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Supporting Information

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# Supporting Information

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## Biological Evaluation: Antiplasmodial and Antitrypanosomal Activity

### Sample Preparation

The compounds were dissolved in DMSO at a concentration of 25 mM – except for strasseriolide D which was prepared at 12.5 mM.

These stock solutions were then diluted with culture media so that the maximum concentration of DMSO for the *P. falciparum* assay was at or below 0.1%, while for the *Trypanosoma cruzi* assay a 500-fold dilution of the stock solution was performed in order to lower the DMSO concentration to 0.2%. In the cytotoxicity assay (L6 cells), the stock solutions were diluted 200 times to achieve 0.5% DMSO.

### Cell Strains and Methods

#### *Plasmodium falciparum*

A *P. falciparum* 3D7 culture was synchronized using 5% sorbitol. After 96 h, the synchronized culture was diluted with complete medium and human erythrocytes to a starting 2% hematocrit and 0.5% parasitaemia. 50 µL per well were dispensed onto the 96-well plates containing the previously plated compounds. Plates were incubated at 37°C for 72 h and eventually frozen for at least 24 h.

Each plate included positive growth controls, where only medium was added, and negative growth controls with 100 nM of chloroquine. Plates were thawed at room temperature for at least 1 h. To evaluate lactate dehydrogenase (LDH) activity, 140 µL per well of freshly made reaction mix, containing 143 mM sodium L-lactate, 143 µM APAD, 178.75 µM NBT, 1 U/mL diaphorase, 0.7% Tween 20 and 100 mM Tris-HCl (pH 8.0) were dispensed. Plates were shaken to ensure mixing and absorbance was measured at 650 nm after 10 min of incubation at room temperature.[1]

#### *Trypanosoma cruzi*

The *Trypanosoma cruzi* Tulahuen C4 strain used is a genetically modified strain that expresses the *Escherichia coli* β-galactosidase gene, lacZ.[2] Intracellular amastigotes were cultured in RPMI-1640 supplemented with 10% inactivated FBS, 1.7 mM L-glutamine, 100 U/mL penicillin, and 100 U/mL streptomycin at 37°C and 5% $CO_2$.

L6 rat skeletal muscle cells were used as host cells and were infected with transgenic *T. cruzi* trypomastigotes (MOI 1) that eventually differentiate to intracellular amastigotes. 90 µL/well of infected L6 culture at a density of 40,000 cells/mL was added with a Multidrop dispenser to 96-well transparent microplates containing 10 µL/well of compound (0.2% DMSO). Benznidazole at 50 µM was routinely used as negative growth control and untreated infected cells as positive in-plate control.

Plates were first incubated for 96 h at 37°C and then 30 µL of lysis buffer (0.5 mM red chlorophenol-β-D-galactopyranoside (CPRG), 0.5% NP40) were added to each well. Plates were further incubated for 4 h in the dark at 37°C. Absorbance was then measured at 585 nm in a microplate reader.[3]

**L6 (cytotoxicity assay)**

A cytotoxicity assay was also performed using the L6 cell line. 100 µL of supplemented RPMI 1640 medium containing the compounds and controls were added to L6 cells previously seeded (4,000 cells per well) in a 96-well plate. 0.5% DMSO was used as positive growth control and 50 µM of tamoxifen as negative growth control.

After 72 h at 37°C, the number of viable cells was determined by resazurin reduction. 20 µL of resazurin at 0.11 mg/mL in PBS 1X were added to each well and incubated in the dark for 2 h at 37°C. Cell viability was estimated by measuring the final fluorescence at 550–590 nm in a Tecan Infinite F200 plate reader.[4]

**Data analysis**

Compound activities were normalized using the in-plate negative and positive controls according to the following equation:

$$\text{Percentage inhibition growth} = \left[1 - \left(\frac{Abs_{well} - Abs_{neg}}{Abs_{pos} - Abs_{neg}}\right)\right] \times 100$$

where $Abs_{well}$ is the absorbance value of a specific well, and $Abs_{pos}$ and $Abs_{neg}$ are the average absorbances measured for the positive and negative controls, respectively.

For cytotoxicity estimation fluorescence measurement was used in the above-mentioned equation for the calculation of $CC_{50}$ values.

Parasite growth inhibition is expressed as $EC_{50}$ values, meaning the concentration of compound that reduces cell growth by 50% versus untreated control cells.

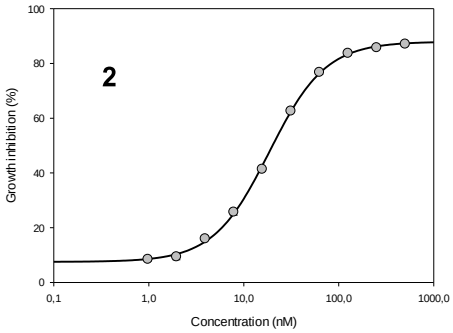
The $CC_{50}$ and $EC_{50}$ of each compound were calculated from 10-point dose-response curves (serial dilutions 1/2), which were analysed with SigmaPlot Software.

All $EC_{50}$ and $CC_{50}$ mean values represent the average of three biological replicates.

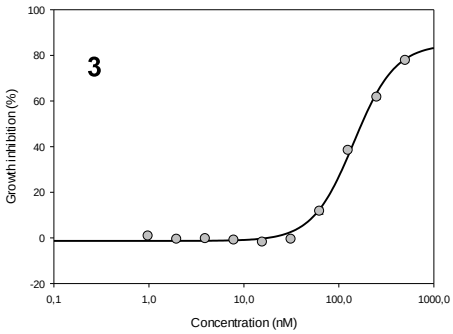
## Dose-Response Curves of Active Compounds

### *P. falciparum*:

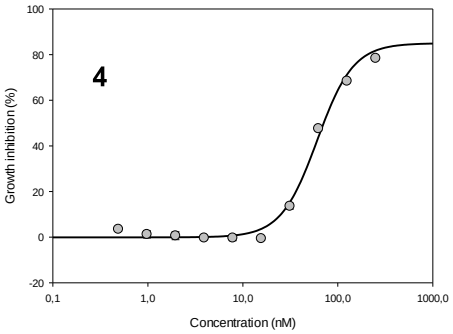
Strasseriolide B (SDI-SA-442)



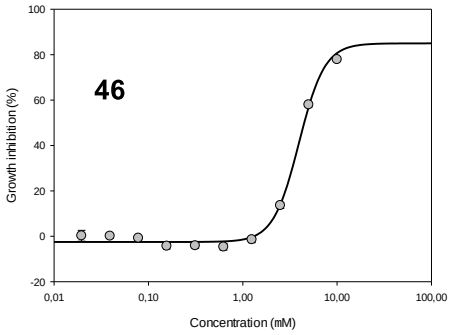

Strasseriolide C (ISE-IA-280)




Strasseriolide D (ISE-IA-214)




ISE-IA-248

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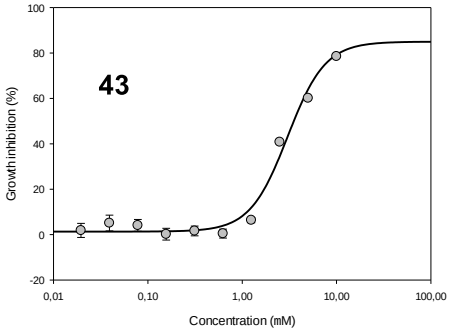
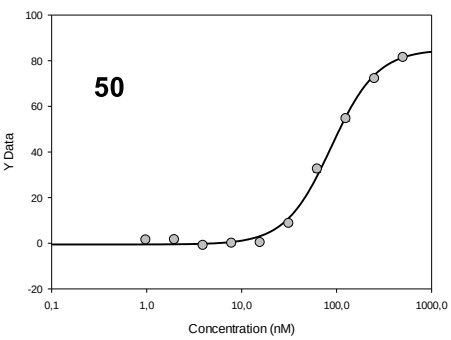
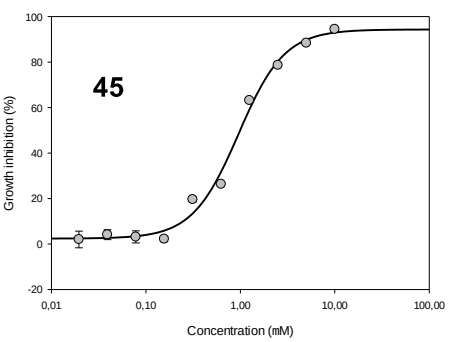



ISE-IA-255

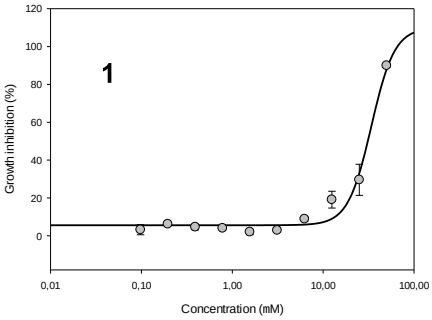



ISE-IA-275

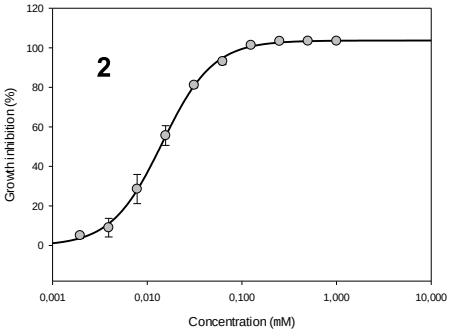


***T. cruzi*:**

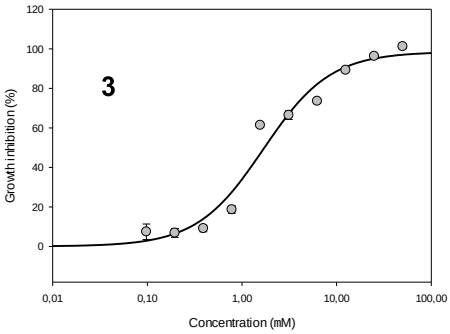
Strasseriolide A (SFS-SD-885)



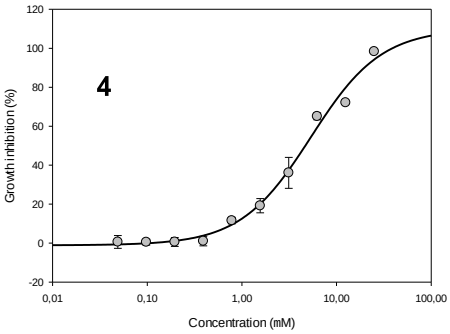

Strasseriolide B (SDI-SA-442)




Strasseriolide C (ISE-IA-280)




Strasseriolide D (ISE-IA-214)

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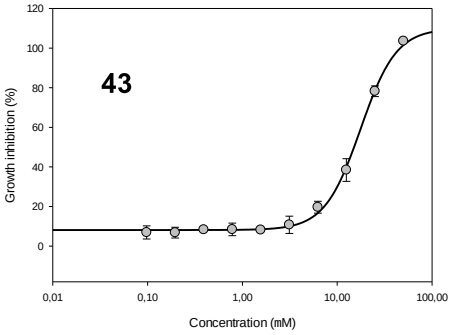
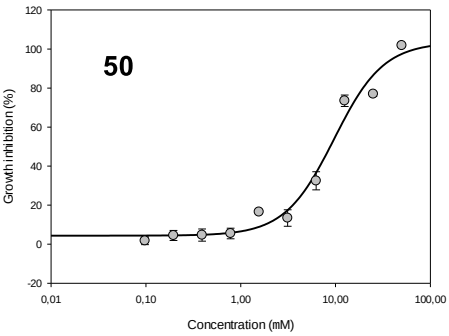



ISE-IA-255



## General Information

Unless stated otherwise, all reactions were carried out in flame-dried glassware using anhydrous solvents under an argon atmosphere. The solvents were purified by distillation over the indicated drying agents and were transferred under argon: THF (magnesium anthracene); diisopropylamine, diisopropylethylamine, 2,6-lutidine, pyridine, *tert*-butyl methyl ether, dichloromethane, NMP, DMPU ($CaH_2$); *n*-pentane, diethyl ether (Na/K alloy); toluene (sodium tetraethylaluminate); MeOH, EtOH, *i*PrOH (Mg; stored over MS 3 Å). DMSO, DMF, $NEt_3$, pentane and pyridine were dried by an adsorption solvent purification system based on molecular sieves. Molecular sieves (5 Å) were activated at 150 °C for 24 h in high vacuum ($1 \times 10^{-3}$ mbar) and stored under argon.

Thin layer chromatography (TLC): Macherey-Nagel precoated plates (POLYGRAM®SIL/UV254); visualization by UV light (254 nm) and by staining with solutions of *p*-anisaldeyhde, $KMnO_4$ or cerium ammonium nitrate.

Flash chromatography: Merck silica gel 60 (40-63 µm or 15-40 µm (referred to as "fine silica") with pre-distilled or HPLC grade solvents.

Preparative LC was performed with an Agilent 1260 infinity system (fraction collector G7159 A + G7166B, diode array detector G7115A); the stationary phase and conditions for each compound are specified below.

NMR: Spectra were recorded on Bruker AV 400, AV 500, AVIII 600 or AVneo 600 spectrometers in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$: $\delta_C$ = 77.16 ppm; residual $CHCl_3$ in $CDCl_3$: $\delta_H$ = 7.26 ppm; $CD_2Cl_2$: $\delta_C$ = 53.84 ppm; residual $CDHCl_2$ in $CD_2Cl_2$: $\delta_H$ = 5.32 ppm; $CD_3OD$: $\delta_C$ = 49.00 ppm, residual $CD_2HOD$ in $CD_3OD$: $\delta_H$ = 3.31 ppm). All spectra were recorded at 25 °C. Multiplicities are indicated by the following abbreviations: s: singlet, d: doublet, t: triplet, q: quartet, p: pentet, h: hextet, hept: heptet, m: multiplet. $^{13}C$ NMR spectra were recorded in $^{1}H$-decoupled manner and the values of the chemical shifts are rounded to one decimal point. Signal assignments were established using HSQC, HMBC, COSY, NOESY and other 2D experiments.

IR: Spectra were recorded on an Alpha Platinum ATR instrument (Bruker); wavenumbers ($\tilde{\nu}$) in $cm^{-1}$.

MS (ESI-MS): Finnigan MAT 8200 (70 eV), ESI-MS: ESQ3000 (Bruker), accurate mass determinations: Bruker APEX III FTMS (7 T magnet) or Mat 95 (Finnigan).

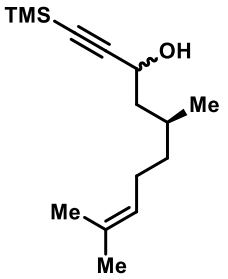
Optical rotations ($[\alpha]_D^{20/25}$) were measured with an A-Krüss Otronic Model P8000-t polarimeter at a wavelength of 589 nm.

Hydrogen gas (N50, ≥99.999 Vol.%) was purchased from Air Liquide and was handled with standard balloon techniques.

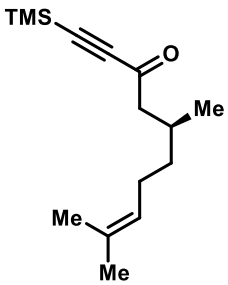
Unless stated otherwise, all commercially available compounds (Alfa Aesar, Sigma Aldrich, TCI, Strem Chemicals, ChemPUR) were used as received.

## The "Eastern" Fragment

**(5*S*)-5,9-Dimethyl-1-(trimethylsilyl)dec-8-en-1-yn-3-ol (S1).** *n*BuLi (1.6 M in hexanes, 20.69 mL, 33.1 mmol) was added dropwise to a solution of trimethylsilylacetylene (4.68 mL, 33.10 mmol) in THF (90 mL) at –78 °C. The resulting mixture was stirred at this temperature for 30 minutes before a solution of (*S*)-citronellal ((*S*)-**5**) (5.00 mL, 27.6 mmol) in THF (370 mL) was added dropwise *via* cannula. Stirring was continued at –78 °C for an additional 3 hours before a saturated aqueous solution of $NH_4Cl$ (400 mL) was added and the mixture was allowed to warm to ambient temperature. The layers were separated and the aqueous layer was extracted with *tert*-butyl methyl ether (3 x 100 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (5% *tert*-butyl methyl ether in pentane) to give the title compound as a clear oil (6.68 g, 96% yield). $[\alpha]_D^{20}$ = 2.5 (*c* = 0.52, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ) δ 5.15 – 5.05 (m, 1H), 4.46 – 4.37 (m, 1H), 2.07 – 1.91 (m, 2H), 1.83 – 1.45 (m, 4H), 1.68 (q, *J* = 1.3 Hz, 3H), 1.61 (bs, 3H), 1.43 – 1.30 (m, 1H), 1.25 – 1.12 (m, 1H), 0.93 (dd, *J* = 6.5, 4.1 Hz, 3H), 0.17 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 131.5, 124.98, 107.4, 107.1, 89.6, 89.3, 61.8, 61.2, 45.3, 45.2, 37.3, 37.2, 29.5, 29.1, 25.9, 25.5, 25.5, 19.9, 19.4, 17.8, 0.0. IR (film, $cm^{-1}$): 3335, 2961, 2915, 2854, 2170, 1452, 1378, 1250, 1099, 1059, 1024, 944, 841, 760, 700, 649, 612. HRMS (EI) *m/z* calcd. for $C_{15}H_{29}OSi$ [$M^+$ + H]: 253.1979; found 253.1982.

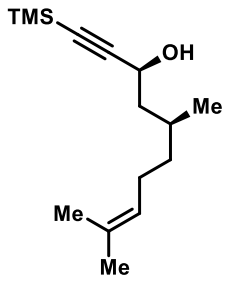



**(*S*)-5,9-Dimethyl-1-(trimethylsilyl)dec-8-en-1-yn-3-one (6).** To a solution of alcohol **S1** (5.47 g, 21.7 mmol) in dichloromethane (220 mL) and DMSO (43 mL) cooled to 0 °C with an ice bath was added triethylamine (12.1 mL, 86.7 mmol), immediately followed by $SO_3$·pyridine complex (10.35 g, 65.0 mmol). The mixture was stirred at 0 °C for 1 hour before the ice bath was removed and the mixture stirred at ambient temperature for an additional 16 hours. A saturated aqueous solution of $NH_4Cl$ was added, the resulting layers were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 100 mL). The combined organic layers were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (2% *tert*-butyl methyl ether in pentane) to yield the title compound as a colorless oil (4.67 g, 86% yield). $[\alpha]_D^{20}$ = –11.5 (*c* = 0.99, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.09 (ddp, *J* = 7.1, 5.7, 1.5 Hz, 1H), 2.55 (dd, *J* = 15.5, 5.8 Hz, 1H), 2.36 (dd, *J* = 15.5, 8.1 Hz, 1H), 2.19 – 2.06 (m, 1H), 1.99 (dp, *J* = 14.7, 7.4 Hz, 2H), 1.68 (d, *J* = 1.4 Hz, 3H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.36 (dddd, *J* = 13.4, 9.1, 6.6, 5.8 Hz, 1H), 1.29 – 1.16 (m, 1H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.24 (s, 9H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 188.0, 131.8, 124.3, 102.5, 97.6, 52.8, 36.9, 29.5, 25.9, 25.5, 19.8, 17.8, –0.6. IR



(film, $cm^{-1}$): 2963, 2914, 2854, 2161, 2148, 2018, 1676, 1455, 1402, 1378, 1252, 1121, 1069, 865, 846, 762, 705, 623. HRMS (ESI) *m/z* calcd. for $C_{15}H_{26}OSiNa$ [$M^+$ + Na]: 273.1647; found 273.1645.

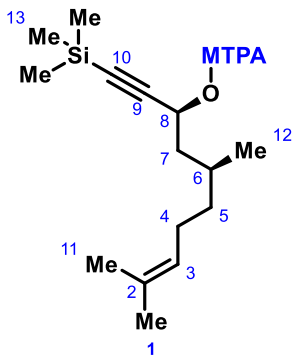
**(3*S*,5*S*)-5,9-Dimethyl-1-(trimethylsilyl)dec-8-en-1-yn-3-ol (7a).** Powdered potassium hydroxide




(65.0 mg, 1.16 mmol) was added to a solution of RuCl[(*S*,*S*)-TsDPEN](mesitylene) (*S,S*-**13**) (75.0 mg, 0.12 mmol) in dichloromethane (10 mL) at ambient temperature. After stirring for 15 minutes, the dark purple solution was transferred to a separatory funnel and washed multiple times with water. The solution was then dried over sodium sulfate and the solvent removed under reduced pressure. The dark blue-purple residue was dissolved in *i*PrOH (8 mL) and added dropwise to a solution of ketone **6** (2.90 g, 11.6 mmol) in *i*PrOH (50 mL). After stirring for 1 hour at ambient temperature, the solvent was removed under reduced pressure. The resulting residue was subjected to flash chromatography (5% *tert*-butyl methyl ether in pentane) to give the title compound as a colorless oil (2.76 g, 94% yield). $[\alpha]_D^{20}$ = – 9.3 (*c* = 0.57, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.10 (tp, *J* = 7.1, 1.4 Hz, 1H), 4.42 (dd, *J* = 7.5, 6.7 Hz, 1H), 2.09 – 1.90 (m, 2H), 1.73 – 1.48 (m, 4H), 1.68 (q, *J* = 1.3 Hz, 3H), 1.61 (bs, 3H), 1.38 (dddd, *J* = 13.3, 9.2, 6.6, 5.2 Hz, 1H), 1.19 (dddd, *J* = 13.5, 9.1, 7.4, 6.4 Hz, 1H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.17 (s, 9H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 131.5, 124.8, 107.1, 89.6, 61.6, 45.2, 37.2, 29.5, 25.9, 25.5, 19.9, 17.8, 0.0. IR (film, $cm^{-1}$): 3317, 2961, 2915, 2854, 21714, 1453, 1378, 1250, 1059, 1023, 945, 840, 760, 699, 649. HRMS (ESI) *m/z* calcd. for $C_{15}H_{28}OSiNa$ [$M^+$ + Na]: 275.1800; found 275.1802.

The absolute configuration was determined by Mosher ester analysis.[5]

**Preparation of the (*S*)-and (*R*)-MTPA Esters of Alcohol 7a. Representative Procedure.** (*S*)-(+)-MTPA-




Cl (7.4 µL, 0.040 mmol) was added to a solution of alcohol **7a** (10 mg, 0.40 mmol), trimethylamine (16.5 µL, 11.9 µmol), and 4-(dimethylamino)-pyridine (1 mg, 7.9 µmol) in dichloromethane (0.8 mL). After stirring for 2 hours, the mixture was poured into a separatory funnel containing dichloromethane (2 mL) and a saturated aqueous solution of $NH_4Cl$ (5 mL). The phases were separated and the aqueous layer was extracted with dichloromethane (3 x 2 mL). The combined organic phases were washed with brine, dried with sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography to give the desired (*R*)-MTPA-ester as a clear oil (16.3 mg, 88% yield). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.55 – 7.52 (m, 2H), 7.44 – 7.36 (m, 3H), 5.57 (t, *J* = 7.6 Hz, 1H), 5.07 (tp, *J* = 7.1, 1.4 Hz, 1H), 3.56 (q, *J* = 1.2 Hz, 3H), 2.05 – 1.90 (m, 2H), 1.86 – 1.78 (m, 1H), 1.71

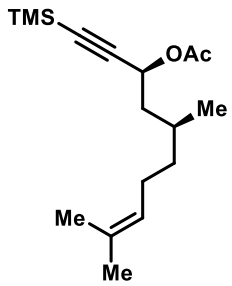
– 1.65 (m, 2H), 1.67 (q, *J* = 1.5 Hz, 3H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.39 (ddt, *J* = 13.9, 9.2, 6.6 Hz, 1H), 1.19 (dtd, *J* = 13.3, 9.1, 5.8 Hz, 1H), 0.94 (d, *J* = 6.1 Hz, 3H), 0.15 (s, 9H).

The (*S*)-MTPA ester (77% yield) was prepared analogously using (*R*)-(-)-MTPA-Cl as the reagent. It analyzed as follows: $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.59 – 7.54 (m, 2H), 7.44 – 7.36 (m, 3H), 5.61 (t, *J* = 7.3 Hz, 1H), 5.06 (tp, *J* = 7.0, 1.5 Hz, 1H), 3.60 (q, *J* = 1.2 Hz, 3H), 2.01 – 1.94 (m, 1H), 1.94 – 1.86 (m, 1H), 1.76 (dt, *J* = 13.5, 6.7 Hz, 1H), 1.68 (q, *J* = 1.4 Hz, 3H), 1.64 (dd, *J* = 13.6, 7.5 Hz, 1H), 1.60 (d, *J* = 1.2 Hz, 3H), 1.59 – 1.54 (m, 1H), 1.35 (ddt, *J* = 13.3, 9.5, 6.5 Hz, 1H), 1.13 (dtd, *J* = 13.5, 9.4, 5.7 Hz, 1H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.17 (s, 9H).

**Table S1**. Analysis of the Mosher esters according to Hoye and co-workers;[5] arbitrary numbering scheme as shown in the insert.

| Atom number | (*S*)-MTPA-ester δ (ppm) | (*R*)-MTPA-ester δ (ppm) | δS – δR (ppm) |
|---|---|---|---|
| **5a** | 1.35 | 1.39 | –0.04 |
| **5b** | 1.13 | 1.19 | –0.06 |
| **12** | 0.88 | 0.94 | –0.06 |
| **6** | 1.58 | 1.68 | –0.10 |
| **7a** | 1.76 | 1.82 | –0.06 |
| **7b** | 1.64 | 1.68 | –0.04 |
| **8** | 5.61 | 5.57 | +0.04 |
| **13** | 0.17 | 0.15 | +0.02 |

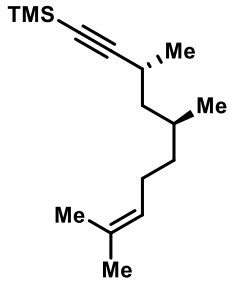

**(3*S*,5*S*)-5,9-dimethyl-1-(trimethylsilyl)dec-8-en-1-yn-3-yl acetate (7b).** 4-Dimethylaminopyridine




(321.4 mg, 2.63 mmol), triethylamine (5.50 mL, 39.5 mmol), and acetic acid anhydride (1.62 mL, 17.1 mmol) were added sequentially to a solution of alcohol **7a** (3.32 g, 13.2 mmol) in dichloromethane (53 mL) at ambient temperature. After 1 hour, the mixture was diluted with water (50 mL) and the phases were separated. The aqueous layer was extracted with *tert*-butyl methyl ether (3 x 50 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash

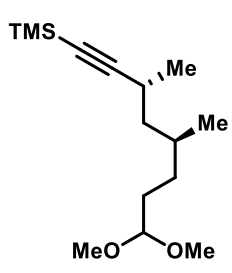
chromatography (2% *tert*-butyl methyl ether in pentane) to yield the title compound as a colorless oil (3.75 g, 97% yield). $[\alpha]_D^{20}$ = – 90.5 (*c* = 0.47, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ $^1$H NMR (400 MHz, $CDCl_3$) δ 5.44 (dd, *J* = 8.1, 6.5 Hz, 1H), 5.08 (tdt, *J* = 7.1, 2.9, 1.5 Hz, 1H), 2.07 (s, 3H), 1.98 (bq, *J* = 7.7 Hz, 2H), 1.75 (ddd, *J* = 12.8, 8.2, 4.9 Hz, 1H), 1.70 – 1.53 (m, 2H), 1.68 (q, *J* = 1.3 Hz, 3H), 1.60 (d, *J* = 1.1 Hz, 3H), 1.43 – 1.31 (m, 1H), 1.27 – 1.14 (m, 1H), 0.94 (d, *J* = 6.4 Hz, 3H), 0.17 (s, 9H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 170.0, 131.6, 124.6, 103.0, 90.5, 63.5, 41.9, 37.1, 29.4, 25.9, 25.4, 21.3, 19.6, 17.8, −0.1. IR (film, $cm^{-1}$): 2962, 2917, 2180, 1745, 1452, 1371, 1249, 1227, 1089, 1019, 989, 945, 841, 760, 700. HRMS (ESI) *m/z* calcd. for $C_{17}H_{30}O_2SiNa$ [$M^+$ + Na]: 317.1911; found 317.1907.

**Trimethyl((3*R*,5*S*)-3,5,9-trimethyldec-8-en-1-yn-1-yl)silane (8).** Methylmagnesium bromide (3 M in




$Et_2O$, 12.4 mL, 37.1 mmol) was added dropwise to a suspension of copper(I) iodide (3.53 g, 18.5 mmol) in THF (83 mL). After 15 minutes, a solution of propargylic acetate **7b** (3.64 g, 12.4 mmol) in THF (41 mL) was added dropwise to the suspension and stirring was continued for an additional 1 hour. The mixture was then cooled with an ice bath and the reaction carefully quenched with a saturated aqueous solution of $NH_4Cl$ (75 mL). The phases were separated and the aqueous layer was extracted with *tert*-butyl methyl ether (3 x 100 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (pentane) to give the title compound as a colorless oil (2.16 g, 70% yield). $[\alpha]_D^{20}$ = –21.5 (*c* = 0.40, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ $^1$H NMR (400 MHz, $CDCl_3$) δ 5.10 (ddq, *J* = 8.5, 5.7, 1.4 Hz, 1H), 2.51 (dp, *J* = 7.9, 6.9 Hz, 1H), 2.08 – 1.87 (m, 2H), 1.71 – 1.56 (m, 1H), 1.68 (q, *J* = 1.3 Hz, 3H), 1.61 (d, *J* = 1.2 Hz, 3H), 1.46 – 1.22 (m, 3H), 1.18 – 1.01 (m, 1H), 1.13 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.14 (s, 9H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ $^{13}$C NMR (101 MHz, $CDCl_3$) δ 131.2, 125.0, 112.7, 83.8, 44.5, 36.6, 30.5, 25.9, 25.6, 24.6, 21.2, 19.9, 17.8, 0.4. IR (film, $cm^{-1}$): 2963, 2916, 2852, 2168, 1453, 1377, 1248, 933, 838, 758, 697, 638. HRMS (ACPI) *m/z* calcd. for $C_{16}H_{31}Si$ [$M^+$ + H]: 521.2190; found 521.2190.

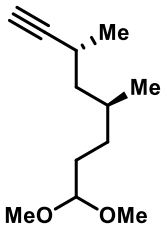
**((3*R*,5*S*)-8,8-Dimethoxy-3,5-dimethyloct-1-yn-1-yl)trimethylsilane (S2).** A stream of ozone was



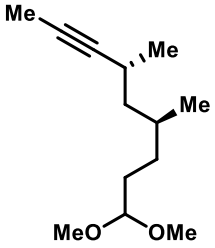

passed through a solution of alkene **19** (2.00 g, 8.00 mmol) and Sudan Red 7B (0.8 mL, 0.05% in MeOH) in dichloromethane (40 mL) and MeOH (40 mL) at –78 °C until a color change from red to a light yellow was observed. A stream of oxygen was then passed through the solution for 5 minutes followed by argon for an additional 5 minutes. Next, dimethylsulfide (2.94 mL, 40.0 mmol) was added in one portion and stirring continued at –78 °C for 30 minutes before the cooling bath was removed and the solution allowed to warm to ambient temperature. Stirring was continued for 16 hours before trimethylorthoformate (2.63 mL, 24.00 mmol) and camphor-10 sulfonic

acid (186 mg, 0.80 mmol) were added. After stirring for 4 hours, an additional portion of MeOH (10 mL) was added and stirring continued for 1 hour. The reaction was then quenched with saturated aqueous $NaHCO_3$ (50 mL). The layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 100 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (0 – 5% *tert*-butyl methyl ether in pentane) to give the title compound as a clear oil (1.98 g, 91% yield). $[\alpha]_D^{20}$ = –40.5 (*c* = 0.47, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 4.34 (t, *J* = 5.7 Hz, 1H), 3.31 (d, *J* = 1.6 Hz, 6H), 2.51 (dp, *J* = 8.2, 6.9 Hz, 1H), 1.71 – 1.49 (m, 3H), 1.48 – 1.23 (m, 3H), 1.18 – 1.02 (m, 1H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.13 (s, 9H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 112.5, 105.0, 84.0, 52.9, 52.7, 44.4, 31.1, 30.7, 30.0, 24.6, 21.2, 19.9, 0.4. IR (film, $cm^{-1}$): 2955, 2930, 2829, 2166, 1456, 1378, 1337, 1249, 1192, 1126, 1059, 963, 929, 916, 862, 840, 759, 698, 638, 564. HRMS (ESI) *m/z* calcd. for $C_{15}H_{30}O_2SiNa$ [$M^+$ + Na]: 293.1904; found 293.1907.

**(3*R*,5*S*)-8,8-Dimethoxy-3,5-dimethyloct-1-yne (S3).** Potassium carbonate (2.22 g, 16.0 mmol) was added to a solution of the TMS-capped alkyne **S2** (1.45 g, 5.34 mmol) in MeOH/$Et_2O$ (1:1, 54 mL). The resulting suspension was stirred at ambient temperature for 18 hours before water was added until a clear solution was formed. The layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 20 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (5% *tert*-butyl methyl ether in pentane) to give the title compound as a colorless oil (993.3 mg, 94% yield). $[\alpha]_D^{20}$ = –41.3 (*c* = 0.66, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 4.34 (t, *J* = 5.7 Hz, 1H), 3.31 (d, *J* = 1.0 Hz, 6H), 2.50 (dpd, *J* = 9.2, 6.8, 2.4 Hz, 1H), 2.02 (d, *J* = 2.4 Hz, 1H), 1.71 – 1.50 (m, 3H), 1.48 – 1.27 (m, 3H), 1.18 – 1.06 (m, 1H), 1.16 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 105.0, 89.5, 68.1, 52.8, 52.8, 44.3, 30.9, 30.6, 29.9, 23.5, 21.2, 20.0. IR (film, $cm^{-1}$): 3279, 2952, 2937, 2839, 2163, 1999, 1737, 1722, 1712, 1454, 1379, 1190, 1174, 1126, 1063. HRMS (ESI) *m/z* calcd. for $C_{12}H_{22}O_2Na$ [$M^+$ + Na]: 221.1512; found 221.1512.

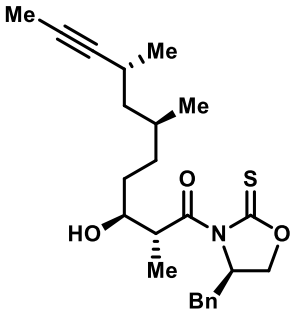



**(4*R*,6*S*)-9,9-Dimethoxy-4,6-dimethylnon-2-yne (9).** *n*BuLi (1.6 M, 3.40 mL, 5.44 mmol) was added dropwise to a solution of alkyne **S3** (980 mg, 4.94 mmol) in THF (9.9 mL) at –78 °C. After stirring for 10 minutes, the solution was warmed to 0 °C and stirring was continued for 30 minutes. The solution was then cooled to –78 °C before *N*,*N*′-dimethylpropyleneurea (DMPU) (1.79 mL, 14.8 mmol) was added. After stirring for 10 minutes, methyl iodide (0.62 mL, 9.89 mmol, 200 mol%) was added and the cooling bath was removed. The reaction mixture was stirred at ambient temperature for 16 hours before it was diluted with $Et_2O$ (20 mL). The mixture was washed with water (2 x 20 mL) and brine,



dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (5% *tert*-butyl methyl ether in pentane) to yield the title compound as a colorless oil (1.08 g, 95% yield). $[\alpha]_D^{20}$ = – 43.4 (*c* = 0.42, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 4.33 (t, *J* = 5.8 Hz, 1H), 3.31 (d, *J* = 0.7 Hz, 6H), 2.44 (dddt, *J* = 10.7, 9.1, 4.7, 2.4 Hz, 1H), 1.77 (d, *J* = 2.4 Hz, 3H), 1.71 – 1.48 (m, 3H), 1.47 – 1.22 (m, 3H), 1.15 – 1.03 (m, 1H), 1.09 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 105.1, 84.3, 75.5, 52.8, 52.7, 44.9, 31.0, 30.6, 29.9, 23.7, 21.6, 20.0, 3.6. IR (film, $cm^{-1}$): 3381, 2954, 2931, 2831, 2191, 2007, 1738, 1715, 1457, 1377, 1192, 1128, 1059, 965, 607, 445. HRMS (ESI) *m/z* calcd. for $C_{13}H_{24}O_2Na$ [$M^+$ + Na]: 235.1670; found 235.1669.

**(2*R*,3*S*,6*S*,8*R*)-1-((*R*)-4-Benzyl-2-thioxooxazolidin-3-yl)-3-hydroxy-2,6,8-trimethylundec-9-yn-1-one**



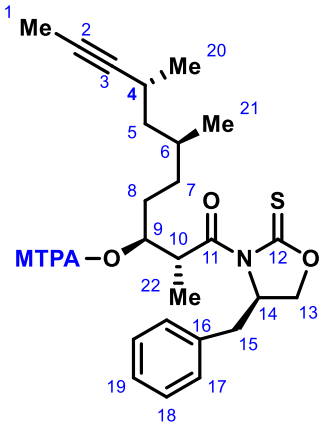

**(11).** HCl (10% *w/w*, 3.80 mL, 12.50 mmol) was added to a stirring solution of acetal **9** (531 mg, 2.50 mmol) in THF (5 mL) at ambient temperature. Stirring was continued for 90 minutes before the mixture was diluted with water and the layers were separated. The aqueous phase was extracted with $Et_2O$ (3 x 5 mL). The combined organic phases were washed with a saturated aqueous $NaHCO_3$, dried over sodium sulfate, and the solvent was removed under reduced pressure. The resulting crude aldehyde was used without further purification.

A solution of titanium tetrachloride (1 M in dichloromethane, 2.50 mL, 2.50 mmol) was added dropwise to a solution of (*R*)-(-)-4-benzyl-3-propionyl-2-oxazolidithione (**16**)[6] in dichloromethane (15 mL) at 0 °C. After stirring for 5 minutes, (–)-sparteine (0.57 mL, 2.50 mmol) was added dropwise and stirring was continued for an additional 20 minutes at 0 °C. The deep red mixture was then cooled to –78 °C for 1.5 hours before *N*-methyl-2-pyrrolidone (0.24 mL, 2.50 mmol) was added dropwise. Stirring was then continued for 10 minutes before a solution of the crude aldehyde in dichloromethane (2.50 mL) was added dropwise, rinsing with dichloromethane (2.5 mL). The resulting mixture was stirred for 1 hour at –78 °C, for 30 minutes at –40 °C, for 30 minutes at –20 °C, and for 10 minutes at –10 °C as well as at 0 °C. For work up, a saturated aqueous solution of $NH_4Cl$ was added dropwise until the mixture became a pale yellow. The phases were quickly separated and the aqueous layer extracted with dichloromethane (3 x 20 mL). The combined extracts were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (65% *tert*-butyl methyl ether in pentane) to give the title compound as a light yellow syrup (856 mg, 83% yield). $[\alpha]_D^{20}$ = – 61.4 (*c* = 0.70, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.38 – 7.27 (m, 3H), 7.24 – 7.19 (m, 2H), 5.01 – 4.91 (m, 1H), 4.70 (qd, *J* = 7.0, 2.8 Hz, 1H), 4.39 – 4.24 (m, 2H), 4.01 – 3.93 (m, 1H), 3.25 (dd, *J* = 13.3, 3.5 Hz, 1H), 2.77 (dd, *J* = 13.4, 10.0 Hz, 1H), 2.75 (d, *J* = 2.7 Hz, 1H), 2.45 (dddd, *J* = 9.2, 8.1, 4.6, 2.4 Hz, 1H), 1.78 (d, *J* = 2.3 Hz, 3H), 1.70 – 1.57 (m, 2H), 1.44 – 1.34 (m, 2H), 1.36 – 1.22 (m, 3H), 1.30 (d, *J* = 7.0 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR

($CDCl_3$, 100 MHz): δ 185.2, 178.6, 135.2, 129.5, 129.2, 127.7, 84.3, 75.5, 72.0, 70.4, 60.1, 44.8, 42.2, 37.7, 32.4, 31.4, 30.6, 23.7, 21.6, 20.0, 10.5, 3.7. IR (film, $cm^{-1}$): 3523, 2961, 2918, 2870, 1697, 1454, 1366, 1351, 1318, 1190, 1155, 1017, 955, 748, 702, 529, 503. HRMS (ESI+) *m/z* calcd. for $C_{24}H_{33}NO_3SNa$ [$M^+$ + Na]: 438.2075; found 438.2073.

The alcohol absolute configuration was determined by Mosher ester analysis.[5]

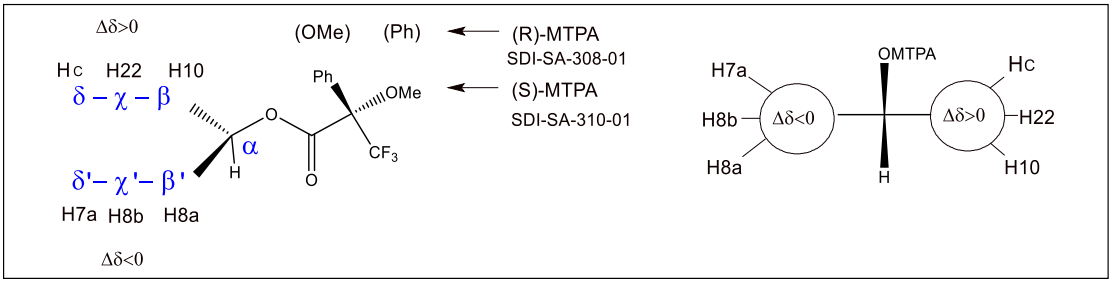
**Preparation of the (*S*)-and (*R*)-MTPA Esters of Alcohol 11. Representative Procedure.** (*S*)-(+)-MTPA-Cl (2.8 µL, 15.0 µmol) was added to a solution of alcohol **11** (6.8 mg, 15.0 µmol), 2,6-lutidine (5.1 µL, 44 µmol), and 4-(dimethylamino)-pyridine (0.5 mg, 4.1 µmol) in dichloromethane (0.3 mL). After stirring for 2 hours, the mixture was poured into a separatory funnel containing dichloromethane (2 mL) and saturated aqueous $NH_4Cl$ (5 mL). The phases were separated and the aqueous layer was extracted with dichloromethane (3 x 2 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (25% *tert*-butyl methyl ether in pentane) to give the (*R*)-MTPA-ester as a clear oil (6.8 mg, 73% yield). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.56 – 7.53 (m, 2H), 7.42 – 7.39 (m, 3H), 7.35 – 7.32 (m, 2H), 7.29 – 7.26 (m, 1H), 7.21 – 7.18 (m, 2H), 5.47 (dt, *J* = 9.1, 4.0 Hz, 1H), 5.05 (qd, *J* = 6.9, 2.7 Hz, 1H), 4.74 (dddd, *J* = 10.5, 7.2, 3.4, 1.9 Hz, 1H), 4.36 (ddd, *J* = 9.1, 7.3, 0.9 Hz, 1H), 4.30 (dd, *J* = 9.1, 1.9 Hz, 1H), 3.54 (q, *J* = 1.4 Hz, 3H), 3.30 (dd, *J* = 13.3, 3.4 Hz, 1H), 2.76 (dd, *J* = 13.3, 10.4 Hz, 1H), 2.42 – 2.34 (m, 1H), 1.83 (dddd, *J* = 14.0, 11.4, 9.1, 4.7 Hz, 1H), 1.77 (d, *J* = 2.3 Hz, 3H), 1.71 – 1.59 (m, 2H), 1.40 – 1.22 (m, 3H), 1.20 (d, *J* = 6.9 Hz, 2H), 1.13 – 1.03 (m, 1H), 1.09 (d, *J* = 6.8 Hz, 1H), 0.86 (d, *J* = 6.7 Hz, 1H).




The (*S*)-MTPA ester (64% yield) was prepared analogously using (*R*)-(-)-MTPA-Cl as the reagent. It analyzed as follows: $^1$H NMR ($CDCl_3$, 400 MHz): δ δ 7.57 – 7.51 (m, 2H), 7.42 – 7.37 (m, 3H), 7.34 (tt, *J* = 8.2, 1.5 Hz, 2H), 7.30 – 7.26 (m, 1H), 7.21 – 7.19 (m, 2H), 5.49 (dt, *J* = 9.5, 3.6 Hz, 1H), 5.12 (qd, *J* = 6.9, 2.4 Hz, 1H), 4.68 (dddd, *J* = 10.6, 7.3, 3.4, 1.7 Hz, 1H), 4.40 (ddd, *J* = 8.9, 7.3, 0.9 Hz, 1H), 4.30 (dd, *J* = 9.0, 1.7 Hz, 1H), 3.64 (q, *J* = 1.3 Hz, 3H), 3.31 (dd, *J* = 13.3, 3.4 Hz, 1H), 2.77 (dd, *J* = 13.4, 10.4 Hz, 1H), 2.31 (qddd, *J* = 9.0, 6.8, 4.5, 2.3 Hz, 1H), 1.77 (d, *J* = 2.3 Hz, 3H), 1.76 – 1.66 (m, 1H), 1.57 – 1.49 (m, 2H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.24 -1.15 (m, 2H), 1.13 – 1.08 (m, 1H), 1.07 (d, *J* = 6.8 Hz, 3H), 0.89 - 0.84 (m, 1H), 0.75 (d, *J* = 6.6 Hz, 3H).

**Table S2**. Analysis of the Mosher esters according to Hoye and co-workers;[5] arbitrary numbering Scheme as shown in the insert.

| Atom number | (*S*)-MTPA-ester δ (ppm) | (*R*)-MTPA-ester δ (ppm) | δS – δR (ppm) |
|---|---|---|---|
| **6** | 1.52 | 1.62 | –0.10 |
| **7a** | 1.18 | 1.36 | –0.18 |
| **7b** | 0.77 | 1.07 | –0.30 |
| **8a** | 1.72 | 1.83 | –0.11 |
| **8b** | 1.54 | 1.66 | –0.12 |
| **9** | 5.49 | 5.47 | +0.02 |
| **10** | 5.12 | 5.05 | +0.07 |
| **22** | 1.26 | 1.20 | +0.06 |
| **14** | 4.68 | 4.74 | –0.06 |



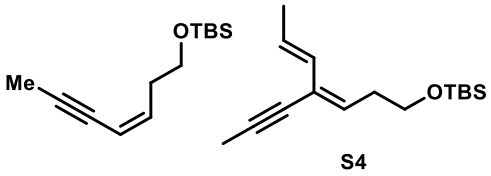

**Methyl (2*R*,3*S*,6*S*,8*R*)-3-hydroxy-2,6,8-trimethylundec-9-ynoate (12).** Potassium carbonate (821 mg, 5.94 mmol) was added to a solution of compound **11** (822 mg, 1.98 mmol) in MeOH (80 mL). Stirring was continued at ambient temperature for 3 hours before a saturated aqueous solution of $NH_4Cl$ (50 mL) was introduced. The phases were separated and the aqueous layer was extracted with *tert*-butyl methyl ether (3 x 30 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (25% *tert*-butyl methyl ether in pentane) to give the title compound as a colorless oil (388 mg, 75% yield). $[\alpha]_D^{20}$ = – 44.2 (*c* = 0.33, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 3.88 (dq, *J* = 8.3, 4.0 Hz, 1H), 3.71 (s, 3H), 2.55 (qd, *J* = 7.2, 3.7 Hz, 1H), 2.44 (dddq, *J* = 11.3, 6.8, 4.5, 2.3 Hz, 1H), 2.21 (brs, 1H),1.78 (d, *J* = 2.3 Hz, 3H), 1.65 (dddd, *J* = 14.2, 7.6, 6.5, 4.3 Hz, 1H), 1.55 – 1.45 (m, 1H), 1.43 – 1.22 (m, 5H), 1.19 (d, *J* = 7.2 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 176.7, 84.2, 75.6, 72.1, 51.9, 44.8, 44.4, 32.3, 31.1, 30.6, 23.6, 21.6, 20.0, 10.9, 3.6. IR (film, $cm^{-1}$): 3526, 2952, 2920, 2874, 1137, 1459, 1436, 1376, 1336, 1256, 1199, 1169, 1114, 1089, 1037, 989, 505. HRMS (ESI+) *m/z* calcd. for $C_{15}H_{26}O_3Na$ [$M^+$ + Na]: 277.1773; found 277.1774.

## The "Western" Fragment Comprising a C13-OR Substituent

***tert*-Butyl((4-iodobut-3-yn-1-yl)oxy)dimethylsilane (18).** *n*-BuLi (1.6 M in hexanes, 18.0 mL, 28.8 mmol) was added dropwise over 5 minutes to a solution of 4-(*tert*-butyldimethylsilyloxy)-1-butyne (**17**) (5.0 g, 27.1 mmol) in THF (50 mL) at −78 °C. After stirring at this temperature for 30 minutes, solid iodine (10.33 g, 40.68 mmol, 1.50 eq.) was added in portions over 15 min with vigorous stirring. The resulting mixture was stirred at −78 °C for 30 minutes and was then allowed to reach ambient temperature, whereby the iodine got fully dissolved. After stirring at ambient temperature for 1 hour, a saturated aqueous solution of $Na_2S_2O_3$ (30 mL) and brine (30 mL) were added. The mixture was diluted with $Et_2O$ (30 mL) and the phases were separated. The aqueous layer was extracted with $Et_2O$ (3 x 50 mL). The combined organic phases were dried over magnesium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (2% *tert*-butyl methyl ether in pentane) to yield the title compound as a pale-yellow oil (8.02 g, 95%). $^1$H NMR ($CDCl_3$, 400 MHz): δ 3.73 (t, *J* = 7.0 Hz, 2H), 2.57 (t, *J* = 7.0 Hz, 1H), 0.90 (s, 9H), 0.07 (s, 6H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 91.9, 61.9, 26.0, 25.3, 18.5, −5.1. HRMS (GC-CI) *m/z* calcd. for $C_{10}H_{19}OSiI$ [$M^+$ + H]: 311.03237; found 311.03227.

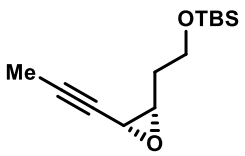
**(*Z*)-*tert*-Butyl((4-iodobut-3-en-1-yl)oxy)dimethylsilane (19).** $BH_3{\cdot}SMe_2$ (14 mL, 147.2 mmol) was added dropwise to a solution of cyclohexene (30.0 mL, 293.2 mmol) in $Et_2O$ (200 mL) at 0 °C. After stirring at this temperature for 1 hour, a solution of the iodoalkyne **18** (15.0 g, 48.3 mmol) in $Et_2O$ (100 mL) was added slowly via cannula. After stirring for an additional 2 hours at 0 °C, glacial acetic acid (42.0 mL, 734 mmol) was slowly introduced over the course of 15 min. The mixture was allowed to warm to room temperature and was stirred for 18 hours. A saturated aqueous solution of $NaHCO_3$ (400 mL) was added, the layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 200 mL). The combined organic extracts were dried with magnesium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (2% *tert*-butyl methyl ether in pentane) to yield the title compound as a pale yellow oil (11.3 g, 75% yield). $^1$H NMR ($CDCl_3$, 400 MHz): δ 6.31 – 6.23 (m, 2H), 3.69 (t, *J* = 6.5 Hz, 2H), 2.42 – 2.30 (m, 2H), 0.90 (s, 9H), 0.06 (s, 6H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 138.4, 83.8, 61.3, 38.5, 26.1, 18.5, −5.1. IR (film, $cm^{-1}$): 2953, 2928, 2895, 2856, 1611, 1471, 1408, 1385, 1361, 1337, 1309, 1287, 1256, 1100, 1059, 1006, 938, 835, 811, 775, 733, 687, 663, 630, 615. HRMS (GC-CI) *m/z* calcd. for $C_{10}H_{21}OSiI$ [$M^+$ + H]: 313.04802; found 313.04792.

**(*Z*)-*tert*-Butyl(hept-3-en-5-yn-1-yloxy)dimethylsilane (20).** Alkenyl iodide **19** (11.0 g, 34.9 mmol) was dissolved in a mixture of THF/diethylamine (120 mL/120 mL) and argon was bubbled through the solution at –15 °C for 15 minutes. Propyne (10 mL, condensed at –78 °C) was then added followed by copper(I) iodide (531 mg, 2.79 mmol), bis(triphenylphosphine)-palladium(II) dichloride (979 mg, 1.40 mmol), and additional propyne (10 mL). The resulting mixture was allowed to reach ambient temperature and was stirred for 2 hours. The mixture was then diluted with hexane (300 mL) and transferred to a separatory funnel. The organic phase was washed with a saturated aqueous solution of $NH_4Cl$ (200 mL) and brine (200 mL), dried over magnesium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (2% *tert*-butyl methyl ether in pentane) to yield the title compound (7.48 g, 92% yield), which was isolated as an inseperable 10:1 mixture with side product **S4** as an orange oil. $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.86 (dtd, *J* = 10.8, 7.3, 0.7 Hz, 1H), 5.52 – 5.45 (m, 1H), 3.66 (t, *J* = 6.8 Hz, 2H), 2.61 – 2.43 (m, 2H), 1.97 (dd, *J* = 2.4, 0.6 Hz, 3H), 0.90 (s, 9H), 0.06 (s, 6H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 138.7, 111.1, 90.2, 76.6, 62.4, 33.9, 26.1, 18.5, 4.5, –5.1. IR (film, cm$^{-1}$): 3206, 2954, 2929, 2897, 2857, 1472, 1443, 1378, 1361, 1254, 1210, 1098, 1006, 939, 834, 812, 775, 740, 663. HRMS (GC-CI) *m/z* calcd. for $C_{13}H_{24}OSi$ [$M^+$ + H]: 225.16669; found 225.16692.



S4

***tert*-Butyldimethyl(2-((*2S,3R*)-3-(prop-1-yn-1-yl)oxiran-2-yl)ethoxy)silane (21).** This compound was prepared by a modified literature procedure.[7] Ti(O$^i$Pr)$_4$ (0.46 mL, 1.56 mmol) was added dropwise to a solution of ligand **29** (924 mg, 1.72 mmol)[8] in dichloromethane (15 mL) at ambient temperature. After stirring for 1 hour, a solution of enyne **20** (3.50 g , 15.60 mmol) in dichloromethane (30 mL) was introduced, followed by 4,4'-thiobis(6-*tert*-butyl-*m*-cresol) (280 mg, 0.78 mmol), pH 7 phosphate buffer (0.05 M, 4.5 mL), and aqueous hydrogen peroxide (35% *w/w*, 7.58 mL, 78.0 mmol). After stirring for 20 hours, solid $NH_4Cl$ (3 g) and hexane (150 mL) were added to the orange mixture. The suspension was filtered through a pad of Celite and the filtrate was washed with a saturated aqueous solution of $NH_4Cl$ (2 x 100 mL) and brine (150 mL). The organic phase was dried over magnesium sulfate and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (2% EtOAc in hexane) to yield the title compound and the as a yellow oil (3.01 g, 73% yield, 96%ee). $[\alpha]_D^{20}$ = –10.7 (*c* = 0.82, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 3.82 (ddd, *J* = 6.4, 5.6, 1.2 Hz, 2H), 3.42 (dq, *J* = 3.7, 1.8 Hz, 1H), 3.17 (ddd, *J* = 6.5, 5.4, 4.0 Hz, 1H), 1.99 – 1.80 (m, 2H), 1.85 (d, *J* = 1.8 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 6H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 82.3, 74.4, 60.2, 55.8, 45.6, 32.9, 26.0, 18.5, 3.9, –5.2. IR (film, cm$^{-1}$): 2955, 2928, 2885, 2857, 1472, 1435, 1388, 1363, 1254, 1171, 1094, 1061, 1007, 942,



884, 834, 812, 776, 734, 664. HRMS (ESI) *m/z* calcd. for $C_{13}H_{24}O_2SiNa$ [$M^+$ + Na]: 263.14369; found 263.14378.

SFS-AA-286-02-Racemat
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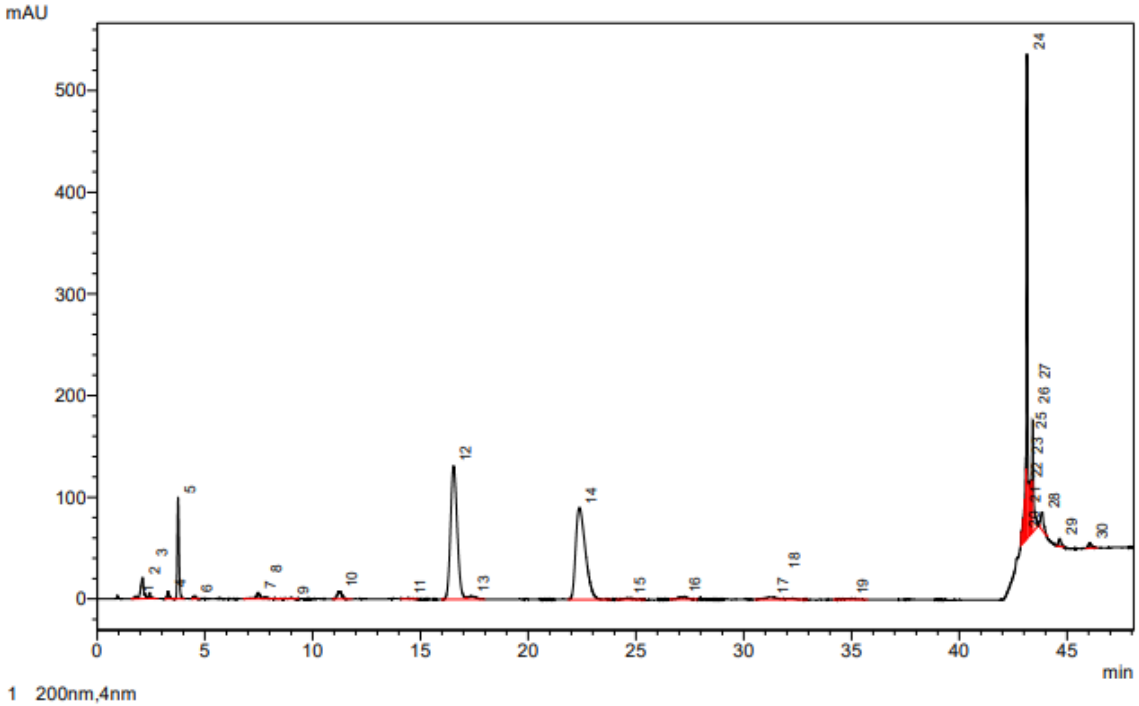
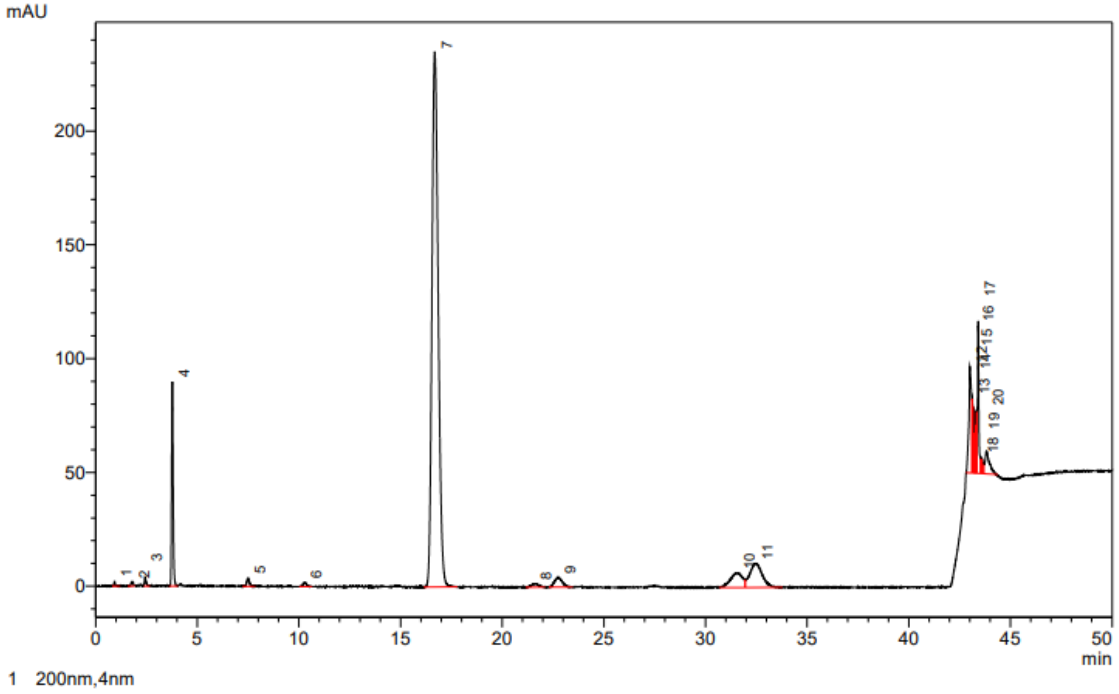
CH3CN / Wasser = 45:55 - 40 min - in 1 min 100 % CH3CN
1.0 ml/min, 167 bar, 298 K




PDA Ch1 200nm

| Peak # | Ret. Time | Area % | Name |
|---|---|---|---|
| 1 | 1,80 | 0,18 | |
| 2 | 2,11 | 1,95 | |
| 3 | 2,43 | 0,34 | |
| 4 | 3,29 | 0,46 | |
| 5 | 3,76 | 5,46 | |
| 6 | 4,52 | 0,21 | |
| 7 | 7,48 | 0,81 | |
| 8 | 7,76 | 0,17 | |
| 9 | 8,99 | 0,15 | |
| 10 | 11,25 | 1,08 | |
| 11 | 14,43 | 0,23 | |
| 12 | 16,54 | 27,18 | 1. Enantiomer |
| 13 | 17,36 | 0,78 | |
| 14 | 22,38 | 27,22 | 2. Enantiomer |
| 15 | 24,61 | 0,42 | |
| 16 | 27,18 | 0,72 | |
| 17 | 31,24 | 0,87 | |
| 18 | 31,78 | 0,37 | |
| 19 | 34,94 | 0,33 | |
| 20 | 42,89 | 0,32 | |
| 21 | 42,96 | 0,79 | |
| 22 | 43,03 | 1,32 | |
| 23 | 43,08 | 2,05 | |
| 24 | 43,14 | 14,62 | |
| 25 | 43,24 | 1,87 | |
| 26 | 43,36 | 2,26 | |

SFS-AA-287-02
150 mm Chiralcel OJ-3R, 3 µm, 4.6 mm i.D.,
CH3CN / Wasser = 45:55 - 40 min - in 1 min 100 % CH3CN
1.0 ml/min, 167 bar, 298 K




1 200nm,4nm

PDA Ch1 200nm

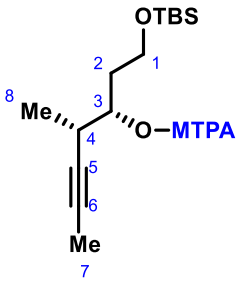
| Peak # | Ret. Time | Area % | Name |
|---|---|---|---|
| 1 | 0,93 | 0,10 | |
| 2 | 1,81 | 0,19 | |
| 3 | 2,43 | 0,29 | |
| 4 | 3,77 | 6,10 | |
| 5 | 7,50 | 0,42 | |
| 6 | 10,26 | 0,26 | |
| 7 | 16,68 | 64,59 | 1. Enantiomer 95.6 % ee |
| 8 | 21,57 | 0,51 | |
| 9 | 22,75 | 1,46 | 2. Enantiomer |
| 10 | 31,56 | 3,47 | |
| 11 | 32,46 | 5,84 | |
| 12 | 43,00 | 5,48 | |
| 13 | 43,12 | 0,79 | |
| 14 | 43,17 | 1,53 | |
| 15 | 43,26 | 1,31 | |
| 16 | 43,33 | 0,95 | |
| 17 | 43,41 | 4,02 | |
| 18 | 43,56 | 0,29 | |
| 19 | 43,61 | 0,38 | |
| 20 | 43,82 | 2,01 | |
| Total | | 100,00 | |

**(*3S*,*4S*)-1-((*tert*-Butyldimethylsilyl)oxy)-4-methylhept-5-yn-3-ol (S5).** Trimethylaluminum (2 M in toluene, 12.5 mL, 25.00 mmol) was added dropwise to a solution of epoxide **21** (3.0 g, 12.5 mmol) in dichloromethane (130 mL) at –78 °C. After stirring at this temperature for 10 minutes, methyllithium (1.6 M in $Et_2O$, 15.6 mL, 25.0 mmol) was added dropwise. Stirring was continued at –78 °C for an additional 20 minutes before boron trifluoride etherate (3.10 mL, 25.1 mmol, 200) was slowly introduced. After stirring for 1 hour, MeOH (20 mL) was added dropwise and the mixture allowed to reach ambient temperature before a saturated solution of $NH_4Cl$ (50 mL) was added. After stirring for 30 minutes the

mixture was diluted with dichloromethane (350 mL) and a saturated solution of Rochelle's salts (250 mL) was added. The mixture was vigorously stirred for 1 hour, the layers were separated and the aqueous phase was extracted with dichloromethane (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (8% EtOAc in hexane) to yield the title compound as a colorless oil (2.52 g, 79% yield). $[\alpha]_D^{20}$ = –13.0 (*c* = 1.18, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 3.94 (ddd, *J* = 10.0, 5.4, 4.4 Hz, 1H), 3.84 (ddd, *J* = 10.2, 8.7, 3.8 Hz, 1H), 3.65 (ddd, *J* = 9.2, 7.0, 2.1 Hz, 1H), 3.51 (bs, 1H), 2.48 (pq, *J* = 7.0, 2.4 Hz, 1H), 1.91 (dddd, *J* = 14.4, 5.7, 3.8, 2.2 Hz, 1H), 1.79 (d, *J* = 2.4 Hz, 3H), 1.73 (dtd, *J* = 14.3, 8.9, 4.4 Hz, 1H), 1.18 (d, *J* = 7.0 Hz, 3H), 0.90 (s, 9H), 0.08 (s, 6H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 81.2, 77.6, 75.5, 62.9, 35.6, 33.1, 26.0, 18.3, 17.2, 3.7, –5.4, –5.4. IR (film, $cm^{-1}$): 3494, 2954, 2929, 2883, 2858, 1472, 1463, 1411, 1389, 1362, 1298, 1255, 1213, 1082, 1005, 974, 937, 896, 835, 813, 777, 729, 663. HRMS (ESI) *m/z* calcd. for $C_{14}H_{28}O_2SiNa$ [$M^+$ + Na]: 279.17519; found 279.17508.

The alcohol absolute configuration was determined by Mosher ester analysis.[5]

**Preparation of the (*S*)-and (*R*)-MTPA Esters of Alcohol S5. Representative Procedure.** (*S*)-(+)-MTPA-Cl

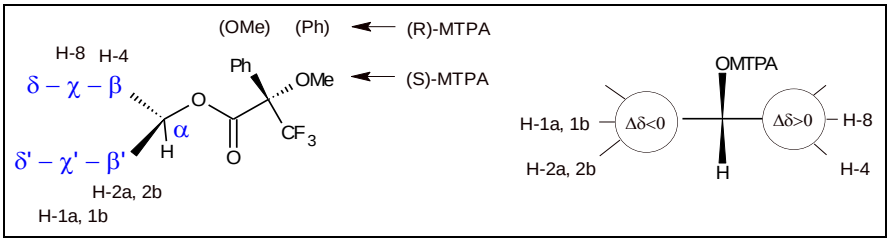



(7.4 µL, 0.039 mmol) was added to a solution of alcohol **S5** (10.0 mg, 0.039 mmol), triethylamine (16.3 µL, 0.12 mmol), and 4-(dimethylamino)pyridine (0.9 mg, 7.8 µmol) in dichloromethane (0.8 mL). After stirring for 24 hours, the mixture was poured into a separatory funnel containing dichloromethane (2 mL) and a saturated aqueous solution of $NH_4Cl$ (5 mL). The phases were separated and the aqueous layer was extracted with dichloromethane (3 x 2 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (2.5% *tert*-butyl methyl ether in pentane) to give the desired (*R*)-MTPA-ester as a colorless oil (8.4 mg, 0.018 mmol, 46%). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.59 – 7.55 (m, 2H), 7.41 – 7.37 (m, 3H), 5.14 (dt, *J* = 6.5, 5.6 Hz, 1H), 3.68 (ddd, *J* = 10.3, 6.3, 5.5 Hz, 1H), 3.62 (ddd, *J* = 10.3, 7.6, 6.9 Hz, 1H), 3.55 (q, *J* = 1.1 Hz, 3H), 2.83 (qtq, *J* = 7.0, 4.7, 2.4 Hz, 1H), 1.99 – 1.94 (m, 2H), 1.70 (d, *J* = 2.4 Hz, 3H), 1.08 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.03 (s, 6H).

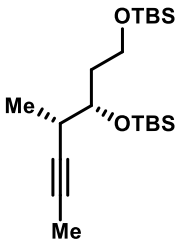
The (*S*)-MTPA ester (46%) was prepared analogously using (*R*)-(-)-MTPA-Cl as the reagent. It analyzed as follows: $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.64 – 7.60 (m, 2H), 7.43 – 7.35 (m, 3H), 5.14 (ddd, *J* = 9.3, 4.6, 3.3 Hz, 1H), 3.61 (q, *J* = 1.2 Hz, 1H), 3.55 (ddd, *J* = 10.2, 6.9, 4.2 Hz, 1H), 3.44 (ddd, *J* = 10.2, 8.6, 5.8 Hz, 1H), 2.92 (ttq, *J* = 7.1, 4.6, 2.4 Hz, 1H), 1.93 (dddd, *J* = 14.4, 9.3, 5.8, 4.3 Hz, 1H), 1.85 (dddd, *J* = 14.4, 8.6, 6.9, 3.4 Hz, 1H), 1.77 (d, *J* = 2.4 Hz, 3H), 1.15 (d, *J* = 7.1 Hz, 3H), 0.88 (s, 9H), 0.00 (d, *J* = 3.5 Hz, 6H).

**Table S3**. Analysis of the Mosher esters according to Hoye and co-workers;[5] arbitrary numbering scheme as shown in the insert.

| Atom number | (*S*)-MTPA-ester δ (ppm) | (*R*)-MTPA-ester δ (ppm) | δS – δR (ppm) |
|---|---|---|---|
| 1a | 3.55 | 3.68 | –0.13 |
| 1b | 3.44 | 3.62 | –0.18 |
| 2a | 1.93 | 1.96 | –0.03 |
| 2b | 1.85 | 1.96 | –0.11 |
| 3 | 5.14 | 5.14 | 0 |
| 4 | 2.92 | 2.83 | +0.09 |
| 8 | 1.15 | 1.08 | +0.07 |
| 7 | 1.77 | 1.70 | +0.07 |

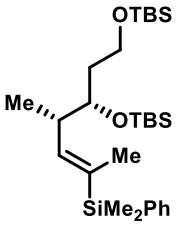



**(S)-2,2,3,3,9,9,10,10-Octamethyl-5-((*S*)-pent-3-yn-2-yl)-4,8-dioxa-3,9-disilaundecane (22).** TBSOTf



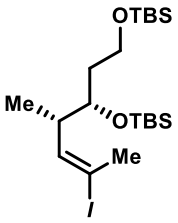

(2.54 mL, 11.1 mmol) was added to a solution of alcohol **S5** (1.42 g, 5.54 mmol) and 2,6-lutidine (1.94 mL, 16.6 mmol) in dichloromethane (55 mL) at –78°C. The mixture was stirred for 1 hour before the reaction was quenched with MeOH (10 mL). The mixture was allowed to reach ambient temperature before a saturated aqueous solution of $NaHCO_3$ (50 mL) was introduced. The layers were separated and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (1% EtOAc in hexanes) to yield the title compound as a colorless oil (1.90 g, 93%). $[\alpha]_D^{20}$ = –33.6 (*c* = 0.91, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 3.76 – 3.65 (m, 3H), 2.52 – 2.43 (m, 1H), 1.86 – 1.69 (m, 2H), 1.77 (d, *J* = 2.4 Hz, 3H), 1.09 (d, *J* = 2.4 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 6H) ppm. $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 82.0, 72.8, 59.8, 37.8, 32.8, 26.1, 26.1, 18.4, 18.3, 17.3, 3.7, –4.3, –4.3, –5.1, –5.1 ppm. IR (film, cm$^{-1}$): 2954, 2929, 2885, 2857, 1472, 1462, 1388, 1361, 1253, 1090, 1027, 1006, 938, 832, 772, 711, 664, 524. HRMS (ESI) *m/z* calcd. for $C_{20}H_{42}O_2Si_2Na$ [$M^+$ + Na]: 393.2616; found 393.2612.

**(*S*)-5-((*S,E*)-4-(Dimethyl(phenyl)silyl)pent-3-en-2-yl)-2,2,3,3,9,9,10,10-octamethyl-4,8-dioxa-3,9-di-**




**silaundecane (23).** $LiSiMe_2Ph$ (0.4 M solution in THF, 32 mL, 12.8 mmol) was added to a suspension of copper(I) cyanide (568 mg, 6.35 mmol) in diethyl ether (40 mL) at 0 °C. The mixture was stirred for 30 minutes before it was cooled to –78 °C. A solution of alkyne **22** (1.81 g, 4.88 mmol) in $Et_2O$ (10 mL) was added via cannula and the resulting mixture was stirred for 1.5 hours. It was then warmed to 0 °C and, after 30 min, the reaction was quenched with a saturated aqueous solution of $NH_4Cl$ (50 mL). The mixture was partitioned between water (25 mL) and *tert*-butyl methyl ether (50 mL), the layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 50 mL). The combined organic layers were dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (1% EtOAc in hexanes) to yield title compound as a pale yellow oil (2.27 g, 92%). $[\alpha]_D^{20}$ = 2.3 (*c* = 1.00, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.52 – 7.46 (m, 2H), 7.36 – 7.31 (m, 3H), 5.76 (dq, *J* = 9.2 Hz, 1.8 Hz, 1H), 3.71 (q, *J* = 5.6 Hz, 1 H), 3.66 (t, *J* = 6.8 Hz, 2H), 2.73 – 2.64 (m, 1H), 1.77 – 1.62 (m, 2H), 1.67 (d, *J* = 1.7 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.89 (s, 9H), 0.32 (s, 6H), 0.06 (s, 3H), 0.04 (m, 6H), 0.03 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 145.1, 139.0, 134.1, 132.9, 128.9, 127.8, 73.1, 60.1, 38.2, 38.0, 26.1, 26.1, 18.4, 18.3, 15.7, 15.1, −3.2, −3.3, −4.1, −4.2, −5.1, −5.1. IR (film, $cm^{-1}$): 2955, 2929, 2866, 2857, 1472, 1462, 1428, 1407, 1387, 1361, 1249, 1091, 1021, 1006, 975, 939, 830, 811, 771, 729, 699, 665, 471, 428. HRMS (ESI) *m/z* calcd. for $C_{28}H_{54}O_2Si_3Na$ [$M^+$ + Na]: 529.3324; found 529.3325.

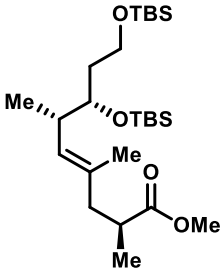
**(*S*)-5-((*S,E*)-4-Iodopent-3-en-2-yl)-2,2,3,3,9,9,10,10-octamethyl-4,8-dioxa-3,9-disilaundecane (24).** in




*NOTE: This reaction was carried out in a dark fume hood*. *N*-Iodosuccinimide (1.50 g, 6.67 mmol) was added to a solution of alkenylsilane **23** (2.27 g, 4.48 mmol) and 2,6-Lutidine (0.39 mL, 3.36 mmol) in a mixture of HFIP and dichloromethane (3:1, 20 mL) at 0 °C. The mixture was stirred for 10 minutes at 0 °C before the reaction was quenched with a saturated aqueous solution of $Na_2S_2O_3$ (20 mL). The mixture was diluted with water (20 mL) and dichloromethane (30 mL), the layers were separated and the aqueous phase was extracted with dichloromethane (3 x 25 mL). The combined extracts were dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (1 – 2% EtOAc in hexanes) to yield title compound as a pale orange oil (1.68 g, 75%). $[\alpha]_D^{20}$ = −30.0 (*c* = 0.95, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 6.08 (dq, *J* = 9.9 Hz, 1.5 Hz, 1H), 3.70 (td, *J* = 5.9 Hz, 4.5 Hz, 1H), 3.64 (t, *J* = 6.6 Hz, 2H), 2.54 – 2.45 (m, 1H), 2.38 (d, *J* = 1.5 Hz, 3H), 1.73-1.58 (m, 2H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.89 (s, 9H), 0.05 (s, 3H), 0.05(s, 3H), 0.04 (s, 6 H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 145.1, 93.5, 72.5, 60.0, 40.9, 37.9, 28.0, 26.1, 18.4, 18.3, 14.9, −4.3, −4.3, −5.1, −5.2. IR (film, $cm^{-1}$): 2954, 2928, 2885, 2856, 1472. 1462, 1937, 1361, 1253, 1093,

1053, 1022, 1006, 980, 939, 833, 812, 774, 671, 665. HRMS (ESI) *m/z* calcd. for $C_{20}H_{43}IO_2Si_2Na$ [$M^+$ + Na]: 521.1749; found 521.1743.

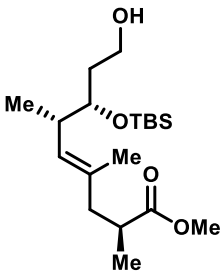
**Methyl (2*S*,6*S*,7*S*,*E*)-7,9-bis((*tert*-butyldimethylsilyl)oxy)-2,4,6-trimethylnon-4-enoate (S6).** (*R*)-(+)-3-




Bromoisobutyric acid methyl ester (**30**) (1.29 mL, 10.1 mmol) was added to a slurry of manganese(II) bromide (217 mg, 1.01 mmol) and copper(I) chloride (66.7 mg, 0.67 mmol) in DMPU (15 mL) at ambient temperature. Then, diethylzink (1 M solution in hexanes, 7.60 mL, 7.60 mmol) was added dropwise and the resulting dark solution was stirred for 22 hours at ambient temperature.

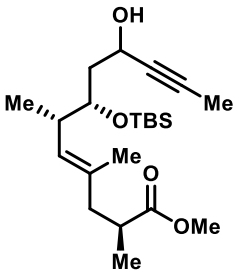
This solution was added dropwise to a mixture of alkenyl iodide **24** (1.68 g, 3.37 mmol) and [$PdCl_2$(dppf)·$CH_2Cl_2$] (138 mg, 0.17 mmol) in THF (50 mL). The mixture was stirred for 48 hours before the reaction was quenched with a saturated aqueous solution of $NH_4Cl$ (50 mL). The mixture was diluted with *tert*-butyl methyl ether (50 mL) and water (50 mL), the layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 75 mL). The combined extracts were washed with brine (3 x 50 mL), dried with magnesium sulfate, filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (2% EtOAc in hexanes) to yield the title compound as a colorless oil (1.46 g, 92%). $[\alpha]_D^{20}$ = –5.8 (*c* = 1.33, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.05 (dq, *J* = 9.8, 1.2 Hz, 1H), 3.66 – 3.58 (m, 3H), 3.64 (s, 3H), 2.66 – 2.57 (m, 1H), 2.47 – 2.39 (m, 1H), 2.34 (ddd, *J* = 13.4, 7.5, 1.1 Hz, 1H), 2.02 (ddd, *J* = 13.4, 7.5, 1.1 Hz, 1H), 1.75 – 1.61 (m, 2H), 1.59 (d, *J* = 1.4 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.89 – 0.86 (m, 21 H), 0.04 – 0.03 (m, 6H), 0.03 (s, 6H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 177.2, 131.4, 130.9, 73.6, 60.1, 51.5, 44.6, 38.2, 38.2, 37.9, 26.1, 26.1, 18.3, 16.8, 16.0, –4.2, –4.2, –5.1, –5.2. IR (film, cm$^{-1}$): 2954, 2930, 2886, 2857, 1741, 1472, 1462, 1386, 1361, 1254, 1194, 1165, 1091, 1041, 1027, 1006, 939, 835, 774, 664. HRMS (ESI) *m/z* calcd. for $C_{25}H_{52}O_4Si_2Na$ [$M^+$ + Na]: 495.3296; found 495.3299.

**Methyl (2*S*,6*S*,7*S*,*E*)-7-((*tert*-butyldimethylsilyl)oxy)-9-hydroxy-2,4,6-trimethylnon-4-enoate (25).**




*para*-Toluene sulfonic acid monohydrate (57 mg, 0.30 mmol) was added to a solution of TBS-ether **S6** (1.42 g, 3.00 mmol) in MeOH (30 mL) at 0 °C. After 1 hour, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (50 mL). The mixture was diluted with EtOAc (100 mL) and water (50 mL), the layers were separated, and the aqueous phase was extracted with EtOAc (3 x 75 mL). The combined organic layers were dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (10 – 20% EtOAc in hexanes) to yield title compound as a colorless oil (792 mg, 74%). $[\alpha]_D^{20}$ = –9.2 (*c* = 0.79, MeOH). $^1$H NMR ($CDCl_3$, 400 MHz): δ 4.96 (d, *J* = 9.8 Hz, 1H), 3.82 – 3.76 (m, 1H), 3.69 – 3.63 (m, 2H), 3.64 (s, 3H), 2.67 – 2.51 (m, 2H), 2.32 (dd, *J* = 13.4, 7.8 Hz, 1H), 2.27 (br, 1H),

2.03(dd, *J* = 13.4, 7.4 Hz, 1H), 1.86 – 1.77 (m, 1H), 1.69 – 1.63 (m, 1H), 1.61 (s, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.92 – 0.90 (m, 12H), 0.10 (s, 3H), 0.07 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 177.1, 132.2, 130.0, 75.8, 60.1, 51.6, 44.3, 382., 37.8, 36.1, 26.0, 18.2, 18.0, 16.9, 16.2, −4.2, −4.4. IR (film, cm$^{-1}$): 3447, 2954, 2930, 2885, 2857, 1739, 1461, 1436, 1376, 1361, 1255, 1196, 1167, 1094, 1060, 1029, 1005, 939, 864, 836, 774, 671, 666. HRMS (ESI) *m/z* calcd. for $C_{19}H_{38}O_4SiNa$ [$M^+$ + Na]: 381. 381.2432; found 381.2431.

**Methyl (2*S*,6*S*,7*S*,*E*)-7-((*tert*-butyldimethylsilyl)oxy)-9-hydroxy-2,4,6-trimethyldodec-4-en-10-ynoate (S7).** 

Dess-Martin-periodinane (1.18 g, 2.79 mmol) was added to a suspension of alcohol **25** (400 mg, 1.12 mmol) and $NaHCO_3$ (469 mg, 5.58 mmol) in wet dichloromethane (11 mL) at 0°C. After 10 min, the mixture was allowed to reach ambient temperature and stirring was continued for 2 hours. The reaction was quenched with a saturated solution of $Na_2S_2O_3$/$NaHCO_3$ (1:1, 20 mL). The biphasic mixture was vigorously stirred for 30 min before the layers were separated. The aqueous phase was extracted with dichloromethane (3 x 20 mL), the combined organic layers were dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure to yield the crude aldehyde as a pale yellow oil, which was immediately used in the next step without further purification.

Propynylmagnesium bromide (0.5 M solution in THF, 6.7 mL, 3.35 mmol) was added to a solution of the crude aldehyde in THF (11 mL) at 0 °C. After 30 min, the reaction was quenched with a saturated aqueous solution of $NH_4Cl$ (10 mL), the mixture was diluted with *tert*-butyl methyl ether (30 mL) and water (10 mL), and the layers were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (3 x 25 mL). The combined extracts were dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (7.5% EtOAc in hexanes) to yield title compound (1:0.7 mixture of diastereomers) as a yellow oil (359 mg, 81%).

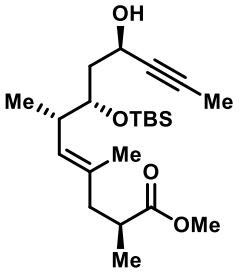
Major diastereomer: $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.08 (dq, *J* = 9.5, 1.3 Hz, 1H), 4.47 – 4.42 (m, 1H), 3.73 – 3.67 (m, 1H), 3.64 (s, 3H), 2.65 − 2.58 (m, 1H), 2.58 – 2.49 (m, 1H), 2.34 (ddd, *J* = 13.5, 7.7, 1.2 Hz, 1H), 2.10 (d, *J* = 4.6 Hz, 1H), 2.03 (ddd, *J* = 13.5, 7.5, 0.7 Hz, 1H), 1.90 – 1.75 (m, 2H), 1.85 (d, *J* = 2.1 Hz, 3H), 1.60 (d, *J* = 1.4 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.89 – 0.87 (m, 12H), 0.08 (s, 3H), 0.06 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 177.1, 132.3, 129.9, 81.5, 80.5, 74.6, 61.3, 51.6, 44.5, 42.4, 38.7, 38.2, 26.1, 18.2, 17.0, 16.9, 16.2, 3.7, −4.0, −4.3.

Minor diastereomer: $^1$H NMR ($CDCl_3$, 400 MHz): δ 4.97 (dq, *J* = 9.7 Hz, 1.3 Hz, 1H), 4.59 – 4.48 (m, 1H), 3.75 – 3.66 (m, 1H), 3.64 (s, 3H), 3.07 (d, *J* = 3.4, 1H), 2.67 – 2.57 (m, 1H), 2.57 – 2.48 (m, 1H), 2.34 (ddd, *J* = 13.5, 7.7, 1.2 Hz, 1H), 2.03 (ddd, *J* = 13.5, 7.4, 0.9 Hz, 1H), 1.90 – 1.75 (m, 2H), 1.82 (d, *J* =

2.1 Hz, 3H), 1.62 (d, *J* = 1.4 Hz, 3H), 1.10 (d, *J* = 7.2 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 177.1, 132.5, 129.6, 80.6, 80.5, 75.1, 59.9, 51.6, 44.3, 41.6, 38.1, 37.8, 26.0, 18.1, 17.9, 16.8, 16.1, 3.7, −4.2, −4.3.

IR (film, cm$^{-1}$): 3466, 2955, 2856, 1738, 1460, 1436, 1377, 1361, 1252, 1197, 1166, 1059, 1023, 1006, 940, 864, 833, 810, 774, 666. HRMS (ESI) *m/z* calcd. for $C_{22}H_{40}O_4SiNa$ [$M^+$ + Na]: 419.2588; found 419.2592.

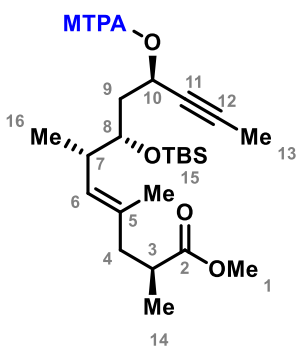
**Methyl (2*S*,6*S*,7*S*,9*R*,*E*)-7-((*tert*-butyldimethylsilyl)oxy)-9-hydroxy-2,4,6-trimethyldodec-4-en-10-ynoate (27).** Manganese(IV) oxide (1.57g, 18.1 mmol) was added to a solution of alcohol **S7** (359 mg, 0.91 mmol) in dichloromethane (9 mL) at ambient temperature. The suspension was stirred for 3 hours and was then filtered through a short pad of Celite© (≈ 2 cm), which was carefully rinsed with dichloromethane (100 mL). The solvent was removed under reduced pressure to yield the crude ynone **26** as a yellow oil, which was immediately used in the next step without further purification.




Powdered potassium hydroxide (940 mg, 16.8 mmol) was added to a solution of complex *R,R*-**32** (100 mg, 0.17 mmol) in $CH_2Cl_2$ (10 mL) at ambient temperature. After stirring for 30 minutes, the suspension was diluted with $CH_2Cl_2$ (10 mL), washed with water (3 x 10 mL), dried over $CaH_2$, and transferred to a Schlenk flask via filter cannulation. The solvent was removed under reduced pressure to give the activated catalyst as a deep purple solid, which was stored under Argon.

The crude ynone **26** was dissolved in *i*PrOH (8 mL) and an orange solution of activated *R,R*-**32** (26.5 mg, 0.05 mmol) in *i*PrOH (1 mL) was added. The mixture was stirred at ambient temperature for 18 hours before the solvent was removed under reduced pressure. The residue was purified by flash chromatography (10% EtOAc in hexanes) to yield title compound as a pale yellow oil (259 mg, dr > 20:1, 72%). $[\alpha]_D^{20}$ = −6.4 (*c* = 0.84, MeOH). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.08 (dq, *J* = 9.5, 1.3 Hz, 1H), 4.47 – 4.42 (m, 1H), 3.73 – 3.67 (m, 1H), 3.64 (s, 3H), 2.65 - 2.58 (m, 1H), 2.58 – 2.49 (m, 1H), 2.34 (ddd, *J* = 13.5, 7.7, 1.2 Hz, 1H), 2.10 (d, *J* = 4.6 Hz, 1H), 2.03 (ddd, *J* = 13.5, 7.5, 0.7 Hz, 1H), 1.90 – 1.75 (m, 2H), 1.85 (d, *J* = 2.1 Hz, 3H), 1.60 (d, *J* = 1.4 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.89 – 0.87 (m, 12H), 0.08 (s, 3H), 0.06 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 177.1, 132.3, 129.9, 81.5, 80.5, 74.6, 61.3, 51.6, 44.5, 42.4, 38.7, 38.2, 26.1, 18.2, 17.0, 16.9, 16.2, 3.7, −4.0, −4.3. IR (film, cm$^{-1}$): 3452, 2956, 2930, 2893, 2857, 1739, 1472, 1460, 1436, 1377, 1361, 1253, 1197, 1166, 1089, 1060, 1024, 1006, 940, 865, 835, 810, 775, 668. HRMS (ESI) *m/z* calcd. for $C_{22}H_{40}O_4SiNa$ [$M^+$ + Na]: 419.2588; found 419.2591.

The alcohol absolute configuration was determined by Mosher ester analysis.[5]

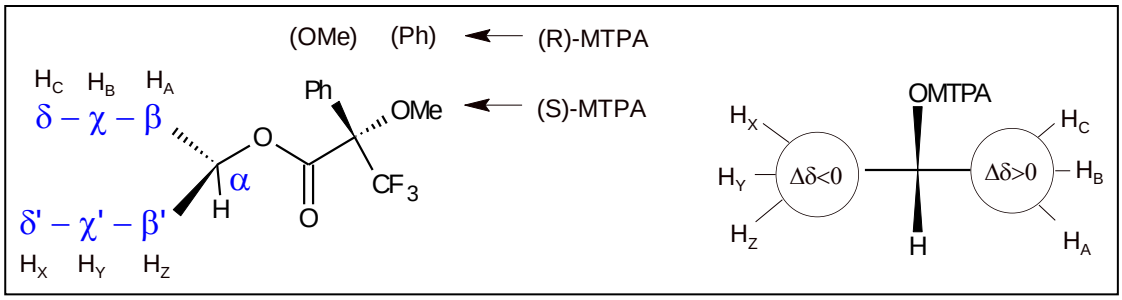



**Preparation of the (*S*)-and (*R*)-MTPA Esters of Alcohol 27. Representative Procedure.** (*S*)-(+)-MTPA-Cl (5.0 µL, 26.7 µmol) was added to a solution of alcohol **27** (10 mg, 25.2 µmol), triethylamine (10.5 µL, 75.6 µmol), and 4-(dimethylamino)pyridine (0.6 mg, 5.0 µmol) in dichloromethane (0.5 mL). After stirring for 18 hours, the mixture was poured into a separatory funnel containing dichloromethane (15 mL) and a saturated aqueous solution of $NH_4Cl$ (10 mL). The phases were separated and the aqueous layer was extracted with dichloromethane (2 x 10 mL). The combined organic phases were dried with magnesium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (5% EtOAc in hexanes) to yield the (*R*)-MTPA ester as a colorless oil (10.9 mg, 71%). $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.55 – 7.50 (m, 2H), 7.42 – 7.37 (m, 3H), 5.58 (ddq, *J* = 10.3, 6.1, 2.1 Hz, 1H), 5.02 (dq, *J* = 9.6 Hz, 1.3 Hz, 1H), 3.68 (ddd, *J* = 7.8, 5.1, 4.3 Hz, 1H), 3.62 (s, 3H), 3.55 (q, *J* = 1.0 Hz, 3H), 2.61 (h, *J* = 7.1 Hz, 1H), 2.49 (dqd, *J* = 9.6, 6.9, 5.1 Hz, 1H), 2.33 (ddd, *J* = 13.5, 7.8, 1.1 Hz, 1H), 2.02 (ddd, *J* = 13.5, 7.3, 1.0 Hz, 1H), 1.94 (ddd, *J* = 13.3, 9.1, 4.3 Hz, 1H), 1.87 (ddd, *J* = 13.5, 7.8, 6.1 Hz, 1H), 1.84 (d, *J* = 2.1 Hz, 3H), 1.54 (d, *J* = 1.4 Hz, 3H), 1.09 (d, J 0 6.9 Hz, 3H), 0.90 (s, 9H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.11 (s, 3H), 0.05 (s, 3H).

