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# Platinum-Catalyzed Cycloisomerizations of a Common Enyne: A Divergent Entry to Cyclopropane Sesquiterpenoids. Formal Synthesis of Sarcandralactone A

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## Supporting Information

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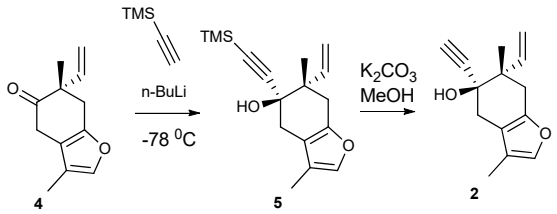
## I. General Information

All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions. Dry diethyl ether ($Et_2O$), and tetrahydrofuran (THF), were obtained by refluxing the solvents with sodium and benzophenone for several hours, whereas methylene chloride ($CH_2Cl_2$) was dried by distillation from $CaH_2$. Dry dimethylformamide (DMF) and toluene were obtained by stirring them with activated molecular sieves 4Å for 2 days and their subsequent distillation under reduced pressure. All the solvents were kept under argon using molecular sieves 4Å in their bottles. Reagents were purchased at the highest commercial quality and used without further purification.

Reactions were monitored by thin-layer chromatography (TLC) carried out on S-2 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and ethanolic *p*-anisaldehyde as developing agent. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Silica gel was neutralized with 1% $Et_3N$ and used in all indicative cases where compounds are sensitive to acidic conditions. Preparative thin-layer chromatography separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254).

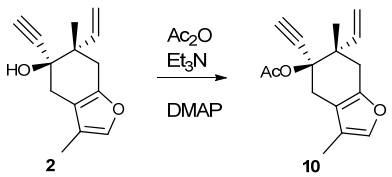
NMR spectra were recorded on Agilent 500 spectrometer and calibrated using solvent residual peaks as an internal reference. The following abbreviations are used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, dd = doublet of doublets. High-resolution mass spectra (HRMS) were recorded on an Agilent ESI-TOF (time of flight) mass spectrometer at a 4000 V emitter voltage. Optical rotations were recorded on a Perkin-Elmer Model 343 polarimeter at 589 nm, and are reported in units of $10^{-1}$(deg $cm^2$ $g^{-1}$).

## II. Experimental procedures and physical properties of compounds




**Compound 2**

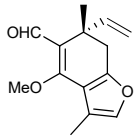
In a flamed dried round bottom flask a solution of *n*-BuLi 2.5 M in THF (0.83 mL, 2.08 mmol) was added dropwise in a solution of TMS-acetylene (0.3 mL, 2.08 mmol) in 1 mL of THF at 0°C. The solution was stirred for 5 min at this temperature before brought at rt to stand for 40 min. The reaction flask was then emerged into an acetone-dry ice cooling mixture at -78 °C before a solution of compound **4**[1] (330 mg, 1.74 mmol) in 4 mL of THF was introduced. The reaction mixture was stirred at the same temperature for 1 h and then quenched by sat. aqueous $NH_4Cl$. The resulting was extracted with ether (3 x 5 mL), dried with $Na_2SO_4$ and evaporated under reduced pressure. The oily residue was dissolved in MeOH (6 mL) and $K_2CO_3$ was added at once at rt and allowed to stir for 1 h at the same temperature. After that, the reaction mixture was quenched by $NH_4Cl$, extracted with ether (3 x 5 mL), dried with $Na_2SO_4$ and evaporated to dryness. Finally, the reaction mixture was chromatographed by neutralized silica gel flash column chromatography (petroleum/$Et_2O$ = 85:1) to provide 289 mg, 77% of pure compound **2** as a clear oil; $R_f$ = 0.46 (petroleum/ $Et_2O$ = 3:1); $[a]_D$ = + 18.9 (*c* 3.2, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$): δ = 7.09 (brs, 1H), 6.19 (brs, 1H), 5.25 (d, *J* = 12 Hz, 1H), 5.21 (d, *J* = 17 Hz, 1H), 2.95-2.80 (m, 2H), 2.77-2.53 (m, 2H), 2.49 (s, 1H), 1.93 (s, 3H), 1.26 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 148.4, 148.3, 137.8, 119.5, 119.4, 115.4, 85.4, 73.0, 72.3, 44.7, 33.8, 26.9, 21.8, 8.1; HRMS: calcd for $C_{14}H_{17}O_2^+$ [M + $H^+$]: 217.1229, found 217.1226.




**Compound 10**

In a round bottom flask, compound **2** (100 mg, 0.46 mmol) was introduced and dissolved in 5 mL of dry DCM. To the resulting solution, $Et_3N$ (0.67 mL, 4.8 mmol), $Ac_2O$ (0.72 mL, 7.2 mmol) and DMAP (6 mg, 0.05 mmol) were introduced sequentially at rt. The reaction was left under stirring for 48 hours at the same temperature. Then, the reaction was washed with $NaHCO_3$ (5 mL), $NH_4Cl$ (5 mL) and brine (5 mL), extracted with DCM (3 x 10 mL) and the organic phase is dried with $Na_2SO_4$ and evaporated under reduced pressure to provide an oily residue which was chromatographed by neutralized silica gel flash column

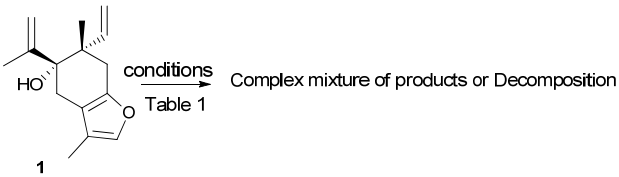
chromatography (petroleum/$Et_2O$ = 80:1) to provide 86 mg, 72% of pure compound **10** as a clear oil; $R_f$ = 0.56 (petroleum/ $Et_2O$ = 3:1); $[a]_D$ = + 14.8 (*c* 1.25, $CH_2Cl_2$); $^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.06 (brs, 1H), 6.09 (brs, 1H), 5.26-5.04 (brd, 2H), 2.94-2.46 (brm, 5H), 2.03 (brs, 3H), 1.89 (brs, 3H), 1.28 (brs, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 169.3, 148.1, 148.0, 137.8, 119.6, 119.5, 114.8, 81.2, 78.5, 75.1, 44.7, 32.5, 29.7, 21.9, 21.8, 8.1; HRMS: calcd for $C_{16}H_{19}O_3^+$ [M + $H^+$]: 259.1334, found 259.1331.




**Compound 7**

When the acetylation conditions described above for compound **10** were ran in the presence of air, a more polar spot was isolated after column chromatography representing the structure of compound **7** in 30% yield as a clear oil; $R_f$ = 0.56 (petroleum/ $Et_2O$ = 3:1); $[a]_D$ = -11.3 (*c* 0.05, $CH_2Cl_2$) $^1H$ NMR (500 MHz, $CDCl_3$): δ = 9.95 (s, 1H), 7.08 (s, 1H), 6.03 (dd, *J* = 17.7 Hz, *J* = 11.1 Hz, 1H), 5.17 (d, *J* = 9.7 Hz, 1H), 5.13 (d, *J* = 17.3 Hz, 1H), 3.71 (s, 3H), 3.35 (d, *J* = 15.0 Hz, 1H), 3.23 (d, *J* = 15.0 Hz, 1H), 2.17 (s, 3H), 1.33 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 186.1, 174.7, 162.0, 140.0, 139.4, 125.5, 123.3, 120.0, 115.0, 52.4, 49.0, 35.9, 20.6, 8.9; HRMS: calcd for $C_{14}H_{17}O_3^+$ [M + $H^+$]: 233.1178, found 233.1175.

## Attempts to cycloisomerize compound 1




<u>General reaction set up for cycloisomerization attempts of compound **1**</u>: Compound **1** (10 mg, 0.043 mmol) was introduced in a 5 mL round bottom flask or screw cap 4 mL vial and dissolved in the indicated reaction solvent (1 mL). The appropriate metal catalyst (5 or 10 mmol%) or acid (5 or 10 mmol%) was then introduced in the solution at once before the flask was capped and emerged to the indicating reaction conditions. TLC samples were taken periodically from the reaction mixture to monitor reaction progress. Then, the reaction was quenched by $NaHCO_3$ and evaporated to dryness under reduced pressure. Aliquots were used for crude $^1H$ NMR of the reaction mixture to estimate the progress of the reaction and its final result.

**Table 1**

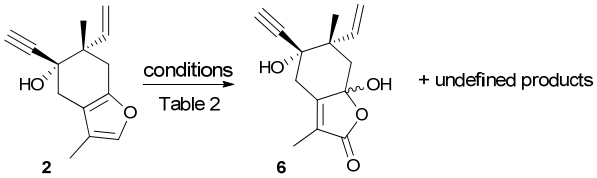
| Entry | Starting material | Lewis Acid Or Acid (mmol%) | Conditions | Result |
|---|---|---|---|---|
| 1 | **1** | $AuCl_3$ (5%) | DCM at rt for 3h and then to reflux for 2.5h | Decomposition |
| 2 | **1** | AuCl (5%) | DCM at rt for 3h and then to reflux for 2.5h | Unidentified mixture of products and decomposition |
| 3 | **1** | pTSA (10%) | Deoxygenation; DCM rt to reflux o/n | Complex mixture of products and Compound **1** |
| 4 | **1** | $Bi(OTf)_3$ (5%) | Deoxygenation; DCM from rt to reflux for 48h | Unreacted **1** |
| 5 | **1** | $Pd(Ph_3P)_4$ (10%) | Deoxygenation; DCM rt for 1h and then 60 $^oC$ o/n | Unreacted **1** |

## Attempts to cycloisomerize compound 2 and optimization conditions for the cycloisomerization of compound 10

General reaction set up for cycloisomerization attempts (**Method A**): Compound **2** (10 mg, 0.046 mmol) or **10** (10 mg, 0.039 mmol) was introduced in a 4 mL screw cap vial and dissolved in the indicated reaction solvent (1 mL). The appropriate metal catalyst (5 or 10 mmol%) was then introduced in the solution as a solid at once before the vial was tightly capped and emerged to the indicating reaction conditions. TLC samples were taken periodically from the reaction mixture to ensure the consumption of the starting material. Then, the reaction was quenched and evaporated to dryness under reduced pressure and chromatographed by neutralized silica gel flash column chromatography.

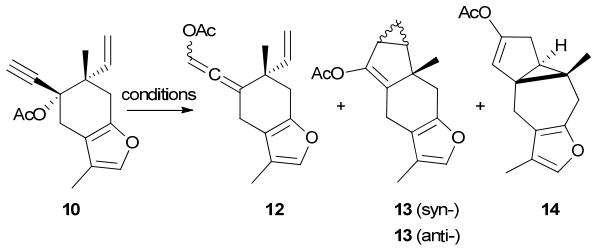
General technique used for deoxygenated reactions (**Method B**): Compound **2** (10 mg, 0.046 mmol) or **10** (10 mg, 0.039 mmol) was introduced in a 25 mL Schlenck apparatus and dissolved in the indicated reaction solvent (2 mL). The appropriate metal catalyst (5 or 10 mmol%) was introduced in the solution as a solid at once under argon before the Schlenk was tightly sealed and deoxygenated under freeze-pump technique. The resulting was emerged to the indicating reaction conditions. Then, the reaction was quenched and evaporated to dryness under reduced pressure and chromatographed by neutralized silica gel flash column chromatography.

**Table 2**



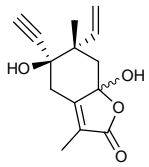

| Entry | Metal (mmol%) | Conditions | Product (% Yield) (ratio of isomers) |
|---|---|---|---|
| 1 | AuCl 5% | Method A; rt, DCM; o/n | **2** (65%) + Decomposition |
| 2 | $AuCl_3$ 5% | Method A; rt, toluene; 2.5h | **6** isomers (75%) (0.6:0.4) |
| 3 | $AuCl_3$ 5% | Method B; Schlenk rt, toluene; o/n | **2** (90%) |
| 4 | $AuCl_3$ 5% | Method B; Schlenk 80 °C, toluene; 2.5h | Decomposition |
| 5 | $PtCl_2$ 5% | Method A; 80 °C, toluene; 1.5h | **2** (70%) + **6** isomers (20%) (0.5:0.5) |
| 6 | $PtCl_2$ 10% | Method B; Schlenk 80 °C, toluene; o/n | Decomposition |

**Table 3**[1]



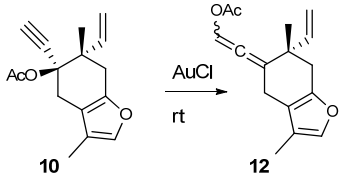

| Entry | Metal (5 mmol%) | Conditions | Product (% Yield) (ratio of isomers) |
|---|---|---|---|
| 1 | AuCl | Method A; rt, toluene, 2h | **12** (100%) |
| 2[2] | $PtCl_2$ | Method A; 100 °C; toluene, o/n | **14** (65%) |
| 3 | $PtCl_2$ | Method A; 60 °C; toluene, 4h | **10** (38%) + **12** (12%) + **13** (30%) *syn:anti* = 1.3:1 |
| 4 | $PtCl_2$ | Method B; 110 °C, toluene, o/n | **13** (45%) *syn:anti* = 2.4:1 + **14** (30%) |
| 5 | $PtCl_2$ | Method B; 90 °C, toluene, 1.5h | **13** (48%) *syn:anti* = 1.6:1 + **14** (27%) |
| 6 | $PtCl_2$ | Method B; 90 °C, 5h toluene, then rt, o/n | **13** (42%) *syn:anti* = 2.3:1 + **14** (14%) |
| 7 | $PtCl_2$ | Method B; 90 °C, $NaHCO_3$, toluene, o/n | **13** (62%) *syn:anti* = 2.4:1 + **14** (8%) |

[1] Reactions were run in sealed vials or Schenck apparatus depending on the deoxygenation conditions required; [2]**12** was used as the starting material.



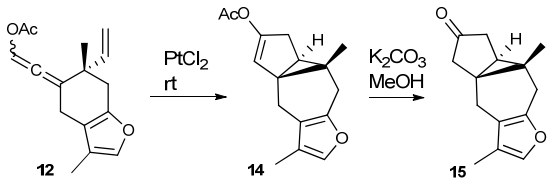

**Compound 6 (mixture isomers)**

Following **Method A**; $R_f$ = 0.24 (petroleum/ $Et_2O$ = 3:1); $^1H$ NMR (500 MHz, $CDCl_3$): δ = 6.25 (dd, *J* = 10.5 Hz, *J* = 17.7 Hz, α-isomer 1H), 6.11 (dd, *J* = 10.5 Hz, *J* = 17.4 Hz, β-isomer 1H), 5.35 (d, *J* = 16.4 Hz, α-isomer 1H), 5.33 (d, *J* = 10.5 Hz, α-isomer 1H), 5.32 (d, *J* = 11.0 Hz, β-isomer 1H), 5.16 (d, *J* = 17.4 Hz, β-isomer 1H), 3.15 (d, *J* = 14.2 Hz, β-isomer 1H), 3.09 (d, *J* = 13.0 Hz, α-isomer 1H), 2.82 (d, *J* = 14.2, β-isomer 1H), 2.64 (d, *J* = 13.0 Hz, a-isomer, 1H), 2.60 (s, β-isomer 1H), 2.50 (d, *J* = 10.8 Hz, 1H), 2.27 (s, a-isomer 1H), 2.14 (d, *J* = 12.4 Hz, 1H), 1.85 (s, a-isomer 3H), 1.84 (s, β-isomer 3H), 1.81 (d, *J* = 10.8 Hz, 1H), 1.79 (d, *J* = 12.4 Hz, 1H), 1.27 (s, a-isomer 3H), 1.26 (s, β-isomer 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$) (Both isomers): δ = 174.3, 173.9, 158.1, 156.7, 141.6, 138.2, 125.5, 123.8, 117.0, 116.6, 107.5, 107.3, 84.3, 83.5, 75.4, 75.3, 74.4, 72.4, 45.4, 45.2, 39.8, 38.1, 36.2, 35.6, 24.1, 22.3, 8.2, 8.1; HRMS: calcd for $C_{14}H_{17}O_4^+$ [M + $H^+$]: 249.1127, found 249.1122




**Allene compound 12**

Following **Method A**: Compound **10** (10 mg, 0.039 mmol) with AuCl (0.5 mg, 5 mmol%) provided compound **12** (10 mg; 100%) as a clear oil; $R_f$ = 0.52 (petroleum/ $Et_2O$ = 3:1); For both isomers: $^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.43 (s, 1H), 7.06 (s, 1H), 5.92 (dd, *J* = 10.5 , *J* = 6.8 Hz, 1H), 5.88 (dd, *J* = 10.5 , *J* = 6.8 Hz, 1H), 5.08 (d, *J* = 17.5 Hz, 1H), 5.04 (pst, *J* = 8.1 Hz, 1H), 3.34-3.19 (m, 2H), 2.82 (d, *J* = 16.4 Hz, 1H), 2.61 (pst, *J* = 16.4 Hz, 1H), 2.15 and 2.14 (s, 3H for both), 1.91 (s, 3H), 1.29 and 1.27 (s, 3H for both); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 189.0, 188.9, 168.6, 168.3, 148.6, 148.5, 143.6, 143.4, 137.8, 137.7, 129.0, 128.2, 120.1, 119.0, 115.2, 115.1, 113.3, 113.2, 111.5, 111.4, 41.4, 41.3, 36.2, 36.1, 26.0, 25.9, 25.8, 25.7, 21.0, 20.9, 8.1, 8.0; HRMS: calcd for $C_{16}H_{19}O_3^+$ [M + $H^+$]: 259.1334, found 259.1332; Anal. calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02 %. Found: C, 74.39; H, 6.99%.

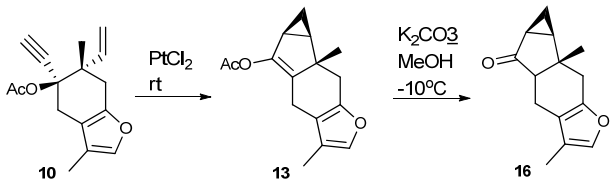



**Myliol derivative 14**

Following **Method B**: Compound **12** (8 mg, 0.030 mmol) with $PtCl_2$ (0.5 mg, 10 % mmol) provided compound **14** (5 mg; 65%) as a clear oil; $R_f$ = 0.49 (petroleum/ $Et_2O$ = 3:1); $[a]_D$ = -18.9 (*c* 0.5, $CH_2Cl_2$) $^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.02 (s, 1H), 5.41 (s, 1H), 2.94 (d, *J* = 16.0 Hz, 1H), 2.86 (d, *J* = 21.3 Hz, 1H), 2.82 (d, *J* = 21.3 Hz, 1H), 2.80-2.71 (m, 2H), 2.29 (d, *J* = 18.1 Hz, 1H), 2.17 (s, 3H), 1.89 (s, 3H), 1.13 (d, *J* = 6.4 Hz), 1.12 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 168.5, 150.6, 147.9, 137.0, 119.3, 116.8, 114.7, 36.4, 31.7, 31.3, 25.0, 23.8, 23.3, 21.0, 15.0, 8.0; HRMS: calcd for $C_{16}H_{19}O_3^+$ [M + $H^+$]: 259.1334, found 259.1330; Anal. calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02 %. Found: C, 74.37; H, 7.02%.

**Myliol derivative 15**

In a round bottom flask containing a solution of compound **14** (5 mg, 0.019 mmol) in MeOH (1 mL), $K_2CO_3$ was inserted as a solid at once at rt. The reaction mixture was allowed to stir at the same temperature for 30 min before quenched by $NH_4Cl$ and extracted with ether. The organic phase was dried with $Na_2SO_4$ and evaporated under reduced pressure to provide crude mixture of **15**. Flash column chromatography by neutralized silica gel (petroleum) gave compound **15** as a colorless oil (3 mg, 70%); $R_f$ = 0.19 (petroleum/ $Et_2O$ = 3:1); $[a]_D$ = -22.1 (*c* 0.8, $CH_2Cl_2$); $^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.05 (s, 1H), 2.99 (d, *J* = 16.3 Hz, 1H), 2.85 (d, *J* = 17.0 Hz, 1H), 2.80 (d, *J* = 17.0 Hz, 1H), 2.69 (d, *J* = 16.3 Hz, 1H), 2.59 (dd, *J* = 20 Hz, *J* = 6.5 Hz, 1H), 2.48 (s, 2H), 2.30 (d, *J* = 20 Hz, 1H), 1.91 (s, 3H), 1.31 (d, *J* = 6.5 Hz, 1H), 1.05 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 219.3, 147.8, 137.3, 119.3, 114.4, 44.4, 38.7, 31.2, 27.9, 25.6, 24.0, 22.6, 15.7, 8.0; HRMS: calcd for $C_{14}H_{17}O_2^+$ [M + $H^+$]: 217.1229, found 217.1232; Anal. calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46 %. Found: C, 77.77; H, 7.52%.



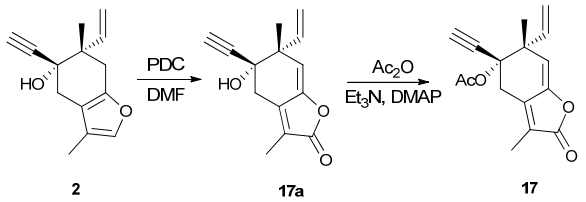

**Lindenane derivative 13**

Following **Method B**: Compound **10** (35 mg, 0.14 mmol) with $PtCl_2$ (2 mg, 10 mmol%) and $NaHCO_3$ provided compound **13** (22 mg; 62%) as a clear oil; $R_f$ = 0.48 (petroleum/ $Et_2O$ = 3:1); $[a]_D$ = -50.4 (*c* 0.1, $CH_2Cl_2$); $^1H$ NMR (500 MHz, $CDCl_3$) (For *trans*-isomer): δ = 7.05 (s, 1H), 2.97 (d, *J* = 18.0 Hz, 1H), 2.86 (d, *J* = 18.0 Hz, 1H), 2.70 (d, *J* = 16.0 Hz, 1H), 2.57 (d, *J* = 16.0 Hz, 1H), 2.2 (s, 3H), 2.04 (m, 1H), 1.90 (s, 3H), 1.54 (m, 1H), 1.30 (s,

3H), 0.79 (m, 1H), 0.36 (m, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 168.5, 149.8, 145.6, 137.5, 125.0, 119.2, 115.7, 43.4, 38.2, 26.1, 22.1, 20.8, 20.5, 17.7, 15.1, 8.1; HRMS: calcd for $C_{16}H_{19}O_3^+$ [M + $H^+$]: 259.1334, found 259.1338; Anal. calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02 %. Found: C, 74.36; H, 7.04%.

