Supporting Information

A hypervalent iodine-induced double annulation enables a concise synthesis of the pentacyclic core structure of the cortistatins

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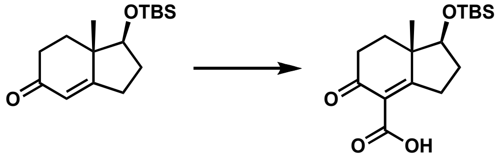
General experimental details

All reactions were carried out under an atmosphere of Ar unless otherwise specified. Tetrahydrofuran (THF), toluene ($PhCH_3$), diethyl ether (Et_2O), benzene, and methylene chloride (CH_2Cl_2) were dried by passing through activated alumina columns. Commercial reagents of high purity were purchased and used without further purification, unless otherwise noted. Reactions were monitored by thin-layer chromatography (TLC) carried out on Whatman Partisil® K6F silica gel 60 Å 250 μM plates using UV light as a visualizing agent in aqueous ceric sulfate / phosphomolybdic acid and heat as a developing agent. Silicycle Silia-P flash ultra pure silica gel (particle size 40-63 μM was used for flash column chromatography.

Instrumentation

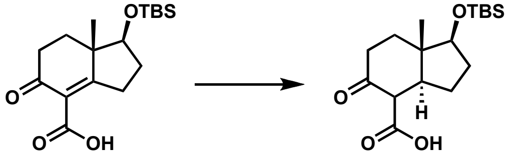
FT-IR spectra were obtained on a Perkin-Elmer Paragon 500 FT-IR. NMR spectra were obtained on Bruker 500 MHz cryoprobe FT-NMR and calibrated to the residual solvent peak (^{1}H NMR: $CDCl_3$: 7.26 ppm; ^{13}C NMR: $CDCl_3$; 77.36 ppm). The multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad signal, dd = doublet of doublets, etc. Optical rotations were recorded on a Perkin-Elmer model 341 polarimeter using a 1 mL, 1 dm cell. Mass spectra were obtained using Agilent 6210 Time of Flight (ESI) with internal standard methyl stearate.

Experimental Details



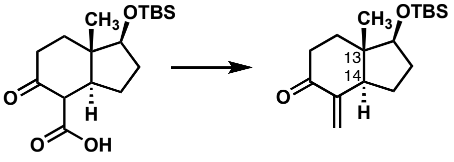
9 **10**

α,β-Unsaturated β-keto acid **10**: To a solution of the enone **9** (6.7 g, 23.9 mmol, 1 equiv) in DMF (52 mL), was added methyl magnesium carbonate (2 M in DMF, 42.0 mL, 3.5 equiv) and the solution was degassed with argon for 20 minutes at room temperature. The reaction vessel was lowered into a pre-heated 130 °C oil bath and heated at this temperature for 3 hours. The solution was then cooled to 0 °C and 2M HCl was added until the solution solidified. The thick suspension was diluted with ether and acidified with conc. HCl until both layers were homogenous. The aqueous phase (now pH ~ 2-3) was extracted at 0 °C with Et_2O (3 x 100 mL) and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was allowed to solidify under vacuum (~ 0.1 mmHg) overnight. The solid was taken up in a minimal amount of hexanes with heating and was precipitated at – 78 °C (acetone/dry ice) to give the α,β-unsaturated β-keto acid **10** (6.5 g, 85% yield).



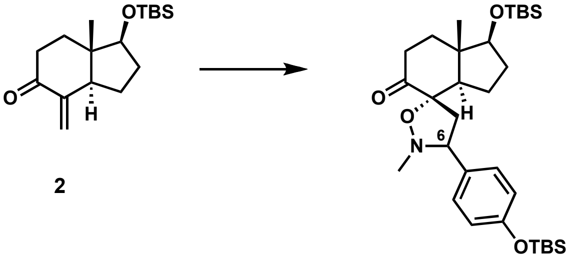
10 **11**

β-Keto acid **11**: To a suspension of $Pd/BaSO_4$ (750 mg, 5% wt/wt) in methanol (25 mL) was added the unsaturated keto acid **10** (4.98 g, 15.4 mmol, 1 equiv) in methanol (75 mL). The flask was evacuated and filled with H_2 (1 atm, double balloon) three times and stirred at room temperature for 5 hours. The reaction mixture was filtered through a pad of celite which was washed with methanol. The filtrate was concentrated under reduced pressure to give the saturated β-keto acid **11** which was taken onto the next step without further purification.



11 **2**

Enone **2**: To a solution of the crude keto acid **11** (~ 15.4 mmol, 1 equiv) in CH_3CN (770mL) was added *N*,*N*-dimethylmethyleneiminium iodide (Eschenmosher's salt; 4.96 g, 26.8 mmol, 1.74 equiv). The suspension was sonicated for 5 min at room temperature and the reaction flask was lowered into a pre-heated 95 °C oil bath. The reaction was refluxed for 1 hour. The reaction mixture was allowed to cool to room temperature and the solution was concentrated under reduced pressure. The concentrate was partitioned between Et_2O and 1N HCl, and the aqueous layer extracted with Et_2O (3 x 150 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and the solution was concentrated under reduced pressure. Purification of the residue via column chromatography (silica gel, 20% ethyl acetate/hexanes) provided enone **12** (4.12 g, 90 % over 2 steps) as a colorless oil.

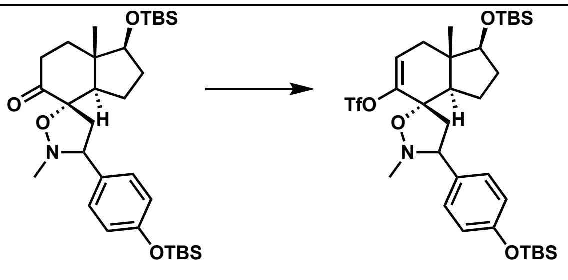


2

13

N-methyl isoxazolidine **13**: Nitrone **12** (5.17 g, 19.5 mmol, 1.5 equiv) was added to a solution of enone **2** (3.82 g, 13 mmol, 1 equiv in 65 mL toluene) and heated to 110 °C in a sealed tube for 15 hours. Once cooled, the reaction mixture was concentrated *in vacuo*. The crude residue was purified by flash column chromatography (silica gel, 10% EtOAc/hexanes) furnishing 13 as a mixture of two C6 diastereomers (3.92 g, 54% as combined yield). **13a**: TLC: R_f = 0.36 (20% EtOAc/hexanes); IR (film) 2943, 2849, 1713, 1509, 1466, 1263, 1102, 898, 839, 771 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.3 Hz, 2H), 6.79 (d, *J* = 8.3 Hz, 2H), 3.66 (app t, *J* = 8.9 Hz, 1H), 3.58 (dd, *J* = 11.4, 5.9 Hz, 1H), 2.65 (s, 3H), 2.72-2.59 (m, 2H), 2.47 (ddd, *J* = 16.1, 4.7, 1.5 Hz, 1H), 2.26 (dd, *J* = 12.8, 5.6 Hz, 1H), 2.06 (dddd, *J* = 15.1, 9.1, 9.1, 5.6 Hz, 1H), 2.05 (dd, *J* = 11.7, 7.8 Hz, 1H), 1.94-1.79 (m, 3H), 1.65-1.56 (m, 1H), 1.41 (ddd, *J* = 12.9, 12.9, 5.0 Hz, 1H), 0.97 (s, 9H), 0.95 (s, 3H), 0.87 (s, 9H), 0.18 (s, 6H), 0.02 (s, 3H), and 0.01 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.8, 155.9, 130.3, 129.0, 120.6, 88.1, 81.1, 71.8, 51.9, 44.7, 43.8, 43.7, 36.3, 35.8, 31.3, 26.1, 26.0, 19.8, 18.5, 18.3, 11.7, -4.1, and -4.6; $[\alpha]^{20}_D$ = +35.6 (c 1.1, $CDCl_3$); HRMS (ESI) calculated for $C_{31}H_{54}NO_4Si_2$ $[M^+H]^+$ 559.3513, found 559.3508.

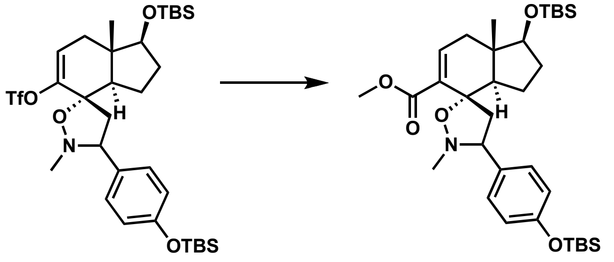
13b: TLC: R_f = 0.30 (30% EtOAc/hexanes); IR (film) 2926, 2849, 1713, 1509, 1458, 1254, 1102, 907, 830, 771 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 8.5 Hz, 2H), 3.63 (app t, *J* = 8.8 Hz, 1H), 3.23 (dd, *J* = 9.5, 7.3 Hz, 1H), 2.60 (ddd, *J* = 15.6, 14.0, 6.5 Hz, 1H), 2.51 (s, 3H), 2.46 (ddd, *J* = 15.2, 4.6, 2.0 Hz, 1H), 2.11 (dd, 12.0, 10.6 Hz, 1H), 2.04 (dddd, *J* = 13.0, 9.3, 9.3, 5.5 Hz, 1H), 1.93 (dd, *J* = 11.6, 7.2 Hz, 1H), 1.86 (ddd, *J* = 12.5, 6.1, 2.3 Hz, 1H), 1.79-1.54 (m, 3H), 1.41 (ddd, *J* = 13.6, 13.6, 4.6 Hz, 1H), 0.99 (s, 3H), 0.96 (s, 9H), 0.87 (s, 9H), 0.17 (s, 6H), 0.01^+ (s, 3H), and 0.01^-(s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 210.8, 155.8, 130.4, 129.2, 120.4, 86.7, 80.8, 74.6, 50.1, 44.6, 43.5, 43.3, 36.2, 35.7, 31.0, 26.0, 25.8, 20.0, 18.4, 18.2, 12.2, -4.2, -4.3, -4.3, and -4.7; $[\alpha]^{20}_{D}$ = -57.1 (c 1.4, $CDCl_3$); HRMS (ESI) calculated for $C_{31}H_{54}NO_4Si_2$ $[M^{+}H]^{+}$ 559.3513, found 559.3508.



13a, b **SI-1a,b**

Enol triflate **SI-1a**: To a solution of **13a** (760 mg, 1.22 mmol, 1 equiv in 2.45 mL THF) was added KHMDS (0.5 M in toluene, 3.42 mL, 1.4 equiv) dropwise at -78 ºC. The reaction mixture was stirred at -78 ºC and then Comins' reagent (526 mg, 1.34 mmol, 1.1 equiv in 1.5 mL THF) was added. The reaction mixture continued to stir at -78 ºC for another hour and was then quenched by addition of NH_4Cl *(aq)* saturated solution. The aqueous layer was extracted three times with Et_2O. The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The residue obtained was purified by a quick silica gel plug (20% EtOAc/hexanes) to furnish enol triflate **SI-1a** (880 mg, 96%) as a solid.

Enol triflate **SI-1b**: To a solution of **13b** (906 mg, 1.46 mmol, 1 equiv in 3 mL THF) was added KHMDS (0.5 M in toluene, 4.1 mL, 1.4 equiv) dropwise at -78 ºC. The reaction mixture was stirred at -78 ºC and then Comins' reagent (632 mg, 1.61 mmol, 1.1 equiv in 1.5 mL THF) was added. The reaction mixture continued to stir at -78 ºC for another hour and was then quenched by addition of NH_4Cl *(aq)* saturated solution. The aqueous layer was extracted three times with Et_2O. The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The residue obtained was purified by a quick silica gel plug (20% EtOAc/hexanes) to furnish enol triflate **SI-1b** (910 mg, 83%) as a solid.



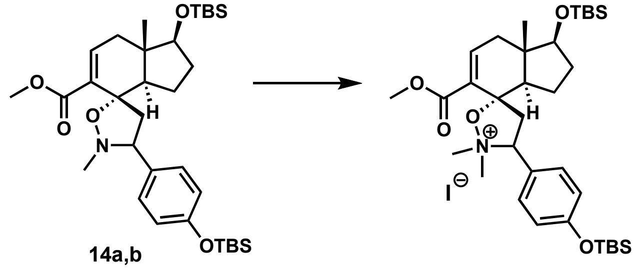
SI-1a, b **14a,b**

Methyl ester **14a**: Enol triflate **SI-1a** (880 mg, 1.17 mmol, 1 equiv) was dissolved in DMF (5 mL) and purged with CO (1 atm, double balloon) for 5 mintues. In a separate flask, a mixture of $PdCl_2(dppf)$ (100 mg, 0.12 mmol, 0.1 equiv), Et_3N (490 µL, 3.51 mmol, 3 equiv) and MeOH (5 mL) was also purged with CO (1 atm, double balloon) for 5 minutes. The DMF solution of enol triflate was then added and the reaction mixture was purged with CO for another 5 minutes. After purging, the mixture was stirred under 1 atm of CO (double balloon) at 60 °C for 15 hours. After cooling, the reaction mixture was filtered through celite and concentrated *in vacuo*. The residue was dissolved in Et_2O, washed with water, dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (silica gel, 20% EtOAc/hexanes) to give methyl ester **14a** (589 mg, 76%) as an oil. TLC: R_f = 0.72 (20% EtOAc/hexanes); IR (film) 2943, 2857, 1721, 1500, 1263, 1102, 899, 839, 771, 670 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.3 Hz, 2H), 6.81 (d, *J* = 8.3 Hz, 2H), 6.52 (dd, *J* = 5.6, 2.0 Hz, 1H), 3.82 (s, 3H), 3.74 (app t, *J* = 8.4 Hz, 1H), 3.26 (dd, *J* = 11.1, 6.5 Hz, 1H), 3.13 (dd, *J* = 12.6, 11.1 Hz, 1H), 2.68 (dd, *J* = 12.5, 6.5 Hz, 1H), 2.43 (s, 3H), 2.14 (dd, *J* = 18.2, 5.6 Hz, 1H), 2.06-1.79 (m, 5H), 1.74 (ddd, *J* = 12.3, 12.3, 5.0 Hz, 1H), 0.98 (s, 9 H), 0.87 (s, 9H), 0.74 (s, 3H), 0.18 (s, 6H), and 0.02 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$)

δ 167.41, 155.34, 141.31, 134.82, 132.90, 129.05, 120.39, 81.82, 81.79, 74.04, 52.41, 51.82, 45.89, 44.14, 43.43, 40.10, 31.22, 26.14, 26.01, 22.33, 12.95, -4.05; $[\alpha]^{20}{}_{D}$ = +113 (c 0.94, $CDCl_3$); HRMS (ESI) calculated for $C_{33}H_{56}NO_5Si_2$ $[M^{+}H]^{+}$ 601.3618, found 601.3619.

Methyl ester **14b**: Enol triflate **SI-1b** (910 mg, 1.21 mmol, 1 equiv) was dissolved in DMF (6 mL) and purged with CO (1 atm, double balloon) for five mintues. In a separate flask, a mixture of $PdCl_2$(dppf) (100 mg, 0.121 mmol, 0.1 equiv), Et_3N (505 μL, 3.63 mmol, 3 equiv) and MeOH (6 mL) was also purged with CO (1 atm, double balloon) for five minutes. The DMF solution of enol triflate was then added and the reaction mixture was purged with CO for another five minutes. After purging, the mixture was stirred under 1 atm of CO (double balloon) at 60 °C for 15 hours. After cooling, the reaction mixture was filtered through celite and concentrated *in vacuo*. The residue was dissolved in Et_2O, washed with water, dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue obtained was purified by flash column chromatography (silica gel, 20% EtOAc/hexanes) to give methyl ester **14b** (586 mg, 73%) as an oil. TLC: R_f = 0.70 (20% EtOAc/hexanes); IR (film) 2954, 2949, 1717, 1508, 1255, 1113, 912, 882, 830, 778 cm^{-1}; ^{1}H NMR (500MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.6 Hz, 2H), 6.87 (dd, *J* = 5.6, 2.3 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 2H), 4.05 (dd, *J* = 9.6, 7.9 Hz, 1H), 3.78 (s, 3H), 3.75 (app t, *J* = 7.9 Hz), 2.73 (dd, *J* = 12.6, 7.9 Hz, 1H), 2.54 (dd, *J* = 12.6, 9.6 Hz, 1H), 2.47 (s, 3H), 2.21-2.10 (m, 2H), 2.08-1.97 (m, 4H), 0.98 (s, 9H), 0.87 (s, 9H), 0.66 (s, 3H), 0.19 (s, 6H), and 0.02 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.70, 155.72, 136.03, 129.72, 120.49, 81.98, 75.00, 52.20, 48.57, 44.01, 43.94, 43.66, 39.41, 30.37, 26.14, 26.03, 20.61, 12.98; $[\alpha]^{20}{}_{D}$ = -15.9 (c 0.93, $CDCl_3$); HRMS (ESI) calculated for $C_{33}H_{56}NO_5Si_2$ $[M^{+}H]^{+}$

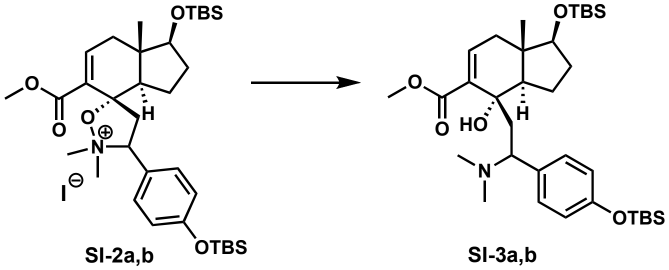
601.3618, found 601.3619.



14a,b **SI-2a,b**

Quaternized isoxazolidine **SI-2a**: Iodomethane (3.5 mL) was added to a solution of methyl ester **2.37** (574 mgs 0.864 mmol, 1 equiv in 8.7 mL THF) and stirred at ambient temperature for 48 hours. The reaction mixture was concentrated *in vacuo* furnishing a solid that was used without further purification.

Quaternized isoxazolidine **SI-2b**: Iodomethane (3.5 mL) was added to a solution of methyl ester **14b** (570 mgs 0.860 mmol, 1 equiv in 8.6 mL THF) and stirred at ambient temperature for 24 hours. The reaction mixture was concentrated *in vacuo* furnishing a solid that was used without further purification.

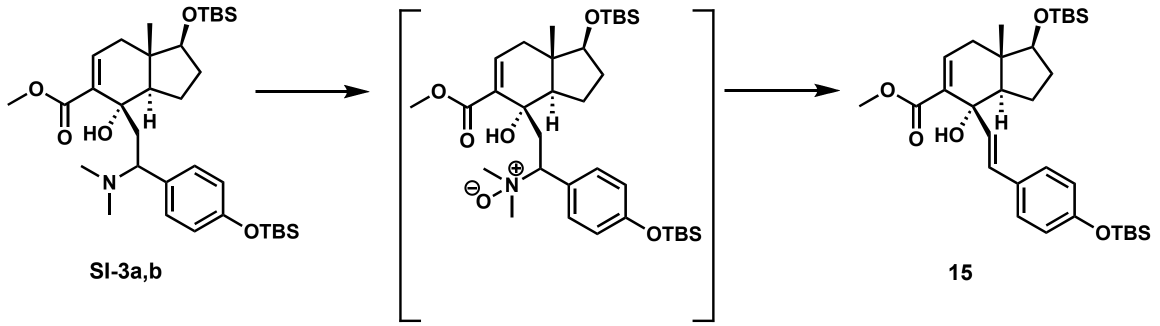


SI-2a,b **SI-3a,b**

Dimethyl amino alcohol **SI-3a**: Methyl ester **SI-2a** (649 mg, 0.872 mmol, 1 equiv) was dissolved in a THF/H_2O (16 mL, 1:1) mixture. To this mixture was added glacial acetic acid (17 mL) followed by zinc dust (313 mg, 4.80 mmol, 5.5 equiv). The reaction mixture was allowed to stir at ambient temperature for 2 hours and then filtered through celite. The celite pad was washed with MeOH several times. The filtrate and MeOH washings were concentrated *in vacuo* and the crude residue was purified by flash column chromatography (silica gel, 20% acetone/hexanes then 100% acetone) to give dimethyl amino alcohol **SI-3a**(526 mg, 97%) as an oil. $R_f = 0.13$ (20% acetone/hexanes); IR (film) 2948, 2850, 1696, 1464, 1255, 1105, 1016, 913, 829, 770 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, J = 8.5 Hz, 2H), 6.88 (dd, J = 5.3, 2.2 Hz, 1H), 6.86 (d, J = 8.5 Hz, 2H), 4.61 (app t, J = 6.8 Hz, 1H), 3.77 (s, 1H), 3.71 (app t, J = 8.2 Hz, 1H), 3.67 (s, 3H), 2.66 (dd, J = 14.7, 5.9 Hz, 1H), 2.43-2.35 (m, 1H), 2.38 (s, 6H), 2.25 (dd, J = 14.6, 7.3 Hz, 1H), 2.21-2.15 (s, 1H), 2.07-1.89 (m, 4H), 1.61-1.51 (m, 1H), 0.99 (s, 9H), 0.88 (s, 9H), 0.85 (s, 3H), 0.21 (s, 3H), 0.03 (s, 3H), and 0.02 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.67, 168.52, 156.48, 142.18, 135.47, 131.69, 131.12, 126.32, 120.14, 81.91, 81.46, 73.29, 65.47, 53.02, 52.39, 52.11, 52.03, 43.69, 42.95, 40.10, 40.08, 35.86, 30.67, 26.13, 26.10, 25.96, 20.81, 18.54, 18.37, 14.05, -4.02, -4.05, -4.50; HRMS (ESI) calculated for $C_{34}H_{60}NO_5Si_2$ $[M^+H]^+$ 617.3931, found 617.3924.

