Supporting Information

Broadly Applicable Stereoselective Syntheses of Serrulatane, Amphilectane Diterpenes and Their Diastereoisomeric Congeners using Asymmetric Hydrovinylation for Absolute Stereochemical Control

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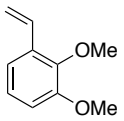
1. General Information

Unless otherwise noted, reagents were purchased from commercial suppliers and used without further purification. Air-sensitive reactions were conducted under an inert atmosphere of argon using Schlenk techniques or a Vacuum Atmospheres glovebox. Solvents were distilled from the appropriate drying agents under nitrogen. Ethylene (99.5%) was purchased from Matheson, Inc., and passed through Drierite® and potassium hydroxide before use. Analytical TLC was performed on E. Merck pre-coated (0.25 mm) silical gel 60 F254 plates. Flash column chromatography was carried out on silica gel 40 (Sorbtech Chemicals), gas chromatographic analysis was conducted on an Agilent 7820A using hydrogen as the carrier gas, equipped with a methyl silicone column (30 m X 0.32 mm, 0.25 µm film thickness). Enantiomeric excess of chiral compounds were determined by chiral stationary phase gas chromatographic (CSP GC) analysis, which was performed on an Agilent 7820A using hydrogen as the carrier gas, equipped with a Cyclosil-B (30 m x 0.25 mm, 0.25 µm film thickness), capillary GC columns purchased from Agilent. Each GC was equipped with FID detectors and integrators or a computer. Optical rotations were recorded on a Rudolph 21CFR 11 polarimeter at the sodium D line in chloroform or dichloromethane on solutions filtered through a 45 micron nylon filter.

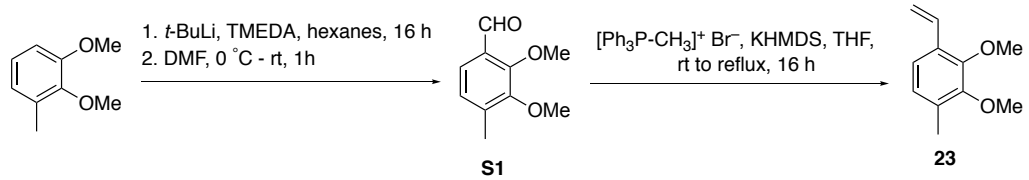
2. Experimental Procedure and Characterization of the Key Compounds

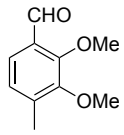
A. Experimental Data of Scheme 2



22

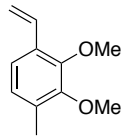
A three-necked 1 L round bottomed flask equipped with magnetic stir bar, glass stoppers and reflux condenser with gas inlet was flame-dried, purged with nitrogen and charged with solid KHMDS (19.15 g, 96.0 mmol). Dry THF (400 mL) was added, and the solution was stirred at rt. Methyltriphenylphosphonium bromide (34.30 g, 96.0 mmol) was added in portions over 10 min, causing a yellow solution to form. This solution was stirred for 3 h at rt, then was treated portionwise with solid 2,3-dimethoxybenzaldehyde (13.30 g, 80.0 mmol, Alfa Aesar). The reaction was heated to reflux and stirred for 18 h, then cooled to rt and diluted with water (100 mL). The whole was transferred to a separatory funnel containing water (300 mL) and was extracted with ether (3 x 300 mL). The organic extracts were combined, dried ($MgSO_4$) and concentrated *in vacuo* to a clear pale yellow oil, which was kept warm *via* heat gun, then purified by vacuum distillation (75 °C at 3 torr) to afford pure styrene **22** as a clear colorless oil that solidified upon standing to a white solid: 9.34 g, 57.0 mmol, 72%. R_f 0.30 (5:95 EtOAc:Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.13 (d, 1H, *J* 6.4 Hz), 7.07 (dd, 1H, *J* 10.8 Hz, 6.8 Hz), 7.04 (d, 1H, *J* 8.4 Hz), 5.77 (dd, 1H, *J* 17.6 Hz, 1.2 Hz), 5.31 (dd, 1H, 10.8 Hz, 1.6 Hz), 3.87 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 152.86, 146.61, 131.62, 131.07, 123.84, 117.68, 114.94, 111.46, 60.67, 55.61; IR (neat) 1628, 1576, 1475, 1298, 1223, 1070 cm^{-1}; [M + Na] Calc. 165.0915 Meas. 165.0914.





S1

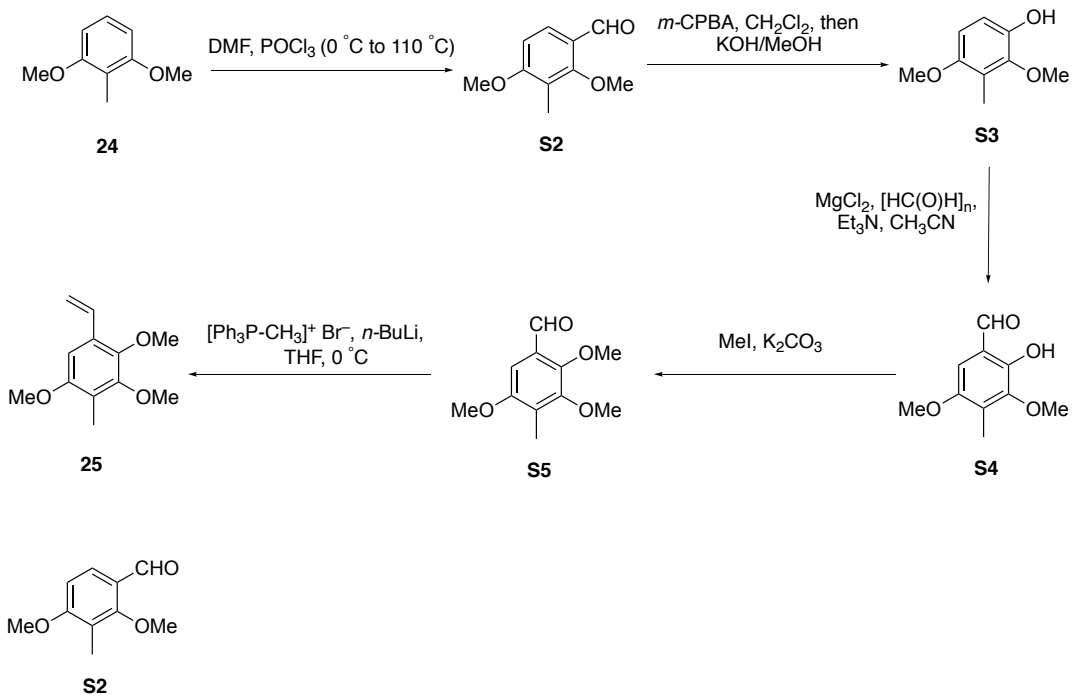
A 500 mL three-necked flask equipped with a magnetic stirring bar, stopper, addition funnel and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with 2,3-dimethoxytoluene (10.0 mL, 67.35 mmol) and freshly distilled TMEDA (2.52 mL, 16.84 mmol, 0.25 equiv.) dissolved in anhydrous hexanes (200 mL). A 1.7 M solution of *t*-butyl lithium in pentane (47.5 mL, 80.82 mmol, 1.2 equiv.) was added dropwise via addition funnel over 30 min. The resulting cloudy yellow solution was allowed to stir at room temperature overnight (16 h). The reaction vessel was cooled to 0° C and freshly distilled, degassed, anhydrous DMF (10.4 mL, 134.70 mmol, 2.0 equiv.) was added dropwise over 10 min. The reaction vessel was warmed to room temperature and allowed to stir for 1 h. The reaction was quenched by the slow addition of water (20 mL) followed by the addition of 2 N HCl until the pH of the solution was neutral. The reaction mixture was poured into water (200 mL) and extracted with ether (3 x 50 mL). The organic layers were combined and dried over $MgSO_4$, filtered, and evaporated to give the crude aldehyde which was purified via flash column chromatography (R_f = 0.40, hexanes-ethyl acetate, 9:1) to yield (**S1**) as a pale yellow oil (8.95 g, 49.68 mmol, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 1H), 7.47 (d, 1H, *J* = 8.0 Hz), 6.99 (d, 1H, *J* = 8.0 Hz), 3.98 (s, 3H), 3.85 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.8, 156.4, 151.7, 140.6, 128.6, 126.3, 123.0, 62.2, 60.4, 16.7. IR (neat) 2855, 2743, 1688, 1596, 1464, 1257, 1253, 1071, 1023 cm^{-1}.



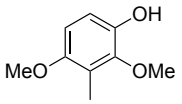
23

A 500 mL three-necked flask equipped with magnetic stirring bar, stoppers and reflux condenser fitted with a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with KHMDS (5.486 g, 27.50 mmol, 1.2 equiv.) dissolved in anhydrous THF (170 mL). Methyltriphenylphosphonium bromide (9.824 g, 27.50 mmol, 1.2 equiv.) was added in small portions and the reaction mixture was allowed to stir for 1 h. A solution of (**S1**) (4.130 g, 22.92 mmol) in anhydrous THF (50 mL) was added dropwise via syringe and then heated to reflux in an oil bath. The reaction was allowed to reflux overnight (16 h). The vessel was allowed to cool to room temperature, then the reaction mixture was diluted with pentane (150 mL) and cooled to 0° C to induce precipitation of triphenylphosphine oxide. The reaction mixture was then passed through a plug of Celite, followed by rinsing of the reaction vessel

with pentane (3 x 50 mL). The crude styrene was purified via flash column chromatography (R_f = 0.36, hexanes-ethyl acetate, 19:1) to yield (**23**) as a colorless oil (3.78 g, 20.98 mmol, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, 1H, J = 8.0 Hz), 6.98 (dd, 1H, $J_{1,2}$ = 10.8, 17.7 Hz), 6.88 (d, 1H, J = 8.0 Hz), 5.72 (dd, 1H, $J_{1,2}$ = 1.4, 17.7 Hz), 5.25 (dd, 1H, $J_{1,2}$ = 1.4, 10.8 Hz), 3.84 (s, 6H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 150.9, 132.1, 131.4, 130.2, 126.0, 120.8, 114.4, 61.0, 60.4, 16.1. IR (neat) 1824, 1625, 1601, 1567, 1284, 1222, 1066, 1024 cm^{-1}. HRMS (ESI); *m/z* 201.0898 ([M + Na]); exact mass calculated for $C_{11}H_{14}O_2Na$, 201.0891. GC (Cyclodex-β, 85 °C isotherm): t_R = 61.41 min.

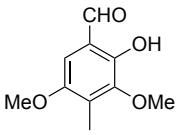


A 250 mL 3-necked flask equipped with a magnetic stirring bar, thermometer, stopper, and a reflux condenser fitted with a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with anhydrous DMF (22.4 mL, 289.11 mmol, 1.1 equiv.) and cooled to 0 °C in an ice/water bath. $POCl_3$ (28.9 mL, 315.40 mmol, 1.2 equiv.) was added dropwise via syringe over 15 min. 2,6-Dimethoxytoluene (40.00 g, 262.83 mmol) was added in a single portion and the flask was placed in an oil bath pre-heated to 110 °C. The reaction mixture was allowed to stir at 110 °C for 16 h, then cooled to ambient temperature and slowly quenched with excess 4 M NaOH (75 mL). The whole was poured into H_2O (1500 mL) and extracted with DCM (4 x 200 mL). The organic layers were combined and dried over $MgSO_4$, filtered, and concentrated to give the crude aldehyde, which was purified by passing through a plug of silica (R_f = 0.26, pentane-diethyl ether, 4:1) to yield **S2** as pale yellow solid (41.68 g, 231.30 mmol, 88%). M.P.: 48-50 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.07 (1H, s), 7.57 (1H, d, J = 9.0 Hz), 6.60 (1H, d, J = 9.0 Hz), 3.76 (3H, s), 3.72 (3H, s), 2.02 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.8, 163.8, 162.4, 127.8, 122.6, 119.9, 106.4, 62.9, 55.7, 8.3. IR (neat) 2948, 1670, 1594, 1458, 1388, 1281, 1260, 1108, 1002, 962. HRMS (ESI); *m/z* 203.0680 ([M + Na]); exact mass calculated for $C_{10}H_{12}O_3Na$, 203.0679.



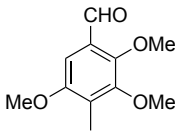
S3

A 2 L 3-necked flask equipped with a magnetic stirring bar, stoppers, and reflux condenser fitted with a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with 70-75% w/w *m*-CPBA (85.53 g, 346.95 mmol, 1.5 equiv.) in DCM (750 mL) and cooled to 0 °C in an ice/water bath. A solution of **S2** (41.68 g, 231.30 mmol) in DCM (175 mL) was added slowly and the flask was allowed to warm to ambient temperatures before refluxing in an oil bath for 16 h. The flask was then cooled to 0 °C and quenched slowly with sat. aq. $NaHCO_3$ with vigorously stirring until bubbling ceased. The whole was poured into a separatory funnel and the organic layer was drained. The aqueous layer was extracted with DCM (5 x 50 mL) and the organic layers were combined and concentrated. The crude formate ester was dissolved in methanol (500 mL), KOH (129.78 g, 2.313 mol, 10.0 equiv.) was added, and the reaction mixture was allowed to stir at ambient temperatures for 6 h. The reaction was quenched by slow addition of 10% H_2SO_4 until acidic pH was achieved. The whole was poured into H_2O (1 L) and extracted with DCM (5 x 100 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated to give **S3** (30.95 g, 184.02 mmol, 80%) which was used in the subsequent reaction without further purification.



S4

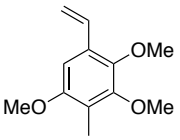
A 1 L 3-necked flask equipped with a magnetic stirring bar, stopper, thermometer, and reflux condenser fitted with a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with $MgCl_2$ (26.28 g, 276.03 mmol, 1.5 equiv.) and paraformaldehyde (28.74 g, 956.90 mmol, 5.2 equiv.). A solution of **S3** (30.95 g, 184.02 mmol) in anhydrous acetonitrile (370 mL) was added via syringe, followed by addition of Et_3N (102.6 mL, 736.08 mmol, 4.0 equiv.). The reaction mixture was heated to 110 °C and allowed to stir for 16 h. **CAUTION**: A strong exotherm is observed when the reaction mixture reaches ~85-90 °C. The reaction mixture was cooled to 0 °C and slowly quenched with 10% H_2SO_4 until acidic pH was achieved. The whole was extracted with DCM (5 x 50 mL), dried over $MgSO_4$, filtered, and concentrated to give a crude mixture of **S4** and a demethylated product. The mixture was used in the subsequent reaction without further purification.



S5

A 2 L 3-necked flask equipped with a magnetic stirring bar, stoppers and reflux condenser fitted with a nitrogen inlet was purged with nitrogen. The flask was charged with K_2CO_3 (129.65 g, 938.07 mmol, 9.0 equiv.) and a solution of **S4** (mixture) (20.45 g) dissolved in acetone (695 mL). MeI (97.3 mL, 1.563 mol,

15.0 equiv.) was added via syringe and the reaction mixture was heated to reflux in an oil bath and allowed to stir for 16 h. The flask was then cooled to ambient temperature, poured into H_2O (1 L), and extracted with DCM (5 x 50 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated to give the crude aldehyde which was purified via flash column chromatography (R_f = 0.26, hexanes-ethyl acetate, 9:1) to give **S5** (25.275 g, 120.23 mmol, 65% over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.27 (s, 1H), 6.96 (s, 1H), 3.89 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.3, 154.6, 152.2, 151.4, 129.7, 127.2, 102.2, 62.5, 60.5, 55.8, 9.7. IR (neat) 2999, 2939, 2856, 1684, 1598, 1466, 1407, 1387, 1332, 1283, 1207, 1133, 1084, 1030 cm^{-1}. HRMS (ESI); *m/z* 233.0782 ([M + Na]); exact mass calculated for $C_{11}H_{14}O_4Na$, 233.0784.



25

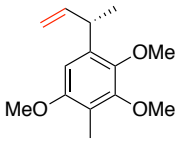
A 100 mL 3-necked flask equipped with a magnetic stirring bar, stoppers, and a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with methyltriphenylphosphonium bromide (1.026 g, 2.872 mmol, 1.2 equiv.) and anhydrous THF (13 mL). 2.5 M n-BuLi (1.05 mL, 2.632 mmol, 1.1 equiv.) was added dropwise via syringe and the reaction mixture was allowed to stir at ambient temperatures for 1 h, then was cooled to 0 °C in an ice/water bath. A solution of **S5** (503 mg, 2.393 mmol) in anhydrous THF (10 mL) was added via syringe and the reaction mixture was allowed to warm to ambient temperature and stir for 1 h. The reaction mixture was concentrated and dissolved in a minimal amount of DCM and purified via flash column chromatography (R_f = 0.36, pentane-ether, 20:1) to yield **25** as a colorless oil (452 mg, 2.170 mmol, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (dd, 1H, $J_{1,2}$ = 11.0, 17.5 Hz), 6.75 (s, 1H), 5.72 (dd, 1H, $J_{1,2}$ = 1.0, 17.5 Hz), 5.28 (dd, 1H, $J_{1,2}$ = 1.0, 11.0 Hz), 3.85 (s, 3H), 3.83 (s, 3H), 3.80 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.5, 152.3, 145.2, 131.6, 128.8, 121.1, 114.1, 102.2, 61.2, 60.6, 55.9, 9.2. IR (neat) 2959, 2933, 1487, 1461, 1400, 1272, 1224, 1072, 1024, 904, 820 cm^{-1}. HRMS (ESI); *m/z* 231.0987 ([M + Na]); exact mass calculated for $C_{12}H_{16}O_3Na$, 231.0992. GC (Cyclosil-B, 125 °C isotherm): t_R = 32.59 min.

B. Experimental Data of Scheme 3

General Procedure of Ni(II)-Catalyzed Asymmetric Hydrovinylation: *Precatalyst preparation*: In a glovebox, NaBARF (0.0586 mmol, 1.0 mol%), ligand (0.0586 mmol, 1.0 mol%), and $[(allyl)NiBr]_2$ (0.0293 mmol, 0.5 mol%) were weighed into separate glass vials. The ligand was dissolved in anhydrous DCM (1.0 mL) and transferred to the vial containing $[(allyl)NiBr]_2$, followed by 1.0 mL rinsing of the source vial. The resulting yellow solution of phosphoramidite ligand and $[(allyl)NiBr]_2$ was transferred to the vial containing NaBARF, followed by 1.0 mL rinsing of the source vial. The resulting orange-yellow solution was allowed to stand for 1.5 h. *Asymmetric hydrovinylation*: A 100 mL three-necked flask equipped with a rubber septum, flow-controlled nitrogen inlet, thermometer, and magnetic stirring bar was flame-dried and purged with nitrogen. The catalyst solution prepared above was transferred to the reaction

vessel via cannula, followed by 1.0 mL rinsing of the source vial. The system was closed at the flow-controlled stopcock and cooled to desired temperature in a cryogenic bath, creating a small vacuum. A strong flow of dry ethylene was introduced via needle through the septum to relieve the vacuum and then the atmosphere of the vessel was evacuated three times via syringe to remove any remaining nitrogen. The flow of ethylene was adjusted to maintain a pressure of 1 atm by releasing excess gas through an oil bubbler. A solution of the Vinyl-styrene substrate (5.858 mmol) in anhydrous DCM (6 mL), followed by 2.0 mL rinsing of the source vial was introduced via syringe as to not increase the reaction temperature above the desired maintained temperature. The reaction mixture was allowed to stir at the desired temp for desired time (reaction progress was monitored by GC-FID analysis). The ethylene needle was then removed and the reaction was exposed to air and NH_4OH (1.0 mL) was added to quench the reaction. The resulting mixture was poured into H_2O (25 mL) and extracted with DCM (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated to give the crude hydrovinylation product, which was then eluted through a plug of silica with pentane-ether (20:1) to remove any nickel salts. The eluent was concentrated to yield the pure hydrovinylated product.

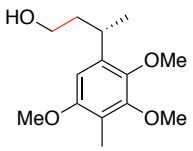
Ligands (**L1**, **L2**, **L3**, **L4**, **L5**, **L6**, **L7**)[1] were synthesized following literature procedures. Hydrovinylated product **26**[1a] and **27**[2] was previously reported from our research group.



28

General procedure of Ni(II)-catalyzed hydrovinylation was followed. (99%, 96% *ee* using complex of **L3**). Authentic racemic sample was obtained via complex of achiral ligand **L6**.). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.45 (s, 1H), 6.10-6.04 (m, 1H), 5.12-5.07 (m, 2H), 3.69 (quintet, 1H, J = 7.0 Hz), 3.86-3.81 (m, 9H, containing: 3.86 (s, 3H), 3.84 (s, 3H), 3.81 (s, 3H)), 2.16 (s, 3H), 1.37 (d, 3H, J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.4, 152.1, 144.7, 143.4, 136.3, 118.8, 113.2, 104.4, 61.1, 60.3, 55.9, 36.0, 20.6, 8.9. $[\alpha]_D^{20}$ -16.8 (*c* 3.00, $CHCl_3$); IR (neat) 2962, 2934, 2832, 1604, 1584, 1484, 1464, 1403, 1224, 1190, 1130, 1060, 1035, 917 cm^{-1}. HRMS (ESI); *m/z* 259.1306 ([M + Na]); exact mass calculated for $C_{14}H_{20}O_3Na$, 259.1305. GC (Cyclosil-B, 125 °C isotherm): t_R = 40.66 (*R*), 41.62 (*S*) min.

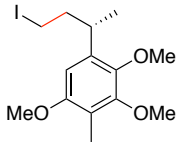
C. Experimental Data of Scheme 5



30

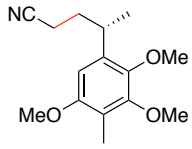
A 100 mL 3-necked flask equipped with a magnetic stirring bar, thermometer, stopper, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with 9-BBN dimer (1.289 g, 5.281 mmol, 1.0 equiv.) and a solution of **28** (1.248 g, 5.281 mmol) in anhydrous THF (50 mL) was added via

syringe. The reaction mixture was allowed to stir at ambient temperature for 2 h, then cooled to 0 °C in an ice/water bath. 4 M NaOH (10.6 mL) was added dropwise, maintaining the internal temperature below 10 °C. A solution of ~30% H_2O_2 (7.9 mL) was added dropwise, maintaining the internal temperature below 10 °C. **CAUTION**: A strong exotherm is observed upon the initial addition of H_2O_2. Once addition was complete, the reaction mixture was allowed to warm to ambient temperature, poured into H_2O (100 mL), and extracted with ether (3 x 25 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated. The crude alcohol was purified via flash column chromatography (R_f = 0.12, hexanes-ethyl acetate, 4:1) to give **30** as a colorless oil (1.341 g, 5.273 mmol, >99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.42 (s, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H), 3.54-3.50 (m, 1H), 3.36-3.31 (m, 2H), 2.47 (bs, 1H), 2.10 (s, 3H), 1.95-1.88 (m, 1H), 1.60-1.54 (m, 1H), 1.28 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 151.8, 144.8, 136.6, 118.7, 103.4, 61.4, 61.1, 60.5, 55.9, 41.4, 28.2, 21.8, 8.9. $[\alpha]_D^{20}$ +47.3 (*c* 2.73, $CHCl_3$); IR (neat) 3427, 2932, 2869, 2833, 1738, 1605, 1583, 1485, 1462, 1403, 1230, 1127, 1042 cm^{-1}. HRMS (ESI); *m/z* 277.1417 ([M + Na]); exact mass calculated for $C_{14}H_{22}O_4Na$, 277.1410.



S6

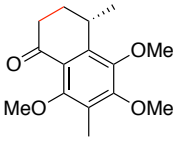
A 100 mL 3-necked flask equipped with a magnetic stirring bar, stoppers, and a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with **30** (1.341 g, 5.273 mmol) in anhydrous THF (55 mL). Imidazole (718 mg, 10.546 mmol, 2.0 equiv.) and triphenylphosphine (1.521 g, 5.800 mmol, 1.1 equiv.) were added to the flask and the reaction mixture was cooled to 0 °C in an ice/water bath. Iodine crystals (1.472 g, 5.800 mmol, 1.1 equiv.) were added in small portions until a red solution persisted, then the reaction mixture was allowed to warm to ambient temperature. The reaction mixture was concentrated and the crude mixture was purified via flash column chromatography (R_f = 0.40, hexanes-ethyl acetate, 19:1) to give **S6** (1.894 g, 5.200 mmol, 99%) as a white chalky oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.39 (s, 1H), 3.83-3.79 (m, 9H, containing: 3.83 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H)), 3.27 (sextet, 1H, *J* = 7.0 Hz), 3.14-3.06 (m, 2H), 2.20-2.06 (m, 5H, containing: 2.12 (s, 3H)), 1.24 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.5, 152.2, 145.2, 136.0, 119.0, 103.8, 61.2, 60.4, 56.0, 41.8, 34.2, 21.4, 9.0, 4.9. $[\alpha]_D^{20}$ +26.8 (*c* 3.16, $CHCl_3$); IR (neat) 2957, 2930, 2867, 2831, 1604, 1583, 1485, 1462, 1403, 1227, 1189, 1130, 1035, 837, 486 cm^{-1}. HRMS (ESI); *m/z* 387.0420 ([M + Na]); exact mass calculated for $C_{14}H_{21}IO_3Na$, 387.0428.



31

A 100 mL single-necked flask equipped a magnetic stirring bar and a reflux condenser fitted with a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with NaCN (463 mg,

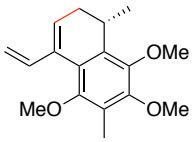
9.445 mmol, 2.0 equiv.) and a solution of **S6** (1.720 g, 4.722 mmol) in anhydrous DMSO (24 mL). The reaction mixture was heated to 60 °C in an oil bath and allowed to stir for 2 h. The flask was then cooled to ambient temperature and the whole was poured into H_2O (100 mL) and extracted with ether (3 x 25 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated to give the crude nitrile which was eluted through a plug of silica (R_f = 0.35, hexanes-ethyl acetate, 4:1) to yield **31** as a colorless oil (1.242 g, 4.716 mmol, >99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.36 (s, 1H), 3.81-3.79 (m, 9H, containing: 3.793 (s, 3H), 3.786 (s, 3H), 3.78 (s, 3H)), 3.26 (sextet, 1H, *J* = 7.0 Hz), 2.24-2.21 (m, 2H), 2.10 (s, 3H), 1.96-1.88 (m, 2H), 1.28 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.4, 152.0, 145.0, 134.9, 119.8, 119.0, 103.2, 60.8, 60.0, 55.7, 33.1, 32.1, 21.3, 15.4, 8.7. $[\alpha]_D^{20}$ +43.8 (*c* 3.43, $CHCl_3$); IR (neat) 2961, 2933, 2869, 2834, 2244, 1604, 1583, 1486, 1458, 1404, 1347, 1319, 1268, 1231, 1122, 1078, 1032, 839, 790 cm^{-1}. HRMS (ESI); *m/z* 286.1422 ([M + Na]); exact mass calculated for $C_{15}H_{21}NO_3Na$, 286.1414.



32

A 100 mL single-necked flask equipped with a magnetic stirring bar and reflux condenser fitted with a nitrogen inlet was purged with nitrogen. The flask was charged with **31** (1.440 g, 5.468 mmol) dissolved in methanol (28 mL). NaOH (10.937 g, 273.42 mmol, 50.0 equiv.) and H_2O (14 mL) were added in sequence and the flask was heated to reflux in an oil bath. The reaction mixture was allowed to reflux overnight (16 h) and then cooled to ambient temperature. Conc. HCl (~20 mL) was added until an acidic pH was achieved. The whole was poured into H_2O (50 mL) and extracted with ethyl acetate (3 x 25 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated to give the crude acid as a pale yellow oil. The crude oil was azeotroped with benzene (20 mL) and dried overnight with a vacuum pump. *Friedel-Crafts Acylation*: A 100 mL three-necked flask equipped with a magnetic stirring bar, stopper, thermometer, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with the crude acid dissolved in anhydrous DCM (55 mL). The flask was then cooled to 0 °C in an ice/water bath and a 2.0 M solution of oxalyl chloride in DCM (3.0 mL, 6.015 mmol, 1.1 equiv.) was added dropwise. The reaction mixture was allowed to warm to ambient temperature and stir for 1 h. The flask was then re-cooled to 0 °C and $AlCl_3$ (1.094 g, 8.202 mmol, 1.5 equiv.) was added in a single portion and the reaction mixture was allowed to stir for 0.5 h. The reaction was quenched by the slow addition of H_2O (10 mL). The whole was poured into H_2O (50 mL) and extracted with ether (3 x 25 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated to give the crude ketone which was purified via flash column chromatography (R_f = 0.36, hexanes-ethyl acetate, 4:1) to yield **32** as a pale yellow oil (1.386 g, 5.244 mmol, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84-3.81 (m, 6H, containing: 3.84 (s, 3H), 3.81 (s, 3H)), 3.72 (s, 3H), 3.42-3.39 (m, 1H), 2.77-2.70 (m, 1H), 2.51-2.46 (m, 1H), 2.16-2.10 (m, 4H, containing: 2.13 (s, 3H)), 1.91-1.86 (m, 1H), 1.25 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.5, 156.2, 155.8, 145.6, 142.1, 125.1, 121.5, 61.0, 60.5, 59.8, 35.0, 28.4, 27.0, 19.8, 8.8.

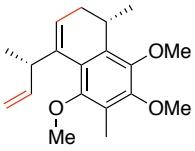
$[\alpha]_D^{20}$ -36.1 (*c* 1.97, $CHCl_3$); IR (neat) 2960, 2932, 2865, 1681, 1576, 1459, 1402, 1316, 1284, 1156, 1107, 1070, 1039, 1019 cm^{-1}. HRMS (ESI); *m/z* 287.1252 ([M + Na]); exact mass calculated for $C_{15}H_{20}O_4Na$, 287.1254.



33

A 50 mL 3-necked flask equipped with a magnetic stirring bar, stopper, thermometer, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with **32** (728 mg, 2.754 mmol) dissolved in anhydrous THF (25 mL) and cooled to 0 °C in an ice/water bath. A 1.0 M solution of vinylmagnesium bromide (3.3 mL, 3.305 mmol, 1.2 equiv.) was added via syringe in a single portion. The reaction mixture was allowed to stir at 0 °C for 30 min. and a saturated aqueous solution of NH_4Cl (5 mL) was slowly added to quench the reaction. The whole was poured into H_2O (50 mL) and extracted with ether (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, filtered, concentrated, and eluted through a plug of silica (hexanes-ethyl acetate, 4:1) to give the crude alcohol which was used in the subsequent reaction without further purification. A 50 mL 3-necked flask equipped with a magnetic stirring bar, stoppers, and a nitrogen inlet was charged with the crude alcohol dissolved in CH_2Cl_2 (25 mL). (+/-)-Camphor-10-sulfonic acid (64 mg, 0.275 mmol, 0.10 equiv.) was added and the reaction mixture was allowed to stir at ambient temperature for 2.5 h, until TLC showed complete consumption of the alcohol. The reaction was concentrated and purified via flash column chromatography (R_f = 0.34, pentane-diethyl ether, 20:1) to yield **33** as a colorless oil (608 mg, 2.216 mmol, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.84 (dd, 1H, $J_{1,2}$ = 10.5, 17.0 Hz), 6.03-6.01 (m, 1H), 5.38 (dd, 1H, $J_{1,2}$ = 2.0, 17.0 Hz), 4.96 (dd, 1H, $J_{1,2}$ = 2.0, 10.5 Hz), 3.87 (s, 3H), 3.85 (s, 3H), 3.46 (s, 3H), 3.29-3.25 (m, 1H), 2.41-2.37 (m, 1H), 2.22-2.18 (m, 4H, containing: 2.19 (s, 3H)), 1.08 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.4, 151.2, 146.1, 139.0, 135.3, 134.5, 124.4, 123.6, 122.9, 110.6, 61.0, 60.8, 60.2, 30.2, 26.4, 18.9, 9.3. $[\alpha]_D^{20}$ -48.8 (*c* 3.18, $CHCl_3$); IR (neat) 2958, 2929, 2866, 2827, 1458, 1402, 1336, 1112, 1078, 1030, 899 cm^{-1}. HRMS (ESI); *m/z* 297.1472 ([M + Na]); exact mass calculated for $C_{17}H_{22}O_3Na$, 297.1461. GC (Cyclosil-B, 150 °C isotherm): t_R = 45.92 (C_1:*R*), 47.92 (C_1:*S*) min.

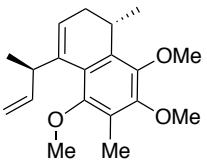
D. Experimental Data of Scheme 6



34

General procedure of Ni(II)-catalyzed hydrovinylation was followed. (98%, >95% *de* as determined by NMR using complex of **L3**). Authentic diastereomeric mixture sample was obtained via complex of achiral ligand **L6**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85 (dd, 1H, $J_{1,2}$ = 1.5, 7.0 Hz), 5.77-5.70 (m, 1H), 4.97 (dd, 1H, $J_{1,2}$ = 1.5, 17.0 Hz), 4.78 (dd, 1H, $J_{1,2}$ = 1.5, 10.0 Hz), 4.16-4.11 (m, 1H), 3.86 (s, 3H), 3.85 (s, 3H),

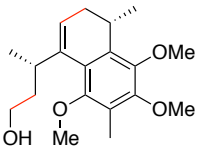
3.57 (s, 3H), 3.26-3.21 (m, 1H), 2.33-2.28 (m, 1H), 2.20 (s, 3H), 2.15-2.10 (m, 1H), 1.36 (d, 3H, J = 7.0 Hz), 1.04 (d, 3H, J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3, 150.7, 145.8, 144.4, 139.6, 135.5, 123.3, 123.1, 121.2, 111.7, 60.65, 60.62, 60.0, 37.9, 30.0, 26.4, 18.7, 18.0, 9.3. $[\alpha]_D^{20}$ -102.5 (c 3.23, $CHCl_3$); IR (neat) 2960, 2931, 2869, 2830, 1462, 1454, 1402, 1362, 1336, 1108, 1079, 1020, 971 cm^{-1}. HRMS (ESI); *m/z* 325.1759 ([M + Na]); exact mass calculated for $C_{19}H_{26}O_3Na$, 325.1774. GC (Cyclosil-B, 150 °C isotherm): t_R = 50.55 (C_{11}:*R* or *S*, C_1:*R*), 52.17 (C_{11}:*R* or *S*, C_1:*S*) min.



11-*epi*-**34**

(*S*)-4-((*R*)-but-3-en-2-yl)-5,7,8-trimethoxy-1,6-dimethyl-1,2-dihydronaphthalene (11-*epi*-34): ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.11 (m, 1H,), 5.74 (d, 1H, J = 6.2 Hz), 5.15-5.10 (m, 2H), 4.06 (m, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.55 (s, 3H), 3.21-3.17 (m, 1H), 2.28-2.25 (m, 1H), 2.17 (s, 3H), 2.08-2.04 (m, 1H), 1.06 (d, 3H, J = 6.8 Hz), 1.02 (d, 3H, J = 7.0 Hz). ^{13}C NMR (175 MHz, $CDCl_3$) δ 151.83, 150.53, 145.71, 143.2, 140.44, 135.65, 123.03, 122.72, 122.15, 113.07, 60.75, 60.6, 60.0, 38.69, 29.77, 26.19, 20.79, 17.9, 9.13. HRMS (ESI); m/z 325.1728 ([M + Na]); exact mass calculated for $C_{19}H_{26}O_3Na$, 325.1774. GC (Cyclosil-B, 150 °C isotherm): t_R = 51.51 min. (C_{11}:*S*, C_1:*S*) minor; t_R = 58.65 min (C_{11}: *R*, C_1: *S*) major.; dr 1.3:98.7.

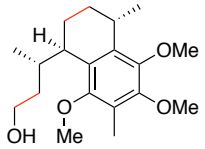
E. Experimental Data of Scheme 7



35a

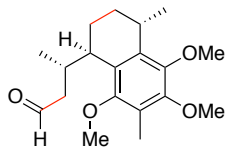
A 50 mL three-necked flask equipped with magnetic stirring bar, stopper, thermometer, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with olefin **34** (226 mg, 0.747 mmol) dissolved in anhydrous THF (8 mL). 9-BBN dimer (365 mg, 1.494 mmol, 2.0 equiv.) was added and the reaction mixture was allowed to stir at room temperature for 3 h. The vessel was cooled to 0 °C in an ice/water bath and 4 M NaOH (1.5 mL) was added dropwise, maintaining the internal temperature of the vessel below 10 °C. A solution of ~30% H_2O_2 (1.1 mL) was then added dropwise, maintaining the internal temperature of the vessel below 10 °C. The vessel was allowed to warm to room temperature and stir for an additional 0.5 h. The vessel was then diluted with ether (10 mL) and neutralized with 10% H_2SO_4 until pH ~7 was achieved. The whole was poured into H_2O (15 mL) and extracted with ether (3 x 10 mL). The organic layers were combined and dried over $MgSO_4$, and concentrated to give crude **35a** which was purified via flash column chromatography (R_f = 0.29, hexanes-ethyl acetate, 3:1) to yield **35a** as

a colorless oil (226 mg, 0.715 mmol, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ AC-6-23 5.81 (d, 1H, J = 6.0 Hz), 3.81-3.80 (m, 6H, containing: 3.81 (s, 3H), 3.80 (s, 3H)), 3.58-3.51 (m, 5H, containing: 3.51 (s, 3H), 3.43 (bs, 1H), 3.20-3.16 (m, 1H), 2.28-2.23 (m, 2H), 2.13 (s, 3H), 2.10-2.05 (m, 1H,), 1.67-1.64 (m, 1H), 1.32-1.26 (m, 1H), 1.21 (d, 3H, J = 7.0 Hz), 0.97 (d, 3H, J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.4, 150.7, 146.1, 141.0, 135.6, 123.4, 123.2, 120.8, 61.2, 60.7, 60.6, 60.1, 41.4, 30.5, 29.9, 26.2, 18.4, 17.9, 9.3. $[\alpha]_D^{20}$ -108.3 (c 1.78, $CHCl_3$); IR (neat) 3446, 2959, 2931, 2874, 1462, 1402, 1336, 1322, 1107, 1079, 1024 cm^{-1}. HRMS (ESI); m/z 343.1882 ([M + Na]); exact mass calculated for $C_{19}H_{28}O_4Na$, 343.1880.



36a

An oven dried 100 mL three necked flask was equipped with a magnetic stirring bar, septum, stopper, and an oven dried cold finger with an attached balloon. The flask was charged with alcohol **35a** (115 mg, 0.359 mmol) dissolved in a minimal amount of 1,4-dioxane (1.5 mL). The vessel was cooled to -60 °C in a cryogenic bath and ammonia (passed through a drying tube of barium oxide) was condensed into the vessel (*ca*. 35 mL). Sodium metal (large pieces in kerosene) (413 mg, 17.945 mmol, 50.0 equiv.) was freshly cut and added in a single portion, resulting in the formation of a blue solution, which was stirred for an additional 2 min. at -60 °C. The reaction was slowly quenched with methanol (10 mL) resulting in a cloudy white mixture. H_2O (10 mL) was slowly added to the reaction mixture and the whole was poured into a separatory funnel and extracted with ether (3 x 10 mL). The organic layers were combined and dried over $MgSO_4$, and concentrated to give crude **36a** which was purified via flash column chromatography (R_f = 0.22, hexanes-ethyl acetate, 3:1) to yield **36a** as a colorless oil (151 mg, 0.468 mmol, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.85 (s, 3H), 3.80-3.74 (m, 4H, containing: 3.80 (s, 3H)), 3.65-3.61 (m, 4H, containing: 3.65 (s, 3H)), 3.20-3.15 (m, 1H), 2.89-2.86 (m, 1H), 2.17 (s, 3H), 2.10-2.05 (m, 1H), 1.99-1.90 (m, 2H), 1.84-1.74 (m, 2H), 1.60-1.52 (m, 2H), 1.50-1.45 (m, 1H), 1.13 (d, 3H, J = 7.0 Hz), 0.79 (d, 3H, J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9, 149.9, 147.3, 135.0, 128.5, 122.5, 61.4, 60.7, 60.6, 60.1, 38.2, 34.9, 34.6, 27.1, 26.7, 23.4, 18.6, 18.5, 9.7. $[\alpha]_D^{20}$ +19.3 (c 0.900, $CHCl_3$); IR (neat) 3368, 2932, 2868, 2826, 1453, 1403, 1326, 1300, 1248, 1101, 1073, 1011 cm^{-1}. HRMS (ESI); m/z 345.2037 ([M + Na]); exact mass calculated for $C_{19}H_{30}O_4Na$, 345.2036.

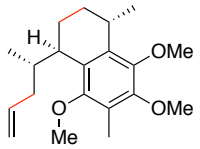


36d

A 25 mL single necked flask charged with alcohol **36a** (151 mg, 0.468 mmol) was equipped with a magnetic stirring bar and nitrogen inlet. The alcohol was dissolved in DCM (12 mL) and $NaHCO_3$ (472 mg, 5.620 mmol, 12.0 equiv.) and DMP (397 mg, 0.937 mmol, 2.0 equiv.) were added in sequence. The flask was purged with nitrogen and the reaction mixture was allowed to stir at ambient temperature for 2.5

h until TLC showed complete consumption of starting material. The mixture was concentrated and then eluted through a plug of silica (hexanes-ethyl acetate, 4:1). The crude aldehyde was purified via flash column chromatography (R_f = 0.34, hexanes-ethyl acetate, 9:1) to give **36d** as a colorless oil (119 mg, 0.371 mmol, 73%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.51 (t, 1H, *J* = 2.0 Hz), 3.84 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H), 3.61 (s, 3H), 3.17-3.11 (m, 1H), 2.78-2.76 (m, 1H), 2.41-2.27 (m, 3H), 2.17 (s, 3H), 2.04-1.97 (m, 1H), 1.84-1.79 (m, 2H), 1.51-1.48 (m, 1H), 1.15 (d, 3H, *J* = 7.0 Hz), 0.97 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.7, 152.8, 150.2, 147.7, 134.8, 127.7, 122.7, 60.7, 60.2, 60.1, 49.3, 36.6, 33.6, 27.3, 25.8, 23.4, 20.1, 19.6, 9.6. $[\alpha]_D^{20}$ +23.4 (*c* 0.950, $CHCl_3$); IR (neat) 2932, 2869, 2826, 2714, 1722, 1591, 1462, 1403, 1300, 1249, 1101, 1072, 1009 cm^{-1}. HRMS (ESI); *m/z* 343.1880 ([M + Na]); exact mass calculated for $C_{19}H_{28}O_4Na$, 343.1880. GC (Cyclosil-B, 175 °C isotherm): t_R = 43.78 (C_4:*R* or *S*, C_{11}:*S*, C_1:*S*), 49.68 (C_4:*R* or *S*, C_{11}:*S*, C_1:*S*) min.

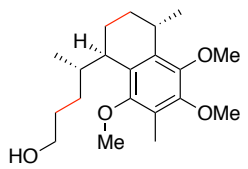
F. Experimental Data of Scheme 8



36e

A 25 mL three necked flask equipped with magnetic stirring bar, stopper, thermometer, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with methyltriphenylphosphonium bromide (321 mg, 0.899 mmol, 1.5 equiv.) dissolved in anhydrous THF (10 mL). A 1.0 M solution of *n*-butyllithium in hexanes (0.72 mL, 0.719 mmol, 1.2 equiv.) was added dropwise and the reaction mixture was allowed to stir at ambient temperature for 1 h. The vessel was cooled to 0 °C in an ice/water bath and a solution of **36d** (192 mg, 0.599 mmol) in anhydrous THF (2 mL) was added dropwise via syringe. The reaction mixture was allowed to stir at 0 °C for an additional 30 min. and was then concentrated and dissolved in a minimal amount of DCM and purified via flash column chromatography (R_f = 0.41, pentane-ether, 20:1) to yield **36e** as a colorless oil (154 mg, 0.484 mmol, 81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83-5.76 (m, 1H), 5.01-4.95 (m, 2H), 3.85 (s, 3H), 3.80 (s, 3H), 3.63 (s, 3H), 3.19-3.15 (m, 1H), 2.88-2.85 (m, 1H), 2.17 (s, 3H), 2.11-1.92 (m, 4H), 1.80-1.75 (m, 2H), 1.49-1.45 (m, 1H), 1.14 (d, 3H, *J* = 7.0 Hz), 0.76 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.2, 149.8, 147.3, 139.2, 135.0, 128.8, 122.5, 115.2, 60.7, 60.4, 60.1, 40.2, 38.1, 35.4, 27.2, 26.7, 23.4, 18.8, 18.3, 9.6. $[\alpha]_D^{20}$ +5.5 (*c* 0.655, $CHCl_3$); IR (neat) 2932, 2869, 2826, 1458, 1404, 1326, 1298, 1249, 1110, 1072, 1034, 1017, 908 cm^{-1}. HRMS (ESI); *m/z* 341.2084 ([M + Na]); exact mass calculated for $C_{20}H_{30}O_3Na$, 341.2087.

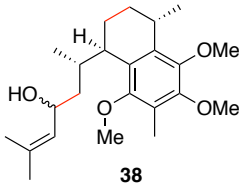
G. Experimental Data of Scheme 10



37

A 25 mL three-necked flask equipped with magnetic stirring bar, stopper, thermometer, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with olefin **36e** (15.0 mg, 0.047 mmol) dissolved in anhydrous THF (2 mL). 9-BBN dimer (23.0 mg, 0.094 mmol, 2.0 equiv.) was added and the reaction mixture was allowed to stir at room temperature for 3 h. The vessel was cooled to 0 °C in an ice/water bath and 4 M NaOH (0.5 mL) was added dropwise, maintaining the internal temperature of the vessel below 10 °C. A solution of ~30% H_2O_2 (0.5 mL) was then added dropwise, maintaining the internal temperature of the vessel below 10 °C. The vessel was allowed to warm to room temperature and stir for an additional 0.5 h. The vessel was then diluted with ether (15 mL) and the whole was poured into H_2O (15 mL) and extracted with ether (3 x 10 mL). The organic layers were combined and dried over $MgSO_4$, and concentrated to give crude **37** which was purified via flash column chromatography (R_f = 0.25, hexanes-ethyl acetate, 4:1) to yield **37** as a colorless oil (14.0 mg, 0. 042 mmol, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ SB-07-284 3.85 (s, 3H), 3.80 (s, 3H), 3.60-3.68 (m, 5H), 3.13-3.19 (m, 1H), 2.84-2.87 (m, 1H), 2.17 (s, 3H,), 1.91-2.17 (m, 2H), 1.75-1.82 (m, 2H), 1.51-1.68 (m, 4H), 1.31-1.38 (m, 2H), 1.14 (d, 3H, *J* = 7.0 Hz), 0.75 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 149.6, 147.1, 134.8, 128.6, 122.2, 63.4, 60.5, 60.2, 59.9, 37.5, 35.5, 31.3, 30.7, 27.0, 26.4, 23.3, 18.6, 18.1, 9.4; $[\alpha]_D^{20}$ +1.7 (*c* 0.7, $CHCl_3$); HRMS (ESI); *m/z* 359.2181 ([M + Na]); exact mass calculated for $C_{20}H_{32}O_4Na$, 359.2193.