The (*S*)-MTPA ester (7.9 mg, 13 µmol, 51%) was prepared analogously using (*R*)-(-)-MTPA-Cl as the reagent. It analyzed as follows: $^1$H NMR ($CDCl_3$, 600 MHz): δ 7.56 – 7.52 (m, 2H), 7.42 – 7.37 (m ,3H), 5.61 (ddq, *J* = 8.7, 6.5, 2.10, 1H), 5.00 – 4.97 (m, 1H), 3.62 (s, 3H), 3.60 – 3.57 (m, 3H), 2.61 (ddq, *J* = 7.8, 7.3, 6.9 Hz, 1H), 2.40 (dqd, *J* = 9.7, 6.8, 4.9, 1H), 2.33 (ddd, *J* = 13.5, 7.8, 1.1 Hz, 1H), 2.02 (ddd, *J* = 13.5, 7.3, 1.0 Hz, 1H), 1.90 (ddd, *J* = 13.4, 8.4, 4.9 Hz, 1H), 1.86, (d, *J* = 2.10, 3H), 1.82 (ddd, *J* = 13.7, 7.3, 6.6, 1H), 1.55 (d, *J* = 1.4 Hz, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.07 (s, 3H), 0.01 (s, 3H).

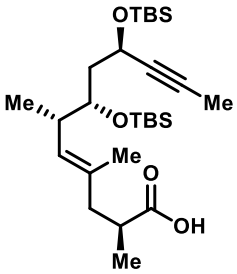
**Table S4**. Analysis of the Mosher esters according to Hoye and co-workers;[5] arbitrary numbering Scheme as shown in the insert.

| Atom number | (*S*)-MTPA-ester δ (ppm) | (*R*)-MTPA-ester δ (ppm) | δS – δR (ppm) |
|---|---|---|---|
| **13** | 1.84 | 1.86 | –0.02 |
| **10** | 5.68 | 5,61 | +0.07 |
| **9a** | 1.94 | 1.90 | +0.04 |
| **9b** | 1.87 | 1.82 | +0.05 |
| **8** | 3.68 | 3.59 | +0.09 |
| **7** | 2.49 | 2.40 | +0.09 |
| **6** | 5.02 | 4.99 | +0.03 |
| **16** | 0.87 | 0.81 | +0.06 |




**Methyl (2*S*,6*S*,7*S*,9*R*,*E*)-7,9-bis((*tert*-butyldimethylsilyl)oxy)-2,4,6-trimethyldodec-4-en-10-ynoate (S8).** Imidazole (130 mg, 1.91 mmol) and TBSCl (192 mg, 1.27 mmol) were added to a solution of alcohol **27** (252 mg, 0.64 mmol) in dichloromethane (6.5 mL) at ambient temperature. The mixture was stirred for 1 hour before water (15 mL) and dichloromethane (15 mL) were introduced. The layers were separated and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried over magnesium sulfate, filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (5% EtOAc in hexanes) to yield the title compound as a colorless oil (304 mg, 94%). $[\alpha]_D^{20}$ = 10.6 (*c* = 1.16, MeOH). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.10 (dq, *J* = 9.7, 1.3 Hz, 1H), 4.42 – 4.37 (m, 1H), 3.70 (dt, *J* = 7.6, 4.5 Hz, 1H), 3.64 (s, 3H), 2.66 – 2.57 (m, 1H), 2.52 – 2.44 (m, 1H), 2.35 (ddd, *J* = 13.3, 7.3, 1.1 Hz, 1H), 2.03 (ddd, *J* = 13.4, 7.7, 1.0 Hz, 1H), 1.83 (d, *J* = 2.1 Hz, 3H), 1.78 – 1.70 (m, 2H), 1,59 (d, *J* = 1.4 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.87 (d, *J* = 9.8 Hz, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 177.2, 131.5, 130.7, 81.0, 80.9, 73.4, 61.7, 51.6, 44.6, 43.8, 38.2, 38.1, 26.1, 26.0, 18.4, 18.3, 16.8, 16.2, 16.1, 3.7, 1.2, –4.1, –4.2, –4.4, –4.8. IR (film, cm$^{-1}$): 2956, 3930, 2887, 1742, 1472, 1462, 1435, 1361, 1254, 1194, 1164, 1094, 1060, 1028, 1006, 943, 836, 775. HRMS (ESI) *m/z* calcd. for $C_{28}H_{54}O_4Si_2Na$ [$M^+$ + Na]: 533.3453; found 533.3457.

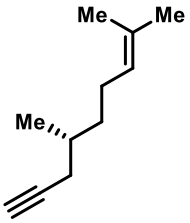
**(2*S*,6*S*,7*S*,9*R*,*E*)-7,9-bis((*tert*-Butyldimethylsilyl)oxy)-2,4,6-trimethyldodec-4-en-10-ynoic acid (28).**




Lithium hydroxide (138 mg, 5.76 mmol) was added to a solution of methyl ester **S8** (294 mg, 0.58 mmol) in a mixture of THF/MeOH/water (2.2 mL/2.2 mL/1.1 mL) at ambient temperature. After 6 hours, the mixture was diluted with dichloromethane (50 mL) and water (50 mL) and the aqueous phase was acidified with HCl (1 M) until a pH ≈ 2 was reached. The layers were separated and the aqueous phase extracted with dichloromethane (3 x 50 mL). The combined organic layers were dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure. The title compound was obtained as a colorless oil (262 mg, 92%) and was used without further purification. $[\alpha]_D^{20}$ = 6.9 (*c* = 1.17, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.14 (dd, *J* = 9.7, 1.3 Hz, 1H), 4.42 – 4.38 (m, 1H), 3.71 (dt, *J* = 7.6, 4.5 Hz, 1H), 2.66 – 2.57 (m, 1H), 2.53 – 2.45 (m, 1H), 2.39 (ddd, *J* = 13.3, 6.8, 1.2 Hz, 1H), 2.05 (ddd, *J* = 13.4, 8.3, 1.0 Hz, 1H), 1.85 – 1.70 (m, 2H), 1.83 (d, *J* = 2.1 Hz, 3H), 1.60 (d, *J* = 1.4 Hz, 3H), 1.13 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.89 – 0.88 (m, 3H), 0.11(s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 182.2, 131.2, 131.0 , 81.0, 80.9, 73.3, 61.7, 44.1, 43.7, 38.2, 37.8, 26.1, 26.0, 18.4, 18.2, 16.4, 16.1, 16.0, 3.7, −4.1, −4.2, −4.4, −4.8. IR (film, cm$^{-1}$): 2956, 2929, 2857, 1708, 1462, 1383, 1361, 1251, 1090, 1062, 1028, 1005, 941, 834, 811, 774, 668. HRMS (ESI) *m/z* calcd. for $C_{27}H_{51}O_4Si_2$ [$M^+$ + Na]: 495.3331; found 495.3332.

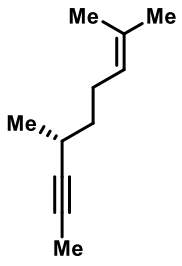
## The "Western" Fragment Devoid of a C13 Substituent

**(*R*)-4,8-Dimethylnon-7-en-1-yne (33).** Ohira-Bestman reagent [dimethyl-(1-diazo-2-oxopropyl)-




phosphonate, **39**] (7.29 mL, 30.3 mmol) was added to a suspension of potassium carbonate (7.62 g, 55.2 mmol) and (*R*)-citronellal ((*R*)-**5**) (5.00 mL, 27.6 mmol) in MeOH (275 mL) at ambient temperature. The mixture was stirred for 18 hours before it was diluted with water. The aqueous layer was separated and extracted with pentane. The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was carefully removed under reduced pressure [*NOTE*: *the compound is volatile; conditions for the evaporation of the solvents: >700 mbar, 40 °C*]. The residue was purified by flash chromatography (pentane) to yield the title compound as a colorless oil (3.58 g, 86% yield). $[\alpha]_D^{20}$ = –0.8 (*c* = 0.86, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.10 (tdt, *J* = 7.1, 2.9, 1.4 Hz, 1H), 2.18 (ddd, *J* = 16.7, 5.6, 2.7 Hz, 1H), 2.08 (ddd, *J* = 16.7, 6.9, 2.7 Hz, 1H), 2.03 – 1.96 (m, 2H), 1.95 (t, *J* = 2.7 Hz, 1H), 1.71 – 1.63 (s, *J* = 6.4 Hz, 1H), 1.68 (q, *J* = 1.3 Hz, 3H), 1.61 (bs, 3H), 1.51 – 1.35 (m, 1H), 1.24 (dddd, *J* = 13.4, 8.8, 7.6, 6.6 Hz, 1H), 1.00 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 131.6, 124.6, 83.5, 69.2, 36.2, 32.1, 25.9, 25.8, 25.7, 19.5, 17.8. IR (film, $cm^{-1}$): 3426, 3288, 2964, 2930, 2873, 1715, 1457, 1379, 1236, 1146, 1067, 1034, 974, 633, 435. HRMS (APCI) *m/z* calcd. for $C_{11}H_{19}$ [$M^+$ + H]: 151.1482; found 151.1481.

**(*R*)-2,6-Dimethylnon-2-en-7-yne (S9).** Potassium *tert*-butoxide (4.95 g, 44.1 mmol) was added to a



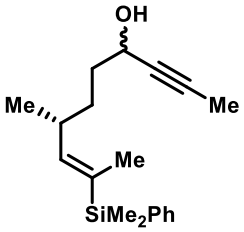

solution of alkyne **33** (3.31 g, 22.0 mmol) in degassed DMSO (70 mL) at ambient temperature. The resulting solution was stirred for 1 hour before it was cooled with an ice bath and the reaction was quenched with aqueous HCl (1 M). The layers were separated and the aqueous phase was extracted with pentane (3 x 100 mL). The combined organic layers were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (pentane) to give the title compound as a colorless oil (3.10 g, 94% yield). [*NOTE*: *the compound is volatile; conditions for the evaporation of the solvents: >700 mbar, 40 °C*]. $[\alpha]_D^{20}$ = –79.9 (*c* = 0.67, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.10 (ddp, *J* = 7.2, 5.8, 1.4 Hz, 1H), 2.43 – 2.30 (m, 1H), 2.21 – 2.00 (m, 2H), 1.79 (d, *J* = 2.3 Hz, 3H), 1.68 (q, *J* = 1.3 Hz, 3H), 1.62 (d, *J* = 1.3 Hz, 3H), 1.50 – 1.31 (m, 2H), 1.12 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 132.0, 124.3, 84.0, 75.7, 37.5, 26.1, 25.9, 25.6, 21.5, 17.8, 3.6. IR (film, $cm^{-1}$): 3429, 2967, 2920, 2858, 2150, 1451, 1376, 1338, 1258, 1146, 1093, 1073, 982, 846, 829, 426. HRMS (EI) *m/z* calcd. for $C_{11}H_{18}$ [$M^+$]: 150.1404; found 150.1403.

**(*R*)-4-Methylhept-5-yn-1-ol (34).** A stream of ozone was passed through a solution of alkene **S9** (1.48 g, 9.88 mmol) and Sudan Red 7B (1.0 mL, 0.05% in MeOH) in dichloromethane (66 mL) and MeOH (33 mL) at –78 °C until a color change from red to light yellow occurred. A stream of oxygen was then passed through the solution for 5 minutes followed by a stream of argon for an additional 5 minutes. Sodium borohydride (486 mg, 12.9 mmol) was added and the mixture stirred at –78 °C for 30 minutes. The cooling bath was then removed and the mixture stirred for 16 hours at ambient temperature. The reaction was quenched with saturated aqueous $NH_4Cl$ (100 mL), the layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 100 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (65% *tert*-butyl methyl ether in pentane) to give the title compound as a colorless syrup (1.12 g, 90% yield). $[\alpha]_D^{20}$ = –40.2 (*c* = 0.44, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 3.66 (t, *J* = 6.5 Hz, 2H), 2.46 – 2.34 (m, 1H), 1.78 (d, *J* = 2.4 Hz, 3H), 1.77 – 1.59 (m, 2H), 1.51 (bs, 1H), 1.56 – 1.37 (m, 2H), 1.14 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 83.7, 76.1, 63.0, 33.5, 30.8, 25.9, 21.6, 3.6. IR (film, $cm^{-1}$): 3321, 2965, 2933, 2921, 2871, 1452, 1374, 1334, 1056, 1022, 897, 671, 666, 643. HRMS (EI) *m/z* calcd. for $C_8H_{14}O$ [$M^+$]: 126.1039; found 126.1039.

**(*R*,*E*)-6-(Dimethyl(phenyl)silyl)-4-methylhept-5-en-1-ol (35).** A solution of $LiSiMe_2Ph$ (0.255 M in THF, 84.60 mL, 21.57 mmol) was added to copper(I) cyanide (966.0 mg, 10.79 mmol) at 0 °C. The resulting mixture was stirred at this temperature for 30 minutes before it was cooled to –78 °C. In a separate flask, *n*BuLi (1.6 M in hexanes, 5.62 mL, 8.99 mmol) was added to a solution of alcohol **34** in $Et_2O$ (9 mL) at –78 °C. The resulting mixture was warmed to 0 °C and stirred for 20 minutes. The solution was then cooled to –78 °C and added slowly *via* cannula to the solution of the silylcuprate, rinsing with $Et_2O$ (2 x 1 mL). The resulting mixture was stirred at –78 °C for 1 hour before a saturated aqueous solution of $NH_4Cl$ (30 mL) was added and the mixture was warmed to ambient temperature. The layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 20 mL). The combined organic phases were washed with water and brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (50% *tert*-butyl methyl ether in pentane) to give the title compound as a light yellow syrup (2.19 g, 93% yield). $[\alpha]_D^{20}$ = – 19.6 (*c* = 0.49, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.52 – 7.45 (m, 2H), 7.37 – 7.30 (m, 3H), 5.57 (dq, *J* = 9.1, 1.7 Hz, 1H), 3.63 (t, *J* = 6.6 Hz, 2H), 2.67 – 2.52 (m, 1H), 1.66 (d, *J* = 1.7 Hz, 3H), 1.62 – 1.46 (m, 2H), 1.45 – 1.37 (m, 1H), 1.35 (bs, 1H), 1.31 – 1.22 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.32 (s, 6H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 147.7, 139.0, 134.1, 132.5, 128.9, 127.8, 63.4, 33.4, 32.5, 31.0, 20.9, 15.1, –3.2. IR (film, $cm^{-1}$): 3306, 3068, 2955, 2928, 2867, 1619, 1453, 1428, 1409, 1374, 1317, 1247, 1110, 1057, 1028, 999,

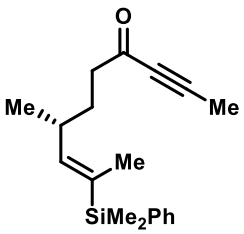
972, 831, 813, 773, 730, 700, 643, 474, 432, 421. HRMS (ESI) *m/z* calcd. for $C_{16}H_{26}OSiNa$ [$M^+$ + Na]: 285.1647; found 285.1645.

**(7*R*,*E*)-9-(Dimethyl(phenyl)silyl)-7-methyldec-8-en-2-yn-4-ol (S10).** Dess-Martin periodinane (7.04 g, 16.6 mmol) was added to a solution of alcohol **35** (2.18 g, 8.29 mmol) in dichloromethane (83 mL) at 0 °C. The mixture was allowed to warm to ambient temperature and stirring was continued for 2 hours. The mixture was diluted with dichloromethane (30 mL) and treated with saturated solutions of $NaHCO_3$ (30 mL) and $Na_2S_2O_3$ (30 mL). The resulting biphasic mixture was stirred for 30 minutes before the phases were separated. The aqueous layer was extracted with dichloromethane (3 x 50 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The crude aldehyde was used in the next step without further purification.



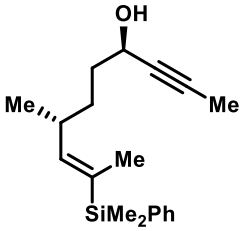

A solution of propynylmagnesium bromide (0.5 M in THF, 49.8 mL, 24.9 mmol) was added dropwise to a solution of the crude aldehyde in THF (166 mL) at 0 °C. The mixture was stirred at 0 °C for 1 hour before the reaction was quenched with saturated aqueous $NH_4Cl$ (150 mL). The layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 50 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (25% *tert*-butyl methyl ether in pentane) to give the title compound as a light yellow-orange syrup (2.17 g, 87% yield over both steps). $[\alpha]_D^{20}$ = –5.3 (*c* = 0.55, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.54 – 7.43 (m, 2H), 7.37 – 7.30 (m, 3H), 5.58 (dp, *J* = 9.2, 1.8 Hz, 1H), 4.31 (tq, *J* = 6.6, 2.1 Hz, 1H), 2.60 (dddt, *J* = 11.8, 6.7, 5.4, 2.6 Hz, 1H), 1.85 (dd, *J* = 2.2, 0.6 Hz, 3H), 1.66 (d, *J* = 1.8 Hz, 3H), 1.65 – 1.58 (m, 3H), 1.58 – 1.29 (m, 2H), 0.97 (dd, *J* = 6.7, 1.0 Hz, 3H), 0.32 (d, *J* = 0.7 Hz, 6H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 147.6, 147.6, 139.0, 134.1, 132.7, 132.6, 128.9, 127.8, 81.1, 80.6, 80.6, 63.1, 63.0, 36.3, 36.3, 32.8, 32.7, 32.4, 32.4, 20.8, 20.8, 15.1, 3.7, –3.2, –3.2. IR (film, $cm^{-1}$): 3351, 3068, 2965, 2920, 2864, 1618, 1454, 1428, 1374, 1318, 1247, 1109, 1082, 1048, 1018, 972, 831, 813, 772, 730, 700, 643, 476. HRMS (EI) *m/z* calcd. for $C_{19}H_{29}OSi$ [$M^+$ + H]: 301.1979; found 301.1982.

**(*R*,*E*)-9-(Dimethyl(phenyl)silyl)-7-methyldec-8-en-2-yn-4-one (S11).** Triethylamine (3.99 mL, 28.6 mmol) was added to a solution of **S10** (2.15 g, 7.15 mmol) in dichloromethane (72 mL) and DMSO (15 mL) at 0 °C. $SO_3$·pyridine complex (3.41 g, 21.4 mmol) was added in portions at this temperature. The mixture was slowly warmed to ambient temperature and stirring was continued overnight. A saturated aqueous solution of $NH_4Cl$ was added, the layers were



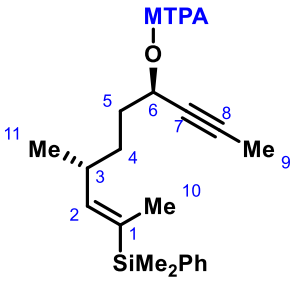
separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 75 mL). The combined organic layers were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (5% *tert*-butyl methyl ether in pentane) to give the title compound as a yellow oil (1.84 g, 86% yield). $[\alpha]_D^{20}$ = – 22.4 (*c* = 0.8, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.52 – 7.45 (m, 2H), 7.37 – 7.31 (m, 3H), 5.52 (dq, *J* = 9.3, 1.7 Hz, 1H), 2.68 – 2.54 (m, 1H), 2.48 (t, *J* = 7.6 Hz, 2H), 2.01 (s, 3H), 1.73 (dtd, *J* = 13.2, 7.7, 5.4 Hz, 1H), 1.65 (d, *J* = 1.7 Hz, 3H), 1.62 – 1.49 (m, 1H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.33 (s, 6H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 188.5, 146.5, 138.8, 134.1, 133.8, 128.9, 127.8, 90.0, 80.4, 43.7, 32.1, 31.2, 20.7, 15.1, 4.2, −3.2, −3.3. IR (film, cm$^{-1}$): 3068, 3049, 2957, 2924, 2686, 2219, 1673, 1619, 1453, 1428, 1374, 1321, 1248, 1174, 1109, 1022, 974, 832, 814, 773, 731, 701, 642, 476, 432. HRMS (EI) *m/z* calcd. for $C_{19}H_{27}OSi$ [$M^+$ + H]: 299.1826; found 299.1826.

**(4*R*,7*R*,*E*)-9-(dimethyl(phenyl)silyl)-7-methyldec-8-en-2-yn-4-ol (S12).** Powdered potassium hydroxide (172.0 mg, 3.07 mmol) was added to a solution of RuCl[(*R*,*R*)-TsDPEN](mesitylene) (*R,R*-**13**) (190.2 mg, 0.31 mmol) in dichloromethane (12 mL) at ambient temperature. After stirring for 15 minutes, the dark purple solution was transferred to a separatory funnel and washed multiple times with water. The solution was then dried over sodium sulfate and the solvent was removed under reduced pressure. The dark blue-purple residue was dissolved in *i*PrOH (8 mL) and the resulting solution was added dropwise to a solution of ketone **S11** (1.83 g, 6.13 mmol) in *i*PrOH (33 mL). After stirring for 1 hour at ambient temperature, the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (25% *tert*-butyl methyl ether in pentane) to give the title compound as a light yellow syrup (1.76 g, 95% yield). $[\alpha]_D^{20}$ = – 6.9 (*c* = 0.36, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.55 – 7.45 (m, 2H), 7.39 – 7.29 (m, 3H), 5.59 (dq, *J* = 9.2, 1.8 Hz, 1H), 4.31 (tq, *J* = 6.4, 2.1 Hz, 1H), 2.67 – 2.54 (m, 1H), 1.86 (d, *J* = 2.1 Hz, 3H), 1.68 (s, 1H), 1.66 (d, *J* = 1.7 Hz, 3H), 1.66 – 1.60 (m, 2H), 1.56 – 1.45 (m, 1H), 1.45 – 1.29 (m, 1H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.33 (s, 6H); $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 147.6, 139.0, 134.1, 132.6, 128.9, 127.8, 81.1, 80.6, 63.0, 36.3, 32.8, 32.4, 20.8, 15.1, 3.7, −3.2, −3.2; IR (film, cm$^{-1}$): 3371, 3067, 3048, 2955, 2921, 2865, 1619, 1454, 1428, 1374, 1315, 1247, 1156, 1110, 1083, 1046, 1018, 973, 832, 814, 773, 731, 700, 643, 476, 432; HRMS (EI) *m/z* calcd. for $C_{19}H_{28}OSi$ [$M^+$]: 300.1901; found 300.1904.




The absolute configuration was determined by Mosher ester analysis.[5]

**Preparation of the (*S*)-and (*R*)-MTPA Esters of Alcohol S12. Representative Procedure.** (*S*)-(+)-MTPA-Cl (4.4 µL, 23 µmol) was added to a solution of alcohol **S12** (7 mg, 23 µmol), triethylamine (9.7 µL, 70 µmol), and 4-(dimethylamino)pyridine (0.6 mg, 4.7 µmol) in dichloromethane (0.46 mL). After stirring for 2 hours, the mixture was poured into a separatory funnel containing $Et_2O$ (2 mL) and a saturated aqueous solution of $NH_4Cl$ (5 mL). The phases were separated and the aqueous layer was extracted with $Et_2O$ (3 x 2 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure to give the desired (*R*)-MTPA-ester as a colorless oil (11.9 mg, 99% yield). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.57 – 7.54 (m, 2H), 7.49 – 7.46 (m, 3H), 7.40 – 7.31 (m, 5 H), 5.52 (ddt, *J* = 8.5, 6.4, 2.1 Hz, 1H), 5.49 (dq, *J* = 9.2, 1.7 Hz, 1H), 3.60 (q, *J* = 1.1 Hz, 3H), 2.57 – 2.48 (m, 1H), 1.86 (d, *J* = 2.1 Hz, 3H), 1.74 – 1.67 (m, 2H), 1.62 (d, *J* = 1.7 Hz, 3H), 1.41 – 1.32 (m, 1H), 1.22 (dddd, *J* = 12.7, 10.1, 6.2, 2.3 Hz, 1H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.31 (s, 6H).

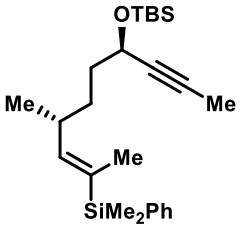



The (*S*)-MTPA ester (92% yield) was prepared analogously using (*R*)-(-)-MTPA-Cl as the reagent. It analyzed as follows: $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.56 – 7.52 (m, 2H), 7.49 – 7.46 (m, 3H), 7.40 – 7.30 (m, 5H), 5.53 (dq, *J* = 9.2, 1.7 Hz, 1H), 5.48 (tq, *J* = 6.5, 2.1 Hz, 1H), 3.54 (q, *J* = 1.2 Hz, 3H), 2.64 – 2.53 (m, 1H), 1.83 (d, *J* = 2.1 Hz, 3H), 1.76 (dtd, *J* = 8.7, 6.7, 1.6 Hz, 2H), 1.64 (d, *J* = 1.8 Hz, 3H), 1.50 (dddd, *J* = 12.9, 9.1, 6.8, 5.3 Hz, 1H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.31 (s, 6H).

**Table S5**. Analysis of the Mosher esters according to Hoye and co-workers;[5] arbitrary numbering Scheme as shown in the insert.

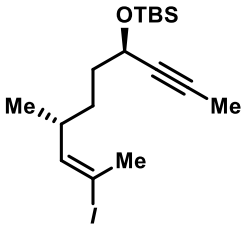
| Atom number | (*S*)-MTPA-ester δ (ppm) | (*R*)-MTPA-ester δ (ppm) | δS – δR (ppm) |
|---|---|---|---|
| **2** | 5.53 | 5.49 | +0.04 |
| **3** | 2.58 | 2.52 | +0.06 |
| **11** | 0.95 | 0.89 | +0.06 |
| **4a** | 1.50 | 1.36 | +0.14 |
| **4b** | 1.33 | 1.22 | +0.11 |
| **5** | 1.76 | 1.71 | +0.05 |
| **6** | 5.48 | 5.52 | –0.04 |
| **9** | 1.83 | 1.88 | –0.05 |

***tert*-Butyl(((4*R*,7*R*,*E*)-9-(dimethyl(phenyl)silyl)-7-methyldec-8-en-2-yn-4-yl)oxy)dimethylsilane (36).**




Imidazole (1.18 g, 17.3 mmol) followed by TBSCl (1.30 g, 8.64 mmol) were added to a solution of alcohol **S12** (1.73 g , 5.76 mmol) in dichloromethane (58 mL) at 0 °C. The cooling bath was removed and the mixture stirred at ambient temperature for 2 hours. The reaction was quenched with a saturated aqueous solution of $NH_4Cl$ (50 mL), the phases were separated and the aqueous layer was extracted with dichloromethane (3 x 50 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (2% *tert*-butyl methyl ether in pentane) to give the title compound as a colorless oil (2.31 g, 97% yield). $[\alpha]_D^{20}$ = +18.8 (*c* = 0.27, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.52 – 7.46 (m, 2H), 7.37 – 7.29 (m, 3H), 5.58 (dq, *J* = 9.1, 1.8 Hz, 1H), 4.30 (tq, *J* = 6.3, 2.1 Hz, 1H), 2.58 (ttt, *J* = 11.9, 8.8, 6.0 Hz, 1H), 1.83 (d, *J* = 2.1 Hz, 3H), 1.65 (d, *J* = 1.7 Hz, 3H), 1.63 – 1.56 (m, 2H), 1.54 – 1.44 (m, 1H), 1.38 – 1.27 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.90 (s, 9H), 0.32 (s, 6H), 0.11 (s, 3H), 0.09 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 148.0, 139.1, 134.1, 132.3, 128.8, 127.8, 81.2, 80.0, 63.5, 37.0, 32.8, 32.3, 26.0, 20.9, 18.5, 15.1, 3.7, −3.2, −3.2, −4.3, −4.8. IR (film, cm$^{-1}$): 2955, 2928, 2856, 1618, 1471, 1462, 1428, 1361, 1247, 1160, 1093, 1070, 1032, 1005, 973, 940, 833, 813, 773, 729, 699, 643, 474. HRMS (ESI+) *m/z* calcd. for $C_{25}H_{42}OSi_2Na$ [$M^+$ + Na]: 437.2671; found 437.2666.

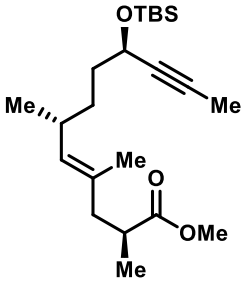
**tert-Butyl(((4*R*,7*R*,*E*)-9-iodo-7-methyldec-8-en-2-yn-4-yl)oxy)dimethylsilane (37).** *N*-Iodosuccin-




imide (338 mg, 1.50 mmol) was added to a solution of silane **36** (415 mg, 1.00 mmol) and 2,6-lutidine (0.12 mL, 1.00 mmol) in HFIP (4 mL) at 0 °C.[9] The mixture was stirred at this temperature for 10 minutes before it was poured into a separatory funnel containing dichloromethane (10 mL) and a saturated aqueous solution of $Na_2SO_3$ (20 mL). The pink solution became colorless on shaking. The layers were separated and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ and brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (2% *tert*-butyl methyl ether in pentane) to give the title compound as a clear oil (368 mg, 0.95 mmol, 95%). [*NOTE*: *The compound is isomerization-prone on storage*]. $[\alpha]_D^{20}$ = –9.3 (*c* = 0.55, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.94 (dq, *J* = 9.8, 1.5 Hz, 1H), 4.27 (tq, *J* = 6.3, 2.1 Hz, 1H), 2.43 – 2.34 (m, 1H), 2.37 (d, *J* = 1.5 Hz, 3H), 1.82 (d, *J* = 2.1 Hz, 3H), 1.66 – 1.50 (m, 2H), 1.50 – 1.40 (m, 1H), 1.36 – 1.25 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 147.4, 92.9, 81.0, 80.3, 63.3, 36.8, 35.7, 32.7, 27.9, 26.0, 20.7, 18.4, 3.7, −4.3, −4.9. IR (film, cm$^{-1}$): 2954, 2927, 2856, 1635, 1471, 1461, 1377, 1360, 1344, 1295, 1251, 1195, 1088, 1074,

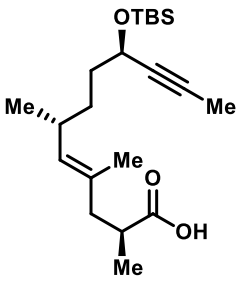
1052, 1030, 1006, 976, 961, 939, 835, 815, 776, 719, 669, 642, 557. HRMS (EI) *m/z* calcd. for $C_{17}H_{31}O_1SiI$ [$M^+$]: 406.1185; found 406.1183.

**Methyl (2*S*,6*R*,9*R*,*E*)-9-((*tert*-butyldimethylsilyl)oxy)-2,4,6-trimethyldodec-4-en-10-ynoate (S13)**. (*R*)-




(+)-3-Bromoisobutyric acid methyl ester (**30**) (0.18 mL, 1.4 mmol) and diethyl zinc (1 M in hexanes, 1.28 mL, 1.28 mmol) were successively added to a suspension of copper(I) chloride (9.2 mg, 0.09 mmol) and manganese(II) bromide (30.1 mg, 0.14 mmol) in DMPU (1.4 mL).[10] The resulting mixture was stirred for 4 hours before being it was transferred via cannula into a solution of [Pd(dppf)$Cl_2$· dichloromethane] (19.1, 23 µmol) and alkenyl iodide **37** (176 mg, 0.43 mmol) in THF (9 mL), rinsing with THF (1 mL). The resulting mixture was stirred overnight before it was diluted with *tert*-butyl methyl ether (15 mL) and water (15 mL). The layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 15 mL). The combined organic layers were washed with water and brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (4% *tert*-butyl methyl ether in pentane) to give the title compound as a colorless oil (141.0 mg, 85%). $[\alpha]_D^{20}$ = + 33.6 (*c* = 0.33, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 4.91 (dq, *J* = 9.4, 1.3 Hz, 1H), 4.26 (tq, *J* = 6.4, 2.1 Hz, 1H), 3.64 (s, 3H), 2.62 (h, *J* = 6.9 Hz, 1H), 2.34 – 2.27 (m, 1H), 2.33 (ddd, *J* = 13.3, 7.5, 1.1 Hz, 1H), 2.02 (ddd, *J* = 13.5, 7.6, 1.0 Hz, 1H), 1.81 (d, *J* = 2.1 Hz, 3H), 1.58 (d, *J* = 1.4 Hz, 3H), 1.57 – 1.50 (m, 2H), 1.44 (ddt, *J* = 13.1, 10.8, 5.5 Hz, 1H), 1.31 – 1.22 (m, 1H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 177.3, 134.0, 130.9, 81.2, 80.0, 63.5, 51.5, 44.4, 38.1, 37.1, 33.3, 32.3, 26.0, 21.4, 18.4, 16.8, 16.0, 3.7, −4.4, −4.9. IR (film, $cm^{-1}$): 3526, 2952, 2920, 2874, 1737, 1459, 1459, 1436, 1376, 1336, 1256, 1199, 1169, 1114, 1089, 1037, 988, 505. HRMS (ESI) *m/z* calcd. for $C_{22}H_{40}O_3SiNa$ [$M^+$ + Na]: 403.2645; found 403.2639.

**(2*S*,6*R*,9*R*,*E*)-9-((*tert*-Butyldimethylsilyl)oxy)-2,4,6-trimethyldodec-4-en-10-ynoic acid (38).** Lithium

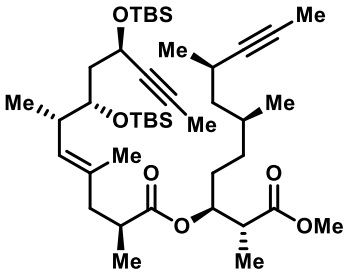



hydroxide (266.4 mg, 11.13 mmol) was added to a solution of methyl ester **S13** (424 mg, 1.11 mmol) in THF/MeOH/$H_2O$ (2:2:1, 11.10 mL). The resulting suspension was stirred at ambient temperature for 3 hours before the mixture was diluted with dichloromethane (25 mL) and the biphasic mixture was acidified (pH ≈ 4) by dropwise addition of aqueous HCl (1 M). The phases were separated and the aqueous layer was extracted with dichloromethane (3 x 25 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure to give the title compound as a gummy opaque oil (386.5 g, 95% yield). $[\alpha]_D^{20}$ = +21.3 (*c* =0.30, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 4.96 (dq, *J* = 9.4, 1.2 Hz, 1H), 4.27 (tq, *J* = 6.3, 2.1 Hz, 1H), 2.63 (dp, *J* = 8.2, 6.9 Hz, 1H), 2.38 (ddd, *J* = 13.6, 6.8, 1.2 Hz, 1H), 2.36 – 2.25

(m, 1H), 2.04 (ddd, *J* = 13.4, 8.1, 1.0 Hz, 1H), 1.82 (d, *J* = 2.1 Hz, 3H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.62 – 1.52 (m, 2H), 1.50 – 1.40 (m, 1H), 1.31 – 1.21 (m, 1H), 1.13 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 134.5, 130.5, 120.4, 81.2, 80.0, 63.5, 44.0, 37.7, 37.1, 33.3, 32.4, 26.0, 21.4, 18.4, 16.4, 16.0, 3.7, −4.3, −4.8. IR (film, $cm^{-1}$): 2954, 2928, 2857, 1708, 1462, 1418, 1387, 1361, 1341, 1294, 1249, 1073, 1034, 1005, 939, 837, 777, 666, 560. HRMS (ESI) *m/z* calcd. for $C_{21}H_{37}O_3Si$ [*M* – H]: 365.2519; found 365.2518.

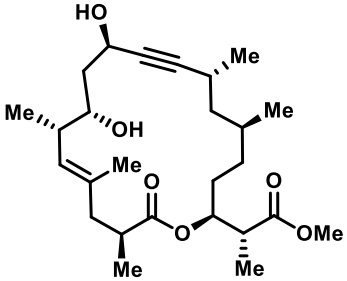
## Total Syntheses of Strasseriolide C and D

**(2*R*,3*S*,6*S*,8*R*)-1-Methoxy-2,6,8-trimethyl-1-oxoundec-9-yn-3-yl (2S,6S,7S,9R,E)-7,9-bis((*tert*-butyl-**




**dimethylsilyl)oxy)-2,4,6-trimethyldodec-4-en-10-ynoate (40).** 4-(Dimethylamino)pyridine (387 mg, 3.16 mmol) and *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (303 mg, 1.58 mmol) were successively added to a stirred solution of crude acid **28** (262 mg, 0.53 mmol) and alcohol **12** (148 mg, 0.58 mmol) in dichloromethane (10 mL) at 0°C. After 10 min, stirring was continued at ambient temperature for 2.5 days. The reaction was quenched with a saturated aqueous solution of $NH_4Cl$ (40 mL) and diluted with water (20 mL) and *tert*-butyl methyl ether (50 mL). The layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 50 mL). The combined organic layers were dried over magnesium sulfate, filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (2.5% EtOAc in hexanes) to yield the title compound as a colorless oil (311 mg, 80%). $[\alpha]_D^{20}$ = −17.5 (*c* = 1.04, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.15 – 5.08 (m, 2H), 4.42 – 4.38 (m, 1H), 3.71 (dt, *J* = 7.5, 4.5 Hz, 1H), 3.67 (s, 3H), 2.68 (dq, *J* = 7.0, 5.3 Hz, 1H), 2.61 – 2.46 (m, 2H), 2.45 – 2.36 (m, 2H), 2.01 – 1.95 (m, 1H), 1.82 (d, *J* = 2.0 Hz, 3H), 1.81 – 1.70 (m, 2H), 1.77 (d, *J* = 2.0 Hz, 3H), 1.67 – 1.46 (m, 3H), 1.59 (br, 3H), 1.37 – 1.21 (m, 3H), 1.15 (d, *J* = 7.1 Hz, 3H), 1.12 – 1.04 (m, 1H), 1.09 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.89 – 0.86 (m, 6H), 0.89 (s, 9H), 0.88 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 167.1, 174.5, 131.3, 131.1, 84.1, 81.0, 80.9, 75.5, 74.1, 73.4, 61.7, 51.9, 44.8, 44.1, 43.7, 43.1, 38.2, 38.0, 31.8, 30.5, 29.2, 26.1, 26.0, 26.0, 23.6, 21.6, 19.8, 18.4, 18.2, 16.3, 16.1, 16.0, 12.0, 3.7, 3.4, −4.1, −4.3, −4.4, −4.8. IR (film, $cm^{-1}$): 2955, 2929, 2857, 1738, 1460, 1379, 1361, 1251, 1161, 1088, 1061, 1028, 1005, 941, 834, 774, 669. HRMS (ESI) *m/z* calcd. for $C_{42}H_{76}O_6Si_2Na$ [$M^+$ + Na]: 755.5073; found 755.5078.

**Methyl (*R*)-2-((2*S*,5*S*,7*R*,10*R*,12*S*,13*S*,17*S*,*E*)-10,12-dihydroxy-5,7,13,15,17-pentamethyl-18-oxo-**

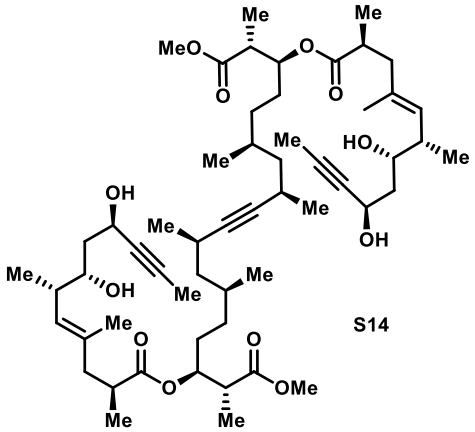



**oxacyclooctadec-14-en-8-yn-2-yl)propanoate (41).** Powdered molecular sieves (5Å, 20 g) were added to a solution of diyne **40** (276 mg, 0.38 mmol) in toluene (190 mL) and the resulting suspension was stirred at 110 °C for 30 min. A solution of complex **54** (27.5 mg, 0.03 mmol, 10 mol%)[11] in toluene (5 mL) was added at this temperature. After stirring for 30 min, another portion of catalyst **54** (27.5 mg, 0.03 mmol, 10 mol%) in toluene (5 mL) was added. The mixture was stirred for another 1 hour before the catalyst was quenched by addition of EtOH (20 mL). After cooling to ambient temperature, the mixture

was filtered through a short pad of Celite© (≈ 3 cm) and the solvent was removed under reduced pressure.

*NOTE*: *This reaction was carried out in a Teflon© vial in a well ventilated fume hood.* The residue was dissolved in THF (8 mL) and pyridine (600 µL, 7.42 mmol). The mixture was cooled to 0 °C before HF·pyridine (600 µL, 7.77 mmol) was added. After 10 min, stirring was continued at ambient temperature for 20 hours. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (50 mL) and diluted with EtOAc (50 mL). The layers were separated and the aqueous phase was extracted with EtOAc (4 x 50 mL). The combined organic layers were dried over magnesium sulfate, filtered, and the solvent was removed under reduced pressure The residue was purified by flash chromatography (40% EtOAc in hexanes) to yield title compound as a colorless, amorphous solid (103 mg, 61% over both steps). $[\alpha]_D^{20}$ = 8.8° (*c* = 0.83, $CHCl_3$). $^1$H NMR ($CDCl_3$, 600 MHz): δ 5.14 (dt, *J* = 6.7, 5.1 Hz, 1H), 4.97 (dq, *J* = 9.3, 1.4 Hz, 1H), 4.59 (td, *J* = 8.0, 2.2 Hz, 1H), 3.67 (s, 3H), 3.49 (td, *J* = 9.6, 1.6 Hz, 1H), 2.76 (p, *J* = 6.9 Hz, 1H), 2.72 – 2.66 (m, 1H), 2.66 – 2.60 (m, 1H), 2.33 (tq, *J* = 9.3, 6.7 Hz, 1H), 2.27 (br, 1H), 2.25 – 2.17 (m, 1H), 2.18 (br, 1H), 2.12 (dd, *J* = 14.8 Hz, 3.1 Hz, 1H), 1.90 (ddd, *J* = 13.8, 8.0, 1.6 Hz, 1H), 1.81 – 1.74 (m, 1H), 1.71 (ddd, *J* = 13.8, 9.6, 6.3 Hz, 1H), 1.67 – 1.52 (m, 3H), 1.64 (d, *J* = 1.3 Hz, 3H) , 1.42 (ddd, *J* = 13.5, 10.6, 3.7 Hz, 1H), 1.30 (ddd, *J* = 13.5, 9.7, 4.3 Hz, 1H), 1.19 (d, *J* = 7.0 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 7.0 Hz, 3H), 1.12 – 1.06 (m, 1H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 174.9, 174.4, 133.4, 128.8, 90.0, 82.0, 75.8, 74.1, 62.5, 52.0, 44.3, 44.2, 43.4, 42.1, 40.6, 39.5, 30.4, 30.0, 29.1, 21.8, 21.1, 18.5, 17.9, 17.0, 12.7. IR (film, $cm^{-1}$): 3391, 2955, 2927, 2874, 1734, 1455, 1377, 1331, 1251, 1197, 1168, 1072, 1047, 915, 732. HRMS (ESI) *m/z* calcd. for $C_{26}H_{42}O_6Na$ [$M^+$ + Na]: 473.2873; found 473.2875.

A second fraction was collected during the flash chromatography which contained dimer **S14**; colorless




**S14**

solid (19.3 mg, 11%). $^1$H NMR ($CDCl_3$, 600 MHz): δ 5.09 (dt, J =8.2, 4.9 Hz, 1H), 5.01 (dd, *J* = 9.7, 1.3 Hz, 1H), 4.56 (ddq, *J* = 8.6, 4.2, 2.0 Hz, 1H), 3.67 – 3.63 (m, 1H), 3.66 (s, 3H), 2.69 (td, *J* = 8.2, 3.6 Hz, 1H), 2.69 (td, *J* = 8.2, 3.6 Hz, 1H), 2.62 (dq, *J* = 8.0, 6.9 Hz, 1H), 2.50 – 2.36 (m, 3H), 2.01 (ddd, *J* = 13.9, 8.1, 1.0 Hz, 1H), 1.87 – 1.83 (m, 1H), 1.84 (d, *J* = 2.1 Hz, 3H), 1.74 (ddd, *J* = 14.3, 10.4, 8.5 Hz, 1H) 1.67 – 1.52 (m ,2H), 1.62 (d, *J* = 1.4 Hz, 3H), 1.53 – 1.44 (m, 1H), 1.33 – 1.10 (m, 3H), 1.15 (d, *J* = 7.1 Hz, 3H), 1.09 (d, *J* = 7.0 Hz, 3H), 1.08 (d, *J* = 6.6 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 4H). $^{13}$C NMR (151 MHz, $CDCl_3$) δ 175.8, 174.5, 133.6, 129.3, 85.1, 81.3, 80.1, 75.7, 74.3, 62.9, 52.0, 44.9, 43.6, 43.0, 42.0, 39.2, 38.2, 32.1, 30.8, 29.2, 23.7,

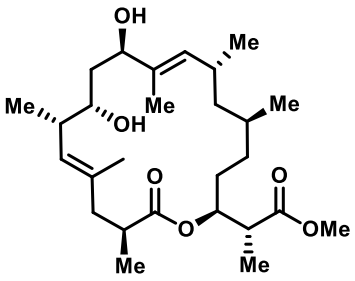
21.7, 19.9, 16.9, 16.6, 16.5, 11.8, 3.7. HRMS (ESI) *m/z* calcd. for $C_{56}H_{90}O_{12}Na$ [$M^+$ + Na]: 977.6324; found 977.6333.

**Methyl (*R*)-2-((2*S*,5*S*,7*R*,8*Z*,10*R*,12*S*,13*S*,14*E*,17*S*)-10,12-dihydroxy-5,7,13,15,17-pentamethyl-18-oxo-9-(tributylstannyl)oxacyclooctadeca-8,14-dien-2-yl)propanoate (42).** $[Cp^*RuCl]_4$ (6.6 mg, 6.1 µmol, 5 mol%) and tributyltin hydride (50 µL, 186 µmol) were successively added to a solution of alkyne **41** (55 mg, 122 µmol) in dichloromethane (2.5 mL) at ambient temperature.[12],[13] After 1 hour, a second portion of tributyltin hydride (50 µL, 186 µmol) was introduced and stirring continued for an additional 30 minutes. The solvent was then removed under reduced pressure and the residue was purified by flash chromatography (20% EtOAc in hexanes) to yield the title compound as a yellow oil (82.3 mg, 91%). $[\alpha]_D^{20}$ = 10.8° (*c* = 0.38, $CHCl_3$). $^1$H NMR ($CDCl_3$, 600 MHz): δ 6.02 (dd, *J* = 9.8, 0.8 Hz, $J_{Sn119\text{-}H}$ = 129.8 Hz, $J_{Sn117\text{-}H}$ = 124.1, 1H), 5.09 (q, *J* = 6.0 Hz, 1H), 4.99 (dq, *J* = 9.4, 1.4 Hz, 1H), 4.35 (td, *J* = 7.0, 2.0 Hz, $J_{Sn\text{-}H}$ = 68.3 Hz, 1H), 3.67 (s, 3H), 3.40 (ddt, *J* = 10.1, 6.9, 3.1 Hz, 1H), 2.74 – 2.68 (m, 2H), 2.61 (d, *J* = 3.0 Hz, 1H), 2.32 – 2.18 (m, 3H), 2.28 (d, *J* = 2.2 Hz, 1H), 2.28 (d, *J* = 2.2 Hz, 1H), 2.10 (dd, *J* = 16.1, 3.1 Hz, 1H), 1.66 – 1.43 (m, 11H), 1.61 (d, *J* = 1.3 Hz, 3H), 1.38 – 1.25 (m, 9H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 7.1 Hz, 3H), 1.09 – 0.99 (m, 1H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.98 – 0.87 (m, 6H), 0.90 (t, *J* = 7.3 Hz, 9H), 0.89 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 175.4, 174.4, 148.3 ($J_{Sn}$ = 25.1 Hz), 146.5 ($J_{Sn119}$ = 373.8 Hz, $J_{Sn117}$ = 356.7 Hz), 133.0, 128.3, 81.6 ($J_{Sn}$ = 25.1 Hz), 75.2, 74.3, 52.0, 44.3 ($J_{Sn}$ = 5.3 Hz), 43.1 ($J_{Sn}$ = 6.8 Hz), 42.4, 41.8, 39.8, 39.5, 35.4 ($J_{Sn}$ = 29.9 Hz), 31.7, 29.4 ($J_{Sn}$ = 18.8 Hz), 29.3, 28.7, 27.7 ($J_{Sn119}$ = 64.9 Hz, $J_{Sn117}$ = 62.3 Hz), 21.5, 21.2, 18.7, 18.6, 16.1, 13.8, 11.7 ($J_{Sn119}$ = 335.0 Hz, $J_{Sn117}$ = 320.1 Hz), 11.7. $^{119}$Sn NMR ($CDCl_3$, 224 MHz): δ −58.7 ppm. IR (film, cm$^{-1}$): 3436, 2953, 2923, 2871, 2854, 1739, 1457, 1376, 1337, 1258, 1197, 1171, 1073, 1047, 962,874, 666, 596. HRMS (ESI) *m/z* calcd. for $C_{38}H_{70}O_6SnNa$ [$M^+$ + Na]: 765.4087; found 765.4085.

**Strasseriolide D Methylester (43) and *E*-Alkene 44.** Tetrakis(triphenylphosphine)palladium (5.4 mg, 4.67 µmol, 5 mol%) was added at ambient temperature to a solution of stannane **42** (69.2 mg, 93.3 µmol) and $[Ph_2PO_2][NBu_4]$ (47.2 mg, 103 µmol) in DMF (0.5 mL). After 5 min, CuTC (53.4 mg, 280 µmol) was added, immediately followed by methyl iodide (26 µL, 418 µmol). The mixture was stirred at 40 °C for 3 hours. The reaction was quenched with triethylamine (3 drops from a glass Pasteur pipette), and the mixture was diluted with EtOAc (10 mL) and a saturated aqueous solution of $NH_4Cl$ (10 mL). The layers were separated and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over magnesium sulfate, filtered and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (30% EtOAc in hexanes) to yield a 4:1 mixture of Strasseriolide D methyl ester **43** and the protodestannylated *E*-alkene **44**. Compounds

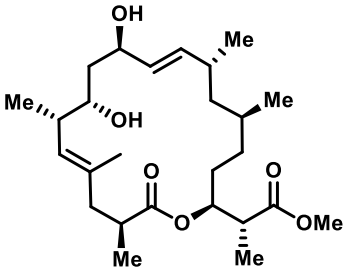
**43** and **44** were separated by preparative HPLC (YMC Triart C18 5 µm, 150 mm x 20.0 mm i.D, 20% MeOH in water, 15 mL/min, λ = 205 nm, t = 6.57 min (**44**), 7.55 min (**43**)).

Methylester **43**: colorless amorphous solid (19.0 mg, 44%); $[\alpha]_D^{20}$ = 39.4° (*c* = 0.51, $CHCl_3$). $^1$H NMR



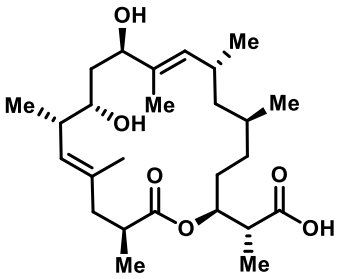

($CDCl_3$, 600 MHz): δ 5.16 (dd, *J* = 9.3, 1.6 Hz, 1H), 5.13 (dt, J =7.5, 4.6 Hz, 1H), 4.86 (d, *J* = 9.5 Hz, 1H), 3.68 (s, 3H), 3.33 (t, *J* = 9.0 Hz, 1H), 2.70 (p, *J* = 7.1 Hz, 2H), 2,62 – 2.50 (m, 2H), 2.28 (ddt, *J* = 15.8, 9.1, 6.6 Hz, 1H), 2.18 – 2.09 (m, 3H), 1.66 (ddd, *J* = 14.4, 6.4, 1.3 Hz, 1H), 1.64 (d, *J* = 1.4 Hz, 3H), 1.61 (d, *J* = 1.4 Hz, 3H), 1.60 – 1.47 (m, 6H), 1.27 (ddd, *J* = 13.5, 10.4, 3.1 Hz, 1H), 1.24 – 1.18 (m, 1H), 1.17 (d, *J* = 7.0 Hz, 3H), 1.13 (d, *J* = 7.0 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.93 – 0.86 (m, 1H) 0.84 (d, *J* = 6.6 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 150 MHz): δ 175.4, 174.4, 135.5, 134.8, 133.5, 129.4, 79.4, 76.3, 74.2, 52.0, 45.8, 43.1, 41.7, 41.4, 40.5, 39.8, 30.0, 29.9, 29.2, 28.8, 21.9, 21.2, 18.8, 18.3, 17.1, 13.3, 10.1. IR (film, $cm^{-1}$): 3321, 2953, 2924, 1737, 1455, 1376, 1252, 1194, 1167, 1048, 1006, 990, 911, 868, 734. HRMS (ESI) *m/z* calcd. for $C_{27}H_{46}O_6Na$ [$M^+$ + Na]: 489.3187; found 489.3193.

Alkene **44:** colorless amorphous solid (7.5 mg, 18%); $[\alpha]_D^{20}$ = 26.2° (*c* = 0.75, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400




MHz): δ 5.45 – 5.34 (m, 2H), 5.14 (dq, *J* = 5.0, 3.4 Hz, 1H), 4.91 (dd, *J* = 9.5, 1.4 Hz, 1H), 4.26 (dtd, *J* = 8.0, 5.4, 2.5 Hz, 1H), 3.68 (s, 3H), 3.39 (t, *J* = 9.2 Hz, 1H), 2.74 (q, *J* = 7.1 Hz, 1H), 2.66 – 2.52 (m, 1H), 2.36 – 2.24 (m, 2H), 2.18 – 2.11 (m, 2H), 1.77 (ddd, *J* = 14.3, 5.4, 1.5 Hz, 1H), 1.65 – 1.47 (m, 5H), 1.62 (d, *J* = 1.4 Hz, 3H), 1.30 – 1.21 (m, 2H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 7.0 Hz, 3H), 0.99 (s, 3H), 0.98 (s, 3H), 0.95 – 0.87 (m, 1H), 0.84 (d, *J* = 6.6 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 175.6, 174.5, 139.9, 133.4, 132.0, 129.1, 76.6, 74.6, 74.4, 52.0, 45.1, 42.8, 42.7, 41.8, 41.4, 39.9, 34.7, 30.0, 29.8, 28.6, 22.6, 21.1, 18.7, 18.6, 17.0, 13.4. IR (film, $cm^{-1}$): 3401, 2952, 2926, 2870, 1737, 1456, 1376, 1259, 1199, 1172, 1155, 1080, 1047, 972. HRMS (ESI) *m/z* calcd. for $C_{26}H_{44}O_6Na$ [$M^+$ + Na]: 475.3030; found 475.3031.

**Strasseriolide D (4).** Trimethyltin hydroxide (28.5 mg, 0.16 mmol) was added to a solution of




methylester **43** (7.1 mg, 15.8 µmol) in 1,2-dichloroethane (0.2 mL). The mixture was irradiated at 120 °C in a microwave oven for 90 min before a second portion of trimethyltin hydroxide (28.5 mg, 0.16 mmol) was introduced and irradiation was continued at 120 °C for another 90 min. The mixture was then filtered through a short pad of Celite© (≈ 1 cm), which was rinsed with dichloromethane (10 mL). The solvent was removed under reduced pressure. The residue was dissolved in EtOAc (10 mL) and the solution washed with HCl (2 M, 3 x 10 mL) and brine (10 mL). The solvent was removed under reduced

pressure and the residue was purified by flash chromatography (60% EtOAc in hexane + 0.5% AcOH) to yield Strasseriolide D as a colorless film (3.8 mg, 54%). An analytically pure sample was obtained by preparative HPLC (YMC Triart C18 5 µm, 150 mm x 10.0 mm i.D, 25% MeOH in water + 0.1% TFA, 4.7 mL/min, t = 5.25 min).

$[\alpha]_D^{25}$ = 19.0° (*c* = 0.15, MeOH) (ref.:[14] $[\alpha]_D^{25}$ = 22.1° (*c* = 0.16, MeOH)). $^1$H NMR ([D$_4$]-MeOH, 600 MHz): δ 5.16 (ddd, *J* = 8.7, 4.3, 4.3 Hz, 1H), 5.14 (dd, *J* = 9.10, 1.1 Hz, 1H), 4.66 (d, *J* = 9.2 Hz, 1H), 4.10 (dd, *J* = 11.0, 3.9 Hz, 1H), 3.04 (ddd, *J* = 9.9, 9.1, 0.7 Hz, 1H), 2.74 (dq, *J* = 8.8, 6.9 Hz, 1H), 2.62 (dqd, *J* = 11.9, 6.9, 3.3 Hz, 1H), 2.58 (m, 1H), 2.26 (m, 1H), 2.25 (t, *J* = 13.3 Hz, 1H), 2.09 (dd, *J* = 13.3, 3.3 Hz, 1H), 1.78 (ddd, *J* = 13.9, 11.0, 1.1 Hz, 2H), 1.78 (m, 1H), 1.65 (d, *J* = 1.3 Hz, 3H), 1.61 (tt, *J* = 12.7 Hz, 4.4 Hz, 1H), 1.58 (d, *J* = 1.3 Hz, 3H), 1.50 (m, 1H), 1.48 (m, 1H), 1.42 (ddd, *J* = 13.9, 8.0, 3.9 Hz, 1H), 1.31 (ddd, *J* = 13.8, 11.1, 3.0 Hz, 1H), 1.25 (ddd, *J* = 13.8, 10.7, 3.7, 1H), 1.21 (d, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 6.9 Hz, 3H), 1.08 (m, 1H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 3H).$^{13}$C NMR ([D$_4$]-MeOH, 150 MHz): δ 177.5, 176.0, 137.1, 135.8, 133.9, 132.0, 78.3, 75.3, 75.2, 48.4, 45.6, 43.1, 42.5, 41.9, 40.8, 31.7, 30.7, 30.5, 29.7, 22.3, 21.6, 18.7, 18.3, 16.6, 14.5, 10.3. IR (film, cm$^{-1}$): 3379, 2954, 2925, 2871, 1714, 1572, 1455, 1407, 1377, 1291, 1259, 1213, 1171, 1050, 985, 546. HRMS (ESI) *m/z* calcd. for $C_{26}H_{44}O_6Na$ [$M^+$ + Na]: 475.3030; found 475.3031.

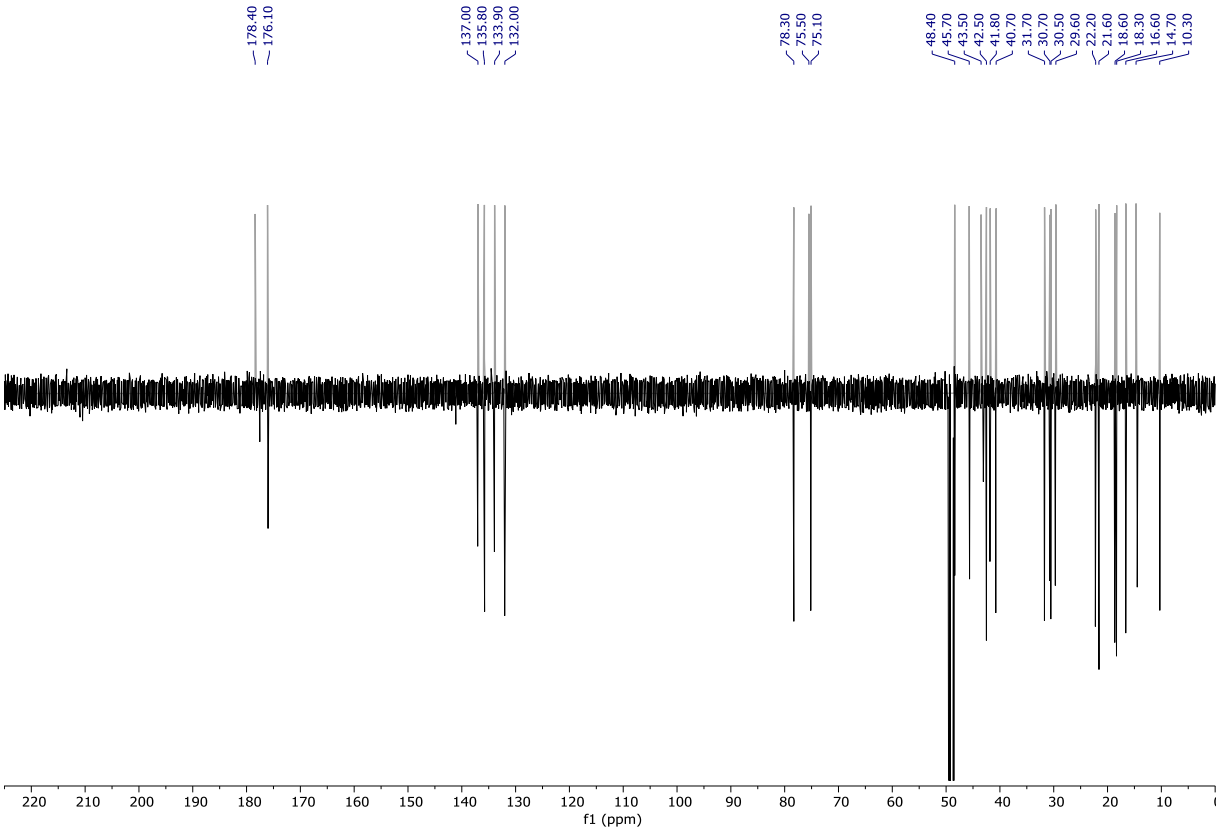
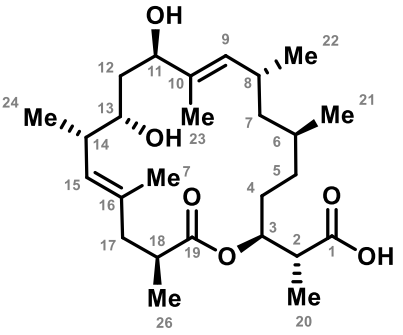



**Figure S1.** Visual comparison of $^{13}$C NMR spectrum of authentic Strasseriolide D (up) and synthetic **4** (down). Note that the spectrum of authentic Strasseriolide D (up) was genereated (MestReNova) by

converting the tabulated $^{13}C$ NMR data of the natural product[14] into a formal spectrum; therefore, the intensity of the lines was arbitrarily set to be identical for all signals. For a tabular survey of the exact numbers, see Table S7.

**Table S6.** NMR assignment of synthetic Strasseriolide D (**4**). All measurements were performed on a Bruker Avance III 600 spectrometer equipped with a cryogenically cooled 5 mm TCI probehead using a classical set of 1D ($^{1}H$, $^{13}C$) and 2D (COSY, HSQC, HMBC, NOESY) experiments. Numbering scheme as shown in the Insert.




| Atom number | δ [ppm] | J [Hz] | COSY | HSQC | HMBC | NOESY |
|---|---|---|---|---|---|---|
| **1 C** | 177.5 | | | | 2, 3, 20 | |
| **2 C** | 43.1 | | | 2 | 3, 4b, 20 | |
| **H** | 2.74 | 8.80 | 3, 20 | 2 | 1, 3, 4, 20 | 3, 5b, 20 |
| **3 C** | 75.3 | | | 3 | 2, 4b, 20 | |
| **H** | 5.16 | 8.70, 4.30, 4.30 | 2, 4a, 4b | 3 | 1, 2, 4, 5, 19, 20 | 2, 4a, 4b, 20 |
| **4 C** | 30.7 | | | 4a, 4b | 2, 3, 5a, 5b | |
| **Ha** | 1.78 | | 3, 4b, 5a, 5b | 4 | | 3, 21 |
| **Hb** | 1.50 | | 4, 4a, 5a, 5b | 4 | 2, 3, 5, 6 | 3 |
| **5 C** | 29.7 | | | 5a, 5b | 3, 4b, 7a, 7b, 21 | |
| **Ha** | 1.61 | 12.70, 4.40 | 4a, 4b, 5b, 6 | 5 | 4, 6, 7, 21 | 8 |
| **Hb** | 1.08 | | 4a, 4b, 5a, 6 | 5 | 4, 6, 7, 21 | 2, 21 |
| **6 C** | 31.7 | | | 6 | 4b, 5a, 5b, 7a, 7b, 21 | |
| **H** | 1.48 | | 5a, 5b, 7a, 7b, 21 | 6 | | 9, 13, 21 |
| **7 C** | 48.4 | | | 7a, 7b | 5a, 5b, 9, 21 ,22 | |
| **Ha** | 1.31 | 13.80, 11.10, 3.00 | 6, 7b, 8, 22 | 7 | 5, 6, 8, 9, 21, 22 | 9, 21, 22 |
| **Hb** | 1.25 | 13.80, 10.70, 3.70 | 7, 7a, 8 ,21 | 7 | 5, 6, 7, 9, 21, 22 | 8, 21, 22 |
| **8 C** | 30.7 | | | 8 | 7a, 7b, 9, 22 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **H** | 2.58 | | 7a, 7b, 9, 22 | 8 | | 5a, 7b, 22, 23 |
| **9 C** | 135.8 | | | 9 | 7a, 7b, 11, 22, 23 | |
| **H** | 5.14 | 9.10, 1.10 | 8, 11, 22, 23 | 9 | 7, 8, 11, 23 | 6, 7a, 11, 13, 22 |
| **10 C** | 137.1 | | | | 12a, 12b, 23, | |
| **11 C** | 78.3 | | | 11 | 9, 12a, 12b, 13, 23 | |
| **H** | 4.10 | 11.00, 3.90 | 8, 11, 22, 23 | 11 | 9, 12, 13, 23 | 9, 12b, 13, 23 |
| **12C** | 41.9 | | | 12a, 12b | 11, 13 | |
| **Ha** | 1.78 | | 11, 12b, 13 | 12 | 10,11, 14 | 13, 14, 23 |
| **Hb** | 1.42 | 13.90, 8.00, 3.90 | 11, 12a, 13 | 12 | 10, 11, 13 | 11, 14 |
| **13 C** | 75.2 | | | 13 | 11, 12b, 14, 15, 24 | |
| **H** | 3.04 | 9.90, 8.10, 0.70 | 12a, 12b, 14, 24 | 13 | 11, 12, 14, 15, 24 | 6, 9, 11, 12a, 14, 15, 23, 24 |
| **14 C** | 40.8 | | | 14 | 12a, 13, 15, 24 | |
| **H** | 2.26 | | 13, 15, 24 | 14 | 13, 24 | |
| **15 C** | 132.1 | | | 15 | 13, 17a, 17b, 24, 25 | |
| **H** | 4.66 | 9.20 | 14, 17b, 24, 25 | 15 | 13, 17a, 17b, 24, 25 | |
| **16 C** | 133.9 | | | | 17a, 17b, 25 | |
| **17 C** | 45.6 | | | 17a, 17b | 15, 25, 26 | |
| **Ha** | 2.25 | 13.30 | 17b, 18, 25, 26 | 17 | 15, 16, 18, 19, 25, 26 | 15, 23, 25, 26 |
| **Hb** | 2.09 | 13.30, 3.30 | 15, 17a, 18, 25 | 17 | 15, 16, 18, 19, 25, 26 | 18, 25, 26 |
| **18 C** | 42.5 | | | 18 | 17a, 17b, 26 | |
| **H** | 2.62 | 11.90, 6.90, 3.30 | 17a, 17b, 26 | 18 | 19, 26 | |
| **19 C** | 176.0 | | | | 3, 17a, 17b, 18, 26 | |
| **20 C** | 14.5 | | | 20 | 2, 3 | |
| **3H** | 1.14 | 6.90 | 2 | 20 | 1, 2, 3 | 2, 3, 26 |
| **21 C** | 21.6 | | | 21 | 5a, 5b, 7a, 7b | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **3H** | 0.88 | 6.70 | | 21 | 5, 6, 7 | 4a, 5b, 6, 7a, 7b |
| **22 C** | 22.3 | | | 22 | 7a, 7b, 23 | |
| **3H** | 0.98 | 6.70 | 7a, 8, 9 | 22 | 7, 8, 9 | 7a, 7b, 8, 9, 23 |
| **23 C** | 10.3 | | | 23 | 9, 11 | |
| **3H** | 1.58 | 1.30 | 9 | 23 | 9, 10, 11, 22 | 8, 11, 12a, 13, 15, 17a, 22 |
| **24 C** | 18.3 | | | 24 | 13, 14,24 | |
| **H** | 0.91 | 6.70 | 13, 14, 15 | 24 | 13, 14, 15 | 13, 14, 15, 25 |
| **25 C** | 16.6 | | | 25 | 15, 17a, 17b | |
| **3H** | 1.65 | 1.30 | 14, 17a, 17b | 25 | 15, 16, 17, 24 | 14, 17a, 17b, 18, 24 |
| **26** | 18.7 | | | 26 | 17a, 17b, 18 | |
| **3H** | 1.21 | 6.90 | 17a, 18 | 26 | 17, 18, 19 | 17a, 17b, 18, 20 |

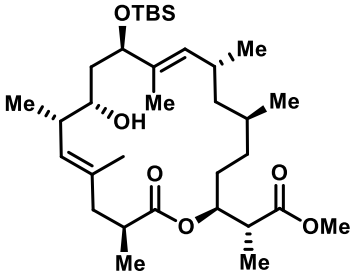
**Table S7.** Comparison of the spectral data for authentic and synthetic Strasseriolide D (**4**).[14]

| Atom number | $^{1}$H δ (lit.) [ppm] | $^{1}$H δ (exp.) [ppm] | ΔδH | $^{13}$C δ (lit.) [ppm] | $^{13}$C δ (exp.) [ppm] | ΔδC |
|---|---|---|---|---|---|---|
| **1** | | | | 178.4 | 177.5 | -0.9[b] |
| **2** | 2.72 | 2.74 | +0.02 | 43.5 | 43.1 | -0.4[b] |
| **3** | 5.17 | 5.16 | +0.01 | 75.5 | 75.3 | -0.2 |
| **4** | 1.78/1.49 | 1.78/1.50 | 0/+0.01 | 30.7 | 30.7 | 0 |
| **5** | 1.61/1.08 | 1.61/1.08 | 0/0 | 29.6 | 29.7 | +0.1 |
| **6** | 1.47 | 1.48 | +0.01 | 31.7 | 31.7 | 0 |
| **7** | 1.43/1.28 | 1.31/1.25 | +0.12[a]/+0.03 | 48.4 | 48.4 | 0 |
| **8** | 2.59 | 2.58 | -0.01 | 30.5 | 30.5 | 0 |
| **9** | 5.14 | 5.14 | 0 | 135.8 | 135.8 | 0 |
| **10** | | | | 137.0 | 137.1 | +0.1 |
| **11** | 4.10 | 4.10 | 0 | 78.3 | 78.3 | 0 |
| **12** | 1.78/1.42 | 1.78/1.42 | 0/0 | 41.8 | 41.9 | +0.1 |
| **13** | 3.05 | 3.04 | -0.01 | 75.1 | 75.2 | +0.1 |
| **14** | 2.26 | 2.26 | 0 | 40.7 | 40.8 | +0.1 |
| **15** | 4.65 | 4.66 | +0.01 | 132.0 | 132.0 | 0 |
| **16** | | | | 133.9 | 133.9 | 0 |
| **17** | 2.25/2.08 | 2.25/2.09 | 0/+0.01 | 45.7 | 45.6 | -0.1 |
| **18** | 2.62 | 2.62 | 0 | 42.5 | 42.5 | 0 |
| **19** | | | | 176.1 | 176.0 | -0.1 |
| **20** | 1.13 | 1.14 | +0.01 | 14.7 | 14.5 | -0.2 |
| **21** | 0.87 | 0.87 | 0 | 21.6 | 21.6 | 0 |
| **22** | 0.98 | 0.98 | 0 | 22.2 | 22.3 | +0.1 |
| **23** | 1.57 | 1.58 | +0.01 | 10.3 | 10.3 | 0 |
| **24** | 0.91 | 0.91 | 0 | 18.3 | 18.3 | 0 |
| **25** | 1.65 | 1.65 | 0 | 16.6 | 16.6 | 0 |
| **26** | 1.21 | 1.21 | 0 | 18.6 | 18.7 | +0.1 |

[a] Our HSQC spectrum shows two cross peaks for C7 at 1.31 ppm and 1.25 ppm. It seems plausible that these signals were overlapping in the spectra of the isolated compound, thus leading *Reyes et. al.* to interpret it as one proton instead of two.[14]

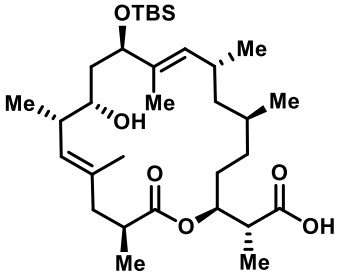
[b] We detect a noticeable difference in the NMR shifts of C1 and C2. This observation is in accordance with previous report by *Rychnovsky et al.* and *Goswami et al.*[15],[16] Both teams noticed concentration effects and suspected H-bonding interactions of the carboxylic acid to form dimeric structures to be the cause of the discrepancy with the isolation paper.

**Methyl (*R*)-2-((2*S*,5*S*,7*R*,8*E*,10*R*,12*S*,13*S*,14*E*,17*S*)-10-((*tert*-butyldimethylsilyl)oxy)-12-hydroxy-**




**5,7,9,13,15,17-hexamethyl-18-oxooxacyclooctadeca-8,14-dien-2-yl)propanoate (51).** Imidazole (2.7 mg, 39.7 µmol) and a solution of TBSCl (3.4 mg, 22.6 µmol) in dichloromethane (0.1 mL) were successively added to a solution of methylester **43** (9.2 mg, 19.7 µmol) in dichloromethane (0.9 mL) at ambient temperature. After stirring for 1 hour, additional imidazole (2.7 mg, 39.7 µmol) and TBSCl (3.4 mg, 22.6 µmol) were introduced and stirring was continued for 16 hours. At this point, a third portion of imidazole (2.7 mg, 39.7 µmol) and TBSCl (3.4 mg, 22.6 µmol) was added and the mixture was stirred for another 6 hours. The reaction was then quenched with water (15 mL) and the mixture diluted with dichloromethane (15 mL). The layers were separated and the aqueous phase was extracted with dichloromethane (3 x 15 mL). The combined organic layers were dried with magnesium sulfate, filtered and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (10% EtOAc in hexanes) to yield the title compound as a pale yellow oil (10.2 mg, 89%). $[\alpha]_D^{20}$ = 41.1° (*c* = 1.02, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.14 (dt, *J* = 8.1, 4.0 Hz, 1H), 5.06 (dd, *J* = 9.2, 1.6 Hz, 1H), 4.85 (d, *J* = 9.4 Hz, 1H), 4.23 (dd, *J* = 7.9 Hz, 6.3 Hz, 1H), 3,68 (s, 3H), 3.27 (t, *J* = 9.0 Hz, 1H), 2.99 (br, 1H), 2.72 – 2.65 (m, 1H), 2.59 – 2.46 (m, 2H), 2.24 (ddt, *J* = 15.8, 9.2, 6.6 Hz, 1H), 2.18 – 2.06 (m, 2H), 1.67 – 1.47 (m, 7H), 1.60 – 1.58 (m, 6H), 1.30 – 1.18 (m, 2H), 1.16 (d, *J* = 6.9 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.82 (d, *J* = 6.6 Hz, 3H), 0.08 (s, 3H), 0.02 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 175.4, 174.5, 136.1, 133.9, 133.3, 129.9, 80.6, 75.9, 74.2, 52.0, 46.0, 43.3, 41.9, 41.8, 1.6, 39.6, 29.9, 29.7, 29.1, 28.6, 26.0, 21.5, 21.1, 18.8, 18.2, 182., 17.3, 13.8, 10.4, –4.2, –4.9. IR (film, $cm^{-1}$): 3519, 2953, 2928, 2858, 1739, 1457, 1376, 1338, 1252, 1195, 1165, 1069, 1048, 868, 836, 777, 535. HRMS (ESI) *m/z* calcd. for $C_{33}H_{60}O_6SiNa$ [$M^+$ + Na]: 603.4051; found 603.4054.

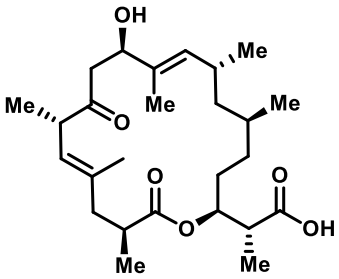
**(*R*)-2-((2*S*,5*S*,7*R*,8*E*,10*R*,12*S*,13*S*,14*E*,17*S*)-10-((*tert*-Butyldimethylsilyl)oxy)-12-hydroxy-**




**5,7,9,13,15,17-hexamethyl-18-oxooxacyclooctadeca-8,14-dien-2-yl)propanoic acid (S15).** Trimethyltin hydroxide (23.7 mg, 0.13 mmol) was added to a solution of methyl ester **51** (7.6 mg, 13.1 µmol) in 1,2-dichloroethane (0.3 mL). The mixture was irradiated in a microwave oven at 120 °C for 2 hours before a second portion of trimethyltin hydroxide (23.7 mg, 0.13 mmol) was introduced and heating was continued for an additional 3 hours. The mixture was filtered through a short pad of Celite© (≈ 1 cm), which was carefully rinsed with dichloromethane (10 mL). The solvent was removed under reduced pressure and the residue was dissolved in EtOAc (15 mL). The solution was washed with a sulfate buffer (pH 2, 1 M, 3 x 10 mL) and brine (10 mL). The organic phase was dried over magnesium sulfate, filtered

and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (30% EtOAc in hexanes + 0.5% AcOH) to yield title compound as a pale yellow oil (6.7 mg, 90%). $[\alpha]_D^{20}$ = 36.5° (*c* = 0.62, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.14 (dt, *J* = 8.1, 4.2 Hz, 1H), 5.08 (d, *J* = 9.1 Hz, 1H), 4.86 (d, *J* = 9.2 Hz, 1H), 3.31 (t, *J* = 9.0 Hz, 1H), 2.70 (p, *J* = 7.1 Hz, 1H), 2.60 – 2.47 (m, 2H), 2.25 (ddt, *J* = 15.9, 9.3, 6.6 Hz, 1H), 2.18 – 2.07 (m, 2H), 1.76 – 1.44 (m, 6H), 1.60 (br s, 6 H), 1.35 – 1.11 (m, 3H), 1.17 (s, 3H), 1.16 (s, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.91 – 0.85 (m, 1H), 0.83 (d, *J* = 6.5 Hz, 3H), 0.09 (s, 3H), 0.02 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 178.4, 175.5, 136.1, 133.9, 133.3, 129.8, 80.8, 76.0, 74.0, 46.0, 43.2, 41.8, 41.8, 41.3, 39.6, 29.9, 29.8, 29.1, 28.5, 26.0, 21.5, 21.1, 18.8, 18.3, 18.2, 17.4, 13.7, 10.4, 1.2, −4.1, −4.9. IR (film, $cm^{-1}$): 2955, 2926, 2858, 1735, 1707, 1457, 1375, 1292, 1254, 1074, 1051, 836, 778. HRMS (ESI) *m/z* calcd. for $C_{32}H_{57}O_6Si$ [$M^-$ − H]: 565.3930; found 565.3937.

**Strasseriolide C (3).** Dess-Martin periodinane (12.6 mg, 29.7 µmol) was added to a solution of alcohol




**S15** (6.2 mg, 10.9 µmol) in dichloromethane (0.5 mL). After 45 minutes, the mixture was diluted with dichloromethane (15 mL) and a saturated aqueous solution of $Na_2S_2O_3$ (15 mL) was introduced. The suspension was stirred for 30 min before the layers were separated. The aqueous phase was extracted with dichloromethane (3 x 10 mL), the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to give the corresponding ketone, which was used in the next step without further purification.

*NOTE: This reaction was carried out in a Teflon© vial*. HF·pyridine (50 µL, 0.56 mmol) was added to a solution of the crude ketone in THF (0.3 mL) at room temperature. After 1 hour of stirring, the solvent and HF·py were removed under a gentle stream of Argon in an empty, well-ventilated fume hood. The residue was purified by flash chromatography (40% EtOAc in hexane + 0.5% AcOH) to yield Strasseriolide C (2.6 mg, 53%) as a pale yellow film.

$[\alpha]_D^{25}$ = 65.4° (*c* = 0.26, MeOH) (ref.:[14] $[\alpha]_D^{25}$ = 35.6° (*c* = 0.23, MeOH)). $^1$H NMR ($CD_3OD$, 600 MHz): δ 5.11 (dt, *J* = 9.8, 3.7 Hz, 1H), 5.04 (dq, *J* = 8.2, 1.3 Hz, 1H), 4.68 (d, *J* = 10.4 Hz, 1H), 4.46 (dd, *J* = 11.1, 4.3 Hz, 1H), 3.37 (dq, *J* = 10.5, 6.6 Hz, 1H), 2.74 (dq, *J* = 9.8, 6.9 Hz, 1H), 2.68 (dqd, *J* = 12.1, 6.9, 3.2 Hz, 1H), 2.49 – 2.40 (m, 1H), 2.23 (t, *J* = 12.8 Hz, 1H), 2.29 (J = 14.7, 4.3 Hz, 1H), 2.20 (dd, *J* = 12.8, 3.2 Hz, 1H), 1.81 (d, *J* = 1.3 Hz, 3H), 1.75 (dddd, *J* = 14.3, 13.3, 4.6, 3.2 Hz, 1H), 1.63 (tt, *J* = 13.1, 2.8 Hz, 1H), 1.57 (d, *J* = 1.3 Hz, 3H), 1.37 – 1.35 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 3H), 1.23 (m, 1H), 1.20 – 1.18 (m, 1H), 1.19 – 1.17 (m, 1H), 1.12 (d, *J* = 6.9 Hz, 3H), 1.01 – 0.99 (m, 1H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 5.9 Hz, 3H). $^{13}$C NMR ($CD_3OD$, 151 MHz): δ 210.8, 177.6, 175.4, 138.5, 136.6, 136.2, 126.3, 76.2, 75.1, 48.9, 48.7, 46.4, 46.3, 43.5, 42.2, 31.3, 30.5, 30.3, 28.9, 22.2, 21.4, 18.5, 16.0, 15.1,

15.0, 10.2. IR (film, $cm^{-1}$): 3402, 2951, 2926, 2870, 1714, 1573, 1455, 1411, 1375, 1341, 1291, 1261, 1045. HRMS (ESI) *m/z* calcd. for $C_{26}H_{41}O_6$ [$M^-$ – H]: 449.2909; found 449.2909.

**Table S8.** Concentration effect on selected $^{13}C$ NMR shifts of Strasseriolide C

| **Atom number** | **$^{13}C$ δ** (lit.) [ppm] | **$^{13}C$ δ** (10 mM) + 10 eq. AcOD [ppm] | **$^{13}C$ δ** (20 mM) [ppm] |
|---|---|---|---|
| **3** | 75.1 | 75.1 | 76.0 |
| **20** | 15.1 | 15.1 | 15.8 |

With a concentration of approx. 20 mM and no additive drastic shifts in the $^{13}C$ NMR spectrum were obtained for the carbon signals of the carboxylic acid moiety (see Table S8). Spectra were then recorded at a concentration of approx. 10 mM with the addition of 10 eq. of AcOD, resulting in an excellent match with the literature data.[14]

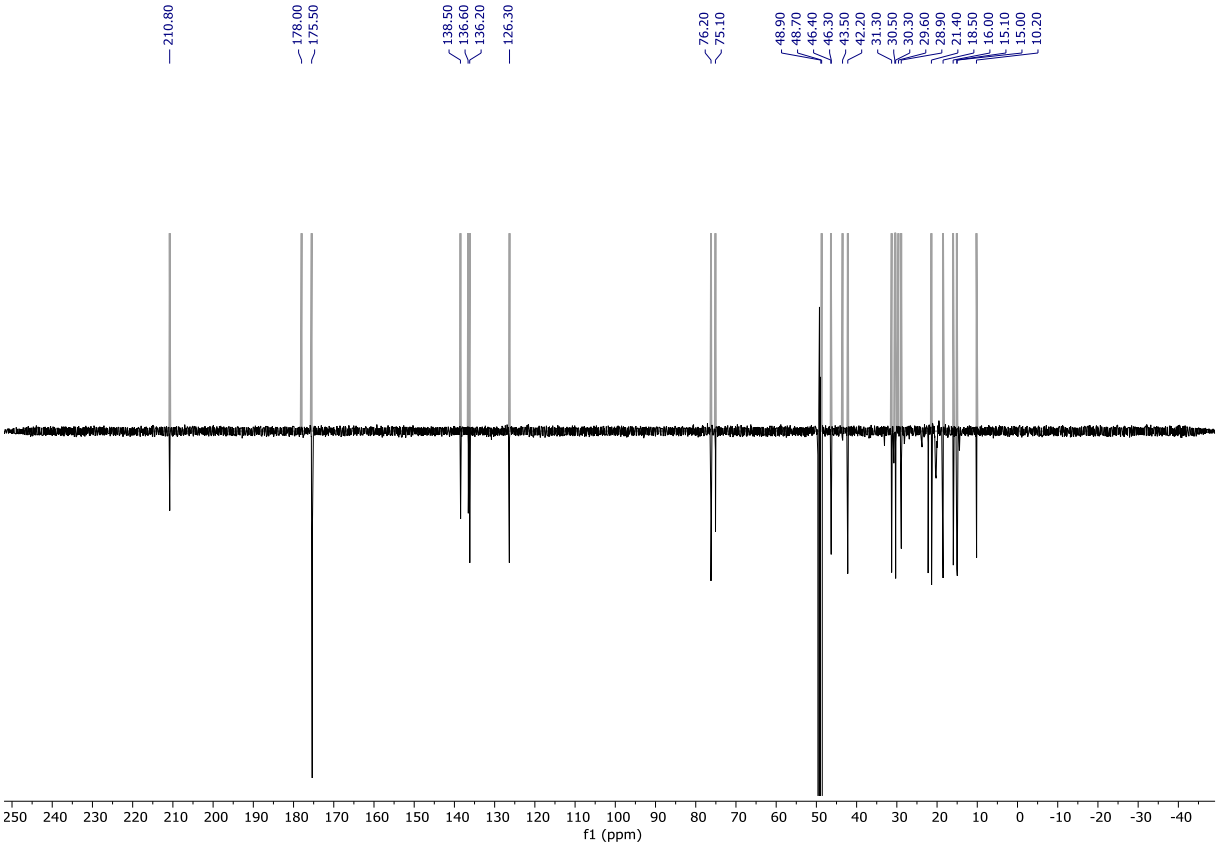
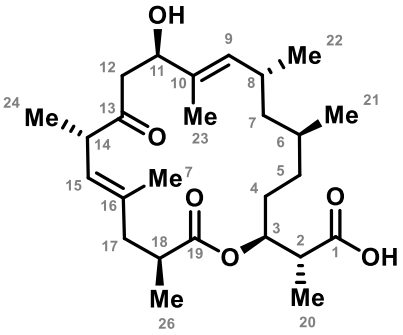



**Figure S2.** Visual comparison of $^{13}C$ NMR spectrum of authentic Strasseriolide C (up) and synthetic **3** (down). Note that the shown spectrum of authentic Strasseriolide C (up) was generated (MestReNova) by converting the tabulated $^{13}C$ NMR data of the natural product into a formal spectrum;[14] therefore the intensity of the lines was arbitrarily set to be identical for all signals. For a tabular survey of the exact numbers, see Table S10.

**Table S9.** NMR assignment of synthetic Strasseriolide C (**3**). All measurements were performed on a Bruker Avance III 600 spectrometer equipped with a cryogenically cooled 5 mm TCI probehead using a classical set of 1D ($^{1}$H, $^{13}$C) and 2D (COSY, HSQC, HMBC, NOESY) experiments. The sample had a concentration of 10 mM and contained 10 eq. of perdeuterated acetic acid. Numbering scheme as shown in the Insert.




| Atom number | δ [ppm] | J [Hz] | COSY | HSQC | HMBC | NOESY |
|---|---|---|---|---|---|---|
| **1C** | 177.6 | | | | 2, 20 | |
| **2C** | 43.5 | | | 2 | 20 | |
| **H** | 2.74 | 6.90, 9.80 | 3, 20 | 2 | 1, 3, 20 | 3, 5b, 20 |
| **3C** | 75.1 | | | 3 | 2, 20 | |
| **H** | 5.11 | 9.80, 3.70, 3.70 | 2, 4a, 4b | 3 | 5, 19, 20 | 2, 4a, 4b, 20 |
| **4C** | 30.5 | | | 4a, 4b | 5a | |
| **H** | 1.75 | 14.30, 13.30, 4.60, 3.20 | 3, 4b, 5a, 5b | 4 | | 3, 5b, 21 |
| **H** | 1.36 | | 3, 4a, 5a, 5b | 4 | 5 | 3, 5a, 6, 15, 24 |
| **5C** | 28.9 | | | 5a, 5b | 3, 4b, 7a, 7b, 21 | |
| **Ha** | 1.63 | 13.10, 2.80 | 4a, 4b, 5b, 6 | 5 | 4 | 4b, 6, 8, 15 |
| **Hb** | 1.18 | | 4a, 4b, 5a, 6 | 5 | 6 | 2, 4a, 21 |
| **6C** | 31.3 | | | 6 | 5b, 7a, 7b, 21 | |
| **H** | 1.18 | | 5a, 5b, 21 | 6 | | 4b, 5a, 9, 15, 21, 22 |
| **7C** | 48.7 | | | 7a, 7b | 9, 21 | |
| **Ha** | 1.23 | | 7b, 8 | 7 | 5, 6, 8, 9, 21, 22 | 9, 21, 22 |
| **Hb** | 1.19 | | 7a, 8 | 7 | 5, 6, 9 | 8, 9 |
| **8C** | 30.3 | | | 8 | 7a, 9, 22 | |
| **H** | 2.44 | 6.80 | 7a, 7b, 9, 22 | 8 | | 5a, 7b, 9, 22, 23 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **9C** | 136.2 | | | 9 | 7a, 7b, 11, 22, 23 | |
| **H** | 5.04 | 8.20, 1.30 | 8, 11, 23 | 9 | 7, 8, 11, 23 | |
| **10C** | 136.6 | | | | 11, 12a, 12b, 23 | |
| **11C** | 76.2 | | | 11 | 9, 12a, 12b, 23 | |
| **H** | 4.46 | 11.10, 4.30 | 9, 12a, 12b | 11 | 9, 10, 12, 13, 23 | 9, 12b, 23 |
| **12C** | 46.4 | | | 12a, 12b | 11 | |
| **Ha** | 3.03 | 14.70, 11.20 | 11, 12b | 12 | 10,11,13 | 14, 15, 23, 25 |
| **Hb** | 2.29 | 14.70, 4.40 | 11, 12a | 12 | 10, 11, 13 | 11, 14 |
| **13C** | 210.8 | | | | 11, 12a, 12b, 14, 15, 24, 25 | |
| **14C** | 48.9 | | | 14 | 15, 24 | |
| **H** | 3,37 | 10.50, 6.60 | 15, 24 | 14 | 13, 15, 16, 24 | 12a, 12b, 15, 24, 25 |
| **15 C** | 126.3 | | | 15 | 14, 17a, 17b, 24, 25 | |
| **H** | 4.68 | 10.50 | 14, 17a, 17b, 25 | 15 | 13, 14, 17, 24, 25 | 4b, 5a, 6, 12a, 14, 17a, 23, 24, 25 |
| **16C** | 138.5 | | | | 14, 17a, 17b, 25 | |
| **17C** | 46.3 | | | 17a, 17b | 15, 25, 26 | |
| **Ha** | 2.32 | 12.80, 12.10 | 15, 17b, 18, 25, 26 | 17 | 15, 16, 18, 19 ,25, 26 | 15, 23, 26 |
| **Hb** | 2.20 | 12.80, 3.20 | 15, 17a, 18, 25 | 17 | 15, 16, 18, 19, 25, 26 | 18, 23, 25, 26 |
| **18C** | 42.2 | | | 18 | | |
| **H** | 2.68 | 12.10, 3.20, 6.90 | 17a, 17b, 26 | 18 | | 17b, 25, 26 |
| **19C** | 175.4 | | | | 3, 17a, 17b, 26 | |
| **20C** | 15.1 | | | 20 | 2, 3 | |
| **H3** | 1.12 | 6.90 | 2 | 20 | 1, 2, 3 | 2, 3, 26 |
| **21C** | 21.4 | | | 21 | 7a,23 | |
| **3H** | 0.83 | 5.90 | 6 | 21 | 5, 6, 7 | 4a, 5b, 6, 7a |
| **22C** | 22.2 | | | 22 | 7a, 23 | |
| **H3** | 0.93 | 6.80 | 8 | 22 | 8, 9 | 6, 7a, 8, 9 |
| **23C** | 10.2 | | | 23 | 9, 11 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **H3** | 1.57 | 1.30 | 9 | 23 | 9, 10, 11, 22 | 8, 9, 11, 12a, 15, 17a, 17b |
| **24C** | 15.0 | | | 24 | 14, 15, 25 | |
| **H3** | 0.90 | 6.60 | 14 | 24 | 13, 14, 15 | 4b, 14, 15 |
| **25C** | 16.0 | | | 25 | 15, 17a, 17b | |
| **H3** | 1.81 | 1.30 | 15, 17a, 17b | 25 | 13, 15, 16, 17, 18, 24 | 12a, 14, 15, 17b, 18 |
| **26C** | 18.5 | | | 26 | 17a, 17b | |
| **H3** | 1.25 | 6.90 | 17a, 18 | 26 | 17, 18, 19 | 17a, 17b, 18, 20 |

**Table S10.** Comparison of spectral data of authentic and synthetic Strasseriolide C (**3**).[14]

| Atom number | $^{1}$H δ (lit.) [ppm] | $^{1}$H δ (exp.) [ppm] | ΔδH | $^{13}$C δ (lit.) [ppm] | $^{13}$C δ (exp.) [ppm] | ΔδC |
|---|---|---|---|---|---|---|
| **1** | | | | 178.0 | 177.6 | -0.4[b] |
| **2** | 2.73 | 2.74 | +0.01 | 43.5 | 43.5 | 0 |
| **3** | 5.11 | 5.11 | 0 | 75.1 | 75.1 | 0 |
| **4** | 1.76/1.36 | 1.75/1.36 | -0.01/0 | 30.5 | 30.5 | 0 |
| **5** | 1.63/1.00 | 1.63/0.99 | 0/-0.01 | 28.9 | 28.9 | 0 |
| **6** | 1.19 | 1.18 | -0.01 | 31.3 | 31.3 | 0 |
| **7** | 1.23/1.19 | 1.23/1.19 | 0/0 | 48.7 | 48.7 | 0 |
| **8** | 2.44 | 2.44 | 0 | 30.3 | 30.3 | 0 |
| **9** | 5.04 | 5.04 | 0 | 136.2 | 136.2 | 0 |
| **10** | | | | 136.6 | 136.6 | 0 |
| **11** | 4.46 | 4.46 | 0 | 76.2 | 76.2 | 0 |
| **12** | 3.03/2.23 | 3.03/2.29 | 0/+0.06[a] | 46.3 | 46.4 | +0.1 |
| **13** | | | | 210.8 | 210.8 | 0 |
| **14** | 3.37 | 3.37 | 0 | 48.9 | 48.9 | 0 |
| **15** | 4.68 | 4.68 | 0 | 126.3 | 126.3 | 0 |
| **16** | | | | 138.5 | 138.5 | 0 |
| **17** | 2.38/2.20 | 2.32/2.20 | +0.06 [a]/0 | 46.4 | 46.3 | -0.1 |
| **18** | 2.68 | 2.68 | 0 | 42.2 | 42.2 | 0 |
| **19** | | | | 175.4 | 175.4 | 0 |
| **20** | 1.12 | 1.12 | 0 | 15.1 | 15.1 | 0 |
| **21** | 0.83 | 0.83 | 0 | 21.4 | 21.4 | 0 |
| **22** | 0.93 | 0.93 | 0 | 22.2 | 22.2 | 0 |
| **23** | 1.57 | 1.57 | 0 | 10.2 | 10.2 | 0 |
| **24** | 0.90 | 0.90 | 0 | 15.0 | 15.0 | 0 |
| **25** | 1.81 | 1.81 | 0 | 16.0 | 16.0 | 0 |
| **26** | 1.25 | 1.25 | 0 | 18.5 | 18.5 | 0 |

[a] There are inconsistencies between the depicted spectra and the reported chemical shifts for protons 12b and 17a in ref.[14] The depicted $^{1}$H NMR spectrum shows the doublet of doublets for proton 17a at 2.33 ppm instead of the reported 2.38 ppm. For proton 12b, the multiplet appears in a range from 2.28 – 2.27 ppm (Figure S19), but these signals are listed in Table S4. Our assignment of the 2D NMR correlations of the protons in question is in agreement with the depicted spectra.

