

SUPPORTING INFORMATION ACCOMPANYING

Enantioselective Total Synthesis of (+)-Euphorikanin A

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5.1 General Methods

Unless stated otherwise, reactions were performed in dry solvents and under an atmosphere of nitrogen. Dry solvents were either purchased from commercial sources, or for larger quantities obtained from a purification column composed of activated alumina.

Generally, chemicals were purchased from commercial sources (Acros, Alfa Aesar, Fluka, TCI) and used without further purification. Martins Sulfurane was stored and weighed in a glove box to avoid contact to air and moisture. SmI_2 was prepared according to the literature procedure of Kagan and co-workers.¹ However, if reactions were performed with a commercial solution of SmI_2 purchased from Sigma-Aldrich, the same yields were achieved.

Aldehyde **8** was prepared according to a literature procedure from Altmann and co-workers, from commercial (*R*)-Roche ester.²

NMR spectra were recorded on Bruker DRX and Avance (400 MHz) or DRXII (500MHz) spectrometers at room temperature. Signals are reported relative to the residual signal of the undeuterated solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, dd = doublet of doublets, etc.) and integration.

Flash column chromatography was performed manually using glass columns with Sigma-Aldrich, 60 Å, 230–400 mesh silica gel using laboratory grade solvents. For small scale column chromatography, Et_2O was distilled prior to use to remove BHT, and stored under Argon in a brown glass bottle, while regularly being checked for peroxide formation

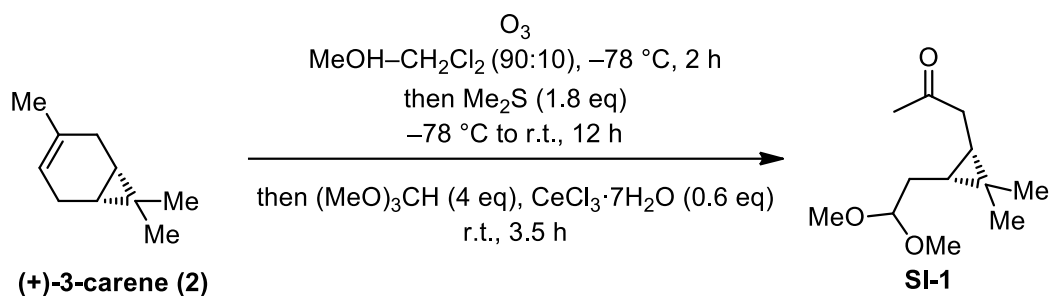
Thin layer chromatography was performed on glass plates pre-coated with silica gel (Merck, Silica gel 60 F₂₅₄). Compounds were visualized using UV light and/or standard staining techniques involving KMnO_4 or Seebach stain.

Infrared spectra (IR) were recorded on a Perkin Elmer Spectrum Two FT-IR (UATR) instrument as thin films and are reported as wavenumbers (cm^{-1}).

Optical rotation: Optical rotations were measured on a Jasco P-2000 Polarimeter, 10 cm, 1.5 mL cell.

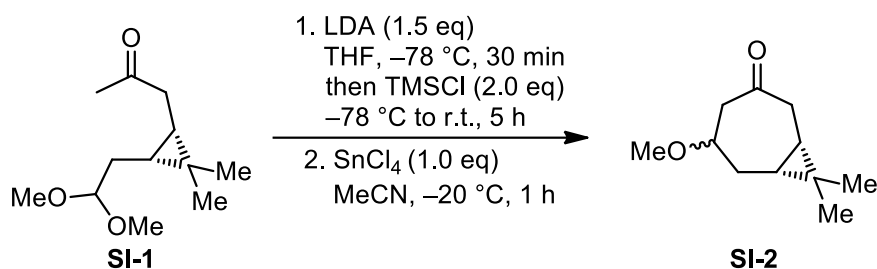
High resolution mass spectra (HRMS) were recorded on a Bruker Daltonics maXis ESI-Q-TOF by the ETH Zurich MS service.

Supporting Information



A nitrogen purged solution of (1S)-(+)-3-carene (**2**) (50 mL, 320 mmol, 90% purity, 1.0 eq) in MeOH-CH₂Cl₂ (90:10, 300 mL) at -78 °C was treated with ozone for 2 hours. After purging with nitrogen, dimethyl sulfide (42 mL, 570 mmol, 1.8 eq) was added and the reaction mixture was stirred for 12 hours while slowly warming up to room temperature. After addition of trimethoxymethane (150 mL, 1.4 mol, 4.3 eq) and cerium(III) chloride heptahydrate (66 g, 180 mmol, 0.60 eq) the reaction was stirred at room temperature for 3.5 hours and concentrated *in vacuo*. The concentrate was dissolved in saturated aqueous NaHCO₃ (250 mL), extracted with ether (3 x 500 mL), dried over Na₂SO₄ and concentrated *in vacuo*. The resulting yellow oil was used in the following step without further purification.

Supporting Information



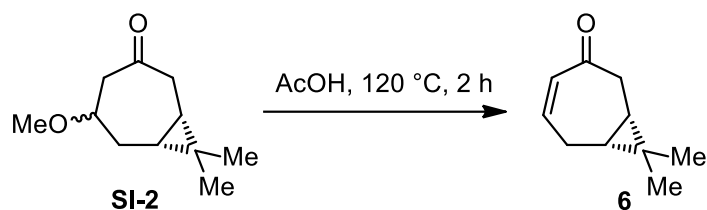
To a solution of freshly prepared 0.5 M solution of LDA in THF (0.60 L, 0.30 mol, 1.4 eq) at $-78\text{ }^{\circ}\text{C}$ was slowly added a solution of **SI-1** (49.0 g, 220 mmol, 1.0 eq) in THF (50 mL) over 30 minutes and the reaction was stirred for 30 minutes before adding freshly distilled TMSCl (57 mL, 450 mmol, 2.0 eq) and stirring for an additional 5 hours while warming to room temperature. After diluting with hexane (500 mL) the reaction mixture was quenched with saturated aqueous NaHCO_3 solution (500 mL), extracted with hexane (3 x 800 mL), dried over Na_2SO_4 and concentrated *in vacuo*.

To a well stirred solution of tin(IV) chloride (27.0 mL, 231 mmol, 1.0 eq) in MeCN (50 mL) at $-20\text{ }^{\circ}\text{C}$ was added dropwise a solution of the crude enol ether in MeCN (450 mL) over 1 hour. After stirring for 5 minutes the reaction was diluted with diethyl ether (200 mL), quenched with saturated aqueous NaHCO_3 (1.5 L), extracted with ether (6 x 2 L), dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (hexane/ Et_2O , 93:7) provided the desired product **SI-2** (13 g, 72 mmol, 33%) in an inconsequential mixture of diastereomers (*anti-syn* 2:1) as a colorless oil.

The analytical data matched previous reports

$^1\text{H-NMR}$: (400 MHz, Chloroform-*d*) δ 3.71 – 3.67 (m, 2H), 3.65 – 3.58 (m, 1H), 3.38 (s, 6H), 3.36 (s, 3H), 3.12 – 3.04 (m, 3H), 2.72 – 2.65 (m, 2H), 2.61 – 2.54 (m, 3H), 2.48 (dd, $J = 11.9, 7.1\text{ Hz}$, 1H), 2.34 (ddd, $J = 14.4, 9.2, 2.8\text{ Hz}$, 3H), 2.21 – 2.12 (m, 3H), 1.33 – 1.25 (m, 1H), 1.13 (s, 7H), 1.10 (s, 3H), 1.08 (s, 3H), 1.03 (s, 6H), 1.01 – 0.96 (m, 2H), 0.85 – 0.78 (m, 2H), 0.72 (dtd, $J = 8.0, 3.0, 1.8\text{ Hz}$, 2H).

$^{13}\text{C-NMR}$: (101 MHz, Chloroform-*d*) δ 209.8, 209.7, 78.6, 76.8, 56.6, 56.5, 49.3, 48.2, 39.7, 39.1, 29.9, 28.6, 28.5, 27.1, 22.7, 22.0, 21.2, 20.2, 20.1, 15.2, 15.2.

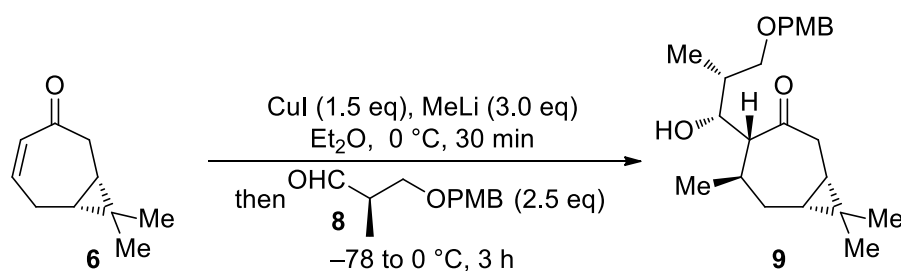


A well stirred solution of **SI-2** (13 g, 72 mmol, 1.0 eq) in acetic acid (0.30 L) was refluxed for 2 hours, quenched with saturated aqueous Na₂CO₃, extracted with ether, dried over Na₂SO₄. After careful concentration *in vacuo*, column chromatography (hexane–Et₂O, 97:3) yielded the desired product **6** (8.1 g, 43 mmol, 59%) as a pale-yellow oil that solidified in the freezer.

The analytical data is in agreement to previous reports of Yamaka³ and co-workers and Wood⁴ and co-workers.

¹H-NMR (400 MHz, Chloroform-*d*) δ 6.81 (ddd, *J* = 11.6, 8.7, 3.8 Hz, 1H), 5.96 (ddd, *J* = 11.6, 3.1, 2.2 Hz, 1H), 2.74 (ddd, *J* = 13.7, 5.0, 2.2 Hz, 1H), 2.56 (ddd, *J* = 16.4, 8.7, 6.1 Hz, 1H), 2.36 – 2.26 (m, 1H), 2.14 – 2.03 (m, 1H), 1.21 – 1.13 (m, 4H), 1.08 (s, 3H), 0.71 (ddd, *J* = 12.0, 9.1, 5.0 Hz, 1H).

¹³C-NMR (101 MHz, Chloroform-*d*) δ 201.7, 148.5, 133.8, 42.1, 31.4, 28.6, 25.8, 24.6, 23.0, 15.7.



To a well stirred solution of copper(I) iodide (4.8 g, 25 mmol, 1.5 eq) in diethyl ether (130 mL) at 0 °C was added a 1.6 M solution of methyl lithium in diethyl ether (32 mL, 0.050 mol, 3.0 eq) and after stirring for 5 minutes the mixture was cooled to –78 °C. At –78 °C **6** (2.5 g, 17 mmol, 1.0 eq) was added and the reaction was stirred for 30 minutes until completion was confirmed by TLC. **8** (8.7 g, 42 mmol, 2.5 eq) in diethyl ether (3 x 7 mL) was added over 10 minutes and the reaction was let warm to 0 °C over 3 hours. After quenching with saturated aqueous NaHCO₃ (250 mL), extracting with diethyl ether (3 x 250 mL), drying over Na₂SO₄, celite filtration and purification via column chromatography (hexane–Et₂O, 95:5 to 80:20) the desired diastereomer **9** (4.9 g, 13 mmol, 79%) was isolated as a yellow oil.

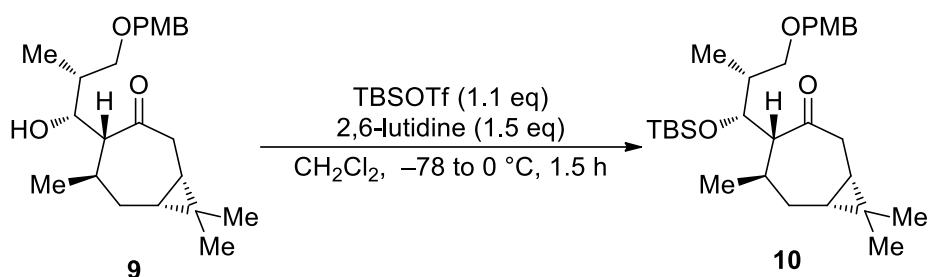
¹H-NMR (400 MHz, CDCl₃): δ 7.25 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.42 (s, 2H), 3.80 (s, 3H), 3.60 (dd, *J* = 9.1, 4.5 Hz, 1H), 3.56 – 3.51 (m, 1H), 3.49 – 3.40 (m, 1H), 2.97 (ddd, *J* = 8.7, 2.9, 0.9 Hz, 1H), 2.68 (dd, *J* = 17.8, 9.9 Hz, 1H), 2.36 – 2.25 (m, 1H), 2.20 (ddd, *J* = 17.8, 6.7, 1.1 Hz, 1H), 1.89 – 1.78 (m, 1H), 1.75 – 1.68 (m, 1H), 1.13 (d, *J* = 6.8 Hz, 3H), 1.08 (s, 3H), 1.07 – 0.99 (m, 1H), 0.95 – 0.87 (m, 7H), 0.76 (ddd, *J* = 9.9, 8.7, 6.7 Hz, 1H).

¹³C-NMR (101 MHz, CDCl₃): δ 218.9, 159.1, 130.6, 129.2, 113.7, 73.5, 72.8, 72.6, 55.3, 55.1, 40.8, 38.7, 32.0, 28.6, 28.0, 26.9, 22.1, 20.0, 19.1, 18.8, 15.2, 15.1.

IR (thin film, cm^{–1}): 3479, 2957, 2934, 2868, 2867, 1685, 1612, 1586, 1513, 1458, 1418, 1417, 1377, 1302, 1246, 1173, 1137, 1083, 1035, 986, 957, 909, 819, 757, 708, 687, 638, 563, 516.

HRMS (ESI) *m/z*: exact mass calculated for C₂₃H₃₄NaO₄ [M+Na]⁺, 397.2349; found: 397.2347.

[α]_D²⁵ = +89.7 (*c* = 0.5, CHCl₃).



To a solution of **9** (4.6 g, 12 mmol, 1.0 eq) in CH₂Cl₂ (125 mL) at -78 °C was added 2,6-lutidine (2.2 mL, 19 mmol, 1.5 eq). After stirring for 30 seconds TBSOTf (3.0 mL, 13 mmol, 1.1 eq) was added and the solution was warmed to RT over 1.5 hours. The mixture was quenched with saturated aqueous NH₄Cl (100 mL) and diluted with water (200 mL). After extracting with CH₂Cl₂ (4 x 200 mL) the combined organic phases were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Flash column chromatography (hexane–Et₂O, 95:5) provided the desired product **10** (4.7 g, 10 mmol, 78%) as a pale oil.

¹H-NMR (400 MHz, CDCl₃): δ 7.24 (d, *J* = 8.7, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.41 (s, 2H), 4.11 (dd, *J* = 8.1, 2.9 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 1H), 3.27 (dd, *J* = 9.4, 7.1 Hz, 1H), 2.64 (dd, *J* = 8.2, 4.0 Hz, 1H), 2.45 (ddd, *J* = 12.9, 7.6, 1.3 Hz, 1H), 2.29 (dd, *J* = 12.9, 9.4 Hz, 1H), 2.13 (qd, *J* = 7.1, 2.8 Hz, 1H), 2.01 – 1.92 (m, 1H), 1.70 (dt, *J* = 15.0, 5.3 Hz, 1H), 1.43 (s, 1H), 1.21 (t, *J* = 7.0 Hz, 1H), 1.06 (s, 3H), 1.02 (s, 3H), 1.00 (d, *J* = 7.0 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.90 (d, *J* = 15.2 Hz, 1H), 0.83 (s, 9H), 0.08 – -0.02 (m, 6H).

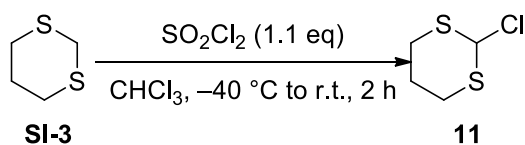
¹³C-NMR (101 MHz, CDCl₃): δ 210.6, 130.6, 129.2, 113.7, 74.8, 72.8, 71.9, 62.7, 55.3, 38.7, 38.6, 31.4, 28.6, 26.1, 26.0, 23.0, 21.3, 20.0, 19.1, 18.4, 15.3, 13.6, -3.8, -4.2.

IR (thin film, cm⁻¹): 2954, 2930, 2857, 1704, 1613, 1587, 1513, 1463, 1378, 1362, 1302, 1248, 1173, 1085, 1084, 1062, 1037, 959, 938, 871, 832, 774, 666, 641, 587, 586, 516.

HRMS (ESI) *m/z*: exact mass calculated for C₂₉H₄₈NaO₄Si [M+Na]⁺, 511.3214; found: 511.3209.

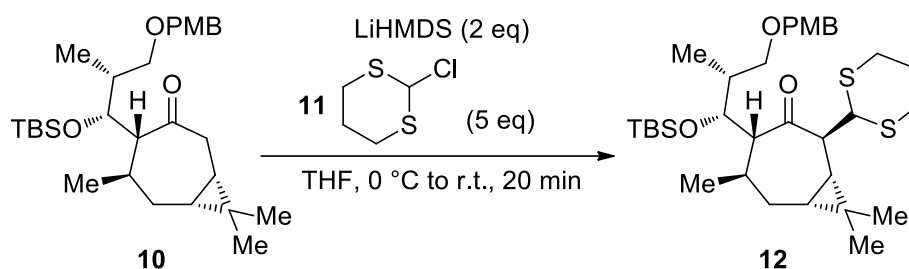
[α]_D²⁵ = +70.1 (*c* = 1, CHCl₃).

Supporting Information



To a well stirred solution of 1,3-dithiane (1.0 g, 0.010 mol, 1.0 eq) in chloroform (25 mL) at $-40\text{ }^\circ\text{C}$ was added dropwise sulfuryl chloride (0.89 mL, 11 mmol, 1.1 eq) in chloroform (5 mL) over 30 minutes. After stirring for an additional 30 minutes the solution was let warm to room temperature and stirred for 2 h. The solution was then cooled to $0\text{ }^\circ\text{C}$ and concentrated in vacuo.

Due to the high sensitivity of the crude product towards water the crude product was never taken out of a N_2 atmosphere. It was rather, dissolved in THF (10 mL), stirred at $0\text{ }^\circ\text{C}$ for 1 hour and used as the crude solution.



A solution of **10** (0.610 g, 1.25 mmol, 1.0 eq) in THF (12.0 mL) at 0 °C was treated with a 1 M solution of LiHMDS in THF (2.50 mL, 2.50 mmol, 2.0 eq) and stirred for 0.75 h. Crude **11** as a an approximately 1 M solution in THF (5.00 mL, 5.00 mmol, 4.0 eq) was added and the solution was warmed to room temperature. After stirring at room temperature for 20 minutes the reaction was quenched with sat. aq. NH₄Cl (15 mL), diluted with water (15 mL), extracted with diethyl ether (3 x 50 mL), dried over Na₂SO₄ and concentrated *in vacuo*. Column chromatography (hexane–Et₂O, 90:10) yielded the product **12** (678 mg, 1.12 mmol, 90%) as a light-yellow oil.

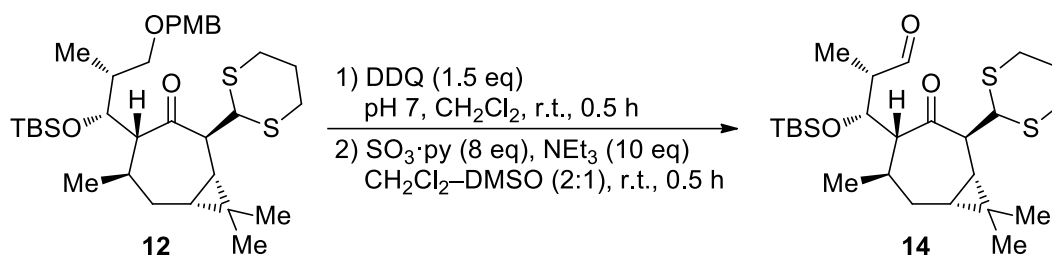
¹H-NMR: (400 MHz, CDCl₃) δ 7.24 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 4.62 (d, *J* = 6.3 Hz, 1H), 4.46 – 4.34 (m, 2H), 3.92 (dd, *J* = 4.9, 2.1 Hz, 1H), 3.80 (s, 3H), 3.60 (dd, *J* = 9.4, 4.1 Hz, 1H), 3.27 (dd, *J* = 9.4, 8.3 Hz, 1H), 3.05 – 2.89 (m, 2H), 2.92 – 2.85 (m, 1H), 2.85 – 2.73 (m, 2H), 2.55 (dd, *J* = 9.3, 6.3 Hz, 1H), 2.27 (ddt, *J* = 8.6, 6.8, 4.5 Hz, 1H), 2.17 – 2.02 (m, 2H), 1.91 – 1.75 (m, 1H), 1.67 – 1.57 (m, 1H), 1.25 – 1.16 (m, 1H), 1.15 – 1.08 (m, 6H), 1.07 (d, *J* = 6.8 Hz, 3H), 1.01 (s, 3H), 0.89 (s, 9H), 0.87 (s, 1H), 0.76 (t, *J* = 9.1 Hz, 1H), 0.11 (s, 3H), 0.04 (s, 3H).

¹³C-NMR: (101 MHz, CDCl₃) δ 212.5, 159.0, 131.0, 129.2, 113.7, 76.2, 72.6, 72.5, 61.4, 55.3, 53.3, 51.6, 37.6, 33.2, 31.1, 30.9, 29.6, 28.2, 26.2, 25.7, 24.2, 22.1, 21.0, 20.6, 18.4, 16.7, 15.8, –3.2, –4.7.