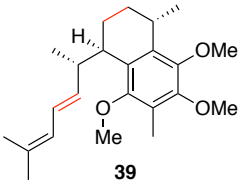
H. Experimental Data of Scheme 11



38

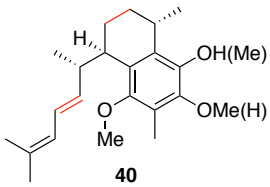
A 25 mL three necked flask equipped with a magnetic stirring bar, stopper, septum, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with a solution of isocrotylmagnesium bromide (303 mg, 2.247 mmol, 10.0 equiv.) in anhydrous THF (3 mL). *Preparation of isocrotylmagnesium bromide:* To a vial charged with magnesium turnings (137 mg, 5.618 mmol, 25.0 equiv.) was added 1-bromo-2-methyl-1-propene (230 μL, 2.247 mmol, 10.0 equiv.) and diluted with anhydrous THF (3 mL). 1,2-Dibromoethane (29 μL, 0.337 mmol, 1.5 equiv.) was added to activate the magnesium turnings and the reaction mixture was heated to 60 °C in an oil bath for 3 h, resulting in a brownish solution that was transferred to the reaction flask via cannula. A solution of aldehyde **36d** (72 mg, 0.225 mmol) in anhydrous THF (2 mL) was added dropwise via syringe to the reaction flask and was allowed to stir at ambient temperature for 15 min. The reaction was quenched by the slow addition of a saturated aqueous solution of $NaHCO_3$ (1 mL) and the whole was poured into H_2O (15 mL) and extracted with Et_2O (3 x 10 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated to give the crude mixture of C_{13} epimeric allylic alcohols, which were purified via flash column chromatography (R_f = 0.26-0.21, hexanes-ethyl acetate, 4:1) to yield **38** as a colorless oil (78 mg, 0.207 mmol, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.20-5.16 (m, 2H), 4.53-4.49 (m, 1H), 4.36-4.32 (m, 1H), 3.844 (s, 3H), 3.840

(s, 3H), 3.80 (s, 3H), 3.79 (s, 3H), 3.67 (s, 3H), 3.63 (s, 3H), 3.20-3.12 (m, 2H), 2.96-2.94 (m, 1H), 2.85-2.82 (m, 1H), 2.42 (bs, 1H), 2.16 (s, 6H), 2.09-2.04 (m, 1H), 1.99-1.92 (m, 2H), 1.83-1.79 (m, 4H), 1.73 (s, 3H), 1.71 (s, 3H), 1.68 (s, 3H), 1.67 (s, 3H), 1.61-1.55 (m, 2H), 1.41-1.36 (m, 1H), 1.25-1.20 (m, 1H), 1.14 (d, 3H, J = 6.9 Hz), 1.13 (d, 3H, J = 6.9 Hz), 0.79 (d, 3H, J = 7.1 Hz), 0.77 (d, 3H, J = 7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.2, 152.9, 149.84, 149.79, 147.2, 147.1, 135.0, 134.9, 134.5, 134.4, 129.0, 128.46, 128.42, 122.5, 122.4, 110.3, 67.5, 66.7, 60.7, 60.6, 60.5, 60.4, 60.03, 60.02, 44.3, 43.5, 37.2, 35.2, 34.6, 34.0, 27.2, 26.9, 26.81, 26.75, 25.94, 25.92, 23.4, 23.3, 19.2, 18.9, 18.5, 18.43, 18.35, 18.2, 9.71, 9.69. $[\alpha]_D^{20}$ +1.82 (c 1.100, $CHCl_3$); IR (neat) 3443, 2932, 2868, 1462, 1454, 1403, 1098, 1074, 1030, 1009 cm^{-1}. HRMS (ESI); m/z 399.2503 ([M + Na]); exact mass calculated for $C_{23}H_{36}O_4Na$, 399.2506.



39

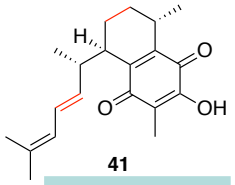
An oven-dried 5 dram vial was equipped with a magnetic stirring bar and charged with a solution of **38** (23 mg, 0.061 dissolved in acetonitrile (2 mL). (+/-)-Camphor-10-sulfonic acid (2 mg, 0.006 mmol, 0.10 equiv.) was added and the reaction mixture was allowed to stir at ambient temperature for 30 min, until TLC showed complete consumption of the starting material. The reaction was concentrated and purified via flash column chromatography (R_f = 0.33, pentane-diethyl ether, 20:1) to yield **39** as a colorless oil (21 mg, 0.059 mmol, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06 (dd, 1H, $J_{1,2}$ = 10.5, 15.0 Hz), 5.78 (broad d, 1H, J = 10.5 Hz), 5.65 (dd, 1H, $J_{1,2}$ = 7.5, 10.5 Hz), 4.85 (broad d, 1H, J = 7.0 Hz), 3.85 (s, 3H), 3.79 (s, 3H), 3.67 (s, 3H), 3.19-3.14 (m, 1H), 2.95-2.92 (m, 1H), 2.87-2.81 (m, 1H), 2.16 (s, 3H), 2.01-1.93 (m, 1H), 1.82-1.77 (m, 2H), 1.74 (s, 3H), 1.70 (s, 3H), 1.49-1.46 (m, 1H), 1.14 (d, 3H, J = 7.0 Hz), 0.87 (d, 3H, J = 7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.8, 149.8, 147.2, 138.2, 134.9, 132.6, 128.0, 125.6, 125.3, 122.5, 60.8, 60.4, 60.1, 41.7, 37.6, 27.1, 26.7, 26.1, 23.4, 19.3, 18.4, 17.6, 9.6. $[\alpha]_D^{20}$ -20.82 (c 0.730, $CHCl_3$); IR (neat) 2956, 2931, 2867, 1457, 1404, 1072, 1026, 967 cm^{-1}. HRMS (ESI); m/z 381.2402 ([M + Na]); exact mass calculated for $C_{23}H_{34}O_3Na$, 381.2400.



40

A 25 mL three necked flask equipped with a magnetic stirring bar, stopper, thermometer, and reflux condenser fitted with a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with **39** (24 mg, 0.067 mmol) dissolved in anhydrous DMF (3.5 mL). Sodium ethanethiolate (56 mg, 0.670 mmol, 10.0 equiv.) was added and the reaction vessel was heated to 100 ºC in an oil bath and allowed to stir for 12 h. The vessel was cooled to ambient temperature, acidified with 1.0 N aq. HCl, and extracted with diethyl ether (3 x 10 mL). The organic layers were combined, washed with H_2O (10 mL) and saturated aqueous NaCl (10 mL), dried over $MgSO_4$, and concentrated. Purification by flash column chromatography (R_f = 0.24, pentane-diethyl ether, 10:1) gave **40** as a ~2:1 mixture of mono-demethylated

products (15 mg, 0.044 mmol, 65%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.08 (dd, 1H, $J_{1,2}$ = 7.5, 10.5 Hz), 5.79 (d, 1H, J = 10.5 Hz), 5.65 (dd, 1H, $J_{1,2}$ = 7.5, 10.5 Hz), 5.50 (s, 1H), 3.77 (s, 3H), 3.67 (s, 3H), 3.11-3.06 (m, 1H), 2.95-2.93 (m, 1H), 2.86-2.80 (m, 1H), 2.16 (s, 3H), 2.05-1.97 (m, 1H), 1.84-1.77 (m, 2H), 1.77 (s, 3H), 1.70 (s, 3H), 1.48-1.45 (m, 1H), 1.15 (d, 3H, J = 7.0 Hz), 0.88 (d, 3H, J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 145.9, 141.2, 138.1, 133.8, 132.6, 125.6, 125.3, 123.9, 115.7, 61.6, 60.6, 41.8, 37.4, 27.5, 26.8, 26.1, 23.2, 19.5, 18.4, 17.4, 9.4 (only signals from the major product are reported). $[\alpha]_D^{20}$ +1.20 (*c* 0.500, $CHCl_3$); IR (neat) 3533, 3418, 2931, 2868, 2830, 1608, 1454, 1416, 1291, 1250, 1099, 1056, 1021, 963 cm^{-1}. HRMS (ESI); *m/z* 367.2244 ([M + Na]); exact mass calculated for $C_{22}H_{32}O_3Na$, 367.2244.

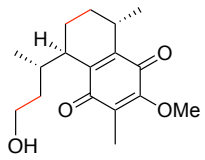


41

nor-elisabethadione

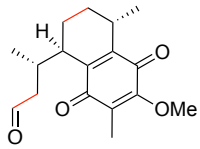
(+)-*nor*-elisabethadione (41): A 5 dram vial equipped with a magnetic stirring bar was charged with **40** (15 mg, 0.044 mmol) dissolved in acetonitrile (4.0 mL) and cooled to 0 °C in an ice/water bath. An aqueous 0.10 M solution of cerium ammonium nitrate (1.3 mL, 0.130 mmol, 3.0 equiv.) was added and the reaction mixture was allowed to stir at 0 °C for an additional 5 min. The red reaction mixture was diluted with H_2O (5 mL) and extracted with diethyl ether (3 x 10 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated to give the crude product, which was used in the subsequent reaction without further purification. An oven-dried 5 dram vial equipped with a magnetic stirring bar and nitrogen inlet was charged with a solution of crude dione dissolved in 2,6-lutidine (2.0 mL). Lithium iodide (17 mg, 0.130 mmol, 3.0 equiv.) was added and the reaction mixture was heated to 80 ºC in an oil bath and allowed to stir for 3 h. The reaction mixture was allowed to cool to ambient temperature and poured into H_2O (15 mL) and extracted with Et_2O (3 x 10 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated. Purification by flash column chromatography (R_f = 0.34, pentane-diethyl ether, 10:1) furnished **41** (6 mg, 0.020 mmol, 46% over 2 steps) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (s, 1H), 5.98 (dd, 1H, $J_{1,2}$ = 10.5, 15.0 Hz), 5.68 (d, 1H, J = 10.5 Hz), 5.32 (dd, 1H, $J_{1,2}$ = 8.5, 15.0 Hz), 2.97-2.93 (m, 2H), 2.43-2.36 (m, 1H), 1.94-1.89 (m, 1H), 1.86 (s, 3H), 1.72 (s, 3H), 1.64 (s, 3H), 1.60-1.57 (m, 1H), 1.50-1.47 (m, 1H), 1.10 (d, 3H, J = 7.0 Hz), 1.03 (d, 3H, J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.6, 183.2, 150.4, 149.1, 142.0, 137.0, 133.8, 125.6, 124.9, 117.3, 41.6, 37.3, 26.3, 26.1, 25.2, 21.1, 19.2, 18.7, 18.4, 8.3. $[\alpha]_D^{20}$ +147.50 (*c* 0.080, $CHCl_3$); IR (neat) 3389, 2961, 2923, 2870, 1650, 1633, 1454, 1376, 1336, 1233, 1154, 1041, 962 cm^{-1}. HRMS (ESI); *m/z* 337.1773 ([M + Na]); exact mass calculated for $C_{20}H_{26}O_3Na$, 337.1774.

I. Experimental Data of Scheme 12



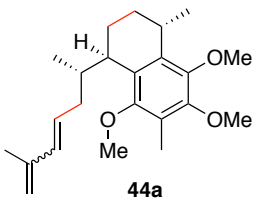
43a

A 25 mL single necked flask charged with alcohol **36a** (100 mg, 0.310 mmol) was equipped with a magnetic stirring bar and nitrogen inlet. The alcohol was dissolved in 4 mL of solvent mixture of CH_3CN:H_2O (1:1). Above reaction flask was cooled down to 0 ˚C and CAN (561 mg, 1.023 mmol) was added. Upon the complete consumption of starting material as judged by TLC (usually within 10-15min) the reaction was poured onto brine, and was extracted with Et_2O three times. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude material was purified *via* flash column chromatography (R_f = 0.21, hexanes-ethyl acetate, 8:2) to give quinone **43a** as a viscous yellow liquid (61.6 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.0 (s, 3H), 3.87-3.80 (m, 1H), 3.71-3.67 (m, 1H), 3.00 (quin, *J* = 6.3 Hz, 1H), 2.87-2.85 (m, 1H), 2.35 (bs, 1H), 2.04-1.96 (m, 1H), 1.92 (s, 3H), 1.85-1.62 (m, 3H), 1.55-1.53 (m, 2H), 1.51-1.46 (m, 1H), 1.07 (d, *J* = 7 Hz, 3H), 0.83 (d, *J* = 7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.06, 183.0, 155.57, 146.46, 144.06, 128.79, 60.85, 60.67, 37.91, 33.03, 32.82, 26.16, 26.01, 20.93, 17.63, 17.21, 8.82. $[\alpha]_D^{20}$ +162.4 (*c* 0.25, $CHCl_3$); HRMS (ESI); *m/z* 315.1563 ([M + Na]); exact mass calculated for $C_{17}H_{24}O_4Na$, 315.1567.



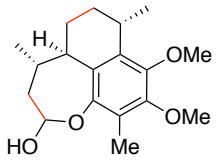
44

A 25 mL single necked flask charged with alcohol quinone **43a** (30 mg, 0.103 mmol) was equipped with a magnetic stirring bar and nitrogen inlet. The alcohol was dissolved in DCM (12 mL) and DMP (65.3 mg, 0.1539 mmol, 1.5 equiv.) and drop of H2O were added in sequence at 0 ˚C. The flask was purged with nitrogen and the reaction mixture was allowed to stir at ambient temperature for 3h until TLC showed complete consumption of starting material. The mixture was concentrated and then eluted through a plug of silica (hexanes-ethyl acetate, 4:1). The crude aldehyde was purified via flash column chromatography (Rf = 0.34, hexanes-ethyl acetate, 9:1) to give quinone aldehyde **44** as a yellow oil (19.1 mg, 0.066 mmol, 64%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.74 (t, *J* = 2.3 Hz, 1H), 3.99 (s, 3H), 2.98 (quin, *J* = 7.0 Hz, 1H), 2.79-2.77 (m, 1H), 2.48-2.44 (m, 1H), 2.34-2.32 (m, 2H), 1.94 (s, 3H), 1.86-1.80 (m, 1H), 1.75-1.72 (m, 1H), 1.68-1.61 (m, 1H), 1.51-1.49 (m, 1H), 1.08 (d, *J* = 7 Hz, 3H), 0.93 (d, *J* = 7 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 202.32, 188.59, 183.07, 155.59, 146.69, 143.42, 128.63, 60.80, 49.85, 35.36, 31.69, 26.34, 25.80, 20.90, 18.56, 18.14, 8.83.



44a

A 25 mL 3-necked flask equipped with a magnetic stirring bar, stoppers, and a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with β-methylallyltriphenylphosphonium chloride (33 mg, 0.094 mmol, 1.5 equiv.) and anhydrous THF (2.0 mL). 1.6 M n-BuLi (47 µL, 0.075 mmol, 1.2 equiv.) was added dropwise via syringe and the reaction mixture was allowed to stir at ambient temperature for 1 h. A solution of **36d** (20 mg, 0.062 mmol) dissolved in anhydrous THF was added and the reaction mixture was allowed to stir at ambient temperature for 3 h. The reaction mixture was concentrated and dissolved in a minimal amount of DCM and purified via flash column chromatography (R_f = 0.44, pentane-ether, 20:1) to yield colorless oil **44a** as a mixture of *E*- and *Z*-isomers (14 mg, 0.040 mmol, 64%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.14 (d, 1H, *J* = 15.8 Hz), 5.85 (d, 1H, *J* = 12.0 Hz), 5.69-5.64 (m, 1H), 5.49-5.43 (m, 1H), 4.91-4.72 (m, 4H), 3.86 (s, 3H), 3.85 (s, 3H), 3.80 (bs, 3H), 3.63 (s, 3H), 3.62 (s, 3H), 3.19-3.10 (m, 2H), 2.87-2.84 (m, 2H), 2.35-2.26 (m, 1H), 2.172 (s, 3H), 2.167 (s, 3H), 2.14-1.93 (m, 6H), 1.85 (s, 3H), 1.83 (s, 3H), 1.80-1.75 (m, 4H), 1.50-1.45 (m, 2H), 1.27-1.22 (m, 2H), 1.14 (d, 6H, *J* = 6.9 Hz), 0.80 (d, 3H, *J* = 7.0 Hz), 0.77 (d, 3H, *J* = 6.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.2, 153.1, 149.80, 149.77, 147.3, 142.5, 142.3, 135.04, 134.97, 133.7, 132.0, 131.14, 131.10, 128.74, 128.68, 122.5, 115.3, 114.1, 60.7, 60.36, 60.34, 60.11, 60.08, 39.3, 39.0, 38.6, 35.8, 35.5, 34.5, 27.2, 26.7, 26.6, 23.6, 23.45, 23.39, 19.0, 18.8, 18.5, 18.4, 9.62, 9.60. $[\alpha]_D^{20}$ -31.60 (*c* 0.500, $CHCl_3$); IR (neat) 2955, 2932, 2867, 1455, 1403, 1326, 1299, 1248, 1102, 1073, 1026, 1010, 967 cm^{-1}. HRMS (ESI); *m/z* 381.2398 ([M + Na]); exact mass calculated for $C_{23}H_{34}O_3Na$, 381.2400.

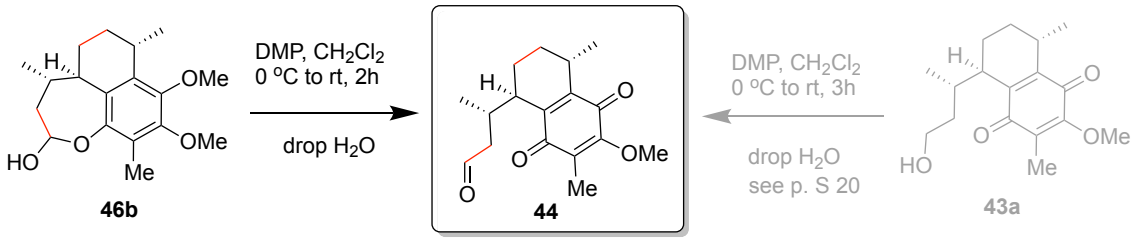


46b

In a glovebox, a 1 dram vial was charged with aldehyde **36d** (30 mg, 0.0936 mmol) dissolved in deuterated chloroform (1.0 mL). Trimethylsilyl iodide (40 µL, 0.281 mmol, 3.0 equiv.) was added and the reaction mixture was transferred to an NMR tube *via* pipette and sealed from the outside environment. Upon completion of the reaction (as judged by NMR analysis after 1.5h), the whole was poured into H_2O (10 mL) and extracted with Et_2O (3 x 5 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated. Purification by flash column chromatography (R_f = 0.26, hexanes-ethyl acetate, 4:1) furnished **46b** (12.9 mg, 0.0421 mmol, 45%) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.67-5.63 (m, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 3.10-3.05 (m, 1H), 2.81 (d, *J* = 5.3 Hz, 1H), 2.68-2.66 (m, 1H), 2.20 (s, 3H), 1.89-1.83 (m, 1H), 1.76-1.59 (m, 4H), 1.54-1.5 (m, 2H), 1.19 (d, *J* = 7 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.74, 147.50, 145.19, 132.71, 127.62, 123.02, 93.72, 60.38, 59.92, 37.47, 37.42, 31.47, 27.38, 25.65, 21.23, 20.57, 19.46, 10.33. $[\alpha]_D^{20}$ + 3.6 (*c* 0.15, $CHCl_3$); HRMS (ESI); *m/z* 329.1719 ([M + Na]); exact mass calculated for $C_{18}H_{26}O_4Na$, 329.1723.

The structure of this hemiacatal (**46b**) was further confirmed by its conversion to the quinone-

aldehyde **44**, which was synthesized independently from the corresponding alcohol **43b** (Scheme below and Scheme 12A in the paper).

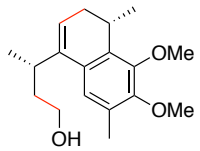


A 10mL single necked flask charged with compound **46b** (10 mg, 0.0326 mmol) was equipped with a magnetic stirring bar and nitrogen inlet. The lactol **46b** was dissolved in DCM (2 mL) and DMP (20.8 mg, 0.0489 mmol, 1.5 equiv.) and drop of H_2O were added in sequence at 0 ˚C. The flask was purged with nitrogen and the reaction mixture was allowed to stir at ambient temperature for 2h until TLC showed complete consumption of starting material. The mixture was concentrated and then eluted through a plug of silica (hexanes-ethyl acetate, 4:1). The crude product was purified via flash column chromatography (R_f = 0.34, hexanes-ethyl acetate, 9:1) and it was identified as compound **44** by comparison with spectra prepared by an alternate route (Scheme 12A).

J. Experimental Data of Scheme 13

Experimental procedures, 1H, 13C spectra and Gas Chromatogram data of compound **27**, **46**, **47**, **48**, **50**, **51** and **52** were reported in our previous communication.[2]

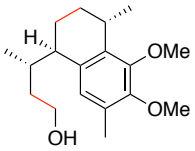
K. Experimental Data of Scheme 15



52

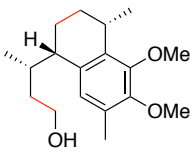
A 50 mL three-necked flask equipped with magnetic stirring bar, stopper, thermometer, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with olefin **51** (231.8 mg, 0.85 mmol) dissolved in anhydrous THF (20 mL). 9-BBN dimer (519.1 mg, 2.13 mmol, 2.5 equiv.) was added in small portions and the reaction mixture was allowed to stir at room temperature for 2 h. The vessel was cooled to 0 °C in an ice/water bath and 4 M NaOH (2.0 mL) was added dropwise, maintaining the internal temperature of the vessel below 10 °C. A solution of ~30% H_2O_2 (1.5 mL) was then added dropwise, maintaining the internal temperature of the vessel below 10 °C. The vessel was allowed to warm to room temperature and stir for an additional 0.5 h. The vessel was then diluted with ether (10 mL) and neutralized with 10% H_2SO_4 until pH ~7 was achieved. The whole was poured into water (15 mL) and

extracted with ether (3 x 10 mL). The organic layers were combined and dried over $MgSO_4$, and concentrated to give crude **52** which was purified via flash column chromatography (R_f = 0.42, hexanes-ethyl acetate, 2:1) to yield **52** as a colorless oil (245.3 mg, 0.85mmol, >99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (s, 1H), 5.69 (d, 1H, *J* = 6.4 Hz), 3.88 (s, 3H), 3.83 (s, 3H), 3.72-3.63 (m, 2H), 3.27 (quintet, 1H, *J* = 6.8 Hz), 2.95 (sextet, 1H, *J* = 6.8 Hz), 2.42 (dd, 1H, $J_{1,2}$ = 6.8, 16.8 Hz), 2.25 (s, 3H), 2.17 (dd, 1H, $J_{1,2}$ = 6.8, 10.0 Hz), 1.87 (sextet, 1H, *J* = 6.8 Hz), 1.66 (sextet, 1H, *J* = 6.8 Hz), 1.22 (d, 3H, *J* = 6.8 Hz), 1.05 (d, 3H, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 149.7, 139.9, 133.7, 130.0, 129.0, 120.5, 119.3, 61.4, 60.8, 60.0, 39.8, 30.3, 25.2, 22.8, 20.4, 19.9, 16.2. $[\alpha]_D^{20}$ -30.4 (*c* 0.63, $CHCl_3$). HRMS (ESI); *m/z* 313.1780 ([M + Na]); exact mass calculated for $C_{18}H_{26}O_3Na$, 313.1780.



53-C_4(*R*)

An oven dried 50 mL three necked flask was equipped with a magnetic stirring bar, septum, stopper, and an oven dried cold finger with an attached balloon. The flask was charged with alcohol **52** (187.8 mg, 0.65 mmol) dissolved in a minimal amount of THF (1 mL). The vessel was cooled to -78 °C in a dry ice/acetone bath and ammonia (passed through a drying tube of barium oxide) was condensed into the vessel (*ca*. 20 mL). Lithium metal (40% dispersion in mineral oil) (168 mg, 9.69 mmol, 15 equiv.) was added, resulting in the formation of a blue solution, which was stirred for an additional 15 min. at -78 °C. The reaction was slowly quenched with methanol (10 mL) resulting in a cloudy white mixture. Water (10 mL) was slowly added to the reaction mixture and the whole was poured into a separatory funnel and extracted with ether (3 x 10 mL). The organic layers were combined and dried over $MgSO_4$, and concentrated to give crude **53-(C_4-*R*)** which was purified via flash column chromatography (R_f = 0.24, hexanes-ethyl acetate, 3:1) to yield **53-(C_4-*R*** as a colorless oil (188.3 mg, 0.64 mmol, >99%). *Note*: ammonia:THF ratio is critical to diastereoselectivity of the reduction. A high ammonia:THF ratio and large excess of lithium gives the best selectivities (>95% *de* determined by GC). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.74 (s, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 3.78-3.67 (m, 2H), 3.16 (quintet, 1H, *J* = 6.0 Hz), 2.62 (q, 1H, *J* = 6.0 Hz), 2.22 (s, 3H), 2.11 (quintet, 1H, *J* = 6.5 Hz), 1.89-1.19 (m, 2H), 1.76-1.65 (m, 2H), 1.64-1.48 (m, 3H), 1.17 (d, 3H, *J* = 7.0 Hz), 0.76 (d, 3H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.7, 149.2, 135.2, 135.1, 128.9, 125.8, 61.8, 60.6, 60.0, 40.4, 38.8, 35.6, 28.1, 27.5, 22.5, 18.9, 16.5, 16.0. $[\alpha]_D^{20}$ +2.51 (*c* 2.11, $CHCl_3$), IR (neat) 3360, 1614, 1236, 1014 cm^{-1}. HRMS (ESI); *m/z* 315.1910 ([M + Na]); exact mass calculated for $C_{18}H_{28}O_3Na$, 315.1936.

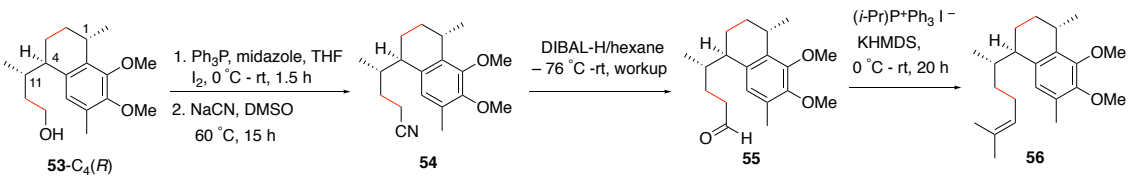


53-C_4(*S*)

A vial containing ~ 0.5 mg sample of alcohol **52** was treated with a stir bar, 30 mol% Pd/C and MeOH (1

mL). A stream of H_2 was introduced and the vial capped. The reaction was allowed to stir overnight, then was poured into water and extracted with ether. The organic extracts were combined, dried (MgSO4) and concentrated *in vacuo* to afford the title compound with its C_4 epimer in a 97:3 ratio (1H NMR). Rf 0.30 (30:70 EtOAc:Hexanes); 1H NMR (500 MHz, CDCl3) δH 6.84 (s, 1H), 3.88 (s, 3H), 3.80 (s, 3H), 3.67-3.62 (m, 1H), 3.54-3.62 (m, 1H), 3.14-3.12 (m, 1H), 2.76-2.71 (m, 1H), 2.38-2.33 (m, 1H), 2.21 (s, 3H), 1.72-1.68 (m, 3H), 1.67-1.51 (m, 2H), 1.41-1.35 (m, 1H), 1.30-1.24 (m, 1H), 1.19 (d, 3H, *J* 7 Hz), 1.09 (d, 3H, *J* 7 Hz).

L. Experimental Data of Scheme 16



A two-necked 15 mL round bottomed flask equipped with magnetic stir bar, gas inlet and glass stopper was flame-dried, purged with nitrogen and charged with a solution of alcohol **53** (100 mg, 0.342 mmol, 92:8 at C_{11} and ~85:15 at C_4) in dry THF (3.0 mL). The solution was cooled to 0 °C and treated with triphenylphosphine (91 mg, 0.345 mmol), imidazole (47 mg, 0.684 mmol), and iodine chips (88 mg, 0.345 mmol). The reaction was warmed to rt and stirred for 1.5 h. The whole was transferred to a dry flask and the solvent removed *in vacuo*. Dry DMSO (2.0 mL) was added to the crude iodide, followed by solid NaCN (34 mg, 0.68 mmol) and a magnetic stir bar. The reaction was heated to 60 °C and stirred for 1.5 h, then poured into water and extracted with ether. The organic phases were combined, dried ($MgSO_4$) and concentrated to an oil. Purification *via* column chromatography (13:87 EtOAc:Hexanes) afforded nitrile **54** as an oil.

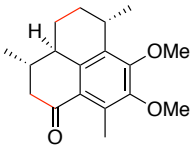
A three-necked 25 mL round bottomed flask equipped with magnetic stir bar, gas inlet, rubber septum, and thermometer adapter was flame-dried, purged with nitrogen and charged with a solution of nitrile **54** (59 mg, 0.196 mmol, 92:8 at C_{11} and ~85:15 at C_{10}) in dry THF (2.0 mL). The solution was cooled to -76 °C and treated with DIBAL-H (0.49 mL, 1.0 M in Hexanes). The reaction was warmed to 0 °C and stirred for 3.5 h, then treated with a satd. solution of NH_4Cl:HCl (6:1, 0.4 mL). The whole was warmed to rt and treated with a solution of Rochelle's salt and stirred for 20 min, then poured into water and extracted with ether. The organic phases were combined, dried ($MgSO_4$) and concentrated to a clear film.

A 2-necked 15 mL round bottomed flask equipped with magnetic stir bar, gas inlet and glass stopper was flame-dried, purged with nitrogen and charged with solid KHMDS (78 mg, 0.392 mmol). Dry THF (2.0 mL) was added, followed by isopropyltriphenylphosphonium iodide (169 mg, 0.392 mmol) in a single portion. The reaction was stirred for 2 h at rt, then cooled to 0 °C and treated with a solution of the aldehyde **55** prepared above in THF (2.0 mL). The reaction was warmed to rt and stirred overnight for 20.5

h. The whole was filtered through a fritté funnel and the ether rinsings/filtrate were concentrated *in vacuo* and the residue purified by column chromatography (isocratic hexanes, then 10:90 EtOAc:Hexanes) to afford alkene **56** as an oil. R_f 0.24 (5:95 EtOAc:Hexanes). The spectral data matched with the literature value.[3] ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.73 (s, 1H), 5.18-5.14 (m, 1H, major diastereomer, 85%), 5.01 (m, 1H, minor diastereomer, 15%), 3.88 (s, 3H), 3.80 (s, 3H), 3.78-3.67 (m, 2H), 3.15 (m, 1H), 2.65-2.63 (m, 1H), 2.22 (s, 3H), 1.88-2.11 (m, 3H), 1.85-1.79 (m, 2H), 1.72 (s, 3H), 1.63 (s, 3H), 1.51-1.33 (m, 4H), 1.17 (d, 3H, J = 7.0 Hz), 0.72 (d, 3H, J = 7.0 Hz).

M. Experimental Data of Scheme 17

Experimental procedures, ^{1}H, ^{13}C spectra and X-ray data of compound **57** were reported in our previous communication.[2]

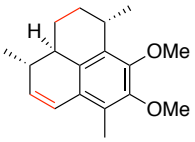


57

A 25 mL three-necked flask equipped with a magnetic stirring bar, septum, thermometer, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with anhydrous DCM (2.0 mL) and dimethyl sulfoxide (0.03 mL) and cooled to -78 °C via dry ice/acetone bath. A 2.0 M solution of oxalyl chloride (0.13 mL) was added and allowed to stir for 15 min. A solution of alcohol **53** (70.5 mg, 0.21 mmol) in anhydrous DCM (1.0 mL) was added and allowed to stir for 30 min. Triethylamine (0.13 mL) was added and allowed to stir for 15 min. The vessel was allowed to warm to room temperature and the whole was poured into water (10 mL) and extracted with ether (3 x 10 mL). The organic layers were combined and dried over $MgSO_4$, and concentrated to give the crude aldehyde, which was used for the next reaction without further purification. Flash column chromatography of crude aldehyde led to the formation of a cyclized product. The crude aldehyde was dissolved in THF (1.0 mL) and *t*-butyl alcohol (1.0 mL) in a 5 dram vial. A solution of 1.0 M 2,3-dimethyl-2-butene in THF (1.0 mL) was added to the vial followed by a solution of $NaClO_2$ (65.4 mg, 0.72 mmol, 3.0 equiv.) and NaH_2PO_4 (86.7 mg, 0.72 mmol, 3.0 equiv.) dissolved in deionized water (1.0 mL). The reaction mixture was allowed to stir for 1 h then the whole was poured into water (10 mL) and extracted with ether (3 x 10 mL). The organic layers were combined and dried over $MgSO_4$, concentrated, and azeotroped with benzene to ensure all water has been removed. A 25 mL three-necked flask equipped with a magnetic stirring bar, septum, thermometer, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with crude acid dissolved in anhydrous DCM (3.0 mL) and cooled to 0 °C via ice/water bath. A 2.0 M solution of oxalyl chloride in DCM (0.14 mL, 0.29 mmol, 1.2 equiv.) was added and the vessel was allowed to warm to room temperature and stir for 1 h. The vessel was re-cooled to 0 °C and $AlCl_3$ (48.2 mg, 0.36 mmol, 1.5 equiv.) was added and the vessel was allowed to warm to room temperature and stir for 30 min. The vessel was re-cooled to 0 °C and the reaction was quenched by the slow addition of water (5 mL). The whole was poured into water and extracted with ether (3 x 10 mL). The organic layers were combined

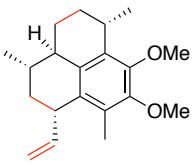
and dried over $MgSO_4$, and concentrated to give crude ketone **57** which was purified via flash column chromatography (R_f = 0.29, hexanes-ethyl acetate, 9:1) to give a mixture of diastereomers as a colorless oily solid. Recrystallization with methanol afforded colorless needles as a single diastereomer of **57** (28.9 mg, 0.10 mmol, 47 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 (s, 3H), 3.75 (s, 3H), 3.23 (sextet, 1H, J = 7.2 Hz), 2.62 (dd, 1H, $J_{1,2}$ = 3.8, 16.4 Hz), 2.52 (s, 3H), 2.36-2.26 (m, 2H), 2.18-2.12 (m, 2H), 1.80-1.77 (m, 1H), 1.42-1.37 (m, 1H), 1.23 (d, 3H, J = 6.8 Hz), 1.13-1.09 (m, 4H containing 1.12 (d, 3H, 6.4 Hz)). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.2, 155.3, 150.3, 142.6, 133.7, 133.2, 127.7, 60.6, 60.2, 49.3, 43.8, 35.6, 31.3, 28.6, 27.2, 23.7, 19.6, 14.0. mp = 101.5-103.5, $[\alpha]_D^{20}$ +59.4 (c 1.33, $CHCl_3$), IR (neat) 1673, 1448, 1254, 1071 cm^{-1}. HRMS (ESI); m/z 311.1624 ([M + Na]); exact mass calculated for $C_{18}H_{24}O_3Na$, 311.1623.

N. Experimental Data of Scheme 18



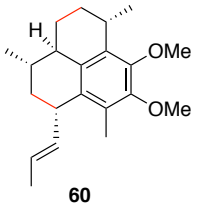
58

Ketone **57** (16 mg, 0.055 mmol) was dissolved in ethanol (1.0 mL) in a 5 dram vial. $NaBH_4$ (6 mg, 0.165 mmol, 3.0 equiv.) was added to the reaction mixture and was allowed to stir at room temperature for 3.5 h. The whole was poured into water and extracted with ether (3 x 10 mL). The organic layers were combined and dried over $MgSO_4$, and concentrated to give the crude alcohol, which was used in the subsequent reaction without further purification. The crude alcohol was dissolved in anhydrous DCM (1.0 mL) in an oven-dried 5 dram vial. Camphorsulfonic acid (3.0 mg, 0.011 mmol, 0.20 equiv.) was added and the reaction was allowed to stir at room temperature for 45 min. The whole was poured into water and extracted with ether (3 x 10 mL). The organic layers were dried over $MgSO_4$, and concentrated to give crude vinylarene **58** which was purified via flash column chromatography (R_f = 0.36, hexanes-ethyl acetate, 19:1) to give **58** as a colorless oil (15 mg, 0.055 mmol, >99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (dd, 1H, $J_{1,2}$ = 2.8, 9.6 Hz), 5.75 (dd, 1H, $J_{1,2}$ = 2.0, 9.6 Hz), 3.86 (s, 3H), 3.79 (s, 3H), 3.11 (sextet, 1H, J = 6.8 Hz), 2.31-2.23 (m, 4H containing 2.23 (s, 3H)), 2.14-2.02 (m, 3H), 1.39-1.26 (m, 5H containing 1.27 (d, 3H, J = 6.8 Hz)), 1.19 (d, 3H, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 149.7, 134.6, 133.5, 132.3, 128.3, 125.2, 123.9, 60.4, 60.3, 41.2, 34.7, 31.8, 29.4, 26.5, 22.6, 19.8, 11.4. $[\alpha]_D^{20}$ +25.9 (c 0.92, $CHCl_3$). HRMS (ESI); m/z 295.1692 ([M + Na]); exact mass calculated for $C_{18}H_{24}O_2Na$, 295.1674. GC (poly(dimethylsiloxane), 200 °C isotherm): t_R = 28.44 (C_{11}:S, C_4:R, C_1:S) min.



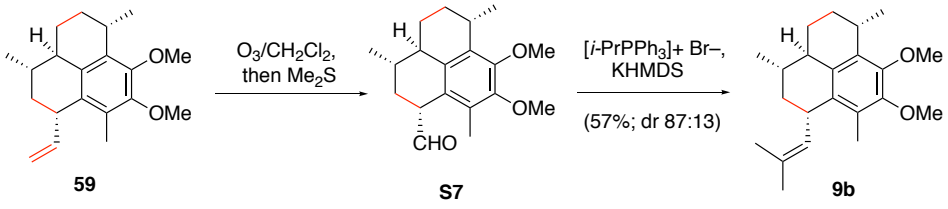
59

General procedure of Ni(II)-catalyzed hydrovinylation was followed. (99%, >99% *de* as determined by NMR using complex of **L1**). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.76 (ddd, 1H, $J_{1,2,3}$ = 7.5, 10.0, 17.5 Hz), 4.95-4.91 (m, 2H), 3.86 (s, 3H), 3.78 (s, 3H), 3.65 (q, 1H, J = 8.0 Hz), 3.20 (sextet, 1H, J = 7.5 Hz), 2.16 (s, 3H), 2.09-2.02 (m, 4H), 1.38-1.34 (m, 2H), 1.29-1.24 (m, 5H containing 1.26 (d, 3H, J = 6.5 Hz)), 1.06 (d, 3H, J = 6.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.6, 144.0 (2 x C), 135.6, 133.4, 132.7, 128.5, 112.9, 60.4, 60.1, 43.2, 42.0, 40.5, 34.4, 31.2, 28.7, 27.0, 24.0, 20.5, 12.8. $[\alpha]_D^{20}$ +29.3 (*c* 0.75, $CHCl_3$). HRMS (ESI); *m/z* 323.1977 ([M + Na]); exact mass calculated for $C_{20}H_{28}O_2Na$, 323.1987. GC (poly(dimethylsiloxane), 200 °C isotherm): t_R = 31.21 (C_{13}:*S*, C_{11}:*S*, C_4:*R*, C_1:*S*) min.

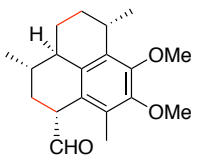


60

A 25 mL three-necked flask equipped with a magnetic stirring bar, stoppers, and a reflux condenser fitted with a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with olefin **59** (17 mg, 0.055 mmol) and 2-methyl-2-butene (5.0 mL). Grubb's 2nd generation catalyst (5 mg, 0.005 mmol, 10.0%) was added and the reaction mixture was heated to reflux in an oil bath (40 °C). The reaction was allowed to stir for 6 h before cooling to ambient temperature. The whole was concentrated and eluted through a plug of silica (R_f = 0.33, hexanes-ethyl acetate, 19:1) to give **60** (14 mg, 0.045 mmol, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37-5.34 (m, 2H), 3.86 (s, 3H), 3.78 (s, 3H), 3.61-3.55 (m, 1H), 3.25-3.15 (m, 1H), 2.15 (s, 3H), 2.08-2.01 (m, 3H), 1.75-1.73 (m, 1H), 1.64 (d, 3H, J = 4.1 Hz), 1.56-1.51 (m, 1H), 1.38-1.30 (m, 2H), 1.28-1.24 (m, 4H, containing 1.26 (d, 3H, J = 6.9 Hz), 1.04 (d, 3H, J = 6.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 149.4, 136.8, 135.5, 133.6, 133.3, 128.5, 123.5, 60.4, 60.1, 43.3, 41.0, 40.9, 34.5, 31.2, 28.7, 27.0, 24.0, 20.5, 18.0, 12.8.



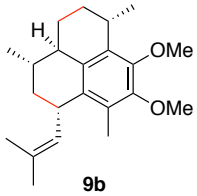
59 **S7** **9b**



S7

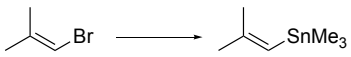
Olefin **59** (22.2 mg, 0.074 mmol) was dissolved in anhydrous DCM (2.0 mL) in a 5 dram vial. The vessel was cooled to -78 °C via acetone/dry ice bath and ozone was introduced via bubbling through a glass pipette until a persistent blue color was observed throughout the solution. The flow of ozone was stopped and nitrogen was bubbled through the solution until the blue color was no longer observed. Dimethyl

sulfide (0.1 mL, 1.48 mmol, 20.0 equiv.) was added and the reaction mixture was allowed to warm to room temperature. The whole was poured into water (10 mL) and extracted with ether (3 x 10 mL). The organic layers were combined and dried over $MgSO_4$, and concentrated to give the crude aldehyde, which was eluted through a small plug of neutral alumina (pentane-ether, 19:1) to yield aldehyde **S7** (17.1 mg, 0.565 mmol, 76%). *Note*: Elution on a silica gel column resulted in significant loss of product most likely due to aldol-type processes. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (d, 1H, *J* = 3.6 Hz), 3.86 (s, 3H), 3.86-3.76 (m, 5H containing 3.79 (s, 3H)), 3.22 (sextet, 1H, *J* = 7.2 Hz), 2.16-2.04 (m, 6H containing 2.10 (s, 3H)), 2.02-1.94 (m, 2H), 1.60-1.52 (m, 2H), 1.25 (d, 3H, *J* = 6.8 Hz), 1.11 (d, 3H, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.3, 150.8, 149.8, 136.3, 134.4, 128.8, 125.3, 60.4, 60.2, 51.4, 43.3, 33.4, 32.0, 31.0, 28.5, 27.0, 24.0, 20.2, 12.8. $[\alpha]_D^{20}$ +5.0 (*c* 0.25, $CHCl_3$). HRMS (ESI); *m/z* 325.1761 ([M + Na]); exact mass calculated for $C_{19}H_{26}O_3Na$, 325.1774.



9b

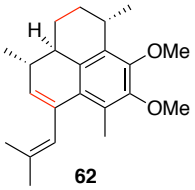
A 25 mL three-necked flask equipped with a magnetic stirring bar, septum, stopper, and nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with KHMDS (8.8 mg, 0.044 mmol, 1.1 equiv.) dissolved in anhydrous THF (1.0 mL). Isopropyltriphenylphosphonium bromide (23.3 mg, 0.060 mmol, 1.5 equiv.) was added and the reaction mixture was allowed to stir at room temperature for 2 h. The reaction mixture was transferred dropwise to a vessel containing aldehyde **S7** (12.2 mg, 0.040 mmol) dissolved in anhydrous THF (1.0 mL) at 0 °C via cannula. The reaction mixture was allowed to stir at 0 °C for 30 min. then allowed to warm to room temperature and stir for an additional 2 h. The reaction mixture was poured into water (10 mL) and extracted with ether (3 x 10 mL). The organic layers were combined and dried over $MgSO_4$, and concentrated to give the crude olefin which was purified via flash column chromatography (R_f = 0.32, hexanes-ethyl acetate, 19:1) to give **9b** (10.0 mg, 0.030 mmol, 75%, 73% *de*) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.97 (d, 1H, *J* = 9.2 Hz), 3.84 (s, 3H), 3.77 (s, 3H), 3.69 (q, 1H, *J* = 9.2 Hz), 3.22 (sextet, 1H, *J* = 7.2 Hz), 2.12-2.03 (m, 6H containing 2.07 (s, 3H)), 1.98-1.93 (m, 1H), 1.73 (s, 3H), 1.68 (s, 3H), 1.40-1.31 (m, 2H), 1.25-1.19 (m, 5H containing 1.24 (d, 3H, *J* = 7.2 Hz)), 1.03 (d, 3H, *J* = 6.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 149.3, 135.5, 134.2, 133.3, 131.1, 128.8, 128.6, 60.4, 60.1, 44.2, 40.3, 37.5, 34.3, 31.5, 28.5, 27.8, 25.6, 24.6, 20.3, 17.8, 12.3. $[\alpha]_D^{20}$ +29.0 (*c* 0.55, $CHCl_3$). HRMS (ESI); *m/z* 351.2302 ([M + Na]); exact mass calculated for $C_{22}H_{32}O_2Na$, 351.2295.



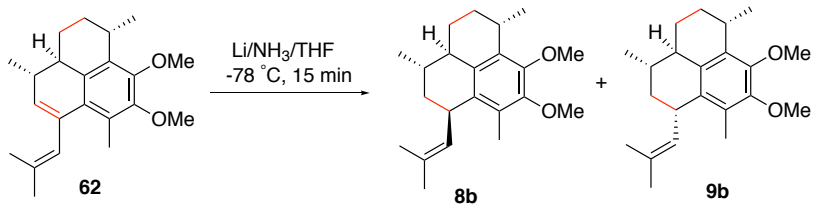
63

2-Methyl-1-tri-*n*-butylstannylpropene (63): A 3-necked 25 mL round bottomed flask equipped with magnetic stir bar, gas inlet, thermometer adapter and rubber septum was flame-dried, purged with nitrogen, and charged with dry tetrahydrofuran (6.5 mL) which was cooled internally to -78 °C. *t*-BuLi (2.3 mL, 3.9

mmol, 1.7 M in pentane) was added *via* syringe, followed by isocrotyl bromide (0.20 mL, 1.95 mmol) over a temperature range of -78 °C→-55 °C, then was allowed to recool to -78 °C. Tributyltin iodide (0.56 mL, 1.95 mmol) was added neat *via* syringe, keeping the temperature below -65 °C and forming a yellow milky color. The cooling bath was removed and the reaction warmed to rt, stirring for 23 h. The mixture was poured into water, washed with saturated KF, and extracted with ether. The organic phases were combined, dried ($MgSO_4$) and concentrated to an oil as stannane **63**, which was of sufficient purity to not warrant any further isolation techniques: 679.8 mg, 1.97 mmol, *ca.* 100%. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 5.43 (s, 1H), 1.90 (d, 3H, *J* 1.2 Hz), 1.77 (s, 3H), 1.51-1.47 (m, 6H), 1.35-1.27 (m, 6H), 0.94-0.88 (m, 15H).

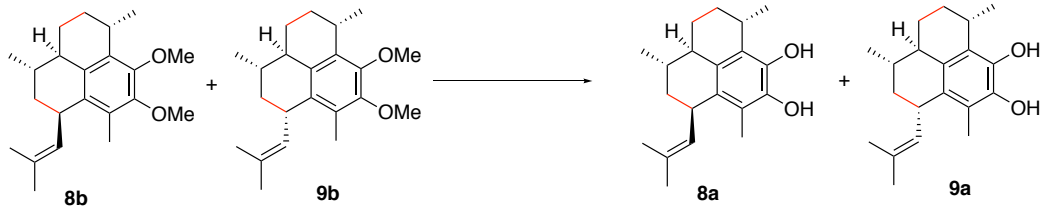


A three-necked 25 mL round bottomed flask equipped with magnetic stir bar, gas inlet, rubber septum, and glass stopper was flame-dried, purged with nitrogen, and charged with solid potassium hexamethyldisilazide (19.3 mg, 0.097 mmol). Dry tetrahydrofuran (1.0 mL) was added *via* syringe, and the clear colorless solution was stirred at rt while being treated dropwise with a solution of *enantiopure* ketone **57** (19.9 mg, 0.069 mmol) in THF (1.0 mL plus 1.0 mL rinse), forming a red clear solution that was stirred for one hour. Solid *N*-phenylbis(triflouromethanesulfonimide) (25.9 mg, 0.073 mmol) was added under a stream of nitrogen in a single portion, causing the solution to gradually become a clear pale yellow. The reaction was stirred for one hour. Lithium chloride (5.8 mg, 0.138 mmol), triphenylarsine (2.1 mg, 10 mol%), and Pd_2dba_3•$CHCl_3$ (3.6 mg, 5 mol%) were added in sequence, followed by a solution of stannane **63** (39 mg, 0.113 mmol) in THF (0.5 mL plus 0.5 mL rinse). The reaction was monitored by GC (fused silica, 170 °C for one minute, then 5 °C per minute to 250 °C; t_R triflate = 16.125, t_R 1,3-diene = 17.906) and judged complete after 6.5 h at rt. The whole was treated with saturated NaF and stirred for 5 minutes, then extracted with ether. The organic extracts were combined, dried ($MgSO_4$) and concentrated *in vacuo* to a brown oil, which was purified by prep TLC (97.5:2.5 petroleum ether [30-60 °C fraction]:diethyl ether) to afford clean 1,3-diene **62**: 16.6 mg, 0.051 mmol, 74% from ketone **57**. R_f 0.31 (2.5:97.5 ether:petroleum ether [30-60 °C fraction]); $[\alpha]_D$ (*c* 1.107, +222.8, $CHCl_3$); UV ($CHCl_3$) λ_{max} 274 nm (ε 1543); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 5.85 (s, 1H), 5.63 (s, 1H), 3.86 (s, 3H), 3.77 (s, 3H), 3.09-3.05 (m, 1H), 2.19 (s, 3H), 2.14-2.04 (m, 3H), 1.91-1.87 (m, 1H), 1.81 (s, 3H), 1.71 (s, 3H), 1.32-1.23 (m, 1H), 1.28 (d, 3H, *J* 7 Hz), 1.17-1.09 (m, 1H), 1.14 (d, 3H, *J* 7 Hz); ^{13}C (125 MHz, $CDCl_3$) δ_C 150.59, 149.88, 135.83, 135.43, 135.11, 132.62, 131.89, 131.37, 127.43, 126.68, 60.03, 59.82, 43.06, 34.32, 32.17, 29.68, 26.33, 26.01, 23.20, 19.53, 18.80, 14.06; IR (neat) 1560, 1458, 1260, 1072 cm^{-1}.



