Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Evolution of an Oxidative Dearomatization Enabled Total Synthesis of Vinigrol

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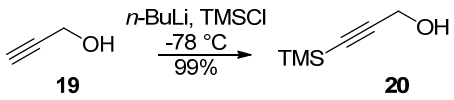
General Information

All reactions were performed using flame-dried glassware under an atmosphere of nitrogen with dry solvents, unless otherwise stated. Dry tetrahydrofuran (THF), diethyl ether, dichloromethane (CH_2Cl_2), toluene (PhMe), methanol (MeOH), acetonitrile (CH_3CN) were obtained by passing these previously degassed solvents through activated alumina columns. Benzene (PhH) was distilled from sodium/benzophenone. All other commercial reagents were used as provided. Reactions were monitored by thin layer chromatography (TLC) carried out on EMD silica gel 60-F254 plates. Visualization was performed by UV light irradiation and ceric ammonium molybdate, or anisaldehyde, or potassium permanganate stain and heat. SiliaFlash F60 silica (particle size 40-63□m) was used for flash column chromatography. Preparative thin layer chromatography (prep-TLC) separations were also carried out on EMD silica gel 60-F254 plates. ^1H and ^{13}C NMR data was acquired on Varian Inova 400, 500, or 600 (Cornell University) or Bruker DRX 400, 500, or 600 (University of Arizona) spectrometer and the spectra were calibrated using residual solvents as an internal reference ($CDCl_3$: 7.26 ppm for ^1H NMR, 77.16 ppm for ^{13}C NMR; C_6D_6: 7.16 ppm for ^1H NMR, 128.06 ppm for ^{13}C NMR; CD_3OD: 3.31 ppm for ^1H NMR, 49.00 ppm for ^{13}C NMR). The following abbreviations (or combinations thereof) were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. Infrared spectra were recorded on a Shimadzu Prestige FT-IR. High resolution mass spectra were acquired at the University of Arizona Mass Spectral Facility.

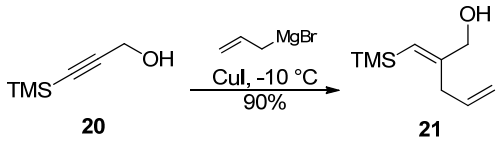
Experimental Procedures



19 **20**

A solution of propargyl alcohol (12.0 mL, 203.1 mmol) in THF (775 mL) was cooled to -78 °C, and *n*-BuLi (2.5 M in hexanes, 170.6 mL, 426.5 mmol) was added slowly. After stirring for 30 min. at -78 °C, trimethylsilyl chloride (57.1 mL, 446.8

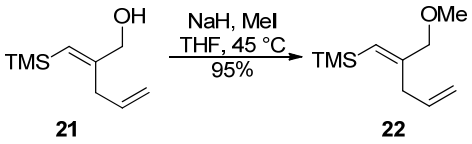
mmol) was added dropwise. Once the addition was completed, the cold bath was removed, and the reaction was stirred at r.t. for 2.0 h. The reaction was cooled to 0 °C, quenched by water (100 mL), then 1 N HCl solution (300 mL) was added to the crude reaction mixture and stirred at r.t. for 1.5h. The complete consumption of the TMS ether was observed by TLC (R_f 0.90 in 10% ethyl acetate/hexanes). The reaction mixture was poured into a separatory funnel, the organic layer was separated and the aqueous layer was extracted with diethyl ether (4 × 150 mL). The combined organic layers were washed with brine (200 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification by vacuum distillation (15 mtor, 50 °C) provided the desired alcohol (25.9 g, 99%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) □ 4.27 (d, J = 6.1 Hz, 2H), 1.53 (t, J = 6.1 Hz, 1H), 0.18 (s, 9H). The spectrum data is consistent with the reported literature data.[1]



A mixture of 3-(trimethylsilyl)prop-2-ynol (11.9 g, 93.0 mmol), diethyl ether (200 mL), and copper iodide (1.92 g, 10.1 mmol) was stirred and cooled at -10 °C (salt/ice bath) and freshly prepared allylmagnesium bromide (0.085M, 300 mL) was added slowly via cannula. The reaction mixture turned from grey to brown to black over time. After the addition was completed, the reaction was warmed to r.t. naturally and stirred for total 12 h. The reaction mixture was cooled to 0 °C and quenched by saturated NH_4Cl solution (100 mL) and diluted with water (300 mL). After phase separation, the aqueous phase was filtered through a Celite pad to remove the precipitate. The solution was then extracted with diethyl ether (3 × 150 mL). All organic phases were combined and washed with brine (200 mL), dried over anhydrous Na_2SO_4 and concentrated. The crude product was distilled under vacuum (15 mtor, 72-73 °C) to afford a light yellow oil (14.2 g, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) □ 5.77 (ddt, J = 17.1, 10.1, 6.5 Hz, 1H), 5.62 (t, J = 1.6 Hz, 1H), 5.08 (dq, J = 17.1, 1.7 Hz,

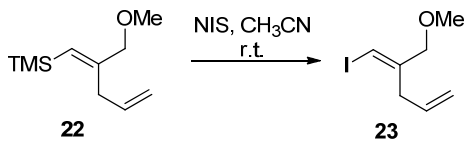
(1) Langille, N. F.; Jamison, T. F. *Org. Lett.* **2006**, 8, 3761-3764.

1H), 5.04 (dq, *J* = 10.1, 1.5 Hz, 1H), 4.06 (dd, *J* = 6.2, 1.5 Hz, 2H), 2.93 (dt, *J* = 6.5, 1.6 Hz, 2H), 1.57 (t, *J* = 6.2 Hz, 1H), 0.14 (s, 9H). The spectrum data is consistent with the reported literature data.[2]



21 **22**

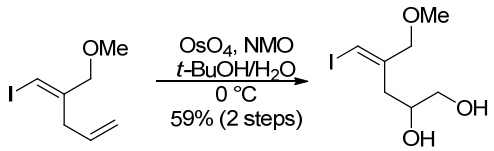
To a suspension of NaH (60 wt%, 5.36 g, 133.9 mmol) and iodomethane (25.1 mL, 401.9 mmol) in THF (160 mL), alcohol (15.2 g, 89.3 mmol) in THF (20 mL) was added dropwise. The reaction mixture was then stirred at 45 °C for 16 h. After that period of time, the starting material was still present by TLC analysis. More NaH (3.56 g, 89.3 mmol) and iodomethane (5.6 mL, 89.3 mmol) were added and stirring continued for 5.0 h. The reaction was cooled to 0 °C and quenched by saturated NH_4Cl solution (50 mL) and diluted with water (50 mL). The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 × 80 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous Na_2SO_4 and concentrated. Purification by column chromatography (5% diethyl ether/pentane) afforded a light yellow oil (15.6 g, 95%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.77 (ddt, *J* = 17.1, 10.1, 6.5 Hz, 1H), 5.61 (t, *J* = 1.5 Hz, 1H), 5.07 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.03 (dq, *J* = 10.1, 1.5 Hz, 1H), 3.83 (d, *J* = 1.4 Hz, 1H), 3.33 (s, 3H), 2.90 (dt, *J* = 6.5, 1.5 Hz, 1H), 0.13 (s, 9H). The spectrum data is consistent with the reported literature data.[2]



22 **23**

(2) Labaudinihe, L.; Hanaizi, J.; Normant, J. *J. Org. Chem.* **1992**, 57, 6903-6908.

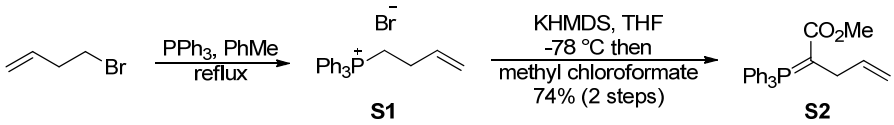
To the solution of TMS-diene (12.1 g, 65.6 mmol) in acetonitrile (230 mL) was added *N*-iodosuccinimide (17.1g, 76.0 mmol) at 0 °C in portions. After the addition was completed, the reaction mixture was stirred at 0 °C for 40 min., then warmed to r.t., covered with aluminum foil and stirred for 40 h. After that period of time, the reaction was quenched by 10% $Na_2S_2O_3$ solution (200 mL). Two phases were separated and the aqueous phase was extracted with pentane (3 × 150 mL) and the organic phase was also extracted with pentane (6 × 200 mL). The combined extracts were washed with brine (200 mL), dried over anhydrous Na_2SO_4 and carefully concentrated on rotovap. The crude product with residual pentane was used in next step without any further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.34 (tt, *J* = 1.4, 0.5 Hz, 1 H), 5.75 (ddt, *J* = 17.1, 10.0, 6.6 Hz, 1 H), 5.15 (dq, *J* = 17.1, 1.6 Hz, 1 H), 5.09 (ddt, *J* = 10.0, 1.8, 1.3 Hz, 1 H), 3.91 (d, *J* = 1.4 Hz, 2 H), 3.30 (s, 3 H), 2.98 (dt, *J* = 6.6, 1.5 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.11, 133.26, 117.06, 79.49, 74.80, 58.12, 39.43; IR (film) 3059, 2980, 2928, 2926, 2820, 1639, 1211, 1095, 993, 916, 781 cm^{-1} ; HRMS (EI) *m/z* calcd. for $C_7H_{11}IO$ $[M]^+$: 237.9855, found: 237.9861.



23 **24**

N-Methylmorpholine *N*-oxide monohydrate (9.34 g, 69.1 mmol) was dissolved in water (140 mL) and cooled to 0 °C, and iododiene from the previous step dissolved in *tert*-butanol (140 mL) was added, followed by a solution of osmium tetroxide (2.5 wt%, 12.0 mL, 1.73 mmol) in *tert*-butanol. The reaction was stirred at 0 °C for 8 h then quenched by 15% $NaHSO_3$ solution (250 mL) and extracted with ethyl acetate (6 × 200 mL). The combined extracts were washed with brine (2 × 200 mL), dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by column chromatography (60% ethyl acetate/hexanes) to afford a light brown oil (10.5 g, 59% yield over 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (td, *J* = 1.1, 0.7 Hz, 1H), 4.00 (d, *J* = 1.1 Hz, 2H), 3.93 (ddtd, *J* = 8.8, 6.5, 3.8, 3.3 Hz, 1H), 3.70 (ddd, *J* = 11.2, 6.8, 3.3 Hz, 1H), 3.61 (d, *J* = 3.9 Hz, 1H), 3.53 (ddd, *J* = 11.2, 6.5, 5.4 Hz, 1H), 3.37 (s,

3H), 2.69 (dd, *J* = 6.8, 5.4 Hz, 1H), 2.51 (ddd, *J* = 13.9, 3.9, 0.7 Hz, 1H), 2.40 (dd, *J* = 13.9, 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 145.17, 83.47, 76.70, 70.57, 66.63, 58.28, 39.84; IR (film) 3358, 2926, 2885, 2821, 1610, 1192, 1087, 1033, 910, 783 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_7H_{13}INaO_3$ $[M+Na]^+$: 294.9802, found: 294.9807.



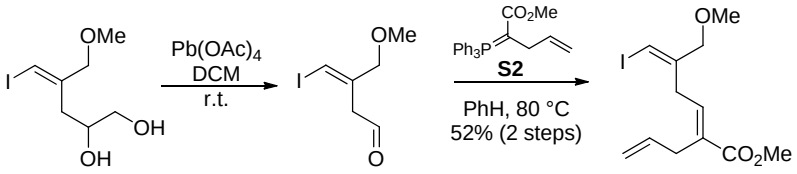
Compound **S2** was prepared according to literature protocol.[3]

A mixture of 4-bromo-1-butene (5.4 mL, 52.7 mmol) and triphenylphosphine (10.6 g, 40.5 mmol) in toluene (150 mL) was heated at reflux for 24 h. The reaction mixture was then cooled to r.t. and filtered over a Buchner funnel. A white solid was collected, which was washed with toluene (2 × 35 mL) then dried under high vacuum to afford desired product **S1** (16.0 g, quantitative yield).

To a solution of phosphonium salt (500 mg, 1.25 mmol) in THF (7.0 mL) was added potassium bis(trimethylsilyl)amide (1.0 M in THF, 5.0 mL) dropwise at -78 °C. After stirring for 1.0 h, methyl chloroformate (0.48 mL, 6.25 mmol) was added. The reaction mixture was stirred at the same temperature for 30 min. then warmed to r.t. and stirred for 1.0 h. The reaction was quenched by saturated $NaHCO_3$ and diluted with dichloromethane. The organic phase was separated and the aqueous phase was extracted with dichloromethane three times. The combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated. The crude product was purified by column chromatography (15% ethanol/ethyl acetate) to afford an off-white solid (348 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) 7.64 – 7.40 (m, 15H), 5.82 (ddt, *J* = 17.0, 10.0, 6.0 Hz, 1H), 4.67 (ddt, *J* = 10.0, 2.6, 1.4 Hz, 1H), 4.56 (dq, *J* = 17.0, 1.7 Hz, 1H), 3.33 (s, 3H), 2.69 (ddt, *J* = 18.6, 6.0, 1.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 170.52, 140.93, 133.42 (d, *J* = 9.7 Hz, 6C), 131.48 (d, *J* = 2.8 Hz, 3C), 128.26 (d, *J* = 12.0 Hz, 6C), 127.61 (d, *J* = 90.4 Hz, 3C), 111.65, 49.17, 37.43 (d, *J* =

(3) Bestmann, H. J.; Schulz, H. *Chem. Ber.* **1962**, 95, 2921- 2927.

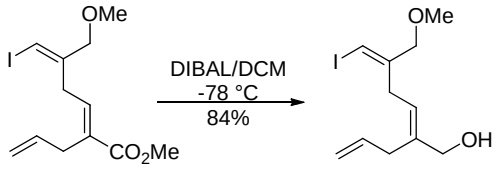
122.0 Hz), 31.14; IR (film) 3057, 2941, 1627, 1600, 1435, 1323, 1159, 1101, 746, 715, 692, 569, 516 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{24}H_{24}O_2P$ $[M+H]^+$: 375.1508, found: 375.1505.



24 **25** **26**

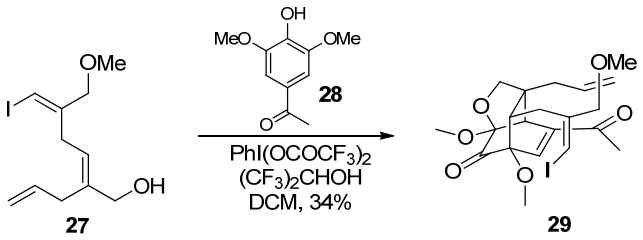
To an ice-water cooled solution of diol (82.0 mg, 0.301 mmol) in CH_2Cl_2 (3.0 mL) was added lead (IV) acetate (155 mg, 0.332 mmol) in one portion. After the addition was completed, the reaction mixture was allowed to warm to r.t. and stirred for 1.0 h. The mixture was then poured directly over a silica gel pad, filtered and the filter cake was washed with ethyl acetate. After the filtrate was concentrated on rotovap, the residue was taken up in diethyl ether and filtered through a Celite pad and washed with ether. The filtrate was concentrated again on rotovap and then placed under high vacuum briefly to remove the residual solvents and formaldehyde by-product. The resultant aldehyde crude product was used immediately.

A mixture of phosphorane (281 mg, 0.753 mmol) and the aforementioned aldehyde in benzene (3.0 mL) was placed in a high-pressure tube, capped and heated at 80 °C for 1.0 h. The reaction mixture was cooled to r.t. and concentrated. The residue was purified by column chromatography (10 % ethyl acetate/hexanes) to afford a colorless oil (53.0 mg, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 6.72 (t, *J* = 7.5 Hz, 1H), 6.41 (s, 1H), 5.84 (ddt, *J* = 17.2, 10.1, 6.1 Hz, 1H), 5.12 – 4.98 (m, 2H), 3.89 (d, *J* = 1.3 Hz, 2H), 3.74 (s, 2H), 3.30 (s, 3H), 3.18 (dt, *J* = 6.1, 1.7 Hz, 2H), 3.15 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 167.73, 145.54, 138.44, 135.08, 131.85, 115.59, 80.67, 75.05, 58.15, 52.02, 34.71, 31.20; IR (film) 2949, 2926, 1712, 1435, 1276, 1205, 1132, 1093, 914, 783, 765 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{12}H_{18}IO_3$ $[M+H]^+$: 337.0295, found: 337.0292.



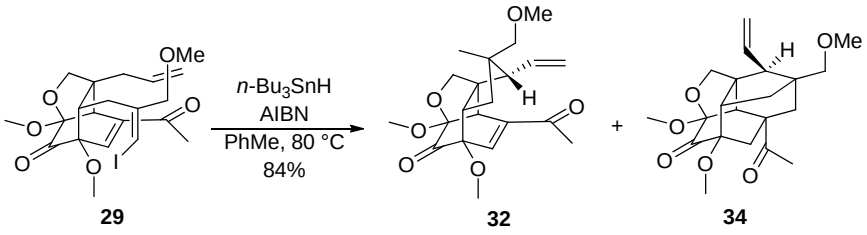
26 **27**

To a solution of ester (455 mg, 1.35 mmol) in dichloromethane (14.0 mL) cooled at -78 °C, DIBAL (1.0 M in CH_2Cl_2, 2.98 mL, 2.98 mmol) was added dropwise. After stirring at -78 °C for 3 h the reaction was quenched by 10% Rochelle's salt (4.0 mL) and warmed to r.t. The mixture was then partitioned between ethyl acetate (25 mL) and Rochelle' salt solution (25 mL) and vigorously stirred for 2 h. The organic layer was separated and the aqueous layer was extracted with ethyl acetate three times. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration and concentration, the residue was purified by column chromatography (30% ethyl acetate/hexanes) to afford a light yellow oil (349 mg, 84% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 6.30 (td, *J* = 1.4, 0.6 Hz, 1H), 5.80 (ddt, *J* = 17.1, 10.0, 6.4 Hz, 1H), 5.45 (dddt, *J* = 8.1, 7.4, 2.2, 1.1 Hz, 1H), 5.10 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.04 (dq, *J* = 10.0, 1.7 Hz, 1H), 4.07 – 4.02 (m, 2H), 3.89 (d, *J* = 1.4 Hz, 2H), 3.29 (s, 2H), 3.02 (d, *J* = 7.4 Hz, 2H), 2.95 (d, *J* = 6.4 Hz, 2H), 1.68 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 146.87, 139.07, 135.52, 122.26, 115.94, 79.22, 74.91, 66.72, 58.08, 33.73, 32.84; IR (film) 3404, 2976, 2924, 2821, 1635, 1612, 1450, 1375, 1298, 1284, 1265, 1192, 1087, 995, 914, 777, 673 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{11}H_{17}IO_2Na$ $[M+Na]^+$: 331.0165, found: 331.0163.



27 **28** **29**

To a solution of alcohol (32.0 mg, 0.104 mmol) and phenol (61.2 mg, 0.312 mmol) in 1,1,1,3,3,3-hexafluoropropan-2-ol (5.0 mL) was added at r.t. a solution of phenyliodine bis(trifluoroacetate) (134 mg, 0.312 mmol) in 1,1,1,3,3,3-hexafluoropropan-2-ol (1.0 mL) over 2.0 h via syringe pump. After the addition was completed, the reaction solution was stirred for further 30 min., then partitioned between ethyl acetate and saturated $NaHCO_3$ solution. The organic phase was separated, and the aqueous phase was extracted with ethyl acetate three times. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (25% ethyl acetate/hexanes) to provide a light yellow oil (18.0 mg, 34% yeild). ^{1}H NMR (400 MHz, $CDCl_3$) □ 7.13 (dd, *J* = 2.2, 1.1 Hz, 1H), 6.31 (t, *J* = 1.1 Hz, 1H), 5.86 (ddt, *J* = 17.2, 10.1, 7.2 Hz, 1H), 5.24 – 5.17 (m, 1H), 5.09 (dq, *J* = 16.9, 1.5 Hz, 1H), 4.09 (d, *J* = 8.2 Hz, 1H), 4.03 (dd, *J* = 3.5, 1.0 Hz, 2H), 4.00 (d, *J* = 2.2 Hz, 1H), 3.86 (d, *J* = 8.2 Hz, 1H), 3.56 (s, 3H), 3.46 (s, 3H), 3.29 (s, 3H), 2.94 (t, *J* = 7.2 Hz, 1H), 2.42 (s, 3H), 2.36 (ddd, *J* = 7.6, 2.7, 1.1 Hz, 2H), 2.21 (dd, *J* = 14.5, 7.6 Hz, 1H), 2.09 (dd, *J* = 14.5, 6.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 198.60, 194.07, 146.95, 139.83, 139.16, 132.60, 120.39, 99.24, 87.20, 80.82, 77.99, 75.55, 57.94, 53.77, 51.32, 49.24, 45.09, 42.33, 35.72, 33.32, 25.12; IR (film) 2976, 2941, 2893, 1766, 1749, 1674, 1249, 1228, 1192, 1089, 1014, 877 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{28}IO_6$ $[M+H]^+$: 503.0925, found: 503.0916.



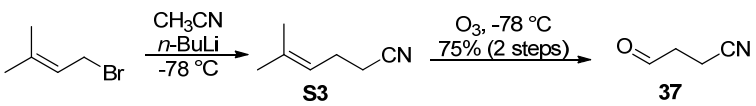
29 **32** **34**

A solution of vinyl iodide (27.0 mg, 0.0538 mmol) in dry toluene (0.80 mL) was heated to 80 °C, to which tributyltin hydride (0.63 M in toluene, 0.10 mL) and azobisisobutyronitrile (0.11 M in toluene, 0.10 mL) were added simultaneously via

syringe pumps over 2.0 h. The reaction was stirred for additional 3.0 h then cooled to r.t. and concentrated. The crude product was purified by column chromatography (25% ethyl acetate/hexanes) to afford two compounds: **32** (higher R_f, colorless oil, 9.0 mg, 44% yield) and **34** (lower R_f, colorless oil, 8.0 mg, 40% yield).

Compound **32**: ^{1}H NMR (600 MHz, $CDCl_3$) □ 6.99 (t, *J* = 1.7 Hz, 1H), 5.53 (dt, *J* = 16.7, 10.2 Hz, 1H), 5.22 (dd, *J* = 10.0, 2.0 Hz, 1H), 5.13 (dd, *J* = 16.7, 2.0 Hz, 1H), 4.07 (d, *J* = 7.7 Hz, 1H), 3.94 (d, *J* = 2.1 Hz, 1H), 3.88 (d, *J* = 7.7 Hz, 1H), 3.60 (s, 3H), 3.43 (s, 3H), 3.24 (s, 3H), 3.02 (d, *J* = 9.3 Hz, 1H), 2.92 (d, *J* = 9.3 Hz, 1H), 2.88 (m, 1H), 2.39 (s, 3H), 2.05 (d, *J* = 10.2 Hz, 1H), 1.65 (dd, *J* = 13.0, 7.6 Hz, 1H), 1.50 (t, *J* = 12.2 Hz, 1H), 0.90 (s, 3H); ^{13}C NMR ($CDCl_3$, extracted from HSQC and HMBC) □ 198.9, 194.5, 140.9, 138.7, 132.2, 120.7, 98.00, 86.1, 77.9, 76.3, 59.2, 57.2, 53.6, 53.3, 51.1, 47.0, 46.0, 41.5, 37.5, 24.8, 19.5; IR (film) 2954, 2927, 2873, 1759, 1714, 1195, 1109, 1087, 1016, 871.86 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{29}O_6$ $[M+H]^+$: 377.1958, found: 377.1958.

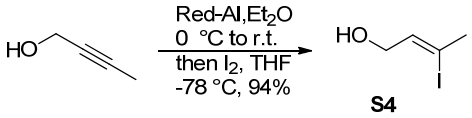
Compound **34**: 1H NMR (600 MHz, $CDCl_3$) □ 5.67 (dt, J = 16.8, 10.1 Hz, 1H), 5.20 (dd, J = 16.9, 1.8 Hz, 1H), 5.16 (dd, J = 10.2, 1.8 Hz, 1H), 3.94 (d, J = 8.7 Hz, 1H), 3.67 (d, J = 8.7 Hz, 1H), 3.52 (s, 3H), 3.46 (s, 3H), 3.29 (s, 3H), 3.26 (d, J = 9.3 Hz, 1H), 3.21 (d, J = 9.3 Hz, 1H), 2.79 (d, J = 1.3 Hz, 1H), 2.45 (d, J = 10.1 Hz, 1H), 2.34 (m, 1H), 2.30 (m, 2H), 2.18 (s, 3H), 2.08 (dt, J = 13.9, 1.6 Hz, 1H), 1.88 (ddd, J = 14.1, 10.2, 1.9 Hz, 1H), 1.83 (d, J = 2.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, extracted from HSQC and HMBC) □ 225.0, 208.2, 132.9, 119.4, 103.4, 79.4, 76.7, 72.7, 59.2, 58.8, 52.8, 51.7, 51.3, 49.0, 47.8, 46.9, 45.9, 41.8, 35.0, 31.1, 25.0; IR (film) 2929, 1756, 1706, 1447, 1354, 1198, 1109, 1008 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{29}O_6$ $[M+H]^+$: 377.1958, found: 377.1962.



3-cyanopropanal **37** was prepared according to literature protocol.[4]

To a solution of acetonitrile (1.0 mL, 20.0 mmol) in THF (50 mL), *n*-BuLi (1.6 M in hexanes, 12.8 mL, 20.5 mmol) was added dropwise at -78 °C while the solution gradually turned to opaque yellow. After stirring for 15 min., 1-bromo-3-methyl-2-butene (2.2 mL, 19.0 mmol) in THF (25 mL) was added dropwise. The reaction mixture was stirred at -78 °C for 4.5 h, then quenched by saturated NH_4Cl solution (30 mL) and warmed to r.t. The organic phase was separated and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered and carefully concentrated to afford a light yellow oil. This crude product was used directly in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) □ 5.22 – 5.05 (m, 1H), 2.34 (m, 4H), 1.73 (s, 3H), 1.66 (s, 3H).

The crude product from the previous step was dissolved in dichloromethane (80 mL) and purged with ozone at -78 °C until the reaction solution turned blue. The mixture was then purged with N_2 for 15 min. and stirred with dimethyl sulfide (5.0 mL) at r.t. for 1.5 h. After evaporation of the solvent, the desired product 3-cyanopropanal (1.19 g, 75% yield over 2 steps) was obtained, which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) □ 9.80 (s, 1H), 2.92 (t, J = 7.0 Hz, 2H), 2.64 (t, J = 7.0 Hz, 2H).

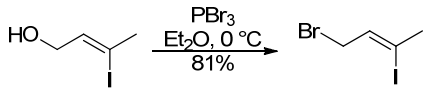


S4

A solution of Red-Al in toluene (65 wt% in toluene, 150.8 mL, 497.6 mmol) was added dropwise to a stirred solution of 2-butyn-1-ol (15.0 mL, 199.0 mmol) in ethyl ether (720 mL) at 0 °C. The resultant clear solution was warmed to r.t. and stirred for 18 h. After cooling to 0 °C, ethyl acetate (29.2 mL) was added and stirred for 30 min. The solution was cooled to -78 °C and iodine (75.8 g, 298.5 mmol) in THF

(4) Shrestha-Dawadi, P. B.; Lugtenburg, J. *Eur. J. Org. Chem.* **2003**, 4654-4663.

(250 mL) was added slowly. After the addition was completed, the reaction mixture was allowed to warm to r.t. and stirred for 2 h. The reaction was cooled to 0 °C and saturated $Na_2S_2O_3$ solution (250 mL) was added. The upper organic phase was decanted and the rest was extracted with ethyl ether (3 × 250 mL). The combined organic phases were washed successively with saturated $Na_2S_2O_3$ solution (2 × 250 mL), water (250 mL), and brine (250 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The resultant crude product was purified by column chromatography (30% ethyl ether/pentane) to afford a light yellow oil (36.8g, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 5.76 (tq, *J* = 6.0, 1.5 Hz, 1H), 4.16 (dq, *J* = 6.0, 1.2 Hz, 2H), 2.53 (dt, J = 1.5, 1.2 Hz; 3H). Spectrum data is consistent with the reported literature data.[5]

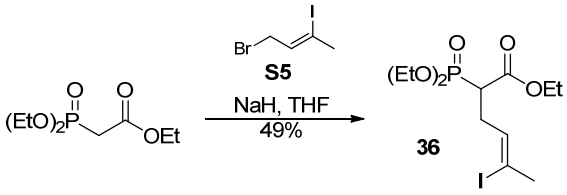


S4 **S5**

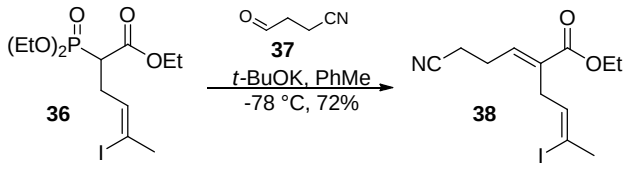
To a solution of allylic alcohol (67.6 g, 270.5 mmol) in ethyl ether (550 mL) was added phosphorus tribromide (12.8 mL, 135.2 mmol) dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 1 h then quenched by brine (100 mL). The organic phase was separated and washed with water (100 mL) and brine (100 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The resultant crude product was purified by column chromatography (pure pentane) to afford a colorless oil (57.1 g, 81%), which rapidly turned purple standing in air. ^{1}H NMR (400 MHz, $CDCl_3$) □ 5.77 (tq, *J* = 7.8, 1.6 Hz, 1H), 3.99 (dq, *J* = 7.8, 0.8 Hz, 2H), 2.58 (dt, *J* = 1.6, 0.8 Hz, 3H). Spectrum data is consistent with the reported literature data.[6]

(5) Kulyk, S.; Dougherty, W. G.; Kassel, W.S.; Zdilla, M. J.; Sieburth, S. M. *Org. Lett.* **2011**, 13, 2180-2183.

(6) Paquette, L. A.; Hormuth, S.; Lovely, C. J. *J. Org. Chem.* **1995**, 60, 4813-4821.



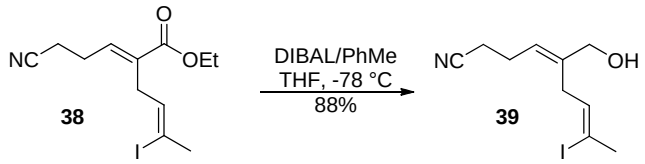
Compound **36** was prepared according to literature procedure.[7] To a suspension of NaH (60 wt%, 1.38 g, 34.4 mmol) in THF (60 mL) was added triethyl phosphonoacetate (6.21 mL, 31.3 mmol) dropwise at 0 °C. After stirring for 30 min., (Z)-1-bromo-3-iodo-but-2-ene (8.99 g, 34.4 mmol) was added dropwise at the same temperature. The reaction was allowed to warm up to r.t. and stirred for 4 h then quenched by saturated NH_4Cl solution (20 mL). The organic phase was separated and the aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (75% ethyl acetate) to afford a colorless oil (6.23 g, 49% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 (dddd, *J* = 6.7, 5.5, 1.9, 0.7 Hz, 1H), 4.28 – 4.10 (m, 6H), 3.04 (ddd, *J* = 22.3, 10.4, 4.7 Hz, 1H), 2.81 – 2.67 (m, 1H), 2.67 – 2.55 (m, 1H), 2.49 (m, 3H), 1.35 (tdd, *J* = 7.1, 2.1, 0.6 Hz, 6H), 1.29 (t, *J* = 7.1 Hz, 3H). The bis-alkylation product was also isolated as a yellow oil (3.66 g, 20% yield).



To a solution of phosphonate (2.89 g, 7.16 mmol) in toluene (20 mL), potassium *tert*-butoxide (803.5 mg, 7.16 mmol) was added at 0 °C in portions. After stirring at 0 °C for 30 min., the mixture was cooled to -78 °C and aldehyde (169.5 mg,

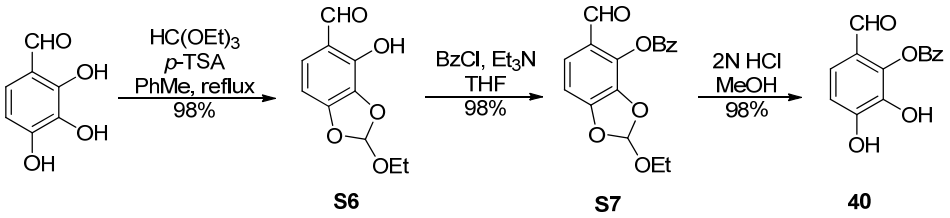
(7) Morton, J. G. M.; Draghici, C.; Njardarson, J. T. *Org. Lett.* **2009**, 11, 4492-4495.

2.04 mmol) in toluene (15 mL) was added dropwise. The reaction was stirred at -78 °C for 1.5 h then quenched by saturated NH_4Cl solution (20 mL) and warmed to r.t. The organic phase was separated and the aqueous phase was extracted with ethyl acetate (2 × 20 mL). The combined organic phases were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography (25% ethyl acetate/hexanes) to afford a light yellow oil (4:1 E/Z mixture, 486.3 mg, 72% yield). The E isomer could be isolated by second column chromatography (10% ethyl acetate/hexanes) and characterized: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (t, *J* = 7.5 Hz, 1H), 5.45 (tq, *J* = 6.6, 1.5 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.14 (dt, *J* = 6.6, 1.2 Hz, 2H), 2.65 (q, *J* = 7.3 Hz, 2H), 2.52 – 2.47 (m, 5H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.80, 138.12, 132.97, 132.37, 118.71, 101.71, 61.16, 35.21, 33.64, 25.13, 16.89, 14.37; IR (film) 2960, 2916, 2247, 1712, 1427, 1282, 1203, 1114, 1093, 1051, 758 cm^{-1}; HRMS (EI) *m/z* calcd. for $C_{12}H_{16}INO_2$ $[M]^+$: 333.0226, found: 333.0237.



To a solution of ester (2.35 g, 7.05 mmol) in THF (35 mL) at -78 °C, was added DIBAL (1.2 M in toluene, 12.2 mL, 14.8 mmol) dropwise. The reaction was stirred at -78 °C for 2.5 h and 0 °C for 2 h. After the reaction was diluted with THF (40 mL), water (0.56 mL), 20% NaOH (0.56 mL) and water (1.2 mL) were added in sequence at 0 °C. The mixture was allowed to warm up to r.t. and stirred for 15 min before anhydrous $MgSO_4$ was added. After stirring for another 15 min., the solid was filtered off and washed with diethyl ether. The filtrate was concentrated and purified by column chromatography (50% ethyl acetate/hexanes) to afford a colorless oil (1.60 g, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.51 (tt, *J* = 7.1, 1.4 Hz, 1H), 5.41 (tq, *J* = 6.7, 1.5 Hz, 1H), 4.05 (s, 2H), 2.91 (dt, *J* = 6.7, 1.3 Hz, 2H), 2.51 (q, *J* = 1.4 Hz, 3H), 2.49 – 2.40 (m, 4H), 2.30 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.94, 132.32, 122.43, 119.39, 102.33, 66.13, 36.12, 33.54, 23.78, 17.52; IR (film) 3419, 2949, 2914,

2866, 2245, 1423, 1139, 1097, 1074, 1006, 850, 580 cm^{-1}; HRMS (EI) *m/z* calcd. for $C_{10}H_{14}INO$ $[M]^+$: 291.0120, found: 291.0111.



Compound **40** was prepared according to literature protocol.[8]

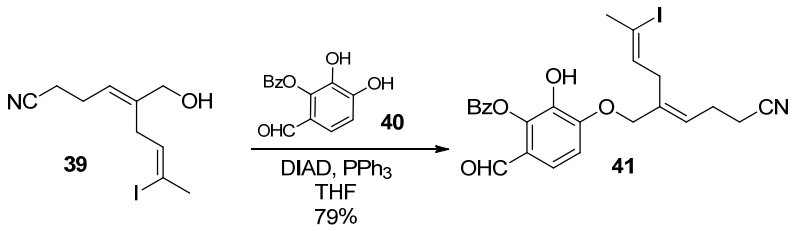
In a 500-mL round-bottom flask equipped with a reflux condenser and a Dean-Stark trap containing 5Å molecular sieves, a mixture of triethylorthoformate (16.7 mL, 100 mmol) and *p*-toluene sulfonic acid (500 mg) in toluene (250 mL) was heated to reflux for 30 min. After the mixture was cooled below refluxing temperature, 2, 3, 4-trihydroxybenzaldehyde (7.71 g, 50 mmol) was added and the mixture was then heated to reflux again. After 3 h, another portion of triethylorthoformate (16.7 mL, 100 mmol) was added and the mixture was refluxed for total 19 h. After the reaction was cooled to r.t., cesium carbonate (750 mg) was added, and the mixture was filtered through a Celite pad and washed with toluene (50 mL). The filtrate was concentrated to afford an off-white solid, which was purified by column chromatography (15-20% ethyl acetate/hexanes) to afford a white solid (10.3 g, 98%). ^{1}H NMR (600 MHz, $CDCl_3$) □ 11.05 (s, 1H), 9.75 (s, 1H), 7.19 (d, *J* = 8.1 Hz, 1H), 6.99 (s, 1H), 6.63 (d, *J* = 8.1 Hz, 1H), 3.78 (qq, *J* = 9.4, 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).

To a solution of phenol (10.3 g, 49.0 mmol) and benzoyl chloride (6.88 mL, 53.9 mmol) in THF (240 mL) was added triethylamine (10.2 mL, 73.5 mmol) dropwise at 0 °C. A white precipitate formed immediately upon addition. The reaction was warmed to r.t. and stirred for 30 min. After that period of time, the reaction

(8) Mills, S. J.; Dozol, H.; Vandeput, F.; Backers, K.; Woodman, T.; Erneux, C.; Spiess, B.; Potter, B. V. L. *ChemBioChem* **2006**, 7, 1696-1706.

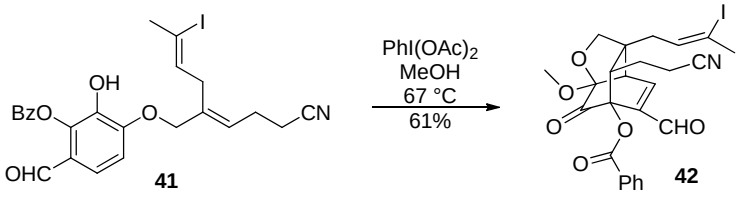
mixture was diluted with ethyl acetate and washed with water and brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (10% ethyl acetate/hexanes) to afford a white solid (15.1 g, 98%). ^{1}H NMR (300 MHz, $CDCl_3$) □ 10.03 (s, 1H), 8.30 – 8.19 (m, 2H), 7.73 – 7.63 (m, 1H), 7.59 – 7.50 (m, 3H), 7.03 (s, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 3.77 (qq, *J* = 9.4, 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

A solution of orthoester (0.27 g, 0.86 mmol) in MeOH/H_2O (2:1 v/v, 8.6 mL) was treated with 2N HCl (16.0 mL, 4.30 mmol) at r.t. for 1 h. The reaction was then concentrated on rotovap. The residue was taken up in ethyl acetate (30 mL) and washed with water (2 × 20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (50 % ethyl acetate/hexanes) to afford a white solid (0.22g, 98%). ^{1}H NMR (500 MHz, $CDCl_3$) □ 11.59 (s, 1H), 9.77 (s, 1H), 8.35 – 8.19 (m, 2H), 7.74 – 7.64 (m, 1H), 7.59 – 7.51 (m, 2H), 7.41 (d, *J* = 8.7 Hz, 1H), 6.71 (d, *J* = 8.7 Hz, 1H), 6.04 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 194.92, 164.15, 155.59, 155.41, 134.48, 132.45, 130.80 (2C), 128.96 (2C), 128.17, 126.23, 116.04, 109.15; IR (film) 3290, 1730, 1627, 1502, 1448, 1317, 1240, 1089, 1055, 796, 704 cm^{-1}; HRMS (MALDI) *m/z* calcd. for $C_{14}H_{10}O_5$ $[M+H]^+$: 259.0601, found: 259.0601.



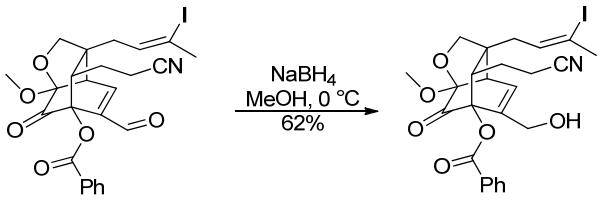
A mixture of alcohol (800.0 mg, 2.75 mmol), phenol (852.1mg, 3.30 mmol) and triphenylphosphine (865.6 mg, 3.30 mmol) in THF (15 mL) was cooled to 0 °C and diisopropyl azodicarboxylate (0.64 mL, 3.30 mmol) was added dropwise. After the addition was completed, the reaction was stirred at 0 °C for 2 h, then warmed to r.t. and stirred for 16 h. The reaction was concentrated and purified by flash column

chromatography (30% ethyl acetate/hexanes) to provide a light yellow oil (1.15 g, 79% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 11.32 (s, 1H), 9.80 (s, 1H), 8.29 – 8.22 (m, 2H), 7.68 – 7.62 (m, 1H), 7.53 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.47 (d, *J* = 8.8 Hz, 1H), 6.66 (d, *J* = 8.8 Hz, 1H), 5.52 (ddd, *J* = 8.3, 6.7, 1.3 Hz, 1H), 5.32 (tq, *J* = 6.9, 1.5 Hz, 1H), 4.56 (s, 2H), 2.88 (d, *J* = 6.9 Hz, 2H), 2.40 (q, *J* = 7.2 Hz, 2H), 2.35 (q, *J* = 1.3 Hz, 3H), 2.29 – 2.24 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-d) 194.92, 164.06, 157.31, 155.26, 134.81, 133.83, 132.65, 131.60, 130.53 (2C), 128.90, 128.72 (2C), 127.44, 125.93, 119.07, 116.52, 104.99, 103.14, 72.29, 36.20, 33.46, 23.97, 17.18; IR (film) 3458,3269, 3062, 2951, 2848, 2752, 2247, 1741, 1645, 1446, 1269, 1176, 1095, 1076, 1056, 1002, 912, 852, 786, 731, 705, 646, 542 cm^{-1}; HRMS (MALDI) *m/z* calcd. for $C_{24}H_{22}INO_5Li$ $[M+Li]^+$: 538.0697, found: 538.0685.



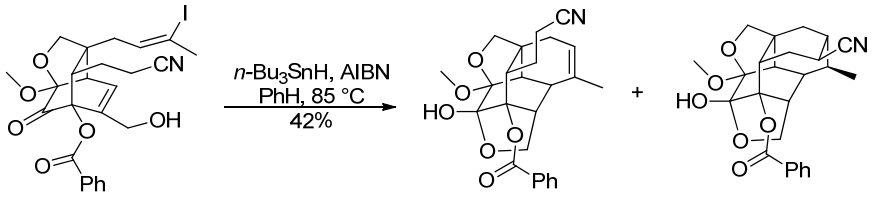
A solution of phenol (10.0 mg, 0.0188 mmol) in methanol (0.90 mL) was heated to 67 °C, to which a solution of iodobenzene diacetate (13.3 mg, 0.0414 mmol) in methanol (0.70 mL) was added over 40 min. via syringe pump. After the addition was completed, the reaction was stirred for additional 2 h then cooled to r.t. and concentrated. The crude product was purified by column chromatography (50-75% diethyl ether/hexanes) to afford a white solid (6.4 mg, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$) 9.69 (s, 1H), 8.11 (d, *J* = 7.7 Hz, 2H), 7.67 – 7.57 (m, 1H), 7.56 – 7.40 (m, 2H), 7.13 (d, *J* = 7.0 Hz, 1H), 5.45 (td, *J* = 6.7, 1.6 Hz, 1H), 4.18 (d, *J* = 8.7 Hz, 1H), 4.11 – 3.95 (m, 1H), 3.63 (s, 3H), 3.31 (d, *J* = 7.0 Hz, 1H), 2.66 – 2.55 (m, 1H), 2.60 (q, *J* = 1.3 Hz, 3H), 2.29 (qd, *J* = 16.4, 15.8, 6.7 Hz, 2H), 1.96 – 1.80 (m, 1H), 1.80 – 1.63 (m, 1H), 1.39 – 0.95 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) 193.75, 187.06, 164.92, 139.48, 133.88, 130.16 (2C), 129.31, 128.82 (2C), 128.74 (2C), 119.29, 107.60, 98.49, 86.64, 78.57, 53.51, 50.72, 49.74, 48.39, 40.20, 34.09, 23.79, 17.46; IR (film) 2954, 2924, 2853, 2245, 1767, 1727, 1692, 1451, 1274, 1175, 1088,

1067, 1049, 710 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{25}H_{25}INO_6$ $[M+H]^+$: 562.0721, found: 562.0721.



42 **43**

Sodium borohydride (1.94 mg, 0.0513 mmol) in methanol (1.0 mL) was added to a solution of □,□-unsaturated aldehyde (57.6 mg, 0.103 mmol) in dichloromethane (0.50 mL) and methanol (1.0 mL) at 0 °C. After stirring at 0 °C for 30 min., the reaction was warmed to r.t. and stirred for 10 min., then quenched by 0.1 M HCl (2.5 mL), extracted with ethyl acetate for three times. The extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (50 % ethyl acetate/hexanes) to afford a white solid (36.2 mg, 62% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 8.13 – 7.98 (m, 2H), 7.68 – 7.56 (m, 1H), 7.54 – 7.41 (m, 2H), 6.26 (dt, *J* = 6.9, 1.6 Hz, 1H), 5.46 (td, *J* = 6.7, 1.6 Hz, 1H), 4.45 (dd, *J* = 5.8, 1.6 Hz, 2H), 4.22 – 4.02 (m, 2H), 3.61 (s, 3H), 3.48 (t, *J* = 6.2 Hz, 1H), 3.07 (d, *J* = 6.9 Hz, 1H), 2.58 (q, *J* = 1.3 Hz, 3H), 2.49 (ddd, *J* = 16.8, 9.1, 6.2 Hz, 1H), 2.40 – 2.21 (m, 3H), 1.99 – 1.77 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 192.83, 164.56, 140.67, 134.05, 130.05 (2C), 129.44, 129.21, 128.94 (2C), 123.50, 119.21, 106.91, 99.69, 89.34, 79.67, 60.85, 53.05, 50.42, 48.23, 46.21, 39.76, 34.10, 23.57, 17.46; IR (film) 3493, 2955, 2924, 2853, 2247, 1758, 1727, 1450, 1267, 1175, 1089, 1061, 711 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{25}H_{27}INO_6$ $[M+H]^+$: 564.0877, found: 564.0878.

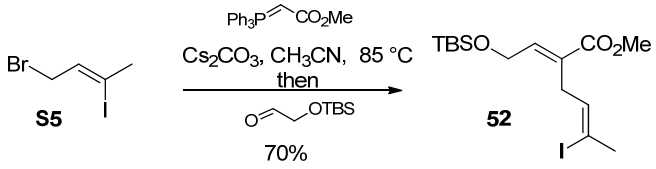


43 **45** **47**

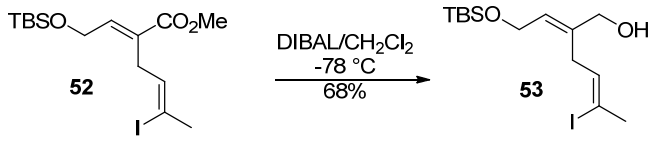
A solution of vinyl iodide (10.0 mg, 0.0178 mmol) in benzene (0.50 mL) was heated to 85 °C, to which tributyltin hydride (0.10 M in benzene, 0.43 mL) and azobisisobutyronitrile (0.01 M in benzene, 0.36 mL) were added simultaneously via syringe pumps over 1 h. After the addition was completed, the reaction was stirred for 30 min. then cooled to r.t. and concentrated. The crude product was purified by column chromatography (50-60% ethyl acetate/hexanes) to afford product **45** (higher R_f, colorless oil, 0.4 mg, 5% yield) and **47** (lower R_f, 2.9 mg, colorless oil, 37% yield).

Compound **45**: ^{1}H NMR (600 MHz, C_6D_6) □ 8.14 – 8.07 (m, 2H), 7.15 – 7.04 (m, 3H), 4.93 (d, *J* = 4.9 Hz, 1H), 4.34 (dd, *J* = 7.6, 3.7 Hz, 1H), 3.95 (s, 1H), 3.67 (s, 3H), 3.52 (d, *J* = 7.4 Hz, 1H), 3.47 (d, *J* = 7.7 Hz, 1H), 3.36 (d, *J* = 7.4 Hz, 1H), 3.21 (d, *J* = 8.3 Hz, 1H), 2.03 (d, *J* = 4.1 Hz, 1H), 1.91 (d, *J* = 3.7 Hz, 1H), 1.89 – 1.75 (m, 2H), 1.74 – 1.68 (m, 2H), 1.61 – 1.52 (m, 1H), 1.52 – 1.46 (m, 1H), 1.45 – 1.37 (m, 1H), 1.36 (s, 3H); ^{13}C NMR (C_6D_6, extracted from HSQC and HMBC) □ 166.35, 136.74, 132.96, 130.02, 129.94 (2C), 128.41 (2C), 120.13, 119.24, 107.49, 106.55, 91.00, 80.70, 73.53, 53.18, 46.51, 42.55, 42.06, 41.12, 40.96, 29.31, 22.98, 21.2, 17.81; IR (film) 3498, 2948, 2927, 2892, 2247, 1713, 1450, 1292, 1257, 1195, 1112, 1070, 994, 958, 710 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{25}H_{27}NNaO_6$ $[M+Na]^+$: 460.1730, found: 460.1731.

Compound **47**: ^{1}H NMR (600 MHz, C_6D_6) □ 8.26 – 8.21 (m, 2H), 7.15 – 7.04 (m, 3H), 4.07 (dd, *J* = 8.1, 4.4 Hz, 1H), 4.01 (s, 1H), 3.68 (s, 3H), 3.21 – 3.17 (m, 2H), 3.02 (d, *J* = 7.3 Hz, 1H), 2.91 (dd, *J* = 11.9, 7.3 Hz, 1H), 2.75 (d, *J* = 4.4 Hz, 1H), 2.51 (d, *J* = 6.1 Hz, 1H), 1.90 (ddd, *J* = 14.8, 7.2, 1.6 Hz, 1H), 1.73 (q, *J* = 3.7 Hz, 1H), 1.52 (t, *J* = 4.2 Hz, 1H), 1.46 (ddd, *J* = 14.8, 11.9, 6.4 Hz, 1H), 1.29 (dd, *J* = 13.2, 3.1 Hz, 1H), 1.25 (d, *J* = 4.1 Hz, 1H), 1.02 – 0.95 (m, 1H), 0.53 (d, *J* = 7.1 Hz, 3H), 0.43 – 0.36 (m, 1H); ^{13}C NMR (C_6D_6, extracted from HSQC and HMBC) □ 166.34, 133.15, 131.39, 130.09 (2C), 128.38 (2C), 123.44, 107.68, 107.66, 88.36, 78.00, 73.50, 53.11, 49.39, 40.85, 39.60, 37.58, 36.87, 36.30, 35.87, 27.49, 22.89, 21.46, 15.19; IR (film) 3499, 2948, 2927, 2875, 2235, 1713, 1454, 1269, 1195, 1112, 1100, 982, 710 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{25}H_{28}NO_6$ $[M+H]^+$: 438.1911, found: 438.1911.

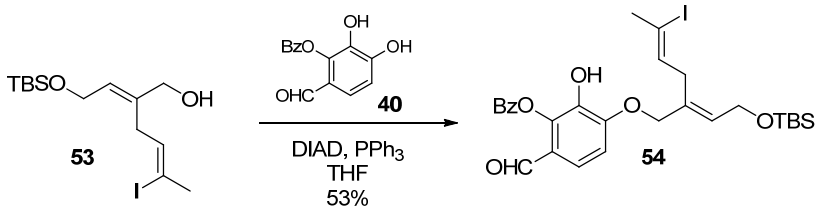


A mixture of methyl (triphenylphosphoranylidene)acetate (5.22 g, 15.6 mmol), vinyl bromide (4.15 g, 15.9 mmol) and cesium carbonate (5.08 g, 15.6 mmol) in acetonitrile (80 mL) was heated at 85 °C for 4 h, and then the hot reaction mixture was filtered through a Celite pad. The filtrate was concentrated on rotovap and placed under vacuum for 15 min to remove any residual bromide. The resultant phosphorane intermediate was re-dissolved in acetonitrile (80 mL) and (*tert*-butyldimethylsilyloxy) acetaldehyde (2.72 g, 15.6 mmol) was added. The solution was stirred at 85 °C for 15 h before cooling to r.t. Acetonitrile was removed on rotovap, and hexanes were added to the residue while a solid crushed out, which was filtered off and washed with ethyl acetate. The filtrate was concentrated and purified by column chromatography (25% diethyl ether/hexanes) to afford a light yellow oil (4.50 g, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) □ 6.85 (t, J = 5.6 Hz, 1H), 5.39 (tq, J = 6.5, 1.5 Hz, 1H), 4.43 (d, J = 5.6 Hz, 2H), 3.76 (s, 2H), 3.07 (d, J = 6.5 Hz, 2H), 2.48 (q, J = 1.5 Hz, 2H), 0.91 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 167.61, 144.14, 132.48, 128.55, 101.41, 61.10, 52.11, 35.49, 33.64, 26.05 (3C), 18.45, -5.06 (2C); IR (film) 2953, 2927, 2856, 2362, 1716, 1463, 1436, 1251, 1205, 1107, 1085, 1041, 837, 777 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{15}H_{28}IO_3Si$ $[M+H]^+$: 411.0847, found: 411.0850.

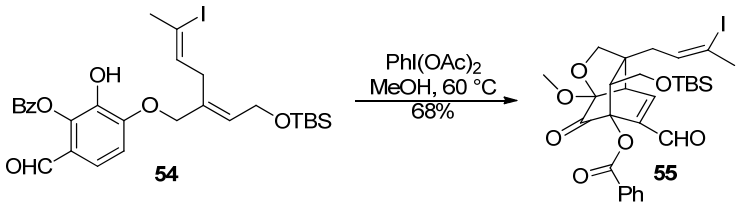


To a solution of ester (7.82 g, 19.1 mmol) in dichloromethane (45 mL) at -78 °C, was added DIBAL (1.0 M in dichloromethane, 47.2 mL) dropwise. The reaction was stirred at -78 °C for 3 h then quenched by saturated Rochelle's salt solution (20 mL) and diluted with ethyl acetate (300 mL). The mixture was allowed to warm to r.t. and stirred vigorously until two clear layers formed. The organic layer was separated

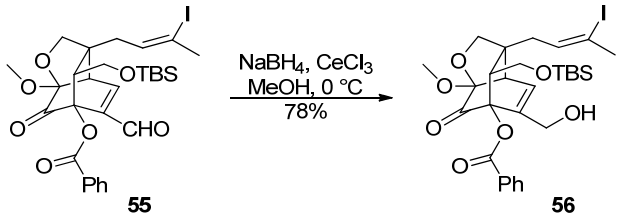
and the aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with brine (100 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (10% ethyl acetate/hexanes) to afford a colorless oil (4.93 g, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.64 (ttd, *J* = 5.3, 1.4, 0.6 Hz, 1H), 5.37 (tq, *J* = 6.8, 1.5 Hz, 1H), 4.27 (dt, *J* = 6.2, 1.2 Hz, 2H), 4.06 (s, 2H), 2.90 (dt, *J* = 6.8, 1.2 Hz, 2H), 2.50 (q, *J* = 1.4 Hz, 3H), 1.47 (s, 1H), 0.91 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.47, 132.74, 127.32, 102.12, 66.71, 60.12, 36.48, 33.68, 26.17 (3C), 18.58, -4.92 (2C); IR (film) 3365, 2953, 2927, 2856, 1463, 1255, 1107, 1066, 835 777 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{14}H_{27}IO_2SiLi$ $[M+Li]^+$: 389.0980, found: 389.0976.



To a solution of triphenylphosphine (850 mg, 3.24 mmol) in THF (8.0 mL) was added diisopropyl azodicarboxylate (0.63 mL, 3.24 mmol) dropwise at 0 °C. After stirring for 30 min., a solution of alcohol (411 mg, 1.08 mmol) and phenol (837 mg, 3.24 mmol) in THF (2.5 mL) was added dropwise. The reaction was allowed to warm to r.t. naturally and stirred for total 24 h. Removal of solvent and purification by column chromatography (20% ethyl acetate/hexanes) afforded a light yellow oil (353 mg, 53% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.33 (s, 1H), 9.76 (s, 1H), 8.31 – 8.18 (m, 2H), 7.70 – 7.57 (m, 1H), 7.54 – 7.46 (m, 2H), 7.43 (d, *J* = 8.8 Hz, 1H), 6.66 (d, *J* = 8.8 Hz, 1H), 5.70 (tt, *J* = 6.0, 1.1 Hz, 1H), 5.28 (tq, *J* = 6.8, 1.5 Hz, 1H), 4.54 (d, *J* = 1.3 Hz, 2H), 4.22 (d, *J* = 6.0 Hz, 2H), 2.86 (d, *J* = 6.8 Hz, 2H), 2.30 (q, *J* = 1.5 Hz, 3H), 0.87 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.85, 163.98, 157.58, 155.23, 133.71, 132.55, 132.00, 131.98, 131.22, 130.52 (2C), 128.92, 128.64 (2C), 127.40, 116.40, 104.99, 102.47, 72.80, 59.94, 36.40, 33.40, 26.00 (3C), 18.36, -5.08 (2C); IR (film) 2953, 2927, 2854, 1743, 1647, 1506, 1242, 1105, 1058, 835, 705 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{28}H_{36}IO_6Si$ $[M+H]^+$: 623.1320, found: 623.1330.

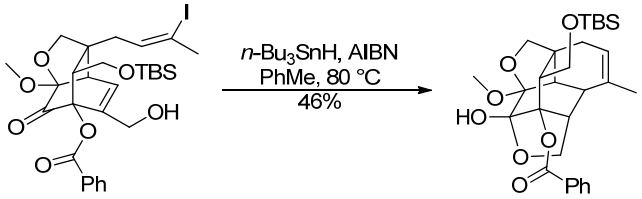


A solution of phenol (153.0 mg, 0.246 mmol) in methanol (16.0 mL) was heated to 60 °C, to which a solution of iodobenzene diacetate (174.2 mg, 0.541mmol) in methanol (8.0 mL) was added over 2.5 h via syringe pump. After stirring for additional 2 h the reaction was cooled to r.t. and concentrated. The crude product was purified by column chromatography (20% diethyl ether/hexanes) to afford a light yellow solid (108.8 mg, 68% yield). ^{1}H NMR (400 MHz, $CDCl_3$) 9.72 (s, 1H), 8.16 (d, J = 7.7 Hz, 2H), 7.65 – 7.56 (m, 1H), 7.52 – 7.42 (m, 2H), 7.08 (d, J = 7.1 Hz, 1H), 5.53 (td, J = 7.0, 1.5 Hz, 1H), 4.15 (d, J = 8.2 Hz, 1H), 4.04 – 3.87 (m, 2H), 3.75 (dd, J = 11.5, 5.9 Hz, 1H), 3.62 (s, 3H), 3.35 (d, J = 7.0 Hz, 2H), 2.71 – 2.42 (m, 2H), 2.59 (d, J = 1.5 Hz, 3H), 0.82 (s, 9H), -0.03 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) 193.15, 185.85, 164.46, 139.68, 138.55, 133.68, 130.24 (2C), 129.69 (2C), 129.54, 128.63 (2C), 106.61, 99.13, 78.81, 59.60, 53.25, 51.68, 48.83 (2C), 37.07, 34.17, 26.17 (3C), 18.45, -5.41, -5.46; IR (film) 2954, 2929, 2856, 1766, 1729, 1695, 1470, 1451, 1274, 1179, 1091, 912, 837, 780, 709 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{29}H_{37}INaO_7Si$ $[M+Na]^+$: 675.1245, found: 675.1250.



To an ice-water cooled mixture of ,-unsaturated aldehyde (20.0 mg, 0.0307 mmol) and cerium (III) chloride heptahydrate (57.0 mg, 0.153 mmol) in methanol (0.62 mL) was added sodium borohydride (3.5 mg, 0.0925 mmol) in one portion. The reaction was stirred at 0 °C for 2 h then quenched by saturated NH_4Cl solution (0.2 mL) and extracted with ethyl acetate (3 × 2 mL). The combined organic layers were

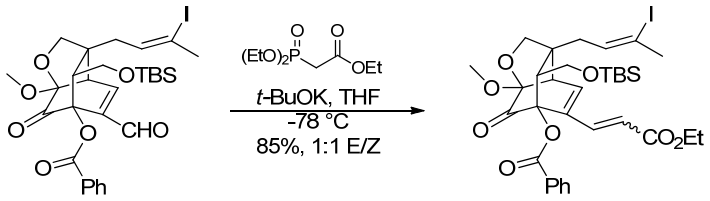
washed with brine (2 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (25% ethyl acetate/hexanes) to afford a colorless oil (15.7 mg, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 – 7.98 (m, 2H), 7.69 – 7.53 (m, 1H), 7.47 (m, 2H), 6.18 (dt, *J* = 6.8, 1.6 Hz, 1H), 5.51 (td, *J* = 7.5, 7.0, 1.8 Hz, 1H), 4.45 (qd, *J* = 14.8, 4.0 Hz, 2H), 4.09 (d, *J* = 8.1 Hz, 1H), 4.05 (d, *J* = 8.1 Hz, 1H), 3.84 (dd, *J* = 11.3, 5.2 Hz, 1H), 3.74 (dd, *J* = 11.3, 5.2 Hz, 1H), 3.62 (s, 3H), 3.58 (t, *J* = 5.4 Hz, 1H), 3.07 (d, *J* = 6.8 Hz, 1H), 2.59 – 2.51 (m, 1H), 2.56 (s, 3H), 2.42 – 2.33 (m, 1H), 2.05 (t, *J* = 5.8 Hz, 1H), 0.76 (s, 9H), -0.11 (s, 3H), -0.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.29, 163.96, 140.98, 133.55, 130.26, 130.01 (2C), 129.96, 128.65 (2C), 122.07, 105.68, 99.82, 87.66, 79.59, 60.96, 60.43, 52.92, 49.82, 47.95 (2C), 38.21, 34.07, 26.06 (3C), 18.45, -5.40, -5.49; IR (film) 3488, 2954, 2927, 2855, 1759, 1729, 1451, 1275, 1251, 1093, 1004, 837, 780, 709 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{29}H_{40}IO_7Si$ $[M+H]^+$: 655.1582, found: 655.1579.



56 **57**

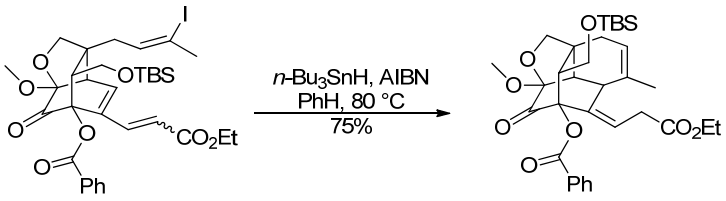
A solution of vinyl iodide (15.0 mg, 0.0229 mmol) in toluene (1.30 mL) was heated to 80 °C, to which tributyltin hydride (0.10 M in toluene, 0.55 mL) and azobisisobutyronitrile (0.01 M in toluene, 0.46 mL) were added simultaneously via syringe pumps over 1 h. After the addition was completed, the reaction was stirred for additional 2h then cooled to r.t. and concentrated. The crude product was purified by column chromatography (20% ethyl acetate/hexanes) to afford a colorless oil (5.6 mg, 46% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (m, 2H), 7.61 – 7.52 (m, 1H), 7.47 – 7.39 (m, 2H), 5.51 (dt, *J* = 5.1, 1.7 Hz, 1H), 4.41 (dd, *J* = 7.9, 3.7 Hz, 1H), 4.29 (s, 1H), 3.87 (d, *J* = 7.1 Hz, 1H), 3.76 – 3.69 (m, 3H), 3.60 (dd, *J* = 10.6, 3.1 Hz, 1H), 3.58 (s, 3H), 3.18 (dd, *J* = 10.0, 3.1 Hz, 1H), 2.85 – 2.77 (m, 1H), 2.59 (d, *J* = 3.5 Hz, 1H), 2.30 (d, *J* = 4.1 Hz, 1H), 2.02 – 1.92 (m, 1H), 1.96 (d, *J* = 4.2 Hz, 1H), 1.77 (dt, *J* = 2.7, 1.4 Hz, 3H), 0.80 (s, 9H), -0.11 (s, 3H), -0.12 (s, 3H); ^{13}C NMR (125 MHz,

$CDCl_3$) □ 166.12, 135.77, 133.38, 130.74, 129.91 (2C), 128.57 (2C), 121.67, 107.81, 107.06, 89.16, 81.58, 73.84, 61.28, 52.86, 45.18, 44.97, 42.43, 42.34, 41.17, 28.34, 25.93 (3C), 21.99, 18.14, -5.37, -5.53; IR (film) 3529, 2952, 2927, 2855, 1722, 1259, 1093, 1070, 993, 837, 777, 708 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{29}H_{41}O_7Si$ $[M+H]^+$: 529.2616, found: 529.2615.



55 **58**

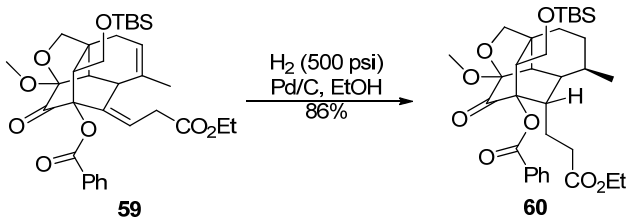
To a solution of triethyl phosphonoacetate (0.041 mL, 0.284 mmol) in THF (0.80 mL) was added potassium *tert*-butoxide (31.9 mg) in portions at 0 °C. After stirring for 15 min., the mixture was cooled to -78 °C and aldehyde (58.0 mg, 0.0945 mmol) in THF (0.20 mL) was added dropwise. The reaction was stirred at -78 °C for 4 h then quenched by saturated NH_4Cl solution (1 mL) and extracted with ethyl acetate (3 × 2 mL). The combined extracts were washed with brine (2 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (20% ethyl acetate/hexanes) to afford a light yellow oil (56.7 mg, 1:1 E/Z mixture, 85% yield), which was used directly without further separation.



58 **59**

A solution of vinyl iodides (1:1 E/Z mixture, 53.0 mg, 0.0733 mmol) in benzene (4.0 mL) was heated to 80 °C, to which tributyltin hydride (0.10 M in benzene, 1.80 mL) and azobisisobutyronitrile (0.01 M in benzene, 1.50 mL) were added simultaneously via syringe pumps over 2 h. After the addition was completed, the reaction was stirred for additional 2 h then cooled to r.t. and concentrated. The

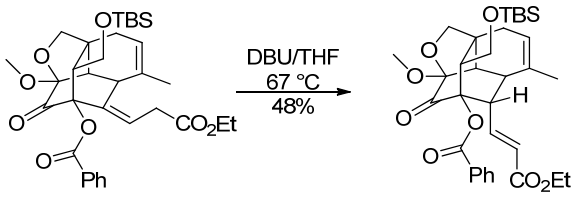
crude product was purified by column chromatography (20% ethyl acetate/hexanes) to afford a colorless oil (32.8 mg, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) □ 8.15 – 8.01 (m, 2H), 7.65 – 7.52 (m, 1H), 7.46 (m, 2H), 6.33 (td, *J* = 7.5, 1.7 Hz, 1H), 5.65 – 5.54 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.08 (d, *J* = 7.4 Hz, 1H), 3.94 (d, *J* = 7.4 Hz, 1H), 3.68 (s, 3H), 3.67 – 3.57 (m, 2H), 3.49 (dd, *J* = 8.6, 3.9 Hz, 1H), 3.33 – 3.28 (m, 3H), 2.86 (ddd, *J* = 18.0, 5.2, 1.8 Hz, 1H), 2.40 (d, *J* = 3.9 Hz, 1H), 2.11 (d, *J* = 18.6 Hz, 1H), 1.87 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.75 (s, 9H), -0.17 (s, 3H), -0.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 194.47, 170.72, 163.68, 134.83, 133.28, 132.57, 130.42, 130.01 (2C), 128.54 (2C), 124.04, 121.40, 104.14, 85.49, 82.21, 61.31, 61.16, 53.16, 47.22, 45.40, 43.19, 36.48, 35.45, 29.71, 25.91 (3C), 24.34, 18.13, 14.30, -5.40, -5.48; IR (film) 2953, 2930, 2856, 1759, 1729, 1268, 1252, 1176, 1091, 1001, 837, 777, 707 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{33}H_{45}O_8Si$ $[M+H]^+$: 597.2878, found: 597.2879.



59 **60**

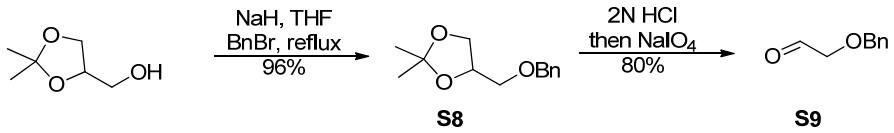
In a 4-mL vial, diene (3.0 mg, 0.00503 mmol) was dissolved in ethanol (0.20 mL) and palladium on carbon (10 wt%, 3.0 mg) was added. The vial was placed in a hydrogenation bomb and stirred at r.t. under 500 psi of H_2 for 16 h. The reaction mixture was then filtered through a Celite pad and washed with ethyl acetate. The filtrate was concentrated and purified by column chromatrography (20% ethyl acetate/hexanes) to afford a colorless oil (2.6 mg, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$) □ 8.07 – 8.00 (m, 2H), 7.58 – 7.52 (m, 1H), 7.47 – 7.39 (m, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.02 (dd, *J* = 10.9, 7.8 Hz, 1H), 3.84 (d, *J* = 6.8 Hz, 1H), 3.80 (dd, *J* = 10.9, 5.3 Hz, 1H), 3.71 (dd, *J* = 6.8, 0.8 Hz, 1H), 3.70 (s, 3H), 3.57 (dd, *J* = 7.7, 5.4 Hz, 1H), 2.57 (ddd, *J* = 15.7, 8.6, 6.9 Hz, 1H), 2.45 (ddd, *J* = 15.7, 8.6, 6.3 Hz, 1H), 2.32 (m, 1H), 2.11 (q, *J* = 6.6 Hz, 1H), 2.01 (ddt, *J* = 15.1, 8.7, 6.4 Hz, 1H), 1.89 (d, *J* = 2.7 Hz, 1H), 1.86 – 1.82 (m, 1H), 1.75 – 1.61 (m, 2H), 1.46 – 1.25 (m, 3H), 1.27 (t,

J = 7.1 Hz, 3H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.75 (s, 9H), -0.14 (s, 3H), -0.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.10, 173.40, 164.15, 133.08, 130.48, 130.00 (2C), 128.45 (2C), 103.95, 85.71, 82.20, 60.52, 58.94, 53.22, 53.16, 44.51, 44.25, 38.92, 36.02, 35.26, 32.91, 28.81, 27.96, 27.71, 25.92 (3C), 19.55, 18.23, 14.44, -5.54 (2C); IR (film) 2953, 2929, 2856, 1759, 1729, 1266, 1256, 1090, 837, 778, 707 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{33}H_{49}O_8Si$ $[M+H]^+$: 601.3191, found: 601.3192.



59 **61**

A mixture of diene (27.7 mg, 0.0464 mmol) and 1, 8-diazabicyclo [5.4.0] undec-7-ene (0.02 mL, 0.139 mmol) in THF (0.20 M, 0.05 mL) was heated to 67 °C and stirred for 3 h. The reaction mixture was then cooled to r.t. and concentrated. Purification by column chromatography (10-20% ethyl acetate/hexanes) provided a colorless oil (13.2 mg, 48%) and unreacted starting material (8.2 mg, 30%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 2H), 7.60 – 7.51 (m, 1H), 7.46 – 7.34 (m, 2H), 6.72 (dd, *J* = 15.5, 9.3 Hz, 1H), 5.99 (dd, *J* = 15.5, 1.0 Hz, 1H), 5.54 (d, *J* = 4.4 Hz, 1H), 4.30 – 4.11 (m, 2H), 4.02 (d, *J* = 7.1 Hz, 1H), 3.89 (d, *J* = 7.1 Hz, 1H), 3.81 (dd, *J* = 10.6, 9.7 Hz, 1H), 3.75 – 3.70 (m, 1H), 3.69 (s, 3H), 3.54 – 3.48 (m, 1H), 2.88 (ddd, *J* = 18.2, 4.9, 1.7 Hz, 1H), 2.67 (dd, *J* = 9.2, 2.9 Hz, 1H), 2.38 (m, 1H), 2.30 (d, *J* = 3.7 Hz, 1H), 2.16 – 2.08 (m, 1H), 1.78 (dt, *J* = 2.8, 1.5 Hz, 3H), 1.29 (t, *J* = 7.1 Hz, 3H), 0.80 (s, 9H), -0.12 (s, 3H), -0.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.32, 165.76, 163.92, 145.82, 136.87, 133.34, 130.04, 129.93 (2C), 128.52 (2C), 124.49, 121.07, 103.59, 83.83, 82.43, 60.77, 60.28, 53.06, 47.47, 47.34, 45.55, 43.12, 36.46, 28.84, 25.91 (3C), 22.10, 18.12, 14.39, -5.33, -5.47; IR (film) 2952, 2928, 2894, 2855, 1757, 1727, 1263, 1095, 836, 707 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{33}H_{45}O_8Si$ $[M+H]^+$: 597.2878, found: 597.2877.

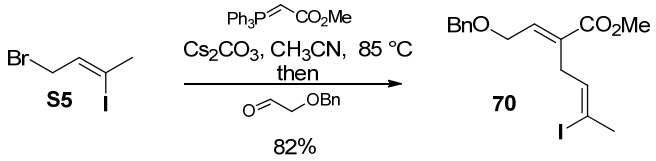


Compound **S9** was prepared according to literature protocol.[9]

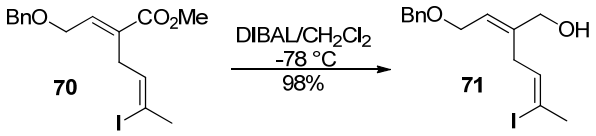
To a suspension of sodium hydride (60 wt%, 8.04g, 201.1 mmol) in THF (600 mL) 2,3-O-isopropylideneglycerol (20.0 mL, 160.9 mmol) was added dropwise over 1 h at r.t. After stirring for 4 h, benzyl bromide (21.1 mL, 177.0 mmol) was added and the reaction mixture was heated to reflux (72 °C) for 18 h. After the reaction was cooled to r.t. and the solvent was removed, hexanes (600 mL) were added to the residue. The solid was filtered off and the filtrate was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by column chromatography (10% ethyl acetate/hexanes) to afford a yellow oil (34.4 g, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 7.40 – 7.24 (m, 5H), 4.64 – 4.51 (m, 2H), 4.30 (tt, *J* = 6.3, 5.6 Hz, 1H), 4.06 (dd, *J* = 8.2, 6.3 Hz, 1H), 3.75 (dd, *J* = 8.2, 6.3 Hz, 1H), 3.56 (dd, *J* = 9.8, 5.6 Hz, 1H), 3.48 (dd, *J* = 9.8, 5.6 Hz, 1H), 1.42 (q, *J* = 0.7 Hz, 3H), 1.37 (q, *J* = 0.7 Hz, 3H).

A solution of acetonide (14.6 g, 65.5 mmol) in THF (60.0 mL) was treated with 2N HCl (33.0 mL, 65.5 mmol) for 4.0 h at r.t. The reaction was concentrated, taken up in dichloromethane (180 mL) and washed with saturated $NaHCO_3$ (3 × 150 mL). The volume of the organic solution was reduced to 90 mL and sodium metaperiodate (28.0 g, 131.0 mmol) in water (180 mL) was added. The two-phase mixture was stirred vigorously at r.t. for 18 h. The organic phase was separated and the aqueous phase was extracted with dichloromethane (50 mL). The combined organic phases were washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated to afford the desired aldehyde (7.83g, 80% yield), which was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) □ 9.73 (t, *J* = 0.9 Hz, 1H), 7.45 – 7.27 (m, 5H), 4.64 (s, 2H), 4.10 (d, *J* = 0.9 Hz, 2H).

(9) Shiao, M.-J.; Yang, C.-Y.; Lee, S.-H.; and Wu, T.-C. *Synth. Commun.* **1988**, 18, 359-366.

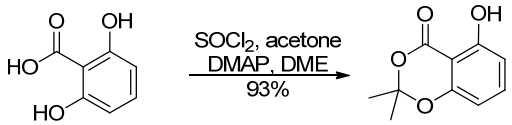


A mixture of methyl (triphenylphosphoranylidene)acetate (18.0 g, 53.8 mmol), bromide (22.1 g, 64.6 mmol) and cesium carbonate (17.5g, 53.8 mmol) in acetonitrile (225 mL) was heated at 85 °C for 5 h then aldehyde (7.61g, 50.7 mmol) in acetonitrile (25 mL) was added dropwise over 1 h. After stirring at 85 °C for 18 h the reaction was cooled to r.t. The solid was filtered off and the filtrate was concentrated. Hexanes were added to the residue and a solid crushed out, which was filtered off and washed with ethyl acetate. This operation was repeated once. The resultant filtrate was concentrated and purified by column chromatography (10% ethyl acetate/hexanes) to afford a colorless oil (16.1 g, 82% yield), which turned light brown while standing in air. ^{1}H NM R (400 MHz, $CDCl_3$) □ 7.41 – 7.26 (m, 5H), 6.93 (t, *J* = 5.9 Hz, 1H), 5.39 (tq, *J* = 6.5, 1.4 Hz, 1H), 4.55 (s, 2H), 4.29 (d, *J* = 5.9 Hz, 2H), 3.75 (s, 3H), 3.07 (d, *J* = 6.5 Hz, 2H), 2.45 (q, *J* = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 167.37, 140.40, 137.81, 132.31, 130.72, 128.57 (2C) , 127.97, 127.93 (2C), 101.54, 73.01, 67.22, 52.12, 35.48, 33.58; IR (film) 2949, 2912, 2854, 1712, 1647, 1452, 1435, 1311, 1274, 1205, 1105, 1124, 1047, 738, 698 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{16}H_{20}IO_3$ $[M+H]^+$: 387.0452, found: 387.0457.



To a solution of ester (12.3 g, 31.9 mmol) in CH_2Cl_2 (250 mL) was added DIBAL (1.0 M in CH_2Cl_2, 70.2 mL) dropwise at -78 °C. The reaction was stirred at -78 °C for 5 h then quenched by 10% Rochelle's salt solution (100 mL). The mixture was warmed to r.t. and stirred vigorously until two clear layers formed. The organic layer was separated and the aqueous layer was extracted with dichloromethane (3 × 50

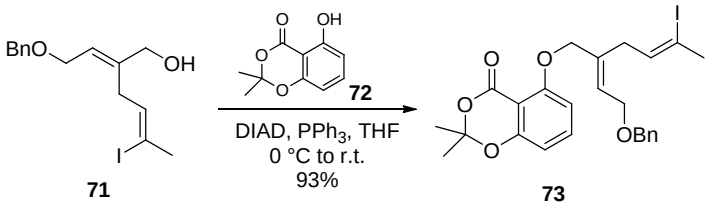
mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated to provide a colorless oil (11.2 g, 98% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.25 (m, 5H), 5.73 (dddd, *J* = 6.6, 5.2, 1.7, 0.9 Hz, 1H), 5.35 (tq, *J* = 6.9, 1.4 Hz, 1H), 4.53 (s, 2H), 4.12 (dt, *J* = 6.6, 1.1 Hz, 2H), 4.05 (s, 2H), 2.89 (d, *J* = 6.9 Hz, 2H), 2.47 (q, *J* = 1.4 Hz, 3H), 1.79 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.54, 138.27, 132.60, 128.53 (2C), 127.97 (2C), 127.80, 123.35, 102.24, 72.66, 66.39, 66.35, 36.41, 33.61; IR (film) 3385, 2912, 2856, 1452, 1425, 1363, 1109, 1070, 1004, 736, 698 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{15}H_{19}INaO_2$ $[M+Na]^+$: 381.0322, found: 381.0316.



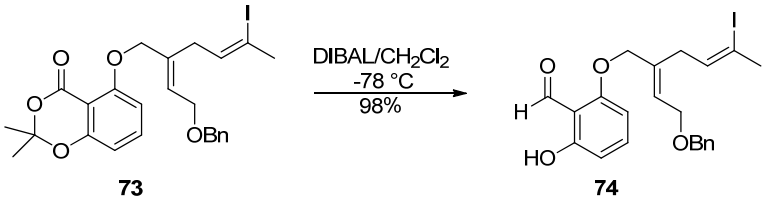
72

Compound **72** was prepared according to literature protocol.[10] A solution of 2,6-dihydroxybenzoic acid (30.0 g, 194.6 mmol), 4-dimethylaminopyridine (1.19 g, 9.74 mmol) and acetone (18.6 mL, 252.9 mmol) in dimethoxyethane (150 mL) was cooled to 0 °C and thionyl chloride (18.4 mL, 252.9 mmol) was added dropwise. Upon completion of the addition, the resultant solution was allowed to stir at 0 °C for 1 h then r.t. 20 h. The reaction solution turned from light yellow to brown to red over time. The reaction was then cooled to 0°C, quenched by slow addition of saturated $NaHCO_3$ (100 mL). The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 × 150 mL). The combined organic layers were washed with brine (200 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The resultant solid was triturated with hexanes and collect by vacuum filtration to provide a light yellow solid (32.0 g, 93% yield). ^{1}H NMR (500 MHz, $CDCl_3$) d 10.34 (s, 1H), 7.41 (t, J = 8.3 Hz, 1H), 6.64 (dd, J = 8.5, 1.0 Hz, 1H), 6.44 (dd, J = 8.1, 0.9 Hz, 1H), 1.75 (s, 6H).

(10) Hadfield, A.; Schweitzer, H.; Trova, M. P.; Green, K. *Synth. Commun.* **1994**, *24*, 1025-1028.

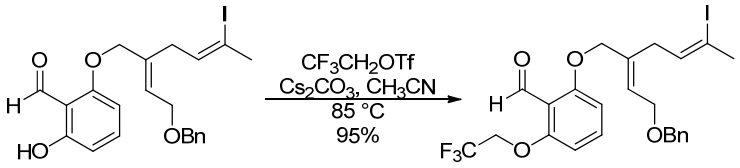


To a solution of allylic alcohol (5.30 g, 14.8 mmol), phenol (3.14 g, 17.8 mmol) and triphenylphosphine (4.67 g, 17.8 mmol) in THF (100 mL) was added diisopropyl azodicarboxylate (3.45 mL, 17.8 mmol) at 0 °C over 30 min. After the addition was completed, stirring continued for 1.0 h at 0 °C, then the reaction was warmed to r.t. and stirred overnight. The reaction was concentrated and the residue was taken up in ethyl acetate. The solid was filtered off and the filtrate was concentrated again. The residue was purified by column chromatography (10% ethyl acetate/hexanes) to afford a colorless oil (7.38 g, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, J = 8.4 Hz, 1H), 7.37 – 7.25 (m, 5H), 6.59 (dd, J = 8.5, 0.9 Hz, 1H), 6.55 (dd, J = 8.3, 0.9 Hz, 1H), 6.02 (tt, J = 6.5, 1.2 Hz, 1H), 5.62 (tq, J = 7.1, 1.4 Hz, 1H), 4.56 (d, J = 1.2 Hz, 2H), 4.54 (s, 2H), 4.20 (d, J = 6.5 Hz, 2H), 3.02 (d, J = 7.1 Hz, 2H), 2.48 (q, J = 1.4 Hz, 3H), 1.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.43, 157.96, 157.94, 138.34, 136.40, 135.31, 132.65, 128.55 (2C), 128.04 (2C), 127.78, 126.85, 109.54, 106.71, 105.35, 103.73, 102.40, 72.64, 72.59, 66.47, 36.82, 33.67, 25.80 (2C); IR (film) 2995, 2941, 2912, 2854, 1737, 1606, 1583, 1481, 1454, 1377, 1330, 1259, 1205, 1080, 921, 802, 738, 690 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{25}H_{27}INaO_5$ $[M+Na]^+$: 557.0795, found: 557.0791.



To a solution of acetonide (13.2 g, 24.7 mmol) in CH_2Cl_2 (170 mL) cooled at -78 °C, DIBAL/CH_2Cl_2 (1.0M, 74.2 mL) was added dropwise. The reaction solution was stirred at -78 °C for 3 h, and then quenched by saturated Rochelle's salt solution

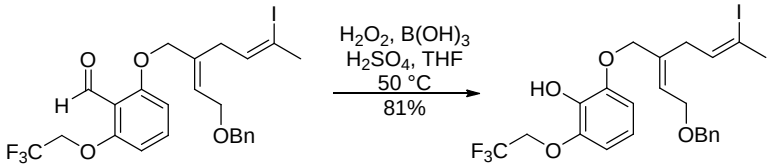
(150 mL). After ethyl acetate (300 mL) was added, the mixture was warmed to r.t. and stirred overnight. Two clear layers formed and the upper organic layer was decanted and the rest aqueous layer was extracted with ethyl acetate (2 × 200 mL). The combined organic layers were washed with water (3 × 150 mL) and brine (150 mL) and dried over anhydrous Na_2SO_4. Filtration and removal of solvent provided a light yellow oil (11.6 g, 98% yield). This crude product was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) □ 11.96 (s, 1H), 10.39 (s, 1H), 7.41 – 7.25 (m, 5H), 7.37 (t, *J* = 8.4 Hz, 1H), 6.52 (dt, *J* = 8.5, 0.7 Hz, 1H), 6.34 (dd, *J* = 8.3, 0.7 Hz, 1H), 5.86 (tt, *J* = 6.4, 1.2 Hz, 1H), 5.35 (tq, *J* = 6.8, 1.4 Hz, 1H), 4.54 (s, 2H), 4.51 (q, *J* = 1.0 Hz, 2H), 4.16 (d, *J* = 6.4 Hz, 2H), 2.99 (d, *J* = 6.8 Hz, 2H), 2.47 (q, *J* = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 194.36, 163.77, 161.45, 138.40, 138.04, 135.37, 131.86, 128.56 (2C), 127.96 (2C), 127.88, 127.14, 111.08, 110.15, 103.04, 102.11, 72.79, 71.85, 66.16, 36.58, 33.61; IR (film) 3219, 3061, 3028, 2883, 2856, 2791, 1643, 1494, 1462, 1334, 1311, 1238, 1170, 1091, 1028, 837, 783, 719, 499 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{22}H_{24}IO_4$ $[M+H]^+$: 479.0714, found: 479.0722.



74 **75**

In a high-pressure flask was charged phenol (12.8 g, 26.8 mmol), cesium carbonate (8.73 g, 26.8 mmol), 2, 2, 2-trifluoroethyl trifluoromethanesulfonate (5.80 mL, 40.2 mmol) and dry acetonitrile (250 mL). The flask was flushed with N_2 for 5 min., capped and heated to 85 °C (bath temperature). The reaction mixture was stirred at 85 °C for 3.0 h and the solution gradually turned from light yellow to colorless. After cooling to r.t., the reaction mixture was partitioned between ethyl acetate (300 mL) and water (200 mL). The organic phase was separated and the aqueous phase was washed with saturated $NaHCO_3$ (3 × 100 mL). The aqueous phase was back-extracted with ethyl acetate (100 mL). The combined organic phases were washed with brine (100 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified

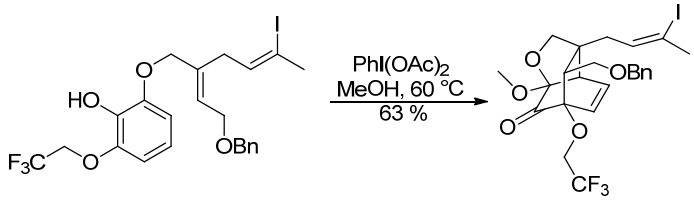
by column chromatography (15% ethyl acetate/hexanes) to afford a light yellow oil (14.3 g, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 10.54 (s, 1H), 7.43 (t, *J* = 8.5 Hz, 1H), 7.37 – 7.26 (m, 5H), 6.68 (d, *J* = 8.5 Hz, 1H), 6.56 (d, *J* = 8.3 Hz, 1H), 5.92 (tt, *J* = 6.5, 1.1 Hz, 1H), 5.45 (tq, *J* = 6.8, 1.4 Hz, 1H), 4.53 (s, 2H), 4.53 (s, 2H), 4.41 (q, *J* = 8.1 Hz, 2H), 4.17 (d, *J* = 6.5 Hz, 2H), 2.99 (d, *J* = 6.8 Hz, 2H), 2.48 (q, *J* = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 188.31, 161.12, 159.58, 138.17, 135.66, 135.31, 132.15, 128.54 (2C), 127.99 (2C), 127.83, 126.95, 123.24 (q, *J* = 278.4 Hz), 116.01, 107.54, 106.97, 102.77, 72.69, 72.29, 67.34 (q, *J* = 35.9 Hz), 66.28, 36.61, 33.60; IR (film) 2860, 2775, 1689, 1597, 1473, 1454, 1284, 1246, 1165, 1122, 1028, 975, 825, 777, 738, 698, 667 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{24}H_{25}F_3IO_4$ $[M+H]^+$: 561.0744, found: 561.0737.



75 **76**

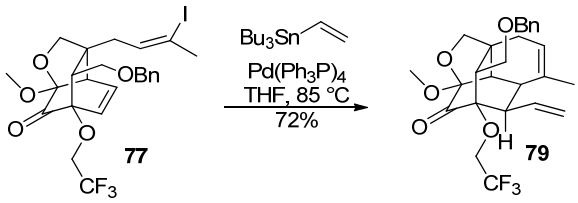
In a high-pressure flask, 10 M sulfuric acid (7.6 mL, 76.0 mmol) was added to a suspension of boric acid (2.36 g, 38.2 mmol) in THF (60 mL) with stirring. Heat was generated during addition. After the flask was cooled to r.t. in air, hydrogen peroxide (30 wt% in water, 1.30 mL, 11.5 mmol) was added slowly. After stirring at r.t. for 1.0 h, aldehyde (4.28 g, 7.64 mmol) in THF (16 mL) was added. The high-pressure flask was then capped and immersed in 50 °C oil bath and heated for 4.0 h. The reaction was cooled to r.t., diluted with ethyl acetate (100 mL), and washed with water (3 × 50 mL) and brine (2 × 50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (10% ethyl acetate/hexanes) to afford a light yellow oil (3.40 g, 81%). ^{1}H NMR (400 MHz, CDCl3) □ 7.39 – 7.25 (m, 5H), 6.74 (t, J = 8.3 Hz, 1H), 6.63 (td, J = 8.1, 1.4 Hz, 2H), 5.84 (tt, J = 6.4, 1.1 Hz, 1H), 5.57 (s, 1H), 5.37 (tq, J = 6.8, 1.5 Hz, 1H), 4.52 (s, 2H), 4.51 (s, 2H), 4.42 (q, J = 8.3 Hz, 2H), 4.15 (d, J = 6.4 Hz, 2H), 2.98 (d, J = 6.8 Hz, 2H), 2.47 (q, J = 1.5 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3) □ 146.81, 145.33,

138.11, 136.81, 135.80, 132.08, 128.55 (2C), 127.98 (2C), 127.87, 127.19, 123.56 (q, J = 278.6 Hz), 119.23, 110.22, 108.39, 102.87, 72.77, 72.68, 67.86 (q, J = 35.3 Hz), 66.22, 36.62, 33.60; IR (film) 3520, 3030, 2947, 2916, 2858, 1610, 1504, 1479, 1454, 1359, 1280, 1211, 1165, 1112, 1087, 968, 736, 698 cm^{-1}; HRMS (ESI) m/z calcd. for C23H24F3INaO4 [M+Na]+: 571.0564, found: 571.0562.

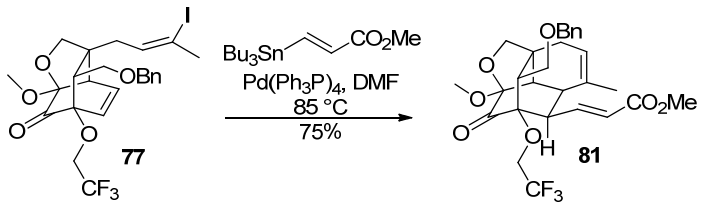


76 **77**

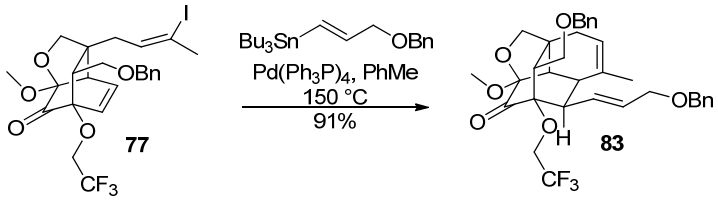
To a 500-mL 3-necked round-bottom flask equipped with a reflux condenser was charged a solution of iodobenzene diacetate (3.03 g, 9.41 mmol) in methanol (290 mL). The solution was heated to 60 °C and a solution of phenol (1.72 g, 3.14 mmol) in methanol (24 mL) was added over 2.5 h via syringe pump. Upon the completion of addition, the reaction was stirred at 60 °C for 2 h then cooled to r.t. and concentrated. The crude product was purified by column chromatography (15% ethyl acetate/hexanes) to provide a light yellow oil (1.14g, 63% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 7.38 – 7.22 (m, 5H), 6.24 – 6.10 (m, 2H), 5.48 (ddq, *J* = 7.9, 6.5, 1.4 Hz, 1H), 4.44 (s, 2H), 4.32 – 4.11 (m, 2H), 4.01 (d, *J* = 8.2 Hz, 1H), 3.82 (d, *J* = 8.2 Hz, 1H), 3.76 (dd, *J* = 10.3, 2.4 Hz, 1H), 3.53 (s, 3H), 3.52 – 3.43 (m, 1H), 3.07 (dd, *J* = 6.6, 1.9 Hz, 1H), 2.68 (ddq, *J* = 15.2, 6.5, 1.4 Hz, 1H), 2.54 (m, 1H), 2.53 (q, *J* = 1.4 Hz, 3H), 2.37 (ddd, *J* = 15.2, 7.7, 1.2 Hz, 1H); ^{13}C NMR (101 MHz, Chloroform-d) □ 198.39, 137.82, 130.22, 129.67, 128.63, 128.50 (2C), 127.96 (2C), 127.87, 123.65 (q, *J* = 277.8 Hz), 105.74, 99.49, 85.17, 78.72, 73.54, 66.45, 64.03 (q, *J* = 35.1 Hz), 52.16, 50.31, 49.17, 47.24, 37.80, 34.06; IR (film) 2949, 2914, 2887, 1755, 1365, 1282, 1205, 1161, 1118, 1091, 1028, 985, 966, 889, 736, 698 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{24}H_{27}F_3IO_5$ $[M+H]^+$: 579.0849, found: 579.0843.



In a 4-mL clear vial was charged a solution of vinyl iodide (5.0 mg, 0.00865 mmol) in THF (0.5 mL). After flushing the solution with N_2 for 10 min, tetrakis(triphenylphosphine)palladium(0) (10 mg, 0.00865 mmol) was added. The vial was capped and heated at 85 °C for 1 h. After which, the reaction was cooled to r.t. and tributyl(vinyl)tin (0.0051 mL, 0.0173 mmol) was added under N_2. The reaction was heated again at 85 °C for 16 h, then cooled to r.t. and concentrated. The residue was purified by column chromatography (15% ethyl acetate/hexanes) to provide a colorless oil (3.0 mg, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.25 (m, 5H), 5.54 (ddq, *J* = 3.8, 2.6, 1.3 Hz, 1H), 5.34 (dt, *J* = 16.1, 10.0 Hz, 1H), 5.18 – 5.15 (m, 1H), 5.15 – 5.10 (m, 1H), 4.51 – 4.41 (m, 2H), 4.19 (dq, *J* = 10.8, 8.6 Hz, 1H), 3.96 (dq, *J* = 10.8, 8.6 Hz, 1H), 3.89 (d, *J* = 7.3 Hz, 1H), 3.78 (d, *J* = 7.3 Hz, 1H), 3.67 (dd, *J* = 9.5, 1.8 Hz, 1H), 3.58 (s, 3H), 3.60 – 3.52 (m, 1H), 2.79 (m, 1H), 2.71 – 2.66 (m, 1H), 2.62 (ddq, *J* = 18.4, 4.7, 1.7 Hz, 1H), 2.46 (dt, *J* = 9.9, 1.7 Hz, 1H), 2.23 (d, *J* = 3.8 Hz, 1H), 2.07 (dtd, *J* = 18.2, 2.6, 1.5 Hz, 1H), 1.71 (dt, *J* = 2.8, 1.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.20, 137.97, 134.90, 133.60, 128.53 (2C), 127.92, 127.90 (2C), 123.73 , 123.72 (q, *J* = 277.8 Hz), 120.94, 103.37, 81.99, 78.84, 73.15, 68.19, 61.85 (q, *J* = 35.0 Hz), 52.09, 46.43, 45.43, 43.73, 42.13, 35.30, 29.83, 25.25; IR (film) 2948, 2923, 2890, 1748, 1454, 1284, 1219, 1161, 1101, 1076, 993, 922, 888, 736, 696 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{26}H_{30}F_3O_5$ $[M+H]^+$: 479.2039, found: 479.2037.

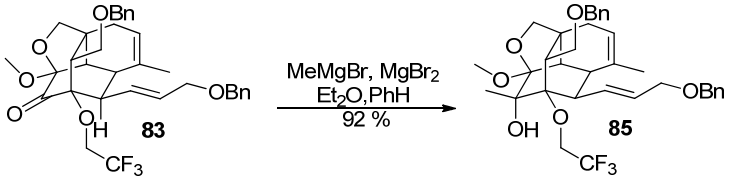


In a high-pressure tube was charged a solution of vinyl iodide (25.0 mg, 0.0432 mmol) in DMF (2.2 mL). After flushing the solution with N_2 for 10 min, tetrakis(triphenylphosphine)palladium(0) (0.5 mg, 0.000432 mmol) and (*E*)-methyl 3-(tributylstannyl)acrylate (32 mg, 0.864 mmol) were added successively. The tube was flushed with N_2 for 10 min again, capped and heated at 85 °C for 18 h. After cooling to r.t. the reaction mixture was poured onto water (10 mL) and extracted with ethyl acetate (3 × 5 mL). The combined extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography (15% ethyl acetate/hexanes) to provide a light yellow solid, which was further purified by trituration with methanol. The resultant white solid was collected by vacuum filtration (17.3 mg, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.26 (m, 5H), 6.43 (dd, *J* = 15.2, 10.6 Hz, 1H), 5.88 (dd, *J* = 15.2, 0.7 Hz, 1H), 5.58 (tt, *J* = 2.8, 1.4 Hz, 1H), 4.47 (s, 2H), 4.19 (dq, *J* = 10.9, 8.5 Hz, 1H), 3.91 (d, *J* = 7.3 Hz, 1H), 3.81 (d, *J* = 7.3 Hz, 1H), 3.75 (dq, *J* = 10.9, 8.5 Hz, 1H), 3.75 (s, 3H), 3.64 – 3.52 (m, 2H), 3.60 (s, 3H), 2.95 – 2.84 (m, 1H), 2.74 – 2.67 (m, 1H), 2.62 (ddd, *J* = 18.4, 4.4, 1.7 Hz, 1H), 2.50 – 2.44 (m, 1H), 2.27 (d, *J* = 3.8 Hz, 1H), 2.09 (dq, *J* = 18.3, 2.3 Hz, 1H), 1.65 (dt, *J* = 2.8, 1.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.29, 166.21, 143.43, 137.70, 134.07, 128.57 (2C), 128.14 (2C), 128.04, 126.13, 124.70, 123.49 (q, *J* = 277.7 Hz), 103.24, 81.99, 79.17, 73.36, 67.72, 61.94 (q, *J* = 35.4 Hz), 52.33, 51.77, 45.75, 44.93, 42.88, 42.24, 35.09, 29.76, 24.79; IR (film) 2950, 2890, 1761, 1722, 1653, 1436, 1283, 1240, 1163, 1092, 991, 733, 700 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{28}H_{31}F_3NaO_7$ $[M+Na]^+$: 559.1914, found: 559.1914.



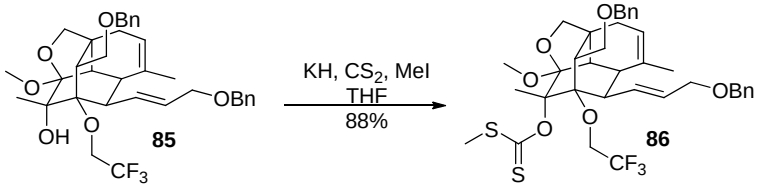
In a 15-mL high-pressure tube was charged a solution of vinyl iodide (400.0 mg, 0.692 mmol) in toluene (7.0 mL). After flushing the solution with N_2 for 15 min., tetrakis(triphenylphosphine)palladium(0) (40.0 mg, 0.0346 mmol) and (*E*)-(3-

(benzyloxy)prop-1-en-1-yl)tributylstannane (0.4 mL, 0.900 mmol) were added successively. The tube was flushed with N_2 for 10 min. again, capped and heated at 150 °C for 18 h. The reaction solution turned from yellow to olive over time and in some occasions a black precipitate formed on the glass wall. After cooling to r.t. the reaction mixture was filtered through a Celite pad and the filtrate was concentrated and purified by column chromatography (10% ethyl acetate/hexanes) to provide a light yellow oil (375.2 mg, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.20 (m, 10H), 5.68 (dt, *J* = 15.2, 5.5 Hz, 1H), 5.54 (dt, *J* = 4.0, 2.2 Hz, 1H), 5.24 (ddt, *J* = 15.2, 10.2, 1.5 Hz, 1H), 4.48 (d, *J* = 4.0 Hz, 2H), 4.41 (d, *J* = 1.4 Hz, 2H), 4.24 (dq, *J* = 11.0, 8.6 Hz, 1H), 4.00 (ddd, *J* = 5.5, 2.3, 1.5 Hz, 2H), 3.95 – 3.85 (m, 2H), 3.79 (d, *J* = 7.3 Hz, 1H), 3.63 (dd, *J* = 9.4, 1.7 Hz, 1H), 3.59 (s, 3H), 3.54 (dd, *J* = 9.7, 9.4 Hz, 1H), 2.84 (dd, *J* = 10.7, 10.2 Hz, 1H), 2.68 (dd, *J* = 10.7, 3.8 Hz, 1H), 2.61 (ddd, *J* = 18.4, 4.4, 2.1 Hz, 1H), 2.47 (dt, *J* = 9.7, 1.7 Hz, 1H), 2.25 (d, *J* = 3.8 Hz, 1H), 2.08 (d, *J* = 18.4 Hz, 1H), 1.70 (dt, *J* = 2.7, 1.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.08, 138.67, 137.89, 134.94, 133.00, 128.55 (2C), 128.50 (2C), 127.98, 127.94 (2C), 127.87, 127.64, 127.58 (2C), 123.83, 123.77 (q, *J* = 277.6 Hz), 103.41, 82.03, 79.11, 73.18, 71.60, 69.86, 68.13, 61.90 (q, *J* = 35.1 Hz), 52.17, 45.51, 45.34, 43.33, 42.18, 35.30, 29.83, 25.25; IR (film) 2943, 2887, 2850, 1751, 1452, 1282, 1161, 1070, 991, 887, 736, 698 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{34}H_{37}F_3NaO_6$ $[M+Na]^+$: 621.2434, found: 621.2439.



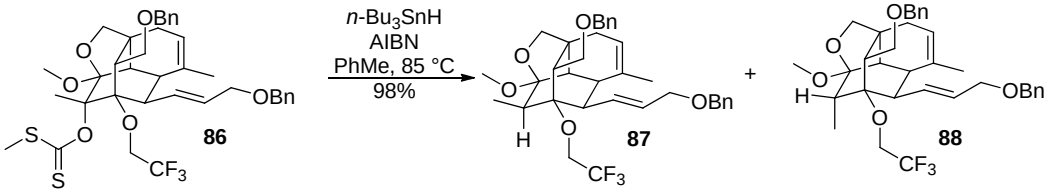
Magnesium bromide diethyl etherate (542.0 mg, 2.10 mmol) in a flask was dried by heating gently under vacuum. After the flask was cooled to r.t., ketone (837.6 mg, 1.40 mmol) in anhydrous ethyl ether (12.0 mL) was added, followed by anhydrous benzene (2.5 mL). The mixture turned into a clear solution. (Note: When $MgBr_2$ dissolves in diethyl ether it forms two layers of liquid. The button layer contains $MgBr_2$ at 39 wt% and the top layer 3 wt%. Addition of benzene can increase

the solubility and make a clear solution. This operation does not seem to affect the yield or stereoselectivity of the reaction and therefore could be omitted.) The solution was cooled to 0 °C while vigorously stirred. Methylmagnesium bromide (3.0 M in diethyl ether, 0.70 mL, 2.10 mmol) was added dropwise while the reaction solution turned form colorless to light yellow. After the addition was completed, the reaction mixture was warmed to r.t. and stirred for 1.0 h, then quenched by saturated NH_4Cl solution at 0 °C and diluted with water and ethyl acetate. The organic layer was separated and the aqueous layer was extracted with ethyl acetate three times. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column (10-15% ethyl acetate/hexanes) to afford a white solid (790.2 mg, 92% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.19 (m, 10H), 5.74 (dt, *J* = 15.3, 5.6 Hz, 1H), 5.53 – 5.39 (m, 2H), 4.48 (s, 2H), 4.47 (d, *J* = 11.9 Hz, 1H), 4.39 (d, *J* = 11.9 Hz, 1H), 4.23 (dq, *J* = 11.3, 8.5 Hz, 1H), 4.02 (dq, *J* = 11.3, 8.5 Hz, 1H), 3.99 (dd, *J* = 5.6, 1.4 Hz, 2H), 3.95 (dd, *J* = 8.9, 1.9 Hz, 1H), 3.80 (td, *J* = 11.3, 2.0 Hz, 1H), 3.71 (d, *J* = 6.8 Hz, 1H), 3.55 (m, 1H), 3.53 (d, *J* = 6.8 Hz, 1H), 3.35 (s, 3H), 3.35 (s, 1H), 2.51 (dd, J = 11.3, 3.5 Hz, 1H), 2.47 (m, 1H), 2.19 (dt, *J* = 10.3, 2.0 Hz, 1H), 1.96 (dtd, *J* = 18.6, 2.7, 1.2 Hz, 1H), 1.89 (d, *J* = 3.5 Hz, 1H), 1.65 (dt, *J* = 2.9, 1.6 Hz, 3H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.71, 138.53, 135.69, 131.88, 131.47, 128.48 (2C), 128.43 (2C), 127.71 (2C), 127.62, 127.60, 127.51 (2C), 124.27 (q, *J* = 277.7 Hz), 122.45, 107.10, 81.38, 79.56, 79.49, 72.69, 71.85, 70.40, 69.10, 61.96 (q, *J* = 34.0 Hz), 49.99, 47.83, 40.78, 39.98, 35.43, 35.10, 29.62, 25.59, 17.48; IR (film) 3535, 2939, 2858, 1452, 1282, 1163, 1118, 1095, 1016, 960, 856, 734, 696 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{35}H_{42}F_3O_6$ $[M+H]^+$: 615.2928, found: 615.2926.



Potassium hydride (30 wt% in mineral oil, 0.98 g, 7.34 mmol) was washed with dry pentane under N_2 for three times, then suspended in THF (15 mL) and cooled

to 0 °C. Alcohol (1.13 g, 1.83 mmol) in THF (3.3 mL) was added dropwise. After the reaction was stirred at 0 °C for 2.0 h, freshly distilled carbon disulfide (1.11 mL, 18.3 mmol) was added dropwise. The reaction was stirred at 0 °C for 30 min. and r.t. 4.0h. After that period of time, the reaction was cooled to 0 °C again and methyl iodide (1.14 mL, 18.3 mmol) was added dropwise. The resultant mixture was allowed to warm up to r.t. and stirred for 20 h. The reaction was then quenched by water at 0 °C and diluted with ethyl acetate. The organic layer was separated and the aqueous layer was extracted with ethyl acetate three times. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was triturated with hexane and an off-white solid was collected by vacuum filtration. The filtrate was concentrated and purified by flash column chromatography (15% ethyl acetate/hexanes) to afford another crop of white solid. All solids were combined and weighed 1.13g (88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 7.43 – 7.20 (m, 10H), 5.82 (dt, *J* = 15.2, 5.5 Hz, 1H), 5.53 – 5.37 (m, 2H), 4.51 (s, 2H), 4.44 (q, *J* = 11.8 Hz, 2H), 4.12 – 3.96 (m, 3H), 3.94 – 3.77 (m, 3H), 3.73 (d, *J* = 7.0 Hz, 1H), 3.62 – 3.54 (m, 1H), 3.54 (d, *J* = 7.2 Hz, 1H), 3.24 (s, 3H), 2.65 (d, *J* = 11.8, 3.5 Hz, 1H), 2.54 (s, 3H), 2.52 – 2.41 (m, 1H), 2.20 (dt, *J* = 10.3, 2.0 Hz, 1H), 2.03 (s, 3H), 2.01 – 1.93 (m, 1H), 1.95 (d, *J* = 3.5 Hz, 1H), 1.69 (dt, *J* = 2.8, 1.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 212.63, 138.60, 138.35, 135.55, 132.83, 130.06, 128.51 (2C), 128.47 (2C), 127.72 (2C), 127.70, 127.67, 127.50 (2C), 123.84 (q, *J* = 277.8 Hz), 122.67, 107.94, 97.60, 81.57, 80.64, 72.79, 72.24, 70.33, 69.04, 61,90 (q, *J* = 34.3 Hz), 49.18, 47.30, 40.95, 40.48, 35.81, 34.94, 29.52, 25.57, 20.08, 15.50; IR (film) 2935, 2860, 1282, 1222, 1163, 1109, 1016, 962, 734, 696 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{37}H_{44}F_3O_6S_2$ $[M+H]^+$: 705.2526, found: 705.2521.

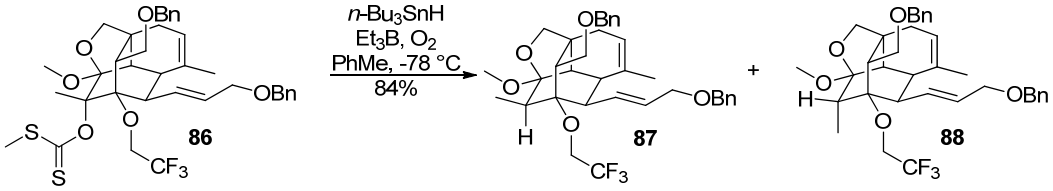


A mixture of xanthate (45.0 mg, 0.0638 mmol), tributyltin hydride (0.085 mL, 0.319 mmol) and azobisisobutyronitrile (5.4 mg, 0.0319 mmol) in toluene (1.3 mL) was heated at 85 °C for 1 h, then cooled to r.t. and concentrated. The crude product was purified by column chromatography (10-15% ethyl acetate/hexanes) to afford product **87** (lower R_f, white solid, 31.2 mg, 82% yield) and **88** (higher R_f, white solid, 6.0 mg, 16% yield).

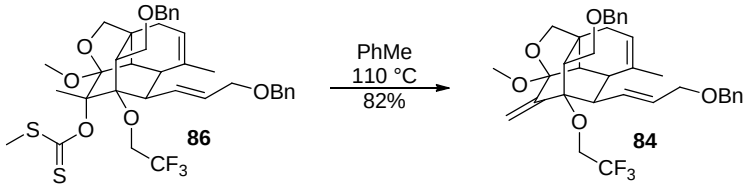
Compound **87**: ^{1}H NMR (500 MHz, $CDCl_3$) □ 7.43 – 7.19 (m, 10H), 5.68 (dt, *J* = 15.3, 5.6 Hz, 1H), 5.50 – 5.36 (m, 2H), 4.49 (s, 2H), 4.48 (d, *J* = 11.8 Hz, 1H), 4.40 (d, *J* = 11.8 Hz, 1H), 4.07 – 3.89 (m, 3H), 3.87 (dd, *J* = 9.0, 1.9 Hz, 1H), 3.73 (d, *J* = 7.0 Hz, 1H), 3.67 (dq, *J* = 10.2, 8.1 Hz, 1H), 3.58 (d, *J* = 7.0 Hz, 1H), 3.52 (dd, *J* = 10.4, 9.0 Hz, 1H), 3.31 (s, 3H), 2.68 (td, *J* = 11.0, 1.8 Hz, 1H), 2.58 (dd, *J* = 11.3, 3.6 Hz, 1H), 2.52 (ddd, *J* = 18.4, 4.3, 2.0 Hz, 1H), 2.21 (dt, *J* = 10.4, 1.9 Hz, 1H), 2.02 (q, *J* = 6.8 Hz, 1H), 1.96 (m, 2H), 1.65 (dt, *J* = 2.9, 1.6 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 138.57, 138.53, 134.70, 131.64, 131.32, 128.53 (2C), 128.45 (2C), 127.77 (2C), 127.69, 127.65, 127.56 (2C), 123.53, 124.05 (q, *J* = 277.1 Hz), 109.63, 81.53, 77.20, 72.78, 71.98, 70.25, 68.64, 59.93 (q, *J* = 34.5 Hz), 49.62, 48.81, 47.52, 46.32, 40.87, 40.49, 35.66, 30.24, 25.60, 7.69; IR (film) 2923, 2855, 1454, 1281, 1161, 1114, 1013, 966, 926, 735, 696 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{35}H_{42}F_3O_5$ $[M+H]^+$: 599.2978, found: 599.2980.

