Supporting Information

Total synthesis of spiro *Ganoderma* meroterpenoids spiroapplanatumines B, D, F, and H

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1. General Information

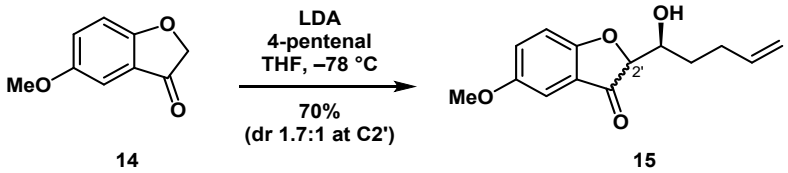
Unless otherwise mentioned, all reactions were carried out under argon atmosphere under anhydrous conditions and all reagents were purchased from commercial suppliers without further purification. Anhydrous solvents were distilled prior to use (toluene, THF, and Et_2O from Na/benzophenone; MeCN, DCM, and pyridine from CaH_2). Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous material, unless otherwise stated. Lower temperatures were maintained using dry ice/acetone (–78 °C), dry ice/MeCN (–40 °C), ice/water (0 °C) baths, and low temperature reactor.

Reactions were monitored by thin layer chromatography on plates (GF254) supplied by Yantai Chemicals (China), using UV light as the visualizing agent and/or ethanolic phosphomolybdic acid, acidic ethanolic anisaldehyde, or basic aqueous $KMnO_4$ and heat as developing agents. If not specially noted, flash column chromatography uses silica gel (200-300 mesh) supplied by Tsingtao Haiyang Chemicals (China) and preparative thin layer chromatography (PTLC) separations were carried out 0.50 mm Yantai (China) silica gel plates.

NMR spectra were recorded on Brüker Avance 600, Brüker Avance 500, and Bruker Brüker Avance 300, and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were recorded on a Bruker Apex IV FTMS mass spectrometer using ESI (electrospray ionization). Infrared spectra were recorded on a Shimadzu IR Prestige 21, using thin films of the sample on KBr plates. Melting points were obtained on an MP450-01 micro-melting point apparatus (Hanon Instrument, Shandong, China) without correction.

2. Synthetic Procedures and Characterization Data

Synthesis of compound 15



To a mixture of 5-methoxybenzofuran-3(2*H*)-one (**14**) (10.0 g, 61.0 mmol, 1 equiv) in THF (120 mL) was added lithium diisopropylamide (LDA, 2.0 M in THF, 39.6 mL, 79.3 mmol, 1.3 equiv) and the resulting mixture was stirred at –78 ℃ for 0.5 h. Then 4-pentenal (7.68 g, 91.5 mmol, 1.5 equiv) was added slowly and stirring was continued for another 1 h. The mixture was quenched with saturated aqueous NH_4Cl (100 mL) at 0 ℃ carefully and extracted with EtOAc (3 × 80 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (50:1 to 5:1) as eluent to afford **15** (10.6 g, 70% yield, 1.7:1 diastereomeric mixture at C2') as a yellow oil.

Data for compound **15**:

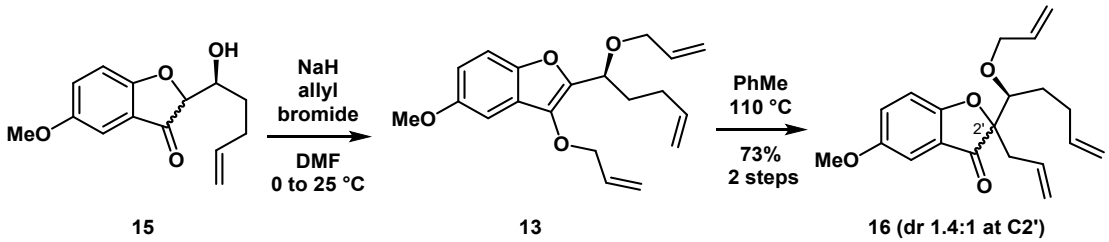
***R**f* = 0.3 (hexane/EtOAc = 5:1);

^{1}H NMR (300 MHz, $CDCl_3$, 1.7:1 diastereomeric mixture) δ 7.23 – 7.14 (m, 1.6H), 7.03 (s, 1H), 7.00 (s, 0.6H), 6.96 (d, *J* = 2.8 Hz, 0.6H), 6.94 (d, *J* = 2.8 Hz, 1H), 5.88 – 5.70 (m, 1.6H), 5.08 – 4.91 (m, 3.2H), 4.59 – 4.41 (m, 1.6H), 4.21 – 4.08 (m, 1H), 4.03 – 3.87 (m, 0.6H), 3.74 (s, 1.8H), 3.72 (s, 3H), 3.18 (s, 0.5H), 2.60 (s, 0.85H), 2.34 – 2.10 (m, 3.28H), 1.93 – 1.49 (m, 3.13H);

^{13}C NMR (75 MHz, $CDCl_3$, 1.7:1 diastereomeric mixture) δ 201.3, 201.1, 168.8, 168.6, 155.1, 155.0, 137.9, 137.7, 128.4, 128.1, 121.6, 121.2, 115.5, 115.3, 114.3 (114.33), 114.3 (114.28), 103.9 (103.91), 103.9 (103.87), 87.9, 87.4, 70.9, 70.7, 55.9 (55.90), 55.9 (55.86), 32.4, 31.1, 29.8, 29.5;

HRMS (*m/z*): calcd for $C_{14}H_{16}NaO_4$ $[M+Na]^+$ 271.0941, found 271.0933.

Synthesis of compound 16



To a stirred solution of alcohol **15** (9.00 g, 36.3 mmol, 1 equiv) in DMF (100 mL) was added NaH (60% dispersion in mineral oil, 3.19 g, 79.8 mmol, 2.2 equiv) at 0 ℃. After 5 min, allyl bromide (9.41 mL, 109 mmol, 3 equiv) was added. The mixture was stirred at 25 ℃ for 1 before it was quenched with saturated aqueous NH_4Cl (50 mL) at 0 ℃ carefully and extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated to give the crude **13**. Compound **13** was dissolved in toluene (36 ml) and refluxed at 110 ℃ for 1 h. At this point, TLC showed complete consumption of **13** (R_f = 0.75, hexane/EtOAc = 5:1). After the reaction mixture was concentrated, the residue was purified by silica gel column chromatography with hexane/EtOAc (100:1 to 50:1) as eluent to afford **16** (8.69 g, 73% yield over 2 steps, 1.4:1 diastereomeric mixture) as a colorless oil.

Note: We found that intermediate **13** underwent Claisen rearrangement slowly at room temperature. Silica gel could accelerate this process during purification by flash column chromatography. However, upon heating, the rearrangement of **13** to give **16** proceeded rapidly.

Data for compound **16**:

R_f = 0.6 (hexane/EtOAc = 5:1);

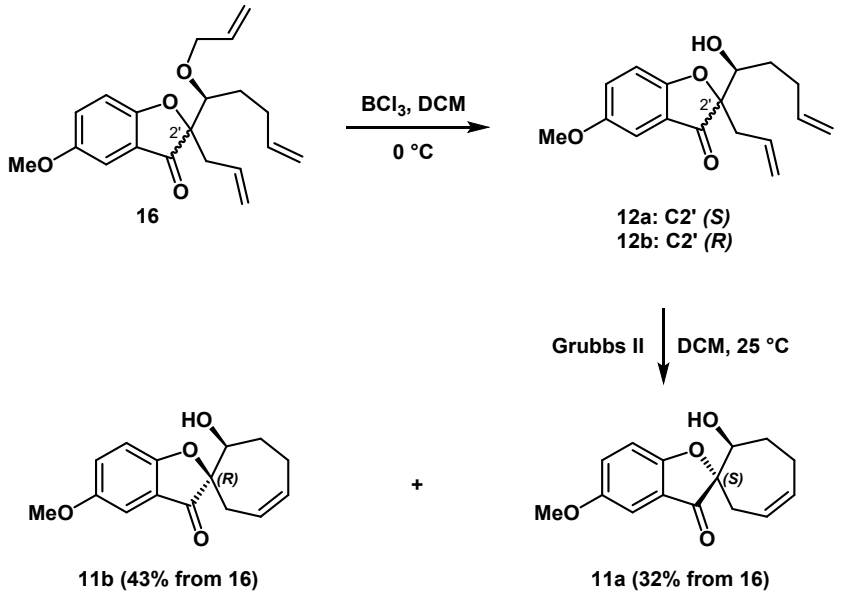
^{1}H NMR (300 MHz, $CDCl_3$, 1.4:1 diastereomeric mixture) δ 7.18 – 7.15 (m, 0.7H), 7.15 – 7.12 (m, 1H), 6.99 (d, *J* = 1.4 Hz, 1H), 6.96 (d, *J* = 1.4 Hz, 0.7H), 6.95 – 6.92 (m, 1.7H), 5.79 – 5.42 (m, 5.1H), 5.12 – 4.86 (m, 10.2H), 4.06 – 3.86 (m, 3.4H), 3.70

(s, 3H), 3.70 (s, 2.1H), 3.64 – 3.56 (m, 1.7H), 2.79 – 2.49 (m, 3.47H), 2.29 – 1.94 (m, 3.62H), 1.85 – 1.62 (m, 2.7H), 1.36 – 1.26 (m, 0.76H);

^{13}C NMR (75 MHz, $CDCl_3$, 1.4:1 diastereomeric mixture) δ 202.9, 202.1, 167.8, 167.6, 154.7, 154.6, 138.0, 137.9, 134.5, 134.4, 130.3, 130.0, 127.9, 127.8, 122.0, 121.9, 119.6 (119.59), 119.6 (119.56), 116.9, 116.6, 115.19, 115.18, 113.9, 113.8, 103.7, 103.6, 95.3, 94.9, 81.6, 80.8, 74.0, 73.6, 55.7 (55.70), 55.7 (55.69), 38.0, 36.9, 30.0, 29.9, 29.0, 28.6;

HRMS (*m/z*): calcd for $C_{20}H_{24}NaO_4$ $[M+Na]^+$ 351.1567, found 351.1555.

Synthesis of compounds 11a and 11b



To a stirred solution of **16** (1.4:1 diastereomeric mixture at C2', 7.60 g, 23.2 mmol, 1 equiv) in DCM (46 mL) was added BCl_3 (1.0 M in DCM, 46.4 mL, 46.4 mmol, 2 equiv) at 0 °C. The resulting mixture was stirred at 0 °C for 1 h before it was quenched with saturated aqueous $NaHCO_3$ (50 mL) and extracted with DCM (3 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated. The residue was disolved in DCM (50 mL) and then filtered through a pad of silica gel rapidly. The silica gel was thoroughly washed with hexane/EtOAc

(2:1, 3 × 50 mL). The filtrate was concentrated in *vacuo*. The crude **12a** and **12b** were azetropically dried with toluene (2 × 30 mL) and then used in the next step.

To a stirred solution of the crude alcohols **12a** and **12b** in DCM (100 mL) was added Grubbs 2nd generation catalyst (Grubbs II, 984 mg, 1.16 mmol, 0.05 equiv) at 25 ℃. The mixture was stirred at 25 ℃ for 5 h. After concentration, the residue was purified by silica gel column chromatography with hexane/EtOAc (10:1 to 3:1) as eluent to give **11a** (1.93 g, 32% yield) as a white solid and **11b** (2.59 g, 43% yield) as a white solid.

Data for compound **11a**:

Note: Using the described route, > 5 g of **11a** was readily prepared after three parallel operations.

$\boldsymbol{R_f}$ = 0.4 (hexane/EtOAc = 3:1);

m.p. = 131 – 133 ℃;

IR (film) $\boldsymbol{\nu_{max}}$ = 2934, 1697, 1630, 1492, 1275, 1221, 1034, 802 cm^{-1};

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.05 (d, *J* = 9.0 Hz, 1H), 7.01 (d, *J* = 2.8 Hz, 1H), 6.11 – 6.02 (m, 1H), 5.58 – 5.51 (m, 1H), 3.93 – 3.88 (m, 1H), 3.78 (s, 3H), 3.44 (t, *J* = 1.7 Hz, 1H), 3.00 – 2.91 (m, 1H), 2.71 – 2.62 (m, 1H), 2.16 (dd, *J* = 15.5, 7.5 Hz, 1H), 2.07 – 1.99 (m, 2H), 1.89 – 1.82 (m, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 204.6, 167.4, 155.2, 134.9, 128.8, 124.2, 119.9, 114.7, 104.3, 89.2, 72.3, 56.0, 28.7, 28.2, 21.4;

HRMS (*m/z*): calcd for $C_{15}H_{16}NaO_4$ $[M+Na]^+$ 283.0941, found 283.0933.

Data for compound **11b**:

Note: Using the described route, > 5 g of **11b** was readily prepared after three parallel operations.

R_f = 0.2 (hexane/EtOAc = 3:1);

m.p. = 135 – 138 °C;

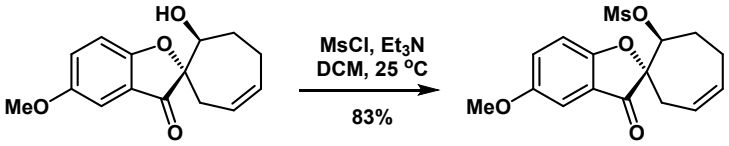
IR (film) ν_{max} = 2934, 1705, 1623, 1487, 1277, 1220, 1031, 774 cm^{-1};

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.06 (d, *J* = 9.0 Hz, 1H), 7.03 (d, *J* = 2.8 Hz, 1H), 6.11 – 6.05 (m, 1H), 5.63 – 5.58 (m, 1H), 4.15 – 4.08 (m, 1H), 3.77 (s, 3H), 2.46 – 2.41 (m, 1H), 2.36 – 2.30 (m, 1H), 2.23 (dd, *J* = 15.7, 8.2 Hz, 1H), 2.14 – 2.07 (m, 1H), 1.99 – 1.93 (m, 2H), 1.80 – 1.73 (m, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 203.8, 167.8, 155.0, 134.2, 127.9, 125.2, 120.8, 114.4, 104.5, 91.7, 76.6, 56.0, 30.6, 29.5, 23.4;

HRMS (*m/z*): calcd for $C_{15}H_{16}NaO_4$ $[M+Na]^+$ 283.0941, found 283.0933.

Synthesis of compound 17a



11a **17a**

To a stirred solution of alcohol **11a** (20.0 mg, 76.9 μmol, 1 equiv) and Et_3N (53.2 μL, 0.385 mmol, 5 equiv) in DCM (2 mL) was added methanesulfonyl chloride (MsCl, 12.0 μL, 0.154 mmol, 2 equiv) at 0 ºC. The reaction mixture was warmed to 25 ºC and stirred for 1 h before it was quenched with saturated aqueous NH_4Cl (5 mL) at 0 ºC and extracted with DCM (3 × 5 mL). The combined organic layers were washed with brine (25mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (50:1 to 10:1) as eluent to afford **17a** (21.5 mg, 83% yield) as a colorless oil.

Data for compound **17a**:

R_f = 0.5 (hexane/EtOAc = 5:1);

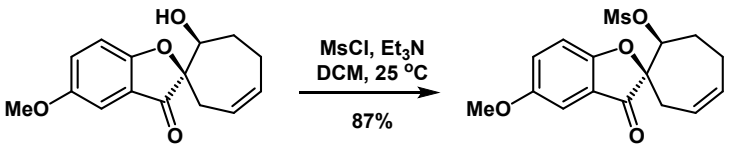
IR (film) ν_{max} = 3412, 1595, 1492, 1355, 1093,1034, 801, 708 cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.03 (d, *J* = 2.8 Hz, 1H), 7.00 (d, *J* = 9.0 Hz, 1H), 6.16 – 6.02 (m, 1H), 5.66 – 5.52 (m, 1H), 4.97 (dd, *J* = 10.7, 3.6 Hz, 1H), 3.80 (s, 3H), 2.85 (s, 3H), 2.55 (d, *J* = 6.8 Hz, 2H), 2.52 – 2.35 (m, 2H), 2.31 – 2.16 (m, 1H), 2.14 – 2.02 (m, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 198.7, 165.9, 155.3, 134.2, 128.3, 122.5, 121.1, 113.9, 104.7, 88.1, 85.2, 56.1, 38.4, 31.3, 28.1, 22.9;

HRMS (*m/z*): calcd for $C_{16}H_{18}NaO_6S$ $[M+Na]^+$ 361.0716, found 361.0721.

Synthesis of compound 17b



11b **17b**

To a stirred solution of alcohol **11b** (20.0 mg, 76.9 μmol, 1 equiv) and Et_3N (53.2 μL, 0.385 mmol, 5 equiv) in DCM (2 mL) was added methanesulfonyl chloride (MsCl, 12.0 μL, 0.154 mmol, 2 equiv) at 0 ºC. The reaction mixture was warmed to 25 ºC and stirred for 1 h before it was quenched with saturated aqueous NH_4Cl (5 mL) at 0 ºC and extracted with DCM (3 × 5 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (50:1 to 10:1) as an eluent to afford **17a** (22.6 mg, 87% yield) as a colorless oil.

Data for compound **17b**:

R_f = 0.5 (hexane/EtOAc = 5:1);

IR (film) ν_{max} = 3423, 1596, 1382, 1353, 1261, 1093, 1035, 801 cm^{-1};

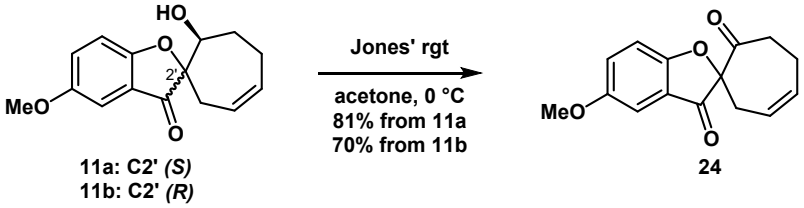
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.09 (d, *J* = 9.0 Hz, 1H),

7.01 (d, J = 2.7 Hz, 1H), 6.18 – 6.03 (m, 1H), 5.70 – 5.53 (m, 1H), 4.99 (dd, J = 10.9, 3.8 Hz, 1H), 3.80 (s, 3H), 2.80 (s, 3H), 2.54 – 2.24 (m, 4H), 2.21 – 2.04 (m, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 202.0, 167.9, 155.4, 134.1, 128.8, 124.6, 119.8, 115.0, 104.1, 89.4, 86.0, 56.1, 38.3, 30.0, 29.1, 22.9;

HRMS (*m/z*): calcd for $C_{16}H_{18}NaO_6S$ $[M+Na]^+$ 361.0716, found 361.0720.

Synthesis of compound 24



From 11a: To a stirred solution of alcohol **11a** (1.50 g, 5.77 mmol, 1 equiv) in acetone (30 mL) was added Jones' reagent (2.0 M in H_2O, 11.5 mL, 23.1 mmol, 4 equiv) dropwise at 0 °C. After being stirred at 0 ℃ for 12 h, the reaction mixture was quenched by slow addition of *i*-PrOH (5 mL). The resulting solution was diluted with EtOAc (200 mL) and then washed with brine (2 × 50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (20:1 to 5:1) as eluent to give diketone **24** (1.21 g, 81% yield) as a white solid.

From 11b: To a stirred solution of alcohol **11b** (2.00 g, 7.69 mmol, 1 equiv) in acetone (40 mL) was added Jones' reagent (2.0 M in H_2O, 15.4 mL, 30.8 mmol, 4 equiv) dropwise at 0 °C. After being stirred at 0 ℃ for 36 h, the reaction mixture was quenched by slow addition of *i*-PrOH (5 mL). The resulting solution was diluted with EtOAc (200 mL) and then washed with brine (2 × 50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (20:1 to 5:1) as eluent to give diketone **24** (1.39 g, 70% yield) as a white solid.

Data for compound **24**:

R_f = 0.6 (hexane/EtOAc = 3:1);

m.p. = 96 – 98 °C;

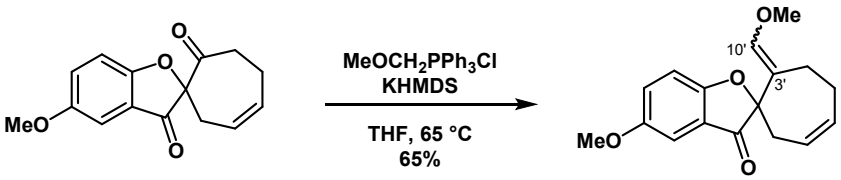
IR (film) ν_{max} = 2922, 2842, 1706, 1489, 1278, 1194, 828, 785, 764 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.15 (d, *J* = 9.0 Hz, 1H), 6.99 (d, *J* = 2.8 Hz, 1H), 5.84 – 5.74 (m, 2H), 3.78 (s, 3H), 3.53 – 3.43 (m, 1H), 3.33 (s, 1H), 2.68 – 2.61 (m, 1H), 2.56 – 2.47 (m, 2H), 2.41 – 2.35 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 200.8, 195.9, 167.9, 155.6, 131.3, 129.0, 124.2, 119.0, 114.6, 104.6, 99.8, 56.1, 37.8, 31.6, 27.2;

HRMS (*m/z*): calcd for $C_{15}H_{14}NaO_4$ $[M+Na]^+$ 281.0784, found 281.0779.

Synthesis of compound 19



24 **19**

To a stirred suspension of (methoxymethyl)triphenylphosphoniumchloride (199 mg, 0.581 mmol, 3 equiv) in THF (4 mL) was added potassium bis(trimethylsilyl)amide (KHMDS, 1.0 M in THF, 0.581 mL, 0.581 mmol, 3.0 equiv) at 0 °C. The resulting mixture was stirred at that temperature for 0.5 h before **24** (50.0 mg, 0.194 mmol, 1 equiv) in THF (2 mL) was added dropwise. The reaction mixture was heated to 65 °C and stirred for 2 h. The mixture was quenched with saturated aqueous NH_4Cl (10 mL) at 0 ºC carefully and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (100:1 to 10:1) as eluent to afford **19** (36.0 mg, 65% yield) as a yellow oil.

Data for compound **19**:

The geometry configuration of C3'–C10' double bond of **19** was not identified.

R_f = 0.5 (hexane/EtOAc = 7:1);

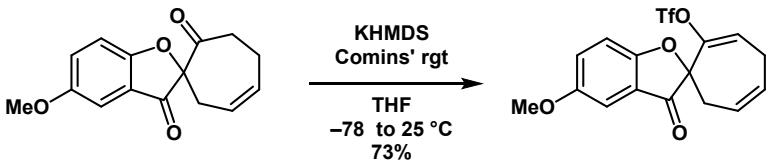
IR (film) ν_{max} = 3429, 1599, 1384, 1356, 1261, 1261, 1096, 1035, 803 cm^{-1};

^{1}H NMR (500 MHz, C_6D_6) δ 7.08 (d, *J* = 2.8 Hz, 1H), 6.96 (dd, *J* = 8.9, 2.8 Hz, 1H), 6.75 (d, *J* = 9.0 Hz, 1H), 6.23 (s, 1H), 5.78 – 5.70 (m, 1H), 5.61 – 5.52 (m, 1H), 3.15 (s, 3H), 3.06 – 3.00 (m, 1H), 2.93 (s, 3H), 2.92 – 2.86 (m, 1H), 2.84 – 2.75 (m, 1H), 2.47 – 2.38 (m, 1H), 2.36 – 2.29 (m, 1H), 2.26 (dd, *J* = 16.0, 7.7 Hz, 1H);

^{13}C NMR (126 MHz, C_6D_6) δ 201.2, 166.4, 155.4, 145.9, 132.7, 128.0, 123.7, 120.4, 115.5, 114.5, 105.1, 94.0, 59.3, 55.3, 34.8, 30.2, 22.8;

HRMS (*m/z*): calcd for $C_{17}H_{19}O_4$ $[M+H]^+$ 287.1278, found 287.1280.

Synthesis of compound 21



24 **21**

To a stirred solution of diketone **24** (1.20 g, 4.65 mmol, 1 equiv) in THF (25 mL) was added potassium bis(trimethylsilyl)amide (KHMDS, 1.0 M in THF, 5.12 mL, 5.12 mmol, 1.1 equiv) dropwise over 10 min at −78 °C. The reaction mixture was stirred at that temperature for 1 h before Comins' reagent (2.01 g, 5.12 mmol, 1.1 equiv) in THF (10 mL) was dropwise over 10 min. The mixture was slowly warmed to 25 ℃ and stirred for another 30 min. The reaction mixture was quenched with saturated aqueous NH_4Cl (25 mL) at 0 ºC carefully and extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (50:1 to 20:1) as eluent to afford triflate **21** (1.32 g, 73% yield) as a

yellow solid.

Data for compound **21**:

R_f = 0.6 (hexane/EtOAc = 5:1);

m.p. = 123 – 125 ℃;

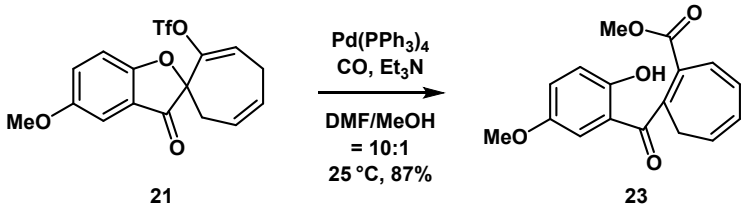
IR (film) ν_{max} = 2922, 2358, 1713, 1629, 1496, 1274, 1215, 1026, 828 cm^{-1};

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.12 (d, *J* = 9.0 Hz, 1H), 7.07 (d, *J* = 2.8 Hz, 1H), 6.37 (dd, *J* = 7.1, 4.8 Hz, 1H), 6.27 – 6.16 (m, 1H), 5.97 – 5.87 (m, 1H), 3.83 (s, 3H), 3.21 – 3.08 (m, 1H), 3.07 – 2.94 (m, 1H), 2.75 (ddt, *J* = 14.8, 6.7, 1.2 Hz, 1H), 2.62 (dd, *J* = 14.7, 7.0 Hz, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 198.1, 166.9, 155.5, 145.0, 133.1, 129.0, 127.7, 125.7, 119.0, 114.9, 104.4, 88.1, 55.9, 32.0, 24.0 (the signal for CF_3 was not observed);

HRMS (*m/z*): calcd for $C_{16}H_{13}F_3NaO_6S$ $[M+Na]^+$ 413.0277, found 413.0262.

Synthesis of compound 23



To a stirred solution of triflate **21** (70.0 mg, 0.179 mmol, 1 equiv) in DMF/MeOH (5 mL/0.5 mL) was added Et_3N (124 μL, 6.65 mmol, 5 equiv) and $Pd(PPh_3)_4$ (10.4 mg, 8.97 μmol, 0.05 equiv) at 25 ºC. The reaction mixture was evacuated/backfilled with CO three times and then stirred under CO atmosphere (balloon) for 12 h. The mixture was quenched with saturated aqueous NH_4Cl (10 mL) at 0 ºC and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (10:1 to 3:1) as eluent to afford **23** (46.5 mg, 87%

yield) as a yellow oil.

Data for compound **23**:

R_f = 0.5 (hexane/EtOAc = 5:1);

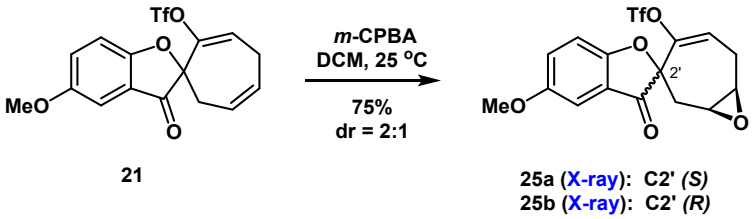
IR (film) ν_{max} = 3410, 1596, 1387, 1356, 1261, 1903, 1037, 806 cm^{-1};

^{1}H NMR (500 MHz, C_6D_6) δ 12.09 (s, 1H), 7.09 (d, *J* = 11.5 Hz, 1H), 6.98 (d, *J* = 3.1 Hz, 1H), 6.95 (d, *J* = 9.0 Hz, 1H), 6.79 (dd, *J* = 9.0, 3.1 Hz, 1H), 6.39 (dd, *J* = 11.5, 5.5 Hz, 1H), 5.91 (dd, *J* = 9.2, 5.5 Hz, 1H), 5.07 – 5.00 (m, 1H), 3.18 (s, 3H), 3.04 (s, 3H), 2.25 (d, *J* = 6.8 Hz, 2H);

^{13}C NMR (126 MHz, C_6D_6) δ 201.8, 165.9, 158.0, 152.2, 137.0, 133.1, 128.2, 128.1, 124.3, 122.1, 119.7, 119.1, 114.5, 55.2, 51.7, 30.8;

HRMS (*m/z*): calcd for $C_{17}H_{16}NaO_5$ $[M+Na]^+$ 324.0890, found 324.0897;

Synthesis of compounds 25a and 25b



To a stirred solution of triflate **21** (1.20 g, 3.08 mmol, 1 equiv) in DCM (30 mL) was added 3-chloroperoxybenzoic acid (*m*-CPBA, 85%, 1.88 g, 9.23 mmol, 3 equiv) at 25 °C. After being stirred at 25 °C for 36 h, the mixture was quenched with saturated aqueous $NaHCO_3$ (15 mL) and saturated aqueous $Na_2S_2O_3$ (15 mL) at 0 °C carefully. The aqueous phase was further extracted with DCM (3 × 30 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (50:1 to 10:1) as an eluent to afford a 2:1 diastereomeric mixture (indicated by ^{1}H NMR analysis) of **25a** and **25b** (937 mg, 75% yield).

Note: For characterization purpose, **25a** and **25b** were separated by PTLC (hexane/EtOAc = 10:1) using a small amount of sample. The structures of **25a** and **25b** were confirmed by X-ray crystallographic analysis after obtaining the pure **25a** and **25b**.

Data for compound **25a**:

R_f = 0.4 (hexane/EtOAc = 5:1);

m.p. = 126 – 128 °C;

IR (film) ν_{max} = 3432, 1716, 1599, 1485, 1421, 1346, 1216, 1143, 822 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.12 (d, *J* = 9.0 Hz, 1H), 7.05 (d, *J* = 2.8 Hz, 1H), 6.23 (dd, *J* = 10.0, 3.8 Hz, 1H), 3.81 (s, 3H), 3.55 – 3.49 (m, 1H), 3.37 – 3.30 (m, 1H), 2.96 – 2.86 (m, 1H), 2.52 – 2.41 (m, 2H), 2.09 – 2.01 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 167.0, 155.9, 145.3, 129.5, 124.9, 118.7, 118.2 (q, *J* = 319.9 Hz, CF_3), 115.1, 104.6, 89.3, 56.0, 55.1, 50.2, 33.9, 25.3;

HRMS (*m/z*): calcd for $C_{16}H_{13}F_3NaO_7S$ $[M+Na]^+$ 429.0226; found 429.0210.

Data for compound **25b**:

R_f = 0.38 (hexane/EtOAc = 5:1);

m.p. = 109 – 111 °C;

IR (film) ν_{max} = 3441, 1721, 1603, 1488, 1416, 1214, 1147, 1035, 614 cm^{-1};

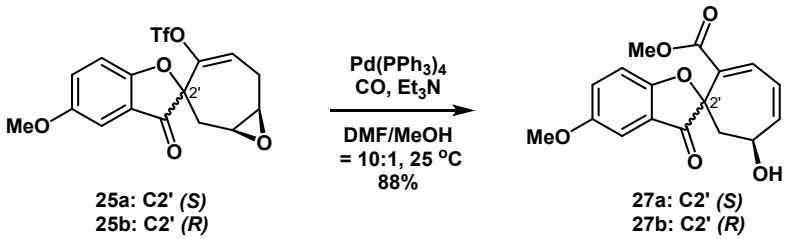
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 9.1, 2.8 Hz, 1H), 7.12 (d, *J* = 9.0 Hz, 1H), 7.04 (d, *J* = 2.8 Hz, 1H), 6.15 (dd, *J* = 8.6, 4.8 Hz, 1H), 3.82 (s, 3H), 3.50 (q, *J* = 5.7 Hz, 1H), 3.33 – 3.28 (m, 1H), 2.97 – 2.89 (m, 1H), 2.62 – 2.51 (m, 2H), 2.30 (dd, *J* = 14.6, 8.3 Hz, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 197.8, 167.1, 155.8, 145.6, 129.3, 123.5, 118.7, 118.1

(q, J = 319.7 Hz, CF_3), 115.1, 104.5, 88.0, 55.9, 55.0, 48.9, 32.9, 25.0;

HRMS (*m/z*): calcd for $C_{16}H_{13}F_3NaO_7S$ $[M+Na]^+$ 429.0226; found 429.0210.

Synthesis of compounds 27a and 27b



To a stirred solution of triflates **25** and **25b** (ca. 2:1 diastereomeric mixture at C2', 900 mg, 2.22 mmol, 1 equiv) in DMF/MeOH (10 mL/1 mL) was added Et_3N (920 μL, 6.65 mmol, 3 equiv) and $Pd(PPh_3)_4$ (128 mg, 0.111 mmol, 0.05 equiv) at 25 ºC. The reaction system was evacuated/backfilled with CO three times before it was stirred at 25 ºC for 12 h. The mixture was quenched with saturated aqueous NH_4Cl (15 mL) at 0 ºC and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (10:1 to 3:1) as eluent to afford a 2:1 diastereomeric mixture of **27a** and **27b** (616 mg, 88% yield).

For characterization purpose, **27a** and **27b** were separated by PTLC (hexane/EtOAc = 5:1) using a small amount of sample to give pure **27a** as a yellow oil and **27b** as a yellow oil.