**Lindenane derivative 16**

Compound **13** (40 mg, 0.15 mmol) was dissolved in MeOH (2 mL) at -10°C and $K_2CO_3$ (20 mg, 0.16mmol) was added at once in one portion. The reaction mixture was allowed to stir at the same temperature for 1 h before quenched by $NH_4Cl$ and extracted with ether. The organic phase was dried with $Na_2SO_4$ and evaporated under reduced pressure to provide crude mixture of **16**. Flash column chromatography by neutralized silica gel (petroleum/ $Et_2O$ = 100:1) gave compound **16** as a colorless oil (22 mg, 69%); $R_f$ = 0.44 (petroleum/ $Et_2O$ = 3:1); $^1$H NMR (500 MHz, $CDCl_3$): δ = 6.98 (s, 1H), 2.84 (dd, *J* = 3.7 Hz, J = 16.5 Hz,, 1H), 2.72-2.54 (m, 2H), 2.48 (dd, *J* = 3.7 Hz, J = 8.8 Hz,, 1H), 2.21-2.14 (m, 1H), 2.00 (dd, *J* = 5.2 Hz, J = 7.9 Hz,, 1H), 1.92 (s, 3H), 1.84-1.87 (m, 1H), 1.32-1.34 (m, 1H), 1.20-1.23 (m, 1H), 1.06 (s, 3H).




**2** **17a** **17**

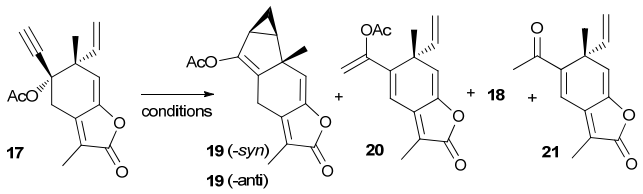
**Compound 17a**

In a round-bottomed flask containing a solution of compound **2** (280 mg, 1.3 mmol) in dry DMF (3.5 mL), PDC (1,47gr, 3.9 mmol) was added at once at rt and the resulting mixture was stirred at the same temperature for 20 h. The reaction was quenched by water, extracted with $Et_2O$ (5x10 mL) and the organic phase is dried with $Na_2SO_4$ and evaporated under reduced pressure. Flash column chromatography by neutralized silica gel of the crude mixture (cyclohexane/ $Et_2O$ = 30:1) afforded compound **17a** as a colorless oil (119 mg, 40%); $R_f$ = 0.50 (petroleum/ $Et_2O$ = 1:3); $[a]_D$ = -12.3 (*c* 0.5, $CH_2Cl_2$); NMR indicates two conformers of compound **17a** at 25 °C. The same sample when heated at 60 °C showed: $^1$H NMR (500 MHz, $CDCl_3$): 6.08 (dd, *J* = 10.5 Hz, *J* = 17.4 Hz, 1H), 5.46 (s, 1H), 5.35 (d, *J* = 10.5 Hz, 1H), 5.22 (d, *J* = 17.4 Hz, 1H), 3.00 (s, 2H), 2.51 (s, 1H), 1.92 (s, 3H), 1.47 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 170.9, 148.5, 141.4, 140.2, 123.0, 118.6, 116.5, 84.2, 74.1, 72.1, 47.7, 34.4, 29.3, 8.6; HRMS: calcd for $C_{14}H_{15}O_3^+$ [M + $H^+$]: 231.1021, found 231.1030; Anal. calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13 %. Found: C, 73.06; H, 6.18%.

**Compound 17**

In a round bottom flask, compound **17a** (70 mg, 0.30 mmol) was introduced and dissolved in 7 mL of dry DCM. To the resulting solution, $Et_3N$ (0.44 mL, 3.2 mmol), $Ac_2O$ (0.47 mL, 4.8 mmol) and DMAP (4 mg, 0.03

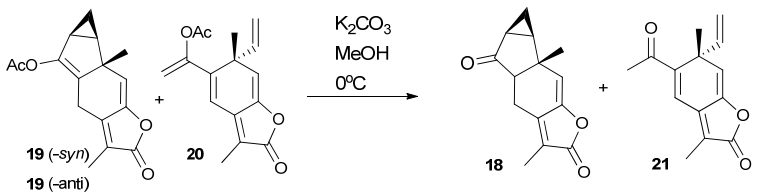
mmol) were introduced sequentially at rt. The reaction was left under stirring for 72 hours at rt. Then, the reaction was washed with $NaHCO_3$ (2 mL), $NH_4Cl$ (2 mL) and brine (2 mL), extracted with DCM (3 x 5 mL) and the combined organic layers were dried with $Na_2SO_4$ and evaporated under reduced pressure to provide an oily residue which was chromatographed by neutralized silica gel flash column chromatography (cyclohexane/$Et_2O$ = 8:1) to afford compound **17** (56 mg, 68%) as a clear oil; $R_f$ = 0.56 (petroleum/ $Et_2O$ = 1:3); NMR indicates two visible conformers of **17**. $^1$H NMR (500 MHz, $CDCl_3$): 6.11 (dd, *J* = 11.5 Hz, *J* =18.0 Hz, 0.5H), 6.01 (dd, *J* = 10.5 Hz, *J* =18.0 Hz, 0.5H), 5,37 (s, 0.5H), 5.33 (s, 0.5H), 5.22 (d, *J* = 10.5 Hz, 0.5H), 5.13 (d, *J* = 18.0 Hz, 0.5H), 3.90 (brs, 0.5H), 3.72 (brs, 0.5H), 3.01 (brs, 1H), 2.67 (s, 0.5H), 2.52 (s, 0.5H), 2.05 (s, 1.5H), 1.97 (s, 1.5H), 1.89 (s, 1.5H), 1.85 (s, 1.5H), 1,48 (s, 1.5H), 1.44 (s, 1.5H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 170.6, 170.5, 168.9, 168.8, 148.6, 148.4, 143.9, 143.2, 140.3, 139.6, 123.5, 123.3, 117.2, 117.0, 110.3, 109.1, 80.0, 79.8, 78.5, 77.8, 76.5, 75.8, 47.8, 47.4, 30.6, 29.8, 24.7, 23.2, 22.3, 21.5, 8.4, 8.3; HRMS: calcd for $C_{16}H_{17}O_4^+$ [M + H$^+$]: 273.1127, found 273.1126.




General reaction set up for cycloisomerization of compound **17** Compound **17** (30 mg, 0.11 mmol) was introduced in a 25 mL Schlenck apparatus and dissolved in the indicated reaction solvent (2 mL). Then, $PtCl_2$ (10 mmol%) was introduced in the solution as a solid at once under argon before the Schlenk was tightly sealed and emerged to the indicating reaction conditions. Finally, the reaction was evaporated to dryness under reduced pressure and chromatographed by a short neutralized silica gel flash column chromatography.

**Table 4**

| Entry | Metal (mmol %) | Conditions | Products (ratio) |
|---|---|---|---|
| 1 | $PtCl_2$ 5% | Deoxygenation 60 °C, toluene; o/n | **17** (90%) + traces of **19** |
| 2 | $PtCl_2$ 5% | Deoxygenation 80 °C, toluene; 3h | **17** (73%) + **19** (8%) + traces of **18** |
| 3 | $PtCl_2$ 10% | Deoxygenation 90 °C, toluene; o/n | **19** (37%) + **18** (15%) *syn:anti* = 5:1 + **20** (19%) + **21** (17%) |
| 4 | $PtCl_2$ 10% | Deoxygenation 110 °C, $NaHCO_3$ toluene; 4h | **20** (16%) + **21** (12%) Extended Decomposition |
| 5 | $PtCl_2$ 10% | Deoxygenation 70 °C, toluene; o/n | **19** (40%) + **18** (17%) *syn:anti* = 5:1 + **20** (21%) + **21** (11%) |

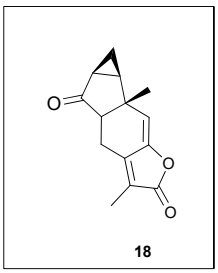



**Compounds 18 and 21**

The inseparable mixture of compounds **19** and **20** (from entry 5, Table 4) (15 mg, 0.06 mmol) was dissolved in MeOH (5 mL) at 0°C and $K_2CO_3$ (15 mg, 0.011 mmol) was added at once in one portion. The reaction mixture was allowed to stir at the same temperature for 30 min before quenched by $NH_4Cl$ and extracted with ether. The organic phase was dried with $Na_2SO_4$ and evaporated under reduced pressure to provide a crude mixture of **18** and **21**. Flash column chromatography by neutralized silica gel (cyclohexane/ EA = 30:1) afforded compounds **18** (5 mg, 38%) and **21** (2 mg, 17%) as brownish oils; For compound **21**: $R_f$ = 0.6 (cyclohaxane/ EtOAc = 1:3); $[a]_D$ = -36.1 (*c* 0.1, $CH_2Cl_2$); $^1$H NMR (500 MHz, $CDCl_3$): 7.37 (s, 1H), 6.16 (dd, *J* = 10.5 Hz, *J* =17.5 Hz, 1H), 5.63 (s, 1H), 5.05 (d, *J* = 10.5 Hz, 1H), 4.98 (d, *J* = 17.5 Hz, 1H), 2.46 (s, 3H), 2.10 (s, 3H), 1.54 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 187.1, 171.0, 150.7, 145.3, 141.3, 140.1, 124.5, 120.8, 115.5, 115.1, 30.3, 29.7, 28.0, 25.6, 8.8; HRMS: calcd for $C_{14}H_{15}O_3^+$ [M + $H^+$]: 231.1021, found 231.1019.

For compound **18**[2]: $R_f$ = 0.29 (cyclohaxane/ EtOAc = 1:3); $[a]_D$ = +138.3 (*c* 0.3, $CH_2Cl_2$) $^1$H NMR (500 MHz, $CDCl_3$): 5.54 (s, 1H), 3.19 (d, *J* = 17.8 Hz, 1H), 2.47 (m, 1H), 2.22 (d, 1H, *J* = 6.5 Hz), 2.05 (m, 1H), 1.91 (s, 3H), 1.86 (dd, 1H, *J* = 5.4 Hz, *J* = 3.0 Hz), 1.40 (s, 3H), 1.28-1.23 (m, 1H), 1.22 (td, 1H, *J* = 5.1 Hz, *J* = 3.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 210.2, 170.9, 147.8, 144.6, 121.9, 112.7, 44.2, 40.4, 32.3, 26.5, 24.1, 17.3, 13.5, 8.7; HRMS: calcd for $C_{14}H_{15}O_3^+$ [M + $H^+$]: 231.1021, found 231.1018.

**NMR comparison of compound 18 with previously synthesized intermediate for the total synthesis of sarcandralactone A[2]**



18

| **$^{1}$H-NMR Shifts ($CDCl_3$) 500MHz** | |
|---|---|
| Synthetic **18** | Previous synthesis |
| 5.54 (s, 1H) | 5.53 (s, 1H) |
| 3.19 (d, *J* = 17.8 Hz, 1H) | 3.18 (d, *J* = 17.8 Hz 1H) |
| 2.47 (m, 1H) | 2.48 (ddd, *J* = 17.7, 6,7, 2 Hz 1H) |
| 2.22 (d, *J* = 6.5 Hz, 1H) | 2.22 (d, *J* = 6.1 Hz, 1H) |
| 2.05 (m, 1H) | 2.07 (dt, *J* = 7.7, 5.0 Hz, 1H) |
| 1.91 (s, 3H) | 1.90 (d, *J* = 1.9 Hz, 3H) |
| 1.86 (dd, *J* = 5.4, 3.0 Hz 1H) | 1.87 (dd, *J* = 5.4, 3.1 Hz, 1H) |
| 1.40 (s, 3H) | 1.39 (s, 3H) |
| 1.23-1.28 (m, 1H) | 1.24-1.30 (m, 1H) |
| 1.22 (td, *J* = 5.1, 3.0 Hz, 1H) | 1.22 (td, *J* = 5.1, 3.2 Hz, 1H) |

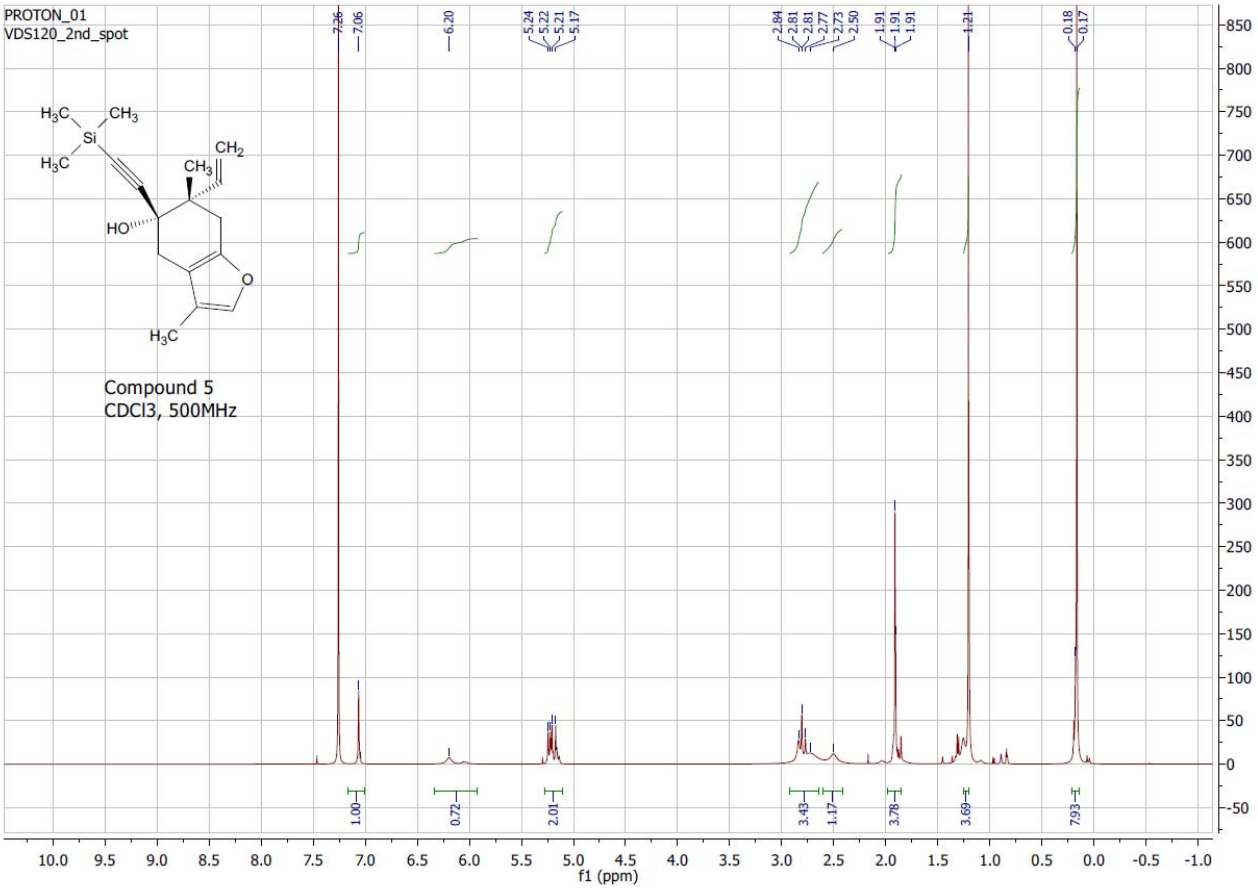
| **$^{13}$C-NMR Shifts ($CDCl_3$) 125 MHz** | |
|---|---|
| Synthetic **18** | Previous synthesis |
| 210.2 | 210.2 |
| 170.9 | 170.9 |
| 147.8 | 148.1 |
| 144.6 | 144.7 |
| 121.9 | 121.9 |
| 112.7 | 112.8 |
| 44.2 | 44.2 |
| 40.4 | 40.5 |
| 32.3 | 32.3 |
| 26.5 | 26.5 |
| 24.1 | 24.1 |

| | |
|---|---|
| 17.3 | 17.3 |
| 13.5 | 13.6 |
| 8.7 | 8.6 |

## References


1. E. E. Anagnostaki and A. L. Zografos, *Org. Lett.*, **2013**, *15*, 152
2. J. M. Eagan, M. Hori, J. Wu, K. S. Kanyiva and S. A. Snyder, *Angew. Chem. Int. Ed.*, **2015**, *54*, 7842

