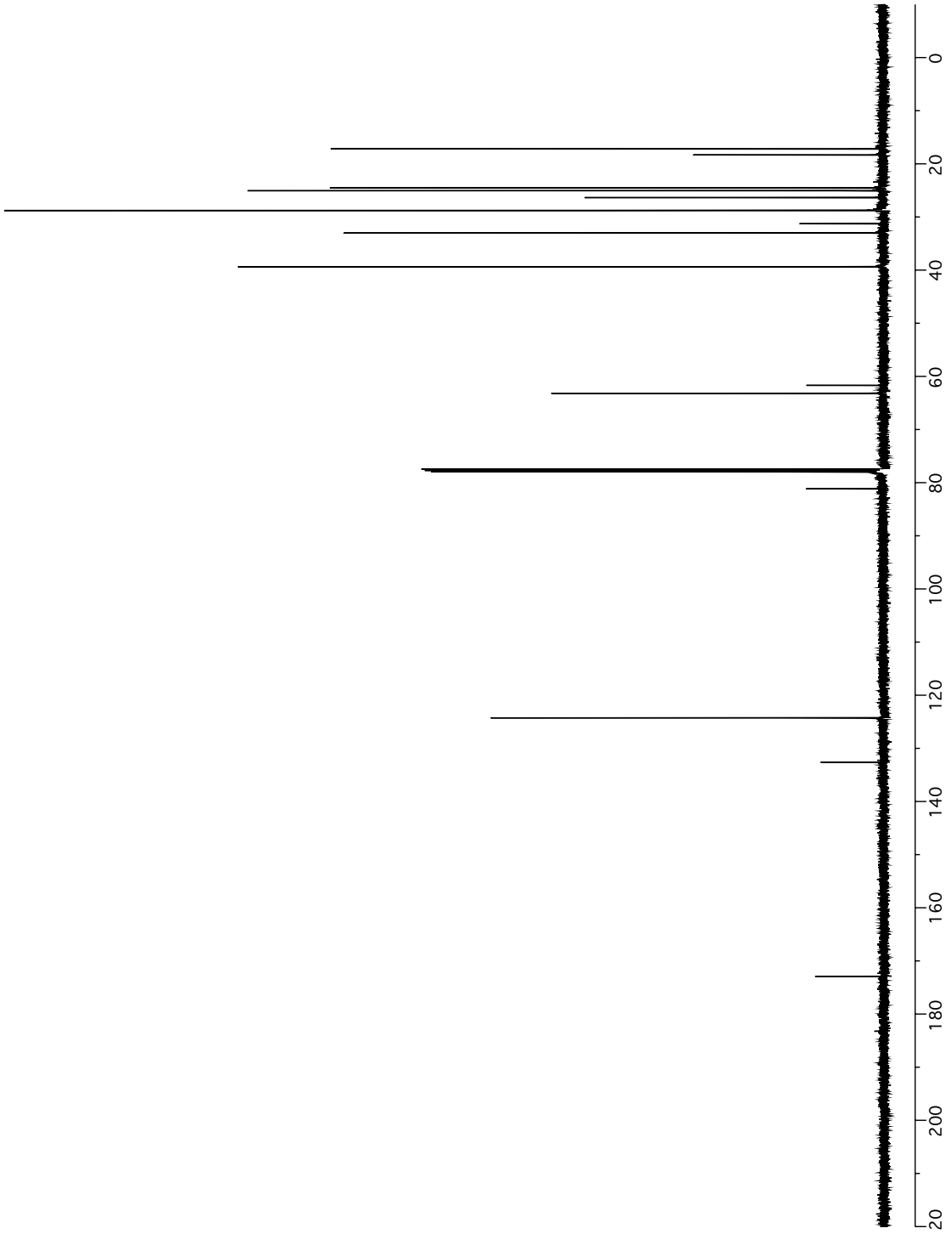

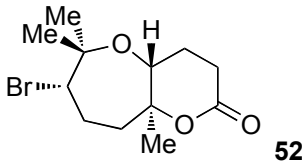

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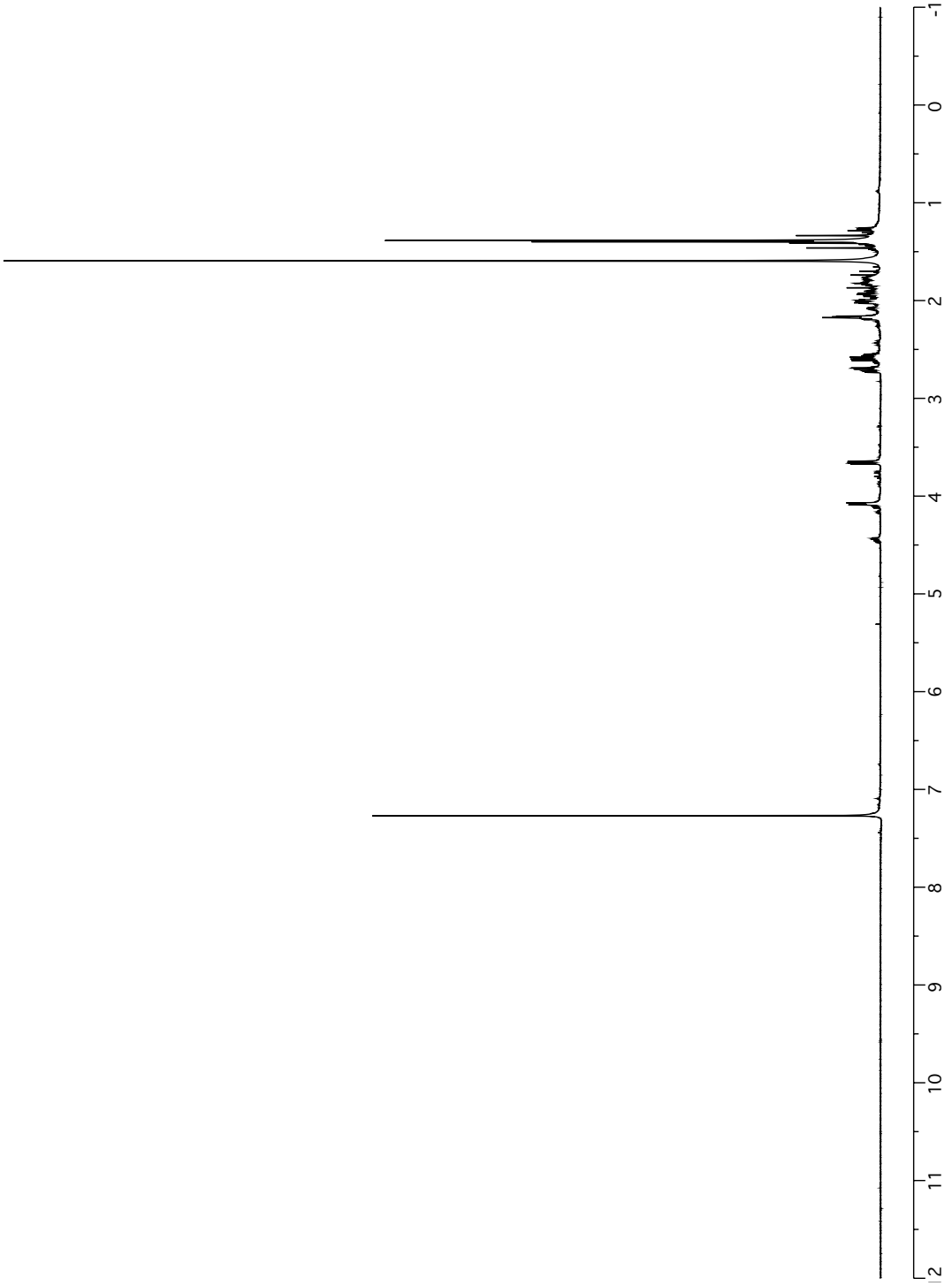

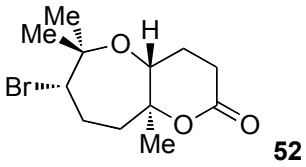

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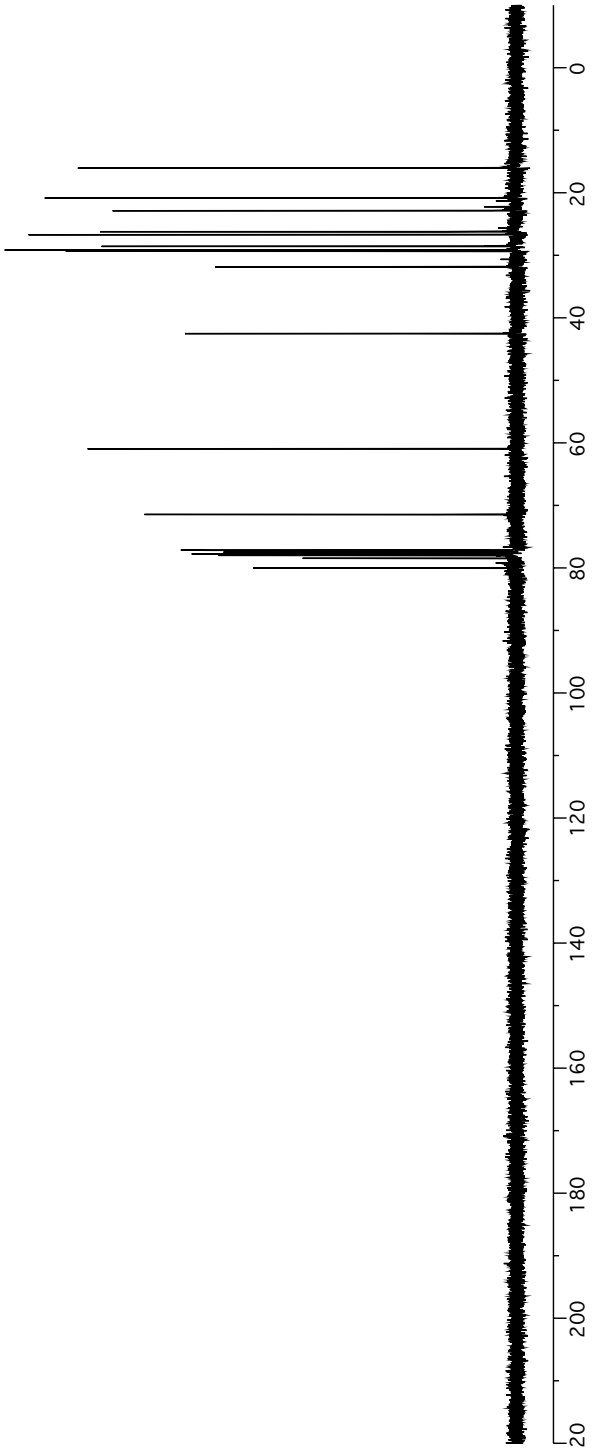

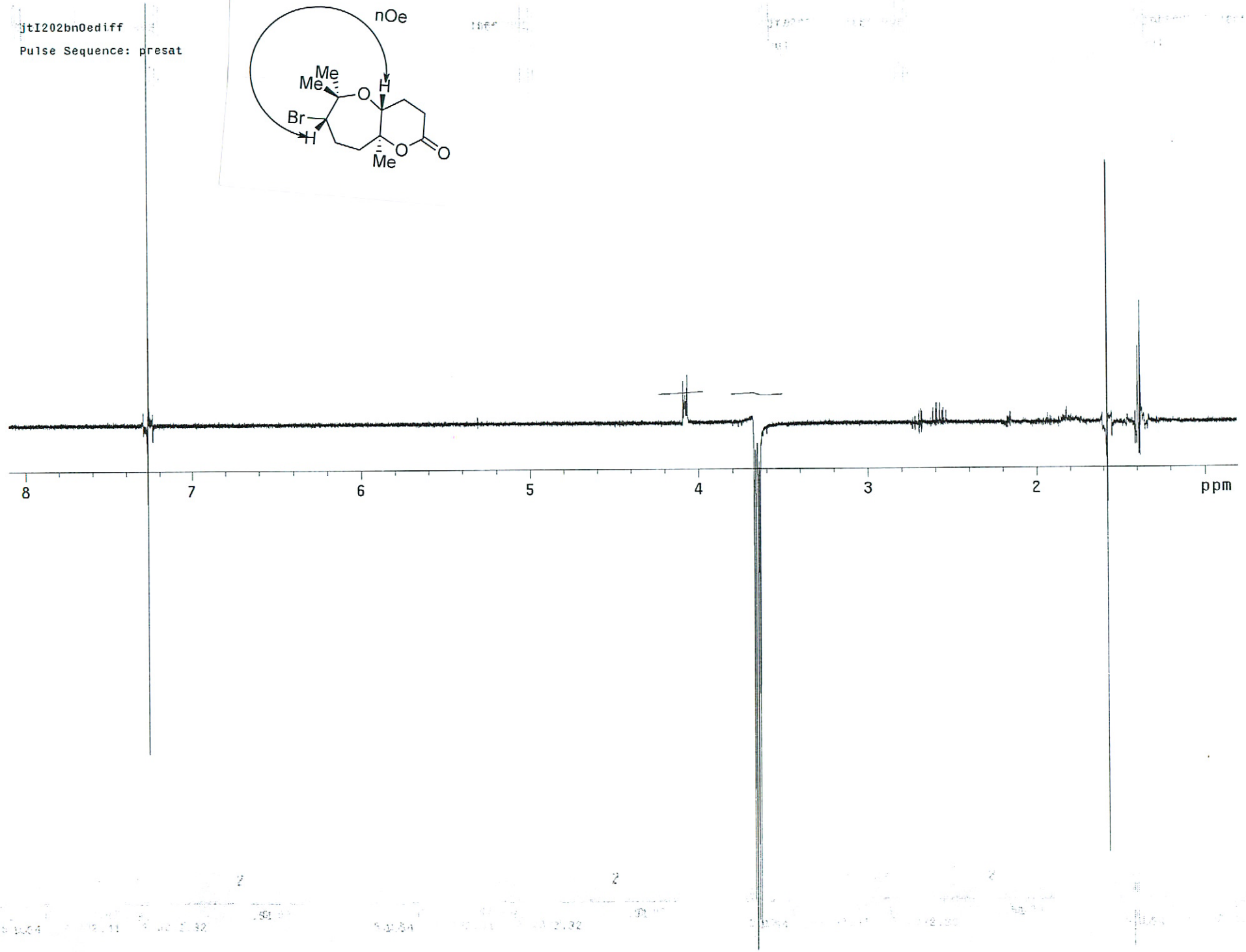
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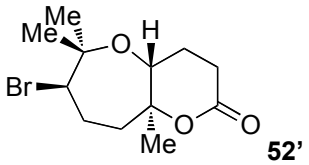

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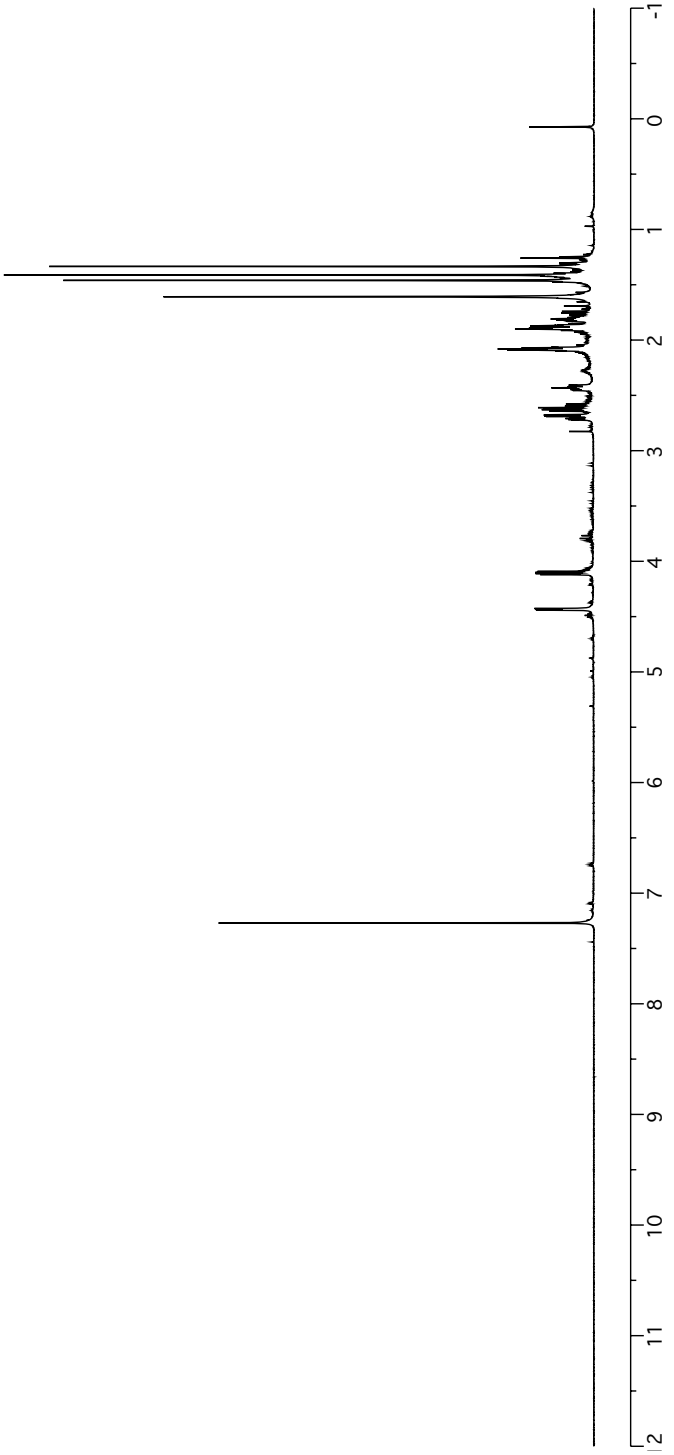

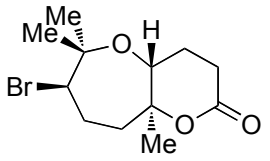

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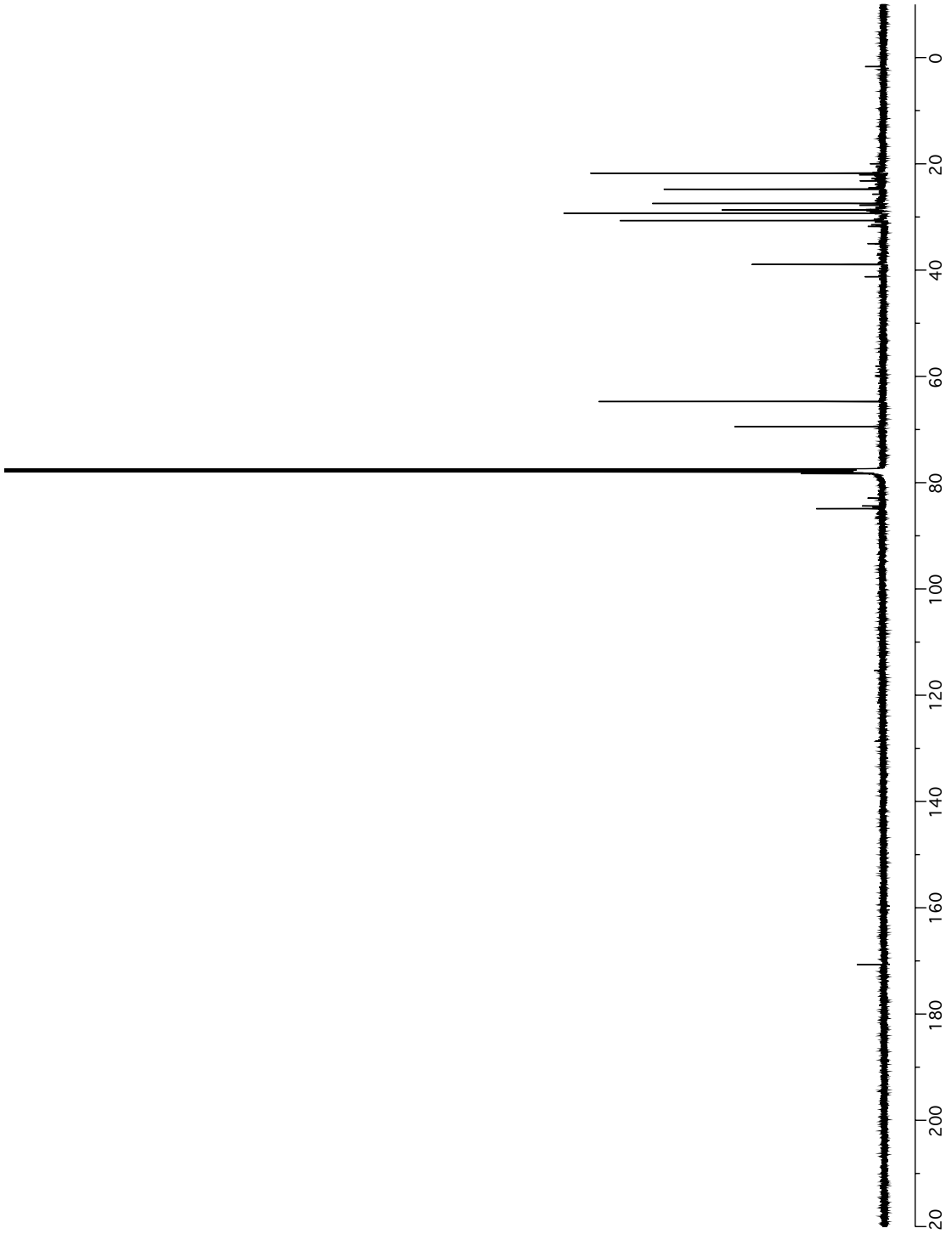

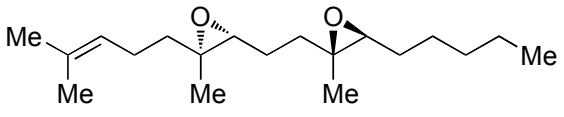

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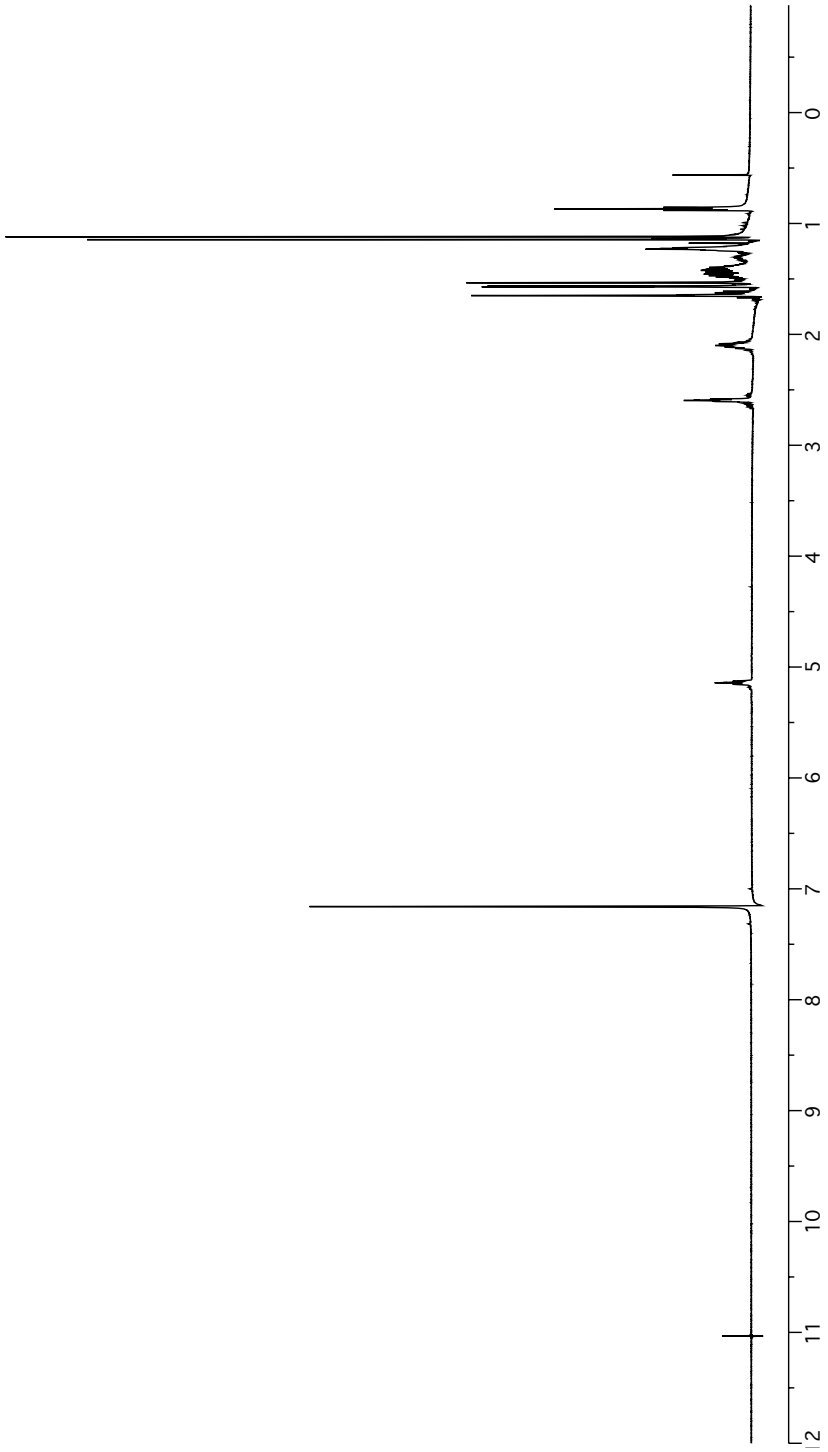

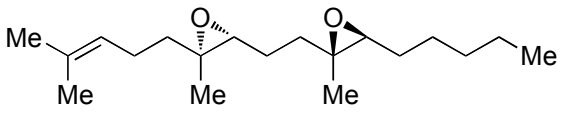

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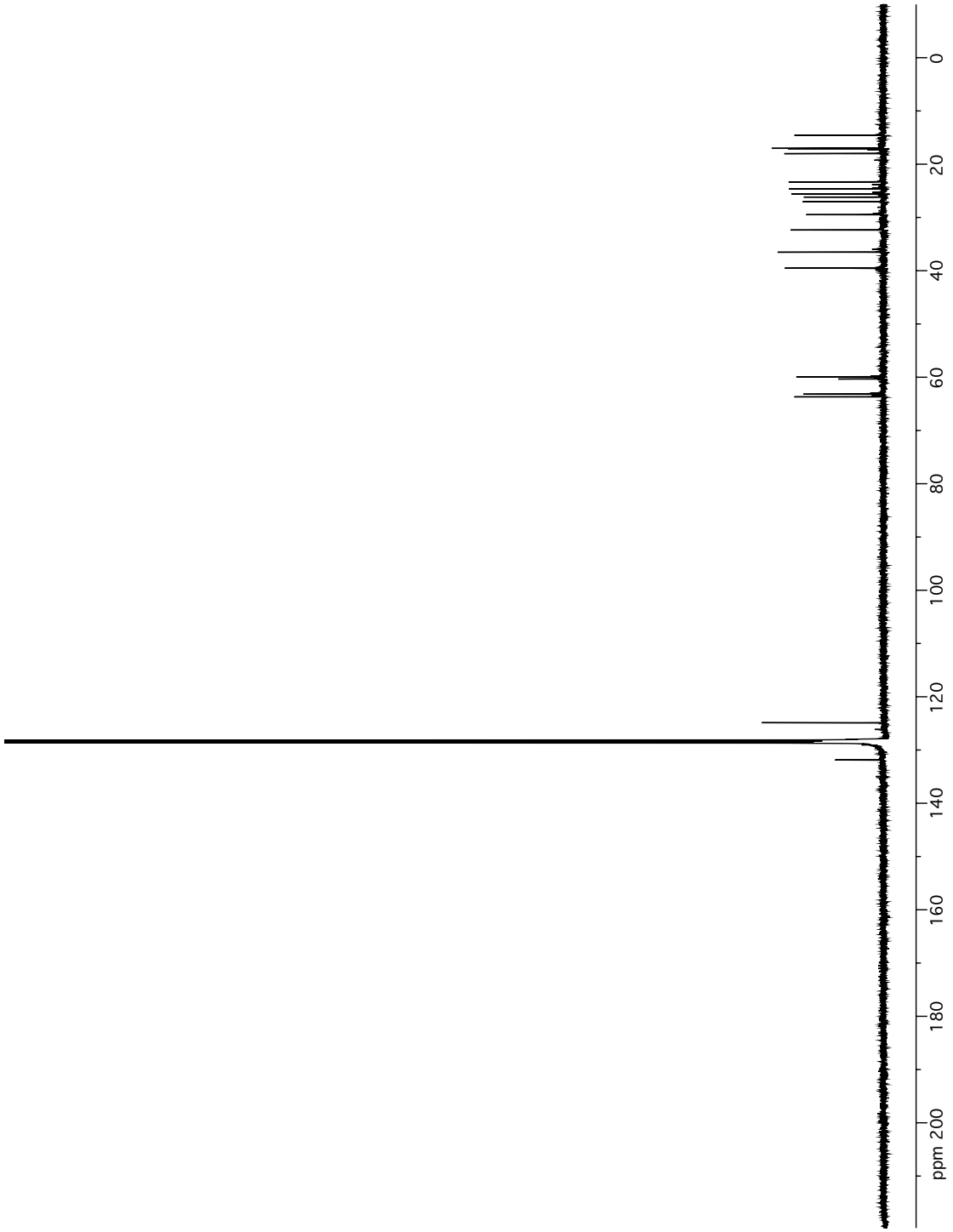

