Stereochemical Determination of the Leupyrrins and Total Synthesis of Leupyrrin A_1

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Supporting Information

Table of Contents:

1 General Methods

All reactions with dry solvents were performed under an atmosphere of argon in flame-dried glassware which had been cooled under argon unless stated otherwise. All flasks were equipped with rubber septa and reactants were handled using standard Schlenk techniques.

Temperatures above room temperature (20 °C) refer to oil bath temperatures which were controlled by a temperature modulator. For cooling, the following baths were used: acetone/dry ice (–78 °C), H_2O/ice (0 °C) for other temperatures below 0 °C a Huber TC100E-F-NR cooler was used.

All reagents were purchased from commercial suppliers (Sigma-Aldrich, TCI, AlfaAesar, Strem) in the highest grade available and used without further purification unless otherwise stated.

Anhydrous solvents (THF, Et_2O, toluene, and CH_2Cl_2) were obtained from a solvent drying system MB SPS-800 (MBraun) and stored over molecular sieves or purchased over molecular sieves (dioxane, DMF, DMSO).

Reactions were monitored via TLC on silica gel 60 F_{254} precoated plates (0.2 mm SiO_2, Machery-Nagel) and visualized using UV light and/or staining with a solution of CAM (1.0 g $Ce(SO_4)_2$, 2.5 g $(NH_4)_6Mo_7O_{24}$, 8 mL conc. H_2SO_4 in 100 mL H_2O) or $KMnO_4$ (1.5 g $KMnO_4$, 10 g K_2CO_3, 1.25 mL 10% NaOH in 200 mL H_2O) or Ninhydrin (1.5 g ninhydrin, 3 mL HOAc in 100 mL H_20 and 100 mL *n*-butanol) or 4-anisaldehyde (3.7 mL 4-anisaldehyde, 1.5 mL HOAc, 5 mL H_2SO_4 in 135 mL abs. EtOH) respectively, and subsequent heating.

For column chromatography, silica gel (pore size 60 Å, 40-63 µm) obtained from Aldrich or Merck was used and the size of the column was adjusted to the recommendations by Still *et al.*[1] Compounds were eluated using the stated mixtures under a positive pressure of air. Solvents were destilled prior to use.

Optical rotations were measured with a Perkin Elmer 241 or 341 polarimeter in a 10 mm cuvette and are uncorrected. Melting points were obtained using a Büchi melting point instrument B-540 or a microscope for determining the melting point of fibres (Reichert, Austria, type 7905) and are uncorrected.

^{1}H- and ^{13}C-NMR spectra were recorded on Bruker AC-300, DRX-300, DPX-300, DPX-400, DRX-500 and Avance-III-600 spectrometers with ^{13}C operating frequencies of 75, 100, 125 and 150 Mhz respectively. Spectra were measured at room temperature unless stated otherwise. Chemical shifts (δ) are reported in ppm relative to tetramethylsilane (δ = 0.00 ppm)

[1] Still, W. C.; Kahn, M.; Mitra A. *J. Org. Chem.* **1978**, *43*, 2923.

and the spectra were calibrated to the residual signal of undeuterated solvents.[2] Data for ^{1}H-NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants in Hertz, number of hydrogens). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), br. (broad).

Mass spectra (MS) and high-resolution-mass spectra (HRMS) were recorded at the Departments of Organic Chemistry in Heidelberg and Bonn on the following mass spectrometers: Bruker ICR APEX-QE, Vacuum Generators ZAB-2F, Finnigan MAT TSQ 700, JEOL JMS-700, Bruker Daltonics micrOTOF-Q and a Thermo Finnigan MAT 95 XL.

IR spectra were recorded on a Thermo Scientific Nicolet 380 FT-IR spectrometer. UV/Vis measurements were carried out using a Perkin Elmer Lambda 18 spectrometer.

The HPLC analytical and preparative analyses were performed by using a system of the company "Knauer Wissenschaftliche Geräte GmbH": Smartline series consisting of a two-channel degasser, two pumps S-1800 (100 mL pump head), an injection assistant 6000 with a feed pump S-100, a mixing chamber Smartmix 350, a UV-detector S-2550 and a fraction valves (16 port). The system was controlled by Chromgate software version 3.3.2. All solvents were purchased from the central chemical store of the University of Bonn in HPLC grade.

List of abbreviations:

Boc	*tert*-butyloxycarbonyl
CSA	10-camphorsulfonic acid
DAST	diethylaminosulfur trifluoride
DiBAl	di-*iso*-butylaluminium hydride
DIPT	di-*iso*-propyltartrate
DMAP	4-(*N*,*N*-dimethylamino)pyridine
HATU	*O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*,*N*·-tetramethyluronium hexafluorophosphate
HWE	Horner-Wadsworth-Emmons
IBX	2-iodoxybenzoic acid
MS	molecular sieve
MW	microwave
pin	pinacole
PPTS	pyridinium-*para*-toluensulfonate
Py	pyridine
rt	*room temperature*
SAE	Sharpless asymmetric epoxidation
Suc	succinimide
TASF	tris(dimethylamino)sulfonium difluorotrimethylsilicate

[2] Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics* **2010**, *29*, 2176.

TBAF	tetra-n-butylammoniumfluoride
TBS	tert-butyldimethylsilyl
TCBC	2,4,6-trichlorbenzoylchloride
Teoc	2-(trimethylsilyl)ethoxycarbonyl

2 Stereochemical Determination

2.1 Fermentation and Isolation

The Leupyrrins A_1 (**1**), A_2, B_1 (**2**), B_2, C and D were produced by the *Sorangium cellulosum* strain So ce690 in a 70 L fermentor (Giovanola Frères SA, Monthey, Switzerland) at 30 °C containing the following medium: Starch 8 g L^{-1}, soybean meal 1.5 g L^{-1}, skim milk 1.5 g L^{-1}, casitone 1 g L^{-1}, glucose × H_2O 2 g L^{-1}, fructose × H_2O 2 g L^{-1}, KH_2PO_4× H_2O 0.25 g L^{-1}, $CaCl_2$ × 2 H_2O 1 g L^{-1}, $MgSO_4$ × 7 H_2O 1 g L^{-1}, Na-Fe-EDTA 8 mg L^{-1}, at pH 7.3 in the presence of 1% of adsorber resin Amberlite XAD-16 (Rohm & Haas). The partial pressure was regulated to an oxygen concentration of 20%. After 14 days of cultivation, starch, glucose and fructose were used up and the culture broth was passed through a process filter to collect the absorber resin.

Residual cells were floated from the XAD-16 resin with water. The resin was eluted with acetone (12 L). The organic solvent was evaporated and the remaining water-layer (1 L) was adjusted to pH 10 with aqueous NH_3 and extracted with ice-cold Et_2O (3 portions of 2 L) after addition of saturated NaCl-solution (500 mL). The Et_2O-layer yielded an oily crude extract after evaporation.[3] A MeOH/*n*-heptane partition was carried out to remove lipophilic by-products in the *n*-heptane layer (700 mL). After evaporation the MeOH-layer yielded 9.80 gof an orange-brown material, which was fractionated into leupyrrins A_1 (**1**), A_2, B_1 (**2**), B_2 (2.39 g), and Leupyrrins C, D (0.42 g) by silica gel flash-chromatography [solvent: *t*-butyl methyl ether/petrol ether, 2:1, with 2% MeOH]. The mixture of Leupyrrins C and D were purified by RP-HPLC [column 250×21 mm, 10 µm: Nucleosil C18 (Macherey-Nagel), solvents MeOH/H_2O 70:30 with 0.05 M NH_4OAc, pH 8.0, FR = 22 mL min^{-1}, UV detection 277 nm]. The fractions at R_t = 23 min and R_t = 27 min were combined, respectively and neutralized with pure acetic acid and extracted with EtOAc before the organic solvent was dried with Na_2SO_4 and evaporated. This yielded pure compounds (leupyrrins C and D). The crude mixture of leupyrrins A_1 (**1**), A_2, B_1 (**2**), B_2 were separated by normal-phase HPLC [column 250×21 mm, 10 µm: Nucleosil (Macherey-Nagel), solvents: *t*-butyl methyl

[3] The water-layer was acidified to pH 3 using aqueous HCl and extracted with EtOAc (1 portion of 2L, 2 portions of 1L). Finally the EtOAc-layer was neutralized and yielded crude material of Sorangicin after evaporation, which was not further purified.

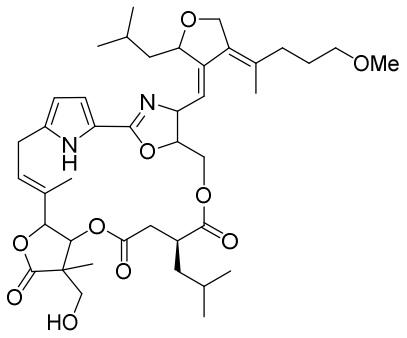
ether/petrol ether 18:82 mit 0.5% MeOH, FR = 34 mL min^{-1}, UV detection 277 nm]. The fractions at R_t = 27 min and R_t = 29 min as well as the fractions of R_t = 44 min and R_t = 50 min were combined and evaporated to yield a mixture of leupyrrins A_1 and A_2 and a mixture of B_1 and B_2. Both mixed fractions were purified by chiral normal-phase HPLC [column 250×20 mm, 5 µm: Chiralpak-IB (Daicel), solvent A: petrol ether; solvent B: *i*-propanol, gradient: starting from 5% B and increasing to 22.5% B in 15 min, maintaining for 1 min, FR = 20 mL min^{-1}, UV detection 277 nm]. The retention was detected by R_t = 7 min for leupyrrin A_1, R_t = 9 min for leupyrrin A_2 and R_t = 6 min for leupyrrin B_1 and R_t = 8 min for leupyrrin B_2. The yields for the purified compounds are as follows:

Table S 1 Quantities of the leupyrrins after isolation

	yield [mg]
leupA_1	47.3
leupA_2	27.1
leupB_1	70.1
leupB_2	73.0
leupC	18.4
leupD	143.9
leupMA[b]	22.9
leupMB[b]	26.6

[a] crude mixtures from in total (purified): leup A/B = 2.39 g (2.39 g), leup C/D = 0.42 g (0.42 g); [b] mixed fractions.

Leupyrrin A_1 (1)



1

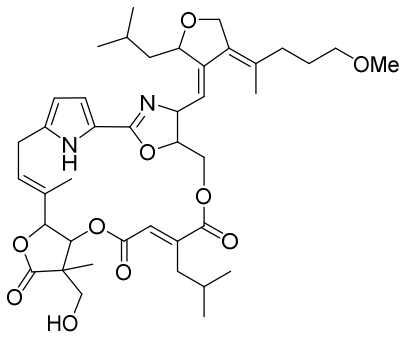
$C_{41}H_{58}N_2O_{10}$, M = 738. 91 g/mol

Isolated material.