NMR Spectra of compounds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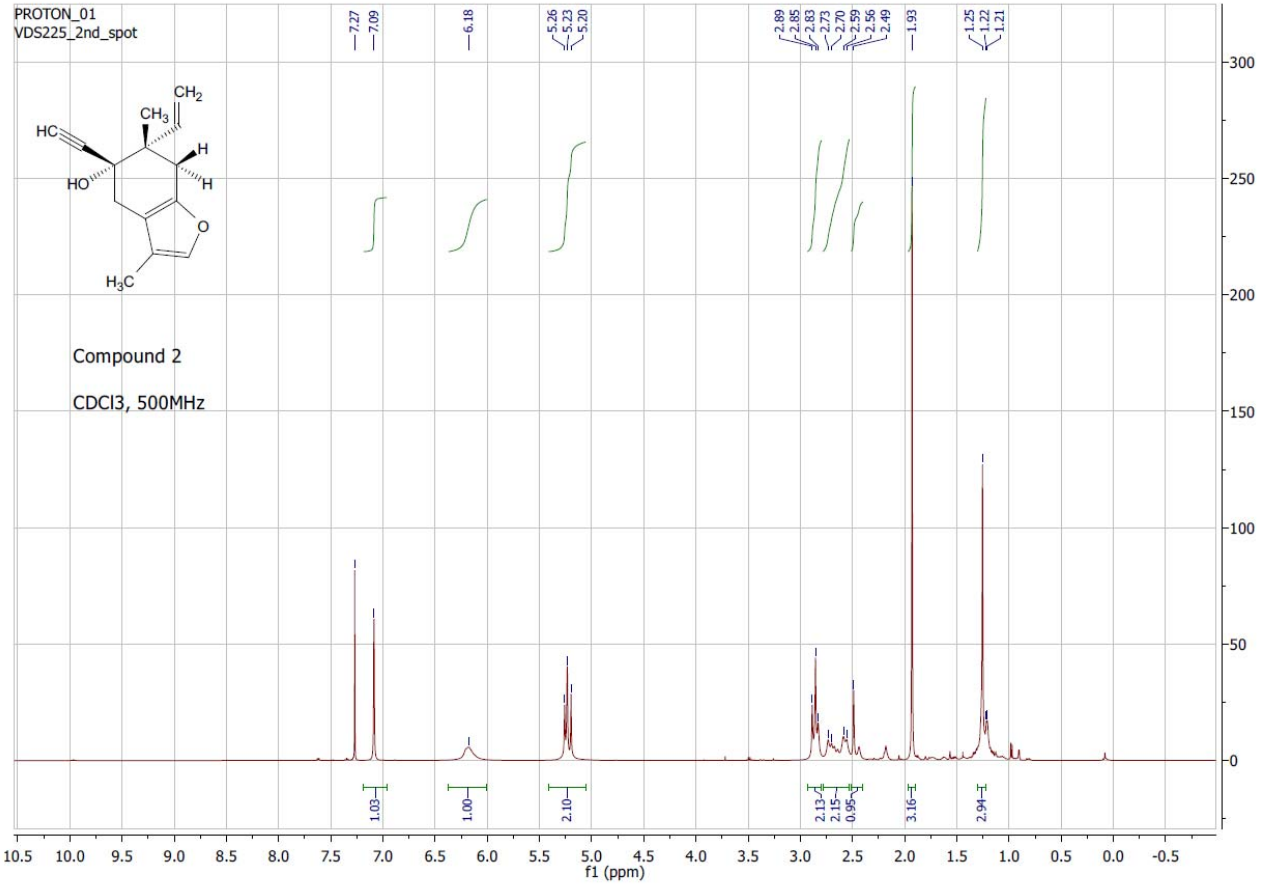
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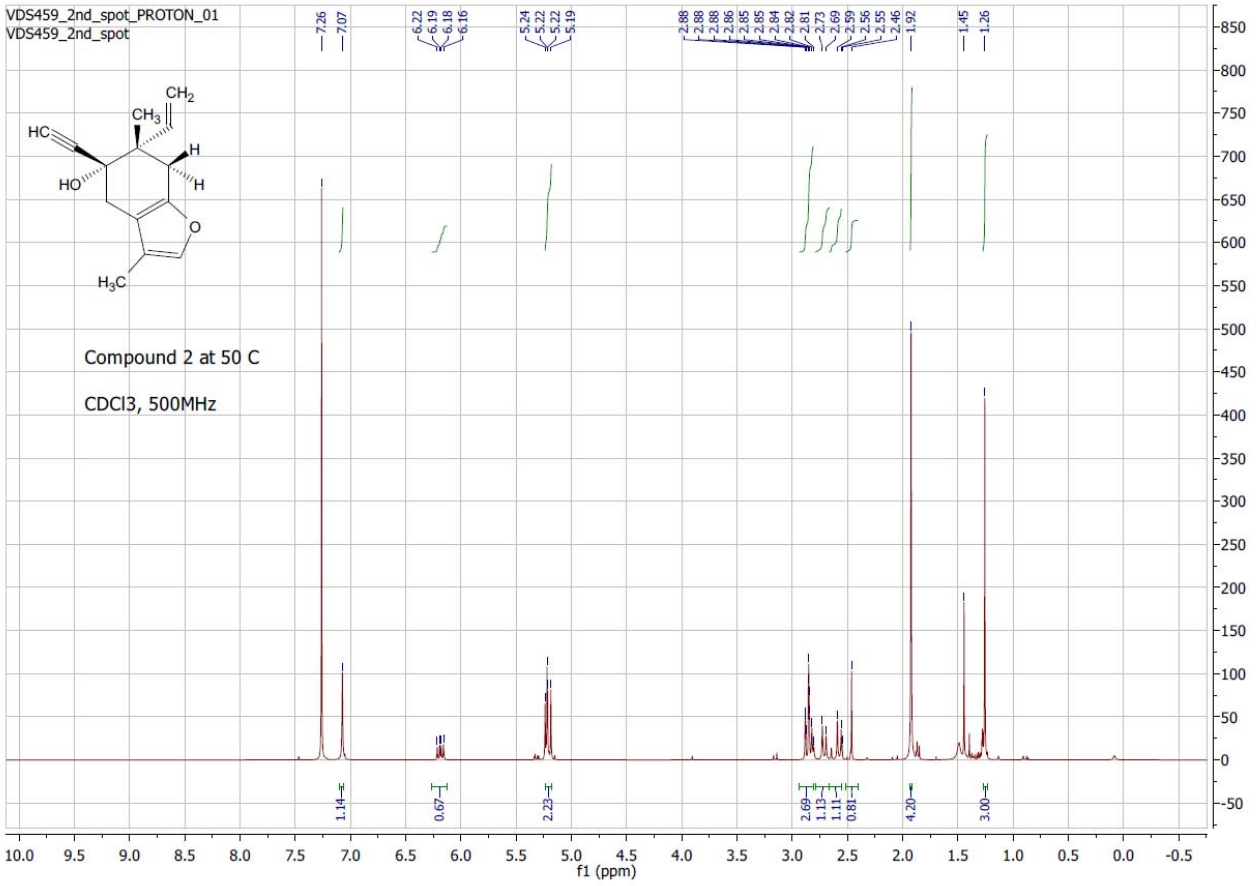
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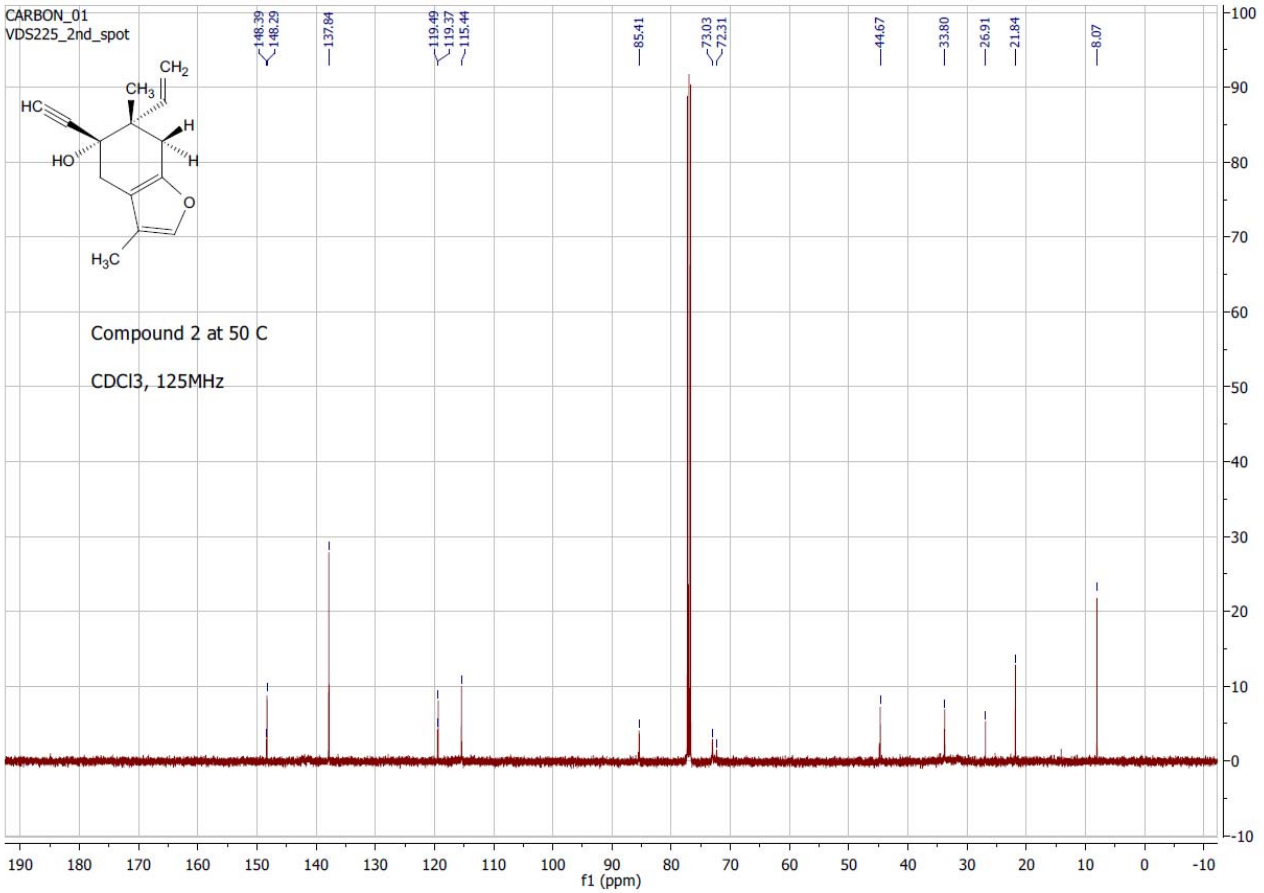
f1 (ppm)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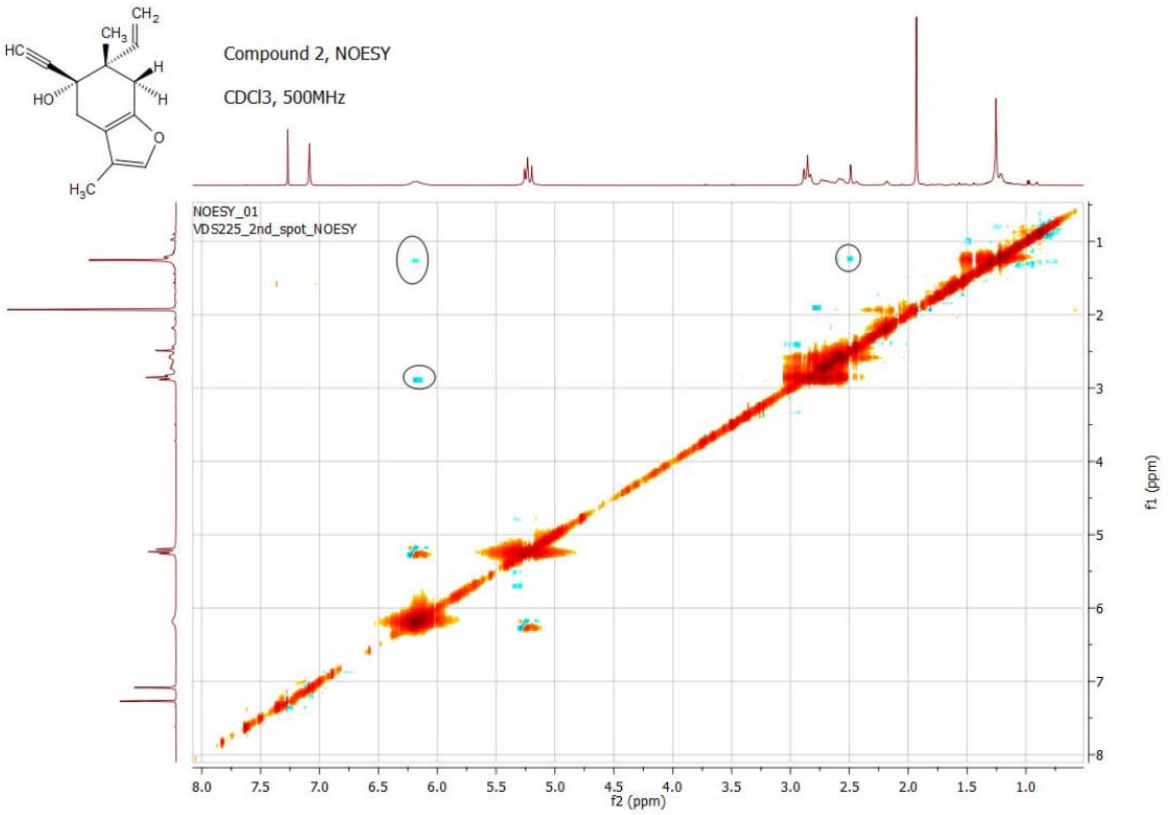
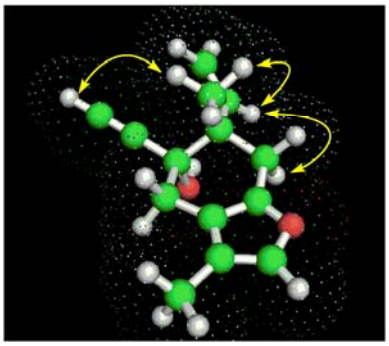
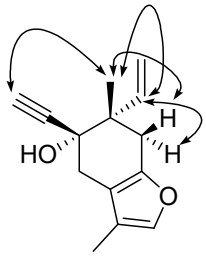
Compound 2 at 50 C
CDCl3, 125MHz
f1 (ppm)



