Supporting Information

Total Syntheses of Secalonic Acids A and D

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I. General Information

A. Instrumentation and methods

^{1}H NMR spectra were recorded at 400 MHz at ambient temperature with $CDCl_3$ (Cambridge Isotope Laboratories, Inc.) as the solvent unless otherwise stated. ^{13}C NMR spectra were recorded at 100.0 MHz at ambient temperature with $CDCl_3$ as the solvent unless otherwise stated. Chemical shifts are reported in parts per million relative to $CDCl_3$ (^{1}H, δ 7.26; ^{13}C, δ 77.0). Data for ^{1}H NMR are reported as follows: chemical shift, integration, multiplicity (app = apparent, br = broad, par obsc = partially obscure, ovrlp = overlapping, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constants. All ^{13}C NMR spectra were recorded with complete proton decoupling. Infrared spectra were recorded on a Nicolet Nexus 670 FT-IR spectrophotometer. High-resolution mass spectra were obtained in the Boston University Chemical Instrumentation Center using a Waters Q-TOF mass spectrometer. Melting points were recorded on a Mel-temp (Laboratory Devices). Analytical thin layer chromatography was performed using 0.25 mm silica gel 60-F plates. Flash chromatography was performed using 200-400 mesh silica gel (Sorbent Technologies, Inc.). Preparative TLC was conducted with glass backed 1000μm silica gel 60-F plates (Silicycle, Inc.) Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. All other reactions were carried out in oven-dried glassware under an argon atmosphere unless otherwise noted. The Arthur™ Suite Reaction Planner (Symyx Technologies, Inc.) was used for experimental procedure planning. Analytical LC-MS experiments were performed using a Waters Acquity UPLC (Ultra Performance Liquid Chromatography) with a Binary solvent manager, SQ mass spectrometer, Water 2996 PDA (PhotoDiode Array) detector, and Evaporative Light Scattering Detector (ELSD). An Acquity UPLC BEH C18 1.7 μm column was used for analytical UPLC-MS analysis. Preparative HPLC purification was performed on a Gilson PLC 2020 Personal Purification System. A Chiralcel®OD (Chiral Technologies Inc., 250 × 4.6 mm I.D.) column was used for enantiomeric excess determination.

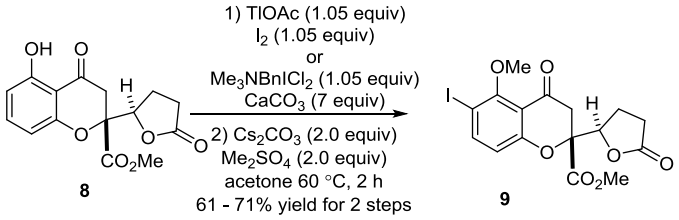
B. Reagents and solvents

HPLC grade tetrahydrofuran, methylene chloride, diethyl ether, toluene and hexanes were purchased from Fisher and VWR and were purified and dried by passing through a PURE SOLV® solvent purification system (Innovative Technology, Inc.). Methanol was purchased from Fisher and used without further purification. Other ACS grade solvents were purchased from Clean Harbors.

Commercial CuCl was purchased from Sigma-Aldrich (≥99.995% trace metals basis) and Strem (99.99%-Cu). Fresh CuCl was prepared following the reported procedure.[S1] All other reagents and relevant catalysts were purchased from Sigma-Aldrich, Acros, Alfa Aesar, and Strem Chemicals.

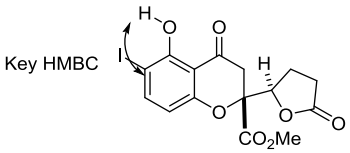
[S1] B. S. Furniss, A. J. Hannaford, P. W. G. Smith, A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, **5th** ed.; John Wiley & Sons: New York, 1989.

II. Experimental Procedures and Compound Characterization



***Ortho*-Iodo Chromone lactone 9: a) $Me_3NBnICl_2$ Method:** Chromone lactone **8** (1.0 g, 3.27 mmol), calcium carbonate (2.29 g, 22.86 mmol, 7.0 equiv), and $Me_3NBnICl_2$ (1.19 g, 3.43 mmol, 1.05 equiv) were added to a solution of CH_2Cl_2/MeOH (5 : 1, 36 mL). After stirring at room temperature for 12 h, the reaction mixture was directly filtered to remove calcium carbonate. After concentration *in vacuo*, the crude product was purified by silica gel chromatography (CH_2Cl_2/EtOAc = 30: 1) to afford a mixture of iodinated chromone lactones. By ^{1}H NMR integration, the ratio of *ortho*: *para*: diiodide: starting material was approximately 63: 5: 12: 10.

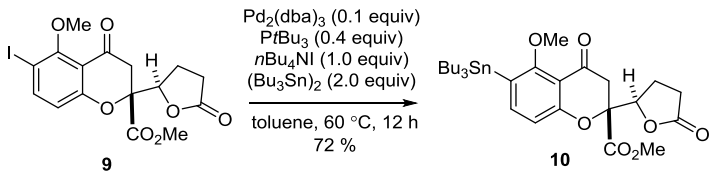
The major *ortho*-iodide product was verified by the following key HMBC correlation:



The aforementioned compound mixture was dissolved in 30 mL of acetone, and cesium carbonate (2.12 g, 6.53 mmol, 2.0 equiv) and dimethyl sulfate (0.824 g, 0.59 mL, 6.53 mmol, 2.0 equiv) were added to the solution. The reaction mixture was warmed to 60 ^{o}C and stirred for 2 h. After cooling to room temperature, cesium carbonate was removed by filtration. After removing volatiles *in vacuo*, the residue was purified by silica gel chromatography (hexanes/EtOAc = 3: 1) to afford the protected *ortho*-iodo chromone lactone **9** (889 mg, 61 %) as a colorless to pale yellow oil. R_f = 0.28 (hexanes/EtOAc = 1: 1); IR (thin film): ν_{max} 2937, 1788, 1753, 1697, 1585, 1458, 1223, 1060, 759 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83 (d, *J* = 8.9 Hz, 1H), 6.65 (d, *J* = 8.9 Hz, 1H), 4.80 (dd, *J* = 8.4, 4.6 Hz, 1H), 3.78 (s, 3H), 3.70 (s, 3H), 3.36 (d, *J* = 16.5 Hz, 1H), 3.01 (d, *J* = 16.5 Hz, 1H), 2.75 (ddd, *J* = 18.0, 10.2, 7.8 Hz, 1H), 2.56 (ddd, *J* = 18.0, 10.5, 5.5 Hz, 1H), 2.43 (m, 1H), 2.33 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 186.2, 175.8, 168.7, 160.9,

159.3, 144.9, 115.8, 115.4, 85.0, 84.6, 79.5, 61.6, 53.6, 41.8, 27.6, 21.6; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{16}IO_7$, 446.9941; found, 446.9933.

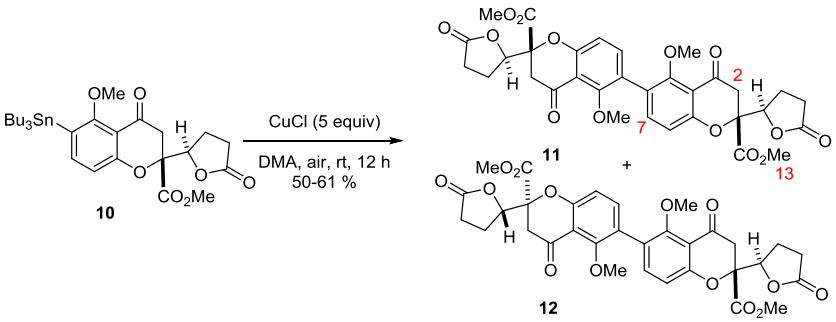
b) TlOAc-directed method:[S2] Chromone lactone **8** (1.0 g, 3.27 mmol), and thallium acetate (0.90 g, 3.43 mmol, 1.05 equiv) were dissolved in 30 mL of CH_2Cl_2, and I_2 (0.51 g, 3.43 mmol, 1.05 equiv) in 10 mL of CH_2Cl_2 was added into the solution by syringe pump over 1 h. After the addition was complete, the reaction was stirred at rt for 12 h during which time a precipitate was formed. The reaction mixture was directly filtered through Celite® to remove thallium salts. After concentration *in vacuo*, the crude product was purified by silica gel chromatography (CH_2Cl_2/EtOAc = 30: 1) to provide a mixture of chromone lactone compounds. The mixture was dissolved in 30 mL of acetone, and cesium carbonate (2.12 g, 6.53 mmol, 2.0 equiv), and dimethyl sulfate (0.824 g, 0.59 mL, 6.53 mmol, 2.0 equiv) were added to the solution. The flask was warmed to 60 ^oC and stirred for 2 h. After cooling to room temperature, cesium carbonate was removed by filtration. After removing volatiles, the residue was purified by silica gel chromatography (hexanes/EtOAc = 3: 1) to afford the protected *ortho*-iodo chromone lactone **9** (1.03 g, 71 %) as a colorless to pale yellow oil.



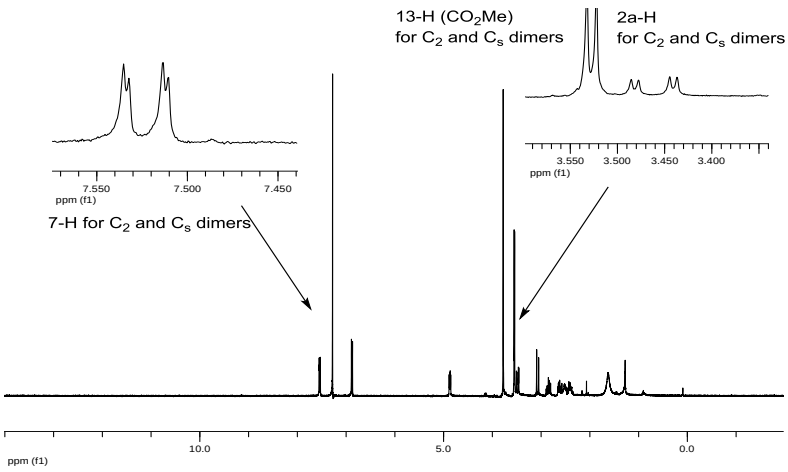
Chromone Lactone Stannane 10: Iodide chromone lactone **9** (889 mg, 1.99 mmol), nBu$_4$NI (736 mg, 1.99 mmol, 1.0 equiv), $Pd_2(dba)_3$ (182 mg, 0.20 mmol, 0.1 equiv), PtBu$_3$ (162 mg, 0.80 mmol, 0.4 equiv) and bis(tributyltin) (2.31 g, 1.53 mL, 3.98 mmol, 2.0 equiv) were added to a flame-dried flask. Under a N_2 atmosphere, 20 mL of anhydrous toluene was added. The flask was warmed to 60 ^oC and stirred for 12 h. The crude mixture was directly purified by silica gel chromatography (hexanes/EtOAc = 4: 1) to afford the chromone lactone stannane **10** (894 mg, 72 %) as a colorless oil. R_f = 0.51 (hexanes/EtOAc = 1: 1); IR (thin film): ν_{max} 2955, 2927, 1790, 1756, 1690, 1580, 1455,

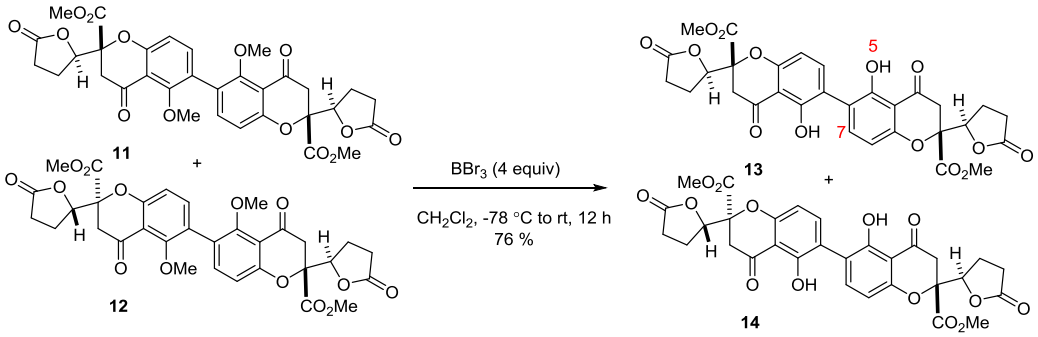
[S2] Both thallium acetate and the produced thallium salt precipitate are highly toxic, please handle with extreme care.

1377, 1287, 1161, 1058, 840 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.46 (d, *J* = 8.1 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 4.81 (dd, *J* = 4.3, 4.3 Hz, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 3.37 (d, *J* = 16.5 Hz, 1H), 3.02 (d, *J* = 16.5 Hz, 1H), 2.80 (ddd, *J* = 17.5, 10.1, 7.8 Hz, 1H), 2.56 (ddd, *J* = 17.8, 10.5, 5.1 Hz, 1H), 2.49 (m, 1H), 2.32 (m, 1H), 1.49 (m, 6H), 1.31 (m, 6H), 1.04 (m, 6H), 0.87 (t, *J* = 7.3 Hz, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 187.4, 176.1, 169.2, 165.0, 161.5, 144.3, 128.7, 113.6, 113.3, 84.2, 79.7, 62.2, 53.4, 42.2, 29.0, 27.7, 27.3, 21.7, 13.6, 9.9; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{28}H_{43}O_7Sn$, 611.2037; found, 611.2049.



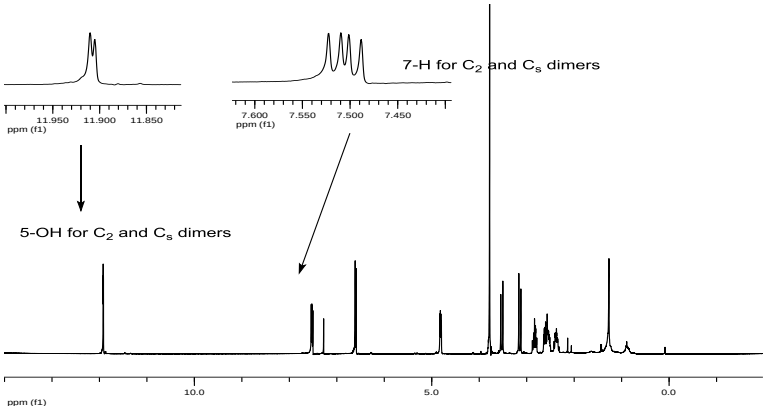
Dimeric Chromone Lactones 11 and 12: Chromanone stannane **10** (100 mg, 0.16 mmol), and freshly prepared CuCl (81 mg, 0.82 mmol, 5 equiv) were placed in an open tube (Note: if commercial CuCl was used, the reaction could proceed under a N_2 atmosphere in comparable yield). Next, 1.6 mL of DMA was added into the tube and the reaction mixture was stirred at room temperature for 12 h. (Note: the reaction mixture turned from clear yellow to cloudy to completely dark). The mixture was quenched with 3 mL of saturated NH_4Cl solution and was extracted 5 times with 5 mL of EtOAc After concentrating the reaction mixture at 40 ^oC *in vacuo*, the crude product was directly purified by column chromatography (hexanes/EtOAc = 1: 2 to pure EtOAc) to afford the dimeric chromone lactones **11** and **12** (26-31 mg, 50-61 %, dr 1: 1, inseparable by silica gel chromatography) as a colorless gel. **11** and **12**: R_f = 0.11 (hexanes/EtOAc = 1: 2); ^1H NMR ($CDCl_3$, 400 MHz) (Note: C_s- and C_2-symmtric compounds have highly overlapping signals in the ^1H NMR spectra except for protons 7, 2a, and 13, see below); HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{32}H_{31}O_{14}$, 639.1714; found, 639.1703.

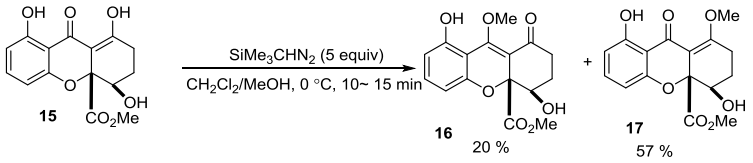




Dimeric Chromone Lactones 13 and 14: Chromanone dimers **11** and **12** (190 mg, 0.30 mmol) were dissolved in 10 mL of CH_2Cl_2 in a 50 mL flask and the reaction mixture was cooled to -78 ^oC. Next, 112 µL (4 equiv) of BBr_3 was added into the flask dropwise and the reaction mixture was slowly warmed to room temperature over 12 h. The reaction mixture was quenched with 20 mL of ice and stirred for an additional 30 min. The reaction mixture was extracted 3 times with 10 mL of EtOAc. After concentrating *in vacuo*, the crude product was directly purified by column chromatography (hexanes/EtOAc = 1: 2 to pure EtOAc) to afford the deprotected dimeric chromone lactones **13** and **14** (135 mg, 76 %, dr 1: 1, inseparable by silica gel chromatography) as a pale yellow foam. **13** and **14**: R_f = 0.33 (hexanes/EtOAc = 1: 2); ^1H NMR ($CDCl_3$, 400 MHz) (Note: C_s- and C_2-symmetric compounds have highly overlapping signals in the ^1H NMR except for protons 5 and 7, see below): dimer 1: δ 11.91 (s, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 6.58 (d, *J* = 8.5 Hz, 2H), 4.79 (dd, *J* = 8.6, 4.3 Hz, 2H), 3.76 (s, 6H), 3.50 (d, *J* = 17.3 Hz, 2H), 3.12 (d, *J* = 17.3 Hz, 2H), 2.81 (ddd, *J* = 18.0, 10.2, 7.1 Hz, 2H), 2.58 (ddd,

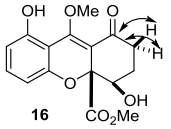
J = 17.7, 10.5, 5.1 Hz, 2H), 2.51 (m, 2H), 2.35 (m, 2H); dimer 2: 11.90 (s, 2H), 7.50 (d, *J* = 8.5 Hz, 2H), 6.58 (d, *J* = 8.5 Hz, 2H), 4.79 (dd, *J* = 8.6, 4.3 Hz, 2H), 3.76 (s, 6H), 3.50 (d, *J* = 17.3 Hz, 2H), 3.12 (d, *J* = 17.3 Hz, 2H), 2.81 (ddd, *J* = 18.0, 10.2, 7.1 Hz, 2H), 2.58 (ddd, *J* = 17.7, 10.5, 5.1 Hz, 2H), 2.51 (m, 2H), 2.35 (m, 2H); HRMS□ESI (m/z): $[M+H]^+$ calcd for $C_{30}H_{27}O_{14}$, 611.1401; found, 611.1415.



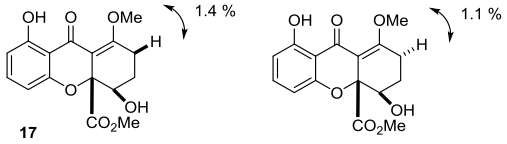


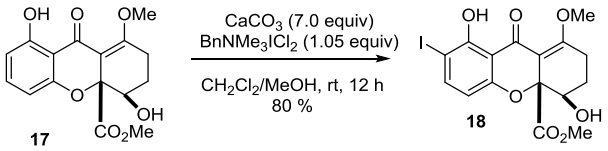
***O*-Methyl-protected Tetrahydroxanthones 16 and 17:** (±)-Tetrahydroxanthone **15** (900 mg, 2.94 mmol) was placed into a flask under a N_2 atmosphere. 30 mL of CH_2Cl_2/MeOH (1: 1) was next added into the flask which was cooled down to 0 ^oC and stirred to fully dissolve the compound. (Note: If solids remain undissolved, an additional 1 ~ 2 mL CH_2Cl_2 was added to the solution.) Next, (trimethylsilyl)diazomethane solution (2M in ether, 7.34 mL, 14.69 mmol, 5 equiv) was added dropwise. After stirring at 0 ^oC for 10 to 15 min, the reaction was quenched with 10 % aqueous AcOH. After warming to room temperature, the reaction was extracted twice with 30 mL of EtOAc. The organic phase was combined, washed with brine, dried over sodium sulfate and calcium carbonate, filtered, and concentrated *in vacuo*. Purification by column chromatography (hexane/EtOAc = 1: 1 to 1: 2) afforded product **16** (188 mg, 20 %) as a pale yellow powder and **17** (531 mg, 57 %) as a yellow solid. **16**: R_f = 0.48 (EtOAc); mp 136-137 °C (CH_2Cl_2); IR (thin film): ν_{max} 3423, 1752, 1730, 1590, 1468, 1325, 1217, 1056, 760 cm^{-1};

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.38 (s, 1H), 7.21 (t, *J* = 8.3 Hz, 1H), 6.59 (d, *J* = 8.1 Hz, 1H), 6.51 (d, *J* = 8.3 Hz, 1H), 4.50 (dd, *J* = 10.5, 7.3 Hz, 1H), 3.92 (s, 3H), 3.69 (s, 3H), 2.99 (d, *J* = 1.5 Hz, 1H, OH, chemical shift and coupling varies with concentration), 2.69 (ddd, *J* = 17.0, 5.1, 2.8 Hz, 1H), 2.54 (ddd, *J* = 17.0, 8.9, 5.5 Hz, 1H), 2.19 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 194.8, 169.6, 160.0, 156.8, 155.4, 134.1, 111.5, 109.7, 108.2, 106.0, 85.0, 73.1, 63.0, 53.0, 38.2, 25.2; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{17}O_7$, 321.0974 ; found, 321.0980.

Observed Key HMBC 

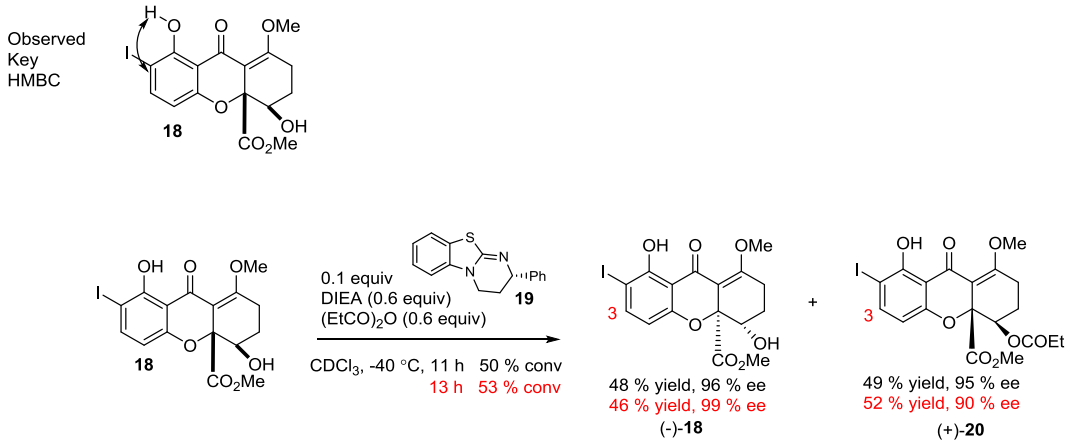
17: R_f = 0.38 (EtOAc); mp 192-193 °C (CH_2Cl_2); IR (thin film): ν_{max} 3448, 3014, 1733, 1633, 1562, 1458, 1356, 1220, 1071, 986, 752 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 12.6 (s, 1H), 7.31 (t, *J* = 8.3 Hz, 1H), 6.49(1) (d, *J* = 8.3 Hz, 1H), 6.48(7) (d, *J* = 8.3 Hz, 1H), 4.27 (dd, *J* = 12.5, 4.5 Hz, 1H), 3.94 (s, 3H), 3.67 (s, 3H), 2.99 (s, 1H, OH, chemical shift and coupling varies with concentration), 2.80 (ddd, *J* = 18.7, 6.2, 1.5 Hz, 1H), 2.65 (ddd, *J* = 18.7, 10.8, 6.7 Hz, 1H), 2.21 (dddd, *J* = 23.7, 13.0, 6.4, 1.4 Hz, 1H), 2.08 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 185.1, 170.0, 169.1, 162.9, 158.5, 137.1, 110.4, 108.2, 106.8, 105.4, 86.1, 71.6, 56.3, 53.2, 24.7, 23.7; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{17}O_7$, 321.0974 ; found, 321.0969.

Observed Key nOe's 



***Ortho*-iodo Tetrahydroxanthone 18:** *O*-Methyl-protected tetrahydroxanthone **17** (500 mg, 1.56 mmol), calcium carbonate (1.09 g, 10.93 mmol, 7.0 equiv), and $Me_3NBnICl_2$ (570 mg, 1.64 mmol, 1.05 equiv) were added to a solution of CH_2Cl_2/MeOH (5 : 1, 16 mL). After stirring at room temperature for 12 h, the reaction mixture was directly filtered to remove calcium carbonate. After concentration *in vacuo*, the crude product was

purified by silica gel chromatography (CH_2Cl_2/EtOAc = 20: 1) to afford iodide **18** (556 mg, 80 %) as a yellow powder. R_f = 0.29 (hexanes/EtOAc = 1: 2) mp decomp 170 °C (CH_2Cl_2); IR (thin film): ν_{max} 3478, 3018, 1748, 1628, 1567, 1425, 1353, 1220, 1066, 759 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 13.57 (s, 1H), 7.73 (d, *J* = 8.7 Hz, 1H), 6.39 (d, *J* = 8.7 Hz, 1H), 4.28 (dd, *J* = 12.6, 4.6 Hz, 1H), 3.96 (s, 3H), 3.68 (s, 3H), 2.82 (ddd, *J* = 18.8, 6.4, 3.9 Hz, 1H), 2.82 (s, 1H, OH, chemical shift and coupling varies with concentration), 2.66 (ddd, *J* = 17.7, 10.8, 6.8 Hz, 1H), 2.21 (dddd, *J* = 24.2, 10.9, 6.5, 2.2 Hz, 1H), 2.10 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 184.3, 170.1, 169.7, 161.5, 158.9, 145.5, 109.3, 108.5, 104.7, 86.4, 75.1, 71.6, 56.5, 53.3, 24.9, 23.7; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{16}O_7I$, 446.9941 ; found, 446.9951.

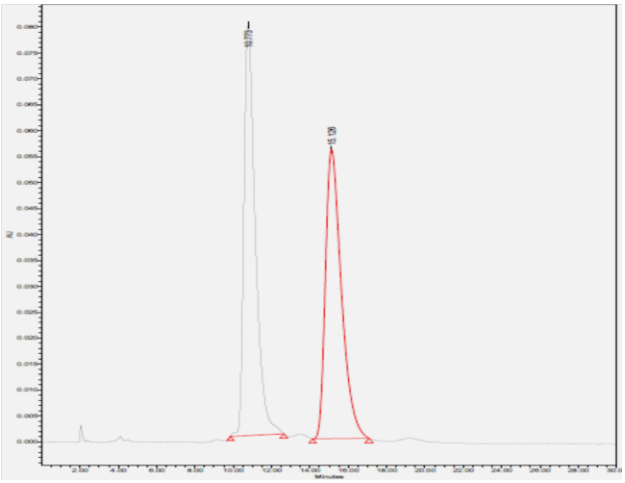


Chiral, Non-Racemic Tetrahydroxanthones (+)-20 and (-)-18: (±)-Tetrahydroxanthone **18** (100 mg, 0.22 mmol) and 5 mL of $CDCl_3$ was added to a flame-dried flask. The solution was gently warmed at 40 °C for 5 min until the substrate was fully dissolved. The solution was cooled to -40 °C. To a flame-dried tube was added (*R*)-HBTM **19**[S3] (6 mg, 0.022 mmol, 0.1 equiv), DIEA (17 mg, 23 µL, 0.13 mmol, 0.6 equiv), and $(EtCO)_2O$ (17 mg, 18 µL, 0.13 mmol, 0.6 equiv) with 1 mL of $CDCl_3$ and the contents were mixed for 3 min. The latter solution was transferred dropwise to a solution of **18**. After stirring at -40 °C for 11 h, the reaction was quenched by 0.2 mL of MeOH and was warmed to room temperature. After concentrating *in vacuo*, the crude reaction product was subjected to ^1H NMR analysis to monitor conversion (δ 6.39, 3-H for (-)-**18**; δ 6.31, 3-H for (+)-**20**). The crude product was purified by silica gel chromatography (CH_2Cl_2/EtOAc = 20: 1 to 10: 1) to afford product (+)-**20** (55 mg, 49 %) as a yellow solid

[S3] For preparation of HBTM catalysts, see: X. Li, V. B. Birman, *Org. Lett.* **2008**, *10*, 1115-1118.