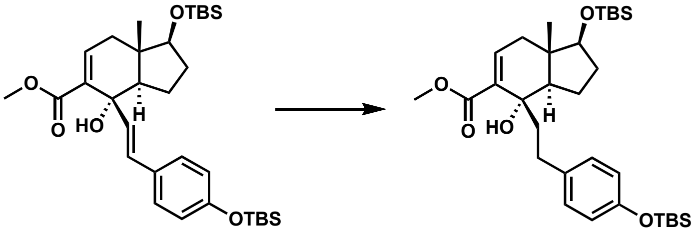
Dimethyl amino alcohol **SI-3b**: Methyl ester **SI-2b** (630 mg, 0.847 mmol, 1 equiv) was dissolved in a THF/H_2O (16 mL, 1:1) mixture. To this mixture was added glacial acetic acid (17 mL) followed by zinc dust (305 mg, 4.66 mmol, 5.5 equiv). The reaction mixture was allowed to stir at ambient temperature for 2 hours and then was filtered through celite. The celite pad was washed with MeOH several times. The filtrate and MeOH washings were concentrated *in vacuo* and the crude residue was purified by flash column chromatography (silica gel, 20% acetone/hexanes then 100% acetone) to give dimethyl amino alcohol **SI-2b** (475 mg, 90%) as an oil. TLC: $R_f = 0.11$ (20% acetone/hexanes); IR (film) 2947, 2849, 1694, 1463, 1254, 1105, 1016, 912, 830, 770 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (d, J = 8.3 Hz, 2H), 6.99 (m, 1H), 6.81 (d, J = 8.3 Hz, 2H), 3.9 (d, J = 12.1 Hz, 1H), 3.79 (s, 3H), 3.69 (app t, J = 8.5 Hz, 1H), 2.93

(dd, J = 14.3, 12.4 Hz, 1H), 2.17 (s, 6H), 2.07-1.89 (m, 5H), 1.79 (d, J = 14.8 Hz, 1H), 1.59 (dddd, J = 12.2, 12.2, 12.2, 5.8 Hz, 1H), 1.40 (dddd, J = 12.5, 12.5, 7.7, 3.5 Hz, 1H), 1.0 (s, 9H), 0.86 (s, 9H), 0.71 (s, 3H), 0.23 (s, 6H), 0.02 (s, 3H), and 0.01 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.73, 167.77, 155.22, 140.26, 139.80, 138.03, 136.87, 130.59, 130.46, 128.63, 128.19, 119.76, 119.56, 119.48, 82.22, 81.78, 73.62, 73.36, 64.99, 64.12, 54.02, 52.56, 51.92, 51.80, 43.65, 42.82, 40.33, 40.26, 40.20, 39.69, 34.75, 32.90, 30.78, 30.69, 30.05, 29.58, 26.14, 26.10, 25.98, 21.74, 20.48, 18.48, 18.37, 18.33, 14.50, 14.26, 13.53, -4.05, -4.09, -4.49, -4.54; HRMS (ESI) calculated for $C_{34}H_{60}NO_5Si_2$ $[M^+H]^+$ 617.3931, found 617.3924.



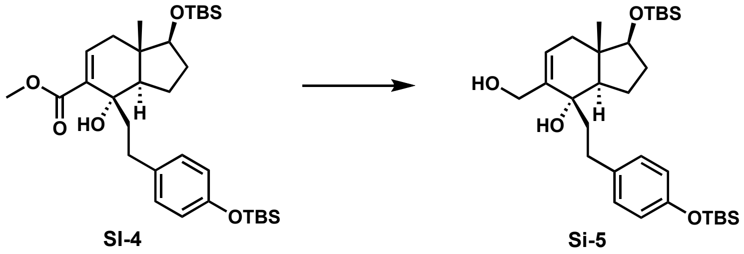
Styrene **15**: To a solution of **SI-3** (45 mg, 0.073 mmol, 1 equiv in 3 mL CH_2Cl_2) was added *m*CPBA (28 mg, 0.161 mmol, 2.2 equiv) at 0 ºC. The reaction mixture was stirred at 0 ºC for 30 minutes and then quenched by the addition of $NaHCO_3$ (*aq)* saturated solution. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The crude *N*-oxide was heated (neat) at 65 ºC for 2 hours to thermally instigate Cope elimination. The crude residue was purified by flash column chromatography (silica gel, 20% acetone/hexanes) to give **15** (30 mg, 73%) as an oil. TLC: R_f = 0.70 (20% acetone/hexanes); IR (film) 2937, 2854, 1717, 1505, 1255, 1107, 913, 830, 774 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, J = 8.5 Hz, 2H), 7.13 (dd, J = 5.8, 2.1 Hz, 1H), 6.77 (d, J = 8.5 Hz, 2H), 6.57

(d, J = 16.2 Hz, 1H), 6.09 (d, J = 16.2 Hz, 1H), 4.47 (s, 1H), 3.73 (s, 3H), 3.73 (app t, J = 7 Hz, 1H, overlapped with 3.73), 2.28 (dd, J = 19.2, 5.9 Hz, 1H), 2.07 (br d, J = 19 Hz, 1H), 2.02 (dd, J = 11.7, 8.0 Hz, 1H), 1.93 (ddd, J = 14.2, 9.3, 5.6 Hz, 1H), 1.78-1.65 (m, 3H), 1.41 (ddd, J = 12.8, 8.1, 5.0 Hz, 1H), 0.97 (s, 9H), 0.87 (s, 9H), 0.80 (s, 3H), 0.18 (s, 6H), 0.03 (s, 3H), and 0.01 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.08, 155.53, 142.66, 133.91, 130.65, 130.15, 130.12, 127.93, 120.46, 81.76, 75.31, 52.19, 51.29, 43.12, 39.86, 30.73, 30.06, 29.73, 26.13, 26.04, 20.21, 18.38, 14.51, 13.91, -4.04, -4.06, -4.50; $[\alpha]^{20}_D$ = +114 (c 0.8, $CDCl_3$); HRMS (ESI) calculated for $C_{32}H_{52}NaO_5Si_2$ $[M^+Na]^+$ 572.3353, found 572.3348.

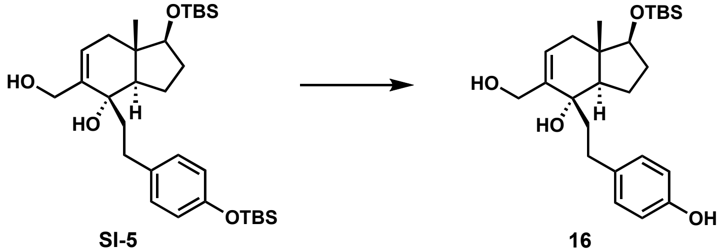


15 **SI-4**

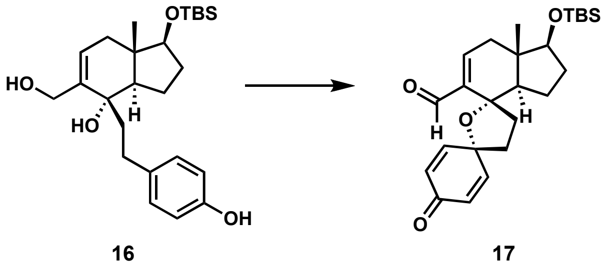
Triol **16**: To a suspension of palladium on carbon (10% w/w) in CH_2Cl_2 (1.5 mL) was added a CH_2Cl_2 (1.5 mL) solution of **15** (30 mg, 0.052 mmol, 1 equiv). The mixture was purged three times with hydrogen (1 atm) and then allowed to stir 3 hours at ambient temperature. The reaction mixture was filtered over celite and washed with a CH_2Cl_2/MeOH mixture. The filtrate and washings were concentrated *in vacuo* furnishing an oil that was used without further purification. TLC: R_f = 0.67 (20% acetone/hexanes); IR (film) 2946, 2853, 1689, 1255, 1107, 903, 830, 774 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, J = 8.2 Hz, 2H), 6.98 (dd, J = 5.7, 2.1 Hz, 1H), 6.73 (d, J = 8.2 Hz, 2H), 4.75 (s, 1H), 3.77 (s, 3H), 3.71 (app t, J = 8.1 Hz, 1H), 2.73-2.62 (m, 2H), 2.22 (dd, J = 18.8, 6.0 Hz, 1H), 2.08-1.79 (m, 7H), 1.54-1.45 (m, 1H), 0.97 (s, 9H), 0.88 (s, 9H), 0.81 (s, 3H), 0.17 (s, 6H), and 0.02 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.46, 153.85, 142.64, 141.73, 135.76, 135.21, 130.14, 129.46, 127.92, 120.45, 120.17, 81.87, 75.30, 73.72, 52.28, 52.18, 51.65, 51.28, 43.16, 39.89, 38.83, 30.72, 30.05, 26.14, 26.03, 21.07, 18.51, 18.37, 13.91, -4.04, -4.09, -4.52; $[\alpha]^{20}_{D}$ = +31.7 (c 0.42, $CDCl_3$); HRMS (ESI) calculated for $C_{32}H_{54}NaO_5Si_2$ $[M^{+}Na]^{+}$ 574.3509, found 574.3506.



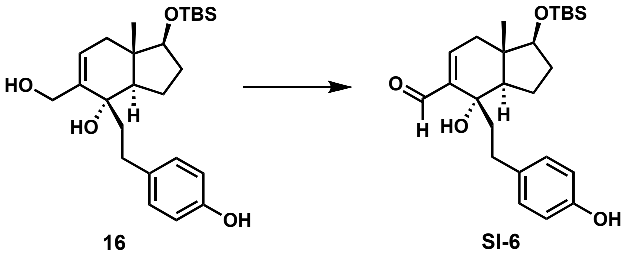
Diol **SI-5**: A solution of **SI-4** (185 mg, 0.324, 1 equiv in 5 mL THF) was added dropwise to a cooled solution (-40 °C dry ice/CH_3CN) of $LiAlH_4$ (2 M in THF, 259 μL, 0.486 mmol). Over a one-hour period, the reaction mixture was allowed to warm to ambient temperature. The excess $LiAlH_4$ was quenched by the slow addition of saturate aqueous solution of potassium sodium tartrate. Once bubbling ceased, the reaction mixture was diluted with Et_2O, filtered over celite. The filtrate was dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (silica gel, 10-20% acetone/hexanes gradient) to afford diol **SI-5** (120 mg, 68%) as an oil. TLC: R_f = 0.40 (20% acetone/hexanes); IR (film) 2937, 2853, 1504, 1245, 1116, 903, 830, 774 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 5.75 (dd, *J* = 5.5, 2.5 Hz, 1H), 4.63 (d, *J* = 12.2 Hz, 1H), 4.13 (d, *J* = 12.2 Hz, 1H), 3.68 (app t, *J* = 8.5 Hz, 1H), 2.8-2.69 (m, 2H), 2.64 (br s, 1H), 2.52 (br s, 1H), 2.1-1.79 (m, 8 H), 1.55-1.46 (m, 1H), 0.98 (s, 9H), 0.88 (s, 9H), 0.78 (s, 3H), 0.19 (s, 6H), 0.03^{+} (s, 3H), and 0.03^{-} (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.0, 141.1, 135.8, 129.4, 128.7, 120.3, 82.0, 66.2, 54.2, 43.8, 39.5, 37.7, 30.81, 30.77, 26.1, 26.0, 20.8, 18.5, 18.4, 13.6, -4.1, and -4.5; $[\alpha]^{20}_{D}$ = +34.3 (c 0.8, $CDCl_3$); HRMS (ESI) calculated for $C_{31}H_{54}NaO_4Si_2$ $[M^{+}Na]^{+}$ 546.3560, found 546.3558.



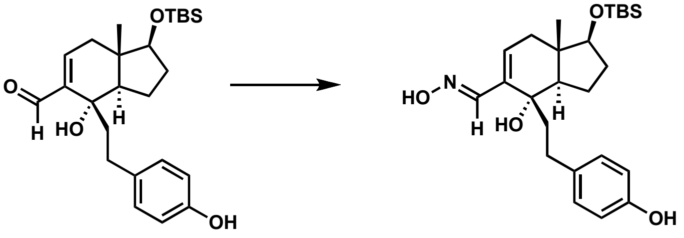
Triol **16**: To a solution of diol **SI-5** (117 mg, 0.214 mmol, 1 equiv in 2 mL CH_2Cl_2) was added TBAF (1 M in THF, 214 µL, 0.214 mmol) at 0 ºC. The reaction mixture was stirred at 0 ºC for 30 minutes and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (silica gel, 50% acetone/hexanes) to furnish triol **16** (93 mg, 99%) as an oil. TLC: R_f = 0.71 (50% acetone/hexanes); IR (film) 3343, 2936, 2854, 1652, 1245, 1116, 829, 774 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 8.5 Hz, 2H), 5.77 (dd, *J* = 5.0, 1.5 Hz, 1H), 4.63 (d, *J* = 12.2 Hz, 1H), 4.14 (d, *J* = 12.2 Hz, 1H), 3.70 (app t, *J* = 8.7 Hz, 1H), 2.84-2.71 (m, 2H), 2.08-1.69 (m, 8H), 1.54-1.46 (m, 1H), 0.88 (s, 9H), 0.78 (s, 3H), 0.03 (s, 3H), and 0.02 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.39, 140.67, 134.83, 129.67, 129.64, 128.93, 115.69, 82.32, 81.98, 77.61, 76.53, 66.23, 65.88, 53.98, 43.78, 39.43, 37.81, 30.78, 30.72, 26.13, 25.97, 21.02, 20.82, 18.37, 18.32, 13.59, -3.26, -4.09, -4.13, -4.51; $[\alpha]^{20}_{D}$ = +40.5 (c 0.37, $CDCl_3$); HRMS (ESI) calculated for $C_{25}H_{40}NaO_4Si$ $[M^{+}Na]^{+}$ 432.2695, found 432.2692.



Aldehyde **17:** To a solution of triol **16** (83 mg, 0.192 mmol, 1 equiv in 2.4 mL CH_2Cl_2) was added $NaHCO_3$ (*s*) (36 mg, 0.422 mmol, 2.2 equiv) and Dess-Martin Periodinane (147 mg, 0.346 mmol, 1.8 equiv) at 0 ºC. The reaction mixture was stirred at 0 ºC for 30 minutes and then quenched by the addition of a 1:1 mixture of $NaHCO_3$ and $Na_2S_2O_3$ (*aq)* saturated solutions. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (silica gel, 10-30% acetone/hexanes gradient to afford **17** (44.4 mg, 54%). TLC: R_f = 0.67 (30% acetone/hexanes); IR (film) 2954, 2925, 2880, 2858, 1697, 1671, 1628, 1463, 1250, 1102, 1028, 857, 836, 776 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.62 (dd, *J* = 10.1, 2.9 Hz, 1H), 6.86 (dd, *J* = 5.7, 2.1 Hz, 1H), 6.79 (dd, *J* = 10.1, 3.0 Hz, 1H), 6.11 (dd, *J* = 10.1, 2.0 Hz, 1H), 6.08 (dd, *J* = 10.1, 2.1 Hz, 1H), 3.77 (app t, *J* = 8.7 Hz, 1H), 2.63-2.48 (m, 2H), 2.40 (dd, *J* = 19.4, 5.6 Hz, 1H) 2.34 (ddd, *J* = 13.3, 9.2, 5.1 Hz, 1H), 2.16 (br d, *J* = 19.5 Hz, 1H), 2.18-2.01 (m, 3H), 1.93-1.70 (m, 3H), 1.64-1.53 (m, 1H), 0.89 (s, 9H), 0.75 (s, 3H), 0.05 (s, 3H), and 0.04 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.69, 186.14, 156.59, 152.06, 151.13, 150.02, 144.71, 128.97, 127.23, 126.89, 87.10, 81.20, 78.33, 51.28, 44.77, 40.59, 38.15, 30.86, 30.50, 30.24, 26.12, 21.57, 12.90, -4.02, -4.50; $[\alpha]^{20}_D$ = -36.3 (c 1.4, $CDCl_3$); HRMS (ESI) calculated for $C_{25}H_{37}O_4Si$ $[M+H]^+$ 428.2383, found 428.2385.



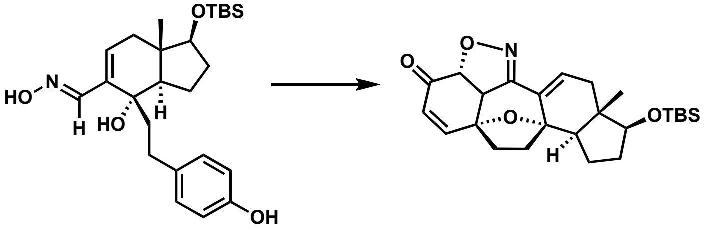
α,β-Unsaturated aldehyde **SI-6**: To a solution of triol **16** (35 mg, 0.081 mmol, 1 equiv in 405 µL 1:8 DMSO/CH_2Cl_2 was added Et_3N (34 µL, 0.243 mmol, 3 equiv) and sulfur trioxide pyridine complex (39 mg, 0.243 mmol, 3 equiv) at 0 ºC. The reaction mixture was stirred at 0 ºC for 20 minutes and then warmed to room temperature and allowed to stir for an additional hour. The reaction was quenched by the addition of H_2O. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by flash column chromatography (silica gel, 30% acetone/hexanes) to furnish the α,β-unsaturated aldehyde **SI-6** (20 mg, 57%). TLC: $R_f = 0.56$ (30% acetone/hexanes): IR (film) 3364 (br), 2954, 2928, 2855, 1670, 1515, 1250, 1134, 1101, 1019, 898, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.43 (s, 1H), 7.01 (d, J = 8.4 Hz, 2H), 6.77 (dd, J = 4.9, 2.3 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 4.92 (br s, 1H), 4.18 (s, 1H), 3.69 (app t, J = 8.5 Hz, 1H), 2.74-2.59 (m, 2H), 2.38 (dd, J = 19.5, 5.3 Hz, 1H), 2.10 (br d, J = 19.5 Hz, 1H), 2.04-1.42 (m, 8 H), 0.85 (s, 9H), 0.79 (s, 3H), 0.00 (s, 3H), and -0.01 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.70, 154.69, 154.65, 153.96, 153.66, 145.69, 135.07, 134.94, 134.62, 129.73, 129.67, 115.54, 82.58, 81.63, 76.95, 74.04, 51.46, 43.12, 40.75, 38.62, 38.57, 31.94, 30.72, 30.55, 26.13, 25.98, 20.61, 14.33, -4.01, -4.11, -4.53; $[\alpha]^{20}_D = +71.9$ (c 1.2, $CDCl_3$); HRMS (ESI) calculated for $C_{25}H_{37}O_3Si$ $[M^+-H_2O+H]^+$ 412.2434, found 412.2430.