Compound **88**: ^{1}H NMR (600 MHz, $CDCl_3$) □ 7.40 – 7.20 (m, 10H), 5.62 (dt, *J* = 15.1, 5.9 Hz, 1H), 5.44 (dt, *J* = 4.3, 2.0 Hz, 1H), 5.27 (dd, *J* = 15.1, 10.1 Hz, 1H), 4.49 (d, *J* = 12.2 Hz, 1H), 4.43 (d, *J* = 12.3 Hz, 2H), 4.37 (d, *J* = 11.7 Hz, 1H), 4.02 (ddd, *J* = 12.8, 5.8, 1.4 Hz, 1H), 3.96 (ddd, *J* = 12.8, 5.8, 1.4 Hz, 1H), 3.77 (d, *J* = 6.9 Hz, 1H), 3.66 – 3.52 (m, 3H), 3.50 (dd, *J* = 9.6, 1.6 Hz, 1H), 3.36 (t, *J* = 9.8 Hz, 1H), 3.32 (s, 3H), 2.72 (t, *J* = 10.6 Hz, 1H), 2.46 – 2.39 (m, 2H), 2.24 (q, *J* = 7.1 Hz, 1H), 2.12 (d, *J* = 10.0 Hz, 1H), 2.01 (d, *J* = 18.2 Hz, 1H), 1.89 (d, *J* = 3.6 Hz, 1H), 1.66 (s, 3H), 0.96 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, extracted for HSQC and MHBC) 128.5 (2C), 127.86(2C), 127.77(3C), 127.5 (3C), 138.94, 138.07, 136.05, 131.73, 130.47, 124.03, 122.26, 108.77, 81.06, 77.01, 73.11, 71.08, 70.42, 68.32, 59.23, 49.87,

47.97, 47.66, 40.14, 39.00, 38.97, 34.78, 29.77, 25.26, 9.07; IR (film) 2923, 2853, 1454, 1368, 1279, 1161, 1114, 1016, 968, 916, 735, 698 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{35}H_{42}F_3O_5$ $[M+H]^+$: 599.2978, found: 599.2978.

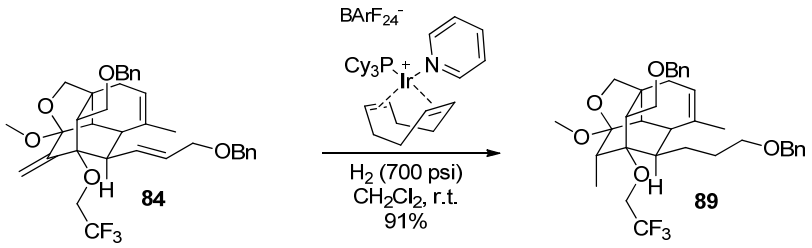


A mixture of xanthate (10.0 mg, 0.0142 mmol), tributyltin hydride (0.009 mL, 0.0355 mmol) and triethylborane (1.0 M in THF, 0.01 mL) in toluene (1.4 mL) was cooled to -78 °C and O_2 was bubbled through for 5 min. The reaction was stirred at -78 °C for 1.0 h under O_2 atmosphere, then warmed to r.t. and concentrated. Crude ^{1}H-NMR showed the ratio of **87** to **88** is about 17:1. The major product **87** was isolated by column chromatography (10% ethyl acetate/hexanes) as a white solid (14.3 mg, 84% yield).



A solution of xanthate (3.02 g, 4.28 mmol) in toluene (43.0 mL) was heated at 110 °C for 4 h. After cooling to r.t. the reaction mixture was concentrated. The residue was triturated with 5% ethyl acetate/hexanes. A white solid was collected by vacuum filtration. The filtrate was concentrated and purified by flash column (10-15% ethyl acetate/hexanes) to afford another crop of white solid. The solids are combined and weighed 2.09 g (82% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.22 (m, 10H), 5.63 (dtd, *J* = 15.1, 5.8, 0.6 Hz, 1H), 5.47 (m, 1H), 5.46 (d, *J* = 0.7 Hz, 1H), 5.25 (ddt, *J* =

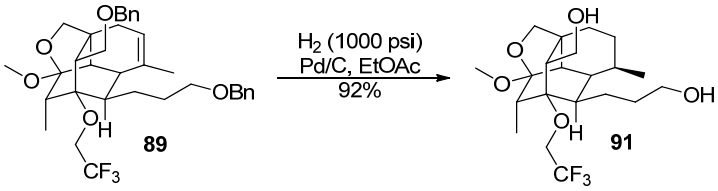
15.1, 10.3, 1.5 Hz, 1H), 5.05 (s, 1H), 4.50 (d, *J* = 12.1 Hz, 1H), 4.46 (d, *J* = 11.8 Hz, 1H), 4.44 (d, *J* = 12.1 Hz, 1H), 4.36 (d, *J* = 11.8 Hz, 1H), 4.05 – 3.93 (m, 3H), 3.80 (d, *J* = 7.0 Hz, 1H), 3.64 (d, *J* = 7.1 Hz, 1H), 3.56 – 3.37 (m, 3H), 3.40 (s, 3H), 2.71 – 2.62 (m, 1H), 2.60 – 2.54 (m, 1H), 2.50 – 2.41 (m, 1H), 2.24 (dt, *J* = 9.4, 1.9 Hz, 1H), 2.16 (d, *J* = 3.5 Hz, 1H), 2.05 (dtd, *J* = 18.2, 2.5, 1.2 Hz, 1H), 1.67 (dt, *J* = 2.8, 1.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 151.30, 138.85, 137.87, 136.06, 132.23, 129.82, 128.52 (2C), 128.42 (2C), 127.97, 127.92 (2C), 127.61 (2C), 127.53, 124.07 (q, *J* = 277.8 Hz), 122.78, 105.96, 104.75, 81.33, 77.79, 73.14, 71.23, 70.26, 67.85, 60.17 (q, *J* = 34.4 Hz), 50.60, 49.78, 45.37, 41.62, 41.41, 35.60, 30.00, 25.31; IR (film) 2931, 2852, 1452, 1367, 1282, 1166, 1103, 1010, 923, 854, 734, 696 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{35}H_{40}F_3O_5$ $[M+H]^+$: 597.2822, found: 597.2828.



In a 4-mL clear glass vial, triene (124.7 mg, 0.209 mmol) was dissolved in CH_2Cl_2 (1.0 mL), and iridium catalyst[11] (8.0 mg, 0.00522 mmol, 0.025 eq.) was added. The resultant red solution was bubbled with H_2 for 1.0 min. and the color was discharged immediately. Six of this vial was placed in a hydrogenation bomb and stirred at r.t. under 700 psi of H_2 for 16 h. The combined reaction mixture was

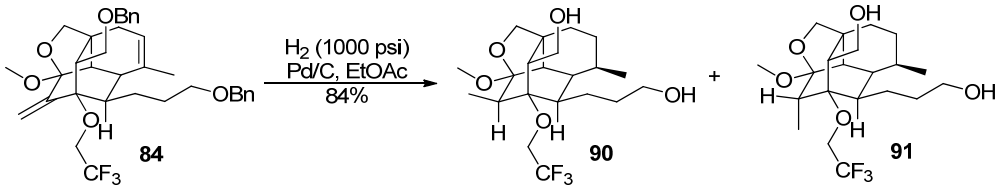
(11) Wustenberg, B.; Pfaltz, A. *Adv. Synth. Catal.* **2008**, *350*, 174-178.

concentrated under reduced pressure and the residue was purified by column chromatography (10% ethyl acetate/hexanes) to afford a white solid (688.6 mg, 91% yield). ^{1}H NMR (600 MHz, $CDCl_3$) □ 7.38 – 7.26 (m, 10H), 5.50 – 5.42 (m, 1H), 4.50 (d, *J* = 11.9 Hz, 1H), 4.47 (d, *J* = 11.8 Hz, 1H), 4.46 (d, *J* = 11.9 Hz, 1H), 4.40 (d, *J* = 11.8 Hz, 1H), 3.74 (d, *J* = 7.0 Hz, 1H), 3.64 – 3.54 (m, 2H), 3.54 – 3.50 (m, 1H), 3.52 (d, *J* = 7.0 Hz, 1H), 3.46 (ddd, *J* = 9.5, 7.8, 5.5 Hz, 1H), 3.38 (dt, *J* = 9.6, 7.1 Hz, 1H), 3.30 (s, 3H), 3.28 (t, *J* = 10.0 Hz, 1H), 2.53 – 2.45 (m, 2H), 2.19 (q, *J* = 7.1 Hz, 1H), 2.07 (dt, *J* = 10.6, 1.9 Hz, 1H), 2.00 – 1.89 (m, 2H), 1.88 (d, *J* = 3.6 Hz, 1H), 1.78 – 1.68 (m, 1H), 1.74 (s, 3H), 1.63 – 1.54 (m, 1H), 1.47 (dtd, *J* = 14.0, 8.2, 2.5 Hz, 1H), 1.11 (dtd, *J* = 13.0, 7.8, 4.9 Hz, 1H), 0.89 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 138.81, 138.25, 136.23 , 128.43 (2C), 128.4 (q, *J* = 278.1 Hz), 128.34 (2C), 127.73, 127.69 (2C), 127.64 (2C), 127.45, 123.19, 108.65, 81.09, 77.91, 73.00, 72.82, 70.48, 68.18, 59.06 (q, *J* = 34.5 Hz), 49.85, 48.01, 47.82, 40.53, 40.43, 35.51, 34.38, 31.85, 29.87, 25.48, 21.10, 8.82; IR (film) 3028, 2929, 2856, 1496, 1454, 1365, 1280, 1201, 1163, 1112, 966, 916, 734, 696 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{35}H_{44}F_3O_5$ $[M+H]^+$: 601.3135, found: 601.3132.

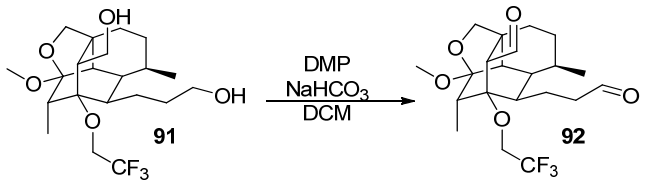


In a 2-mL clear glass vial, palladium on carbon (10 wt%, 35.0 mg, 0.0328 mmol) was added to a solution of alkene (19.7 mg, 0.0328 mmol) in ethyl acetate (0.82 mL). Seven of this reaction vial were placed in a hydrogenation bomb and stirred at r.t. under 1000 psi of H_2 for 22 h. The reaction mixtures were filtered through a Celite pad and the filtrates were combined and triturated with 30% ethyl acetate/hexanes. A white solid was collected by vacuum filtration and the filtrate was concentrated and purified by column chromatography (50% ethyl acetate/hexanes) to afford another crop of white solid. The solids were combined and weighed 89.3 mg (92% yield). ^{1}H NMR (400 MHz, CD_3OD) □ 3.99 – 3.71 (m, 4H), 3.60 – 3.49 (m, 1H),

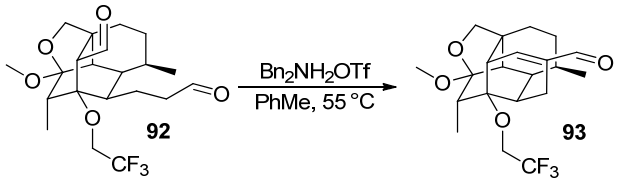
3.57 (d, *J* = 6.5 Hz, 1H), 3.48 – 3.40 (m, 1H), 3.37 (d, *J* = 6.5 Hz, 1H), 3.28 (s, 3H), 2.31 – 2.24 (m, 1H), 2.22 – 2.16 (m, 1H), 2.14 (q, *J* = 7.1 Hz, 1H), 2.03 (dt, *J* = 10.6, 2.5 Hz, 1H), 1.98 – 1.90 (m, 1H), 1.77 – 1.56 (m, 5H), 1.59 (d, *J* = 2.5 Hz, 1H), 1.54 – 1.36 (m, 3H), 1.22 (d, *J* = 6.4 Hz, 3H), 0.87 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 124.28 (q, *J* = 277.6 Hz), 108.35, 81.35, 80.88, 62.20, 59.78 (q, *J* = 34.3 Hz), 59.15, 49.97, 49.35, 47.17, 47.15, 41.65, 38.23, 35.42, 34.50, 33.21, 28.81, 27.91, 21.24, 18.89, 9.07; IR (film) 3373, 2941, 2875, 2499, 1390, 1282, 1159, 1122, 1045, 983, 970 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{34}F_3O_5$ $[M+H]^+$: 423.2353, found: 423.2346.



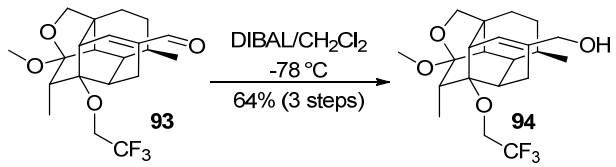
In a 2-mL clear glass vial, palladium on carbon (10 wt%, 17.8 mg, 0.0168 mmol) was added to a solution of diene (10.0 mg, 0.0168 mmol) in ethyl acetate (0.60 mL). Five of this vial were placed in a hydrogenation bomb and stirred at r.t. under 1000 psi H_2 for 36 h. The reaction mixtures were filtered through a Celite pad and the filtrates were combined, concentrated and purified by column chromatography (70% ethyl acetate/hexanes) to afford a white solid (6.5:1 inseparable mixture of **90** and **91**, 29.7 mg, 84% yield). Major diastereomer compound **90**: ^{1}H NMR (500 MHz, CD_3OD) 4.02 (dd, *J* = 11.0, 3.6 Hz, 1H), 3.87 – 3.79 (m, 2H), 3.63 (dq, *J* = 11.0, 8.5 Hz, 1H), 3.55 (d, *J* = 6.5 Hz, 1H), 3.51 (t, *J* = 6.4 Hz, 2H), 3.40 (d, *J* = 6.5 Hz, 1H), 3.27 (s, 3H), 2.33 (m, 2H), 2.07 – 2.00 (m, 1H), 1.97 – 1.84 (m, 3H), 1.83 – 1.56 (m, 4H), 1.70 (d, *J* = 2.7 Hz, 1H), 1.53 – 1.34 (m, 3H), 1.23 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 123.90 (q, *J* = 277.7 Hz), 109.06, 82.95, 81.23, 62.76, 60.30, 60.30 (q, *J* = 34.6 Hz), 49.43, 48.81, 47.22, 47.17, 44.38, 41.96, 38.67, 35.49, 33.13, 29.04, 28.50, 21.63, 20.77, 7.37; IR (film) 3413, 2944, 2917, 2875, 2514, 1458, 1281, 1163, 1118, 1093, 1025, 966 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{34}F_3O_5$ $[M+H]^+$: 423.2353, found: 423.2355.



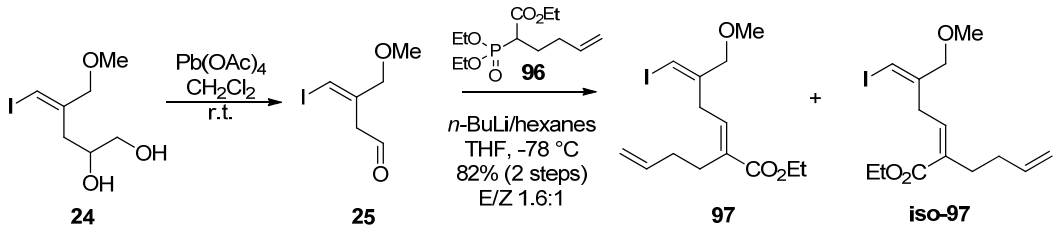
To a mixture of diol (51.7 mg, 0.122 mmol) and $NaHCO_3$ (51.2 mg, 0.610 mmol) in CH_2Cl_2 (4.8 mL) was added Dess-Martin periodinane (129.8 mg, 0.306 mmol) in one portion at r.t. After stirring for 1.5 h the reaction mixture was filtered through a Celite pad. The filtrate was concentrated, then taken up in diethyl ether (50 mL) and filtered again. The etheral solution was washed with saturated $NaHCO_3$/10% $Na_2S_2O_3$ mixture solution (1:2 v/v, 5 × 6 mL) and brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product (50.0 mg) was used directly without further purification.



A mixture of dialdehyde (50.0 mg, 0.119 mmol) and dibenzylammonium trifluoroacetate (40.9 mg, 0.131 mmol) in toluene (2.4 mL) was heated at 55 °C for 16 h, while the reaction solution turned to light yellow gradually. After that period of time, the reaction was cooled to r.t. and concentrated. The residue was taken up in diethyl ether and the solid was filtered off. The filtrate was concentrated again, then loaded onto a short silica gel pad and eluted with 30% ethyl acetate/hexanes. The eluate was concentrated to afford a colorless oil (50.9 mg), which was used directly in the next step.



To a solution of □,□-unsaturated aldehyde (50.9 mg, 0.127 mmol) in CH_2Cl_2 (2.3 mL) was added DIBAL (1.0 M in CH_2Cl_2, 0.25 mL) dropwise at -78 °C. The reaction was stirred at -78 °C for 1.5 h then quenched by 10% Rochelle's salt solution (5.0 mL). The mixture was warmed to r.t. and stirred vigorously until two clear layers formed. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (30% ethyl acetate/hexanes) to provide a white solid (31.3 mg, 64% yield over 3 steps). ^{1}H NMR (400 MHz, $CDCl_3$) □ 5.71 (dp, *J* = 7.2, 1.5 Hz, 1H), 4.04 (s, 2H), 3.69 – 3.56 (m, 2H), 3.43 – 3.34 (m, 2H), 3.33 (s, 3H), 2.42 (m, 1H), 2.38 – 2.30 (m, 1H), 2.36 (s, 1H), 2.27 (dt, *J* = 11.5, 2.7 Hz, 1H), 2.19 (dd, *J* = 7.2, 3.0 Hz, 1H), 2.12 (q, *J* = 7.2 Hz, 1H), 1.80 – 1.72 (m, 1H), 1.61 (dqd, *J* = 10.4, 7.4, 3.3 Hz, 1H), 1.42 – 1.23 (m, 5H), 1.20 (d, *J* = 7.2 Hz, 3H), 0.98 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 142.08, 124.35 (q, *J* = 278.7 Hz), 116.52, 108.17, 80.55, 79.56, 66.48, 60.31 (q, *J* = 34.3 Hz), 50.18, 47.48, 44.65, 43.04, 41.88, 37.29, 34.86, 29.81, 28.59, 26.86, 25.43, 22.23, 9.17; IR (film) 3427, 2978, 2929, 2891, 1456, 1386, 1280, 1165, 1151, 1120, 968, 864, 732 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{30}F_3O_4$ $[M+H]^+$: 403.2091, found: 403.2096.



To an ice-water cooled solution of diol (2.03 g, 7.47 mmol) in CH_2Cl_2 (30.0 mL) was added lead (IV) acetate (3.64 g, 8.21 mmol) in portions. After the addition was completed, the reaction mixture was allowed to warm to r.t. and stirred for 1.0 h. The reaction mixture was poured directly over a silica gel pad, filtered and the filter cake was washed with ethyl acetate. The filtrate was concentrated on rotovap and the residue was taken up in ether and filtered through a Celite pad and washed with ethyl ether. The filtrate was concentrated again on rotovap and then placed under high

vacuum briefly to remove residual solvents and formaldehyde by-product. The resultant aldehyde crude product was used immediately.

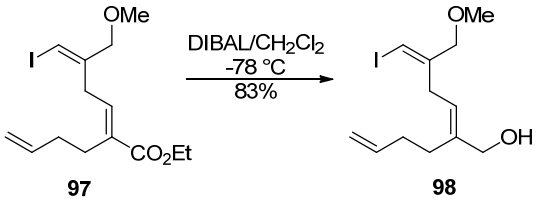
To a solution of phosphonate[12] (11.43 g, 41.1 mmol) in THF (10 mL), *n*-BuLi (2.5 M in hexane, 14.9 mL, 37.4 mmol) was added dropwise at -78 °C with stirring. After 2.0 h, the aforementioned aldehyde in THF (5.0 mL) was added dropwise and the stirring was continued for 6.0 h. The reaction was quenched by saturated NH_4Cl solution (5 mL), warmed to r.t., diluted with water (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (10% ethyl acetate/hexanes to straight ethyl acetate) to afford the desired product mixture (colorless oil, 2.24 g, E/Z 1.6:1, yield 82%) and unreacted phosphonate. The E/Z mixture was further separated by column chromatography (5% ethyl ether/hexanes): high R_f fraction, Z isomer **iso-97**, colorless oil, 0.86 g; low R_f fraction, E isomer **97**, colorless oil, 1.38 g.

Z isomer **iso-97**: ^{1}H NMR (400 MHz, $CDCl_3$) □ 6.34 (td, *J* = 1.4, 0.7 Hz, 1H), 5.85 – 5.71 (m, 2H), 5.01 (ddt, *J* = 17.1, 2.0, 1.5 Hz, 1H), 4.96 (ddt, *J* = 10.2, 2.0, 1.2 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.90 (d, *J* = 1.4 Hz, 2H), 3.39 (dq, *J* = 7.5, 0.8 Hz, 2H), 3.31 (s, 3H), 2.37 (ddt, *J* = 8.7, 6.2, 1.0 Hz, 2H), 2.23 – 2.13 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 167.78, 146.41, 137.81, 136.17, 133.71, 115.29, 79.41, 75.10, 60.48, 58.24, 35.79, 34.12, 33.31, 14.44; IR (film) 2980, 2927, 1708, 1639, 1448, 1377, 1201, 1095, 1026, 912, 785 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{14}H_{21}INaO_3$ $[M+Na]^+$: 387.0428, found: 387.0429.

E isomer **97**: ^{1}H NMR (400 MHz, $CDCl_3$) □ 6.64 (tt, *J* = 7.5, 0.6 Hz, 1H), 6.40 (td, *J* = 1.3, 0.6 Hz, 1H), 5.84 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1H), 5.04 (ddt, *J* = 17.1, 2.0, 1.5 Hz, 1H), 4.97 (ddt, *J* = 10.2, 2.0, 1.1 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.90 (d, *J* = 1.3 Hz, 2H), 3.31 (s, 3H), 3.14 (dd, *J* = 7.5, 0.6 Hz, 2H), 2.54 – 2.45 (m, 2H), 2.25 – 2.15 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 167.51, 145.69,

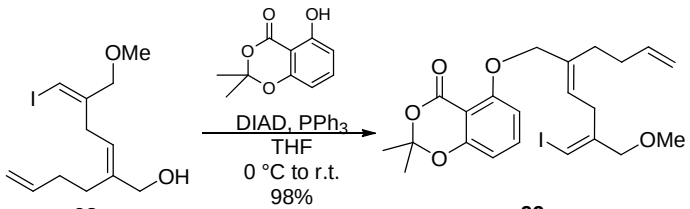
(12) Petter, R. C.; Banerjee, S.; Englard, S. *J. Org. Chem.* **1990**, 55, 3088-3097.

137.97, 137.21, 134.03, 115.25, 80.49, 74.98, 60.66, 58.11, 34.70, 33.37, 26.72, 14.37; IR (film) 2978, 2929, 2819, 1708, 1639, 1448, 1371, 1261, 1199, 1095, 912, 783 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{14}H_{22}IO_3$ $[M+H]^+$: 365.0608, found: 365.0603.



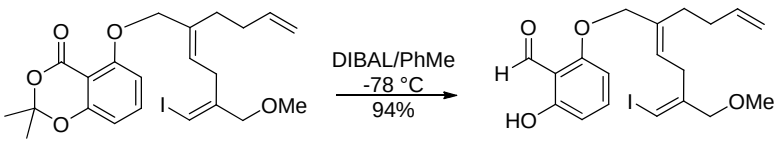
97 **98**

To a solution of □,□-unsaturated ester (10.1 g, 27.8 mmol) in CH_2Cl_2 (200 mL) was added DIBAL (1.0 M in CH_2Cl_2, 69.5 mL) dropwise at -78 °C. The reaction was stirred at -78 °C for 6.5 h then quenched by 10% Rochelle's salt solution (150 mL), diluted with CH_2Cl_2 (200 mL), warmed to r.t. and stirred vigorously until two clear layers formed. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 150 mL). The combined organic layers were washed with brine (200 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (10-25% ethyl acetate/hexanes) to provide a colorless oil (7.54 g, 83% yield). ^1H NMR (400 MHz, $CDCl_3$) □ 6.30 (td, *J* = 1.4, 0.6 Hz, 1H), 5.85 (ddt, *J* = 17.1, 10.2, 6.5 Hz, 1H), 5.39 (dddt, *J* = 7.3, 6.7, 1.2, 0.8 Hz, 1H), 5.06 (ddt, *J* = 17.1, 2.0, 1.5 Hz, 1H), 4.98 (ddt, *J* = 10.2, 2.0, 1.2 Hz, 1H), 4.07 (dq, *J* = 6.1, 1.2 Hz, 2H), 3.89 (d, *J* = 1.4 Hz, 2H), 3.30 (s, 3H), 3.02 (dq, *J* = 7.3, 0.8 Hz, 2H), 2.34 – 2.25 (m, 2H), 2.20 (dddt, *J* = 8.3, 6.5, 5.7, 1.4 Hz, 2H), 1.33 (t, *J* = 6.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 147.03, 141.10, 138.31, 121.76, 115.11, 79.12, 74.90, 66.85, 58.08, 33.71, 32.70, 27.84; IR (film) 3385, 2926, 2856, 2819, 1639, 1448, 1087, 1064, 912 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{12}H_{19}INaO_2$ $[M+Na]^+$: 345.0322, found: 345.0318.



98 **99**

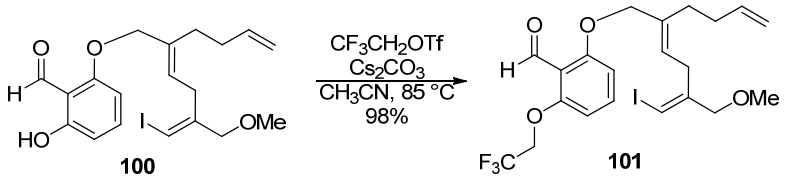
To an ice-water cooled solution of alcohol (2.39g, 7.42 mmol), phenol (1.57 g, 8.90 mmol) and triphenylphosphine (2.33 g, 8.90 mmol) in THF (50 mL) was added diisopropyl azodicarboxylate (1.73 mL, 8.90 mmol) slowly. After the addition was completed, stirring continued for 1.0 h at 0 °C and then the reaction mixture was warmed to r.t. naturally and stirred overnight. The reaction was concentrated and the residue was taken up in ethyl acetate. After the solid was filtered off, the filtrate was concentrated again and the residue was purified by column chromatography (20% ethyl acetate/hexanes) to provide a light yellow oil (3.61 g, 98% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 7.40 (t, *J* = 8.4 Hz, 1H), 6.59 (dd, *J* = 8.4, 0.9 Hz, 1H), 6.54 (dd, *J* = 8.4, 0.9 Hz, 1H), 6.31 – 6.26 (m, 1H), 5.87 (ddt, *J* = 17.1, 10.2, 6.6 Hz, 1H), 5.65 (ddt, *J* = 8.4, 7.3, 1.1 Hz, 1H), 5.07 (ddt, *J* = 17.1, 2.0, 1.5 Hz, 1H), 4.97 (ddt, *J* = 10.2, 2.0, 1.2 Hz, 1H), 4.58 (q, *J* = 1.1 Hz, 2H), 3.90 (d, *J* = 1.4 Hz, 2H), 3.30 (s, 3H), 3.07 (d, *J* = 7.3 Hz, 2H), 2.41 (dd, *J* = 9.2, 6.3 Hz, 2H), 2.34 – 2.20 (m, 2H), 1.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 160.55, 157.89, 157.85, 146.88, 138.29, 136.23, 136.14, 124.26, 115.13, 109.30, 106.96, 105.23, 103.73, 79.06, 74.86, 72.67, 58.14, 33.85, 32.38, 27.83, 25.74 (2C); IR (film) 3074, 2993, 2927, 2821, 1735, 1606, 1583, 1479, 1330, 1259, 1203, 1080, 918, 802, 761, 690 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{22}H_{28}IO_5$ $[M+H]^+$: 499.0976, found: 499.0982.



99 **100**

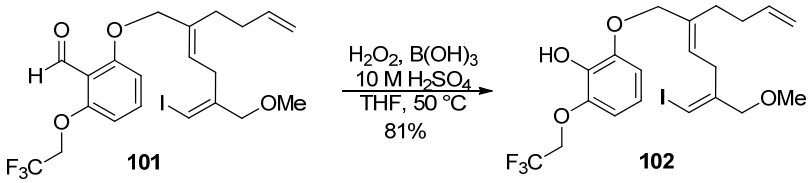
To a solution of acetonide (4.19 g, 8.41 mmol) in toluene (70 mL) cooled at -78 °C, DIBAL (1.2M in toluene, 14.7 mL, 17.7 mmol) was added dropwise. After stirring at -78 °C for 3 h, the reaction was quenched by 10% Rochelle's salt solution (100 mL), diluted with ethyl acetate (200 mL), warmed to r.t. and vigorously stirred overnight. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (5 × 100 mL). The combined organic layers were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. After filtration and concentration, the crude product was purified by column chromatography (10% ethyl acetate/hexanes) to

afford a light yellow oil (3.48g, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 11.95 (s, 1H), 10.37 (d, *J* = 0.6 Hz, 1H), 7.38 (t, *J* = 8.4, 1H), 6.52 (dt, *J* = 8.4, 0.8 Hz, 1H), 6.37 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.33 (dq, *J* = 1.3, 0.7 Hz, 1H), 5.85 (ddt, *J* = 17.1, 10.2, 6.6 Hz, 1H), 5.54 (ddt, *J* = 7.3, 6.4, 1.0 Hz, 1H), 5.07 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.01 (ddt, *J* = 10.2, 1.9, 1.2 Hz, 1H), 4.52 (q, *J* = 1.0 Hz, 2H), 3.88 (d, *J* = 1.3 Hz, 2H), 3.29 (s, 3H), 3.07 (d, *J* = 7.3 Hz, 2H), 2.42 – 2.33 (m, 2H), 2.31 – 2.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 194.32, 163.80, 161.75, 146.60, 138.45, 137.84, 136.17, 125.64, 115.49, 111.18, 110.05, 102.27, 79.70, 75.01, 72.65, 58.10, 33.86, 32.45, 28.00; IR (film) 3074, 3061, 2926, 2887, 1639, 1618, 1456, 1240, 1074, 914, 783, 717 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{19}H_{23}INaO_4$ $[M+Na]^+$: 465.0533, found: 465.0542.



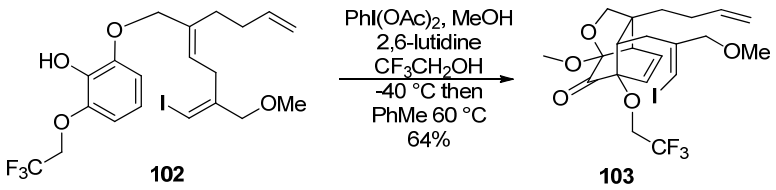
In a high-pressure flask was charged phenol (9.94 g, 22.5 mmol), cesium carbonate (7.33 g, 22.5 mmol), 2, 2, 2-trifluoroethyl trifluoromethanesulfonate (4.86 mL, 33.7 mmol) and dry acetonitrile (112 mL). The flask was flushed with N_2 for 5 minutes, capped and heated at 85 °C (bath temperature) for 2.0 h. The reaction solution gradually turned from light yellow to colorless. After cooling to r.t., the reaction mixture was diluted with ethyl acetate (150 mL) and filtered through a Celite pad. The filtrate was washed with saturated $NaHCO_3$ solution (3 × 100 mL) and brine (150 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography (15% ethyl acetate/hexanes) to afford a light yellow oil (11.5 g, 98% yield). ^{1}H NMR (400 MHz, $CDCl_3$) □ 10.52 (s, 1H), 7.43 (t, *J* = 8.4 Hz, 1H), 6.70 (d, *J* = 8.4, 1H), 6.56 (d, *J* = 8.4 Hz, 1H), 6.31 (td, *J* = 1.4, 0.6 Hz, 1H), 5.85 (ddt, *J* = 17.1, 10.2, 6.6 Hz, 1H), 5.58 (tt, *J* = 7.3, 1.1 Hz, 1H), 5.06 (dq, *J* = 17.1, 1.6 Hz, 1H), 4.99 (ddt, *J* = 10.2, 1.9, 1.2 Hz, 1H), 4.54 (q, *J* = 1.1 Hz, 2H), 4.42 (q, *J* = 8.1 Hz, 2H), 3.88 (d, *J* = 1.4 Hz, 2H), 3.29 (s, 3H), 3.06 (d, *J* = 7.3 Hz, 2H), 2.42 – 2.34 (m, 2H), 2.29 – 2.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 188.30, 161.38, 159.50, 146.70, 138.00, 136.15, 135.58, 125.07, 123.25 55 (q, *J* = 278.72 Hz), 116.08, 115.31,

107.77, 106.89, 79.37, 74.92, 72.84, 67.37 (q, J = 35.8 Hz), 58.09, 33.84, 32.36, 27.84; IR (film) 3076, 2978, 2927, 2877,2823, 2779, 1693, 1598, 1473, 1288, 1246, 1166, 1122, 777 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{21}H_{24}F_3INaO_4$ $[M+Na]^+$: 547.0564, found: 547.0566.



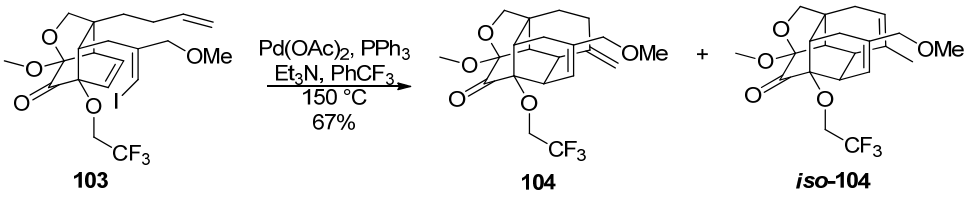
In a high-pressure flask, 10 M sulfuric acid (3.9 mL, 39.3 mmo) was added to a suspension of boric acid (1.21 g, 19.6 mmol) in THF (30 mL) with stirring. Heat was generated during addition. After the flask had been cooled to r.t. in air, hydrogen peroxide (30 wt% in water, 0.98 mL, 8.65 mmol) was added slowly. After stirring at r.t. for 1.0 h, phenyl aldehyde (2.06 g, 3.93 mmol) in THF (10 mL) was added. The high-pressure flask was capped and immersed in 50 °C oil bath and heated for 4.0h. The reaction mixture turned from colorless to light yellow gradually. After the reaction was cooled to r.t., ethyl acetate (100 mL) was added and the mixture was washed with water (3 × 50 mL) and brine (50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (10% ethyl acetate/hexanes) to yield a colorless oil (1.63 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) □ 6.74 (dd, J = 8.3, 8.3 Hz, 1H), 6.65 (dd, J = 8.3, 1.4 Hz, 1H), 6.62 (dd, J = 8.3, 1.4 Hz, 1H), 6.31 (td, J = 1.3, 0.6 Hz, 1H), 5.85 (ddt, J = 17.1, 10.2, 6.5 Hz, 1H), 5.57 (s, 1H), 5.51 (tt, J = 7.3, 1.0 Hz, 1H), 5.07 (dq, J = 17.1, 1.4 Hz, 1H), 5.00 (ddt, J = 10.2, 1.9, 1.1 Hz, 1H), 4.52 (q, J = 1.0 Hz, 2H), 4.43 (q, J = 8.3 Hz, 2H), 3.84 (d, J = 1.3 Hz, 2H), 3.27 (s, 3H), 3.05 (d, J = 7.3, 2H), 2.40 – 2.31 (m, 2H), 2.30 – 2.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 146.99, 146.65, 145.27, 138.00, 136.78, 136.64, 125.52, 123.55 (q, J = 278.72 Hz), 119.21, 115.38,

110.01, 108.54, 79.46, 74.90, 73.42, 67.84 (q, J = 35.3 Hz), 58.03, 33.87, 32.52, 27.90; IR (film) 3535, 3076, 2978, 2931, 2823, 1612, 1479, 1280, 1163, 1087, 1031, 966, 914, 777, 717 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{20}H_{24}F_3INaO_4$ $[M+Na]^+$: 535.0564, found: 535.0570.



To a solution of phenol (440.7 mg, 0.860 mmol) and 2,6-lutidine (0.5 mL, 4.30 mmol) in 2,2,2-triflouroethanol (76 mL) was added a solution of iodobenzene diacetate (290.9 mg, 0.903 mmol) in MeOH (10 mL) dropwise at -40 °C (acetonitrile/dry ice bath). After the addition was completed, the reaction was stirred at the same temperature for 1.0 h then transferred via cannula to pre-heated (70 °C) toluene (340 mL) in a 1 L 3-neck round-bottom flask equipped with a condenser. The resultant solution was stirred at 60 °C for 16 h while the reaction solution turned from yellow to light yellow gradually. After that period of time, the reaction was cooled to r.t., the solvent was removed on rotovap and the residue was placed under vacuum for a few hours to remove residual 2, 6-lutidine. Purification of the crude product by column chromatography (10-15% ethyl acetate/hexanes) gave a light yellow oil, 298.2 mg (64% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.27 (m, 2H), 5.77 (ddt, J = 17.1, 10.2, 6.3 Hz, 1H), 5.05 (dq, J = 17.1, 1.7 Hz, 1H), 5.00 (dq, J = 10.2, 1.5 Hz, 1H), 4.31 (dq, J = 11.3, 8.6 Hz, 1H), 4.13 (dq, J = 11.3, 8.6 Hz, 1H), 4.09 (d, J = 8.3 Hz, 1H), 4.04 (dd, J = 12.2, 0.9 Hz, 1H), 3.99 (dd, J = 12.2, 1.3 Hz, 1H), 3.85 (d, J = 8.3 Hz, 1H), 3.53 (s, 3H), 3.26 (s, 3H), 3.14 (dd, J = 5.5, 3.0 Hz, 1H), 2.81 (t, J = 7.1 Hz, 1H), 2.47 (ddd, J = 15.6, 6.6, 1.3 Hz, 1H), 2.35 (ddd, J = 15.6, 7.7, 1.1 Hz, 1H), 2.11 (dddt, J = 13.1, 7.8, 6.3, 1.5 Hz, 2H), 1.63 – 1.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.95, 146.95, 137.48, 129.97, 128.60, 123.64 (q, J = 277.5 Hz), 115.50, 99.64, 86.83, 80.72, 78.18, 75.50, 63.59 (q, J = 35.1 Hz), 57.68, 51.93, 50.24, 47.04, 45.38,

32.53, 30.73, 29.48; IR (film) 3074, 2976, 2937, 2893, 1755, 1641, 1454, 1284, 1161, 1093, 968, 889, 783, 688 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{21}H_{27}F_3IO_5$ $[M+H]^+$: 543.0850, found: 543.0841.



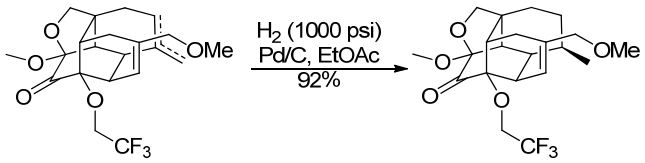
103 **104** ***iso*-104**

In a high-pressure flask charged with vinyl iodide (600 mg, 1.11 mmol) in trifluorotoluene (110 mL) was added triphenylphosphine (349.4 mg, 1.33 mmol) and triethylamine (0.77 mL, 5.55 mmol). The solution was purged with N_2 for 30 min and palladium (II) acetate (24.8 mg, 0.111 mmol) was added. After addition, the solution was purged with N_2 again for 30 min before the flask was capped and immersed in 150 °C oil bath. The reaction solution was stirred at 150 °C for 2 h and turned from light yellow to yellow over time. After cooling to r.t. the reaction mixture was filtered through a Celite pad and the filtrate was concentrated. The residue was purified by column chromatography (10-15% ethyl acetate/hexanes) to afford two white solids, the higher R_f product being *exo*-olefin **104** (257.6 mg, 56% yield) and the lower R_f product being *endo*-olefin ***iso*-104** (50.6 mg, 11% yield).

Exo-olefin **104**: ^{1}H NMR (400 MHz, $CDCl_3$) □ 5.58 (dq, *J* = 7.1, 1.5 Hz, 1H), 4.83 (m, 1H), 4.77 (tt, *J* = 1.7, 0.9 Hz, 1H), 4.10 (dq, *J* = 10.7, 8.6 Hz, 1H), 3.89 (d, *J* = 12.3 Hz, 1H), 3.86 (dq, *J* = 10.7, 8.6 Hz, 1H), 3.83 (d, *J* = 7.4 Hz, 1H), 3.75 (d, *J* = 12.3 Hz, 1H), 3.71 (d, *J* = 7.4 Hz, 1H), 3.59 (s, 3H), 3.29 (s, 3H), 3.21 (dd, *J* = 11.3, 2.8 Hz, 1H), 2.79 (ddd, *J* = 10.9, 7.1, 3.0 Hz, 1H), 2.51 (dt, *J* = 5.7, 2.5 Hz, 1H), 2.42 – 2.26 (m, 3H), 2.21 (dd, *J* = 17.1, 8.1 Hz, 1H),), 2.08 (dd, *J* = 13.7, 7.7 Hz, 1H), 1.91 (d, *J* = 2.8 Hz, 1H), 1.48 (ddd, *J* = 13.7, 12.3, 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 204.99, 145.34, 137.70, 123.82 (q, *J* = 277.6 Hz), 119.42, 113.29, 103.14, 82.85, 80.05, 76.02, 63.05 (q, *J* = 34.8 Hz), 58.23, 52.19, 48.39, 45.45, 40.15, 37.72, 36.11, 28.24, 28.03, 24.88; IR (film) 3072, 2978, 2922, 2873, 1749, 1639, 1462, 1284,

1161, 1107, 972, 896, 734, 682 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{21}H_{26}F_3O_5$ $[M+H]^+$: 415.1727, found: 415.1729.

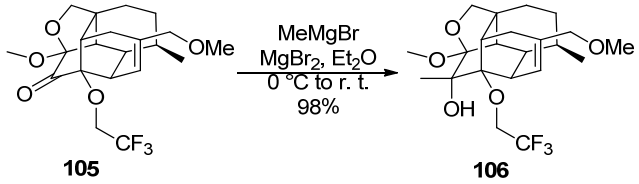
Endo-olefin ***iso*-104**: ^1H NMR (400 MHz, $CDCl_3$) □ 5.55 (dt, *J* = 6.5, 1.6 Hz, 1H), 5.35 (ddd, *J* = 4.3, 2.8, 1.5 Hz, 1H), 4.14 (dq, *J* = 10.7, 8.5 Hz, 1H), 3.89 (d, *J* = 7.3 Hz, 1H), 3.88 (dq, *J* = 10.7, 8.5 Hz, 1H), 3.84 (d, *J* = 7.3 Hz, 1H), 3.79 (s, 2H), 3.61 (s, 3H), 3.24 (s, 3H), 2.85 – 2.71 (m, 2H), 2.45 – 2.34 (m, 2H), 2.24 (d, *J* = 2.8 Hz, 1H), 2.26 – 2.16 (m, 1H), 2.11 – 2.01 (m, 2H), 1.54 (dt, *J* = 2.8, 1.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 204.66, 138.57, 137.60, 123.82 (q, *J* = 277.6 Hz), 121.09, 117.78, 103.15, 82.36, 79.61, 76.01, 63.10 (q, *J* = 34.8 Hz), 57.33, 52.17, 45.61, 44.51, 38.24, 36.84, 36.09, 30.43, 25.01, 24.83; IR (film) 2929, 2845, 1749, 1454, 1284, 1157, 1107, 1066, 993, 883, 844, 736 cm^{-1} ; HRMS (MALDI) *m/z* calcd. for $C_{21}H_{25}F_3O_5Li$ $[M+Li]^+$: 421.1809, found: 421.1804.



104/*iso*-104 **105**

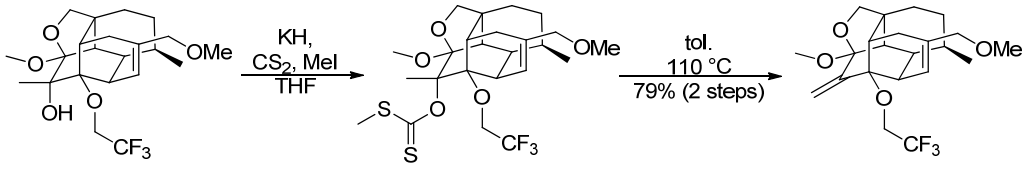
In a 4-mL clear vial, palladium on carbon (10 wt%, 6.9 mg, 0.00647 mmol) was added to a solution of diene (exo- or endo-olefin form the previous step, 26.8 mg, 0.0647 mmol) in ethyl acetate (2.0 mL). Six of this vial were placed in a hydrogenation bomb and stirred at r.t. under 1000 psi H_2 for 8.0 h. The reaction mixtures were filtered through a Celite pad and the filtrates were combined and concentrated to afford a white solid (161.0 mg, 92% yield). This solid was used without further purification. (Note: The hydrogenation of the endo-olefin usually requires high pressure, however for the exo-olefin, the pressure requirement varies depending on the suppliers and batches of the palladium catalyst. In some cases the reaction was conducted under a hydrogen balloon.) ^1H NMR (600 MHz, $CDCl_3$) □ 5.76 (dt, *J* = 7.0, 1.7 Hz, 1H), 4.10 (dq, *J* = 10.7, 8.6 Hz, 1H), 3.88 (d, *J* = 12.8, 1H), 3.79 (dq, *J* = 10.7, 8.6 Hz, 1H), 3.79 (d, *J* = 7.3 Hz, 1H), 3.77 (d, *J* = 12.8, 1H), 3.71 (d, *J* = 7.3 Hz, 1H), 3.61 (s, 2H), 3.32 (s, 3H), 2.76 (ddd, *J* = 10.7, 7.3, 3.1 Hz, 1H), 2.50 –

2.43 (m, 2H), 2.29 (dd, *J* = 19.0, 7.7 Hz, 1H), 2.20 (dt, *J* = 19.0, 1.1 Hz, 1H), 2.09 (dd, *J* = 13.5, 6.0 Hz, 1H), 1.83 (d, *J* = 2.4 Hz, 1H), 1.67 (dddd, *J* = 12.8, 7.0, 5.8, 3.7 Hz, 1H), 1.63 – 1.54 (m, 1H), 1.47 – 1.42 (m, 1H), 1.42 – 1.35 (m, 2H), 1.12 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 205.88, 137.96, 123.87 (d, *J* = 277.6 Hz), 118.91, 103.09, 82.92, 80.72, 76.00, 63.08 (q, *J* = 34.7 Hz), 58.48, 52.44, 51.13, 45.58, 37.76, 37.52, 35.94 (2C), 28.87, 25.77, 24.59, 21.18; IR (film) 2980, 2914, 2875, 2827, 1751, 1284, 1157, 1103, 1070, 975, 885, 732 cm^{-1} ; HRMS (MALDI) *m/z* calcd. for $C_{21}H_{27}F_3O_5Li$ $[M+Li]^+$: 423.1965, found: 423.1954.



Magnesium bromide diethyl etherate (1.59 g, 6.16 mmol) in a flask was dried by heating gently under vacuum. After the flask was cooled to r.t., anhydrous diethyl ether (15 mL) was added. Magnesium bromide dissolved in ether and two layers of liquid were resulted. Ketone (854.8 mg, 2.05 mmol) in diethyl ether (25 mL) was then added. A white cloudy suspension was formed with a layer of oil on the bottom of the flask. The mixture was cooled to 0 °C with vigorous stirring. Methylmagnesium bromide (3.0 M in diethyl ether, 2.06 mL, 6.18 mmol) was added dropwise while the suspension turned to a clear solution and the oil layer remained unchanged. After the addition was completed, the reaction mixture was warmed to r.t. and stirred for 1.5 h, during that period of time a white precipitate formed and the oil layer gradually disappeared. The reaction was then cooled to 0 °C, quenched by saturated NH_4Cl solution (30 mL) and diluted with water (30 mL) and ethyl acetate (50 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (10% ethyl acetate/hexanes) to afford a colorless oil (868.8 mg, 98% yield). ^{1}H NMR (400 MHz, $CDCl_3$) 5.77 (dt, *J* = 7.2, 1.6 Hz, 1H), 4.17 (dq, *J* = 10.8, 8.8 Hz, 1H), 3.86 (ddd, *J* = 12.5, 1.5, 0.7 Hz,

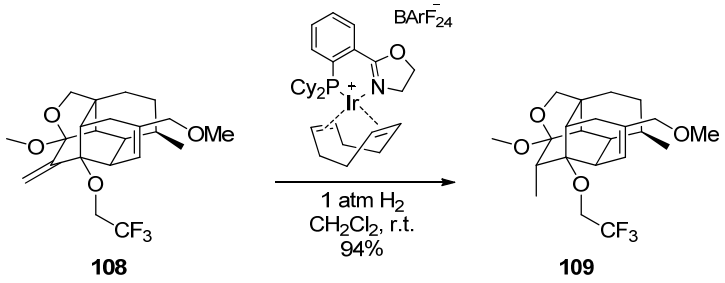
1H), 3.75 (ddd, *J* = 12.5, 1.5, 0.7 Hz, 1H), 3.57 (d, *J* = 6.8 Hz, 1H), 3.48 (dq, *J* = 10.8, 8.8 Hz, 1H), 3.42 (d, *J* = 6.8 Hz, 1H), 3.34 (s, 3H), 3.31 (s, 3H), 3.12 (ddt, *J* = 10.6, 7.4, 3.1 Hz, 1H), 2.91 (s, 1H), 2.40 – 2.25 (m, 2H), 2.11 – 1.89 (m, 3H), 1.76 – 1.51 (m, 2H), 1.48 (d, *J* = 2.2 Hz, 1H), 1.34 – 1.20 (m, 2H), 1.23 (s, 3H), 1.11 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 138.88, 124.50 (q, *J* = 277.5 Hz), 120.44, 106.63, 82.18, 80.98, 78.53, 76.30, 62.82 (q, *J* = 33.9 Hz), 58.44, 49.59, 44.29, 44.04, 40.40, 37.87, 36.15, 28.75, 28.55, 26.12, 25.60, 21.45, 16.92; IR (film) 3552, 2981, 2933, 2912, 2872, 1463, 1375, 1282, 1165, 1147, 989, 862 cm^{-1} ; HRMS (MALDI) *m/z* calcd. for $C_{22}H_{31}F_3O_5Li$ $[M+Li]^+$: 439.2278, found: 439.2275.



Potassium hydride (30 wt% in mineral oil, 1.06 g, 7.95 mmol) was washed with dry pentane for three times under N_2 then suspended in THF (10 mL). Alcohol (0.86 g, 1.99 mmol) in THF (10 mL) was added dropwise at 0 °C. After stirring at 0 °C for 2.0 h, freshly distilled carbon disulfide (1.20 mL, 19.9 mmol) was added dropwise. The reaction was stirred at 0 °C for 1.0 h and r.t. 6.0h. After that period of time, the reaction was cooled to 0 °C again and methyl iodide (1.24 mL, 19.9 mmol) was added dropwise. The resultant mixture was allowed to warm up to r.t. and stirred for 12 h. The reaction was then quenched by water (10 mL) at 0 °C and diluted with ethyl acetate (20 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 15 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated.

The crude product from the previous operation was dissolved in toluene (200 mL, 0.01 M) and heated at 110 °C for 2.0 h. After cooling to r.t. the reaction mixture was concentrated. The residue was purified by column chromatography (10% ethyl acetate/hexanes) to afford a light yellow solid (0.65 g, 79% yield over 2 steps). (Note: To assure the success of the subsequent iridium catalyzed hydrogenation, this solid

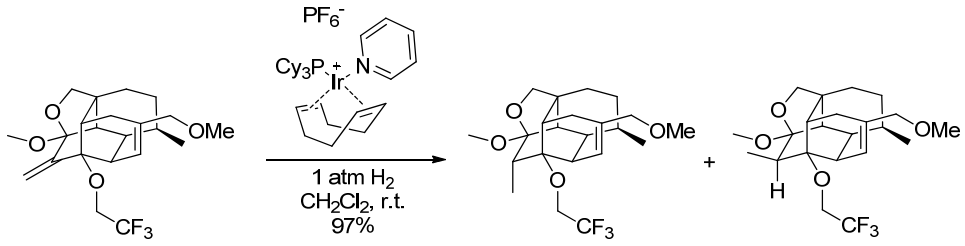
should be further purified by trituration with hexanes and filtration to remove the tiny amount of colored impurities.) ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (dt, *J* = 7.5, 1.4 Hz, 1H), 5.53 (d, *J* = 1.1 Hz, 1H), 5.14 (t, *J* = 0.9 Hz, 1H), 3.94 (dq, *J* = 10.8, 8.8 Hz, 1H), 3.91 (d, *J* = 12.5 Hz, 1H), 3.75 (d, *J* = 12.5Hz, 1H), 3.70 (dq, *J* = 10.8, 8.8 Hz, 1H), 3.66 (d, *J* = 7.1 Hz, 1H), 3.52 (d, *J* = 7.1 Hz, 1H), 3.39 (s, 3H), 3.30 (s, 3H), 2.48 – 2.39 (m, 1H), 2.32 – 2.12 (m, 4H), 2.03 (dd, *J* = 13.2, 5.5 Hz, 1H), 1.71 (d, *J* = 2.2 Hz, 1H), 1.68 – 1.50 (m, 2H), 1.44 – 1.25 (m, 2H),1.07 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, CDCl3) δ 149.23, 135.85, 124.15 (q, *J* = 277.3 Hz), 122.80, 106.65, 105.52, 82.11, 79.29, 76.29, 61.60 (q, *J* = 34.3 Hz), 57.82, 49.53, 46.57, 44.69, 41.17, 38.40, 37.42, 36.78, 29.00, 26.06, 24.84, 21.30; IR (film) 2980, 2916, 2873, 1276, 1161, 1103, 1083, 964, 866 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{22}H_{30}F_3O_4$ $[M+H]^+$: 415.2091, found: 415.2086.



108 **109**

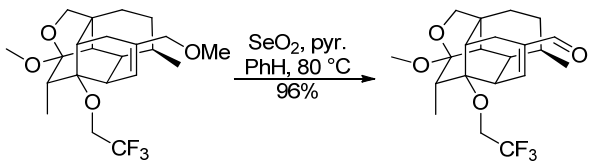
To a solution of diene (464.0 mg, 1.12 mmol) in CH_2Cl_2 (11.2 mL), iridium catalyst[11] (16.9 mg, 0.0112 mmol) was added in one portion. Hydrogen was bubbled into the resultant pink solution for 5.0 min. The color was quickly discharged and the solution turned to light yellow. The reaction was stirred at r.t. under H_2 balloon for 22 h. After removal of solvent, the residue was purified by column chromatography (15% ethyl acetate/hexanes) to afford a white solid (439.4 mg, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.76 (dt, *J* = 7.2, 1.5 Hz, 1H), 3.88 (d, *J* = 12.1 Hz, 1H), 3.74 (d, *J* = 12.1 Hz, 1H), 3.72 (dq, *J* = 10.8, 8.8 Hz, 1H), 3.63 (dq, *J* = 10.8, 8.8 Hz, 1H), 3.58 (d, *J* = 6.9 Hz, 1H), 3.40 (d, *J* = 6.9 Hz, 1H), 3.33 (s, 3H), 3.29 (s, 3H), 2.56 (ddd, *J* = 10.5, 7.2, 2.8 Hz, 1H), 2.28 (ddd, *J* = 11.3, 3.5, 2.1 Hz, 1H), 2.19 (q, *J* = 7.2 Hz, 1H), 2.15 – 2.08 (m, 3H), 1.95 (dd, *J* = 13.4, 6.3 Hz, 1H), 1.74 – 1.62 (m, 1H), 1.58 (dddd, *J* = 12.5, 7.0, 5.5, 3.5 Hz, 1H), 1.41 (d, *J* = 2.1 Hz, 1H), 1.37 – 1.18 (m, 2H), 1.09 (d, *J*

= 7.0 Hz, 3H), 0.97 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.87, 124.18 (q, *J* = 277.7 Hz), 123.50, 107.97, 81.39, 79.85, 76.45, 60.58 (q, *J* = 34.4 Hz), 57.83, 49.98, 46.49, 44.15, 43.46, 39.06, 37.46, 36.06, 33.16, 28.19, 26.21, 25.25, 21.40, 9.02; IR (film) 2980, 2926, 2875, 1463, 1384, 1280, 1161, 1109, 1020, 862, 678 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{22}H_{32}F_3O_4$ $[M+H]^+$: 417.2247, found: 417.2250.



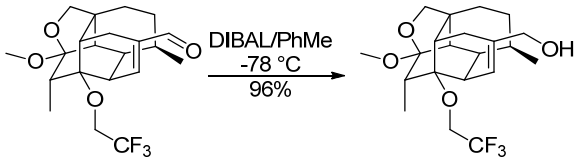
108 **109** **110**

To a solution of diene (138.2 mg, 0.334 mmol) in CH_2Cl_2 (6.7 mL) Crabtree's catalyst (13.4 mg, 0.0167 mmol) was added in one portion. Hydrogen was bubbled into the resultant pink solution for 5.0 min. The color was quickly discharged and the solution turned to bright yellow. The reaction was stirred at r.t. under H_2 balloon for 2 h. After concentration, the residue was purified by column chromatography (15% ethyl acetate/hexanes) to afford two white solids: **110** (higher R_f, 74.5 mg, 54% yield) and **109** (lower R_f, 60.2 mg, 43% yield). Undesired diastereomer **110**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.73 (dt, *J* = 6.9, 1.6 Hz, 1H), 3.85 (d, *J* = 12.7 Hz, 1H), 3.74 (d, *J* = 12.7 Hz, 1H), 3.59 (d, *J* = 6.9 Hz, 1H), 3.54 (dq, *J* = 10.1, 8.3 Hz, 1H), 3.45 (d, *J* = 6.9 Hz, 1H), 3.39 (dq, *J* = 10.1, 8.3 Hz, 1H), 3.30 (s, 3H), 3.30 (s, 3H), 2.36 (ddd, *J* = 10.4, 6.8, 3.0 Hz, 1H), 2.33 – 2.25 (m, 2H), 2.11 (dd, *J* = 7.6, 3.1 Hz, 1H), 2.05 (d, *J* = 18.6 Hz, 1H), 1.97 (m, 2H), 1.64 – 1.56 (m, 2H), 1.51 (d, *J* = 2.2 Hz, 1H), 1.35 – 1.24 (m, 2H), 1.10 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.08, 124.18 (q, *J* = 277.6 Hz), 119.84, 108.96, 82.07, 78.44, 76.15, 60.94 (q, *J* = 34.3 Hz), 58.28, 49.20, 45.14, 43.60, 43.47, 38.99, 37.51, 36.29, 36.07, 28.93, 26.19, 25.35, 21.39, 6.89; IR (film) 2981, 2911, 2875, 2829, 1462, 1451, 1279, 1165, 1130, 1120, 1088, 1013, 970 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{22}H_{32}F_3O_4$ $[M+H]^+$: 417.2247, found: 417.2242.



109 **111**

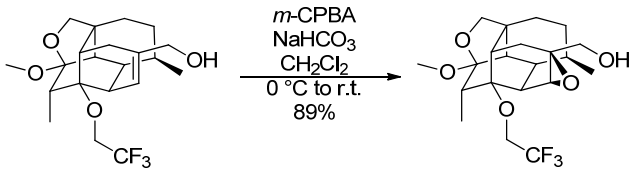
A high-pressure tube charged with a solution of vinyl ether (110 mg, 0.264 mmol) in benzene (5.0 mL), selenium dioxide (146.5 mg, 1.32 mmol) and pyridine (0.21 mL, 2.64 mmol) was sealed and heated to 80 °C. The reaction solution turned from colorless to light yellow and a pink precipitate formed on the flask wall and turned black over time. After 42 h the reaction mixutre was cooled to r.t. and filtered through a Celite pad. The filtrate was concentrated and purified by column chromatography (20% ethyl acetate/hexanes) to afford a white solid (101.8 mg, 96% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.48 (s, 1H), 7.00 (dt, *J* = 7.3, 1.8 Hz, 1H), 3.69 (dq, *J* = 11.0, 8.4 Hz, 1H), 3.63 (d, *J* = 7.1 Hz, 1H), 3.57 (dq, *J* = 10.9, 8.5 Hz, 1H), 3.44 (d, *J* = 7.2 Hz, 1H), 3.35 (s, 3H), 2.84 (ddd, *J* = 11.1, 7.3, 3.2 Hz, 1H), 2.50 – 2.44 (m, 2H), 2.28 (ddt, *J* = 19.5, 7.6, 1.1 Hz, 1H), 2.25 – 2.19 (m, 2H), 1.97 – 1.89 (m, 1H), 1.62 (ddt, *J* = 14.3, 7.0, 3.7 Hz, 1H), 1.47 (d, *J* = 2.1 Hz, 1H), 1.38 – 1.19 (m, 3H), 1.10 (d, *J* = 7.1 Hz, 3H), 0.99 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.87, 150.60, 142.77, 123.90 (q, *J* = 277.7 Hz), 107.71, 81.20, 79.90, 60.45 (q, *J* = 34.6 Hz), 50.09, 46.26, 44.17, 43.29, 38.08, 37.23, 36.92, 34.82, 27.96, 26.09, 21.62, 21.11, 8.95; IR (film) 2981, 2933, 2877, 1678, 1282, 1163, 1147, 1111, 1018, 731 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{28}F_3O_4$ $[M+H]^+$: 401.1934, found: 401.1936.



111 **112**

To a solution of α,β-unsaturated aldehyde (156.6 mg, 0.391 mmol) in toluene (7.8 mL) was added DIBAL (1.0 M in toluene, 0.59 mL) dropwise at -78 °C. The reaction was stirred at -78 °C for 1.0 h then quenched by 15% Rochelle's salt solution (10 mL). The mixture was diluted with ethyl acetate (10 mL), warmed to r.t. and

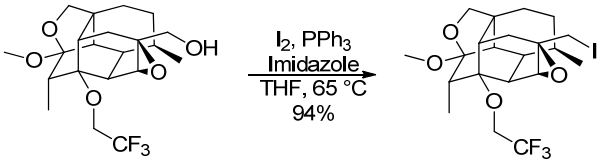
stirred vigorously until two clear layers formed. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (30% ethyl acetate/hexanes) to afford a white solid (151.3 mg, 96% yield). ^{1}H NMR (600 MHz, $CDCl_3$) □ 5.79 (dt, *J* = 6.9, 1.5 Hz, 1H), 4.08 – 3.97 (m, 2H), 3.70 (dq, *J* = 10.9, 8.5 Hz, 1H), 3.62 (dq, *J* = 10.9, 8.5 Hz, 1H), 3.59 (d, *J* = 6.9 Hz, 1H), 3.41 (d, *J* = 6.9 Hz, 1H), 3.34 (s, 3H), 2.55 (ddd, *J* = 10.7, 7.1, 2.8 Hz, 1H), 2.29 (dt, *J* = 11.2, 2.7 Hz, 1H), 2.22 – 2.11 (m, 4H), 1.96 (dd, *J* = 13.7, 6.3 Hz, 1H), 1.70 – 1.54 (m, 2H), 1.42 (d, *J* = 2.1 Hz, 1H), 1.37 – 1.24 (m, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 138.42, 124.26 (q, *J* = 277.8 Hz), 121.84, 108.07, 81.41, 79.79, 66.78, 60.60 (q, *J* = 34.2 Hz), 50.05, 46.42, 44.11, 43.62, 38.89, 37.47, 36.01, 33.04, 28.22, 26.35, 24.81, 21.45, 9.04; IR (film) 3429, 2980, 2929, 2875, 1463, 1280, 1161, 1116, 1055, 1037, 1018, 862, 734 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{21}H_{30}F_3O_4$ $[M+H]^+$: 403.2091, found: 403.2089.



112 **113**

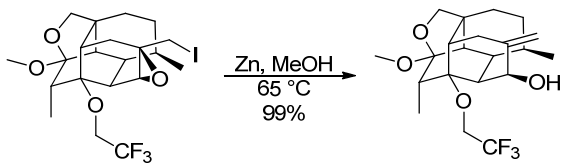
A mixture of allylic alcohol (82.2 mg, 0.204 mmol), $NaHCO_3$ (51.4 mg, 0.612 mmol) in CH_2Cl_2 (4.0 mL) was cooled to 0 °C, to which *meta*-chloroperoxybenzoic acid (70-75 wt% with benzoic acid and water, 75.6 mg, 0.306 mmol) was added in one portion. The reaction was allowed to warm to r.t. naturally and stirred for total 15 h. After that period of time, the reaction mixture became cloudy, and then water (2 mL) and ethyl acetate (10 mL) were added. The organic phase was separated and washed with saturated $NaHSO_3$ (3 × 2 mL), saturated $NaHCO_3$ (3 × 2 mL) and brine (2 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (50% ethyl acetate/hexanes) to afford a white solid (75.8 mg, 89% yield). ^{1}H NMR (500 MHz, $CDCl_3$) □ 3.82 (dd, *J* = 12.7, 2.4 Hz,

1H), 3.77 – 3.59 (m, 4H), 3.51 (d, *J* = 6.9 Hz, 1H), 3.35 (d, *J* = 6.9 Hz, 1H), 3.32 (s, 3H), 2.70 (dt, *J* = 10.8, 2.7 Hz, 1H), 2.41 (dt, *J* = 10.8, 2.4 Hz, 1H), 2.12 (q, *J* = 7.2 Hz, 1H), 2.00 (dd, *J* = 16.0, 6.8 Hz, 1H), 1.96 – 1.89 (m, 2H), 1.86 – 1.75 (m, 3H), 1.69 – 1.47 (m, 3H), 1.47 – 1.44 (m, 1H), 1.21 (d, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 124.21 (q, *J* = 278.1 Hz), 107.00, 81.22, 81.00, 63.38, 60.20 (q, *J* = 34.7 Hz), 58.36, 56.38, 50.12, 49.06, 44.14, 44.01, 39.52, 37.27, 34.17, 32.38, 27.00, 26.90, 23.21, 21.70, 8.97; IR (film) 3449, 2932, 2880, 1736, 1464, 1279, 1166, 1149, 1118, 1049, 1012, 964, 931, 782 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{21}H_{30}F_3O_5$ $[M+H]^+$: 419.2040, found: 419.2032.



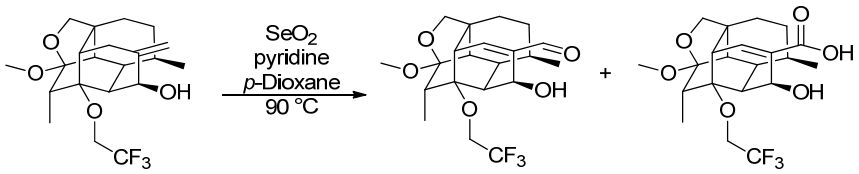
113 **114**

To a solution of epoxy alcohol (75.8 mg, 0.181 mmol) in THF (3.6 mL), triphenylphosphine (71.1 mg, 0.272 mmol), imidazole (24.4 mg, 0.363 mmol) and iodine (69.1 mg, 0.272 mmol) were added in sequence. The reaction mixture was stirred at 65 °C for 16 h then cooled to r.t. and diluted with ethyl acetate (10 mL). After washing with 10% $Na_2S_2O_3$ (5 mL) and brine (5 mL) the solution was dried over anhydrous Na_2SO_4, filtered and concentrated. Purification of the crude product by column chromatography (20% ethyl acetate/hexanes) afforded a white solid (90.0 mg, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) 3.80 – 3.57 (m, 5H), 3.51 (d, *J* = 6.9 Hz, 1H), 3.39 – 3.32 (m, 1H), 3.31 (s, 3H), 3.10 (d, *J* = 10.1 Hz, 1H), 2.59 (dt, *J* = 10.9, 2.7 Hz, 1H), 2.41 (dt, *J* = 10.8, 2.4 Hz, 1H), 2.31 – 2.20 (m, 1H), 2.10 (q, *J* = 7.2 Hz, 1H), 2.00 – 1.74 (m, 3H), 1.74 – 1.59 (m, 1H), 1.58 – 1.42 (m, 3H), 1.23 (d, *J* = 7.2 Hz, 3H), 1.01 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 124.14 (q, *J* = 278.3 Hz), 106.94, 81.11, 80.26, 63.74, 60.26 (q, *J* = 34.7 Hz), 55.97, 50.16, 49.06, 44.10, 44.08, 40.16, 37.34, 34.02, 33.61, 27.43, 27.11, 26.81, 21.80, 15.12, 9.05; IR (film) 2975, 2932, 2878, 1462, 1279, 1150, 1116, 1014, 965, 732 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{21}H_{29}F_3IO_4$ $[M+H]^+$: 529.1057, found: 529.1058.



114 **115**

In a high-pressure tube a mixture of epoxide (90.0 mg, 0.170 mmol), zinc powder (111.0 mg, 1.70 mmol, used as received from commercial supplier without further treatment) in MeOH (8.5 mL) was heated at 65 °C for 20 h then cooled to r.t. The unreacted zinc solid was filtered off over a Celite pad and the filtrate was concentrated then purified by column chromatography (15% ethyl acetate/hexanes) to afford a white solid (68.4 mg, 99% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.32 (s, 1H), 5.12 (s, 1H), 4.78 (d, *J* = 11.7 Hz, 1H), 3.79 (dq, *J* = 11.0, 8.3 Hz, 1H), 3.66 (dq, *J* = 11.0, 8.3 Hz, 1H), 3.51 (d, *J* = 6.9 Hz, 1H), 3.37 (d, *J* = 6.9 Hz, 1H), 3.31 (s, 2H), 3.06 (d, *J* = 11.7 Hz, 1H), 2.71 (dq, *J* = 18.8, 1.8 Hz, 1H), 2.67 – 2.59 (m, 1H), 2.51 (dd, *J* = 12.2, 3.1 Hz, 1H), 2.37 (dt, *J* = 12.2, 2.4 Hz, 1H), 2.17 (q, *J* = 7.2 Hz, 1H), 2.07 – 2.02 (m, 1H), 1.98 – 1.90 (m, 1H), 1.77 – 1.62 (m, 2H), 1.47 – 1.39 (m, 1H), 1.45 (d, *J* = 2.0 Hz, 1H), 1.33 (ddd, *J* = 14.0, 12.0, 6.9 Hz, 1H), 1.22 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.94, 123.94 (q, *J* = 277.9 Hz), 114.97, 107.79, 83.16, 80.80, 68.70, 59.95 (q, *J* = 34.8 Hz), 50.14, 48.61, 43.77, 43.50, 40.32, 39.24, 37.66, 34.38, 28.61, 27.39, 26.35, 21.74, 9.05; IR (film) 3564, 2926, 2881, 2858, 1454, 1282, 1273, 1165, 1109, 1024, 979, 678 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{21}H_{30}F_3O_4$ $[M+H]^+$: 403.2090, found: 403.2091.



115 **116** **117**

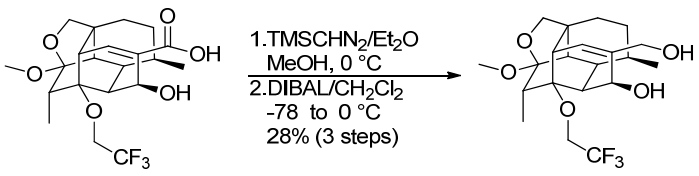
In a 4-mL clear vial, a mixture of allylic alcohol (15.0 mg, 0.0373 mmol), pyridine (0.03 mL, 0.373 mmol) and selenium dioxide (20.7 mg, 0.186 mmol) in *p*-dioxane (1.2 mL) was heated to 90 °C and stirred for 16 h. After cooling to r.t., the reaction mixture was filtered through a Celite pad and the filtrate was concentrated.

The residue was dissolved in ethyl acetate (10 mL) and washed with saturated $NaHCO_3$ (3 × 5 mL) and brine (5 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated to afford the aldehyde product. The aqueous phase was acidified to pH 1.0 by 1 N HCl, and then extracted with ethyl acetate (3 × 10 mL). The extracts were combined and washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated to afford the acid product. Both crude products were converted to alcohol and purified afterward.

116 **95**

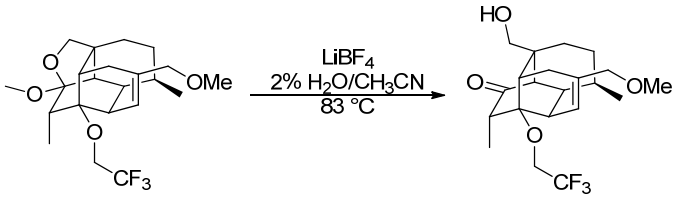
The aforementioned crude aldehyde was dissolved in CH_2Cl_2 (0.30 mL) and cooled to -78 °C, DIBAL (1.0 M in CH_2Cl_2, 0.11 mL) was added dropwise. The reaction was stirred at -78 °C for 2 h then quenched by 10% Rochelle's salt solution (1 mL). The mixture was diluted with ethyl acetate (5 mL), warmed to r.t. and stirred vigorously until two clear layers formed. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 2 mL). The combined organic layers were washed with brine (3 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography (40% ethyl acetate/hexanes) to provide a colorless oil (3.2 mg, 20% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (d, *J* = 7.2 Hz, 1H), 4.56 (d, *J* = 11.4 Hz, 1H), 4.30 (m, 2H), 3.71 – 3.60 (dq, *J* = 10.7, 8.4 Hz, 1H), 3.62 (d, *J* = 7.1 Hz, 1H), 3.47 (dq, *J* = 10.7, 8.4 Hz, 1H), 3.33 (d, *J* = 7.1 Hz, 1H), 3.32 (s, 3H), 3.03 (d, *J* = 11.4 Hz, 1H), 2.56 – 2.46 (m, 2H), 2.36 (dt, *J* = 11.9, 2.6 Hz, 1H), 2.26 (dd, *J* = 7.2, 2.9 Hz, 1H), 2.18 (q, *J* = 7.2 Hz, 1H), 1.80 – 1.58 (m, 2H), 1.45 – 1.37 (m, 2H), 1.36 – 1.26 (m, 2H), 1.23 (d, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.21, 123.91 (q, *J* = 277.6 Hz), 119.12, 107.66, 81.60, 80.29, 67.43, 65.33, 59.68 (q, *J* = 34.7 Hz), 50.23, 49.05, 44.03, 42.87, 42.19, 40.61, 37.03, 33.62, 28.26, 26.88, 22.16, 9.16; IR

(film) 3553, 3441, 2975, 2927, 2878, 1281, 1165, 1110, 1017, 733 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{21}H_{30}F_3O_5$ $[M+H]^+$: 419.2039, found: 419.2043.



117 **95**

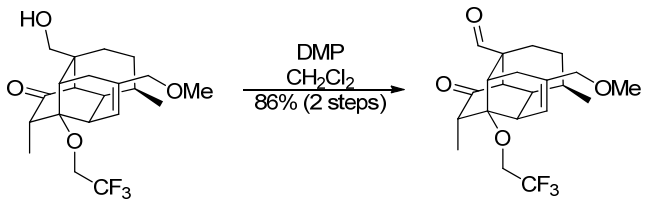
The aforementioned crude acid was dissolved in methanol (0.30 mL) and cooled to 0 °C, and then trimethylsilyldiazomethane (2.0 M in diethyl ether, 0.10 mL) was added dropwise. The reaction was stirred at 0 °C for 1 h then diluted with ethyl acetate and concentrated. The residue was re-dissolved in CH_2Cl_2 (0.30 mL) and cooled to -78 °C, DIBAL (1.0 M in CH_2Cl_2, 0.20 mL) was added dropwise. The reaction was stirred at -78 °C for 2 h then warmed to 0 °C and stirred for 1 h. The reaction was quenched by 10% Rochelle's salt solution (1 mL), diluted with ethyl acetate (5 mL), warmed to r.t. and stirred vigorously until two clear layers formed. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 2 mL). The combined organic layers were washed with brine (3 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography (40% ethyl acetate/hexanes) to provide the same alcohol (4.4 mg, 28% yield over 3 steps).



109 **119**

In a high-pressure flask, a mixture of acetal (0.35 g, 0.841 mmol) and lithium tetrafluoroborate (0.39 g, 4.160 mmol) in 2% H_2O/CH_3CN (42 mL) was heated at 83 °C for 24 h. The reaction mixture was cooled to r.t., diluted with ethyl acetate (100 mL) and washed with saturated $NaHCO_3$ solution (3 × 30 mL) and brine (30 mL). The

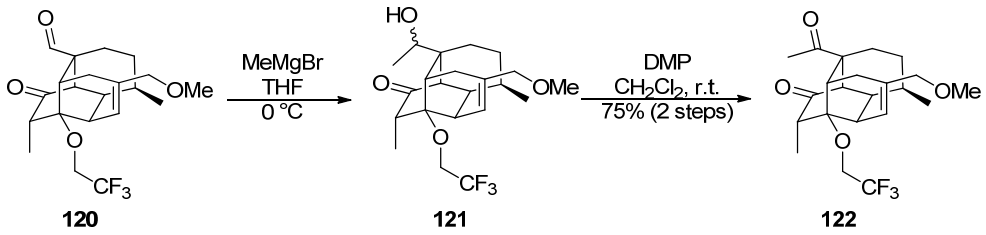
organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated. The resultant solid was triturated with 15% ethyl acetate/hexanes to give a white solid (0.34 g), which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (dt, *J* = 7.3, 1.6 Hz, 1H), 3.91 (d, *J* = 12.2 Hz, 1H), 3.79 (d, *J* = 12.2 Hz, 1H), 3.80 – 3.66 (m, 2H), 3.32 (s, 3H), 3.29 (d, *J* = 4.0 Hz, 2H), 2.71 (ddd, *J* = 10.7, 7.1, 3.1 Hz, 1H), 2.62 (q, *J* = 7.3 Hz, 1H), 2.35 (dt, *J* = 4.8, 3.3 Hz, 1H), 2.22 – 2.18 (m, 2H), 2.10 (ddd, *J* = 11.2, 3.7, 1.9 Hz, 1H), 1.94 – 1.77 (m, 3H), 1.68 (m, 2H), 1.34 (dt, *J* = 13.4, 6.8 Hz, 1H), 1.23 (ddd, *J* = 14.3, 12.2, 7.6 Hz, 1H), 1.16 (d, *J* = 7.3 Hz, 3H), 1.09 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 216.02, 136.75, 124.06 (q, *J* = 277.6 Hz), 122.65, 79.48, 76.42, 72.44, 60.94 (q, *J* = 34.6 Hz), 58.14, 56.97, 46.05, 40.63, 39.46, 35.76, 35.45, 34.17, 29.23, 26.14, 25.25, 21.32, 9.92; IR (film) 3425, 3390, 2943, 2914, 2873, 2812, 1705, 1278, 1153, 1105, 1074, 958, 906, 727, 617 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{21}H_{30}F_3O_4$ $[M+H]^+$: 403.2091, found: 403.2089.



119 **120**

To a solution of alcohol (0.40 g, 0.99 mmol) in CH_2Cl_2 (50 mL), Dess-Martin periodinane (505.9 mg, 1.19 mmol) was added at r.t. in portions. After stirring for 2 h, the reaction mixture was diluted with ethyl acetate (100 mL), washed with a mixture solution of saturated $NaHCO_3$ and 10% $Na_2S_2O_3$ (1:1 v/v, 4 × 30 mL) and brine (30 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (30% ethyl acetate/hexanes) to afford a white solid (0.34 g, 86% over 2 steps). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.28 (s, 1H), 5.84 (dt, *J* = 7.1, 1.6 Hz, 1H), 3.90 (d, *J* = 12.2 Hz, 1H), 3.79 (d, *J* = 12.2 Hz, 1H), 3.79 (dq, *J* = 10.6, 8.3 Hz, 1H), 3.71 (dq, *J* = 10.6, 8.3 Hz, 1H), 3.32 (s, 3H), 2.94 (dd, *J* = 7.2, 3.2 Hz, 1H), 2.75 (ddd, *J* = 10.7, 7.1, 3.2 Hz, 1H), 2.33 (q, *J* = 7.3 Hz, 1H), 2.28 (dd, *J* = 19.5, 7.4 Hz, 1H), 2.21 (ddd, *J* = 11.1, 3.8, 2.1 Hz, 1H), 2.15 (d, *J* = 19.5 Hz, 1H), 2.10 (d, *J* = 2.1 Hz, 1H), 1.99 – 1.85 (m, 2H), 1.80 – 1.72 (m, 1H), 1.69 (ddd, *J* = 13.6,

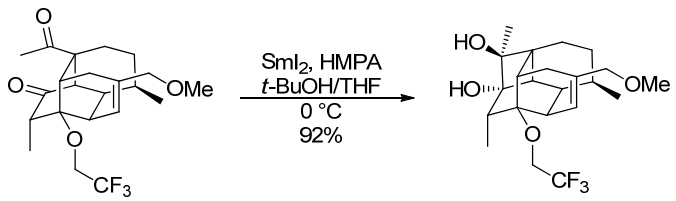
12.1, 7.4 Hz, 1H), 1.49 (ddd, *J* = 13.3, 7.4, 6.0 Hz, 1H), 1.14 (d, *J* = 7.3 Hz, 3H), 1.13 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 212.03, 202.52, 136.57, 123.89 (d, *J* = 277.5 Hz), 122.02, 78.93, 76.15, 61.03 (q, *J* = 34.8 Hz), 58.31, 53.93, 50.22, 46.56, 38.30, 35.27, 34.49, 31.88, 26.79, 25.24, 24.87, 21.25, 9.73; IR (film) 2980, 2924, 2877, 2823, 1728, 1452, 1280, 1163, 1124, 1109, 966, 727 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{21}H_{28}F_3O_4$ $[M+H]^+$: 401.1934, found: 401.1934.



To a solution of ketoaldehyde (7.3 mg, 0.0182 mmol) in THF (0.36 mL), methylmagnesium bromide (1.4 M in 3:1 THF/toluene, 0.06 mL, 0.084 mmol) was added dropwise at 0 °C. After stirring at 0 °C for 1.0 h, the reaction was quenched by saturated NH_4Cl solution (0.5 mL), diluted with water (1.0 mL) and extracted with ethyl acetate (3 × 1.5 mL). The extracts were combined, washed with brine (2.0 mL), dried over anhydrous Na_2SO_4, filtered and concentrated to afford a colorless oil. ^{1}H-NMR analysis indicated a mixture of two diastereomers (dr 2:1). The crude product was used directly in the next step.

The crude product from the previous step was dissolved in CH_2Cl_2 (0.36 mL), to which Dess-Martin periodinane (11.6 mg, 0.0273 mmol) was added at r.t. After stirring for 2 h, the reaction mixture was diluted with ethyl acetate (5 mL), washed with a mixture solution of saturated $NaHCO_3$ and 10% $Na_2S_2O_3$ (1:1 v/v, 4 × 3 mL) and brine (3 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by prep-TLC (50% ethyl acetate/hexanes) to give a white solid (5.7 mg, 75% over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) 5.83 (d, *J* = 7.1 Hz, 1H), 3.92 (d, *J* = 12.1 Hz, 1H), 3.80 (d, *J* = 12.1 Hz, 1H), 3.77 – 3.61 (m, 2H), 3.33 (s, 3H), 2.69 (ddd, *J* = 11.0, 7.0, 2.9 Hz, 1H), 2.55 (dt, *J* = 5.9, 2.6 Hz, 1H), 2.40 – 2.26 (m, 3H), 2.19 – 2.11 (m, 3H), 2.15 (s, 3H), 1.91 (qd, *J* = 12.9, 6.5 Hz, 1H), 1.73 (dtd, *J* =

13.0, 6.6, 3.6 Hz, 1H), 1.60 – 1.50 (m, 1H), 1.43 (dt, *J* = 13.8, 6.7 Hz, 1H), 1.15 (d, *J* = 7.2 Hz, 3H), 1.10 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 212.37, 210.36, 136.45, 123.89 (q, *J* = 278.8 Hz), 122.26, 79.42, 76.28, 61.17 (q, *J* = 34.5 Hz), 58.39, 54.82, 52.21, 46.72, 39.68, 35.51, 35.22, 33.88, 29.28, 26.03, 25.47, 24.97, 21.14, 9.58; IR (film) 2980, 2932, 2913, 2878, 1725, 1281, 1161, 1119, 965 cm^{-1} ; HRMS (ESI) *m/z* calcd. for $C_{22}H_{30}F_3O_4$ $[M+H]^+$: 415.2090, found: 415.2086.

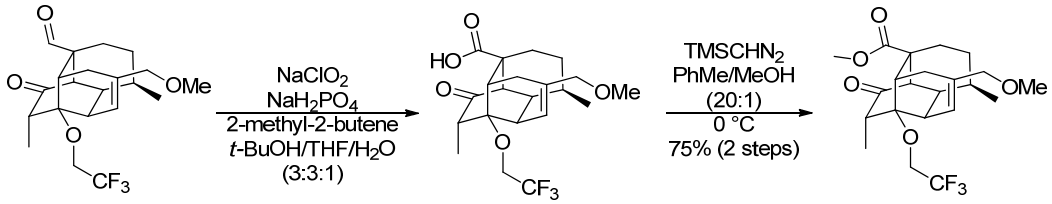


122 **123**

Preparation of SmI_2/HMPA/THF solution (0.10 M): fresh samarium filings (48.4 mg, 0.322 mmol) in a dry two-neck flask, sealed with a septum on one neck, were flame-dried, evacuated and back-filled with N_2 for three times. 1, 2-diiodoethane (45.3 mg, 0.161 mmol) in THF (1.6 mL) was added via syringe under N_2. The solution turned from light yellow to dark blue in a few seconds. After 2 h, HMPA (0.22 mL, 1.26 mmol) was added dropwise under N_2. The color of the solution changed quickly from dark blue to purple. After the mixture was stirred for 10 min., it was allowed to settle for 10 min before use.

Diketone (5.4 mg, 0.0130 mmol) was dissolved in *t*-BuOH/THF (1:20 v/v, 0.26 mL) and cooled to 0°C. N_2 was flushed for 10 min before SmI_2/HMPA/THF solution (0.10 M, 1.30 mL) was added dropwise. The purple reaction solution was stirred at 0 °C for 3.0 h before being opened to air and stirred vigorously for 1 min while the purple color faded away. The reaction was further quenched by 10% $Na_2S_2O_3$ (1 mL) and diluted with water (10 mL), extracted with ethyl acetate (3 × 5 mL). The extracts were combined and washed with brine (3 × 10 mL), dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by prep-TLC (60% ethyl acetate/hexanes) to give a white solid (5.0 mg, 92% yield). ^{1}H NMR (600 MHz, CD_3OD) □ 5.79 (d, *J* = 7.3 Hz, 1H), 3.93 – 3.83 (m, 2H), 3.82 – 3.70 (m, 2H),

3.29 (s, 3H), 3.20 (dd, *J* = 7.8, 3.2 Hz, 1H), 2.58 (ddd, *J* = 10.7, 7.2, 3.2 Hz, 1H), 2.52 (q, *J* = 7.1 Hz, 1H), 2.40 (dt, *J* = 10.9, 2.8 Hz, 1H), 2.13 (dd, *J* = 19.3, 7.8 Hz, 1H), 2.04 (d, *J* = 19.3 Hz, 1H), 1.74 (dd, *J* = 12.8, 5.7 Hz, 1H), 1.66 – 1.57 (m, 2H), 1.34 (s, 3H), 1.33 – 1.24 (m, 2H), 1.06 (d, *J* = 2.1 Hz, 1H), 1.02 (d, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (CD_3OD, extracted from HSQC and HMBC) δ 133.99, 126.65, 125.79, 81.85, 80.67, 77.43, 77.30, 61.12, 57.70, 46.27, 44.21, 40.00, 39.88, 35.60, 34.08, 29.58, 28.55, 27.57, 26.28, 22.04, 18.73, 9.02; IR (film) 3345, 2935, 2910, 1277, 1150, 1112, 1027, 970 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{31}F_3NaO_4$ $[M+Na]^+$: 439.2066, found: 439.2068.

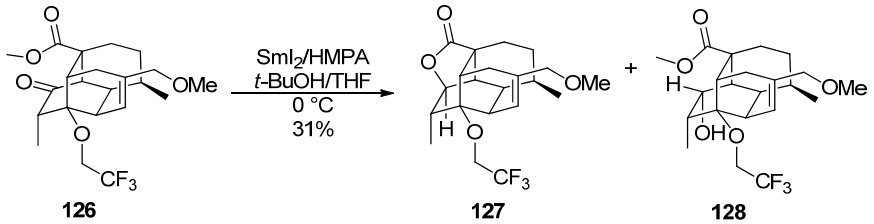


120 **125** **126**

To a mixture of ketoaldehyde (6.0 mg, 0.0150 mmol) and sodium dihydrogen phosphate (6.4 mg, 0.0533 mmol) in *t*-BuOH/THF/H_2O (3:3:1 v/v/v, 0.5 mL) was added 2-methyl-2-butene (0.03 mL, 0.284 mmol), followed by sodium chlorite (5.6 mg, 0.0621 mmol). The reaction mixture was stirred at r.t. for 1.5 h then diluted with saturated NH_4Cl solution (1.0 mL), extracted with ethyl acetate (3 × 1.0 mL). The extracts were combined and washed with brine (2.0 mL), dried over anhydrous Na_2SO_4, filtered and concentrated to give a light yellow oil, which was used directly in the next step.

The crude product from the previous step was dissolved in toluene/methanol (20:1 v/v, 0.50 mL) then cooled to 0°C. Trimethylsilyldiazomethane (2.0 M in diethyl ether, 0.05 mL) was added dropwise. After stirring at 0 °C for 30 min., the reaction was concentrated and purified by column chromatography (30% ethyl acetate/hexanes) to give a white solid (4.8 mg, 75% yield for two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (d, *J* = 6.9 Hz, 1H), 3.91 (d, *J* = 12.4, 1H), 3.79 (d, *J* = 12.4 Hz, 1H), 3.76 – 3.65 (m, 2H), 3.68 (s, 3H), 3.32 (s, 3H), 2.70 (m, 2H), 2.51 (q, *J* = 7.2

Hz, 1H), 2.34 – 2.28 (m, 2H), 2.28 – 2.21 (m, 1H), 2.21 (d, *J* = 2.0 Hz, 1H), 2.12 (ddd, *J* = 11.2, 4.0, 2.2 Hz, 1H), 1.90 – 1.79 (m, 1H), 1.77 – 1.63 (m, 2H), 1.38 (dt, *J* = 13.7, 6.6 Hz, 1H), 1.17 (d, *J* = 7.2 Hz, 3H), 1.08 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 212.37, 177.63, 136.56, 123.92 (q, *J* = 277.6 Hz), 121.99, 79.09, 76.18, 61.14 (q, *J* = 34.7 Hz), 58.31, 55.30, 52.84, 46.65, 46.38, 39.52, 37.28, 35.43, 33.70, 29.99, 25.98, 25.34, 21.15, 9.67; IR (film) 2979, 2926, 2878, 1729, 1454, 1436, 1281, 1250, 1161, 1120, 1103, 967 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{30}F_3O_5$ $[M+H]^+$: 431.2039, found: 431.2038.

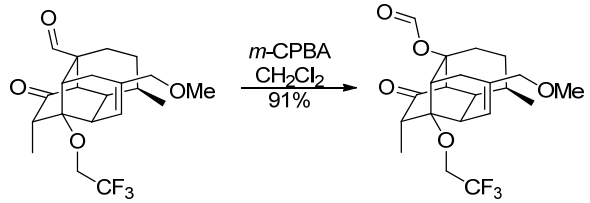


Ketoester (5.6 mg, 0.0130 mmol) was dissolved in *t*-BuOH/THF (1:20 v/v, 0.26 mL) and cooled to 0°C. N_2 was flushed for 10 min before SmI_2/HMPA/THF solution (0.10 M, 1.30 mL) was added dropwise. The purple reaction solution was stirred at 0 °C for 3.0 h before being opened to air and stirred vigorously for 1 min while the purple color faded away. The reaction was further quenched by 10% $Na_2S_2O_3$ (1 mL) and diluted with water (10 mL), extracted with ethyl acetate (3 × 5 mL). The extracts were combined and washed with brine (3 × 10 mL), dried over anhydrous Na_2SO4 and concentrated. The residue was purified by prep-TLC (60% ethyl acetate/hexanes) to give product **127** (higher R_f, white solid, 1.0 mg, 19% yield), **128** (lower R_f, colorless oil, 0.7 mg, 12% yield) and starting material (white solid, 2.0 mg, 36%).

Lactone **127**: ^{1}H NMR (600 MHz, $CDCl_3$) □ 5.78 (d, *J* = 7.2 Hz, 1H), 4.31 (d, *J* = 5.7 Hz, 1H), 3.88 (d, *J* = 12.2 Hz, 1H), 3.75 (d, *J* = 12.2 Hz, 1H), 3.70 (dq, *J* = 10.9, 8.4 Hz, 1H), 3.60 (dq, *J* = 10.9, 8.4 Hz, 1H), 3.30 (s, 3H), 2.60 (ddd, *J* = 10.6, 7.2, 2.9 Hz, 1H), 2.36 (dt, *J* = 11.3, 2.7 Hz, 1H), 2.25 – 2.11 (m, 5H), 1.85 (dd, *J* = 5.6, 2.2 Hz, 1H), 1.69 – 1.55 (m, 2H), 1.48 (m, 1H), 1.44 – 1.37 (m, 1H), 1.10 (d, *J* = 6.6 Hz, 3H),

1.05 (d, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, extracted from HSQC and HMBC) δ 180.27, 135.14, 123.8, 122.12, 81.67, 78.27, 75.98, 60.79, 58.1, 44.9, 42.9, 37.42, 37.07, 36.34, 35.32, 32.54, 26.01, 25.72, 24.73, 21.13, 12.41; IR (film) 2981, 2925, 2851, 1766, 1283, 1163, 1152, 1112, 1099, 1024, 956, 858 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{28}F_3O_4$ $[M+H]^+$: 401.1934, found: 401.1935.

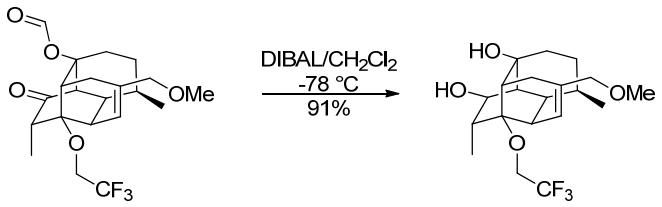
Alcohol **128**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.77 (d, J = 7.0 Hz, 1H), 4.02 (dt, J = 10.5, 3.1 Hz, 1H), 3.87 (d, J = 12.2 Hz, 1H), 3.75 (d, J = 12.2 Hz, 1H), 3.72 – 3.66 (m, 2H), 3.70 (s, 3H), 3.30 (s, 3H), 2.87 (dt, J = 4.8, 3.5 Hz, 1H), 2.60 (ddd, J = 10.7, 7.1, 3.2 Hz, 1H), 2.49 (ddd, J = 11.4, 3.8, 2.1 Hz, 1H), 2.19 – 2.11 (m, 3H), 2.02 – 1.97 (m, 1H), 1.88 – 1.76 (m, 2H), 1.74 – 1.63 (m, 2H), 1.44 – 1.40 (m, 1H), 1.35 – 1.27 (m, 1H), 1.08 (d, J = 7.0 Hz, 3H), 0.99 (d, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, extracted from HSQC and HMBC) δ 179.14, 135.8, 124.3, 123.51, 78.32, 76.61, 66.39, 60.58, 58.03, 52.38, 48.06, 45.36, 36.19, 35.38, 35.05, 34.85, 33.45, 32.25, 26.75, 25.33, 21.48, 7.59; IR (film) 3474, 2925, 1723, 1281, 1158, 1102, 1005, 863 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{31}F_3NaO_5$ $[M+Na]^+$: 455.2015, found: 455.2016.



120 **129**

To a solution of ketoaldehyde (150.0 mg, 0.374 mmol) in CH_2Cl_2 (7.5 mL), *meta*-chloroperoxybenzoic acid (70-75 wt% with benzoic acid and water, 98.0 mg, 0.412 mmol) were added at r.t. in one portion. After stirring for 17 h, the reaction mixture was diluted with ethyl acetate (20 mL), washed with 10% $NaHSO_3$ solution (10 mL), saturated $NaHCO_3$ solution (3 × 10 mL) and brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (20% ethyl acetate/hexanes) to afford a white foam (141.2 mg, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 0.9 Hz, 1H), 5.79 (ddd, J =

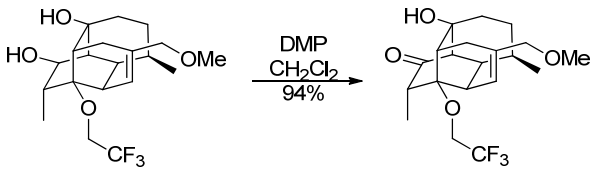
7.1, 2.0, 1.2 Hz, 1H), 3.91 (ddd, *J* = 12.4, 1.5, 0.7 Hz, 1H), 3.80 (ddd, *J* = 12.4, 1.5, 0.7 Hz, 1H), 3.73 – 3.63 (m, 2H), 3.33 (s, 3H), 3.04 – 2.97 (m, 1H), 2.82 – 2.69 (m, 2H), 2.52 – 2.47 (m, 1H), 2.49 (q, *J* = 7.3 Hz, 1H), 2.38 – 2.28 (m, 1H), 2.31 (d, *J* = 2.1 Hz, 1H), 2.27 – 2.18 (m, 1H), 1.95 – 1.70 (m, 2H), 1.59 – 1.41 (m, 2H), 1.20 (d, *J* = 7.3 Hz, 3H), 1.09 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 211.28, 159.77, 137.18, 123.67 (q, *J* = 277.8 Hz), 120.85, 85.02, 78.82, 75.69, 61.11 (q, *J* = 34.8 Hz), 58.61, 58.24, 46.65, 43.09, 39.14, 35.14, 33.49, 31.70, 27.02, 24.95, 20.30, 9.93; IR (film) 2980, 2929, 2877, 2823, 2249, 1712, 1452, 1375, 1282, 1165, 968, 867, 734 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{27}F_3NaO_5$ $[M+Na]^+$: 439.1703, found: 439.1706.



129 **130**

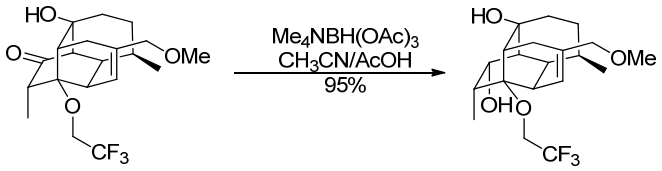
To a solution of ketone-ester (488.4 mg, 1.17 mmol) in CH_2Cl_2 (10 mL) was added DIBAL (1.0 M in CH_2Cl_2, 3.51 mL) dropwise at -78 °C. The reaction was stirred at -78 °C for 2.0 h then quenched by 10% Rochelle's salt solution (20 mL). The mixture was diluted with ethyl acetate (40 mL), warmed to r.t. and stirred vigorously until two clear layers formed. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (60% ethyl acetate/hexanes) to give a white solid (415.7 mg, 91% yield). ^{1}H NMR (600 MHz, $CDCl_3$) 5.72 (d, *J* = 7.1 Hz, 1H), 3.86 (d, *J* = 12.2 Hz, 1H), 3.78 (br s, 1H), 3.74 (d, *J* = 12.2 Hz, 1H), 3.72 (dq, *J* = 10.8, 8.5 Hz, 1H), 3.64 (dq, *J* = 10.8, 8.5 Hz, 1H), 3.51 (s, 1H), 3.29 (s, 3H), 3.14 (br s, 1H), 2.47 (ddd, *J* = 10.8, 7.1, 3.1 Hz, 1H), 2.30 (dd, *J* = 7.4, 3.1 Hz, 1H), 2.25 (d, *J* = 18.9 Hz, 1H), 2.20 – 2.08 (m, 2H), 1.98 (tt, *J* = 7.2, 3.5 Hz, 1H), 1.94 (dt, *J* = 11.0, 2.7 Hz, 1H), 1.82 – 1.62 (m, 2H), 1.53 – 1.42 (m, 2H), 1.35 (dt, *J* = 13.5, 6.3 Hz, 1H), 1.09 (d, *J* = 7.2 Hz, 3H), 1.05 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz,

$CDCl_3$) □ 136.06, 124.15 (q, *J* = 277.6 Hz), 123.19, 79.79, 78.60, 78.32, 76.25, 60.69 (q, *J* = 34.5 Hz), 57.97, 48.17, 45.58, 42.56, 41.29, 37.51, 36.76, 32.77, 27.37, 24.79, 20.88, 15.16; IR (film) 3346, 2980, 2914, 2875, 1452, 1379, 1282, 1155, 1001, 966, 920, 854, 734 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{20}H_{29}F_3NaO_4$ $[M+Na]^+$: 413.1910, found: 413.1916.



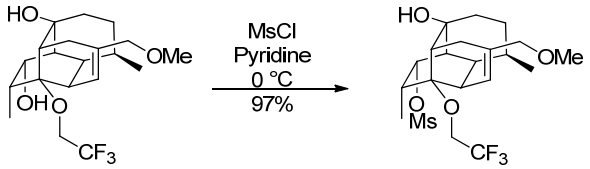
130 **131**

To a solution of diol (349.6 mg, 0.895 mmol) in water-saturated dichloromethane (18 mL), Dess-Martin periodinane (455.7 mg, 1.07 mmol) were added at r.t. in one portion. After stirring for 2 h, another portion of Dess-Martin periodinane (380 mg, 0.895 mmol) was added and the reaction was stirred for further 7 h. The reaction mixture was diluted with ethyl acetate (120 mL), washed with a mixture solution of saturated $NaHCO_3$ and 10% $Na_2S_2O_3$ (1:1 v/v, 4 × 30 mL) and brine (30 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was triturated with 50% ethyl acetate/hexanes and a white solid was collected by vacuum filtration. Purification of the filtrate by column chromatography (35% ethyl acetate/hexanes) gave another crop of white solid. Combined white solids weighed 326.8 mg (94% yield). ^{1}H NMR (600 MHz, $CDCl_3$) □ 5.78 (d, *J* = 7.1 Hz, 1H), 3.91 (d, *J* = 12.3 Hz, 1H), 3.78 (d, *J* = 12.3 Hz, 1H), 3.71 (q, *J* = 8.4 Hz, 2H), 3.32 (s, 3H), 2.71 (ddd, *J* = 10.6, 7.1, 2.9 Hz, 1H), 2.53 (q, *J* = 7.4 Hz, 1H), 2.39 – 2.17 (m, 6H), 2.04 (d, *J* = 2.1 Hz, 1H), 1.87 – 1.64 (m, 2H), 1.52 – 1.38 (m, 2H), 1.16 (d, *J* = 7.3 Hz, 3H), 1.07 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) □ 214.19, 136.66, 123.93 (d, *J* = 277.6 Hz), 122.16, 79.14, 76.08, 74.03, 61.89, 61.06 (q, *J* = 34.7 Hz), 58.17, 45.91, 43.56, 40.33, 37.03, 35.38, 33.65, 27.57, 24.83, 20.70, 9.79; IR (film) 3396, 2981, 2927, 2879, 2825, 1712, 1456, 1280, 1161, 1120, 1020, 966, 920, 732 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{20}H_{27}F_3NaO_4$ $[M+Na]^+$: 411.1754, found: 411.1756.



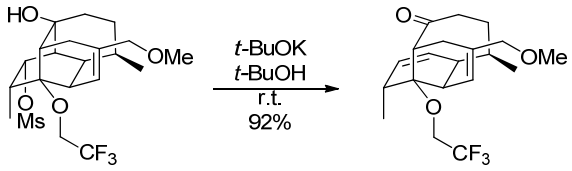
131 **132**

To a solution of ketone-alcohol (173.4 mg, 0.446 mmol) in acetonitrile (5 mL) and acetic acid (10 mL), was added a suspension of tetramethylammonium triacetoxyborohydride (587.4 mg, 2.23 mmol) in acetonitrile (5 mL) at r.t. The reaction mixture was stirred for 3 h before it was quenched by saturated NH_4Cl solution (5 mL). After effervescence had ceased, the solution was diluted with water (10 mL) and ethyl acetate (30 mL). The organic phase was separated and the aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was triturated with hexanes and a white solid was collected by vacuum filtration. Purification of the filtrate by column chromatography (75% ethyl acetate/hexanes) gave another crop of white solid. The combined white solids weighed 165.4 mg (95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) □ 5.74 (dt, *J* = 7.0, 1.5 Hz, 1H), 4.58 (dd, *J* = 10.4, 3.2 Hz, 1H), 3.87 (d, *J* = 12.2 Hz, 1H), 3.74 (d, *J* = 12.2 Hz, 1H), 3.73 (dq, *J* = 10.8, 8.5 Hz, 1H), 3.61 (dq, *J* = 10.8, 8.5 Hz, 1H), 3.29 (s, 3H), 2.60 (ddd, *J* = 10.4, 7.0, 2.9 Hz, 1H), 2.55 – 2.47 (m, 1H), 2.33 (dq, *J* = 10.4, 7.3 Hz, 1H), 2.27 – 2.03 (m, 4H), 1.80 (m, 1H), 1.67 (m, 1H), 1.44 – 1.33 (m, 3H), 1.05 (d, *J* = 7.0 Hz, 3H), 1.01 (d, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 135.87, 124.23 (d, *J* = 277.8 Hz), 123.76, 79.02, 76.44, 74.78, 64.27, 60.58 (q, *J* = 34.3 Hz), 58.03, 51.29, 43.78, 38.46, 36.55, 36.45, 35.46, 33.52, 28.11, 24.82, 21.12, 7.74; IR (film) 3373, 2981, 2926, 2833, 1448, 1280, 1161, 1105, 1002, 966, 916, 864, 732 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{20}H_{29}F_3NaO_4$ $[M+Na]^+$: 413.1910, found: 413.1909.



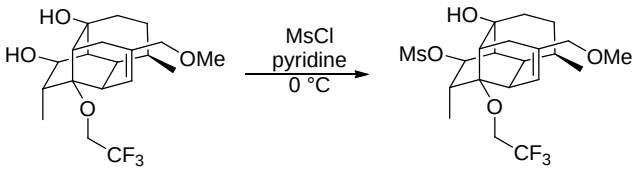
132 **133**

To a solution of diol (276.0 mg, 0.707 mmol) in anhydrous pyridine (12.0 mL), methanesulfonyl chloride (0.55 mL, 7.07 mmol) was added dropwise at 0 °C. The reaction was stirred at 0 °C for 15 h then quenched by 1 N HCl solution (10 mL) and diluted with ethyl acetate (200 mL). The mixture was washed with 1 N HCl solution (3 × 50 mL) and brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was triturated with 10% ethyl acetate/hexanes and a white solid was collected by vacuum filtration. Purification of the filtrate by column chromatography (60% ethyl acetate/hexanes) gave another crop of white solid. The combined white solids weighed 321.3 mg (97% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.73 (dt, *J* = 6.9, 1.5 Hz, 1H), 5.48 (dd, *J* = 10.6, 3.4 Hz, 1H), 3.86 (dd, *J* = 12.2, 1.1 Hz, 1H), 3.74 (dd, *J* = 12.2, 1.1 Hz, 1H), 3.72 (dq, *J* = 10.6, 8.4 Hz, 1H), 3.62 (dq, *J* = 10.6, 8.4 Hz, 1H), 3.29 (s, 3H), 3.05 (s, 3H), 2.62 (ddd, *J* = 10.6, 7.0, 2.9 Hz, 1H), 2.52 (dq, *J* = 11.0, 7.5 Hz, 1H), 2.47 (ddd, *J* = 11.4, 3.7, 2.1 Hz, 1H), 2.25 (d, *J* = 18.0 Hz, 1H), 2.20 (dd, *J* = 12.8, 6.3 Hz, 1H), 2.16 – 2.06 (m, 2H), 2.00 (s, 1H), 1.84 – 1.74 (m, 1H), 1.69 (m, 1H), 1.62 (dd, *J* = 3.4, 2.1 Hz, 1H), 1.47 – 1.34 (m, 2H), 1.06 (d, *J* = 7.0 Hz, 3H), 1.05 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.13, 124.03 (d, *J* = 277.6 Hz), 122.96, 78.48, 77.01, 76.24, 74.28, 60.70 (q, *J* = 34.6 Hz), 58.13, 49.80, 43.53, 38.17, 38.01, 36.86, 36.09, 34.61, 33.23, 27.85, 24.70, 20.97, 8.91; IR (film) 3412, 2983, 2926, 1448, 1350, 1330, 1282, 1168, 1107, 966, 927, 918, 871, 732, 528 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{31}F_3NaO_6S$ $[M+Na]^+$: 491.1686, found: 491.1684.



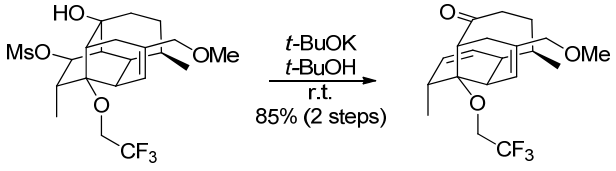
133 **134**

To a solution of mesylate (220.8 mg, 0.471 mmol) in anhydrous *tert*-butanol (44 mL), potassium *tert*-butoxide (1.0 M in THF, 1.41 mL) was added dropwise at r.t. The solution became cloudy and turned yellow. After stirring for 1.5 h, the reaction was quenched by saturated NH_4Cl solution (10 mL) and diluted with ethyl acetate (50 mL) and water (50 mL). The organic phase was separated and the aqueous phase was extracted with ethyl acetate (3 × 50 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was triturated with hexanes and a white solid was collected by vacuum filtration. Purification of the filtrate by column chromatography (15% ethyl acetate/hexanes) afforded another crop of white solid. The combined white solids weighed 161.4 mg (92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) □ 5.93 (dt, *J* = 5.7, 1.5 Hz, 1H), 5.58 – 5.47 (m, 2H), 3.99 (d, *J* = 11.8, 1H), 3.85 (d, *J* = 11.8 Hz, 1H), 3.82 – 3.67 (m, 2H), 3.33 (s, 3H), 2.95 (d, *J* = 7.2 Hz, 1H), 2.83 – 2.78 (m, 1H), 2.74 (ddd, *J* = 14.9, 7.1, 4.0 Hz, 1H), 2.65 (qd, *J* = 7.0, 3.4 Hz, 1H), 2.60-2.53 (m, 1H), 2.46 – 2.38 (m, 1H), 2.25 (d, *J* = 18.6 Hz, 1H), 2.30-2.17 (m, 1H), 1.90 – 1.72 (m, 2H), 1.72 – 1.54 (m, 1H), 1.09 (d, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) □ 211.79, 132.60, 131.32, 130.87, 125.45, 124.84 (d, *J* = 277.8 Hz), 78.93, 76.65, 60.91 (q, *J* = 33.8 Hz), 57.99, 54.19, 44.17, 38.23, 38.10, 37.56, 34.86, 29.76, 25.92, 23.46, 16.33; IR (film) 2927, 2875, 1676, 1280, 1155, 1105, 968, 856 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{20}H_{28}F_3O_3$ $[M+H]^+$: 373.1985, found: 373.1983.



130 **135**

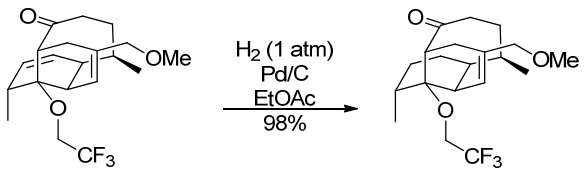
To a solution of diol (15.8 mg, 0.0404 mmol) in anhydrous pyridine (0.80 mL) methanesulfonyl chloride (0.03 mL, 0.404 mmol) was added dropwise at 0 °C. The reaction was stirred at 0 °C for 3 h then quenched by water (2 mL) and diluted with ethyl acetate (10 mL). The mixture was washed with 1 N HCl (5 × 2 mL) and brine (2 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (50% ethyl acetate/hexanes) to afford a white solid (18.9 mg, quantitative yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.71 (d, *J* = 7.2 Hz, 1H), 4.54 (dd, *J* = 4.6, 2.7 Hz, 1H), 3.86 (d, *J* = 12.3 Hz, 1H), 3.74 (d, *J* = 12.3 Hz, 1H), 3.67 (qd, *J* = 8.3, 2.5 Hz, 2H), 3.29 (s, 3H), 3.08 (s, 3H), 2.52 (ddd, *J* = 10.7, 7.1, 3.1 Hz, 1H), 2.34 (s, 1H), 2.32 – 2.20 (m, 3H), 2.19 – 2.12 (m, 2H), 2.09 – 1.97 (m, 1H), 1.84 – 1.74 (m, 2H), 1.69 (qd, *J* = 13.0, 6.3 Hz, 1H), 1.49 – 1.40 (m, 1H), 1.37 (m, 1H), 1.15 (d, *J* = 7.0 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.59, 123.96 (q, *J* = 277.7 Hz), 122.03, 88.47, 78.16, 76.58, 76.10, 60.97 (q, *J* = 34.5 Hz), 58.21, 47.81, 45.32, 41.82, 39.23, 39.07, 37.69, 36.72, 32.96, 27.47, 24.91, 20.80, 14.32; IR (film) 3529, 2925, 2876, 1456, 1333, 1281, 1170, 966, 935, 916, 845 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{31}F_3NaO_6S$ $[M+Na]^+$: 491.1686, found: 491.1689.



135 **134**

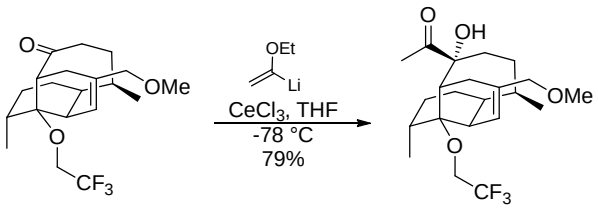
To a solution of mesylate (18.9 mg, 0.0404 mmol) in anhydrous *tert*-butanol (5.3 mL), potassium *tert*-butoxide (1.0 M in THF, 0.16 mL) was added dropwise at r.t. The reaction solution became cloudy and turned yellow. After stirring for 15 h, the reaction was quenched by saturated NH_4Cl (1 mL) and diluted with ethyl acetate (5

mL) and water (5 mL). The organic phase was separated and the aqueous phase was extracted with ethyl acetate (3 × 5 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (10% ethyl acetate/hexanes) to afford a white solid (12.8 mg, 85% yield over 2 steps).



134 **136**

To a solution of diene (247.3 mg, 0.664 mmol) in ethyl acetate (13.3 mL) was added palladium on carbon (10 wt%, 35.3 mg, 0.0332 mmol). The mixture was bubbled with H_2 for 5 min. then stirred at r.t. under H_2 balloon for 3.0 h. After that period of time the reaction mixture was filtered through a Celite pad and the filtrate was concentrated and then purified by column chromatography (15% ethyl acetate/hexanes) to give a colorless oil (243.6 mg, 98% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (ddd, *J* = 4.6, 2.4, 1.2 Hz, 1H), 3.97 (d, *J* = 11.9 Hz, 1H), 3.91 – 3.76 (m, 3H), 3.36 (s, 3H), 2.99 (dq, *J* = 5.9, 1.4 Hz, 1H), 2.73 (ddd, *J* = 12.1, 8.4, 3.9 Hz, 1H), 2.60 (q, *J* = 4.1 Hz, 1H), 2.44 (ddt, *J* = 18.2, 5.7, 2.7 Hz, 1H), 2.25 – 2.11 (m, 2H), 1.99 – 1.83 (m, 3H), 1.82 – 1.71 (m, 1H), 1.68 – 1.57 (m, 1H), 1.53 – 1.28 (m, 4H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 215.76, 132.95, 127.03, 124.25 (q, *J* = 278.3 Hz), 78.93, 76.60, 61.98 (q, *J* = 34.0 Hz), 58.45, 54.04, 42.15, 38.83, 37.96, 37.44, 33.88, 31.44, 27.70, 27.09, 25.95, 24.03, 14.69; IR (film) 2933, 2873, 2821, 1674, 1454, 1377, 1280, 1153, 1103, 972, 850, 667, 536 cm^{-1}; HRMS (MALDI) *m/z* calcd. for $C_{20}H_{29}F_3O_3Li$ $[M+Li]^+$: 381.2224, found: 381.2235.