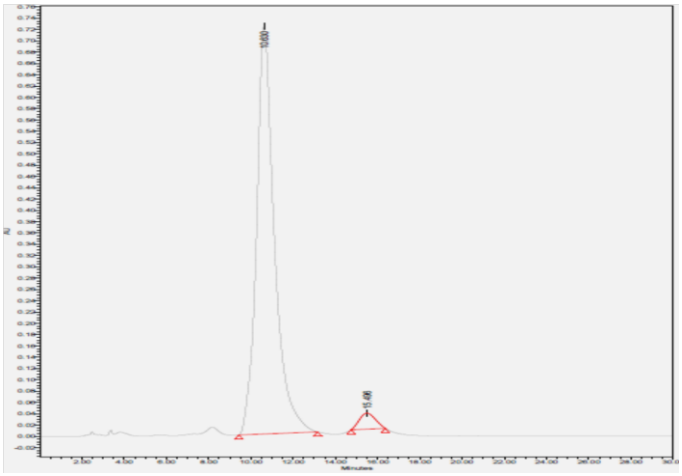
and (-)-**18** (48 mg, 48 %) as a yellow powder. (+)-**20**: R_f = 0.63 (hexanes/EtOAc = 1: 2) mp decomp 180 °C (CH_2Cl_2); IR (thin film): ν_{max} 1750, 1633, 1572, 1427, 1356, 1278, 1226, 1073, 761 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 13.44 (s, 1H), 7.68 (d, *J* = 8.7 Hz, 1H), 6.31 (d, *J* = 8.7 Hz, 1H), 5.40 (d, *J* = 12.1, 4.4 Hz, 1H), 3.92 (s, 3H), 3.65 (s, 3H), 2.77 (ddd, *J* = 18.7, 6.4, 2.6 Hz, 1H), 2.71 (ddd, *J* = 18.7, 12.4, 6.3 Hz, 1H), 2.35 (q, *J* = 7.5 Hz, 2H), 2.34 (m, 1H), 2.08 (m, 1H), 1.14 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 184.3, 173.0, 169.3 (two carbons overlapped, CO_2Me and C=COMe), 161.2, 159.1, 145.4, 109.5, 108.4, 104.8, 84.0, 74.5, 71.7, 56.5, 53.1, 27.6, 24.3, 22.5, 8.9; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{20}O_8I$, 503.0203; found, 503.0212. Enantiomers were separated using chiral UPLC analysis [10% IPA Chiralcel®OD (Chiral Technologies Inc., 250 × 4.6 mm I.D.) column]. The enantiomeric excess for (+)-**20** after kinetic resolution was 96 %. $[\alpha]_D^{28}$= 55.4 ° (*c*= 0.1, CH_2Cl_2).

(±)- **20**:



	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		10.773	3265506	50.40	79170	bb			Unknown	
2		15.126	3213604	49.60	55737	bb			Unknown	

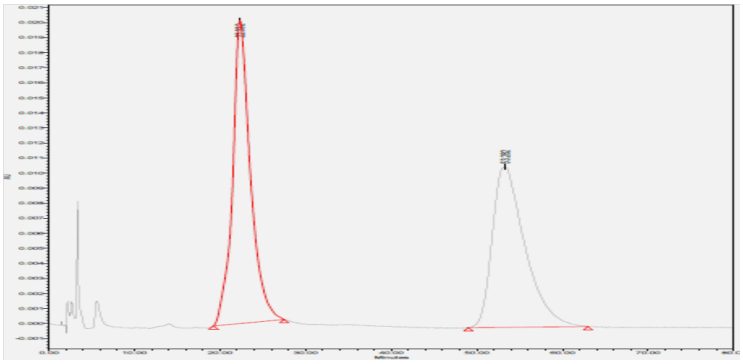
96 % ee (+)-**20**:



	Name	Retention Time (min)	Area (μV*sec)	% Area	Height (μV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		10.630	42574819	96.63	721655	bb			Unknown	
2		15.496	1484288	3.37	28240	bb			Unknown	

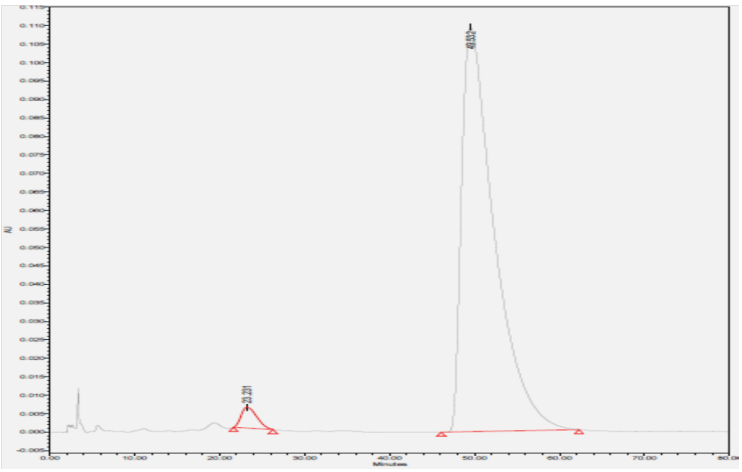
(-)-**18:** ^{1}H NMR, ^{13}C NMR, IR, and HRMS for (-)-**28** were identical to data reported for (±)-**18**. Enantiomers were separated by 10% IPA Chiralcel®OD (Chiral Technologies Inc., 250 × 4.6 mm I.D.) column. The enantiomeric excess for (-)-**18** after kinetic resolution was 95 %.

(±)-**18**:



	Name	Retention Time (min)	Area (μV*sec)	% Area	Height (μV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		22.332	2923674	50.78	20136	bb			Unknown	
2		53.282	2834308	49.22	10661	bb			Unknown	

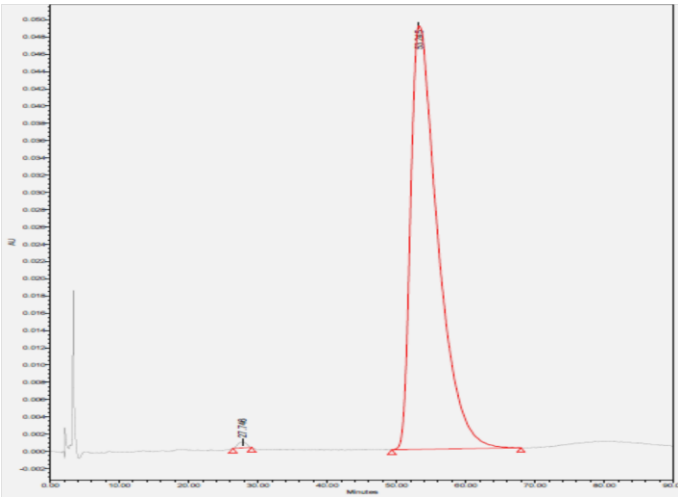
95 % ee (-)-**18**:



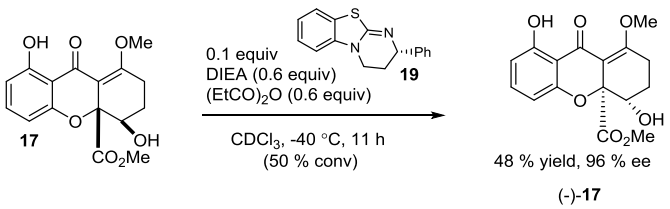
	Name	Retention Time (min)	Area (μV*sec)	% Area	Height (μV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		23.231	721148	2.41	5601	bb			Unknown	
2		49.532	29242612	97.59	109451	bb			Unknown	

>99 % ee (-)-**18**: Follow the previous procedure (Kinetic resolution was performed at -40 ^{o}C for 13 h). Following this protocol, (-)-**18** (46 mg, 46 %) was obtained. $[\alpha]_D^{27}$= -84.5° (*c*= 0.1, CH_2Cl_2).

>99 % ee (-)-**18**:



	Name	Retention Time (min)	Area (μV*sec)	% Area	Height (μV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		27.746	60659	0.45	677	bb			Unknown	
2		53.245	13361534	99.55	49070	bb			Unknown	

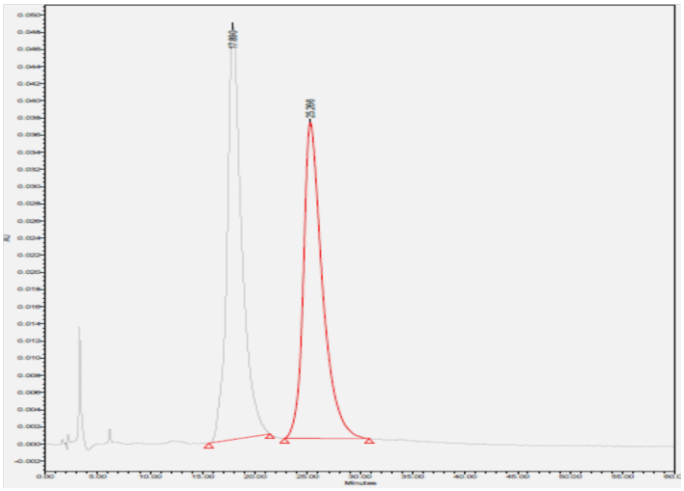


48 % yield, 96 % ee

(-)-**17**

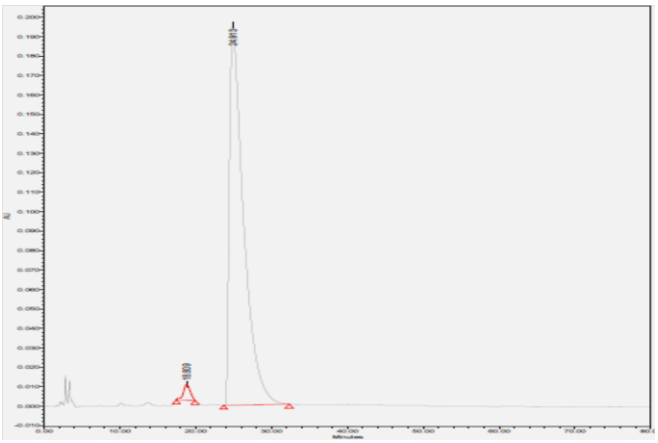
Chiral Tetrahydroxanthone (-)-17: (±)-Tetrahydroxanthone **17** (100 mg, 0.22 mmol) and 5 mL of $CDCl_3$ was added to a flame-dried flask. The solution was gently warmed at 40 ^oC for 5 min until the substrate was fully dissolved. The solution was cooled to -40 ^oC. To a flame-dried tube was added (*R*)-HBTM **19** (6 mg, 0.022 mmol, 0.1 equiv), DIEA (17 mg, 23 µL, 0.13 mmol, 0.6 equiv) and $(EtCO)_2O$ (17 mg, 18 µL, 0.13 mmol, 0.6 equiv) with 1 mL of $CDCl_3$ and the contents were mixed for 3 min. The latter solution was transferred dropwise to the solution of **18**. After stirring at -40 ^oC for 11 h, the reaction was quenched by 0.2 mL MeOH and warmed to room temperature. The crude product was purified by silica gel chromatography (CH_2Cl_2/EtOAc = 20: 1 to 10: 1) to afford product (-)-**17** (48 mg, 48 %) as a yellow powder (X-ray data see page 34). (-)-**17**: ^1H NMR, ^{13}C NMR, IR, and HRMS for **(-)-17** were identical to data reported for (±)-**17**. Enantiomers were separated by 10% IPA Chiralcel®OD (Chiral Technologies Inc., 250 × 4.6 mm I.D.) column. The enantiomeric excess for (-)-**17** after kinetic resolution was 96 %. $[\alpha]_D^{31}$= -129.0 ° (*c*= 0.1, CH_2Cl_2).

(±)-**17**:

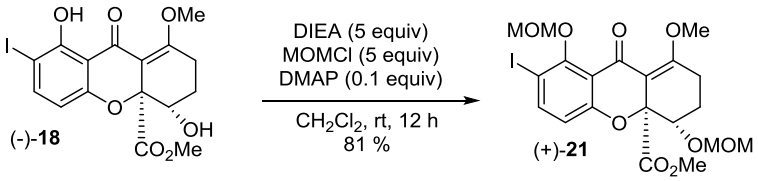


	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		17.890	4681634	50.27	48179	bb			Unknown	
2		25.266	4630776	49.73	36817	bb			Unknown	

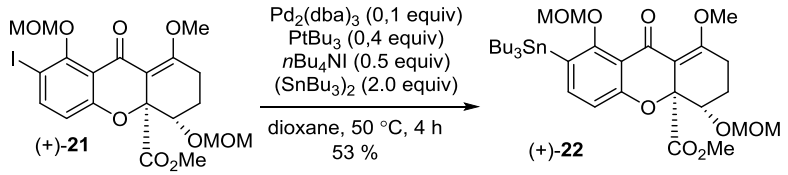
96 % ee (-)-**17**:



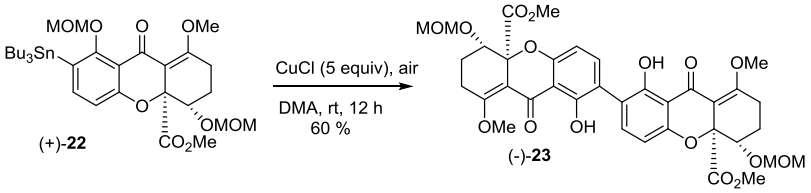
	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		18.809	509919	1.96	8116	bb			Unknown	
2		24.913	25450903	98.04	195503	bb			Unknown	



MOM-Protected Tetrahydroxanthone (+)-21: Enanotiopure tetrahydroxanthone (-)-**18** (46 mg, 0.10 mmol) was dissolved in 1 mL of CH_2Cl_2 in a flame-dried flask. DMAP (1.2 mg, 0.01 mmol, 0.1 equiv), DIEA (64 mg, 87 µL, 0.50 mmol, 5 equiv), and MOMCl (40 mg, 38 µL, 0.50 mmol, 5 equiv) were added into the solution. The reaction was stirred for 12 h at room temperature. After concentration *in vacuo*, the crude product was purified by silica gel chromatography (hexanes/EtOAc = 1: 1 to 1: 2) to afford product (+)-**21** (45 mg, 81 %) as a colorless to pale yellow oil. (+)-**21**: R_f = 0.27 (hexanes/EtOAc = 1: 2); IR (thin film): ν_{max} 1750, 1664, 1583, 1447, 1376, 1285, 1212, 1154, 1036, 921, 737 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.77 (d, *J* = 8.8 Hz, 1H), 6.59 (d, *J* = 8.8 Hz, 1H), 5.33 (d, *J* = 6.6 Hz, 1H), 4.95 (d, *J* = 6.7 Hz, 1H), 4.85 (d, *J* = 6.6 Hz, 1H), 4.71 (d, *J* = 6.7 Hz, 1H), 4.22 (dd, *J* = 11.3, 4.0 Hz, 1H), 3.85 (s, 3H), 3.62 (s, 3H), 3.60 (s, 3H), 3.42 (s, 3H), 2.71 (ddd, *J* = 18.3, 5.7, 5.2, 4.0 Hz, 1H), 2.58 (ddd, *J* = 18.3, 9.8, 5.9 Hz, 1H), 2.26 (m, 1H), 2.03 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 177.4, 169.9, 167.5, 161.0, 158.1, 144.1, 115.7, 114.7, 106.8, 101.9, 96.2, 86.2, 83.4, 75.0, 58.5, 56.4, 55.8, 52.9, 24.4, 23.9; HRMS–ESI (m/z): $[M+Na]^+$ calcd for $C_{20}H_{23}O_9INa$, 557.0285; found, 557.0295; $[\alpha]_D^{30}$= 148.6 ° (*c*= 0.1, CH_2Cl_2).

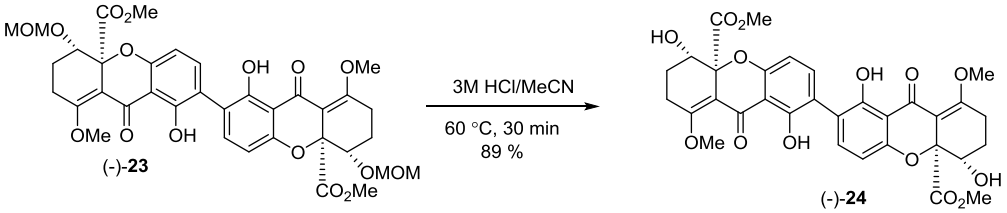


MOM-Protected Stannane (+)-22: MOM-protected tetrahydroxanthone (+)-**21** (45 mg, 0.084 mmol), *n*Bu_4NI (16 mg, 0.042 mmol, 0.5 equiv), $Pd_2(dba)_3$ (7 mg, 0.008 mmol, 0.1 equiv), P*t*Bu_3 (7 mg, 0.034 mmol, 0.4 equiv), and bis(tributyltin) (97 mg, 85 µL, 0.17 mmol, 2.0 equiv) were added to a flame-dried flask. Under a N_2 atmosphere, 0.9 mL of anhydrous dioxane was added. The flask was warmed to 50 ^oC and stirred for 4 h. After cooling to room temperature, solvent was removed in *vacuo*. The crude mixture was directly purified by silica gel chromatography (hexanes/EtOAc = 2: 1) to afford MOM-protected stannane (+)-**22** (31 mg, 53 %) as a colorless to pale yellow oil. (+)-**22**: R_f = 0.30 (hexanes/EtOAc = 1: 1); IR (thin film): ν_{max} 2956, 1737, 1665, 1581, 1450, 1369, 1229, 1154, 1038, 823 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.38 (d, *J* = 8.0 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 5.32 (d, *J* = 6.1 Hz, 1H), 5.00 (d, *J* = 6.7 Hz, 1H), 4.72 (d, *J* = 6.1 Hz, 2H), 4.24 (dd, *J* = 11.2, 3.9 Hz, 1H), 3.85 (s, 3H), 3.62 (s, 3H), 3.44 (s, 3H), 3.38 (s, 3H), 2.71 (ddd, *J* = 18.2, 4.8, 4.8 Hz, 1H), 2.58 (ddd, *J* = 18.2, 9.8, 5.7 Hz, 1H), 2.51 (m, 1H), 2.04 (m, 1H), 1.49 (m, 6H), 1.31 (m, 6H), 1.07 (m, 6H), 0.87 (t, *J* = 7.3 Hz, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 178.8, 170.3, 166.4, 163.5, 161.2, 143.3, 126.9, 113.9, 112.2, 108.0, 100.8, 96.3, 85.9, 75.2, 58.0, 56.2, 55.8, 52.7, 29.1, 27.4, 24.4, 24.1, 13.7, 10.0; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{32}H_{51}O_9Sn$, 699.2562; found, 699.2593; $[\alpha]_D^{30}$= 122.1 ° (*c*= 0.1, CH_2Cl_2).



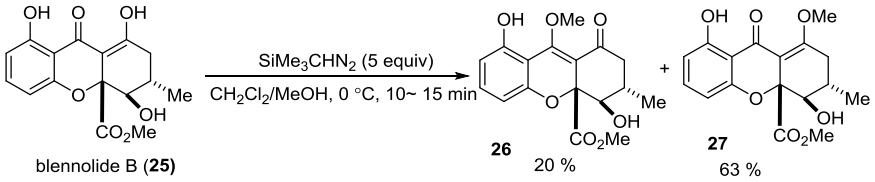
Dimeric Tetrahydroxanthone (-)-23: MOM-protected stannane (+)-**22** (30 mg, 0.043 mmol), and freshly prepared CuCl (21 mg, 0.22 mmol, 5 equiv) were placed in an open tube (Note: if commercial CuCl was used, the reaction could proceed under a N_2 atmosphere in comparable yield). Next, 0.5 mL of DMA was added into the tube and the reaction mixture was stirred at room temperature for 12 h. (Note: Note: the reaction turns

from clear yellow to cloudy to completely dark). The mixture was quenched with 3 mL of saturated NH_4Cl solution and was extracted 5 times with 3 mL. After concentrating at 40 ^oC *in vacuo*, the crude product was directly purified by preparative TLC (EtOAc) to afford the dimeric tetrahydroxanthone (-)-**23** (9 mg, 60 %) as a yellow solid. (-)-**23**: R_f = 0.44 (pure EtOAc); melting point: >220 ^oC (CH_2Cl_2/MeOH); IR (thin film): ν_{max} 2950, 1777, 1633, 1584, 1560, 1432, 1224, 1039, 818 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 12.95 (s, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 6.52 (d, *J* = 8.5 Hz, 2H), 5.04 (d, *J* = 6.7 Hz, 2H), 4.75 (d, *J* = 6.7 Hz, 2H), 4.24 (dd, *J* = 11.9, 4.3 Hz, 2H), 3.89 (s, 6H), 3.69 (s, 6H), 3.45 (s, 6H), 2.76 (ddd, *J* = 18.1, 6.0, 2.9 Hz, 2H), 2.62 (ddd, *J* = 18.1, 10.4, 6.1 Hz, 2H), 2.32 (m, 2H), 2.06 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 185.7, 170.0, 167.8, 160.3, 158.3, 139.6, 117.7, 108.2, 106.4, 106.1, 96.4, 86.1, 75.3, 56.3, 55.8, 53.0, 24.6, 23.9; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{36}H_{39}O_{16}$, 727.2238; found, 727.2233; $[\alpha]_D^{28}$= -23.5 ° (*c*= 0.1, CH_2Cl_2).



Dimeric Tetrahydroxanthone (-)-24: Dimeric tetrahydroxanthone (-)-**23** (5.0 mg, 0.0069 mmol) was dissolved in 1.5 mL of acetonitrile and 1.5 mL of 3M aqueous HCl. The reaction was warmed up to 60 ^oC and was stirred for 30 min. After cooling to room temperature, the solution was purified by preparative HPLC (C_{18}, 10-75% CH_3CN/water). The fractions were extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated to afford (-)-**24** (3.8 mg, 89 %) as a pale yellow solid. (-)-**24**: mp: 223-225 ^oC (CH_2Cl_2); IR (thin film): ν_{max} 3462, 2926, 1737, 1607, 1590, 1562, 1430, 1243, 1059 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) (Note: Compound (-)-**24** has moderate solubility in $CDCl_3$; however, decomposition or isomerization was not observed in $CDCl_3$): δ 13.93 (s, 2H), 11.75 (s, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 6.63 (d, *J* = 8.5 Hz, 2H), 4.34 (dd, *J* = 11.8, 5.2 Hz, 2H), 3.74 (s, 6H), 2.83 (d, *J* = 1.0 Hz, 1H, OH, chemical shift and coupling varies with concentration), 2.68 (m, 4H), 2.22 (m, 2H), 2.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) : δ 187.2, 178.4, 170.1, 159.4, 158.2, 140.2, 118.3, 107.6, 106.9, 101.3, 84.4, 72.0,

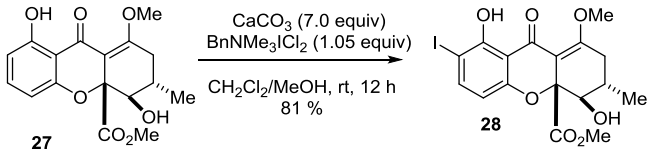
53.3, 27.6, 23.8; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{30}H_{27}O_{14}$, 611.1401; found, 611.1398; $[\alpha]_D^{29}$= -54.3° (*c*= 0.1, CH_2Cl_2).



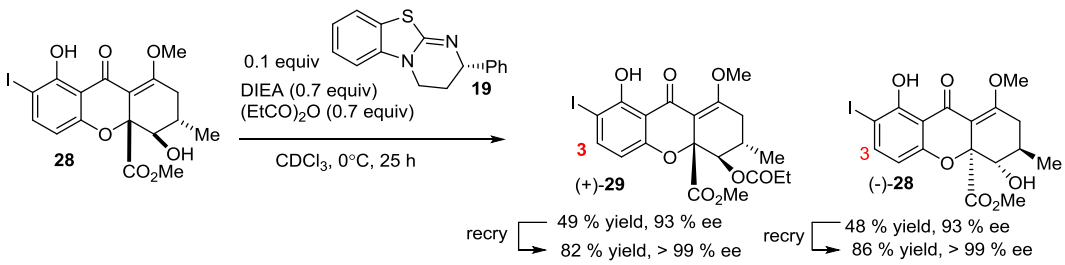
***O*-Methyl-protected Tetrahydroxanthones 26 and 27:** (±)-Blennolide B **25** (900 mg, 2.81 mmol) was placed into a flask under a N_2 atmosphere. 28 mL of CH_2Cl_2/MeOH (1: 1) was next added into the flask which was cooled down to 0 ^oC and stirred to fully dissolve the compound. (Note: If solid remains undissolved, an additional 1 ~ 2 mL CH_2Cl_2 was added to the solution.) Next, (trimethylsilyl)diazomethane solution (2M in ether, 7.03 mL, 14.05 mmol, 5 equiv) was added dropwise. After stirring at 0 ^oC for 10 to 15 min, the reaction was quenched with 10% aqueous AcOH. After warming to room temperature, the reaction was extracted twice with 30 mL of EtOAc. The organic phase was combined, washed with brine, dried over sodium sulfate and calcium carbonate, filtered, and concentrated *in vacuo*. Purification by column chromatography (hexane/EtOAc = 2: 1 to 1: 1) afforded product **26** (189 mg, 20 %) as a white powder and **27** (594 mg, 63 %) as a yellow solid. **26**: R_f = 0.37 (hexanes/EtOAc = 1: 1); mp 174-176 °C (CH_2Cl_2); IR (thin film): ν_{max} 3466, 2959, 1744, 1678, 1593, 1469, 1326, 1227, 1058, 756 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.35 (s, 1H), 7.20 (t, *J* = 8.2 Hz, 1H), 6.59 (d, *J* = 8.1 Hz, 1H), 6.51 (d, *J* = 8.3 Hz, 1H), 4.07 (d, *J* = 11.0 Hz, 1H), 3.91 (s, 3H), 3.67 (s, 3H), 2.95 (s, 1H, OH, chemical shift and coupling varies with concentration), 2.68 (dd, *J* = 16.2, 4.6 Hz, 1H), 2.38 (m, 1H), 2.23 (dd, *J* = 16.1, 12.6 Hz, 1H), 1.15 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 194.4, 169.7, 159.5, 156.8, 155.4, 134.0, 111.5, 110.2, 108.2, 106.0, 85.2, 78.4, 62.9, 52.9, 47.1, 30.6, 18.4; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{19}O_7$, 335.1131 ; found, 335.1129.

27: R_f = 0.35 (hexanes/EtOAc = 1: 2); mp 202-203 °C (CH_2Cl_2); IR (thin film): ν_{max} 3469, 2956, 1733, 1635, 1565, 1458, 1356, 1222, 1045, 991, 817, 733 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 12.61 (s, 1H), 7.31 (t, *J* = 8.3 Hz, 1H), 6.49 (d, *J* = 8.3 Hz, 2H), 3.94 (s, 3H), 3.88 (dd, *J* = 11.6, 2.6 Hz, 1H), 3.66 (s, 3H), 2.87 (d, *J* = 2.6 Hz, 1H, OH,

chemical shift and coupling varies with concentration), 2.84 (dd, *J* = 18.4, 5.7 Hz, 1H), 2.40 (m, 1H), 2.23 (dd, *J* = 18.4, 10.7 Hz, 1H), 1.17 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 185.1, 170.1, 168.3, 162.9, 158.5, 137.1, 110.3, 108.2, 106.8, 105.6, 86.5, 76.5, 56.3, 53.2, 33.5, 28.9, 17.7; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{19}O_7$, 335.1131 ; found, 335.1132.

