

Supplementary Material

A Biomimetic Synthetic Approach to the Frondosins

Kevin K. W. Kuan, Aylin M. C. Hirschvogel and Jonathan H. George*

Department of Chemistry, University of Adelaide, Adelaide, SA 5005, Australia.

**Email: jonathan.george@adelaide.edu.au*

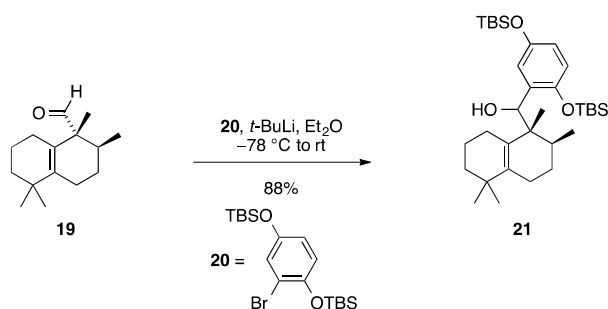
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1. General methods

All chemicals used were purchased from commercial suppliers and used as received. All reactions were performed under an inert atmosphere of N₂. All organic extracts were dried over anhydrous magnesium sulfate. Thin layer chromatography was performed using aluminium sheets coated with silica gel. Visualization was aided by viewing under a UV lamp and staining with ceric ammonium molybdate stain followed by heating. All R_f values were measured to the nearest 0.05. Flash chromatography was performed using 40-63 micron grade silica gel. Melting points were recorded on a digital melting point apparatus and are uncorrected. Infrared spectra were recorded using an FT-IR spectrometer as the neat compounds. High field NMR was recorded using a 600 MHz spectrometer (¹H at 600 MHz, ¹³C at 150 MHz) or a 500 MHz spectrometer (¹H at 500 MHz, ¹³C at 125 MHz). The solvent used for NMR spectra was CDCl₃ unless otherwise specified. ¹H chemical shifts are reported in ppm on the δ-scale relative to TMS (δ 0.0) and ¹³C NMR are reported in ppm relative to chloroform (δ 77.0). Multiplicities are reported as (br) broad, (s) singlet, (d) doublet, (t) triplet, (q) quartet and (m) multiplet. All *J*-values were rounded to the nearest 0.1 Hz. ESI high resolution mass spectra were recorded on a Q-TOF mass spectrometer. Low resolution electron impact ionisation mass spectra were recorded on a GC mass spectrometer. Optical rotations were measured on a modular circular polarimeter.

2. Experimental procedures



To a solution of aryl bromide **20** (3.43 g, 10.8 mmol) in anhydrous Et₂O (40 mL) was added *t*-BuLi (1.7 M in pentane, 5.80 mL, 9.86 mmol) dropwise at -78 °C. The reaction was stirred at -78 °C for 30 min and a solution of aldehyde **19** (1.08 g, 4.91 mmol) in anhydrous Et₂O (40 mL) was added dropwise. The resulting mixture was stirred at -78 °C for 30 min, then allowed to warm to room temperature. The mixture was quenched with saturated aqueous NH₄Cl solution (50 mL) and extracted with Et₂O (3 × 30 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (petrol/EtOAc, 50:1 → 20:1) to give alcohol **21** as a colourless oil (2.42 g, 88%).

Data for **21**:

R_f = 0.6 (petrol/EtOAc, 20:1)

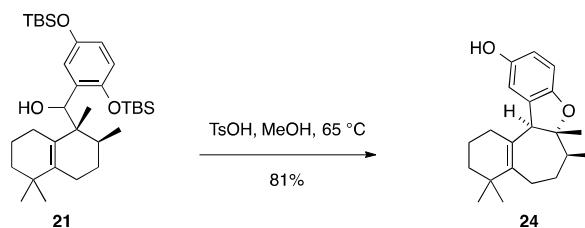
$[\alpha]_D^{25} = -84.3$ (c 0.04, CHCl₃)

IR (film): 3508, 2956, 2929, 1253, 911, 837, 778 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 6.82 (d, *J* = 2.9 Hz, 1H), 6.60 (d, *J* = 8.7 Hz, 1H), 6.55 (dd, *J* = 8.7, 2.9 Hz, 1H), 4.90 (d, *J* = 5.1 Hz, 1H), 2.80 (d, *J* = 5.1 Hz, 1H), 2.17 – 2.14 (d, *J* = 16.8 Hz, 1H), 2.10 – 1.99 (m, 2H), 1.93 – 1.88 (m, 2H), 1.84 – 1.80 (m, 1H), 1.67 – 1.57 (m, 2H), 1.52 – 1.47 (m, 1H), 1.44 – 1.39 (m, 1H), 1.33 – 1.29 (m, 1H), 1.07 (s, 3H), 0.99 (s, 3H), 0.99 (overlapped s, 9H), 0.97 (s, 9H), 0.94 (s, 3H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.24 (s, 3H), 0.21 (s, 3H), 0.16 (s, 6H).

¹³C NMR (125 MHz, CDCl₃): δ 149.1, 147.6, 138.8, 134.7, 130.1, 119.7, 118.7, 118.5, 76.7, 46.9, 39.8, 36.2, 34.7, 28.8, 28.7, 28.3, 26.0, 25.9, 25.7, 20.8, 19.8, 19.1, 18.4, 18.2, 16.4, -3.9, -4.0, -4.5.

HRMS (C₃₃H₅₈O₃Si₂Na, ESI): calculated 581.3821 [M+Na]⁺, found 581.3822 (100%), 582.3861 (43%), 583.3094 (19%).



To a solution of alcohol **21** (1.55 g, 2.78 mmol) in MeOH (140 mL) was added *p*-TsOH (0.63 g, 3.33 mmol) at room temperature. The reaction mixture was heated at 65 °C for 2 h and then allowed to cool to room temperature. The reaction mixture was quenched with saturated NaHCO₃ solution (30 mL) and extracted with Et₂O (2 × 30 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (petrol/EtOAc, 10:1 → 4:1) to give dihydrobenzofuran **24** as a white foam (0.70 g, 81%).

Data for **24**:

R_f = 0.5 (petrol/EtOAc, 4:1)

$[\alpha]_{\text{D}}^{25} = -107.5$ (c 1.09, CHCl₃)

IR (film): 3364, 2956, 2922, 2850, 1605, 1485, 1457, 1375, 1340, 1266, 1205 cm⁻¹.

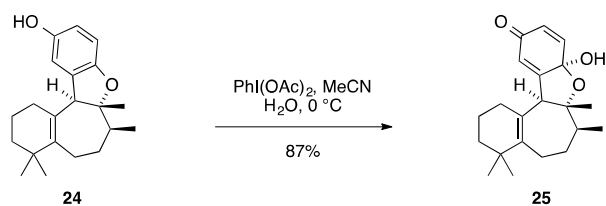
¹H NMR (600 MHz, CDCl₃): δ 6.69 (s, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 6.55 (dd, *J* = 8.4, 2.5 Hz, 1H), 4.43 (s, 1H), 4.28 (s, 1H), 2.40 – 2.17 (m, 4H), 1.93 – 1.90 (m, 1H), 1.73 – 1.68 (m, 1H), 1.65 – 1.60 (m, 1H), 1.54 – 1.44 (m, 3H), 1.07 – 1.05 (overlapped m, 1H), 1.04 (d, *J* = 6.7 Hz, 3H), 1.02 (s, 3H), 1.02 (s, 6H).

¹³C NMR (150 MHz, CDCl₃): δ 153.2, 148.9, 142.6, 130.6, 129.0, 114.1, 113.6, 109.6, 92.2, 55.6, 46.1, 39.6, 35.6, 32.4, 30.1, 28.3, 27.4, 27.0, 19.8, 17.3, 13.3.

¹H NMR (600 MHz, C₆D₆): δ 6.73 (d, *J* = 8.4 Hz, 1H), 6.57 – 6.56 (m, 1H), 6.31 – 6.29 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.24 (s, 1H), 3.71 (s, 1H), 2.30 – 2.24 (m, 1H), 2.13 – 2.08 (m, 1H), 2.07 – 1.97 (m, 2H), 1.85 – 1.83 (m, 1H), 1.51 – 1.47 (m, 1H), 1.43 – 1.37 (m, 4H), 1.11 (d, *J* = 6.7 Hz, 3H), 1.02 (s, 3H), 0.96 (s, 3H), 0.90 (s, 3H), 0.93 – 0.86 (overlapped m, 1H).

¹³C NMR (150 MHz, C₆D₆): δ 153.9, 150.0, 142.3, 130.7, 129.8, 128.4, 114.4, 114.1, 110.1, 56.1, 46.5, 40.0, 35.7, 32.6, 30.4, 28.4, 27.6, 27.1, 20.2, 17.5, 13.5.

HRMS (C₂₁H₂₉O₂, ESI): calculated 313.2168 [M+H]⁺, found 313.2162 (100%), 314.2197 (21%).



To a solution of dihydrobenzofuran **24** (100 mg, 0.33 mmol) in degassed MeCN-H₂O (2:1, 6 mL) was added PhI(OAc)₂ (0.16 g, 0.49 mmol) at 0 °C. The reaction mixture was stirred for 15 min at 0 °C. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (petrol/EtOAc, 4:1) to give hemiacetal **25** as a yellow oil (94 mg, 87%).

Data for 25:

R_f = 0.3 (petrol/EtOAc, 4:1)

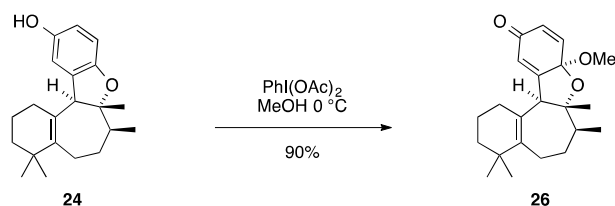
$[\alpha]_{\text{D}}^{25} = +2.2$ (c 0.86, CHCl₃)

IR (film): 3358, 2957, 2925, 2851, 1677, 1650, 1615, 1458 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 6.95 (d, *J* = 10.0 Hz, 1H), 6.26 (dd, *J* = 3.0, 1.5 Hz, 1H), 6.07 (dd, *J* = 10.0, 1.5 Hz, 1H), 4.39 (d, *J* = 3.0 Hz, 1H), 2.99 (s, 1H), 2.32 – 2.25 (m, 3H), 2.18 – 2.12 (m, 2H), 1.74 – 1.64 (m, 2H), 1.56 – 1.51 (m, 1H), 1.47 – 1.40 (m, 2H), 1.01 – 0.99 (overlapped m, 1H), 1.00 (s, 6H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.93 (s, 3H).

¹³C NMR (125 MHz, CDCl₃): δ 186.5, 161.7, 144.7, 143.2, 127.3, 126.9, 121.7, 93.8, 89.3, 51.8, 48.9, 39.3, 35.8, 33.3, 30.4, 28.5, 27.4, 26.8, 19.9, 17.1, 16.5.

HRMS (C₂₁H₂₉O₃, ESI): calculated 329.2111 [M+H]⁺, found 329.2105 (100%), 330.2145 (21%).



To a solution of dihydrobenzofuran **24** (44 mg, 0.14 mmol) in degassed MeOH (3 mL) was added $\text{PhI}(\text{OAc})_2$ (68 mg, 0.21 mmol) at $0\text{ }^\circ\text{C}$. The reaction mixture was stirred for 15 min at $0\text{ }^\circ\text{C}$. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (petroleum ether/EtOAc, 10:1) to give acetal **26** as a yellow oil (44 mg, 90%).

Data for **26**:

$R_f = 0.6$ (petrol/EtOAc, 4:1)

$[\alpha]_D^{25} = -183.0$ (c 0.20, CHCl_3)

IR (neat): 2956, 2926, 2850, 1679, 1653, 1618, 1458 cm^{-1} .

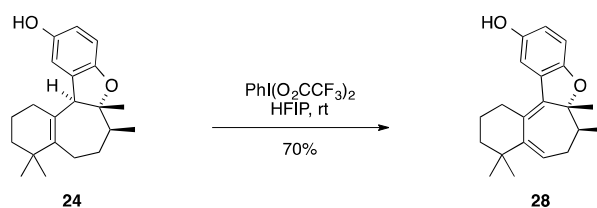
$^1\text{H NMR}$ (500 MHz, CDCl_3): δ 6.92 (d, $J = 10.0$ Hz, 1H), 6.32 (s, 1H), 6.19 (d, $J = 10.0$ Hz, 1H), 4.22 (d, $J = 2.0$ Hz, 1H), 3.21 (s, 3H), 2.31 – 2.25 (m, 3H), 2.16 – 2.09 (m, 2H), 1.74 – 1.63 (m, 2H), 1.56 – 1.51 (m, 1H), 1.48 – 1.40 (m, 2H), 1.01 (overlapped d, $J = 7.0$ Hz, 3H), 1.01 – 0.99 (overlapped m, 1H), 1.00 (s, 6H), 0.95 (s, 3H).

$^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 186.2, 160.4, 144.4, 140.8, 128.9, 127.4, 122.9, 97.1, 89.5, 51.8, 50.0, 48.4, 39.3, 35.8, 33.2, 30.4, 28.5, 27.4, 26.8, 19.9, 17.0, 16.7.

$^1\text{H NMR}$ (500 MHz, C_6D_6): δ 6.60 (d, $J = 10.2$ Hz, 1H), 6.35 (dd, $J = 2.7, 1.7$ Hz, 1H), 6.07 (dd, $J = 10.2, 1.7$ Hz, 1H), 4.19 (d, $J = 2.7$ Hz, 1H), 2.98 (s, 3H), 2.13 – 2.07 (m, 1H), 1.98 – 1.96 (m, 2H), 1.91 – 1.81 (m, 2H), 1.41 – 1.35 (m, 3H), 1.24 – 1.18 (m, 2H), 1.02 (d, $J = 6.7$ Hz, 3H), 0.89 (s, 3H), 0.84 (s, 3H), 0.83 (s, 3H), 0.81 – 0.77 (overlapped m, 1H).

$^{13}\text{C NMR}$ (125 MHz, C_6D_6): δ 185.5, 159.8, 143.9, 140.7, 129.2, 128.4, 123.2, 97.5, 89.1, 52.1, 49.7, 48.6, 39.6, 35.8, 33.4, 30.3, 28.6, 27.6, 26.9, 20.1, 17.2, 16.8.

HRMS ($\text{C}_{22}\text{H}_{30}\text{O}_3\text{Na}$, ESI): calculated 365.2084 $[\text{M}+\text{Na}]^+$, found 365.2093 (100%), 366.2108 (22%).



To a solution of dihydrobenzofuran **24** (26 mg, 0.08 mmol) in degassed HFIP (1.5 mL) was added $\text{PhI}(\text{O}_2\text{CCF}_3)_2$ (36 mg, 0.08 mmol) at room temperature. The reaction mixture was stirred for 4 h at room temperature. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (petrol/EtOAc, 4:1) to give diene **28** as a yellow oil (18 mg, 70%).

Data for 28:

$R_f = 0.5$ (petrol/EtOAc, 4:1)

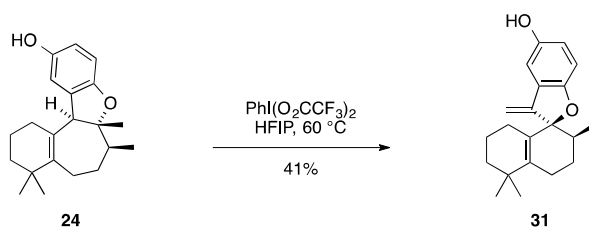
$[\alpha]_D^{25} = +210.4$ (c 0.24, CHCl_3)

IR (film): 3368, 2960, 2929, 1593, 1482, 1460, 1375, 1367, 1223 cm^{-1} .

^1H NMR (600 MHz, CDCl_3): δ 7.16 (d, $J = 2.5$ Hz, 1H), 6.68 (d, $J = 8.4, 2.5$ Hz, 1H), 6.65 (d, $J = 8.4$ Hz, 1H), 5.87 (dd, $J = 8.2, 6.2$ Hz, 1H), 4.36 (s, 1H), 3.07 (dt, $J = 15.0, 4.8$ Hz, 1H), 2.74 (pd, $J = 7.3, 1.7$ Hz, 1H), 2.30 – 2.19 (m, 2H), 1.81 – 1.73 (m, 2H), 1.70 – 1.65 (m, 1H), 1.52 – 1.46 (m, 2H), 1.27 (s, 3H), 1.16 (s, 3H), 1.10 (d, $J = 7.3$ Hz, 3H), 1.08 (s, 3H).

^{13}C NMR (150 MHz, CDCl_3): δ 155.2, 149.7, 148.8, 141.8, 130.5, 126.9, 122.2, 115.9, 111.9, 109.9, 92.8, 55.1, 40.4, 36.3, 32.3, 30.2, 29.4, 29.2, 21.1, 21.0, 15.6.

HRMS ($\text{C}_{21}\text{H}_{27}\text{O}_2$, ESI): calculated 311.2006 $[\text{M}+\text{H}]^+$, found 311.2002 (100%), 312.2037 (22%).



To a solution of dihydrobenzofuran **24** (109 mg, 0.35 mmol) in degassed HFIP (7 mL) was added $\text{PhI}(\text{O}_2\text{CCF}_3)_2$ (180 mg, 0.42 mmol) at room temperature. The reaction mixture was heated at 60 °C for 12 h and then allowed to cool to room temperature. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (gradient elution, petrol/EtOAc, 10:1 \rightarrow 4:1) to give alkene **31** as a yellow oil (44 mg, 41%).

Data for 31:

$R_f = 0.5$ (petrol/EtOAc, 4:1)

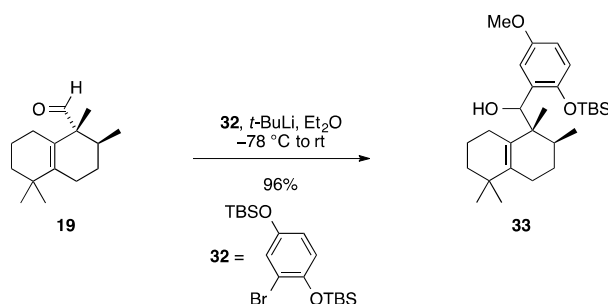
$[\alpha]_D^{25} = -31.7$ (c 0.02, CHCl_3)

IR (film): 3391, 2962, 2929, 2871, 1636, 1484, 1466, 1361, 1215 cm^{-1} .

$^1\text{H NMR}$ (500 MHz, CDCl_3): δ 6.85 (s, 1H), 6.70 (s, 2H), 5.37 (s, 1H), 4.72 (br s, 1H), 4.71 (s, 1H), 2.22 – 2.19 (m, 1H), 2.09 – 2.01 (m, 1H), 1.94 – 1.87 (m, 1H), 1.64 – 1.45 (m, 7H), 1.35 – 1.32 (m, 1H), 1.06 (s, 3H), 1.02 (s, 3H), 0.77 (d, $J = 6.3$ Hz, 3H).

$^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 157.1, 150.9, 149.3, 142.2, 128.2, 128.1, 117.8, 110.0, 106.8, 100.3, 93.9, 43.0, 39.4, 34.5, 28.9, 27.4, 27.1, 25.4, 25.0, 19.1, 14.9.

HRMS ($\text{C}_{23}\text{H}_{29}\text{O}_4$, ESI): calculated 369.2071 $[\text{M}+\text{CH}_3\text{CO}_2]^-$, found 369.2077 (100%), 370.2082 (21%).



To a solution of aryl bromide **32** (0.59 g, 1.84 mmol) in anhydrous Et₂O (6 mL) was added *t*-BuLi (1.7 M in pentane, 0.85 mL, 1.45 mmol) dropwise at -78 °C. The reaction mixture was stirred at -78 °C for 30 min and a solution of aldehyde **19** (0.16 g, 0.74 mmol) in anhydrous Et₂O (6 mL) was added dropwise. The resulting mixture was stirred at -78 °C for 30 min, then allowed to warm to room temperature. The mixture was quenched with saturated aqueous NH₄Cl solution (30 mL) and extracted with Et₂O (3×10 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (gradient elution, petrol/EtOAc, 50:1 \rightarrow 20:1) to give alcohol **33** as a colourless oil (0.32 g, 96%).

Data for **33**:

$R_f = 0.4$ (petrol/EtOAc, 10:1)

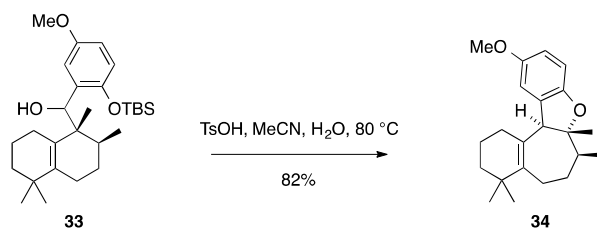
$[\alpha]_D^{25} = +53.4$ (c 0.23, CHCl₃)

IR (film): 3524, 2929, 2860, 1603, 1491, 1259, 1211 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 6.91 (d, $J = 3.0$ Hz, 1H), 6.68 (d, $J = 8.8$ Hz, 1H), 6.63 (dd, $J = 8.8, 3.0$ Hz, 1H), 4.94 (d, $J = 5.3$ Hz, 1H), 3.75 (s, 3H), 2.80 (d, $J = 5.3$ Hz, 1H), 2.17 – 2.14 (m, 1H), 2.08 – 2.03 (m, 2H), 1.94 – 1.89 (m, 2H), 1.84 – 1.80 (m, 1H), 1.66 – 1.58 (m, 2H), 1.52 – 1.48 (m, 1H), 1.45 – 1.39 (m, 1H), 1.34 – 1.30 (m, 1H), 1.07 (s, 3H), 1.00 (s, 12H), 0.94 (s, 3H), 0.82 (d, $J = 6.9$ Hz, 3H), 0.24 (s, 3H), 0.21 (s, 3H).

¹³C NMR (125 MHz, CDCl₃): δ 153.4, 147.2, 138.9, 134.8, 130.0, 118.8, 113.8, 112.5, 76.6, 55.7, 46.9, 39.8, 36.3, 34.7, 28.82, 28.75, 28.3, 26.0, 25.9, 20.9, 19.8, 19.2, 16.4, -3.9 , -4.0 .

HRMS (C₂₈H₄₆O₃SiNa, ESI): calculated 481.3108 [M+Na]⁺, found 481.3110 (100%), 482.3140 (33%), 483.3187 (25%).



To a solution of alcohol **33** (1.14 g, 2.48 mmol) in MeCN-H₂O (2:1, 150 mL) was added *p*-TsOH (0.94 g, 4.96 mmol) at room temperature. The reaction mixture was heated at 80 °C for 2 h and then allowed to cool to room temperature. The reaction mixture was quenched with saturated NaHCO₃ solution (50 mL) and extracted with Et₂O (2 × 50 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (petrol/EtOAc, 10:1) to give dihydrobenzofuran **34** as a colourless oil (0.67 g, 82%).

Data for **34**:

R_f = 0.55 (petrol/EtOAc, 10:1)

$[\alpha]_D^{25} = -51.5$ (c 2.44, CHCl₃)

IR (film): 2954, 2923, 2852, 1482, 1263, 1228 cm⁻¹.

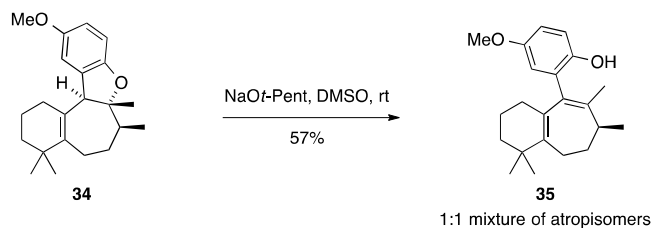
¹H NMR (600 MHz, CDCl₃): δ 6.75 (s, 1H), 6.67 – 6.63 (m, 2H), 4.30 (s, 1H), 3.76 (s, 3H), 2.34 – 2.29 (m, 1H), 2.33 – 2.18 (m, 3H), 1.95 – 1.91 (m, 1H), 1.73 – 1.69 (m, 1H), 1.64 – 1.62 (m, 1H), 1.54 – 1.45 (m, 3H), 1.10 – 1.02 (overlapped m, 1H), 1.05 (d, *J* = 6.7 Hz, 3H), 1.03 (overlapped s, 3H), 1.02 (s, 6H).