IR (thin film, cm^{–1}): 2953, 2928, 2857, 1698, 1612, 1586, 1513, 1463, 1422, 1378, 1361, 1302, 1275, 1248, 1172, 1087, 1039, 1005, 903, 869, 834, 775, 704, 669, 639, 587, 514, 432.

HRMS (ESI): *m/z*: exact mass calculated for C₃₃H₅₅O₄S₂Si [M+H]⁺, 607.3306; found: 607.3296.

[α]_D²⁵ = 169.3 (*c* = 1.0, CHCl₃)



To a well stirred solution of **12** (58 mg, 0.097 mmol, 1.0 eq) in CH_2Cl_2 -aqueous pH 8 buffer (10:1, 1.1 mL) was added DDQ (38 mg, 0.17 mmol, 1.8 eq), and the reaction was stirred at room temperature for 0.5 h. After quenching with sat. aq. NaHCO_3 (2 mL), extracting with CH_2Cl_2 (4 x 5 mL), drying over Na_2SO_4 , and concentrating *in vacuo* the crude product was redissolved in CH_2Cl_2 -DMSO (2:1, 1 mL). While constantly stirring at room temperature dry triethylamine (0.13 mL, 1.0 mmol, 10 eq) and $\text{SO}_3\cdot\text{py}$ (0.12 g, 0.76 mg, 8.0 mmol) were added consecutively. After stirring at room temperature for 0.5 h the reaction was quenched with sat. aq. NaHCO_3 (2 mL), extracted with diethyl ether (3 x 5 mL), dried over Na_2SO_4 , and concentrated *in vacuo*. Purification via column chromatography (hexane- Et_2O , 90:10) yielded the product **14** as a colorless oil (21 mg, 0.043 mmol, 45%).

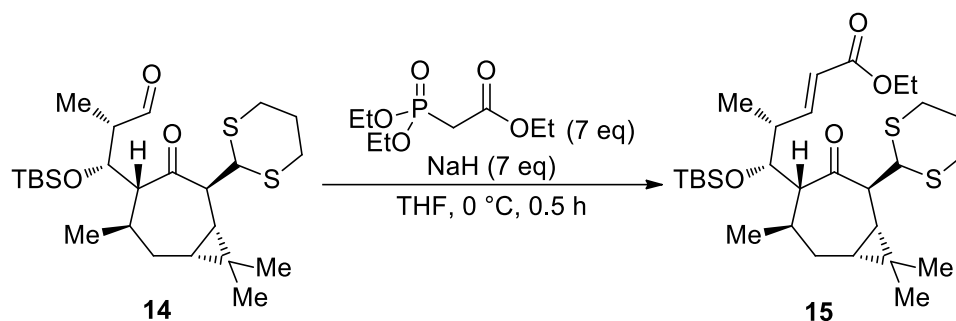
$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 9.86 (d, J = 3.5 Hz, 1H), 4.59 (d, J = 5.2 Hz, 1H), 4.13 (t, J = 2.3 Hz, 1H), 3.19 (ddd, J = 9.4, 2.0, 0.9 Hz, 1H), 3.03 – 2.92 (m, 3H), 2.81 (ddd, J = 14.1, 4.5, 3.2 Hz, 2H), 2.44 (dd, J = 8.5, 5.2 Hz, 1H), 2.20 (dtt, J = 9.4, 4.6, 2.4 Hz, 1H), 2.13 – 2.05 (m, 1H), 1.85 (dtt, J = 14.1, 12.4, 3.2 Hz, 1H), 1.69 – 1.56 (m, 1H), 1.21 (dd, J = 6.9, 4.9 Hz, 6H), 1.16 (s, 3H), 1.07 – 1.00 (m, 2H), 0.97 (s, 3H), 0.95 – 0.92 (m, 1H), 0.89 (s, 9H), 0.16 (s, 3H), 0.06 (s, 3H).

$^{13}\text{C-NMR}$: (101 MHz, CDCl_3) δ 214.3, 206.0, 76.0, 60.7, 54.0, 52.6, 49.9, 33.1, 31.1, 30.7, 30.1, 28.2, 25.9, 25.4, 23.2, 21.9, 20.8, 20.3, 18.1, 15.6, 14.4, 3.4, 5.2.

IR (thin film, cm^{-1}): 2954, 2929, 2899, 2858, 1720, 1698, 1463, 1422, 1389, 1378, 1361, 1309, 1276, 1253, 1223, 1186, 1144, 1092, 1034, 1005, 938, 902, 869, 833, 812, 775, 732, 704, 670, 646, 586, 502, 449, 407.

HRMS (ESI): m/z : exact mass calculated for $\text{C}_{25}\text{H}_{44}\text{NaO}_3\text{S}_2\text{Si}$ $[\text{M}+\text{Na}]^+$, 507.2393; found: 507.2396.

$[\alpha]_{\text{D}}^{25}$ = 79.7 (c = 0.75, CHCl_3)



To a well stirred solution of NaH (7 mg, 0.2 mmol, 7 eq) in THF (0.3 mL) was added ethyl 2-(diethoxyphosphoryl)acetate (0.03 mL, 0.2 mmol, 7 eq) at 0 °C. After 10 min **14** (11 mg, 0.023 mmol, 1.0 eq) in THF (0.3 mL) was added. After stirring at 0 °C for 0.5 h the reaction was quenched with sat. aq. NH₄Cl (2 mL), diluted with water (2 mL), extracted with diethyl ether (3 x 5 mL), dried over Na₂SO₄, and concentrated *in vacuo*. Column chromatography (hexane–Et₂O, 90:10) yielded the product **15** (8 mg, 0.02 mmol, 65%) as a colorless oil.

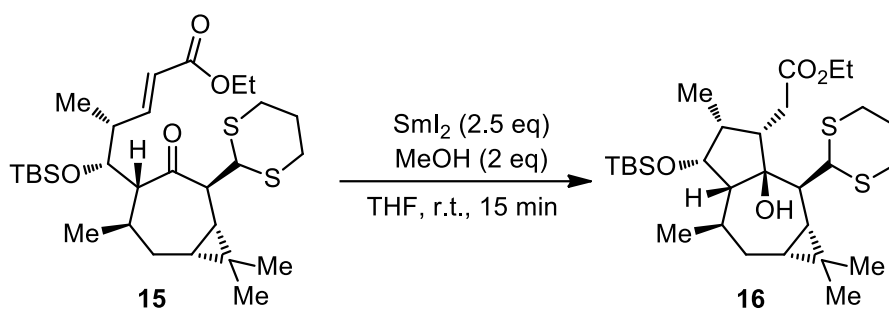
¹H-NMR: (500 MHz, Chloroform-*d*) δ 7.26 – 7.20 (m, 1H), 5.79 (dd, J = 15.9, 0.9 Hz, 1H), 4.61 (d, J = 5.8 Hz, 1H), 4.22 – 4.11 (m, 2H), 3.91 (dd, J = 3.3, 2.0 Hz, 1H), 3.11 – 2.92 (m, 4H), 2.84 – 2.79 (m, 2H), 2.47 (dd, J = 9.0, 5.7 Hz, 1H), 2.17 (dddd, J = 9.3, 6.8, 4.6, 2.9 Hz, 1H), 2.12 – 2.07 (m, 1H), 1.90 – 1.81 (m, 1H), 1.56 (s, 1H), 1.27 (t, J = 7.1 Hz, 4H), 1.14 – 1.12 (m, 6H), 0.98 (s, 3H), 0.93 (s, 10H), 0.86 (d, J = 6.9 Hz, 1H), 0.14 (s, 3H), 0.06 (s, 3H).

¹³C-NMR: (126 MHz, Chloroform-*d*) δ 152.9, 120.3, 61.2, 60.0, 53.7, 52.1, 40.7, 32.8, 31.1, 30.8, 30.0, 28.2, 26.1, 25.5, 23.8, 22.0, 20.8, 20.4, 20.2, 18.3, 15.7, 14.3, -3.1, -4.9.

IR (thin film, cm⁻¹): 2954, 2928, 2857, 1718, 1698, 1649, 1463, 1422, 1377, 1304, 1254, 1180, 1146, 1089, 1054, 1034, 1005, 989, 938, 904, 835, 776, 729, 670, 588

HRMS (ESI): m/z : exact mass calculated for C₂₉H₅₁O₄S₂Si [M+H]⁺, 555.2993; found: 555.2991.

[α]_D²⁵ = 273.5 (c = 0.4, CHCl₃)



To a solution of **15** (8.0 mg, 0.014 mmol, 1.0 eq) in degassed THF (2 mL) under argon was added MeOH (2.3 μL , 0.058 mmol, 2.5 eq). While stirring a 0.1 M Sml_2 solution in THF (0.36 mL, 0.036 mmol, 2.5 eq) was added until the blue color persisted. After stirring at room temperature for 25 minutes the reaction was quenched with sat. aq. NaHCO_3 (3 mL) and sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$ (3 mL), extracted with diethyl ether (3 x 10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. After purification via flash column chromatography (hexane– Et_2O , 75:25) the purified product **16** (6.3 mg, 0.011 mmol, 78%) was obtained as a pale-yellow oil.

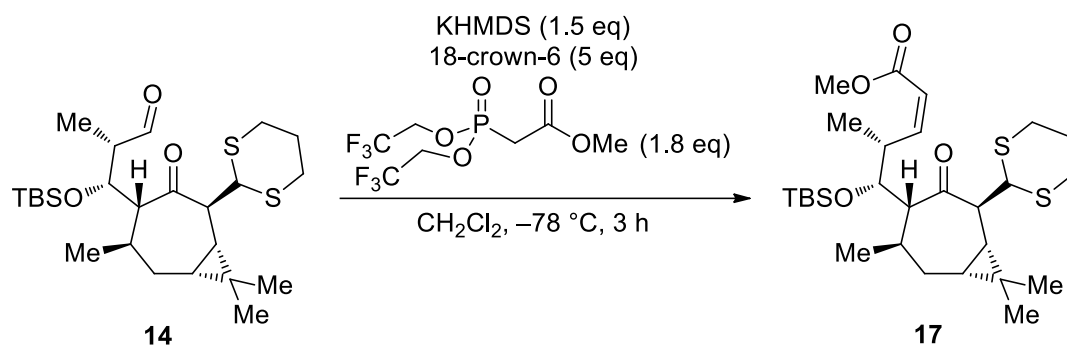
$^1\text{H-NMR}$ (500 MHz, Chloroform-*d*) δ 4.46 (d, J = 2.3 Hz, 1H), 4.39 (t, J = 6.5 Hz, 1H), 4.19 – 4.09 (m, 2H), 3.06 – 2.99 (m, 2H), 2.82 – 2.71 (m, 4H), 2.55 (ddd, J = 9.5, 6.4, 3.2 Hz, 1H), 2.37 – 2.29 (m, 1H), 2.16 (ddt, J = 8.8, 6.4, 3.2 Hz, 1H), 2.11 – 2.06 (m, 1H), 1.98 – 1.85 (m, 3H), 1.51 – 1.47 (m, 1H), 1.41 – 1.35 (m, 1H), 1.26 (d, J = 6.7 Hz, 3H), 1.12 (d, J = 2.4 Hz, 6H), 1.02 (d, J = 6.6 Hz, 3H), 0.96 – 0.90 (m, 13H), 0.85 (dd, J = 5.9, 3.2 Hz, 1H), 0.07 (s, 3H), 0.05 (s, 3H).

$^{13}\text{C-NMR}$: (126 MHz, Chloroform-*d*) δ 90.2, 61.9, 60.6, 52.5, 50.6, 43.8, 38.1, 33.0, 32.2, 32.1, 29.9, 29.2, 29.1, 28.7, 26.6, 26.4, 25.1, 24.9, 20.9, 19.0, 17.4, 14.3, 12.3, -3.0, -3.9.

IR (thin film, cm^{-1}): 2930, 2926, 2820, 1756, 1750, 1733, 1490, 1375, 1249, 830.

HRMS (ESI): m/z : exact mass calculated for $\text{C}_{29}\text{H}_{52}\text{NaO}_4\text{S}_2\text{Si}$ [$\text{M}+\text{Na}$] $^+$, 579.2968; found: 579.2964.

$[\alpha]_{\text{D}}^{25}$ = -0.4 (c = 0.2, CHCl_3).



To a well stirred solution of 18-crown-6 (1.36 g, 5.16 mmol, 5.00 eq) in THF (16 mL) at $-78\text{ }^\circ\text{C}$ was added 0.5 M solution of KHDMS in PhMe (3.09 mL, 1.55 mmol, 1.5 eq) and the reaction was stirred for 20 minutes. After addition of **14** (0.500 g, 1.03 mmol, 1.0 eq) and stirring for 3 hour the reaction was quenched with sat. aq. NH_4Cl (10 mL), extracted with diethyl ether (3 x 50 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography (hexane– Et_2O , 97:3) yielded the product **17** (435 mg, 0.804 mmol, 78%) as a pure, pale yellow, amorphous solid. No *E*-isomer was observed.

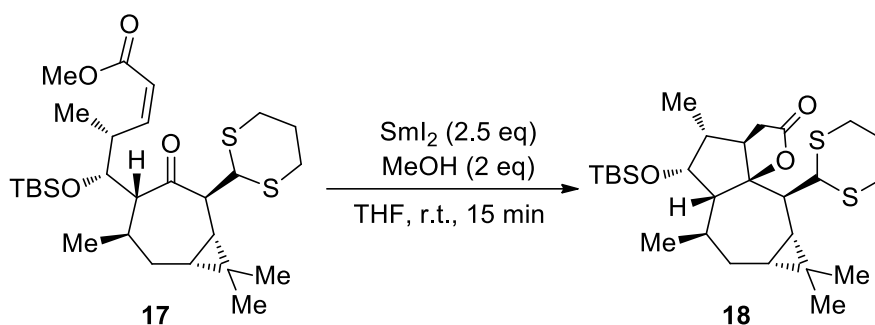
$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 6.71 (dd, $J = 11.8, 10.1$ Hz, 1H), 5.70 (d, $J = 11.8$ Hz, 1H), 4.61 (d, $J = 5.2$ Hz, 1H), 4.24 – 4.07 (m, 1H), 3.98 (s, 1H), 3.70 (s, 3H), 3.10 (d, $J = 8.3$ Hz, 1H), 3.05 – 2.88 (m, 2H), 2.86 – 2.76 (m, 2H), 2.42 (dd, $J = 8.4, 5.3$ Hz, 1H), 2.23 – 2.10 (m, 1H), 2.13 – 2.02 (m, 1H), 1.99 – 1.78 (m, 1H), 1.55 – 1.47 (m, 1H), 1.17 – 1.08 (m, 9H), 0.97 (d, $J = 2.2$ Hz, 2H), 0.95 (s, 3H), 0.92 (s, 9H), 0.87 (d, $J = 7.4$ Hz, 1H), 0.17 (s, 3H), 0.06 (s, 3H).

$^{13}\text{C-NMR}$: (101 MHz, CDCl_3) δ 213.9, 166.8, 153.2, 116.9, 75.9, 61.6, 53.8, 52.5, 51.1, 36.5, 32.0, 31.0, 30.6, 30.1, 28.2, 26.1, 25.5, 23.3, 21.9, 21.2, 20.8, 20.3, 18.2, 15.6, -3.3 , -5.1 .

IR (thin film, cm^{-1}): 2953, 2929, 2858, 1723, 1697, 1463, 1435, 1276, 1253, 1193, 1176, 1114, 1088, 1053, 1034, 1023, 1006, 902, 836, 775.

HRMS (ESI): m/z : exact mass calculated for $\text{C}_{28}\text{H}_{48}\text{NaO}_4\text{S}_2\text{Si}$ $[\text{M}+\text{Na}]^+$, 563.2655; found: 563.2645.

$[\alpha]_{\text{D}}^{25}$ = 69.5 ($c = 1.0$, CHCl_3)



To a solution of **17** (412 mg, 0.609 mmol, 1.0 eq) in degassed THF (20 mL) under argon was added MeOH (99.0 μL , 2.44 mmol, 4.0 eq). While stirring a 0.1 M Sml_2 solution in THF (14.8 mL, 1.48 mmol, 2.5 eq) was added until the blue color persisted. After stirring at room temperature for 15 minutes the reaction was quenched with sat. aq. NaHCO_3 (15 mL) and sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$ (15 mL), extracted with diethyl ether (3 x 50 mL), dried over Na_2SO_4 and concentrated *in vacuo*. After purification via flash column chromatography (hexane– Et_2O , 90:10) the purified product **18** (277 mg, 0.542 mmol, 89%) was obtained as a pale-yellow oil.

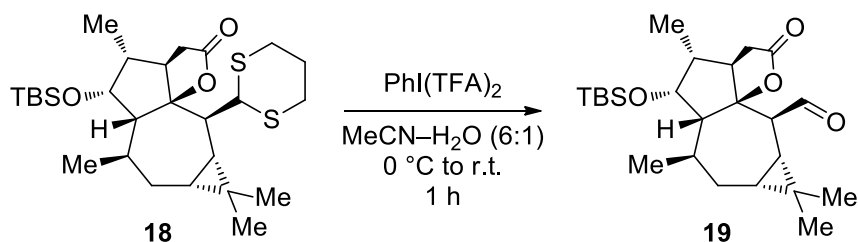
$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 4.40 (d, J = 3.1 Hz, 1H), 4.03 (t, J = 2.6 Hz, 1H), 3.25 – 3.12 (m, 1H), 3.01 – 2.79 (m, 4H), 2.65 (td, J = 10.4, 2.5 Hz, 1H), 2.32 (dd, J = 10.1, 3.1 Hz, 1H), 2.29 – 2.17 (m, 1H), 2.06 (dt, J = 13.5, 4.0, 2.5 Hz, 1H), 1.94 – 1.53 (m, 6H), 1.08 (s, 7H), 1.05 (d, J = 6.7 Hz, 3H), 0.92 (s, 9H), 0.89 (d, J = 6.1 Hz, 3H), 0.80 (ddd, J = 10.0, 6.9, 1.9 Hz, 1H), 0.06 (d, J = 9.8 Hz, 6H).

$^{13}\text{C-NMR}$: (101 MHz, CDCl_3) δ 177.7, 98.4, 78.0, 66.1, 53.7, 46.4, 46.1, 45.1, 37.3, 32.2, 32.0, 31.2, 29.5, 27.5, 26.4, 26.1, 25.8, 23.1, 22.9, 19.0, 18.4, 16.2, 14.1, –3.4, –4.3.

IR (thin film, cm^{-1}): 2954, 2929 2892, 2858, 1767, 1461, 1422, 1413, 1376, 1361, 1333, 1303, 1276, 1254, 1208, 1194, 1152, 1138, 1099, 1081, 1022, 987, 963, 941, 914, 859, 835, 802, 773, 756, 710, 666, 646, 607, 547, 465.

HRMS (ESI): m/z : exact mass calculated for $\text{C}_{27}\text{H}_{46}\text{NaO}_3\text{S}_2\text{Si}$ $[\text{M}+\text{Na}]^+$, 533.255; found: 533.2548.

$[\alpha]_{\text{D}}^{25}$ = 65.9 (c = 1.0, CHCl_3)



To a solution of lactone **18** (211 mg, 0.413 mmol, 1.0 eq) in MeCN–H₂O (6:1, 7 mL) was added PIFA (444 mg, 1.03 mmol, 2.5 eq) at 0 °C. The mixture was warmed to room temperature and stirred for 1 h. After complete consumption of starting material, the mixture was transferred to a separation funnel and extracted with Et₂O (3 x 30 mL). The organic phases were combined, dried over Na₂SO₄, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexane–Et₂O, 80:20) to give **19** as colorless oil (165 mg, 0.392 mmol, 95%), which solidified in the freezer.

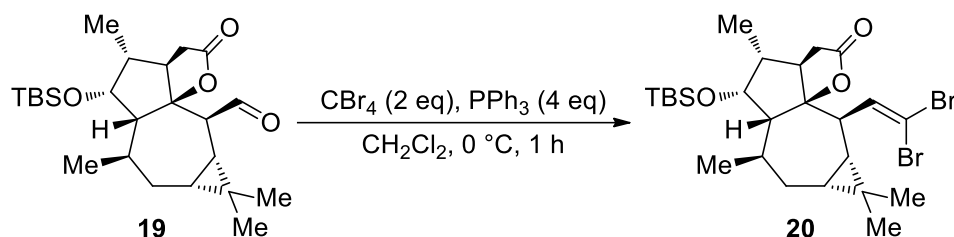
¹H-NMR (400 MHz, CDCl₃) δ 9.55 (d, *J* = 2.4 Hz, 1H), 4.00 (t, *J* = 3.0 Hz, 1H), 3.01 (dd, *J* = 18.4, 10.4 Hz, 1H), 2.79 (dd, *J* = 11.3, 2.4 Hz, 1H), 2.36 (td, *J* = 10.6, 2.8 Hz, 1H), 2.24 (dd, *J* = 18.6, 2.8 Hz, 1H), 2.07 (ddd, *J* = 6.8, 4.2, 2.5 Hz, 1H), 1.83 (dd, *J* = 4.7, 3.0 Hz, 1H), 1.82 – 1.77 (m, 2H), 1.68 (dq, *J* = 9.8, 6.7, 2.9 Hz, 1H), 1.14 (s, 3H), 1.10 (d, *J* = 7.0 Hz, 3H), 1.07 (s, 3H), 0.99 – 0.94 (m, 4H), 0.92 (s, 9H), 0.84 (dd, *J* = 11.3, 9.4 Hz, 1H), 0.08 – 0.07 (m, 6H).