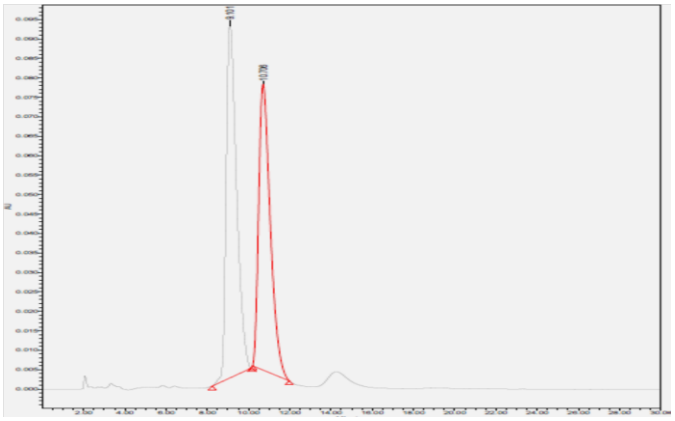


***Ortho*-iodo Tetrahydroxanthone 28:** *O*-Methyl-protected blennolide B **27** (500 mg, 1.50 mmol), calcium carbonate (1.05 g, 10.50 mmol, 7.0 equiv), and $Me_3NBnICl_2$ (548 mg, 1.58 mmol, 1.05 equiv) were added to a solution of CH_2Cl_2/MeOH (5 : 1, 15 mL). After stirring at room temperature for 12 h, the reaction mixture was directly filtered to remove calcium carbonate. After concentration *in vacuo*, the crude product was purified by silica gel chromatography (CH_2Cl_2/EtOAc = 30: 1) to afford product **28** (557 mg, 81 %) as a yellow powder. R_f = 0.41 (hexanes/EtOAc = 1: 2) mp >230 °C (CH_2Cl_2); IR (thin film): ν_{max} 3529, 2951, 1732, 1628, 1566, 1425, 1217, 1071, 1029, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 13.56 (s, 1H), 7.73 (d, *J* = 8.7 Hz, 1H), 6.39 (d, *J* = 8.7 Hz, 1H), 3.96 (s, 3H), 3.89 (d, *J* = 11.6 Hz, 1H), 3.67 (s, 3H), 2.86 (dd, *J* = 18.5, 5.7 Hz, 1H), 2.77 (d, *J* = 1.0 Hz, 1H, OH, chemical shift and coupling varies with concentration), 2.42 (m, 1H), 2.25 (dd, *J* = 18.5, 10.7 Hz, 1H), 1.18 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 184.2, 169.8, 169.3, 161.5, 159.0, 145.5, 109.3, 108.5, 104.8, 86.7, 76.5, 75.0, 56.4, 53.3, 33.5, 28.9, 17.8; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{18}O_7I$, 461.0097 ; found, 461.0101.



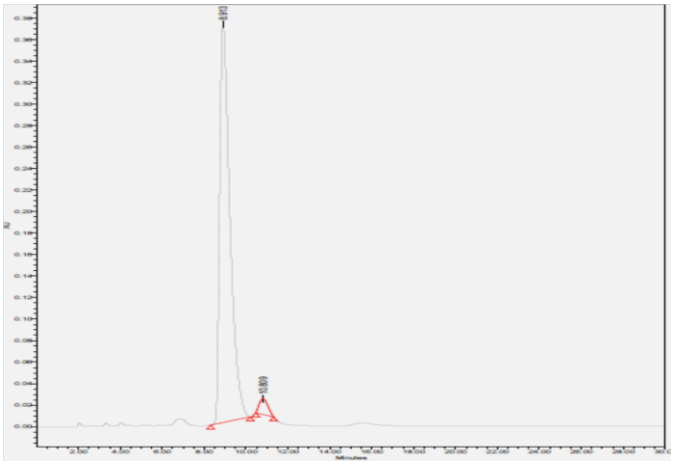
Chiral, Non-Racemic Tetrahydroxanthones (+)-29 and (-)-28: (±)-Tetrahydroxanthone **28** (200 mg, 0.43 mmol) and 20 mL of $CDCl_3$ were added to a flame-dried flask. The solution was gently warmed at 40 ^oC for 5 min until the substrate was fully dissolved. The solution was cooled to 0 ^oC. To a flame-dried tube was added ®-HBTM **19** (11.5mg, 0.043 mmol, 0.1 equiv), DIEA (38.9 mg, 52.3 µL, 0.30 mmol, 0.7 equiv), and $(EtCO)_2O$ (39.0 mg, 38.5 µL, 0.30 mmol, 0.7 equiv) with 2 mL of $CDCl_3$ and the contents were mixed for 3 min. The latter solution was transferred dropwise to a solution of **28**. After stirring at 0 ^oC for 25 h, the reaction was quenched by 0.2 mL of MeOH, and was warmed to room temperature. After concentrating *in vacuo*, the crude reaction product was subjected to ^1H NMR analysis to monitor conversion (δ 6.49, 3-H for (-)-**28**; δ 6.39, 3-H for (+)-**29**). The crude product was purified by silica gel chromatography (CH_2Cl_2/EtOAc = 30: 1 to 10: 1) to afford product (+)-**29** (110 mg, 49 %) as a yellow solid and (-)-**28** (96 mg, 48 %) as a yellow powder. (+)-**29**: R_f = 0.33 (hexanes/EtOAc = 1: 1) mp >230 °C (CH_2Cl_2); IR (thin film): ν_{max} 2951, 1751, 1634, 1570, 1426, 1351, 1218, 1079, 734 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 13.44 (s, 1H), 7.70 (d, *J* = 8.7 Hz, 1H), 6.31 (d, *J* = 8.7 Hz, 1H), 5.36 (d, *J* = 12.1 Hz, 1H), 3.95 (s, 3H), 3.67 (s, 3H), 2.88 (dd, *J* = 18.4, 5.6 Hz, 1H), 2.62 (m, 1H), 2.41 (q, *J* = 7.7 Hz, 2H), 2.36 (dd, *J* = 18.4, 10.8 Hz, 1H), 1.20 (t, *J* = 7.6 Hz, 3H), 1.03 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 184.2, 173.4, 169.4, 168.5, 161.2, 159.2, 145.5, 109.7, 108.4, 105.2, 85.0, 75.5, 74.6, 56.6, 53.2, 33.3, 28.4, 27.6, 17.1, 9.2; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{20}H_{22}O_8I$, 517.0359 ; found, 517.0358. Enantiomers were separated using a 10% IPA Chiralcel®OD (Chiral Technologies Inc., 250 × 4.6 mm I.D.) column. The enantiomeric excess for (+)-**29** after kinetic resolution was 93 %.

(±)-**29**:



	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		9.101	3188785	52.66	91142	bb			Unknown	
2		10.706	2866903	47.34	73482	bb			Unknown	

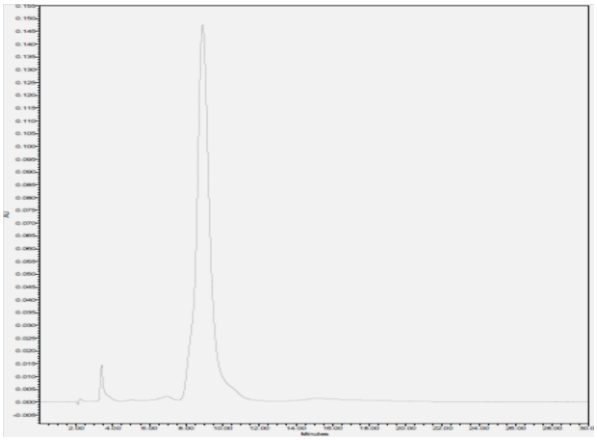
93 % ee (+)-**29**:



	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		8.913	12624063	96.75	370578	bb			Unknown	
2		10.809	423700	3.25	14601	bb			Unknown	

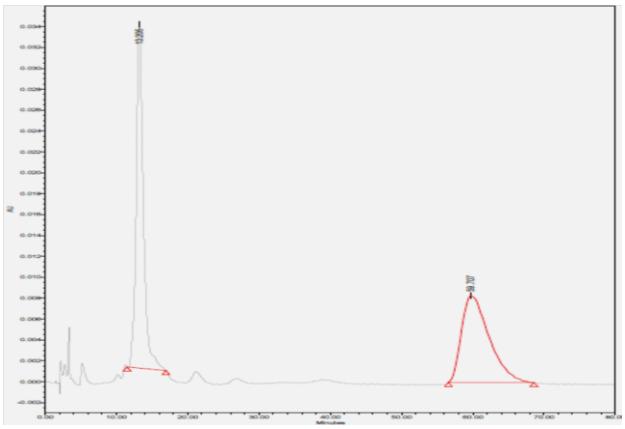
Recrystallization of (+)-**29**: 110 mg 93 % ee (+)-**29** was dissolved in 3 mL of CH_2Cl_2, which followed by the addition of hexanes (10 mL). The reaction mixture was placed in a -20 °C refrigerator overnight in which case the racemate precipitated from the solution. After filtration of the solid, the solution was concentrated *in vacuo*, to afford (+)-**29** (91 mg, 83 %). $[\alpha]_D^{27}$= 84.3 ° (*c*= 0.1, CH_2Cl_2).

>99 % ee (+)-**29**:



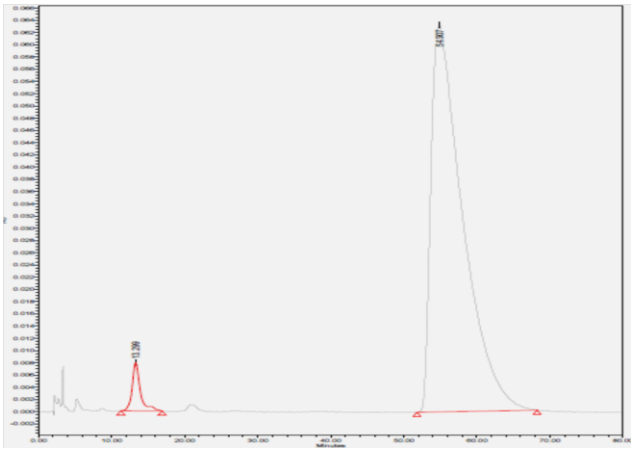
(-)-28: ^{1}H NMR, ^{13}C NMR, IR, and HRMS for (-)-**28** were identical to data reported for (±)-**28**. Enantiomers were separated by 10% IPA Chiralcel®OD (Chiral Technologies Inc., 250 × 4.6 mm I.D.) column. The enantiomeric excess for (-)-**28** after kinetic resolution was 93 %.

(±)-**28**:



	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		13.205	2305039	50.69	32913	bb			Unknown	
2		59.707	2242396	49.31	8325	bb			Unknown	

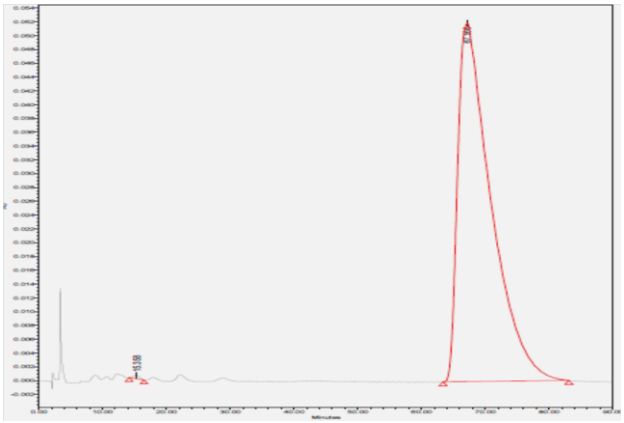
93 % ee (-)-**28**:



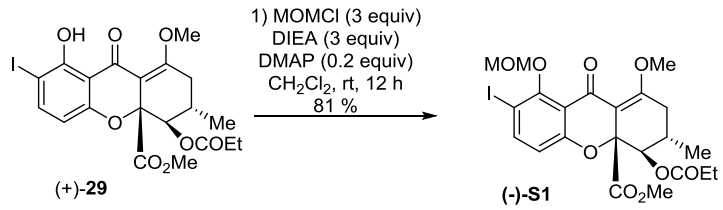
	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		13.299	613441	3.11	7880	bb			Unknown	
2		54.907	19111680	96.89	63226	bb			Unknown	

Recrystallization of (-)-28: 96 mg 93 % ee (-)-**28** was dissolved in CH_2Cl_2, followed by rotovaping of the solvent afforded an oily residue. The corresponding oil was left on the bench overnight in which case (-)-**28** was obtained as clear yellow crystals. After removal of the residue oil, (-)-**28** (82 mg, 85 %) was obtained. $[\alpha]_D^{28}$= -55.3 ° (*c*= 0.1, CH_2Cl_2).

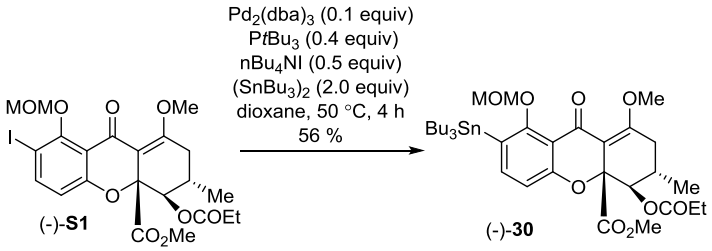
>99 % ee (-)-**28**:



	Name	Retention Time (min)	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		15.358	36986	0.20	498	bb			Unknown	
2		67.166	18787143	99.80	51945	bb			Unknown	

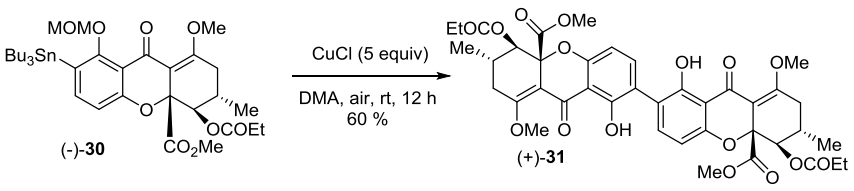


MOM-Protected Tetrahydroxanthone (-)-S1: Enanotiopure tetrahydroxanthone (+)-**29** (91 mg, 0.18 mmol) was dissolved in 2 mL of CH_2Cl_2 in a flame-dried flask. DMAP (2.2 mg, 0.018 mmol, 0.1 equiv), DIEA (70 mg, 94 µL, 0.54 mmol, 3 equiv) and MOMCl (43 mg, 41 µL, 0.54 mmol, 3 equiv) were added into the solution. The reaction was stirred at room temperature for 12 h. After concentrating *in vacuo*, the crude product was purified by silica gel chromatography (hexanes/EtOAc = 2: 1 to 1: 1) to afford product (-)-**S1** (80 mg, 81 %) as a colorless to pale yellow oil. (-)-**S1**: R_f = 0.42 (hexanes/EtOAc = 1: 2); IR (thin film): ν_{max} 2951, 1750, 1665, 1583, 1447, 1377, 1208, 1158, 1030, 926, 733 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.76 (d, *J* = 8.8 Hz, 1H), 6.55 (d, *J* = 8.8 Hz, 1H), 5.34 (d, *J* = 12.0 Hz, 1H), 5.30 (d, *J* = 6.5 Hz, 1H), 4.84 (d, *J* = 6.5 Hz, 1H), 3.88 (s, 3H), 3.62 (s, 3H), 3.59 (s, 3H), 2.80 (dd, *J* = 18.2, 5.4 Hz, 1H), 2.54 (m, 1H), 2.40 (q, *J* = 7.6 Hz, 2H), 2.32 (dd, *J* = 18.2, 10.8 Hz, 1H), 1.18 (t, *J* = 7.6 Hz, 3H), 1.00 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 177.0, 173.4, 169.5, 166.7, 161.0, 157.9, 144.2, 115.5, 114.9, 107.1, 101.9, 85.3, 83.5, 75.5, 58.5, 56.7, 53.0, 33.6, 28.6, 27.6, 16.9, 9.1; HRMS–ESI (m/z): $[M+Na]^+$ calcd for $C_{22}H_{25}O_9INa$, 583.0441; found, 583.0440; $[\alpha]_D^{27}$= -71.7 ° (*c*= 0.1, CH_2Cl_2).



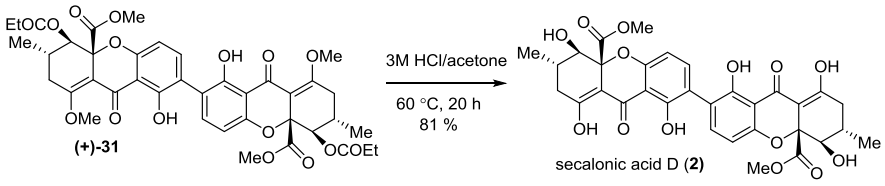
MOM-Protected Stannane (-)-30: MOM-protected tetrahydroxanthone **(-)-S1** (80 mg, 0.14 mmol), *n*Bu_4NI (26 mg, 0.07 mmol, 0.5 equiv), $Pd_2(dba)_3$ (13 mg, 0.014 mmol, 0.1 equiv), P*t*Bu_3 (11 mg, 0.056 mmol, 0.4 equiv) and bis(tributyltin) (162 mg, 141 µL, 0.28 mmol, 2.0 equiv) were added to a flame-dried flask. Under a N_2 atmosphere, 1.5 mL of anhydrous dioxane was added. The flask was warmed to 50 ^oC and stirred for 4 h. After cooling to room temperature, the solvent was removed in *vacuo*. The crude mixture was directly purified by silica gel chromatography (hexanes/EtOAc = 2: 1) to afford the MOM-protected stannane (-)-**30** (57 mg, 56 %) as a colorless oil. (-)-**30**: R_f = 0.48 (hexanes/EtOAc = 1: 1); IR (thin film): ν_{max} 2954, 1756, 1664, 1581, 1461, 1225, 1158, 1073 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37 (d, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 8.0 Hz,

1H), 5.36 (d, *J* = 12.0 Hz, 1H), 5.30 (d, *J* = 6.1 Hz, 1H), 4.71 (d, *J* = 6.1 Hz, 1H), 3.86 (s, 3H), 3.61 (s, 3H), 3.36 (s, 3H), 2.79 (dd, *J* = 18.1, 5.4 Hz, 1H), 2.54 (m, 1H), 2.40(1) (q, *J* = 7.6 Hz, 1H), 2.39(8) (q, *J* = 7.6 Hz, 1H), 2.32 (dd, *J* = 18.1, 11.8 Hz, 1H), 1.49 (m, 6H), 1.31 (m, 6H), 1.19 (dd, *J* = 7.6, 7.6 Hz, 3H), 1.06 (m, 6H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.85 (t, *J* = 7.3 Hz, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 178.4, 173.5, 169.9, 165,7, 163.3, 161.3, 143.4, 126.9, 113.8, 112.4, 108.2, 100.8, 84.9, 75.7, 58.0, 56.5, 52.8, 33.5, 29.1, 28.8, 27.7, 27.4, 17.0, 13.7, 10.0, 9.1; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{34}H_{53}O_9Sn$, 725.2719; found, 725.2726; $[\alpha]_D^{26}$= -59.9 ° (*c*= 0.1, CH_2Cl_2).



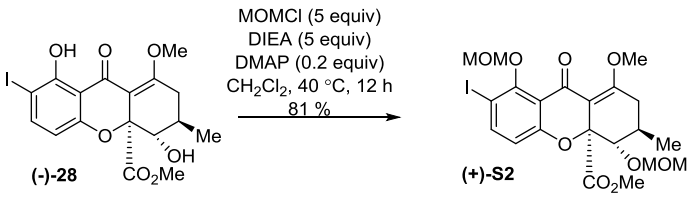
Ester Dimeric Tetrahydroxanthone (+)-31: MOM-protected stannane (-)-**30** (50 mg, 0.069 mmol), and freshly prepared CuCl (34 mg, 0.35 mmol, 5 equiv) were placed in an open tube (Note: if commercial CuCl was used, the reaction could proceed under a N_2 atmosphere in comparable yield). Next, 0.7 mL of DMA was added into the tube and the reaction mixture was stirred at room temperature for 12 h. (Note: the reaction turned from clear yellow to cloudy to completely dark). The mixture was quenched with 3 mL of saturated NH_4Cl solution and was extracted 5 times with 3 mL EtOAc. After concentrating at 40 ^oC *in vacuo*, the crude product was directly purified by preprative TLC (hexanes/EtOAc = 1: 2) to afford dimeric tetrahydroxanthone (+)-**31** (16 mg, 60 %) as a yellow solid (for X-ray data, see page S41). (Note: The C_2 and C_s dimers have similar ^{1}H NMR spectra, and were inseparable by silica gel chromatography. If the C_s compound was present, an additional phenol signal δ = 12.93 could be observed in the ^{1}H NMR spectrum). (+)-**31**: R_f = 0.31 (hexanes/EtOAc = 1: 2); melting point: >230 ^oC (CH_2Cl_2); IR (thin film): ν_{max} 2962, 1754, 1633, 1584, 1566, 1422, 1357, 1220, 1042, 816 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 12.90 (s, 2H), 7.40 (d, *J* = 8.5 Hz, 2H), 6.45 (d, *J* = 8.5 Hz, 2H), 5.37 (d, *J* = 12.0 Hz, 2H), 3.91 (s, 6H), 3.69 (s, 6H), 2.85 (dd, *J* = 18.3, 5.5 Hz, 2H), 2.61 (m, 2H), 2.42(1) (q, *J* = 7.6 Hz, 2H), 2.41(5) (q, *J* = 7.6 Hz, 2H), 2.36 (dd, *J* = 18.3, 10.8 Hz, 2H), 1.21 (dd, *J* = 7.6, 7.6 Hz, 6H), 1.03 (d, *J* = 6.5 Hz, 6H); ^{13}C NMR

($CDCl_3$, 100 MHz) : δ 185.2, 173.5, 169.7, 167.1, 160.1, 158.1, 139.7, 117.7, 108.0, 106.6, 106.2, 84.8, 75.8, 56.5, 53.1, 33.4, 28.5, 27.7, 17.1, 9.2; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{40}H_{43}O_{16}$, 779.2551; found, 779.2559; $[\alpha]_D^{25}$= 52.7 ° (*c*= 0.1, CH_2Cl_2).

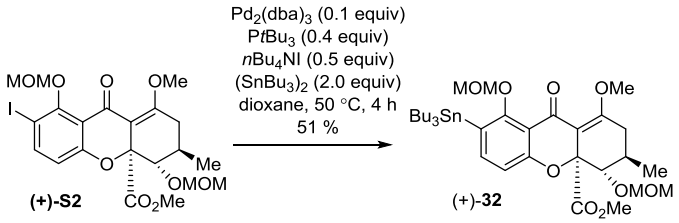


Secalonic Acid D (2): Dimeric tetrahydroxanthone (+)-**31** (7.0 mg, 0.0090 mmol) was dissolved in 4 mL of acetone and 2 mL of 3M HCl solution was added. The reaction was warmed to 60 ^oC and was stirred under argon for 20 h. After cooling down to room temperature, the solution was diluted with 5 mL of ethyl acetate and the organics were washed 1 x 5 mL water, followed by brine, dried over sodium sulfate, filtered, and concentrated *in vacuo* to afford a yellow residue which was purified by preparative HPLC (C_{18}, 10-75% CH_3CN/water). The fractions were extracted with EtOAc, washed with brine, dried over sodium sulfate, and concentrated to afford secalonic acid D **2** (4.6 mg, 81 %) as a pale yellow solid. **2**: melting point: >230 ^oC (CH_2Cl_2) (lit: 281-283 ^oC in evacuated capillary, 255-259 ^oC on hot stage[S4]; 253-255 ^oC[S5]); IR (thin film): ν_{max} 3464, 1726, 1610, 1585, 1566, 1436, 1233, 1067 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 13.78(s, 2H), 11.75(s, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 6.63 (d, *J* = 8.5 Hz, 2H), 3.93 (dd, *J* = 11.3, 1.6 Hz, 2H), 3.73 (s, 6H), 2.81 (d, *J* = 2.2 Hz, 2H), 2.74 (dd, *J* = 19.1, 6.2 Hz, 2H), 2.41 (m, 2H), 2.32 (dd, *J* = 19.1, 10.6 Hz, 2H), 1.17 (d, *J* = 6.4 Hz, 6H); ^1H NMR (D_6-DMSO, 500 MHz): δ 13.60(s, 2H), 11.66(s, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 6.62 (d, *J* = 8.5 Hz, 2H), 6.01 (d, *J* = 5.4 Hz, 2H), 3.81 (dd, *J* = 10.9, 5.6 Hz, 2H), 3.60 (s, 6H), 2.66 (dd, *J* = 19.2, 5.4 Hz, 2H), 2.47 (dd, *J* = 19.2, 10.8 Hz, 2H), 2.41 (m, 2H), 1.03 (d, *J* = 5.5 Hz, 6H);^{13}C NMR ($CDCl_3$, 125 MHz) : δ 187.2, 177.5, 170.3, 159.4, 158.3, 140.2, 118.2, 107.6, 106.9, 101.5, 84.7, 76.9(7), 53.3, 36.3, 29.2, 18.0; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{32}H_{31}O_{16}$, 639.1714; found, 639.1716; $[\alpha]_D^{26}$= 62.0 ° (*c*= 0.1, $CHCl_3$) (lit. $[\alpha]_D^{26}$= 64.0 ° (*c*= 0.14, $CHCl_3$)).

[S4] R. Andersen, G. Büchi, B. Kobbe, A. L. Demain *J. Org. Chem.* **1977**, *42*, 352-353.
[S5] P. S. Steyn, *Tetrahedron* **1970**, *26*, 51-57.

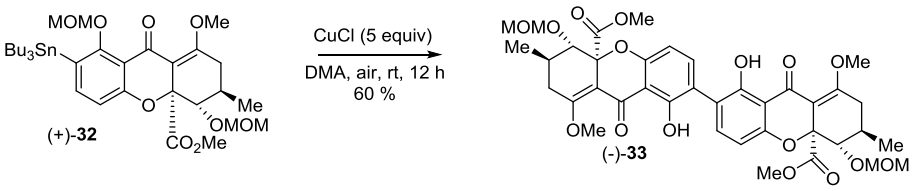


MOM-Protected Tetrahydroxanthone (+)-S2: Enanotiopure tetrahydroxanthone (-)-**28** (82 mg, 0.18 mmol) was dissolved in 2 mL of CH_2Cl_2 in a flame-dried flask. DMAP (2.2 mg, 0.018 mmol, 0.1 equiv), DIEA (116 mg, 157 µL, 0.90 mmol, 5 equiv) and MOMCl (72 mg, 68 µL, 0.90 mmol, 5 equiv) were added into the solution. The reaction was warmed to 40 ^{o}C and stirred for 12 h. After concentrating *in vacuo*, the crude product was purified by silica gel chromatography (hexanes/EtOAc = 2: 1 to 1: 1) to afford product (+)-**S1** (79 mg, 81 %) as a colorless to pale yellow oil. (+)-**S1**: R_f = 0.43 (hexanes/EtOAc = 1: 2); IR (thin film): ν_{max} 2953, 1751, 1663, 1582, 1446, 1377, 1215, 1153, 1027, 920, 816, 730 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.77 (d, *J* = 8.8 Hz, 1H), 6.57 (d, *J* = 8.8 Hz, 1H), 5.32 (d, *J* = 6.5 Hz, 1H), 5.20 (d, *J* = 6.7 Hz, 1H), 4.83 (d, *J* = 6.5 Hz, 1H), 4.70 (d, *J* = 6.7 Hz, 1H), 3.86 (d, *J* = 3.8 Hz, 1H), 3.84 (s, 3H), 3.61 (s, 3H), 3.58 (s, 3H), 3.46 (s, 3H), 2.74 (dd, *J* = 18.2, 5.2 Hz, 1H), 2.46 (m, 1H), 2.23 (dd, *J* = 18.2, 11.0 Hz, 1H), 1.14 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 177.3, 169.7, 166.8, 161.1, 158.0, 144.2, 115.6, 114.7, 107.2, 101.9, 97.3, 88.1, 83.4, 80.1, 58.5, 56.5(3), 56.4(6), 52.9, 33.7, 29.8, 17.9; HRMS–ESI (m/z): $[M+Na]^+$ calcd for $C_{21}H_{25}O_9INa$, 571.0441; found, 571.0432; $[\alpha]_D^{26}$= 108.9 ° (*c*= 0.1, CH_2Cl_2).