¹³C NMR (150 MHz, CDCl₃): δ 153.4, 153.3, 142.6, 130.4, 129.1, 113.3, 111.9, 109.4, 92.2, 56.1, 55.6, 46.1, 39.6, 35.6, 32.4, 30.1, 28.3, 27.4, 27.0, 19.8, 17.3, 13.3.

¹H NMR (500 MHz, C₆D₆): δ 6.86 (s, 1H), 6.78 (d, *J* = 8.5 Hz, 1H), 6.55 (dd, *J* = 8.5, 2.3 Hz, 1H), 4.26 (s, 1H), 3.37 (s, 3H), 2.41 – 2.36 (m, 1H), 2.14 – 2.08 (m, 1H), 2.04 – 2.00 (m, 2H), 1.88 – 1.85 (m, 1H), 1.47 – 1.43 (m, 1H), 1.42 – 1.34 (m, 4H), 1.10 (d, *J* = 6.7 Hz, 3H), 0.93 (s, 3H), 0.87 (s, 3H) 0.90 – 0.86 (overlapped m, 3H).

¹³C NMR (125 MHz, C₆D₆): δ 154.4, 154.2, 142.4, 130.7, 129.9, 128.4, 114.0, 112.4, 110.0, 92.0, 56.2, 55.6, 46.5, 40.0, 35.8, 32.6, 30.4, 28.4, 27.7, 27.1, 20.2, 17.5, 13.6.

GCMS (EI, m/z): 326 [M⁺] (100%).



To a solution of dihydrobenzofuran **34** (29 mg, 0.09 mmol) in DMSO (2 mL) was added sodium *tert*-pentoxide (49 mg, 0.45 mmol) at room temperature. The reaction mixture was stirred for 1 h at room temperature. The resulting mixture was quenched with water (10 mL) and extracted with Et₂O (2 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (petrol /EtOAc, 4:1) to give diene **35** as a colourless oil (17 mg, 57%).

Data for **35**:

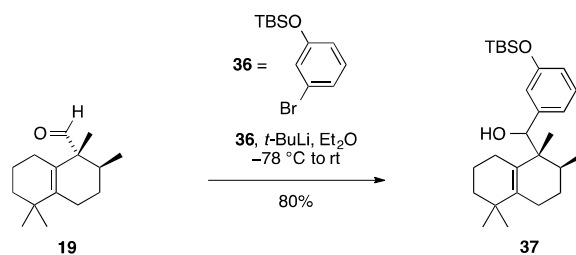
$R_f = 0.65$ (petrol/EtOAc, 4:1)

$[\alpha]_D^{25} = -12.6$ (c 0.02, CHCl₃)

IR (film): 3462, 2931, 1709, 1615, 1490, 1273, 1222 cm⁻¹.

¹H NMR (500 MHz, CDCl₃) δ 6.83 (d, $J = 8.8$ Hz, 1H), 6.76 (d, $J = 8.7$ Hz, 1H), 6.73 – 6.71 (m, 2H), 6.59 (d, $J = 2.9$ Hz, 1H), 6.39 (d, $J = 3.0$ Hz, 1H), 5.25 (s, 1H), 5.02 (s, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 2.67 – 2.63 (m, 1H), 2.50 – 2.53 (m, 1H), 2.18 – 2.05 (m, 6H), 1.92 – 1.86 (m, 2H), 1.78 – 1.74 (overlapped m, 2H), 1.76 (s, 3H), 1.67 – 1.65 (overlapped m, 2H), 1.65 (s, 3H), 1.52 – 1.45 (m, 8H), 1.15 (s, 3H), 1.13 (s, 3H), 1.09 (d, $J = 6.9$ Hz, 1H), 1.08 (d, $J = 6.5$ Hz, 1H), 1.06 (s, 3H), 1.05 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ 153.2, 152.7, 148.5, 147.2, 146.7, 144.4, 141.9, 141.7, 132.8, 132.6, 132.4, 132.2, 127.9, 127.3, 117.2, 115.7, 114.6, 114.5, 113.4, 113.0, 55.74, 55.67, 46.2, 45.7, 39.5, 39.3, 35.5, 35.40, 35.35, 35.1, 30.1, 29.9, 28.6, 28.1, 28.00, 27.95, 26.9, 26.5, 19.5 (2 signals overlapped), 17.5, 17.3, 16.4, 15.4.



To a solution of aryl bromide **36** (2.81 g, 9.79 mmol) in anhydrous Et₂O (30 mL) was added *t*-BuLi (1.7 M in pentane, 5.50 mL, 9.32 mmol) dropwise at $-78\text{ }^\circ\text{C}$. The reaction was stirred at $-78\text{ }^\circ\text{C}$ for 30 min and a solution of aldehyde **19** (1.03 g, 4.66 mmol) in anhydrous Et₂O (30 mL) was added dropwise. The resulting mixture was stirred at $-78\text{ }^\circ\text{C}$ for 30 min, then allowed to warm to room temperature. The mixture was quenched with saturated aqueous NH₄Cl solution (50 mL) and extracted with Et₂O ($3 \times 50\text{ mL}$). The combined organic extracts were dried over MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (petrol/EtOAc, 20:1) to give alcohol **37** as a colourless, viscous oil (1.59 g, 80%).

Data for **37**:

$R_f = 0.4$ (petrol/EtOAc, 10:1)

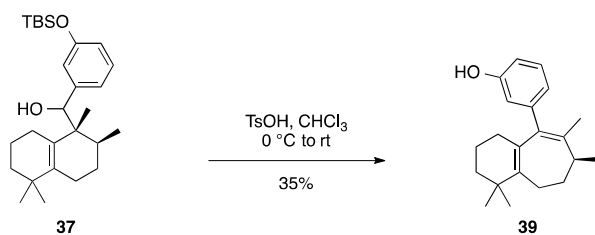
$[\alpha]_D^{25} = +1.7$ (c 1.25, CHCl₃)

IR (film): 3480, 2955, 2929, 2861, 1601, 1584, 1483, 1472, 1440, 1381, 1361, 1275 cm⁻¹.

¹H NMR (600 MHz, CDCl₃): δ 7.86 (t, $J = 7.8\text{ Hz}$, 1H), 6.90 (d, $J = 7.7\text{ Hz}$, 1H), 6.85 (s, 1H), 6.70 (dd, $J = 7.9, 2.3\text{ Hz}$, 1H), 4.89 (d, $J = 3.7\text{ Hz}$, 1H), 2.32 – 2.28 (m, 1H), 2.08 – 1.95 (m, 2H), 1.84 (d, $J = 3.7\text{ Hz}$, 1H), 1.79 – 1.74 (m, 1H), 1.70 – 1.60 (m, 3H), 1.57 – 1.51 (m, 1H), 1.49 – 1.42 (m, 2H), 1.22 – 1.16 (m, 1H), 1.04 (s, 3H), 1.02 (s, 3H), 1.02 (s, 3H), 1.00 (s, 3H), 0.98 (s, 9H), 0.84 (d, $J = 6.9\text{ Hz}$, 1H), 0.18 (s, 6H).

¹³C NMR (150 MHz, CDCl₃): δ 155.0, 144.8, 138.2, 130.4, 128.2, 120.1, 118.9, 118.4, 79.6, 46.1, 39.9, 34.7, 33.0, 28.6, 28.5, 28.0, 26.5, 25.7, 21.8, 20.0, 19.1, 18.2, 16.8, -4.37 , -4.39 .

HRMS (C₂₇H₄₅O₂Si, ESI): calculated 429.3189 [M+H]⁺, found 429.3171 (100%), 430.3278 (13%), 431.3372 (12%).



To a solution of alcohol **37** (0.11 g, 0.27 mmol) in CHCl_3 (13 mL) was added *p*-TsOH (0.30 g, 1.59 mmol) at 0 °C. The reaction mixture was allowed to gradually warm up to room temperature and stirred for 12 h. The resulting mixture was quenched with saturated NaHCO_3 solution (10 mL) and extracted with Et_2O (2×10 mL). The combined organic extracts were washed with brine (20 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel (petrol/EtOAc, 10:1) to give diene **39** as a colourless oil (28 mg, 35%).

Data for 39:

$R_f = 0.3$ (petrol/EtOAc, 10:1)

$[\alpha]_D^{25} = -305.1$ (c 1.17, CHCl_3)

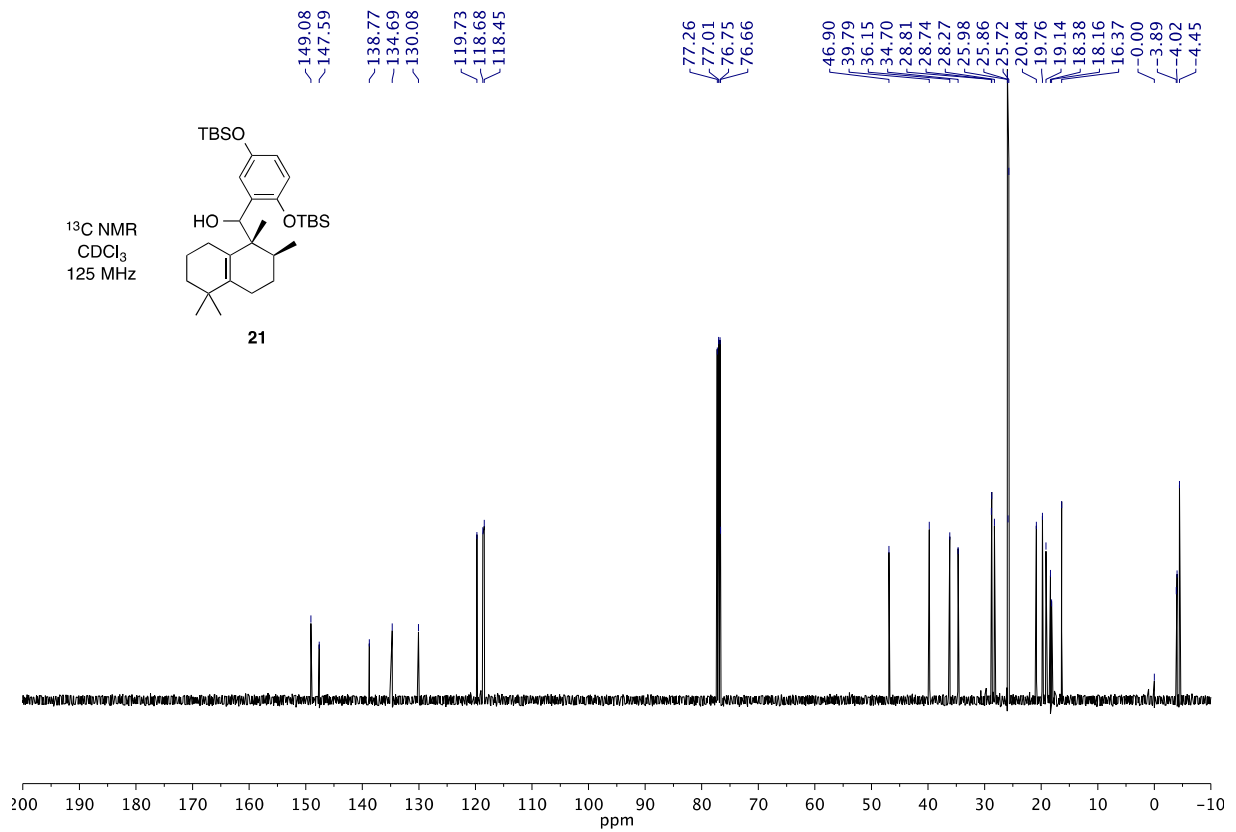
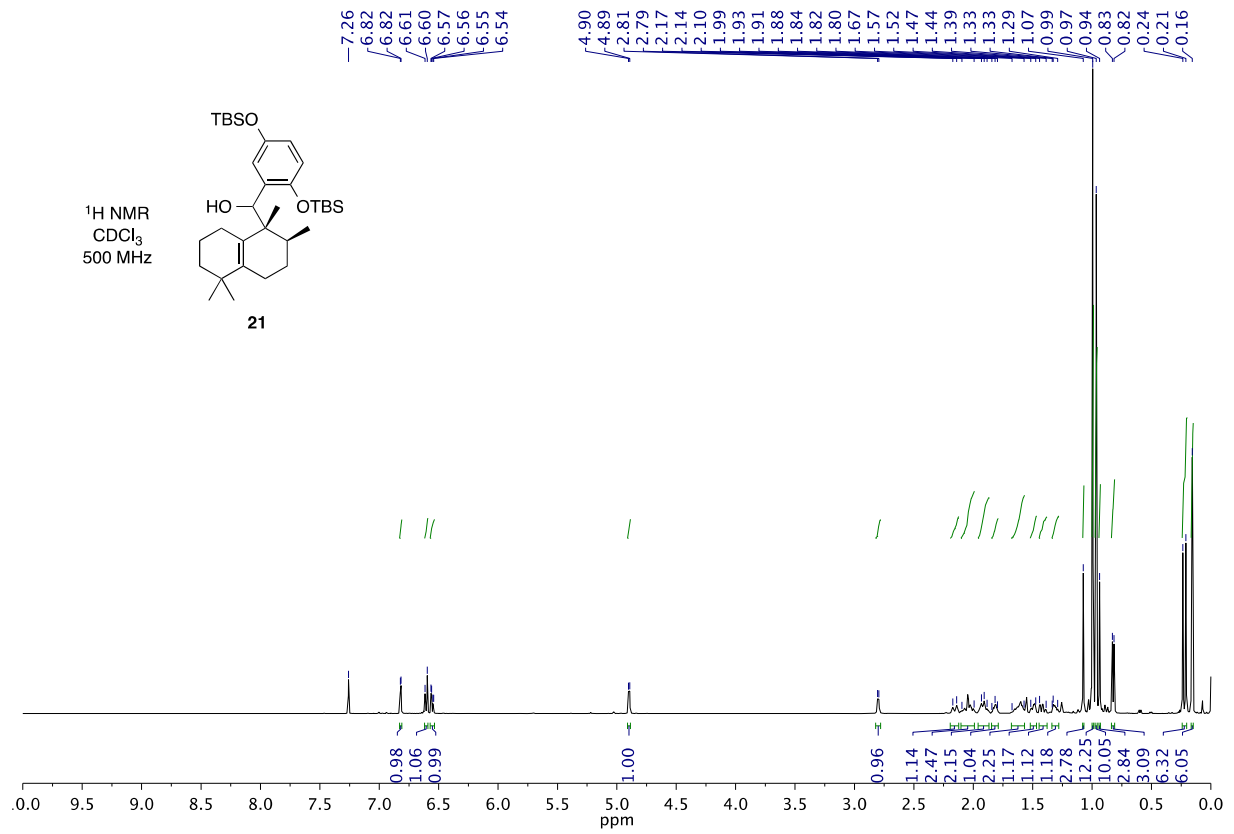
IR (film): 3438, 3246, 2922, 2852, 1600, 1454, 1380, 1258 cm^{-1} .

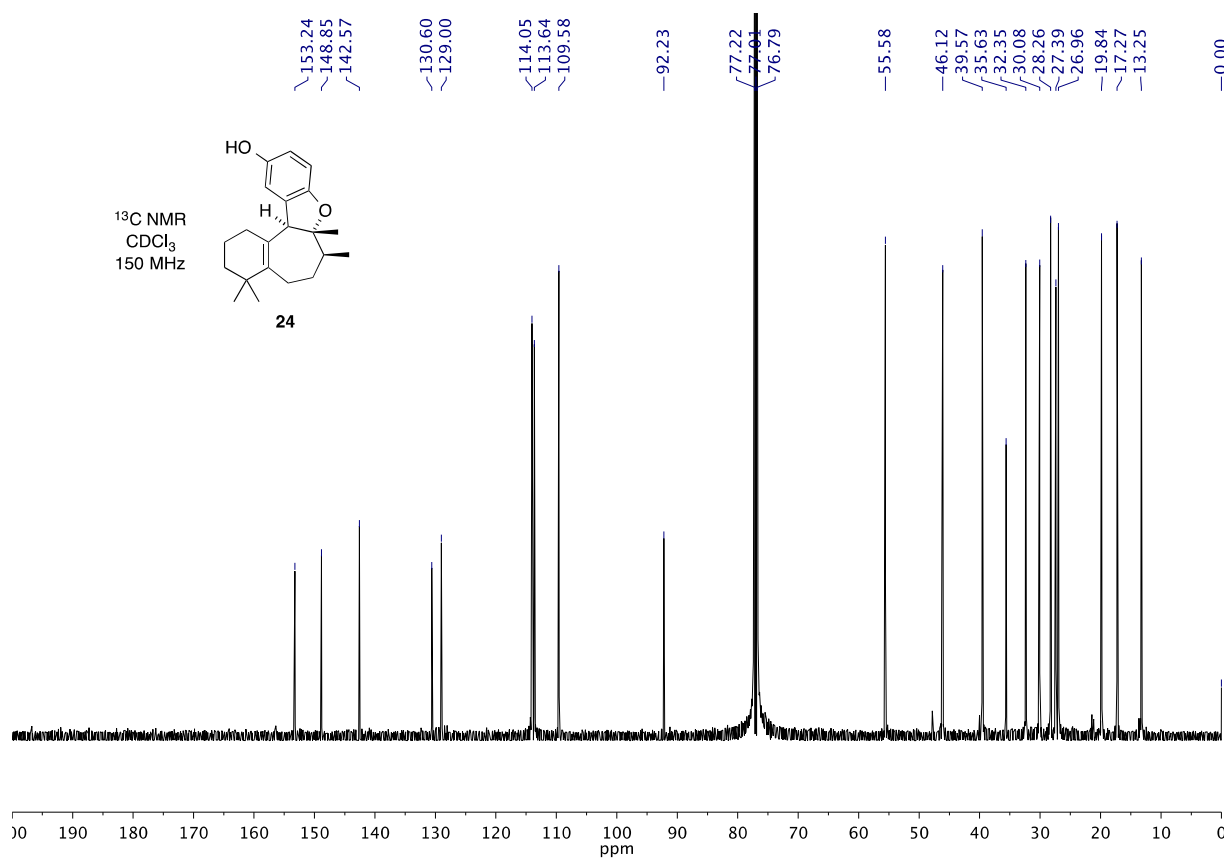
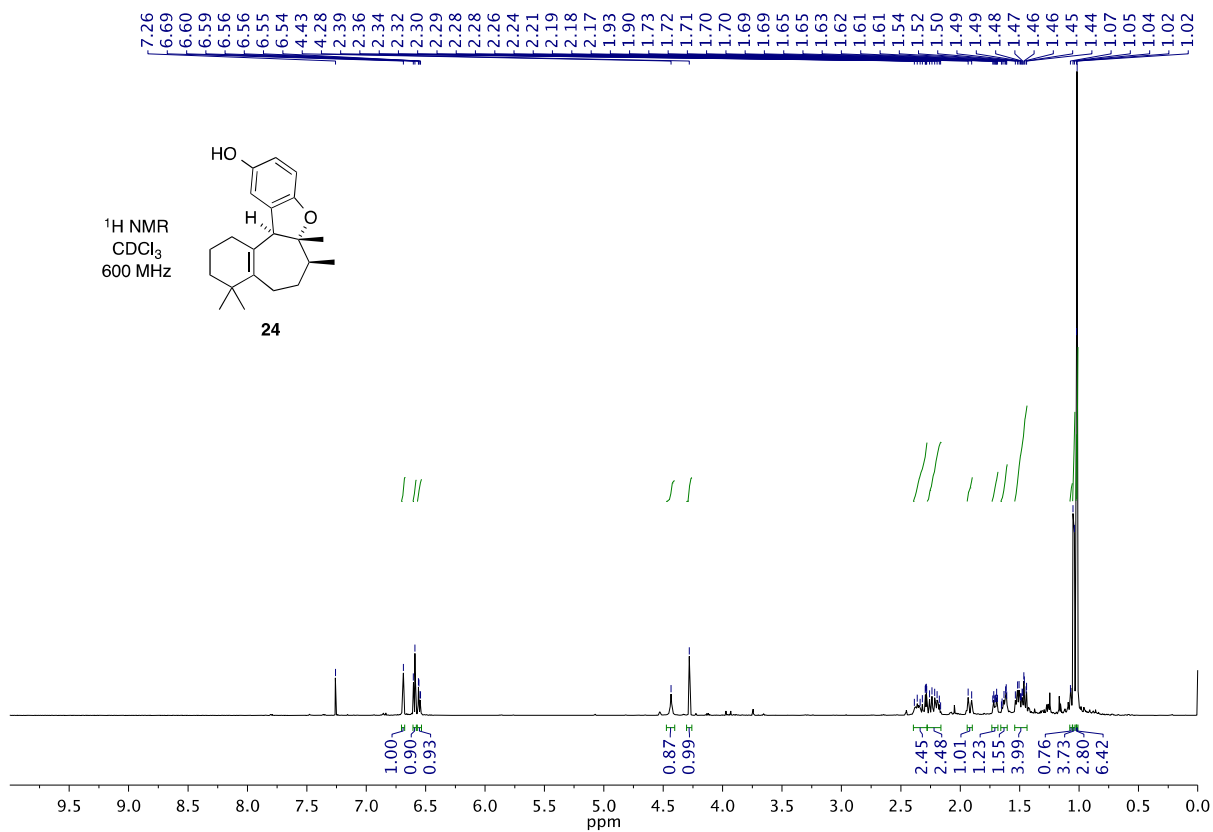
^1H NMR (500 MHz, CDCl_3): δ 7.15 (t, $J = 7.8$ Hz, 1H), 6.68 – 6.63 (m, 2H), 6.52 (s, 1H), 4.62 (s, 1H), 2.58 – 2.50 (m, 1H), 2.06 – 1.99 (m, 3H), 1.84 – 1.79 (m, 1H), 1.70 (s, 3H), 1.68 – 1.65 (m, 2H), 1.51 – 1.45 (m, 4H), 1.12 (s, 3H), 1.06 (overlapped d, $J = 6.6$ Hz, 3H), 1.06 (s, 3H).