[b] The signal of C1 is broadened in the $^{13}$C NMR spectrum and of very low intensity. However, 2D NMR experiments allowed for unambiguous determination.

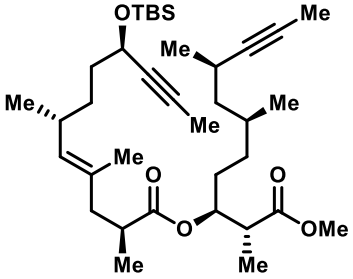
**Strasseriolide C Methyl Ester (52).** Dess-Martin periodinane (18.6 mg, 43.9 µmol) was added to a suspension of the alcohol **51** (10.2 mg, 17.6 µmol) and $NaHCO_3$ (7.4 mg, 87.8 µmol) in $CH_2Cl_2$ at ambient temperature. The mixture was stirred for 2 hours before the reaction was quenched with a mixture of saturated aqueous $NaHCO_3/Na_2S_2O_3$ (1:1, 10 mL). The mixture was diluted with $CH_2Cl_2$ (20 mL) and water (10 mL) and stirred for 30 min before the layers were separated. The aqueous phase was extracted with $CH_2Cl_2$ (3 x 10 mL) and the combined organic extracts were dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure.

*NOTE: This reaction was carried out in a Teflon© vial*. The resulting crude ketone was dissolved in THF (1 mL). Pyridine (15 µL, 0.19 mmol) and HF·py (20 µL, 0.22 mmol) were successively added at rt and the mixture was stirred for 20 h. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (5 mL) and the mixture diluted with EtOAc (15 mL) and water (10 mL). The layers were seperated and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined extracts were dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (30% EtOAc in hexane) to give the title compound as a colorless foam (6.2 mg, 76%). $[\alpha]_D^{20}$ = 134.7° (*c* = 0.62, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.20 – 5.07 (m, 2H), 4.72 (d, *J* = 10.3 Hz, 1H), 4.57 (dd, *J* = 9.4, 5.4 Hz, 1H), 3.67 (s, 3H), 3.22 (dq, *J* = 10.3, 6.6 Hz, 1H), 2.96 (dd, *J* = 15.2, 9.5 Hz, 1H), 2.75 – 2.71 (m, 1H), 2.71 (m, 1H), 2.47 – 2.24 (m, 3H), 2.11 (dd, *J* = 13.4, 3.2 Hz, 1H), 1.76 (d, *J* = 1.4 Hz, 3H), 1.66 – 1.47 (m, 4H), 1.59 (d, *J* = 1.3 Hz, 3H), 1.44 – 1.34 (m, 1H), 1.30 – 1.15 (m, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.13 (d, *J* = 6.9 Hz, 3H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 5.9 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 209.5, 174.3, 173.8, 136.9, 135.8, 134.5, 125.2, 75.5, 73.7, 51.9, 47.9, 46.8, 45.4, 44.6, 42.0, 40.9, 30.0, 29.2, 28.5, 22.0, 21.3, 18.5, 16.7, 14.7, 13.9, 9.9. IR (film, $cm^{-1}$): 3462, 2952, 2927, 1736, 1715, 1455, 1375, 1336, 1289, 1170, 1045, 866, 734, 553, 535. HRMS (ESI) *m/z* calcd. for $C_{27}H_{44}O_6$ [$M^+$ + Na]: 487.3030; found 487.3034.

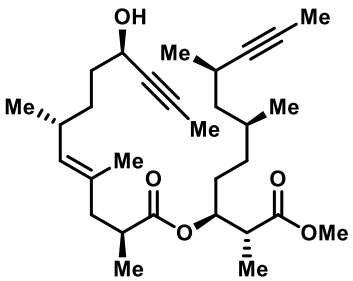
**Methyl (2*R*,3*S*,6*S*,8*R*,*E*)-2,6,8,10-tetramethyl-11-oxo-3-(((2*S*,6*S*,*E*)-2,4,6-trimethyl-7-oxooct-4-enoyl)oxy)undec-9-enoate (53).** Trimethyltinhydroxide (23.4 mg, 0.13 mmol) was added to a solution of strasseriolide C methylester **52** (6.0 mg, 12.9 µmol) in 1,2-dichloroethane (0.3 mL). The reaction mixture was heated to 120 °C in the microwave oven for 2 h. The mixture was then filtered through a short pad of Celite© (ca. 1 cm), which was rinsed with dichloromethane (10 mL). The solvent was removed under reduced pressure. The residue was taken up in EtOAc (10 mL) and the solution was washed with HCl (1 M, 3 x 10 mL) and brine (10 mL). The solvent was removed under reduced pressure and the residue purified

by flash chromatography (40% EtOAc in hexane) to yield title compound as a colorless film (1.0 mg, 17%). Because of the low stability of this compound, no analytically pure sample could be obtained; the spectra indicate a purity of $\leq$ 90%. $^{1}$H NMR ($CDCl_3$, 400 MHz): δ 9.38 (s, 1H), 6.25 (dd, *J* = 9.9, 1.4 Hz, 1H), 5.14 – 5.05 (m, 2H), 3.67 (s, 3H), 3.35 (dq, *J* = 9.6, 8.8 Hz, 1H), 2.77 (dq, *J* = 9.7, 6.8 Hz, 1H), 2.70 – 2.57 (m, 2H), 2.45 (dd, *J* = 13.6, 6.3 Hz), 2.10 (s, 3H), 2.08 – 2.00 (m, 1H), 1.75 (d, *J* = 1.3 Hz, 3H), 1.69 (d, *J* = 1.4 Hz, 3H), 1.65 – 1.15 (m, 7H), 1.15 (d, *J* = 7.1 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 7.0 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H).$^{13}$C NMR ($CDCl_3$, 100 MHz): δ 195.7, 175.6, 174.3, 160.8, 135.6, 127.3, 126.8, 124.8, 74.2, 52.0, 47.3, 44.0, 43.6, 43.0, 38.1, 32.7, 31.2, 30.6, 29.4, 27.9, 19.8, 19.6, 16.7, 16.5, 16.3, 12.0, 9.4. IR (film, $cm^{-1}$): 2958, 2935, 1737, 1716, 1688, 1459, 1424, 1379, 1319, 1259, 1168, 1038, 1015, 666. HRMS (ESI) *m/z* calcd. for $C_{27}H_{44}O_6Na$ [$M^+$ + Na]: 487.3030; found 487.3031.

**(2*R*,3*S*,6*S*,8*R*)-1-Methoxy-2,6,8-trimethyl-1-oxoundec-9-yn-3-yl-(2*S*,6*R*,9*R*,*E*)-9-((*tert*-butyldimethylsilyl)oxy)-2,4,6-trimethyldodec-4-en-10-ynoate (S16).** 4-(Dimethylamino)pyridine (567 mg, 4.64 mmol) and *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (445 mg, 2.32 mmol) were added to a solution of acid **38** (284 mg, 0.77 mmol) and alcohol **12** (197 mg, 0.77 mmol) in dichloromethane (40 mL) at 0 °C. The mixture was stirred at this temperature for 10 minutes and at ambient temperature for 18 hours. The reaction was then quenched with saturated aqueous $NH_4Cl$ (50 mL) and the layers were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (3 x 50 mL), the combined organic phases were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (5% *tert*-butyl methyl ether in pentane) to give the title compound as a colorless syrup (413 mg, 88% yield). $[\alpha]_D^{20}$ = –21.8 (*c* = 0.34, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.10 (dt, *J* = 8.3, 5.0 Hz, 1H), 4.95 (dq, *J* = 9.4, 1.2 Hz, 1H), 4.26 (tq, *J* = 6.3, 2.1 Hz, 1H), 3.67 (s, 3H), 2.69 (qd, *J* = 7.1, 5.4 Hz, 1H), 2.57 (dtt, *J* = 12.7, 9.1, 6.3 Hz, 1H), 2.44 – 2.37 (m, 2H), 2.36 – 2.26 (m, 1H), 1.97 (ddd, *J* = 13.5, 9.1, 0.9 Hz, 1H), 1.81 (d, *J* = 2.1 Hz, 3H), 1.77 (d, *J* = 2.3 Hz, 3H), 1.69 – 1.40 (m, 6H), 1.58 (d, *J* = 1.3 Hz, 3H), 1.38 – 1.20 (m, 5H), 1.16 (d, *J* = 7.1 Hz, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 1.08 (d, *J* = 7.1 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.87 (d, *J* = 6.7 Hz, 3H), 0.10 (s, 3H), 0.08 (s, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 176.0, 174.5, 134.3, 130.6, 84.1, 81.2, 80.0, 75.6, 74.1, 63.5, 51.9, 44.8, 43.9, 43.1, 38.0, 37.1, 33.3, 32.4, 31.8, 30.5, 29.2, 26.0, 23.6, 21.6, 21.4, 19.8, 18.4, 16.5, 15.9, 12.1, 3.7, 3.6, −4.3, −4.9. IR (film, $cm^{-1}$): 2954, 2927, 2856, 1740, 1460, 1378, 1361, 1343, 1251, 1200, 1163, 1075, 995, 961, 940, 837, 777. HRMS (ESI) *m/z* calcd. for $C_{36}H_{62}O_5SiNa$ [$M^+$ + Na]: 625.4260; found 625.4259.

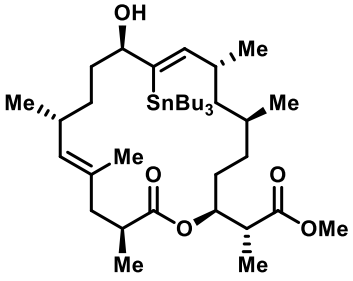



**(2*R*,3*S*,6*S*,8*R*)-1-Methoxy-2,6,8-trimethyl-1-oxoundec-9-yn-3-yl-(2S,6R,9R,E)-9-hydroxy-2,4,6-trimethyldodec-4-en-10-ynoate (56).** HF·pyridine (0.91 mL, 10.11 mmol) was added to a solution of the silyl ether **S16** (406 mg, 0.67 mmol) and pyridine (0.82 mL, 10.11 mmol) in THF (6.74 mL) at 0 °C. After stirring for 10 minutes, the ice bath was removed and stirring was continued at ambient temperature for 16 hours before the mixture was diluted with water and *tert*-butyl methyl ether. A saturated aqueous solution of $NaHCO_3$ was then slowly added to quench the remaining HF. The layers were separated and the aqueous phase extracted with *tert*-butyl methyl ether (3 x 20 mL). The combined organic layers were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (35% *tert*-butyl methyl ether in



pentane) to give the title compound as a colorless syrup (317.3 mg, 96% yield). $[\alpha]_D^{20}$ = – 58.7 (*c* = 0.30, $CHCl_3$). $^1$H NMR ($CDCl_3$, 400 MHz): δ 5.10 (dt, *J* = 8.2, 5.0 Hz, 1H), 4.95 (dq, *J* = 9.5, 1.3 Hz, 1H), 4.34 – 4.24 (m, 1H), 3.67 (s, 3H), 2.69 (qd, *J* = 7.0, 5.3 Hz, 1H), 2.63 – 2.54 (m, 1H), 2.45 – 2.29 (m, 3H), 1.98 (ddd, *J* = 13.6, 8.8, 0.9 Hz, 1H), 1.84 (d, *J* = 2.1 Hz, 3H), 1.78 (d, *J* = 2.3 Hz, 3H), 1.67 – 1.38 (m, 6H), 1.59 (d, *J* = 1.3 Hz, 3H), 1.38 – 1.21 (m, 5H), 1.16 (d, *J* = 7.1 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.09 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ 176.0, 174.5, 133.8, 131.0, 84.1, 81.1, 80.6, 75.6, 74.2, 63.0, 51.9, 44.8, 43.8, 43.1, 38.1, 36.3, 33.2, 32.4, 31.8, 30.5, 29.2, 23.6, 21.6, 21.4, 19.8, 16.6, 16.1, 12.0, 3.7, 3.6. IR (film, $cm^{-1}$): 3514, 2953, 2921, 2870, 1738, 1456, 1379, 1343, 1255, 1201, 1165, 1088, 1048, 1021, 897.

**Methyl-(*R*)-2-((2*S*,5*S*,7*R*,8*Z*,10*R*,13*R*,14*E*,17*S*)-10-hydroxy-5,7,13,15,17-pentamethyl-18-oxo-9-(tributylstannyl)oxacyclooctadeca-8,14-dien-2-yl)propanoate (58).** Argon was bubbled through a

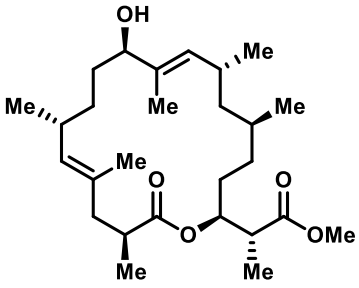



suspension comprising diyne **56** (259.5 mg, 0.53 mmol) and powdered molecular sieves (5 Å, 7.5 g; dried at 150 °C under high vacuum overnight) in toluene (265 mL) for 5 minutes before the mixture was heated to 110 °C. A solution of complex **54** (78.7 mg, 0.11 mmol)[11] in toluene (5 mL) was then added dropwise to the mixture. Stirring was continued at 110 °C for 30 minutes, when TLC showed full consumption of the starting material. EtOH (5 mL) was added to quench the catalyst and the resulting mixture was allowed reach ambient temperature. The mixture was filtered through a pad of silica, rinsing carefully with EtOAc, and the combined filtrates were evaporated.

The residue of crude **57** was dissolved in dichloromethane (35 mL). $[Cp^*RuCl]_4$ (14.4 mg, 13 µmol) was added, followed by tributyltin hydride (0.18 mL, 0.64 mmol). The resulting dark brown mixture was stirred for 1 hour before an additional portion of tributyltin hydride (0.18 mL, 0.64 mmol) was introduced. Stirring was continued for another 1 hour before the solvent was removed under reduced pressure. The residue was purified by flash chromatography (10% *tert*-butyl methyl ether in pentane) to give the title compound as a yellow oil (229.8 mg, 60% yield over both steps). $[\alpha]_D^{20}$ = +30.0 (*c* = 0.2, $CH_2Cl_2$). $^1$H NMR ($CD_2Cl_2$, 600 MHz): δ 5.89 (dd, *J* = 9.5, 1.0 Hz, $J_{Sn–H}$ = 130.7 Hz, 1H), 5.04 (q, *J* = 6.2 Hz, 1H), 4.83 (dq, *J* = 8.9, 1.4 Hz, 1H), 3.99 – 3.82 (m, $J_{Sn–H}$ = ~70 Hz, 1H), 3.64 (s, 3H), 2.72 (p, *J* = 7.0 Hz, 1H), 2.65 (dqd, *J* = 11.8, 7.0, 3.3 Hz, 1H), 2.30–2.16 (m, 3H), 2.01 (dt, *J* = 15.5, 2.3 Hz, 1H), 1.65–1.59 (m, 2H), 5.89 (dd, *J* = 9.5, 1.0 Hz, 3H), 1.53 – 1.44 (m, 9 H), 1.33 (h, *J* = 7.4 Hz, 6H), 1.35–1.22 (m, 3H), 1.18 – 1.13 (m, 3H), 1.15 (d, *J* = 7.0 Hz, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.07–1.00 (m, 1H), 0.99–0.94 (m, 9H), 0.90 (t, *J* = 7.3 Hz, 9H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR (151 MHz, $CD_2Cl_2$) δ 174.8, 174.6, 148.7, 147.1, 132.3, 132.0, 82.4, 74.2, 52.0, 45.3, 43.1, 41.9, 40.3, 36.5, 35.5, 33.9, 33.0, 31.5, 29.7, 29.7, 28.9, 28.0, 21.3, 21.2, 21.0, 18.9, 17.7, 13.8, 12.1, 11.9. $^{119}$Sn NMR (224 MHz, $CD_2Cl_2$)

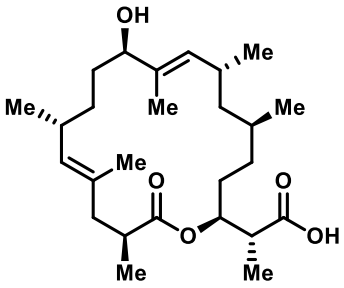
δ −60.4. IR (film, $cm^{-1}$): 2953, 2925, 2870, 2854, 2349, 1739, 1457, 1375, 1339, 1288, 1252, 1200, 1171, 1071, 1047, 1016, 1002, 671, 665. HRMS (ESI+) *m/z* calcd. for $C_{38}H_{70}O_5SnNa$ [$M^+$ + Na]: 749.4138; found 749.4137.

**Strasseriolide B Methyl Ester (59).** $Pd(PPh_3)_4$ (2.3 mg, 2 µmol) was added to a solution of stannane **58**




(28.7 mg, 39.6 µmol) and $[Ph_2PO_2][NBu_4]$ (20 mg, 43.5 µmol) in DMF (0.2 mL) at ambient temperature. After stirring for 5 min, CuTC (22.6 mg, 119 µmol) was added, followed immediately by methyl iodide (11 µL, 178 µmol).[17] The resulting mixture was stirred at 40 °C for 2 hours before it was cooled to ambient temperature. A few drops of triethylamine were added and the mixture was diluted with *tert*-butyl methyl ether (5 mL). The slurry was transferred to a separatory funnel containing a saturated solution of $NH_4Cl$ (1 mL). The layers were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 x 5 mL). The combined organic layers were washed with brine, dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (35% *tert*-butyl methyl ether in pentane) to give the title compound as a colorless sticky syrup (11.1 mg, 62% yield). $[\alpha]_D^{20}$ = +28.9 (*c* = 0.25, MeOH). $^1$H NMR ($CD_3OD$, 600 MHz): δ 5.13 (ddd, *J* = 7.5, 5.4, 4.5 Hz, 1H), 5.07 (dq, *J* = 8.8, 1.7 Hz, 1H), 4.74 (dq, *J* = 8.9, 1.2 Hz, 1H), 3.77 (ddd, *J* = 10.1, 4.7, 0.5 Hz, 1H), 3.68 (s, 3H), 2.80 (p, *J* = 7.0 Hz, 1H), 2.65–2.54 (m, 2H), 2.26–2.19 (m, 2H), 2.09 (dd, *J* = 14.0, 3.3 Hz, 1H), 1.66–1.62 (m, 1H), 1.62 (dd, *J* = 1.4, 0.5 Hz, 3H), 1.59 (d, *J* = 1.4 Hz, 3H), 1.57–1.48 (m, 4H), 1.42–1.38 (m, 1H), 1.34–1.22 (m, 3H), 1.19 (d, *J* = 6.9 Hz, 3H), 1.13 (d, *J* = 7.0 Hz, 3H), 1.07–1.01 (m, 1H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.93–0.90 (m, 1H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR ($CD_3OD$, 151 MHz): δ 176.3, 175.9, 136.7, 135.7, 134.7, 133.6, 80.2, 75.2, 52.4, 47.7, 44.9, 42.8, 42.3, 34.9, 33.9, 33.1, 31.6, 30.6, 30.5, 30.4, 22.2, 22.1, 21.7, 18.7, 17.1, 13.3, 10.4. IR (film, $cm^{-1}$): 3441, 2950, 2925, 2865, 1738, 1455, 1377, 1329, 1287, 1251, 1199, 1166, 1079, 1047, 911, 868, 756, 560, 533. HRMS (ESI+) *m/z* calcd. for $C_{27}H_{46}O_5Na$ [$M^+$ + Na]: 473.3243; found 473.3238 .

**Strasseriolide B (2).** Trimethyltin hydroxide (38.1 mg, 210 µmol) was added to a solution of methyl




ester **59** (9.2 mg, 21 µmol) in 1,2-dichloroethane (0.21 mL) in a microwave vial. The vial was sealed and the mixture heated under microwave conditions at 120 °C for 90 minutes. A second portion of trimethyltin hydroxide (38.1 mg, 210 µmol) was introduced and the vial resealed. Microwave heating to 120 °C was continued for an additional 2 hours. The mixture was allowed to stand until the solids had precipitated. The suspension was then filtered through a pad of Celite, washing carefully with dichloromethane, and the combined filtrates were concentrated under reduced pressure. The residue

was dissolved in EtOAc (5 mL) and the solution washed several times with HCl (1 M). The organic phase was dried over sodium sulfate and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (20% EtOAc in hexane + 1% formic acid) to give strasseriolide B as a white amorphous solid (7.7 mg, 84% yield).

$[\alpha]_D^{25}$ = +23.0 (*c* = 0.40, MeOH) (ref.:[14] $[\alpha]_D^{25}$ = +32.6 (*c* = 0.25, MeOH). $^1$H NMR ($CD_3OD$, 600 MHz): δ 5.15 (ddd, *J* = 8.2, 5.2, 1.4 Hz, 1H), 5.06 (dq, *J* = 8.9, 1.5 Hz, 1H), 4.73 (dq, *J* = 9.1, 1.2 Hz, 1H), 3.77 (dd, *J* = 10.1, 4.6 Hz, 1H), 2.73 (dq, *J* = 8.1, 6.9 Hz, 1H), 2.62 (dqd, *J* = 11.9, 7.0, 3.3 Hz, 1H), 2.58 (m, 1H), 2.25 (dd, *J* = 13.8, 11.9 Hz, 1H), 2.23 (m, 1H), 2,09 (dd, *J* = 13.9, 3.3 Hz, 1H), 1.74 (tdd, *J* = 11.2, 5.7, 4.2 Hz, 1H), 1.62 (d, *J* = 1.3 Hz, 3H), 1.62 (m, 1H),1.59 (d, *J* = 1.4 Hz, 3H), 1.54 (m, 1H), 1.52 (m, 1H), 1.50 (m, 1H), 1.42 (dddd, *J* = 13.0, 10.3, 7.7, 3.9 Hz, 1H), 1,32 (m, 1H), 1.26 (m, 2H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.14 (d, *J* = 6.9 Hz, 3H), 1.06 (dddd, *J* = 13.4, 11.1, 8.8, 4.9 Hz, 1H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.90 (m, 1H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR (151 MHz, [$D_4$]-MeOH) δ[a] 177.7, 176.4, 136.7, 135.7, 134.7, 133.6, 80.2, 75.5, 49.4, 49.3, 49.1, 49.0, 48.9, 48.7, 48.6, 48.0, 45.0, 43.0, 42.4, 34.8, 34.0, 33.1, 31.7, 30.7, 30.5, 30.2, 22.2, 22.2, 21.6, 18.7, 17.0, 14.1, 10.4. IR (film, $cm^{-1}$): 3398, 2949, 2925 2867, 1734, 1713, 1454, 1377, 1289, 1252, 1205, 1176, 1047, 1018, 1011, 968, 907, 864, 561, 536. HRMS (ESI+) *m/z* calcd. for $C_{26}H_{43}O_5$ [*M* – H]: 435.3116; found 435.3116.

[a] *NOTE*: *In the general information of Reyes et. al.,*[14] *the reference for the chemical shift of [$D_4$]-MeOH is given as $\delta_C$ = 49.10 ppm. However, the tabulated data (Tables S2 – S5) shows a consistent difference of –0.15 ppm. To compare the data of our synthetic material, we therefore referenced our $^{13}$C NMR spectra to $\delta_C$ = 49.00 ppm to match the tabulated data*.

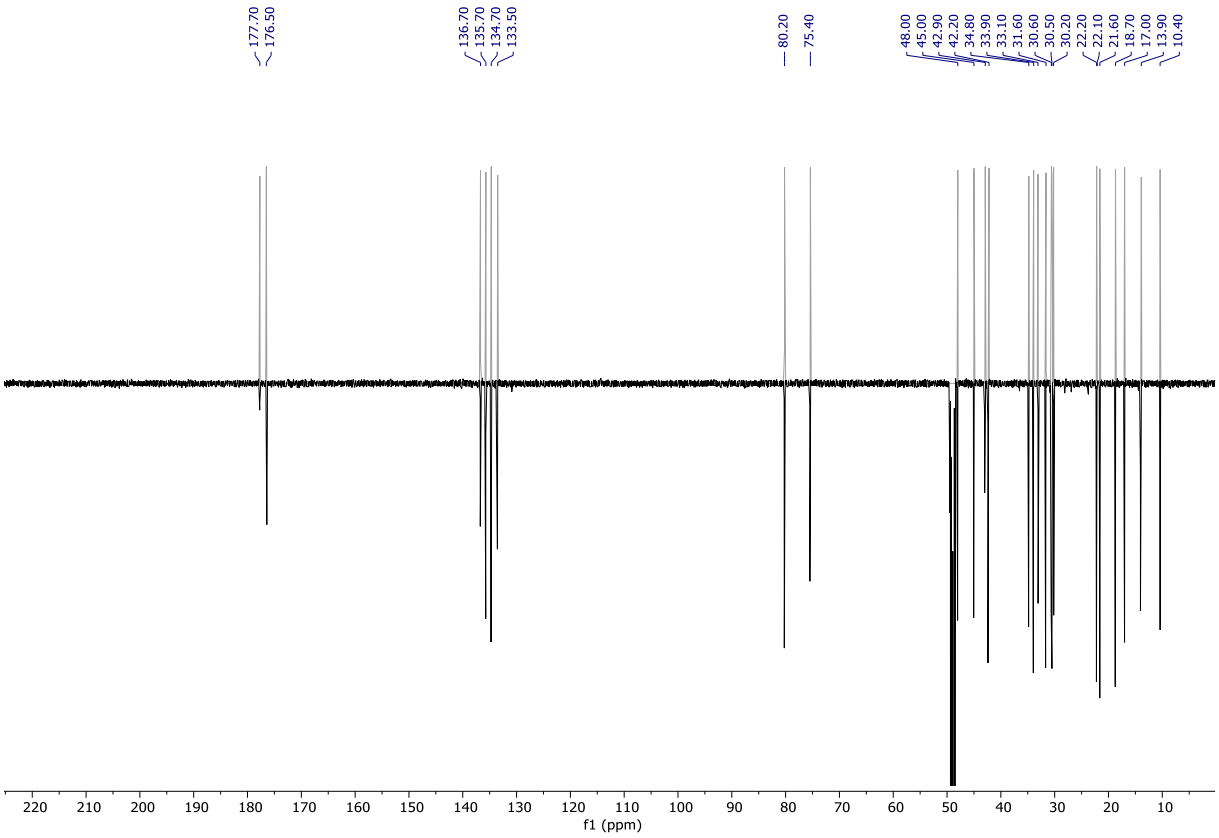
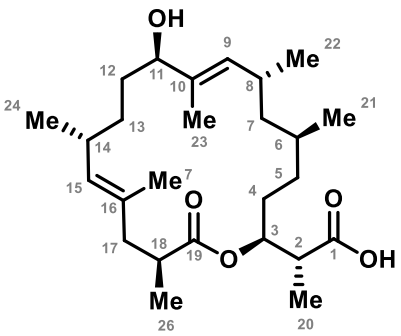



**Figure S3.** Visual comparison of $^{13}C$ NMR spectrum of authentic Strasseriolide B (up) and synthetic **2** (down). Note that the spectrum of authentic Strasseriolide B (up) was generated (MestReNova) by converting the tabulated $^{13}C$ NMR data of the natural product into a formal spectrum;[14] therefore, the intensity of the lines was arbitrarily set to be identical for all signals. For a tabular survey of the exact numbers, see Table S12.

**Table S11.** NMR assignment of synthetic Strasseriolide B (**2**). All measurements were performed on a Bruker Avance III 600 spectrometer equipped with a cryogenically cooled 5 mm TCI probehead using a classical set of 1D ($^{1}$H, $^{13}$C) and 2D (COSY, HSQC, HMBC, NOESY) experiments. Numbering scheme as shown in the Insert.




| Atom number | δ [ppm] | J [Hz] | COSY | HSQC | HMBC | NOESY |
|---|---|---|---|---|---|---|
| **1C** | 177.7 | | | | 2, 3, 20 | |
| **2C** | 43.0 | | | 2 | 3, 4a, 4b, 20 | |
| **H** | 2.73 | 8.10, 6.90 | 3, 20 | 2 | 1, 3, 4, 20 | 5a, 5b, 20 |
| **3C** | 75.5 | | | 3 | 2, 4a, 5b, 5a, 5b, 20 | |
| **H** | 5.15 | 8.20, 5.20, 4.10 | 2, 4a, 4b | 3 | 1, 2, 4, 5, 19, 20 | 4a, 4b, 20 |
| **4C** | 30.7 | | | 4a, 4b | 2, 3, 5a, 5b | |
| **Ha** | 1.75 | 14.20, 1.10, 4.50 | 3, 4b, 5a, 5b | 4 | 2, 3, 5, 6 | 3, 21 |
| **Hb** | 1.52 | 14.20, 11.00, 5.20 | 3, 4a, 5a, 5b | 4 | 2, 3, 5, 6 | 3, 15, 21, 24 |
| **5C** | 30.2 | | | 5a, 5b | 3, 4a, 4b, 6, 7, 21 | |
| **Ha** | 1.62 | | 4a, 4b, 5b, 6 | 5 | 5 | 2, 8 |
| **Hb** | 1.06 | 13.20, 11.50, 9.00, 5.00 | 4a, 4b, 5a, 6 | 5 | 5a, 5b, 9, 21, 22 | 2, 21 |
| **6C** | 31.7 | | | 6 | 4a, 4b, 5a, 5b, 7, 21, 22 | |
| **H** | 1.50 | | 5a, 5b, 7, 21 | 6 | 5 | 9, 15, 21 |
| **7C** | 48.0 | | | 7 | 5a, 5b, 9, 21, 22 | |
| **2H** | 1.26 | | 6, 8 | 7 | 5, 6, 8, 9, 21, 22 | 8, 9, 21, 22 |
| **8C** | 30.5 | | | 8 | 7, 9, 22 | |
| **H** | 2.58 | | 7, 9, 22 | 8 | 22 | 5a, 7, 22, 23 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **9C** | 135.7 | | | 9 | 7, 11, 22, 23 | |
| **H** | 5.06 | 8.90, 1.50 | 8, 23 | 9 | 7, 8, 11, 22, 23 | 6, 7, 11, 13b, 22 |
| **10C** | 136.7 | | | | 11, 12b, 23 | |
| **11C** | 80.24 | | | 11 | 9, 12a, 12b, 13b, 23 | |
| **H** | 3.77 | 10.10, 4.60 | 12a, 12b | 11 | 9, 10, 12, 13, 23 | 9, 13a, 13b, 23 |
| **12C** | 33.1 | | | 12a, 12b | 11, 13a, 13b | |
| **Ha** | 1.54 | | 11, 12b, 13a, 13b | 12 | 11, 13 | |
| **Hb** | 1.32 | | 11, 12a, 13a, 13b | 12 | 10, 11, 13, 14 | 13b, 14, 15, 23 |
| **13C** | 34.8 | | | 13a, 13b | 11, 12a, 12b, 15, 24, 25 | |
| **Ha** | 1.42 | 13.0, 10.30, 7.70, 3.90 | 12a, 12b, 13b, 14 | 13 | 12, 14, 15, 24 | 11, 14, 24 |
| **Hb** | 0.90 | | 12a, 12b, 13a, 14 | 13 | 11, 12, 14, 15, 24 | 9, 11, 12b, 15 |
| **14C** | 34.0 | | | 14 | 12b, 13a, 13b, 15, 24, 25 | |
| **H** | 2.23 | | 13a, 13b, 15, 24 | 14 | 24 | 12b, 13a, 24, 25 |
| **15 C** | 134.7 | | | 15 | 13a, 13b, 17a, 17b, 24, 25 | |
| **H** | 4.73 | 9.10, 1.20 | 14, 17a, 17b, 25 | 15 | 13, 14, 17, 24, 25 | 4b, 6, 12b, 13b, 17a, 18, 23, 24 |
| **16C** | 133.6 | | | | 17a, 17b, 18, 25 | |
| **17C** | 45.1 | | | 17a, 17b | 15, 18, 25, 26 | |
| **Ha** | 2.25 | 13.80, 11.90 | 15, 17b, 18, 26 | 17 | 15, 16, 18, 19, 25, 26 | 15, 26 |
| **Hb** | 2.09 | 13.90, 3.30 | 15, 17a, 18, 25 | 17 | 15, 16, 18, 19, 25, 26 | 18, 25, 26 |
| **18C** | 42.4 | | | 18 | 17a, 17b, 26 | |
| **H** | 2.62 | 11.90, 7.00, 3.30 | 17a, 17b, 26 | 18 | 16, 17, 19, 26 | 15, 17b, 25, 26 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **19C** | 176.4 | | | | 3, 17a, 17b, 18, 26 | |
| **20C** | 14.1 | | | 20 | 2, 3 | |
| **H3** | 1.14 | 6.90 | 2 | 20 | 1, 2, 3 | 2, 3, 26 |
| **21C** | 21.6 | | | 21 | 5a, 5b, 7 | |
| **3H** | 0.89 | 6.70 | 6 | 21 | 5, 6, 7 | 4a, 4b, 5b, 6, 7 |
| **22C** | 22.2 | | | 22 | 7, 8, 9, 23 | |
| **H3** | 0.97 | 6.70 | 8 | 22 | 6, 7, 8, 9 | 7, 8, 9, 23 |
| **23C** | 10.4 | | | 23 | 9,11 | |
| **H3** | 1.59 | 1.40 | 9 | 23 | 9, 10, 11, 22 | 8, 11, 12b, 15, 22 |
| **24C** | 22.2 | | | 24 | 13a, 13b, 14, 15, 25 | |
| **H3** | 0.86 | 6.70 | 14 | 24 | 13, 14, 15 | 4b, 13a, 14, 15, 25 |
| **25C** | 17.0 | | | 25 | 15, 17a, 17b | |
| **H3** | 1.62 | 1.30 | 15, 17b | 25 | 13, 14, 15, 16, 17, 24 | 14, 17b, 18, 24 |
| **26C** | 18.7 | | | 26 | 17a, 17b, 18 | |
| **H3** | 1.20 | 7.00 | 17a, 18 | 26 | 17, 18, 19 | 17a, 17b, 18, 20 |

**Table S12.** Comparison of spectral data for authentic and synthetic Strasseriolide B (**2**).[14]

| Atom number | $^{1}$H δ (lit.) [ppm] | $^{1}$H δ (exp.) [ppm] | ΔδH | $^{13}$C δ (lit.) [ppm] | $^{13}$C δ (exp.) [ppm] | ΔδC |
|---|---|---|---|---|---|---|
| **1** | | | | 177.7 | 177.7 | 0 |
| **2** | 2.73 | 2.73 | 0 | 42.9 | 43.0 | +0.1 |
| **3** | 5.15 | 5.15 | 0 | 75.4 | 75.5 | +0.1 |
| **4** | 1.74 / 1.52 | 1.75 / 1.52 | +0.01 / 0 | 30.2 (30.6)[b] | 30.7 | -0.5 (-0.1) |
| **5** | 1.61 / 1.06 | 1.62 / 1.06 | +0.01 / 0 | 30.2 | 30.2 | 0 |
| **6** | 1.51 | 1.50 | -0.01 | 31.6 | 31.7 | +0.1 |
| **7** | 1.26 / 1.43 | 1.26 | 0 / -0.17 [a] | 48.0 | 48.0 | 0 |
| **8** | 2.58 | 2.58 | 0 | 30.5 | 30.5 | 0 |
| **9** | 5.06 | 5.06 | 0 | 135.7 | 135.7 | 0 |
| **10** | | | | 136.9 | 136.7 | -0.2 |
| **11** | 3.77 | 3.77 | 0 | 80.2 | 80.2 | 0 |
| **12** | 1.55 / 1.33 | 1.54 / 1.32 | -0.01 / -0.01 | 33.1 | 33.1 | 0 |
| **13** | 1.42 / 0.91 | 1.42 / 0.90 | 0 / -0.01 | 34.8 | 34.8 | 0 |
| **14** | 2.23 | 2.23 | 0 | 33.9 | 34.0 | +0.1 |
| **15** | 4.73 | 4.73 | 0 | 134.7 | 134.7 | 0 |
| **16** | | | | 133.5 | 133.6 | +0.1 |
| **17** | 2.24 / 2.09 | 2.25 / 2.09 | +0.01 / 0 | 45.0 | 45.0 | 0 |
| **18** | 2.62 | 2.62 | 0 | 42.2 | 42.4 | +0.2 |
| **19** | | | | 176.5 | 176.4 | -0.1 |
| **20** | 1.14 | 1.14 | 0 | 13.9 | 14.1 | +0.2 |
| **21** | 0.87 | 0.89 | +0.02 | 21.6 | 21.6 | 0 |
| **22** | 0.97 | 0.97 | 0 | 22.1 | 22.2 | +0.1 |
| **23** | 1.59 | 1.59 | 0 | 10.4 | 10.4 | 0 |
| **24** | 0.85 | 0.86 | +0.01 | 22.2 | 22.2 | 0 |
| **25** | 1.62 | 1.62 | 0 | 17.0 | 17.0 | 0 |
| **26** | 1.20 | 1.20 | 0 | 18.7 | 18.7 | 0 |

[a] Our HSQC spectrum shows no correlation to a signal at 1.43. This is in agreement with the findings of *Rychnovsky et. al.* who report only one proton for the signal at 1.42.[14]

[b] The data in the supporting information of ref.[14] gives a chemical shift of 30.2 ppm for C4 (Table S3). In the text of the SI (page S8), however, a signal with the chemical shift of 30.6 ppm is listed instead.

**Strasseriolide A Methyl Ester (60).** Dess-Martin periodinane (19.7 mg, 46.6 µmol) was added to a solution of **59** (10 mg, 22.2 µmol) in $CH_2Cl_2$ (0.4 mL) at 0 °C. The mixture was stirred for 3 hours at ambient temperature until TLC showed full conversion of the starting material. A sat. aq. solution of $NaHCO_3$ (0.5 mL) was added, the layers were separated and the aqueous phase was extracted with dichloromethane (3 x 1 mL). The combined organic phases were dried over sodium sulfate and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (12.5% *tert*-butyl methyl ether in hexane) to give the title compound as a colorless oil (3.2 mg, 33% yield). $[\alpha]_D^{20}$ = –0.8 (*c* = 0.77, MeOH). $^1$H NMR ($CD_3OD$, 600 MHz): δ 6.59 (dq, *J* = 9.3, 1.3 Hz, 1H), 5.09 (dt, *J* = 7.0, 5.0, 5.0 Hz, 1H), 4.80 (dm, *J* = 9.4, 0.9, 1.3 Hz, 1H), 3.68 (s, 3H), 2.94 (dd, *J* = 15.9, 8.2, 4.6 Hz, 1H), 2.84-2.76 (m, 2H), 2.61 (dqd, *J* = 6.9, 11.5, 3.2 Hz, 1H), 2.44–2.37 (m, 2H), 2.17 (ddd, *J* = 11.5, 14.6, 0.9 Hz, 1H), 2.03 (ddd, *J* = 14.6, 3.2, 1.3 Hz, 1H), 1.88-1.80 (m, 1H), 1.75 (d, *J* = 1.3 Hz, 3H), 1.73-1.71 (m, 1H), 1.70-1.68 (m, 1H), 1.65-1.63 (m,1H), 1.55-1.52 (m, 1H), 1.51 (dd, *J* = 1.4, 0.5 Hz, 3H), 1.50-1.40 (m, 3H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.10 (d, *J* = 7.0 Hz, 3H), 1.08-1.05 m, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR ($CD_3OD$, 151 MHz): δ 205.2, 176.6, 175.8, 150.6, 136.9, 134.0, 132.7, 75.3, 52.4, 45.5, 44.3, 43.0, 42.3, 36.6, 34.5, 32.9, 31.7, 31.5, 30.6, 30.6, 27.2, 22.0, 21.0, 20.7, 19.1, 17.8, 13.1, 11.6. IR (film, cm$^{-1}$): 2953, 2926, 2870, 1735, 1666, 1454, 1435, 1375, 1285, 1249, 1198, 1165, 1130, 1100, 1073, 1046, 994, 963, 907, 870, 747. HRMS (ESI+) *m/z* calcd. for $C_{27}H_{44}O_5Na$ [$M^+$ + Na]: 471.3082; found 471.3081.

**Strasseriolide A (1).** Trimethyltin hydroxide (34.3 mg, 190 µmol) was added to a solution of methyl ester **60** (8.5 mg, 18.9 µmol) in 1,2-dichlorethane (0.22 mL) in a microwave vial. The vial was sealed and the mixture heated under microwave conditions to 120 °C for 5 hours. The mixture was allowed to stand until the solids had precipitated. The suspension was then filtered through a pad of Celite, washing carefully with dichloromethane, and the solvent of the combined filtrates was removed under reduced pressure. The residue was dissolved in EtOAc (5 mL) and the solution washed several times with HCl (1 M). The organic phase was dried over sodium sulfate and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (20% EtOAc in hexane + 1% formic acid) to give the natural product as a colorless oil. An analytically pure sample was obtained by preparative LC (150 mm YMC Triart C18, 5 µm, 10.0 mm; MeOH /water + 0.1% TFA = 80:20 with 4.7 mL/min, 9.0 MPa) as a white amorphous solid (2.7 mg, 33% yield).

$[\alpha]_D^{25}$ = +10.5 (*c* = 0.22, MeOH) (ref.:[14] $[\alpha]_D^{25}$ = +9.8 (*c* = 0.45, MeOH)). $^1$H NMR ($CD_3OD$, 600 MHz): δ 6.60 (dq, *J* = 9.2, 1.3 Hz, 1H), 5.11 (dt, *J* = 7.7, 4.8 Hz, 1H), 4.80 (dm, *J* = 9.4 Hz, 1H), 2.96 (dd, *J* = 15.7, 8.0, 4.6 Hz, 1H), 2.86-2.76 (m, 1H), 2.71 (p, *J* = 7.0, 7.7 Hz, 1H), 2.59 (dtd, *J* = 11.6, 7.0, 3.3 Hz, 1H), 2.44-2.36 (m, 2H), 2.18 (ddd, *J* = 11.6, 14.4, 0.8 Hz, 1H), 2.02 (ddd, *J* = 14.4, 3.3, 1.3 Hz, 1H), 1.87-1.77 (m, 2H), 1.75 (d, *J* = 1.3 Hz, 3H), 1.73-1.67 (m, 1H), 1.64 (ddd, *J* = 13.9, 10.2, 3.8 Hz 1H), 1.59-1.46 (m, 3H), 1.53 (d, *J* = 1.4 Hz, 3H), 1.43 (ddd, *J* = 13.9, 9.0, 3.7 Hz, 1H), 1.18 (d, *J* = 7.0 Hz, 3H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.10-1.05 (m, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H) [*O-$^1$H not detected*]. $^{13}$C NMR ($CD_3OD$, 151 MHz): δ 13C NMR (151 MHz, [$D_4$]-MeOH) δ 205.3, 177.3, 176.7, 150.6, 136.9, 134.0, 132.8, 75.4, 49.4, 49.3, 49.1, 49.0, 48.9, 48.7, 48.6, 45.7, 44.4, 42.9, 42.5, 36.7, 34.7, 33.0, 31.8, 31.5, 30.6, 30.1, 22.0, 21.1, 20.7, 19.1, 17.7, 13.6, 11.6. IR (film, cm$^{-1}$): 3439, 3201, 2955, 2926, 2870, 1733, 1711, 1666, 1455, 1377, 1285, 1253, 1203, 1100, 1053. HRMS (ESI+) *m/z* calcd. for $C_{26}H_{42}O_5Na$ [$M^+$ + Na]: 457.2923; found 457.2924.

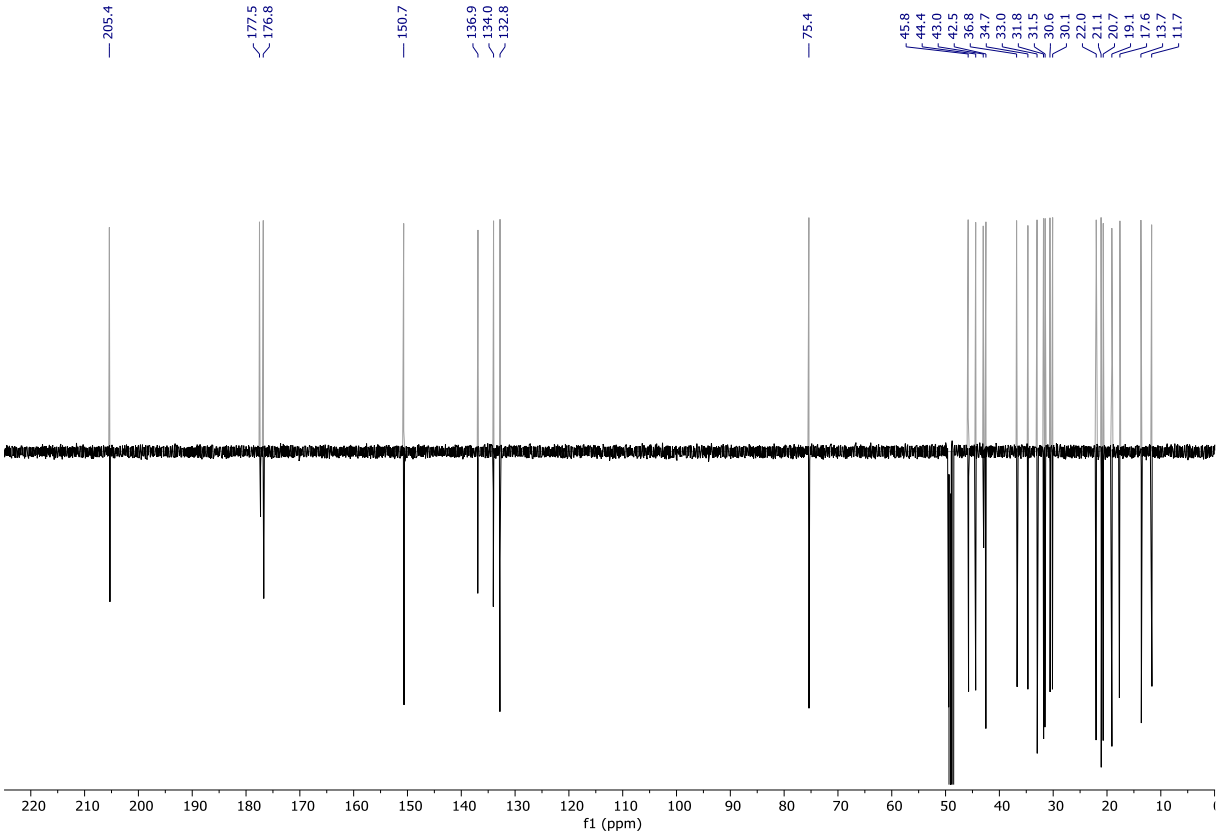
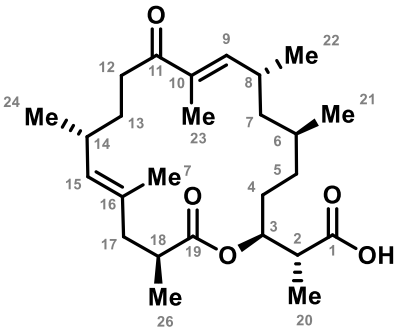



**Figure S4.** Visual comparison of $^{13}$C NMR spectrum of authentic Strasseriolide A (up) and synthetic **1** (down). Note that the shown spectrum of authentic Strasseriolide A (up) was generated (MestReNova) by converting the tabulated $^{13}$C NMR data of the natural product into a formal spectrum;[14] therefore the intensity of the lines is arbitrarily set to be identical for all signals. For a tabular survey of the exact numbers, see Table S14.

**Table S13.** NMR assignment of synthetic Strasseriolide A (**1**). All measurements were performed on a Bruker Avance III 600 spectrometer equipped with a cryogenically cooled 5 mm TCI probehead using a classical set of 1D ($^{1}H$, $^{13}C$) and 2D (COSY, HSQC, HMBC, NOESY) experiments. Numbering scheme as shown in the Insert.




| Atom number | δ [ppm] | J [Hz] | COSY | HSQC | HMBC | NOESY |
|---|---|---|---|---|---|---|
| **1C** | 177.3 | | | | 2, 3, 20 | |
| **2C** | 42.9 | | | 2 | 3, 4a, 4b, 20 | |
| **H** | 2.71 | 7.00, 7.70 | 3, 20 | 2 | 1, 3, 4, 20 | 3, 5b, 20 |
| **3C** | 75.4 | | | 3 | 2, 4a, 4b, 5a, 5b, 20 | |
| **H** | 5.11 | 7.70, 4.80 | 2, 4a, 4b | 3 | 1, 2, 4, 5, 10,20 | 2, 4a, 4b, 6, 20 |
| **4C** | 30.6 | | | 4a, 4b | 2, 3, 5a, 5b | |
| **H** | 1.79 | | 3, 4b, 5a, 5b | 4 | 2, 3, 5, 6 | 3, 21 |
| **H** | 1.49 | | 3, 4a, 5a, 5b | 4 | 2, 3, 5, 6 | 3 |
| **5C** | 30.1 | | | 5a, 5b | 3, 4a, 4b, 7a, 7b, 21 | |
| **Ha** | 1.56 | | 4a, 4b, 5b, 6 | 5 | 3, 4, 6, 7, 21 | 8 |
| **Hb** | 1.07 | | 4a, 4b, 5a, 6 | 5 | 3, 4, 5, 7, 21 | 2,21 |
| **6C** | 31.8 | | | 6 | 4a, 4b, 5a, 5b, 7a, 7b, 21 | |
| **H** | 1.70 | 6.60 | 5a, 5b, 7a, 7b, 21 | 6 | 7, 21 | 3, 9, 13b, 21 |
| **7C** | 45,7 | | | 7a, 7b | 5a, 5b, 6, 8, 9, 21, 22 | |
| **Ha** | 1.64 | 13.90, 10.20, 3.80 | 6, 7b, 8 | 7 | 5, 6, 8, 9, 21, 22 | 8, 9, 21, 22 |
| **Hb** | 1.43 | 13.90, 9.00, 3.70 | 6, 7a, 8 | 7 | 5, 6, 7, 8, 21, 22 | 8, 21, 22 |
| **8C** | 31.5 | | | 8 | 7a, 7b, 9, 22 | |

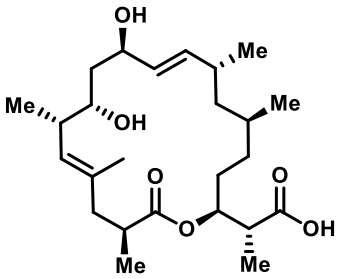
| | | | | | | |
|---|---|---|---|---|---|---|
| **H** | 2.81 | 6.80 | 7a, 7b, 9, 22 | 8 | 7, 10, 22 | 5a, 7a, 7b, 9, 21, 22, 23 |
| **9C** | 150.6 | | | 9 | 7a, 7b, 22, 23 | |
| **H** | 2.81 | 1.30, 9.20 | 8, 23 | 9 | 7, 8, 11, 22, 23 | 6, 7a, 8, 12a, 12b, 13b, 22, 23 |
| **10C** | 136.9 | | | | 8, 12b, 23 | |
| **11C** | 205.3 | | | | 9, 12a, 12b, 13a, 13b, 23 | |
| **12C** | 36.7 | | | 12a, 12b | 13a, 13b, 14 | |
| **Ha** | 2.96 | 15.70, 8.00, 4.60 | 12b, 13a, 13b | 12 | 11, 13, 14 | 9, 13b |
| **Hb** | 2.39 | 15.70 | 12a, 13a, 13b | 12 | 10, 11, 13, 14, 24 | 9 |
| **13C** | 34.7 | | | 13a, 13b | 12a, 12b, 15, 25 | |
| **Ha** | 1.84 | 13.60, 8.10, 4.60, 3.60 | 12a, 12b, 13b, 14 | 13 | 11, 12, 14, 15, 24 | 24 |
| **Hb** | 1.53 | | 12a, 12b, 13a, 14 | 13 | 11, 12, 14, 15, 24 | 6, 9 ,12a 15, 24 |
| **14C** | 33.0 | | | 14 | 12a, 12b, 13a, 13b, 15, 24 | |
| **H** | 2.40 | 6.80, 9.40 | 13a, 13b, 15, 24 | 14 | 12, 15, 16 | |
| **15 C** | 132.8 | | | 15 | 13a, 13b, 14,a 17a, 17b, 24, 25 | |
| **H** | 4.80 | 9.40 | 14, 17a, 17b, 25 | 16 | 13, 14, 17, 24, 25 | 13b, 17a, 17b, 18, 23, 24 |
| **16C** | 134.1 | | | | 14, 17a, 17b, 18, 25 | |
| **17C** | 44.4 | | | 17a, 17b | 15, 18, 25, 26 | |
| **Ha** | 2.18 | 11.60, 14.40, 0.80 | 15, 17b, 18, 25 | 17 | 15, 16, 18, 19, 25, 26 | 15, 23, 25, 26 |
| **Hb** | 2.02 | 14.4, 3.30, 1.30 | 15, 17a, 18, 25 | 17 | 15, 16, 18, 19, 25, 26 | 15, 18, 25, 26 |
| **18C** | 42.5 | | | 18 | 17a, 17b, 26 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **H** | 2.59 | 11.60, 7.00, 3.30 | 17a, 17b, 26 | 18 | 16, 17, 19, 26 | 15, 17b, 25, 26 |
| **19C** | 176.7 | | | | 3, 17a, 17b, 18, 26 | |
| **20C** | 13.6 | | | 20 | 2, 3 | |
| **H3** | 1.11 | 7.00 | 2 | 20 | 1, 2, 3 | 2, 3, 26 |
| **21C** | 21.1 | | | 21 | 5a, 5b, 6, 7a, 7b | |
| **3H** | 0.94 | 6.60 | 6 | 21 | 5, 6, 7, 22 | 4a, 5b, 6, 7a, 7b, 8 |
| **22C** | 20.7 | | | 22 | 7a, 7b, 8, 9, 21, 23 | |
| **H3** | 1.03 | 6.80 | 8 | 22 | 7, 8, 9 | 7a, 7b, 8, 9, 23 |
| **23C** | 11.7 | | | 23 | 9 | |
| **H3** | 1.75 | 1.30 | 9 | 23 | 9, 10, 11, 22 | 8, 9, 15, 17a, 22 |
| **24C** | 22.0 | | | 24 | 12b, 13a, 13b, 15 | |
| **H3** | 0.91 | 6.80 | 14 | 24 | 13, 14, 16 | 13a, 13b, 15 |
| **25C** | 17.70 | | | 25 | 15, 17a, 17b | |
| **H3** | 1.53 | 1.40 | 15, 17b | 25 | 15, 16, 17 | 17a, 17b, 18, 26 |
| **26C** | 19.09 | | | 26 | 17a, 17b, 18 | |
| **H3** | 1.18 | 7.00 | 17a, 18 | 26 | 17, 18, 19 | 17a, 17b, 18, 20, 25 |

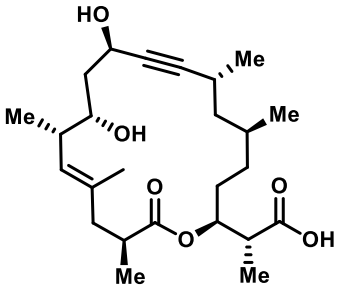
**Table S14.** Comparison of spectral data of authentic and synthetic Strasseriolide A (**1**).[14]

| Atom number | $^{1}$H δ (lit.) [ppm] | $^{1}$H δ (exp.) [ppm] | ΔδH | $^{13}$C δ (lit.) [ppm] | $^{13}$C δ (exp.) [ppm] | ΔδC |
|---|---|---|---|---|---|---|
| **1** | | | | 177.5 | 177.3 | -0.2 |
| **2** | 2.71 | 2.71 | 0 | 43.0 | 42.9 | -0.1 |
| **3** | 5.11 | 5.11 | 0 | 75.4 | 75.4 | 0 |
| **4** | 1.80 / 1.49 | 1.79 / 1.49 | -0.01 / 0 | 30.6 | 30.6 | 0 |
| **5** | 1.56 / 1.08 | 1.56 / 1.0 7 | 0 / -0.01 | 30.1 | 30.1 | 0 |
| **6** | 1.69 | 1.70 | +0.01 | 31.8 | 31.8 | 0 |
| **7** | 1.63 / 1.43 | 1.64 / 1.43 | +0.01 / 0 | 45.8 | 45.7 | -0.1 |
| **8** | 2.81 | 2.81 | 0 | 31.5 | 31.5 | 0 |
| **9** | 6.60 | 6.60 | 0 | 150.7 | 150.6 | -0.1 |
| **10** | | | | 136.9 | 136.9 | 0 |
| **11** | | | | 205.4 | 205.3 | -0.1 |
| **12** | 2.97 / 2.39 | 2.96 / 2.39 | -0.01 / 0 | 36.8 | 36.7 | -0.1 |
| **13** | 1.84 / 1.54 | 1.84 / 1.53 | 0 / -0.01 | 34.7 | 34.7 | 0 |
| **14** | 2.40 | 2.40 | 0 | 33.0 | 33.0 | 0 |
| **15** | 4.79 | 4.80 | +0.01 | 132.8 | 132.8 | 0 |
| **16** | | | | 134.0 | 134.1 | +0.1 |
| **17** | 2.18 / 2.02 | 2.18 / 2.02 | 0 / 0 | 44.4 | 44.4 | 0 |
| **18** | 2.59 | 2.59 | 0 | 42.5 | 42.5 | 0 |
| **19** | | | | 176.8 | 176.7 | -0.1 |
| **20** | 1.11 | 1.11 | 0 | 13.7 | 13.6 | -0.1 |
| **21** | 0.94 | 0.94 | 0 | 21.1 | 21.1 | 0 |
| **22** | 1.03 | 1.03 | 0 | 20.7 | 20.7 | 0 |
| **23** | 1.75 | 1.75 | 0 | 11.7 | 11.7 | 0 |
| **24** | 0.91 | 0.91 | 0 | 22.0 | 22.0 | 0 |
| **25** | 1.52 | 1.53 | +0.01 | 17.6 | 17.7 | +0.1 |
| **26** | 1.18 | 1.18 | 0 | 19.1 | 19.1 | 0 |

## Preparation of Analogues by Diverted Total Synthesis

**(*R*)-2-((2*S*,5*S*,7*R*,8*E*,10*R*,12*S*,13*S*,14*E*,17*S*)-10,12-dihydroxy-5,7,13,15,17-pentamethyl-18-oxooxacyclooctadeca-8,14-dien-2-yl)propanoic acid (45).** 

Trimethyltin hydroxide (19.6 mg, 0.11 mmol) was added to a solution of methylester **44** (4.9 mg, 10.8 µmol) in 1,2-dichloroethane (0.3 mL). The mixture was irradiated at 120 °C in a microwave oven for 2 hours before another portion of trimethyltin hydroxide (19.6 mg, 0.11 mmol) was introduced and irradiation at 120 °C was continued for 3 hours. The mixture was filtered through a short pad of Celite© (≈ 1 cm), which was carefully rinsed with dichloromethane (10 mL). The solvent was removed under reduced pressure, the residue was dissolved in EtOAc (15 mL) and the solution was washed with sulfate buffer (1 M, pH 2, 3 x 10 mL) and brine (10 mL). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (50% EtOAc in hexane + 0.5% AcOH) to yield the title compound as a colorless amorphous solid (2.9 mg, 61%). $[\alpha]_D^{20}$ = 15.4° (*c* = 0.28, MeOH). $^1$H NMR ($CD_3OD$, 600 MHz): δ 5.36 (dd, *J* = 15.2, 9.1 Hz, 1H), 5.22 (dd, *J* = 15.2, 8.9 Hz, 1H), 5.17 (dt, *J* = 8.8, 4.5 Hz, 1H), 4.79 (d, *J* = 9.3 Hz, 1H), 4.11 (ddd, *J* = 10.2, 8.9, 4.5 Hz, 1H), 3.08 (ddd, *J* = 9.8, 8.5, 1.3 Hz, 1H), 2.74 (dq, *J* = 8.8, 6.9 Hz, 1H), 2.67 – 2.61 (m, 1H), 2.36 – 2.23 (m, 3H), 2.17 (dd, *J* = 13.9, 3.3 Hz, 1H), 1.79 (ddt, *J* = 14.2, 11.9, 4.7 Hz, 1H), 1.69 – 1.66 (m, 1H), 1.65 (d, *J* = 1.3 Hz, 3H), 1.64 – 1.46 (m, 4H), 1.28 – 1.24 (m, 2H), 1.23 (d, *J* = 7.0 Hz, 3H), 1.14 (d, *J* = 6.9 Hz, 3H), 1.13 – 1.08 (m, 1H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR ([$D_4$]-MeOH, 151 MHz): δ 177.8, 176.3, 140.9, 134.1, 133.7, 131.50, 75.5, 75.3, 73.4, 47.3, 44.8, 44.6, 43.4, 42.2, 41.0, 36.2, 31.5, 30.8, 30.3, 29.7, 23.4, 21.5, 18.4, 18.2, 17.1, 14.4. IR (film, cm$^{-1}$): 3365, 2953, 2924, 2871, 1733, 1715, 1457, 1377, 1255, 1210, 1175, 1083, 1047, 970. HRMS (ESI) *m/z* calcd. for $C_{25}H_{42}O_6Na$ [$M^+$ + Na]: 461.2874; found 461.2873.

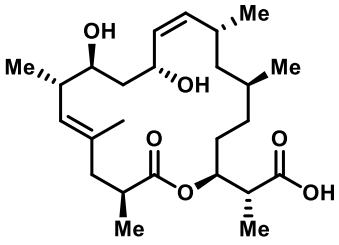
**(*R*)-2-((2*S*,5*S*,7*R*,10*R*,12*S*,13*S*,17*S*,*E*)-10,12-Dihydroxy-5,7,13,15,17-pentamethyl-18-oxooxacyclooctadec-14-en-8-yn-2-yl)propanoic acid (46).** 

Trimethyltin hydroxide (28.9 mg, 0.16 mmol) was added to a solution of methylester **41** (7.2 mg, 16.0 µmol) in 1,2-dichloroethane (0.25 mL). The mixture was irradiated at 120 °C in a microwave oven for 5 hours before another portion of trimethyltin hydroxide (28.9 mg, 0.16 mmol) was introduced and irradiation continued at 120 °C for another 2 hours. The mixture was filtered through a short pad of Celite© (≈ 1 cm), which was carefully rinsed with dichloromethane (10 mL). The solvent was removed under reduced pressure, the residue was dissolved in EtOAc (10 mL) and the resulting solution was washed with HCl (2 M, 3 x 10 mL) and brine (10 mL). The solvent was removed under reduced pressure and the residue was purified by flash

chromatography (60% EtOAc in hexane + 0.5% AcOH) to yield the title compound as a colorless amorphous solid (4.8 mg, 69%). $[\alpha]_D^{20}$ = 19.6° (*c* = 0.25, MeOH). $^1$H NMR ($CD_3OD$, 600 MHz): δ 5.18 (dt, *J* = 8.7, 4.4 Hz, 1H), 4.97 (d, *J* = 8.9 Hz, 1H), 4.43 (ddd, *J* = 11.5, 4.0, 2.3 Hz, 1H), 3.37 (t, *J* = 9.4 Hz, 1H), 2.73 (dq, *J* = 8.7, 7.0 Hz, 1H), 2.70 – 2.60 (m, 2H), 2.32 – 2.20 (m, 2H), 2.14 (dd, *J* = 13.5, 3.5 Hz, 1H), 1.90 (ddd, *J* = 13.1, 11.5, 1.0 Hz, 1H), 1.85 – 1.78 (m, 2H), 1.69 – 1.63 (m, 1H), 1.67 (d, *J* = 1.3 Hz, 3H), 1.59 (ddd, *J* = 13.3, 9.2, 4.1 Hz, 1H), 1.56 – 1.53 (m, 1H), 1.42 (ddd, *J* = 13.3, 11.3, 3.7 Hz, 1H), 1.31 (ddd, *J* = 13.3, 10.5, 4.3 Hz, 1H), 1.26 – 1.19 (m, 1H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.18 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 3H). $^{13}$C NMR ([$D_4$]-MeOH, 151 MHz): δ 177.8, 175.9, 133.9, 131.7, 89.7, 83.8, 75.4, 75.2, 62.0, 46.6, 46.6, 45.8, 43.6, 42.1, 40.6, 31.9, 30.2, 29.6, 24.7, 22.4, 21.0, 18.4, 18.3, 16.5, 14.4. IR (film, cm$^{-1}$): 3370, 2962, 2925, 2873, 1732, 1714, 1456, 1378, 1330, 1291, 1254, 1193, 1175, 1076, 1048, 1022, 969. HRMS (ESI) *m/z* calcd. for $C_{25}H_{40}O_6Na$ [$M^+$ + Na]: 459.2717; found 459.2716.

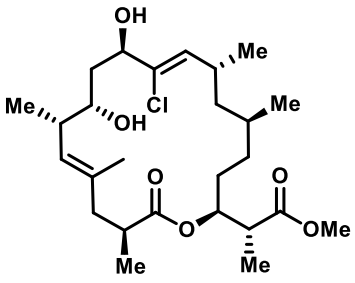
**Methyl (*R*)-2-((2*S*,5*S*,7*R*,8*Z*,10*R*,12*S*,13*S*,14*E*,17*S*)-10,12-dihydroxy-5,7,13,15,17-pentamethyl-18-oxooxacyclooctadeca-8,14-dien-2-yl)propanoate (47).** Lindlar catalyst (5 mol% Pd on $CaCO_3$, poisoned with Pb; 9.0 mg, 20 mol% *w/w*) was added to a solution of alkyne **41** (9.5 mg, 21.1 µmol) and quinoline (5 µL, 42.4 µmol) in EtOAc (1 mL). The mixture was purged with hydrogen before it was stirred under a hydrogen atmosphere (1 bar) at ambient temperature for 45 min. The catalyst was then filtered off over a short pad of Celite© (≈ 1 cm), which was rinsed with EtOAc (15 mL). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (30% EtOAc in hexane) to yield the title compound as a colorless solid (7.9 mg, 83%). $[\alpha]_D^{20}$ = –45.6° (*c* = 0.66, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$) δ 5.42 (dd, *J* = 11.1, 7.9 Hz, 1H), 5.32 (dd, *J* = 9.4, 2.0 Hz, 1H), 5.07 (t, *J* = 10.7 Hz, 1H), 4.99 – 4.95 (m, 1H), 4.43 (td, *J* = 8.9, 4.6 Hz, 1H), 3.68 – 3.60 (m, 4H), 3.20 (br, 1H), 2.90 (dqd, *J* = 10.4, 6.9, 3.3 Hz, 1H), 2.70 (qd, *J* = 7.1, 4.5 Hz, 1H), 2.42 – 2.31 (m, 2H), 2.28 – 2.15 (m , 2H), 1.91 (ddd, *J* = 14.3, 9.6, 4.8 Hz, 1H), 1.74 – 1.57 (m, 2H), 1.68 (s, 3H), 1.55 – 1.46 (m, 1H), 1.46 – 1.37 (m, 1H), 1.36 – 1.27 (m, 2H), 1.23 (d, *J* = 7.0 Hz, 3H), 1.19 – 0.84 (m, 4H) 1.13 (d, *J* = 7.1 Hz, 3H), 1.02 (d, *J* = 6.7 Hz, 3H). 0.93 (d, *J* = 6.7 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 176.6, 174.2, 136.0, 133.0, 132.1, 127.6, 74.7, 73.9, 65.9, 51.9, 45.9, 45.6, 43.2, 42.2, 40.2, 39.2, 30.7, 30.4, 29.6, 28.2, 22.5, 20.8, 18.9, 18.7, 18.6, 11.9. IR (film, cm$^{-1}$): 3438, 2953, 2926, 1737, 1455, 1378, 1260, 1201, 1050, 1019, 754. HRMS (ESI) *m/z* calcd. for $C_{26}H_{44}O_6Na$ [$M^+$ + Na]: 475.3030; found 475.3033.

**(*R*)-2-((2*S*,5*S*,7*R*,8*Z*,10*R*,12*S*,13*S*,14*E*,17*S*)-10,12-dihydroxy-5,7,13,15,17-pentamethyl-18-oxooxa-**



**cyclooctadeca-8,14-dien-2-yl)propanoic acid (48).** Trimethyltin hydroxide (26.4 mg, 0.15 mmol) was added to a solution of methylester **47** (6.6 mg, 14.6 µmol) in 1,2-dichloroethane (0.3 mL). The mixture was irradiated at 120 °C in a microwave oven for 2 hours before another portion of trimethyltin hydroxide (26.4 mg, 0.15 mmol) was introduced and irradiation was continued at 120 °C for 3 hours. The mixture was then filtered through a short pad of Celite© (≈ 1 cm), which was carefully rinsed with dichloromethane (10 mL). The solvent was removed under reduced pressure, the residue was dissolved in EtOAc (15 mL) and the solution was washed with HCl (2 M, 3 x 15 mL) and brine (10 mL). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (50% EtOAc in hexane + 0.5% AcOH) to yield the title compound as a colorless oil (3.1 mg, 48%). $[\alpha]_D^{20}$ = −20.0° (*c* = 0.31, MeOH). $^1$H NMR (600 MHz, [D$_4$]-MeOH) δ 5.34 (ddd, *J* = 11.1, 7.5, 0.8 Hz, 1H), 5.32 (dd, *J* = 9.6, 1.5 Hz, 1H), 5.05 – 5. 00 (m, 2H), 4.50 (dddd, *J* = 11.2, 7.5, 3.3, 1.3 Hz, 1H), 3.58 (dded, J = 8.6, 8.1, 4.4 Hz, 1H), 2.85 (dqd, *J* = 10.2, 6.9, 3.3 Hz, 1H), 2.65 (p, *J* = 6.9 Hz, 1H), 2.46 (ddq, *J* = 9.7, 8.6, 6.8 Hz, 1H), 2.41 (ddd, *J* = 16.7, 10.3, 1.4 Hz, 1H), 2.38 – 2.32 (m, 1H), 2.15 (d, *J* = 16.6 Hz, 1H), 1.78 (ddd, *J* = 14.1, 11.2, 4.4 Hz, 1H), 1.71 (d, *J* = 1.3 Hz, 3H), 1.73 – 1.65 (m, 1H), 1.62 – 1.55 (m, 2H), 1.53 – 1.44 (m, 1H), 1.39 – 1.28 (m, 1H), 1.25 (d, *J* = 7.0 Hz, 3H), 1.22 – 1.10 (m, 3H), 1.12 (d, *J* = 7.1 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H). $^{13}$C NMR (151 MHz, [D$_4$]-MeOH) δ 178.6, 177.7, 136.5, 134.5, 133.3, 129.1, 76.5, 73.9, 67.6, 47.2, 46.4, 45.9, 43.7, 42.0, 40.4, 31.7, 31.4, 31.2, 29.5, 23.1, 21.1, 19.2, 19.1, 18.8, 13.8. IR (film, cm$^{-1}$): 3376, 2953, 2925, 1713, 1572, 1456, 1406, 1379, 1298, 1265, 1202, 1053, 1019. HRMS (ESI) *m/z* calcd. for $C_{25}H_{41}O_6$ [$M^-$ − H]: 437.2909; found 437.2916.

**Methyl (*R*)-2-((2*S*,5*S*,7*R*,8*Z*,10*R*,12*S*,13*S*,14*E*,17*S*)-9-chloro-10,12-dihydroxy-5,7,13,15,17-pentameth**



**yl-18-oxooxacyclooctadeca-8,14-dien-2-yl)propanoate (49).** 2,6-Lutidine (16 µL, 0.14 mmol) and copper(II) chloride (36.6 mg, 0.27 mmol) were added to a solution of stannane **42** (10.1 mg, 13.6 µmol) in THF (1 mL). The mixture was stirred at ambient temperature for 14 days. It was then diluted with EtOAc (15 mL) and saturated aqueous $NH_4Cl$ (15 mL). The layers were separated and the aqueous phase was extracted with EtOAc (4 x 15 mL). The combined extracts were dried over magnesium sulfate, filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (30 – 50% EtOAc in hexane) to yield the title compound as a colorless solid (4.2 mg, 63%). $[\alpha]_D^{20}$ = 32.7° (*c* = 0.41, $CHCl_3$). $^1$H NMR ($CD_3OD$, 600 MHz): δ 5.58 (d, *J* = 9.1 Hz, 1H), 5.14 (dt, *J* = 6.7, 5.2 Hz, 1H), 4.90 (d, *J* = 9.2 Hz, 1H), 4.43 (dt, *J* = 7., 5.9 Hz, 1H), 3.67 (s, 3H), 3.26 (ddd, *J* = 9.8, 6.7, 2.5 Hz, 1H), 2.83 – 2.81 (m, 1H), 2.76 (p, *J* = 7.0 Hz, 1H), 2.69 – 2.60 (m, 1H), 2.36 –

2.26 (m, 2H), 2.24 – 2.08 (m, 2H), 1.86 (dd, *J* = 14.0, 7.9 Hz, 1H), 1.68 (ddd, *J* = 14.1, 6.2 Hz, 1H), 1.62 (s, 3H), 1.62 – 1.43 (m, 3H), 1.39 – 1.21 (m, 2H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 7.0 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.96 – 0.90 (m, 1H), 0.88 (d, *J* = 6.6 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl3) δ 175.3, 174.4, 135.1, 135.0, 133.5, 129.0, 75.6, 75.1, 74.1, 52.0, 44.6, 43.1, 41.8, 41.0, 40.4, 39.3, 30.6, 30.5, 30.2, 29.3, 21.3, 20.8, 18.6, 18.2, 16.4, 12.6. IR (film, cm$^{-1}$): 3312, 2955, 2924, 2968, 1738, 1455, 1377, 1334, 1251, 1192, 1163, 1078, 1039, 969, 867, 841. HRMS (ESI) *m/z* calcd. for $C_{26}H_{43}O_6ClNa$ [$M^+$ + Na]: 509.2640; found 509.2642.

**(*R*)-2-((2*S*,5*S*,7*R*,8*Z*,10*R*,12*S*,13*S*,14*E*,17*S*)-9-Chloro-10,12-dihydroxy-5,7,13,15,17-pentamethyl-18-oxooxacyclooctadeca-8,14-dien-2-yl)propanoic acid (50).** Trimethyltin hydroxide (14.8 mg, 82.1 µmol) was added to a solution of methylester **49** (4.0 mg, 8.2 µmol) in 1,2-dichloroethane (0.3 mL). The mixture was irradiated at 120 °C in a microwave oven for 2 hours before another portion of trimethyltin hydroxide (14.8 mg, 82.1 µmol) was introduced and the irradiation was continued at 120 °C for another 3 hours. The mixture was then filtered through a short pad of Celite© (≈ 1 cm), which was carefully rinsed with dichloromethane (10 mL). The solvent was removed under reduced pressure, the residue was dissolved in EtOAc (15 mL) and the solution washed with HCl (2 M, 3 x 10 mL) and brine (10 mL). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (60% EtOAc in hexane + 0.5% AcOH) to yield the title compound as a colorless amorphous solid (1.6 mg, 41%). $[\alpha]_D^{20}$ = 8.2° (*c* = 0.11, $CHCl_3$). $^1$H NMR (600 MHz, [$D_4$]-MeOH) δ 5.57 (d, *J* = 8.8 Hz, 1H), 5.19 (dt, *J* = 8.9, 4.5 Hz, 1H), 4.74 (d, *J* = 9.0 Hz, 1H), 4.31 (dd, *J* = 11.2, 3.4 Hz, 1H), 2.98 (dd, *J* = 10.3, 8.1 Hz, 1H), 2.91 – 2.81 (m, 1H), 2.70 (p, *J* = 7.1 Hz, 1H), 2.61 (dqd, *J* = 11.9, 6.9, 3.3 Hz, 1H), 2.33 (dd, *J* = 13.4, 11.9 Hz, 1H), 2.25 (tq, *J* = 10.3, 6.7 Hz, 1H), 2.08 – 2.02 (m, 2H), 1.86 – 1.79 (m, 1H), 1.65 (d, *J* = 1.3 Hz, 3H), 1.61 (tt, *J* = 12.9, 4.0 Hz, 1H), 1.51 (tt, *J* = 13.6, 4.3 Hz, 1H), 1.44 – 1.25 (m, 4H), 1.21 (d, *J* = 6.9 Hz, 3H), 1.18 – 1.12 (m, 1H), 1.13 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H). $^{13}$C NMR (151 MHz, [$D_4$]-MeOH) δ 179.2, 176.2, 137.4, 136.0, 133.9, 131.9, 76.0, 75.3, 74.9, 49.4, 49.3, 49.1, 49.0, 48.9, 48.7, 48.6, 47.5, 45.6, 44.4, 42.5, 41.4, 40.4, 32.2, 32.0, 31.0, 29.8, 21.6, 21.1, 18.6, 18.3, 16.6, 14.7. IR (film, cm$^{-1}$): 3365, 2956, 2924, 2871, 1712, 1573, 1454, 1405, 1377, 1291, 1256, 1081, 1040, 998. HRMS (ESI) *m/z* calcd. for $C_{25}H_{40}O_6Cl$ [$M^-$ – H]: 471.2519; found 471.2527.

## Conformational Aspects

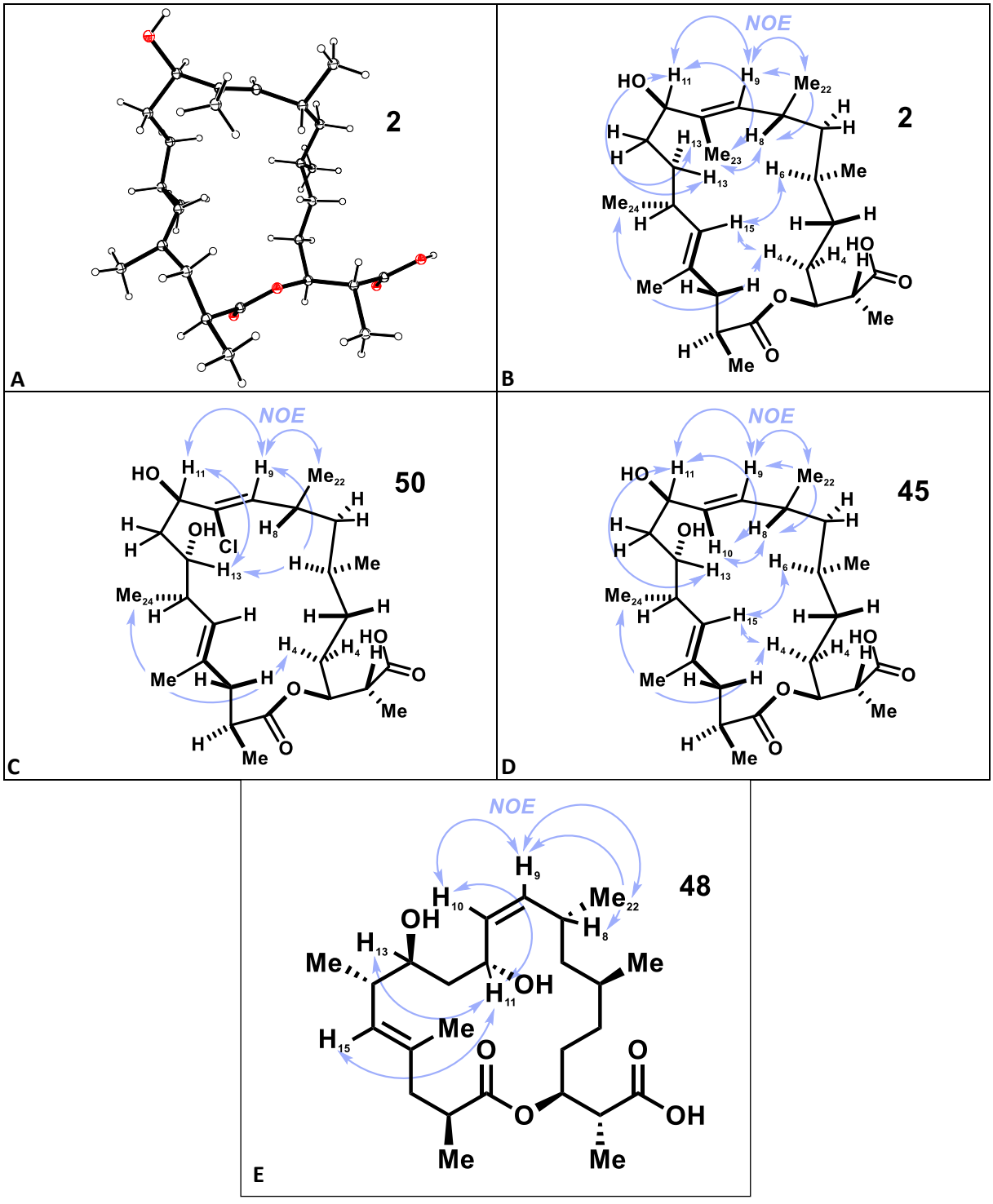



**Chart S1**. A) Molecular structure of Strasseriolide B (**2**) in the solid state, cf. ref[14] B) key NOESY correlations in the region of the allylic alcohol C11-OH and transannular NOESY correlations recorded for synthetic strasseriolide B (**2**); C) relevant NOESY correlations observed with the chloro-alkene derivative **50**; D) relevant NOESY correlation observed with nor-methyl-strasseriolide B (**45**); E) 2D-representation of analogue **48** comprising a *Z*-alkene unit with indication of key NOESY correlations.

All NOESY correlations recorded for strasseriolide B (**2**) can be mapped onto close contact of the respective protons in the X-ray structure, which suggests that the conformation of **2** adopted in solution is similar to the structure in the solid state. The pattern of NOESY cross-peaks for $H_9$ and $H_{11}$ in the synthetic analogues **45** and **50** is similar to that of **2**, which implies that their conformations also bear close resemblance at least in the northern sector of the macrocyclic system. However, the cross peak between $H_8$ and $H_9$ observed for **2** and **45** was missing in the NOESY spectrum of compound **50**. Compounds **2** and **45** show transannular contacts between $H_{24}$ – $H_4$, $H_{15}$ – $H_4$ and $H_{15}$ – $H_6$, while the spectrum of **50** only shows the cross peak between $H_{24}$ – $H_4$.

A detailed conformational analysis of compound **48** comprising a *Z*-configured alkene is not possible on the basis of the available data. However, the NOESY-spectrum is notably different from those of the *E*-configured analogues. A correlation between $H_9$ and $H_{11}$ is missing, whereas there is a cross-peak for $H_{11}$ – $H_{15}$, which was not observed in any derivative containing an *E*-configured olefin.