Data for compound **27a**:

$\boldsymbol{R_f}$ = 0.53 (hexane/EtOAc = 2:1);

IR (film) $\boldsymbol{\nu_{max}}$ = 3432, 2832, 1594, 1493, 1358, 1280, 1058, 770 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, J = 8.1 Hz, 1H), 7.23 (dd, J = 8.9, 2.8 Hz, 1H), 7.15 (d, J = 2.8 Hz, 1H), 6.98 (d, J = 9.0 Hz, 1H), 6.46 (dd, J = 11.7, 3.8 Hz, 1H), 6.02 – 5.97 (m, 1H), 5.00 – 4.91 (m, 1H), 3.82 (s, 3H), 3.57 (s, 3H), 2.65 (dd, J = 14.2, 8.7 Hz, 1H), 2.14 – 2.10 (m, 1H), 1.76 (bs, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 201.7, 166.1, 165.1, 155.1, 146.3, 138.3, 131.3, 127.3, 120.7, 120.3, 114.1, 105.1, 88.6, 65.0, 55.9, 52.3, 39.8;

HRMS (*m/z*): calcd for $C_{17}H_{16}NaO_6$ $[M+Na]^+$ 339.0839; found 339.0829.

Data for compound **27b**:

R_f = 0.5 (hexane/EtOAc = 2:1);

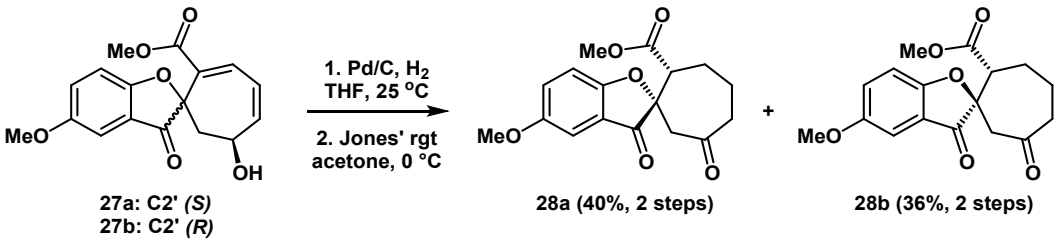
IR (film) ν_{max} = 3507, 2832, 1707, 1596, 1358, 1358, 1263, 775 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.9 Hz, 1H), 7.23 (dd, *J* = 8.9, 2.8 Hz, 1H), 7.13 (d, *J* = 2.8 Hz, 1H), 6.99 (d, *J* = 8.9 Hz, 1H), 6.55 (dt, *J* = 11.5, 2.0 Hz, 1H), 6.06 – 5.99 (m, 1H), 4.76 – 4.69 (m, 1H), 3.81 (s, 3H), 3.58 (s, 3H), 2.31 (dd, *J* = 14.0, 11.4 Hz, 1H), 1.99 (dt, *J* = 14.0, 1.8 Hz, 1H), 1.89 (bs, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 201.5, 166.3, 164.6, 155.2, 149.5, 140.7, 130.8, 127.3, 121.4, 120.2, 114.4, 105.0, 87.2, 67.9, 56.0, 52.5, 44.3;

HRMS (*m/z*): calcd for $C_{17}H_{16}NaO_6$ $[M+Na]^+$ 339.0839; found 339.0829.

Synthesis of compounds 28a and 28b



27a: C2' *(S)*
27b: C2' *(R)*

28a (40%, 2 steps)

28b (36%, 2 steps)

To a solution of **27a** and **27b** (500 mg, 1.58 mmol, 1 equiv) in THF (15 mL) was added 10% Pd/C (2.50 g, m × 5) at 25 ºC. The reaction system was evacuated/backfilled with H_2 three times. After being stirred under H_2 atmosphere (balloon) at 25 ºC for 1 h, the reaction mixture was filtered through a pad of silica gel. The filtrate was concentrated under reduced pressure. The residue was dissolved in acetone (8 mL) and

then cooled to 0 ºC. Jones' reagent (2.0 M in H_2O, 3.16 mL, 6.33 mmol, 4 equiv) was slowly. After 2 h, the reaction was quenched by addition of *i*-PrOH (5 mL). The resulting solution was diluted with EtOAc (50 mL) and then washed with brine (2 × 10 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (20:1 to 10:1) as eluent to give **28a** (201 mg, 40% yield over 2 steps) as a yellow solid and **28b** (181 mg, 36% yield over 2 steps) as a yellow oil.

Data for compound **28a**:

$\boldsymbol{R_f}$ = 0.58 (hexane/EtOAc = 2:1);

m.p. = 135 – 137 ℃;

IR (film) $\boldsymbol{\nu_{max}}$ =2951, 2830, 1707, 1605, 1493, 1367, 770 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 9.0, 2.8 Hz, 1H), 6.96 (d, *J* = 2.8 Hz, 1H), 6.86 (d, *J* = 9.0 Hz, 1H), 3.69 (s, 3H), 3.46 (s, 3H), 3.08 (dd, *J* = 9.9, 3.4 Hz, 1H), 2.93 – 2.83 (m, 2H), 2.76 – 2.66 (m, 1H), 2.59 – 2.53 (m, 1H), 2.28 – 2.21 (m, 1H), 2.12 – 2.05 (m, 2H), 1.81 – 1.72 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.8, 200.6, 171.8, 165.3, 155.4, 128.1, 120.8, 114.3, 104.7, 86.8, 56.0, 53.4, 52.2, 49.9, 43.4, 26.9, 21.7;

HRMS (*m/z*): calcd for $C_{17}H_{18}NaO_6$ $[M+Na]^+$ 341.0996; found 341.0984.

Data for compound **28b**:

$\boldsymbol{R_f}$ = 0.55 (hexane/EtOAc = 2:1);

IR (film) $\boldsymbol{\nu_{max}}$ = 2955, 2832, 1714, 1603, 1490, 1362, 1277, 1213, 772 cm^{-1};

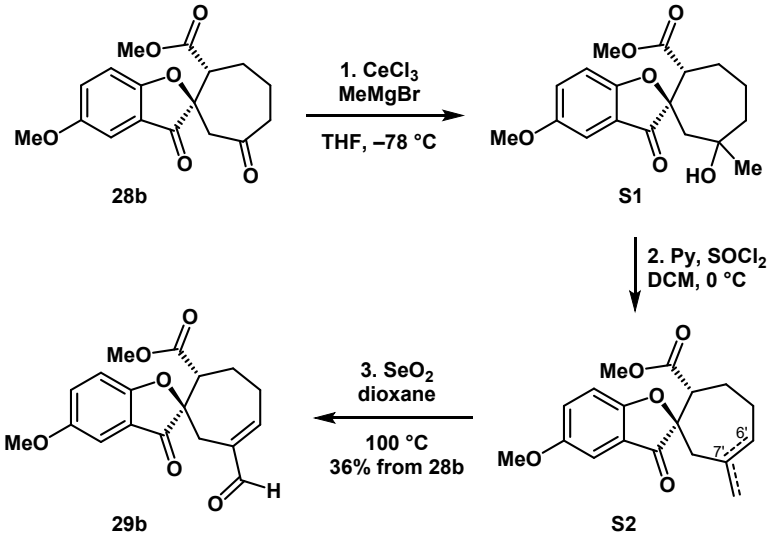
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.07 (d, *J* = 2.8 Hz, 1H), 7.03 (d, *J* = 9.0 Hz, 1H), 3.80 (s, 3H), 3.47 (s, 3H), 3.27 (dd, *J* = 11.6, 3.8 Hz, 1H), 2.98 (d, *J* = 15.3 Hz, 1H), 2.77 – 2.66 (m, 2H), 2.62 (d, *J* = 15.3 Hz, 1H), 2.48 – 2.40 (m,

1H), 2.18 – 2.09 (m, 2H), 1.89 – 1.79 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.6, 202.1, 171.5, 166.0, 155.4, 128.0, 120.0, 114.5, 104.8, 86.9, 56.0, 52.2, 51.6, 47.7, 43.8, 28.2, 22.1;

HRMS (*m/z*): calcd for $C_{17}H_{18}NaO_6$ $[M+Na]^+$ 341.0996; found 341.0984.

Synthesis of compound 29b



The procedure was adapted from Imamoto's protocol.[S1] $CeCl_3$ (232 mg, 0.943 mmol, 2 equiv) was placed in a 50 mL Schlenk tube and dried under vacuum (0.1 mmHg, with oil pump) at 140 ºC for 2 h before it was cooled to 25 ºC. A solution of compound **28b** (150 mg, 0.472 mmol, 1 equiv) in THF (4 mL) was added. The resulting suspension was vigorously stirred for 2 h before it was cooled to −78 ºC. MeMgBr (1.0 M in THF, 0.943 mL, 0.943 mmol, 2 equiv) was added dropwise over 5 min. Stirring was continued at −78 ºC for 30 min. The reaction mixture was quenched aqueous NH_4Cl (10 mL) at 0 ºC and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated to give the crude **S1**, which was used in next step without further purification.

The crude **S1** was dissolved in DCM (4 ml) and then cooled to 0 ºC. Pyridine (Py, 380 μL, 4.72 mmol, 10 equiv) and $SOCl_2$ (171 μL, 2.36 mmol, 5 equiv) was added

sequentially. After 30 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL) and extracted with DCM (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated. The residue was taken in DCM (5 mL) and then filtered through a pad of silica gel rapidly. The silica gel was thoroughly washed with hexane/EtOAc (1:1, 3 × 5 mL). The filtrate was concentrated under vaccum to give crude **S2** as a mixture of *endo* and *exo* olefins (C6'–C7' olefin dominated). The crude **S2** was directly used in the next step.

To a stirred mixture of crude **S2** in dioxane (4 mL) was added SeO_2 (209 mg, 1.89 mmol, 4 equiv) at 25 ºC. The resulting mixture was heated to 110 ºC and stirred for 6 h. The reaction mixture was cooled to room temperature and filtered through a pad of silica gel. The filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography with hexane/EtOAc (10:1 to 5:1) as eluent to give aldehyde **29b** (56.0 mg, 36% yield over 3 steps) as a yellow oil.

Data for compound **29b**:

$\boldsymbol{R_f}$ = 0.4 (hexane/EtOAc = 2:1);

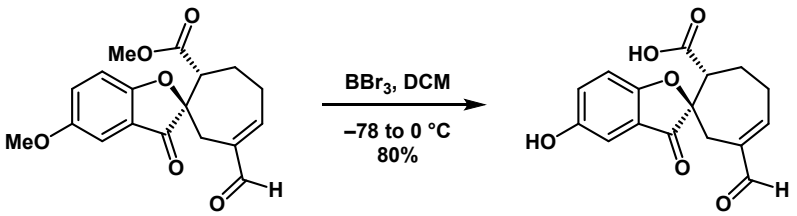
IR (film) $\boldsymbol{\nu_{max}}$ = 3441, 1709, 1596, 1490, 1273, 1207, 1025, 772 cm^{-1};

^{1}H NMR (500 MHz, CD_3OD) δ 9.34 (s, 1H), 7.27 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.24 – 7.18 (m, 1H), 7.03 (s, 1H), 7.01 (d, *J* = 5.0 Hz, 1H), 3.80 (s, 3H), 3.47 (s, 3H), 3.37 (dd, *J* = 11.8, 2.9 Hz, 1H), 2.94 (d, *J* = 14.8 Hz, 1H), 2.87 – 2.80 (m, 1H), 2.77 (d, *J* = 14.8 Hz, 1H), 2.68 – 2.60 (m, 1H), 2.37 – 2.28 (m, 1H), 2.04 – 1.97 (m, 1H);

^{13}C NMR (126 MHz, CD_3OD) δ 202.2, 194.4, 173.5, 166.6, 158.0, 156.7, 139.4, 128.3, 123.1, 115.0, 105.4, 86.9, 56.7, 56.4, 52.4, 31.1, 28.7, 24.4;

HRMS (*m/z*): calcd for $C_{18}H_{18}NaO_6$ $[M+Na]^+$ 353.0996; found 353.0988.

Synthesis of spiroapplanatumine H (8)



29b **Spiroapplanatumine H (8)**

To a stirred solution of **29b** (30.0 mg, 90.9 μmol, 1 equiv) in DCM (2 mL) was added BBr_3 (1.0 M in DCM, 0.909 mL, 0.909 mmol, 10 equiv) dropwise at −78 ºC. After 10 min, the reaction mixture was warmed to 0 ºC and stirred for another 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL) and extracted with DCM (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (2:1 to 1:5) as eluent to give spiroapplanatumine H (**8**) (22.1 mg, 80% yield) as a yellow oil.

Data for spiroapplanatumine H (**8**):

$\boldsymbol{R_f}$ = 0.2 (hexane/EtOAc = 1:2);

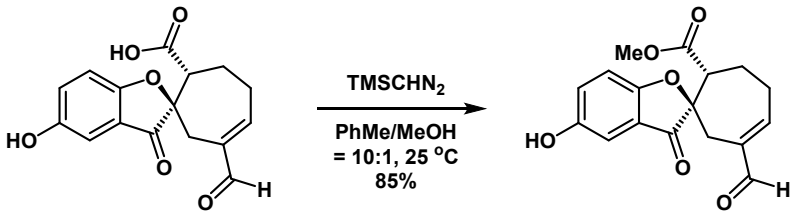
IR (film) $\boldsymbol{\nu_{max}}$ = 2919, 2852, 2356, 1706, 1482, 1258, 1094, 1035, 804 cm^{-1};

^{1}H NMR (500 MHz, CD_3OD) δ 9.34 (s, 1H), 7.21 (t, *J* = 6.0 Hz, 1H), 7.12 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 1H), 6.86 (d, *J* = 2.6 Hz, 1H), 3.28 (dd, *J* = 9.5, 3.0 Hz, 1H), 2.92 (d, *J* = 14.7 Hz, 1H), 2.87 – 2.79 (m, 1H), 2.74 (d, *J* = 14.6 Hz, 1H), 2.68 – 2.60 (m, 1H), 2.41 – 2.31 (m, 1H), 2.09 – 2.01 (m, 1H);

^{13}C NMR (126 MHz, CD_3OD) δ 202.9, 194.5, 175.0, 165.7, 158.1, 153.8, 139.5, 127.5, 123.5, 114.6, 108.3, 86.6, 57.3, 31.4, 29.0, 24.6;

HRMS (*m/z*): calcd for $C_{16}H_{13}O_6$ $[M-H]^-$ 301.0718; found 301.0720.

Synthesis of spiroapplanatumine R (10)



Spiroapplanatumine H (8) **Spiroapplanatumine R (10)**

To a stirred solution of spiroapplanatumine H (**8**) (7.0 mg, 23.2 μmol, 1 equiv) in PhMe/MeOH (2 mL/0.2 mL) was added $TMSCHN_2$ (2.0 M in hexane, 28.9 μL, 57.9 μmol, 2.5 equiv) at 0 ºC. After 10 min, the solution was warmed to 25 ºC and stirred for 30 min. The reaction mixture was concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (3:1 to 1:1) as eluent to give spiroapplanatumine R (**10**) (6.2 mg, 85% yield) as a yellow oil.

Data for spiroapplanatumine R (**10**):

$\boldsymbol{R_f}$ = 0.5 (hexane/EtOAc = 1:2);

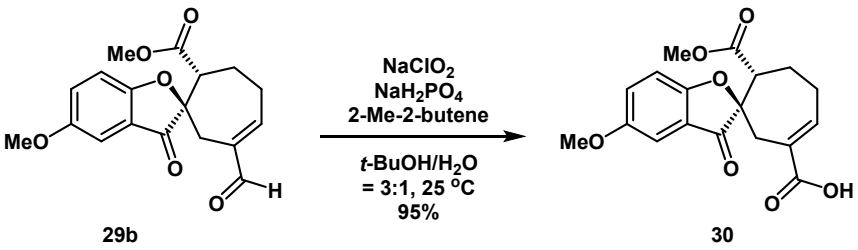
IR (film) $\boldsymbol{\nu_{max}}$ = 2957, 2852, 2363, 1711, 1685, 1482, 1213, 1022, 799 cm^{-1};

^{1}H NMR (500 MHz, CD_3OD) δ 9.34 (s, 1H), 7.24 – 7.17 (m, 1H), 7.15 (dd, *J* = 8.9, 2.7 Hz, 1H), 6.94 (d, *J* = 8.9 Hz, 1H), 6.88 (d, *J* = 2.6 Hz, 1H), 3.47 (s, 3H), 3.34 (dd, *J* = 11.8, 2.9 Hz, 1H), 2.93 (d, *J* = 14.8 Hz, 1H), 2.87 – 2.80 (m, 1H), 2.76 (d, *J* = 14.8 Hz, 1H), 2.67 – 2.59 (m, 1H), 2.37 – 2.25 (m, 1H), 2.03 – 1.96 (m, 1H);

^{13}C NMR (126 MHz, CD_3OD) δ 202.6, 194.5, 173.5, 165.7, 158.0, 154.0, 139.5, 127.8, 123.2, 114.7, 108.2, 86.6, 56.7, 52.4, 31.2, 28.7, 24.4;

HRMS (*m/z*): calcd for $C_{17}H_{16}NaO_6$ $[M+Na]^+$ 339.0839; found 339.0829.

Synthesis of compound 30



To a stirred mixture of **29b** (17.0 mg, 51.5 μmol, 1 equiv), 2-methyl-2-butene (109 μL, 1.03 mmol, 20 equiv), NaH_2PO_4 (61.8 mg, 0.515 mmol, 10 equiv) in *t*-BuOH/H_2O (1.5 mL/0.5 mL) was added $NaClO_2$ (46.3 mg, 0.515 mmol, 10 equiv) at 0 ºC. The reaction mixture was warmed to 25 ºC. After being stirred at 25 ºC for 15 min, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ (5 mL) at 0 ºC and extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (5:1 to 1:1) as eluent to give **30** (16.9 mg, 95% yield) as a yellow oil.

Data for compound **30**:

$\boldsymbol{R_f}$ = 0.3 (hexane/EtOAc = 2:1);

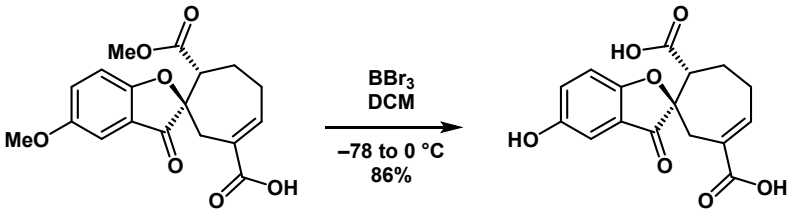
IR (film) $\boldsymbol{\nu_{max}}$ = 2964, 2363, 1734, 1624, 1489, 1269, 1101, 1038, 804 cm^{-1};

^{1}H NMR (500 MHz, CD_3OD) δ 7.41 (t, *J* = 6.7 Hz, 1H), 7.26 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.05 (d, *J* = 2.7 Hz, 1H), 7.01 (d, *J* = 9.0 Hz, 1H), 3.80 (s, 3H), 3.47 (s, 3H), 3.35 – 3.32 (m, 1H), 2.98 (d, *J* = 14.7 Hz, 1H), 2.93 (d, *J* = 14.8 Hz, 1H), 2.70 – 2.62 (m, 1H), 2.50 – 2.42 (m, 1H), 2.32 – 2.24 (m, 1H), 2.00 – 1.94 (m, 1H);

^{13}C NMR (126 MHz, CD_3OD) δ 202.5, 173.6, 170.0, 166.6, 156.6, 146.4, 128.9, 128.0, 123.4, 115.0, 105.5, 86.9, 57.0, 56.4, 52.3, 34.9, 27.8, 24.6;

HRMS (*m/z*): calcd for $C_{18}H_{18}NaO_7$ $[M+Na]^+$ 369.0945; found 369.0932.

Synthesis of spiroapplanatumine B (2)



30 Spiroapplanatumine B (2)

To a stirred solution of **30** (13.0 mg, 37.6 μmol, 1 equiv) in DCM (2 mL) was added BBr_3 (1.0 M in DCM, 0.376 mL, 0.376 mmol, 10 equiv) dropwise at –78 ºC. After 10 min, the reaction mixture was warmed to 0 ºC and stirred for another 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL) and extracted with DCM (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (3:1 to 1:5) as eluent to give spiroapplanatumine B (**2**) (10.3 mg, 86% yield) as a yellow oil.

Data for spiroapplanatumine B (**2**):

$\boldsymbol{R_f}$ = 0.2 (hexane/EtOAc = 1:2);

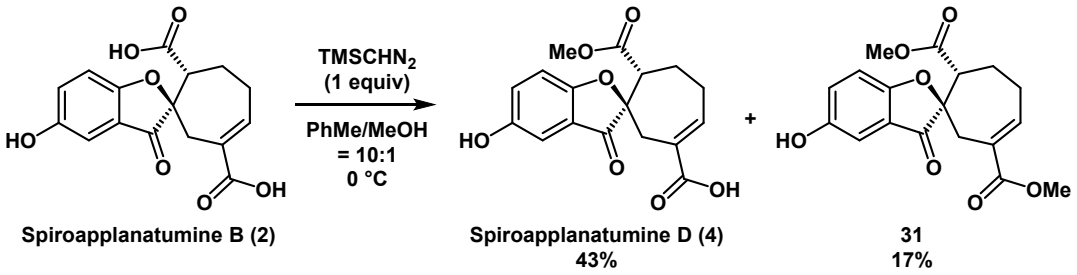
IR (film) $\boldsymbol{\nu_{max}}$ = 2962, 2927, 2367, 1708, 1480, 1087, 1030, 807 cm^{-1};

^{1}H NMR (600 MHz, CD_3OD) δ 7.42 (t, *J* = 6.2 Hz, 1H), 7.11 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 1H), 6.90 (d, *J* = 2.7 Hz, 1H), 3.29 – 3.21 (m, 1H), 2.96 (d, *J* = 14.4 Hz, 1H), 2.91 (d, *J* = 14.5 Hz, 1H), 2.70 – 2.62 (m, 1H), 2.51 – 2.42 (m, 1H), 2.35 – 2.26 (m, 1H), 2.06 – 1.99 (m, 1H);

^{13}C NMR (126 MHz, CD_3OD) δ 203.3, 165.7, 153.7, 146.4, 129.1, 127.2, 123.9, 114.6, 108.3, 86.7, 57.8, 35.2, 28.1, 24.8 (the signals for the two carboxy groups were not observed);

HRMS (*m/z*): calcd for $C_{16}H_{14}NaO_7$ $[M+Na]^+$ 341.0632; found 341.0623.

Synthesis of spiroapplanatumine D (4) and 31



To a stirred solution of spiroapplanatumine B (**2**) (8.0 mg, 25.2 μmol, 1 equiv) in PhMe/MeOH (2 mL/0.2 mL) was added $TMSCHN_2$ (2.0 M in hexane, 12.6 μL, 25.2 μmol, 1 equiv) at 0 ºC. The reaction mixture was stirred at 0 ºC for 15 min before it was quenched by addition of acetic acid (one drop). The reaction mixture was concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (10:1 to 1:5) as eluent to give spiroapplanatumine D (**4**) (3.6 mg, 43% yield) as a yellow oil and **31** (1.5 mg, 17% yield) as a yellow oil.

Data for spiroapplanatumine D (**4**):

$\boldsymbol{R_f}$ = 0.5 (hexane/EtOAc = 1:2);

IR (film) $\boldsymbol{\nu_{max}}$ = 2922, 2368, 1708, 1699, 1217, 1054, 1024, 792 cm^{-1};

^{1}H NMR (500 MHz, CD_3OD) δ 7.40 (t, *J* = 6.4 Hz, 1H), 7.13 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 6.91 (d, *J* = 2.7 Hz, 1H), 3.46 (s, 3H), 3.31 – 3.28 (m, 1H), 2.98 (d, *J* = 14.7 Hz, 1H), 2.91 (d, *J* = 14.7 Hz, 1H), 2.69 – 2.61 (m, 1H), 2.49 – 2.40 (m, 1H), 2.32 – 2.21 (m, 1H), 1.99 – 1.91 (m, 1H);

^{13}C NMR (126 MHz, CD_3OD) δ 202.9, 173.7, 170.2, 165.6, 153.8, 146.3, 129.2, 127.5, 123.6, 114.6, 108.3, 86.6, 57.0, 52.3, 34.9, 27.8, 24.6;

HRMS (*m/z*): calcd for $C_{16}H_{14}NaO_7$ $[M+Na]^+$ 355.0788; found 355.0777.

Data for compound **31**:

$\boldsymbol{R_f}$ = 0.7 (hexane/EtOAc = 1:2);

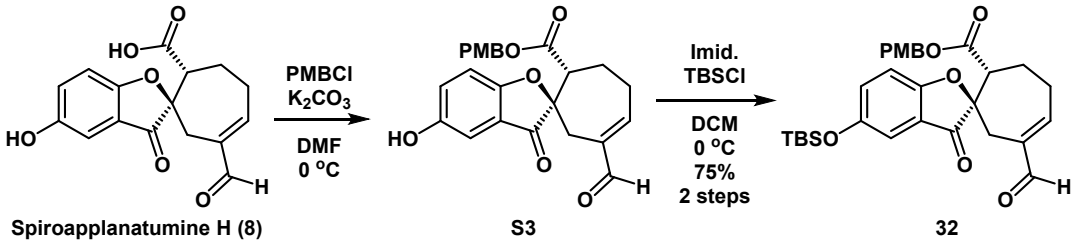
IR (film) $\boldsymbol{\nu_{max}}$ = 3451, 1731, 1593, 1385, 1352, 1156, 518 cm^{-1};

^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.37 – 7.33 (m, 1H), 7.13 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.97 (dd, *J* = 2.8, 0.4 Hz, 1H), 6.93 (dd, *J* = 8.8, 0.4 Hz, 1H), 3.66 (s, 3H), 3.48 (s, 3H), 3.22 (dd, *J* = 11.9, 3.1 Hz, 1H), 3.00 (d, *J* = 14.9 Hz, 1H), 2.85 (dt, *J* = 14.8, 1.2 Hz, 1H), 2.68 – 2.63 (m, 1H), 2.41 – 2.35 (m, 1H), 2.31 – 2.25 (m, 1H), 1.99 – 1.95 (m, 1H);

^{13}C NMR (151 MHz, CD_2Cl_2) δ 200.6, 172.4, 167.6, 164.9, 151.4, 145.1, 127.8, 126.2, 122.8, 114.1, 108.3, 85.8, 56.0, 52.4, 52.3, 34.4, 27.5, 23.8;

HRMS (*m/z*): calcd for $C_{18}H_{17}O_7$ $[M-H]^-$ 345.0980, found 345.0973.

Synthesis of compound 32



Spiroapplanatumine H (8) S3 32

To a stirred mixture of spiroapplanatumine H (**8**) (12.5 mg, 41.4 μmol, 1 equiv) amd K_2CO_3 (57.1 mg, 0.414 mmol, 10 equiv) in DMF (1.5 mL) was added *p*-methoxybenzyl chloride (PMBCl, 56.0 μL, 0.414 mmol, 10 equiv) was added at 0 ºC. After 2 h, the reaction mixture was quenched with H_2O (5 mL) at 0 ºC and extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated to afford crude **S3**. which was directly used in the next step. The crude **S3** was dissolved in DCM (1.5 ml) and cooled to 0 ºC. Imidazole (Imid., 42.2 mg, 0.621 mmol, 15 equiv) and *tert*-butyldimethylsilyl chloride (TBSCl, 62.5 mg, 0.414 mmol, 10 equiv) were added sequentially. After 30 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL) and extracted with DCM (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (10:1 to 2:1) as eluent to give **32** (16.7

mg, 75% yield over 2 steps) as a yellow oil.

Data for compound **32**:

$\boldsymbol{R_f}$ = 0.45 (hexane/EtOAc = 2:1);

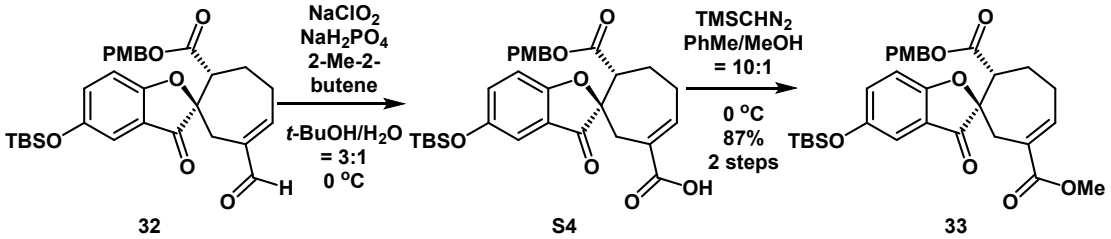
IR (film) $\boldsymbol{\nu_{max}}$ = 2917, 2361, 1627, 1522, 1255, 1099, 1040, 802 cm^{-1};

^{1}H NMR (600 MHz, C_6D_6) δ 9.13 (s, 1H), 7.21 (d, *J* = 2.7 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 2H), 6.80 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.68 (d, *J* = 8.8 Hz, 1H), 6.66 (d, *J* = 8.6 Hz, 2H), 6.11 (t, *J* = 6.4 Hz, 1H), 4.83 (d, *J* = 11.9 Hz, 1H), 4.72 (d, *J* = 11.9 Hz, 1H), 3.28 (d, *J* = 14.9 Hz, 1H), 3.25 (s, 3H), 3.11 (dd, *J* = 11.6, 2.5 Hz, 1H), 2.49 (d, *J* = 14.9 Hz, 1H), 2.46 – 2.39 (m, 1H), 2.02 – 1.95 (m, 1H), 1.70 – 1.64 (m, 2H), 0.91 (s, 9H), -0.05 (s, 6H);

^{13}C NMR (151 MHz, C_6D_6) δ 199.7, 191.6, 171.2, 165.3, 160.2, 154.1, 150.9, 138.3, 130.5, 130.2, 128.3, 123.1, 114.1, 113.8, 113.5, 86.0, 66.7, 55.8, 54.7, 30.9, 27.8, 25.7, 23.5, 18.2, -4.72, -4.74;

HRMS (*m/z*): calcd for $C_{30}H_{36}NaO_7Si$ $[M+Na]^+$ 559.2123; found 559.2107.

Synthesis of compound 33



To a stirred mixture of **32** (11.0 mg, 20.5 μmol, 1 equiv), 2-methyl-2-butene (43.5 μL, 0.410 mmol, 20 equiv), NaH_2PO_4 (24.6 mg, 0.205 mmol, 10 equiv) in *t*-BuOH/H_2O (1.5 mL/0.5 mL) was added $NaClO_2$ (18.4 mg, 0.205 mmol, 10 equiv) at 0 ºC. After being stirred at 0 ºC for 15 min, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated to

afford crude **S4**, which was used in the next step without further purification.

To a stirred solution of crude **S4** in PhMe/MeOH (2 mL/0.2 mL) was added $TMSCHN_2$ (2.0 M in hexane, 41.0 μL, 81.9 μmol, 4 equiv) at 0 ºC. After 30 min, the reaction mixture was concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (20:1 to 5:1) as eluent to give **33** (10.1 mg, 87% yield over 2 steps) as a yellow oil.

Data for compound **33**:

$\boldsymbol{R_f}$ = 0.4 (hexane/EtOAc = 5:1);

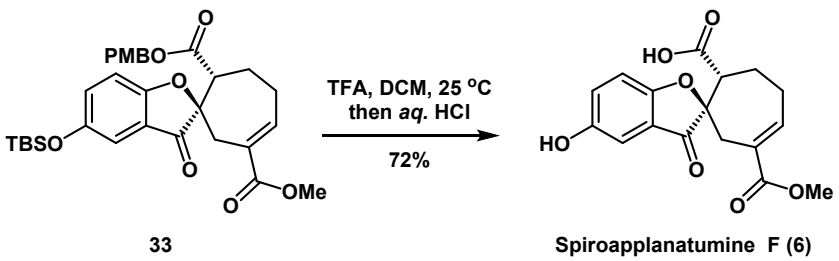
IR (film) $\boldsymbol{\nu_{max}}$ = 2924, 2368, 2368, 1723, 1624, 1480, 1260 cm^{-1};

^{1}H NMR (500 MHz, C_6D_6) δ 7.26 (d, *J* = 2.6 Hz, 1H), 7.22 (t, *J* = 6.5 Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 2H), 6.80 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.70 (d, *J* = 8.8 Hz, 1H), 6.65 (d, *J* = 8.6 Hz, 2H), 4.82 (d, *J* = 11.6 Hz, 1H), 4.70 (d, *J* = 11.6 Hz, 1H, the phase at this position is reversed in the provided spectrum), 3.37 (d, *J* = 14.8 Hz, 1H), 3.30 (s, 3H), 3.25 (s, 3H), 3.17 (dd, *J* = 12.0, 2.7 Hz, 1H), 2.77 (d, *J* = 14.7 Hz, 1H), 2.52 – 2.41 (m, 1H), 2.05 – 1.94 (m, 1H), 1.73 – 1.66 (m, 2H), 0.92 (s, 9H), -0.04 (d, *J* = 2.1 Hz, 6H);

^{13}C NMR (126 MHz, C_6D_6) δ 199.9, 171.3, 166.9, 165.3, 160.1, 150.8, 144.5, 130.5, 130.0, 123.5, 114.1, 113.9, 113.5, 86.0, 66.6, 56.1, 54.7, 51.6, 34.7, 27.1, 25.8, 23.7, 18.2, -4.7 (the signals for two carbons are not observed);

HRMS (*m/z*): calcd for $C_{31}H_{38}NaO_8Si$ $[M+Na]^+$ 589.2228; found 589.2212.

Synthesis of spiroapplanatumine F (6)



33 **Spiroapplanatumine F (6)**

To a stirred solution of **33** (8.0 mg, 14.1 μmol, 1 equiv) in DCM (1 mL) was added trifuluoracetic acid (TFA, 100 μL) at 25 °C. After 1 h, aqueous HCl (2.0 M, 1 mL) was added to the reaction mixture. After being stirred for another 3 h, the reaction mixture was diluted with DCM (10 mL) and washed with brine (2 × 5 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography with hexane/EtOAc (10:1 to 2:1) as eluent to give spiroapplanatumine F (**6**) (3.4 mg, 72% yield) as a yellow oil.