NOESY correlations



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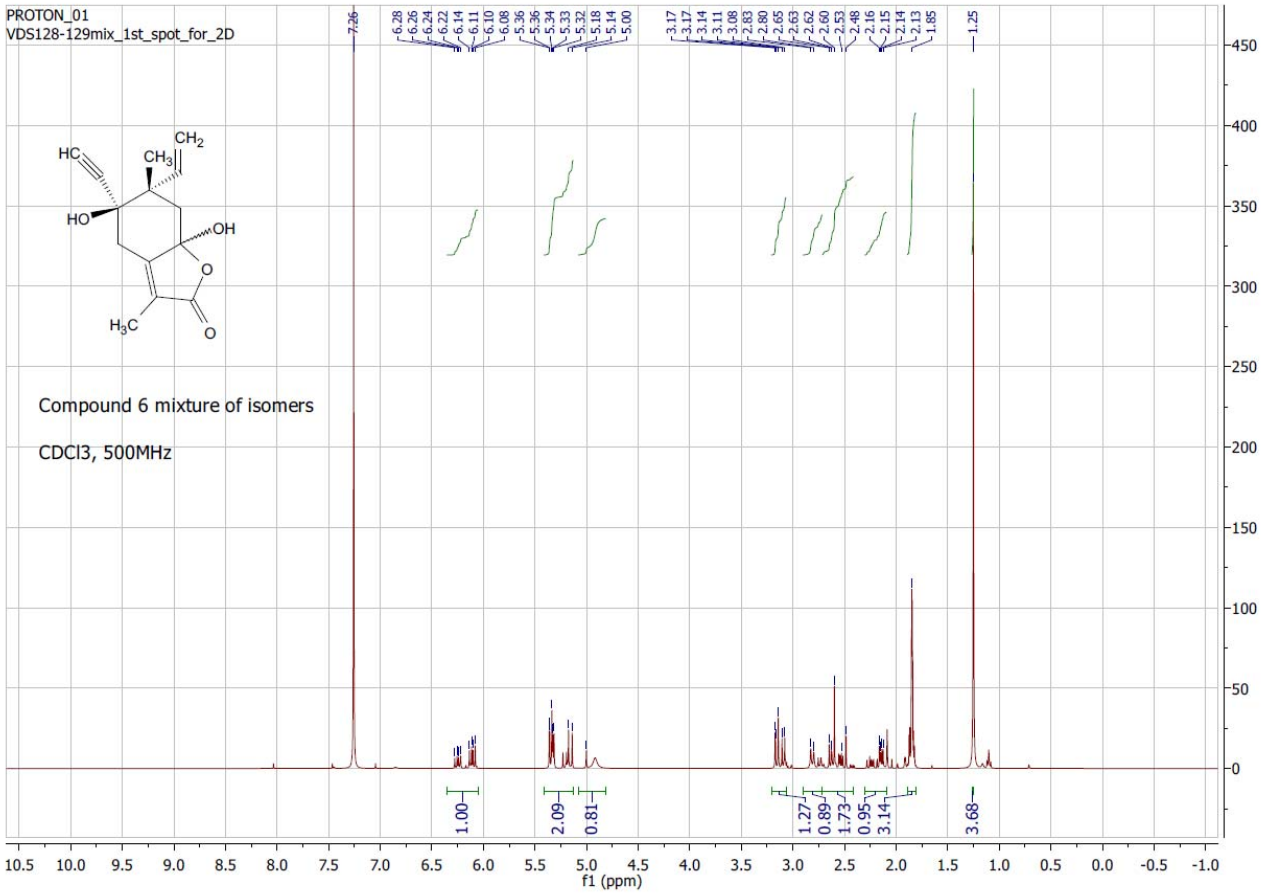
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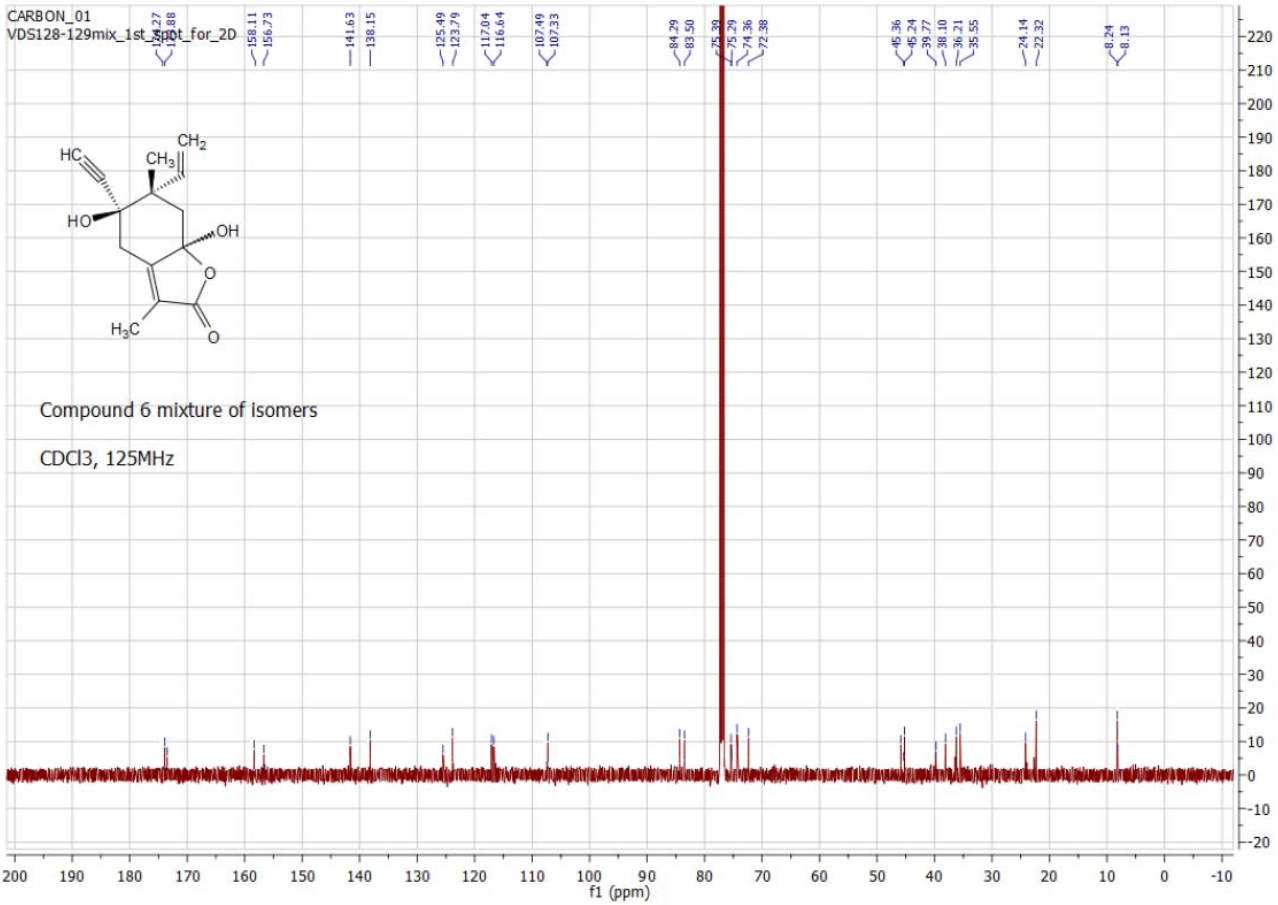
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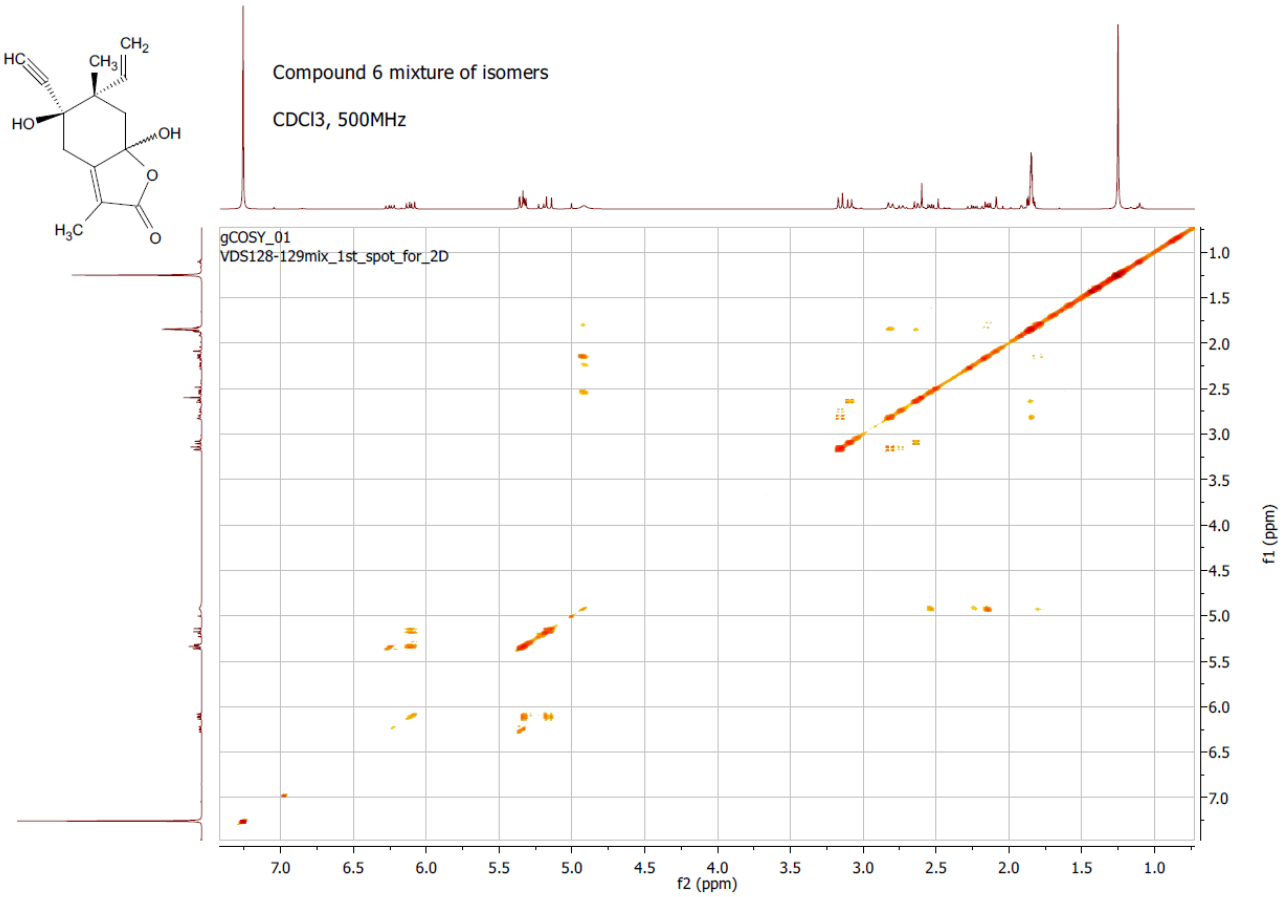
f1 (ppm)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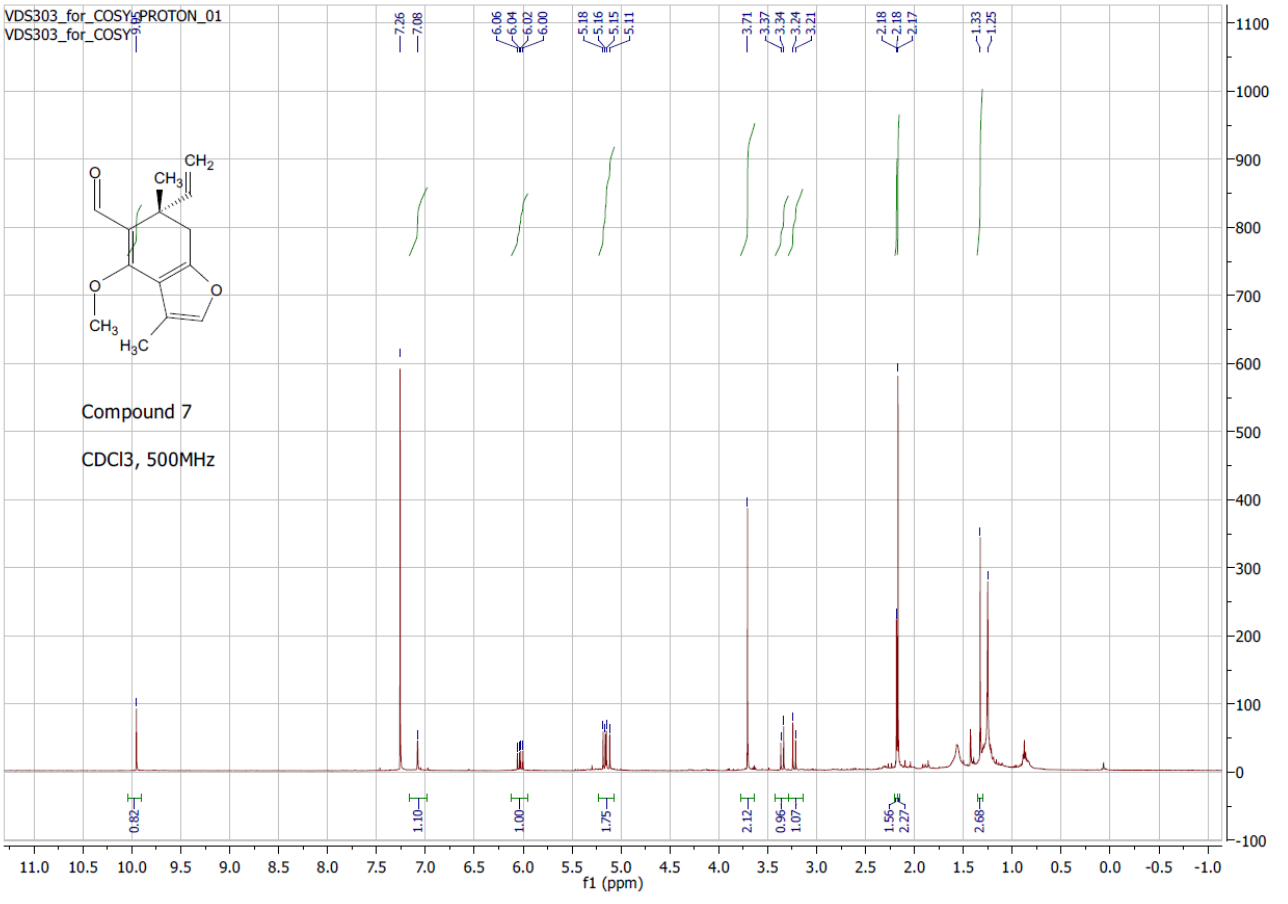
f2 (ppm)
f1 (ppm)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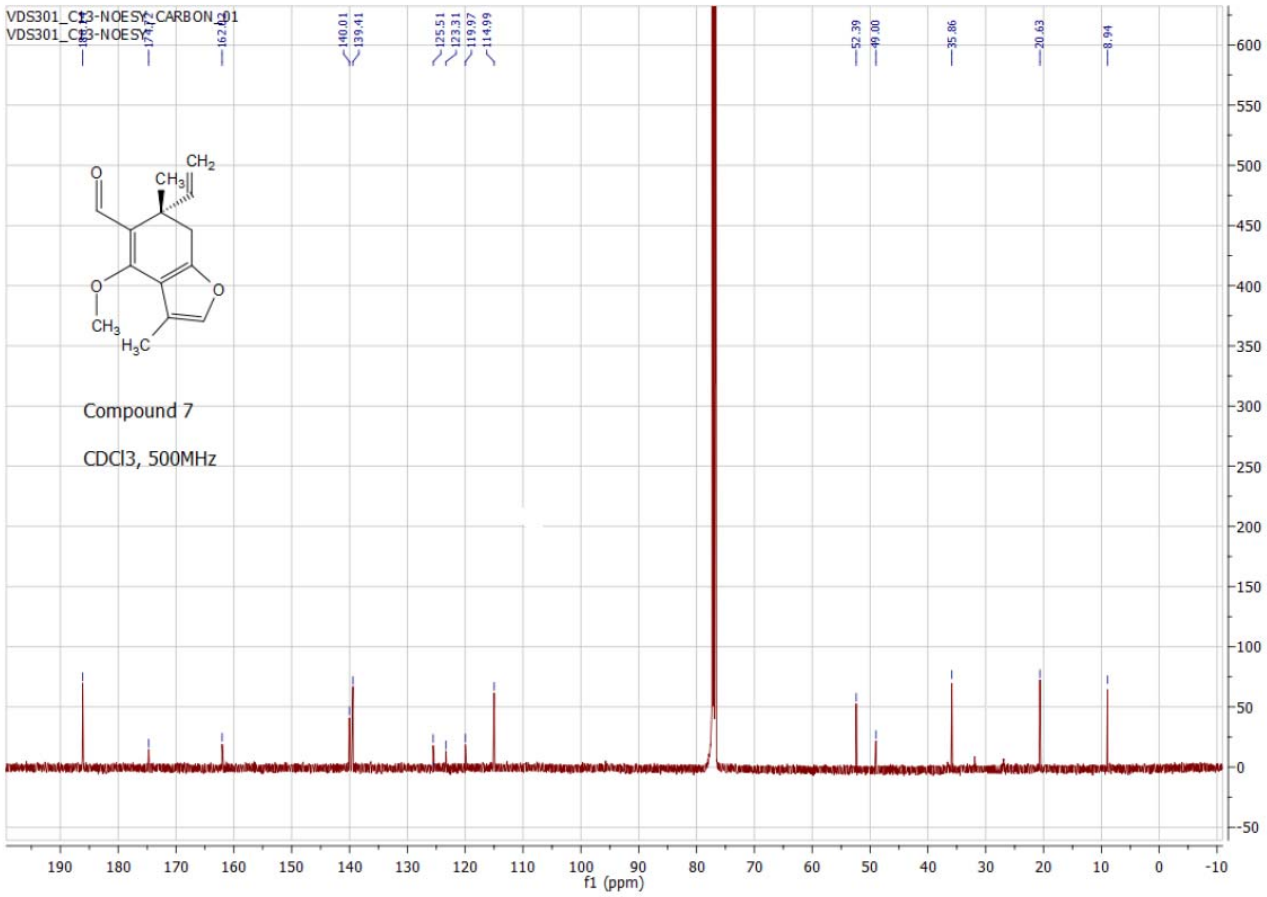
f1 (ppm)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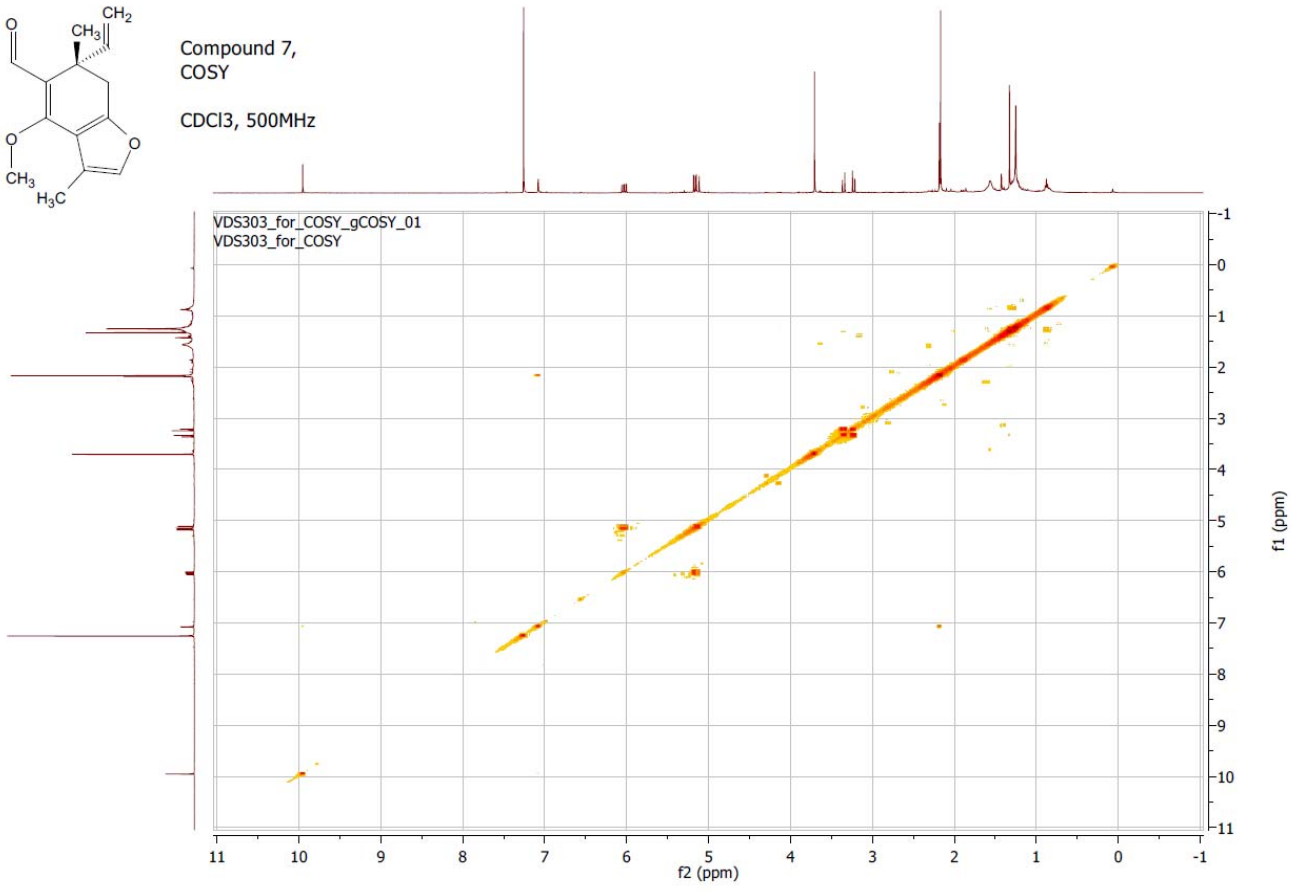
f1 (ppm)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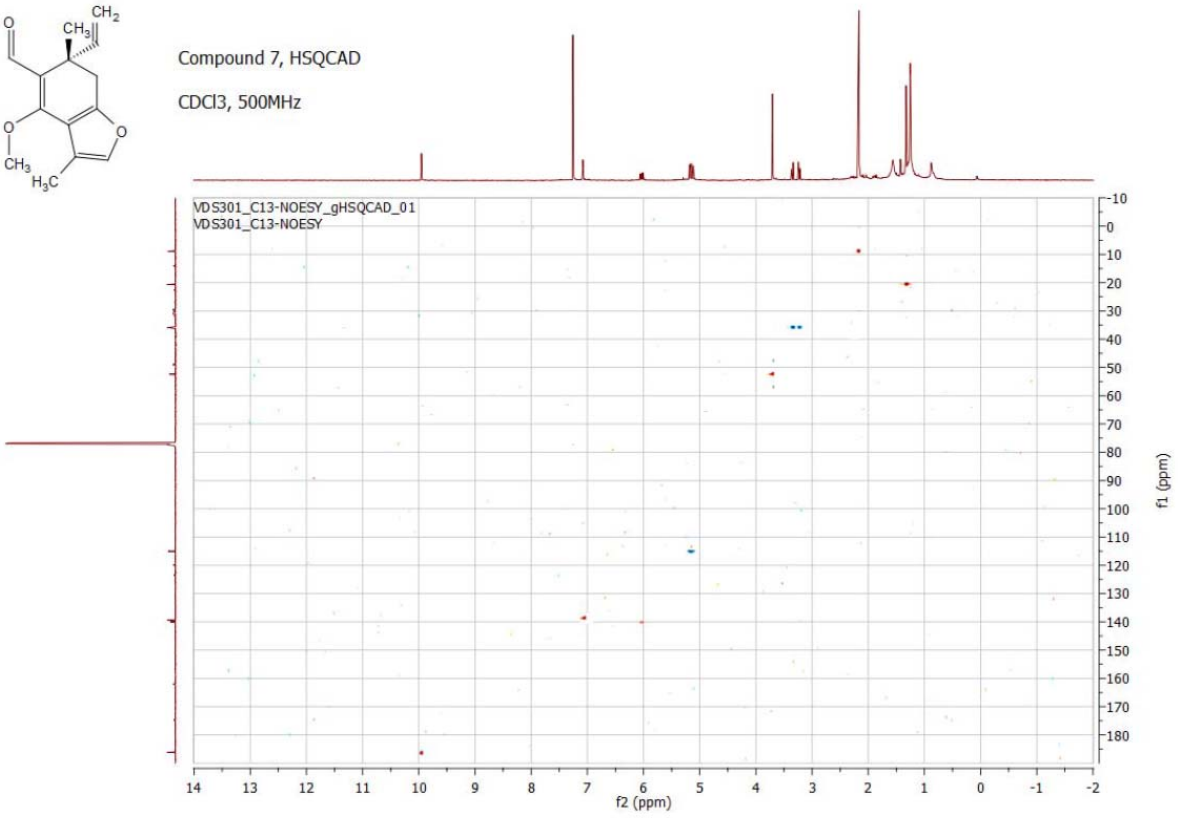
f2 (ppm)
f1 (ppm)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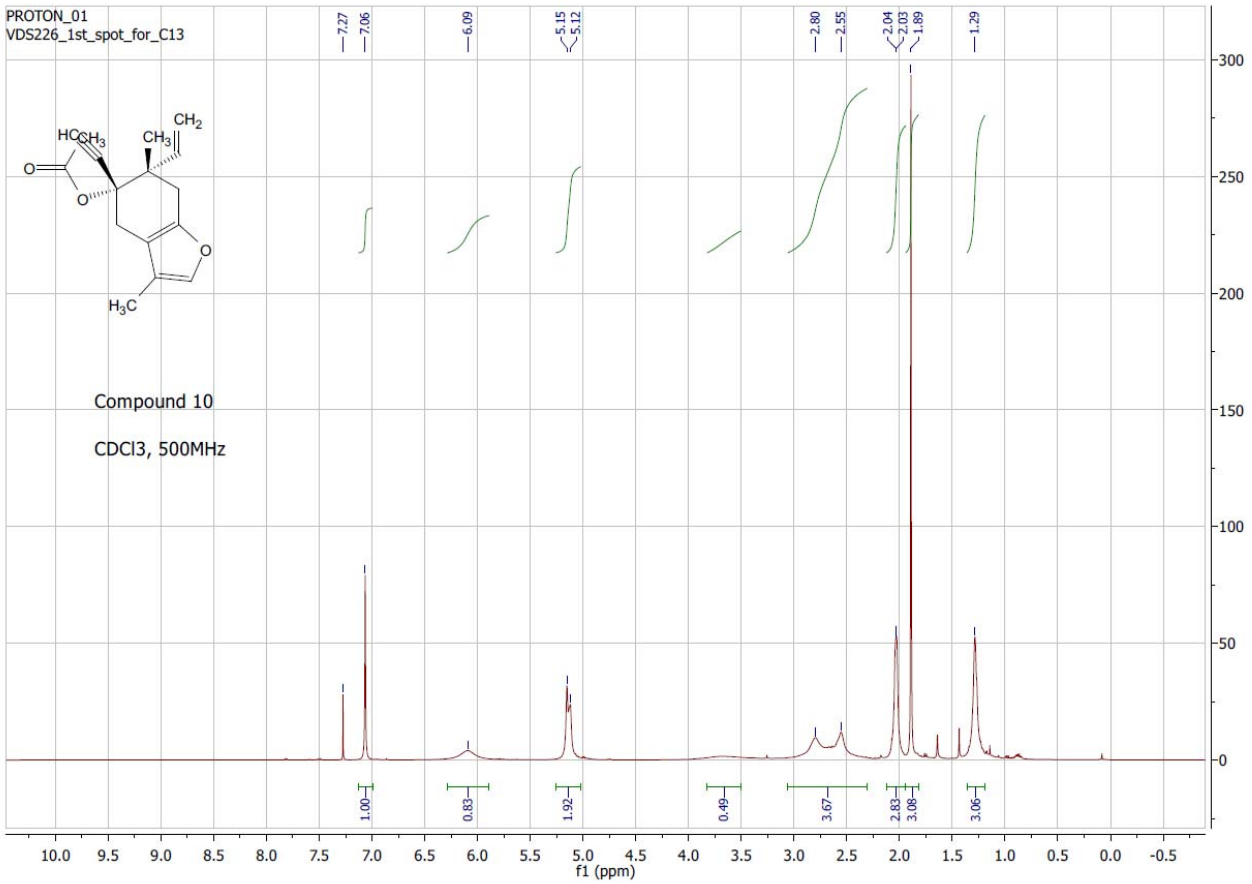
f2 (ppm)