SI-6 **19**

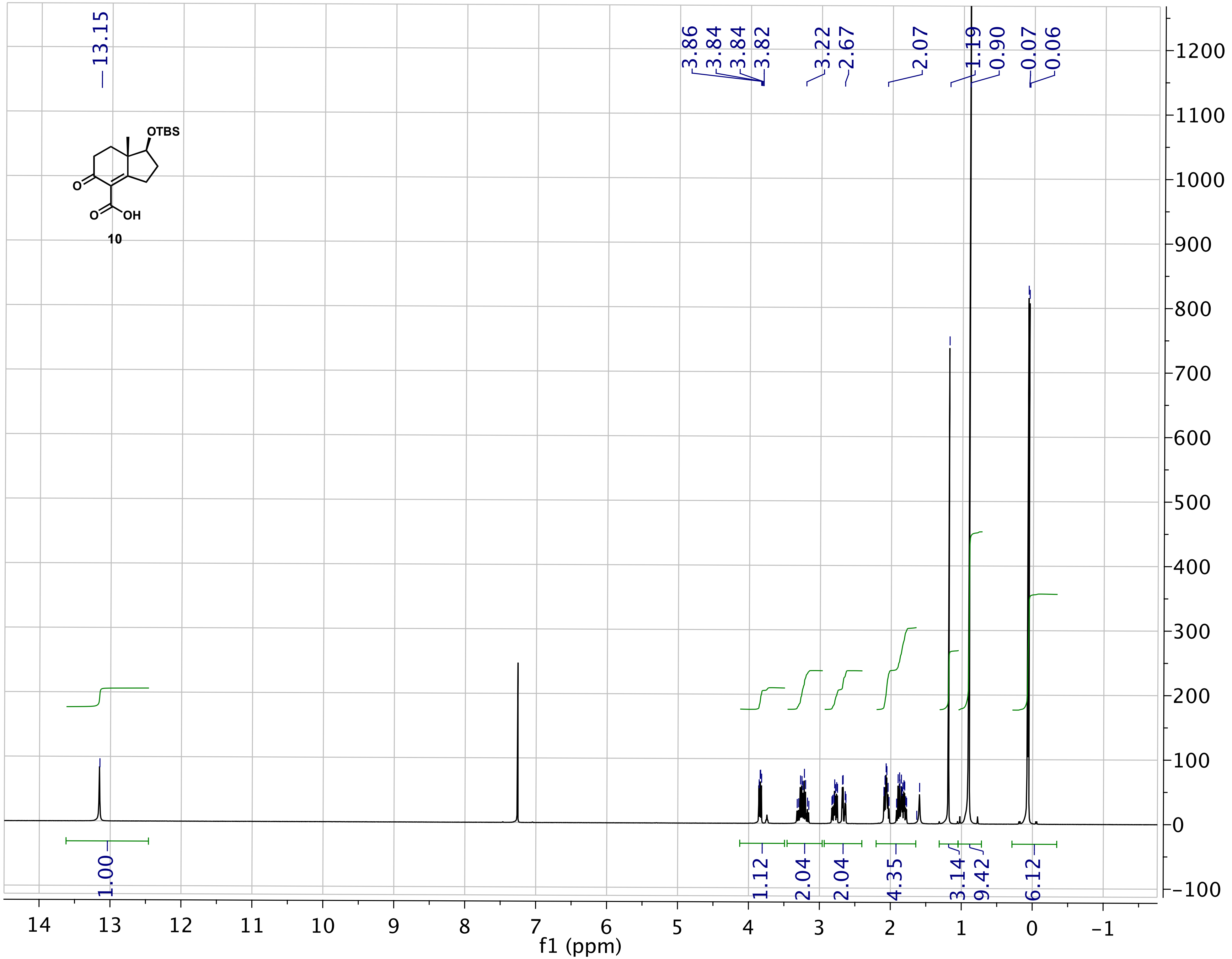
Oxime **18**: To a solution of **SI-5** (2.5 mg, 0.006 mmol, 1 equiv in 300 μL of EtOH) was added sodium acetate (1 mg, 0.012 mmol, 2 equiv) and hydroxylamine hydrochloride (1 mg, 0.012 mmol, 2 equiv). The reaction mixture was heated to 60 ºC for 30 minutes. Once cooled, the reaction mixture was diluted with H_2O and extracted three time with EtOAc. The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo* furnishing the oxime **18** oil that was used without further purification. TLC: R_f = 0.50 (30% acetone/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (br s, 1H), 7.01 (d, *J* = 7.9 Hz, 2H), 6.72 (d, *J* = 7.9 Hz, 2H), 5.98 (dd, *J* = 5.4, 2.3 Hz, 1H), 4.46 (br s, 1H), 3.71 (app t, *J* =8.5 Hz, 1H), 2.76-2.63 (m, 2H), 2.21 (dd, *J* = 18.6, 5.9 Hz, 1H), 2.16 (ddd, *J* = 13.0, 12.2, 6.6 Hz, 1H), 2.00 (dd, *J* = 18.6, 2.0 Hz, 1H), 2.10-1.80 (m, 5H), 1.55 (dddd, *J* = 11.0, 11.0, 8.0, 2.8 Hz, 1H), 0.88 (s, 9H), 0.81 (s, 3H), and 0.03 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.85, 153.54, 138.42, 138.23, 135.48, 129.73, 115.48, 81.94, 74.68, 51.68, 42.96, 40.07, 37.89, 31.03, 30.72, 30.05, 26.14, 20.97, 18.38, 14.06, -4.06, -4.52. HRMS (ESI) calculated for $C_{25}H_{39}NO_4Si$ $[M +H]^+$ 445.2648, found 445.2646.

Isoxazoline **20**:



18 **20**

A solution of PhI(OAc)$_2$ (4 mg, 0.013 mmol, 2.2 equiv in 75 μL 2,2,2-trifluoroethanol) was added dropwise over 15 minutes to a solution of oxime **18** (2.7 mg, 0.006 mmol, 1 equiv in 50 μL 2,2,2-trifluoroethanol) After addition was complete, the reaction mixture was allowed to stir at room temperature for one hour and then concentrated *in vacuo*. The crude residue was quickly flushed through plug of silica gel (30% acetone/hexanes). The oily residue was then heated to 50 ºC for 75 minutes. The crude material was purified via flash column chromatography (20 % acetone:hexanes) and provided the isoxazoline **20** (1.9 mg, 73%). TLC: R_f = 0.44 (30% acetone/hexanes); ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.67 (d, *J* = 10.4, 1H), 6.50 (dd, *J* = 4.9, 3.0 Hz, 1H), 6.33 (d, *J* = 10.4 Hz, 1H), 4.99 (d, *J* = 13.4 Hz, 1H), 3.90 (d, *J* = 13.4 Hz, 1H), 3.76 (app t, *J* = 8.3 Hz, 1H), 2.58 (dd, *J* = 14.0, 10.0 Hz, 1H), 2.24 (dd, *J* = 18.7 Hz, 4.3 Hz, 1H), 2.18 (m, 1H), 2.07-1.48 (m, 8H), 0.88 (s, 9H), 0.82 (s, 3H), 0.03 (s, 3H), and 0.02 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 193.5, 153.7, 146.5, 133.7, 133.4, 126.5, 82.2, 81.8, 79.7, 74.5, 53.1, 46.7, 43.3, 41.6, 40.1, 31.0, 30.7, 26.4, 20.0, 18.1, 14.1, and 0.05. HRMS calculated for $C_{25}H_{36}NO_4Si$ $[M+H]^+$ 442.2407, found 442.2406.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O
OH
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1.00
1.12
2.04
2.04
4.35
3.14
9.42
6.12
14
13
12
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10
9
8
7
6
5
4
3
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f1 (ppm)
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1000
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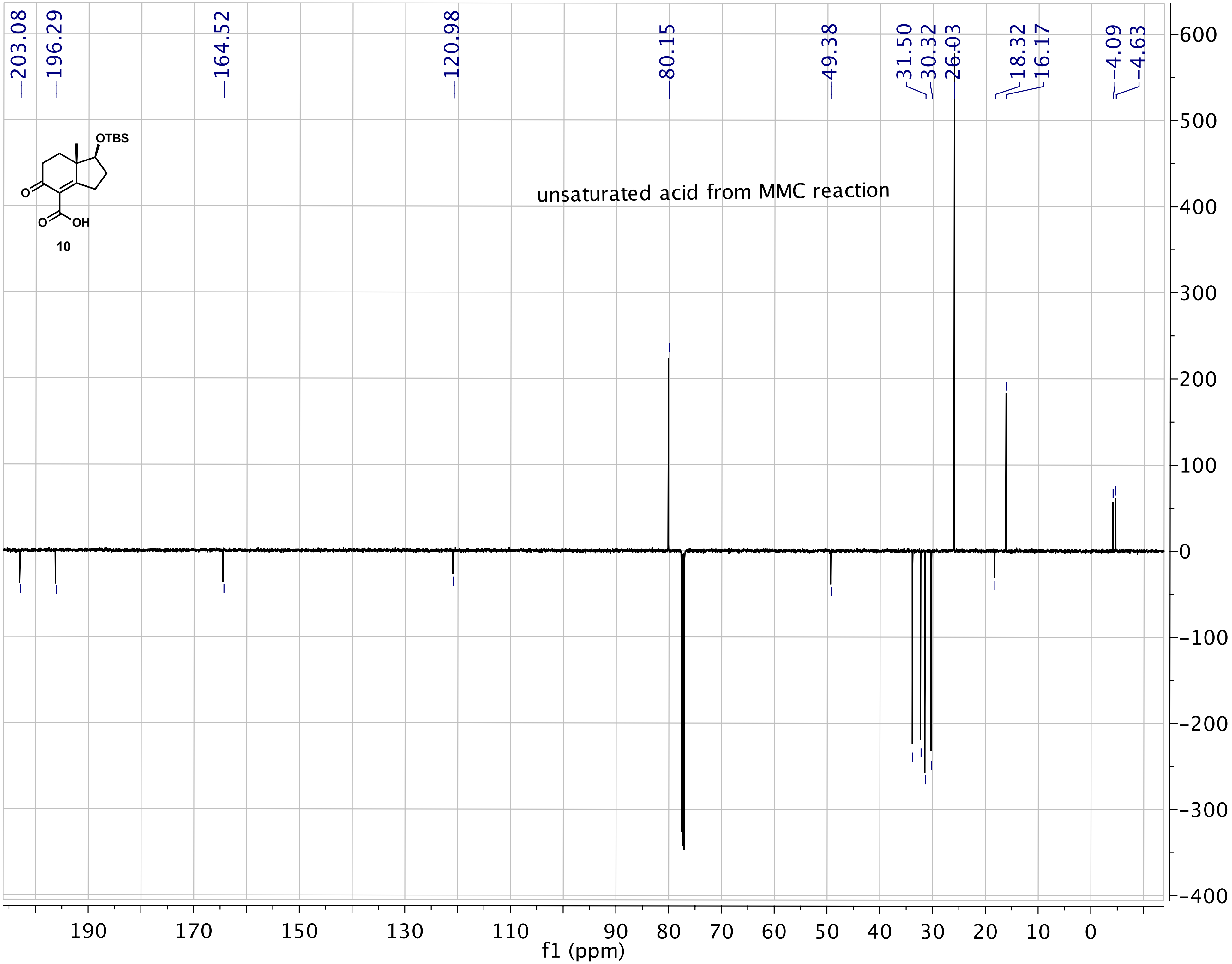

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unsaturated acid from MMC reaction
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O
O
OH
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500
400
300
200
100
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-100
-200
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-400
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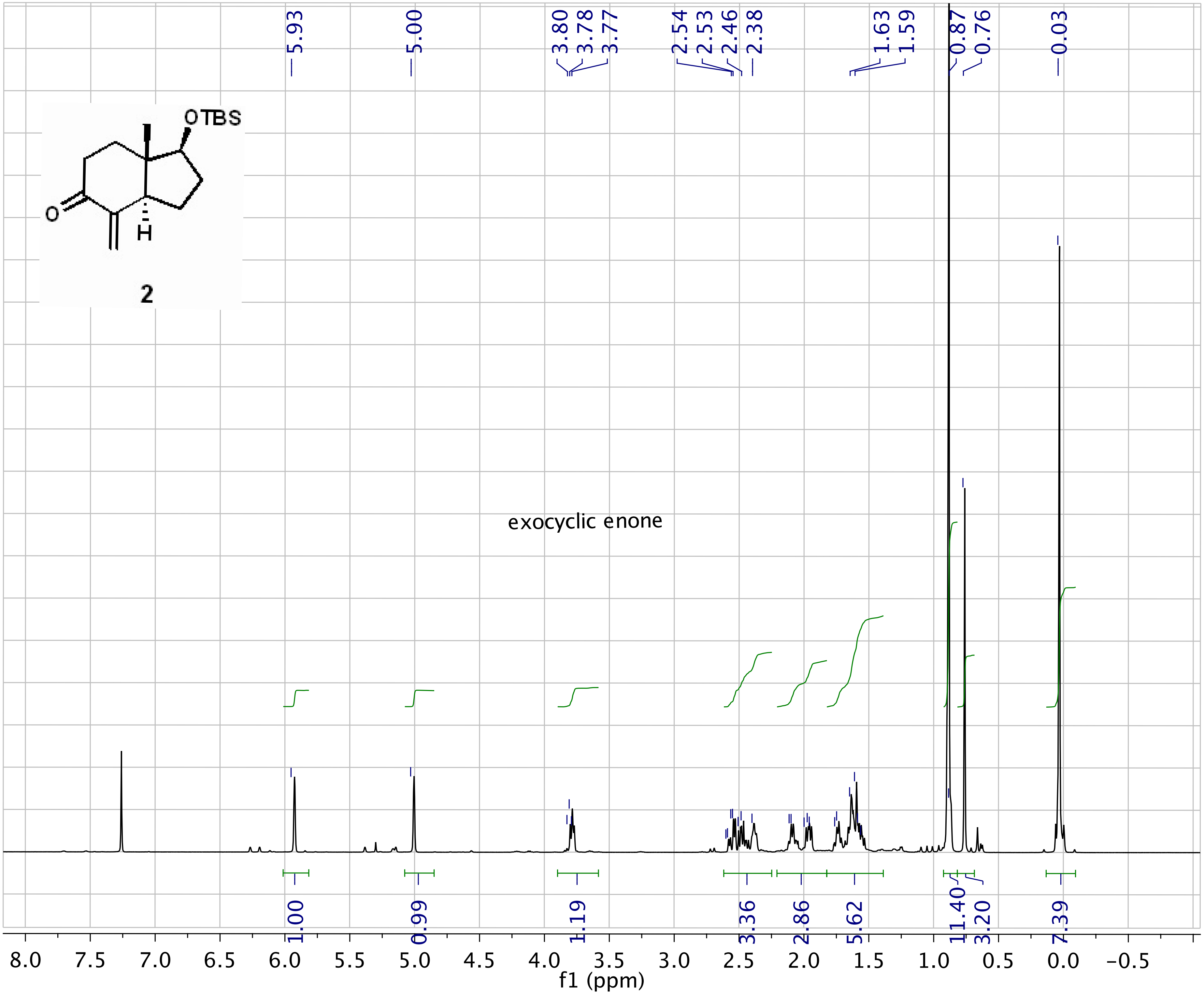
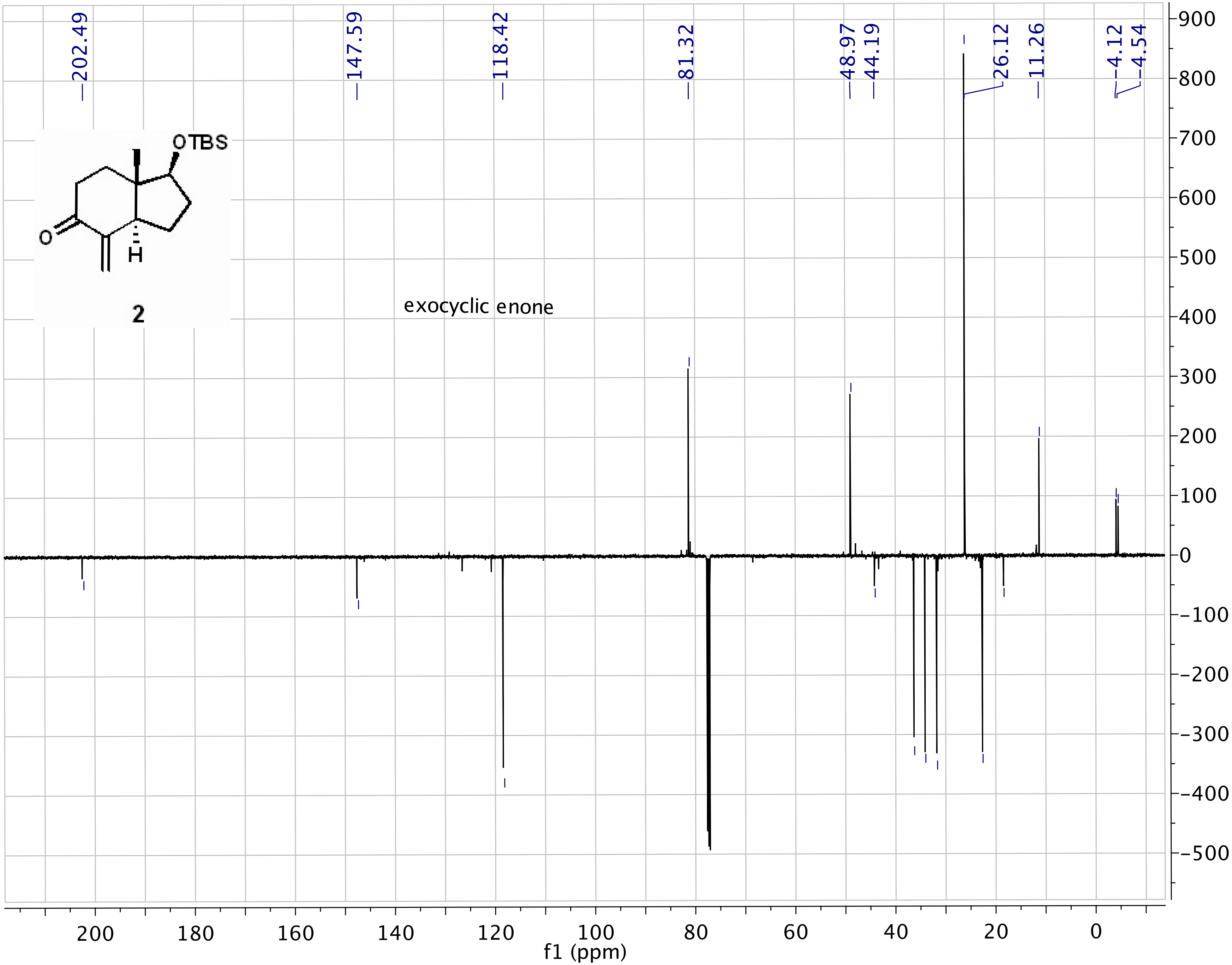
f1 (ppm)