8b:**9b** = 1:2 (80%)

An oven-dried three-necked 25 mL round bottomed flask was equipped (under air) with a dry magnetic stir bar, oven-dried cold finger with gas inlet, a glass stopper, and a drying tube packed with barium oxide. A solution of diene **62** (16.1 mg, 0.049 mmol) in dry THF (1.0 mL plus 1.0 mL rinse) was added *via* pipette, and ammonia (*ca.* 10 mL, passed through a drying tube packed with barium oxide) was condensed into the vessel. Lithium metal (40% dispersion in mineral oil, *ca.* 10-fold excess) was added, forming a blue solution which was stirred for 15 minutes, then was slowly quenched with methanol until a white cloudy mixture formed. The cooling bath was removed and the mixture poured into a large beaker containing dry ether cooled by an ice bath. Excess methanol was added, and the mixture was swirled with addition of a few drops of water (*CAUTION*!). More water was added until all the excess lithium had been killed, leaving behind a clear colorless solution, which was poured into a separatory funnel and extracted from water with ether. The organics were combined, dried ($MgSO_4$) and concentrated *in vacuo* to a white oily mix, which was filtered through a column of silica gel eluting with isocratic hexane to remove the mineral oil, then with 95:5 hexane:ether to afford a mixture of semipure **8b** and **9b**. Purification by prep TLC (97.5:2.5 petroleum ether [30-60 °C]:diethyl ether) afforded **8b** and **9b** as a 1:2 mixture of *R*:*S* epimers at the newly created C_{13} stereogenic center: 12.7 mg, 0.039 mmol, 80%. R_f 0.23 (97.5:2.5 petroleum ether [30-60 °C]:diethyl ether); *Diagnostic* ^{1}H NMR[4] (400 MHz, $CDCl_3$) δ_H 4.97 (d, 1H, *J* 9.2 Hz); IR (neat) 1560, 1541, 1462, 1438, 1260, 1073 cm^{-1}; [M + Na] calc. 351.2300 meas. 351.2293.

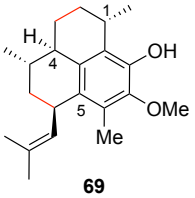


8b:**9b** = 1:2 (80%) **8a**:**9a** = 1:2 (60%)

Pseudopterosin G-J & A-F aglycones (9a and 8a)[4] A three-necked 25 mL round bottomed flask equipped with magnetic stir bar, reflux condenser with gas inlet, rubber septum and thermometer adapter was flame-dried, purged with nitrogen and charged with sodium hydride (8.6 mg, 0.216 mmol, 60% in mineral oil). Dry dimethylformamide (1.0 mL) was added, and the grey slurry was stirred at rt. Dropwise treatment with ethanethiol (0.02 mL, 0.27 mmol) afforded a clear, colorless solution of sodium thiolate. A solution of dimethyl ethers **8b** and **9b** (1:2, 7.9 mg, 0.024 mmol, prepared *via* lithium reduction of diene

62) in DMF (2.0 mL) was added *via* syringe, and the reaction was heated to 150 °C for 2 h, then cooled to rt. Water was added to quench the excess thiolate, and the whole was poured into water and extracted with ether. The organic phases were combined, dried ($MgSO_4$) and concentrated to an oil containing significant amounts of DMF. The excess DMF was removed *via* high-vacuum, and the residual film was purified by prep TLC (17:83 EtOAc:Hexanes) to afford the known title compounds as a 2:1 *S*:*R* mixture of C_{13} epimers: 4.3 mg, 0.0144 mmol, 60%. R_f 0.28 (20:80 EtOAc:Hexanes); *Diagnostic* ^{1}H NMR[4] (400 MHz, $CDCl_3$) δ_H (G-J Aglycone) 5.05 (s, 1H), 4.94 (d, 1H, *J* 9.2 Hz), 4.79 (s, 1H), 3.73-3.67 (m, 1H), 3.15-3.10 (m, 1H); (A-F aglycone) 5.10 (d, 1H, *J* 9.2 Hz), 5.03 (s, 1H), 4.82 (s, 1H), 3.63-3.56 (br, 1H), 3.27-3.20 (m, 1H). See the attached ^{1}H NMR Spectra.

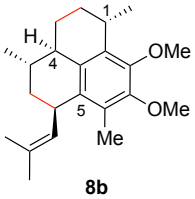
O. Experimental Data of Scheme 19



69

In a glovebox, a 1 dram vial was charged with compound **38** (30.0 mg, 0.08 mmol) dissolved in deuterated chloroform (1.0 mL). Trimethylsilyl iodide (22.7 µL, 0.159 mmol, 2.0 equiv.) was added slowly to the above reaction mixture. Upon completion of the starting material judged by TLC the whole was poured into H_2O (10 mL) and extracted with Et_2O (3 x 10 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated. Purification by flash column chromatography (R_f = 0.35, hexanes-ethyl acetate, 9:1) furnished **69** (16.2 mg, 0.051 mmol, 65%) as white powder. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.63 (s, 1H), 5.10 (br d, *J* = 8.3 Hz, 1H), 3.74 (s, 3H), 3.57-3.55 (m, 1H), 3.33-3.30 (m, 1H), 2.18-2.13 (m, 2H), 2.07 (s, 3H), 2.05-2.01 (m, 1H), 1.74 (s, 3H), 1.67 (s, 3H), 1.65-1.57 (m, 3H), 1.47-1.43 (m, 1H), 1.25 (d, *J* = 6.8 Hz, 3H), 1.14-1.08 (m, 1H), 1.04 (d, *J* = 5.9 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.40, 143.54, 134.13, 130.13, 129.69, 129.56, 126.37, 126.06, 60.81, 43.45, 39.51, 35.39, 30.93, 29.89, 28.20, 27.43, 25.66, 22.88, 21.01, 17.63, 11.20. $[\alpha]_D^{20}$ + 27.8 (*c* 0.18, $CHCl_3$). HRMS (ESI); *m/z* 337.2123 ([M + Na]); exact mass calculated for $C_{21}H_{30}O_2Na$, 337.2138.

Also see the attached spectra. The structure was confirmed by comparison of ^{1}H and ^{13}C spectra of this compound which was isolated during isolation from natural sources.[12b] Further it was converted into **8b**, which has been described in the literature.[13]



8b

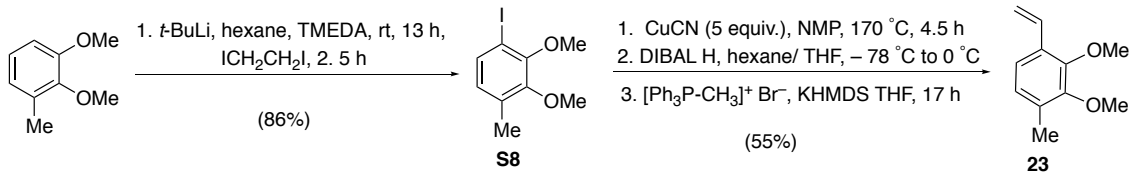
In a glovebox, a 1 dram vial was charged with compound **69** (8 mg, 0.232 mmol) dissolved in DME (1.0

mL). To the resulting solution was added CH_3I (26 uL, 0.4178 mmol, 1.8 equiv.) and cooled down to 0 ˚C then added KH (14 mg, 0.348 mmol, 1.5 equiv.). The progress of the reaction was monitored by TLC, after 30 min TLC shows complete conversion of starting material. Above reaction was quenched using a saturated aqueous solution of NH_4Cl (5 mL), the whole was poured into H_2O (5 mL) and extracted with ether (3 x 5 mL). The organic layers were combined, dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (R_f = 0.50, hexanes-ethyl acetate, 9:1) to give **8b** (7.5 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.13 (br d, *J* = 9.0 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.60-3.57 (m, 1H), 3.41-3.35 (m, 1H), 2.21-2.16 (m, 1H), 2.12-2.07 (m, 1H), 2.06 (s, 3H)), 2.04-1.99 (m, 1H), 1.75 (s, 3H), 1.68 (s, 3H), 1.67-1.58 (m ,3H), 1.54-1.50 (m, 1H), 1.21 (d, *J* = 7.2 Hz, 3H), 1.16-1.09 (m, 1H), 1.04 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.15, 148.57, 133.97, 133.67, 133.38, 129.92, 129.74, 127.87, 60.49, 60.0, 42.16, 39.42, 35.7, 30.37, 29.74, 27.67, 27.08, 25.64, 23.44, 20.99, 17.64, 10.82. $[\alpha]_D^{20}$ -73.2 (*c* 0.08, $CHCl_3$); IR (neat) cm^{-1}. HRMS (ESI); *m/z* 351.2290 ([M + Na]); exact mass calculated for $C_{22}H_{32}O_2Na$, 351.2295.

3. Additional Discussion

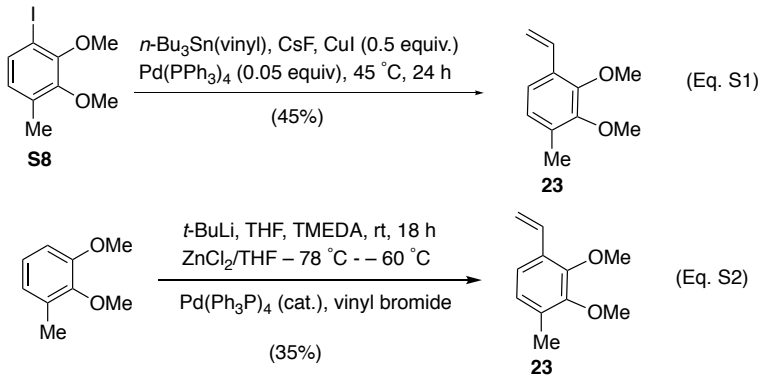
A. Alternative routes to synthesize compound 23 from aryl iodide

We have investigated several routes to synthesize compound **23** in higher yields. Directed *ortho*-metalation and subsequent iodination to synthesize **S8** has been published by Kocienski.[5] The crude iodide **S8** was subjected to a painstaking Ullmann-type coupling using 5 equivalents of copper cyanide in NMP at 170 °C to afford nitrile in 86% overall yield. Reduction of the cyano group with DIBAL-H afforded aldehyde in 73% yield. Wittig olefination and column chromatography finally produced clean vinylarene **23**, in 45% overall yield on a 10 gram scale (Scheme S1).



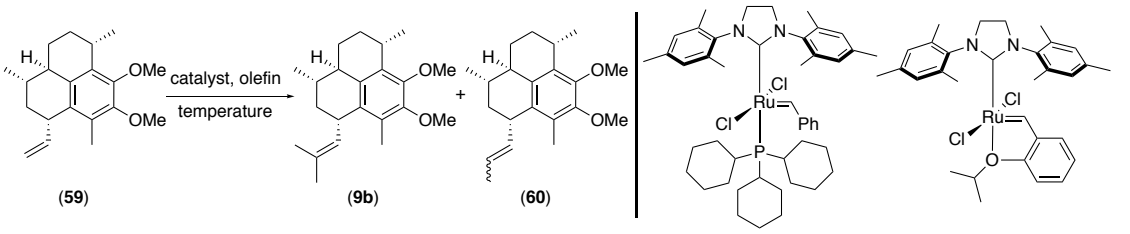
Scheme S1. Synthesis of vinylarene **23** from Kocienski iodide **S8**

Attempts at cross coupling iodoarene **S8** under traditional Stille[6] (with vinyltributyltin, Eq. S1), Kumada[7] (vinylmagnesium bromide, Eq. s2), and Heck[8] (Hermann-Beller palladacycle with ethylene) conditions all suffered from either poor conversion or low yields.



B. Efforts on metathesis reaction to synthesize compound 9b and 60

The ruthenium-catalyzed cross-metathesis reaction was investigated to append the appropriate side chain at C_{13}. Although several reports have disclosed the efficient cross-metathesis of sterically hindered olefins,[9] intermediate **59** failed to give acceptable results under a variety of conditions with multiple olefin partners (Table S1). Although cross-metathesis with 2-methyl-2-butene proceeded with complete conversion of substrate **59**, the product (**60**) contained the incorrect appendage as a result of the cross-metathesis of the thermodynamically less favorable fragment of the olefin (entry 1). Several attempts were made to generate the more stable product, including modification of the catalyst, increasing the reaction temperature, and employing olefinic partners that could not result in the formation of undesired disubstituted olefin **9b**.



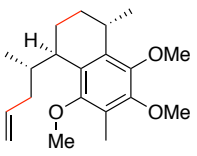
Attempted cross-metathesis conditions with olefin **59**

entry[a]	catalyst	olefin	temp (°C)	Conv.[b] (%)	**9b**	**60**
1	**S9**	2-methyl-2-butene	23[c]	100	0	100
2	**S9**	2-methyl-2-butene	36[d]	100	0	100
3	**S9**	2-methyl-2-butene	60[e]	100	0	100
4	**S10**	2-methyl-2-butene	23[c]	100	0	100
5	**S10**	2-methyl-2-butene	36[d]	100	0	100
6	**S10**	2-methyl-2-butene	60[e]	100	0	100
7	**S9**	2-methylpropene	23[c]	0	0	-
8	**S9**	2-methylpropene	60[e]	0	0	-
9	**S9**	2-methylpropene	23[c]	0	0	-
10	**S10**	2-methylpropene	60[e]	0	0	-
11	**S9**	2,3-dimethyl-2-butene	23[c]	0	0	-
12	**S9**	2,3-dimethyl-2-butene	73[d]	0	0	-
13	**S9**	2,3-dimethyl-2-butene	85[e]	<10	*n.d.*[f]	-
14	**S10**	2,3-dimethyl-2-butene	23[c]	0	o	-
15	**S10**	2,3-dimethyl-2-butene	73[d]	10	*n.d.*[f]	-
16	**S10**	2,3-dimethyl-2-butene	85[e]	100	*n.d.*[f]	-

[a] Reactions conducted with 10 mol% catalyst and the olefin as the solvent at the given temperature. [b] Conversion determined by GC analysis. [c] Reaction conducted at room temperature. [d] Reaction conducted in refluxing solvent. [e] Reaction conducted above the boiling point of solvent in a sealed tube. [f] Complex mixture as a result of decomposition.

4. Comparison of NMR spectra with known literature values

A. Comparison of spectra of compound 36e with literature[10]



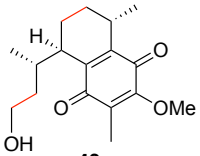
36e

(See attached spectra)

^{1}H NMR		^{13}C NMR	
Davies (400 MHz)	Present Work (500 MHz)[a]	Davies (75 MHz)	Present Work (125 MHz)[b]
5.80 (m, 1H)	5.83-5.76 (m, 1H)	153.0	153.0
5.02-4.95 (m, 2H)	5.01-4.95 (m, 2H)	149.5	149.5
3.85 (s, 3H)	3.85 (s, 3H)	147.0	147.0
3.80 (s, 3H)	3.80 (s, 3H)	138.9	138.9
3.63 (s, 3H)	3.63 (s, 3H)	134.8	134.8
3.16 (m, 1H)	3.19-3.15 (m, 1H)	128.5	128.5
2.86 (m, 1H)	2.88-2.85 (m, 1H)	122.2	122.2
2.17 (s, 3H)	2.17 (s, 3H)	114.9	115.0
2.10-1.92 (m, 4H)	2.11-1.92 (m, 4H)	60.5	60.5
1.80-1.75 (m, 2H)	1.80-1.75 (m, 2H)	60.1	60.2
1.49-1.45 (m, 1H)	1.49-1.45 (m, 1H)	59.9	59.9
1.14 (d, J = 7.0 Hz, 3H)	1.14 (d, J = 7.0 Hz, 3H)	40.0	40.0
0.76 (d, J = 7.0 Hz, 3H)	0.76 (d, J = 7.0 Hz, 3H)	37.8	37.8
		35.2	35.2
		27.0	27.0
		26.5	26.5
		23.2	23.2
		18.6	18.5
		18.1	18.1
		9.4	9.4

[a] Spectrum calibrated to the chloroform peak (7.26 ppm). [b] Spectrum recalibrated to the chloroform peak (77.0 ppm).

B. Comparison of spectra of compound 43a with literature[11]



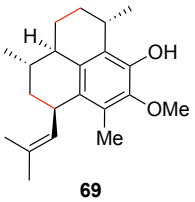
43a

(See attached spectra)

^{1}H NMR		^{13}C NMR	
Mulzer (400 MHz)	Present work (400 MHz)[a]	Mulzer (100 MHz)	Present work (100 MHz)[b]
4.00 (s, 3H)	4.0 (s, 3H)	189.1	189.1
3.85 (m, 1H)	3.87-3.79 (m, 1H)	183.0	183.0
3.70 (m, 1H)	3.71-3.67 (m, 1H)	155.6	155.6
3.00 (quin, *J* = 6.3 Hz, 1H)	3.00 (quin, *J* = 6.3 Hz, 1H)	146.5	146.5
2.86 (bs, 1H)	2.87-2.85 (m, 1H)	144.1	144.1
	2.34 (bs, 1H)	128.8	128.8
2.01 (qd, *J* = 11.9, 3.3 Hz, 1H)	2.04-1.96 (m, 1H)	60.9	60.8
1.93 (s, 3H)	1.92 (s, 3H)	60.7	60.7
1.72 (m, 4H)	1.85-1.62 (m, 3H)	37.9	37.9
1.56 (m, 2H)	1.55-1.53 (m, 2H)	33.0	33.0
1.49 (m, 1H)	1.51-1.46 (m, 1H)	32.8	32.8
1.07 (d, *J* =7.0 Hz, 3H)	1.07 (d, *J* = 7 Hz, 3H)	26.2	26.2
0.84 (d, *J* = 7.3 Hz, 3H)	0.83 (d, *J* = 7 Hz, 3H)	26.0	26.0
		21.0	20.9
		17.7	17.6
		17.2	17.2
		8.9	8.8

[a]Spectrum calibrated to the chloroform peak (7.26 ppm). [b]Spectrum recalibrated to the chloroform peak (77.0 ppm).

C. Comparison of spectra of compound 69 with literature[12]



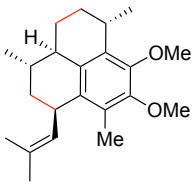
69

(From biomimetic route, **Scheme 20**. Also See attached spectra)

^{1}H NMR		^{13}C NMR	
Literature reported (360 MHz) [12a]	Present work (600 MHz)[a]	Literature reported (50 MHz) [12b]	Present work (150 MHz)[b]
5.65 (s, 1H)	5.63 (s, 1H)	144.5	144.40
5.10 (br d, *J* = 8.2 Hz, 1H)	5.10 (br d, *J* = 8.3 Hz, 1H)	143.7	143.54
3.74 (s, 3H)	3.74 (s, 3H)	134.1	134.13
3.55 (m, 1H)	3.57-3.55 (m, 1H)	130.3	130.13
3.32 (m, 1H)	3.33-3.30 (m, 1H)	130.3	129.69
2.15 (m, 1H)	2.18-2.13 (m, 2H)	129.6	129.56
2.07 (s, 3H)	2.07 (s, 3H)	126.5	126.37
2.02 (m, 1H)	2.05-2.01 (m, 1H)	126.0	126.06
1.74 (s, 3H)	1.74 (s, 3H)	60.7	60.81
1.67 (s, 3H)	1.67 (s, 3H)	43.5	43.45
1.65 (m, 1H)	1.65-1.57 (m, 3H)	39.6	39.51
1.61 (m, 3H)		35.5	35.39
1.45 (m, 1H)	1.47-1.43 (m, 1H)	31.0	30.93
1.25 (d, *J* = 6.9 Hz, 3H)	1.25 (d, *J* = 6.8 Hz, 3H	30.0	29.89
1.14 (m, 1H)	1.14-1.08 (m, 1H)	28.3	28.20
1.04 (d, *J* = 5.9 Hz, 3H)	1.04 (d, *J* = 5.9 Hz, 3H)	27.5	27.43
		25.6	25.66
		22.9	22.88
		20.9	21.01
		17.6	17.63
		11.2	11.20

[a]Spectrum calibrated to the chloroform peak (7.26 ppm). [b]Spectrum recalibrated to the chloroform peak (77.0 ppm).

D. Comparison of spectra of compound 8a, 8b and 9a with literature[4,13]

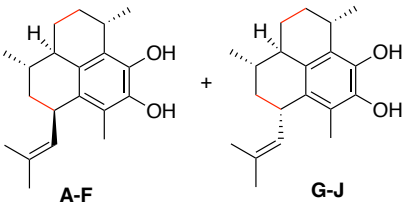


8b pseudopterosin A-F dimethyl ether

(see attached spectra)

^{1}H NMR		^{13}C NMR	
Kocieñski [13] (500 MHz)	Present work (600 MHz)[a]	Kocieñski [13] (75 MHz)	Present work (100 MHz)[b]
5.13 (dhept, *J* = 9.0, 1.5, 1H)	5.13 (br d, *J* = 9.0 Hz, 1H)	149.2	149.15
3.84 (s, 3H)	3.85 (s, 3H)	148.7	148.57
3.78 (s, 3H)	3.78 (s, 3H)	134.1	133.97
3.59 (ddd, *J* = 9.4, 4.5, 2.4 Hz, 1H)	3.60-3.57 (m, 1H)	133.9	133.67
3.43-3.34 (m, 1H)	3.41-3.35 (m, 1H)	133.6	133.38
2.18 (ddt, *J* = 12.7, 7.3, 4.5 Hz, 1H)	2.21-2.16 (m, 1H)	130.2	129.92
2.13-2.06 (m, 1H)	2.12-2.07 (m, 1H)	129.8	129.74
2.06 (s, 3H)	2.06 (s, 3H))	128.1	127.87
2.02 (dddd, *J* = 13.6, 8.4, 7.6, 4.3 Hz, 1H)	2.04-1.99 (m, 1H)	60.7	60.49
1.75 (d, *J* = 1.5 Hz, 3H)	1.75 (s, 3H)	60.2	60.00
1.68 (d, *J* = 1.5 Hz, 3H)	1.68 (s, 3H)	42.3	42.16
1.67-1.60, 2H)	1.67-1.58 (m ,3H)	39.5	39.42
1.60–1.49 (m, 2H)	1.54-1.50 (m, 1H)	35.8	35.70
1.21 (d, *J* = 7.2 Hz, 3H)	1.21 (d, *J* = 7.2 Hz, 3H)	30.5	30.37
1.17-1.08 (m, 1H)	1.16-1.09 (m, 1H)	29.9	29.74
1.04 (d, *J* = 6.2 Hz, 3H)	1.04 (d, *J* = 6.2 Hz, 3H)	27.8	27.67
		27.2	27.08
		25.9	25.64
		23.7	23.44
		21.2	20.99
		17.9	17.64
		11.0	10.82

[a]Spectrum calibrated to the chloroform peak (7.26 ppm). [b]Spectrum recalibrated to the chloroform peak (77.0 ppm).



(see attached spectra)

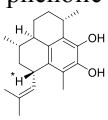
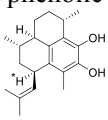
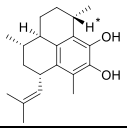
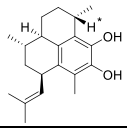
G-J Proton	Observed shift and multiplicity	Corey[4]	A-F Proton	Observed shift and multiplicity	Corey[4]
phenolic	5.05, s	5.05, s	phenolic	5.03, s	5.03, br s
vinyl	4.94, d, *J* 9.2 Hz	4.94, br d, *J* 9.3 Hz	vinyl	5.10, d, *J* 9.2 Hz	5.11, dt, *J* 9.2, 1.4 Hz
phenolic	4.79, s	4.79, s	phenolic	4.82, s	4.82, br s
	3.73-3.67, m	3.69, m		3.63-3.56, m	3.58, m
	3.15-3.10, m	3.12, m		3.27-3.20, m	3.22, m

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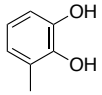
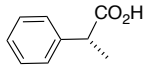
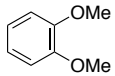
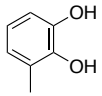
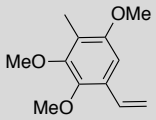
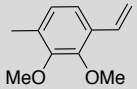
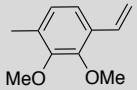
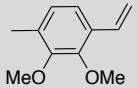
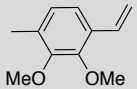
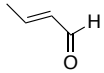
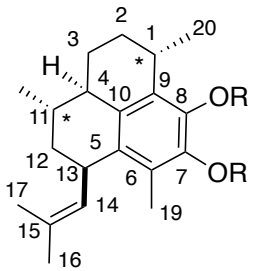
Table S1. A. Comparison of the hydrovinylation approach (highlighted) with others for the synthesis of pseudopterosins[a]

natural product or key intermediate[a]	pseudopter-osin, R, R'	starting material	no. of steps	yield[b]	source of chirality	limiting selectivity[c]	comments	ref.
pseudopterosin A-F	Me, Me		15	1.9	racemic	C_4 (*R**:*S**) 5:4 C_{13} (*R**:*S**) 9:1	• racemic route • efficient C-ring annulation	1
pseudopterosin A-F	$-CH_2Ph$, H	(–)-limonene	30	1.7	chiral pool	C_1 (*R*:*S*) 1:1 C_{13} (*R*:*S*) 1.1:1.0	low selectivity, right protect group (PG) for glycosylation	2
pseudopterosin A-F	Me, Me		21	<2[a]	chiral pool	C_4 (*R*:*S*) 58:42	low selectivity and overall yield	3
pseudopterosin A-F	H, H	(*S*)-(–)-citronellal	18	3.1	chiral pool	C_1 (*R*:*S*) 3:97	exceptional diastereoselectivity. diastereomer synthesis (C_{13}, C_{11}) likely challenging.	4,5
pseudopterosin A-F	H, H	(–)-limonene	16	6	chiral pool	C_{11} (*R*:*S*) 54:46	C_{11} via kinetic resolution	6
pseudopterosin A-F	Me, Me		20	13.5	via resolved $Cr(CO)_3$ complex	• stoichiometric resolution • C_{11} diastereosel. hydroboration • C_{13} (*R*:*S*) 16:1	• exceptional diastereo-selectivity • synthesis of diastereomers (C_4, C_1) likely challenging	8
pseudopterosin A-F	Me, Me		25	4.4	[3,3]-sigmatropic rearr., Pd-catalyzed allylation	C_1 (*R*:*S*) 3:1 C_{13} (*R*:*S*) 15:1	erosion of C_1 configuration during hydrogenation	10

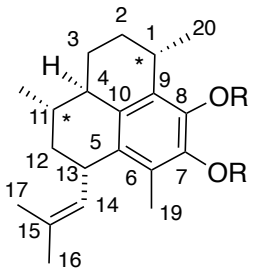
pseudopterosin A-F	-CH_2Ph, H		12	4.4	Cu-cat enantiosel. Me_2Zn add	C_1 (*R:S*) 5:95 C_{13} (*R:S*) 52:48	correct PG for further glycosylation	12
pseudopterosin A-F	Me, H		15	25.6	Enantiosele-ctive hydrov-inylation (HV)	C_{13} (*R:S*) >99:1 C_{11} (*R:S*) 1:99 C_4 (*R:S*) >85:15 C_1 (*R:S*) 2:98	• HV to install C_{11}, C_1, • diastereosel. Birch (C_4), diastereosel. cycliz. (C_{13}) • configurations at C_{11}, C_4, C_1 controllable • correct PG for further glycosylation	13
pseudopterosin A-F	Me, Me		18	17	enantiosel. HV	C_{13} (*R:S*) >99:1 C_{11} (*R:S*) 8:92 C_4 (*R:S*) 97:3 C_1 (*R:S*) <1:99	• HV to install C_{11}, C_1 diastereosel. Birch (C_4), diastereosel. epoxide (C_{13}) • configurations at C_{11}, C_4, C_1 controllable	13,14
pseudopterosin A-F[c]	Me, Me		14	21	enantiosel. (HV)	C_{13} (*R:S*) 86:14 C_{11} (*R:S*) 8:92 C_4 (*R:S*) 97:3 C_1 (*R:S*) <1:99	• HV to install C_{11}, C_1 diastereosel. Birch (C_4), diastereosel cycliz. (C_{13}) • configurations at C_{11}, C_4, C_1 controllable	13,1[d]
pseudopterosin G-J	Me, Me		20	13.6	enantiosel. HV	C_{13} (*R:S*) <1:99 C_{11} (*R:S*) 8:92 C_4 (*R:S*) 97:3 C_1 (*R:S*) <1:99	• HV to install C_{13}, C_{11}, C_1 diastereosel. Birch (C_4) • configurations at C_{11}, C_4, C_1 controllable	13,14
pseudopterosin A-F: G-J aglycones (1:2, Scheme 18) (Stille route)	H, H		18	16.6	enantiosel. HV	C_{13} (*R:S*) 1:2 C_{11} (*R:S*) 8:92 C_4 (*R:S*) 97:3 C_1 (*R:S*) <1:99	C_{13} installed by Li/NH_3 reduction of a dihydronaphthalene	13,14

pseudopterosin G-J	-CH_2Ph, H		12	5.5	Cu-cat enantiosel. Me_2Zn addition	C_1 (*R:S*) 5:95 C_{13} (*R:S*) 52:48	correct PG for further glycosylation	12
ent-pseudopterosin G-J aglycone	H, H		13	0.95	chiral pool	C_4,C_{11} (*S,R*): diastereo-mer + two diasteromers. dr = 5:2	• shortest route • use of exceptionally innovative allene chemistry • need specialized high pressure reactor • stoichiometric Rh used for double decarbonylation, • overall low yield.	11
ent-pseudopterosin G-J aglycone	H, H		15	0.51	enantiosel. hydrogen-ation	(see previous entry)	(also previous entry)	11
pseudopterosin G-J aglycone	H, H	(–)-limonene	15	5.5	chiral pool	C_{11} (*R:S*) 54:46 C_{13} (*R:S*) 1:8	C_{11} via kinetic resolution. Diastereomer synthesis (C_4, C_1) may require new chemistry	6, 7
pseudopterosin A-F aglycone	H, H	(–)-citronellal	18	1	chiral pool	Wittig Reaction *E:Z* 9:1	diastereomer synthesis (C_4, C_1) – see previous row	9
pseudopterosin K-L aglycone	H, H	(–)-isopulegol	15	5.2	chiral pool	C_{13} (*R:S*) 1:10	diastereomer synthesis (C_4, C_1) – see previous row	9

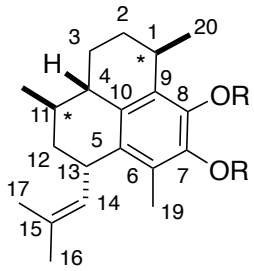
a. A uniform numbering for serrulatanes and amphilectanes is followed (see Figure 1 in the paper).



8a pseudopterosin A-F



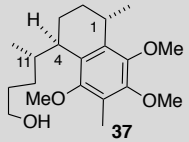
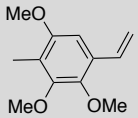
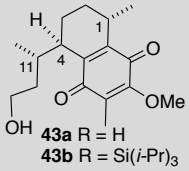
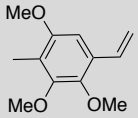
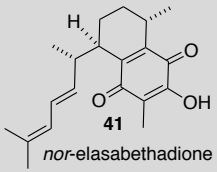
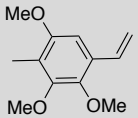
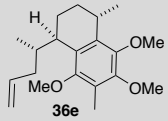
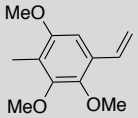
9a pseudopterosin G-J

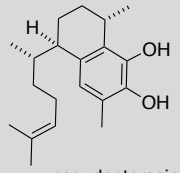
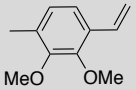
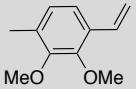
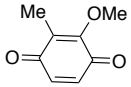
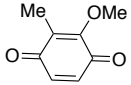
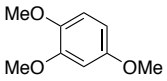
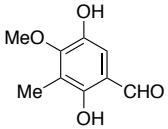


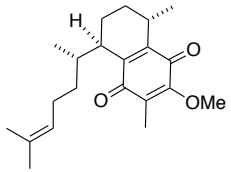
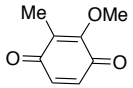
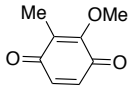
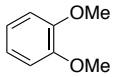
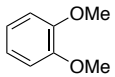
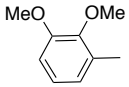
***ent*-8a** pseudopterosin K-L

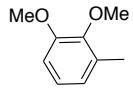
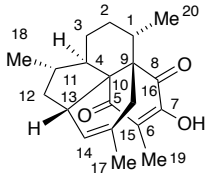
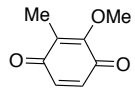
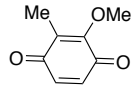
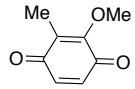
b. Yields uncertain in a few cases since required data is not available. c. The lowest stereoselectivities among the reactions to reach the final target are shown, except for our work (highlighted rows), where all selectivities are shown. d. Combination of RajanBabu,[13,14] Harrowven[1] routes (post-installation of stereogenic centers) gives the shortest (14 steps, ~ 21 %) with excellent stereoselectivity to pseudopterosins A-F aglycone, and, flexibility to make diastereomers at any of the centers.

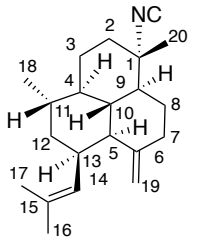
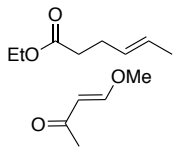
Table S1. B. Comparison of the hydrovinylation approach (highlighted) with others for the synthesis of prototypical serrulatanes and amphilectanes[a]

natural product or key intermediate[a]	starting material	number of steps	overall yield[b]	source of chirality	limiting selectivity[c]	comments	ref.
intermediate for elisabethadione (**37**) 		15	27.8	enantioselective HV	C_1 (*S:R*) 98:2 C_4 (*R:S*) 85:15 C_{11} (*S:R*) 99:1	C_1(*S*) and C_{11} (S) selectivity >99:1. C_4-isomers separated by column (>99:1 *R*). Demonstrated flexibility in diastereomer (C_1, C_4, C_{11}) synthesis	13
intermediate for colombiasin, elisapterosin 		13	36 (**43a**)	enantioselective HV	C_1 (*S:R*) 98:2 C_4 (*R:S*) 85:15 C_{11} (*S:R*) 99:1	C_1(*S*) and C_{11} (S) selectivity >99:1. C_4-isomers separated by column (>99:1 *R*). Demonstrated flexibility in diastereomer (C_1, C_4, C_{11}) synthesis	13
		18	17.4	enantioselective HV	C_1 (*S:R*) 98:2 C_4 (*R:S*) 85:15 C_{11}(*S:R*) 99:1)	C_1(*S*) and C_{11} (S) selectivity >99:1. C_4-isomers separated by column (>99:1 *R*). Demonstrated flexibility in diastereomer (C_1, C_4, C_{11}) synthesis	13
Intermediate for a *p*-benzoquione natural product 		14	30.7	enantioselective HV	C_1 (*S:R*) 98:2 C_4 (*R:S*) 85:15 C_{11}(*S:R*) 99:1)	C_1(*S*) and C_{11} (S) selectivity >99:1. C_4-isomers separated by column (>99:1 *R*). Demonstrated flexibility in diastereomer (C_1, C_4, C_{11}) synthesis	13

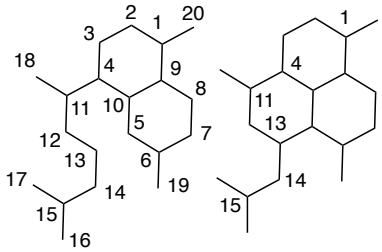
 *seco*-pseudopterosin A aglycone (**56b**)		16	32.2	enantioselective HV	C_1 (*S:R*) >99:1 C_4 (*S:R*) 3:97 C_{11} (*S:R*) 92:8	• independent control of all stereogenic centers	13
helioporin D (**56c**)		17	29.3	enantioselective HV	C_1 (*S:R*) >99:1 C_4 (*S:R*) 3:97 C_{11} (*S:R*) 92:8	• independent control of all stereogenic centers	13
36e		10	17	Rh-cat C-H insertion. Kinetic resolution	C_1 (*S:R*) 96:4	• C_1 kinetic resolution (yield 41%). C_4, C_{11} • diastereomers might require new chemistry	15, 17
37		8	22.8	Rh-cat C-H insertion. Kinetic resolution	C_1 (*S:R*) 96:4	• C_1 kinetic resolution (yield 41%). C_4, C_{11} • diastereomers might require new chemistry	15, 17
ent-37		11	8.9	enantsel. crotylation, 3,3-sigmatropic rear.	C_1 (*S:R*) 1:3	• C_4, C_{11} diastereoselective [3,3]-sigmatropic rearr. • diastereomers separated by prep-HPLC.	17
43a		17	5	racemic	C_1, C_4 config. linked through Diels-Alder dr 1.0:0.0	• C_{11} installed by diastereoselective hydrogeantion	19

43b	Pseudoephedri-nepropionamide	9	17	stoichiometric auxiliary assisted enolate alkylation	C_1, C_4 config. linked through Diels-Alder regioisom. (1.7:1.0)	• C_1, C_4 diastereomeric mixture carried through synthesis	20
 OMe-elisabethadione-		11	15.4	Rh-cat C-H insertion. Kinetic resolution	C_1 (*S:R*) 97:3	independent control of C_4, C_{11} configurations might require redesign of route	15, 16
O-methyl-*nor*-elisabethadione		12	7.8	Rh-cat C-H insertion. Kinetic resolution	C_1 (*S:R*) 97:3	independent control of C_4, C_{11} configurations might require redesign of route.	15, 16
seco-pseudoptrosin A aglycone (**56b)**		18	26.3	via resolved $Cr(CO)_3$ complex	• stoichiome-tric reaction to install C_1	• exceptional diastereo-selectivity • synthesis of diastereo-mers (C_4, C_{11}) challenging	8
helioporin D (**56c**)		17	25.5	via resolved $Cr(CO)_3$ complex	• stoichiome-tric reaction to install C_1	• exceptional diastereo-selectivity • synthesis of diastereo-mers (C_4, C_{11}) challenging	21
helioporin E	(–)-limonene	17	0.55[c]	chiral pool	C_{11} (*R:S*) 54:46	• C_{11} via kinetic resolution. • diastereomer synthesis	6, 7
helioporin E		17	4.5	• enantiosel. L*Cu-cat S_N2' addition of MeMgBr • enantiosel. Ir-cat. hydrogen.	C_4 (*R:S*) 4:1	• efficient route • potentially useful route for synthesis of various diastereomers	25

helioporin C		16	5.7	• enantiosel. L*Cu-cat S_N2' addition of MeMgBr • enantiosel. Ir-cat. hydrogen.	C_4 (*R:S*) 4:1	• efficient route • potentially useful route for synthesis of various diastereomers	25
 **4** colombiasin A		20	1.1	enantiosel. DA	• C_1,C_4 linked through DA dr 85:15, er 97:3 • C_{11} (*R:S*) 1:1	• first synthesis • established the absolute configuration • demonstrated the intra-molecular DA in the last step used by others later.	22
colombiasin A		12	11.5	• enantiosel. DA used twice	• C_{11} 93:7 enantsel. DA • C_1,C_4 linked through DA dr >10:1	• Exceptionally short and practical synthesis • independent control of stereogenic centers could be challenging.	23
colombiasin A	Pseudoephedri-nepropionamide	16	3.4	stoichiometric auxiliary assisted enolate alkylation	C_1, C_4 config. linked through Diels-Alder dr 1.7:1.0	C_1, C_4 Diastereomeric mixture carried through synthesis	20
colombiasin A	(–)-dihydrocarvone	12	1.1	chiral pool, $[(-)\text{-ipc}]_2BH$	C_1,C_4 config. linked- di-hydrocarvone)	C_{11} Configuration by stoichiometric asymmetric hydroboration	24
colombiasin A		14	5.3	kinetic resolution by Rh-cat. C-H insertion	C_1 (*S:R*) 98:2	C_1 kinetic resolution (yield 41%). C_4, C_{11} configurat-ions tied to that of C_1. Practical synthesis	15

 (*rac*)-7-isocyano-11(20), 14-epiamphilectadiene		9	6.4	racemic	C_1 S_N1 with retention dr 88:12. C_4, C_{10}, C_{11} linked thru Diels-Alder dr >10:1	C_5, C_9 config. installed via diastereosel. protonation. C_{13} config. Cu-catalyzed 1,4-addition. Shortest route (spectacularly so!) to the most complex amphilectane to-date. Racemic synthesis. Making specific diastereomers challenging.	30

a. Carbon numbering



1 serrulatane skeleton **2** amphilectane skeleton

b. Yields uncertain in a few cases since required data is not available. c. The lowest stereoselectivities among the reactions to reach the final target are shown, except for our work (highlighted rows), where all selectivities are shown. d. Formation of the methylenedioxy derivative (last step) has been reported (ref 21) to give a better yield (83%) than 10% reported in ref. 7.

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Other notable examples of syntheses of serrulatanes and amphilectanes

The examples cited in **Table S1A** and **Table S1B** list only molecules and intermediates whose syntheses *closely* map a possible hydrovinylation approach. There are many other notable molecules in these classes of compounds that will be helped by this approach. The following references provide a partial list of some of the most notable syntheses in the area.