¹³C-NMR (101 MHz, CDCl₃) δ 200.3, 177.6, 95.9, 80.7, 63.2, 55.4, 48.8, 46.4, 35.5, 30.3, 29.1, 29.0, 26.4, 23.6, 22.9, 22.4, 19.9, 18.3, 15.7, 13.9, -3.4, -4.3.

IR (thin film, cm⁻¹): 2927, 1776, 1728, 1462, 1253, 1029, 836, 775.

HRMS (ESI): *m/z*: exact mass calculated for C₂₄H₄₀NaO₄Si [M+Na]⁺, 443.2588; found: 443.2589.

[α]_D²⁵ = -1.3 (*c* = 0.3, CHCl₃).



To a well stirred solution of tetrabromomethane (237 mg, 0.713 mmol, 2.0 eq) in CH_2Cl_2 (3.5 mL) at $0\text{ }^\circ\text{C}$ was added triphenylphosphine (374 mg, 1.43 mmol, 4.0 eq) and the solution was stirred for 30 min at $0\text{ }^\circ\text{C}$. After addition of **19** (150 mg, 0.357 mmol, 1.0 eq) in CH_2Cl_2 (0.5 mL) and stirring at $0\text{ }^\circ\text{C}$ for 1 h, the reaction was quenched with sat. aq. NH_4Cl (10 mL), extracted with CH_2Cl_2 (3 x 20 mL), dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography (hexane– Et_2O 90:10) yielded the pure product **20** (148 mg, 0.257 mmol, 72%) as a colorless oil.

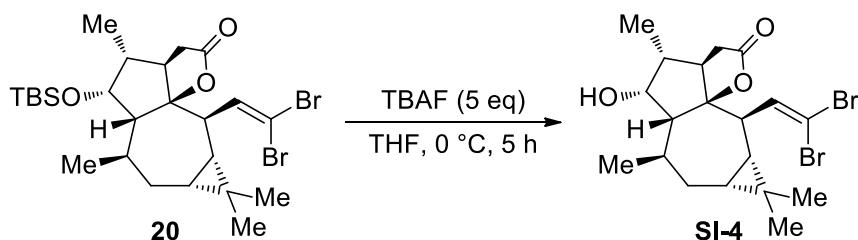
$^1\text{H-NMR}$ (400 MHz, Chloroform-*d*) δ 6.27 (d, $J = 10.2\text{ Hz}$, 1H), 4.00 (t, $J = 3.3\text{ Hz}$, 1H), 2.73 – 2.60 (m, 2H), 2.34 – 2.16 (m, 3H), 1.93 (t, $J = 3.1\text{ Hz}$, 1H), 1.79 – 1.62 (m, 3H), 1.15 (d, $J = 7.2\text{ Hz}$, 3H), 1.10 (s, 3H), 1.03 (s, 3H), 0.99 (d, $J = 6.7\text{ Hz}$, 3H), 0.93 (s, 9H), 0.80 (dd, $J = 9.6, 5.7\text{ Hz}$, 1H), 0.73 (t, $J = 9.6\text{ Hz}$, 1H), 0.08 (s, 6H).

$^{13}\text{C-NMR}$ (101 MHz, Chloroform-*d*) δ 138.6, 99.7, 81.9, 62.5, 48.8, 48.8, 45.8, 35.0, 31.4, 29.2, 28.3, 26.7, 26.5, 23.7, 22.6, 20.1, 18.5, 16.3, 14.1, -3.6, -3.9.

IR: 2955, 2929, 2859, 1775, 1462, 1377, 1257, 1193, 1154, 1118, 1072, 1024, 1004, 959, 940, 872, 836, 800, 774, 751.

HRMS (ESI) m/z : exact mass calculated for $\text{C}_{25}\text{H}_{40}\text{Br}_2\text{NaO}_3\text{Si}$ $[\text{M}+\text{Na}]^+$, 597.1006; found: 597.1011.

$[\alpha]_{\text{D}}^{25}$ = -0.4 ($c = 1.0$, CHCl_3).



To a well stirred solution of **20** (0.050 g, 0.087 mmol, 1.0 eq) in THF (1.7 mL) at 0 °C was added a 1 M solution of TBAF in THF (0.434 mL, 0.434 mmol, 5.0 eq) and the reaction was stirred at 0 °C for 5 h. After quenching the reaction with sat. aq. NaHCO₃ and extracting with diethyl ether (3 x 20 mL), the organic phases were dried over Na₂SO₄, concentrated *in vacuo*, and purified by flash column chromatography (hexane-Et₂O 80:20 to 50:50), yielding the desired product **SI-4** (36 mg, 0.078 mmol, 90%) colorless oil.

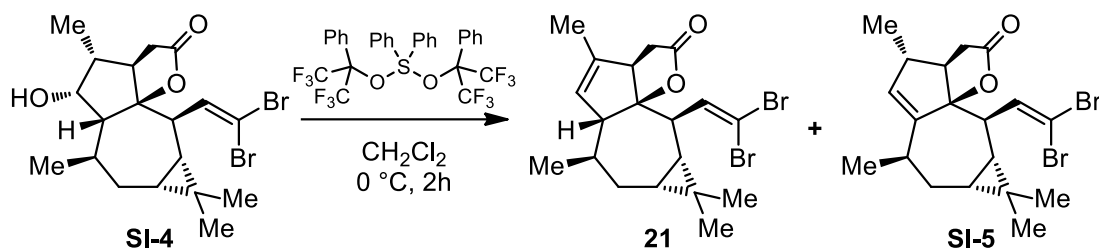
¹H-NMR (400 MHz, Chloroform-*d*) δ 6.29 (d, *J* = 10.2 Hz, 1H), 4.03 (q, *J* = 3.3 Hz, 1H), 2.79 (t, *J* = 9.9 Hz, 1H), 2.70 (dd, *J* = 18.2, 9.3 Hz, 1H), 2.37 – 2.25 (m, 2H), 2.05 – 1.91 (m, 2H), 1.88 – 1.74 (m, 2H), 1.66 (ddd, *J* = 10.4, 6.8, 3.2 Hz, 1H), 1.12 (s, 3H), 1.07 (d, *J* = 5.3 Hz, 3H), 1.05 (d, *J* = 5.2 Hz, 3H), 1.03 (s, 3H), 0.79 (ddd, *J* = 9.6, 7.3, 4.2 Hz, 1H), 0.69 (t, *J* = 9.6 Hz, 1H).

¹³C-NMR (101 MHz, Chloroform-*d*) δ 177.3, 138.8, 99.1, 90.4, 78.9, 62.4, 48.2, 47.2, 44.2, 34.7, 31.5, 30.1, 29.4, 28.2, 23.5, 22.2, 19.2, 16.1, 12.6.

IR: 3483, 2954, 2926, 1761, 1459, 1377, 1198, 1155, 1136, 1089, 1066, 1021, 1002, 961, 921, 805, 777, 747, 695, 540.

HRMS (ESI) *m/z*: exact mass calculated for C₁₉H₂₆Br₂NaO₃ [M+Na]⁺, 483.0141; found: 483.0132.

[α]_D²⁵ = –29.2 (*c* = 0.9, CHCl₃)



To a solution of alcohol **SI-4** (0.030 g, 0.065 mmol, 1.0 eq) in CH_2Cl_2 was added Martin's Sulfurane (66 mg, 0.097 mmol, 1.5 eq) at 0 °C and the solution was stirred at the same temperature for 2 h. Sat. aq. NaHCO_3 (5 mL) was added to the mixture to quench the reaction. The mixture was transferred to a separation funnel and extracted with Et_2O (3 x 20 mL). The combined organic phases were dried over Na_2SO_4 , filtered and concentrated under reduced pressure, to give crude **21**. Purification by flash column chromatography (hexane– Et_2O , 90:10) gave **21** (12 mg, 0.027 mmol, 42%) and **SI-5** (8.5 mg, 0.019 mmol, 30%) as colorless oils that solidified in the freezer.

Analytical data for **21**:

$^1\text{H-NMR}$ (400 MHz, Chloroform-*d*) δ 6.34 (d, J = 10.3 Hz, 1H), 5.50 (d, J = 2.3 Hz, 1H), 2.91 (ddd, J = 7.2, 4.9, 2.2 Hz, 1H), 2.82 (dd, J = 18.4, 10.4 Hz, 1H), 2.45 – 2.27 (m, 4H), 1.95 (ddd, J = 14.5, 6.0, 4.8 Hz, 1H), 1.37 – 1.28 (m, 1H), 1.25 (d, J = 7.4 Hz, 3H), 1.11 (d, J = 7.0 Hz, 3H), 1.08 (s, 3H), 1.08 (s, 3H), 0.92 (ddd, J = 11.6, 9.3, 6.0 Hz, 1H), 0.83 (t, J = 9.6 Hz, 1H).

$^{13}\text{C-NMR}$: (101 MHz, Chloroform-*d*) δ 177.1, 148.6, 138.0, 136.7, 103.8, 89.9, 50.0, 49.3, 45.4, 36.6, 36.2, 29.5, 29.0, 27.7, 24.1, 21.2, 20.0, 18.9, 16.4.

IR (thin film, cm^{-1}): 2927, 1775, 1459, 1377, 1198, 1146, 1007, 960, 801.

HRMS (ESI): m/z : exact mass calculated for $\text{C}_{19}\text{H}_{24}\text{Br}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$, 465.0035; found: 465.0028.

$[\alpha]_{\text{D}}^{25} = -71.6$ (c = 0.5, CHCl_3)

Analytical data for **SI-5**:

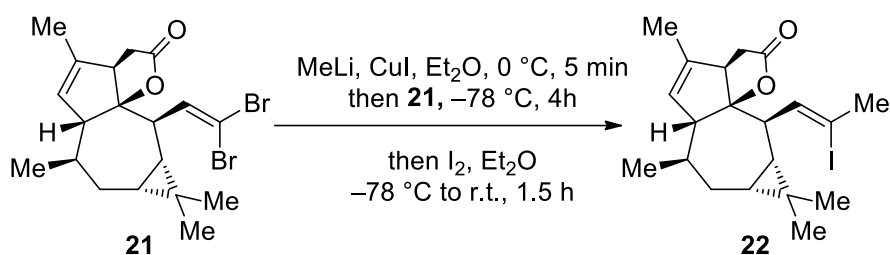
$^1\text{H-NMR}$ (400 MHz, Chloroform-*d*) δ 6.41 (d, J = 10.0 Hz, 1H), 5.41 (dt, J = 2.8, 1.6 Hz, 1H), 3.03 (dq, J = 9.3, 1.5 Hz, 1H), 2.73 (dd, J = 10.0, 2.2 Hz, 1H), 2.70 – 2.58 (m, 2H), 2.40 (dt, J = 18.2, 0.9 Hz, 1H), 1.83 (ddd, J = 15.3, 6.0, 3.6 Hz, 1H), 1.75 – 1.68 (m, 1H), 1.66 (p, J = 1.6 Hz, 3H), 1.39 (ddd, J = 16.7, 10.4, 6.1 Hz, 1H), 1.03 (s, 6H), 0.99 (dd, J = 10.5, 9.4 Hz, 1H), 0.90 (d, J = 6.5 Hz, 3H), 0.75 (td, J = 9.5, 3.5 Hz, 1H).

$^{13}\text{C-NMR}$: (101 MHz, Chloroform-*d*) δ 176.5, 138.3, 137.3, 128.4, 100.9, 58.0, 51.0, 45.9, 33.9, 33.3, 32.3, 29.1, 28.6, 21.7, 21.5, 18.9, 16.4, 14.4.

IR (thin film, cm^{-1}): 1145, 1011, 970, 937, 918, 855, 820, 799, 781, 737, 540, 459,

HRMS (ESI): m/z : exact mass calculated for $\text{C}_{19}\text{H}_{25}\text{Br}_2\text{O}_2$ $[\text{M}+\text{H}]^+$, 443.0216; found: 443.0218

$[\alpha]_{\text{D}}^{25} = -5.5$ (c = 0.3, CHCl_3)



MeLi (1.6M in Et₂O, 0.093 mL, 0.15 mmol, 6.0 eq) was added to a suspension of CuI (14 mg, 0.074 mmol, 3.0 eq) in Et₂O (0.5 mL) at 0 °C and stirred for 5 min. The now clear solution as cooled to -78 °C and a solution of **21** (11 mg, 0.025 mmol, 1.0 eq) in Et₂O (0.2 mL) was added dropwise. The temperature was maintained, and the solution was stirred for 5 h. Iodine (38 mg, 0.15 mmol, 6.0 eq) in Et₂O (3 mL) was added dropwise and the mixture was stirred for 20 min at -78 °C and 1h at room temperature. Sat aq. Na₂SO₃ (10 mL) was added, and the mixture was transferred to a separation funnel with distilled water (10 mL). The mixture was extracted with Et₂O (3 x 15 mL), the organic phases were combined, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexane–Et₂O, 90:10) to give **22** (contaminated by small amounts of the bromomethyl and dimethyl species) as a colorless oil (7.8 mg, 0.018 mmol, 74%).

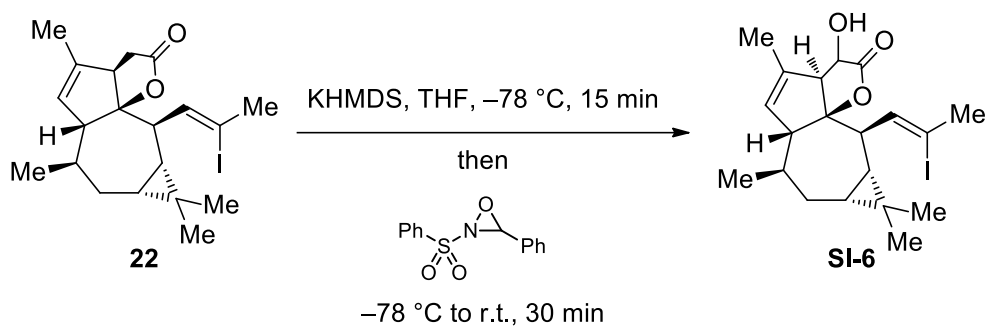
¹H-NMR (400 MHz, Chloroform-*d*) δ 5.48 (d, *J* = 2.1 Hz, 1H), 5.37 (dd, *J* = 9.6, 1.5 Hz, 1H), 2.91 (dtd, *J* = 9.7, 4.9, 2.3 Hz, 1H), 2.77 – 2.69 (m, 1H), 2.56 (d, *J* = 1.5 Hz, 3H), 2.38 – 2.30 (m, 4H), 1.95 – 1.89 (m, 1H), 1.39 – 1.33 (m, 1H), 1.25 (s, 3H), 1.15 (s, 3H), 1.12 (s, 3H), 1.05 (s, 3H), 0.89 – 0.82 (m, 2H).

¹³C-NMR: (101 MHz, Chloroform-*d*) δ 177.7, 148.9, 136.8, 135.3, 105.0, 101.9, 52.6, 48.9, 45.7, 36.7, 36.3, 34.4, 29.3, 29.2, 28.0, 23.8, 21.3, 20.0, 19.2, 17.4.

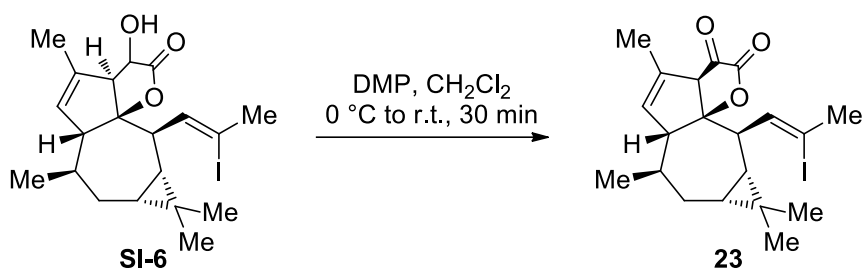
IR (thin film, cm⁻¹): 2915, 2868, 1775, 1444, 1417, 1376, 1299, 1247, 1218, 1187, 1147, 1066, 1014, 979, 967, 937, 915, 865, 787, 753, 653, 574, 539, 508, 470, 423, 410.

HRMS (ESI): *m/z*: exact mass calculated for C₂₀H₂₇INaO₂ [M+Na]⁺, 449.0948; found: 449.0943.

[α]_D²⁵ = -53.7 (*c* = 1.0, CHCl₃)



A solution of **22** (7.8 mg, 0.048 mmol, 1.0 eq) in THF (0.9 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and KHMDS (0.5 M in PhMe, 0.045 mL, 0.023 mmol, 1.25 eq) was added dropwise over the side of the flask. After stirring for 15 min, Davis' oxaziridine (24 mg, 0.091 mmol, 5.0 eq) was added in one portion and the mixture was stirred for 20 min at $-78\text{ }^{\circ}\text{C}$ and 10 min at room temperature. The mixture was transferred to a separation funnel and extracted with Et₂O (3 x 10 mL). The organic phases were combined, dried over Na₂SO₄, filtered over a plug of SiO₂ and concentrated under reduced pressure. The crude product was used without further purification in the next step.



To a solution of crude **SI-6** in CH_2Cl_2 was added DMP (15 mg, 0.036 mmol, 2.0 eq) at $0\text{ }^\circ\text{C}$. The mixture was warmed to room temperature and stirred for 30 min. After completion of the reaction sat. aq. NaHCO_3 (2 mL) and sat. aq. Na_2SO_3 (2 mL) was added, and the mixture was stirred for 5 min. The mixture was added to a separation funnel and extracted with Et_2O (3 x 10 mL). The organic phases were combined, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexane– Et_2O , 95:5) to give **23** as a yellowish oil (3.9 mg, 0.0088 mmol, 49%).

It has to be noted that **23** was contaminated with impurities generated during vinyl iodide formation step, which were not separated at this point and amount to maximally about 5% total. They include dimethyl derivative, protodehalogenated, derivative, and vinyl bromide. The product was carried as is into the next step.

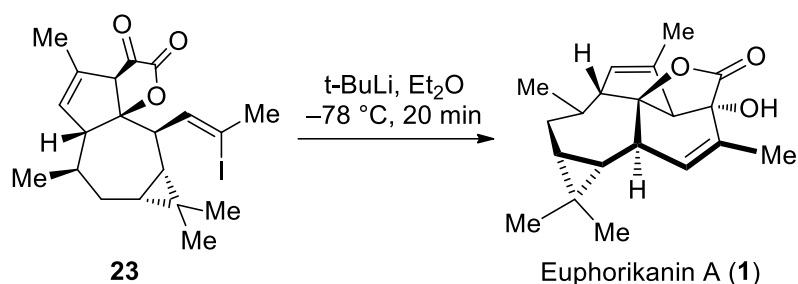
^1H -NMR (400 MHz, CDCl_3) δ (500 MHz, Chloroform-*d*) δ 5.73 (td, $J = 2.6, 1.5\text{ Hz}$, 1H), 5.29 (dd, $J = 9.1, 1.5\text{ Hz}$, 1H), 3.60 (dq, $J = 2.5, 1.3\text{ Hz}$, 1H), 2.91 – 2.85 (m, 1H), 2.68 (dd, $J = 10.5, 9.2\text{ Hz}$, 1H), 2.46 (d, $J = 1.5\text{ Hz}$, 3H), 1.93 – 1.86 (m, 1H), 1.79 – 1.74 (m, 1H), 1.67 (q, $J = 1.6\text{ Hz}$, 3H), 1.07 (s, 3H), 1.04 (s, 3H), 0.96 (d, $J = 6.6\text{ Hz}$, 3H), 0.89 – 0.87 (m, 1H), 0.82 – 0.79 (m, 1H).

^{13}C -NMR: (101 MHz, CDCl_3) δ (126 MHz, Chloroform-*d*) δ 189.7, 160.3, 134.3, 133.5, 125.7, 107.2, 61.1, 57.4, 48.7, 34.2, 33.6, 32.9, 30.5, 28.6, 21.4, 21.3, 19.3, 16.9, 15.4, 14.0.

IR (thin film, cm^{-1}): 2954, 2925, 1789, 1784, 1481, 1390, 1242.

HRMS (ESI): m/z : exact mass calculated for $\text{C}_{20}\text{H}_{25}\text{NaO}_3$ $[\text{M}+\text{Na}]^+$, 463.0741; found: 463.0738.

$[\alpha]_{\text{D}}^{25}$ = -3.7 ($c = 0.2$, CHCl_3).



To a solution of *t*-BuLi (1.7 M in pentane, 20 μL , 0.034 mmol, 3.0 eq) in Et₂O (0.4 mL) was added ketolactone **23** (3.9 mg, 0.0088 mmol, 1.0 eq) in Et₂O (0.5 mL) at $-78\text{ }^{\circ}\text{C}$. The mixture was stirred for 30 min and quenched by the addition of sat. aq. NH₄Cl (2 mL) at the same temperature. After warming to room temperature, the mixture was transferred to a separation funnel and extracted with EtOAc (3 x 10 mL). the organic phases were dried over Na₂SO₄, filtered and concentrated und reduced pressure. The crude product was purified by flash column chromatography (hexane–EtOAc, 70:30) to give **1** as a colorless solid (1.1 mg, 3.54 μmol , 40%).