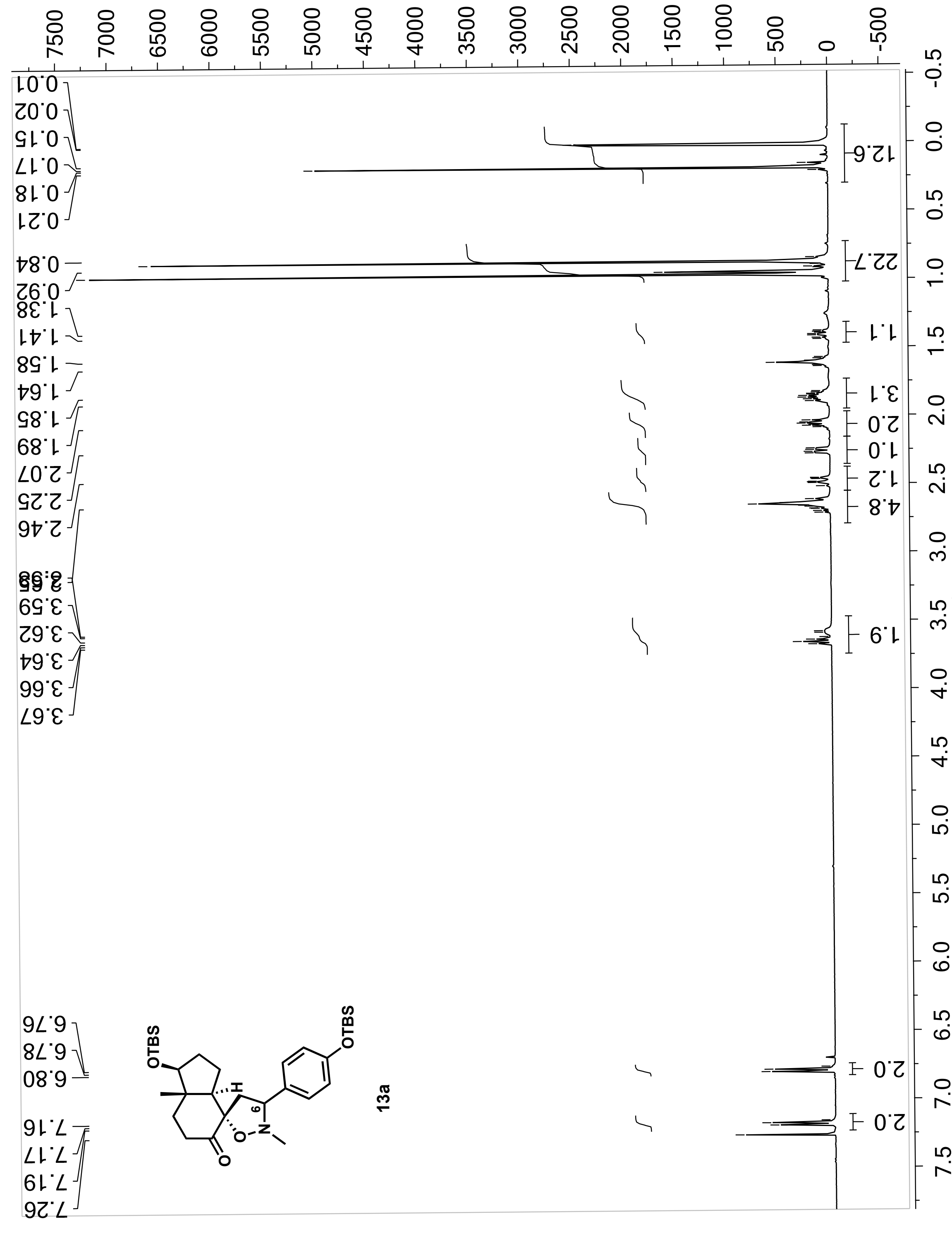
2

exocyclic enone

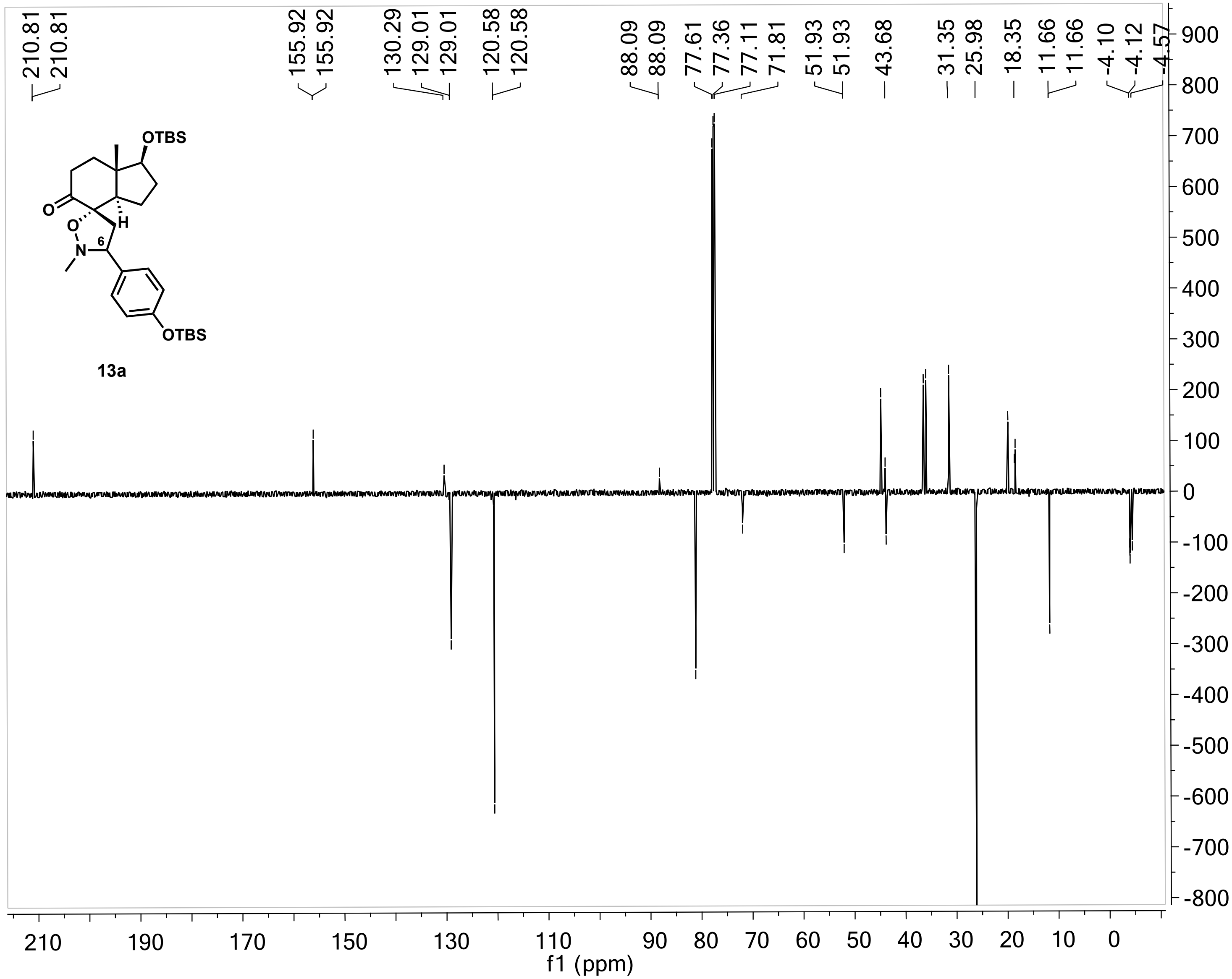

2

exocyclic enone

E.5 Selected NMR spectra



13a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51.93
51.93
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11.66
11.66
-4.10
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O
O
N
6
H
OTBS
13a
900
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700
600
500
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200
100
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-200
-300
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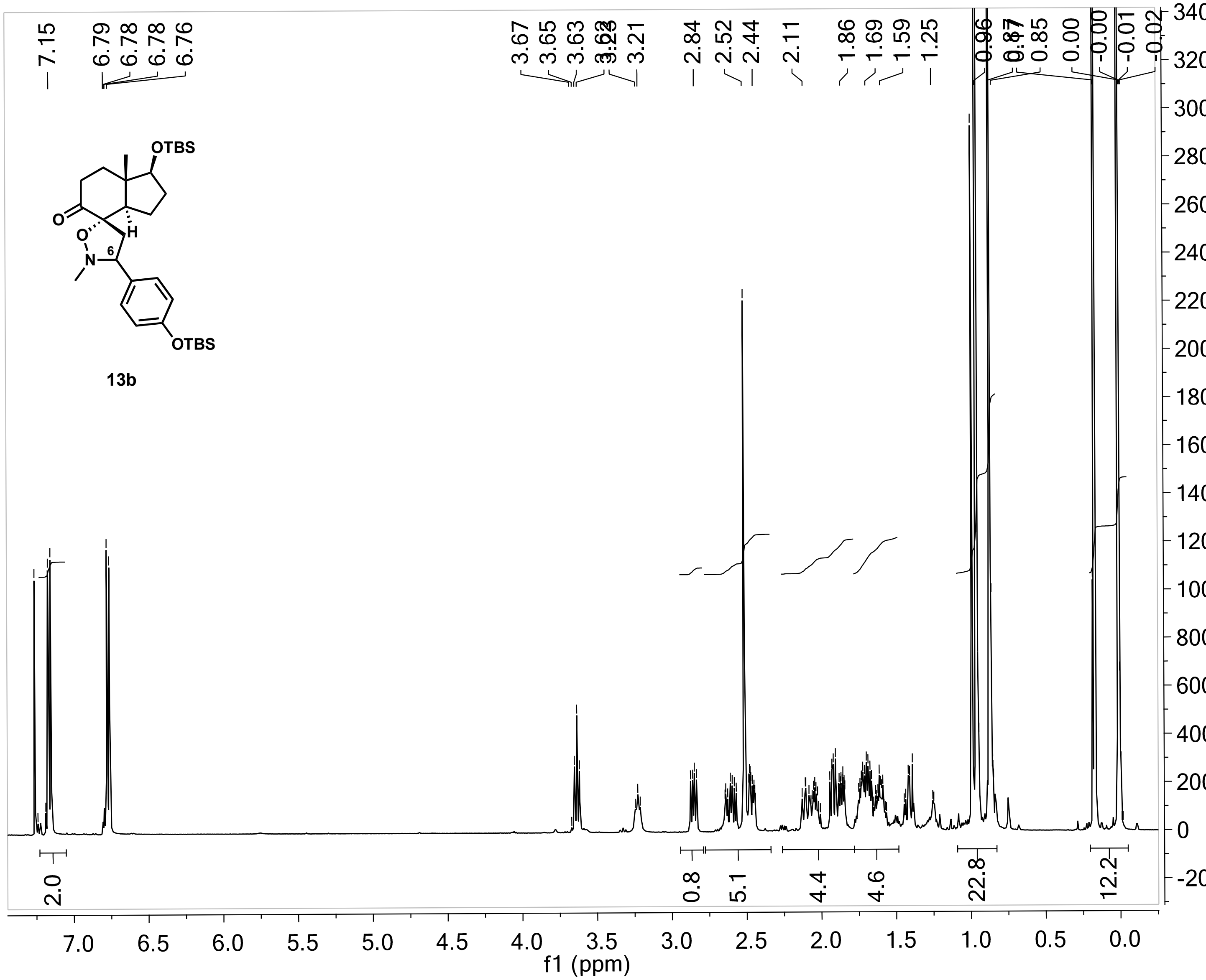
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1.69
1.59
1.25
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0.87
0.85
0.00
-0.00
-0.01
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OTBS
O
O
N
6
H
OTBS
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4.6
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6.5
6.0
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4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
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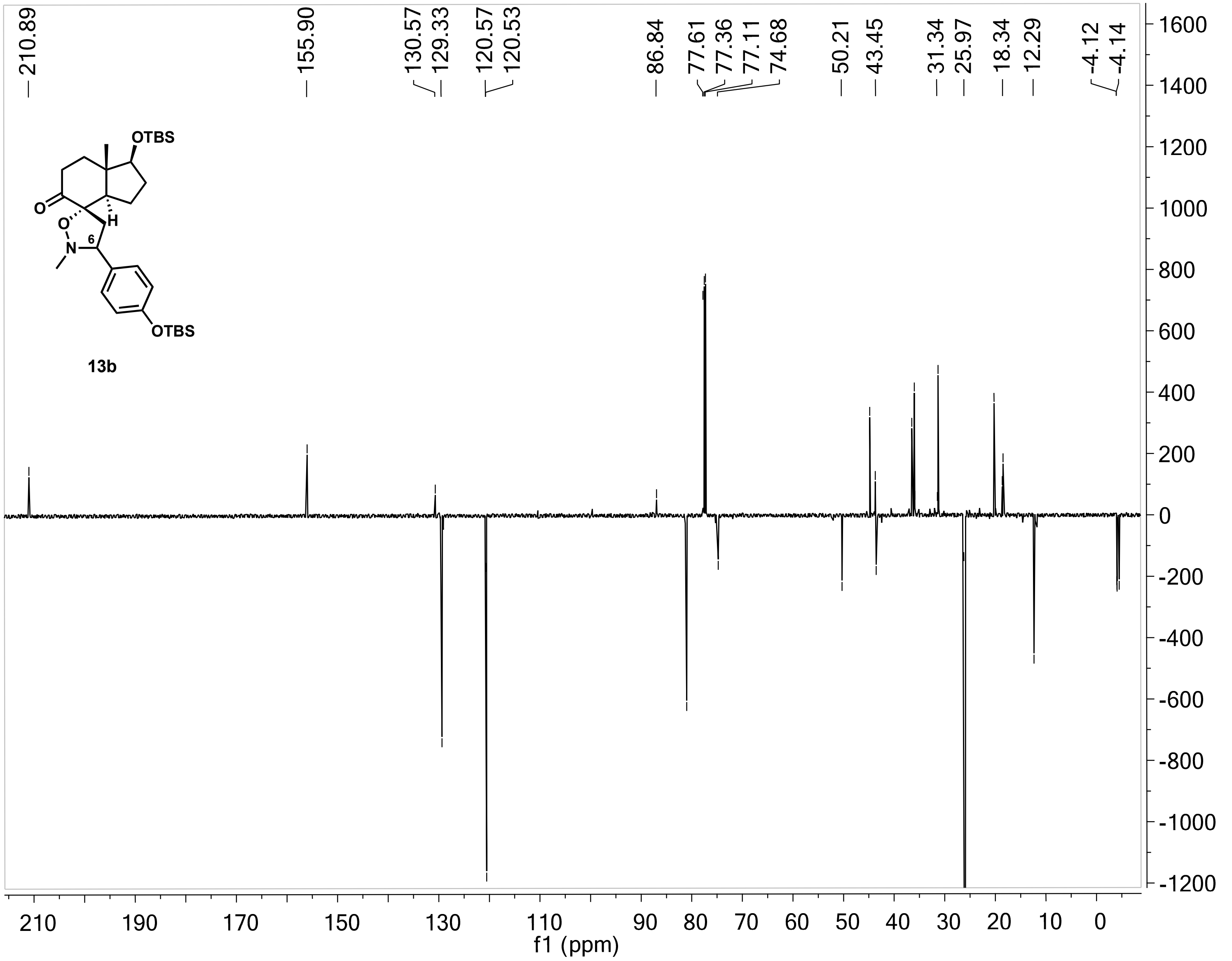
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O
O
N
6
H
OTBS
13b
1600
1400
1200
1000
800
600
400
200
0
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-600
-800
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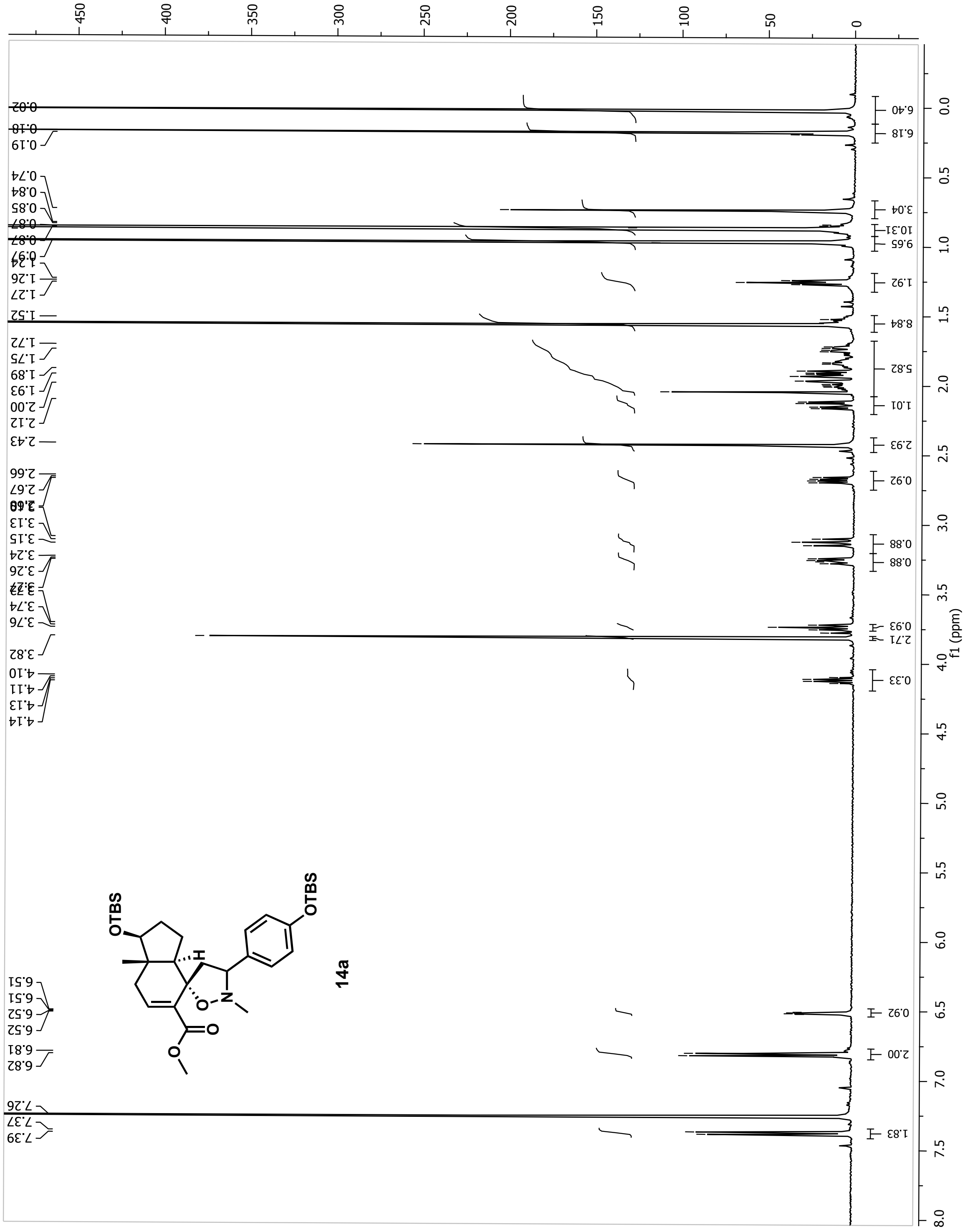
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6.18
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2.00
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OTBS
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O
N
O
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f1 (ppm)
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0.5
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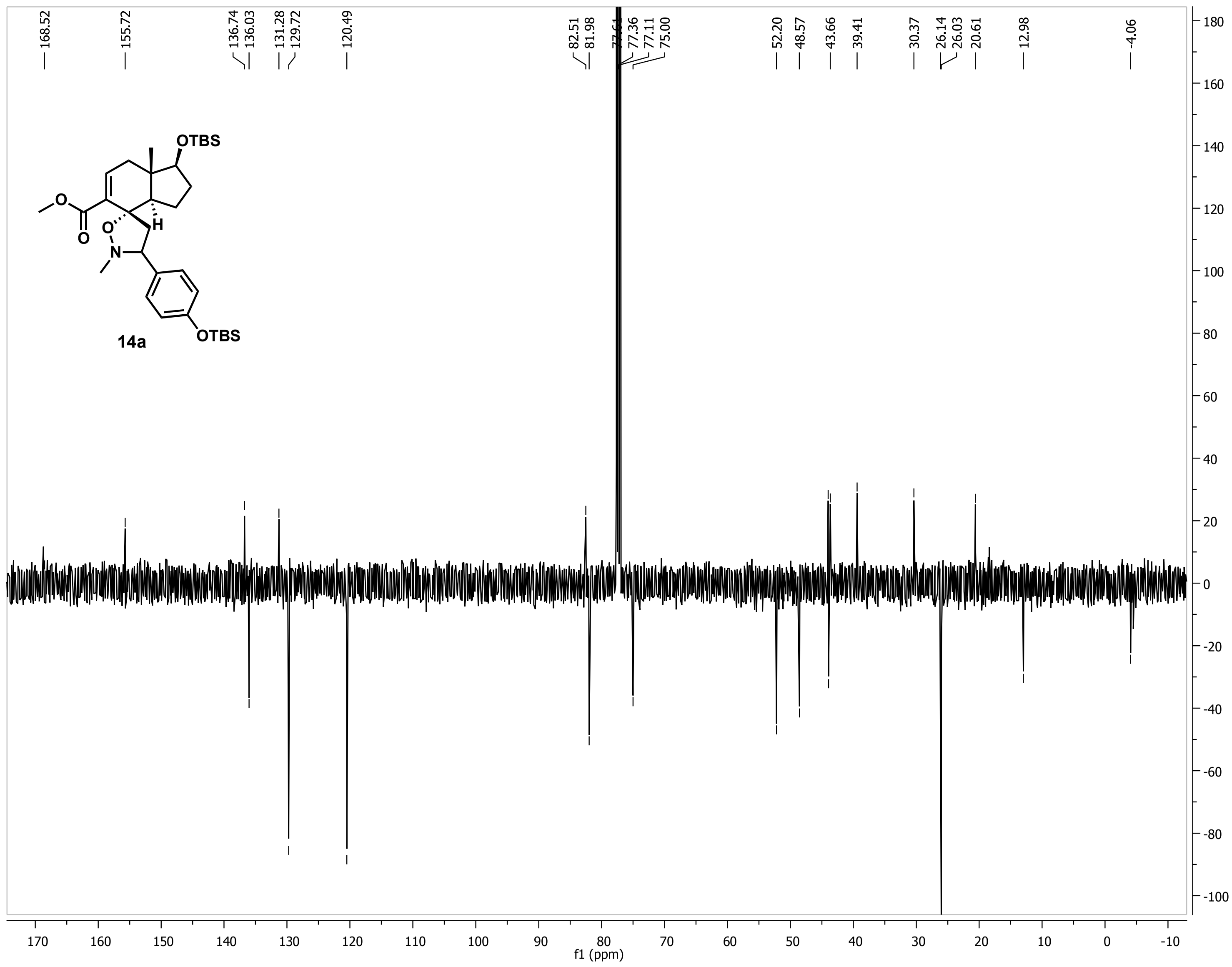
14a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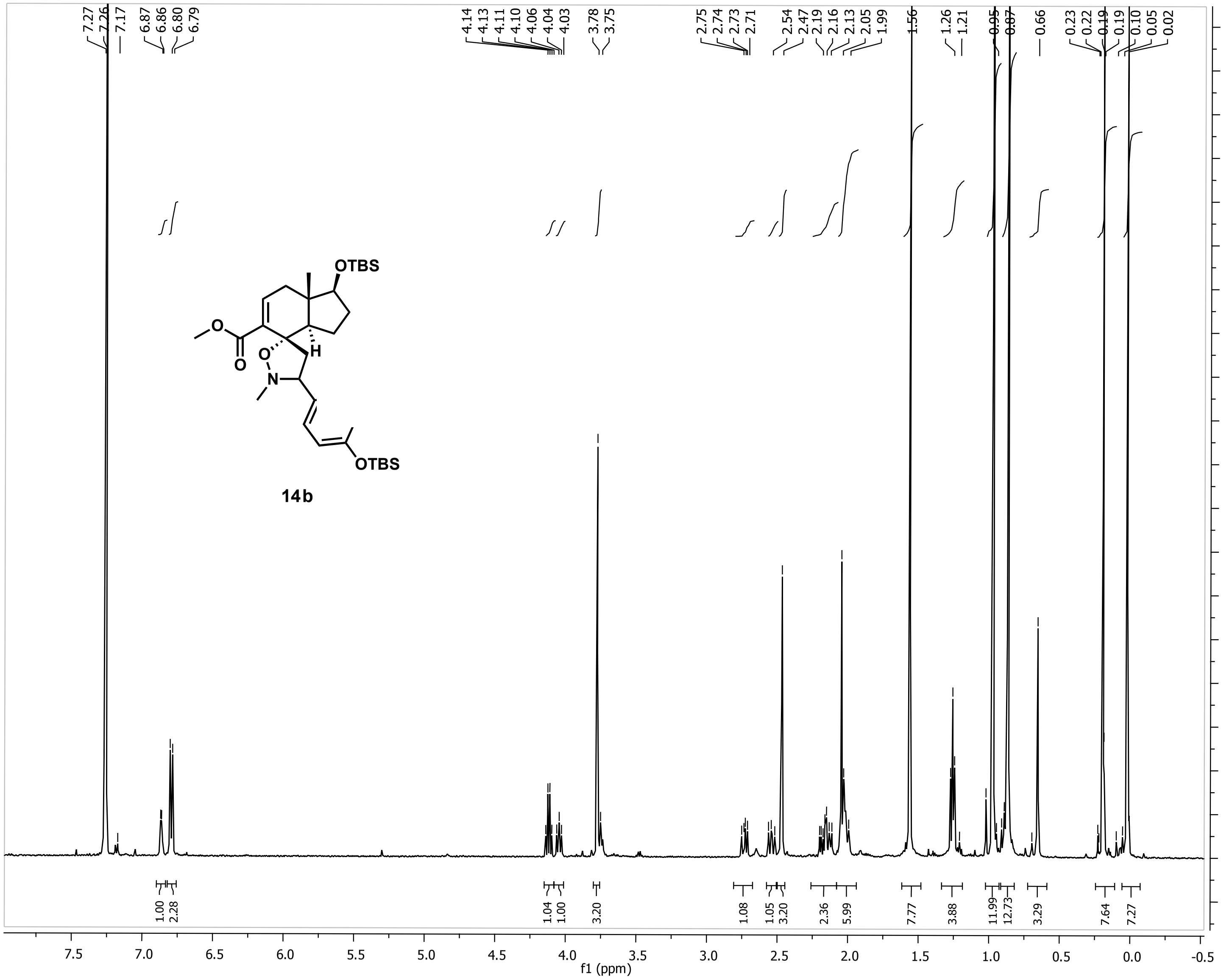
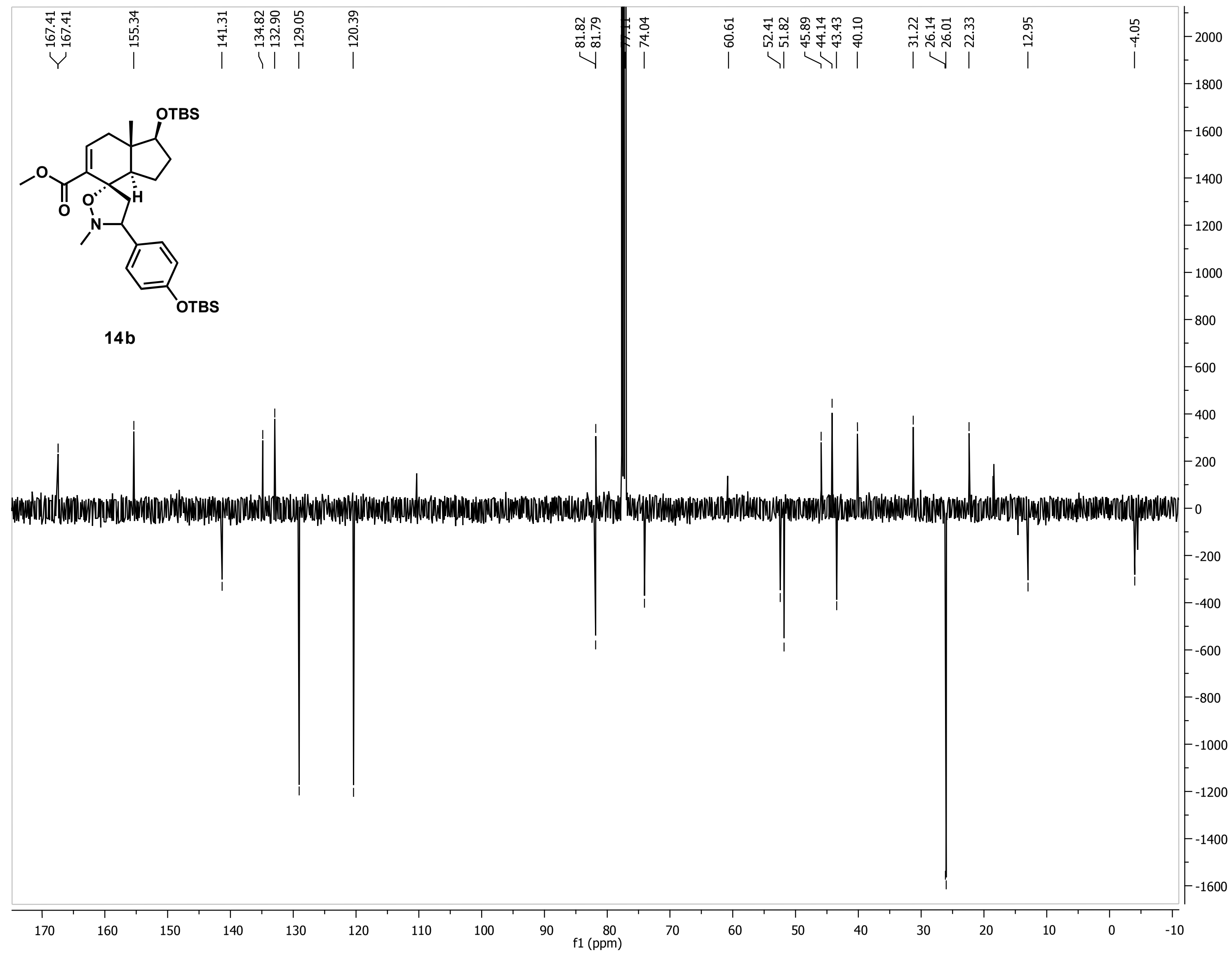
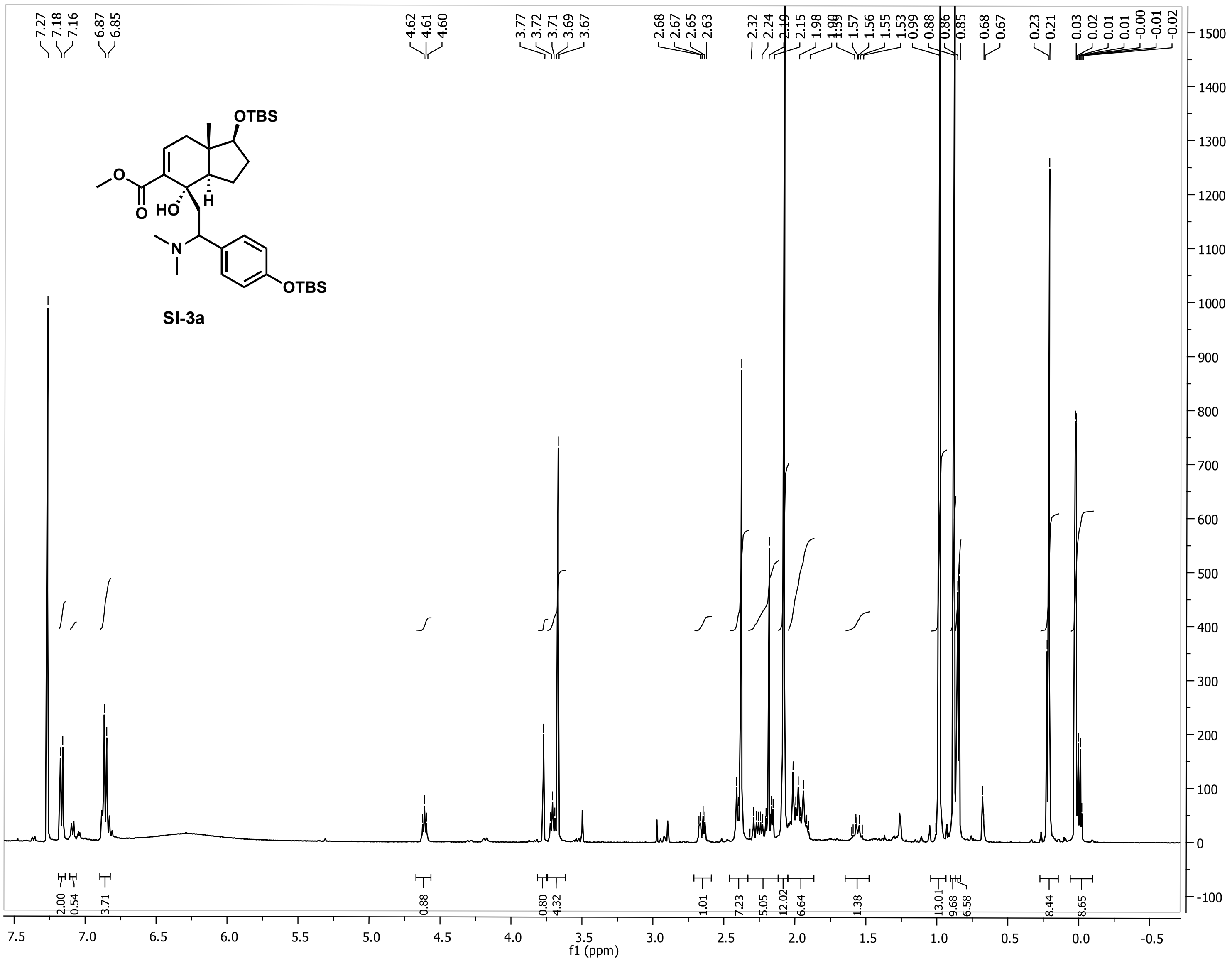
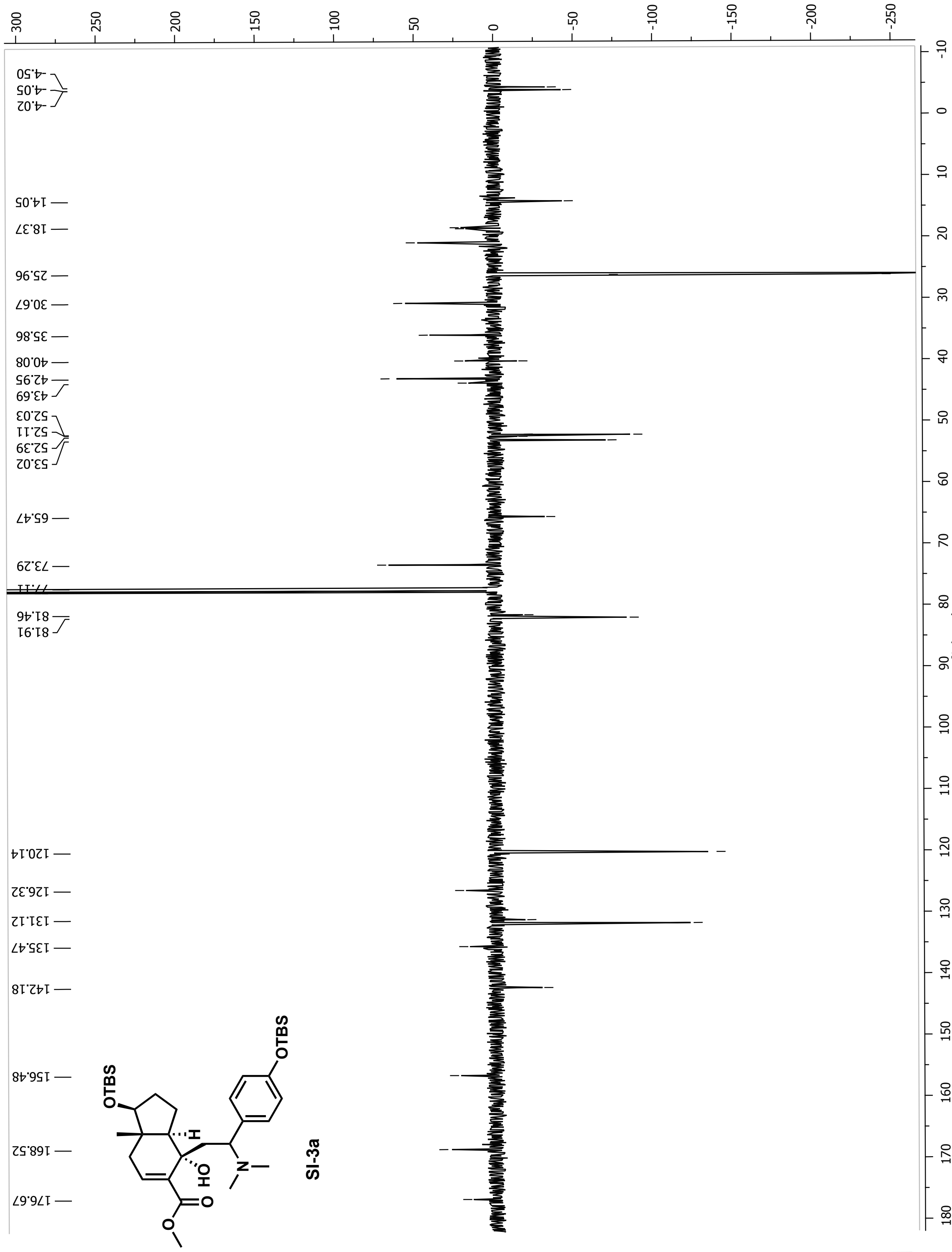
-4.06
OTBS
O
O
O
N
H
OTBS
14a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
180
160
140
120
100
80
60
40
20
0
-20
-40
-60
-80
-100