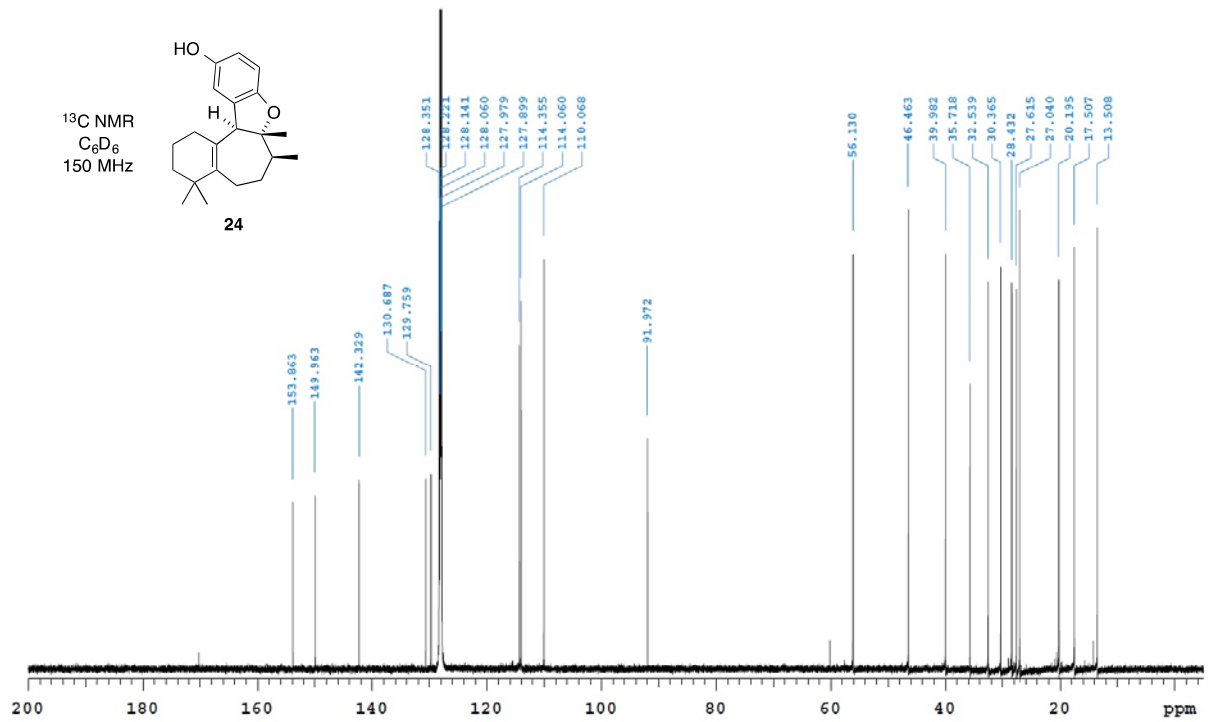
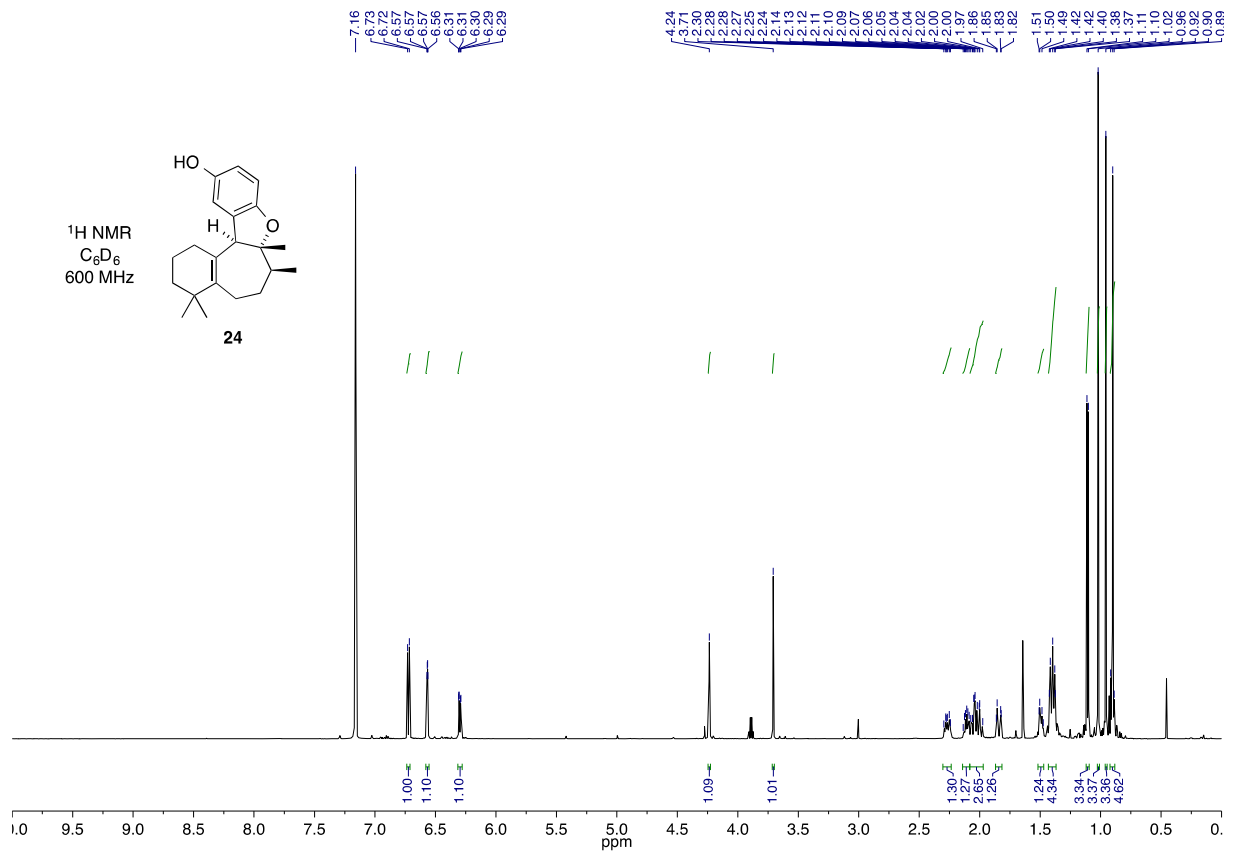
^{13}C NMR (125 MHz, CDCl_3): δ 155.1, 143.6, 143.3, 137.5, 137.4, 132.5, 128.8, 122.4, 116.3, 112.7, 45.7, 39.6, 35.4, 35.0, 30.1, 28.5, 28.3, 26.5, 19.8, 17.4, 15.7.

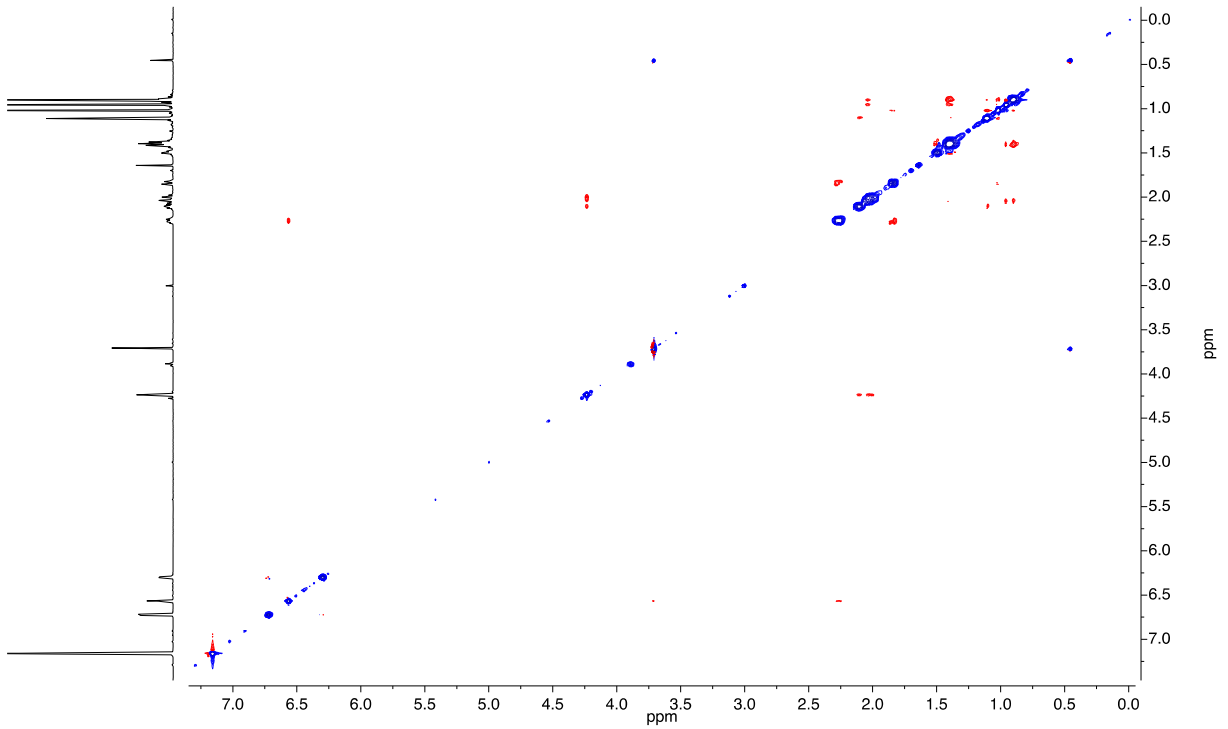
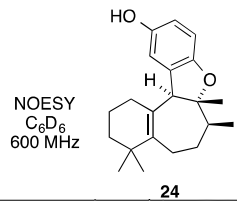
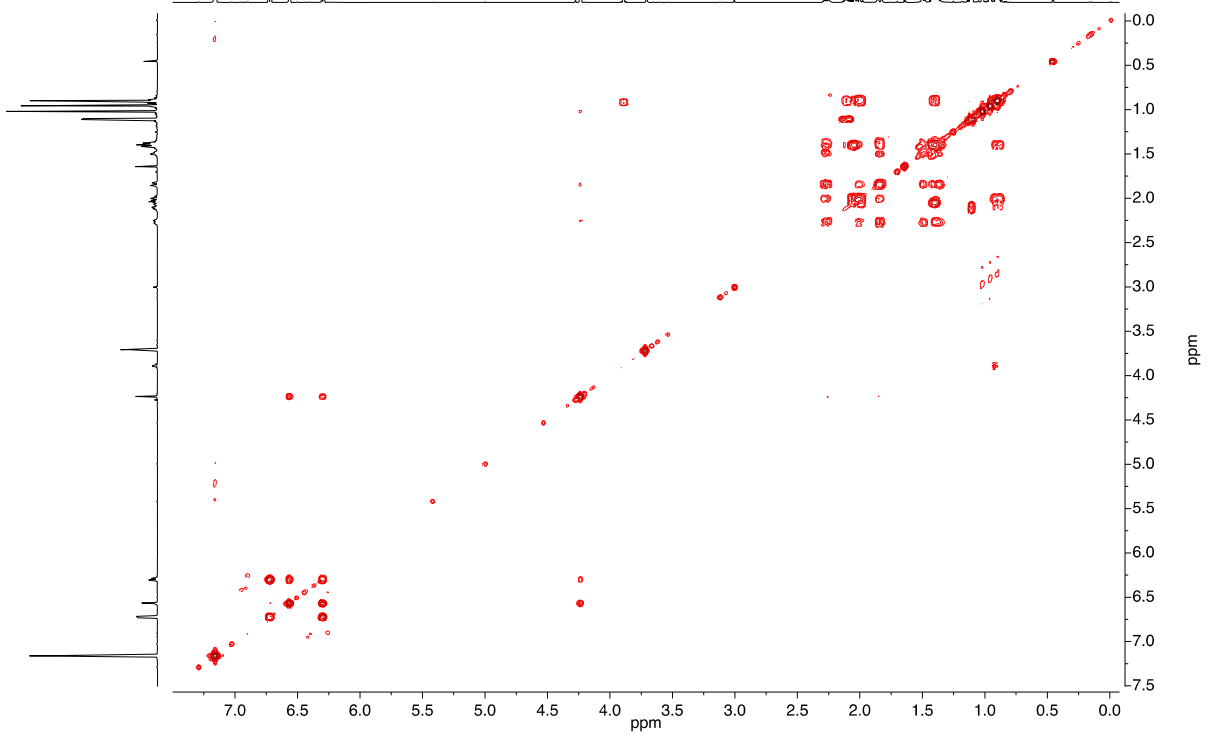
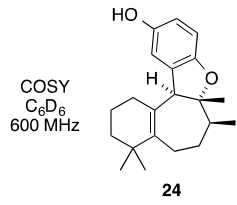
GCMS (EI, m/z): 296 [M^+] (100%).

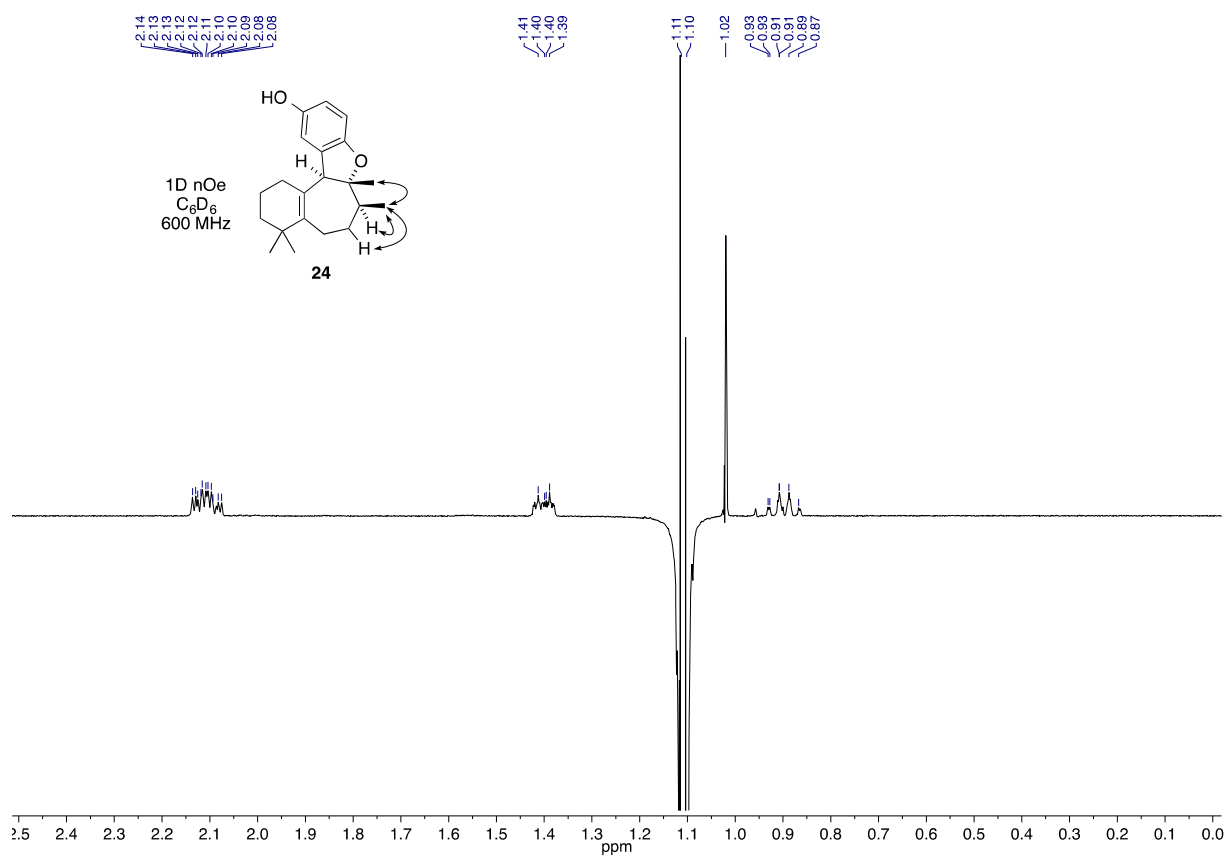
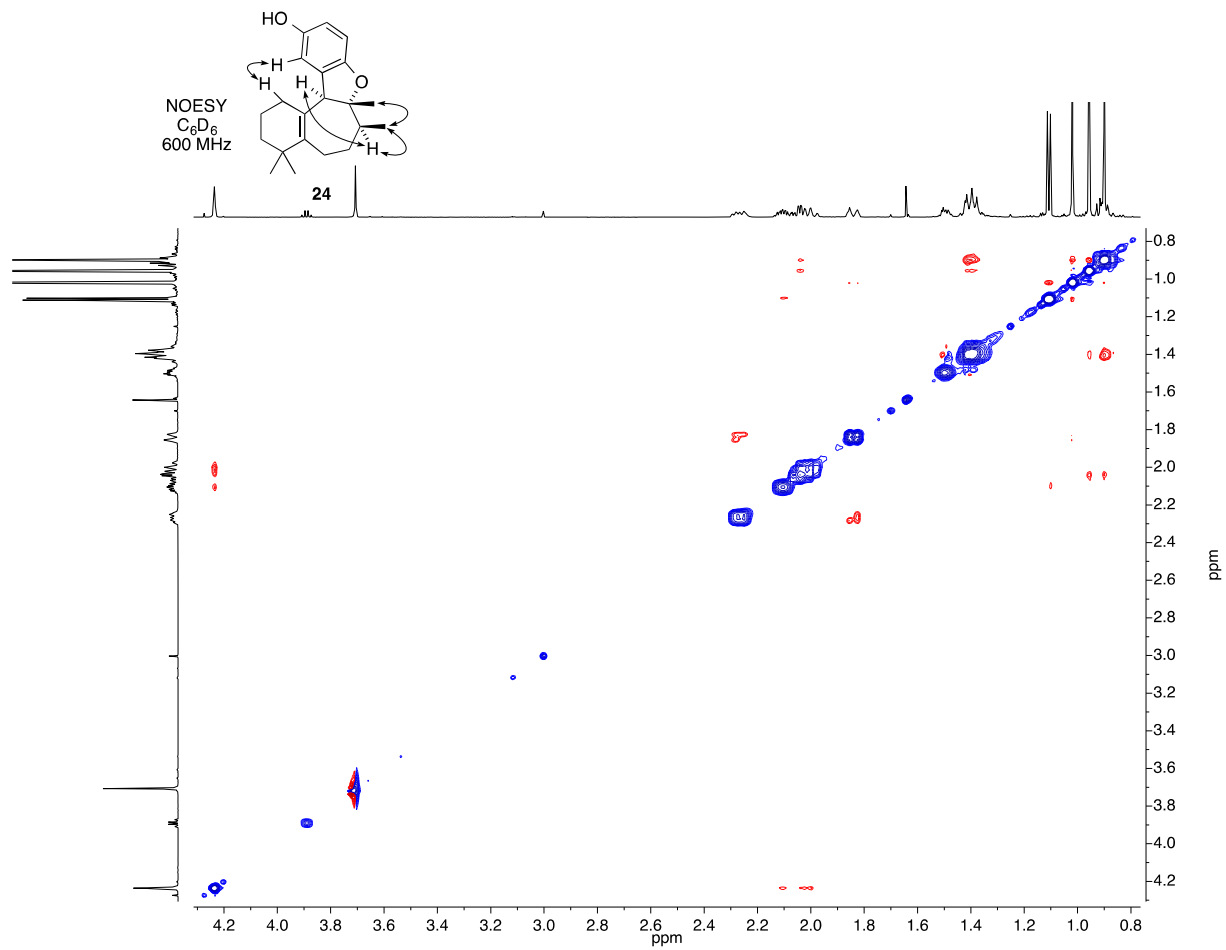
3. NMR spectra

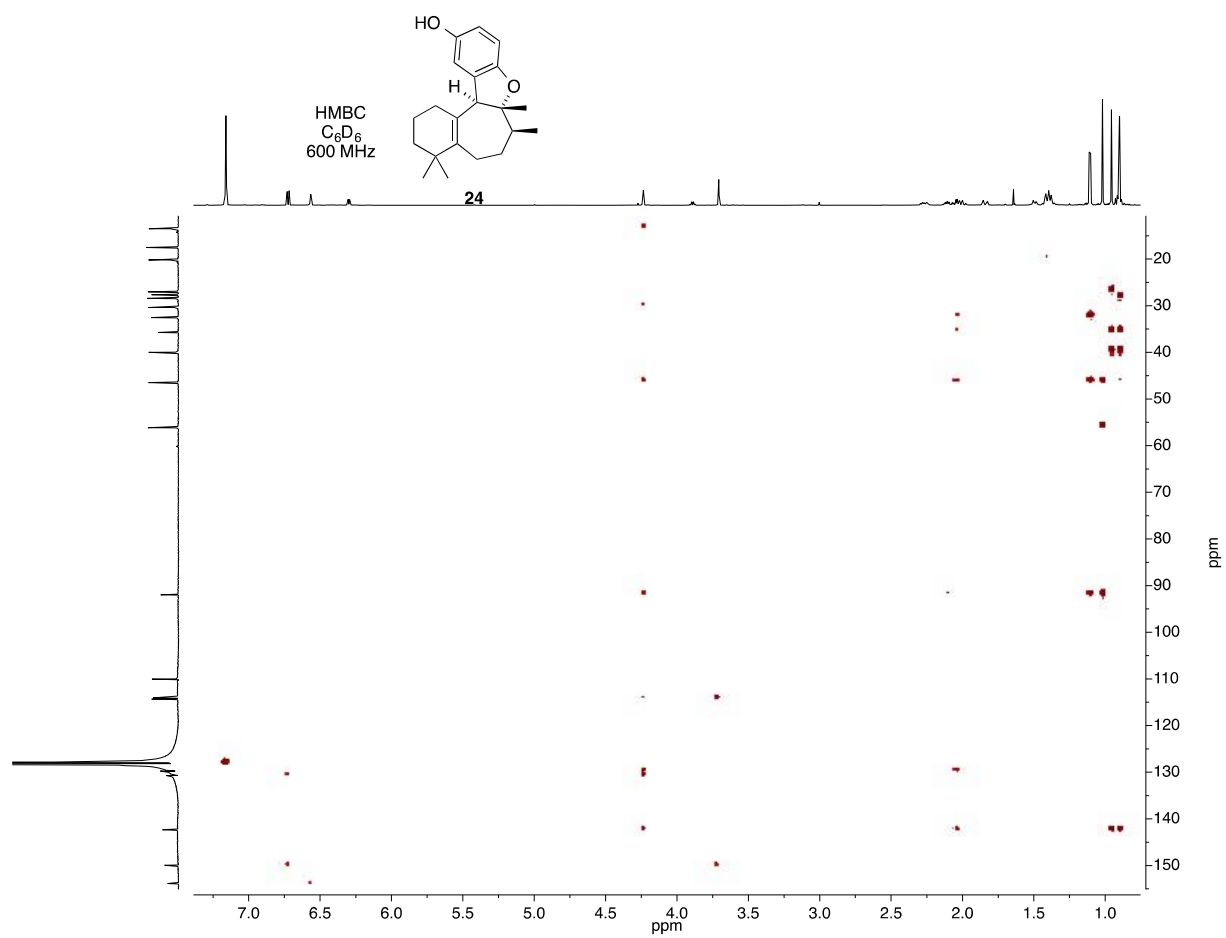
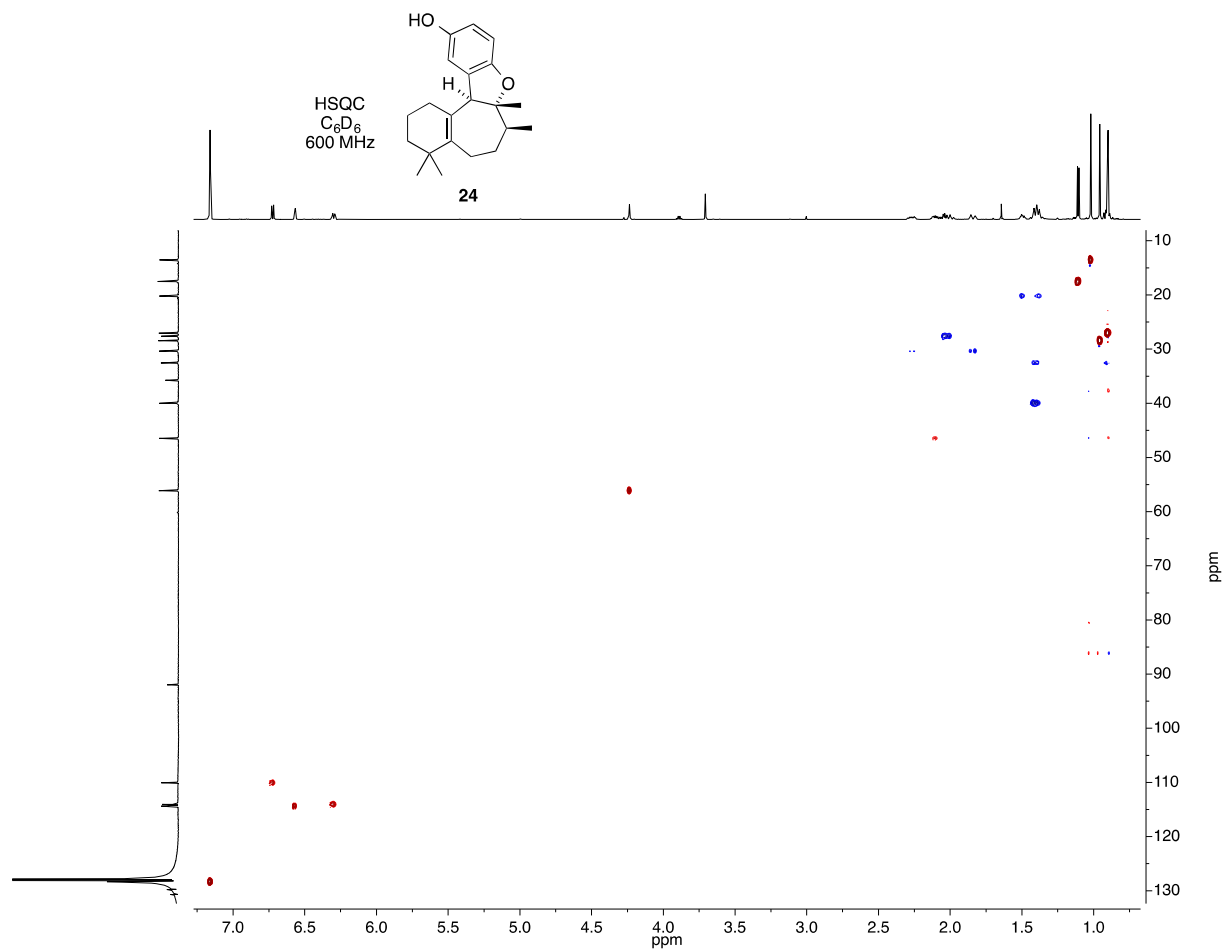