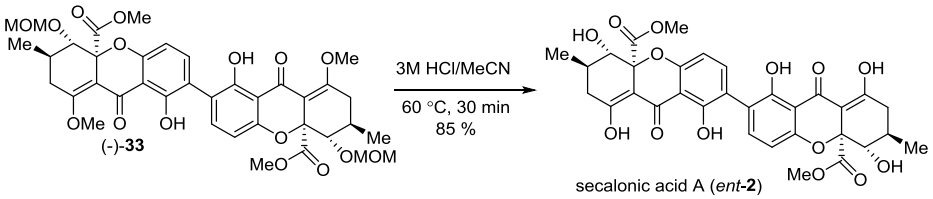
MOM-Protected Stannane (+)-32: MOM-protected tetrahydroxanthone (+)-**S2** (79 mg, 0.14 mmol), *n*Bu_4NI (26 mg, 0.07 mmol, 0.5 equiv), $Pd_2(dba)_3$ (13 mg, 0.014 mmol, 0.1 equiv), P*t*Bu_3 (11 mg, 0.056 mmol, 0.4 equiv) and bis(tributyltin) (162 mg, 141 µL, 0.28 mmol, 2.0 equiv) were added to a flame-dried flask. Under a N_2 atmosphere, 1.5 mL of anhydrous dioxane was added. The flask was warmed to 50 ^{o}C and stirred for 4 h. After cooling to room temperature, the solvent was removed in *vacuo*. The crude mixture was directly purified by silica gel chromatography (hexanes/EtOAc = 2: 1) to afford MOM-

protected stannane (+)-**31** (52 mg, 51 %) as a pale yellow oil. (+)-**32**: R_f = 0.43 (hexanes/EtOAc = 1: 1); IR (thin film): ν_{max} 2956, 1757, 1665, 1581, 1449, 1230, 1032, 962 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.38 (d, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 5.30 (d, *J* = 6.1 Hz, 1H), 5.25 (d, *J* = 6.7 Hz, 1H), 4.72(5) (d, *J* = 6.7 Hz, 1H), 4.71(7) (d, *J* = 6.1 Hz, 1H), 3.90 (d, *J* = 11.5 Hz, 1H), 3.84 (s, 3H), 3.61 (s, 3H), 3.48 (s, 3H), 3.36 (s, 3H), 2.74 (dd, *J* = 18.1, 5.2 Hz, 1H), 2.45 (m, 1H), 2.24 (dd, *J* = 18.1, 11.0 Hz, 1H), 1.49 (m, 6H), 1.31 (m, 6H), 1.15 (d, *J* = 6.5 Hz, 3H), 1.06 (m, 6H), 0.87 (t, *J* = 7.3 Hz, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 178.7, 170.2, 165.7, 163.4, 161.4, 143.3, 127.0, 113.9, 112.2, 108.5, 100.8, 97.4, 87.8, 80.3, 58.1, 56.5, 56.3, 52.7, 33.8, 29.9, 29.1, 27.4, 18.0, 13.7, 10.0; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{33}H_{53}O_9Sn$, 713.2719; found, 713.2737; $[\alpha]_D^{26}$= 66.8 ° (*c*= 0.1, CH_2Cl_2).



Dimeric Tetrahydroxanthone (-)-33: MOM-protected stannane (+)-**32** (50 mg, 0.071 mmol), and freshly prepared CuCl (34 mg, 0.35 mmol, 5 equiv) were placed in an open tube (Note: if commercial CuCl was used, the reaction could proceed under a N_2 atmosphere in comparable yield). Next, 0.7 mL of DMA was added into the tube and the reaction mixture was stirred at room temperature for 12 h. (Note: the reaction turned from clear yellow cloudy to completely dark). The mixture was quenched with 3 mL of a saturated NH_4Cl solution and was extracted 5 times with 3 mL EtOAc. After concentrating at 40 ^oC *in vacuo*, the crude product was directly purified by preparative TLC (hexane/EtOAc = 1: 2) to afford dimeric tetrahydroxanthone (-)-**33** (16 mg, 60 %) as a yellow solid. (Note: The C_2 and C_s dimers have similar ^1H NMR spectra and were inseparable by silica gel chromatography. If any C_s compound was present, an additional phenol signal δ = 12.95 could be observed). (-)-**33**: R_f = 0.33 (hexanes/EtOAc = 1: 2); melting point: >230 ^oC (CH_2Cl_2/MeOH); IR (thin film): ν_{max} 2953, 1753, 1632, 1586, 1566, 1426, 1354, 1220, 1034, 816 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 12.92 (s, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 6.50 (d, *J* = 8.5 Hz, 2H), 5.26 (d, *J* = 6.7 Hz, 2H), 4.76 (d, *J* =

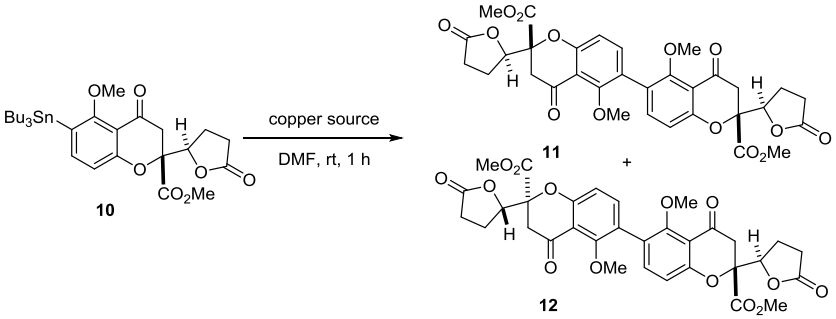
6.7 Hz, 2H), 3.90 (d, *J* = 12.8 Hz, 2H), 3.88 (s, 6H), 3.68 (s, 6H), 3.49 (s, 6H), 2.79 (dd, *J* = 18.2, 5.3 Hz, 2H), 2.53 (m, 2H), 2.26 (dd, *J* = 18.3, 11.1 Hz, 2H), 1.17 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) : δ 185.6, 169.9, 167.1, 160.2, 158.3, 139.6, 117.7, 108.2, 106.5, 106.4, 97.6, 87.7, 80.5, 56.6, 56.3, 53.0, 33.6, 29.7, 18.1; HRMS–ESI (m/z): $[M+H]^+$ calcd for $C_{38}H_{43}O_{16}$, 755.2551; found, 755.2563; $[\alpha]_D^{29}$= -56.5 ° (*c*= 0.1, CH_2Cl_2).



Secalonic Acid A (*ent*-2): Dimeric tetrahydroxanthone (-)-**33** (5.0 mg, 0.0066 mmol) was dissolved in 1.5 mL of acetonitrile and 1.5 mL of 3M HCl solution. The reaction was warmed to 60 ^{o}C and stirred for 30 min. After cooling to room temperature, the solution was directly purified by preparative HPLC (C_{18}, 10-75% CH_3CN in water). The fractions were extracted with EtOAc, washed with brine, dried over sodium sulfate, and concentrated *in vacuo* to afford secalonic acid A (*ent*-**2)** (3.6 mg, 85 %) as a pale yellow solid. ***ent-2*:** ^{1}H NMR, ^{13}C NMR, IR, and HRMS for ***ent-2*** were identical to data reported for 2. $[\alpha]_D^{26}$= -64.1 ° (*c*= 0.1, $CHCl_3$).

III. COPPER-MEDIATED STANNANE COUPLING SCREENING

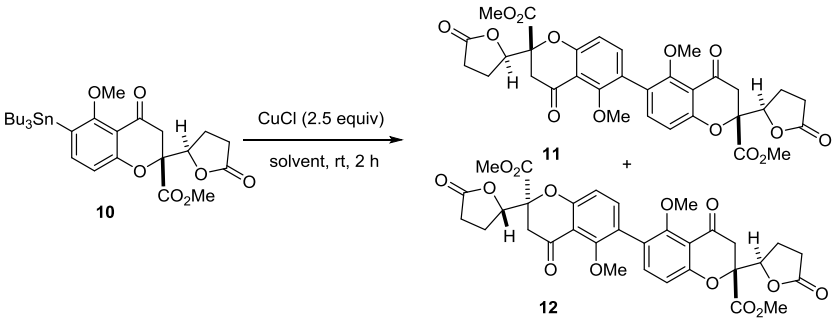
1. Screening of copper sources.



General procedure: Chromanone stannane **10** (10 mg, 0.016 mmol), and commercially available copper compounds (2.5 equiv) were placed under a N_2 atmosphere Next, 0.2 mL of DMF was added into the tube and the reaction mixture was stirred at room temperature for 1 h. The mixture was quenched with 3 mL of saturated NH_4Cl solution and was extracted 5 times with 5 mL of EtOAc After concentration, the reaction was monitored by ^1H NMR.

copper source	11+12	starting material	deiodination product
CuI	0	100	0
CuBr SMe_2	13	74	13
CuCl	38	24	42
CuTC	0	0	100
$Cu(MeCN)_6PF_6$	0	0	100
$CuCl_2$	0	100	0
$Cu(OAc)_2 \cdot H_2O$	0	0	100
$Cu(NO_3)_2 \cdot 3H_2O$	37	6	59

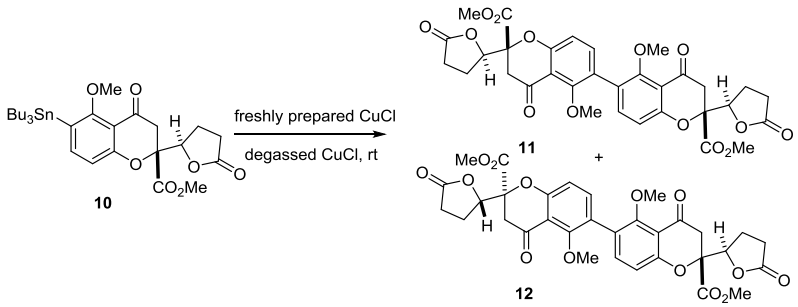
2. Solvent screening.



General procedure: Chromanone stannane **10** (10 mg, 0.016 mmol) and commercially available CuCl (2.5 equiv) were placed under a N_2 atmosphere Next, 0.2 mL of solvent was added into the tube and the reaction mixture was stirred at room temperature for 2 h. The mixture was quenched with 3 mL of saturated NH_4Cl solution and was extracted 5 times with 5 mL of EtOAc After concentrating the reaction was monitored by ^1H NMR.

copper source	11+12	starting material	deiodination product
Dioxane	0	85	15
Acetone	0	56	44
MeOH	0	0	100
MeCN	0	84	16
HMPU	0	0	100
NMP	47	0	53
$MeNO_2$	0	58	42
CCl_4	0	41	59
DMA	65	0	32
DME	0	76	34
DMSO	0	46	30

3. Oxidant Screening.

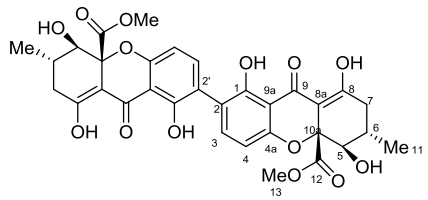


General procedure: Chromanone stannane **10** (100 mg, 0.016 mmol) and freshly prepared CuCl were placed under a N_2 atmosphere Next, 1.6 mL of degassed DMF was added into the tube and the reaction mixture was stirred at room temperature. The mixture was quenched with 3 mL of saturated NH_4Cl solution and was extracted 5 times with 5 mL of EtOAc After concentration, the reaction was monitored by ^1H NMR.

copper source	11+12	starting material	deiodination product
5 eq CuCl, 2 h	<5	0	>95
5 eq CuCl, 2 h, quench with air	31	9	60
5 eq CuCl and 1 eq $CuCl_2$, 2h	42	22	36
5 eq CuCl open air, 12 h	60	24	8
5 eq CuCl and 1 eq $CuCl_2$, 12 h	61	27	12
5 eq $Cu(NO_3)_2 \cdot 3(H_2O)$, 2 h	40	0	60

IV. NMR Data and UPLC Comparisons for Secalonic Acid D

A) ^{1}H NMR spectrum of synthetic secalonic acid D in comparison with literature data ($CDCl_3$, 7.26 ppm):



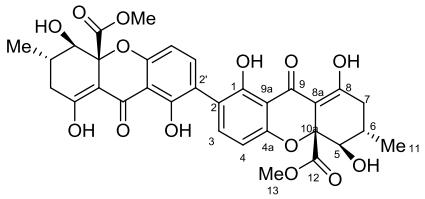
Position	δ ($J_{H\text{-}H}$ in Hz)		
	Natural Product (this work) (400 MHz, $CDCl_3$)[S6]	Natural Products (100 MHz, $CDCl_3$)[S7]	Synthetic (this work) (500 MHz, $CDCl_3$)
3/3'	7.46 (d, *J* = 8.5, 2H)	7.74 (d, *J* = 8, 2H)	7.46 (d, *J* = 8.5, 2H)
4/4'	6.63 (d, *J* = 8.5, 2H)	6.60 (d, *J* = 8, 2H)	6.63 (d, *J* = 8.5, 2H)
5/5'	3.93 (dd, *J* = 11.2, 1.9, 2H)	3.88 (br d, *J* = 11, 2H)	3.93 (dd, *J* = 11.3, 1.6, 2H)
6/6'	2.41 (m, 2H)	--	2.41 (m, 2H)
7α/7α'	2.32 (dd, *J* = 18.8, 10.6, 2H)	--	2.32 (dd, *J* = 19.1, 10.6, 2H)
7β/7β'	2.74 (dd, *J* = 18.8, 5.9, 2H)	2.74 (br d, 2H)	2.74 (dd, *J* = 19.1, 6.2, 2H)
11/11'	1.17 (d, *J* = 6.3, 6H)	1.16 (d, *J* = 6, 6H)	1.17 (d, *J* = 6.4, 6H)
13/13'	3.73 (s, 6H)	3.68 (s, 6H)	3.73 (s, 3H)
1-OH/1'-OH	11.76 (s, 2H)	11.70 (s, 2H)	11.75 (s, 2H)
5-OH/5'-OH*	2.81 (d, *J* = 2.2, 2H)	1.54 (br s, 2H)	2.81 (d, *J* = 2.2, 2H)
8-OH/8'-OH	13.78 (s, 2H)	13.78 (s, 2H)	13.78 (s, 2H)

*The chemical shift of the 5-OH peak was found to vary with concentration.

[S6] We thank Prof. Shu-Hua Qi (South China Sea Institute of Oceanology, CAS) for kindly providing a natural sample of secalonic acid D.

[S7] ^{1}H NMR data for secalonic acid A, see: C. C. Howard, R. A. W. Johnstone *J. Chem. Soc., Perkin I*, **1973**, 2440-2444.

B) ^{1}H NMR spectrum of synthetic secalonic acid D in comparison with literature data (D_6-DMSO, 2.50 ppm):

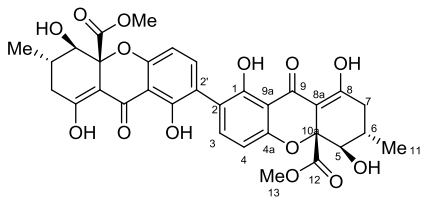


Position	δ (J_{H-H} in Hz)		
	Natural Product (this work) (400 MHz, D_6-DMSO)	Natural Product (600 MHz, D_6-DMSO)[S8]	Synthetic (this work) (500 MHz, D_6-DMSO)
3/3'	7.46 (d, *J* = 8.5, 2H)	7.45 (d, *J* = 8.42, 2H)	7.45 (d, *J* = 8.5, 2H)
4/4'	6.63 (d, *J* = 8.5, 2H)	6.63 (d, *J* = 8.42, 2H)	6.62 (d, *J* = 8.5, 2H)
5/5'	3.81 (dd, *J* = 11.1, 5.7, 2H)	3.81 (d, *J* = 9.51, 2H)	3.81 (dd, *J* = 10.9, 5.6, 2H)
6/6'	2.30 (m, 2H)	2.31 (m, 2H)	2.30 (m, 2H)
7α/7α'	2.48 (dd, *J* = 19.1, 10.9, 2H)	2.49 (dd, *J* = 19.80, 6.22, 2H)	2.47 (dd, *J* = 19.2, 10.8, 2H)
7β/7β'	2.66 (dd, *J* = 19.0, 6.0, 2H)	2.65 (dd, *J* = 19.80, 8.42, 2H)	2.66 (dd, *J* = 19.2, 5.4, 2H)
11/11'	1.03 (d, *J* = 6.5, 6H)	1.03 (d, *J* = 6.22, 6H)	1.03 (d, *J* = 5.5, 6H)
13/13'	3.61 (s, 6H)	3.61 (s, 6H)	3.60 (s, 3H)
1-OH/1'-OH	11.64 (s, 2H)	11.62 (s, 2H)	11.66 (s, 2H)
5-OH/5'-OH*	6.04 (d, *J* = 5.8, 2H)	--	6.01 (d, *J* = 5.4, 2H)
8-OH/8'-OH	13.60 (s, 2H)	13.60 (s, 2H)	13.60 (s, 2H)

*The chemical shift of the 5-OH peak was found to vary with concentration.

[S8] R. Hong, *Pharm. Bio.* **2011**, *49*, 796-799.

C) ^{13}C NMR spectrum of synthetic secalonic acid D in comparison with literature data:

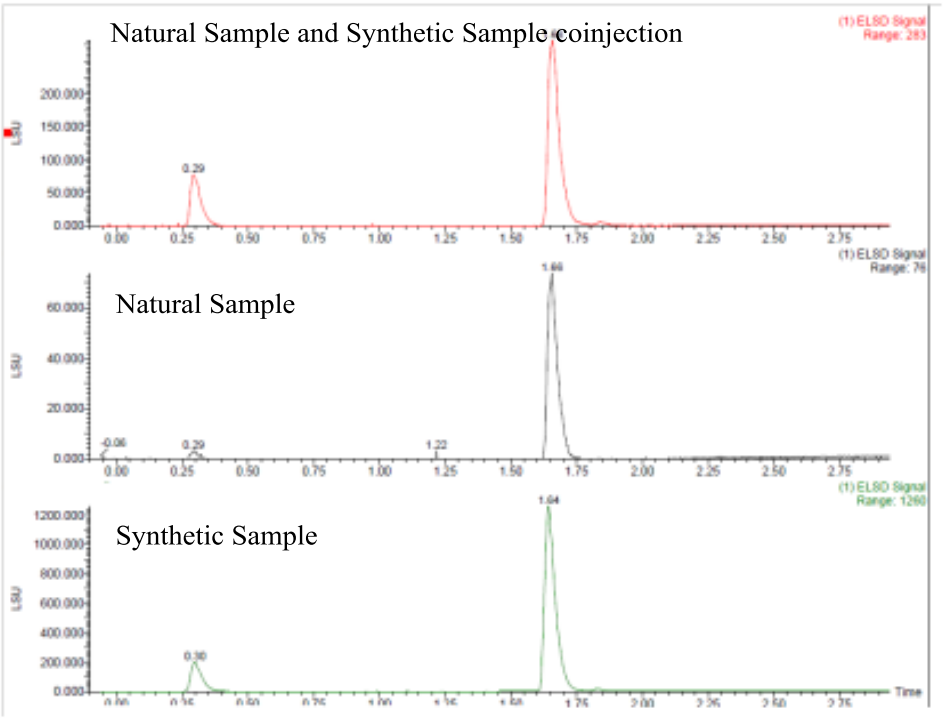


Position	δ		
	Natural Product (this work) (100 MHz, $CDCl_3$)	Synthetic (this work) (125 MHz, $CDCl_3$)	Natural Product (150 MHz, D_6-DMSO)[S8]
1	159.4	159.4	158.9
2	118.2	118.2	117.3
3	140.2	140.2	140.2
4	107.6	107.6	107.5
4a	158.3	158.3	158.5
5	--*	76.9(7)**	75.2
6	29.2	29.2	29.9
7	36.2	36.3	35.8
8	177.5	177.5	178.2
8a	101.5	101.5	101.7
9	187.1	187.2	186.6
9a	106.8	106.9	106.3
10a	84.7	84.7	85.2
11	18.0	18.0	17.8
12	170.3	170.3	170.0
13	53.3	53.3	52.6

*Due to limited amount, the signal was overlapped with the $CDCl_3$ peak.

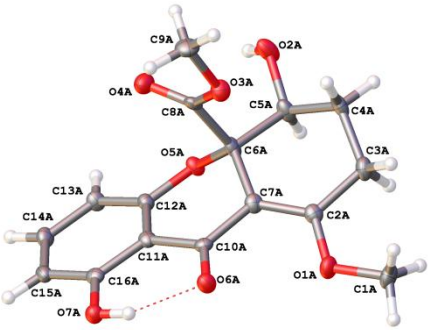
**This chemical shift was also verified by HMQC correlation (see page S70).

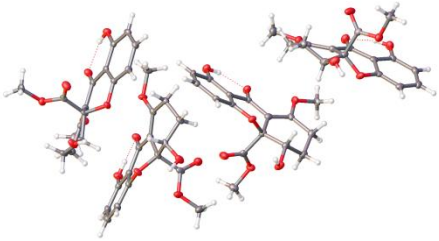
D) UPLC comparison between synthetic secalonic acid D and the natural sample:



V. X-ray Crystallographic Data

X-ray crystallographic data for compound **(-)-17**:[S9]





Crystals of compound **(-)-17** suitable for X-ray analysis were obtained by slow evaporation from $CHCl_3$/MeOH. Crystallographic data have been deposited with the Cambridge Cystallograhic Data Centre (CCDC# 961591). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Data collection: *APEX2* (Bruker, 2006); cell refinement: *SAINT* (Bruker, 2006); data reduction: *SAINT* (Bruker, 2006); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELX*, G.M. Sheldrick, Acta Cryst. (2008). A64, 112-122; molecular graphics: O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Cryst.* **2009**, *42*, 339-341.; software used to prepare material for publication: O. V. Dolomanov,

[S9] (a) Sheldrick, G. M. (1996). SADABS. University of Göttingen, Germany. (b) Sheldrick, G. M. (1997). SHELXL97. University of Göttingen, Germany. (c) Bruker (2006). SAINT. Bruker Analytical X-ray Instruments Inc., Madison, Wisconsin, USA. (d) Bruker (2006). APEX2. Bruker Analytical X-ray Instruments Inc., Madison, Wisconsin, USA. (e) O. V. Dolmanov, L. J. Bourhis, R. J. Cildea, J. A. K. Howard, H. Puschmann *J. Appl. Cryst.* **2009**, *42*, 339-341.

L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Cryst.* **2009**, *42*, 339-341.

Crystal data

$C_{16}H_{16}O_7$	$Z = 4$
$M_r = 320.29$	$F(000) = 672$
Triclinic, $P1$	$D_x = 1.432$ Mg m^{-3}
$a = 7.5282$ (2) Å	Cu $K\alpha$ radiation, $\lambda = 1.54178$ Å
$b = 13.8718$ (4) Å	Cell parameters from 9941 reflections
$c = 14.4637$ (4) Å	$\theta = 3.1–66.6°$
$\alpha = 95.790$ (1)°	$\mu = 0.96$ mm^{-1}
$\beta = 97.794$ (1)°	$T = 100$ K
$\gamma = 92.714$ (1)°	, colorless
$V = 1485.99$ (7) Å^3	0.14 × 0.04 × 0.03 mm

Data collection

Bruker Proteum-R diffractometer	9780 independent reflections
Radiation source: rotating anode	9524 reflections with $I > 2\sigma(I)$
multilayer	$R_{int} = 0.040$
ϕ & ω scans	$\theta_{max} = 66.6°$, $\theta_{min} = 3.1°$
Absorption correction: multi-scan *SADABS* (Sheldrick, 1997)	$h = -8 \varnothing 8$
$T_{min} = 0.684$, $T_{max} = 0.753$	$k = -16 \varnothing 15$
27726 measured reflections	$l = -17 \varnothing 17$

Refinement

Refinement on F^2	Hydrogen site location: mixed
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)] = 0.045$	$w = 1/[\sigma^2(F_o^2) + (0.0667P)^2 + 1.193P]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.130$	$(\Delta/\sigma)_{max} = 0.018$
$S = 1.12$	$\Delta\rangle_{max} = 0.24$ e Å^{-3}
9780 reflections	$\Delta\rangle_{min} = -0.28$ e Å^{-3}

847 parameters	Absolute structure: Flack x determined using 4416 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons and Flack (2004), Acta Cryst. A60, s61).
3 restraints	Flack parameter: 0.02 (14)

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Refinement. CheckCIF Alerts and Discussion:

PLAT089_ALERT_3_C Poor Data / Parameter Ratio (Zmax < 18) .. 6.19 PLAT340_ALERT_3_C Low Bond Precision on C-C Bonds .. 0.0064 Ang.

Discussion: The low data-to-parameter ratio is intrinsic for this sample in P1 with Z' = 4 and copper radiation. The resolution limit on this instrument is 0.84 Angstroms, and to that resolution there are not enough data to achieve a ratio of greater than 8 for 847 parameters. An attempt was made to use restraints via the SHELX SAME command to relate the two pairs of isostructural independent residues, however the imposition of these restraints led to a significantly poorer model as evidenced by the eleveated R1 value of over 9%.