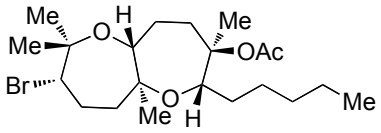

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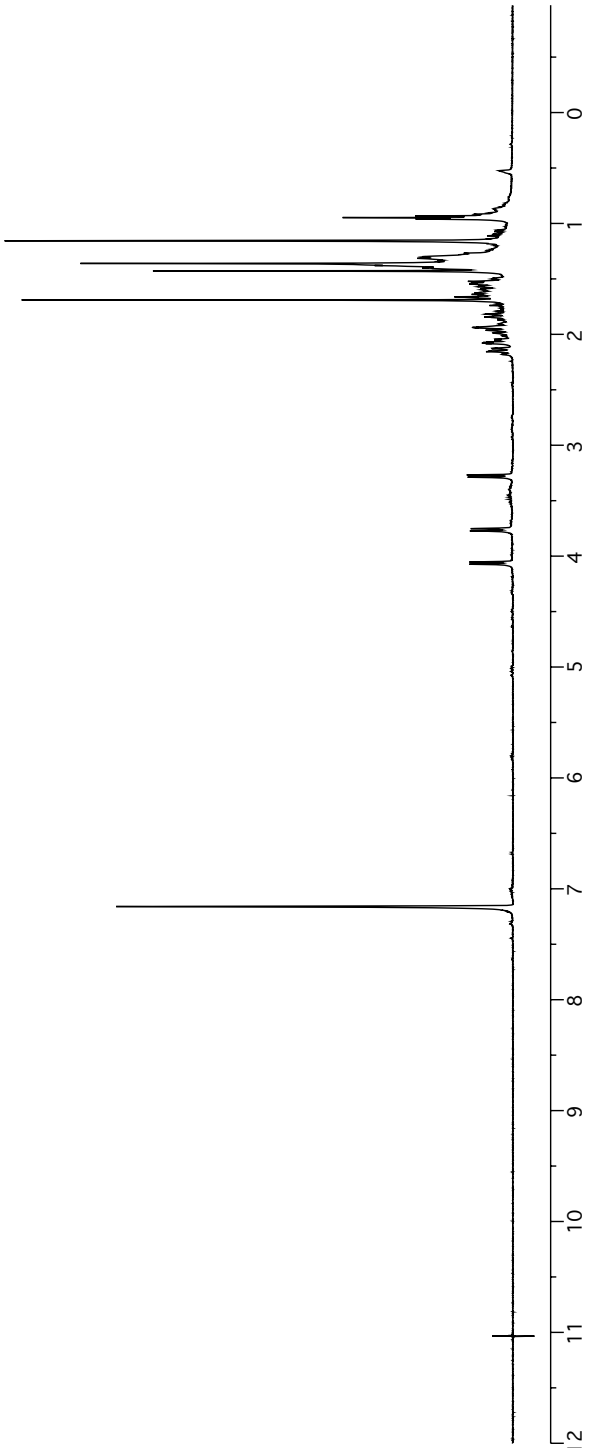

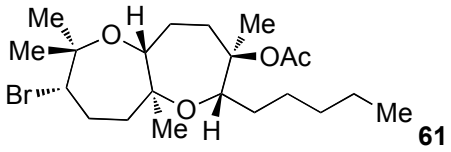

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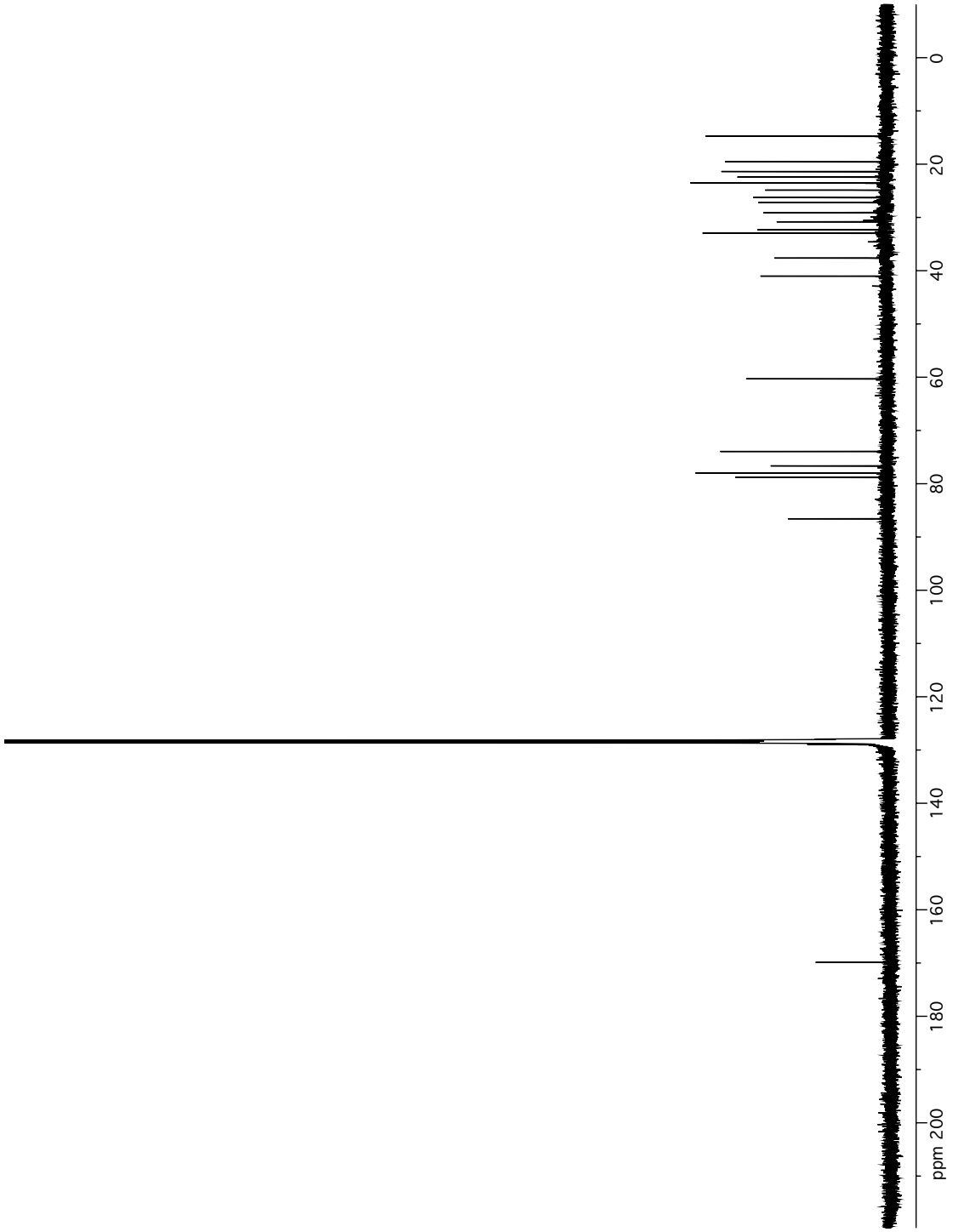

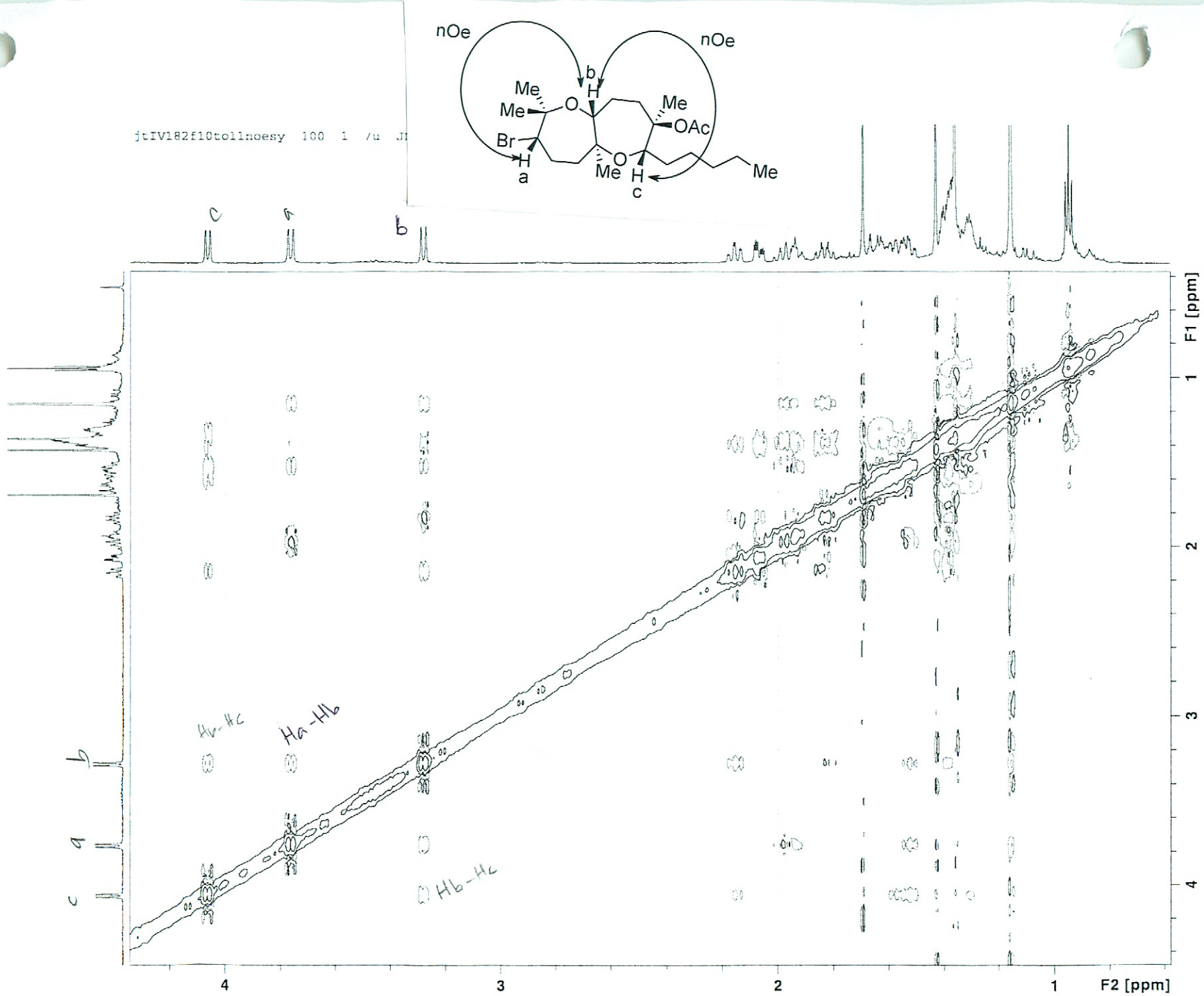
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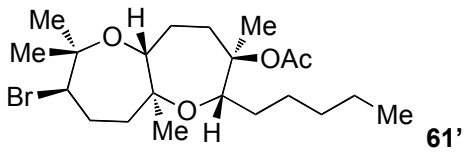

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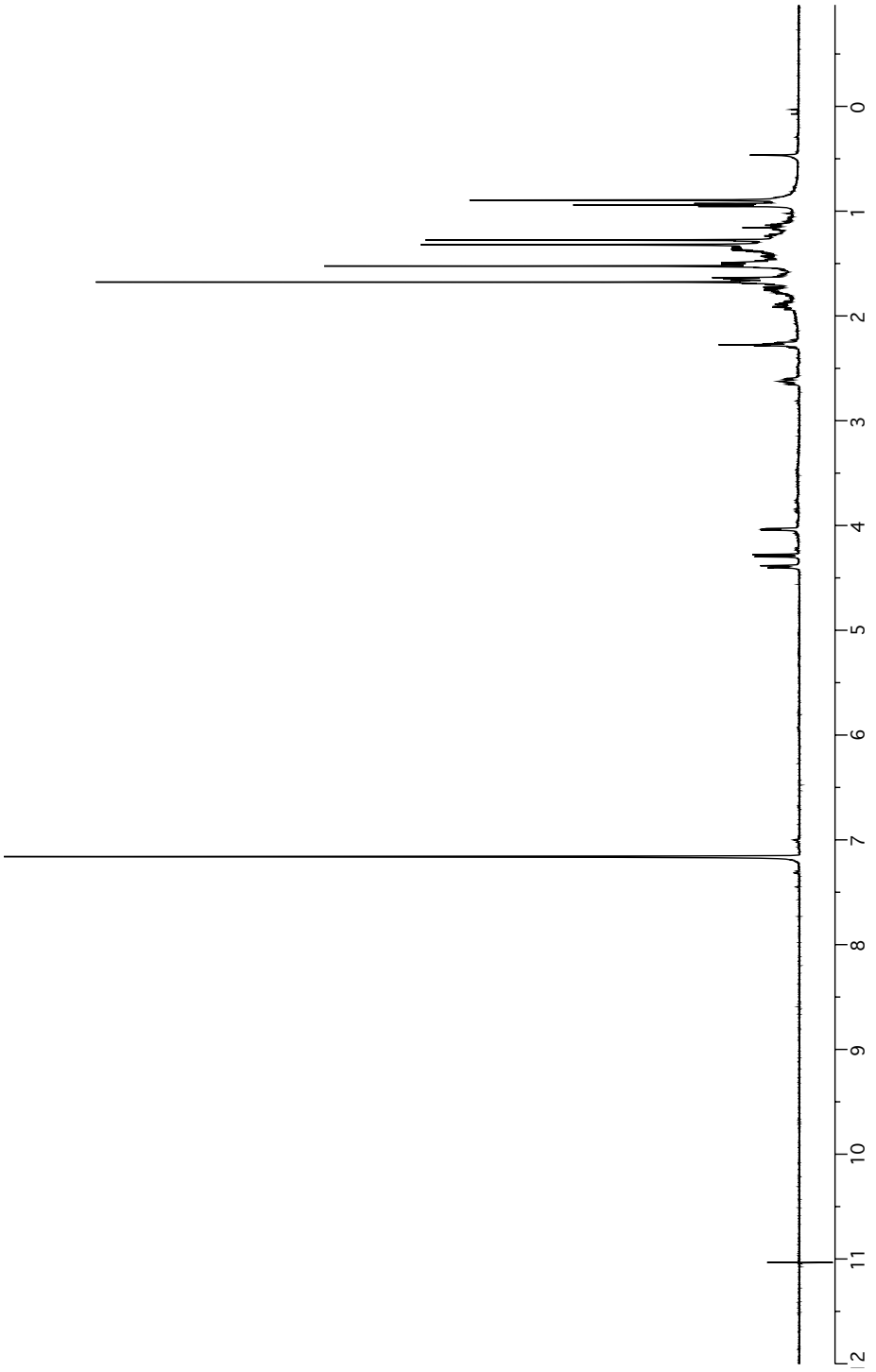

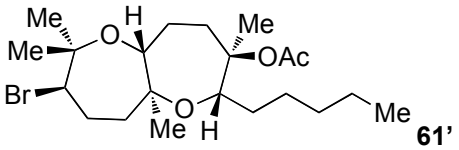

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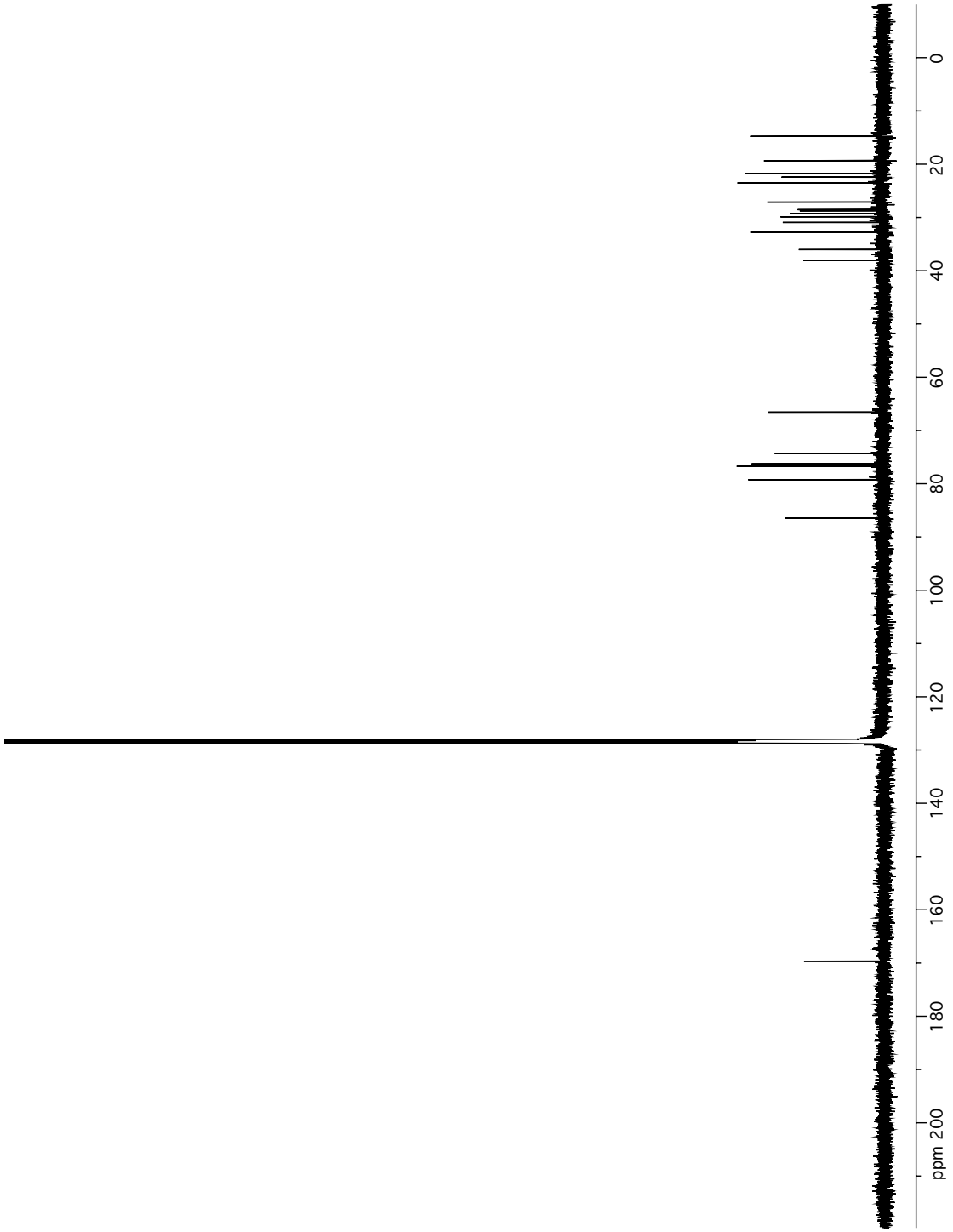

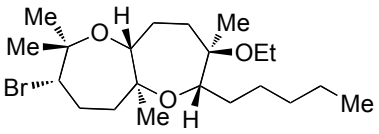

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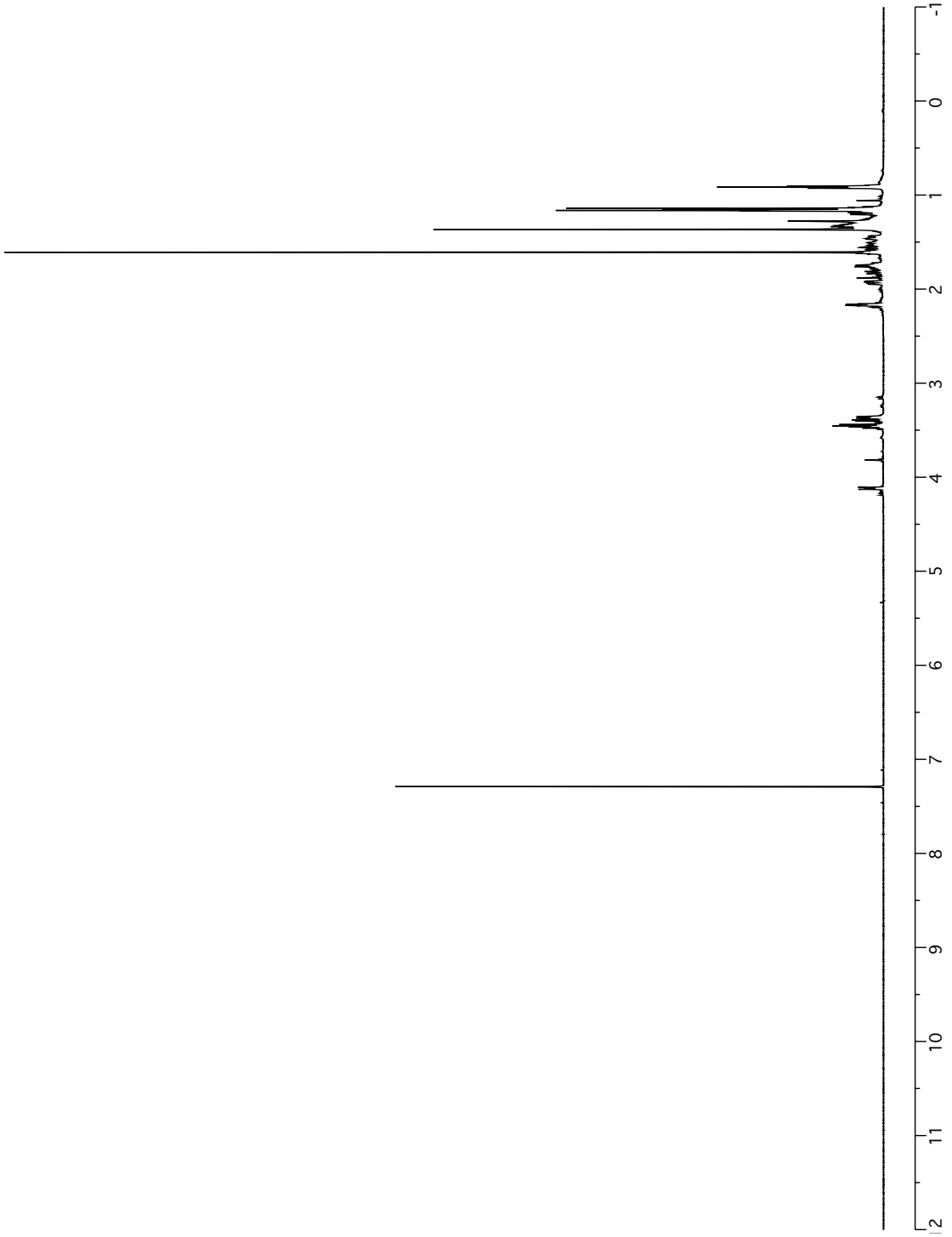

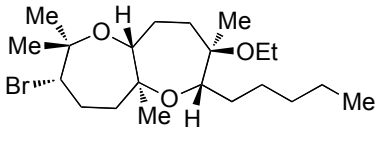

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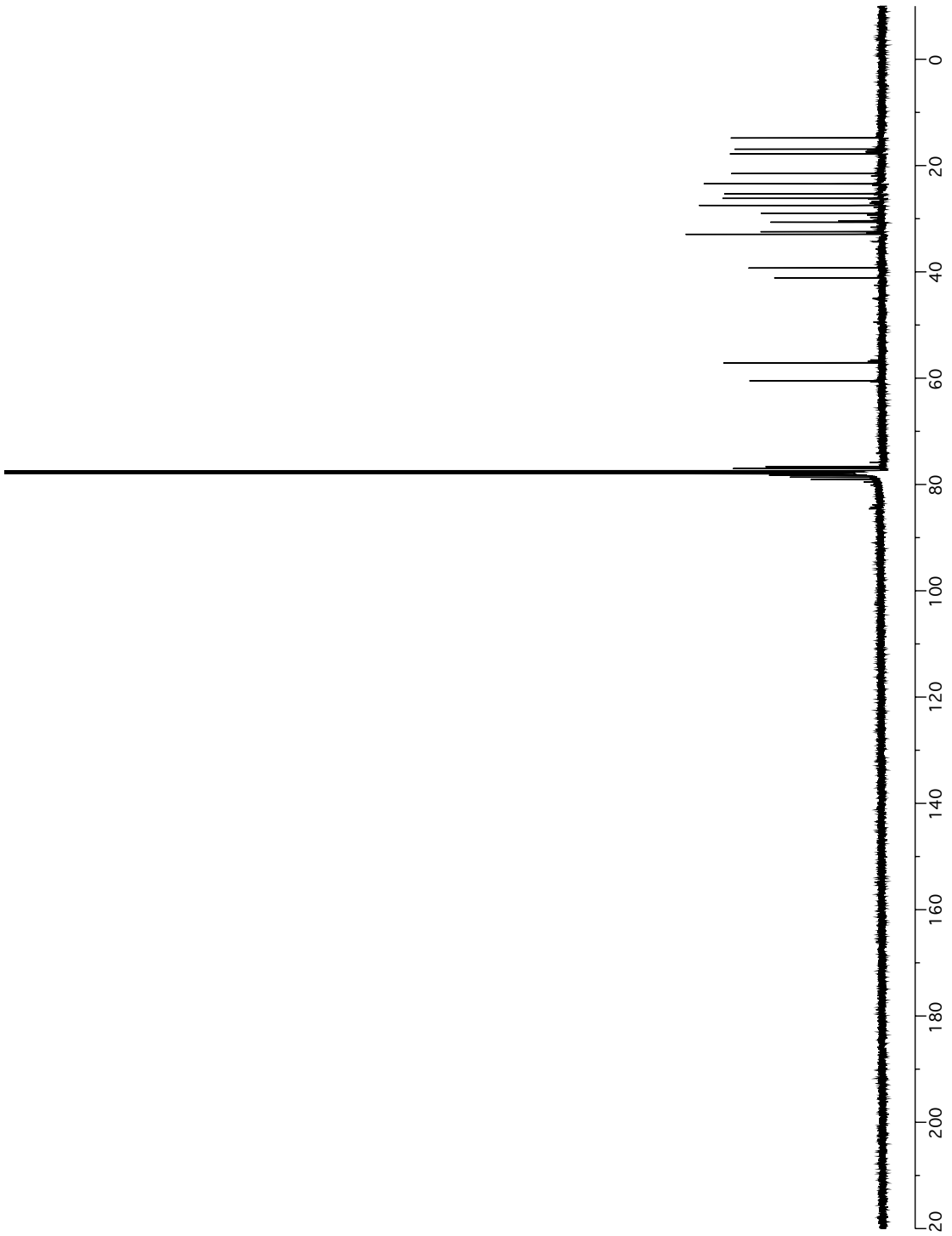

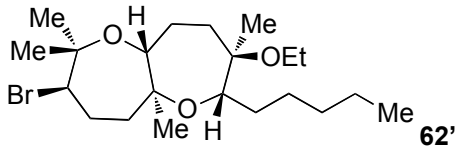

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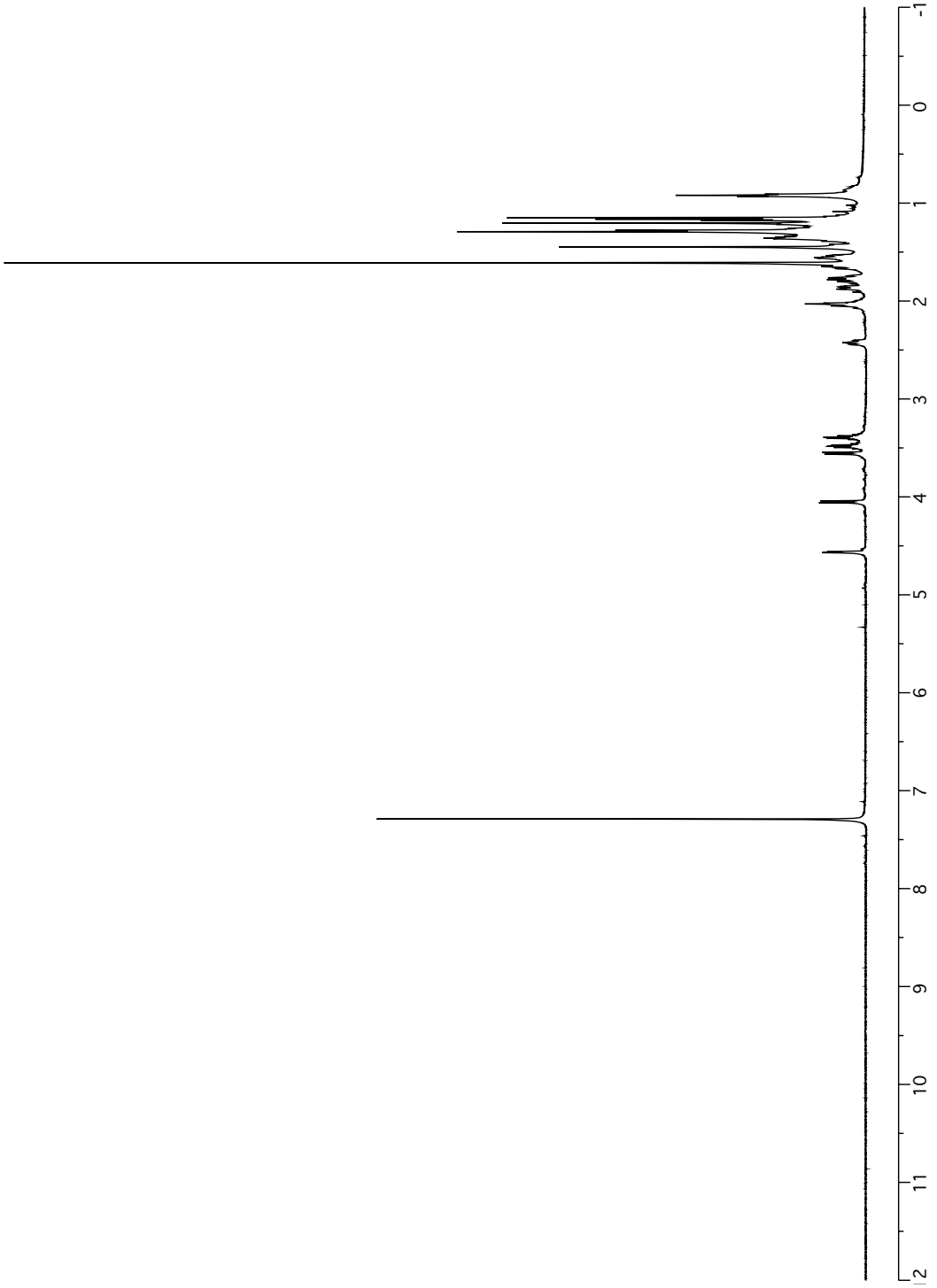