R_f = 0.60 (petroleum ether/EtOAc = 1/2); $[\alpha]_D^{20}$= +11.7 (c = 1.0, MeOH) [Lit: $[\alpha]_D^{20}$= +12 (c 4.06, MeOH)];[4] **UV** (MeOH) λ_{max} (log ε) 260 (1.09) nm, 286 (1.98) nm; **IR** (film) ν_{max} 2955, 2872, 1782, 1741, 1649, 1159, 1115, 1068, 1036, 1003 cm^{-1};**^{1}H-NMR** (600 MHz, CD_3OD): δ [ppm] = 6.80 (d, *J* = 3.7 Hz, 1 H), 6.07 (d, *J* = 3.7 Hz, 1 H), 5.90 (m, 1 H), 5.59 (d, *J* = 7.7 Hz, 1 H), 5.56 (d, *J* = 9.9 Hz, 1 H), 5.01 (m, 1 H), 4.78 (d, *J* = 7.7 Hz, 1 H), 4.71 (ddd, *J* = 8.1, 5.5, 2.6 Hz, 1 H), 4.61-4.55 (m, 4 H), 4.49 (d, *J* = 12.5 Hz, 1 H), 4.21 (dd, *J* = 12.1, 2.6 Hz, 1 H), 3.78 (d, *J* = 11.0 Hz, 1 H), 3.61 (d, *J* = 11.0 Hz, 1 H), 3.42-3.39 (m, 3 H), 3.36 (s, 3 H), 2.85-2.79 (m, 2 H), 2.72-2.67 (m, 1 H), 2.19-2.07 (m, 2 H), 1.98 (s, 3 H), 1.95-1.89 (m, 1 H), 1.82-1.59 (m, 5 H), 1.77 (s, 3 H), 1.49-1.44 (m, 2 H), 1.11 (s, 3 H), 1.08 (d, *J* = 6.6 Hz, 3 H), 1.03 (d, *J* = 6.6 Hz, 3 H), 0.94 (d, *J* = 6.0 Hz, 3 H), 0.93 (d, *J* = 6.0 Hz, 3 H); **^{13}C-NMR** (100 MHz, CD_3OD): δ [ppm] = 179.5, 175.6, 172.3, 160.8, 145.0, 136.6, 135.3, 134.1, 131.4, 128.6, 123.2, 119.5, 115.3, 109.7, 85.5, 84.7, 80.6, 75.6, 73.0, 70.3, 68.2, 66.1, 65.9, 58.9, 51.3, 44.5, 40.2, 40.0, 36.5, 35.0, 28.5, 27.0[5], 26.3, 24.3, 23.0, 22.8, 22.2, 20.3, 14.7, 11.5; **HRMS** (ESI+): calculated for $C_{41}H_{59}N_2O_{10}^+$ $[M+H]^+$: 739.4164, found 739.4166.

[4] Bode, H. B.; Irschik, H.; Wenzel, S. C.; Reichenbach, H.; R. Müller, R.; Höfle, G. *J. Nat. Prod.* **2003**, *66*, 1203.
[5] Signal contains two carbon atoms.

Leupyrrin B_1 (2)



2

$C_{41}H_{56}N_2O_{10}$, M = 736.89 g/mol

Isolated material.

R_f = 0.60 (silica, petroleum ether/EtOAc = 1/2); $[\alpha]_D^{20}$= +2.7 (c = 1.0, MeOH) [Lit: $[\alpha]_D^{20}$= + 11 (*c* = 4.6, MeOH)][6]; **UV** (MeOH) λ_{max} (log ε) 236 (0.82) nm, 260 (0.80) nm, 287 (1.29) nm; **IR** (film) ν_{max} 2954, 2868, 1780, 1725, 1653, 1209, 1132, 1116, 1038, 1008 cm^{-1}; **^{1}H-NMR** (600 MHz, CD_3OD): δ [ppm] = 6.69 (d, *J* = 3.6 Hz, 1 H), 6.58 (s, 1 H), 5.96 (d, *J* = 3.6 Hz, 1 H), 5.86-5.81 (m, 1 H), 5.48 (d, *J* = 10.3 Hz, 1 H), 5.40 (d, *J* = 9.1 Hz, 1 H), 4.99-4.95 (m, 1 H), 4.70-4.64 (m, 3 H), 4.59 (dd, *J* = 10.2, 4.0 Hz, 1 H), 4.53 (d, *J* = 12.9 Hz, 1 H), 4.49 (dd, *J* = 12.4, 2.7 Hz, 1 H), 4.44 (d, *J* = 12.9 Hz, 1 H), 3.77 (d, *J* = 10.7 Hz, 1 H), 3.69 (d, *J* = 10.7 Hz, 1 H), 3.58 (dd, *J* = 14.4, 10.7 Hz, 1 H), 3.34 (t, *J* = 6.1 Hz, 2 H), 3.23 (dd, *J* = 14.5, 5.3 Hz, 1 H), 3.30 (s, 3 H), 2.57 (dd, *J* = 12.6, 7.3 Hz, 1 H), 2.50 (dd, *J* = 12.6, 7.3 Hz, 1 H), 2.13-2.00 (m, 2 H), 1.91 (s, 3 H), 1.88-1.82 (m, 1 H), 1.77- 1.62 (m, 3 H), 1.74 (s, 3 H), 1.57 (ddd, *J* = 14.5, 11.0, 4.3 Hz, 1 H), 1.35 (ddd, *J* = 14.2, 9.5, 2.7 Hz, 1 H), 1.01 (s, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 0.82 (d, *J* = 1.5 Hz, 3 H), 0.81 (d, *J* = 1.5 Hz, 3 H); **^{13}C-NMR** (150 MHz, CD_3OD): δ [ppm] = 179.1, 167.7, 166.2, 161.4, 148.3, 144.6, 136.9, 134.1, 131.6, 131.3, 131.1, 128.1, 123.4, 119.6, 115.8, 109.3, 85.2, 84.3, 80.7, 74.8, 73.0, 70.5, 68.9, 66.9, 65.3, 58.9, 51.1, 44.8, 37.2, 35.1, 29.8, 28.5, 27.3, 26.3, 24.3, 23.0, 22.9, 22.1, 20.3, 13.7, 10.0; **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] = 9.0 (bs, 1 H), 6.70 (s, 1 H), 6.67 (d, *J* = 3.7 Hz, 1 H), 6.03 (d, *J* = 3.7 Hz, 1 H), 5.56 (d, *J* = 9.2 Hz, 1 H), 5.55-5.52 (m, 1 H), 5.46 (d, *J* = 9.9 Hz, 1 H), 4.89-4.85 (m, 1 H), 4.63-4.59 (m, 3 H), 4.57 (dd, *J* = 9.5, 3.7 Hz, 1 H), 4.57 (d, *J* = 9.2 Hz, 1 H), 4.53 (d, *J* = 12.1 Hz, 1 H), 4.47 (d,

[6] Bode, H. B.; Irschik, H.; Wenzel, S. C.; Reichenbach, H.; R. Müller, R.; Höfle, G. *J. Nat. Prod.* **2003**, *66*, 1203.

J = 12.1 Hz, 1 H), 4.33 (dd, *J* = 12.7, 2.8 Hz, 1 H), 3.96 (d, *J* = 11.4 Hz, 1 H), 3.71 (d, *J* = 11.4 Hz, 1 H), 3.54 (dd, *J* = 15.4, 11.0 Hz, 1 H), 3.35-3.31 (m, 3 H), 3.33 (s, 3 H), 2.60 (dd, *J* = 12.7, 7.5 Hz, 1 H), 2.49 (dd, *J* = 12.7, 7.2 Hz, 1 H), 2.10-2.00 (m, 2 H), 1.89 (s, 3 H), 1.83-1.66 (m, 3 H), 1.81 (s, 3 H), 1.61 (ddd, *J* = 14.3, 10.5, 4.2 Hz, 1 H), 1.35 (ddd, *J* = 14.3, 9.4, 2.8 Hz, 1 H), 1.15 (s, 3 H), 0.97 (d, *J* = 6.2 Hz, 3 H), 0.99 (d, *J* = 6.2 Hz, 3 H), 0.85 (d, *J* = 6.6 Hz, 3 H), 0.82 (d, *J* = 6.6 Hz, 3 H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ [ppm] = 176.4, 166.0, 165.6, 161.7, 146.9, 143.8, 134.5, 132.9, 131.5, 129.9, 129.3, 126.8, 121.3, 119.1, 113.9, 108.5, 83.8, 82.7, 79.5, 72.8, 71.9, 69.4, 67.5, 66.4, 64.8, 58.6, 49.4, 43.3, 36.4, 34.1, 29.7, 28.5, 27.4, 26.8, 24.9, 23.7, 22.4, 22.3, 20.1, 13.2, 10.1; **HRMS** (ESI+): calculated for $C_{41}H_{57}N_2O_{10}^+$ $[M+H]^+$: 737.4008, found: 737.4007.

2.2 Assignment of the relative configuration of the C-1 to C-6 subunit of Leupyrrin B_1

As shown in Figure S 1 for the C-1 to C-6 subunit of leupyrrin B_1, characteristic NOE correlations were observed from H-3 to H-22 and H-24 as well as from H-4 to H-6 and H-23. In combination with an antiperiplanar relationship of H-3 and H-4 as deduced from a large vicinal coupling constant between these protons (9.2 Hz) these data suggest an *anti*-, *anti*-configuration between H-2 and H-3 and between H-3 and Me-23, in agreement with the proposal of Bode and Höfle for leupyrrin A_1 and a partial synthesis from our laboratory.[7,8]

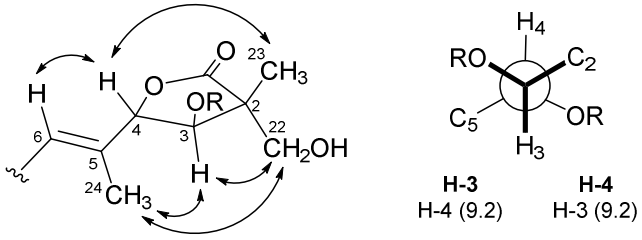
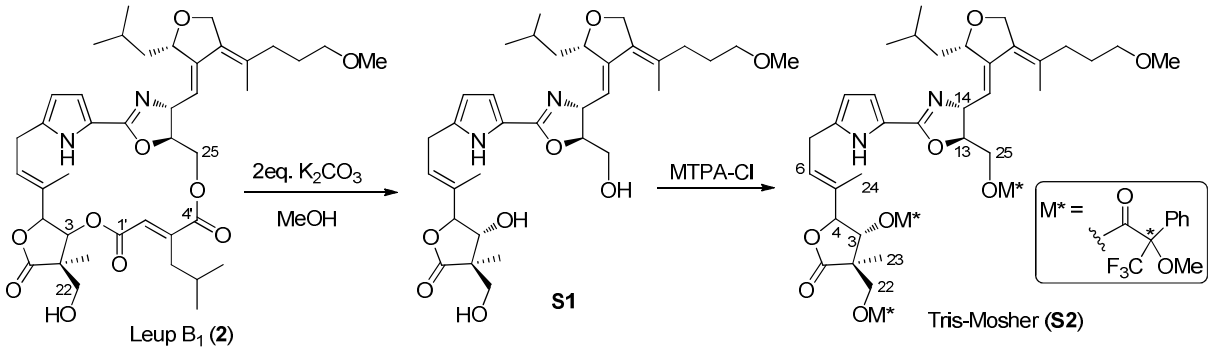


Figure S 1: Rotamers determined for the C-1 to C-6 subunit of leupyrrin B_1; coupling constants, $^3J_{H,H}$ (Hz) in parentheses.