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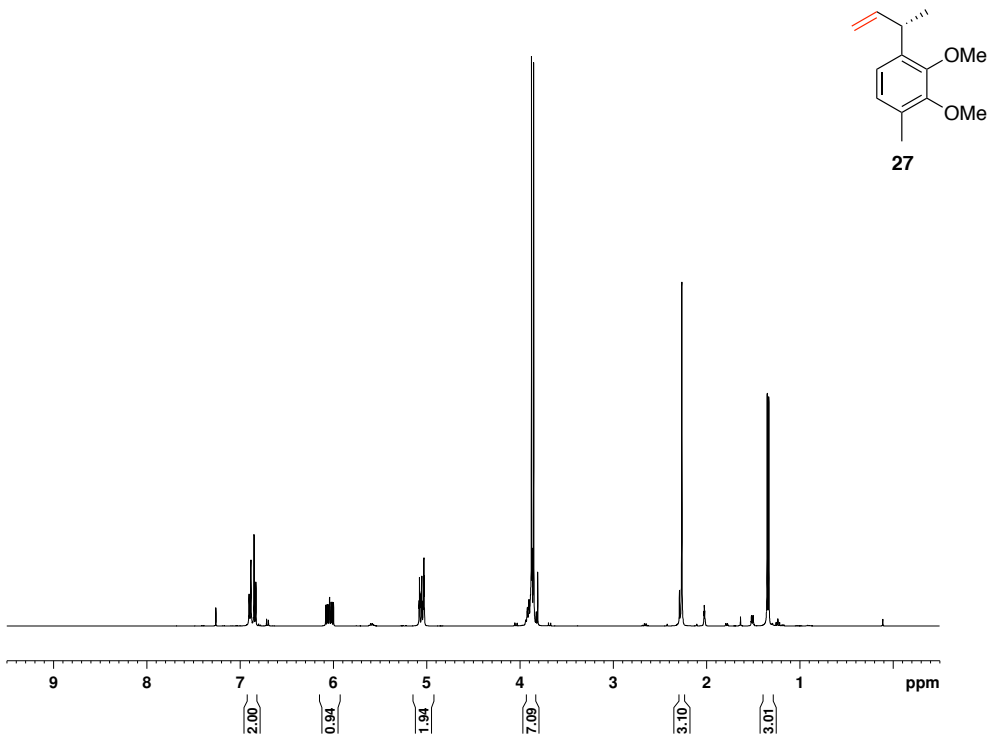
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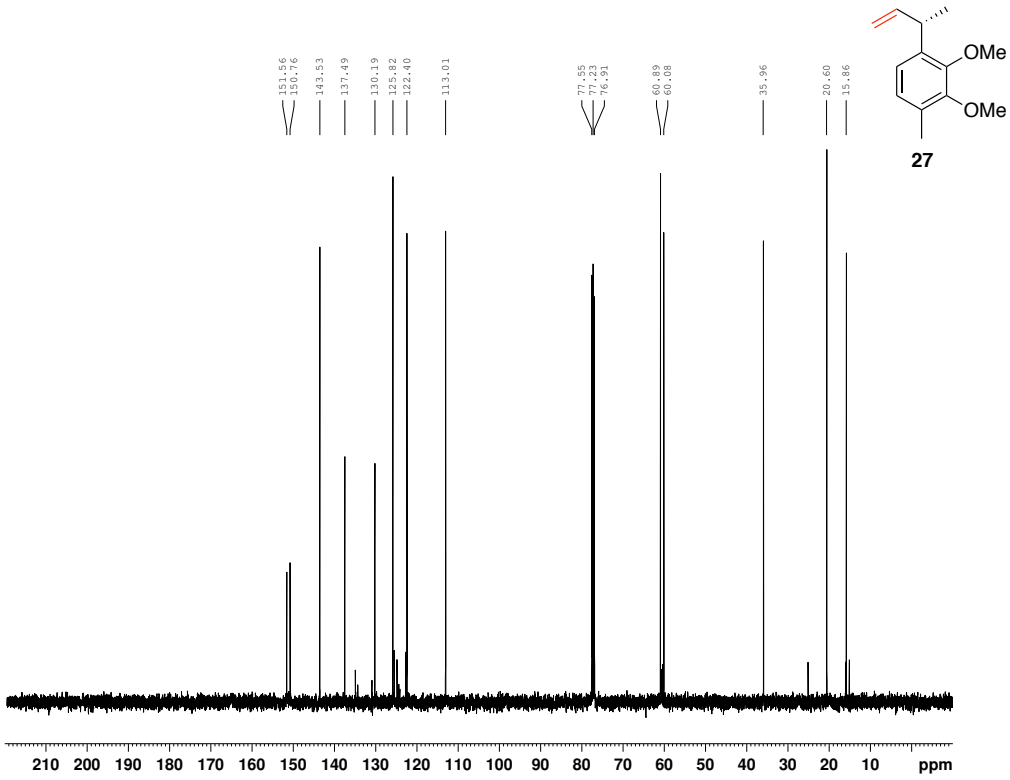
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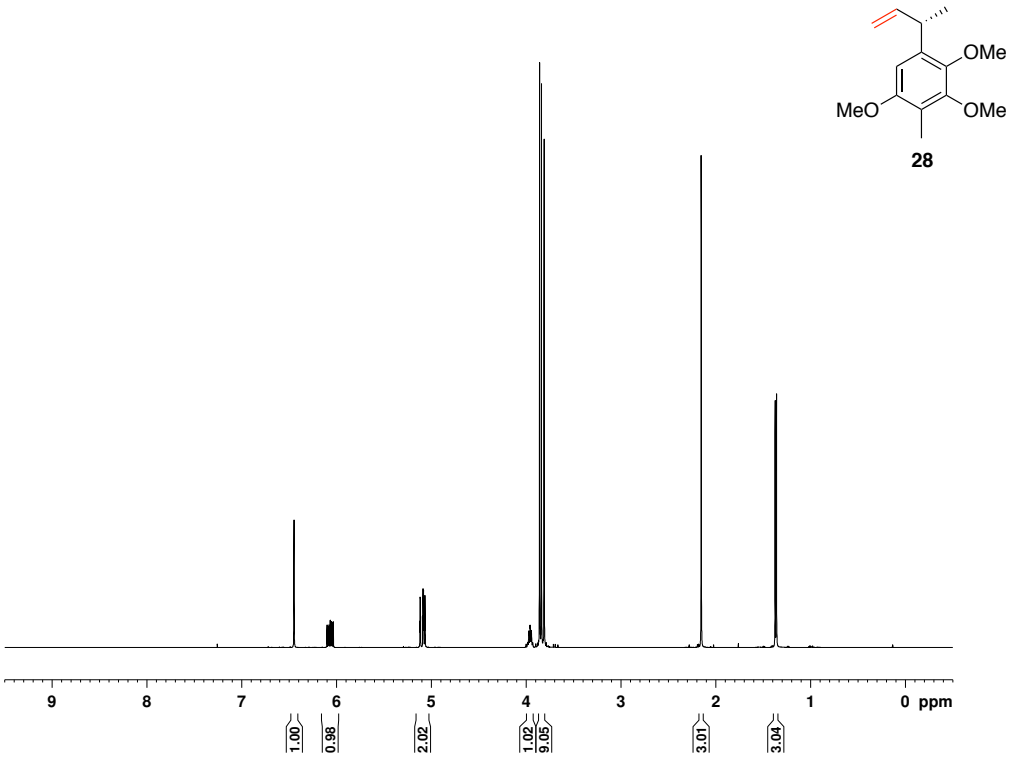
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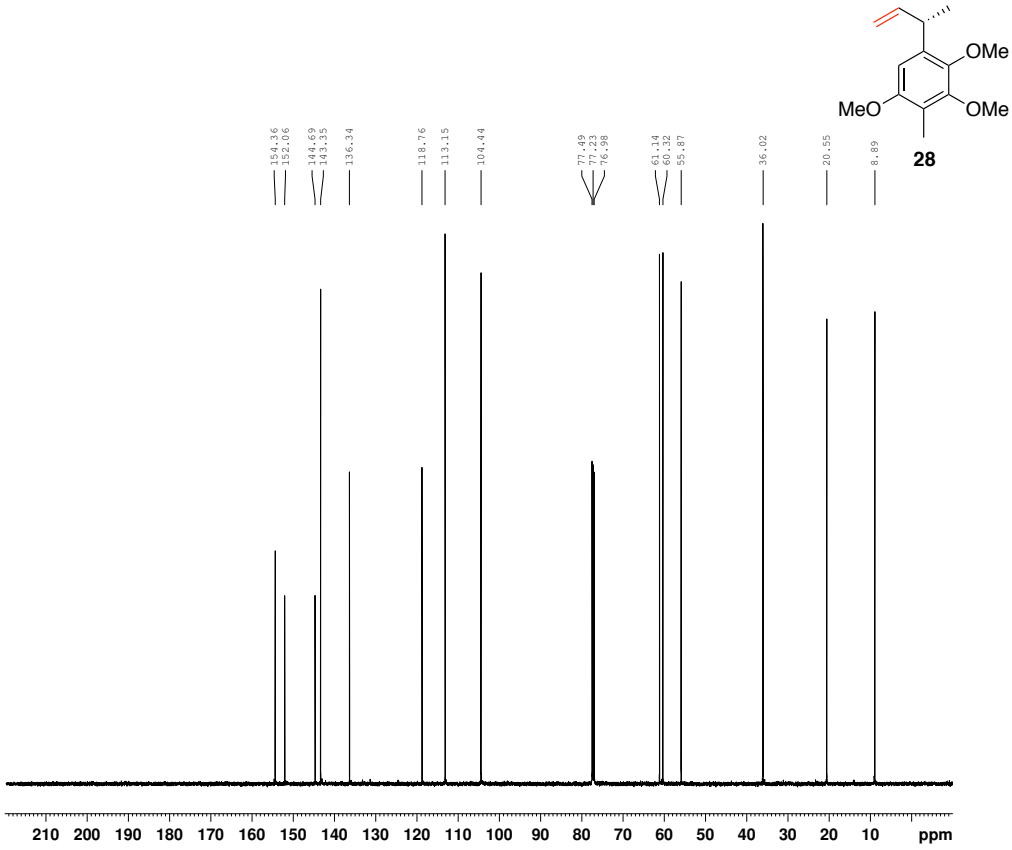
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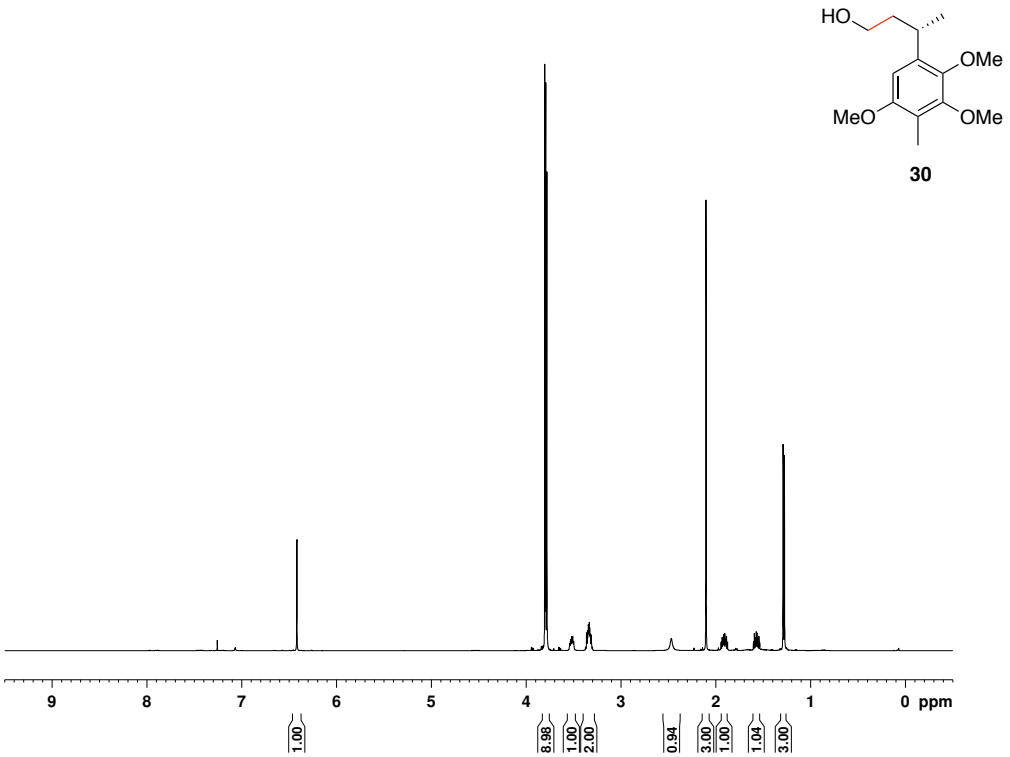
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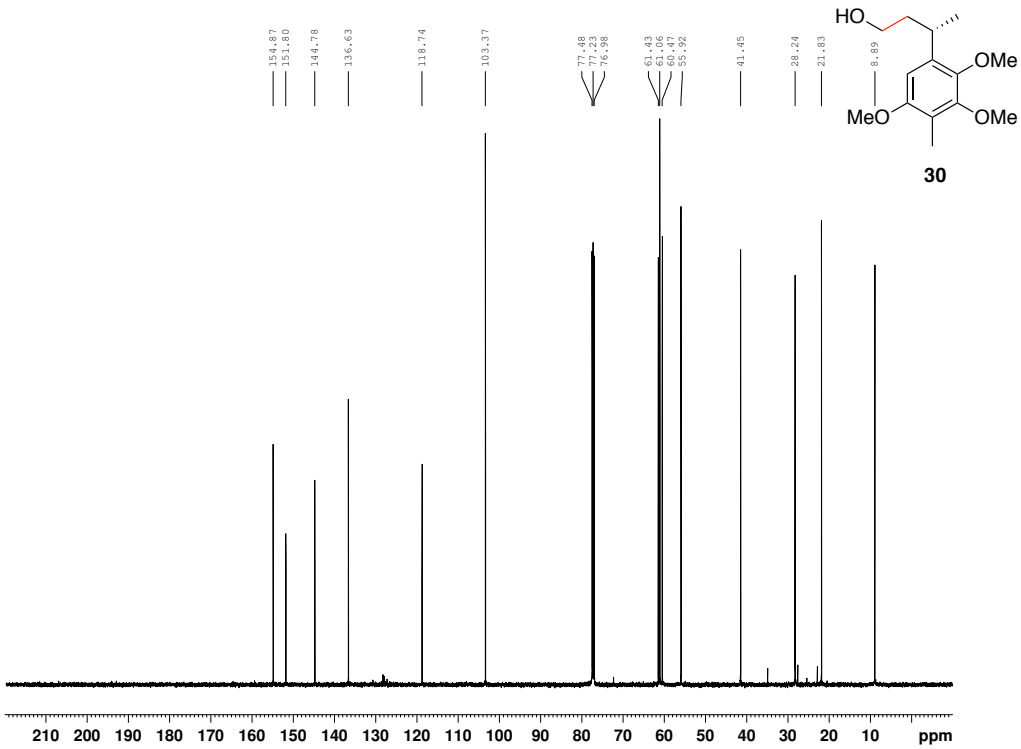
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8.89
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MeO
OMe
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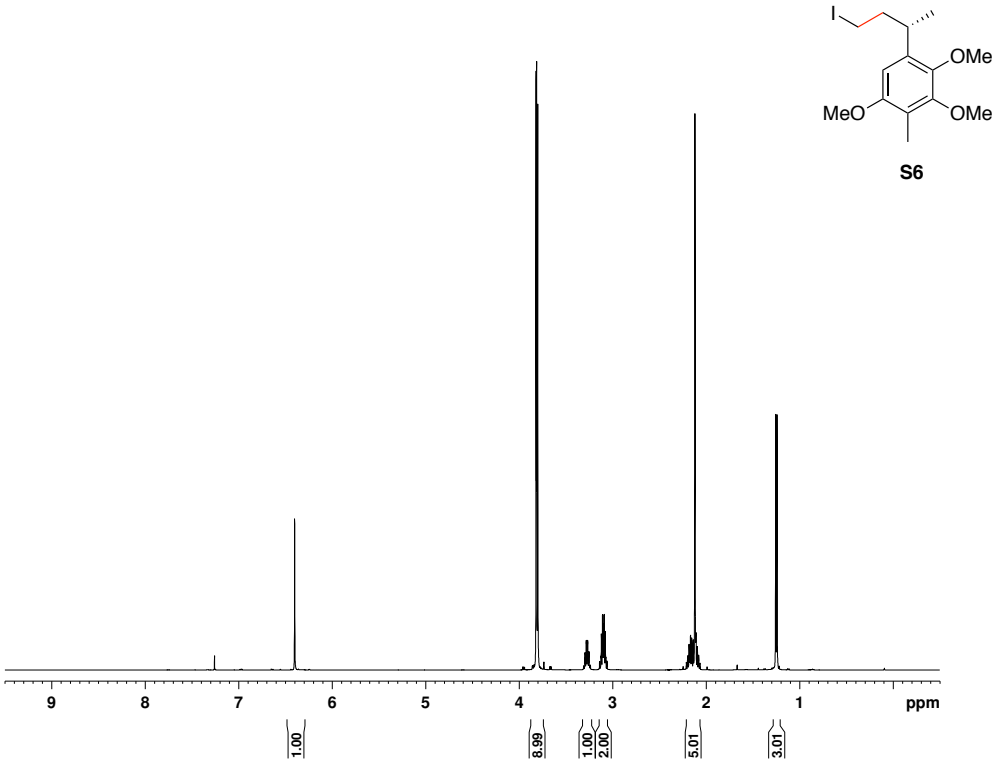
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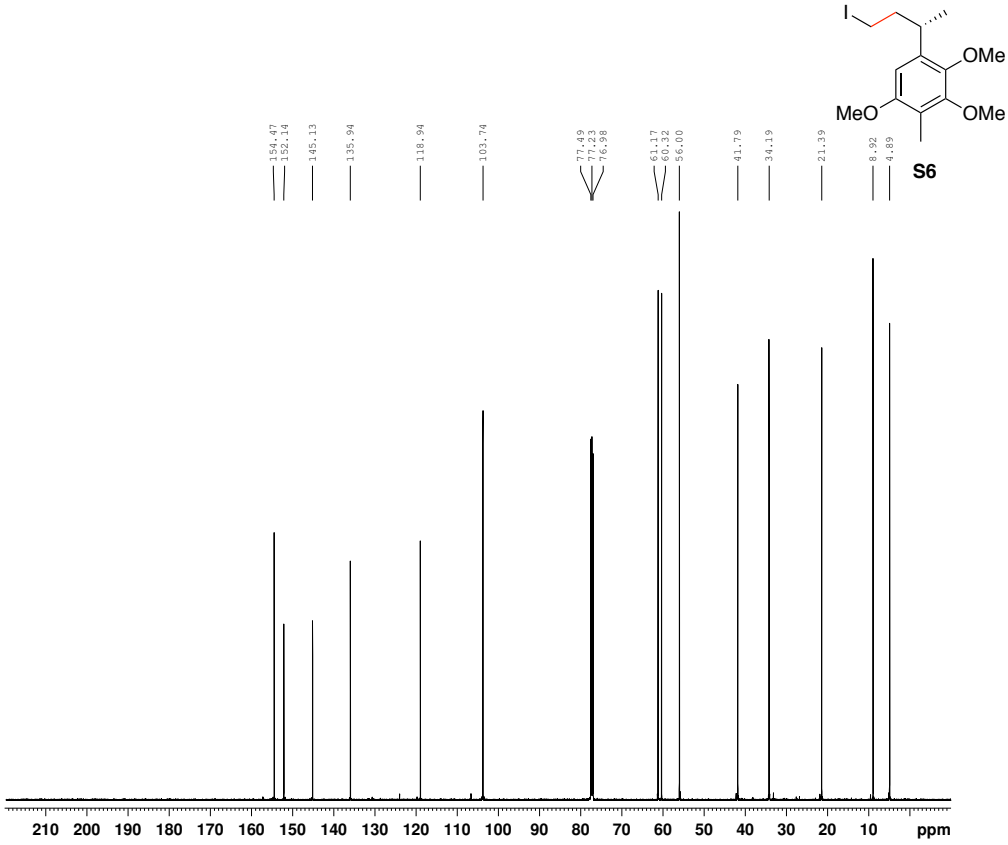
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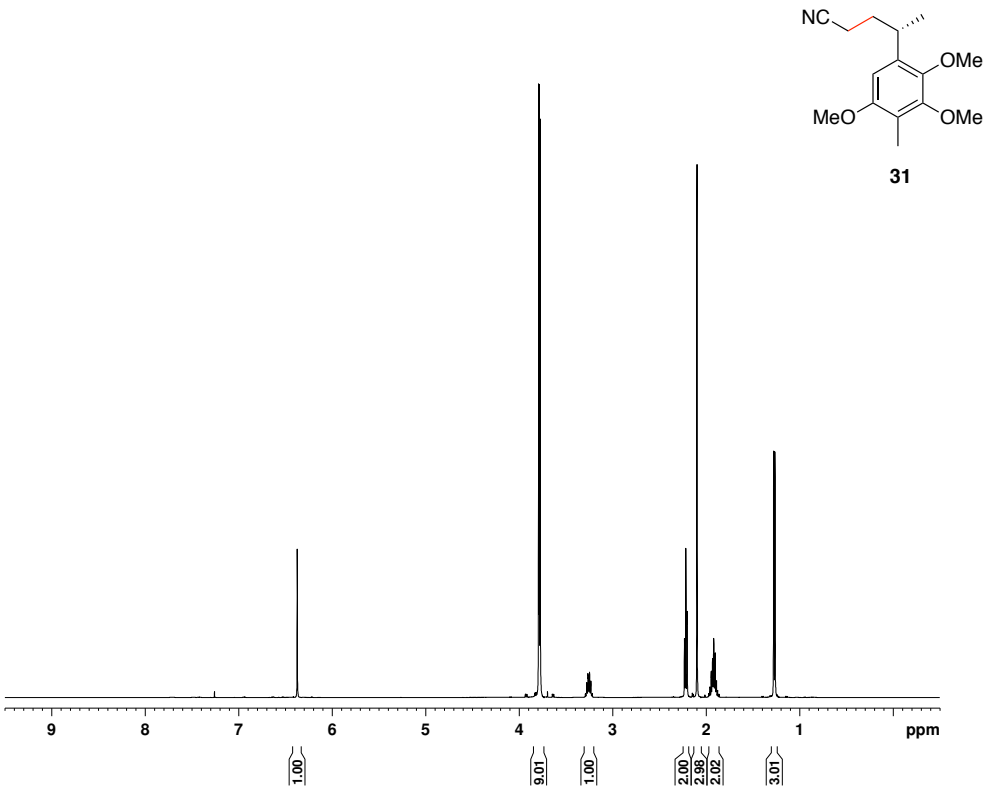
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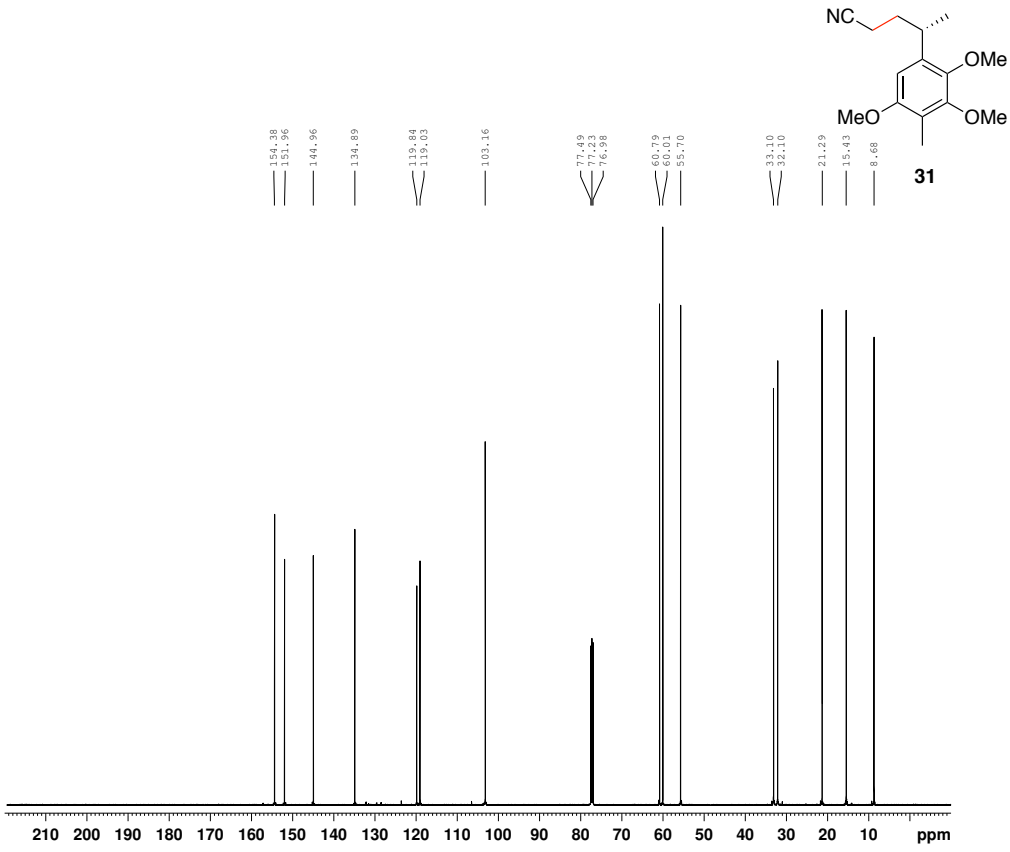
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32.10
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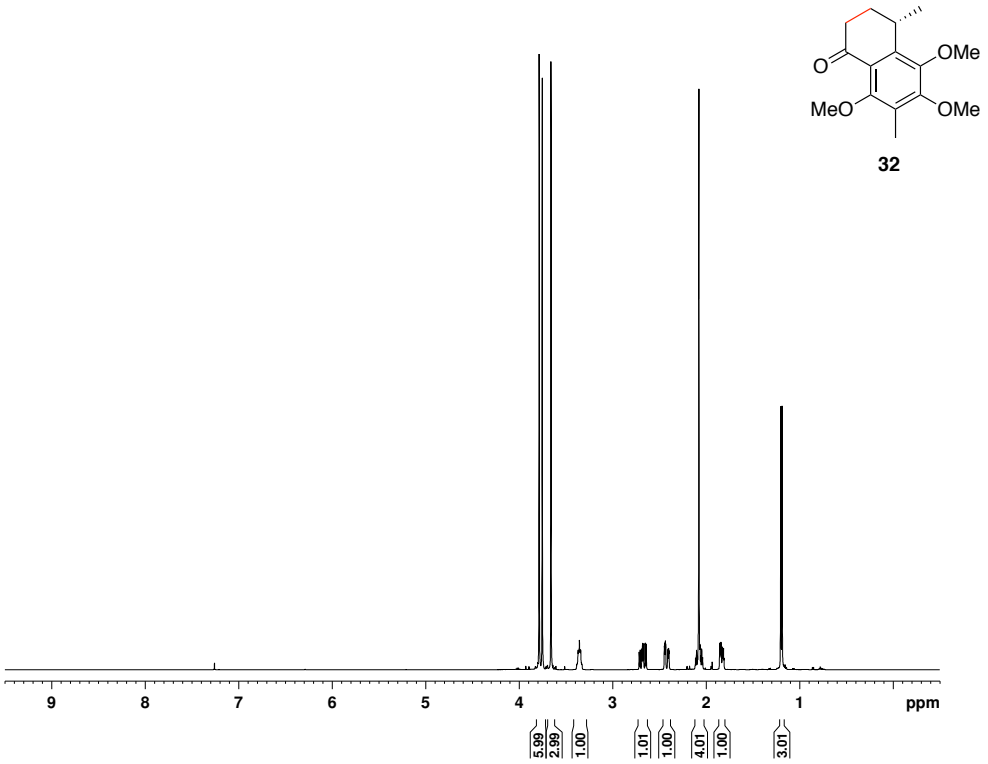
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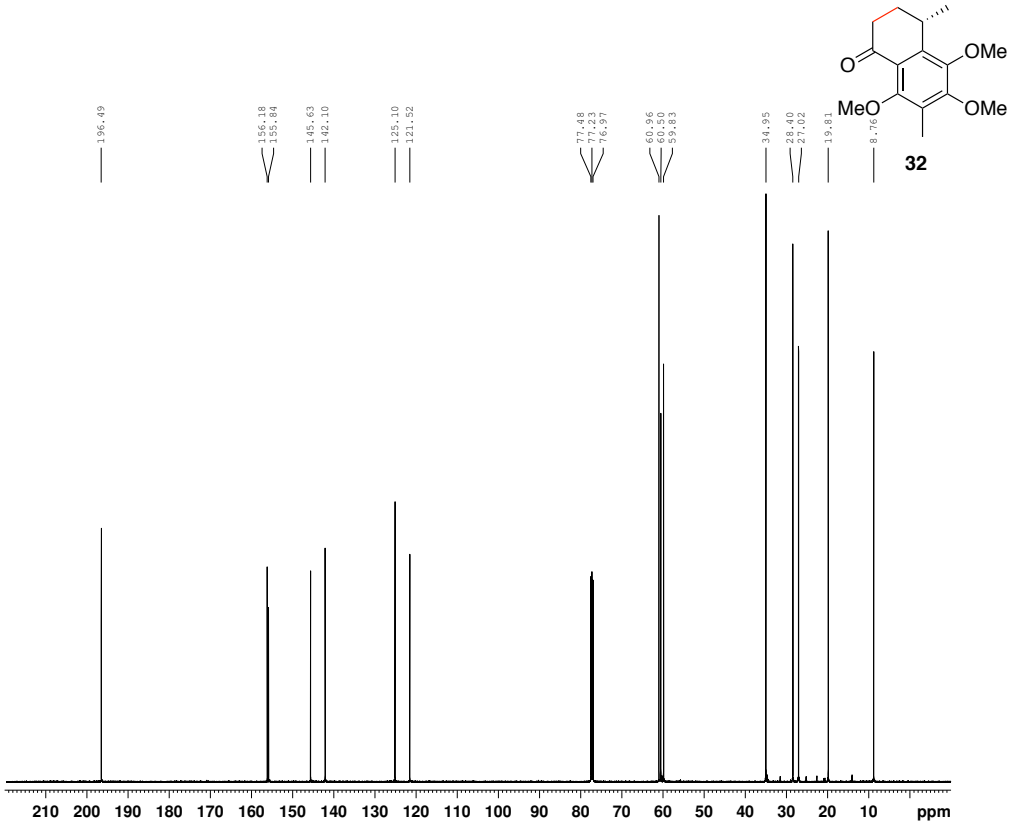
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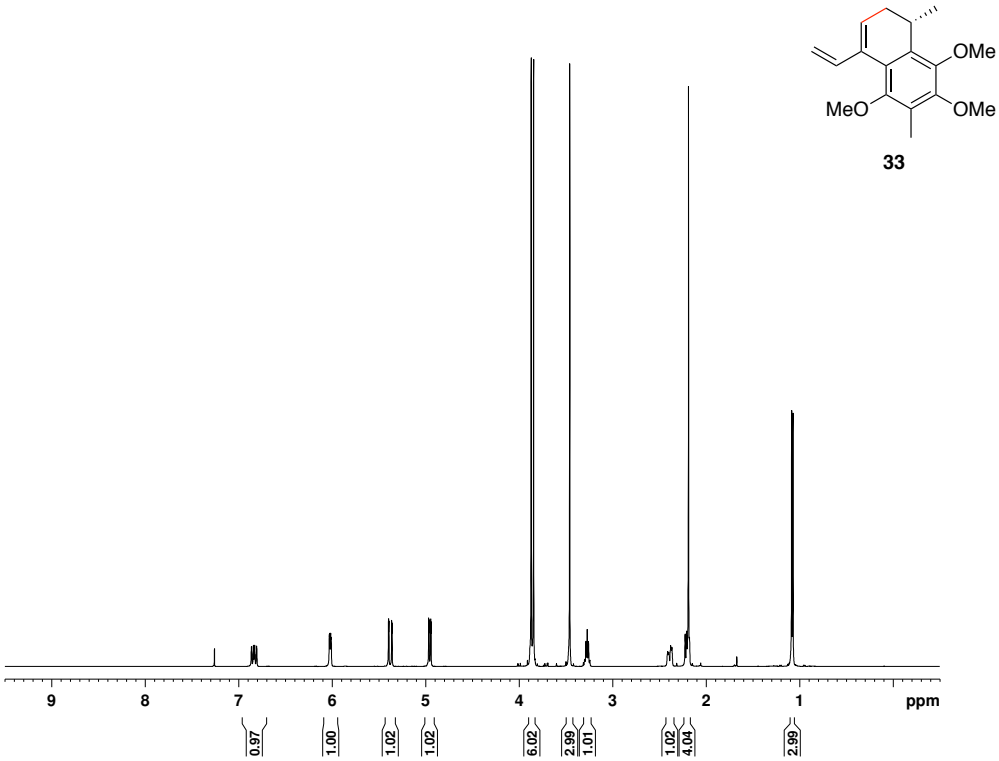
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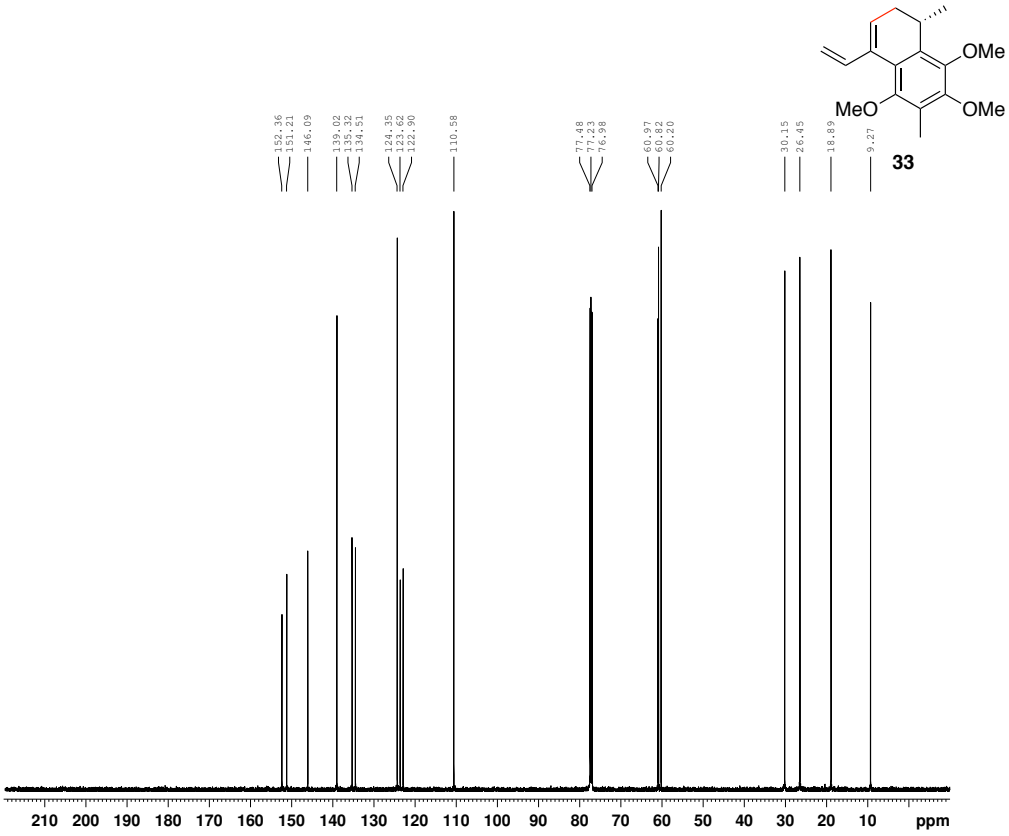
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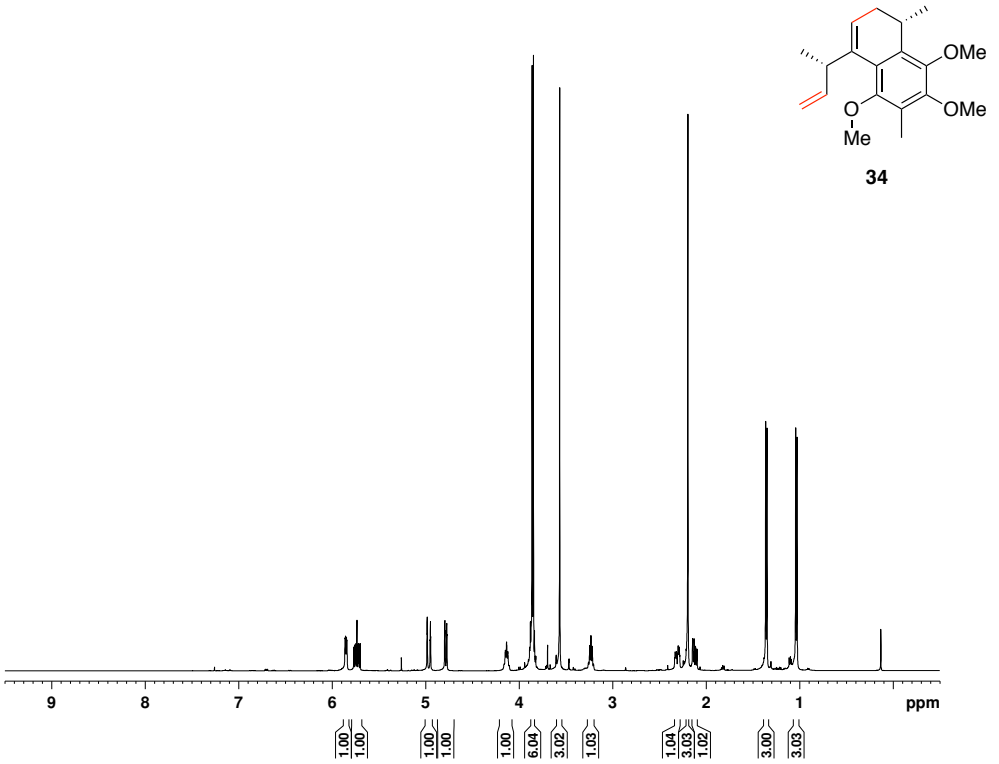
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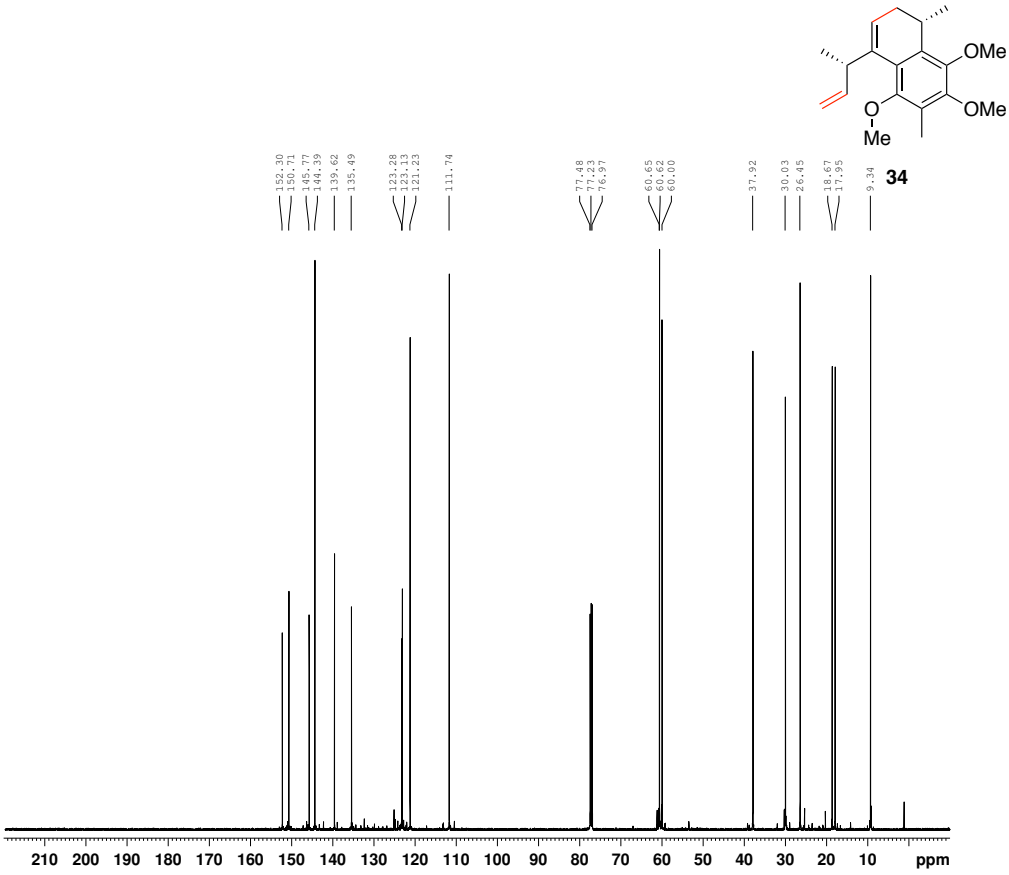
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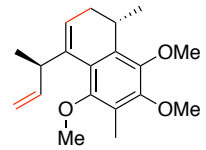

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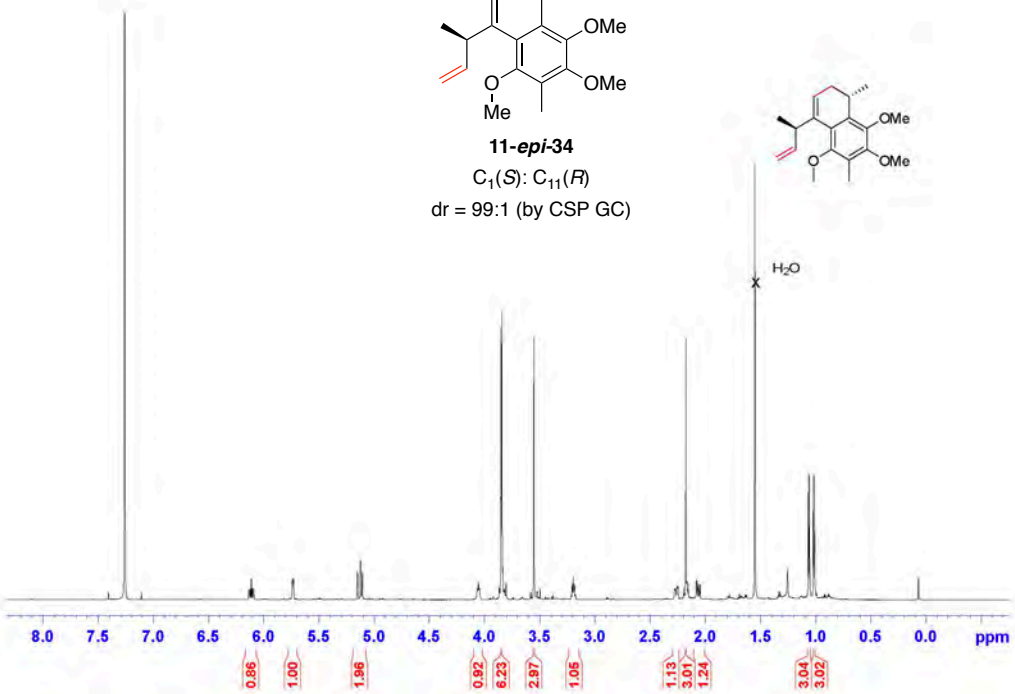
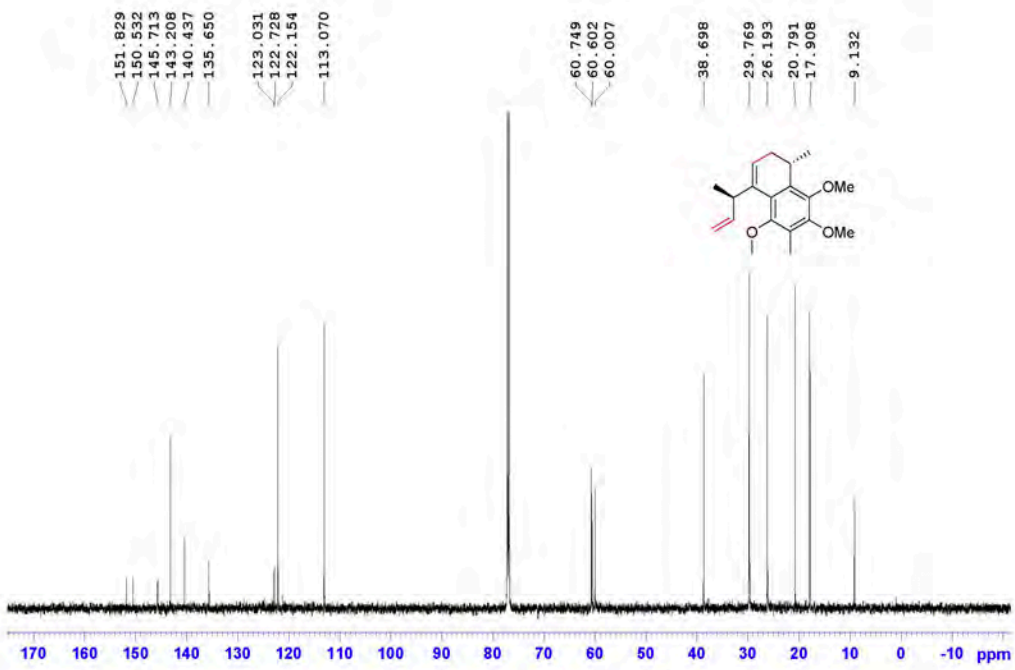
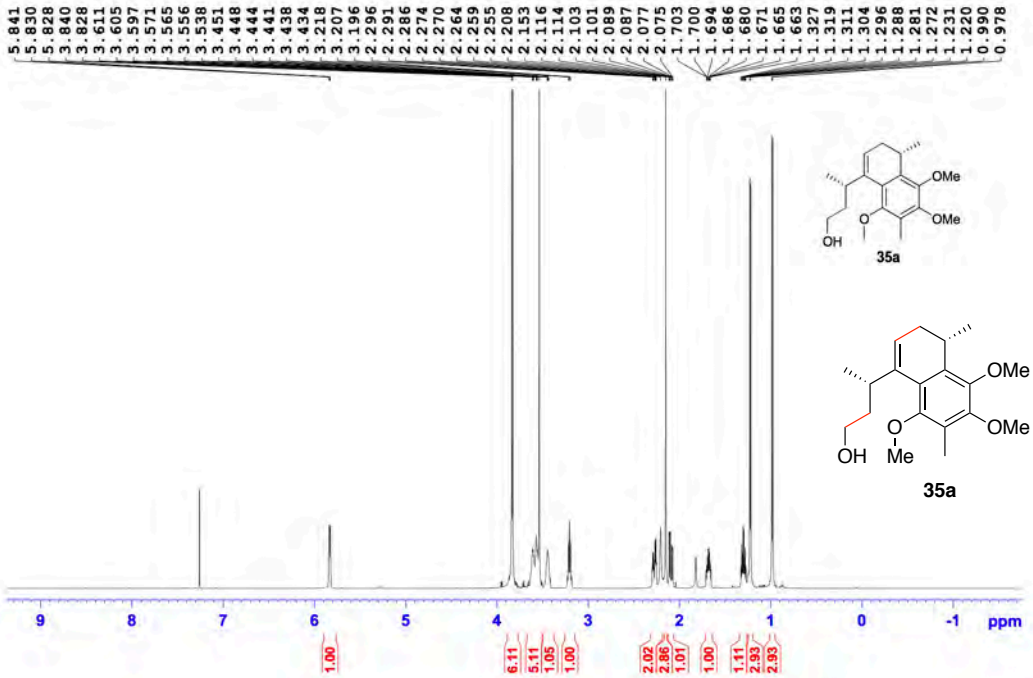
$C_1(S)$: $C_{11}(R)$

dr = 99:1 (by CSP GC)