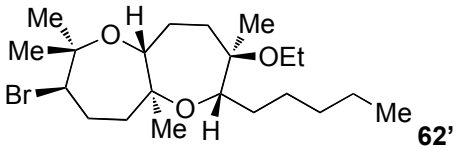

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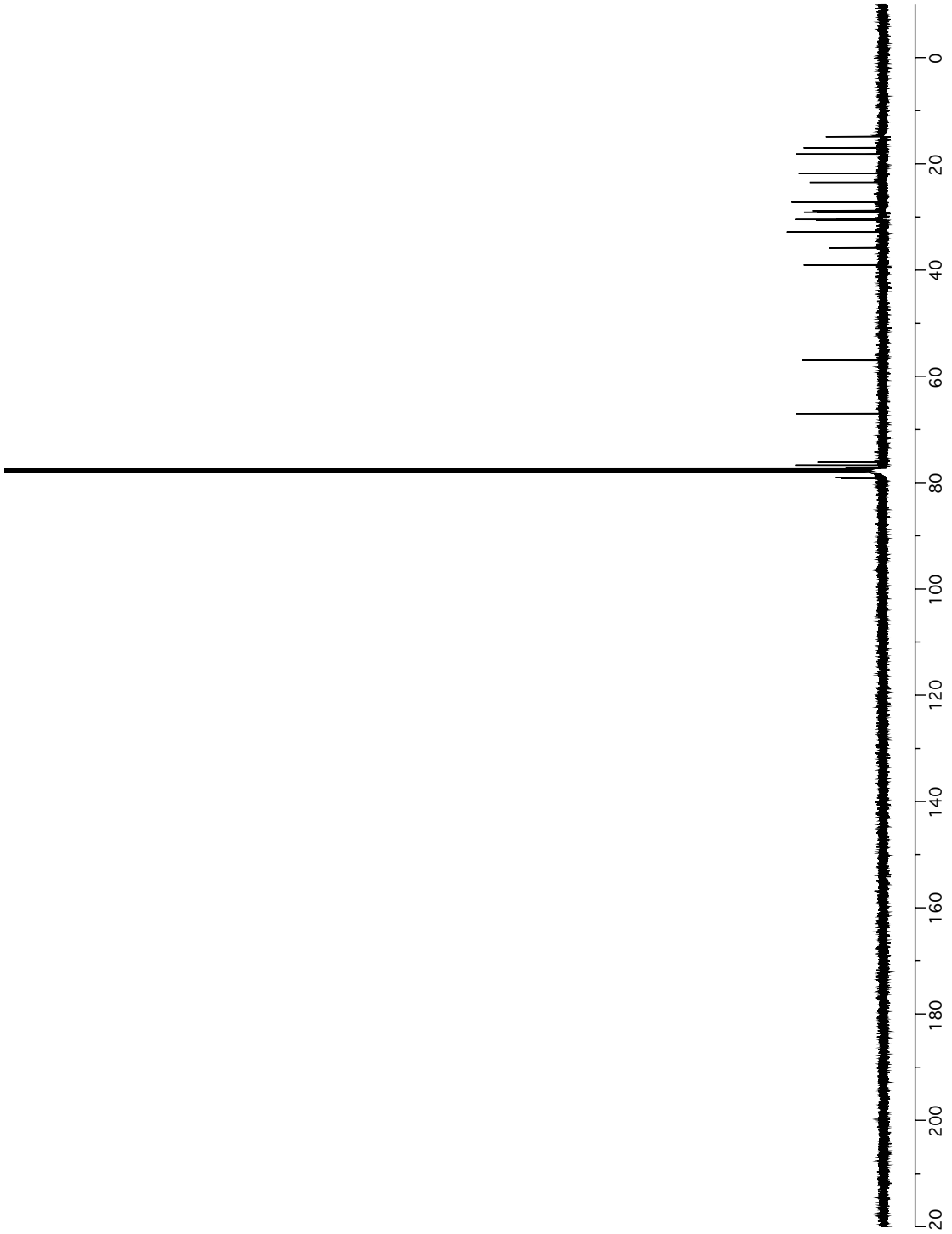
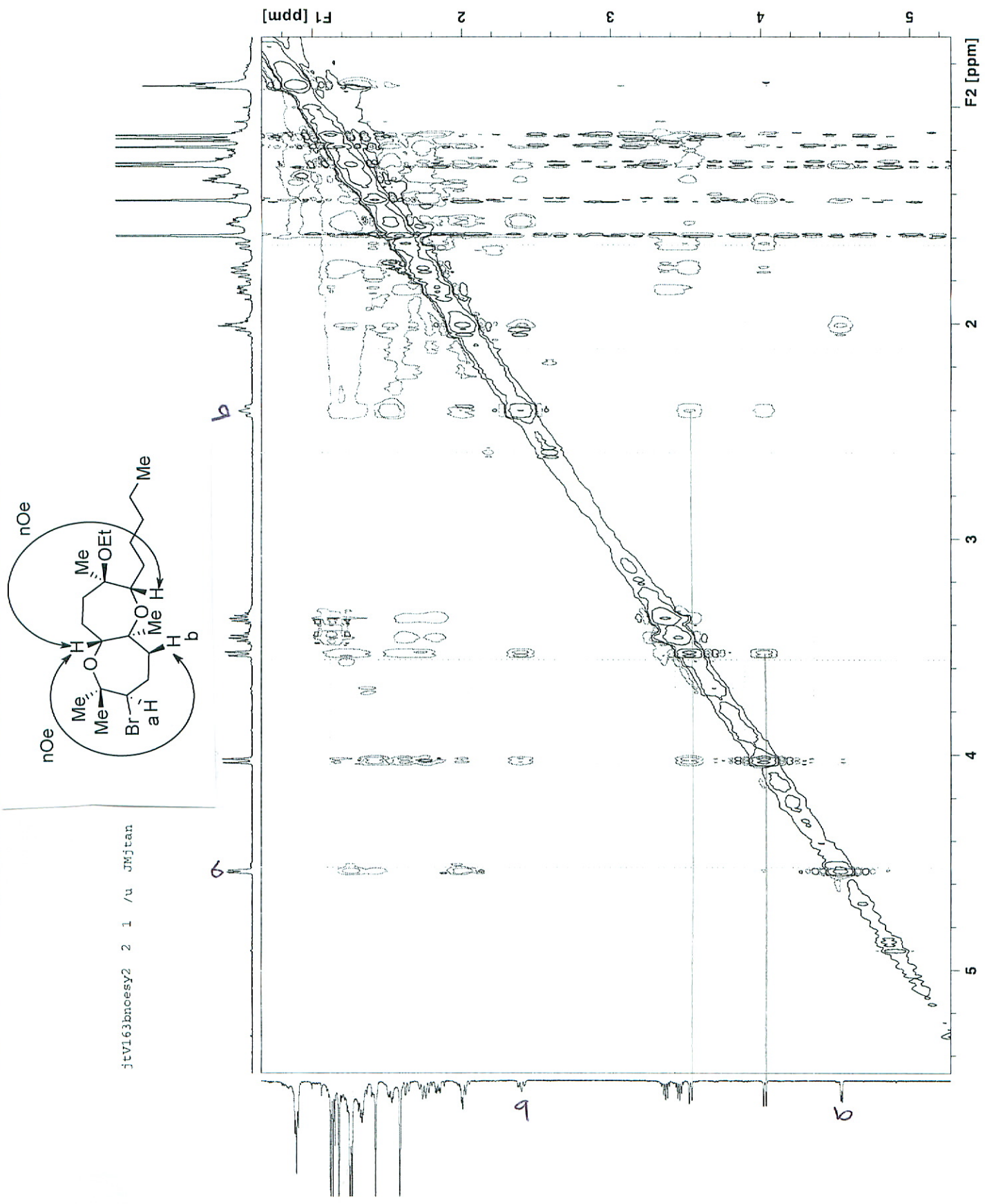
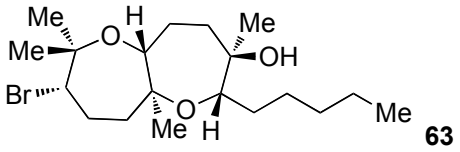



F1 [ppm]
F2 [ppm]
nOe
nOe
Me
OEt
Me
H
O
Me
H
H
b
O
Me
Me
Br
a H
jtV163bnoesy2 2 1 /u JMjtan



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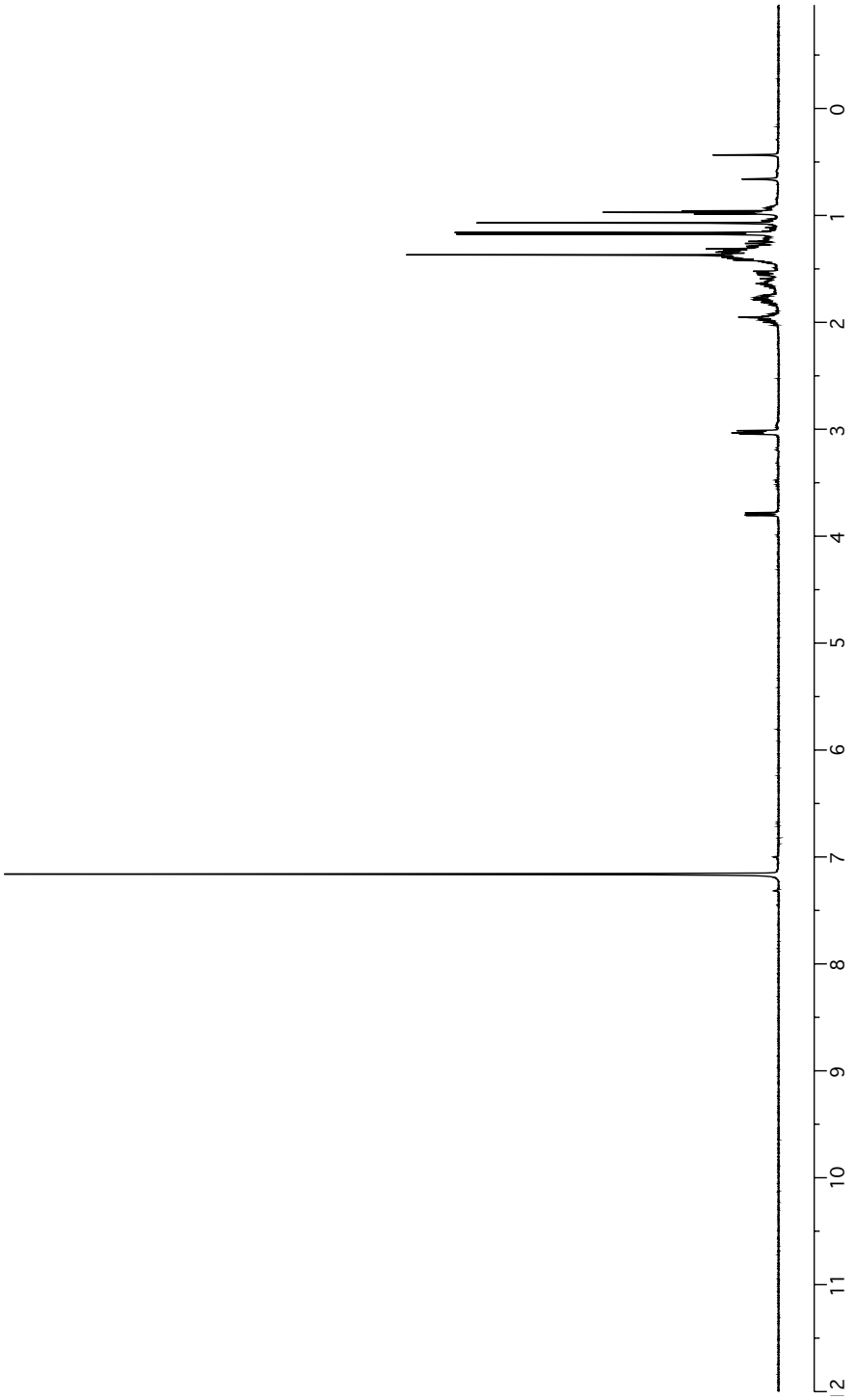

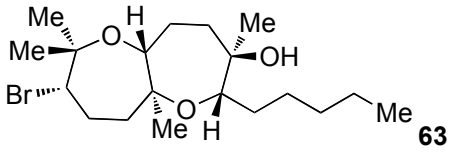

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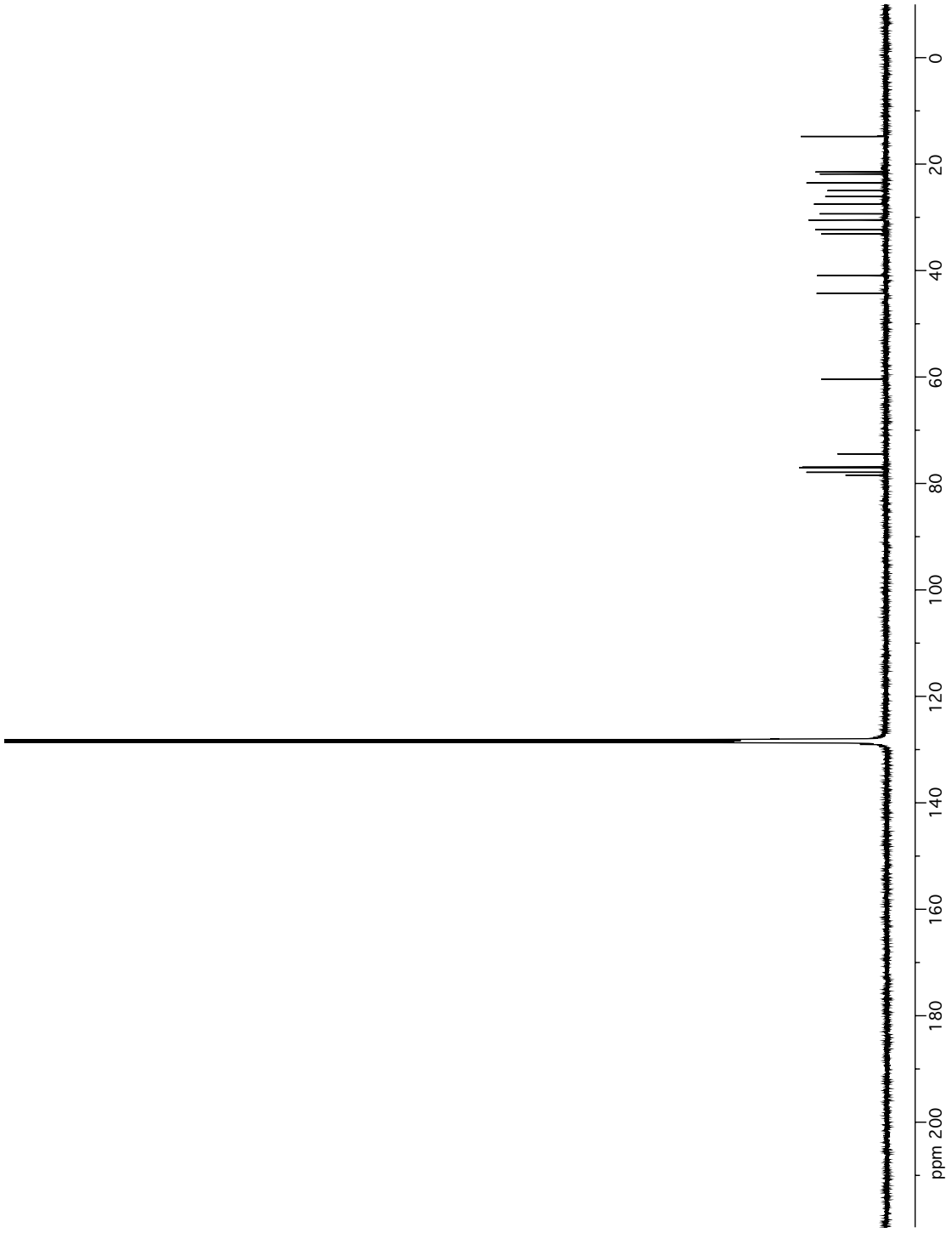

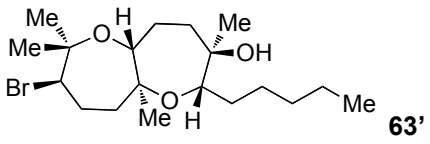

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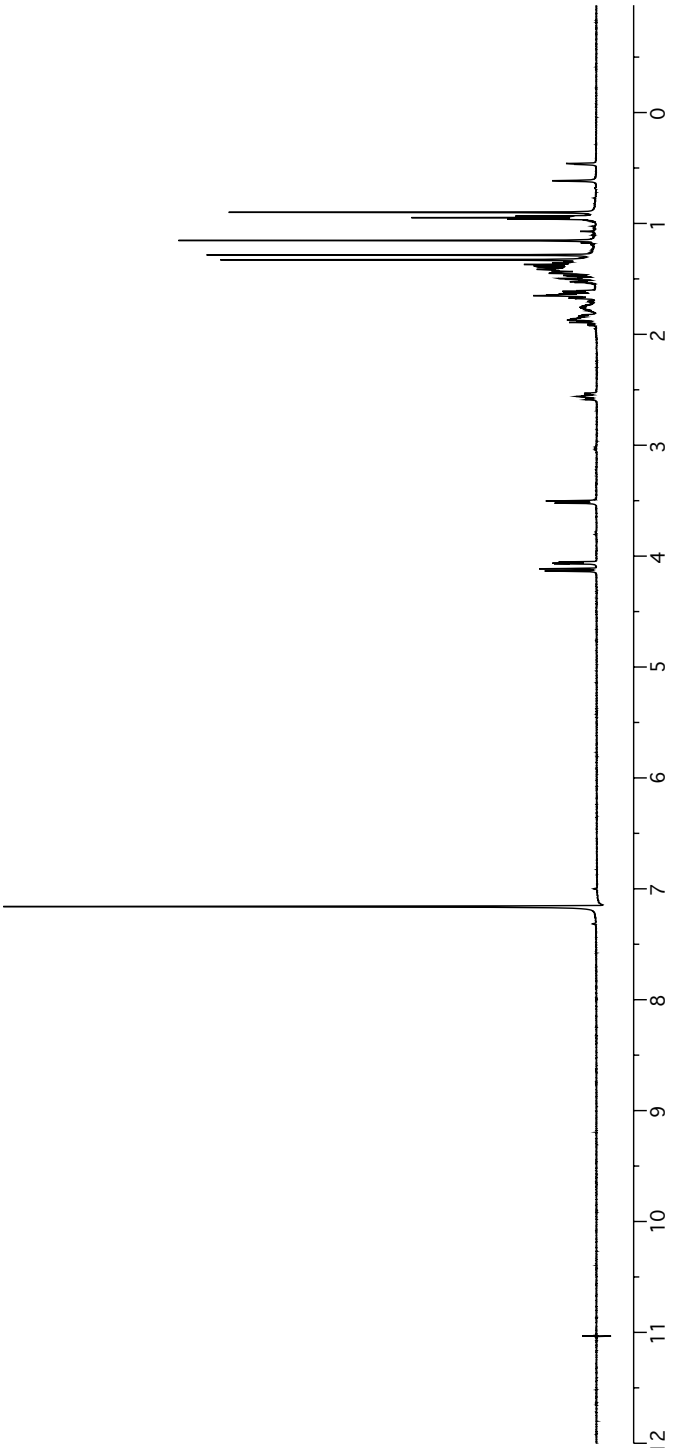

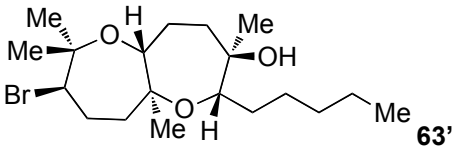

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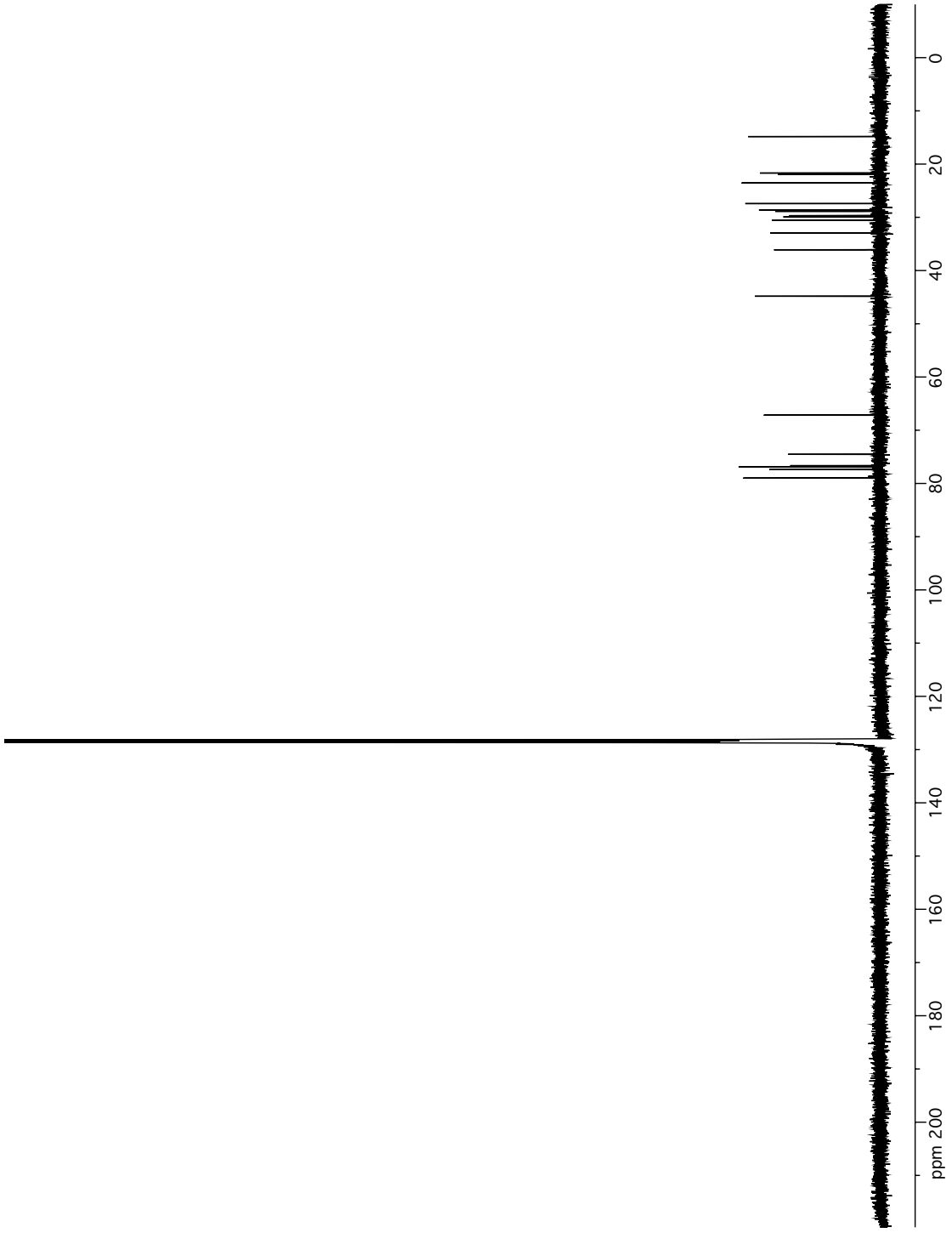

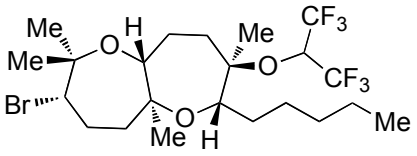

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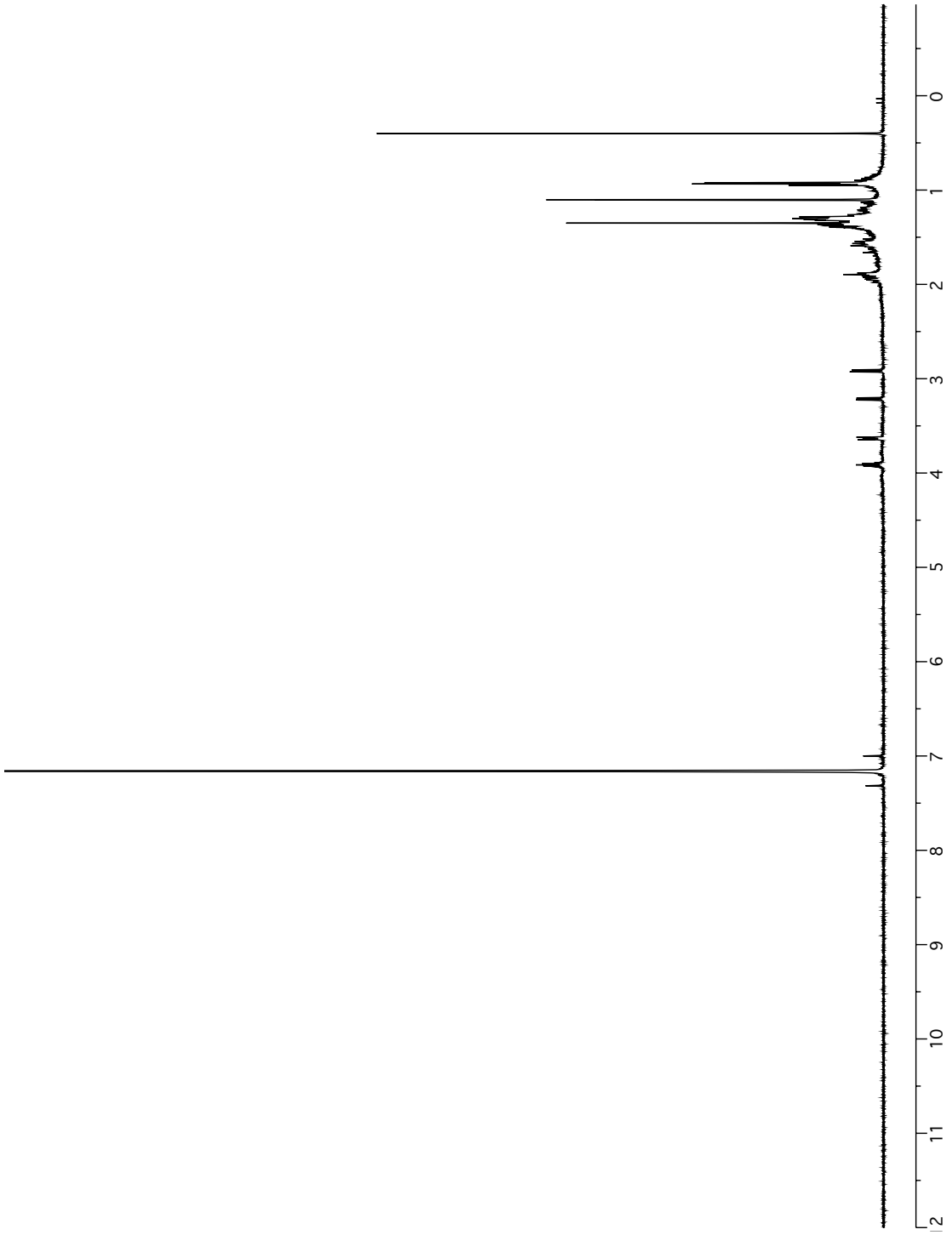
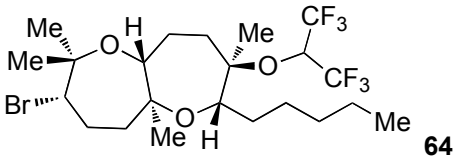
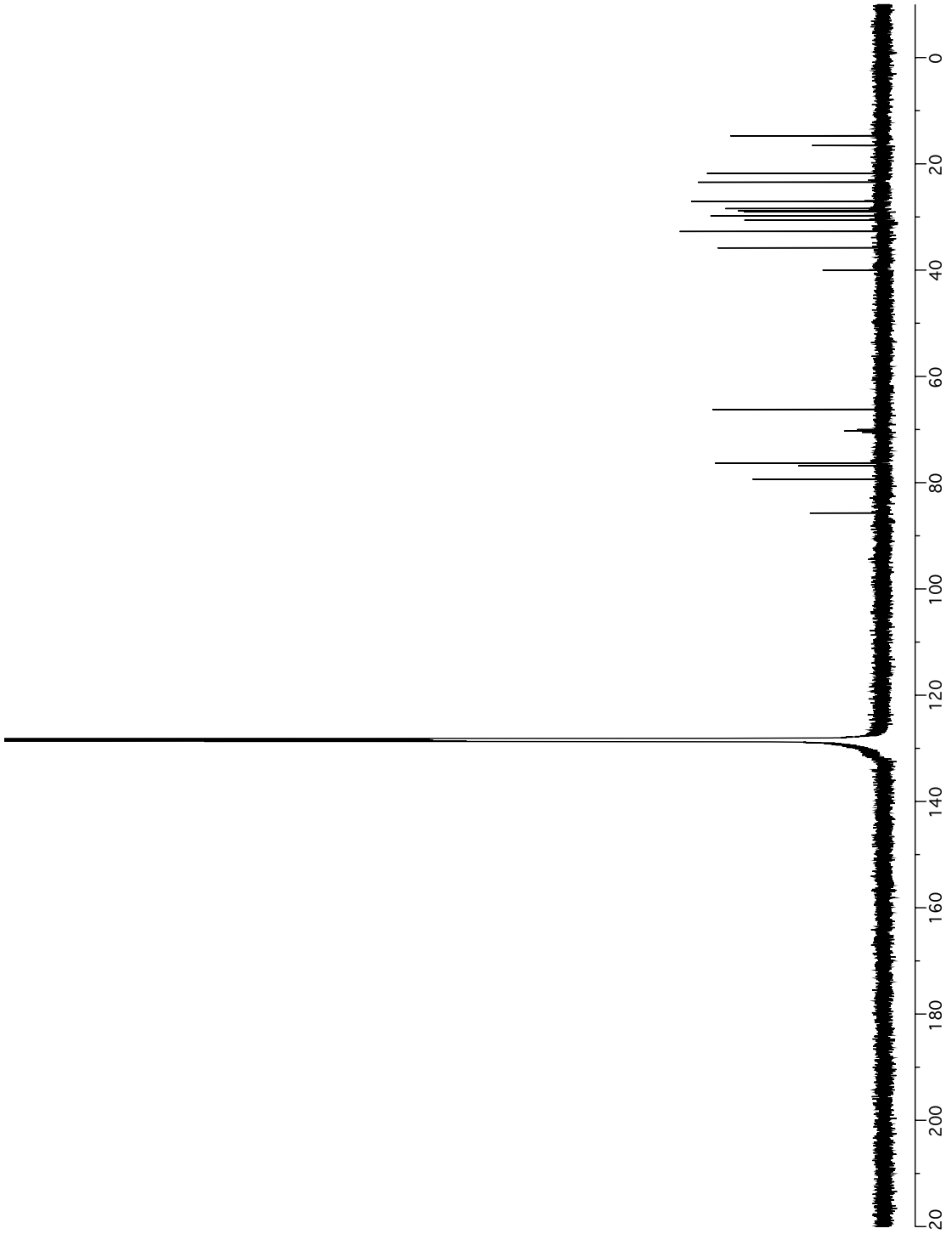
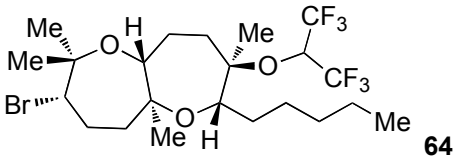