¹H-NMR (600 MHz, Chloroform-*d*) δ 5.53 (tt, $J = 3.2, 1.6\text{ Hz}$, 1H), 5.39 (dq, $J = 3.2, 1.6\text{ Hz}$, 1H), 3.09 (dt, $J = 2.4, 1.3\text{ Hz}$, 1H), 2.71 (m, 2H), 2.34 (dt, $J = 11.4, 2.4\text{ Hz}$, 1H), 1.84 (q, $J = 1.7\text{ Hz}$, 3H), 1.81 (dd, $J = 2.3, 1.6\text{ Hz}$, 3H), 1.79 (dd, $J = 6.2, 3.7\text{ Hz}$, 1H), 1.72 – 1.68 (m, 1H), 1.34 (m, 2H), 1.05 (s, 3H), 1.00 (s, 3H), 0.88 (s, 3H), 0.82 – 0.79 (m, 1H), 0.69 (td, $J = 9.7, 3.6\text{ Hz}$, 1H).

¹³C-NMR: (151 MHz, Chloroform-*d*) δ 130.6, 126.1, 59.7, 54.6, 39.1, 32.7, 31.9, 31.9, 31.3, 29.7, 28.6, 26.6, 20.9, 18.8, 16.6, 16.2, 15.3, 1.0.

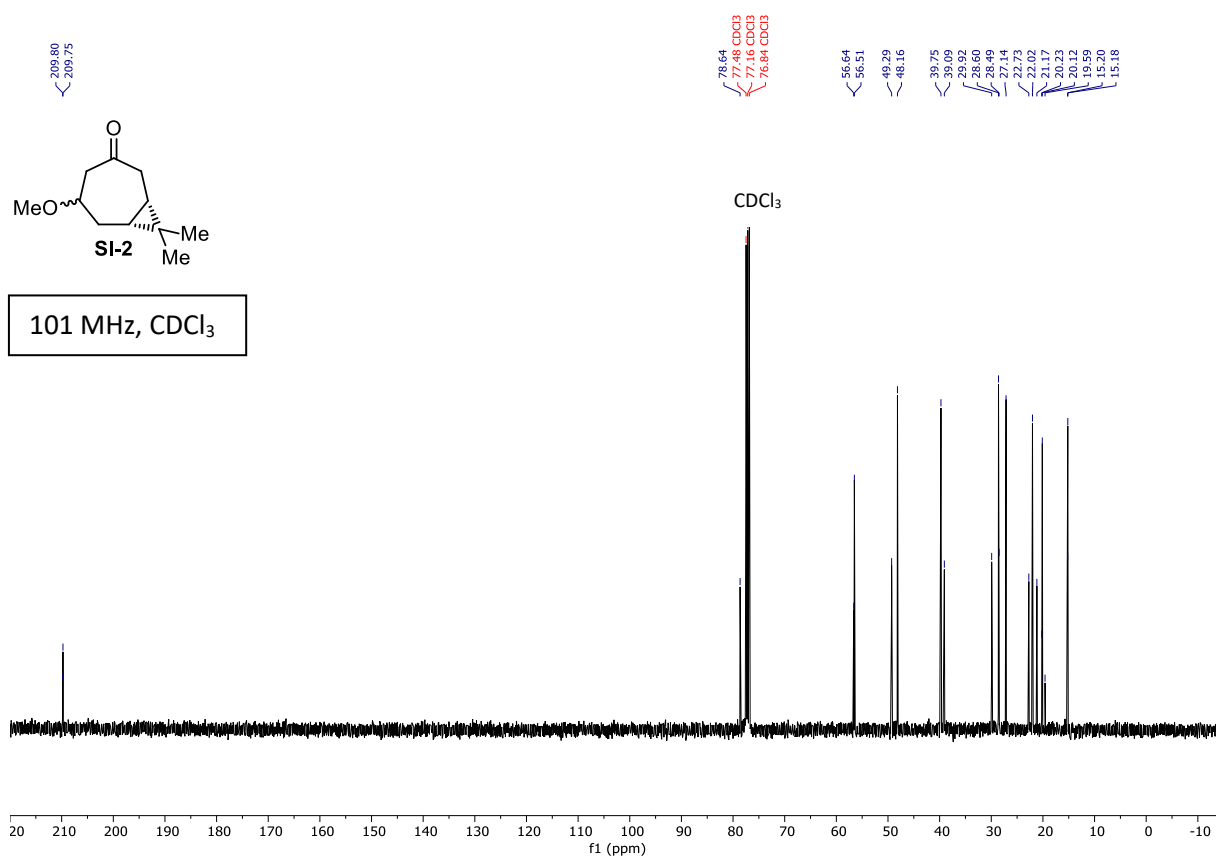
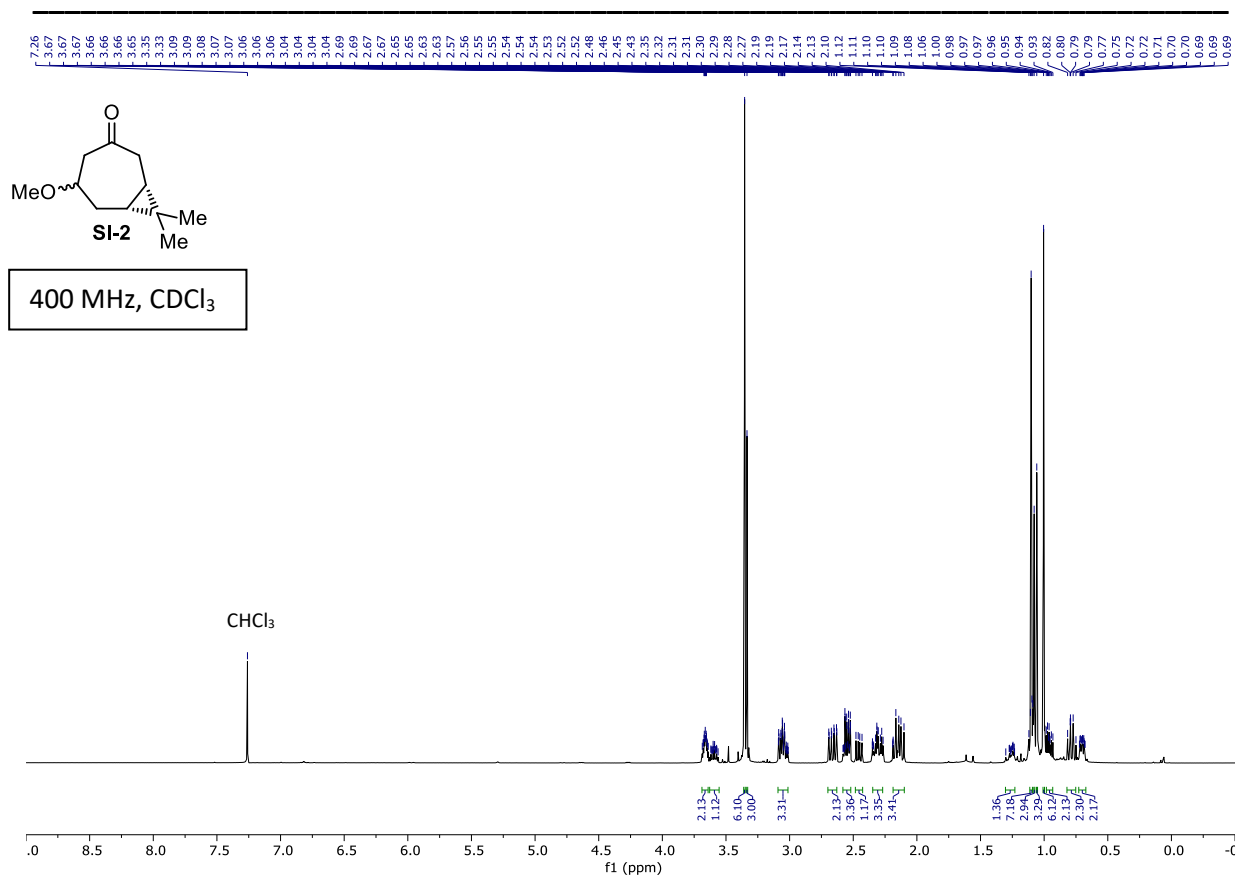
IR (thin film, cm⁻¹): 3442, 2923, 2854, 1758, 1665, 1447, 1378, 1260, 1211, 1182, 1158, 1146, 1084, 1012, 954, 929, 881, 838, 800, 725, 708, 685, 660, 635, 521, 497.

HRMS (ESI): m/z : exact mass calculated for C₂₀H₂₆NaO₃ [M+Na]⁺, 337.1774; found: 337.1773.

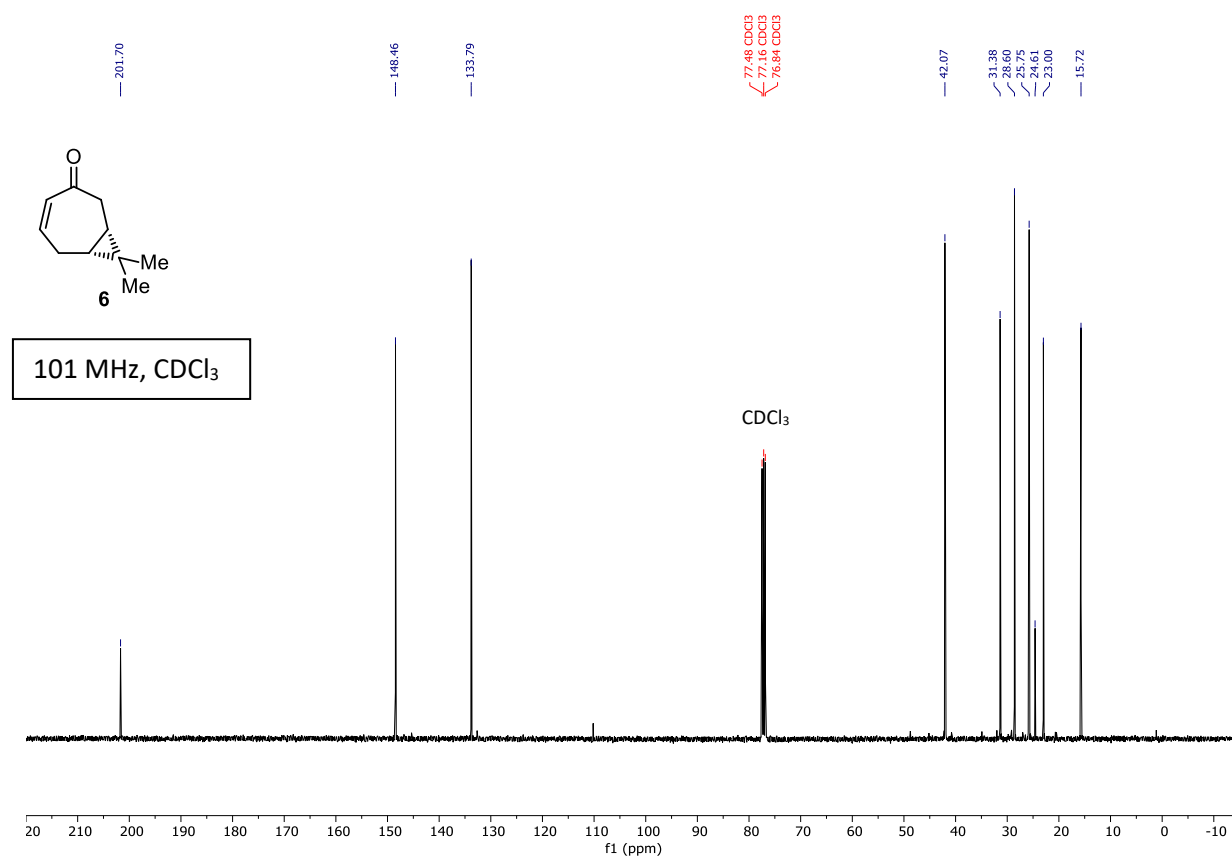
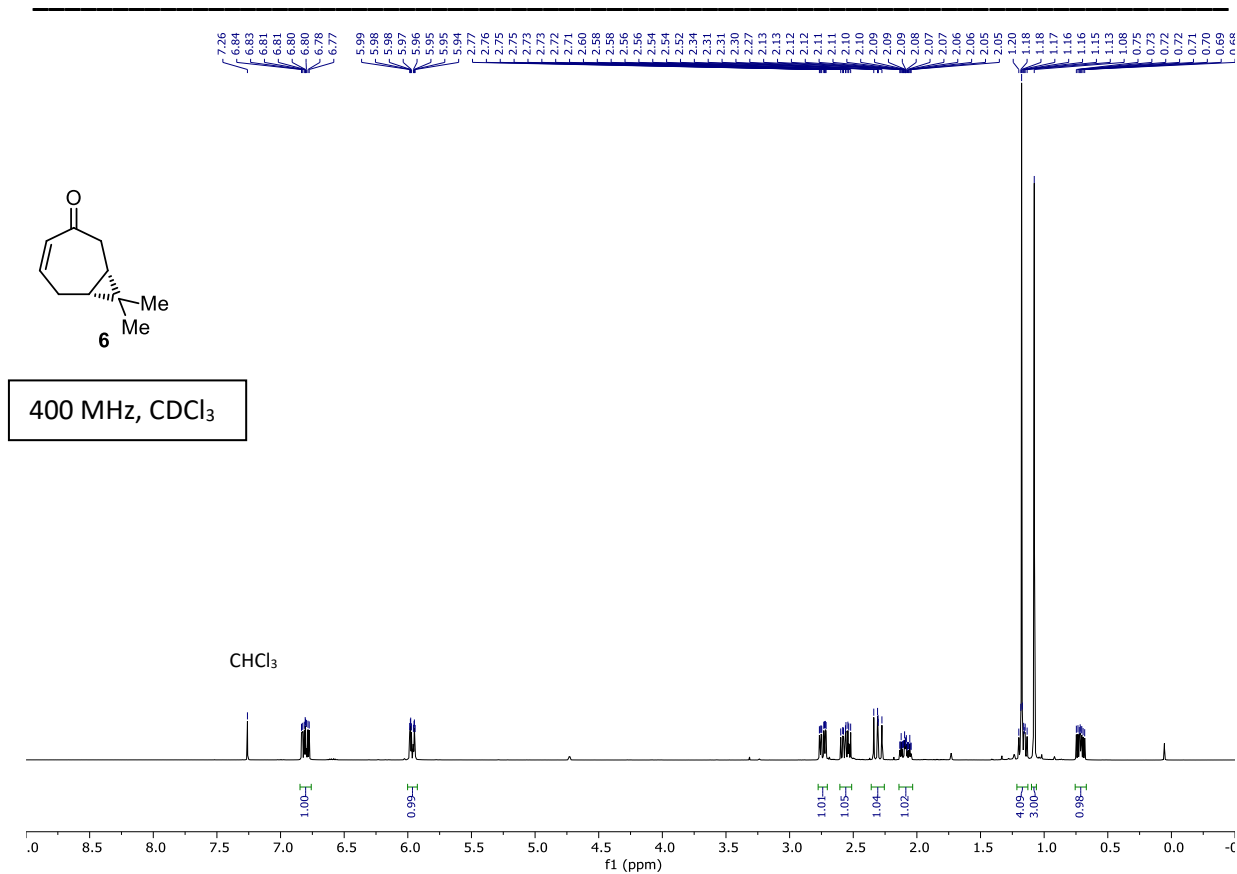
[α]_D²⁵ = +6 ($c = 0.02$, CHCl₃).

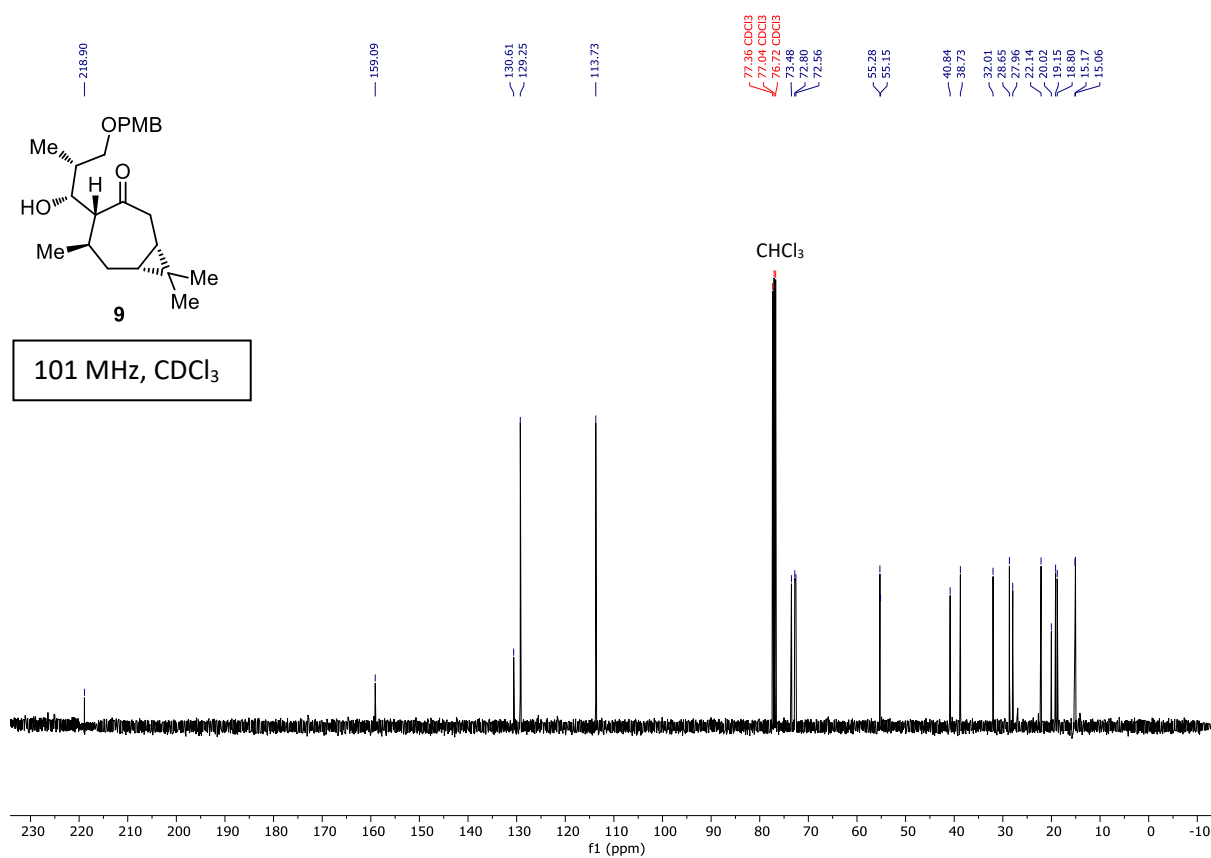
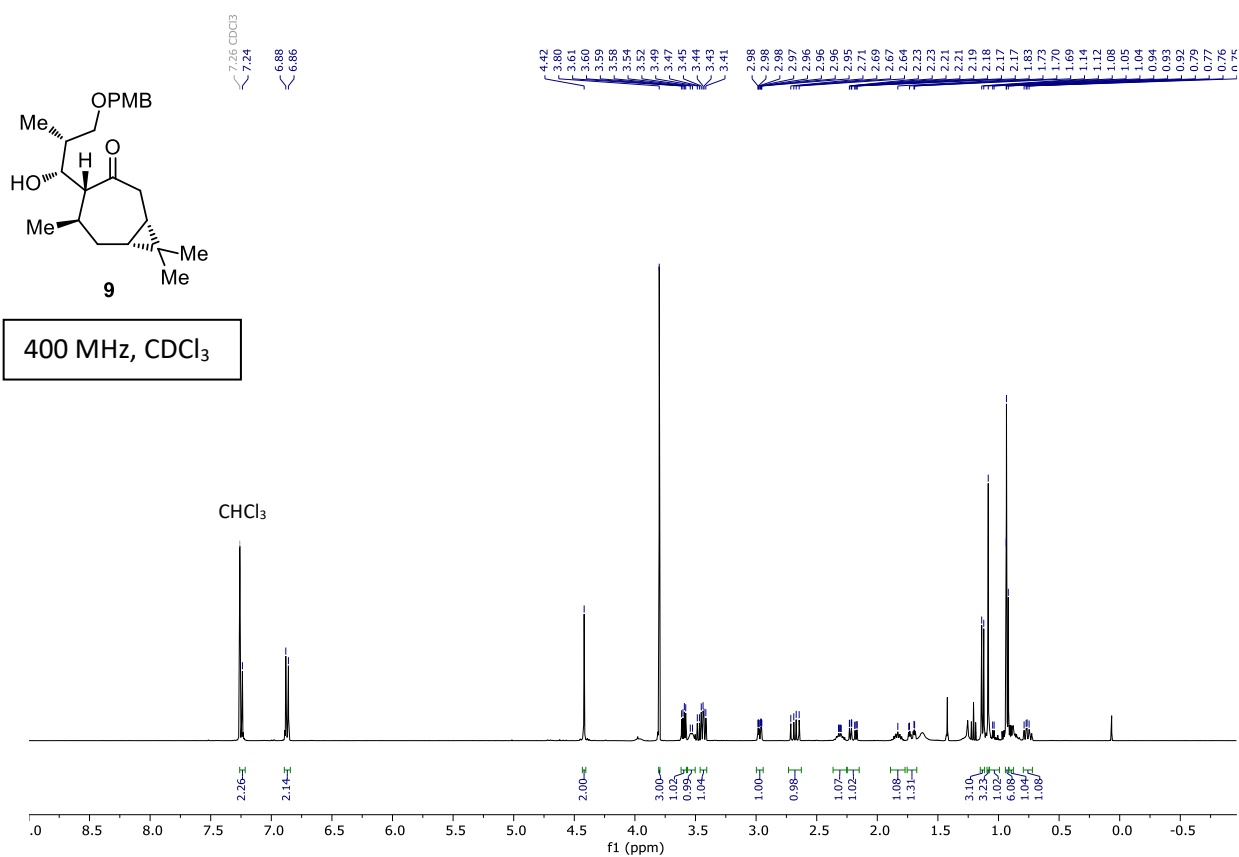
NMR Spectra