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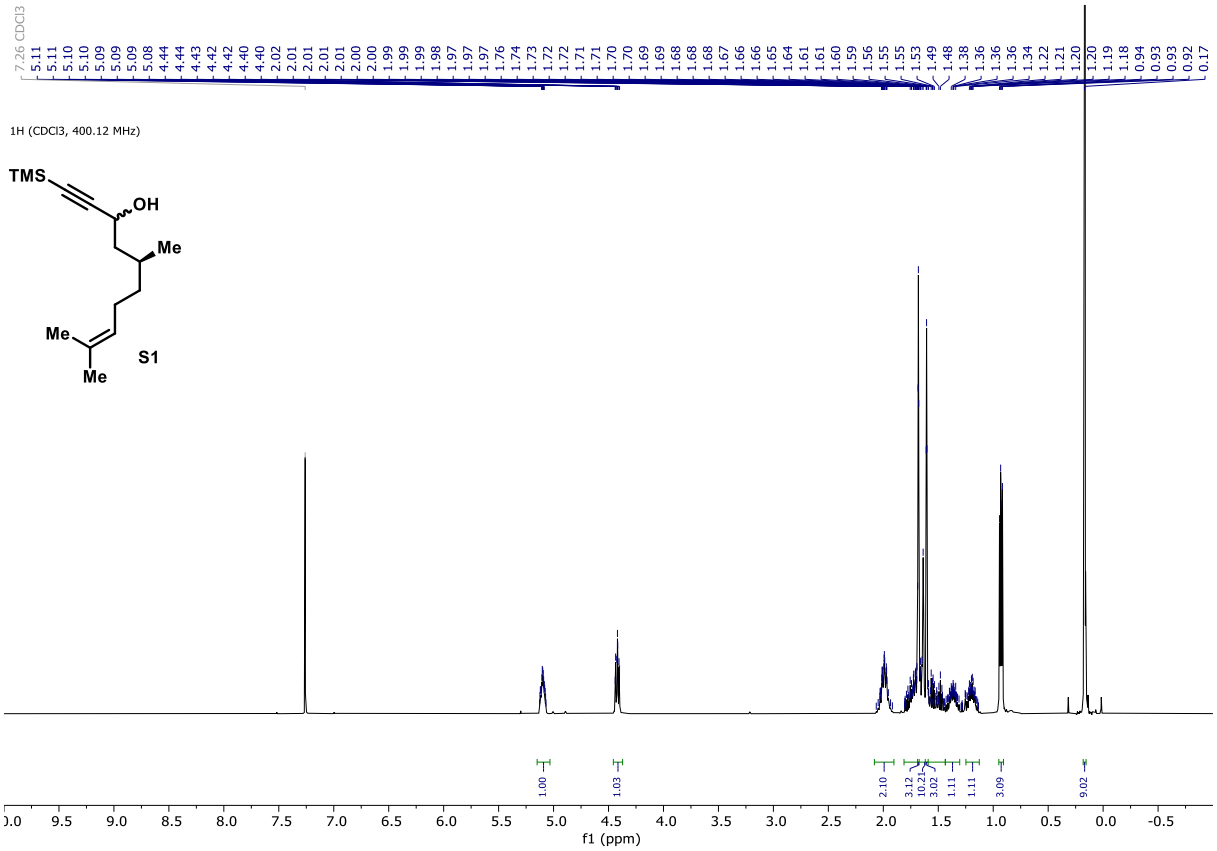
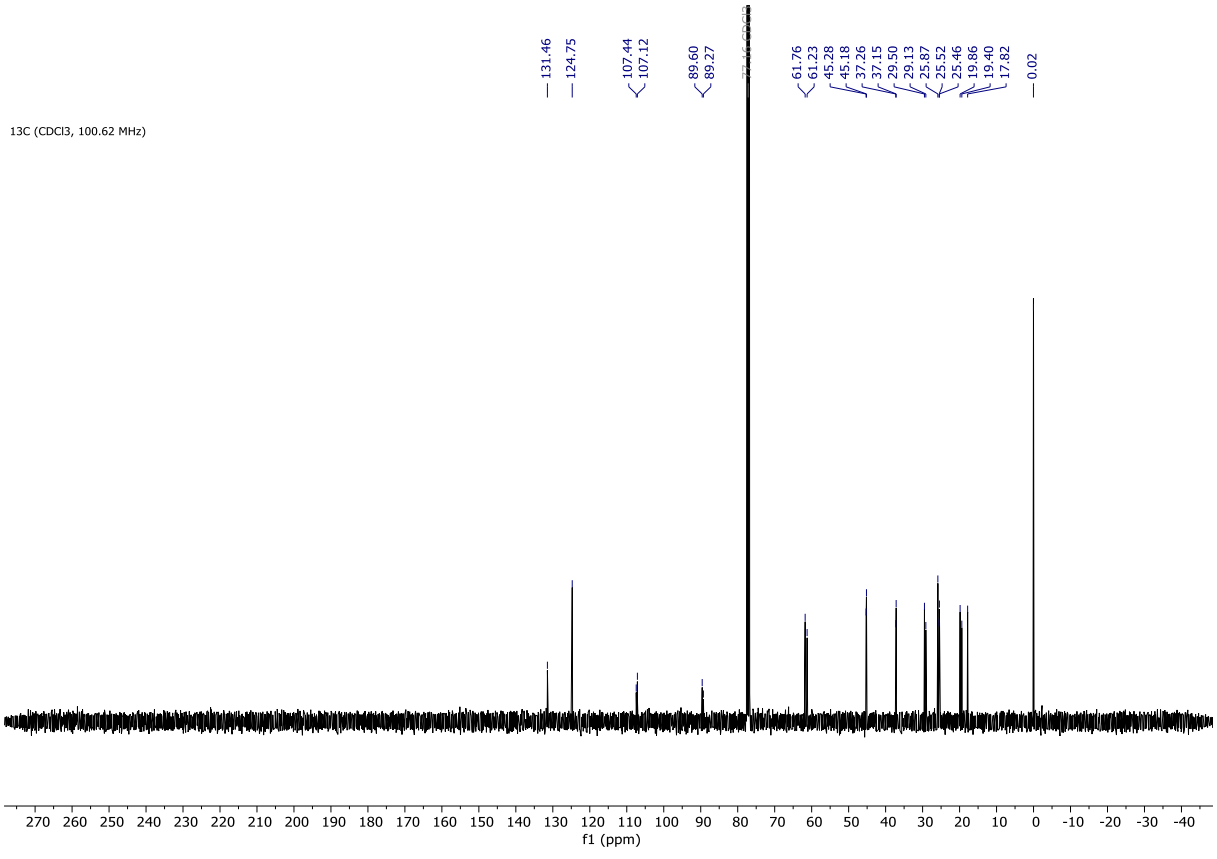
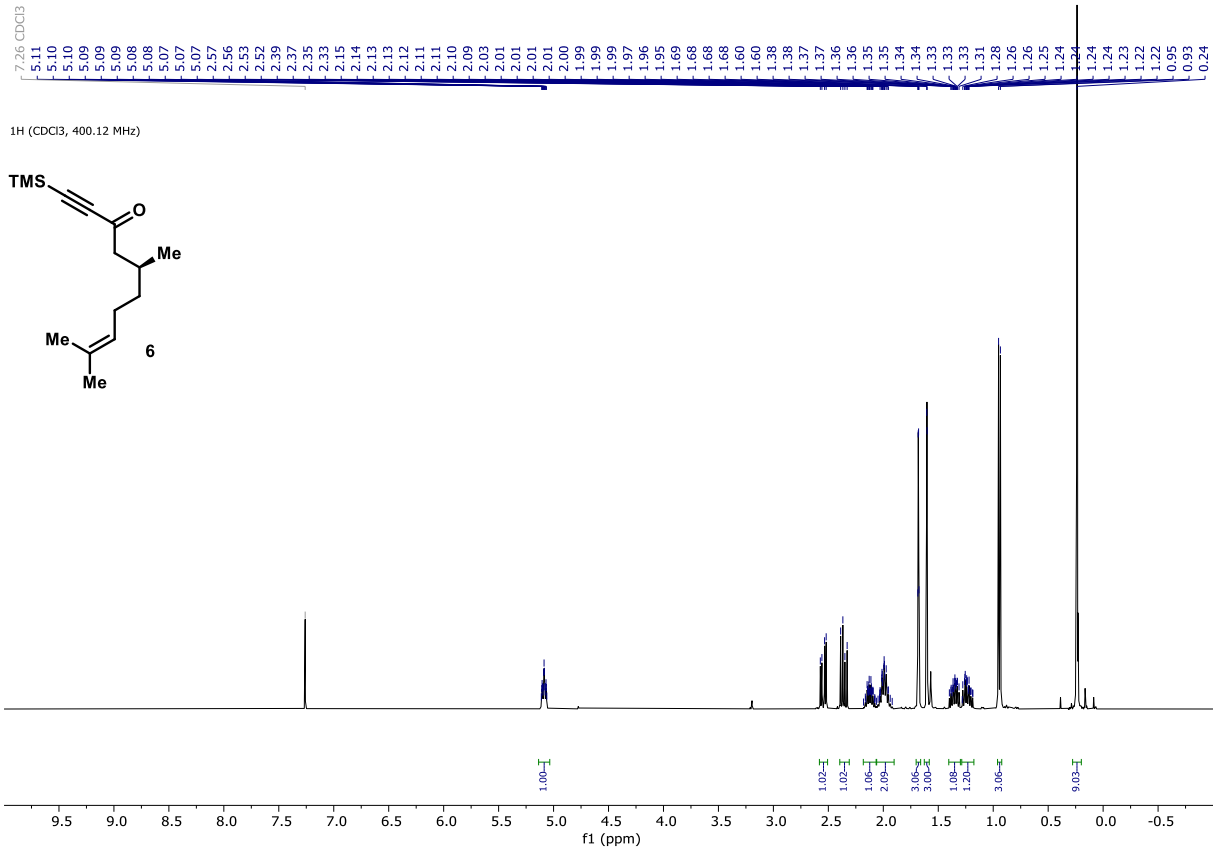
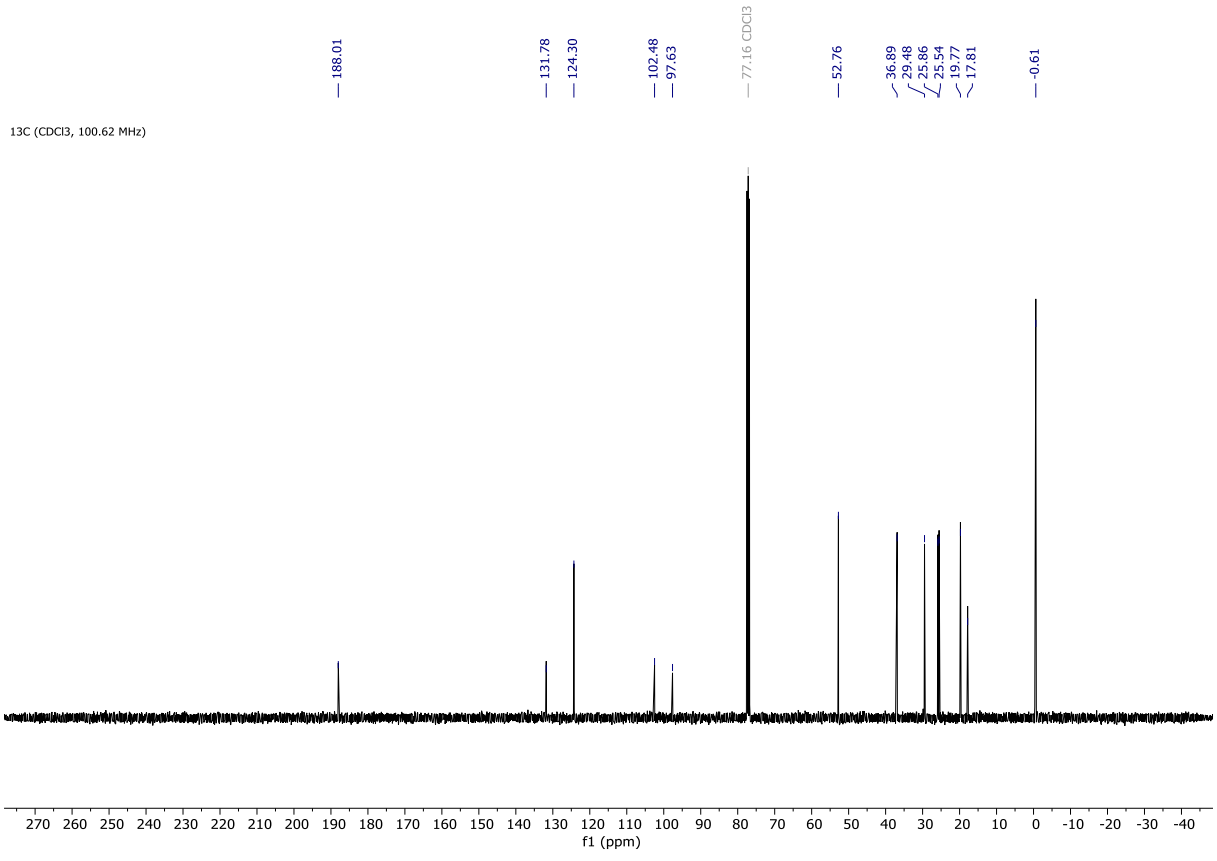
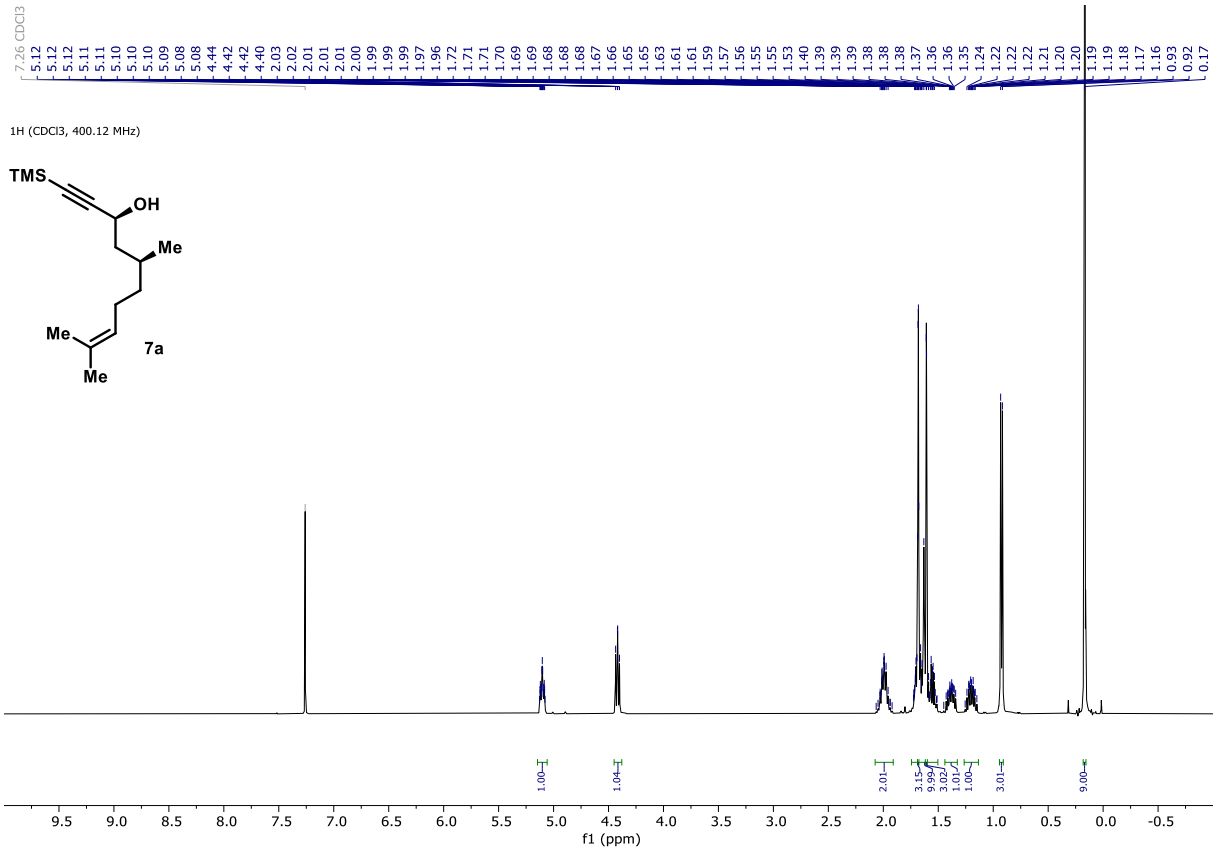
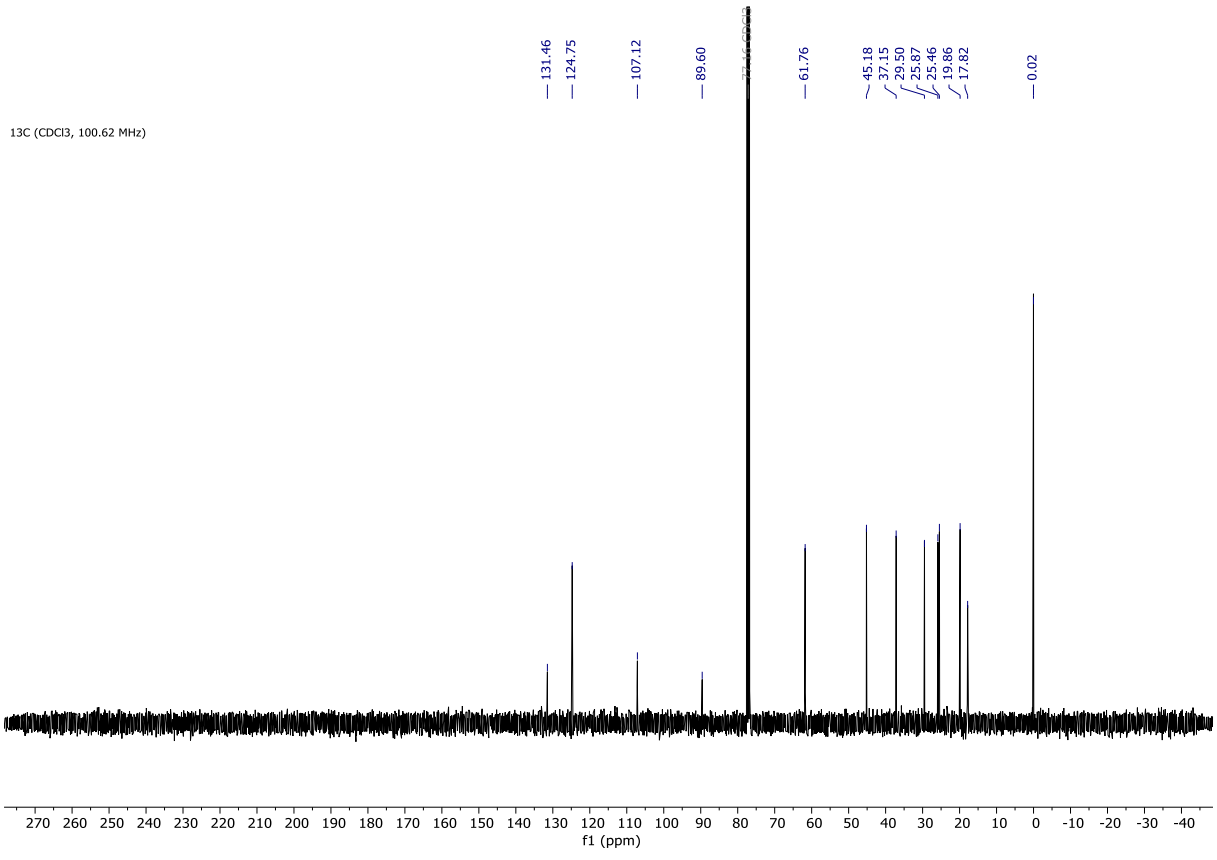

1H (CDCl3, 400.12 MHz)
TMS
OH
Me
Me
Me
S1
Me
f1 (ppm)

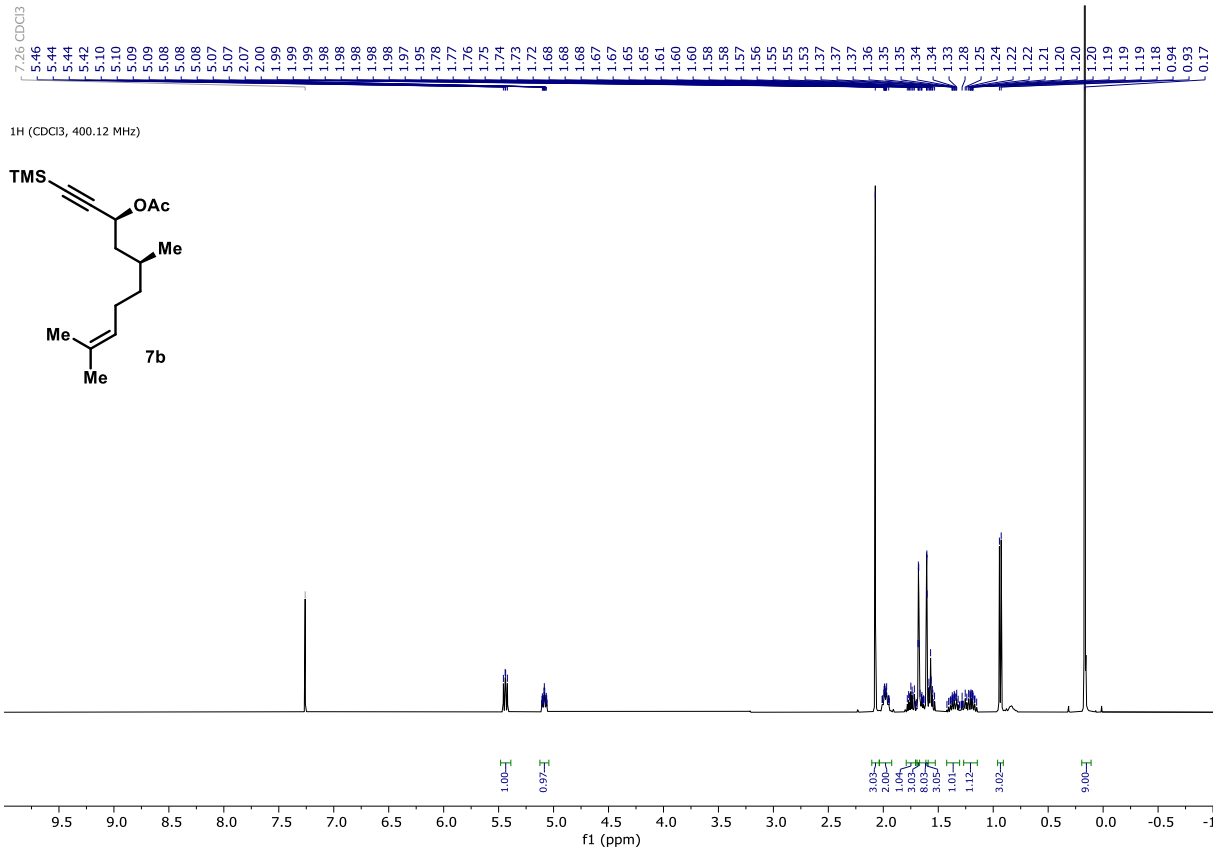

13C (CDCl3, 100.62 MHz)
f1 (ppm)

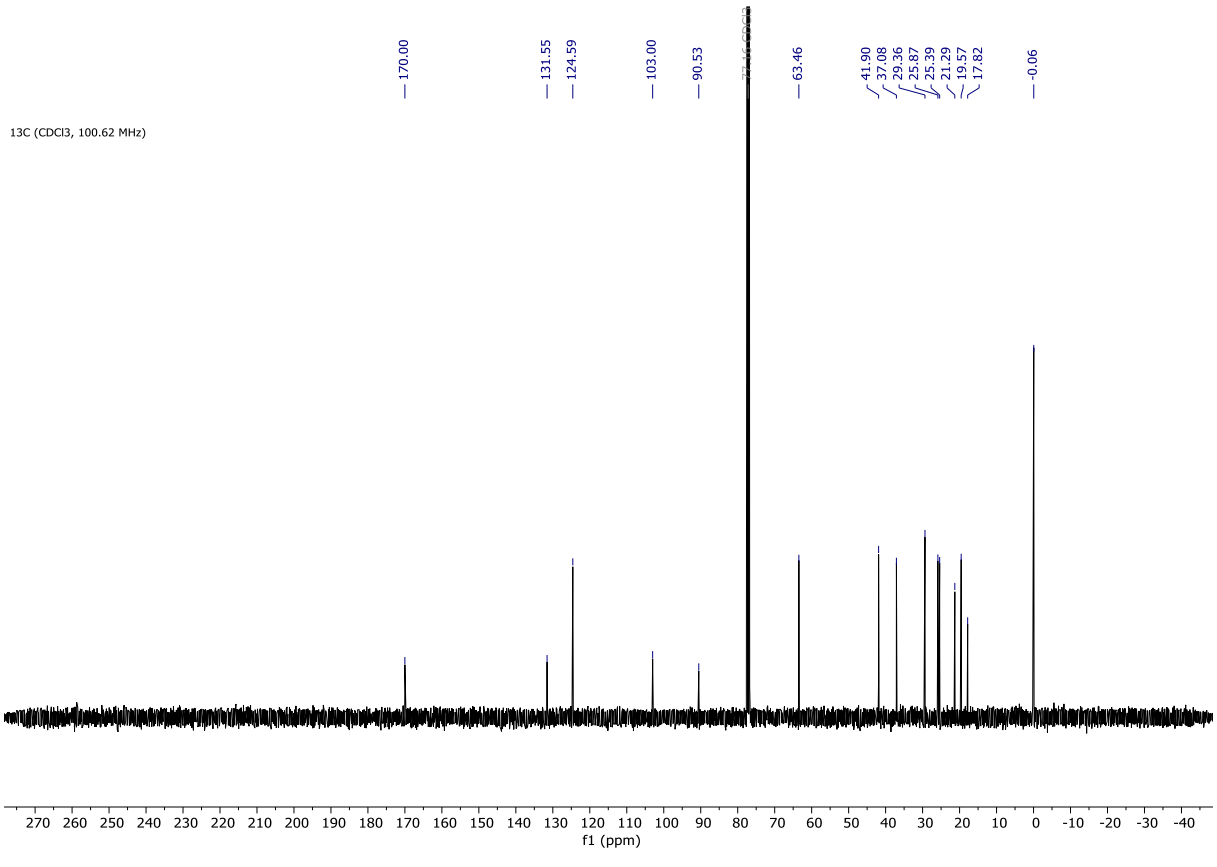

7.26 CDCl3
5.11 5.10 5.10 5.09 5.09 5.09 5.08 5.08 5.07 5.07 5.07 2.57 2.56 2.53 2.52 2.39 2.37 2.35 2.33 2.15 2.14 2.13 2.13 2.12 2.11 2.11 2.10 2.09 2.03 2.01 2.01 2.01 2.00 1.99 1.99 1.97 1.96 1.95 1.69 1.68 1.68 1.68 1.60 1.60 1.38 1.38 1.37 1.37 1.36 1.36 1.35 1.35 1.34 1.34 1.33 1.33 1.33 1.31 1.28 1.26 1.26 1.25 1.24 1.24 1.24 1.24 1.23 1.22 1.22 0.95 0.93 0.24
1H (CDCl3, 400.12 MHz)
TMS
O
Me
Me
Me
6
1.00
1.02
1.02
1.06
2.09
3.06
3.00
1.08
1.20
3.06
9.03
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

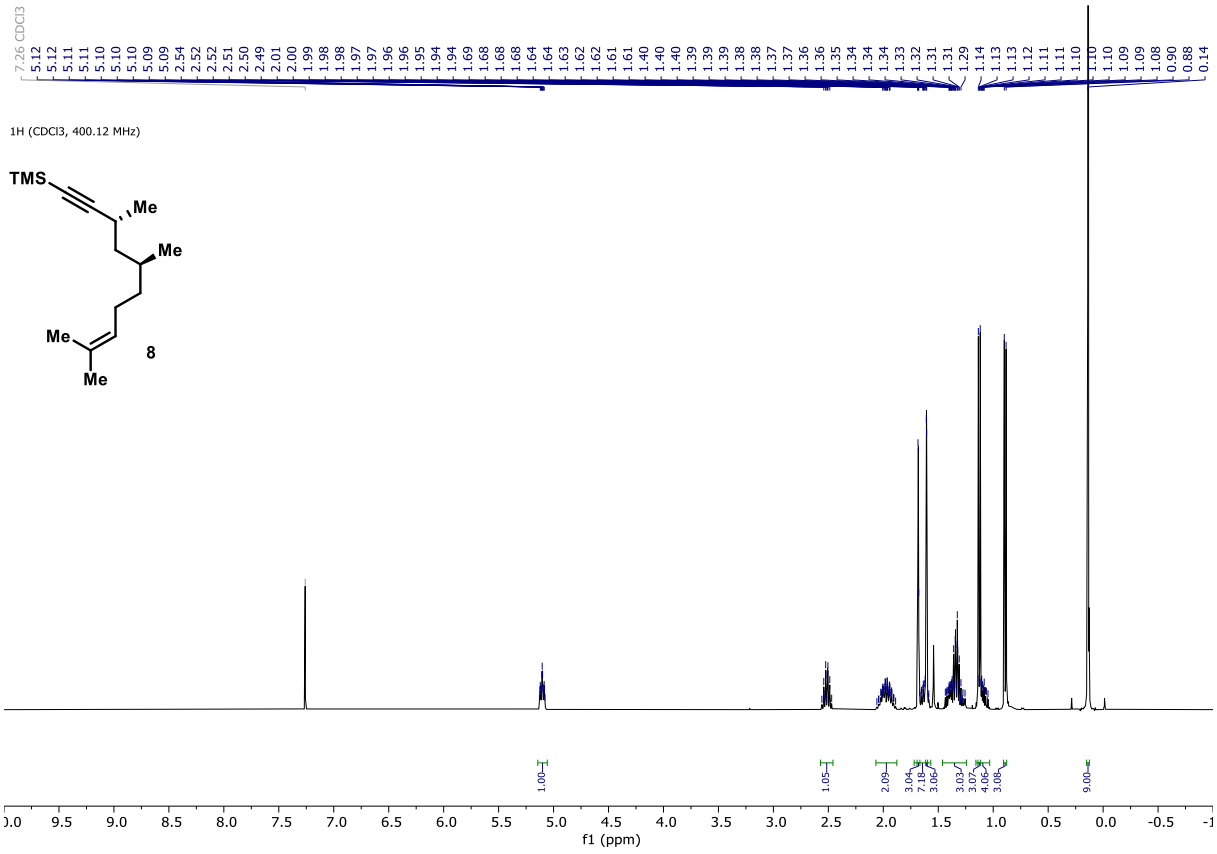

188.01
131.78
124.30
102.48
97.63
77.16 CDCl3
52.76
36.89
29.48
25.86
25.54
19.77
17.81
-0.61
13C (CDCl3, 100.62 MHz)
270 260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

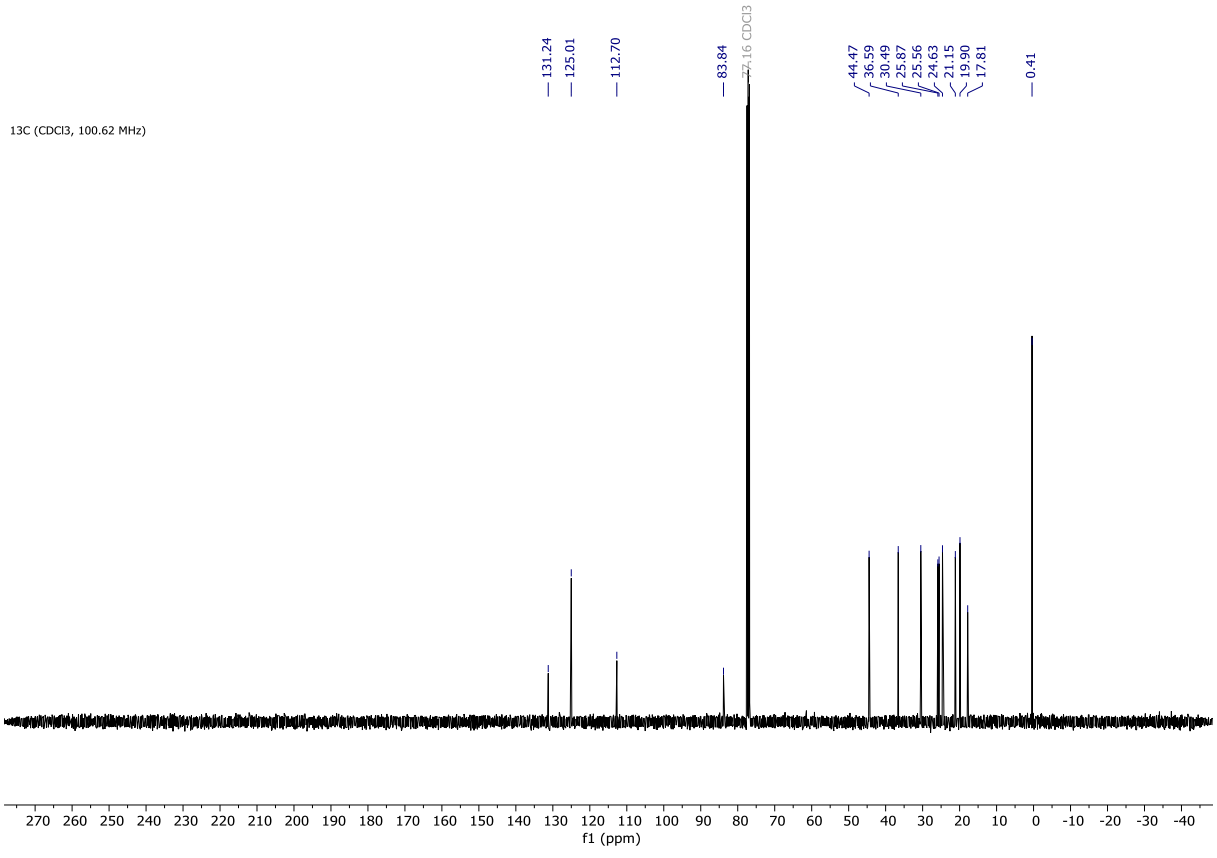

7.26 CDCl3
1H (CDCl3, 400.12 MHz)
TMS
OH
Me
Me
Me
Me
7a
1.00
1.04
2.01
3.15
9.99
3.02
1.01
1.00
3.01
9.00
f1 (ppm)

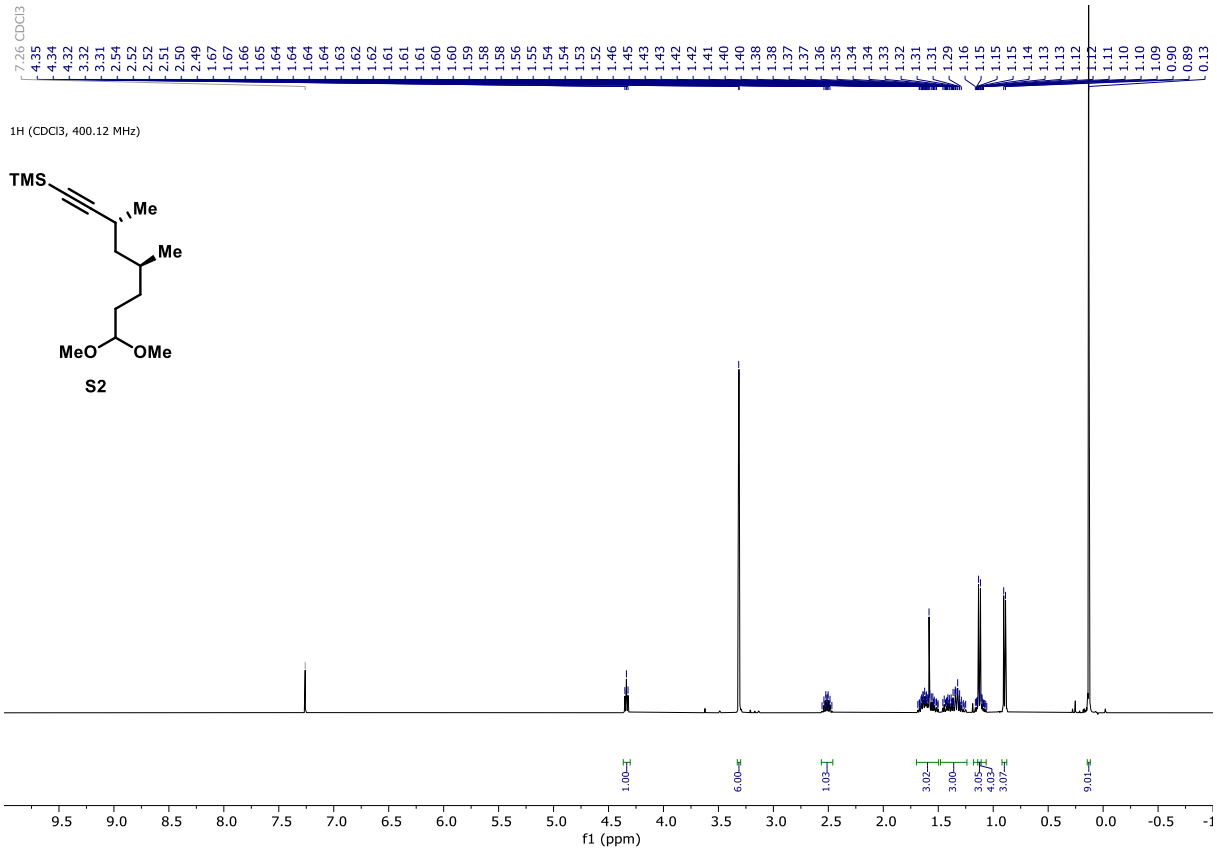

131.46
124.75
107.12
89.60
77.16 CDCl3
61.76
45.18
37.15
29.50
25.87
25.46
19.86
17.82
0.02
13C (CDCl3, 100.62 MHz)
f1 (ppm)

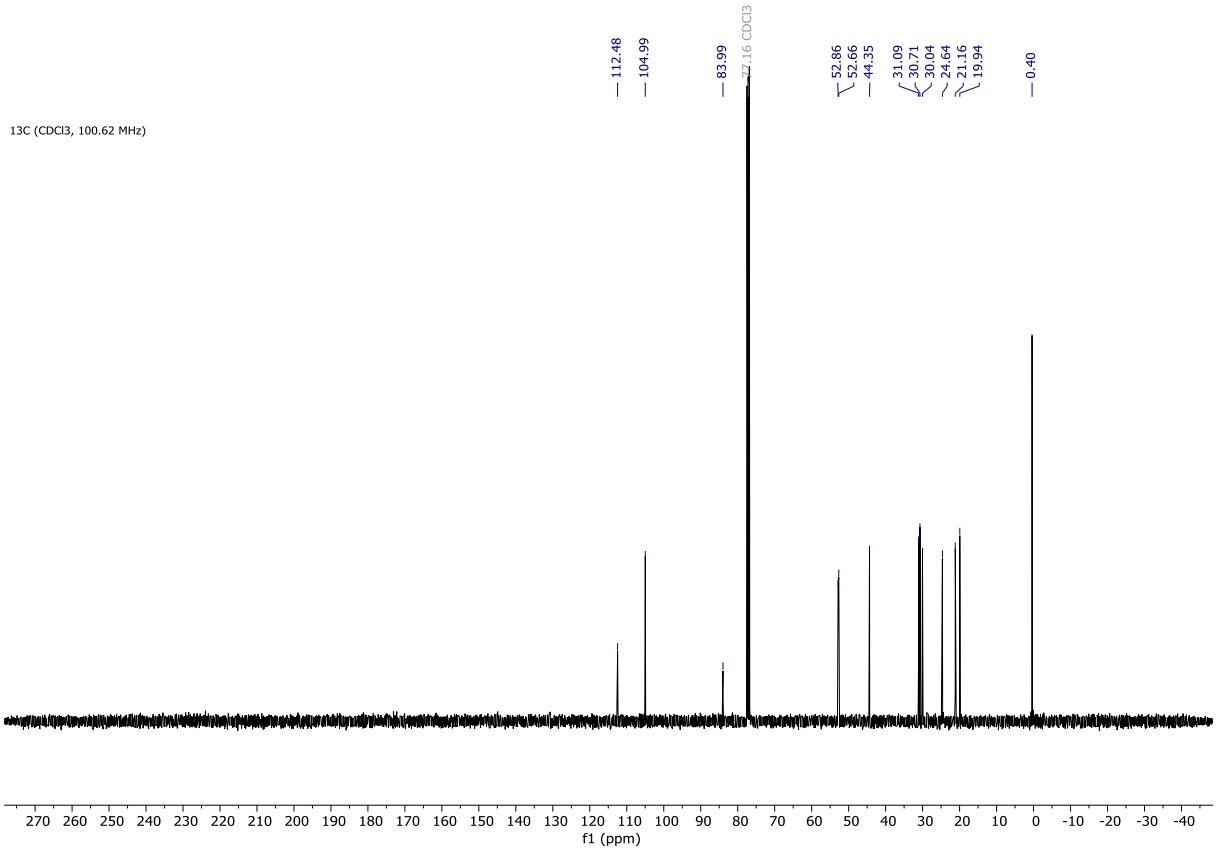

7.26 CDCl3
1H (CDCl3, 400.12 MHz)
TMS
OAc
Me
Me
Me
7b
f1 (ppm)

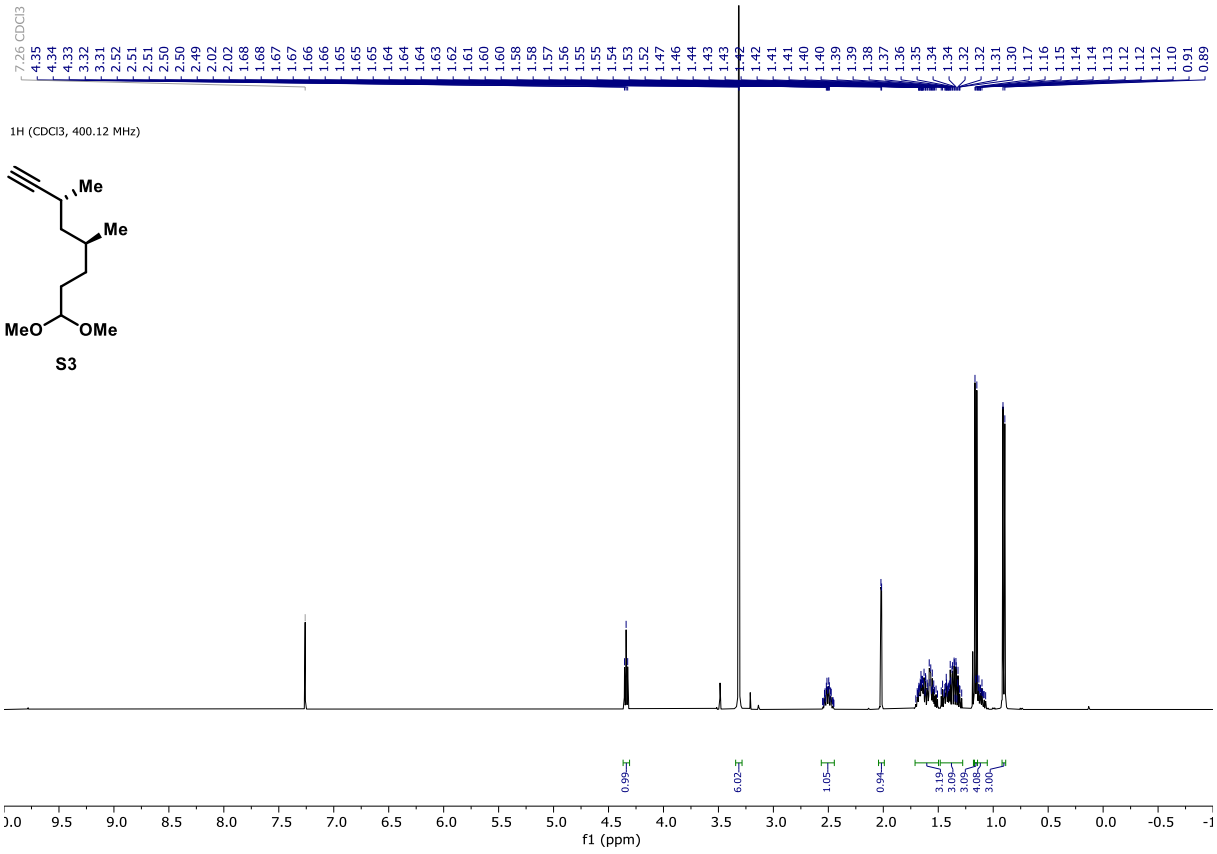

170.00
131.55
124.59
103.00
90.53
77.16 CDCl3
63.46
41.90
37.08
29.36
25.87
25.39
21.29
19.57
17.82
-0.06
13C (CDCl3, 100.62 MHz)
f1 (ppm)

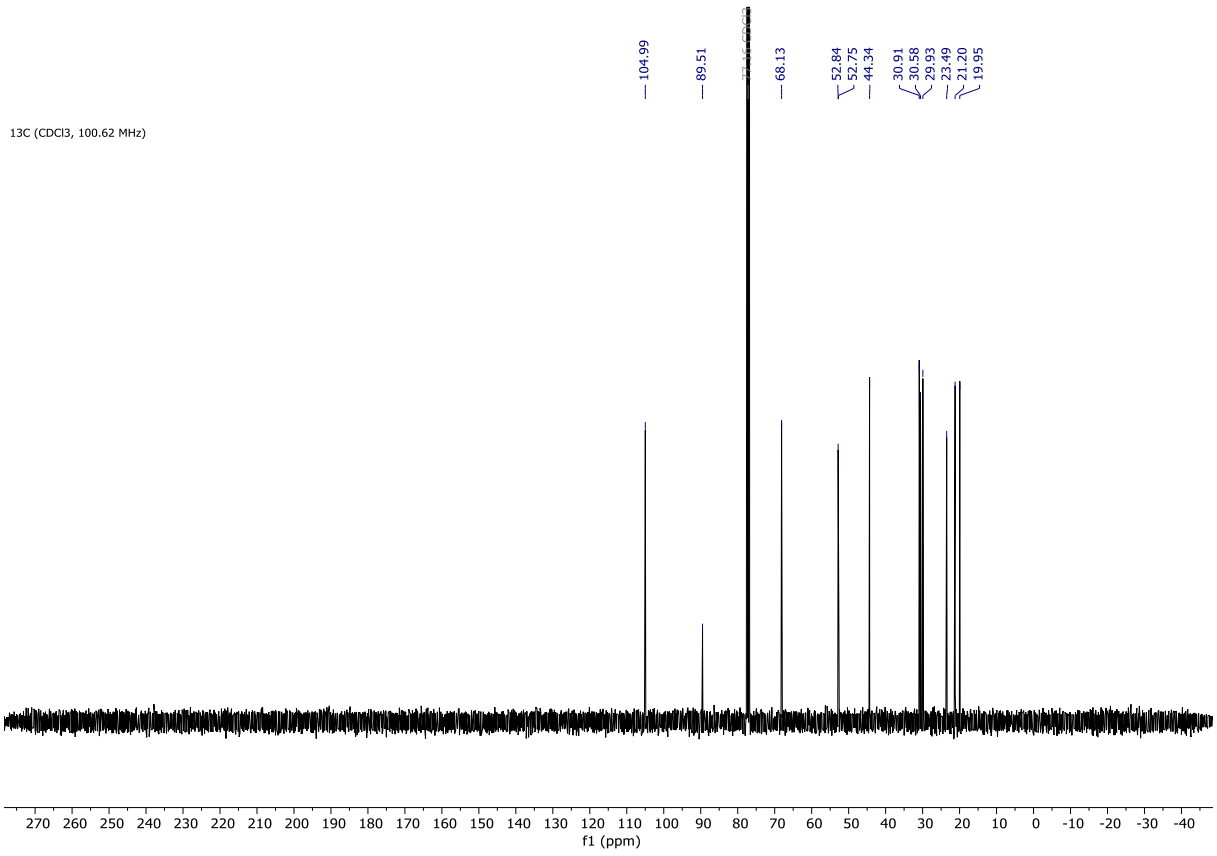

7.26 CDCl3
1H (CDCl3, 400.12 MHz)
TMS
Me
Me
Me
Me
8
f1 (ppm)

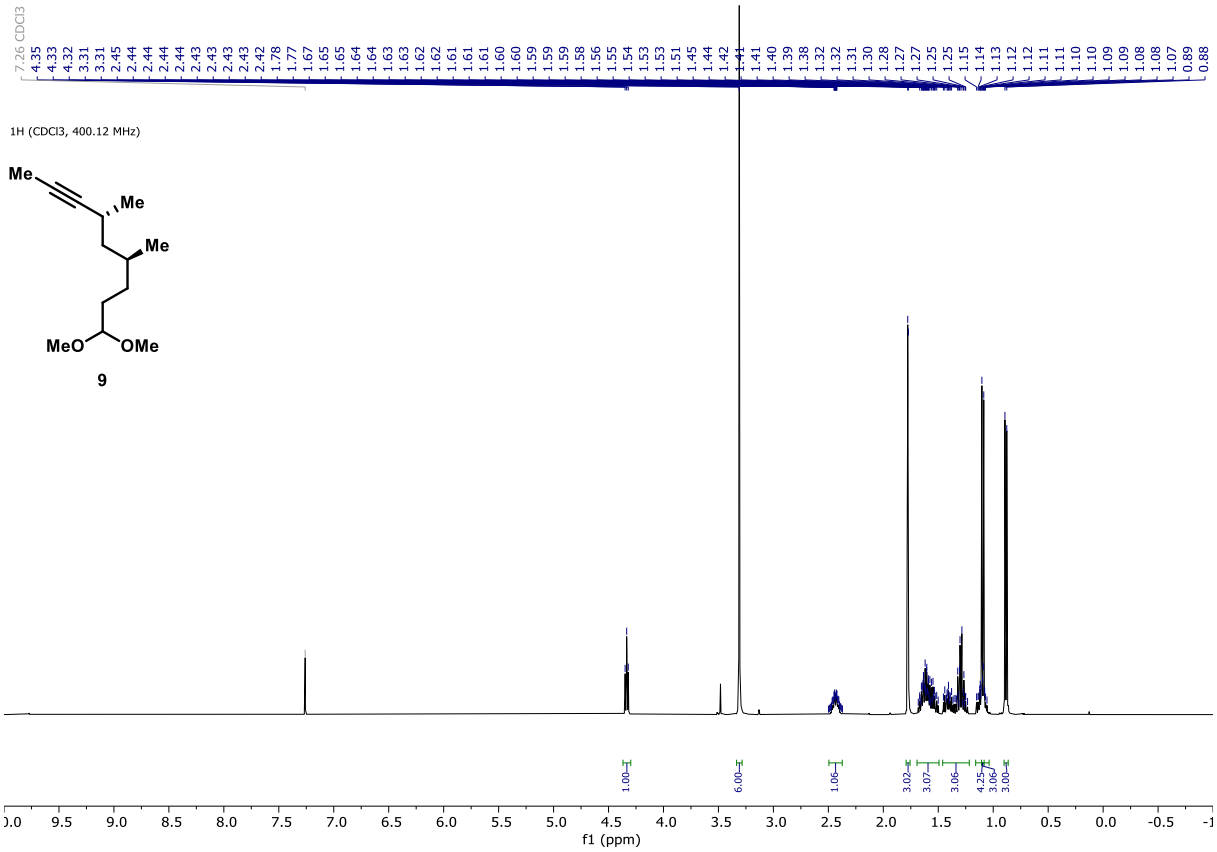

131.24
125.01
112.70
83.84
77.16 CDCl3
44.47
36.59
30.49
25.87
25.56
24.63
21.15
19.90
17.81
0.41
13C (CDCl3, 100.62 MHz)
f1 (ppm)

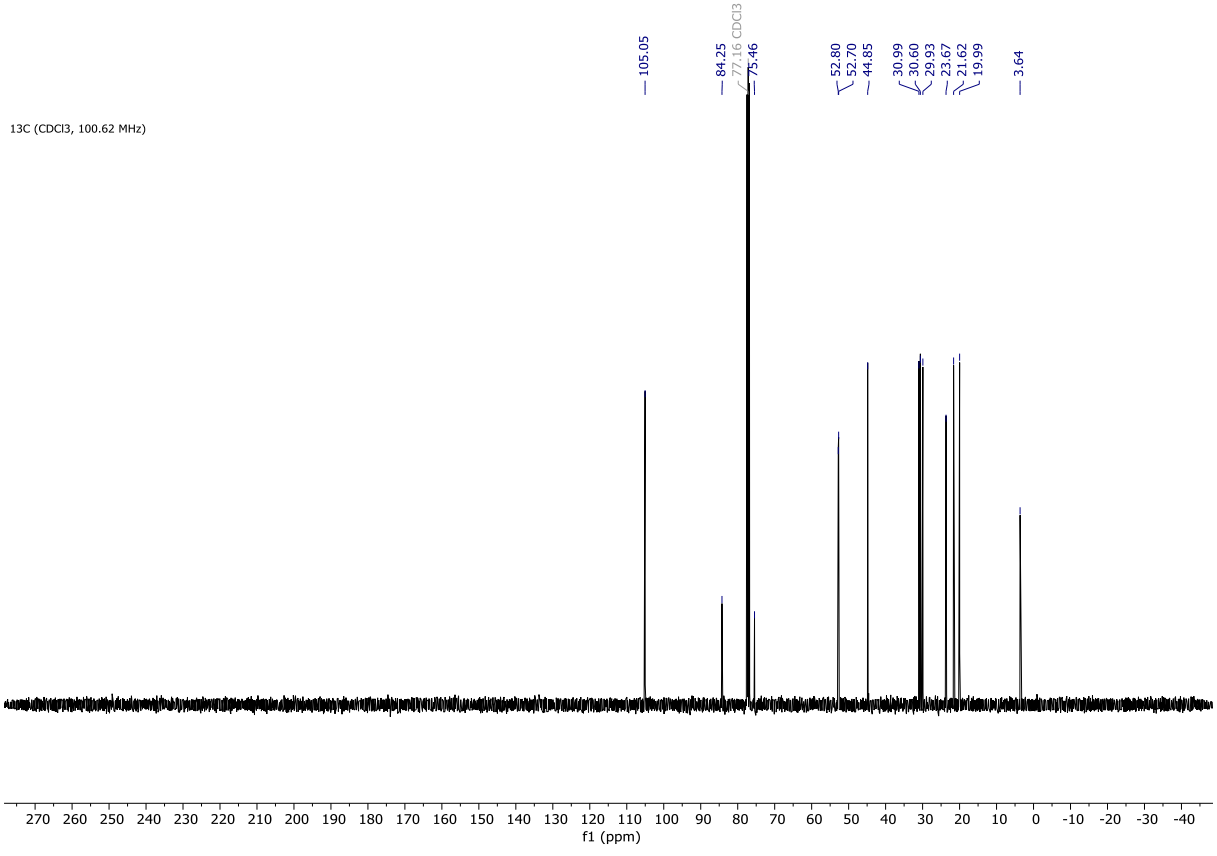

7.26 CDCl3
1H (CDCl3, 400.12 MHz)
TMS
Me
Me
MeO
OMe
S2
1.00
6.00
1.03
3.02
3.00
3.05
4.07
3.07
9.01
f1 (ppm)


112.48
104.99
83.99
77.16 CDCl3
52.86
52.66
44.35
31.09
30.71
30.04
24.64
21.16
19.94
0.40
13C (CDCl3, 100.62 MHz)
f1 (ppm)

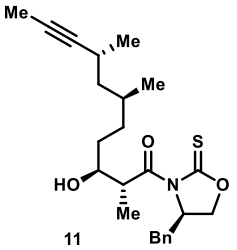

7.26 CDCl3
1H (CDCl3, 400.12 MHz)
Me
Me
MeO
OMe
S3
0.99
6.02
1.05
0.94
3.19
3.09
3.08
4.08
3.00
f1 (ppm)


104.99
89.51
77.16 CDCl3
68.13
52.84
52.75
44.34
30.91
30.58
29.93
23.49
21.20
19.95
13C (CDCl3, 100.62 MHz)
f1 (ppm)


7.26 CDCl3
4.35 4.33 4.32 3.31 3.31 2.45 2.44 2.44 2.44 2.44 2.43 2.43 2.43 2.43 2.42 1.78 1.77 1.67 1.65 1.65 1.64 1.64 1.63 1.63 1.62 1.62 1.61 1.61 1.61 1.60 1.60 1.59 1.59 1.59 1.58 1.56 1.55 1.54 1.53 1.53 1.51 1.45 1.44 1.42 1.41 1.41 1.40 1.39 1.38 1.32 1.32 1.31 1.30 1.28 1.27 1.27 1.25 1.25 1.15 1.14 1.13 1.12 1.12 1.11 1.11 1.10 1.10 1.09 1.09 1.08 1.08 1.07 0.89 0.88
1H (CDCl3, 400.12 MHz)
Me
Me
Me
MeO
OMe
9
1.00
6.00
1.06
3.02
3.07
3.06
4.25
3.06
3.00
f1 (ppm)

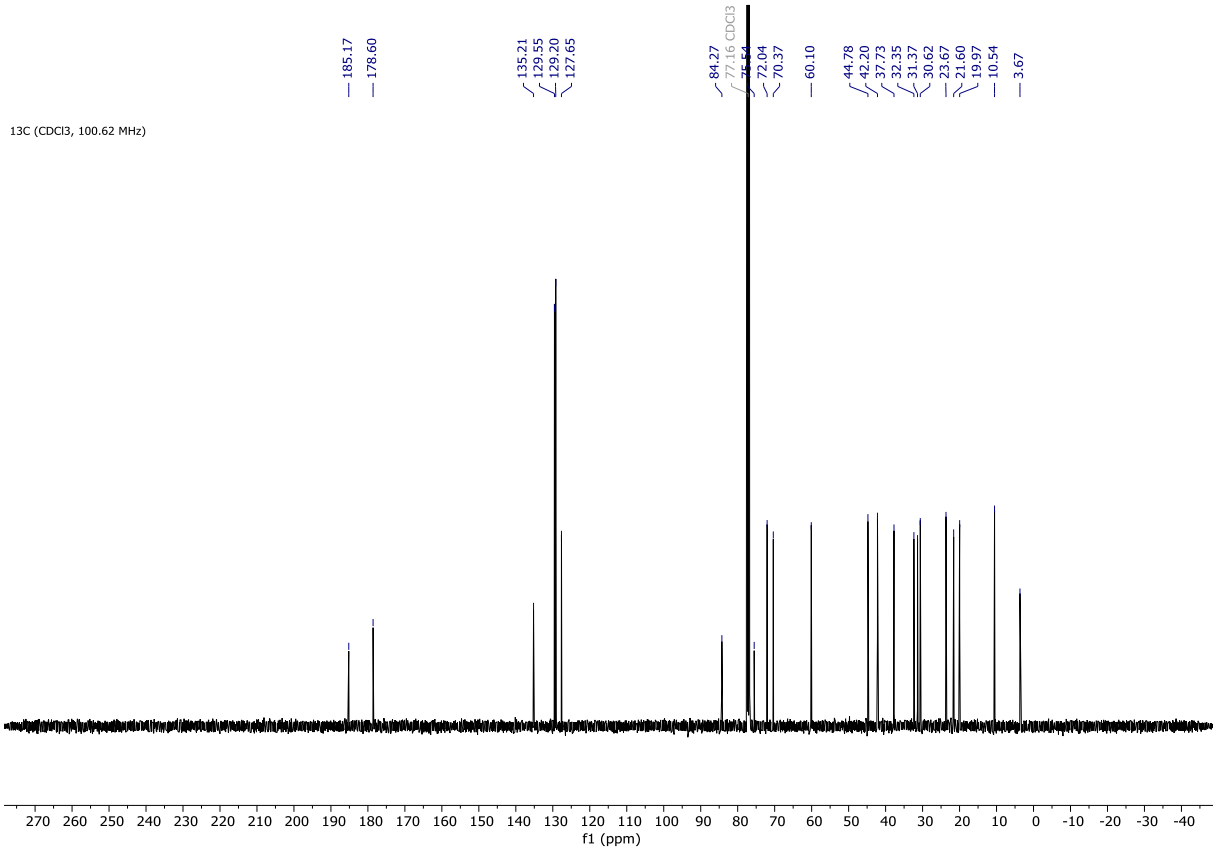

105.05
84.25
77.16 CDCl3
75.46
52.80
52.70
44.85
30.99
30.60
29.93
23.67
21.62
19.99
3.64
13C (CDCl3, 100.62 MHz)
f1 (ppm)


1H (CDCl3, 400.12 MHz)

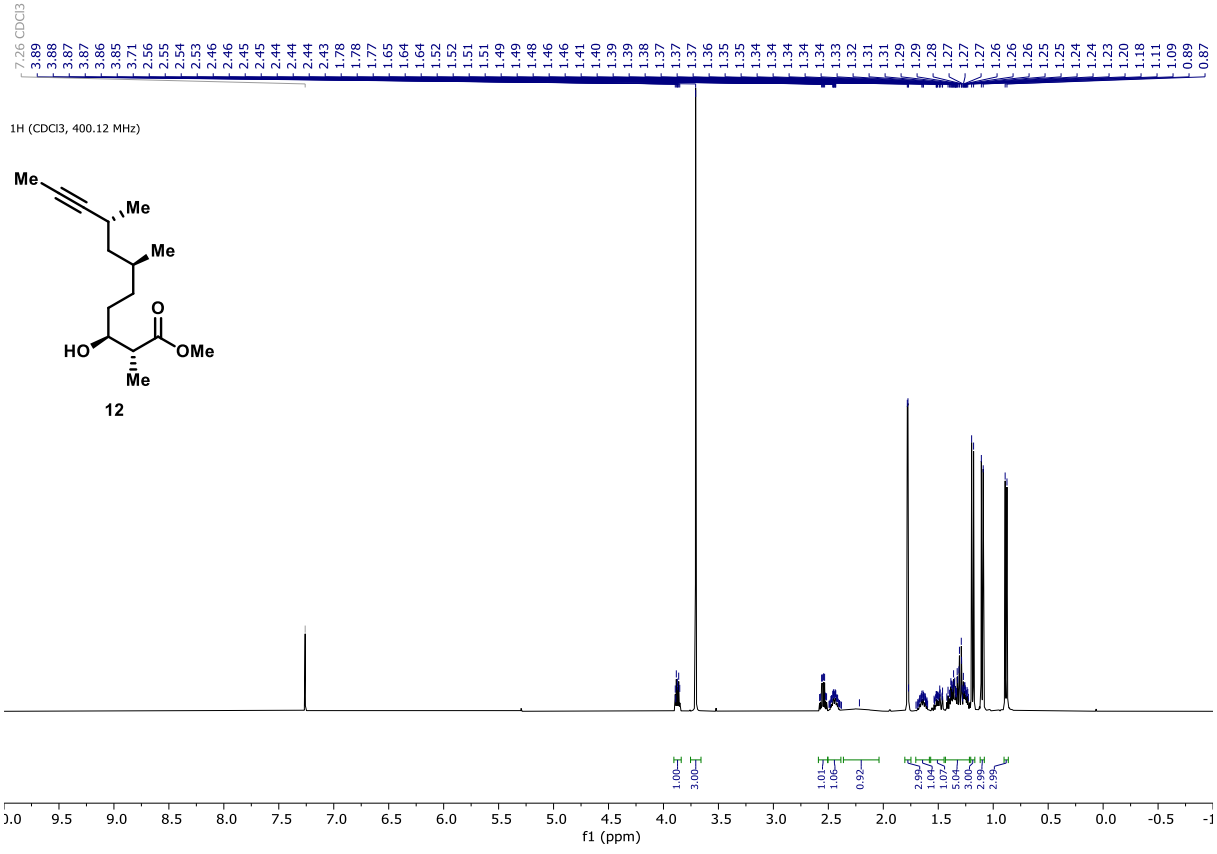


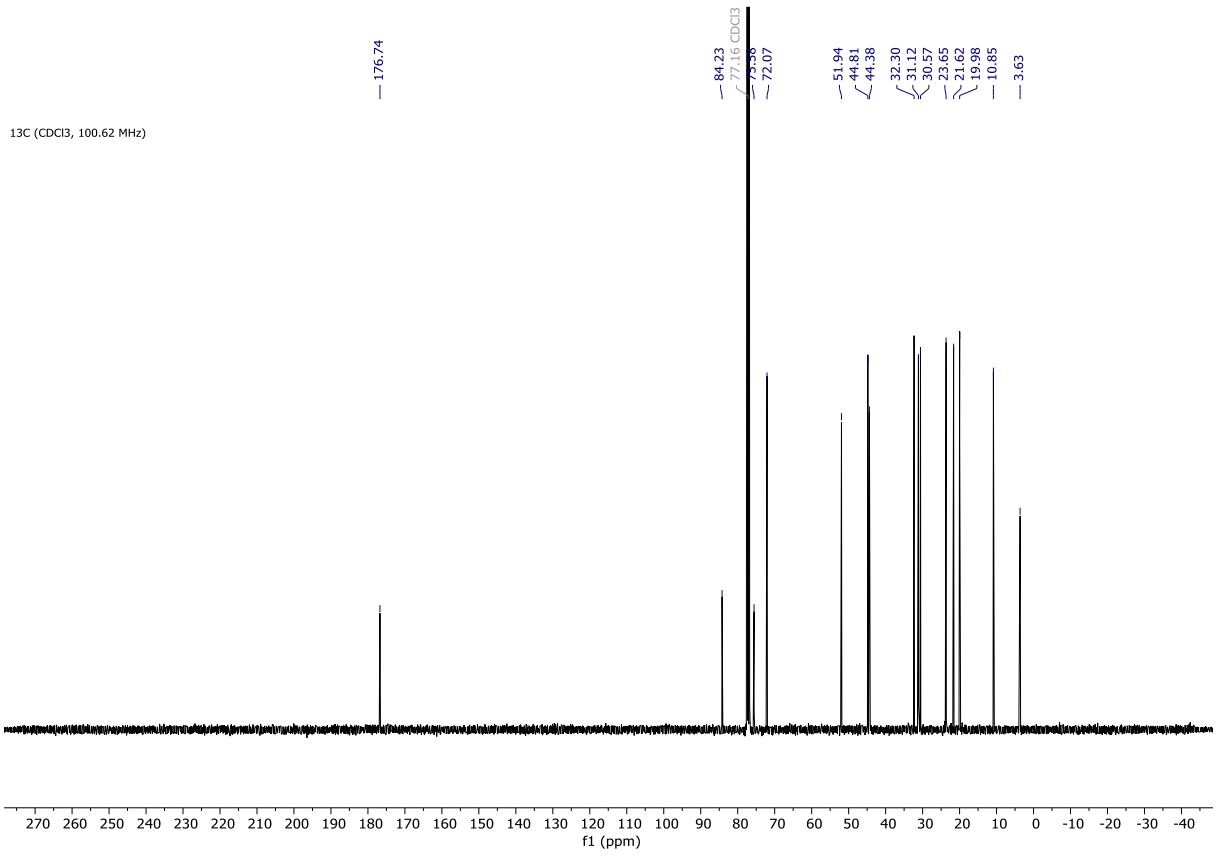

11

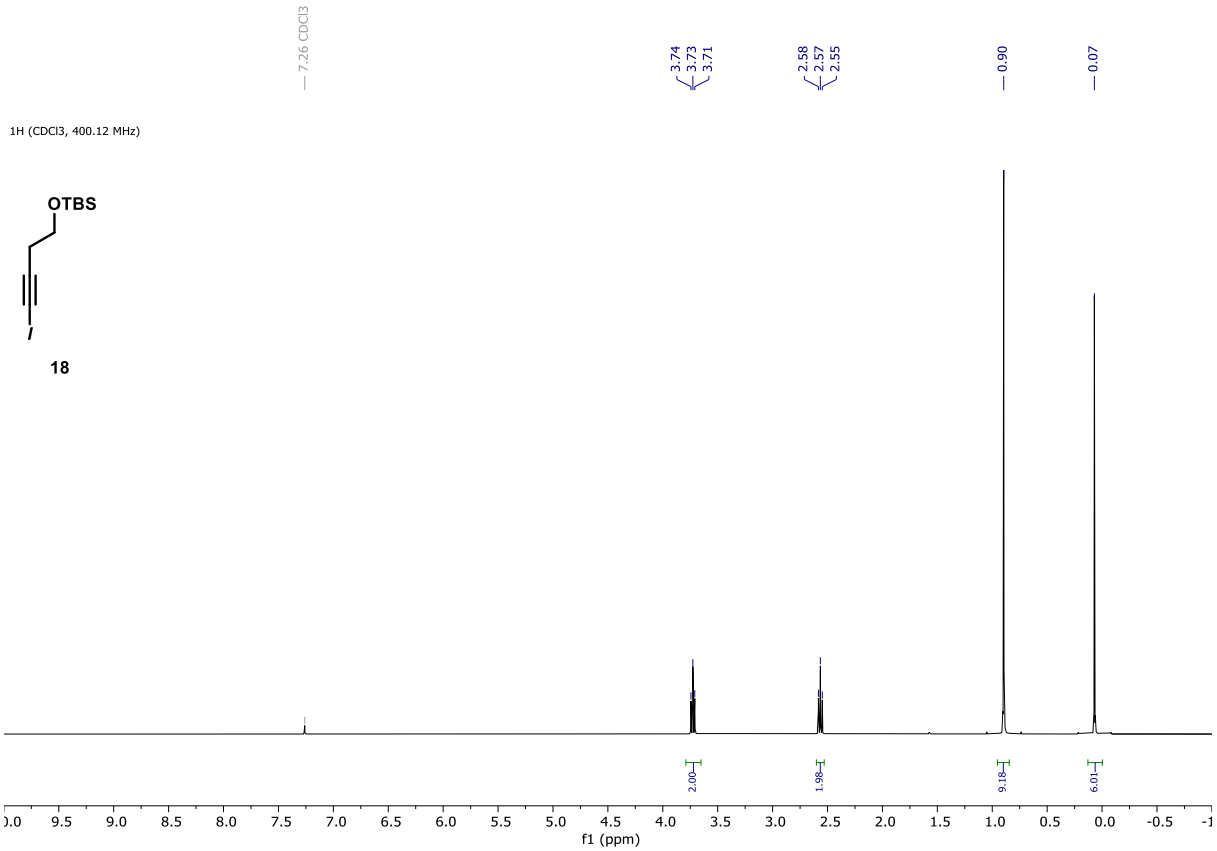


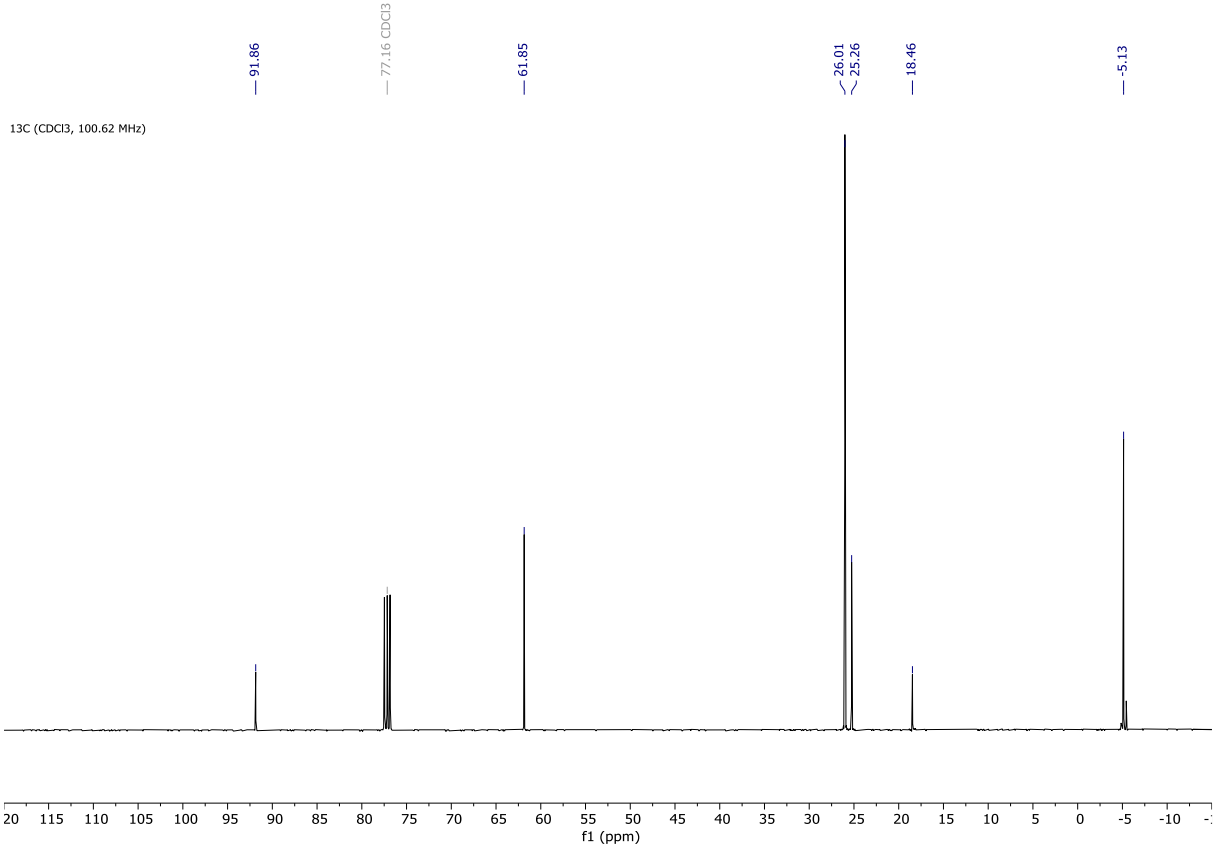



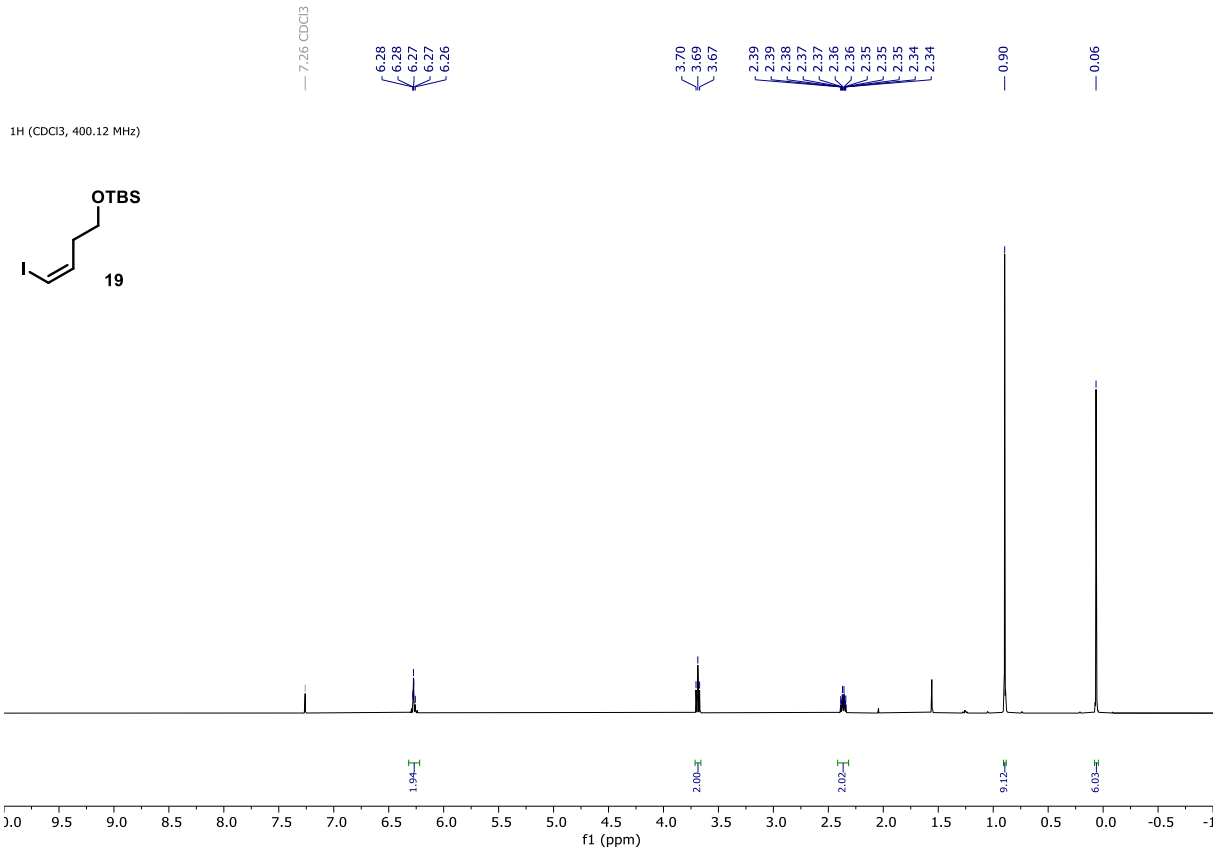

13C (CDCl3, 100.62 MHz)

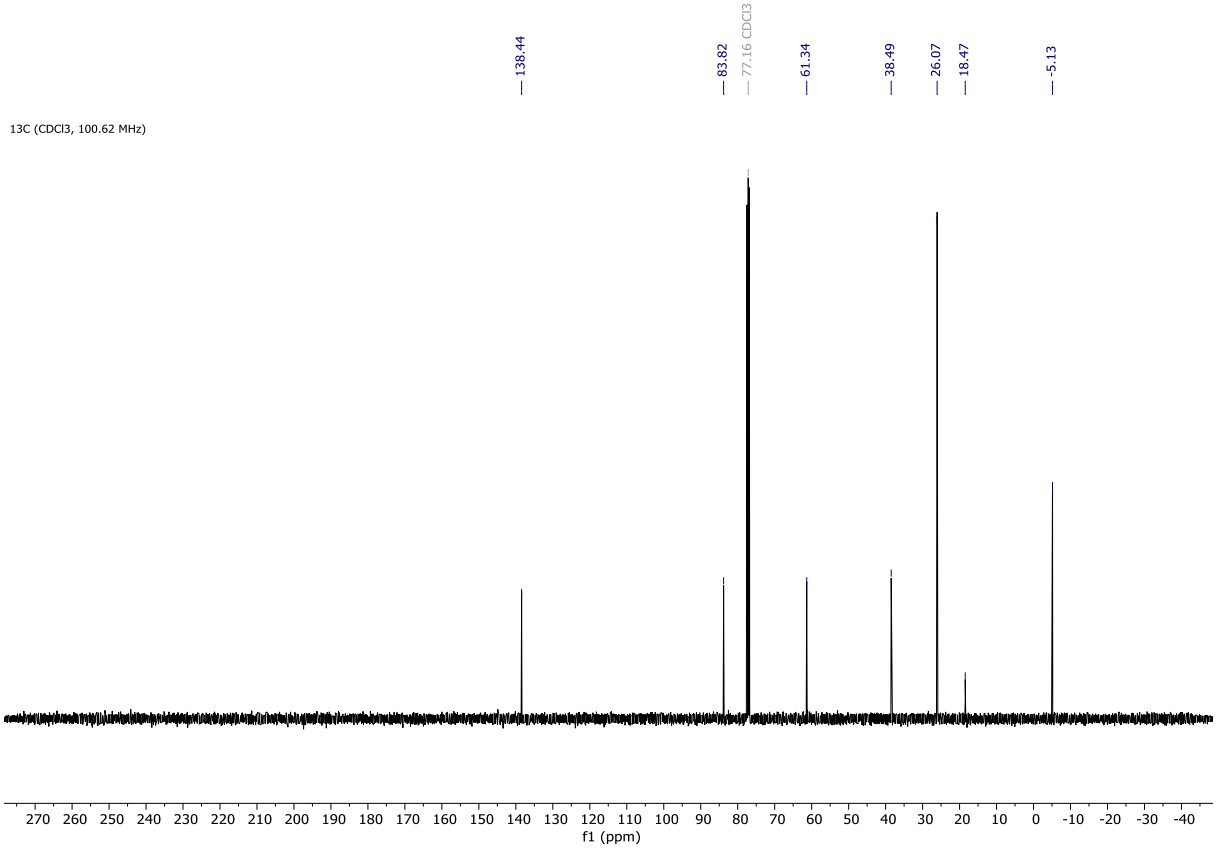

1H (CDCl3, 400.12 MHz)
Me
Me
Me
O
HO
OMe
Me
12
f1 (ppm)

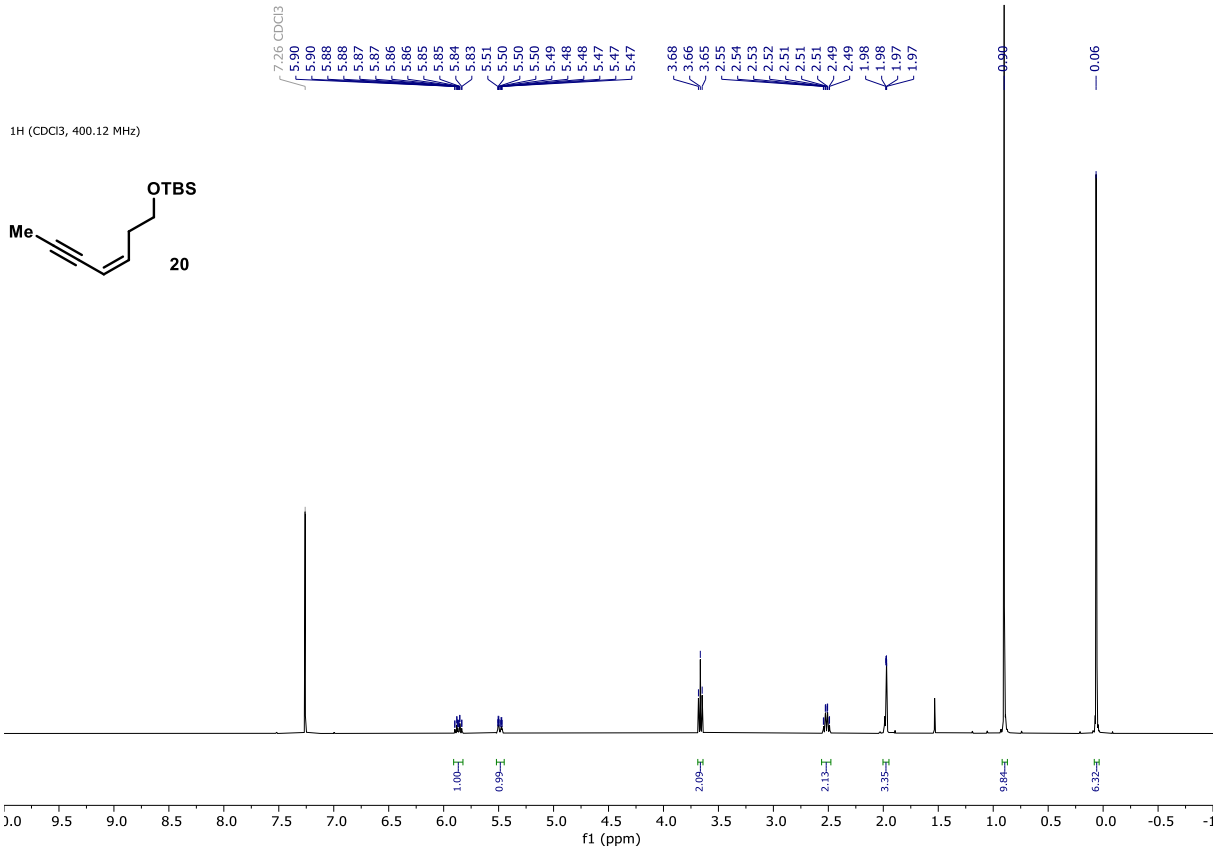

13C (CDCl3, 100.62 MHz)
176.74
84.23
77.16 CDCl3
72.07
51.94
44.81
44.38
32.30
31.12
30.57
23.65
21.62
19.98
10.85
3.63
f1 (ppm)

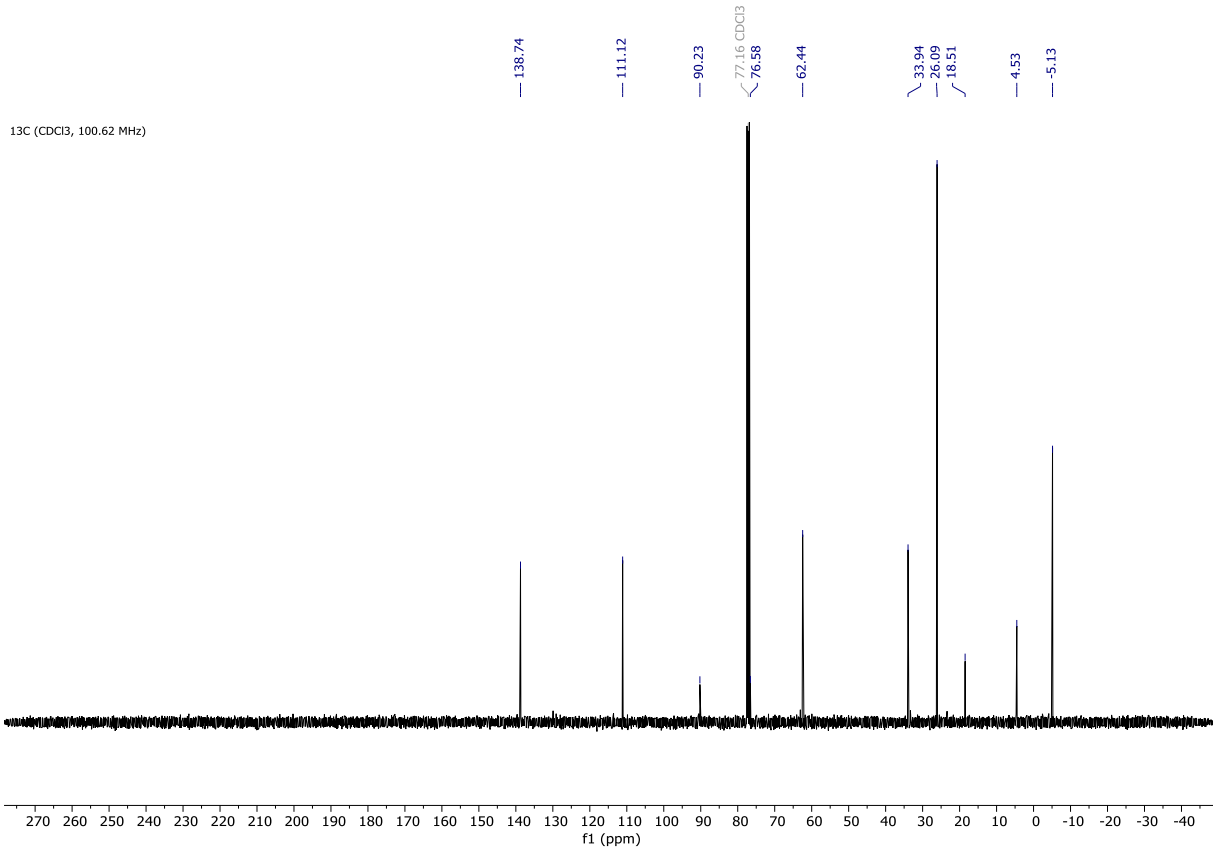

7.26 CDCl3
3.74
3.73
3.71
2.58
2.57
2.55
0.90
0.07
1H (CDCl3, 400.12 MHz)
OTBS
18
2.00
1.98
9.18
6.01
f1 (ppm)

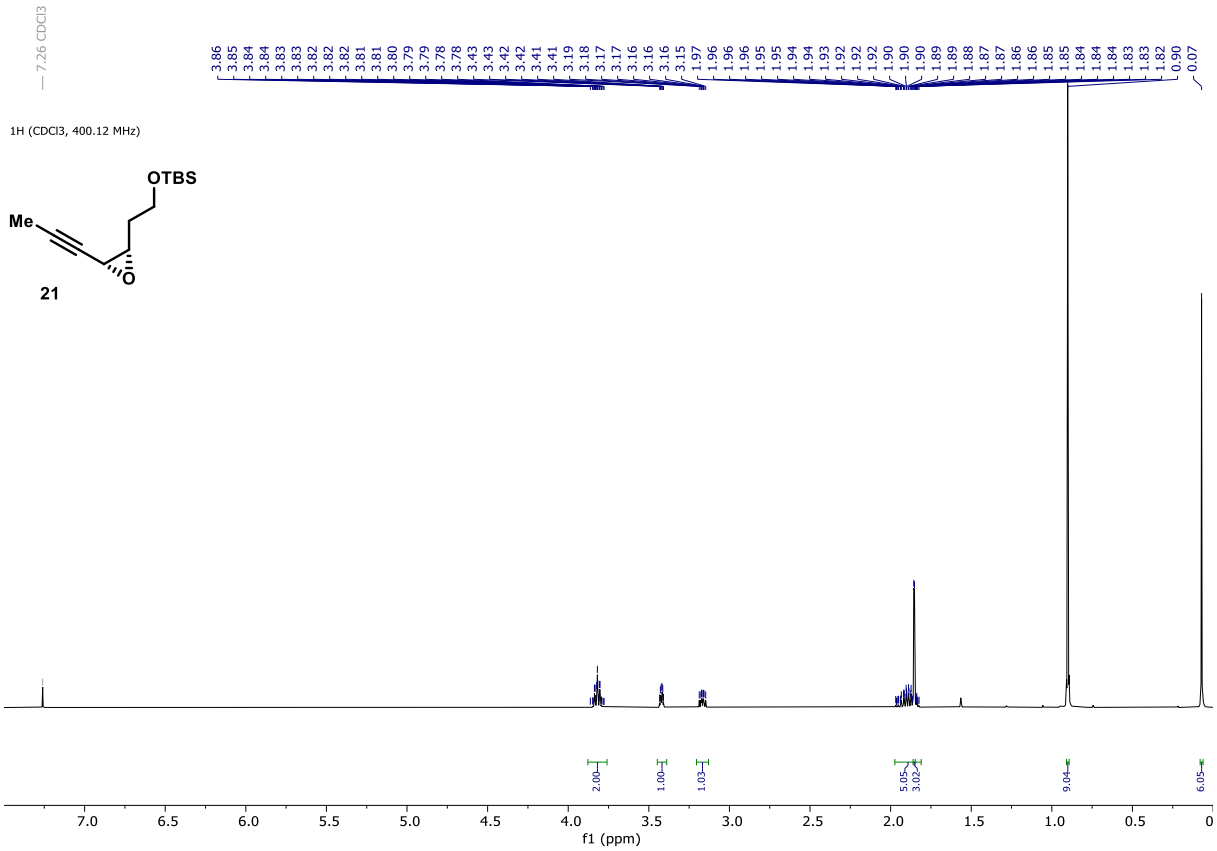

91.86
77.16 CDCl3
61.85
26.01
25.26
18.46
-5.13
13C (CDCl3, 100.62 MHz)
f1 (ppm)

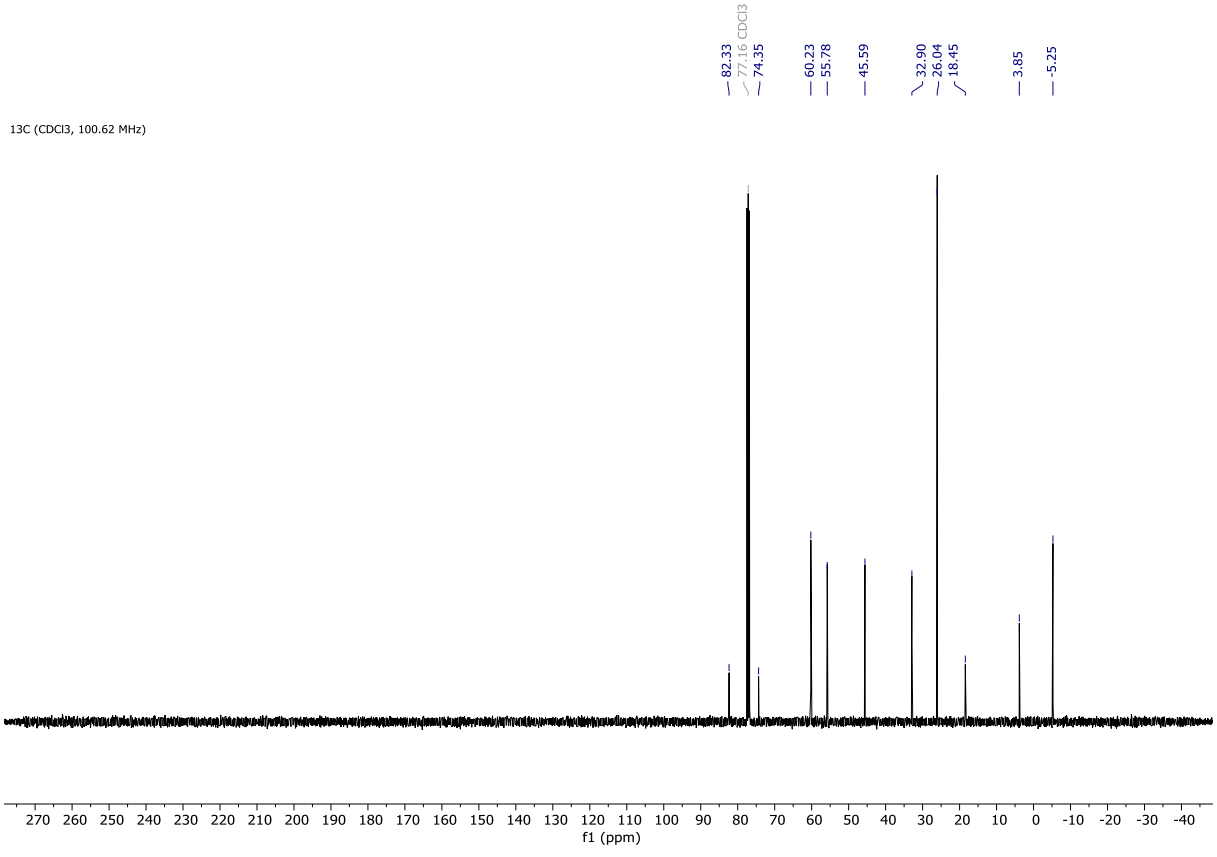

7.26 CDCl3
6.28
6.28
6.27
6.27
6.26
3.70
3.69
3.67
2.39
2.39
2.38
2.37
2.37
2.36
2.36
2.35
2.35
2.35
2.34
2.34
0.90
0.06
1H (CDCl3, 400.12 MHz)
OTBS
I
19
1.94
2.00
2.02
9.12
6.03
f1 (ppm)

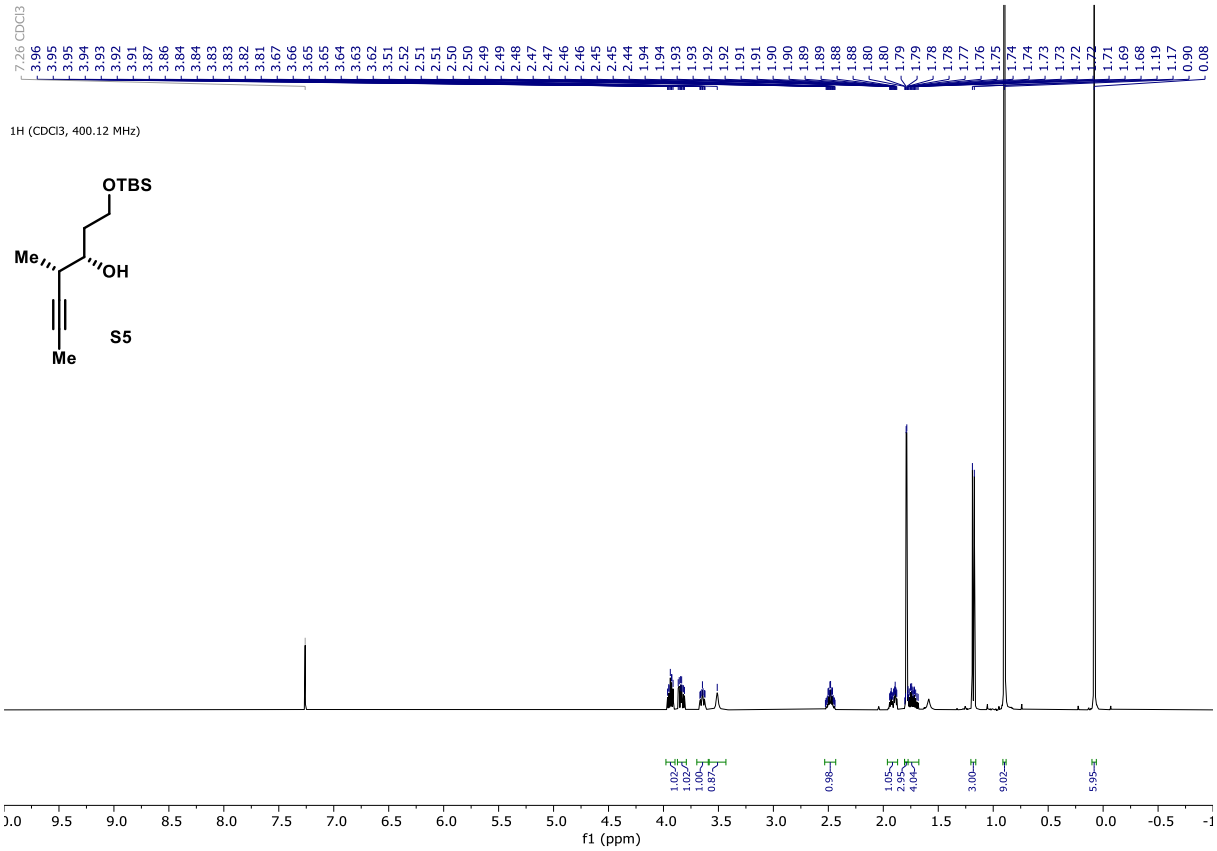

138.44
83.82
77.16 CDCl3
61.34
38.49
26.07
18.47
-5.13
13C (CDCl3, 100.62 MHz)
f1 (ppm)

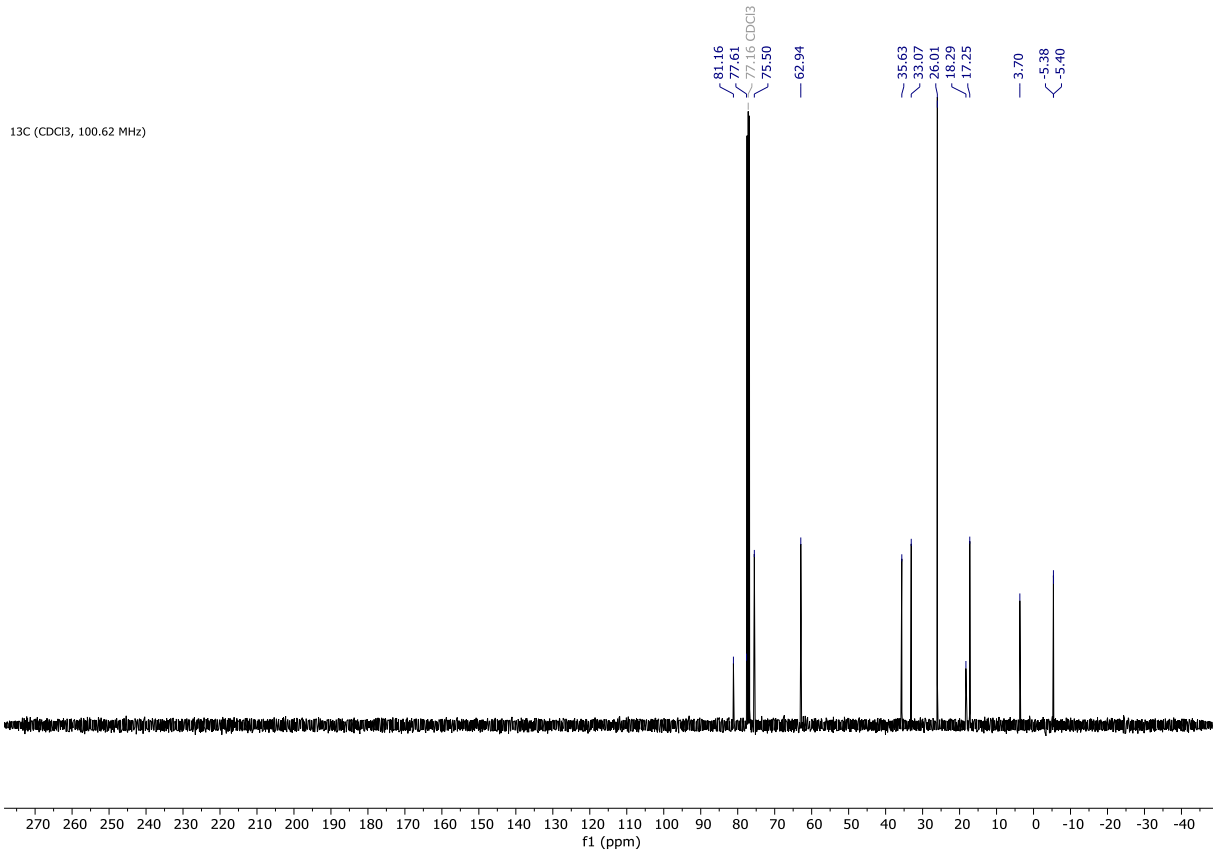

1H (CDCl3, 400.12 MHz)
OTBS
Me
20
7.26 CDCl3
5.90
5.90
5.88
5.88
5.87
5.87
5.86
5.86
5.85
5.85
5.84
5.83
5.51
5.50
5.50
5.50
5.49
5.48
5.48
5.47
5.47
5.47
3.68
3.66
3.65
2.55
2.54
2.53
2.52
2.51
2.51
2.51
2.49
2.49
1.98
1.98
1.97
1.97
0.90
0.06
1.00
0.99
2.09
2.13
3.35
9.84
6.32
f1 (ppm)