7.27
7.26
7.17
6.87
6.86
6.80
6.79
4.14
4.13
4.11
4.10
4.06
4.04
4.03
3.78
3.75
2.75
2.74
2.73
2.71
2.54
2.47
2.19
2.16
2.13
2.05
1.99
1.56
1.26
1.21
0.95
0.87
0.66
0.23
0.22
0.19
0.19
0.10
0.05
0.02
OTBS
O
O
O
N
H
OTBS
14b
1.00
2.28
1.04
1.00
3.20
1.08
1.05
3.20
2.36
5.99
7.77
3.88
11.99
12.73
3.29
7.64
7.27
f1 (ppm)


167.41
167.41
155.34
141.31
134.82
132.90
129.05
120.39
81.82
81.79
74.04
60.61
52.41
51.82
45.89
44.14
43.43
40.10
31.22
26.14
26.01
22.33
12.95
-4.05
OTBS
H
O
N
O
O
OTBS
14b
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
-400
-600
-800
-1000
-1200
-1400
-1600
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

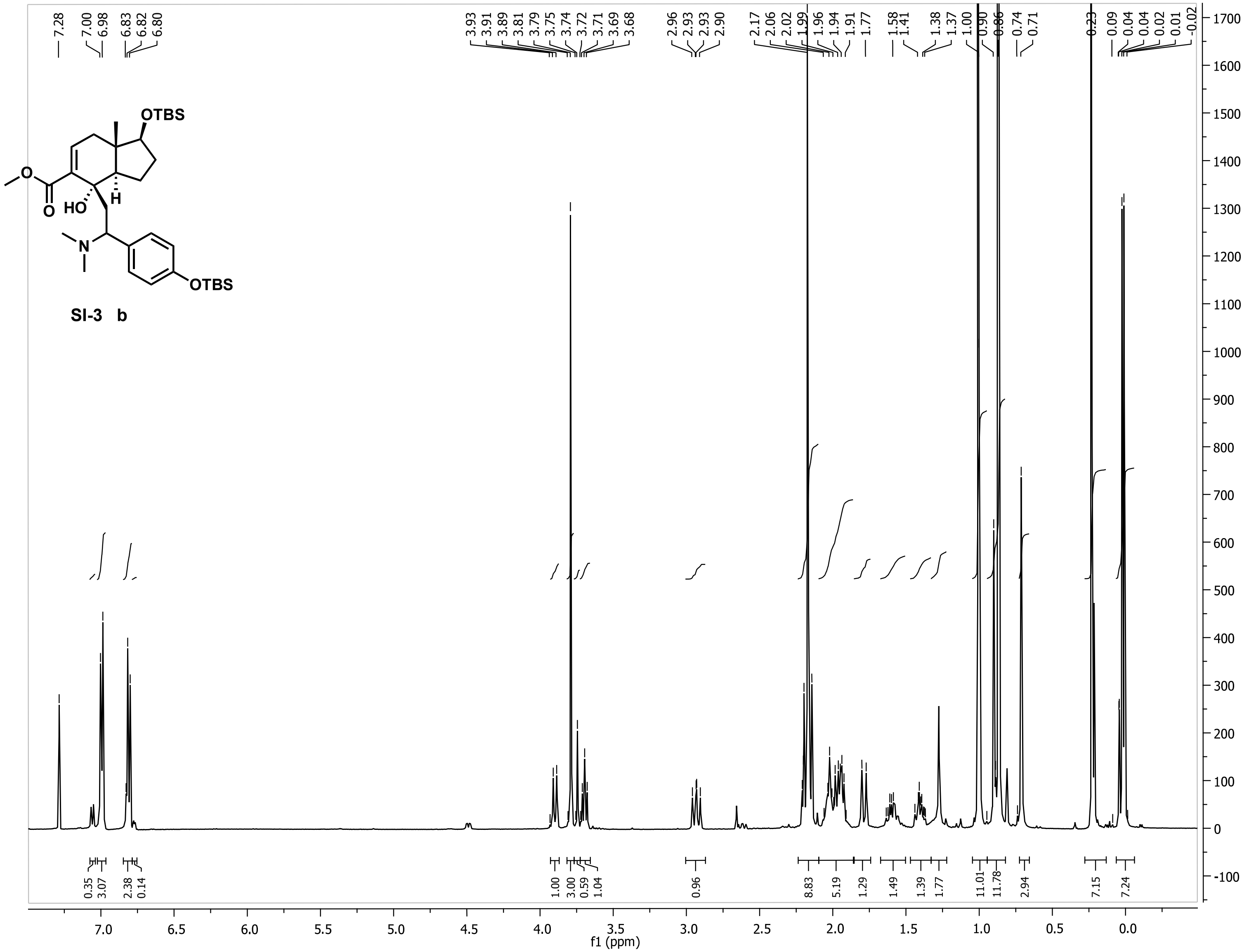

SI-3a

7.27
7.18
7.16
6.87
6.85
4.62
4.61
4.60
3.77
3.72
3.71
3.69
3.67
2.68
2.67
2.65
2.63
2.32
2.24
2.19
2.15
1.98
1.90
1.59
1.57
1.56
1.55
1.53
0.99
0.88
0.86
0.85
0.68
0.67
0.23
0.21
0.03
0.02
0.01
0.01
-0.00
-0.01
-0.02
OTBS
O
O
HO
H
N
OTBS
2.00
0.54
3.71
0.88
0.80
4.32
1.01
7.23
5.05
12.02
6.64
1.38
13.01
9.68
6.58
8.44
8.65
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100



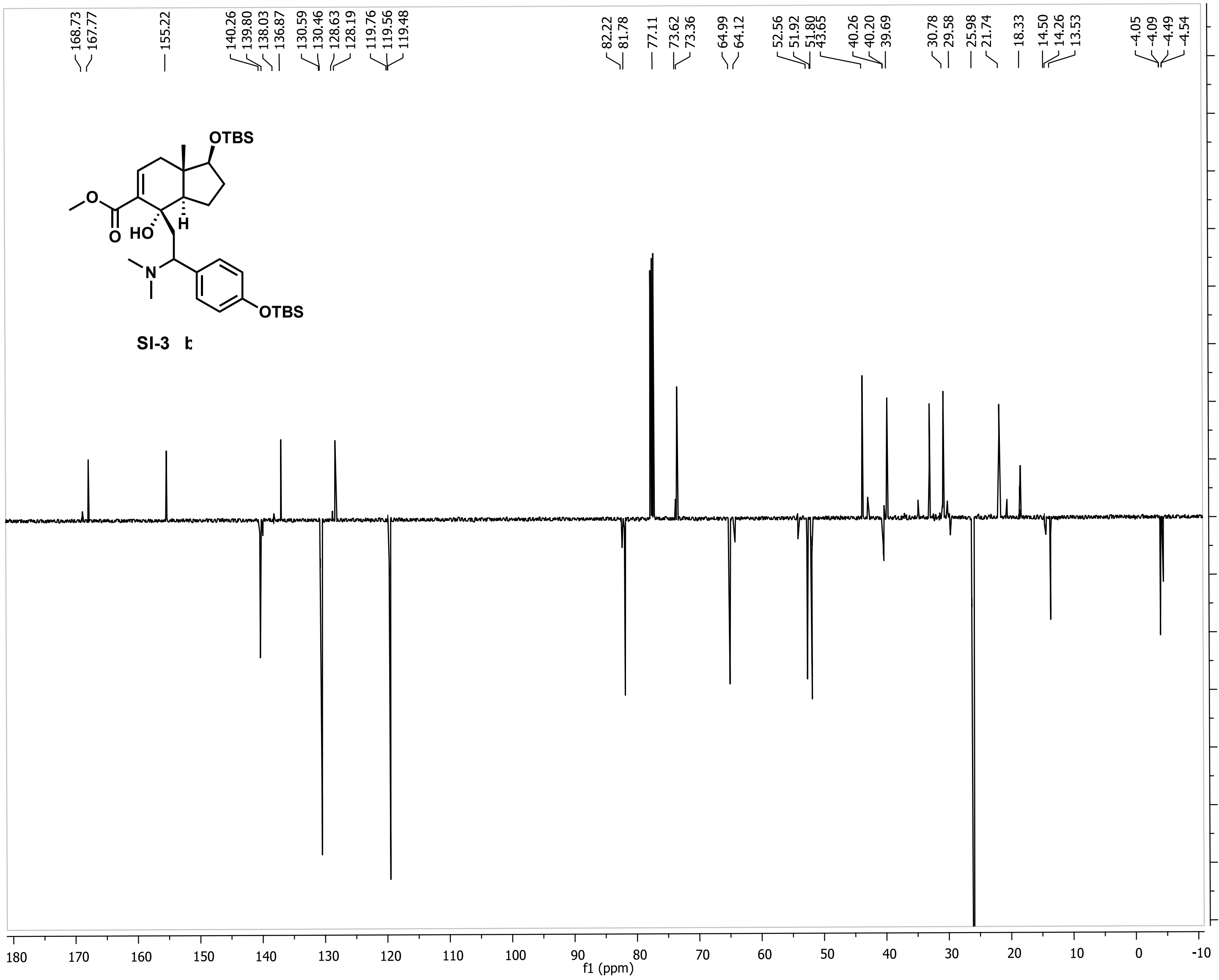
-4.50
-4.05
-4.02
14.05
18.37
25.96
30.67
35.86
40.08
42.95
43.69
52.03
52.11
52.39
53.02
65.47
73.29
77.11
81.46
81.91
120.14
126.32
131.12
135.47
142.18
156.48
168.52
176.67
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
f1 (ppm)
OTBS
OTBS
H
HO
N
O
O