[7] Bode, H. B.; Irschik, H.; Wenzel, S. C.; Reichenbach, H.; R. Müller, R.; Höfle, G. *J. Nat. Prod.* **2003**, *66*, 1203.
[8] Debnar, T.; Wang, T.; Menche, D. *Org. Lett.* **2013**, *15*, 2774.

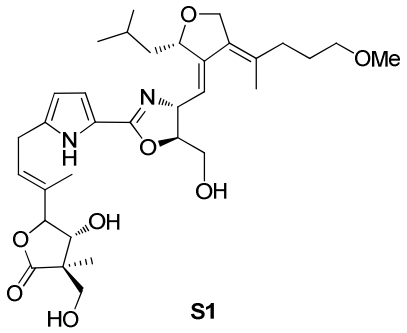
2.3 Derivatization

For determination of the absolute configuration at C3 of leupyrrin B_1, basic cleavage of the dicarboxylic acid (K_2CO_3/MeOH) yielded triol **S1**, which was subsequently transformed to *tris*-Mosher esters **S2** with MTPA-Cl (Scheme S 1, see below for further details).



Scheme S 1: Synthesis of *tris*-Mosher esters (**S2**).

(3*R*,4*R*,5*S*)-4-Hydroxy-3-(hydroxymethyl)-5-((*E*)-4-(5-((4*R*,5*S*)-5-(hydroxymethyl)-4-((*Z*)-((*S*,*Z*)-2-isobutyl-4-(5-methoxypentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)-methyl)-4,5-dihydrooxazol-2-yl)-1*H*-pyrrol-2-yl)but-2-en-2-yl)-3-methyldihydrofuran-2(3*H*)-one (S1)



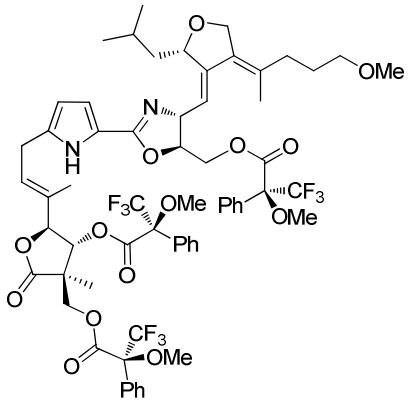
$C_{33}H_{48}N_2O_8$, M = 600.7 g/mol

To a stirred solution of leupyrrin B_1 **2** (16.0 mg, 21.7 µmol) in MeOH (200 µL) at room temperature K_2CO_3 (6.00 mg, 43.4 µmol) was added. The mixture was stirred for 10 minutes until the conversion was completed. After addition of sat. aq. NaCl solution (3 mL), the aqueous portion was extracted with EtOAc (3 × 7 mL). The combined organic portions were dried over $MgSO_4$, filtered and concentrated at reduced pressure. Purification by flash column

chromatography (SiO_2, petroleum ether/EtOAc, 1:2) gave triol **S1** (6.80 mg, 52%) as a colorless oil.

R_f = 0.23 (petroleum ether/EtOAc = 1/4), **^{1}H-NMR** (600 MHz, $CDCl_3$): δ [ppm] = 9.79 (bs, 1H), 6.71 (d, *J* = 3.6 Hz, 1H), 6.00 (d, *J* = 3.3 Hz, 1H), 5.86-5.82 (m, 1H), 5.47 (d, *J* = 10.1 Hz, 1H), 4.90 (d, *J* = 10.2 Hz, 1H), 4.63 (d, *J* = 6.2 Hz, 1H), 4.60-4.56 (m, 1H), 4.54-4.47 (m, 3H), 4.42-4.38 (m, 1H), 3.95 (dd, *J* = 12.2, 2.9 Hz, 1H), 3.81 (d, *J* = 10.3 Hz, 1H), 3.74 (dd, *J* = 12.2, 4.6 Hz, 1H), 3.53-3.47 (m, 5H), 3.36 (t, 6.3 Hz, 2H), 3.34 (s, 3H), 2.12-2.02 (m, 2H), 1.93 (s, 3H), 1.91-1.84 (m, 2H), 1.76-1.69 (m, 2H), 1.72 (s, 3H), 1.62-1.56 (m, 1H), 1.25-1.22 (m, 1H), 1.17 (s, 3H), 0.97 (d, *J* = 6.3 Hz, 3H), 0.95 (d, *J* = 6.3 Hz, 3H); **^{13}C-NMR** (150 MHz, $CDCl_3$): δ [ppm] = 179.1, 159.6, 144.3, 135.6, 135.2, 133.2, 129.8, 122.2, 121.4, 116.9, 115.2, 107.3, 86.3, 79.1, 72.7, 71.9, 69.4, 65.7, 65.2, 62.7, 58.6, 50.8, 49.7, 43.7, 34.3, 27.4, 25.6, 24.9, 23.7, 21.4, 20.3, 13.5, 11.4; **HRMS** (ESI+): calculated for $C_{33}H_{49}N_2O_8^+$ $[M+H]^+$: 601.3483, found: 601.3481.

2-Methoxy-2-phenylpropanoyloxy)-4-(((*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyloxy)methyl)tetrahydrofuran-2-yl)but-2-enyl)-1*H*-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate ((*S*)-S2)



(*S*)-**S2**

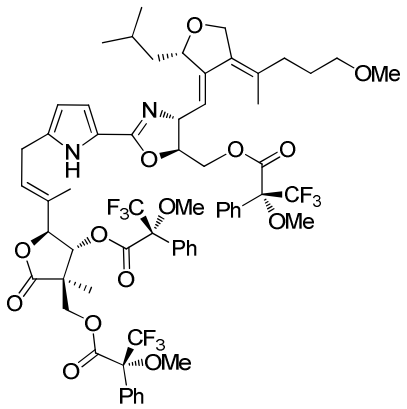
$C_{63}H_{69}F_9N_2O_{14}$, M = 1249.2 g/mol

To a stirred solution of triol **S1** (2.00 mg, 3.40 µmol) in CH_2Cl_2 (100 µL) at room temperature were added pyridine (280 µL, 3.40 mmol), DMAP (100 µL of a stock solution containing 12.6 mg in 1 mL CH_2Cl_2) and (*R*)-MTPA-chloride (11.8 µL, 68.6 µmol). The reaction was stirred for 1 hour, diluted with EtOAc (2 mL), washed with aq. $NaHCO_3$ solution (1.5 mL, 1%) and H_2O (1.0 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column

chromatography (SiO_2, petroleum ether/EtOAc, 4:1) of the residue afforded the corresponding (*S*)-Mosher ester (*S*)-**S2** (3.30 mg, 94%) as a colorless oil.

$\mathbf{R_f}$ = 0.63 (petroleum ether/EtOAc 1:1); **^{1}H-NMR** (600 MHz, CD_3OD): δ [ppm] = 7.50-7.47 (m, 2H), 7.45-7.39 (m, 8H), 7.38-7.34 (m, 2H), 7.33-7.29 (m, 1H), 7.25-7.21 (m, 2H), 6.63 (d, *J* = 3.6 Hz, 1H), 5.85 (d, *J* = 3.6 Hz, 1H), 5.64 (d, *J* = 8.5 Hz, 1H), 5.63-5.59 (m, 1H), 5.48 (d, *J* = 9.7 Hz, 1H), 4.91-4.88 (m, 2H), 4.74 (d, *J* = 8.4 Hz, 1H), 4.67 (d, *J* = 11.3 Hz, 1H), 4.62-4.54 (m, 2H), 4.52 (d, *J* = 12.2 Hz, 1H), 4.46 (dd, *J* = 12.5, 3.1 Hz, 1H), 4.43 (d, *J* = 12.2 Hz, 1H), 4.24 (d, *J* = 11.3 Hz, 1H), 3.52 (s, 3H), 3.47 (s, 3H), 3.44 (s, 3H), 3.40-3.27 (m, 2H), 3.33 (t, *J* = 6.2 Hz, 2H), 3.30 (s, 3H), 2.12-2.10 (m, 2H), 1.90 (s, 3H), 1.81-1.74 (m, 1H), 1.73-1.61 (m, 2H), 1.55-1.49 (m, 1H), 1.38 (s, 3H), 1.29-1.21 (m, 1H), 1.23, (s, 3H), 0.90 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.7 Hz, 3H); **HRMS** (ESI+): calculated for $C_{63}H_{70}F_9N_2O_{14}^+$ $[M+H]^+$: 1249.4678, found: 1249.4617.