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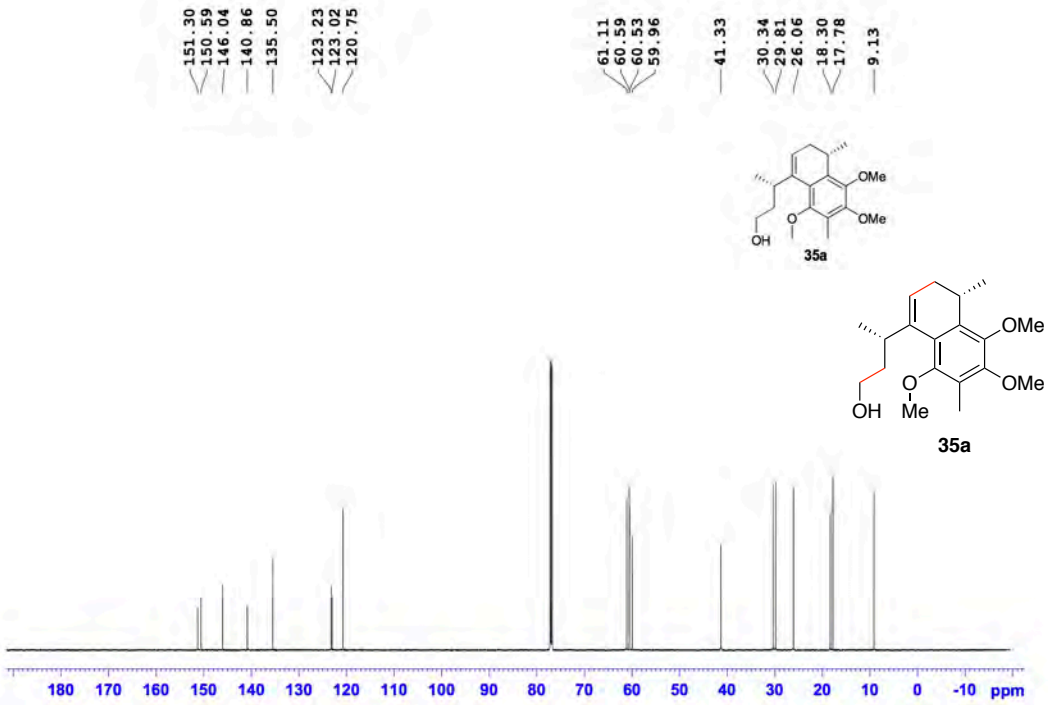
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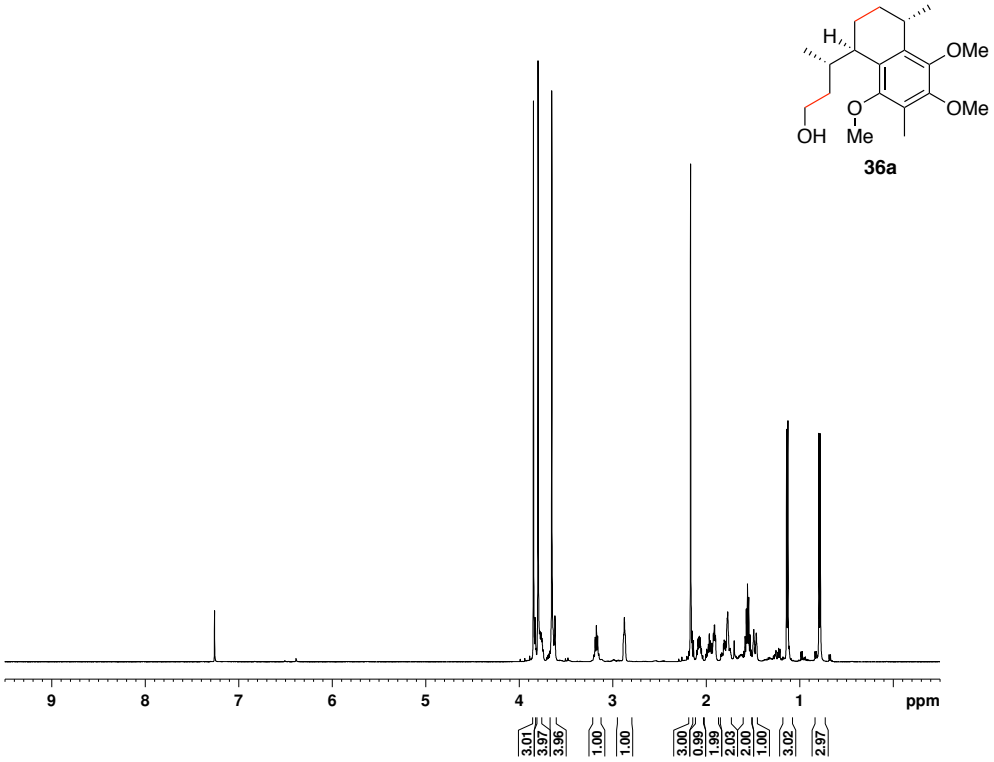
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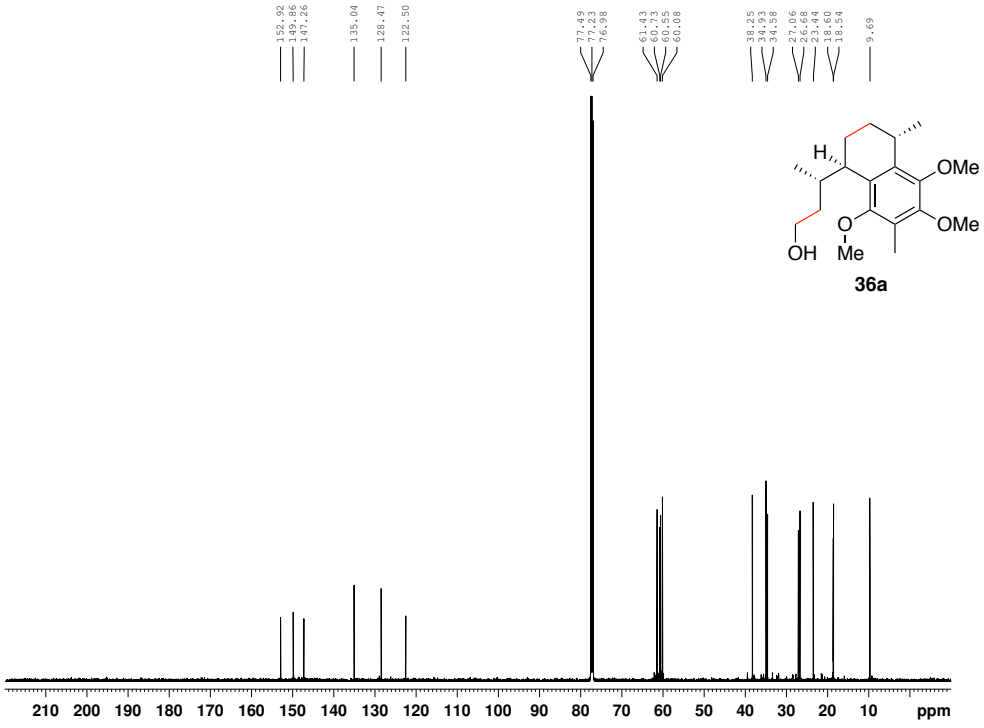
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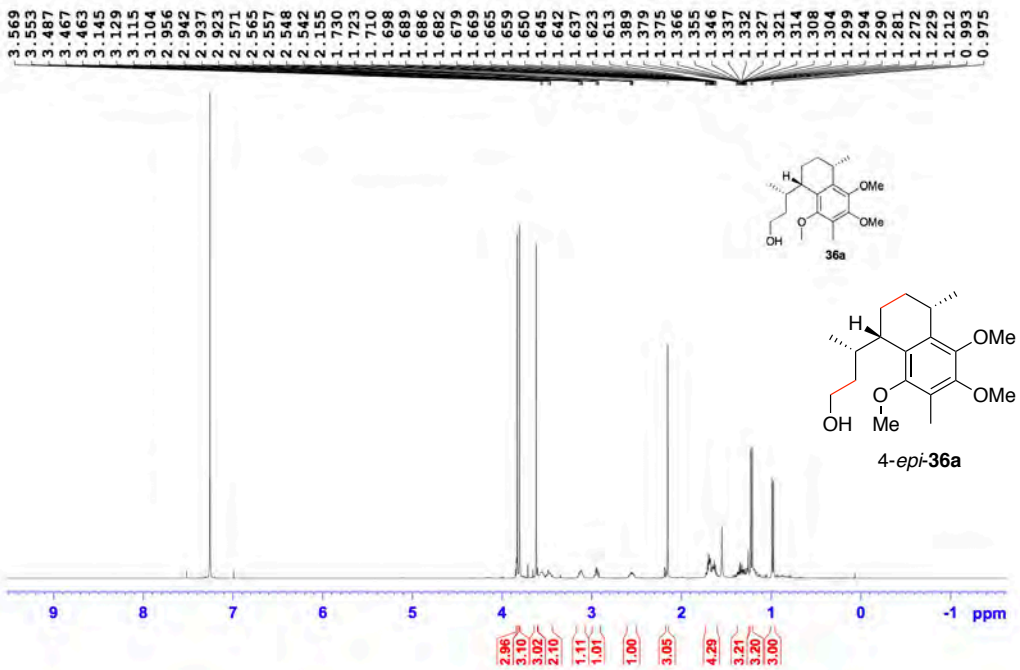
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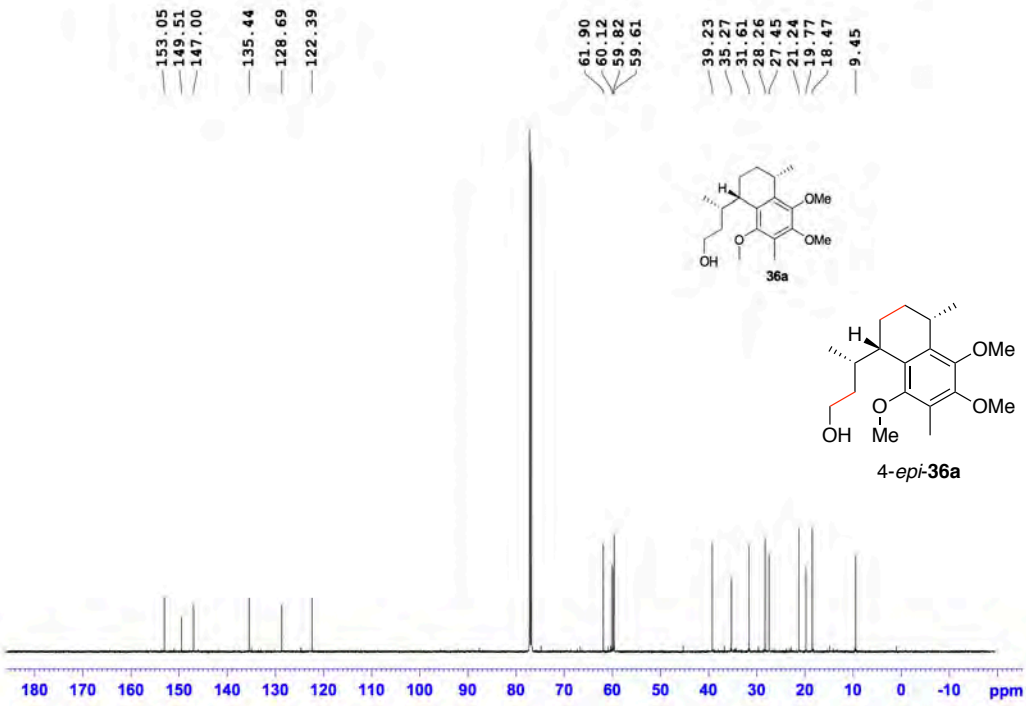
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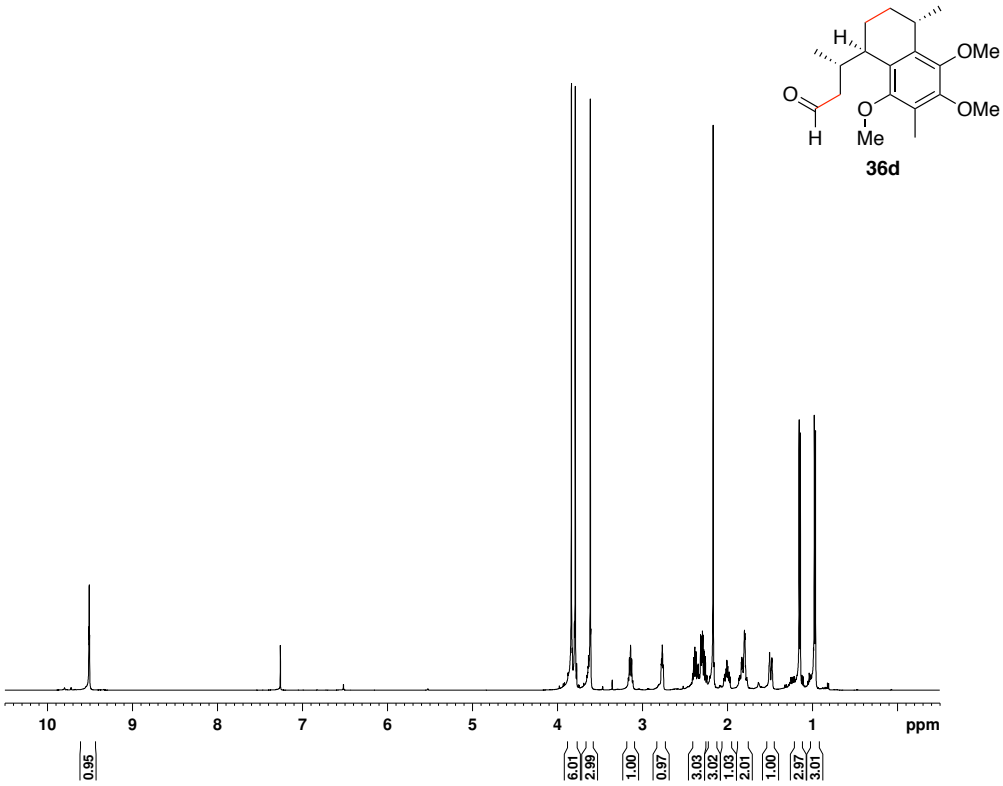
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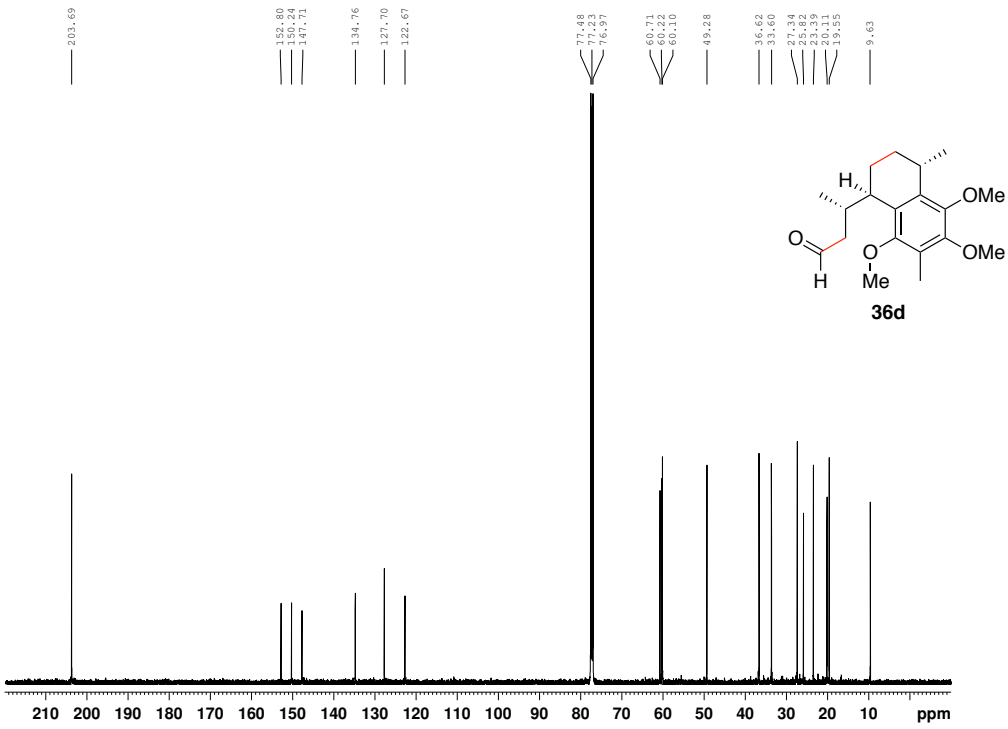
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OMe
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36d
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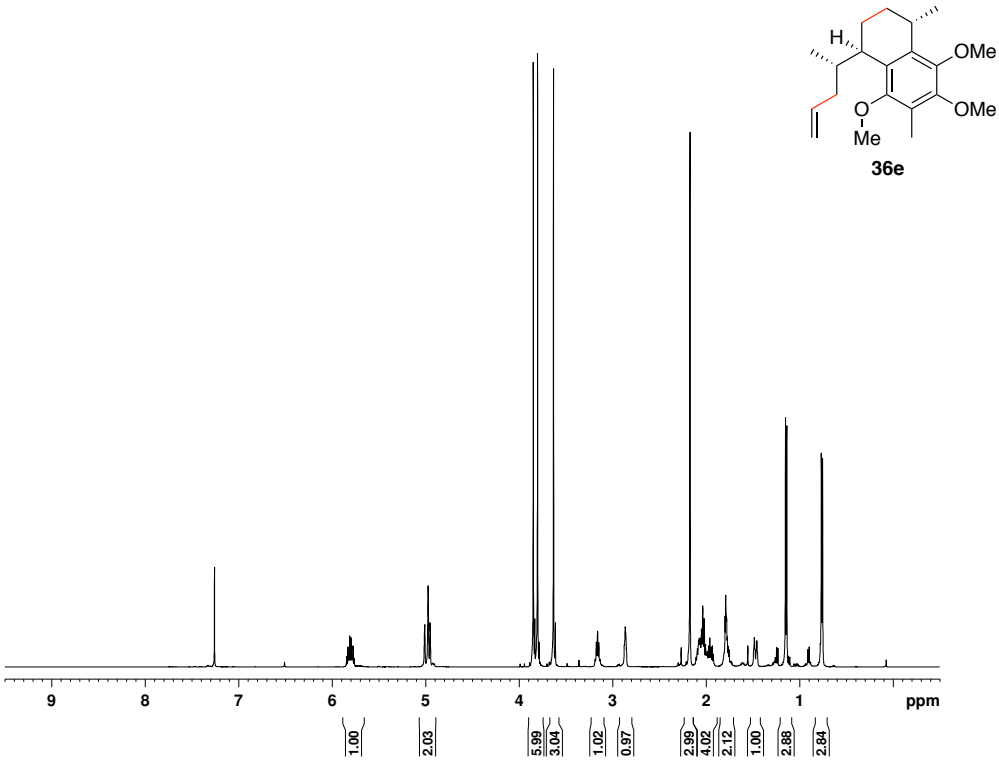
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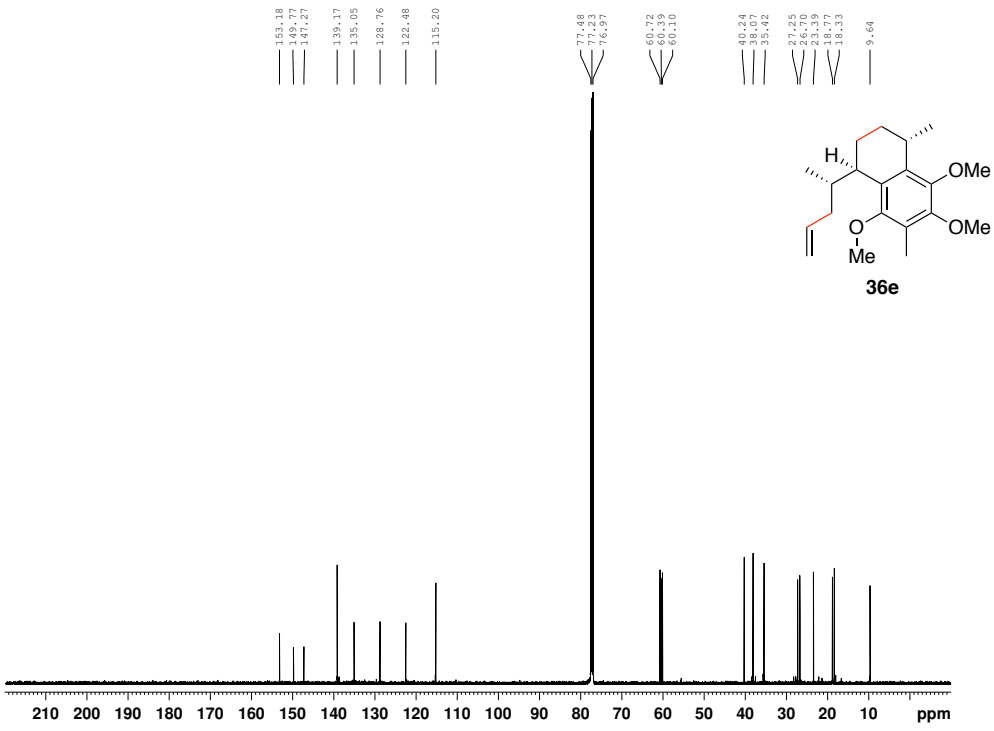
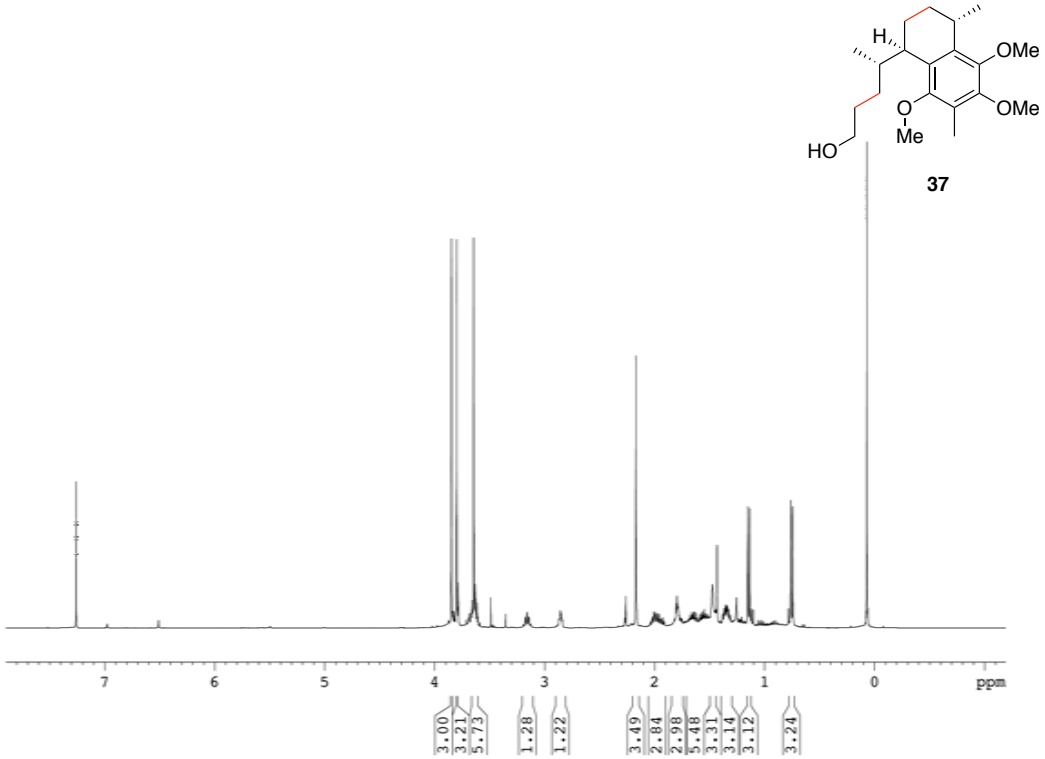
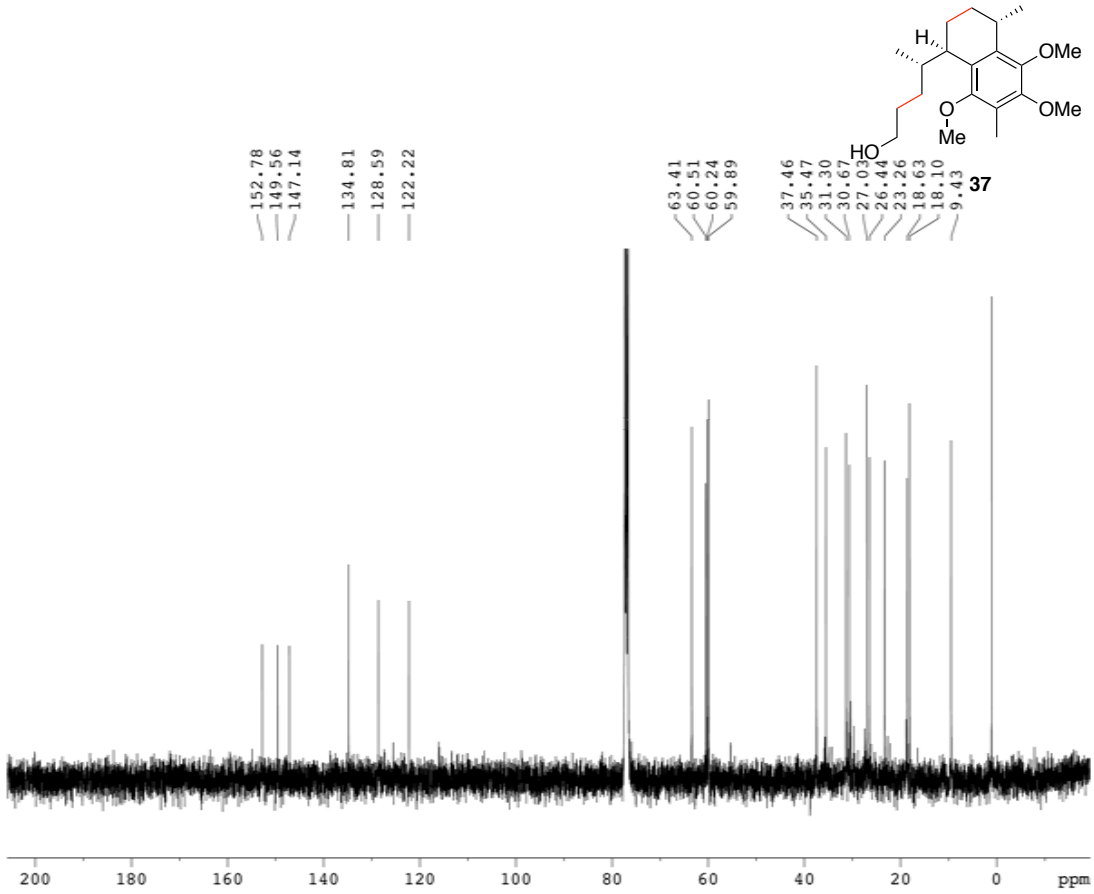
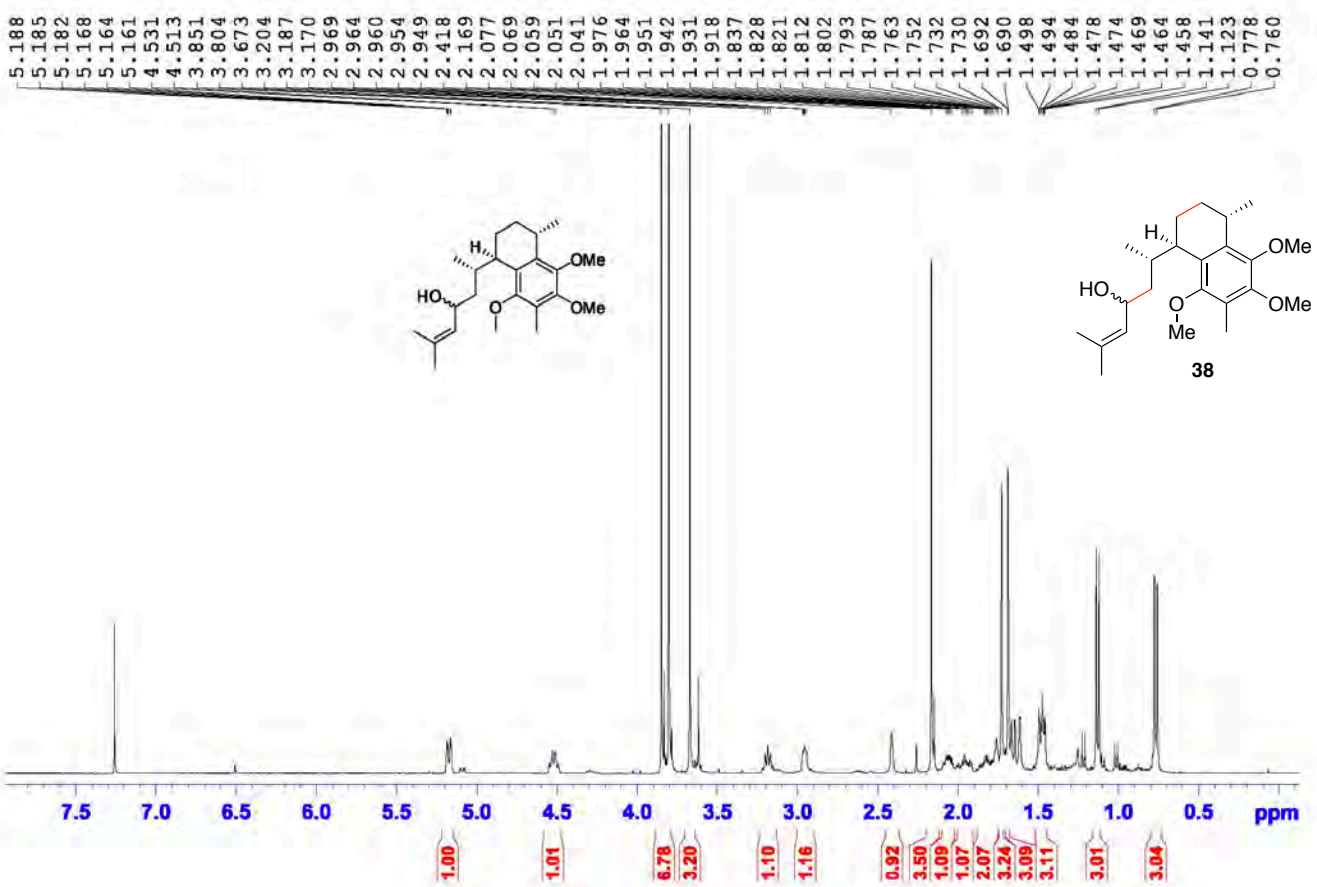
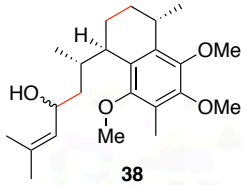
9
8
7
6
5
4
3
2
1
ppm
1.00
2.03
5.99
3.04
1.02
0.97
2.99
4.02
2.12
1.00
2.88
2.84


153.18
149.77
147.27
139.17
135.05
128.76
122.48
115.20
77.48
77.23
76.97
60.72
60.39
60.10
40.24
38.07
35.42
27.25
26.70
23.39
18.77
18.33
9.64
H
OMe
OMe
O
Me
36e
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


H
OMe
OMe
O
Me
HO
37
7
6
5
4
3
2
1
0
ppm
3.00
3.21
5.73
1.28
1.22
3.49
2.84
2.98
5.48
3.31
3.14
3.12
3.24

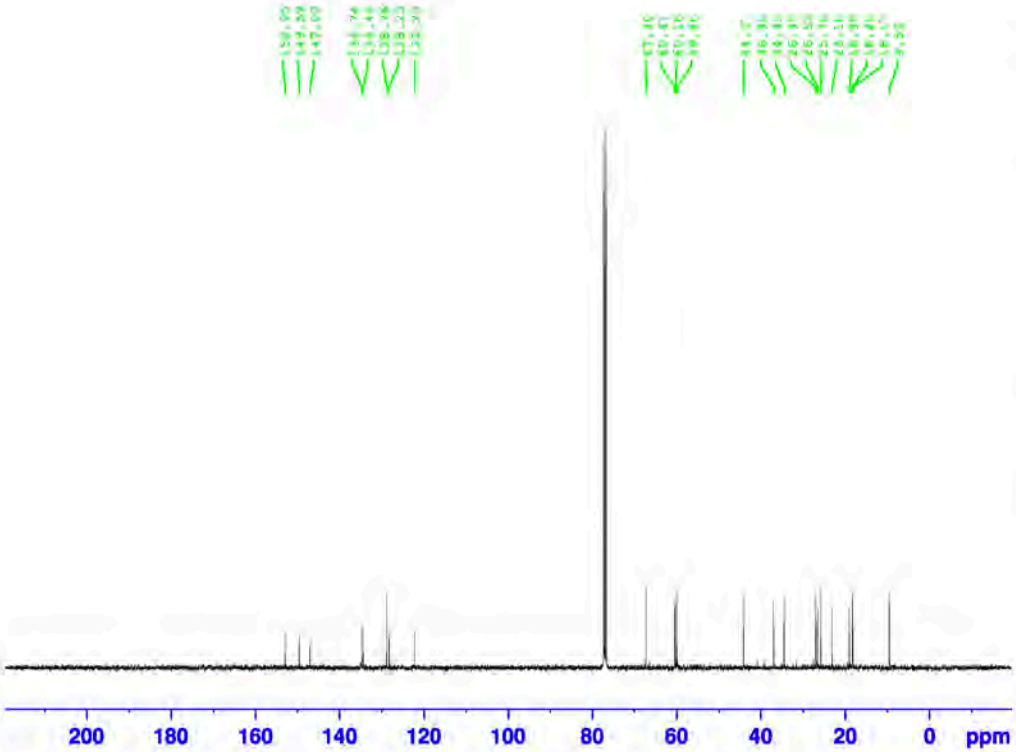

H
OMe
OMe
O
Me
HO
37
152.78
149.56
147.14
134.81
128.59
122.22
63.41
60.51
60.24
59.89
37.46
35.47
31.30
30.67
27.03
26.44
23.26
18.63
18.10
9.43
200
180
160
140
120
100
80
60
40
20
0
ppm


5.188
5.185
5.182
5.168
5.164
5.161
4.531
4.513
3.851
3.804
3.673
3.204
3.187
3.170
2.969
2.964
2.960
2.954
2.949
2.418
2.169
2.077
2.069
2.059
2.051
2.041
1.976
1.964
1.951
1.942
1.931
1.918
1.837
1.828
1.821
1.812
1.802
1.793
1.787
1.763
1.752
1.732
1.730
1.692
1.690
1.498
1.494
1.484
1.478
1.474
1.469
1.464
1.458
1.141
1.123
0.778
0.760
H
OMe
HO
O
OMe
H
OMe
HO
O
Me
OMe
38
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.01
6.78
3.20
1.10
1.16
0.92
3.50
1.09
1.07
2.07
3.24
3.09
3.11
3.01
3.04

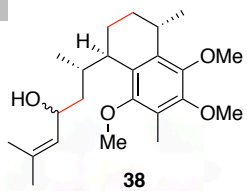


38

Faculty Group Rajanbabu 2163
ST-01-223-GRIG-NP
CARBON_OSU CDCl3 (C:\Bruker\TopSpin3.5pl5) tenneti.3 63

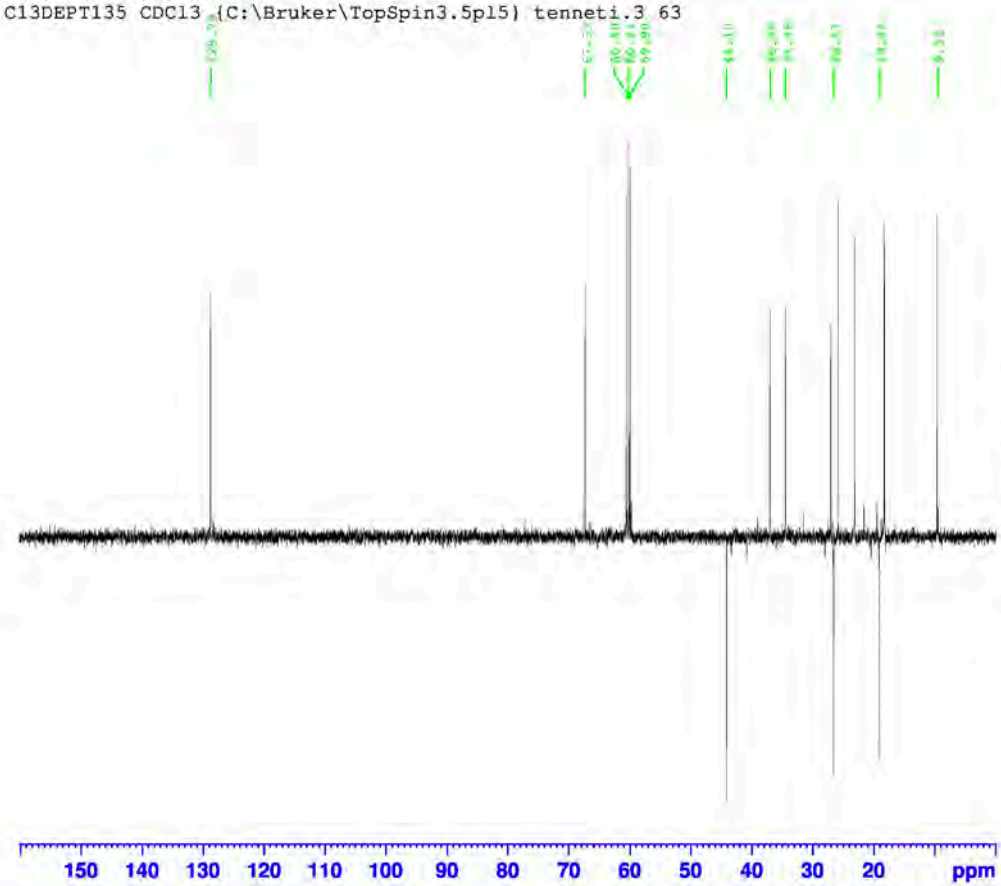



```
Current Data Parameters
NAME      ST-01-223-GRIG-NP
EXPNO                    11
PROCNO                    1

F2 - Acquisition Parameters
Date_            20170414
Time                 1.00 h
INSTRUM             spect
PROBHD    Z108618_0433 (
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH            24038.461 Hz
FIDRES          0.733596 Hz
AQ             1.3631488 sec
RG                  2050
DW                20.800 usec
DE                  6.50 usec
TE                 300.1 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1         100.6328883 MHz
NUC1                 13C
P1                  9.50 usec
PLW1         53.29999924 W
SFO2         400.1716007 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              90.00 usec
PLW2         14.60000038 W
PLW12         0.40555999 W
PLW13         0.20399000 W

F2 - Processing parameters
SI                 32768
SF          100.6228295 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

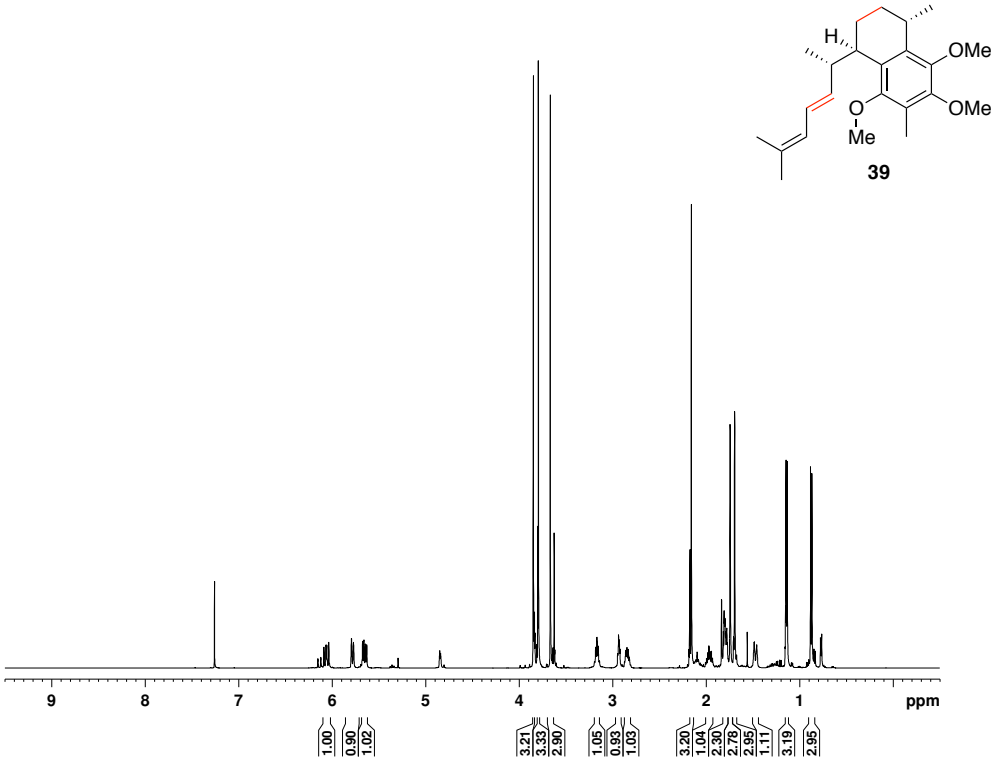


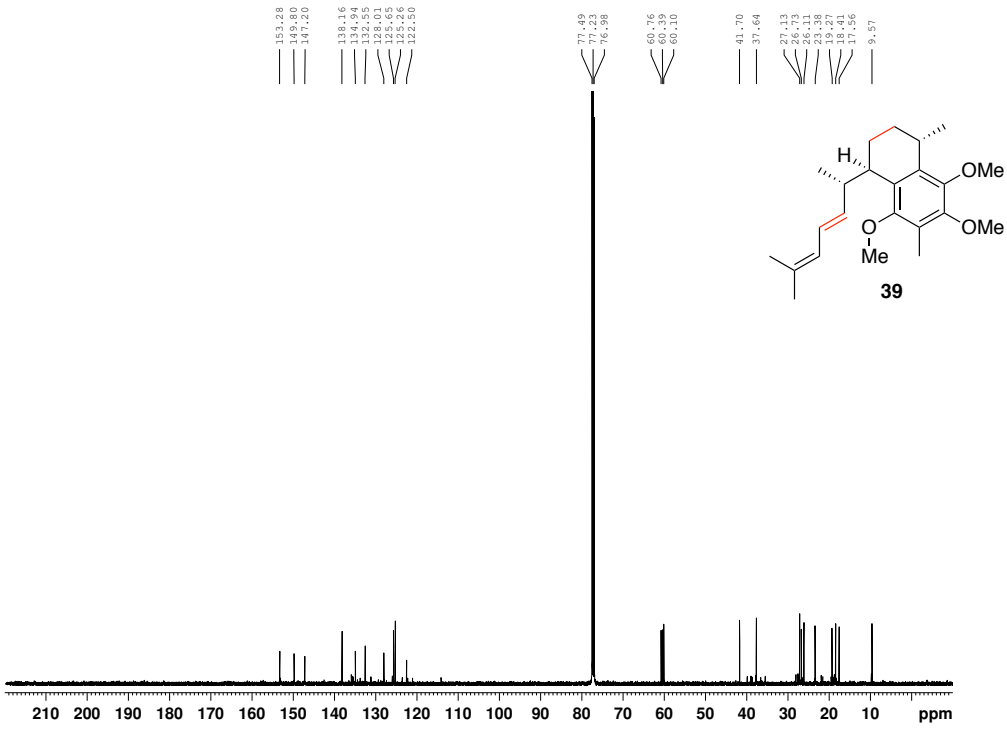
38

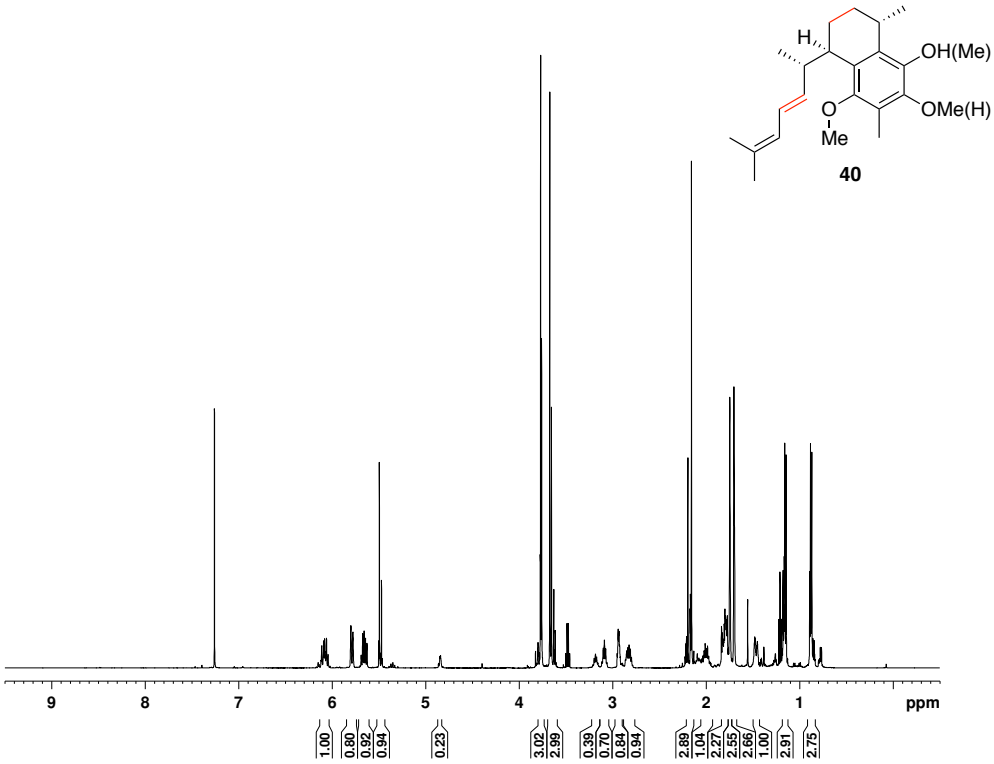
Faculty Group Rajanbabu 2163
ST-01-223-GRIG-NP
C13DEPT135 CDCl3 (C:\Bruker\TopSpin3.5pl5) tenneti.3 63

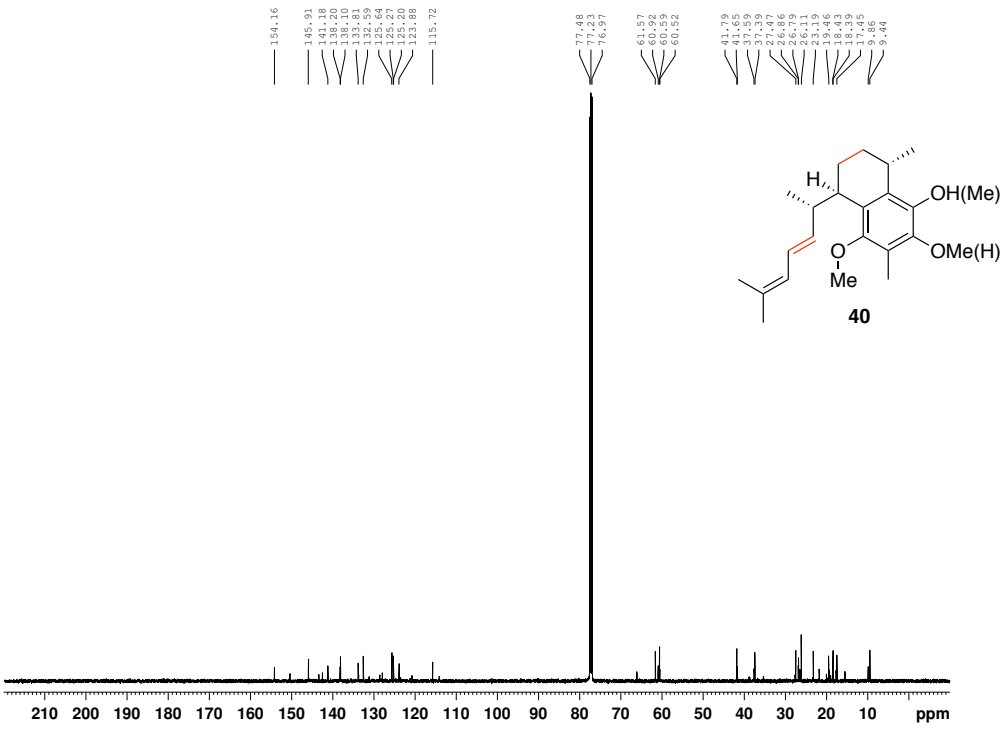


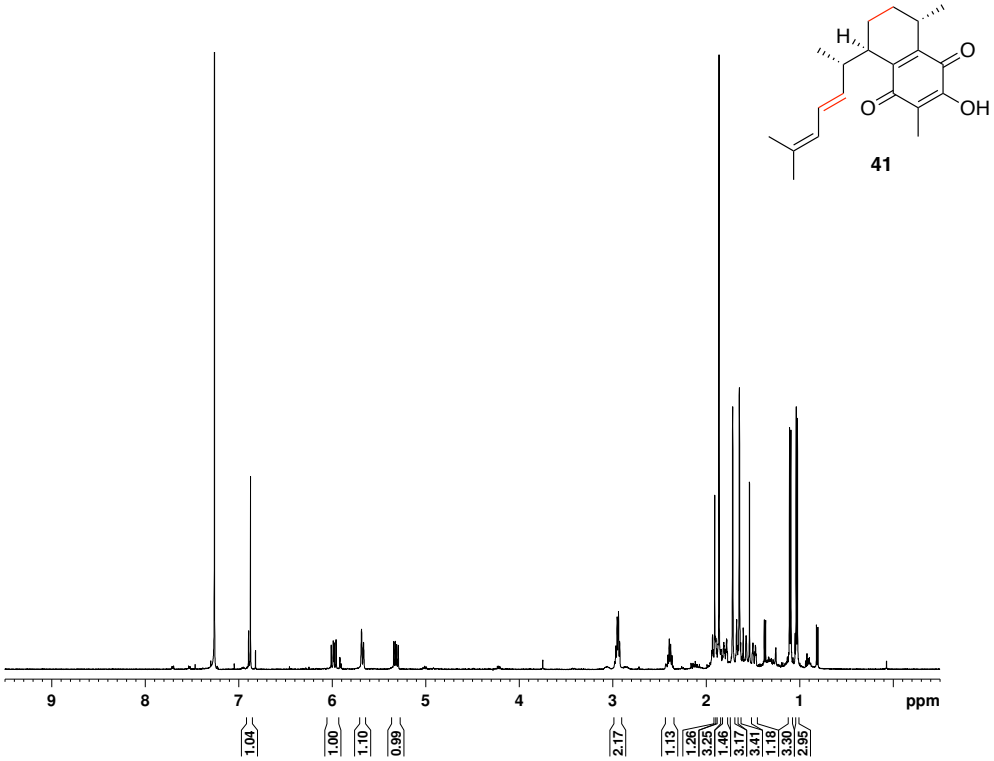

```
C
NAME        ST-01-223-GRIG-NP
EXPNO                      12
PROCNO                      1

F2 - Acquisition Parameters
Date_               20170414
Time                    1.37 h
INSTRUM                 spect
PROBHD     Z108618_0433 (
PULPROG            deptsp135
TD                     65536
SOLVENT                 CDCl3
NS                        512
DS                          8
SWH                16129.032 Hz
FIDRES              0.492219 Hz
AQ                 2.0316160 sec
RG                       2050
DW                     31.000 usec
DE                       6.50 usec
TE                      300.1 K
CNST2             145.0000000
D1                 2.00000000 sec
D2                 0.00344828 sec
D12                0.00002000 sec
TD0                         1
SFO1              100.6308764 MHz
NUC1                       13C
P1                        9.50 usec
P13                    2000.00 usec
PLW0        0 W
PLW1               53.29999924 W
SPNAM[5]           Crp60comp.4
SPOAL5                   0.500
SPOFFS5     0 Hz
SPW5                7.34959984 W
SFO2              400.1716007 MHz
NUC2                        1H
CPDPRG[2                waltz16
P3                       15.00 usec
P4                       30.00 usec
PCPD2                    90.00 usec
PLW2               14.60000038 W
PLW12               0.40555999 W