136 **137**

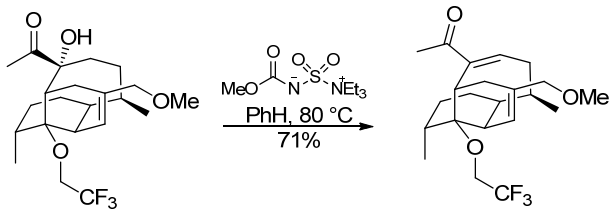
Cerium (III) chloride heptahydrate[13] (190 mg, 0.510 mmol) was grounded to a fine powder and placed in a flask equipped with a stir bar. The flask was heated slowly to 90 °C with evacuation and maintained at 90 °C for 3.5 h. After that period of time, the temperature was increased to 140 °C and the flask was heated for 15 h. The flask was then cooled to r.t., nitrogen was introduced and THF (2.5 mL) was added. The resultant slurry was stirred vigorously under N_2 for 2 h.

In a separate flask, *t*-BuLi (1.7 M in pentane, 1.5 mL, 2.5 mmol) was added dropwise to a solution of ethyl vinyl ether (0.57 mL, 6.0 mmol) in THF (3.0 mL) at -78 °C. The solution turned yellow and a precipitate formed. After the addition was completed, the cooling bath was removed and the mixture was allowed to warm to 0 °C over an ice-water bath and stirred at 0 °C for 15 min. while the yellow color was gradually discharged.

The resultant colorless 1-ethoxyvinyllithium solution (0.5 M, 0.80 mL) was added via syringe to the $CeCl_3$ suspension (cooled to -78 °C before the addition). A canary yellow mixture was formed and stirred for 1.0 h before ketone (45.0 mg, 0.134 mmol) in THF (0.50 mL) was added. The reaction mixture was stirred at -78 °C for 45 min. and quenched by saturated NH_4Cl solution (3 mL) and extracted with ethyl acetate (5 × 6 mL). The combined organic layers were washed with brine (6 mL) and split into two portions; each was diluted with ethyl acetate to 50 mL and washed quickly with cold 1N HCl solution (10 mL) and brine (5 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (15% ethyl acetate/hexanes) to give a colorless oil

(13) Dimitrov, V.; Kostova, K.; Genov, M. *Tetrahedron Letters.* **1996**, 37, 6787-6790.

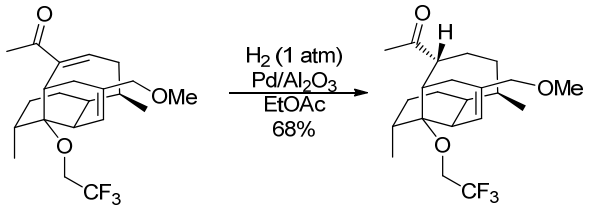
(44.3 mg, 79% yield). (Note: Prolonged exposure of the vinyl ether intermediate to acid during work-up could lead to its decomposition.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.71 (t, *J* = 3.2 Hz, 1H), 3.92 – 3.67 (m, 4H), 3.30 (s, 3H), 2.85 (ddt, *J* = 13.4, 11.4, 6.8 Hz, 1H), 2.64 (s, 1H), 2.57 (s, 1H), 2.37 (d, *J* = 8.1 Hz, 1H), 2.34 – 2.27 (m, 1H), 2.33 (s, 3H), 2.27 – 2.20 (m, 1H), 2.20 – 2.11 (m, 1H), 2.07 (ddt, *J* = 15.4, 7.5, 2.3 Hz, 1H), 1.97 (ddd, *J* = 15.6, 7.9, 2.2 Hz, 1H), 1.81 – 1.72 (m, 2H), 1.55 (d, *J* = 17.9 Hz, 1H), 1.48 – 1.36 (m, 3H), 1.32 – 1.23 (m, 1H), 1.08 (d, *J* = 7.4 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.45, 132.02, 126.42, 124.49 (q, *J* = 278.7 Hz), 82.45, 82.30, 76.80, 62.07 (q, *J* = 33.8 Hz), 58.20, 43.08, 41.02, 39.38, 36.82, 36.27, 30.63, 27.79, 25.82, 25.31, 24.71, 22.22, 22.19, 15.42; IR (film) 3441, 2931, 2872, 2825, 1703, 1456, 1377, 1357, 1280, 1157, 1107, 972, 910, 734 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{33}F_3O_4Li$ $[M+Li]^+$: 425.2485, found: 425.2486.



137 **139**

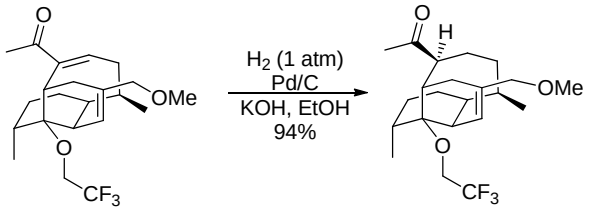
In a high-pressure tube, Burgess's reagent (37.8 mg, 0.159 mmol) was added to a solution of hydroxy ketone (33.2 mg, 0.0793 mmol) in benzene (8.0 mL) under N_2. The tube was then capped and heated at 80 °C for 1.0 h. The reaction solution turned from colorless to light yellow over time. After cooling to r.t. the reaction was concentrated, diluted with diethyl ether (30 mL) and washed with brine (3 × 10 mL). The aqueous phase was back-extracted with ether (3 × 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (10% ethyl acetate/hexanes) to afford a white solid (22.4 mg, 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.06 (t, *J* = 9.0 Hz, 1H), 5.72 (dt, *J* = 5.1, 1.6 Hz, 1H), 4.05 (d, *J* = 9.8 Hz, 1H), 3.97 – 3.79 (m, 3H), 3.77 (d, *J* = 12.1 Hz, 1H), 3,29 – 3.22 (m, 1H), 3.27 (s, 3H), 2.59 (t, *J* = 6.1 Hz, 1H), 2.46 (ddt, *J* = 19.1, 10.2, 2.4 Hz, 1H), 2.39 (s, 3H), 2.03 – 1.93 (m, 2H), 1.90 – 1.83 (m, 1H), 1.81 (d, *J* = 19.1 Hz, 1H), 1.72 (ddd, *J* = 13.0, 9.2, 2.6 Hz, 1H), 1.70 – 1.62 (m, 1H), 1.56 –

1.47 (m, 1H), 1.29 (dq, *J* = 13.7, 5.4 Hz, 1H), 1.14 (dtd, *J* = 13.7, 5.1, 2.4 Hz, 1H), 1.09 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 200.08, 146.73, 145.62, 136.10, 125.76, 124.58 (q, *J* = 278.2 Hz), 81.97, 76.71, 60.94 (q, *J* = 33.8 Hz), 57.70, 42.64, 41.24, 41.10, 33.22, 31.63, 31.52, 30.86, 28.51, 28.48, 27.79, 26.03, 15.43; IR (film) 2954, 2927, 2875, 1662, 1448, 1375, 1274, 1244, 1157, 1109, 968, 856 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{31}F_3O_3Na$ $[M+Na]^+$: 423.2118, found: 423.2113.



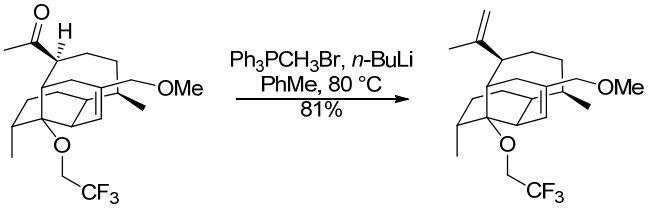
139 **141**

To a solution of ,-unsaturated ketone (1.9 mg, 0.00474 mmol) in ethyl acetate (0.40 mL) was added palladium on activated alumina (10 wt%, 2.0 mg, 0.00188 mmol). The mixture was bubbled with H_2 for 5 min. then stirred at r.t. under H_2 balloon for 16 h. After that period of time the reaction mixture was filtered through a Celite pad, the filtrate was concentrated and purified by column chromatography (25% ethyl acetate/hexanes) to give a colorless oil (1.3 mg, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 5.66 (s, 1H), 3.92 – 3.74 (m, 4H), 3.32 (s, 3H), 3.00 (dd, *J* = 7.4, 3.2 Hz, 1H), 2.73 – 2.63 (m, 1H), 2.51 (dt, *J* = 6.5, 3.2 Hz, 2H), 2.22 (s, 3H), 2.04 – 1.88 (m, 3H), 1.81 – 1.50 (m, 6H), 1.44 – 1.22 (m, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 1.00 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (C_6D_6, extracted from HSQC and HMBC) 208.61, 134.38, 125.63, 125.35, 82.38, 77.04, 62.48, 59.97, 58.18, 41.78, 39.07, 37.54, 37.05, 36.04, 32.83, 29.64, 28.23, 28.00, 27.63, 22.91, 20.82, 16.41; IR (film) 2927, 2874, 1706, 1462, 1279, 1157, 1105, 973, 857 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{33}F_3NaO_3$ $[M+Na]^+$: 425.2274, found: 425.2274.



139 **140**

Enone (70.0 mg, 0.175 mmol) was dissolved in absolute ethanol (8.8 mL) containing potassium hydroxide (28.0 mg), to which palladium on carbon (10 wt%, 18.6 mg, 0.0175 mmol) was added. The mixture was bubbled with H_2 for 5 min. then stirred at r.t. under H_2 balloon for 27 h. The reaction mixture was filtered through a Celite pad and the filter cake was washed with ethyl acetate. After brine (20 mL) was added to the filtrate, the mixture was extracted with ethyl acetate (3 × 15 mL). The combined extracts were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (15% ethyl acetate/hexanes) to give a colorless oil (66.2 mg, 94% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.64 (m, 1H), 3.93 – 3.85 (m, 2H), 3.82 – 3.75 (m, 2H), 3.33 (s, 3H), 2.78 (d, *J* = 11.7 Hz, 1H), 2.44 (s, 1H), 2.35 (d, *J* = 6.8 Hz, 1H), 2.23 – 2.12 (m, 2H), 2.20 (s, 3H), 2.02 – 1.94 (m, 1H), 1.91 (d, *J* = 18.0 Hz, 1H), 1.68 – 1.43 (m, 6H), 1.34 (m, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.07, 133.68, 124.48 (q, *J* = 276.8 Hz), 124.66, 81.42, 76.14, 62.56 (q, *J* = 33.9 Hz), 58.34, 49.86, 42.62, 38.13, 37.23, 36.60, 33.29, 30.73, 29.16, 28.23, 26.88, 24.18, 24.04, 21.93, 14.53; IR (film) 2956, 2933, 2872, 2821, 1708, 1460, 1377, 1354, 1280, 1157, 1126, 1105, 972, 927, 850 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{33}F_3O_3Na$ $[M+Na]^+$: 425.2274, found: 425.2270.

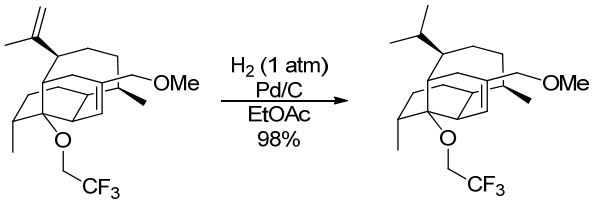


140 **142**

In a high-pressure tube, *n*-BuLi (1.6 M in hexanes, 0.39 mL, 0.624 mmol) was added dropwise to a suspension of methyltriphenylphosphonium bromide (277.4 mg, 0.739 mmol) in toluene (3.5 mL) at 0 °C. The mixture turned to light yellow gradually. After stirring for 15 min., ketone (99.2 mg, 0.246 mmol) in toluene (1.0 mL) was added. The reaction tube was then sealed, warmed to r.t. and heated to 80 °C. After 20 h at 80 °C, the reaction was cooled to r.t., quenched by saturated NH_4Cl solution (5.0 mL), and extracted with ethyl acetate (3 × 10 mL). The combined extracts were washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was loaded on a silica gel plug and eluted with 5% ethyl acetate/hexanes. To remove the trace amount of triphenylphosphine,[14] the eluate was concentrated, to which acetone (9.0 mL), sodium iodide (540 mg) and Merrifield resin (600 mg) were added. The resultant slurry was stirred at r.t. for 24 h then filtered through a Celite pad and washed with small amount of ethyl acetate. The filtrate was concentrated, re-dissolved in ethyl acetate, washed with water and brine and concentrated again. The residue was purified by column chromatography (5% ethyl ether/hexanes) to give a colorless oil (79.8 mg, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) □ 5.62 (m, 1H), 4.76 (t, *J* = 1.5 Hz, 1H), 4.62 (d, *J* = 1.3 Hz, 1H), 3.95 – 3.83 (m, 2H), 3.83 – 3.72 (m, 2H), 3.33 (s, 3H), 2.42 (s, 1H), 2.32 – 2.17 (m, 2H), 2.17 – 2.08 (m, 1H), 2.06 (d, *J* = 7.0 Hz, 1H), 2.03 – 1.89 (m, 2H), 1.83 – 1.78 (s, 3H), 1.62 (m, 1H), 1.56 – 1.28 (m, 8H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 152.22, 134.01, 124.63 (q, *J* = 278.4 Hz), 125.25, 110.04, 81.89, 76.65, 62.56 (q, *J* = 33.8 Hz), 58.25, 42.88, 42.02, 38.88, 38.39, 36.75, 32.99, 31.78, 28.34, 27.04, 25.98, 24.43, 24.21, 23.78, 14.58; IR (film) 2933, 2870, 1280,

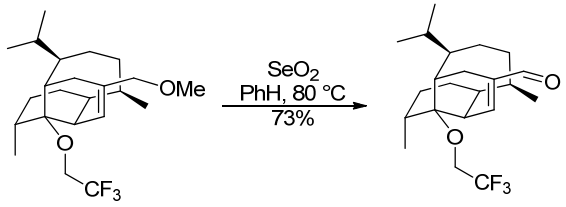
(14) Lipshutz, B.H; Blomgren, P. A. *Org. Lett.* **2001**, 3, 1869-1871.

1155, 1124, 1105, 1089, 974, 891 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{23}H_{35}F_3O_2Li$ $[M+Li]^+$: 407.2744, found: 407.2739.



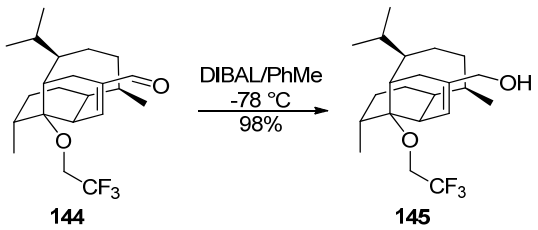
142 **143**

To a solution of diene (89.0 mg, 0.222 mmol) in ethyl acetate (2.2 mL) was added palladium on carbon (10 wt%, 23.6 mg, 0.0222 mmol). The mixture was bubbled with H_2 for 5 min. then stirred at r.t. under H_2 balloon for 36 h. After that period of time the reaction mixtures were filtered through a Celite pad and washed with ethyl acetate. The filtrate was concentrated to give a colorless oil (87.8 mg, 98% yield), which solidified in freezer to a white solid. (Note: The R_f of the product is as same as that of the starting material in ethyl acetate/hexanes solvent system, therefore the reaction was monitored by ^{1}H-NMR of aliquots.) ^{1}H NMR (600 MHz, $CDCl_3$) □ 5.60 (m, 1H), 3.92 – 3.83 (m, 2H), 3.81 – 3.72 (m, 2H), 3.31 (s, 3H), 2.41 (m, 1H), 2.24 (m, 1H), 2.19 – 2.09 (m, 2H), 2.00 – 1.94 (m, 1H), 1.91 (d, *J* = 17.8 Hz, 1H), 1.75 – 1.63 (m, 1H), 1.54 – 1.25 (m, 9H), 1.25 – 1.14 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.1 Hz, 3H), 0.90 (d, *J* = 6.4 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 134.11, 124.72 (d, *J* = 278.5 Hz), 125.63, 82.09, 76.81, 62.38 (q, *J* = 33.7 Hz), 58.07, 42.62, 40.98, 38.21, 37.75, 37.48, 36.14, 33.12, 31.73, 28.85, 27.59, 25.47, 25.43, 24.44, 22.18, 20.94, 14.64; IR (film) 2956, 2933, 2872, 2819, 1463, 1456, 1375, 1280, 1155, 1122, 1101, 975, 850, 659 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{23}H_{37}F_3O_2Li$ $[M+Li]^+$: 409.2900, found: 409.2900.



143 **144**

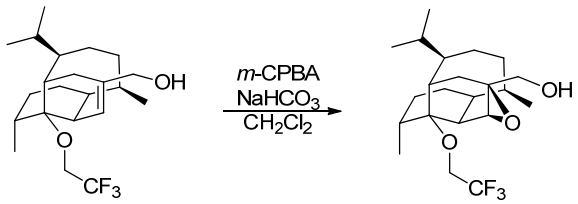
In a high-pressure tube, a mixture of methylvinylether (18.0 mg, 0.0447 mmol), selenium dioxide (24.8 mg, 0.224 mmol) and benzene (1.0 mL) was heated at 80 °C for 60 h. The reaction was cooled to r.t., filtered through a Celite pad and washed with ethyl acetate. The filtrate was concentrated and purified by column chromatography (10% ethyl acetate/hexanes) to afford a white solid (12.6 mg, 73% yield). ^{1}H NMR (600 MHz, $CDCl_3$) □ 9.50 (s, 1H), 6.77 (m, 1H), 3.85 (dq, *J* = 10.8, 8.4 Hz, 1H), 3.75 (dq, *J* = 10.8, 8.4 Hz, 1H), 2.70 (m, 1H), 2.40 (d, *J* = 17.8 Hz, 1H), 2.35 – 2.24 (m, 2H), 2.21 (ddp, *J* = 13.8, 6.9, 3.7 Hz, 1H), 2.06 (dtt, *J* = 12.2, 6.0, 2.9 Hz, 1H), 1.75 (td, *J* = 9.2, 4.4 Hz, 1H), 1.63 –1.32 (m, 10H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 193.65, 152.46, 139.88, 124.19 (q, *J* = 278.7 Hz), 82.21, 62.01 (q, *J* = 34.0 Hz), 43.28, 40.84, 40.18, 37.26, 36.71, 35.88, 33.00, 32.19, 28.60, 27.55, 25.30, 24.19, 22.13, 20.92, 20.61, 14.68; IR (film) 2956, 2933, 2872, 1681, 1649, 1278, 1157, 1118, 972 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{33}F_3O_2Li$ $[M+Li]^+$: 393.2587, found: 393.2581.



144 **145**

To a solution of □,□-unsaturated aldehyde (53.3 mg, 0.138 mmol) in toluene (10 mL) was added DIBAL (1.0 M in toluene, 0.21 mL) dropwise at -78 °C. The reaction was stirred at -78 °C for 1.5 h then quenched by 10% Rochelle's salt solution (5 mL). The mixture was diluted with ethyl acetate (5 mL), warmed to r.t. and stirred vigorously until two clear layers formed. The organic layer was separated and the

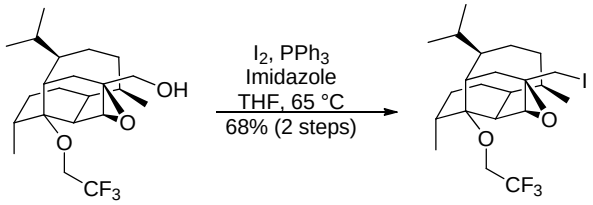
aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (10% ethyl acetate/hexanes) to afford a colorless oil (52.5 mg, 98% yield). ^{1}H NMR (600 MHz, $CDCl_3$) □ 5.62 (m, 1H), 4.06 (q, *J* = 13.1 Hz, 2H), 3.86 (dq, *J* = 10.7, 8.6 Hz, 1H), 3.76 (dq, *J* = 10.7, 8.6 Hz, 1H), 2.46 – 2.37 (m, 1H), 2.29 (ddt, *J* = 17.8, 6.5, 2.9 Hz, 1H), 2.21 – 2.09 (m, 2H), 2.03 – 1.90 (m, 2H), 1.76 – 1.62 (m, 1H), 1.62 – 1.15 (m, 11H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.4 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 136.37, 124.72 (d, *J* = 278.6 Hz), 124.29, 82.12, 67.15, 62.31 (q, *J* = 33.7 Hz), 42.62, 40.86, 38.06, 37.71, 37.49, 36.19, 33.11, 31.77, 28.83, 27.58, 25.52, 25.16, 24.47, 22.14, 20.90, 14.66; IR (film) 3342, 2956, 2933, 2872, 2358, 2341, 1466, 1278, 1155, 1124, 975, 734 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{35}F_3O_2Li$ $[M+Li]^+$: 395.2744, found: 395.2730.



145 **146**

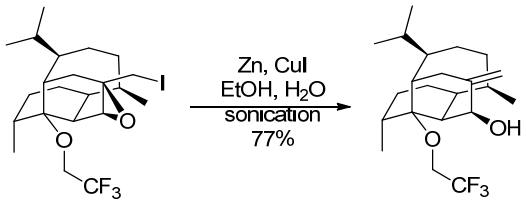
A mixture of allylic alcohol (40.0 mg, 0.103 mmol) and $NaHCO_3$ (43.3 mg, 0.515 mmol) in CH_2Cl_2 (2.0 mL) was cooled to 0 °C, to which *meta*-chloroperoxybenzoic acid (70-75 wt% with benzonic acid and water, 36.8 mg, 0.154 mmol) was added in one portion. The mixture was allowed to warm to r.t. naturally and stirred for total 18 h. After water (2 mL) and ethyl acetate (10 mL) were added to the mixture, the organic phase was separated and washed with saturated $NaHSO_3$ solution (3 × 2 mL), saturated $NaHCO_3$ solution (3 × 2 mL) and brine (2 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The resultant solid (43.4 mg) was used in the next step without further purification. An analytical sample was obtained by triturating the solid with hexanes. ^{1}H NMR (600 MHz, $CDCl_3$) □ 4.19 (m, 1H), 3.81 – 3.70 (m, 2H), 3.65 (dd, *J* = 12.3, 9.7 Hz, 1H), 3.38 (s, 1H), 2.69 (d, *J* = 3.9 Hz, 1H), 2.26 (dd, *J* = 15.8, 8.0 Hz, 1H), 2.14 (dqd, *J* = 13.7, 7.2, 3.9 Hz, 1H), 2.09 – 1.99 (m,

1H), 1.97 (d, *J* = 8.0 Hz, 1H), 1.75 (d, *J* = 9.2 Hz, 1H), 1.69 (td, *J* = 9.8, 4.0 Hz, 1H), 1.63 – 1.43 (m, 7H), 1.43 – 1.23 (m, 4H), 0.95 – 0.89 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 124.75 (q, *J* = 278.3 Hz), 80.78, 62.59, 61.89 (q, *J* = 33.6 Hz), 60.63, 59.00, 42.25, 40.77, 37.44, 36.90, 35.35, 34.74, 33.23, 29.93, 28.78, 28.29, 26.37, 24.59, 23.25, 21.87, 21.16, 14.23; IR (film) 3431, 2954, 2937, 2873, 1456, 1278, 1155, 1122, 974 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{35}F_3O_3Li$ $[M+Li]^+$: 411.2693, found: 411.2693.



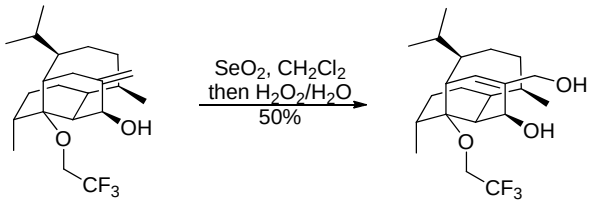
146 **147**

In a high-pressure tube, a mixture of triphenylphosphine (32.6 mg, 0.124 mmol), imidazole (11.2 mg, 0.165 mmol), iodine (31.5 mg, 0.124 mmol) and epoxy alcohol (33.5 mg, 0.0828 mmol) in THF (1.5 mL) was heated to 65 °C and stirred for 5.0 h. The reaction was cooled to r.t., diluted with ethyl acetate (5 mL), washed with 10% $Na_2S_2O_3$ solution (2 × 3 mL) and brine (3 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was loaded on a silica gel column and eluted with 5% diethyl ether/hexanes. The eluate was collected, concentrated on rotovap and placed under high vacuum briefly to give a white solid (27.8 mg, 68% for two steps). The product was used immediately afterward. (Note: This product was unstable when concentrated; partial decomposition was observed after it was dried under high vacuum overnight at room temperature.)



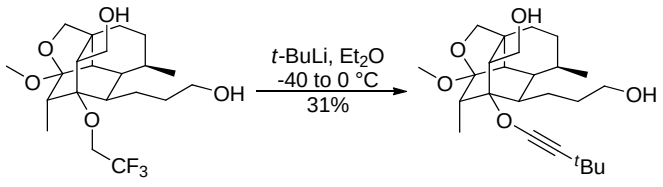
147 **148**

Commercial zinc powder was stirred with 1 N HCl solution for 5 min, and then the acid solution was removed by a pipette. The zinc residue was washed with water (3 ×), absolute ethanol (3 ×) and dry diethyl ether (3 ×). (The wash solutions were removed each time by a pipette.) The material was then dried under high vacuum overnight. The pre-treated zinc powder (73.4 mg, 1.12 mmol) and copper(I) iodide (106.6 mg, 0.560 mmol) are sonicated under N_2 in ethanol/H_2O (2:3 v/v, 4.5 ml) for 5 min. A mixture of iodide (28.8 mg, 0.0560 mmol) in ethanol (2.0 ml) was added to the resultant black suspension and the sonication was continued for 1.5 h. The reaction was quenched by saturated NH_4Cl solution (1.0 mL), filtered through a Celite pad and washed with diethyl ether. The filtrate was extracted with ether (3 × 5 mL), and the combined extracts were washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (10% diethyl ether/hexanes) to give a colorless oil (16.7 mg, 77%). ^{1}H NMR (600 MHz, $CDCl_3$) □ 5.09 (s, 1H), 5.03 (s, 1H), 4.26 (d, *J* = 7.9 Hz, 1H), 4.05 (dq, *J* = 10.3, 8.3 Hz, 1H), 3.81 (dq, *J* = 10.3, 8.3 Hz, 1H), 2.75 (d, *J* = 7.8 Hz, 1H), 2.71 – 2.62 (m, 1H), 2.41 (d, *J* = 4.8 Hz, 1H), 2.31 (d, *J* = 16.2 Hz, 1H), 2.16 (pd, *J* = 7.1, 4.1 Hz, 1H), 2.06 (d, *J* = 7.6 Hz, 1H), 1.93 (dq, *J* = 13.6, 7.0 Hz, 1H), 1.84 (dtd, *J* = 14.0, 6.8, 4.3 Hz, 1H), 1.78 (m, 1H), 1.71 (m, 1H), 1.68 – 1.46 (m, 4H), 1.46 – 1.21 (m, 4H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.97 – 0.91 (m, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) □ 148.36, 124.50 (q, *J* = 277.9 Hz), 113.11, 84.37, 75.62, 60.78 (q, *J* = 33.8 Hz), 47.92, 44.98, 40.61, 38.69, 36.02, 36.00, 33.35, 31.23, 29.04, 28.89, 28.56, 26.67, 25.36, 21.66, 20.76, 15.87; IR (film) 3417, 2954, 2931, 2875, 1454, 1393, 1276, 1159, 1118, 972, 906, 879, 734 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{35}F_3O_2Li$ $[M+Li]^+$: 395.2744, found: 395.2734.



148 **150**

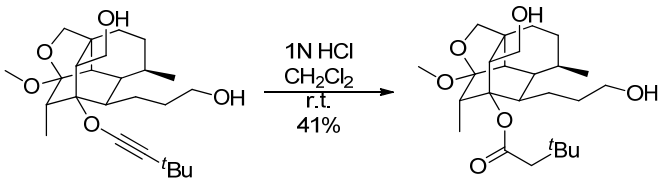
A mixture of exo-olefin (12.0 mg, 0.0309 mmol) and selenium dioxide (17.1 mg, 0.154 mmol) in CH_2Cl_2 (3.0 mL) was stirred at r.t. for 6 h then hydrogen peroxide (30 wt% in water, 0.035 mL, 0.309 mmol) was added and stirred for 16 h. The reaction was diluted with ethyl acetate (6 mL) and washed with 10% $NaHSO_3$ solution (2 mL), saturated $NaHCO_3$ solution (2 mL) and brine (2 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (15% ethyl acetate/hexanes) to give a colorless oil (6.3 mg, 50% yield). ^{1}H NMR (600 MHz, $CDCl_3$) □ 5.72 (d, *J* = 5.8 Hz, 1H), 4.34 – 4.16 (m, 2H), 4.06 (d, *J* = 11.1 Hz, 1H), 3.71 – 3.52 (m, 2H), 2.84 (d, *J* = 11.2 Hz, 1H), 2.60 (s, 1H), 2.40 (d, *J* = 4.6 Hz, 1H), 2.27 (d, *J* = 5.7 Hz, 1H), 2.22 – 2.07 (m, 2H), 2.06 – 1.96 (m, 1H), 1.88 (ddt, *J* = 25.5, 12.9, 4.8 Hz, 2H), 1.66 (pd, *J* = 6.8, 3.9 Hz, 1H), 1.60 – 1.49 (m, 1H), 1.49 – 1.31 (m, 4H), 1.31 – 1.12 (m, 2H), 1.10 (d, *J* = 7.0 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 139.93, 124.47, 124.38 (q, *J* = 278.3 Hz), 83.60, 72.61, 66.83, 59.81 (q, *J* = 33.8 Hz), 50.87, 45.86, 40.27, 37.64, 35.85, 33.80, 33.28, 30.63, 29.82, 28.91, 28.46, 26.52, 21.14, 19.73, 17.54; IR (film) 3429, 2953, 2927, 2358, 2345, 1269, 1161, 1111, 1006, 974, 894 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{35}F_3O_3Li$ $[M+Li]^+$: 411.2693, found: 411.2682.



91 **151**

To a mixture of diol (50.0 mg, 0.118 mmol) in diethyl ether (5.0 mL) cooled to -40 °C, was added *tert*-butyllithium (1.7 M in pentane, 1.0 mL) dropwise. After the

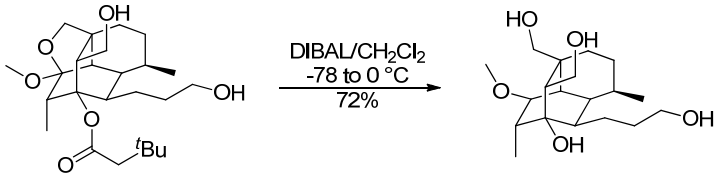
addition was completed, the reaction mixture was allowed to warm up to 0 °C naturally (over 2.0 h). The reaction was stirred at 0 °C for further 30 min. then quenched by methanol (0.5 mL) and saturated NH_4Cl solution (1.0 mL). The mixture was extracted with ethyl acetate (3 × 2 mL) and the combined extracts were washed with brine (2 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. ^{1}H-NMR analysis of the crude product indicated 50% conversion of starting material to product. The crude product was re-subjected to the same reaction conditions and ^{1}H-NMR analysis indicated complete consumption of the starting material. The crude product was purified by column chromatography (40% ethyl acetate/hexanes) to afford a white solid (15.4 mg, 31% yield). ^{1}H NMR (600 MHz, $CDCl_3$) □ 4.07 (dd, *J* = 11.0, 3.6 Hz, 1H), 3.95 – 3.85 (m, 1H), 3.65 (d, *J* = 6.7 Hz, 1H), 3.60 (m, 2H), 3.39 (d, *J* = 6.7 Hz, 1H), 3.31 (s, 3H), 2.56 (q, *J* = 7.2 Hz, 1H), 2.32 (dt, *J* = 9.4, 2.7 Hz, 1H), 2.29 – 2.24 (m, 1H), 2.22 (dt, *J* = 11.8, 2.7 Hz, 1H), 2.07 – 1.98 (m, 1H), 1.76 – 1.59 (m, 5H), 1.53 – 1.43 (m, 3H), 1.43 – 1.30 (m, 3H), 1.19 (s, 9H), 1.18 (d, *J* = 7.5 Hz, 3H), 0.93 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 108.34, 89.16, 83.42, 81.29, 62.66, 59.75, 51.53, 51.09, 49.96, 49.05, 47.61, 41.96, 38.32, 35.08, 34.82, 33.62, 32.16 (3C), 28.68, 28.00, 26.90, 21.39, 19.62, 9.50; IR (film) 3425, 2957, 2927, 2867, 1464, 1205, 1138, 1046, 985, 958, 910, 732 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{25}H_{41}O_5$ $[M+H]^+$: 421.2948, found: 421.2948.



151 **152**

Alkynyl ether (13.3 mg, 0.0316 mmol) was dissolved in dichloromethane (1.5 mL) and treated with 1 N HCl (1.5 mL) for 2.0 h with vigorous stirring. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 2 mL). The combined organic phase was washed with saturated $NaHCO_3$ solution (3 × 3 mL) and brine (3 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by prep-TLC (75% ethyl acetate/hexanes) to afford a white solid

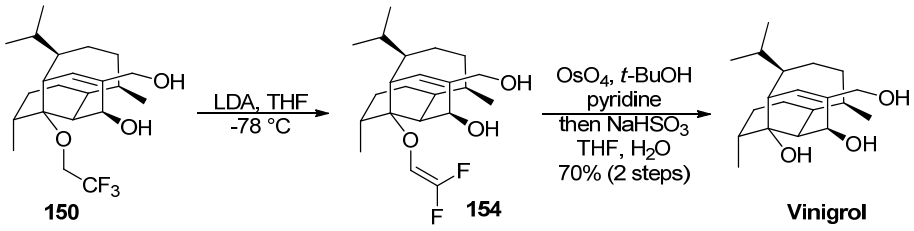
(5.7 mg, 41%). ^{1}H NMR (500 MHz, $CDCl_3$) □ 3.93 (t, *J* = 10.9 Hz, 1H), 3.74 (dd, *J* = 11.2, 3.3 Hz, 1H), 3.69 – 3.56 (m, 3H), 3.37 (d, *J* = 6.7 Hz, 1H), 3.30 (s, 2H), 3.18 (dt, *J* = 10.2, 2.6 Hz, 1H), 3.05 (q, *J* = 7.2 Hz, 1H), 2.32 – 2.24 (m, 1H), 2.21 (dt, *J* = 11.4, 2.0 Hz, 1H), 2.18 (s, 2H), 2.02 (m, 1H), 1.80 – 1.67 (m, 1H), 1.67 – 1.58 (m, 6H), 1.53 (m, 1H), 1.48 (d, *J* = 2.6 Hz, 1H), 1.43 – 1.27 (m, 3H), 1.21 – 1.17 (m, 3H), 1.04 (s, 9H), 0.90 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) □ 171.78, 108.43, 87.31, 81.56, 62.90, 60.26, 50.43, 50.11, 49.08, 47.76, 46.95, 41.95, 38.38, 36.07, 35.54, 32.94, 30.91, 29.85 (3C), 28.76, 27.81, 21.38, 20.34, 9.95; IR (film) 3438, 2954, 2871, 1725, 1475, 1228, 1134, 1046, 1012, 986, 916, 732 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{25}H_{43}O_6$ $[M+H]^+$: 439.3054, found: 439.3054.



152 **153**

To a solution of ester (5.7 mg, 0.0130 mmol) in CH_2Cl_2 (0.80 mL) cooled at -78 °C, DIBAL (1.0M in CH_2Cl_2, 0.13 mL) was added dropwise. The reaction solution was stirred at -78 °C for 30 min. then warmed to 0 °C and stirred for 2 h. The reaction was quenched by saturated Rochelle's salt solution (0.50 mL) and diluted with ethyl acetate (2.0 mL). The mixture was warmed to r.t. and stirred vigorously for 30 min. A clear two layers were formed and the upper organic layer was separated and the rest aqueous layer was extracted with ethyl acetate (3 × 2 mL). The combined organic layers were washed with brine (3.0 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by prep-TLC (10% MeOH/CH_2Cl_2) to give a colorless oil (3.2 mg, 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) □ 4.24 (dd, *J* = 10.6, 7.3 Hz, 1H), 3.88 – 3.70 (m, 3H), 3.62 (dt, *J* = 9.5, 4.4 Hz, 2H), 3.48 (d, *J* = 10.1 Hz, 1H), 3.32 (d, *J* = 10.2 Hz, 1H), 3.26 (s, 3H), 2.89 (bs, 1H), 2.38 (dt, *J* = 11.9, 2.6 Hz, 1H), 2.14 – 2.07 (m, 1H), 2.07 – 2.01 (m, 1H), 1.97 (dq, *J* = 10.3, 7.2 Hz, 1H), 1.92 – 1.83 (m, 1H), 1.83 – 1.70 (m, 2H), 1.69 – 1.53 (m, 4H), 1.45 (m, 2H), 1.32 (m, 1H), 1.15 (d, *J* = 5.8 Hz, 3H), 0.97 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) □ 76.91,

76.00, 73.16, 61.48, 60.88, 57.22, 55.06, 46.94, 42.51, 38.69, 38.06, 35.83, 34.10, 33.55, 31.79, 29.60, 21.68, 19.58, 8.14; IR (film) 3340, 2921, 2875, 1458, 1375, 1193, 1062, 1015, 909, 731 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{19}H_{35}O_5$ $[M+H]^+$: 343.2479, found: 343.2478.

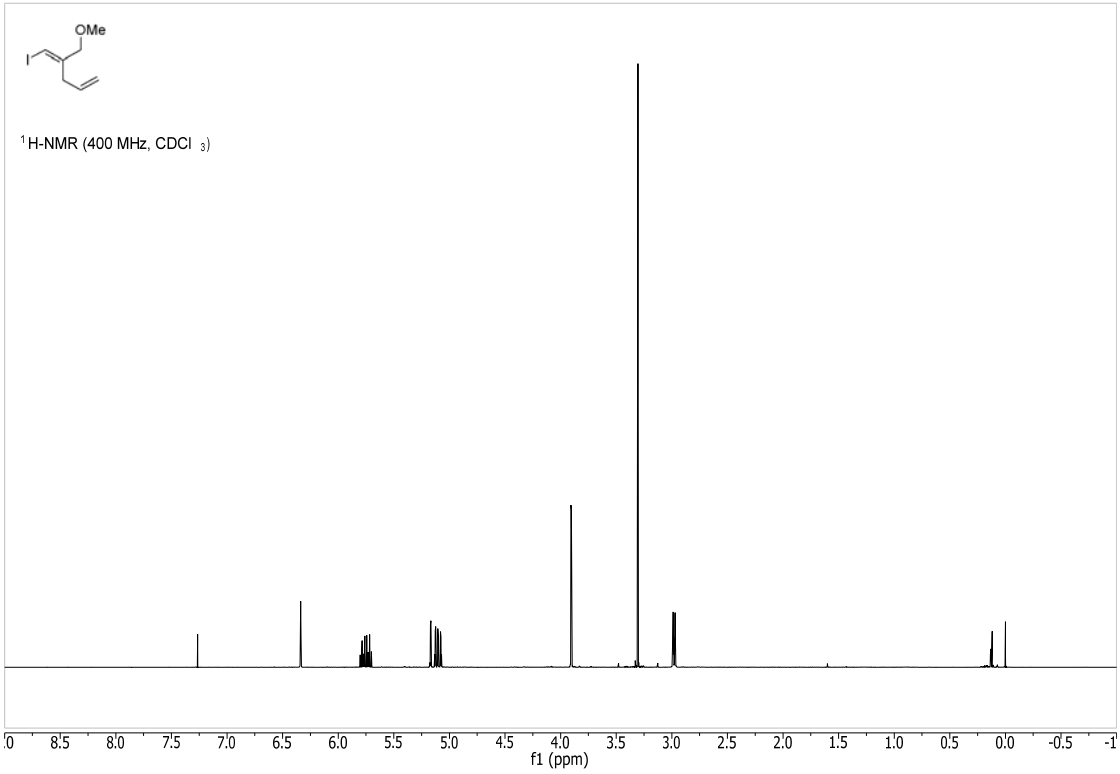


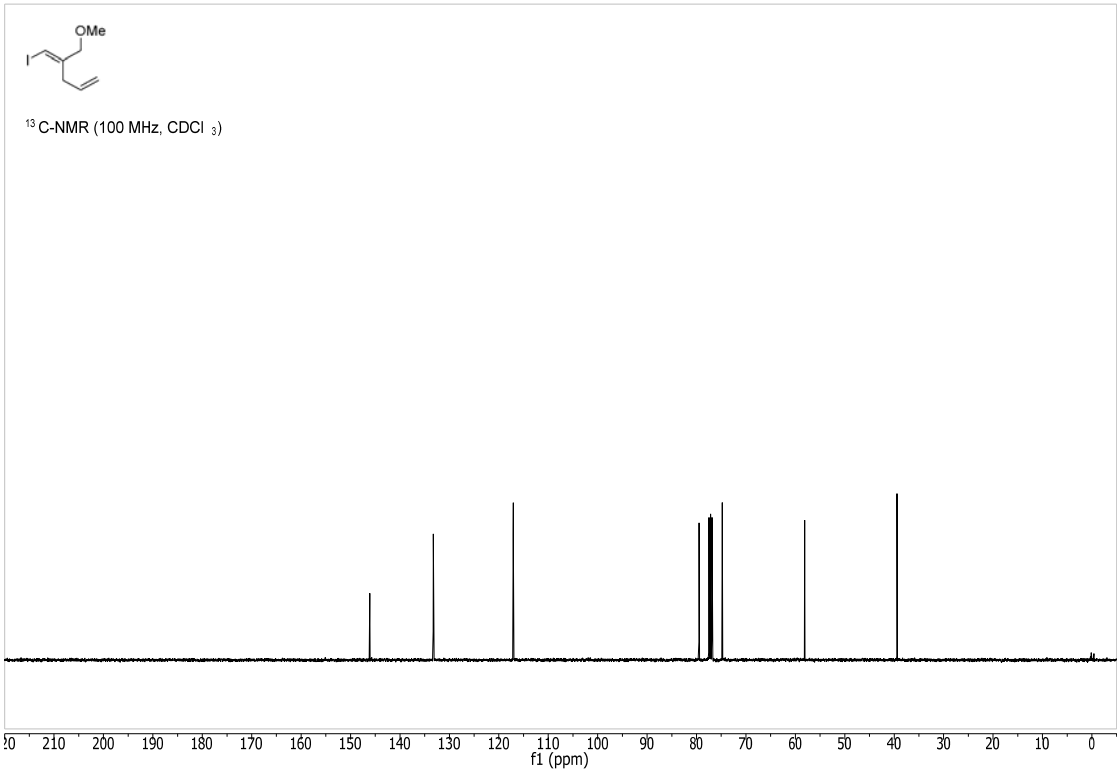
To a solution of trifluoroethyl ether (0.7 mg, 0.0017 mmol) in THF (0.15 mL), freshly prepared LDA (0.5 M in THF, 0.27 mL, 0.136 mmol) was added slowly at -78 °C. After the addition was completed, the reaction was stirred at -78 °C for 30 min. then quenched by saturated NH_4Cl solution (0.5 mL) and extracted with ethyl acetate (3 × 1.0 mL). The combined extracts were washed with brine (1.5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. ^{1}H-NMR analysis of crude product indicated 25% conversion of starting material to product. The crude product was purified by prep-TLC (60% diethyl ether/hexanes) to provide the unreacted starting material and difluorovinyl ether. The isolated starting material was re-subjected to the same reaction conditions. After three iterations, approximate 0.6 mg of difluorovinyl ether was obtained (judging by the integration of the ^{1}H-NMR peaks of solvent and product).

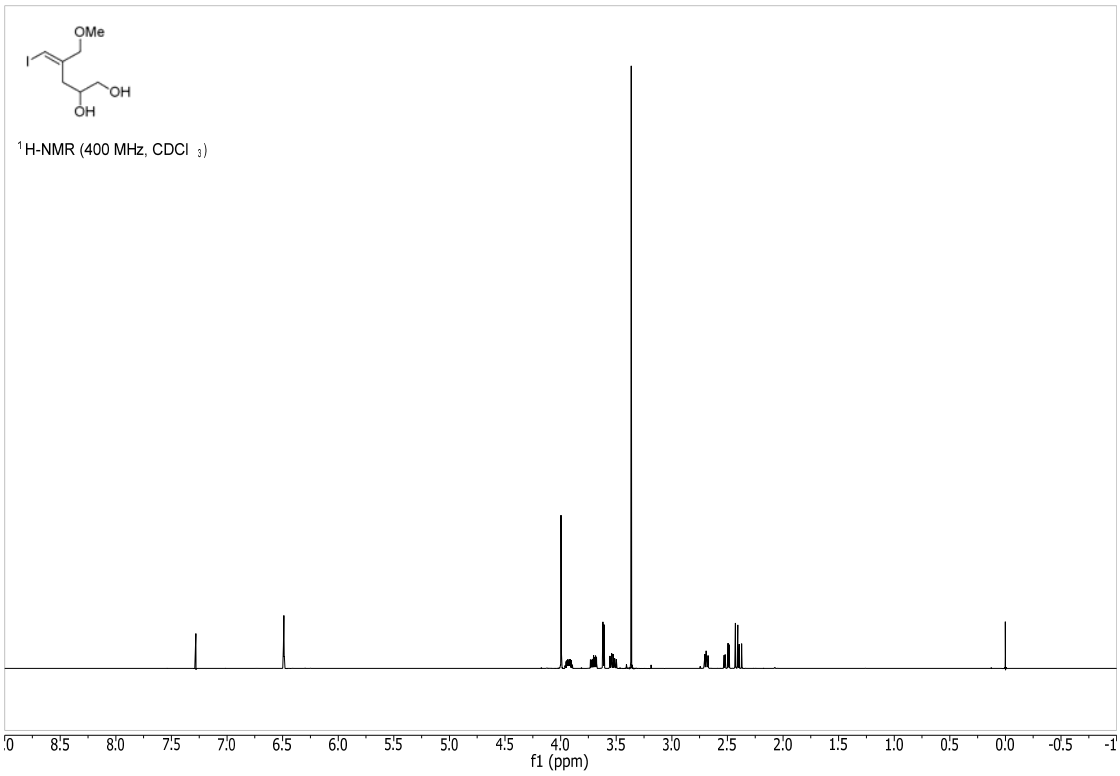
The aforementioned difluorovinyl ether was dissolved in pyridine (0.30 mL) and osmium tetroxide (2.5 wt% in *tert*-butanol, 0.05 mL, 0.0039 mmol) was added at r.t. After stirring for 30 min., the reaction was quenched by saturated $NaHSO_3$ solution (1.5 mL), diluted with THF (1.0 mL) and stirred vigorously at r.t. for 8.0 h. The reaction mixture was extracted with ethyl acetate (3 × 2.0 mL), washed with brine (2.0 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by a short silica gel column (50% acetonitrile/benzene) to give approximate 0.4 mg of product (judging by the integration of the ^{1}H-NMR peaks of solvent and

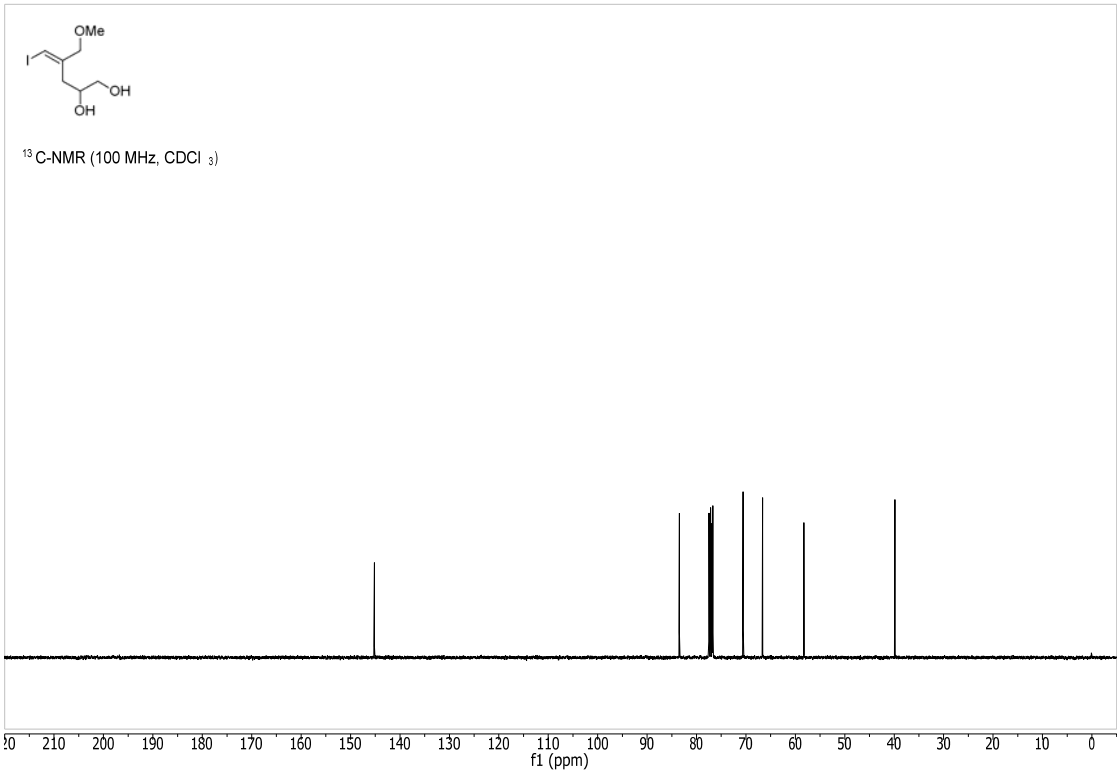
product, 70% yield for two steps). ^{1}H NMR (600 MHz, $CDCl_3$) □ 5.84 (d, *J* = 5.6 Hz, 1H), 4.30 (AB q, *J* = 12.0 Hz, 2H), 4.19 (s, 1H), 3.30 (bs, 1H), 2.45 (bs, 1H), 2.30 (d, *J* = 5.6 Hz, 1H), 2.26 (d, *J* = 3.9 Hz, 1H), 2.15 – 2.09 (m, 1H), 2.03 – 1.93 (m, 2H), 1.81 – 1.71 (m, 2H), 1.66 – 1.53 (m, 3H), 1.40 – 1.10 (m, 6H), 1.00 – 0.95 (m, 9H), 0.90 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (extracted from HSQC and HMBC spectra) □ 136.8, 128.4, 75.6, 72.8, 67.9, 51.3, 45.8, 44.2, 40.4, 35.9, 34.7, 33.1, 29.6, 29.0, 28.7, 27.3, 24.9, 21.5, 20.6, 15.4; IR (film) 3405, 2954, 2925, 2869, 2855, 1559, 1462, 1386, 1106, 1017, 998, 904, 736, 701 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{20}H_{34}O_3Li$ $[M+Li]^+$: 329.2662, found: 329.2662.

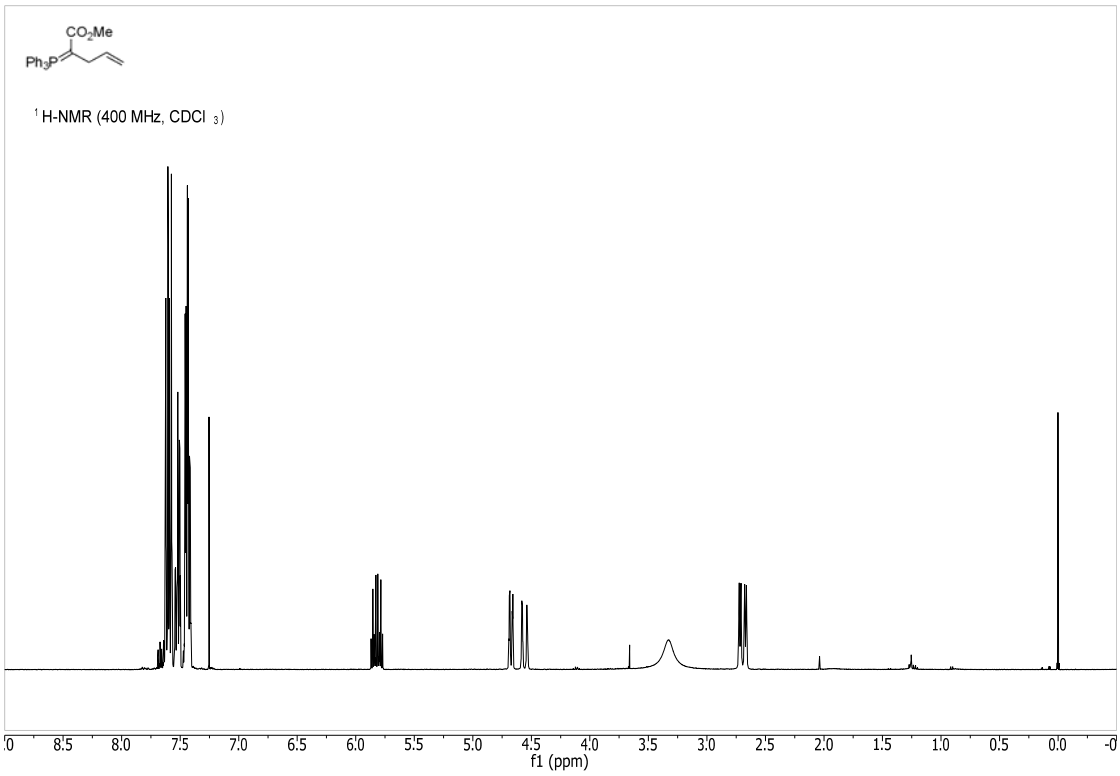
^{1}H and ^{13}C NMR spectra

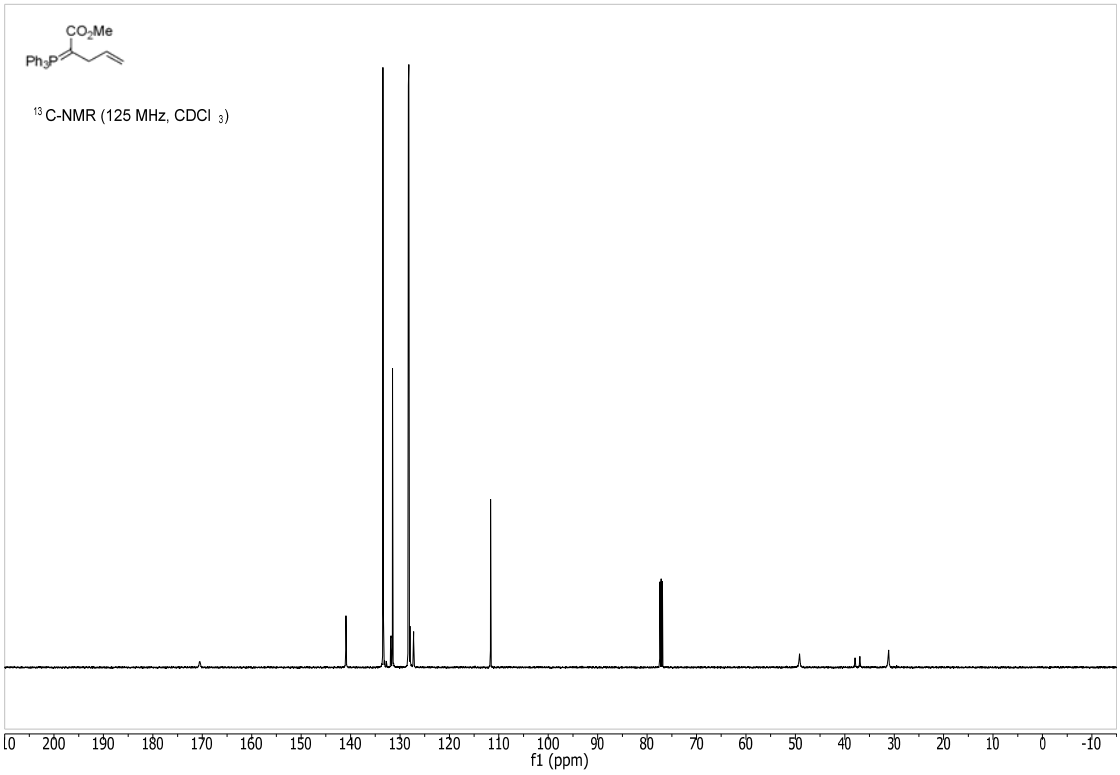


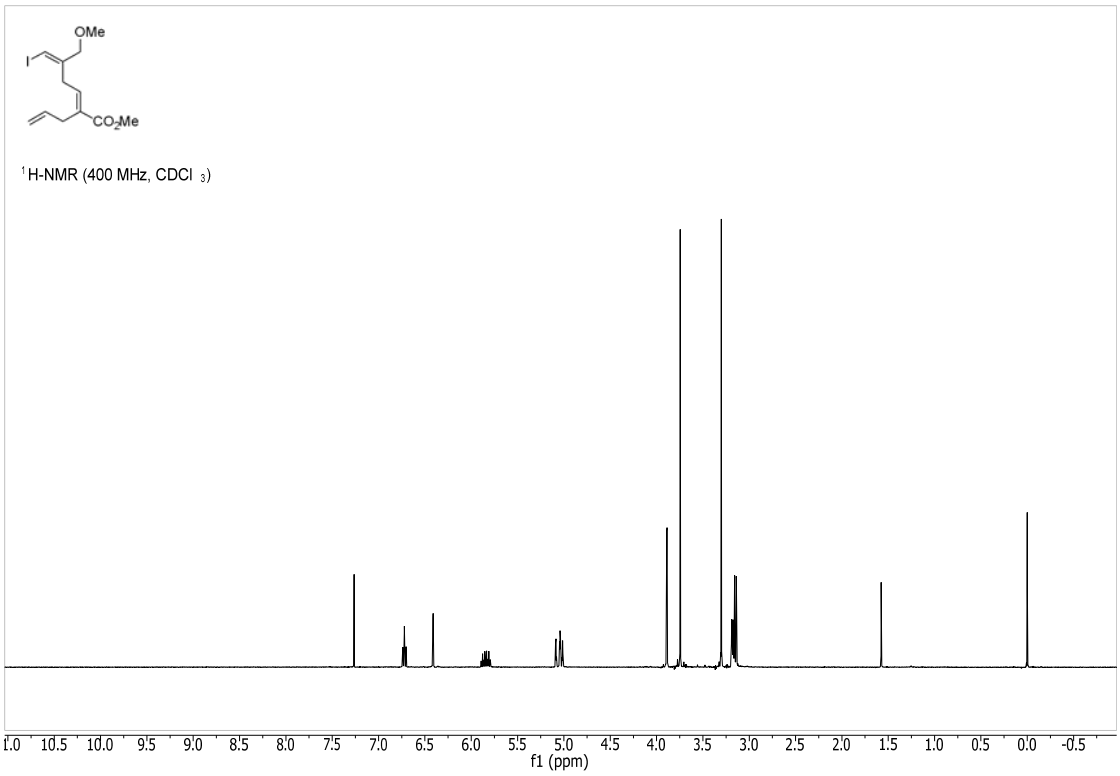


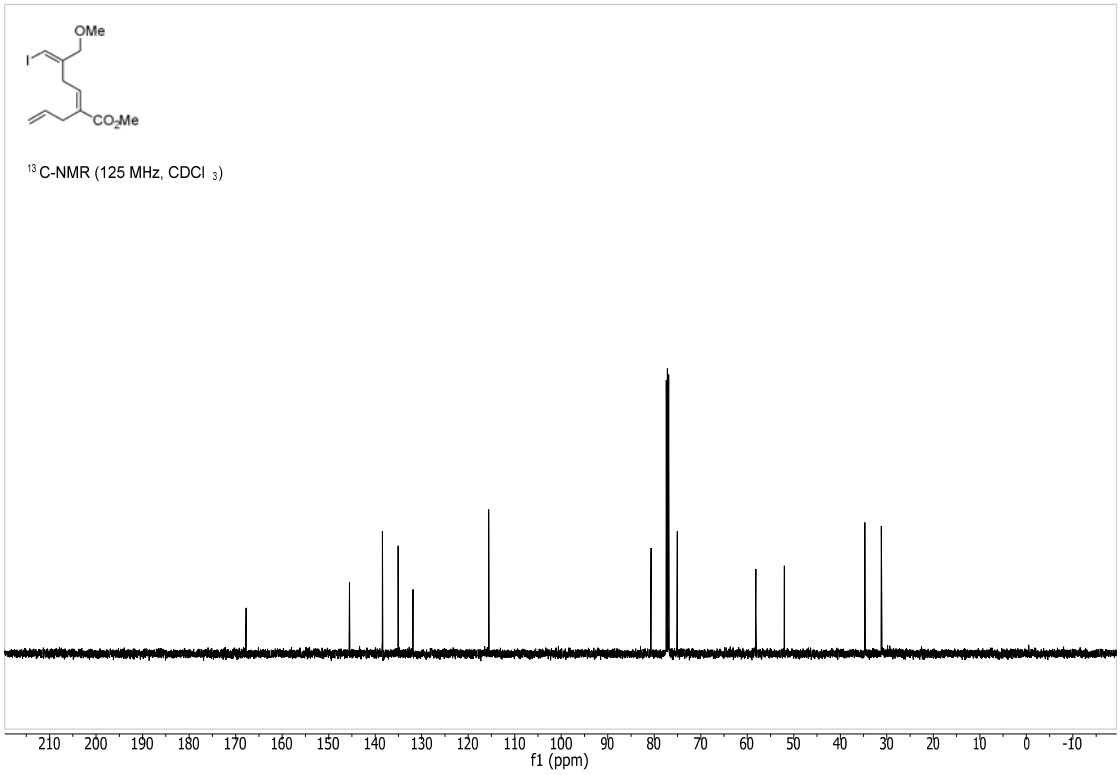


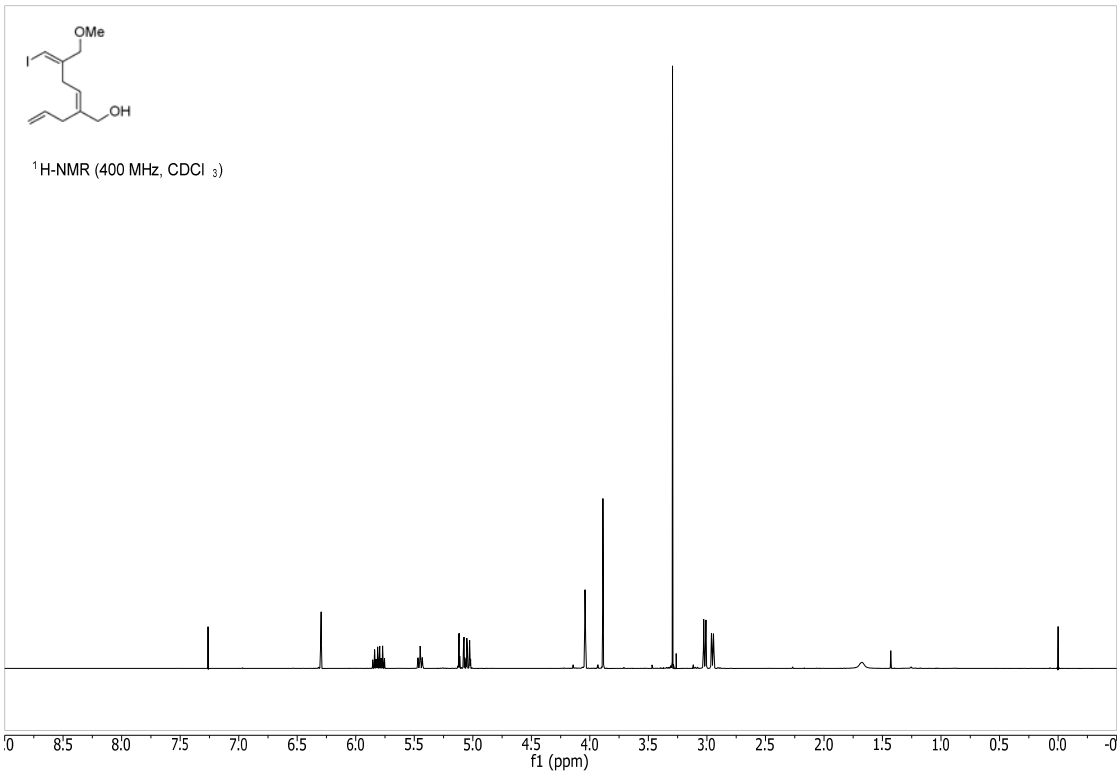


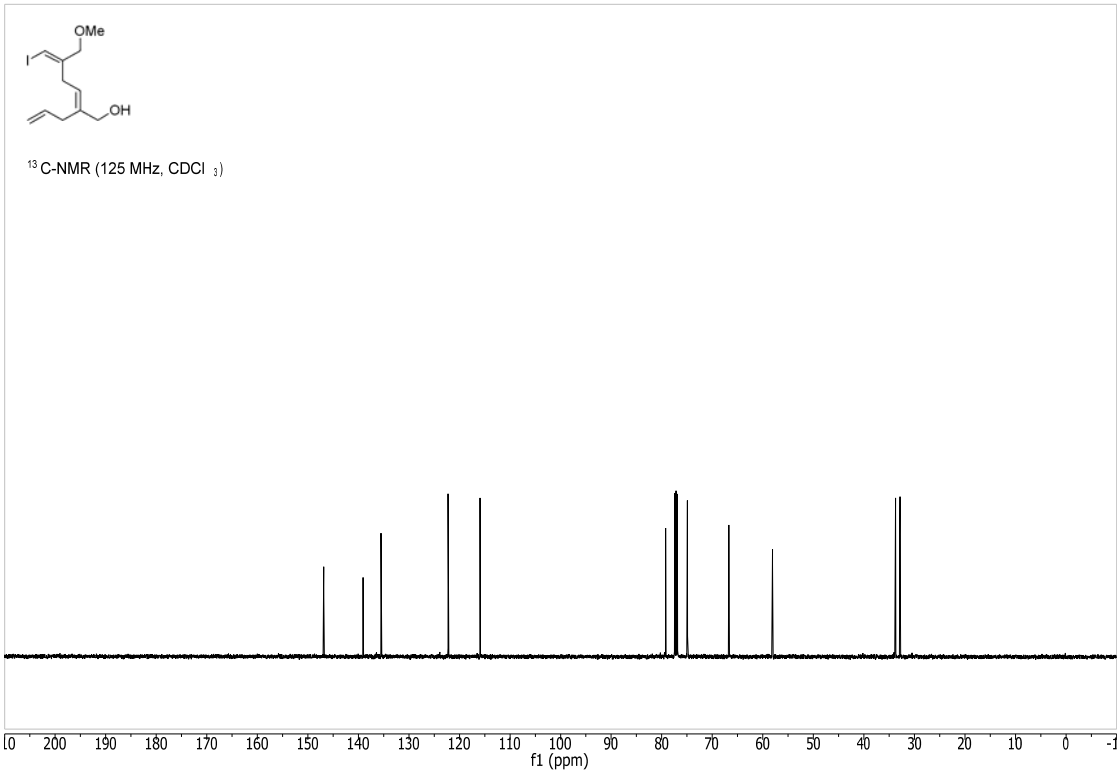


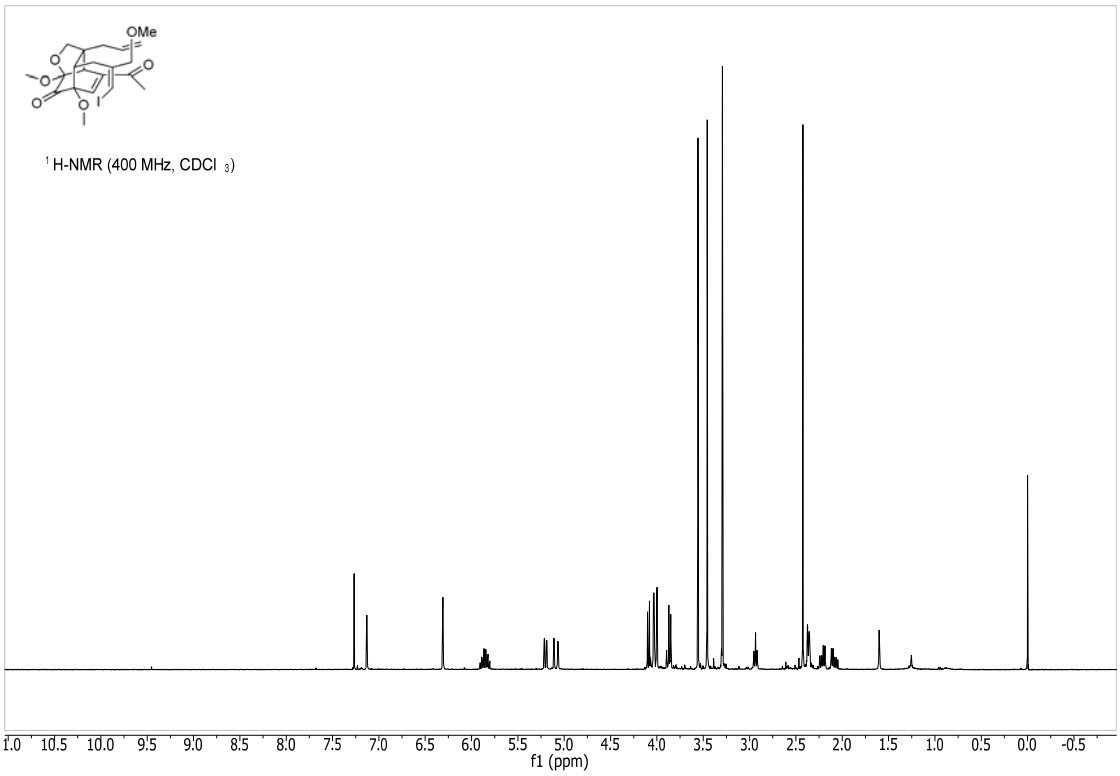


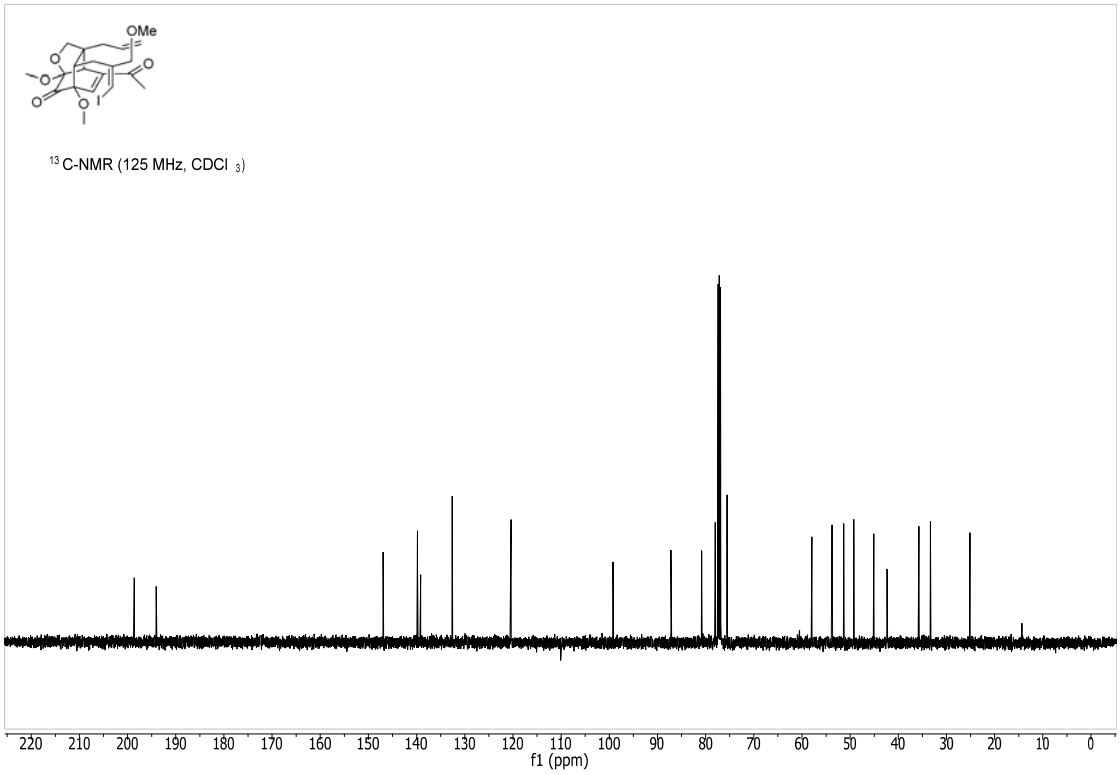

OMe
I
CO2Me
1H-NMR (400 MHz, CDCl 3)
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

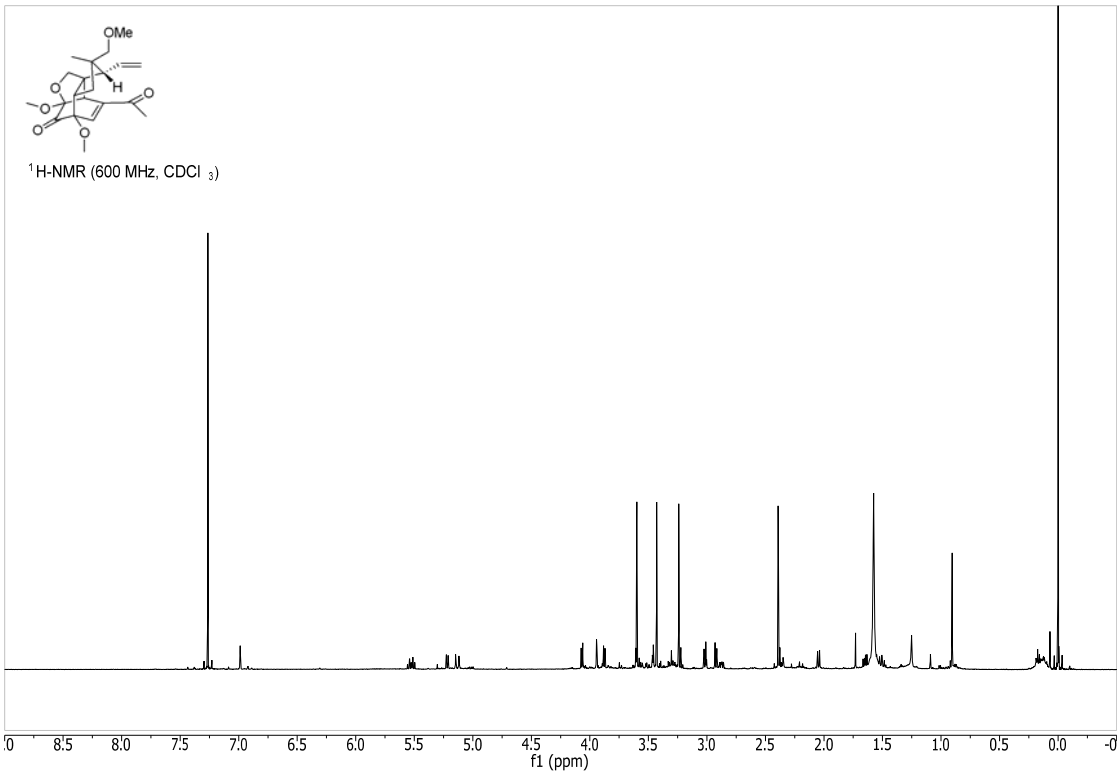

OMe
I
CO2Me
13C-NMR (125 MHz, CDCl 3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

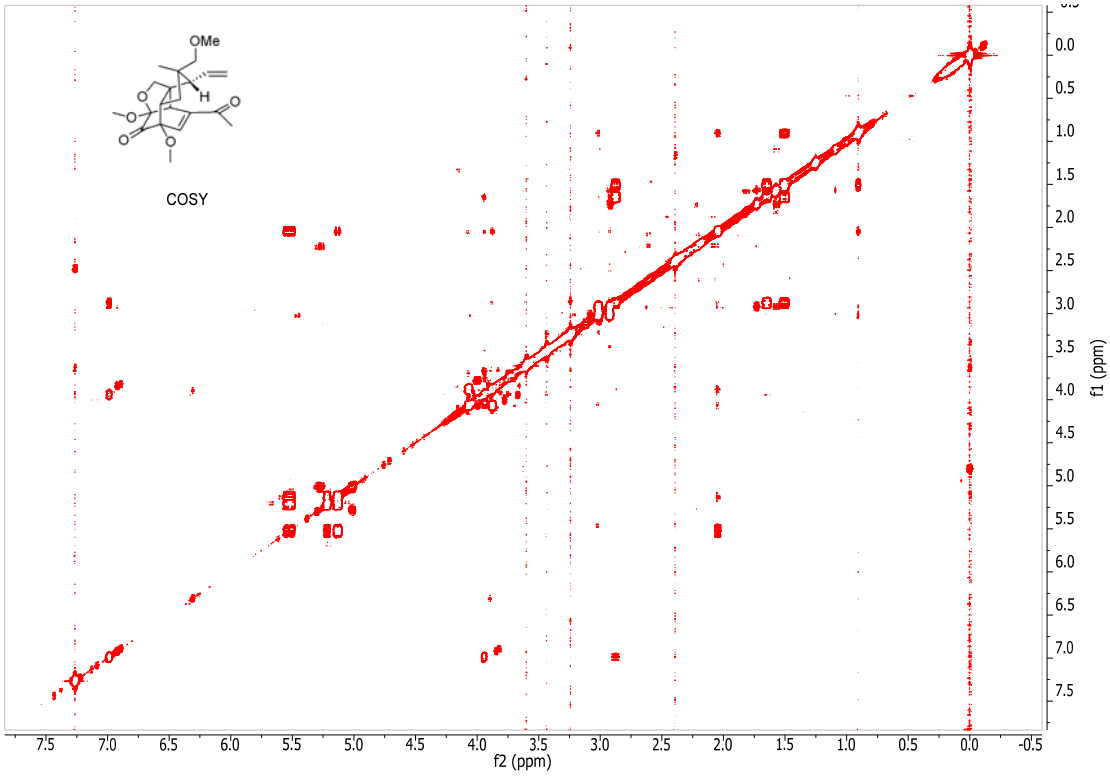


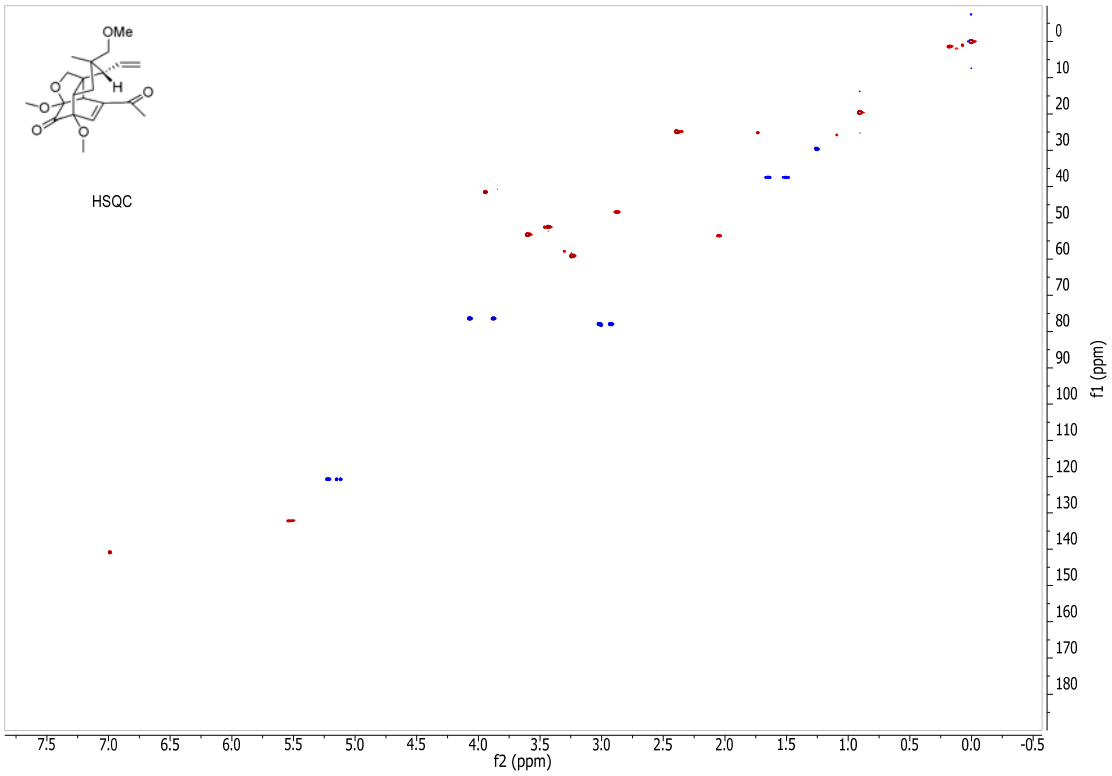


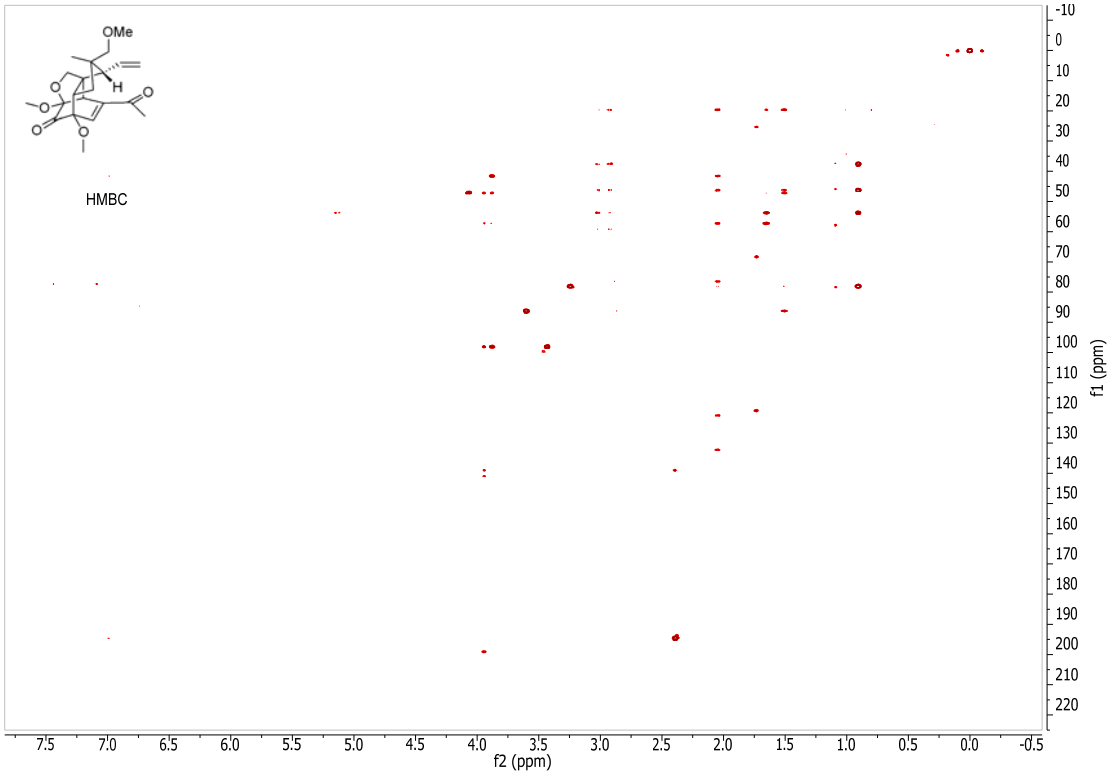












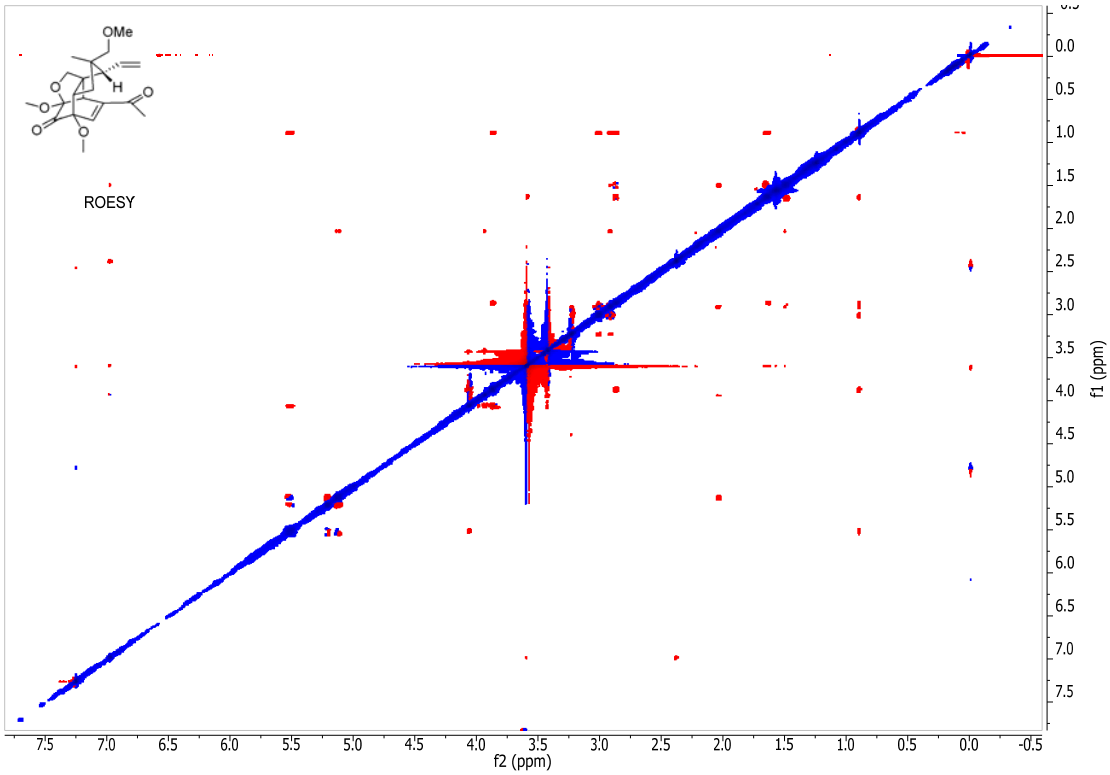
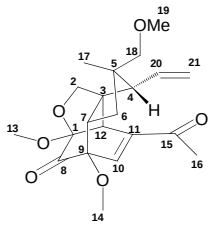
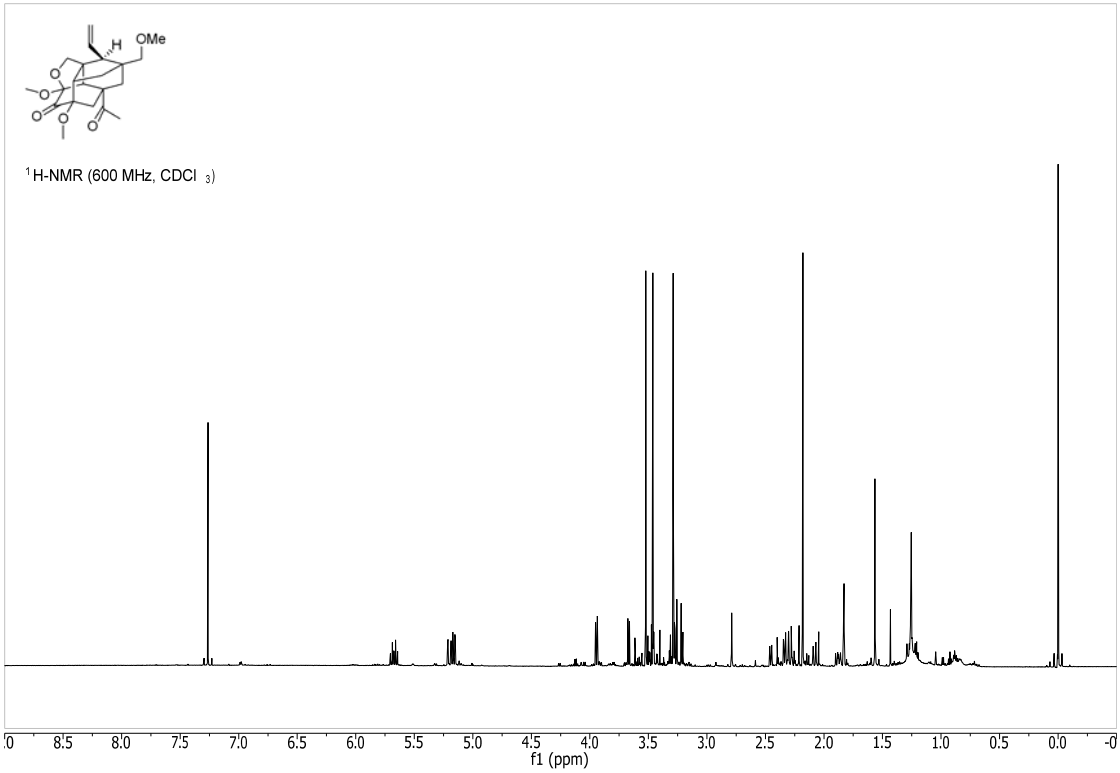
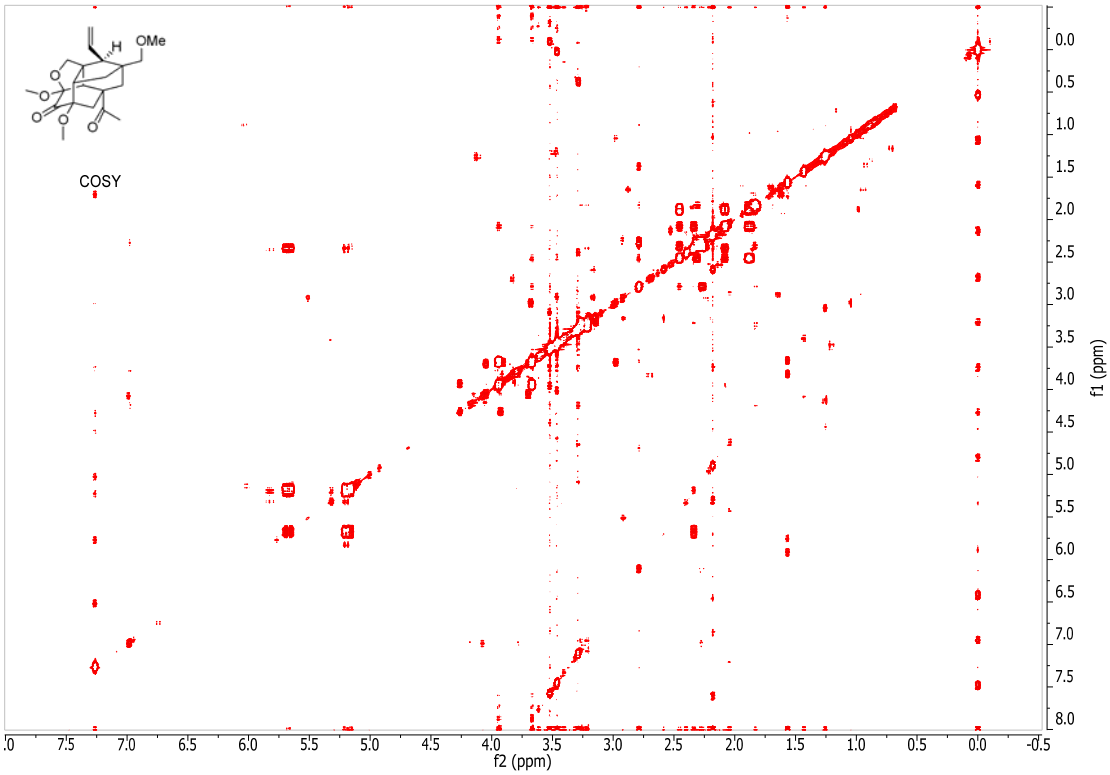


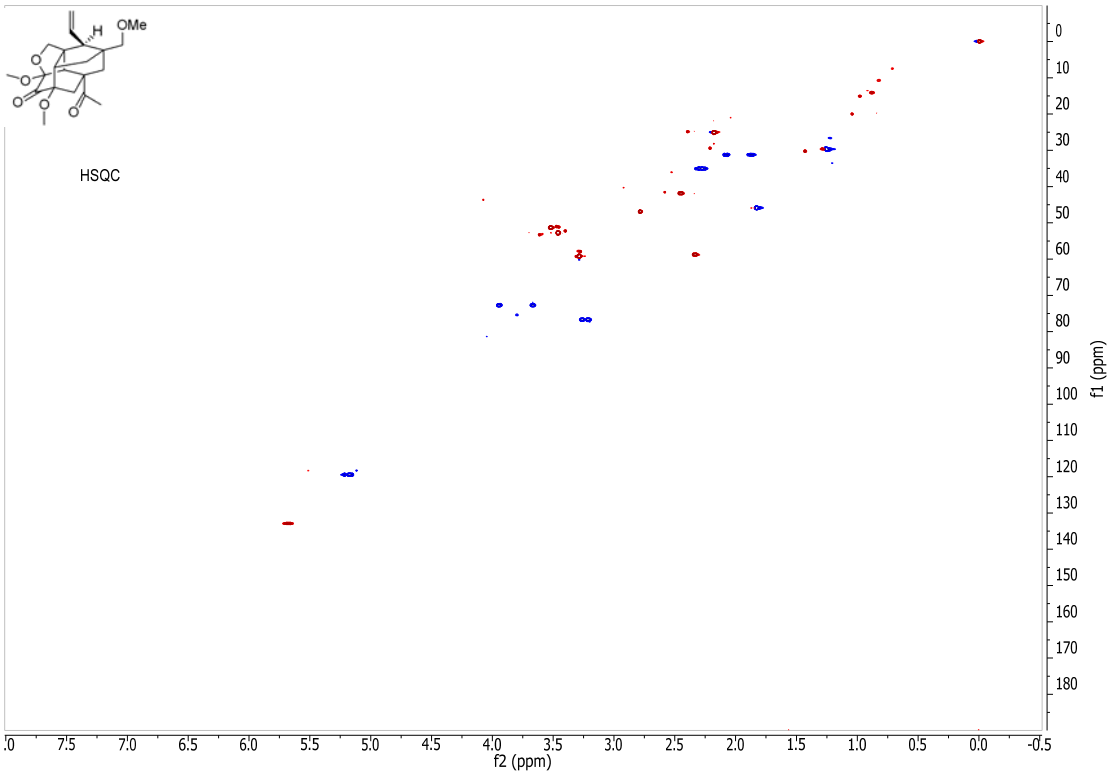
Table 1. 2D-NMR Data of Compound **32**

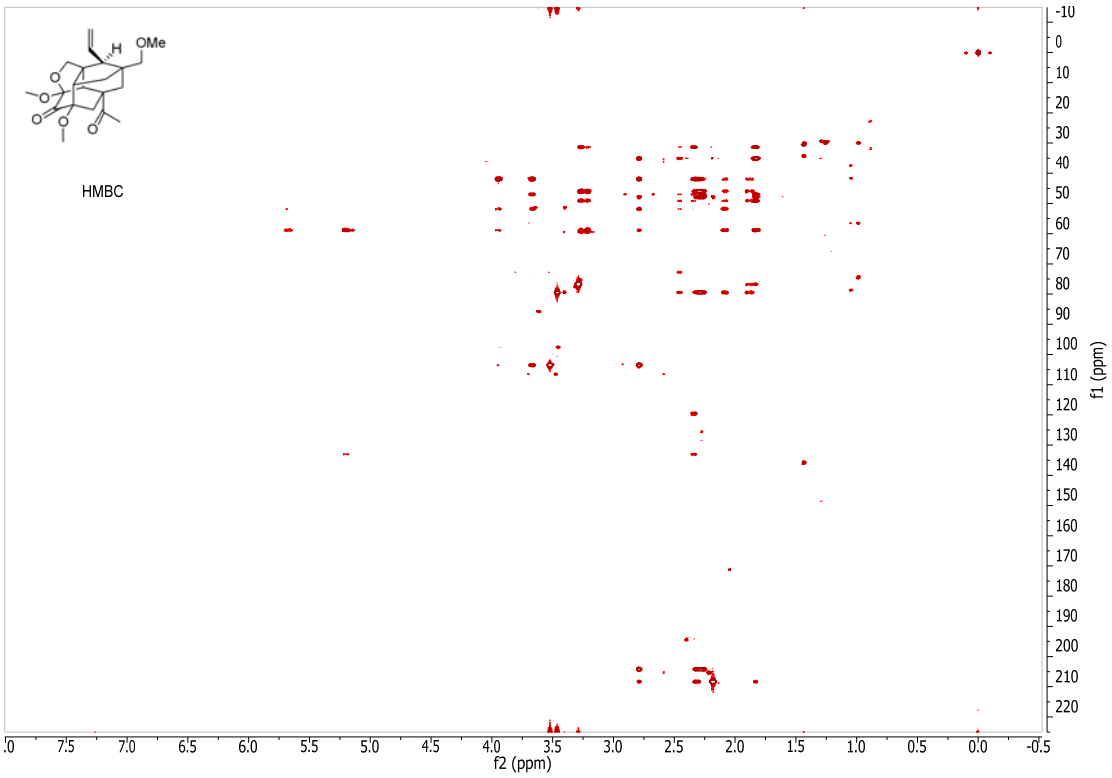


Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations	ROESY correlations
1	98.0		Cq			
2a	76.3	4.07	CH_2	H-2b, H-4	C-7	H-12, H-20
2b		3.88	CH_2	H-2a, H-4, H-7	C-1, C-12	H-7
3	57.2		Cq			
4	53.6	2.05	CH	H-2a, H-2b, H-17, H-20, H-21b	C-3, C-5, C-12, C-20, C-21	H-6b, H-12, H-18b, H-21b
5	46.0		Cq			
6a	37.5	1.65	CH_2	H-6b, H-7	C-3, C-4, C-17	H-7, H-14
6b		1.51	CH_2	H-6a, H-7, H-17	C-5, C-7, C-9, C-17	H-4, H-10
7	47.0	2.88	CH	H-2b, H-6a, H-6b, H-10	C-2, C-9, C-10	H-2b, H-6a, H-18a, H-18b
8	198.9		Cq			
9	86.1		Cq			
10	140.9	6.99	CH_3	H-7, H-12	C-15	H-6b, H-14, H-16
11	138.7		Cq			
12	41.5	3.94	CH	H-10	C-1, C-3, C-8, C-10, C-11	H-2a, H-4
13	51.1	3.43	CH_3		C-1	
14	53.3	3.60	CH_3		C-9	H-6a, H-10
15	194.5		Cq			
16	24.8	2.39	CH_3		C-11, C-15	H-10
17	19.5	0.91	CH_3	H-4, H-6b, H-18a	C-4, C-5, C-6, C-18	H-2b, H-6a, H-7, H-18a, H-18b, H-20
18a	77.9	3.02	CH_2	H-17, H-18b	C-5, C-6, C-19	H-7
18b		2.92	CH_2	H-18a	C-5, C-6, C-17, C-19	H-4, H-7
19	59.2	3.24	CH_3		C-18	
20	132.2	5.53	CH	H-4, H-21a, H-21b		H-17, H-2a
21a	120.7	5.22	CH_2	H-20, H-21b		
21b		5.13	CH_2	H-4, H-20, H-21a	C-4	H-4









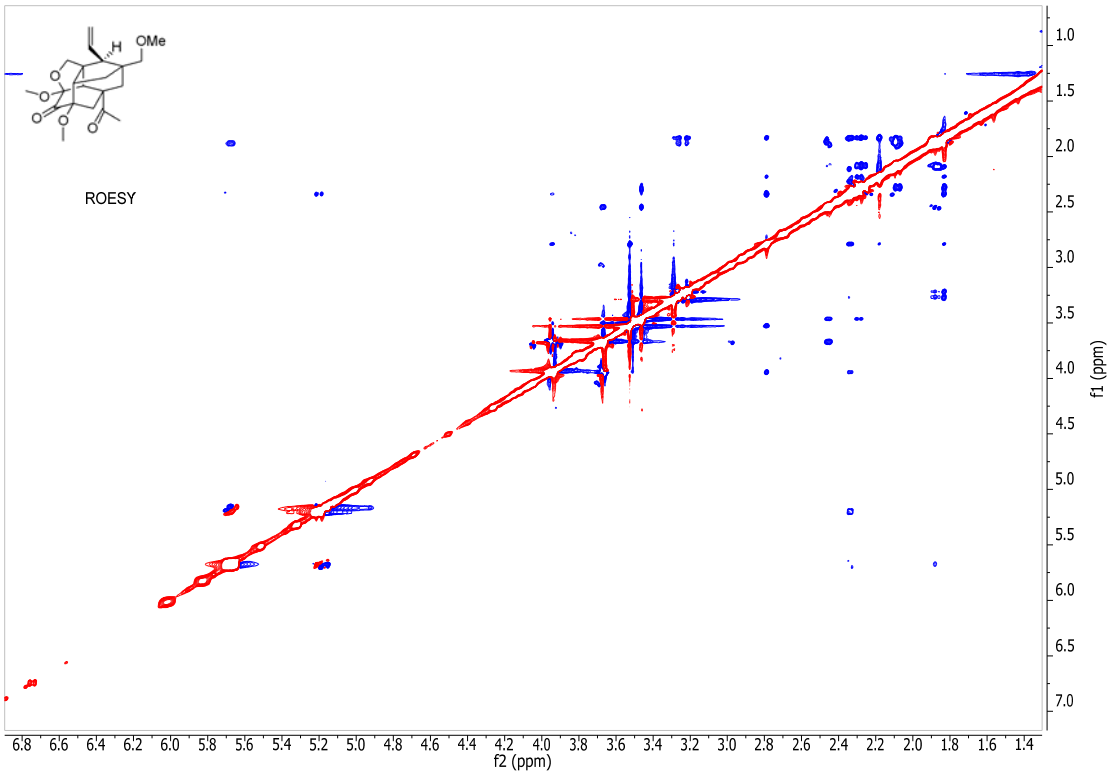
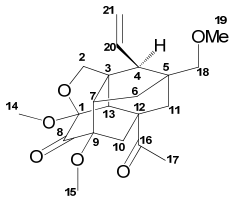
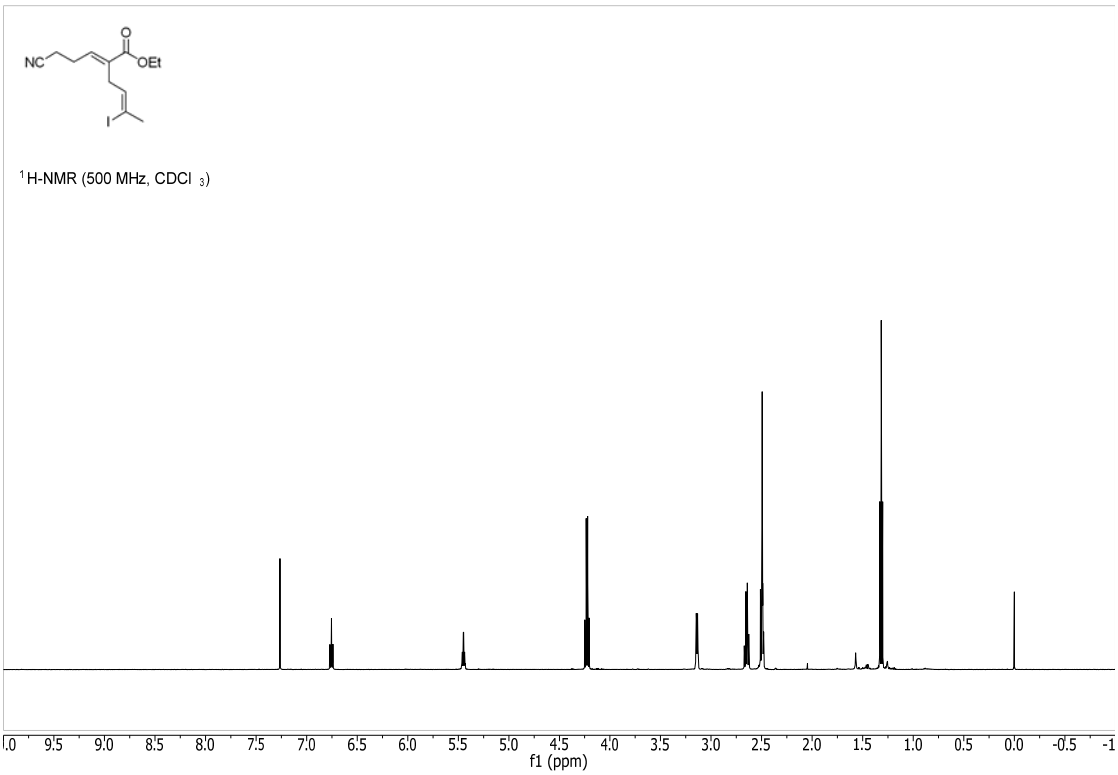
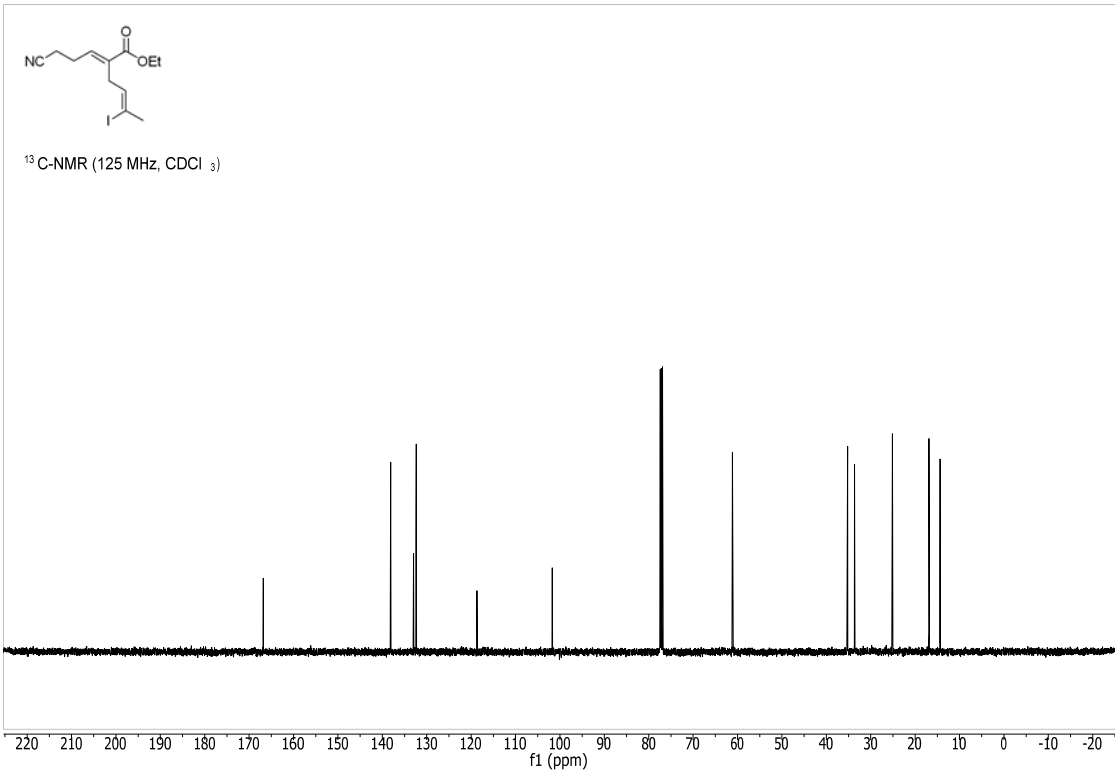


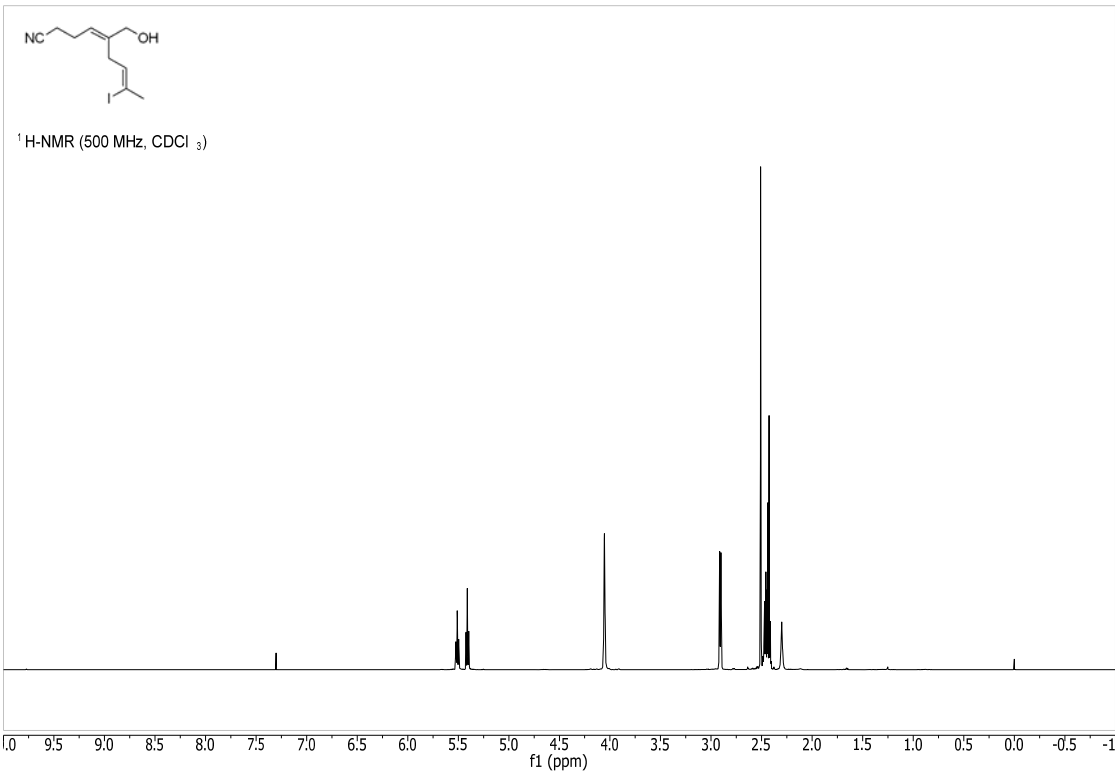
Table 2. 2D-NMR Data of Compound **34**

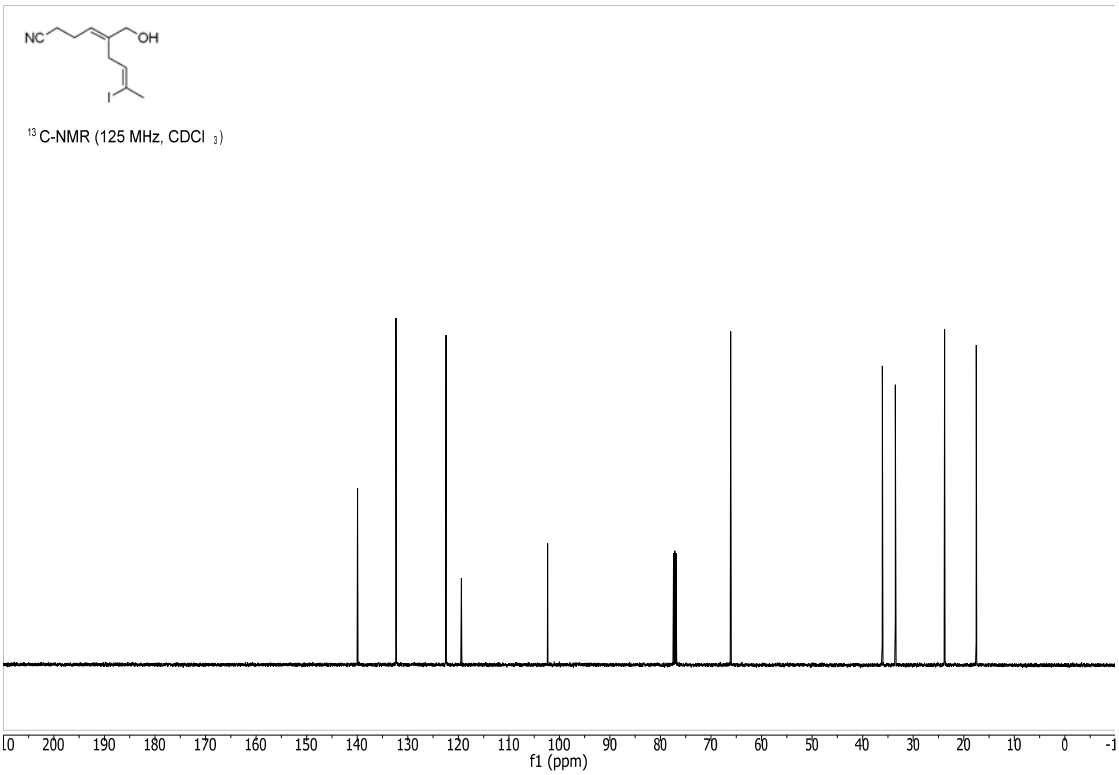


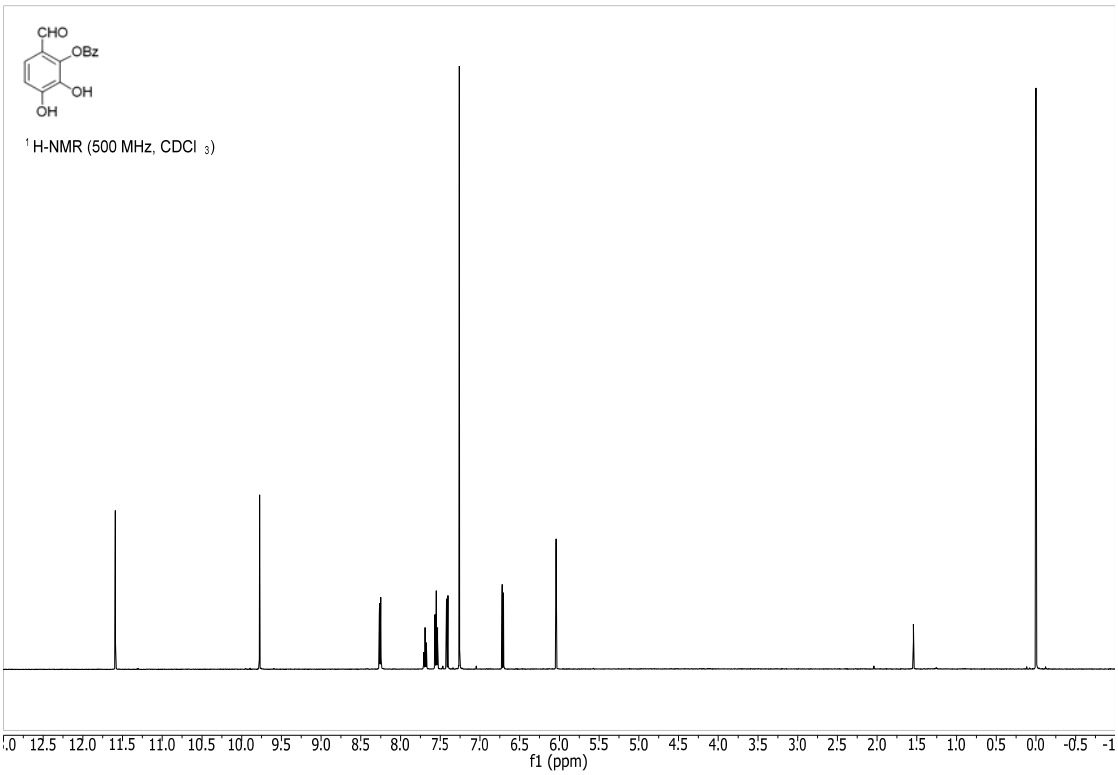
Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations	ROESY correlations
1	103.4		Cq			
2a	72.7	3.95	CH_2	H-2b	C-3, C-4, C-7	H-4, H-13
2b		3.67	CH_2	H-2a	C-1, C-3, C-7, C-13	H-7
3	51.7		Cq			
4	58.8	2.34	CH	H-6a	C-6, C-20, C-21	H-11, H-13, H-21a
5	49.0		Cq			
6a	31.1	2.08	CH_2		C-3, C-4, C-9	H-6b, H-10b
6b		1.88	CH_2		C-5, C-9, C-11	H-6a, H-20
7	41.8	2.46	CH	H-6b	C-9, C-10	H-2b, H-6b
8	225.0		Cq			
9	79.4		Cq			
10a	35.0	2.30	CH_2	H-10b	C-9, C-11, C-12	
10b		2.29	CH_2	H-10a	C-9, C-11, C-12	H-6a, H-11
11	45.9	1.83	CH_2		C-4, C-5, C-6, C-10, C-12, C-13	H-4, H-6a, H-10b, H-18b
12	47.8		Cq			
13	46.9	2.80	CH		C-1, C-3, C-7, C-12	H-2a, H-4, H-11, H-14
14	51.3	3.52	CH_3		C-1, C-8	H-13
15	52.8	3.46	CH_3		C-8, C-9	H-7, H-10a, H-10b
16	208.2		Cq			
17	25.0	2.18	CH_3		C-12, C-16	H-11, H-13
18a	76.7	3.28	CH_2	H-18b	C-5, C-6, C-11	
18b		3.23	CH_2	H-18a	C-4, C-5, C-11	H-11
19	59.2	3.29	CH_3		C-18	
20	132.9	5.68	CH	H-4, H-21a, H-21b	C-4, C-3, C-20	H-6b
21a	119.4	5.20	CH_2	H-20, H-21b	C-4	H-4
21b		5.16	CH_2	H-21a	C-4	