The low data-to-parameter ratio also gives rise to the low C-C bond precision. Despite these limitations the resulting model is more than adequate to satisfy the goals of this crystallographic experiment.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}	
C1B	0.9772 (6)	0.2553 (4)	0.7593 (3)	0.0218 (10)	
H1BA	0.8794	0.2169	0.7181	0.033*	

H1BB	1.0857	0.2188	0.7636	0.033*	
H1BC	1.0010	0.3165	0.7335	0.033*	
C2B	0.7678 (6)	0.3113 (3)	0.8617 (3)	0.0157 (9)	
C3B	0.6278 (6)	0.3108 (4)	0.7771 (3)	0.0182 (9)	
H3BA	0.5813	0.2431	0.7557	0.022*	
H3BB	0.6835	0.3364	0.7257	0.022*	
C4B	0.4721 (6)	0.3719 (4)	0.7983 (3)	0.0197 (10)	
H4BA	0.5120	0.4416	0.8048	0.024*	
H4BB	0.3728	0.3600	0.7453	0.024*	
C5B	0.4048 (6)	0.3474 (3)	0.8878 (3)	0.0167 (9)	
H5B	0.3664	0.2768	0.8814	0.020*	
C6B	0.5546 (6)	0.3704 (3)	0.9723 (3)	0.0162 (9)	
C7B	0.7375 (6)	0.3415 (3)	0.9508 (3)	0.0162 (9)	
C8B	0.5569 (6)	0.4811 (4)	1.0028 (3)	0.0192 (10)	
C9B	0.4424 (8)	0.6018 (4)	1.0986 (4)	0.0307 (12)	
H9BA	0.5604	0.6364	1.1172	0.046*	
H9BB	0.3722	0.6093	1.1509	0.046*	
H9BC	0.3790	0.6288	1.0443	0.046*	
C10B	0.8728 (6)	0.3447 (3)	1.0328 (3)	0.0155 (9)	
C11B	0.8044 (6)	0.3439 (3)	1.1235 (3)	0.0175 (9)	
C12B	0.6199 (6)	0.3287 (3)	1.1266 (3)	0.0160 (9)	
C13B	0.5537 (6)	0.3179 (3)	1.2105 (3)	0.0183 (9)	
H13B	0.4288	0.3054	1.2115	0.022*	
C14B	0.6745 (6)	0.3259 (4)	1.2926 (3)	0.0200 (10)	
H14B	0.6301	0.3203	1.3504	0.024*	
C15B	0.8589 (6)	0.3420 (3)	1.2934 (3)	0.0183 (9)	
H15B	0.9387	0.3472	1.3507	0.022*	
C16B	0.9238 (6)	0.3503 (3)	1.2089 (3)	0.0163 (9)	
O1B	0.9261 (4)	0.2756 (3)	0.8518 (2)	0.0204 (7)	
O2B	0.2550 (4)	0.4026 (3)	0.8990 (2)	0.0223 (7)	
H2B	0.1887	0.3748	0.9317	0.033*	
O3B	0.4652 (4)	0.5004 (3)	1.0744 (2)	0.0249 (8)	
O4B	0.6286 (5)	0.5409 (3)	0.9633 (2)	0.0255 (8)	
O5B	0.4994 (4)	0.3179 (3)	1.0458 (2)	0.0192 (7)	
O6B	1.0385 (4)	0.3465 (3)	1.0312 (2)	0.0205 (7)	
O7B	1.1034 (4)	0.3628 (3)	1.2094 (2)	0.0211 (7)	
H7B	1.1254	0.3642	1.1541	0.032*	

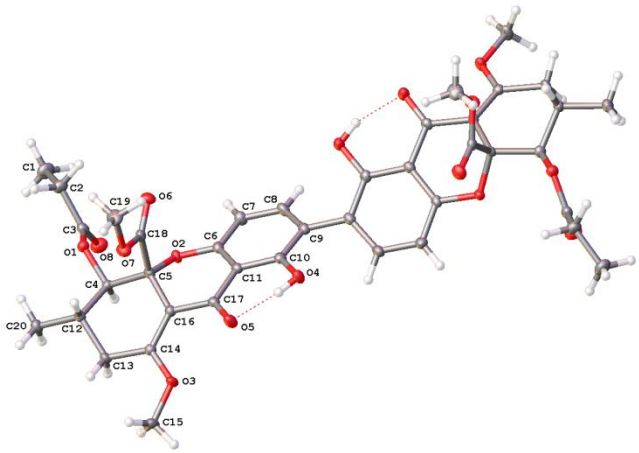
O2C	-0.3640 (4)	0.6661 (3)	0.6765 (2)	0.0233 (7)	
H2C	-0.444 (9)	0.626 (5)	0.641 (5)	0.035*	
C1C	0.3724 (6)	0.8163 (3)	0.5485 (3)	0.0197 (9)	
H1CA	0.2858	0.8521	0.5105	0.029*	
H1CB	0.4826	0.8120	0.5196	0.029*	
H1CC	0.4005	0.8504	0.6119	0.029*	
C2C	0.1400 (6)	0.7086 (3)	0.5868 (3)	0.0157 (9)	
C3C	0.0290 (6)	0.7942 (4)	0.6004 (3)	0.0200 (10)	
H3CA	-0.0229	0.8117	0.5382	0.024*	
H3CB	0.1078	0.8502	0.6326	0.024*	
C4C	-0.1221 (6)	0.7758 (4)	0.6572 (3)	0.0216 (10)	
H4CA	-0.2072	0.8278	0.6512	0.026*	
H4CB	-0.0720	0.7774	0.7243	0.026*	
C5C	-0.2221 (6)	0.6775 (3)	0.6236 (3)	0.0182 (9)	
H5C	-0.2739	0.6773	0.5562	0.022*	
C6C	-0.0954 (6)	0.5942 (3)	0.6319 (3)	0.0170 (9)	
C7C	0.0851 (6)	0.6164 (4)	0.6006 (3)	0.0170 (9)	
C8C	-0.0764 (5)	0.5645 (4)	0.7327 (3)	0.0173 (9)	
C9C	0.0270 (7)	0.6102 (4)	0.8918 (3)	0.0251 (11)	
H9CA	-0.0923	0.5912	0.9063	0.038*	
H9CB	0.0770	0.6678	0.9337	0.038*	
H9CC	0.1062	0.5568	0.9005	0.038*	
C10C	0.1897 (6)	0.5325 (3)	0.5845 (3)	0.0147 (9)	
C11C	0.0899 (6)	0.4379 (4)	0.5674 (3)	0.0167 (9)	
C12C	-0.0994 (6)	0.4316 (3)	0.5601 (3)	0.0156 (9)	
C13C	-0.1983 (6)	0.3429 (3)	0.5370 (3)	0.0156 (9)	
H13C	-0.3257	0.3395	0.5319	0.019*	
C14C	-0.1067 (6)	0.2597 (4)	0.5218 (3)	0.0189 (9)	
H14C	-0.1732	0.1989	0.5061	0.023*	
C15C	0.0789 (6)	0.2623 (3)	0.5287 (3)	0.0169 (9)	
H15C	0.1383	0.2040	0.5189	0.020*	
C16C	0.1773 (6)	0.3508 (4)	0.5502 (3)	0.0170 (9)	
O1C	0.2967 (4)	0.7206 (2)	0.5535 (2)	0.0190 (7)	
O3C	0.0123 (4)	0.6323 (2)	0.7945 (2)	0.0206 (7)	
O4C	-0.1364 (4)	0.4872 (3)	0.7514 (2)	0.0249 (8)	
O5C	-0.1919 (4)	0.5129 (2)	0.5718 (2)	0.0167 (6)	
O6C	0.3555 (4)	0.5370 (2)	0.5822 (2)	0.0198 (7)	

O7C	0.3582 (4)	0.3528 (3)	0.5536 (2)	0.0207 (7)	
H7C	0.4004	0.4106	0.5622	0.031*	
C1D	0.5586 (7)	0.5644 (4)	0.3786 (4)	0.0278 (11)	
H1DA	0.4976	0.5343	0.4251	0.042*	
H1DB	0.6884	0.5704	0.3997	0.042*	
H1DC	0.5340	0.5238	0.3182	0.042*	
C2D	0.3212 (6)	0.6686 (4)	0.3362 (3)	0.0198 (10)	
C3D	0.1922 (6)	0.5822 (4)	0.3309 (3)	0.0224 (10)	
H3DA	0.1770	0.5688	0.3954	0.027*	
H3DB	0.2438	0.5250	0.3004	0.027*	
C4D	0.0090 (7)	0.5955 (4)	0.2768 (4)	0.0243 (10)	
H4DA	0.0163	0.5871	0.2086	0.029*	
H4DB	-0.0785	0.5450	0.2900	0.029*	
C5D	-0.0559 (6)	0.6944 (4)	0.3029 (3)	0.0221 (10)	
H5D	-0.0646	0.7023	0.3716	0.027*	
C6D	0.0758 (6)	0.7755 (4)	0.2811 (3)	0.0191 (10)	
C7D	0.2707 (6)	0.7576 (3)	0.3138 (3)	0.0167 (9)	
C8D	0.0459 (6)	0.7794 (3)	0.1735 (3)	0.0176 (9)	
C9D	-0.1176 (7)	0.8383 (4)	0.0447 (3)	0.0275 (11)	
H9DA	-0.0132	0.8583	0.0159	0.041*	
H9DB	-0.2148	0.8812	0.0298	0.041*	
H9DC	-0.1581	0.7713	0.0203	0.041*	
C10D	0.3943 (6)	0.8413 (4)	0.3160 (3)	0.0186 (10)	
C11D	0.3151 (6)	0.9357 (4)	0.3128 (3)	0.0183 (9)	
C12D	0.1326 (6)	0.9451 (4)	0.3226 (3)	0.0180 (9)	
C13D	0.0585 (6)	1.0337 (4)	0.3289 (3)	0.0210 (10)	
H13D	-0.0639	1.0386	0.3372	0.025*	
C14D	0.1675 (6)	1.1165 (4)	0.3229 (3)	0.0202 (10)	
H14D	0.1173	1.1781	0.3261	0.024*	
C15D	0.3472 (6)	1.1109 (4)	0.3123 (3)	0.0210 (10)	
H15D	0.4184	1.1682	0.3077	0.025*	
C16D	0.4227 (6)	1.0216 (4)	0.3085 (3)	0.0183 (9)	
O1D	0.4937 (4)	0.6596 (2)	0.3678 (2)	0.0218 (7)	
O2D	-0.2272 (4)	0.6985 (3)	0.2527 (3)	0.0263 (8)	
H2D	-0.2835	0.7406	0.2806	0.039*	
O3D	-0.0680 (4)	0.8445 (3)	0.1462 (2)	0.0218 (7)	
O4D	0.1140 (5)	0.7242 (3)	0.1216 (2)	0.0312 (9)	

O5D	0.0242 (4)	0.8640 (2)	0.3285 (2)	0.0186 (7)	
O6D	0.5610 (4)	0.8378 (3)	0.3219 (2)	0.0236 (7)	
O7D	0.5989 (4)	1.0178 (3)	0.3022 (2)	0.0231 (7)	
H7D	0.6301	0.9611	0.3079	0.035*	
C1A	1.0019 (6)	0.1167 (4)	1.0952 (3)	0.0237 (10)	
H1AA	0.9355	0.1555	1.1378	0.036*	
H1AB	1.1176	0.1509	1.0922	0.036*	
H1AC	1.0225	0.0536	1.1185	0.036*	
C2A	0.7284 (6)	0.0669 (3)	0.9911 (3)	0.0172 (9)	
C3A	0.6326 (6)	0.0642 (4)	1.0758 (3)	0.0222 (10)	
H3AA	0.6136	0.1315	1.1007	0.027*	
H3AB	0.7099	0.0352	1.1253	0.027*	
C4A	0.4521 (6)	0.0066 (4)	1.0549 (3)	0.0214 (10)	
H4AA	0.4720	-0.0636	1.0506	0.026*	
H4AB	0.3821	0.0219	1.1071	0.026*	
C5A	0.3451 (6)	0.0296 (4)	0.9637 (3)	0.0216 (10)	
H5A	0.3206	0.1000	0.9694	0.026*	
C6A	0.4488 (6)	0.0074 (4)	0.8799 (3)	0.0180 (9)	
C7A	0.6471 (6)	0.0379 (3)	0.9023 (3)	0.0174 (9)	
C8A	0.4138 (5)	-0.1009 (3)	0.8431 (3)	0.0157 (9)	
C9A	0.4802 (7)	-0.2607 (4)	0.8718 (4)	0.0248 (10)	
H9AA	0.3512	-0.2791	0.8597	0.037*	
H9AB	0.5370	-0.2956	0.9224	0.037*	
H9AC	0.5339	-0.2774	0.8147	0.037*	
C10A	0.7401 (6)	0.0348 (3)	0.8194 (3)	0.0147 (9)	
C11A	0.6257 (6)	0.0370 (3)	0.7293 (3)	0.0156 (9)	
C12A	0.4421 (6)	0.0547 (3)	0.7265 (3)	0.0153 (9)	
C13A	0.3354 (6)	0.0679 (3)	0.6437 (3)	0.0179 (9)	
H13A	0.2126	0.0812	0.6432	0.022*	
C14A	0.4125 (6)	0.0613 (4)	0.5611 (3)	0.0193 (9)	
H14A	0.3402	0.0700	0.5038	0.023*	
C15A	0.5915 (6)	0.0424 (3)	0.5599 (3)	0.0178 (9)	
H15A	0.6399	0.0367	0.5024	0.021*	
C16A	0.6993 (6)	0.0319 (3)	0.6438 (3)	0.0158 (9)	
O1A	0.8990 (4)	0.1021 (3)	1.0028 (2)	0.0226 (7)	
O2A	0.1803 (4)	-0.0261 (3)	0.9514 (2)	0.0256 (8)	
H2A	0.1042	-0.0008	0.9149	0.038*	

O3A	0.5076 (4)	-0.1560 (2)	0.8994 (2)	0.0211 (7)	
O4A	0.3150 (4)	-0.1314 (3)	0.7729 (2)	0.0252 (7)	
O5A	0.3645 (4)	0.0612 (2)	0.8071 (2)	0.0172 (7)	
O6A	0.9060 (4)	0.0298 (2)	0.8217 (2)	0.0201 (7)	
O7A	0.8753 (4)	0.0177 (2)	0.6421 (2)	0.0188 (7)	
H7A	0.9274	0.0173	0.6973	0.028*	

X-ray crystallographic data for compound (+)-**31:**[S9]



Crystals of compound (+)-**31** suitable for X-ray analysis were obtained by slow evaporation from CH_2Cl_2/MeOH. Crystallographic data have been deposited with the Cambridge Cystallograhic Data Centre (CCDC# 961592). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Data collection: *APEX2* (Bruker, 2006); cell refinement: *SAINT* (Bruker, 2006); data reduction: *SAINT* (Bruker, 2006); program(s) used to refine structure: *SHELX*, G.M. Sheldrick, Acta Cryst. (2008). A64, 112-122; molecular graphics: O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Cryst.* **2009**, *42*, 339-341.; software used to prepare material for publication: O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Cryst.* **2009**, *42*, 339-341.

Crystal data

$C_{40}H_{42}O_{16}$	$F(000)$ = 820

M_r = 778.73	D_x = 1.415 Mg m^{-3}
Monoclinic, *C*2	Cu *K*α radiation, λ = 1.54178 Å
Hall symbol: C 2y	Cell parameters from 9067 reflections
a = 14.7105 (5) Å	θ = 5.4–66.5°
b = 7.6108 (3) Å	μ = 0.93 mm^{-1}
c = 16.3778 (5) Å	*T* = 100 K
β = 94.668 (1)°	Block, yellow
V = 1827.55 (11) Å^3	0.12 × 0.09 × 0.08 mm
Z = 2	

Data collection

Bruker Proteum-R diffractometer	3173 independent reflections
Radiation source: rotating anode	3166 reflections with $I > 2\sigma(I)$
multilayer	R_{int} = 0.034
ω & ϕ scans	θ_{max} = 66.6°, θ_{min} = 2.7°
Absorption correction: multi-scan *SADABS* (Sheldrick, 1997)	*h* = -17→17
T_{min} = 0.717, T_{max} = 0.753	*k* = -8→9
46030 measured reflections	*l* = -19→19

Refinement

Refinement on F^2	Secondary atom site location: inferred from neighbouring sites
Least-squares matrix: full	Hydrogen site location: mixed
$R[F^2 > 2\sigma(F^2)]$ = 0.025	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2)$ = 0.085	$w = 1/[\sigma^2(F_o^2) + (0.0553P)^2 + 0.3657P]$ where $P = (F_o^2 + 2F_c^2)/3$
S = 1.25	$(\Delta/\sigma)_{max}$ = 0.002
3173 reflections	$\Delta\rangle_{max}$ = 0.28 e Å^{-3}
260 parameters	$\Delta\rangle_{min}$ = -0.33 e Å^{-3}
1 restraint	Absolute structure: Flack x determined using 1426 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons and Flack (2004), Acta Cryst. A60, s61).
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.03 (3)

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Refinement. CheckCIF Alert and Discussion:

PLAT089_ALERT_3_C Poor Data / Parameter Ratio (Zmax < 18) .. 6.73

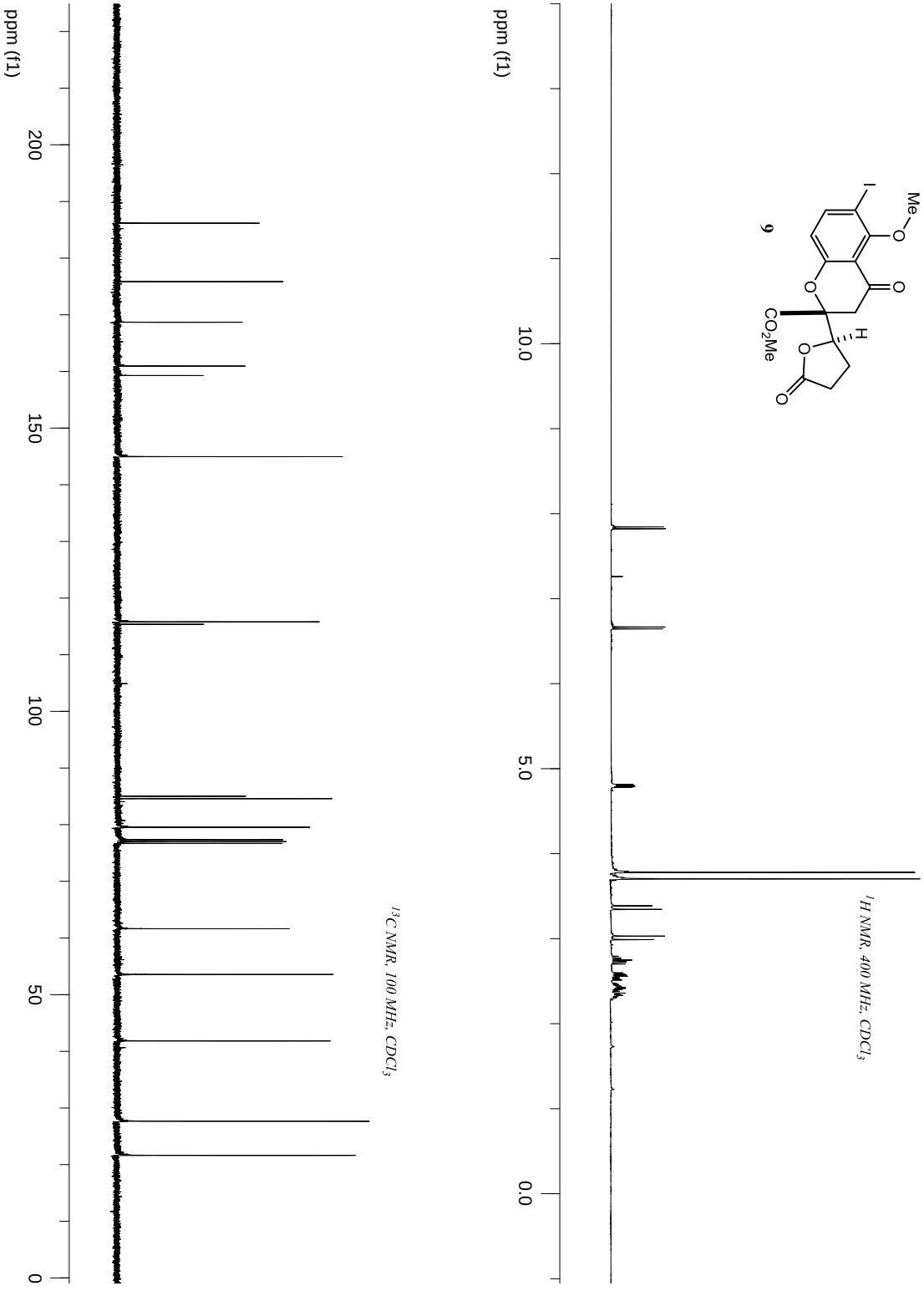
Discussion:

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}	
O1	0.24591 (8)	0.3284 (2)	0.10722 (7)	0.0157 (3)	
O2	0.17302 (8)	0.47131 (19)	0.25419 (8)	0.0149 (3)	
O3	0.45263 (8)	0.4489 (2)	0.40019 (8)	0.0184 (3)	
O4	0.15792 (9)	0.3418 (2)	0.54045 (8)	0.0194 (3)	
O5	0.30708 (9)	0.3181 (2)	0.47298 (8)	0.0208 (3)	
O6	0.13743 (9)	0.1296 (2)	0.22556 (9)	0.0219 (3)	
O7	0.28237 (9)	0.0523 (2)	0.26256 (9)	0.0203 (3)	
O8	0.18022 (10)	0.5851 (2)	0.06538 (9)	0.0253 (4)	
C1	0.09083 (17)	0.4160 (3)	-0.07583 (13)	0.0282 (5)	
H1A	0.1379	0.4774	-0.1038	0.042*	
H1B	0.0480	0.5019	-0.0563	0.042*	
H1C	0.0580	0.3346	-0.1141	0.042*	
C2	0.13537 (14)	0.3136 (3)	-0.00324 (12)	0.0214 (5)	
H2A	0.0875	0.2500	0.0240	0.026*	
H2B	0.1774	0.2251	-0.0236	0.026*	
C3	0.18762 (13)	0.4287 (3)	0.05864 (12)	0.0171 (4)	
C4	0.29700 (13)	0.4106 (3)	0.17597 (11)	0.0145 (4)	

H4A	0.2944	0.5411	0.1692	0.017*	
C5	0.25174 (12)	0.3587 (3)	0.25375 (11)	0.0140 (4)	
C6	0.12662 (13)	0.4611 (3)	0.32366 (11)	0.0144 (4)	
C7	0.03663 (13)	0.5134 (3)	0.31714 (12)	0.0181 (4)	
H7	0.0079	0.5503	0.2659	0.022*	
C8	-0.01161 (13)	0.5112 (3)	0.38706 (12)	0.0183 (4)	
H8	-0.0733	0.5496	0.3825	0.022*	
C9	0.02670 (12)	0.4550 (3)	0.46333 (11)	0.0162 (4)	
C10	0.11853 (13)	0.4002 (3)	0.46859 (12)	0.0154 (4)	
C11	0.16966 (13)	0.4044 (3)	0.39897 (12)	0.0146 (4)	
C12	0.39583 (12)	0.3500 (3)	0.17799 (11)	0.0149 (4)	
H12	0.3975	0.2200	0.1870	0.018*	
C13	0.44894 (12)	0.4384 (3)	0.25071 (11)	0.0155 (4)	
H13A	0.5107	0.3860	0.2581	0.019*	
H13B	0.4561	0.5647	0.2383	0.019*	
C14	0.40392 (13)	0.4210 (3)	0.32927 (11)	0.0137 (4)	
C15	0.54787 (12)	0.4936 (3)	0.40078 (12)	0.0215 (5)	
H15A	0.5711	0.5272	0.4564	0.032*	
H15B	0.5552	0.5921	0.3634	0.032*	
H15C	0.5820	0.3919	0.3830	0.032*	
C16	0.31381 (13)	0.3827 (3)	0.33106 (11)	0.0141 (4)	
C17	0.26768 (13)	0.3640 (3)	0.40634 (11)	0.0145 (4)	
C18	0.21525 (12)	0.1679 (3)	0.24524 (11)	0.0148 (4)	
C19	0.25591 (17)	-0.1312 (3)	0.25702 (15)	0.0261 (5)	
H19A	0.3089	-0.2052	0.2730	0.039*	
H19B	0.2331	-0.1586	0.2006	0.039*	
H19C	0.2078	-0.1537	0.2937	0.039*	
C20	0.43957 (14)	0.3899 (3)	0.09859 (12)	0.0197 (5)	
H20A	0.5017	0.3424	0.1020	0.030*	
H20B	0.4417	0.5173	0.0904	0.030*	
H20C	0.4034	0.3355	0.0524	0.030*	
H4	0.209 (2)	0.318 (4)	0.5288 (17)	0.030*	