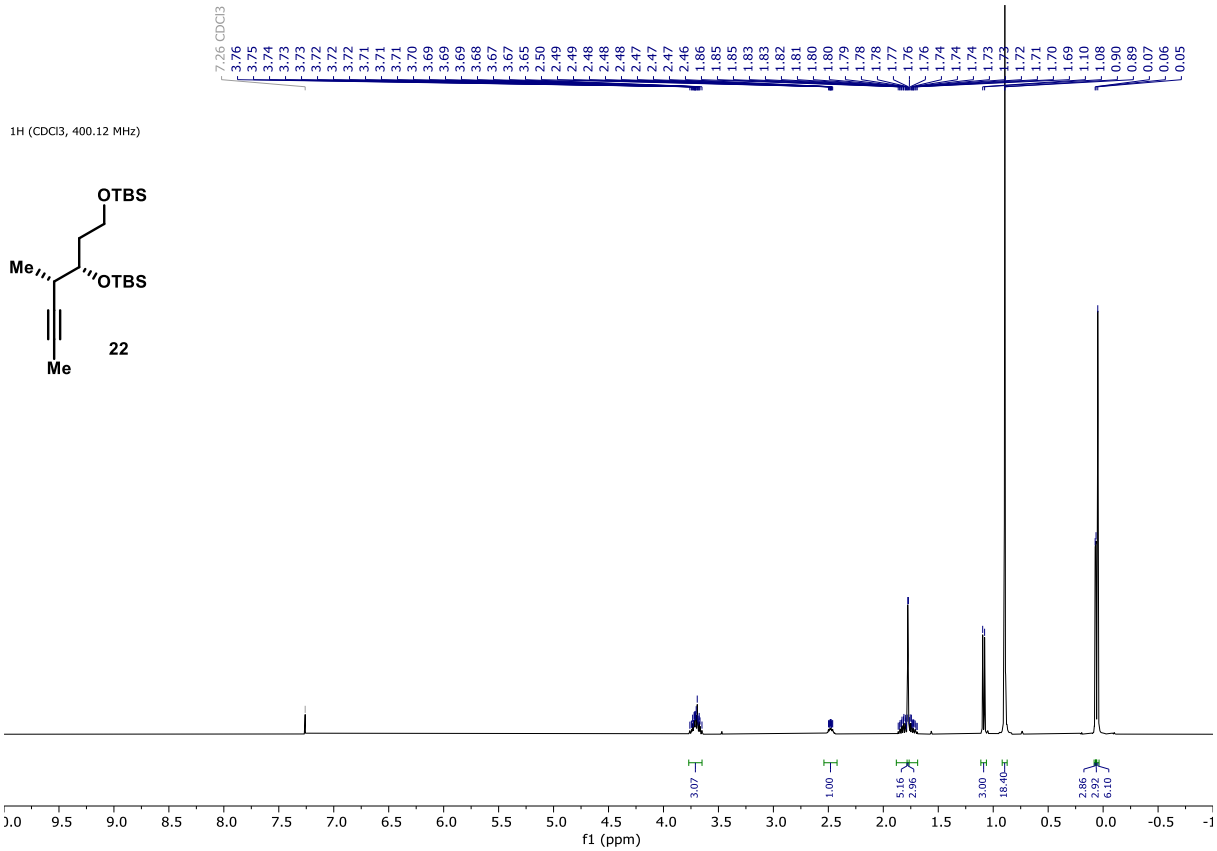

13C (CDCl3, 100.62 MHz)
138.74
111.12
90.23
77.16 CDCl3
76.58
62.44
33.94
26.09
18.51
4.53
-5.13
f1 (ppm)

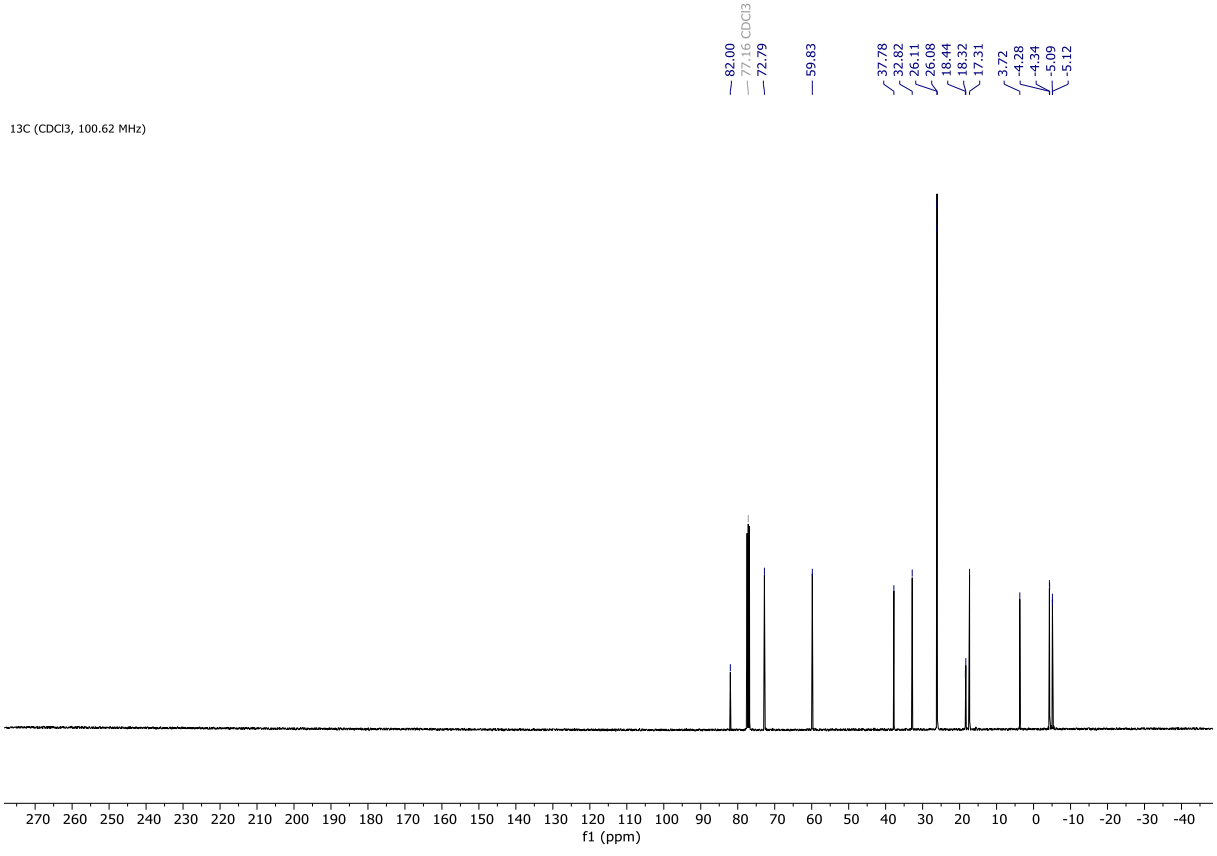

7.26 CDCl3
3.86 3.85 3.84 3.84 3.83 3.83 3.82 3.82 3.82 3.81 3.81 3.80 3.79 3.79 3.78 3.78 3.43 3.42 3.42 3.41 3.41 3.19 3.18 3.17 3.17 3.16 3.16 3.16 3.15 1.97 1.96 1.96 1.95 1.95 1.94 1.94 1.93 1.92 1.92 1.90 1.90 1.90 1.89 1.89 1.88 1.87 1.87 1.86 1.86 1.85 1.85 1.84 1.84 1.84 1.83 1.83 1.82 0.90 0.07
1H (CDCl3, 400.12 MHz)
OTBS
Me
O
21
2.00
1.00
1.03
5.05
3.02
9.04
6.05
7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

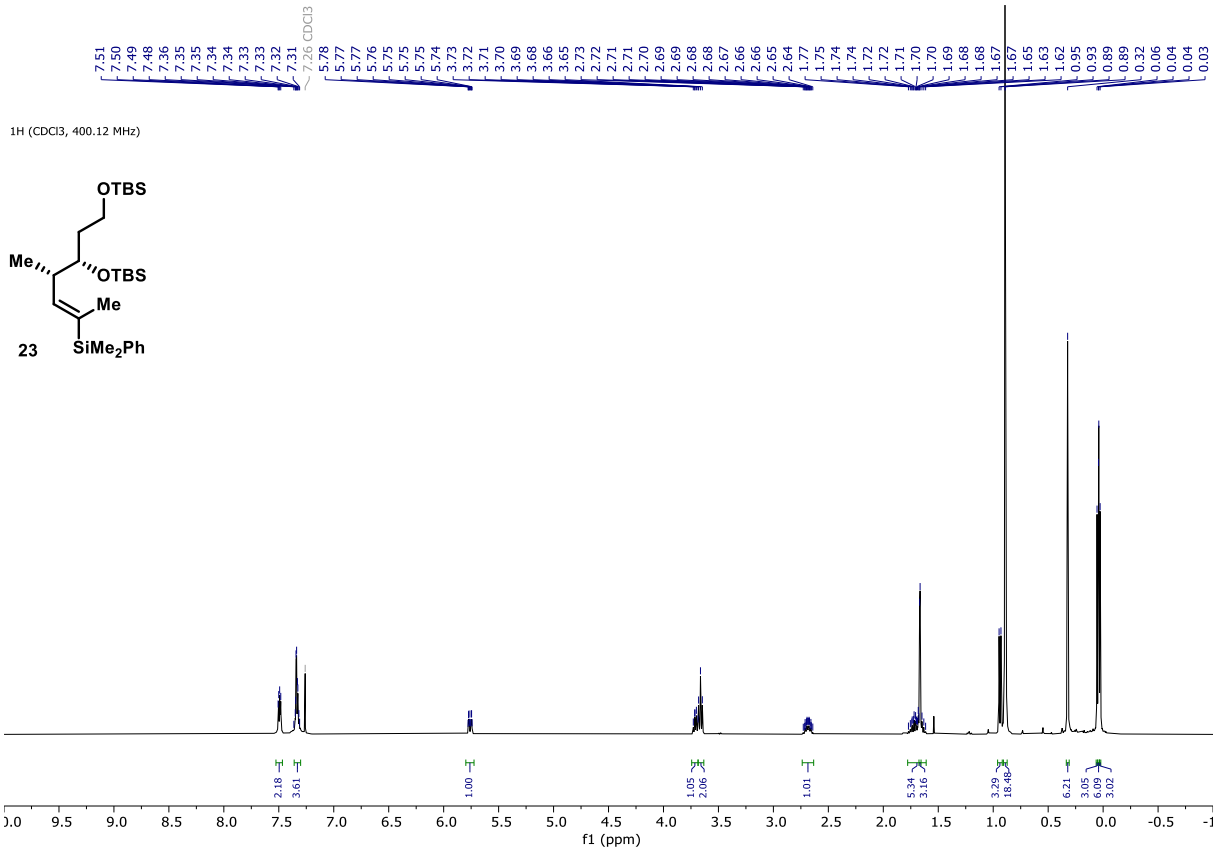

82.33
77.16 CDCl3
74.35
60.23
55.78
45.59
32.90
26.04
18.45
3.85
-5.25
13C (CDCl3, 100.62 MHz)
270 260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

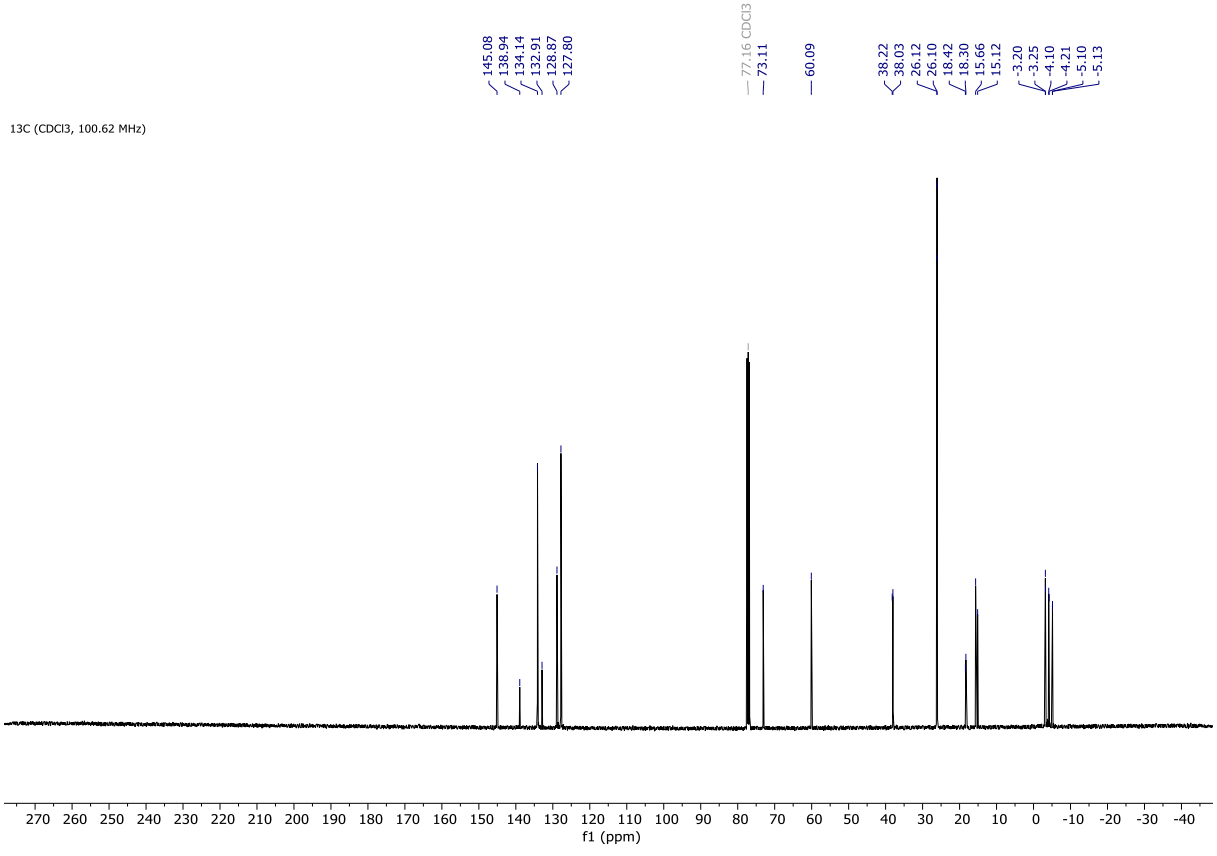

7.26 CDCl3
1H (CDCl3, 400.12 MHz)
OTBS
Me
OH
S5
Me
f1 (ppm)

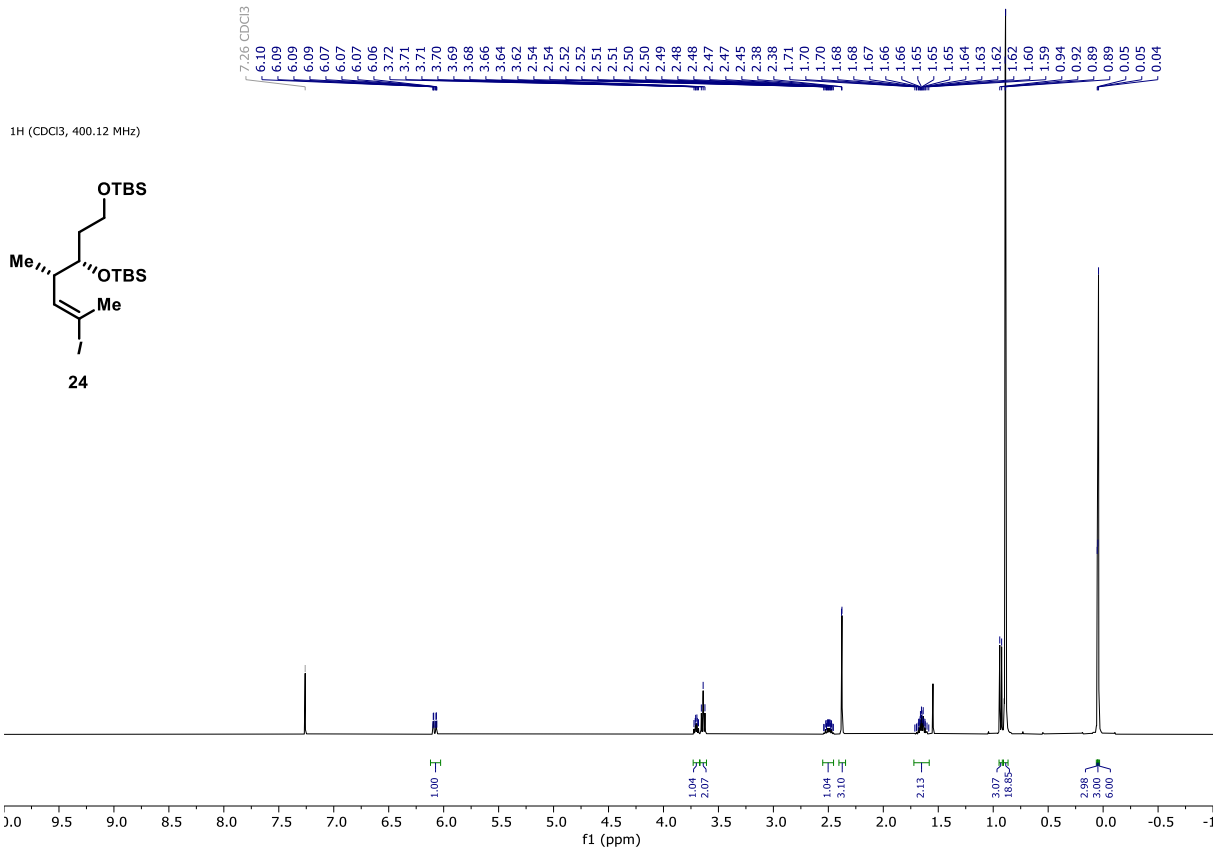

81.16
77.61
77.16 CDCl3
75.50
62.94
35.63
33.07
26.01
18.29
17.25
3.70
-5.38
-5.40
13C (CDCl3, 100.62 MHz)
f1 (ppm)

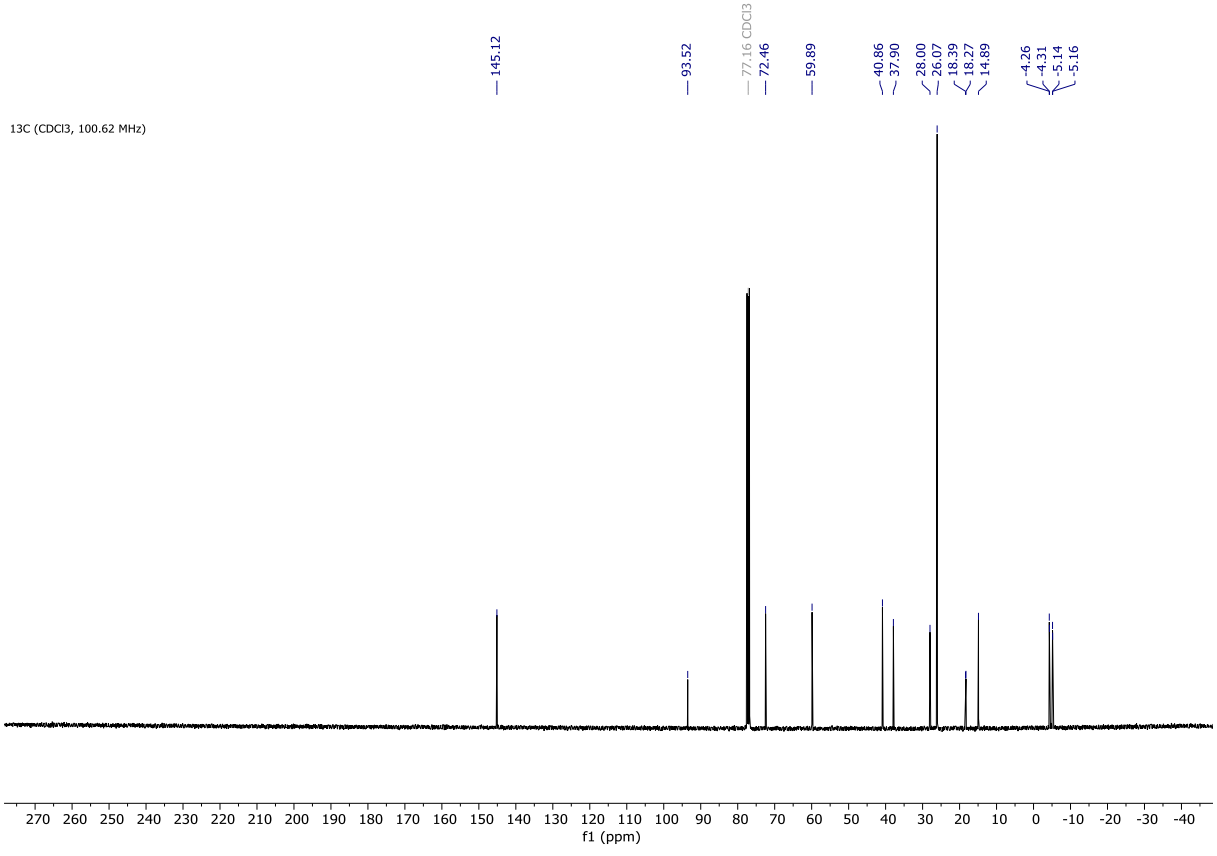

7.26 CDCl3
3.76 3.75 3.74 3.73 3.72 3.72 3.72 3.71 3.71 3.71 3.70 3.69 3.69 3.69 3.68 3.67 3.67 3.65 2.50 2.49 2.49 2.48 2.48 2.48 2.47 2.47 2.47 2.46 1.86 1.85 1.85 1.83 1.83 1.82 1.81 1.80 1.80 1.79 1.78 1.78 1.77 1.76 1.76 1.74 1.74 1.73 1.73 1.72 1.71 1.70 1.69 1.10 1.08 0.90 0.89 0.07 0.06 0.05
1H (CDCl3, 400.12 MHz)
OTBS
Me
OTBS
22
Me
3.07
1.00
5.16
2.96
3.00
18.40
2.86
2.92
6.10
f1 (ppm)

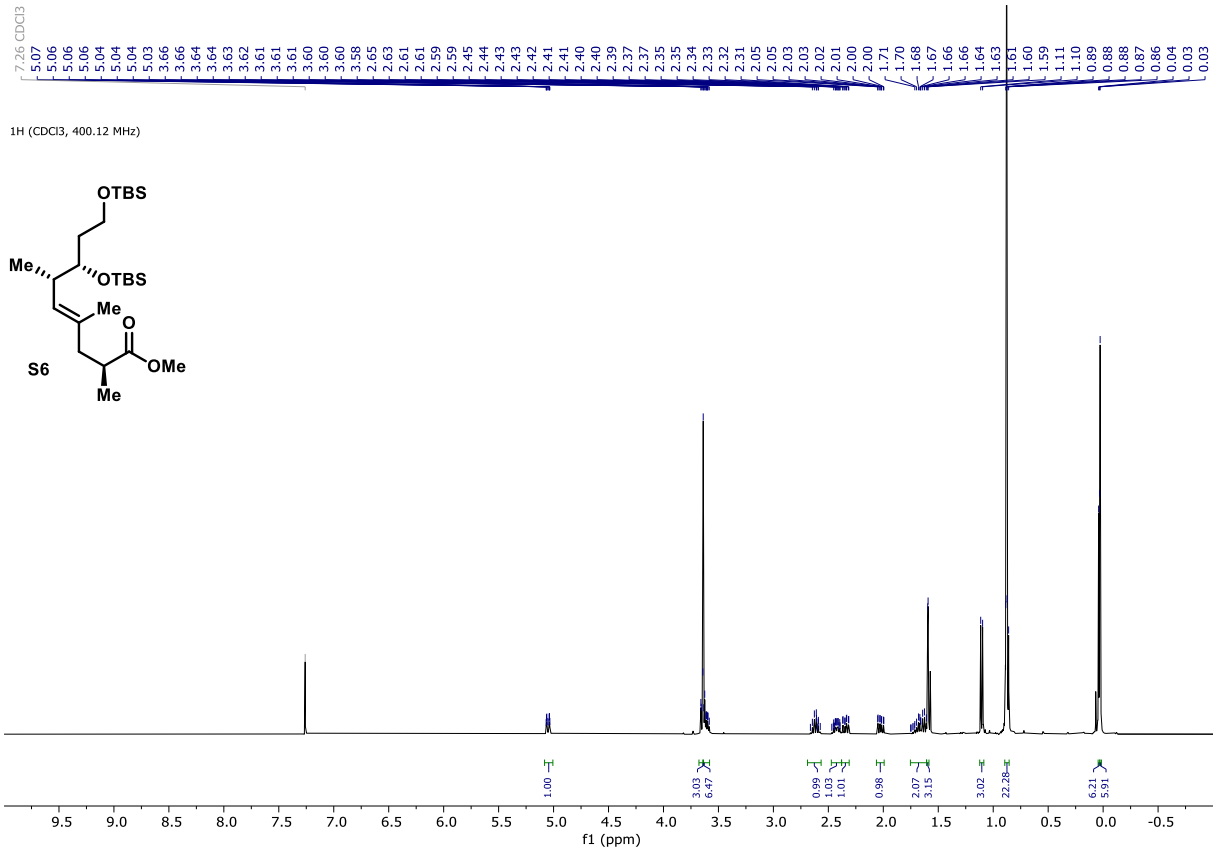

82.00
77.16 CDCl3
72.79
59.83
37.78
32.82
26.11
26.08
18.44
18.32
17.31
3.72
-4.28
-4.34
-5.09
-5.12
13C (CDCl3, 100.62 MHz)
f1 (ppm)

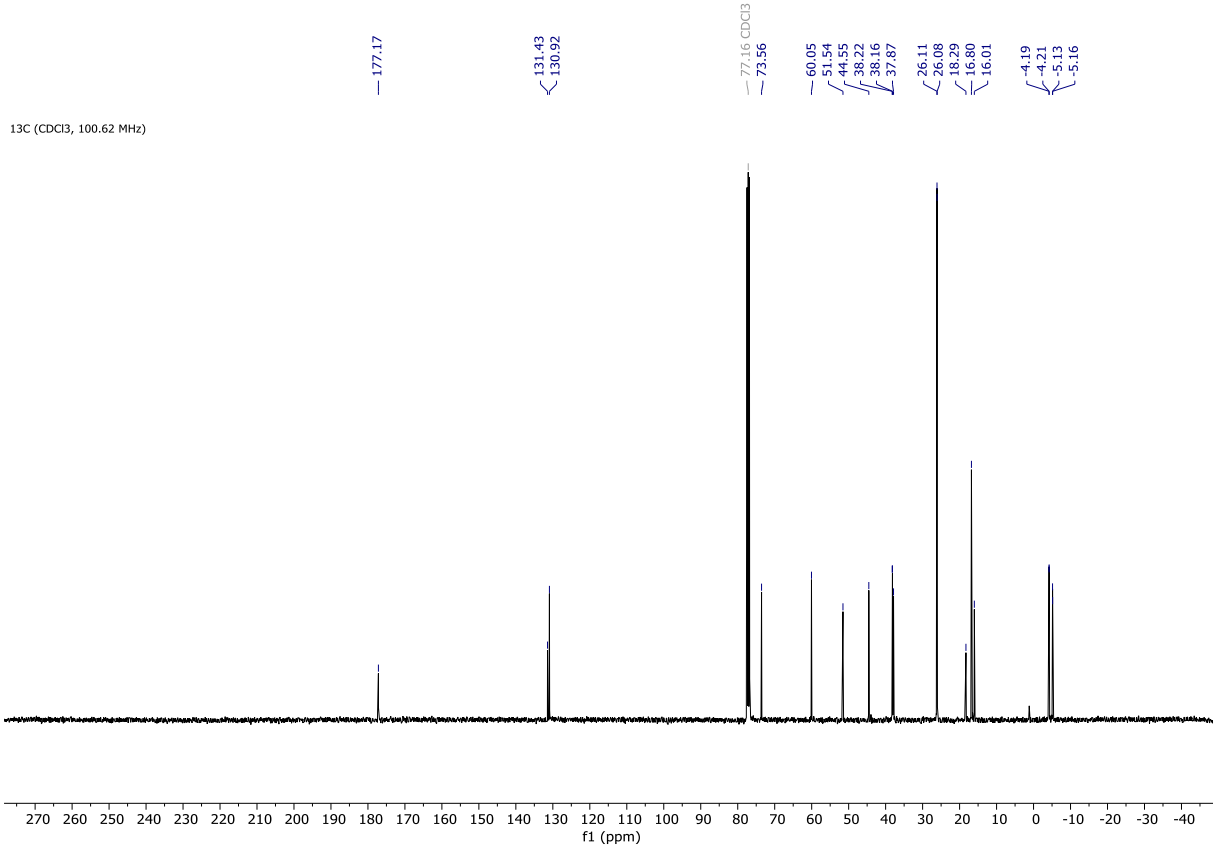

1H (CDCl3, 400.12 MHz)
OTBS
Me
OTBS
Me
SiMe2Ph
23
f1 (ppm)

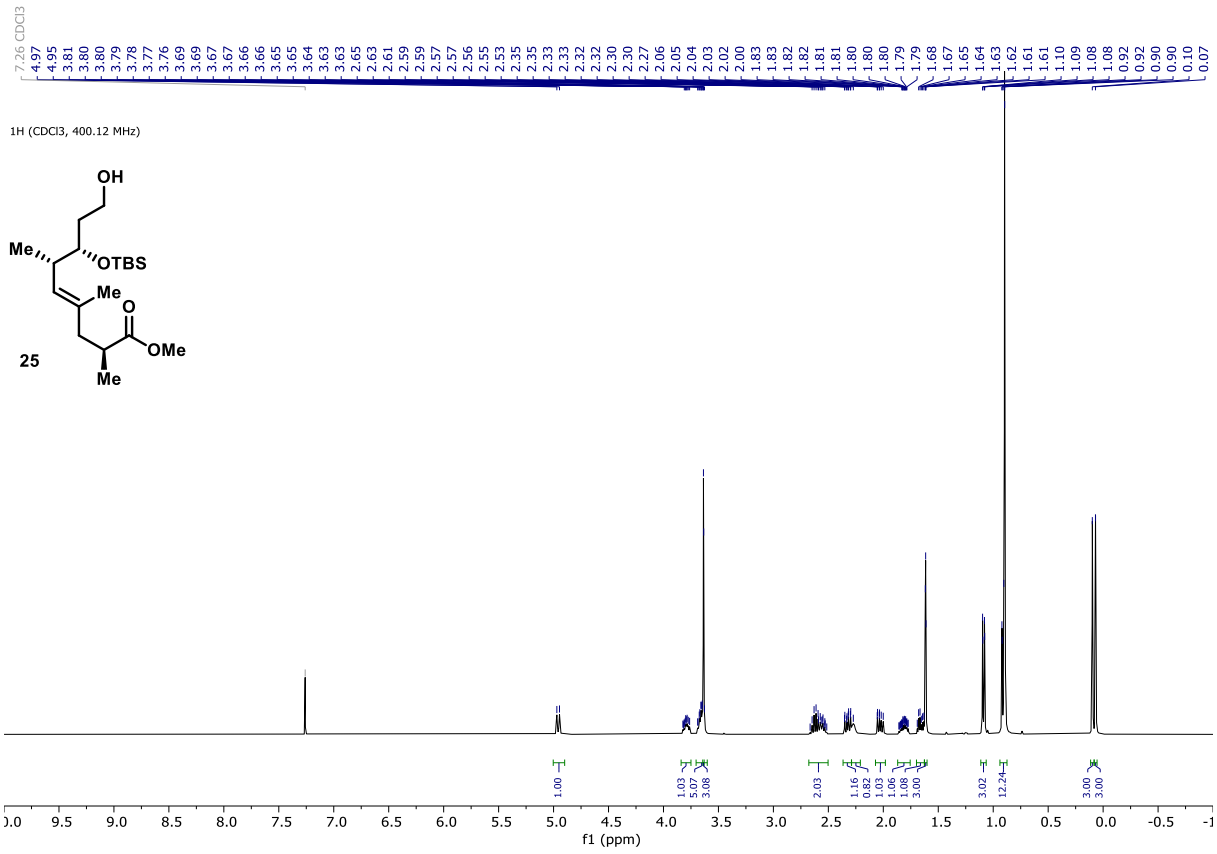

13C (CDCl3, 100.62 MHz)
f1 (ppm)

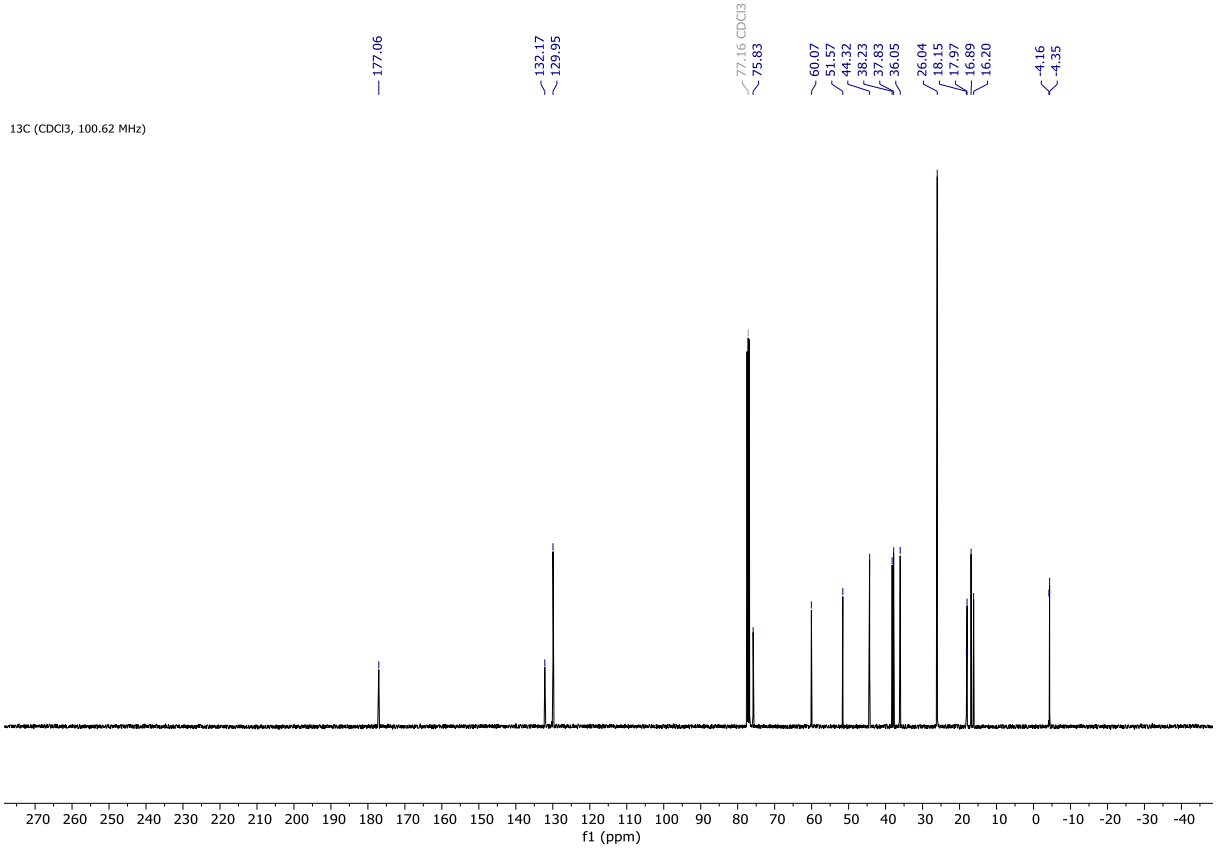

1H (CDCl3, 400.12 MHz)
OTBS
Me
OTBS
Me
24
f1 (ppm)

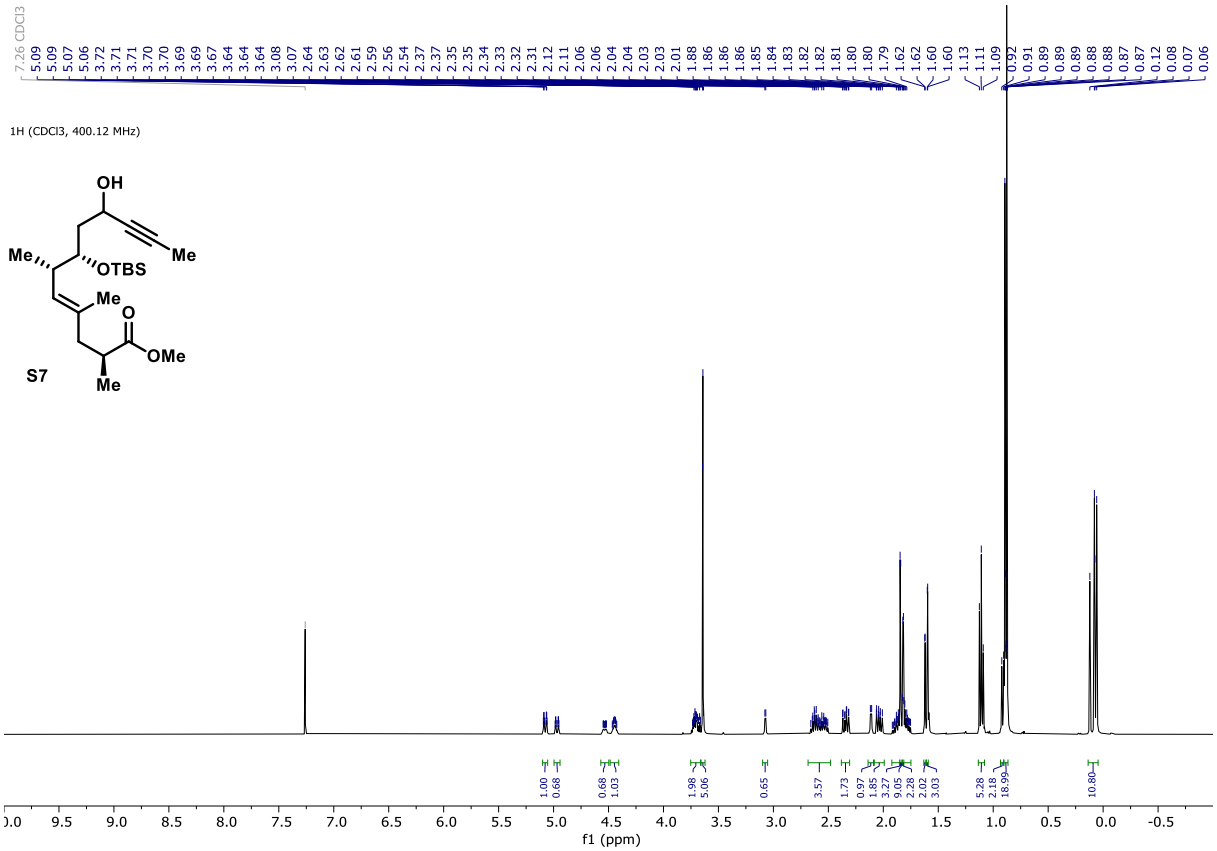

13C (CDCl3, 100.62 MHz)
f1 (ppm)

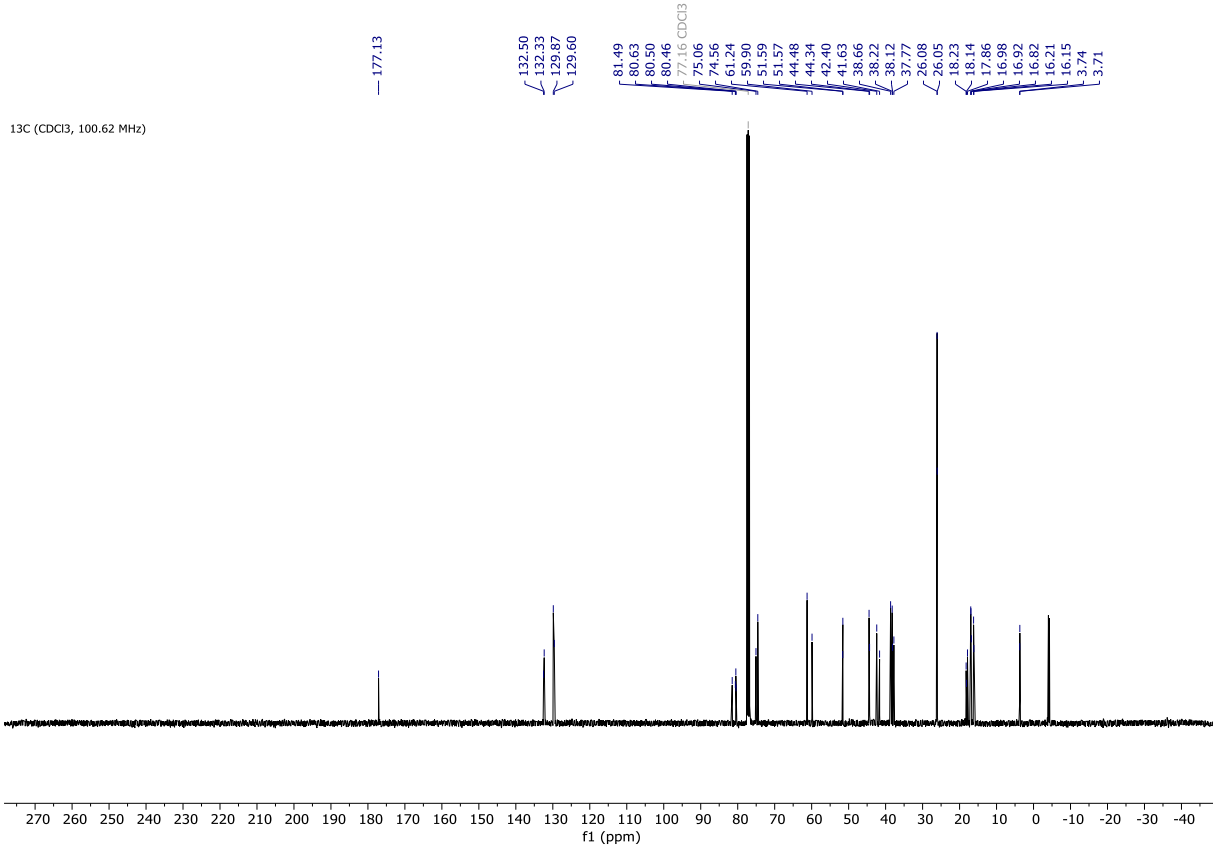

7.26 CDCl3
5.07 5.06 5.06 5.06 5.04 5.04 5.04 5.03 3.66 3.64 3.63 3.62 3.61 3.61 3.60 3.60 3.60 3.58 2.65 2.63 2.61 2.61 2.59 2.59 2.45 2.44 2.43 2.42 2.41 2.41 2.40 2.40 2.39 2.37 2.37 2.35 2.35 2.34 2.33 2.32 2.31 2.05 2.05 2.03 2.03 2.02 2.01 2.00 2.00 1.71 1.70 1.68 1.67 1.66 1.66 1.64 1.63 1.61 1.60 1.59 1.11 1.10 0.89 0.88 0.88 0.87 0.86 0.04 0.03 0.03
1H (CDCl3, 400.12 MHz)
OTBS
Me
OTBS
Me
O
S6
OMe
Me
1.00
3.03
6.47
0.99
1.03
1.01
0.98
2.07
3.15
3.02
22.28
6.21
5.91
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

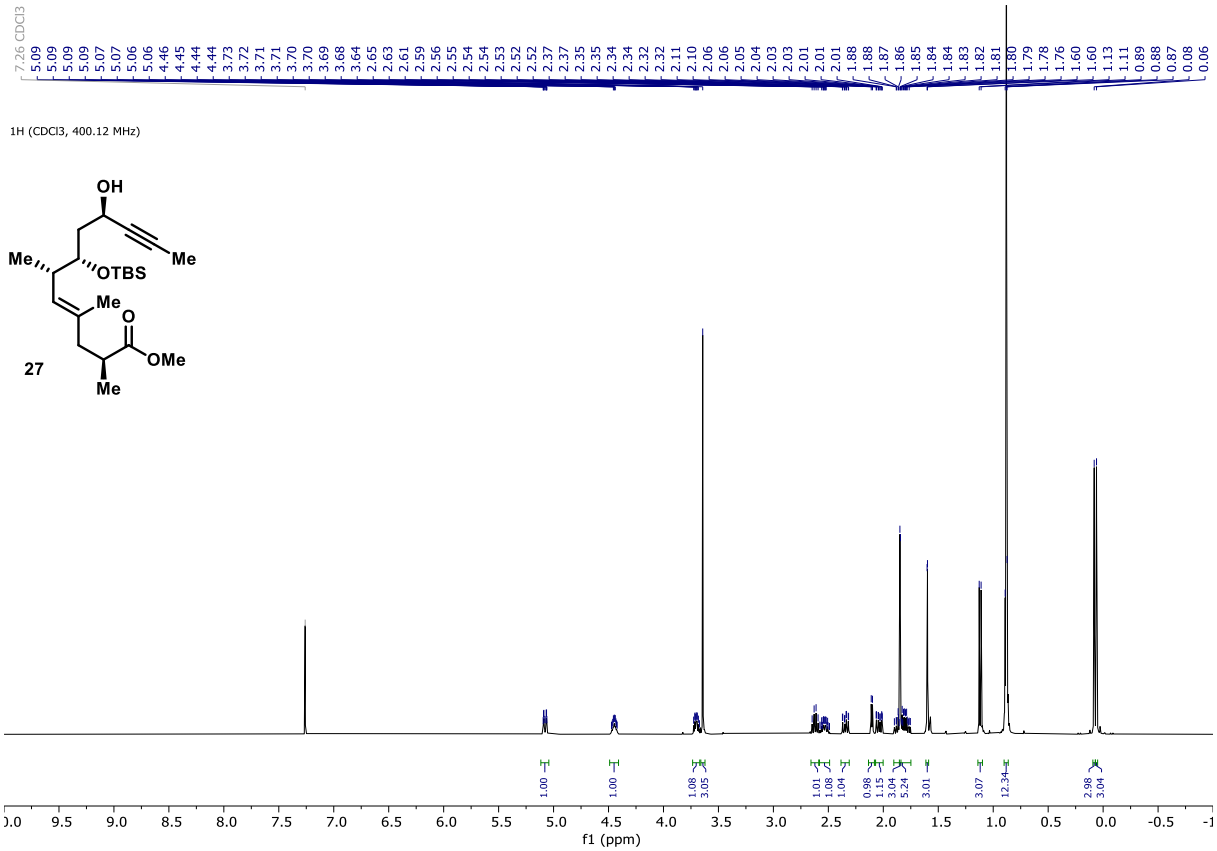

177.17
131.43
130.92
77.16 CDCl3
73.56
60.05
51.54
44.55
38.22
38.16
37.87
26.11
26.08
18.29
16.80
16.01
-4.19
-4.21
-5.13
-5.16
13C (CDCl3, 100.62 MHz)
270 260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

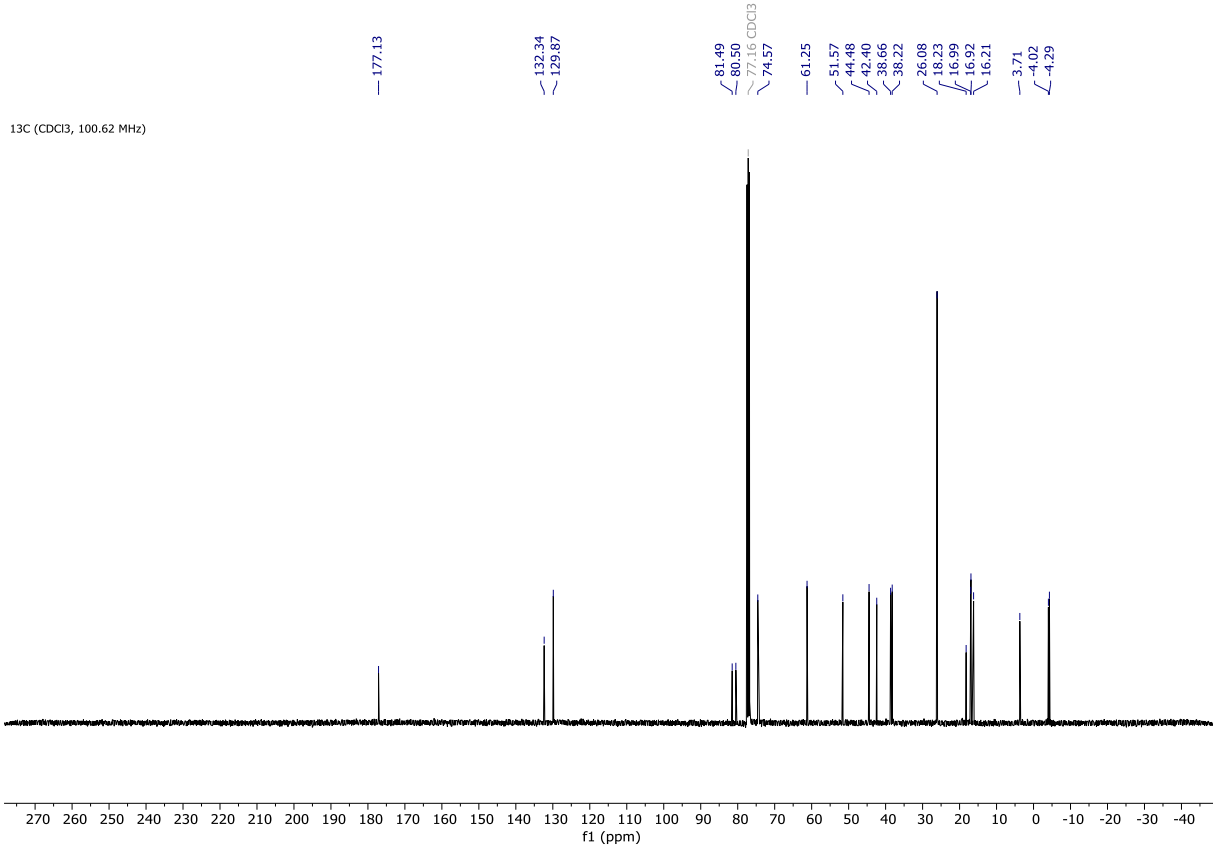

1H (CDCl3, 400.12 MHz)
OH
Me
OTBS
Me
O
OMe
25
Me
f1 (ppm)

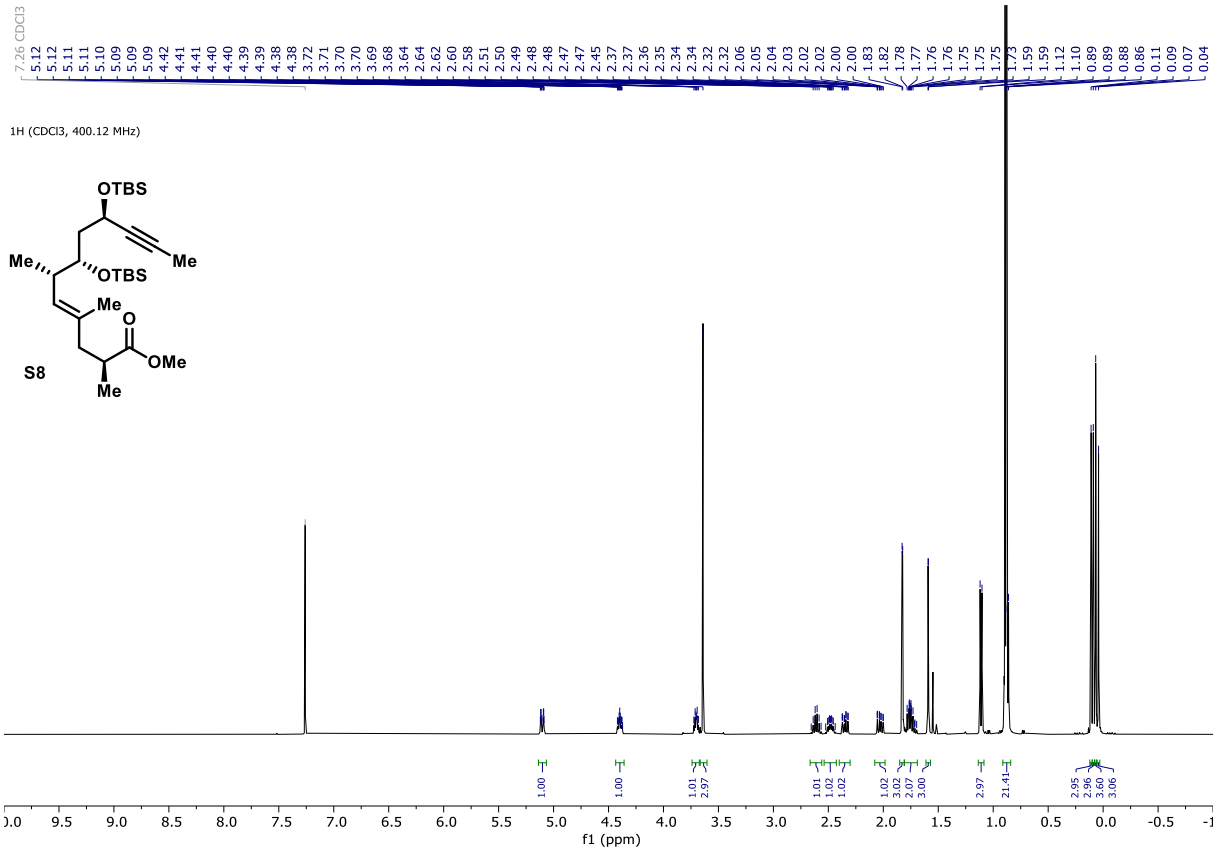

13C (CDCl3, 100.62 MHz)
f1 (ppm)

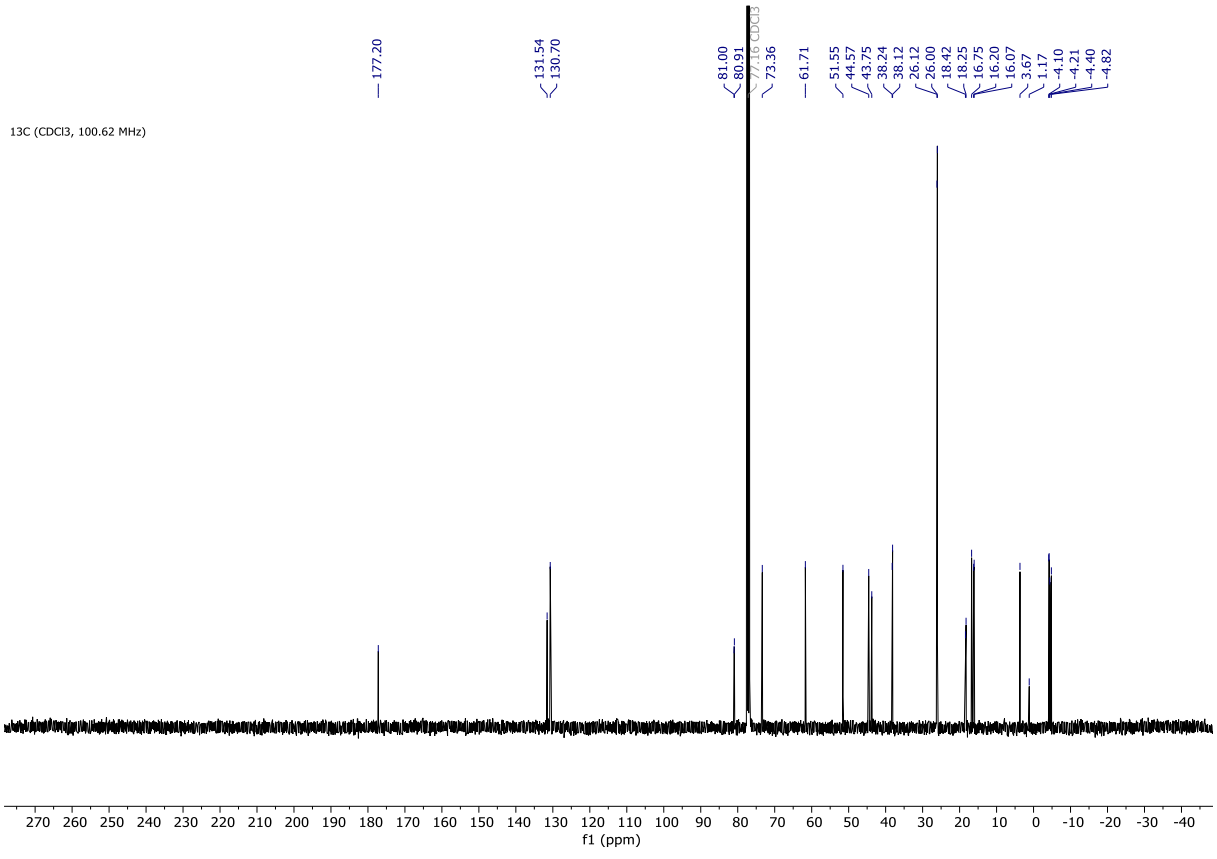

1H (CDCl3, 400.12 MHz)
OH
Me
OTBS
Me
Me
O
OMe
Me
S7
f1 (ppm)

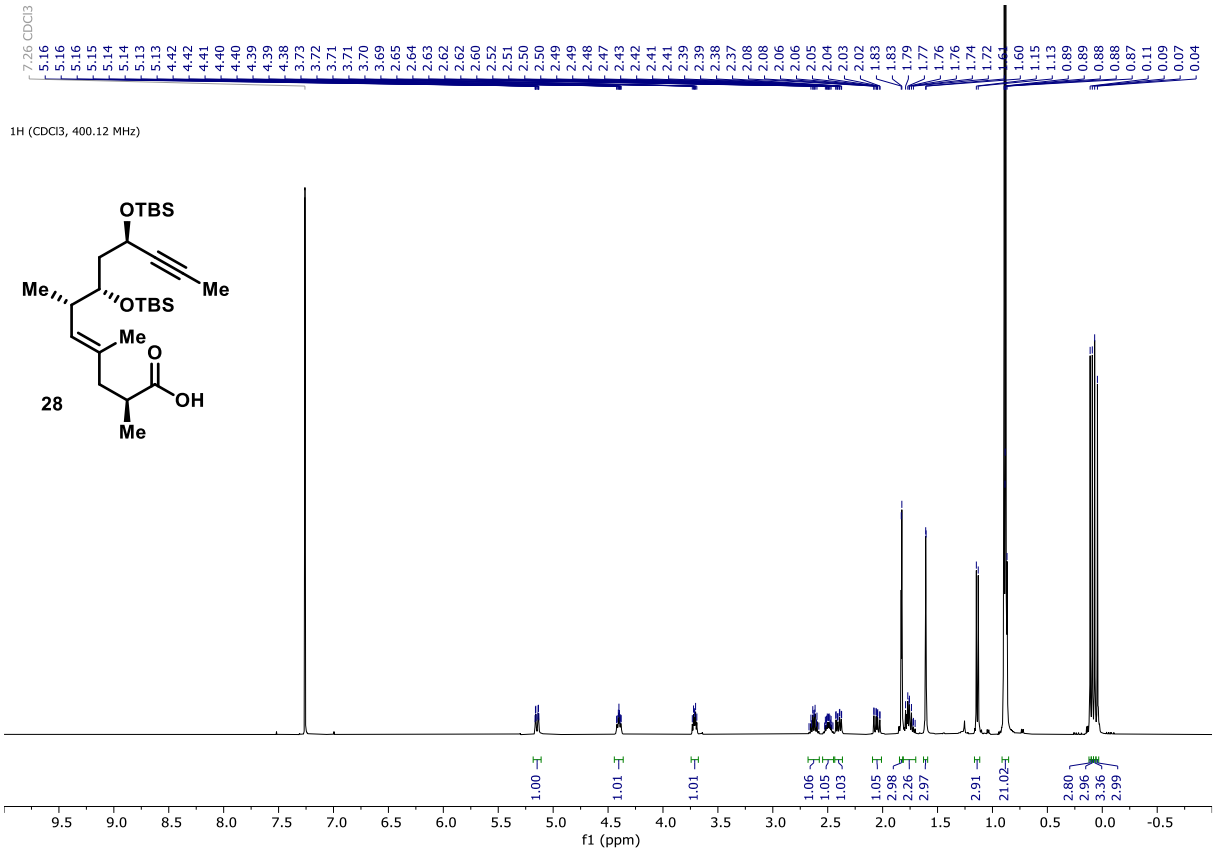

13C (CDCl3, 100.62 MHz)
f1 (ppm)

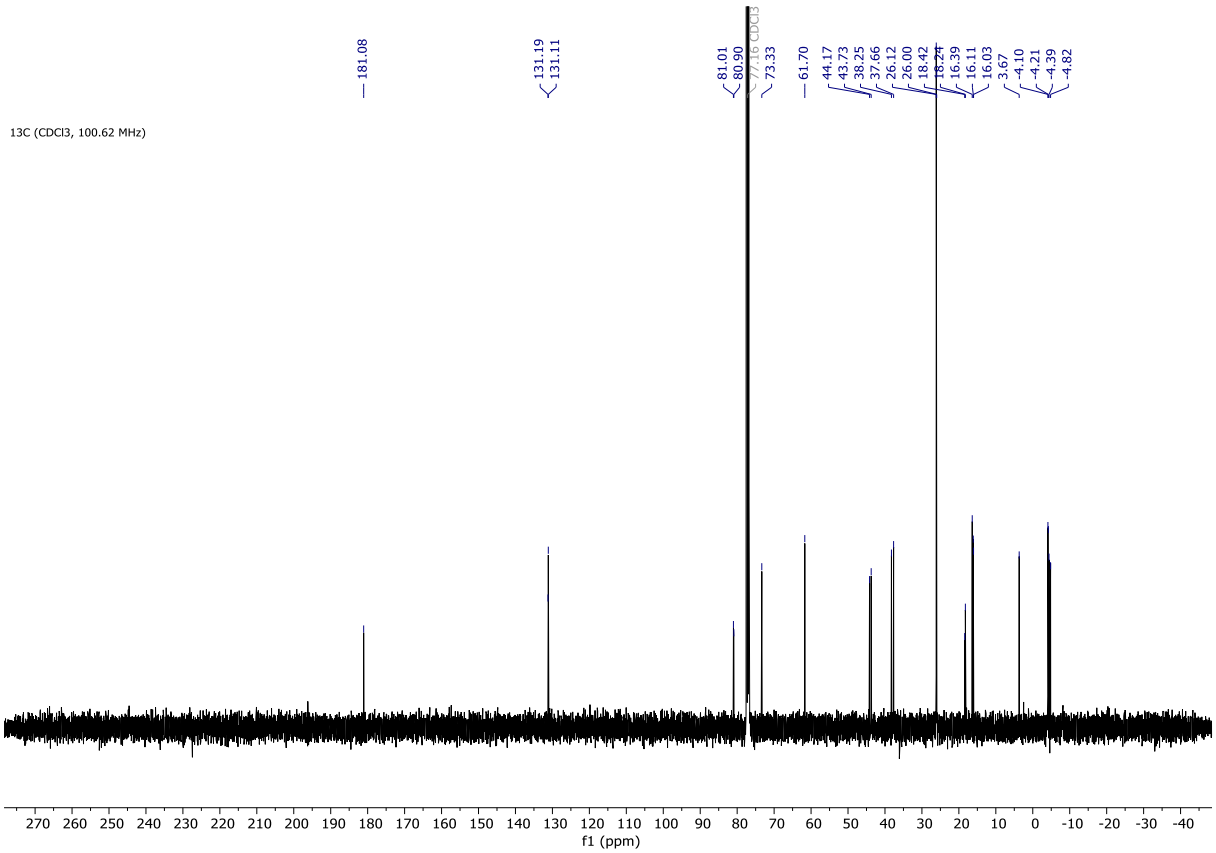

7.26 CDCl3
5.09 5.09 5.09 5.09 5.07 5.07 5.06 5.06 4.46 4.45 4.44 4.44 3.73 3.72 3.71 3.71 3.70 3.70 3.69 3.68 3.64 2.65 2.63 2.61 2.59 2.56 2.55 2.54 2.54 2.53 2.52 2.52 2.37 2.37 2.35 2.35 2.34 2.34 2.32 2.32 2.11 2.10 2.06 2.06 2.05 2.04 2.03 2.03 2.01 2.01 2.01 1.88 1.88 1.87 1.86 1.85 1.84 1.84 1.83 1.82 1.81 1.80 1.79 1.78 1.76 1.60 1.13 1.11 0.89 0.88 0.87 0.08 0.06
1H (CDCl3, 400.12 MHz)
OH
Me
Me
OTBS
Me
O
OMe
27
Me
1.00 1.00 1.08 3.05 1.01 1.08 1.04 0.98 1.15 3.04 5.24 3.01 3.07 12.34 2.98 3.04
f1 (ppm)

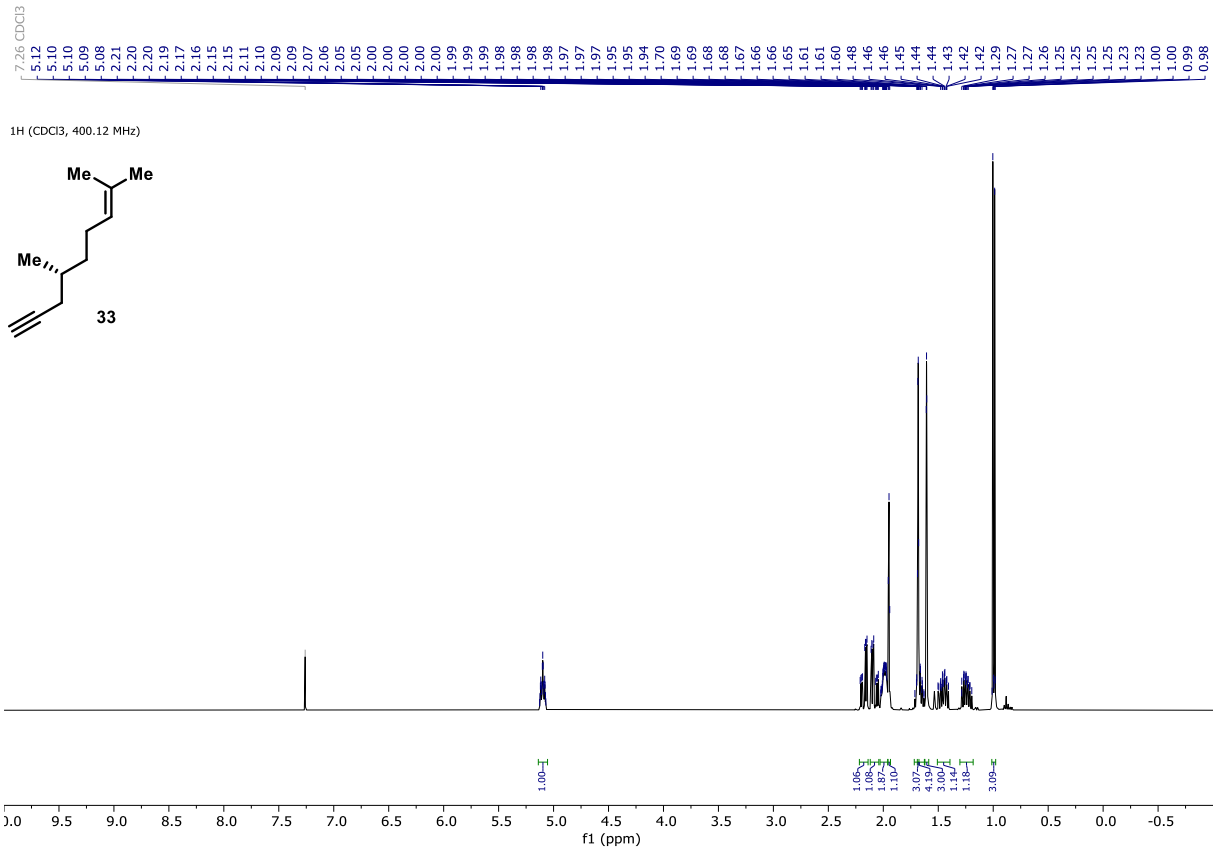

177.13
132.34 129.87
81.49 80.50 77.16 CDCl3 74.57
61.25
51.57 44.48 42.40 38.66 38.22
26.08 18.23 16.99 16.92 16.21
3.71 -4.02 -4.29
13C (CDCl3, 100.62 MHz)
f1 (ppm)

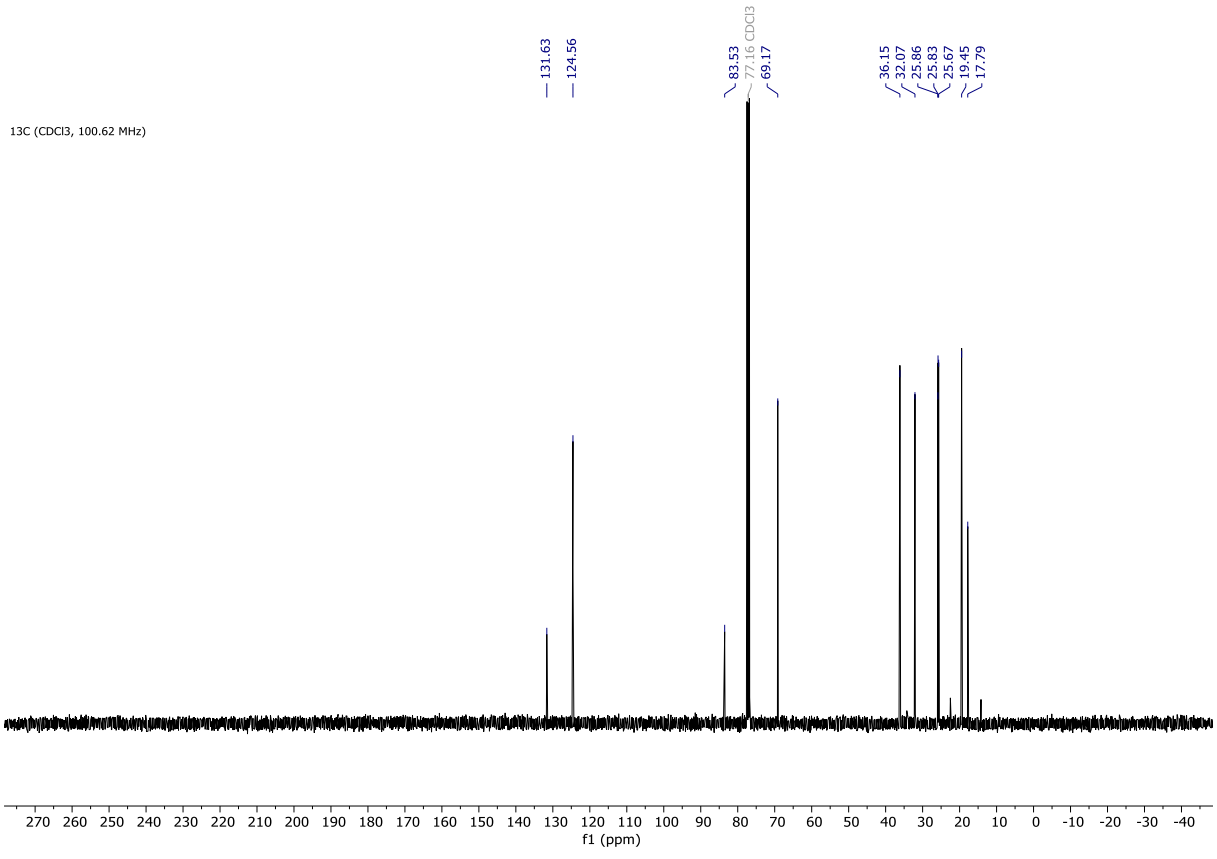

1H (CDCl3, 400.12 MHz)
OTBS
Me
OTBS
Me
Me
O
OMe
S8
Me
f1 (ppm)

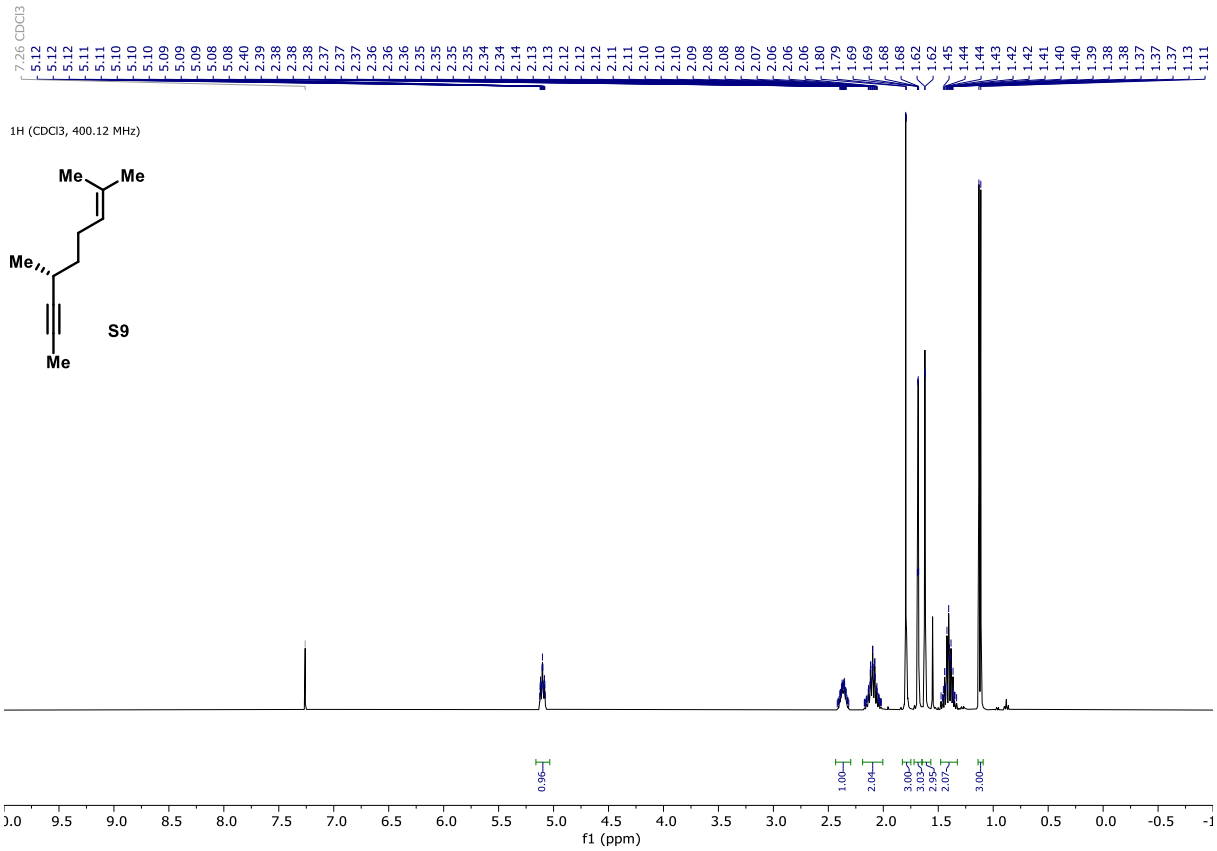

13C (CDCl3, 100.62 MHz)
177.20
131.54
130.70
81.00
80.91
77.16 CDCl3
73.36
61.71
51.55
44.57
43.75
38.24
38.12
26.12
26.00
18.42
18.25
16.75
16.20
16.07
3.67
1.17
-4.10
-4.21
-4.40
-4.82
f1 (ppm)

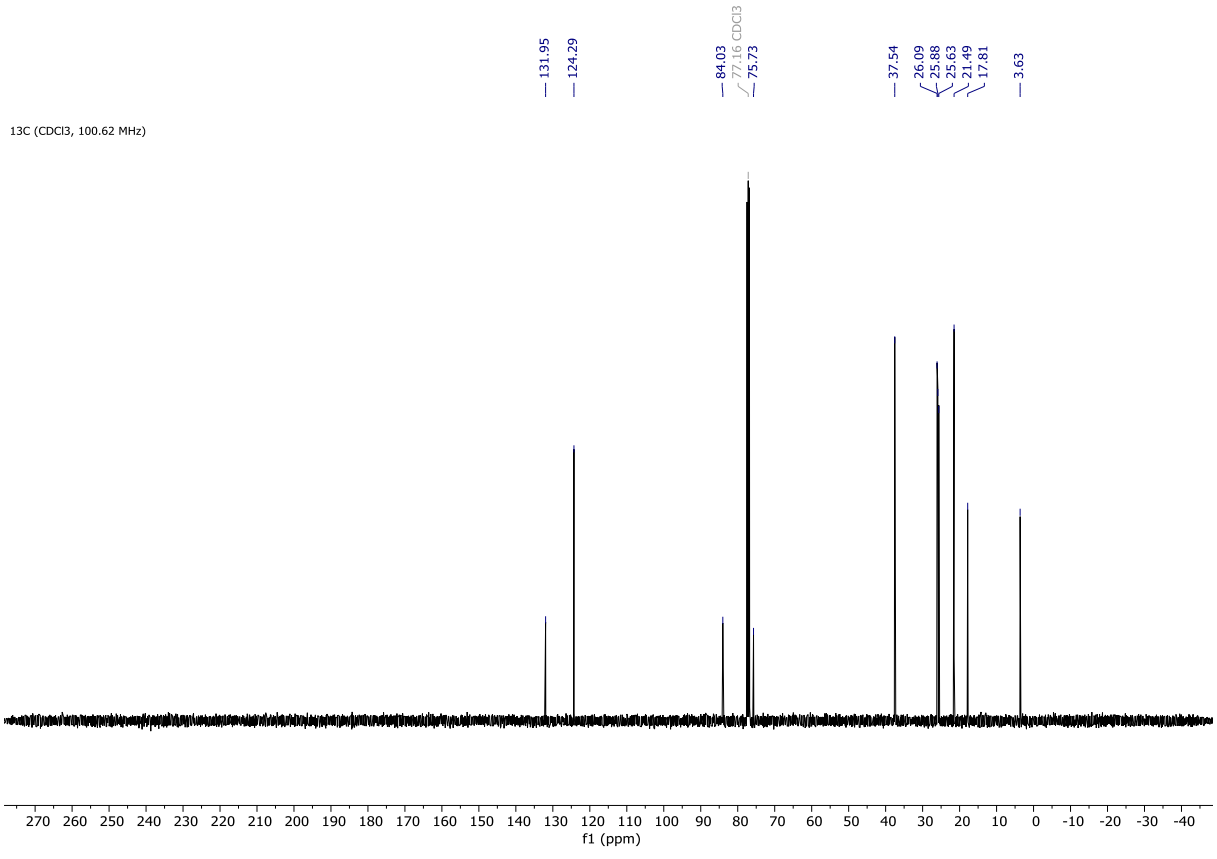

1H (CDCl3, 400.12 MHz)
OTBS
Me
OTBS
Me
Me
O
OH
28
Me
1.00
1.01
1.01
1.06
1.05
1.03
1.05
2.98
2.26
2.97
2.91
21.02
2.80
2.96
3.36
2.99
f1 (ppm)

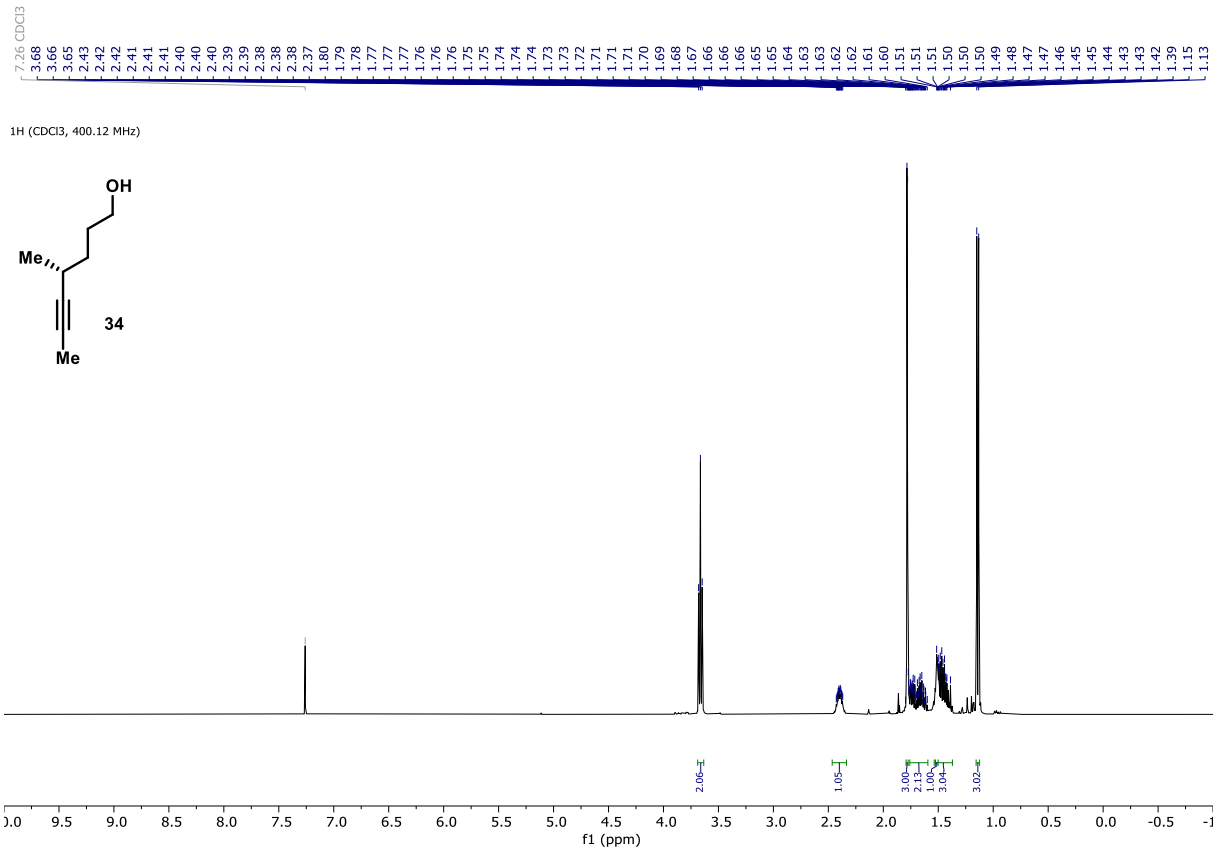

13C (CDCl3, 100.62 MHz)
181.08
131.19
131.11
81.01
80.90
77.16 CDCl3
73.33
61.70
44.17
43.73
38.25
37.66
26.12
26.00
18.42
18.24
16.39
16.11
16.03
3.67
-4.10
-4.21
-4.39
-4.82
f1 (ppm)

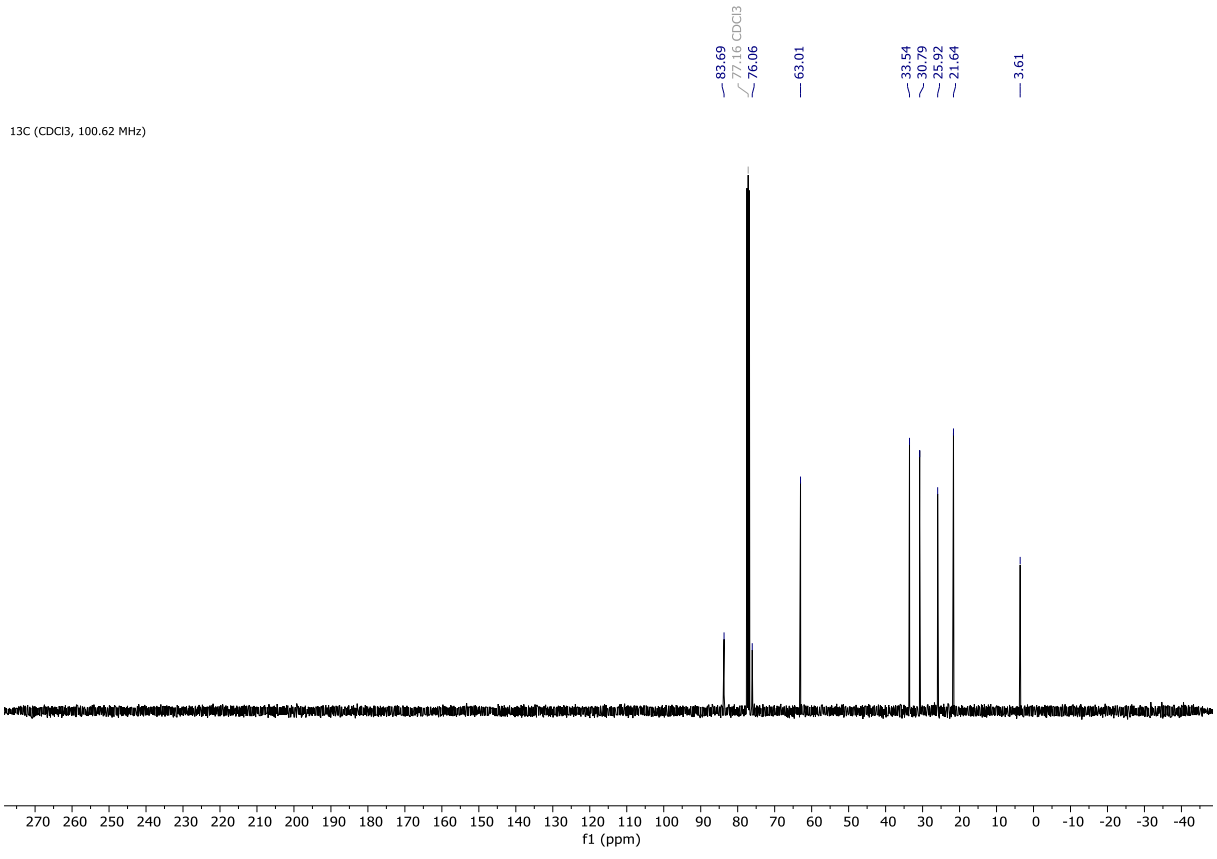

7.26 CDCl3
5.12 5.10 5.10 5.09 5.08 2.21 2.20 2.20 2.19 2.17 2.16 2.15 2.15 2.11 2.10 2.09 2.09 2.07 2.06 2.05 2.05 2.00 2.00 2.00 2.00 2.00 1.99 1.99 1.98 1.98 1.98 1.97 1.97 1.97 1.95 1.94 1.70 1.69 1.69 1.68 1.68 1.67 1.66 1.66 1.65 1.61 1.61 1.60 1.48 1.46 1.46 1.45 1.44 1.44 1.43 1.42 1.42 1.29 1.27 1.27 1.26 1.25 1.25 1.25 1.23 1.23 1.00 1.00 0.99 0.98
1H (CDCl3, 400.12 MHz)
Me
Me
Me
33
1.00
1.06
1.08
1.87
1.10
3.07
4.19
3.00
1.14
1.18
3.09
f1 (ppm)

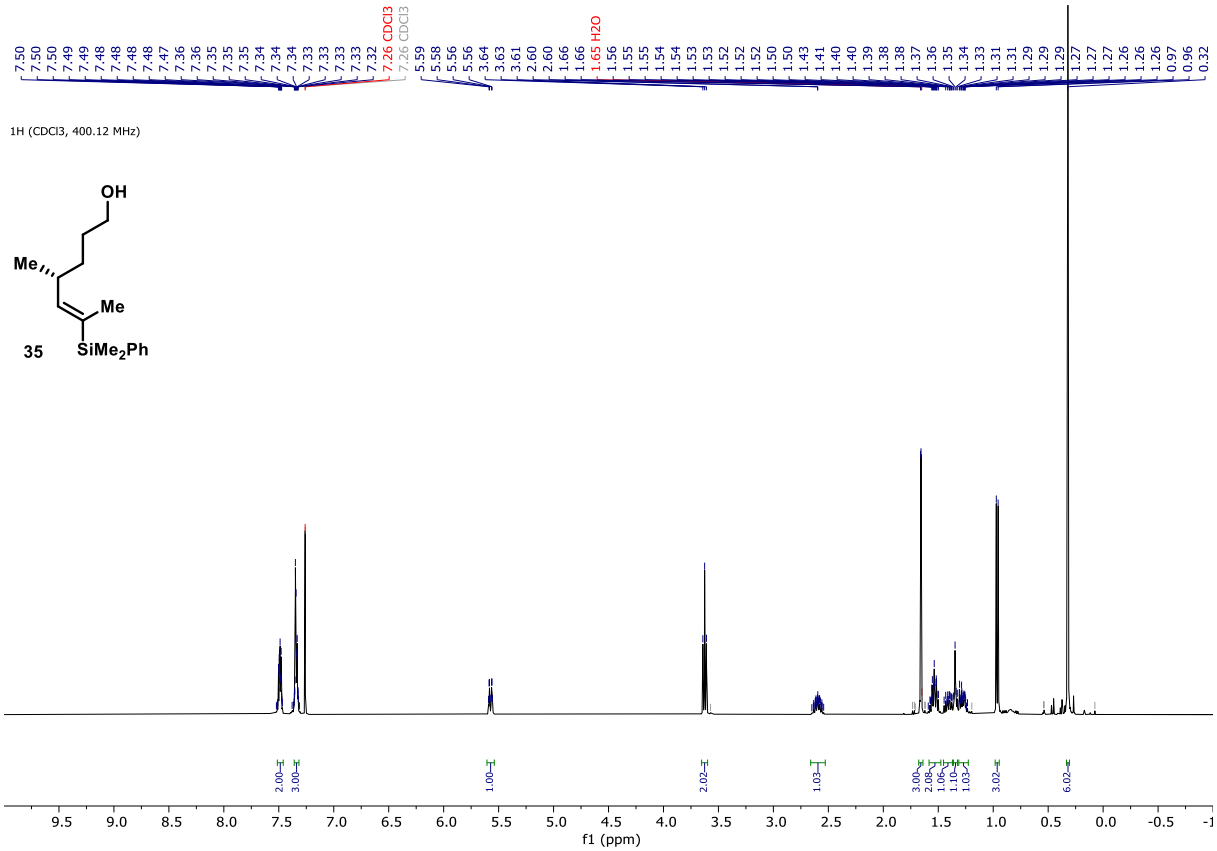

131.63
124.56
83.53
77.16 CDCl3
69.17
36.15
32.07
25.86
25.83
25.67
19.45
17.79
13C (CDCl3, 100.62 MHz)
f1 (ppm)

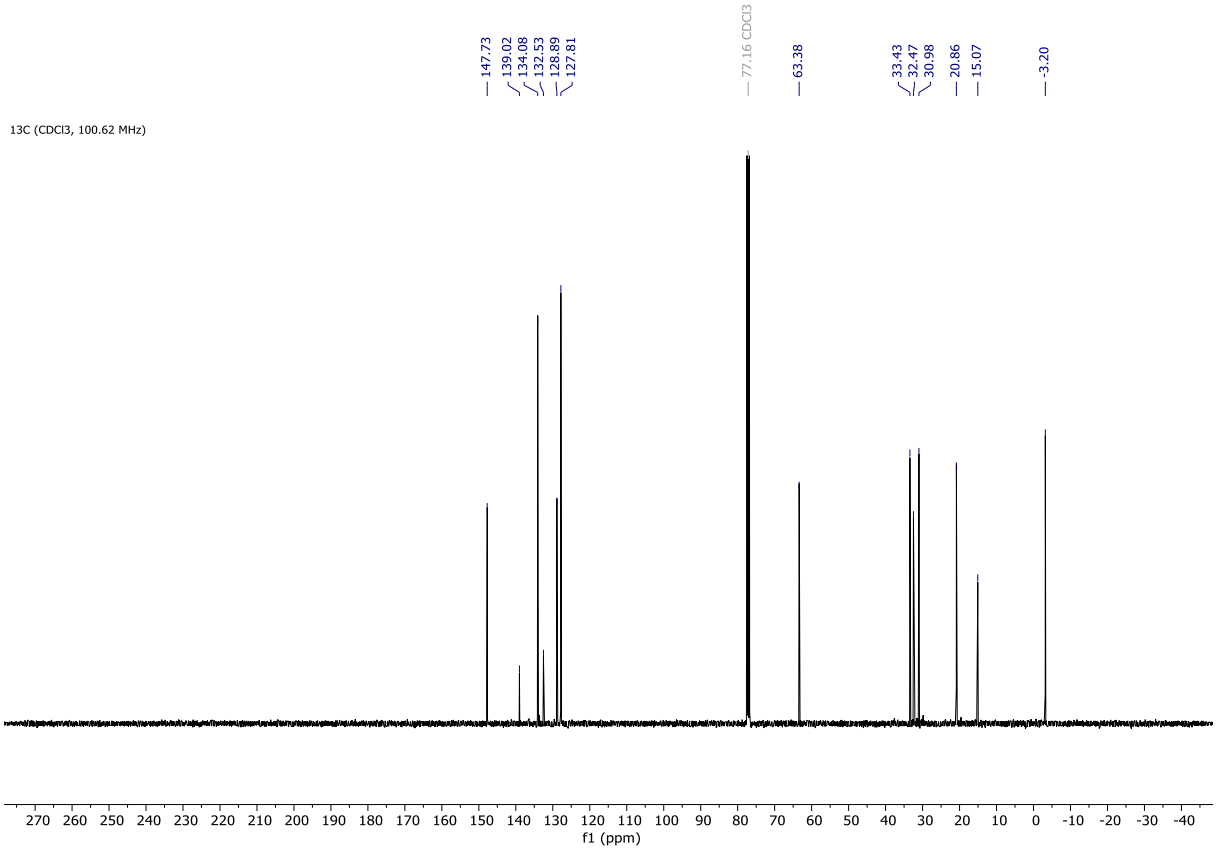

1H (CDCl3, 400.12 MHz)
Me
Me
Me
S9
Me
f1 (ppm)