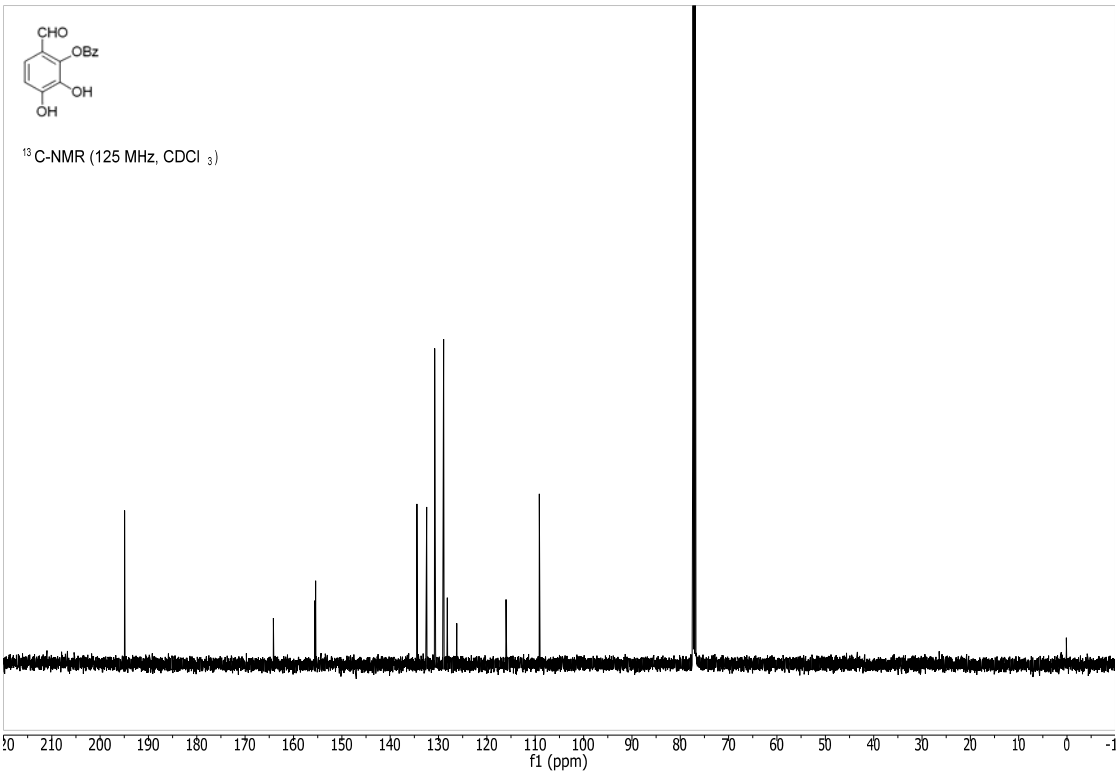

NC
O
OEt
I
1H-NMR (500 MHz, CDCl 3)
f1 (ppm)

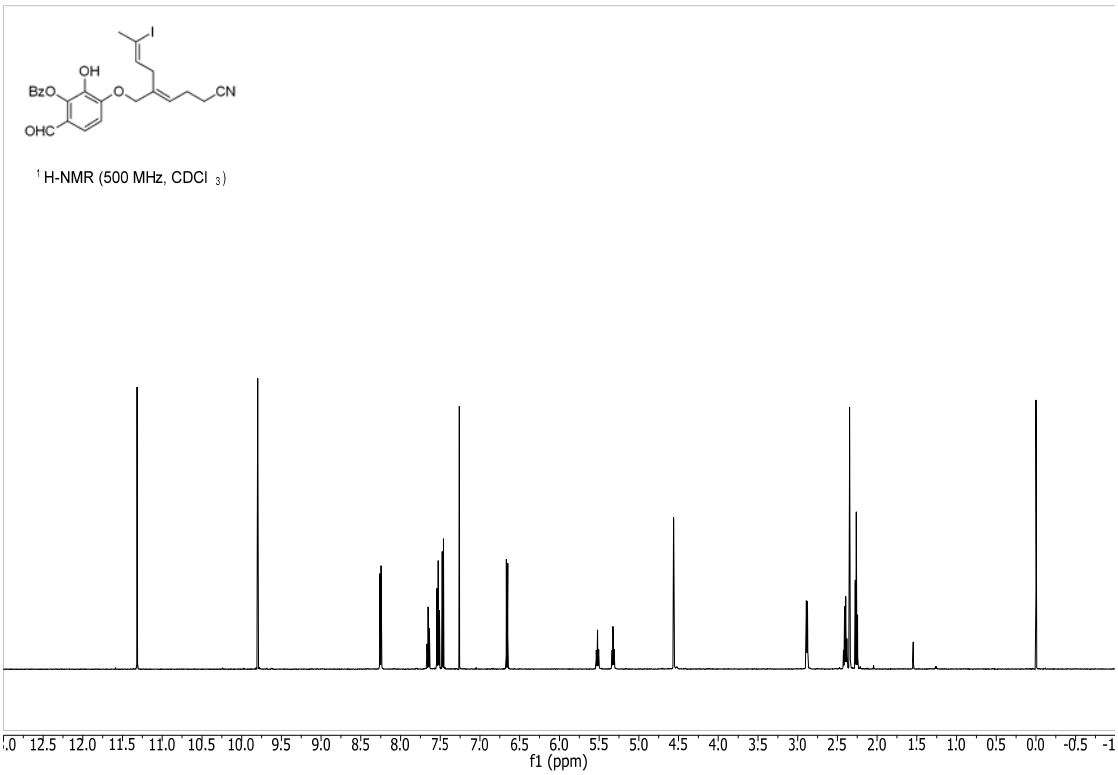

NC
O
OEt
I
13C-NMR (125 MHz, CDCl 3)
f1 (ppm)

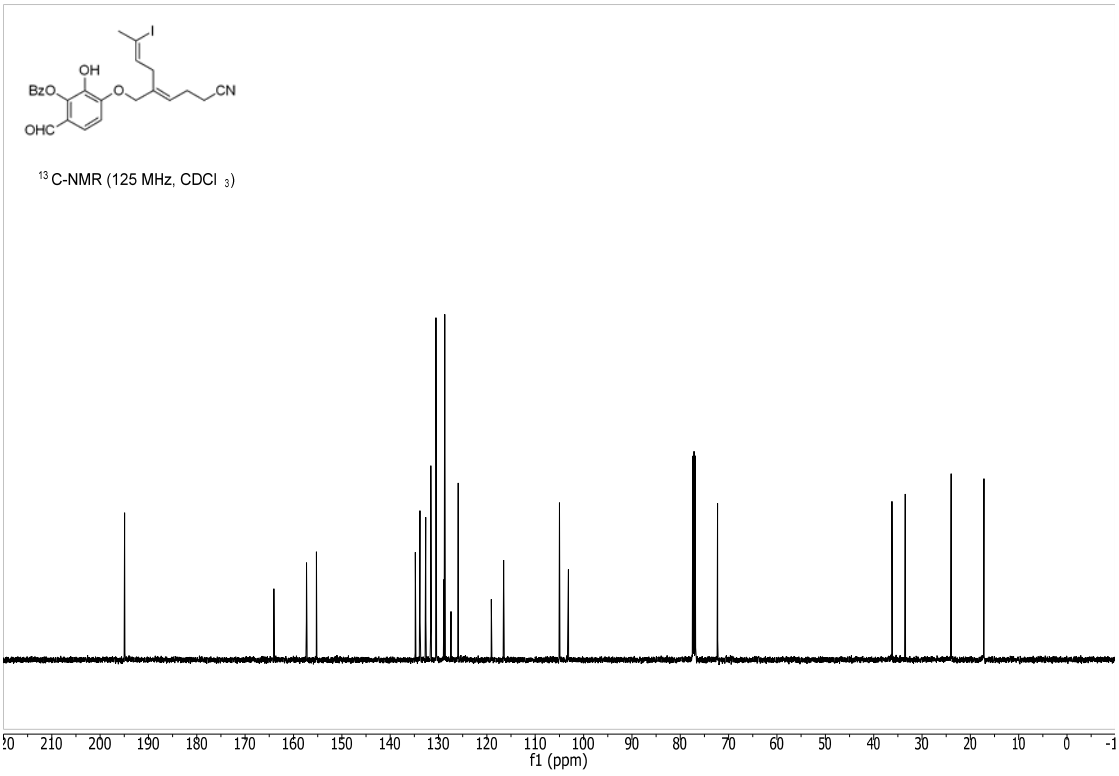

NC
OH
I
1 H-NMR (500 MHz, CDCl 3)
f1 (ppm)

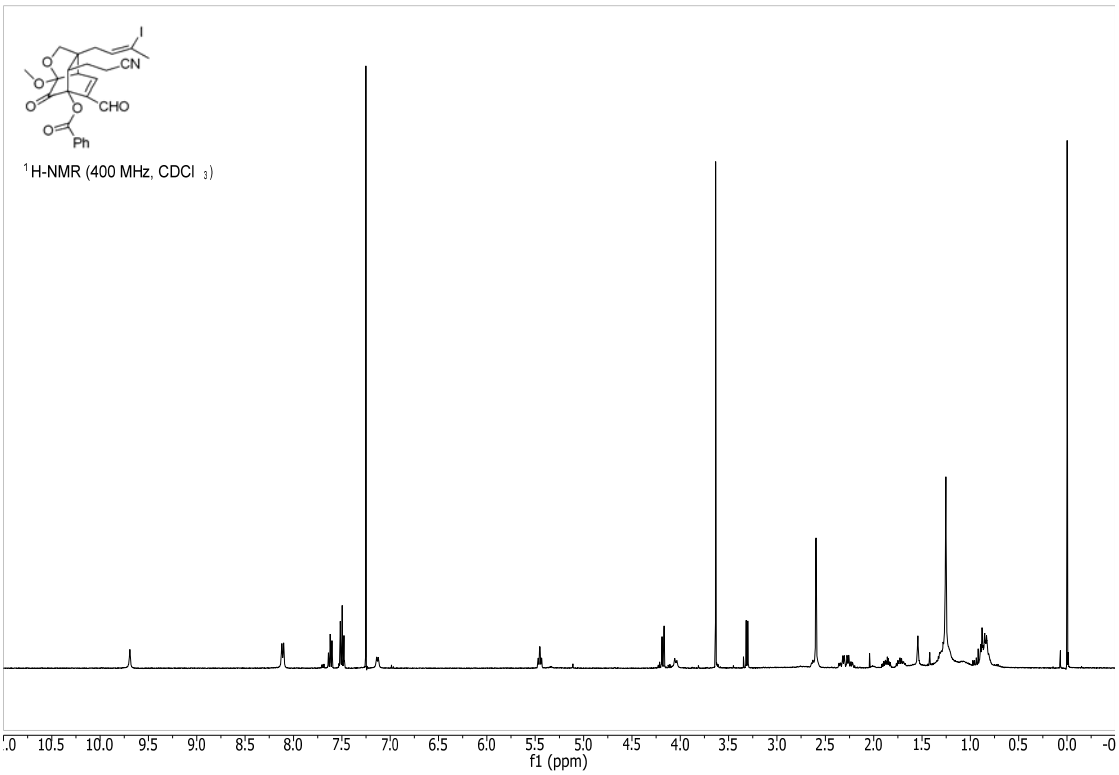

NC
OH
I
13 C-NMR (125 MHz, CDCl 3)
f1 (ppm)

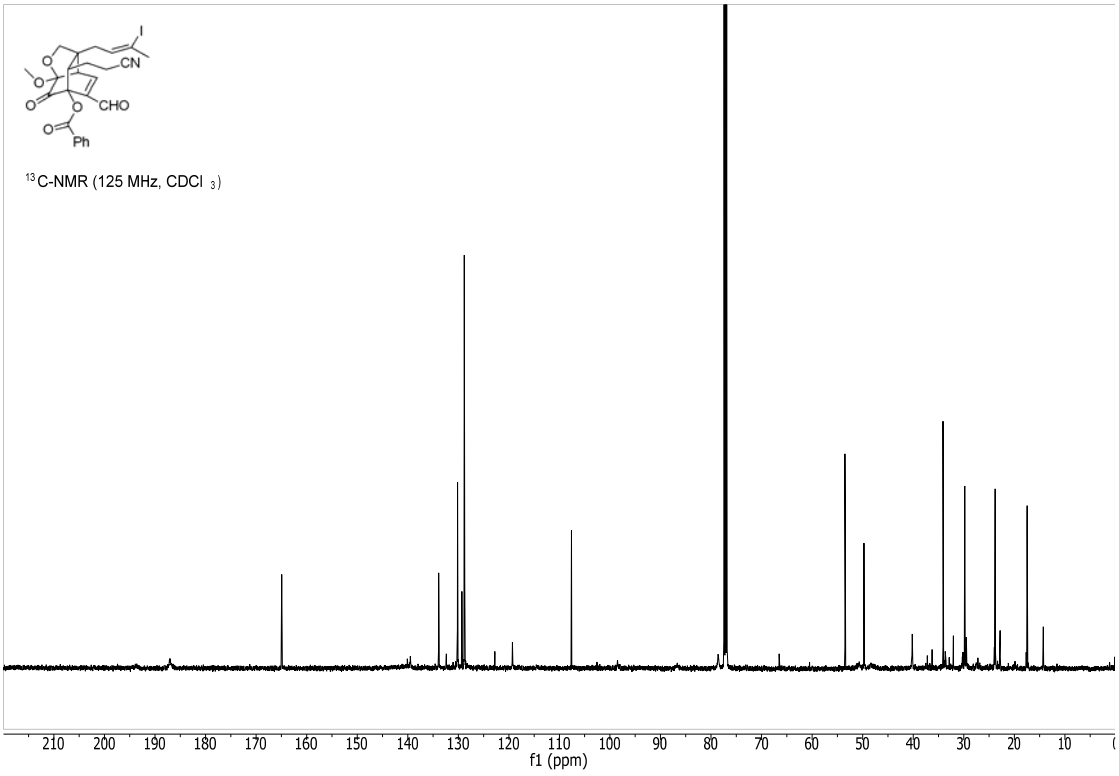


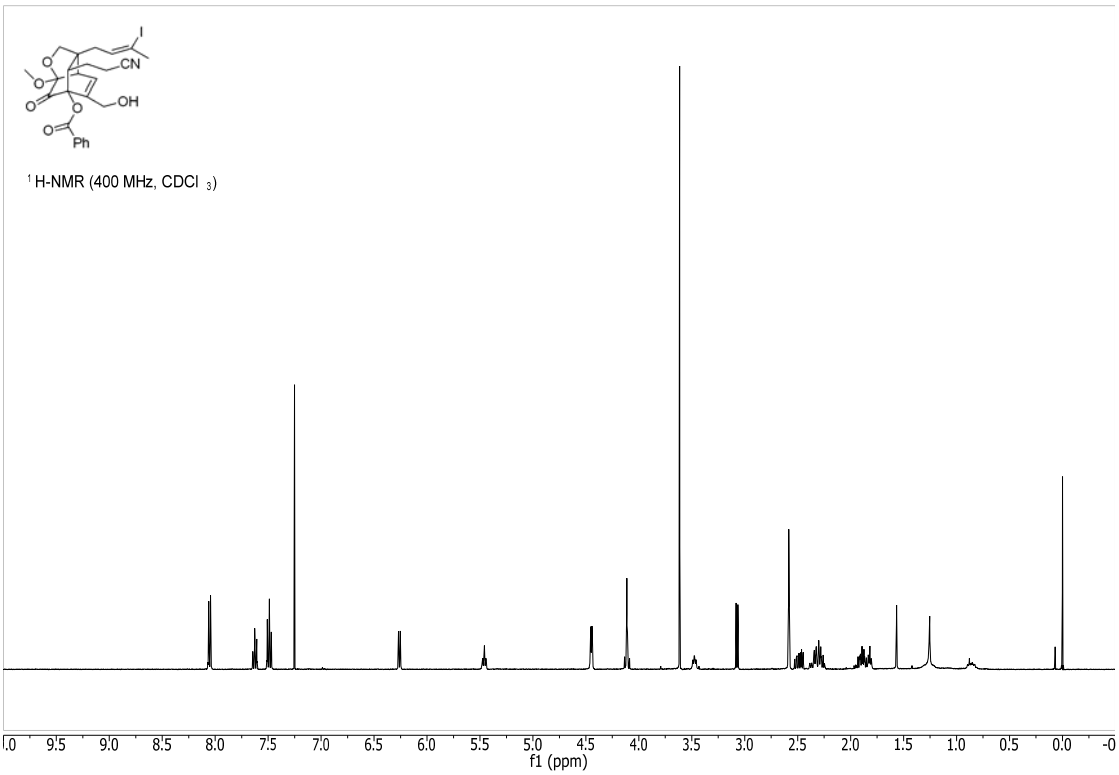


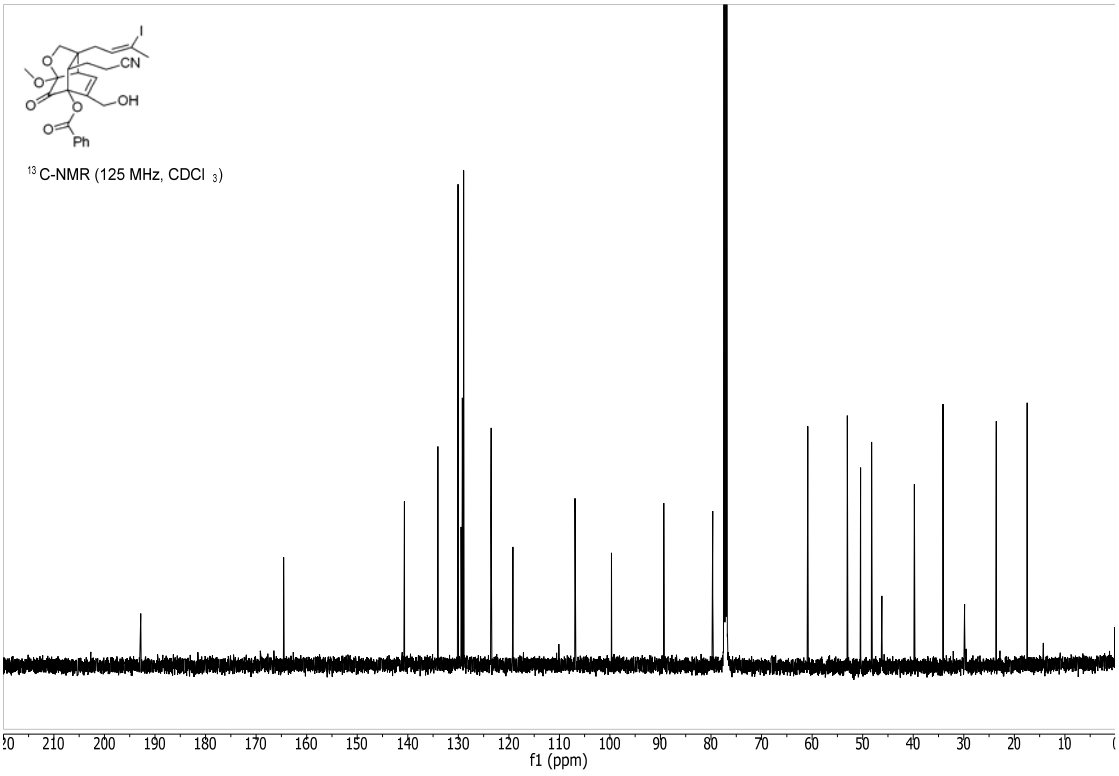

OH
BzO
O
CN
OHC
I
1 H-NMR (500 MHz, CDCl 3)
f1 (ppm)

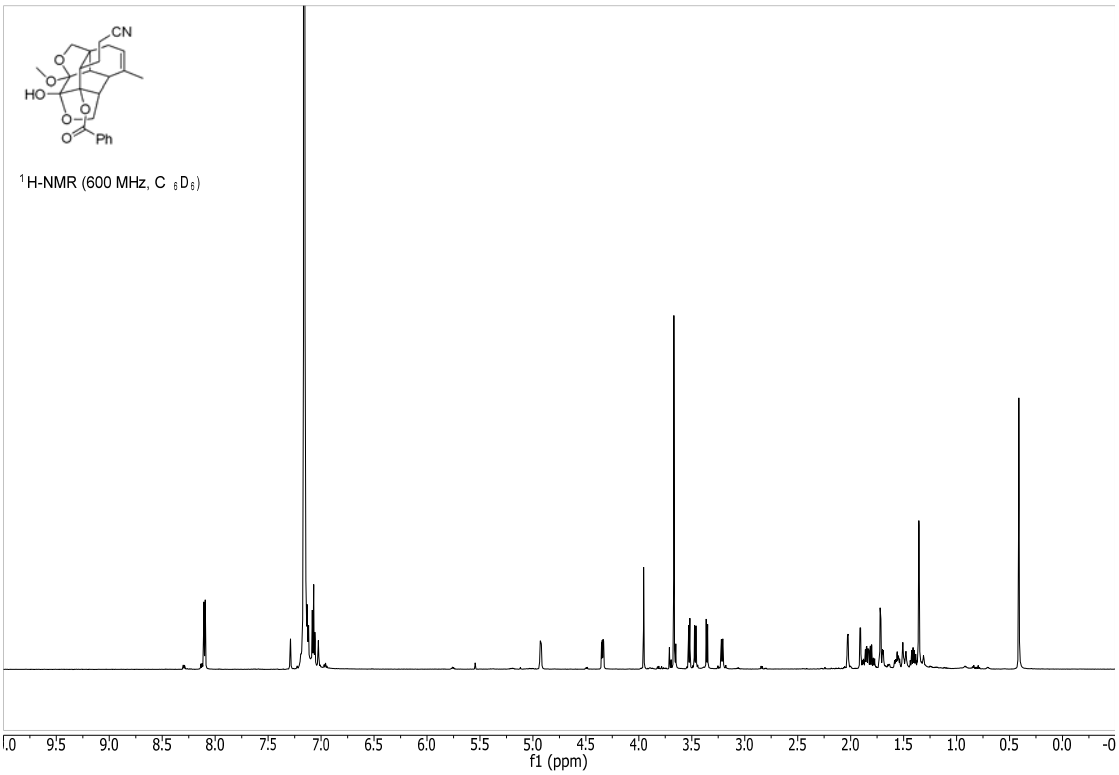

OH
BzO
O
CN
OHC
I
13 C-NMR (125 MHz, CDCl 3)
f1 (ppm)

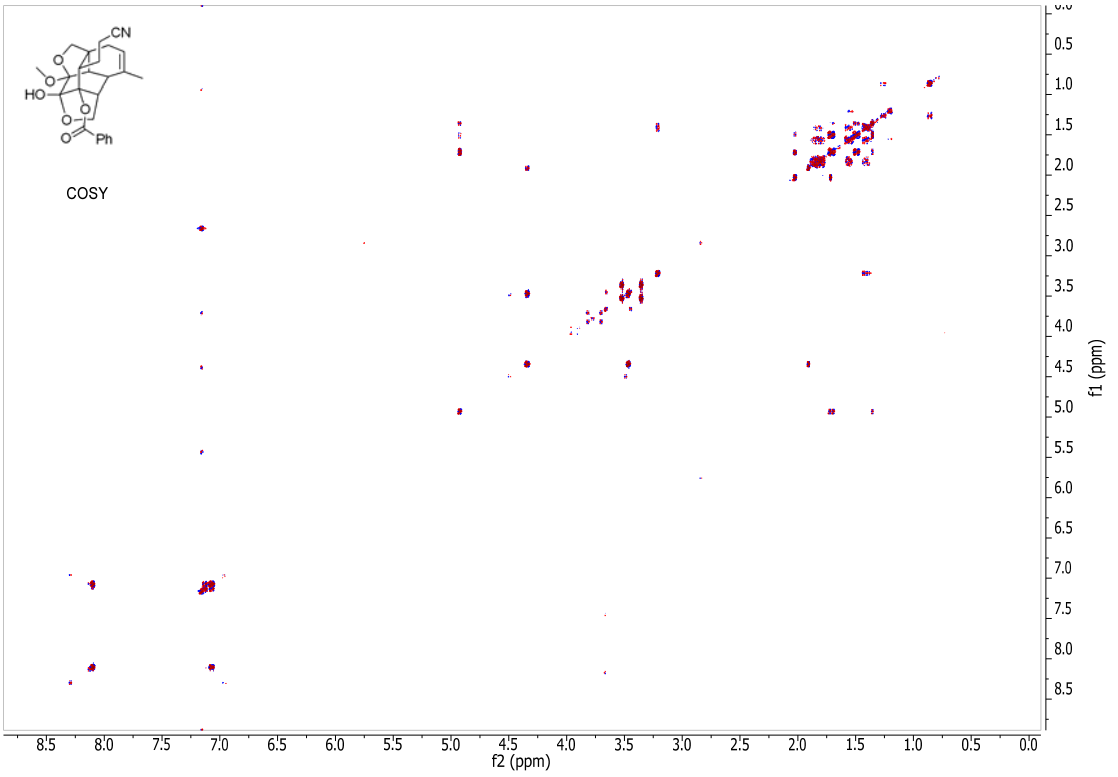


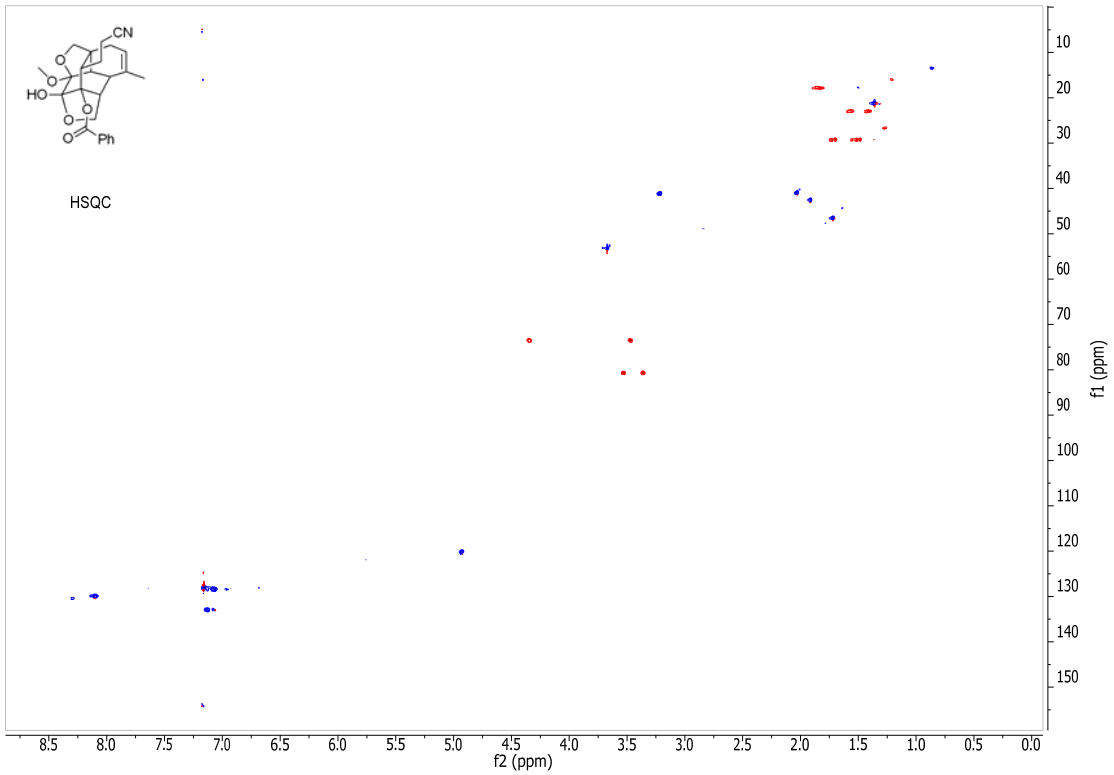


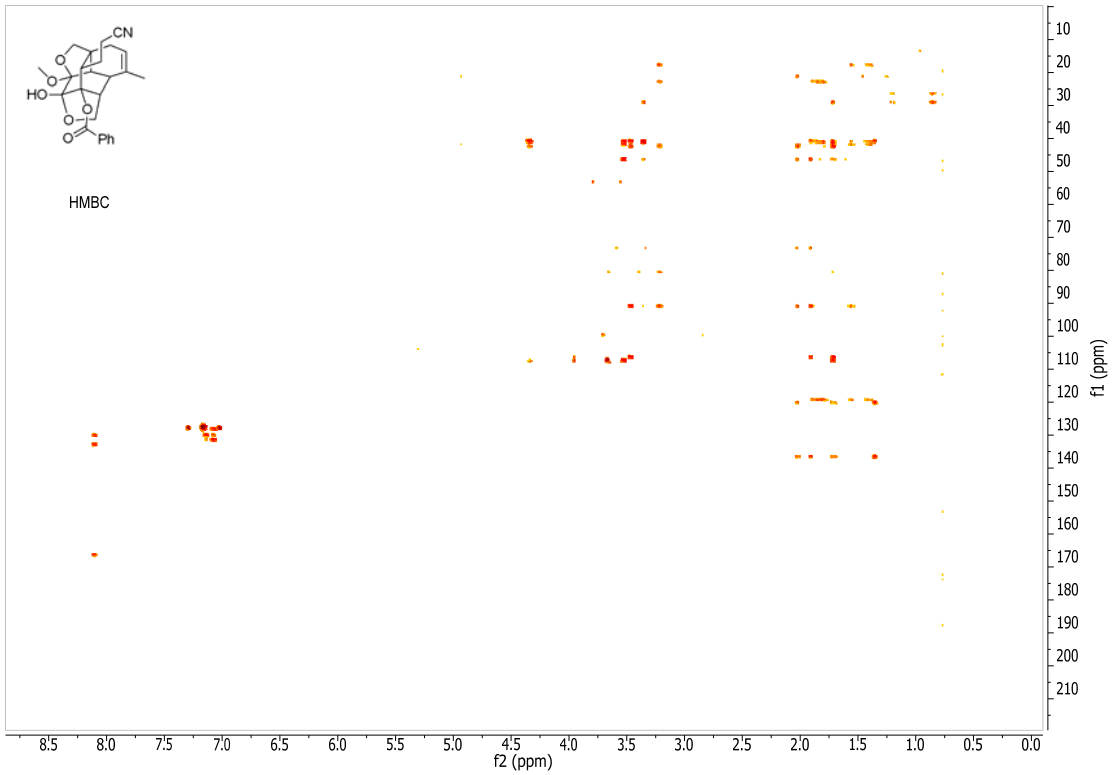












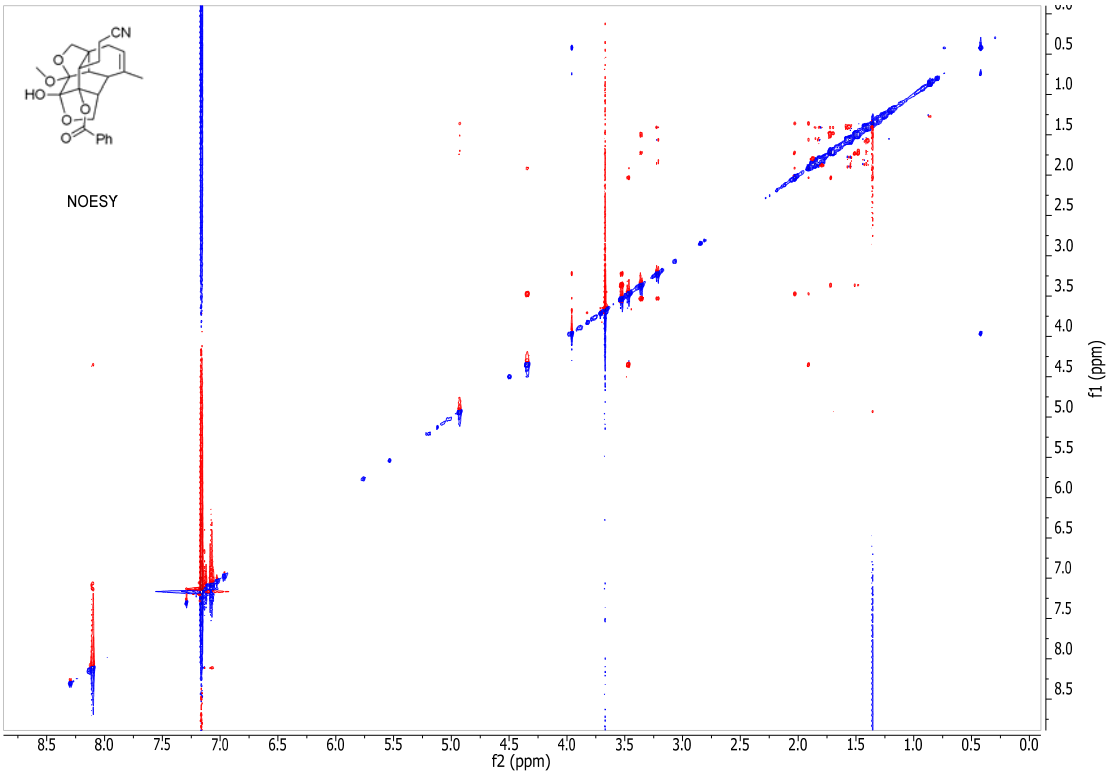
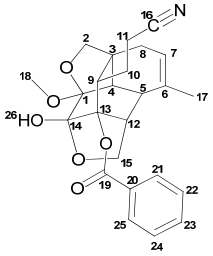
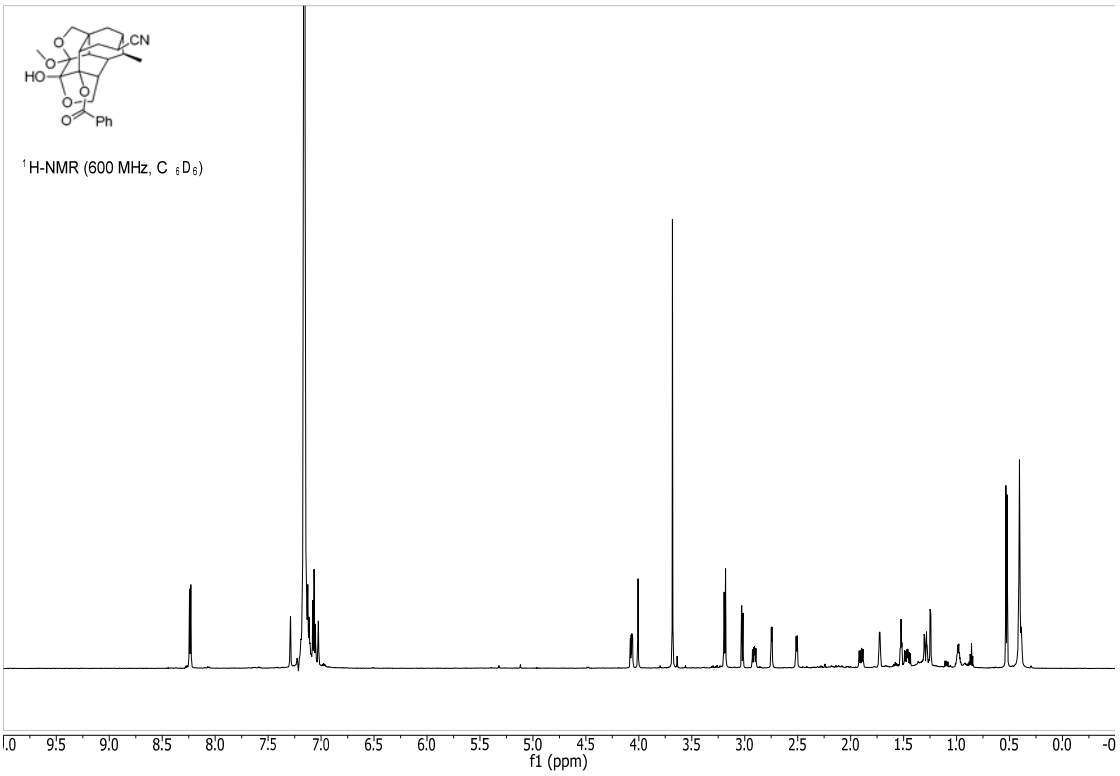


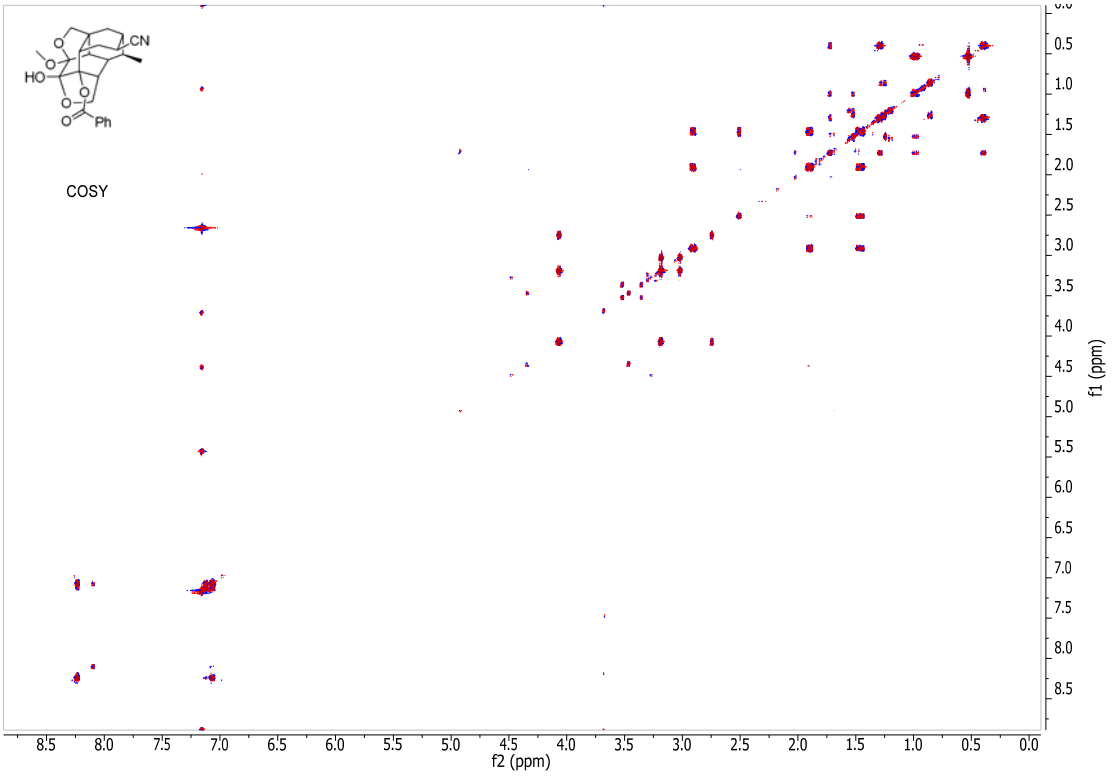
Table 3. 2D-NMR Data of Compound **45**

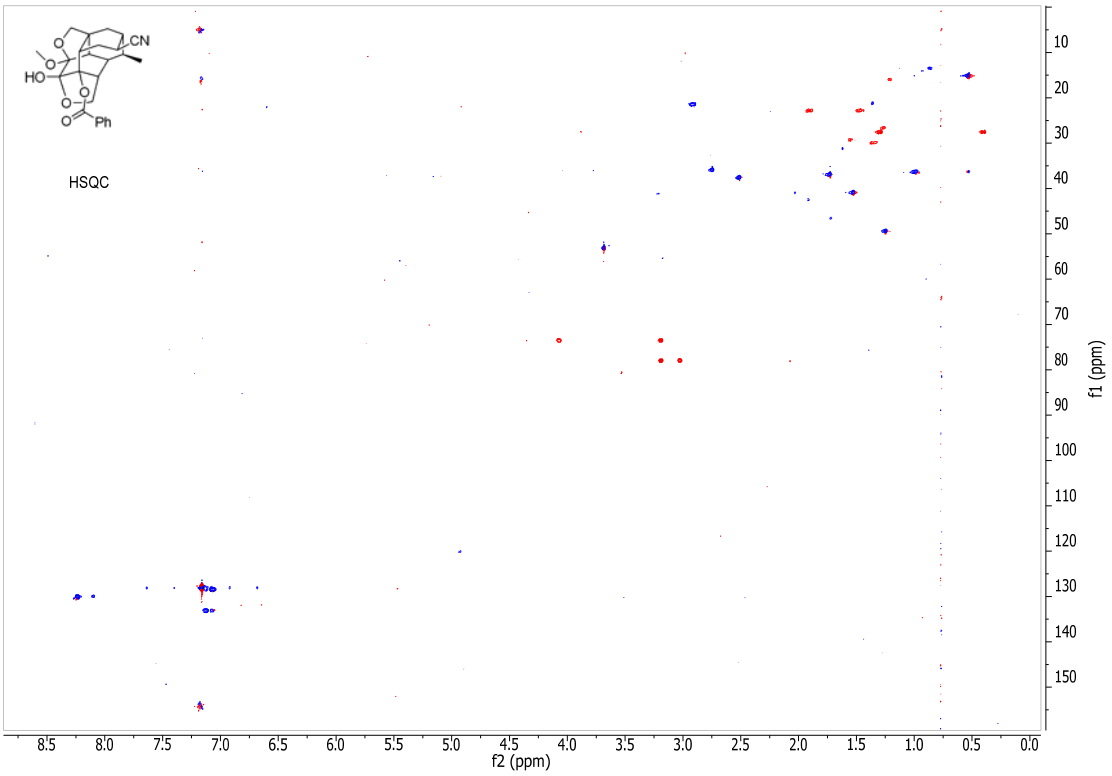


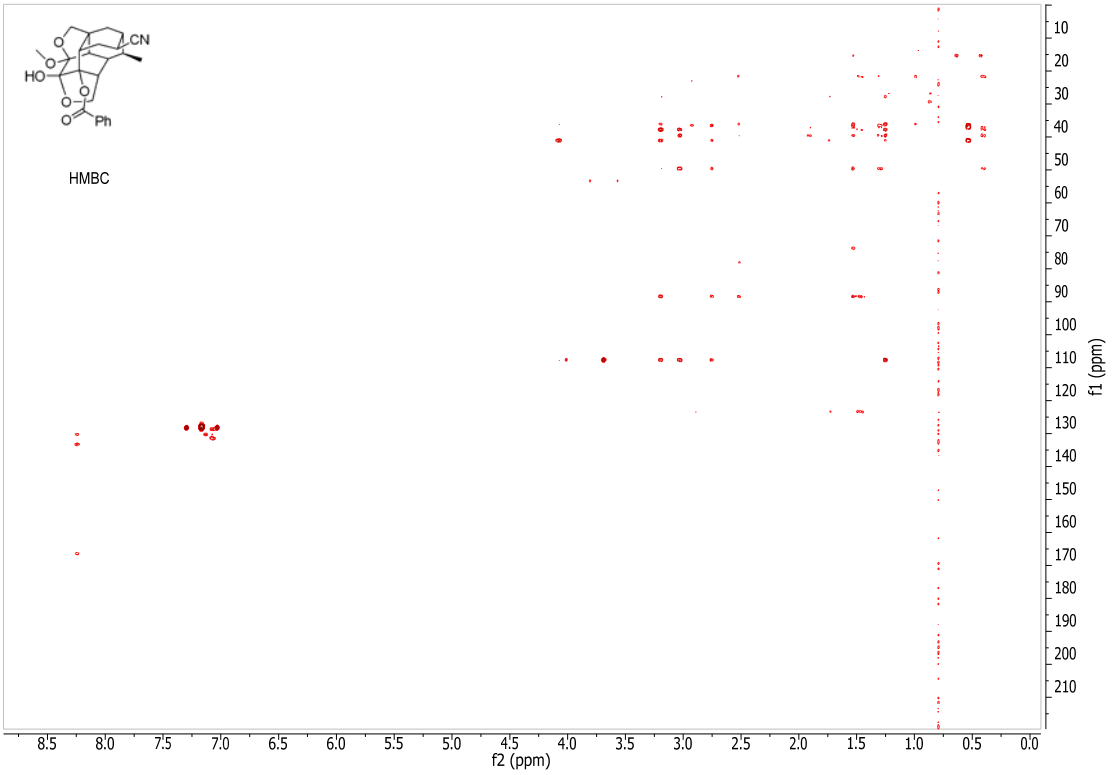
Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations	NOESY correlations
1	107.49		Cq			
2a	80.7	3.36	CH_2	H-2b	C-14, C-13, C-4, C-9, C-8	H-2b, H-4, H-8a
2b		3.53		H-2a	C-1, C-4, C-3, C-9	H-2a, H-9
3	42.06		Cq			
4	46.51	1.72	CH	H-5	C-1, C-14, C-12, C-9, C-8	H-2a, H-8a
5	40.96	2.03	CH	H-8a, H-4	C-7, C-13, C-15, C-4, C-12, C-3, C-17	H-15a, H-4, H-17
6	136.74		Cq			

7	120.13	4.93	CH	H-8b, H-8a, H-17	C-3, C-17	H-8b, H-8a, H-17
8a	29.31	1.5	CH_2	H-7, H-5, H-8b, H-17		H-2a, H-8b
8b		1.71		H-7, H-8a, H-17	C-7, C-4	H-7
9	41.12	3.22	CH	H-10a	C-13, C-2, C-12, C-3, C-10, C-11	H-26, H-11a, H-11b, H-10a
10a	22.98	1.41	CH_2	H-9, H-11a, H-11b, H-10b	C16, C-3, C-9, C-11	H-10b
10b		1.57		H-9, H-11a, H-11b, H-10a	C16, C-13, C-3, C-9, C-11	H-9, H-10a
11a	17.81	1.82	CH_2	H-10a, H-10b	C-16, C-9, C-10	H-9
11b		1.85		H-10a, H-10b	C-16, C-9, C-10	H-9
12	42.55	1.91	CH	H-15b	C-14, C-13, C-15, C-4, C-9	H-19b, H-19a, H-17
13	91		Cq			
14	106.55		Cq			
15a	73.53	3.47	CH_2	H-15b	C-14, C-13, C-12, C-5	H-15b, H-5
15b		4.34		H-15a, H-12	C-1, C-12, C-5	H-15a, H-12
16	119.24		Cq			
17	21.2	1.36	CH_3	H-7, H-8b, H-8a	C-7, C-5	H-7
18	53.18	3.67	CH_3		C-1	
19	166.35		Cq			
20	130.02		Cq			
21	129.94	8.1	CH	H-22	C-19, C-23, C-25	H-22, H-5b
22	128.41	7.07	CH	H-21, H-23	C-20, C-24	H-21
23	132.96	7.13	CH	H-21, H-25, H-22, H-24	C-21, C-25	
24	128.41	7.07	CH			
25	129.94	8.1	CH			
26		3.96	OH		C-1, C-14	H-9









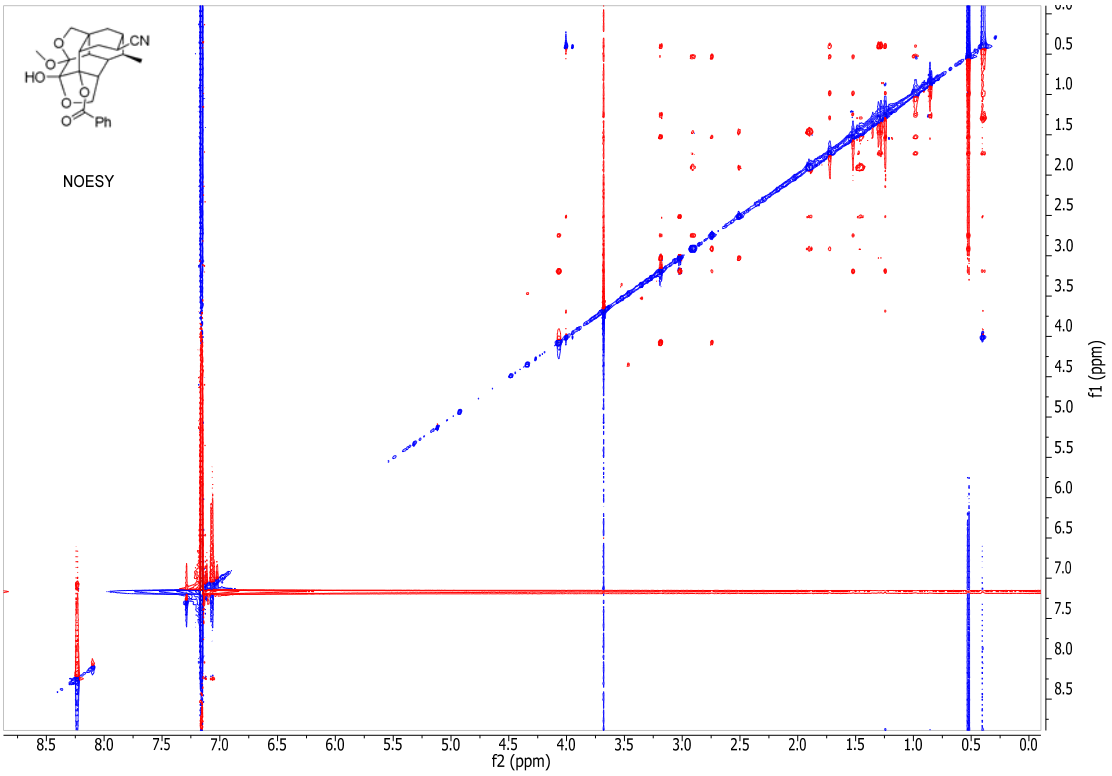
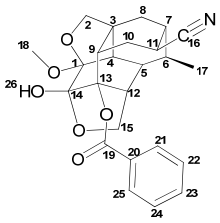
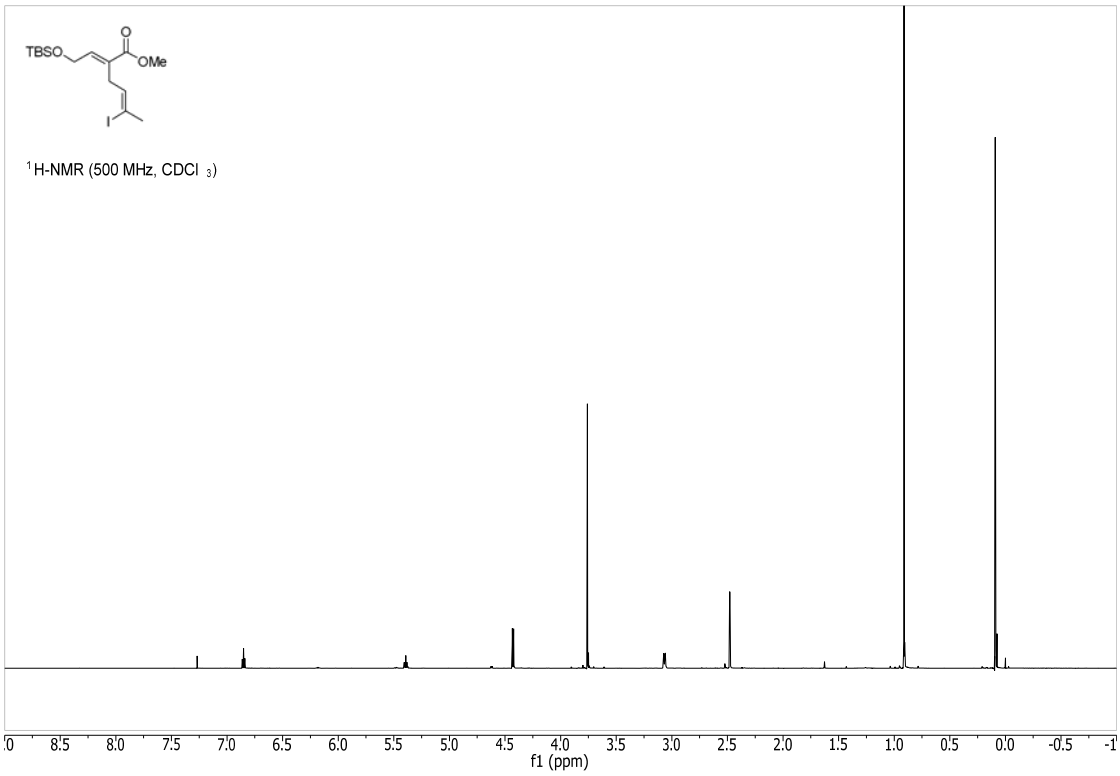


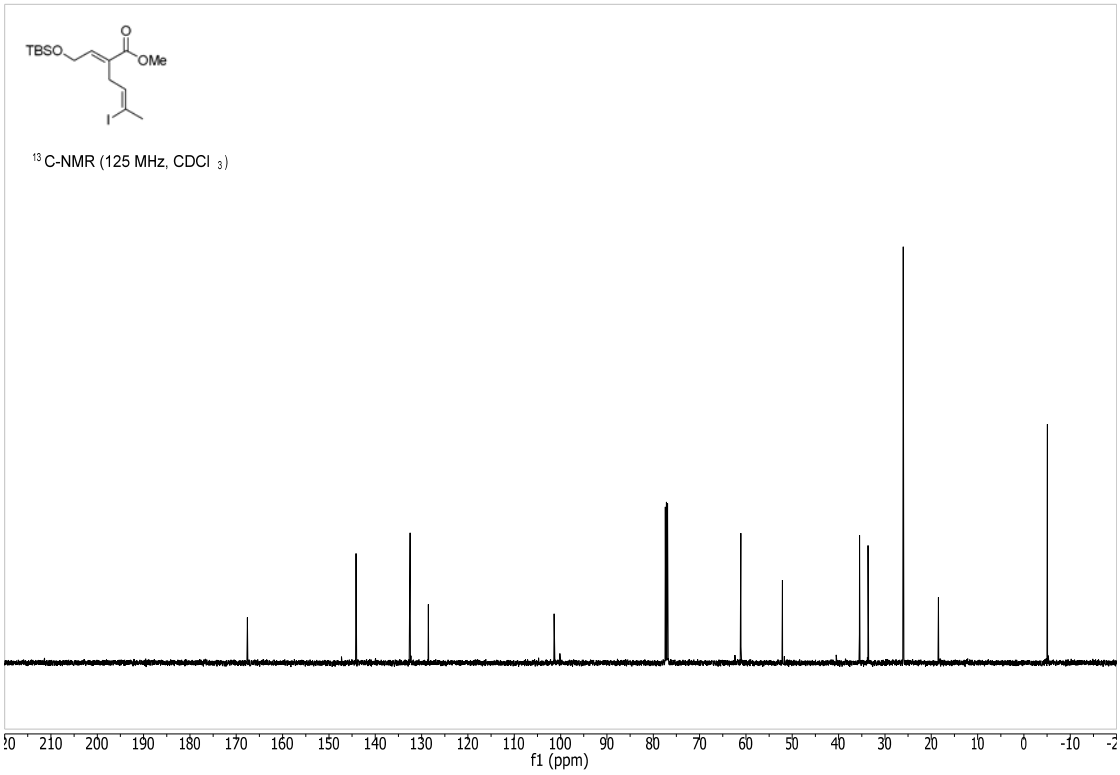
Table 4. 2D-NMR Data of Compound **47**

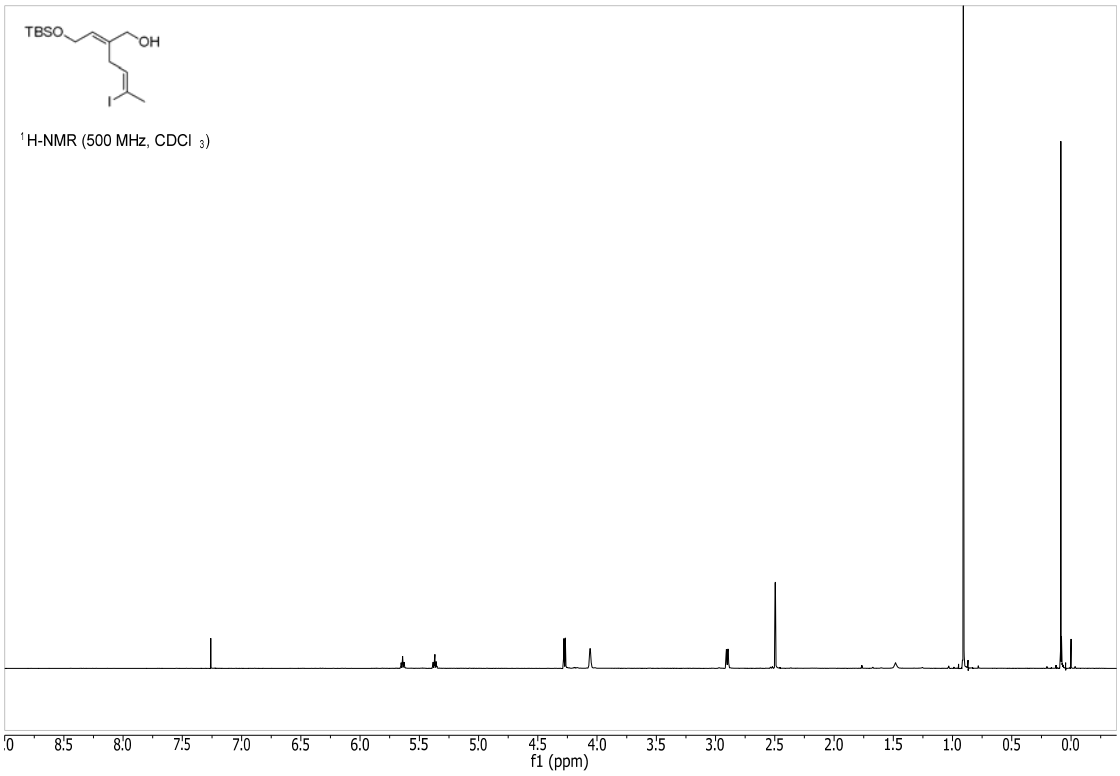


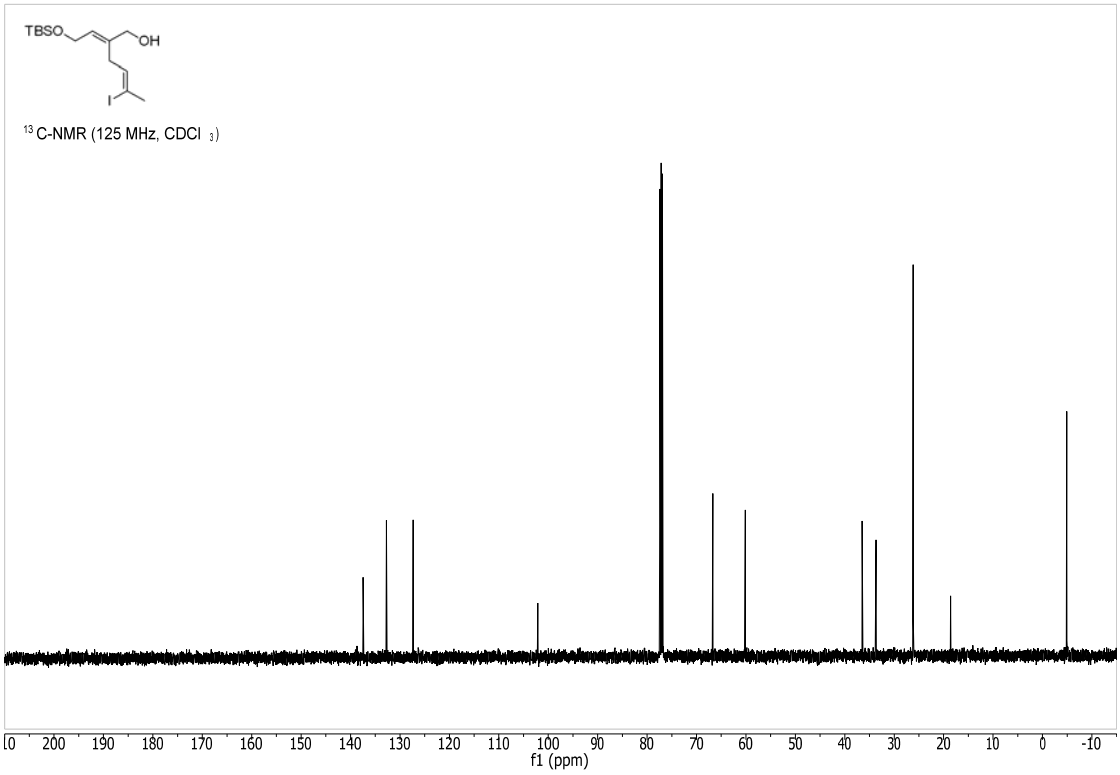
Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations	ROESY correlations
1	107.66		Cq			
2a	78	3.02	CH_2	H-2b	C-1, C-4, C-3, C-9	H-2b, H-9, H-8b
2b		3.19		H-2a	C-1, C-9, C-8	H-2a, H-8b, H-8a
3	39.6		Cq			
4	49.39	1.25	CH	H-5	C-14, C-5, C-3, C-9, C-12, C-8	H-2b, H-5, H-6, H-8a
5	40.85	1.52	CH	H-7, H-4, H-6	C-13, C-4, C-3, C-7, C-17, C-6	H-15a, H-12, H-4, H-6, H-17
6	36.3	0.98	CH	H-7, H-5, H-17	C-12, C-11	H-7, H-5, H-4, H-17, H-8a
7	36.87	1.73	CH	H-5, H-8b, H-6, H-8a	C-16, C-5, C-3, C-6, C-	H-11, H-8b, H-6, H-17, H-

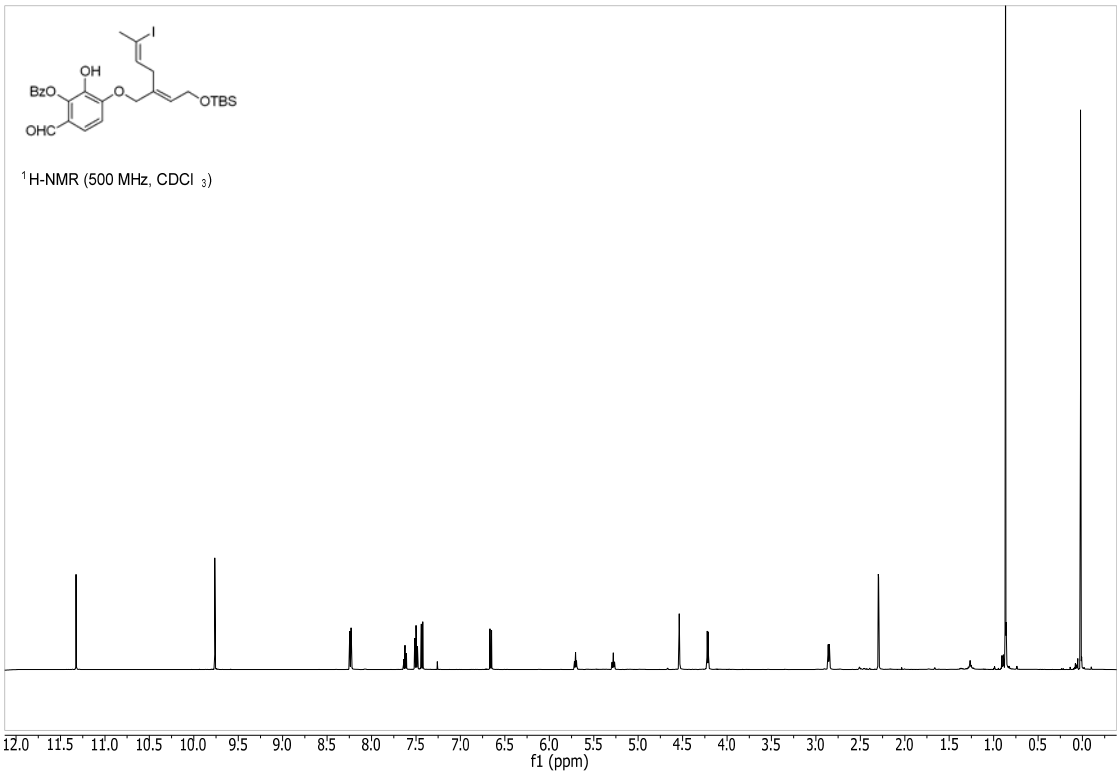
					8, C-10, C-11	8a
8a	27.49	0.4	CH_2	H-7, H-8b	C-4, C-3, C-9, C-11, C-17	H-2b, H-7, H-8b, H-6
8b		1.29		H-7, H-8a	C-4, C-3, C-7, C-6, C-11	H-7, H-8a
9	37.58	2.5	CH	H-10b, H-10a	C-13, C-2, C-3, C-12, C-10, C-11	H-2a, H-10b, H-10a
10a	22.89	1.47	CH_2	H-11, H-9, H-10a	C-16, C-13, C-9, C-11	H-11, H-9, H-10b, H-8b
10b		1.91		H-10b, H-10a	C-3, C-9	H-11, H-9, H-10a
11	21.46	2.92	CH	H-15b	C-16, C-7, C-8, C-10	H-12, H-10b, H-10a, H-17, H-7
12	35.87	2.74	CH		C-14, C-13, C-4, C-5, C-6	H-15b, H-15a, H-11, H-5, H-17
13	88.36		Cq			
14	107.68		Cq			
15a	73.5	3.19	CH_2	H-15b	C-14, C-13, C-5, C-12	H-15b, H-12, H-5
15b		4.07		H-15a, H-12	C-4, C-5, C-12	H-15a, H-12
16	123.44		Cq			
17	15.19	0.53	CH_3	H-6	C-5, C-7	H-11, H-12, H-7, H-5, H-6
18	53.11	3.68	CH_3		C-1	H-4
19	166.34		Cq			
20	131.39		Cq			
21	130.09	8.24	CH	H-22	C-19, C-23	H-22
22	128.38	7.07	CH	H-21, H-24	C-20	H-21
23	133.15	7.12	CH	H-21, H-25, H-22, H-24	C-21	
24	128.38	7.07	CH			
25	130.09	8.24	CH			
26		4.01	OH		C-14	H-9

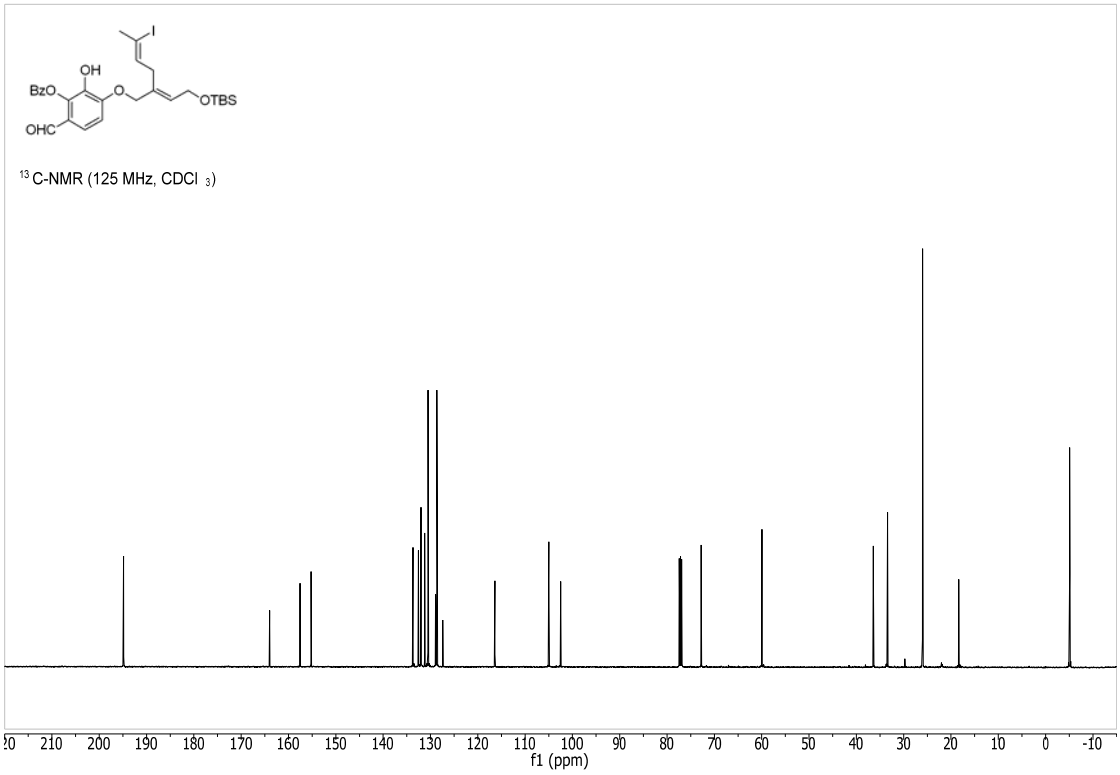


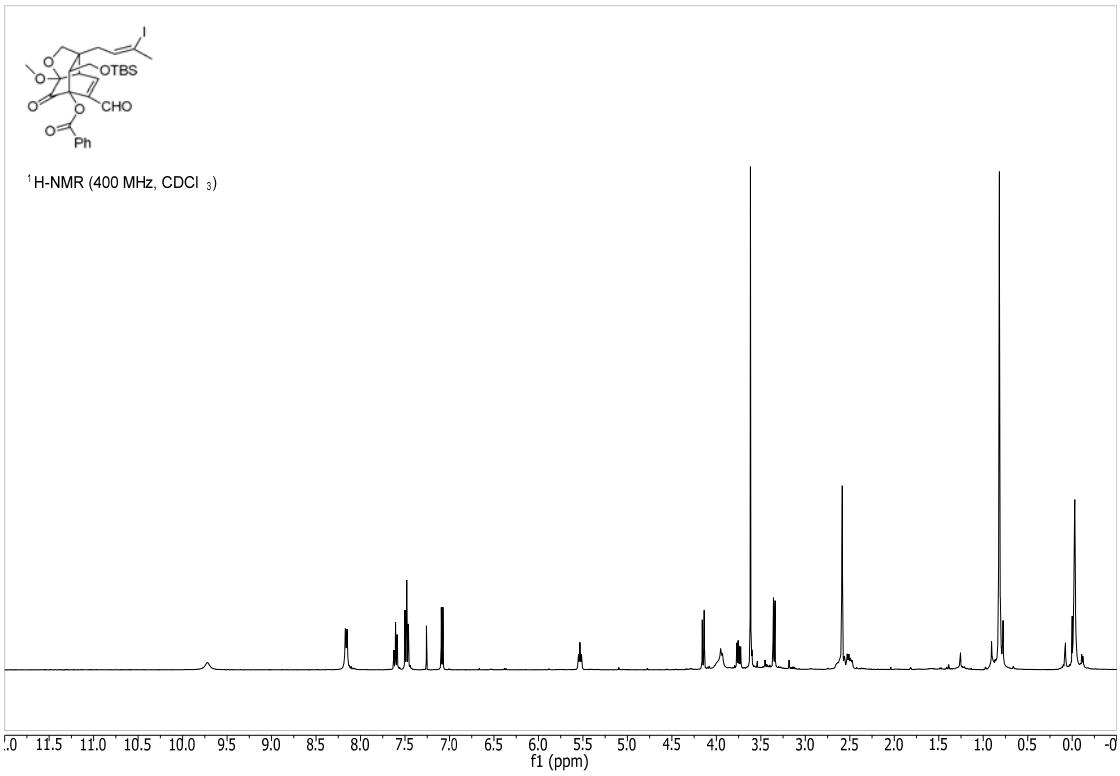


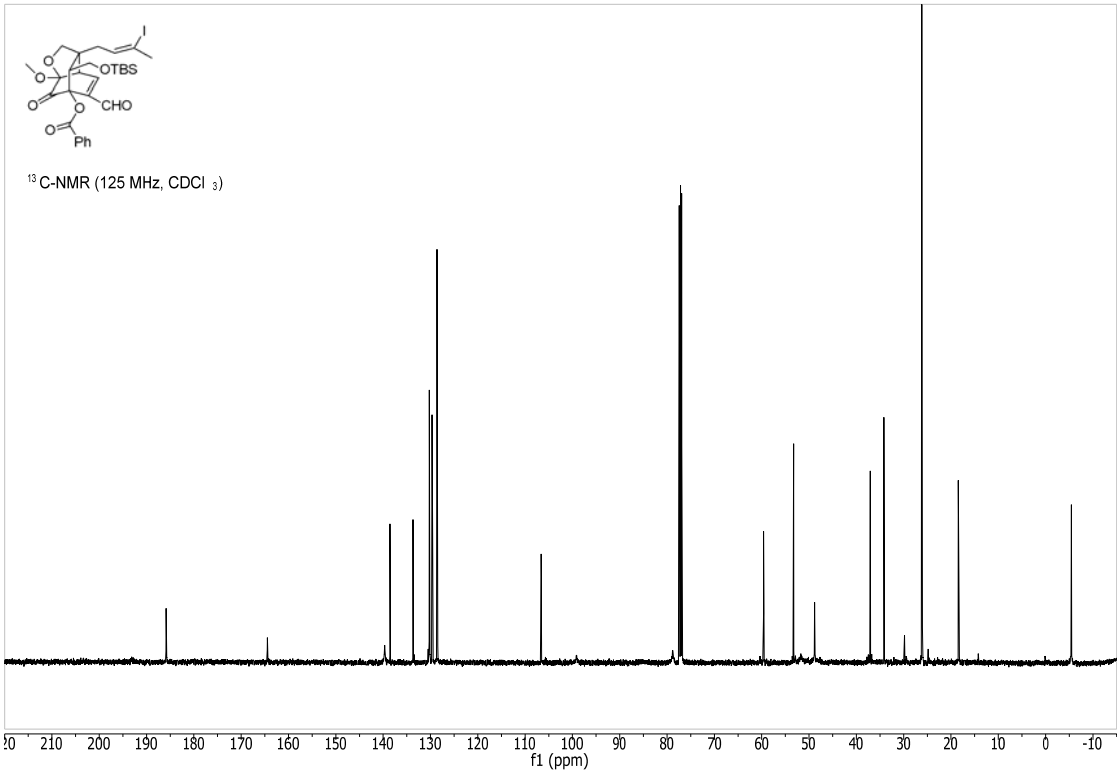


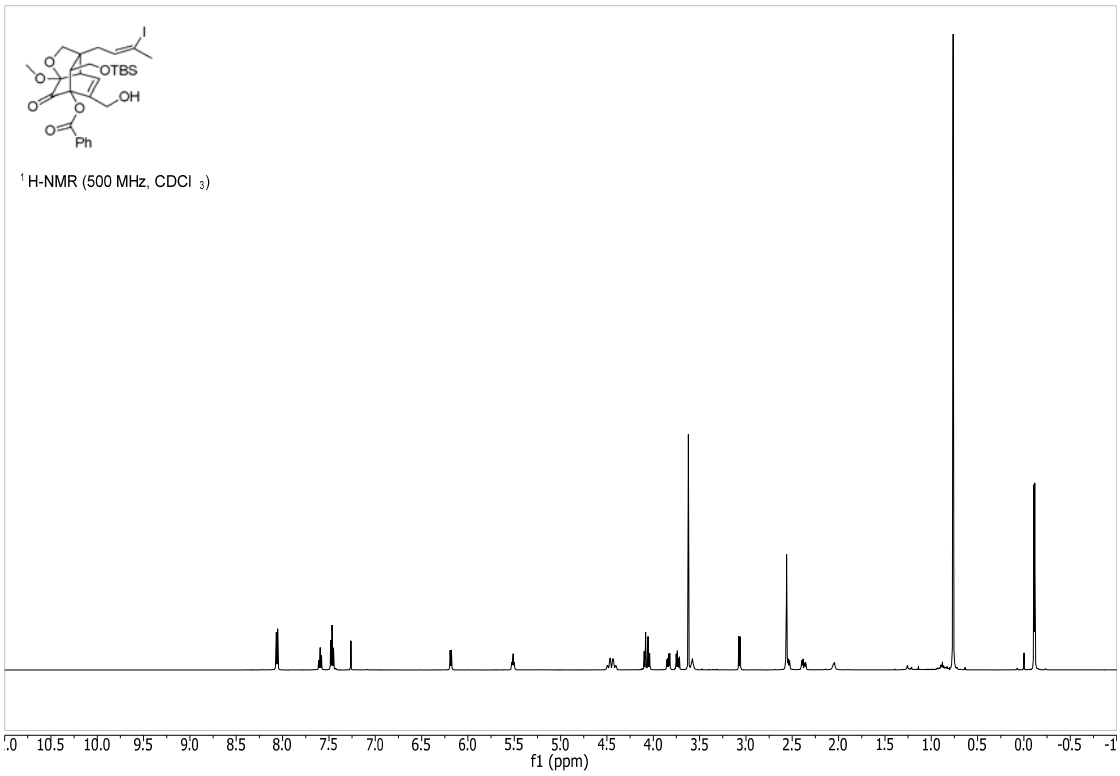


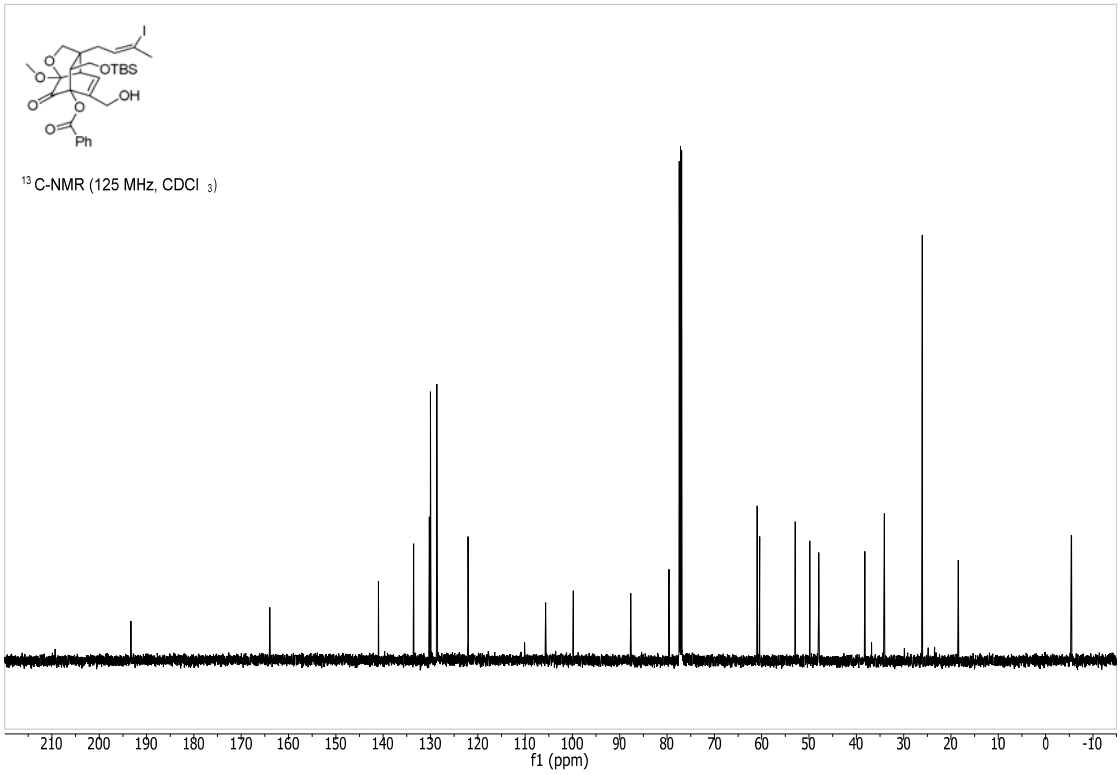


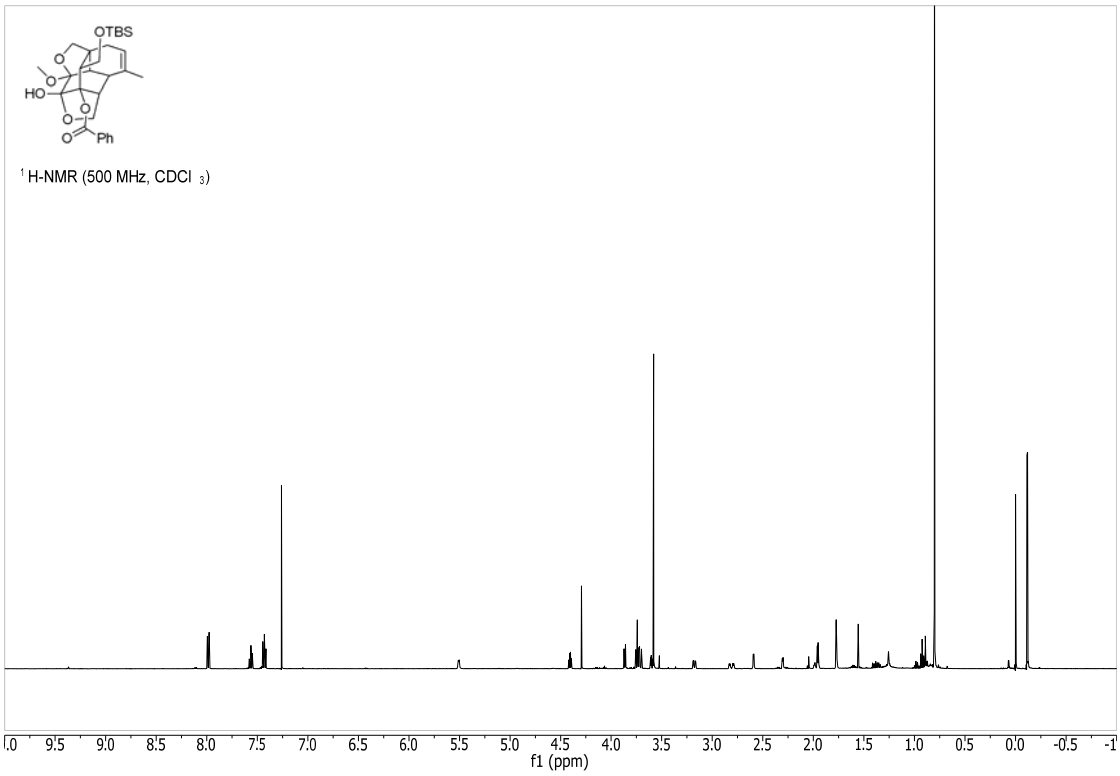


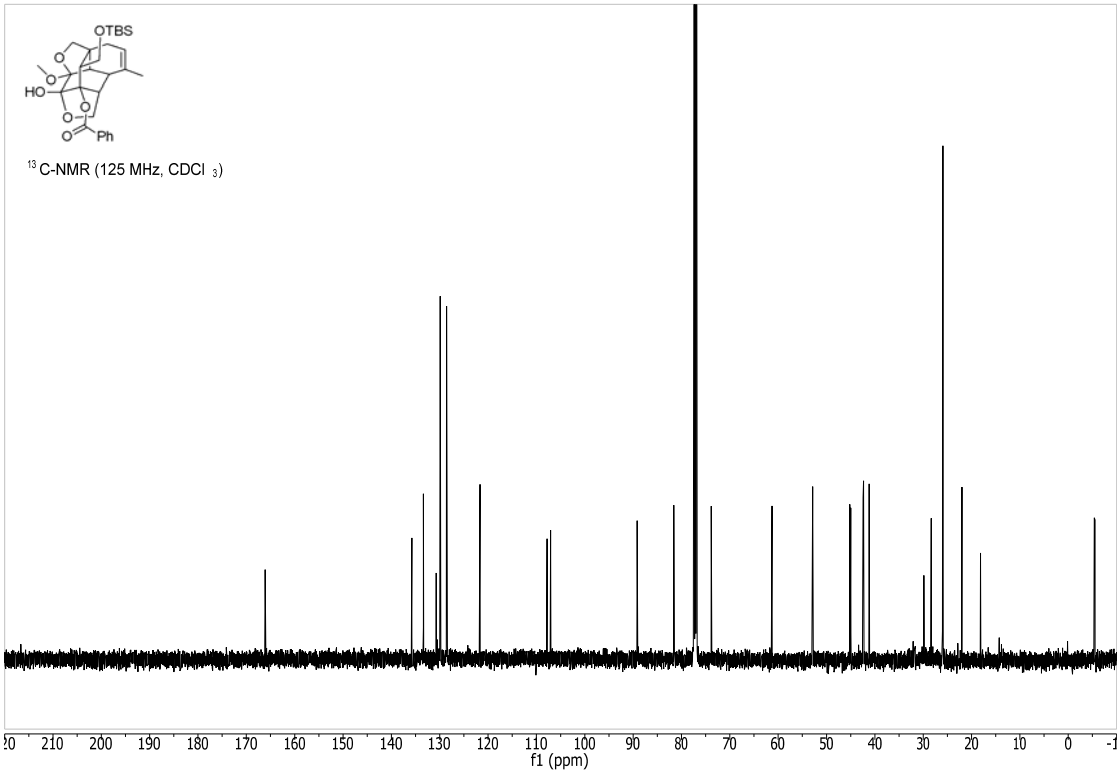


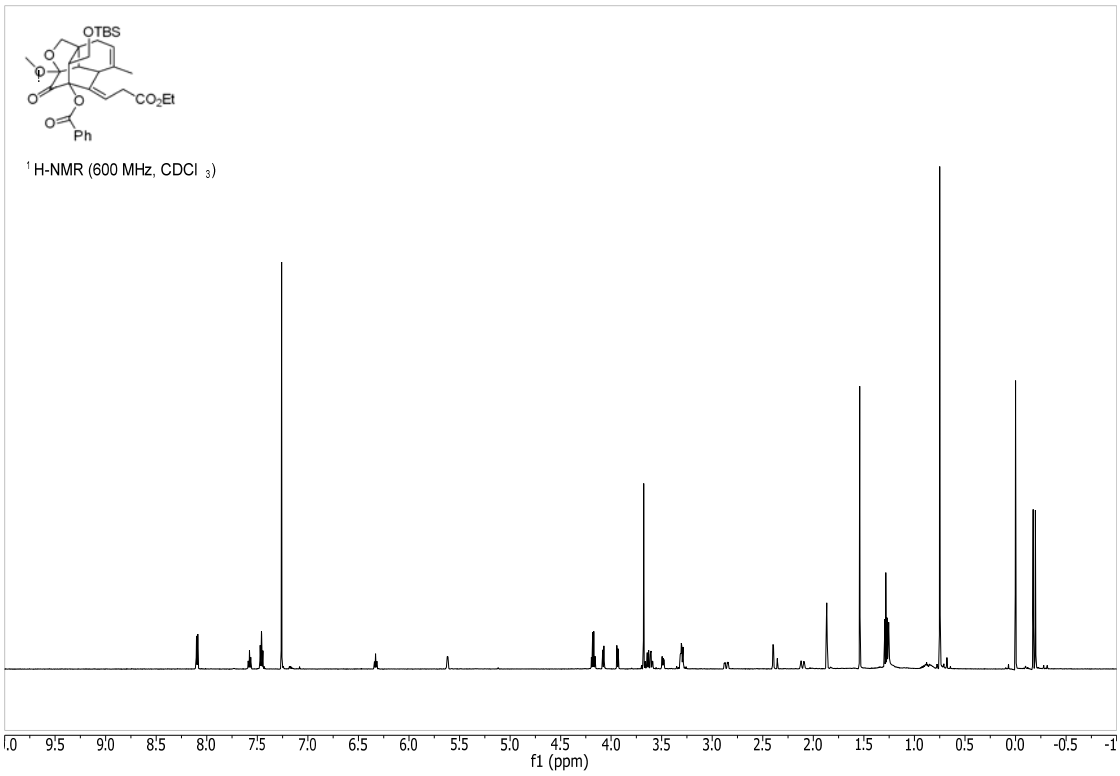


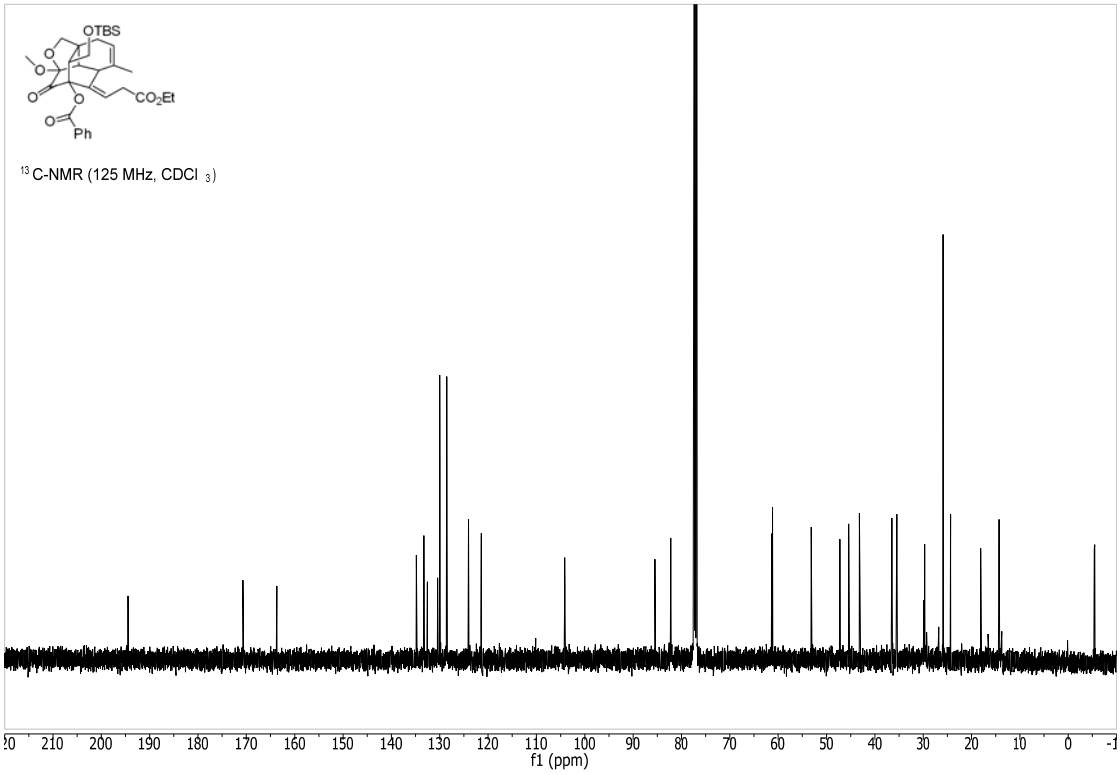


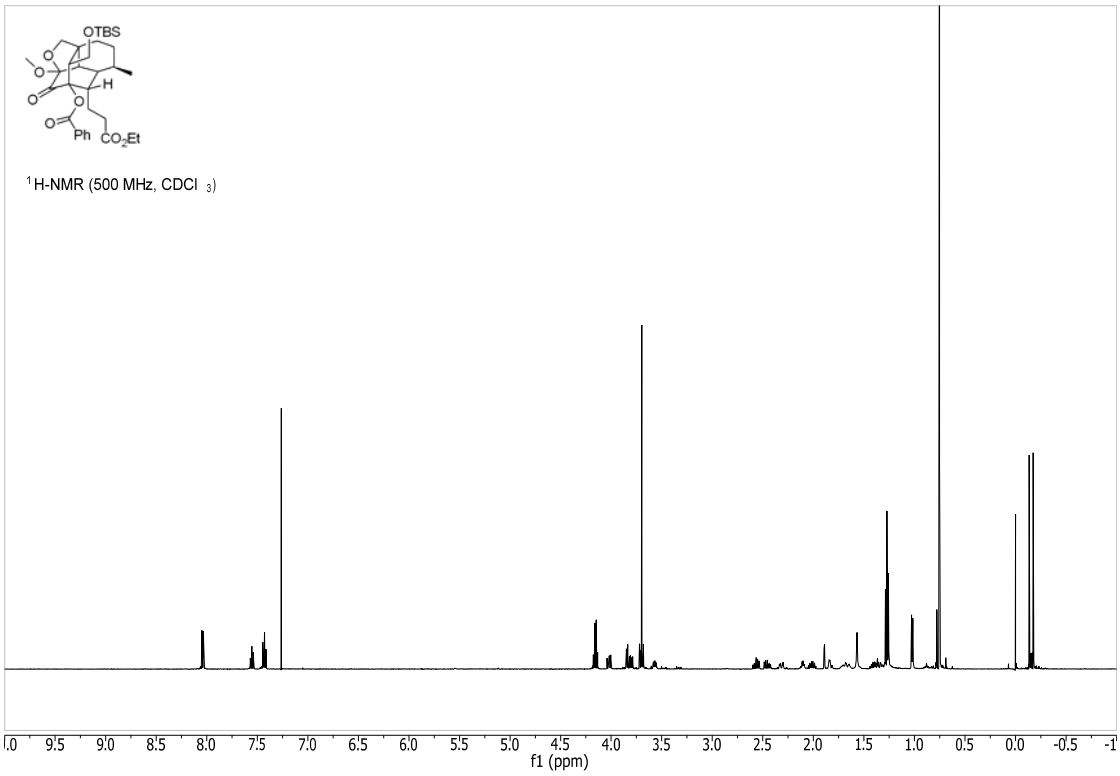


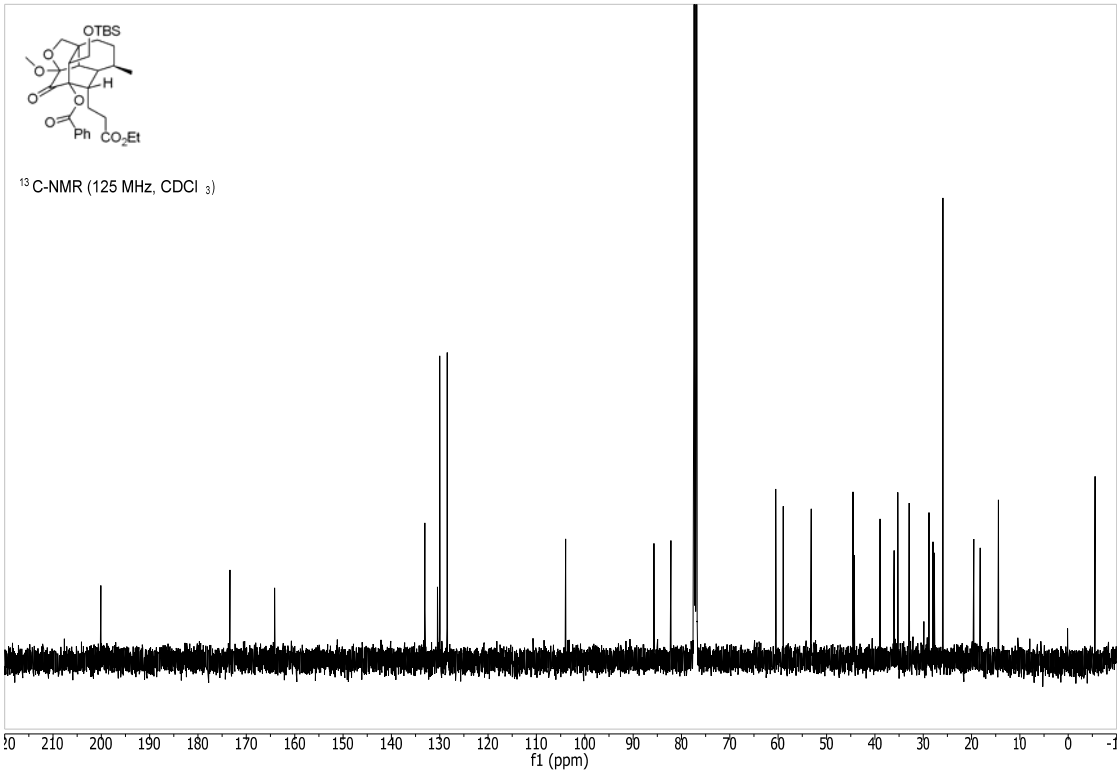


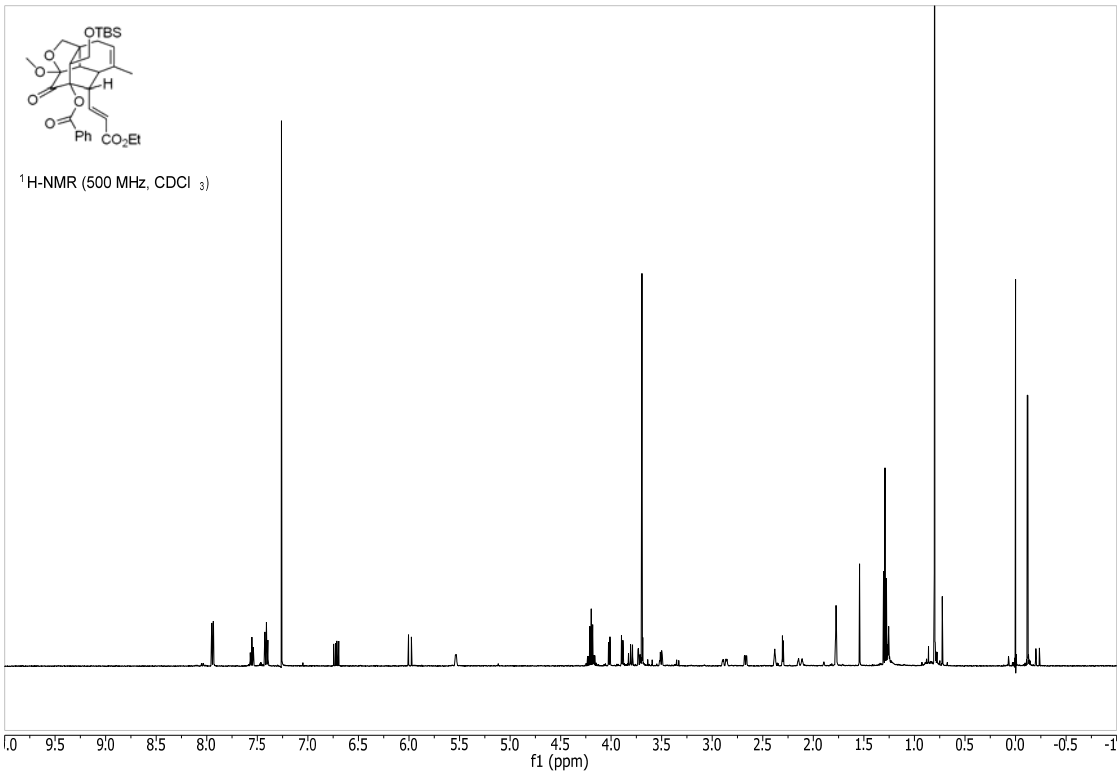


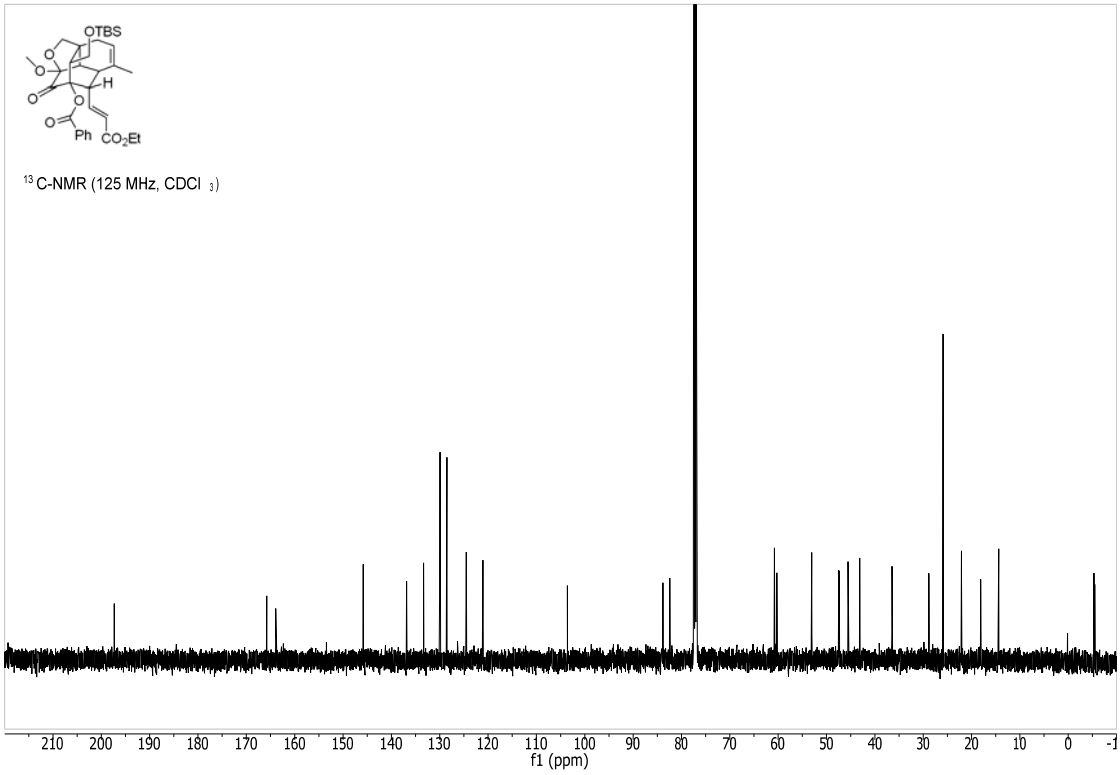


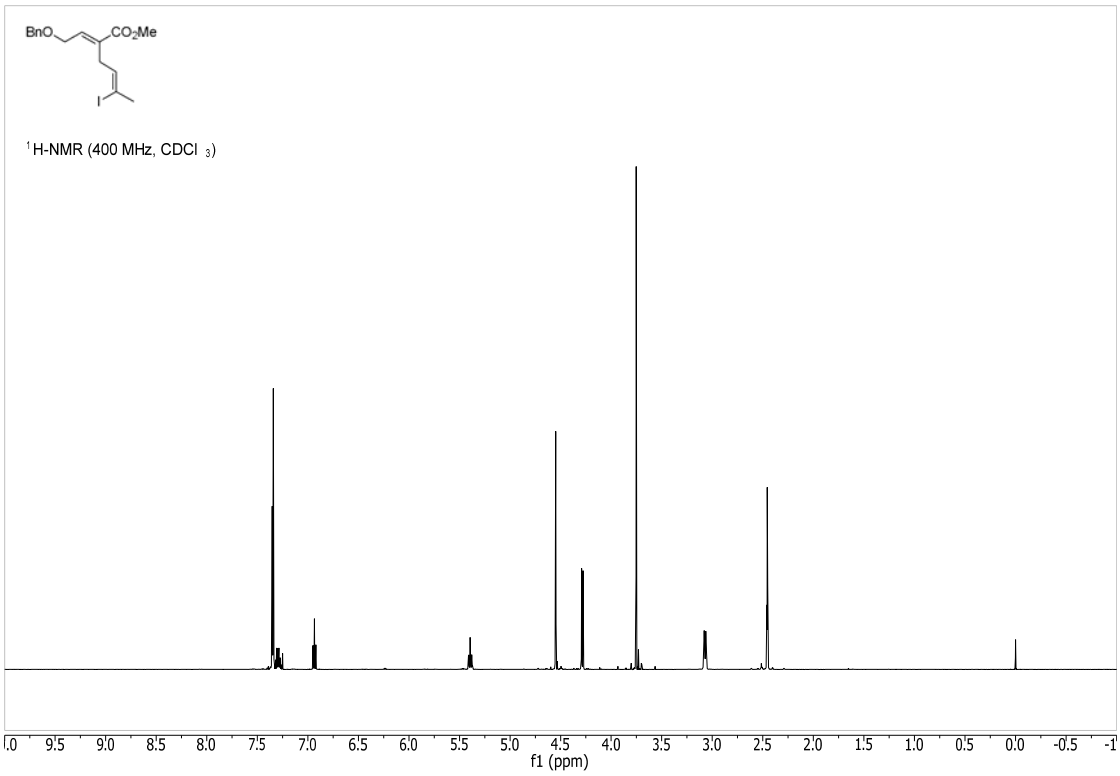


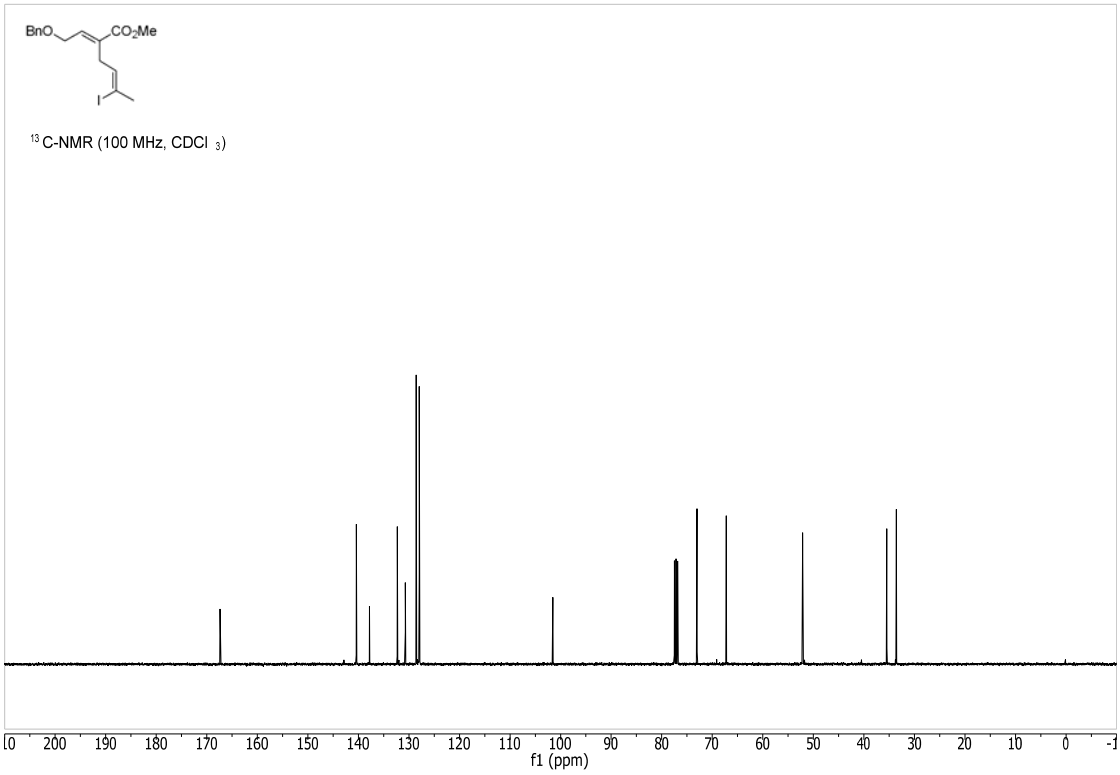


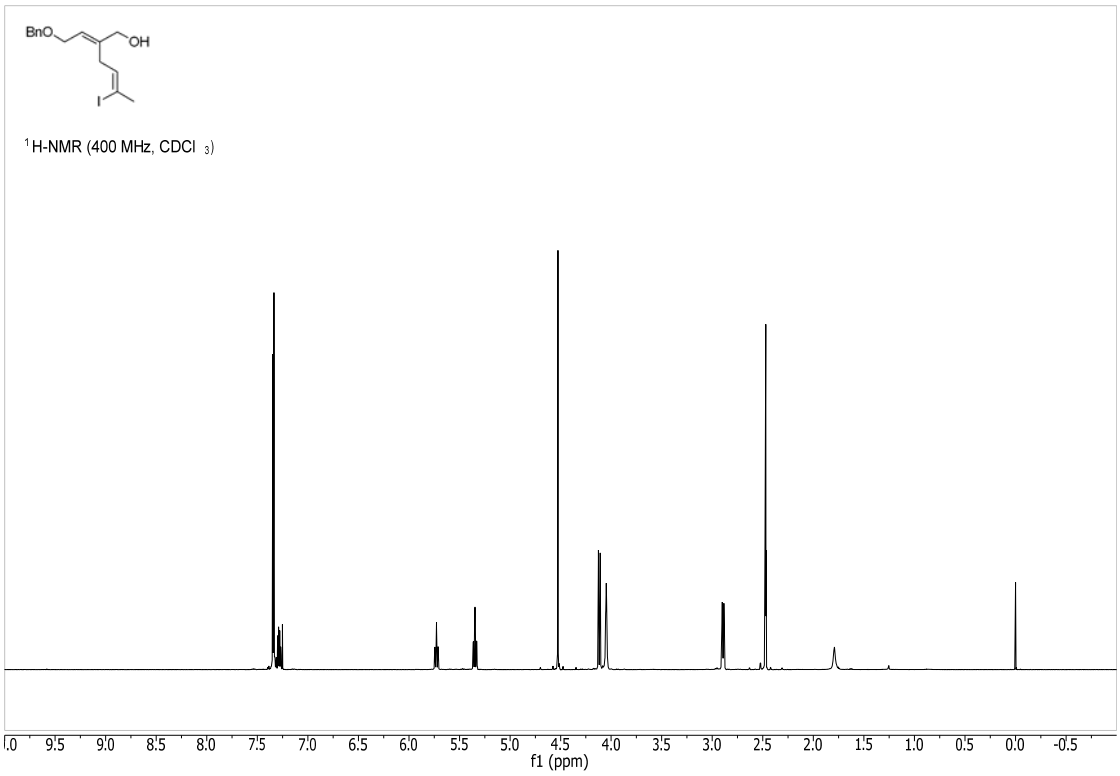


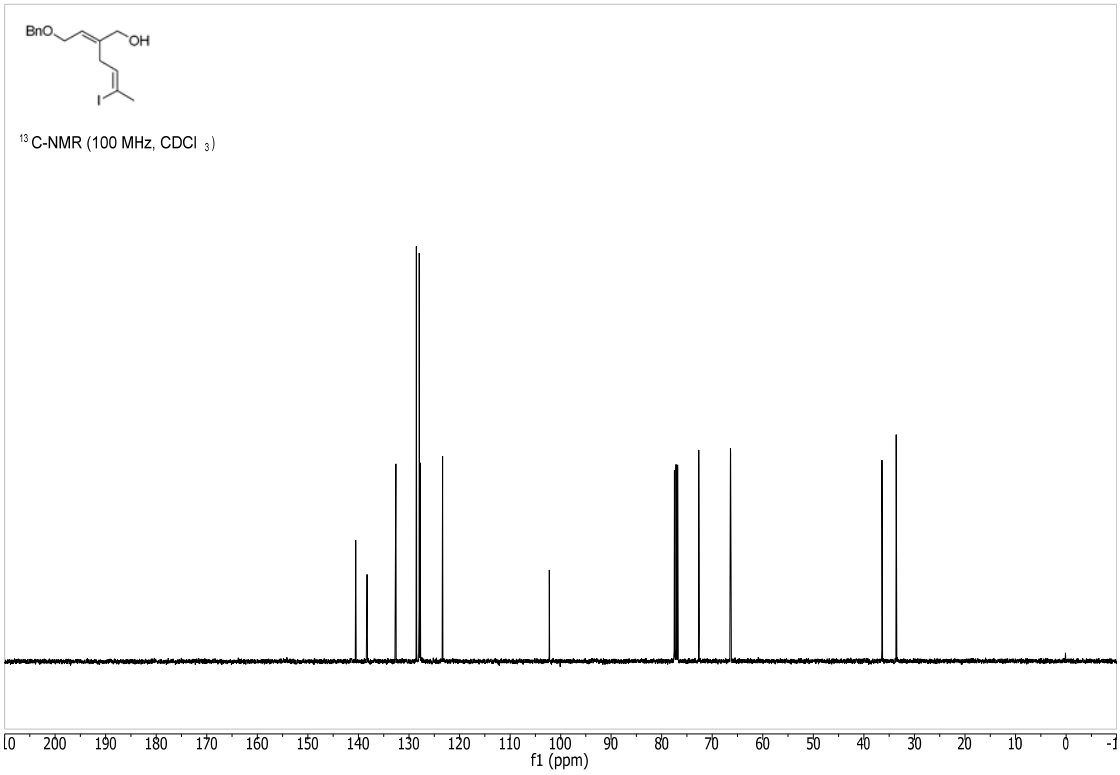


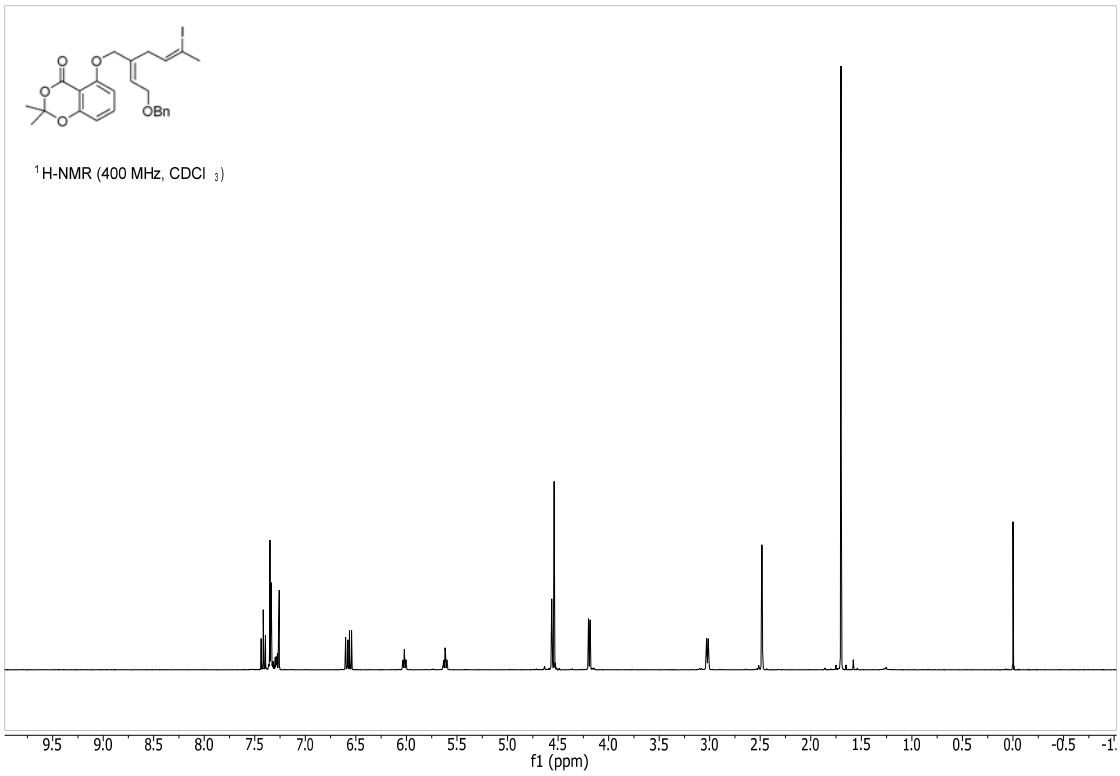


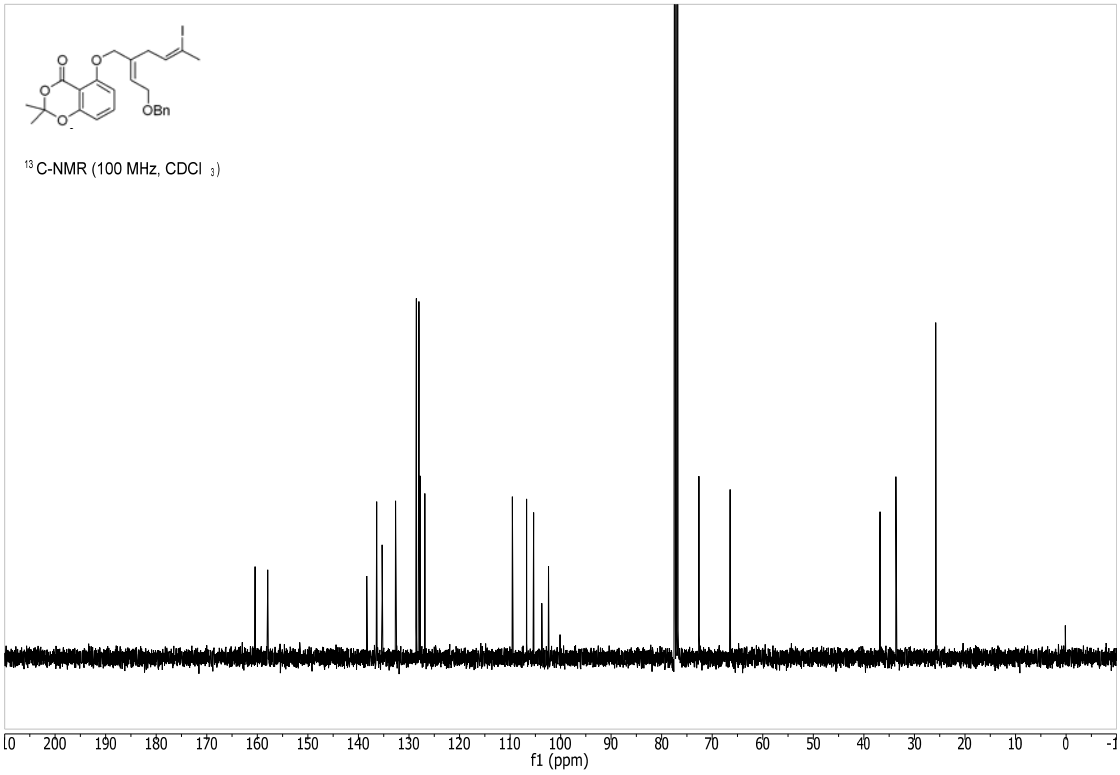

BnO
CO2Me
I
1H-NMR (400 MHz, CDCl 3)
f1 (ppm)