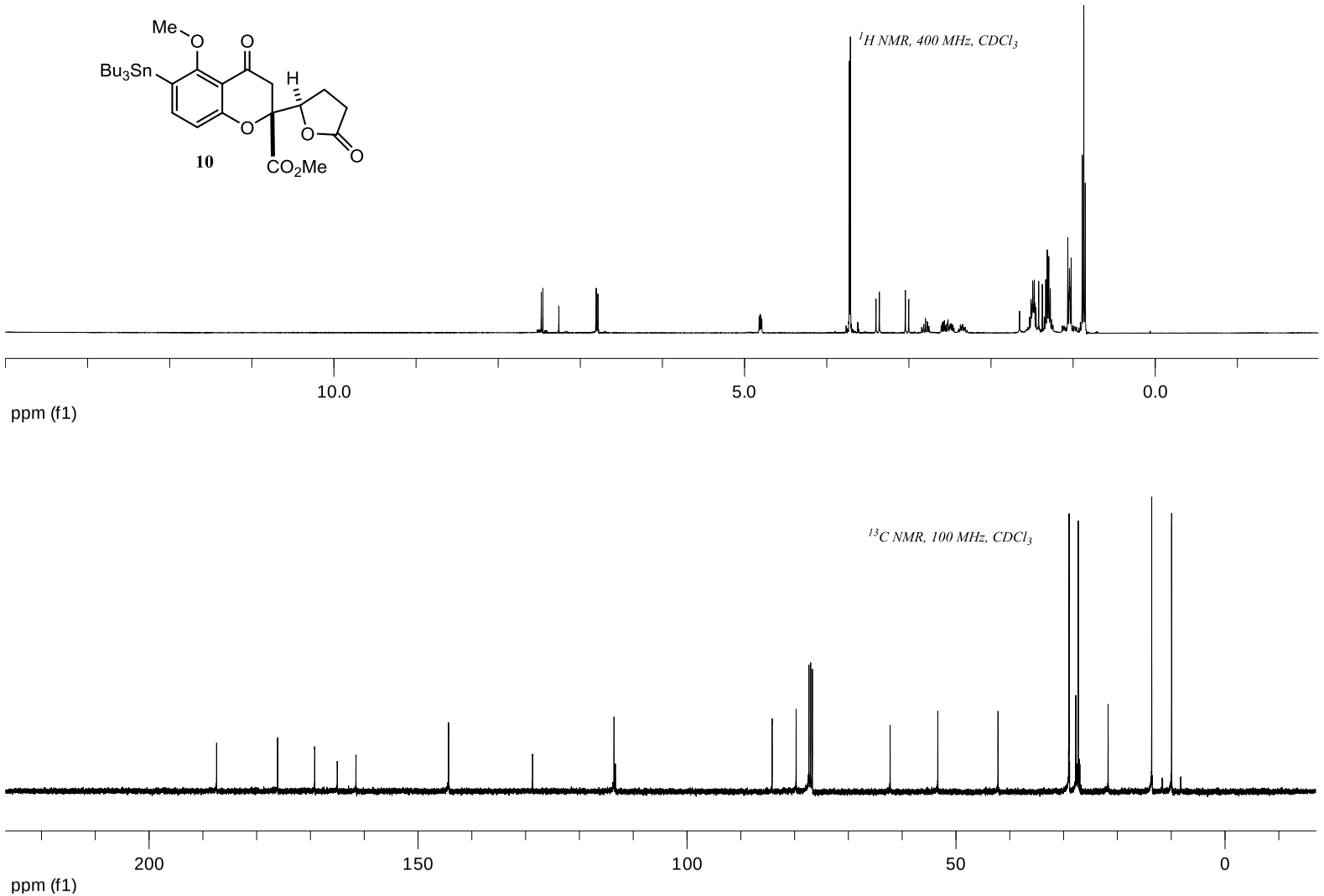
VI. Select NMR Spectra

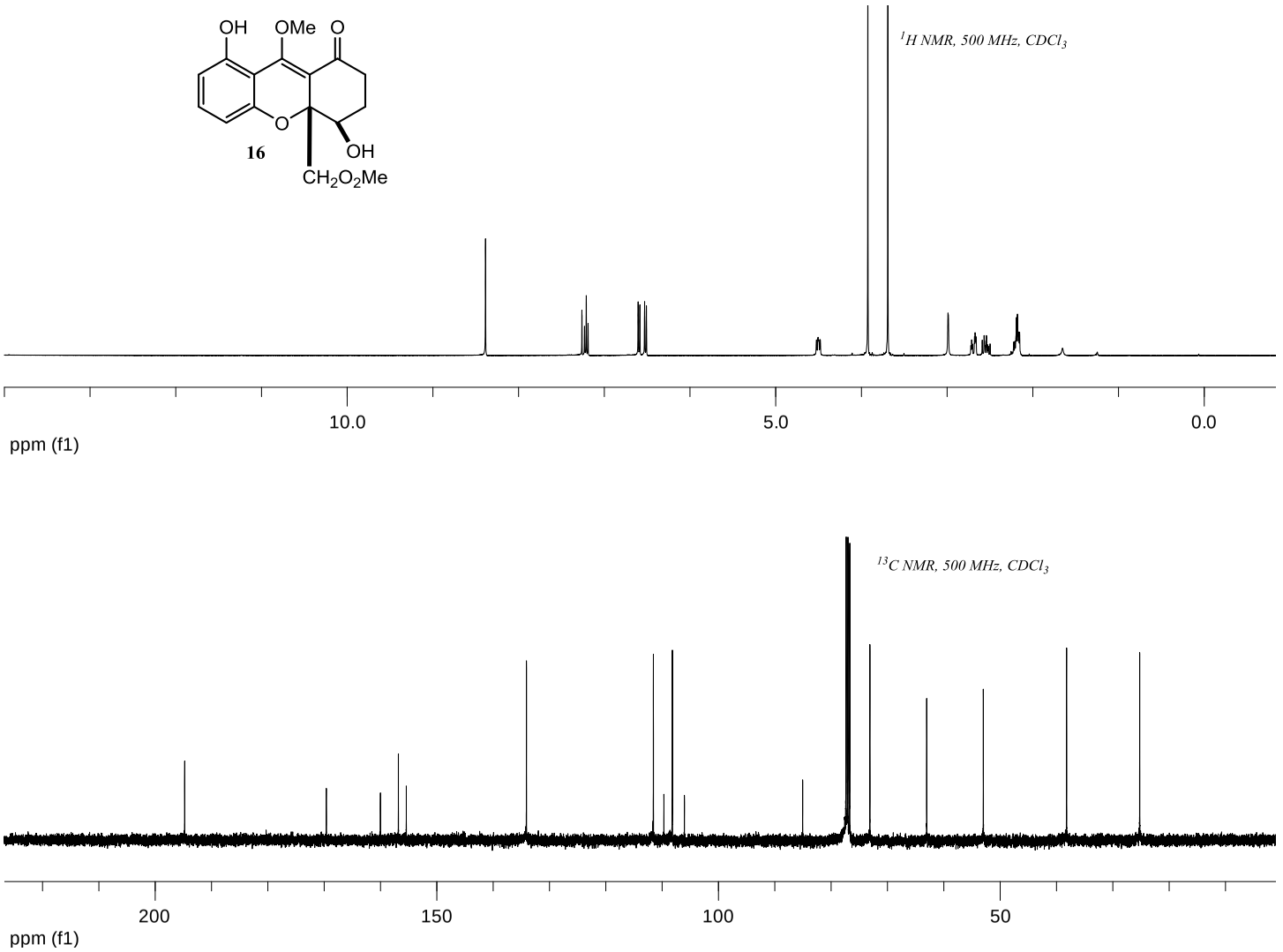


9

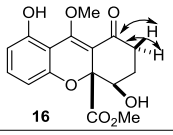
^{1}H NMR, 400 MHz, $CDCl_3$

^{13}C NMR, 100 MHz, $CDCl_3$

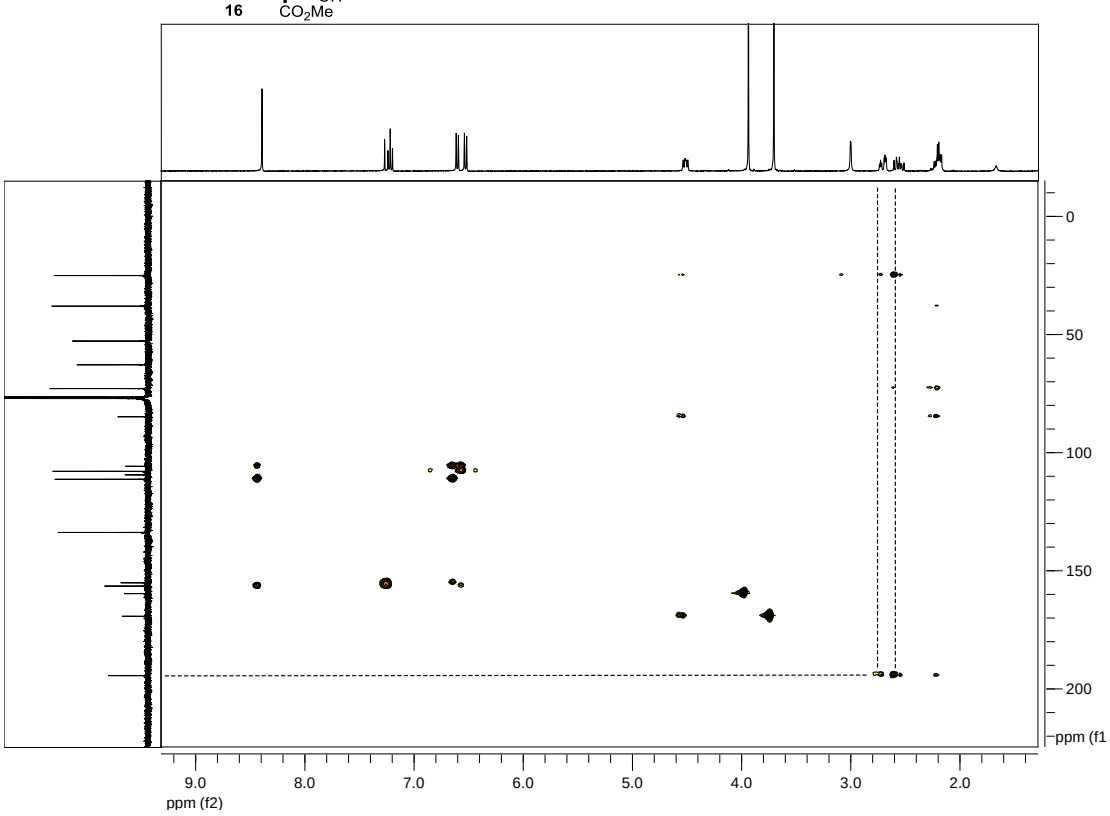

Me
O
O
Bu3Sn
H
O
O
O
O
CO2Me
10
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)

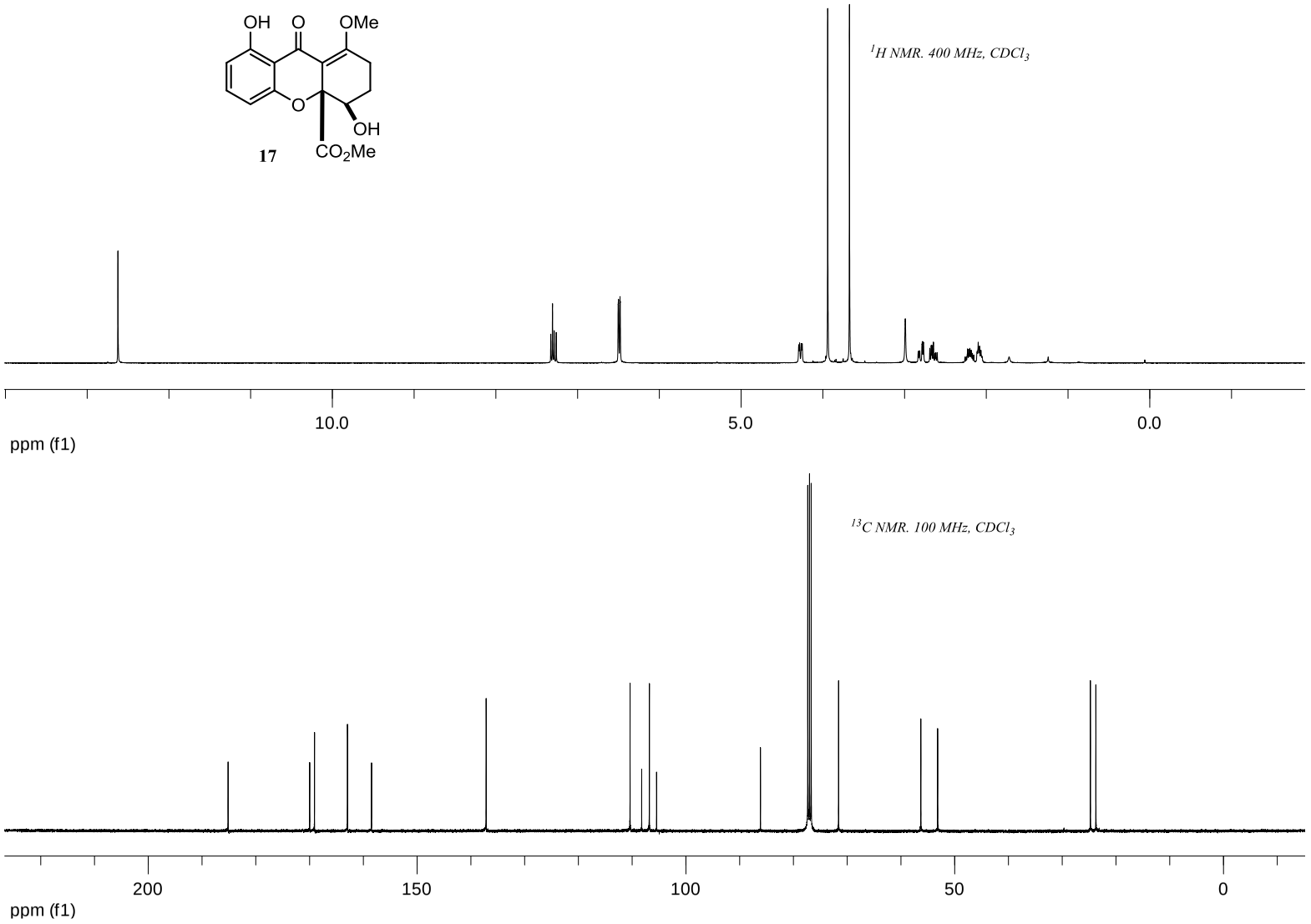

OH
OMe
O
O
16
OH
CH2O2Me
1H NMR, 500 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 500 MHz, CDCl3
200
150
100
50
ppm (f1)

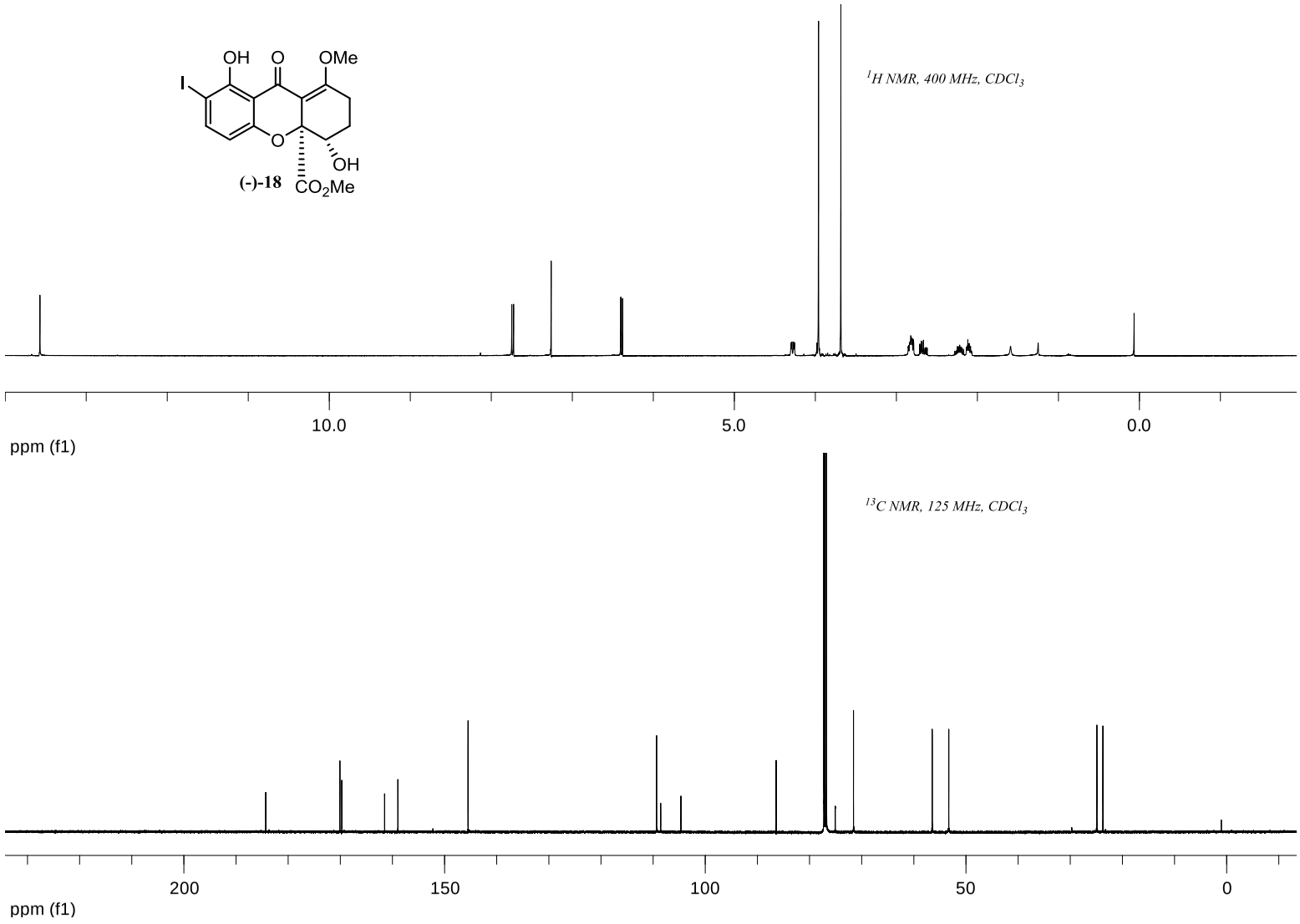
Observed Key HMBC

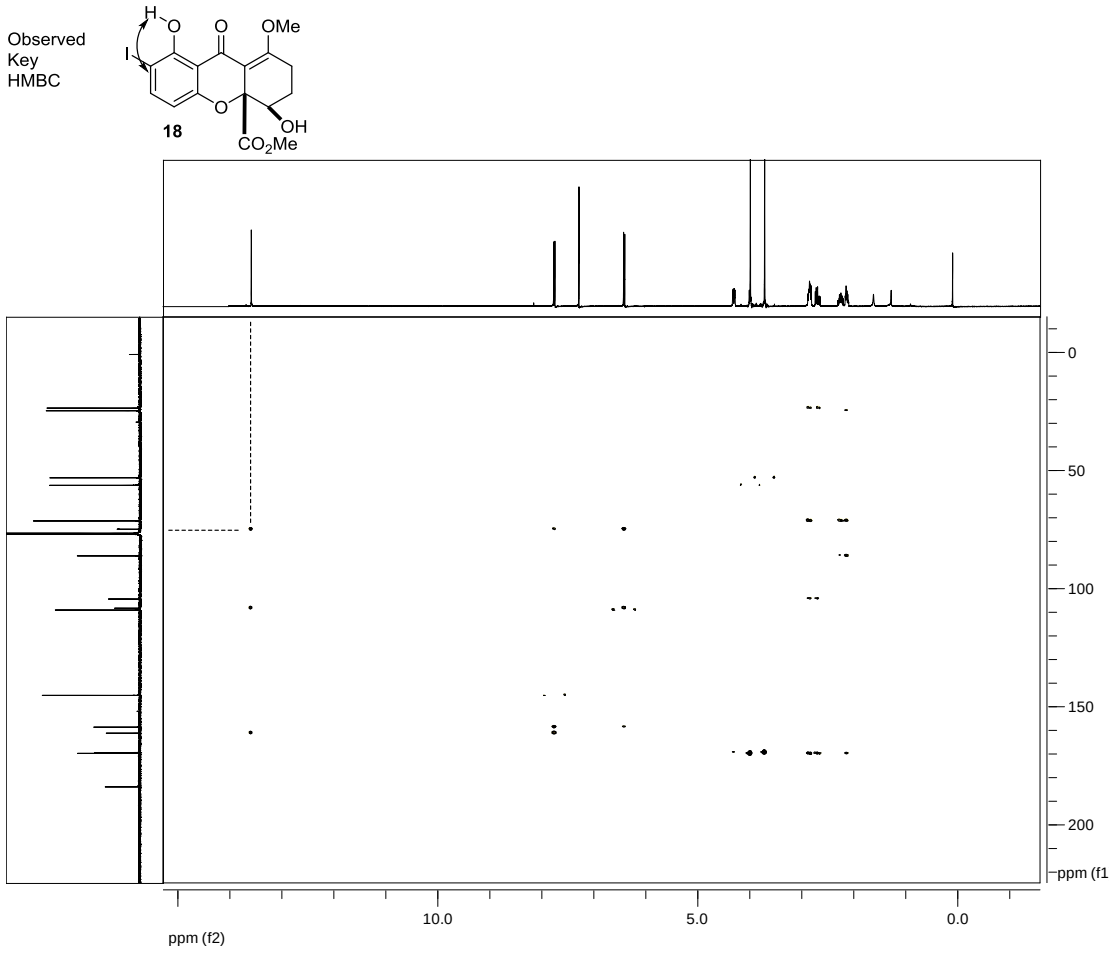


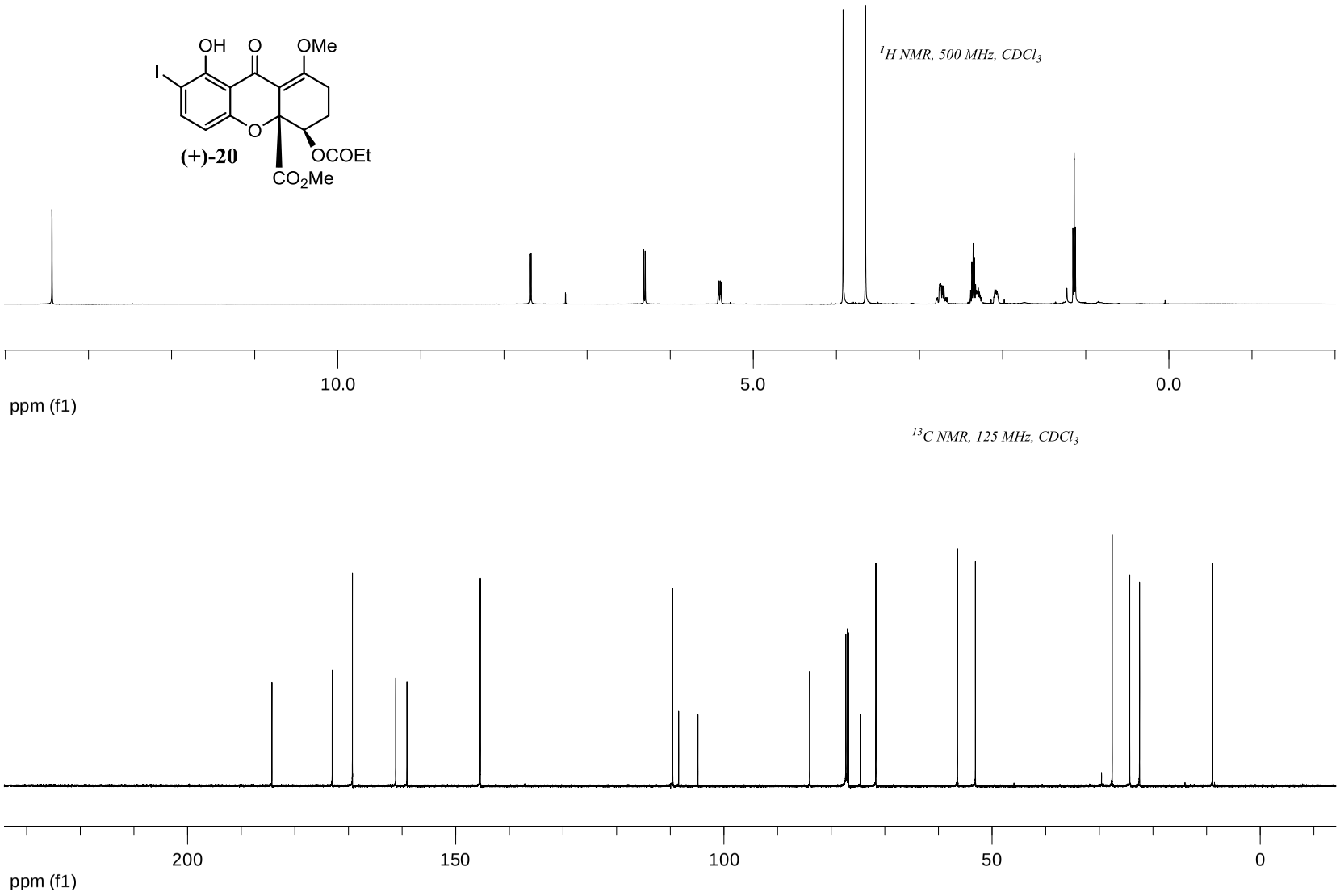
16

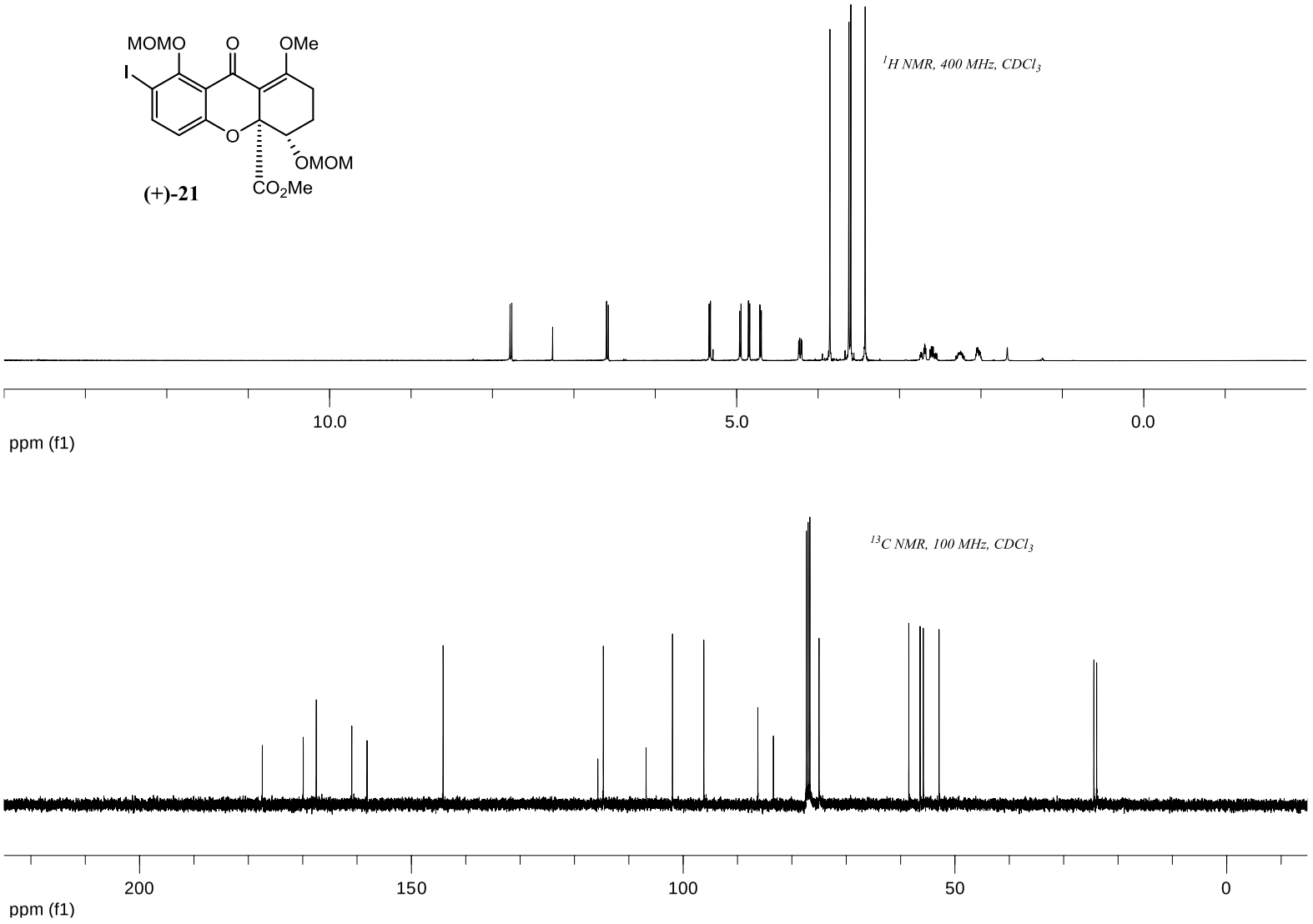


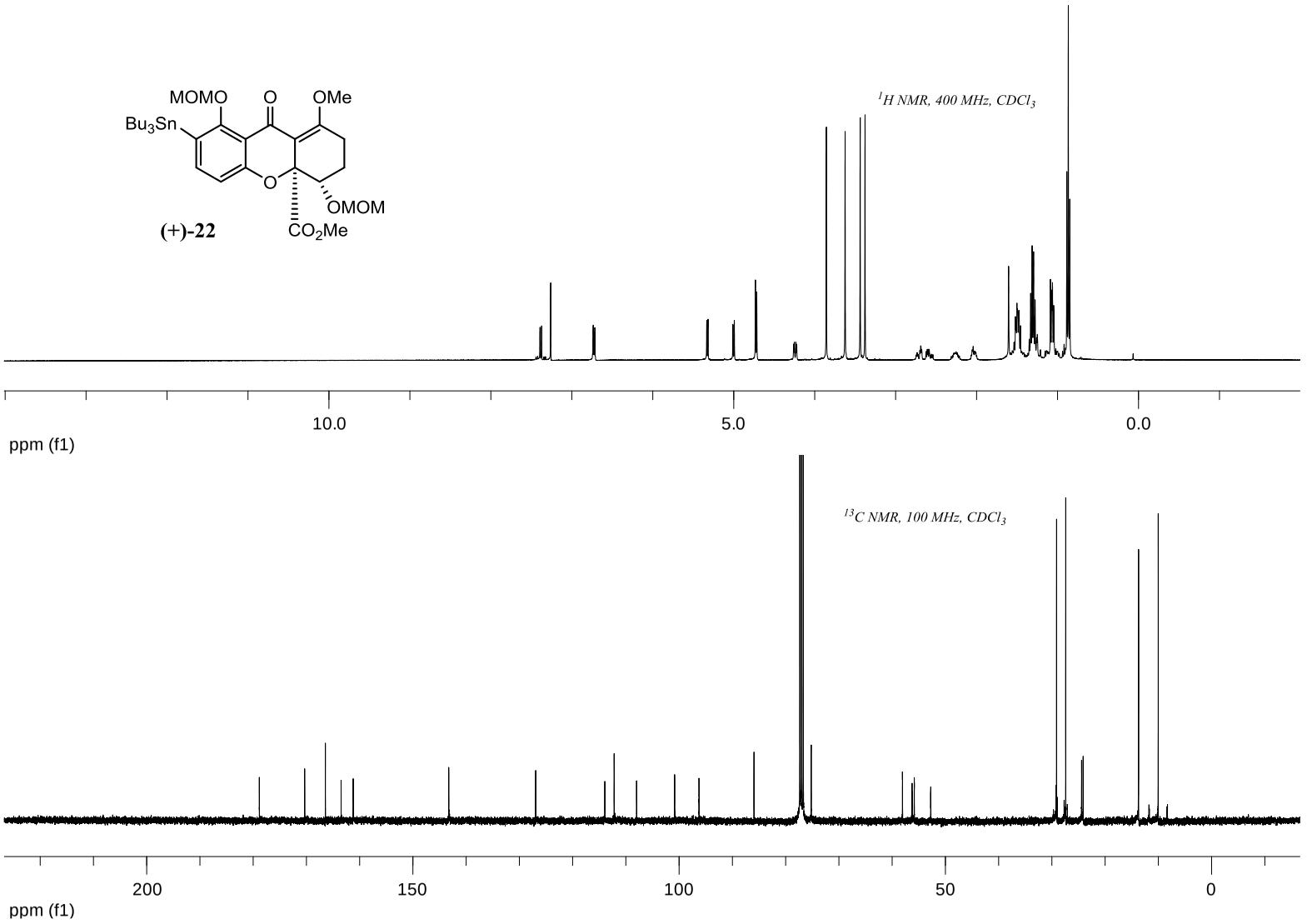

OH
O
OMe
O
OH
CO2Me
17
1H NMR. 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR. 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)

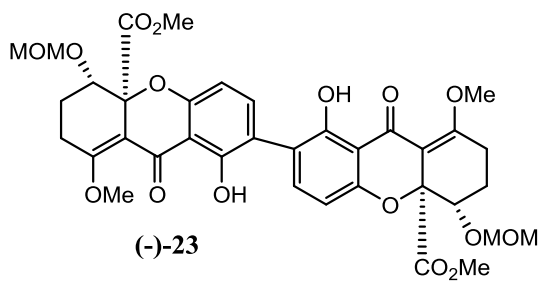

OH
O
OMe
I
O
OH
(-)-18
CO2Me
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 125 MHz, CDCl3
200
150
100
50
0
ppm (f1)


Observed
Key
HMBC
H
O
O
OMe
I
O
OH
CO2Me
18
0
50
100
150
200
ppm (f1
10.0
5.0
0.0
ppm (f2)


OH
O
OMe
I
O
OCOEt
(+)-20
CO2Me
1H NMR, 500 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 125 MHz, CDCl3
200
150
100
50
0
ppm (f1)


MOMO
O
OMe
I
O
OMOM
CO2Me
(+)-21
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)