(*R*)-((4*R*,5*S*)-4-((*Z*)-((*S*,*Z*)-2-*Iso*butyl-4-(5-methoxypentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)methyl)-2-(5-((*E*)-3-((2*S*,3*R*,4*R*)-4-methyl-5-oxo-3-((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyloxy)-4-(((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyloxy)methyl)tetrahydrofuran-2-yl)but-2-enyl)-1*H*-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate ((*R*)-S2)



(*R*)-**S2**

$C_{63}H_{69}F_9N_2O_{14}$, M = 1249.2 g/mol

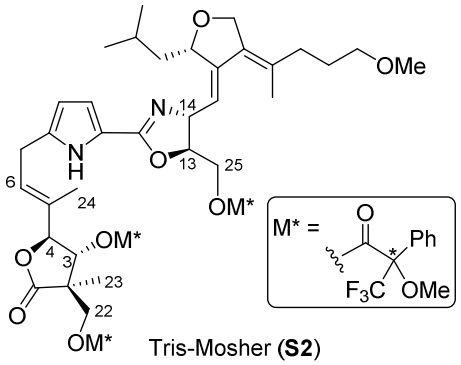
To a stirred solution of triol **S1** (2.30 mg, 4.00 µmol) in CH_2Cl_2 (100 µL) at room temperature were added pyridine (320 µL, 4.00 mmol), DMAP (100 µL of a stock solution containing 16.1 mg in 1 mL CH_2Cl_2) and (*S*)-MTPA-chloride (13.8 µL, 78.9 µmol). The reaction was stirred for 1 hour, diluted with EtOAc (2 mL), washed with aq. $NaHCO_3$ solution (1.5 mL,

1%) and H_2O (1.0 mL), dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography (SiO_2, petroleum ether/EtOAc, 4:1) of the residue afforded the corresponding (*R*)-Mosher ester (*R*)-**22** (3.60 mg, 73%) as a colorless oil.

R_f = 0.63 (petroleum ether/EtOAc = 1/1), **^{1}H-NMR** (600 MHz, CD_3OD): δ = 7.52-7.48 (m, 2H), 7.45-7.36 (m, 10H), 7.35-7.31 (m, 1H), 7.24-7.20 (m, 2H), 6.70 (d, *J* = 3.6 Hz, 1H), 5.89 (d, *J* = 3.5 Hz, 1H), 5.79-5.75 (m, 1H), 5.53-5.49 (m, 1H), 5.35 (d, *J* = 8.6 Hz, 1H), 4.97-4.93 (m, 1H), 4.87-4.84 (m, 1H), 4.83 (d, *J* = 8.6 Hz, 1H), 4.68-4.64 (m, 2H), 4.53-4.49 (d, *J* = 12.2 Hz, 1H), 4.43 (d, *J* = 11.2 Hz, 1H), 4.42 (d, *J* = 12.2 Hz, 1H), 4.38 (dd, *J* = 12.6, 2.1 Hz, 1H), 4.24 (d, *J* = 11.2 Hz, 1H), 3.54 (s, 3H), 3.44 (s, 3H), 3.38-3.32 (m, 4H), 3.34 (s, 3H), 3.30 (s, 3H), 2.13-2.01 (m, 2H), 1.92 (s, 3H), 1.82-1.74 (m, 1H), 1.74-1.63 (m, 2H), 1.56-1.50 (m, 1H), 1.35-1.29 (m, 1H), 1.32 (s, 3H), 0.95 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H) ppm; **HRMS** (ESI^+): calculated for $C_{63}H_{70}F_9N_2O_{14}^+$ $[M+H]^+$: 1249.4678, found: 1249.4617.

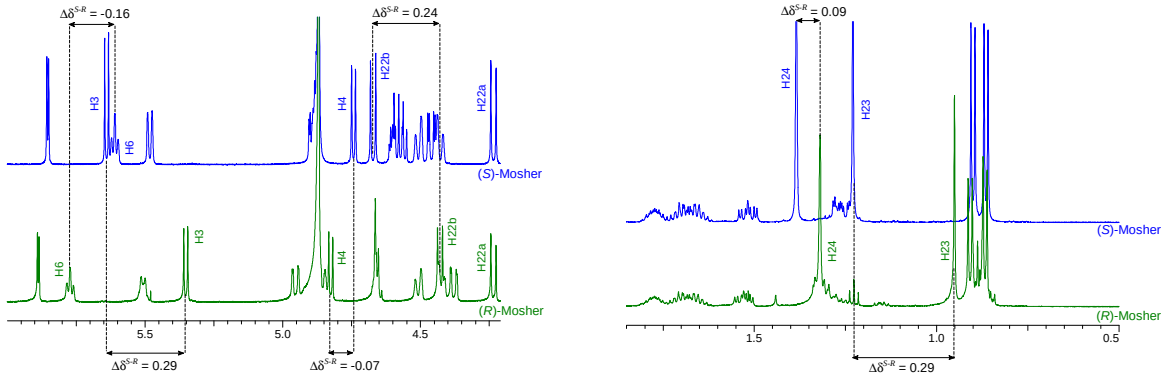
Table S 2: Mosher ester analysis of triol S2.

	^{1}H NMR (CD_3OD)		
	δ(*S*)	δ(*R*)	$\Delta\delta^{S-R}$
H4	4.76	4.83	-0.07
Me23	1.24	0.95	0.29
H3	5.64	5.35	0.29[a]
H24	1.32	1.23	0.09
H6	5.61	5.77	-0.16[a]
H22b	4.67	4.4	0.24



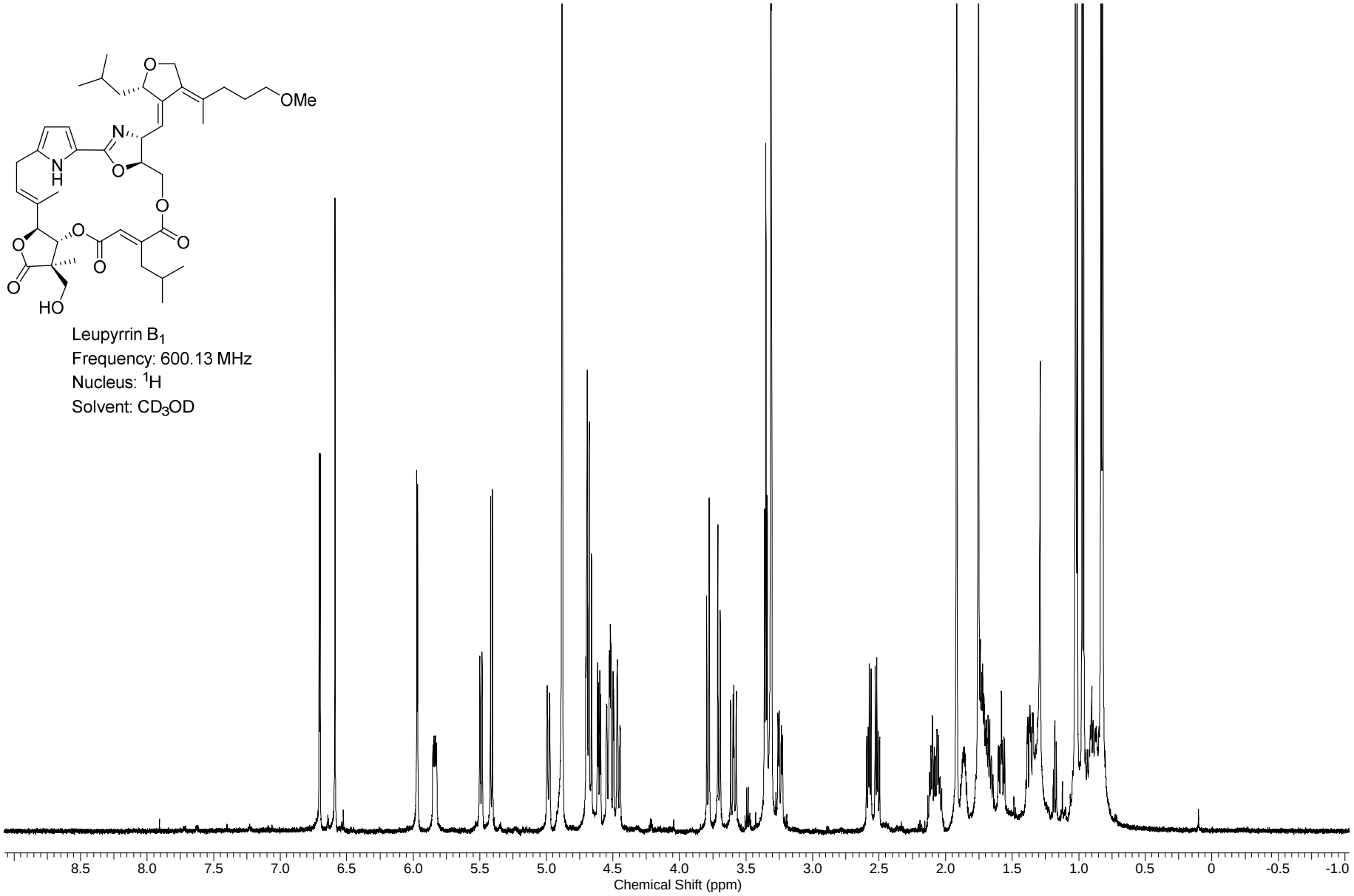
Tris-Mosher (**S2**)

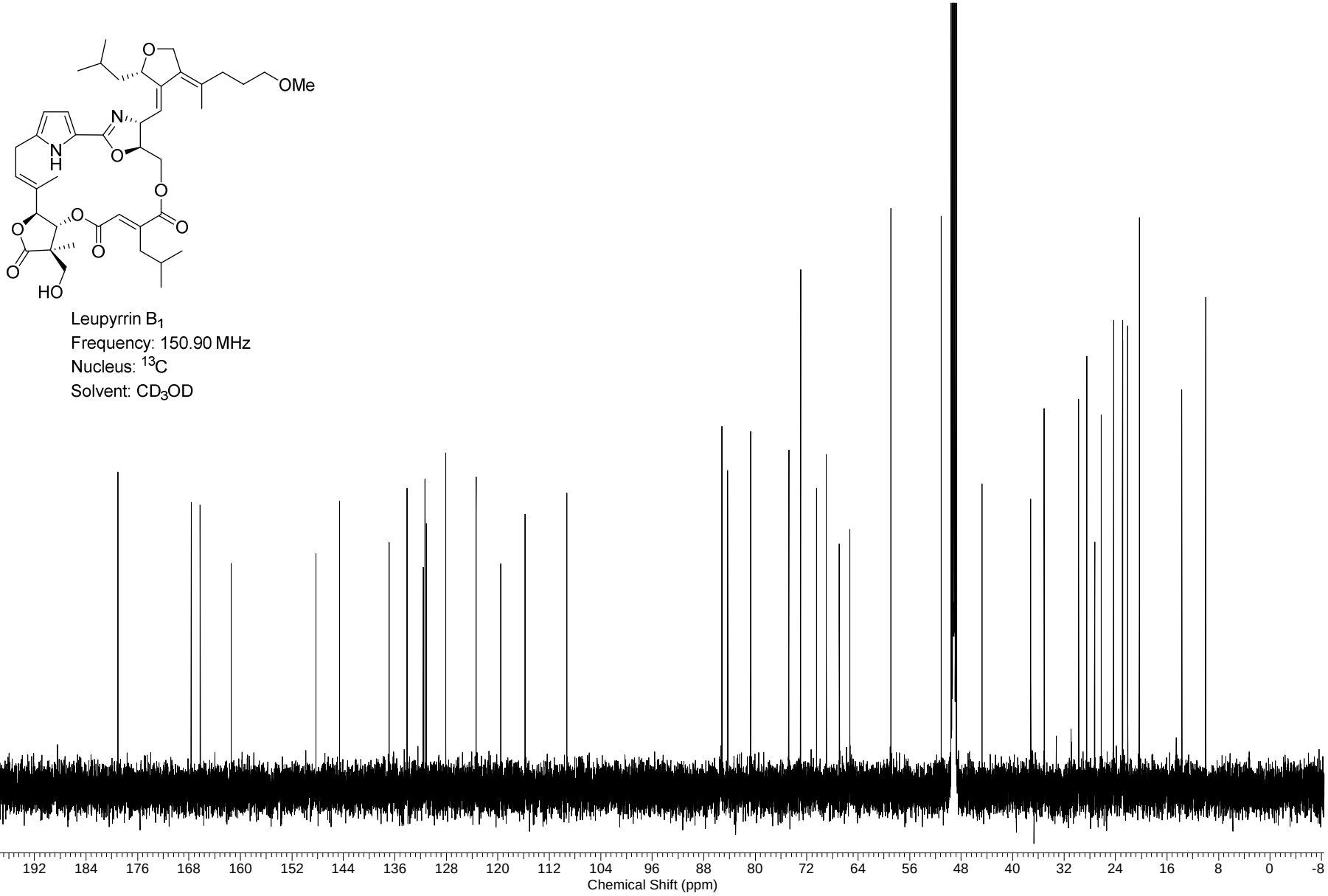
[a] high $\Delta\delta^{S-R}$ value for H3 indicates a gauche conformation between H3 and the CF_3-group. This conformational change also results in a negative $\Delta\delta^{S-R}$ value at H6.[9]