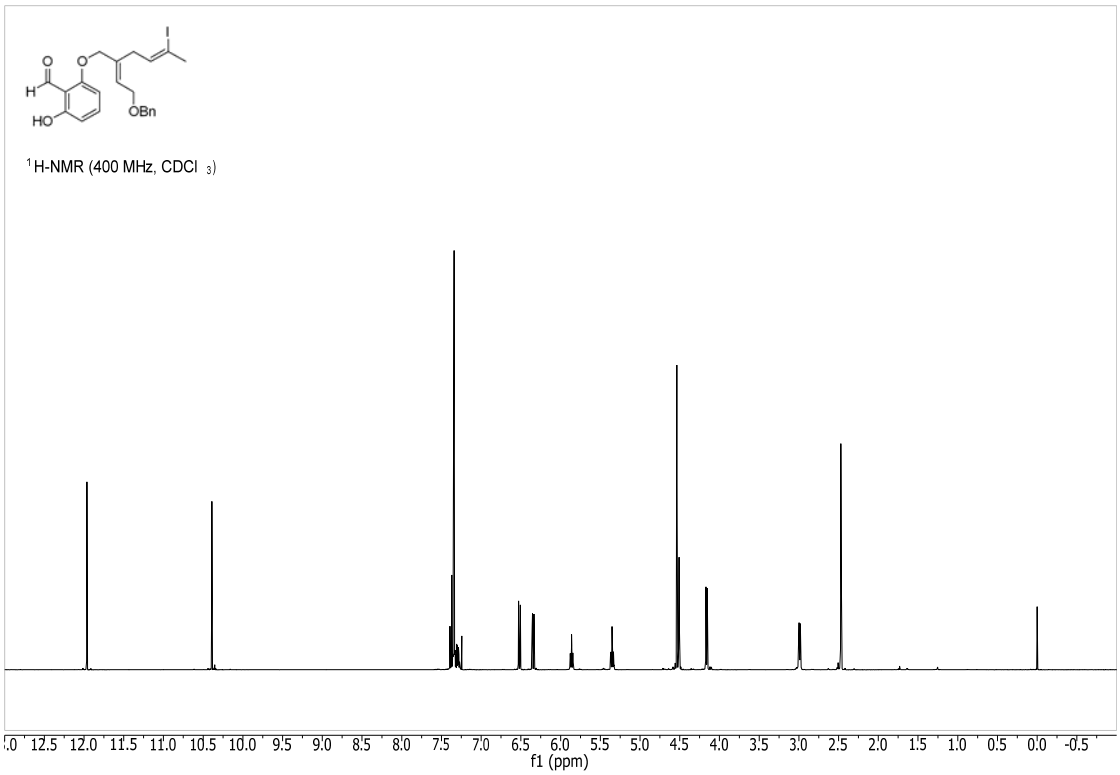

BnO
CO2Me
I
13C-NMR (100 MHz, CDCl 3)
f1 (ppm)

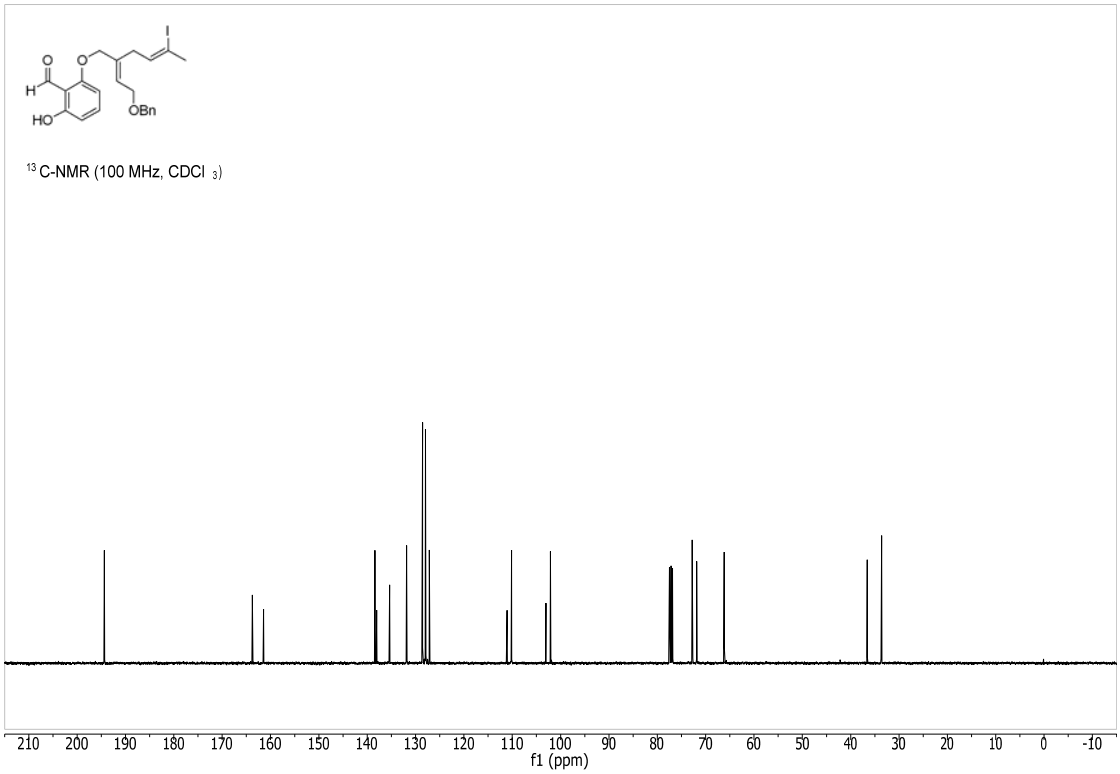


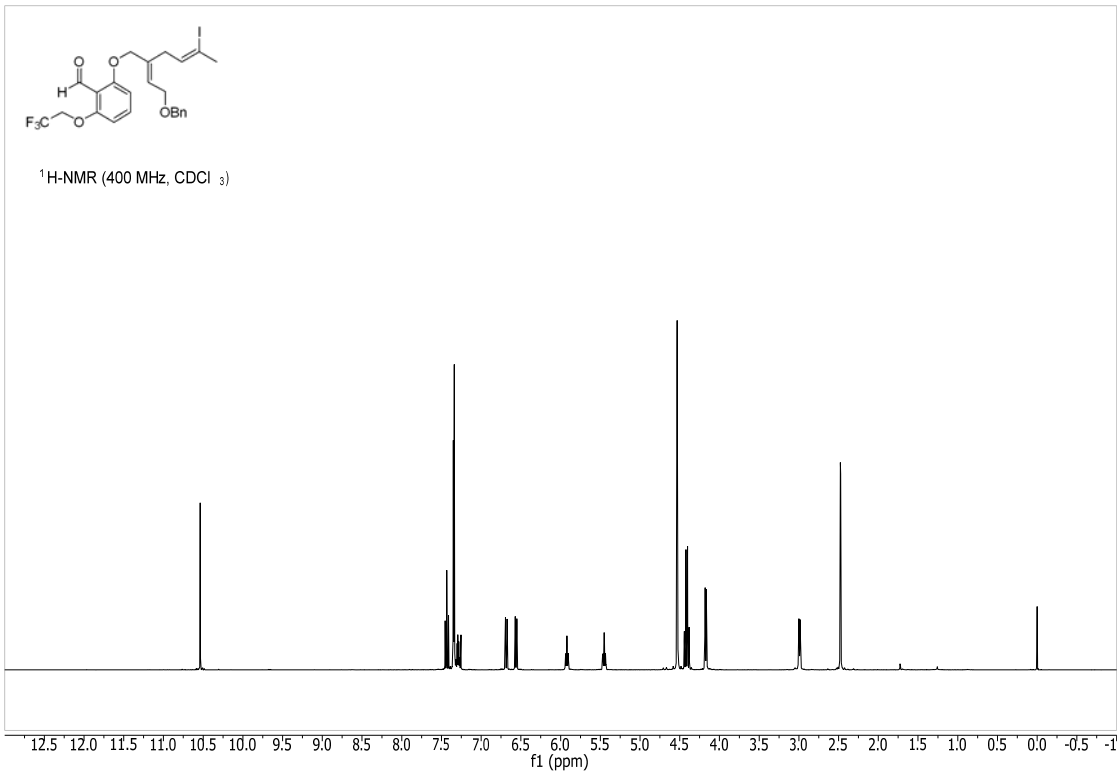


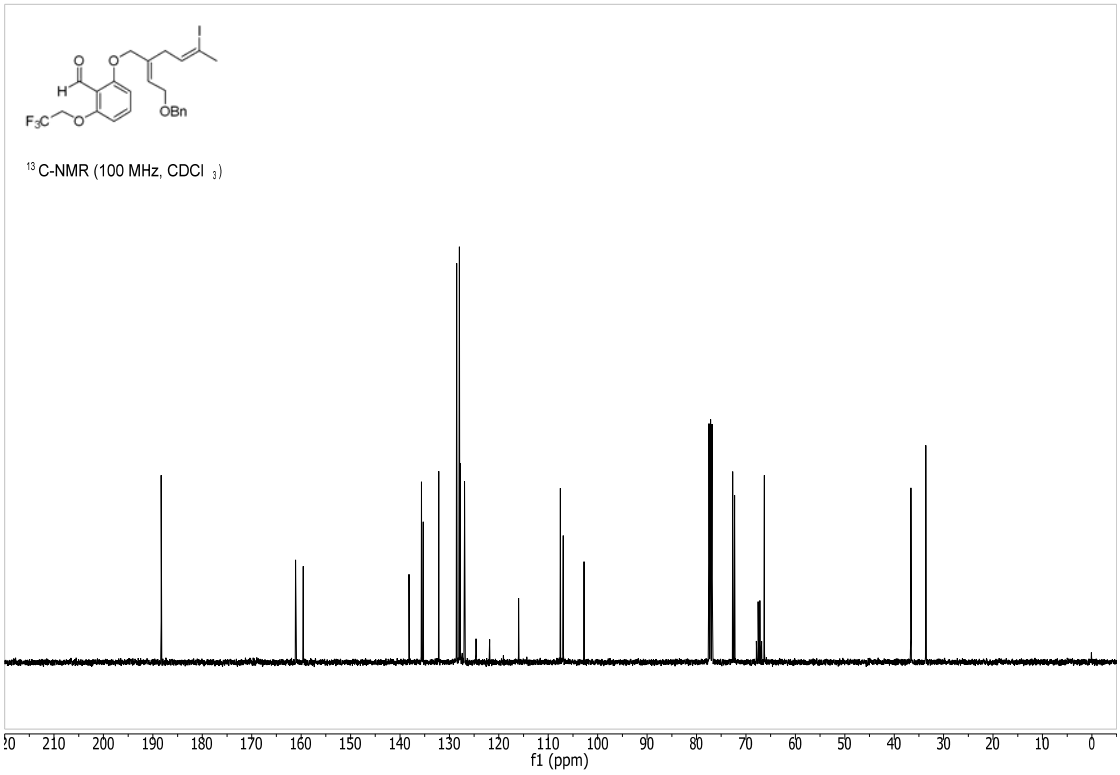


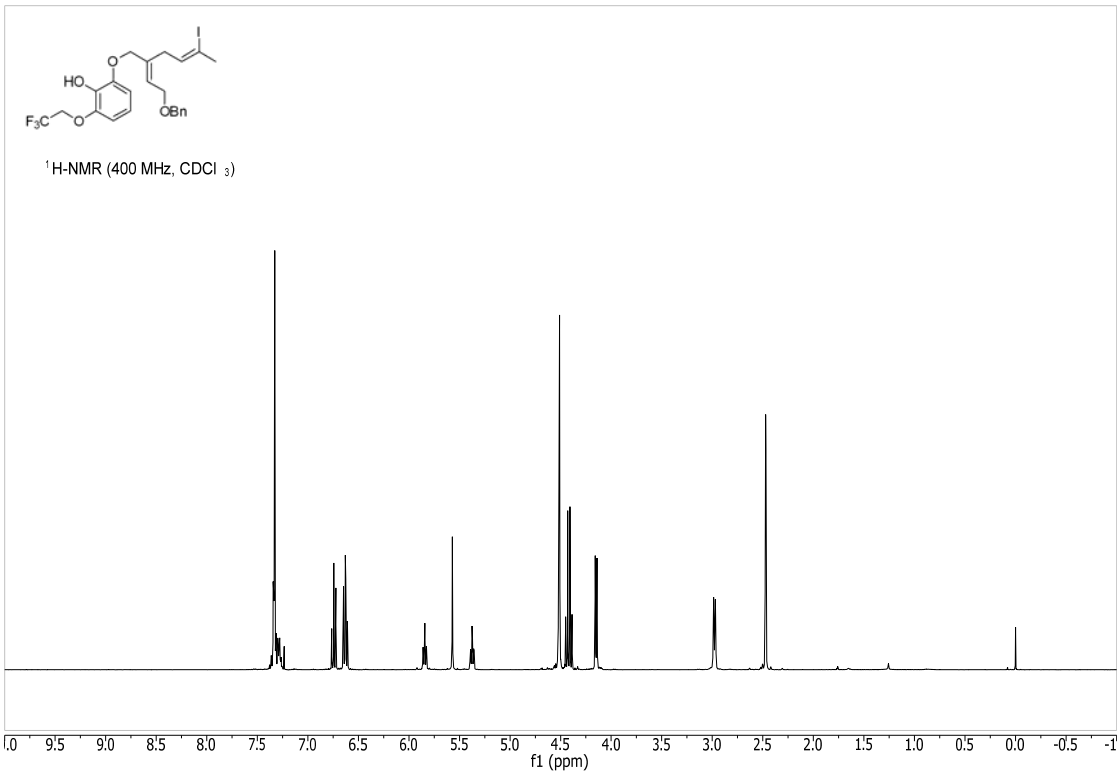


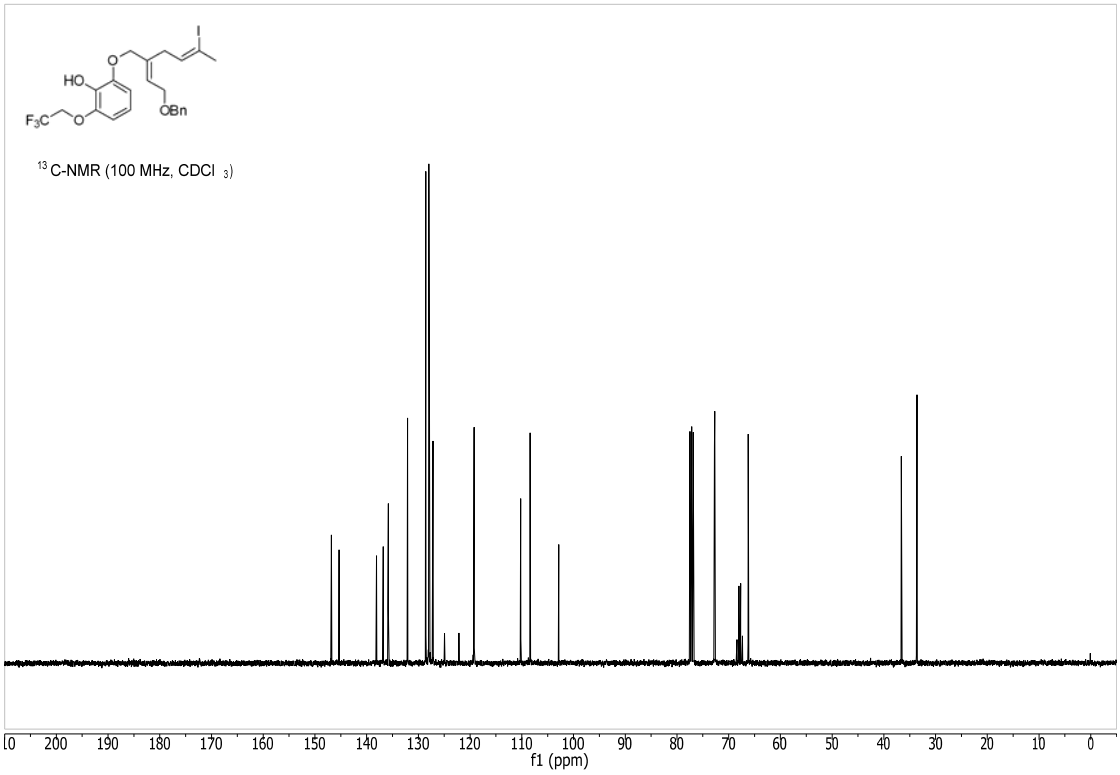


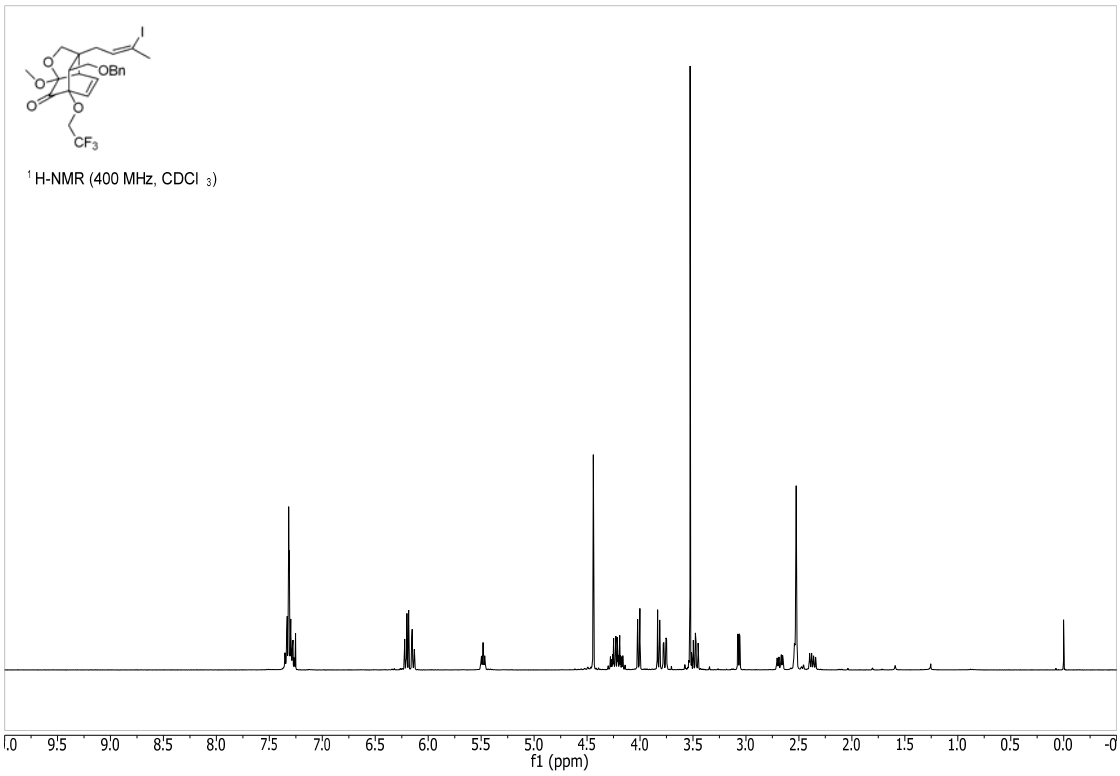


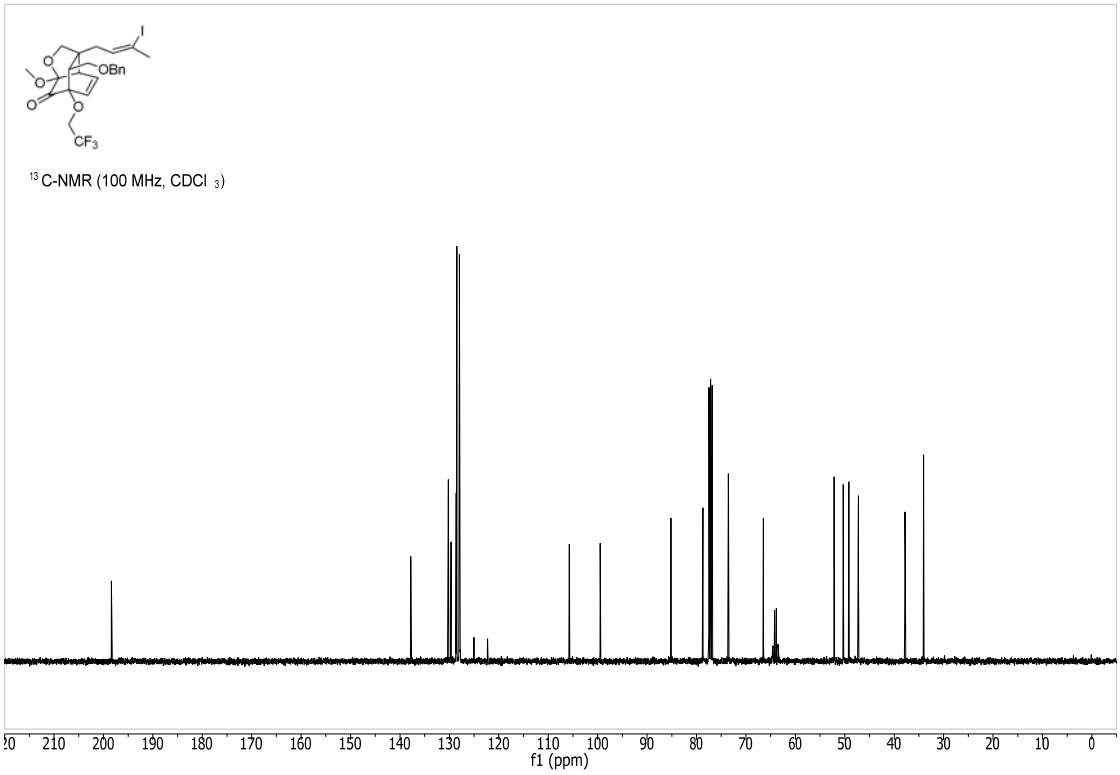


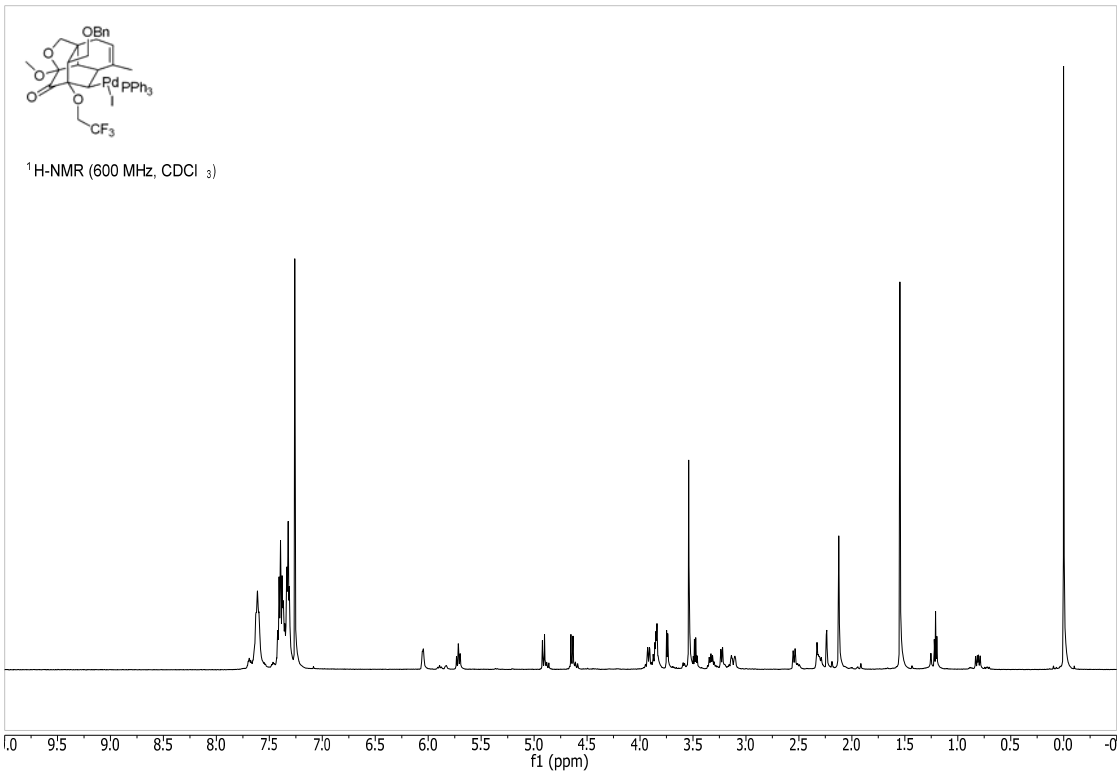


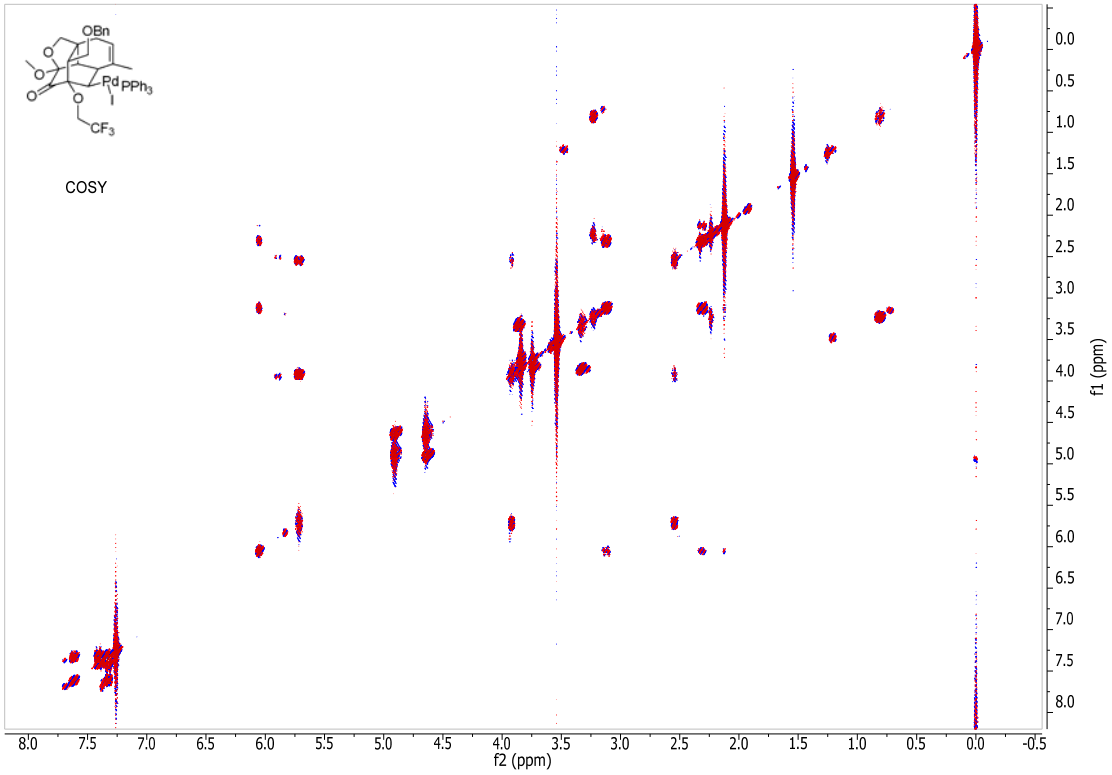

HO
O
I
OBn
F3C
O
1H-NMR (400 MHz, CDCl 3)
f1 (ppm)

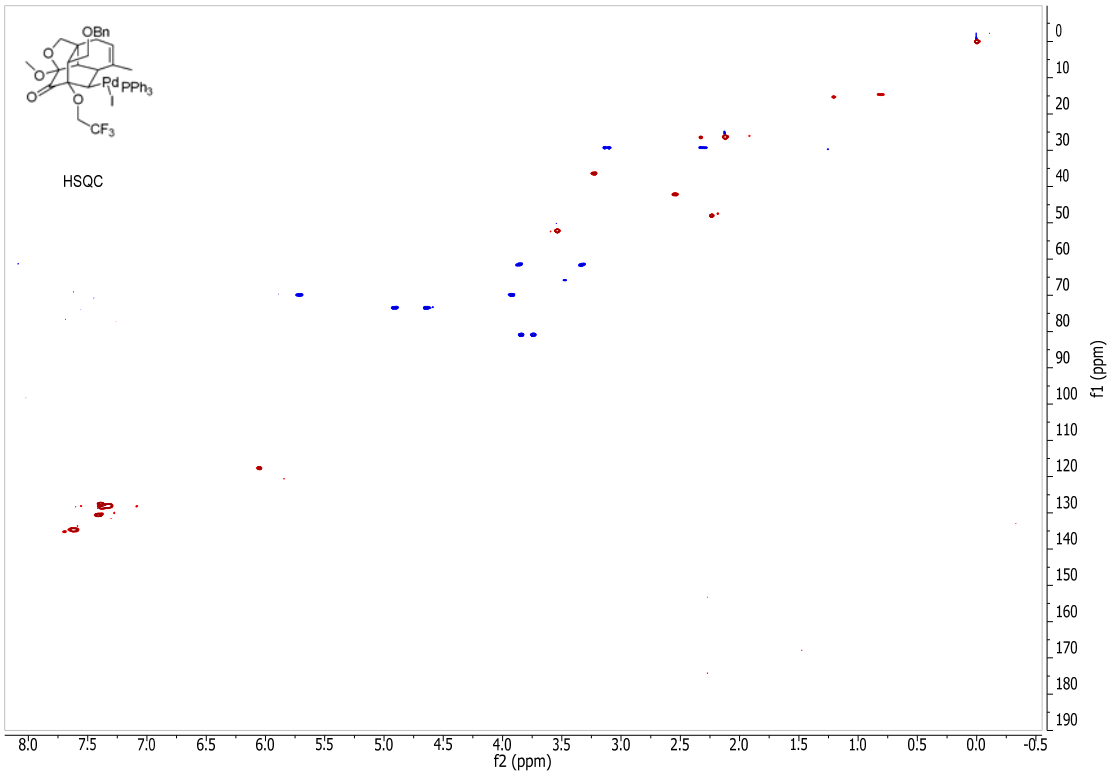

HO
O
I
OBn
F3C
O
13C-NMR (100 MHz, CDCl 3)
f1 (ppm)

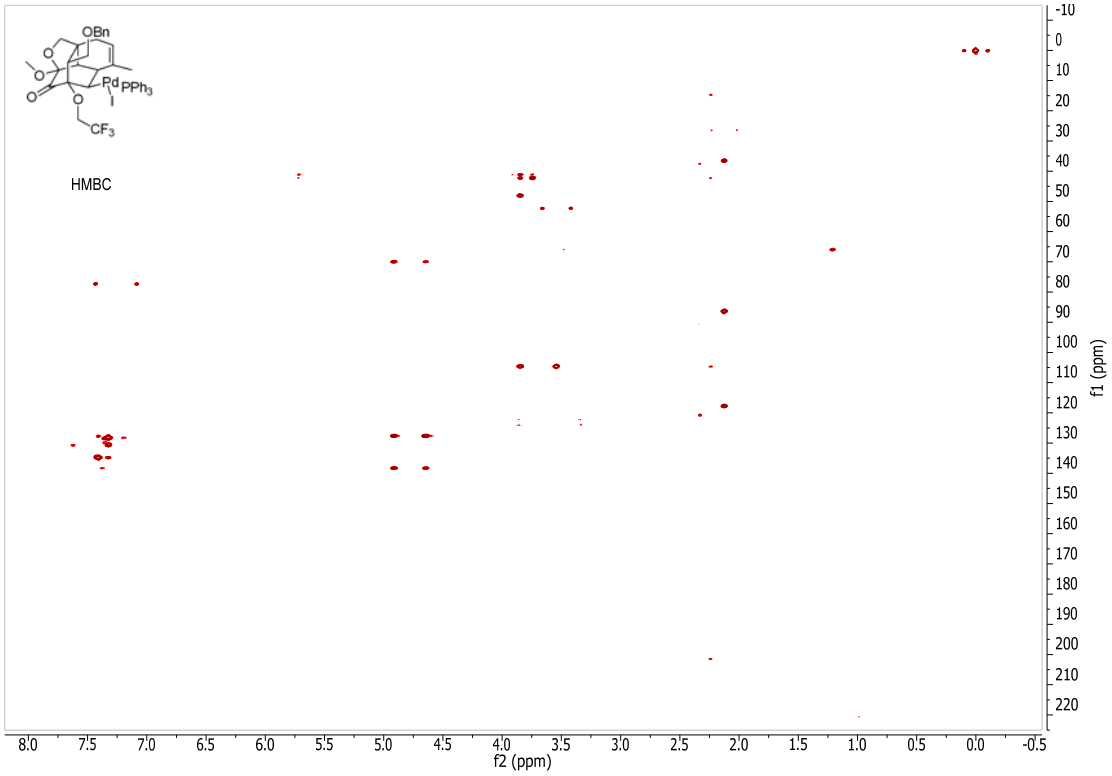


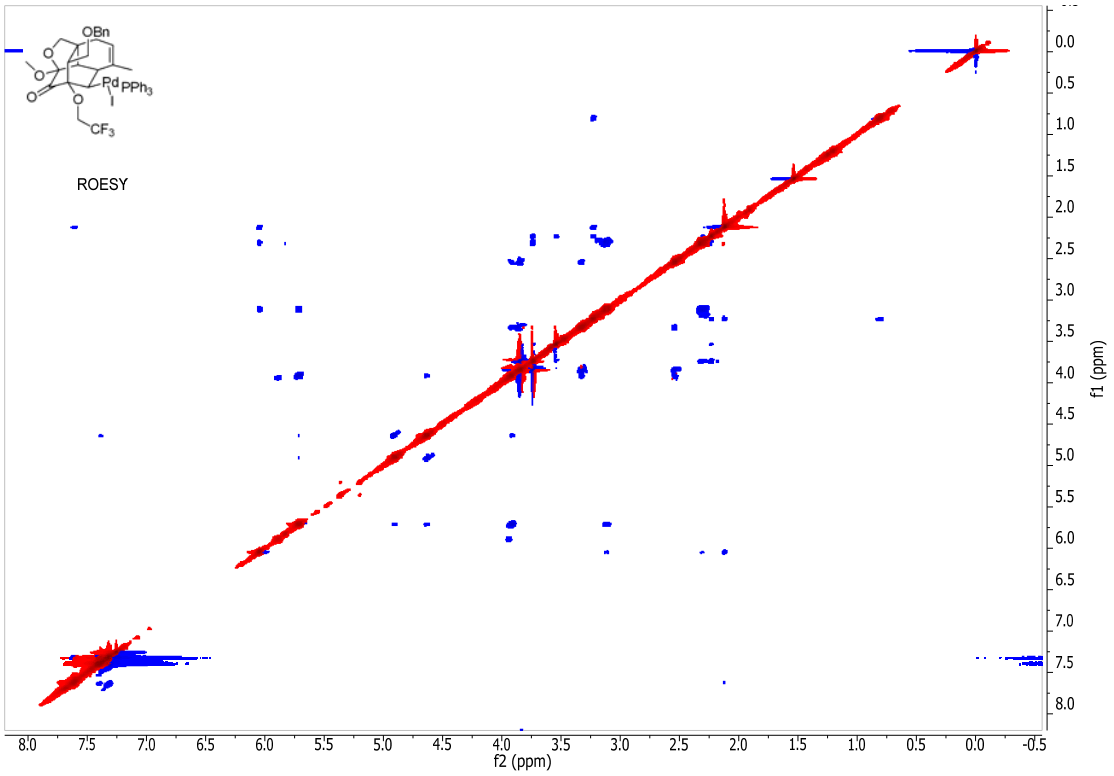












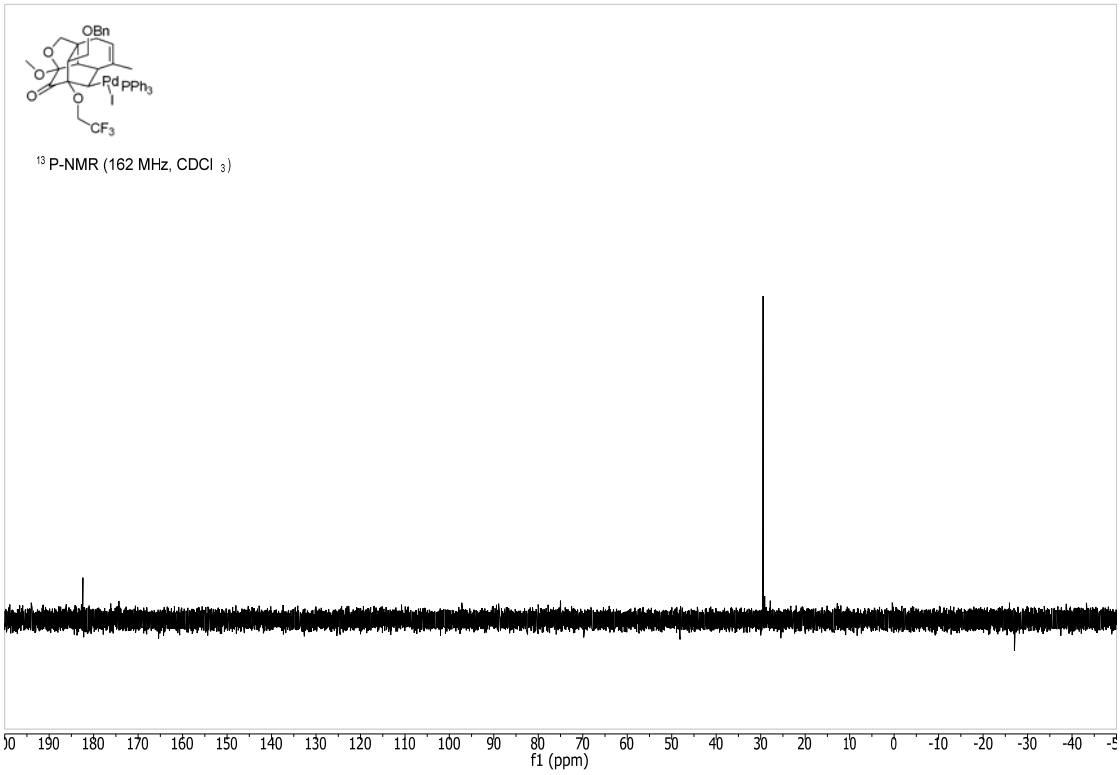
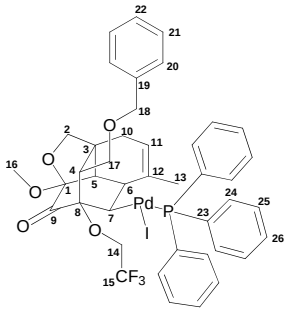
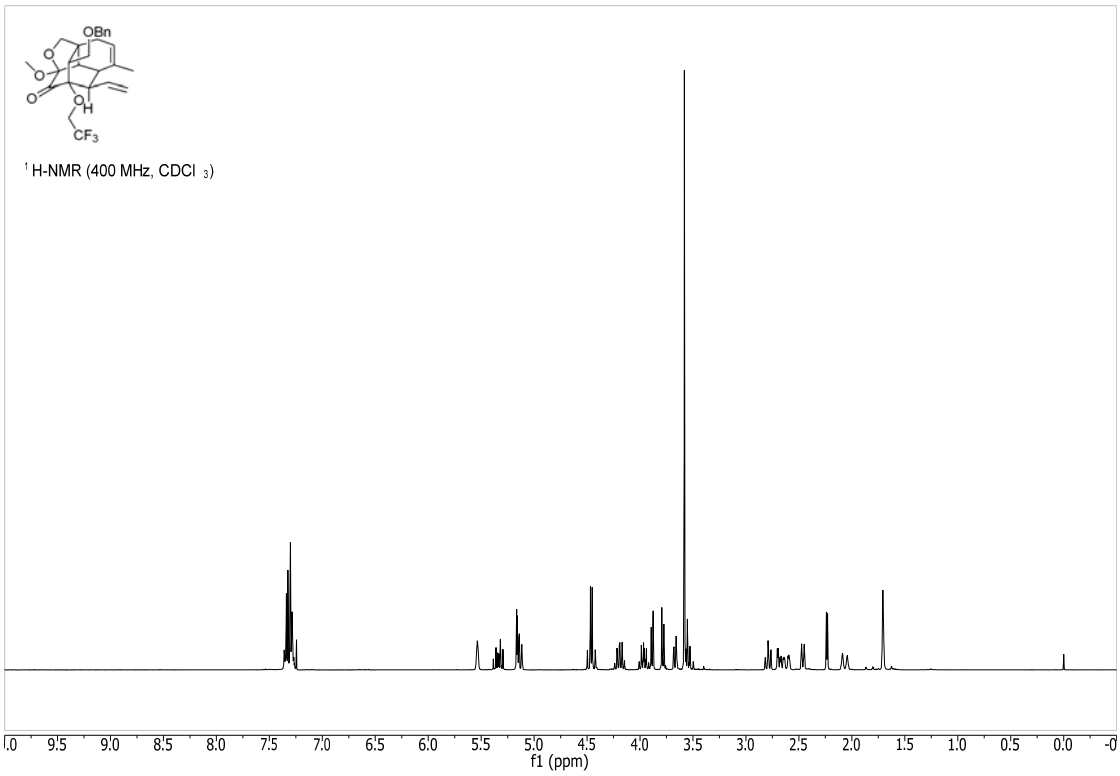


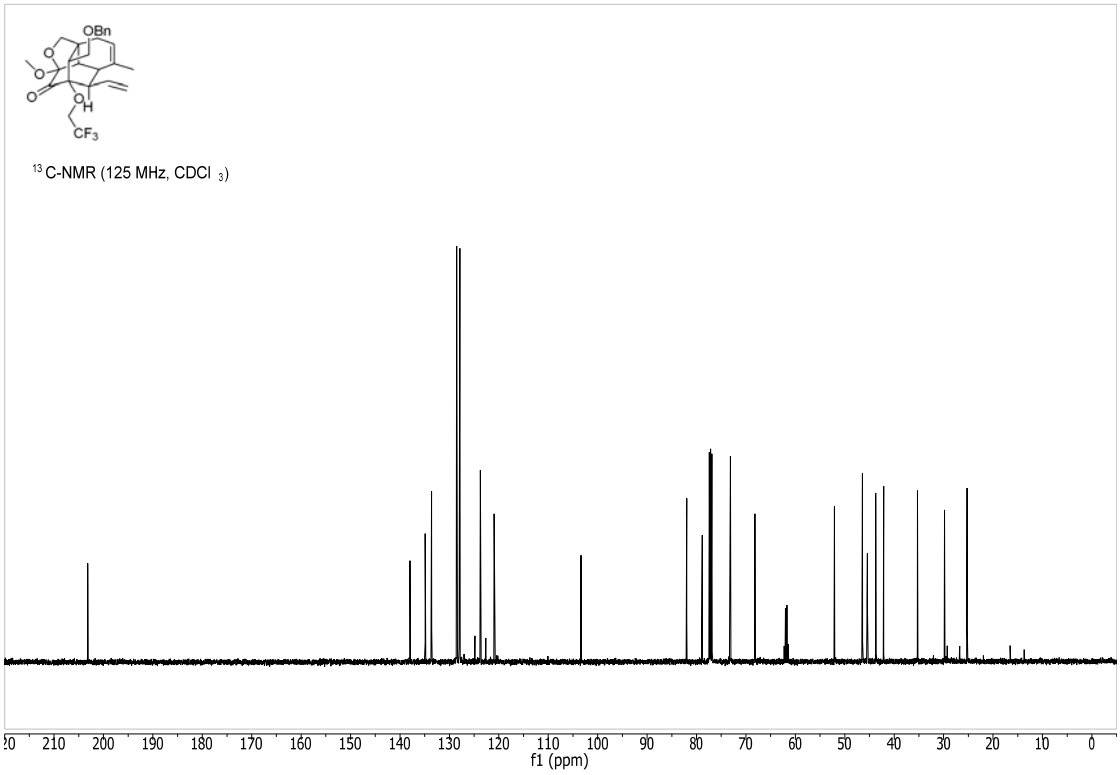
Table 5. 2D-NMR Data of Compound **78**

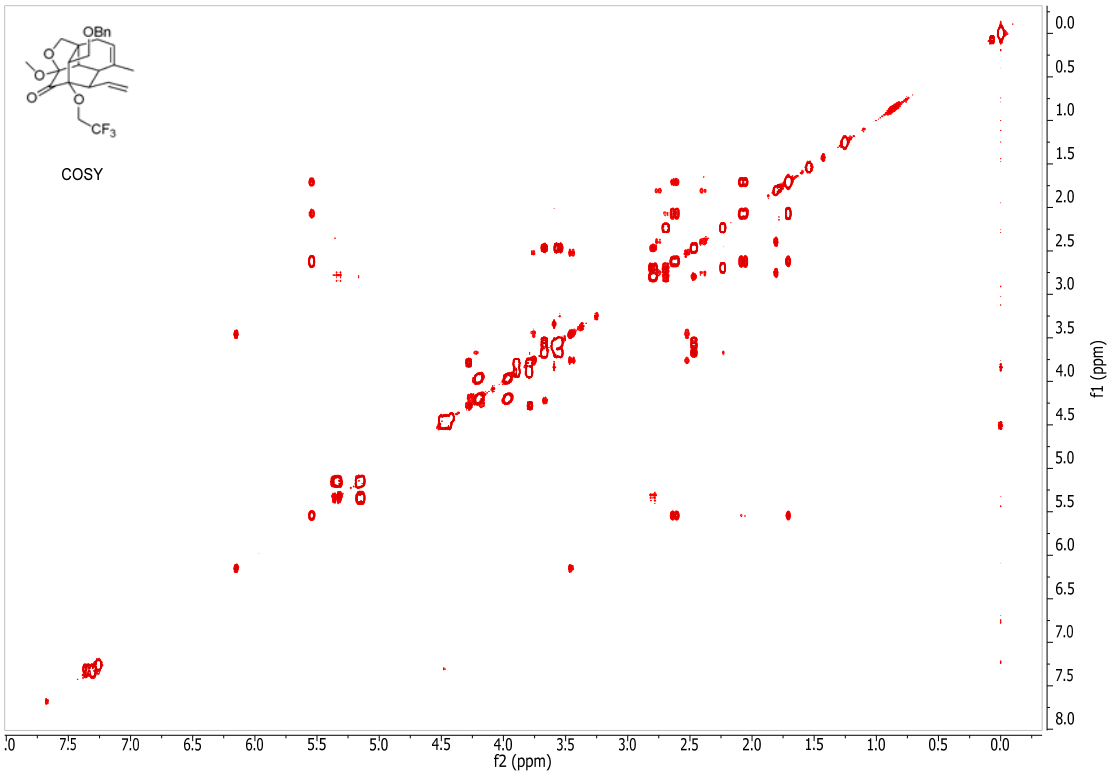


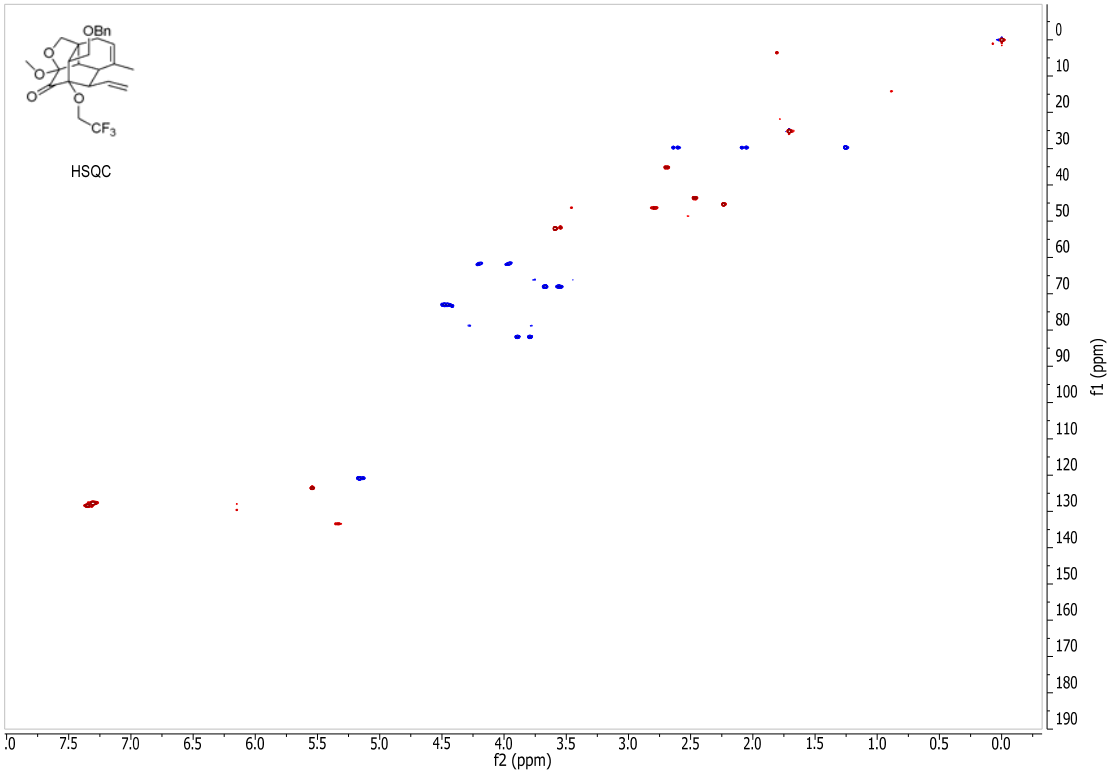
Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations	ROESY correlations
1	104.5		Cq			
2a	80.9	3.84	CH_2	H-2b	C-1, C-3, C-4, C-5	H-4
2b		3.74	CH_2	H-2a	C-3, C-4	H-5, H-10b
3	41.0		Cq			
4	42.2	2.55	CH	H-17a		H-2a, H-14b, H-17b
5	48.0	2.24	CH	H-6	C-1, C-4, C-7, C-9	H-2b, H-6
6	36.4	3.23	CH	H-5, H-7		H-5, H-13
7	14.6	0.81	CH	H-4, H-6		H-6
8	122.1		Cq			
9	201.4		Cq			
10a	29.3	3.12	CH_2	H-10b, H-11		H-10b, H-11
10b		2.31	CH_2	H-10a, H-11, H-13		H-10a
11	117.7	6.05	CH	H-10a, H-10b, H-13		H-10a, H-10b, H-13
12	86.3		Cq			
13	26.3	2.12	CH_3	H-11	C-6, C-11, C-12	H-6, H-11
14a	61.5	3.86	CH_2	H-14b	C-8, C-15	H-14b
14b		3.33	CH_2	H-14a	C-8, C-15	H-4, H-14a
15	123.9		Cq			
16	52.2	3.54	CH_3		C-1	H-5
17a	69.9	5.72	CH_2	H-4, H-17b	C-3, C-4	H-10a, H-17b
17b		3.92	CH_2	H-17a		H-4, H-11, H-14b, H-18b
18a	73.4	4.91	CH_2	H-18b	C-17, C-19, C-20	H-17a, H-18b
18b		4.64	CH_2	H-18a	C-17, C-19, C-20	H-17a, H-17b, H-18a
19	138.1		Cq			
20	127.5	7.39	CH		C-19	H-18b
21	128.5	7.37	CH			
22	128.3	7.36	CH			

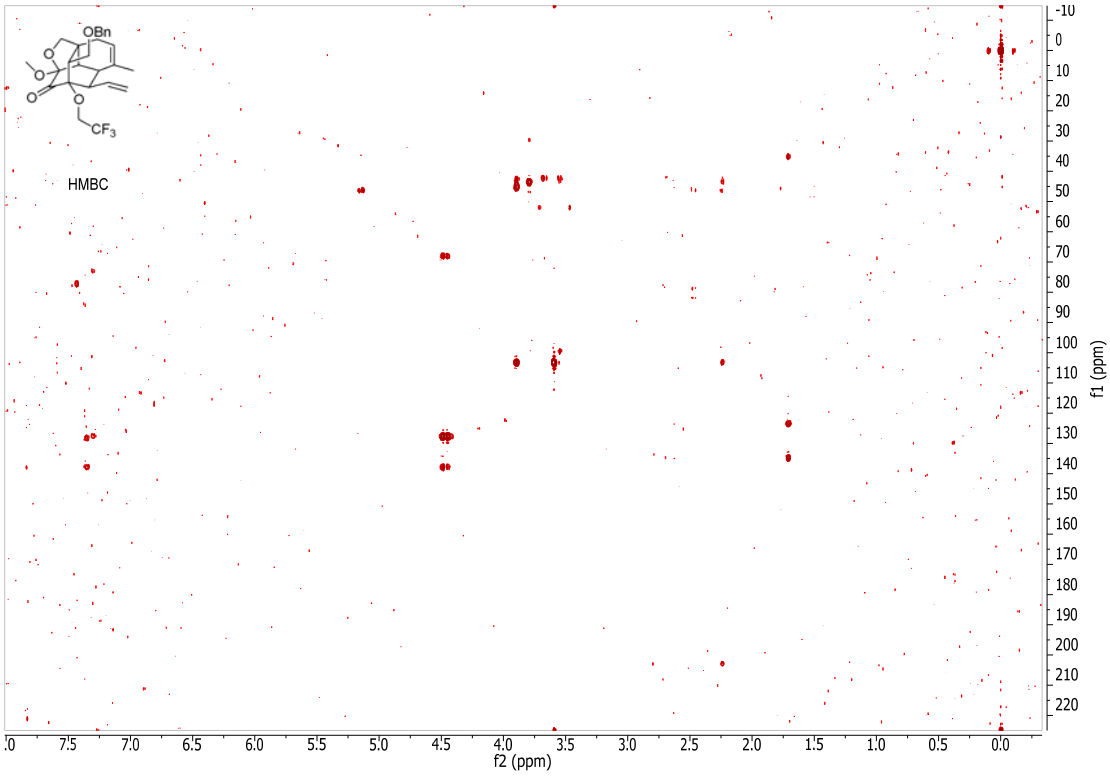
23	129.7		Cq			
23	128.2	7.32	CH	H-25, H-26	C-25, C-26	H-13
25	134.8	7.61	CH	H-24, H-26	C-26	H-7, H-13, H-17a, H-17b
26	130.6	7.41	CH	H-24, H-25	C-25	











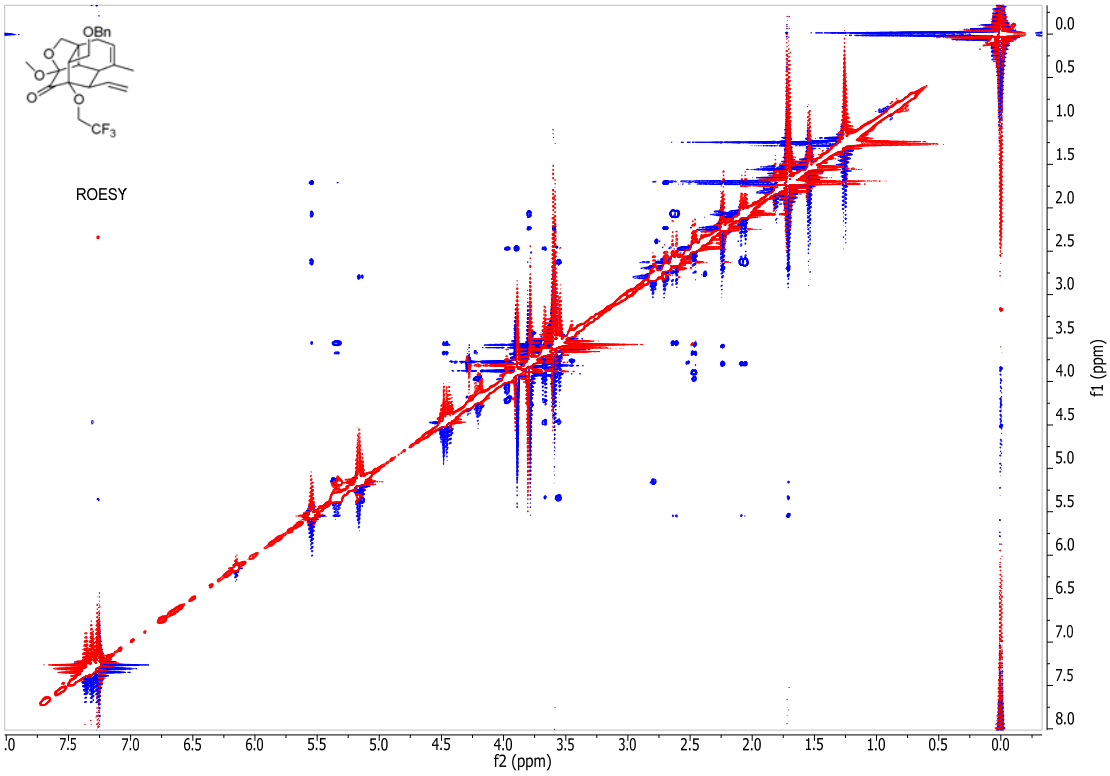
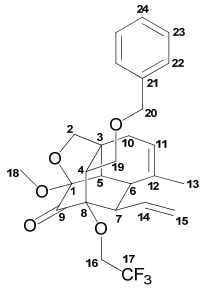
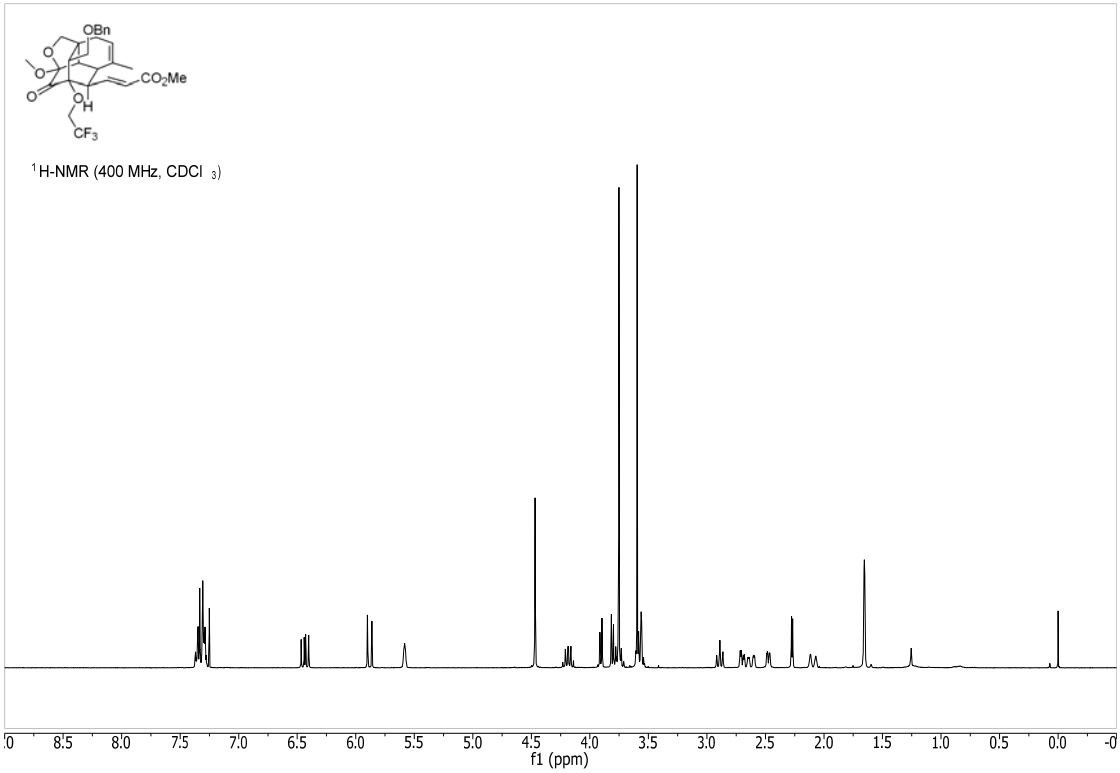
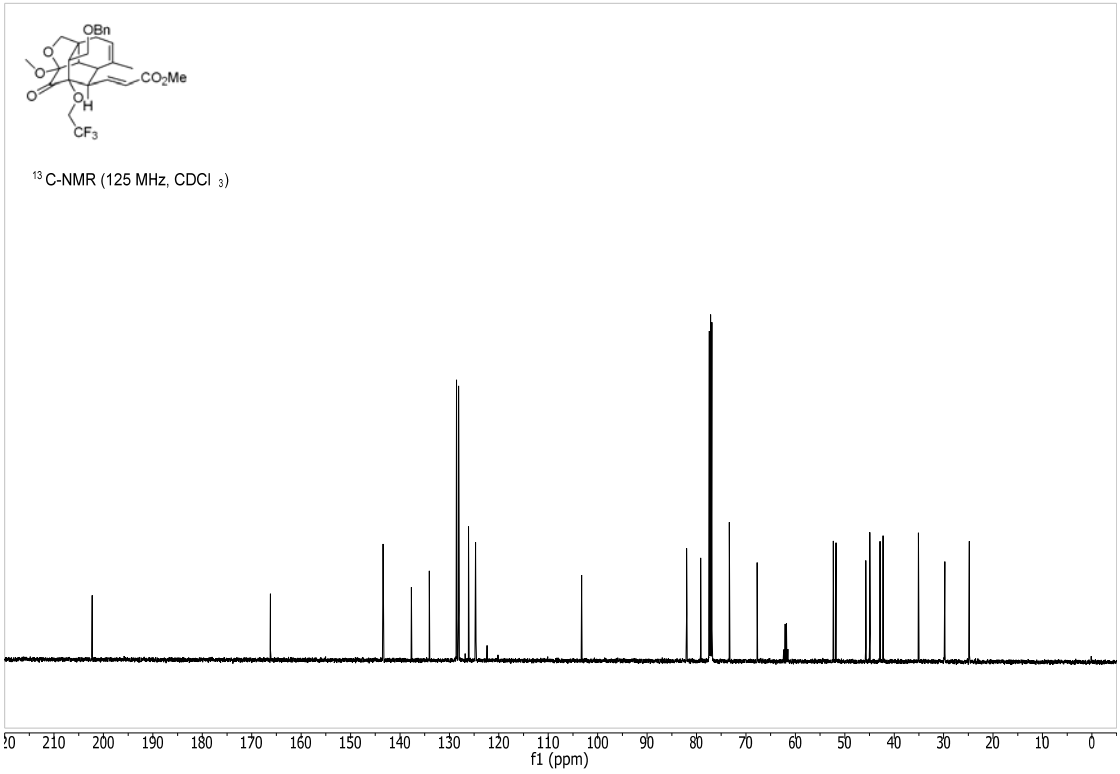


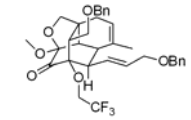
Table 6. 2D-NMR Data of Compound **79**



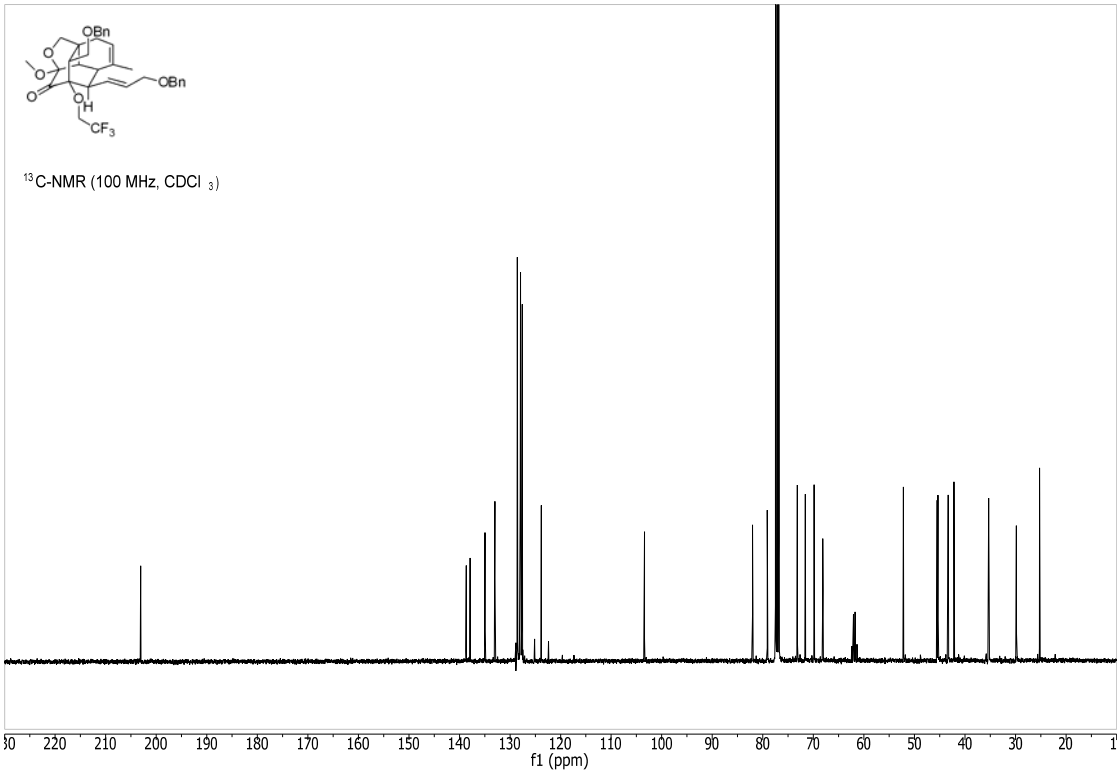
Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations	ROESY correlations
1	103.4		Cq			
2a	82.0	3.90	CH_2	H-2b	C-1, C-4, C-5	H-4
2b		3.79	CH_2	H-2a	C-3, C-4	H-5, H-10b
3	42.1		Cq			
4	43.7	2.47	CH	H-7, H-19a, H-19b		H-2a, H-16b, H-19a
5	45.4	2.25	CH	H-6	C-3, C-4	H-2b, H-6, H-18
6	35.3	2.70	CH	H-5, H-7		H-5, H-13
7	46.4	2.80	CH	H-4, H-6, H-14		H-15a
8	78.8		Cq			
9	203.2		Cq			
10a	29.8	2.62	CH_2	H-10b, H-11, H-13		H-10b, H-19b
10b		2.07	CH_2	H-10a, H-13		H-2b, H-10a
11	123.7	5.55	CH	H-10a, H-13		H-10a, H-10b, H-13
12	134.9		Cq			
13	25.2	1.71	CH_3	H-10a, H-10b, H-11	C-6, C-11, C-12	H-6, H-11, H-14
14	133.6	5.34	CH	H-7, H-15a, H-15b		H-19b
15a	120.9	5.17	CH_2	H-14, H-15b		H-7
15b		5.15	CH_2	H-14, H-15a	C-7	
16a	61.7	4.20	CH_2	H-16b		
16b		3.97	CH_2	H-16a		H-4
17	123.7		Cq			
18	52.0	3.59	CH_3		C-1	
19a	68.2	3.67	CH_2	H-4, H-19b	C-3	H-4, H-20b
19b		3.56	CH_2	H-4, H-19a	C-4, C-8	H-10a, H-14, H-2a
20a	73.1	4.48	CH_2	H-20b, H-23	C-19, C-21, C-22	H-19a
20b		4.46	CH_2	H-20a, H-23	C-19, C-21, C-22	H-19b
21	138.0		Cq			
22	127.9	7.30	CH	H-20b, H-23	C-23	
23	128.5	7.35	CH	H-22, H-24	C-21, C-24	
24	127.9	7.31	CH	H-23		



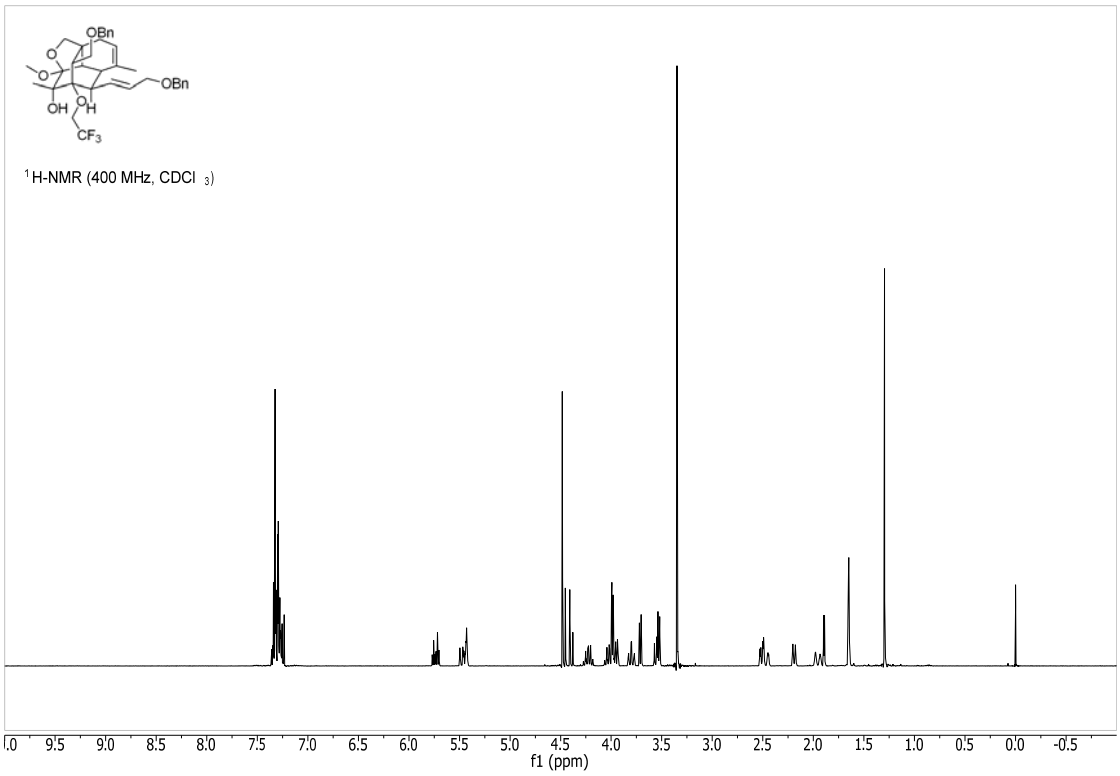


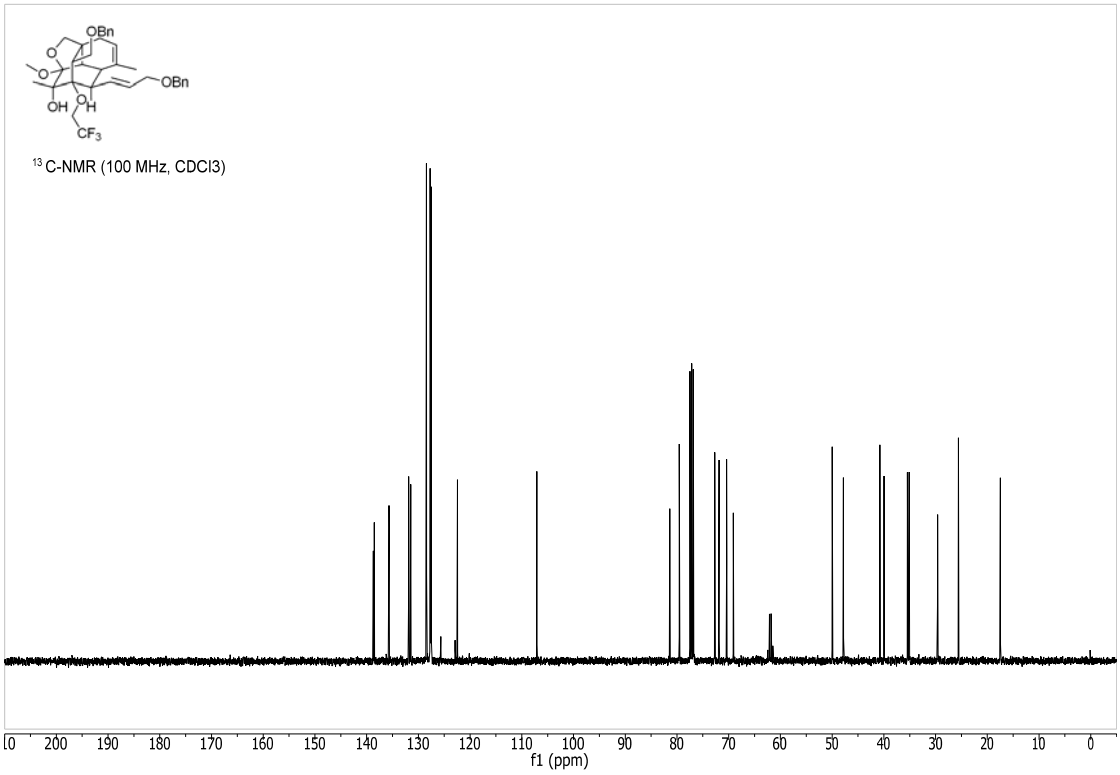


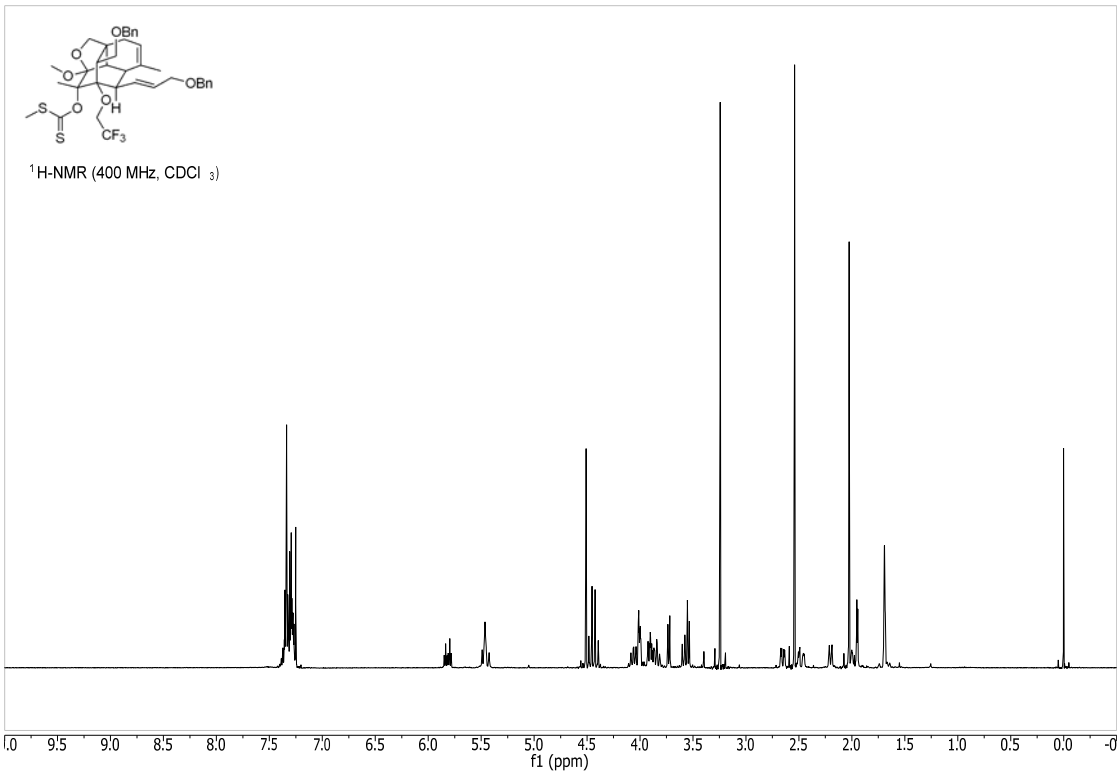
^{1}H-NMR (400 MHz, $CDCl_3$)

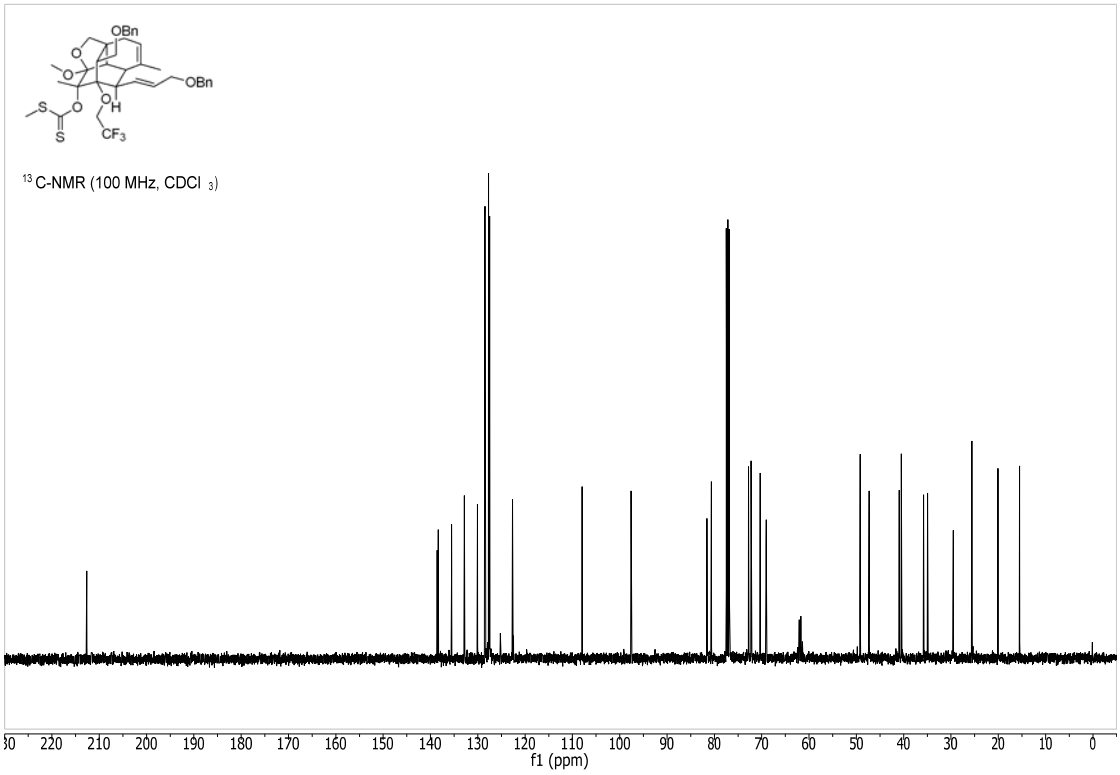


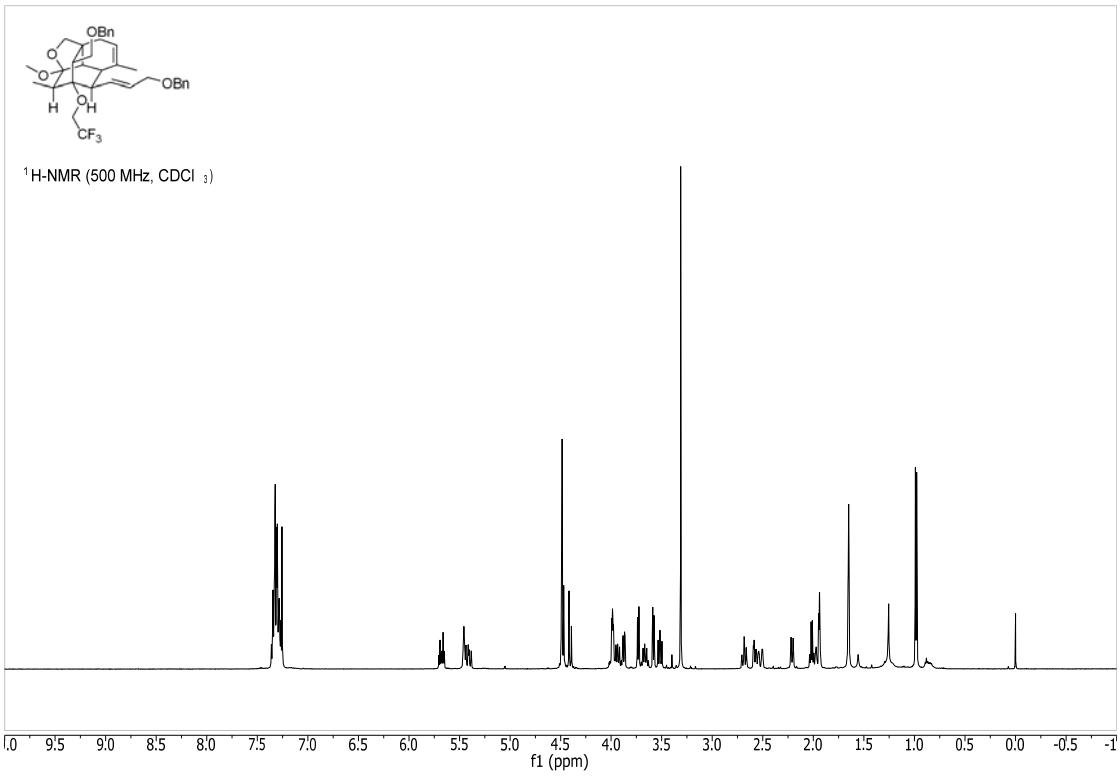
^{13}C-NMR (100 MHz, $CDCl_3$)

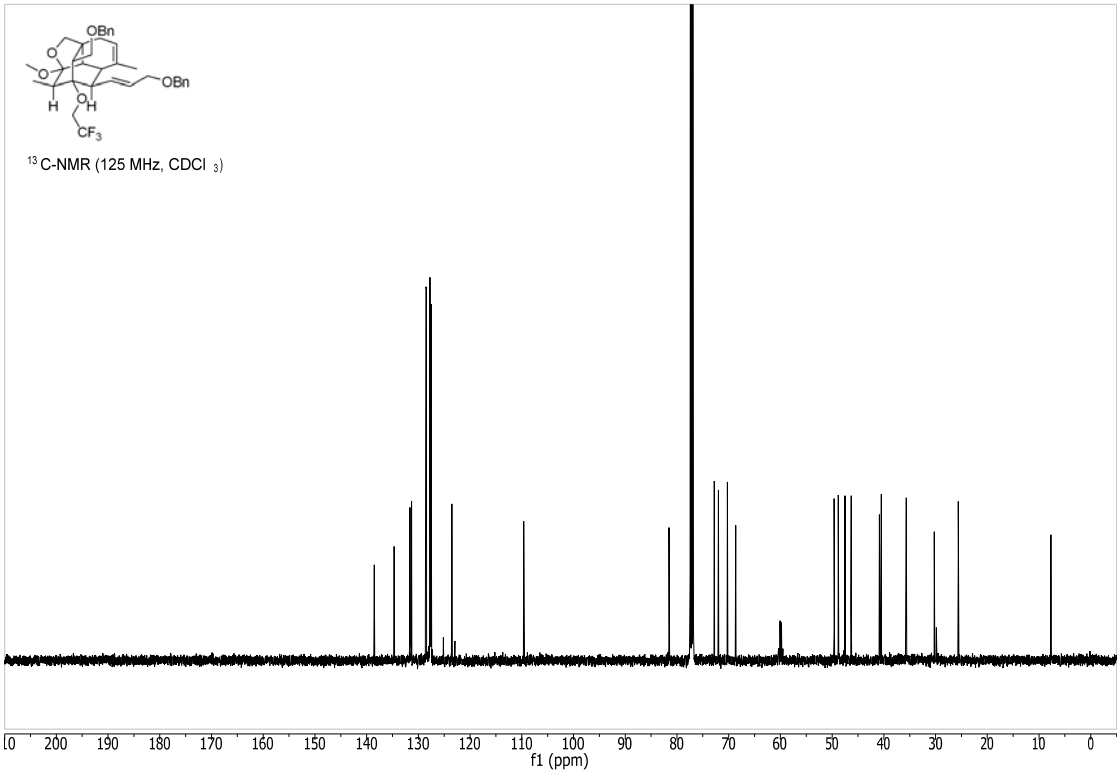


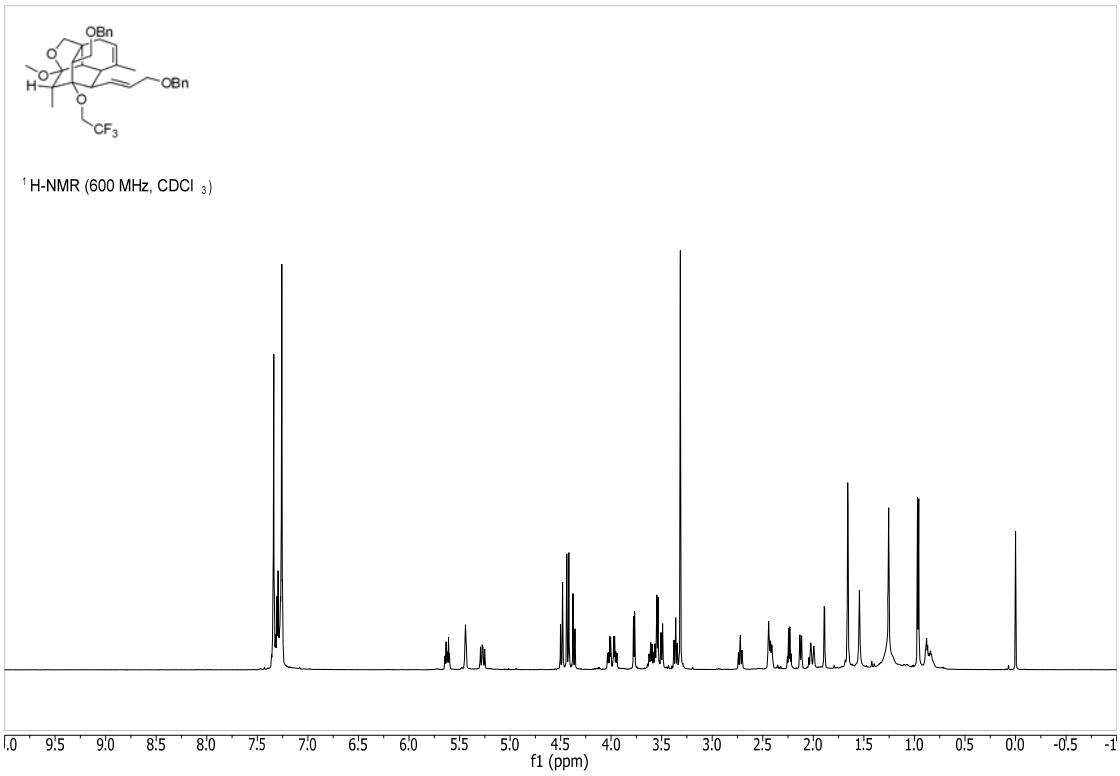


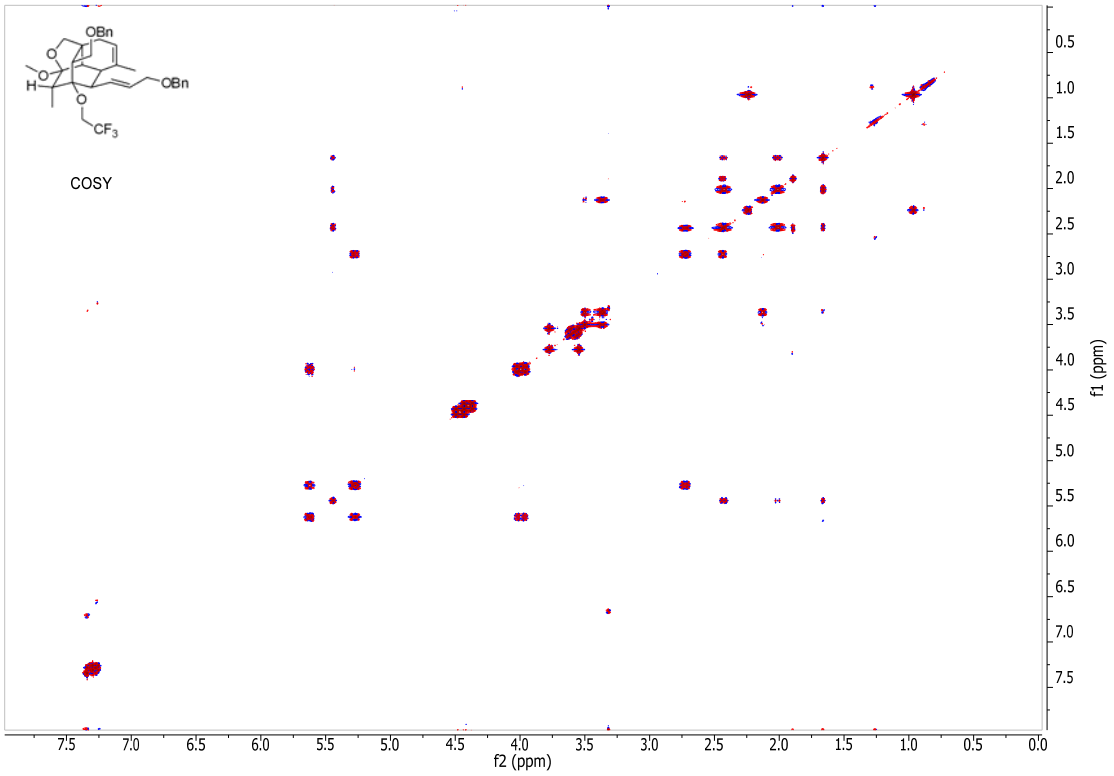


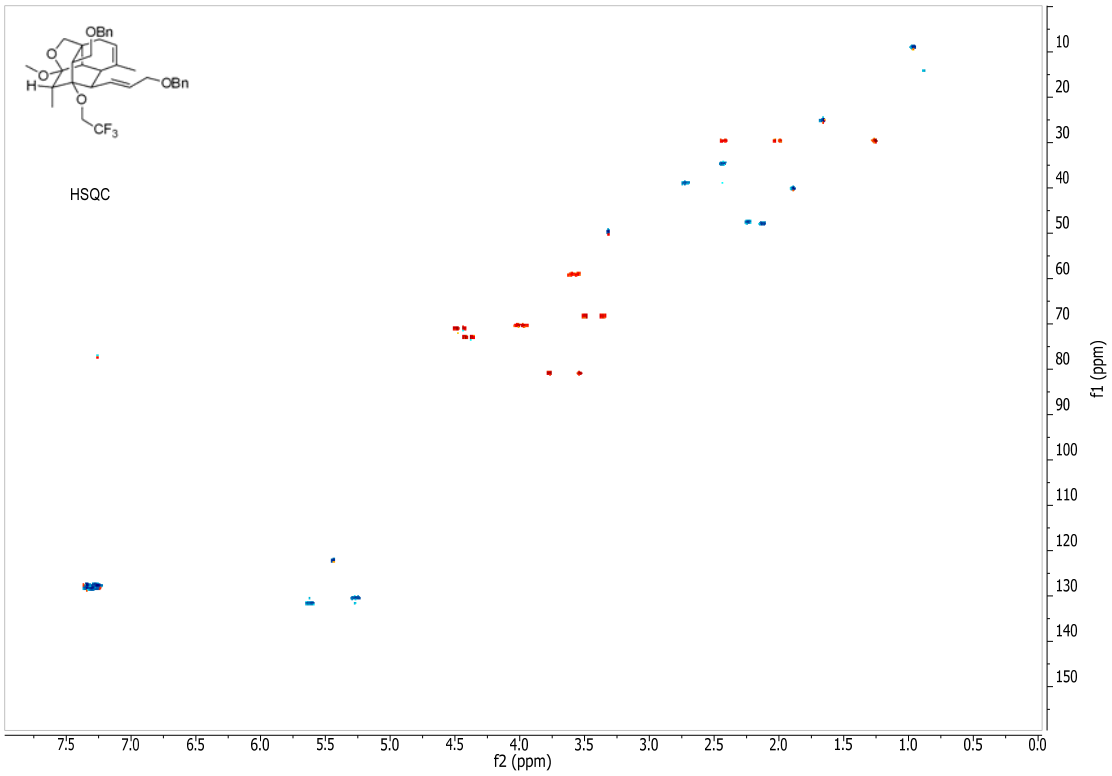


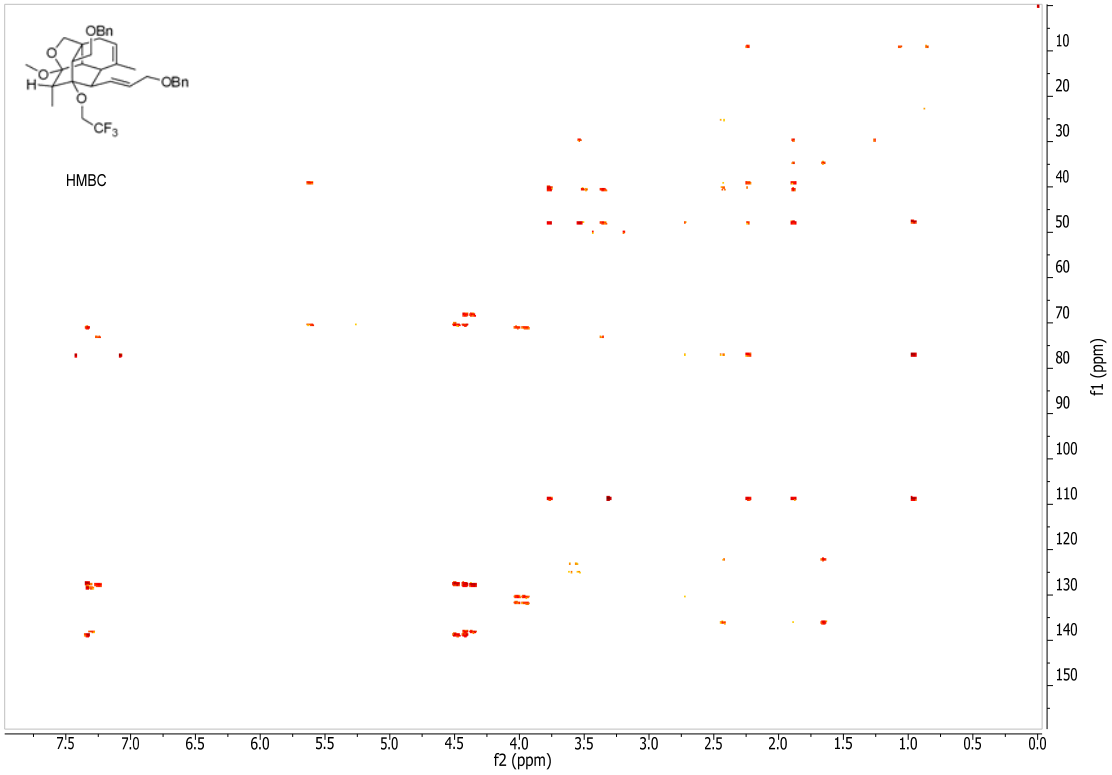












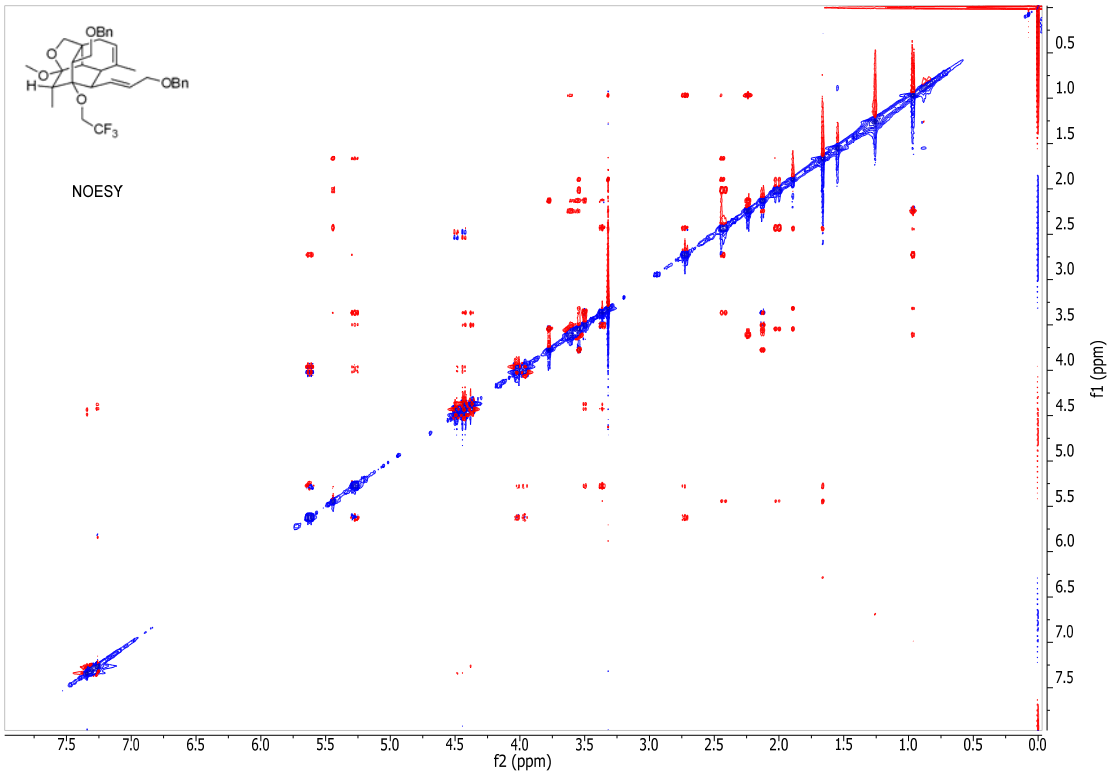
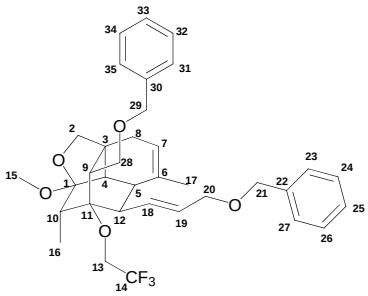
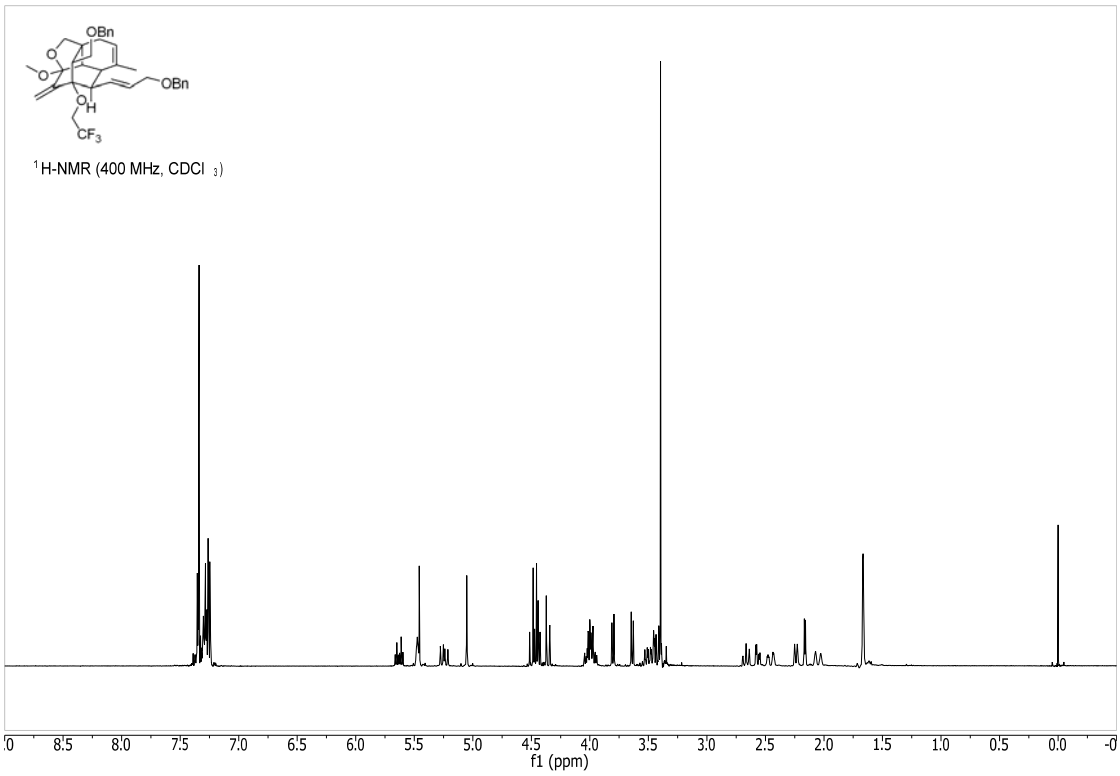


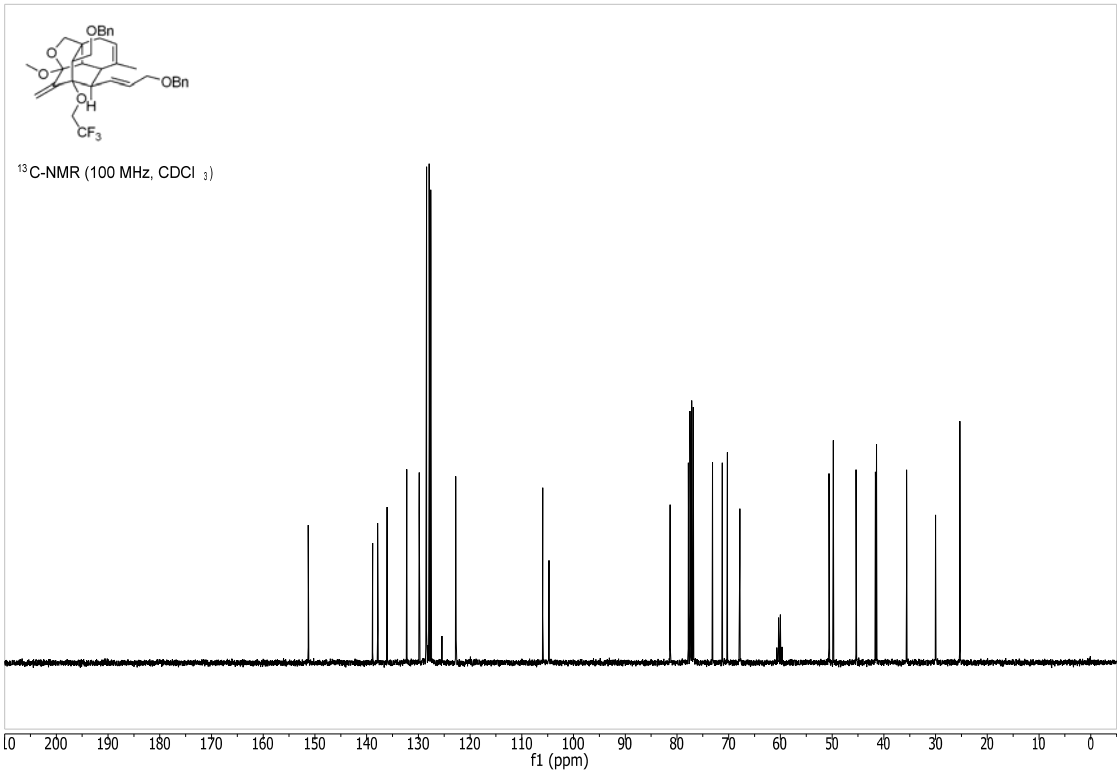
Table 7. 2D-NMR Data of Compound **88**

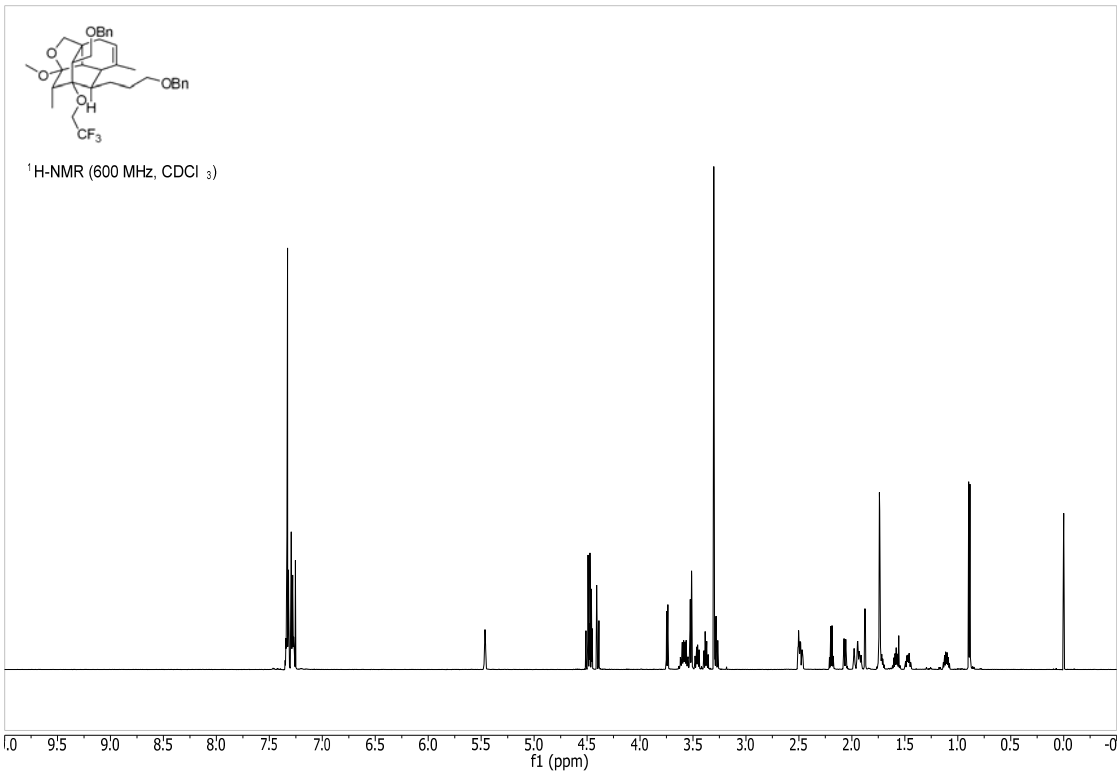


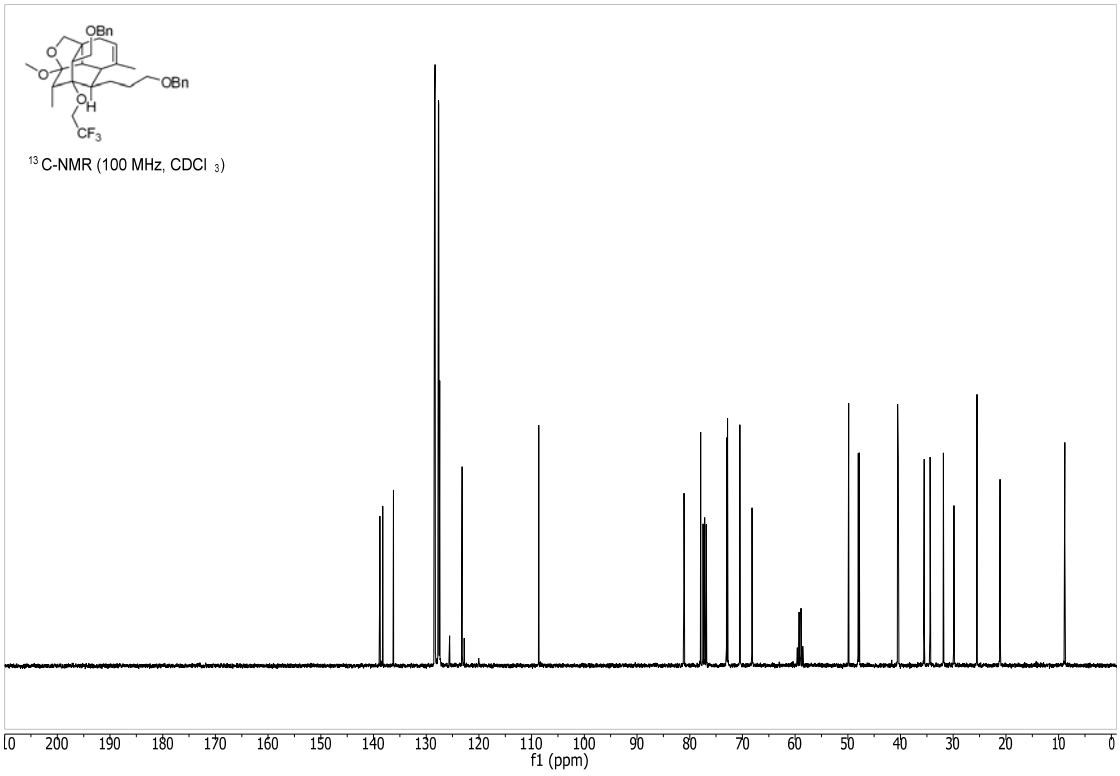
Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations	NOESY correlations
1	108.77		Cq			
2a	81.06	3.54	CH_2	H-2b	C-9, C-3, C-8	H-15, H-81, H-4
2b		3.77		H-2a	C-1, C-9, C-3	H-8b, H-10, H-9
3	39.00		Cq			
4	40.14	1.88	CH	H-5	C-1, C-2, C-11, C-10, C-4, C-3, C-5, C-8	H-2a, H-15, H-5
5	34.78	2.42	CH	H-7, H-12, H-8a, H-17		H-17, H-4
6	136.05		Cq			
7	122.26	5.44	CH	H-8b, H-8a, H-17		H-28a, H-8b, H-8a, H-17