Data for spiroapplanatumine F (**6**):

$\boldsymbol{R_f}$ = 0.35 (hexane/EtOAc = 2:1);

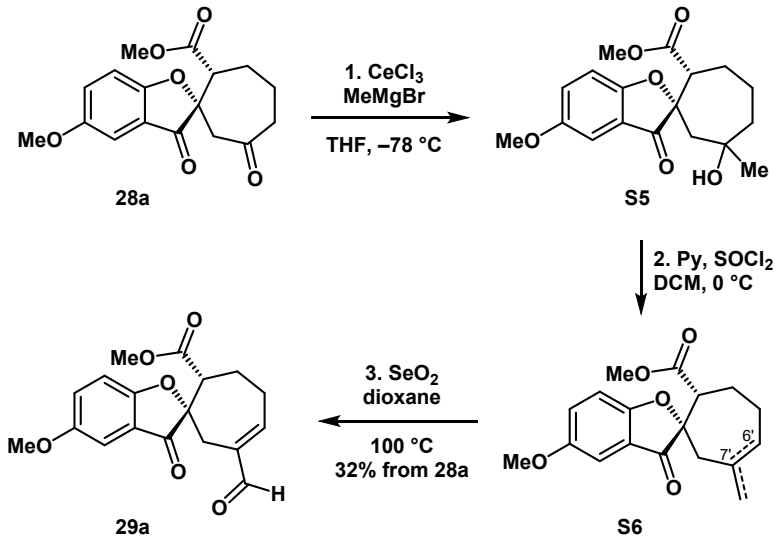
IR (film) $\boldsymbol{\nu_{max}}$ = 2924, 2366, 2323, 1706, 1624, 1412, 1260, 1040, 804 cm^{-1};

^{1}H NMR (500 MHz, CD_3OD) δ 7.39 (dd, *J* = 8.4, 5.6 Hz, 1H), 7.12 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 1H), 6.89 (d, *J* = 2.7 Hz, 1H), 3.66 (s, 3H), 3.25 (dd, *J* = 12.2, 3.1 Hz, 1H), 2.94 (s, 2H), 2.70 – 2.62 (m, 1H), 2.51 – 2.42 (m, 1H), 2.32 – 2.22 (m, 1H), 2.04 – 1.98 (m, 1H);

^{13}C NMR (126 MHz, CD_3OD) δ 203.2, 175.1, 168.8, 165.6, 153.7, 146.7, 128.7, 127.3, 123.9, 114.6, 108.2, 86.5, 57.6, 52.5, 35.2, 28.0, 24.8;

HRMS (*m/z*): calcd for $C_{17}H_{16}NaO_7$ $[M+Na]^+$ 355.0788; found 355.0777.

Synthesis of compound 29a



The procedure was adapted from Imamoto's protocol.[S1] $CeCl_3$ (77.4 mg, 0.314 mmol, 2 equiv) was placed in a 25 mL Schlenk tube and dried under vacuum (0.1 mmHg, with oil pump) at 140 ºC for 2 h before it was cooled to 25 ºC. A solution of compound **28a** (50.0 mg, 0.157 mmol, 1 equiv) in THF (1 mL) was added. The resulting suspension was vigorously stirred for 2 h before it was cooled to −78 ºC. MeMgBr (1.0 M in THF, 0.314 mL, 0.314 mmol, 2 equiv) was added dropwise over 5 min. Stirring was continued at −78 ºC for 30 min. The reaction mixture was quenched aqueous NH_4Cl (10 mL) at 0 ºC and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated to give the crude **S5**, which was used in next step without further purification.

The crude **S5** was dissolved in DCM (2 ml) and then cooled to 0 ºC. Pyridine (Py, 127 μL, 1.57 mmol, 10 equiv) and $SOCl_2$ (57.0 μL, 0.786 mmol, 5 equiv) was added sequentially. After 30 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (5 mL) and extracted with DCM (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated. The residue was taken in DCM (5 mL) and then filtered through a pad of silica gel rapidly. The silica gel was thoroughly washed with hexane/EtOAc (1:1, 3 × 5 mL). The filtrate was concentrated under vaccum to give crude **S6** as a mixture of *endo* and *exo* olefins (C6'−C7' olefin dominated). The crude **S6** was directly used in the next step.

To a stirred mixture of crude **S6** in dioxane (3 mL) was added SeO_2 (69.8 mg, 0.629 mmol, 4 equiv) at 25 ºC. The resulting mixture was heated to 110 ºC and stirred for 6 h. The reaction mixture was cooled to room temperature and filtered through a pad of silica gel. The filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography with hexane/EtOAc (10:1 to 5:1) as eluent to give aldehyde **29a** (16.6 mg, 32% yield over 3 steps) as a yellow oil.

Data for compound **29a**:

$\boldsymbol{R_f}$ = 0.4 (hexane/EtOAc = 2:1);

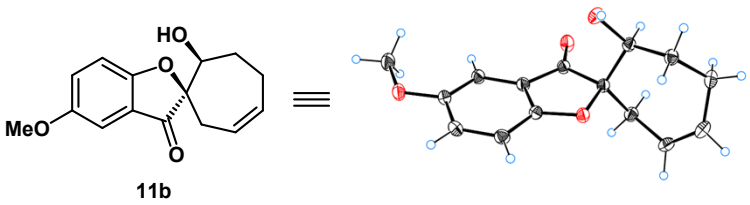
IR (film) $\boldsymbol{\nu_{max}}$ = 3373,2921,2851,1598,1387,2353,769 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.19 (dd, *J* = 8.9, 2.7 Hz, 1H), 7.10 (d, *J* = 2.6 Hz, 1H), 6.99 (t, *J* = 5.0 Hz, 1H), 6.91 (d, *J* = 9.0 Hz, 1H), 3.81 (s, 3H), 3.39 (dd, *J* = 8.1, 4.0 Hz, 1H), 3.34 (s, 3H), 3.01 (d, *J* = 16.1 Hz, 1H), 2.96 – 2.88 (m, 1H), 2.66 – 2.58 (m, 1H), 2.53 (d, *J* = 16.1 Hz, 1H), 2.34 – 2.24 (m, 1H) (there are some impurities in the high field area);

^{13}C NMR (126 MHz, $CDCl_3$) δ 202.3, 193.2, 171.0, 166.2, 155.8, 139.1, 130.1, 127.7, 120.3, 114.1, 105.0, 88.6, 56.0, 51.8, 50.5, 27.8, 27.4, 23.5 (there are some impurities in the high field area);

HRMS (*m/z*): calcd for $C_{18}H_{18}NaO_6$ $[M+Na]^+$ 353.0996; found 353.0988.

3. X-ray Crystallographic Data

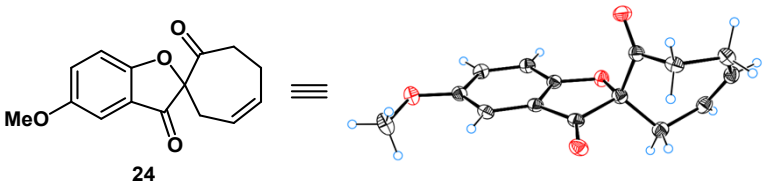


11b

Crystal data and structure refinement for **11b** (CCDC 2363816):

Identification code	**11b**
Empirical formula	$C_{15}H_{16}O_4$
Formula weight	260.28
Temperature/K	293.15
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	9.7545(2)
b/Å	8.7863(2)
c/Å	15.2338(3)
α /°	90
β /°	96.718(2)
γ /°	90
Volume/Å^3	1296.66(5)
Z	4
ρ_{calc}g/cm^3	1.333
μ /mm^{-1}	0.794
F(000)	552.0
Crystal size/mm^3	0.14 × 0.13 × 0.12
Radiation	Cu K α (λ = 1.54184)
2Θ range for data collection/°	10.25 to 147.444
Index ranges	-11 ⩽ h ⩽ 10, -10 ⩽ k ⩽ 10, -18 ⩽ l ⩽ 18
Reflections collected	4915

Independent reflections	2536 [R_{int} = 0.0188, R_{sigma} = 0.0254]
Data/restraints/parameters	2536/0/174
Goodness-of-fit on F^2	1.055
Final R indexes [I>=2 σ (I)]	R_1 = 0.0391, wR_2 = 0.1031
Final R indexes [all data]	R_1 = 0.0427, wR_2 = 0.1071
Largest diff. peak/hole / e $Å^{-3}$	0.15/-0.28

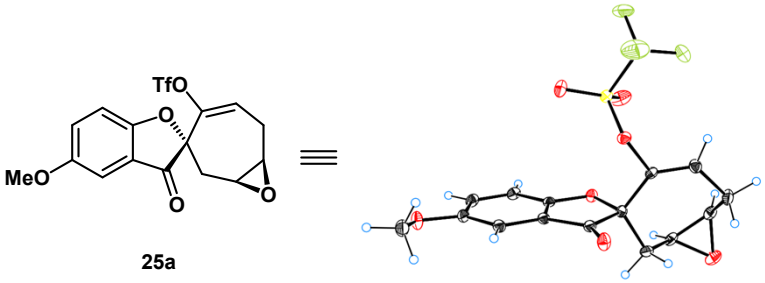


24

Crystal data and structure refinement for **24** (CCDC 2363817):

Identification code	**24**
Empirical formula	$C_{15}H_{14}O_4$
Formula weight	258.26
Temperature/K	169.99(10)
Crystal system	triclinic
Space group	P-1
a/Å	7.3842(8)
b/Å	9.3169(9)
c/Å	10.2980(11)
α /°	71.253(10)
β /°	70.522(10)
γ /°	76.976(9)
Volume/$Å^3$	626.93(13)
Z	2
ρ_{calc}g/cm^3	1.368
μ /mm^{-1}	0.821
F(000)	272.0
Crystal size/mm^3	0.18 × 0.15 × 0.12

Radiation	Cu K α (λ = 1.54184)
2 Θ range for data collection/°	9.456 to 147.902
Index ranges	-8 ⩽ h ⩽ 9, -11 ⩽ k ⩽ 8, -11 ⩽ l ⩽ 12
Reflections collected	3925
Independent reflections	2432 [R_{int} = 0.0248, R_{sigma} = 0.0336]
Data/restraints/parameters	2432/0/173
Goodness-of-fit on F^2	1.135
Final R indexes [I>=2 σ (I)]	R_1 = 0.0469, wR_2 = 0.1246
Final R indexes [all data]	R_1 = 0.0576, wR_2 = 0.1315
Largest diff. peak/hole / e $Å^{-3}$	0.33/-0.25

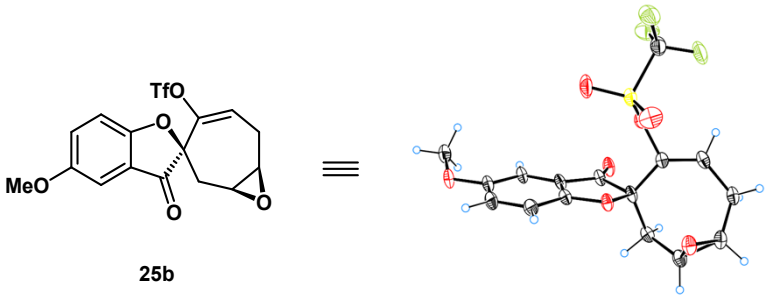


25a

Table 1 Crystal data and structure refinement for **25a** (CCDC 2363818):

Identification code	**25a**
Empirical formula	$C_{16}H_{13}F_3O_7S$
Formula weight	406.32
Temperature/K	170.00(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.8244(6)
b/Å	14.0485(7)
c/Å	11.0895(6)
α /°	90
β /°	101.020(6)
γ /°	90
Volume/Å^3	1655.24(16)
Z	4
ρ_{calc}g/cm^3	1.630
μ /mm^{-1}	0.267
F(000)	832.0
Crystal size/mm^3	0.15 × 0.13 × 0.12
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.734 to 49.992
Index ranges	-12 ⩽ h ⩽ 12, -16 ⩽ k ⩽ 13, -10 ⩽ l ⩽ 13
Reflections collected	6755
Independent reflections	2909 [R_{int} = 0.0282, R_{sigma} = 0.0387]
Data/restraints/parameters	2909/0/245

Goodness-of-fit on F^2	1.032
Final R indexes [I>=2 σ (I)]	R_1 = 0.0385, wR_2 = 0.0912
Final R indexes [all data]	R_1 = 0.0463, wR_2 = 0.0962
Largest diff. peak/hole / e $Å^{-3}$	0.23/-0.41

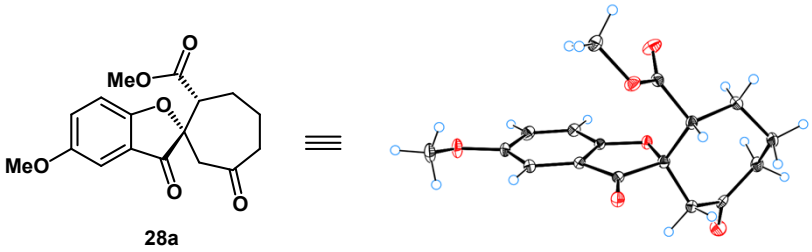


25b

Crystal data and structure refinement for **25b** (CCDC 2363819).

Identification code	**25b**
Empirical formula	$C_{16}H_{13}F_3O_7S$
Formula weight	406.32
Temperature/K	169.99(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.7585(10)
b/Å	14.0755(16)
c/Å	11.0794(11)
α /°	90
β /°	100.732(9)
γ /°	90
Volume/Å^3	1648.4(3)
Z	4
ρ_{calc}g/cm^3	1.637
μ /mm^{-1}	2.436
F(000)	832.0
Crystal size/mm^3	0.14 × 0.13 × 0.1
Radiation	Cu K α (λ = 1.54184)
2Θ range for data collection/°	10.272 to 133.166
Index ranges	-10 ⩽ h ⩽ 12, -16 ⩽ k ⩽ 16, -12 ⩽ l ⩽ 13
Reflections collected	5943
Independent reflections	2900 [R_{int} = 0.0625, R_{sigma} = 0.0639]

Data/restraints/parameters	2900/0/245
Goodness-of-fit on F^2	1.062
Final R indexes [I>=2 σ (I)]	R_1 = 0.0759, wR_2 = 0.2127
Final R indexes [all data]	R_1 = 0.0872, wR_2 = 0.2404
Largest diff. peak/hole / e $Å^{-3}$	0.58/-0.58



28a

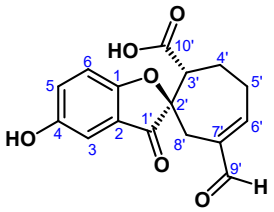
Table 1 Crystal data and structure refinement for **28a** (CCDC 2363820).

Identification code	**28a**
Empirical formula	$C_{17}H_{18}O_6$
Formula weight	318.31
Temperature/K	150.01(14)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	8.5810(6)
b/Å	7.0851(5)
c/Å	24.335(2)
α /°	90
β /°	97.198(8)
γ /°	90
Volume/Å^3	1467.8(2)
Z	4
ρ_{calc}g/cm^3	1.440
μ /mm^{-1}	0.109
F(000)	672.0
Crystal size/mm^3	0.16 × 0.11 × 0.1
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.784 to 49.992
Index ranges	-10 ≤ h ≤ 10, -6 ≤ k ≤ 8, -21 ≤ l ≤ 28
Reflections collected	5629
Independent reflections	2572 [R_{int} = 0.0568, R_{sigma} = 0.0661]
Data/restraints/parameters	2572/0/210

Goodness-of-fit on F^2	1.055
Final R indexes [I>=2 σ (I)]	R_1 = 0.0539, wR_2 = 0.1342
Final R indexes [all data]	R_1 = 0.0635, wR_2 = 0.1438
Largest diff. peak/hole / e $Å^{-3}$	0.28/-0.31

4. Comparison of NMR Data of Natural and Synthetic Products

Table S1. Comparison of ^{1}H NMR spectroscopic data of the natural (Cheng)[S2] and synthetic spiroapplanatumine H (8).

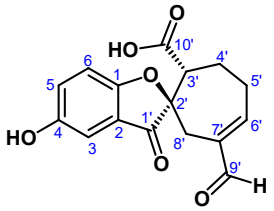


Spiroapplanatumine H (8)

Position	Natural (Cheng)[a] (600 M, CD_3OD)	Synthetic (us)[a] (500 M, CD_3OD)	Δδ (*Nat-Syn*)
3	6.87, d (2.7)	6.86, d (2.6)	+0.01
5	7.13, dd (8.8, 2.7)	7.12, dd, (8.8, 2.7)	+0.01
6	6.94, d (8.8)	6.94, d (8.8)	0
3'	3.27, dd (9.5, 3.0)	3.28, dd (9.5, 3.0)	–0.01
4'	2.36, m	2.36, m	0
	2.05, m	2.05, m	0
5'	2.83, m	2.83, m	0
	2.63, m	2.65, m	–0.02
6'	7.22, t (6.1)	7.21, t (6.0)	+0.01
8'	2.92, d (14.6)	2.92, d (14.7)	0
	2.74, d (14.6)	2.74, d (14.6)	0
9'	9.34, s	9.34, s	0

[a] Chemical shifts referenced to residual undeuterated MeOH at 3.31 ppm.

Table S2. Comparison of ^{13}C NMR spectroscopic data of the natural (Cheng)[S2] and synthetic spiroapplanatumine H (8).

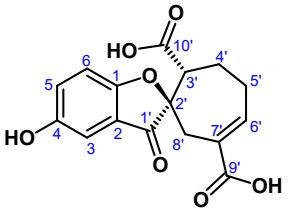


Spiroapplanatumine H (8)

Position	Natural (Cheng)[a] (150 M, CD_3OD)	Synthetic (us)[a] (126 M, CD_3OD)	Δδ (*Nat-Syn*)
1	165.7	165.7	0
2	123.5	123.5	0
3	108.3	108.3	0
4	153.7	153.8	–0.1
5	127.5	127.5	0
6	114.7	114.6	+0.1
1'	202.9	202.9	0
2'	86.6	86.6	0
3'	57.2	57.3	–0.1
4'	24.6	24.6	0
5'	28.9	29.0	–0.1
6'	158.3	158.1	+0.2
7'	139.4	139.5	–0.1
8'	31.4	31.4	0
9'	194.5	194.5	0
10'	175.0	175.0	0

[a] Chemical shifts referenced to CD_3OD at 49.00 ppm.

Table S3. Comparison of ^{1}H NMR spectroscopic data of the natural (Cheng)[S2] and synthetic spiroapplanatumine B (2).

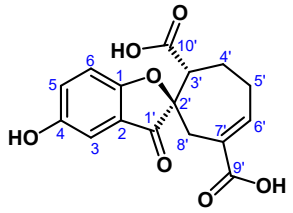


Spiroapplanatumine B (2)

Position	Natural (Cheng)[a] (600 M, CD_3OD)	Synthetic (us)[a] (600 M, CD_3OD)	Δδ (*Nat-Syn*)
3	6.91, d (2.7)	6.90, d (2.7)	+0.01
5	7.13, dd (8.8, 2.7)	7.11, dd (8.8, 2.7)	+0.02
6	6.96, d (8.8)	6.94, d (8.8)	+0.02
3'	3.27, dd (12.2, 3.0)	3.26, m	+0.01
4'	2.29, m	2.31, m	–0.02
	2.01, m	2.01, m	0
5'	2.65, m	2.66, m	–0.01
	2.45, m	2.46, m	–0.01
6'	7.42, t (6.3)	7.42, t (6.2 Hz)	0
8'	2.96, d (14.7)	2.96, d (14.4)	0
	2.91, d (14.7)	2.91, d (14.5)	0

[a] Chemical shifts referenced to residual undeuterated MeOH at 3.31 ppm.

Table S4. Comparison of ^{13}C NMR spectroscopic data of the natural (Cheng)[S2] and synthetic spiroapplanatumine B (2).



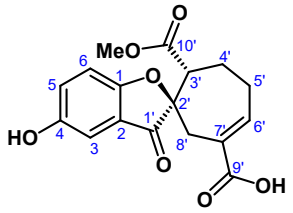
Spiroapplanatumine B (2)

Position	Natural (Cheng)[a] (150 M, CD_3OD)	Synthetic (us)[a] (126 M, CD_3OD)	Δδ (*Nat-Syn*)
1	165.6	165.7	–0.1
2	123.8	123.9	–0.1
3	108.3	108.3	0
4	153.6	153.7	–0.1
5	127.3	127.2	+0.1
6	114.6	114.6	0
1'	203.2	203.3	–0.1
2'	86.6	86.7	–0.1
3'	57.5	57.8	–0.3
4'	24.7	24.8	–0.1
5'	28.0	28.1	–0.1
6'	146.6	146.4	+0.2
7'	128.9	129.1	–0.2
8'	35.1	35.2	–0.1
9'	170.1	-[b]	\
10'	175.2	-[b]	\

[a] Chemical shifts referenced to CD_3OD at 49.00 ppm.

[b] Not observed

Table S5. Comparison of ^{1}H NMR spectroscopic data of the natural (Cheng)[S2] and synthetic spiroapplanatumine D (4).

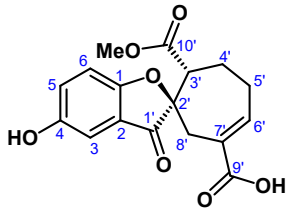


Spiroapplanatumine D (4)

Position	Natural (Cheng)[a] (600 M, CD_3OD)	Synthetic (us)[a] (500 M, CD_3OD)	Δδ (*Nat-Syn*)
3	6.91, d (2.7)	6.91, d (2.7)	0
5	7.13, dd (8.8, 2.7)	7.13, dd (8.8, 2.7)	0
6	6.93, d (8.8)	6.93, d (8.8)	0
3'	3.30, dd (12.0, 3.3)	3.29, m	+0.01
4'	2.27, m	2.27, m	0
	1.95, m	1.96, m	–0.01
5'	2.65, m	2.65, m	0
	2.45, m	2.44, m	+0.01
6'	7.40, t (6.3)	7.40, t (6.4)	0
8'	2.98, d (14.9)	2.98, d (14.7)	0
	2.91, d (14.9)	2.91, d (14.7)	0
10'-OMe	3.46, s	3.46, s	0

[a] Chemical shifts referenced to residual undeuterated MeOH at 3.31 ppm.

Table S6. Comparison of ^{13}C NMR spectroscopic data of the natural (Cheng)[S2] and synthetic spiroapplanatumine D (4).

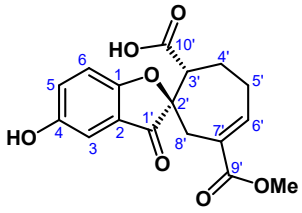


Spiroapplanatumine D (4)

Position	Natural (Cheng)[a] (150 M, CD_3OD)	Synthetic (us)[a] (126 M, CD_3OD)	Δδ (*Nat-Syn*)
1	165.6	165.6	0
2	123.6	123.6	0
3	108.3	108.3	0
4	153.8	153.8	0
5	127.5	127.5	0
6	114.6	114.6	0
1'	202.9	202.9	0
2'	86.6	86.6	0
3'	57.0	57.0	0
4'	24.6	24.6	0
5'	27.8	27.8	0
6'	146.2	146.3	–0.1
7'	129.2	129.2	0
8'	35.0	34.9	+0.1
9'	170.3	170.2	+0.1
10'	173.7	173.7	0
10'-OMe	52.3	52.3	0

[a] Chemical shifts referenced to CD_3OD at 49.00 ppm.

Table S7. Comparison of ^{1}H NMR spectroscopic data of the natural (Cheng)[S2] and synthetic spiroapplanatumine F (6).

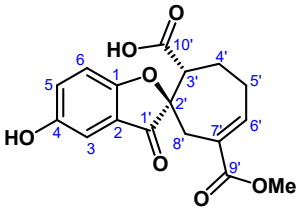


Spiroapplanatumine F (6)

Position	Natural (Cheng)[a] (600 M, CD_3OD)	Synthetic (us)[a] (500 M, CD_3OD)	Δδ (*Nat-Syn*)
3	6.89, d (2.5)	6.89, d (2.7)	0
5	7.11, dd (8.8, 2.5)	7.12, dd (8.8, 2.7)	–0.01
6	6.93, d (8.8)	6.94, d (8.8)	–0.01
3'	3.23, dd (10.3, 3.0)	3.25, dd (12.2, 3.1)	–0.02
4'	2.27, m	2.28, m	–0.01
	2.01, m	2.02, m	–0.01
5'	2.65, m	2.66, m	–0.01
	2.45, m	2.47, m	–0.02
6'	7.39, dd (8.3, 5.5)	7.39, dd (8.4, 5.6)	0
8'	2.92, s	2.94, s	–0.02
9'-OMe	3.65, s	3.66, s	–0.01

[a] Chemical shifts referenced to residual undeuterated MeOH at 3.31 ppm.

Table S8. Comparison of ^{13}C NMR spectroscopic data of the natural (Cheng)[S2] and synthetic spiroapplanatumine F (6).



Spiroapplanatumine F (6)

Position	Natural (Cheng)[a] (150 M, CD_3OD)	Synthetic (us)[a] (126 M, CD_3OD)	Δδ (*Nat-Syn*)
1	165.6	165.6	0
2	124.0	123.9	+0.1
3	108.3	108.2	+0.1
4	153.7	153.7	0
5	127.2	127.3	–0.1
6	114.6	114.6	0
1'	203.4	203.2	+0.2
2'	86.6	86.5	+0.1
3'	58.2[b]	57.6	+0.6
4'	24.8	24.8	0
5'	28.1	28.0	+0.1
6'	146.8	146.7	+0.1
7'	128.7	128.7	0
8'	35.2	35.2	0
9'	168.8	168.8	0
10'	175.8[c]	175.1	+0.7
9'-OMe	52.5	52.5	0

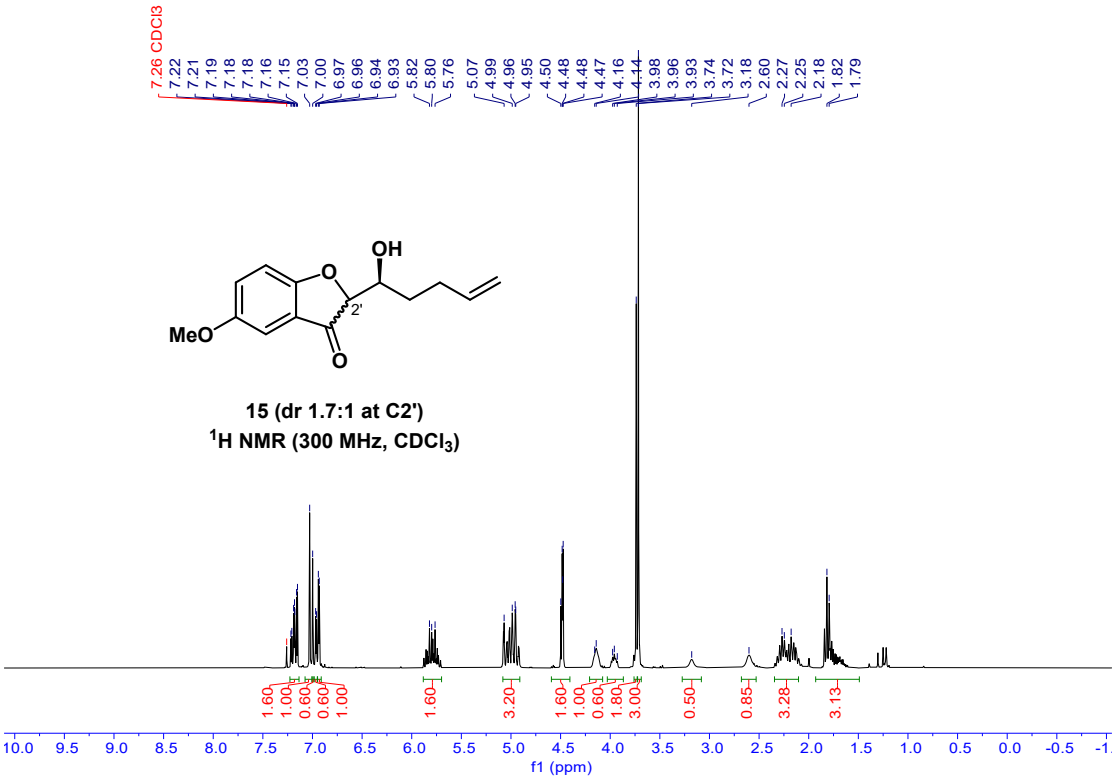
[a] Chemical shifts referenced to CD_3OD at 49.00 ppm.

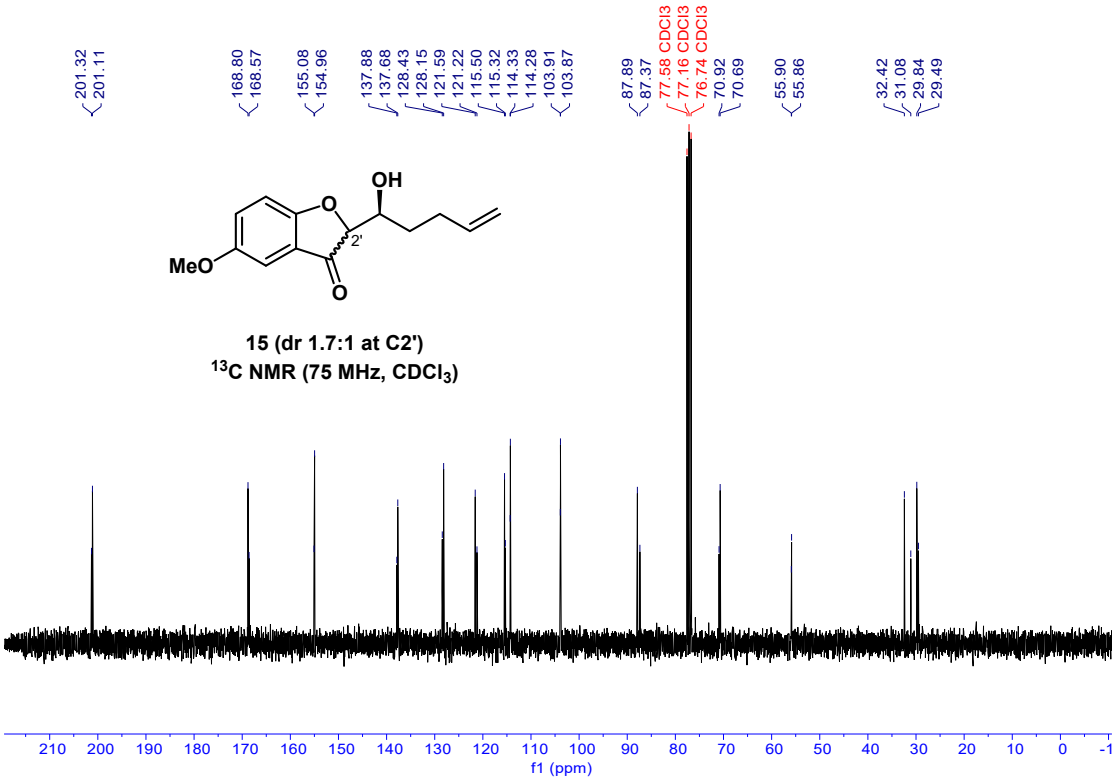
[b] In the ^{13}C NMR spectrum provided by Cheng,[S2] there are some impurities. There is

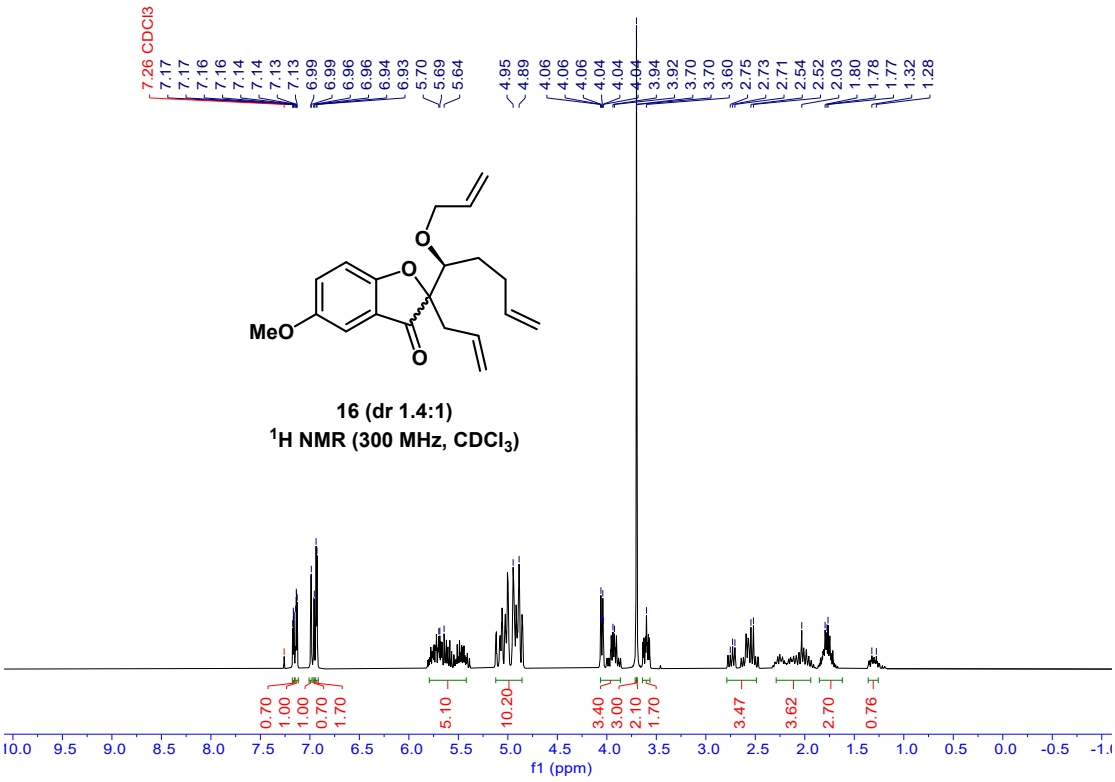
an unassigned peak near this signal (see Page S75).