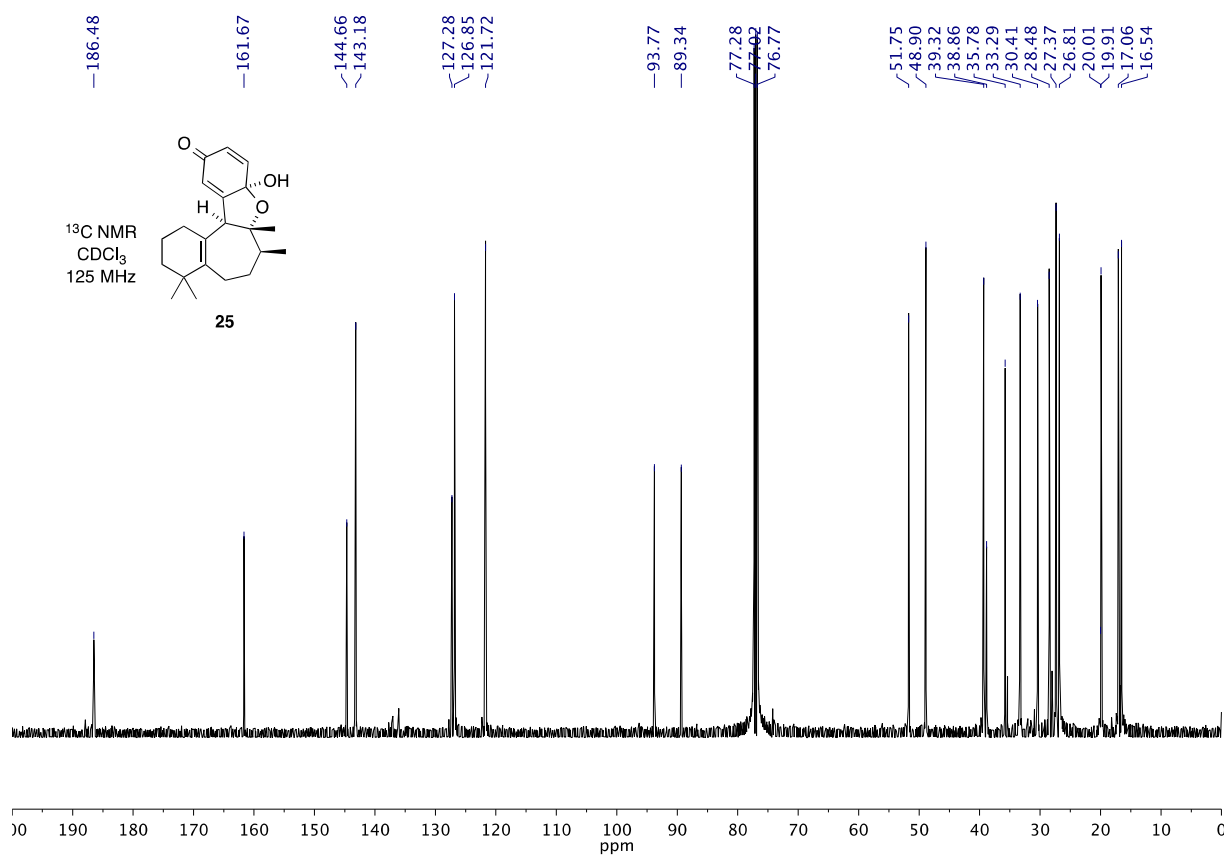
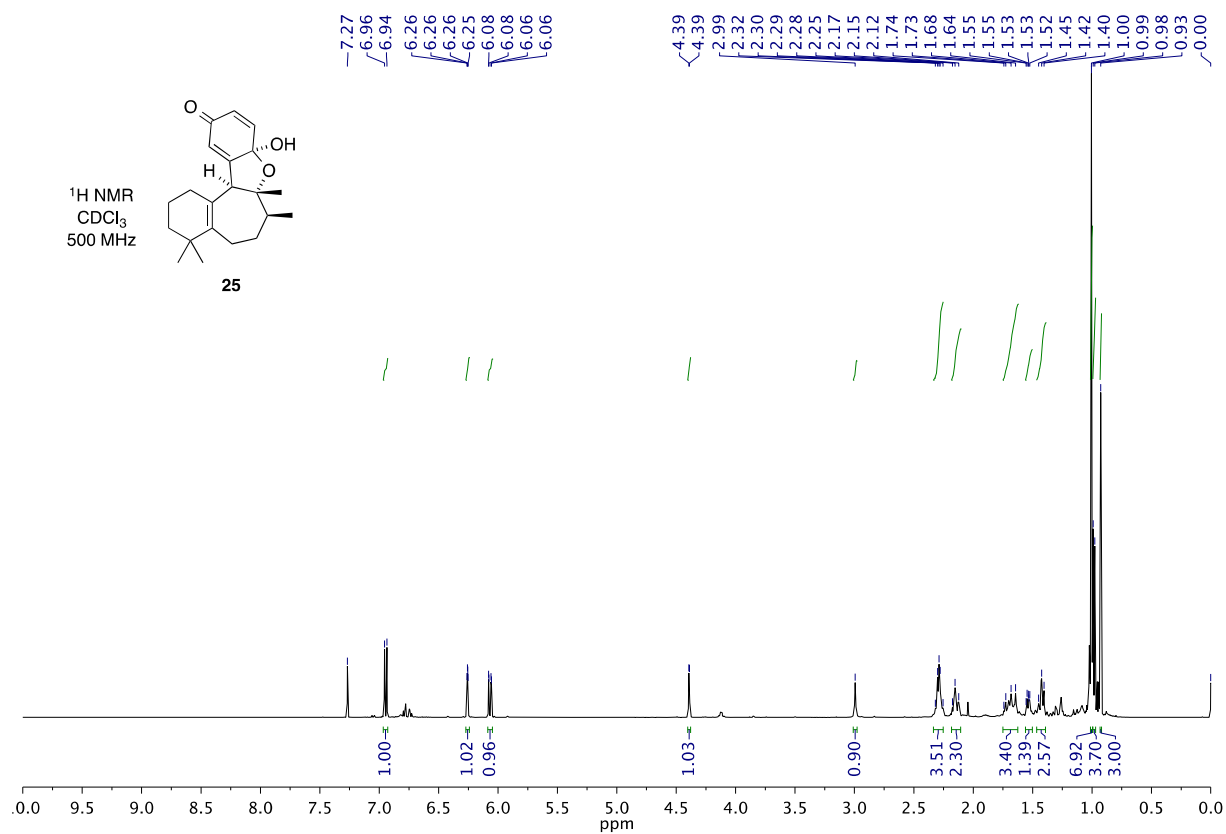


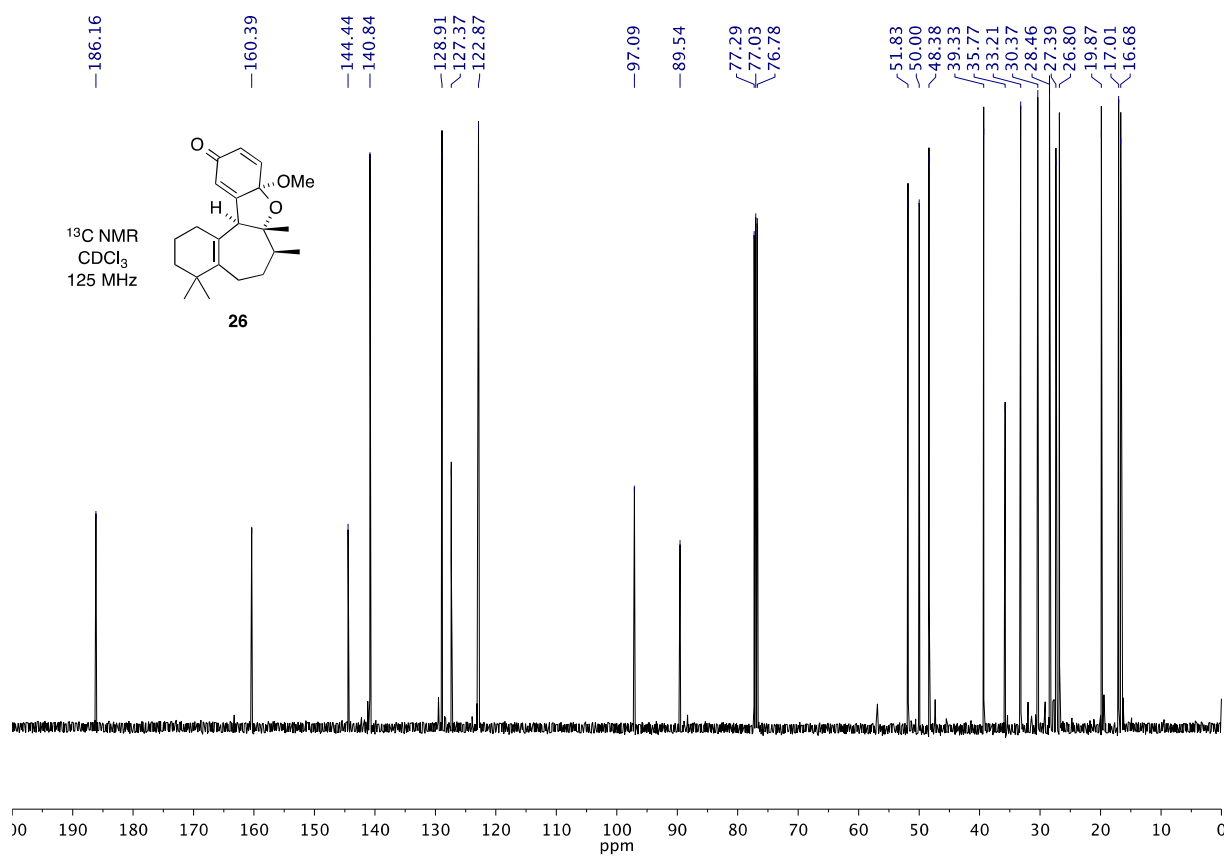
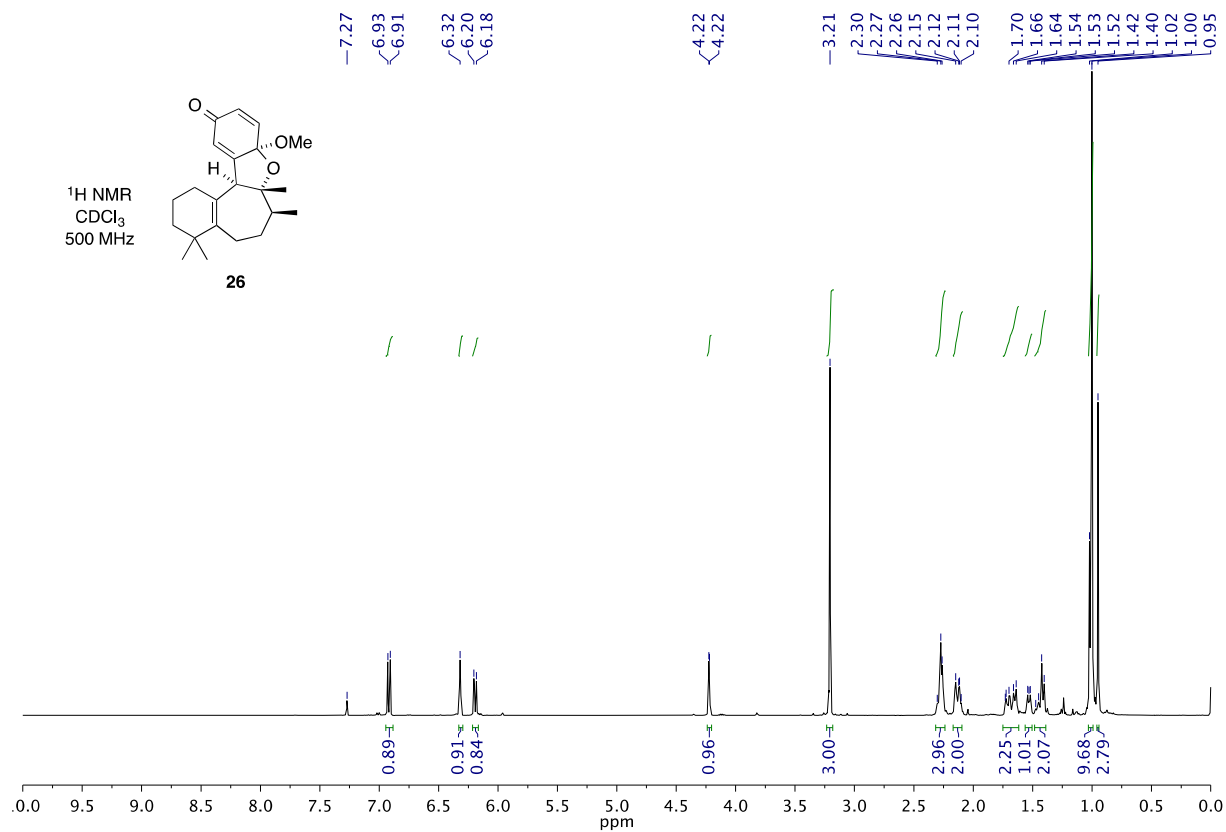


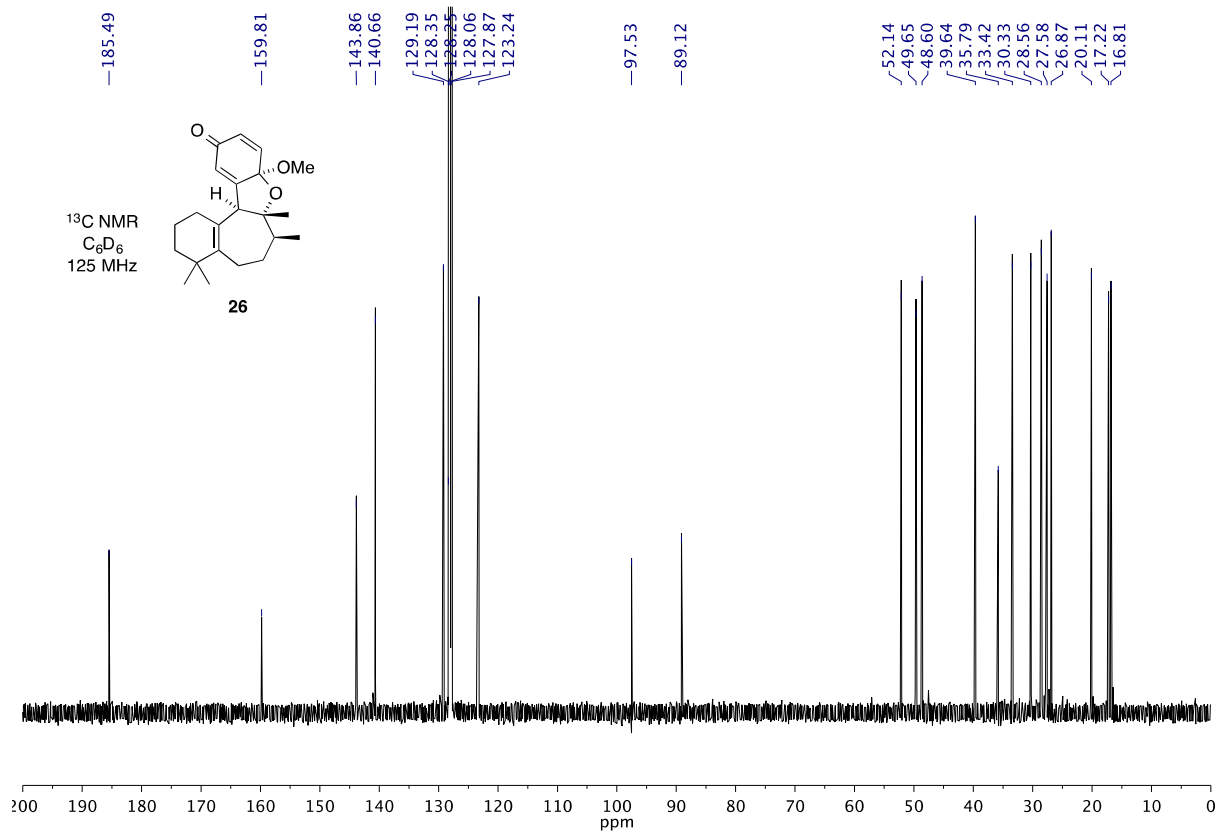
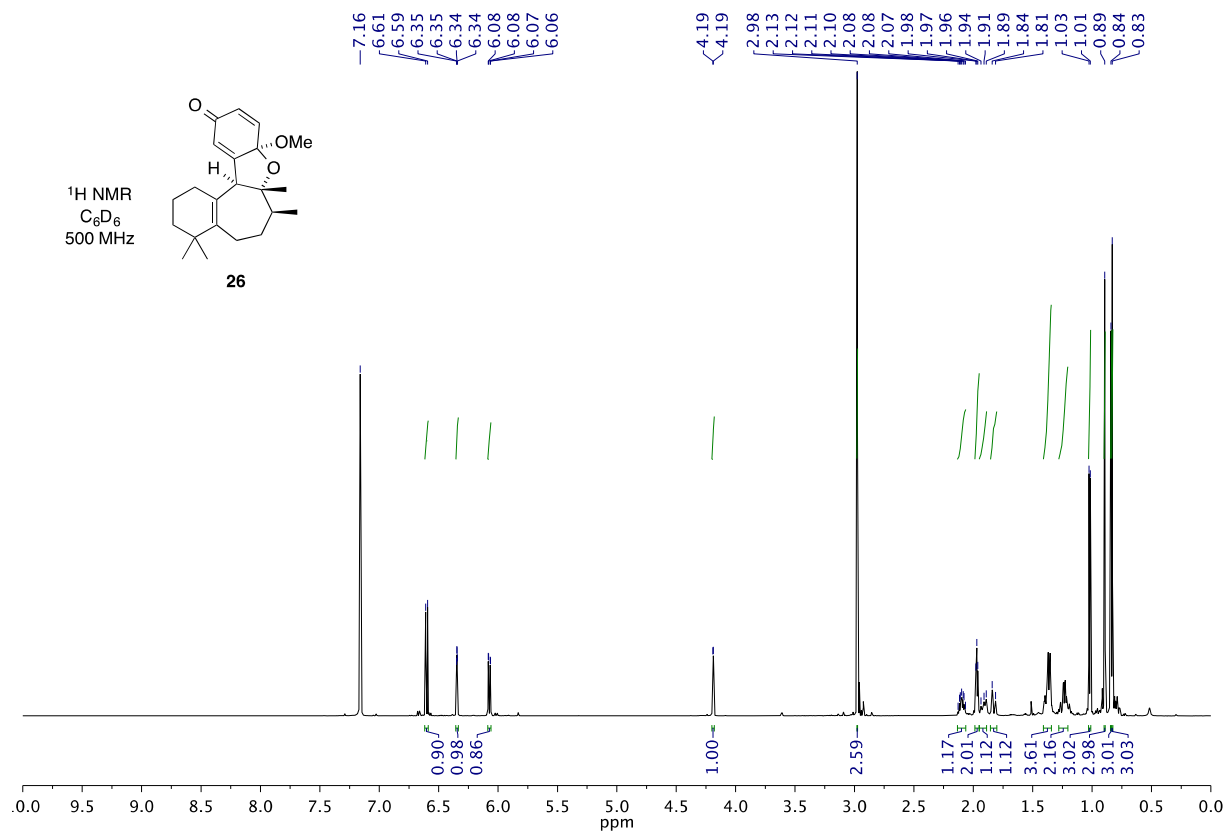


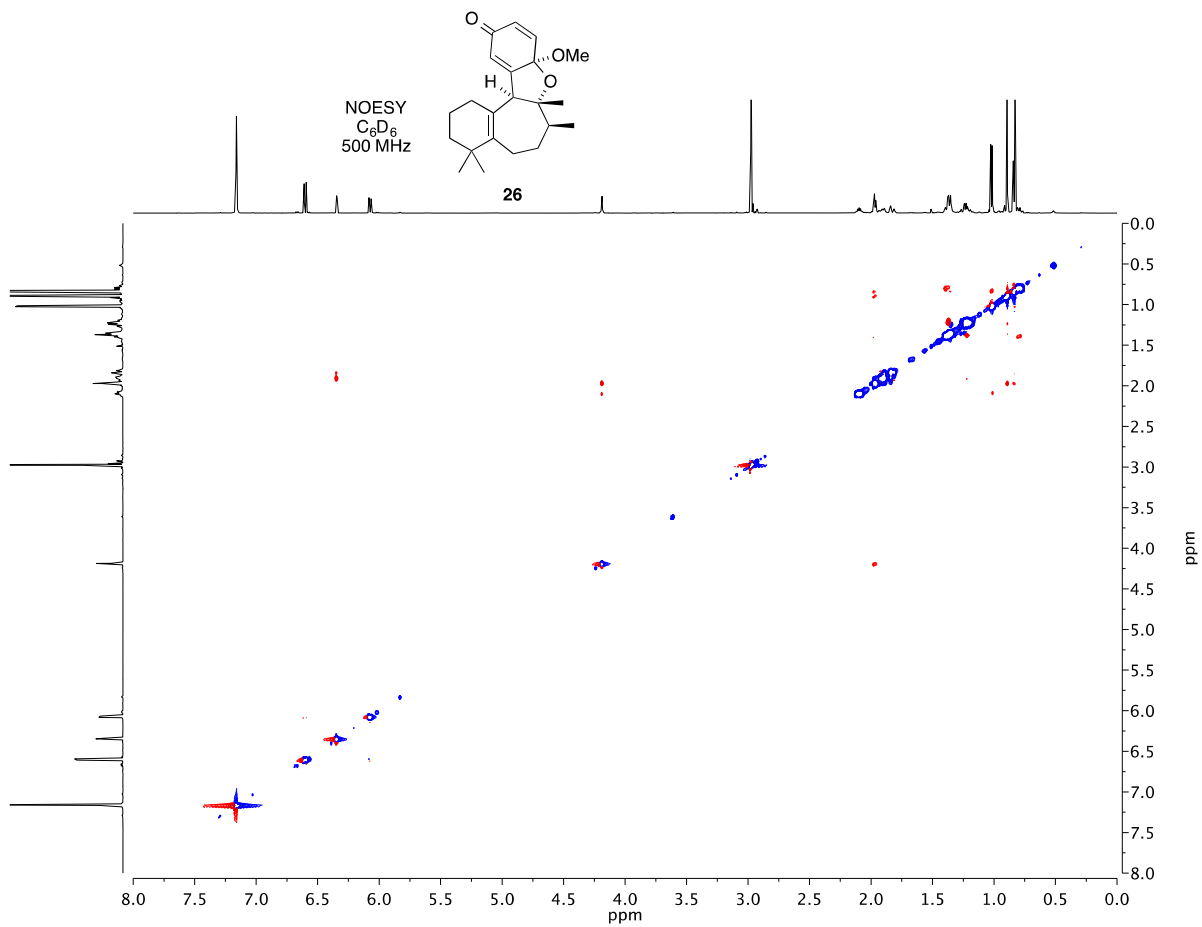
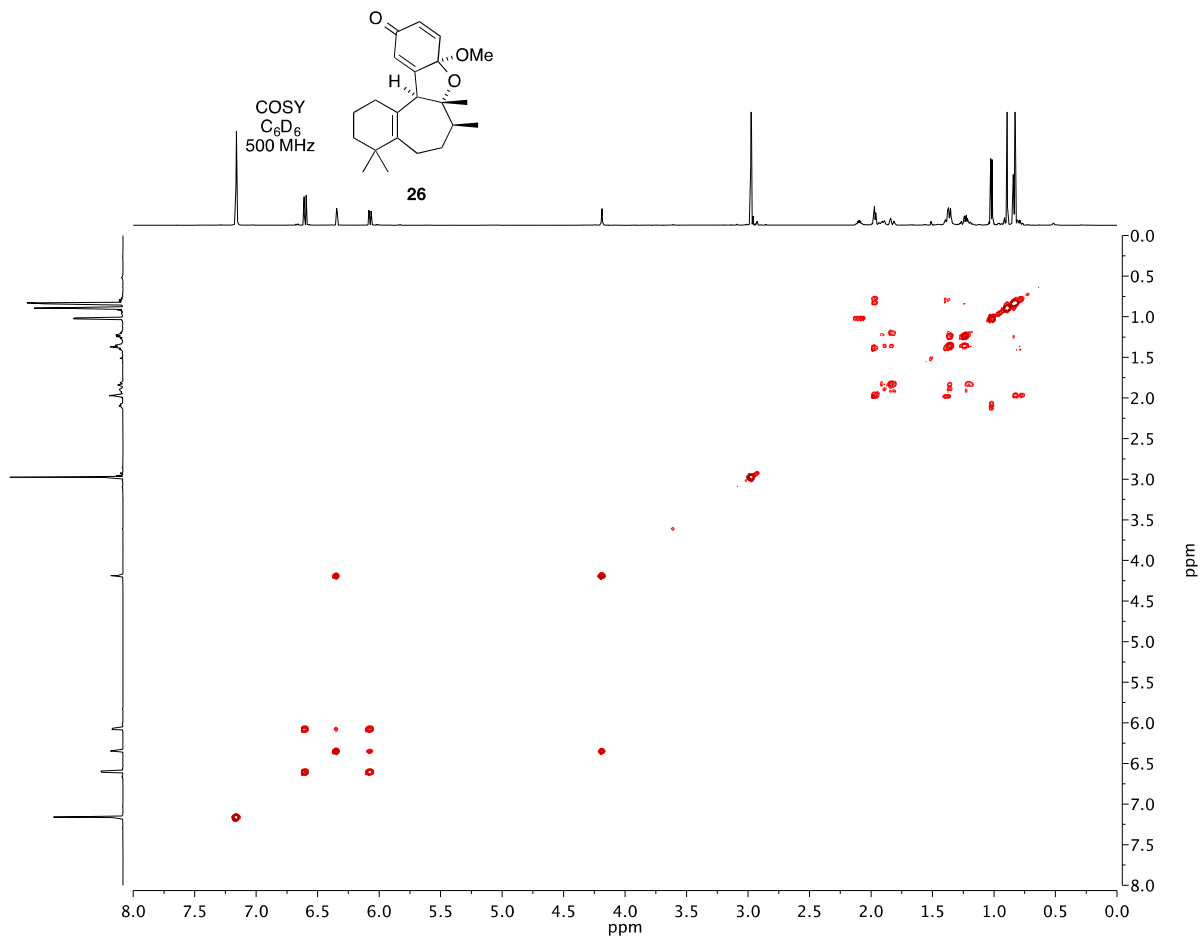