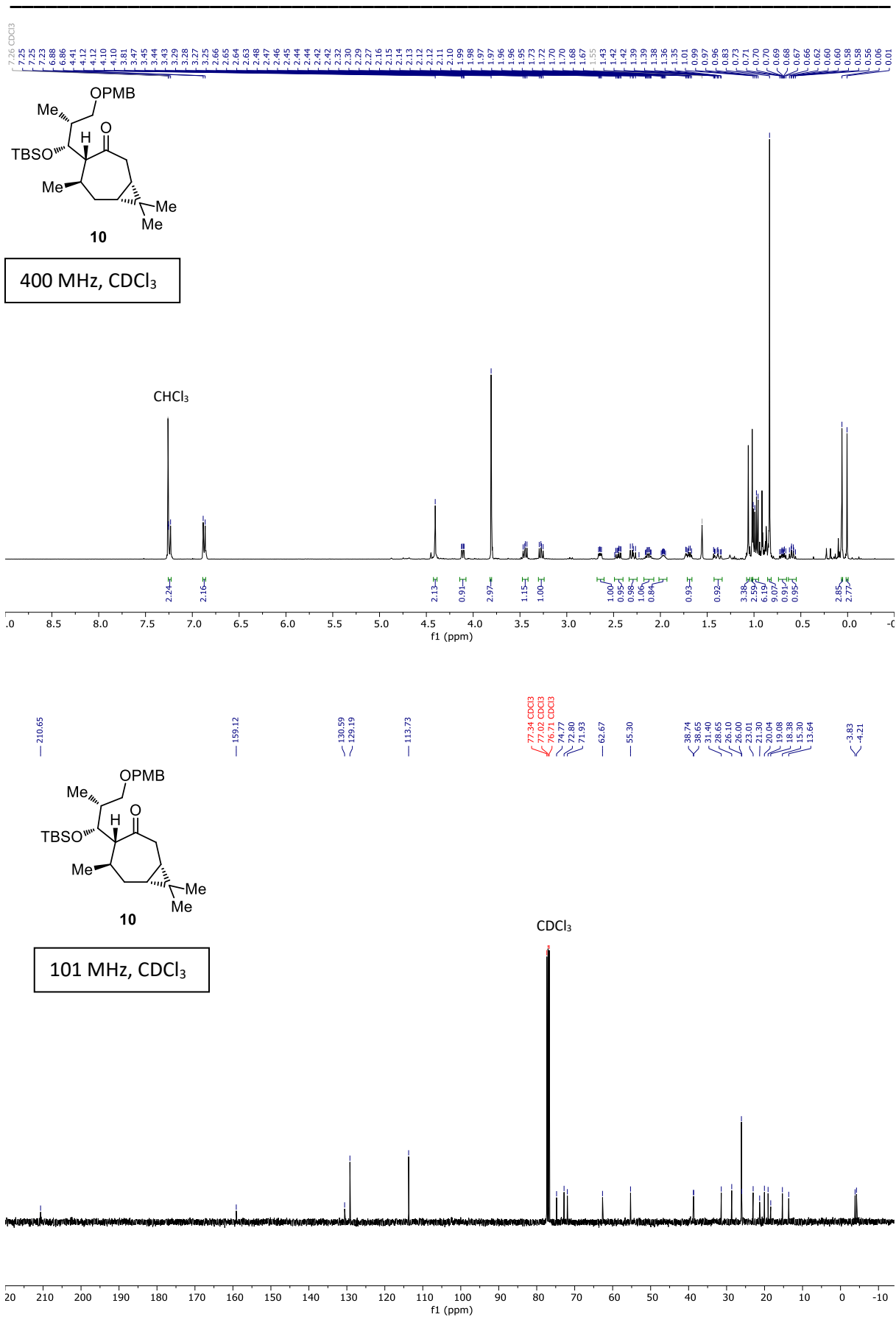
Supporting Information



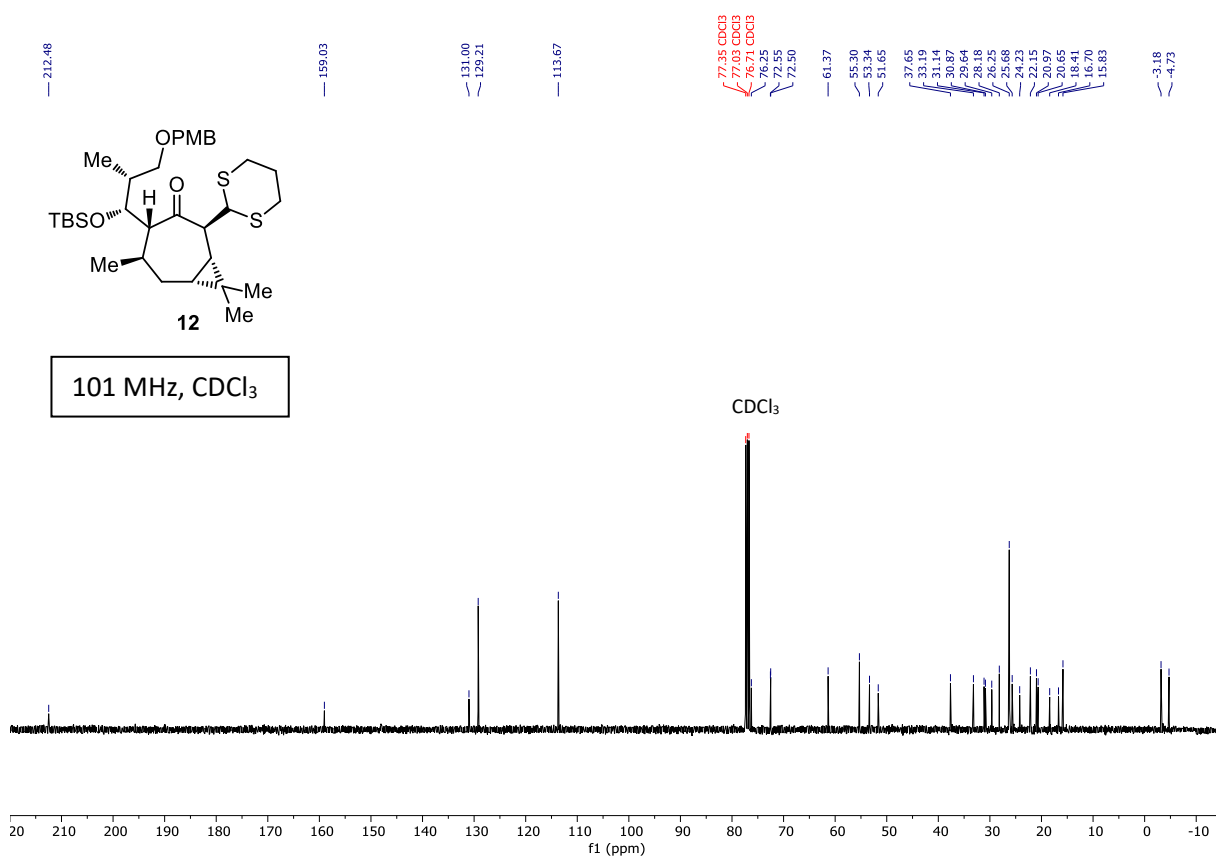
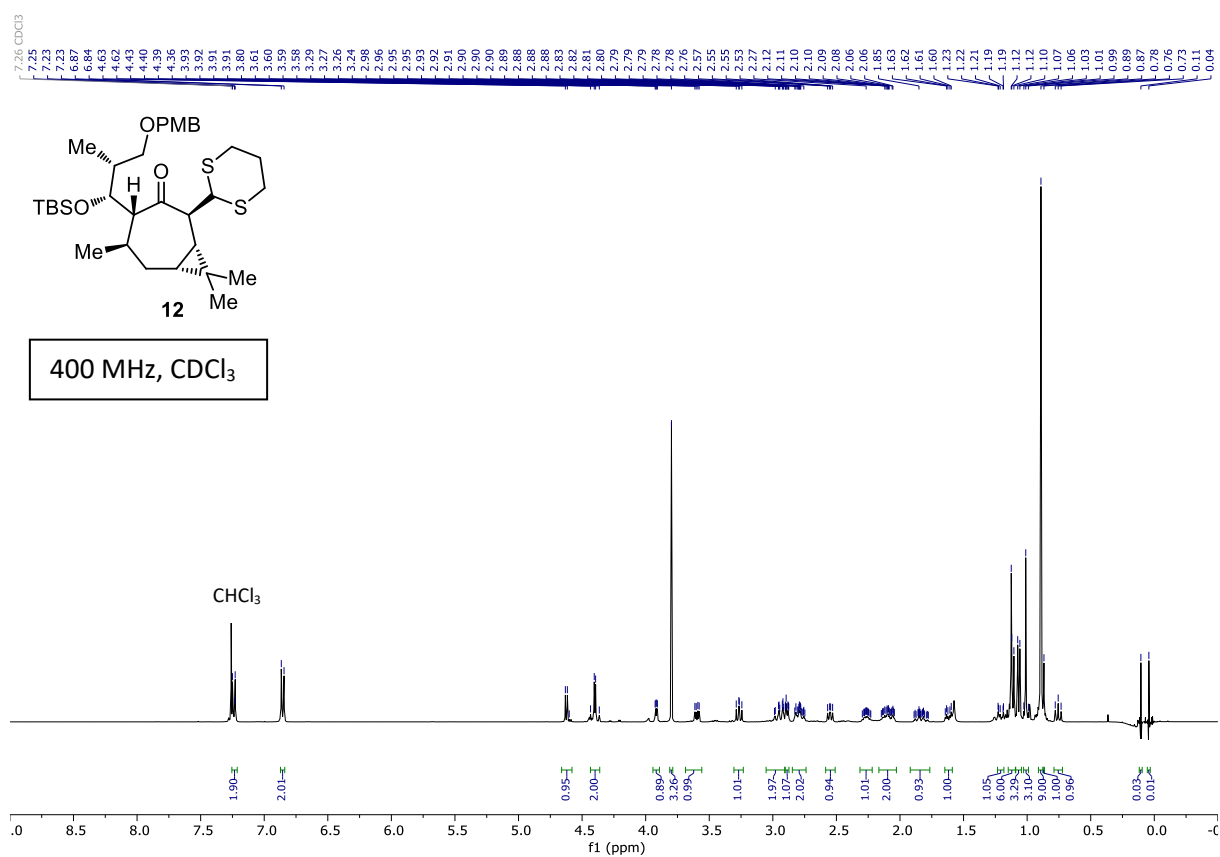
Supporting Information



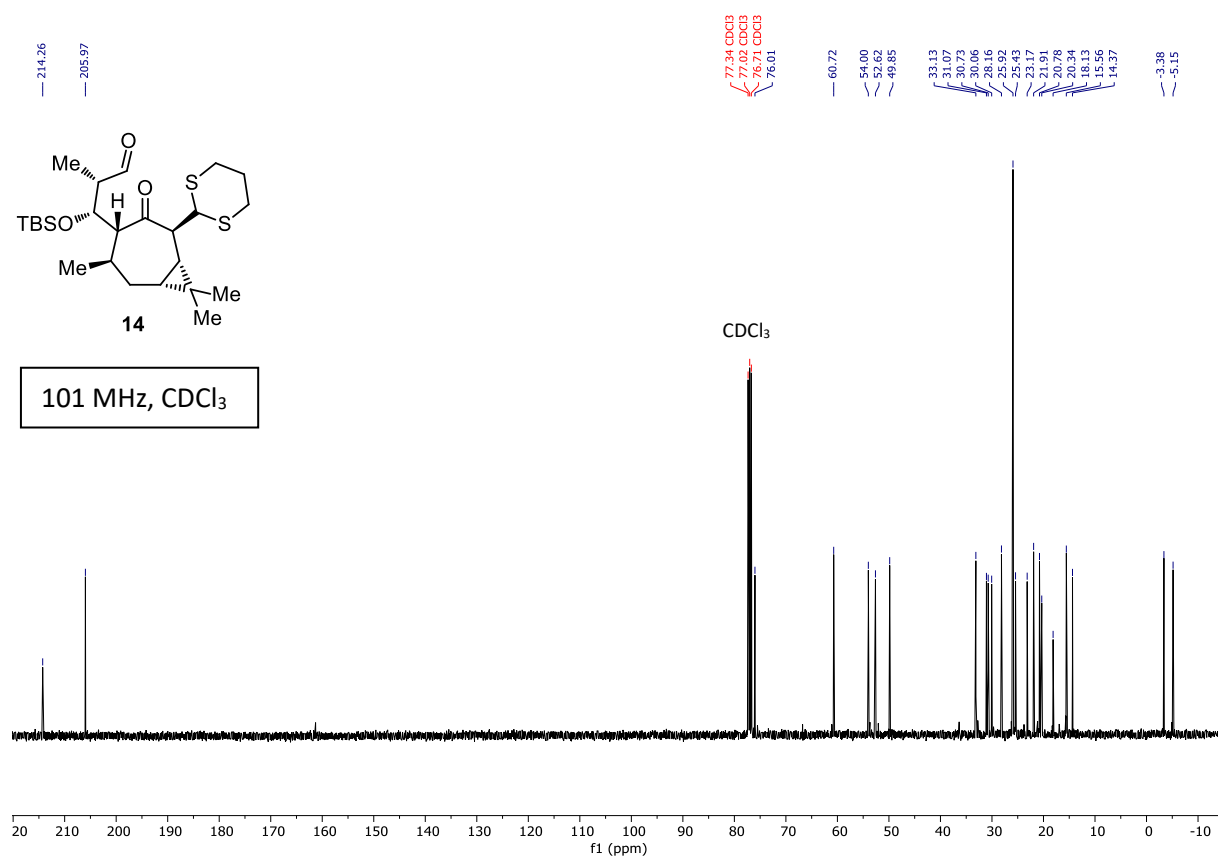
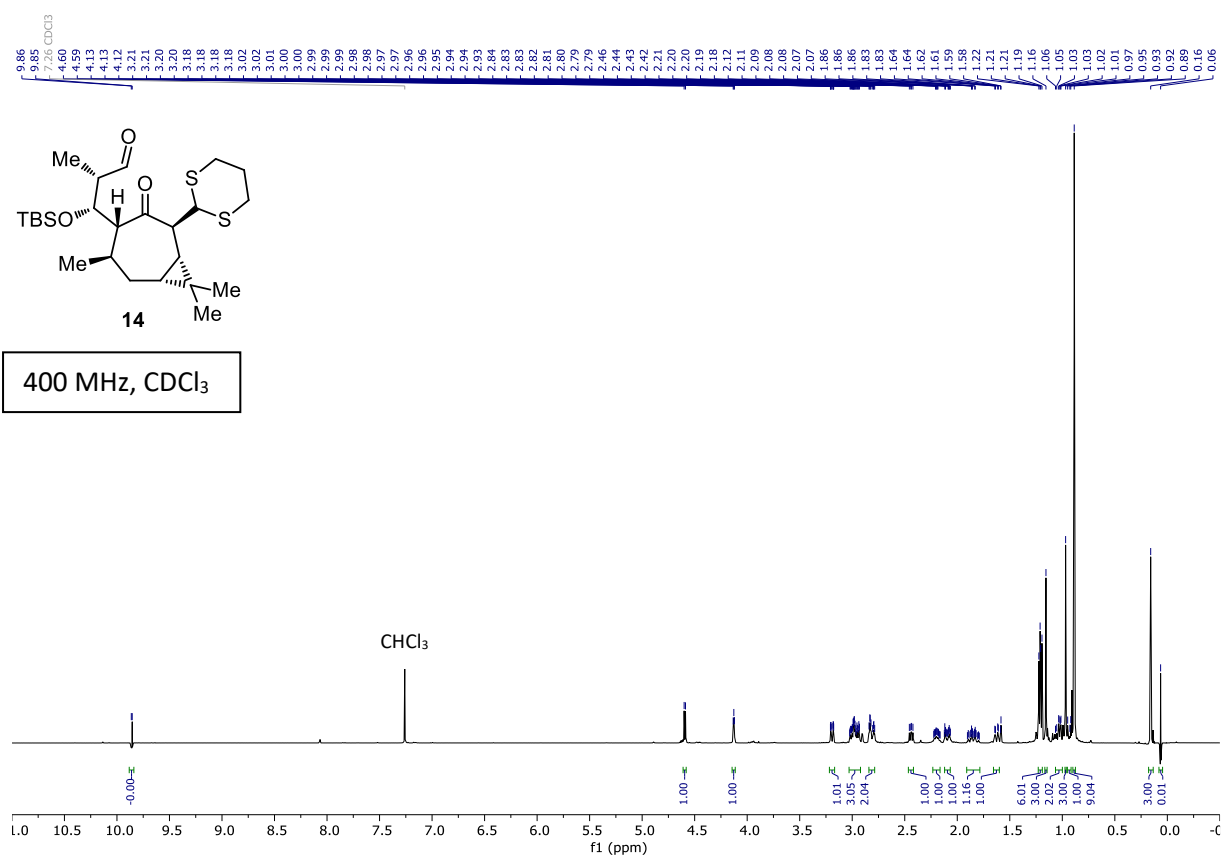




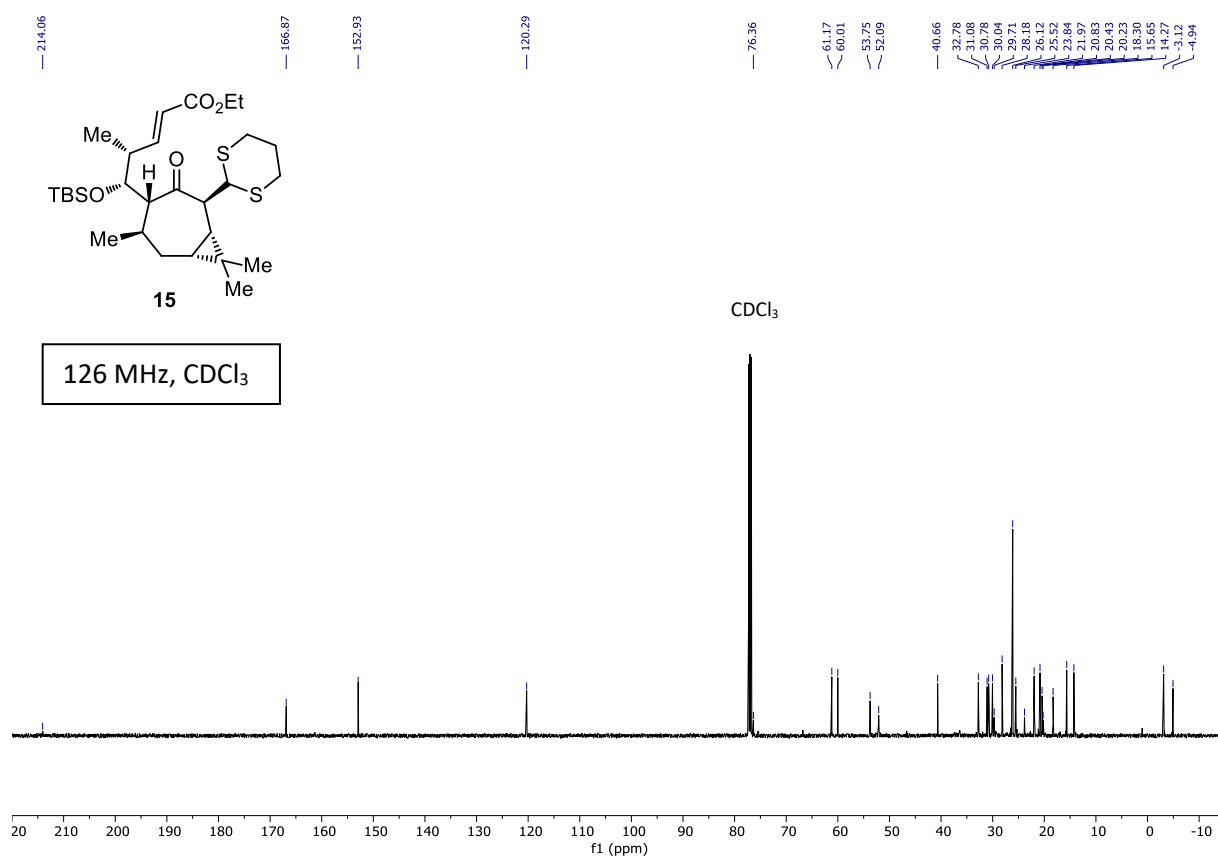
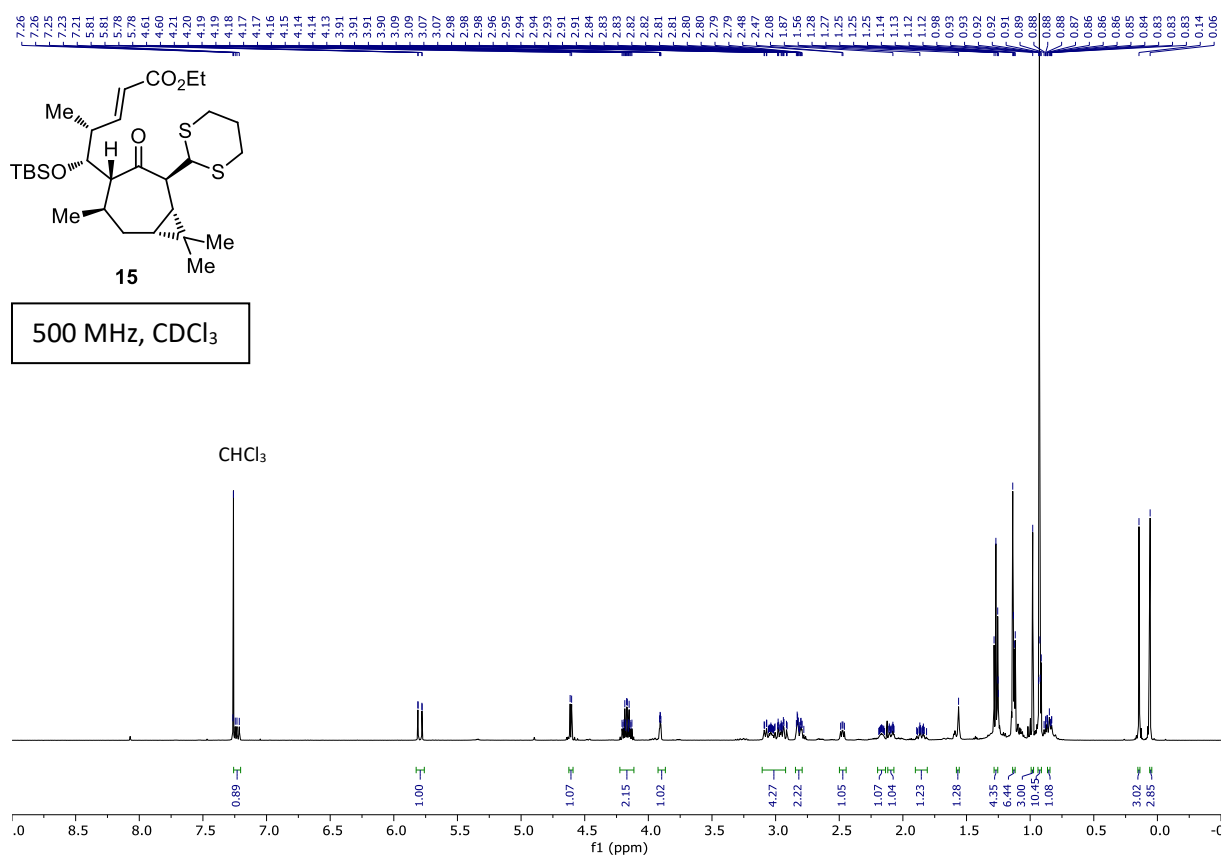
Supporting Information