[c] This signal is very weak in the original ^{13}C NMR spectrum provided by Cheng (see Page S75).[S2]

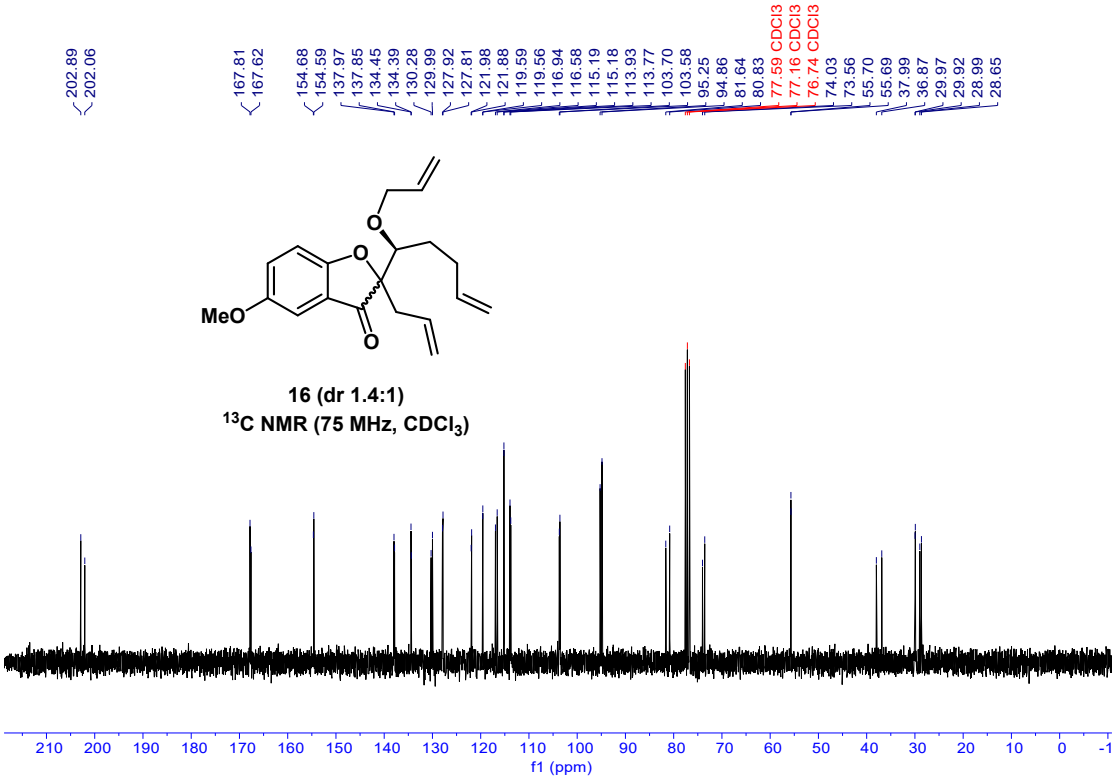
5. NMR Spectra



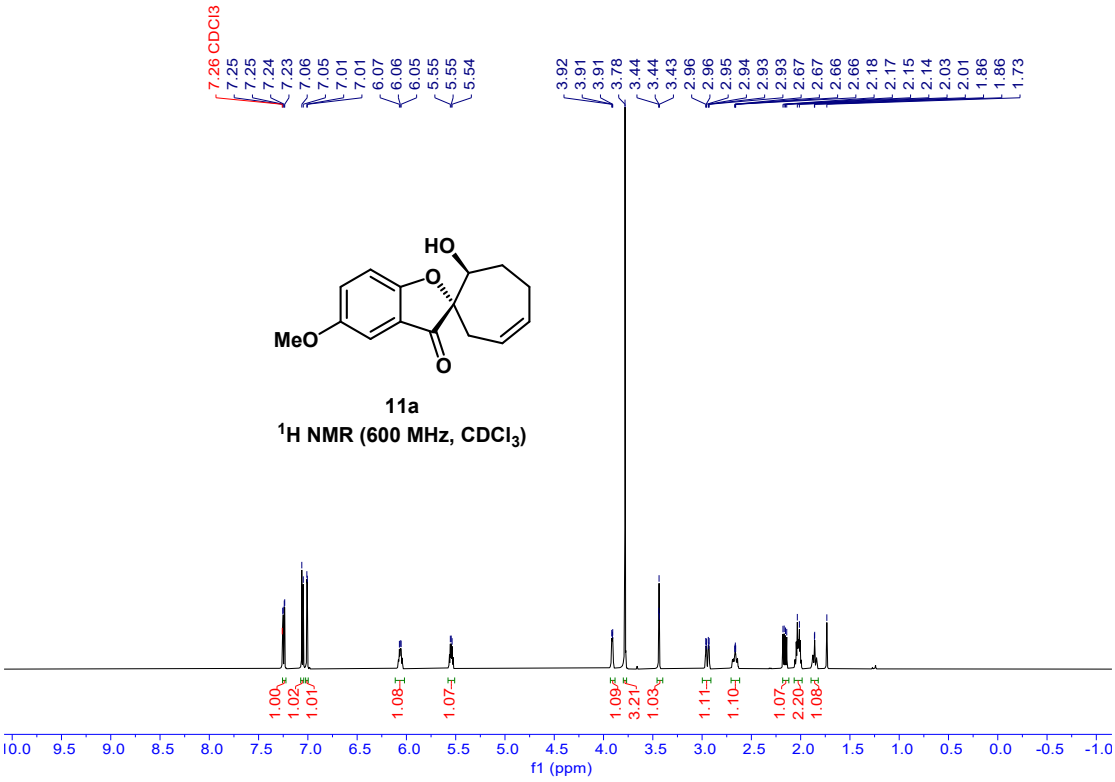




16 (dr 1.4:1)
^{1}H NMR (300 MHz, $CDCl_3$)

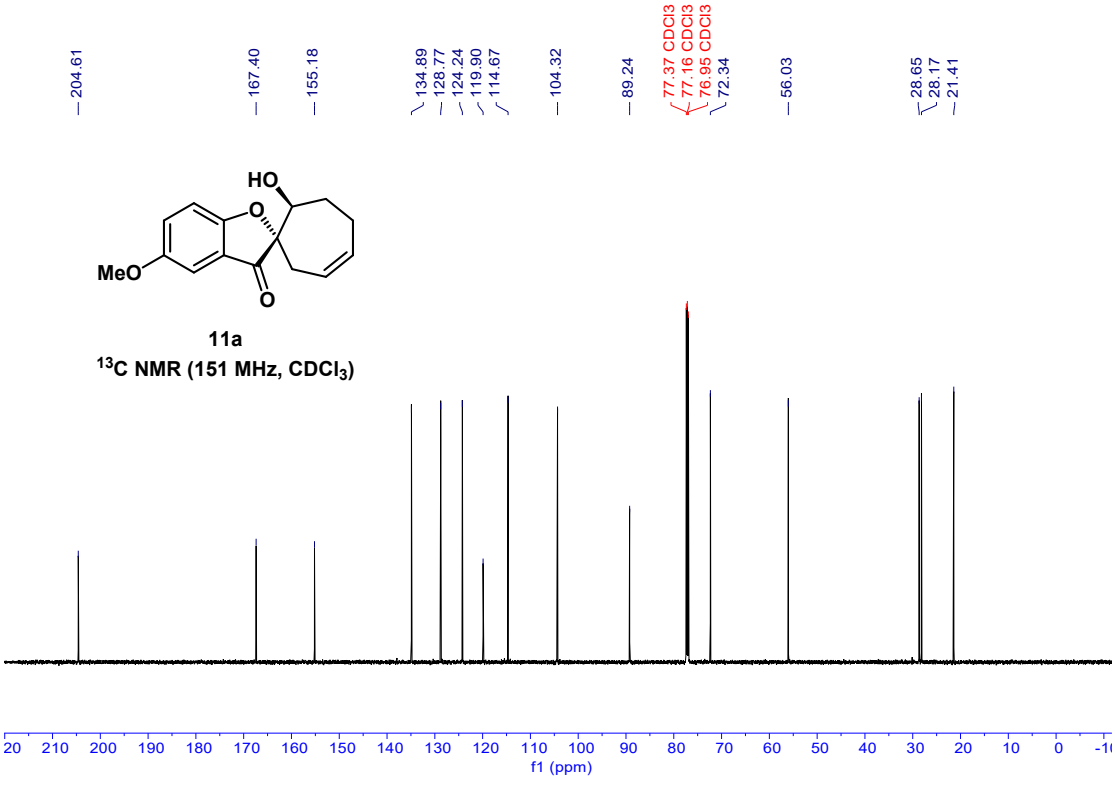


16 (dr 1.4:1)
^{13}C NMR (75 MHz, $CDCl_3$)



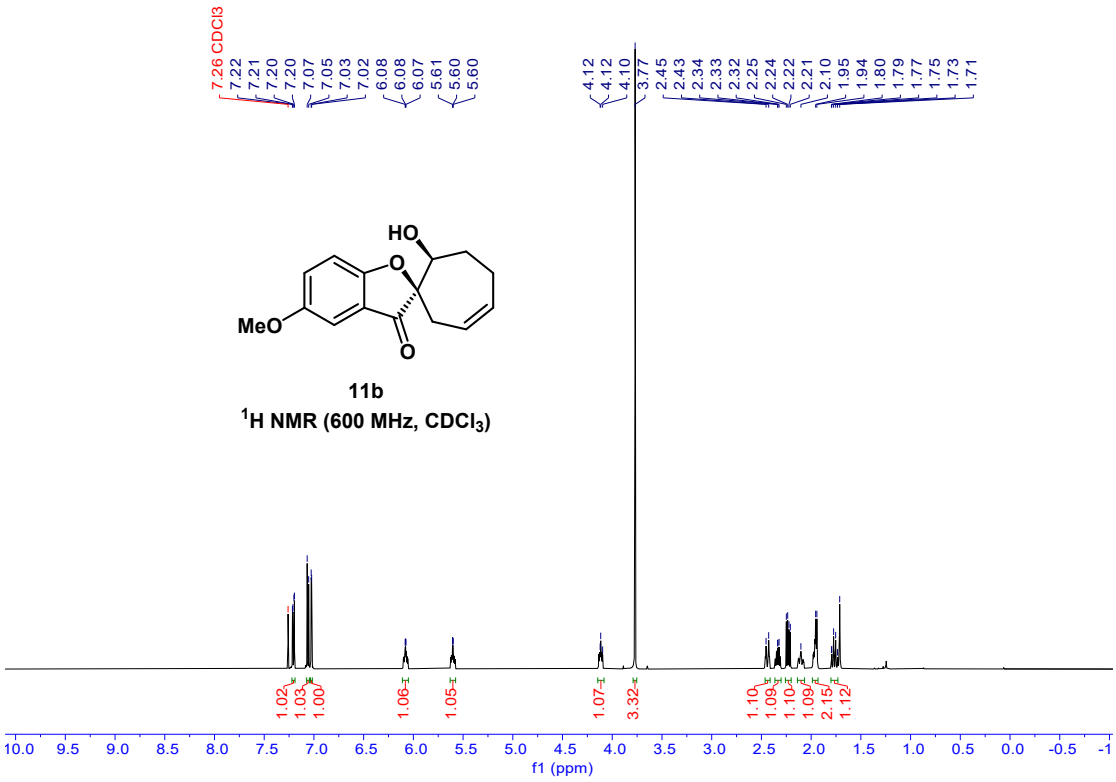
11a

^{1}H NMR (600 MHz, $CDCl_3$)



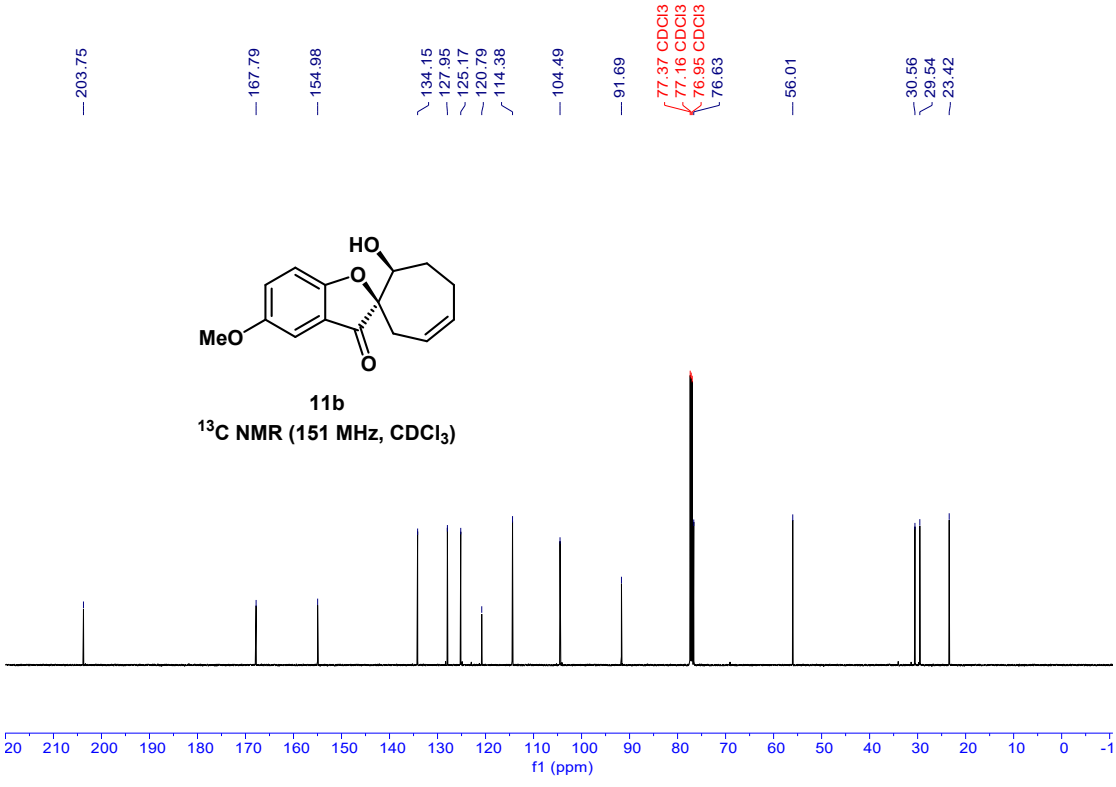
11a

^{13}C NMR (151 MHz, $CDCl_3$)



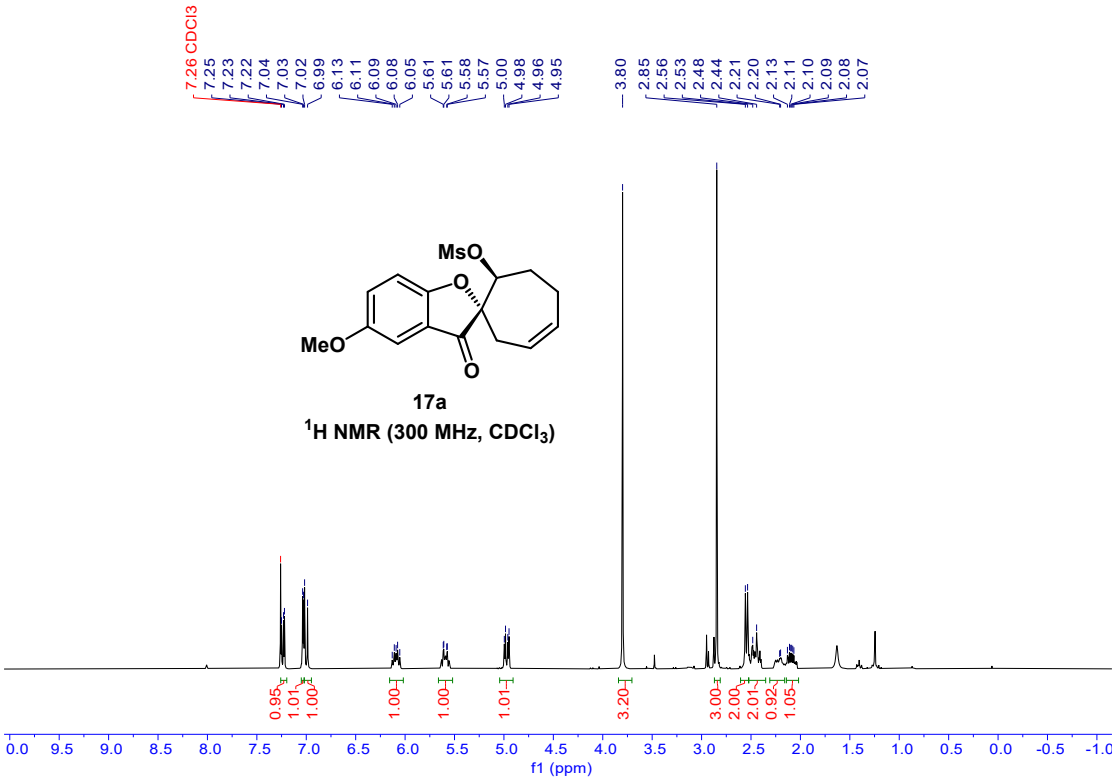
11b

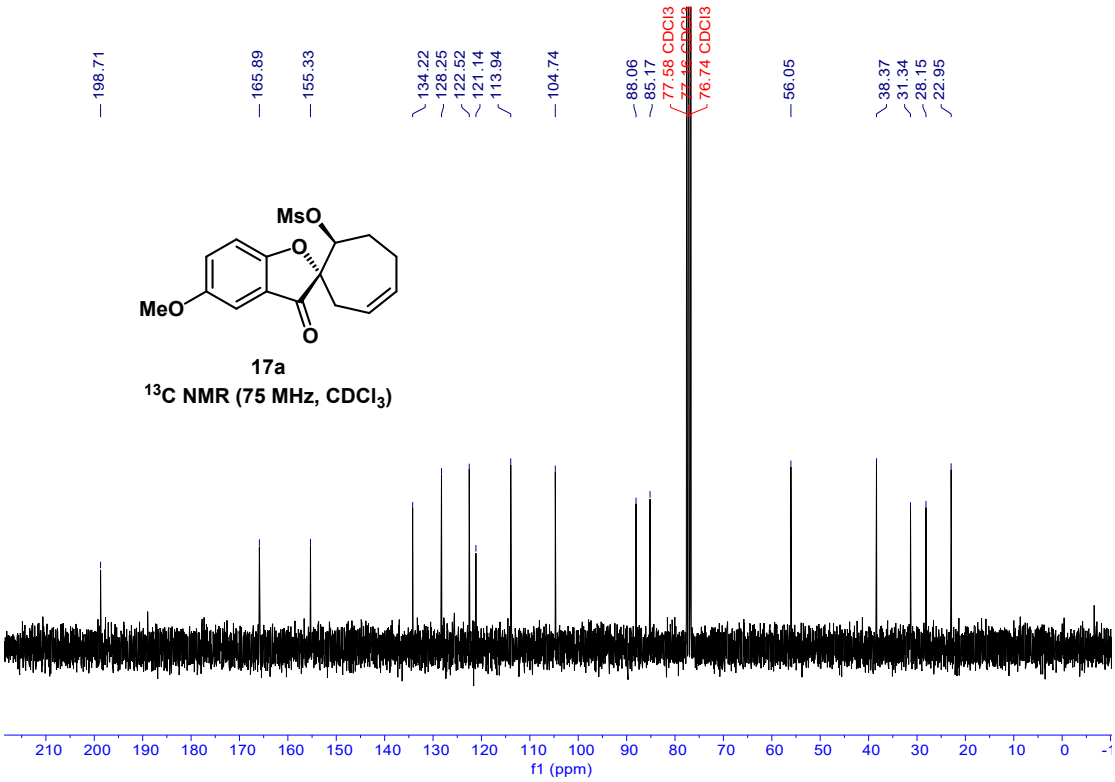
^{1}H NMR (600 MHz, $CDCl_3$)

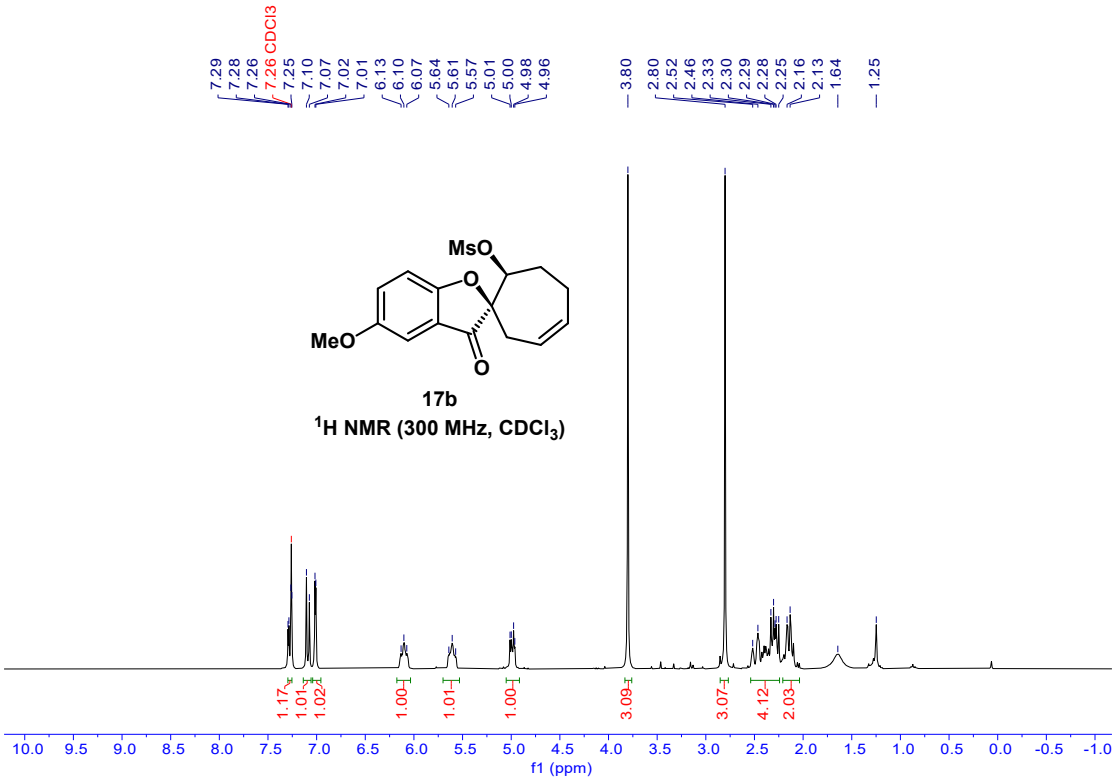


11b

^{13}C NMR (151 MHz, $CDCl_3$)

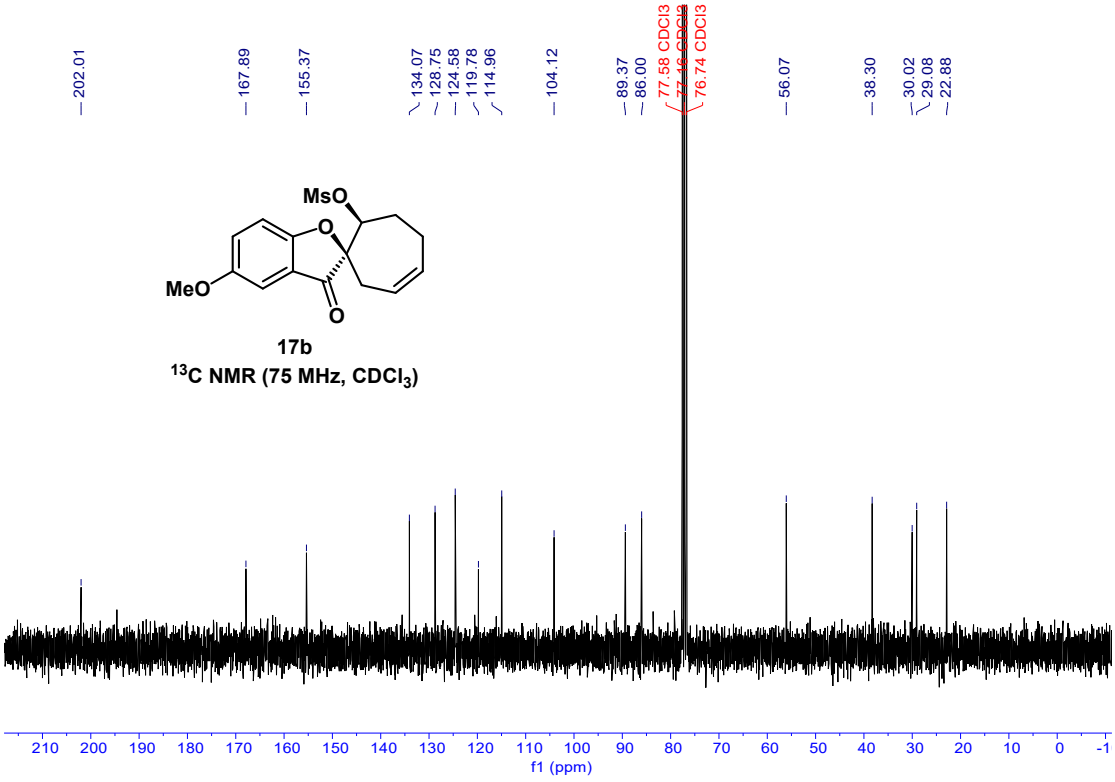

MsO
O
MeO
O
17a
^{1}H NMR (300 MHz, CDCl$_3$)
f1 (ppm)


MsO
O
MeO
O
17a
^{13}C NMR (75 MHz, CDCl$_3$)
f1 (ppm)



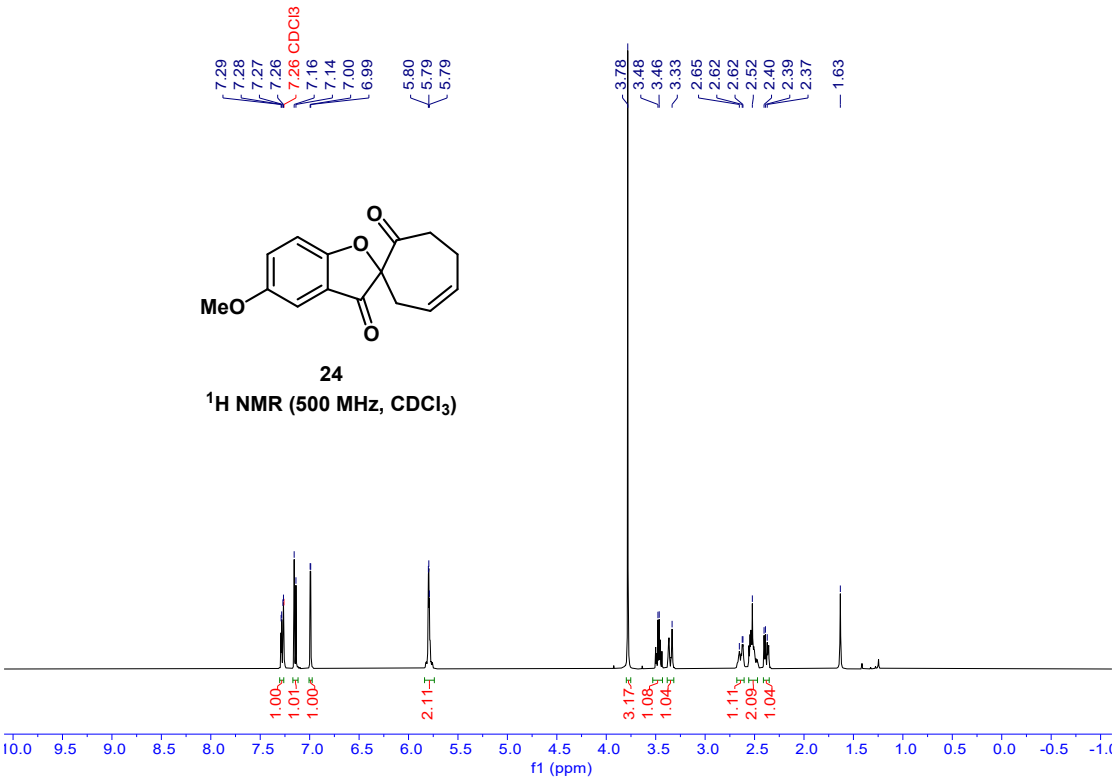
17b

^{1}H NMR (300 MHz, $CDCl_3$)



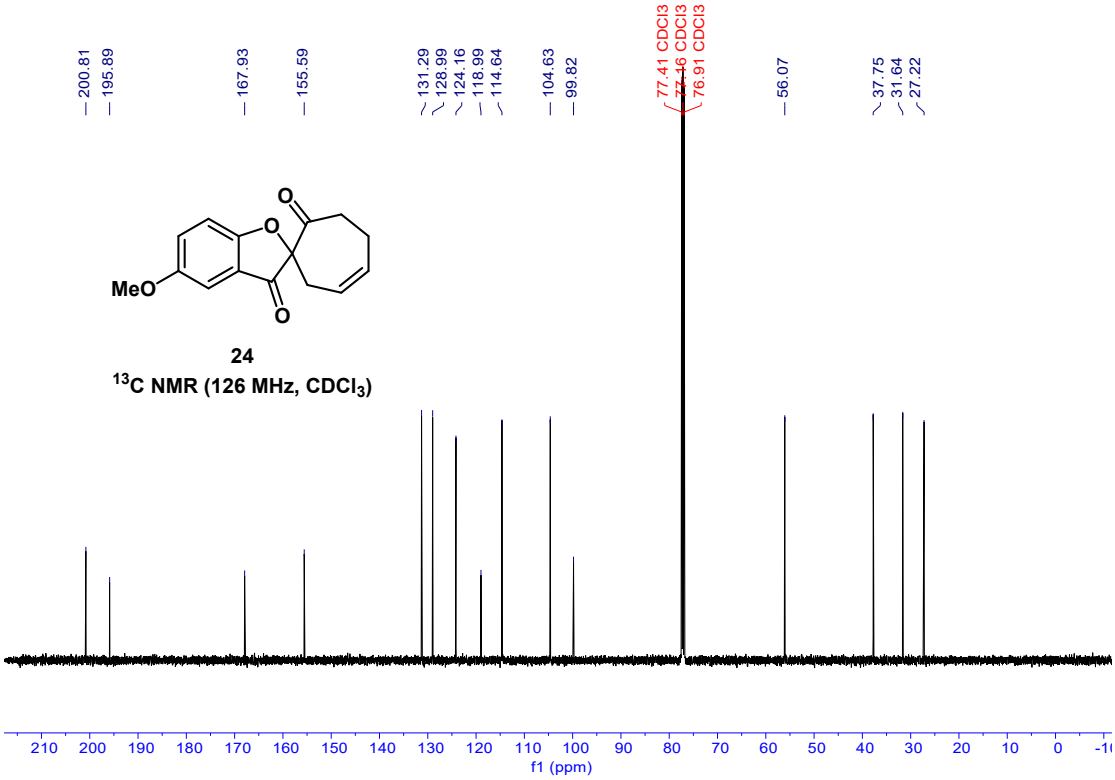
17b

^{13}C NMR (75 MHz, $CDCl_3$)



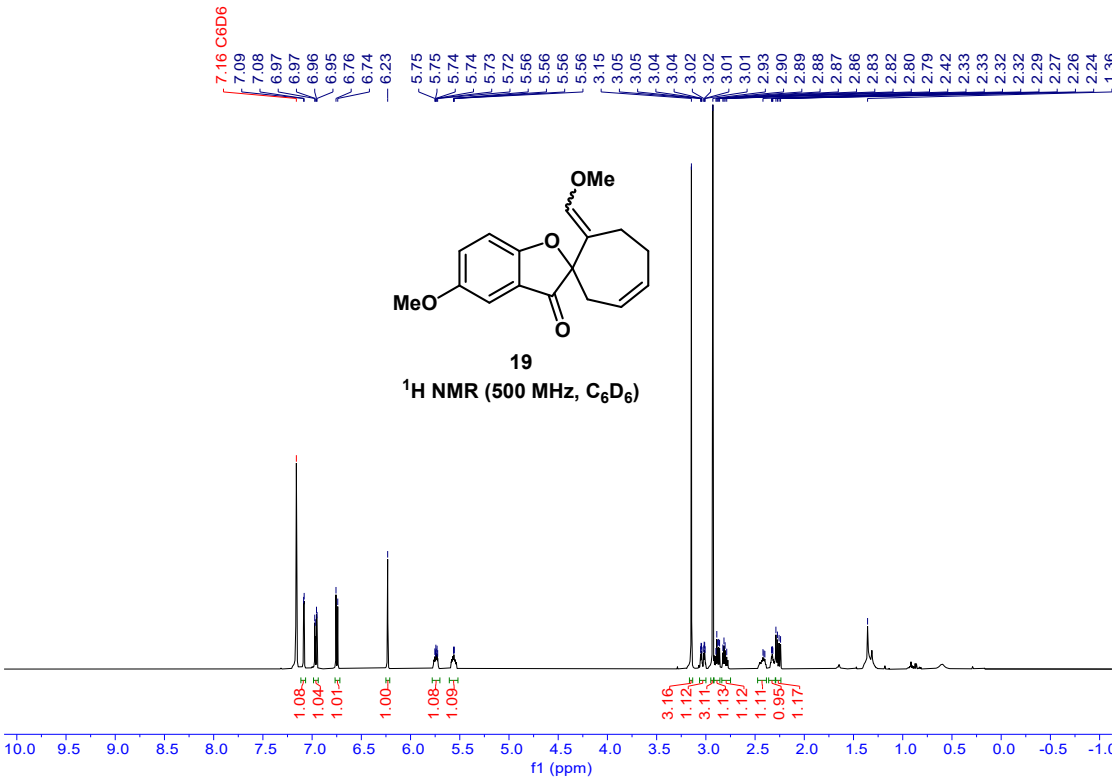
24

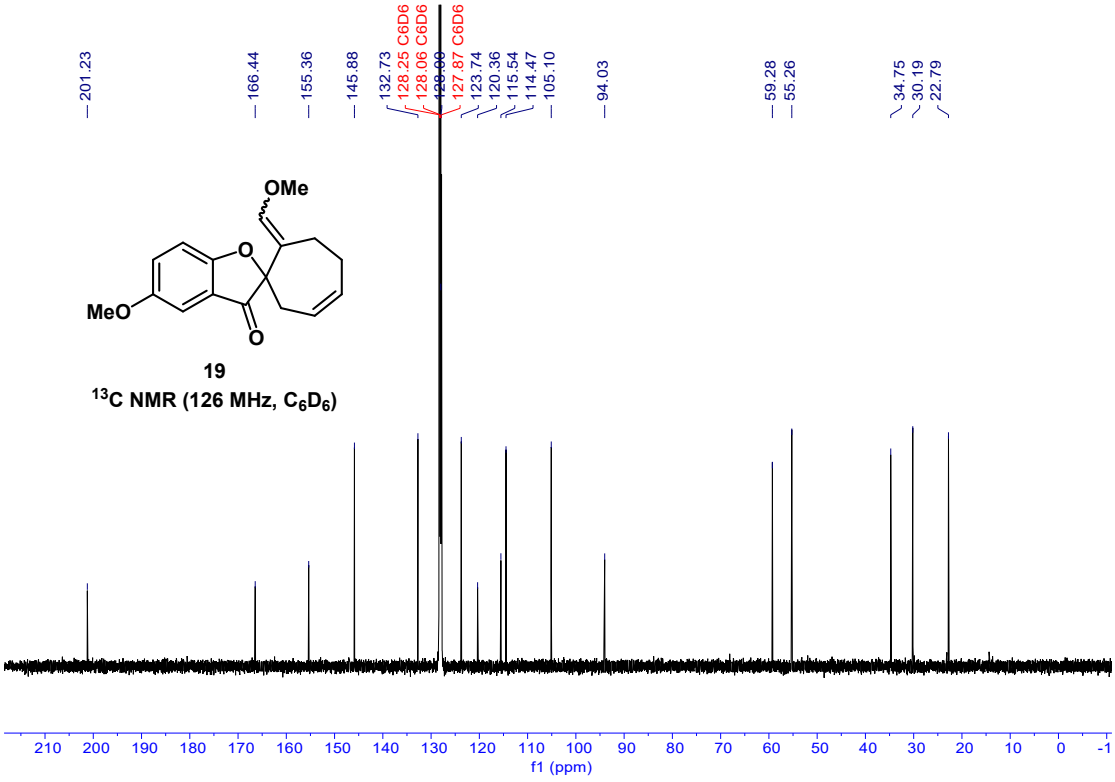
^{1}H NMR (500 MHz, $CDCl_3$)