[9] Seco, J. M.; Quiñoa, E.; Riguera, R. *Chem. Rev*. **2004**, *104*, 17.

2.4 Copies of NMR spectra




OMe
N
H
HO
Leupyrrin B1
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Nucleus: 13C
Solvent: CD3OD
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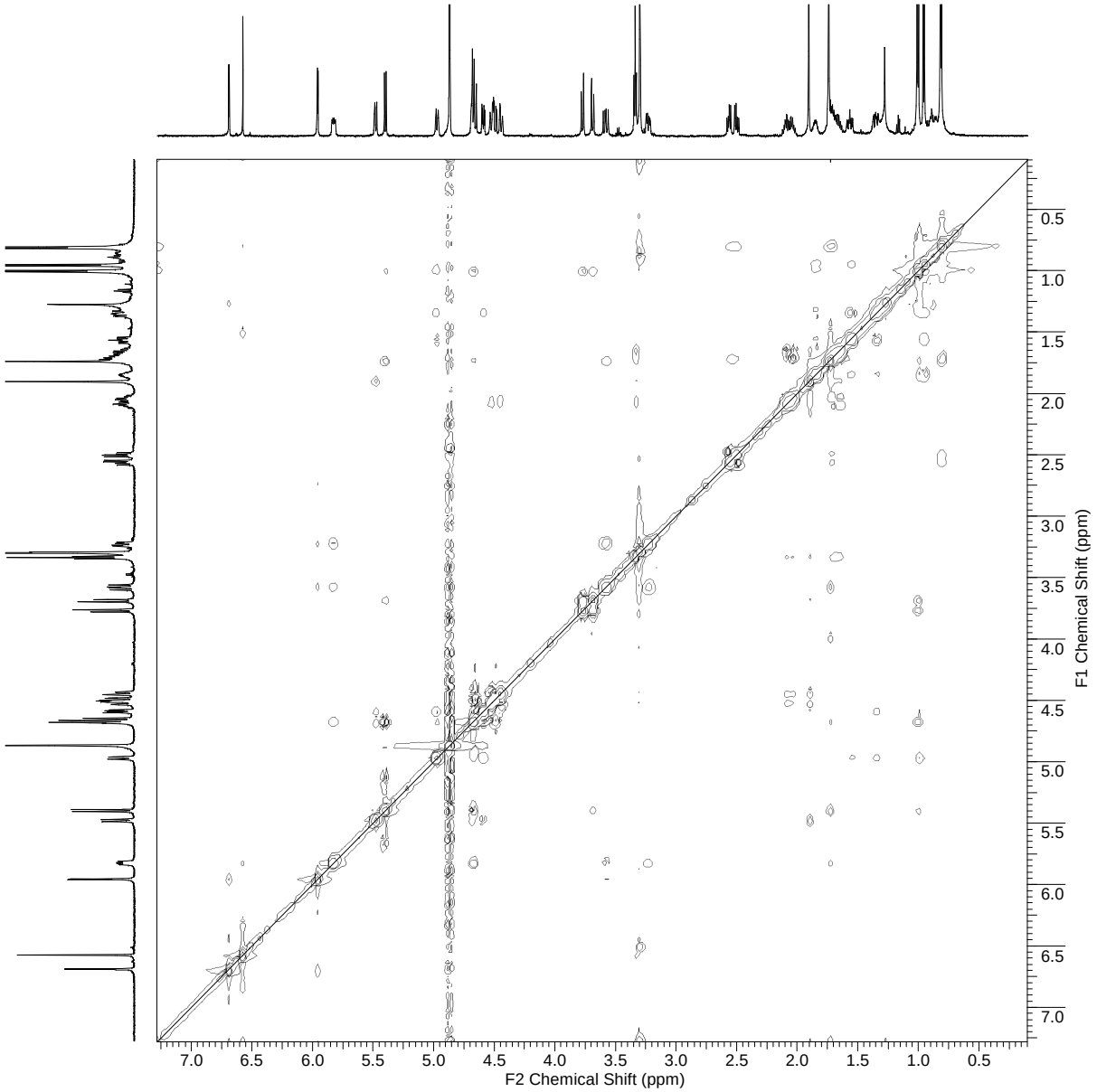
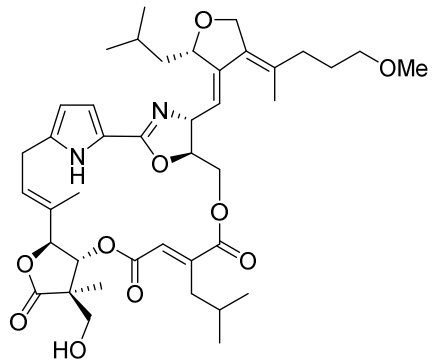
Chemical Shift (ppm)





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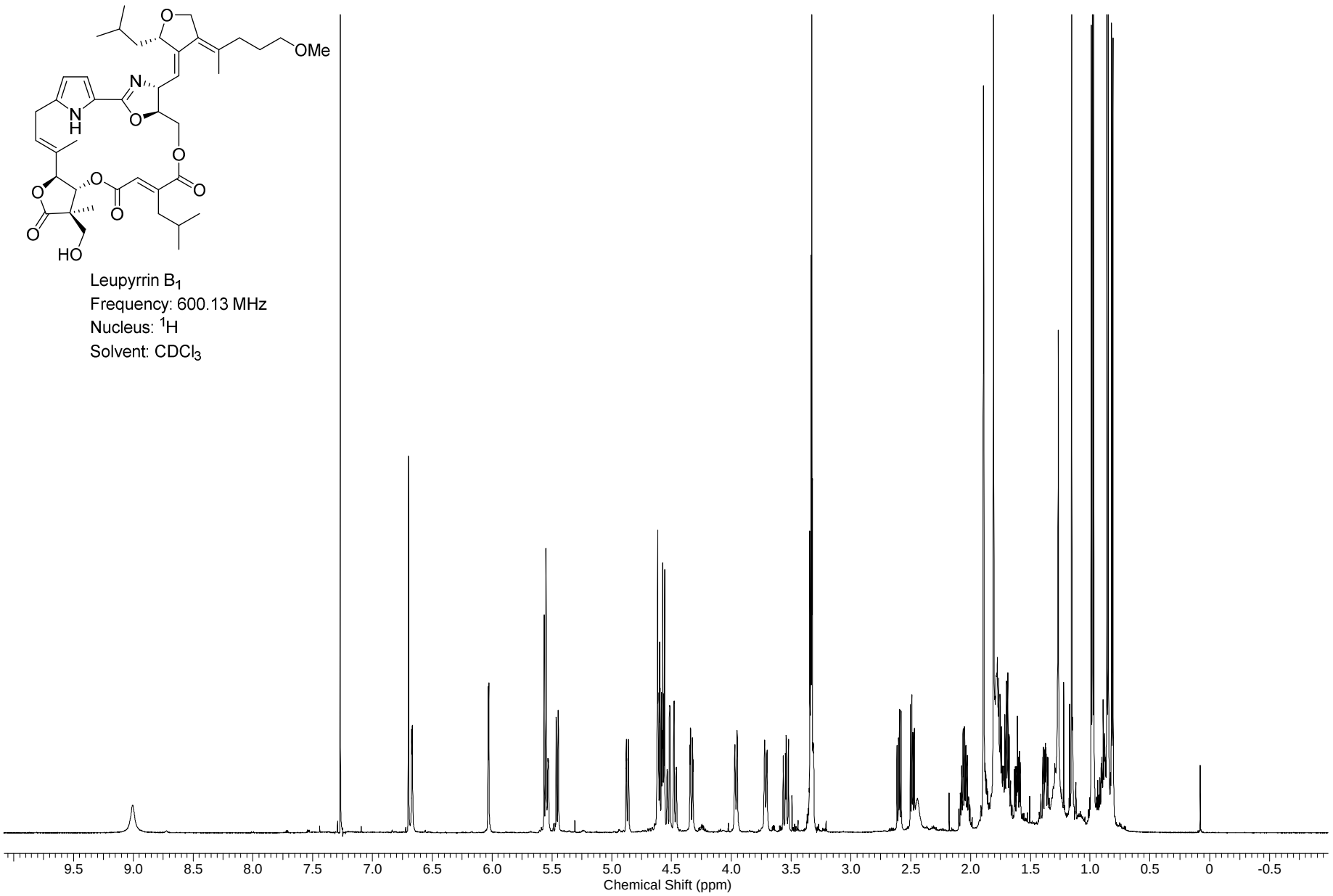
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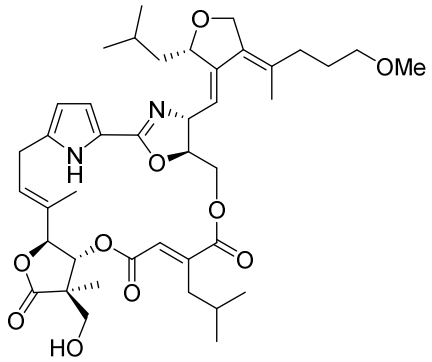
N
H
N
O
O
O
O
O
O
O
O
HO
Leupyrrin B1
Frequency: 600.13 MHz
Nucleus: 1H
Solvent: CDCl3
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)