f1 (ppm)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2.03
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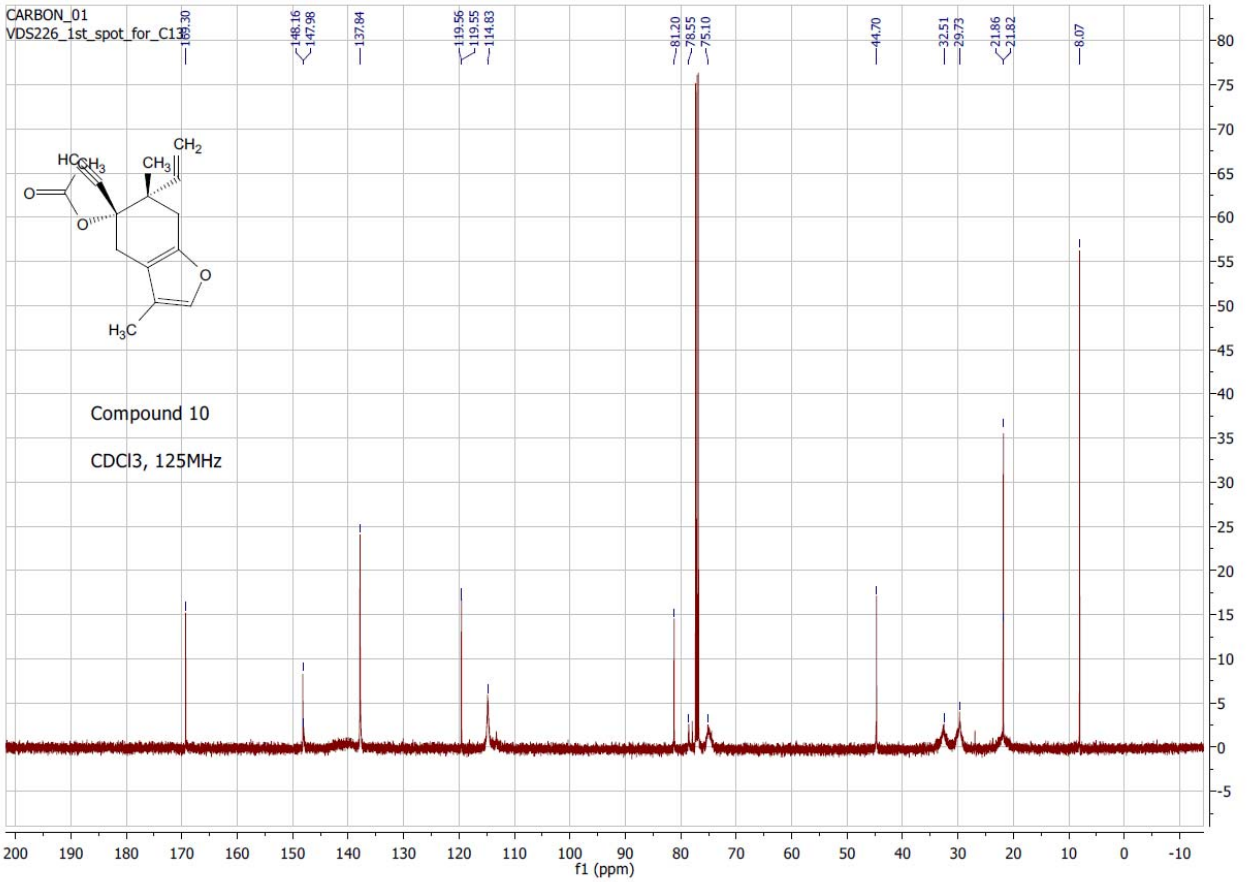
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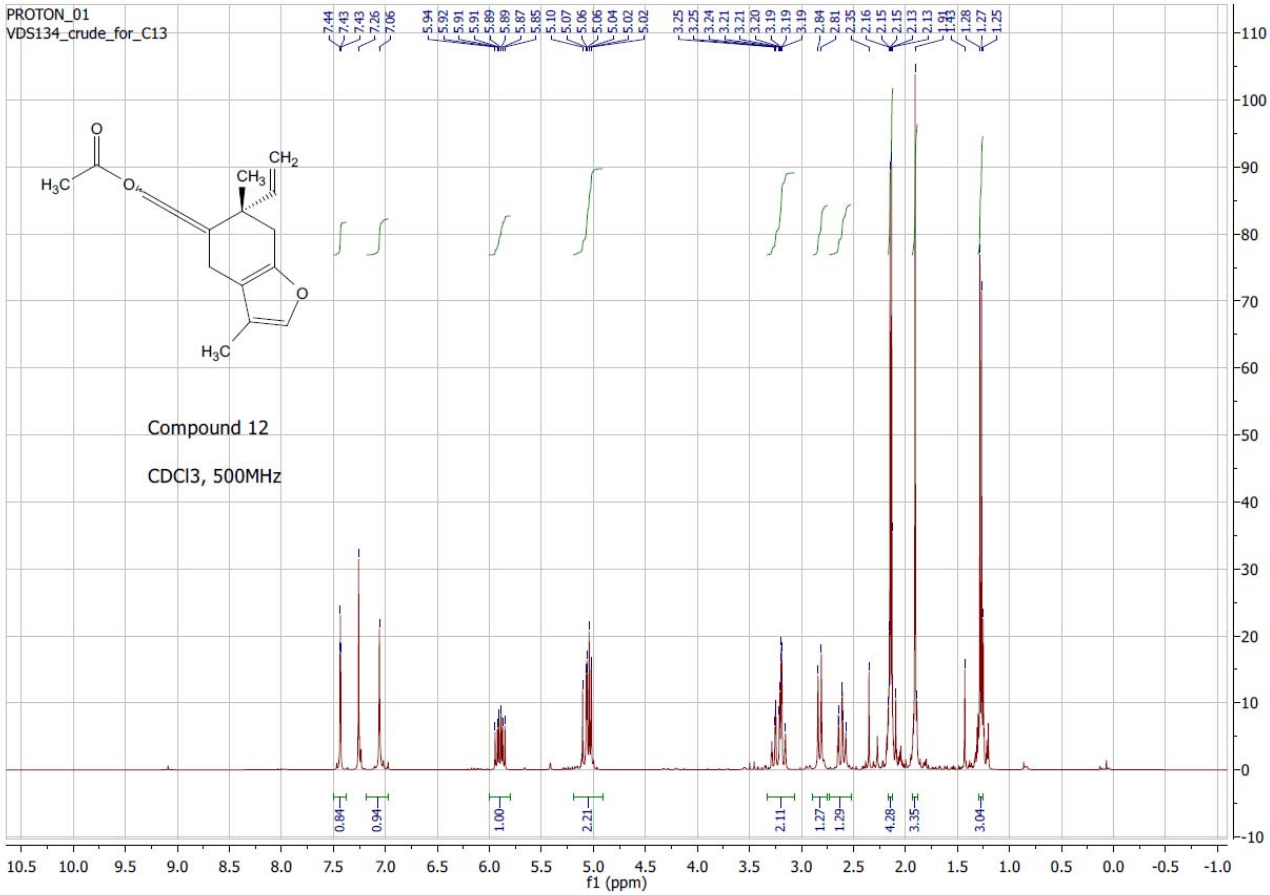
f1 (ppm)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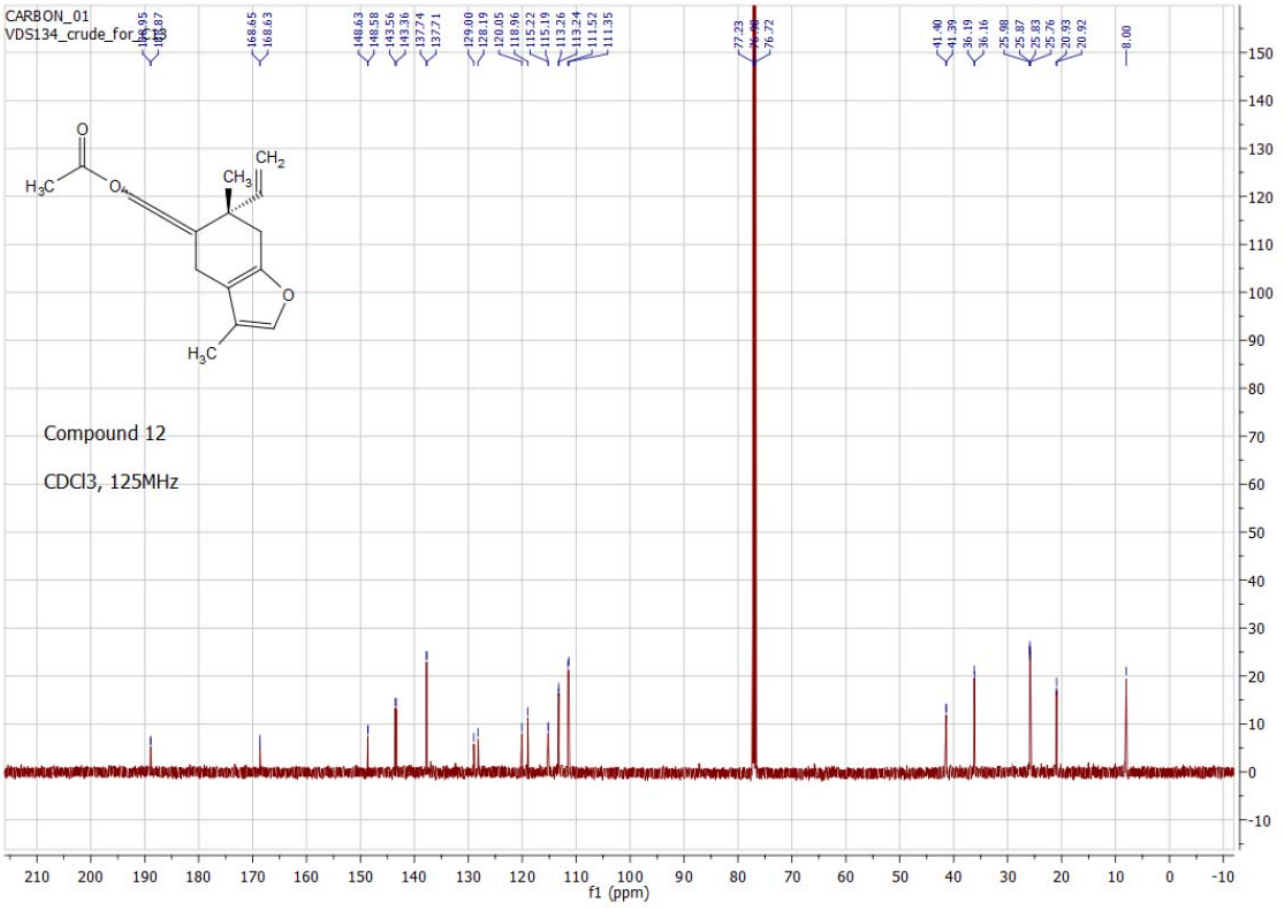
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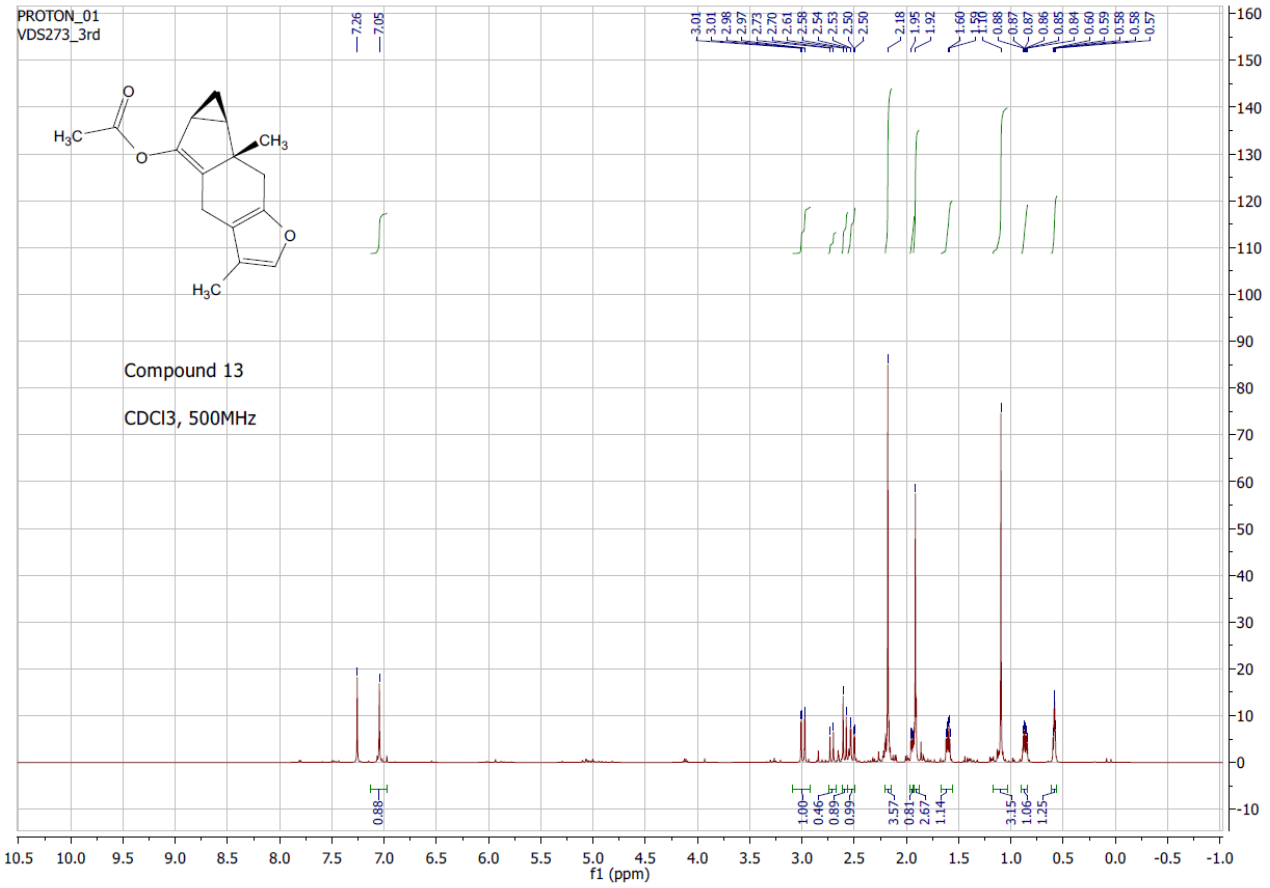
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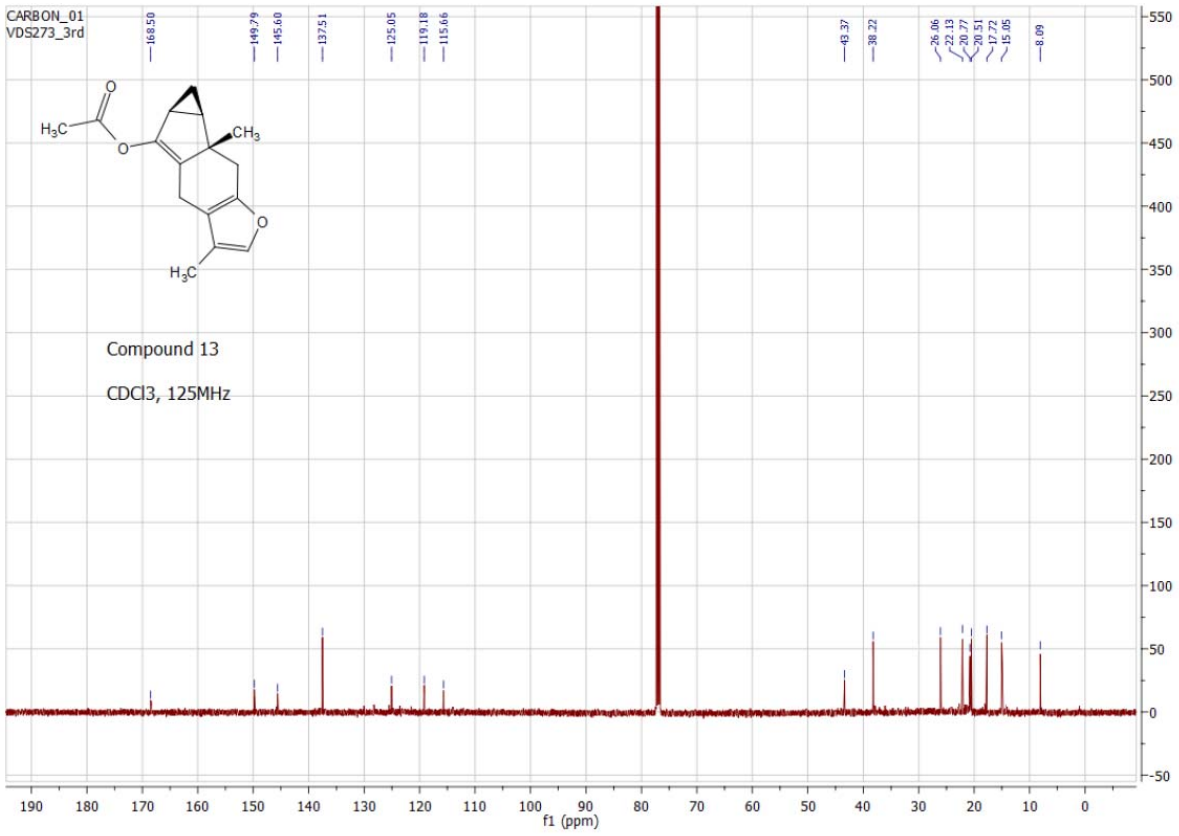
f1 (ppm)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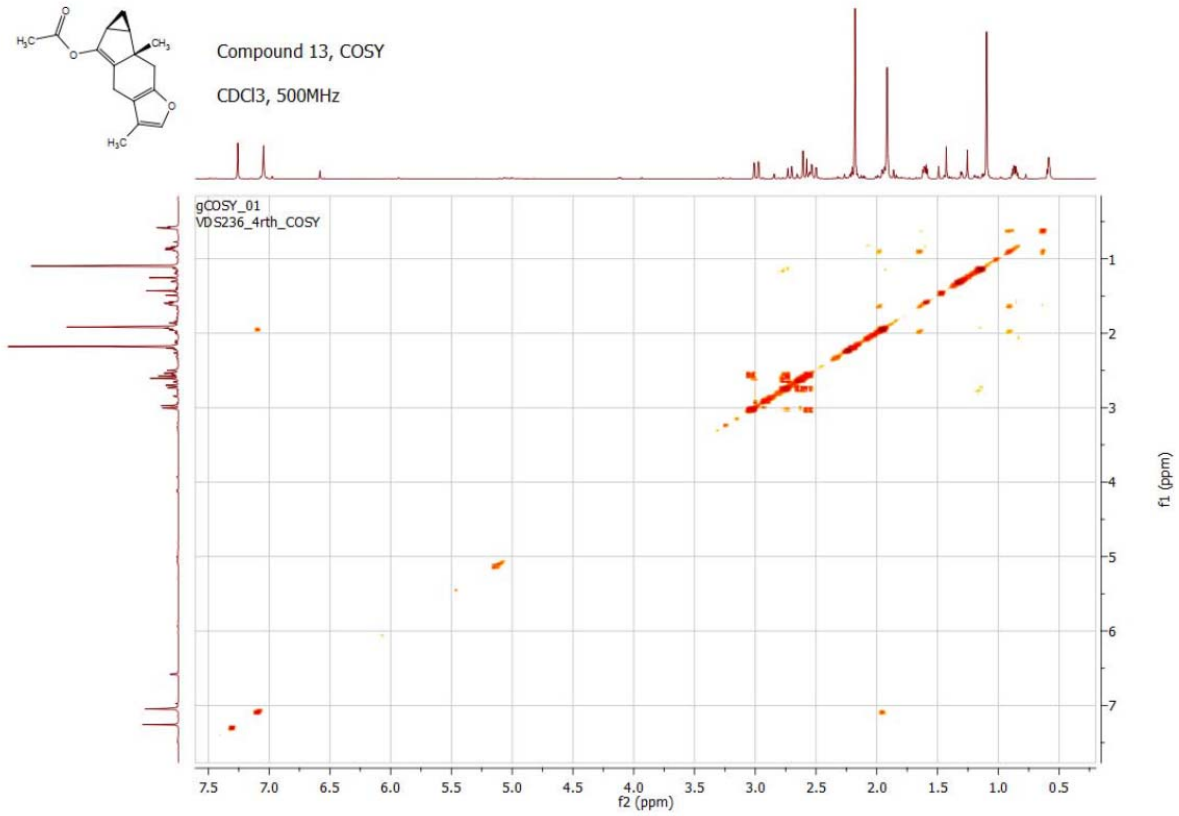
f1 (ppm)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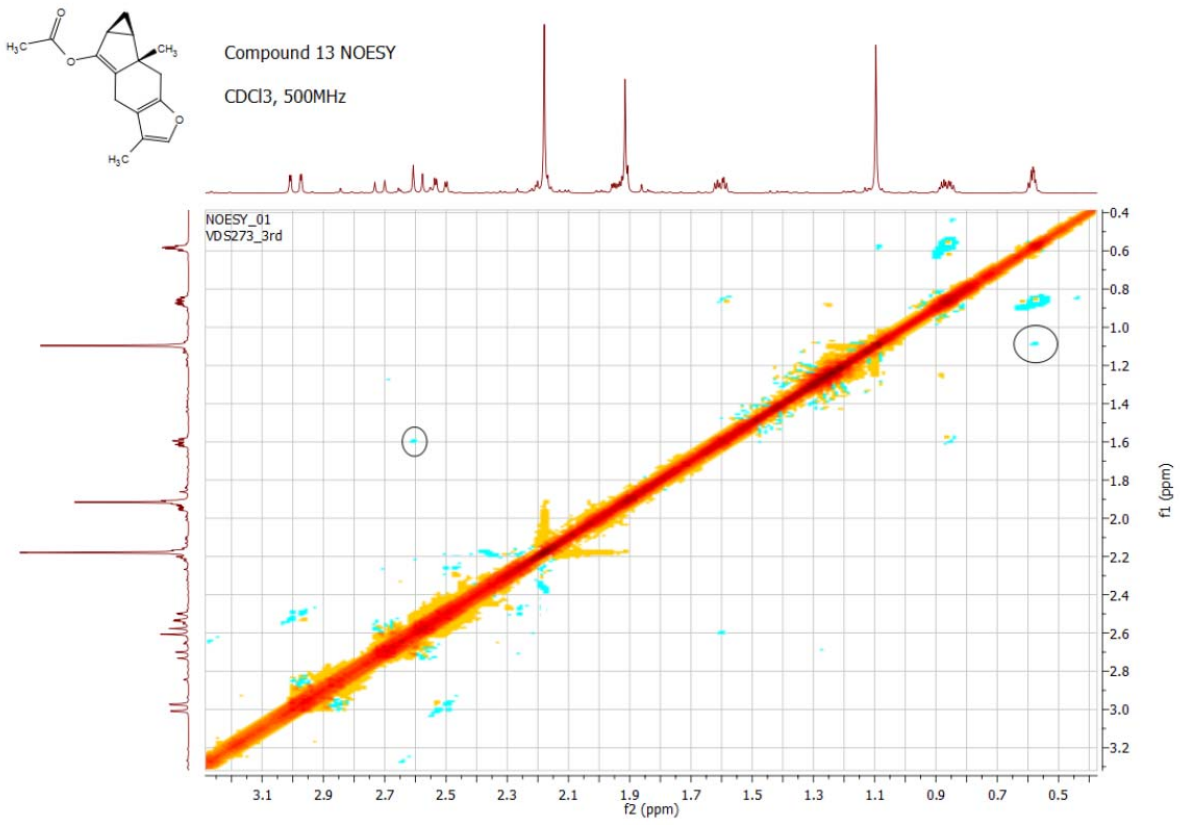
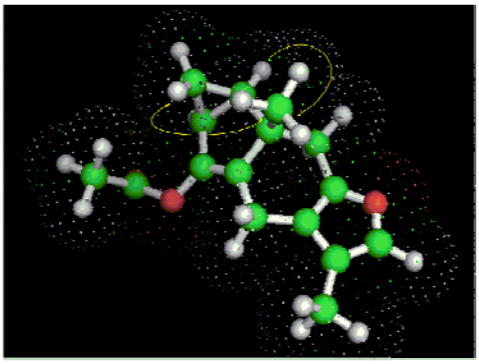
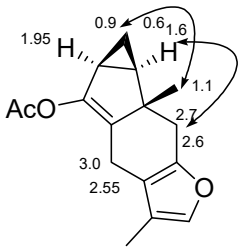
f1 (ppm)