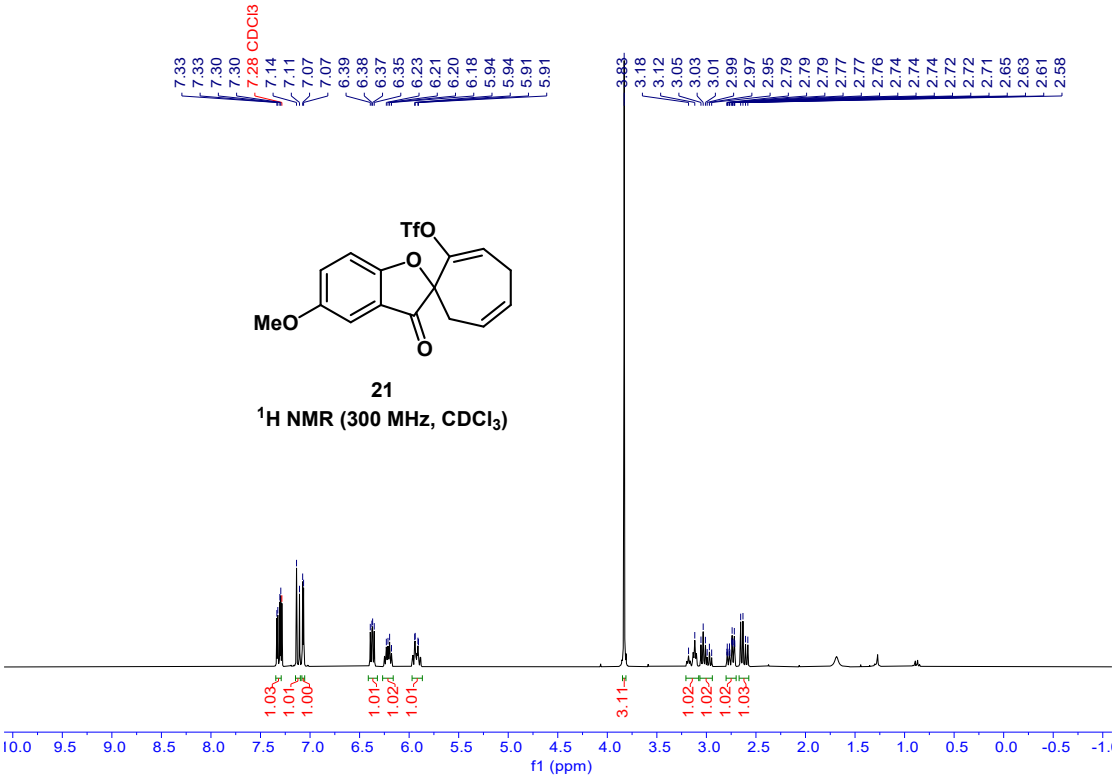


24

^{13}C NMR (126 MHz, $CDCl_3$)

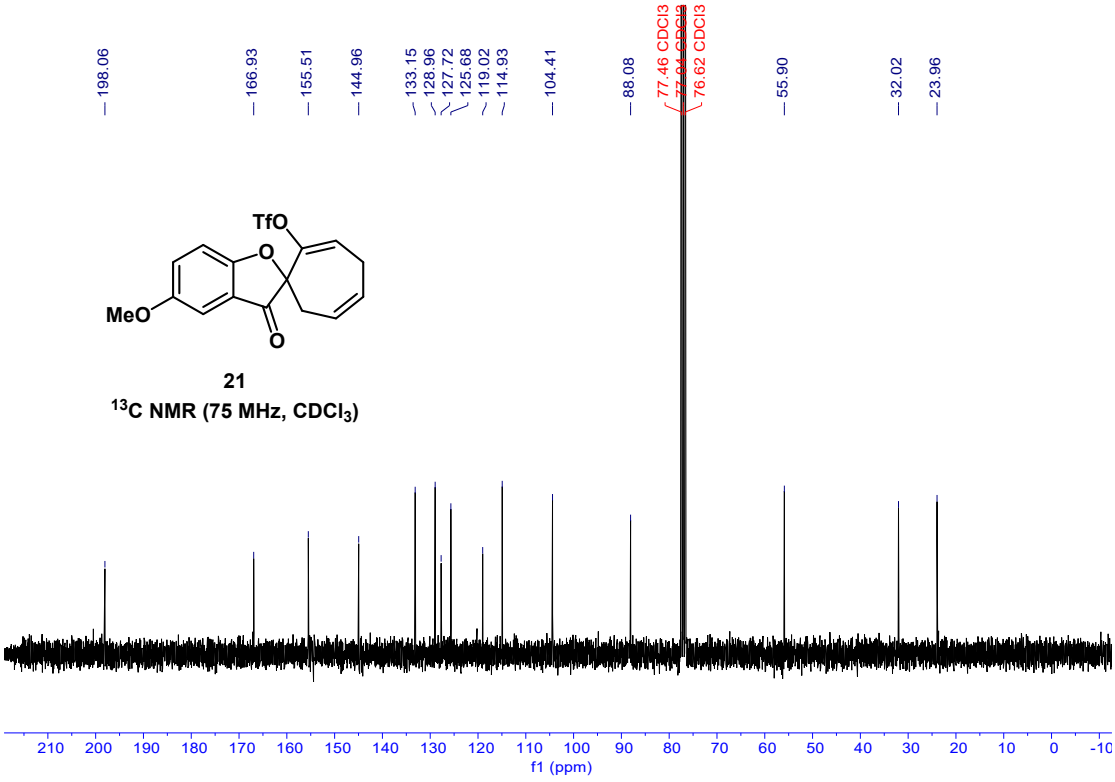

OMe
MeO
O
O
19
^{1}H NMR (500 MHz, C_6D_6)
f1 (ppm)


OMe
MeO
O
O
19
^{13}C NMR (126 MHz, C_6D_6)
f1 (ppm)



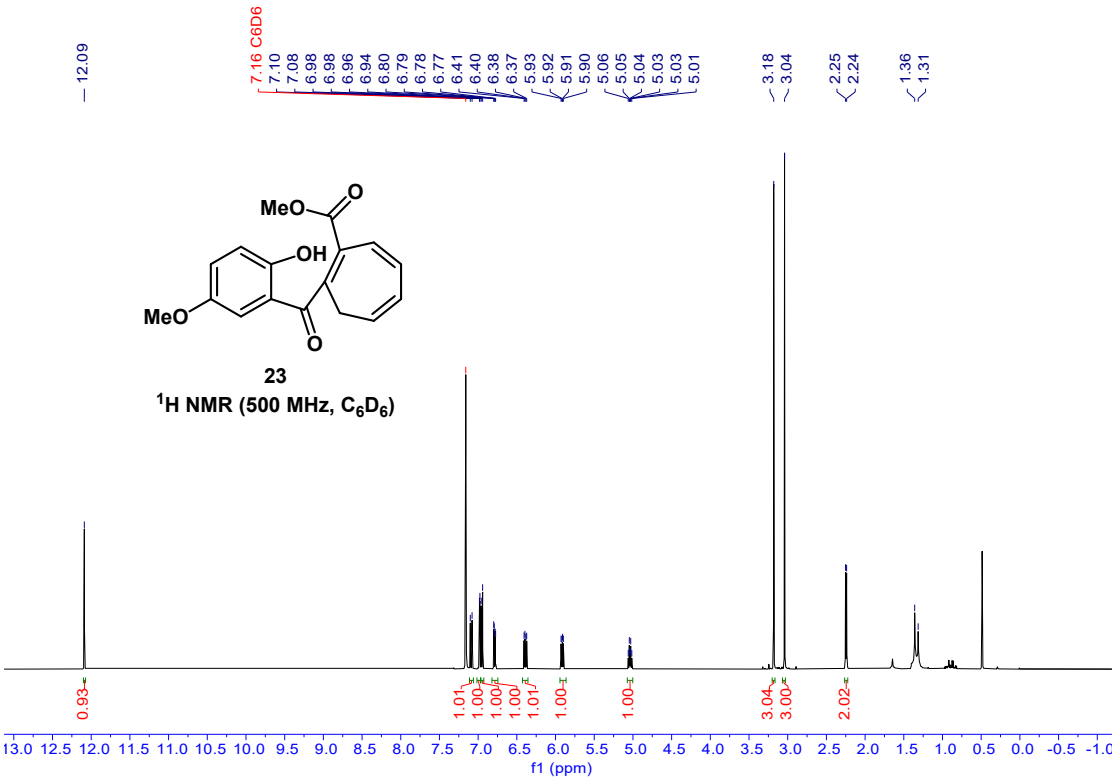
21

^{1}H NMR (300 MHz, $CDCl_3$)



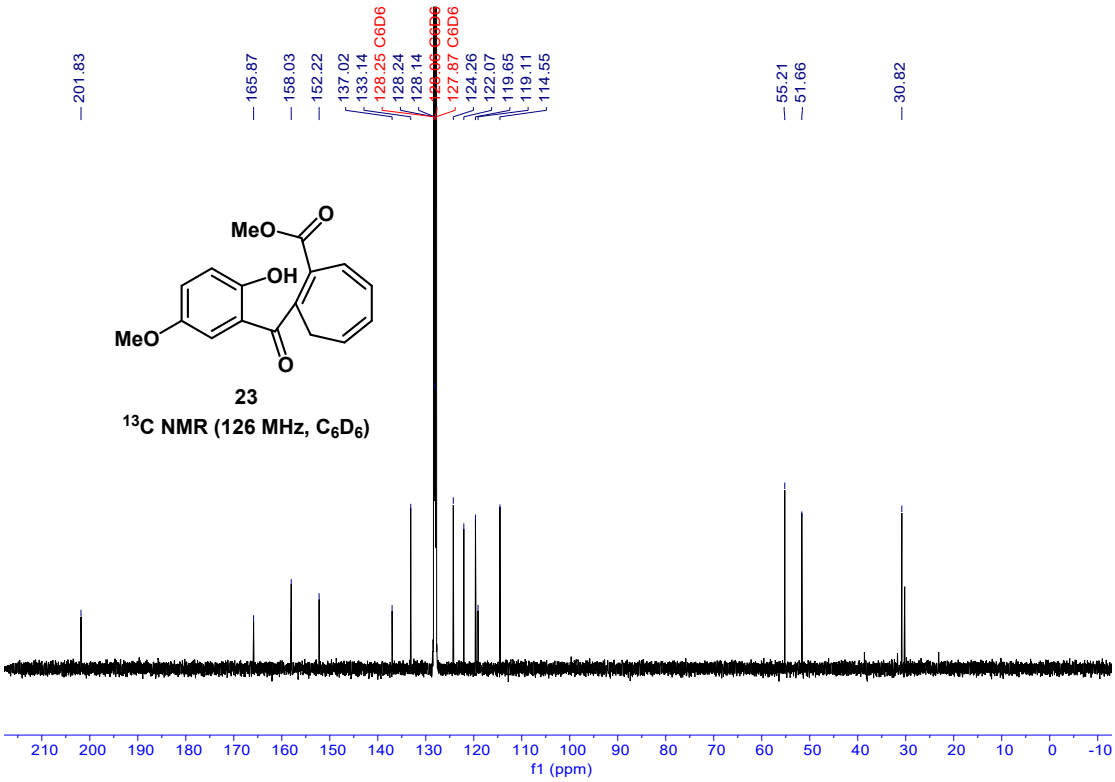
21

^{13}C NMR (75 MHz, $CDCl_3$)



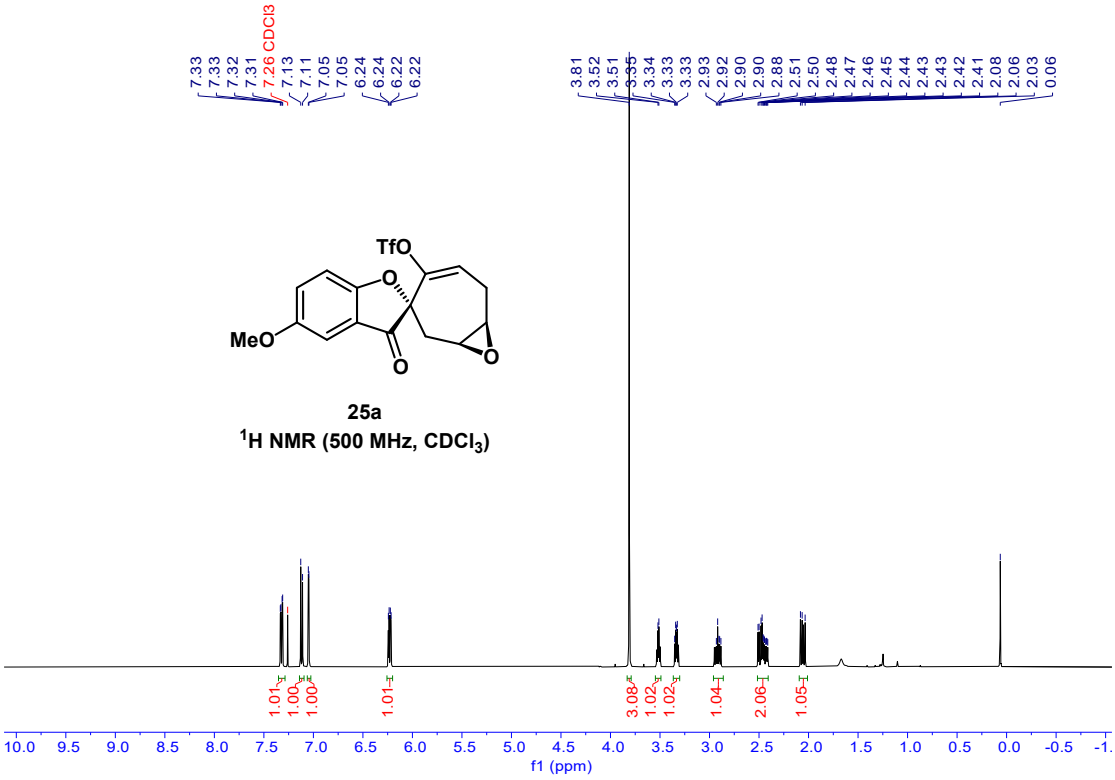
23

^{1}H NMR (500 MHz, C_6D_6)



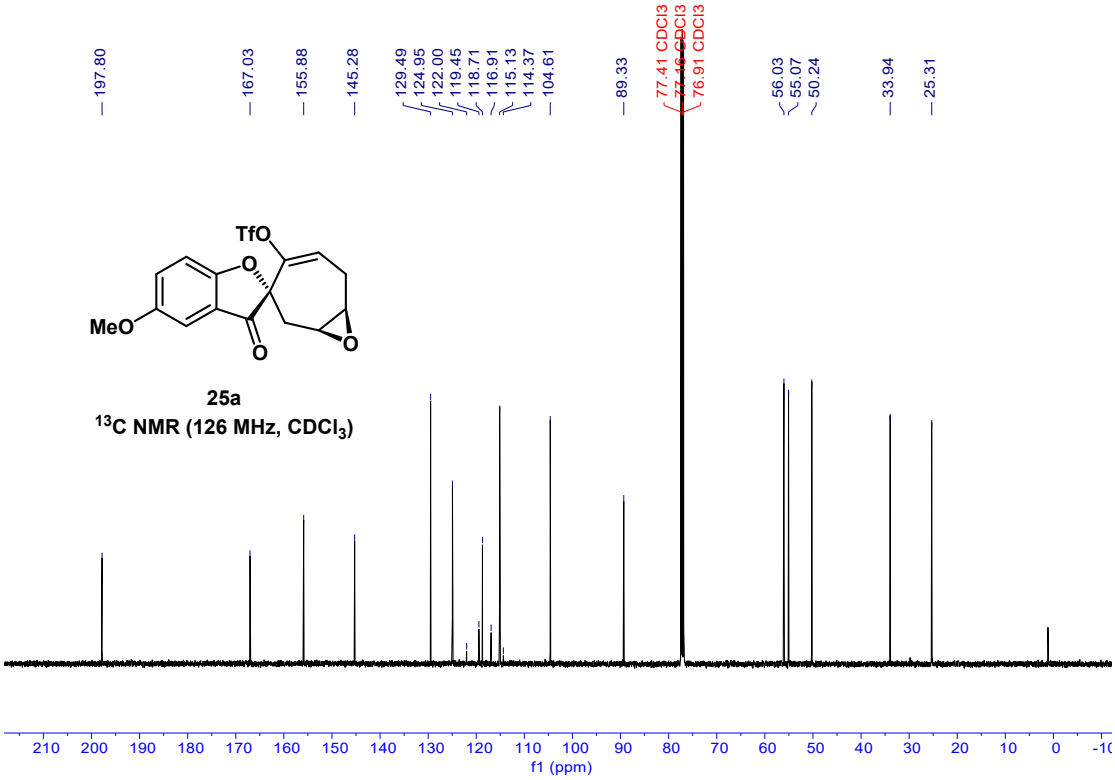
23

^{13}C NMR (126 MHz, C_6D_6)



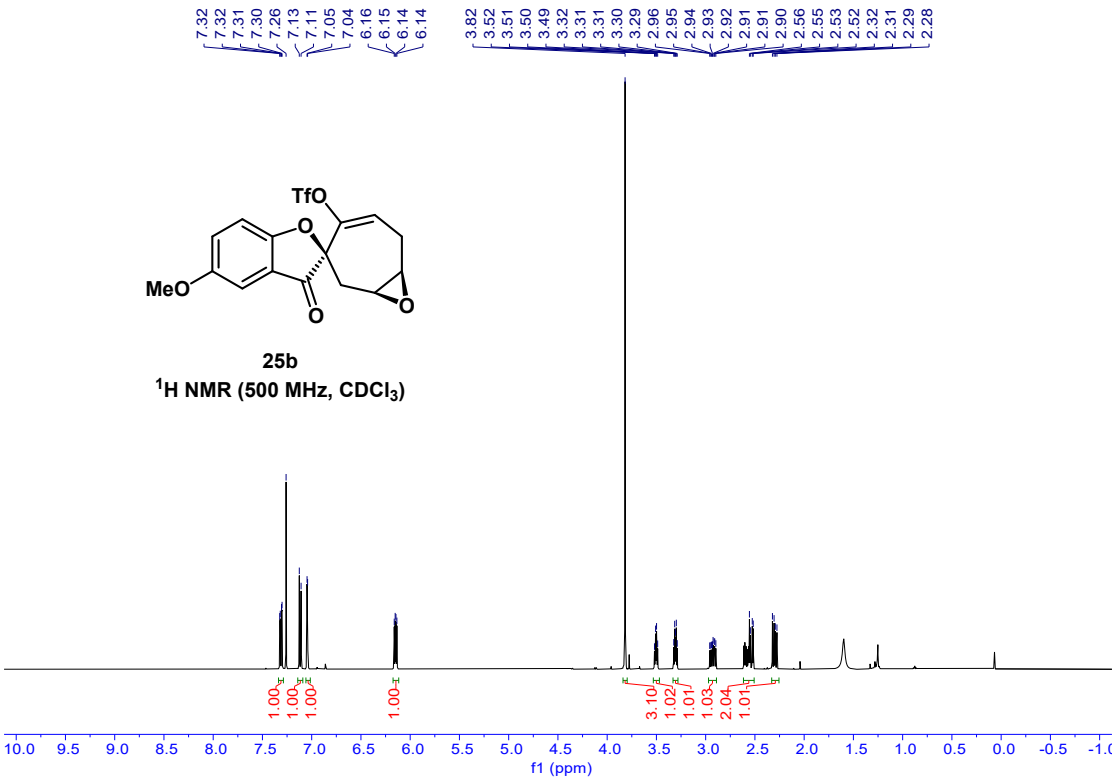
25a

^{1}H NMR (500 MHz, $CDCl_3$)



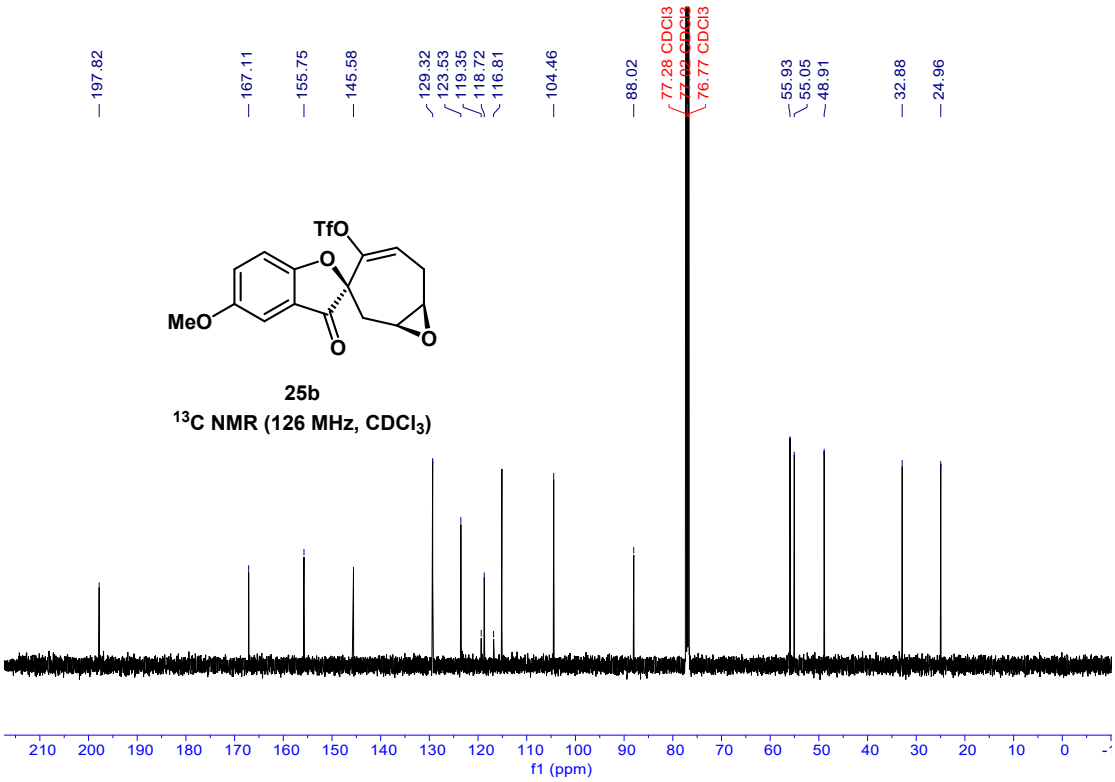
25a

^{13}C NMR (126 MHz, $CDCl_3$)



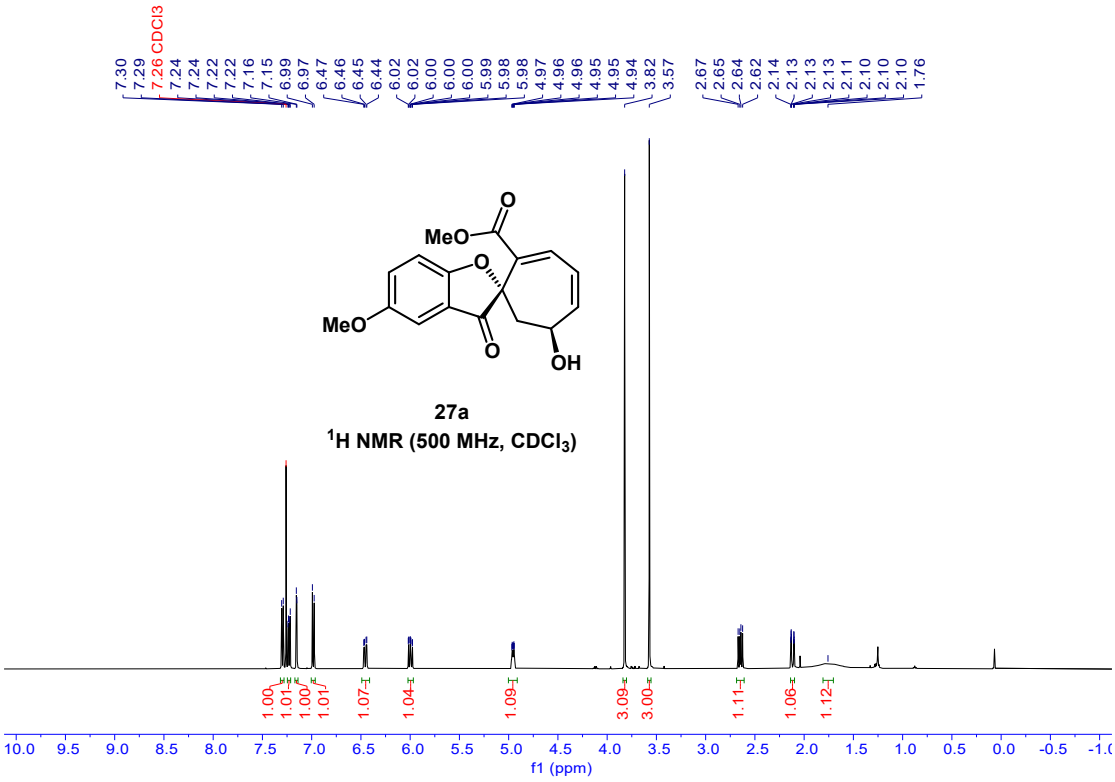
25b

^{1}H NMR (500 MHz, $CDCl_3$)



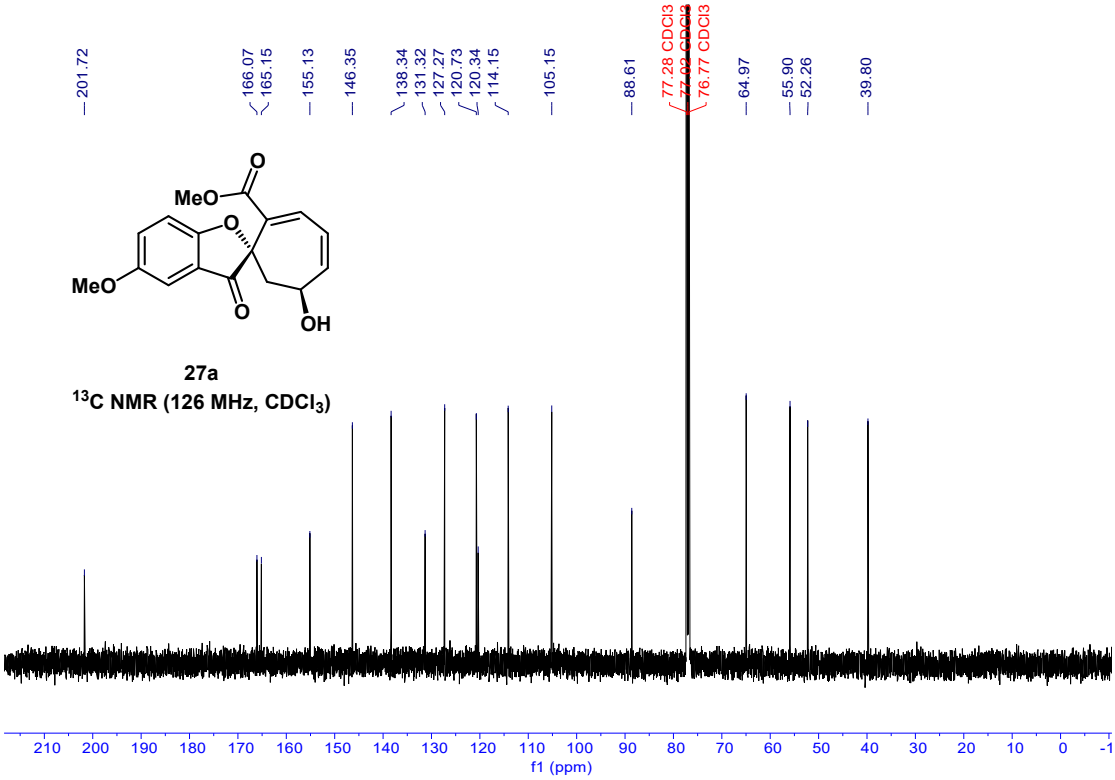
25b

^{13}C NMR (126 MHz, $CDCl_3$)



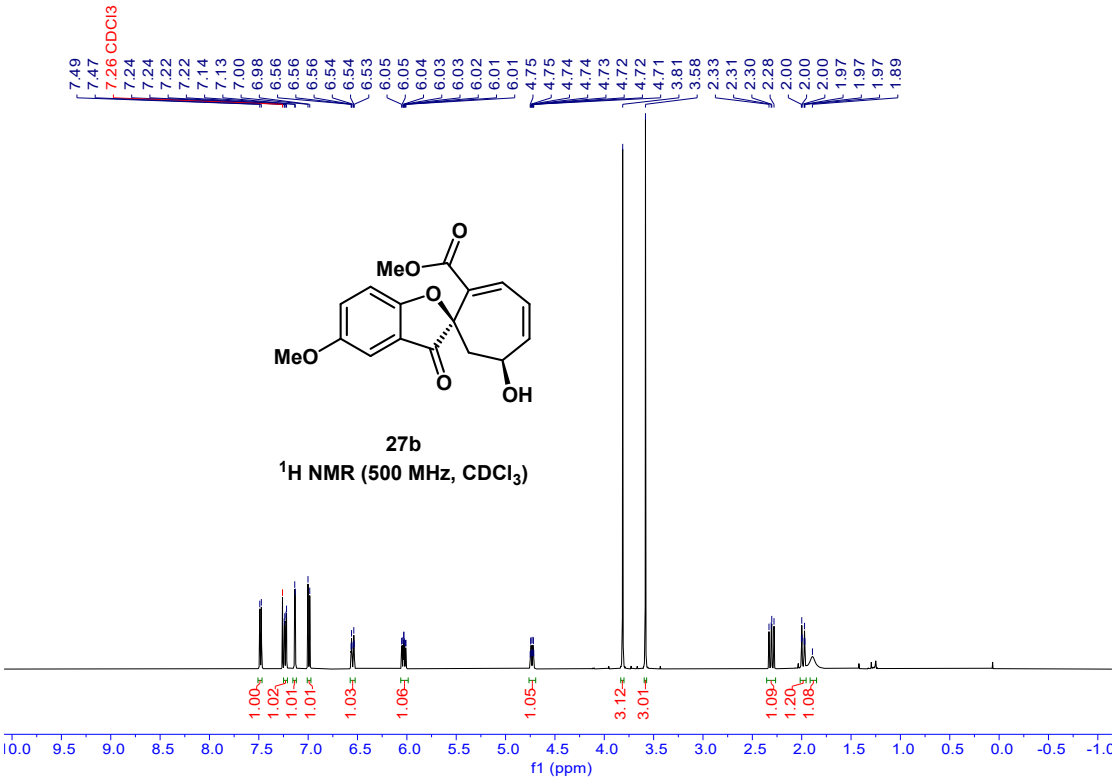
27a

^{1}H NMR (500 MHz, $CDCl_3$)