Leupyrrin B_1
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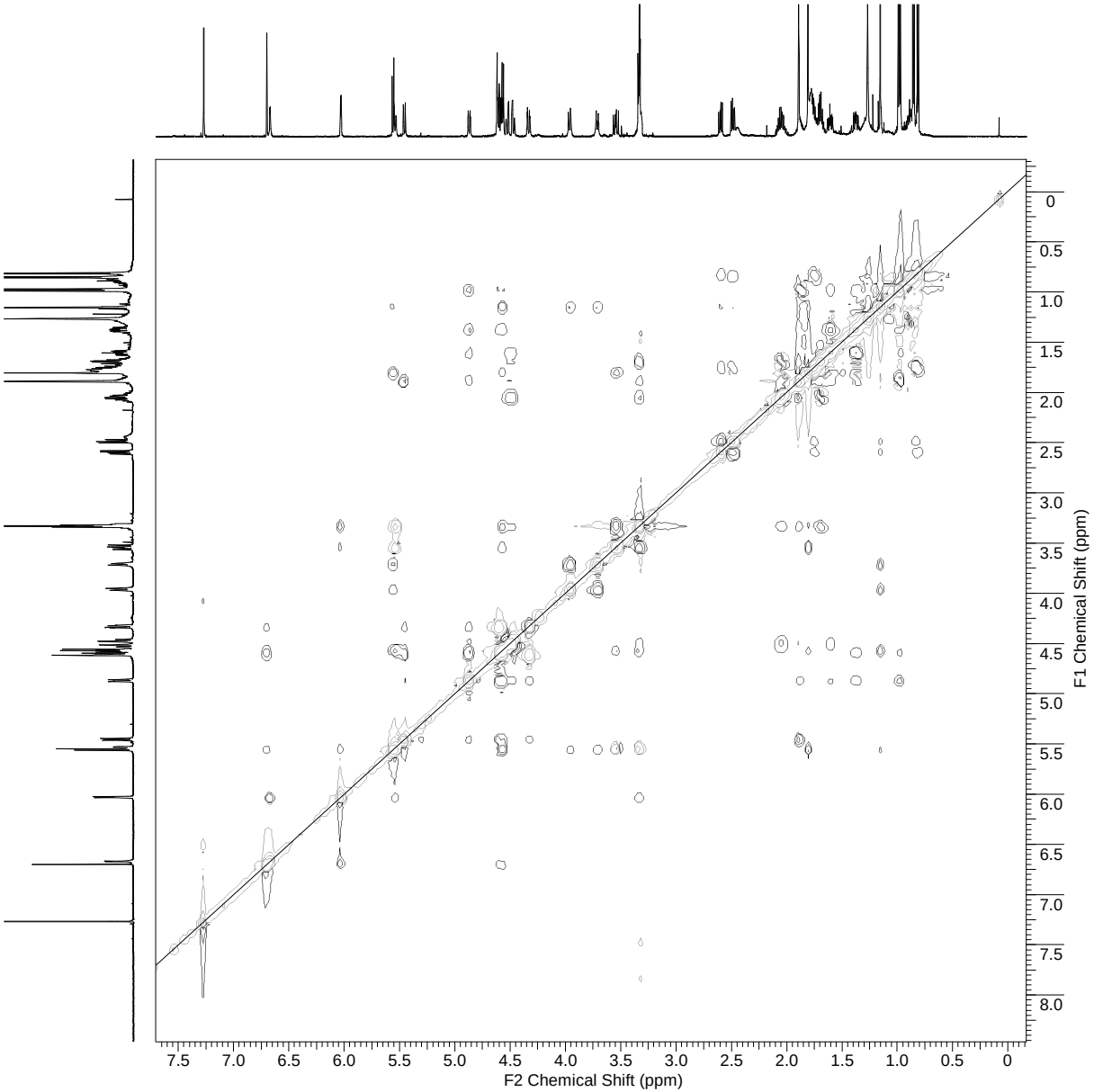
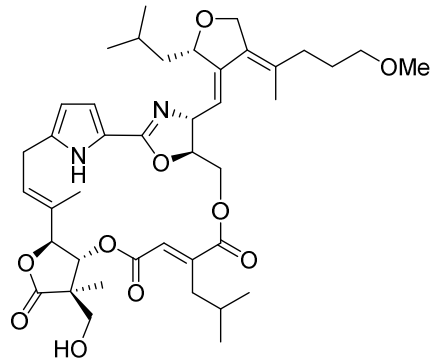
Nucleus: ^{13}C
Solvent: $CDCl_3$