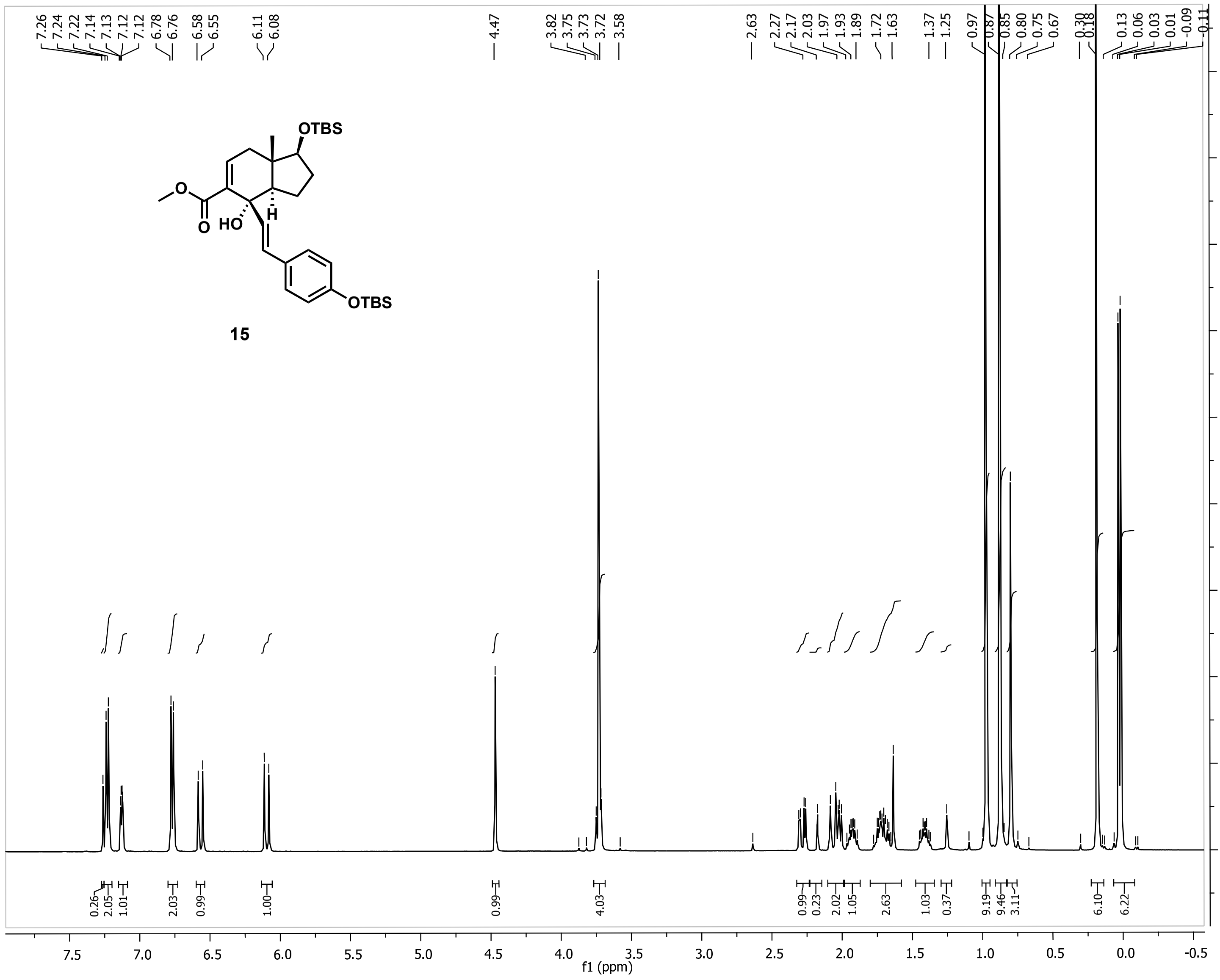
SI-3a



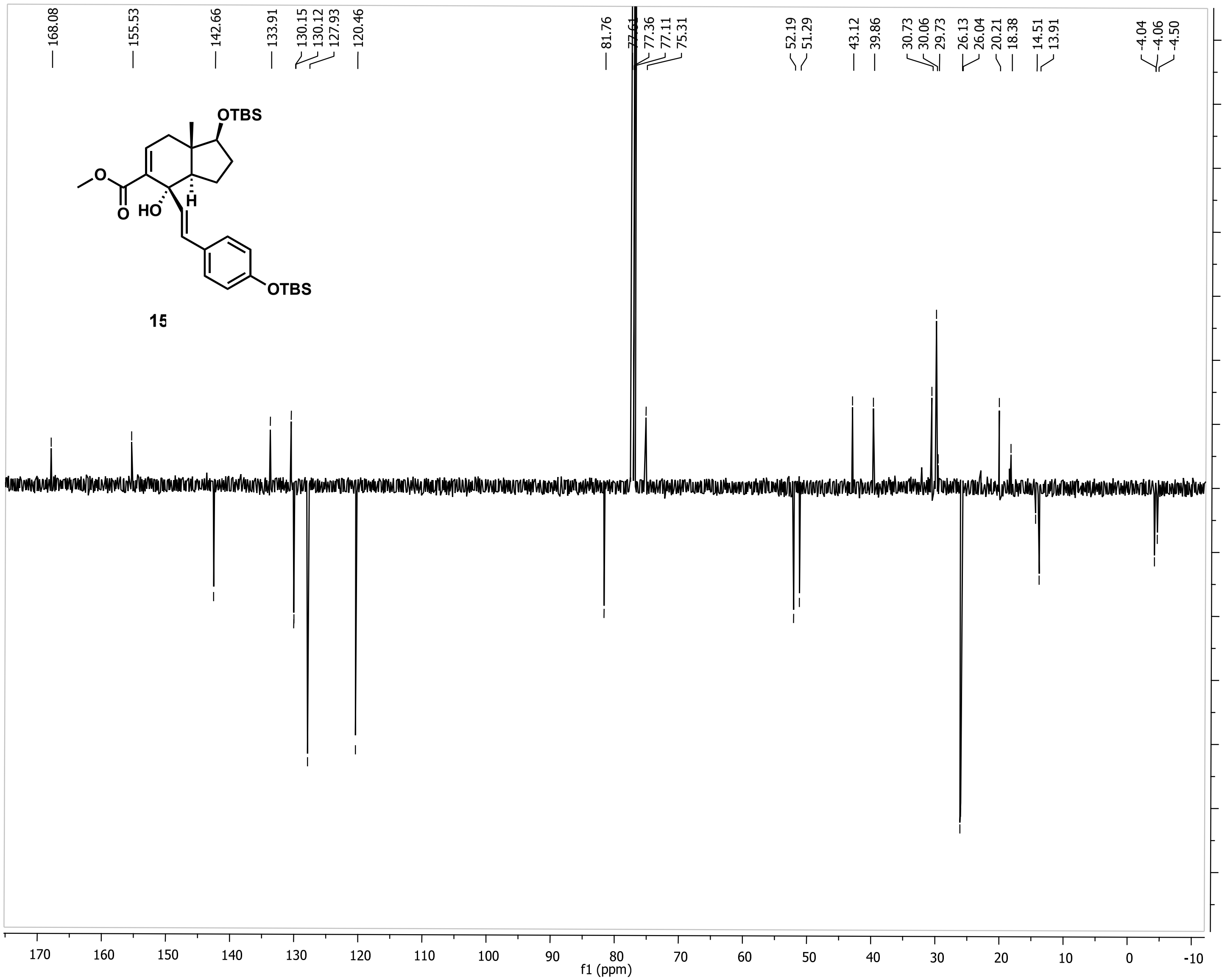
SI-3 b

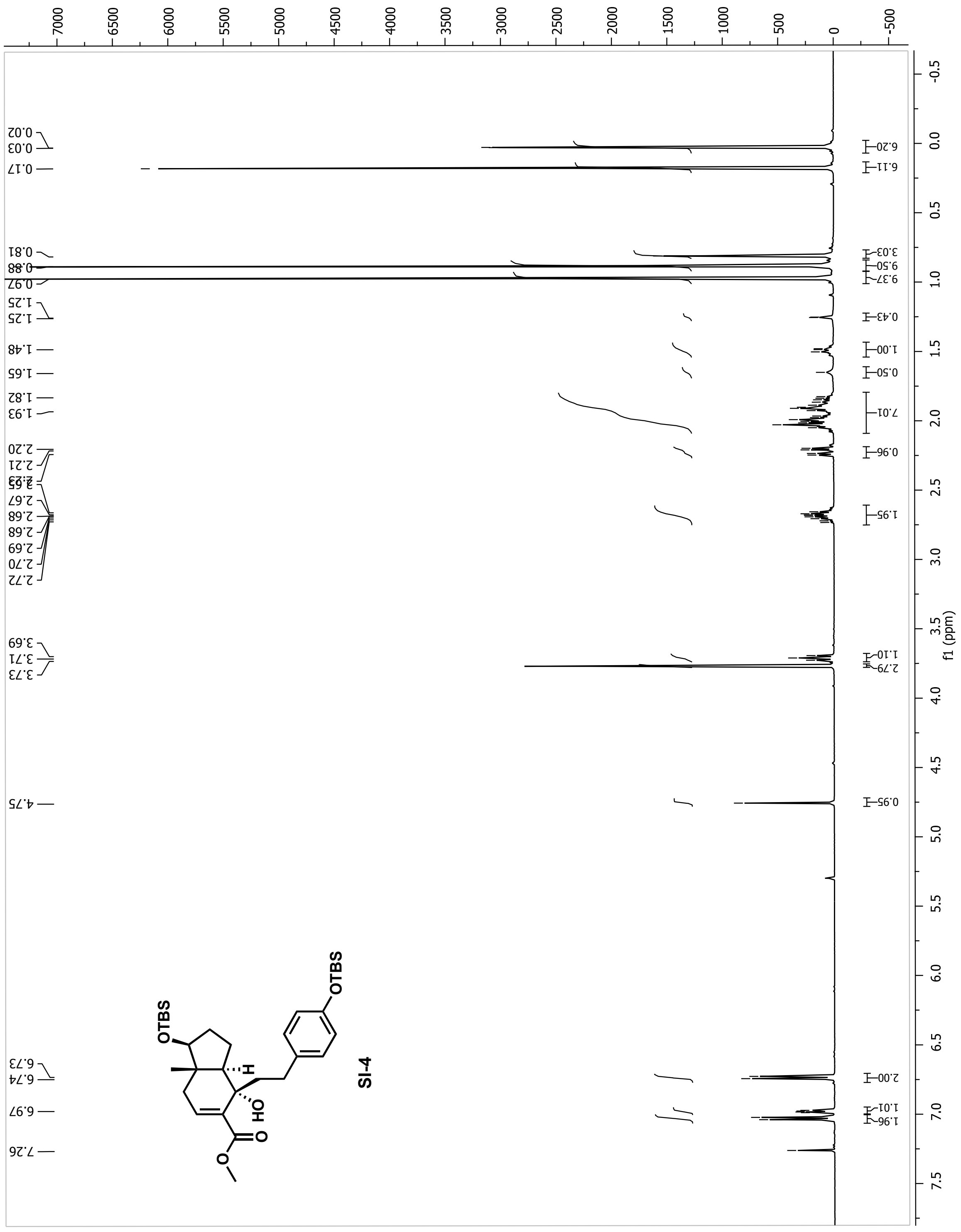
7.28
7.00
6.98
6.83
6.82
6.80
3.93
3.91
3.89
3.81
3.79
3.75
3.74
3.72
3.71
3.69
3.68
2.96
2.93
2.93
2.90
2.17
2.06
2.02
1.99
1.96
1.94
1.91
1.77
1.58
1.41
1.38
1.37
1.00
0.90
0.86
0.74
0.71
0.23
0.09
0.04
0.04
0.02
0.01
-0.02
OTBS
HO
H
O
N
OTBS
0.35
3.07
2.38
0.14
1.00
3.00
0.59
1.04
0.96
8.83
5.19
1.29
1.49
1.39
1.77
11.01
11.78
2.94
7.15
7.24
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100


168.73
167.77
155.22
140.26
139.80
138.03
136.87
130.59
130.46
128.63
128.19
119.76
119.56
119.48
82.22
81.78
77.11
73.62
73.36
64.99
64.12
52.56
51.92
51.80
43.65
40.26
40.20
39.69
30.78
29.58
25.98
21.74
18.33
14.50
14.26
13.53
-4.05
-4.09
-4.49
-4.54
OTBS
O
O
HO
H
N
OTBS
SI-3 b
1600
1400
1200
1000
800
600
400
200
0
-200
-400
-600
-800
-1000
-1200
-1400
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

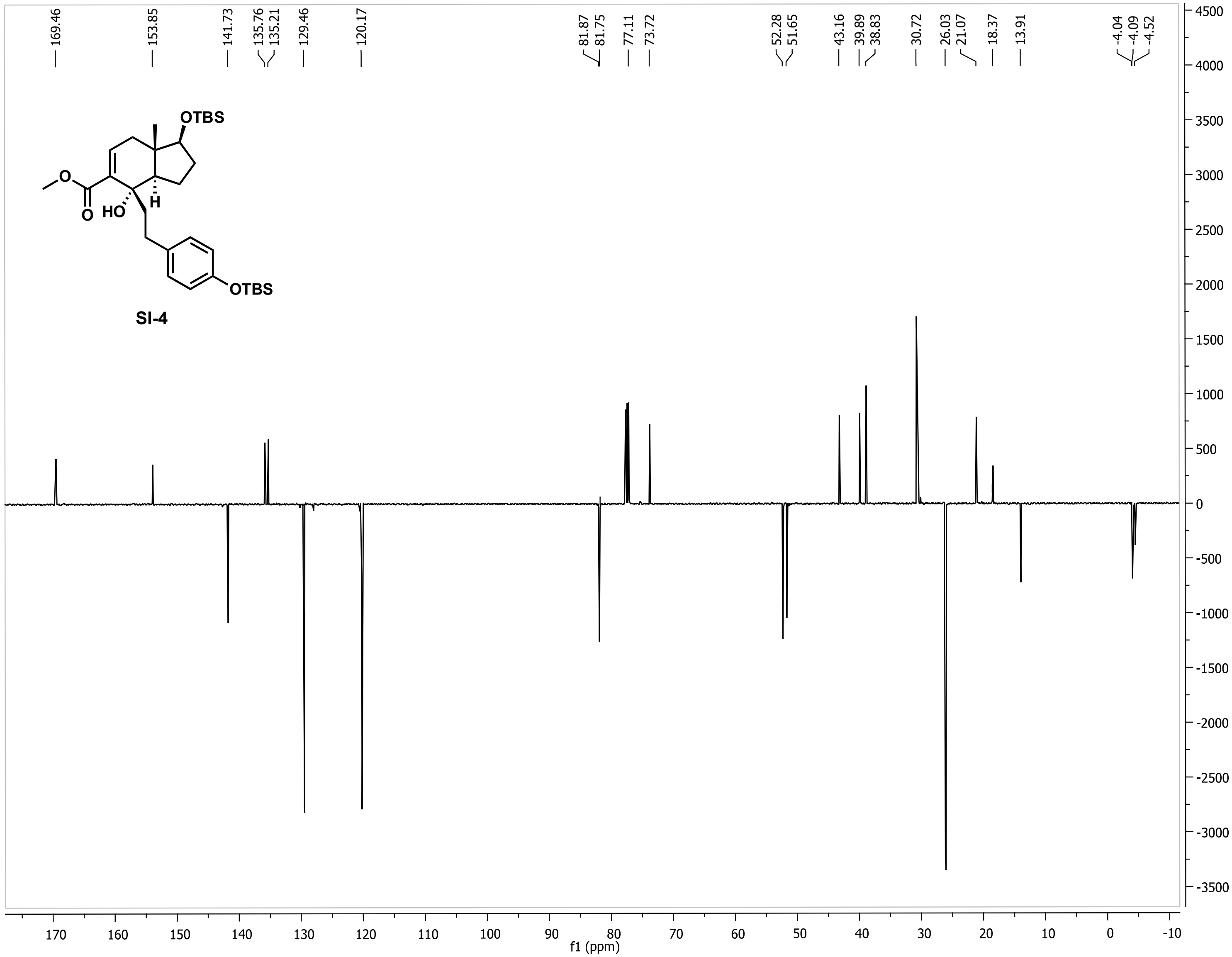

15

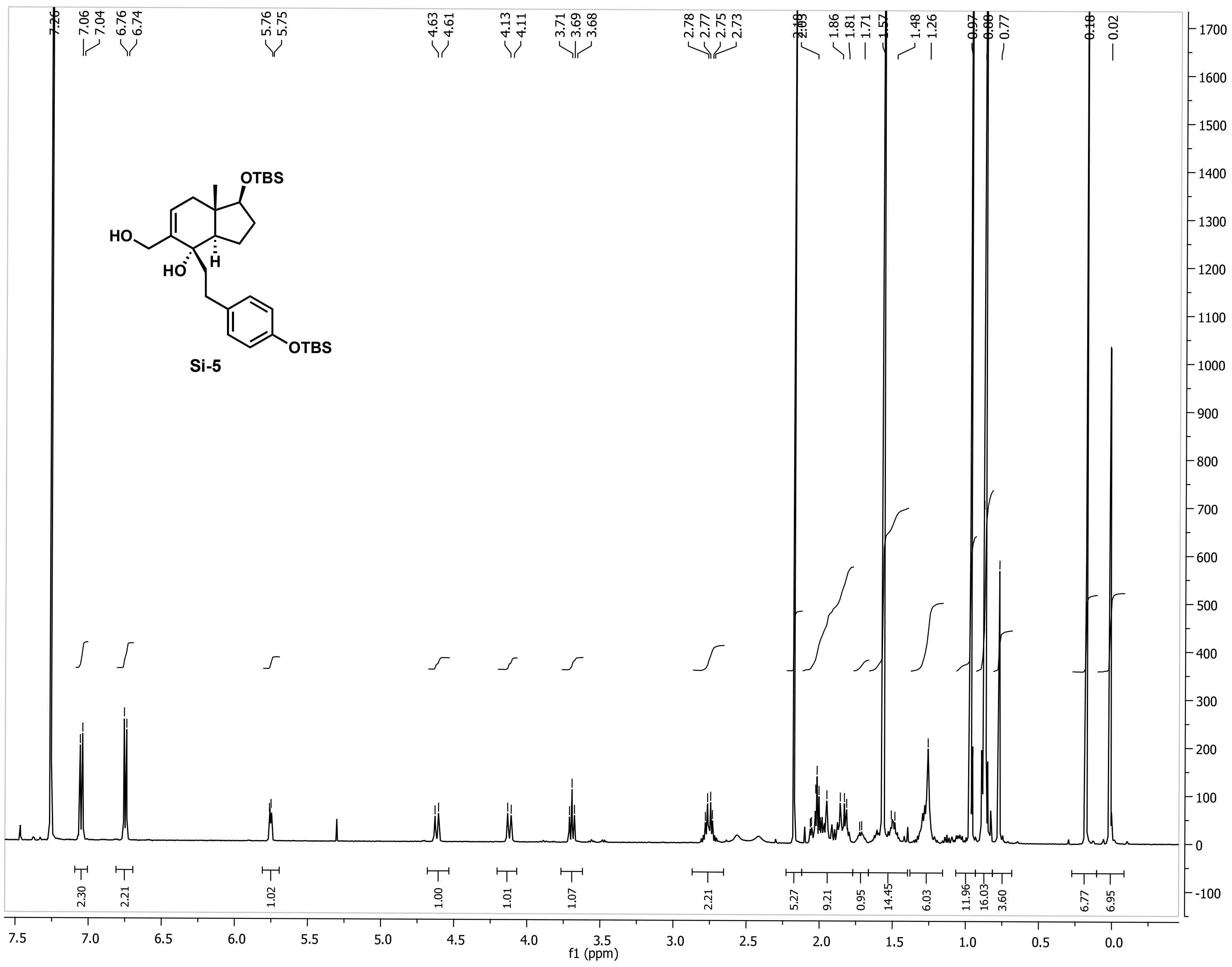
7.26
7.24
7.22
7.14
7.13
7.12
7.12
6.78
6.76
6.58
6.55
6.11
6.08
4.47
3.82
3.75
3.73
3.72
3.58
2.63
2.27
2.17
2.03
1.97
1.93
1.89
1.72
1.63
1.37
1.25
0.97
0.87
0.85
0.80
0.75
0.67
0.30
0.18
0.13
0.06
0.03
0.01
-0.09
-0.11
OTBS
OTBS
O
O
HO
H
0.26
2.05
1.01
2.03
0.99
1.00
0.99
4.03
0.99
0.23
2.02
1.05
2.63
1.03
0.37
9.19
9.46
3.11
6.10
6.22
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


168.08
155.53
142.66
133.91
130.15
130.12
127.93
120.46
81.76
77.61
77.36
77.11
75.31
52.19
51.29
43.12
39.86
30.73
30.06
29.73
26.13
26.04
20.21
18.38
14.51
13.91
-4.04
-4.06
-4.50
OTBS
HO
H
O
O
OTBS
15
350
300
250
200
150
100
50
0
-50
-100
-150
-200
-250
-300
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