F2 - Processing parameters
SI                       32768
SF                 100.6228265 MHz
WDW                         EM
SSB         0
LB                        1.00 Hz
GB          0
PC                        1.40
```

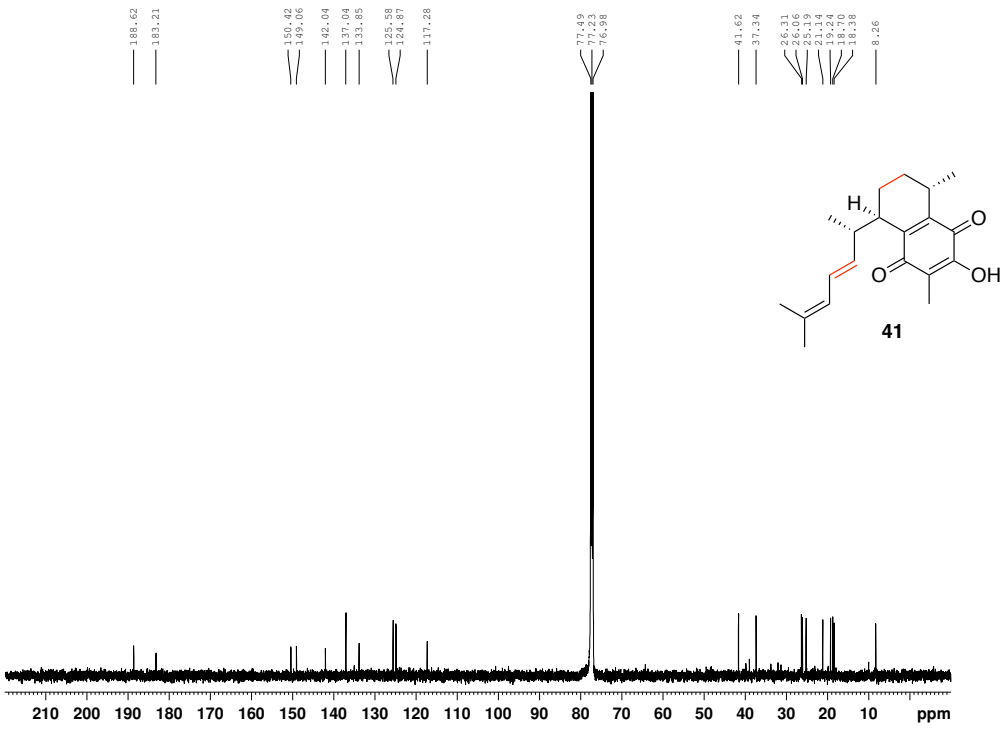

H
OMe
OMe
O
Me
39
9
8
7
6
5
4
3
2
1
ppm
1.00
0.90
1.02
3.21
3.33
2.90
1.05
0.93
1.03
3.20
1.04
2.30
2.78
2.95
1.11
3.19
2.95

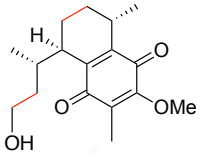

153.28
149.80
147.20
138.16
134.94
132.55
132.01
125.65
125.26
122.50
77.49
77.23
76.98
60.76
60.39
60.10
41.70
37.64
27.13
26.73
26.11
23.38
19.27
18.41
17.56
9.57
H
OMe
OMe
O
Me
39
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


H
OH(Me)
OMe(H)
O
Me
40
9
8
7
6
5
4
3
2
1
ppm
1.00
0.80
0.92
0.94
0.23
3.02
2.99
0.39
0.70
0.84
0.94
2.89
1.04
2.27
2.55
2.66
1.00
2.91
2.75

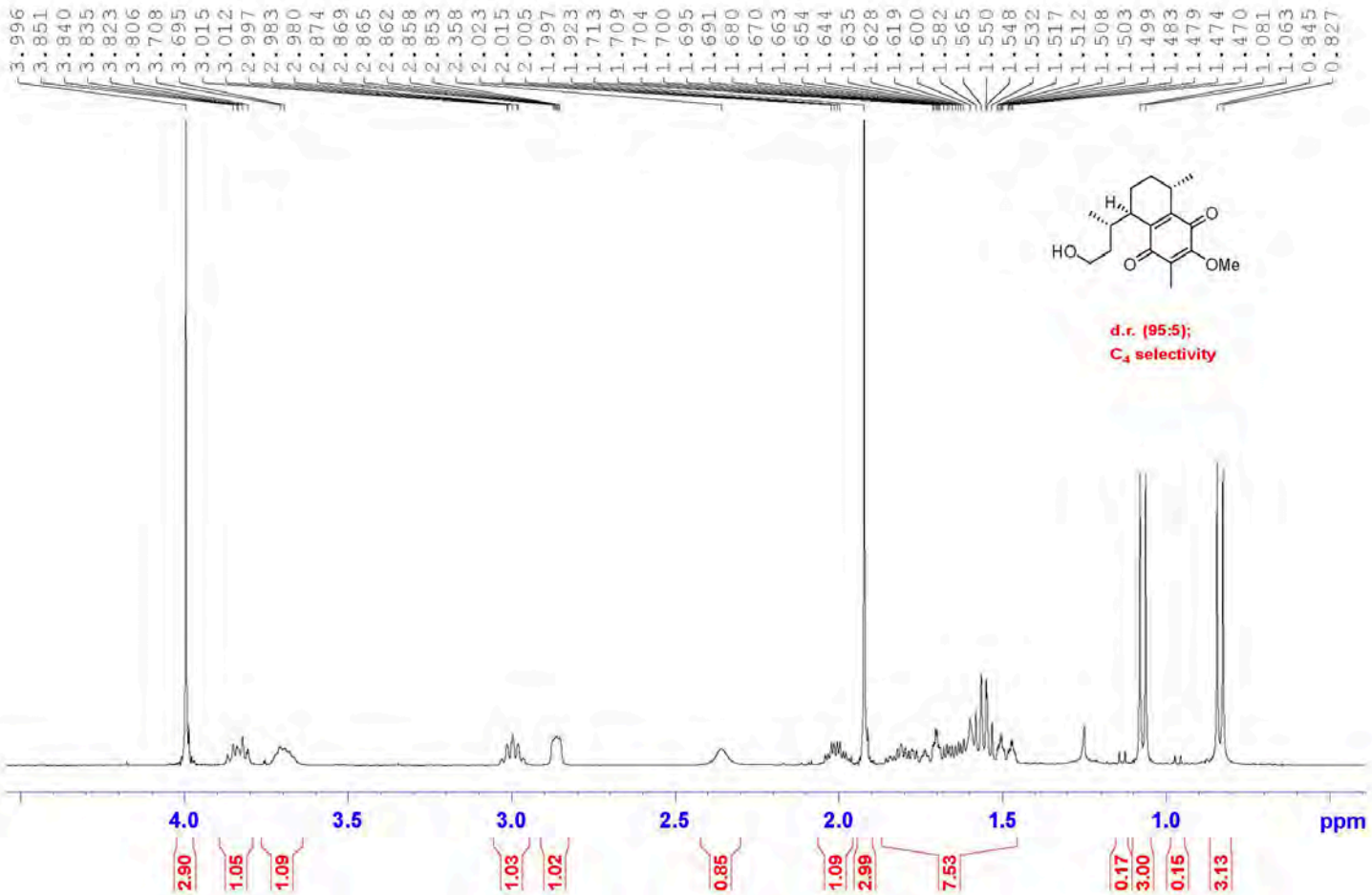

154.16
145.91
141.18
138.20
138.10
133.81
132.59
125.64
125.27
125.20
123.88
115.72
77.48
77.23
76.97
61.57
60.92
60.59
60.52
41.79
41.65
37.59
37.39
37.17
26.86
26.79
26.11
23.19
19.46
19.45
18.39
17.45
9.86
9.44
H
OH(Me)
OMe(H)
O
Me
40
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

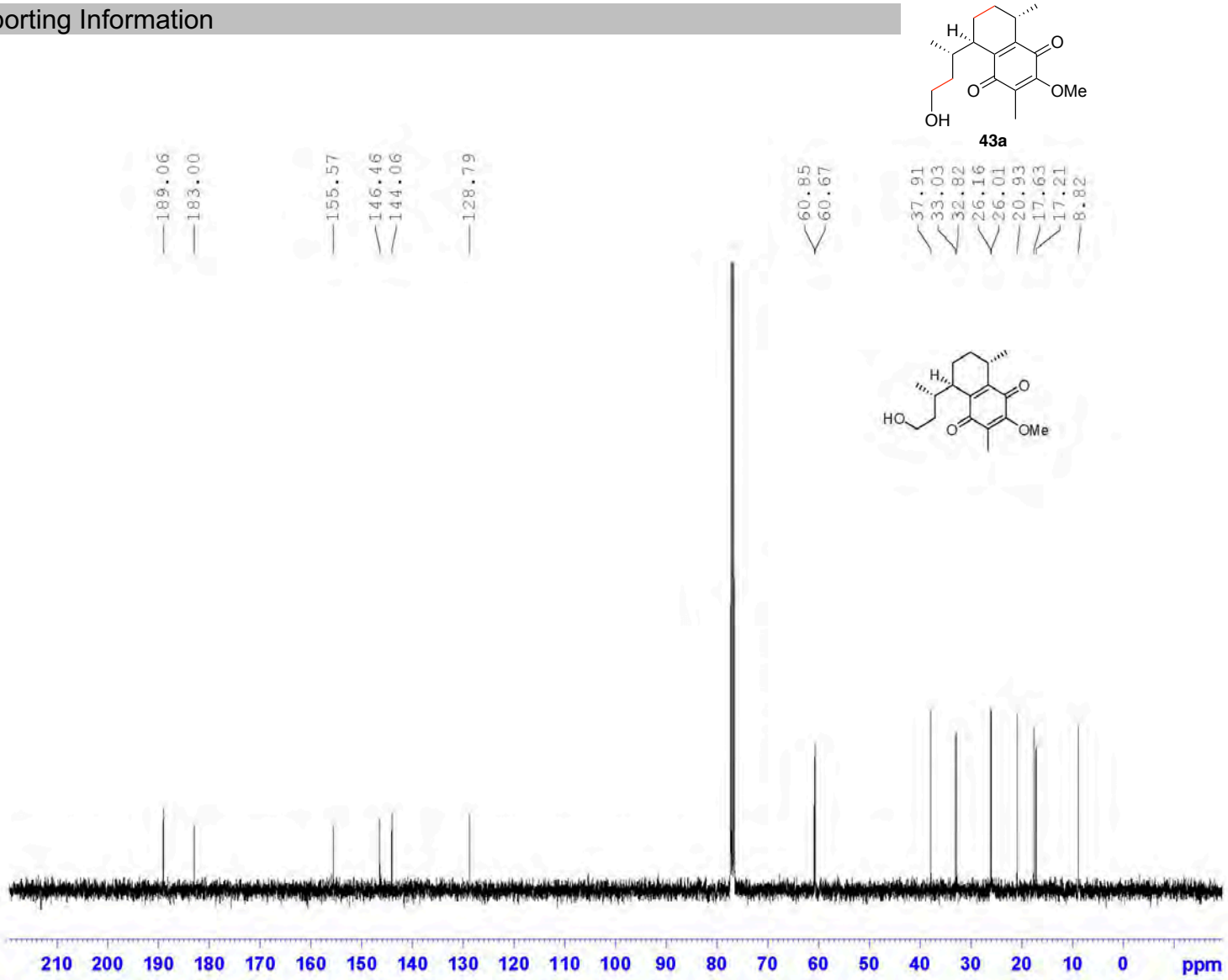

H
O
O
OH
41
9
8
7
6
5
4
3
2
1
ppm
1.04
1.00
1.10
0.99
2.17
1.13
1.26
3.25
1.46
3.17
3.41
1.18
3.30
2.95

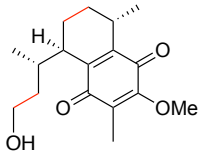

188.62
183.21
150.42
149.06
142.04
137.04
133.85
125.58
124.87
117.28
77.49
77.23
76.98
41.62
37.34
26.31
26.06
25.19
21.14
19.24
18.70
18.38
8.26
H
O
O
OH
41
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


H
O
O
OMe
OH

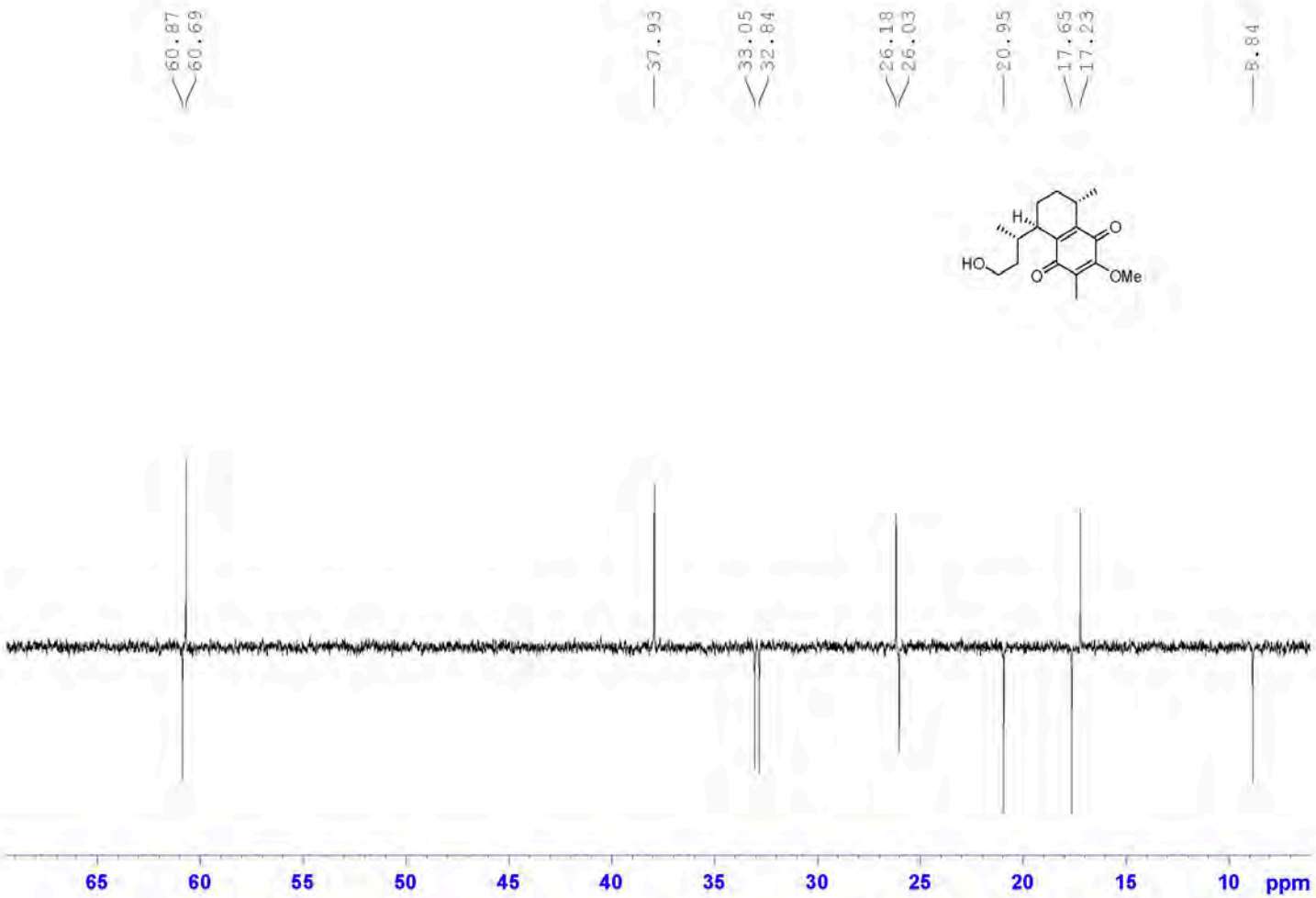
43a

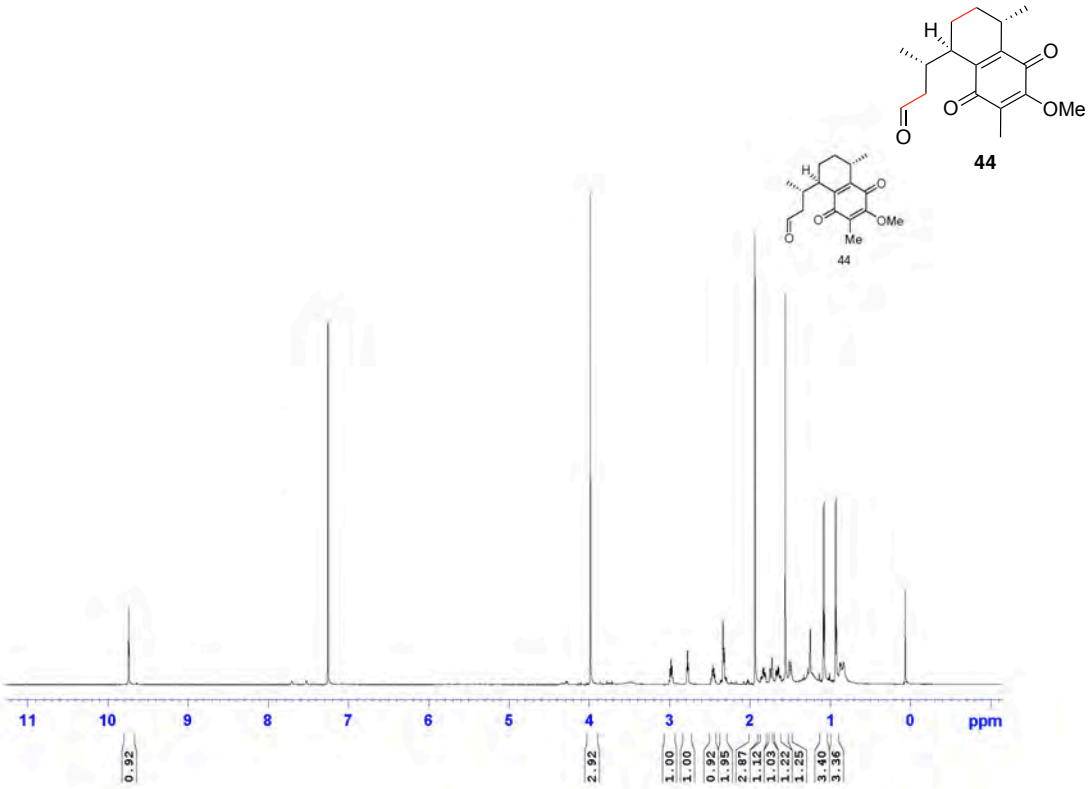

3.996 3.851 3.840 3.835 3.823 3.806 3.708 3.695 3.015 3.012 2.997 2.983 2.980 2.874 2.869 2.865 2.862 2.858 2.853 2.358 2.023 2.015 2.005 1.997 1.923 1.713 1.709 1.704 1.700 1.695 1.691 1.680 1.670 1.663 1.654 1.644 1.635 1.628 1.619 1.600 1.582 1.565 1.550 1.548 1.532 1.517 1.512 1.508 1.503 1.499 1.483 1.479 1.474 1.470 1.081 1.063 0.845 0.827
H
O
HO
O
OMe
d.r. (95:5);
C4 selectivity
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.90
1.05
1.09
1.03
1.02
0.85
1.09
2.99
7.53
0.17
3.00
0.15
3.13

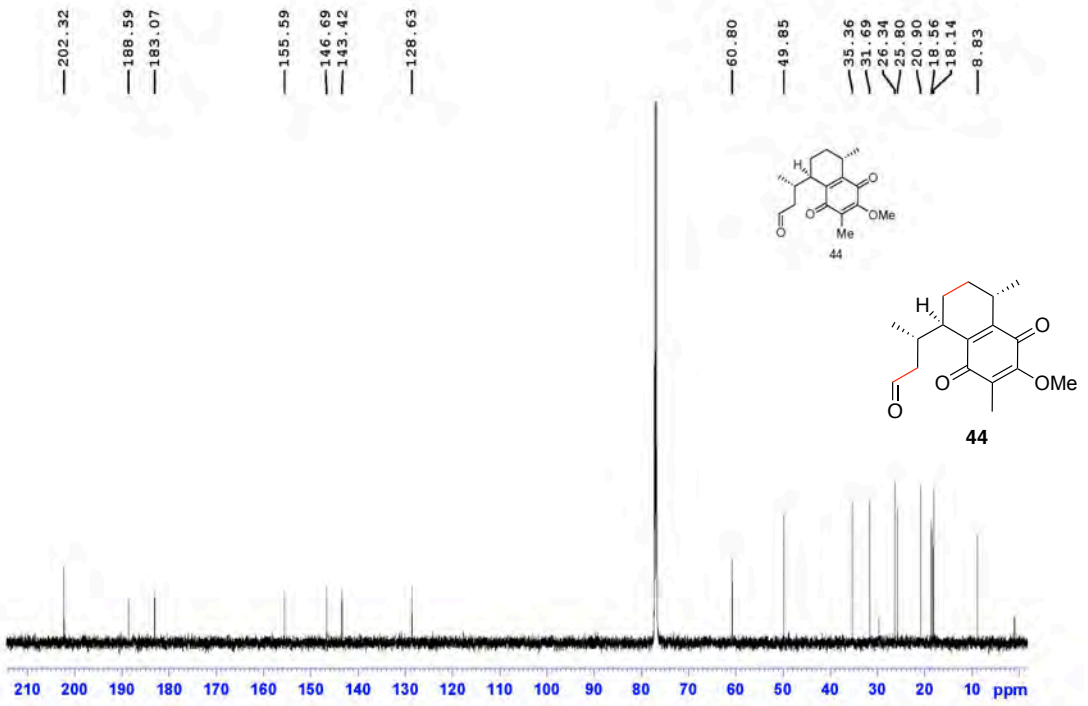

43a
189.06
183.00
155.57
146.46
144.06
128.79
60.85
60.67
37.91
33.03
32.82
26.16
26.01
20.93
17.63
17.21
8.82
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

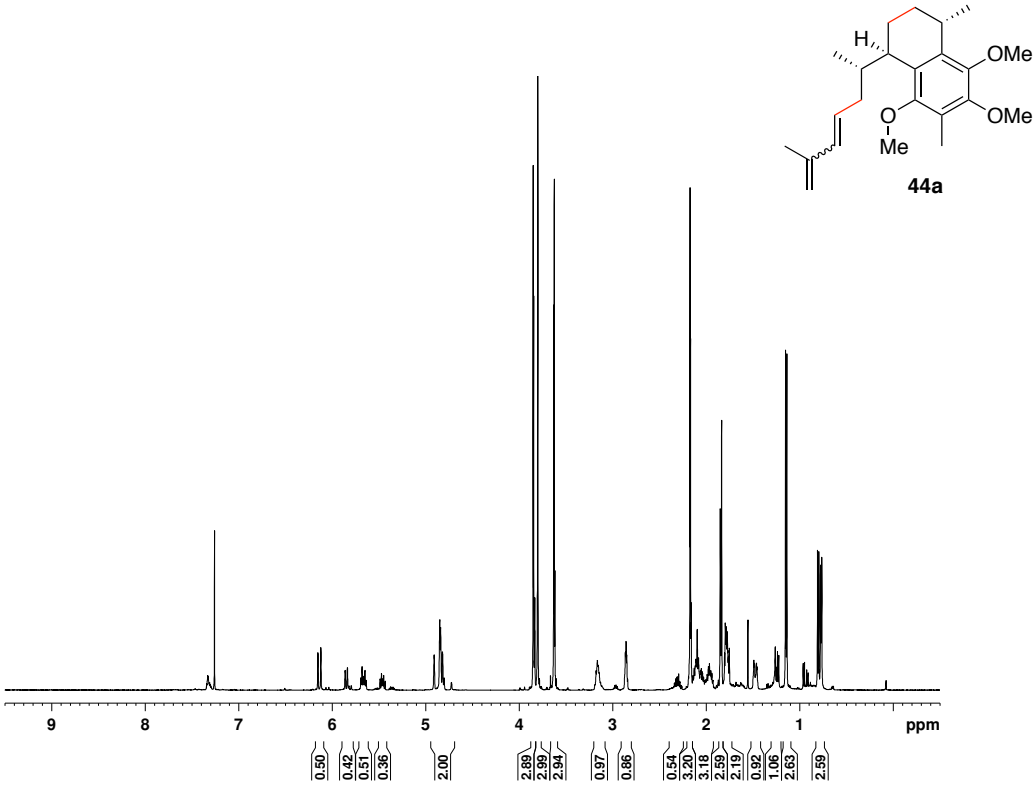

H
O
O
OMe
OH

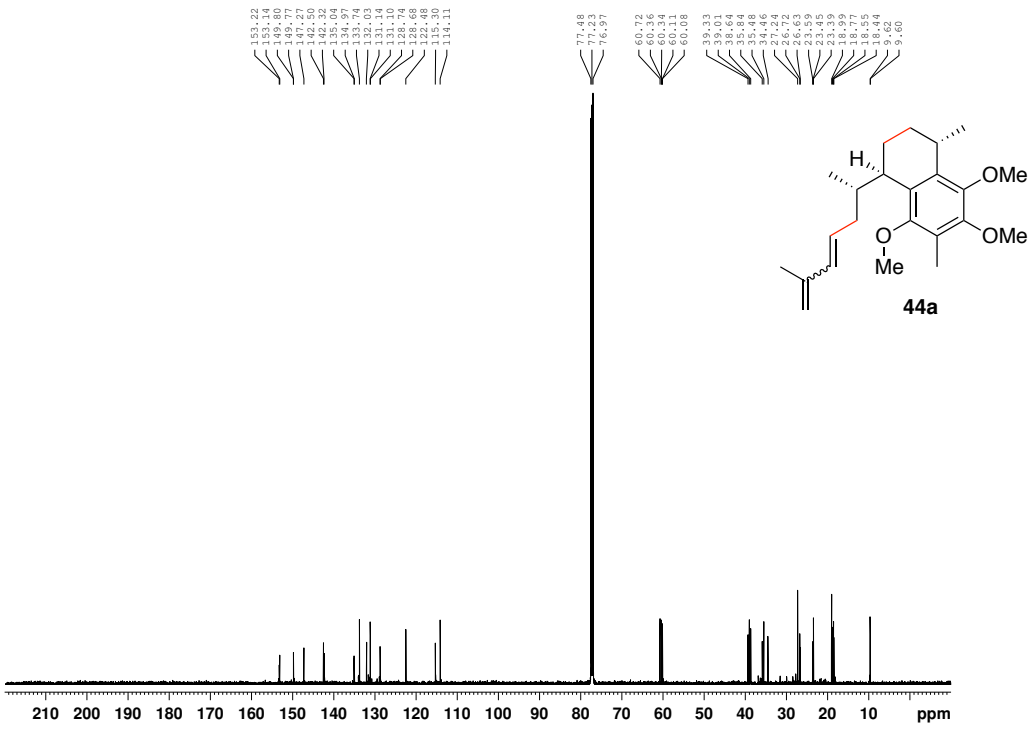
43a

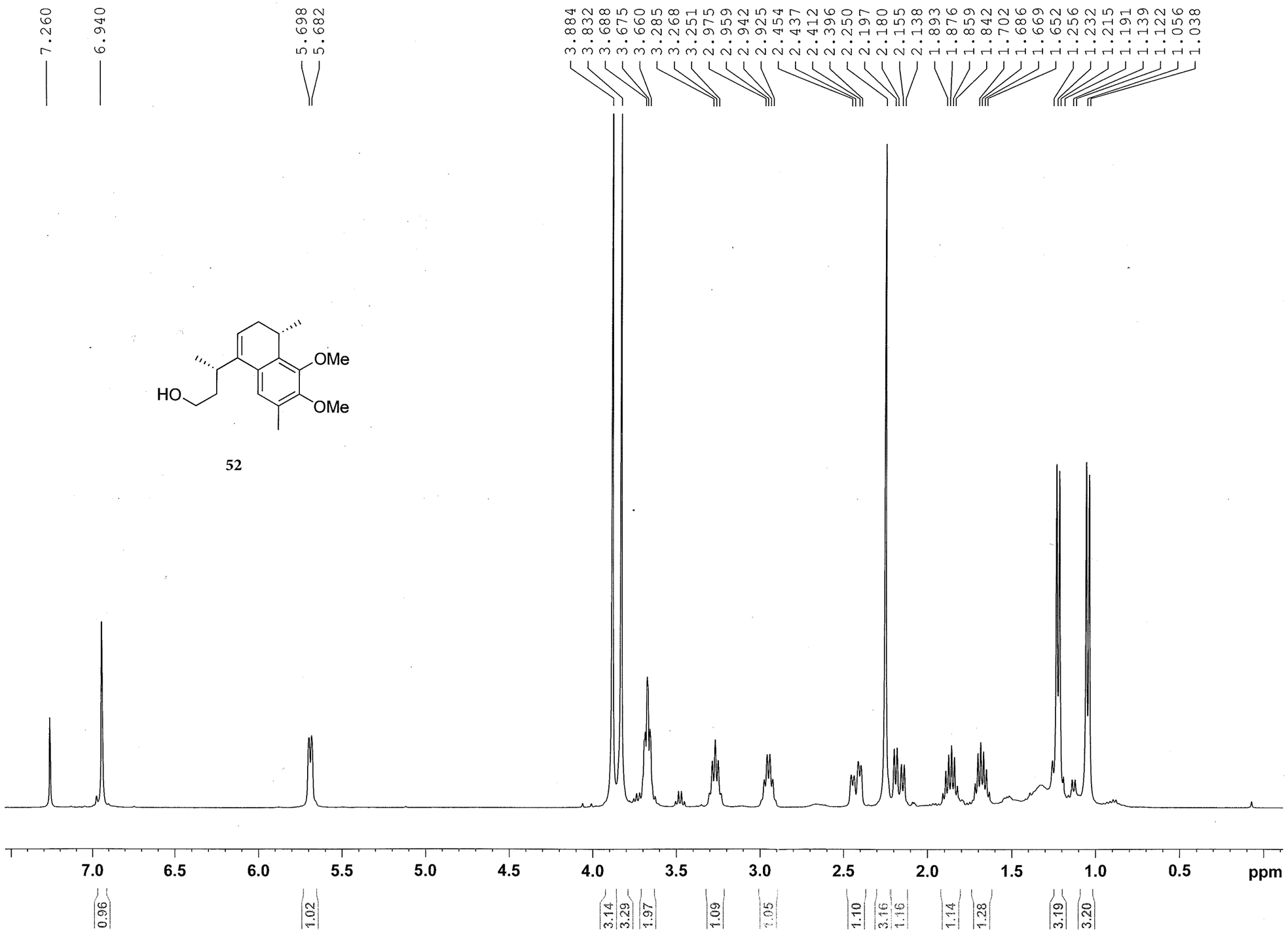

60.87
60.69
37.93
33.05
32.84
26.18
26.03
20.95
17.65
17.23
8.84
H
O
O
HO
OMe
65
60
55
50
45
40
35
30
25
20
15
10
ppm


44
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.92
2.92
1.00
1.00
0.92
1.95
2.87
1.12
1.03
1.22
1.25
3.40
3.36


202.32
188.59
183.07
155.59
146.69
143.42
128.63
60.80
49.85
35.36
31.69
26.34
25.80
20.90
18.56
18.14
8.83
44
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


H
OMe
OMe
O
Me
44a
9
8
7
6
5
4
3
2
1
ppm
0.50
0.42
0.51
0.36
2.00
2.89
2.99
2.94
0.97
0.86
0.54
3.20
3.18
2.59
2.19
0.92
1.06
2.63
2.59


153.22
153.14
149.80
149.77
147.27
142.50
142.32
135.04
134.97
133.74
132.03
131.14
131.10
128.74
128.68
122.48
115.30
114.11
77.48
77.23
76.97
60.72
60.36
60.34
60.11
60.08
39.33
39.01
38.64
35.84
35.48
34.46
27.24
26.72
26.65
23.59
23.45
23.39
18.99
18.79
18.77
18.55
18.44
9.62
9.60
H
OMe
OMe
O
Me
44a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

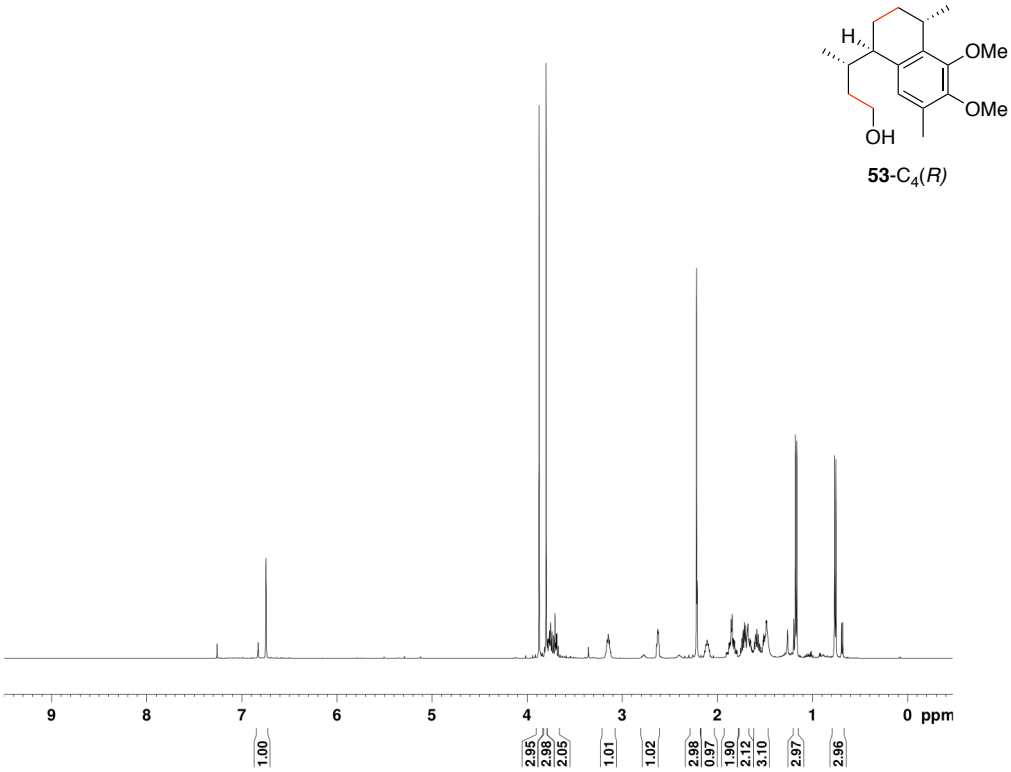


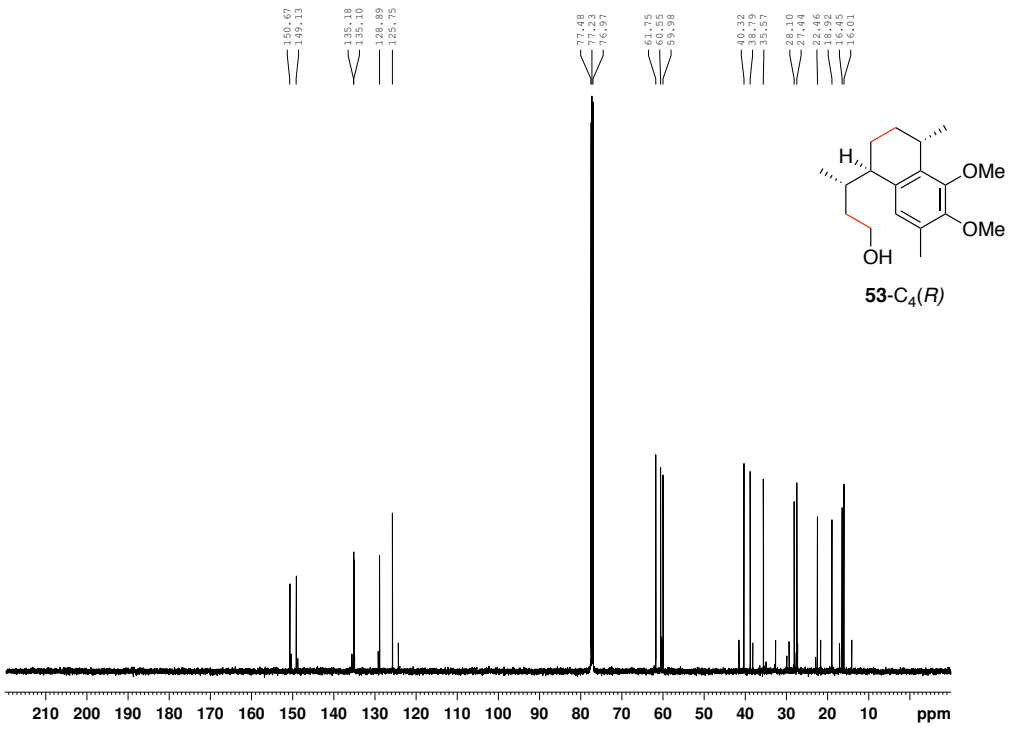
Current Data Parameters
NAME 8-265
EXPNO 9
PROCNO 1

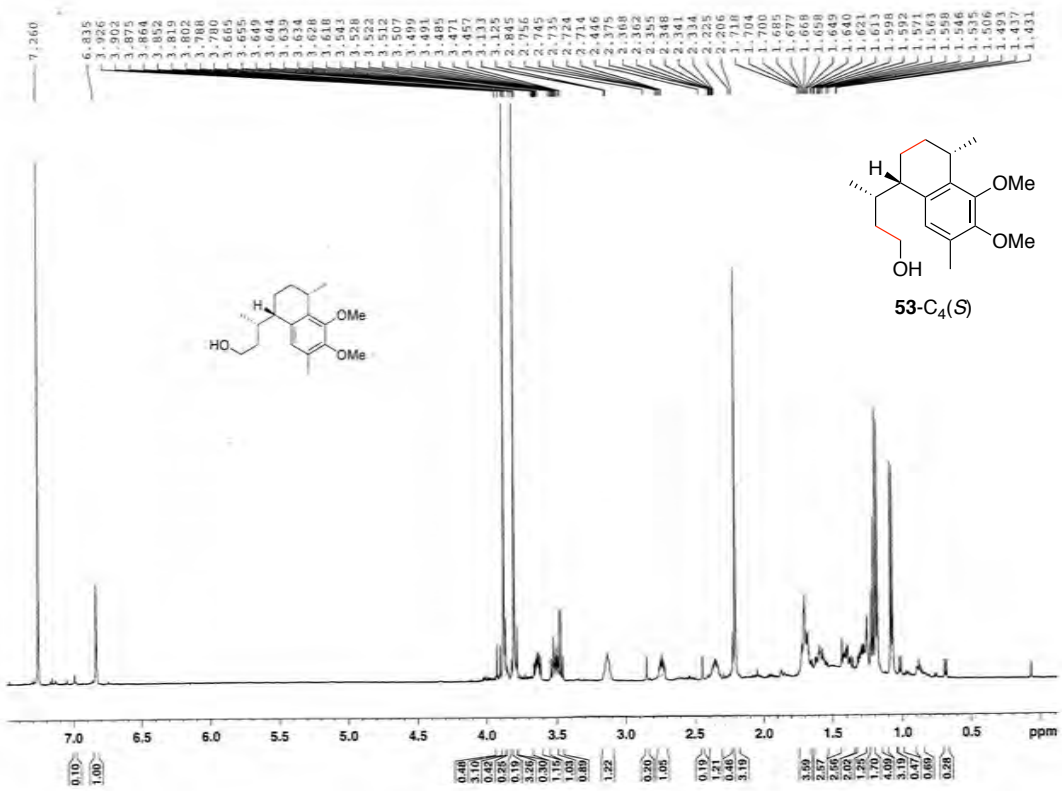
F2 - Acquisition Parameters
Date_ 20071015
Time 12.49
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 128
DW 60.400 usec
DE 6.00 usec
TE 0.0 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 13.00 usec
PL1 0.00 dB
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300101 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


H
OMe
OMe
OH
53-C4(R)
9 8 7 6 5 4 3 2 1 0 ppm
1.00
2.95
2.98
2.05
1.01
1.02
2.98
0.97
1.90
2.12
3.10
2.97
2.96


150.67
149.13
135.18
135.10
128.89
125.75
77.48
77.23
76.97
61.75
60.55
59.98
40.32
38.79
35.57
28.10
27.44
22.46
18.22
16.45
16.01
H
OMe
OMe
OH
53-C4(R)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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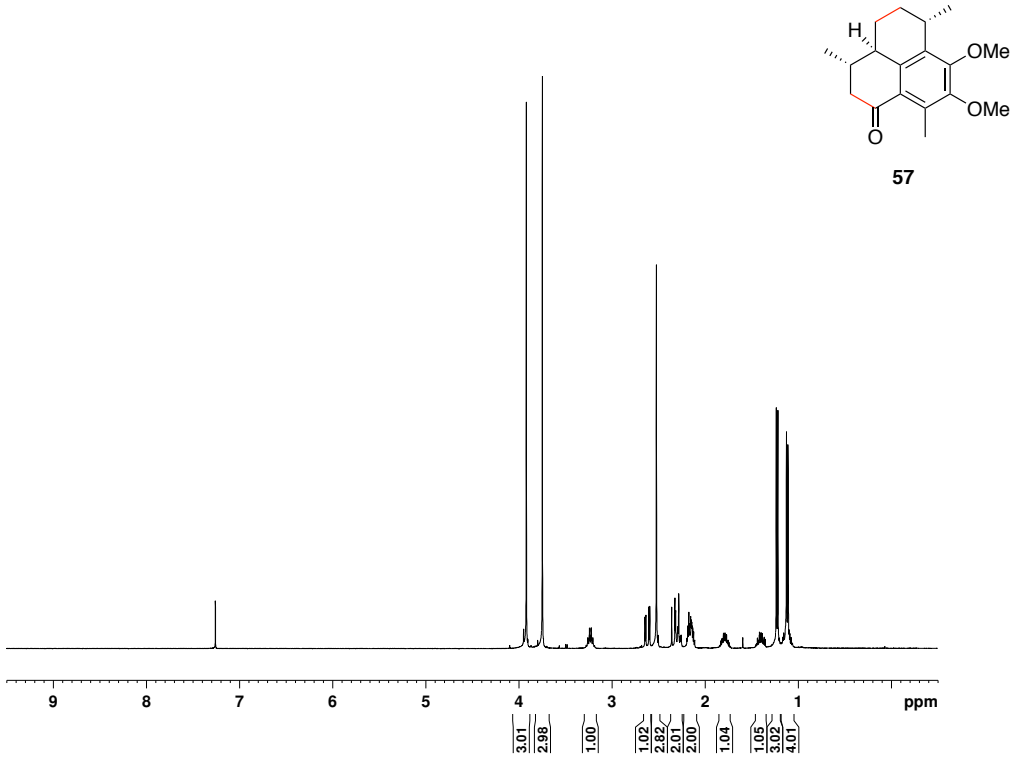