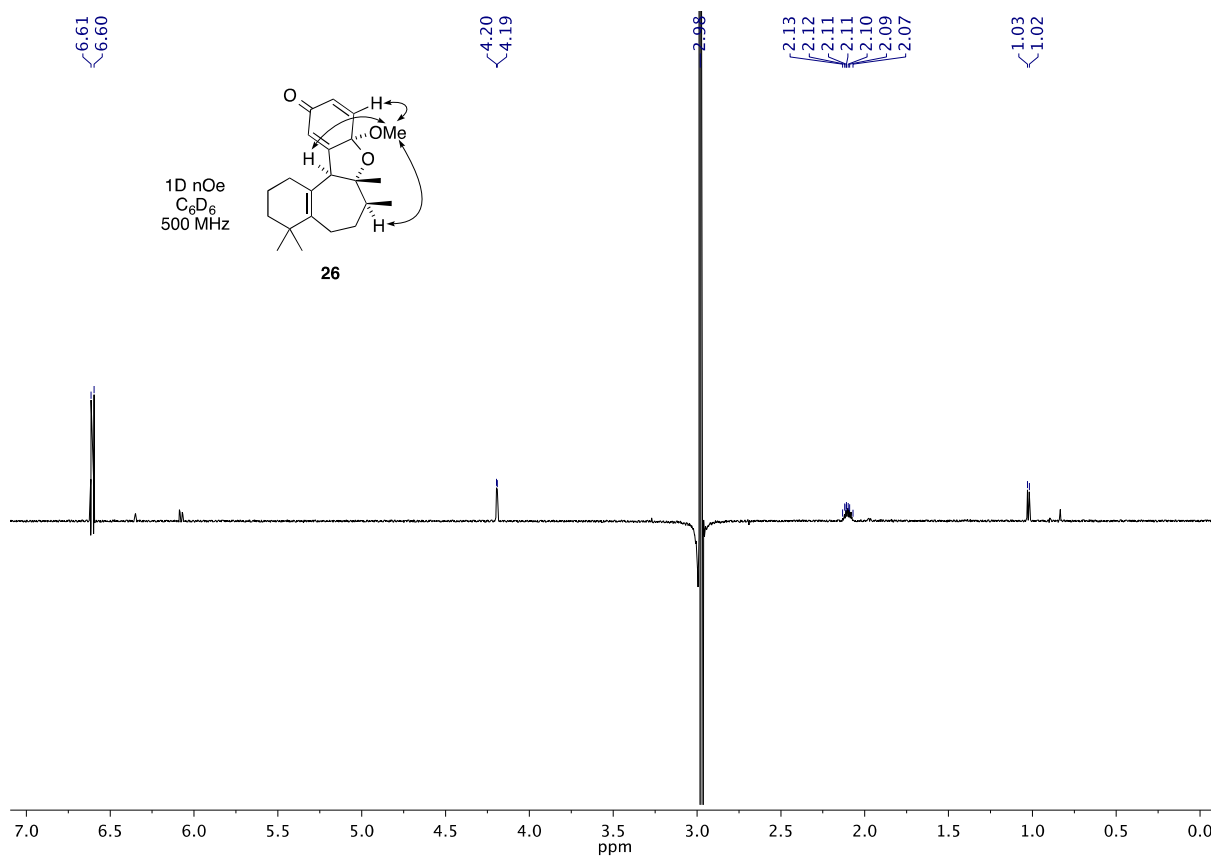
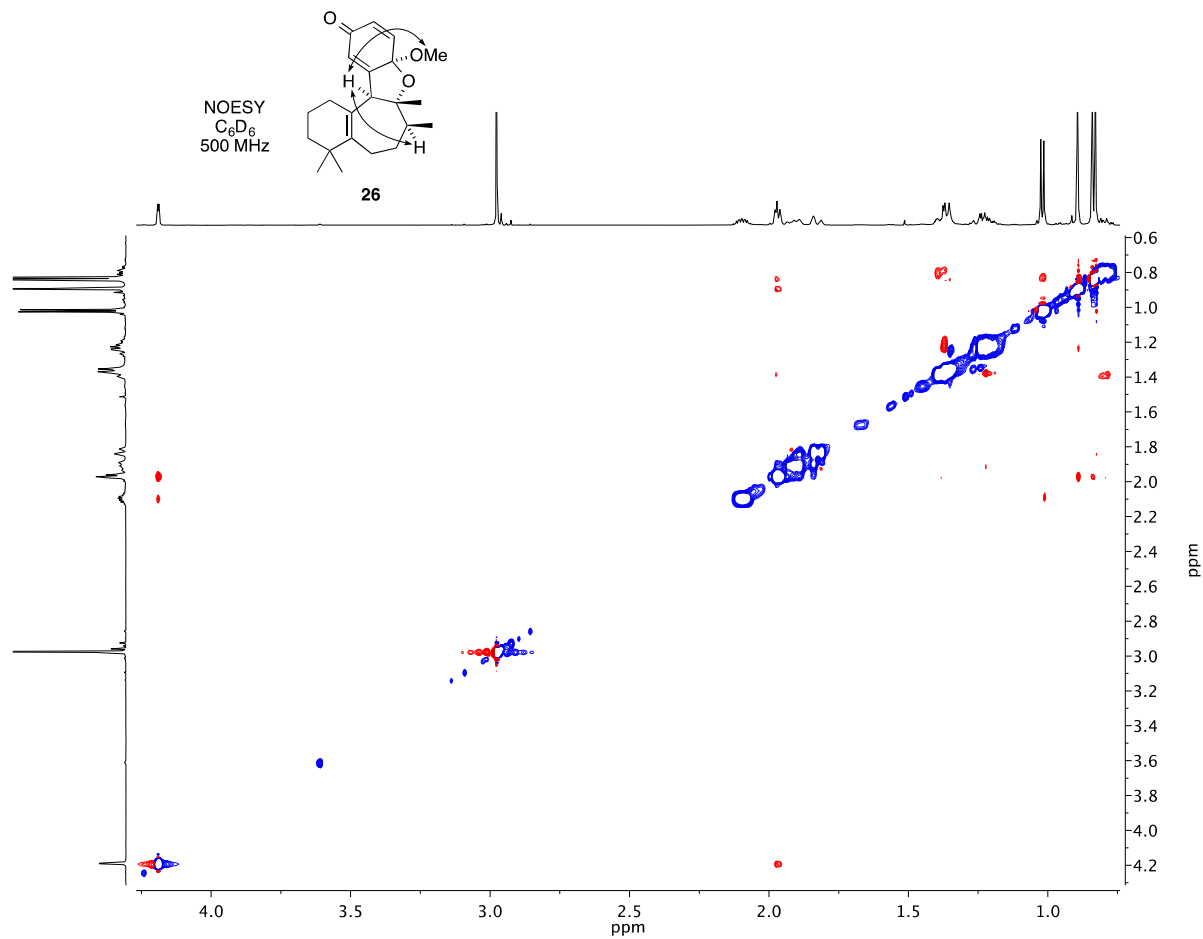


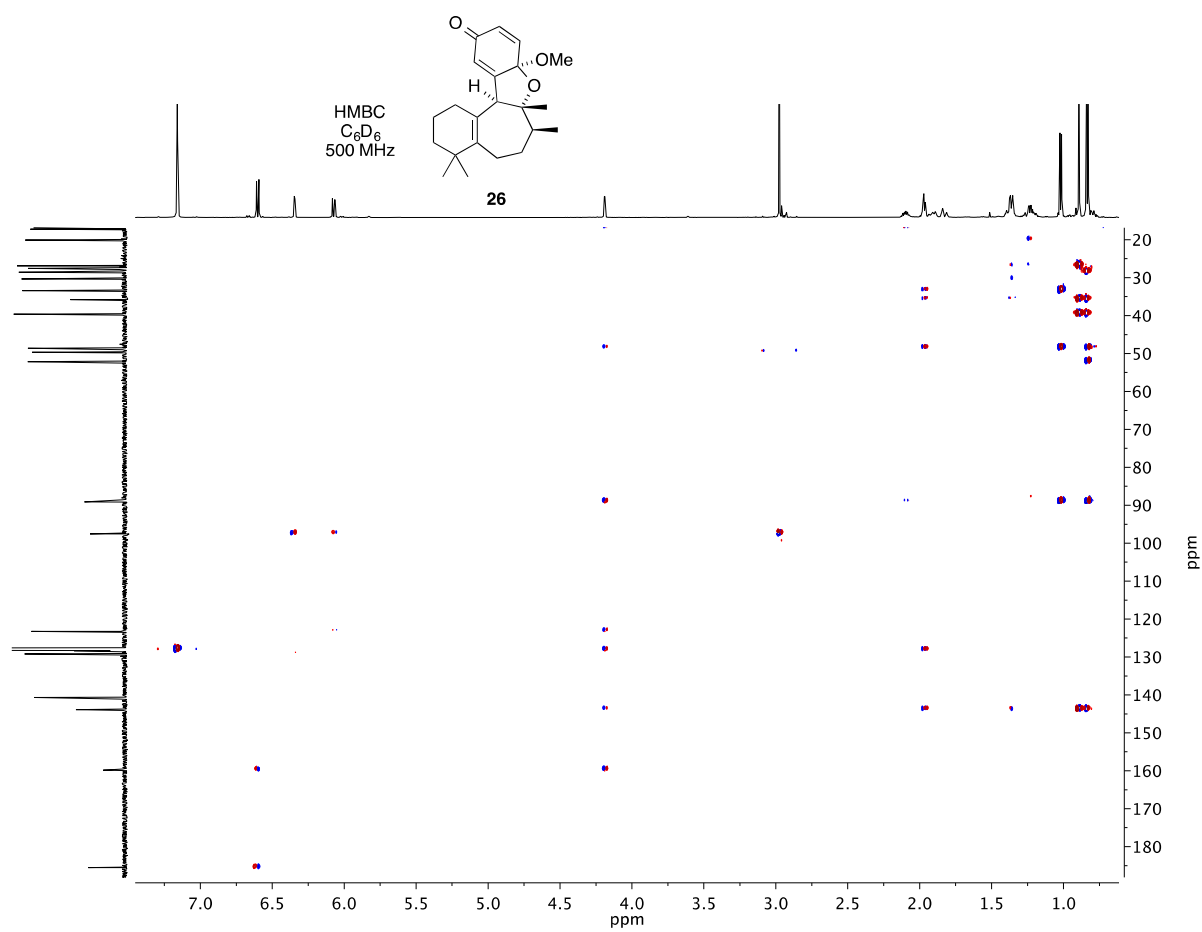
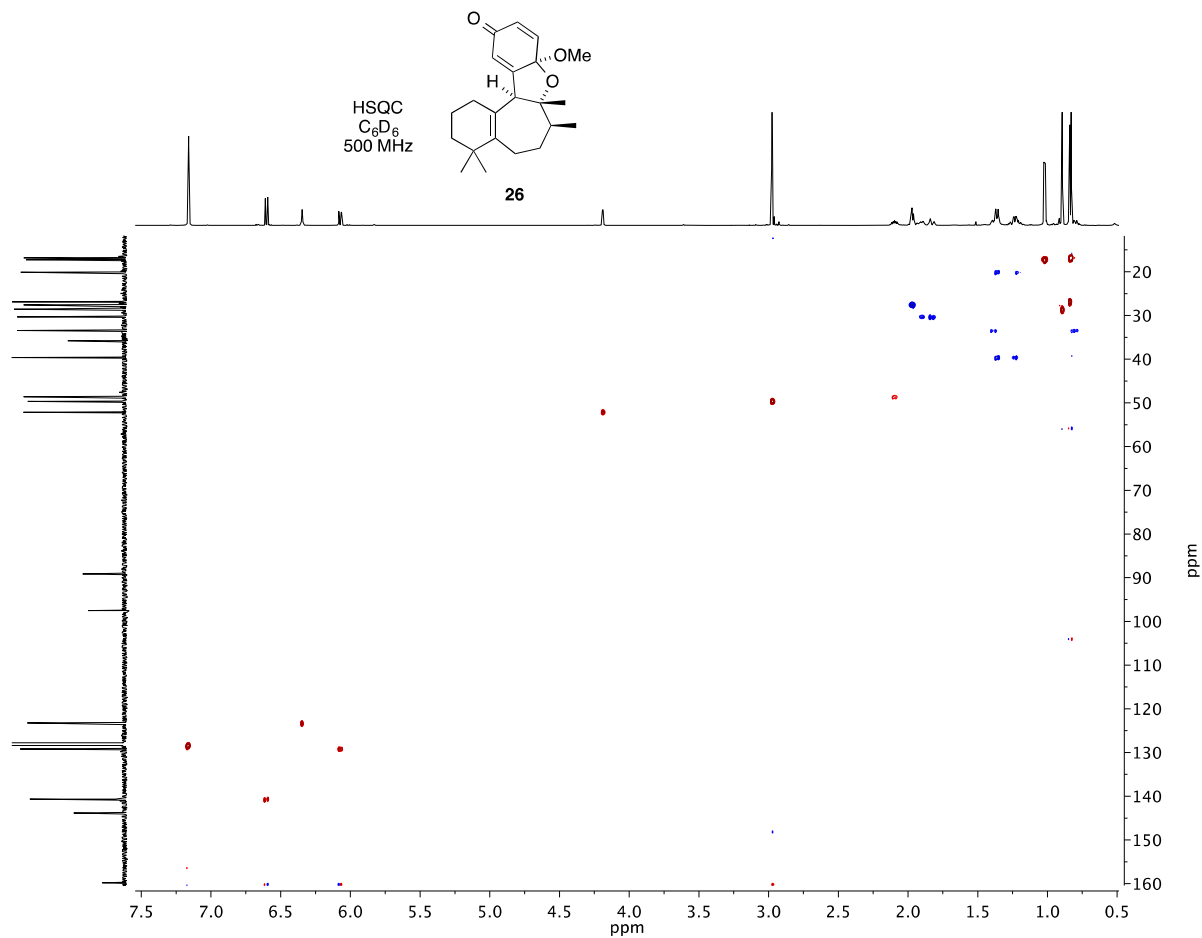


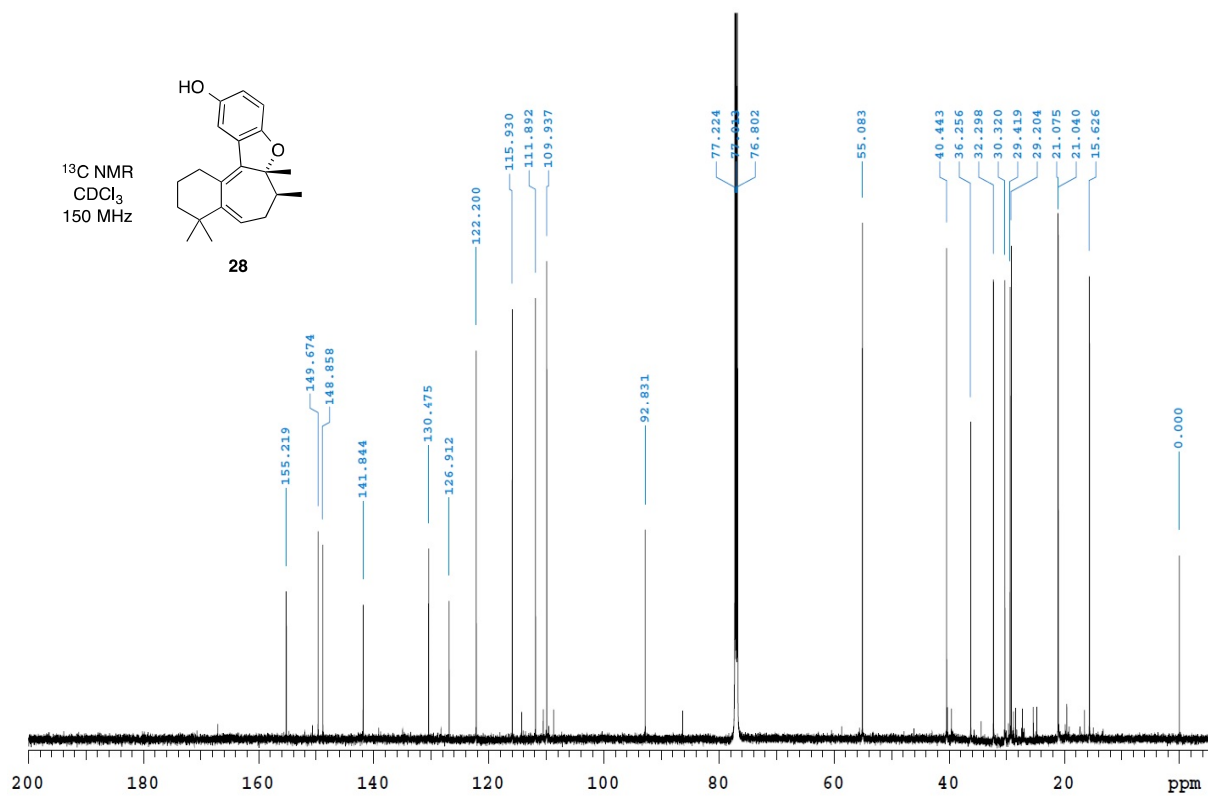
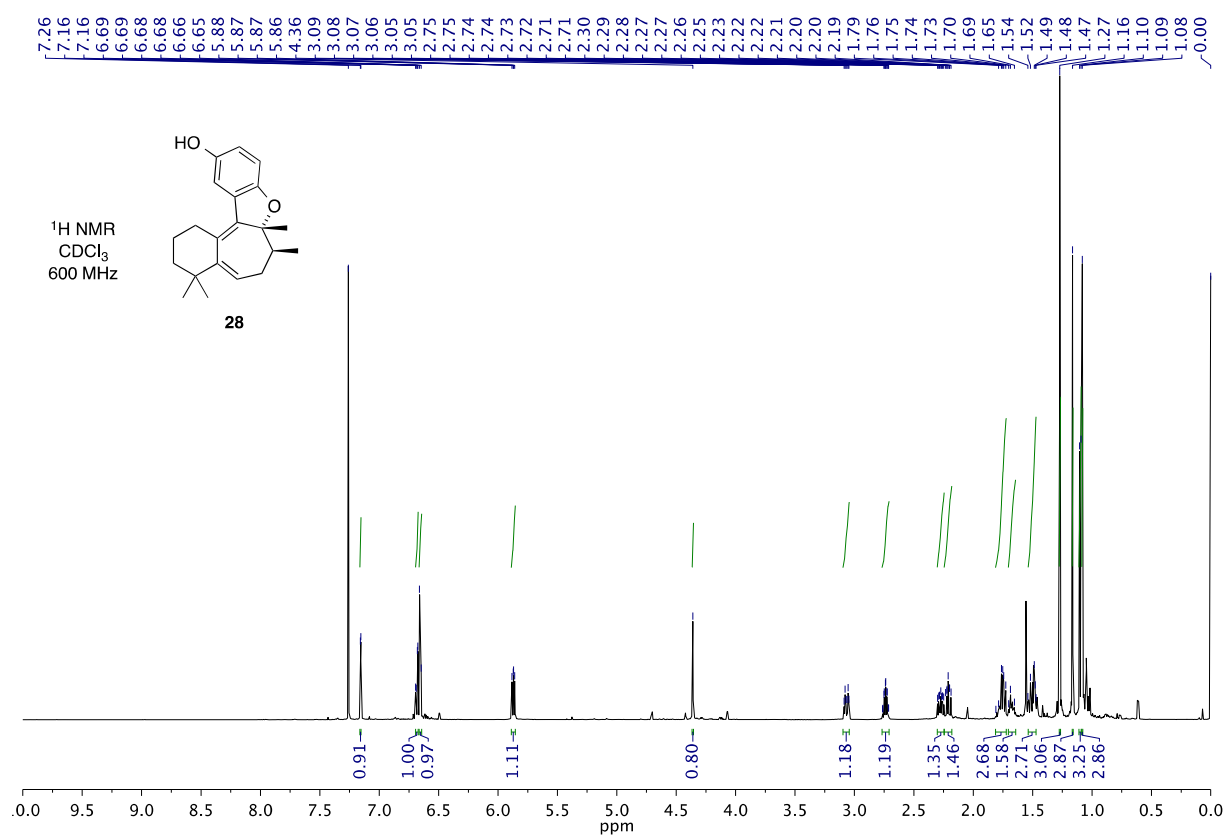