Supporting Information



Supporting Information



Chemical structure of compound **16** is shown above the ¹H NMR spectrum. The structure is a complex polycyclic molecule featuring a TBSO group, a hydroxyl group, a methyl group, a methoxycarbonyl group, and a thioether bridge.

The ¹H NMR spectrum (500 MHz, CDCl₃) displays chemical shifts (ppm) on the x-axis, ranging from 0.0 to 10.0. The spectrum shows several peaks corresponding to the protons in compound **16**, including aromatic protons, aliphatic protons, and the TBSO group.

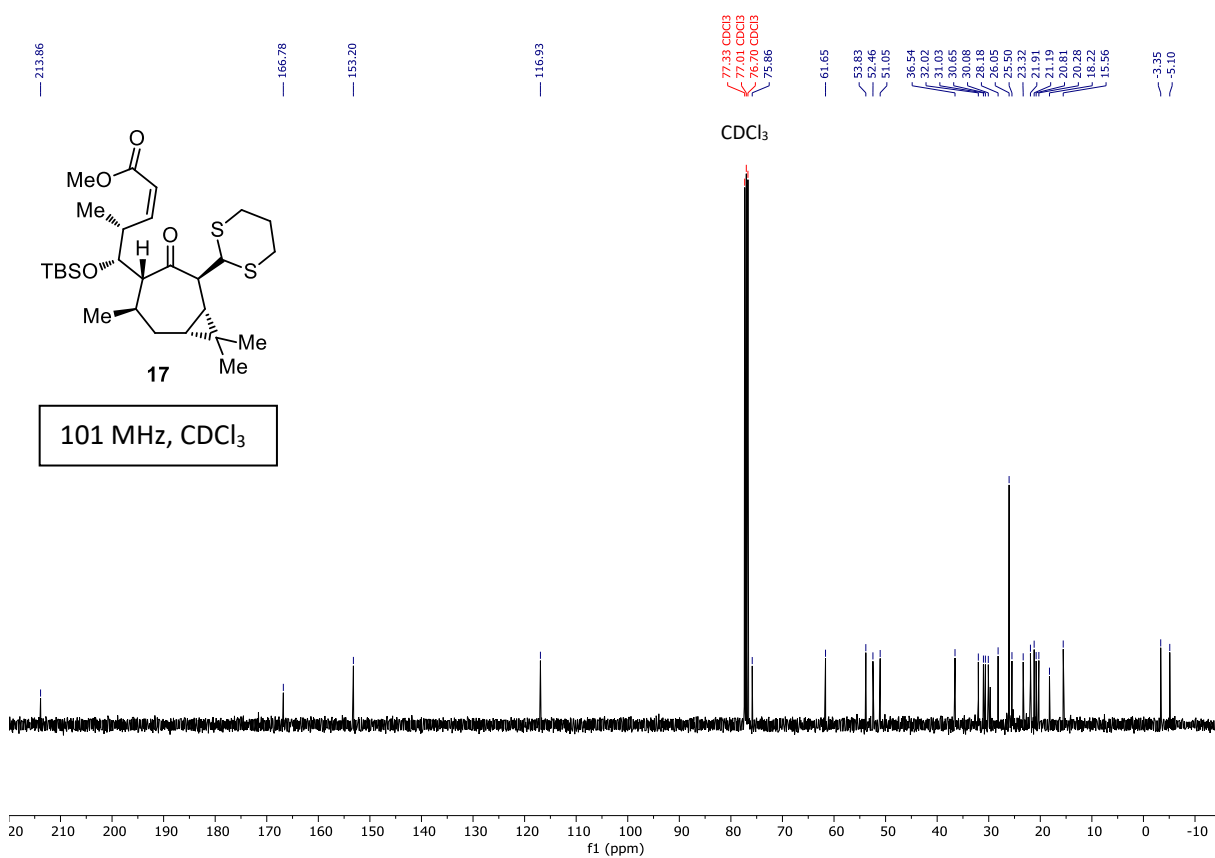
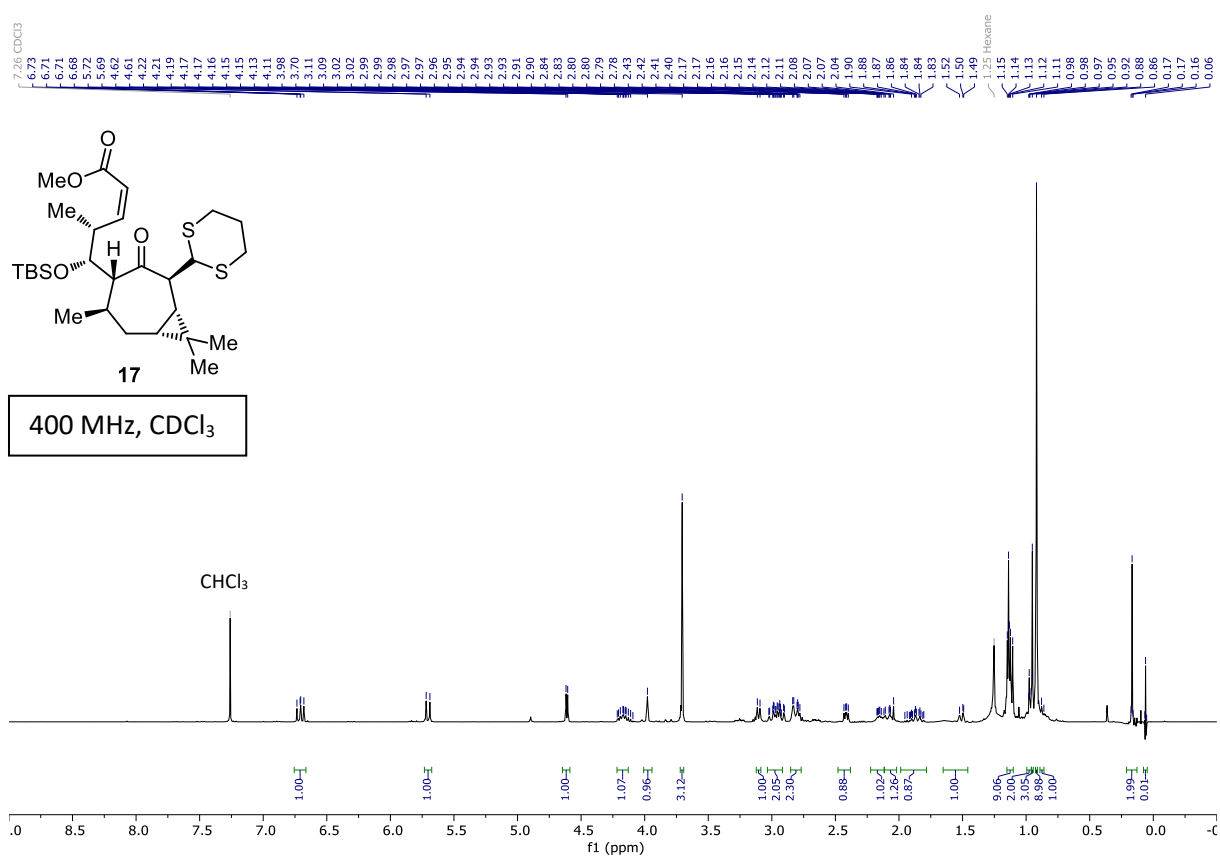
Key peaks in the spectrum include:

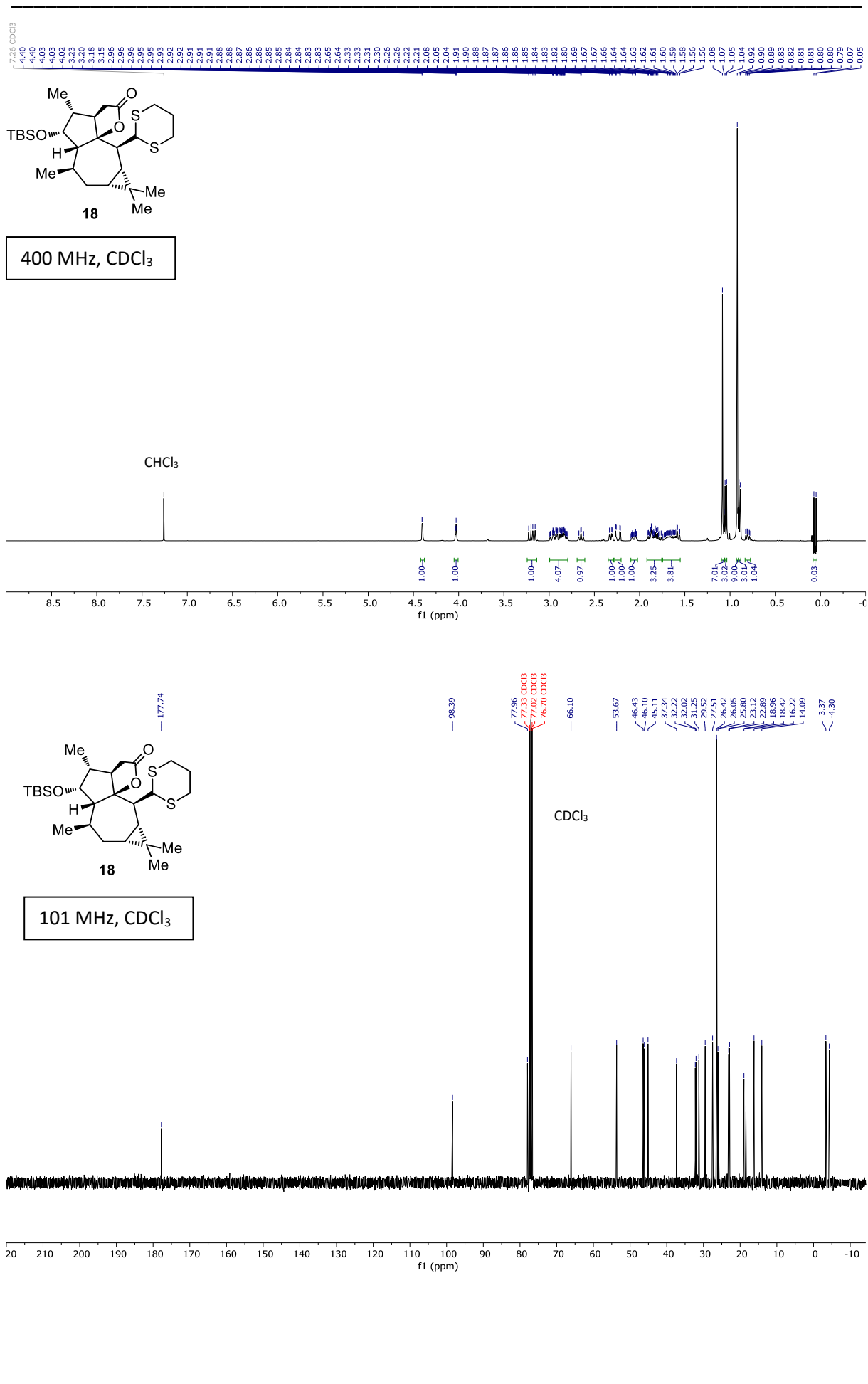
- Aromatic protons (7.0-7.5 ppm)
- Aliphatic protons (4.0-5.5 ppm)
- Thioether bridge protons (2.0-3.0 ppm)
- Methoxycarbonyl group protons (3.5-4.0 ppm)
- TBSO group protons (0.1-0.5 ppm)

The spectrum is labeled with "500 MHz, CDCl₃" and "CHCl₃".

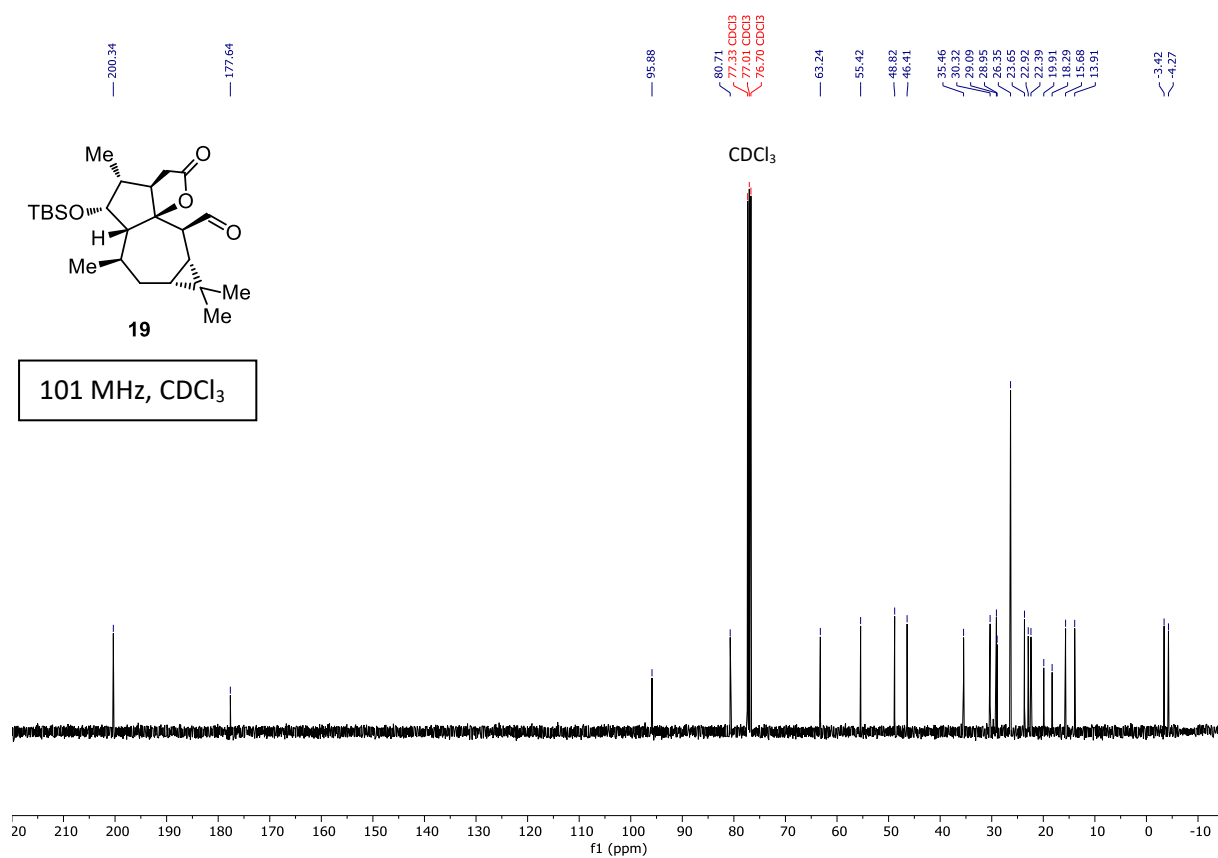
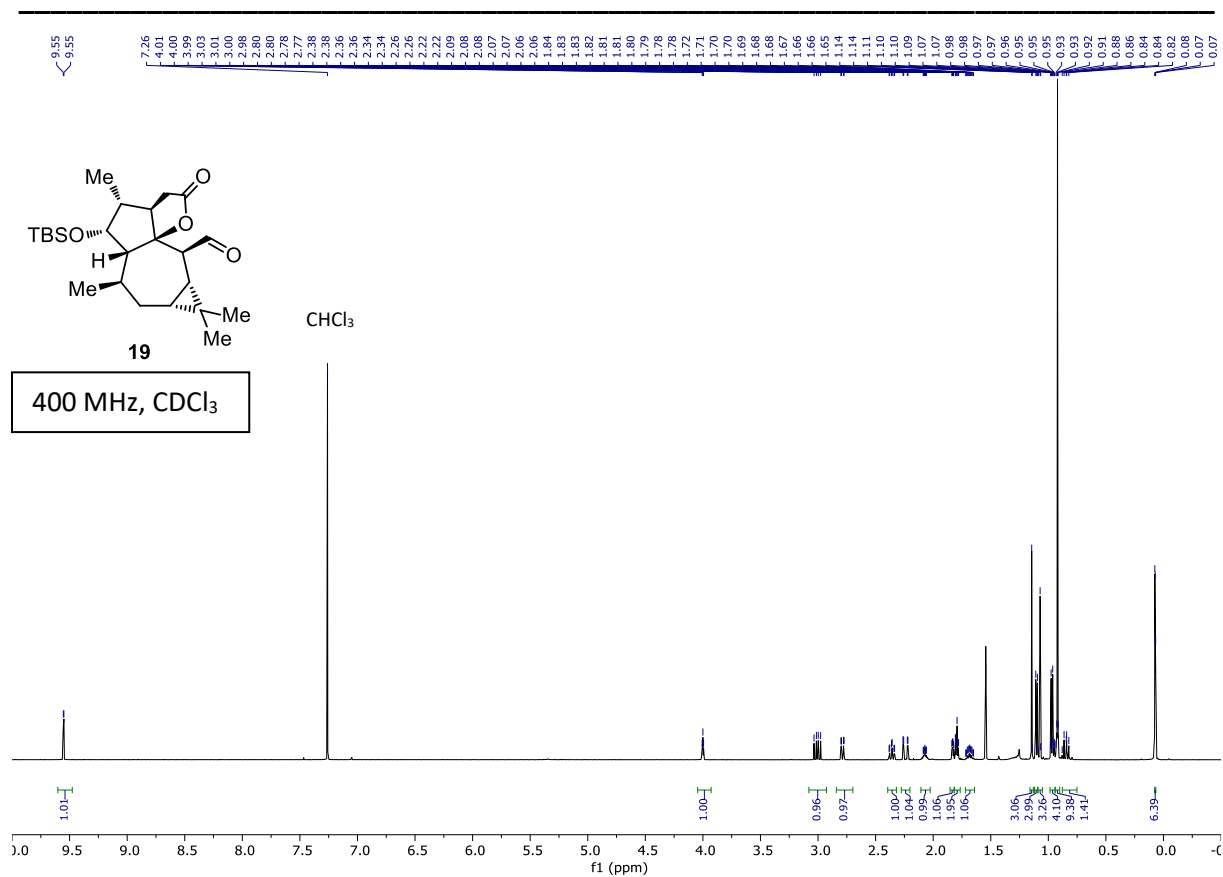


Supporting Information





Supporting Information



Chemical structure of compound **20** is shown above the spectrum. The structure is a complex polycyclic molecule featuring a TBSO group, a ketone, and a bromomethyl group.