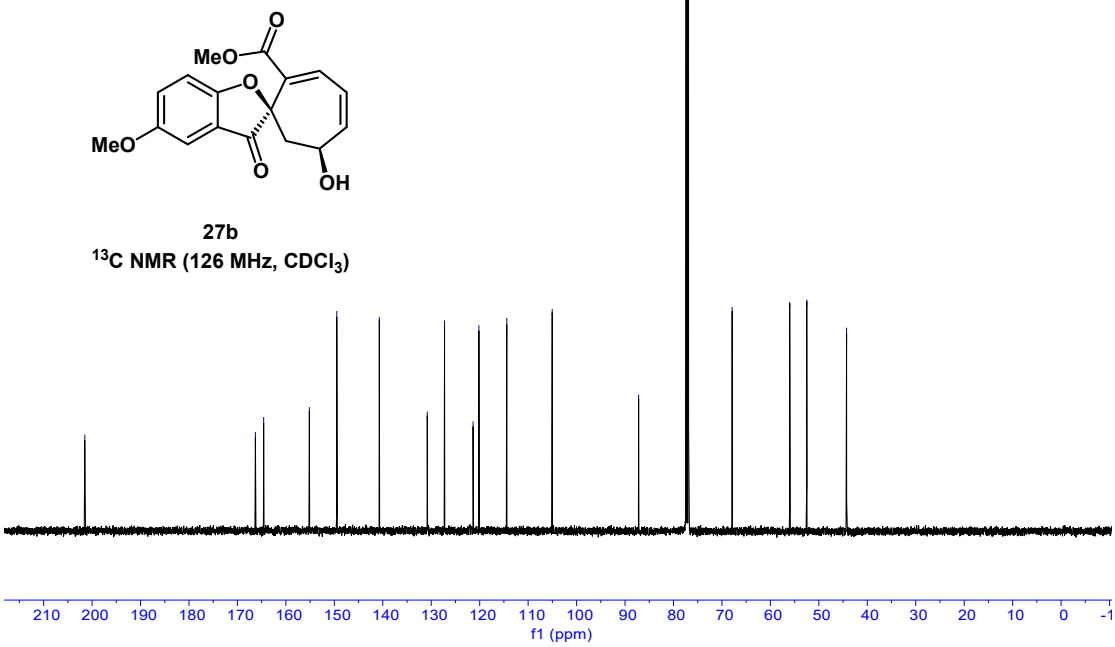
27a

^{13}C NMR (126 MHz, $CDCl_3$)



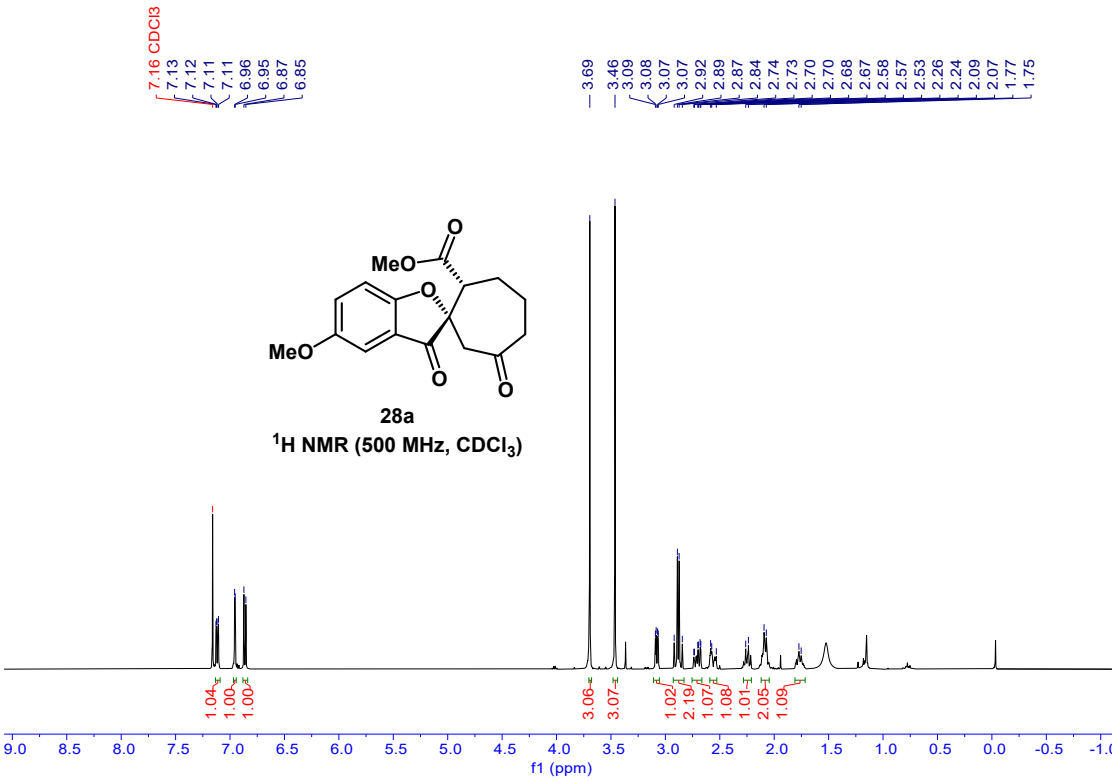
27b

^{1}H NMR (500 MHz, $CDCl_3$)



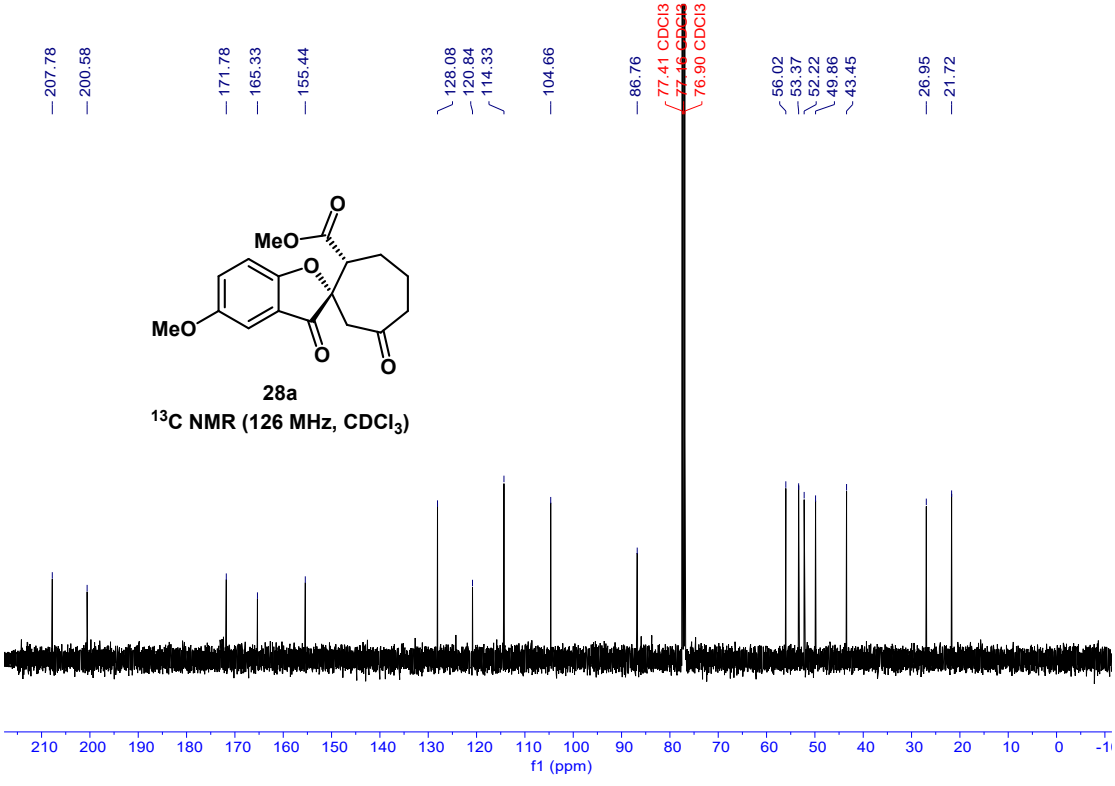
27b

^{13}C NMR (126 MHz, $CDCl_3$)



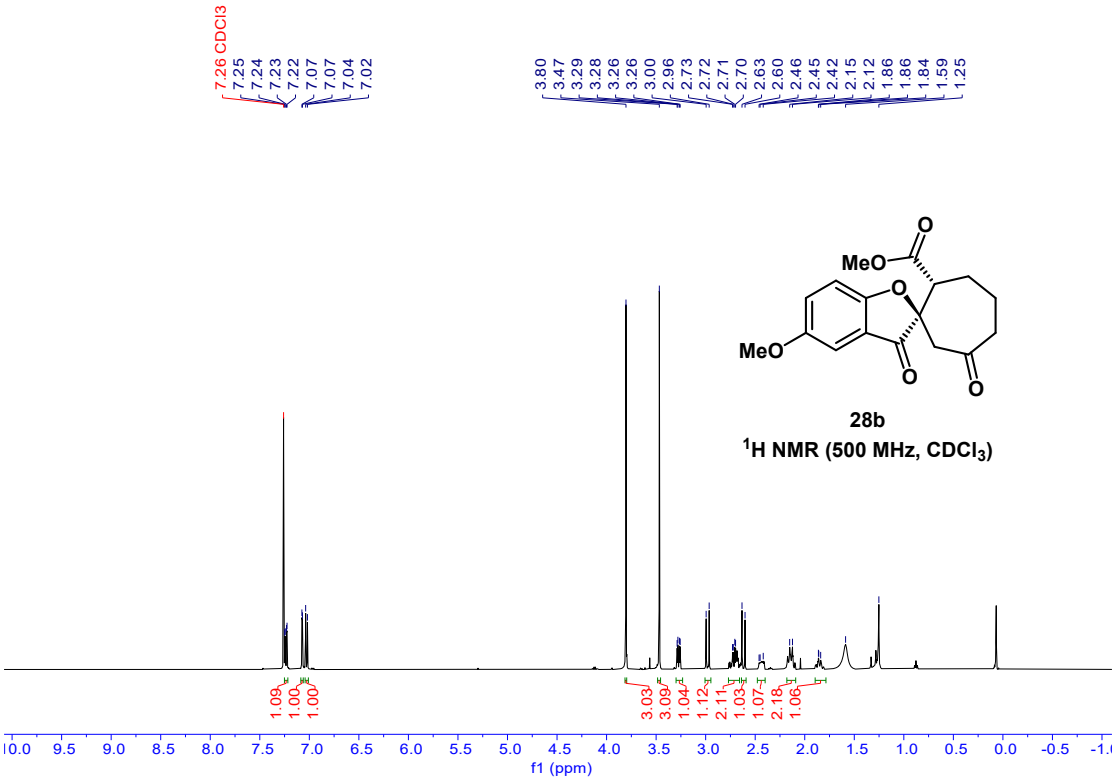
28a

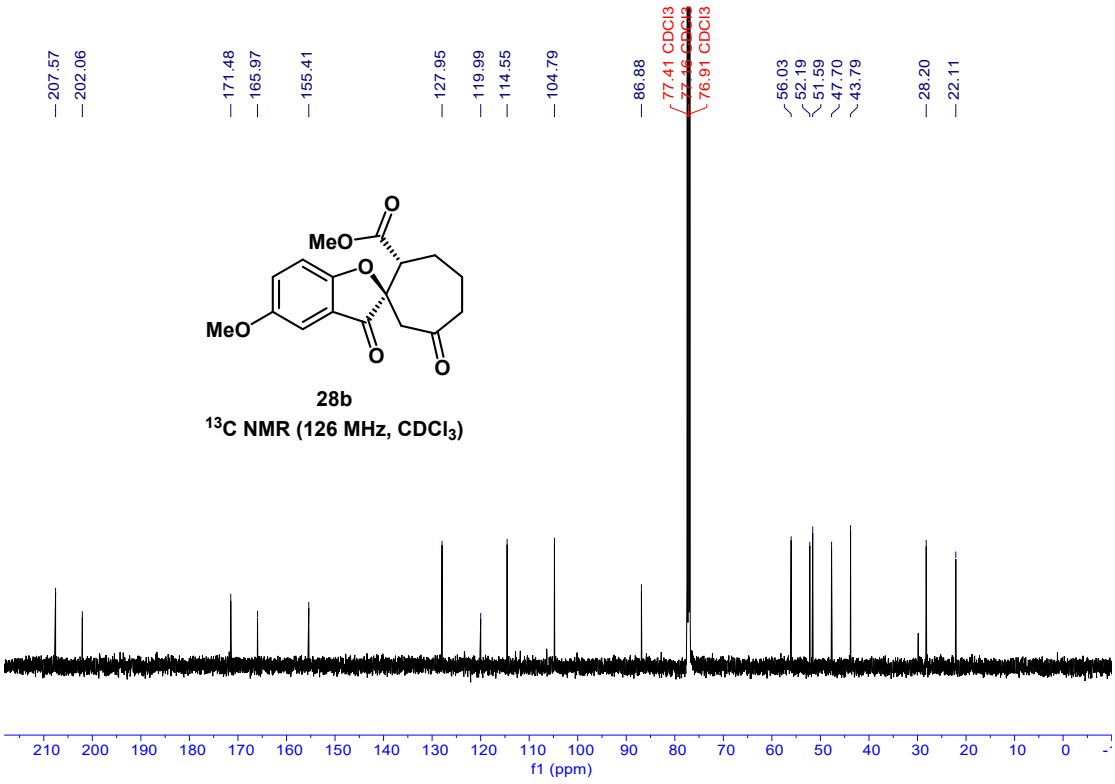
^{1}H NMR (500 MHz, $CDCl_3$)

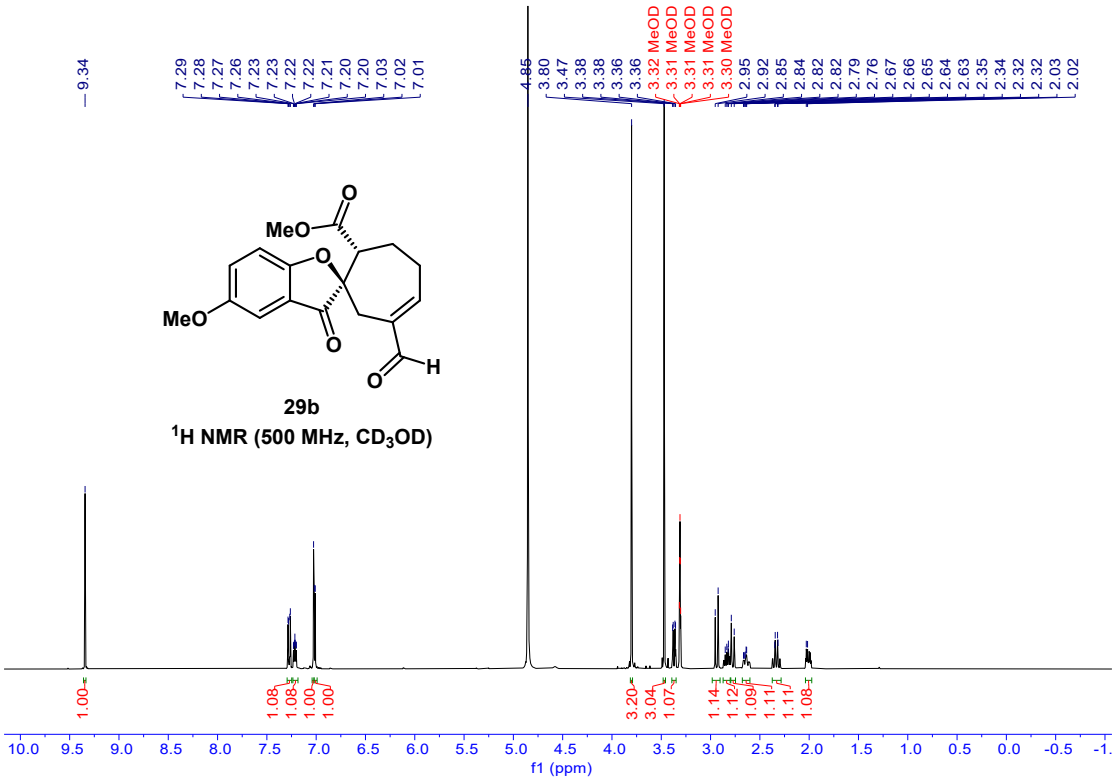


28a

^{13}C NMR (126 MHz, $CDCl_3$)

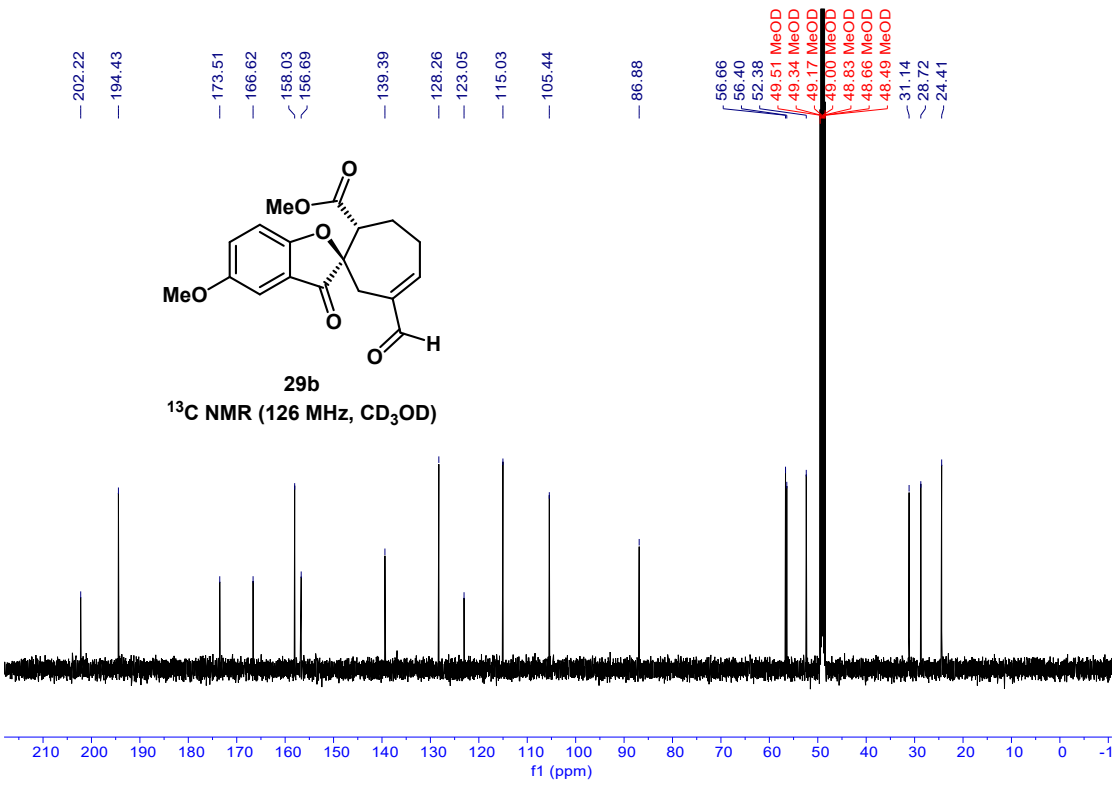

7.26 CDCl3
7.25
7.24
7.23
7.22
7.07
7.07
7.04
7.02
3.80
3.47
3.29
3.28
3.26
3.26
3.00
2.96
2.73
2.72
2.71
2.70
2.63
2.60
2.46
2.45
2.42
2.15
2.12
1.86
1.86
1.84
1.59
1.25
MeO
MeO
O
O
O
O
28b
1H NMR (500 MHz, CDCl3)
1.09
1.00
1.00
3.03
3.09
1.04
1.12
2.11
1.03
1.07
2.18
1.06
f1 (ppm)


207.57
202.06
171.48
165.97
155.41
127.95
119.99
114.55
104.79
86.88
77.41 CDCl3
76.91 CDCl3
56.03
52.19
51.59
47.70
43.79
28.20
22.11
MeO
MeO
O
O
O
O
28b
13C NMR (126 MHz, CDCl3)
f1 (ppm)



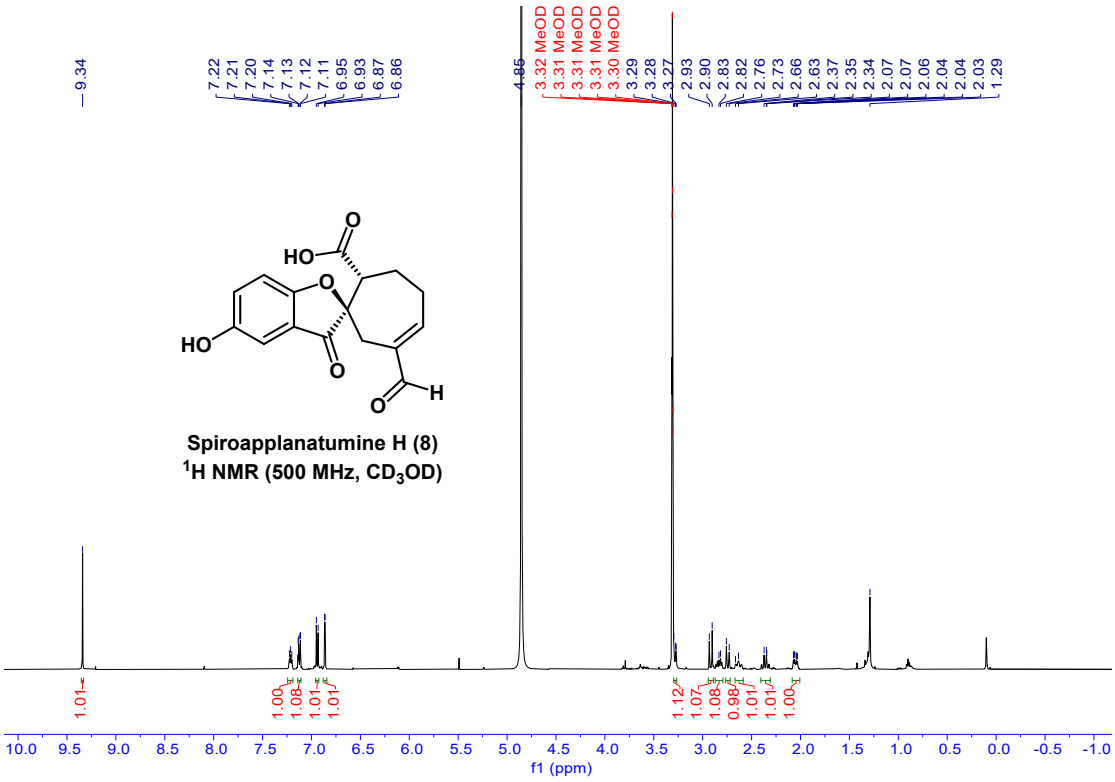
29b

^{1}H NMR (500 MHz, CD_3OD)

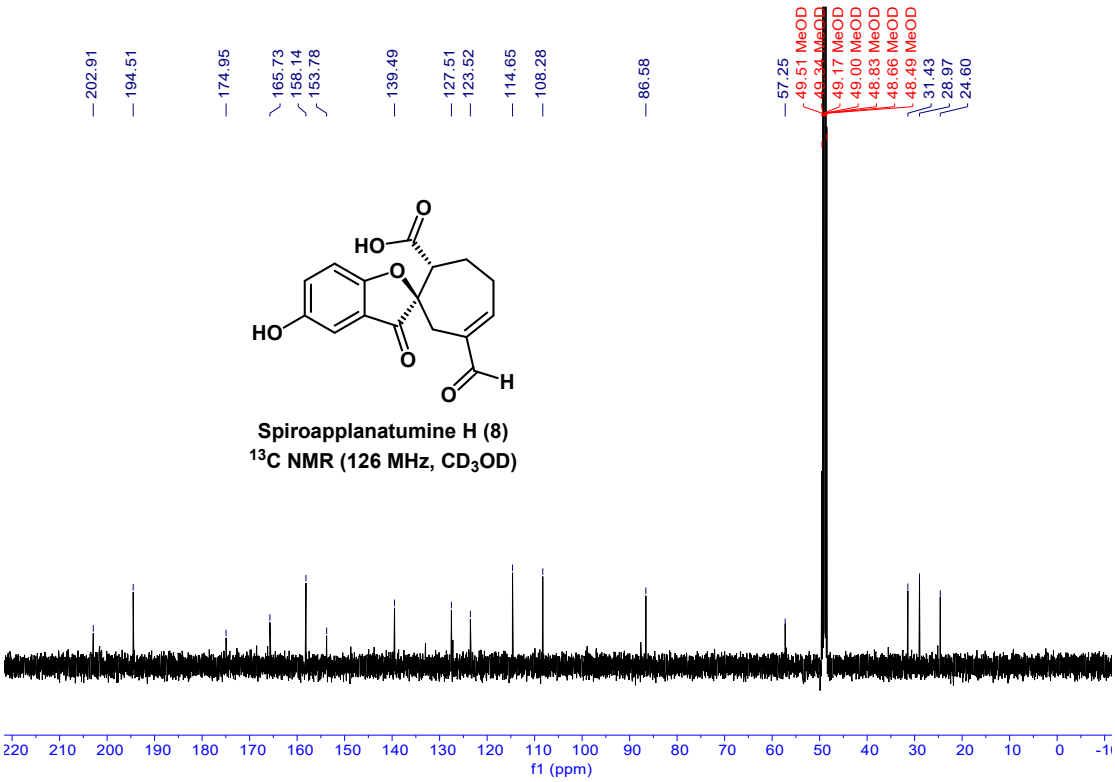


29b

^{13}C NMR (126 MHz, CD_3OD)

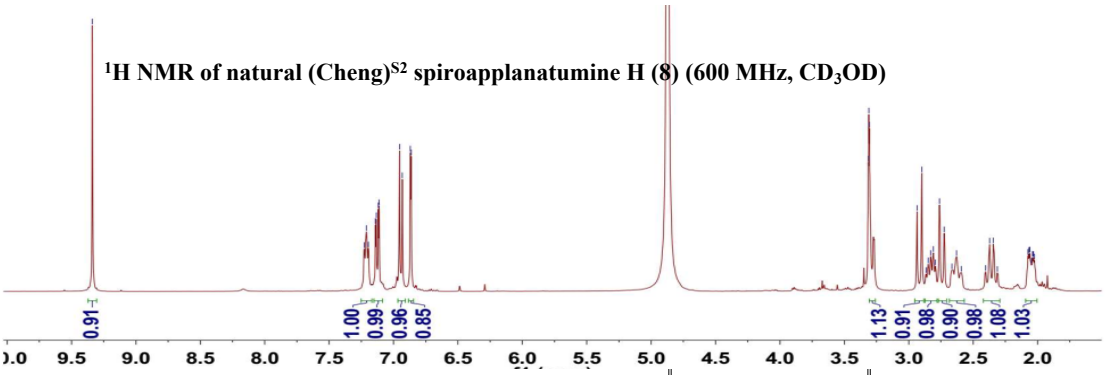


Spiroapplanatumine H (8)
^{1}H NMR (500 MHz, CD_3OD)

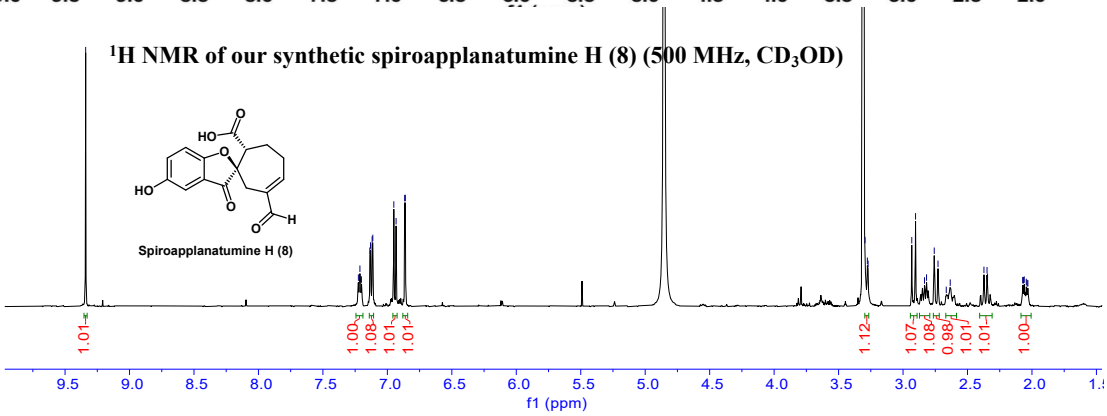


Spiroapplanatumine H (8)
^{13}C NMR (126 MHz, CD_3OD)

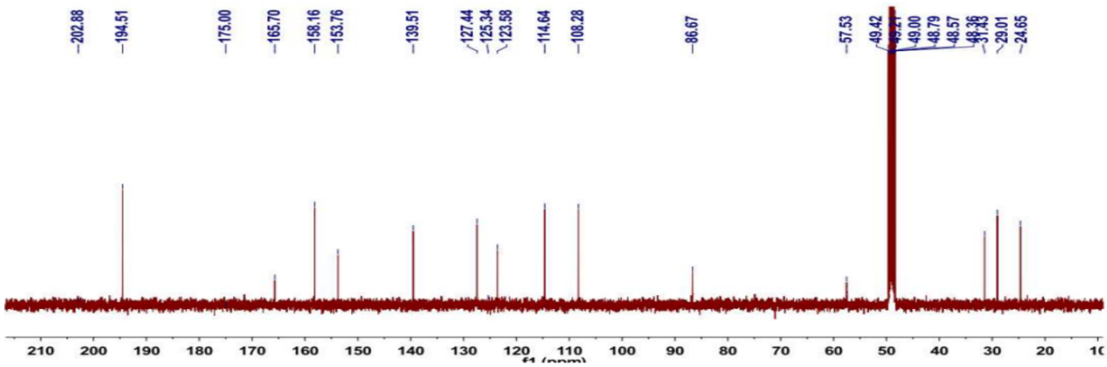
^{1}H NMR of natural (Cheng)[S2] spiroapplanatumine H (8) (600 MHz, CD_3OD)



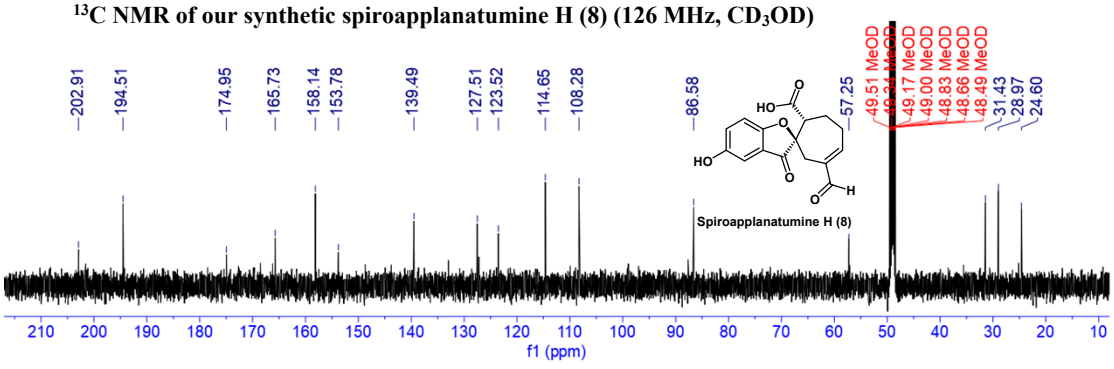
^{1}H NMR of our synthetic spiroapplanatumine H (8) (500 MHz, CD_3OD)

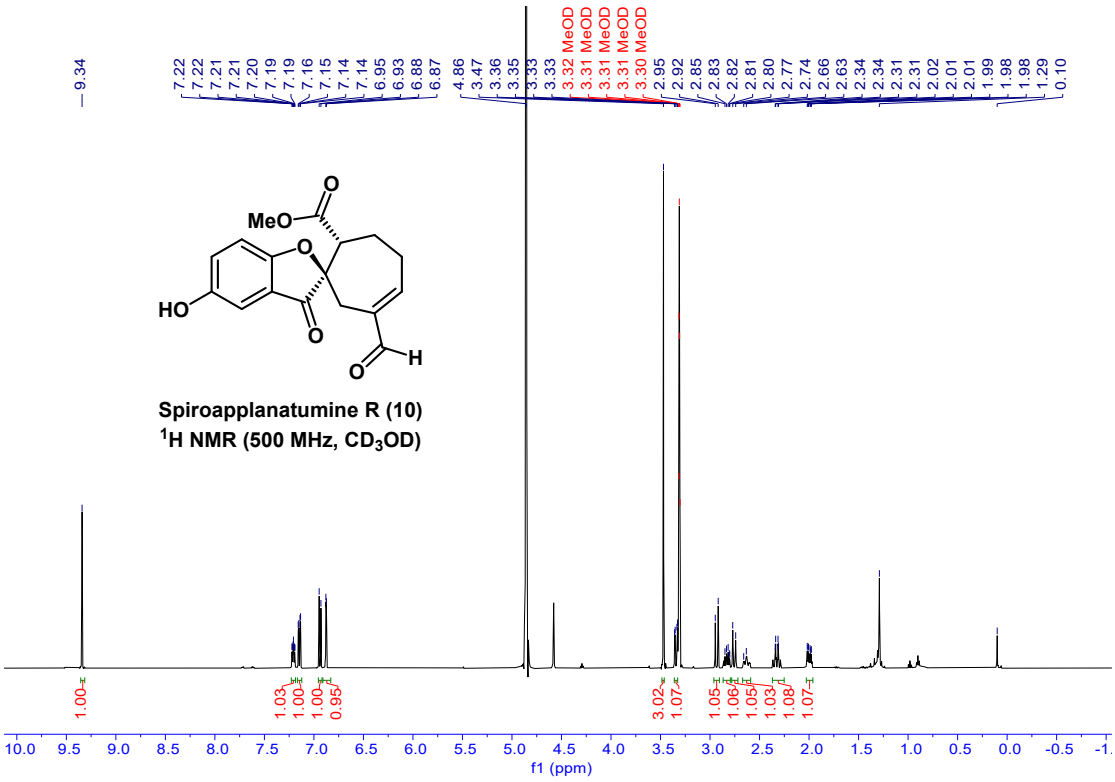


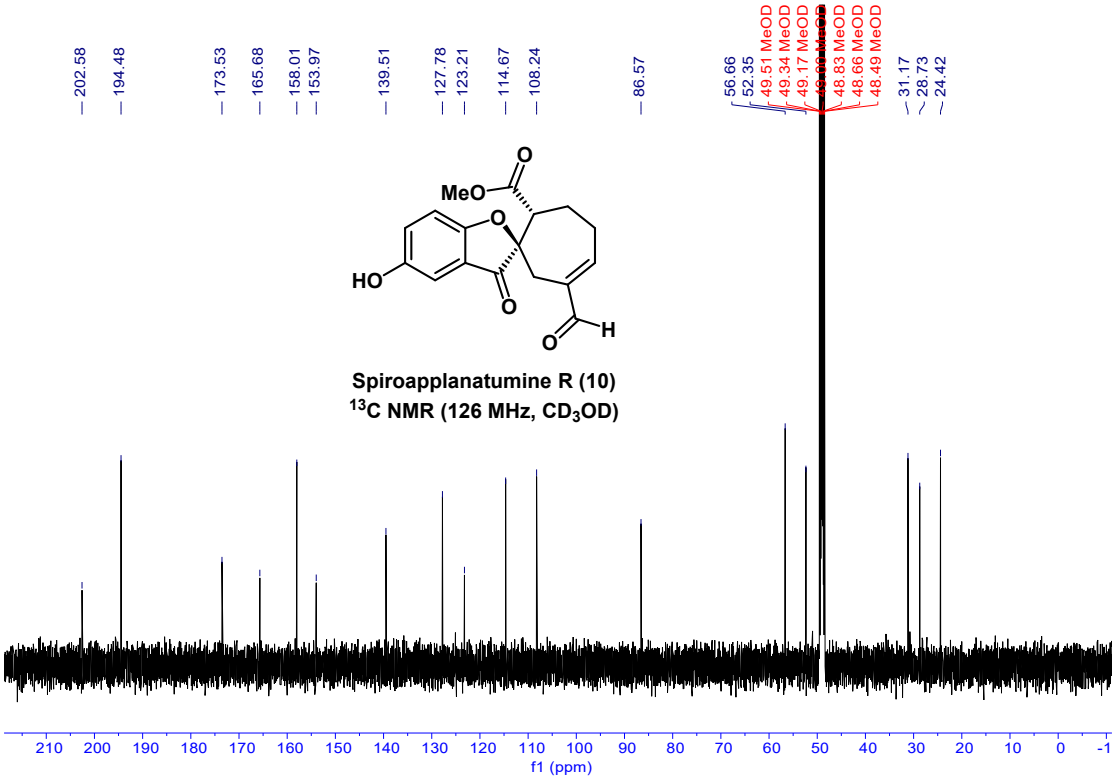
^{13}C NMR of natural (Cheng)[S2] spiroapplanatumine H (8) (150 MHz, CD_3OD)