Me
Me
Br
O
H
Me
O
Me
H
O
CF3
CF3
Me

64


0
20
40
60
80
100
120
140
160
180
200
220



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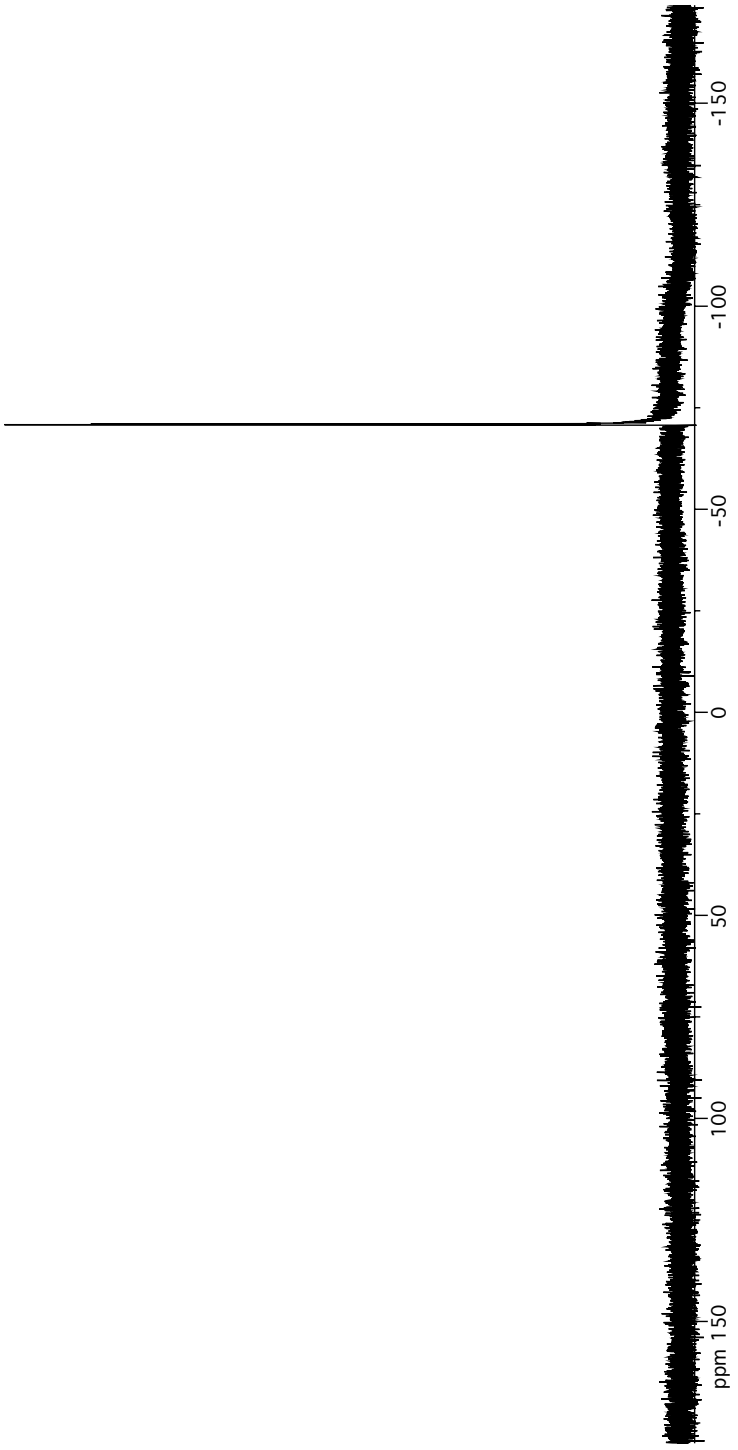
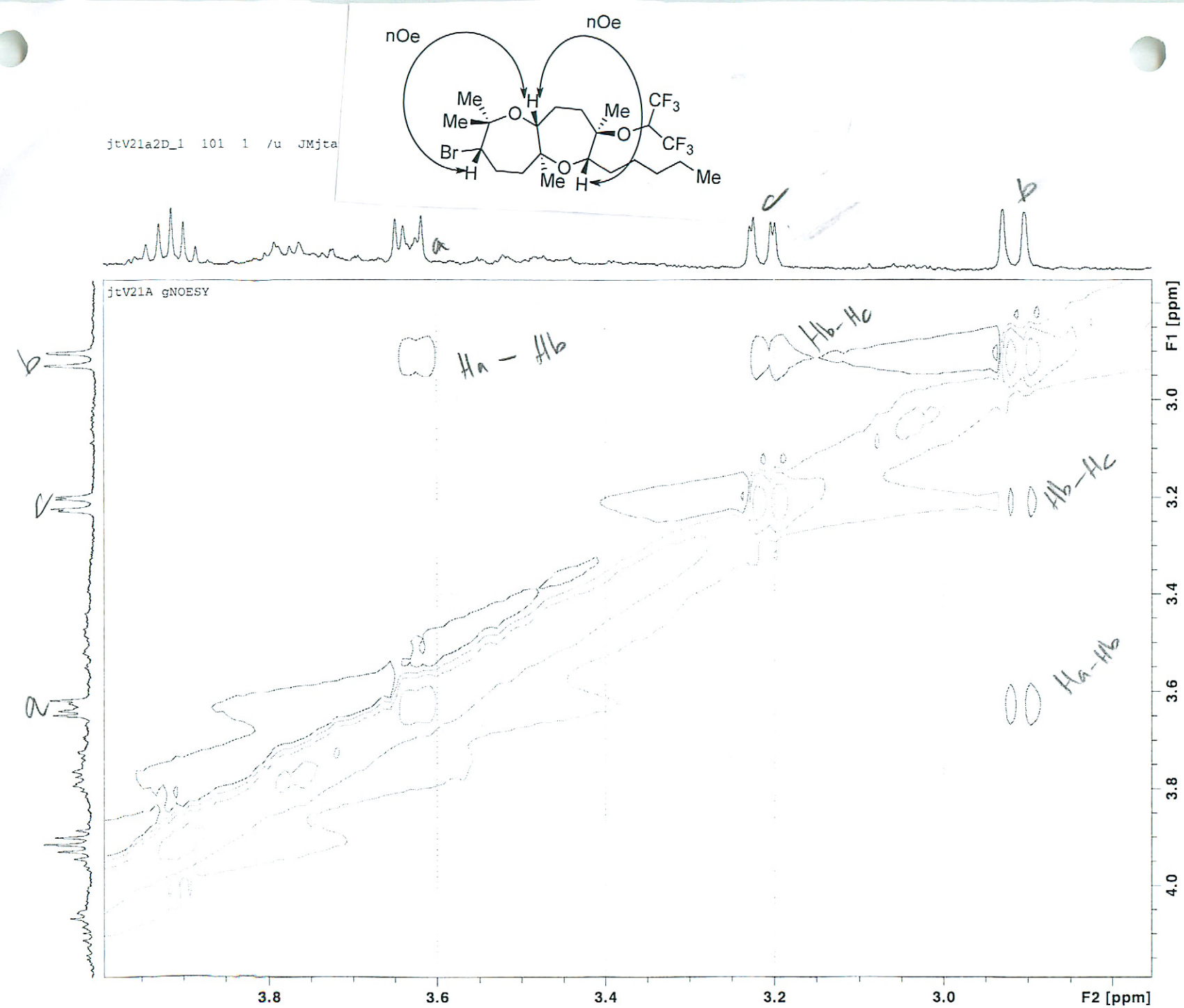
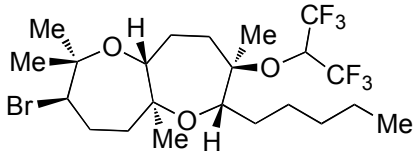



nOe
nOe
Me
Me
O
H
Me
CF3
O
CF3
Br
H
O
Me
H
Me
jtV21a2D_1 101 1 /u JMjta
a
c
b
jtV21A gNOESY
Ha – Hb
Hb-Hc
Hb-Hc
Ha-Hb
b
a
3.8
3.6
3.4
3.2
3.0
F2 [ppm]
F1 [ppm]
3.0
3.2
3.4
3.6
3.8
4.0



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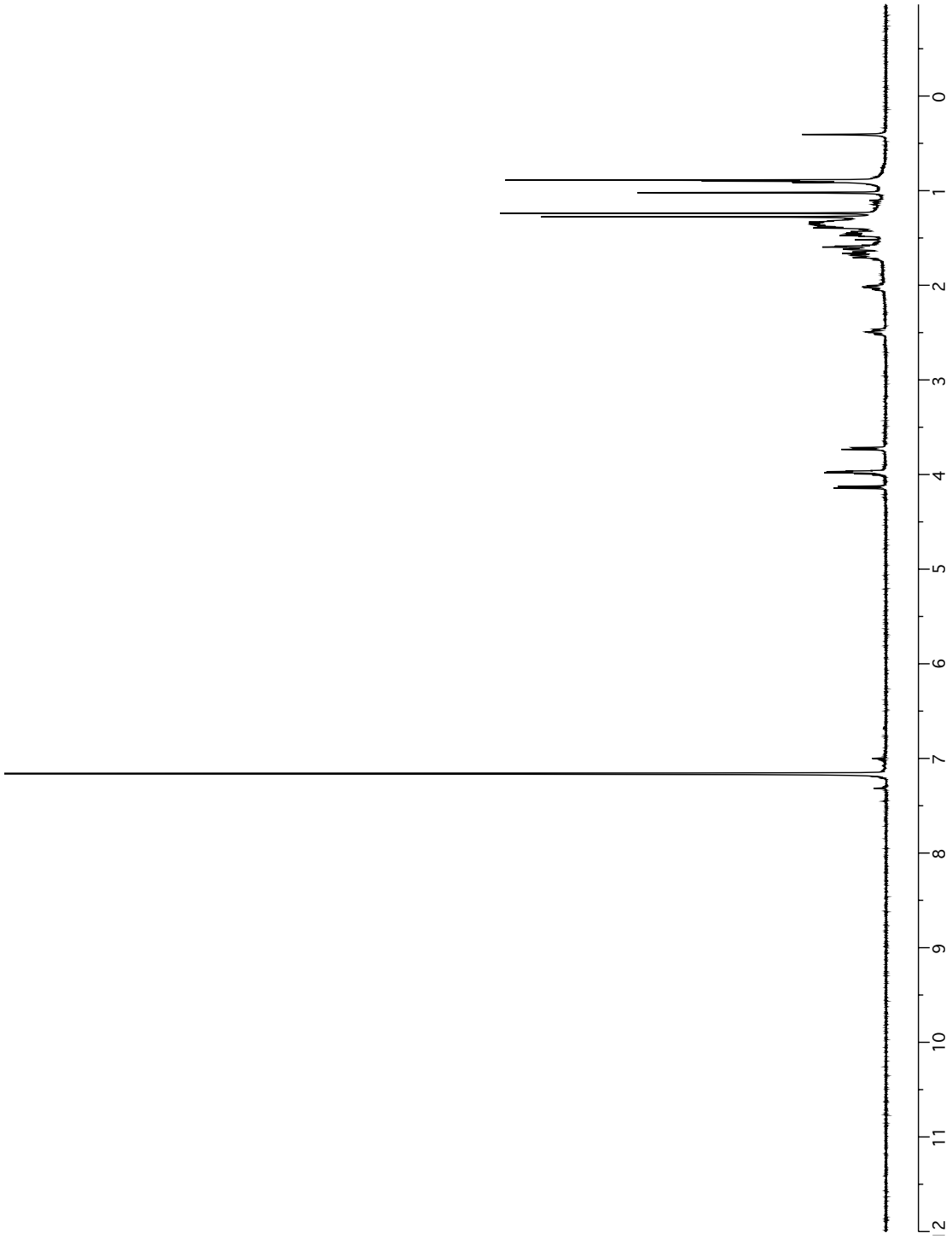

14.744
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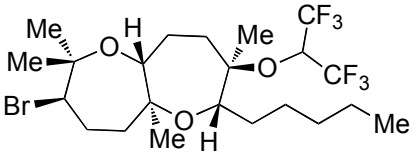
21.821
23.473
27.112
28.426
28.847
29.048
29.799
30.605
32.733
35.823
40.029
66.225
70.262
76.336
76.354
76.798
79.339
85.720
128.206
128.398
128.590
128.691
128.833
jtv21b_carbon
ppm
Me
CF3
CF3
Me
O
H
O
Me
H
O
Me
Me
Br



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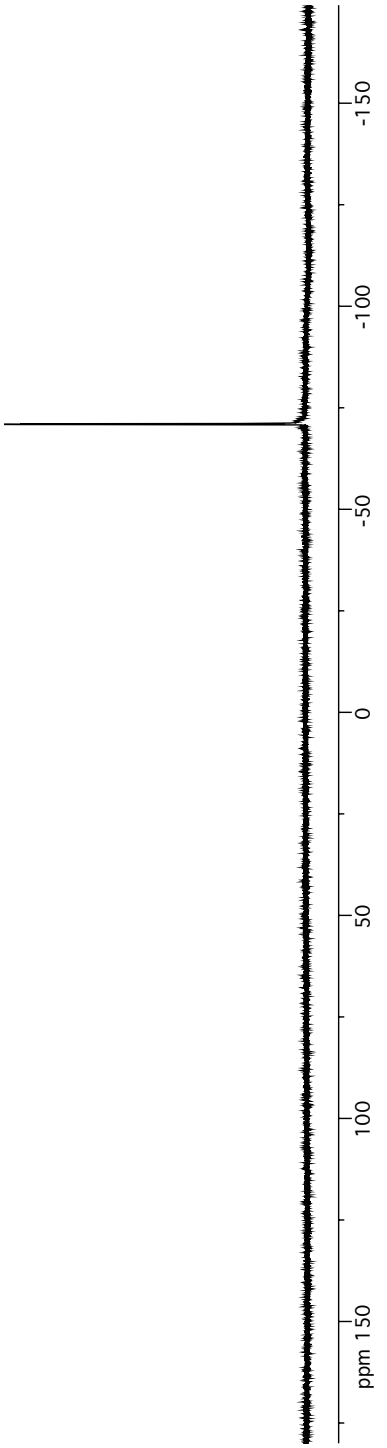
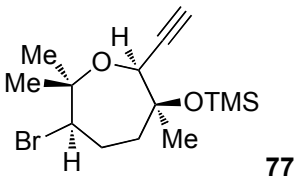
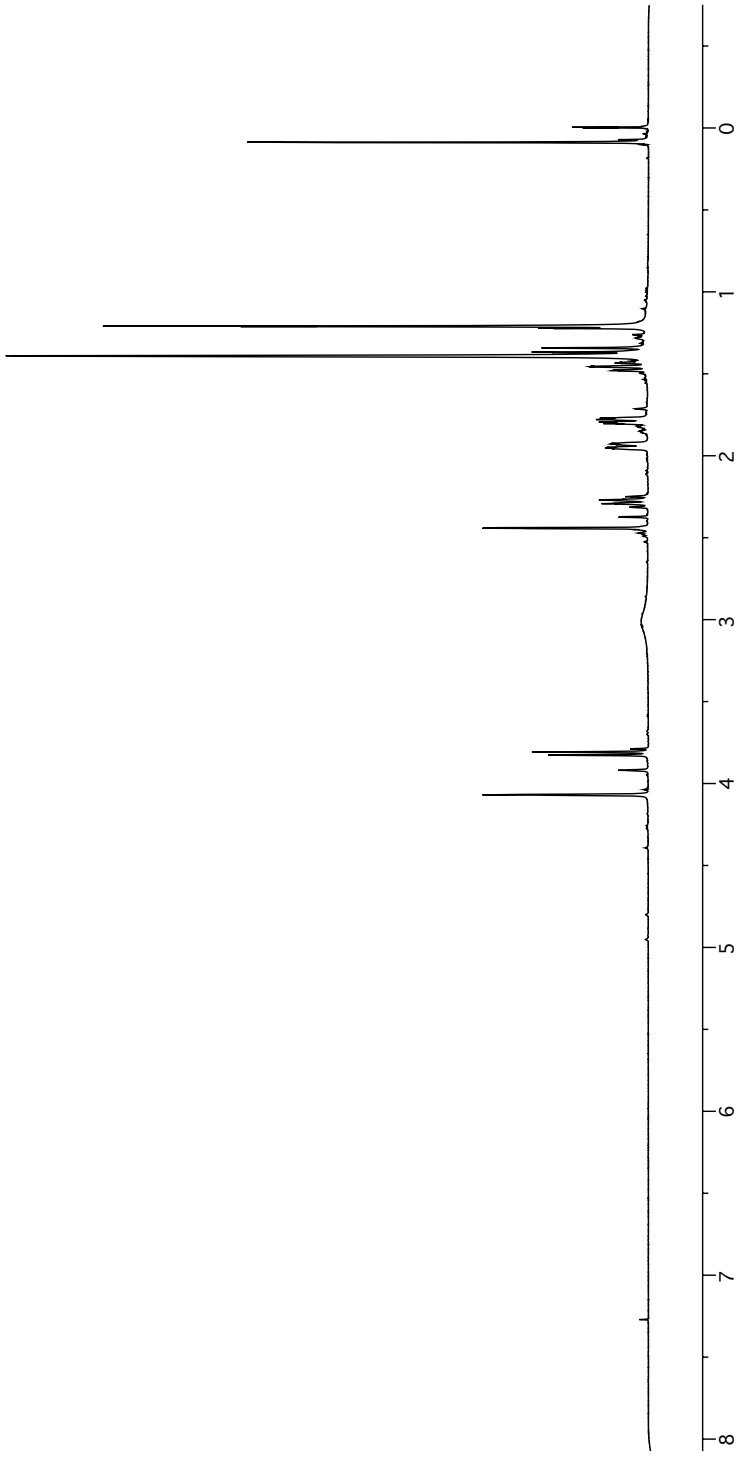
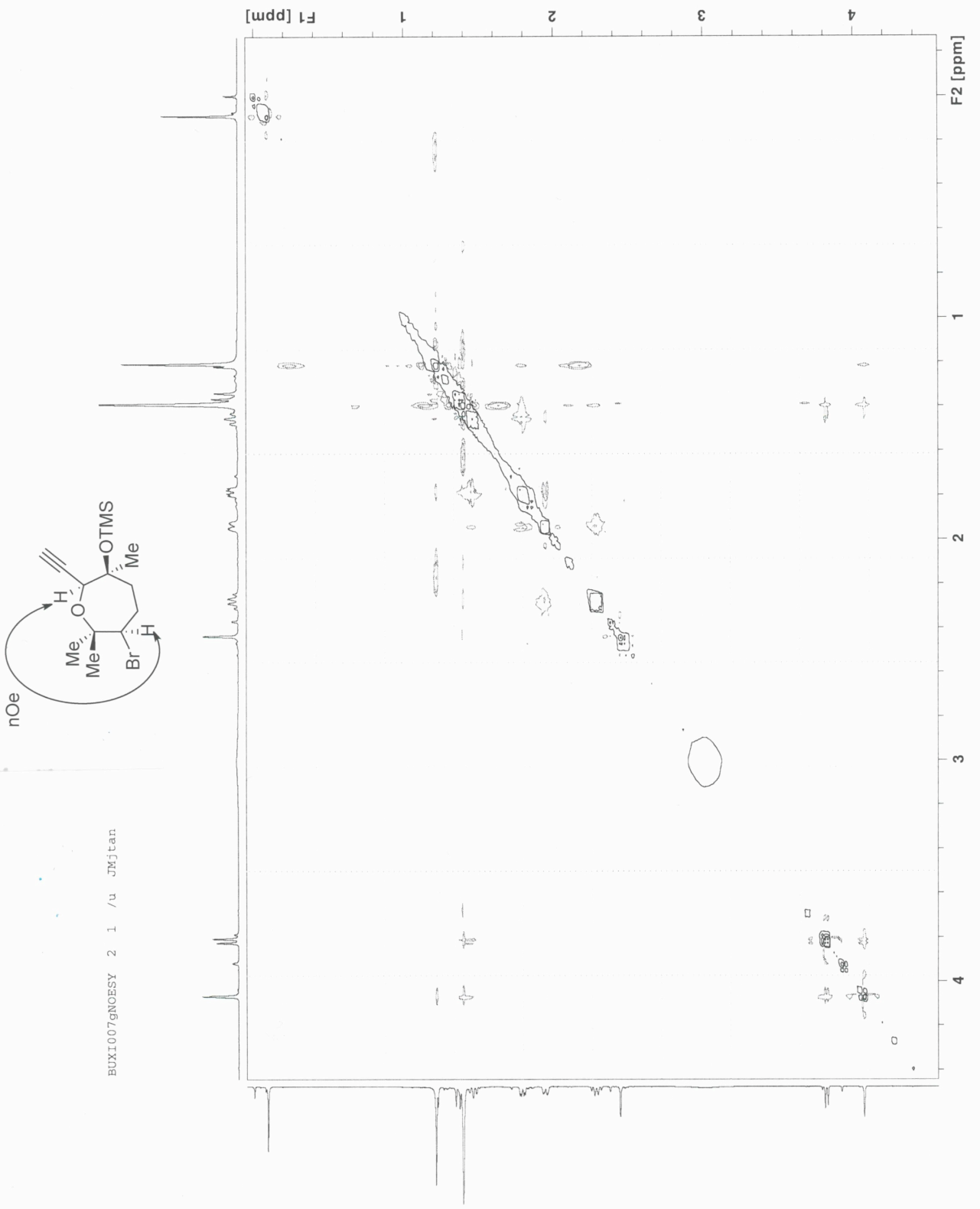
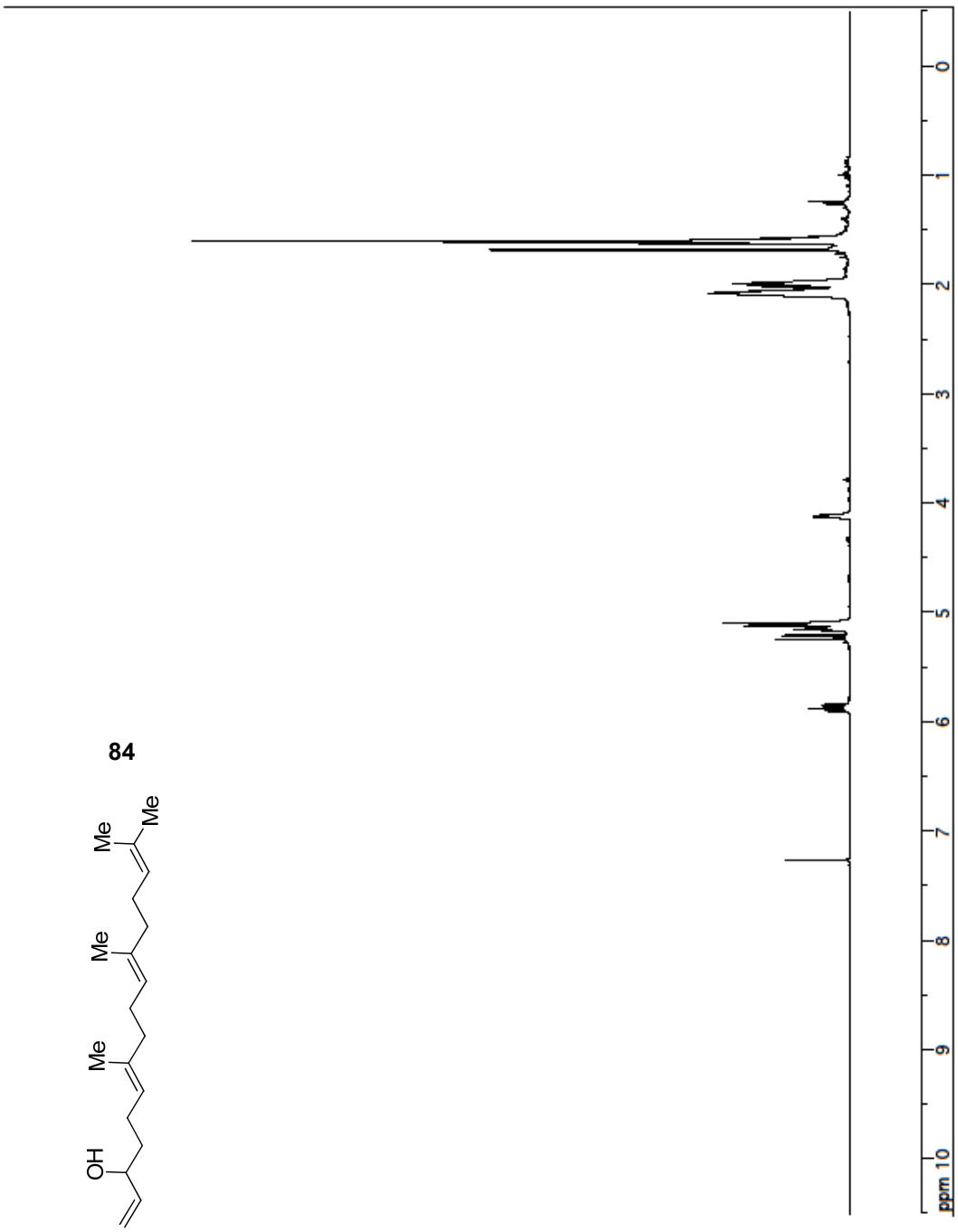