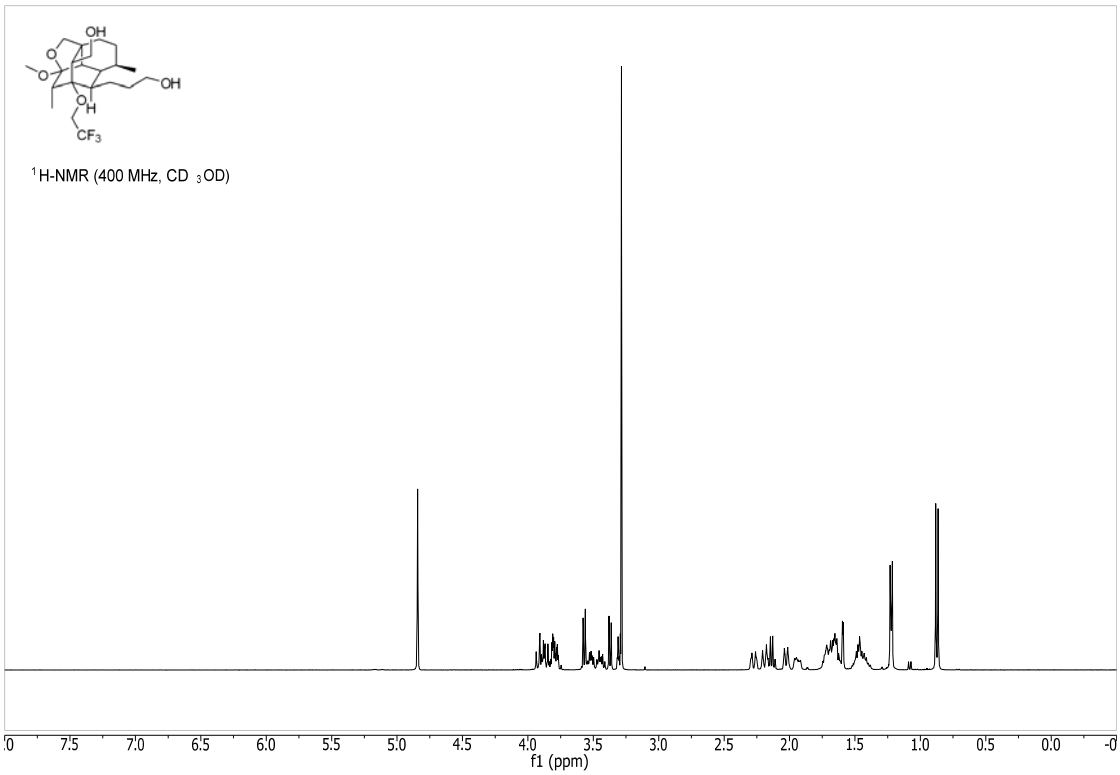
8a	29.77	2.01	CH_2	H-7, H-5, H-17		H-7, H-2a
8b		2.43			C-6, C-7, C-11, C-4, C-3, C-17	H-7, H-28a
9	47.97	2.12	CH	H-28a, H-28b, H-12	C-2, C-11, C-10, C-4, C-3	H-2b
10	47.66	2.24	CH	H-16	C-1, C-11, C-9, C-4, C-3, C-16	H-13b, H-9, H-16
11	77.01		Cq			
12	38.97	2.72	CH	H-18, H-5, H-9	C-6, C-19, C-18, C-11, C-10, C-5	H-19, H-18, H-5, H-16
13a	59.23	3.55	CH_2		C-14	H-10
13b		3.61			C-14	H-10, H-16
14	124.03		Cq			
15	49.87	3.32	CH_3		C-1	H-4, H-16
16	9.07	0.96	CH_3	H-10	C-1, C-11, C-10	H-13b, H-15, H-12,H- 5, H-10
17	25.26	1.66	CH_3	H-7, H-5, H-8a	C-6, C-7, C-5	H-7, H-18, H-5
18	130.47	5.27	CH	H-19, H-20a, H-20b, H-12	C-20, C-12, C-5	H-20a, H-20b, H-28b, H-28a, H-12, H-17
19	131.73	5.62	CH	H-18, H-20a, H-20b, H-12	C-20, C-12	H-12
20a	70.42	3.96	CH_2	H-19, H-18	C-19, C-18, C-21	H-18, H-19
20b		4.02		H-19. H-18	C-19, C-18, C-21	H-18, H-19
21a	71.08	4.42	CH_2		C-22, C-23, C-27, C-20	H-23, H-27, H-20a, H-20b
21b		4.49			C-22, C-23, C-27, C-20	H-23, H-27, H-20a, H-20b
22	138.94		Cq			
23	127.50	7.34	CH			
24	128.50		CH			
25	127.50		CH			
26	128.50		CH			
27	127.50	7.34	CH			
28a	68.32	3.36	CH_2	H-9, H-28b	C-29, C-9, C-3	H-18, H-29a, H-29b, H-9
28b		3.5		H-9, H-28a	C-11, C-29, C-9, C-3	H-18, H-29a, H-29b, H-9, H-8b
29a	73.11	4.37	CH_2		C-30, C-31, C-35, C-28	H-31, H-35, H-28a, H-28b
29b		4.44			C-30, C-31, C-35, C-28	H-31, H-35, H-28a, H-28b
30	138.07		Cq			
31	127.77	7.26	CH			
32	127.86		CH			
33	127.77		CH			
34	127.86		CH			
35	127.77	7.26	CH			

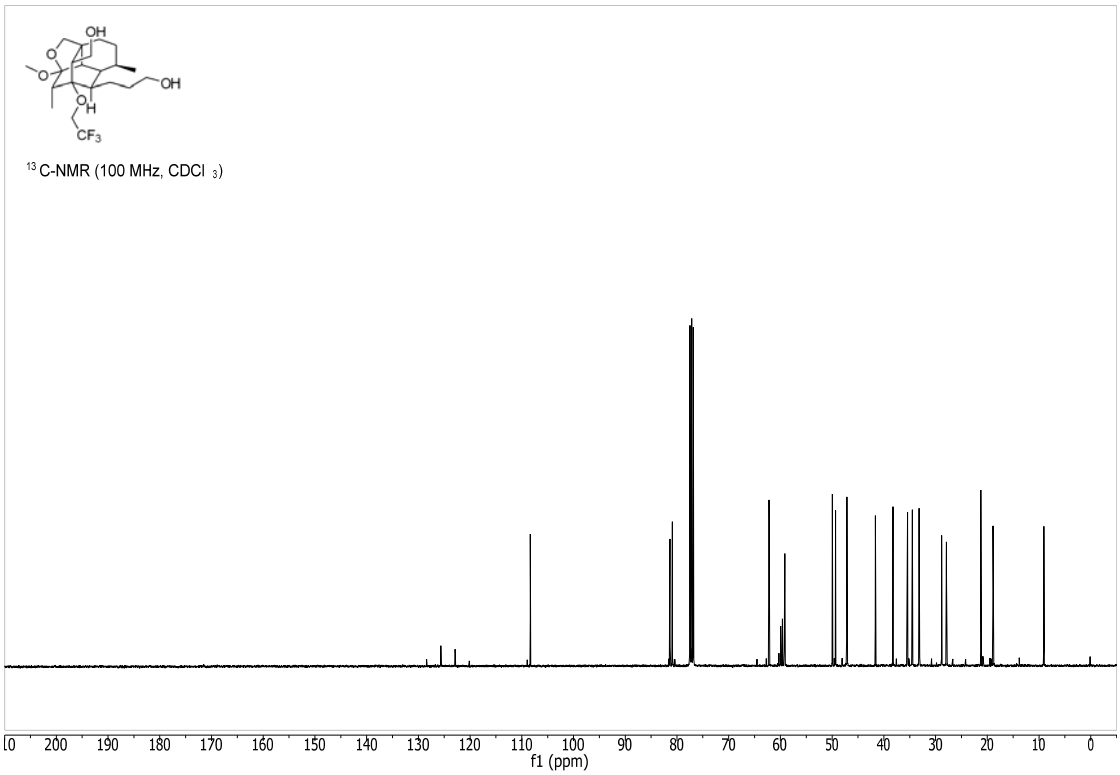


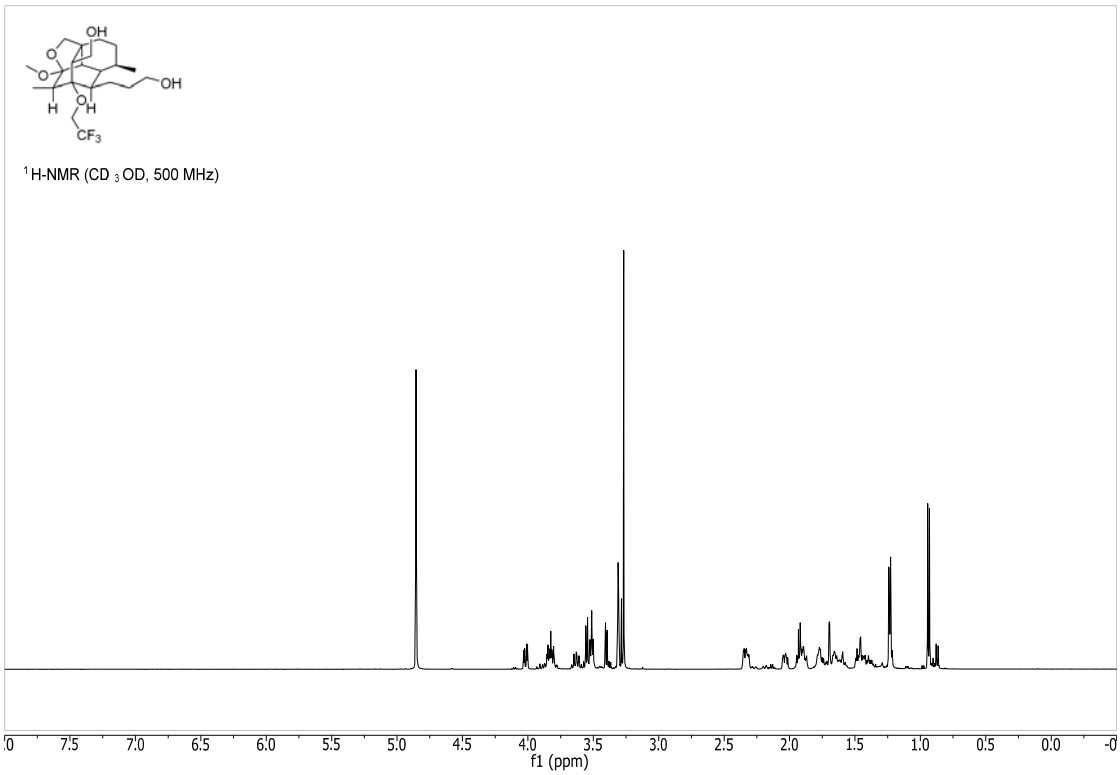


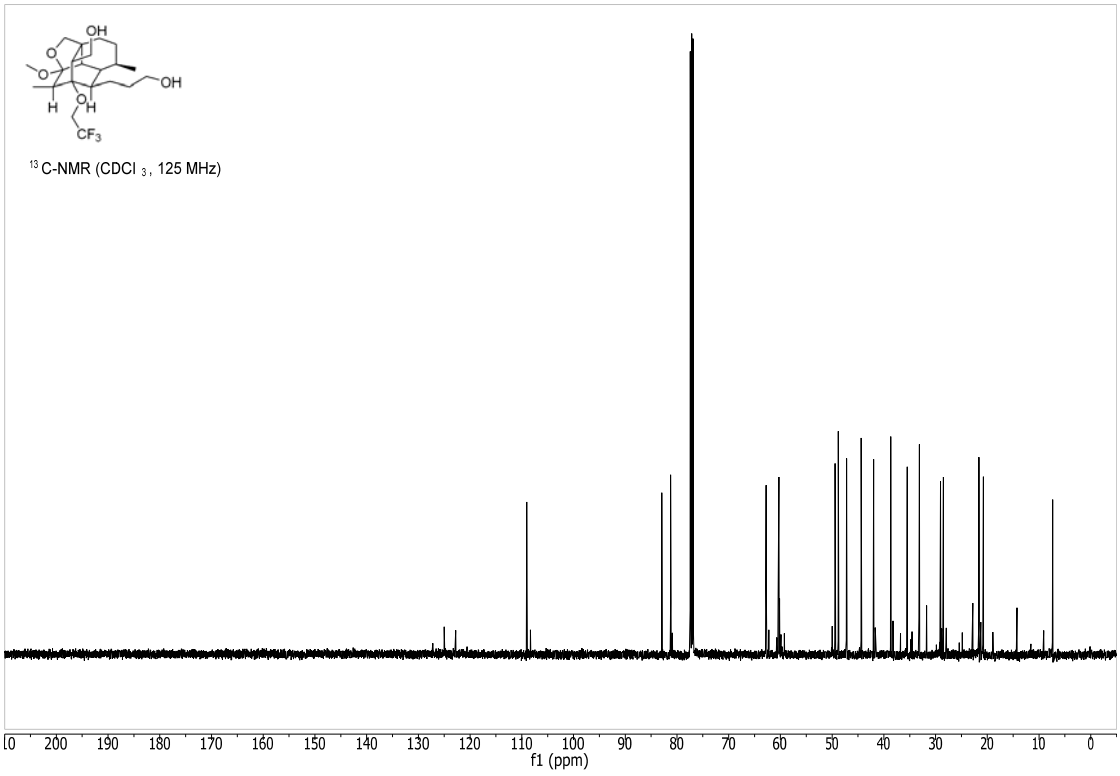


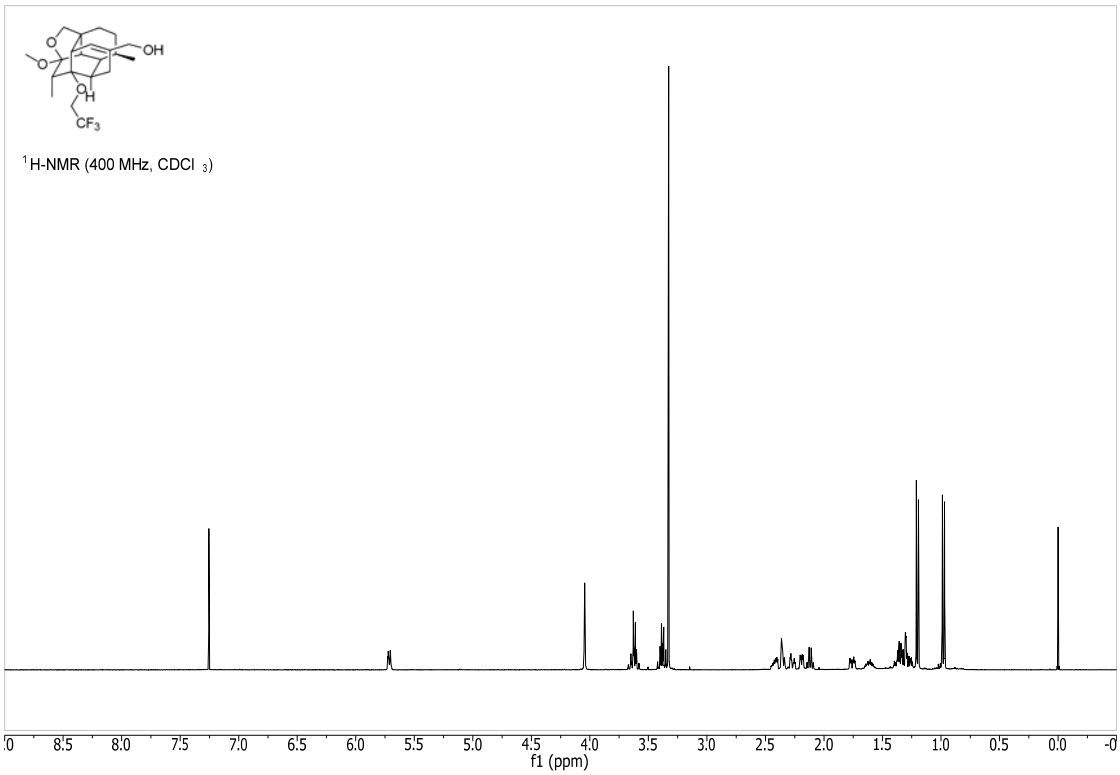


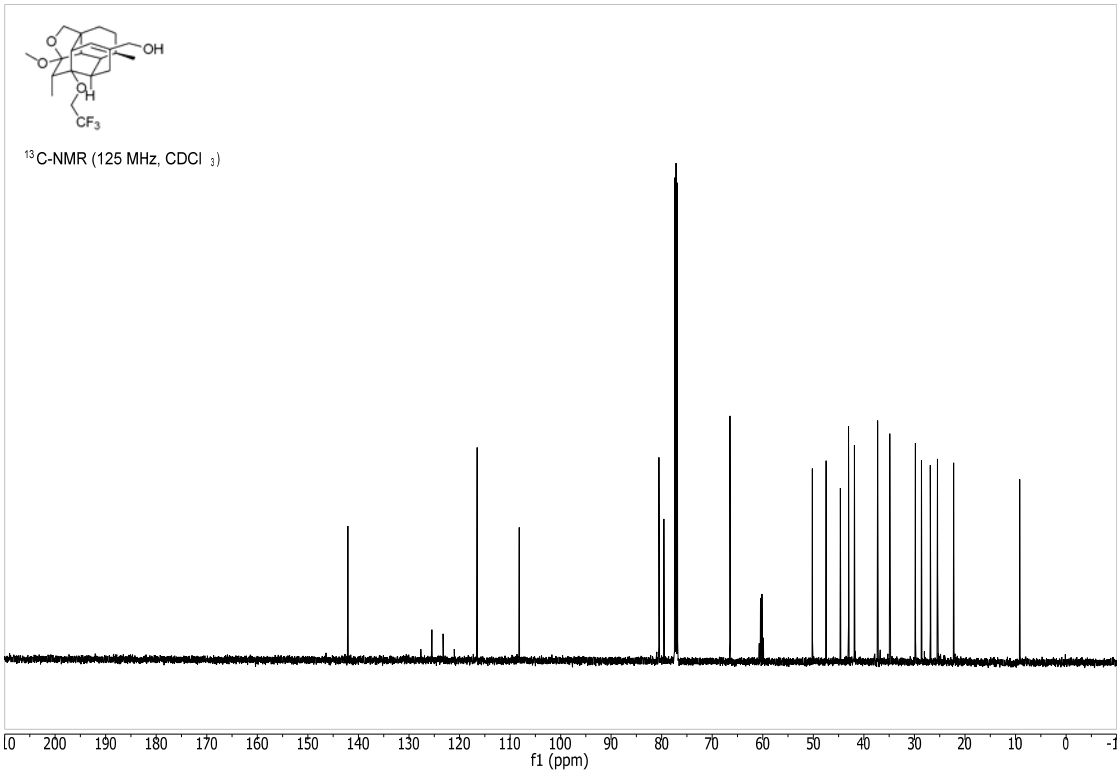


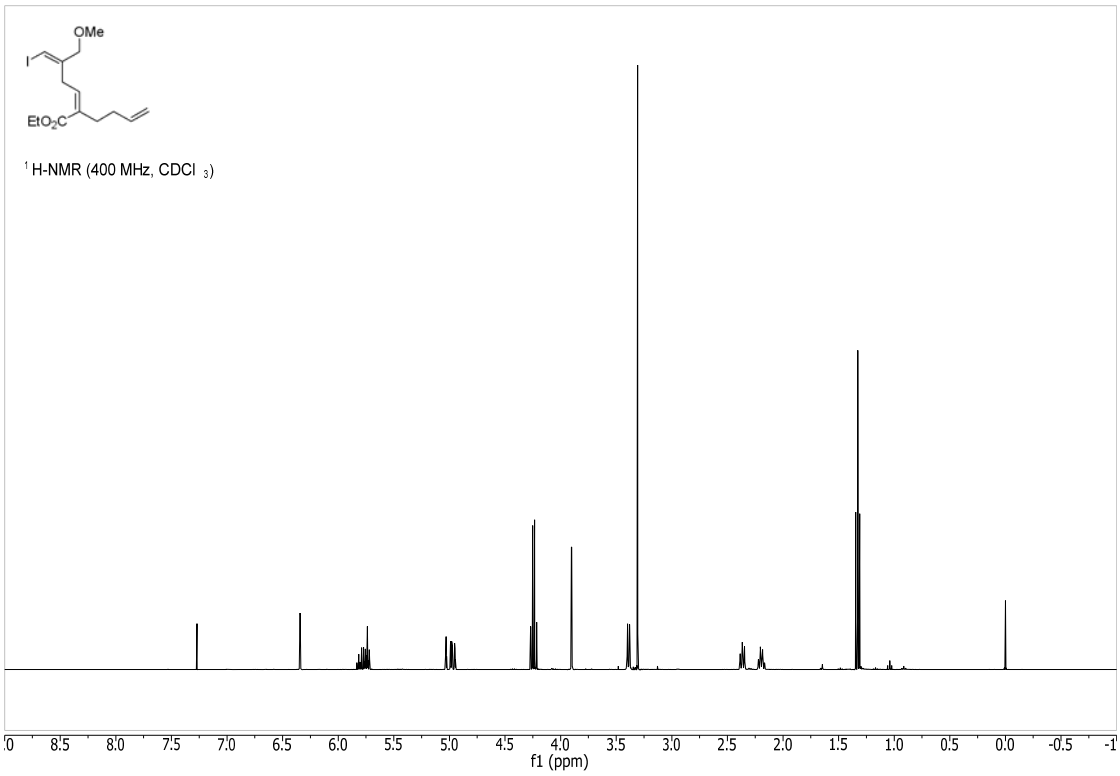


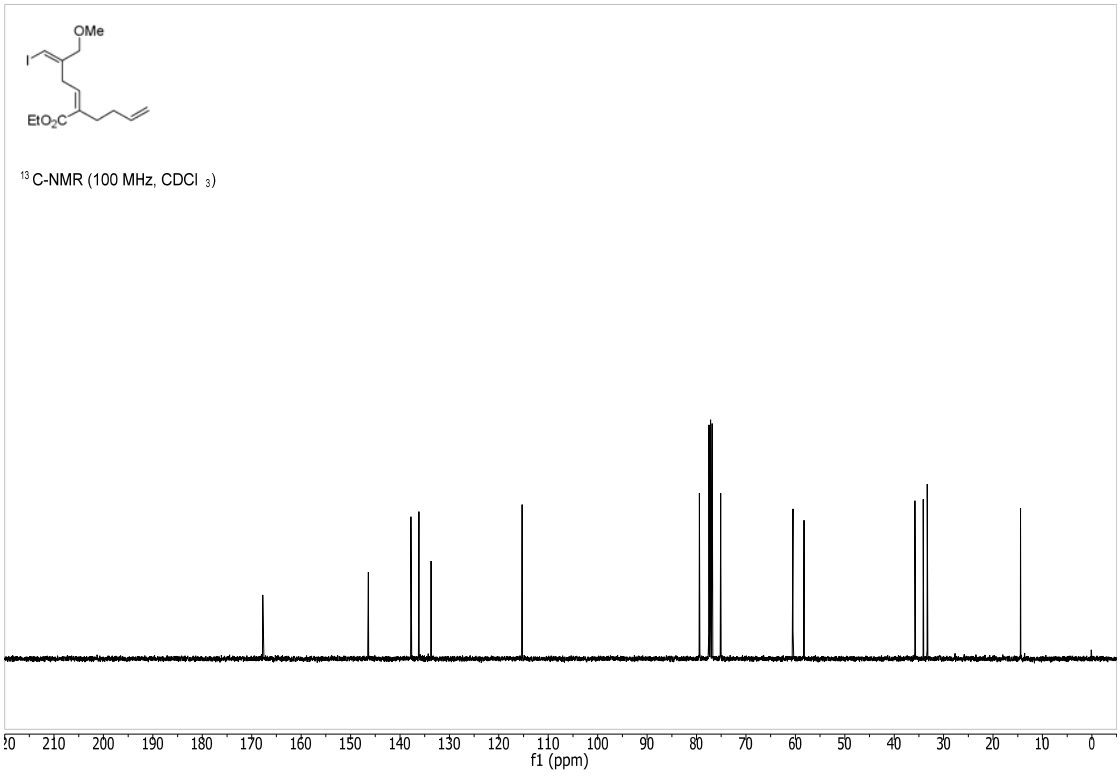


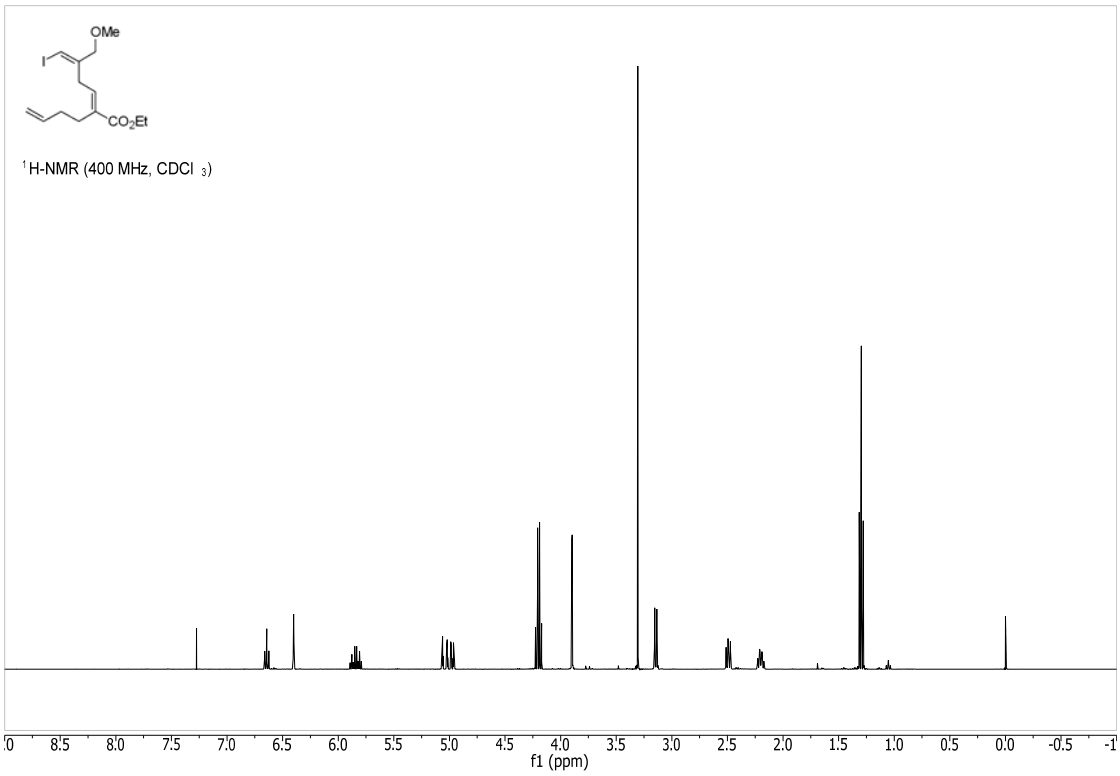


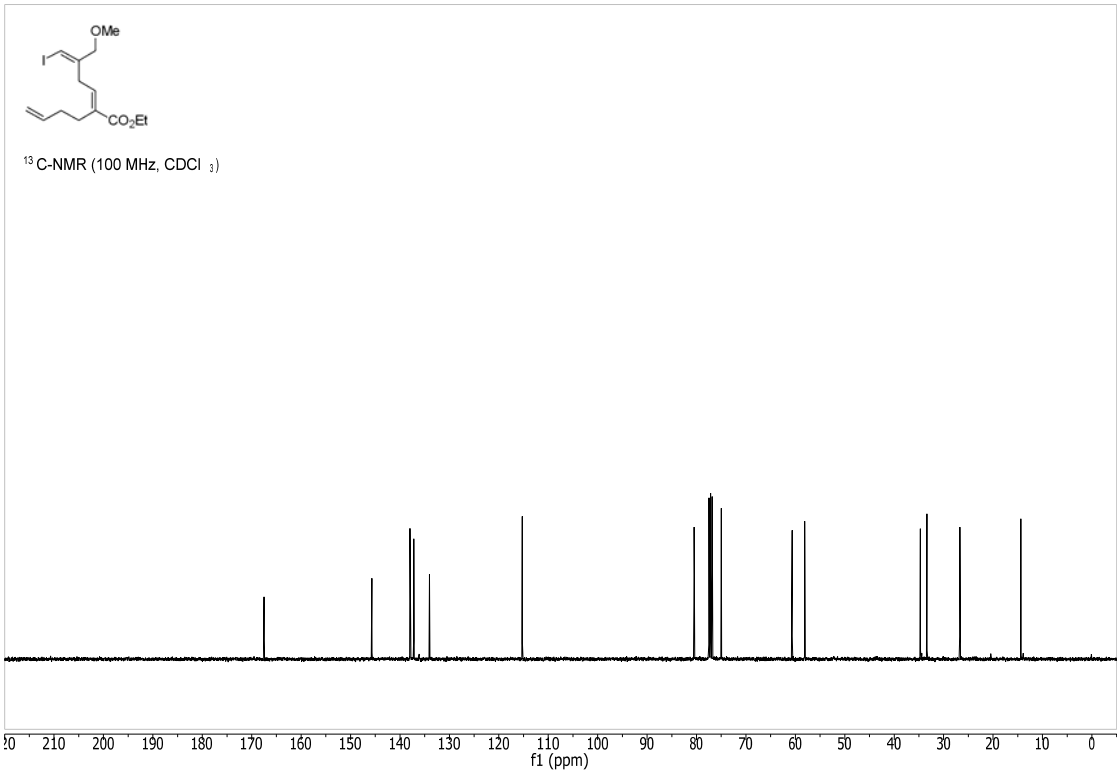


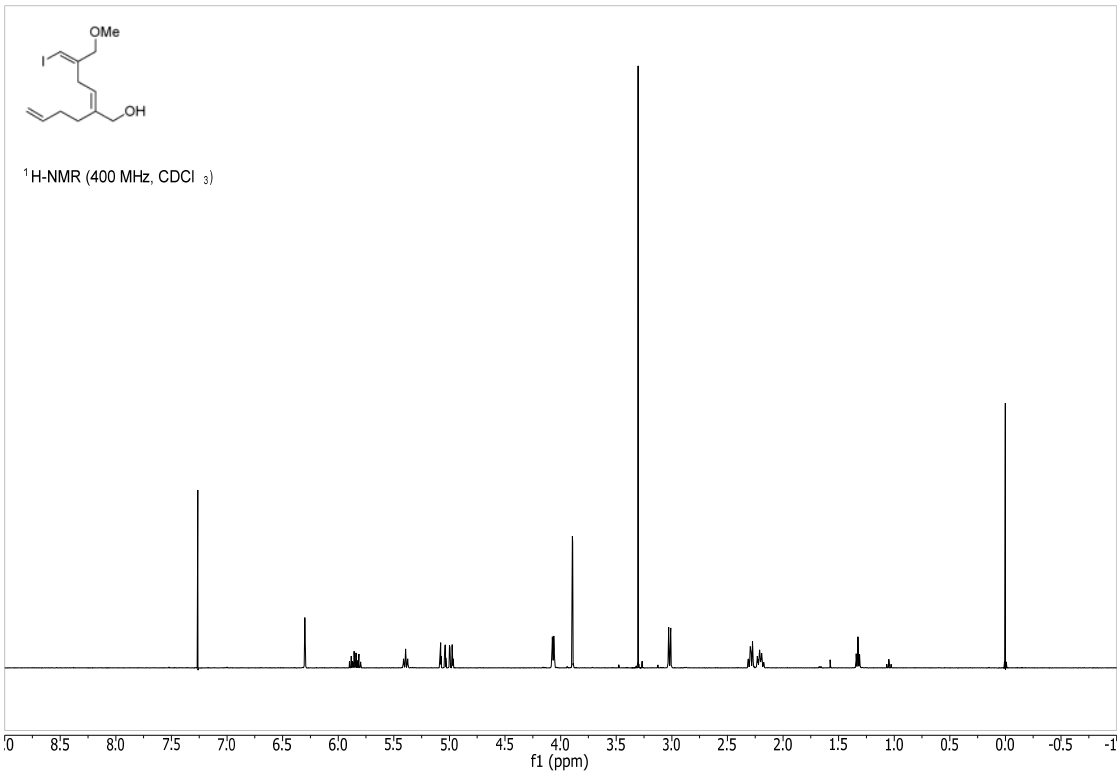


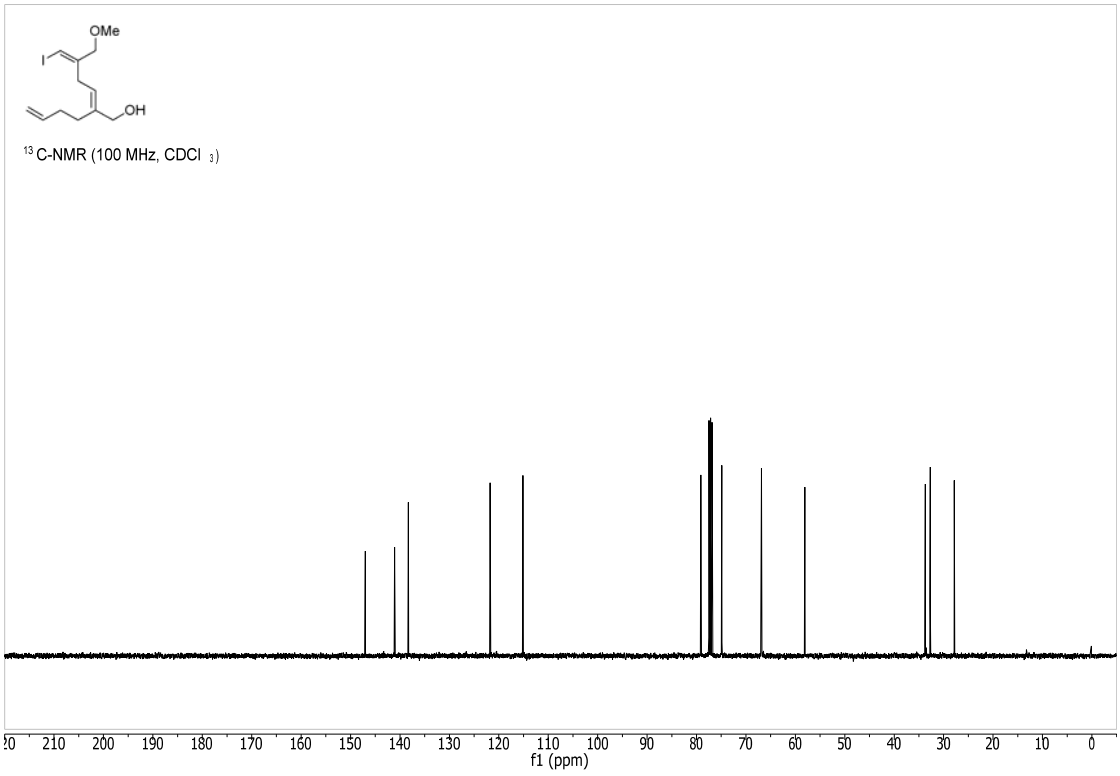


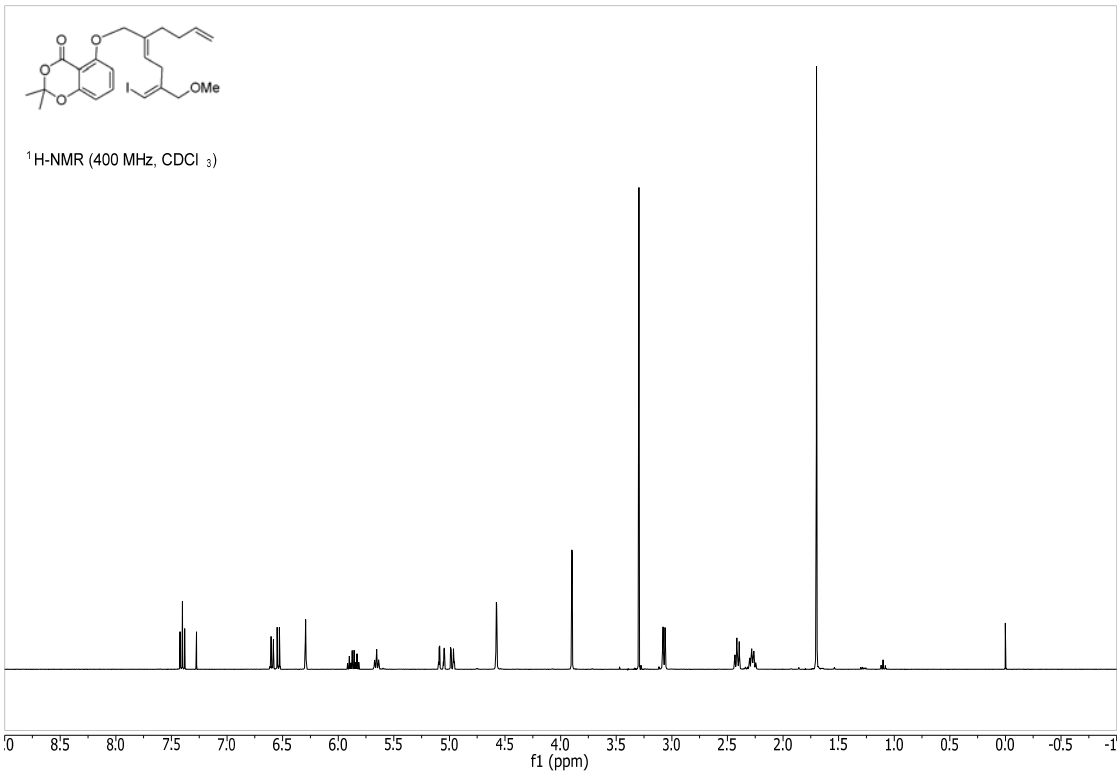


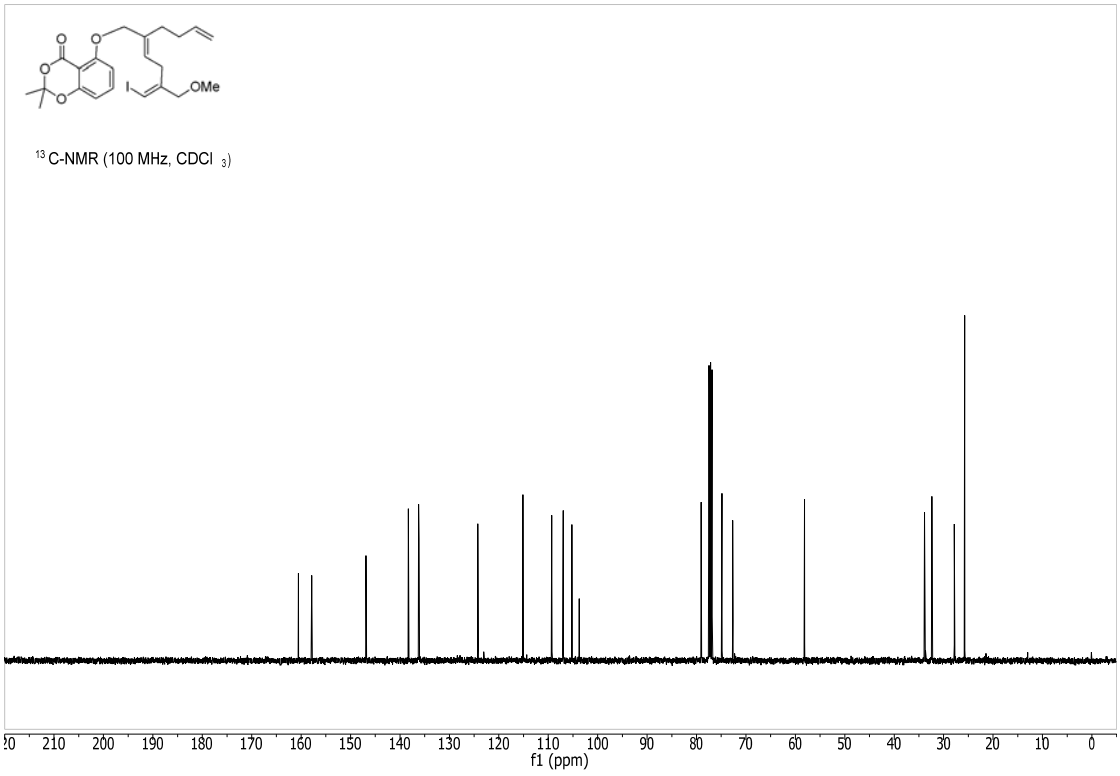


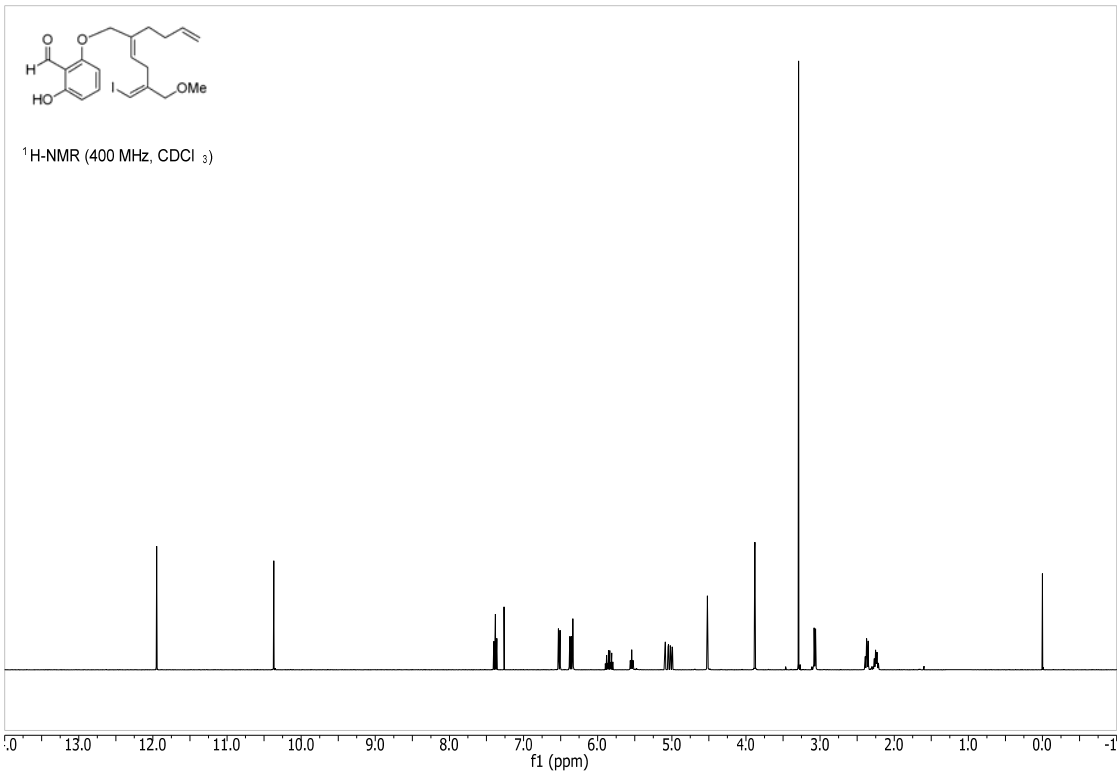


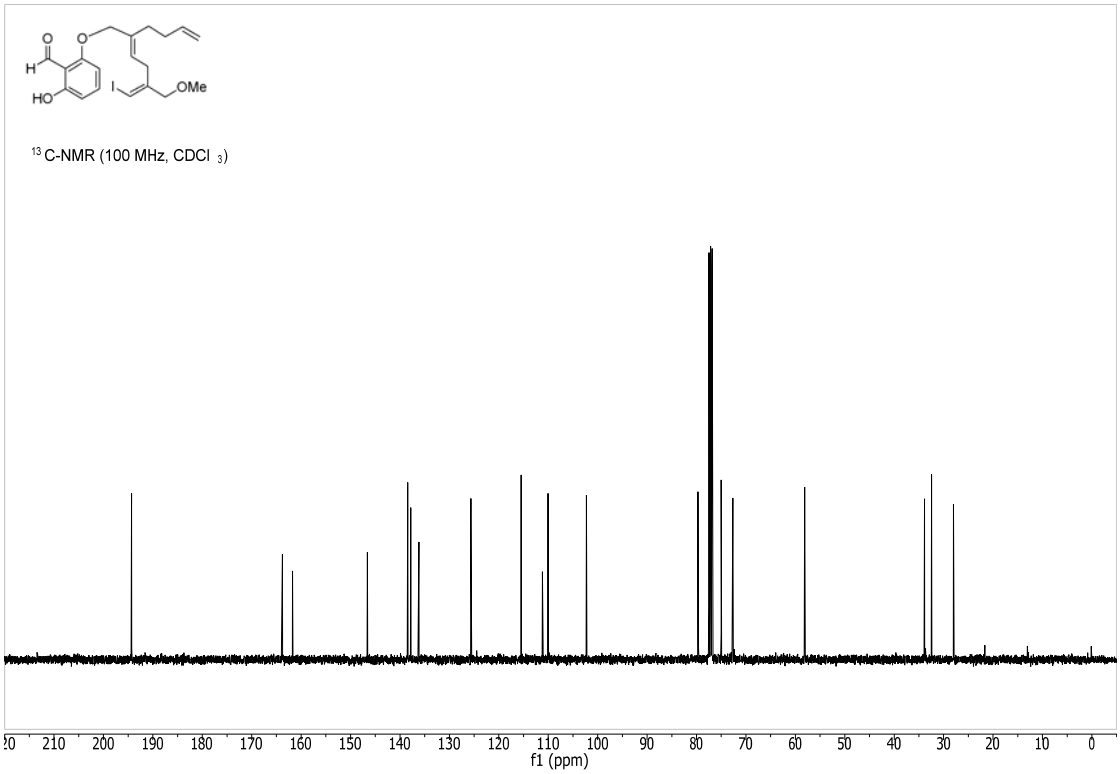


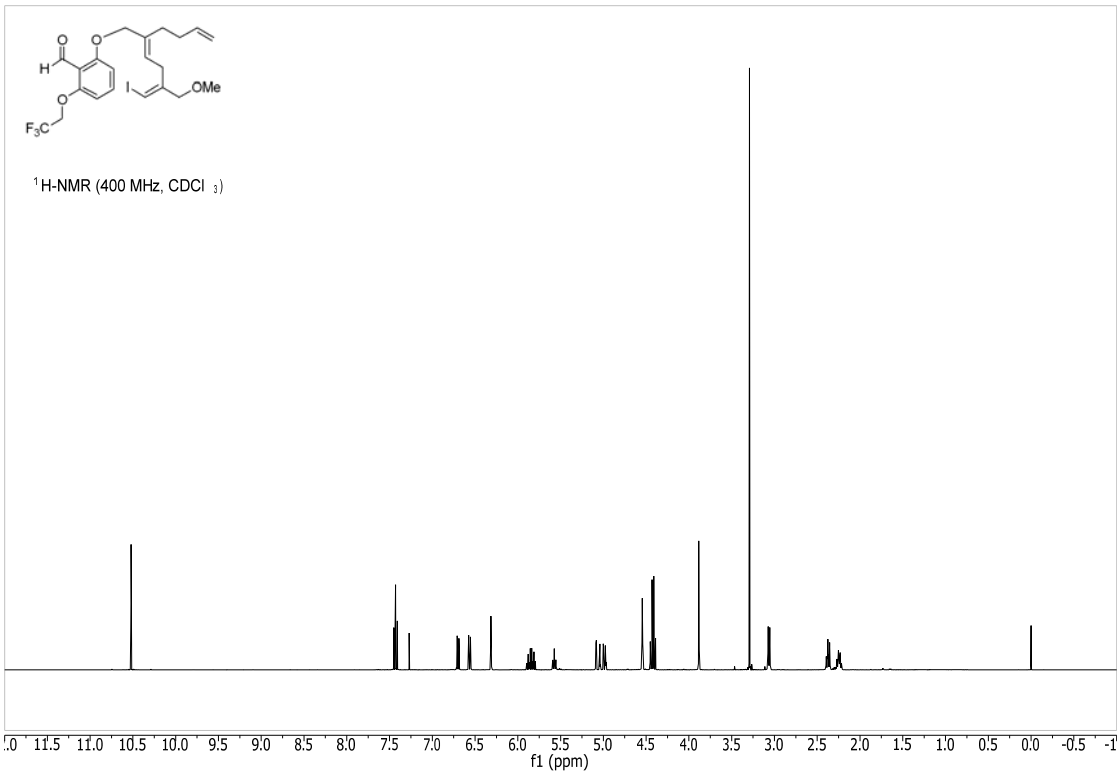


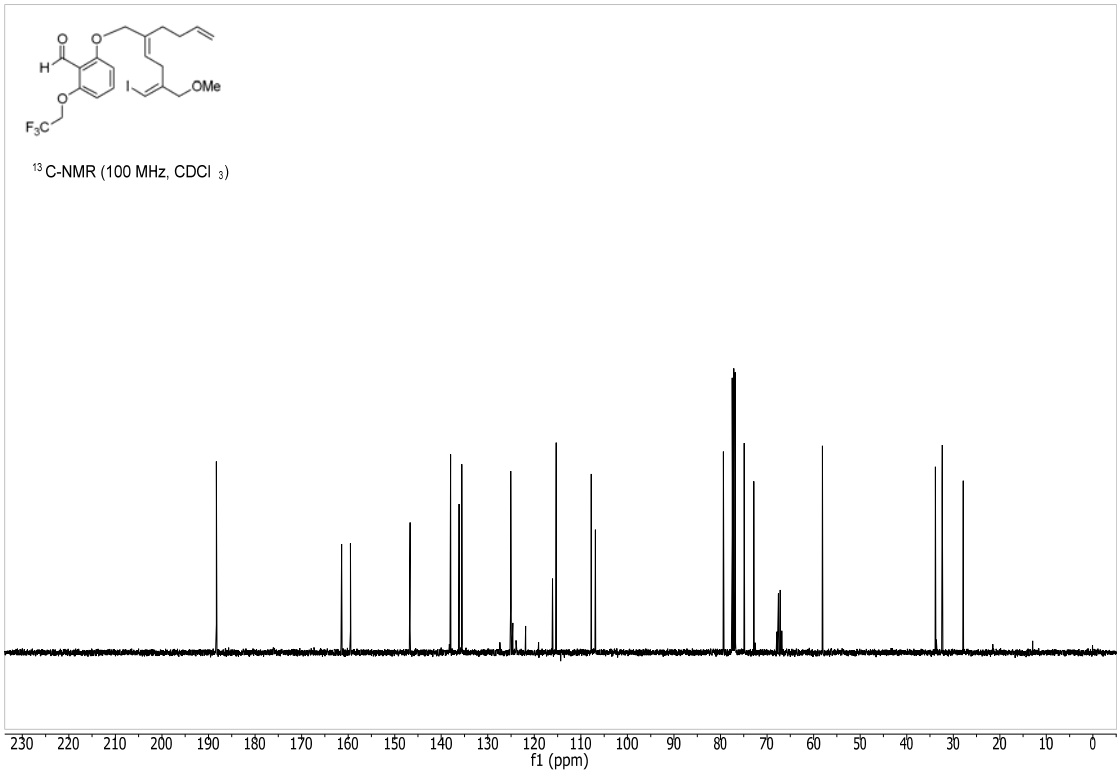


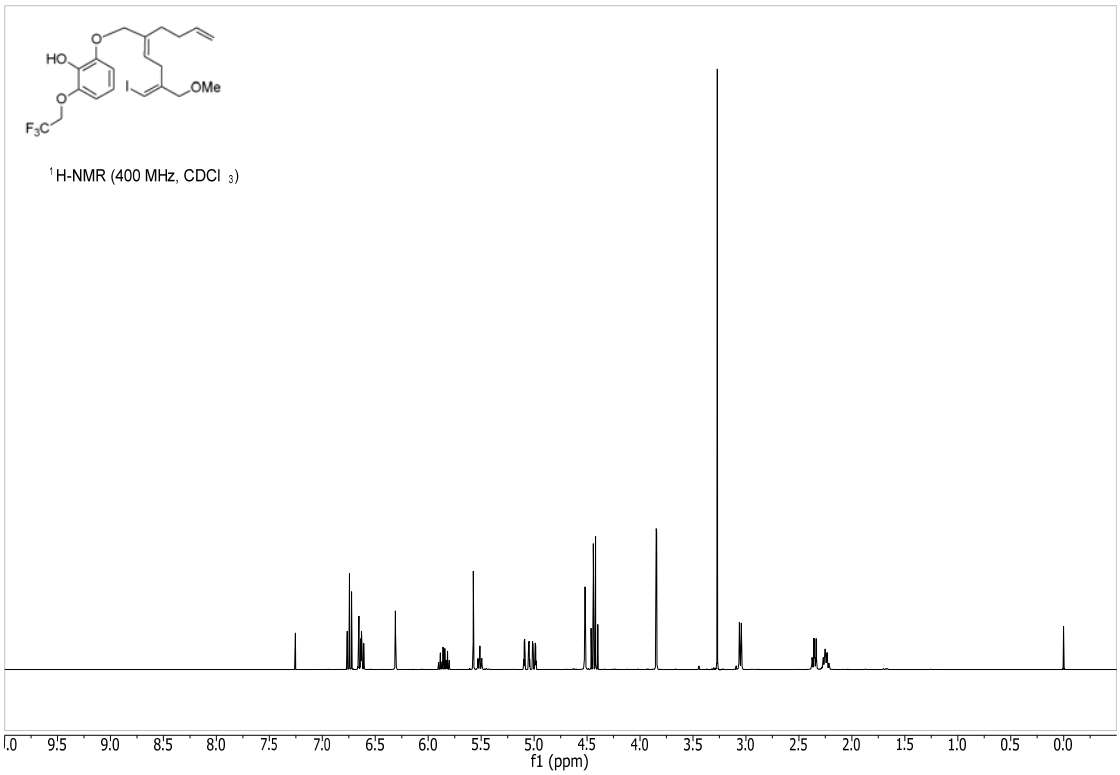


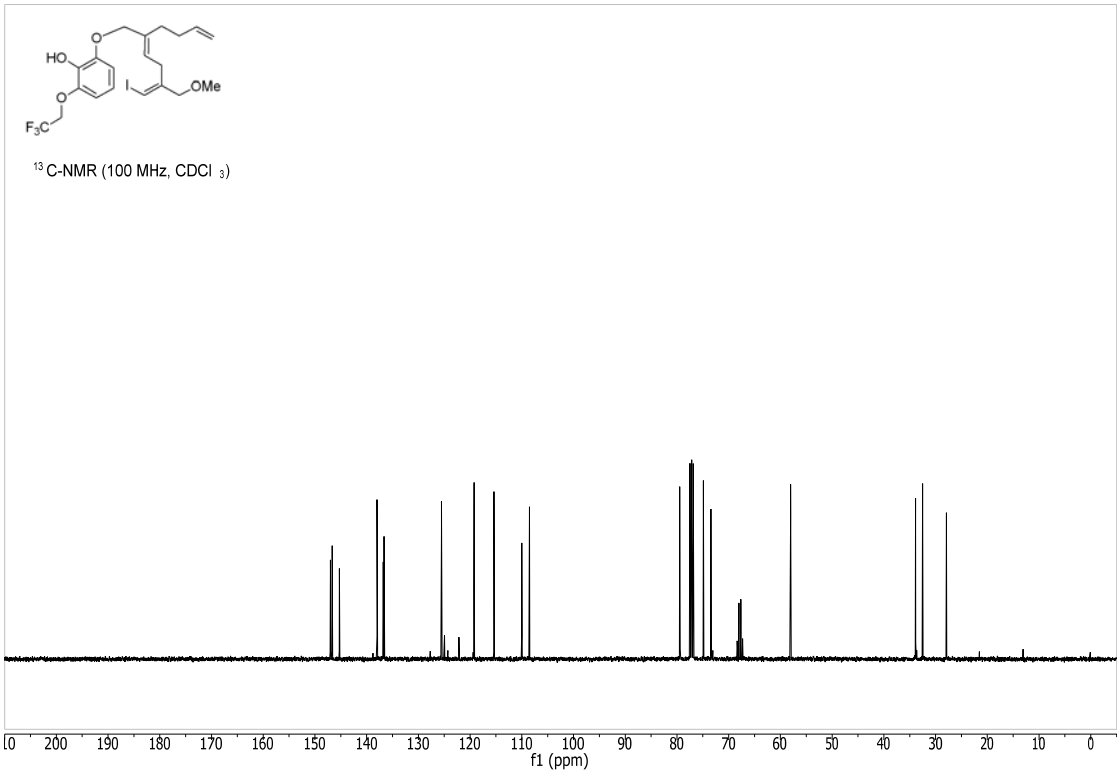


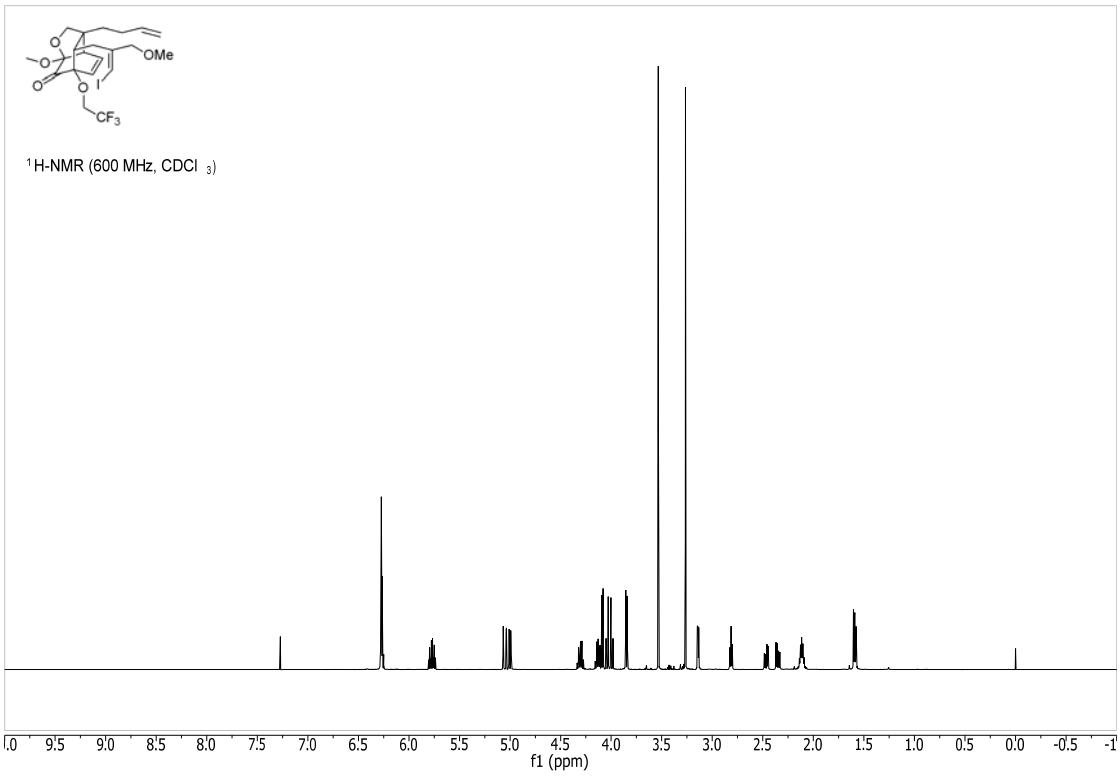


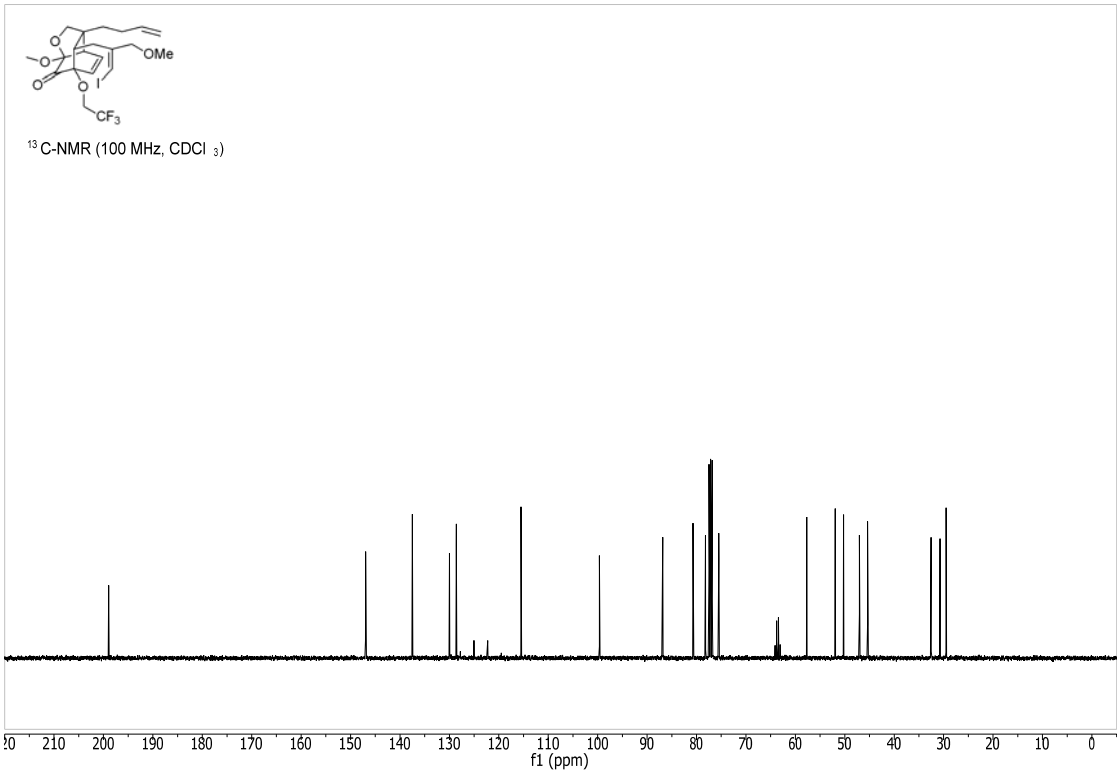


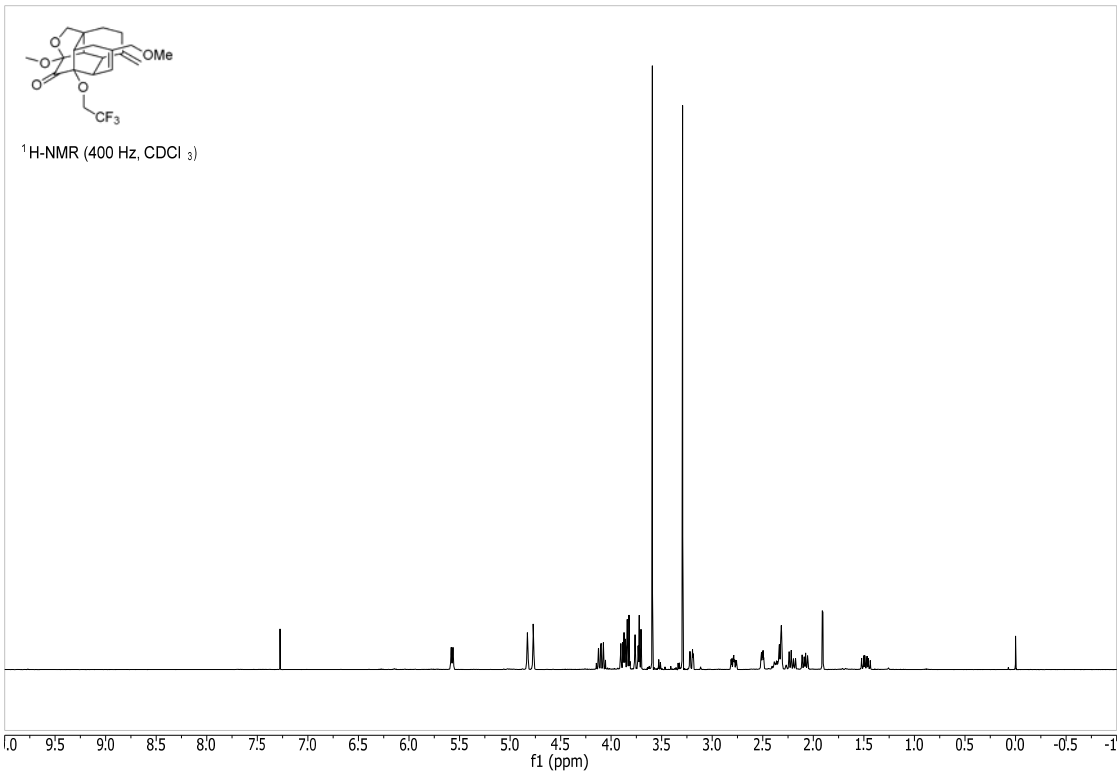


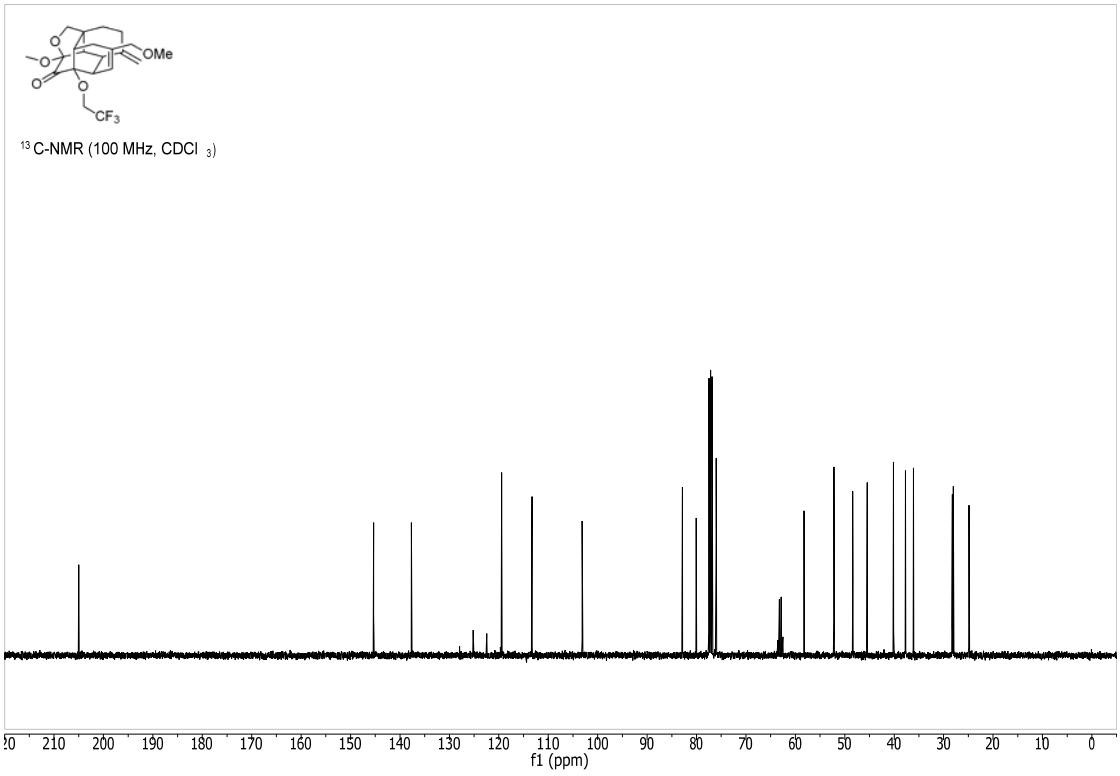


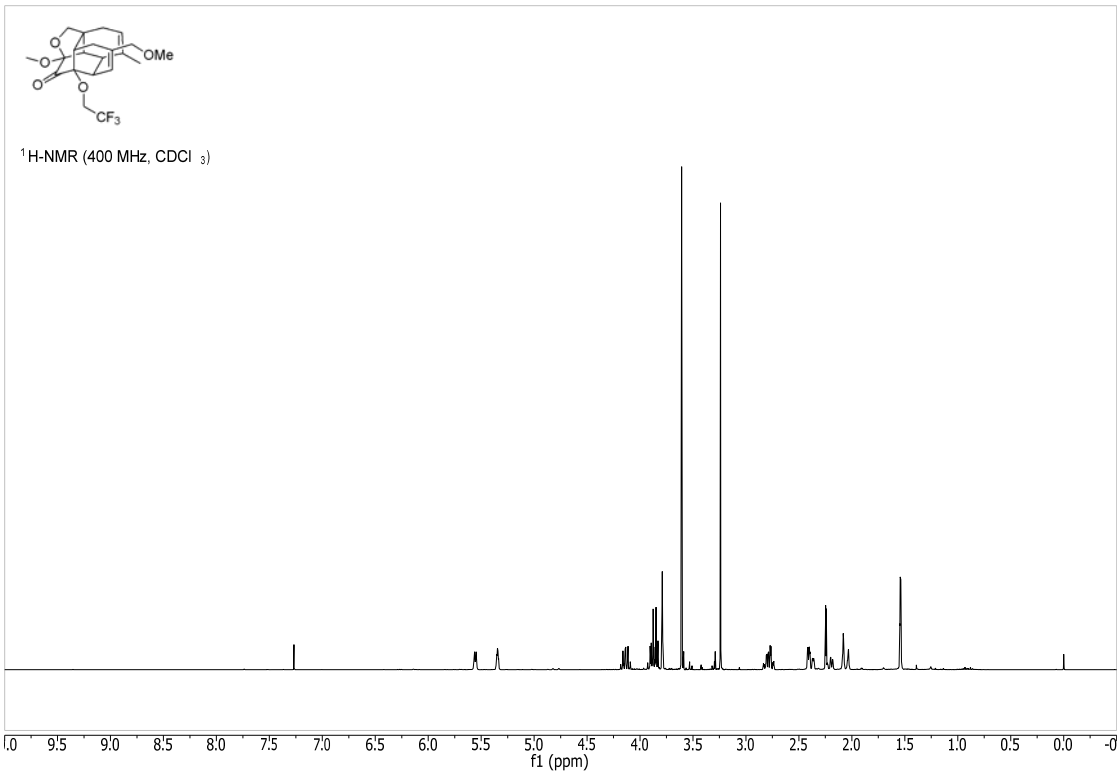








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CF3
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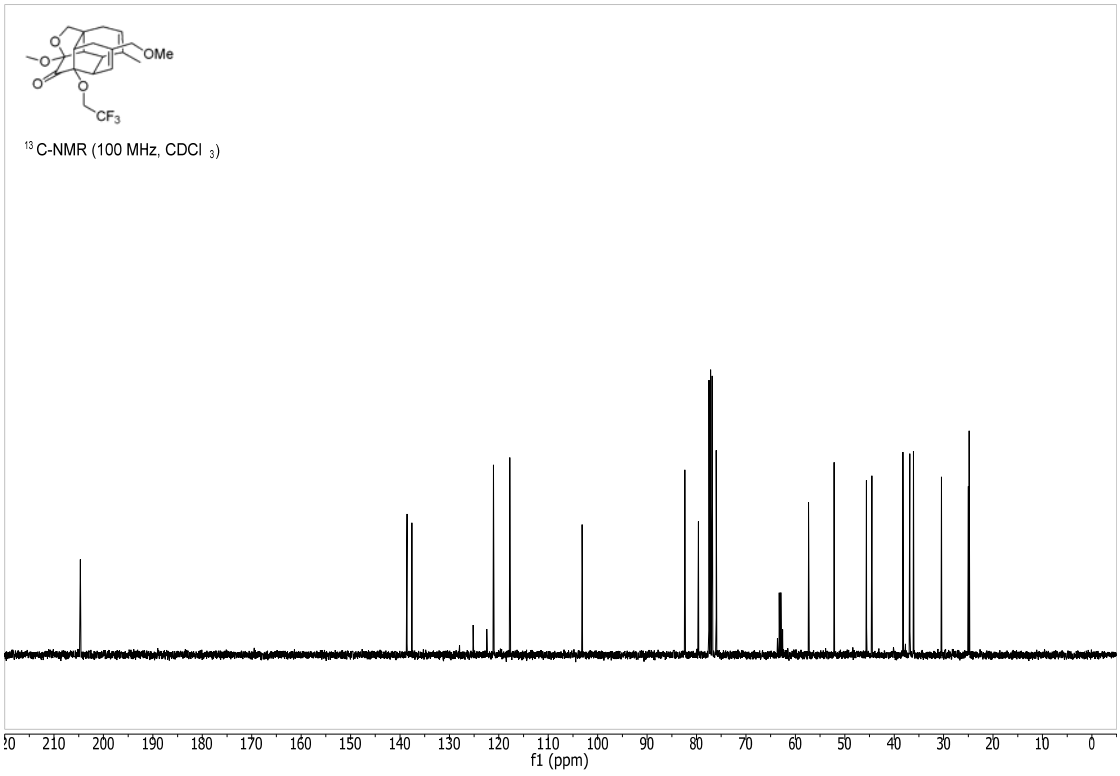
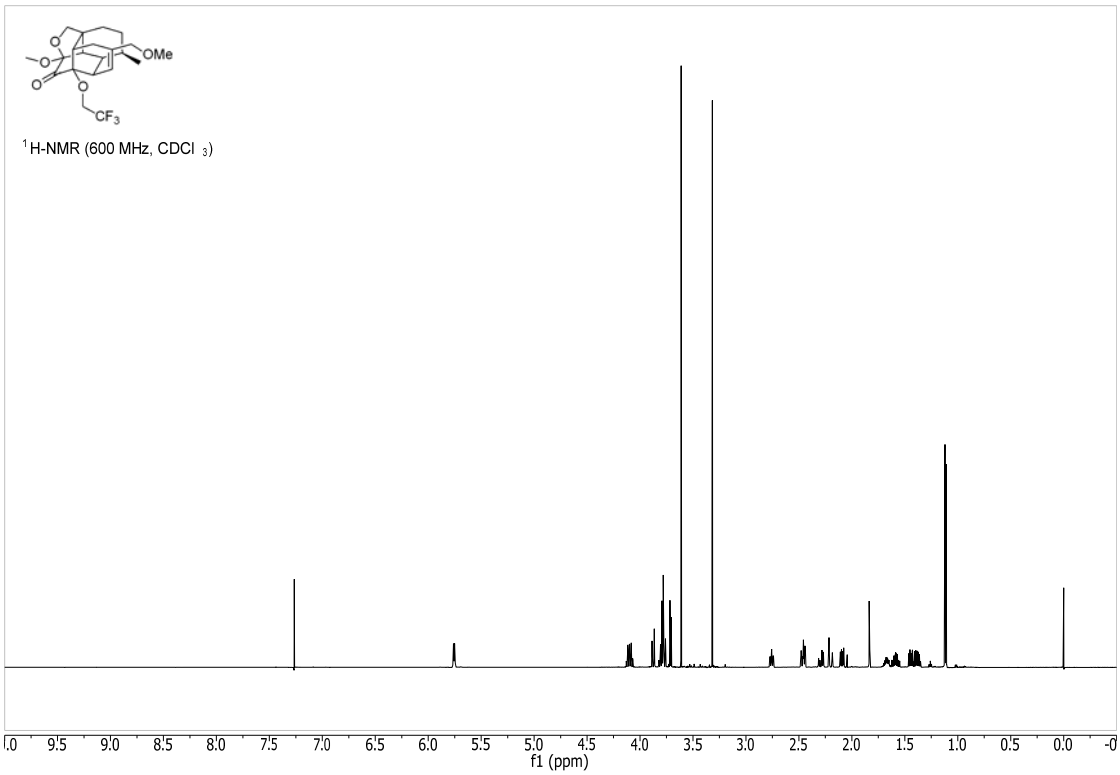
f1 (ppm)


OMe
CF3
13C-NMR (100 MHz, CDCl 3)
f1 (ppm)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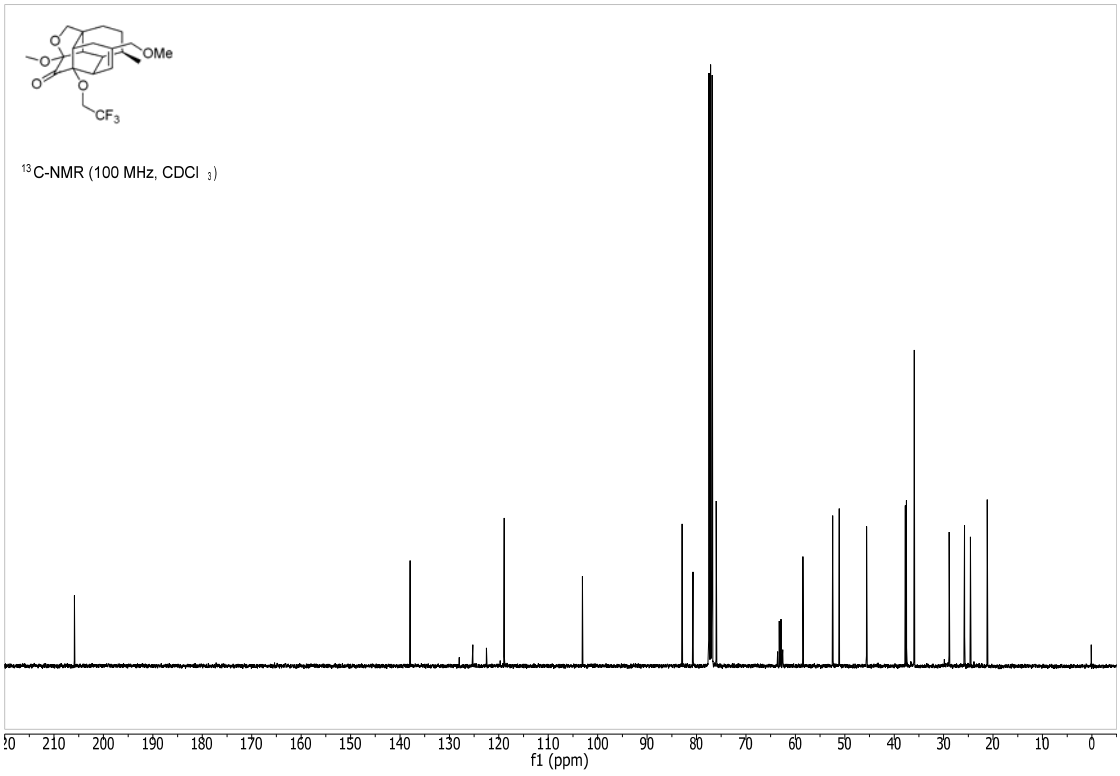
f1 (ppm)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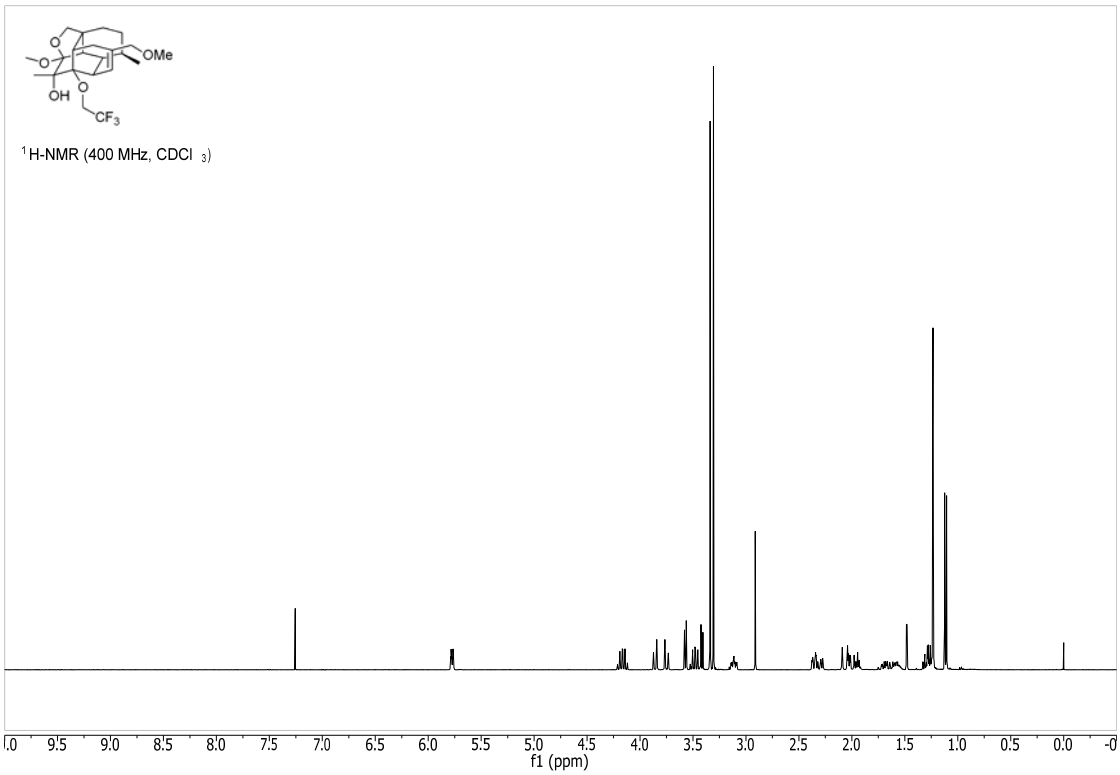
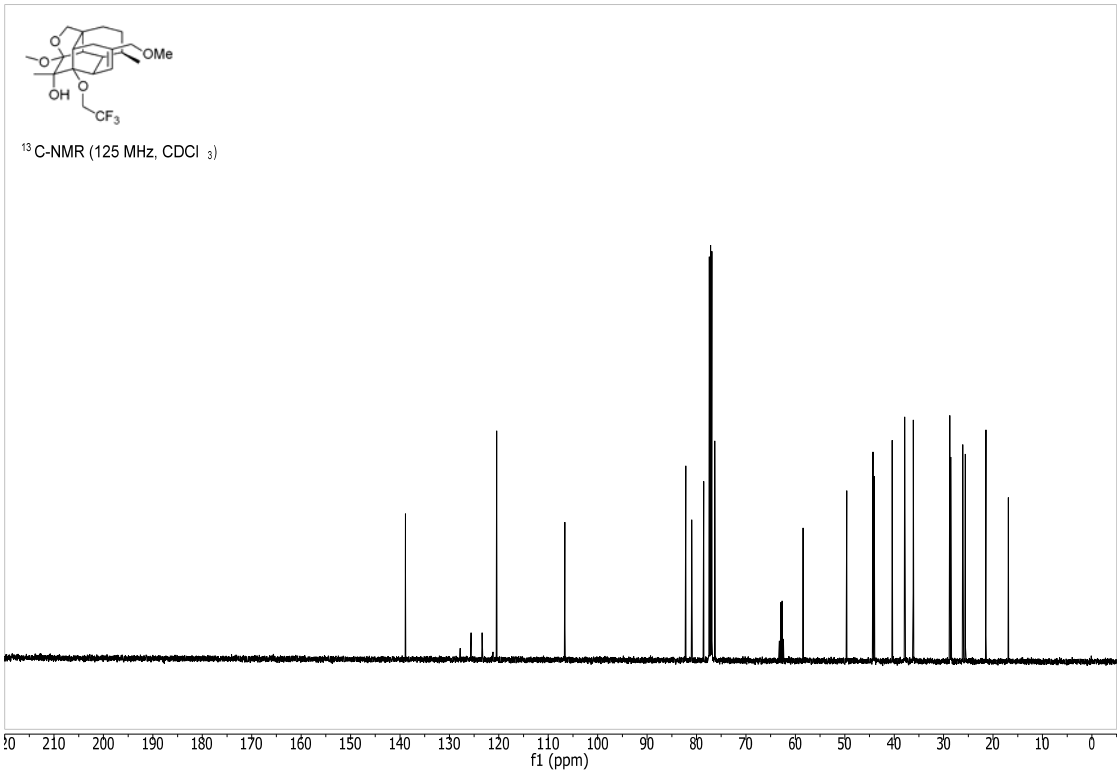
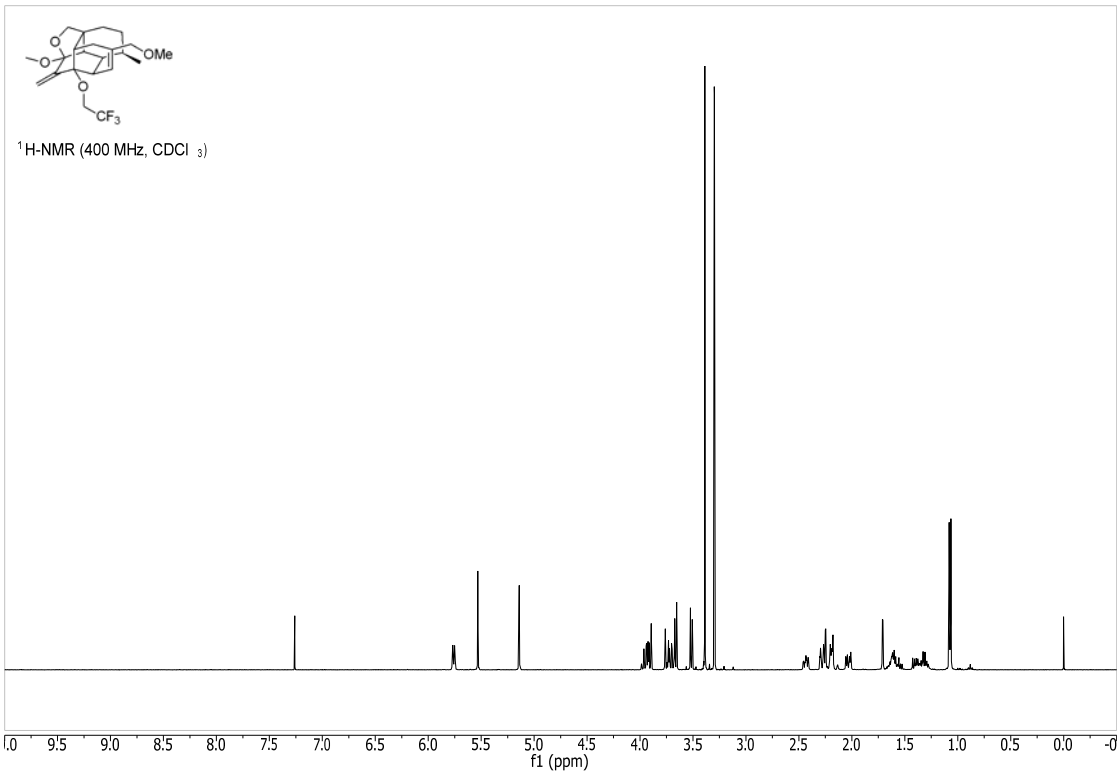
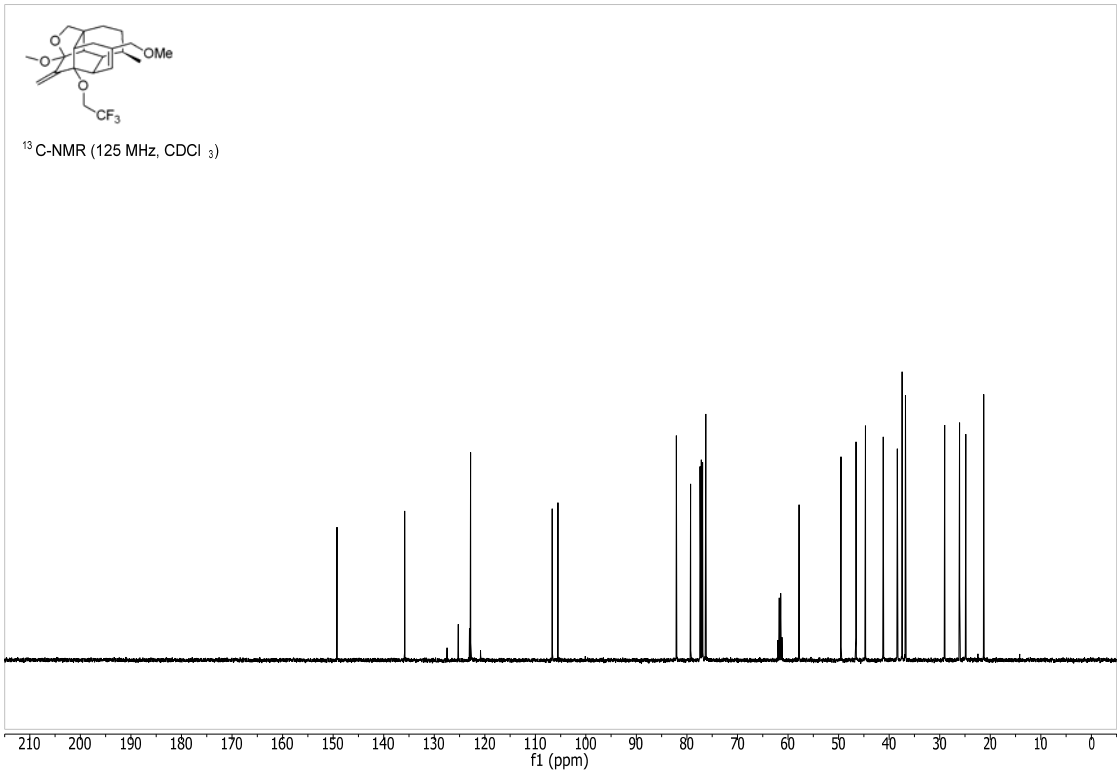
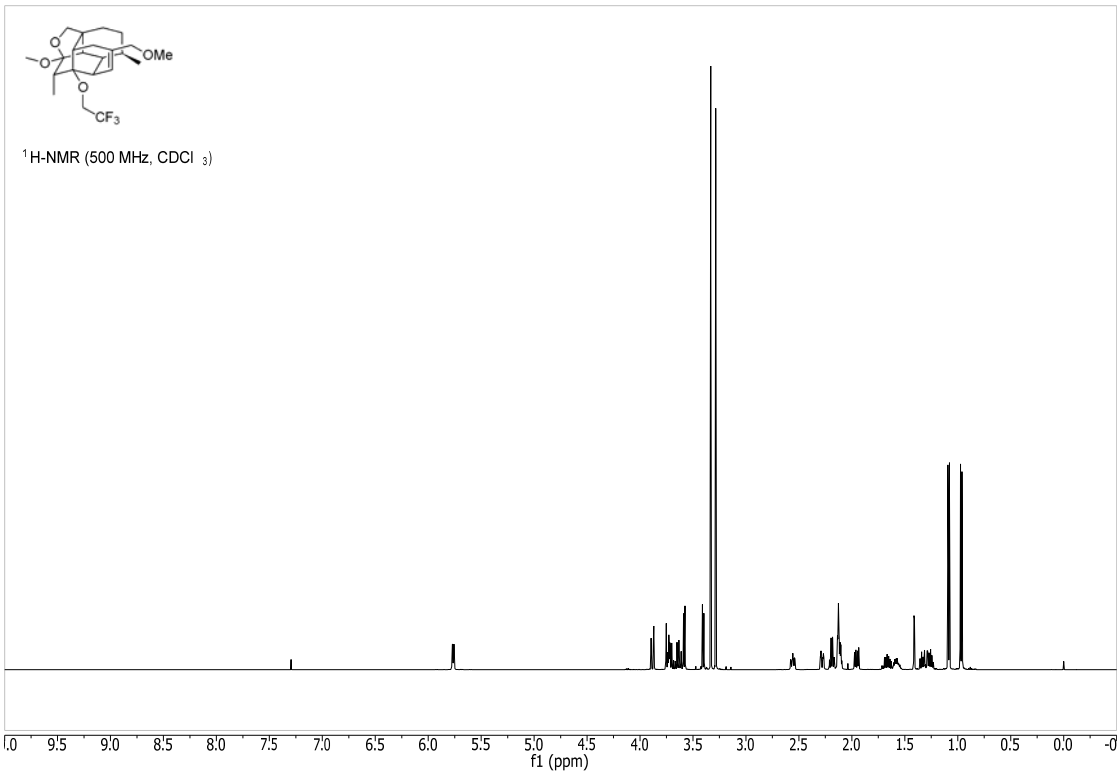
CF3
13C-NMR (100 MHz, CDCl 3)
f1 (ppm)

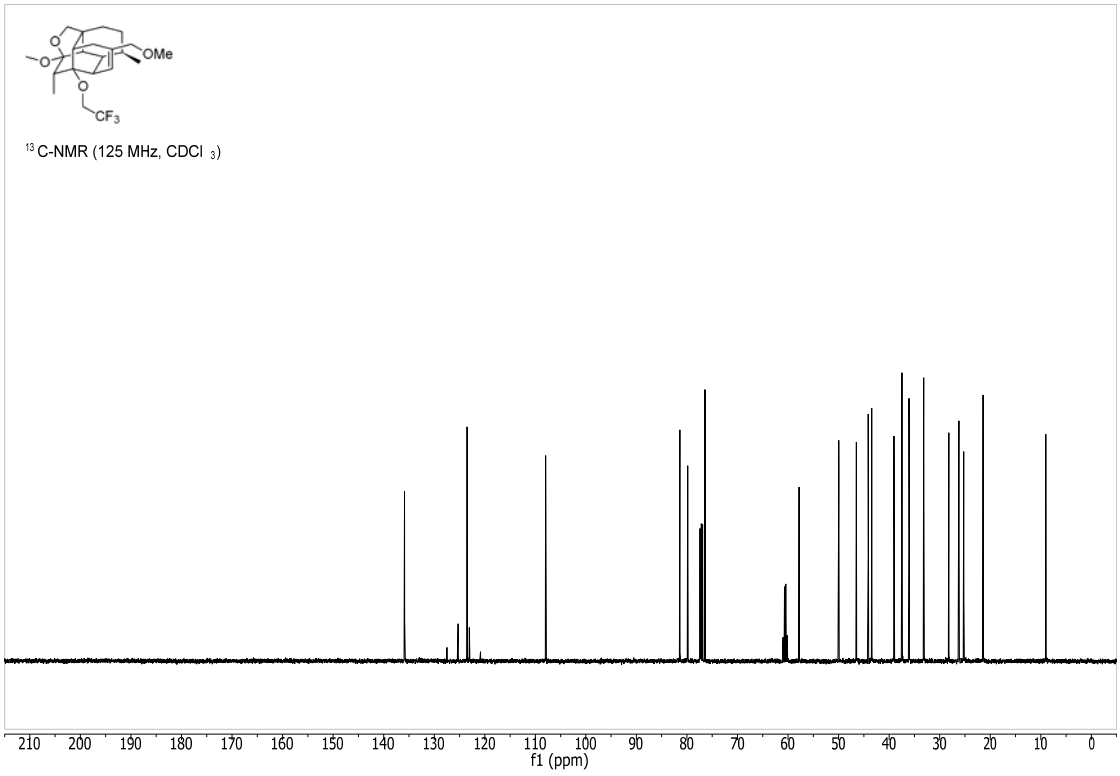

OMe
O
OH
O
CF3
1H-NMR (400 MHz, CDCl 3)
f1 (ppm)

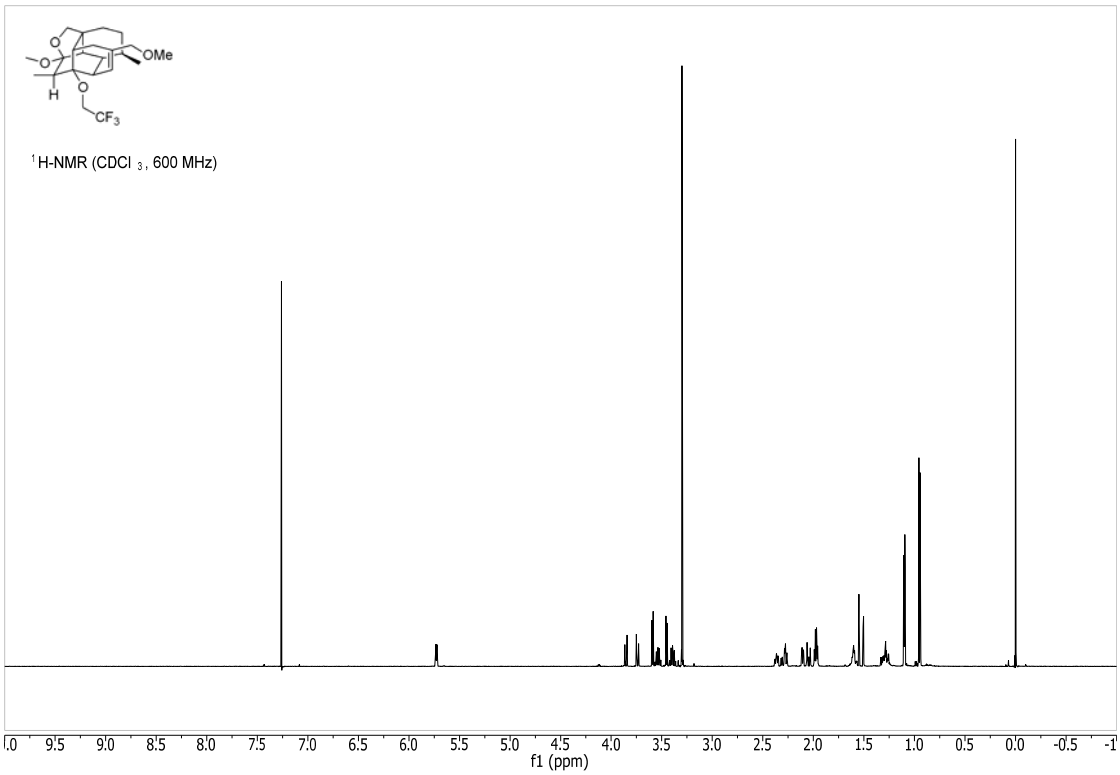

OMe
O
OH
O
CF3
13C-NMR (125 MHz, CDCl 3)
f1 (ppm)

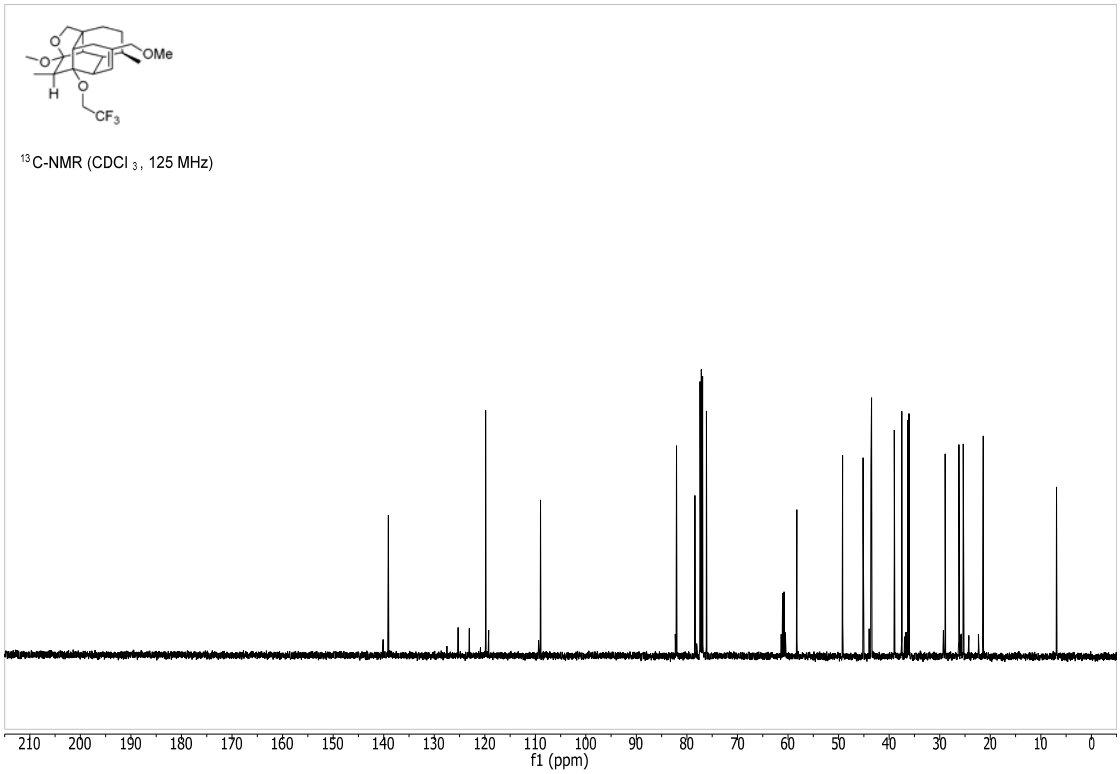

OMe
CF3
1H-NMR (400 MHz, CDCl 3)
f1 (ppm)

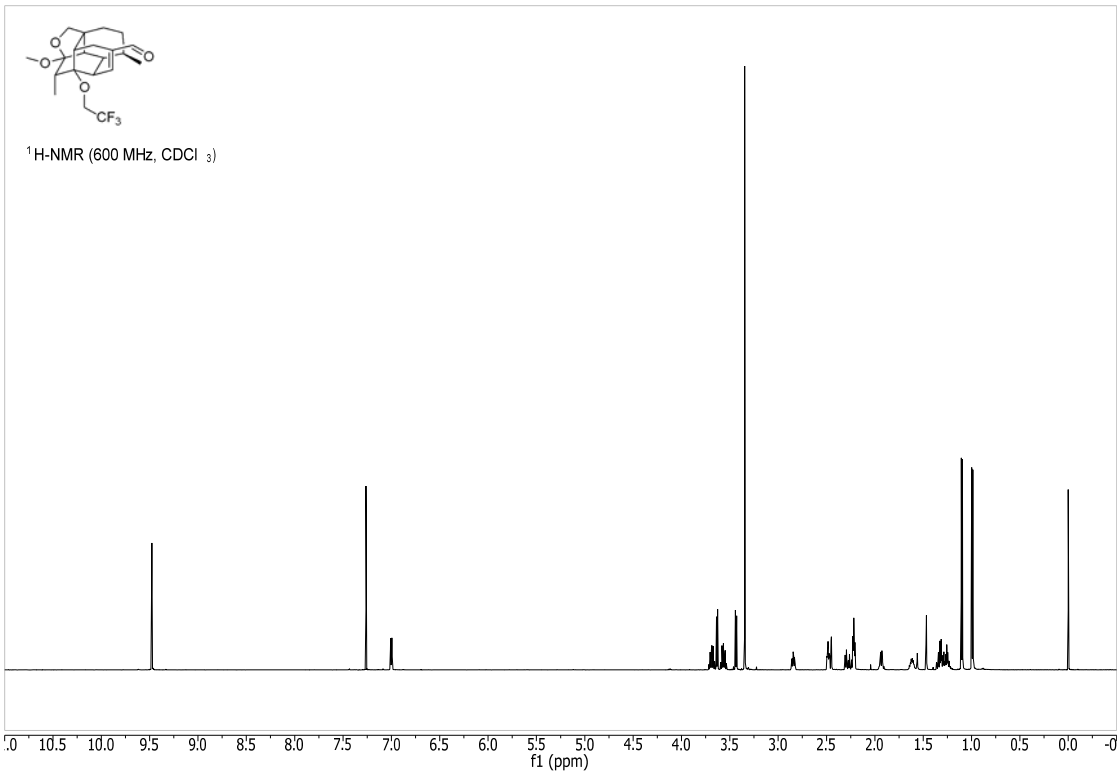

OMe
CF3
13C-NMR (125 MHz, CDCl 3)
f1 (ppm)

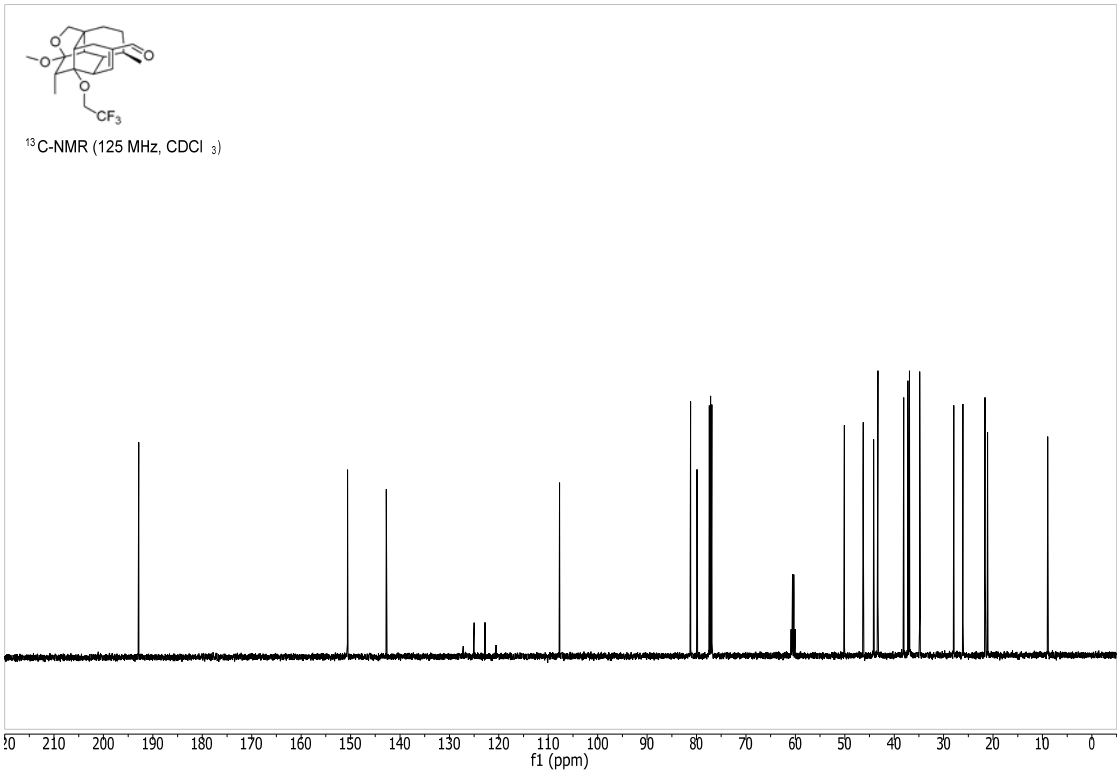


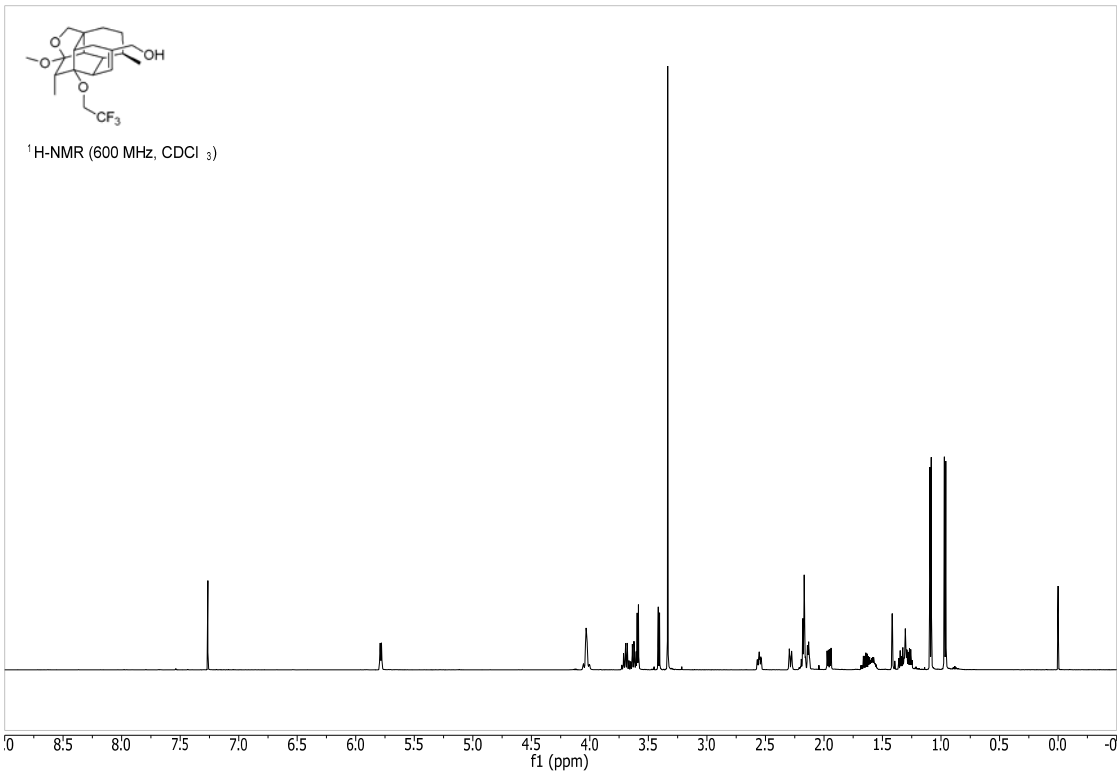


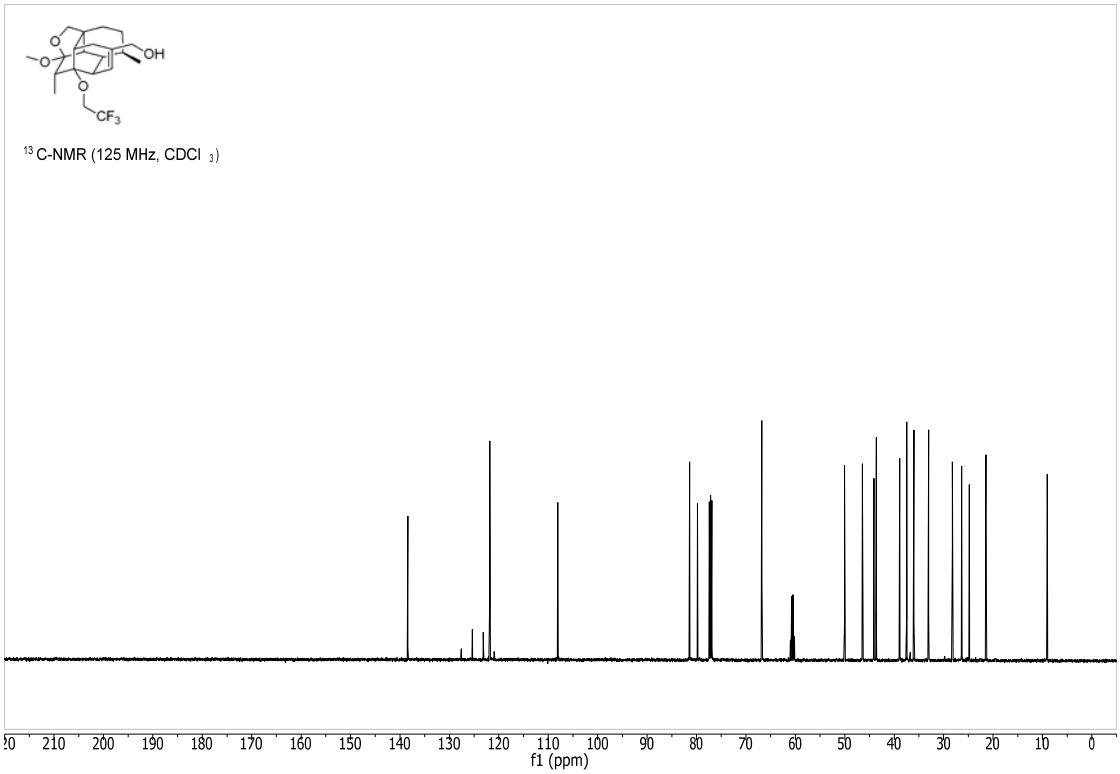


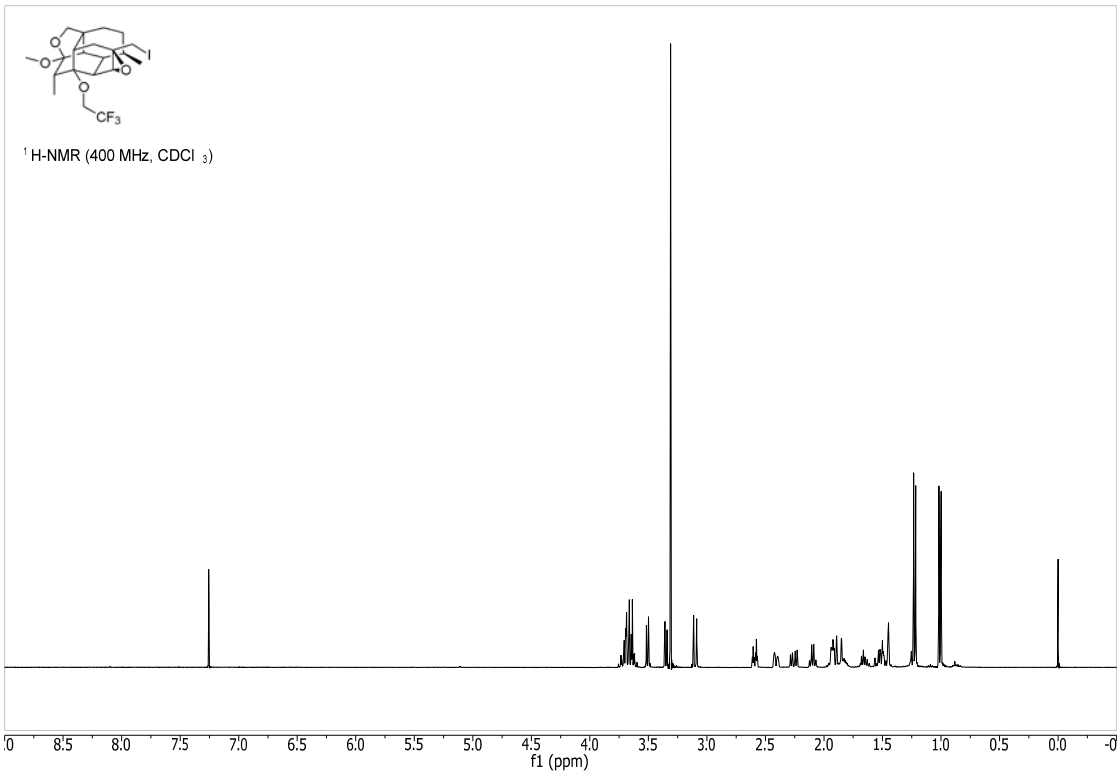


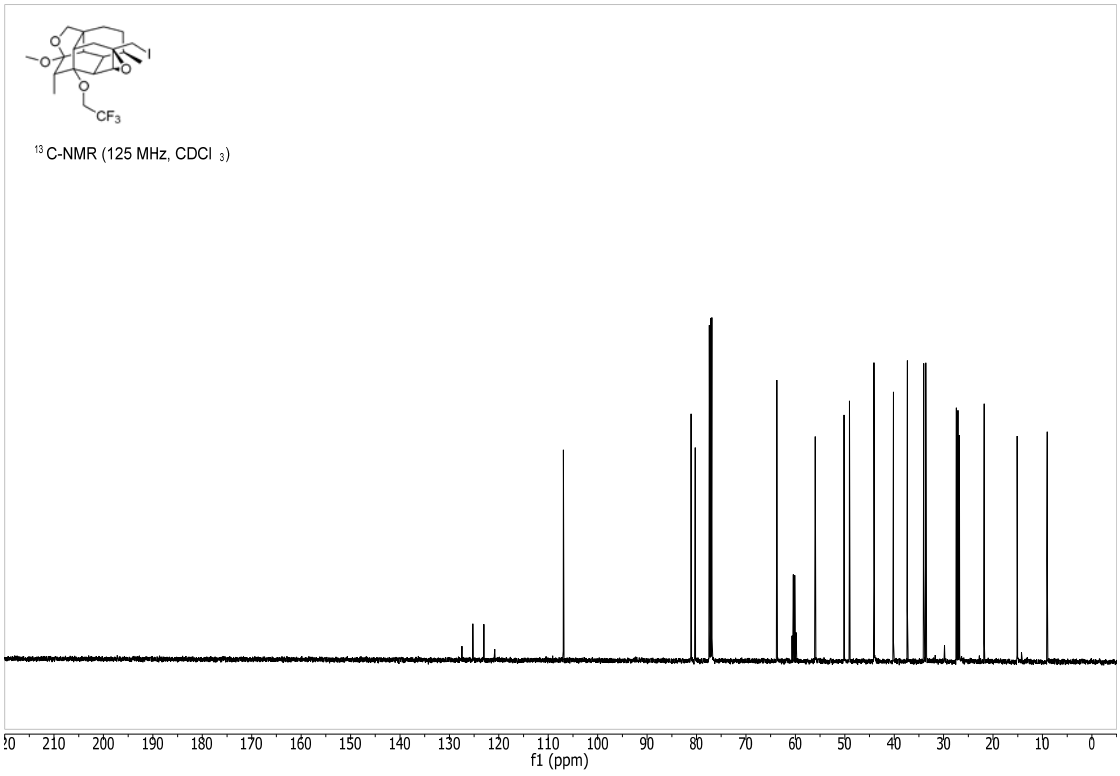

CF3
1H-NMR (600 MHz, CDCl 3)
f1 (ppm)