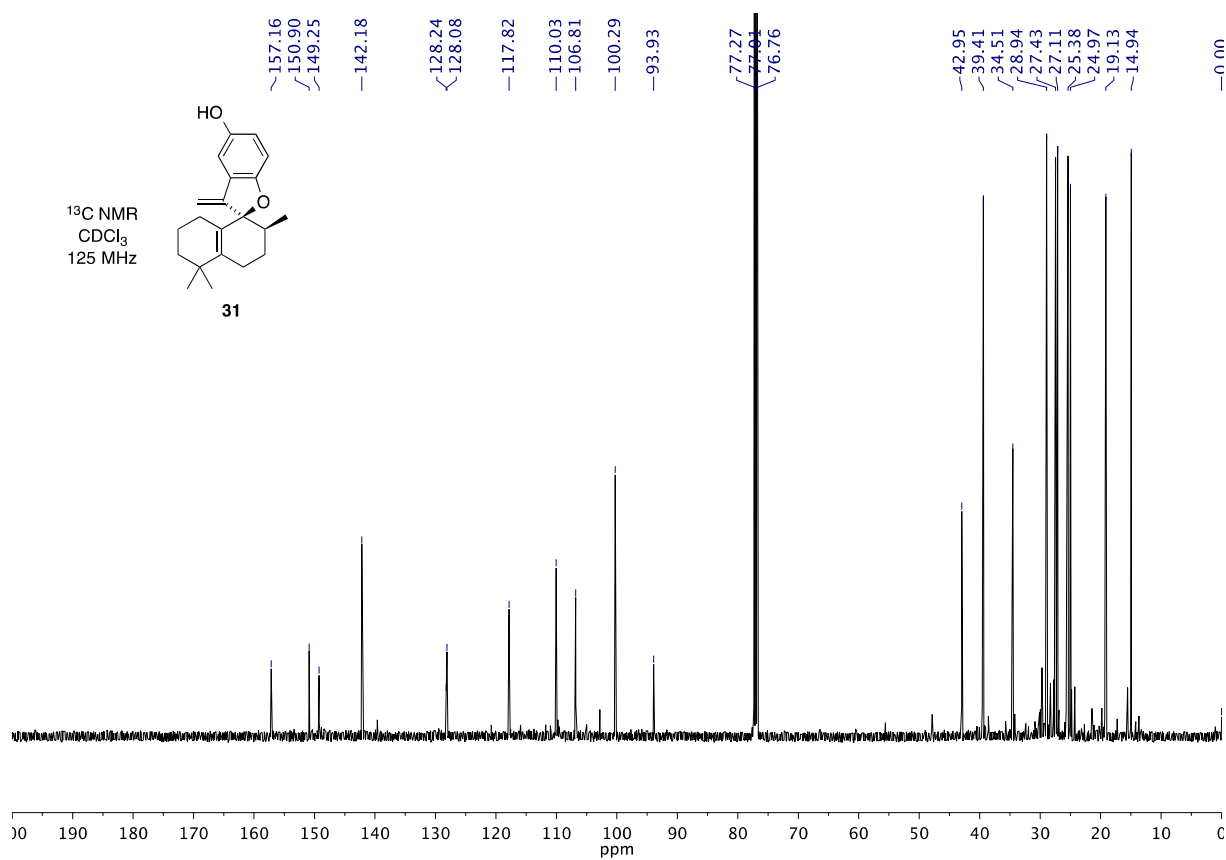
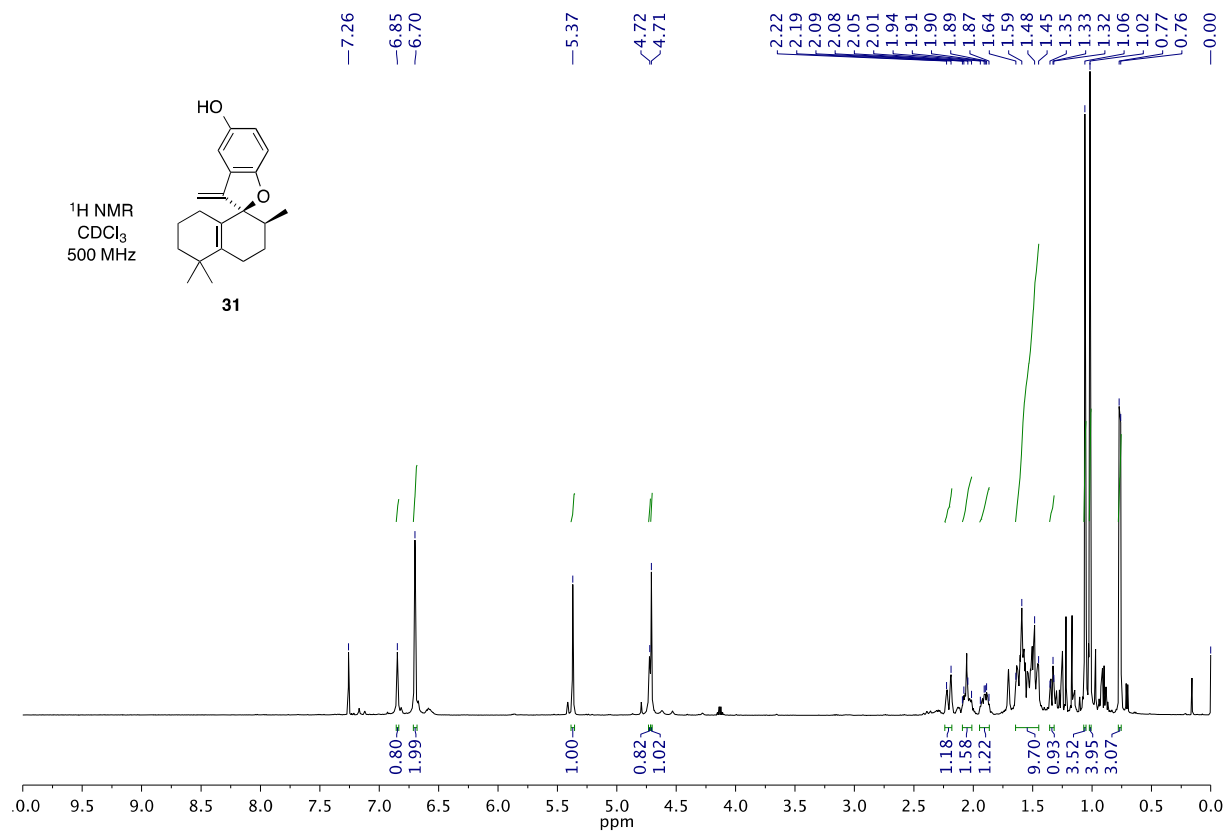


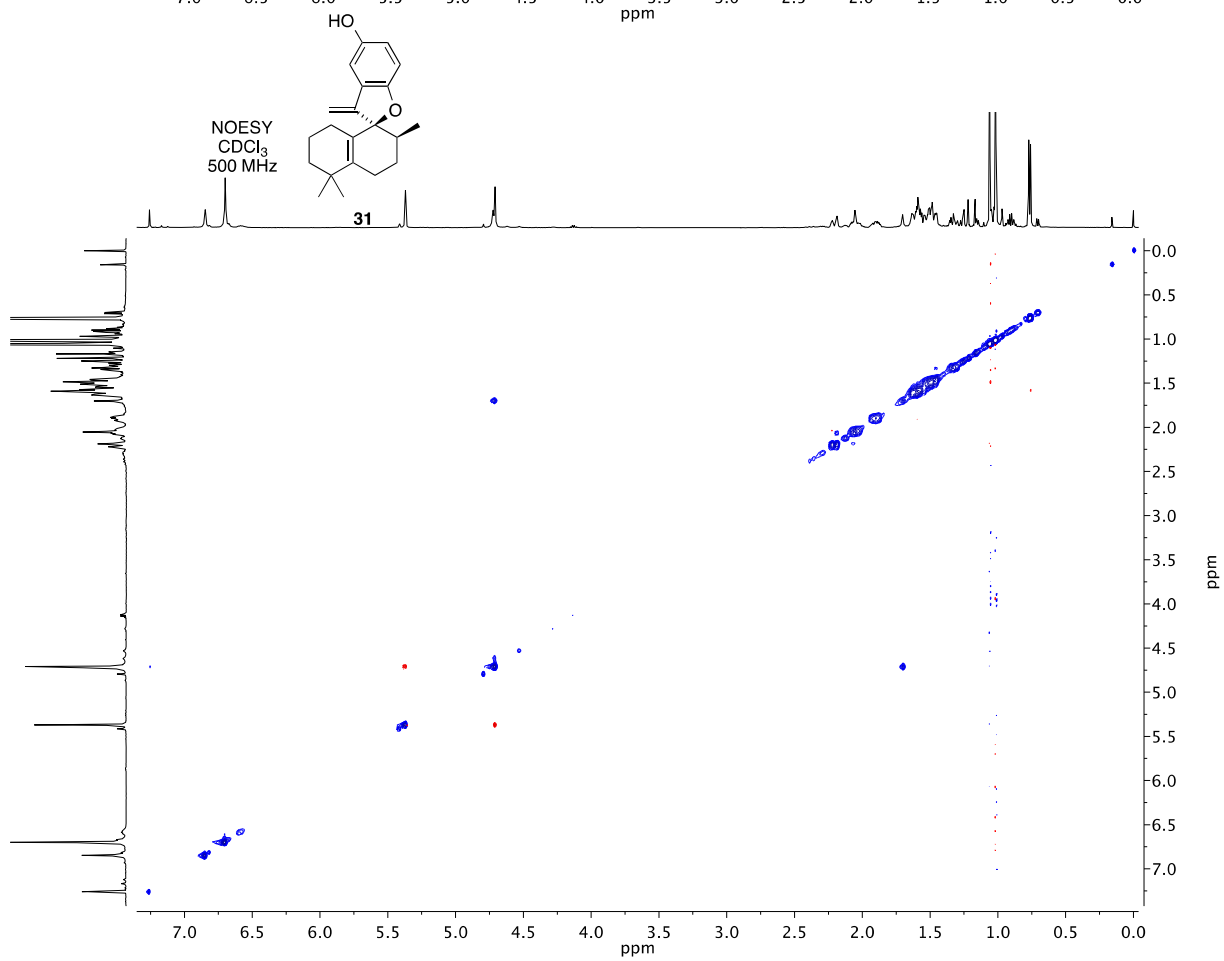
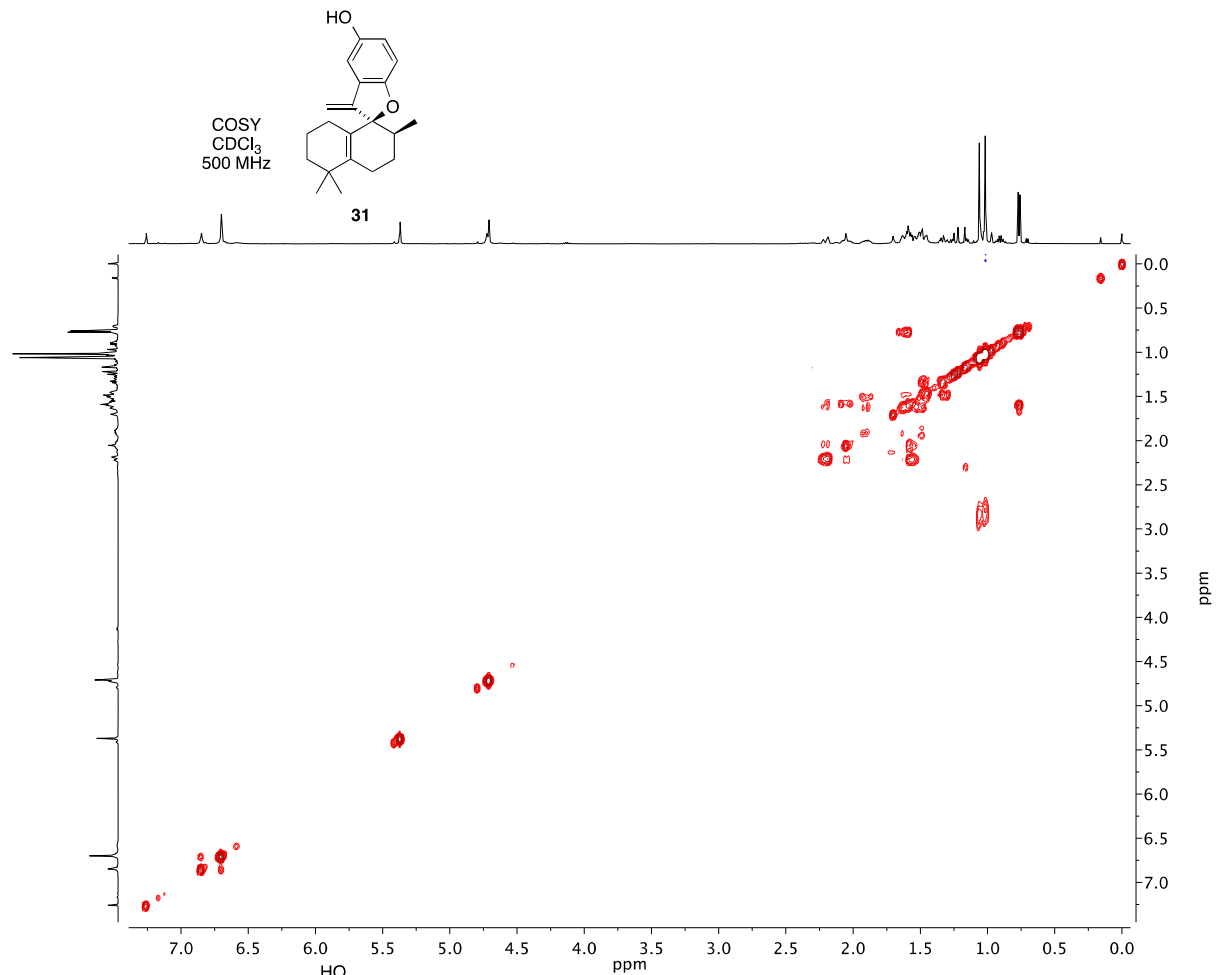


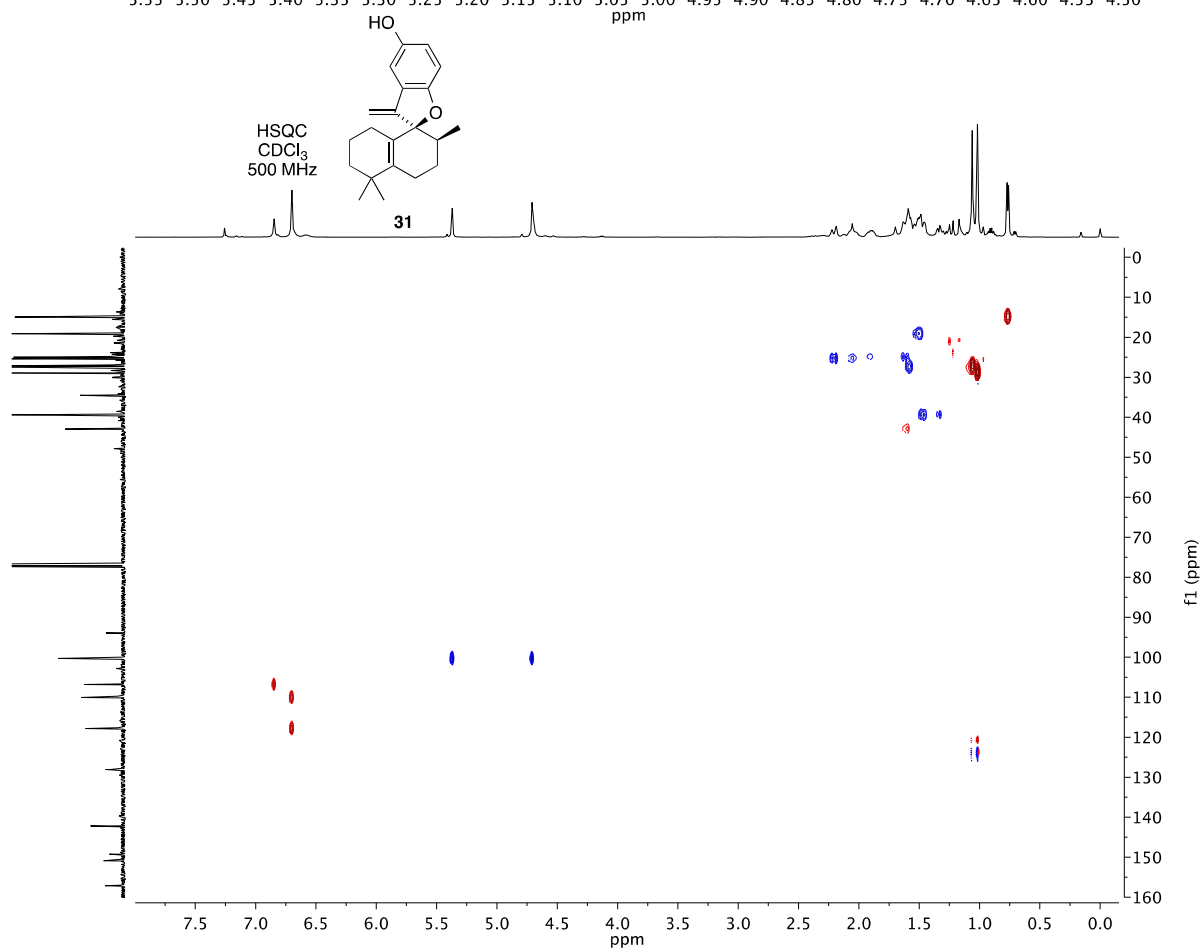
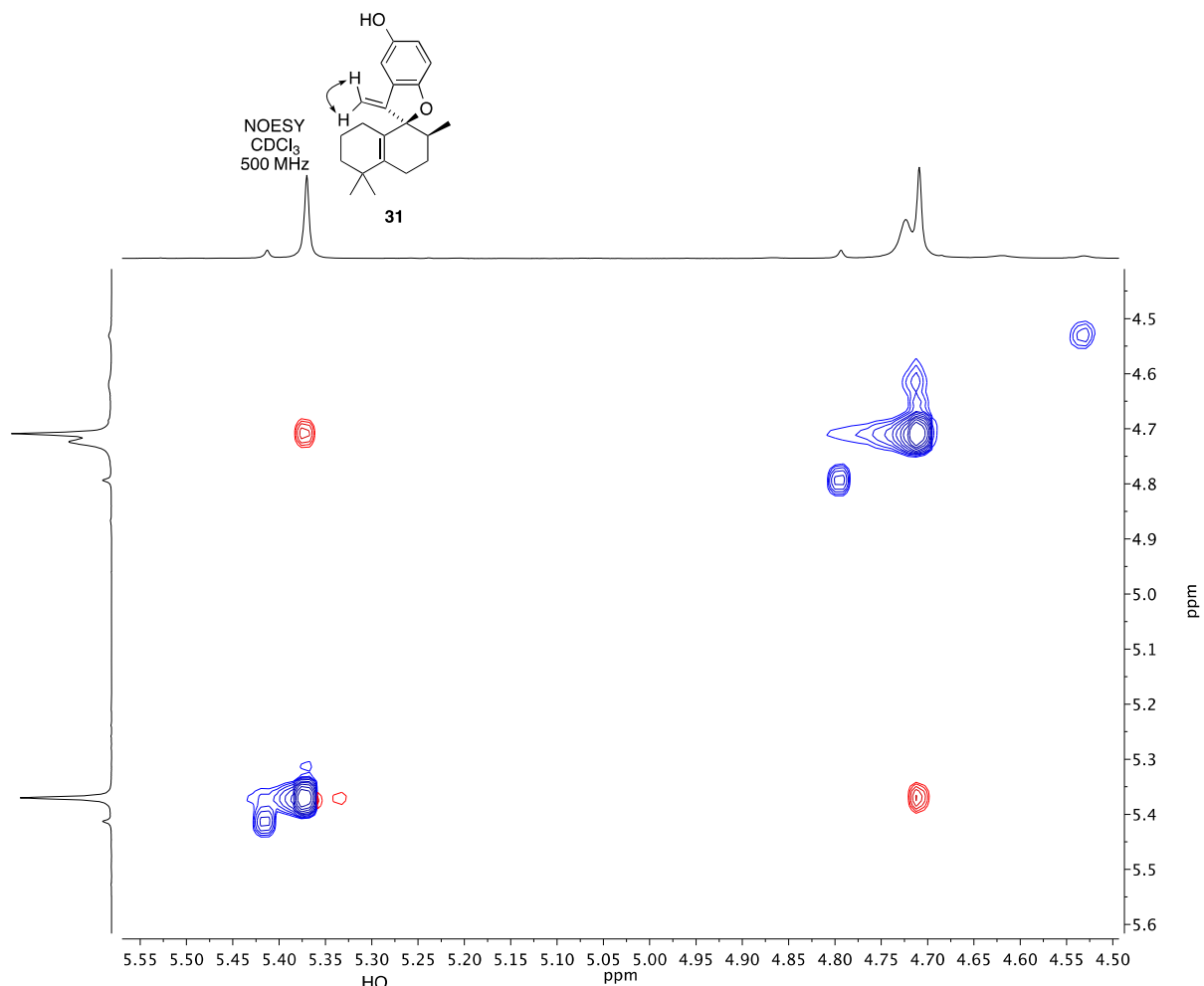