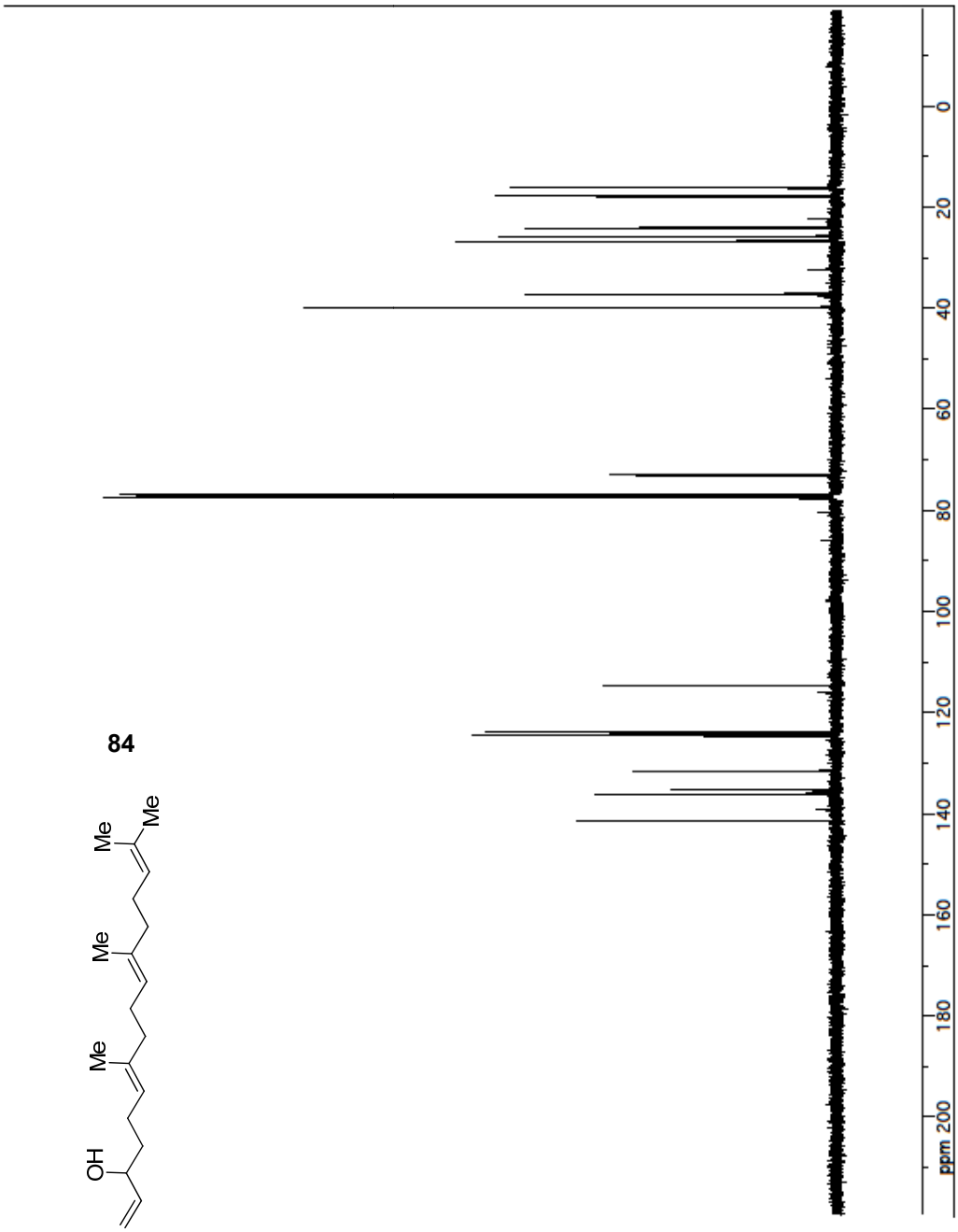


77




F1 [ppm]
F2 [ppm]
1
2
3
4
OTMS
Me
Me
Me
Br
H
H
O
nOe
BUXI007gNOESY 2 1 /u JMjtan


84
OH
Me
Me
Me
Me
ppm 10
9
8
7
6
5
4
3
2
1
0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Me
Me
Me
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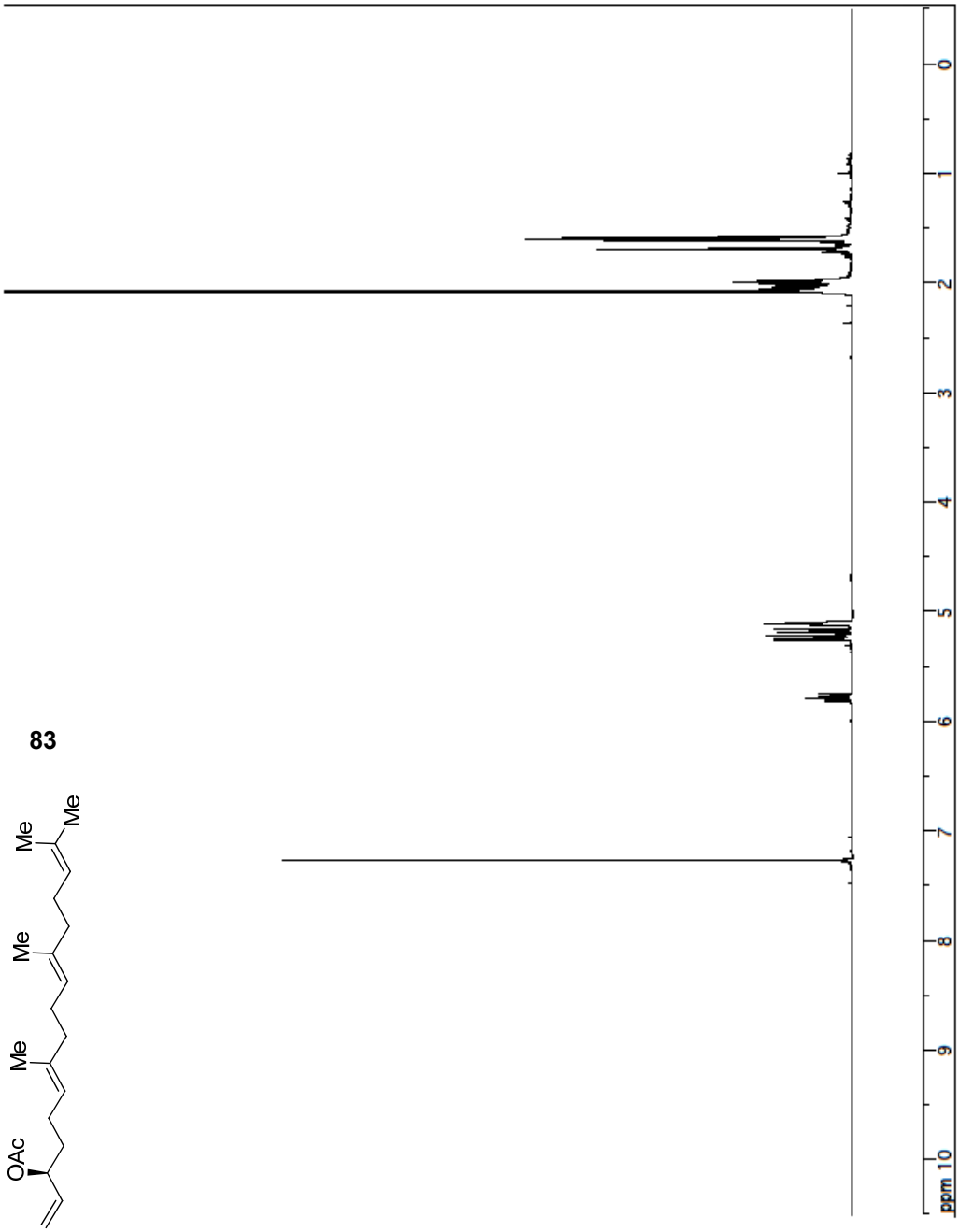
80
100
120
140
160
180
200
ppm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OAc
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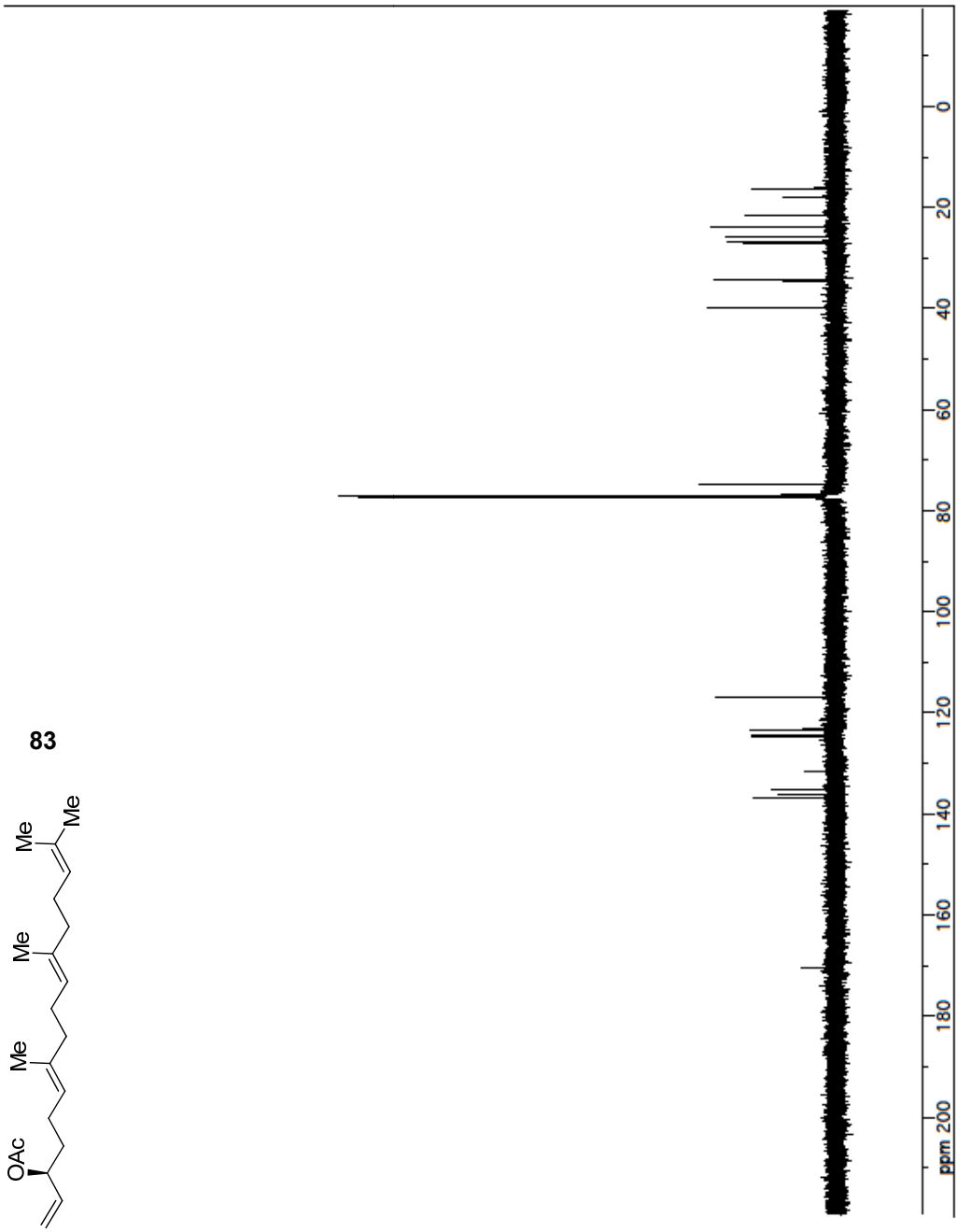
Me
Me
Me
ppm 10
9
8
7
6
5
4
3
2
1
0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Me
Me
Me
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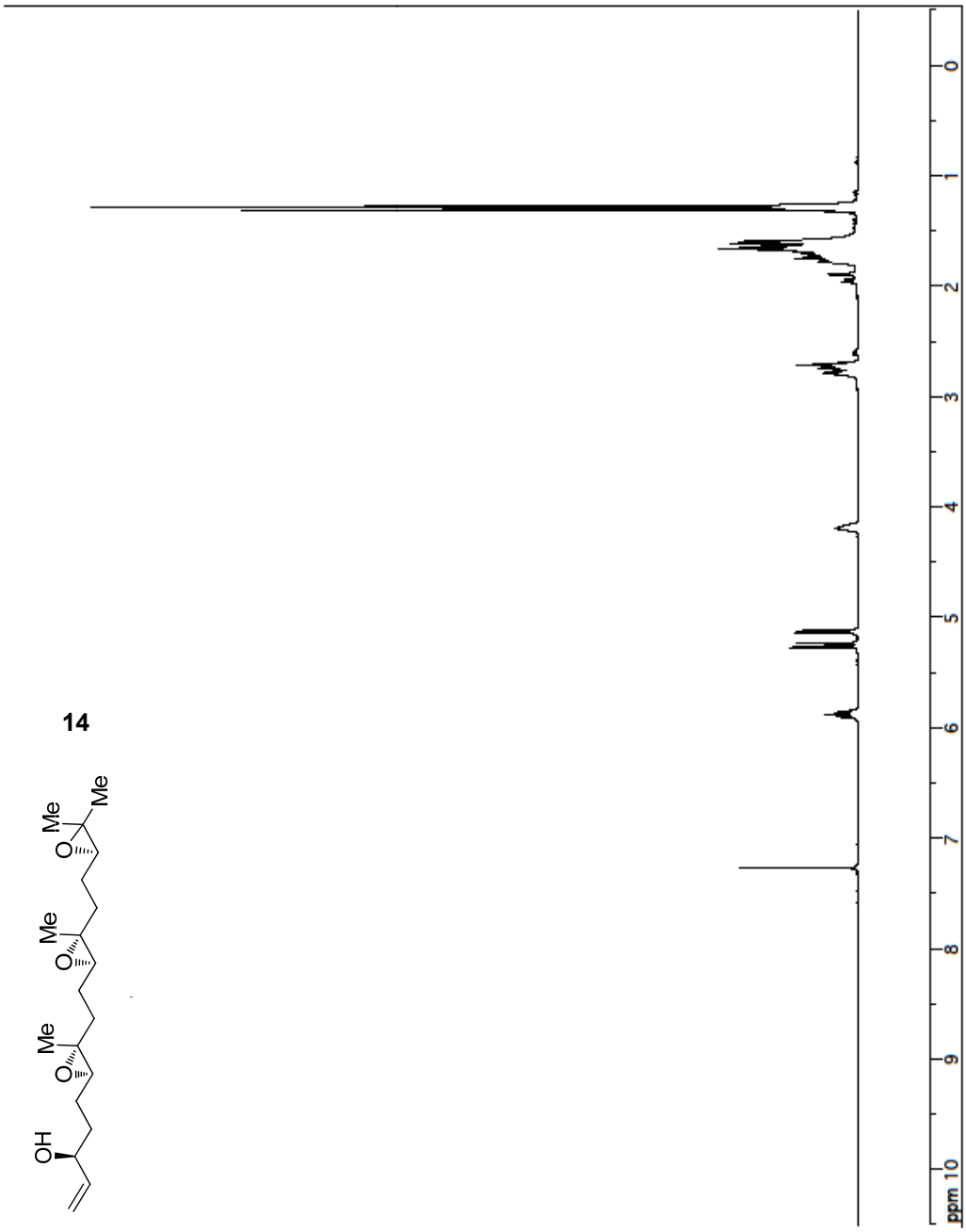
60
40
20
0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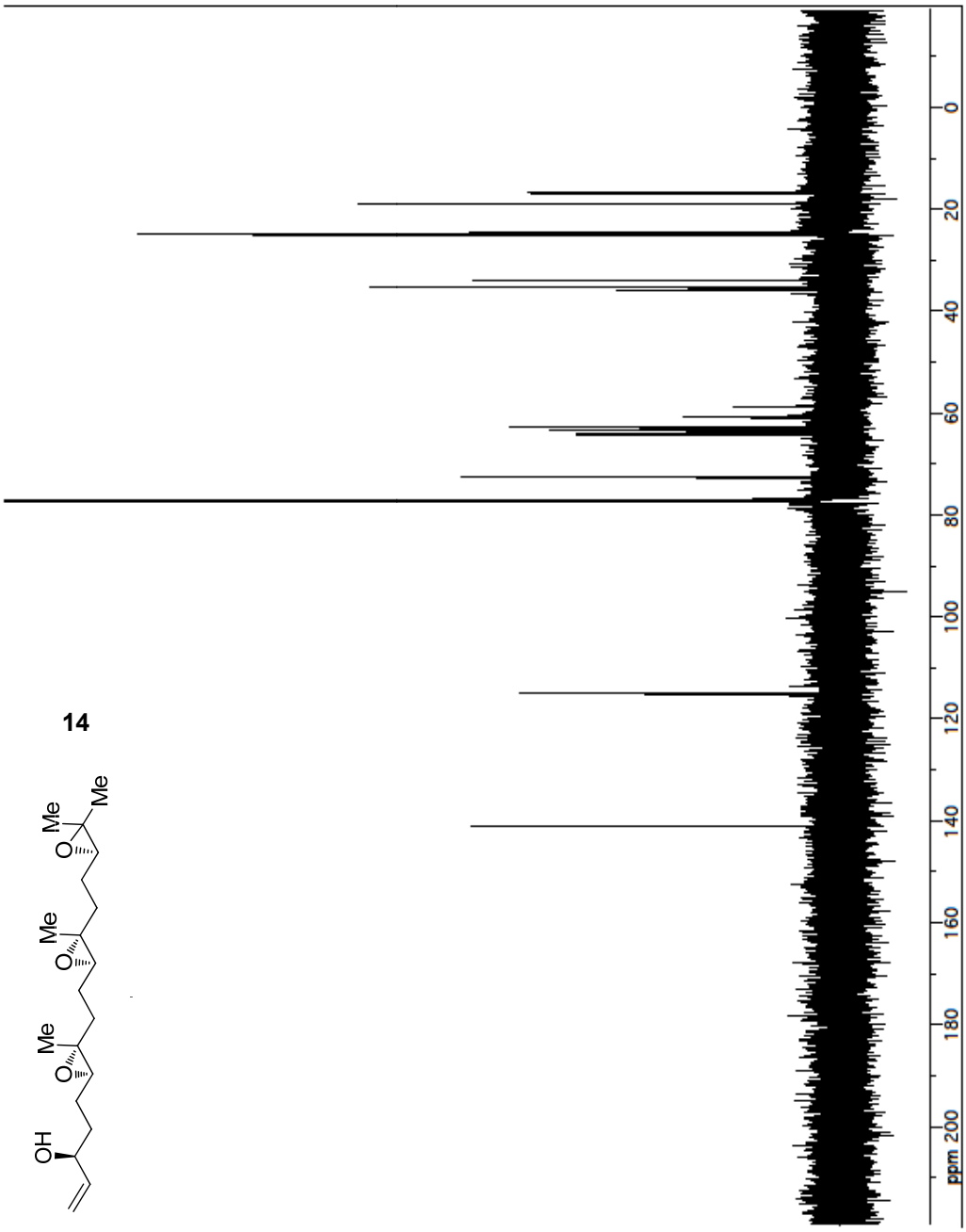
Me
Me
Me
O
O
O
O
ppm
0
1
2
3
4
5
6
7
8
9
10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O
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O
ppm
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20
40
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80
100
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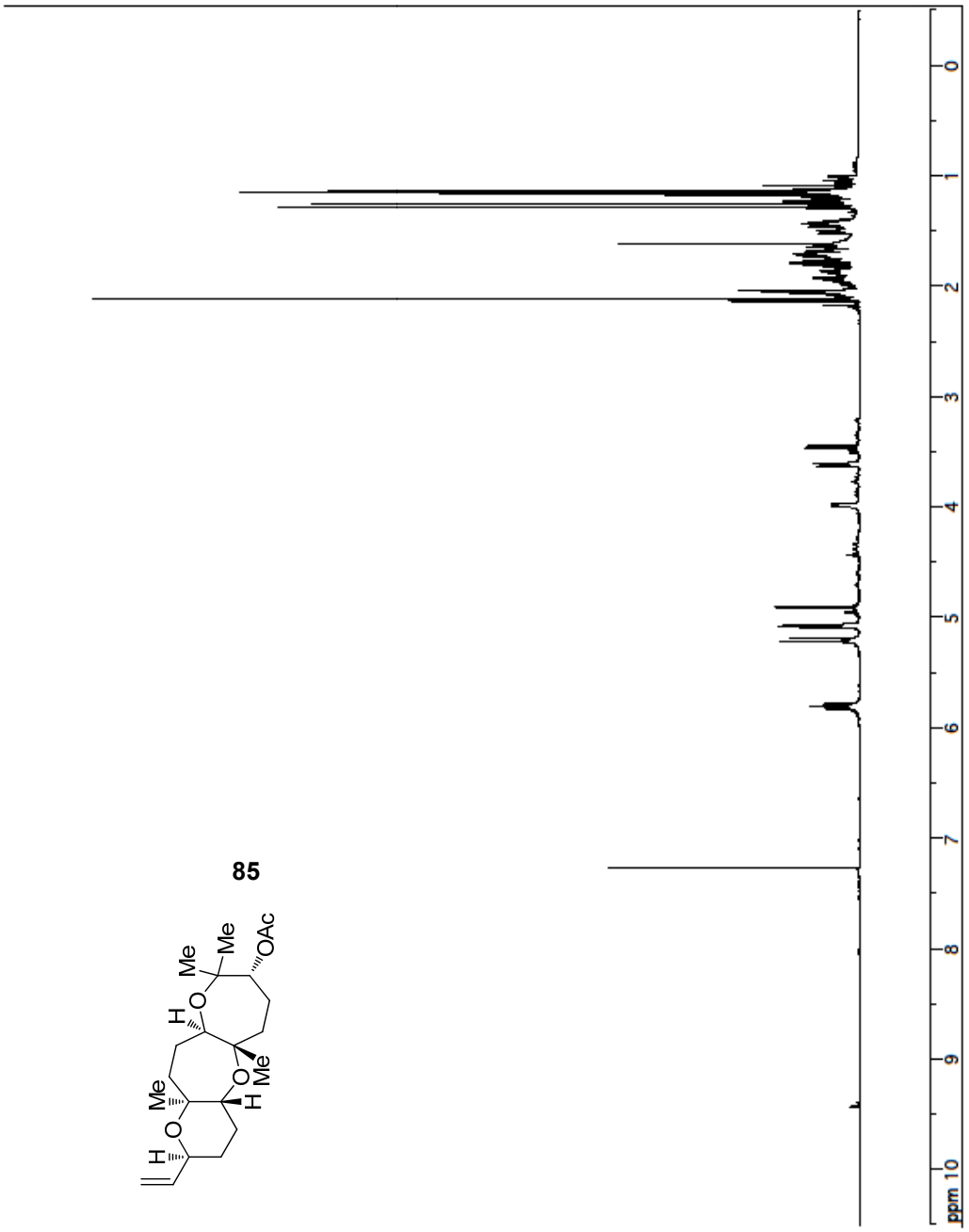
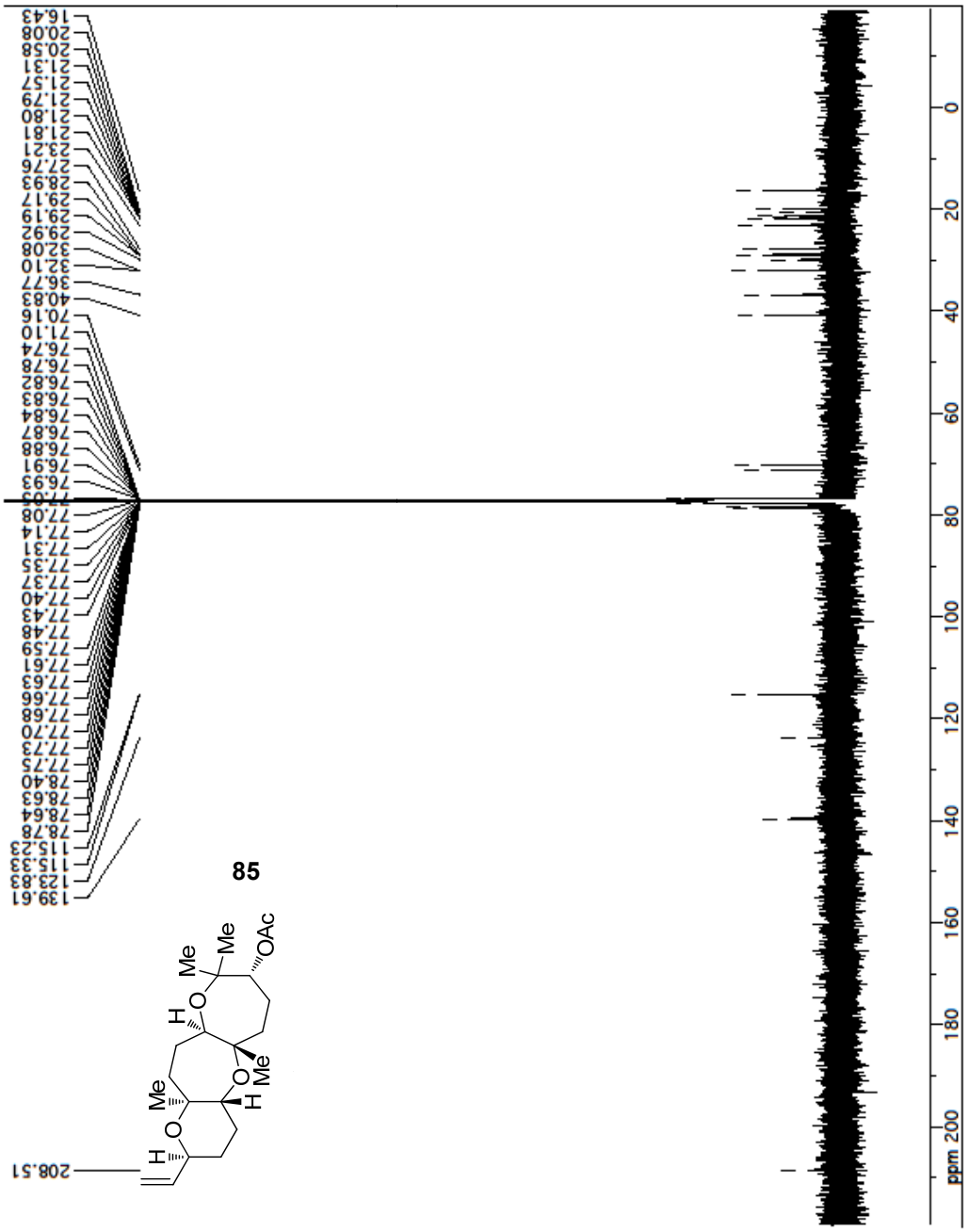
140
160
180
200


85
Me
Me
OAc
H
O
O
Me
H
Me
O
H
ppm
10
9
8
7
6
5
4
3
2
1
0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OAc
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Me
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123.83
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78.40
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77.70
77.68
77.66
77.63
77.61
77.59
77.48
77.43
77.40
77.37
77.35
77.31
77.14
77.08
77.03
76.93
76.91
76.88
76.87
76.84
76.83
76.82
76.78
76.74
71.10
70.16
40.83
36.77
32.10
32.08
29.92
29.19
29.17
28.93
27.76
23.21
21.81
21.80
21.79
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21.31
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20.08
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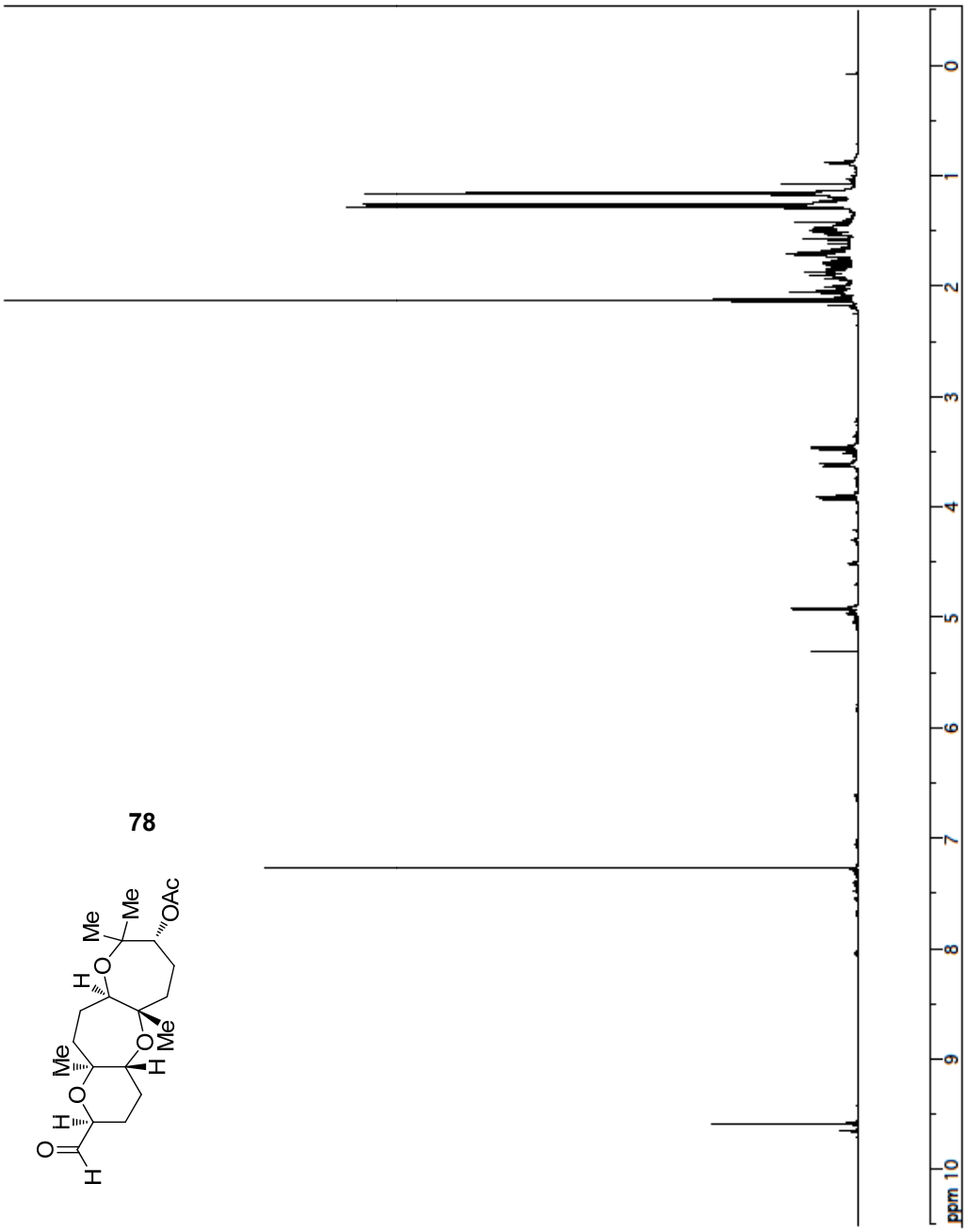
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O
H
O
Me
Me
O
H
Me
O
H
Me
OAc
ppm 10
9
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7
6
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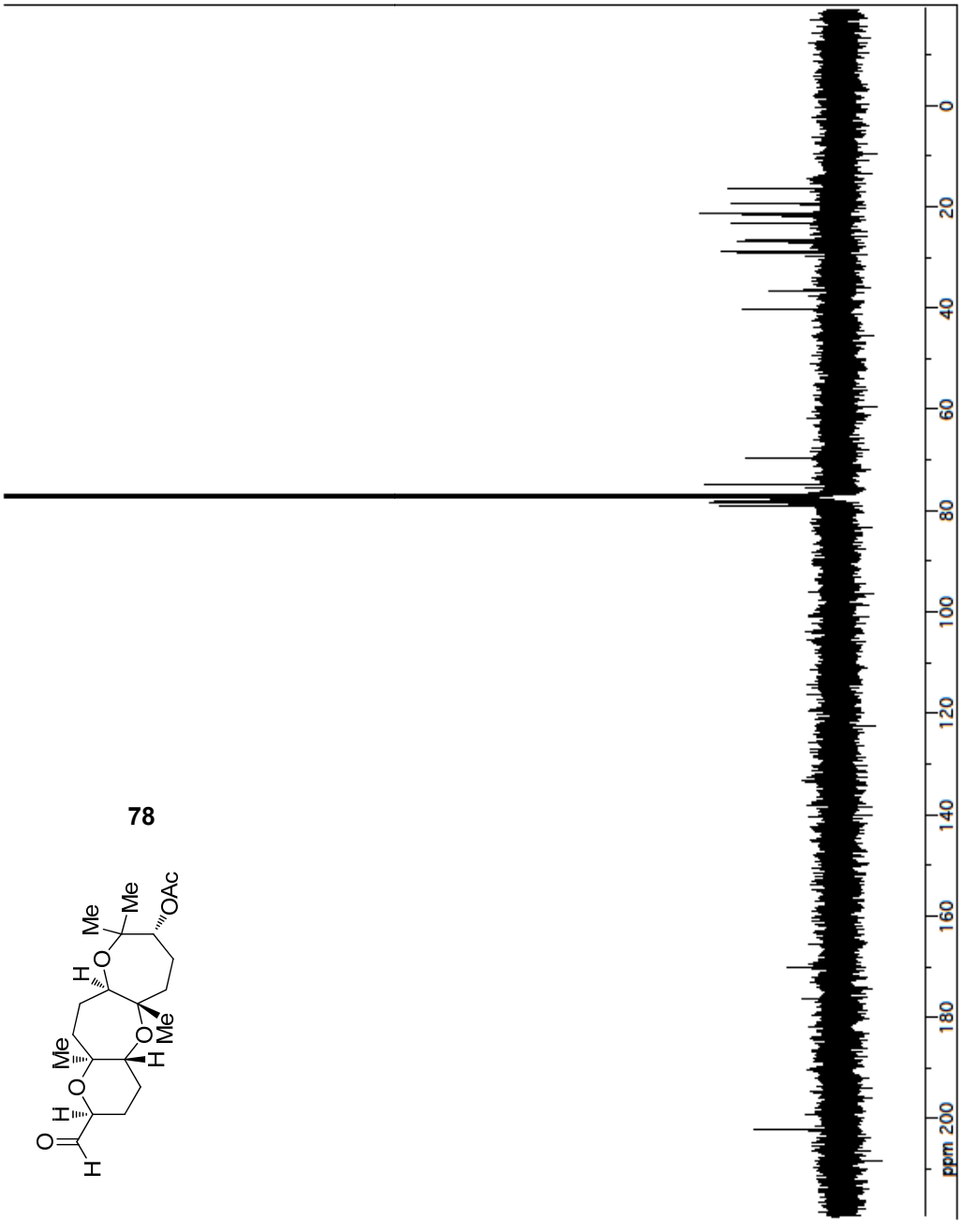
4
3
2
1
0