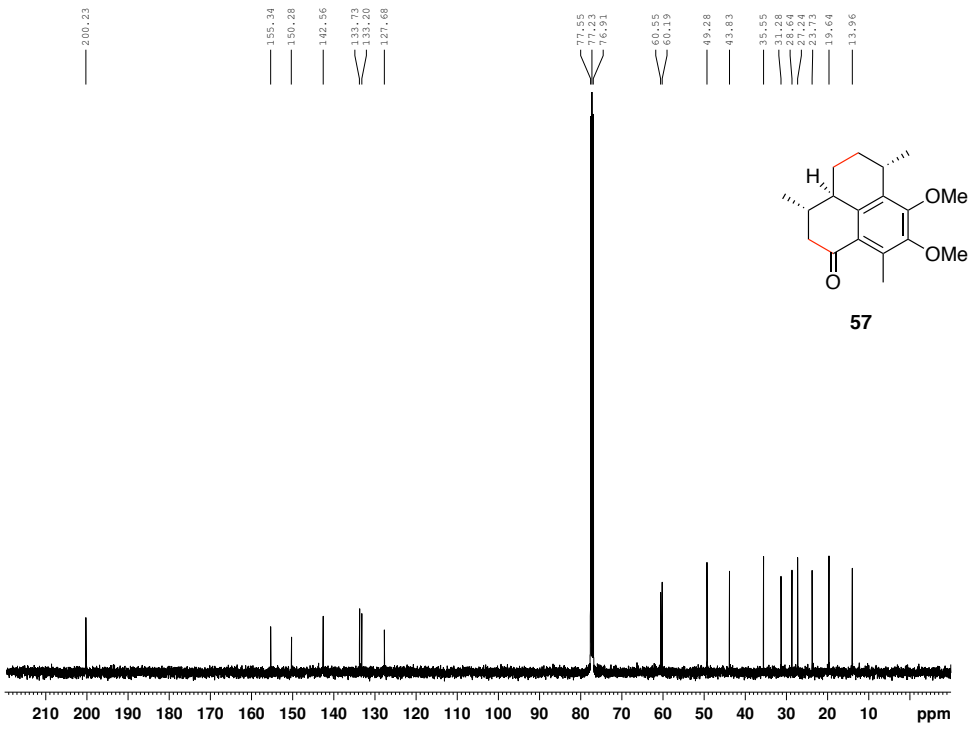
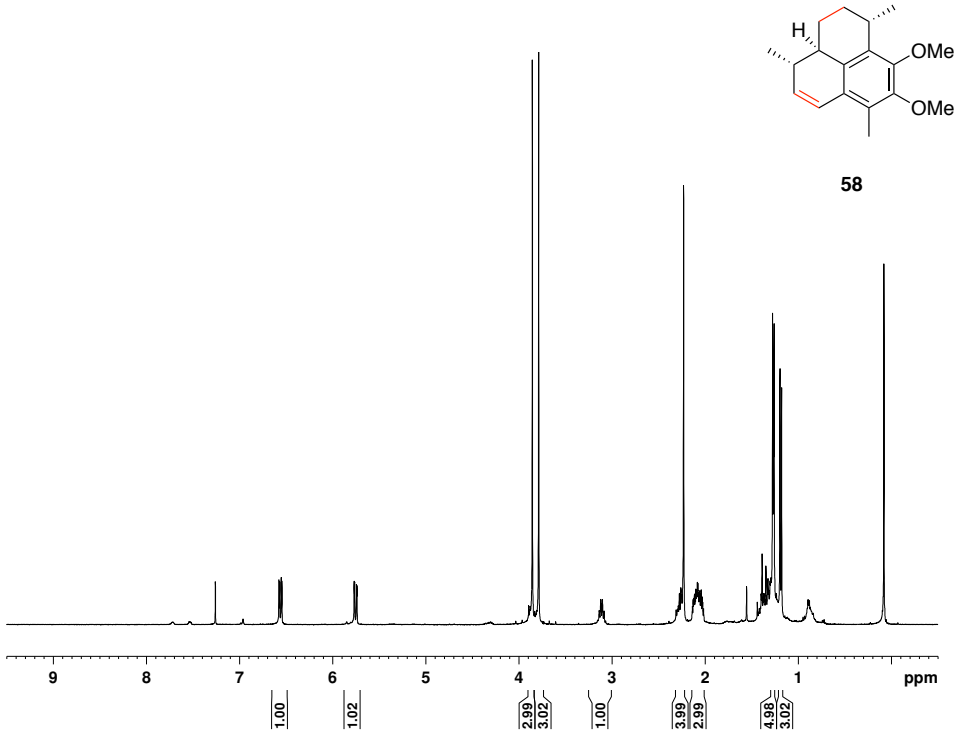
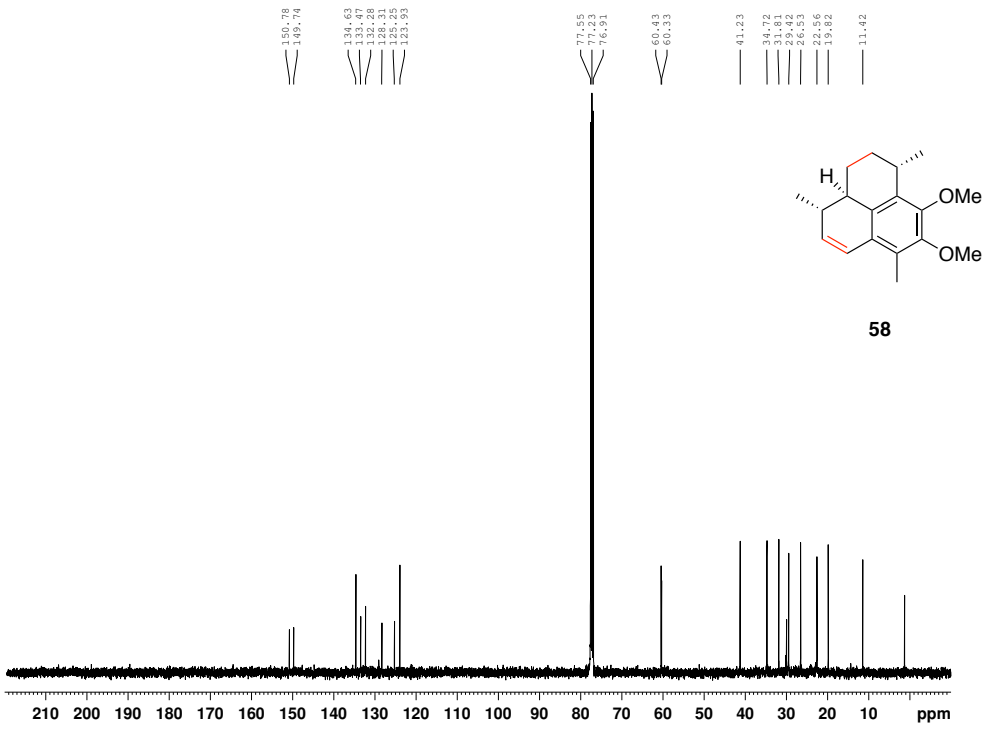
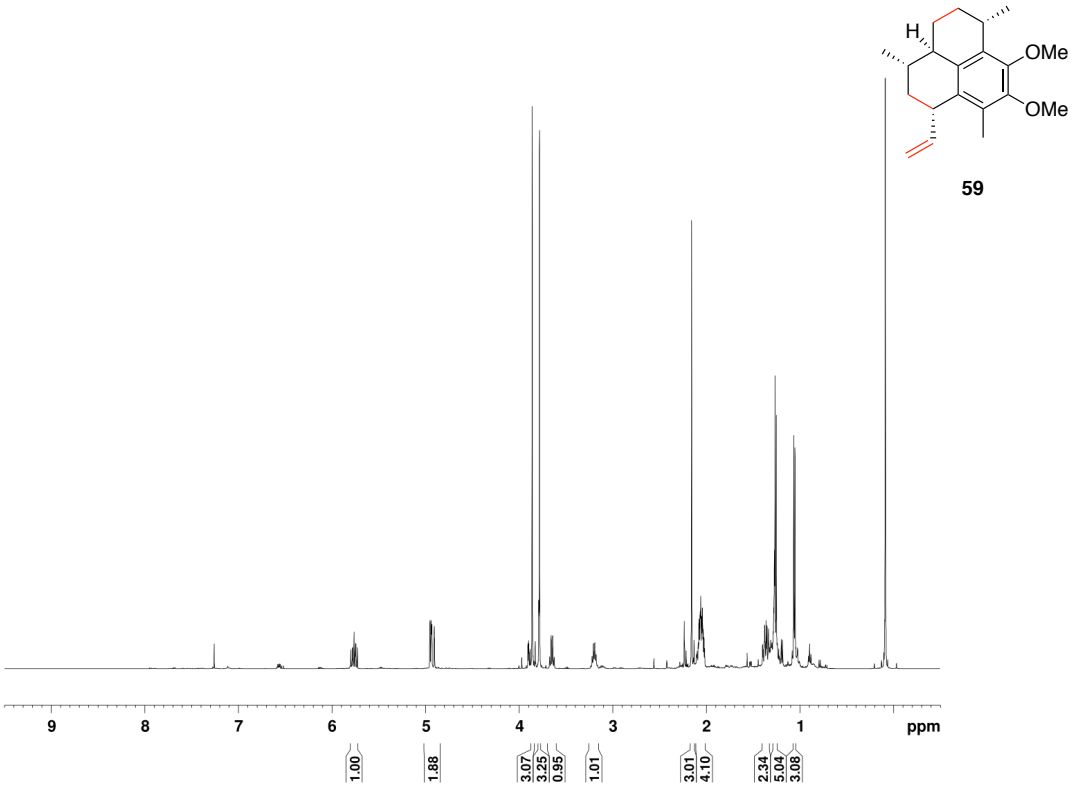
6.835
3.926
3.902
3.875
3.864
3.852
3.819
3.802
3.788
3.780
3.665
3.655
3.649
3.644
3.639
3.634
3.628
3.618
3.543
3.528
3.522
3.512
3.507
3.499
3.491
3.485
3.471
3.457
3.133
3.125
2.845
2.756
2.745
2.735
2.724
2.714
2.446
2.375
2.368
2.362
2.355
2.348
2.341
2.334
2.225
2.206
1.718
1.704
1.700
1.685
1.677
1.668
1.658
1.649
1.640
1.621
1.613
1.598
1.592
1.571
1.563
1.558
1.546
1.535
1.506
1.493
1.437
1.431
H
OMe
OMe
OH
53-C4(S)
H
OMe
HO
OMe
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

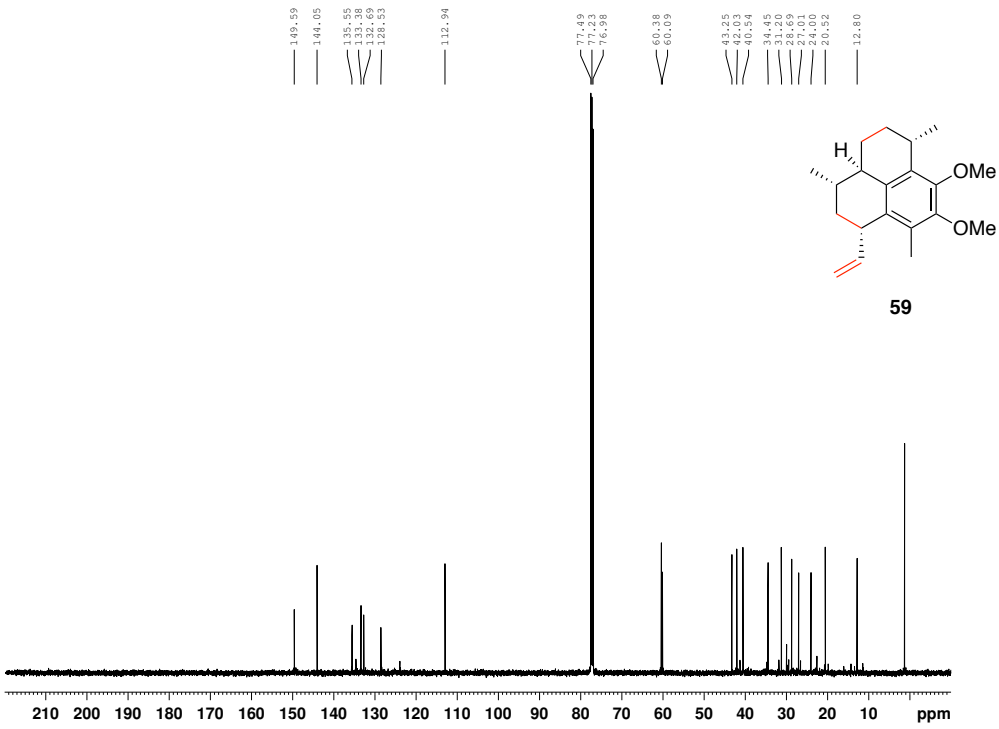

H
OMe
OMe
O
57
9
8
7
6
5
4
3
2
1
ppm
3.01
2.98
1.00
1.02
2.82
2.01
2.00
1.04
1.05
3.02
4.01


200.23
155.34
150.28
142.56
133.73
133.20
127.68
77.55
77.23
76.91
60.55
60.19
49.28
43.83
35.55
31.28
28.64
27.24
23.73
19.64
13.96
H
OMe
OMe
O
57
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


H
OMe
OMe
58
9
8
7
6
5
4
3
2
1
ppm
1.00
1.02
2.99
3.02
1.00
3.99
2.99
4.98
3.02


150.78
149.74
134.63
133.47
132.28
128.31
125.25
123.93
77.55
77.23
76.91
60.43
60.33
41.23
34.72
31.81
29.42
26.53
22.56
19.82
11.42
H
OMe
OMe
58
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


H
OMe
OMe
59
9
8
7
6
5
4
3
2
1
ppm
1.00
1.88
3.07
3.25
0.95
1.01
3.01
4.10
2.34
5.04
3.08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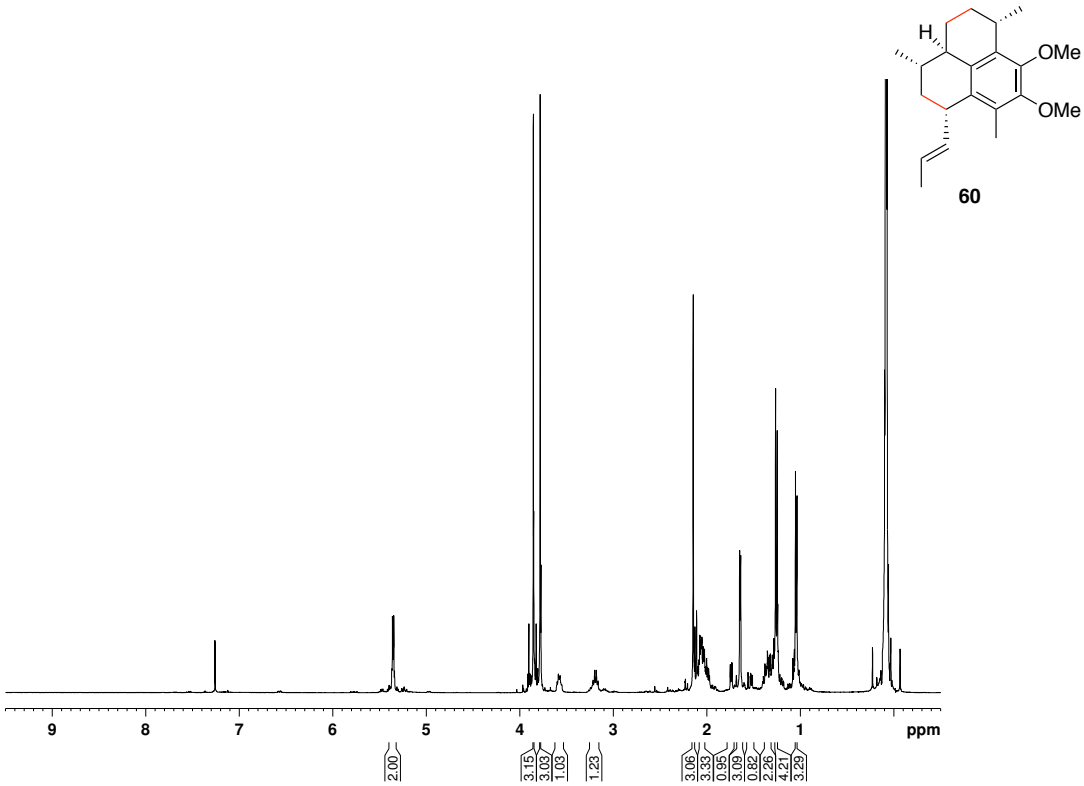
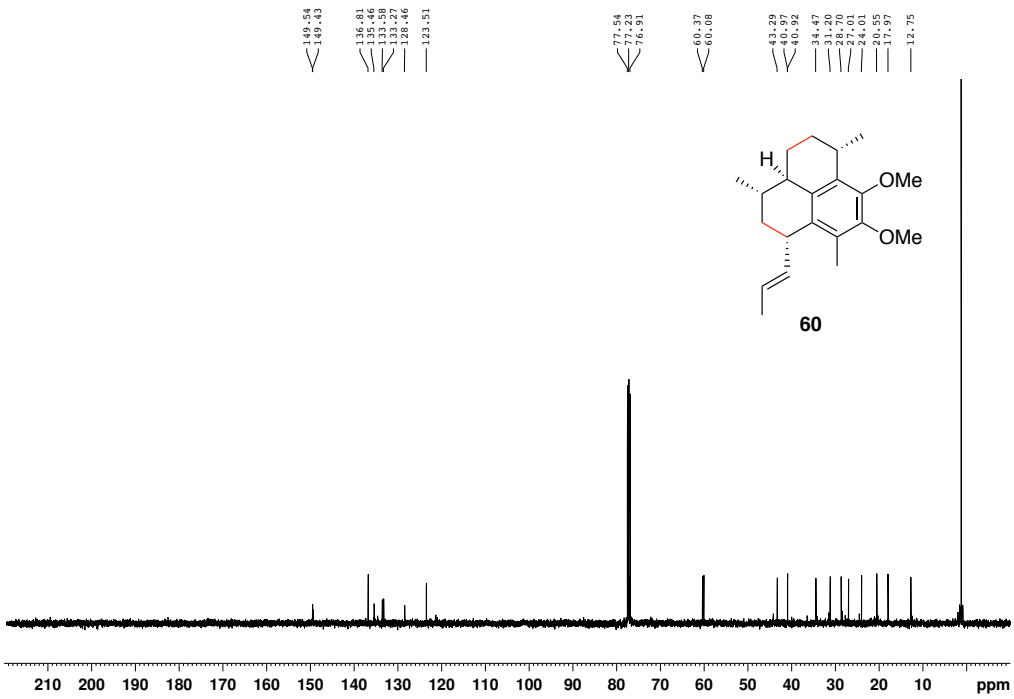
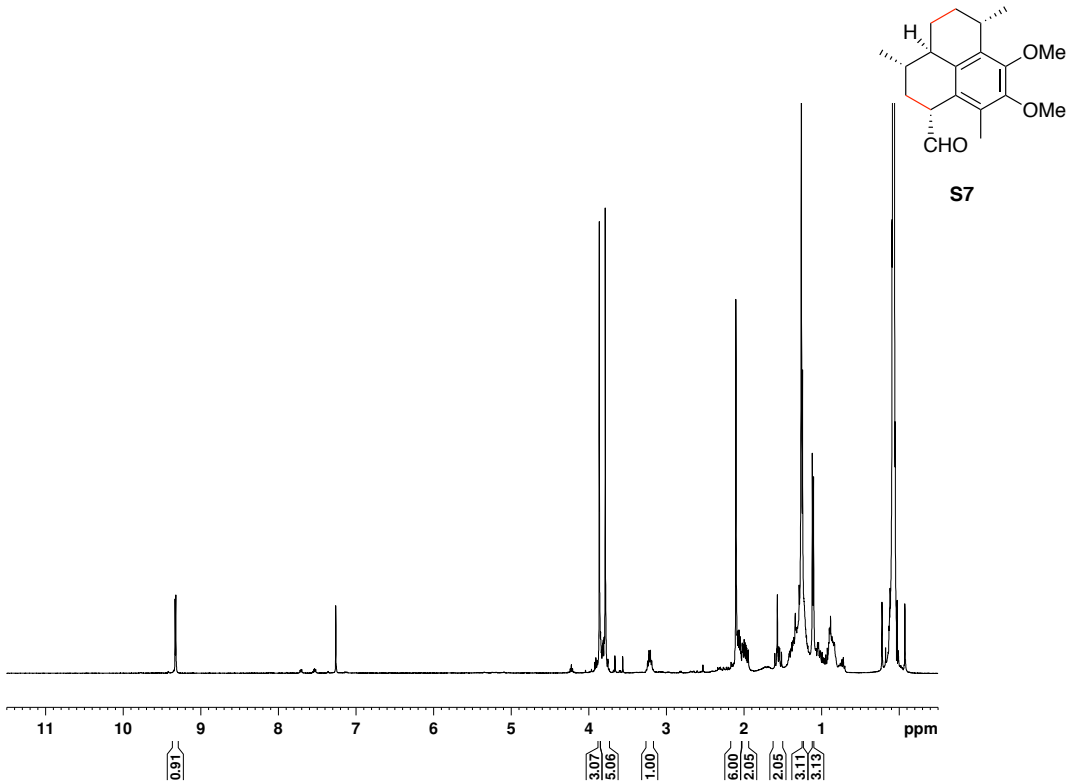
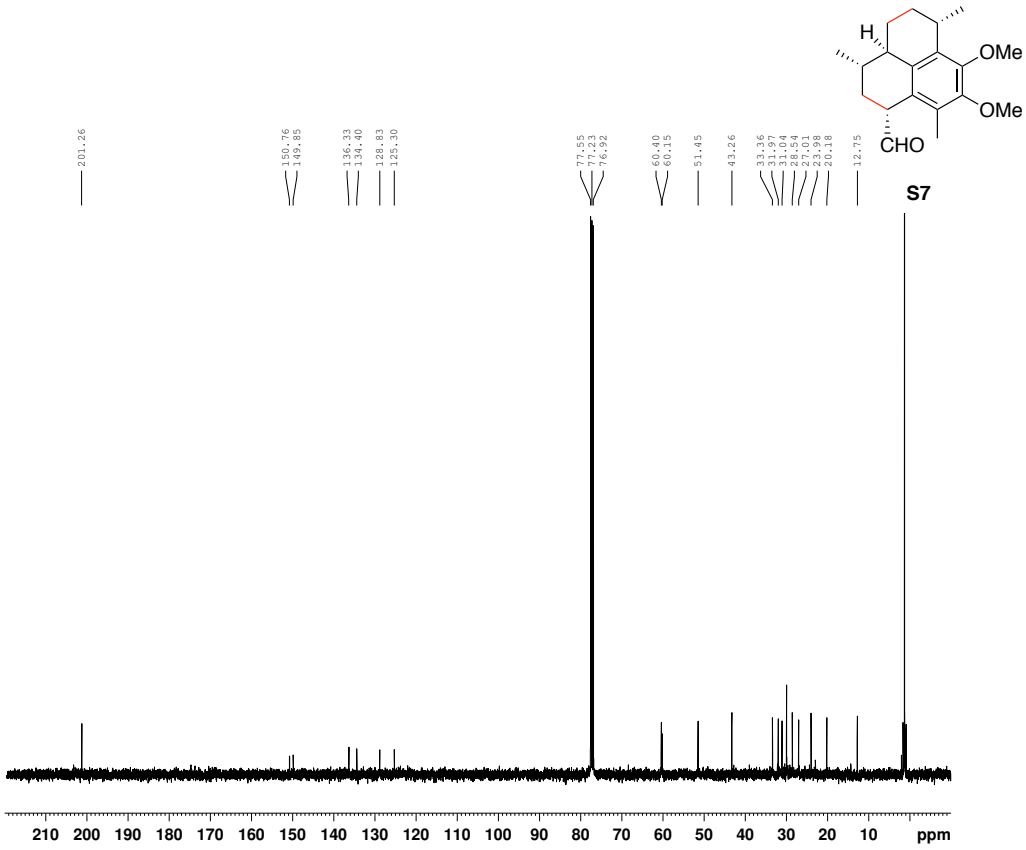
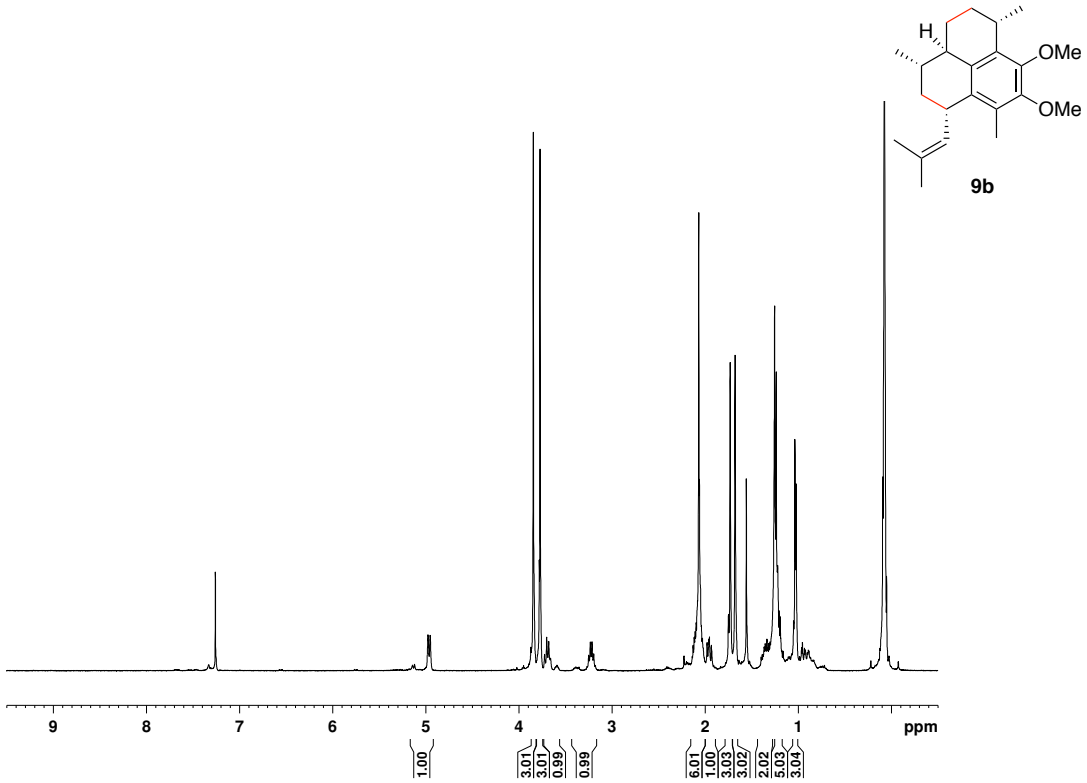
144.05
135.55
133.38
132.69
128.53
112.94
77.49
77.23
76.98
60.38
60.09
43.25
42.03
40.54
34.45
31.20
28.69
27.01
24.00
20.52
12.80
H
OMe
OMe
59
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

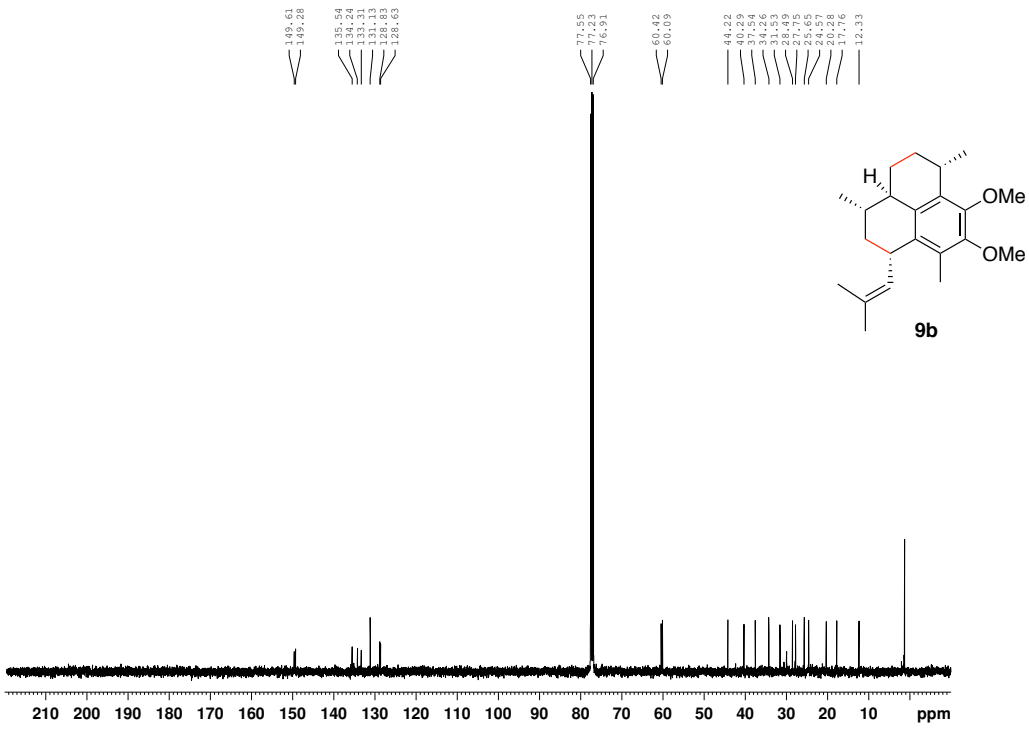

H
OMe
OMe
60
9
8
7
6
5
4
3
2
1
ppm
2.00
3.15
3.03
1.03
1.23
3.06
3.33
0.95
3.09
0.82
2.26
4.21
3.29

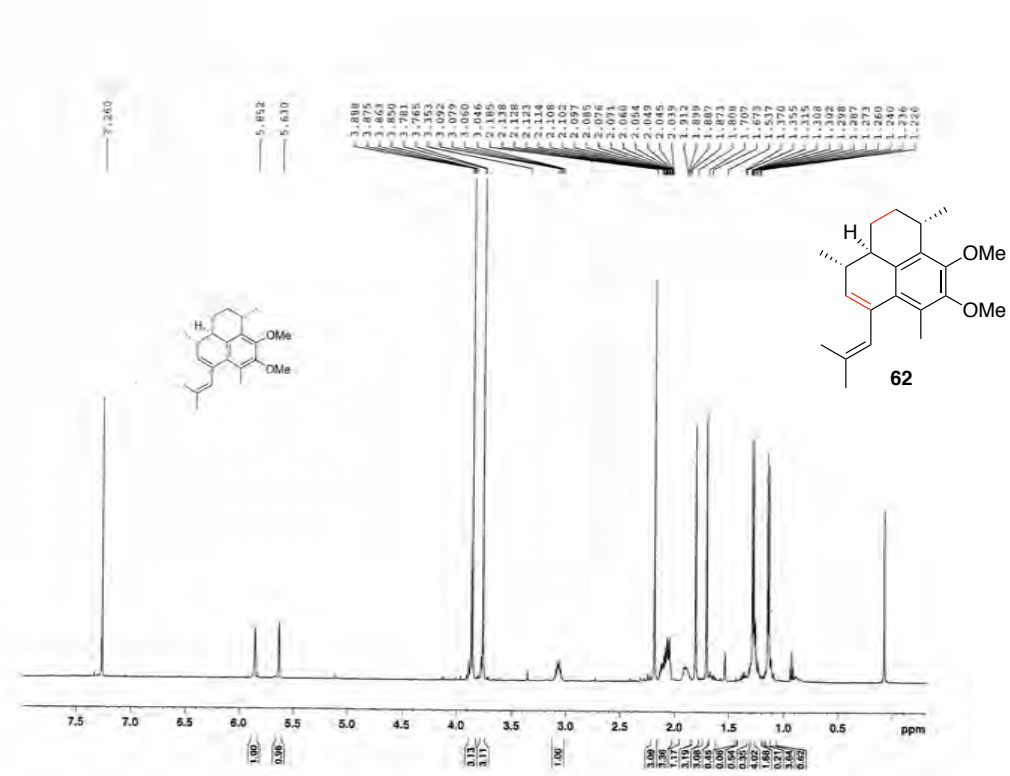

149.54
149.43
136.81
135.46
133.58
133.27
128.46
123.51
77.54
77.23
76.91
60.37
60.08
43.39
40.97
40.92
34.47
31.20
31.20
28.00
27.01
24.01
20.55
17.97
12.75
H
OMe
OMe
60
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

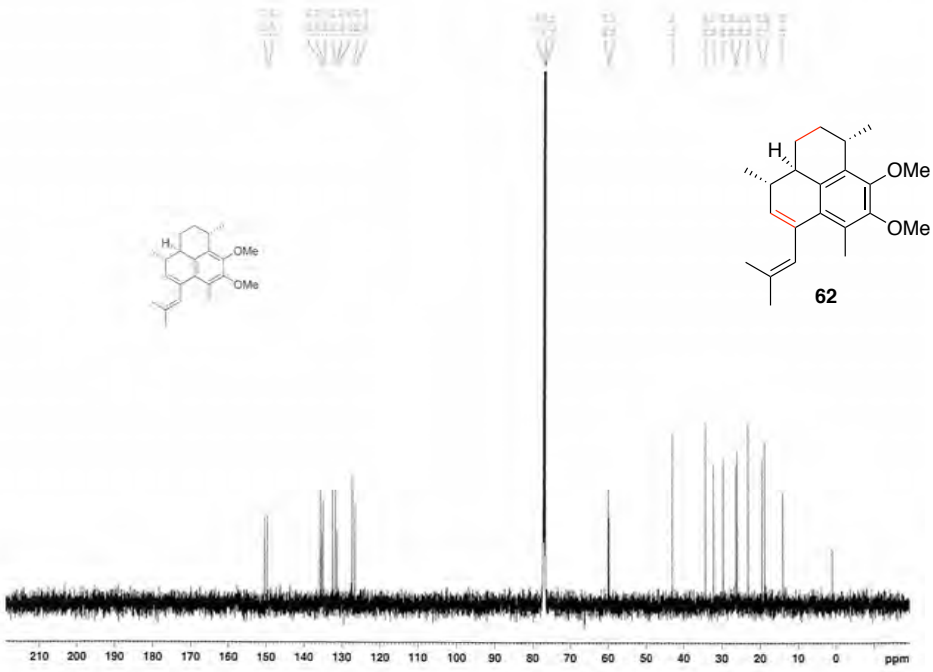

H
OMe
OMe
CHO
S7
11 10 9 8 7 6 5 4 3 2 1 ppm
0.91
3.07
5.06
1.00
6.00
2.05
2.05
3.11
3.13

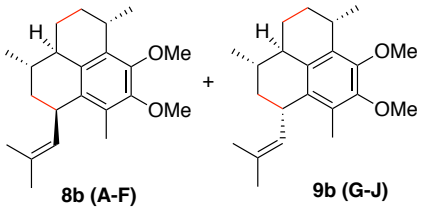

H
OMe
OMe
CHO
S7
201.26
150.76
149.85
136.33
134.40
128.83
125.30
77.55
77.23
76.92
60.40
60.15
51.45
43.26
33.36
31.97
31.94
28.54
27.01
23.98
20.18
12.75
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

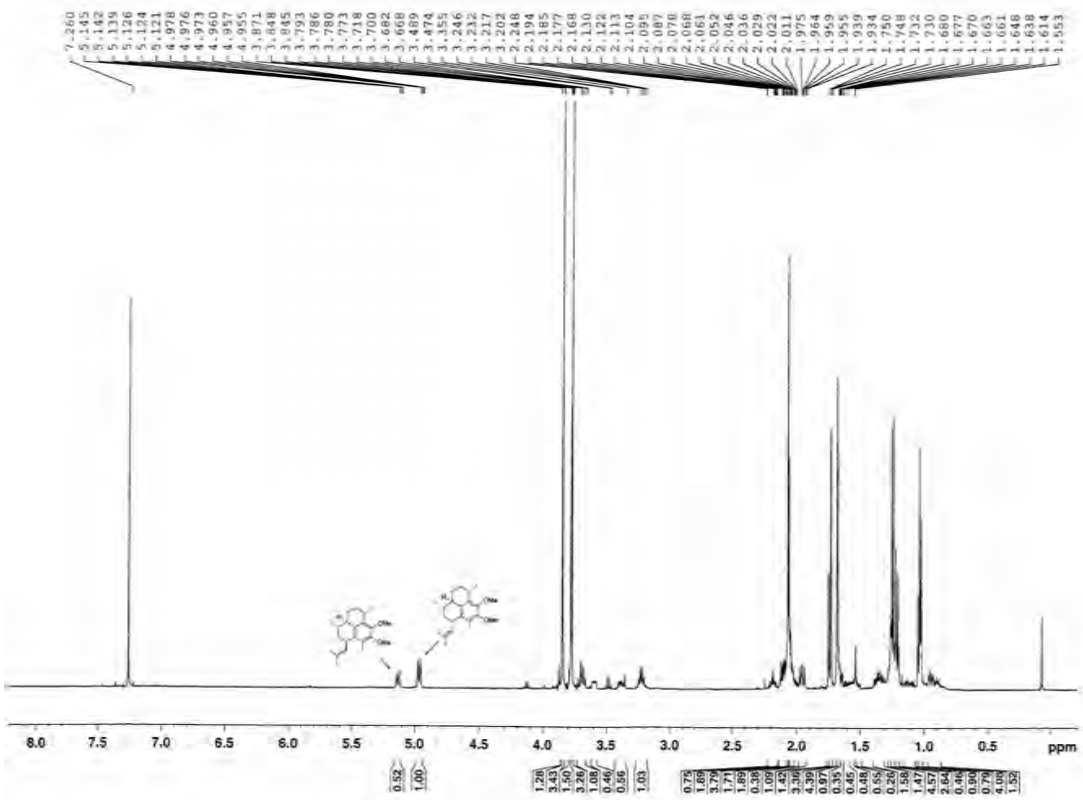

H
OMe
OMe
9b
9
8
7
6
5
4
3
2
1
ppm
1.00
3.01
3.01
0.99
0.99
6.01
1.00
3.03
3.02
2.02
5.03
3.04

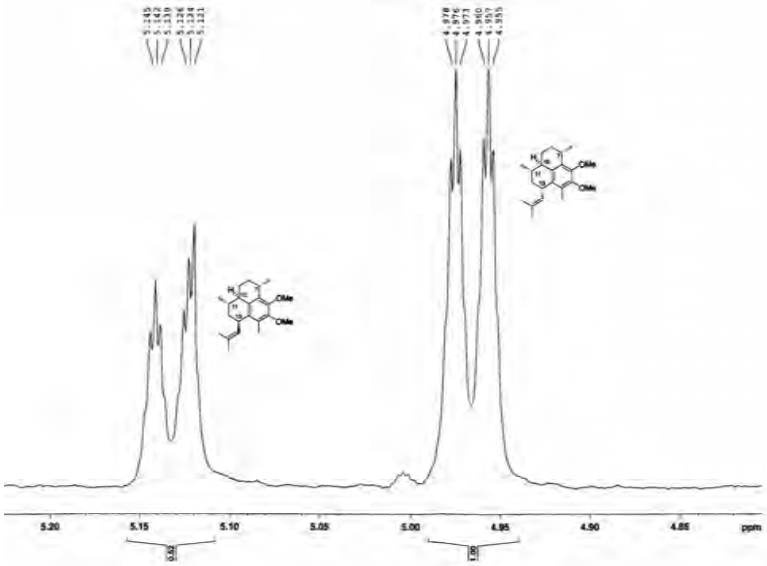

149.61
149.28
135.54
134.24
133.31
131.13
128.83
128.63
77.55
77.23
76.91
60.42
60.09
44.22
40.29
37.54
34.26
31.53
28.49
27.75
25.65
24.57
20.28
17.76
12.33
H
OMe
OMe
9b
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

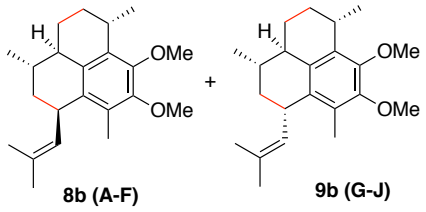

H
OMe
OMe
62
ppm

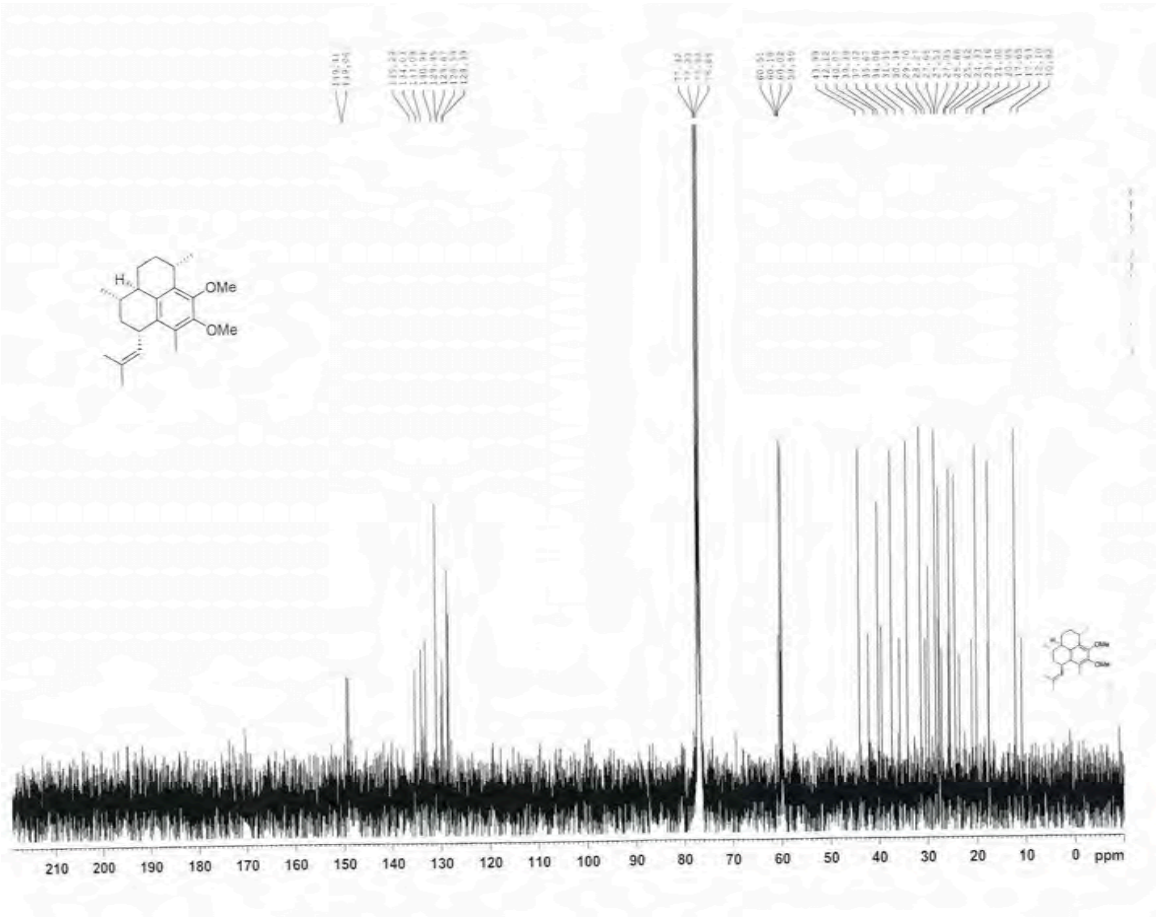

H
OMe
OMe
62
ppm

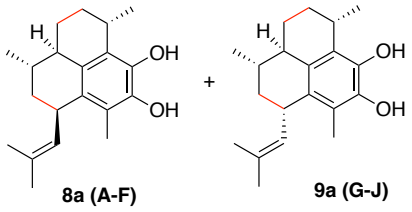

H
OMe
OMe
+
H
OMe
OMe
8b (A-F)
9b (G-J)

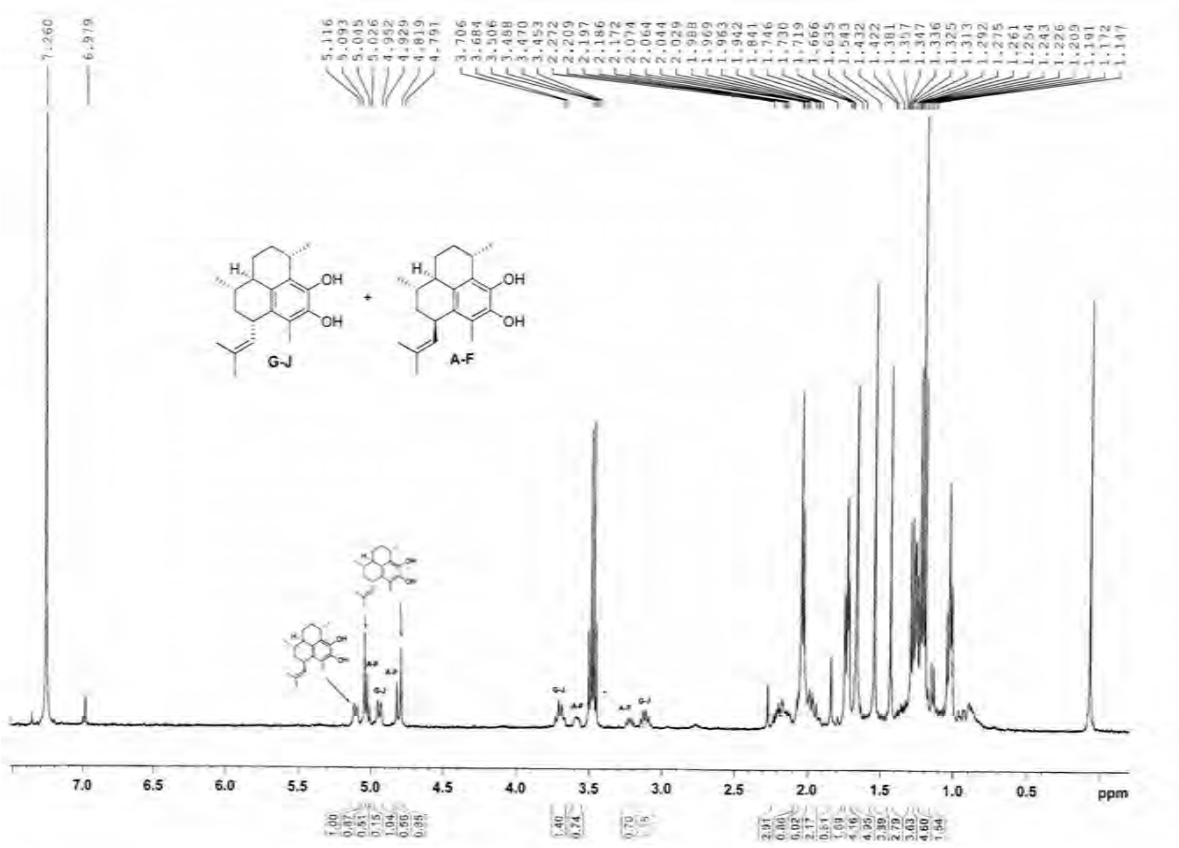

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

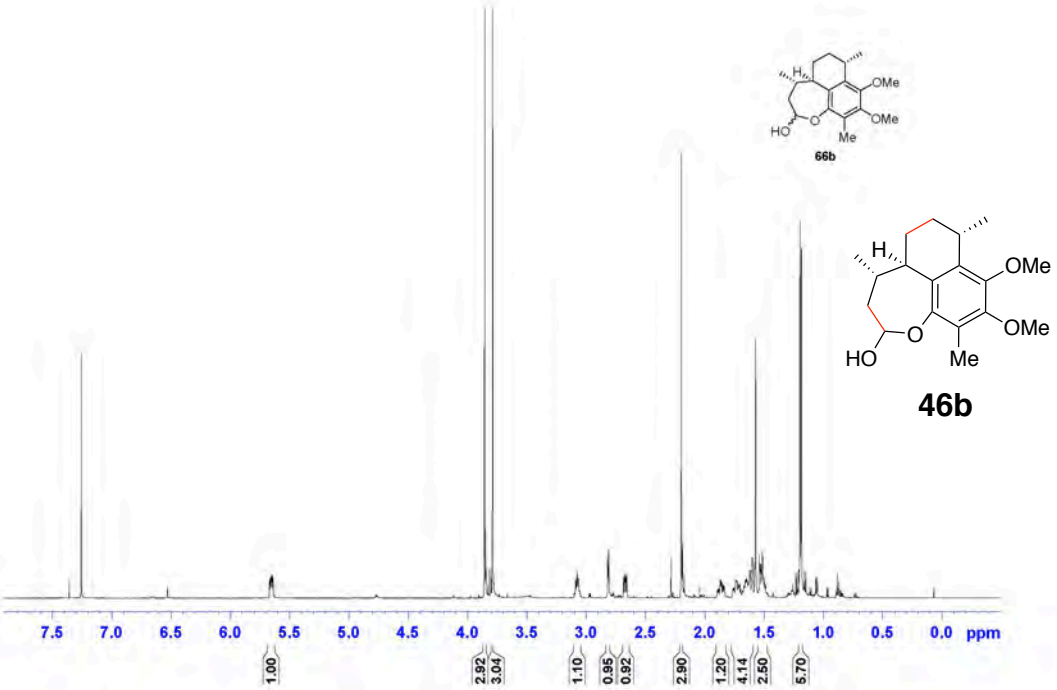

5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
ppm

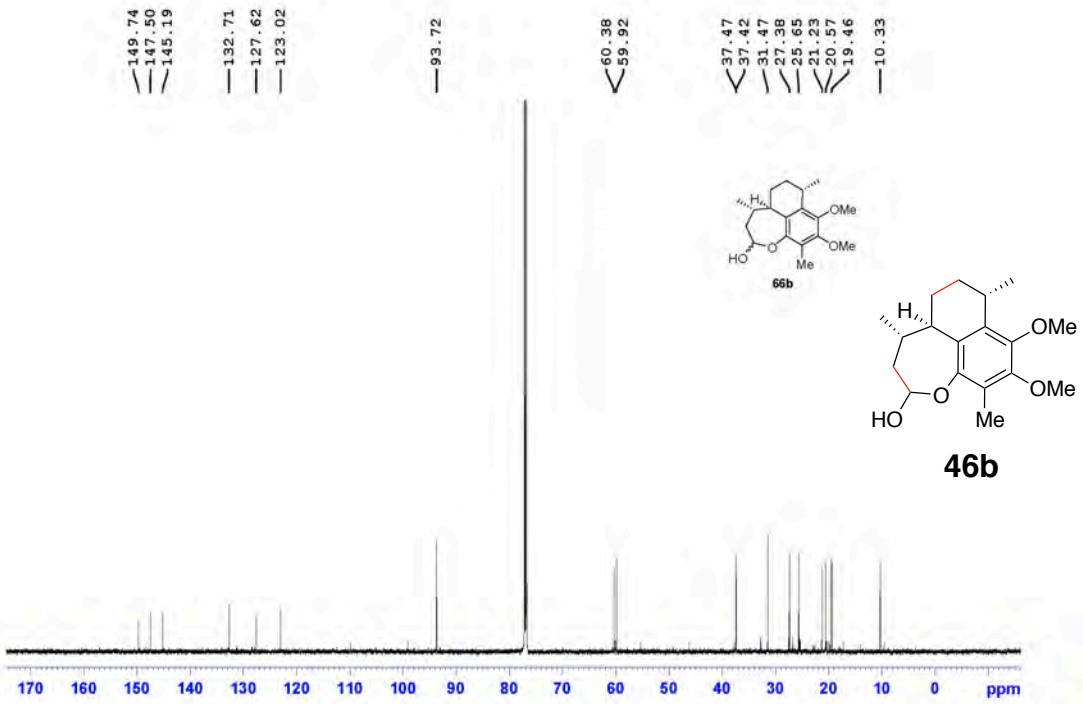

H
OMe
OMe
+
H
OMe
OMe
8b (A-F)
9b (G-J)

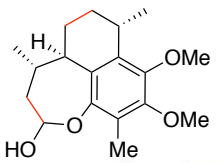

OMe
OMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


H
OH
OH
+
H
OH
OH
8a (A-F)
9a (G-J)

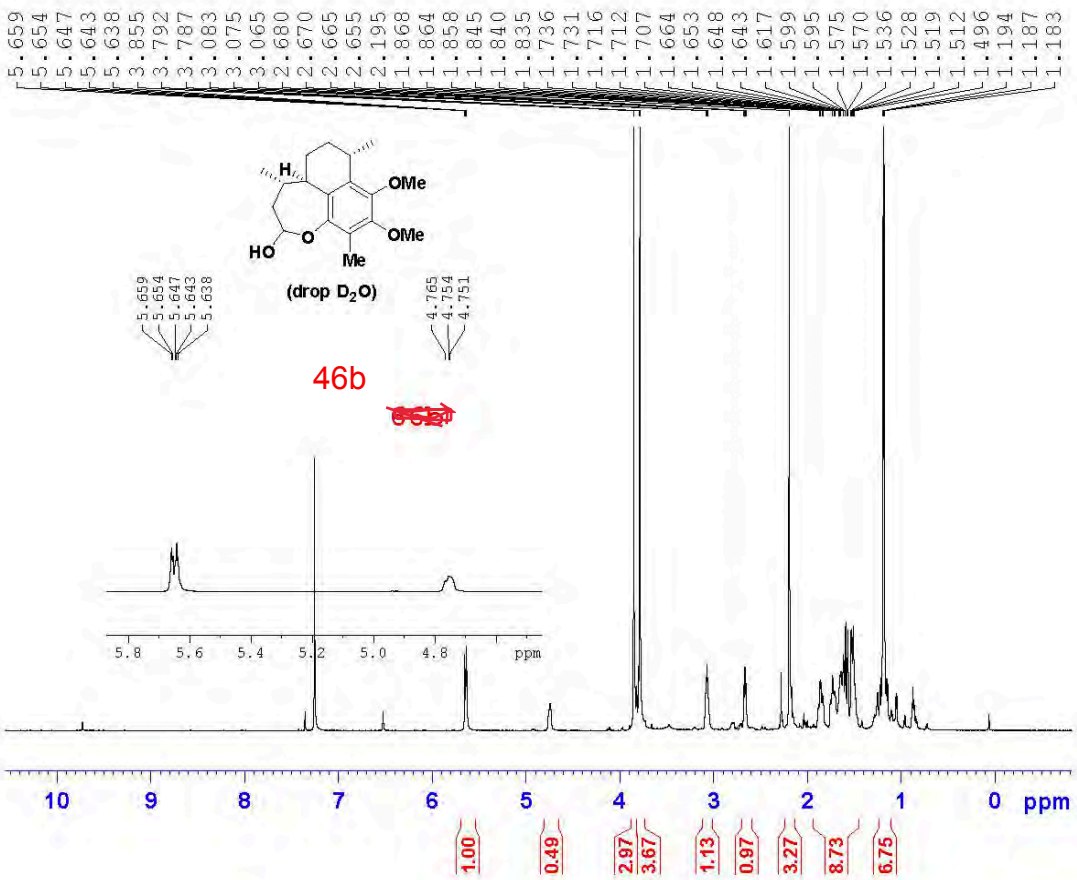

7.260
6.979
G-J
A-F
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


66b
46b
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00 2.92 3.04 1.10 0.95 0.92 2.90 1.20 4.14 2.50 5.70

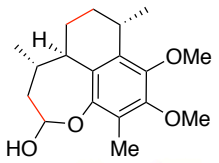

149.74 147.50 145.19 132.71 127.62 123.02 93.72 60.38 59.92 37.47 37.42 31.47 27.38 25.65 21.23 20.57 19.46 10.33
66b
46b
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



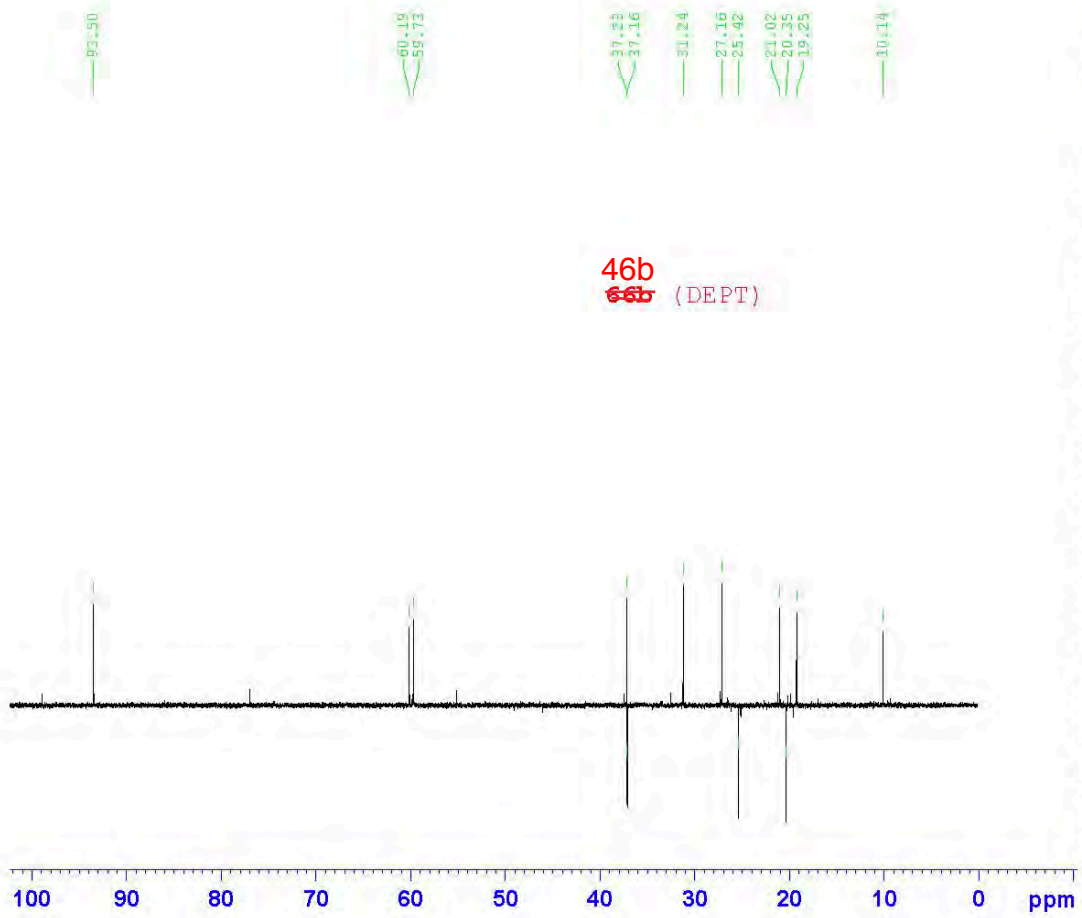
66b



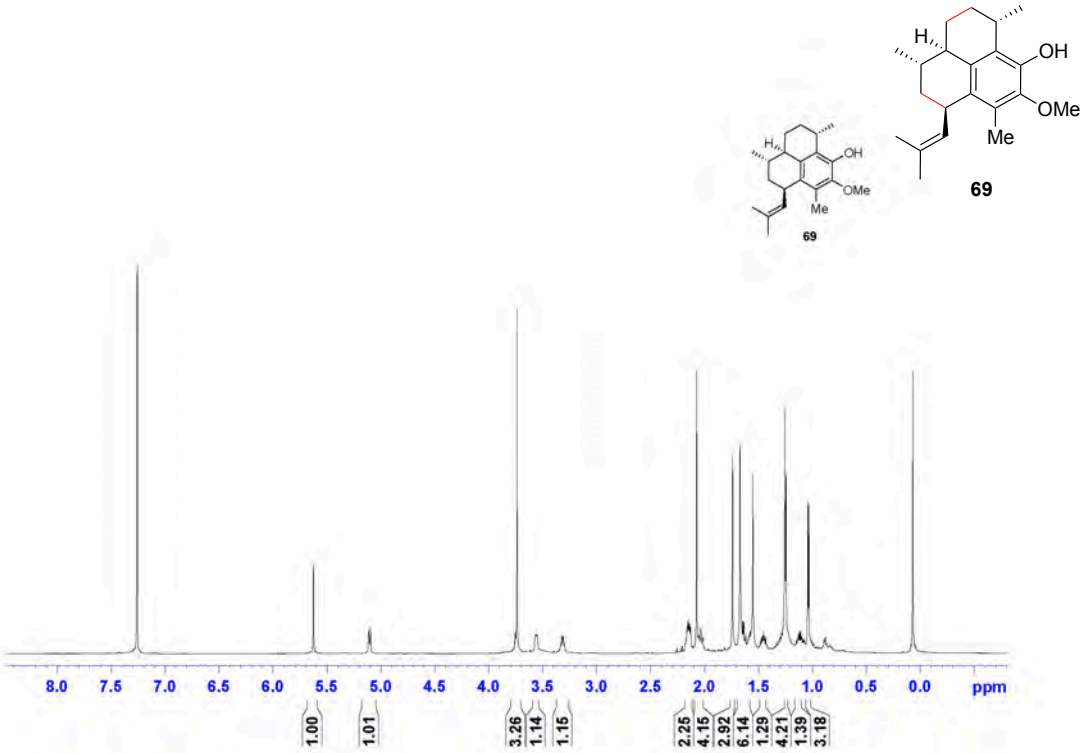