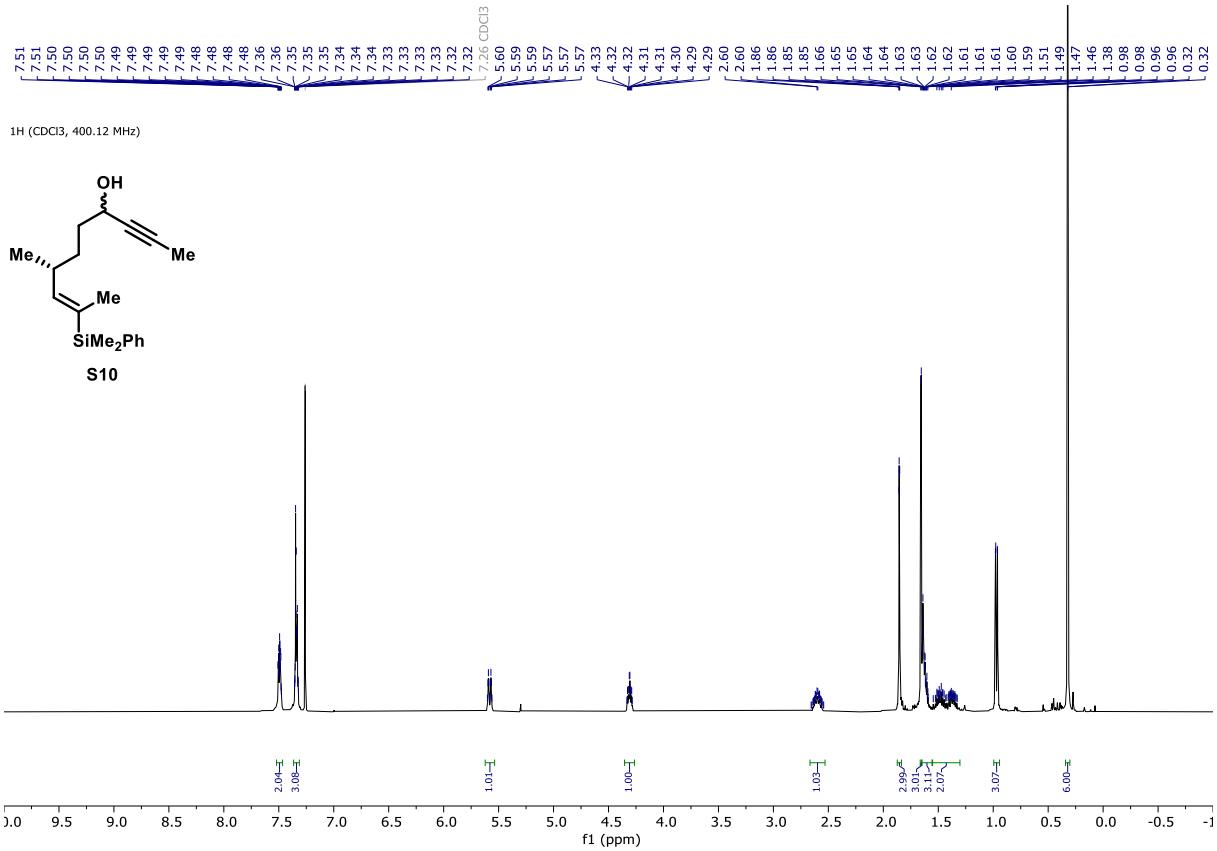

131.95
124.29
84.03
77.16 CDCl3
75.73
37.54
26.09
25.88
25.63
21.49
17.81
3.63
13C (CDCl3, 100.62 MHz)
f1 (ppm)

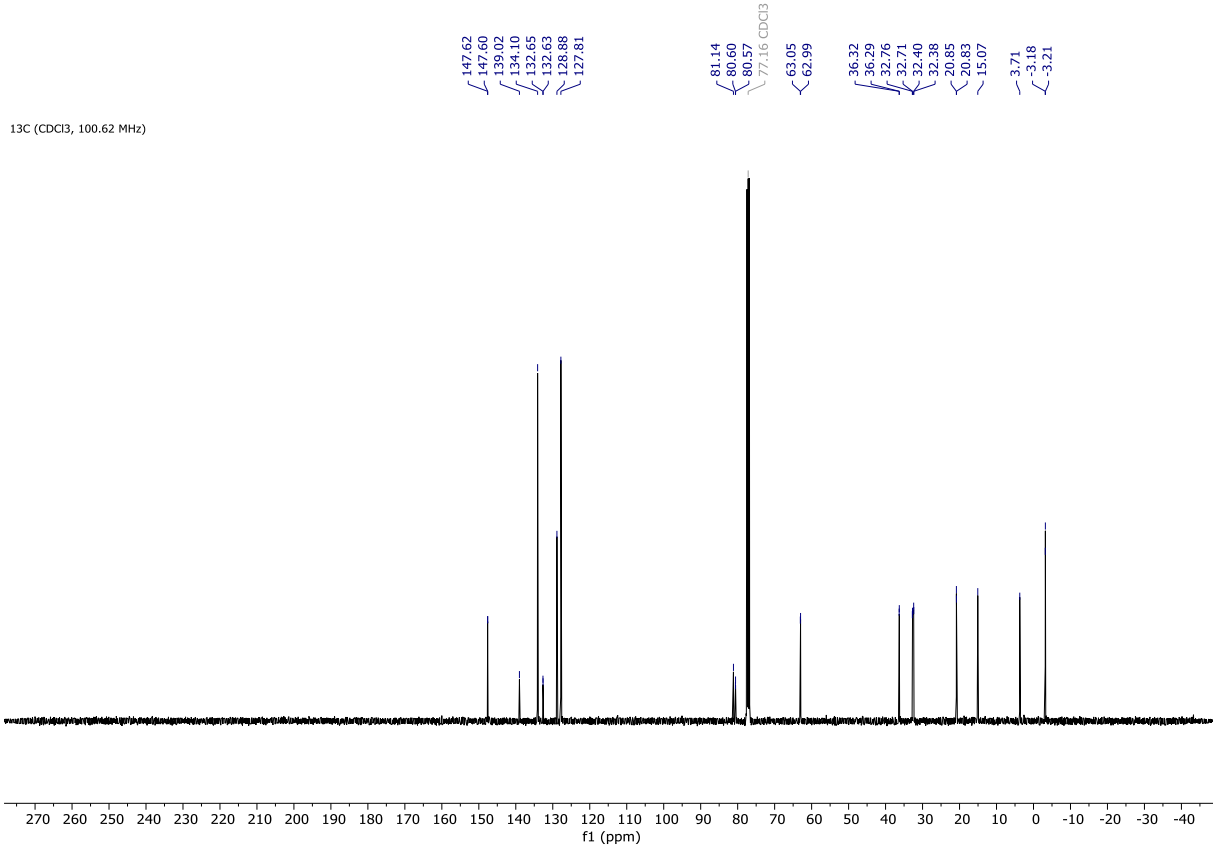

7.26 CDCl3
3.68 3.66 3.65 2.43 2.42 2.42 2.41 2.41 2.41 2.40 2.40 2.40 2.39 2.39 2.38 2.38 2.38 2.37 1.80 1.79 1.78 1.77 1.77 1.77 1.76 1.76 1.76 1.75 1.75 1.74 1.74 1.74 1.73 1.73 1.72 1.71 1.71 1.71 1.70 1.69 1.68 1.67 1.66 1.66 1.66 1.65 1.65 1.64 1.63 1.63 1.62 1.62 1.61 1.60 1.51 1.51 1.51 1.50 1.50 1.50 1.49 1.48 1.47 1.47 1.46 1.45 1.45 1.44 1.43 1.43 1.42 1.39 1.15 1.13
1H (CDCl3, 400.12 MHz)
OH
Me
34
Me
2.06
1.05
3.00
2.13
1.00
3.04
3.02
f1 (ppm)

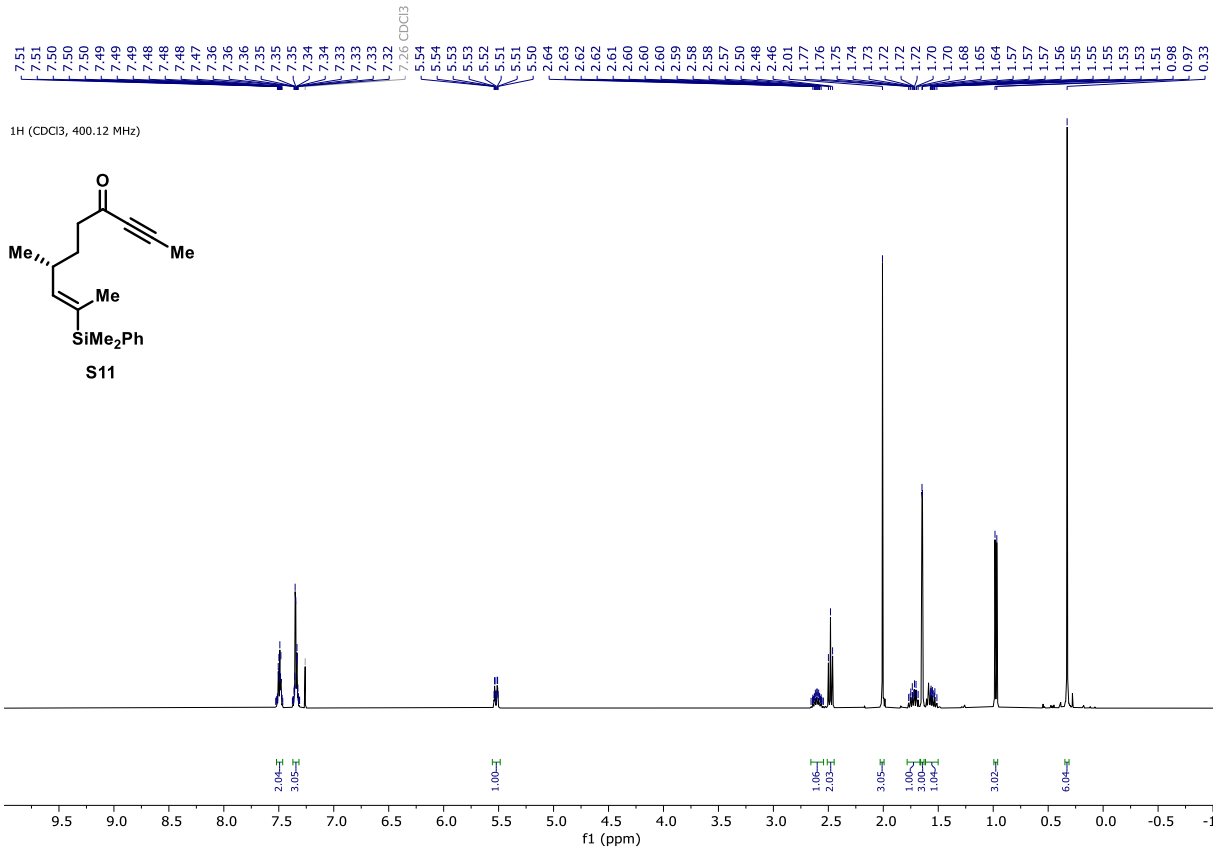

83.69
77.16 CDCl3
76.06
63.01
33.54
30.79
25.92
21.64
3.61
13C (CDCl3, 100.62 MHz)
f1 (ppm)

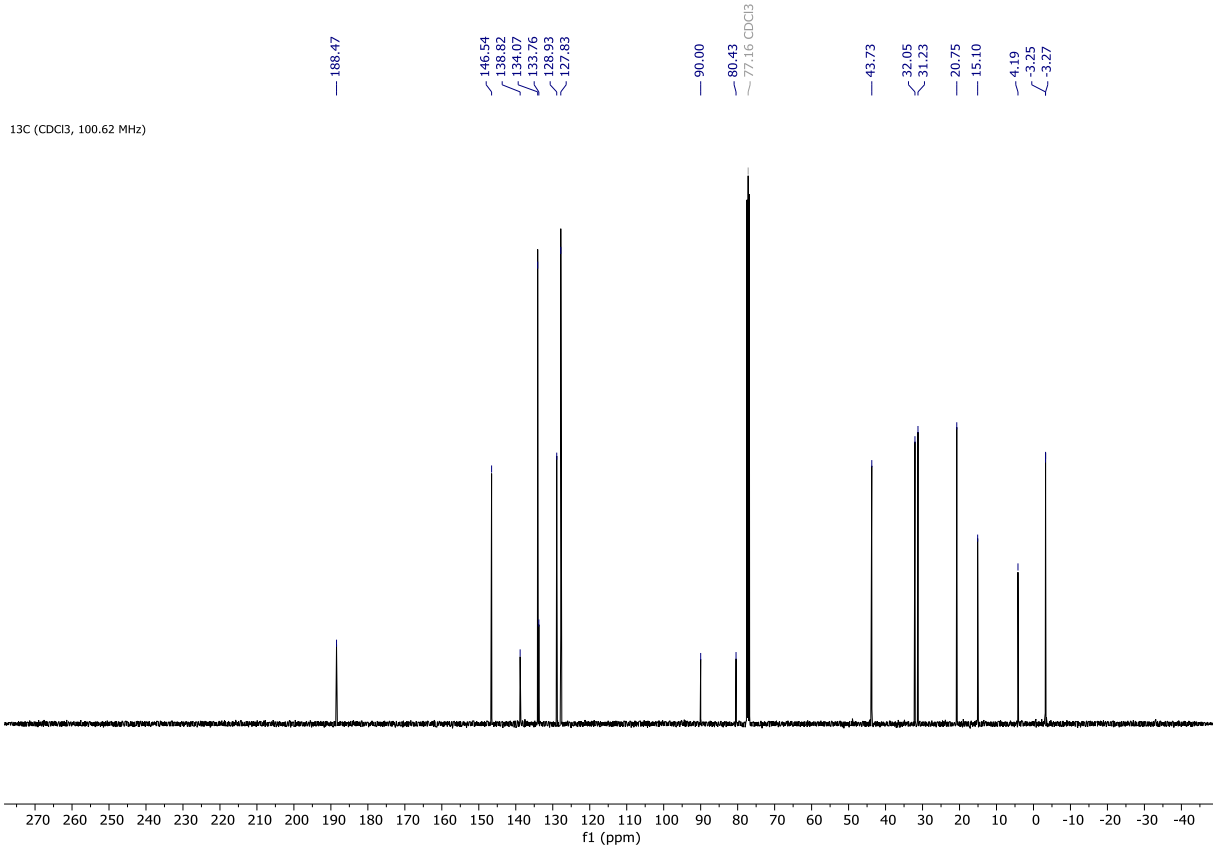

1H (CDCl3, 400.12 MHz)
OH
Me
Me
35
SiMe2Ph
f1 (ppm)

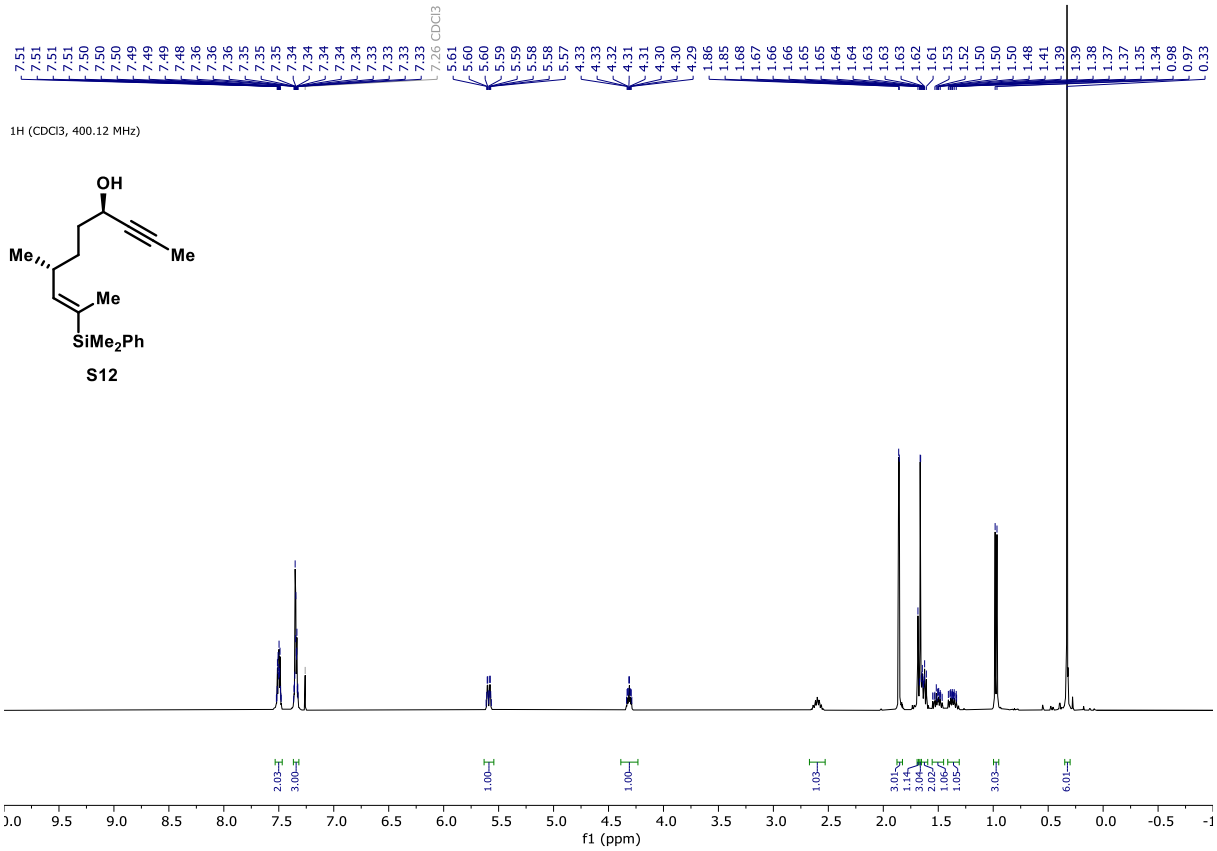

13C (CDCl3, 100.62 MHz)
147.73
139.02
134.08
132.53
128.89
127.81
77.16 CDCl3
63.38
33.43
32.47
30.98
20.86
15.07
-3.20
f1 (ppm)

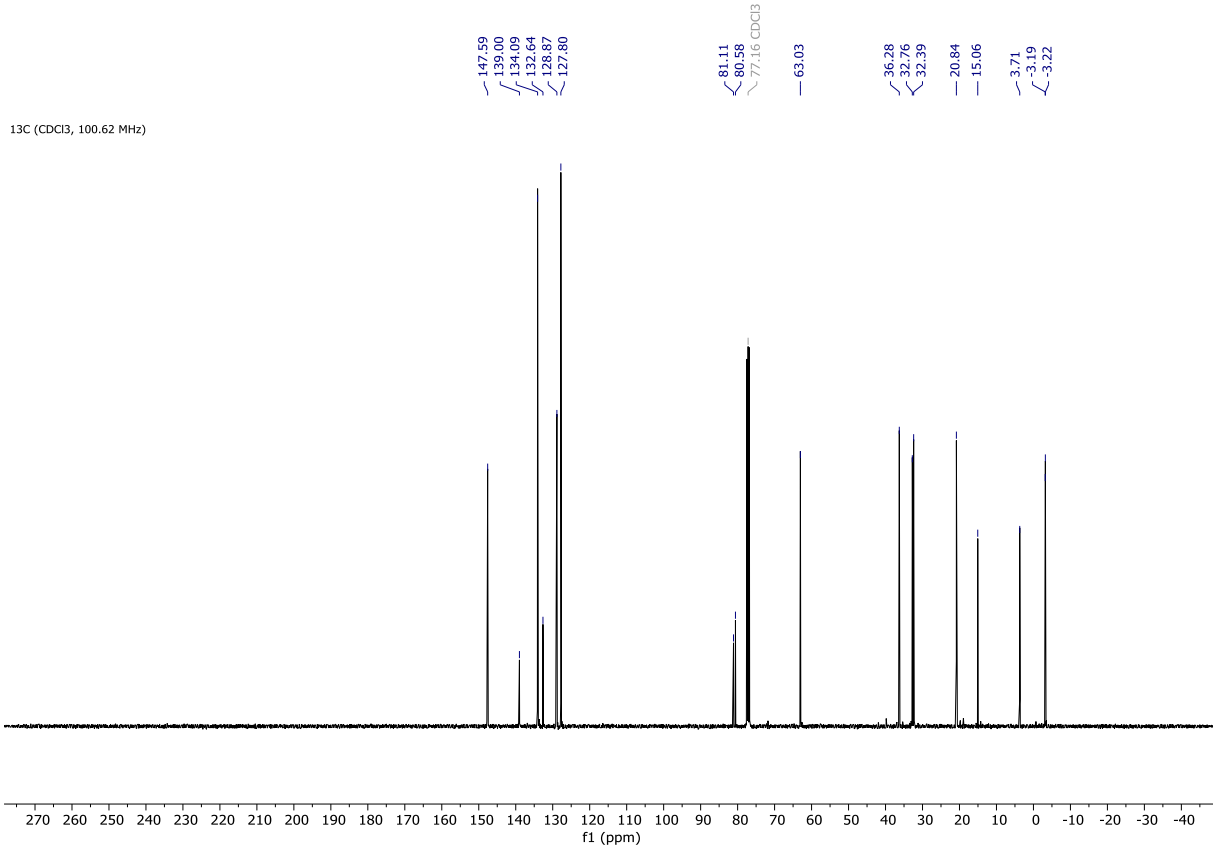

1H (CDCl3, 400.12 MHz)
OH
Me
Me
Me
SiMe2Ph
S10
f1 (ppm)

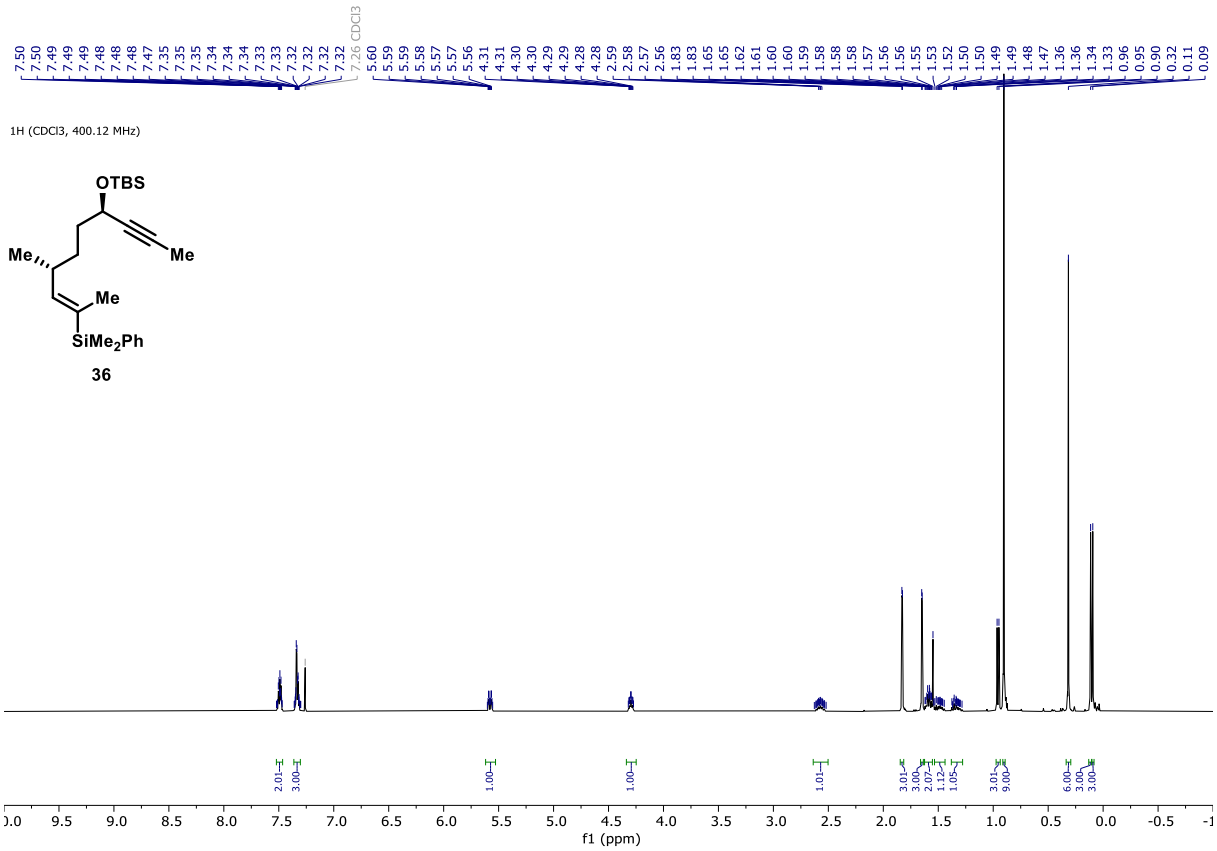

13C (CDCl3, 100.62 MHz)
f1 (ppm)

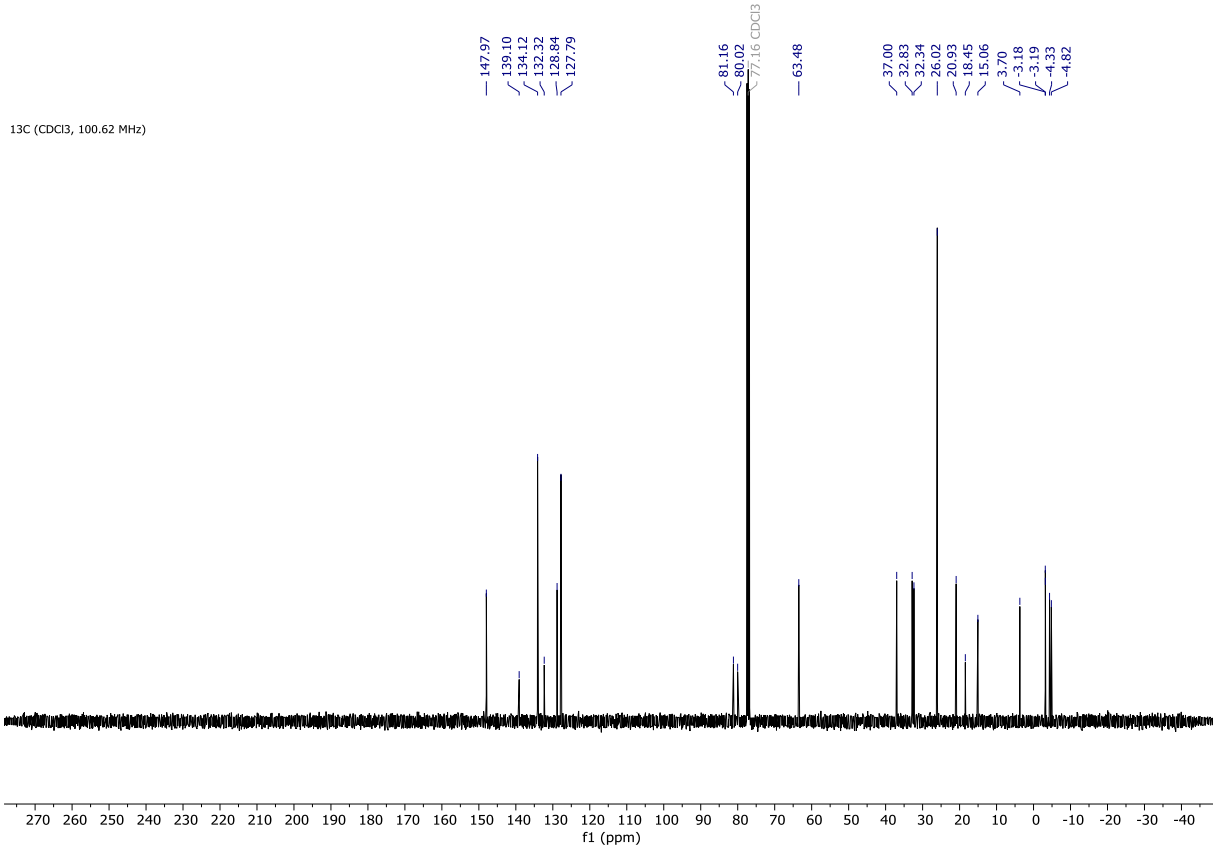

1H (CDCl3, 400.12 MHz)
Me
Me
Me
SiMe2Ph
S11
f1 (ppm)

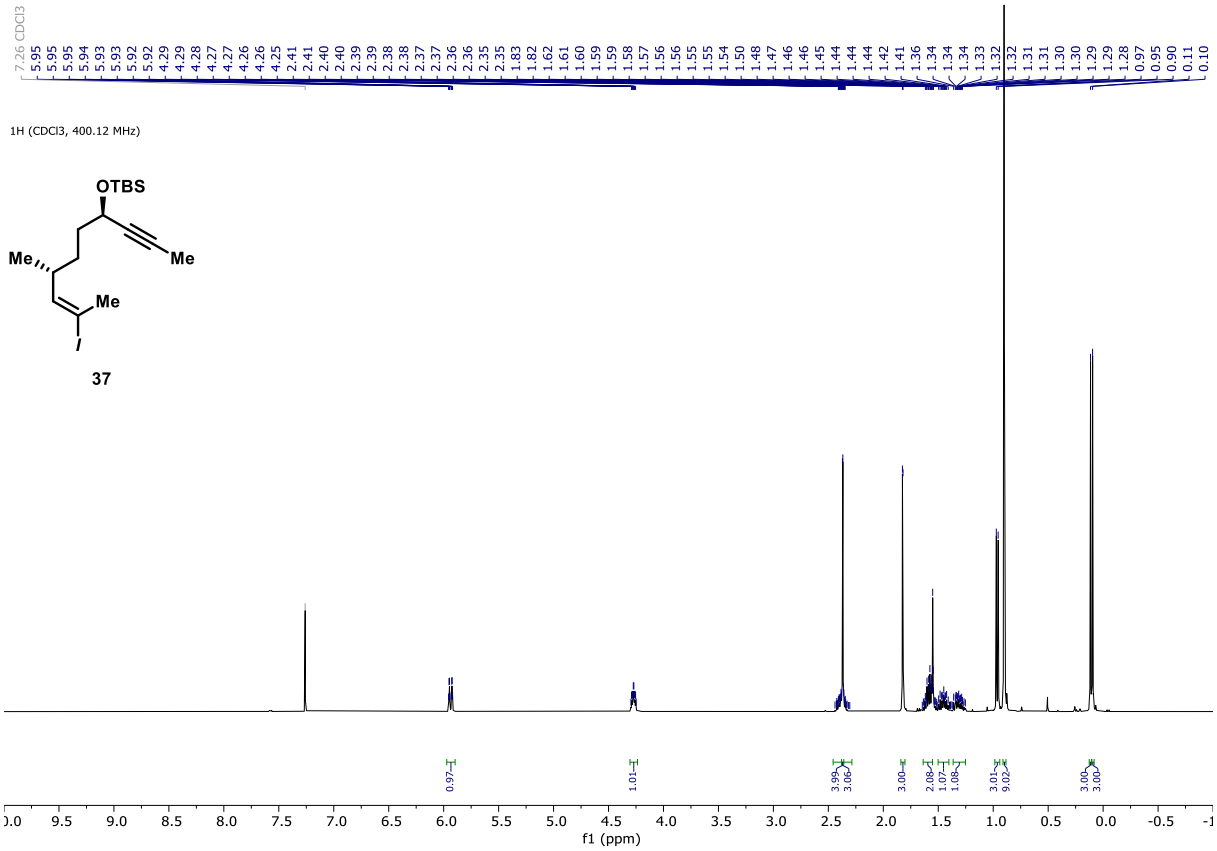

13C (CDCl3, 100.62 MHz)
f1 (ppm)

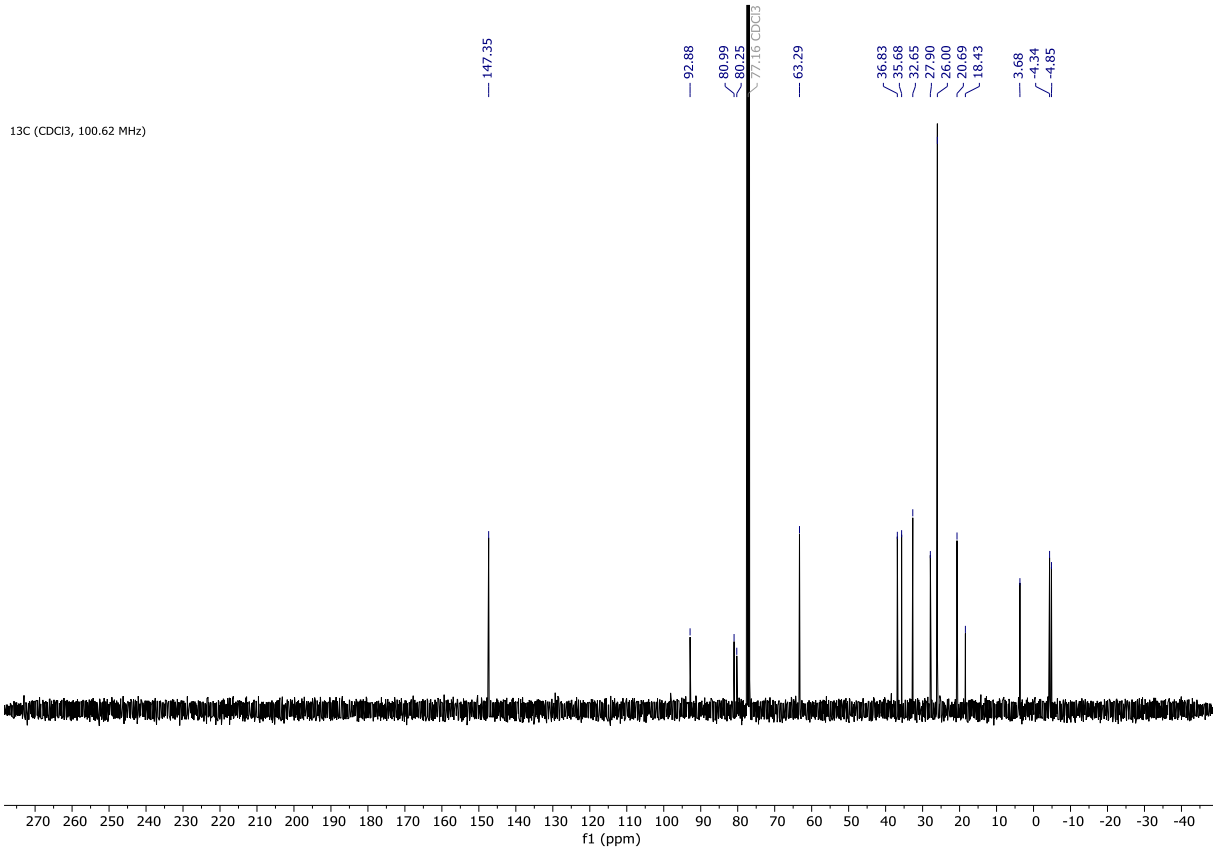

1H (CDCl3, 400.12 MHz)
OH
Me
Me
Me
SiMe2Ph
S12
f1 (ppm)

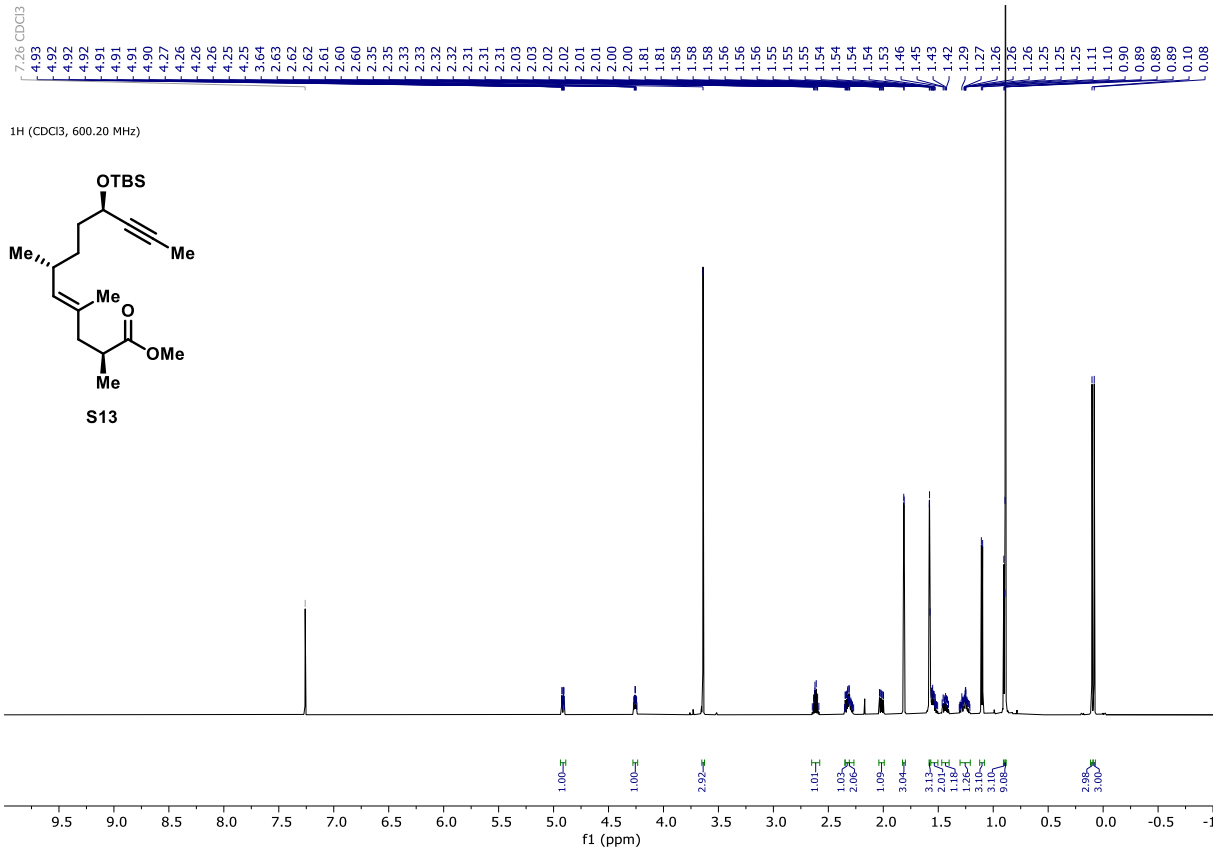

13C (CDCl3, 100.62 MHz)
f1 (ppm)

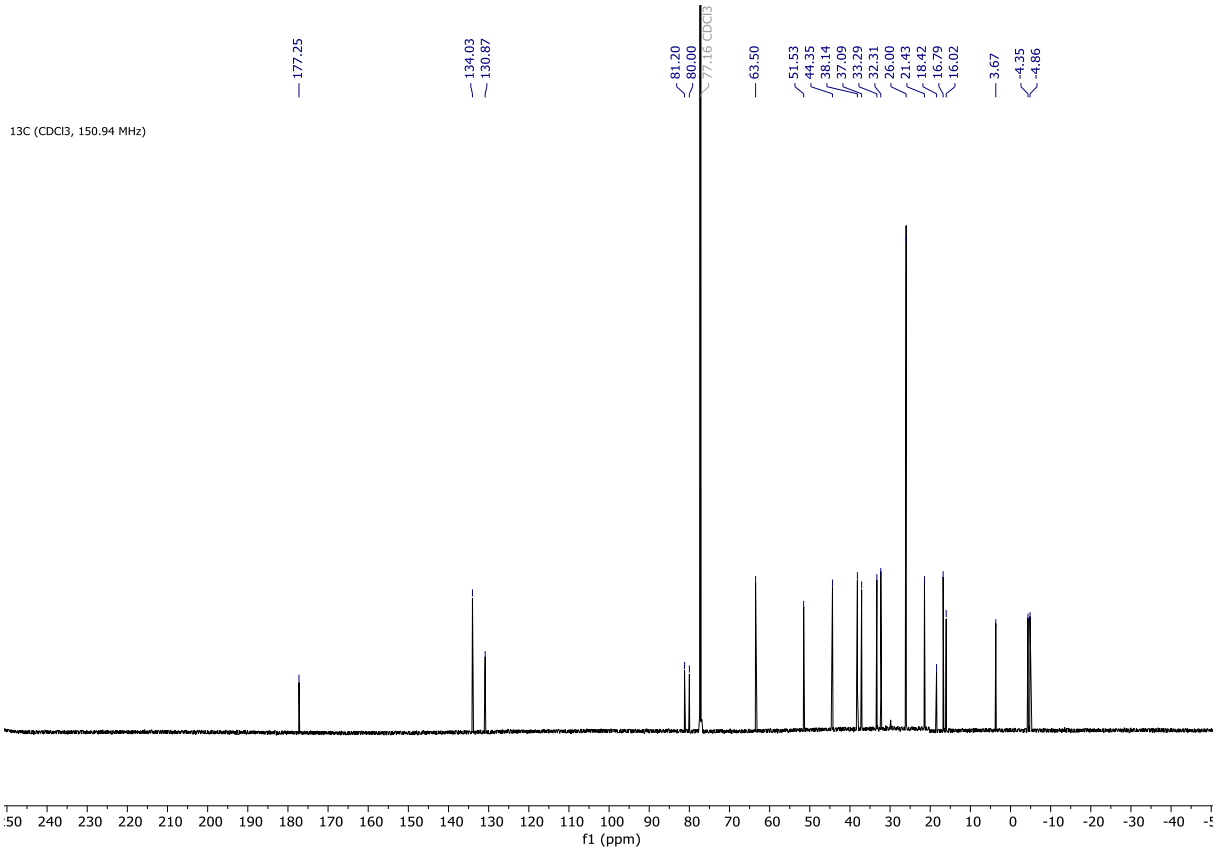

1H (CDCl3, 400.12 MHz)
OTBS
Me
Me
Me
SiMe2Ph
36
f1 (ppm)

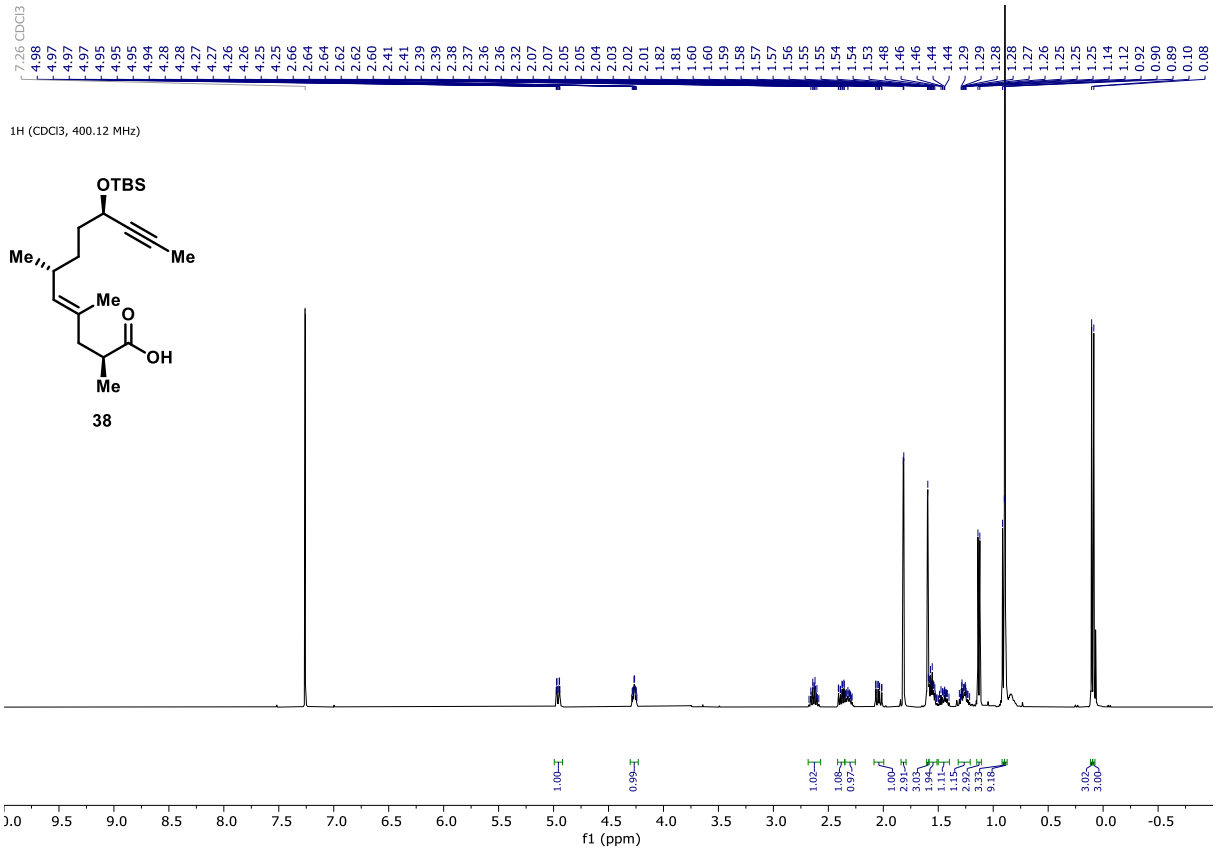

13C (CDCl3, 100.62 MHz)
f1 (ppm)

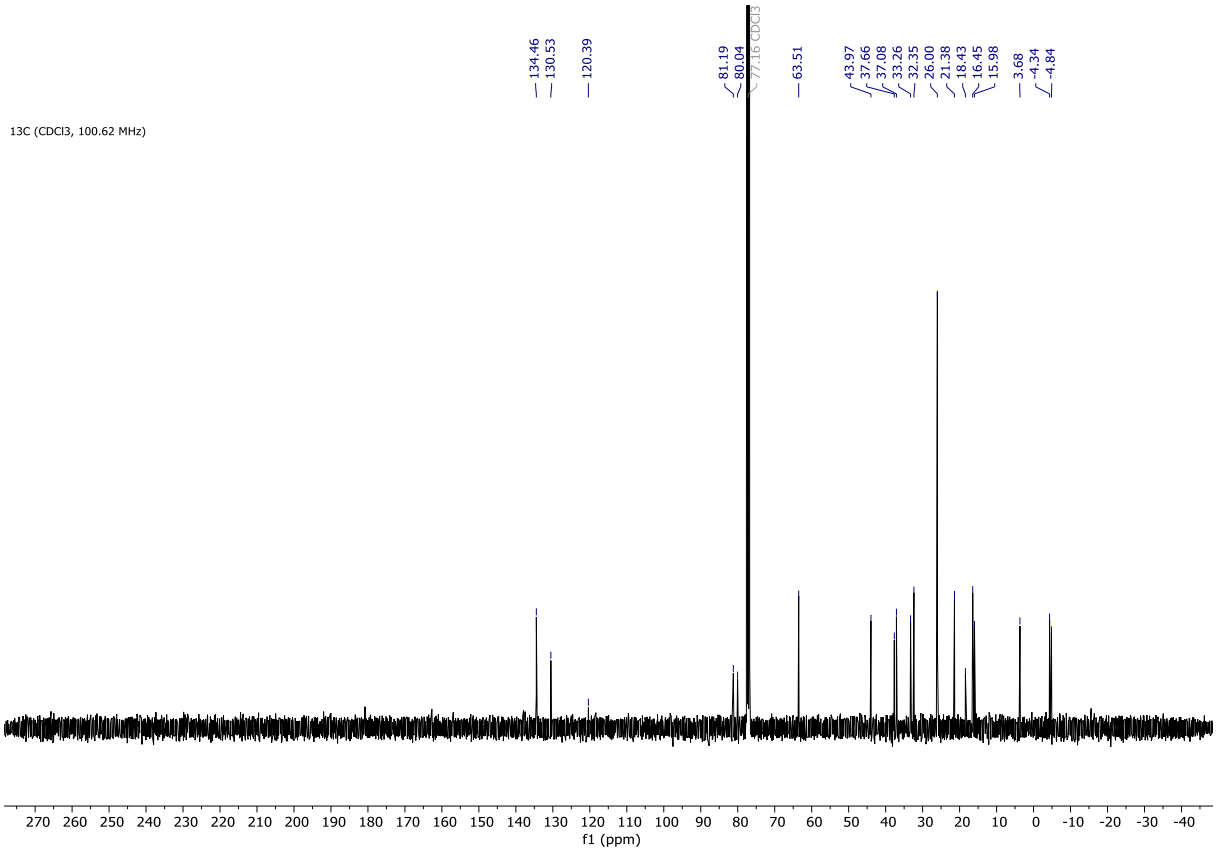

1H (CDCl3, 400.12 MHz)
OTBS
Me
Me
Me
I
37
f1 (ppm)

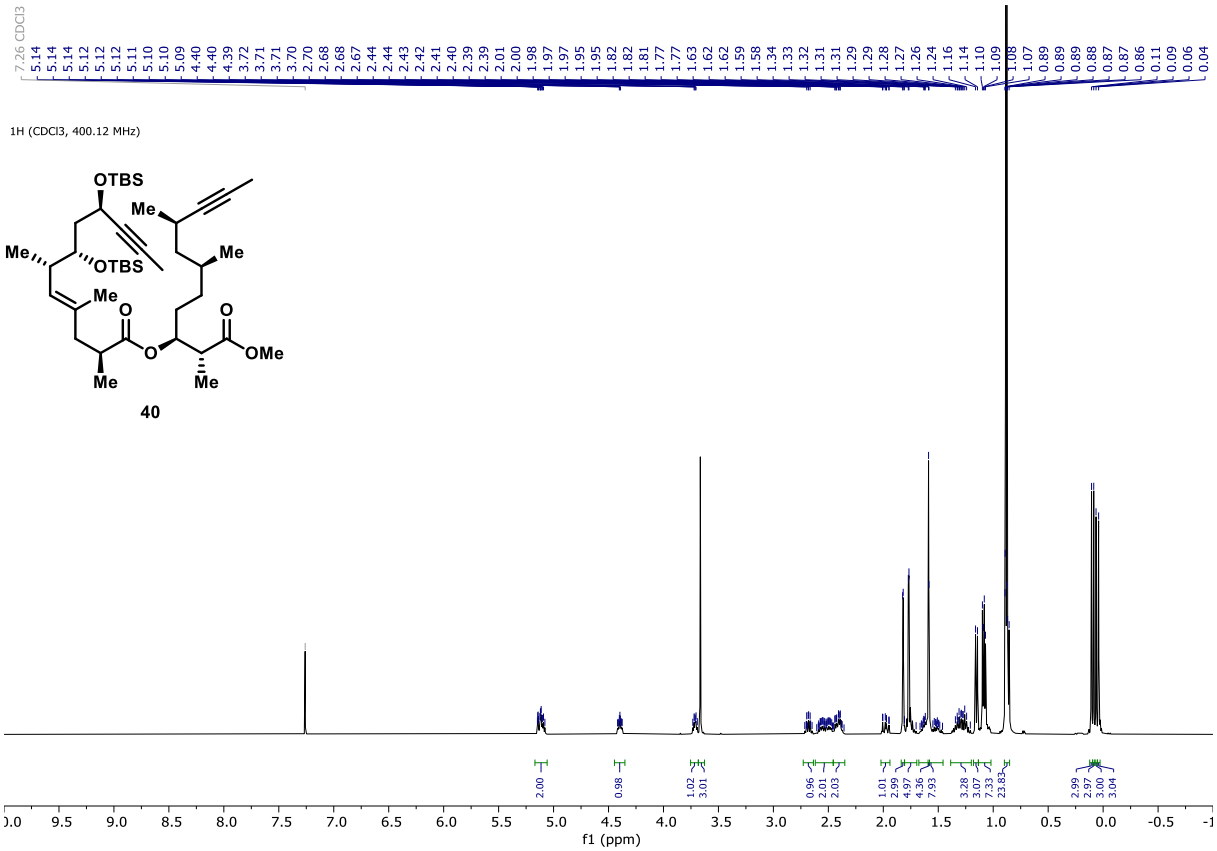

13C (CDCl3, 100.62 MHz)
147.35
92.88
80.99
80.25
77.16 CDCl3
63.29
36.83
35.68
32.65
27.90
26.00
20.69
18.43
3.68
-4.34
-4.85
f1 (ppm)

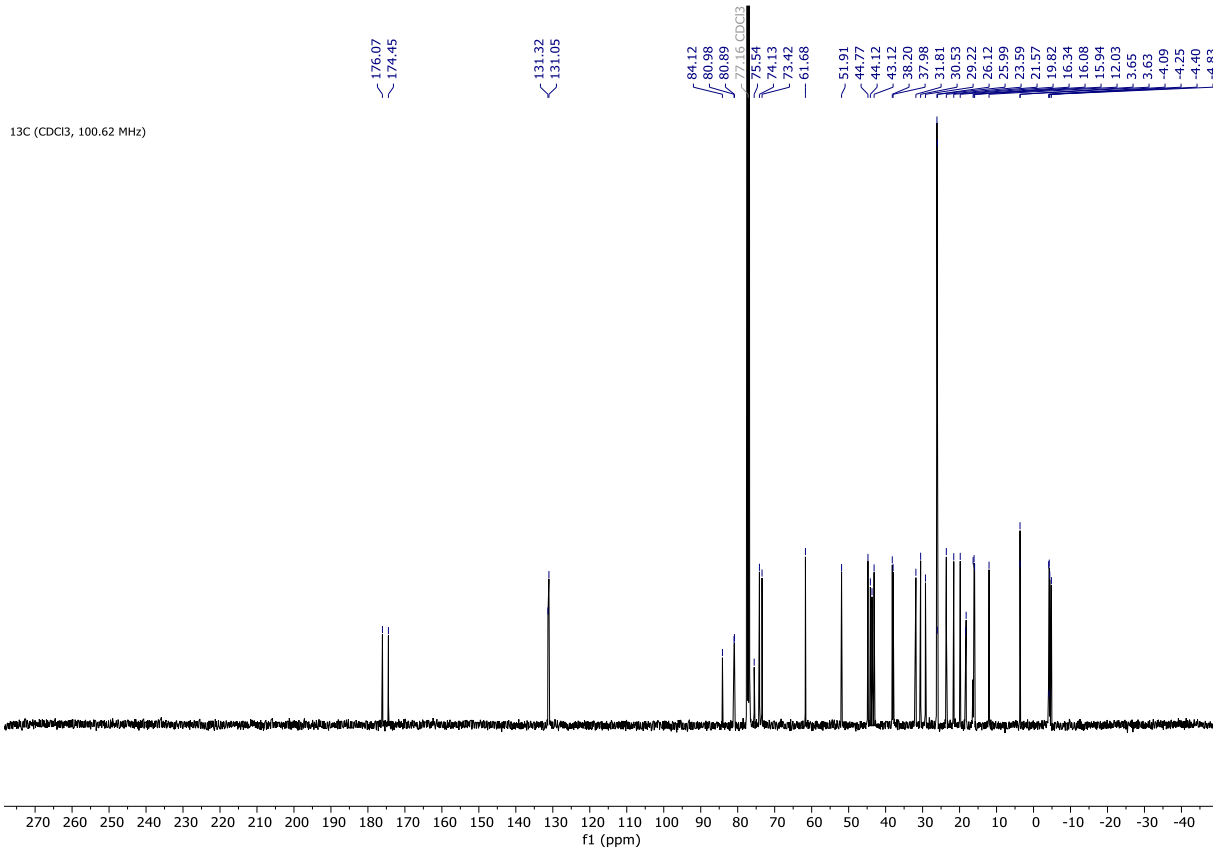

7.26 CDCl3
1H (CDCl3, 600.20 MHz)
OTBS
Me
Me
Me
O
OMe
Me
S13
1.00
1.00
2.92
1.01
1.03
2.06
1.09
3.04
3.13
2.01
1.18
1.26
3.10
3.10
9.08
2.98
3.00
f1 (ppm)

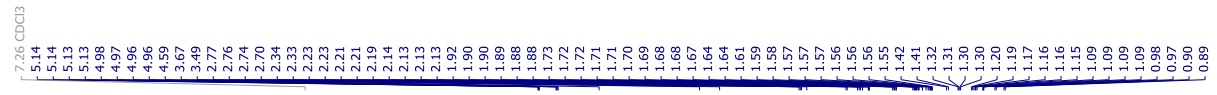

13C (CDCl3, 150.94 MHz)
177.25
134.03
130.87
81.20
80.00
77.16 CDCl3
63.50
51.53
44.35
38.14
37.09
33.29
32.31
26.00
21.43
18.42
16.79
16.02
3.67
-4.35
-4.86
f1 (ppm)


1H (CDCl3, 400.12 MHz)
OTBS
Me
Me
Me
O
OH
Me
38
f1 (ppm)

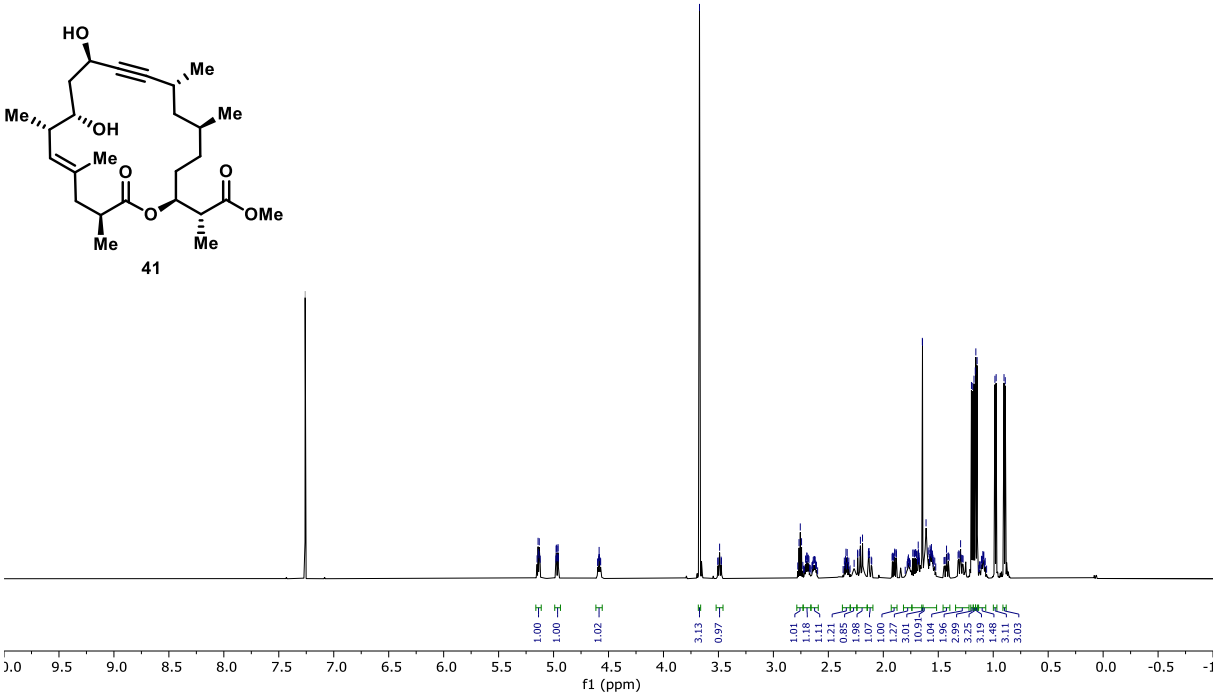

13C (CDCl3, 100.62 MHz)
134.46
130.53
120.39
81.19
80.04
77.16 CDCl3
63.51
43.97
37.66
37.08
33.26
32.35
26.00
21.38
18.43
16.45
15.98
3.68
-4.34
-4.84
f1 (ppm)


1H (CDCl3, 400.12 MHz)
OTBS
Me
Me
OTBS
Me
Me
Me
O
O
O
OMe
Me
Me
40
f1 (ppm)

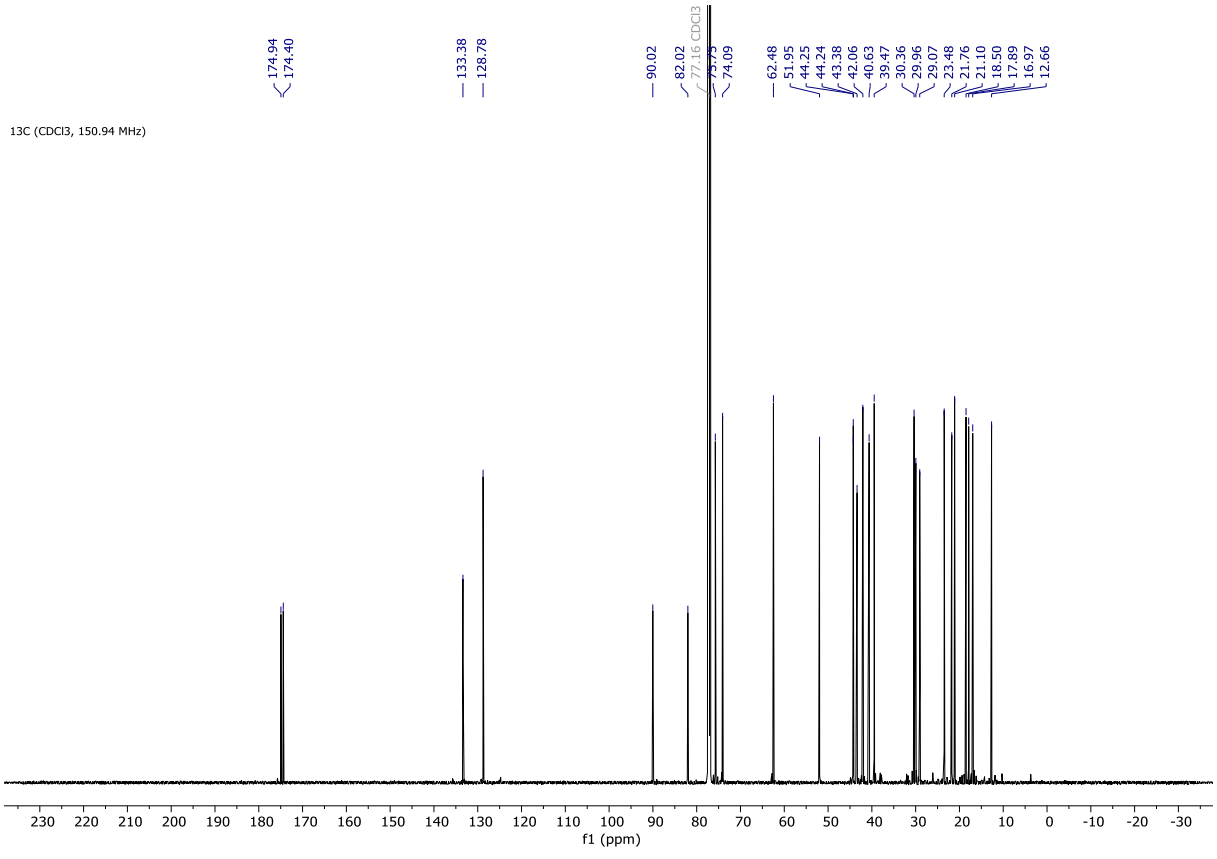

13C (CDCl3, 100.62 MHz)
f1 (ppm)

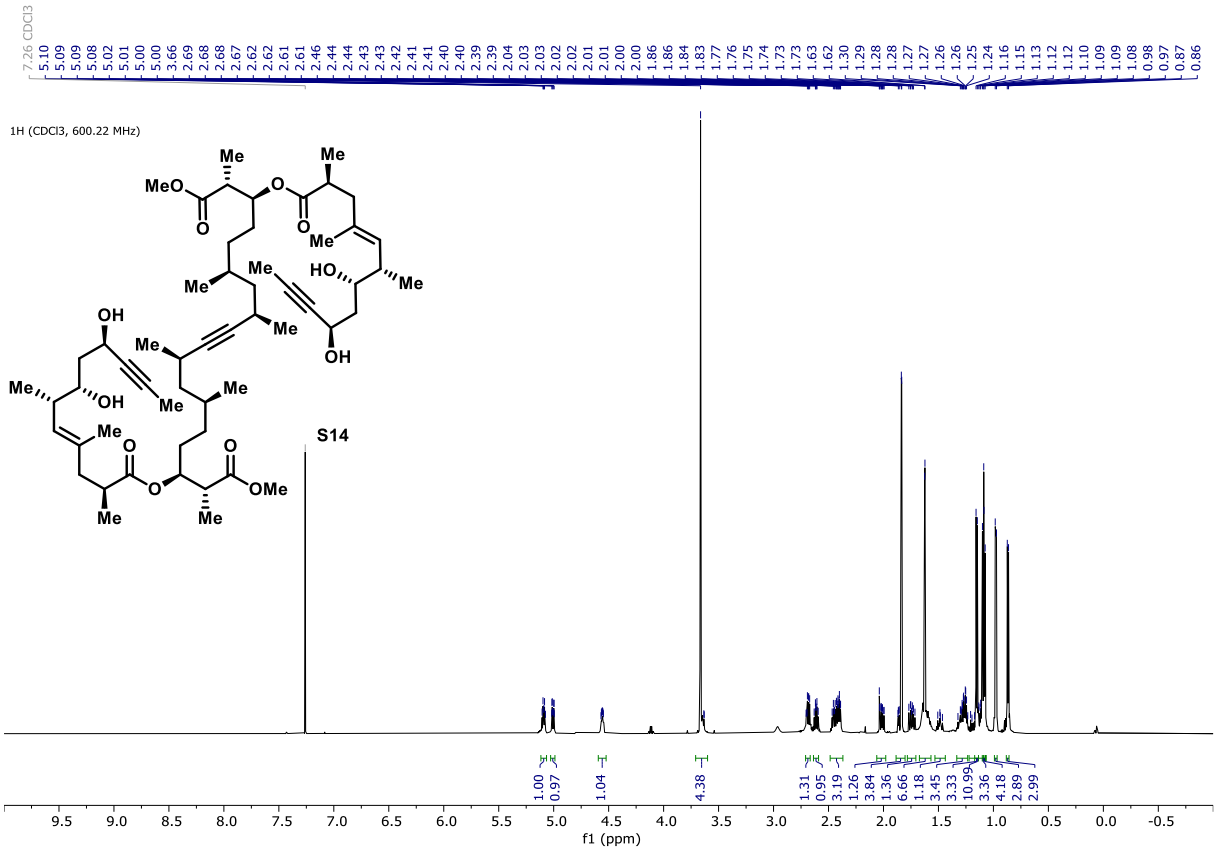


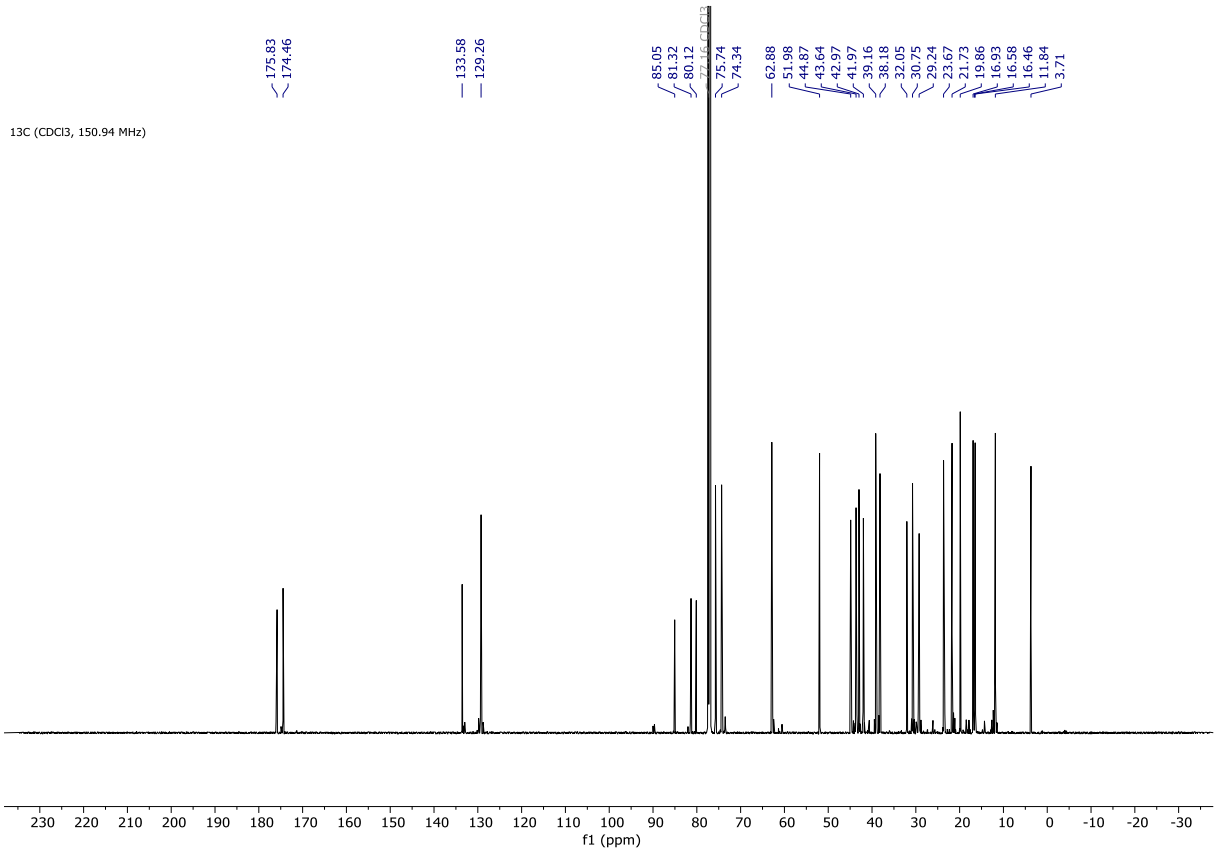

1H (CDCl3, 600.20 MHz)

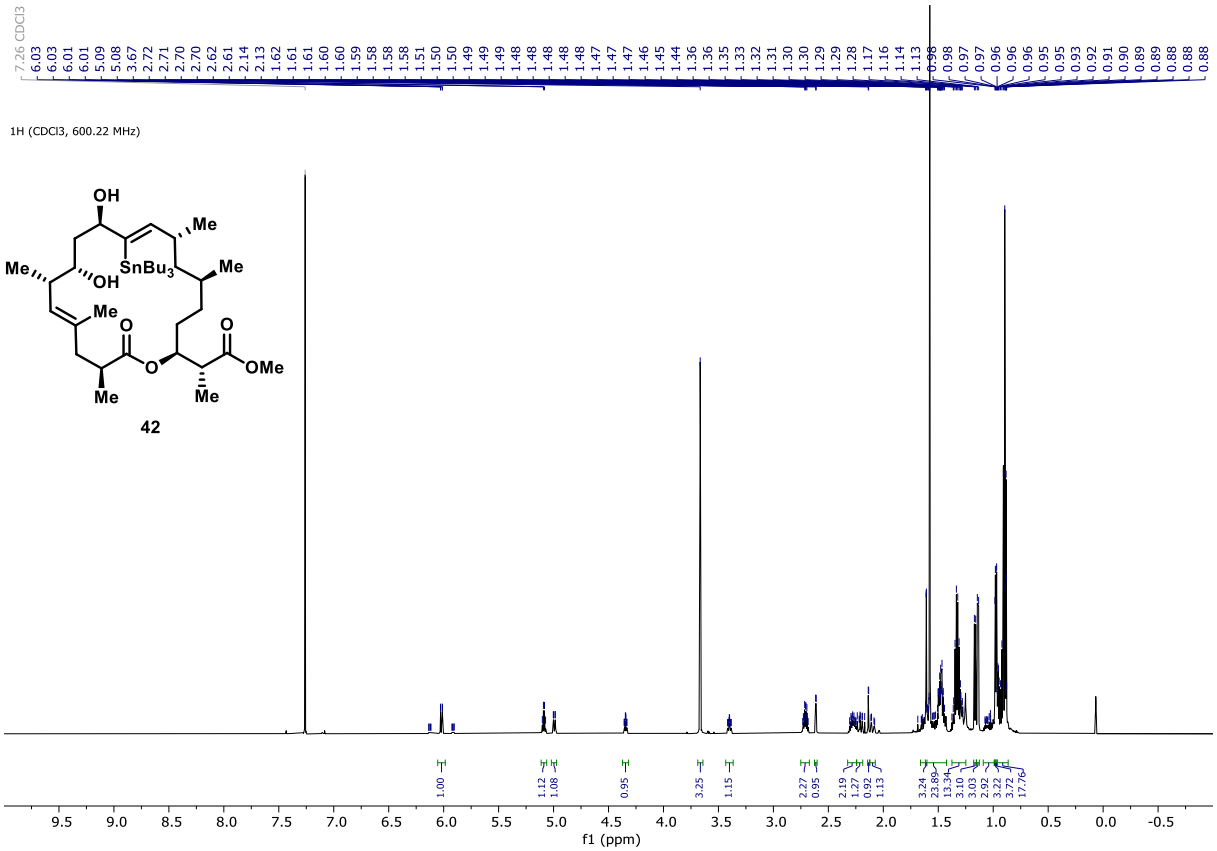



13C (CDCl3, 150.94 MHz)



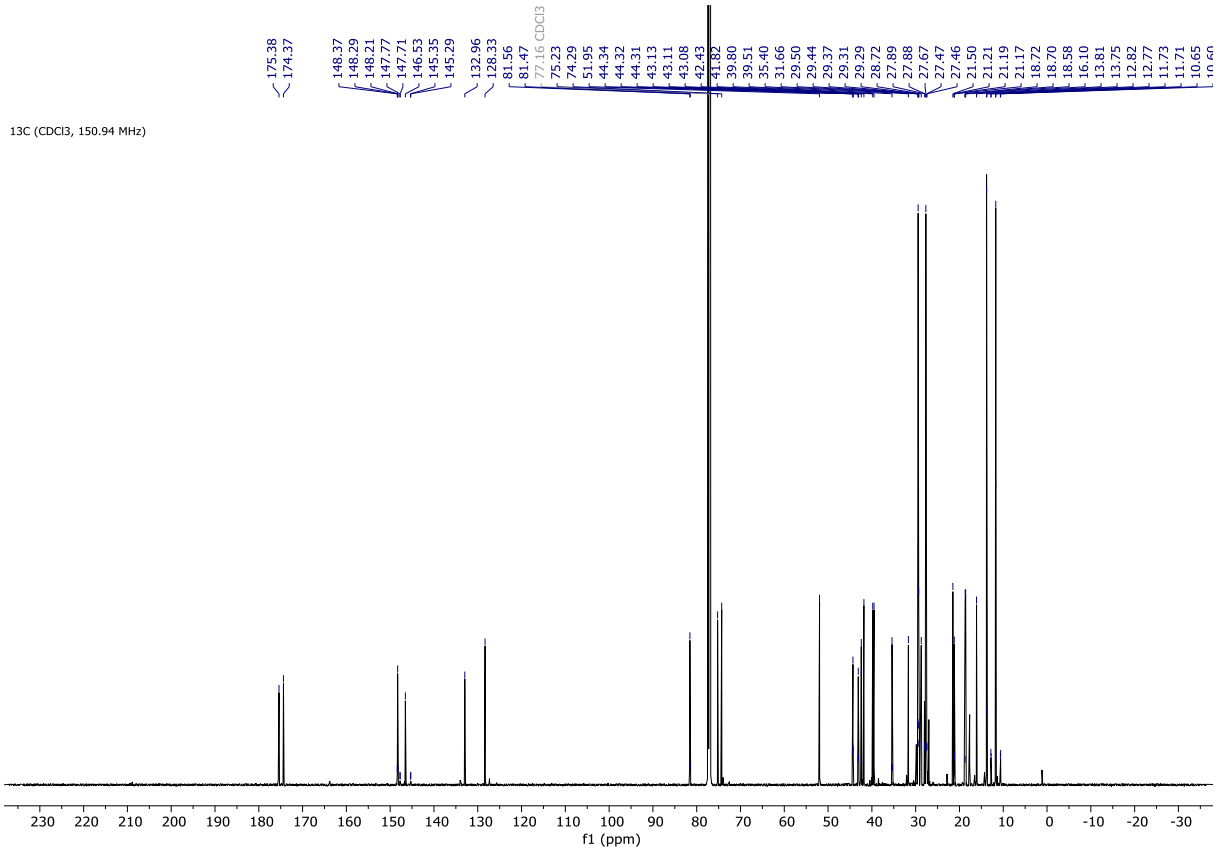

1H (CDCl3, 600.22 MHz)
S14
f1 (ppm)

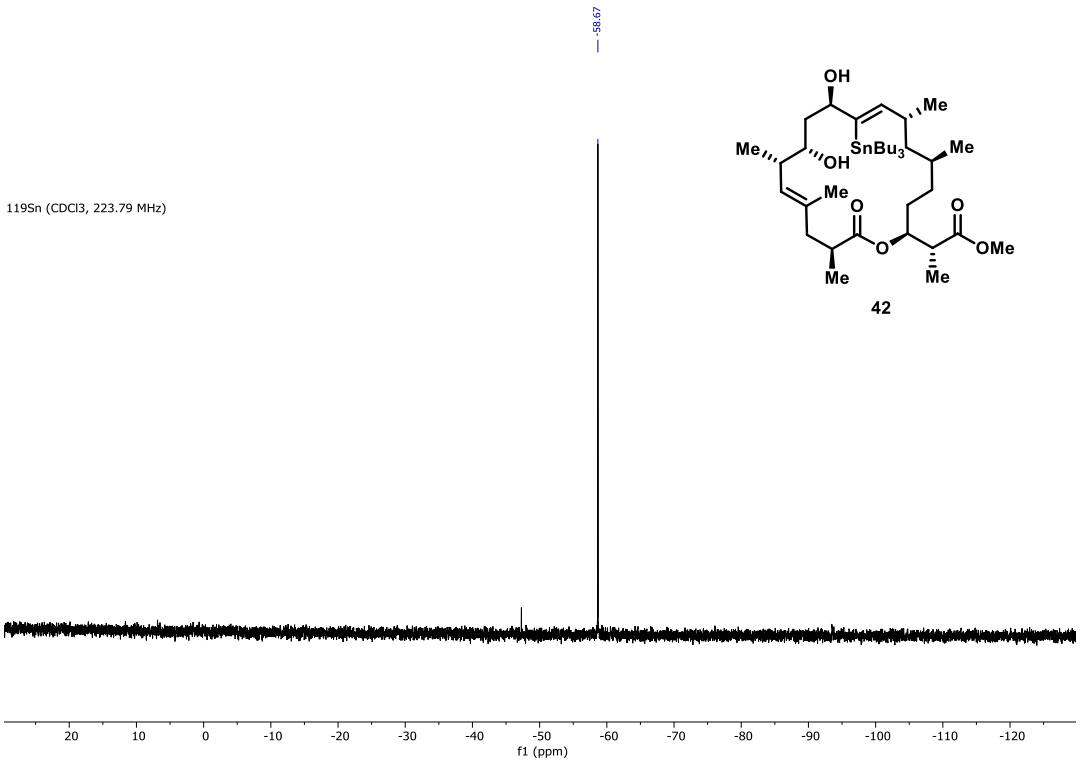

13C (CDCl3, 150.94 MHz)
f1 (ppm)


1H (CDCl3, 600.22 MHz)
7.26 CDCl3
f1 (ppm)


OH
Me
Me
OH
SnBu3
Me
Me
O
O
O
OMe
Me
Me

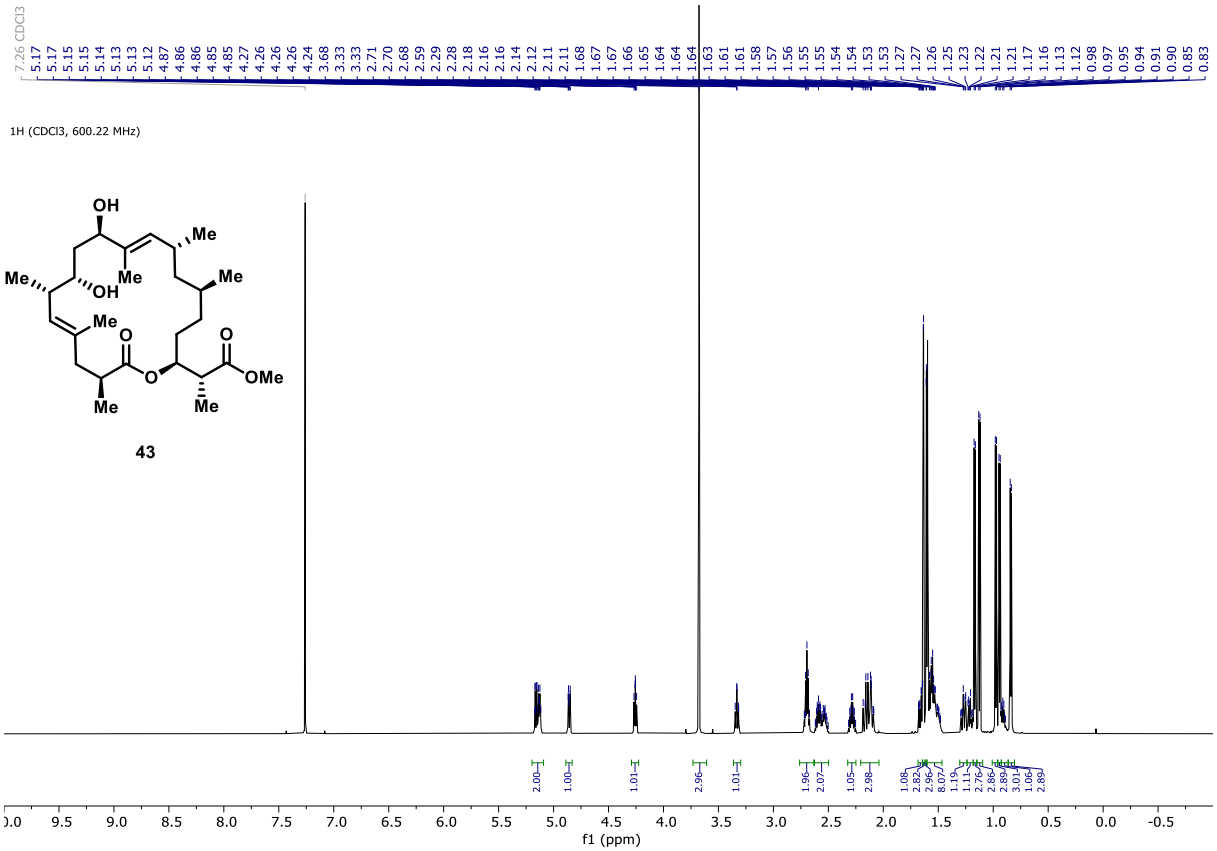
42


13C (CDCl3, 150.94 MHz)
77.16 CDCl3
f1 (ppm)

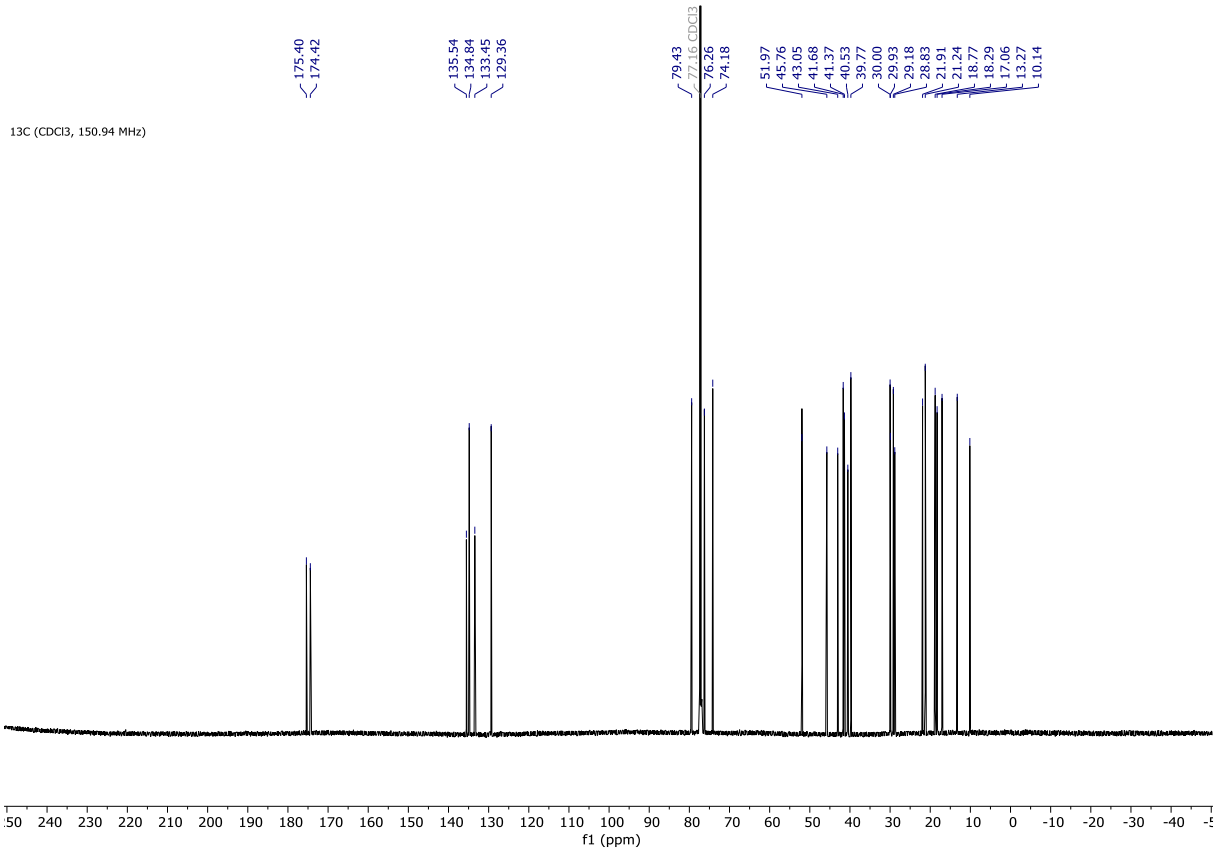

119Sn (CDCl3, 223.79 MHz)
-58.67
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
f1 (ppm)

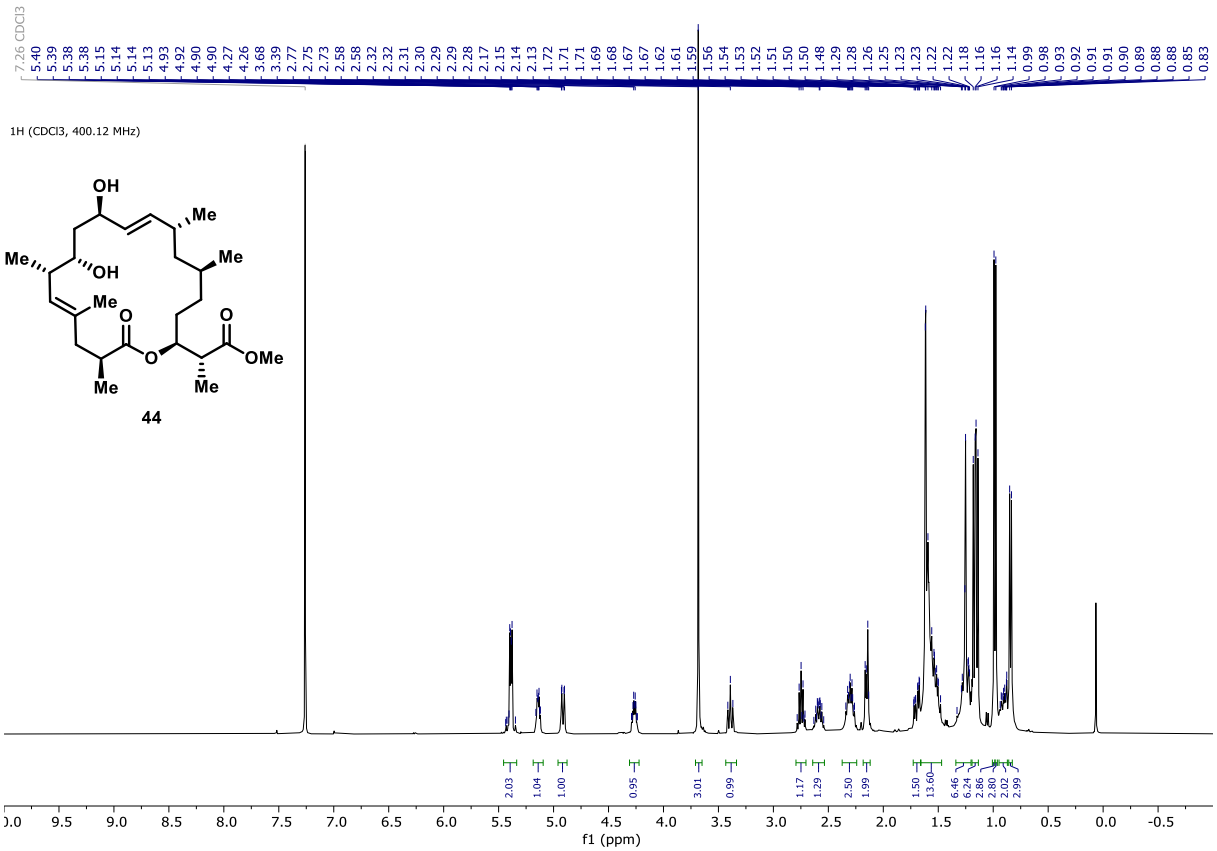

OH
Me
Me
SnBu3
OH
Me
Me
O
O
O
OMe
Me
Me

**42**

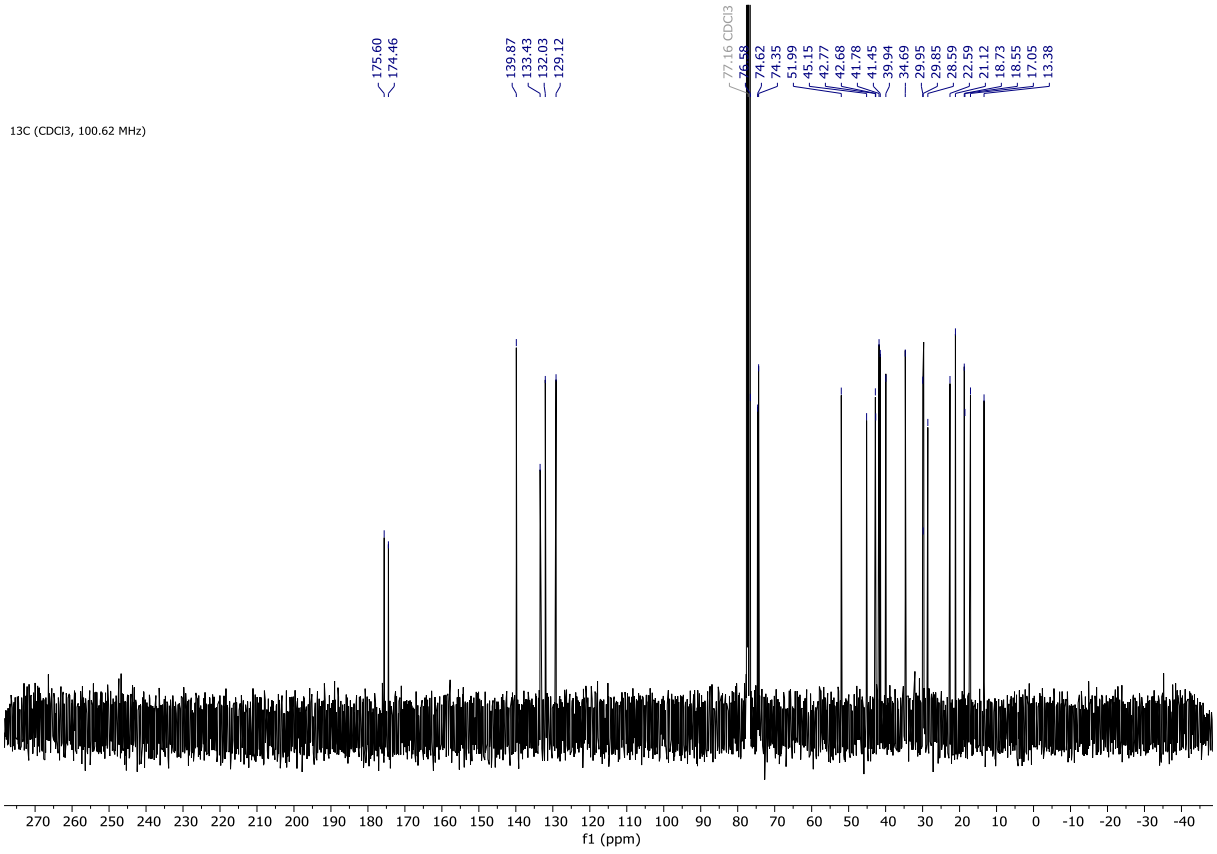

1H (CDCl3, 600.22 MHz)
7.26 CDCl3
5.17 5.17 5.15 5.15 5.14 5.13 5.13 5.12 4.87 4.86 4.86 4.85 4.85 4.27 4.26 4.26 4.24 3.68 3.33 3.33 2.71 2.70 2.68 2.59 2.29 2.28 2.18 2.16 2.16 2.14 2.12 2.11 2.11 1.68 1.67 1.67 1.66 1.65 1.64 1.64 1.64 1.63 1.61 1.61 1.58 1.57 1.56 1.55 1.55 1.54 1.54 1.53 1.53 1.27 1.27 1.26 1.25 1.23 1.22 1.21 1.21 1.17 1.16 1.13 1.12 0.98 0.97 0.95 0.94 0.91 0.90 0.85 0.83
OH
Me
Me
Me
OH
Me
Me
O
O
O
OMe
Me
Me
2.00 1.00 1.01 2.96 1.01 1.96 2.07 1.05 2.98 1.08 2.82 2.96 8.07 1.19 1.11 2.76 2.86 2.89 3.01 1.06 2.89
f1 (ppm)