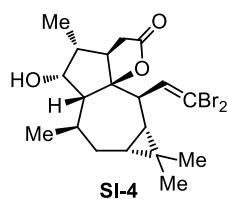
The spectrum was recorded at 400 MHz in CDCl₃. The solvent peak for CHCl₃ is visible at approximately 7.26 ppm.

The spectrum displays several peaks, with the following chemical shifts (ppm) and integrations:

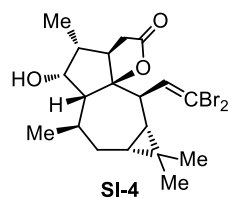
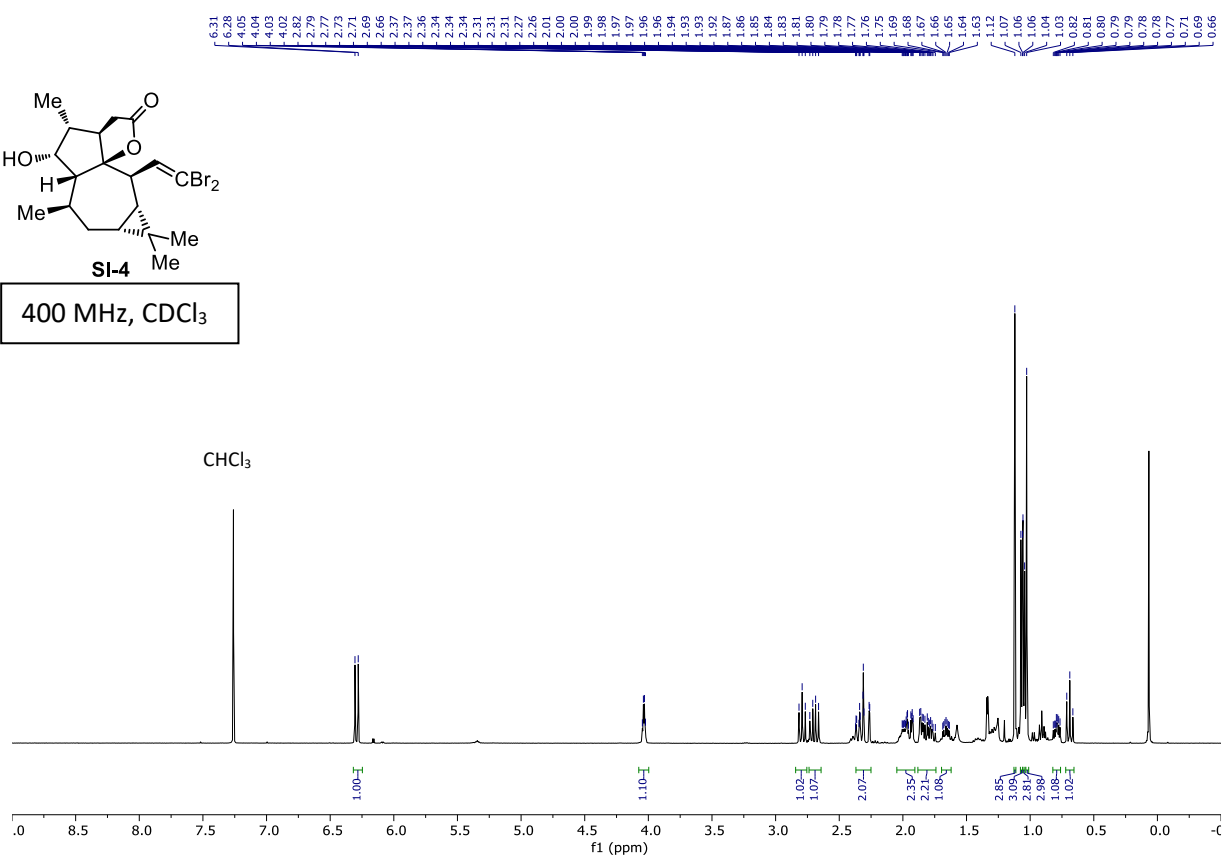
- 7.26 (CHCl₃ solvent)
- 6.28, 6.26 (doublet, integration 1.00)
- 4.01, 3.99, 3.97, 3.95, 3.93, 3.91, 3.89, 3.87, 3.85, 3.83, 3.81, 3.79, 3.77, 3.75, 3.73, 3.71, 3.69, 3.67, 3.65, 3.63, 3.61, 3.59, 3.57, 3.55, 3.53, 3.51, 3.49, 3.47, 3.45, 3.43, 3.41, 3.39, 3.37, 3.35, 3.33, 3.31, 3.29, 3.27, 3.25, 3.23, 3.21, 3.19, 3.17, 3.15, 3.13, 3.11, 3.09, 3.07, 3.05, 3.03, 3.01, 2.99, 2.97, 2.95, 2.93, 2.91, 2.89, 2.87, 2.85, 2.83, 2.81, 2.79, 2.77, 2.75, 2.73, 2.71, 2.69, 2.67, 2.65, 2.63, 2.61, 2.59, 2.57, 2.55, 2.53, 2.51, 2.49, 2.47, 2.45, 2.43, 2.41, 2.39, 2.37, 2.35, 2.33, 2.31, 2.29, 2.27, 2.25, 2.23, 2.21, 2.19, 2.17, 2.15, 2.13, 2.11, 2.09, 2.07, 2.05, 2.03, 2.01, 1.99, 1.97, 1.95, 1.93, 1.91, 1.89, 1.87, 1.85, 1.83, 1.81, 1.79, 1.77, 1.75, 1.73, 1.71, 1.69, 1.67, 1.65, 1.63, 1.61, 1.59, 1.57, 1.55, 1.53, 1.51, 1.49, 1.47, 1.45, 1.43, 1.41, 1.39, 1.37, 1.35, 1.33, 1.31, 1.29, 1.27, 1.25, 1.23, 1.21, 1.19, 1.17, 1.15, 1.13, 1.11, 1.09, 1.07, 1.05, 1.03, 1.01, 0.99, 0.97, 0.95, 0.93, 0.91, 0.89, 0.87, 0.85, 0.83, 0.81, 0.79, 0.77, 0.75, 0.73, 0.71, 0.69, 0.67, 0.65, 0.63, 0.61, 0.59, 0.57, 0.55, 0.53, 0.51, 0.49, 0.47, 0.45, 0.43, 0.41, 0.39, 0.37, 0.35, 0.33, 0.31, 0.29, 0.27, 0.25, 0.23, 0.21, 0.19, 0.17, 0.15, 0.13, 0.11, 0.09, 0.07, 0.05, 0.03, 0.01
- 5.82 (broad peak, integration 5.82)
- 2.99, 2.97, 2.95, 2.93, 2.91, 2.89, 2.87, 2.85, 2.83, 2.81, 2.79, 2.77, 2.75, 2.73, 2.71, 2.69, 2.67, 2.65, 2.63, 2.61, 2.59, 2.57, 2.55, 2.53, 2.51, 2.49, 2.47, 2.45, 2.43, 2.41, 2.39, 2.37, 2.35, 2.33, 2.31, 2.29, 2.27, 2.25, 2.23, 2.21, 2.19, 2.17, 2.15, 2.13, 2.11, 2.09, 2.07, 2.05, 2.03, 2.01, 1.99, 1.97, 1.95, 1.93, 1.91, 1.89, 1.87, 1.85, 1.83, 1.81, 1.79, 1.77, 1.75, 1.73, 1.71, 1.69, 1.67, 1.65, 1.63, 1.61, 1.59, 1.57, 1.55, 1.53, 1.51, 1.49, 1.47, 1.45, 1.43, 1.41, 1.39, 1.37, 1.35, 1.33, 1.31, 1.29, 1.27, 1.25, 1.23, 1.21, 1.19, 1.17, 1.15, 1.13, 1.11, 1.09, 1.07, 1.05, 1.03, 1.01, 0.99, 0.97, 0.95, 0.93, 0.91, 0.89, 0.87, 0.85, 0.83, 0.81, 0.79, 0.77, 0.75, 0.73, 0.71, 0.69, 0.67, 0.65, 0.63, 0.61, 0.59, 0.57, 0.55, 0.53, 0.51, 0.49, 0.47, 0.45, 0.43, 0.41, 0.39, 0.37, 0.35, 0.33, 0.31, 0.29, 0.27, 0.25, 0.23, 0.21, 0.19, 0.17, 0.15, 0.13, 0.11, 0.09, 0.07, 0.05, 0.03, 0.01



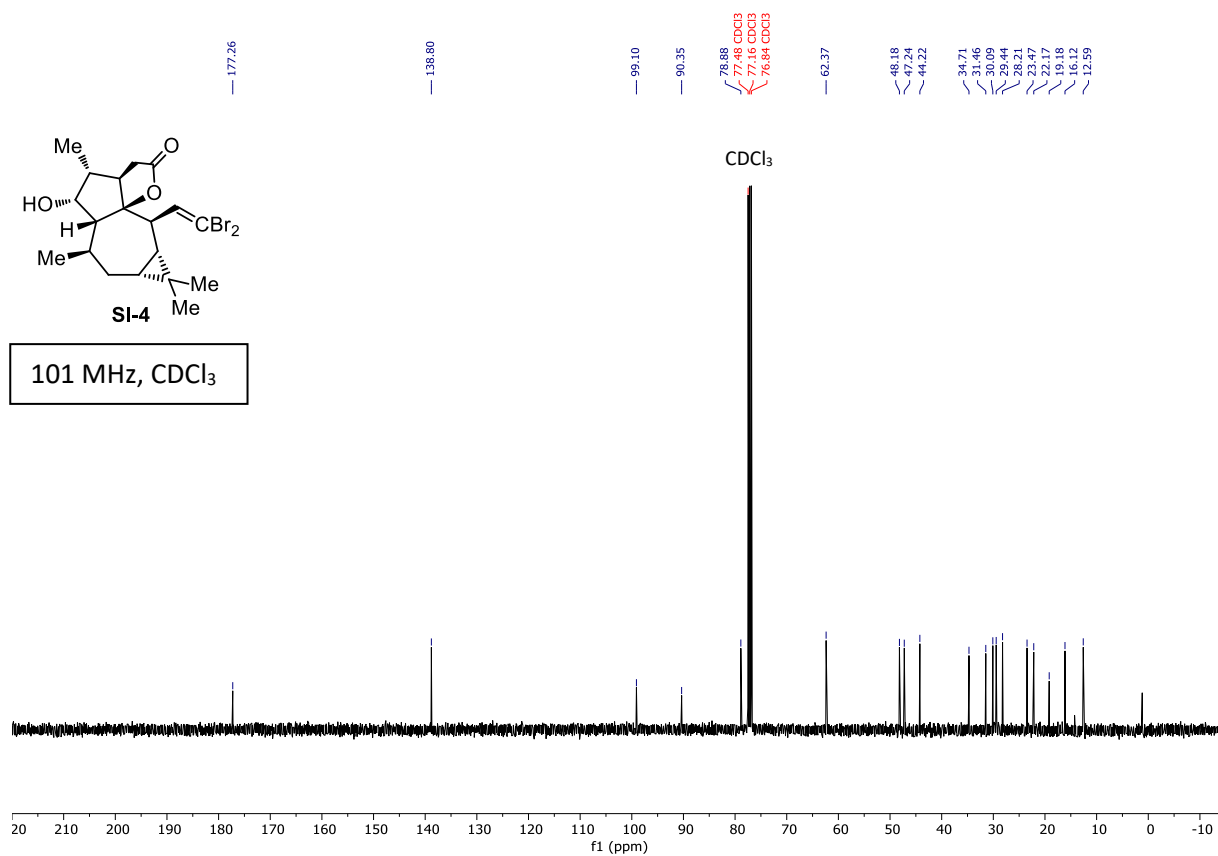
Supporting Information



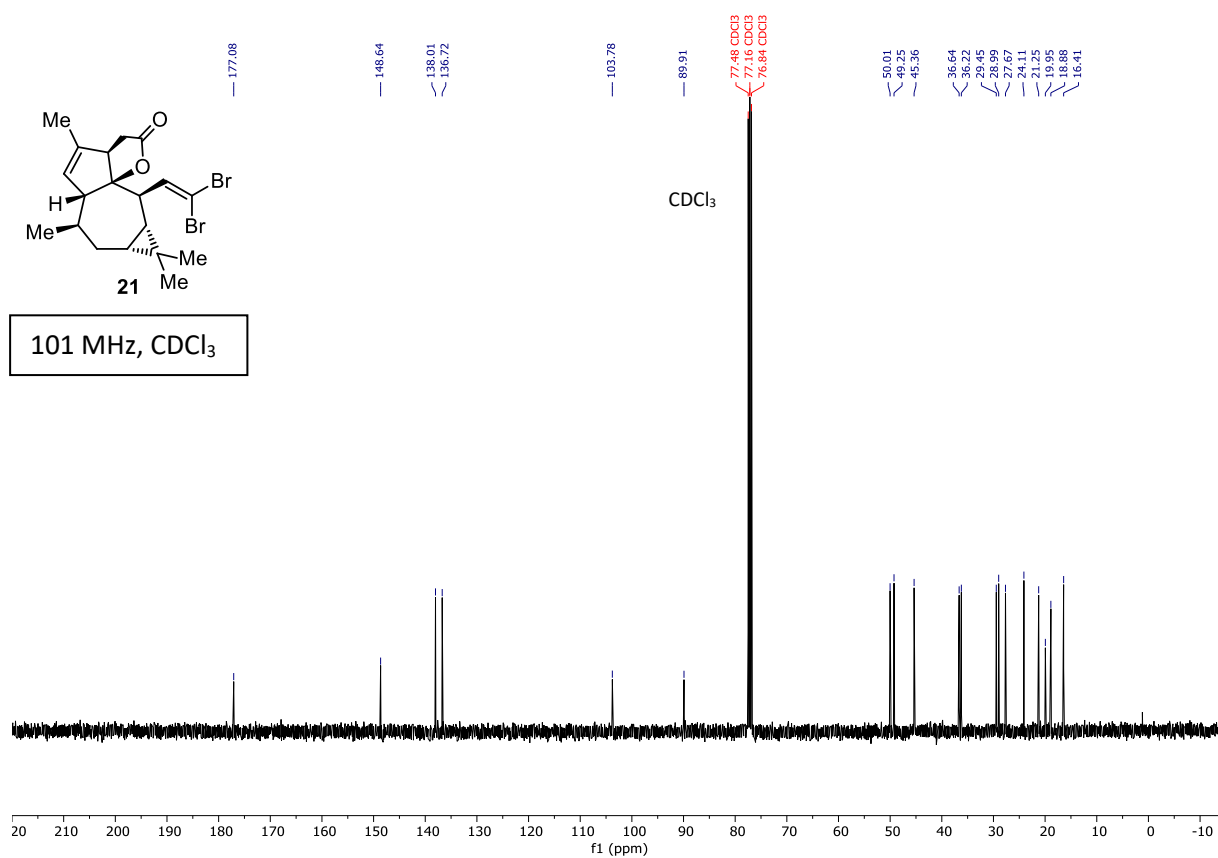
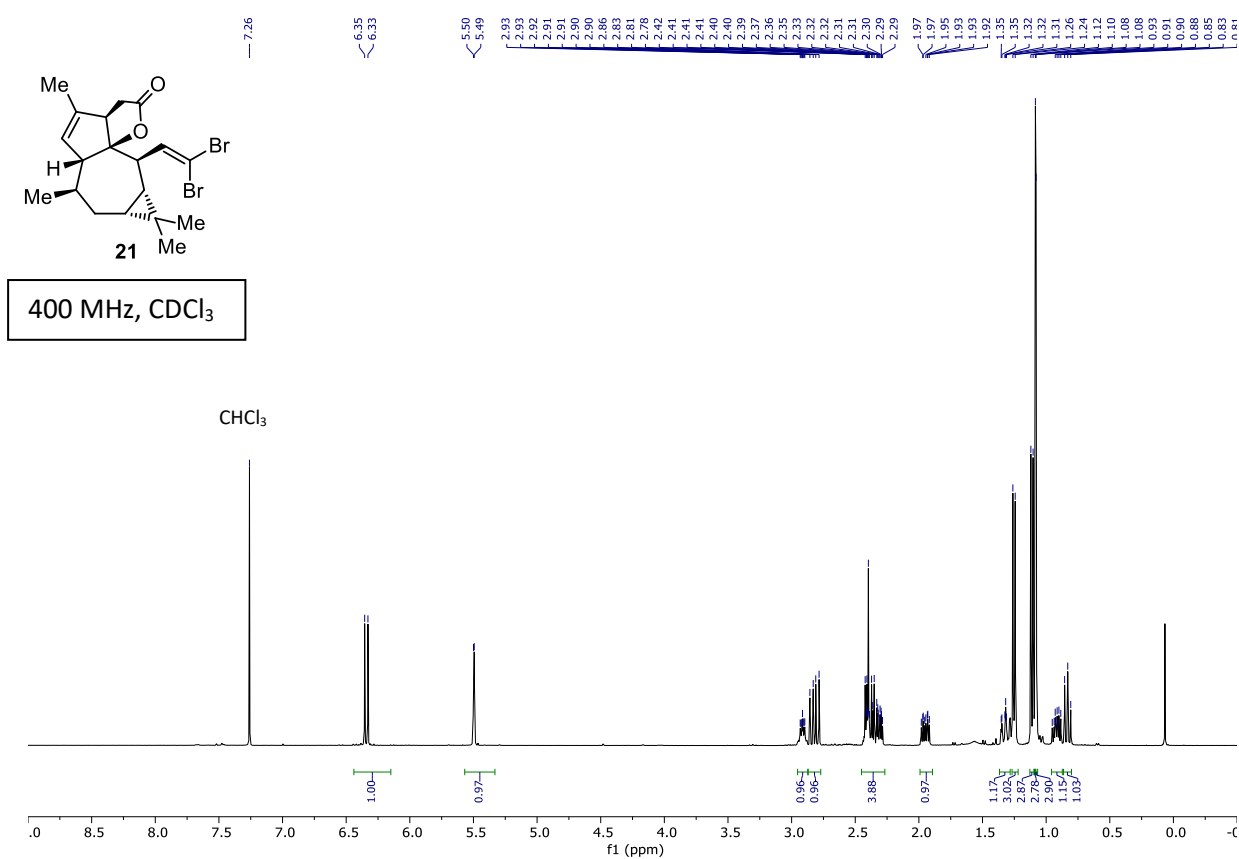
400 MHz, CDCl₃