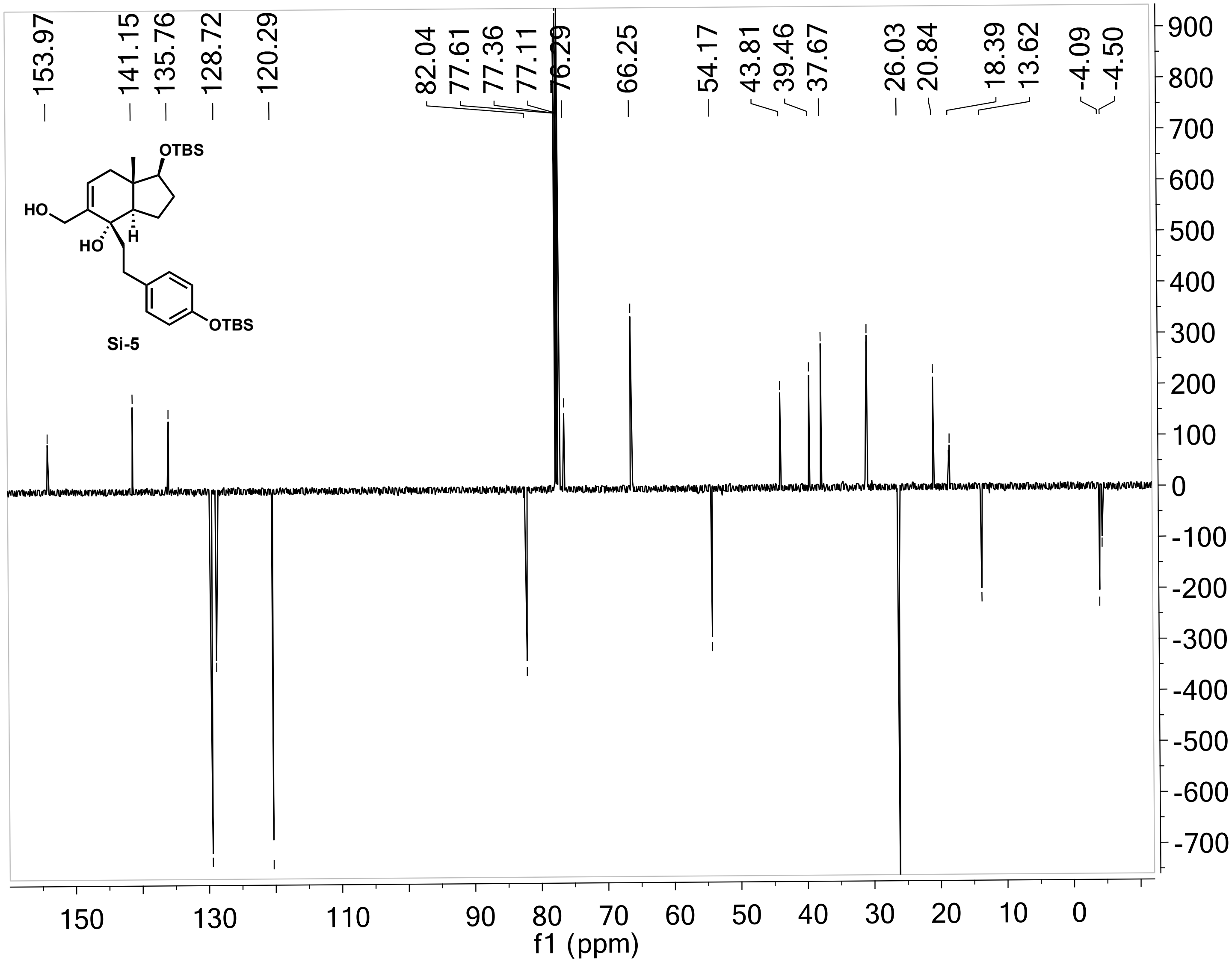

SI-4

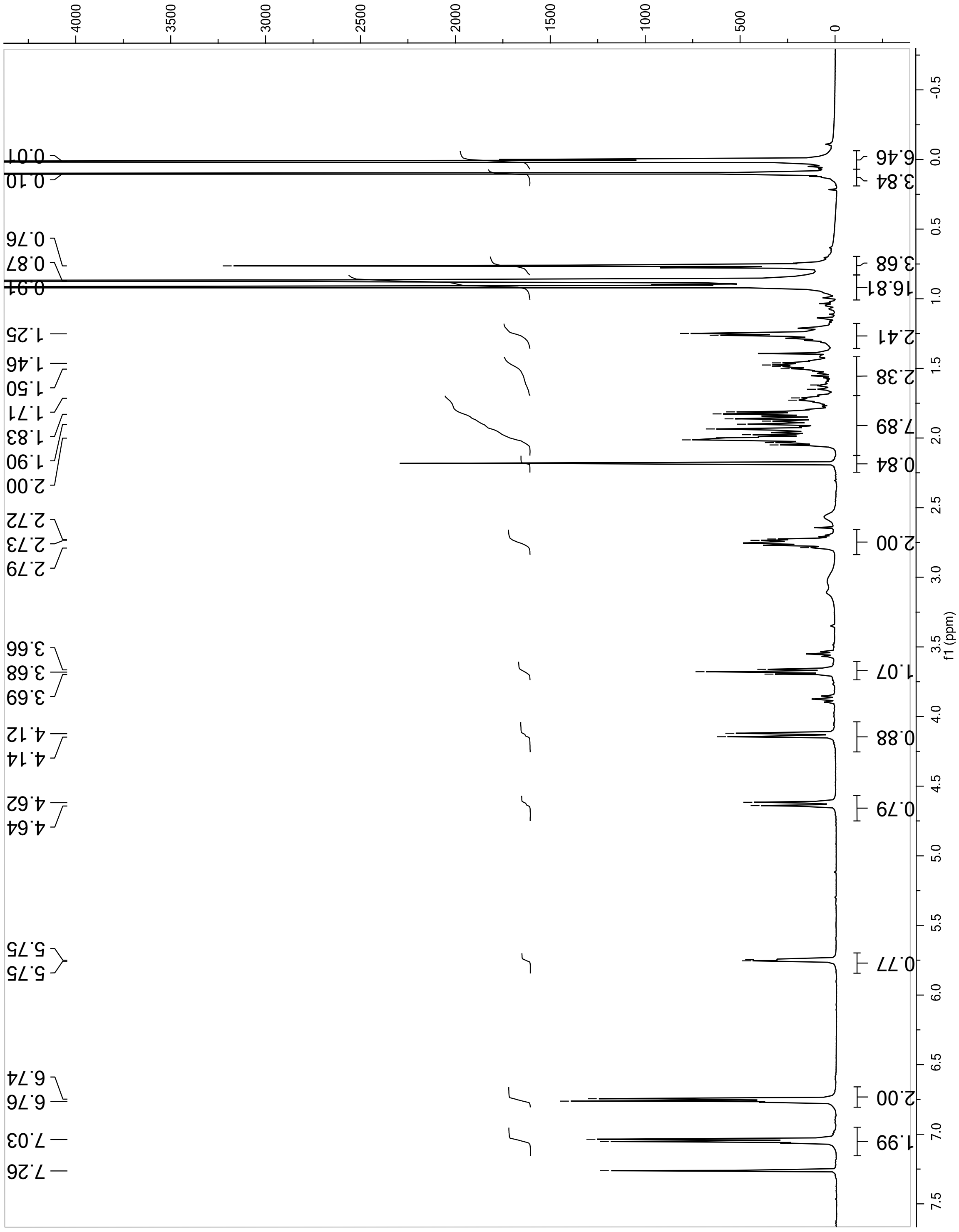
OTBS
OTBS
H
HO
O
O
0.02
0.03
0.17
0.81
0.88
0.97
1.25
1.25
1.48
1.65
1.82
1.93
2.20
2.21
2.23
2.65
2.67
2.68
2.68
2.69
2.70
2.72
3.69
3.71
3.73
4.75
6.73
6.74
6.97
7.26
6.20
6.11
3.03
9.50
9.37
0.43
1.00
0.50
7.01
0.96
1.95
1.10
2.79
0.95
2.00
1.01
1.96
f1 (ppm)
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

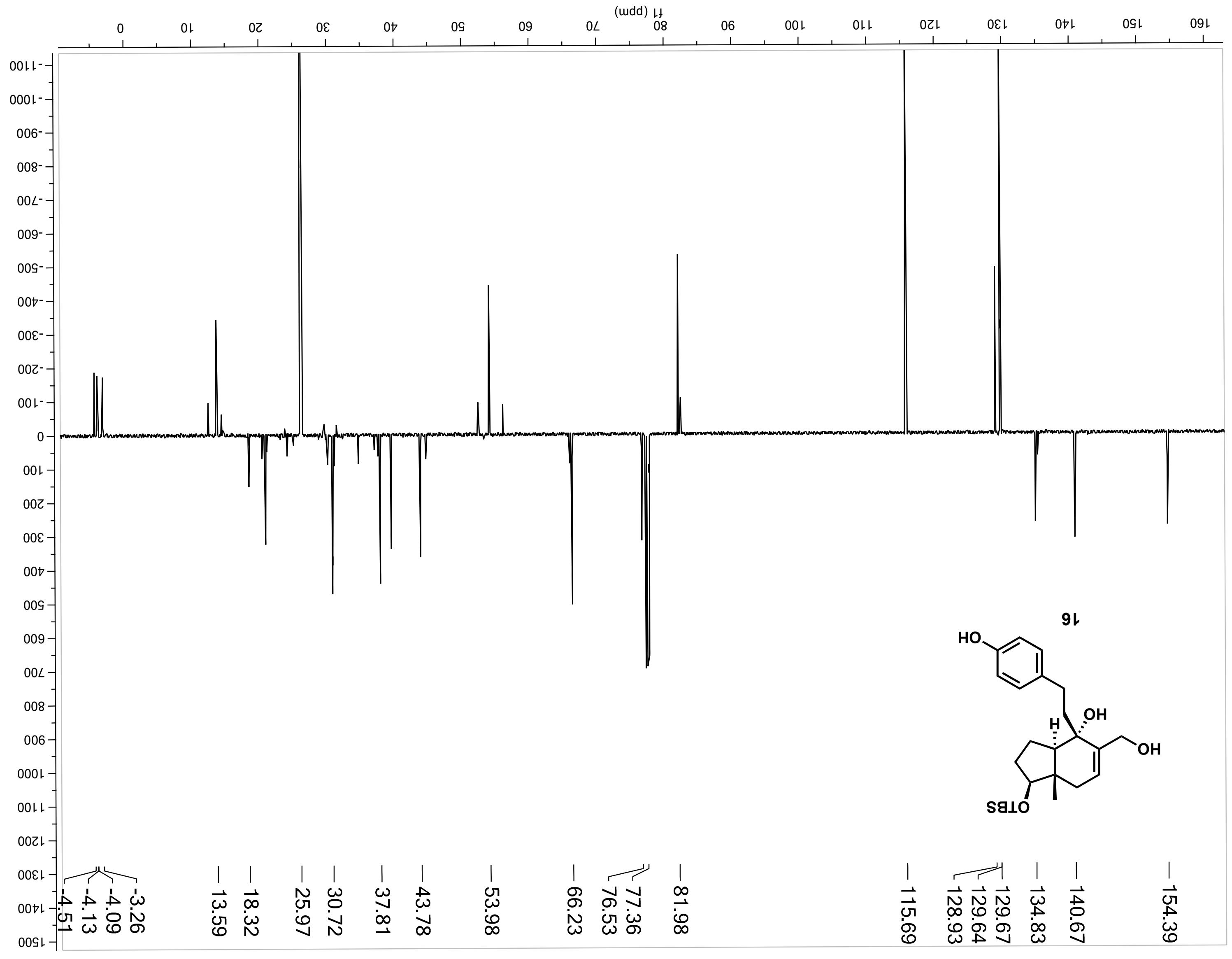
169.46
153.85
141.73
135.76
135.21
129.46
120.17
81.87
81.75
77.11
73.72
52.28
51.65
43.16
39.89
38.83
30.72
26.03
21.07
18.37
13.91
-4.04
-4.09
-4.52
OTBS
O
HO
H
O
OTBS
SI-4
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
-1000
-1500
-2000
-2500
-3000
-3500
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.26
7.06
7.04
6.76
6.74
5.76
5.75
4.63
4.61
4.13
4.11
3.71
3.69
3.68
2.78
2.77
2.75
2.73
2.18
2.09
1.86
1.81
1.71
1.57
1.48
1.26
0.97
0.88
0.77
0.18
0.02
OTBS
HO
HO
H
OTBS
2.30
2.21
1.02
1.00
1.01
1.07
2.21
5.27
9.21
0.95
14.45
6.03
11.96
16.03
3.60
6.77
6.95
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

Si-5

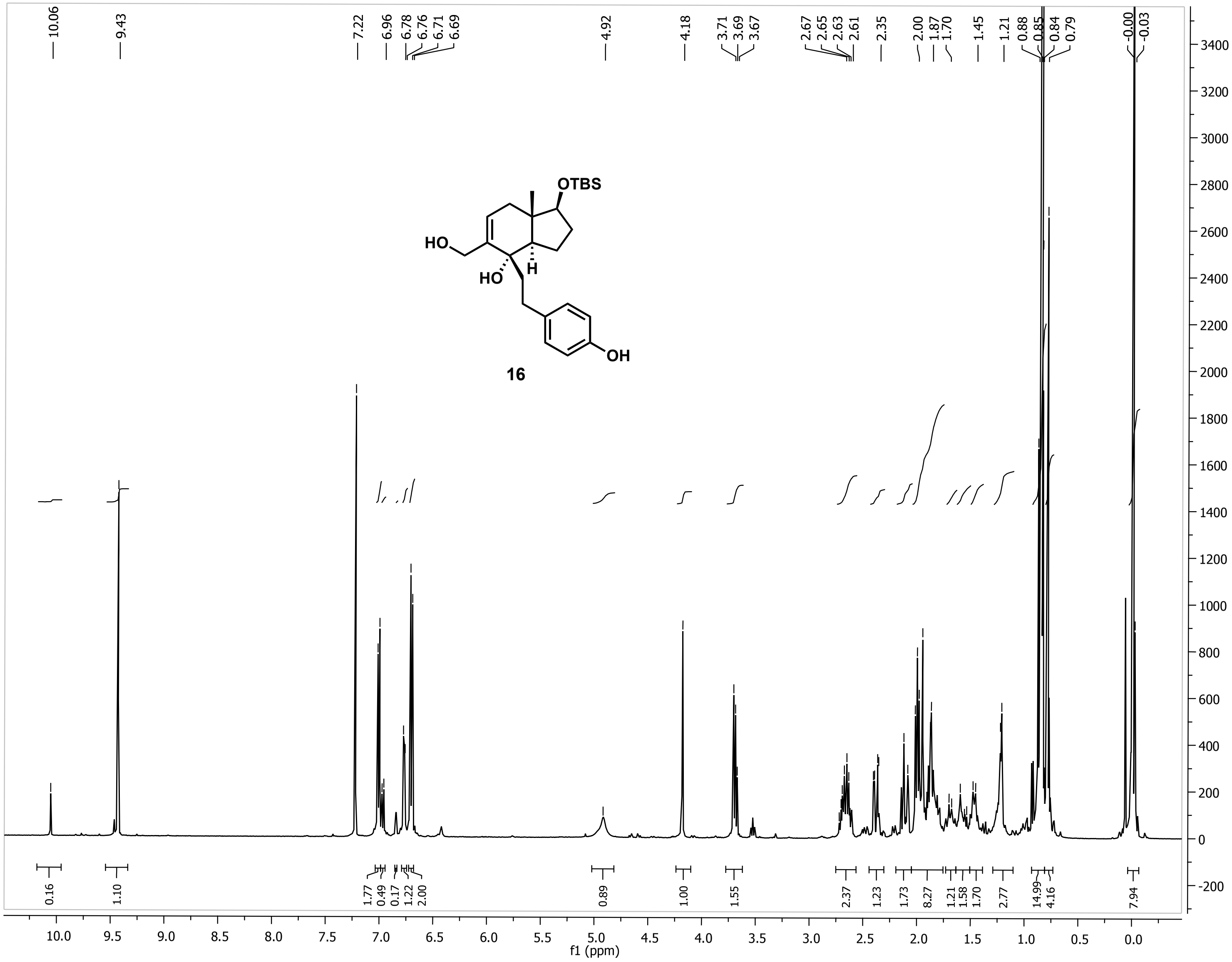

153.97
141.15
135.76
128.72
120.29
82.04
77.61
77.36
77.11
76.29
66.25
54.17
43.81
39.46
37.67
26.03
20.84
18.39
13.62
-4.09
-4.50
HO
HO
H
OTBS
OTBS
Si-5
900
800
700
600
500
400
300
200
100
0
-100
-200
-300
-400
-500
-600
-700
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


0.01
0.10
0.76
0.87
0.91
1.25
1.46
1.50
1.71
1.83
1.90
2.00
2.72
2.73
2.79
3.66
3.68
3.69
4.12
4.14
4.62
4.64
5.75
5.75
6.74
6.76
7.03
7.26
6.46
3.84
3.68
16.81
2.41
2.38
7.89
0.84
2.00
1.07
0.88
0.79
0.77
2.00
1.99
4000
3500
3000
2500
2000
1500
1000
500
0
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
f1 (ppm)



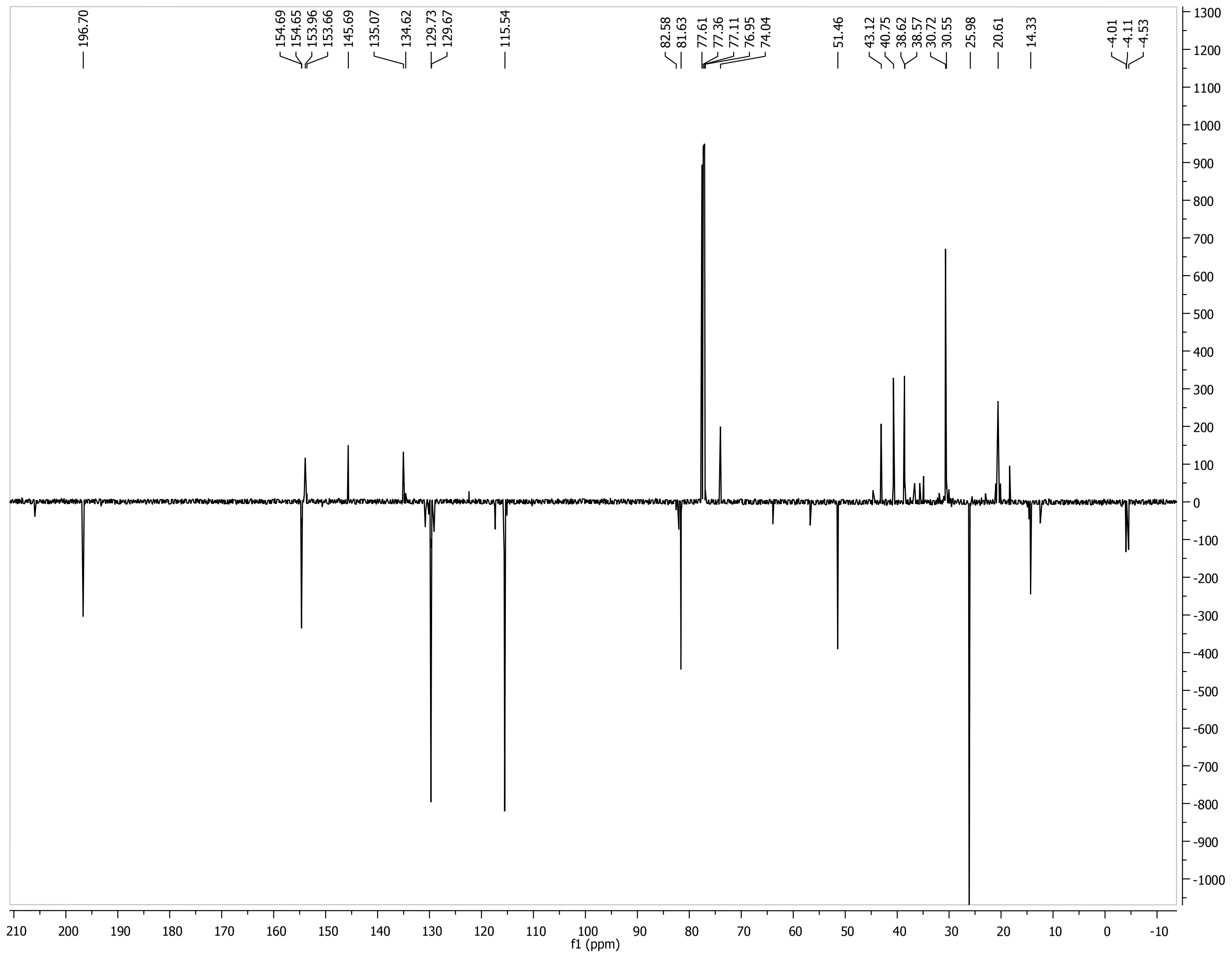
-4.51
-4.13
-4.09
-3.26
13.59
18.32
25.97
30.72
37.81
43.78
53.98
66.23
76.53
77.36
81.98
115.69
128.93
129.64
129.67
134.83
140.67
154.39
OTBS
H
OH
OH
HO
f1 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
-300
-400
-500
-600
-700
-800
-900
-1000
-1100