78
O
H
O
Me
Me
O
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Me
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H
Me
OAc
H
ppm 200
180
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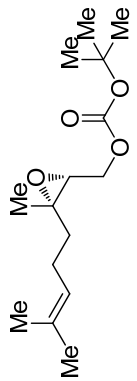
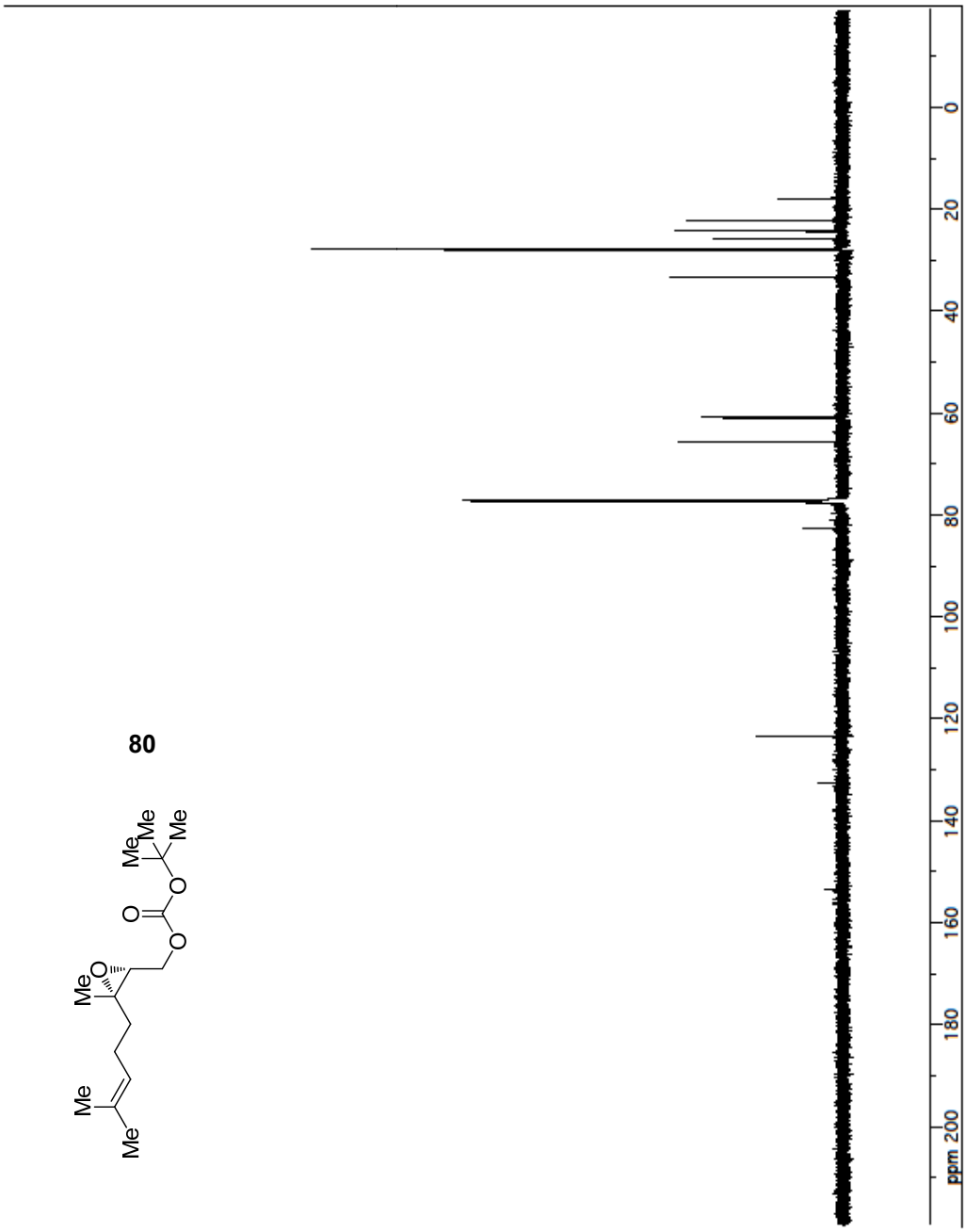
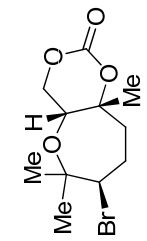
140
120
100
80
60
40
20
0

80

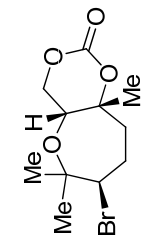



80
Me
Me
Me
O
O
O
Me
O
Me
Me
0
20
40
60
80
100
120
140
160
180
200
ppm

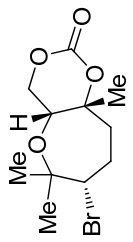
79'

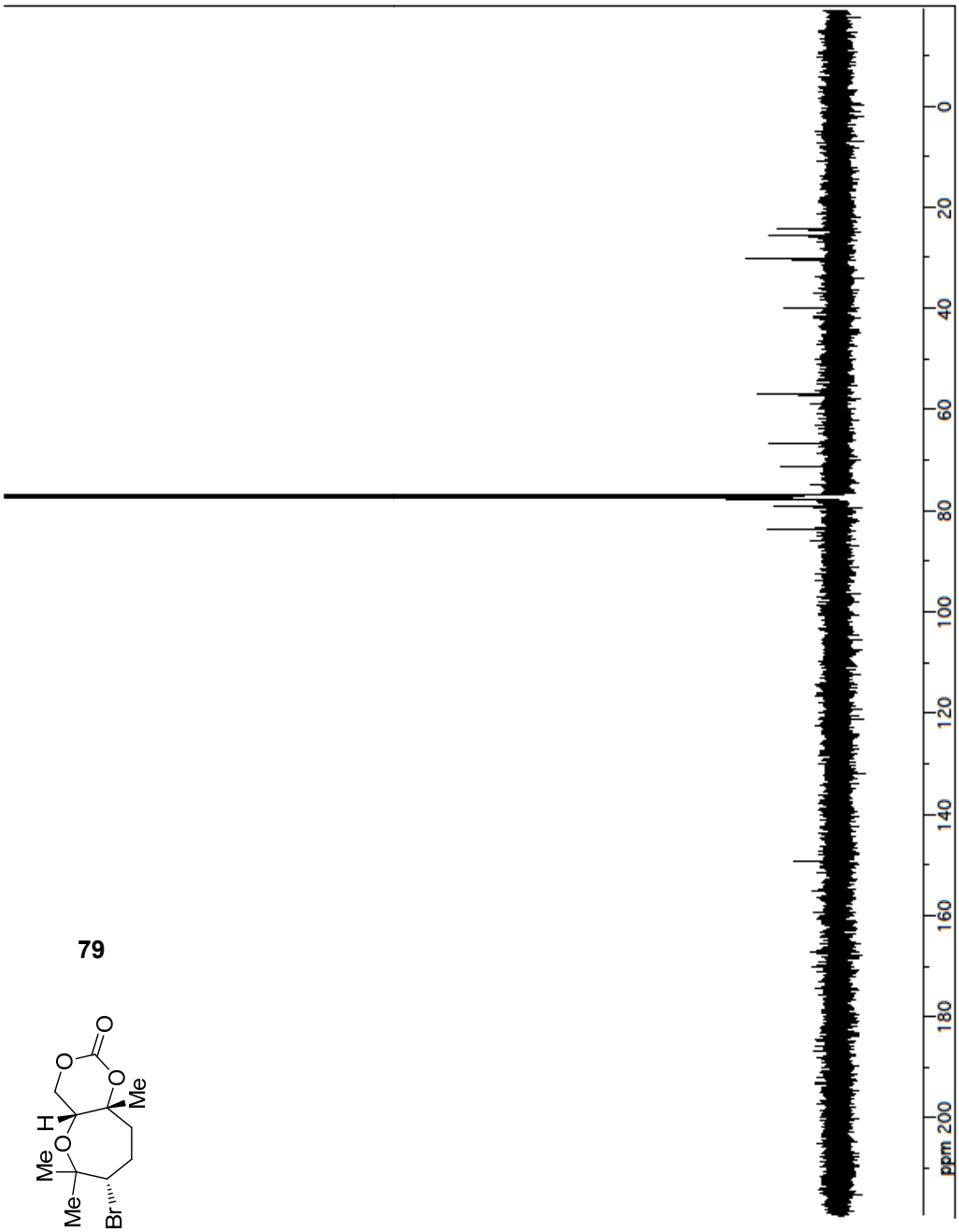


79'



79




79
Me
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O
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O
Me
ppm 200
180
160
140
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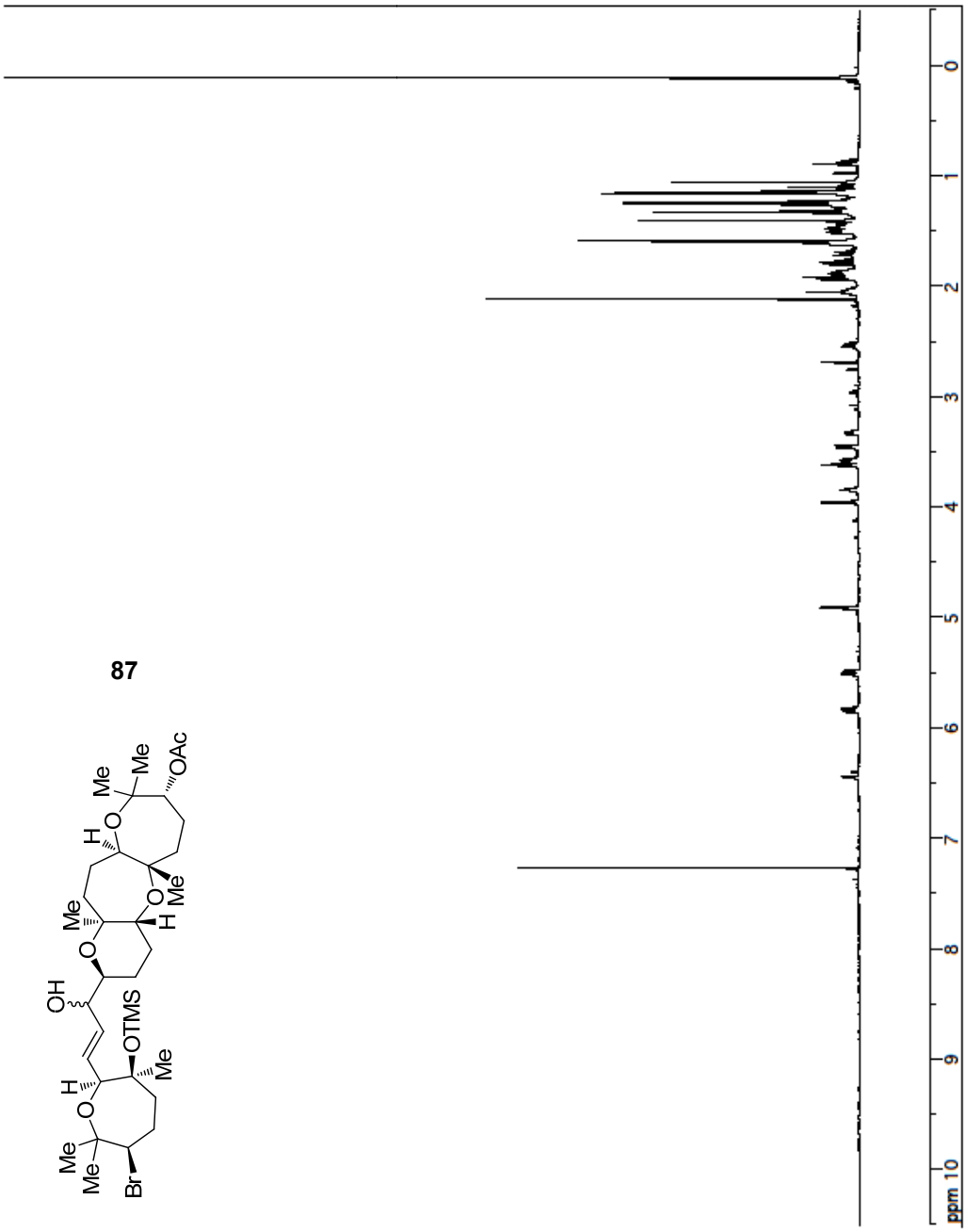
20
0


87
OAc
Me
Me
O
H
Me
O
H
Me
Me
O
OH
OTMS
H
O
Me
Me
Me
Br
ppm
10
9
8
7
6
5
4
3
2
1
0

87
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OTMS
Me
Br
OAc
ppm
0
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60
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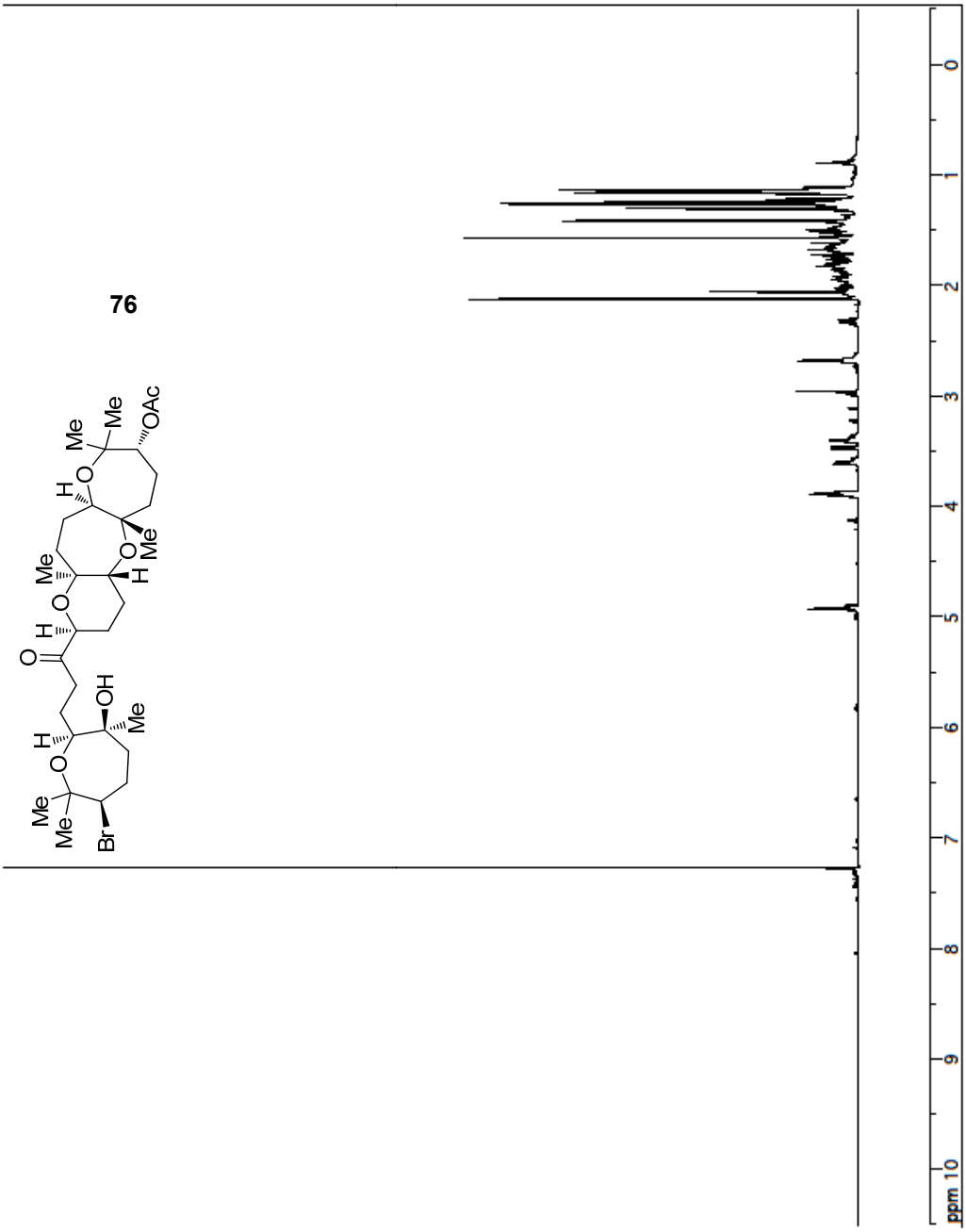
100
120
140
160
180
200


76
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Me
OAc
H
O
Me
O
Me
H
O
Me
O
H
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Me
H
O
Me
Me
Br
ppm
10
9
8
7
6
5
4
3
2
1
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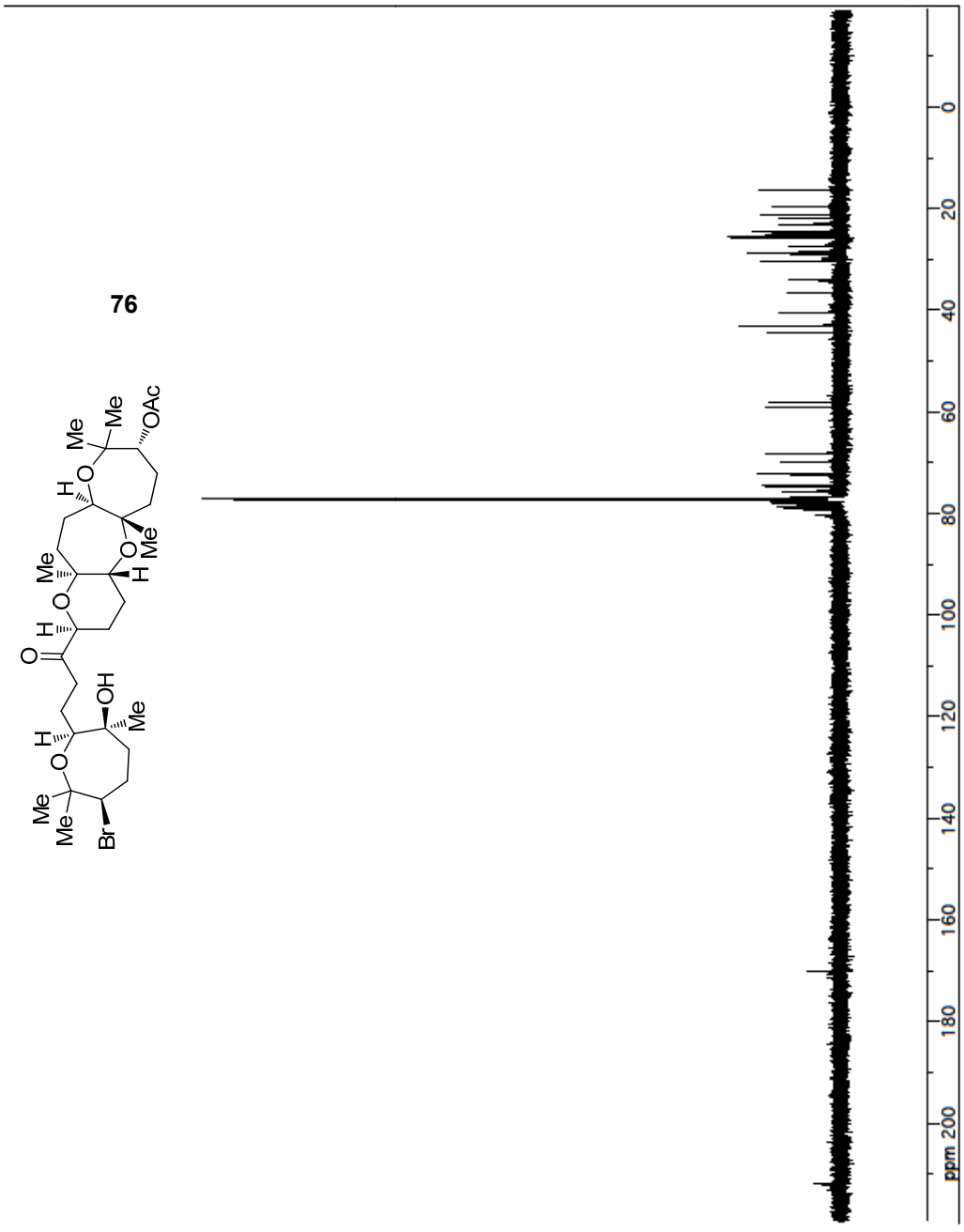
76
Me
Me
OAc
H
O
Me
O
Me
H
Me
O
H
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OH
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Me
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Br
ppm 200
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20
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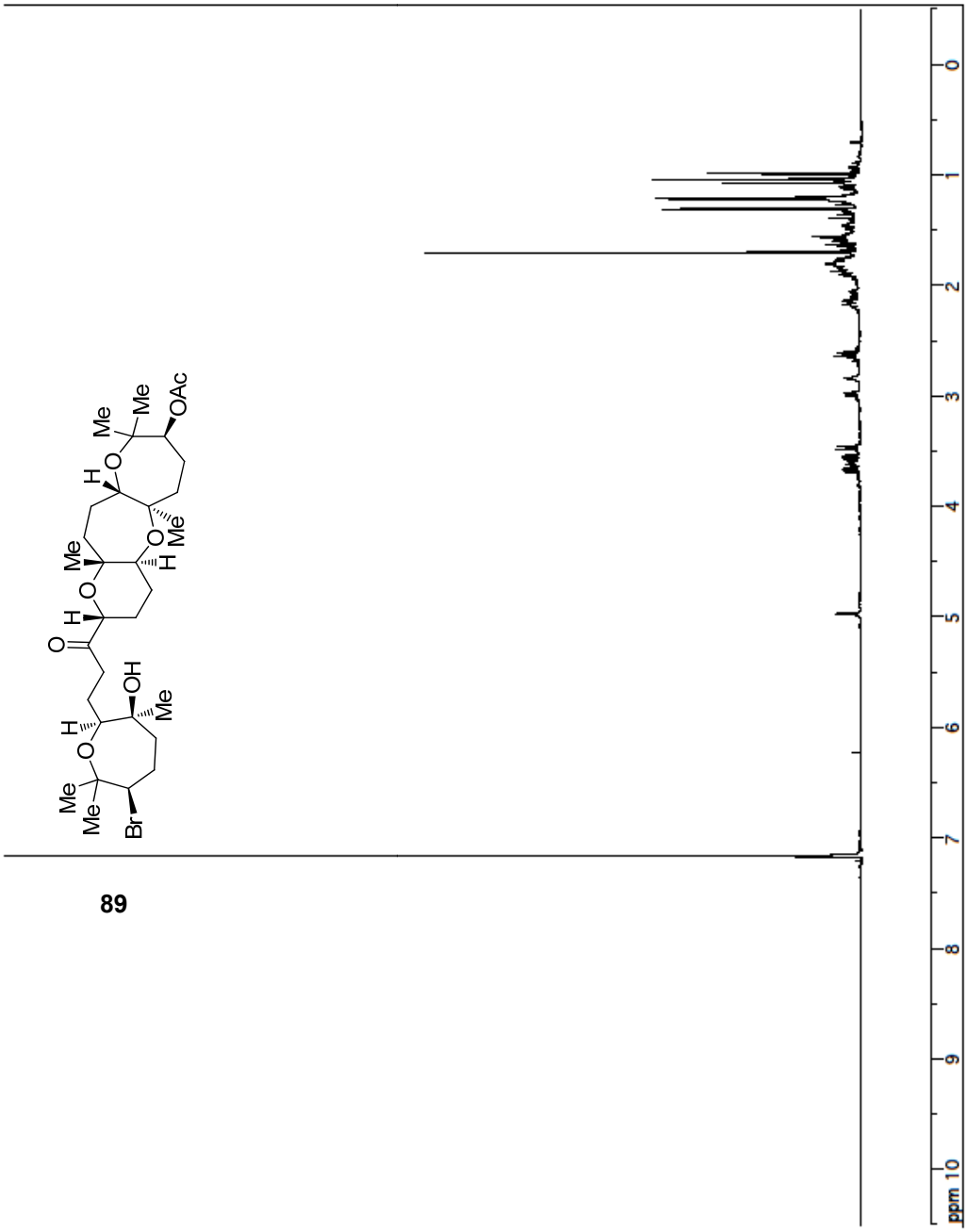
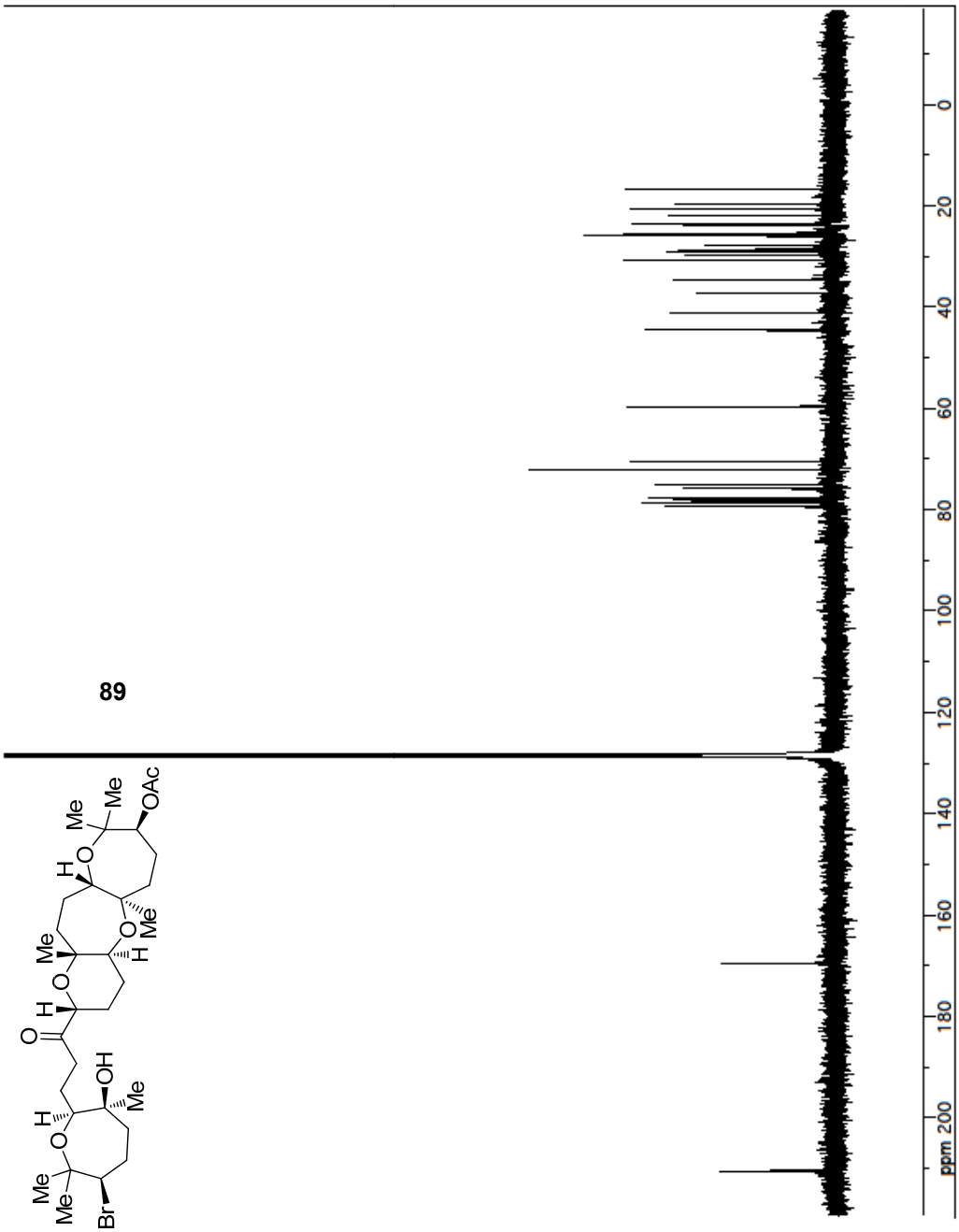


89


89
Me
Me
Br
H
O
OH
Me
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O
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Me
H
O
Me
OAc
ppm 200
180
160
140
120
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20
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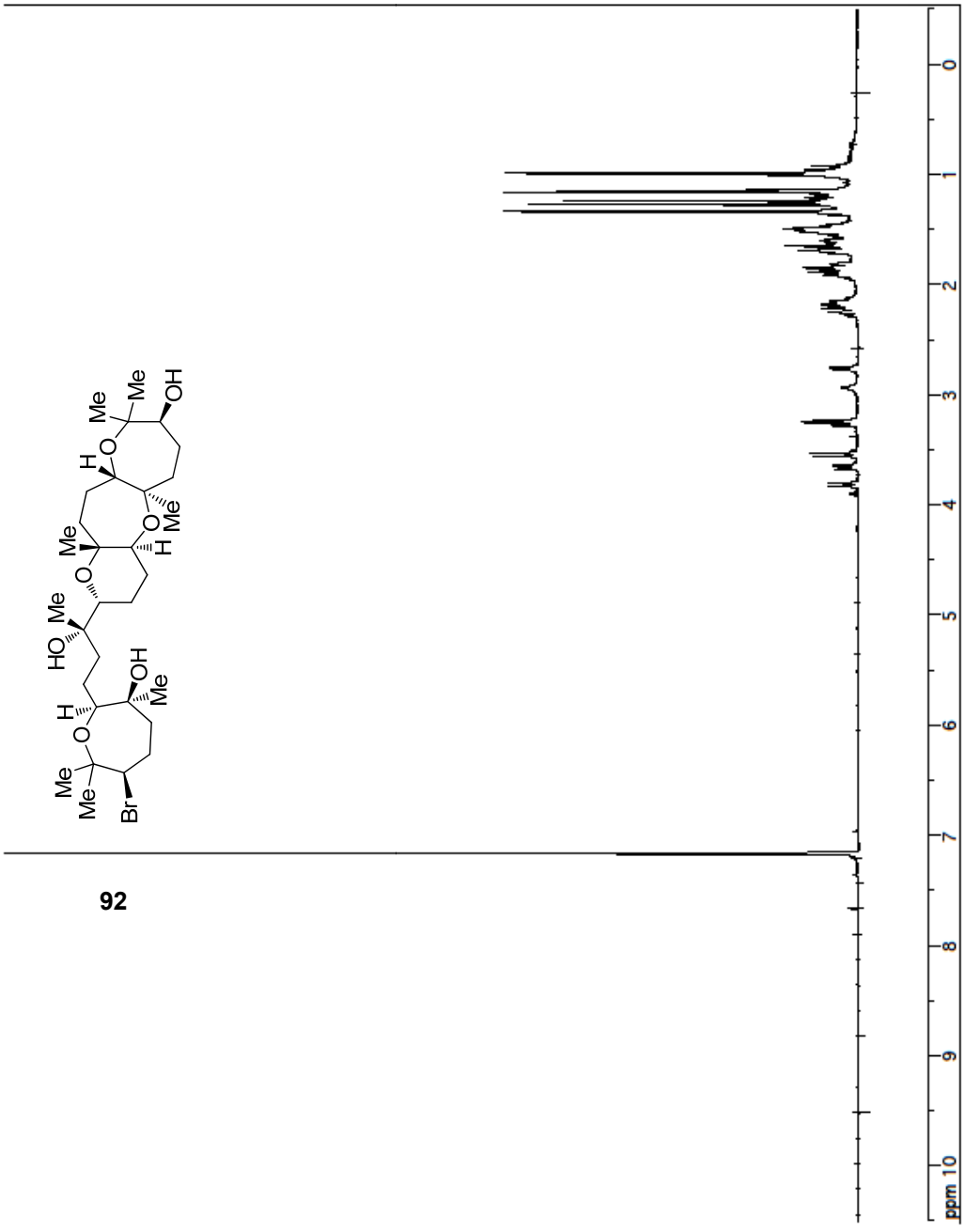