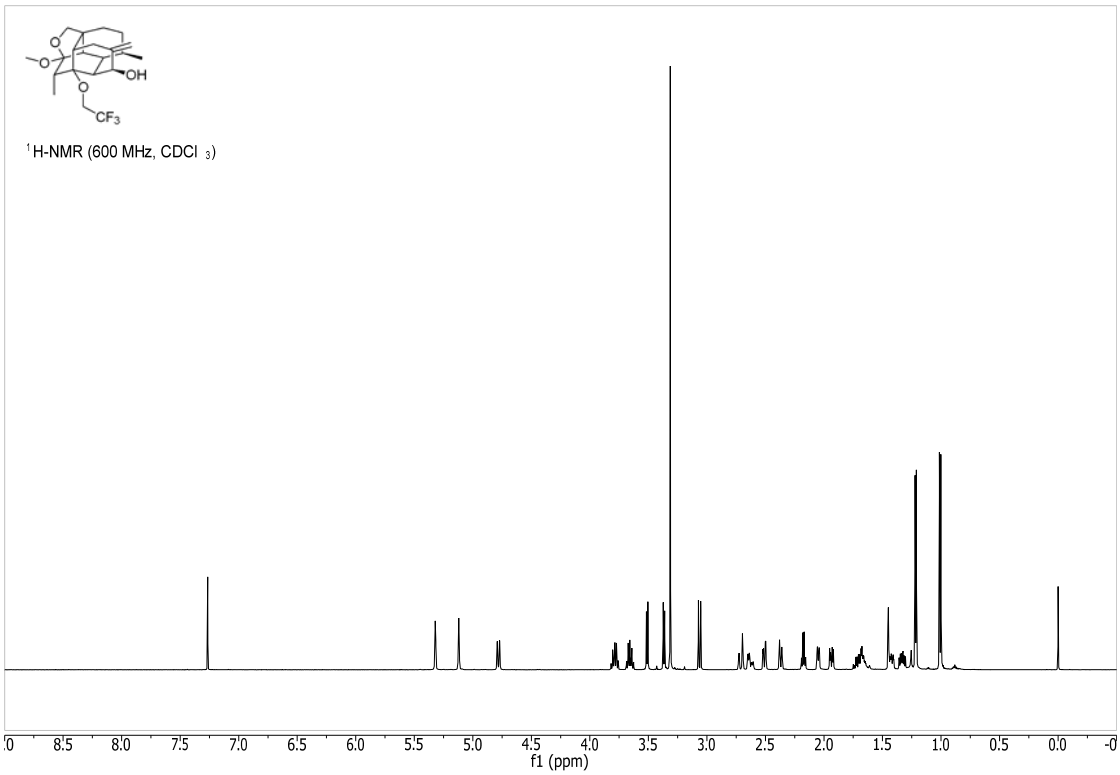

CF3
13C-NMR (125 MHz, CDCl 3)
f1 (ppm)

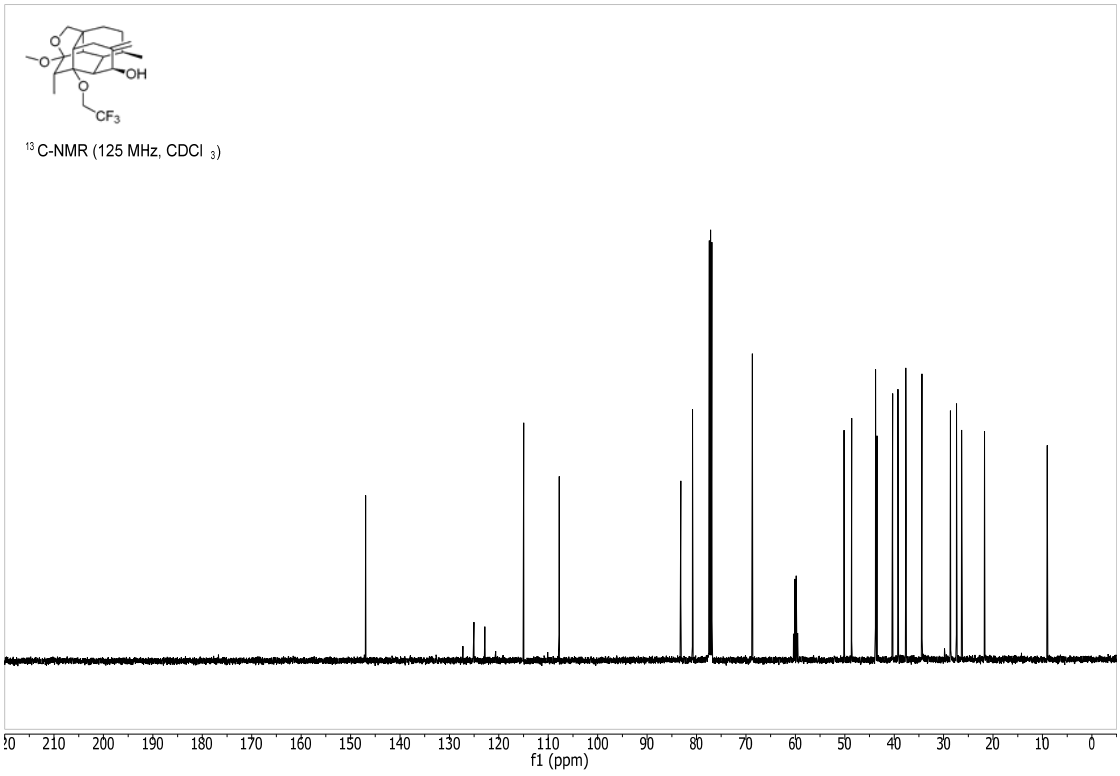


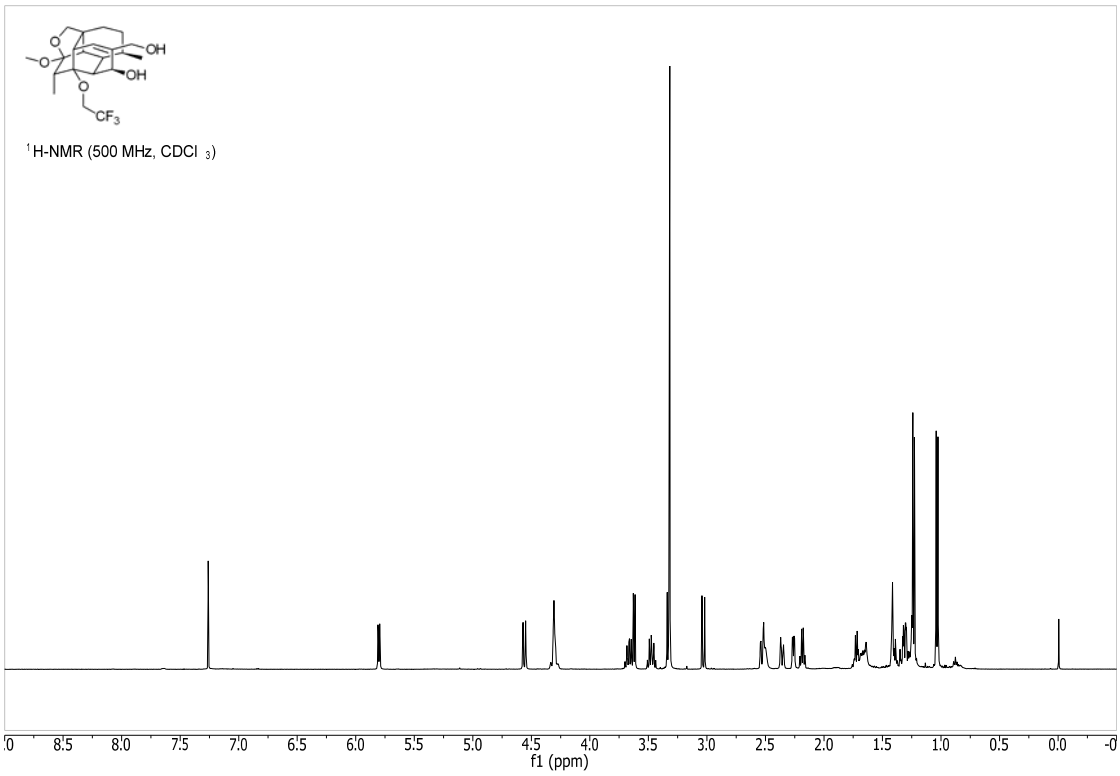


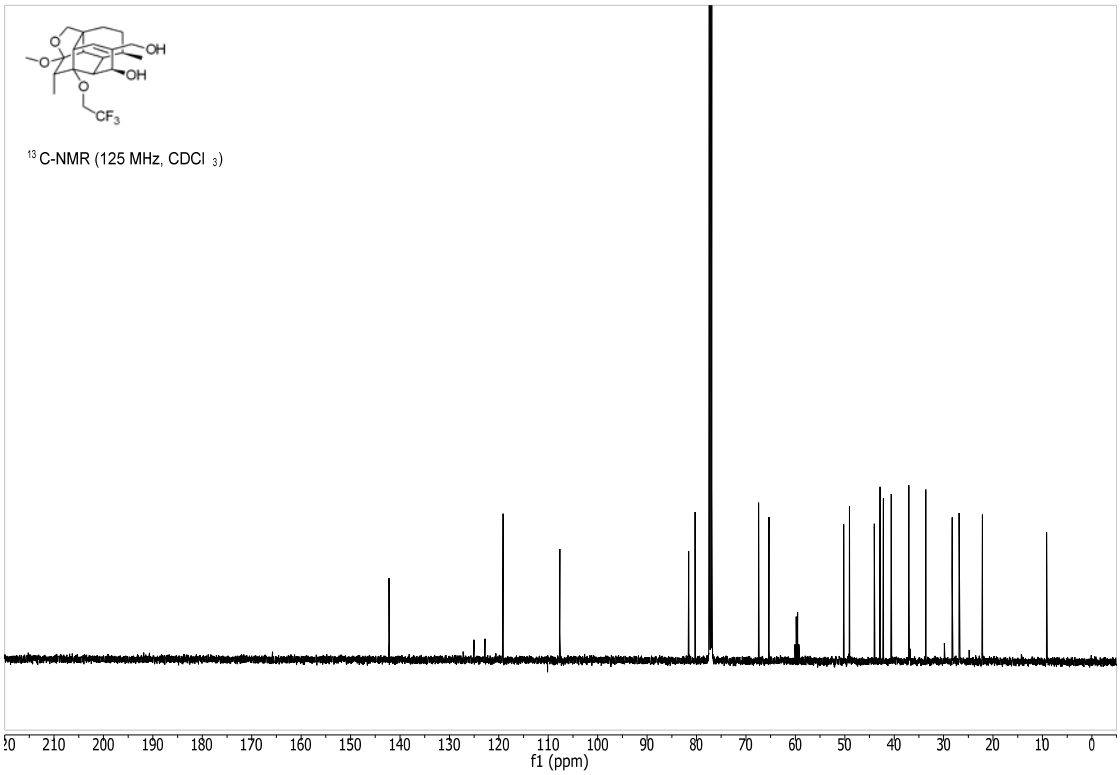


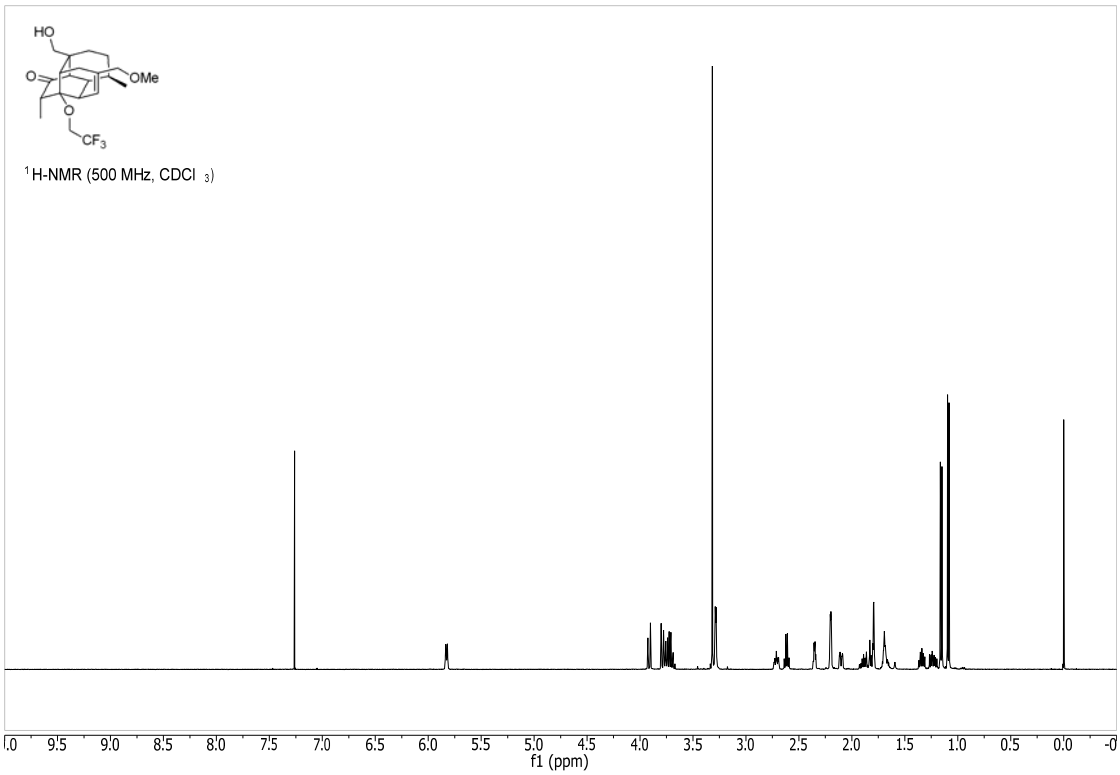


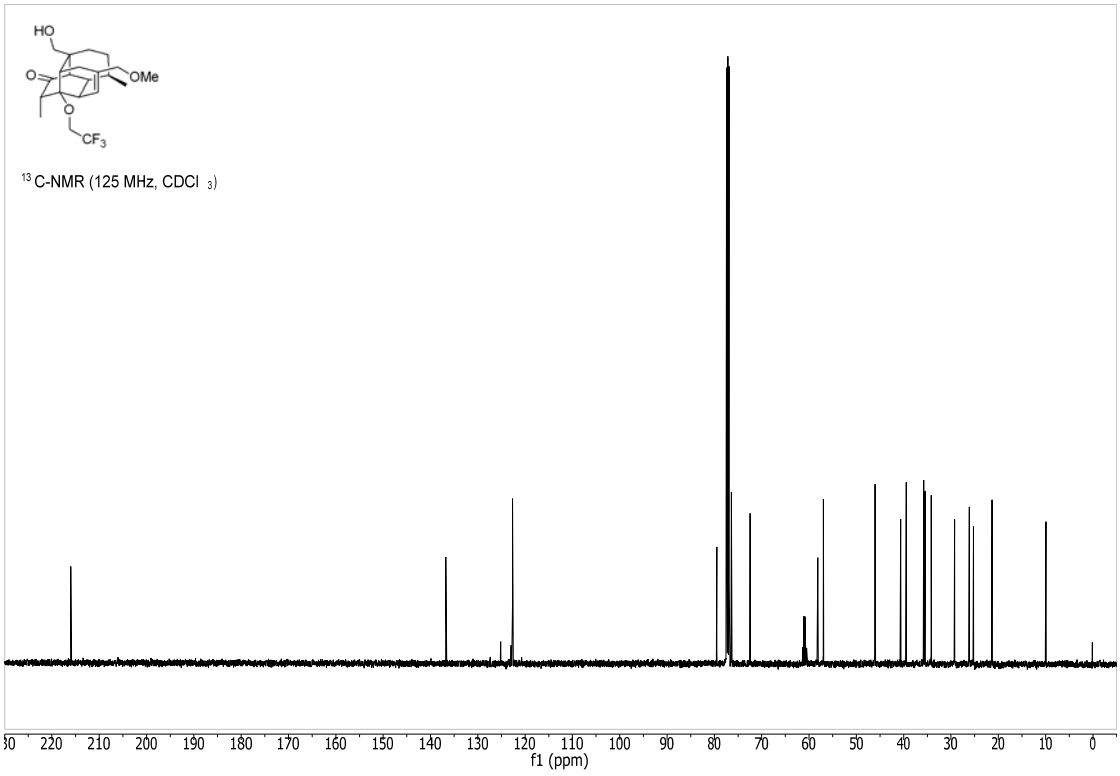

OH
CF3
1H-NMR (600 MHz, CDCl 3)
f1 (ppm)

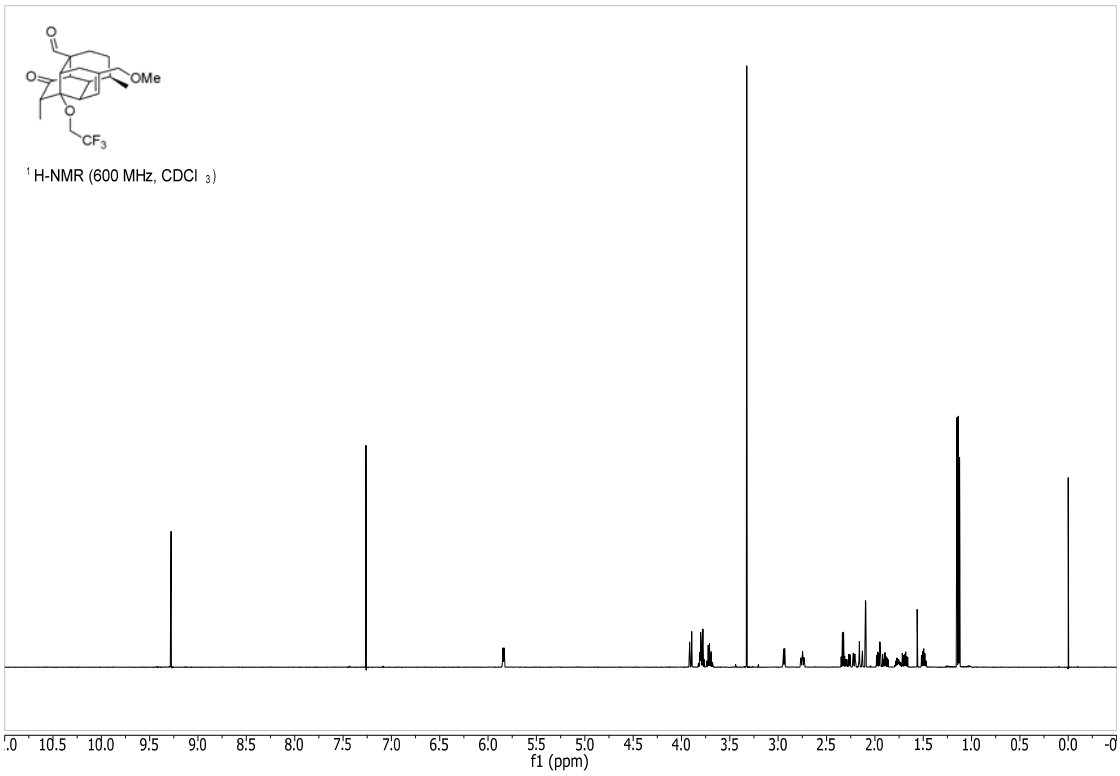

OH
CF3
13C-NMR (125 MHz, CDCl 3)
f1 (ppm)

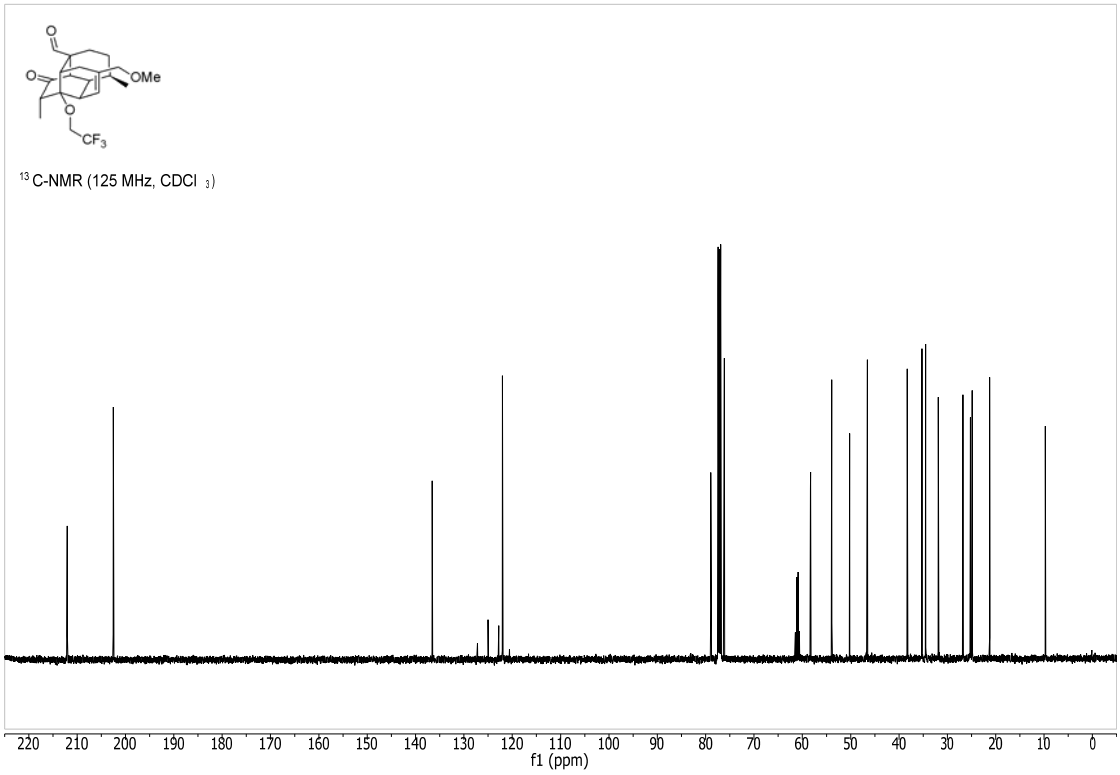


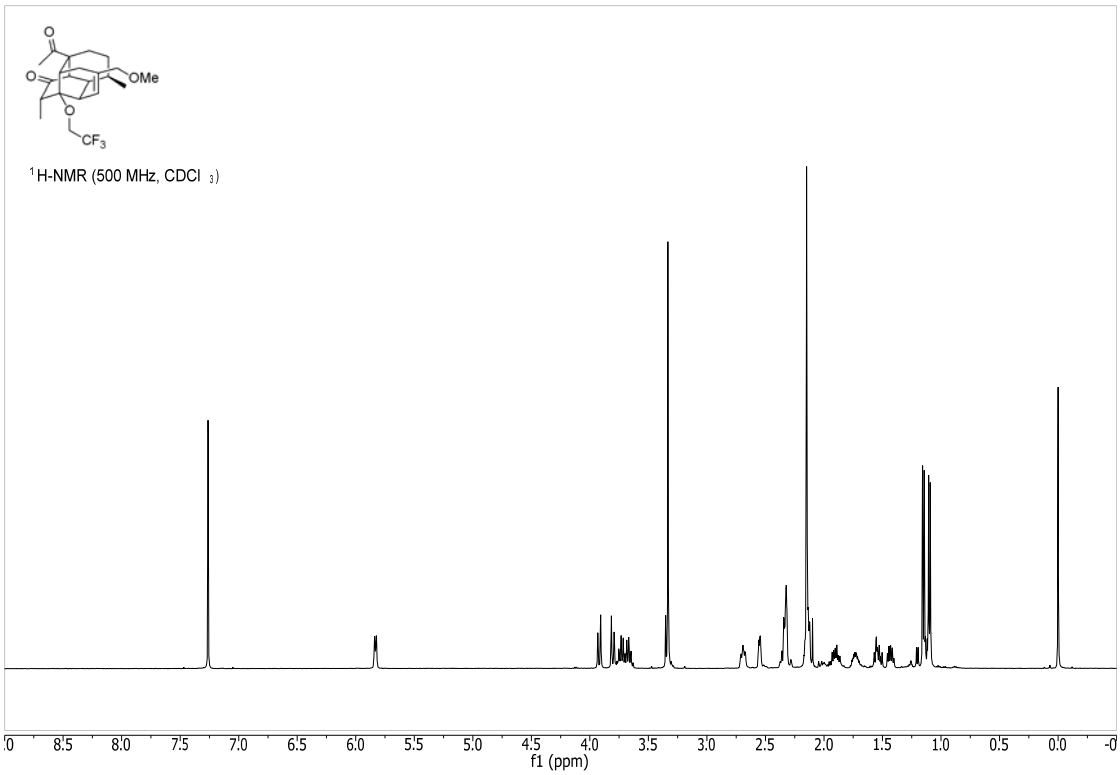


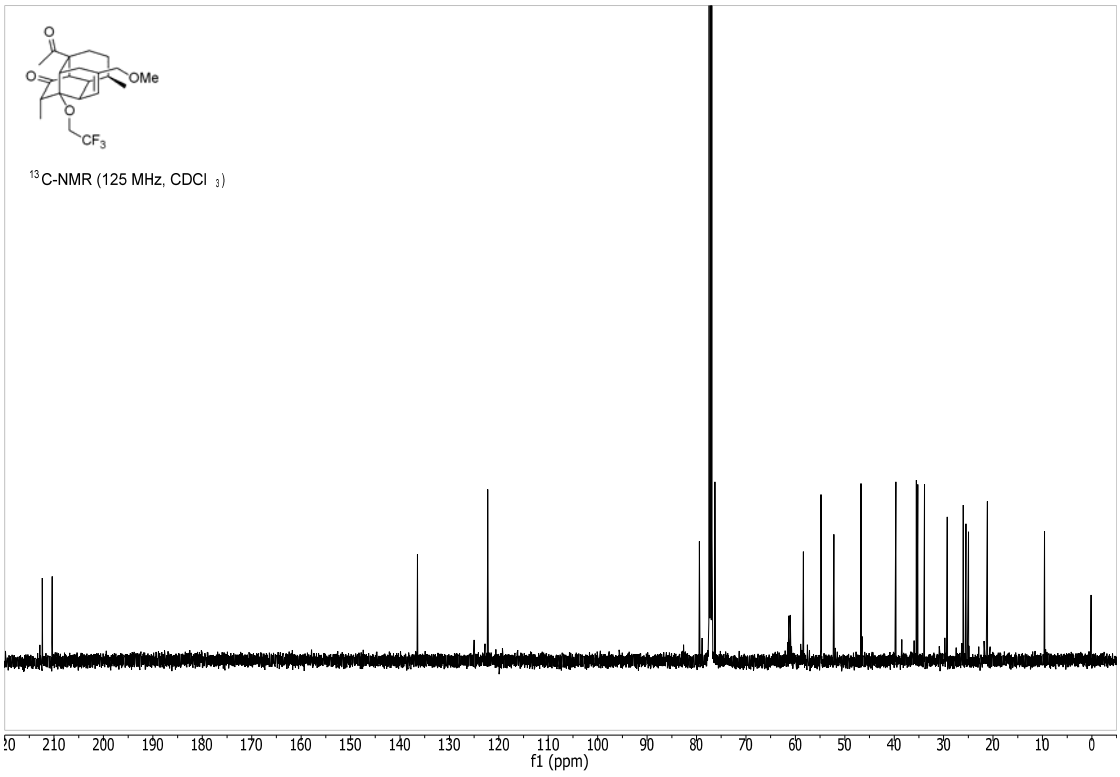

HO
O
OMe
O
CF3
1H-NMR (500 MHz, CDCl 3)
f1 (ppm)

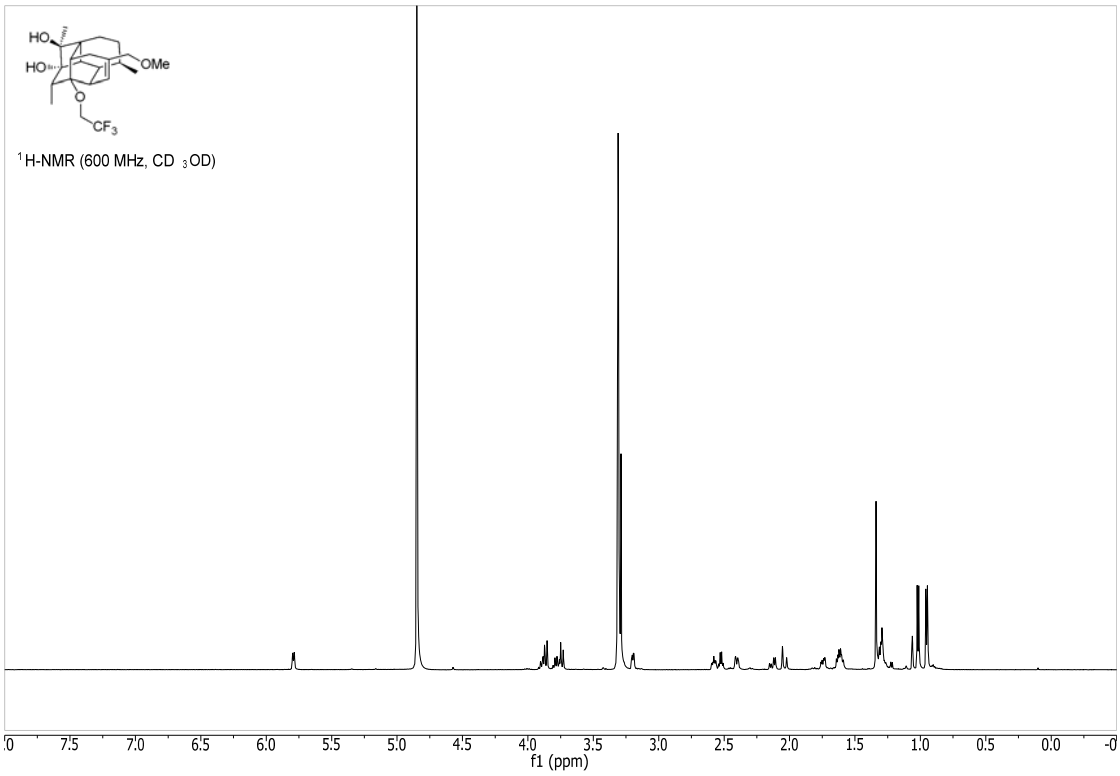

HO
O
OMe
O
CF3
13C-NMR (125 MHz, CDCl 3)
f1 (ppm)

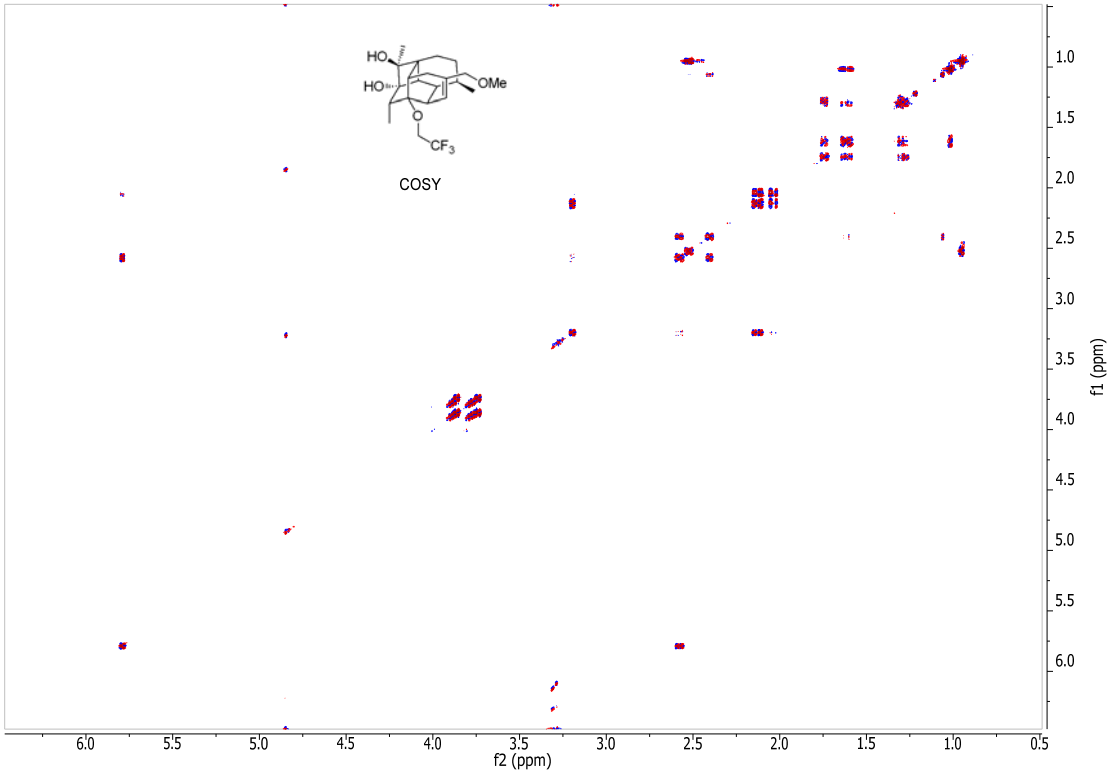


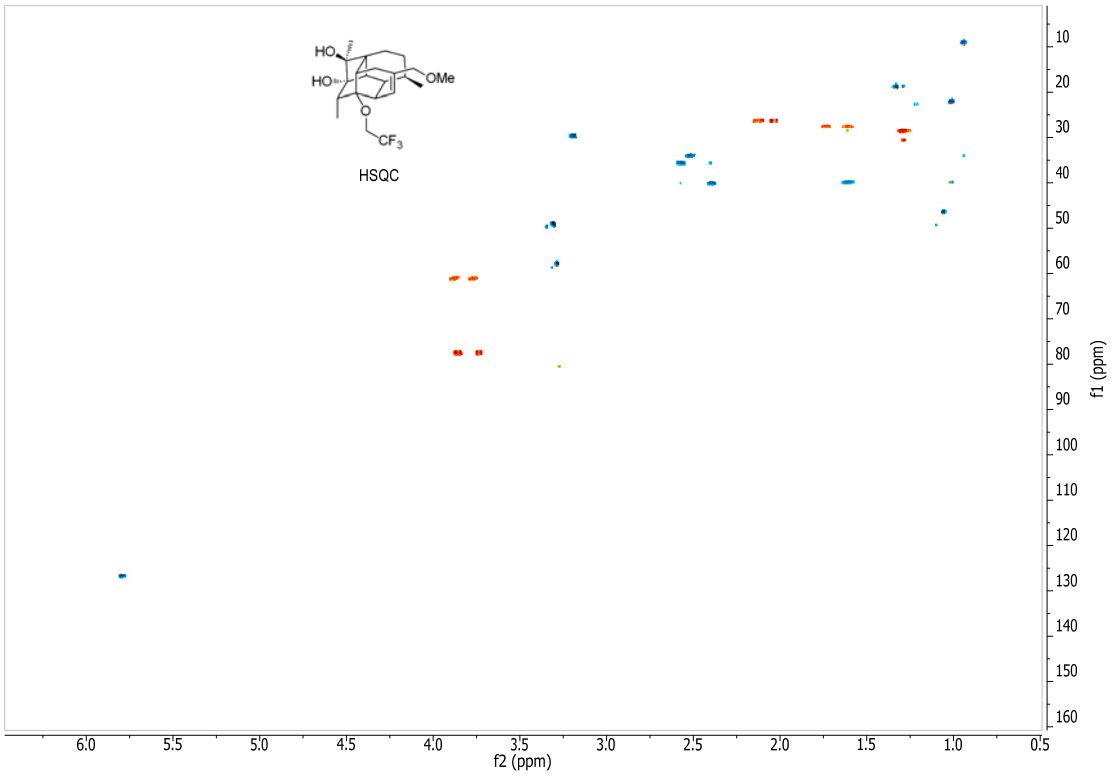


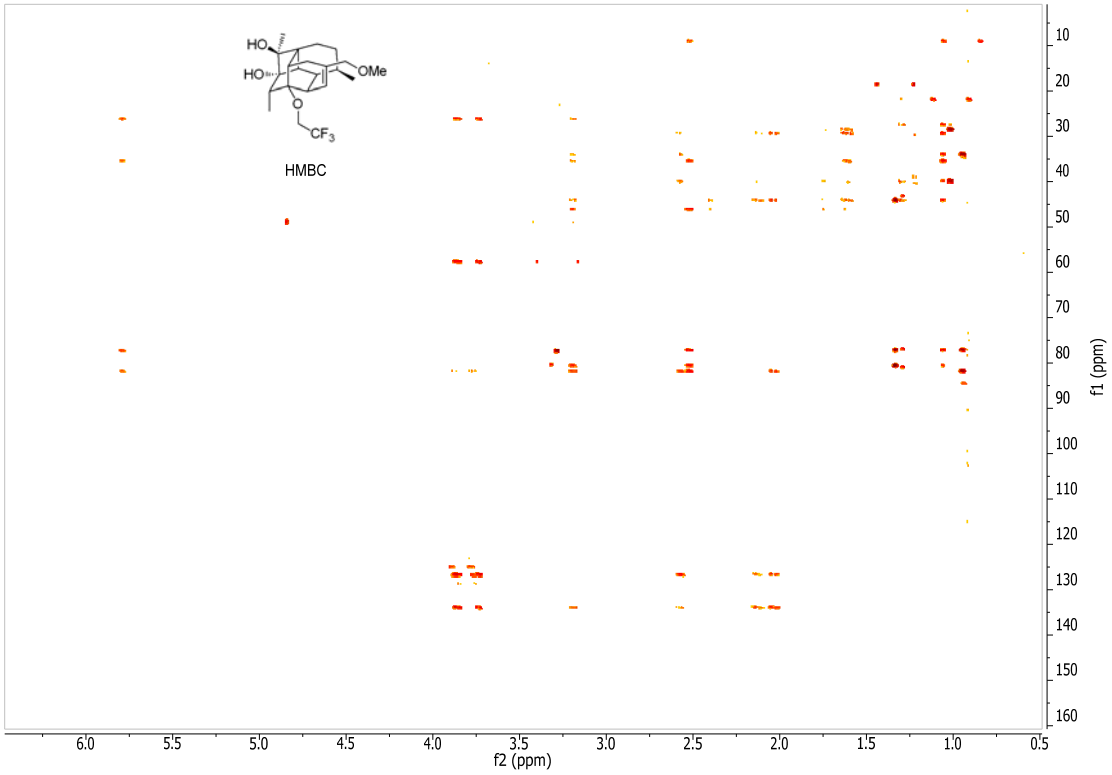












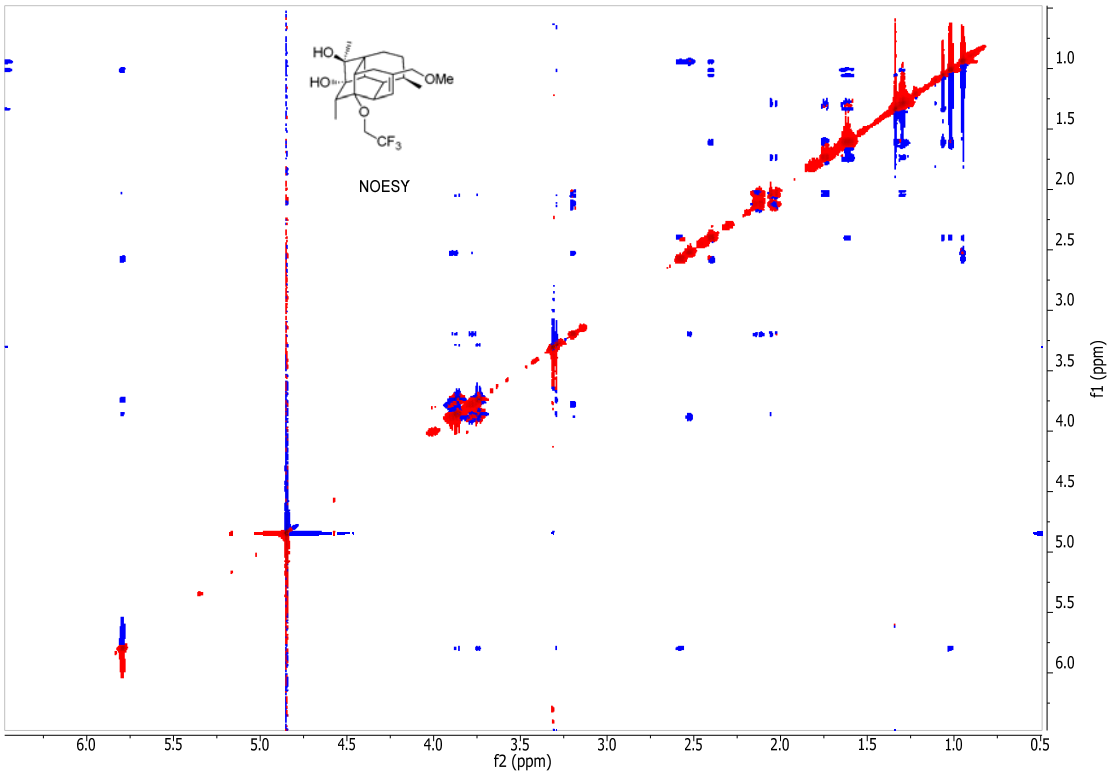
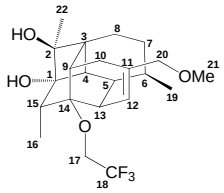
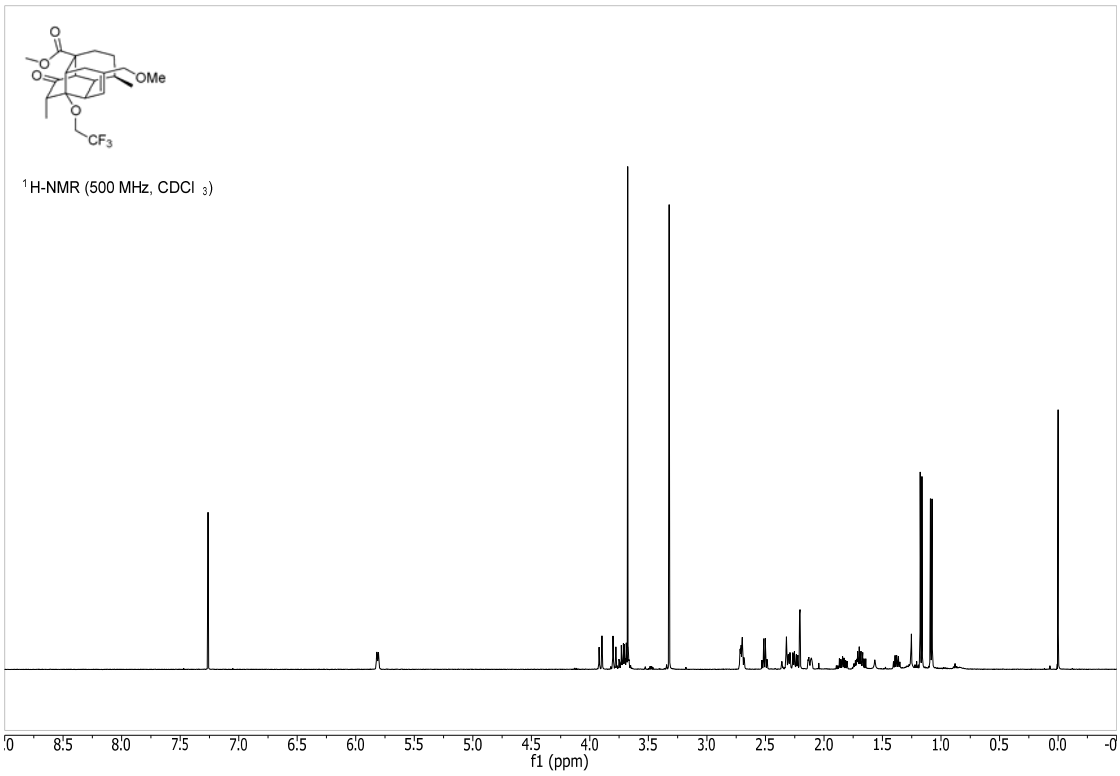
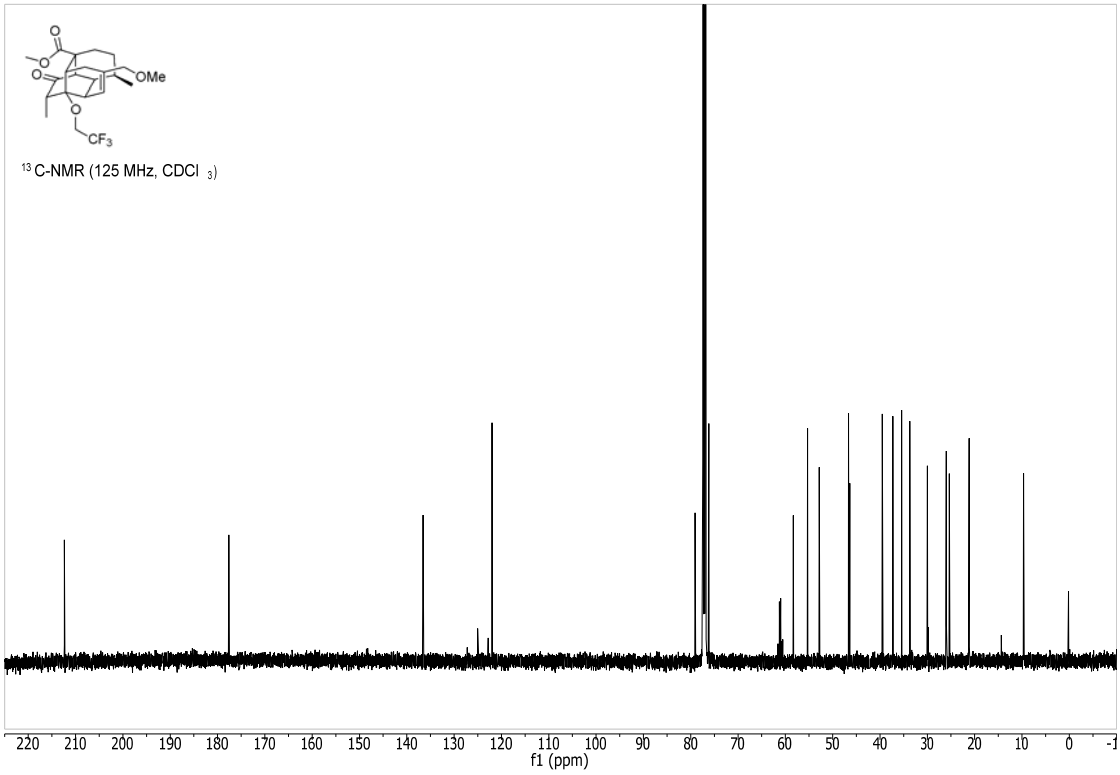


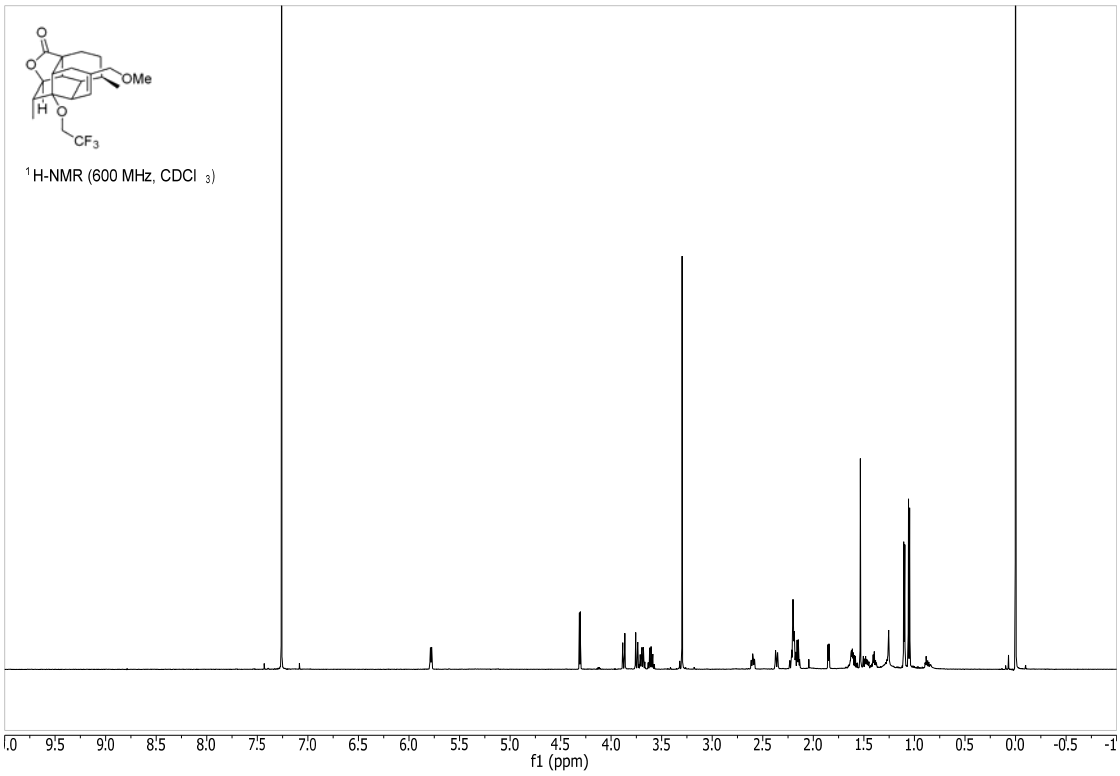
Table 8. 2D-NMR Data of Compound **123**

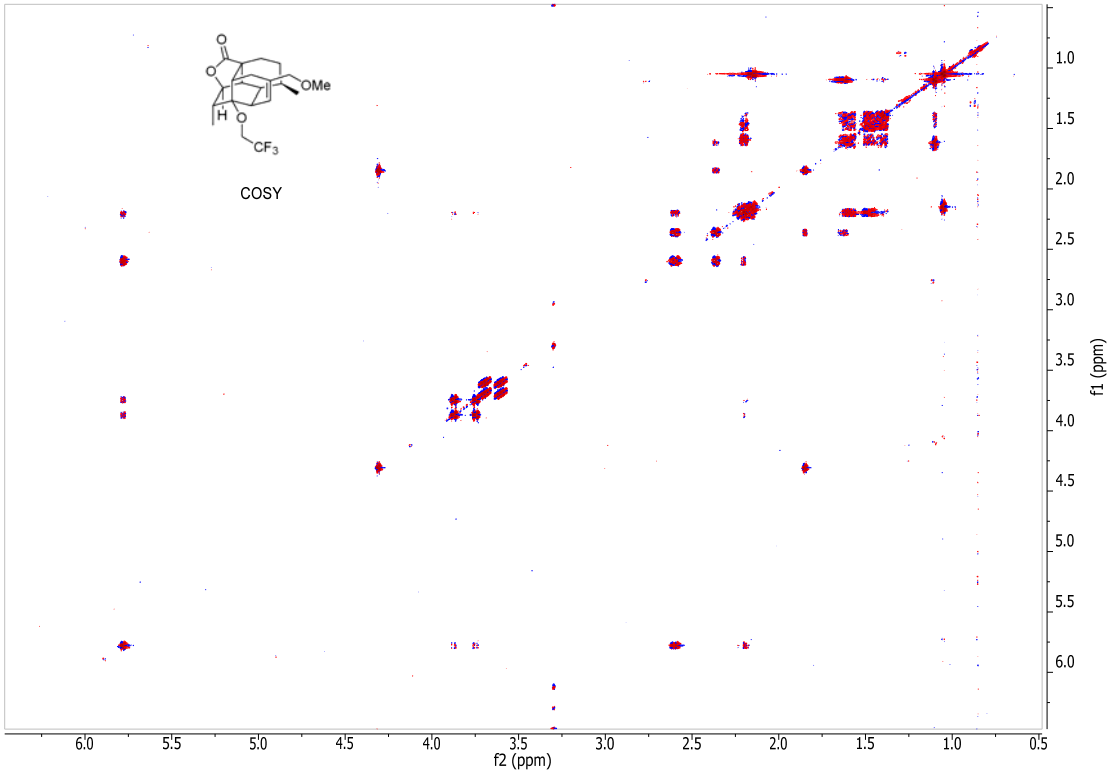


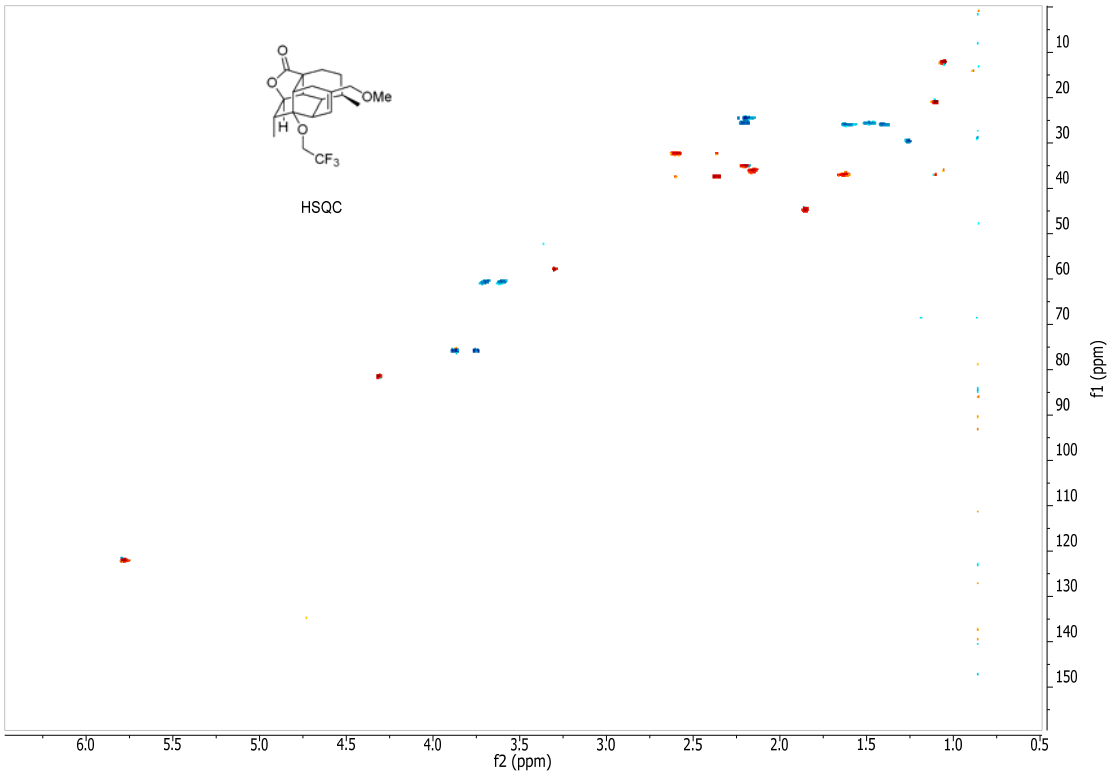
Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations	NOESY correlations
1	77.30		Cq			
2	80.67		Cq			
3	44.21		Cq			
4	46.27	1.06	CH	H-5	C-2, C-1, C-3, C-6, C-13, C-15, C-9, C-7, C-16	H-22
5	40.00	2.40	CH	H-13, H-4	C-3	H-6, H-19, H-16
6	39.88	1.61	CH	H-19, H-5	C-13	H-5, H-8a
7a	27.57	1.62	CH_2	H-8a, H-8b, H-7b	C-4, C-3, C-8, C-9	
7b		1.75		H-7a, H-8a, H-8b	C-4,C-3, C-8, C-9	H-10a
8a	28.55	1.30	CH_2	H-7b, H-7a		
8b		1.30			C-1, C-2, C-3	
9	29.58	3.20	CH	H-13, H-10a, H-10b	C-11, C-14, C-2, C-3, C-4, C-13, C-15, C-10	H-17a, H-15, H-10b, H-10a
10a	26.28	2.04	CH_2	H-12, H-9, H-10b	C-11, C-12, C-3, C-9	H-8a, H-7b
10b		2.13		H-12, H-9, H-10b	C-11, C-12, C-3, C-9	
11	133.99		Cq			
12	126.65	5.79	CH	H-20a, H-20b, H-13, H-10a, H-10b	C-14, C-20, C-13, C-10	H-20a, H-20b, H-13, H-19
13	35.60	2.57	CH	H-12, H-9, H-5	C-11, C-12, C-14, C-5, C-15, C-9	H-12, H-5, H-16
14	81.85		Cq			
15	34.08	2.52	CH	H-16	C-14, C-2, C-1, C-4, C-13, C-16	H-17b, H-16
16	9.02	0.95	CH_3	H-15	C-14, C-1, C-15	
17a	61.12	3.77	CH_2	H-17b	C-14, C-18	H-9, H-15
17b		3.89		H-17a	C-14, C-18	H-9, H-15
18	125.79		Cq			
19	22.04	1.02	CH_3	H-6	C-6, C-18	H-5
20a	77.43	3.74	CH_2	H-10a, H-12, H-20b	C-11, C-12, C-21, C-10	H-12, H-21, H-10a
20b		3.86		H-10a, H-12, H-20a	C-11, C-12, C-21, C-10	H-12, H-21, H-10a
21	57.70	3.29	CH_3		C-20	
22	18.73	1.34	CH_3		C-2, C-1, C-3	

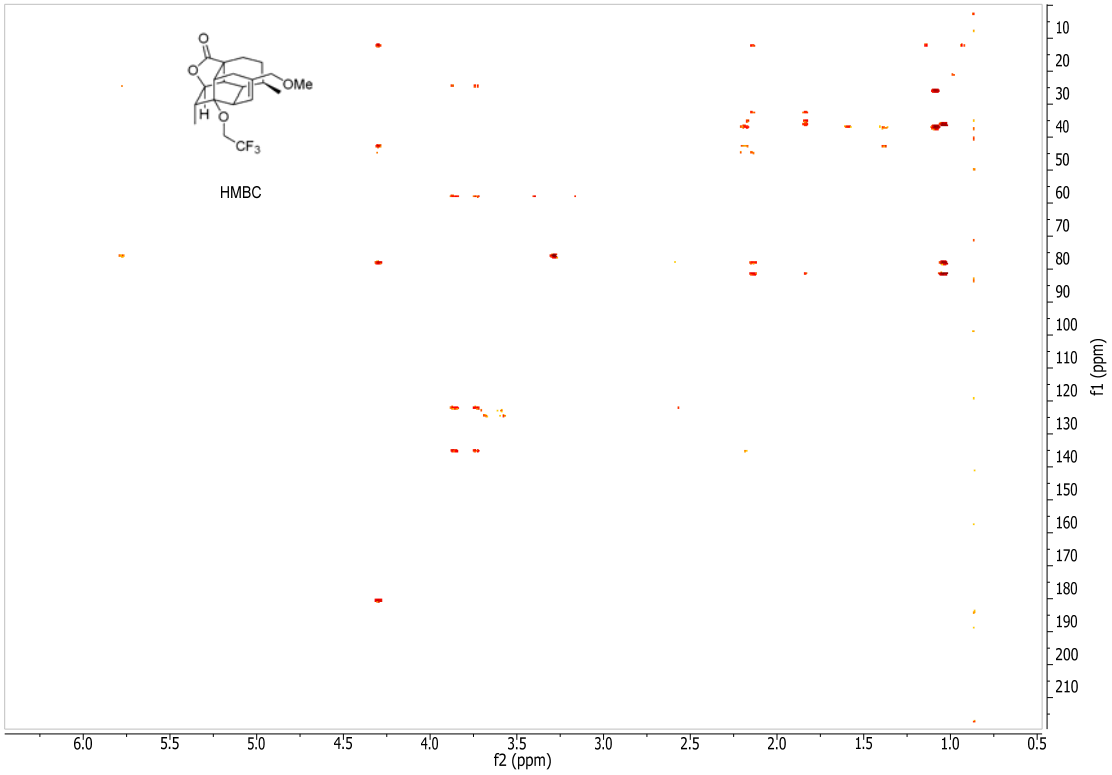












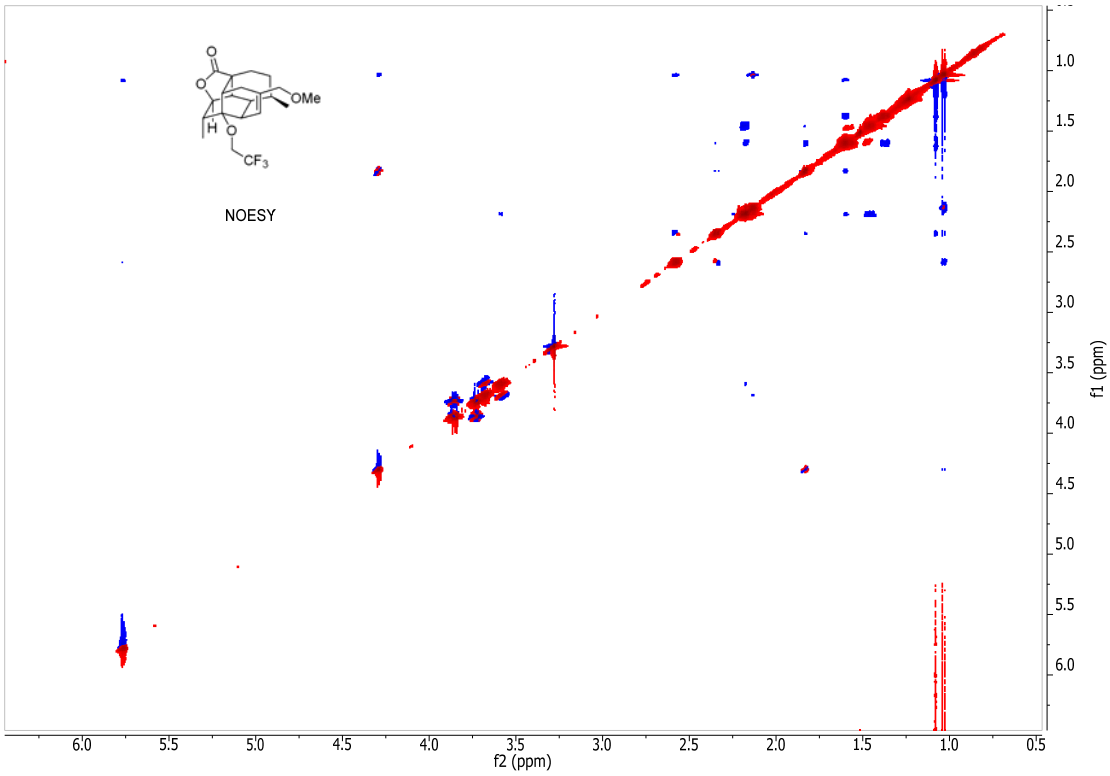
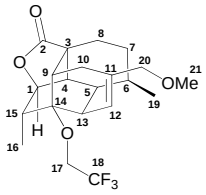
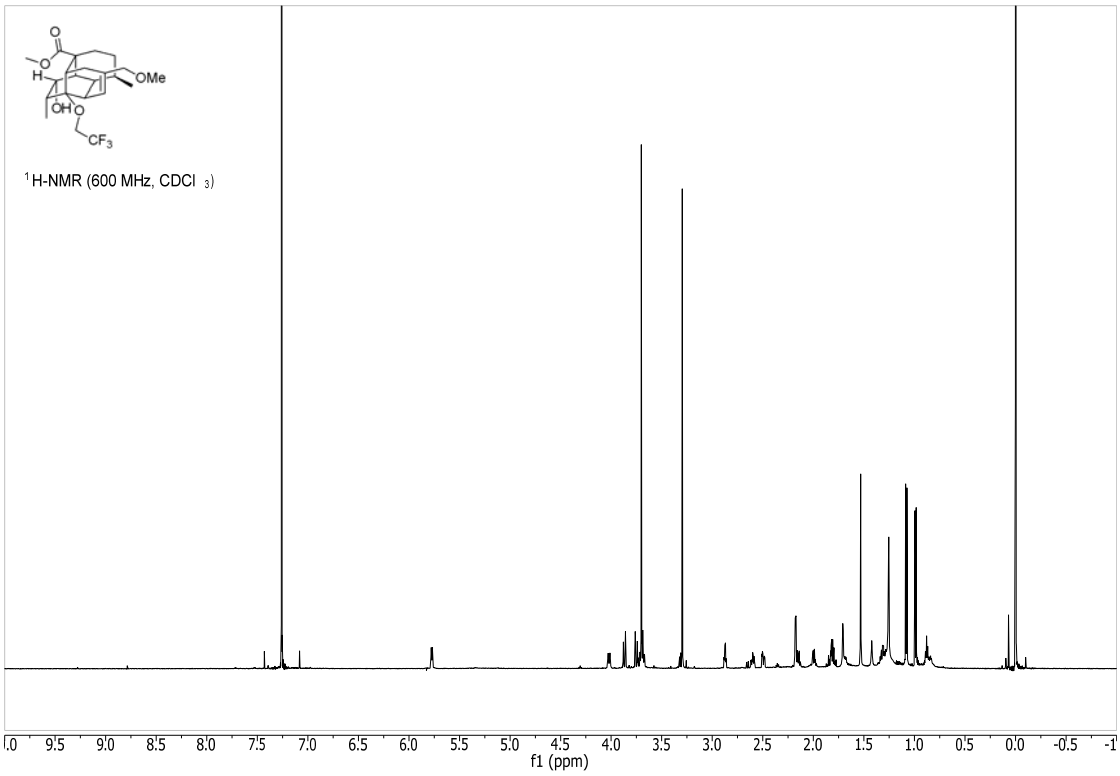
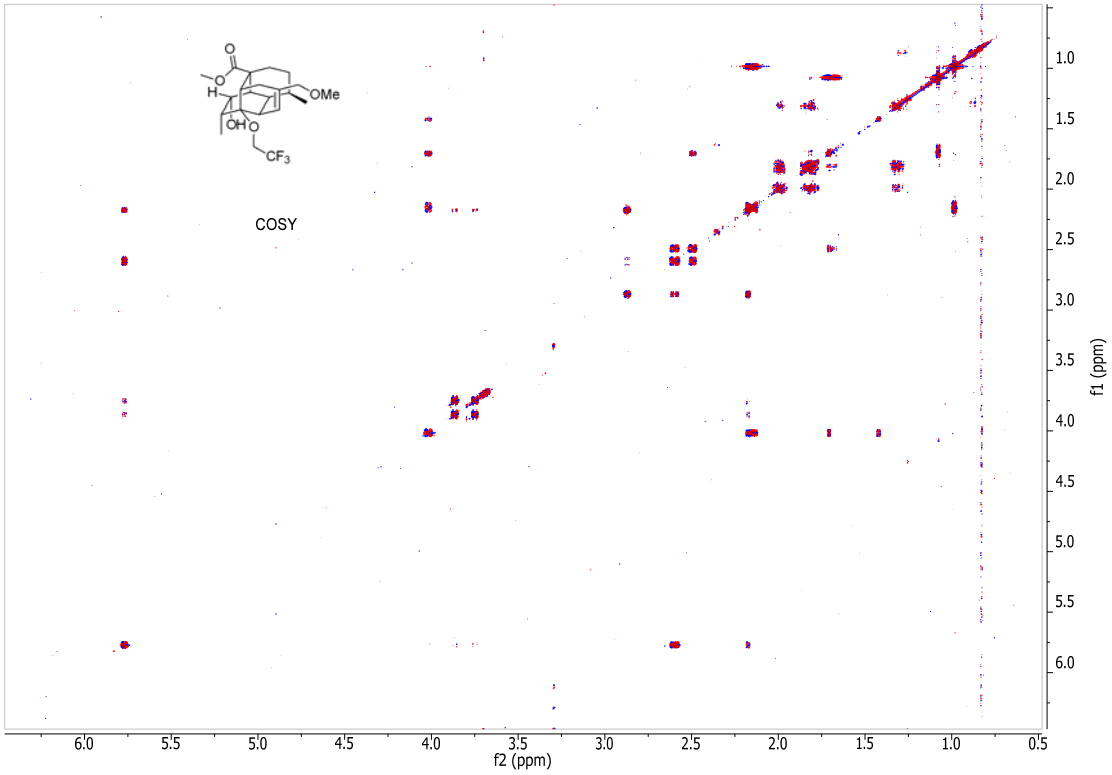


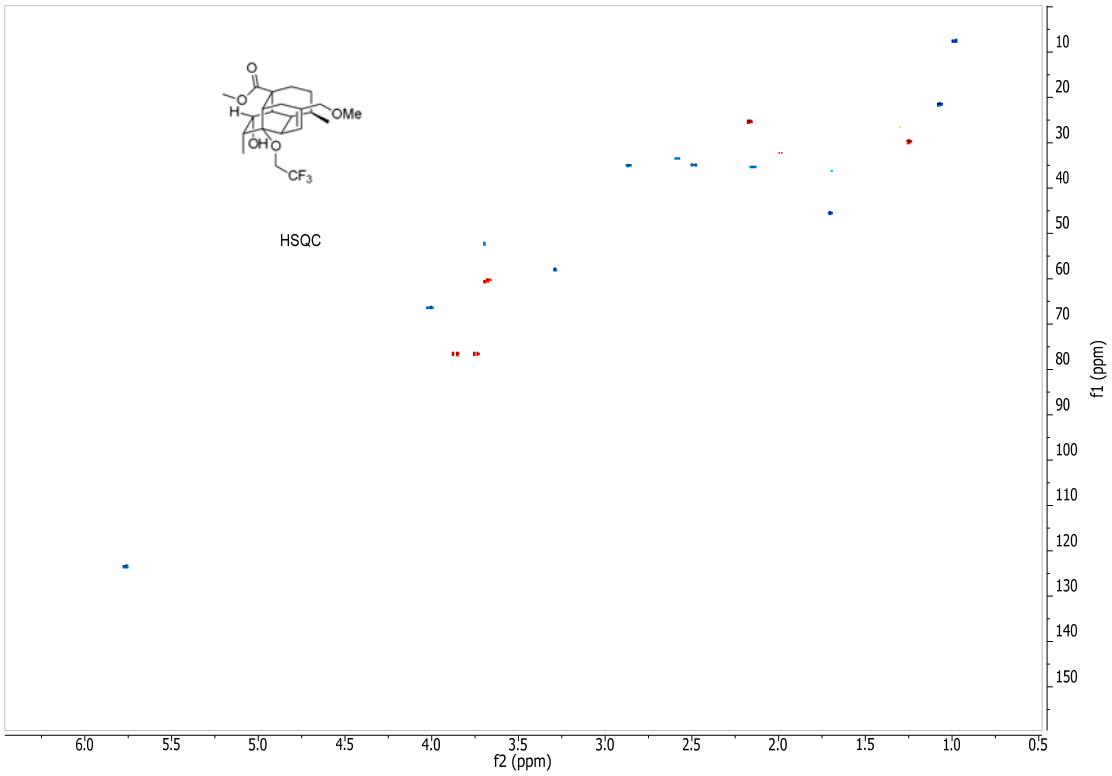
Table 9. 2D-NMR Data of Compound **127**

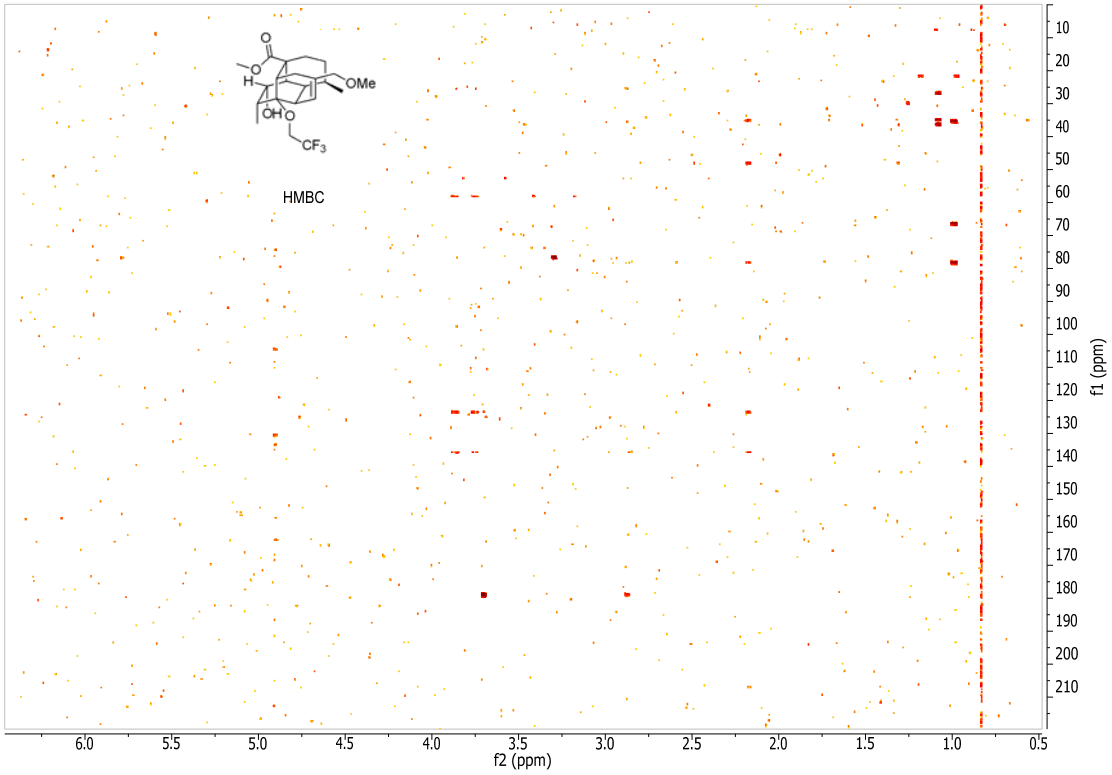


Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations	NOESY correlations
1	81.67	4.31	CH	H-4	C-2, C-14, C-4, C-3, C-16	H-16
2	189.27		Cq			
3	42.90		Cq			
4	44.90	1.85	CH	H-1, H-5	C-1, C-15, C-9, C-13	H-5, H-6, H-8b, H-7a
5	37.42	2.36	CH	H-13, H-4, H-6		H-4, H-6, H-19, H-16
6	37.07	1.63	CH	H-5, H-19		H-5
7a	25.72	1.48	CH_2	H-7b, H-8b		
7b		2.20		H-8b, H-7a, H-8a		
8a	26.01	1.40	CH_2	H-7b, H-8b	C-3, C-6	
8b		1.61		H-7b, H-8a	C-6	
9	35.32	2.20	CH	H-13		H-17a
10a	24.73	2.20	CH_2	H-12, H-20a, H-20b		
10b		2.20		H-12, H-20a, H-20b		
11	135.14		Cq			
12	122.12	5.78	CH	H-20a, H-20b, H-13, H-10a, H-10b	C-14, C-20, C-13, C-10	H-20a, H-20b, H-13
13	32.54	2.60	CH	H-12, H-5, H-9	C-12, C-14	H-12, H-19
14	78.27		Cq			
15	36.34	2.15	CH	H-16	C-1, C-14, C-4, C-9, C-13, C-16	H-17b, H-16
16	12.41	1.05	CH_3	H-15	C-1, C-14, C-15	H-13, H-15
17a	60.79	3.59	CH_2	H-17b	C-18	H-9
17b		3.69		H-17a	C-18	H-15
18	123.80		Cq			
19	21.13	1.10	CH_3	H-6	C-6, C-7	H-5
20a	75.98	3.75	CH_2	H-12, H-10a, H-10b, H-20b	C-11, C-12, C-21, C-10	H-12, H-21, H-10a, H-10b
20b		3.88		H-12, H-10a, H-10b, H-20a	C-11, C-12, C-21, C-10	H-12, H-21, H-10a, H-10b
21	58.10	3.30	CH_3		C-20	









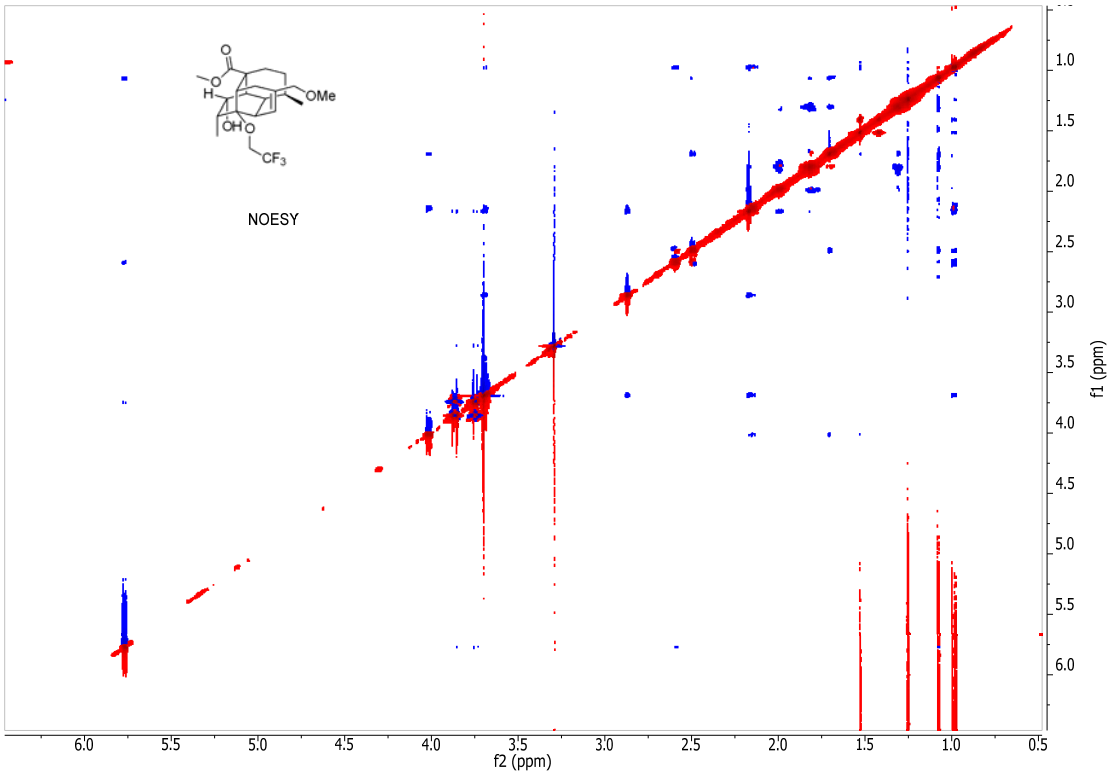
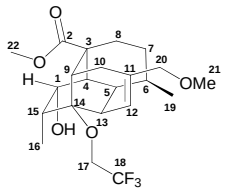
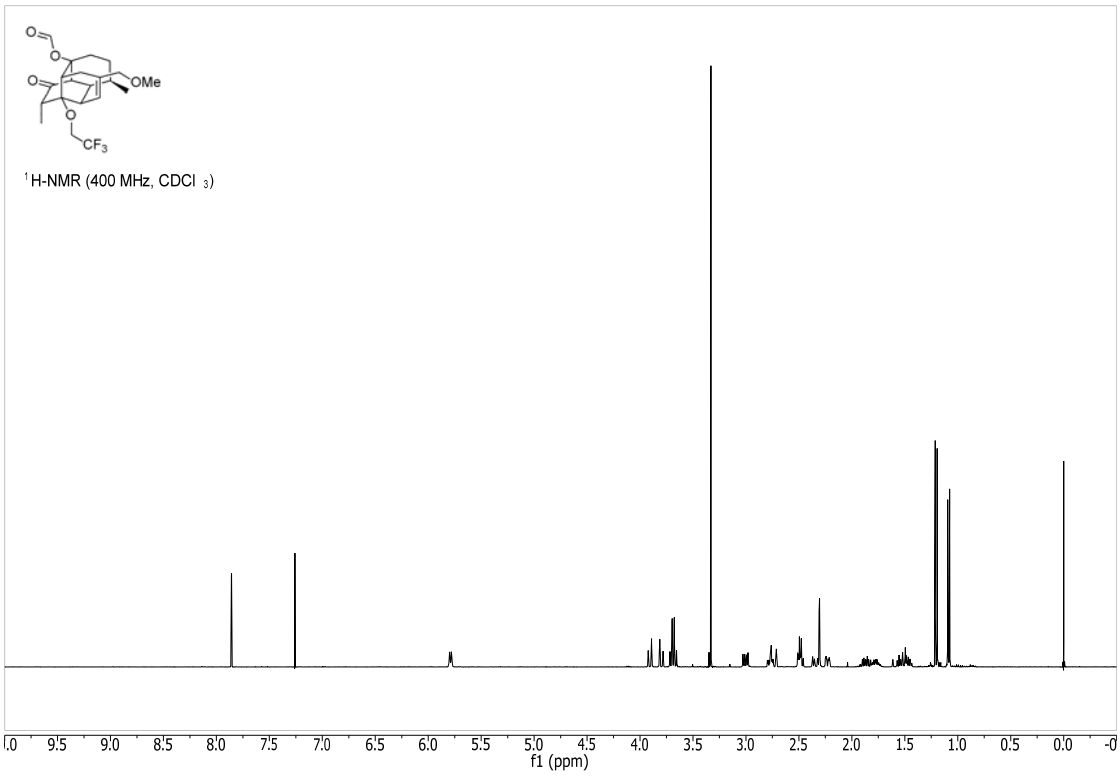
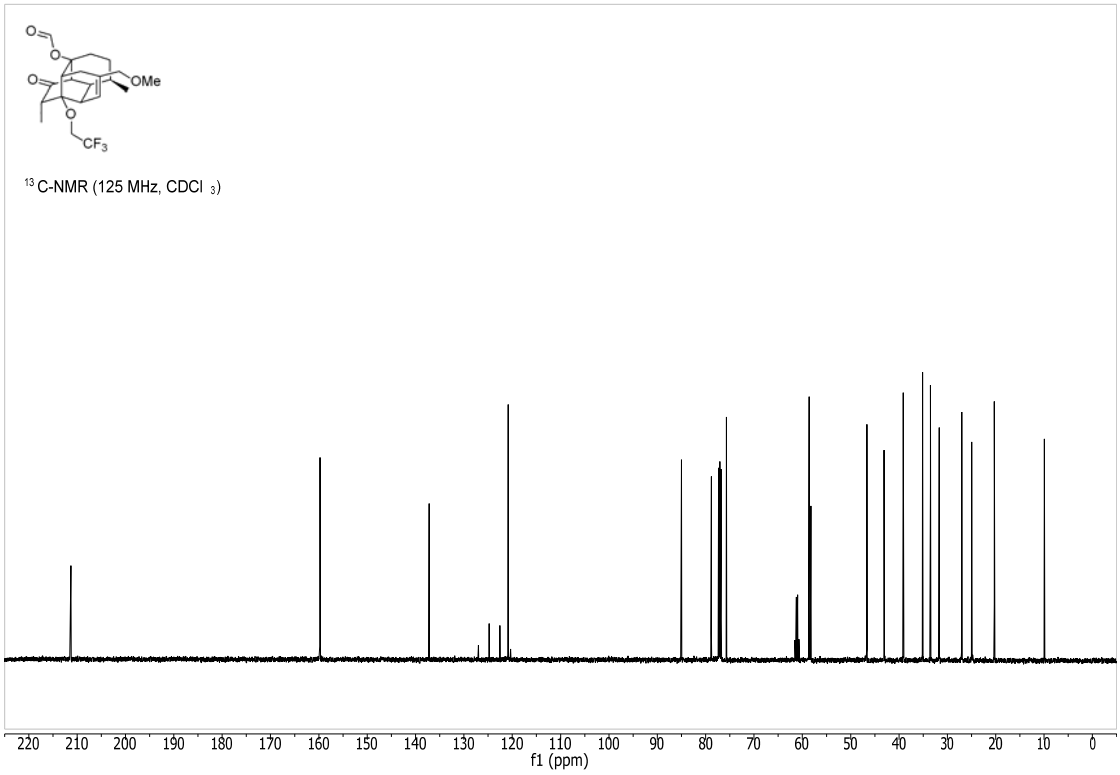


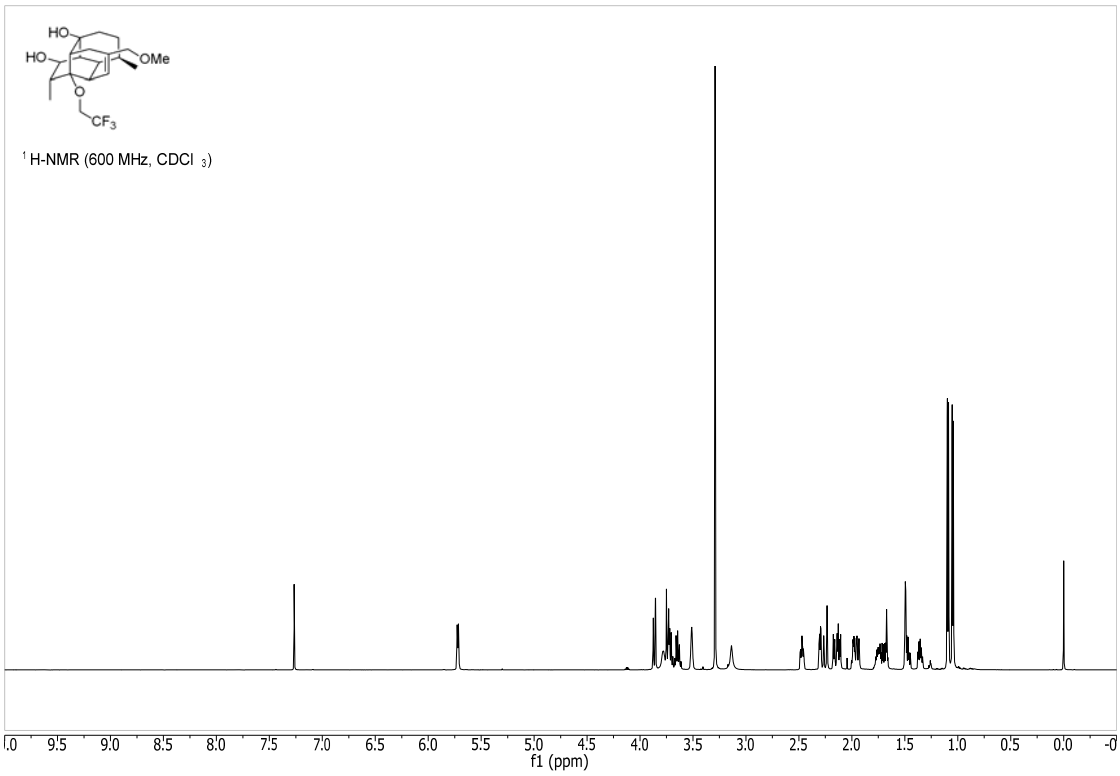
Table 10. 2D-NMR Data of Compound **128**

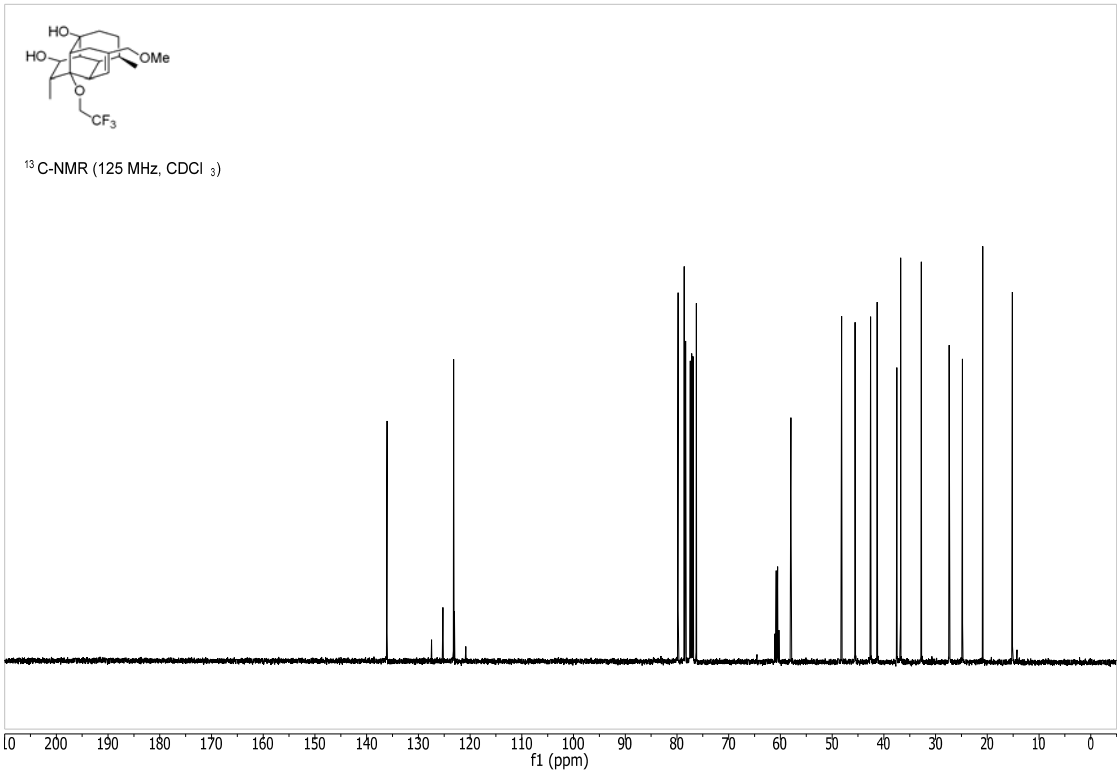


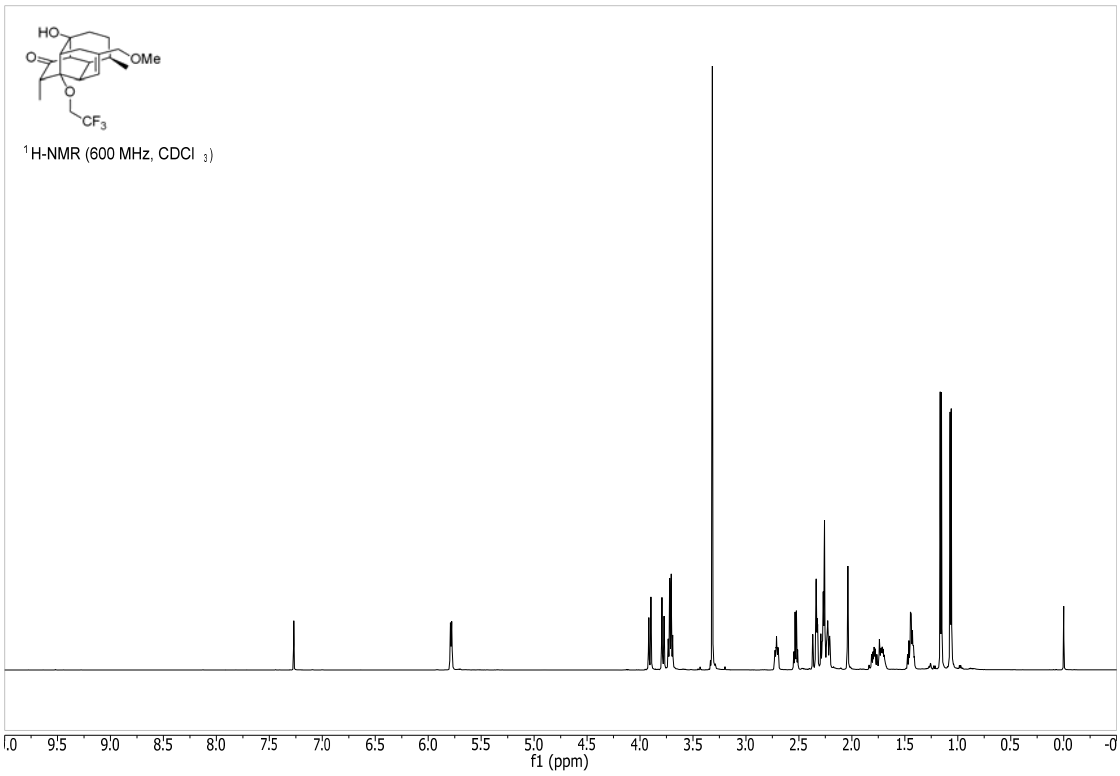
Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations	NOESY correlations
1	66.39	4.02	CH	H-15, H-4, H-23		H-15, H-4
2	179.14		Cq			
3	48.06		Cq			
4	45.36	1.71	CH	H-1, H-5	C-14, C-5	H-5
5	34.85	2.50	CH	H-13, H-6		H-4, H-19, H-16
6	36.19	1.69	CH	H-7b, H-19		H-7a, H-19
7a	26.75	1.31	CH_2	H-8b, H-7b		H-8b, H-6
7b		1.83		H-8b, H-7a		
8a	32.25	1.81	CH_2	H-8b, H-7a		
8b		2.00		H-8a, H-7a		H-10, H-8a, H-7a
9	35.05	2.87	CH	H-13, H-10	C-2, C-11, C-10	H-22, H-15
10a	25.33	2.17	CH_2	H-12, H-9	C-11, C-12, C-3, C-9	H-9
10b		2.17				
11	135.80		Cq			
12	123.51	5.77	CH	H-20a, H-20b, H-13, H-10	C-20	H-20a, H-20b, H-13, H-19
13	33.45	2.60	CH	H-12, H-9, H-5		H-12, H-16
14	78.32		Cq			
15	35.38	2.15	CH	H-1, H-16	C-14	H-1, H-22, H-9, H-16
16	7.59	0.99	CH_3	H-15	C-14, C-1, C-15	H-13, H-17, H-5, H-15
17a	60.58	3.69	CH_2			H-16
17b		3.69				H-16
18	124.30		Cq			
19	21.48	1.08	CH_3	H-6	C-6, C-5, C-7	
20a	76.61	3.75	CH_2	H-20b, H-10	C-11, C-12, C-21	H-10, H-12
20b		3.87		H-20a, H-10	C-11, C-12, C-21	H-10, H-12
21	58.03	3.30	CH_3		C-20	
22	52.38	3.70	CH_3		C-2	H-9
23		1.42	OH	H-1		

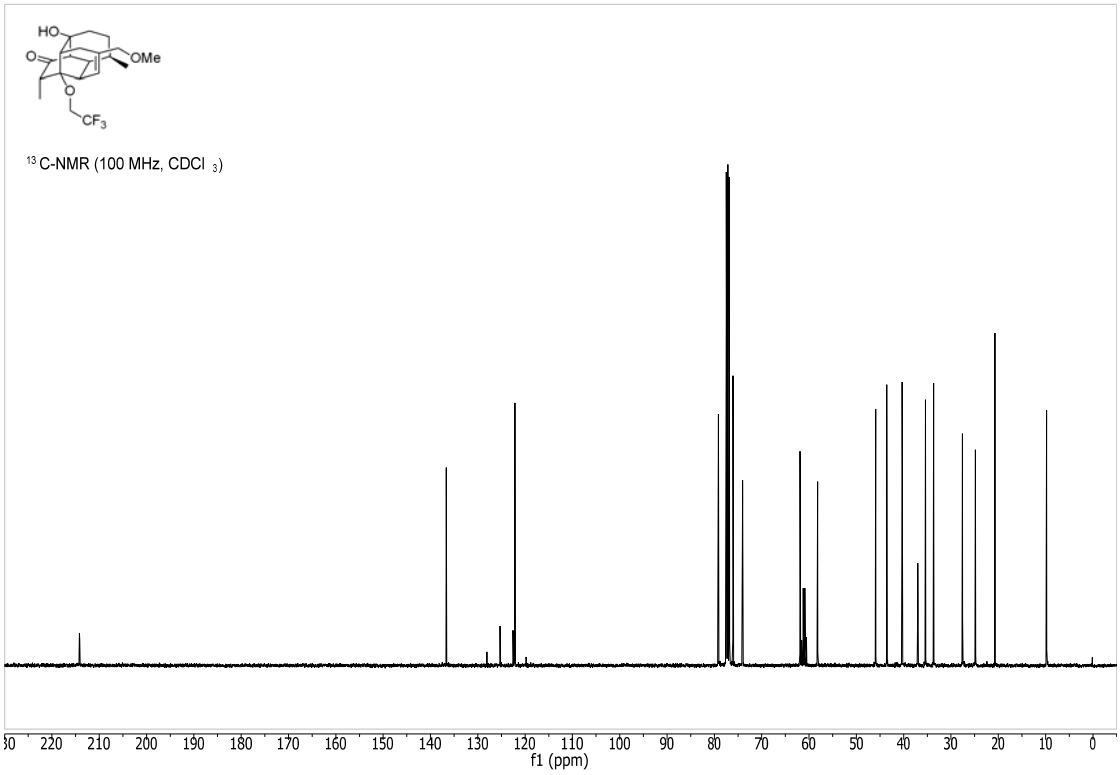


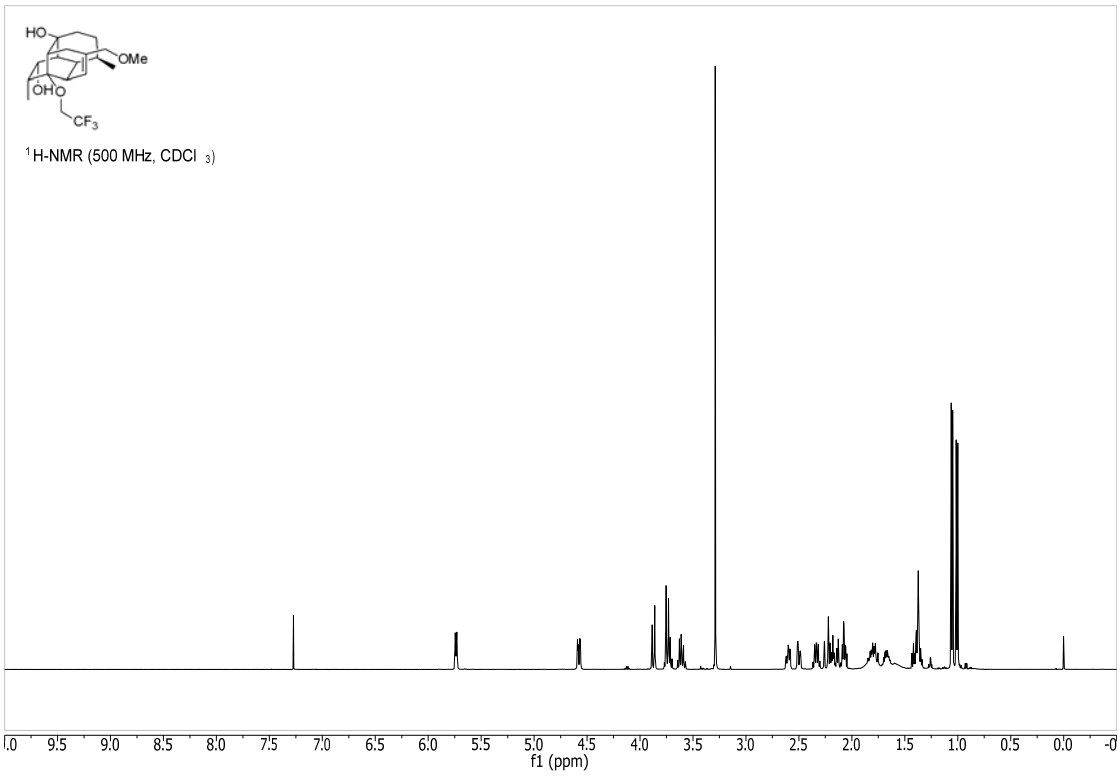


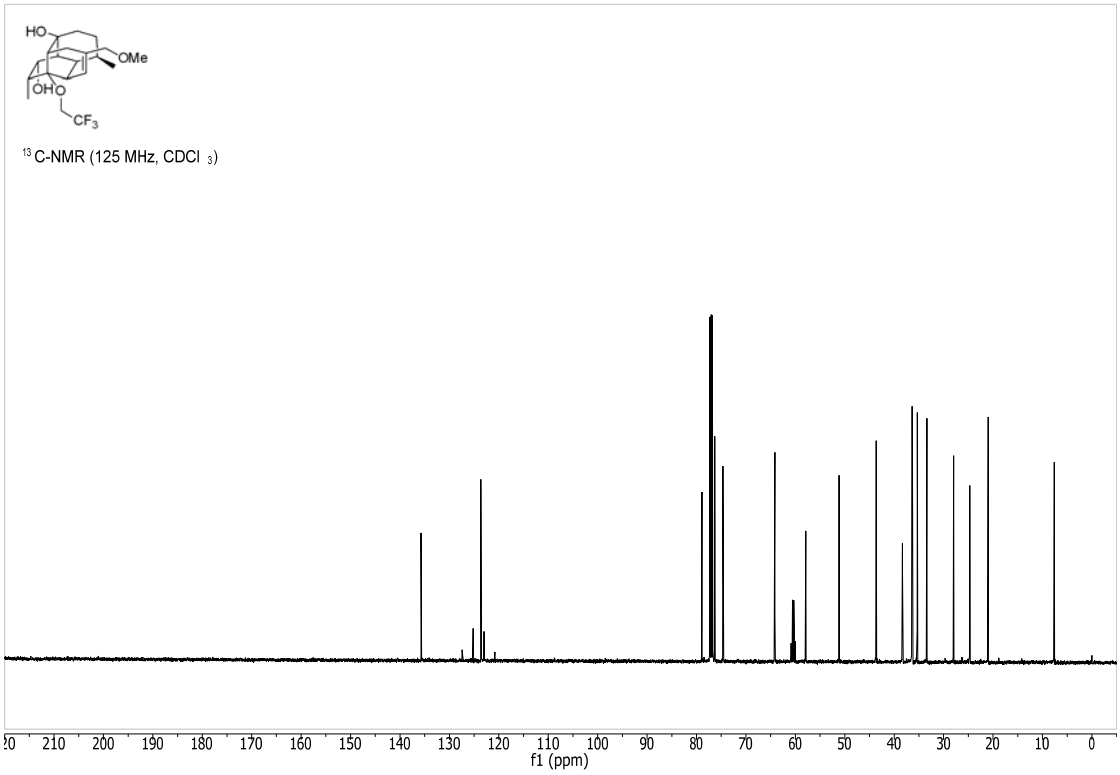


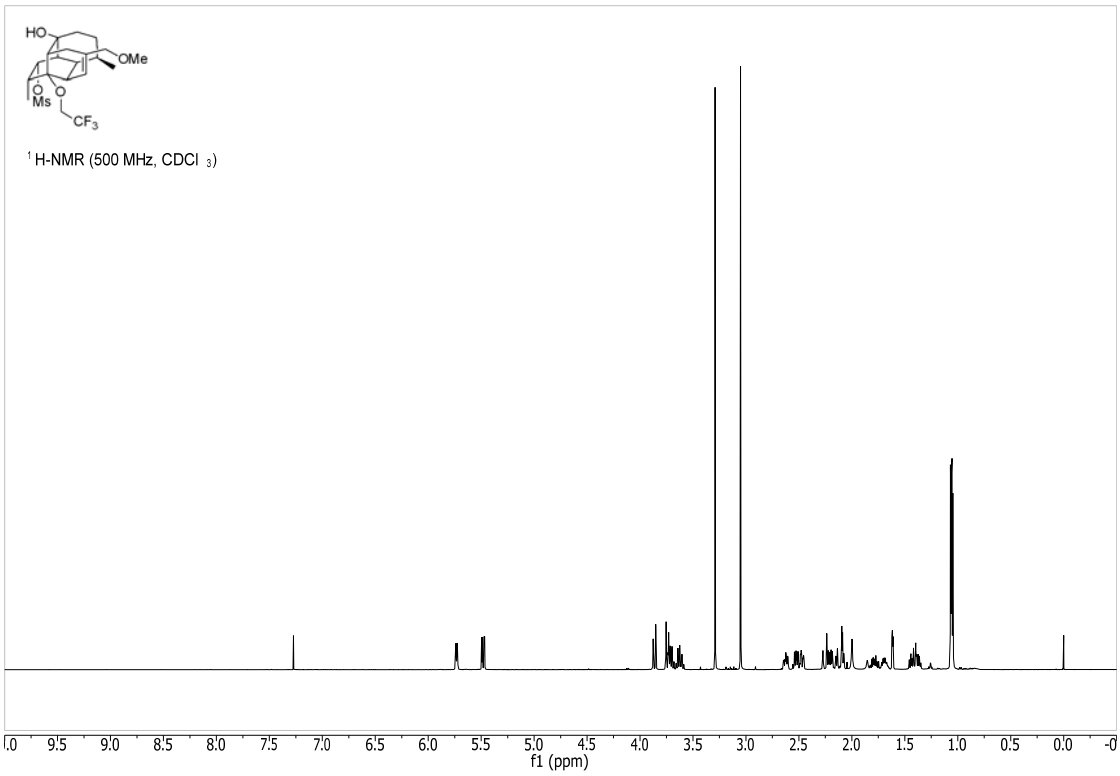


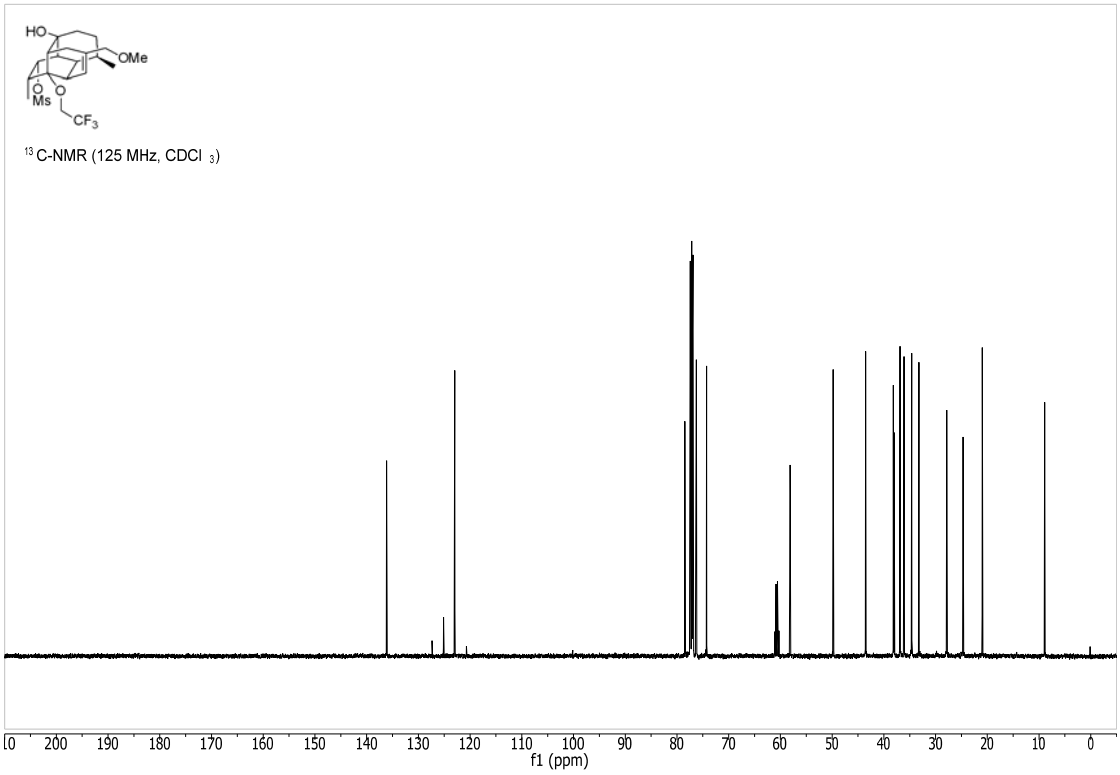


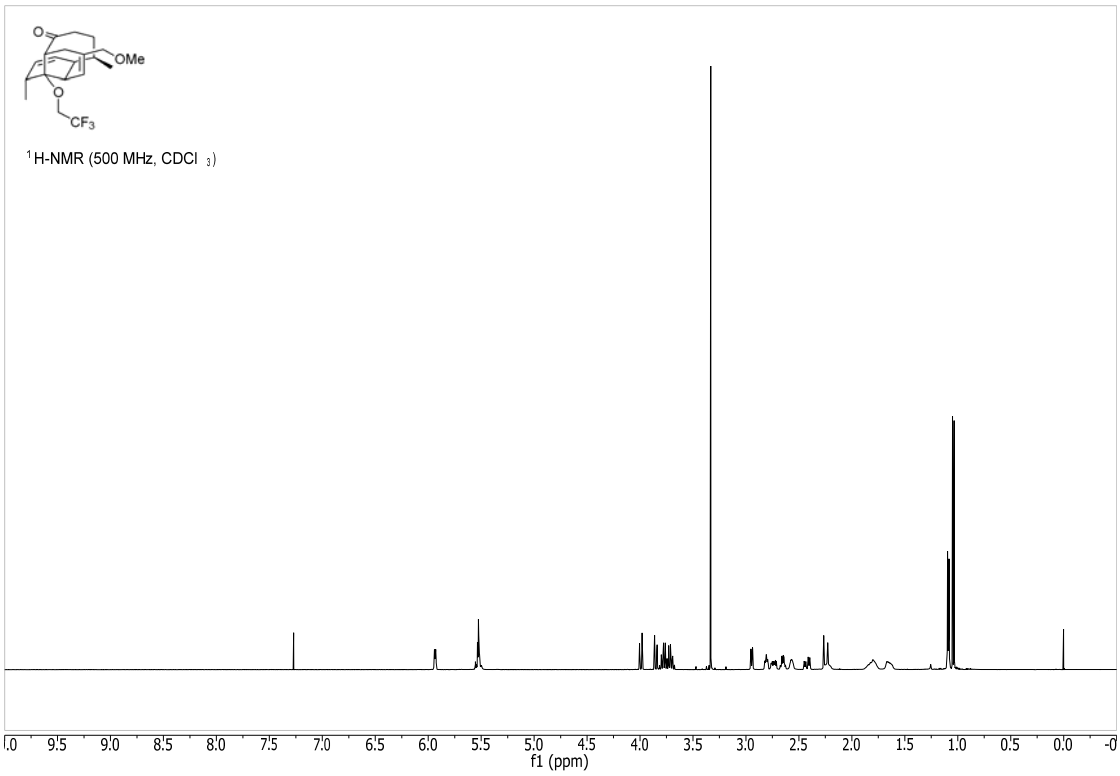








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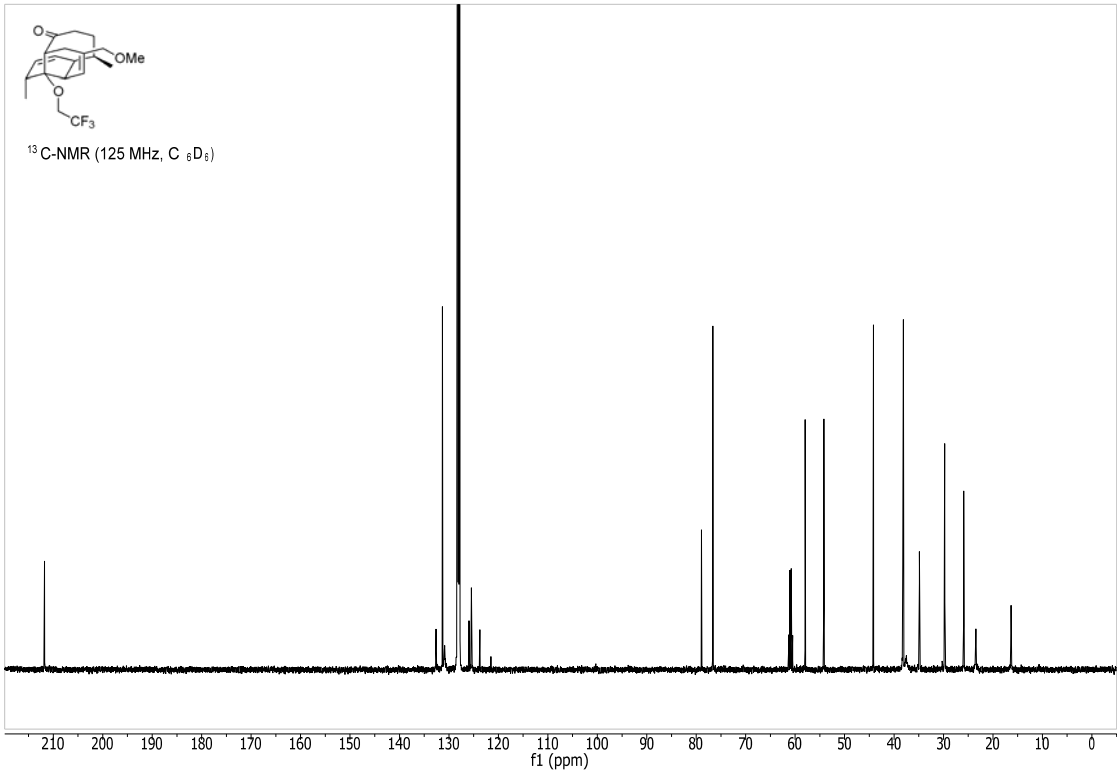
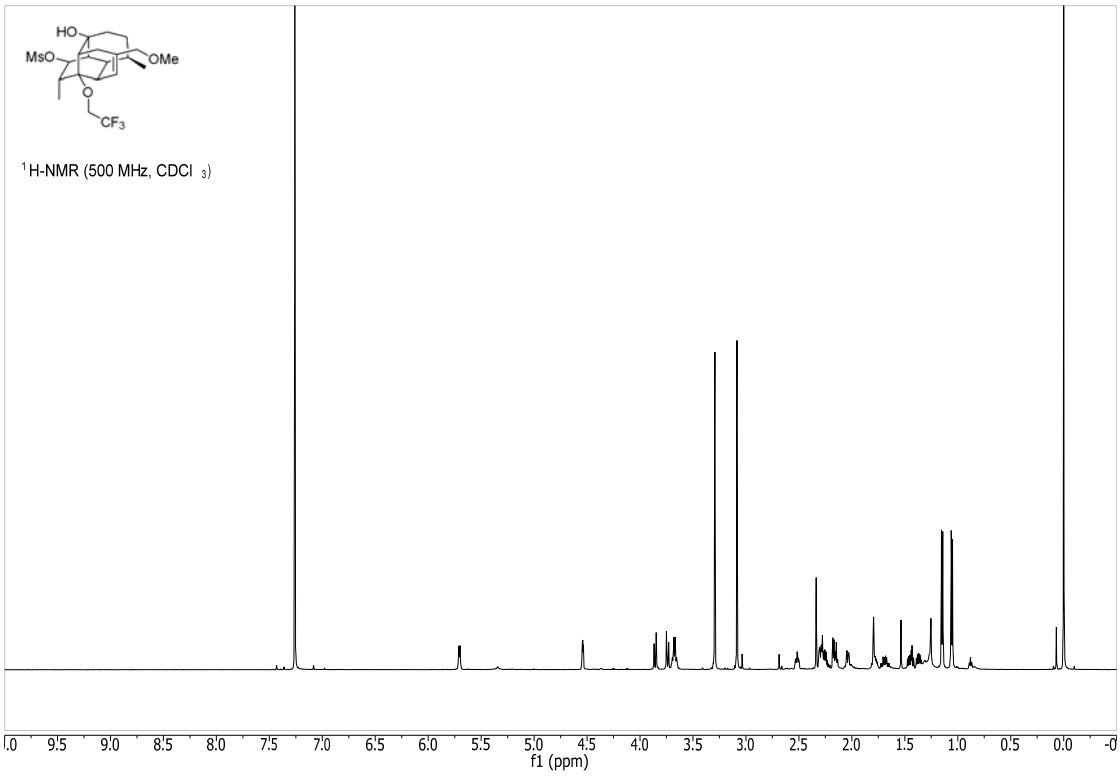
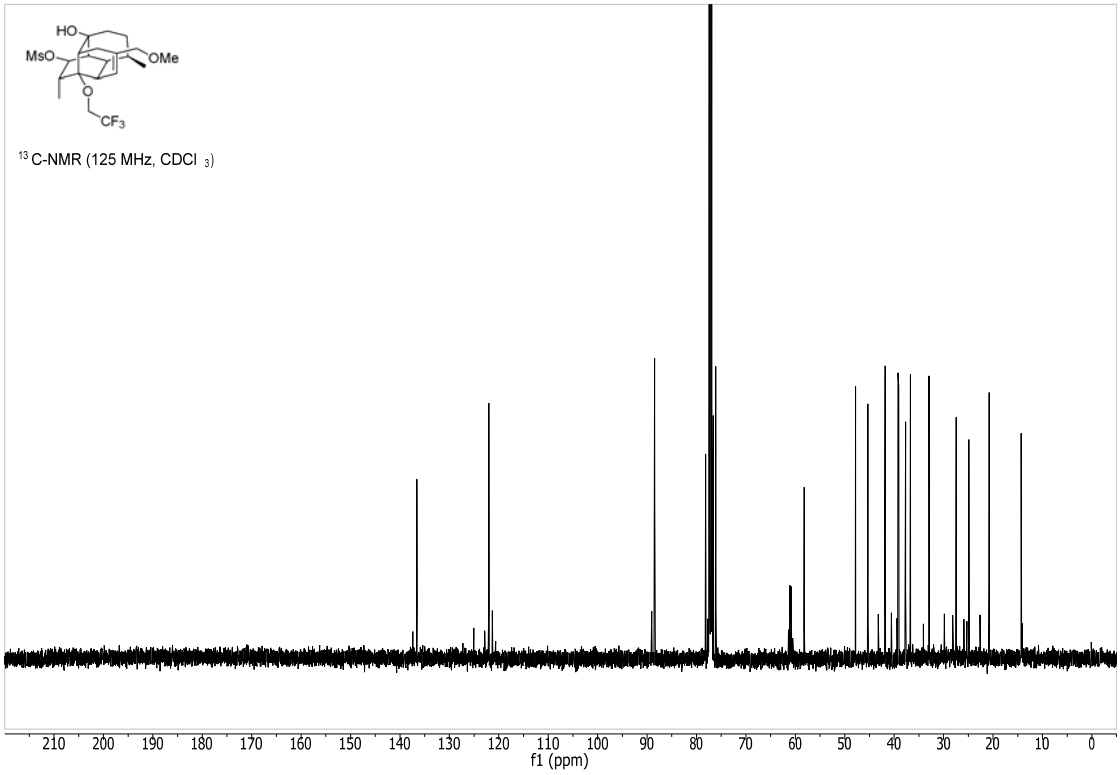
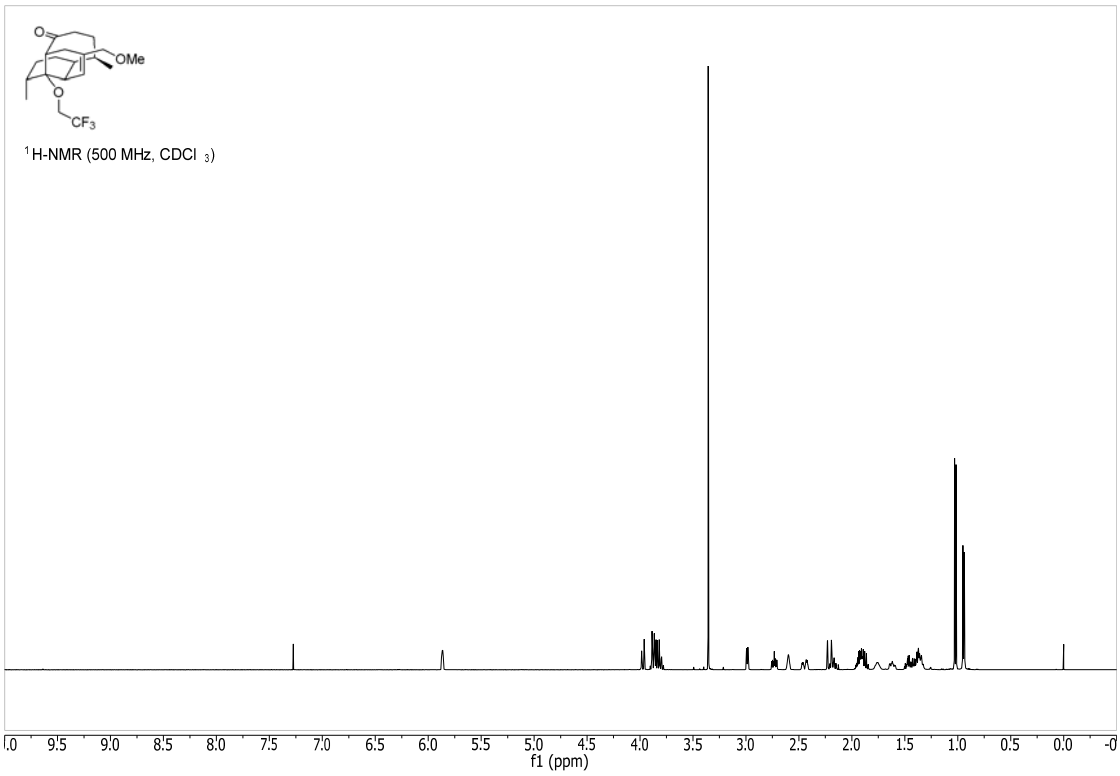
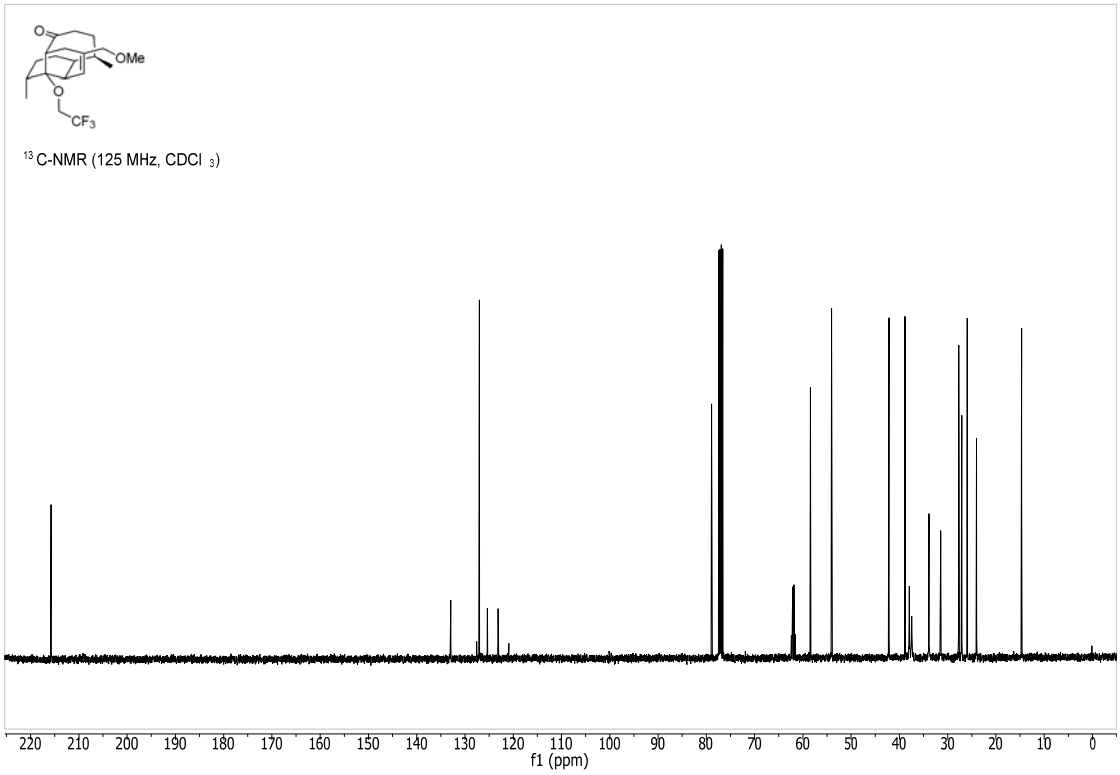
CF3
1H-NMR (500 MHz, CDCl 3)
f1 (ppm)