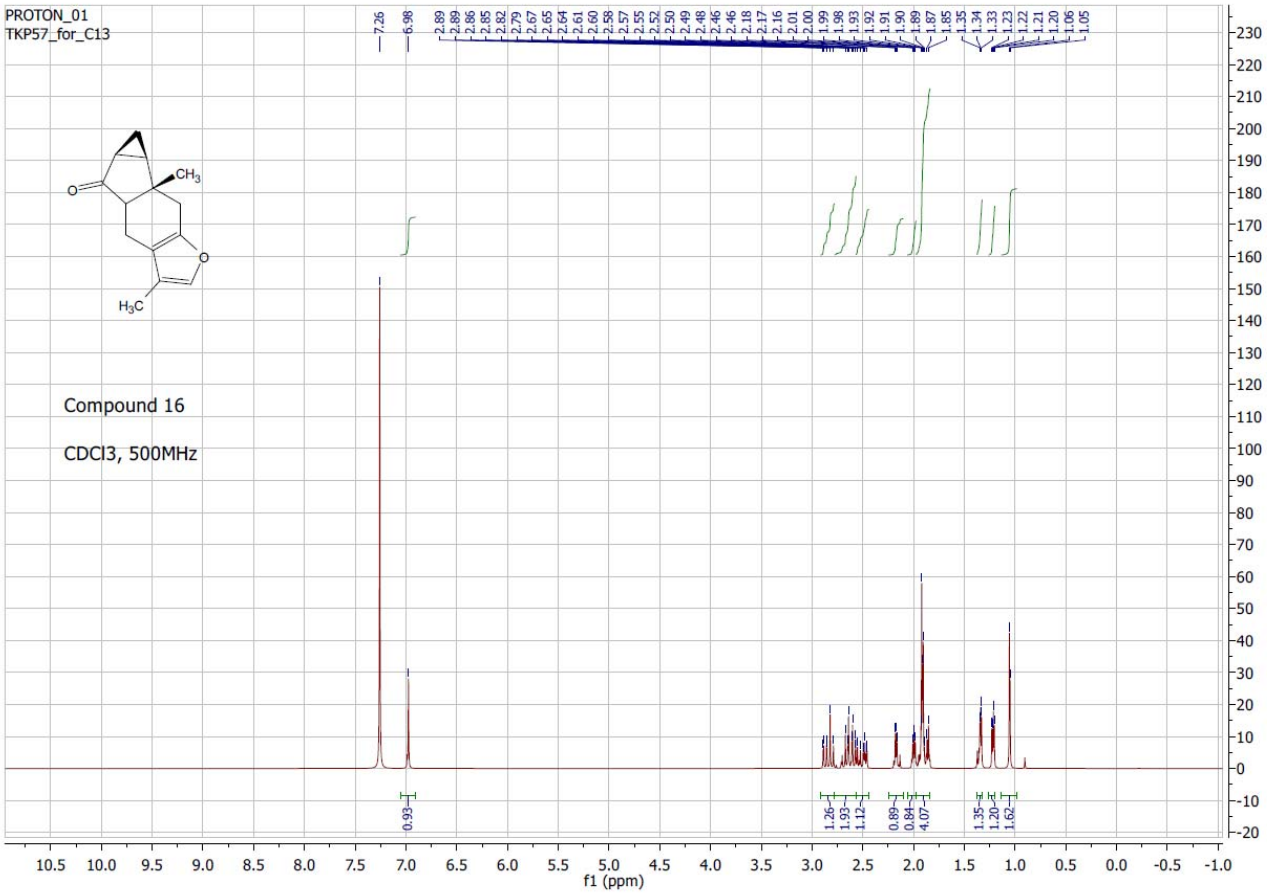


NOESY Correlations




Compound **13**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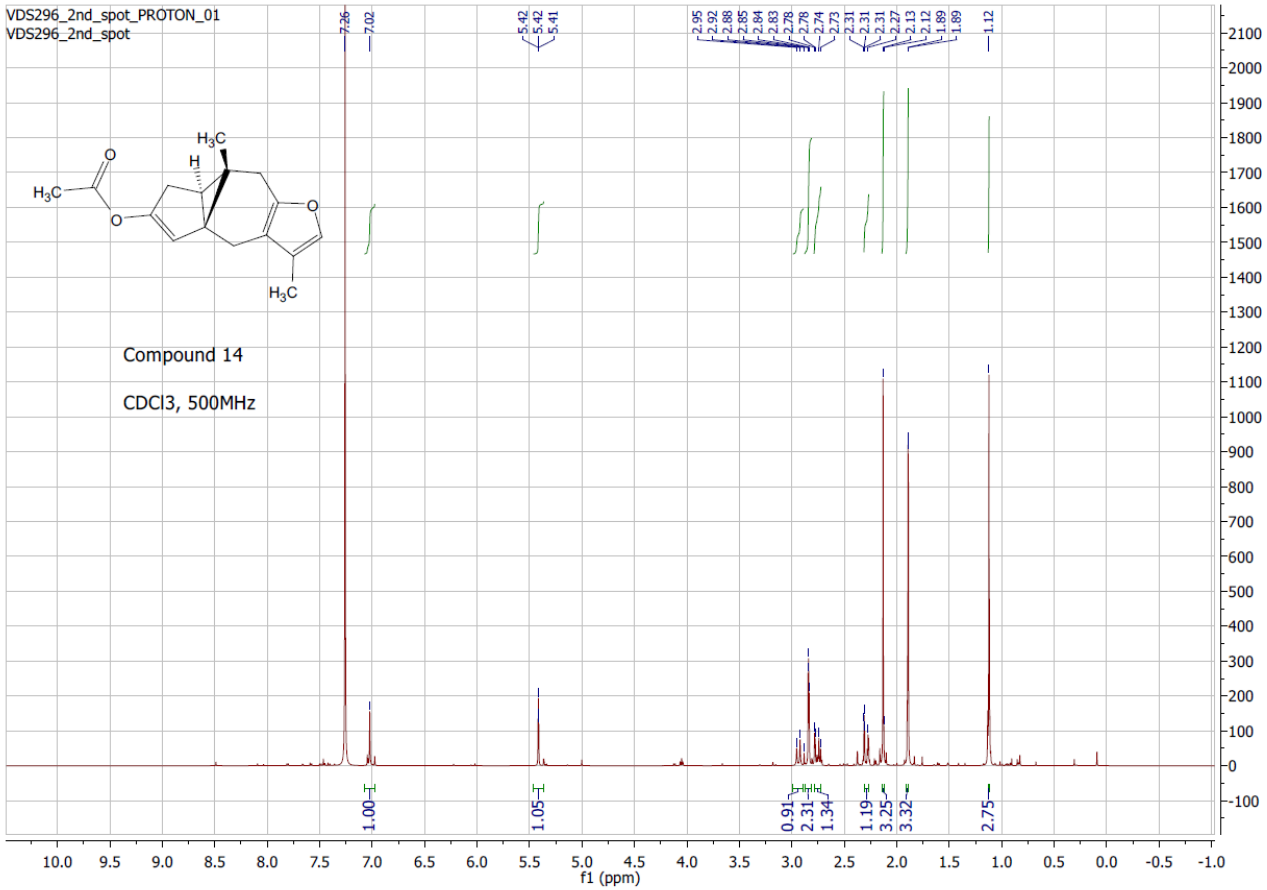
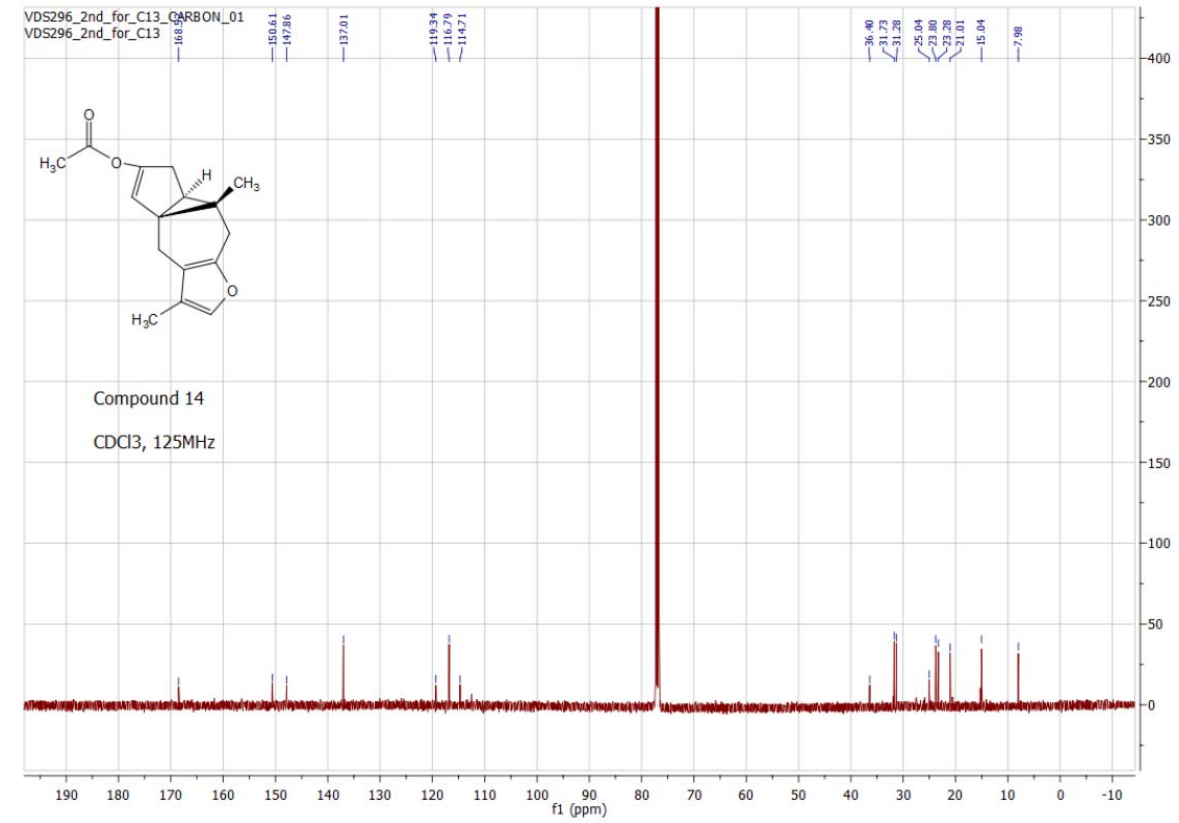
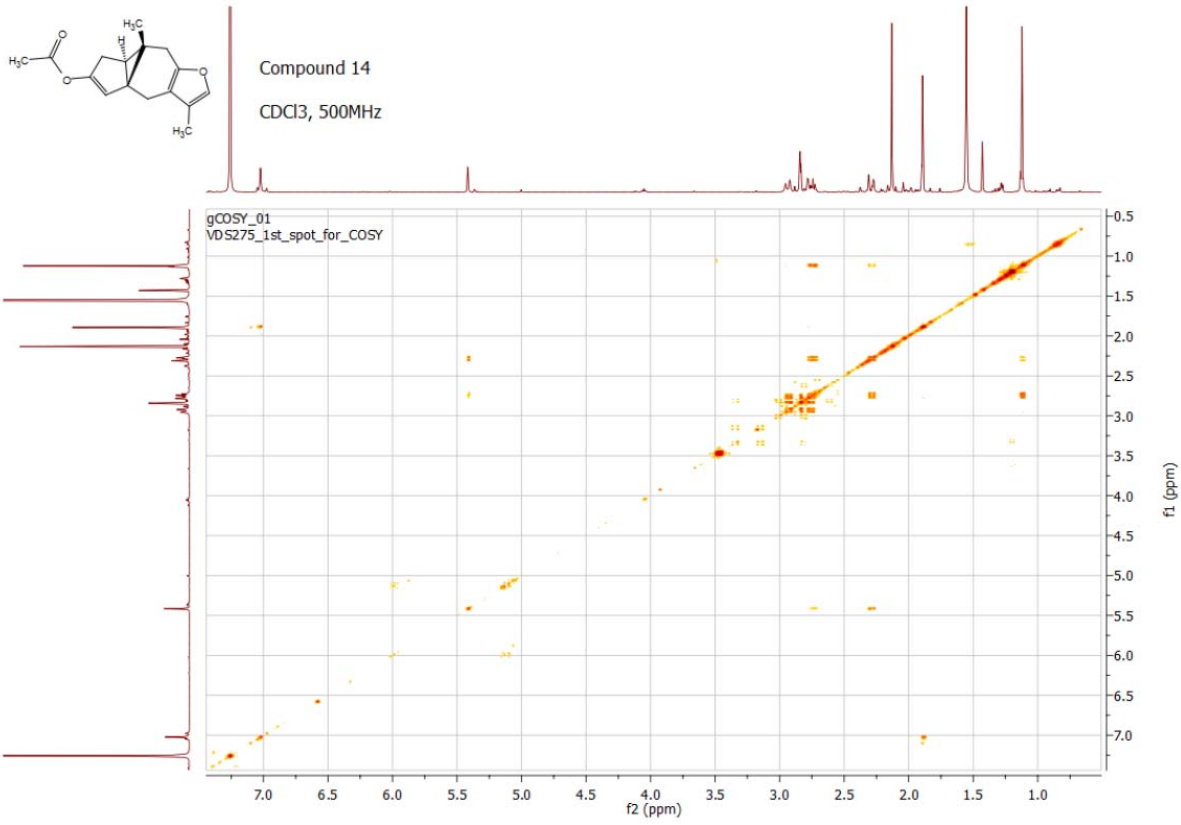
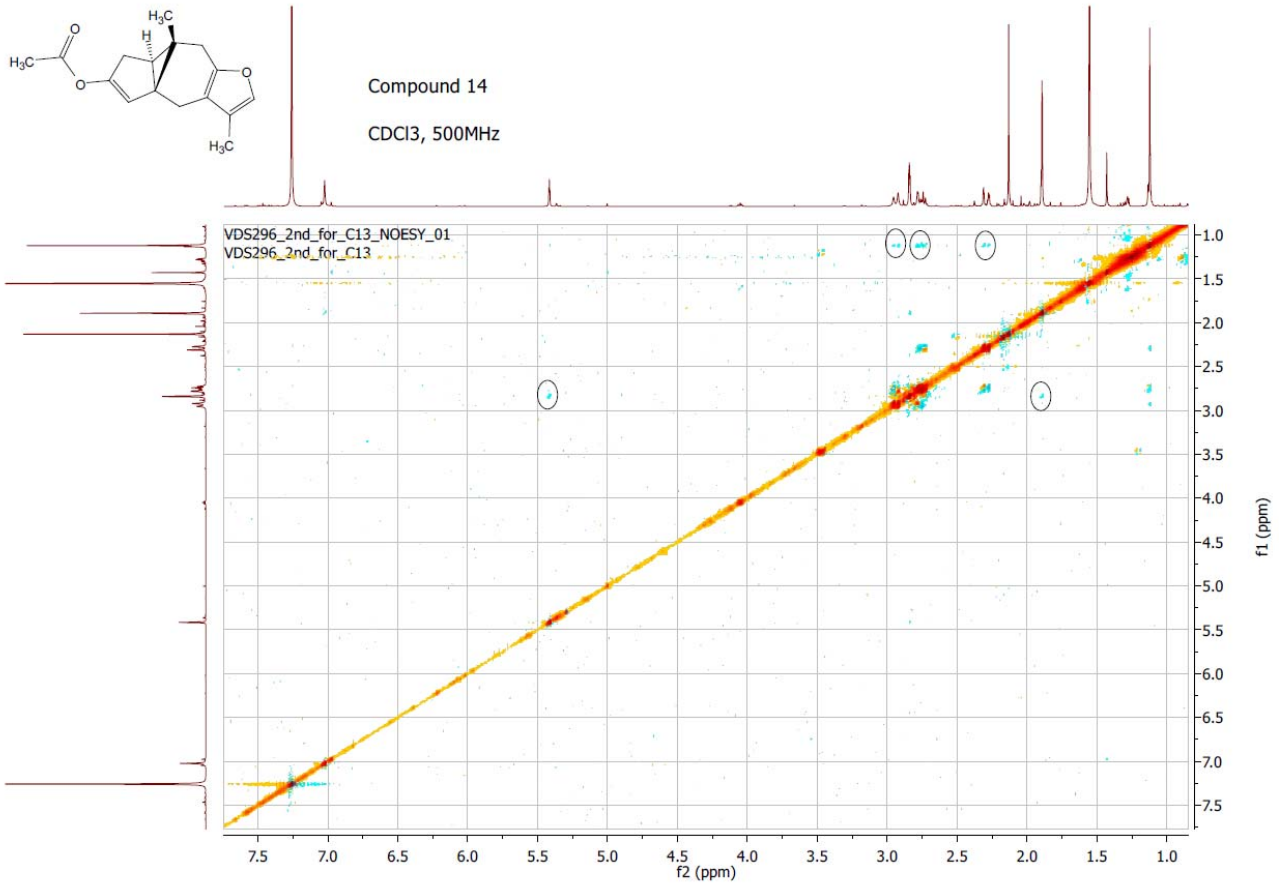
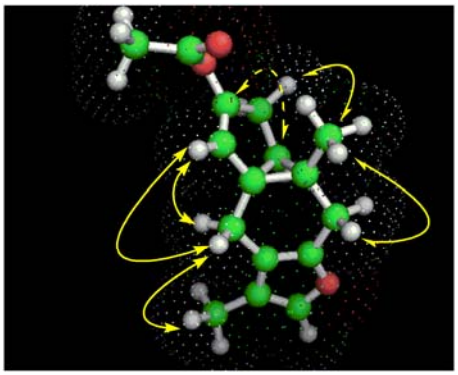
CDCl3, 500MHz
f1 (ppm)

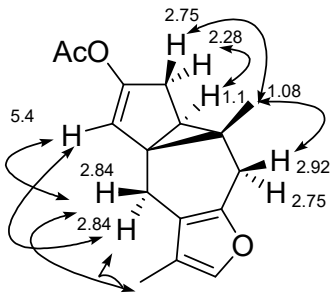

VDS296_2nd_spot_PROTON_01
VDS296_2nd_spot
Compound 14
CDCl3, 500MHz
f1 (ppm)


VDS296_2nd_for_C13_CARBON_01
VDS296_2nd_for_C13
168.57
150.61
147.86
137.01
119.34
116.79
114.71
36.40
31.73
31.28
25.04
23.80
23.28
21.01
15.04
7.98
Compound 14
CDCl3, 125MHz
f1 (ppm)

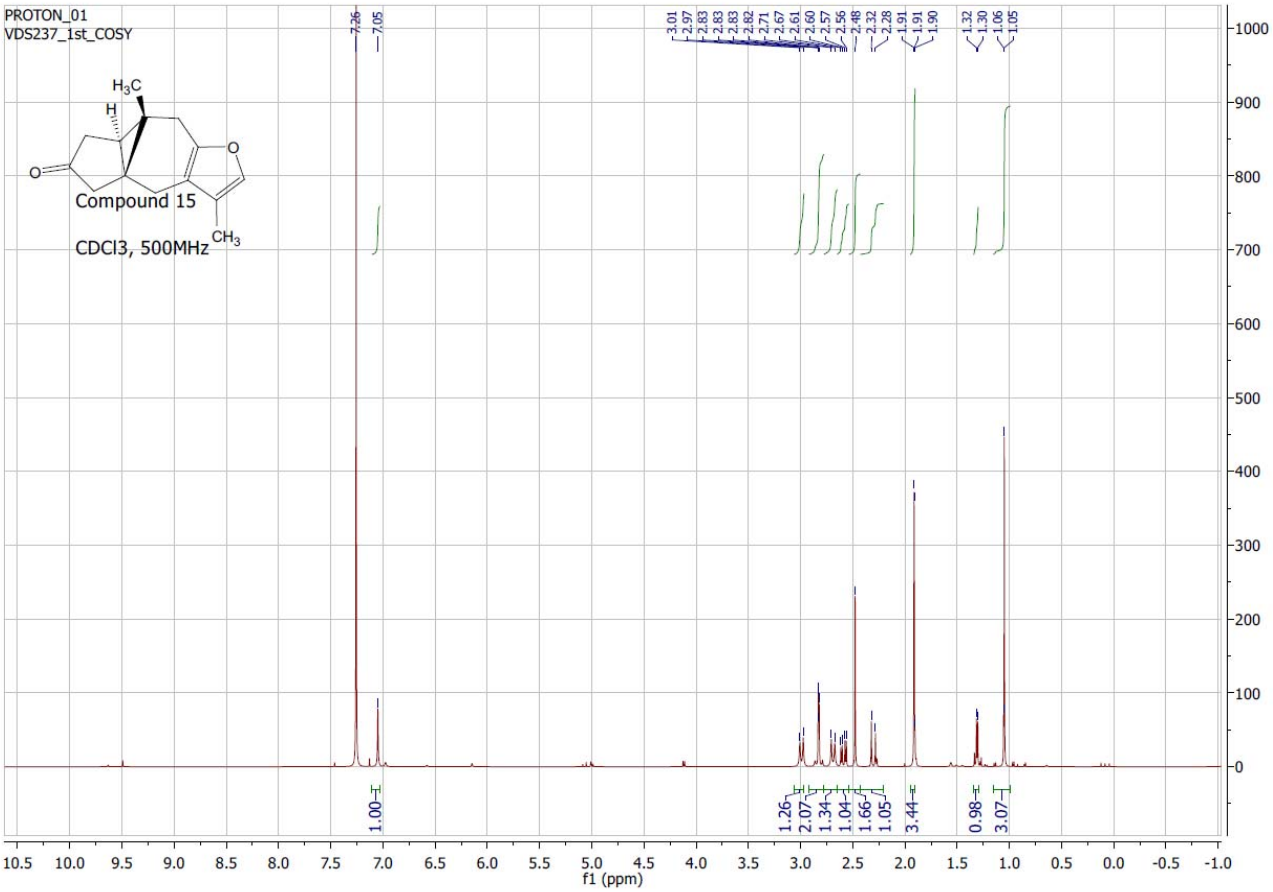

Compound 14
CDCl3, 500MHz
gCOSY_01
VDS275_1st_spot_for_COSY
f2 (ppm)
f1 (ppm)

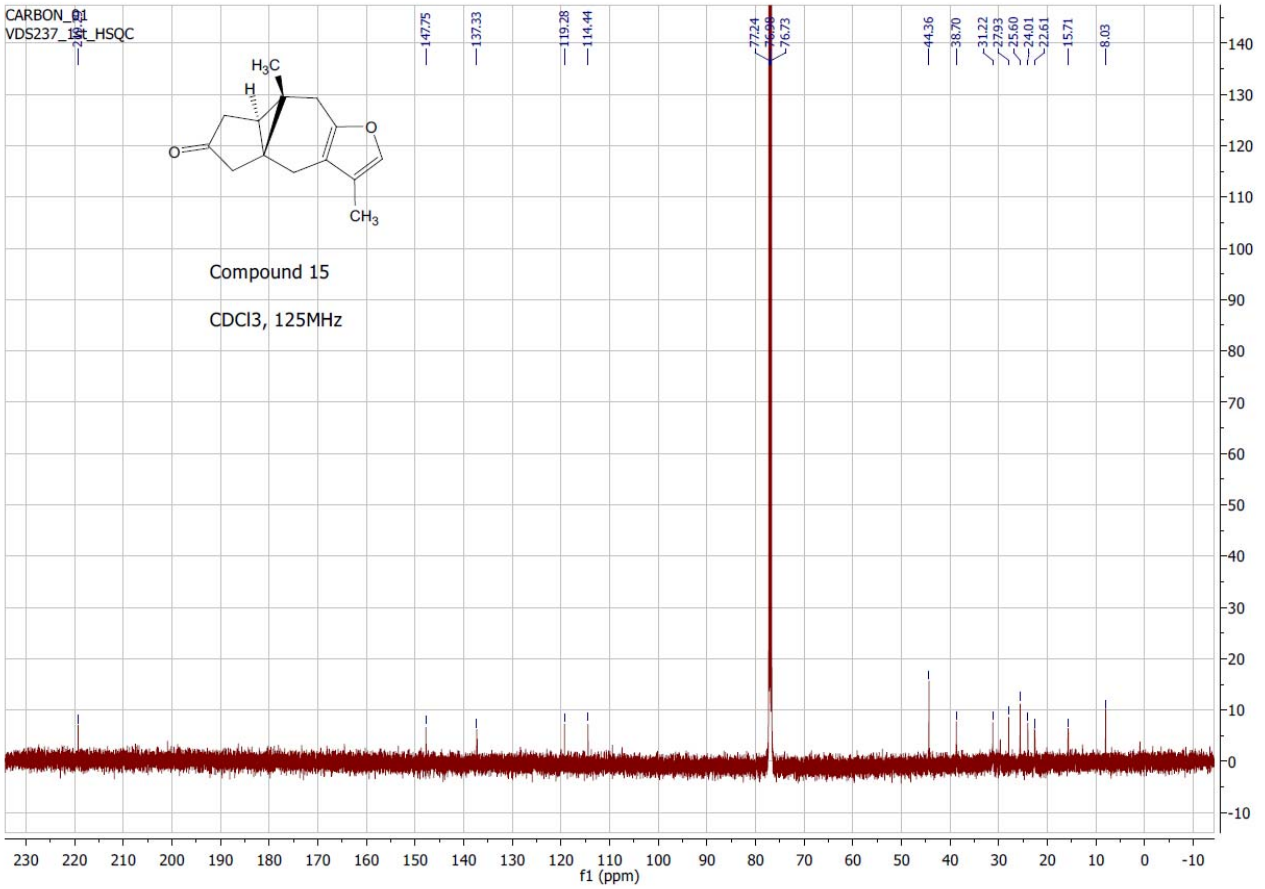

Compound 14
CDCl3, 500MHz
VDS296_2nd_for_C13_NOESY_01
VDS296_2nd_for_C13
f2 (ppm)
f1 (ppm)