Leupyrrin B_1
$^1H,^1H$-ROESY
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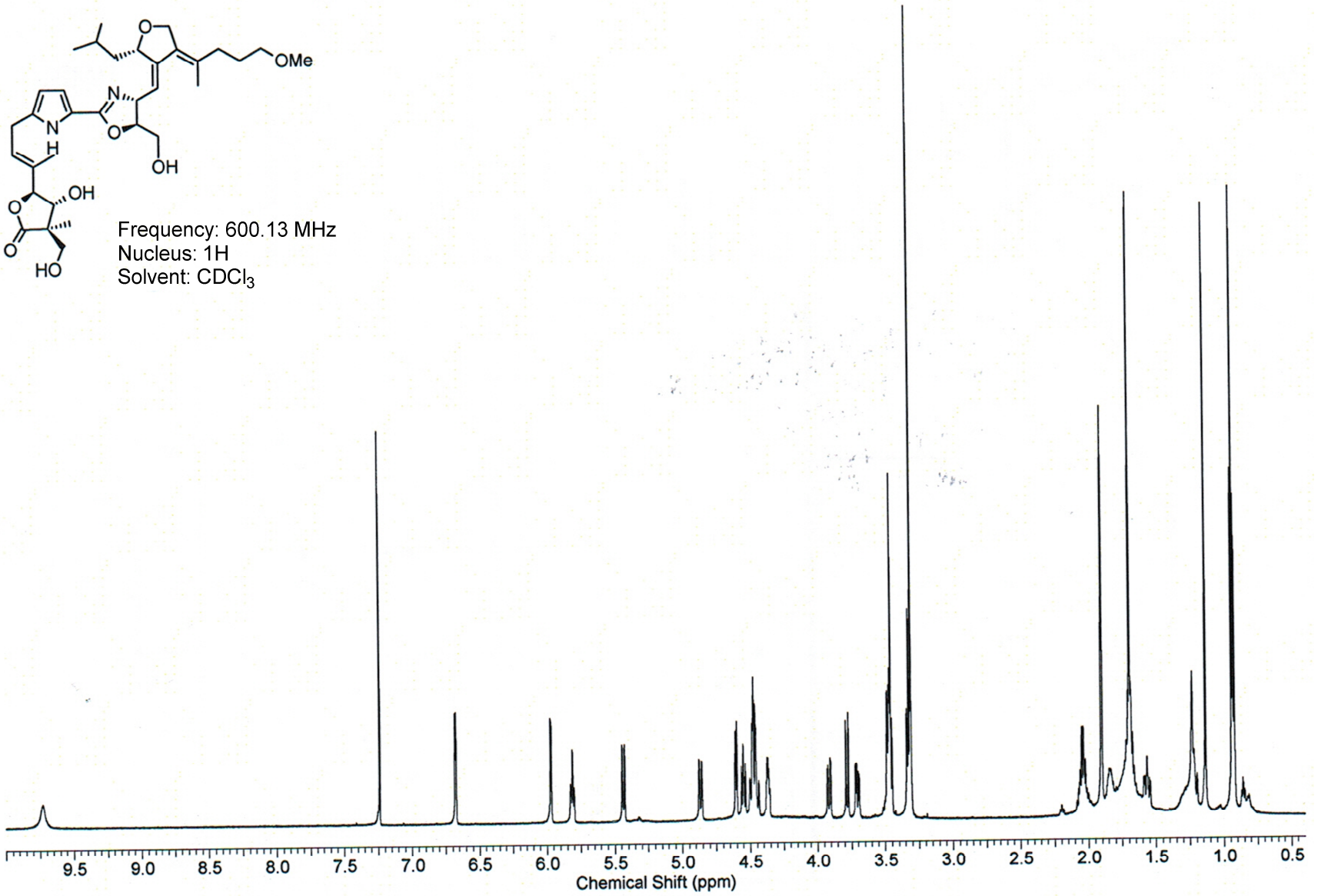
Solvent: $CDCl_3$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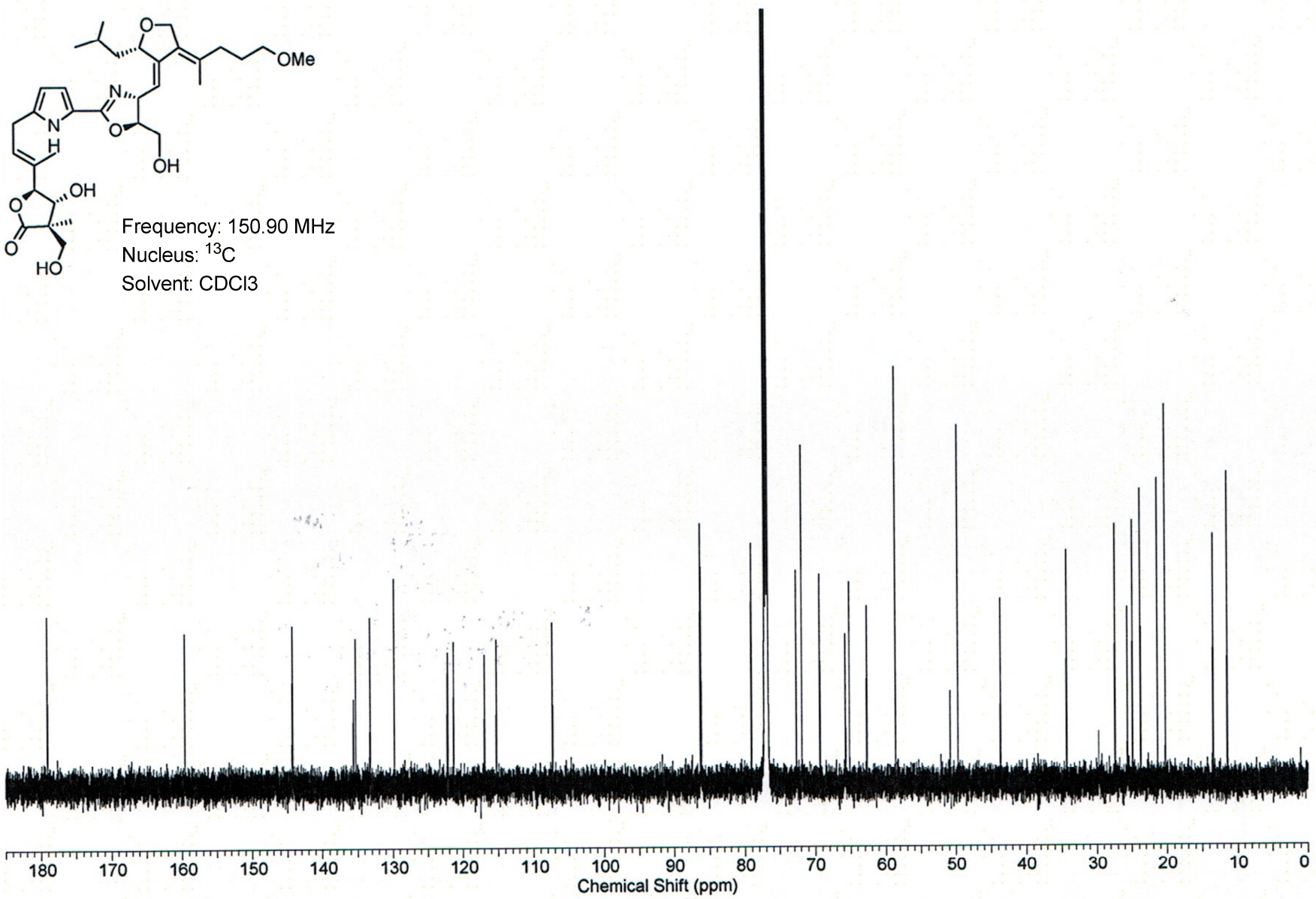
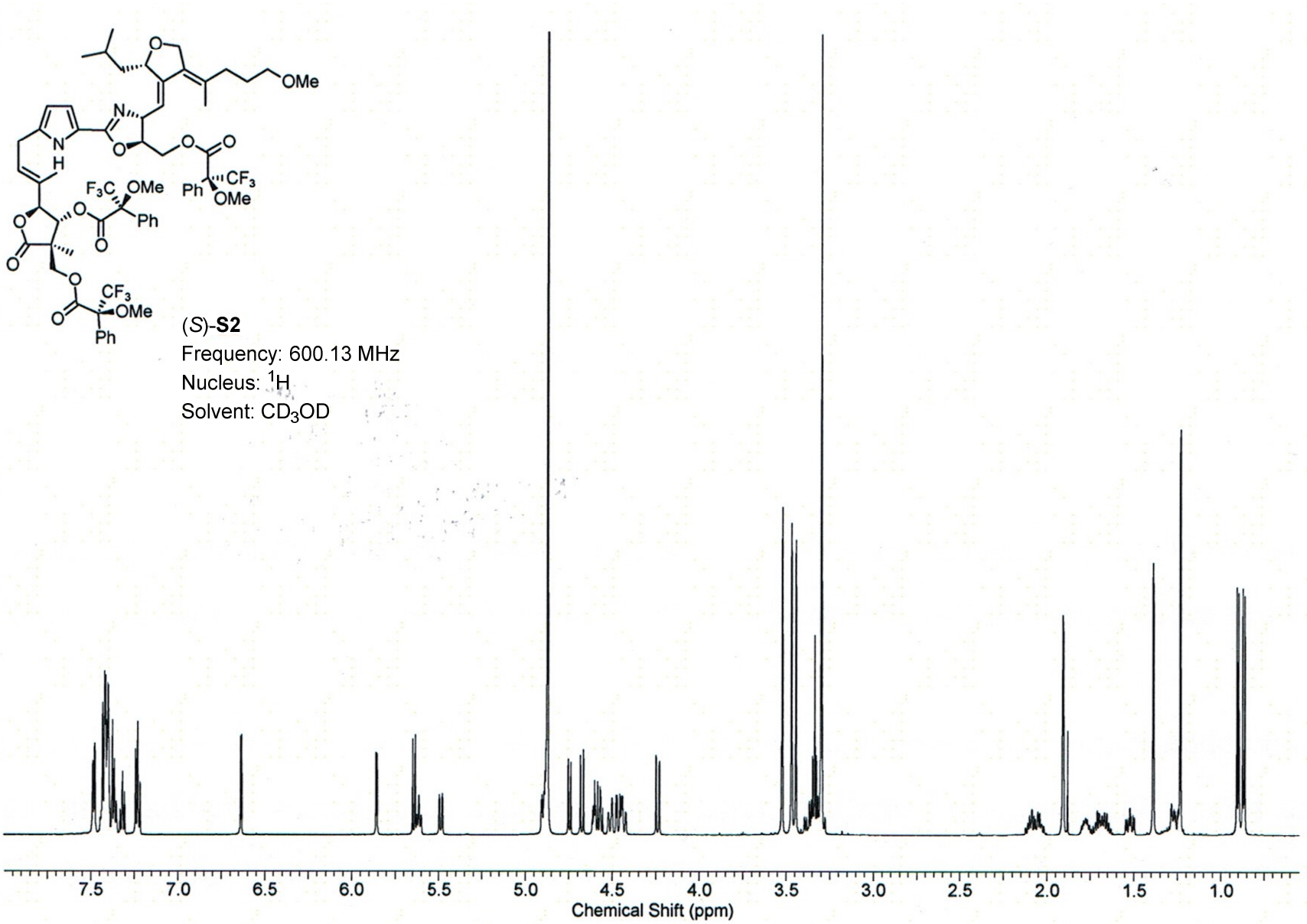
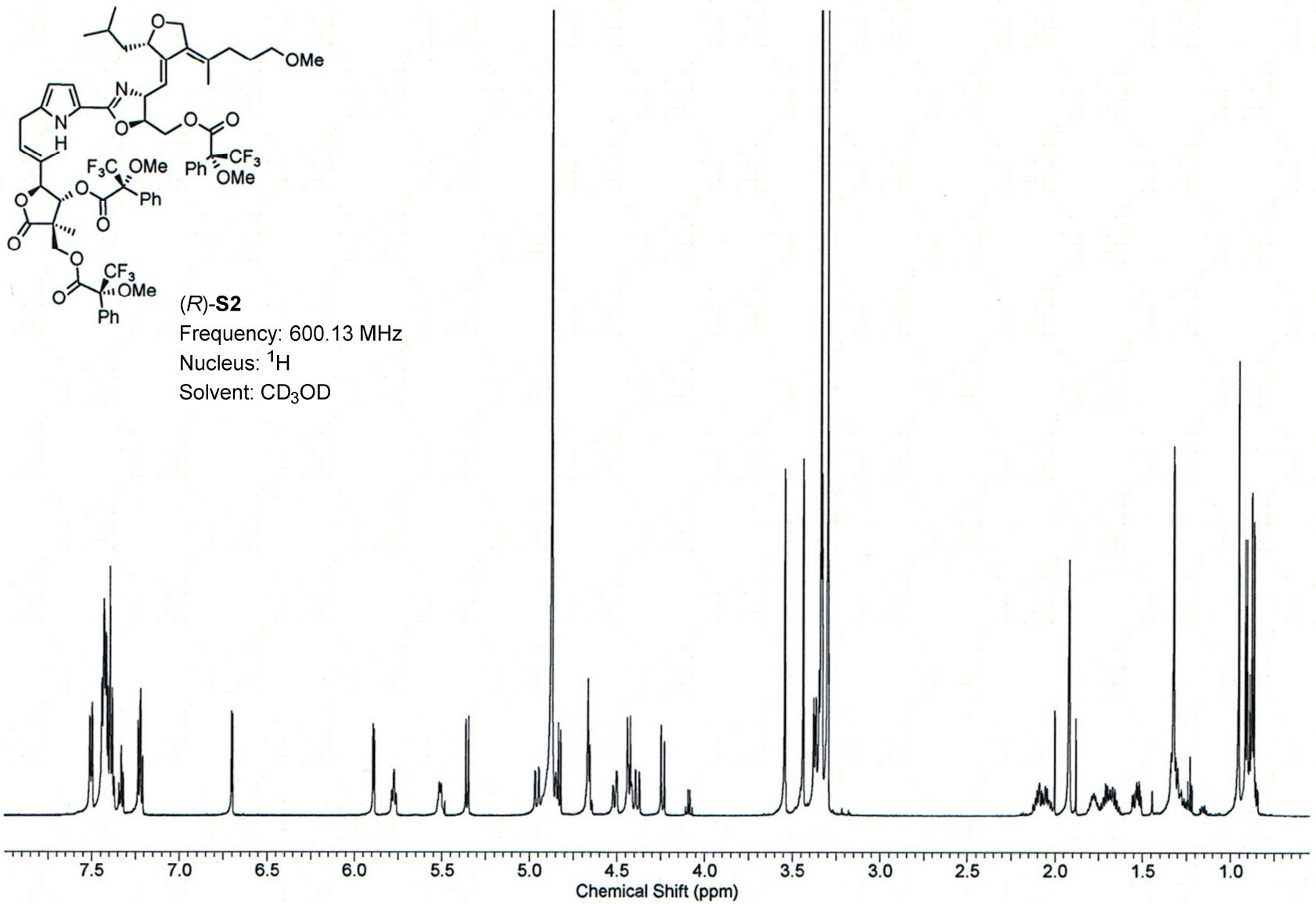
N
H
N
O
O
OH
OH
O
O
HO
Frequency: 600.13 MHz
Nucleus: 1H
Solvent: CDCl3
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


OMe
N
H
N
O
OH
OH
O
O
HO
Frequency: 150.90 MHz
Nucleus: 13C
Solvent: CDCl3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Chemical Shift (ppm)


(S)-S2
Frequency: 600.13 MHz
Nucleus: 1H
Solvent: CD3OD
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
Chemical Shift (ppm)


OMe
N
H
O
F3C
OMe
Ph
CF3
Ph
OMe
CF3
OMe
Ph
(R)-S2
Frequency: 600.13 MHz
Nucleus: 1H
Solvent: CD3OD
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
Chemical Shift (ppm)

2.5 Molecular Modelling

The molecules were built using the Maestro9.2 work suite.[10] If possible, pre-assembled fragments were used to provide a more realistic picture of the angles and bond lengths. The structures were pre-minimized with 500 iterations using MacroModel9.7 (MM).[11] For conformational analysis the mixed torsion/low-mode sampling algorithm as implemented in MM was used. The torsional sampling option was set as "Extended" mode. Default values were used for the other parameters related to conformational sampling, exept that the number of steps was set to 10000. The conformational searches were done for aqueous solution with the Generalized Born/Solvent Accessible surface (GB/SA) continuum solvation model with water or chloroform as solvents. The energy minimization was carried out with the Polak-Ribiere conjugate gradient *algorithm* (PRCG),[12,13] the minimization steps were set to 5000 and the final convergence was set as 0.05 kcal mol^{-1} $Å^{-1}$.