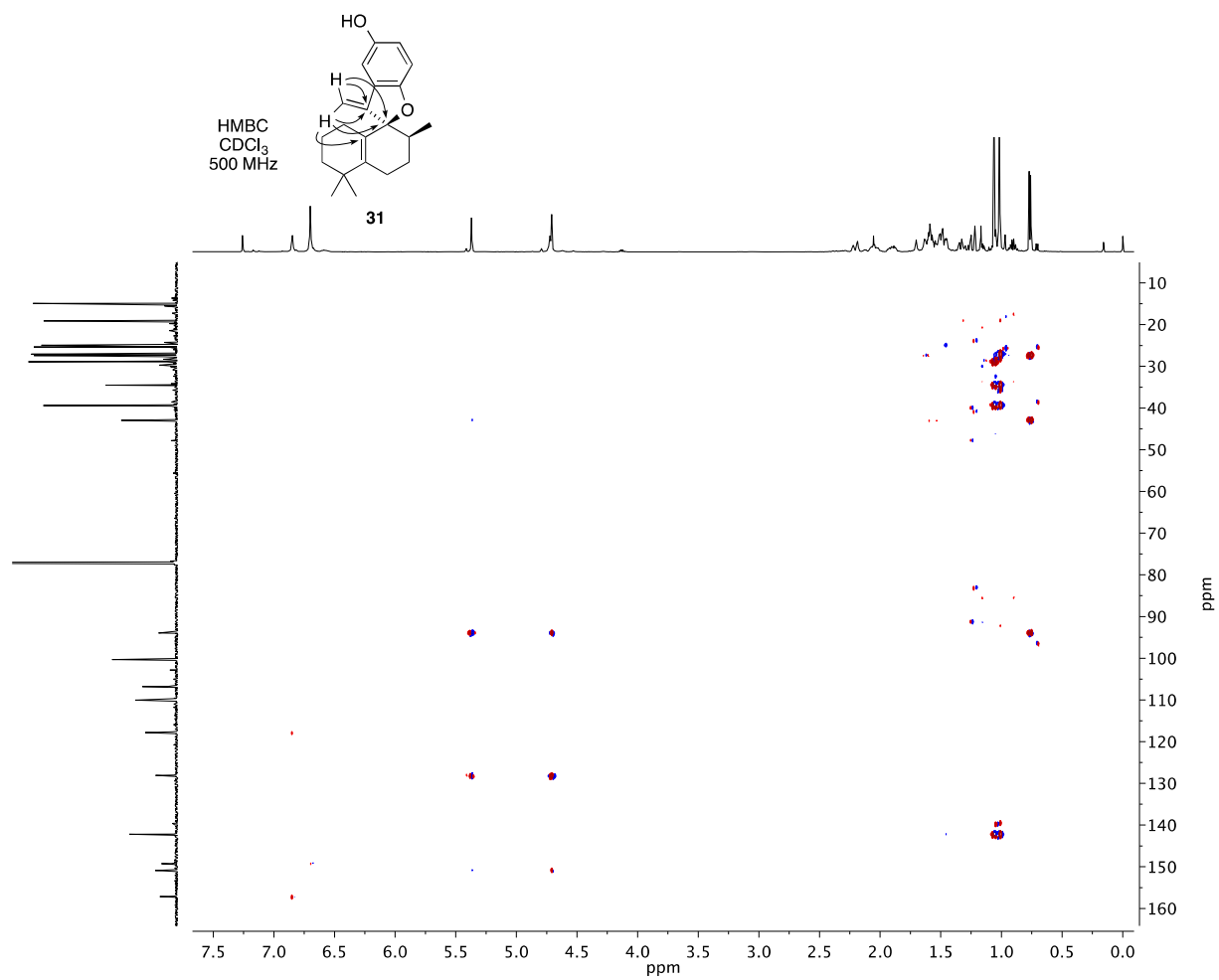


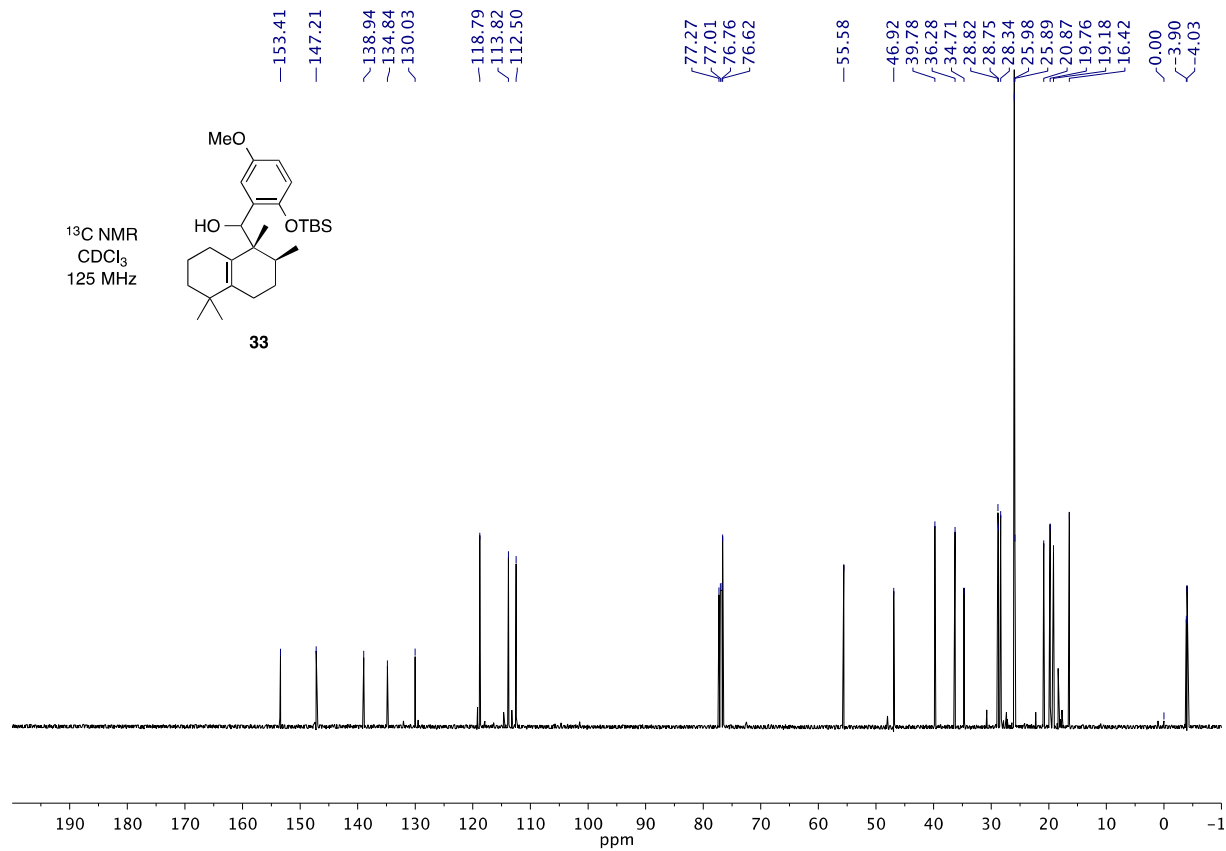
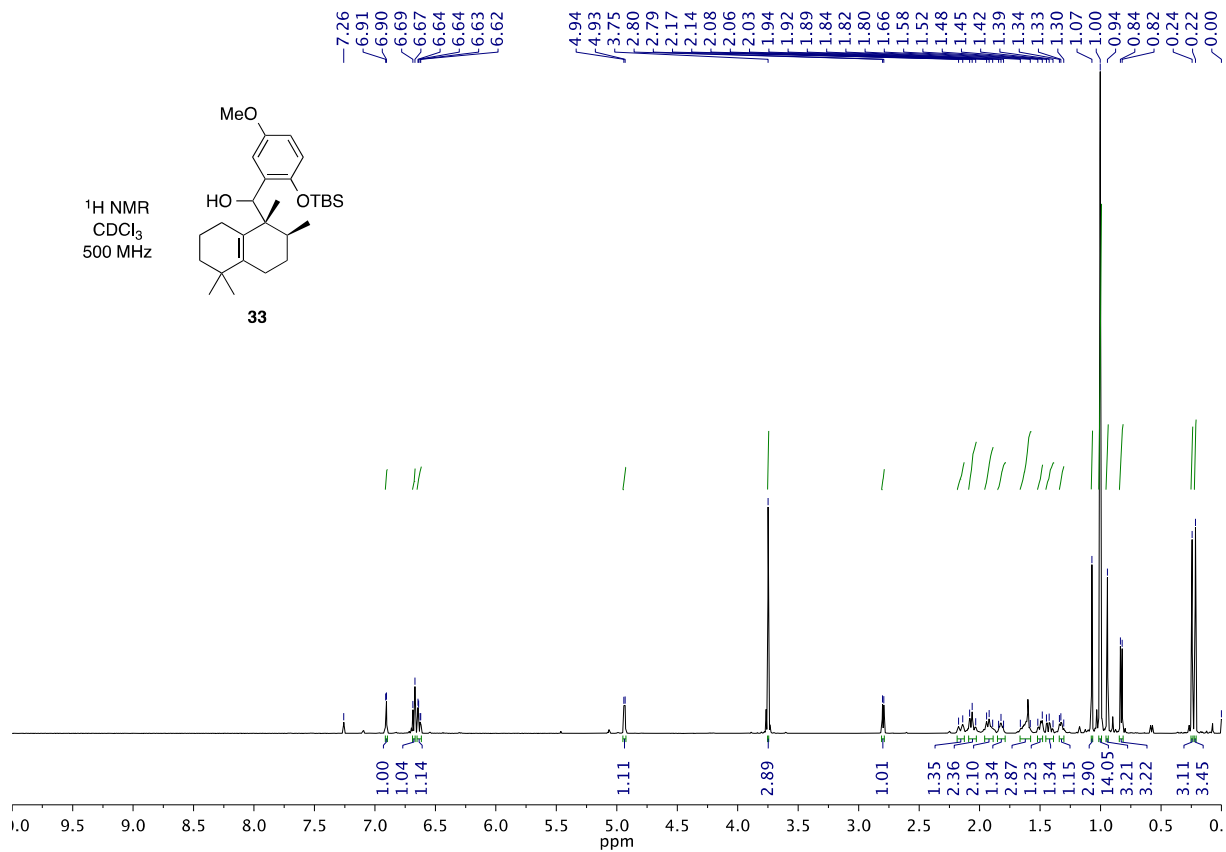


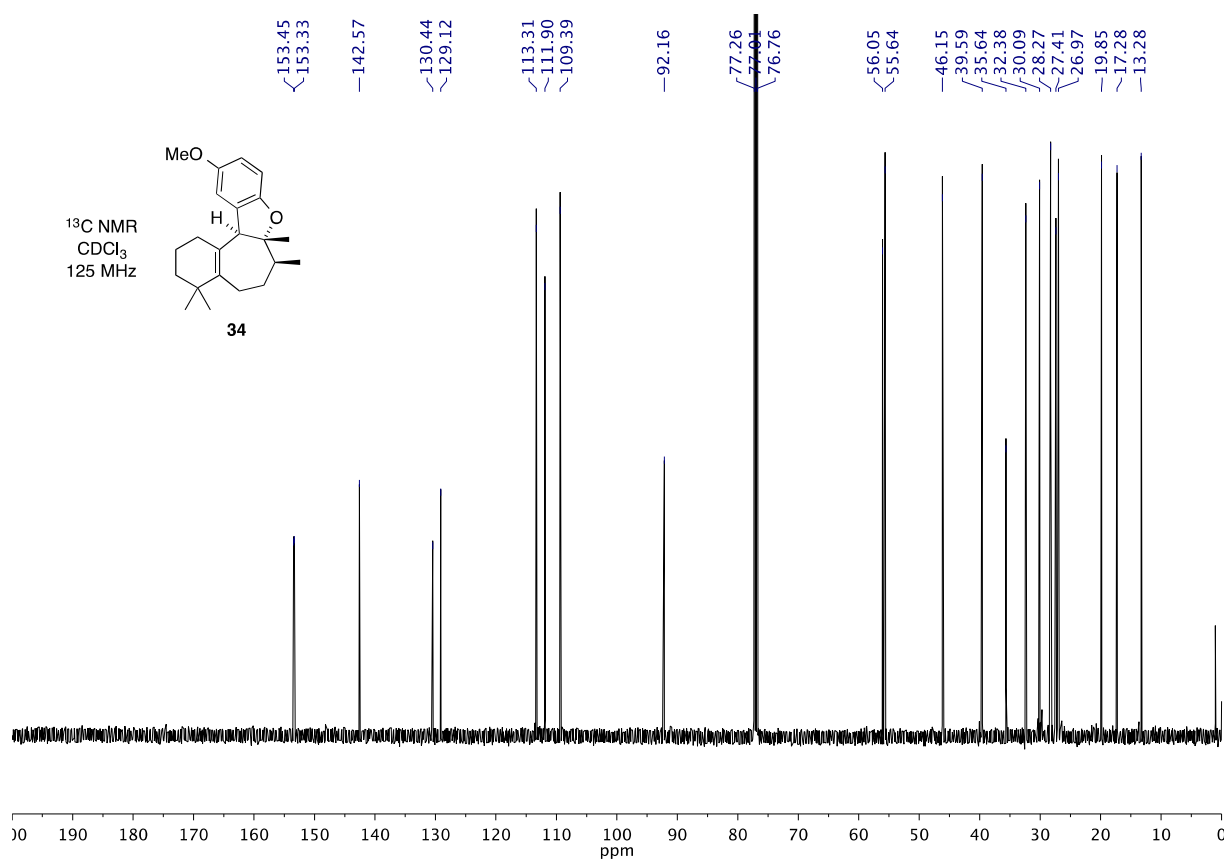
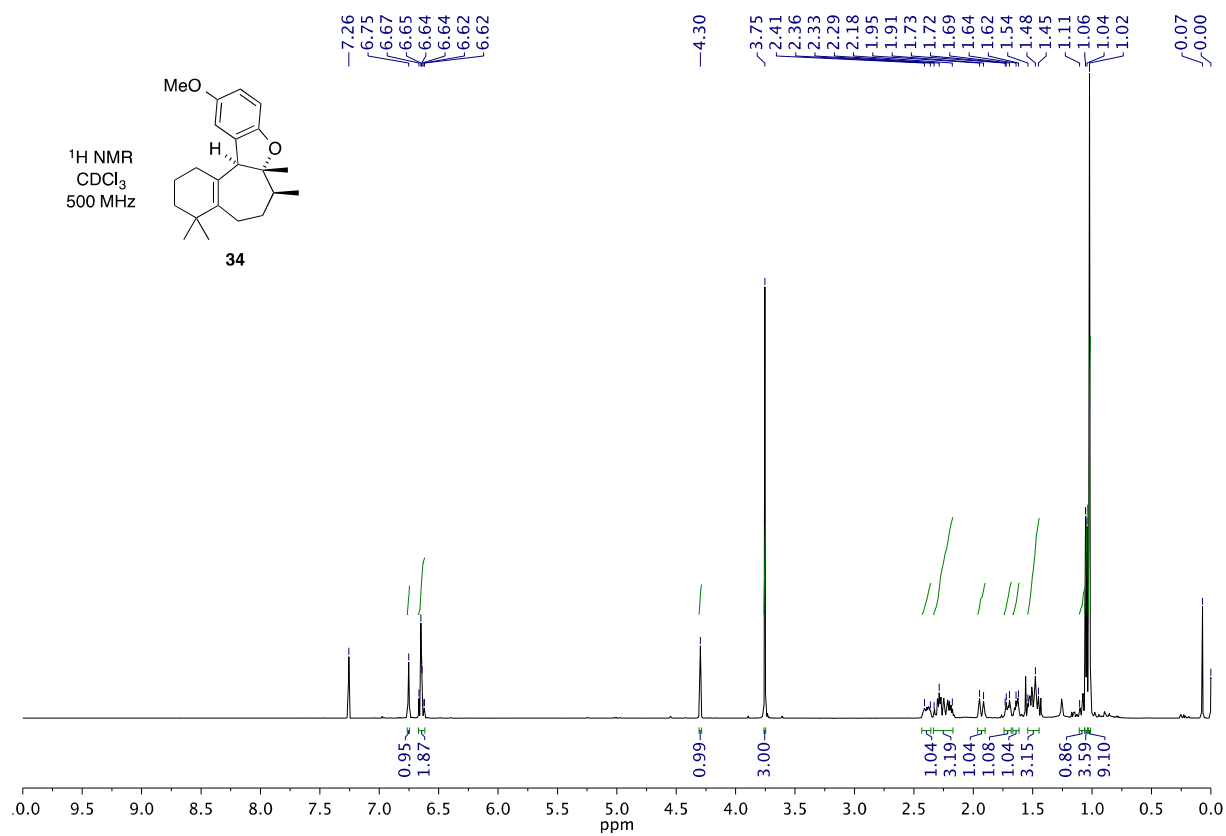


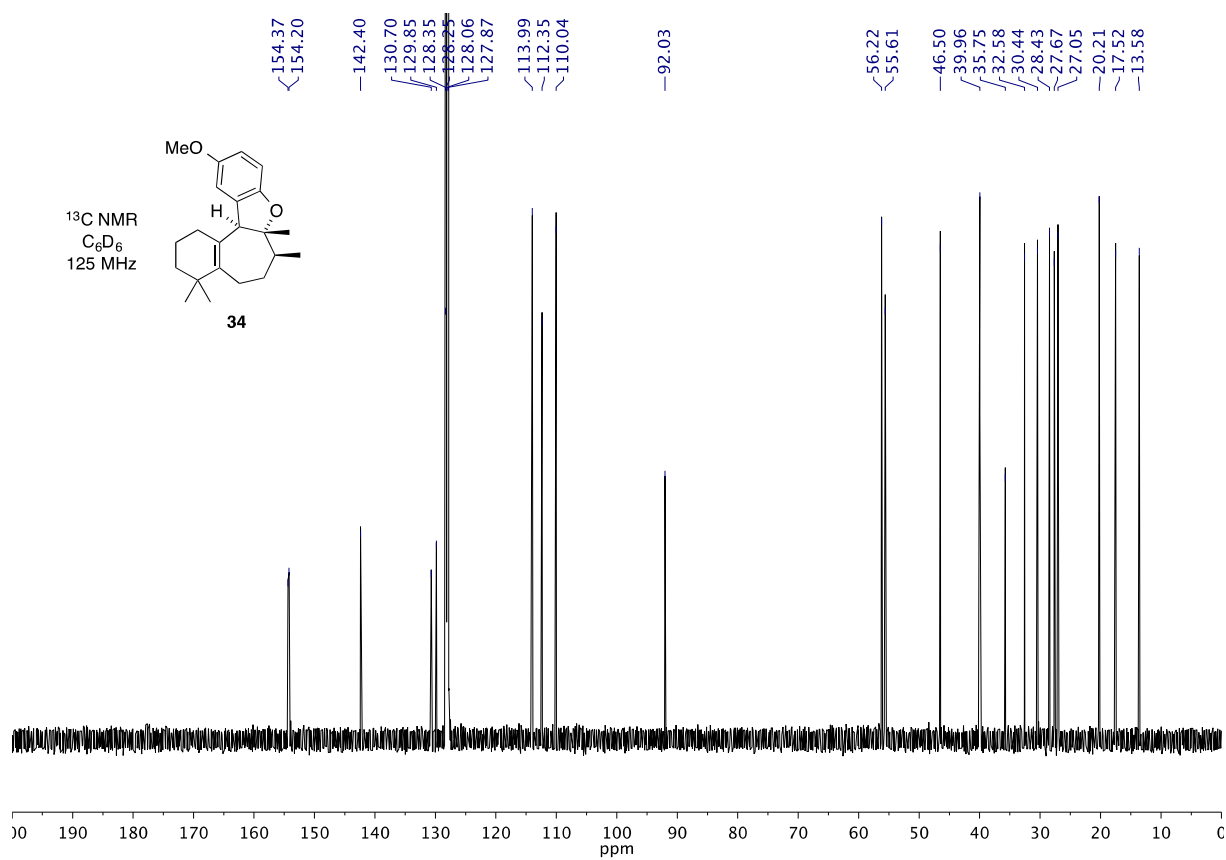
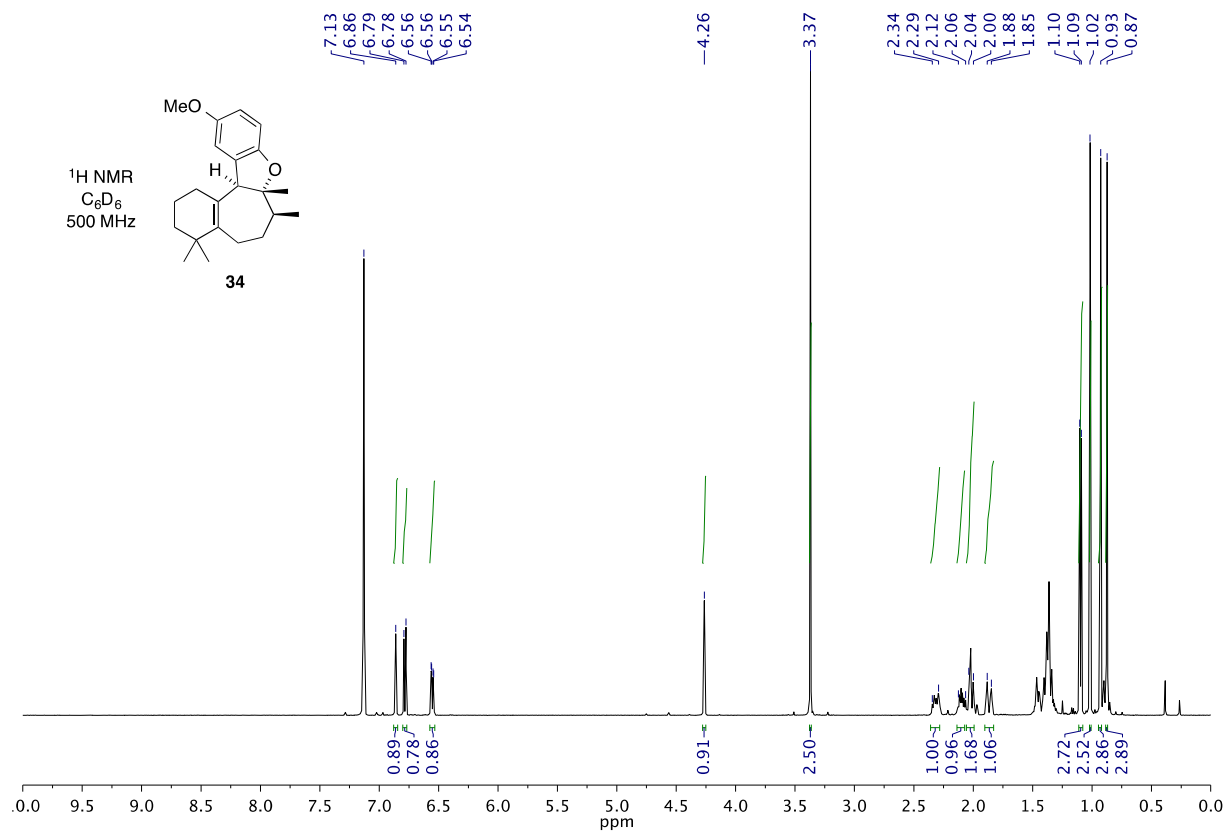


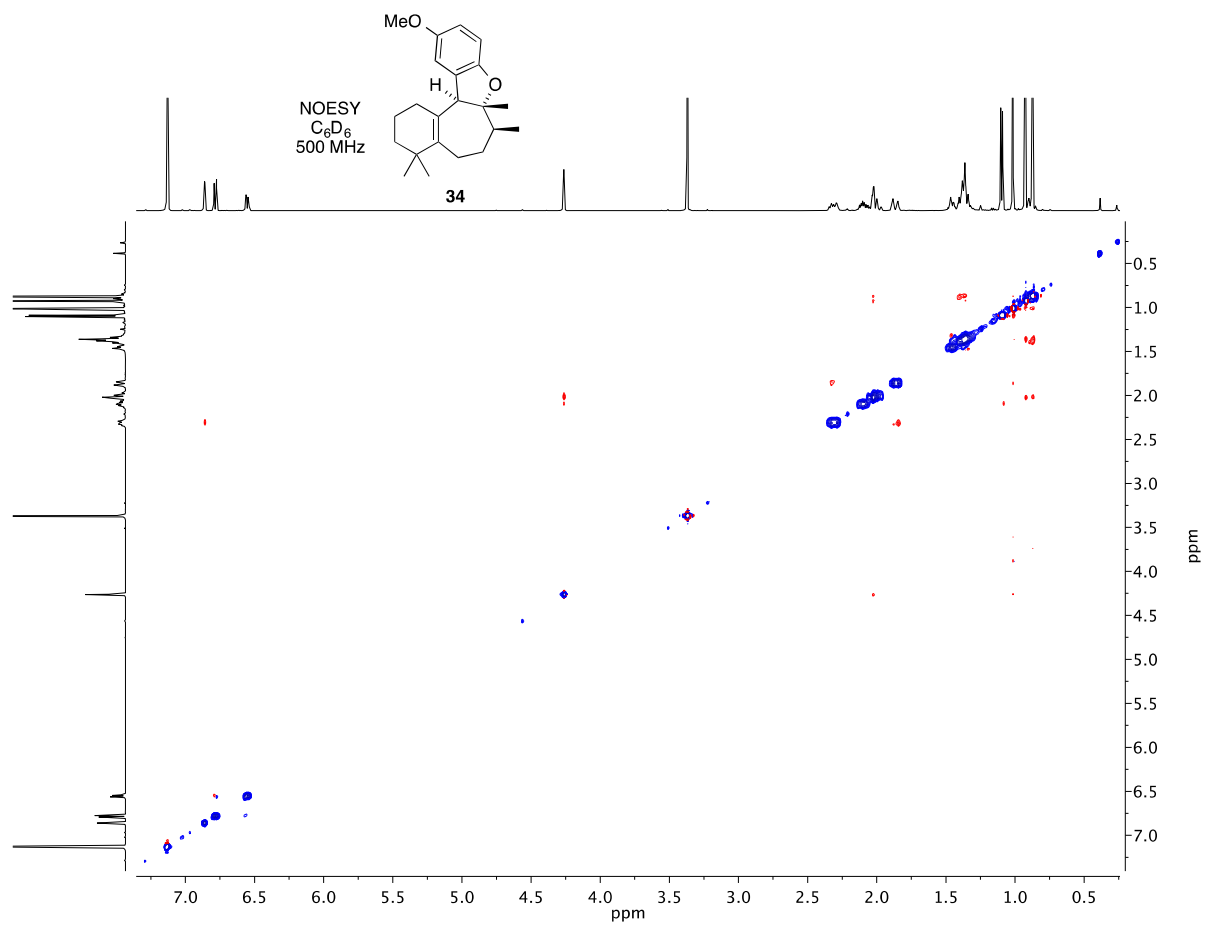
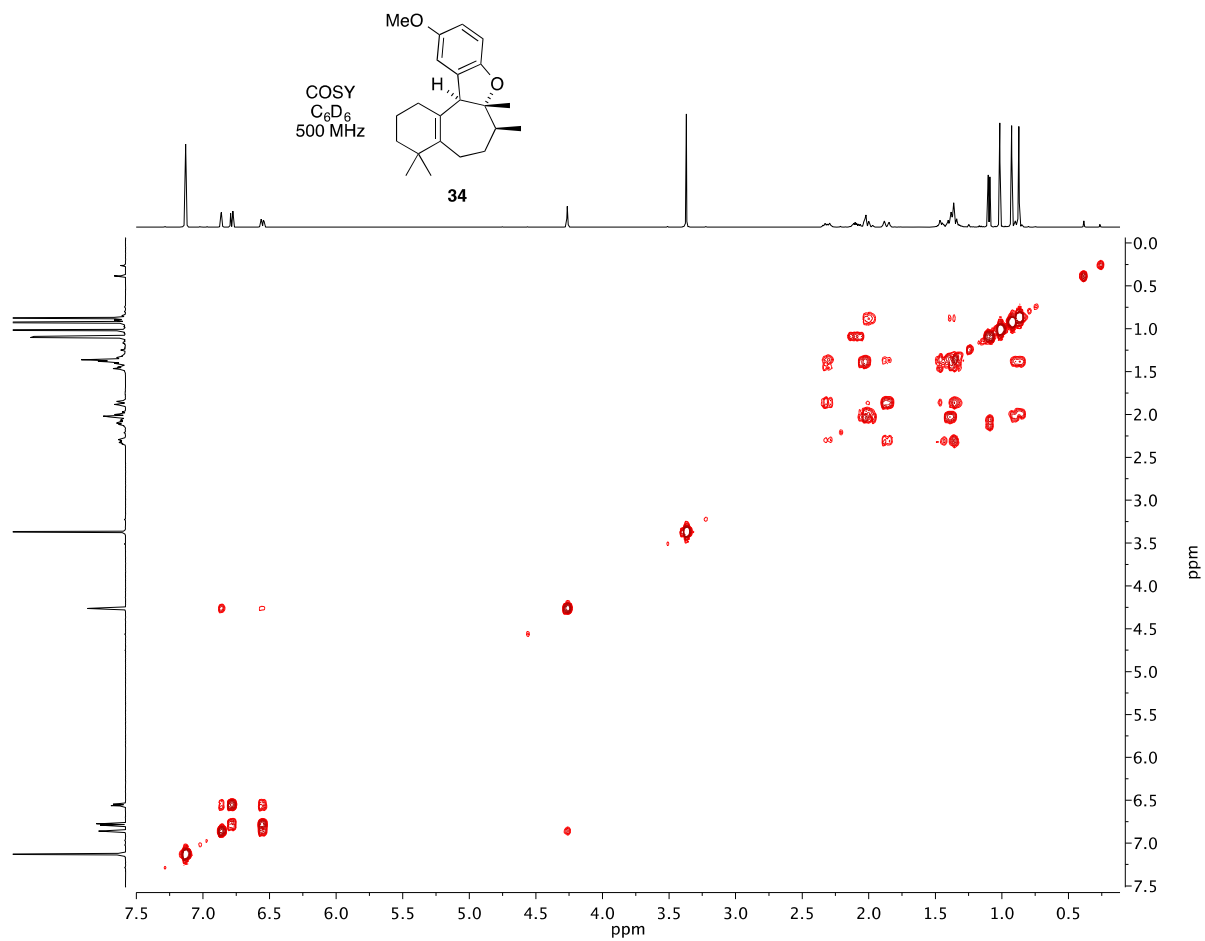