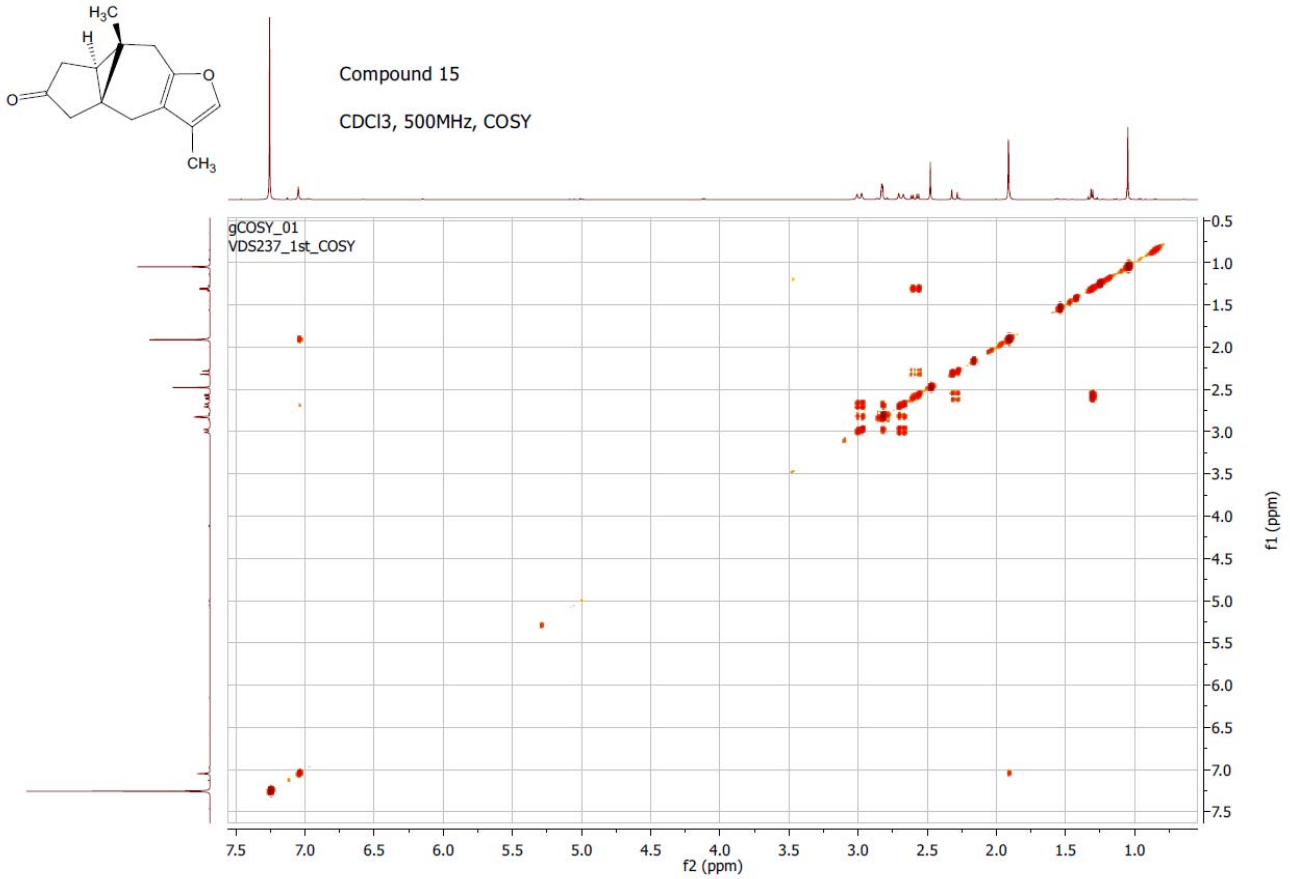


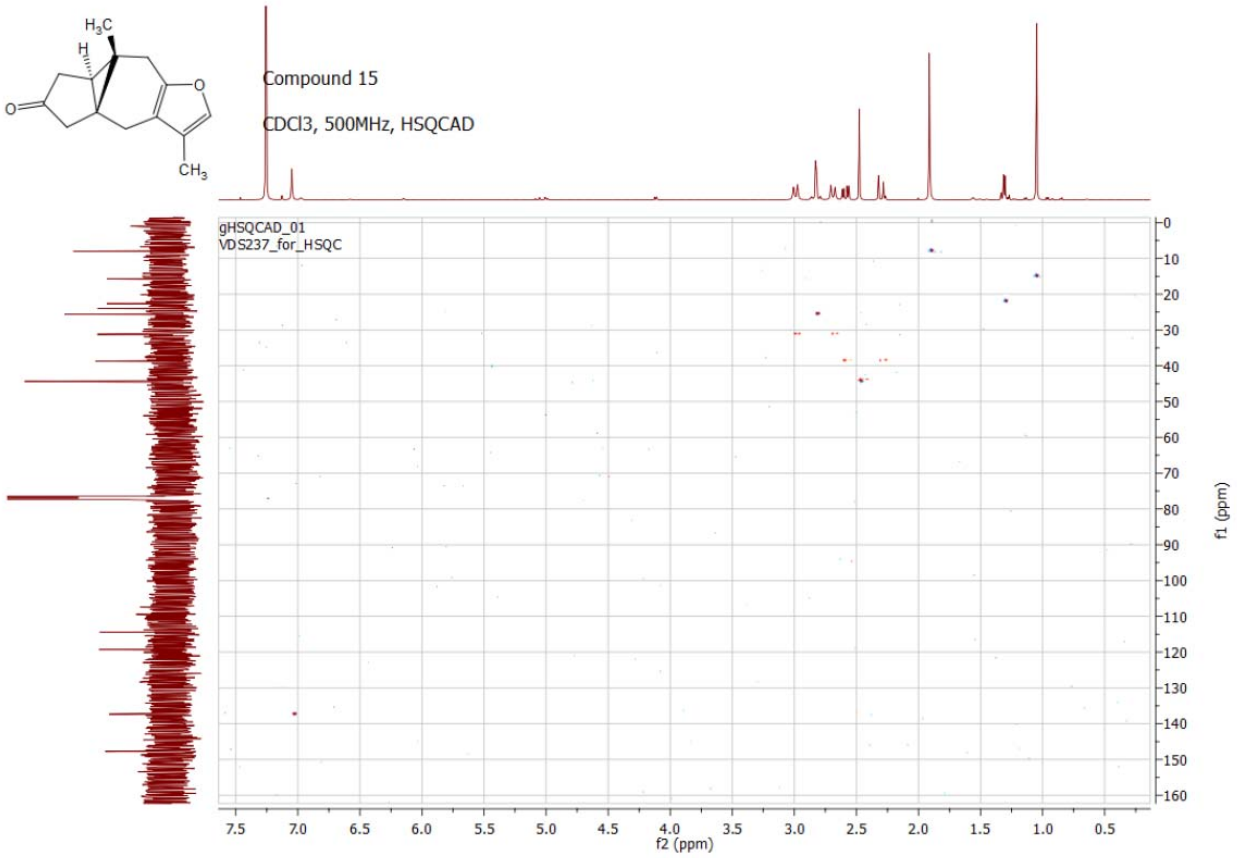

AcO
2.75
2.28
1.1
1.08
5.4
2.84
2.92
2.75
2.84
O

Compound **14**

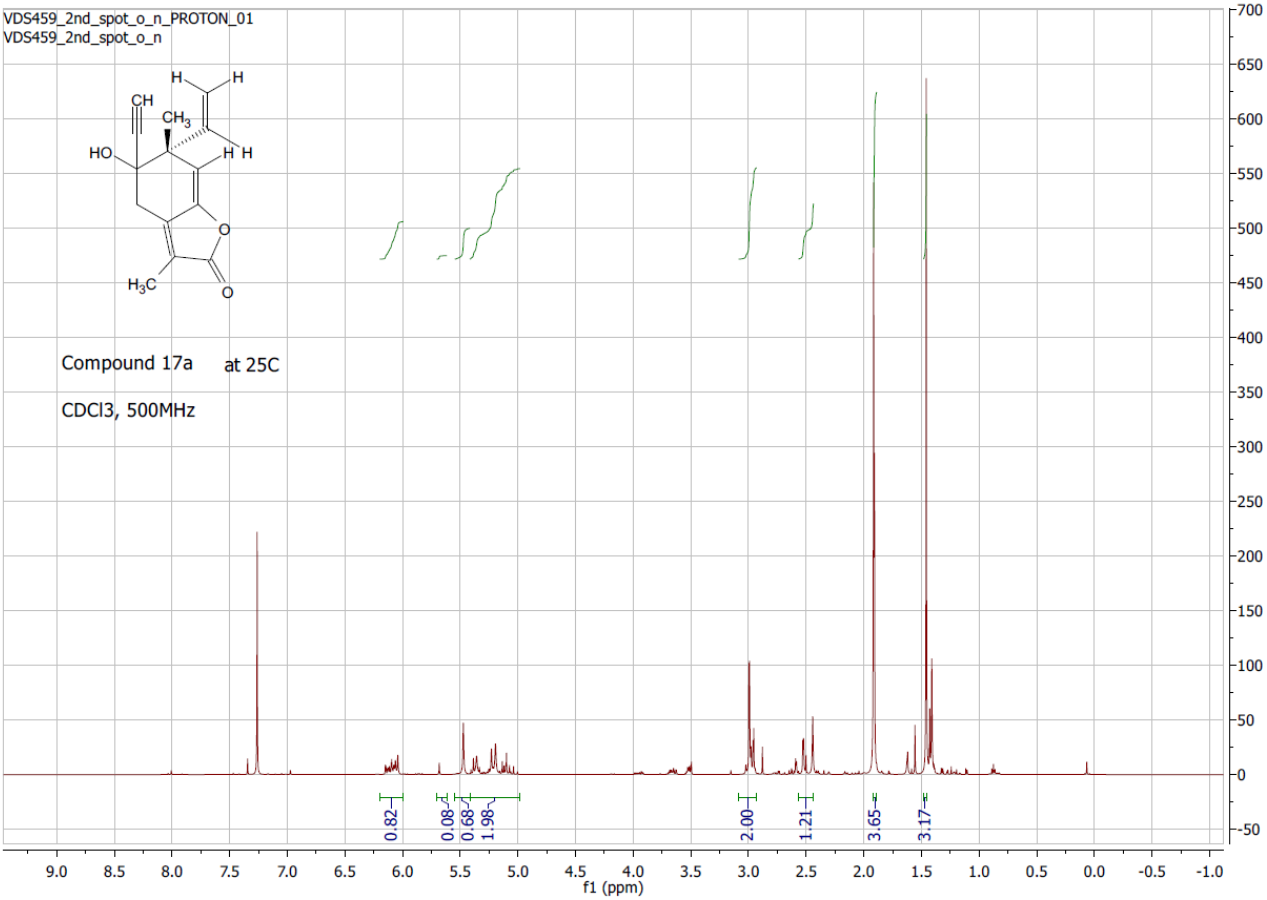

PROTON_01
VDS237_1st_COSY
Compound 15
CDCl3, 500MHz
f1 (ppm)

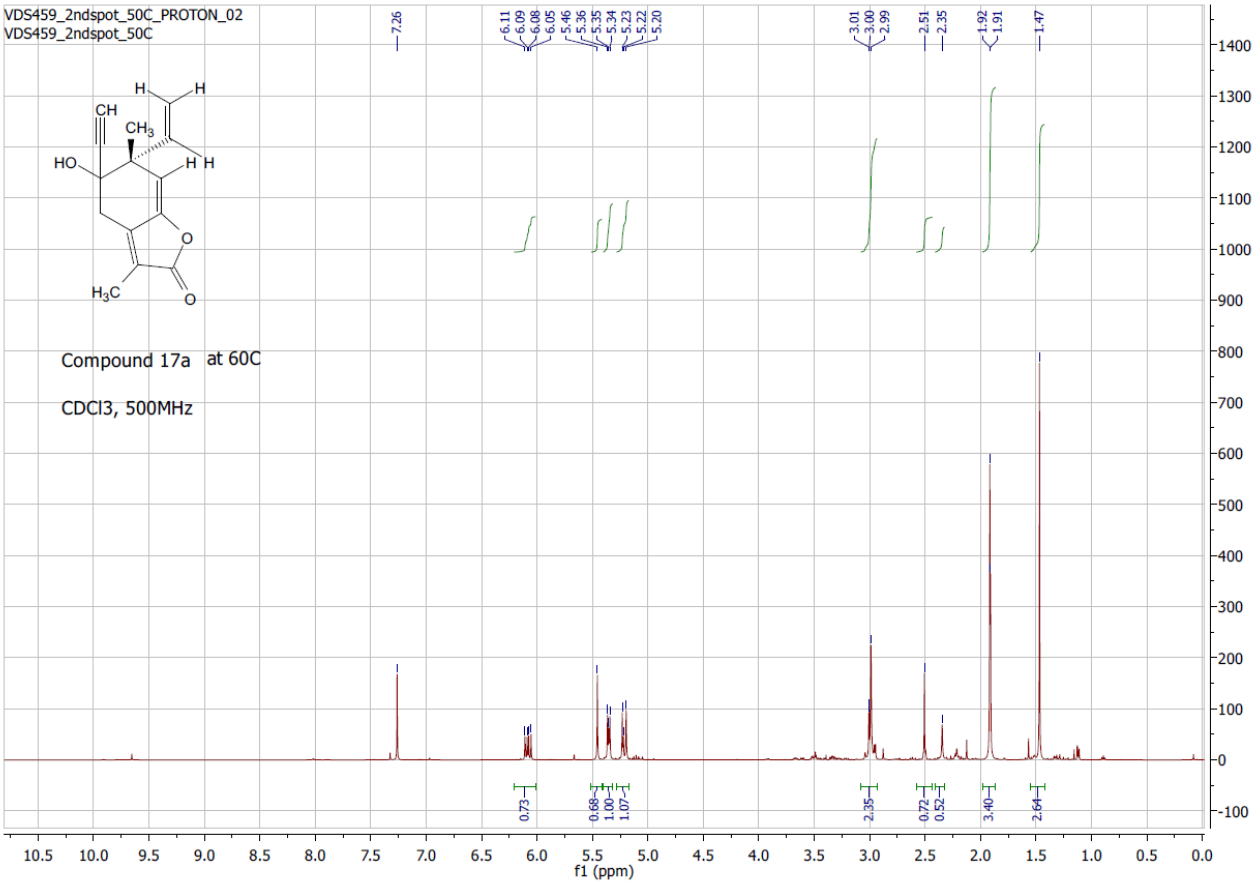

CARBON_01
VDS237_1st_HSQC
Compound 15
CDCl3, 125MHz
f1 (ppm)

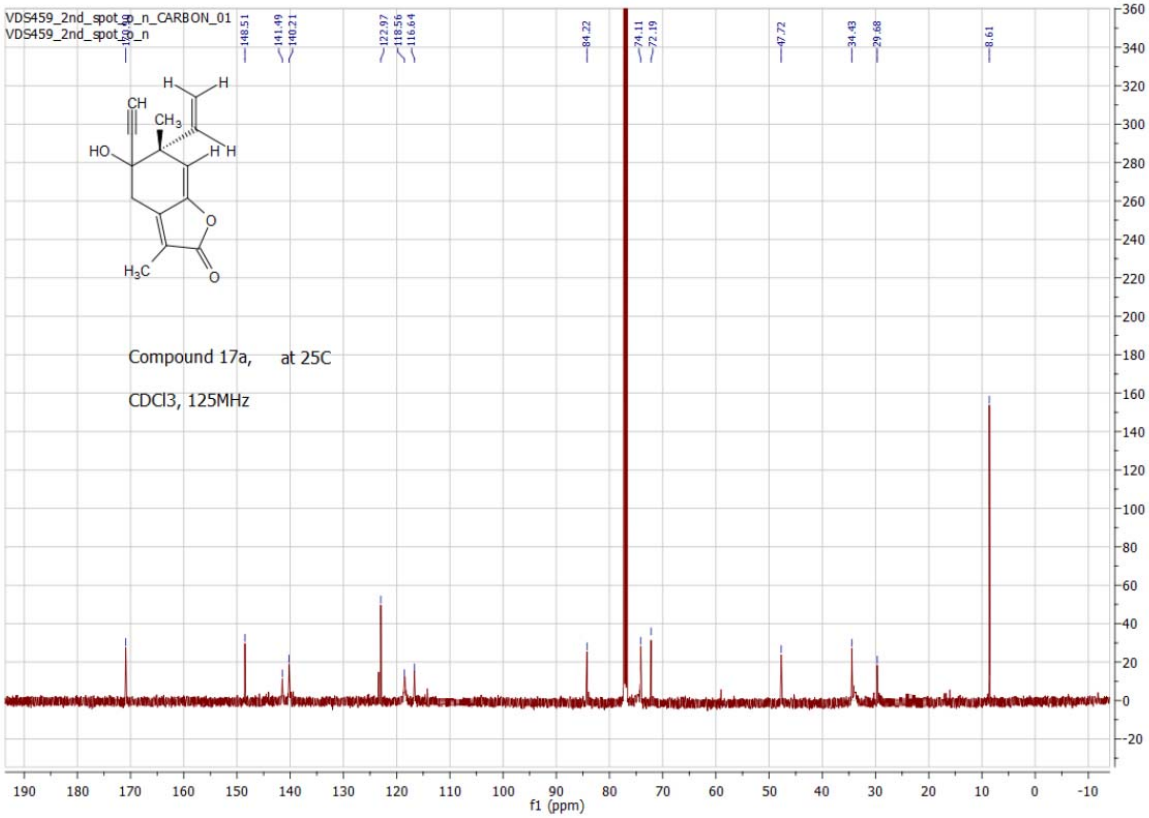

Compound 15
CDCl3, 500MHz, COSY
gCOSY_01
VDS237_1st_COSY
f2 (ppm)
f1 (ppm)

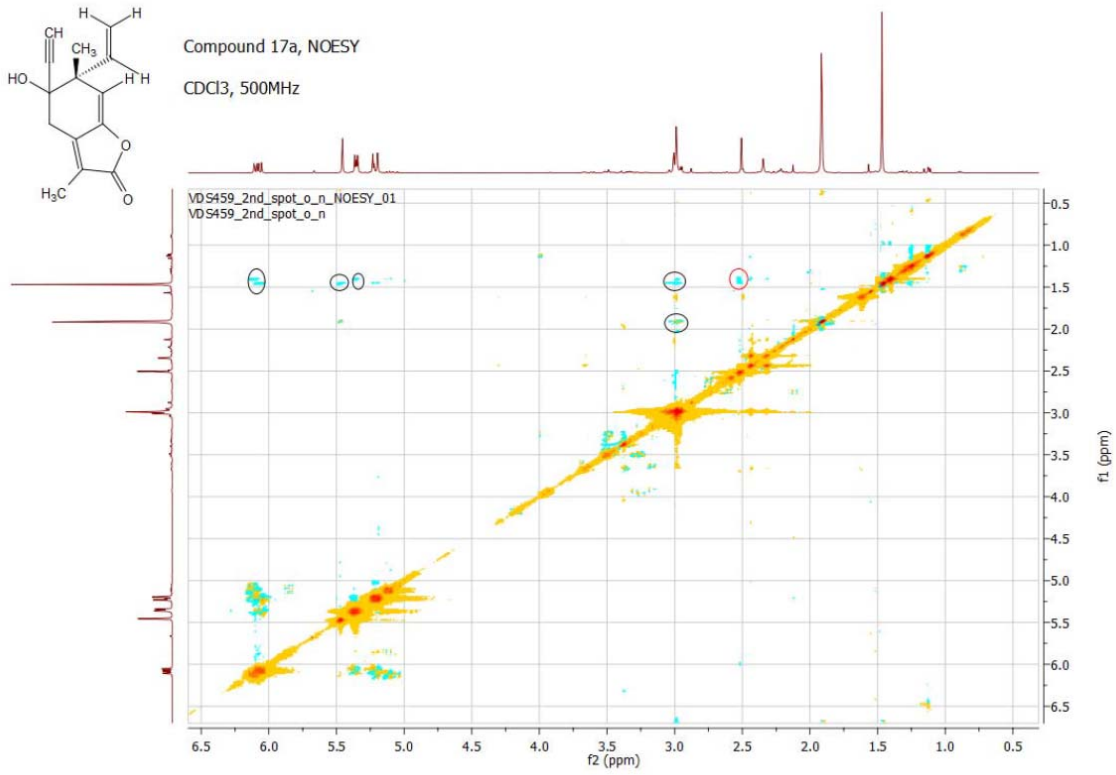

Compound 15
CDCl3, 500MHz, HSQCAD
gHSQCAD_01
VDS237_for_HSQC
f2 (ppm)
f1 (ppm)