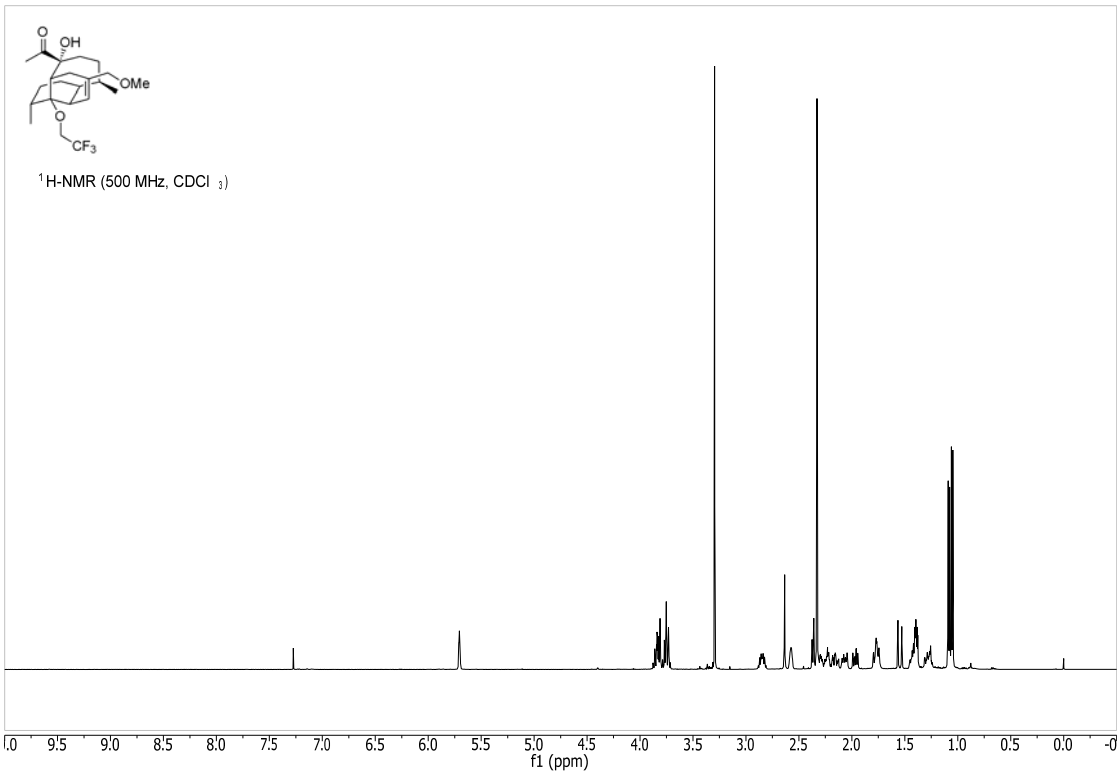

OMe
O
CF3
13C-NMR (125 MHz, C 6D6)
f1 (ppm)

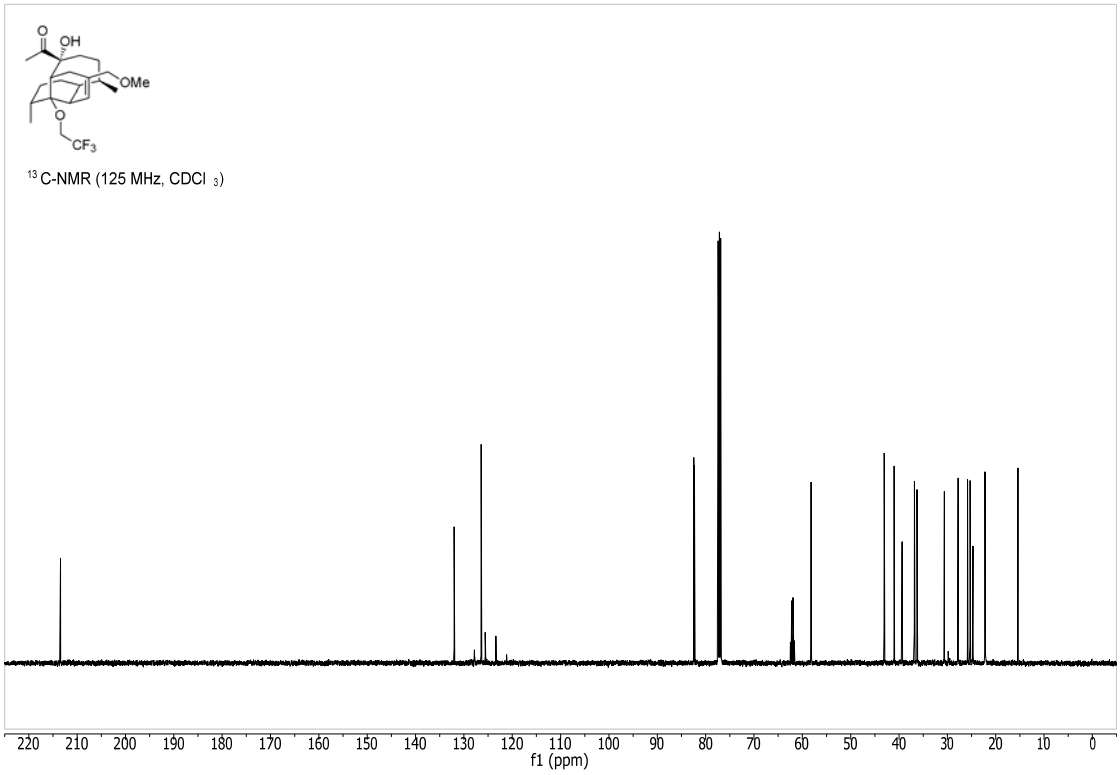


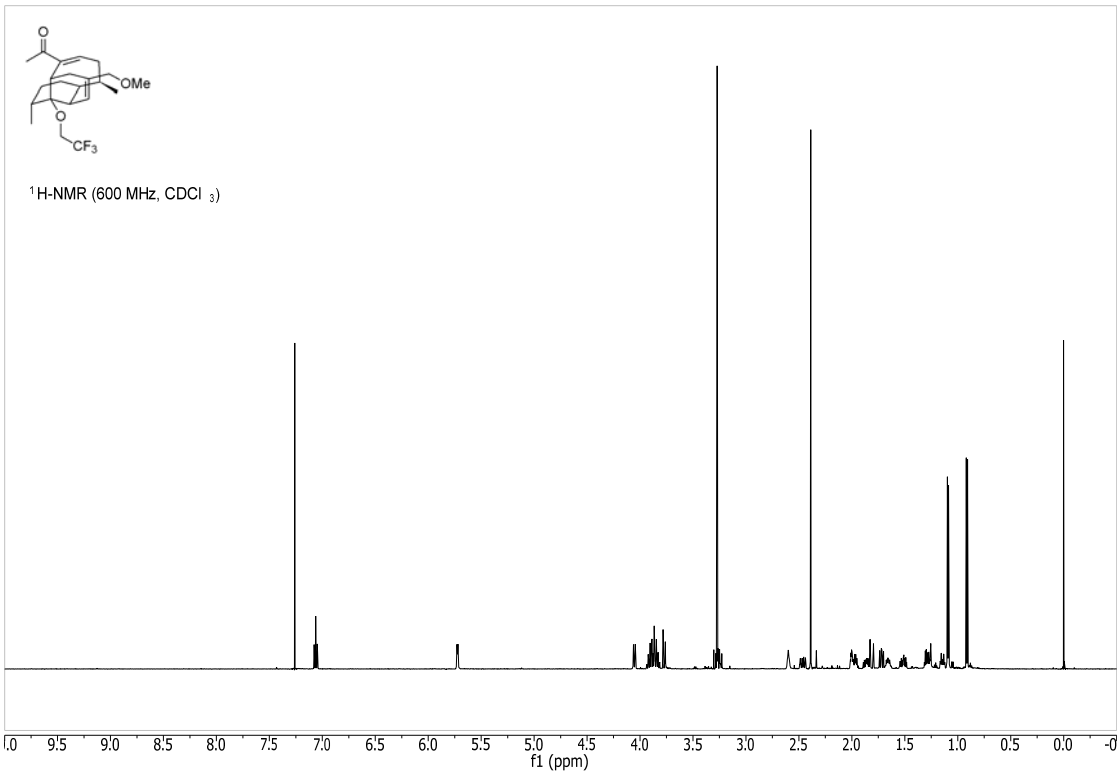








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CF3
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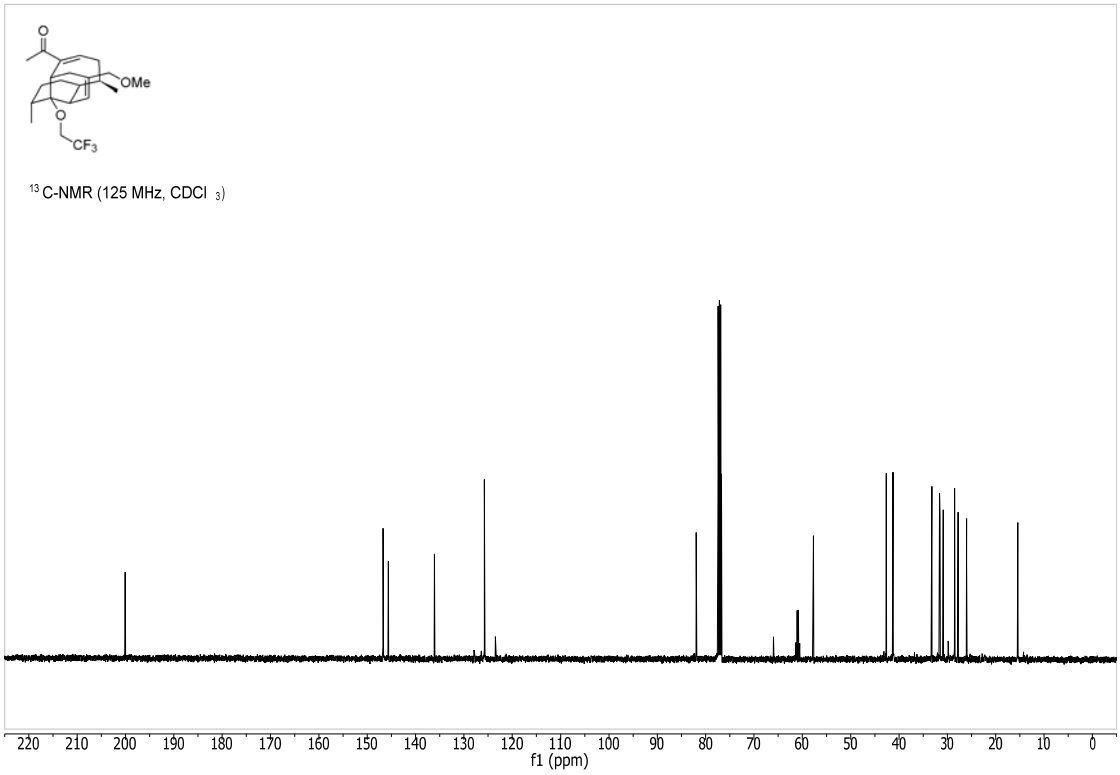
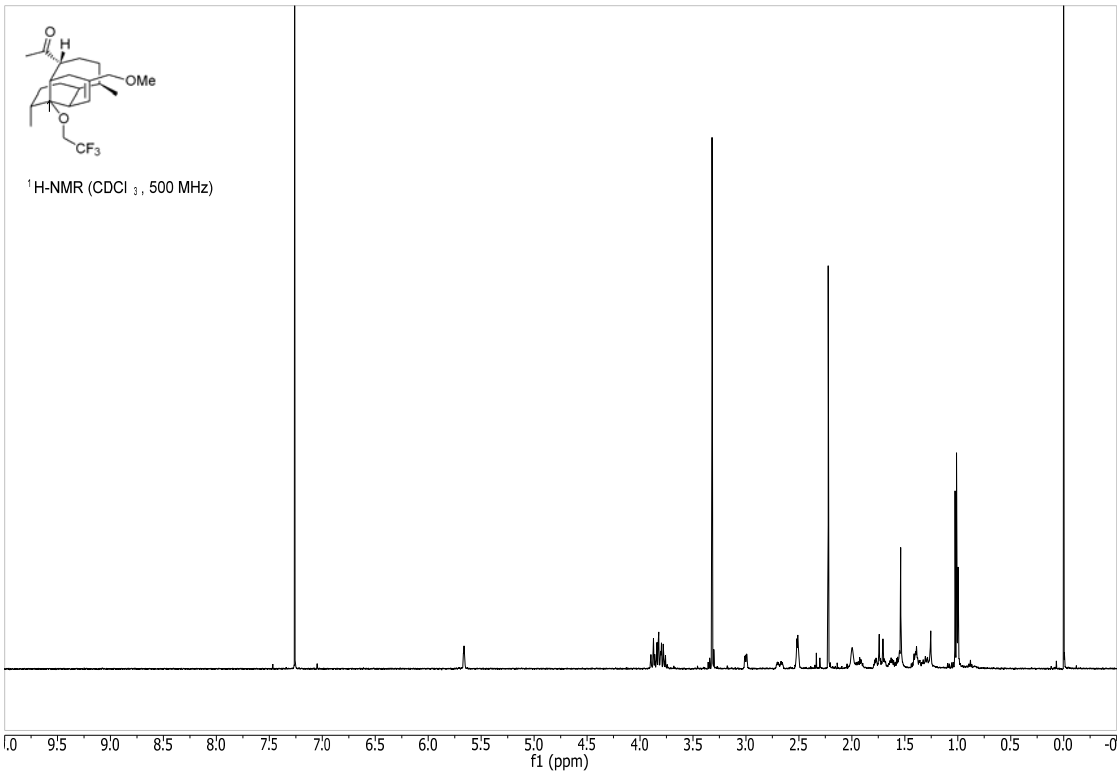
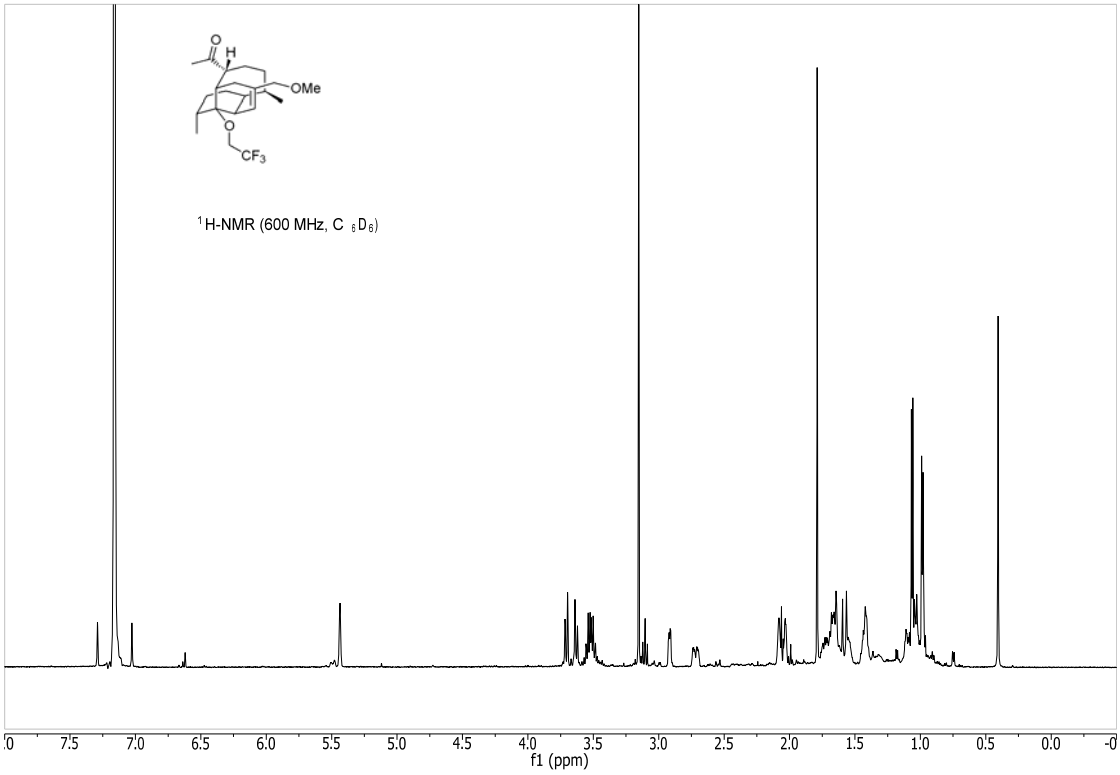
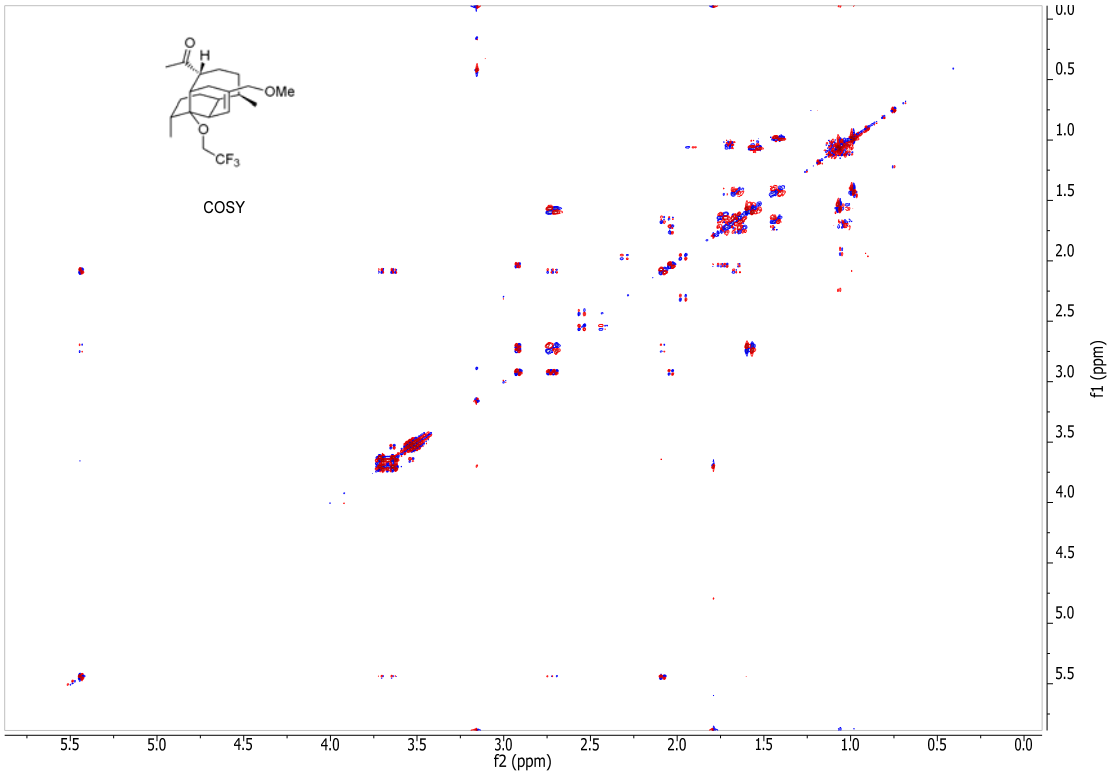
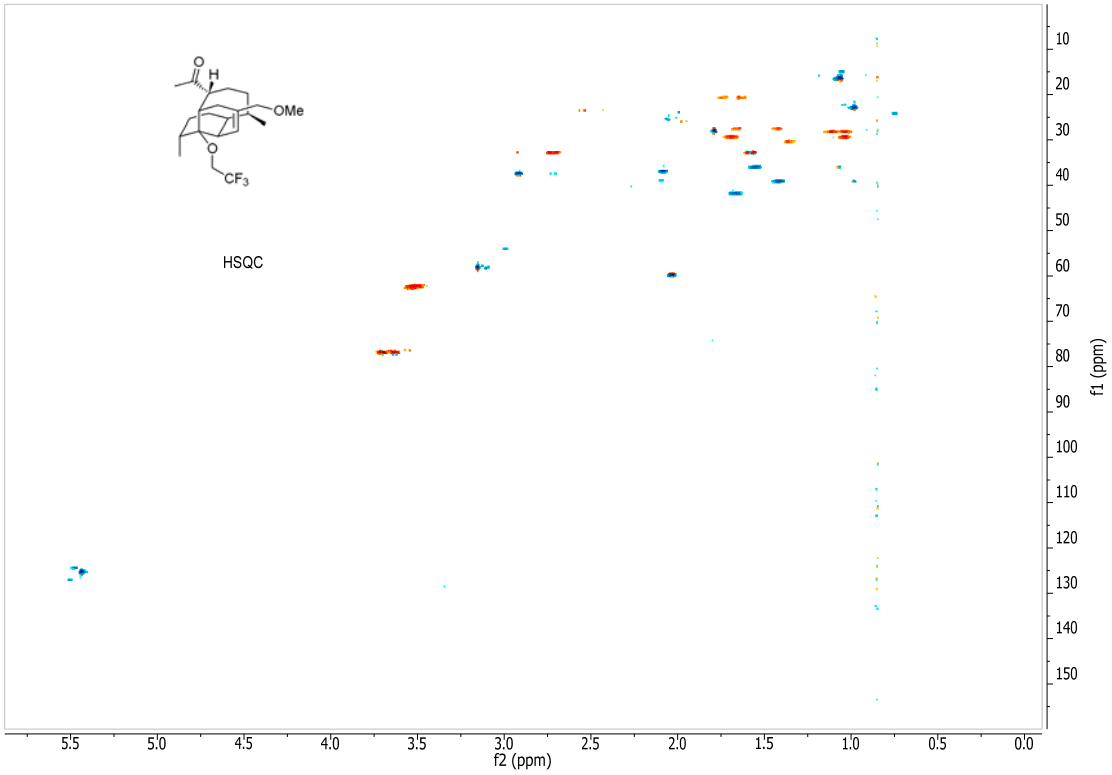
f1 (ppm)

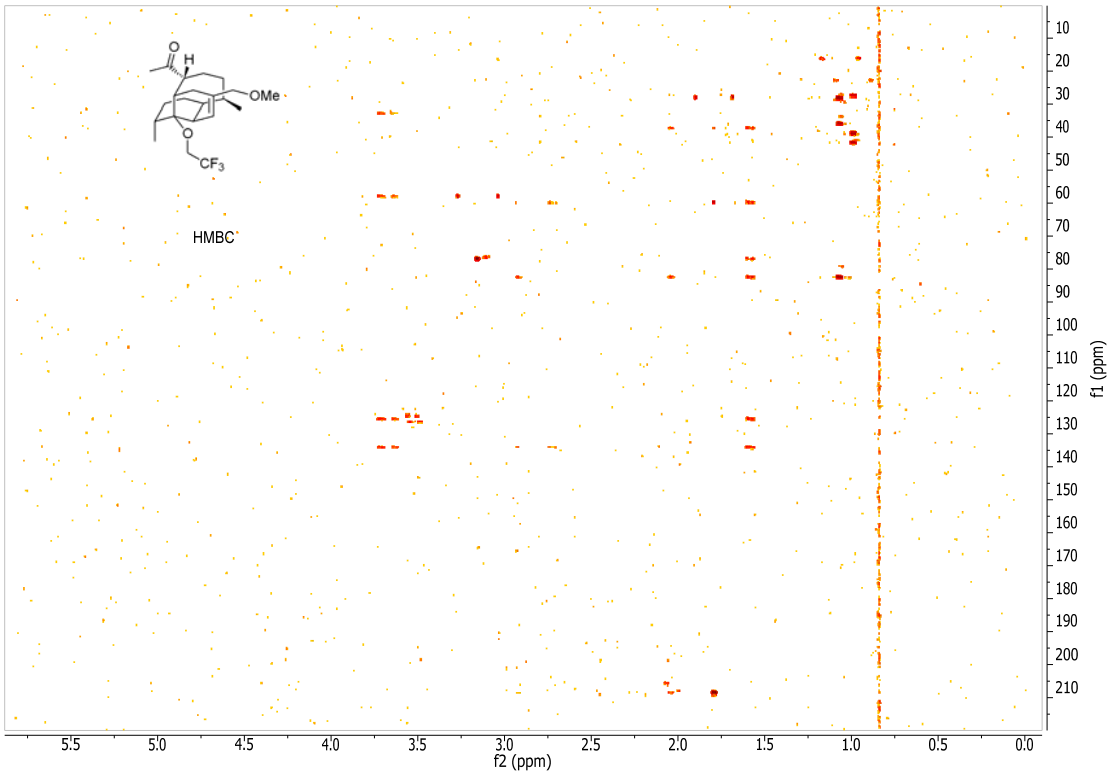

OMe
CF3
13C-NMR (125 MHz, CDCl 3)
f1 (ppm)











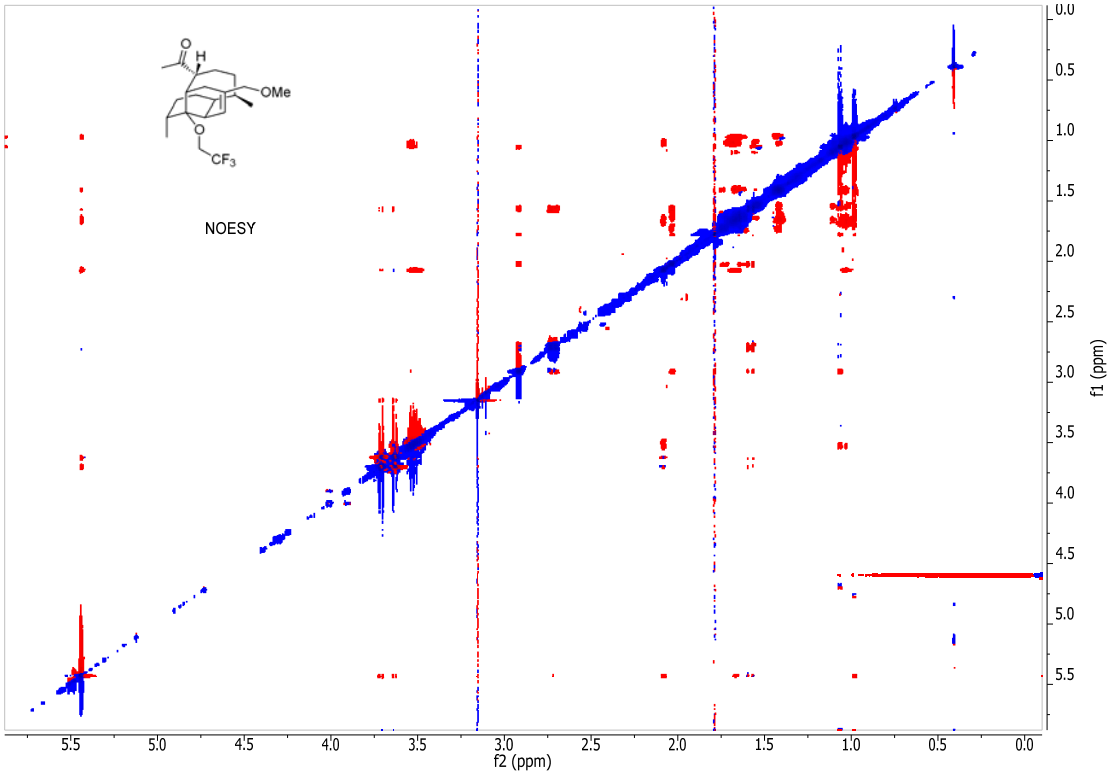
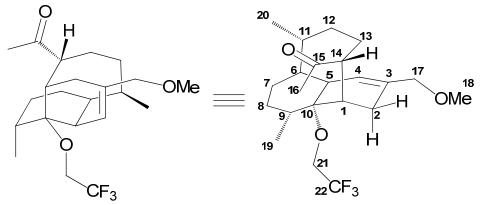
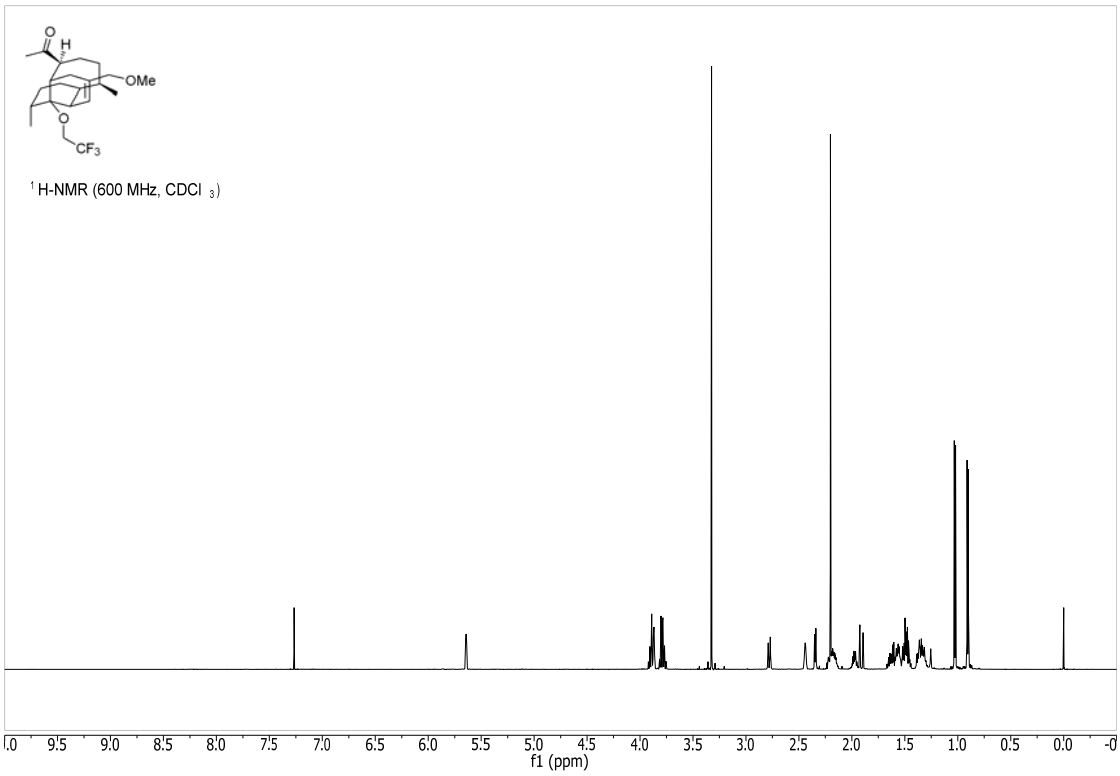
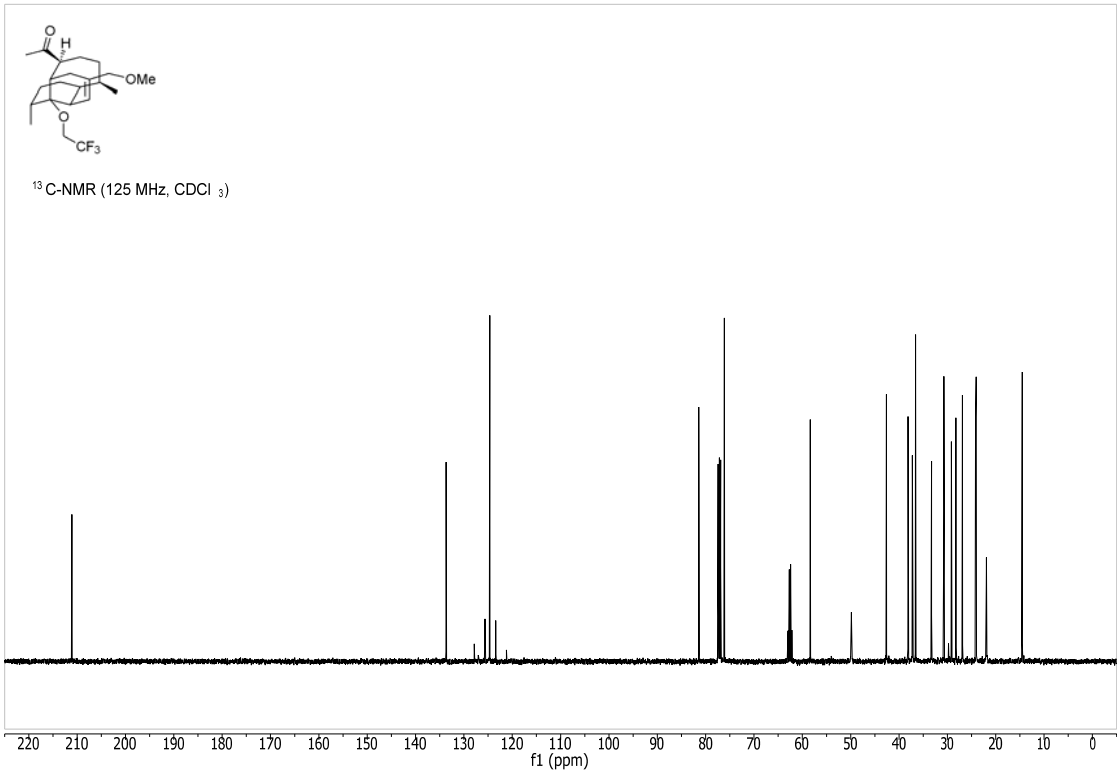


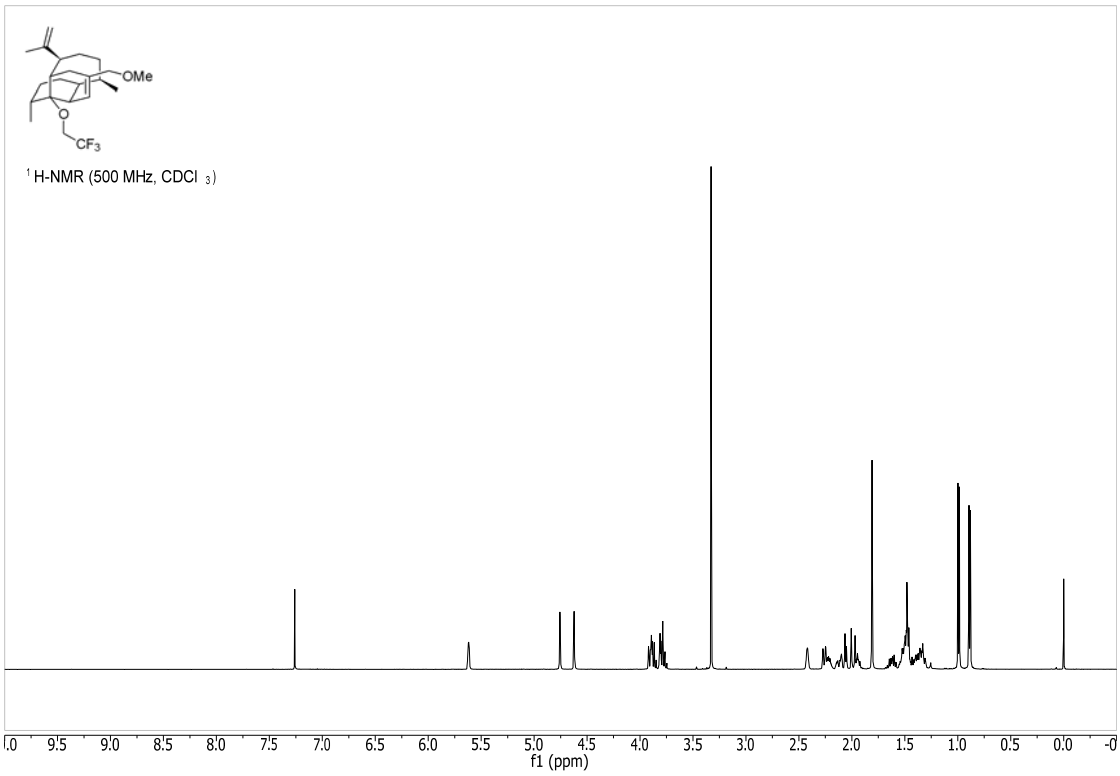
Table 11. 2D-NMR Data of Compound **141**

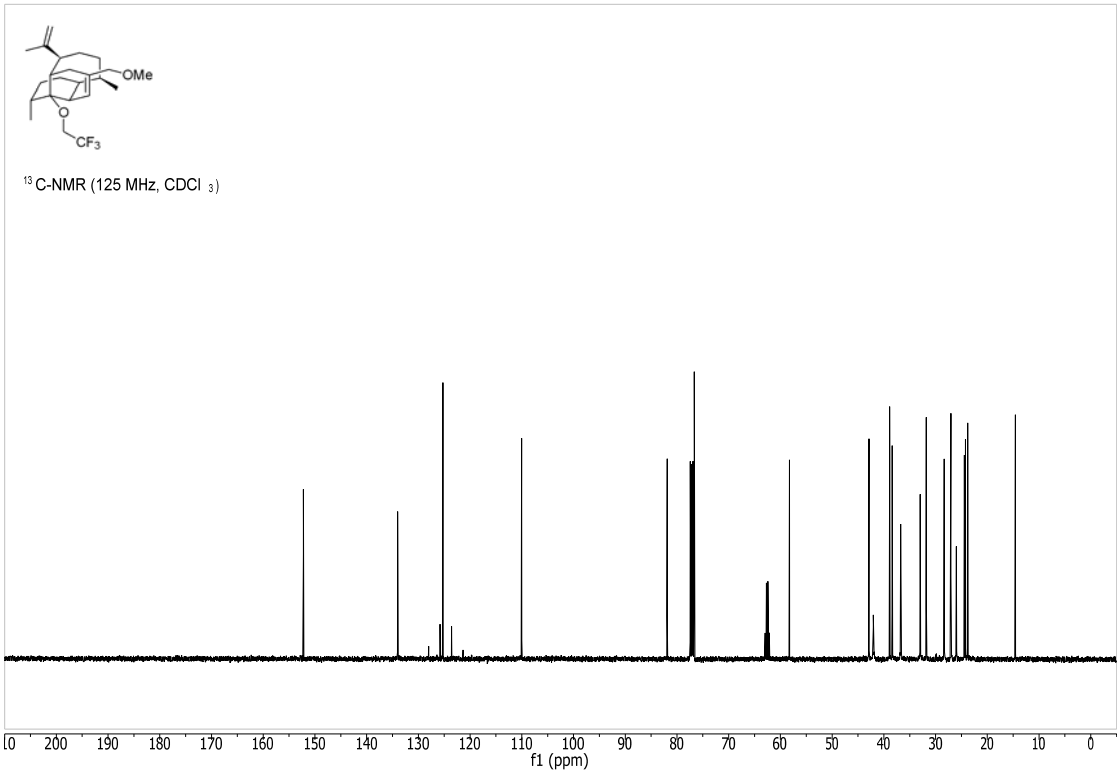


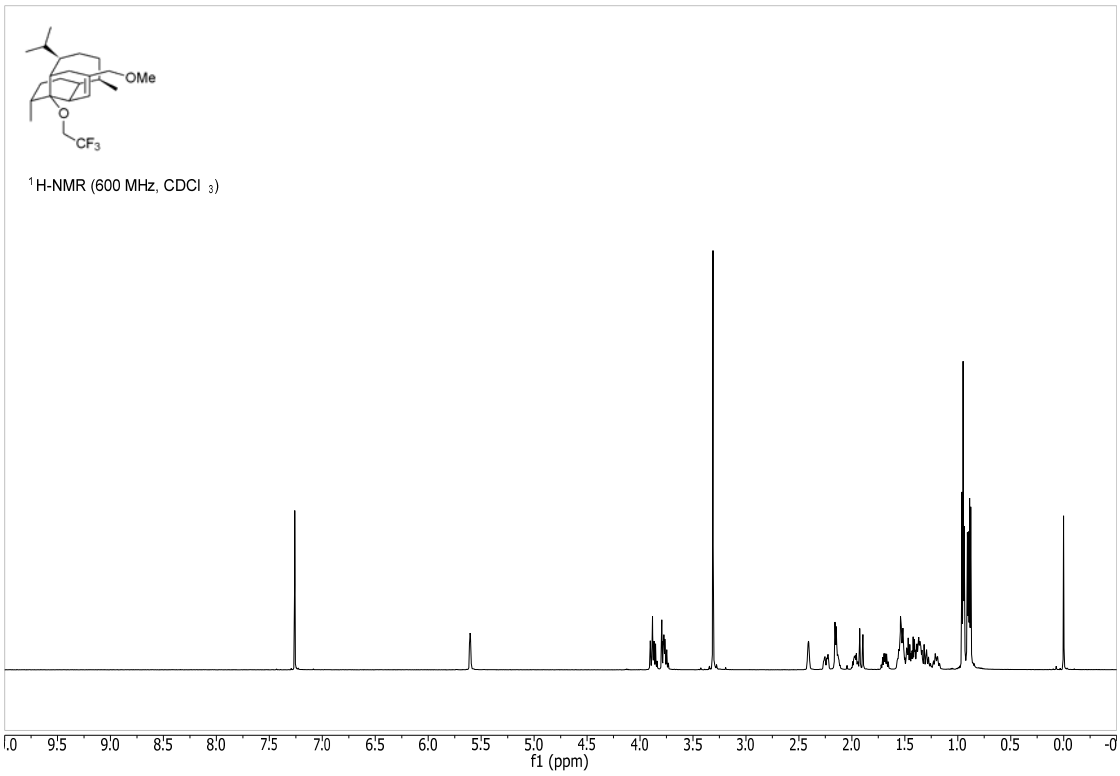
Position	δ 13C (ppm)	δ 1H (ppm)	Type	COSY correlations	HMBC correlations	ROESY correlations
1	37.54	2.92	CH	H-2, H-14	C-3, C-10	H-14, H-16, H-2a, H-19
2a	32.83	1.58	CH_2	H-2b	C-3, C-4, C-10, C-17, C-14, C-5	H-17a, H-17b, H-1, H-2b, H-14
2b		2.72		H-4, H-1, H-5, H-2a	C-3, C-14	H-2a
3	134.38		Cq			
4	125.35	5.44	CH	H-17a, H-17b, H-2b, H-5		H-17a, H-17b, H-5, H-6, H-12a, H-13a
5	37.05	2.08	CH	H-4, H-17a, H-17b, H-2b, H-6		H-4, H-21b, H-6, H-7, H-8
6	41.78	1.66	CH			H-4, H-5, H-12a, H-7a, H-20
7a	29.64	1.02	CH_2	H-8b, H-7b		
7b		1.68		H-8a, H-7a		
8a	28.23	1.04	CH_2	H-9, H-7b, H-8b		
8b		1.11		H-8a		H-9, H-7b
9	36.04	1.55	CH	H8a		
10	82.38		Cq			
11	39.07	1.42	CH	H-20		H-9
12a	27.63	1.43	CH_2	H-12b, H-13b		H-13b, H-12b
12b		1.66		H-12a		
13a	20.82	1.62	CH_2	H-13b		
13b		1.74		H-14, H-13a, H-12a		H-14, H-12a
14	59.97	2.04	CH	H-1, H-13a, H-13b	C-15, C-10, C-1	H-1, H-13b, H-13a, H-2a
15	208.61		Cq			
16	28.00	1.79	CH_3		C-14, C-15	
17a	77.04	3.63	CH_2	H-4, H-5	C-3, C-4, C-18, C-2	H-4, H-18, H-2a
17b		3.71		H-4, H-5	C-3, C-4, C-18, C-2	H-4, H-18, H-2a
18	58.18	3.15	CH_3		C-17	
19	16.41	1.06	CH_3	H-9	C-10, C-9, C-8	H-21b, H-1, H-16
20	22.91	0.99	CH_3	H-11	C-6, C-11, C-12	H-4
21a	62.48	3.49	CH_2			H-2b, H-5, H-8
21b		3.55				H-2b, H-5, H-8
22	125.63		Cq			

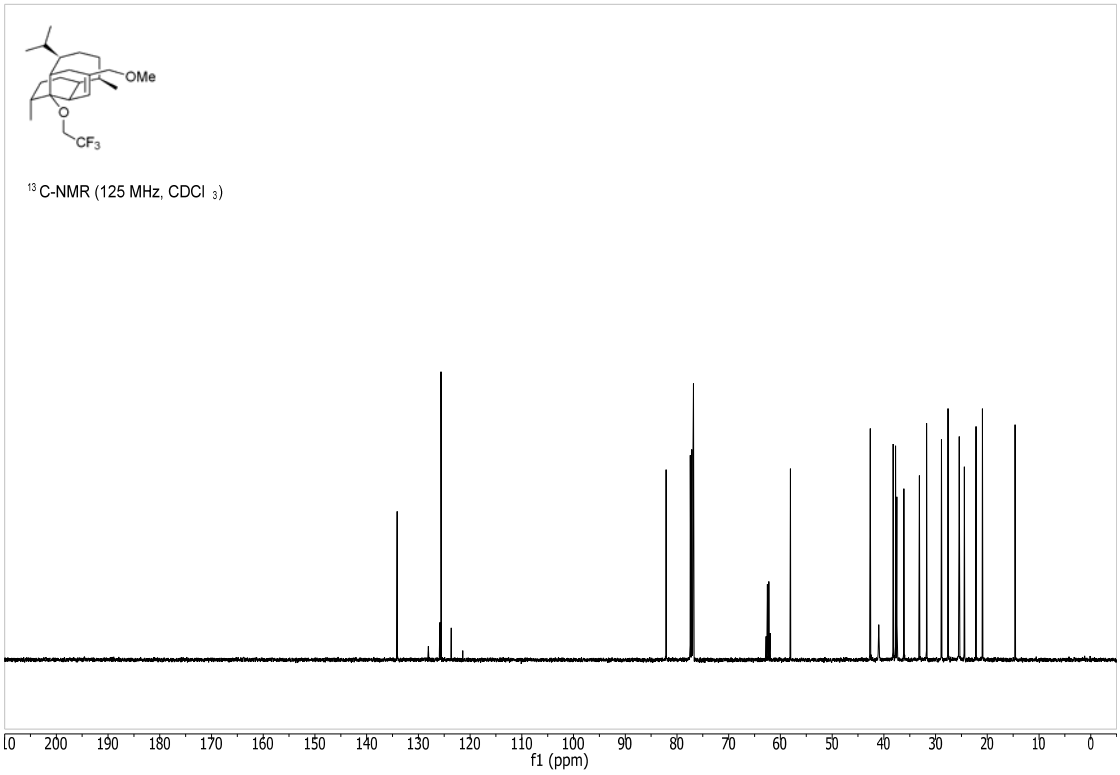

OMe
CF3
1 H-NMR (600 MHz, CDCl 3)
f1 (ppm)

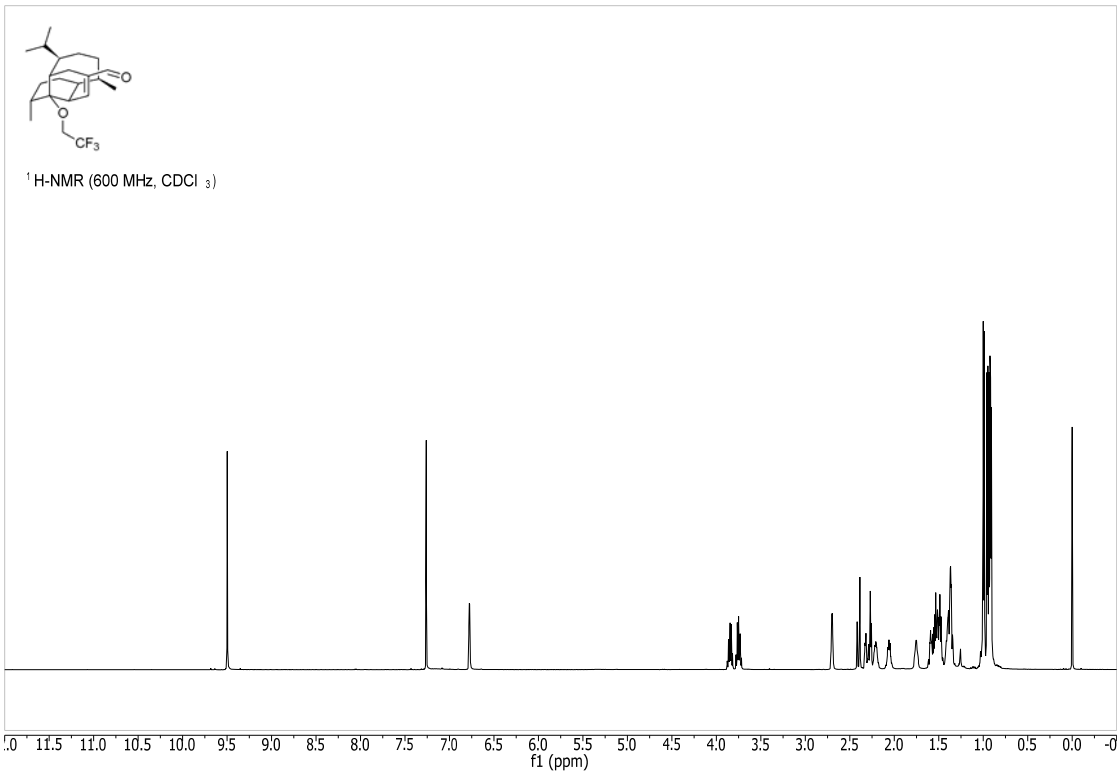

OMe
CF3
13 C-NMR (125 MHz, CDCl 3)
f1 (ppm)

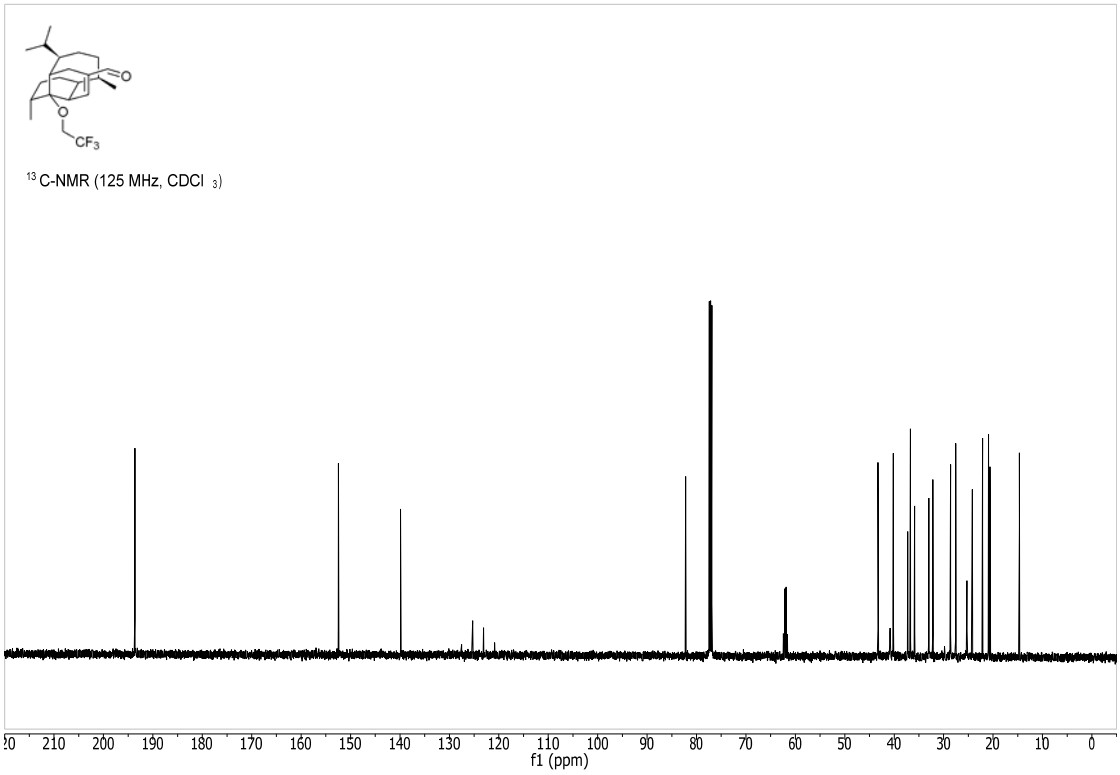


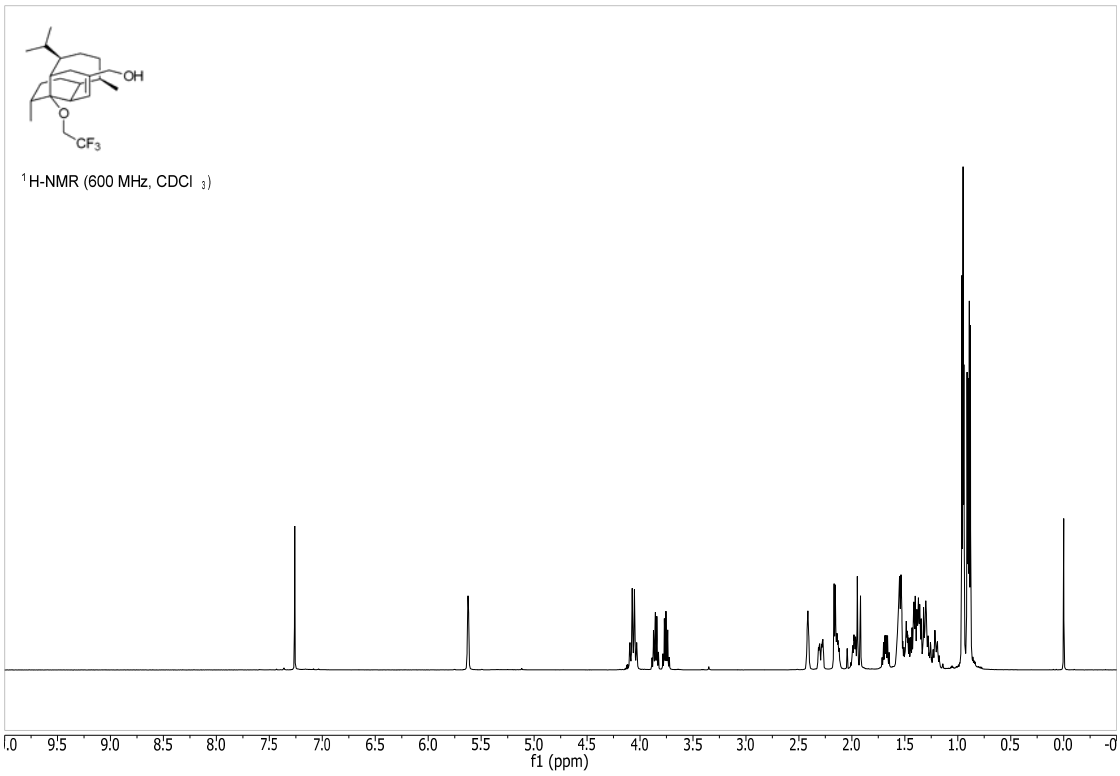


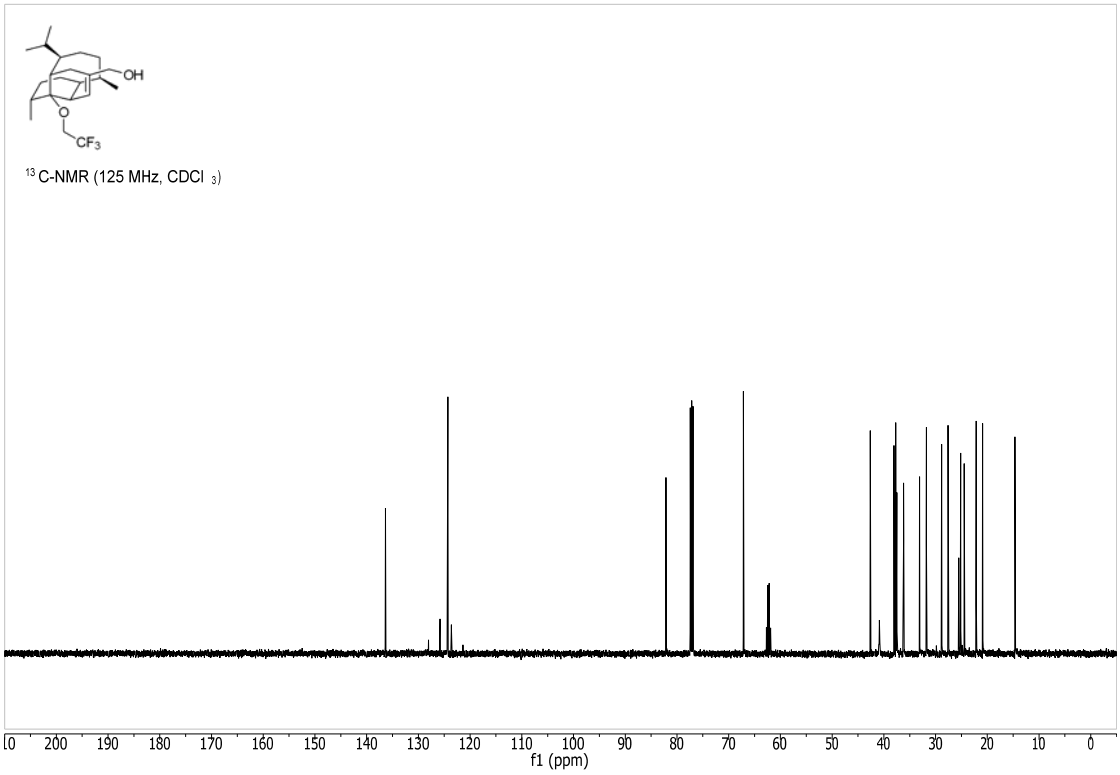

OMe
O
CF3
1H-NMR (600 MHz, CDCl 3)
f1 (ppm)

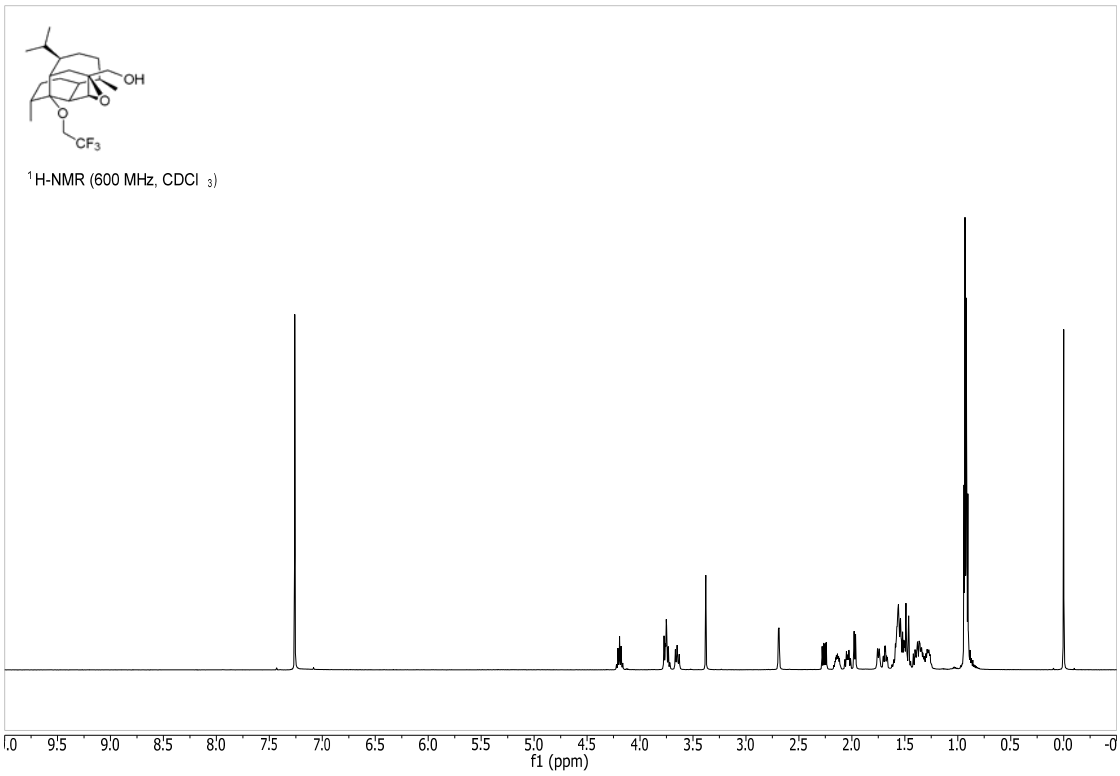

OMe
O
CF3
13C-NMR (125 MHz, CDCl 3)
f1 (ppm)

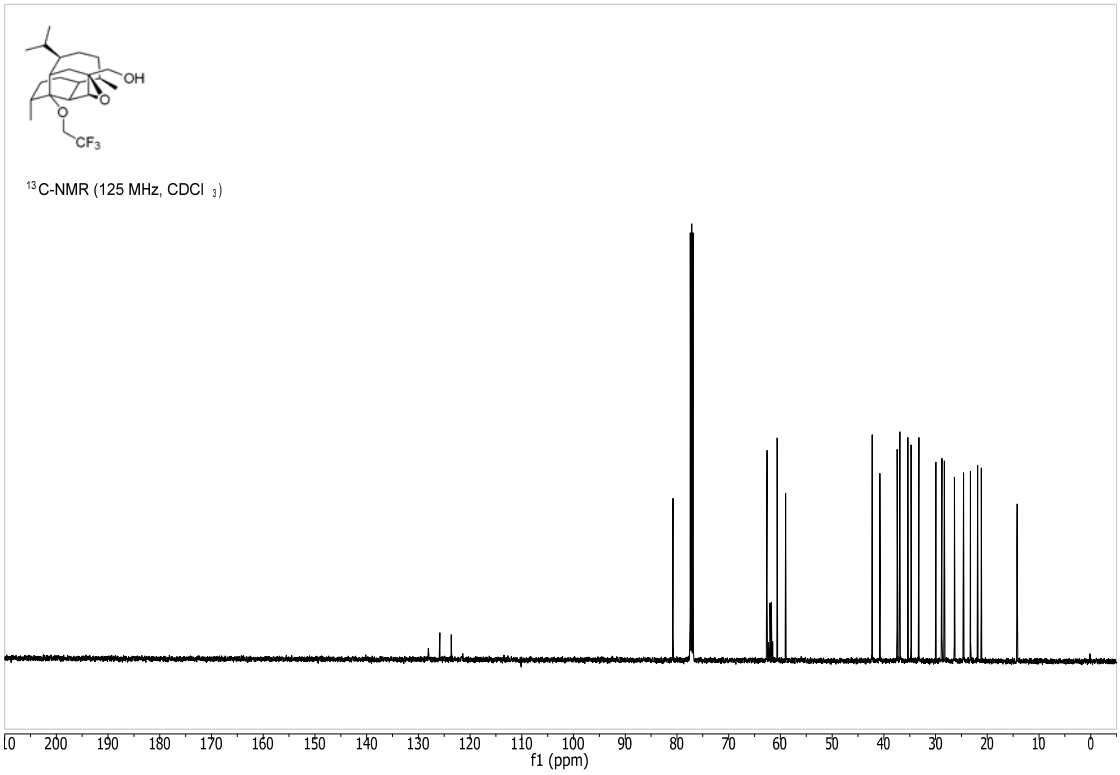


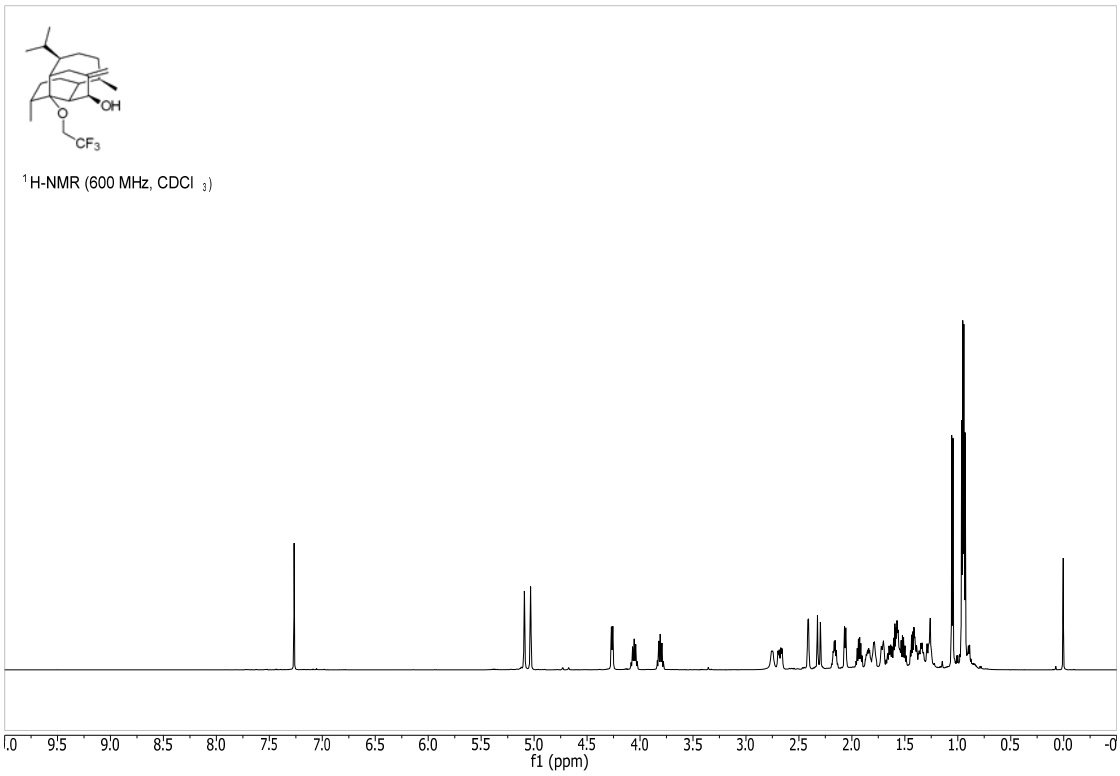


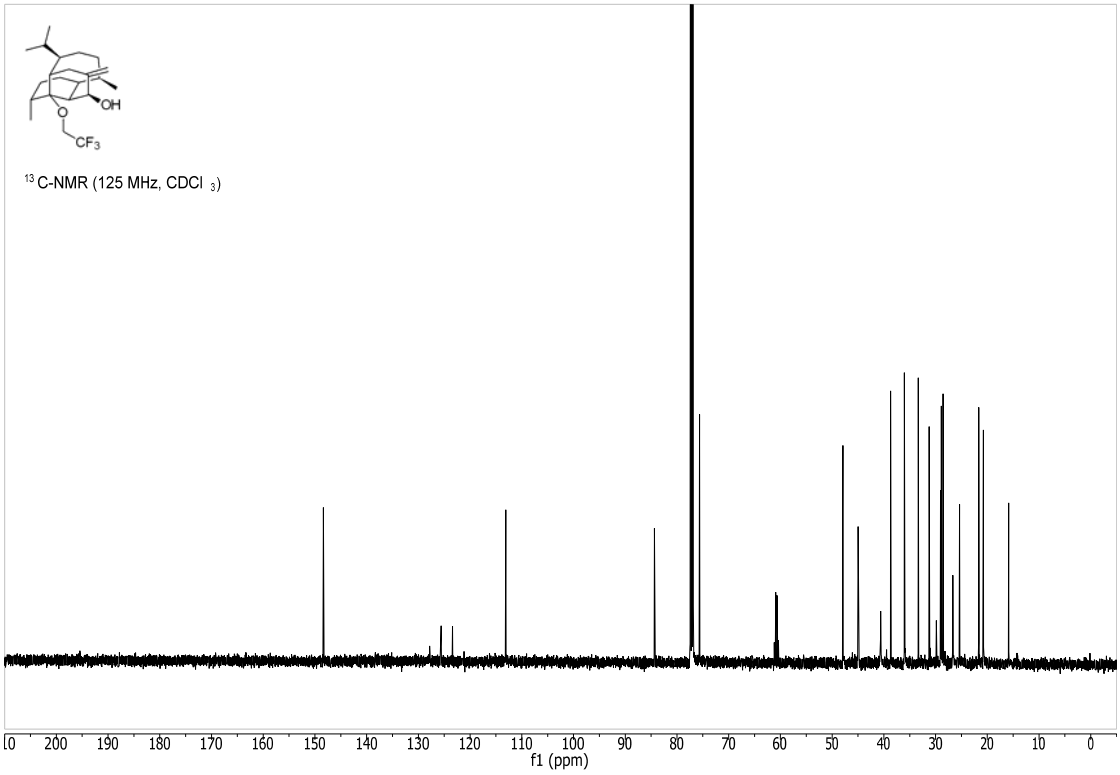


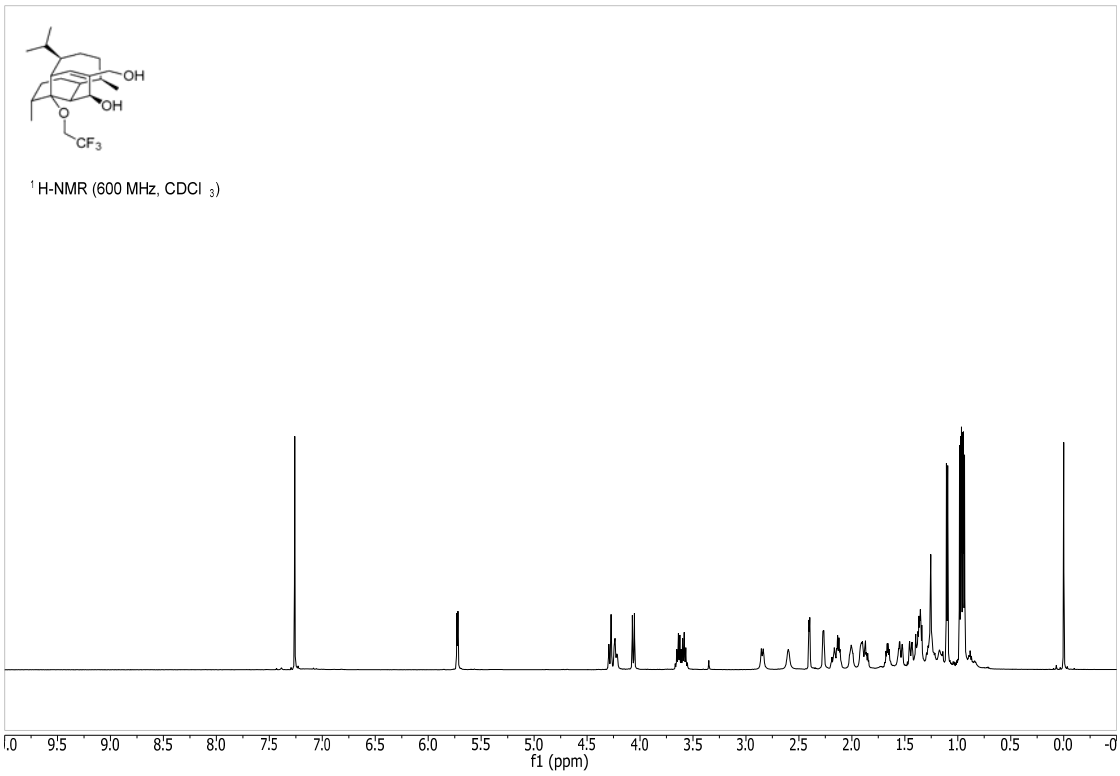


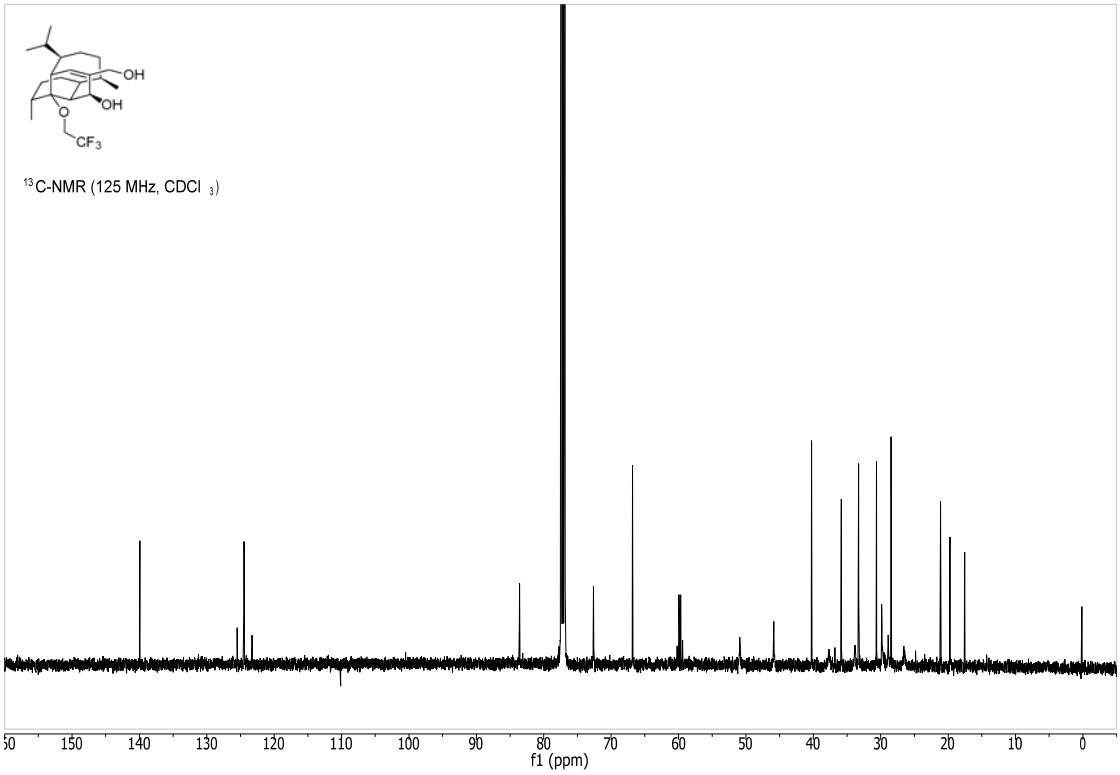


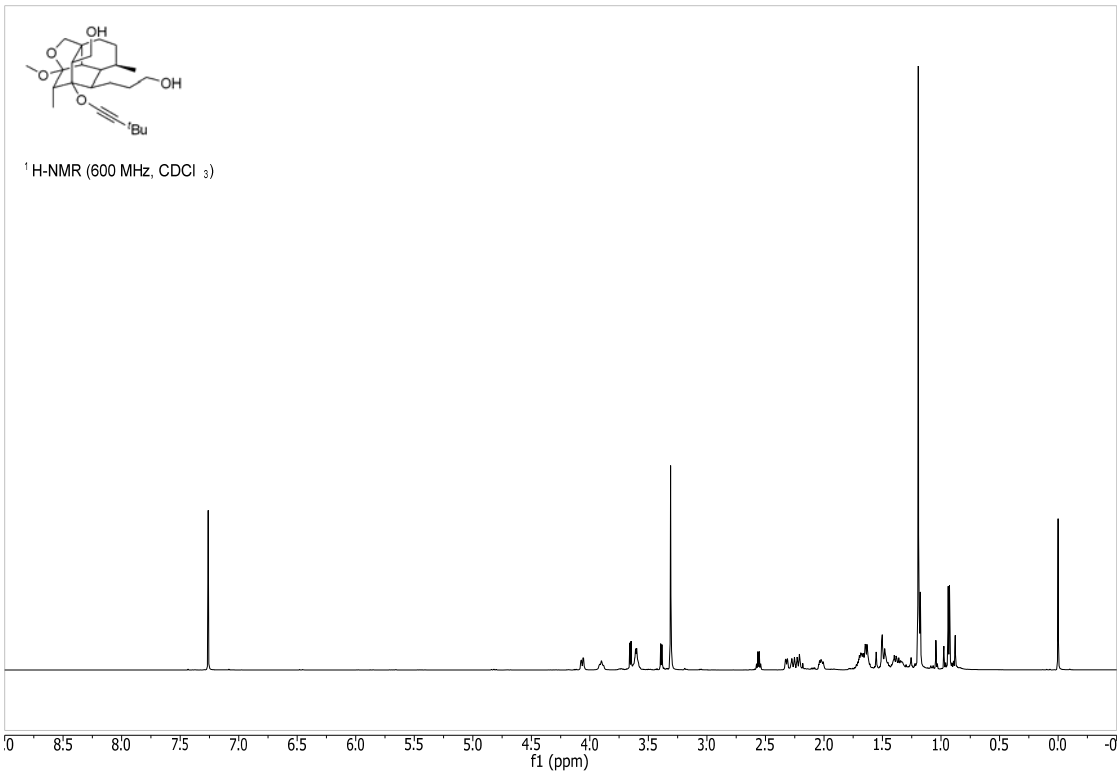


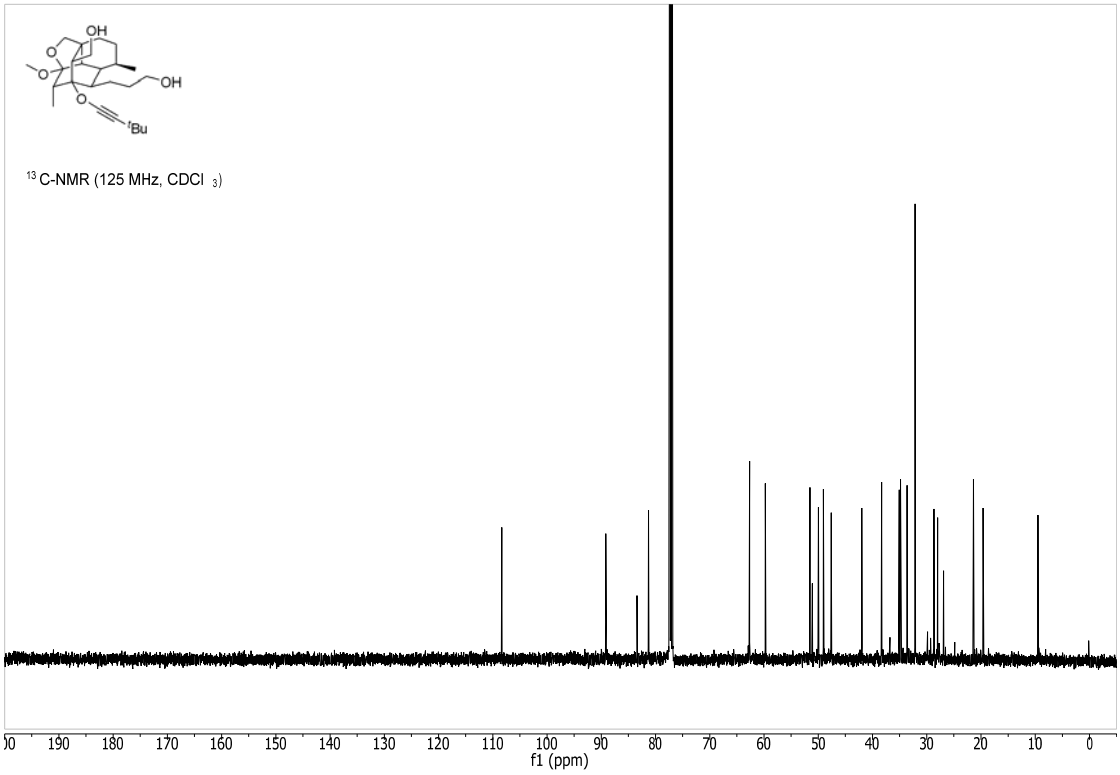


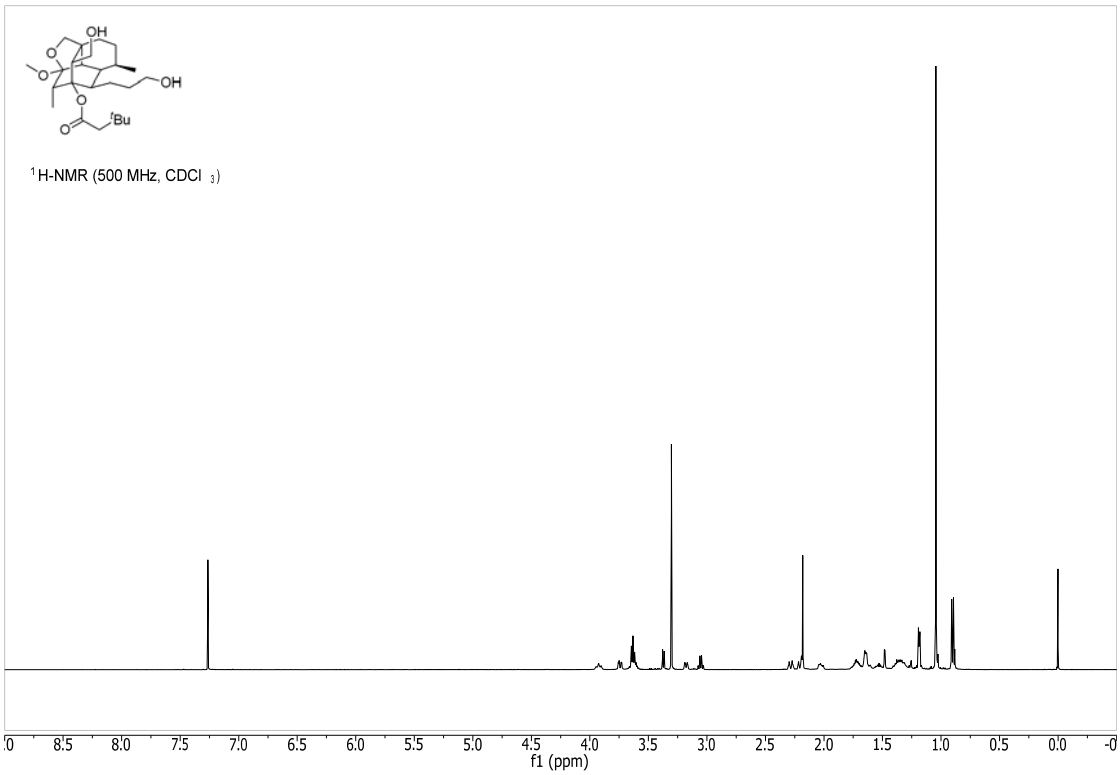


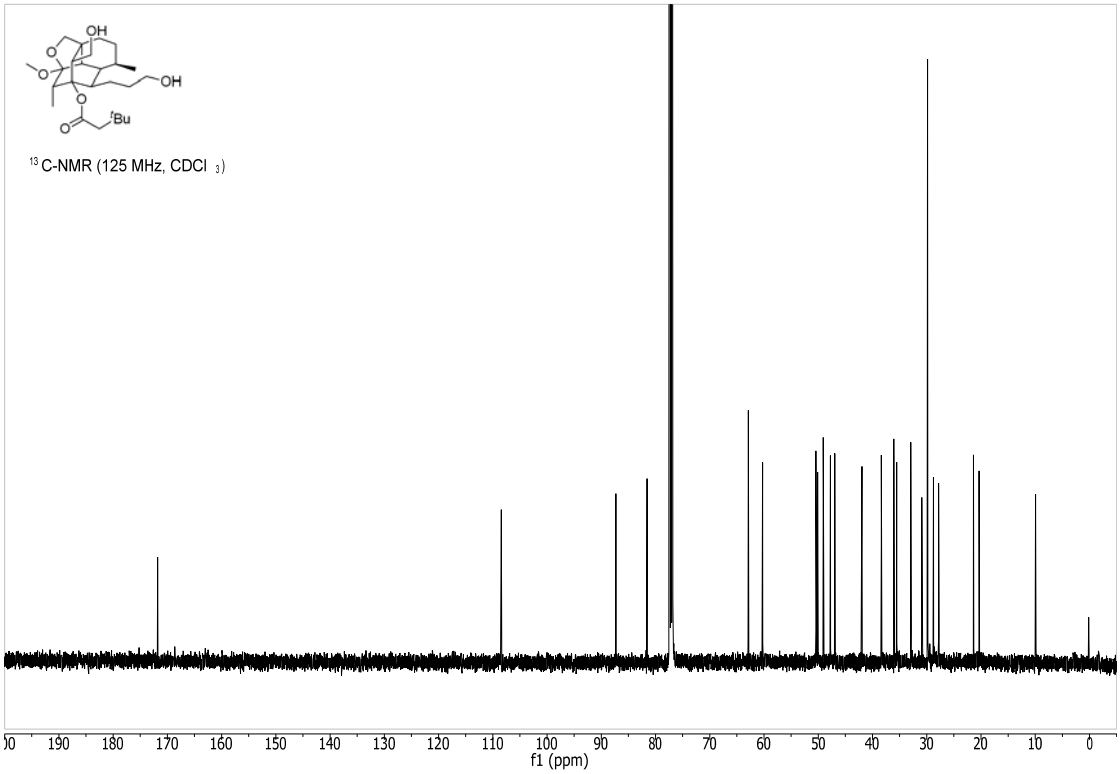


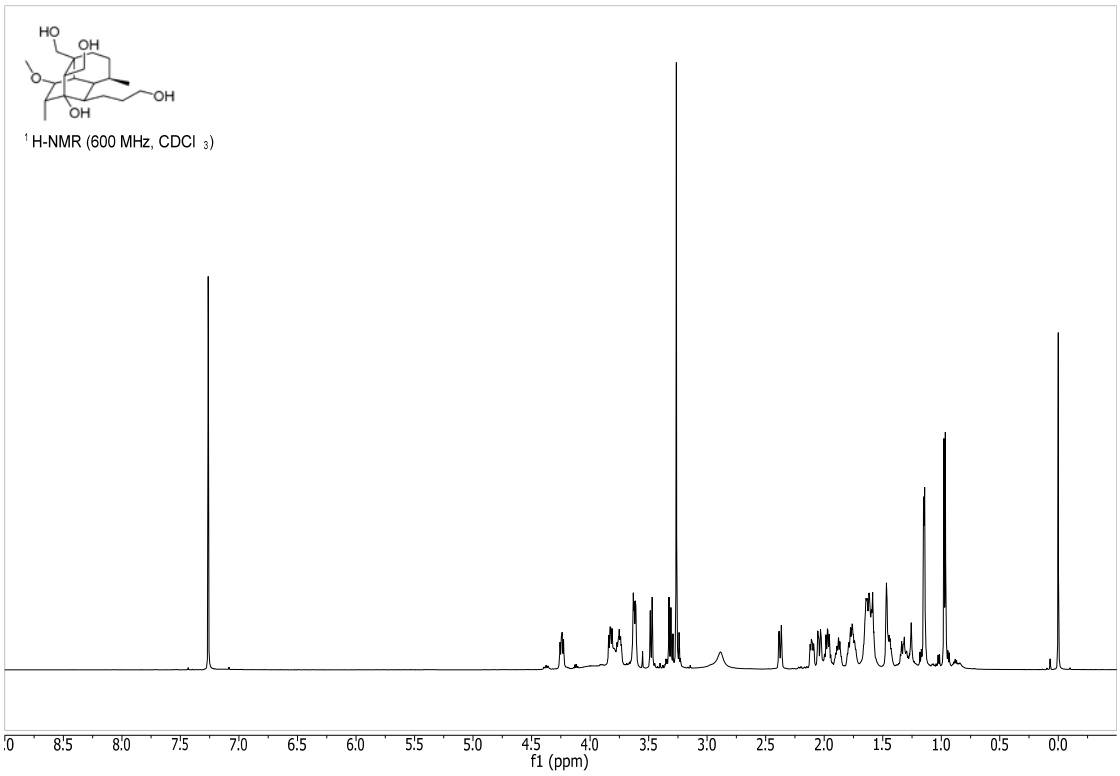


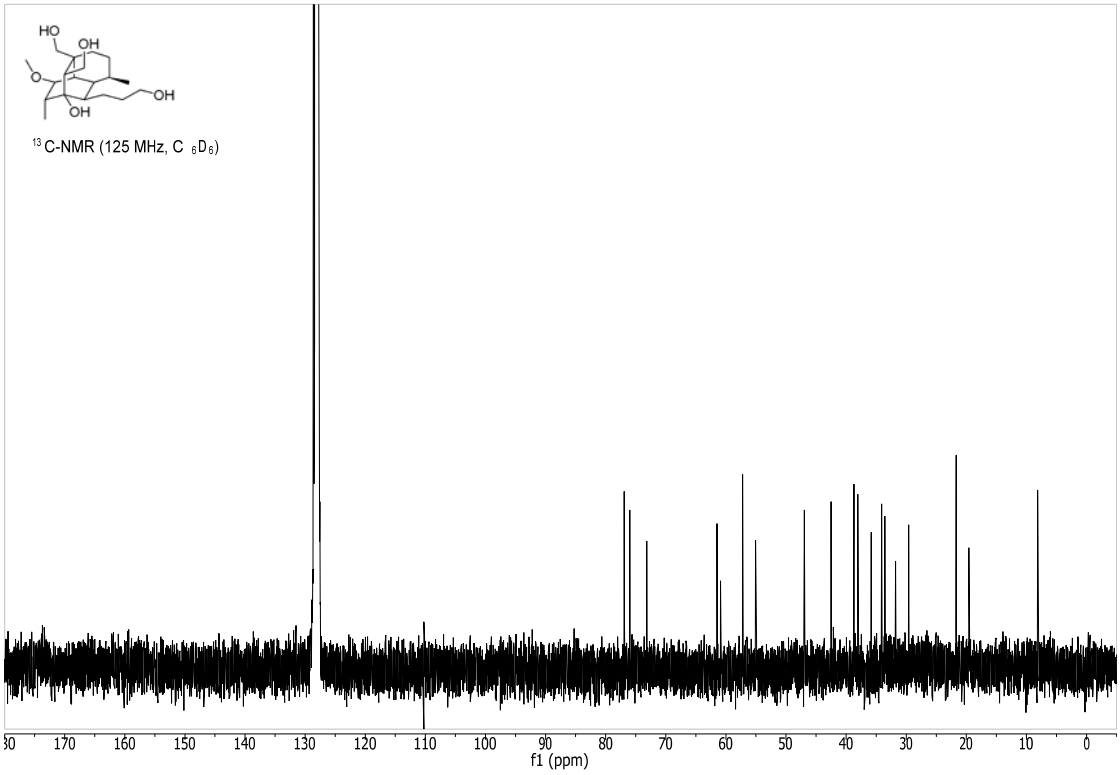


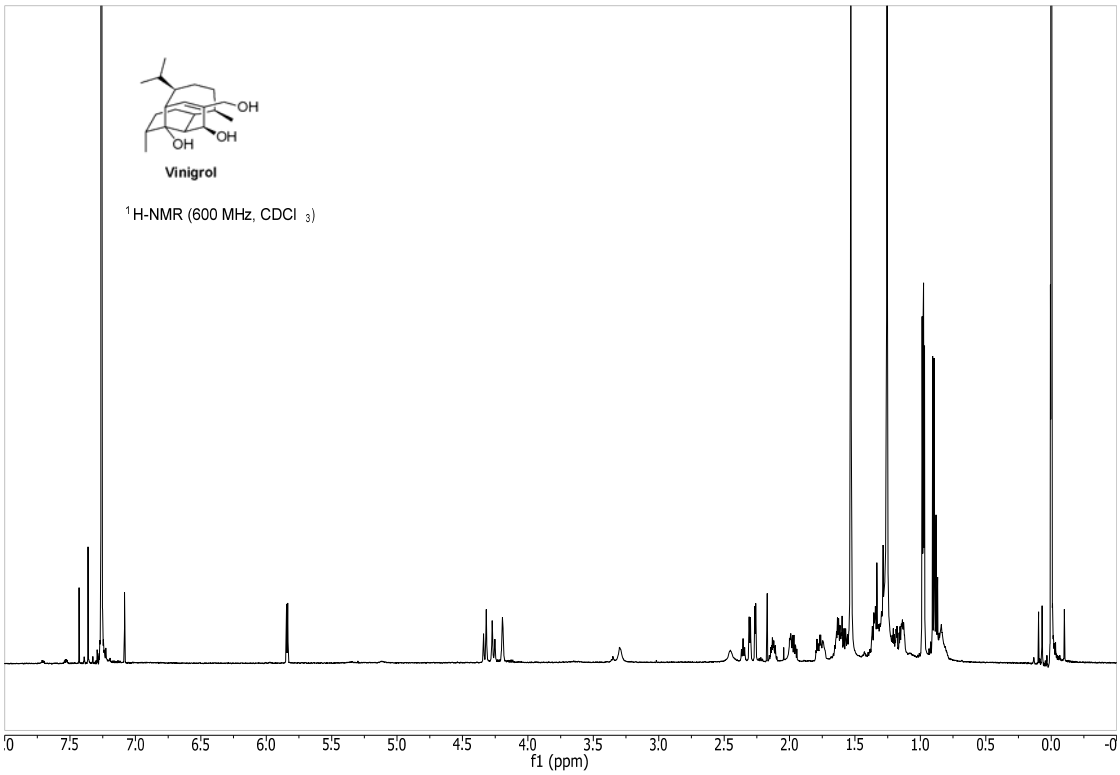


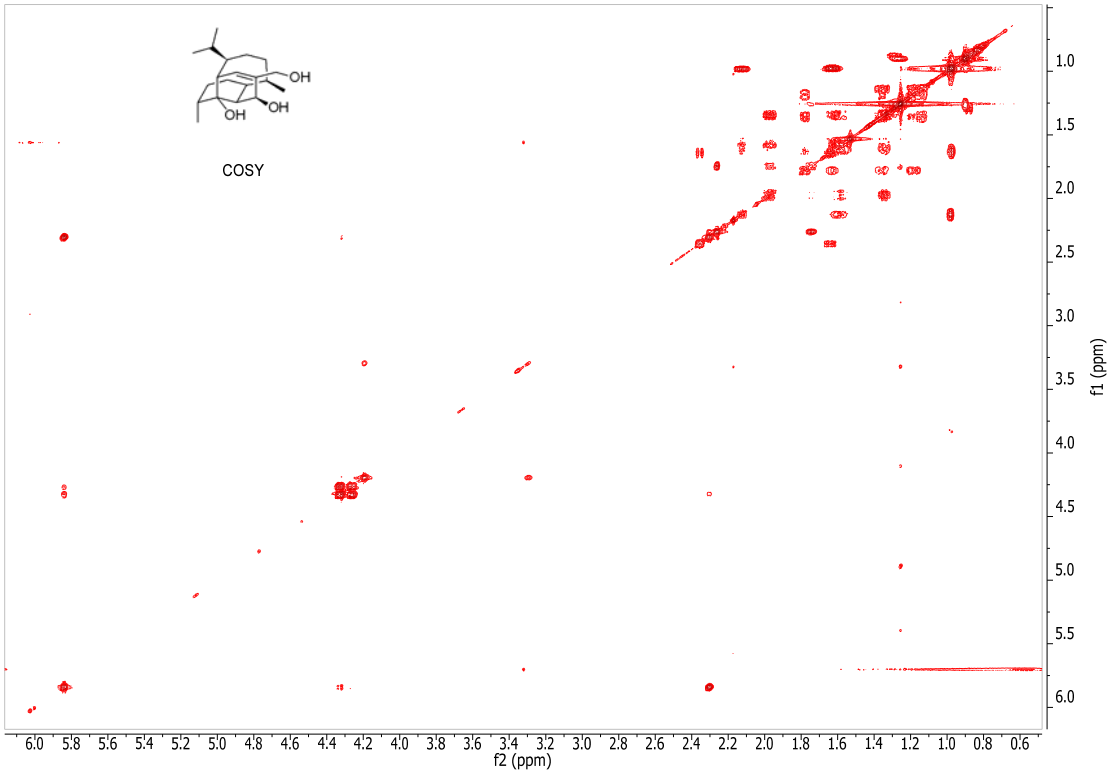


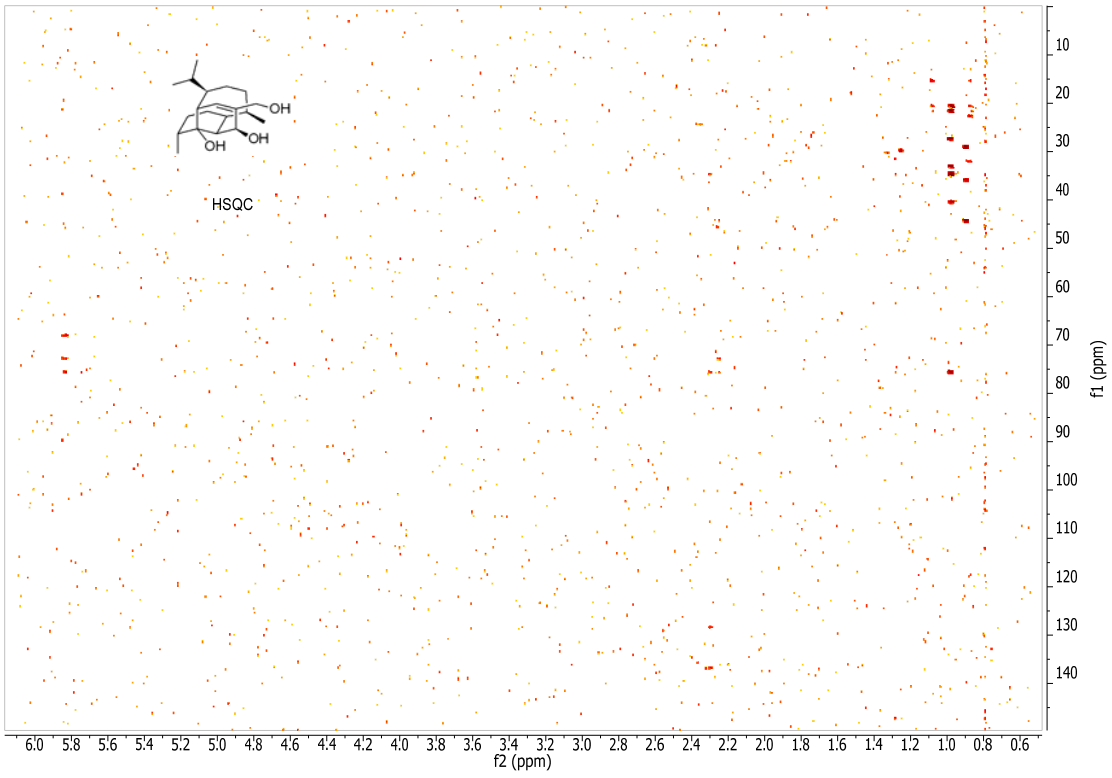



HO
OH
O
OH
OH
1 H-NMR (600 MHz, CDCl 3)
f1 (ppm)


HO
OH
O
OH
OH
13 C-NMR (125 MHz, C 6D6)
f1 (ppm)







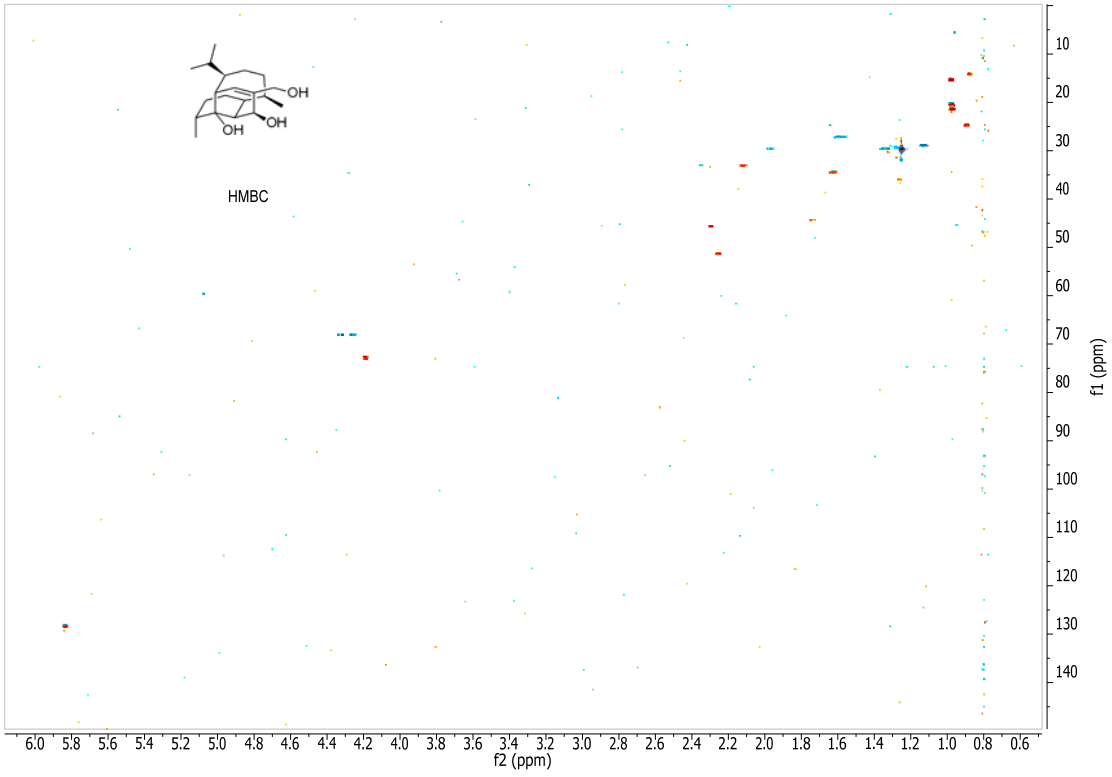
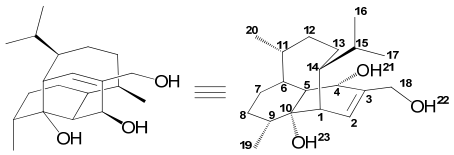


Table 12. 2D-NMR Data of Vinigrol



Position	δ ^{13}C (ppm)	δ ^{1}H (ppm)	Type	COSY correlations	HMBC correlations
1	45.8	2.30	CH	H-2, H-18a, H-18b	C-3, C-2, C-10, C-15
2	128.4	5.84	CH	H-18a, H-18b, H-1	C-10, C-4, C-18, C-1
3	136.4		Cq		
4	72.8	4.19	CH	H-21	
5	51.3	2.26	CH	H-4, H-6	C-4, C-1
6	44.2	1.74	CH	H-5, H-7b	
7a	29.6	1.35	CH_2	H-7b, H-8b	
7b		1.97		H-6, H-8a, H-8b, H-7a	
8a	27.3	1.59	CH_2	H-9, H-7b, H-7a, H-8b	
8b		1.59		H-8a, H-7b, H-7a	
9	33.1	2.12	CH	H-8a, H-8b, H-19	
10	75.6		Cq		
11	35.9	1.26	CH	H-20	
12a	28.9	1.13	CH_2	H-12b	
12b		1.34		H-12a	
13a	28.6	1.19	CH_2	H-14, H-13b	
13b		1.35		H-14, H-13a	
14	40.4	1.77	CH	H-15, H-13b, H-13a	
15	34.7	1.63	CH	H-14, H-16, H-17	
16	21.5	0.98	CH_3	H-15	C-14, C-15, C-17
17	20.5	0.98	CH_3	H-15	C-14, C-15, C-16
18a	67.9	4.26	CH_2	H-2, H-18b, H-22, H-1	
18b		4.33		H-2, H-18a, H-22, H-1	
19	15.3	0.98	CH_3	H-9	C-10, C-9,C-8
20	24.9	0.90	CH_3	H-11	C-6, C-11, C-12
21		3.30	OH	H-4	
22		2.46	OH	H-18a, H-18b	
23		1.99	OH		

Table 13. Vinigrol's ^{1}H NMR Data Comparison (δ in ppm)

Our synthetic sample ($CDCl_3$, 600 MHz) (multiplicity, coupling constant)	**Baran's sample ($CDCl_3$, 600 MHz)[1] (multiplicity, coupling constant)**
5.84 (d, 5.6 Hz)	5.83 (d, 5.5 Hz)
4.30 (AB q, 12.0 Hz)	4.30 (AB q, 12.0 Hz)
4.19 (s)	4.20 (s)
3.30 (bs)	3.40 (bs)
2.45 (bs)	2.65 (bs)
2.30 (d, 5.6 Hz)	2.30 (d, 5.4 Hz)
2.26 (d, 3.9 Hz)	2.25 (d, 3.7 Hz)
2.15 – 2.09 (m)	2.15– 2.09 (m)
2.03 – 1.93 (m)	1.99 – 1.93 (m)
1.81 – 1.71 (m)	1.80 – 1.70 (m)
1.66 – 1.53 (m)	1.65 – 1.50 (m)
1.40 – 1.10 (m)	1.40 – 1.05 (m)
1.00 – 0.95 (m)	1.00 – 0.95 (m)
0.90 (d, 6.8 Hz)	0.90 (d, 6.8 Hz)

Table 14. Vinigrol's ^{13}C NMR Data Comparison (δ in ppm)

Our synthetic sample ($CDCl_3$)	**Baran's sample ($CDCl_3$, 150 MHz)[1]**
136.8	136.5
128.4	128.4
75.6	75.5
72.8	72.8
67.9	67.9
51.3	51.1
45.8	45.5
44.2	44.2
40.4	40.2
35.9	35.8
34.7	34.5
33.1	33.0
29.6	29.6
29.0	28.9
28.7	28.6
27.3	27.2
24.9	24.8
21.5	21.5
20.6	20.5
15.4	15.3

(1) Maimone, T. J.; Shi, J.; Ashida, S.; Baran, P.S. *J. Am. Chem. Soc.* **2009**, 131, 17066-17067.