92

92
Me
Me
Br
H
O
HO
Me
OH
Me
Me
O
H
Me
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O
H
Me
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OH
ppm 200
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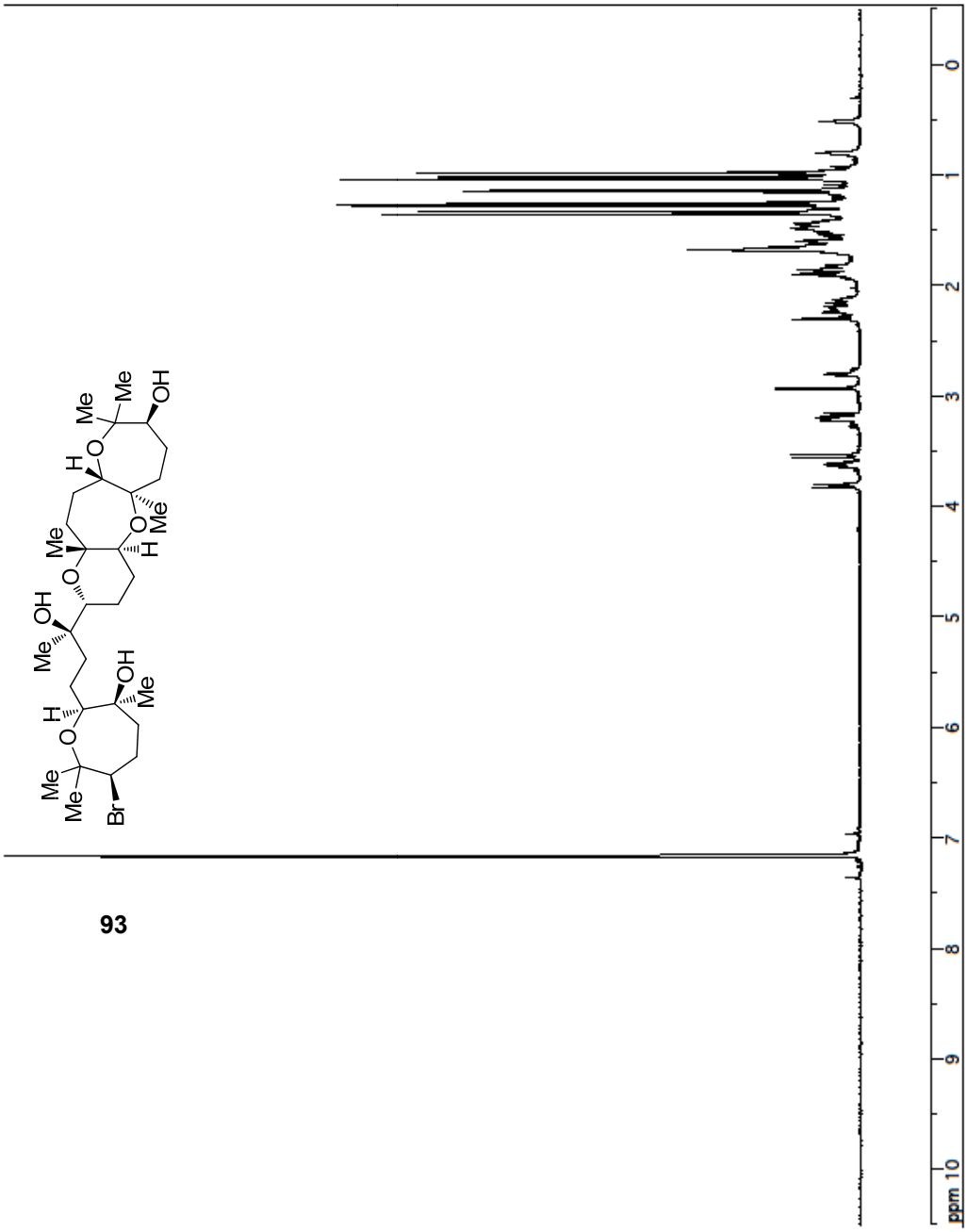

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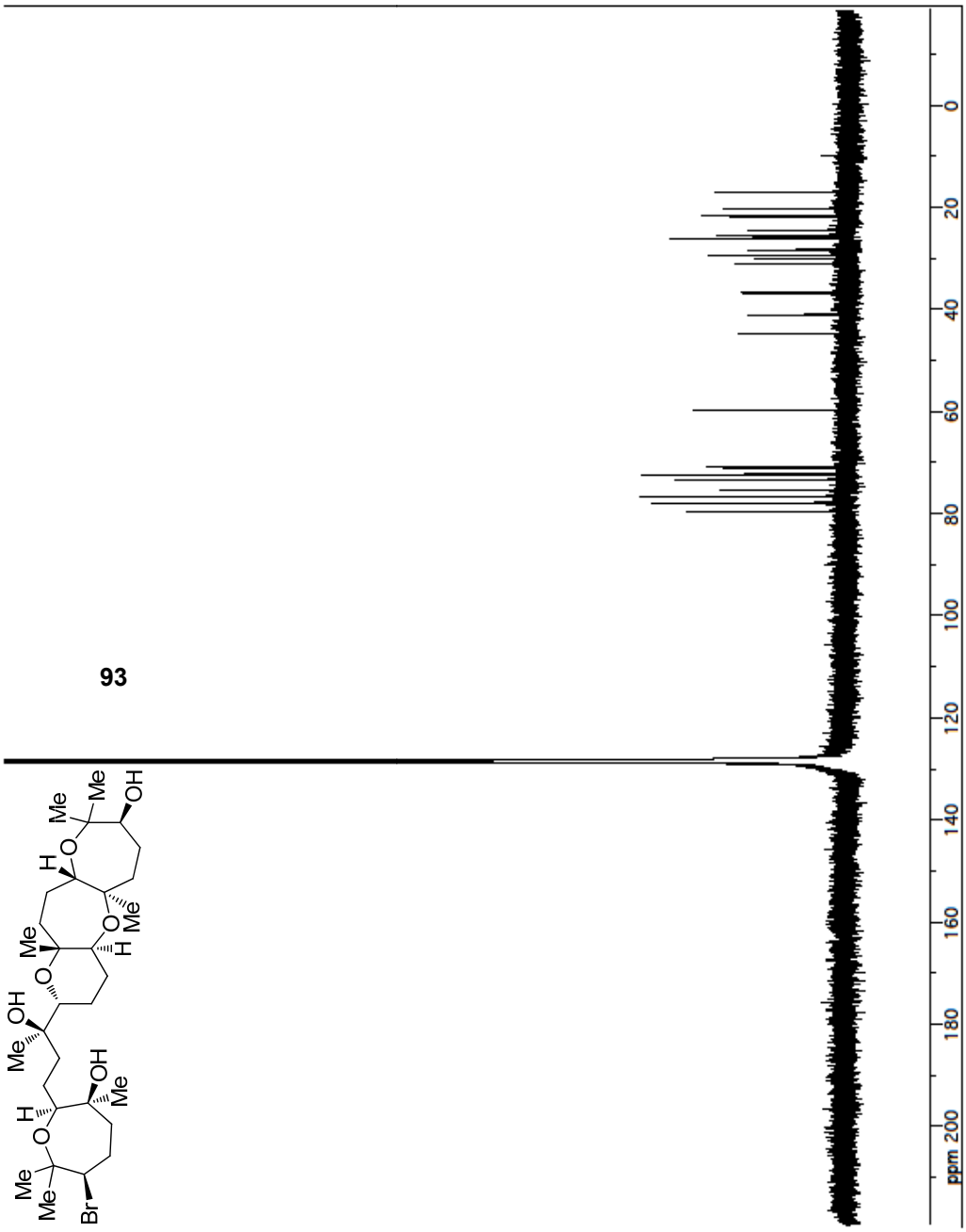
93
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Me
OH
H
O
Me
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H
Me
Me
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Me
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Me
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20
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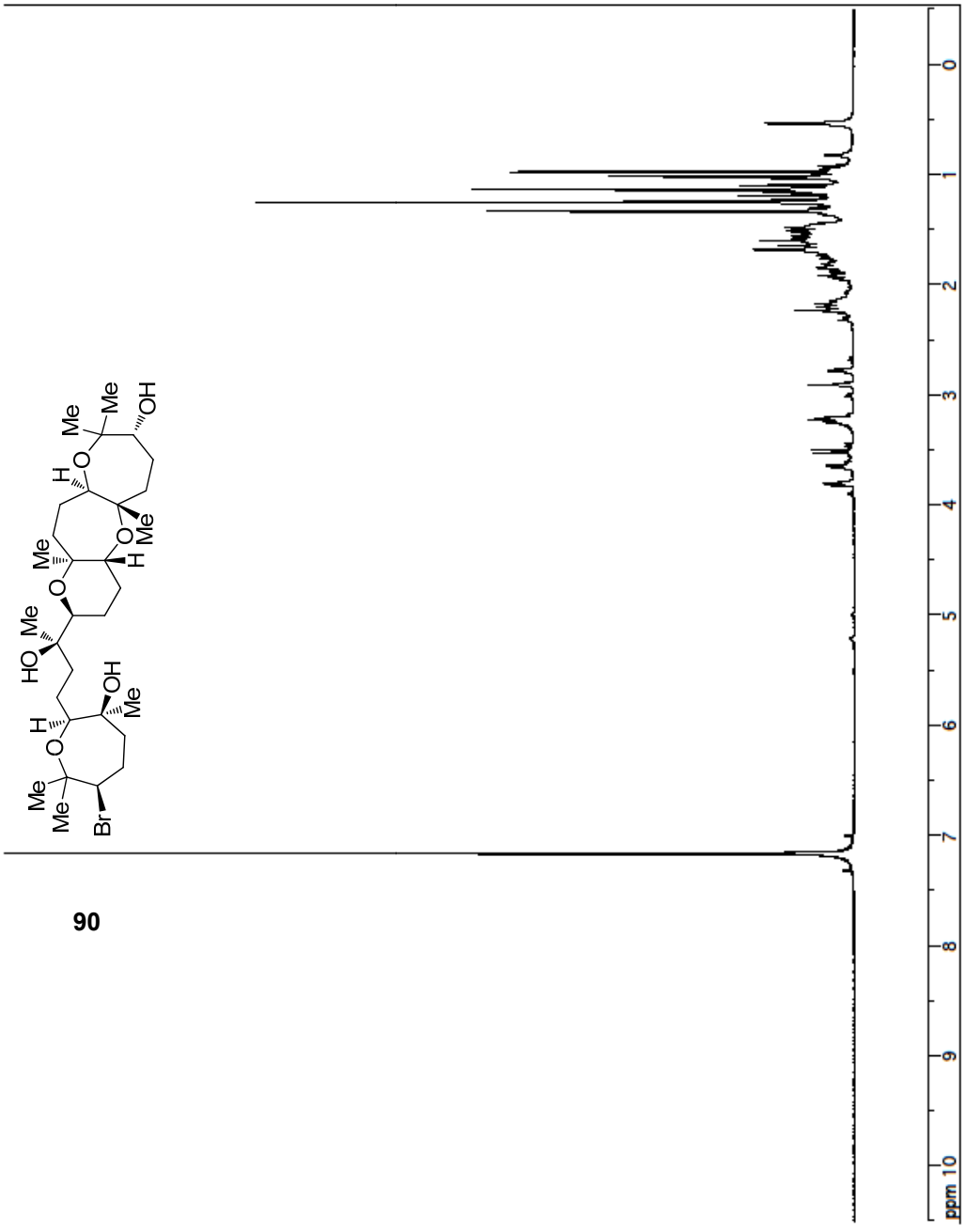
Me
Me
OH
H
O
Me
Me
O
H
Me
Me
O
HO
Me
H
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Me
Me
Me
Br
ppm 10
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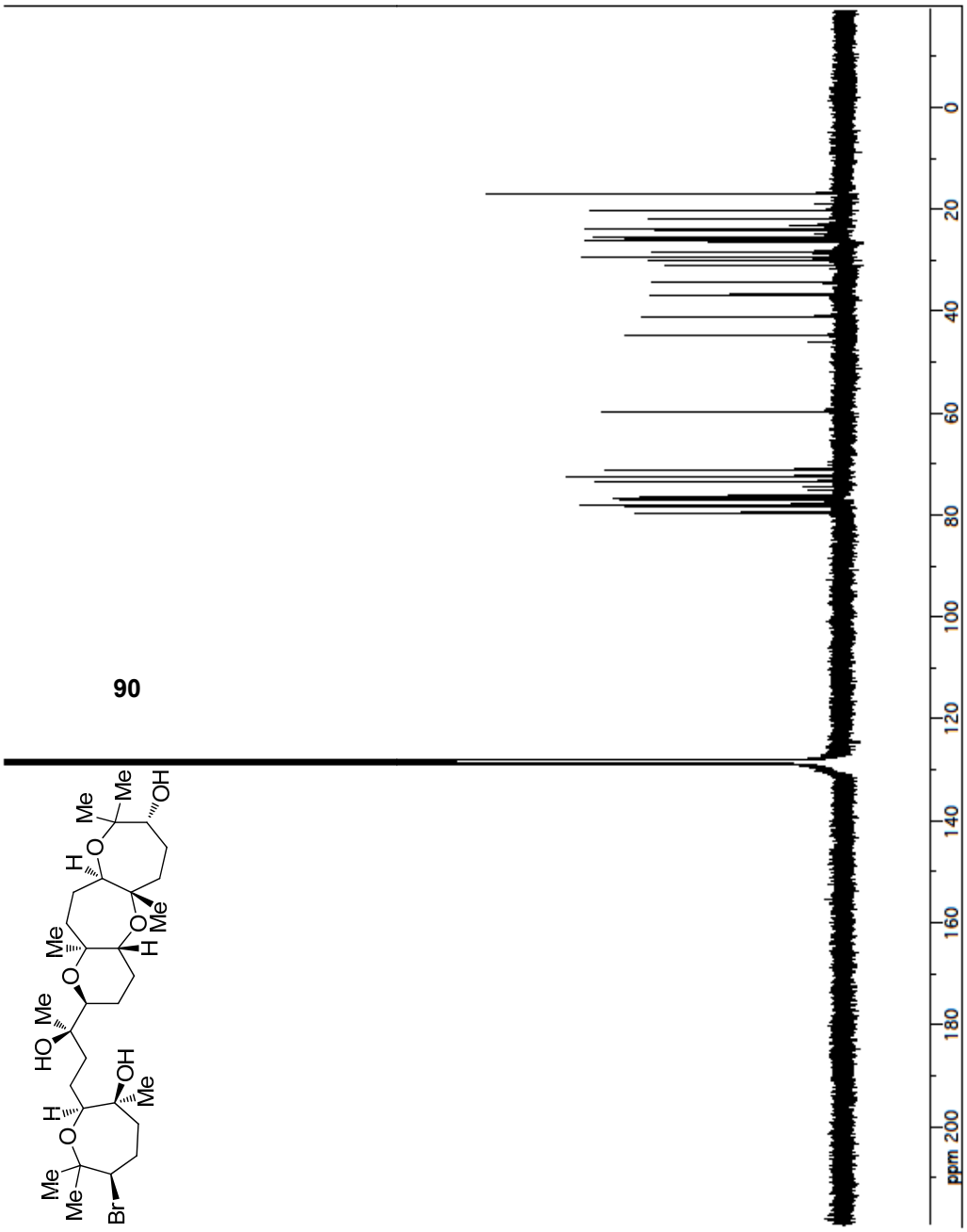
8
7
6
5
4
3
2
1
0

90


90
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Me
OH
H
O
Me
O
H
Me
Me
O
HO
Me
OH
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Me
Me
Me
Br
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80
100
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160
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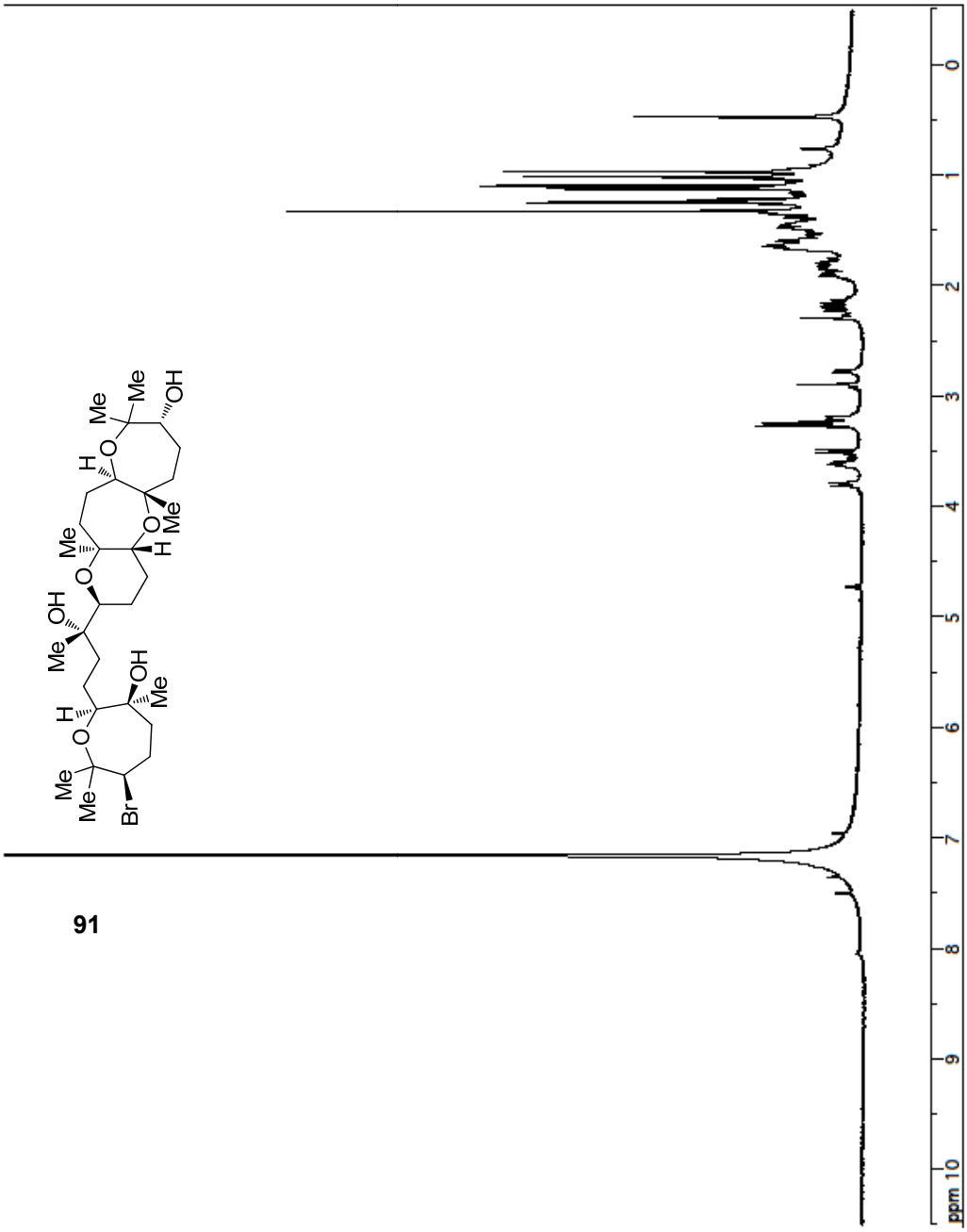
200
ppm



91

91
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OH
H
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H
Me
Me
O
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OH
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OH
Me
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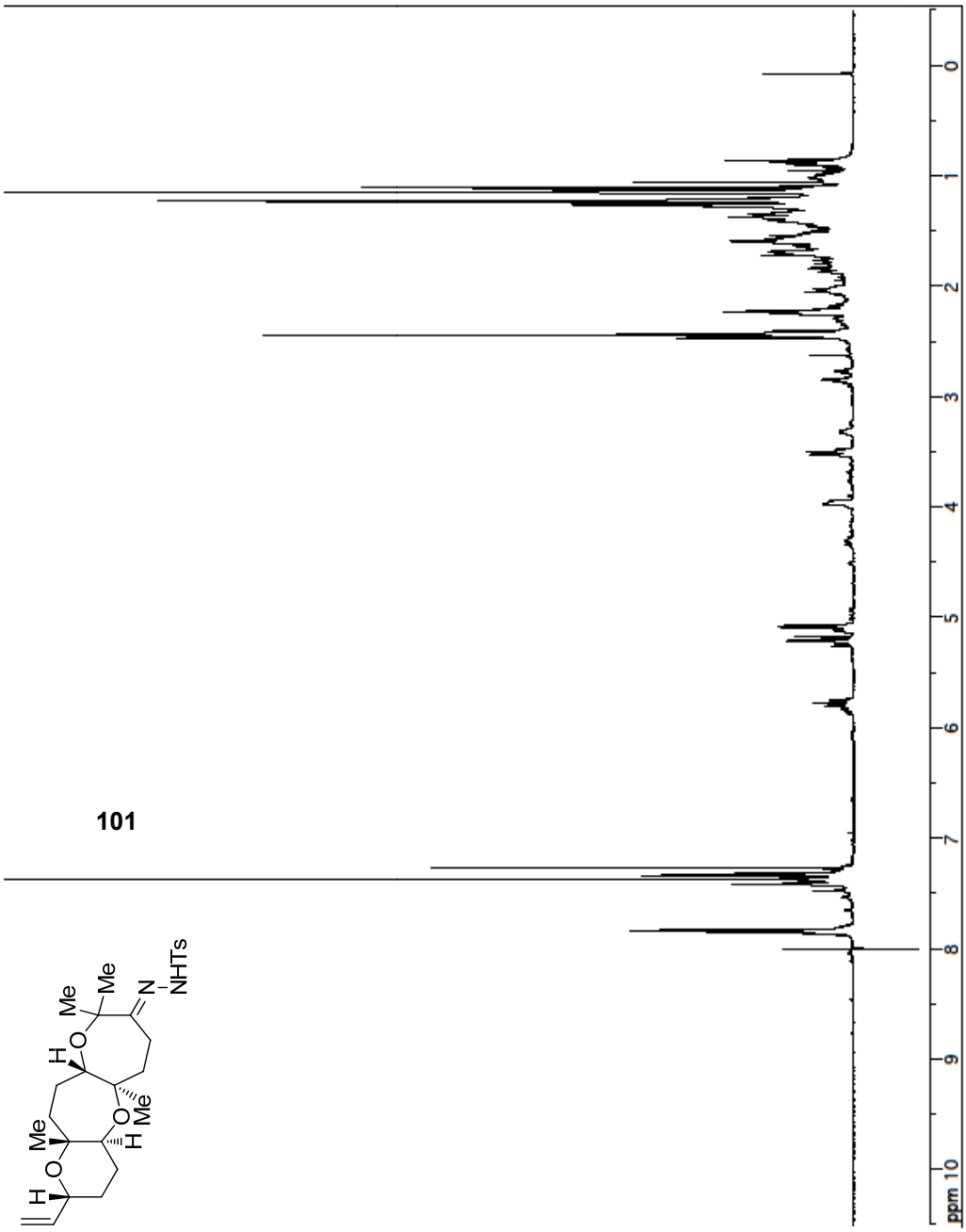
20
0


101
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Me
Me
H
O
N
NHTs
H
O
Me
O
H
Me
ppm
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7
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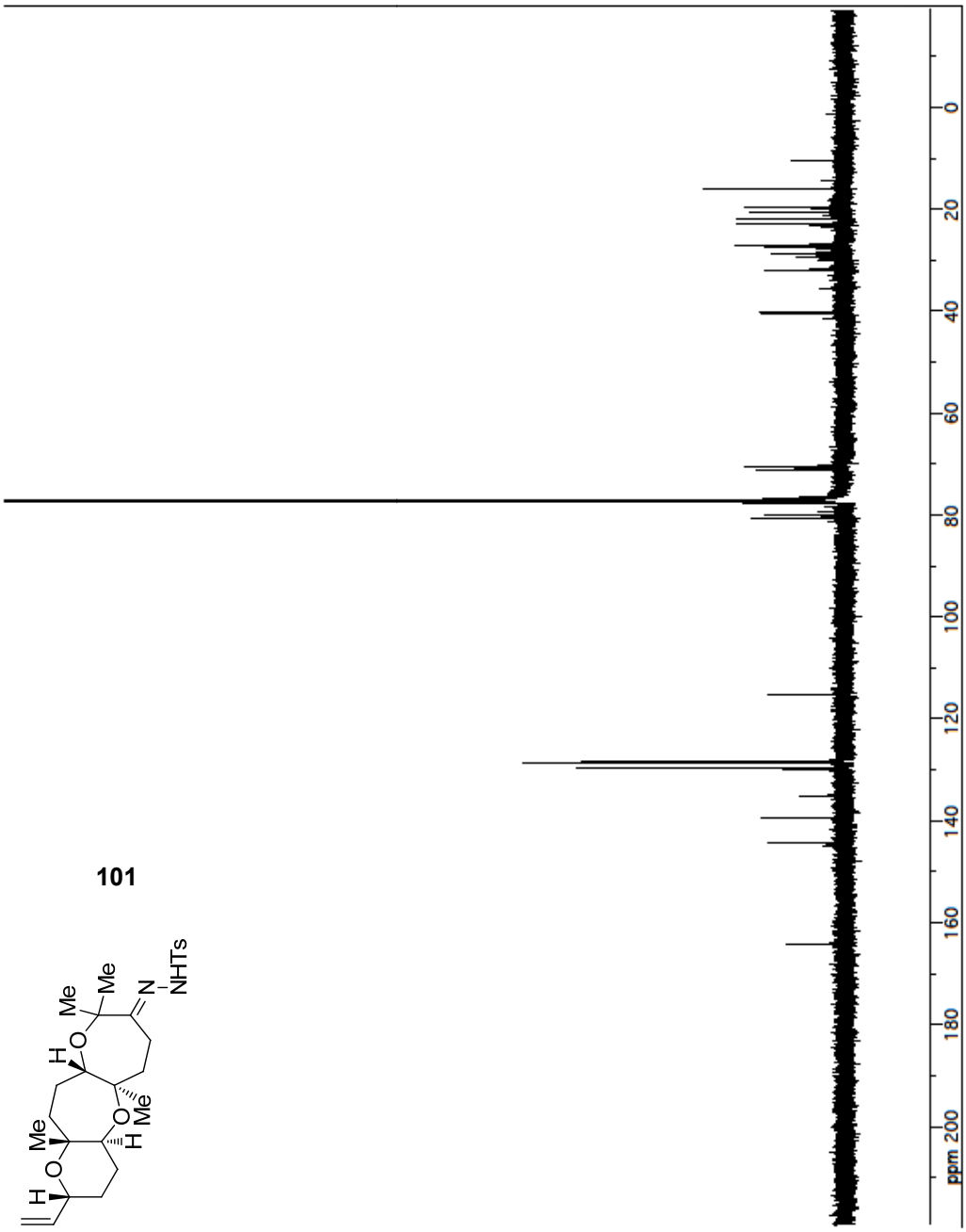
5
4
3
2
1
0


101
Me
Me
Me
H
O
N
NHTs
H
O
Me
O
H
Me
ppm 200
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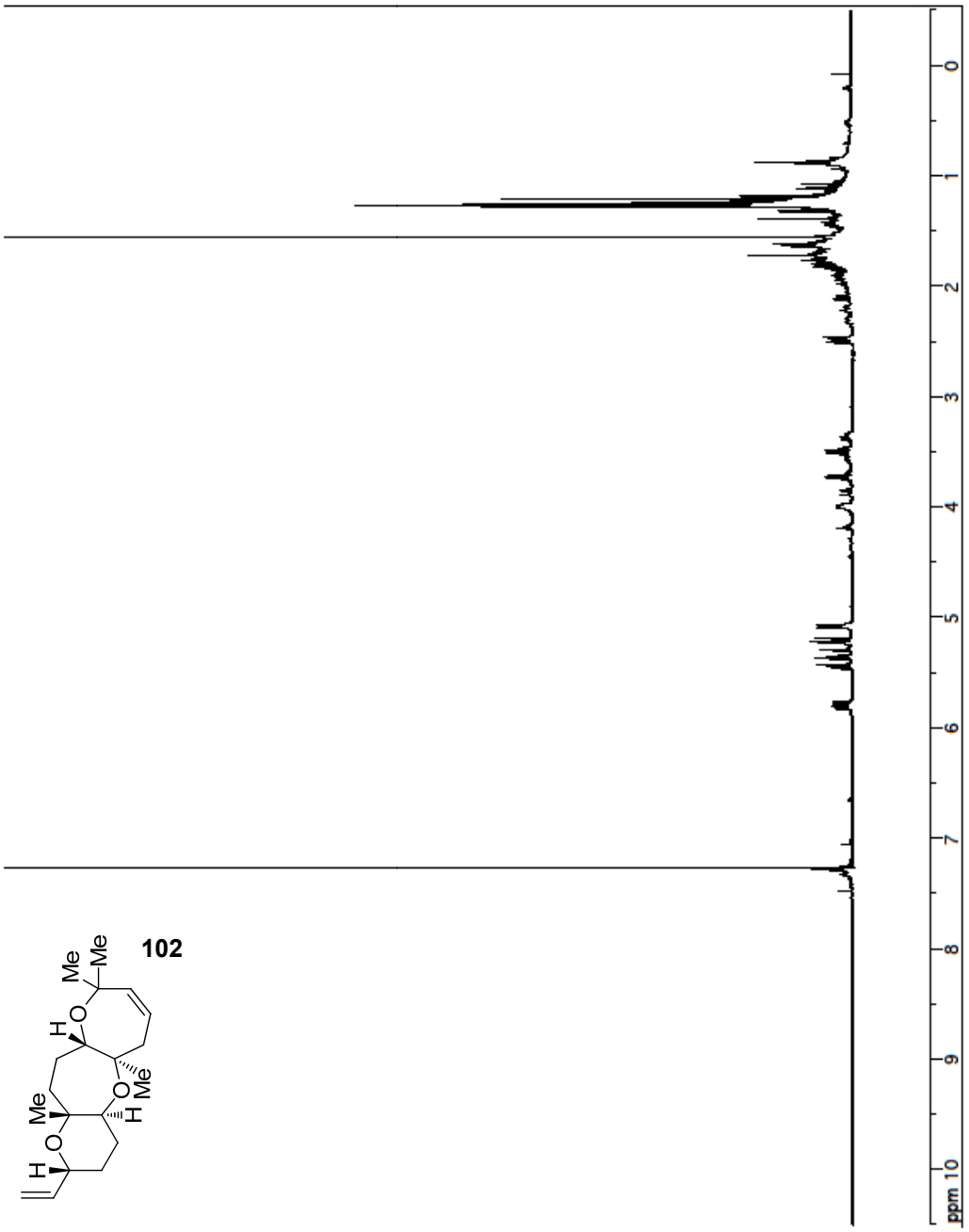
140
120
100
80
60
40
20
0