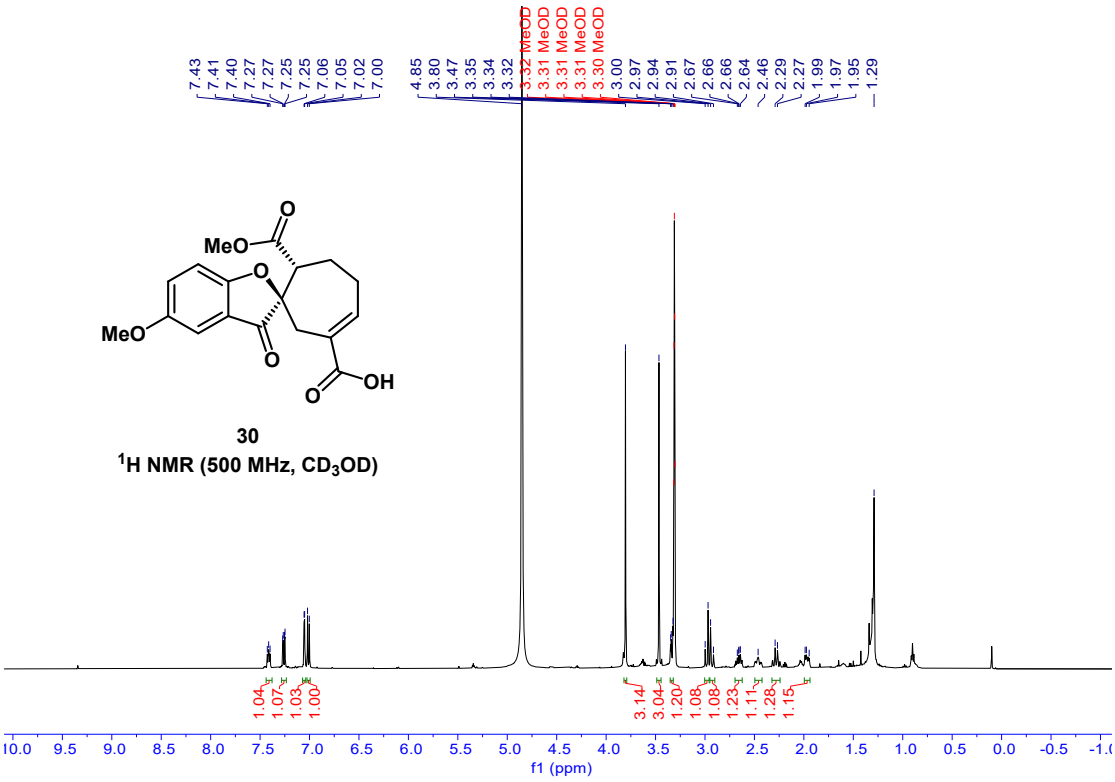


^{13}C NMR of our synthetic spiroapplanatumine H (8) (126 MHz, CD_3OD)



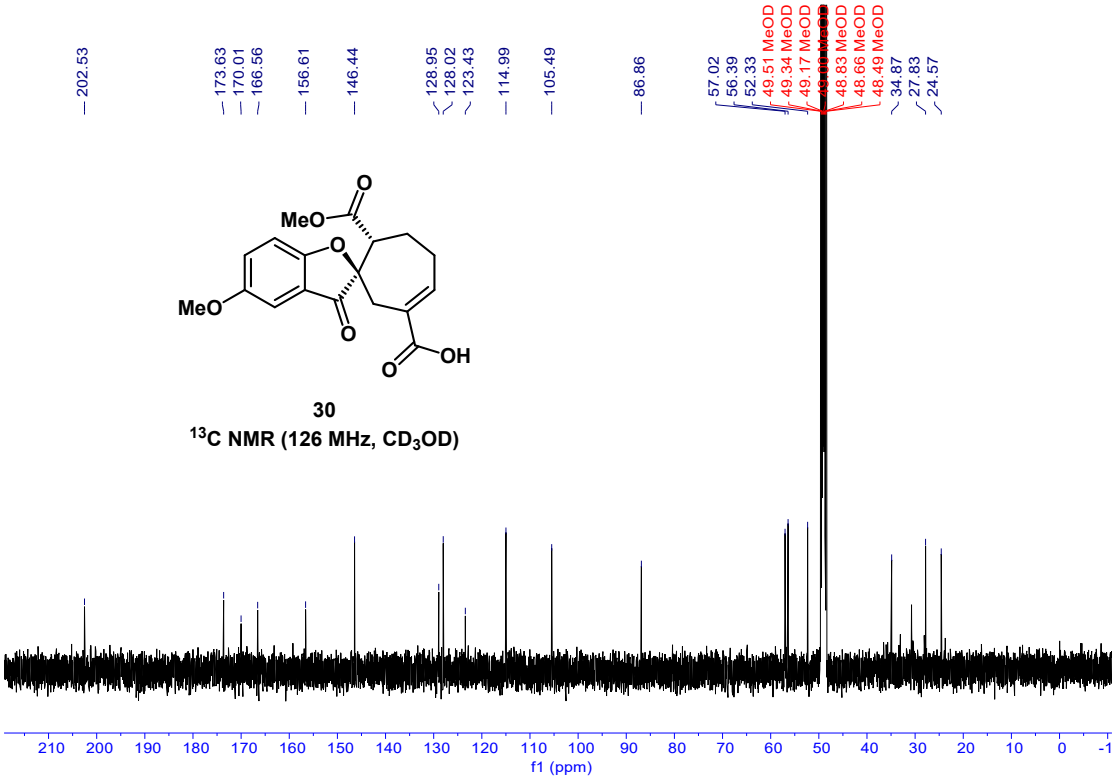

Spiroapplanatumine R (10)
1H NMR (500 MHz, CD3OD)
f1 (ppm)


Spiroapplanatumine R (10)
13C NMR (126 MHz, CD3OD)
f1 (ppm)



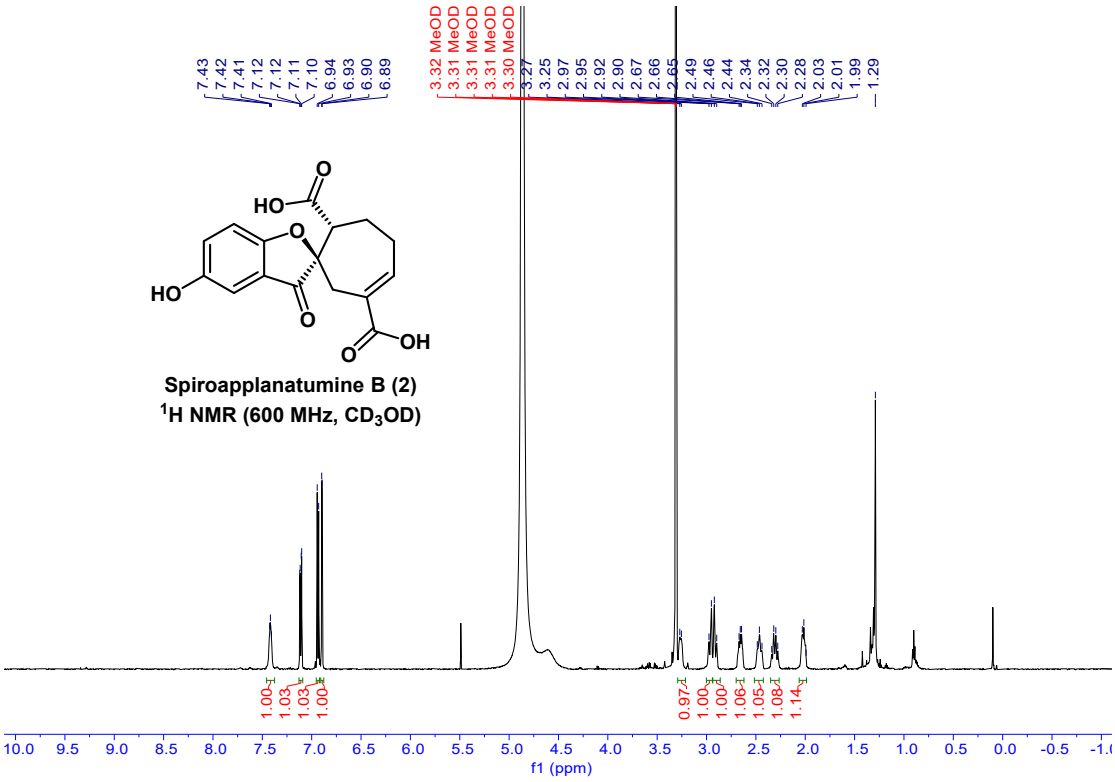
30

^{1}H NMR (500 MHz, CD_3OD)

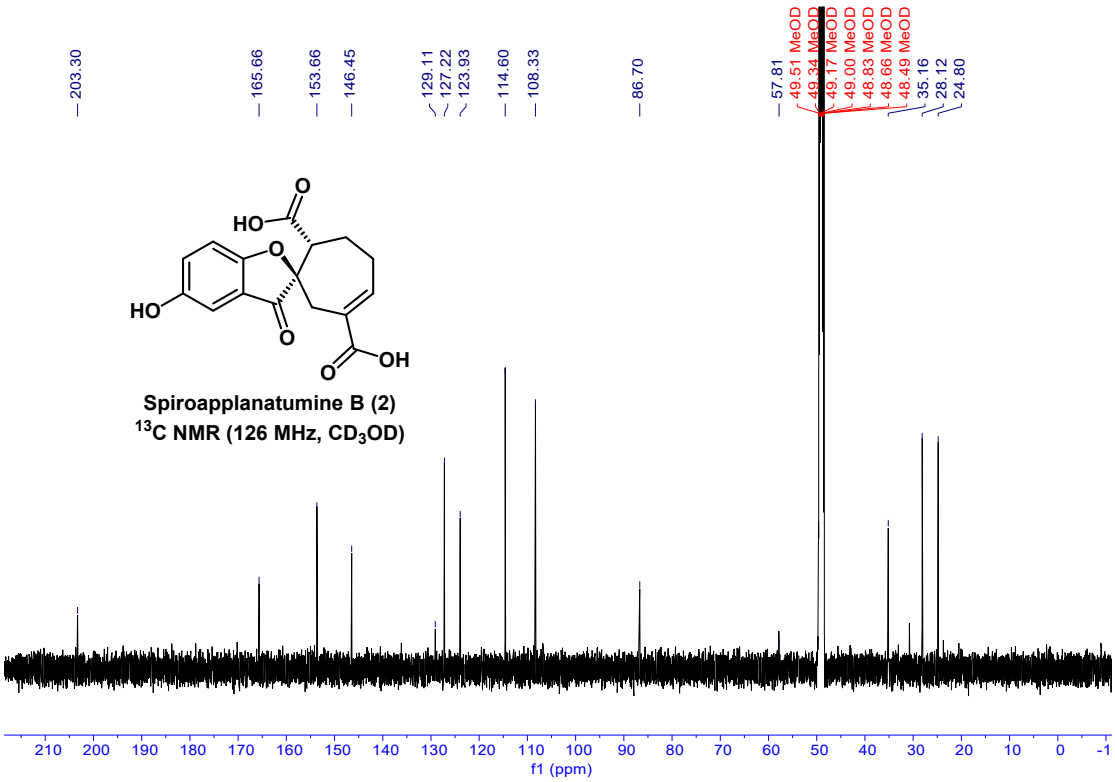


30

^{13}C NMR (126 MHz, CD_3OD)

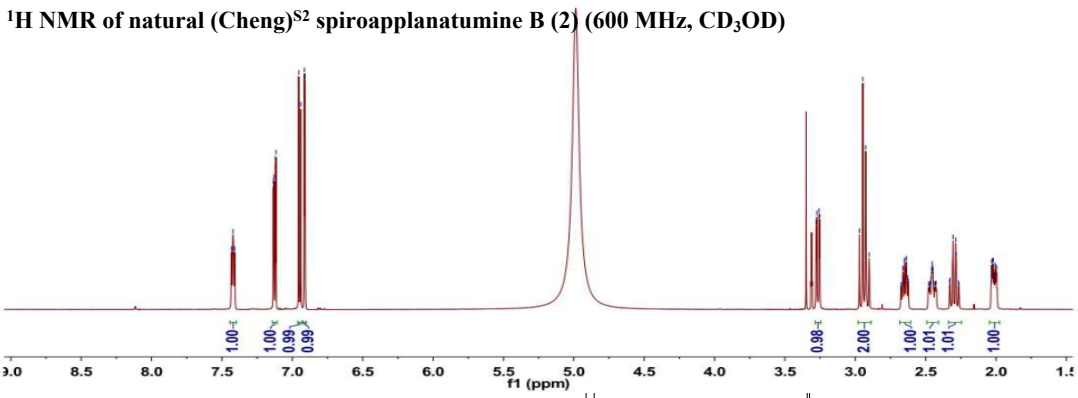


Spiroapplanatumine B (2)
^{1}H NMR (600 MHz, CD_3OD)

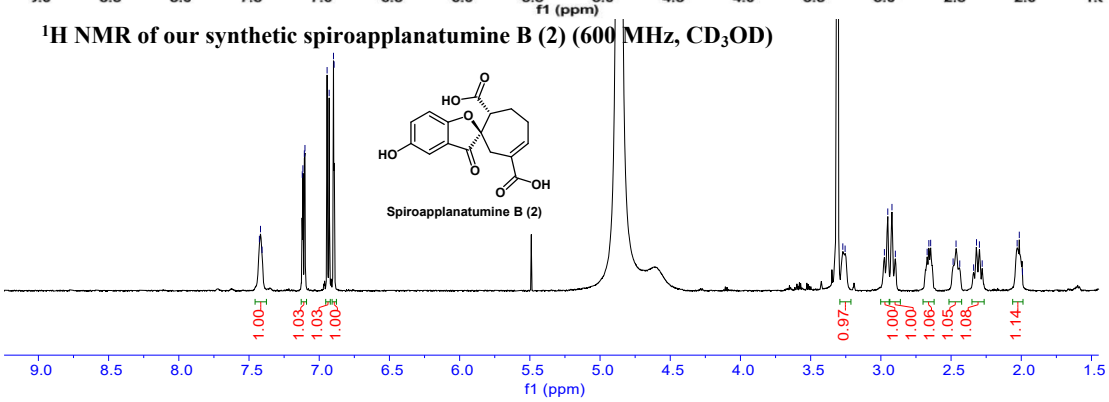


Spiroapplanatumine B (2)
^{13}C NMR (126 MHz, CD_3OD)

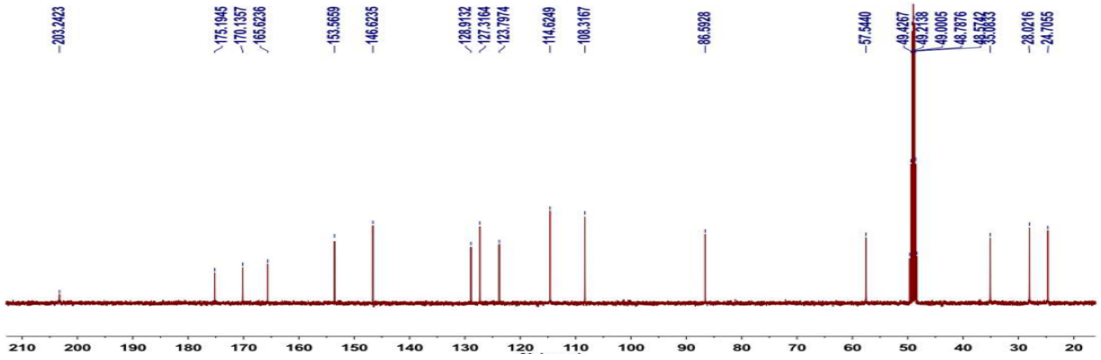
^{1}H NMR of natural (Cheng)[S2] spiroapplanatumine B (2) (600 MHz, CD_3OD)



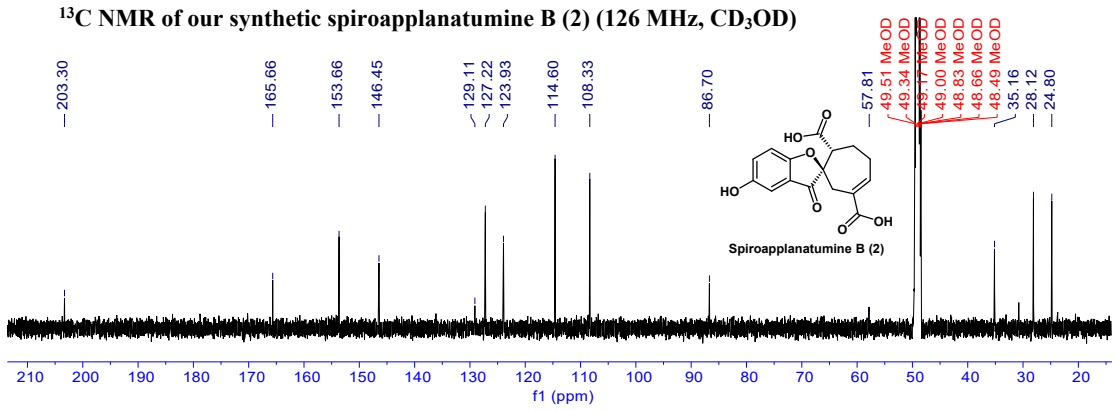
^{1}H NMR of our synthetic spiroapplanatumine B (2) (600 MHz, CD_3OD)

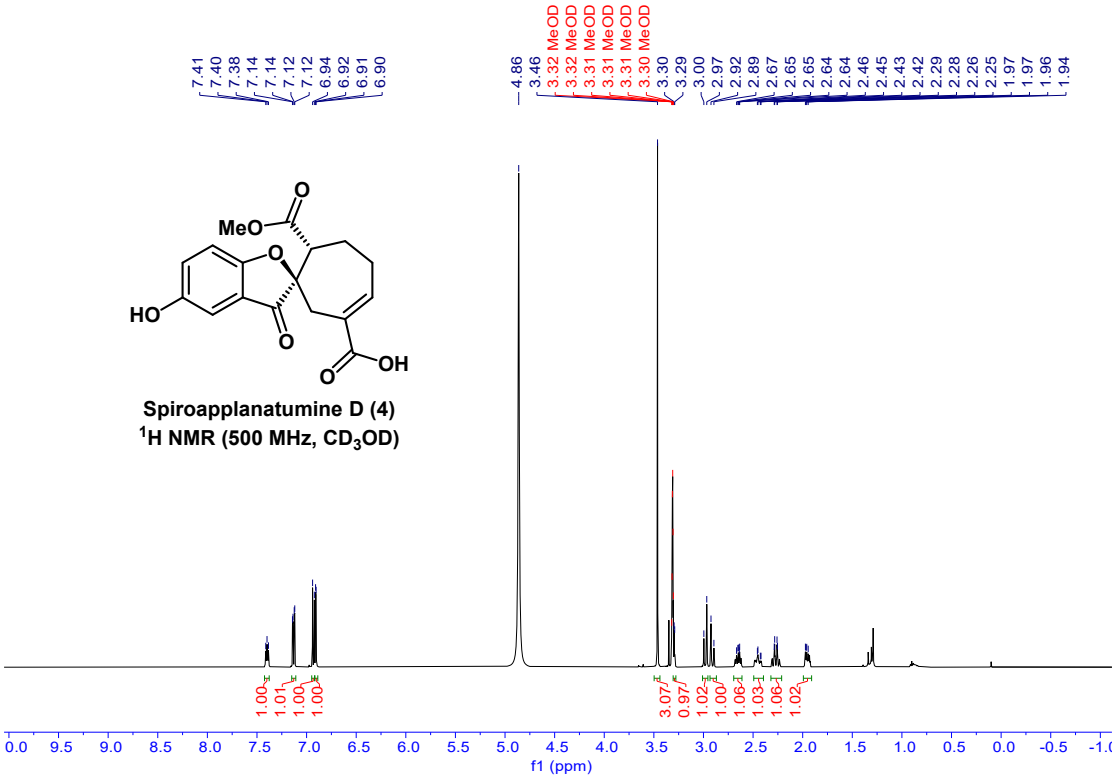


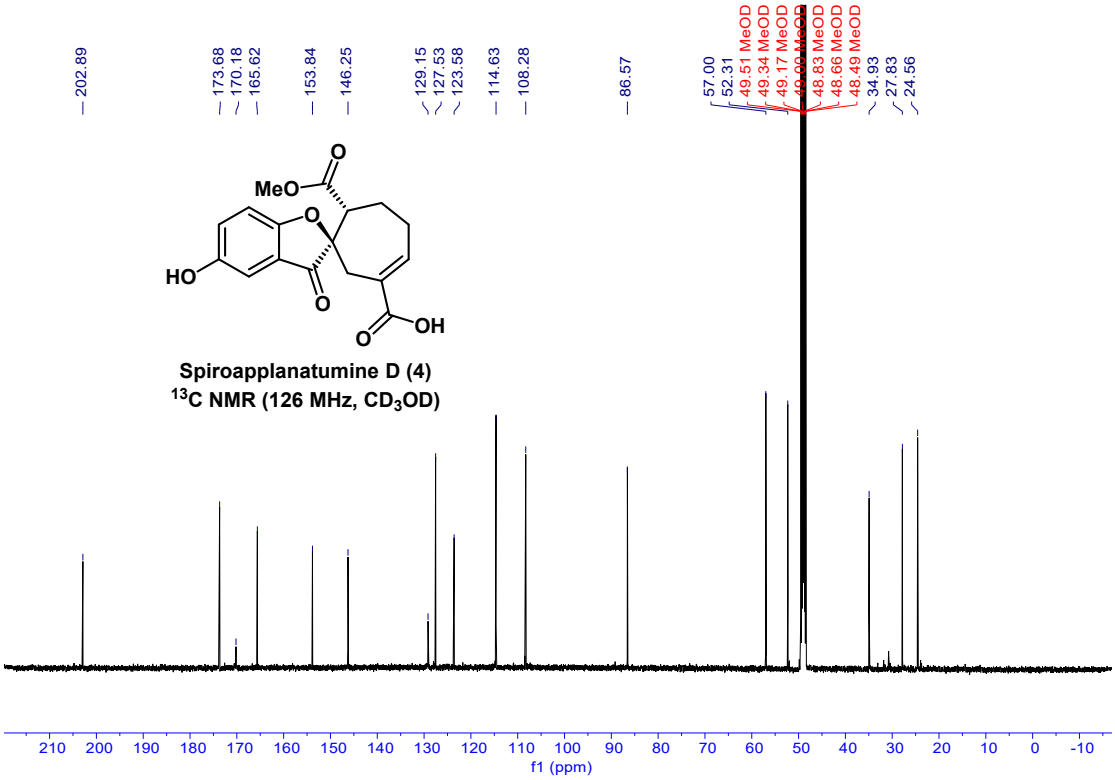
^{13}C NMR of natural (Cheng)[S2] spiroapplanatumine B (2) (150 MHz, CD_3OD)



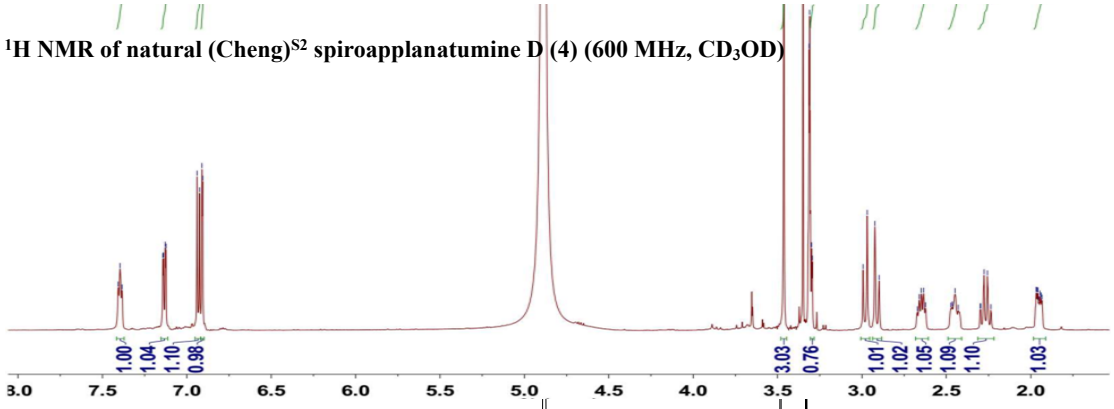
^{13}C NMR of our synthetic spiroapplanatumine B (2) (126 MHz, CD_3OD)



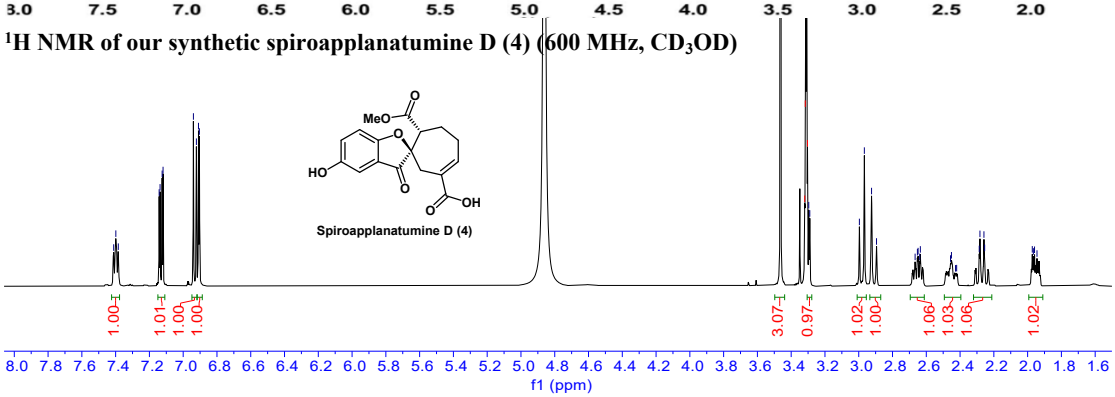

7.41
7.40
7.38
7.14
7.14
7.12
7.12
6.94
6.92
6.91
6.90
4.86
3.46
3.32 MeOD
3.32 MeOD
3.31 MeOD
3.31 MeOD
3.31 MeOD
3.30 MeOD
3.30
3.29
3.00
2.97
2.92
2.89
2.67
2.65
2.65
2.64
2.64
2.46
2.45
2.43
2.42
2.29
2.28
2.26
2.25
1.97
1.97
1.96
1.94
MeO
O
O
HO
O
O
OH
Spiroapplanatumine D (4)
1H NMR (500 MHz, CD3OD)
1.00
1.01
1.00
1.00
3.07
0.97
1.02
1.00
1.06
1.03
1.06
1.02
f1 (ppm)


202.89
173.68
170.18
165.62
153.84
146.25
129.15
127.53
123.58
114.63
108.28
86.57
57.00
52.31
49.51 MeOD
49.34 MeOD
49.17 MeOD
48.83 MeOD
48.66 MeOD
48.49 MeOD
34.93
27.83
24.56
MeO
O
O
HO
O
O
OH
Spiroapplanatumine D (4)
13C NMR (126 MHz, CD3OD)
f1 (ppm)

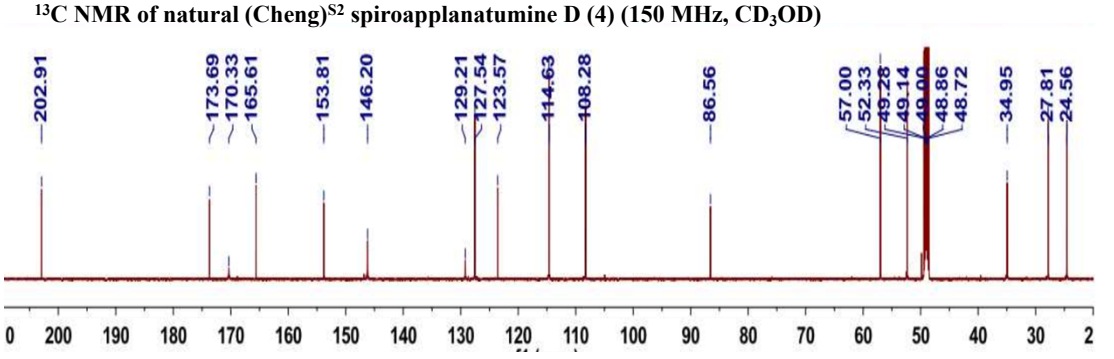
^{1}H NMR of natural (Cheng)[S2] spiroapplanatumine D (4) (600 MHz, CD_3OD)



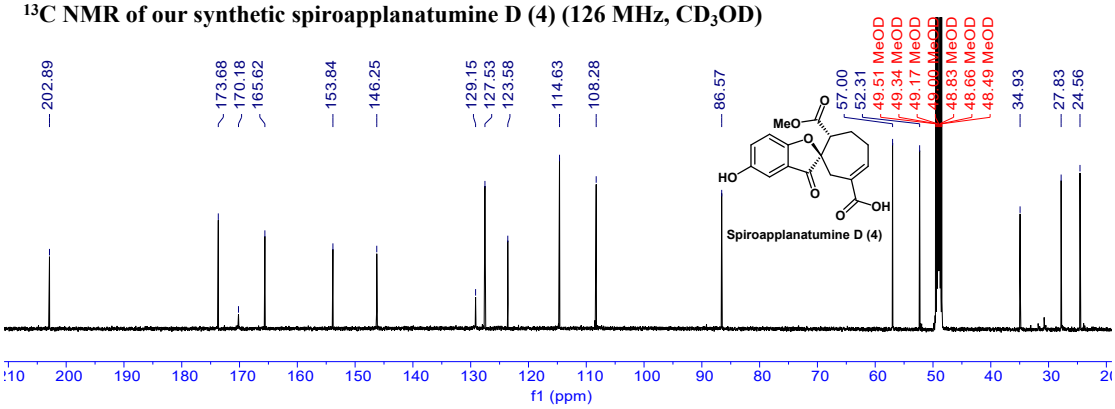
^{1}H NMR of our synthetic spiroapplanatumine D (4) (600 MHz, CD_3OD)