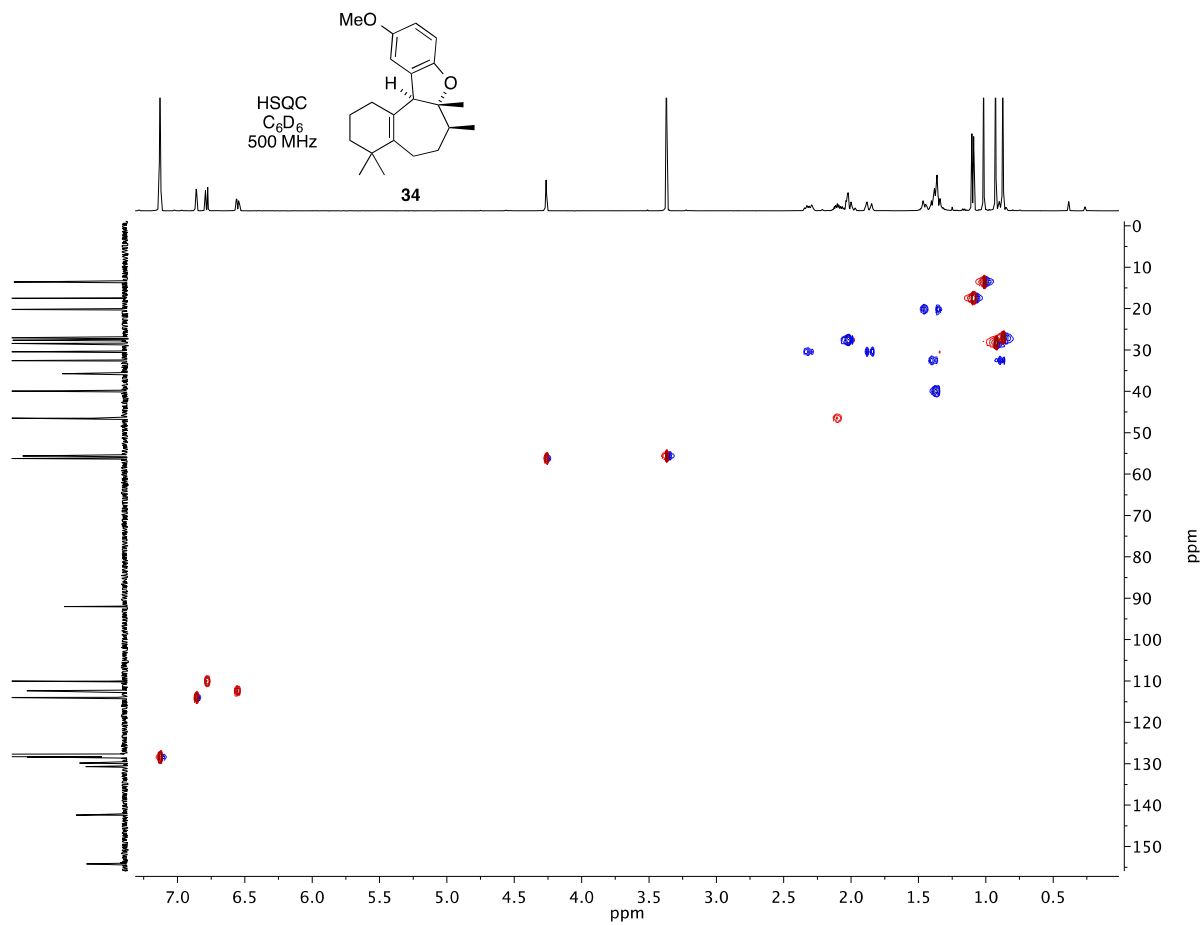
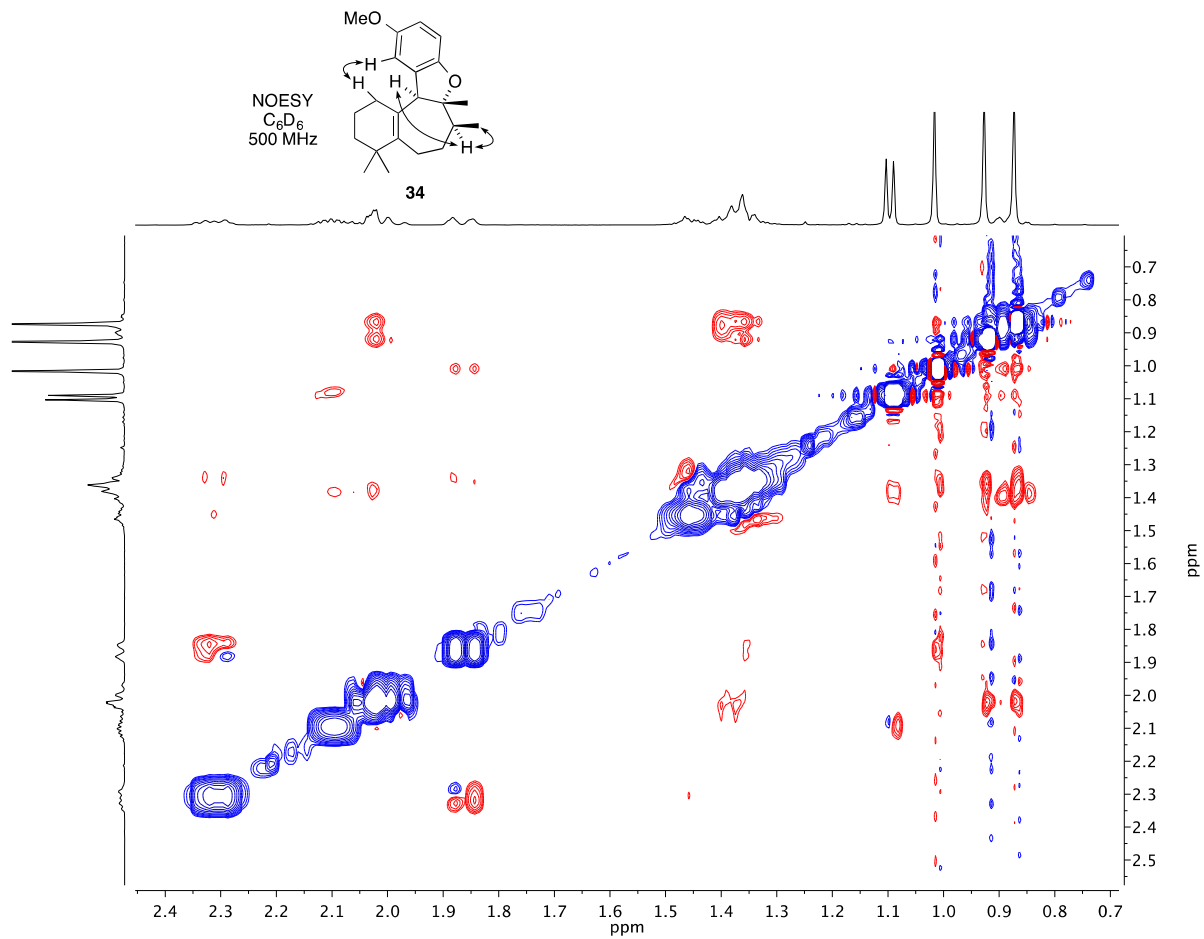


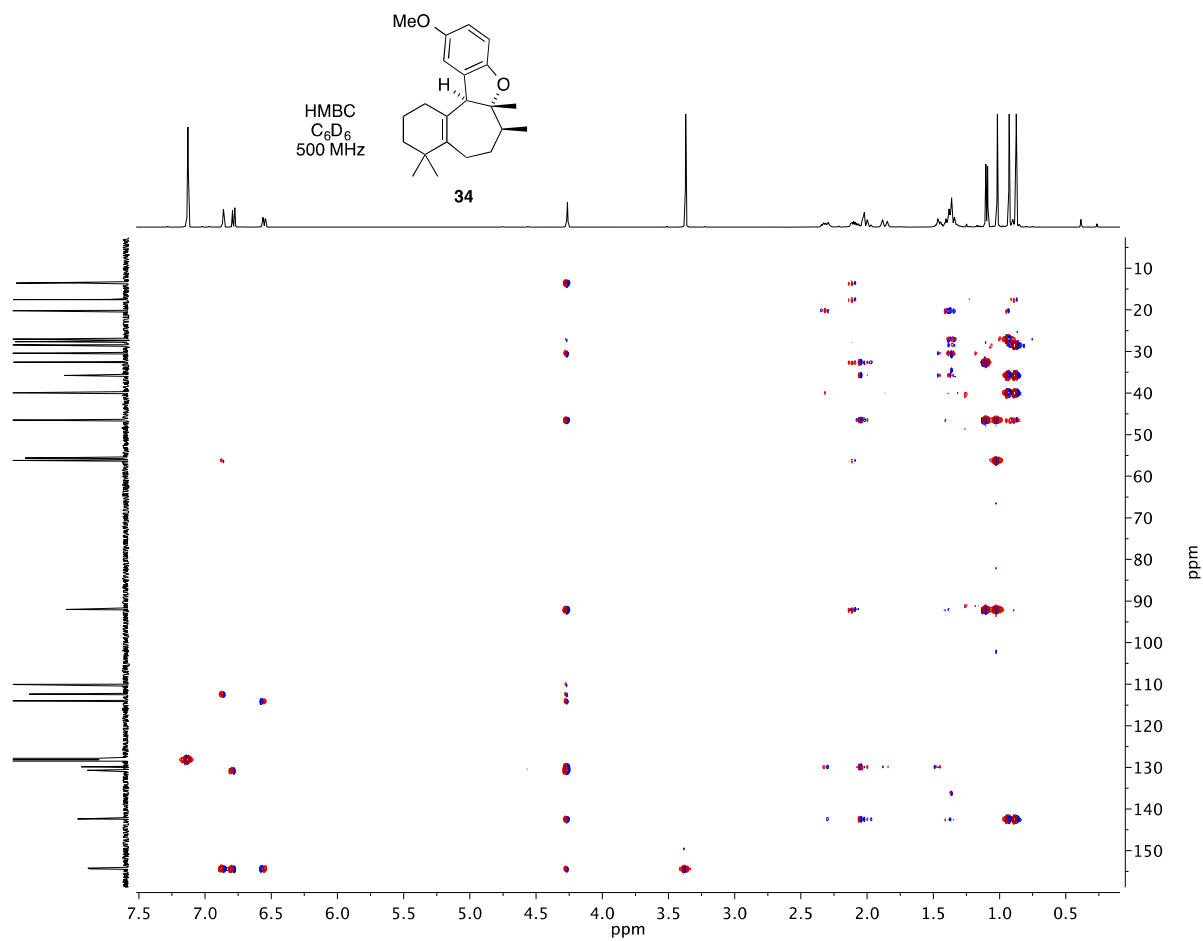


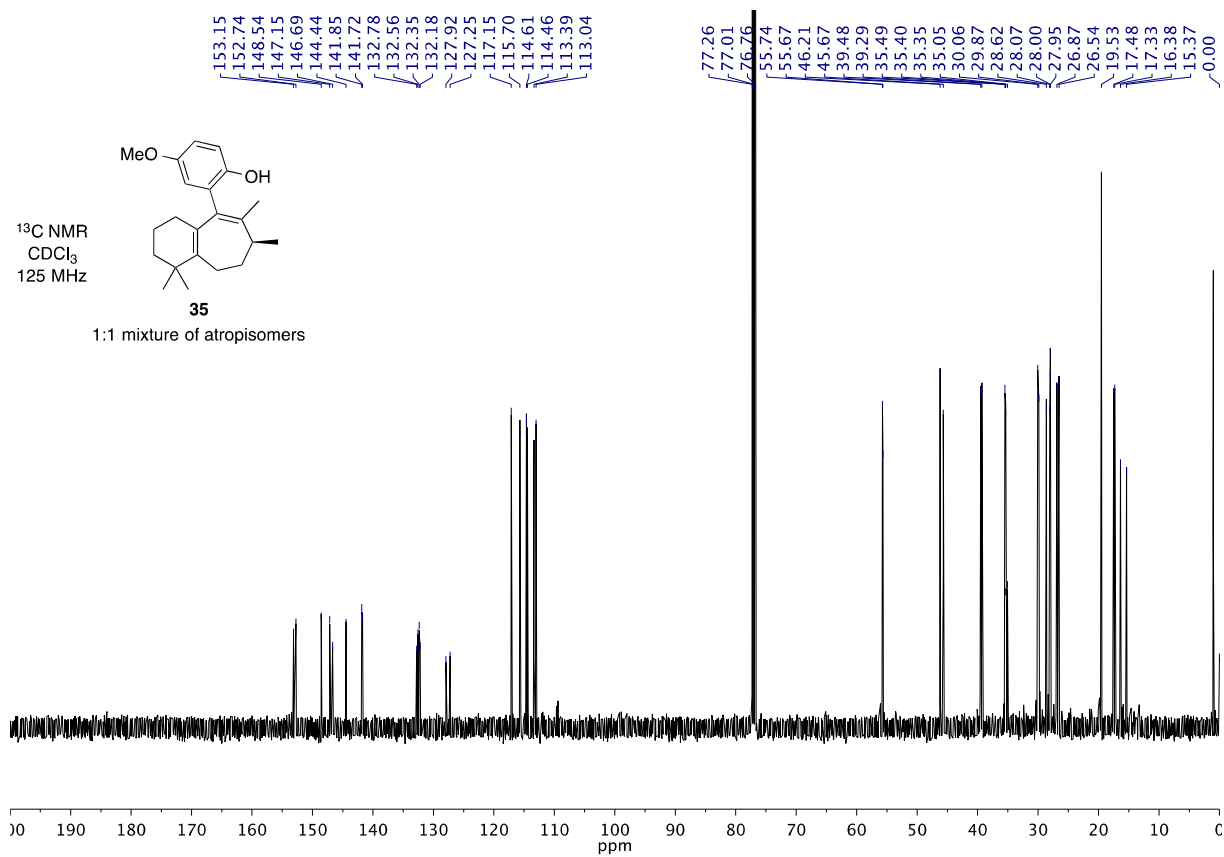
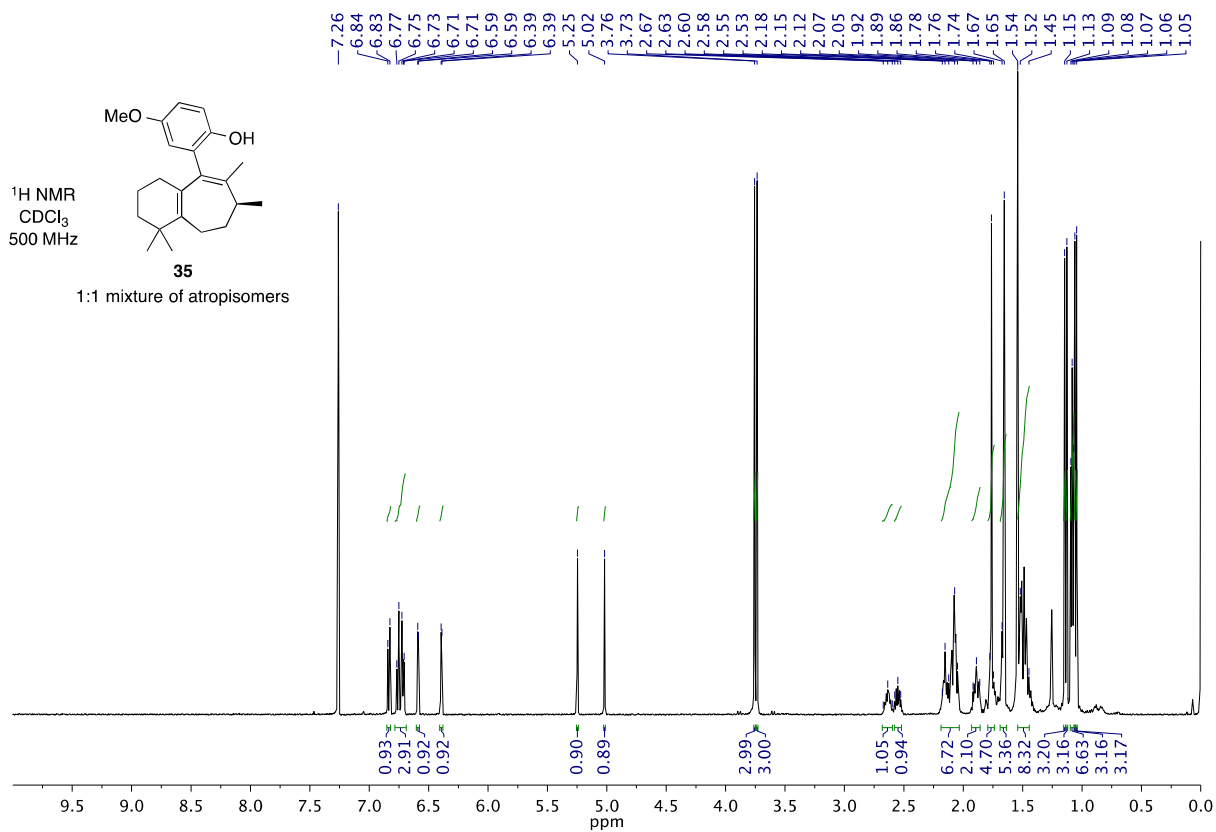


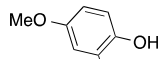








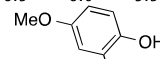
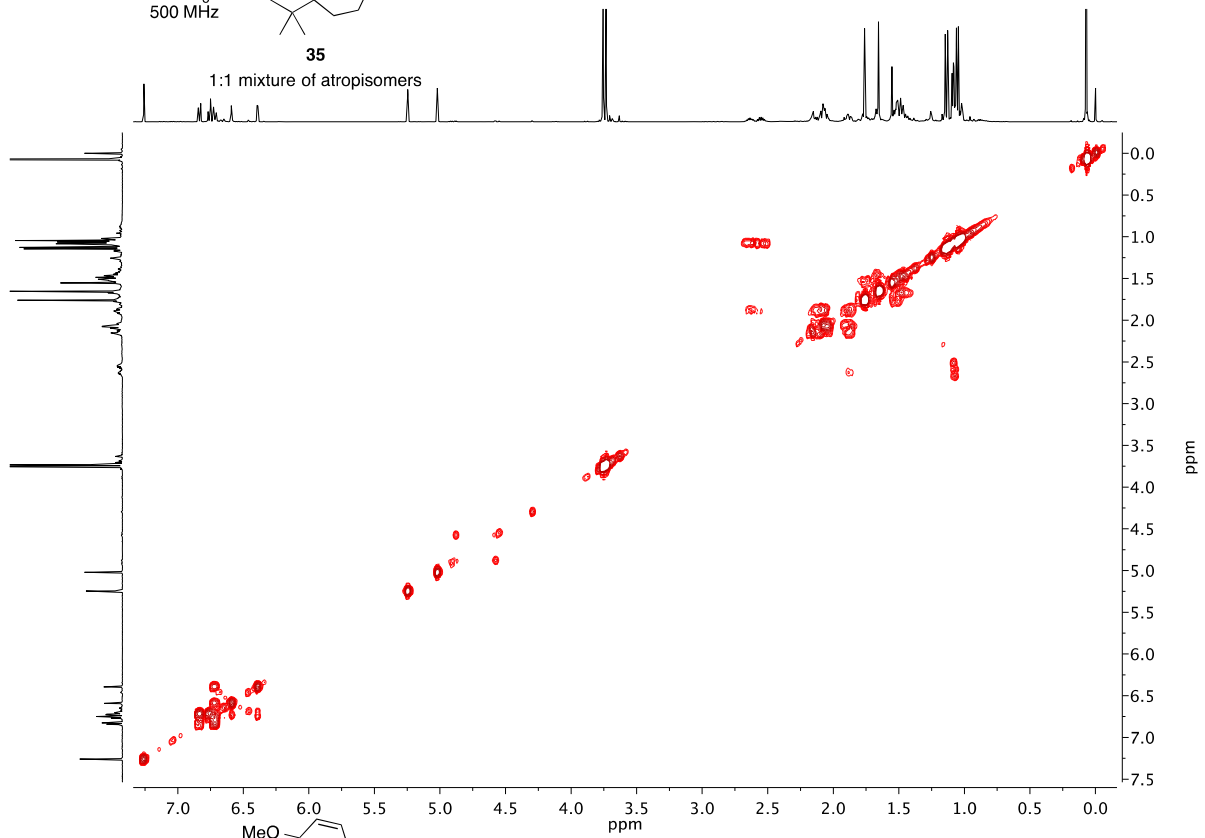




COSY
CDCl₃
500 MHz

35

1:1 mixture of atropisomers



NOESY
CDCl₃
500 MHz

35

1:1 mixture of atropisomers