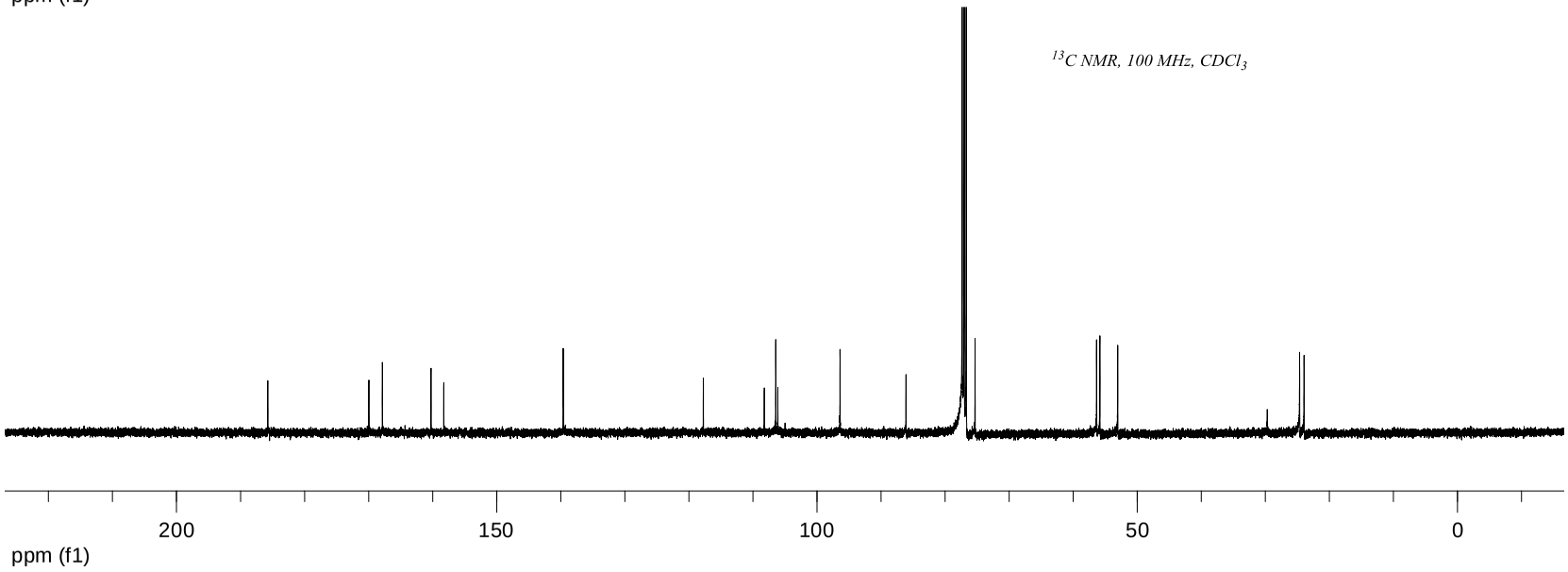

MOMO
O
OMe
Bu3Sn
O
OMOM
CO2Me
(+)-22
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)

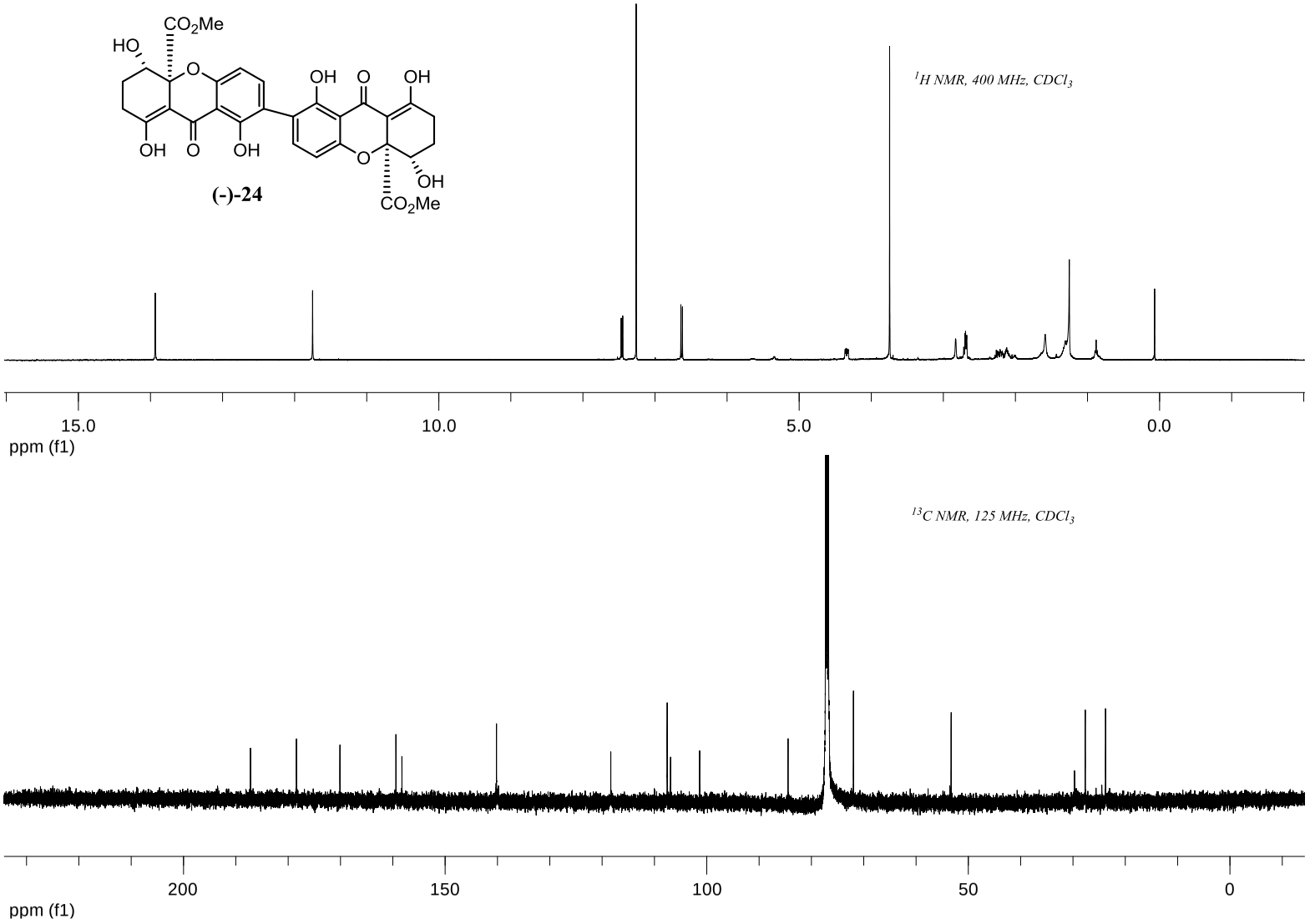


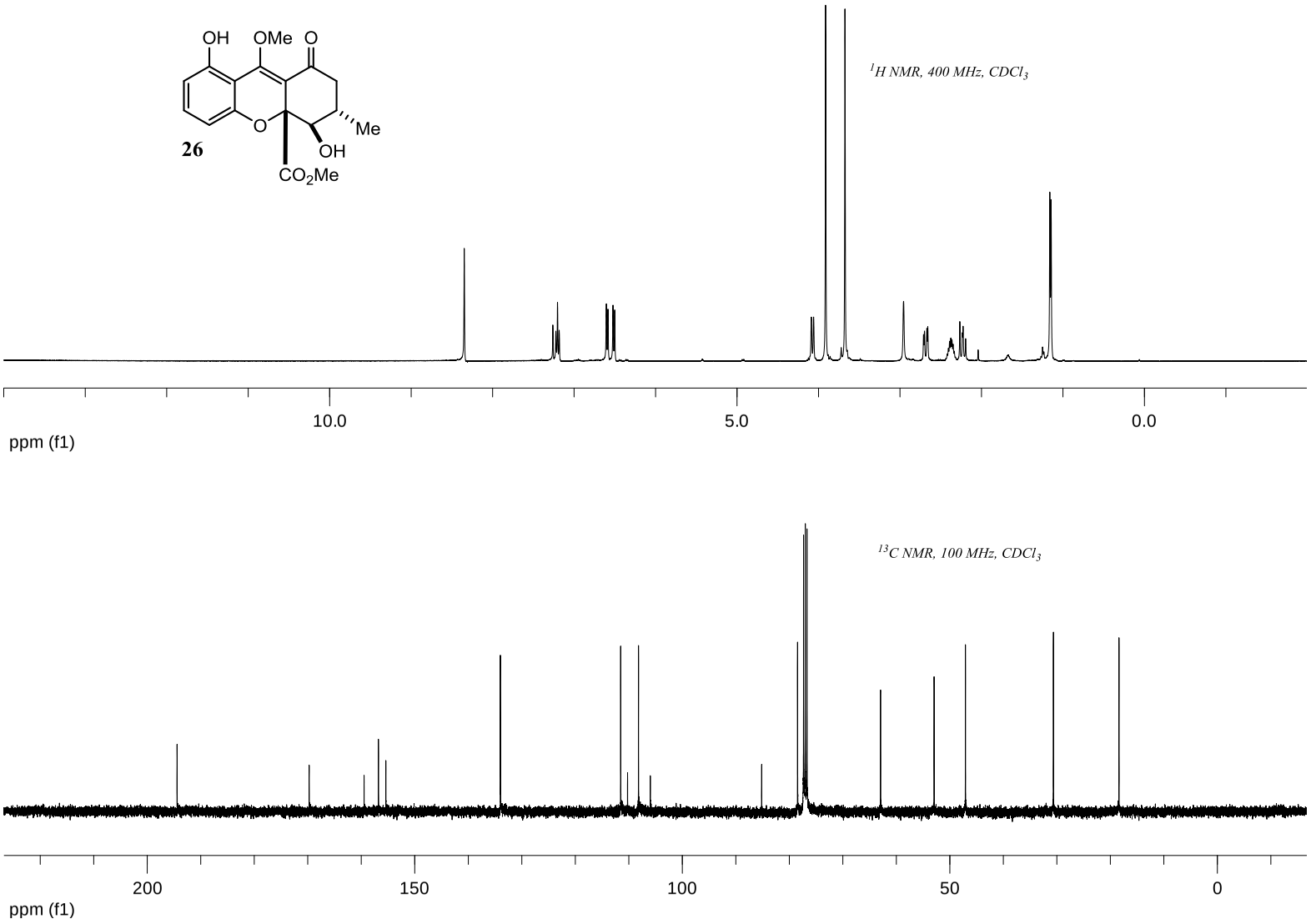
(-)-23

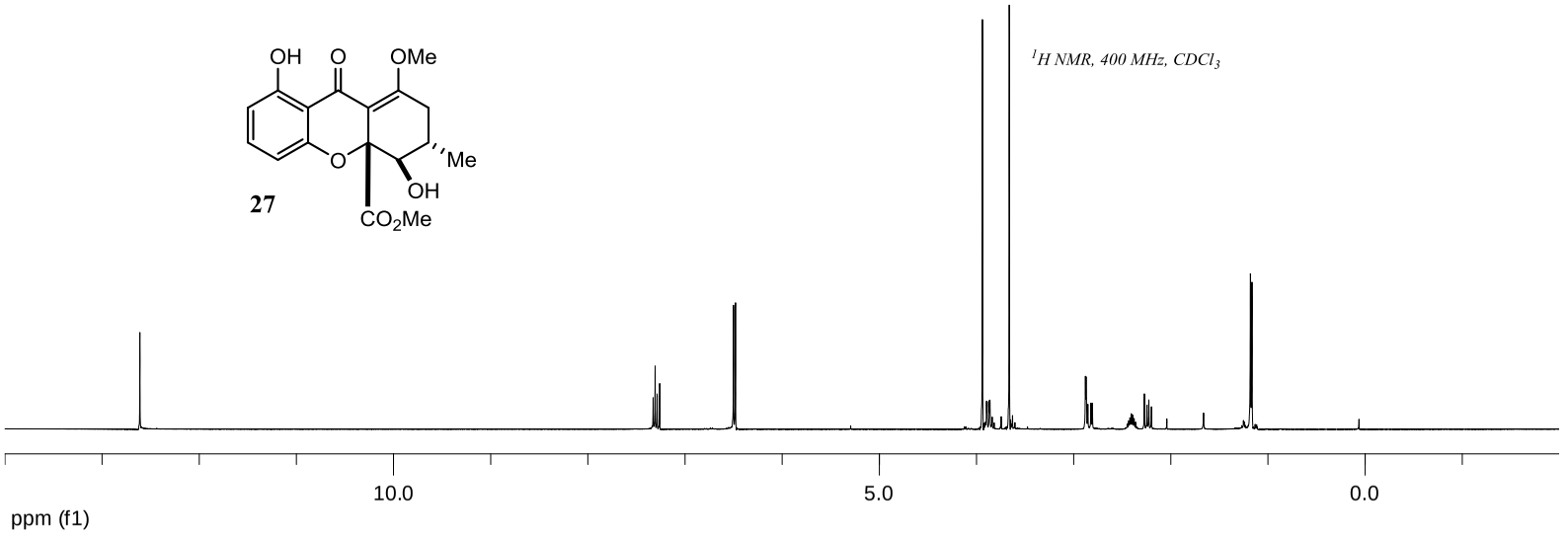
^{1}H NMR, 400 MHz, $CDCl_3$

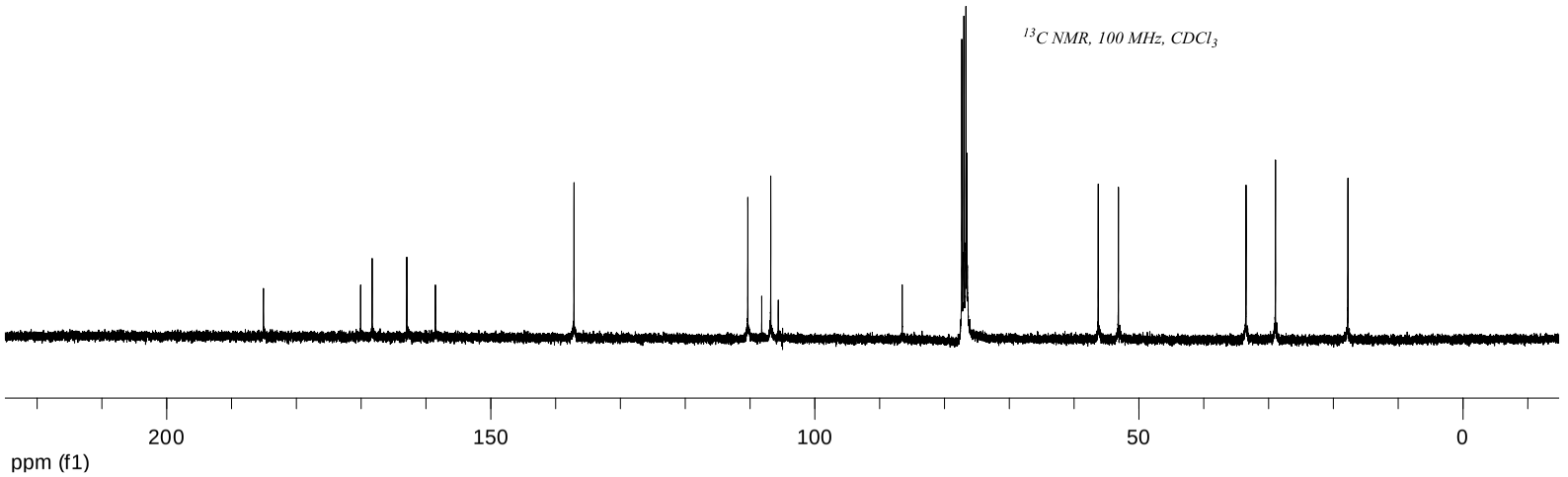
^{13}C NMR, 100 MHz, $CDCl_3$

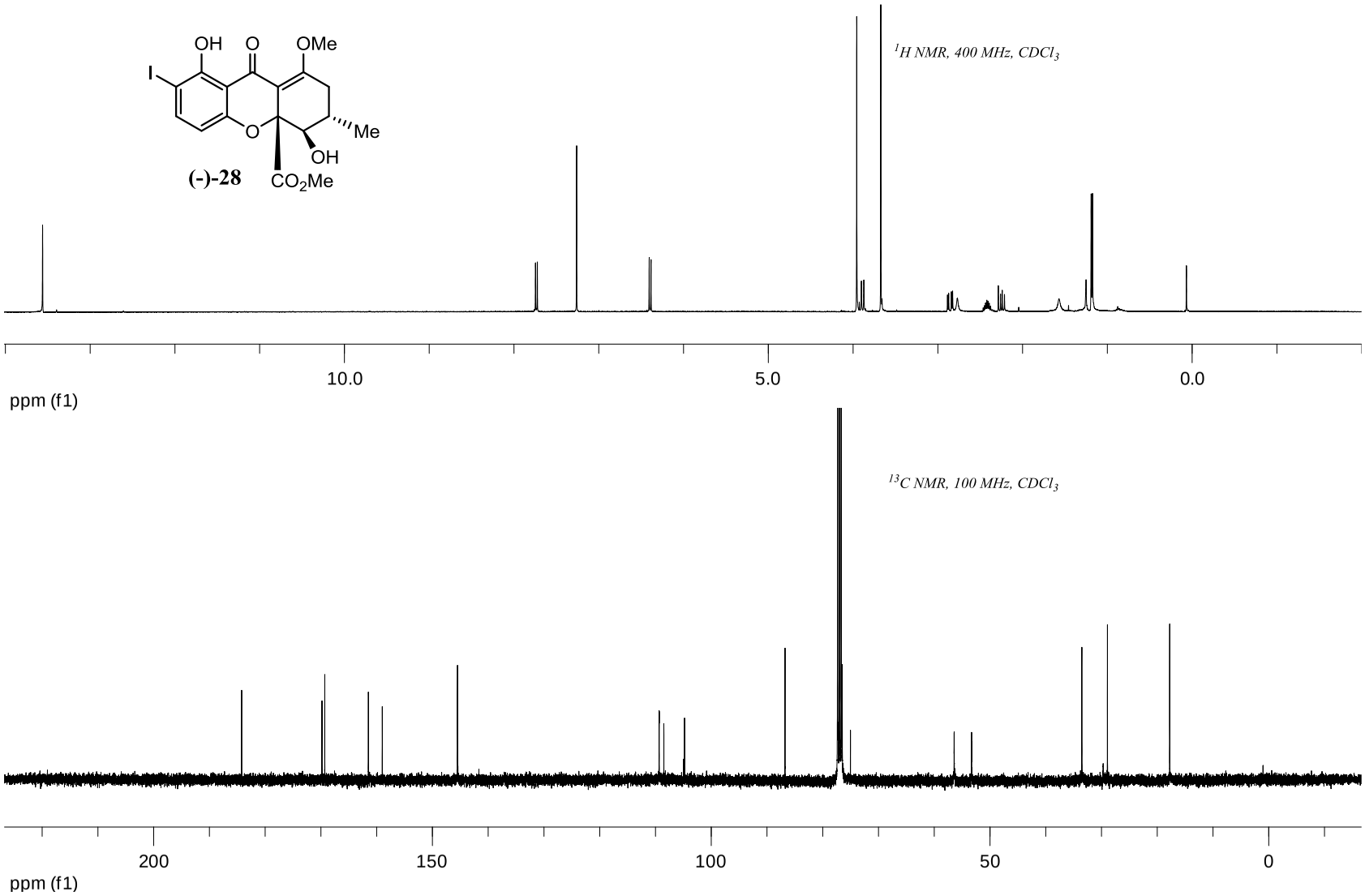


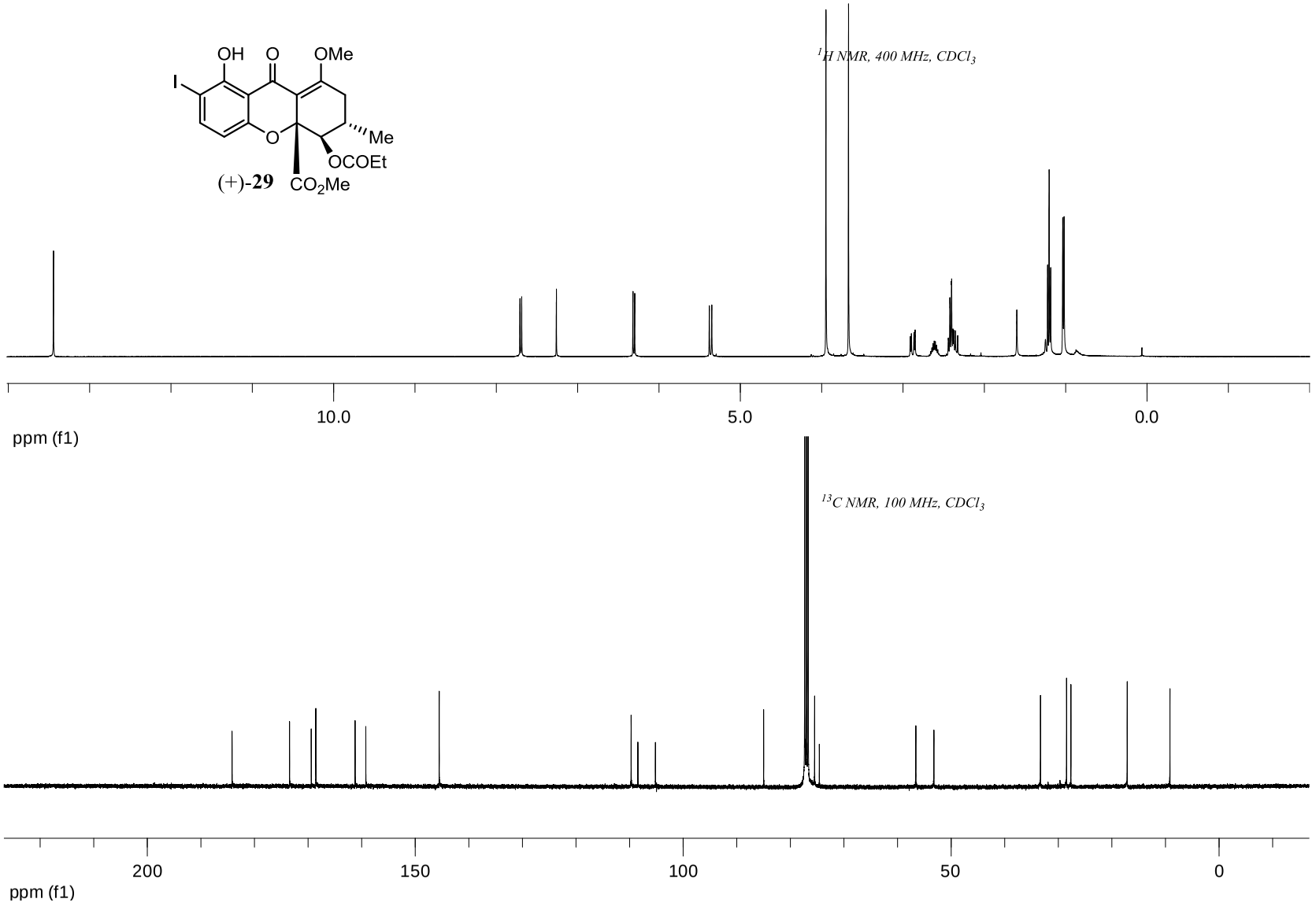

CO2Me
HO
O
OH
O
OH
OH
O
OH
O
OH
CO2Me
(-)-24
1H NMR, 400 MHz, CDCl3
15.0
10.0
5.0
0.0
ppm (f1)
13C NMR, 125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

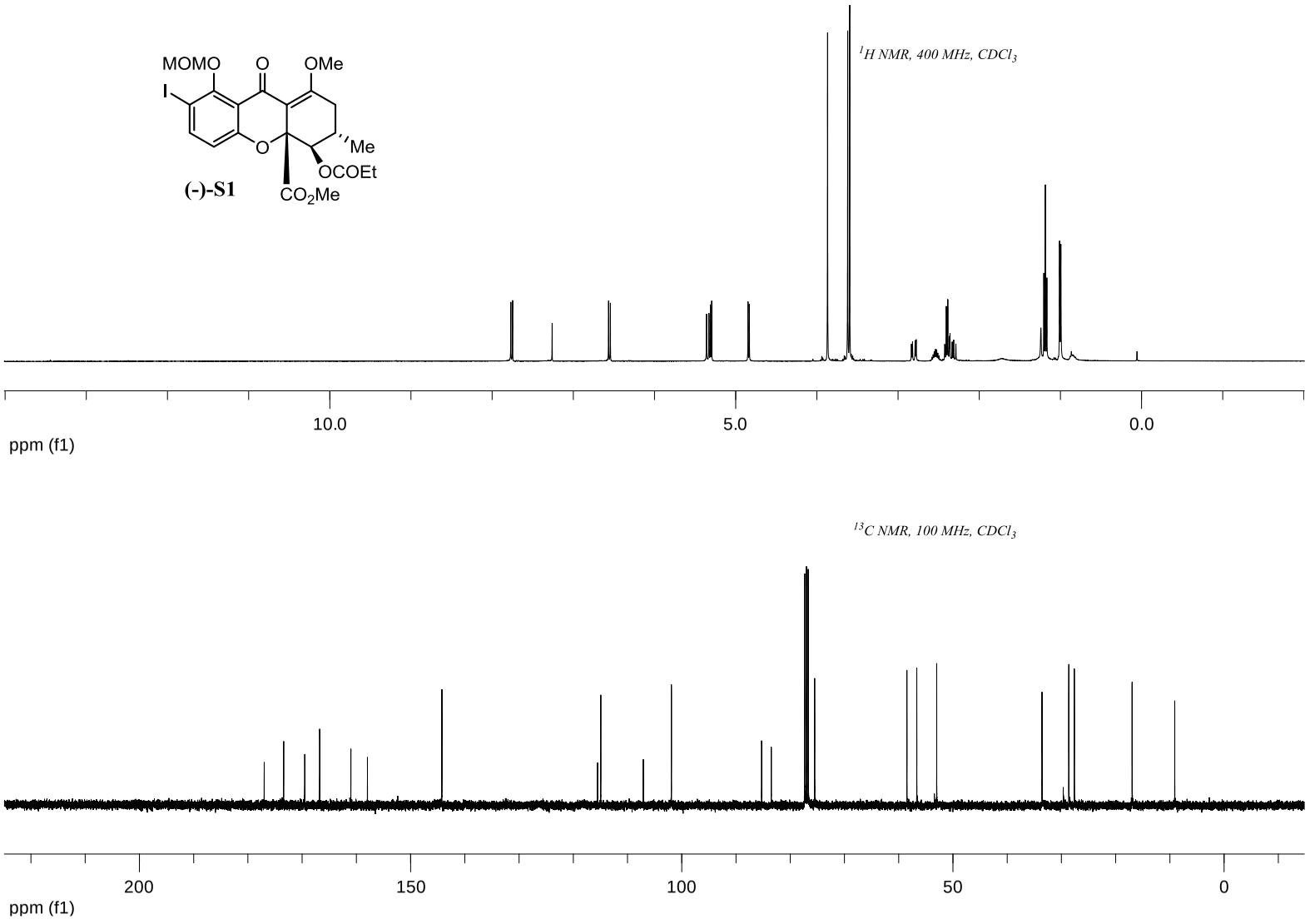

OH
OMe
O
Me
OH
CO2Me
26
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)

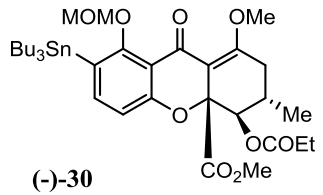

OH
O
OMe
Me
OH
CO_2Me
27
^1H NMR, 400 MHz, $CDCl_3$
10.0
5.0
0.0
ppm (f1)


^{13}C NMR, 100 MHz, $CDCl_3$
200
150
100
50
0
ppm (f1)


OH
O
OMe
I
Me
OH
O
CO2Me
(-)-28
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)