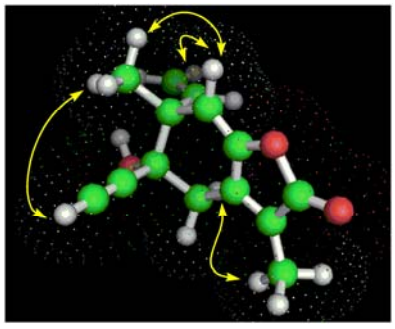
Compound **17a** conformer's dependence at temperature



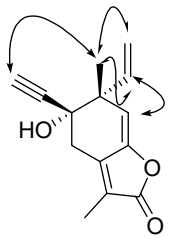





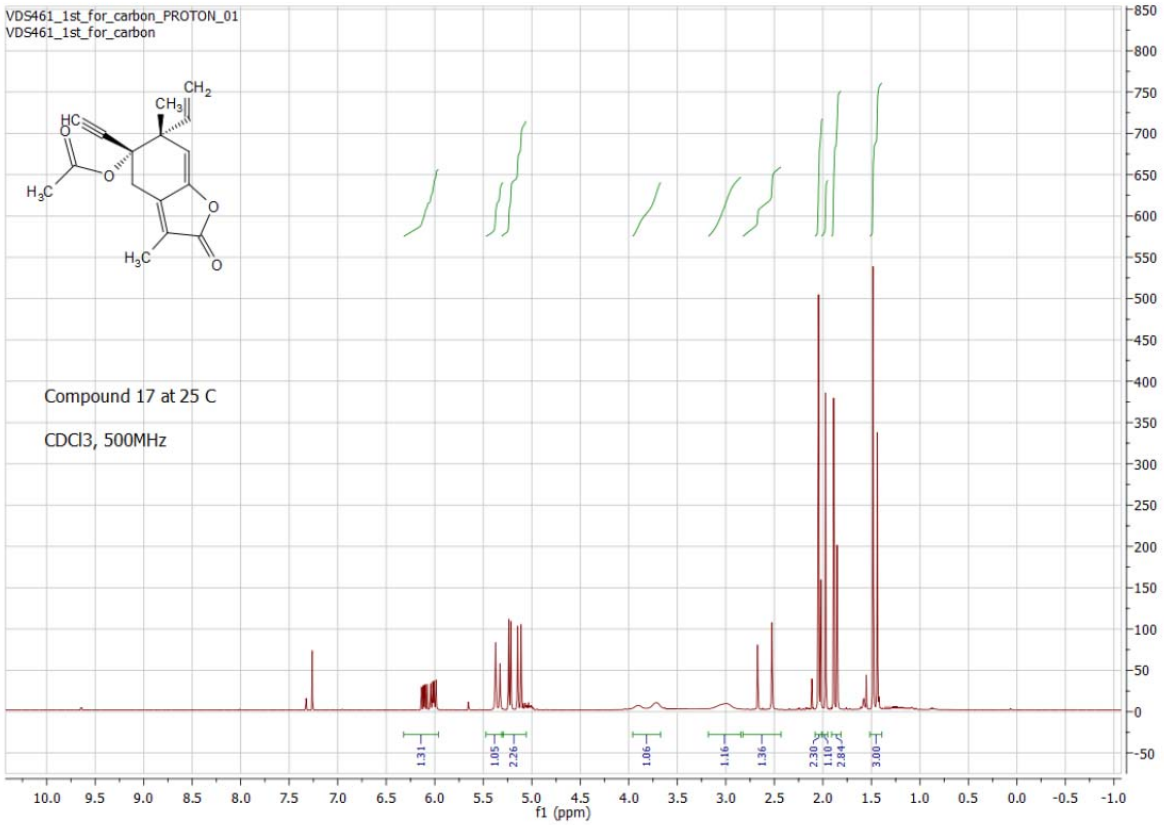



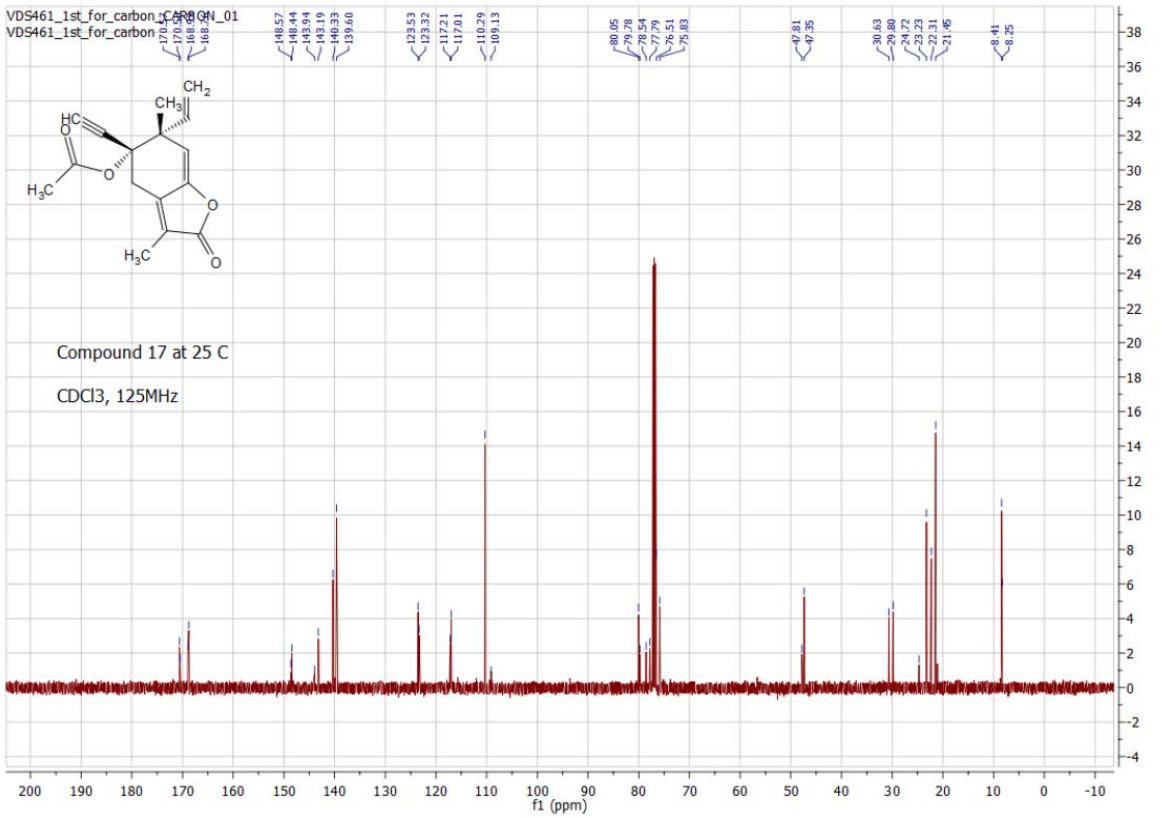
NOESY correlations

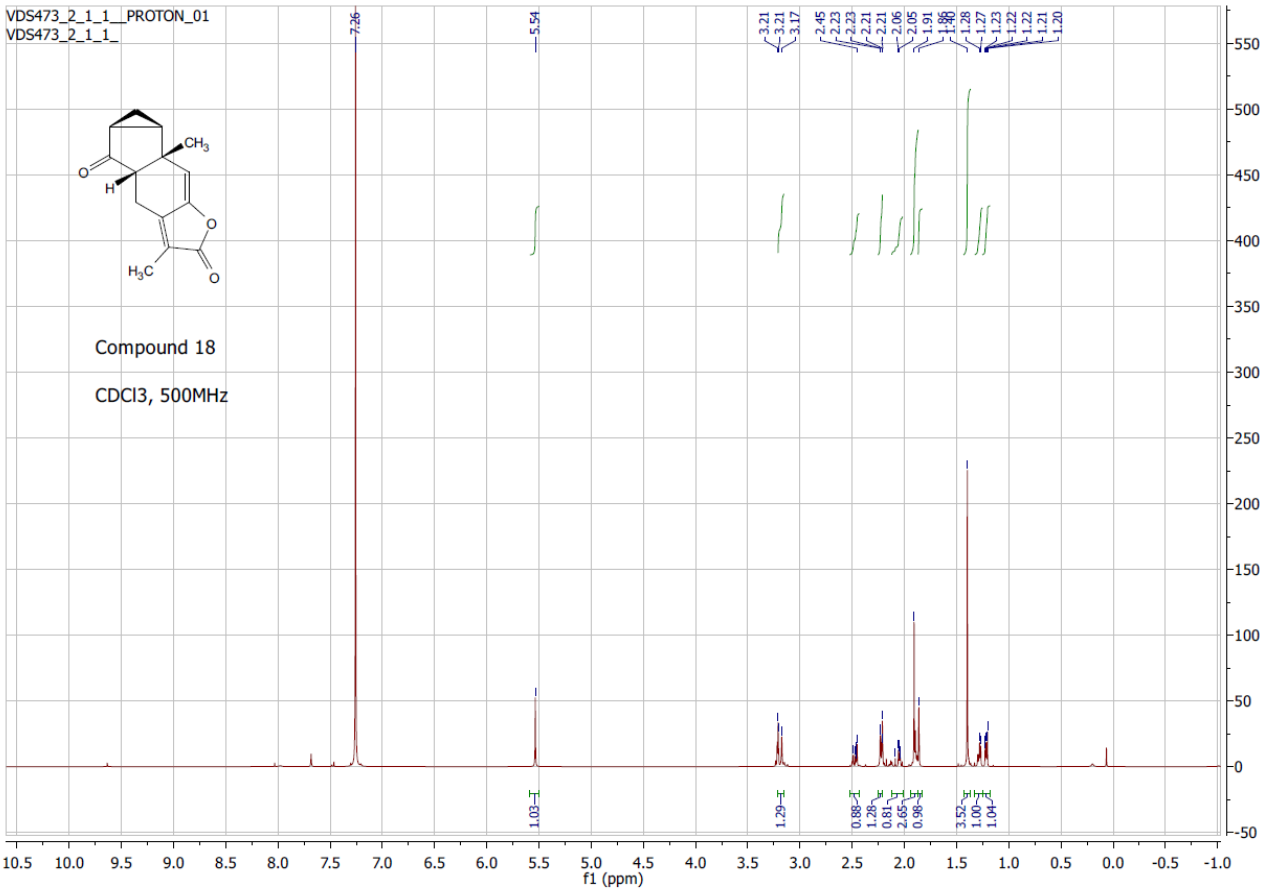


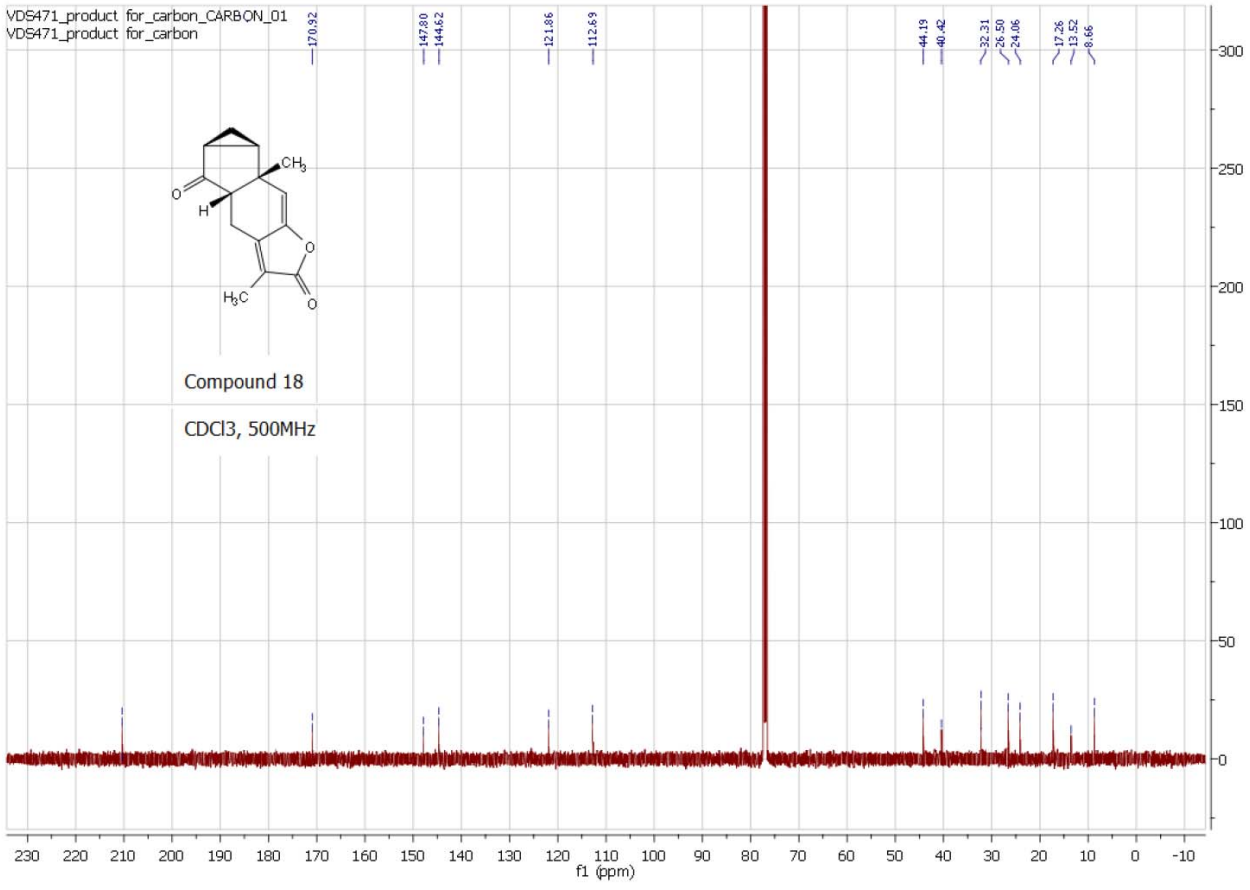
Compound **17a**

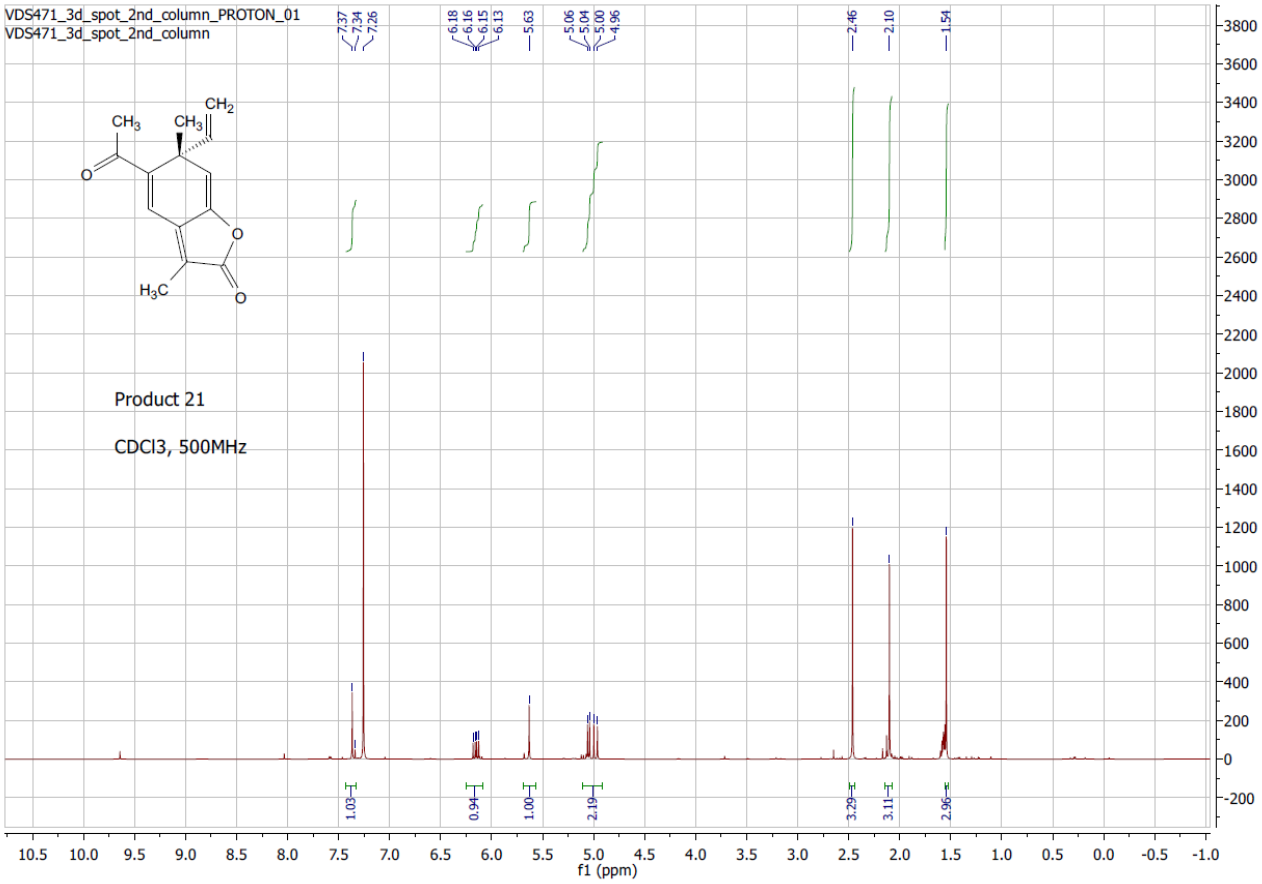
Visible conformers of compound **17** at room temperature

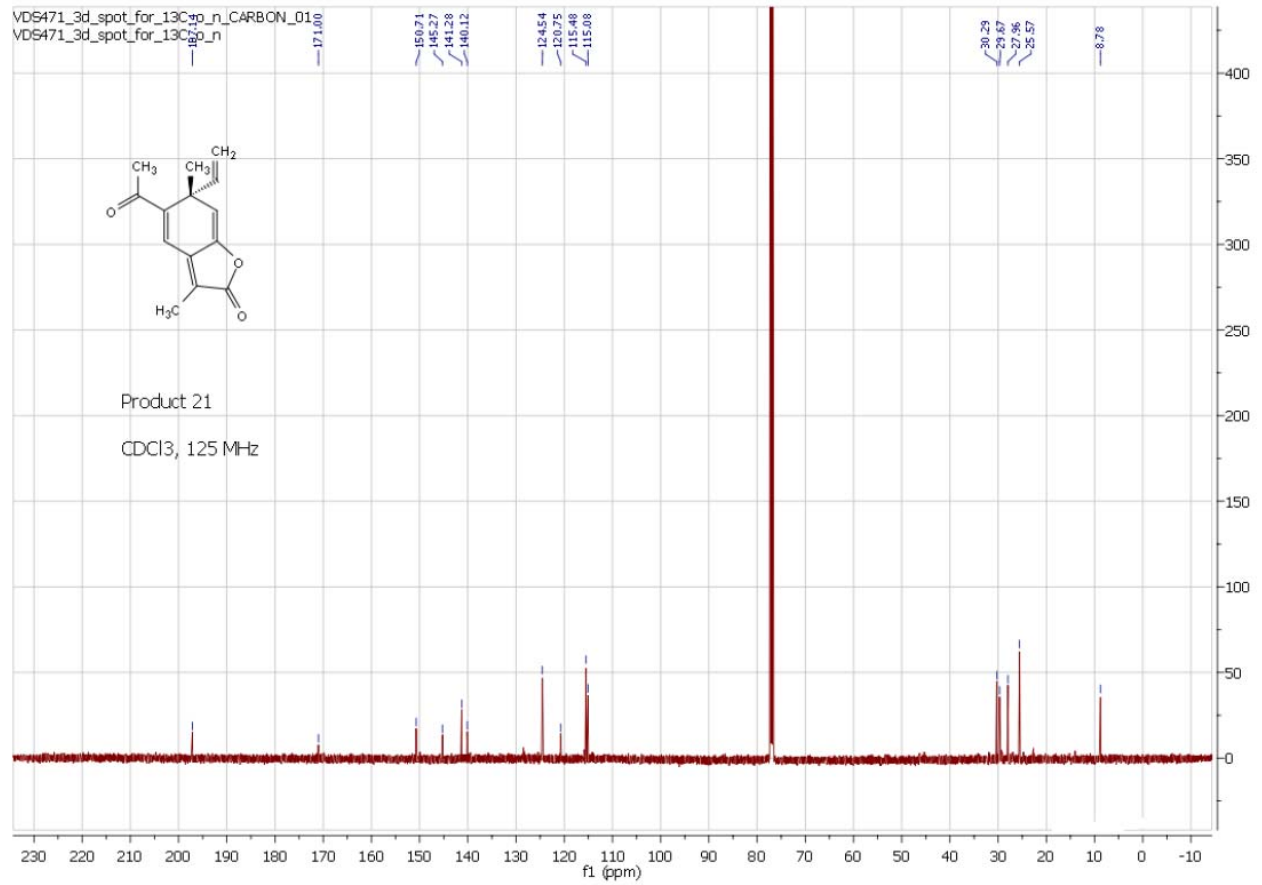



VDS473_2_1_1__PROTON_01
VDS473_2_1_1_
Compound 18
CDCl3, 500MHz
f1 (ppm)


VDS471_product for_carbon_CARBON_01
VDS471_product for_carbon
Compound 18
CDCl3, 500MHz
f1 (ppm)


VDS471_3d_spot_2nd_column_PROTON_01
VDS471_3d_spot_2nd_column
7.37
7.34
7.26
6.18
6.16
6.15
6.13
5.63
5.06
5.04
5.00
4.96
2.46
2.10
1.54
CH3
CH3
CH2
O
O
H3C
O
Product 21
CDCl3, 500MHz
1.03
0.94
1.00
2.19
3.29
3.11
2.96
f1 (ppm)


VDS471_3d_spot_for_13C_n_CARBON_01
VDS471_3d_spot_for_13C_n
171.00
150.71
145.27
141.28
140.12
124.54
120.75
115.48
115.08
30.29
29.67
27.96
25.57
8.78
CH3
CH3
CH2
O
O
H3C
O
Product 21
CDCl3, 125 MHz
f1 (ppm)