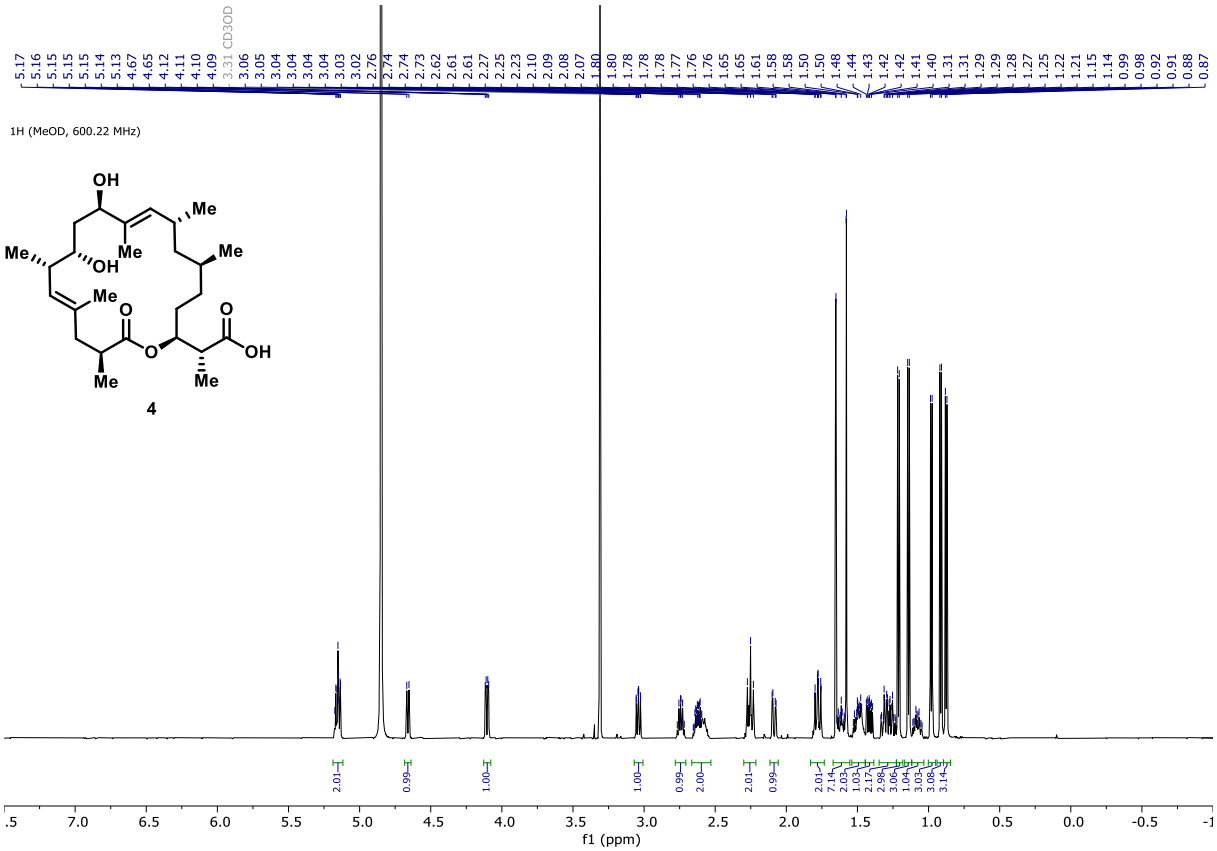
43

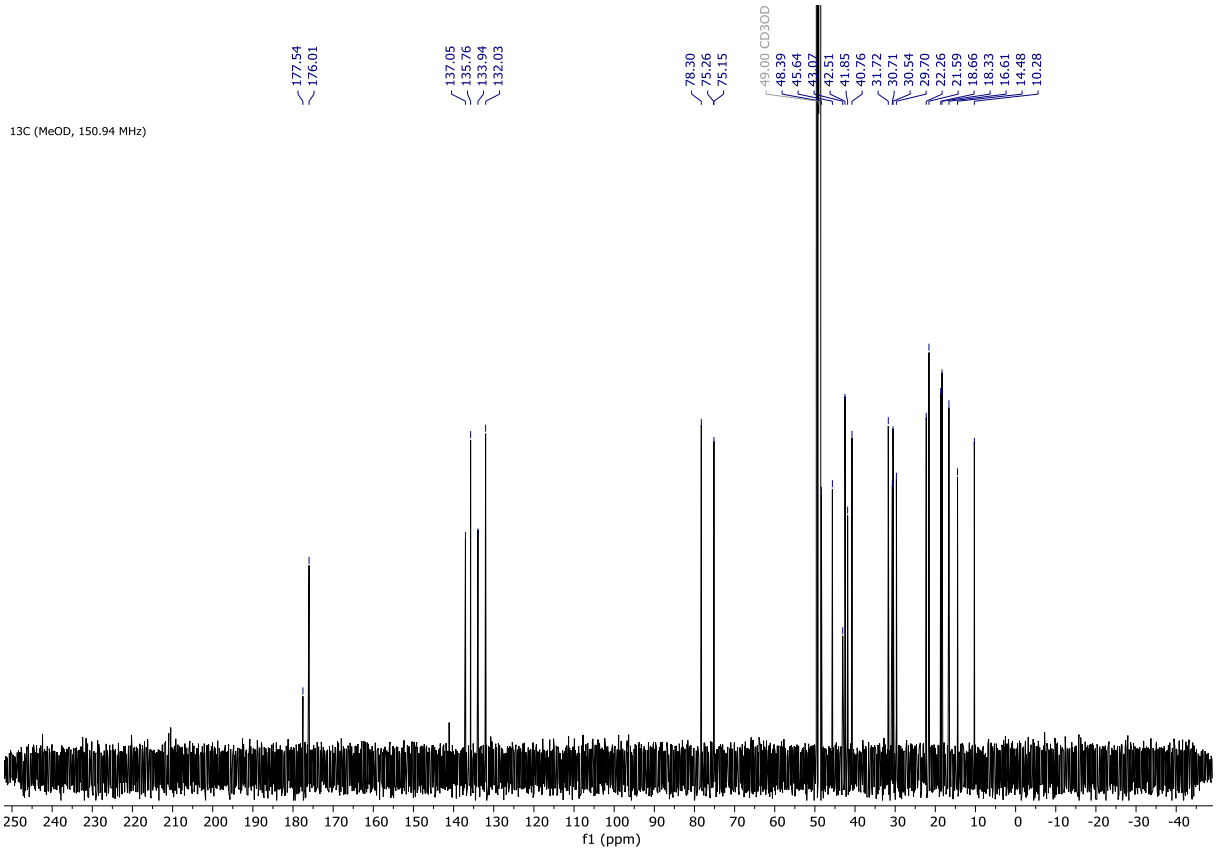

13C (CDCl3, 150.94 MHz)
175.40 174.42 135.54 134.84 133.45 129.36 79.43 77.16 CDCl3 76.26 74.18 51.97 45.76 43.05 41.68 41.37 40.53 39.77 30.00 29.93 29.18 28.83 21.91 21.24 18.77 18.29 17.06 13.27 10.14
f1 (ppm)

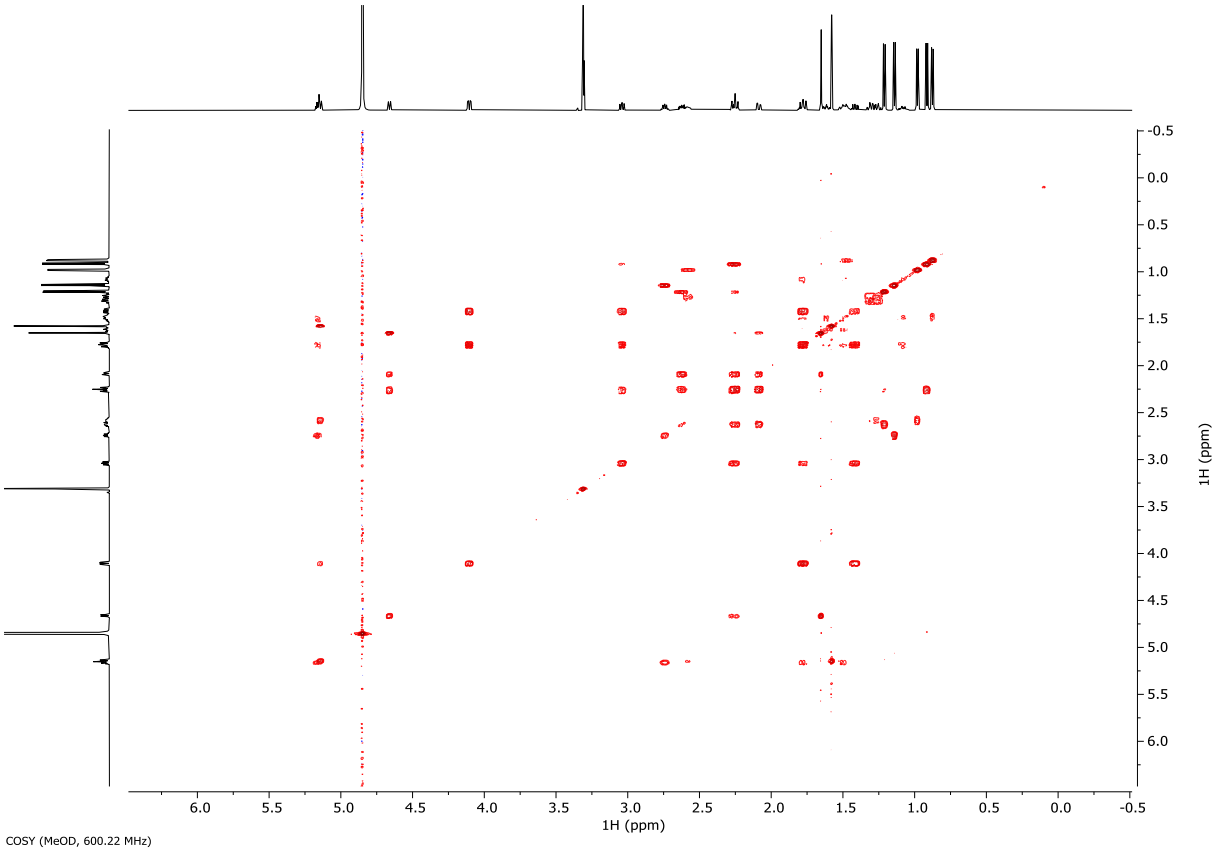



44

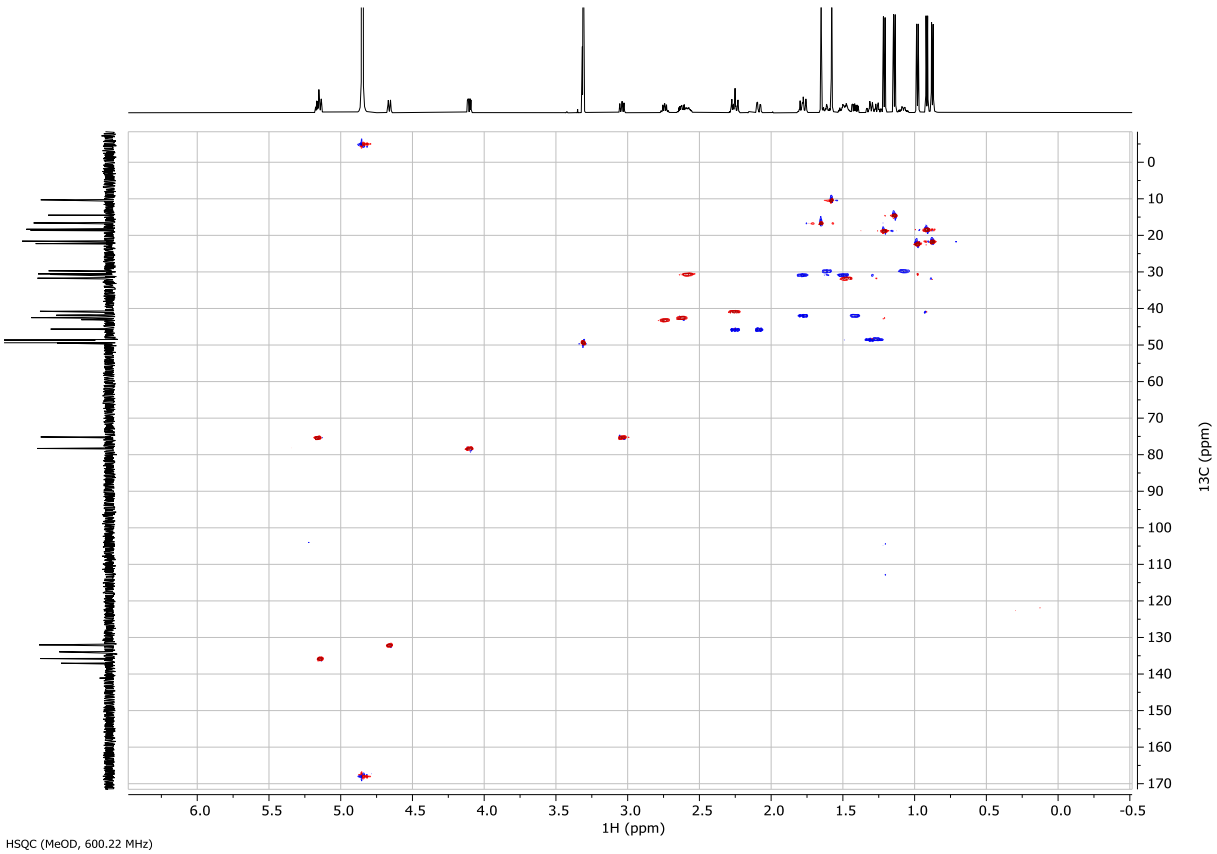



1H (MeOD, 600.22 MHz)
3.31 CD3OD
OH
Me
Me
Me
OH
Me
Me
O
O
O
OH
Me
Me
4
f1 (ppm)

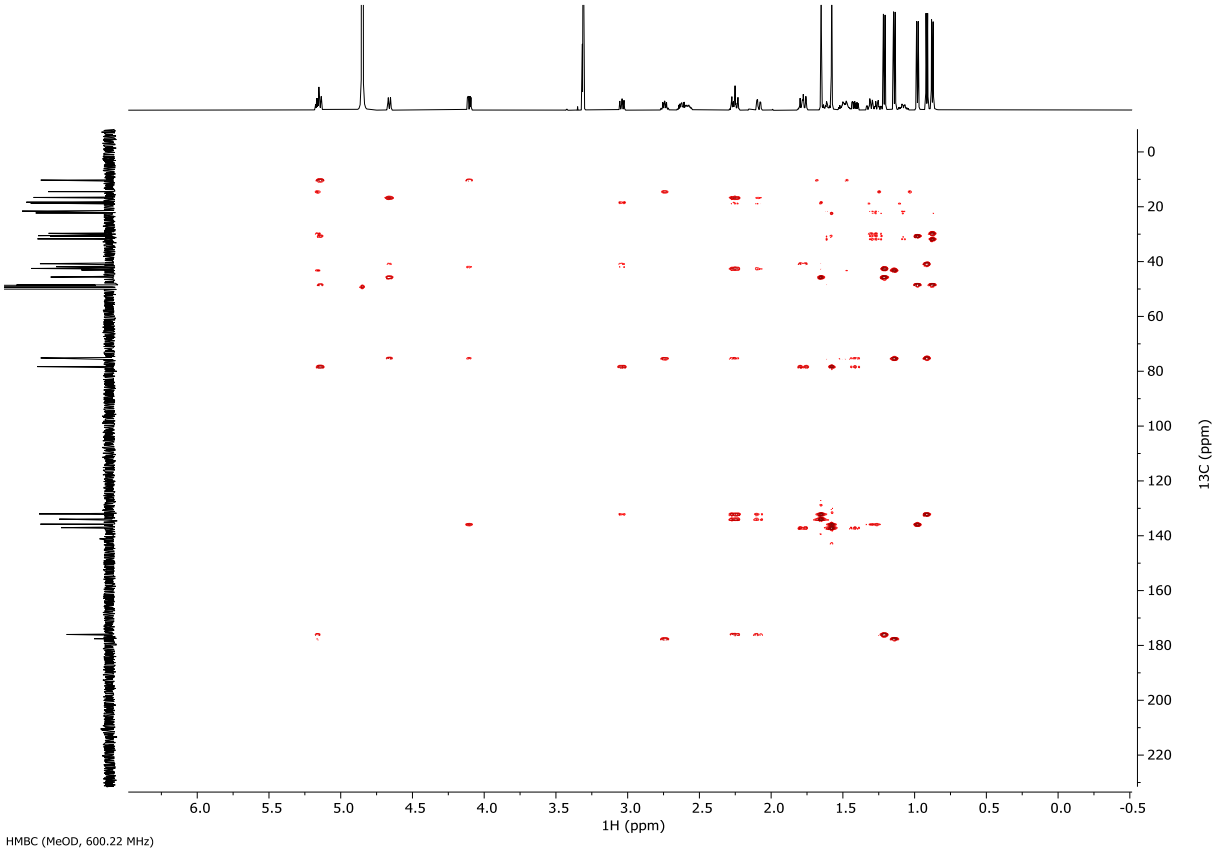

13C (MeOD, 150.94 MHz)
177.54
176.01
137.05
135.76
133.94
132.03
78.30
75.26
75.15
49.00 CD3OD
48.39
45.64
43.07
42.51
41.85
40.76
31.72
30.71
30.54
29.70
22.26
21.59
18.66
18.33
16.61
14.48
10.28
f1 (ppm)



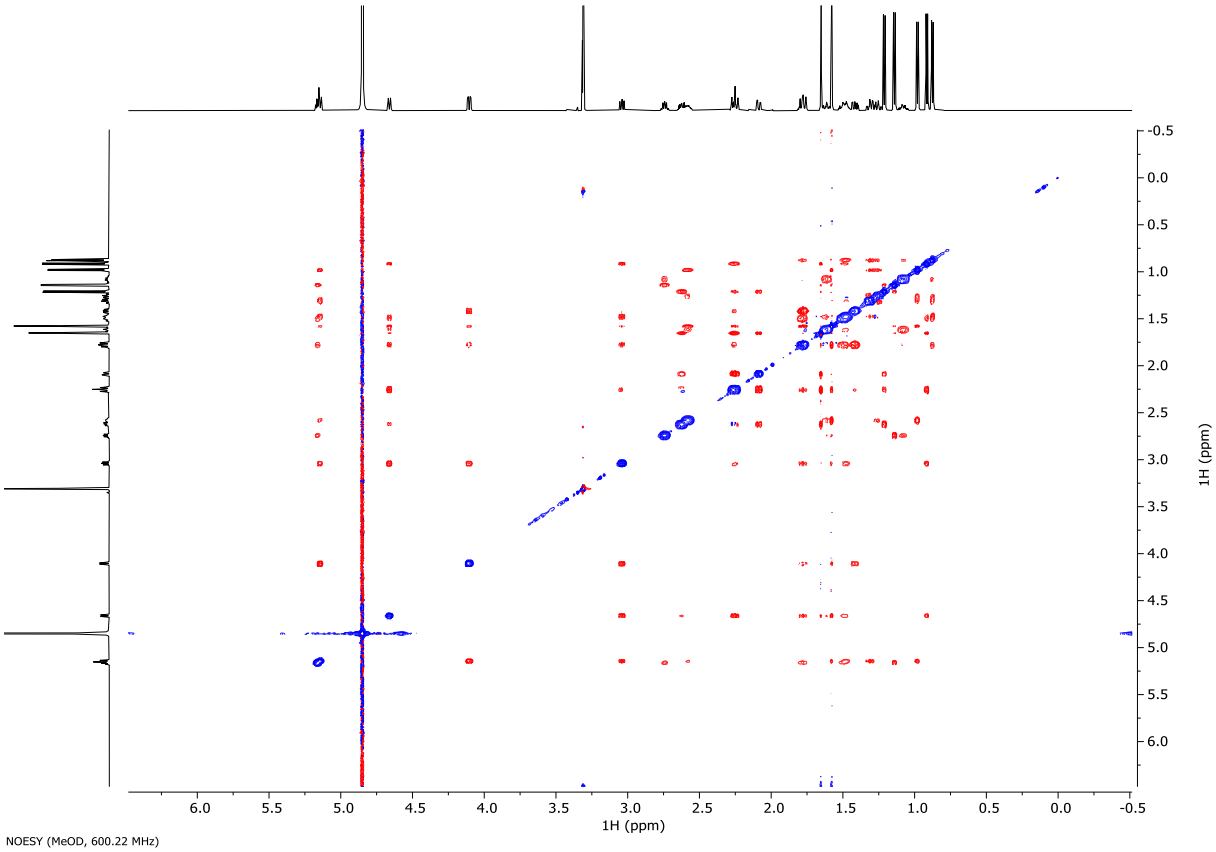

COSY (MeOD, 600.22 MHz)



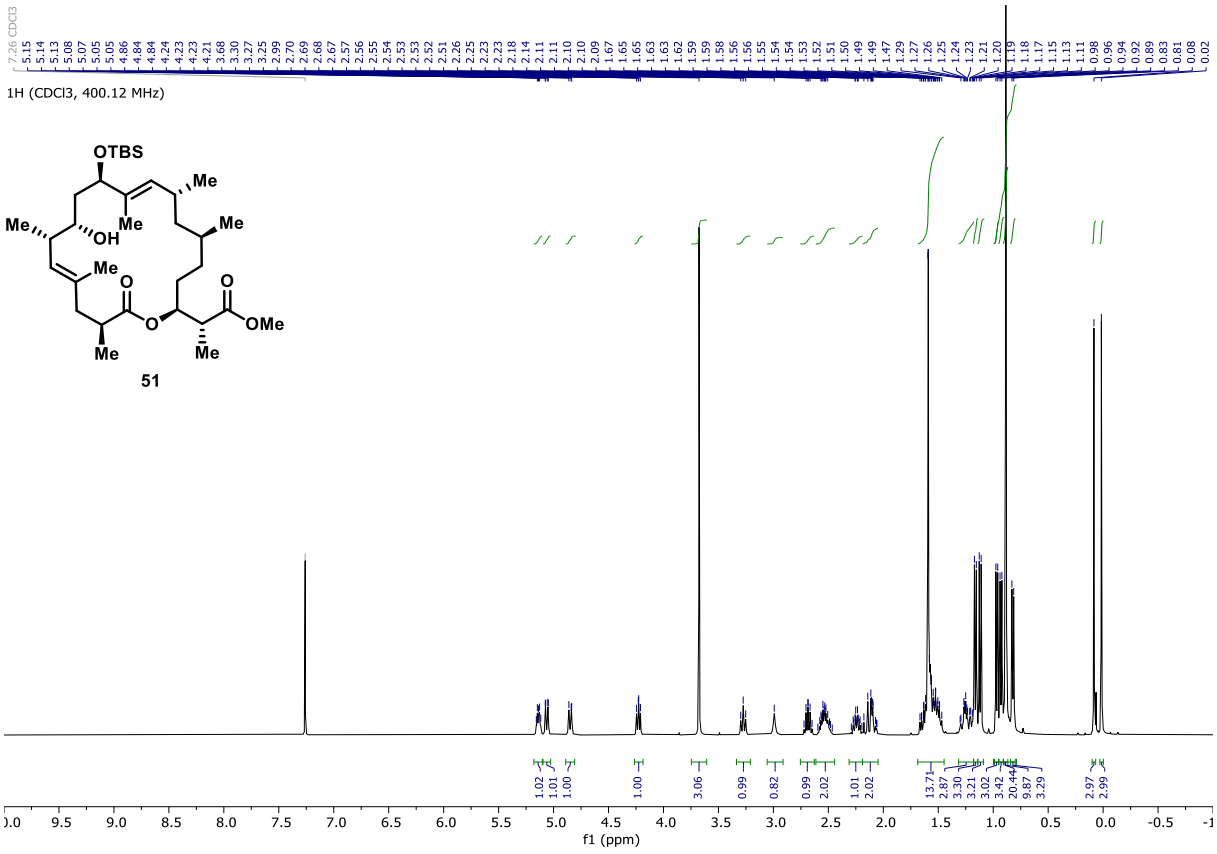

HSQC (MeOD, 600.22 MHz)

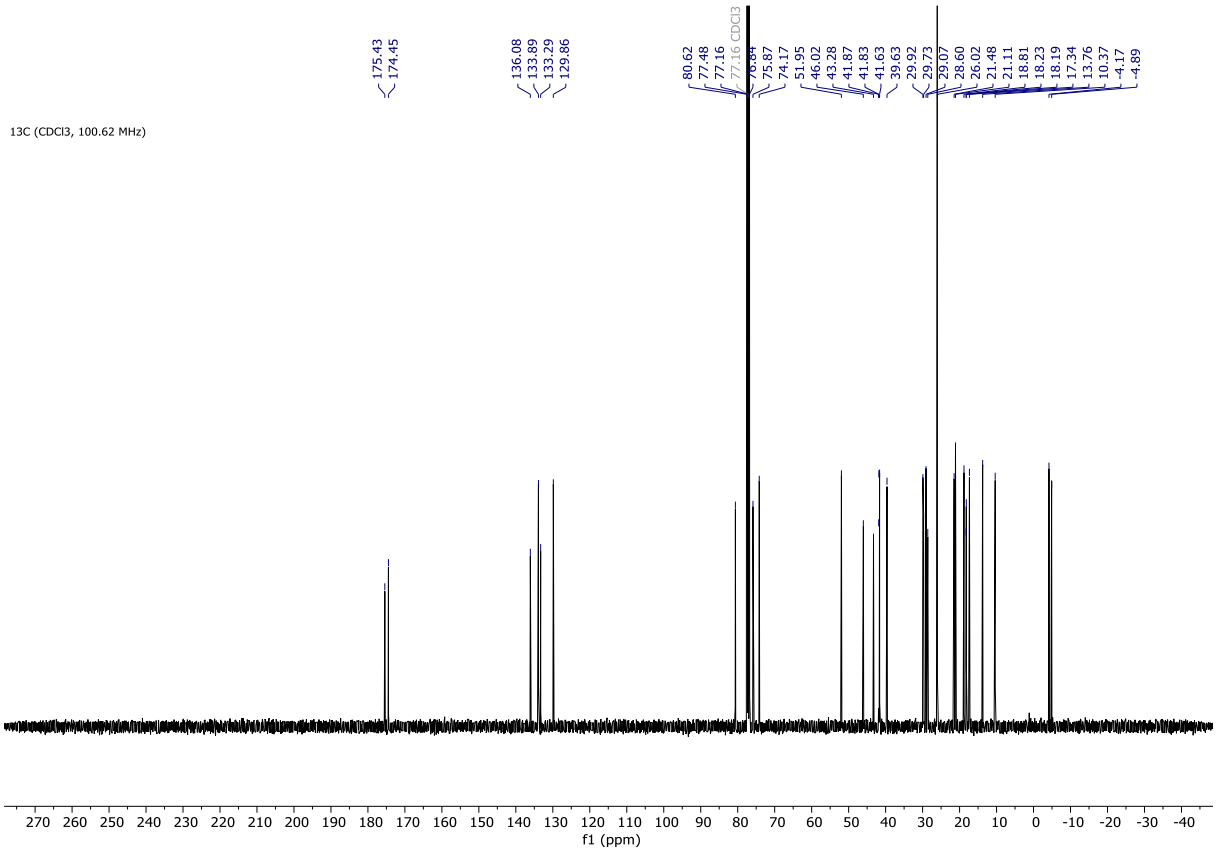


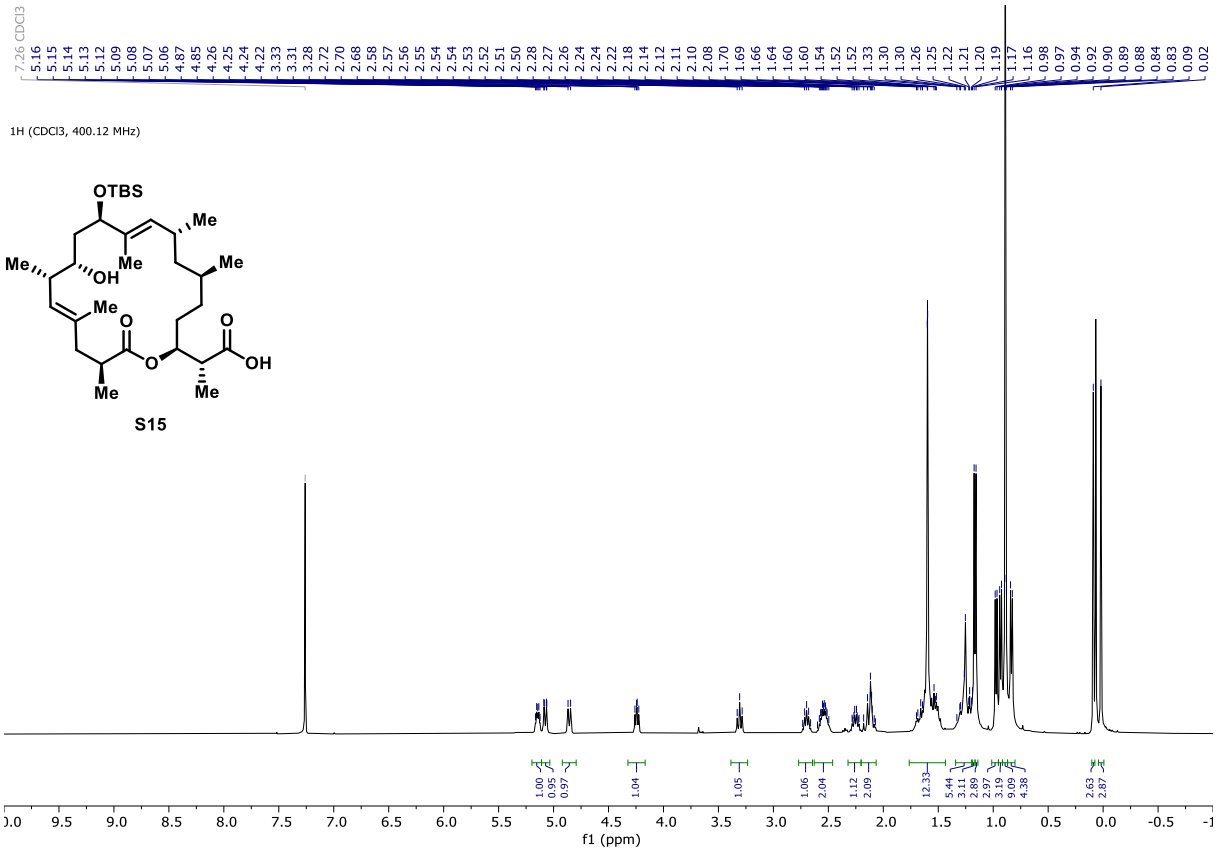

HMBC (MeOD, 600.22 MHz)

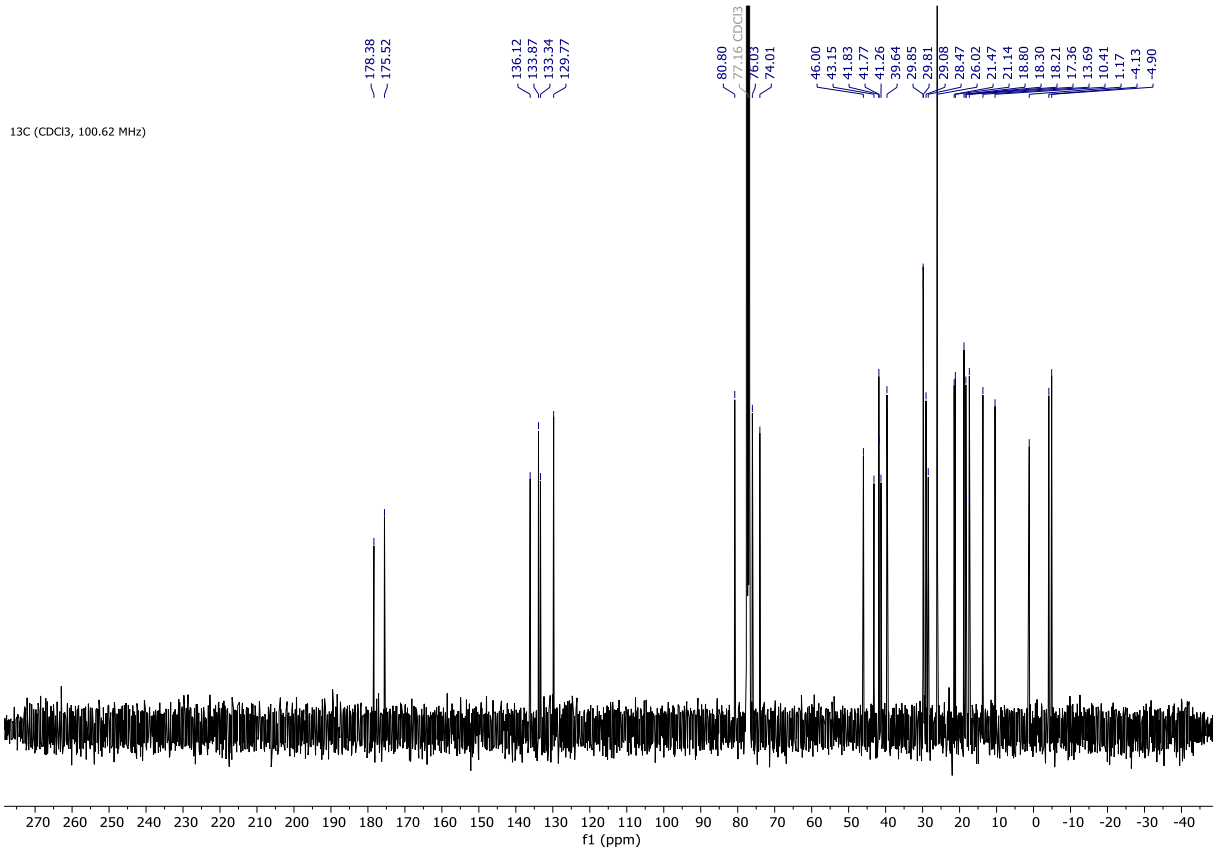


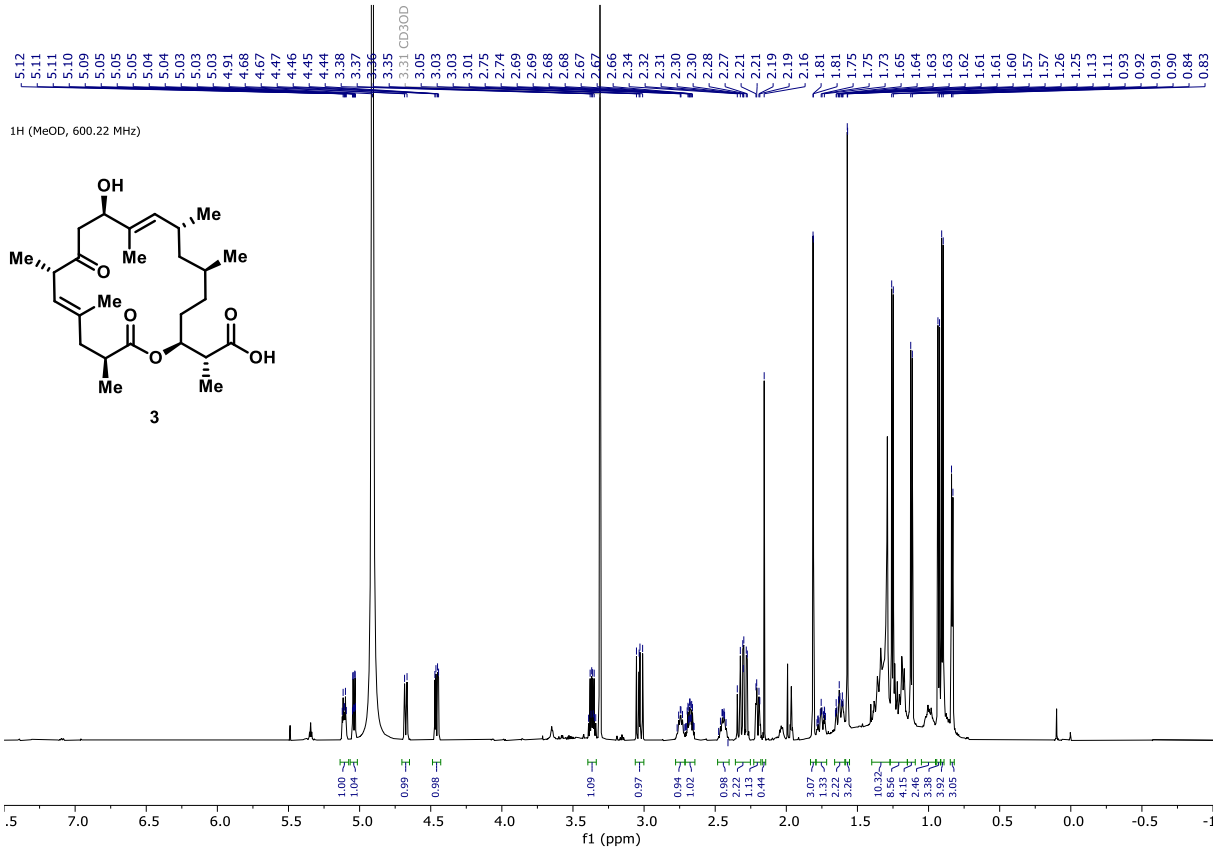

NOESY (MeOD, 600.22 MHz)

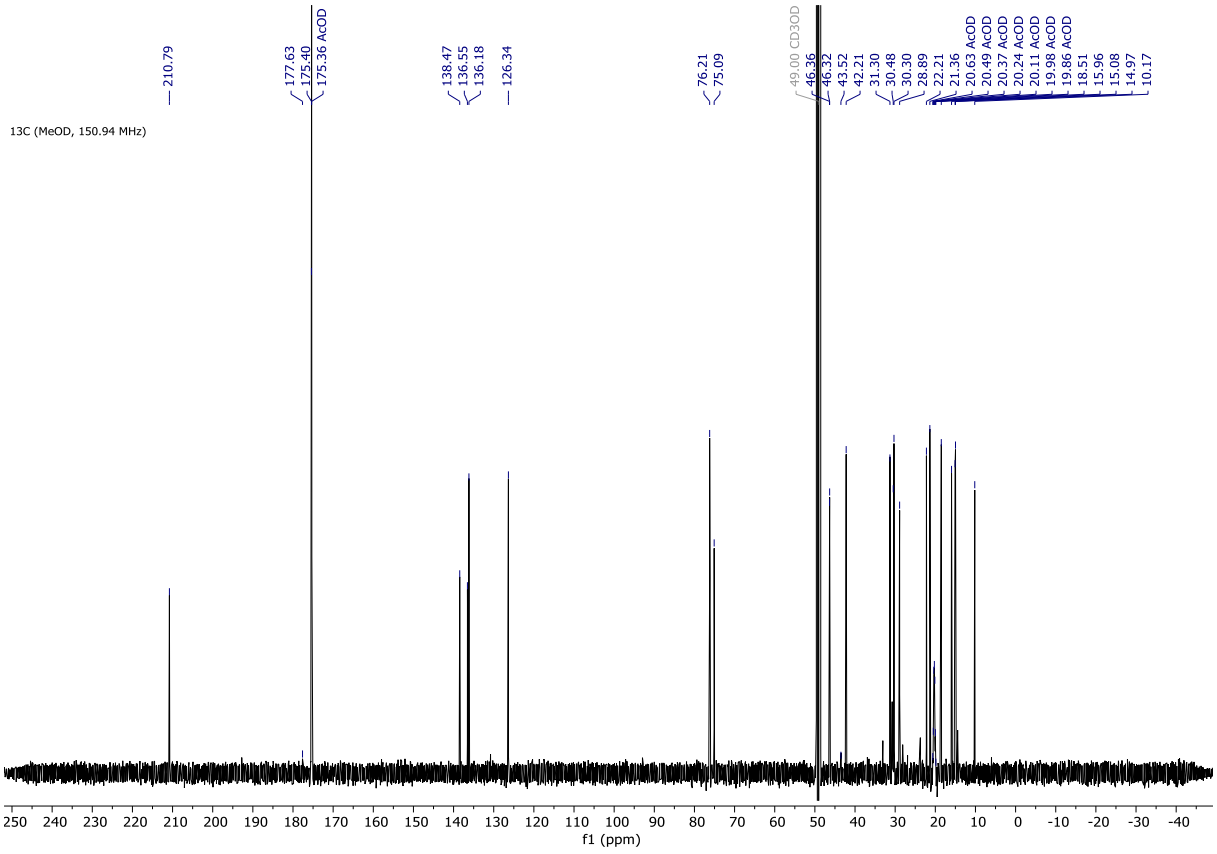

1H (CDCl3, 400.12 MHz)
OTBS
Me
Me
Me
Me
OH
Me
O
O
O
OMe
Me
Me
51
f1 (ppm)

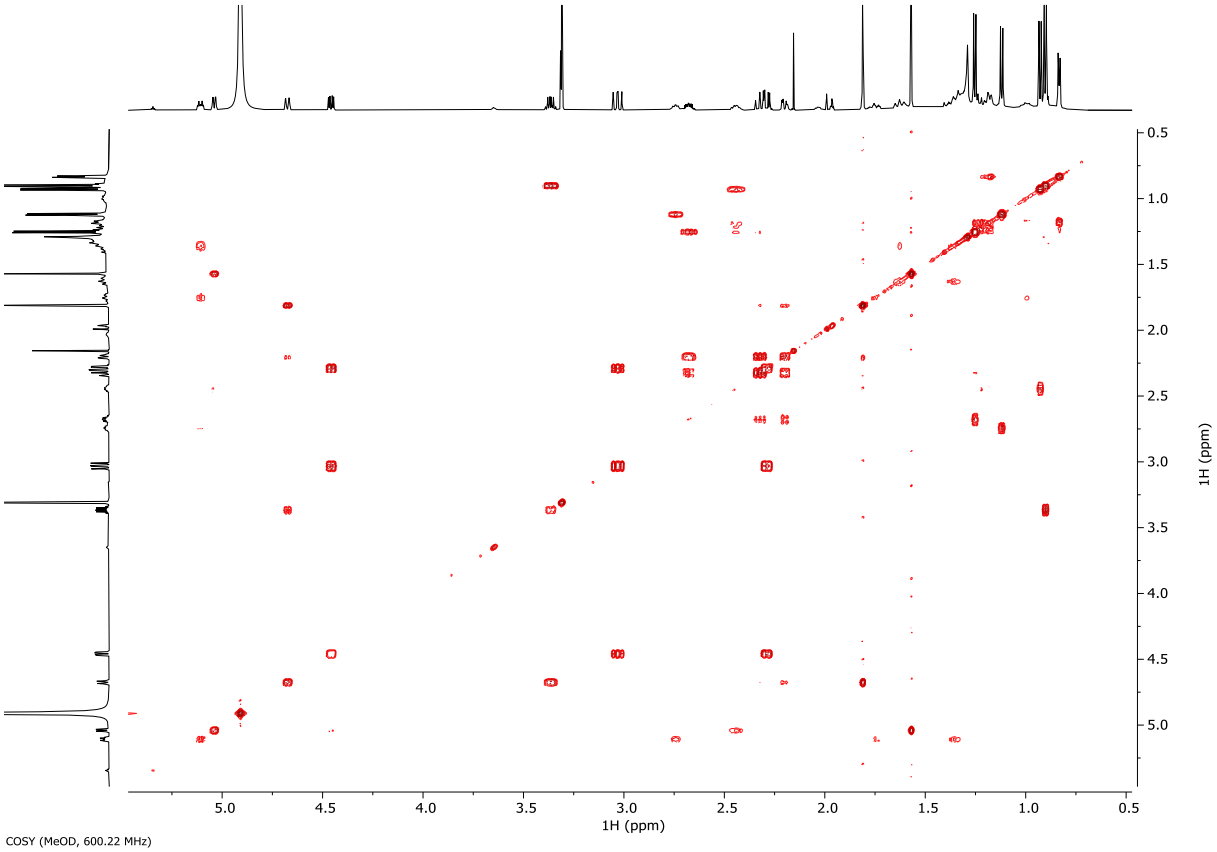

13C (CDCl3, 100.62 MHz)
f1 (ppm)


1H (CDCl3, 400.12 MHz)
OTBS
Me
Me
Me
OH
Me
Me
O
O
O
OH
Me
Me
S15
f1 (ppm)

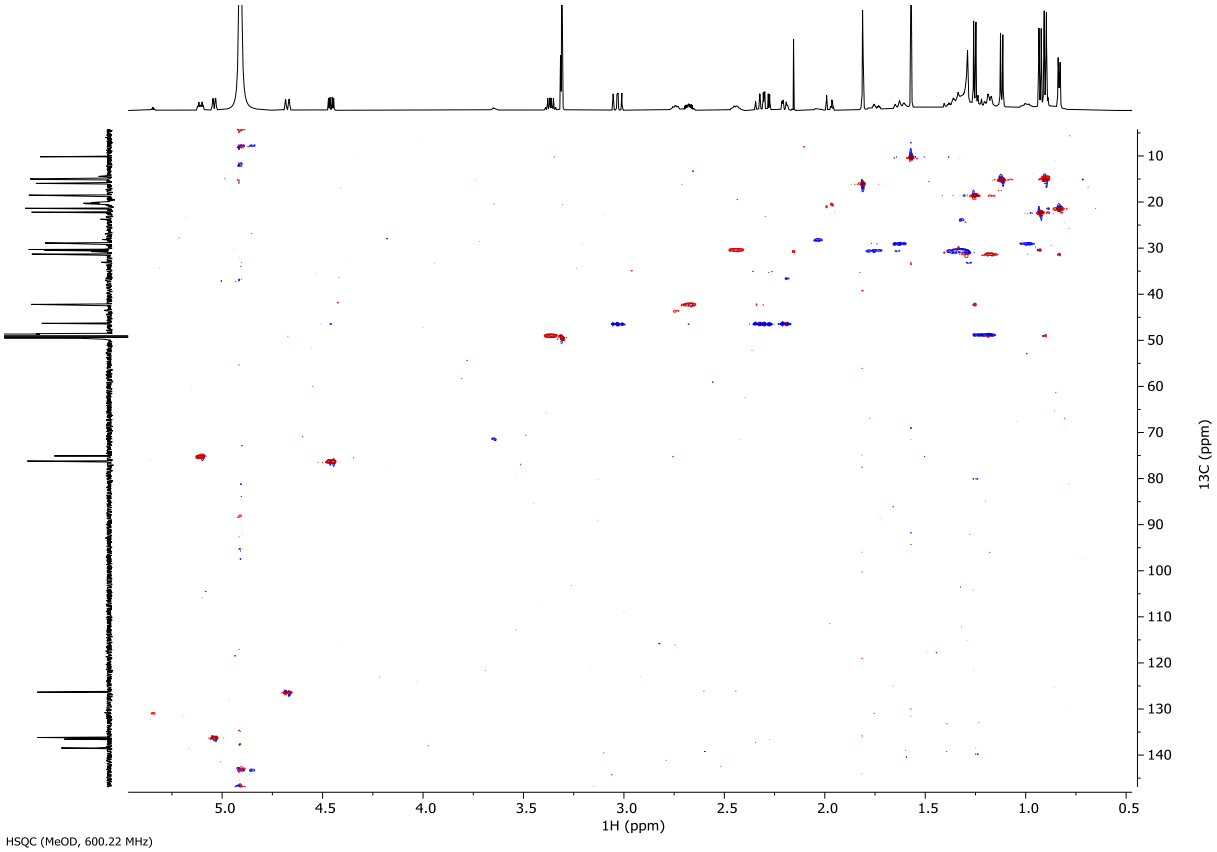

13C (CDCl3, 100.62 MHz)
f1 (ppm)


1H (MeOD, 600.22 MHz)
OH
Me
Me
Me
O
Me
Me
O
O
O
OH
Me
Me
3
f1 (ppm)

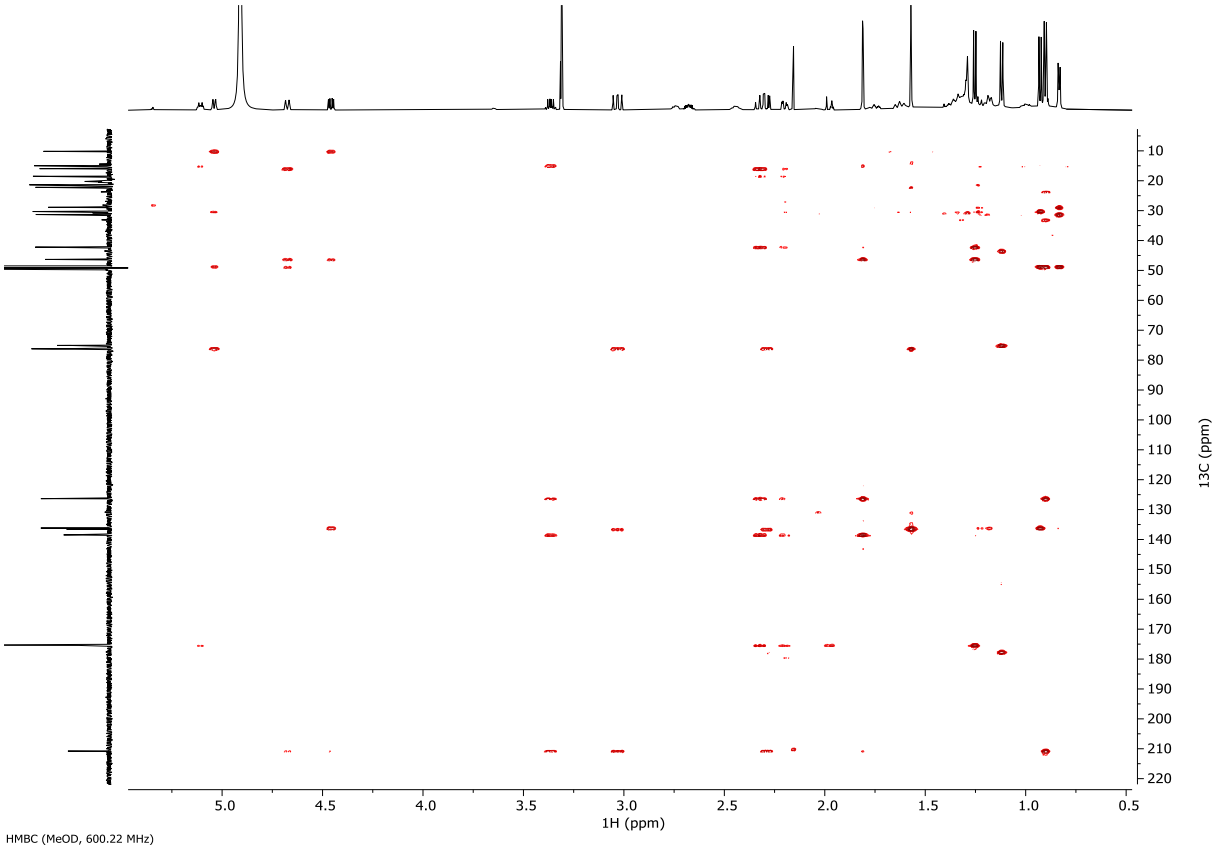

13C (MeOD, 150.94 MHz)
f1 (ppm)



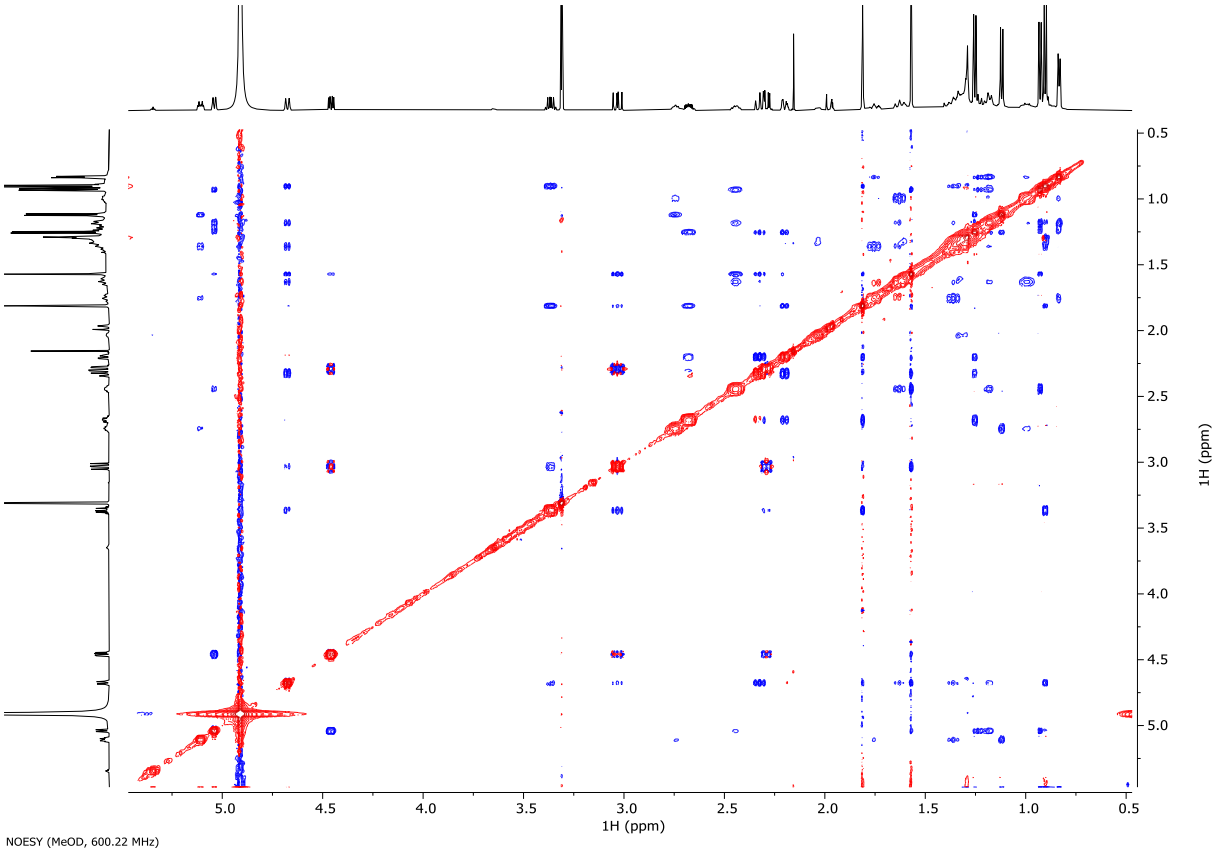

COSY (MeOD, 600.22 MHz)



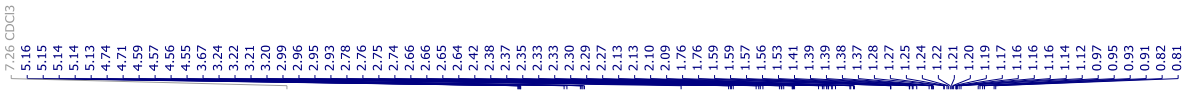

HSQC (MeOD, 600.22 MHz)



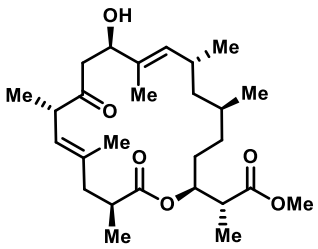

HMBC (MeOD, 600.22 MHz)




NOESY (MeOD, 600.22 MHz)

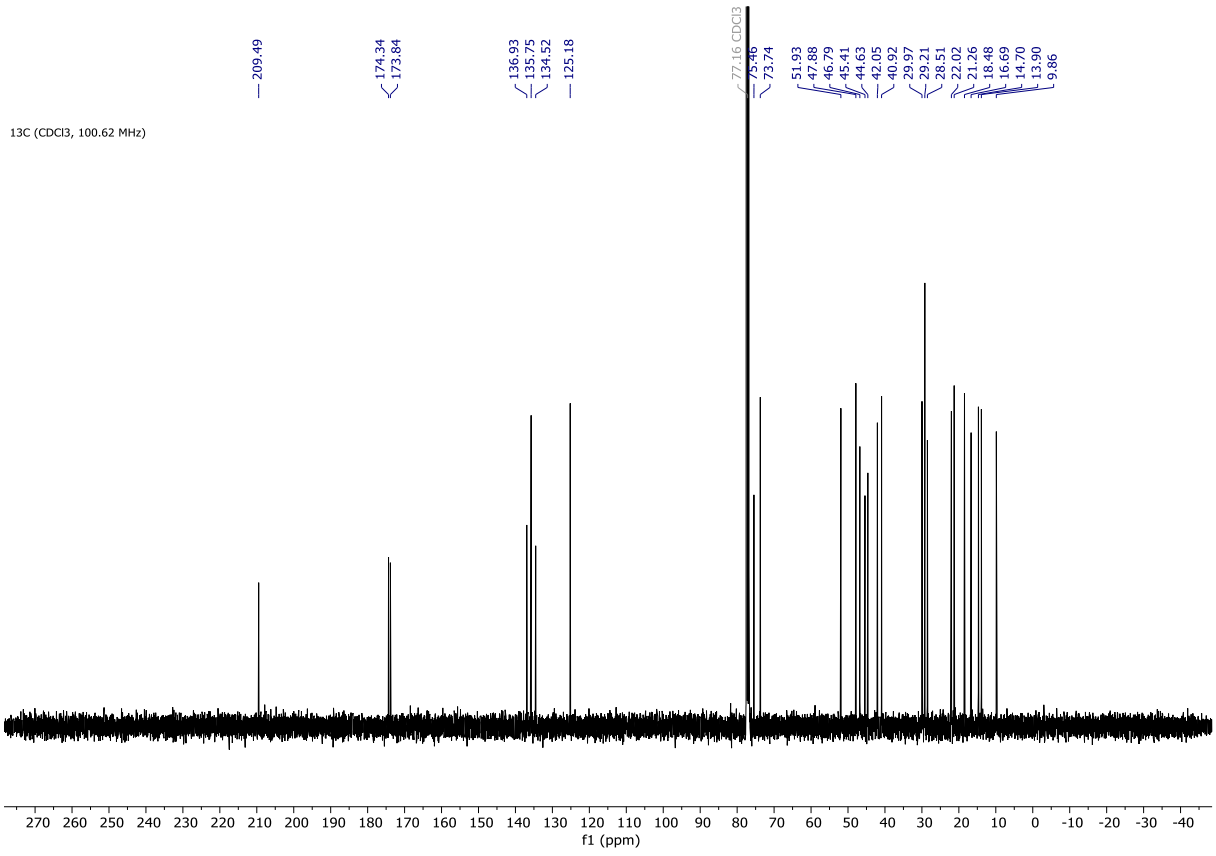


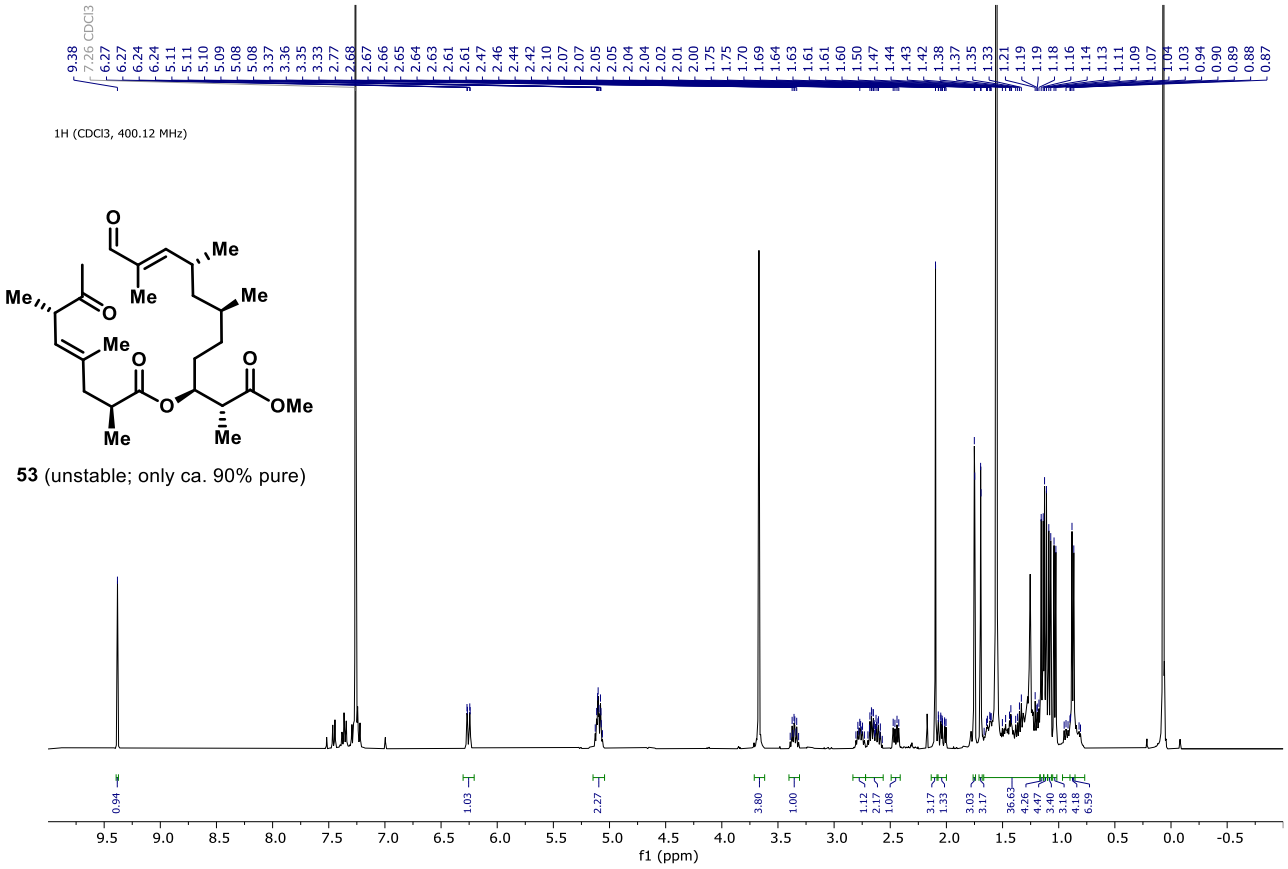

1H (CDCl3, 400.12 MHz)



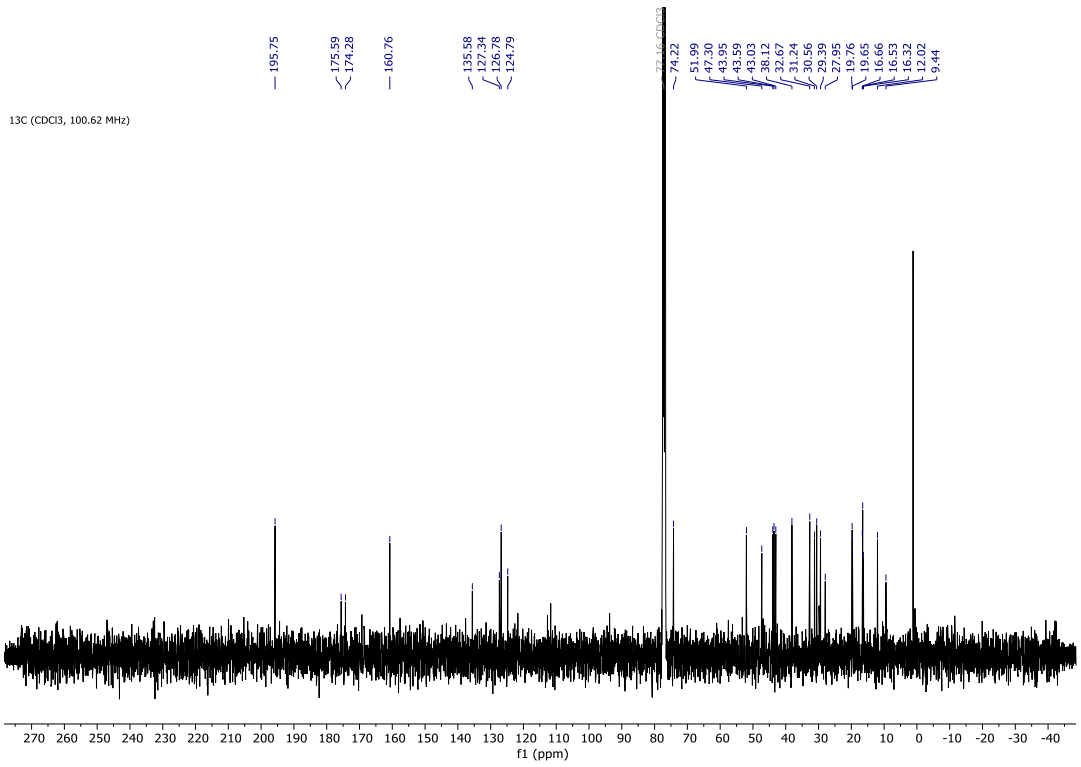

52

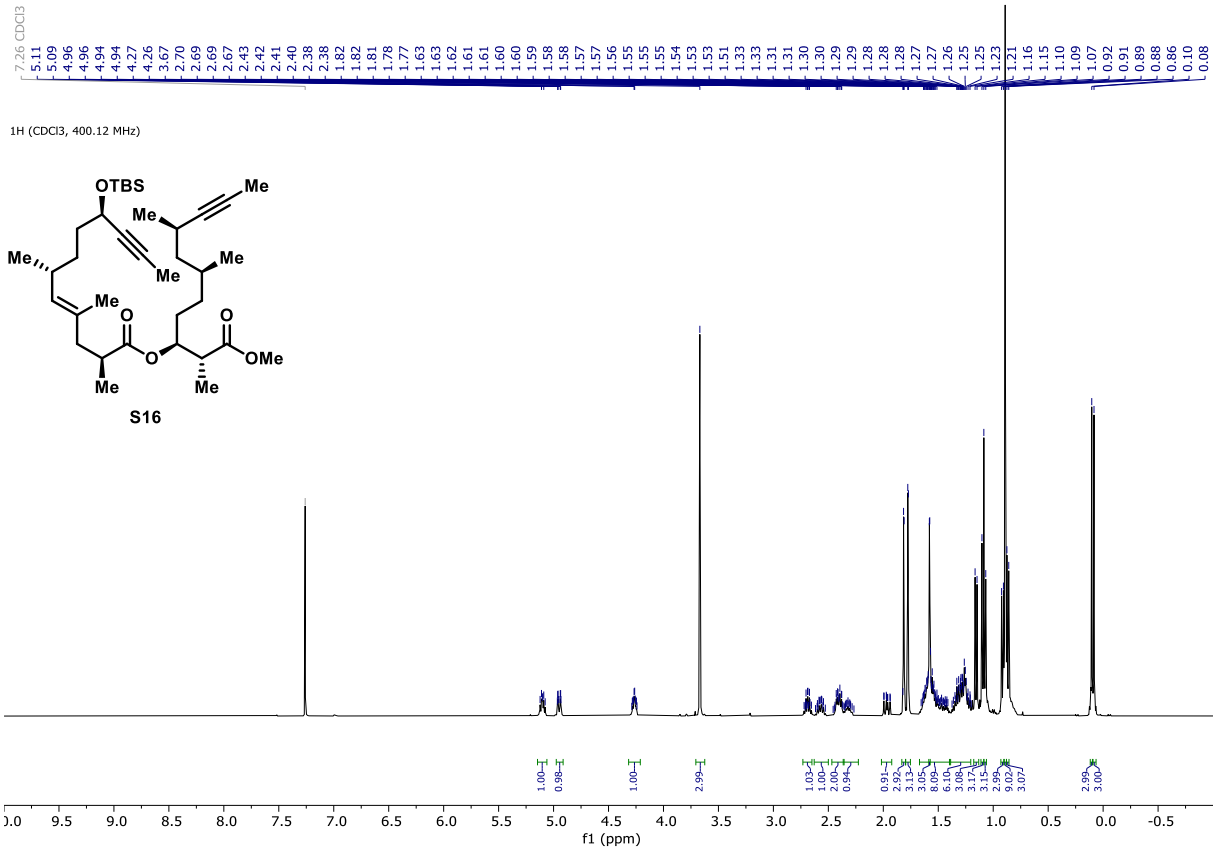


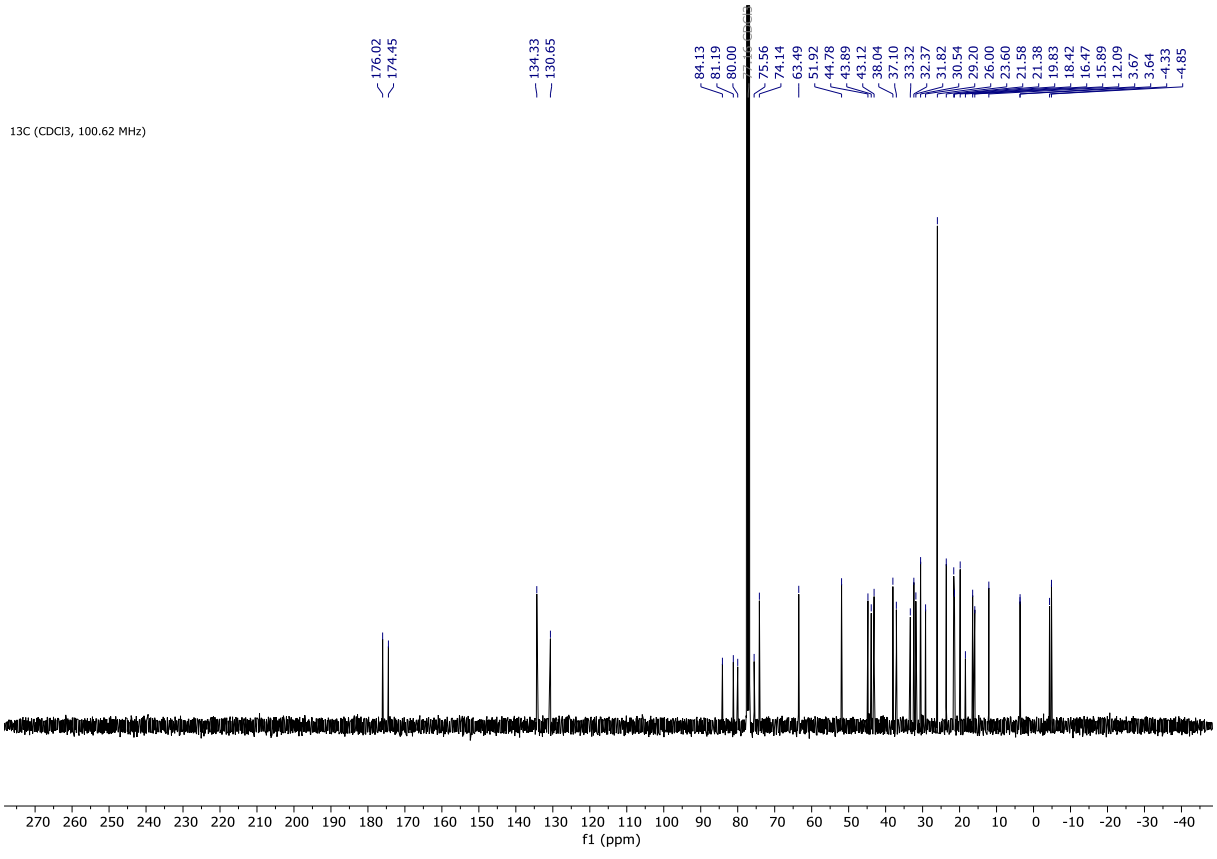



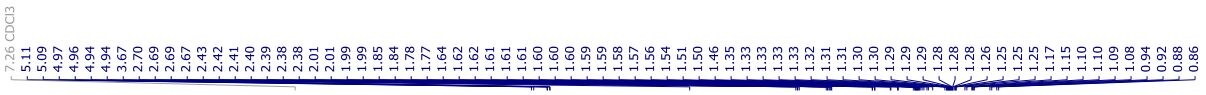



**53** (unstable; only ca. 90% pure)

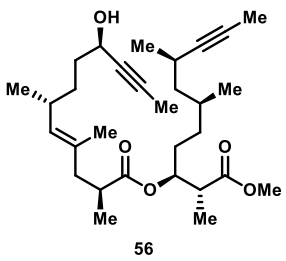



1H (CDCl3, 400.12 MHz)
OTBS
Me
Me
Me
Me
Me
Me
Me
O
O
O
OMe
Me
Me
S16
f1 (ppm)


13C (CDCl3, 100.62 MHz)
f1 (ppm)




1H (CDCl3, 400.12 MHz)

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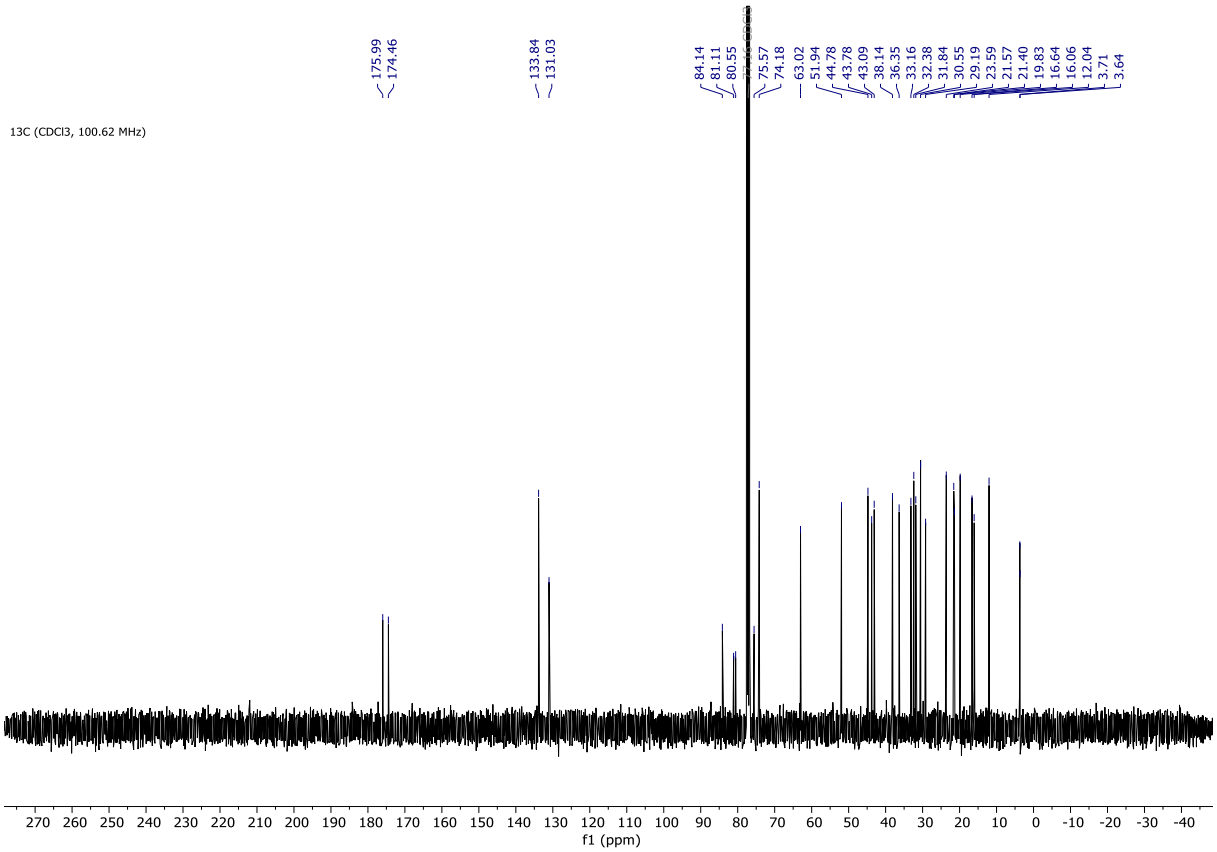
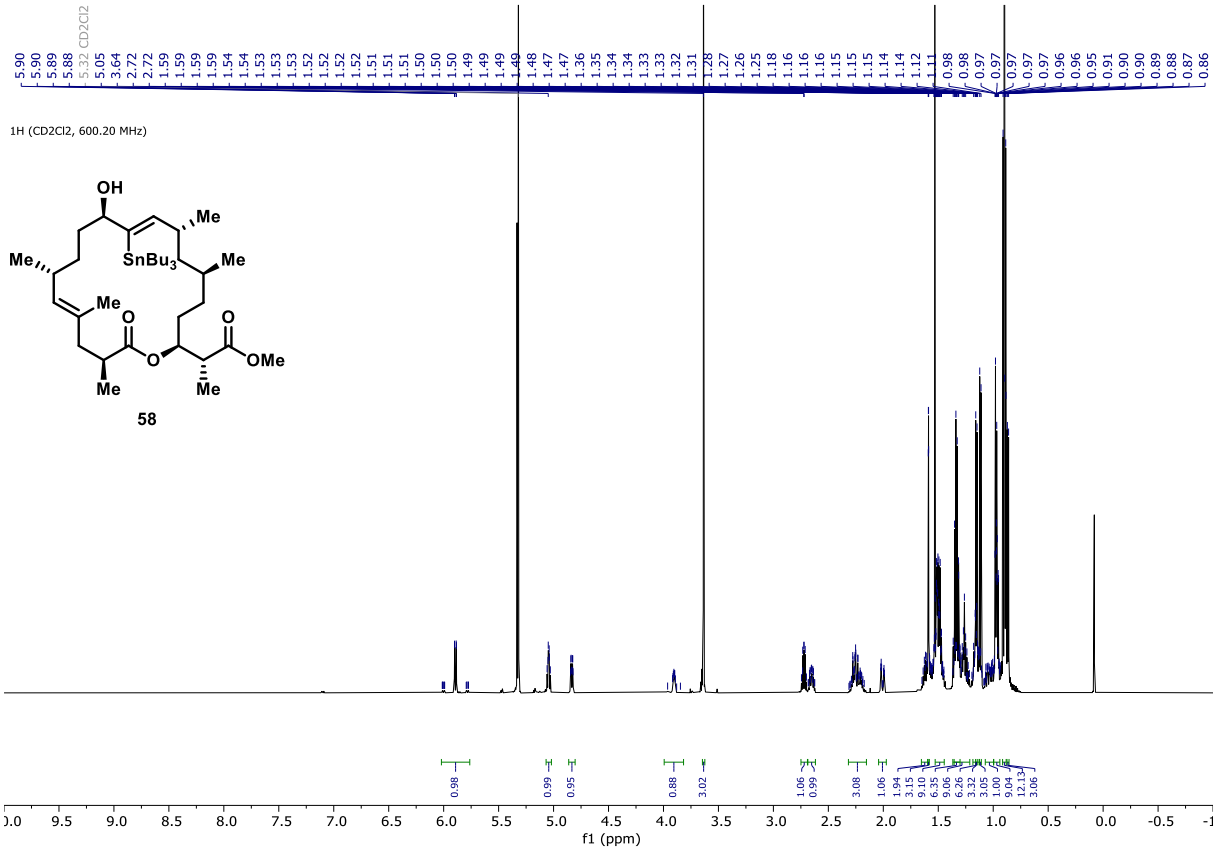
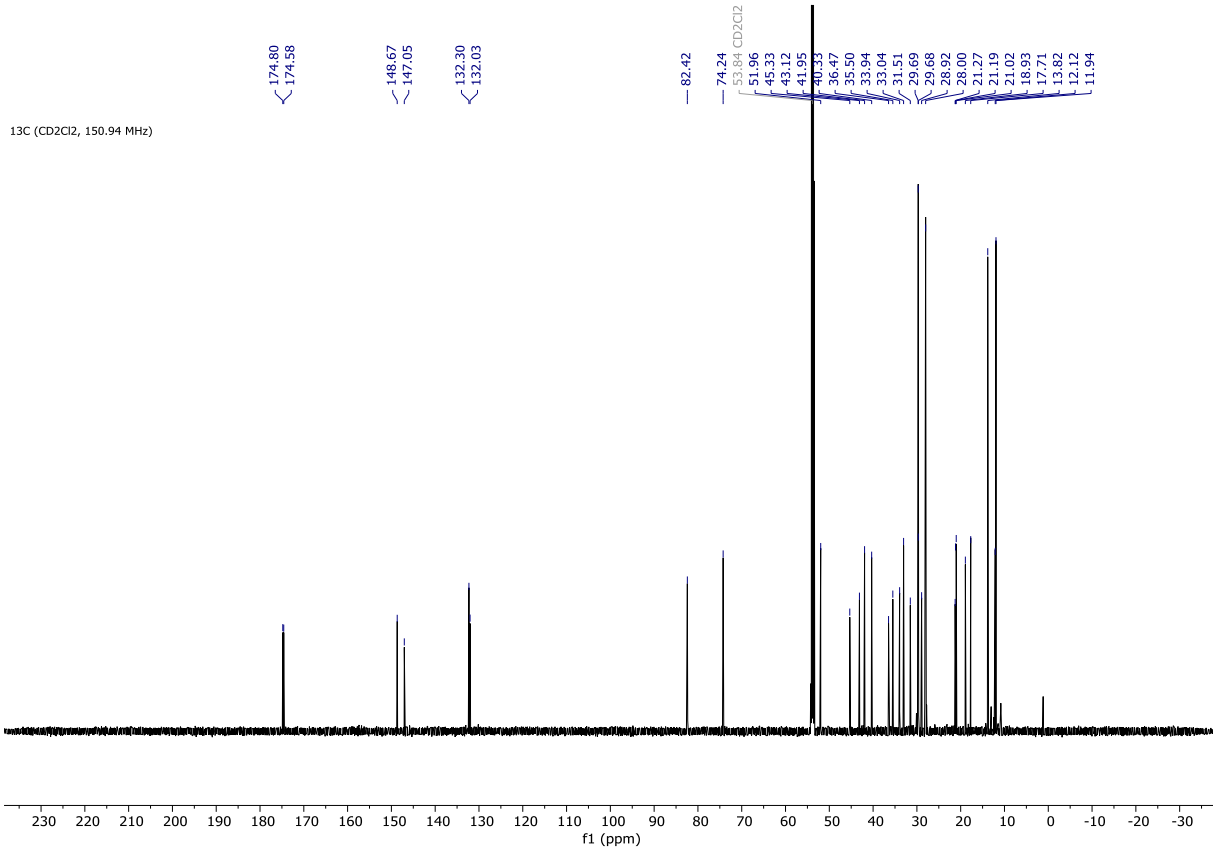
13C (CDCl3, 100.62 MHz)

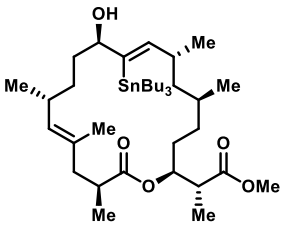



1H (CD2Cl2, 600.20 MHz)
OH
Me
SnBu3
Me
Me
Me
O
O
O
OMe
Me
Me
58
f1 (ppm)

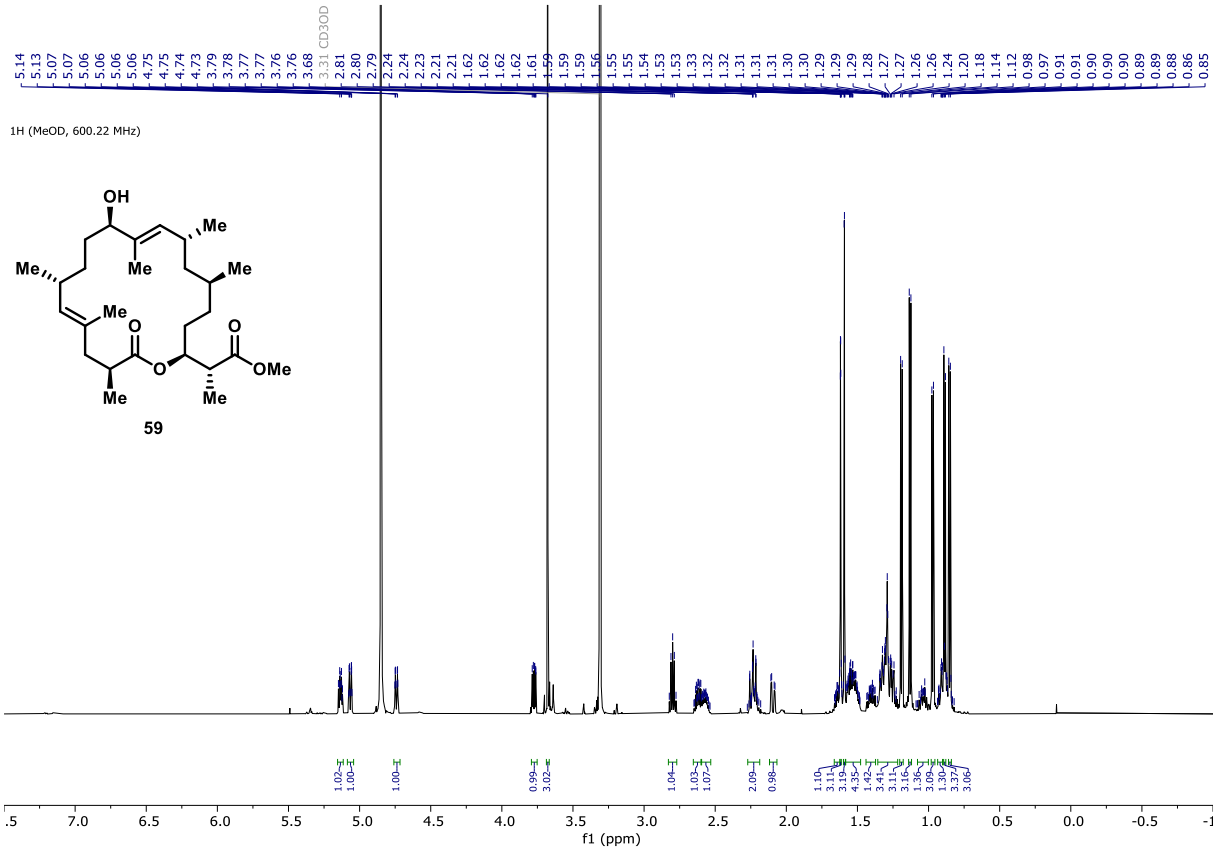

13C (CD2Cl2, 150.94 MHz)
f1 (ppm)

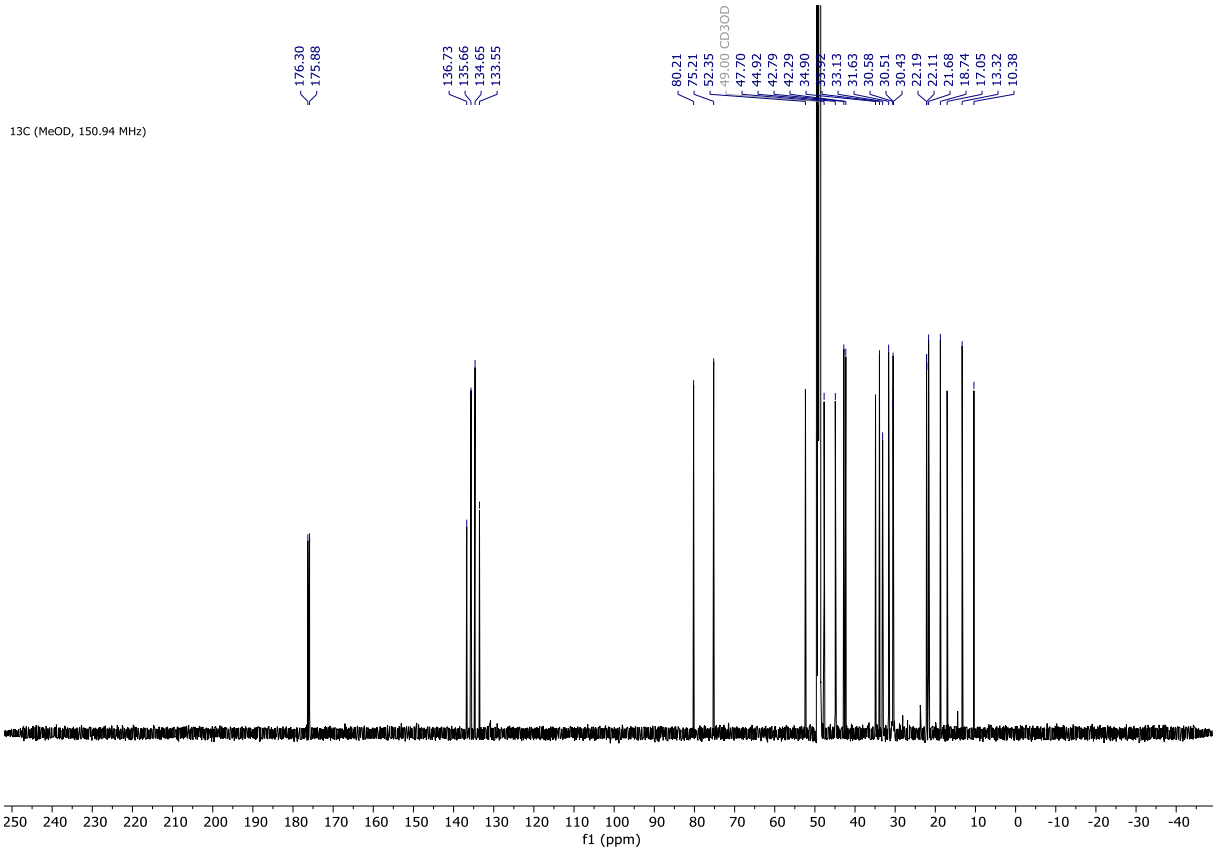
119Sn (CD2Cl2, 223.82 MHz)