```
Current Data Parameters
NAME      ST-01-274-drop D2O
EXPNO                   11
PROCNO                   1

F2 - Acquisition Parameters
Date_            20170811
Time                15.35 h
INSTRUM             spect
PROBHD    Z114607_0174 (
PULPROG              zg30
TD                  96152
SOLVENT             CDCl3
NS                     16
DS                      2
SWH            12019.230 Hz
FIDRES          0.250005 Hz
AQ             3.9999232 sec
RG                 99.15
DW                41.600 usec
DE                 6.50 usec
TE                296.6 K
D1            1.00000000 sec
TD0                     1
SFO1          600.0478245 MHz
NUC1                   1H
P1                 10.00 usec
PLW1          25.10000038 W

F2 - Processing parameters
SI                  65536
SF            600.0450147 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

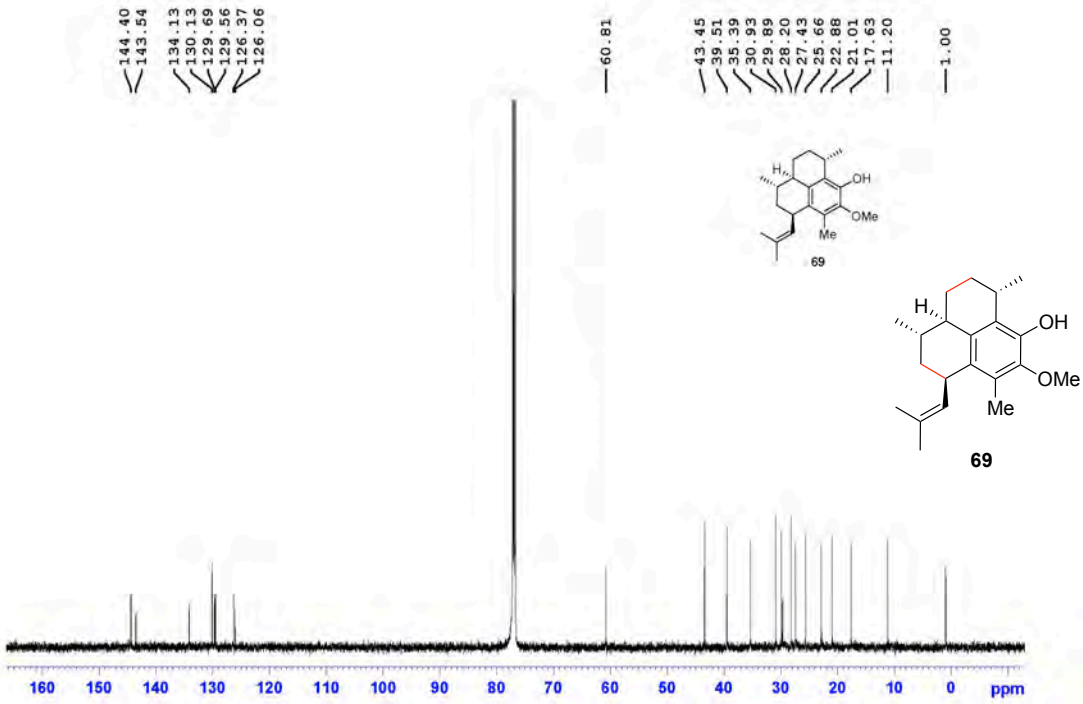


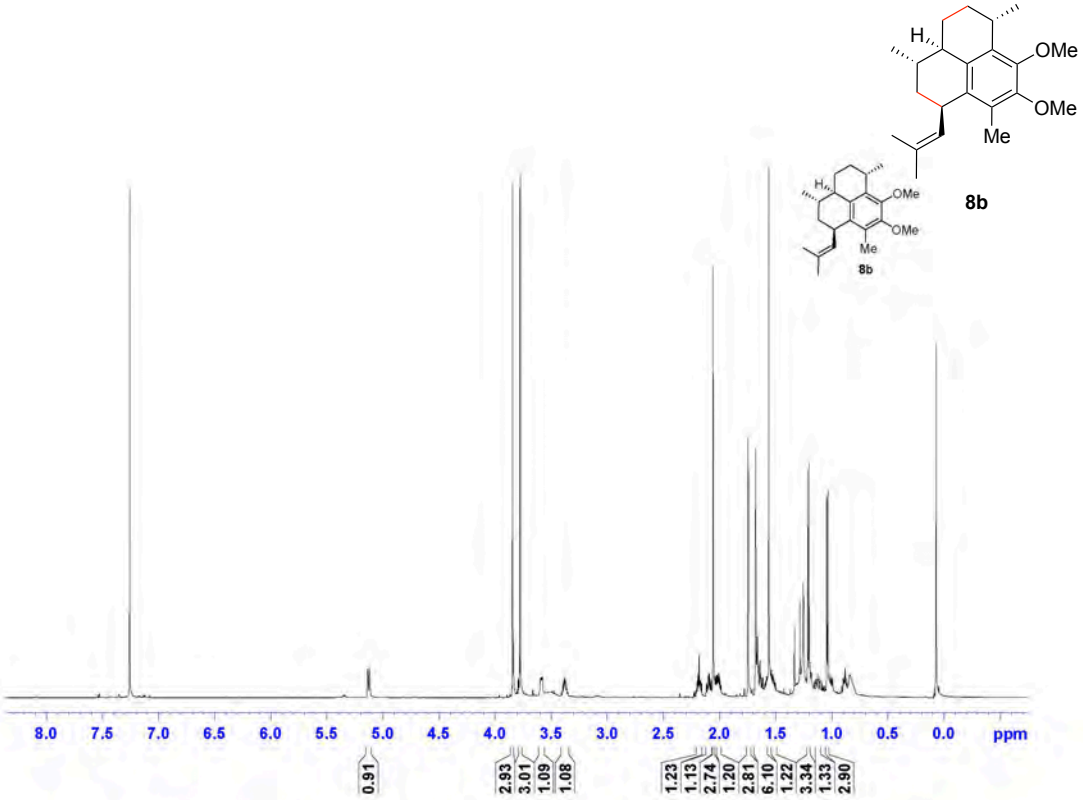
66b

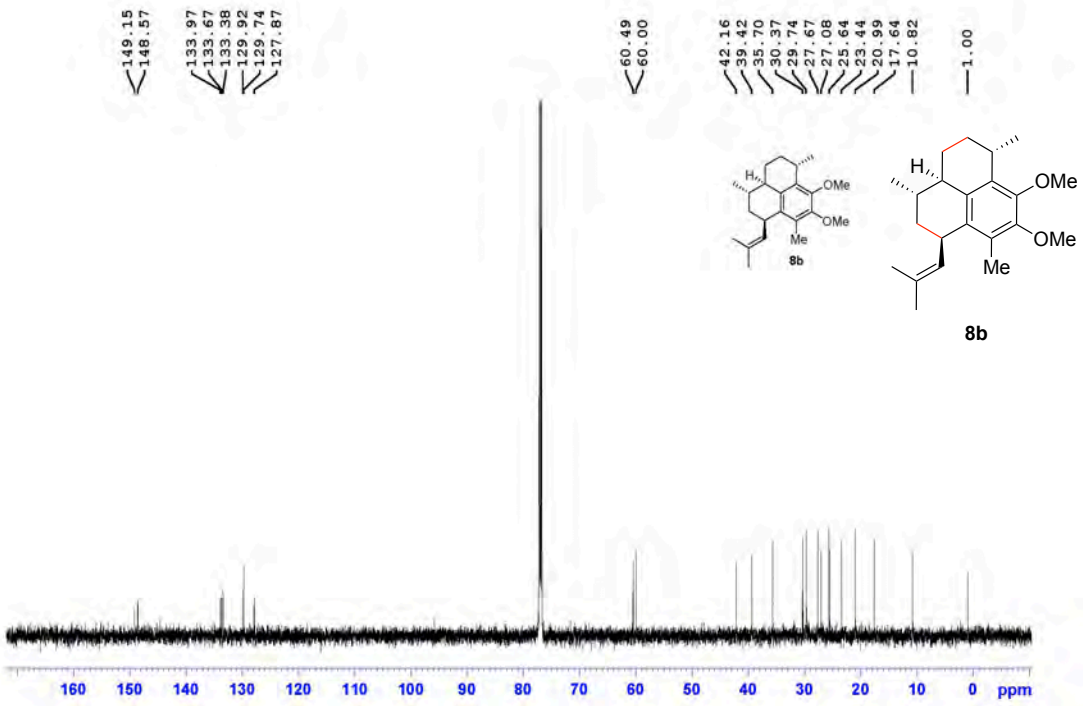



```
Current Data Parameters
NAME      ST-01-274-TMSI-CHO-i
EXPNO                       12
PROCNO                       1

F2 - Acquisition Parameters
Date_              20170810
Time                   6.34 h
INSTRUM               spect
PROBHD    Z114607_0174 (
PULPROG        deptsp135
TD                     65536
SOLVENT                CDCl3
NS                      1000
DS                         4
SWH               24038.461 Hz
FIDRES             0.733596 Hz
AQ                1.3631488 sec
RG                   189.17
DW                   20.800 usec
DE                    6.50 usec
TE                   299.2 K
CNST2            145.0000000
D1                2.00000000 sec
D2                0.00344828 sec
D12               0.00002000 sec
TD0                        1
SFO1             150.8935051 MHz
NUC1                     13C
P1                     12.00 usec
P13                 2000.00 usec
PLW0        0 W
PLW1             78.16000366 W
SPNAM[5]         Crp60comp.4
SPOAL5                 0.500
SPOFFS5     0 Hz
SPW5             17.19599915 W
SFO2             600.0469190 MHz
NUC2                      1H
CPDPRG[2             waltz16
P3                     10.00 usec
P4                     20.00 usec
PCPD2                  70.00 usec
PLW2             28.00000000 W
PLW12             0.57143003 W

F2 - Processing parameters
SI                     32768
SF               150.8814666 MHz
WDW                        EM
SSB         0
LB                      1.00 Hz
GB          0
PC                      1.40
```


H
OH
OMe
Me
69
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.01
3.26
1.14
1.15
2.25
4.15
2.92
6.14
1.29
4.21
1.39
3.18

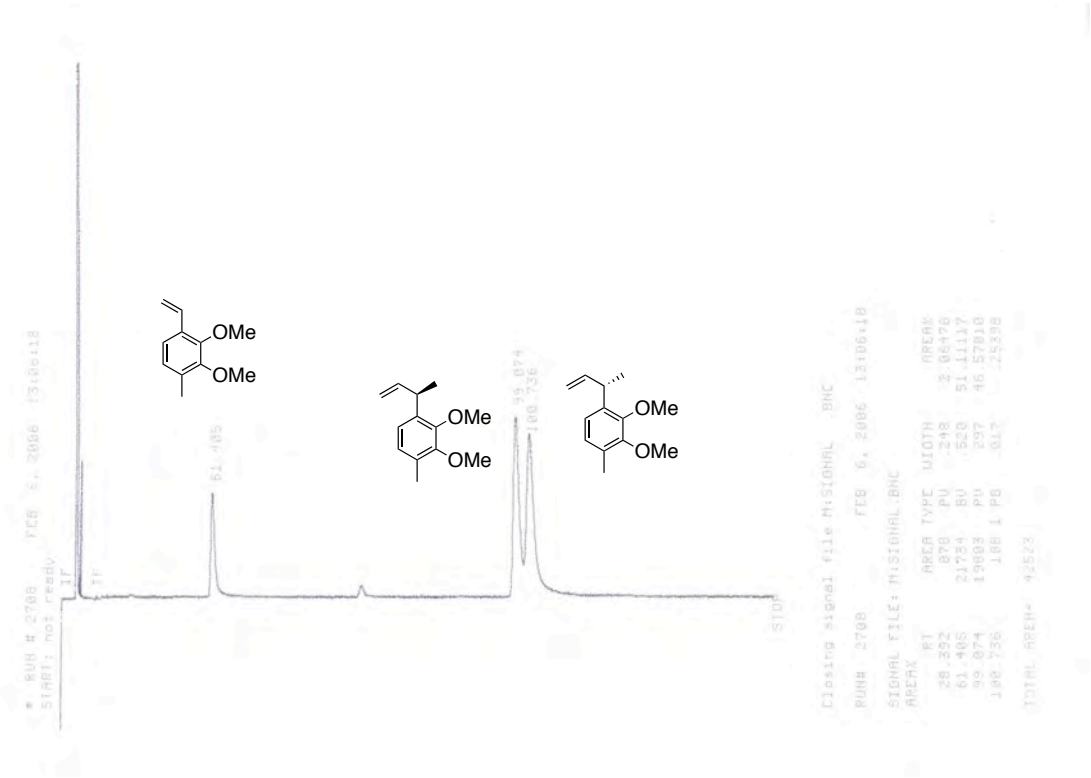

144.40
143.54
134.13
130.13
129.69
129.56
126.37
126.06
60.81
43.45
39.51
35.39
30.93
29.89
28.20
27.43
25.66
22.88
21.01
17.63
11.20
1.00
H
OH
OMe
Me
69
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

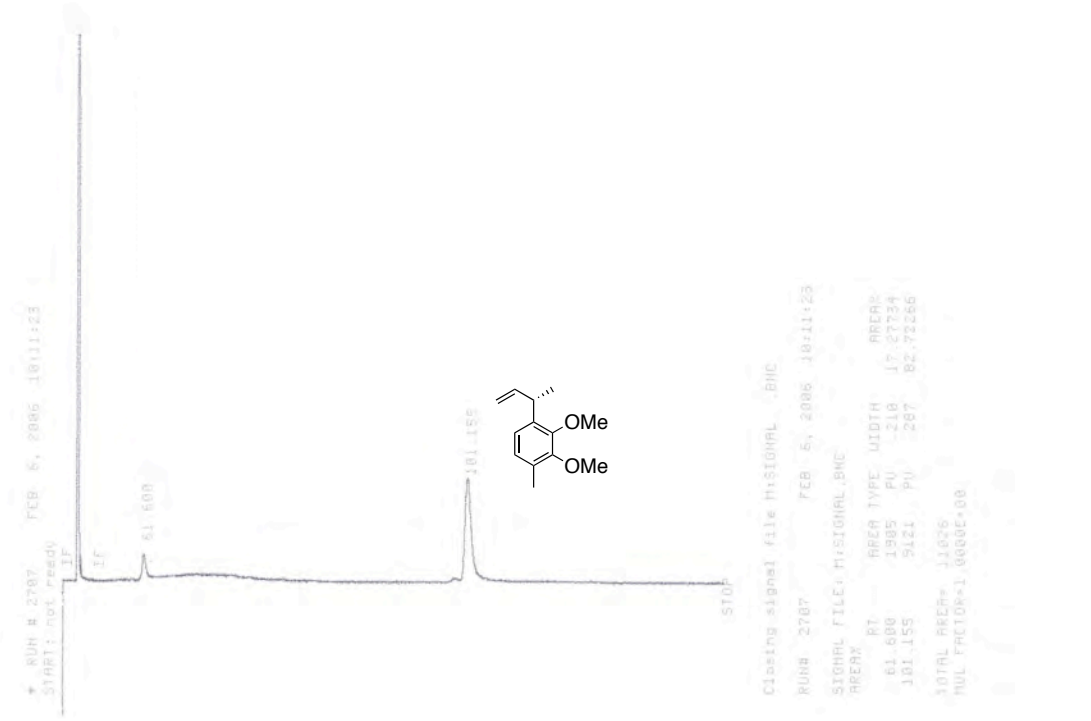

H
OMe
OMe
Me
8b
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.91
2.93
3.01
1.09
1.08
1.23
1.13
2.74
1.20
2.81
6.10
1.22
3.34
1.33
2.90


149.15
148.57
133.97
133.67
133.38
129.92
129.74
127.87
60.49
60.00
42.16
39.42
35.70
30.37
29.74
27.67
27.08
25.64
23.44
20.99
17.64
10.82
1.00
H
OMe
OMe
Me
8b
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

8. Gas Chromatograms of Crude Products Showing Selectivites of Reactions

Compound 22, Racemic-27 and Enantioenriched 27

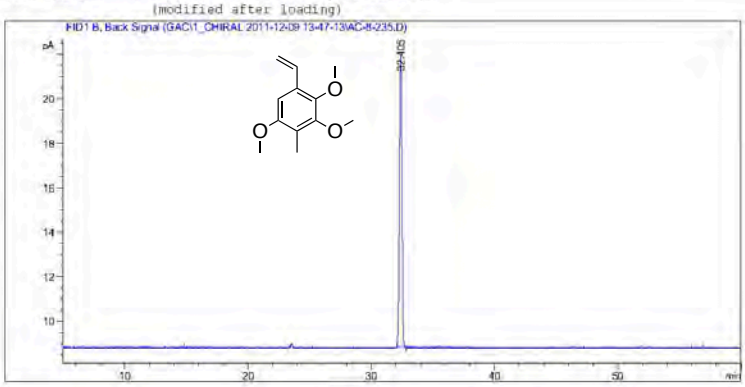




Compound 25

Data File C:\CHEM32\1\DATA\GAC\1_CHIRAL 2011-12-09 13-47-13\AC-8-235.D
Sample Name: AC-8-235

Acq. Operator : Adam Cox
Acq. Instrument : Babu
Injection Date : 12/9/2011 1:48:16 PM
Seq. Line : 1
Location : Vial 201
Inj : 1
Inj Volume : 1 µl
Acq. Method : C:\CHEM32\1\DATA\GAC\1_CHIRAL 2011-12-09 13-47-13\AC_HV_1_CHIRAL.M
Last changed : 12/9/2011 1:47:13 PM by Adam Cox
Analysis Method : C:\CHEM32\1\METHODS\JP_CHIRALTETRALONE.M
Last changed : 1/20/2012 9:02:16 AM by Jordan Page
(modified after loading)



Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	32.405	BB	0.2216	184.86386	13.14775	1.000e2
Totals :				184.86386	13.14775	

*** End of Report ***

Racemic 28 and Enantioenriched 28

Data File C:\CHEM32\1\DATA\GAC\1_CHIRAL 2010-08-25 08-48-06\AC-4-253.D
Sample Name: AC-4-253

Acq. Operator : Adam Cox
Acq. Instrument : Babu
Injection Date : 8/25/2010 8:49:09 AM
Seq. Line : 1
Location : Vial 201
Inj : 1
Inj Volume : 1 µl
Acq. Method : C:\CHEM32\1\DATA\GAC\1_CHIRAL 2010-08-25 08-48-06\AC_HV_1_CHIRAL.M
Last changed : 8/25/2010 8:48:06 AM by Adam Cox
Analysis Method : C:\CHEM32\1\METHODS\JP_CHIRALTETRALONE.M
Last changed : 1/20/2012 9:52:50 AM by Jordan Page
(modified after loading)

Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 B, Back Signal

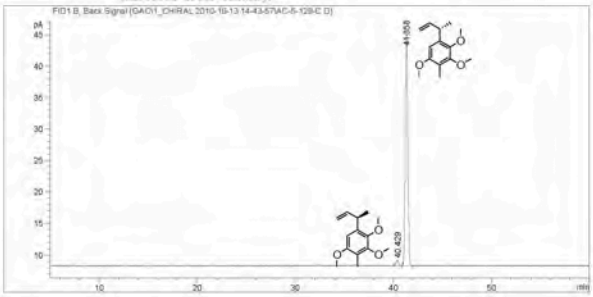
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	40.746	BV	0.2763	1082.52563	61.29282	49.62636
2	41.663	VB	0.2855	1098.82629	60.49282	50.37364

Totals : 2181.35193 121.78574

*** End of Report ***

Data File C:\CHEM32\1\DATA\GAC\1_CHIRAL 2010-10-13 14-43-57\AC-5-129-C.D
Sample Name: AC-5-129-C

Acq. Operator : Adam Cox
Acq. Instrument : Babu
Injection Date : 10/13/2010 2:44:57 PM
Seq. Line : 1
Location : Vial 201
Inj : 1
Inj Volume : 1 µl
Acq. Method : C:\CHEM32\1\DATA\GAC\1_CHIRAL 2010-10-13 14-43-57\AC_HV_1_CHIRAL.M
Last changed : 10/13/2010 2:43:57 PM by Adam Cox
Analysis Method : C:\CHEM32\1\METHODS\JP_CHIRALTETRALONE.M
Last changed : 1/20/2012 9:08:50 AM by Jordan Page
(modified after loading)



Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	40.429	BB	0.2750	15.25805	8.70239e-1	2.24197
2	41.358	BB	0.2803	665.30713	36.98756	97.75803

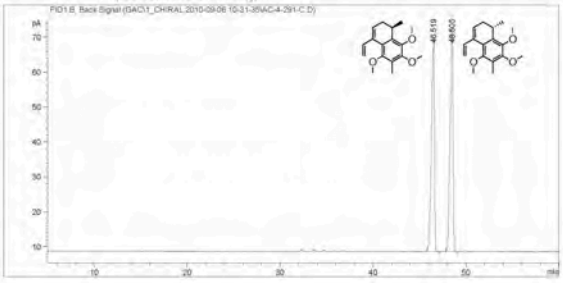
Totals : 680.56518 37.85780

*** End of Report ***

Racemic 33 and Enantioenriched 33

Data File C:\CHEM32\1\DATA\GAC\1_CHIRAL 2010-09-06 10-31-35\AC-4-291-C.D
Sample Name: AC-4-291-C

Acq. Operator : Adam Cox
Acq. Instrument : Babu
Injection Date : 9/6/2010 10:30:31 AM
Seq. Line : 1
Location : Vial 201
Inj : 1
Inj Volume : 1 µl
Acq. Method : C:\CHEM32\1\DATA\GAC\1_CHIRAL 2010-09-06 10-31-35\AC_HV_2_CHIRAL.M
Last changed : 9/2/2010 8:34:13 AM by Jordan Page
Analysis Method : C:\CHEM32\1\METHODS\JP_CHIRALTETRALONE.M
Last changed : 1/20/2012 9:55:15 AM by Jordan Page
(modified after loading)



Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 B, Back Signal

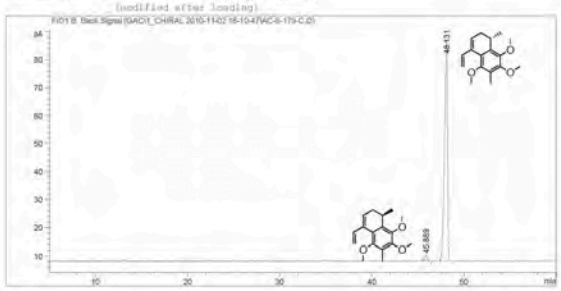
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	46.519	BB	0.3353	1367.23975	60.73857	49.60075
2	49.605	BB	0.3284	1384.16992	63.36748	50.39925

Totals : 2748.40967 124.72603

*** End of Report ***

Data File C:\CHEM32\1\DATA\GAC\1_CHIRAL 2010-11-02 16-10-47\AC-5-179-C.D
Sample Name: AC-5-179-C

Acq. Operator : Adam Cox
Acq. Instrument : Babu
Injection Date : 11/2/2010 4:11:50 PM
Seq. Line : 1
Location : Vial 201
Inj : 1
Inj Volume : 1 µl
Acq. Method : C:\CHEM32\1\DATA\GAC\1_CHIRAL 2010-11-02 16-10-47\AC_HV_2_CHIRAL.M
Last changed : 9/30/2010 3:40:25 PM by Adam Cox
Analysis Method : C:\CHEM32\1\METHODS\JP_CHIRALTETRALONE.M
Last changed : 1/20/2012 9:59:55 AM by Jordan Page
(modified after loading)



Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	45.889	BB	0.3212	40.62482	1.99155	2.21604
2	49.131	BB	0.3376	1792.77026	78.29953	97.78396

Totals : 1833.39918 80.29108

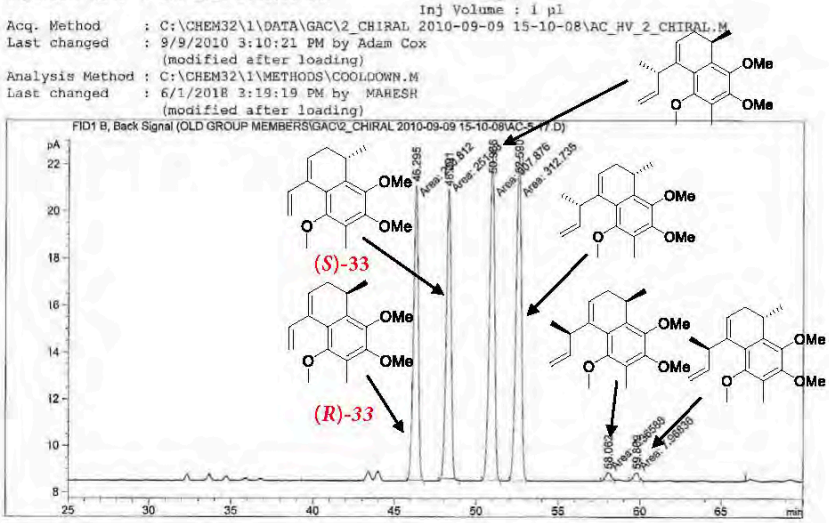
*** End of Report ***

Hydrovinylation of Racemic and Enantioenriched 34

Data File C:\CHEM32\1\DATA\OLD GROUP MEMBERS\GAC\2_CHIRAL 2010-09-09 15-10-08\AC-5-17.D
Sample Name: AC-5-17

Chiral GC (Cyclosil-B, 150 °C isotherm)

```
Acq. Operator   : Adam Cox                          Seq. Line :  1
Acq. Instrument : Babu                               Location : Vial 201
Injection Date  : 9/9/2010 3:11:10 PM                     Inj :  1
                                                   Inj Volume : 1 µl
Acq. Method     : C:\CHEM32\1\DATA\GAC\2_CHIRAL 2010-09-09 15-10-08\AC_HV_2_CHIRAL.M
Last changed    : 9/9/2010 3:10:21 PM by Adam Cox
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\COOLDOWN.M
Last changed    : 6/1/2018 3:19:19 PM by  MAHESH
                  (modified after loading)
```




```
                          Area Percent Report

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```

HV of racemic **33** using achiral ligand **L6** showing retention times of starting materials and products

Signal 1: FID1 B, Back Signal

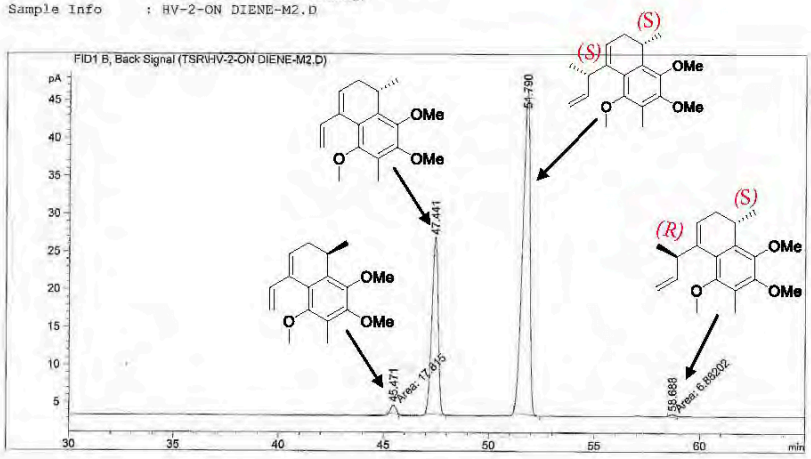
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	46.295	MM	0.3316	250.81210	12.60628	22.02738
2	48.291	MM	0.3400	251.88042	12.34704	22.12121
3	50.966	MM	0.3725	307.87582	13.77690	27.03896
4	52.590	MM	0.3766	312.73526	13.84143	27.46574
5	58.062	MM	0.3500	7.36588	3.50733e-1	0.64690
6	59.809	MM	0.3726	7.96836	3.56461e-1	0.69982
Totals :				1138.63785	53.27884	

Babu 6/1/2018 3:20:17 PM MAHESH Page 1 of 2

Data File C:\CHEM32\1\DATA\TSR\HV-2-ON DIENE-M2.D
Sample Name: HV-2-ON DIENE-M2.D

Chiral GC (Cyclosil-B, 150 °C isotherm)

```
Acq. Operator    : SRINI
Acq. Instrument  : Babu                          Location : Vial 201
Injection Date   : 4/6/2017 12:29:08 PM
                                                 Inj Volume : Manually
Acq. Method      : C:\CHEM32\1\METHODS\150_C-ISO_CHIRAL.M
Last changed     : 4/6/2017 12:26:58 PM by SRINI
                   (modified after loading)
Analysis Method  : C:\CHEM32\1\METHODS\COOLDOWN.M
Last changed     : 5/25/2018 12:15:57 PM by  MAHESH
                   (modified after loading)
Sample Info      : HV-2-ON DIENE-M2.D
```



Area Percent Report

HV of enriched (*S*)-**33** **using** (*Sc,Sc*)-ligand **L3** showing retention times of starting material(s) and products (incomplete reaction)

```
Sorted By              :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Sample Amount:                :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: FID1 B, Back Signal

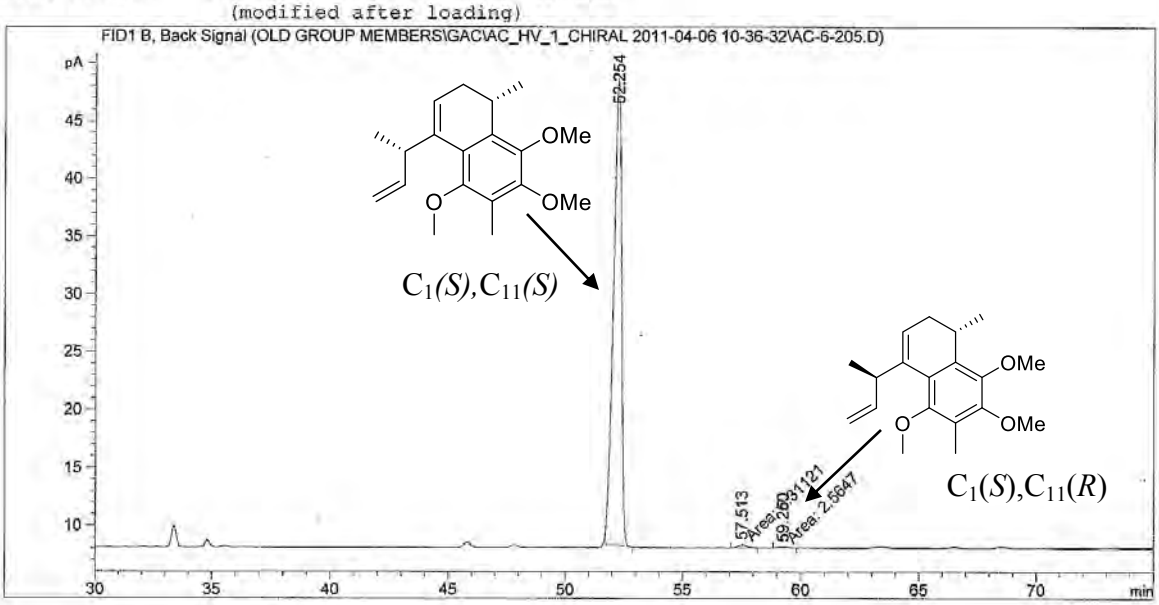
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	45.471	MM	0.2732	17.81499	1.08695	1.16246
2	47.441	BB	0.2847	487.12689	23.37669	31.78599
3	51.790	BB	0.2846	1020.69672	42.80774	66.60248
4	58.688	MM	0.3449	6.88202	3.32605e-1	0.44907

Babu 5/25/2018 12:16:34 PM MAHESH Page 1 of 2

Data File C:\CHEM32\...OLD GROUP MEMBERS\GAC\AC_HV_1_CHIRAL 2011-04-06 10-36-32\AC-6-205.D
Sample Name: AC-6-205

CSP GC (Cyclosil-B), 150 oC isotherm)

```
Acq. Operator   : Adam Cox                          Seq. Line :   1
Acq. Instrument : Babu                               Location : Vial 201
Injection Date  : 4/6/2011 10:38:15 AM                    Inj :   1
                                                   Inj Volume : 1 µl
Acq. Method     : C:\CHEM32\1\DATA\GAC\AC_HV_1_CHIRAL 2011-04-06 10-36-32\AC_HV_2_CHIRAL.M
Last changed    : 4/6/2011 10:36:25 AM by Adam Cox
Analysis Method : C:\CHEM32\1\METHODS\COOLDOWN.M
Last changed    : 5/25/2018 5:51:42 PM by  MAHESH
                  (modified after loading)
```




```
Area Percent Report

Sorted By              :      Signal
Multiplier:                    :      1.0000
Dilution:                      :      1.0000
Use Multiplier & Dilution Factor with ISTDs
```

Asym HV of (*S*)-**33** using (*Sc,Sc*)-ligand (L3) (complete reaction)

Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	52.254	BB	0.2843	956.61475	40.39579	99.08068
2	57.513	MM	0.3728	6.31121	2.82174e-1	0.65368
3	59.250	MM	0.3997	2.56470	1.06943e-1	0.26564

Totals : 965.49065 40.78490

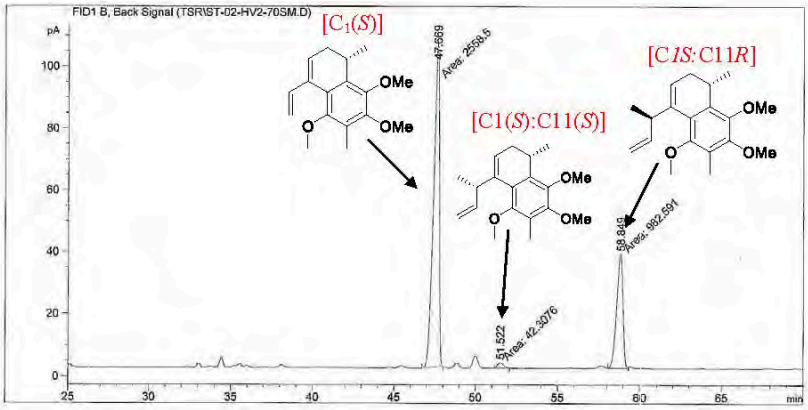
*** End of Report ***

Babu 5/25/2018 5:51:47 PM MAHESH Page 1 of 1

Data File C:\CHEM32\1\DATA\TSR\ST-02-HV2-70SM.D
Sample Name: ST-02-hv2-70sm

Chiral GC (Cyclosil-B, 150 °C isotherm)

```
Acq. Operator    : SRINI
Acq. Instrument  : Babu                          Location : Vial 201
Injection Date   : 5/24/2018 3:21:48 PM
                                                 Inj Volume : Manually
Acq. Method      : C:\CHEM32\1\METHODS\150_C-ISO_CHIRAL.M
Last changed     : 5/24/2018 3:18:51 PM by SRINI
                   (modified after loading)
Analysis Method  : C:\CHEM32\1\METHODS\COOLDOWN.M
Last changed     : 6/1/2018 11:15:50 AM by  MAHESH
                   (modified after loading)
Sample Info      : ST-02-hv2-70% sm and 30% hv2 pro
```




```
                    Area Percent Report

Sorted By              :      Signal
Multiplier:                    :      1.0000
Dilution:                      :      1.0000
Sample Amount:                 :      1.00000  [ng/ul]   (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

HV of (*S*)-**33** using (Rc,Rc)-ligand *ent*- **L3** showing retention times of starting material and products (incomplete reaction)

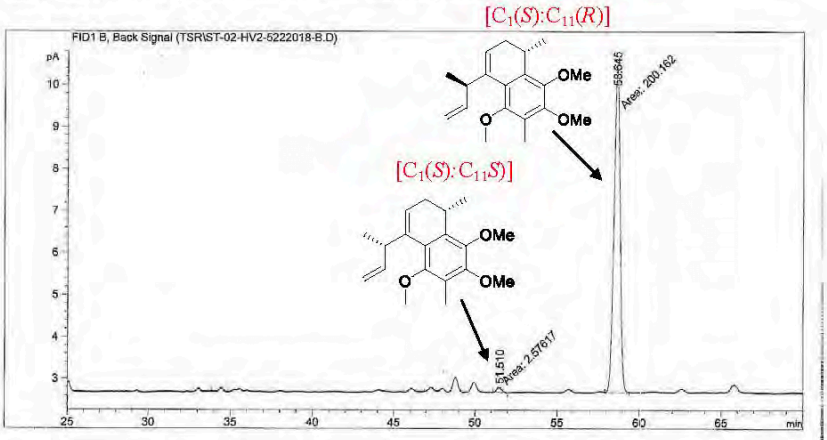
```
Signal 1: FID1 B, Back Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [pA*s]      [pA]       %
----|-------|----|-------|----------|----------|--------|
   1  47.669 MM   0.4061 2558.49756  105.00091 71.39868
   2  51.522 MM   0.4057   42.30760    1.73804  1.18066
   3  58.849 MM   0.4476  982.59088   36.58854 27.42066
```

Babu 6/1/2018 11:17:31 AM MAHESH Page 1 of 2

Data File C:\CHEM32\1\DATA\TSR\ST-02-HV2-5222018-B.D
Sample Name: ST-02-HV2-5222018-B

Chiral GC (Cyclosil-B, 150 °C isotherm)

Acq. Operator : SRINI
Acq. Instrument : Babu Location : Vial 201
Injection Date : 5/23/2018 3:57:29 PM
Inj Volume : 1 µl
Different Inj Volume from Sequence ! Actual Inj Volume : 3 µl
Acq. Method : C:\CHEM32\1\METHODS\150_C-ISO_CHIRAL.M
Last changed : 5/23/2018 3:23:24 PM by SRINI
Analysis Method : C:\CHEM32\1\METHODS\COOLDOWN.M
Last changed : 6/1/2018 11:15:50 AM by MAHESH
(modified after loading)
Sample Info : ST-02-HV2-5222018-B (RE-INJECTED SAMPLE)



Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Sample Amount: : 1.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

HV of (*S*)-33 using (*Rc*,*Rc*)-ligand L3 showing product (complete reaction)

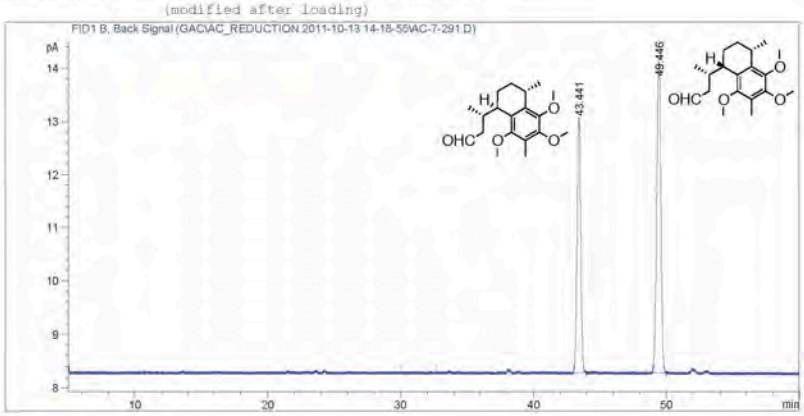
Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	51.510	MM	0.3263	2.57617	1.31567e-1	1.27069
2	58.645	MM	0.4325	200.16246	7.71282	98.72931
Totals :				202.73863	7.84439	

Babu 6/1/2018 11:22:10 AM MAHESH Page 1 of 2

Diastereomeric (C_4) mixture 36d

```
Data File C:\CHEM32\1\DATA\GAC\AC_REDUCTION 2011-10-13 14-18-55\AC-7-291.D
Sample Name: AC-7-291

==========================================================================
Acq. Operator   : Adam Cox                          Seq. Line :   1
Acq. Instrument : Babu                               Location : Vial 201
Injection Date  : 10/13/2011 2:19:59 PM                   Inj :   1
                                                   Inj Volume : 1 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 2 µl
Acq. Method     : C:\CHEM32\1\DATA\GAC\AC_REDUCTION 2011-10-13 14-18-55\AC_RESOLUTION_CHIRAL.
                  M
Last changed    : 10/10/2011 5:14:53 PM by Adam Cox
Analysis Method : C:\CHEM32\1\METHODS\JP_CHIRALTETRALONE.M
Last changed    : 1/20/2012 10:20:15 AM by Jordan Page
                  (modified after loading)
```

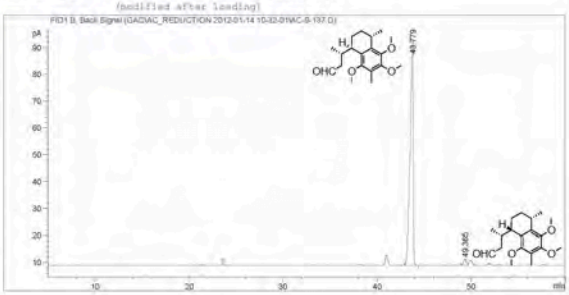



```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: FID1 B, Back Signal

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]   [pA*s]      [pA]        %
----|-------|----|-------|----------|----------|--------|
   1  43.441 BB    0.3002   91.12803    4.75941 41.69753
   2  49.446 BB    0.3384  127.41734    5.89898 58.30247

Totals :                  218.54537   10.65839


==========================================================================
                        *** End of Report ***
```

36d (C_4-*R*) and 36d (C_4-*S*)

Data File C:\CHEM32\1\DATA\GAC\AC_REDUCTION 2012-01-14 10-32-01\AC-8-137.D
Sample Name: AC-8-137

Acq. Operator : Adam Cox
Acq. Instrument : Babu
Injection Date : 1/14/2012 10:33:33 AM
Seq. Line : 1
Location : Vial 201
Inj : 1
Inj Volume : 1 µl
Acq. Method : C:\CHEM32\1\DATA\GAC\AC_REDUCTION 2012-01-14 10-32-01\AC_RESOLUTION_CHIRAL.M
Last changed : 1/13/2012 9:37:08 AM by Adam Cox
Analysis Method : C:\CHEM32\1\METHODS\JP_CHIRALTETRALONE.M
Last changed : 1/30/2012 10:14:06 AM by Jordan Page
(modified after loading)



Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	43.779	BB	0.3224	1964.68225	83.53130	97.46265
2	49.365	BV	0.3370	51.14456	2.34265	2.53715

Totals : 2015.82681 85.87396

*** End of Report ***

Data File C:\CHEM32\1\DATA\GAC\AC_REDUCTION 2011-10-13 12-17-29\AC-8-43.D
Sample Name: AC-8-43

Acq. Operator : Adam Cox
Acq. Instrument : Babu
Injection Date : 10/13/2011 12:19:35 PM
Seq. Line : 1
Location : Vial 201
Inj : 1
Inj Volume : 1 µl
Different Inj Volume from Sequence : Actual Inj Volume : 2 µl
Acq. Method : C:\CHEM32\1\DATA\GAC\AC_REDUCTION 2011-10-13 12-17-29\AC_RESOLUTION_CHIRAL.M
Last changed : 10/10/2011 5:14:53 PM by Adam Cox
Analysis Method : C:\CHEM32\1\METHODS\JP_CHIRALTETRALONE.M
Last changed : 1/20/2012 10:11:44 AM by Jordan Page
(modified after loading)

Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

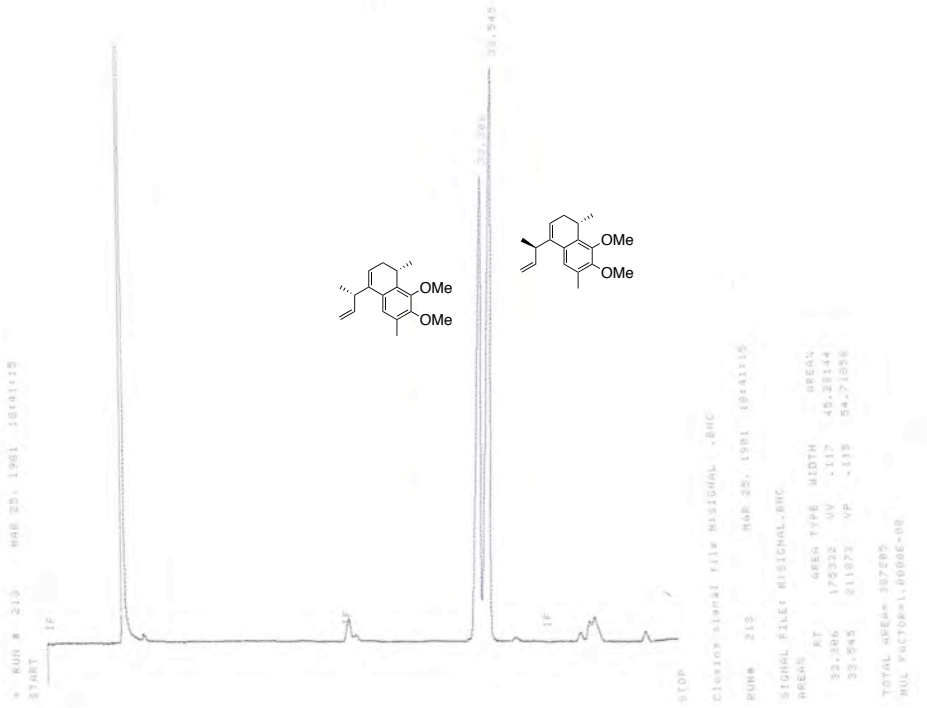
Signal 1: FID1 B, Back Signal

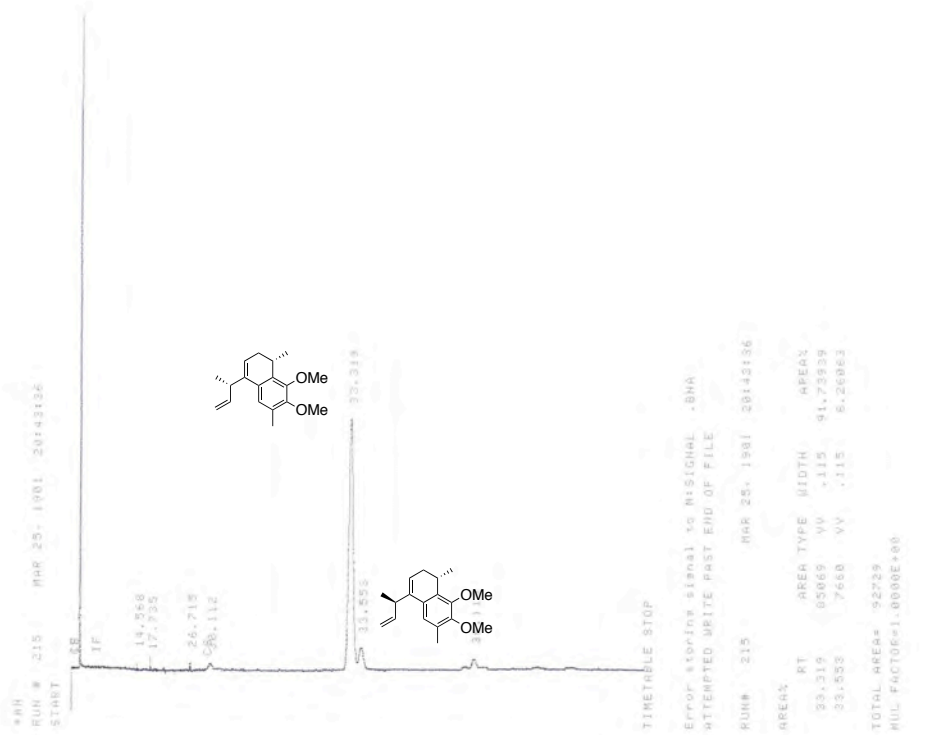
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	49.602	BB	0.3482	870.92203	36.98273	1.00000

Totals : 870.92203 36.98273

*** End of Report ***

Racemic 51 and Enantioenriched 51





Compound 58 and Hydrovinylated Product 59