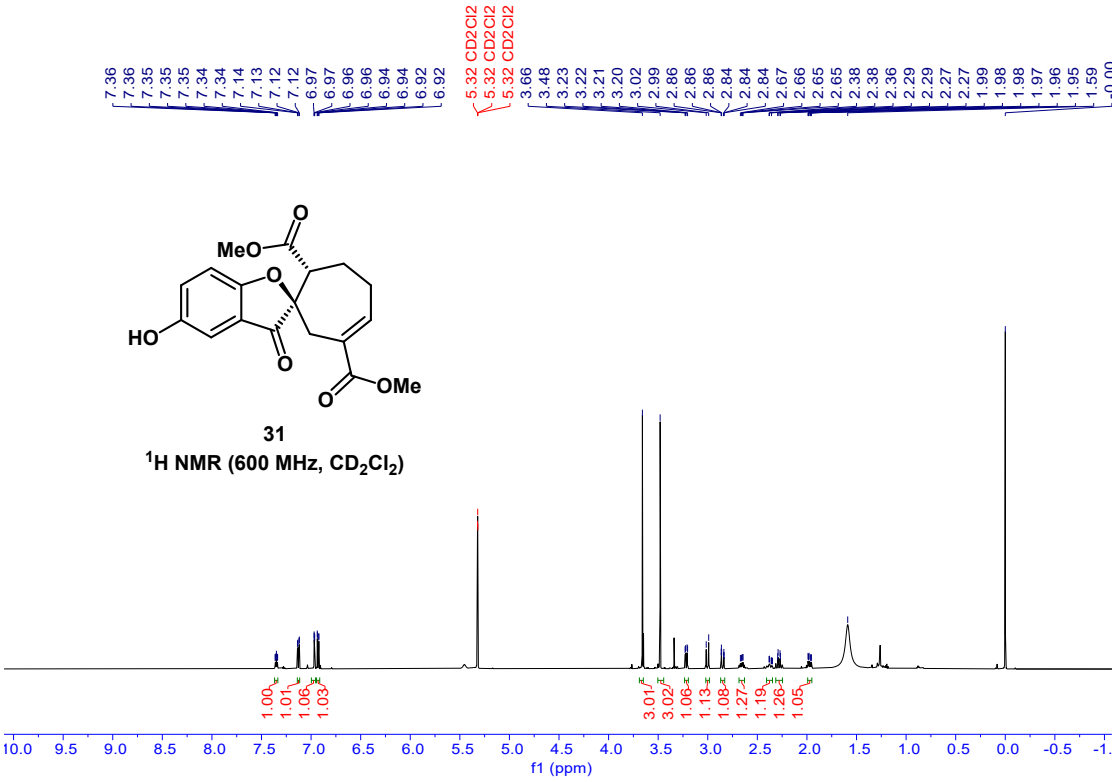


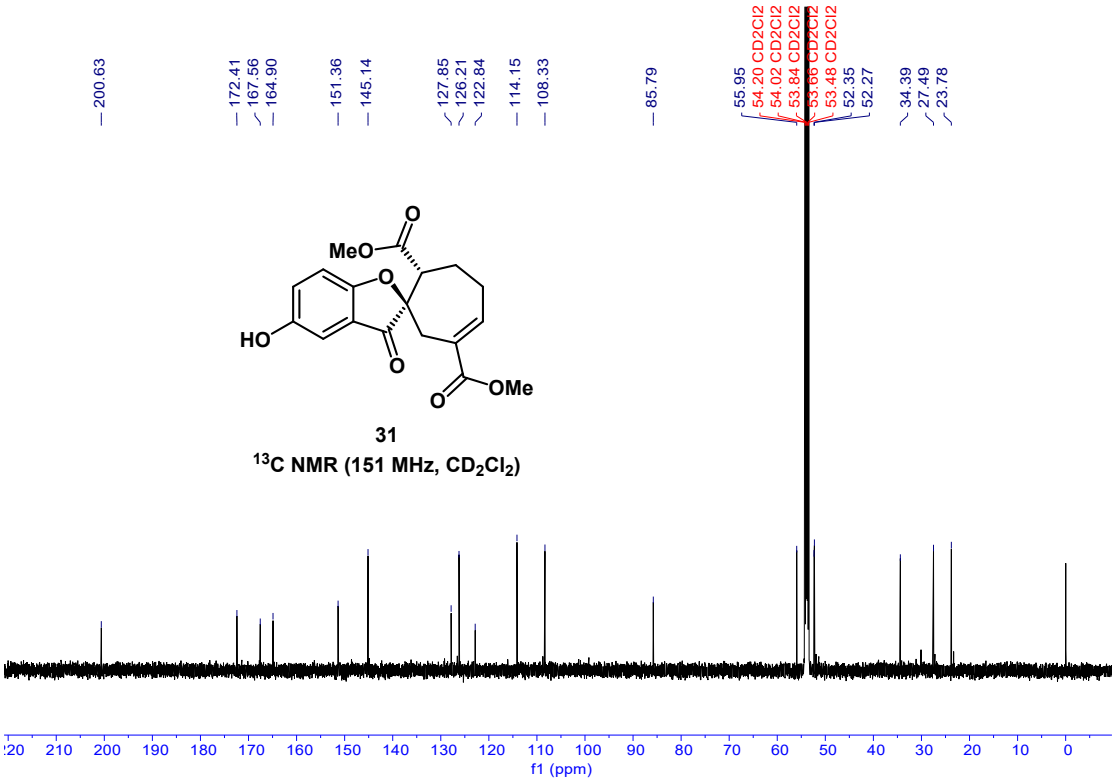
^{13}C NMR of natural (Cheng)[S2] spiroapplanatumine D (4) (150 MHz, CD_3OD)

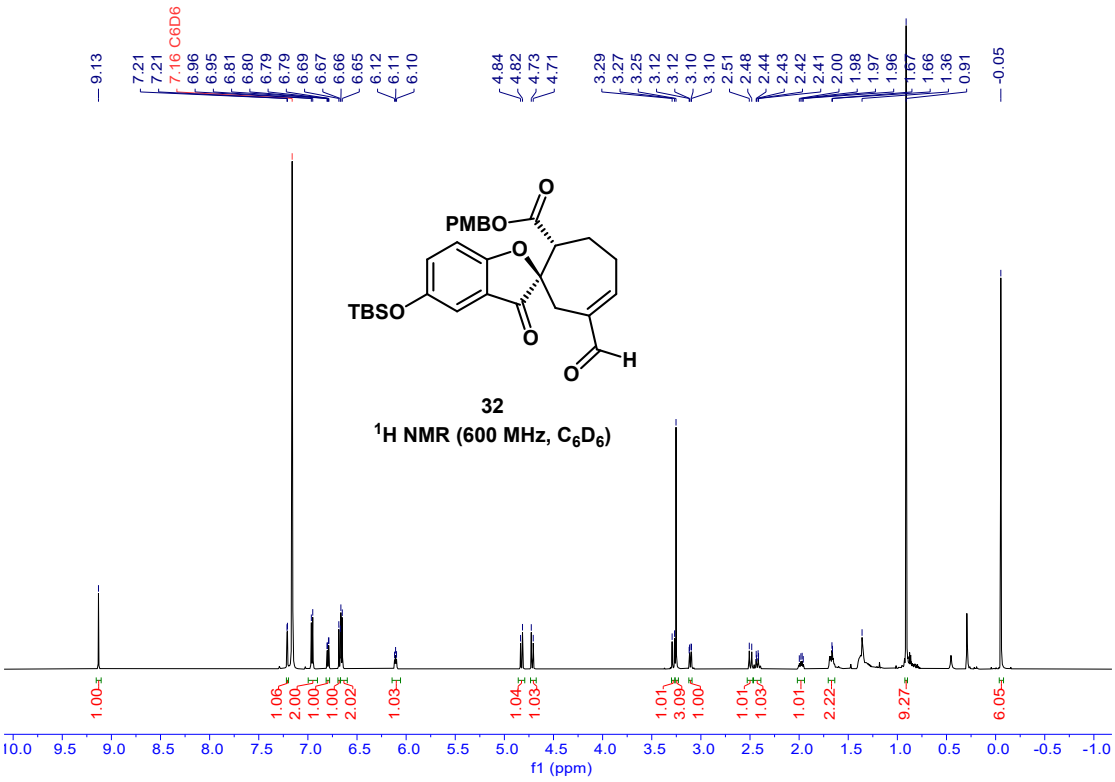


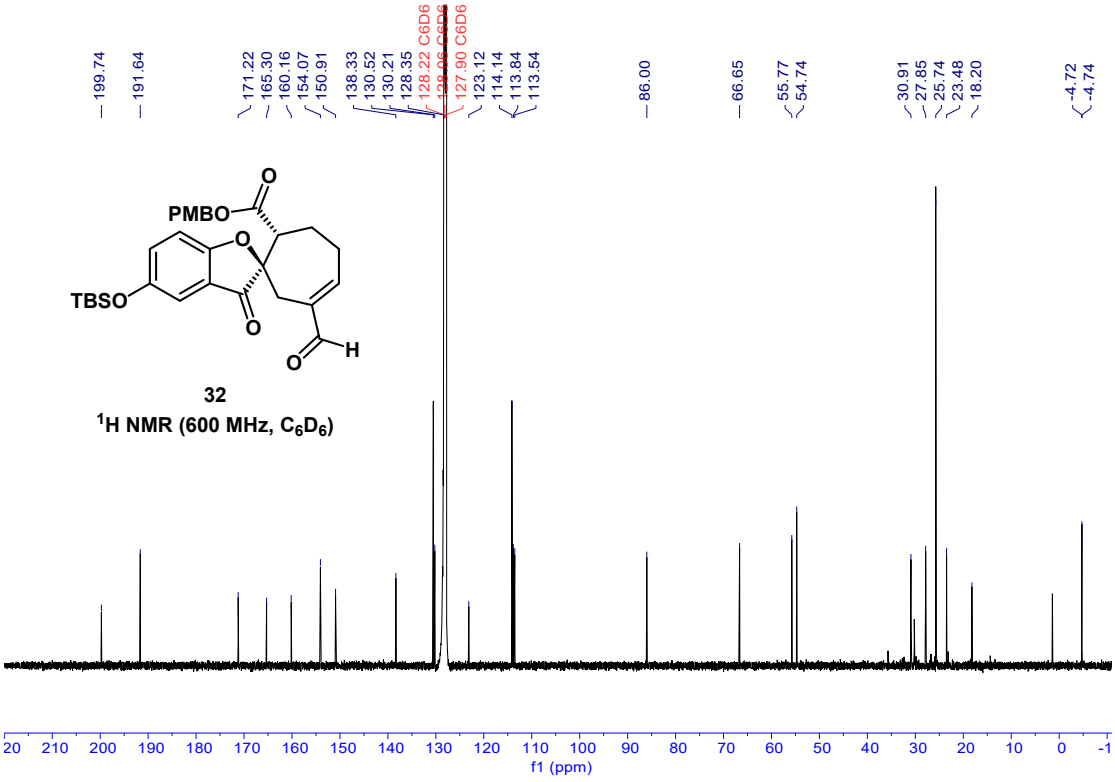
^{13}C NMR of our synthetic spiroapplanatumine D (4) (126 MHz, CD_3OD)

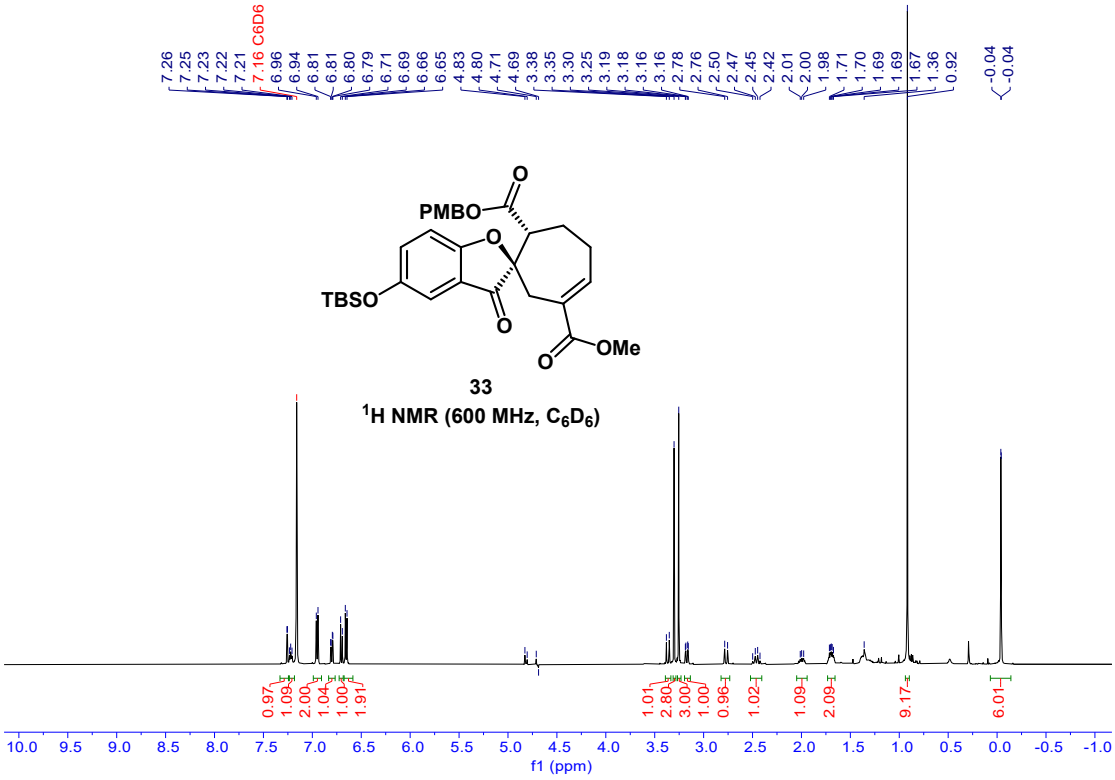


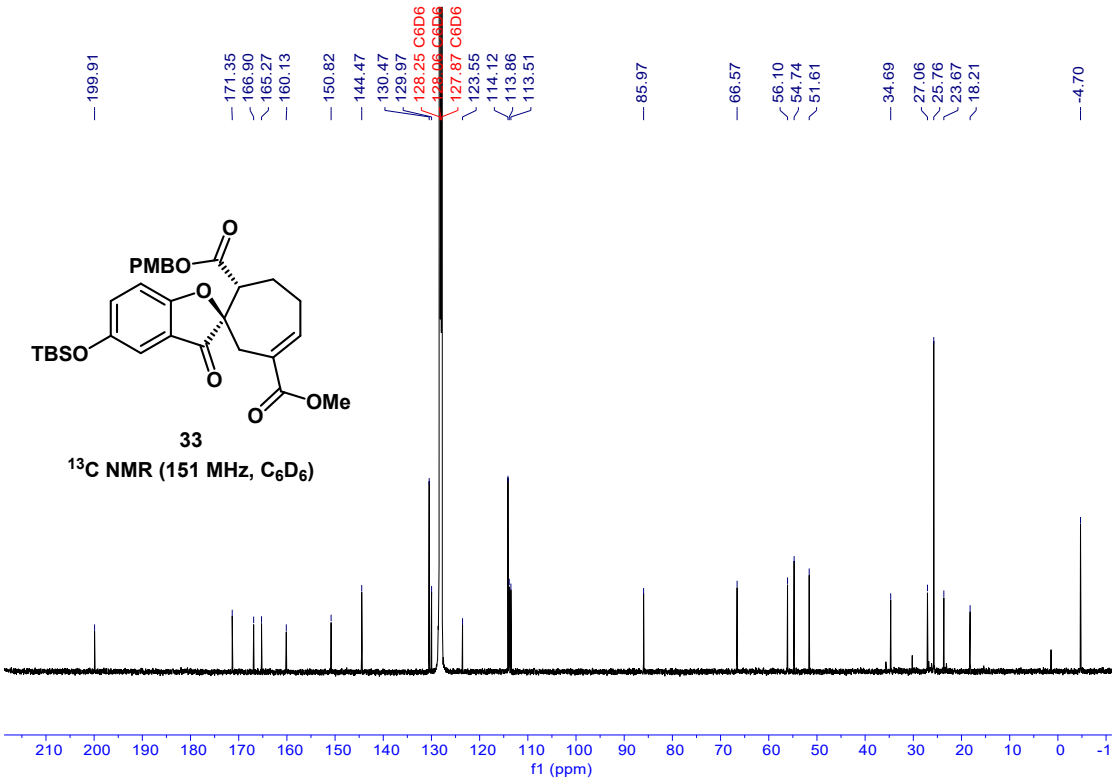

MeO
HO
OMe
31
1H NMR (600 MHz, CD2Cl2)
f1 (ppm)

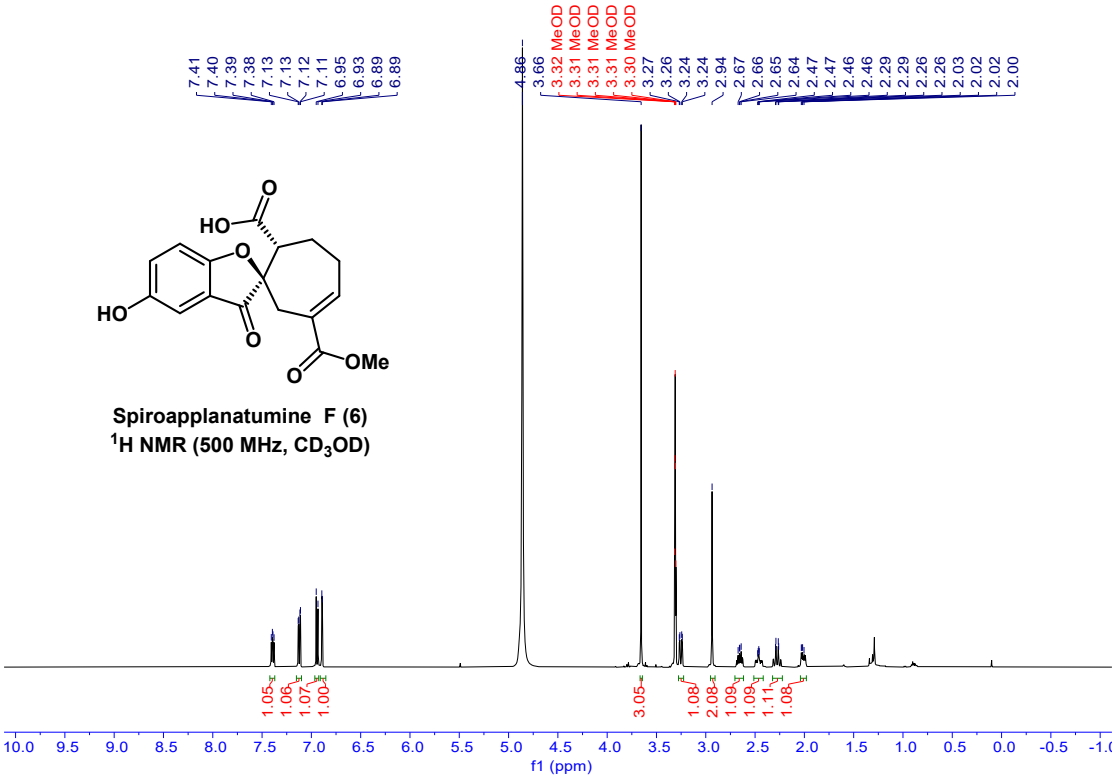

MeO
HO
OMe
31
13C NMR (151 MHz, CD2Cl2)
f1 (ppm)

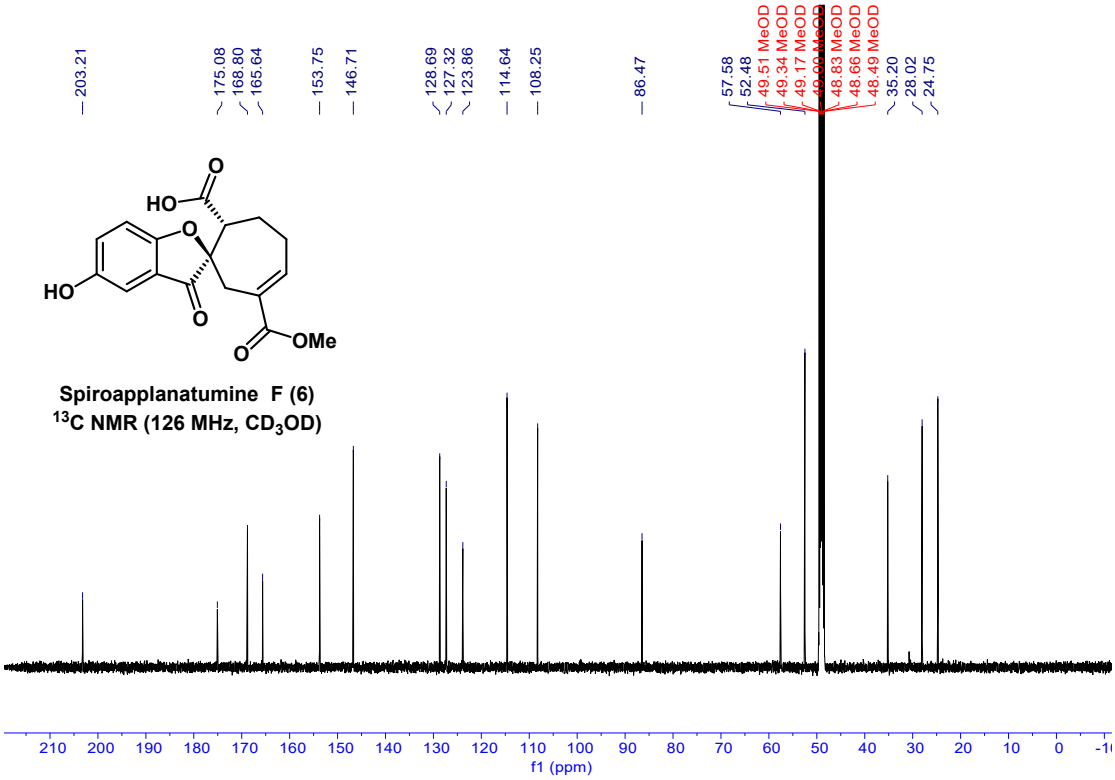

PMBO
TBSO
O
H
32
^{1}H NMR (600 MHz, C_6D_6)
f1 (ppm)


PMBO
TBSO
O
H
32
^{1}H NMR (600 MHz, C_6D_6)
f1 (ppm)

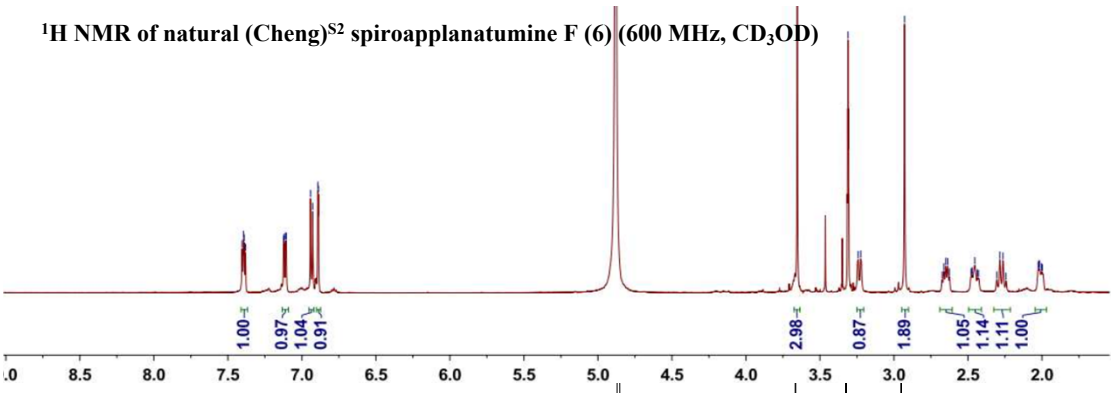

PMBO
TBSO
OMe
33
^{1}H NMR (600 MHz, C_6D_6)
f1 (ppm)


PMBO
TBSO
OMe
33
^{13}C NMR (151 MHz, C_6D_6)
f1 (ppm)

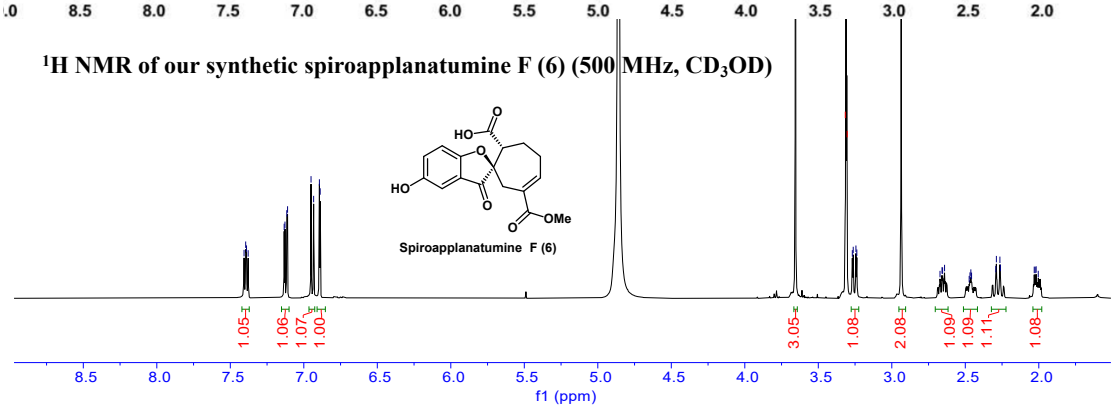

Spiroapplanatumine F (6)
^{1}H NMR (500 MHz, CD$_3$OD)
f1 (ppm)


Spiroapplanatumine F (6)
^{13}C NMR (126 MHz, CD$_3$OD)
f1 (ppm)

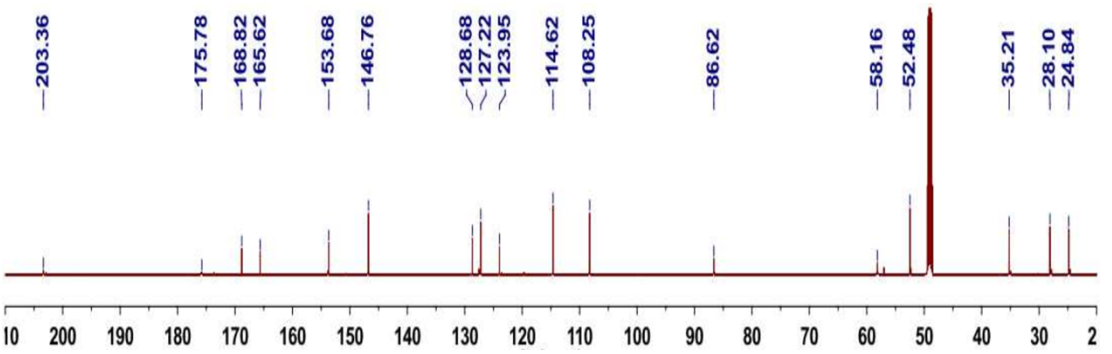
^{1}H NMR of natural (Cheng)[S2] spiroapplanatumine F (6) (600 MHz, CD_3OD)



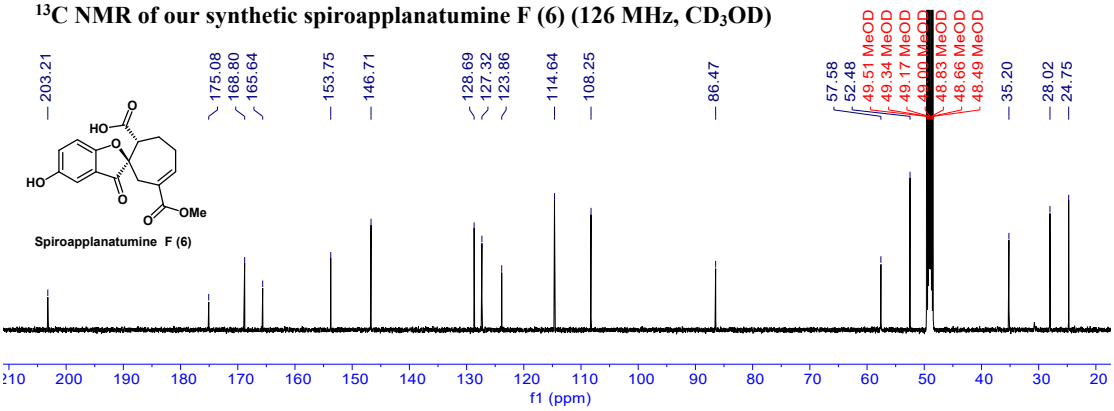
^{1}H NMR of our synthetic spiroapplanatumine F (6) (500 MHz, CD_3OD)

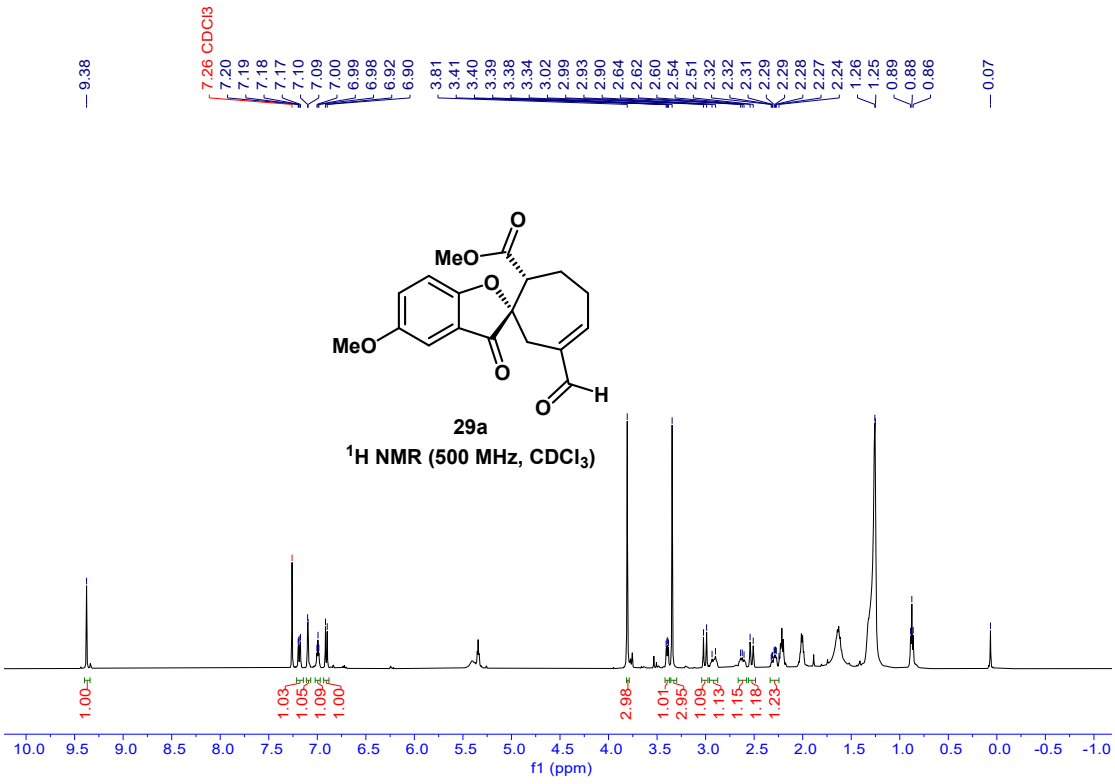


^{13}C NMR of natural (Cheng)[S2] spiroapplanatumine F (6) (150 MHz, CD_3OD)



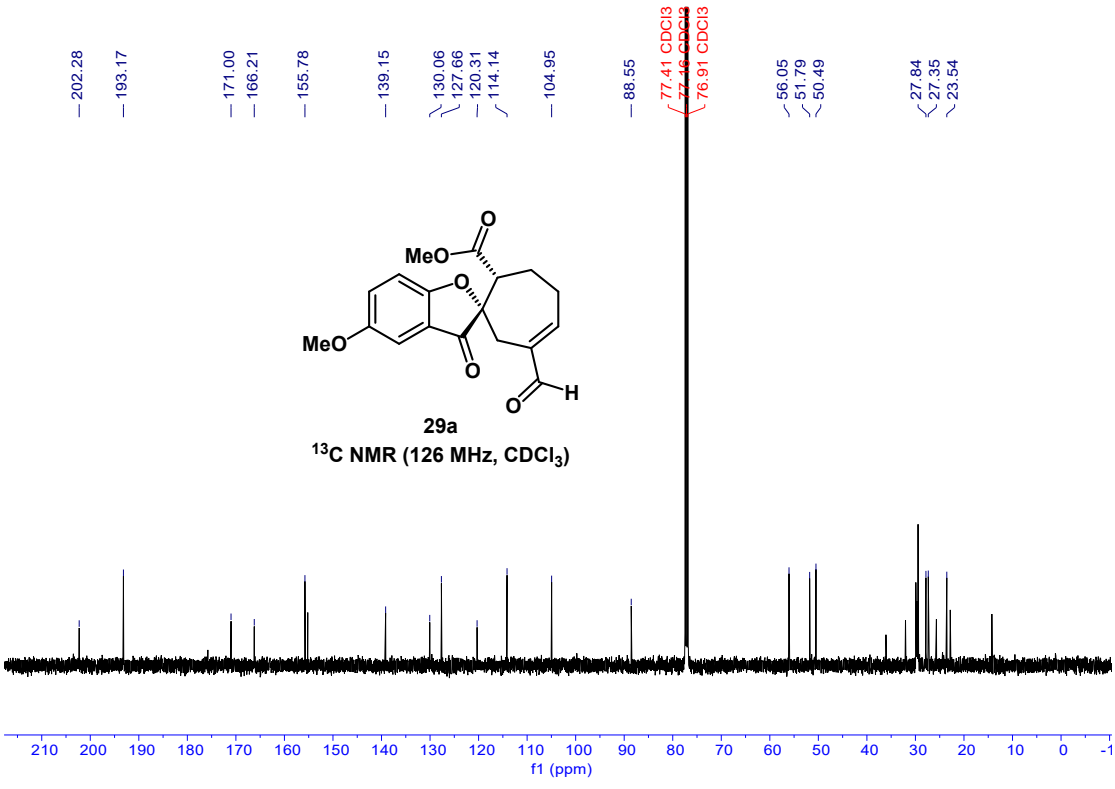
^{13}C NMR of our synthetic spiroapplanatumine F (6) (126 MHz, CD_3OD)





29a

^{1}H NMR (500 MHz, $CDCl_3$)



29a

^{13}C NMR (126 MHz, $CDCl_3$)

6. References

S1. T. Imamoto, N. Takiyama, K. Nakamura, T. Hatajima, and Y. Kamiya, Reactions of Carbonyl Compounds with Grignard Reagents in the Presence of Cerium Chloride, *J. Am. Chem. Soc.*, 1989, **111**, 4392-4398.

S2. Q. Luo, X.-Y. Wei, J. Yang, J.-F. Luo, R. Liang, Z.-C. Tu, and Y.-X. Cheng, Spiro Meroterpenoids from *Ganoderma applanatum*, *J. Nat. Prod.*, 2017, **80**, 61-70.