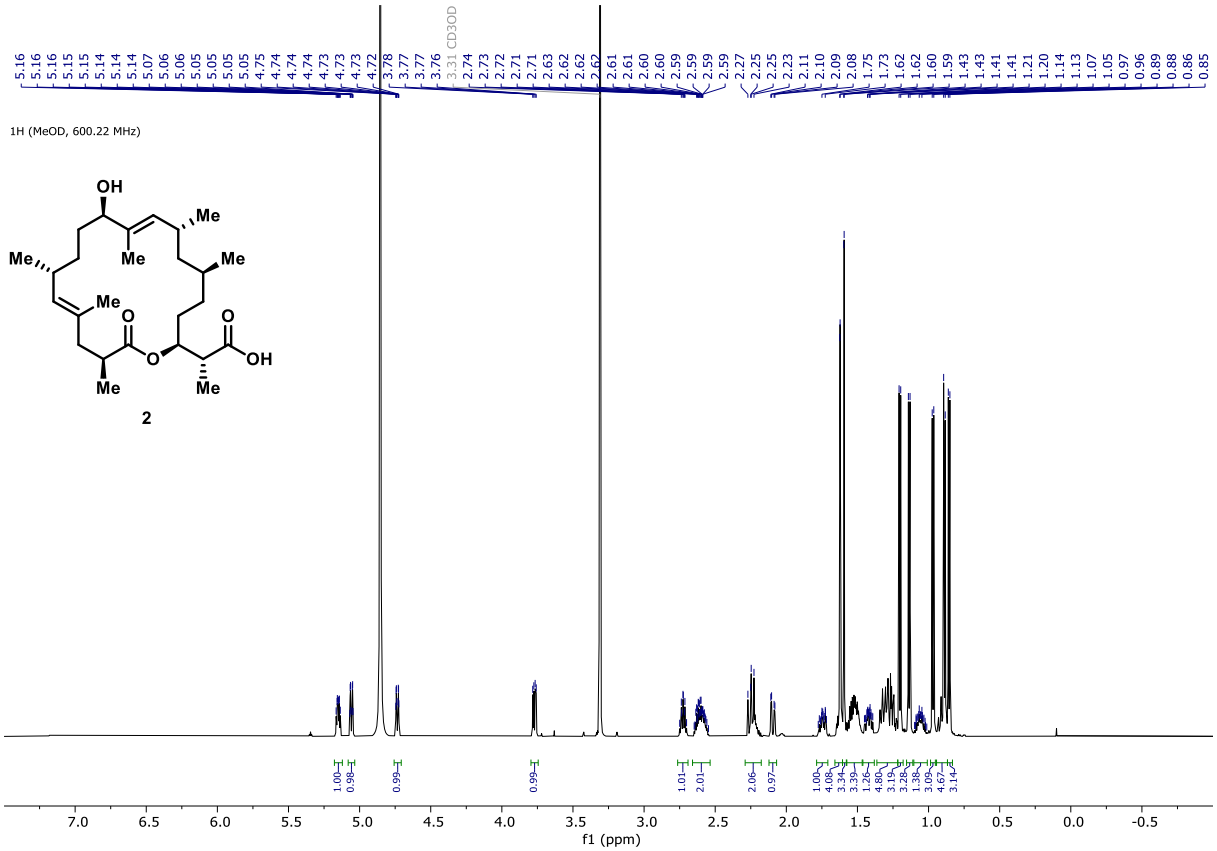
119Sn{1H}

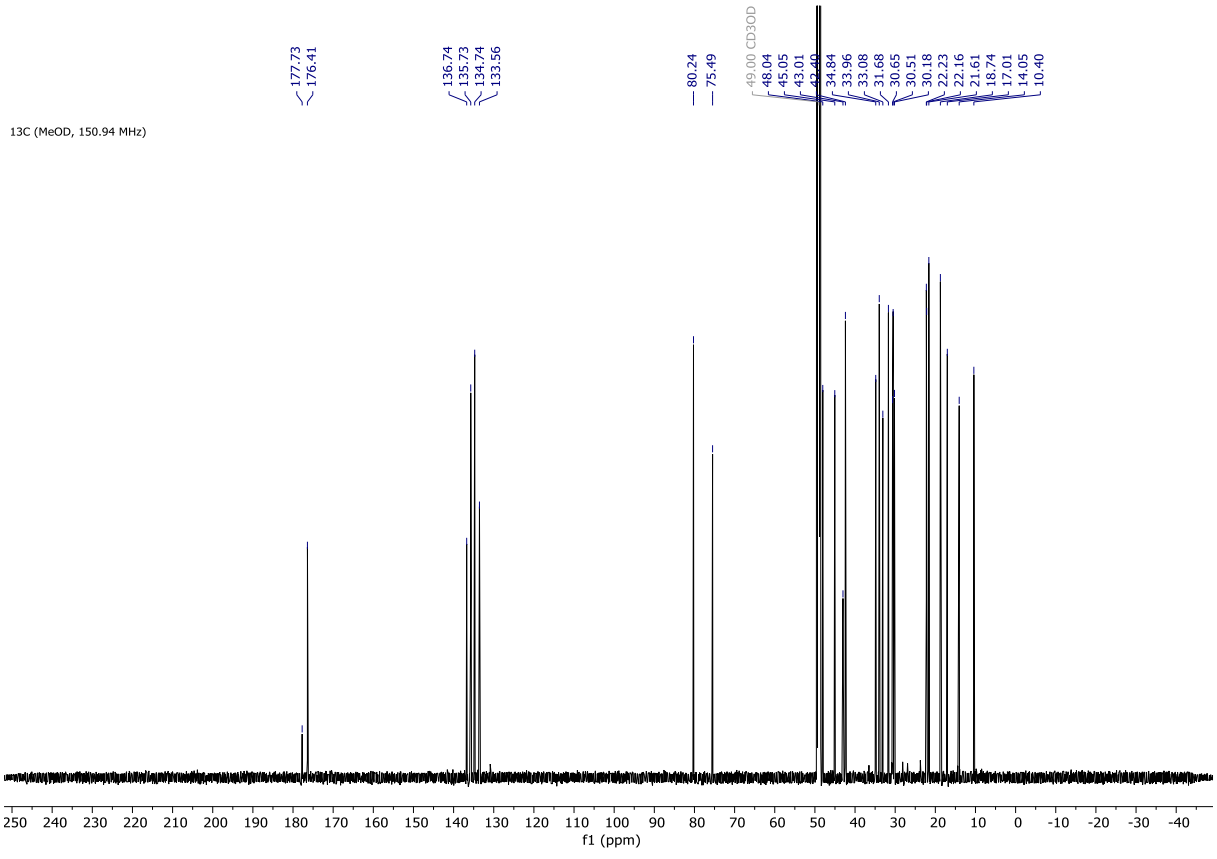


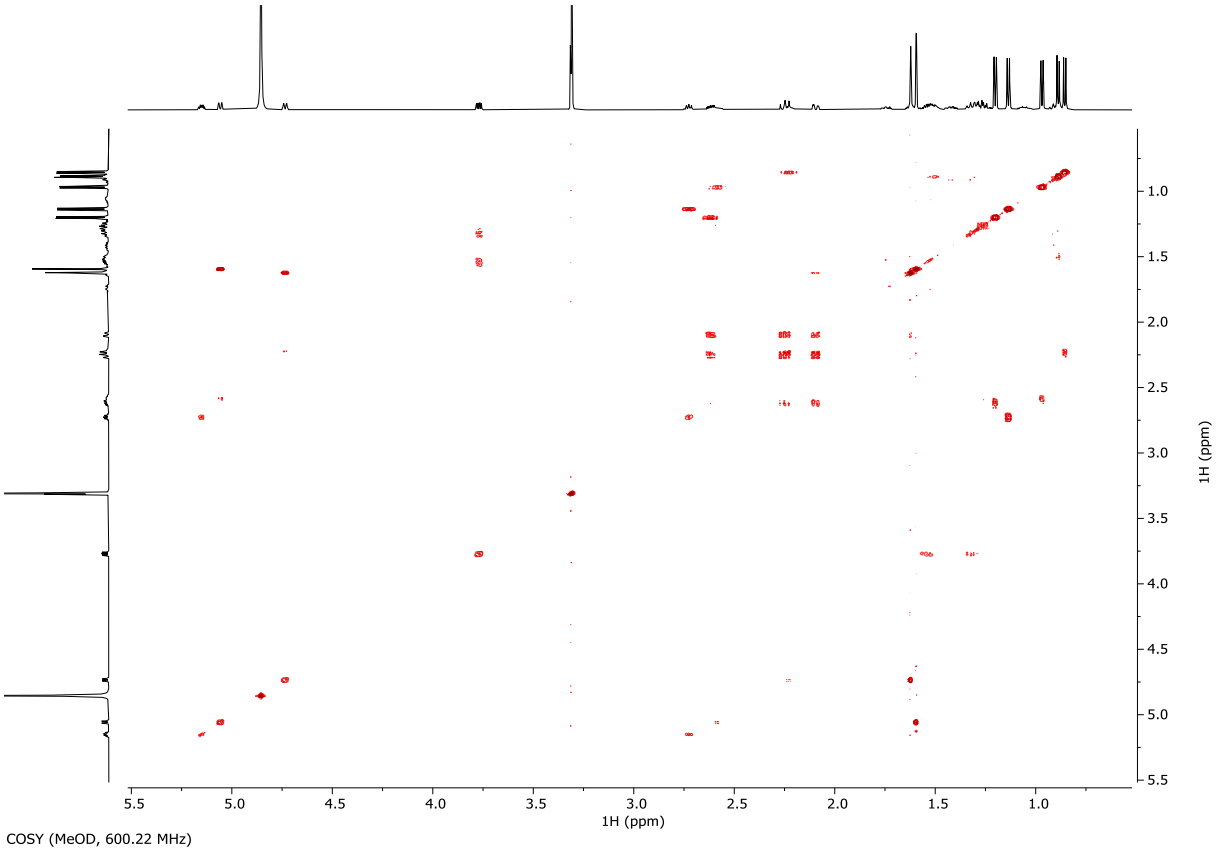

58


1H (MeOD, 600.22 MHz)
OH
Me
Me
Me
Me
Me
Me
O
O
O
O
OMe
Me
Me
59
f1 (ppm)

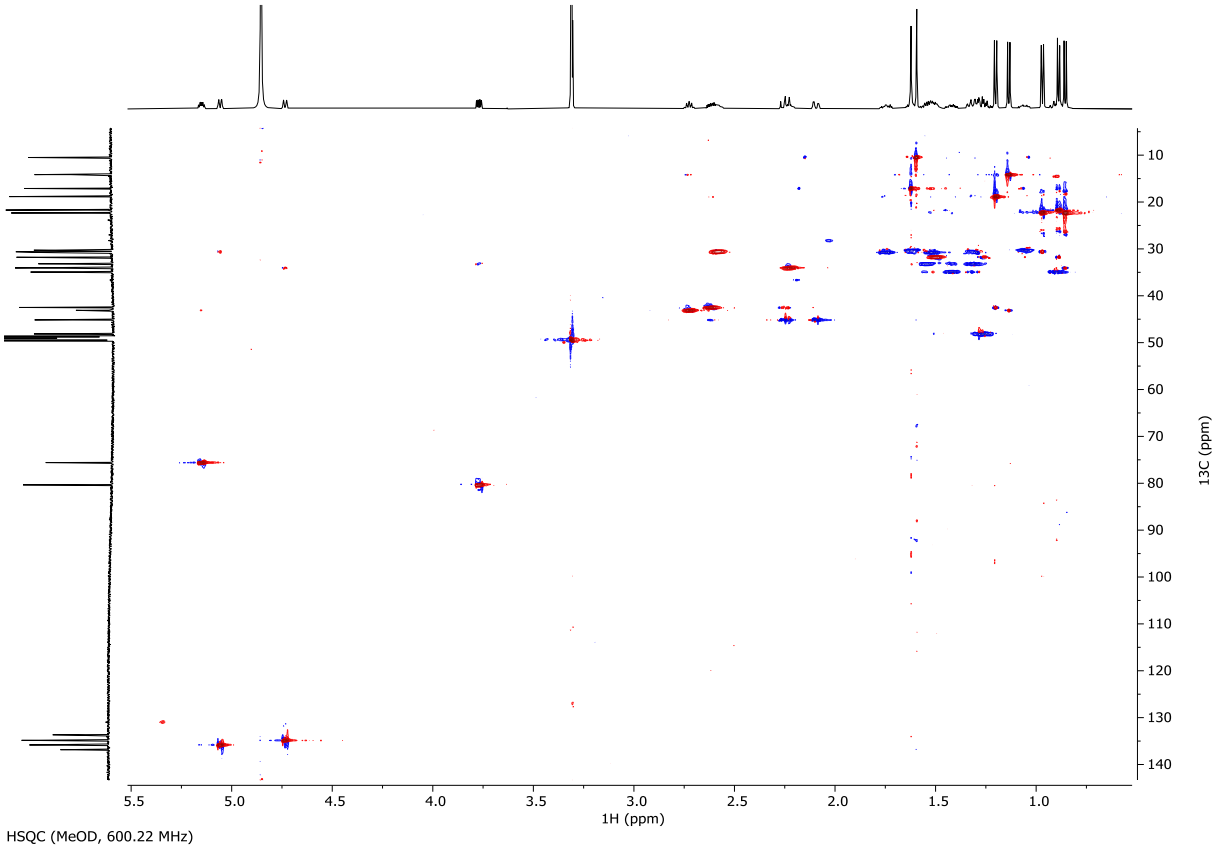

13C (MeOD, 150.94 MHz)
f1 (ppm)


1H (MeOD, 600.22 MHz)
OH
Me
Me
Me
Me
Me
O
O
O
OH
Me
Me
2
f1 (ppm)

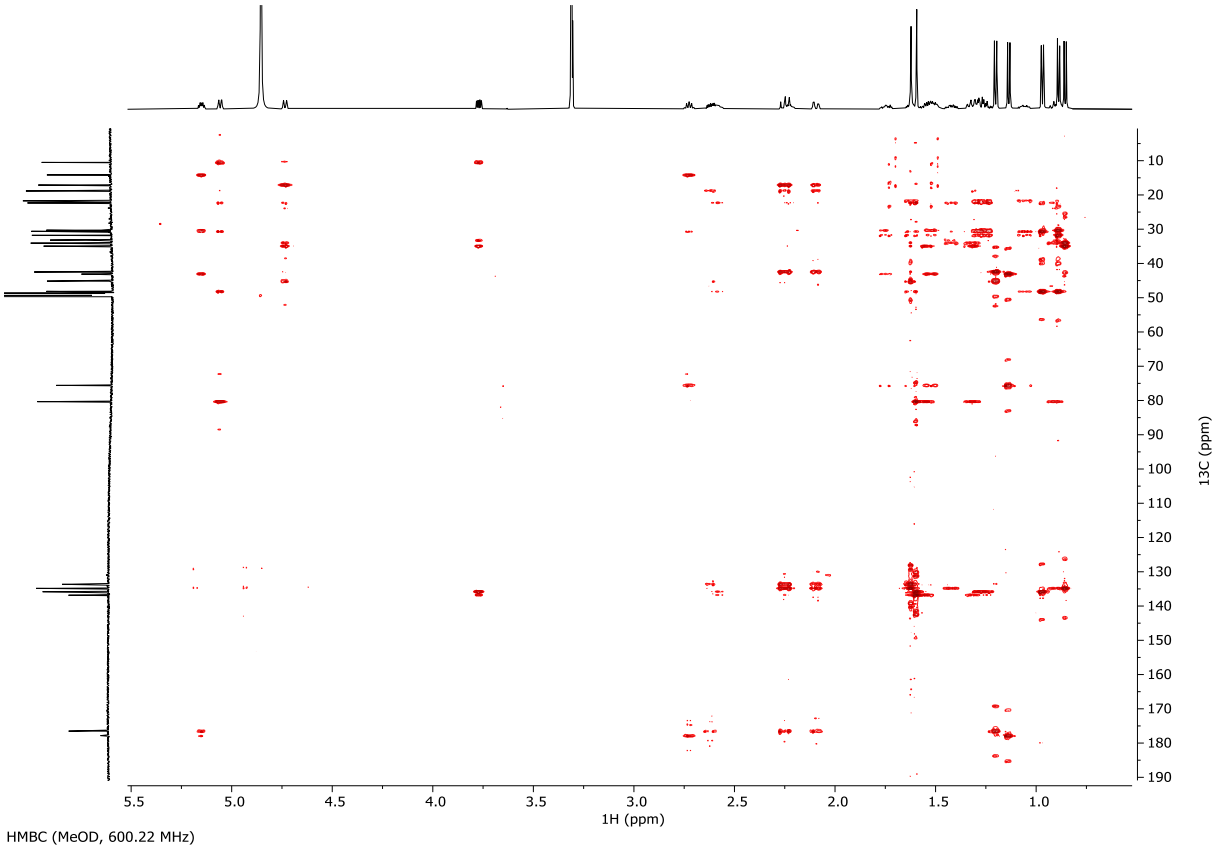

13C (MeOD, 150.94 MHz)
f1 (ppm)



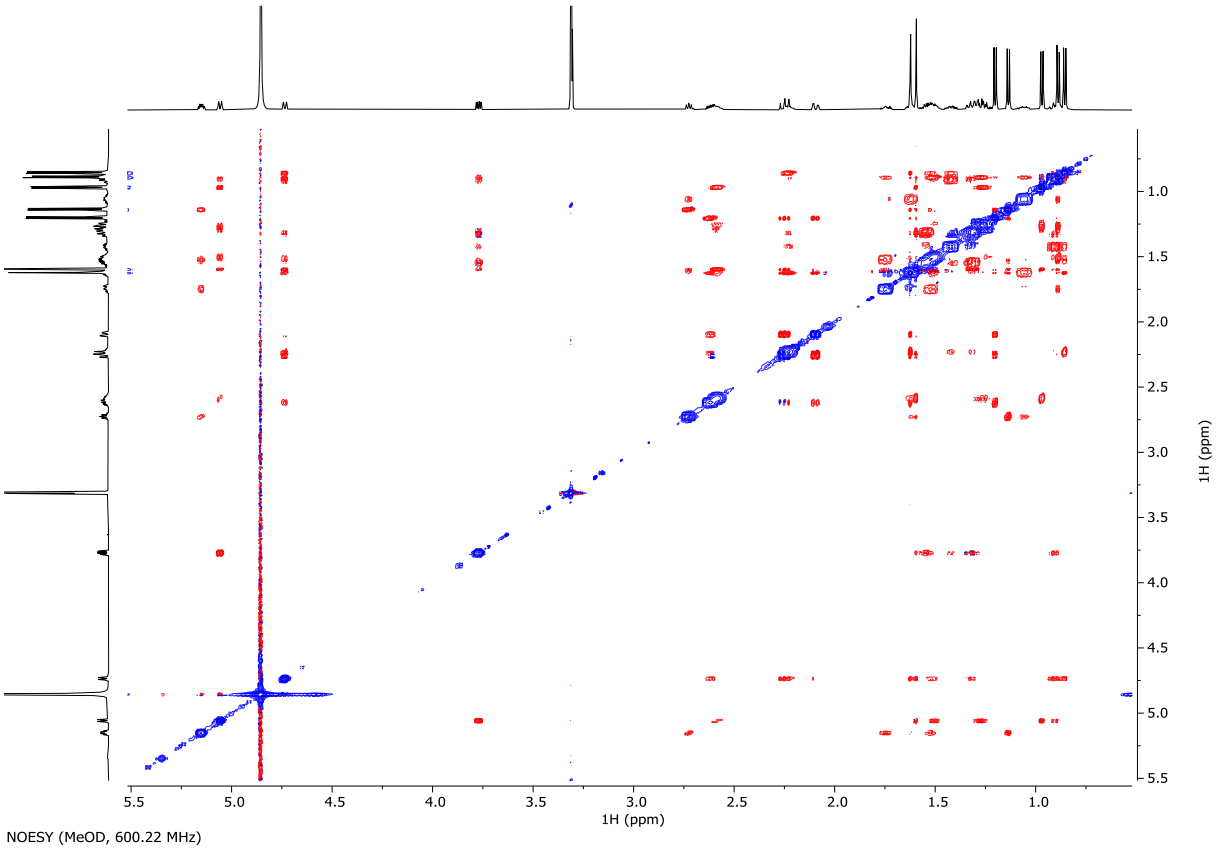

COSY (MeOD, 600.22 MHz)



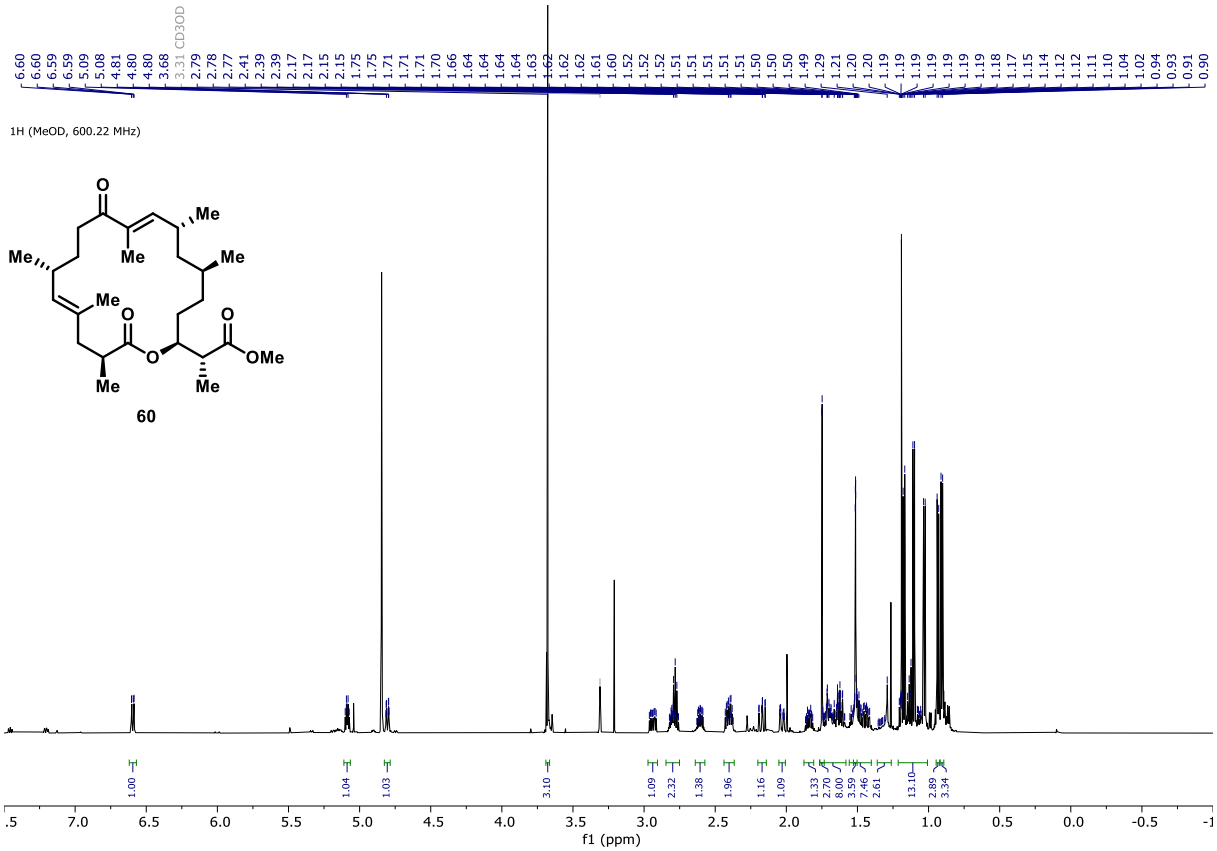

HSQC (MeOD, 600.22 MHz)

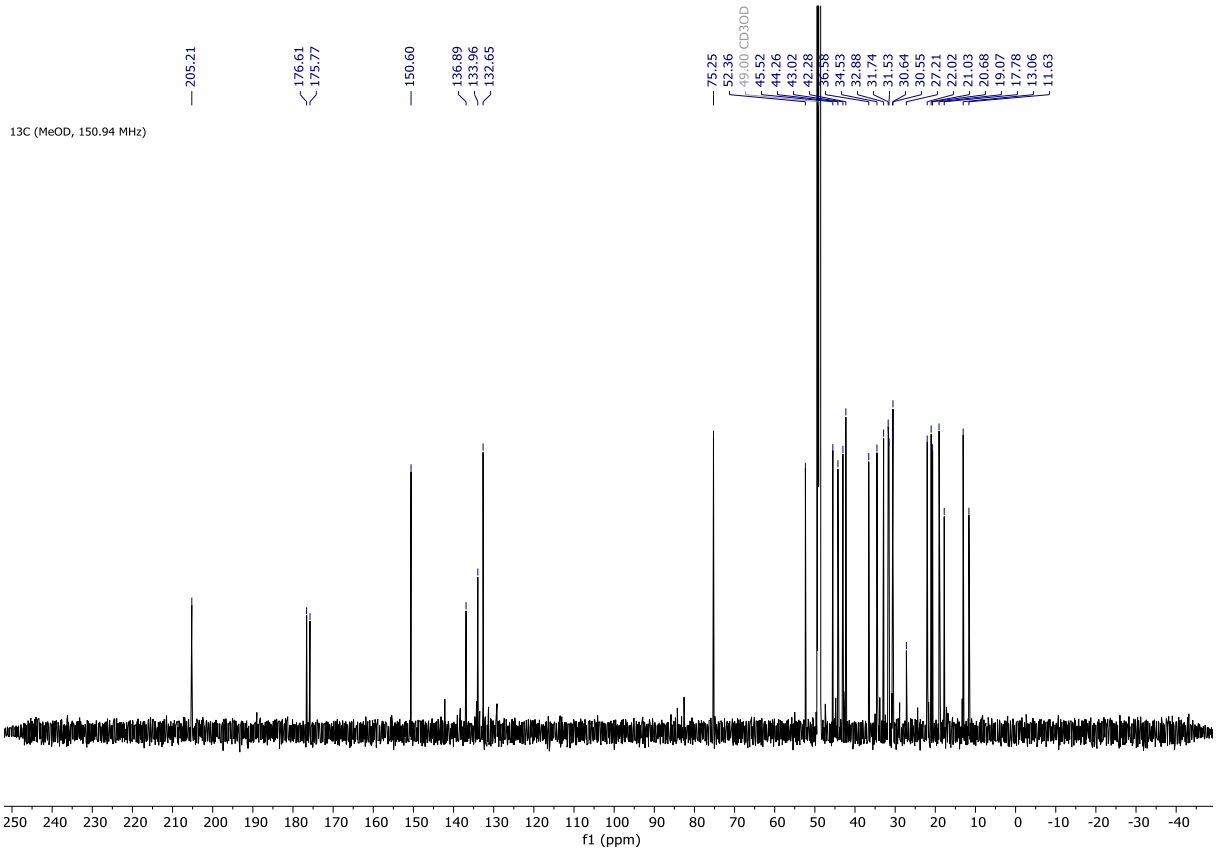


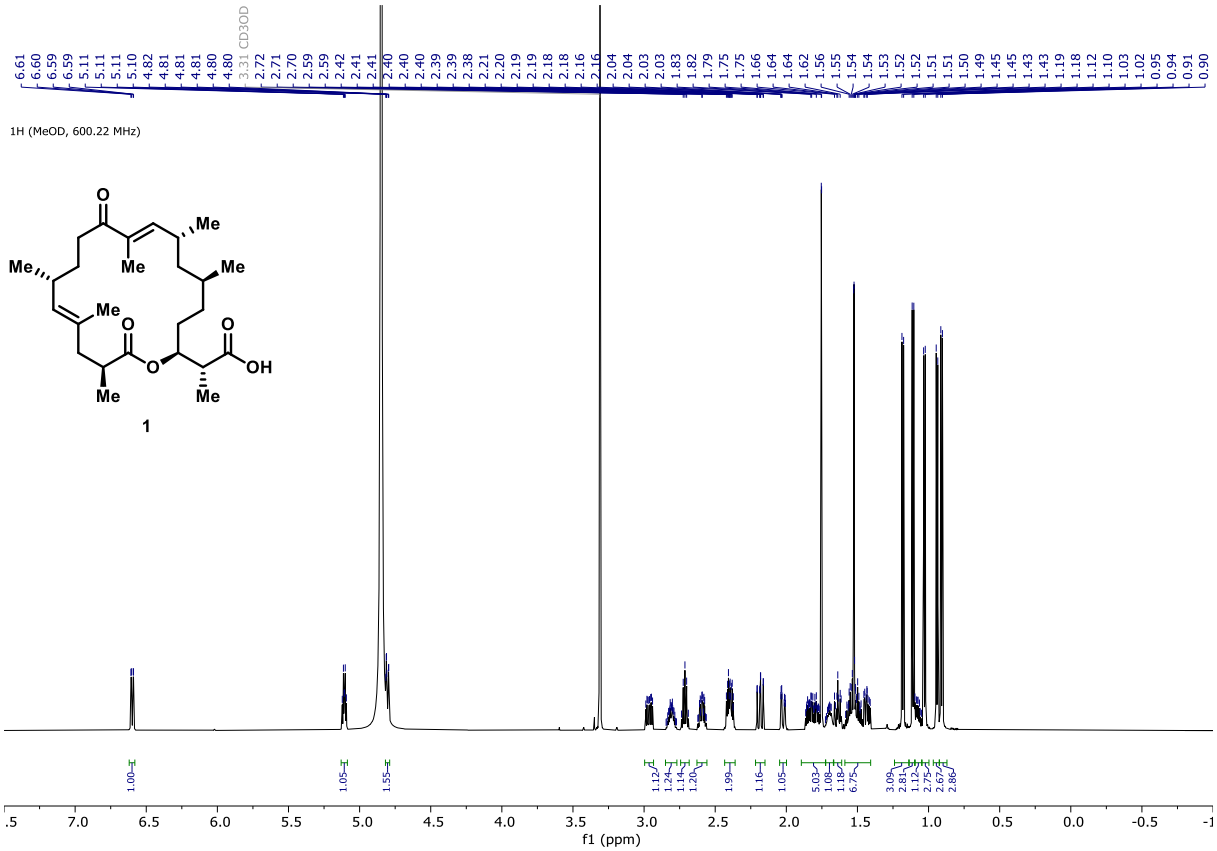

HMBC (MeOD, 600.22 MHz)

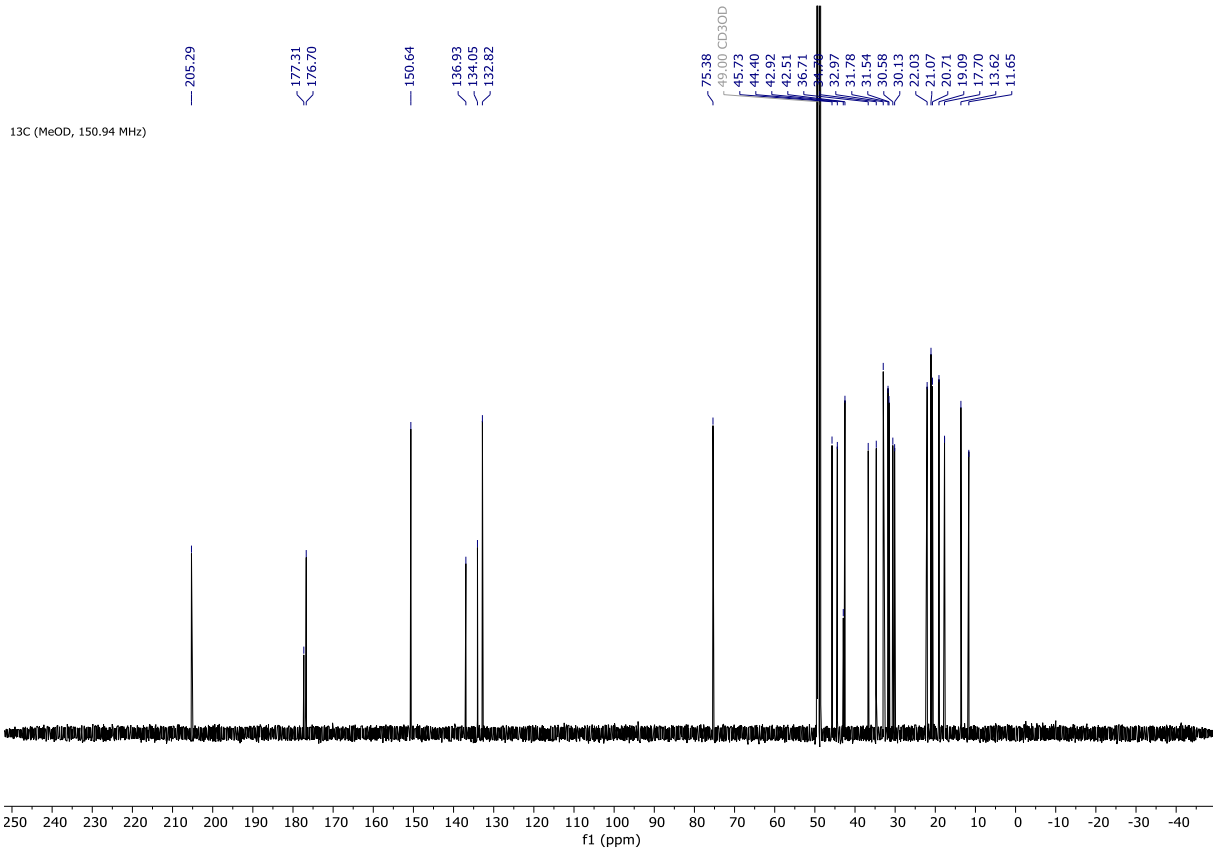


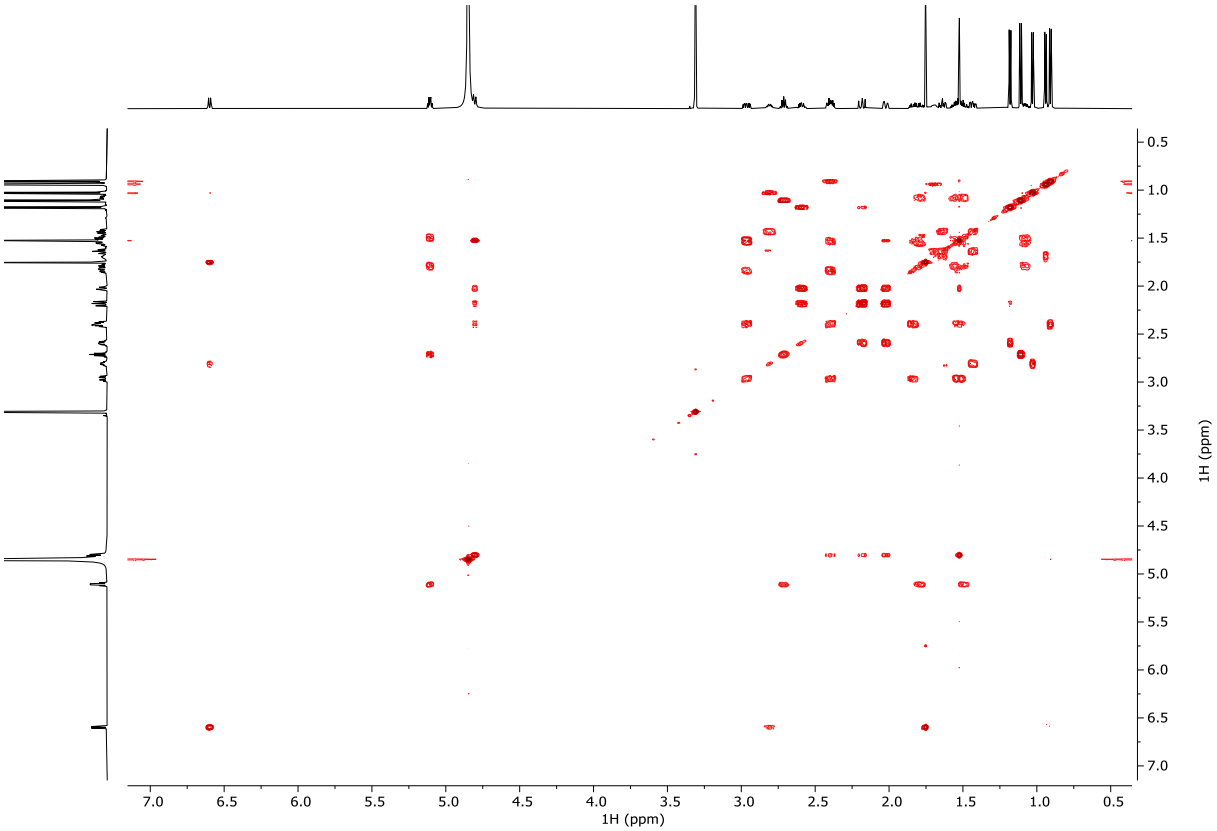

NOESY (MeOD, 600.22 MHz)


1H (MeOD, 600.22 MHz)
60
f1 (ppm)

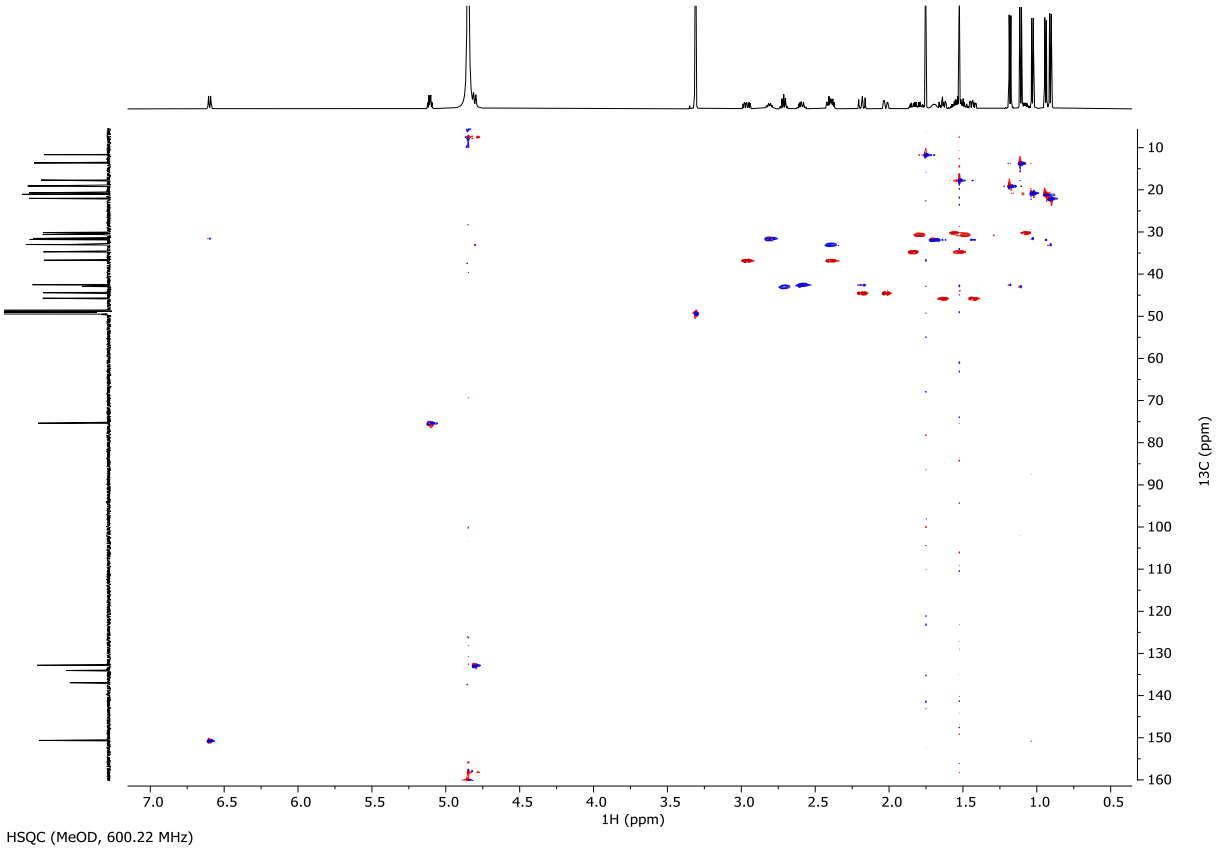

13C (MeOD, 150.94 MHz)
f1 (ppm)


1H (MeOD, 600.22 MHz)
3.31 CD3OD
Me
Me
Me
Me
Me
Me
O
O
O
O
OH
1
f1 (ppm)

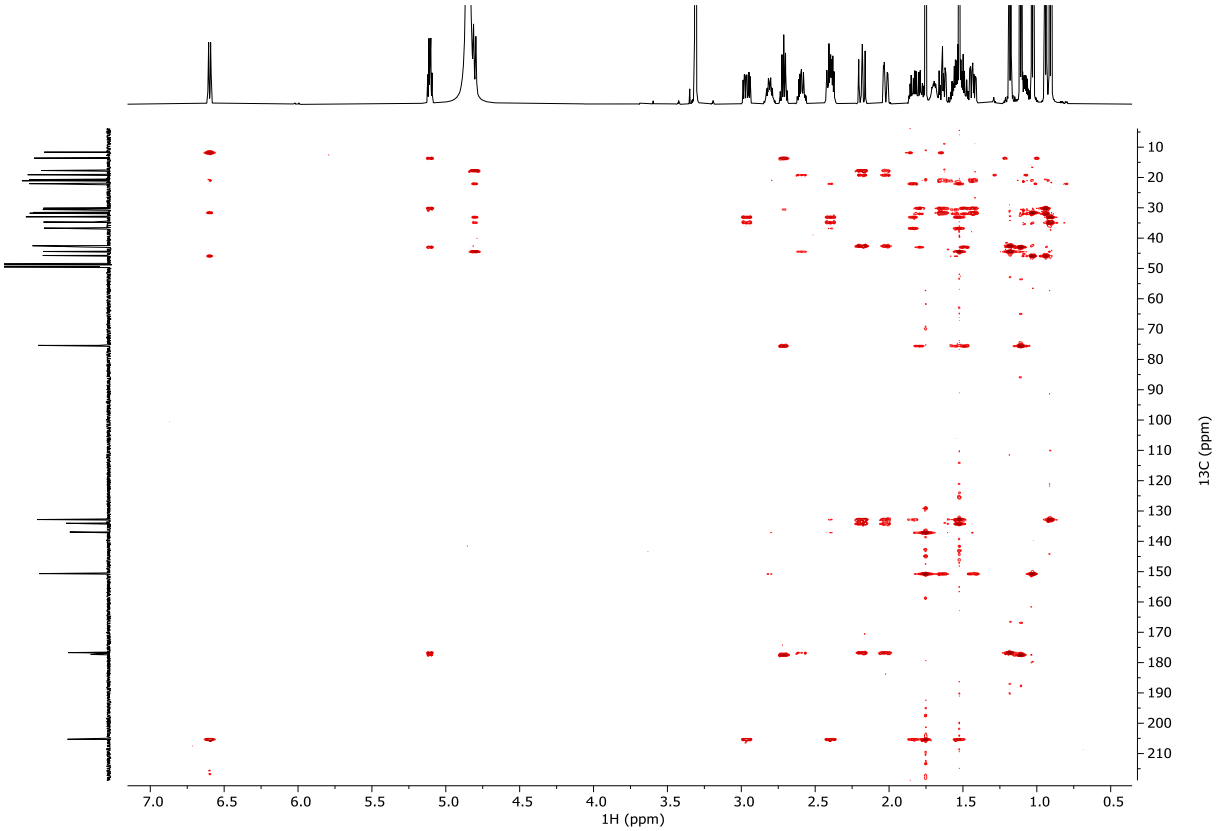

13C (MeOD, 150.94 MHz)
205.29
177.31
176.70
150.64
136.93
134.05
132.82
75.38
49.00 CD3OD
45.73
44.40
42.92
42.51
36.71
34.38
32.97
31.78
31.54
30.58
30.13
22.03
21.07
20.71
19.09
17.70
13.62
11.65
f1 (ppm)



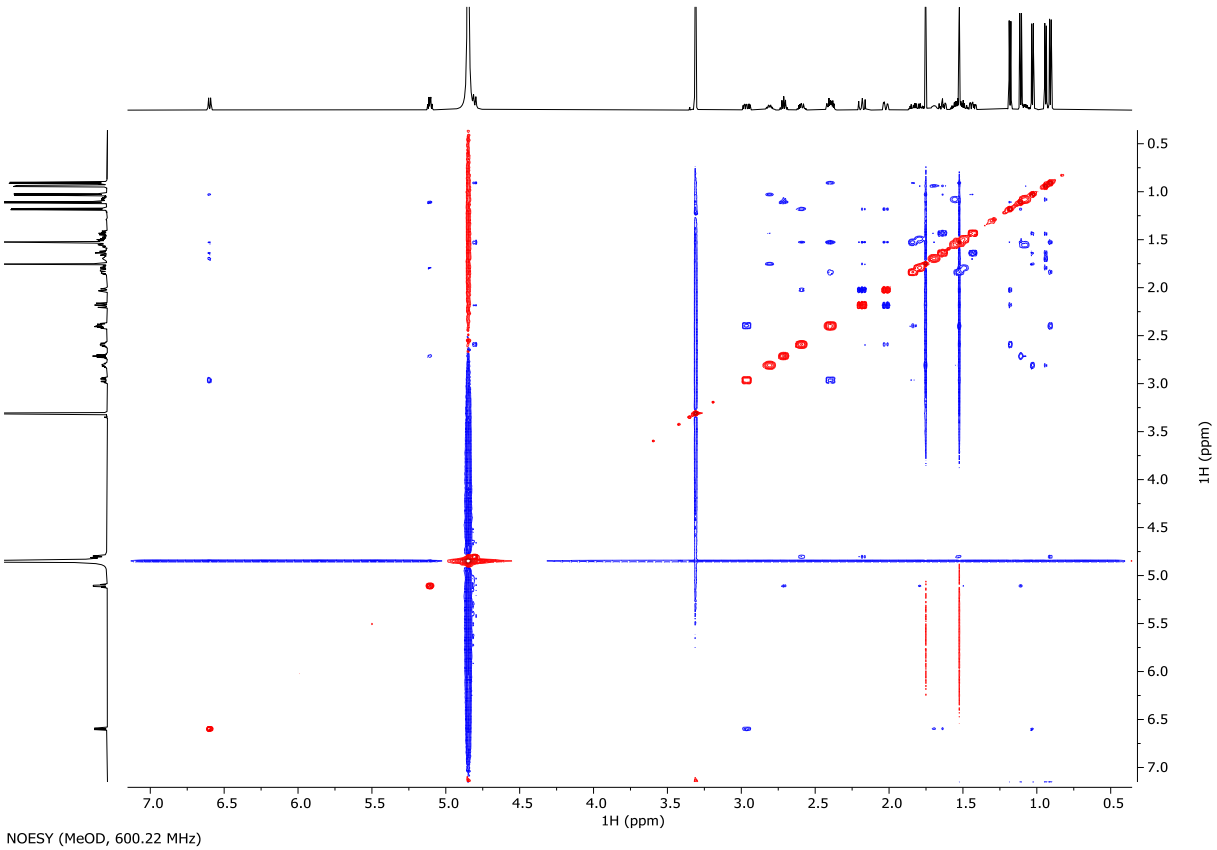

COSY (MeOD, 600.22 MHz)



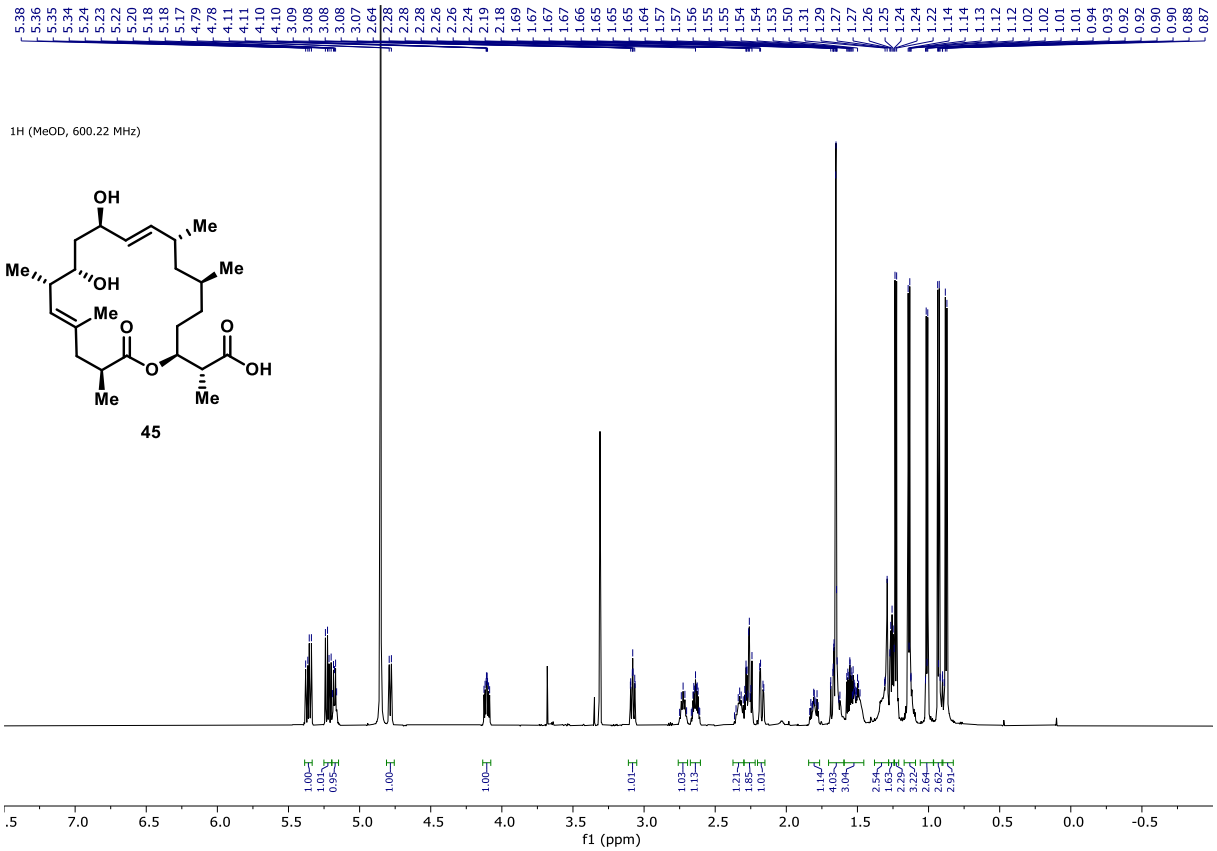

HSQC (MeOD, 600.22 MHz)

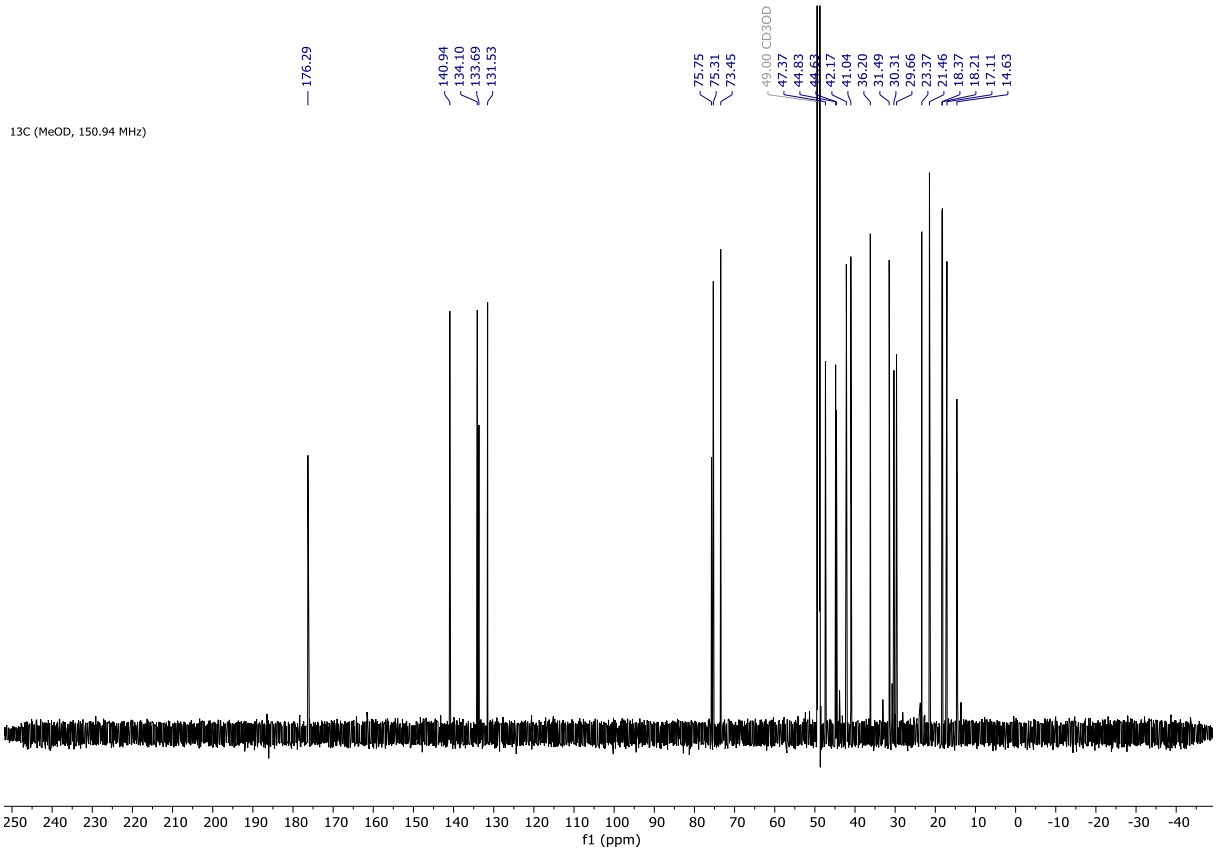


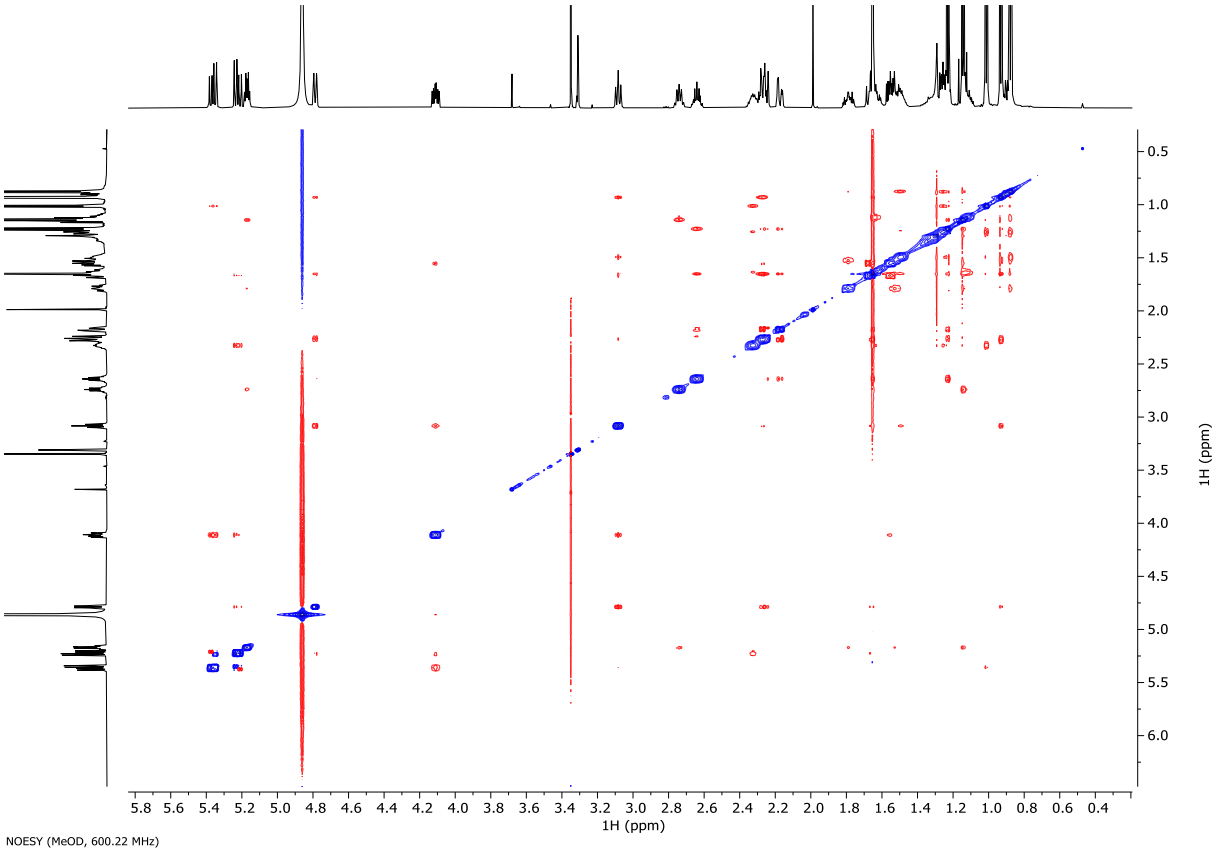

HMBC (MeOD, 600.22 MHz)



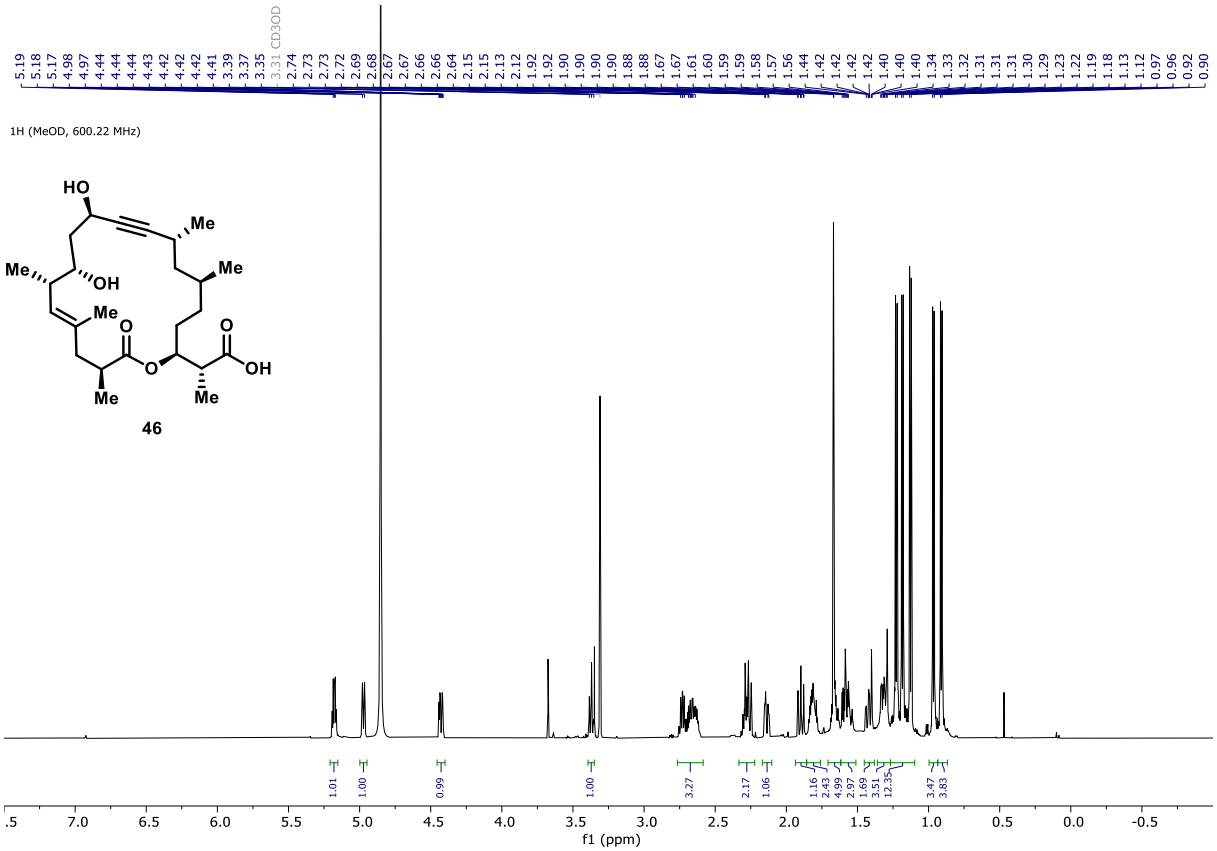

NOESY (MeOD, 600.22 MHz)

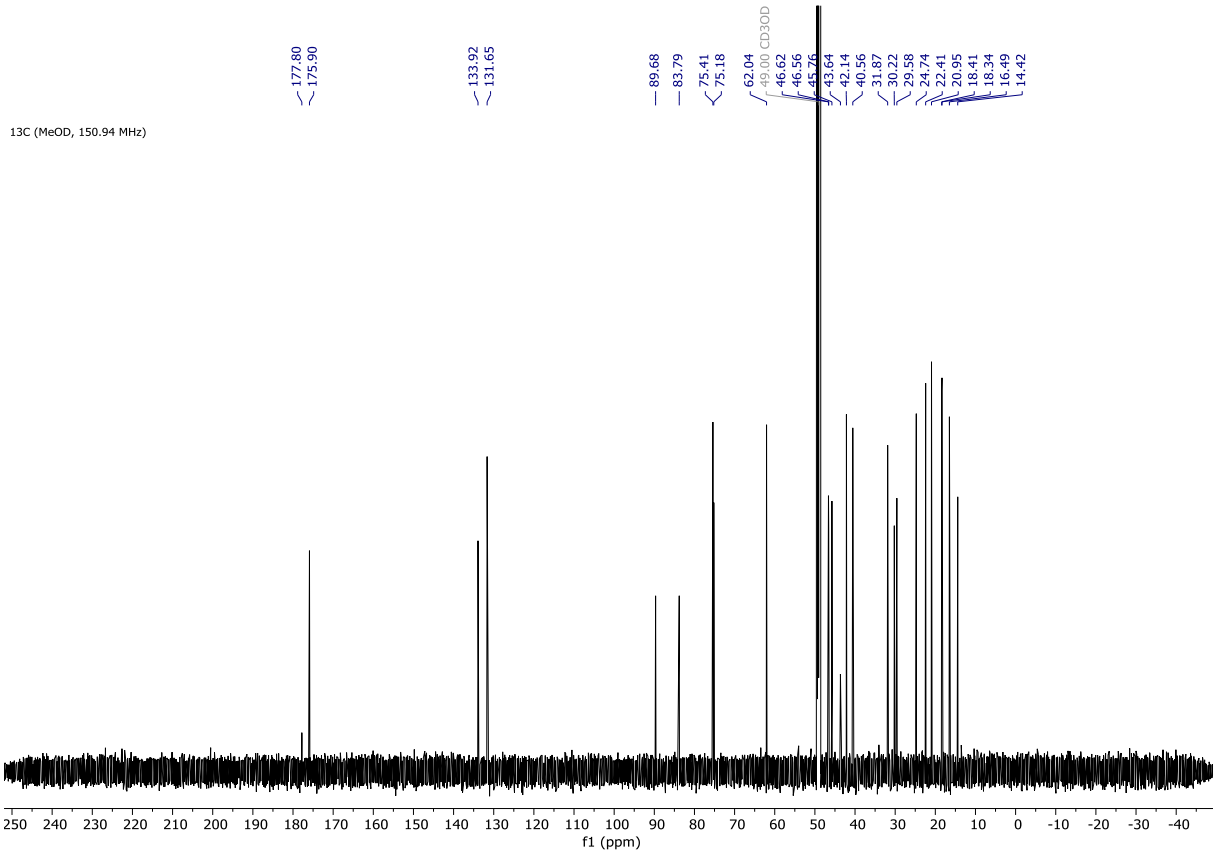

1H (MeOD, 600.22 MHz)
OH
Me
Me
OH
Me
Me
O
O
O
OH
Me
Me
45
f1 (ppm)

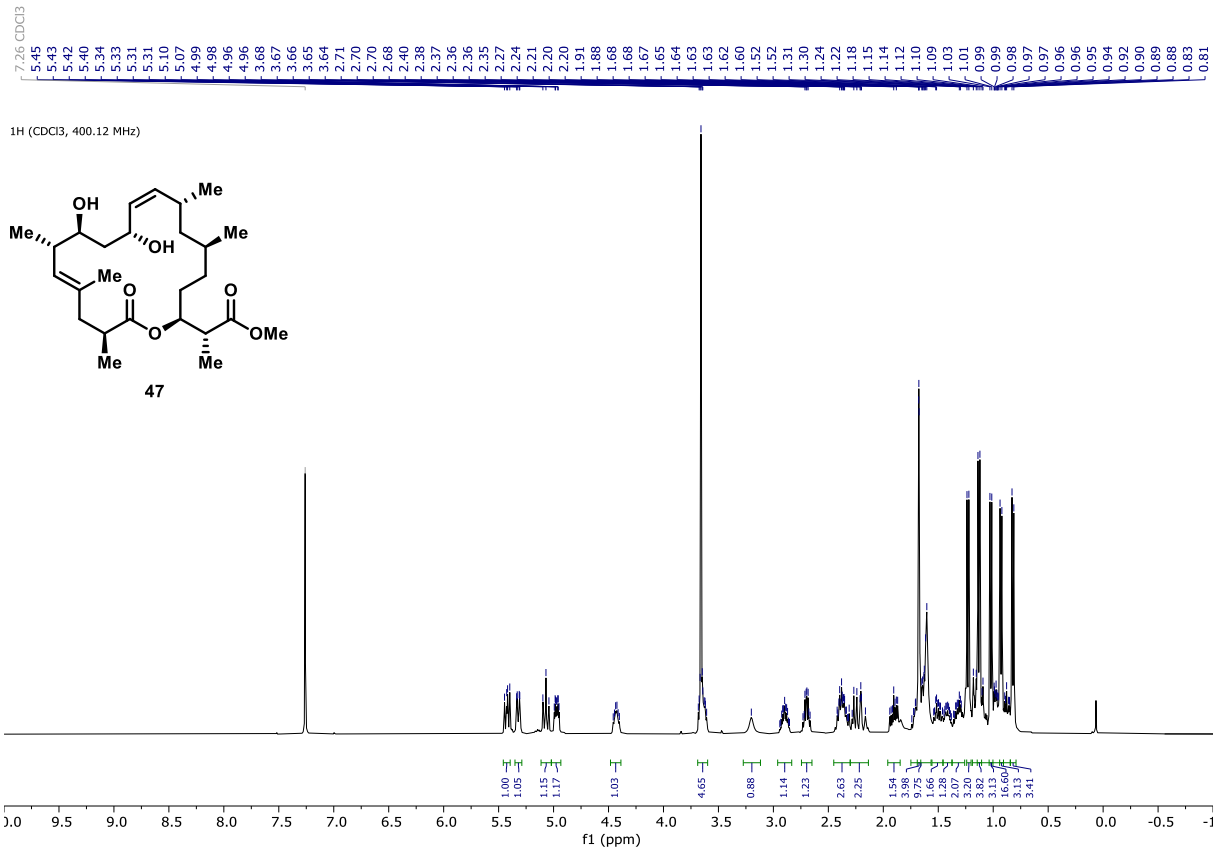

13C (MeOD, 150.94 MHz)
176.29
140.94
134.10
133.69
131.53
75.75
75.31
73.45
49.00 CD3OD
47.37
44.83
44.63
42.17
41.04
36.20
31.49
30.31
29.66
23.37
21.46
18.37
18.21
17.11
14.63
f1 (ppm)

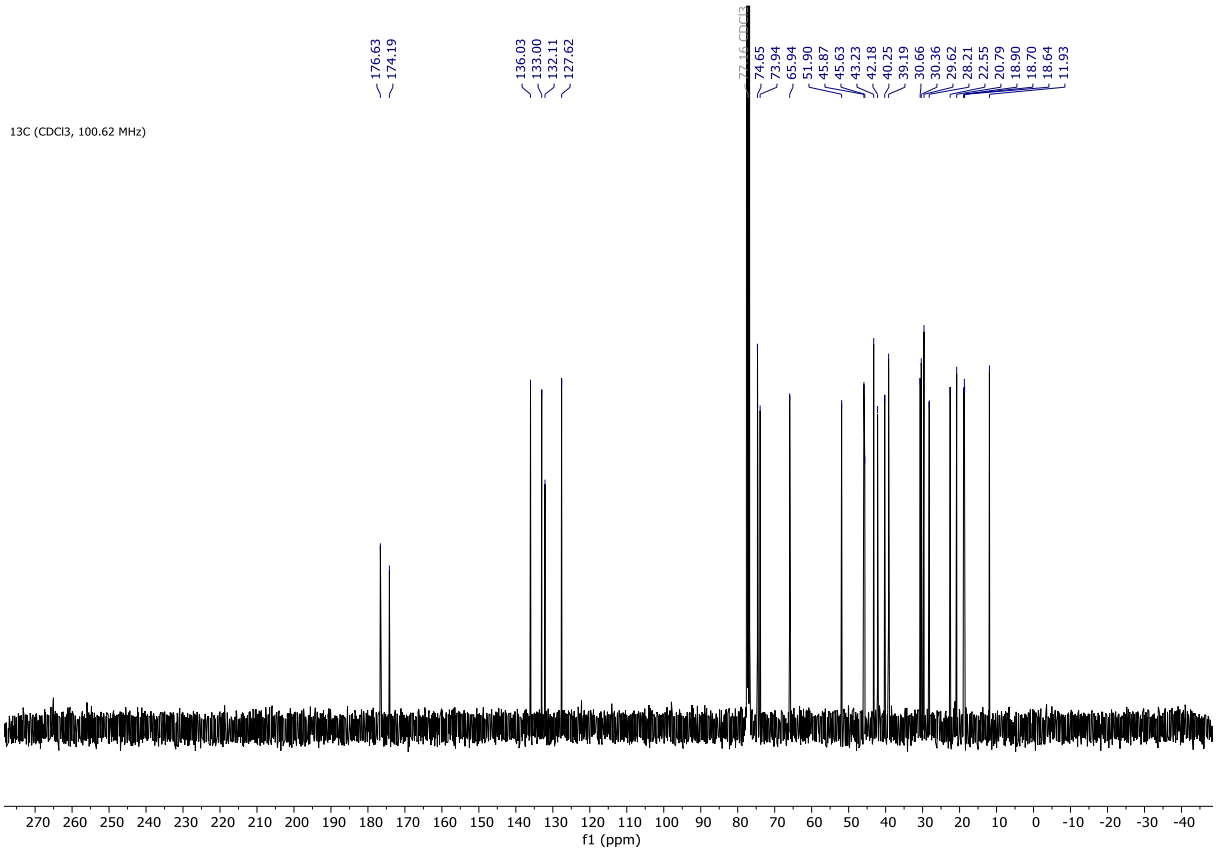


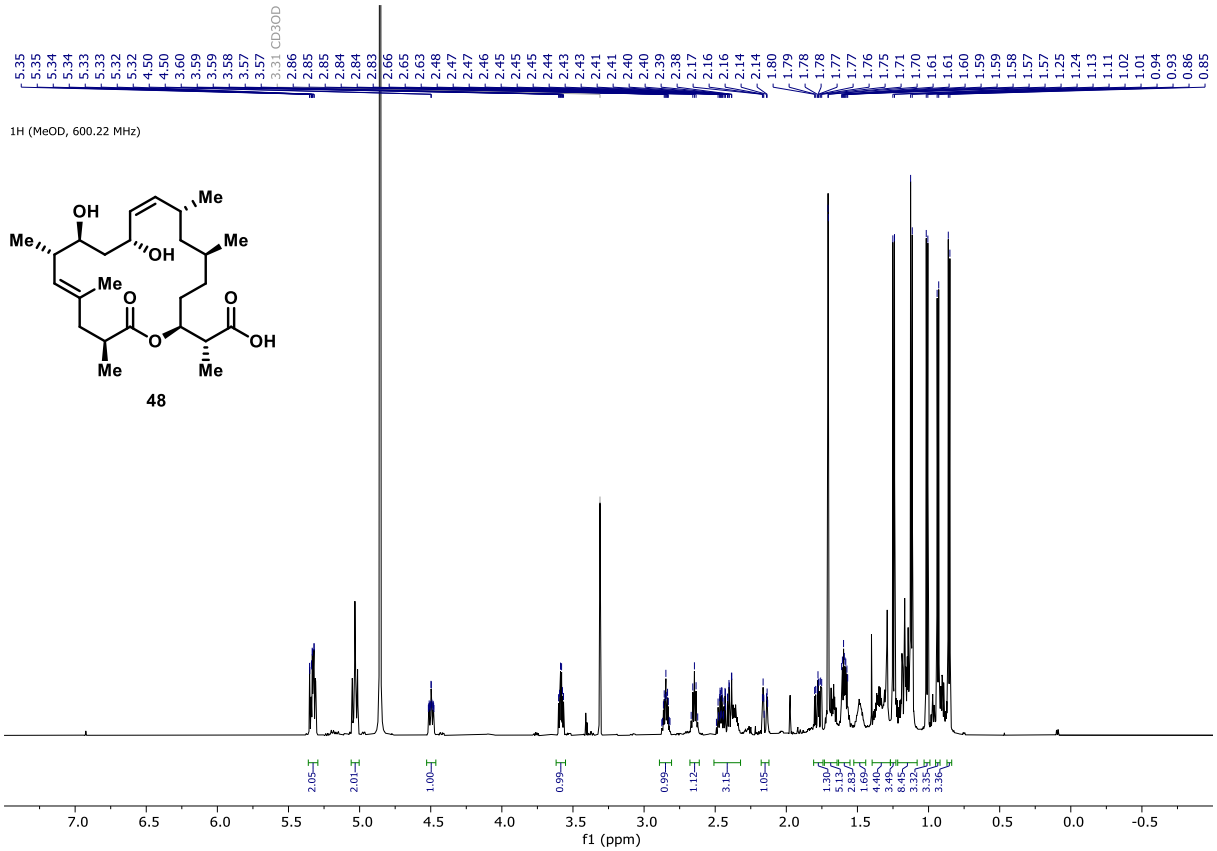

NOESY (MeOD, 600.22 MHz)


1H (MeOD, 600.22 MHz)
HO
Me
Me
OH
Me
Me
O
O
O
OH
Me
Me
46
f1 (ppm)

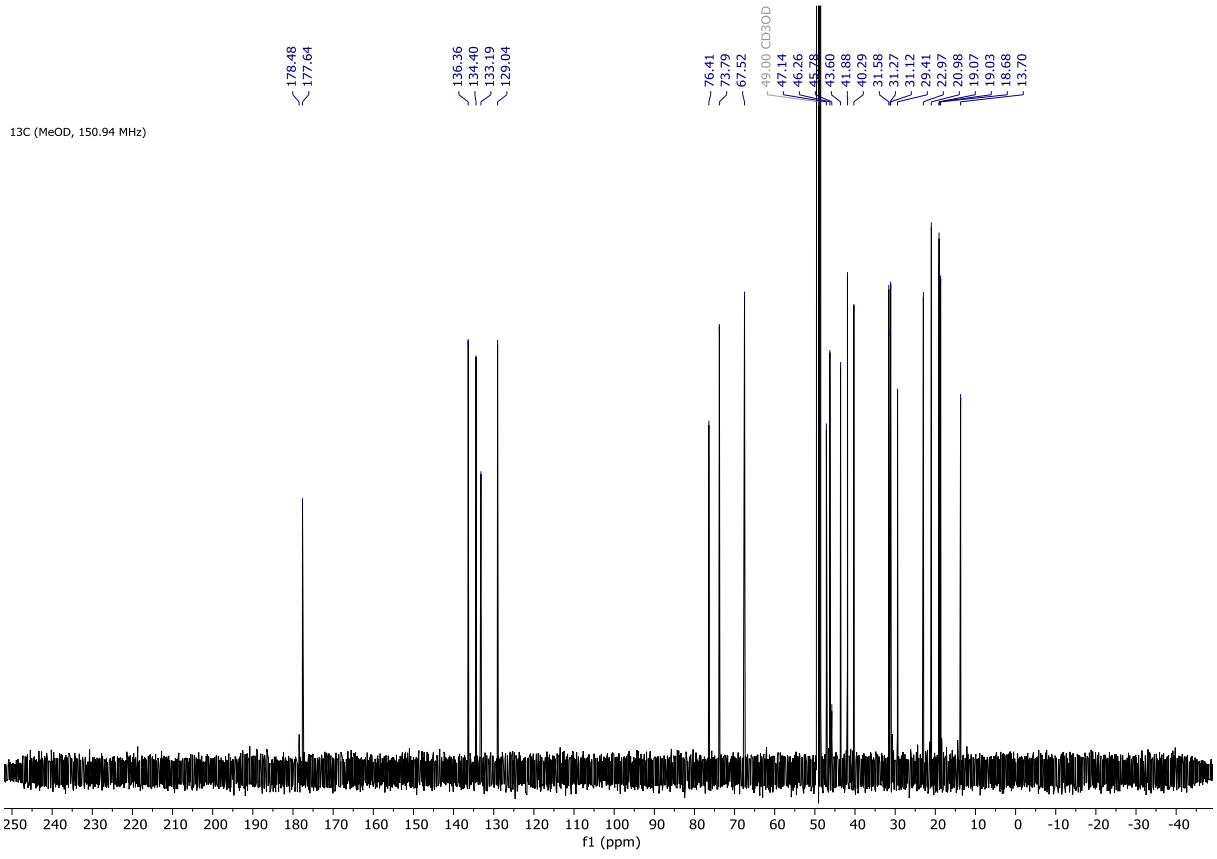

13C (MeOD, 150.94 MHz)
f1 (ppm)

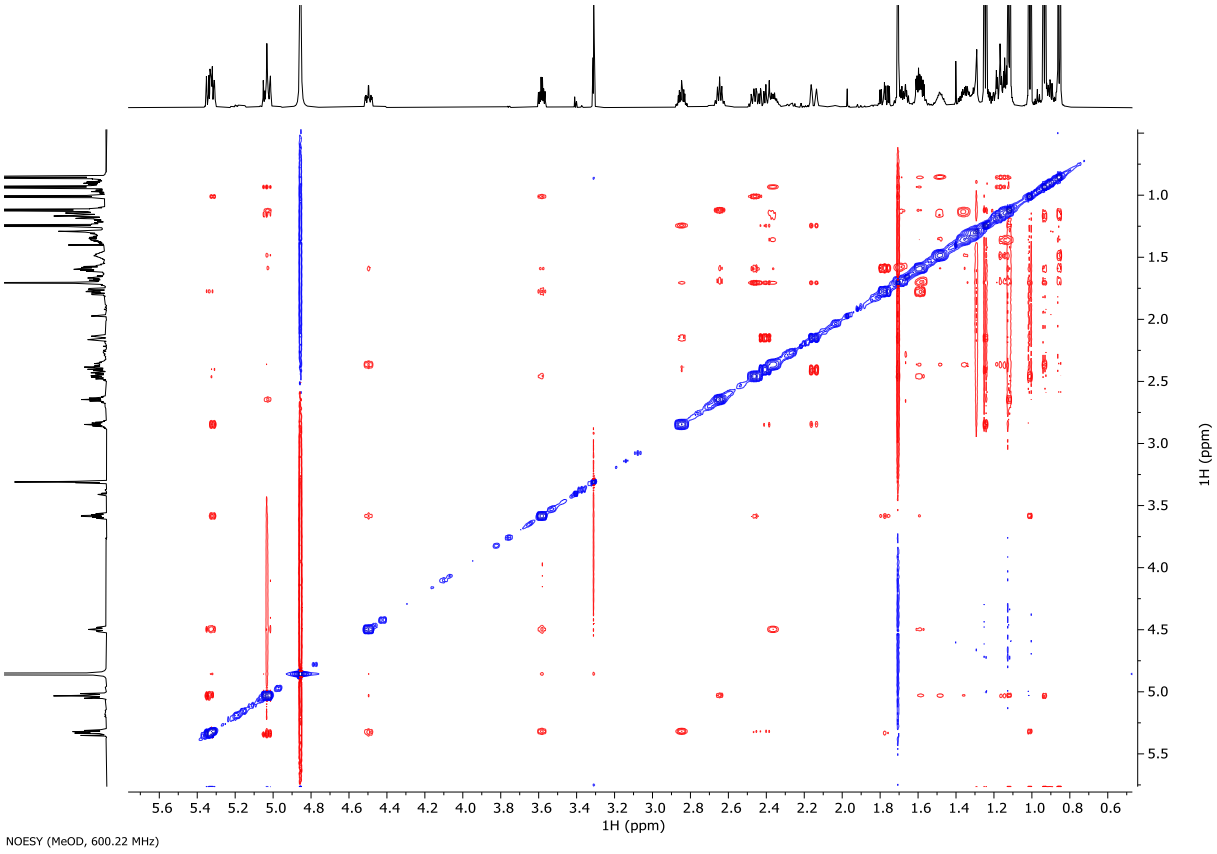

1H (CDCl3, 400.12 MHz)
OH
Me
Me
OH
Me
Me
O
O
O
OMe
Me
Me
47
f1 (ppm)


13C (CDCl3, 100.62 MHz)
f1 (ppm)

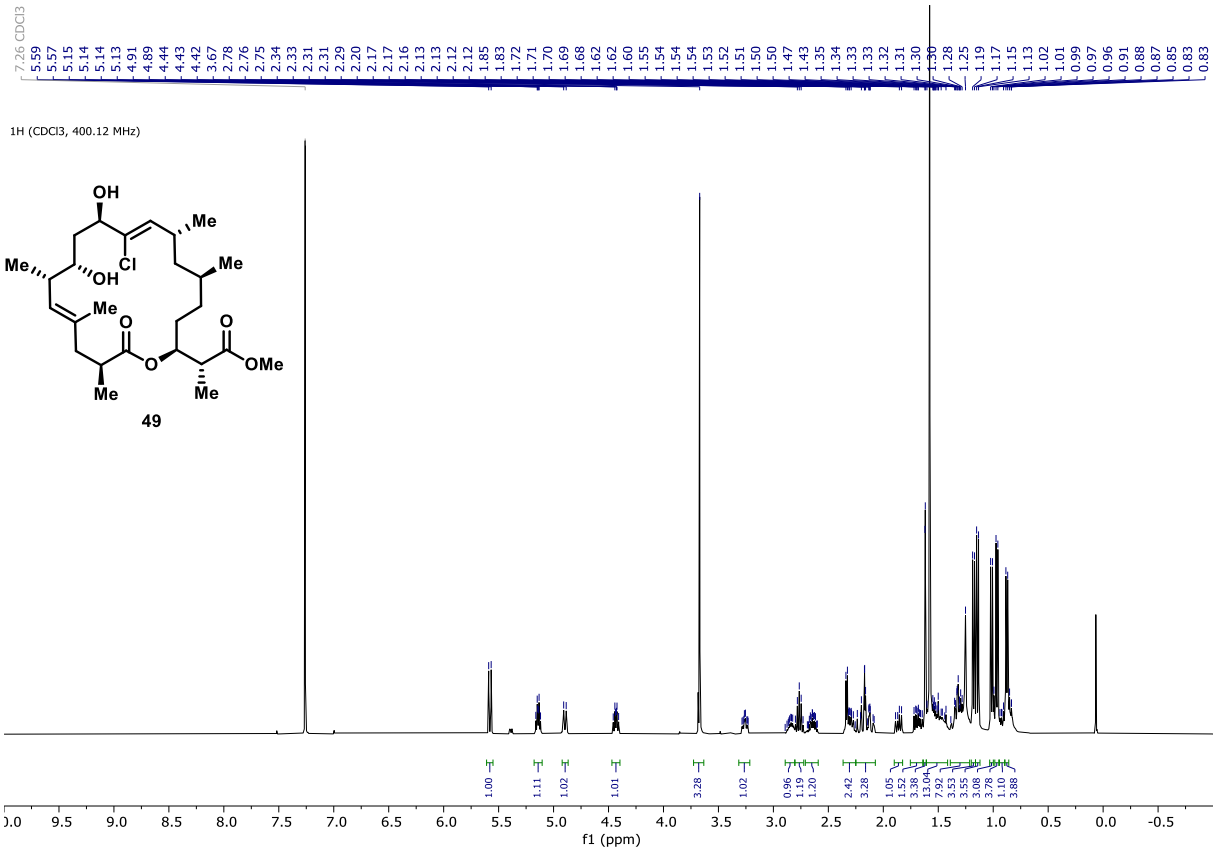

1H (MeOD, 600.22 MHz)
3.31 CD3OD
f1 (ppm)

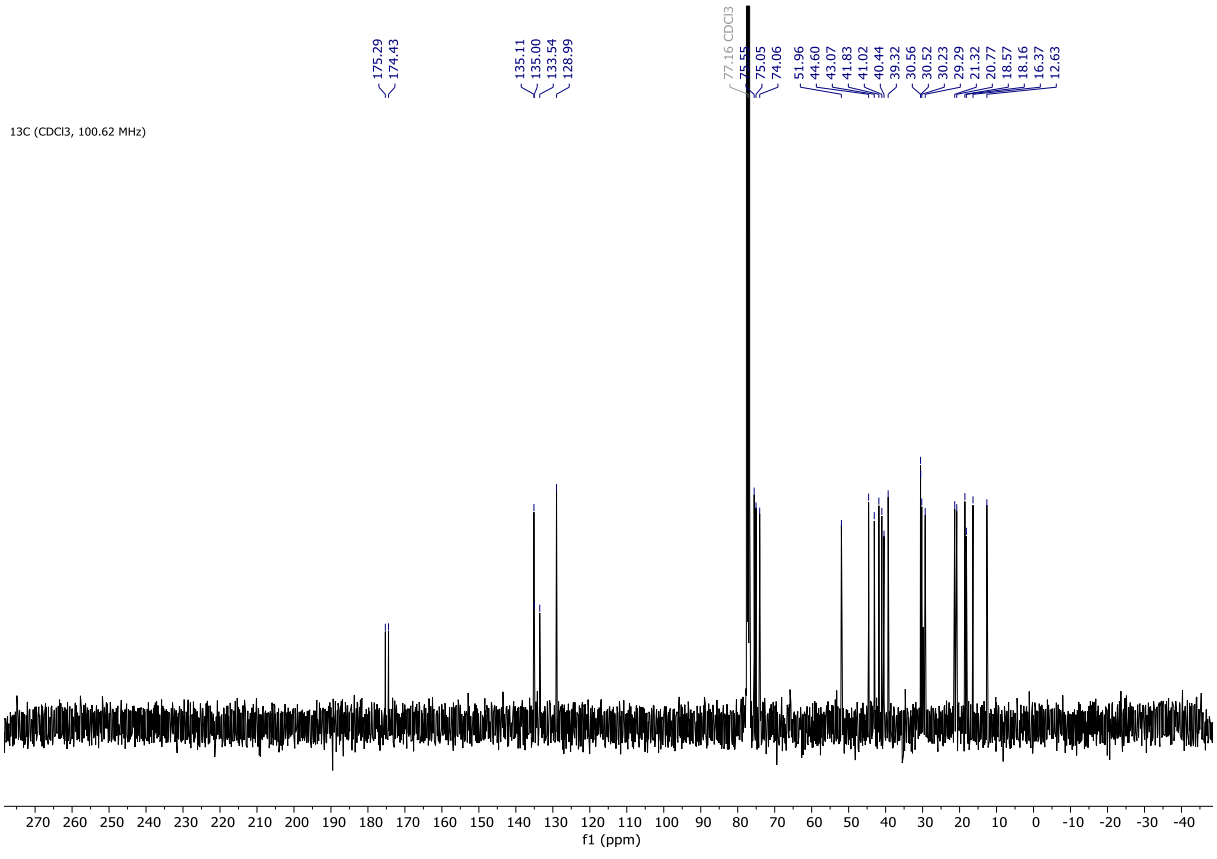
48

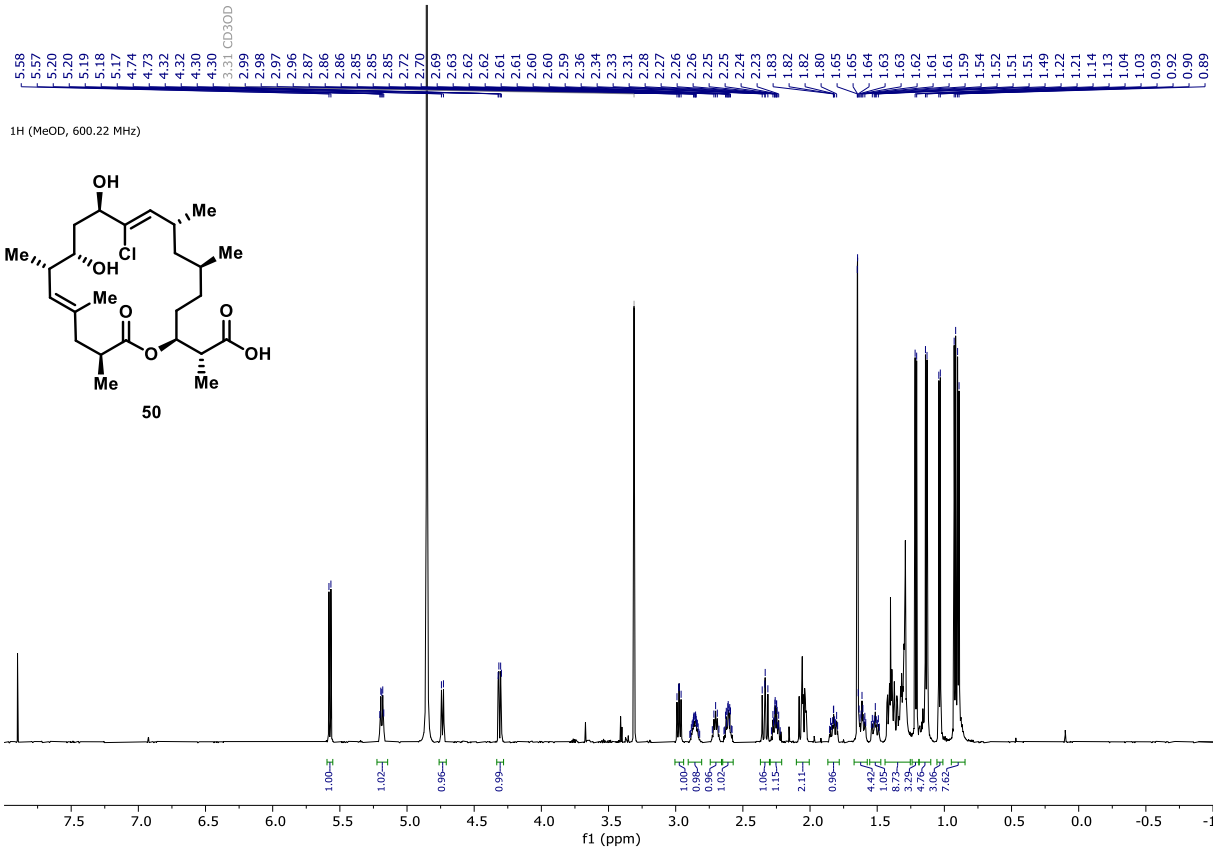

13C (MeOD, 150.94 MHz)
49.00 CD3OD
f1 (ppm)

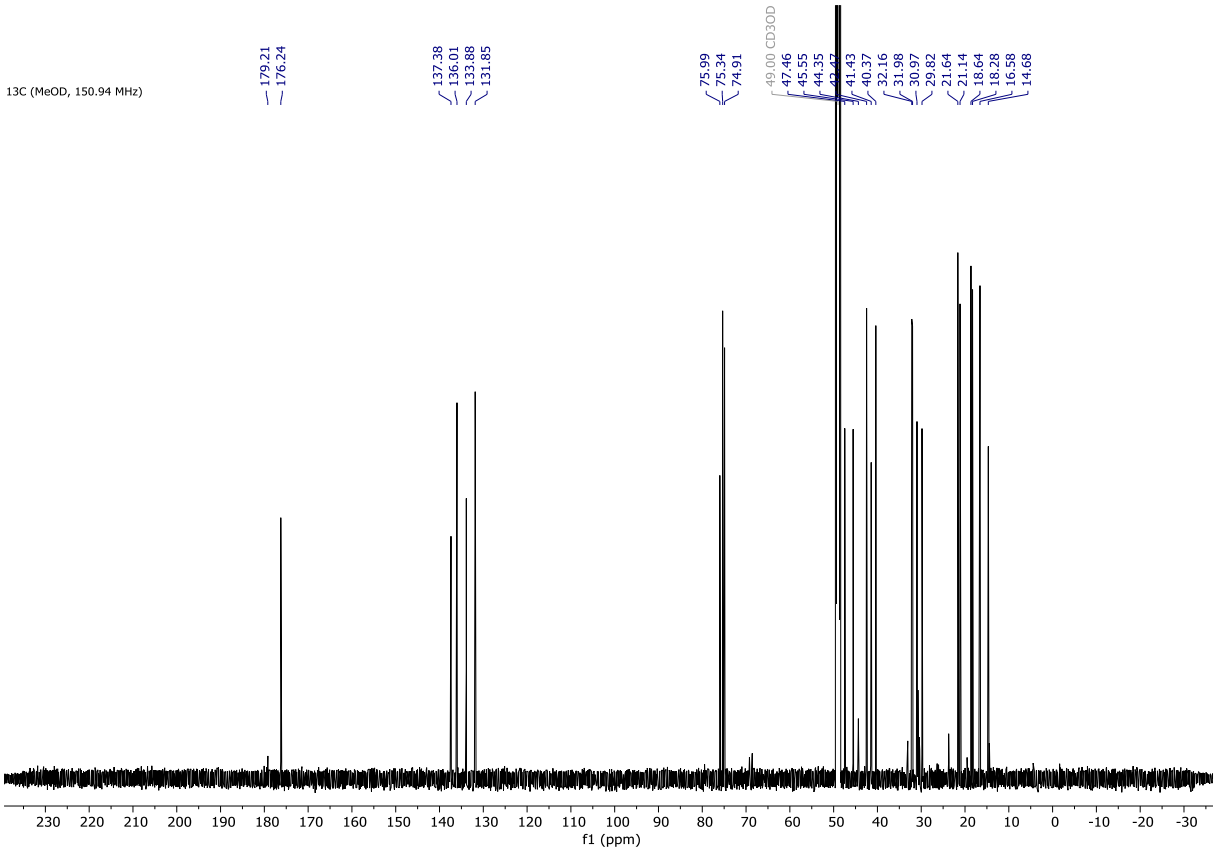


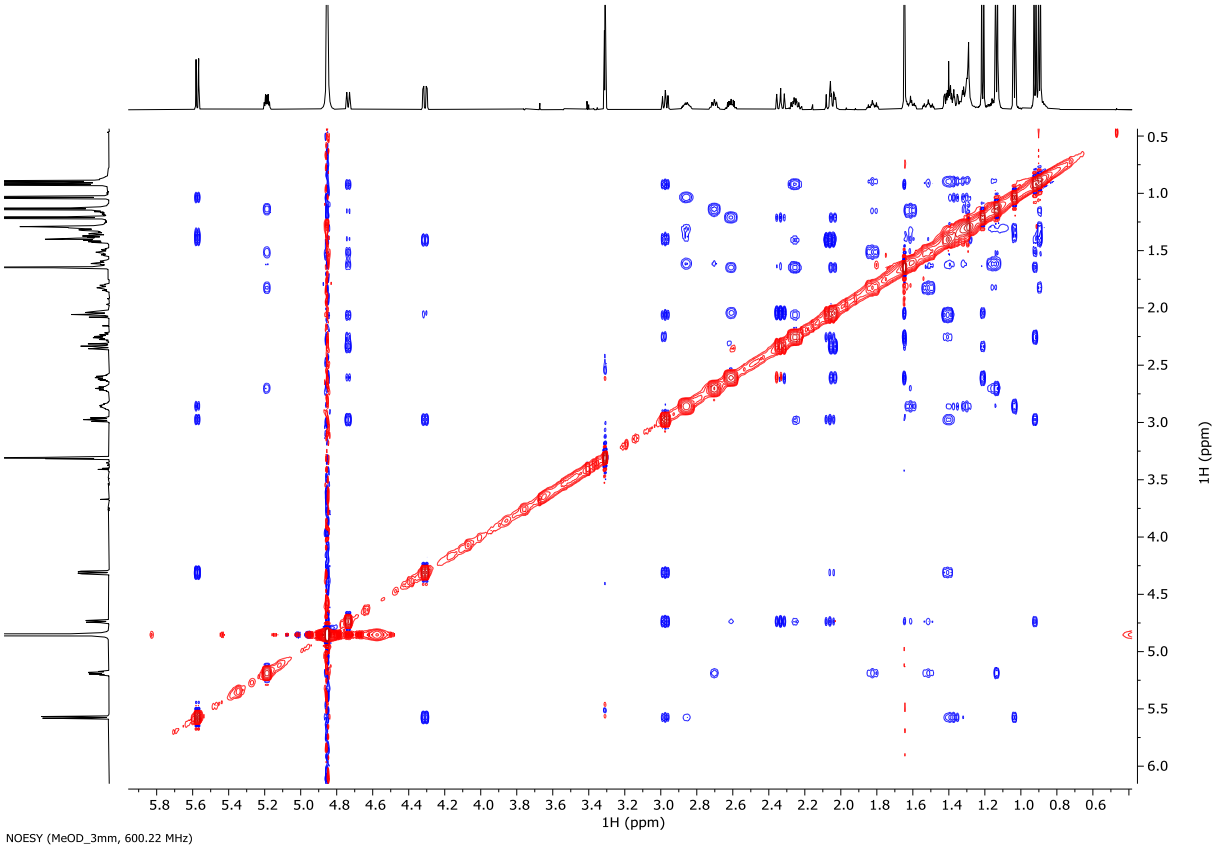

NOESY (MeOD, 600.22 MHz)


1H (CDCl3, 400.12 MHz)
OH
Me
Me
Cl
OH
Me
Me
O
O
O
OMe
Me
Me
49
f1 (ppm)


13C (CDCl3, 100.62 MHz)
f1 (ppm)


1H (MeOD, 600.22 MHz)
OH
Me
Me
Cl
OH
Me
Me
O
O
O
OH
Me
Me
50
f1 (ppm)


13C (MeOD, 150.94 MHz)
179.21
176.24
137.38
136.01
133.88
131.85
75.99
75.34
74.91
49.00 CD3OD
47.46
45.55
44.35
41.43
40.37
32.16
31.98
30.97
29.82
21.64
21.14
18.64
18.28
16.58
14.68
f1 (ppm)




NOESY (MeOD_3mm, 600.22 MHz)