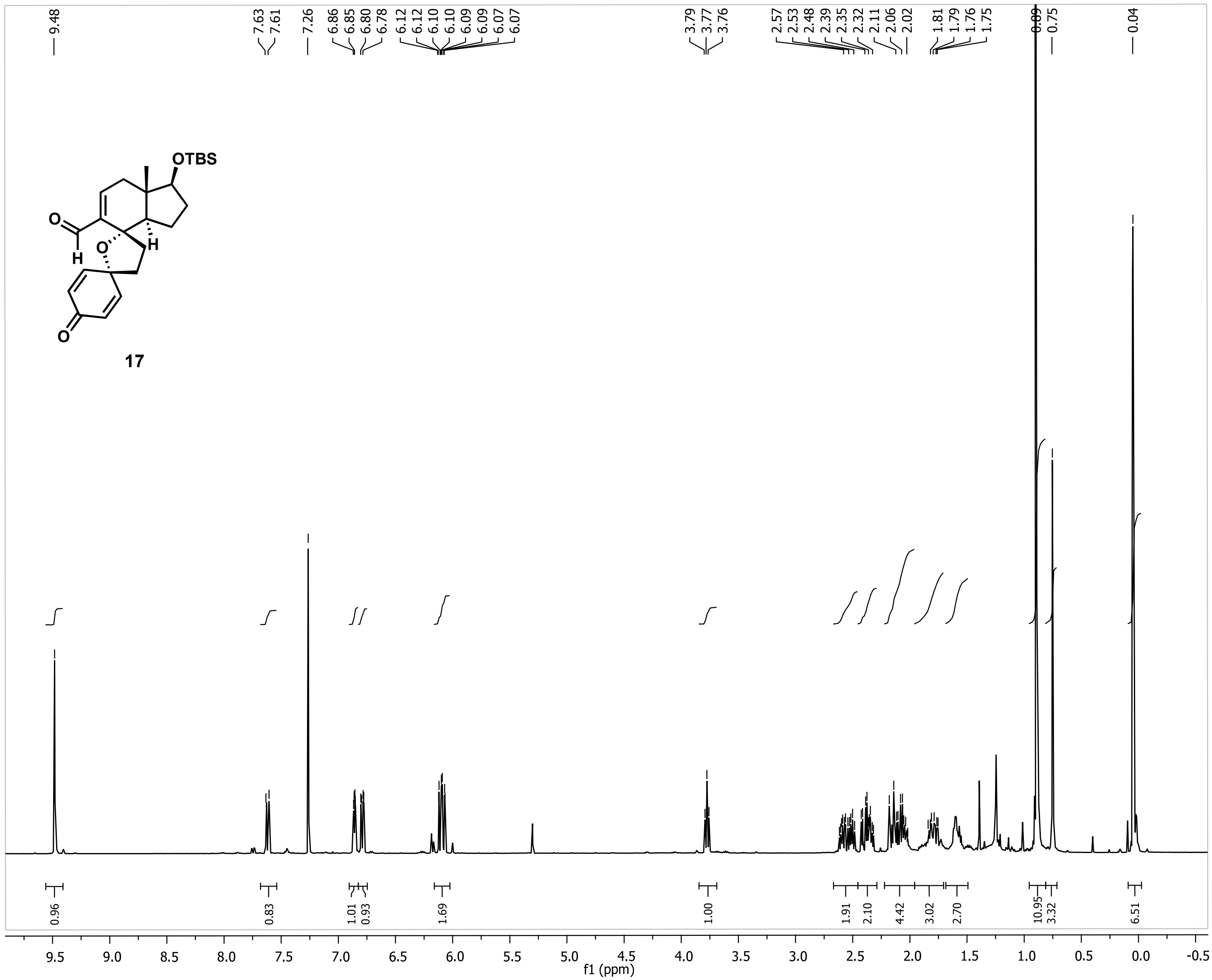
16



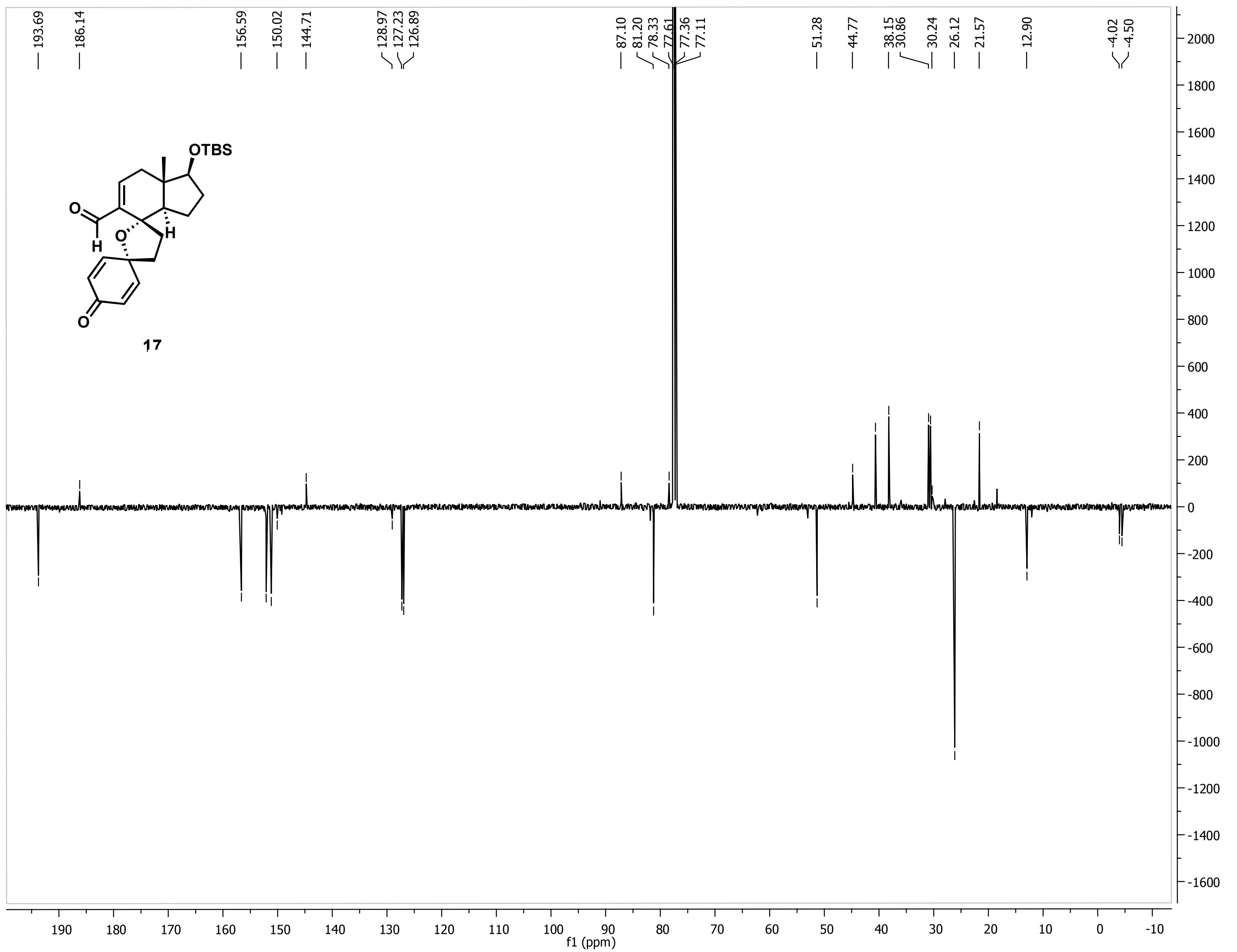
16

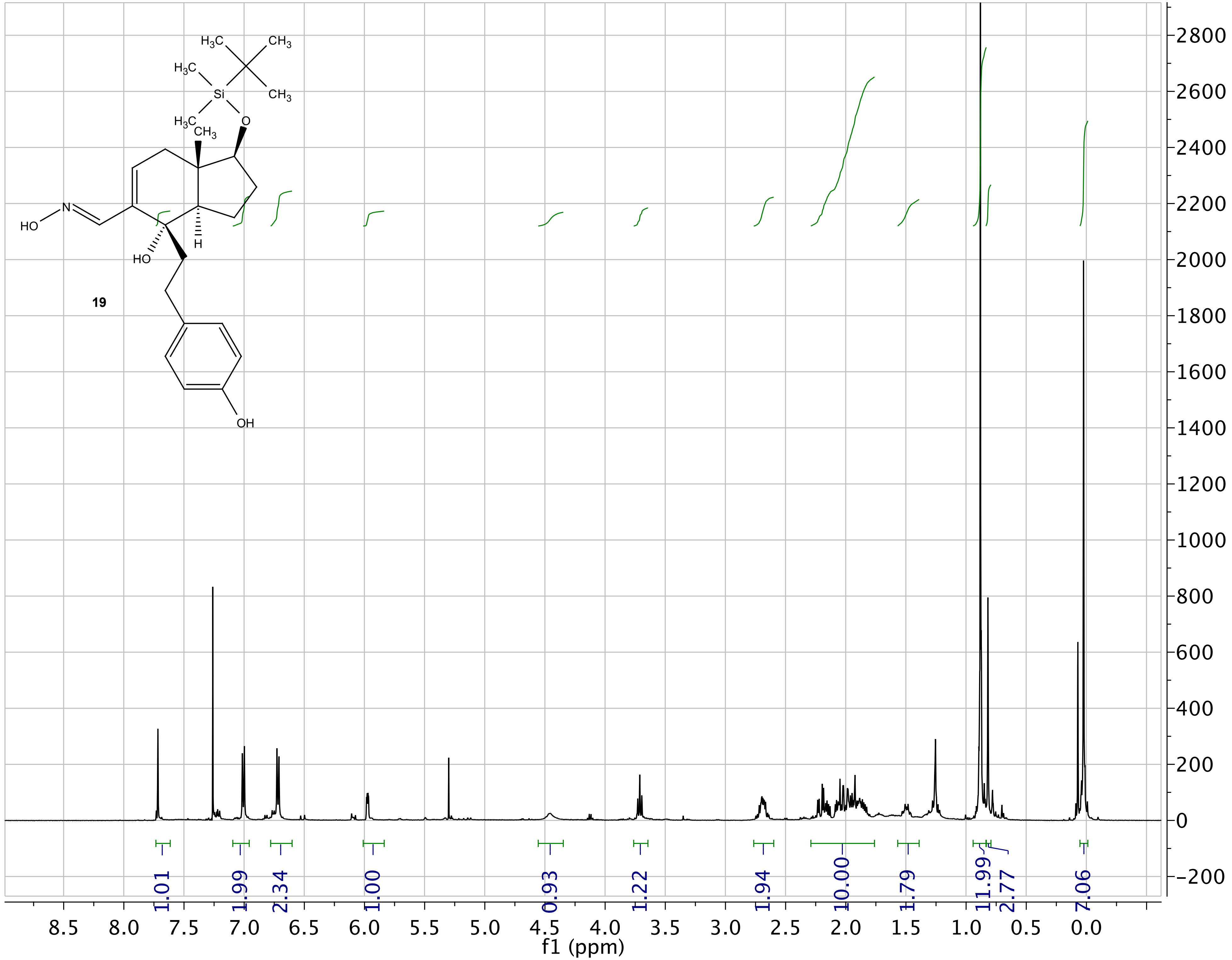
OTBS
HO
HO
H
OH
10.06
9.43
7.22
6.96
6.78
6.76
6.71
6.69
4.92
4.18
3.71
3.69
3.67
2.67
2.65
2.63
2.61
2.35
2.00
1.87
1.70
1.45
1.21
0.88
0.85
0.84
0.79
-0.00
-0.03
0.16
1.10
1.77
0.49
0.17
1.22
2.00
0.89
1.00
1.55
2.37
1.23
1.73
8.27
1.21
1.58
1.70
2.77
14.99
4.16
7.94
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200


196.70
154.69
154.65
153.96
153.66
145.69
135.07
134.62
129.73
129.67
115.54
82.58
81.63
77.61
77.36
77.11
76.95
74.04
51.46
43.12
40.75
38.62
38.57
30.72
30.55
25.98
20.61
14.33
-4.01
-4.11
-4.53
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
-300
-400
-500
-600
-700
-800
-900
-1000

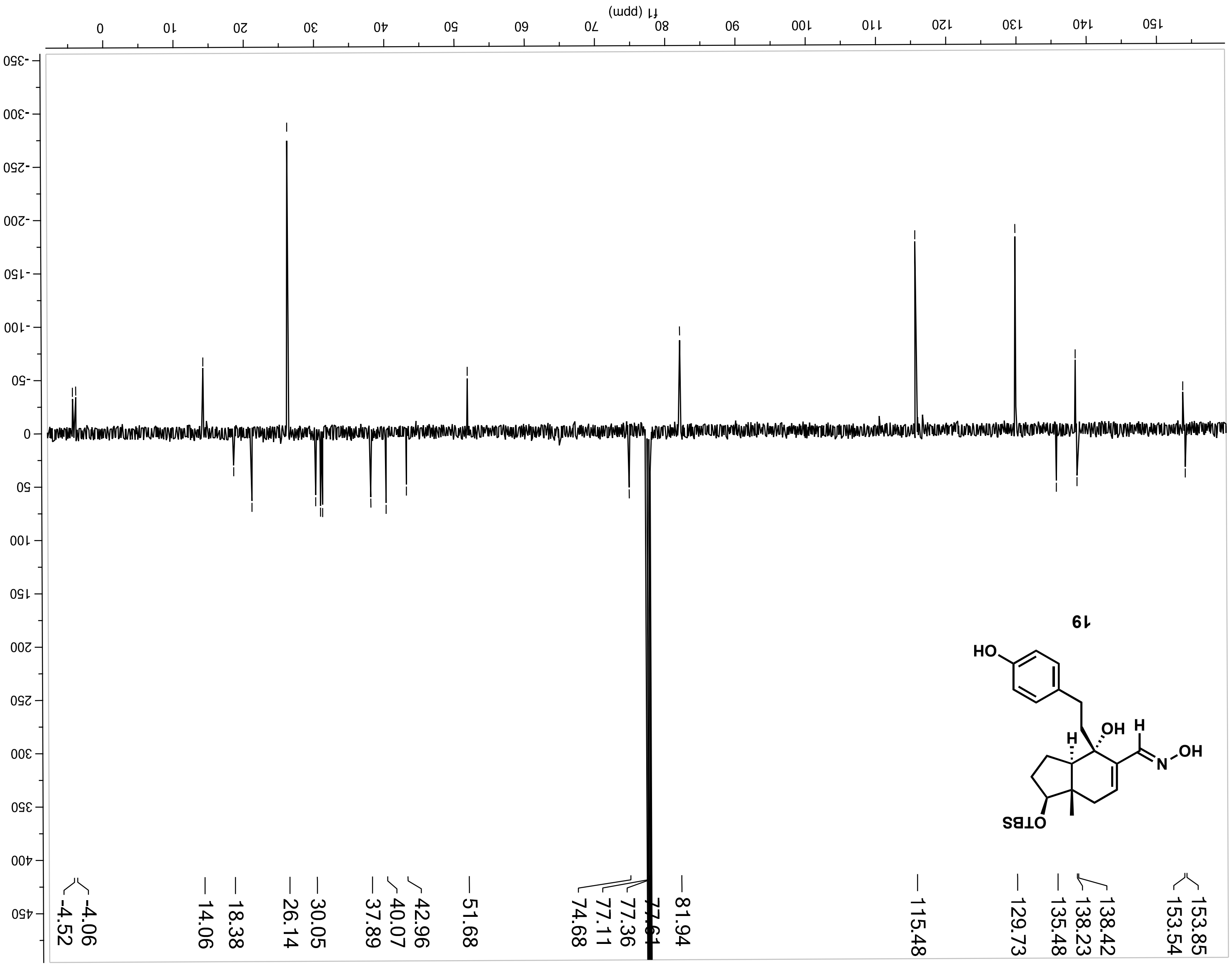

17

9.48
7.63
7.61
7.26
6.86
6.85
6.80
6.78
6.12
6.12
6.10
6.10
6.09
6.09
6.07
6.07
3.79
3.77
3.76
2.57
2.53
2.48
2.39
2.35
2.32
2.11
2.06
2.02
1.81
1.79
1.76
1.75
0.89
0.75
0.04
OTBS
O
H
O
H
O
0.96
0.83
1.01
0.93
1.69
1.00
1.91
2.10
4.42
3.02
2.70
10.95
3.32
6.51
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
4500
4000
3500
3000
2500
2000
1500
1000
500
0

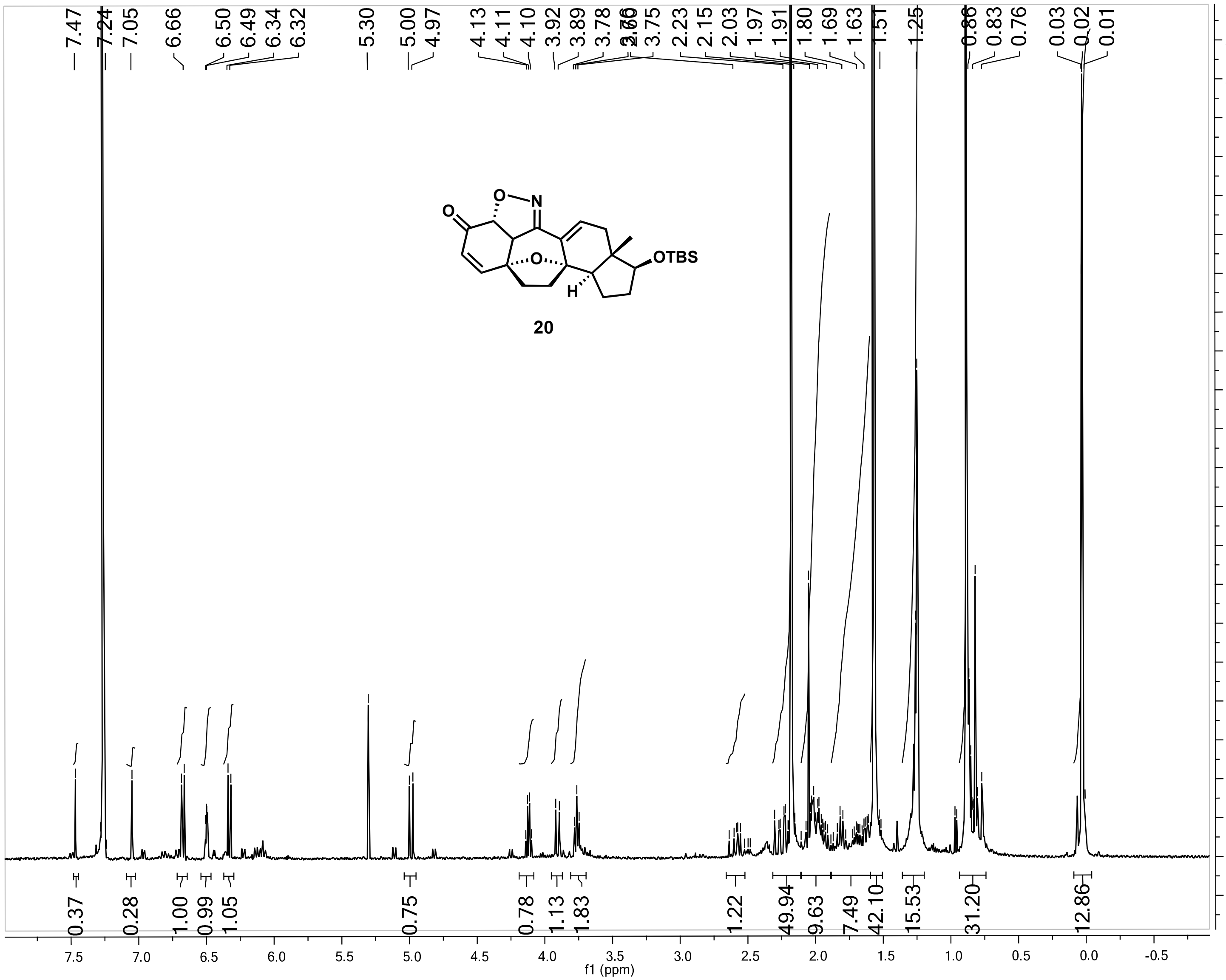

193.69
186.14
156.59
150.02
144.71
128.97
127.23
126.89
87.10
81.20
78.33
77.61
77.36
77.11
51.28
44.77
38.15
30.86
30.24
26.12
21.57
12.90
-4.02
-4.50
OTBS
O
H
O
H
O
17
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
-400
-600
-800
-1000
-1200
-1400
-1600
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


H3C
CH3
H3C
Si
CH3
H3C
CH3
O
HO
N
HO
H
OH
1.01
1.99
2.34
1.00
0.93
1.22
1.94
10.00
1.79
11.99
2.77
7.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200

19


f1 (ppm)
-4.06
-4.52
14.06
18.38
26.14
30.05
37.89
40.07
42.96
51.68
74.68
77.11
77.36
77.61
81.94
115.48
129.73
135.48
138.23
138.42
153.54
153.85
OTBS
H
OH
H
N
OH
HO

19


7.47
7.24
7.05
6.66
6.50
6.49
6.34
6.32
5.30
5.00
4.97
4.13
4.11
4.10
3.92
3.89
3.78
3.76
2.60
3.75
2.23
2.15
2.03
1.97
1.91
1.80
1.69
1.63
1.51
1.25
0.86
0.83
0.76
0.03
0.02
0.01
O
O
N
O
OTBS
H
20
0.37
0.28
1.00
0.99
1.05
0.75
0.78
1.13
1.83
1.22
49.94
9.63
7.49
42.10
15.53
31.20
12.86
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10