102
Me
Me
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Me
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Me
Me
O
H
ppm
10
9
8
7
6
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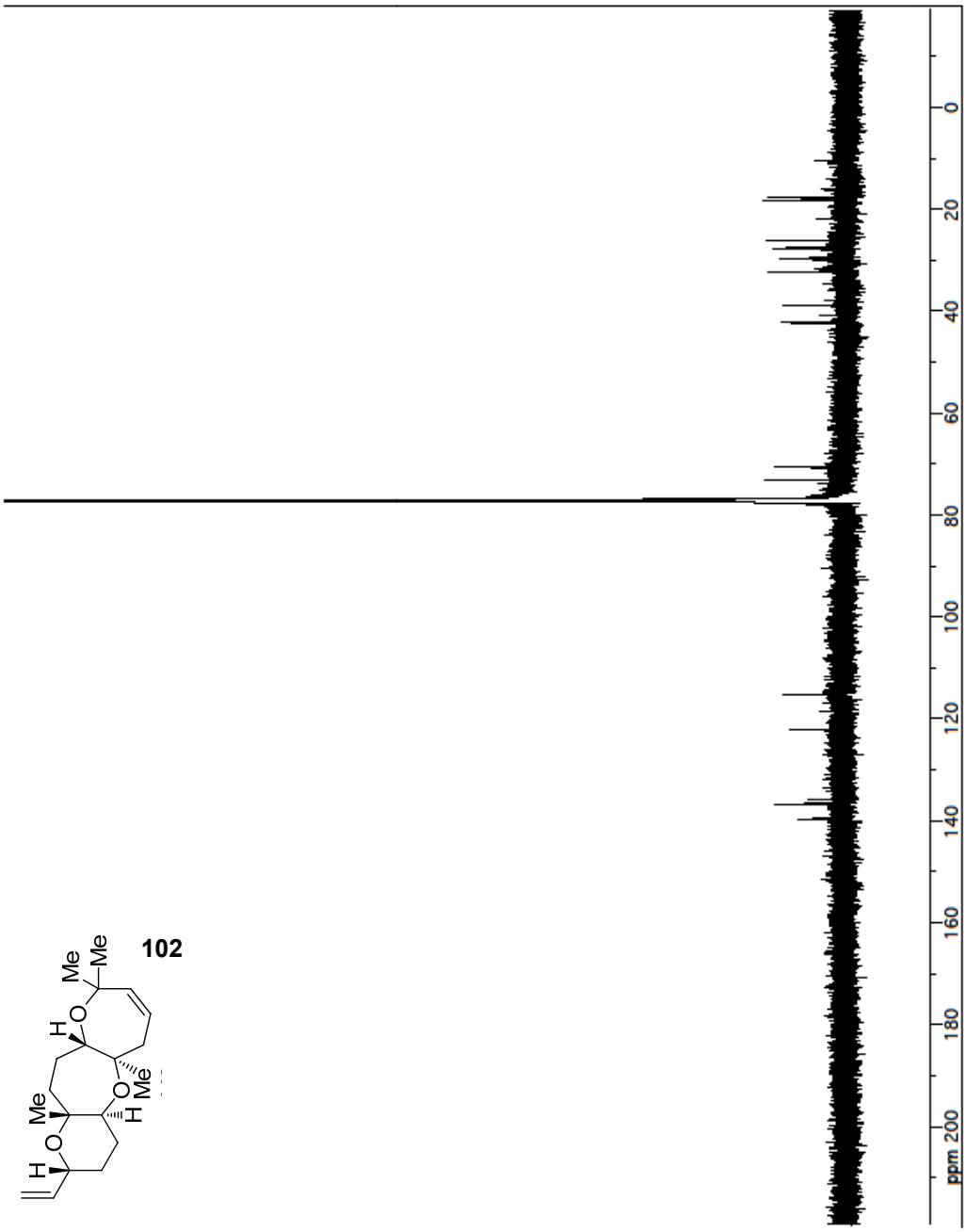
1
0


102
Me
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O
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O
H
Me
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H
ppm 200
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160
140
120
100
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60
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20
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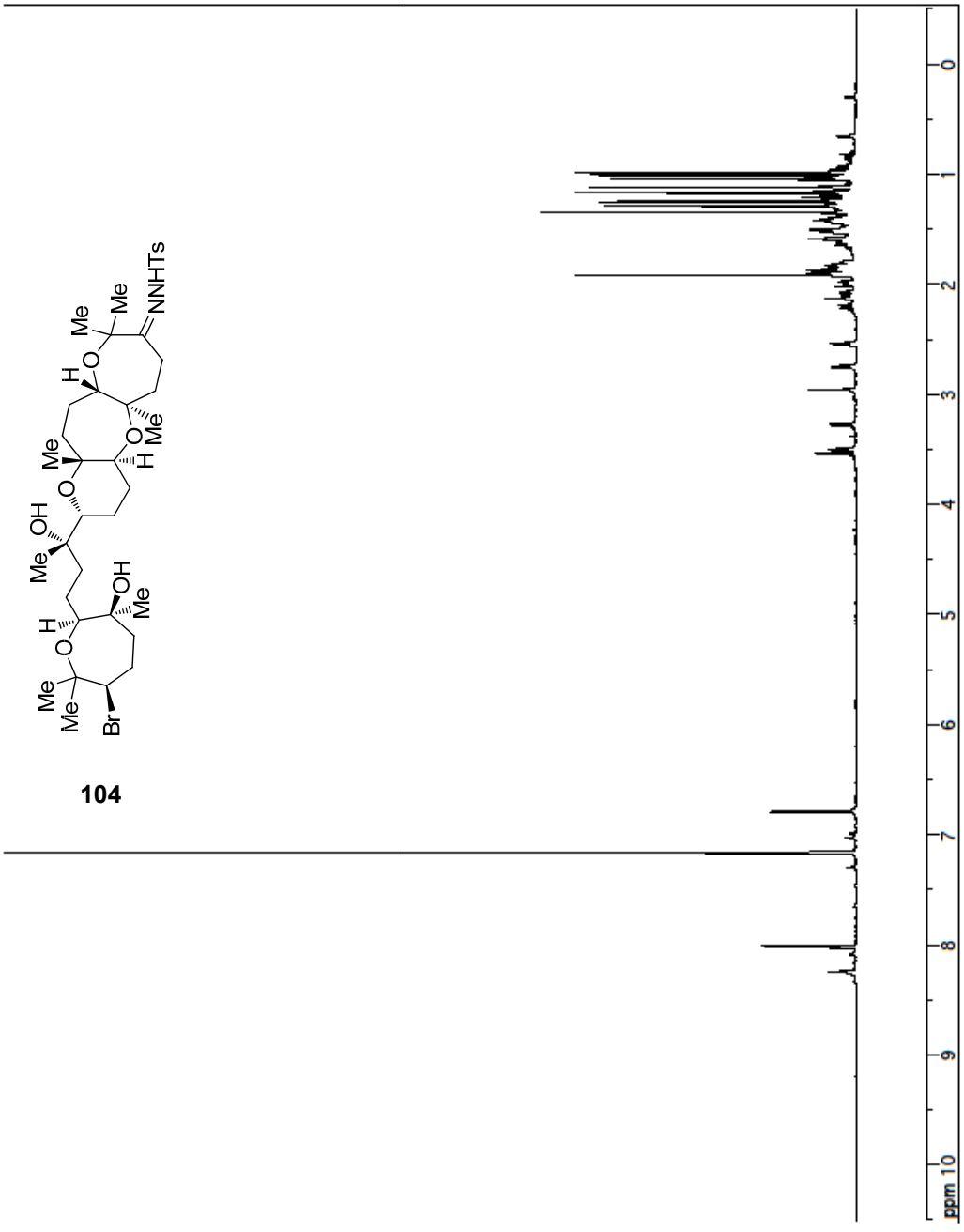
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NNHTs
H
O
Me
O
H
Me
Me
OH
O
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Me
Me
Me
Br
104
ppm 10
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7
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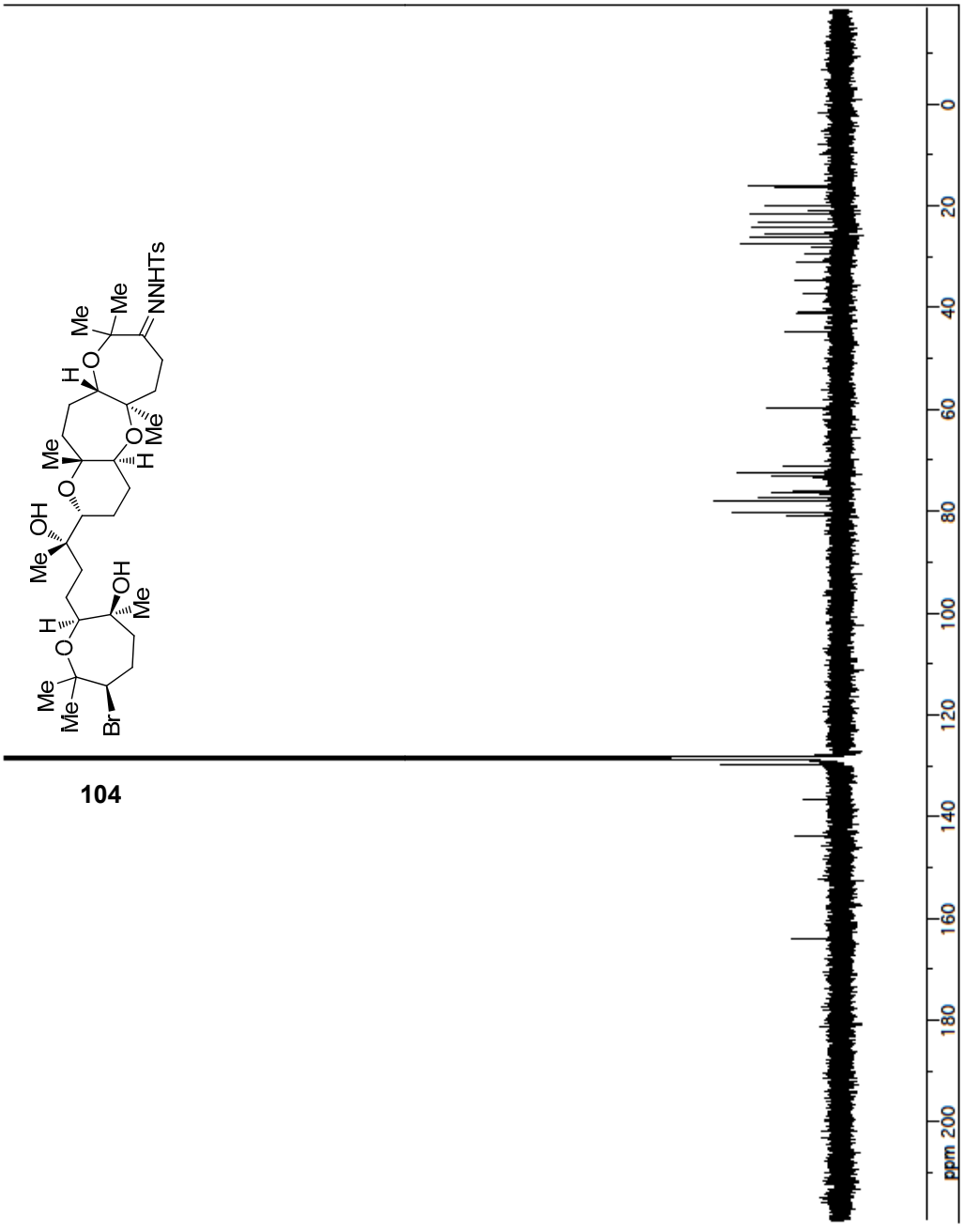
4
3
2
1
0


104
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Me
Br
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O
OH
Me
Me
OH
Me
O
Me
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O
Me
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NNHTs
ppm 200
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140
120
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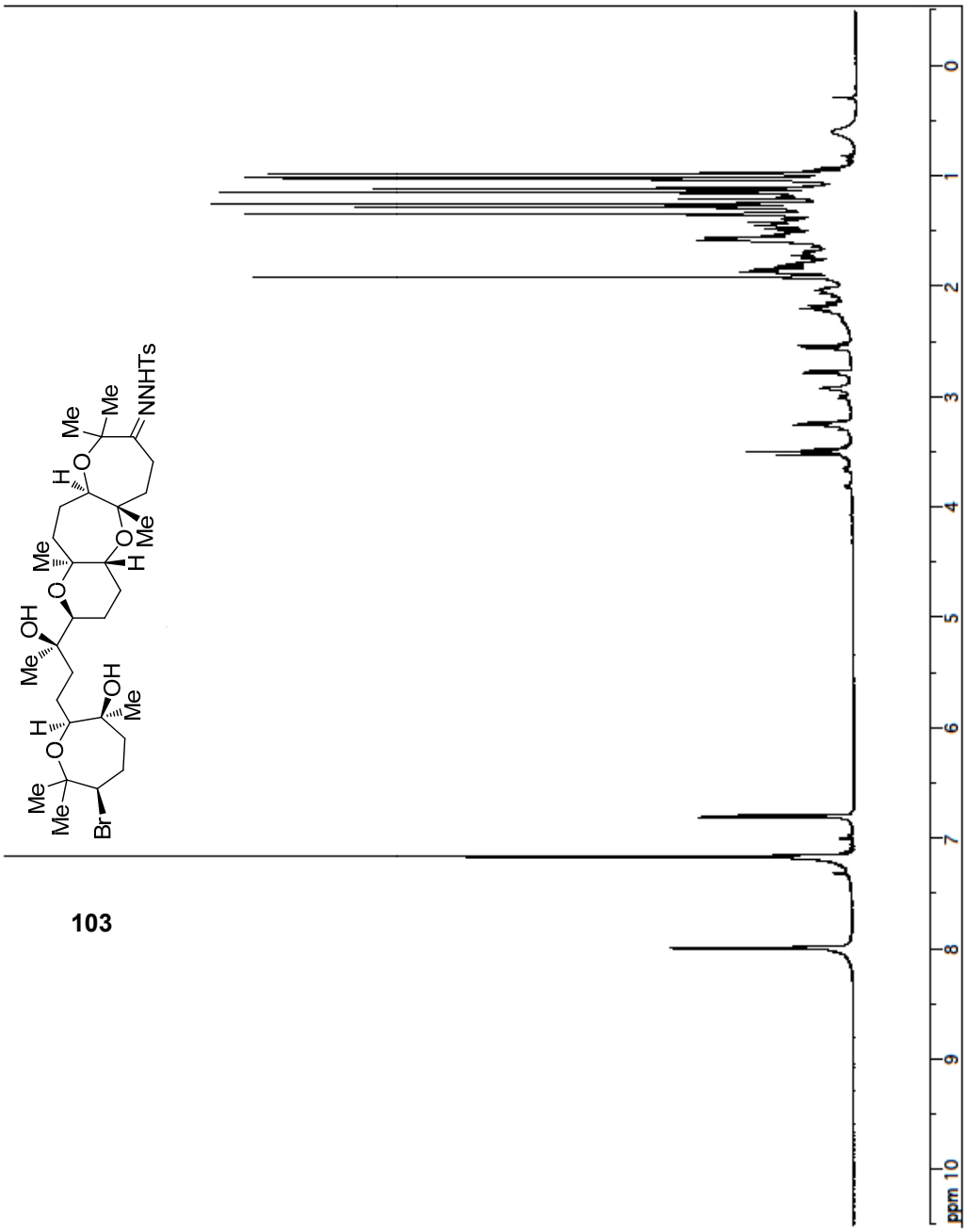
60
40
20
0


Me
Me
NNHTs
H
O
Me
Me
O
H
Me
OH
Me
O
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OH
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Me
Me
Br
ppm 10
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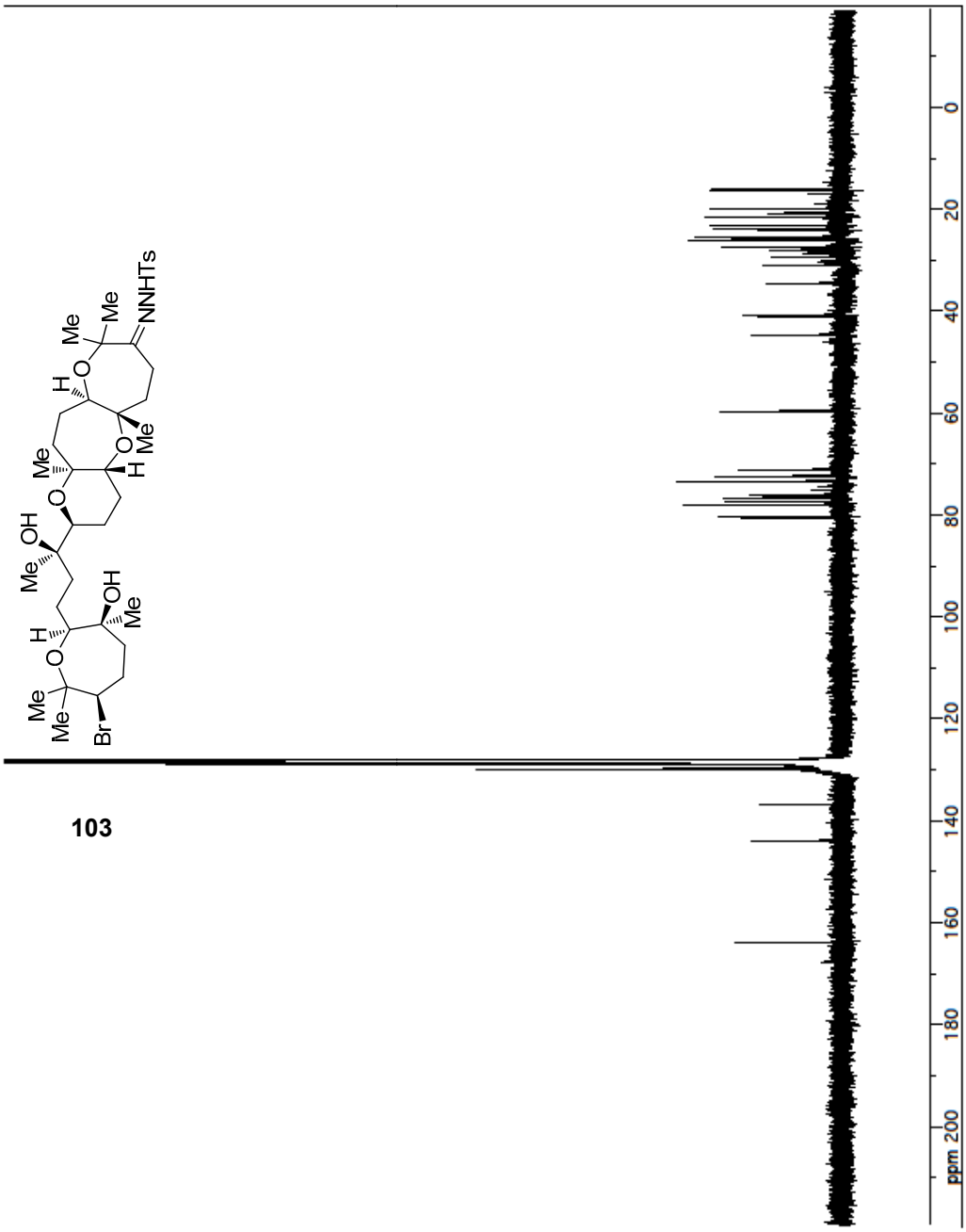
8
7
6
5
4
3
2
1
0

103


Me
Me
NNHTs
H
O
Me
O
H
Me
Me
OH
O
Me
OH
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O
Me
Me
Br
103
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20
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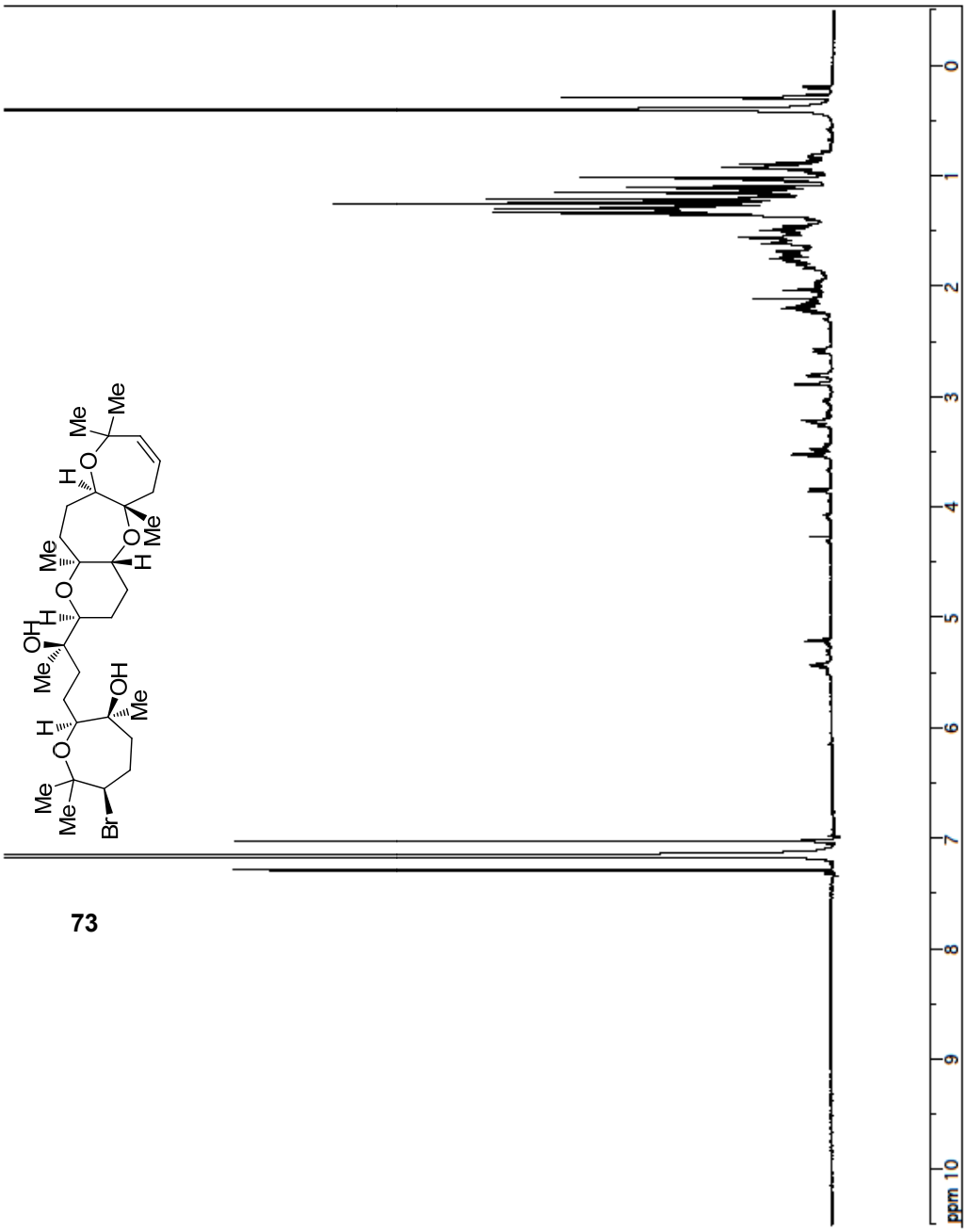
60
80
100
120
140
160
180
200
ppm



73

73
Me
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O
H
O
Me
Me
O
H
Me
OH
H
O
Me
H
OH
Me
Me
Me
Br
ppm 200
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160
140
120
100
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60
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20
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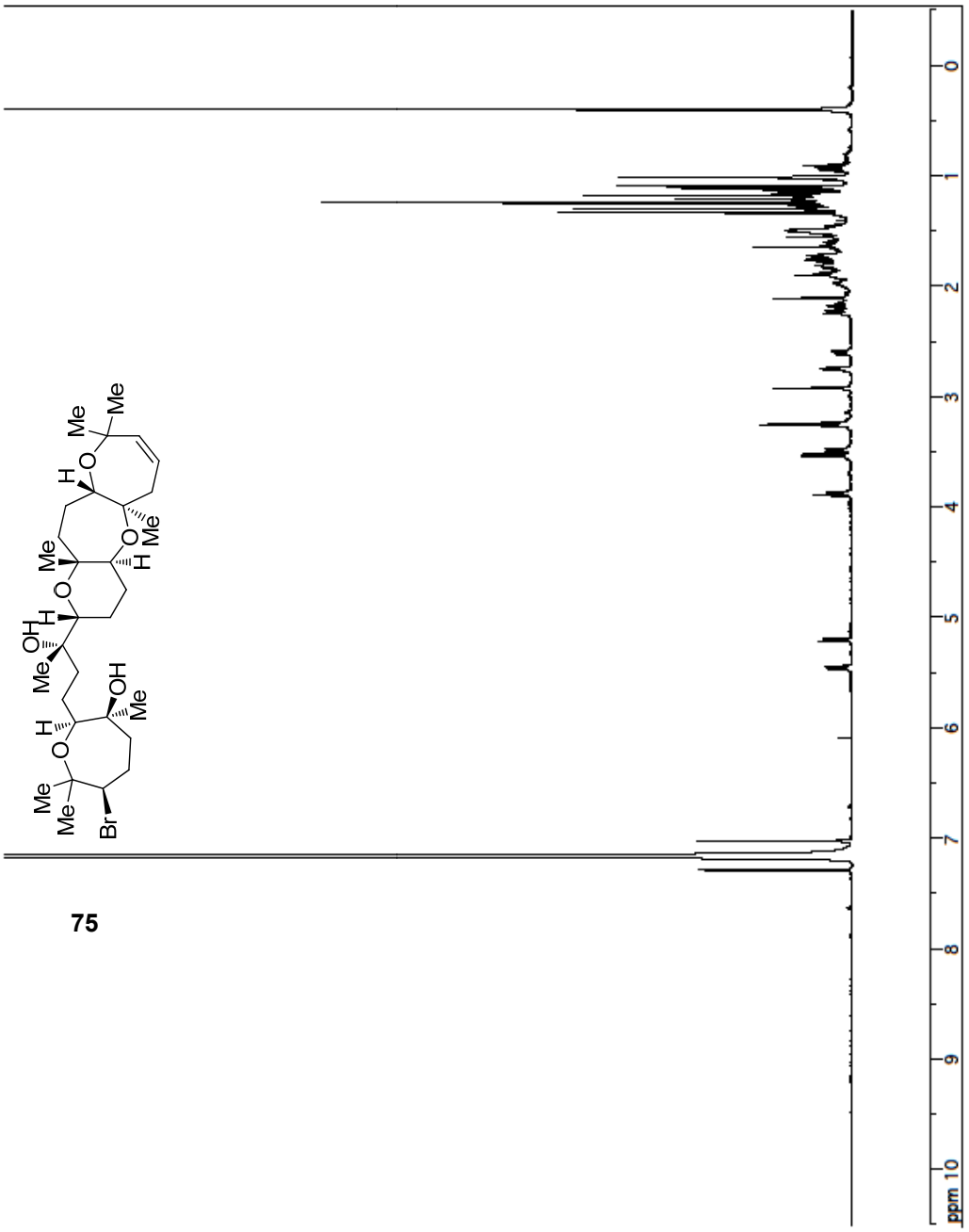
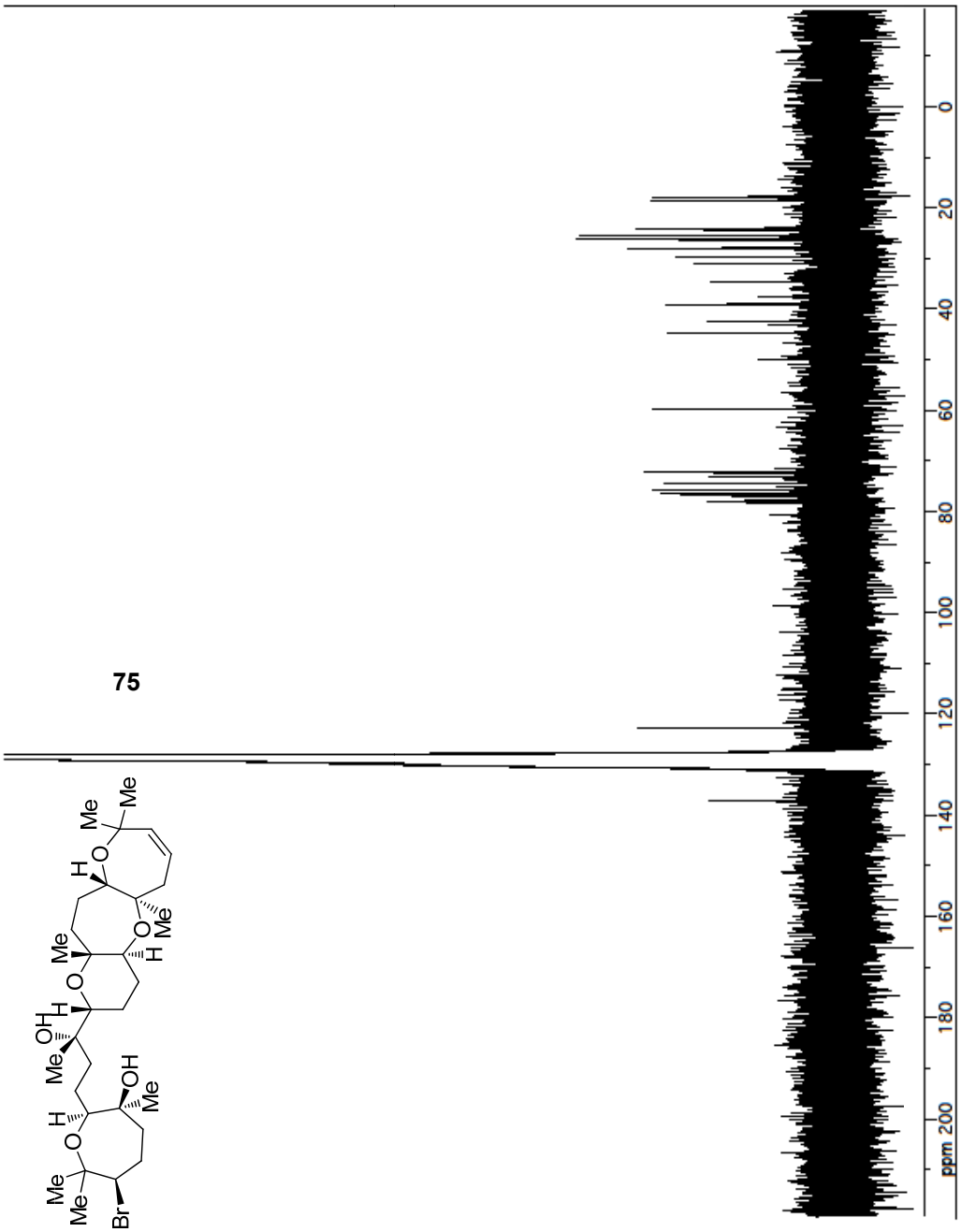


75


75
Me
Me
O
H
O
Me
H
Me
Me
O
H
OH
Me
OH
H
Me
O
Me
Me
Br
ppm 200
180
160
140
120
100
80
60
40
20
0