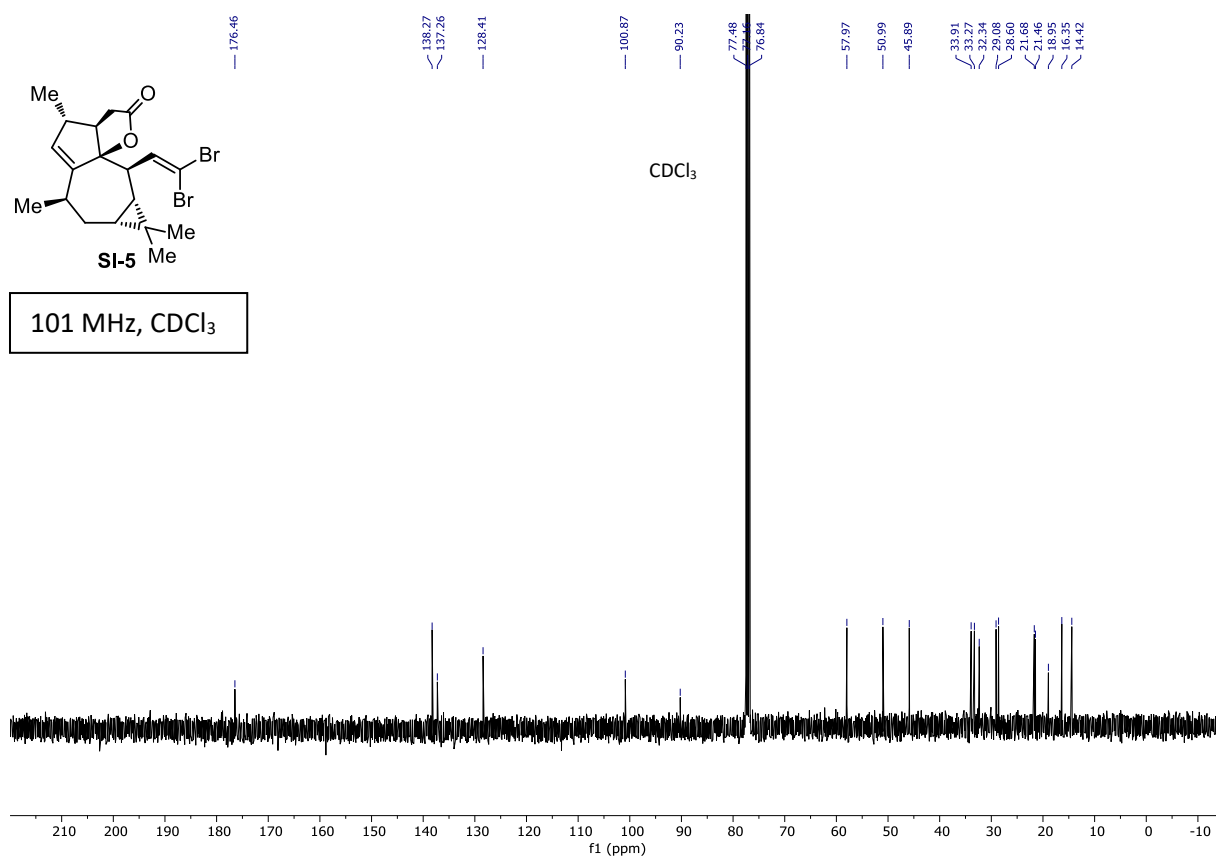
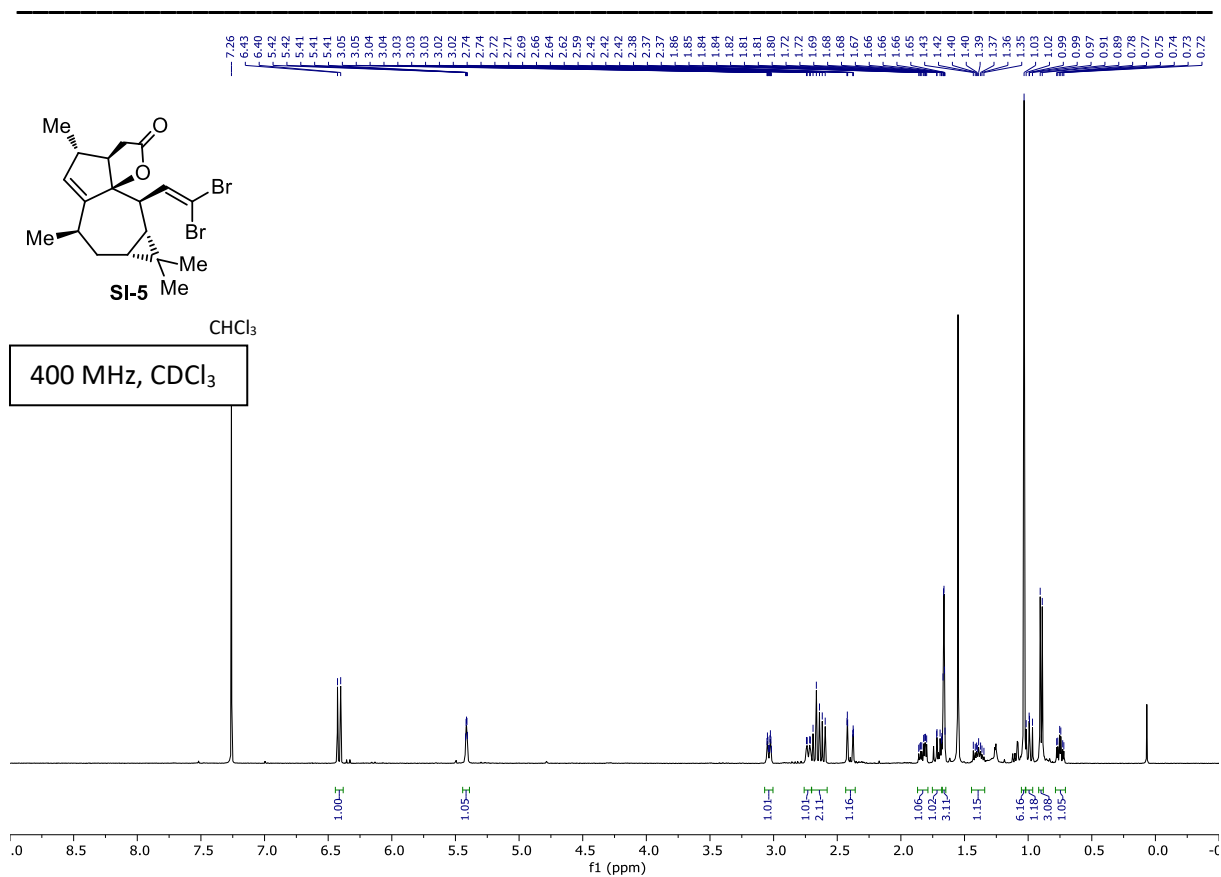
101 MHz, CDCl₃



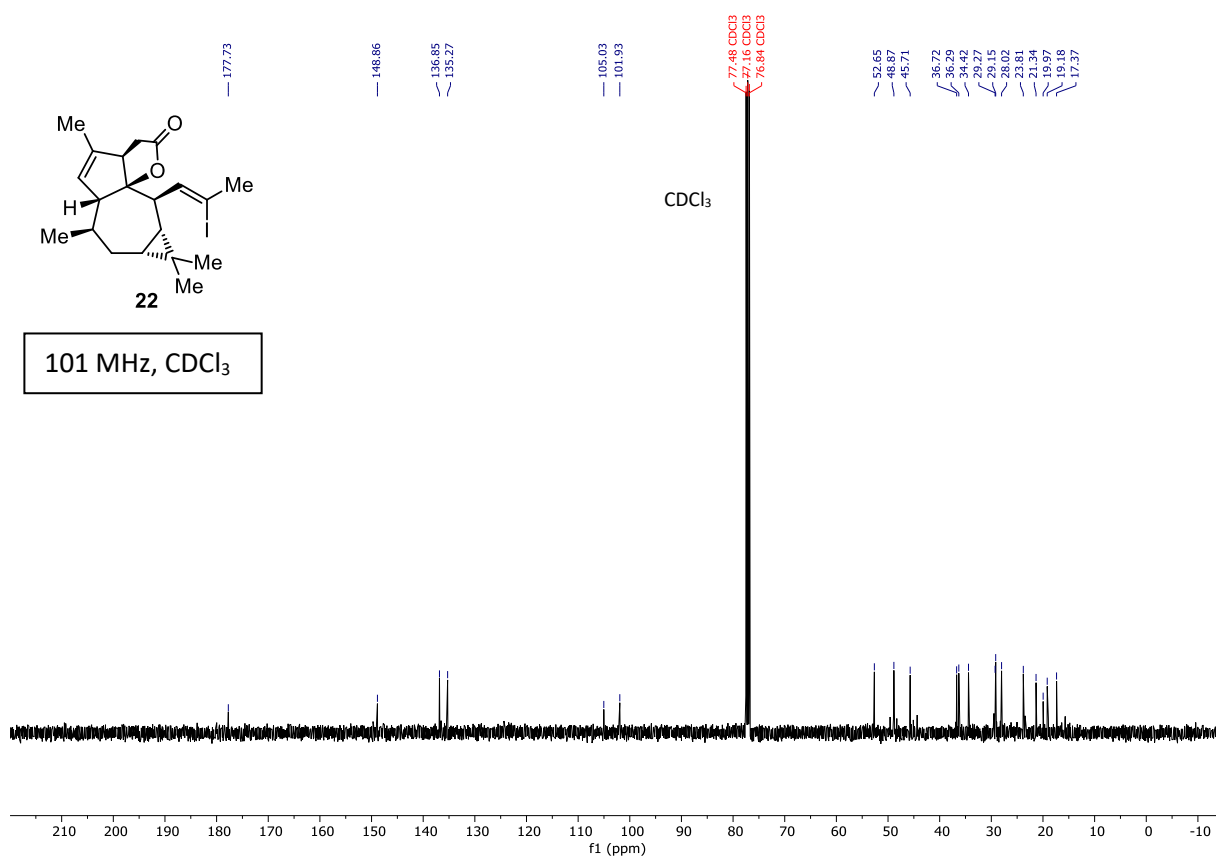
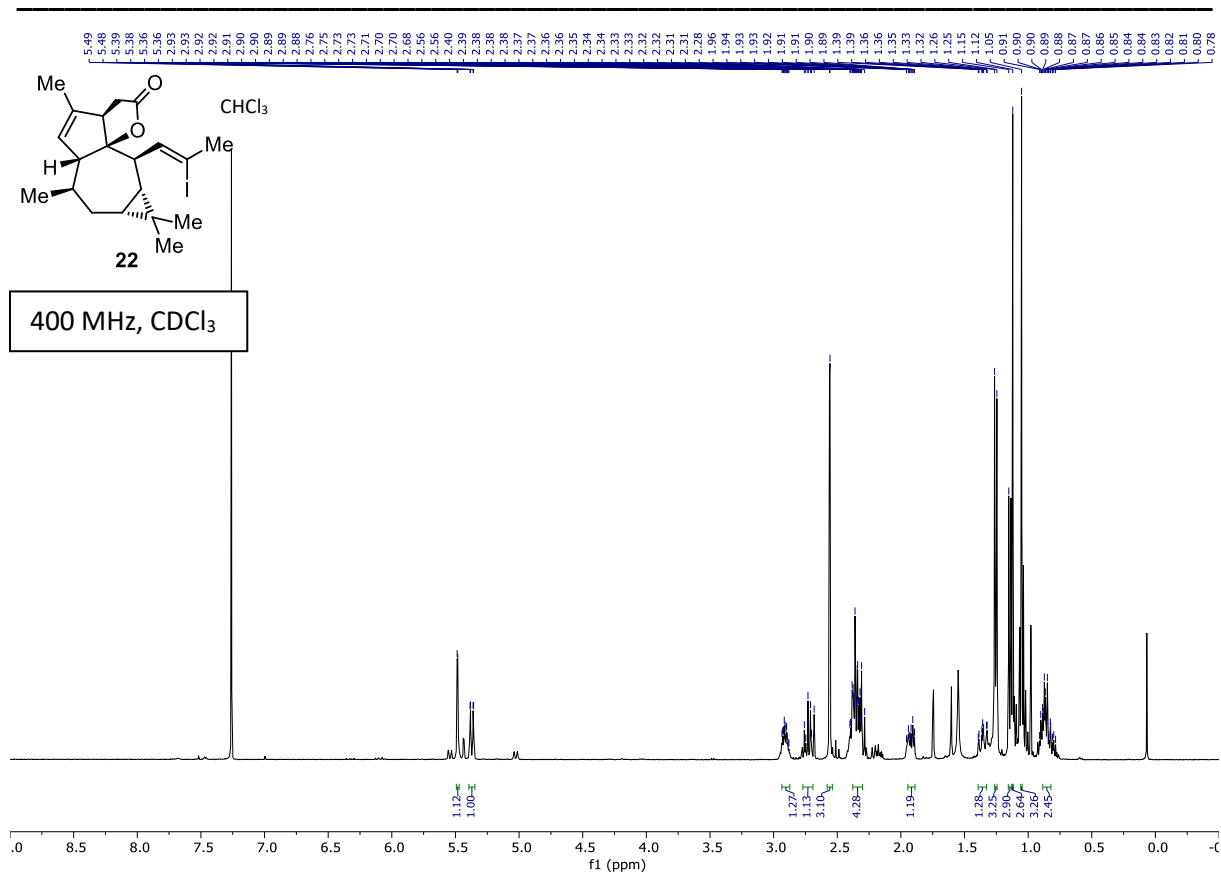
Supporting Information



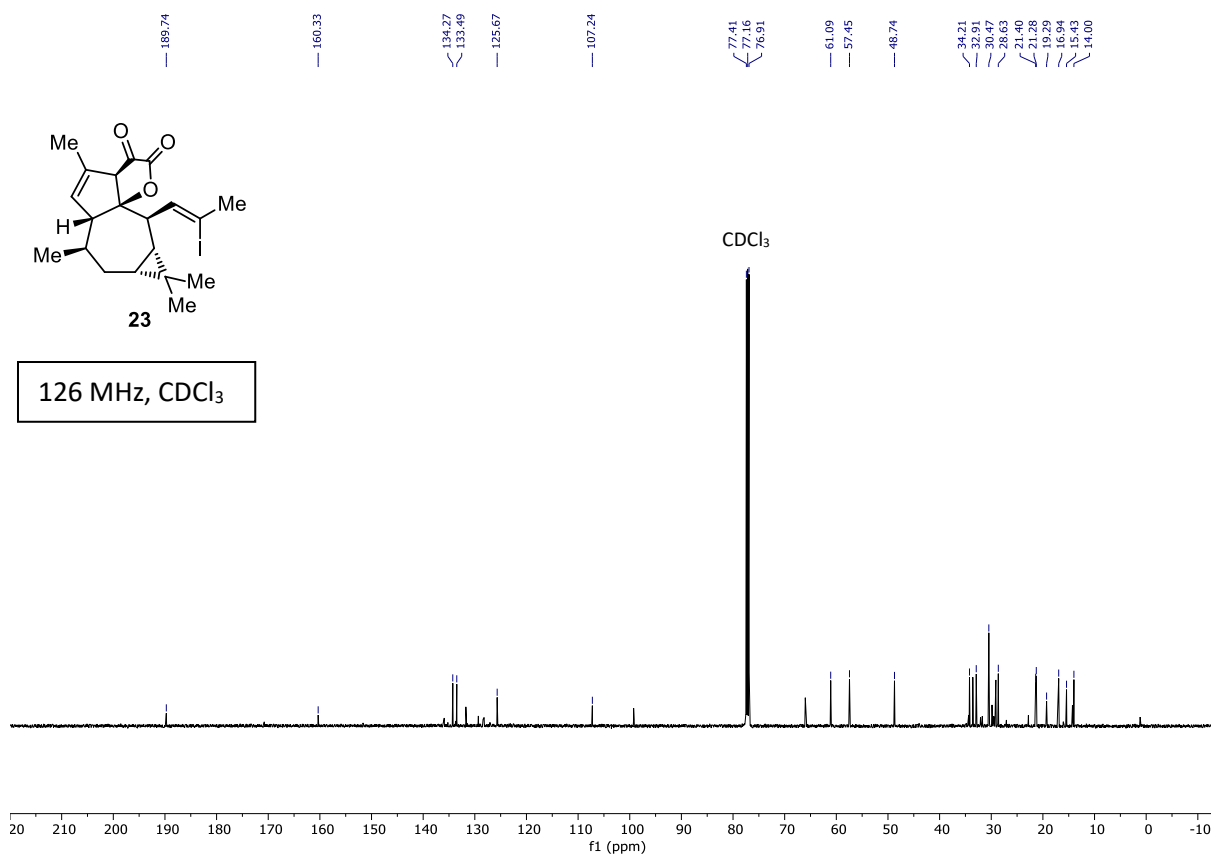
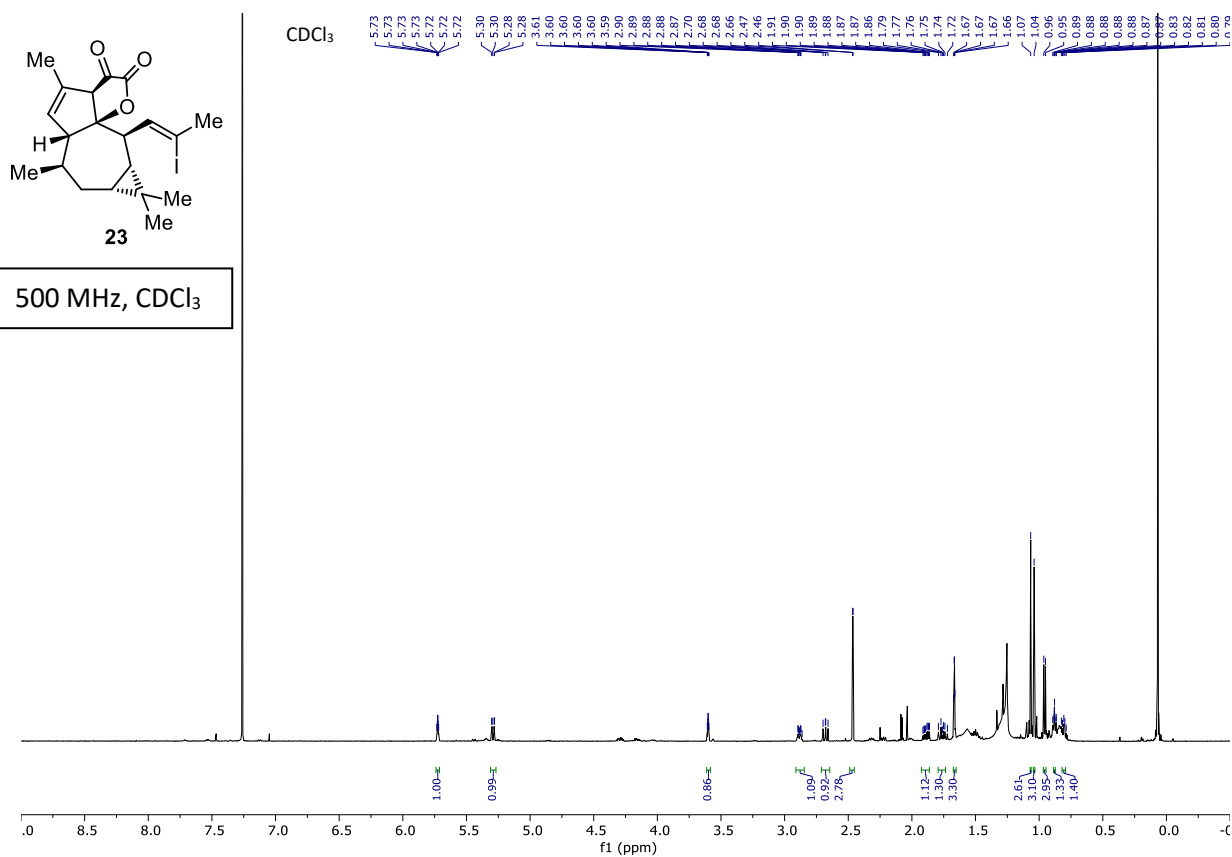
Supporting Information



Supporting Information



Supporting Information



Chemical structure of compound **1** is shown in the top left corner. The structure is a complex polycyclic molecule with multiple methyl groups and a hydroxyl group.

The ^1H NMR spectrum (600 MHz, CDCl_3) is displayed below the structure. The x-axis represents the chemical shift in ppm, ranging from 0.0 to 7.26. The spectrum shows several distinct signals, with integration values provided below the baseline for various peak groups.

Integration values (from left to right):

- 1.00
- 1.00
- 0.94
- 1.87
- 1.16
- 3.08
- 2.94
- 0.91
- 1.20
- 2.48
- 3.40
- 3.28
- 3.41
- 1.35
- 1.13



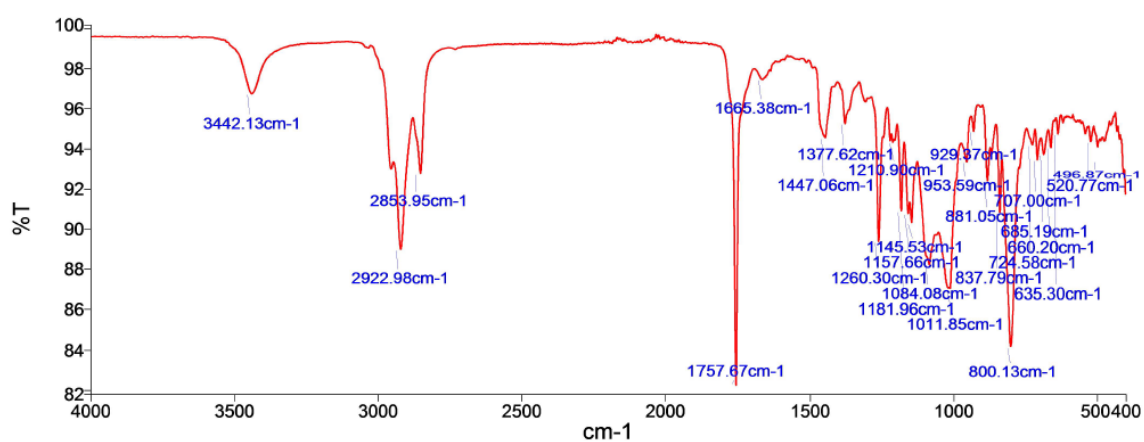
Comparison of natural and synthetic 1.

H	Natural [ppm]⁵	Synthetic [ppm]
1	5.53	5.53
2	-	-
3	3.09	3.09
4	-	-
5	2.71	2.71
6	1.34	1.34
7	1.79, 1.68	1.79, 1.72-1.68
8	0.68	0.69
9	-	-
10	0.81	0.79-0.82
11	2.34	2.34
12	5.40	5.39
13	-	-
14	-	-
15	-	-
16	1.84	1.84
17	0.89	0.88
18	1.05	1.05
19	1.00	1.00
20	1.81	1.81

Supporting Information

C	Natural [ppm] ⁵	Synthetic [ppm]
1	130.6	130.6
2	137.3	137.3
3	59.6	59.7
4	97.3	97.3
5	54.5	54.6
6	31.3	31.3
7	32.7	32.7
8	20.8	20.9
9	18.8	18.8
10	26.5	26.6
11	39.1	39.1
12	126.1	126.1
13	139.5	139.5
14	80.4	80.4
15	177.0	177.0
16	16.2	16.2
17	20.9	20.9
18	28.6	28.6
19	15.3	15.3
20	16.6	16.6

IR spectrum of 1:



Sources

1. P. Girard; J. L. Namy; H. B. Kagan, Divalent lanthanide derivatives in organic synthesis. 1. Mild preparation of samarium iodide and ytterbium iodide and their use as reducing or coupling agents. *J Am Chem Soc* **1980**, *102* (8), 2693-2698.
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3. T. Satoh; Y. Kaneko; T. Okuda; S. Uwaya; K. Yamakawa, Studies on the Terpenoids and Related Alicyclic Compounds. XXXV. Studies Directed toward a Total Synthesis of Ingenol Esters : Synthesis of the C/D-Ring Moiety of Ingenol Esters from (+)-3-Carene via Tin (IV) Chloride-Promoted Intramolecular Directed Aldol Reaction. *CHEMICAL & PHARMACEUTICAL BULLETIN* **1984**, *32* (9), 3452-3460.
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