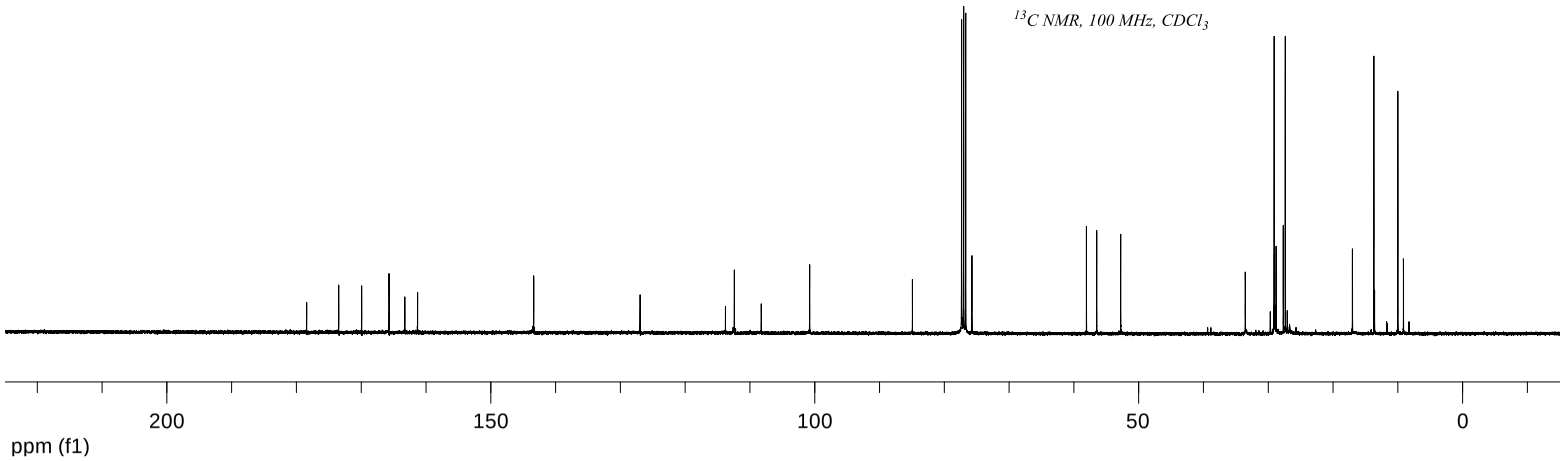

OH
O
OMe
I
Me
OCOEt
(+)-29
CO2Me
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)

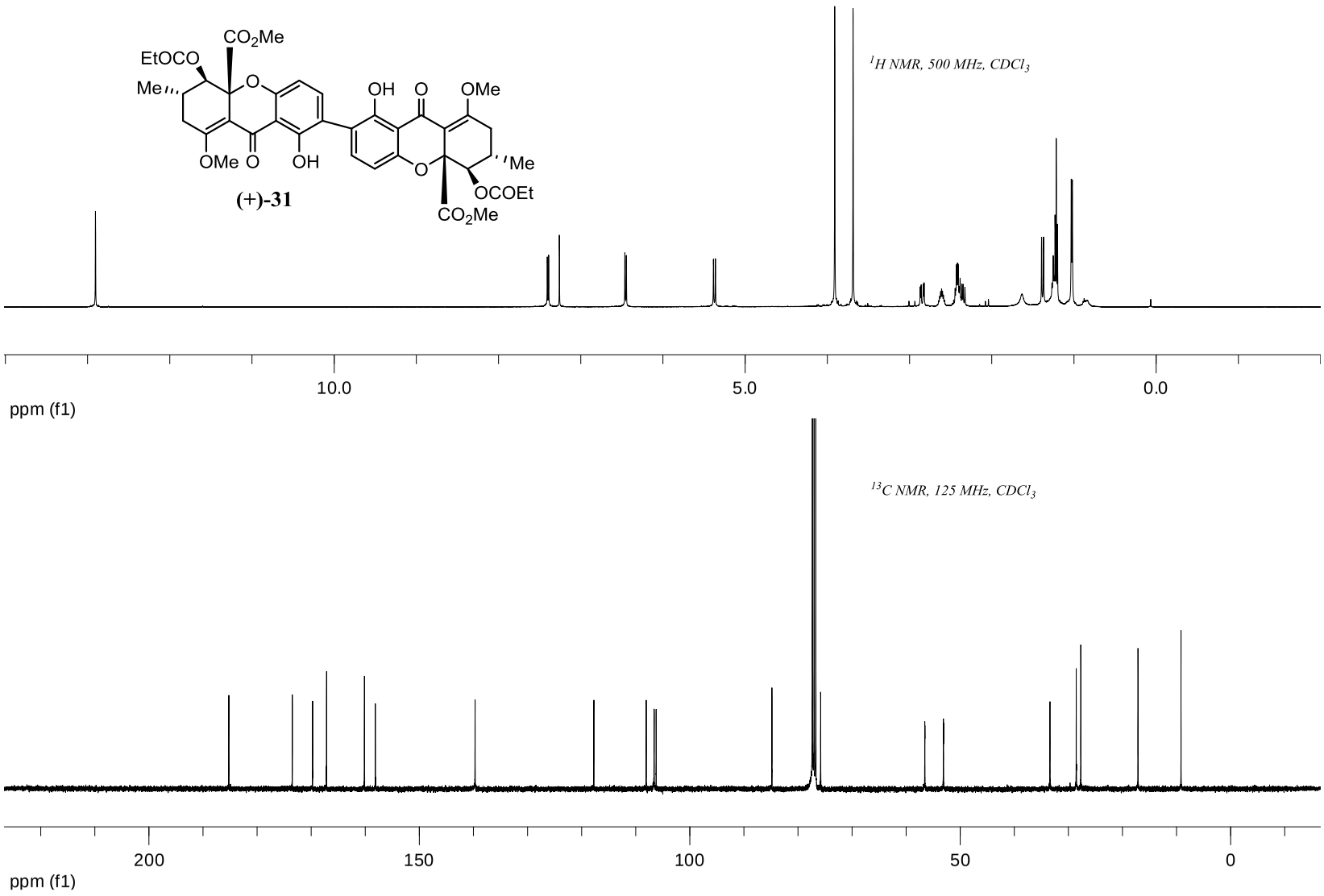

MOMO
O
OMe
I
O
Me
OCOEt
(-)-S1
CO2Me
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)

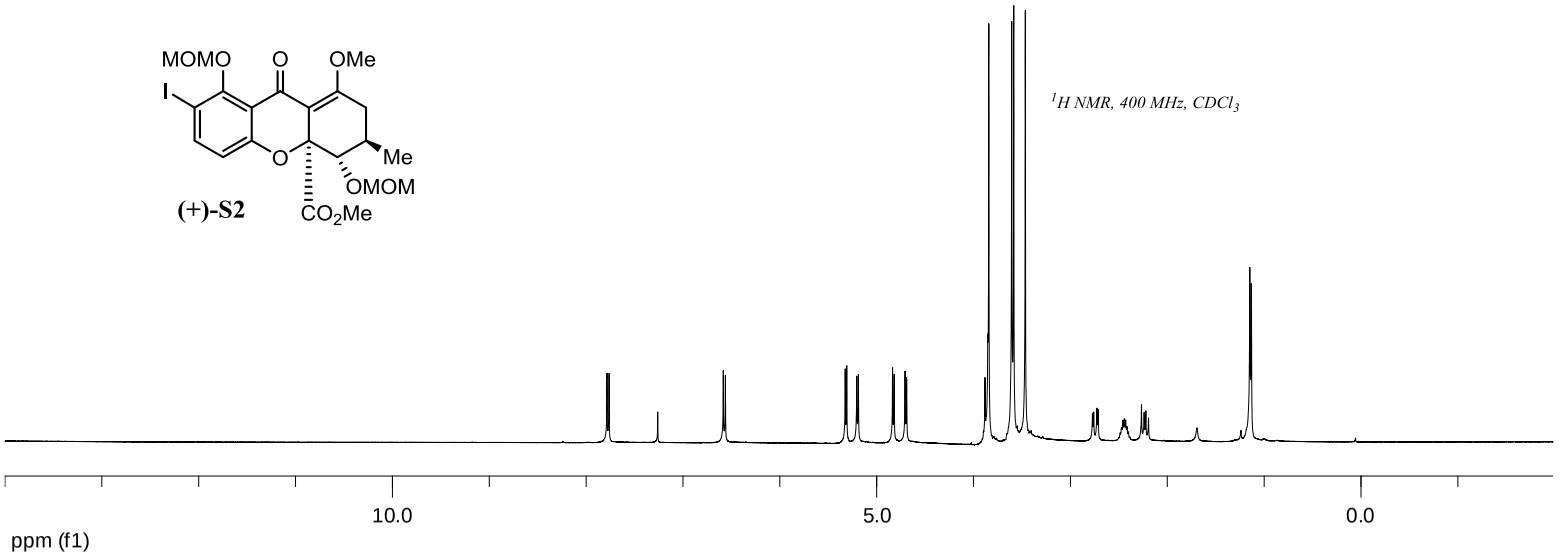

MOMO
O
OMe
Bu3Sn
O
Me
OCOEt
CO2Me

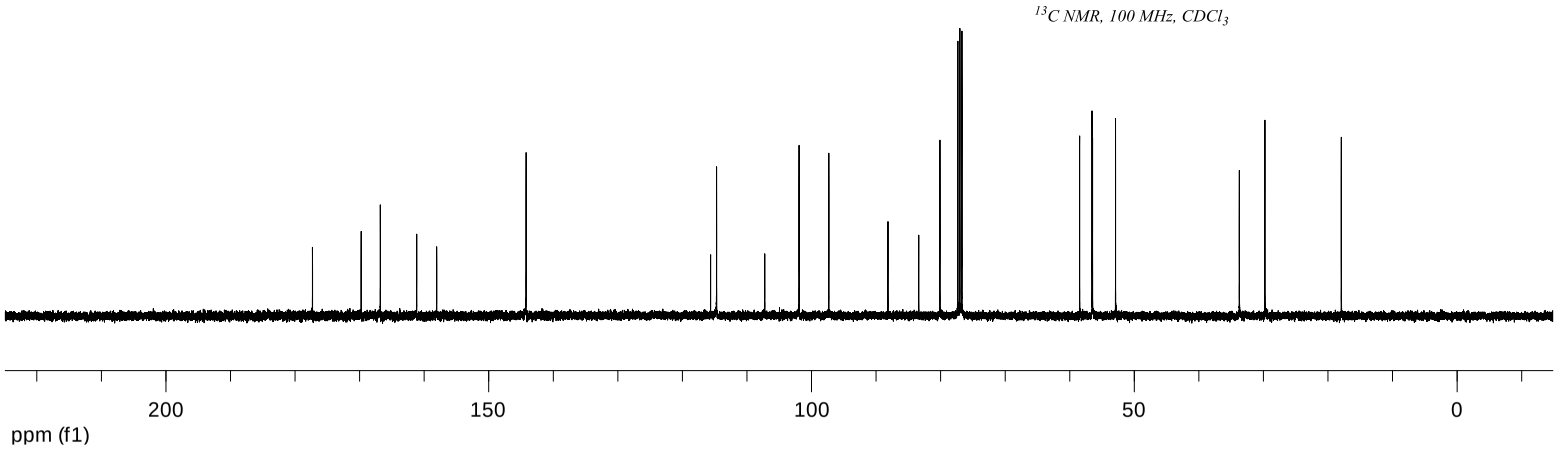
(-)-30

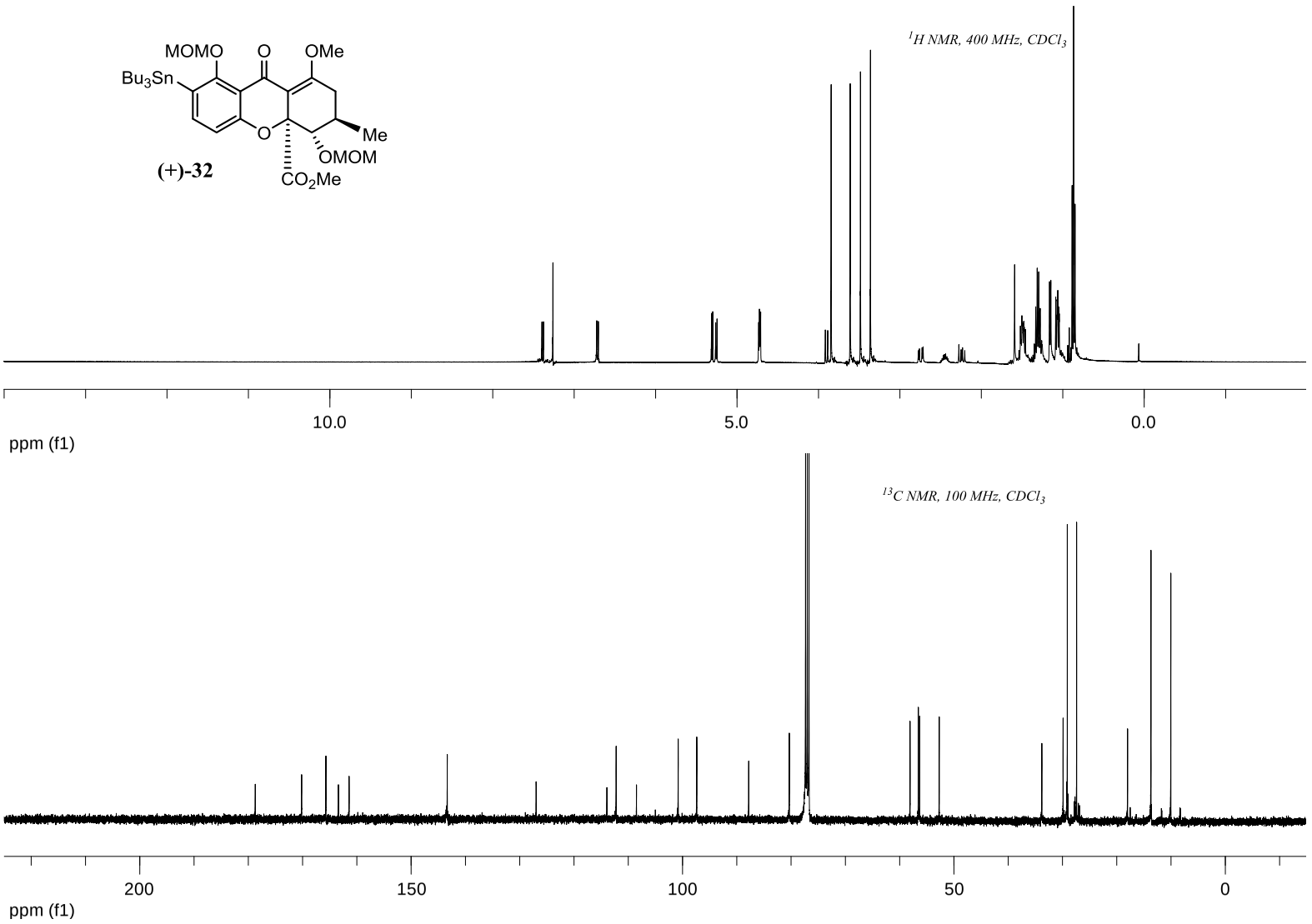
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)

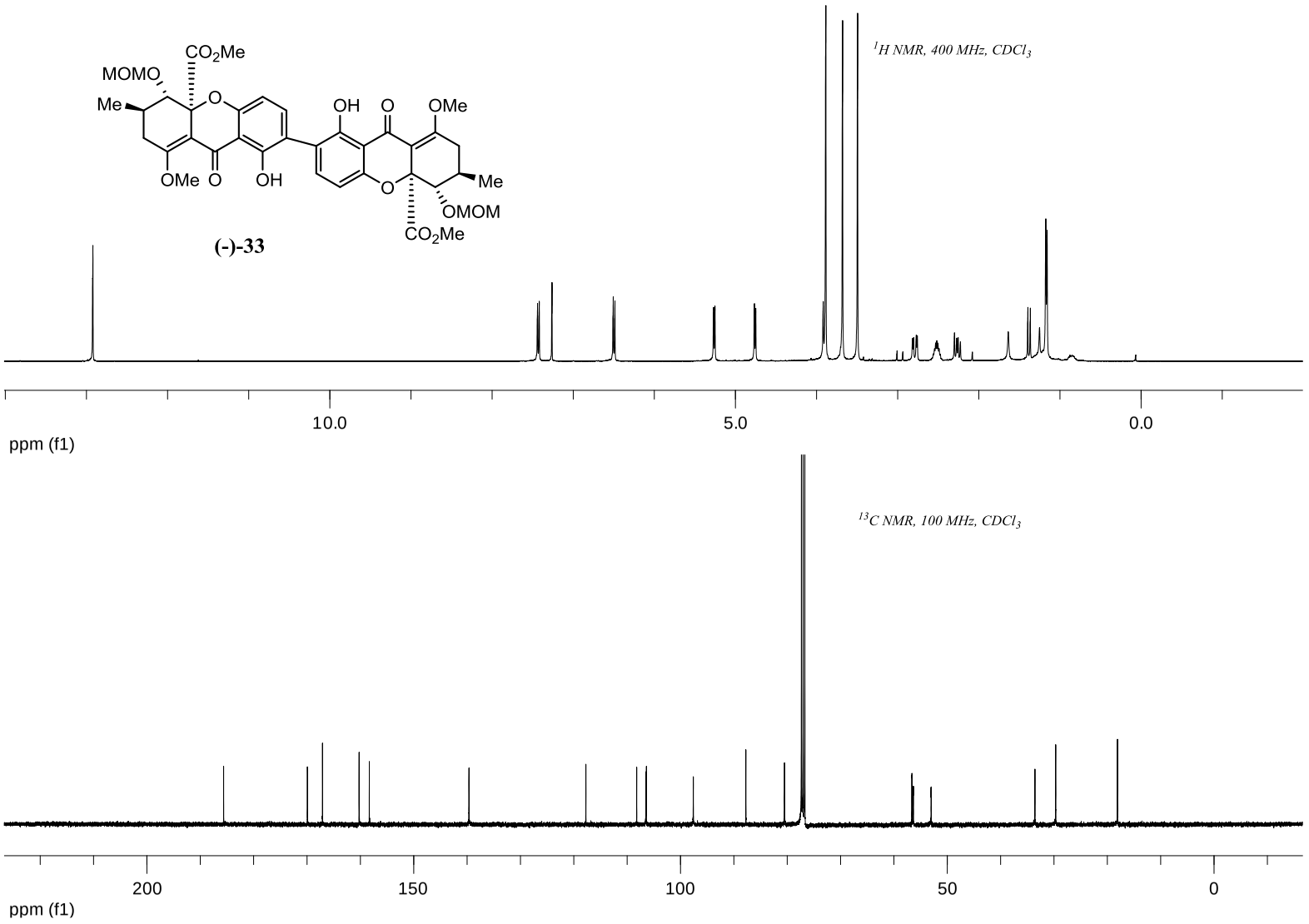

13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)

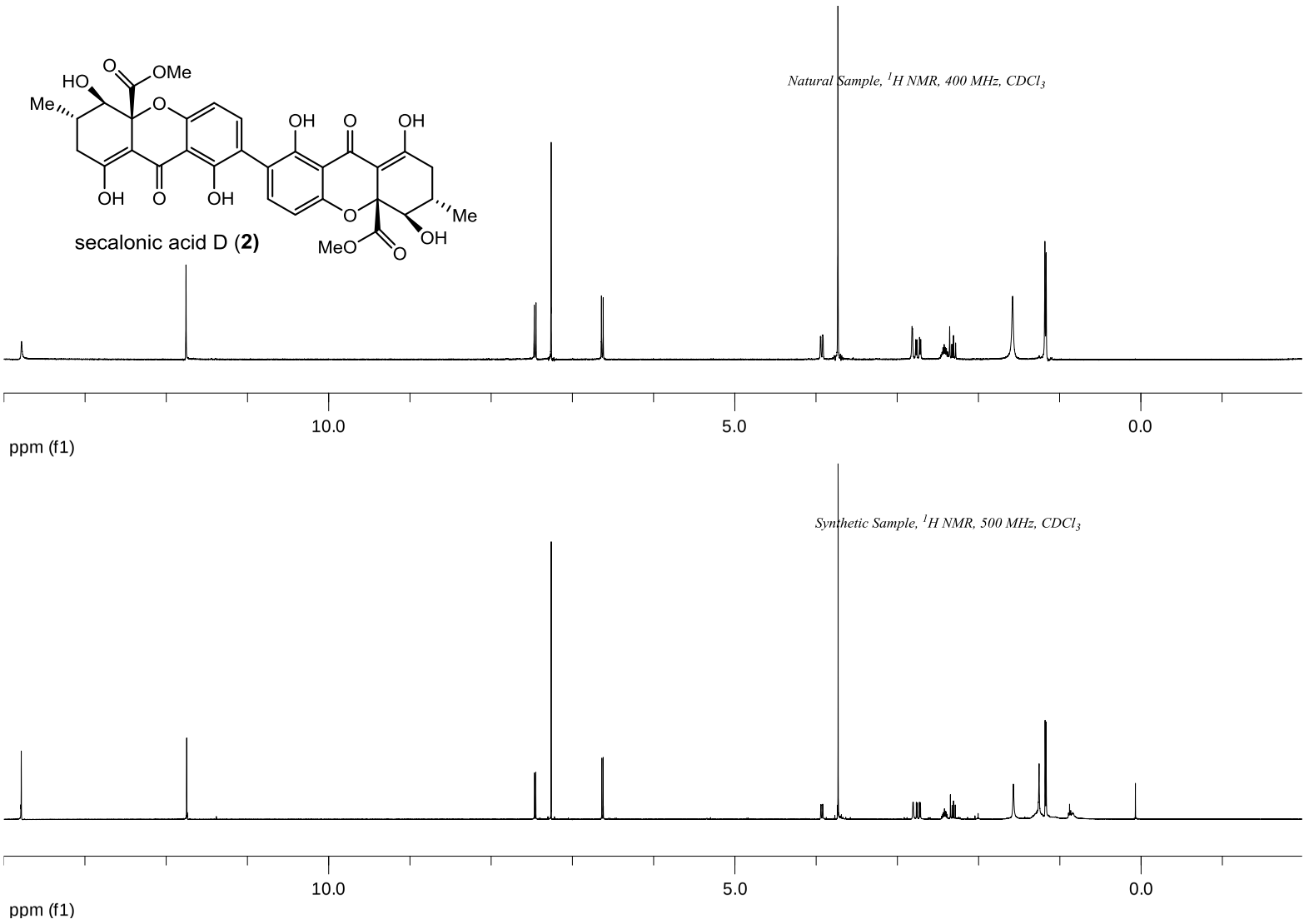

CO2Me
EtOCO
Me
O
OH
O
OMe
OMe
O
OH
O
Me
OCOEt
CO2Me
(+)-31
1H NMR, 500 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 125 MHz, CDCl3
200
150
100
50
0
ppm (f1)

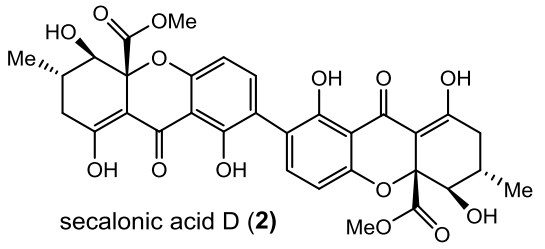

MOMO
O
OMe
I
O
Me
OMOM
CO2Me
(+)-S2
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)


13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)

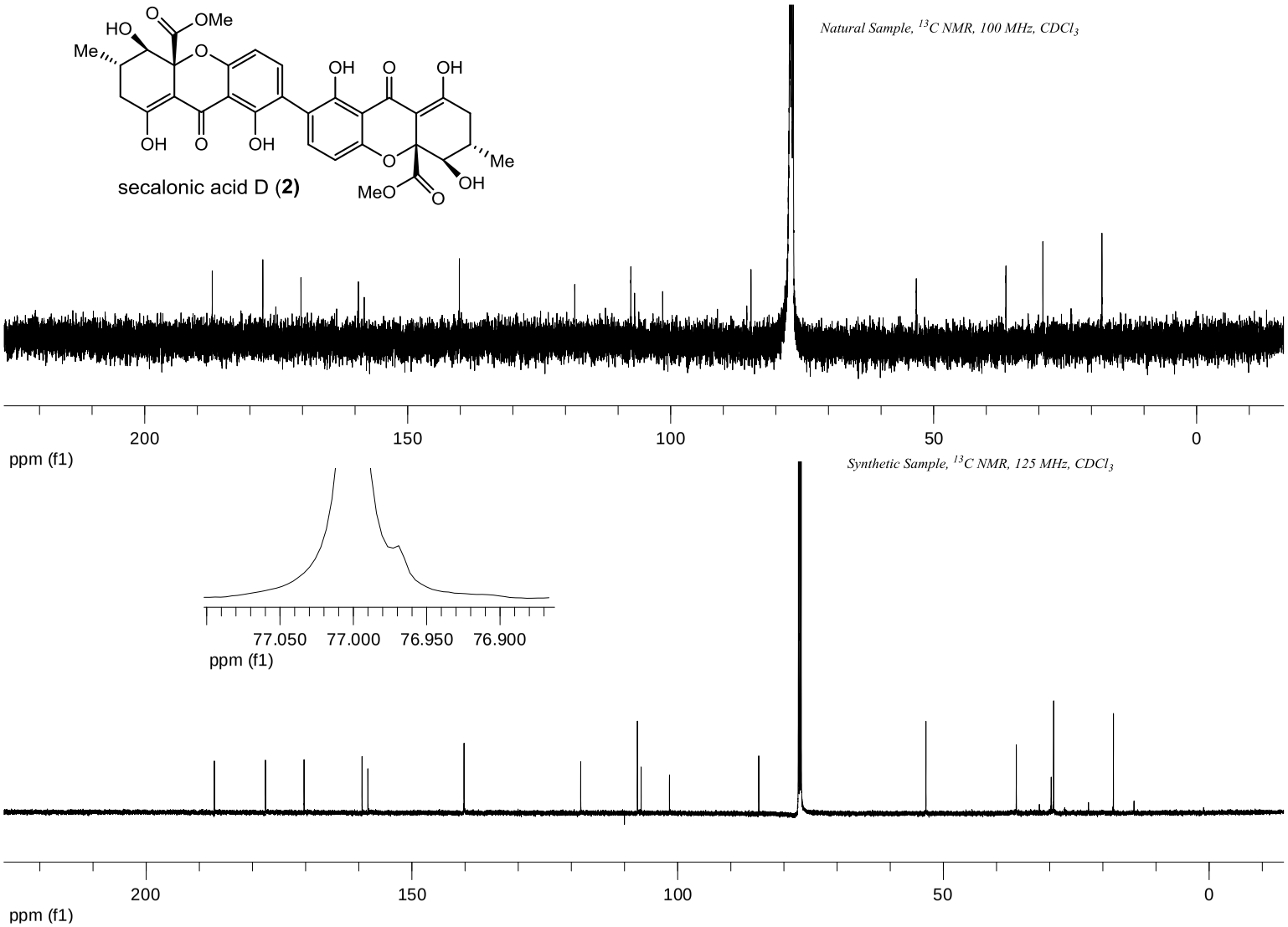

MOMO
O
OMe
Bu3Sn
O
Me
OMOM
CO2Me
(+)-32
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)


CO2Me
MOMO
Me
O
OH
O
OMe
OMe
O
OH
Me
O
OMOM
CO2Me
(-)-33
1H NMR, 400 MHz, CDCl3
10.0
5.0
0.0
ppm (f1)
13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)


secalonic acid D (2)
Natural Sample, ^1H NMR, 400 MHz, $CDCl_3$
10.0
5.0
0.0
ppm (f1)
Synthetic Sample, ^1H NMR, 500 MHz, $CDCl_3$
10.0
5.0
0.0
ppm (f1)



secalonic acid D (**2**)


secalonic acid D (2)
Natural Sample, 13C NMR, 100 MHz, CDCl3
200
150
100
50
0
ppm (f1)
Synthetic Sample, 13C NMR, 125 MHz, CDCl3
77.050
77.000
76.950
76.900
ppm (f1)
200
150
100
50
0
ppm (f1)

Key HMQC data for secalonic acid D