For analysis of the conformers, all structures were superimposed and identical conformations of the macrocycle were clustered. The conformer with lowest energy of each cluster was taken as "cluster representative". The ensemble of all structures for each cluster is given in the appendix. Finally distances between selected atoms were measured and compared to experimental NOE-values.

Conformational Search

Typical INPUT-File (.com)

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[10] Maestro, version 9.2, Schrödinger, LLC, New York, NY, 2011.
[11] Macromodel, version 9.7, Schrödinger, LLC, New York, NY, 2009.
[12] E. Polak, G. Ribiere, *Review Francaise Inf. Rech. Oper.* **1969**, *16 RI*, 35-43.
[13] R. Klessig, E. Polak, *SIAM J. Control* **1972**, *10*, 524-529.

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Typical OUTPUT-File

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 MacroModel. Copyright Schrodinger, LLC.
 All rights reserved.

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Low-frequency-Mode Conformational Search.
 Probability of TORS/MOLS steps:   0.5000000
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   Numbers of high, medium and low quality bend parameters    =  135    0    0
   Numbers of high, medium and low quality torsion parameters =  183   11    0
   Interactions examined:        403 of        403 total, including unused
params.
      Stretch total=       74   constrained=        0
         Bend total=      135   constrained=        0        linear=        0
      Torsion total=      209   constrained=        2  out-of-plane=       13
    Nonbonded total=     2276      H-bonded=        0      ordinary=     2276
  Nonbonded cutoffs: CutVdw=   8.00    ;  CutEs=   20.0
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x86_64/../../data/water.slv
    Block specifies desired NFIELD -- accepting block
 Starting conjugate gradient minimization.
          Step     1 New global minimum.  E (kJ/mol) =        2.62
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  Search initialized with            1  structures from the input structure file
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          Step     4 New global minimum.  E (kJ/mol) =       -2.70
 Conf     4 E =    -2.70 (  0.048) is unique and stored as structure     3
 Conf     5 E =    -1.06 (  0.037) is unique and stored as structure     4
 Conf     6 E =    -1.05 (  0.048) rejected by starting structure     4
          Step     7 New global minimum.  E (kJ/mol) =       -2.73
 Conf     7 E =    -2.73 (  0.038) replaces starting structure     3
 Conf     8 E =    -1.01 (  0.049) rejected by starting structure     4
 Conf     9 E =     3.51 (  0.028) is unique and stored as structure     5
 Conf    10 E =     3.51 (  0.048) rejected by starting structure     5
 Conf    11 E =     5.23 (  0.040) is unique and stored as structure     6
 Conf    12 E =     5.23 (  0.047) rejected by starting structure     6
          :
          :
          :
          :
          :
 Conf   997 E =   -15.15 (  0.045) rejected by starting structure    65
 Conf   998 E =   -15.16 (  0.047) rejected by starting structure    65
 Conf   999 E =   -15.17 (  0.036) rejected by starting structure    65
 Conf  1000 E =   -14.94 (  0.030) replaces structure    64

Final report:
   65 unique conformations found
   65 minimized with good convergence
Found    10 confs within  1.00 kcal/mol ( 4.18 kJ/mol) of glob. min.
Found    17 confs within  2.00 kcal/mol ( 8.37 kJ/mol) of glob. min.
Found    22 confs within  3.00 kcal/mol (12.55 kJ/mol) of glob. min.
Found    65 confs within  5.00 kcal/mol (20.92 kJ/mol) of glob. min.
Global minimum E =    -34.23 found     3 times.

 Total number of structures processed =        1000
 Conformations with poor convergence marked with a *
 Conformation       1 (   -34.23270     kJ/mol) was found     3 times
 Conformation       2 (   -33.05400     kJ/mol) was found     3 times
 Conformation       3 (   -33.00788     kJ/mol) was found     6 times
 Conformation       4 (   -32.83193     kJ/mol) was found     4 times
 Conformation       5 (   -32.53358     kJ/mol) was found     4 times
 Conformation       6 (   -32.51785     kJ/mol) was found     3 times
 Conformation       7 (   -32.22464     kJ/mol) was found     7 times
 Conformation       8 (   -31.55818     kJ/mol) was found     3 times
 Conformation       9 (   -31.53876     kJ/mol) was found     1 times
```

```
Conformation      10 (   -31.16801     kJ/mol) was found     3 times
Conformation      11 (   -29.14901     kJ/mol) was found     2 times
Conformation      12 (   -28.81111     kJ/mol) was found     4 times
Conformation      13 (   -27.21439     kJ/mol) was found     4 times
Conformation      14 (   -27.15058     kJ/mol) was found     1 times
Conformation      15 (   -26.33642     kJ/mol) was found     4 times
Conformation      16 (   -26.26876     kJ/mol) was found     3 times
Conformation      17 (   -26.00729     kJ/mol) was found     3 times
Conformation      18 (   -24.61562     kJ/mol) was found    15 times
Conformation      19 (   -24.50722     kJ/mol) was found     4 times
Conformation      20 (   -23.29960     kJ/mol) was found     3 times
Conformation      21 (   -23.17010     kJ/mol) was found    11 times
Conformation      22 (   -22.81053     kJ/mol) was found     3 times
Conformation      23 (   -21.54195     kJ/mol) was found     1 times
Conformation      24 (   -21.11463     kJ/mol) was found     2 times
Conformation      25 (   -20.77334     kJ/mol) was found     2 times
Conformation      26 (   -20.36103     kJ/mol) was found     2 times
Conformation      27 (   -19.81793     kJ/mol) was found     1 times
Conformation      28 (   -19.71051     kJ/mol) was found     1 times
Conformation      29 (   -19.63368     kJ/mol) was found     5 times
Conformation      30 (   -19.53134     kJ/mol) was found     4 times
Conformation      31 (   -18.90831     kJ/mol) was found     5 times
Conformation      32 (   -18.15746     kJ/mol) was found     3 times
Conformation      33 (   -18.03578     kJ/mol) was found     1 times
Conformation      34 (   -16.54380     kJ/mol) was found     1 times
Conformation      35 (   -16.44508     kJ/mol) was found     2 times
Conformation      36 (   -16.22871     kJ/mol) was found     3 times
Conformation      37 (   -16.02226     kJ/mol) was found     1 times
Conformation      38 (   -15.60071     kJ/mol) was found     5 times
Conformation      39 (   -15.35244     kJ/mol) was found     2 times
Conformation      40 (   -15.34888     kJ/mol) was found     5 times
Conformation      41 (   -15.29989     kJ/mol) was found     1 times
Conformation      42 (   -15.17048     kJ/mol) was found     1 times
Conformation      43 (   -15.10410     kJ/mol) was found     3 times
Conformation      44 (   -14.99823     kJ/mol) was found     1 times
Conformation      45 (   -14.93663     kJ/mol) was found     2 times
Conformation      46 (   -14.80637     kJ/mol) was found     2 times
Conformation      47 (   -14.75907     kJ/mol) was found     1 times
Conformation      48 (   -14.69354     kJ/mol) was found     1 times
Conformation      49 (   -14.59277     kJ/mol) was found     4 times
Conformation      50 (   -14.56575     kJ/mol) was found     3 times
Conformation      51 (   -14.53808     kJ/mol) was found     7 times
Conformation      52 (   -14.49261     kJ/mol) was found     1 times
Conformation      53 (   -14.48515     kJ/mol) was found     4 times
Conformation      54 (   -14.46269     kJ/mol) was found     2 times
```

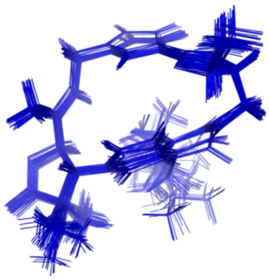
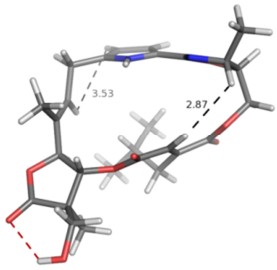
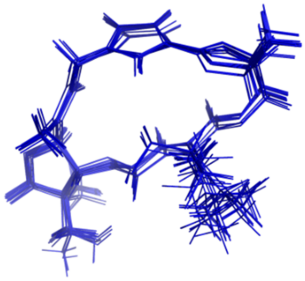
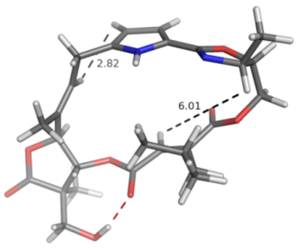
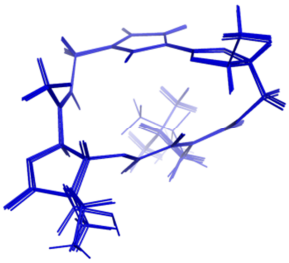
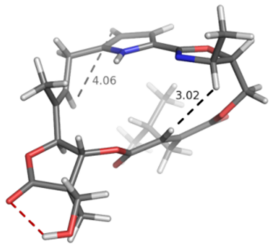
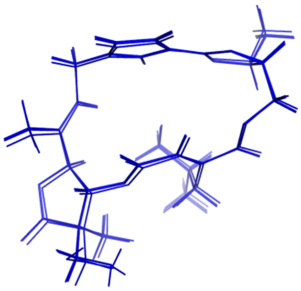
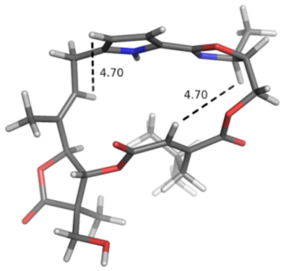
```
 Conformation      55 (   -14.31369     kJ/mol) was found     2 times
 Conformation      56 (   -14.18426     kJ/mol) was found     1 times
 Conformation      57 (   -14.09200     kJ/mol) was found     2 times
 Conformation      58 (   -13.93190     kJ/mol) was found     1 times
 Conformation      59 (   -13.91110     kJ/mol) was found     3 times
 Conformation      60 (   -13.76007     kJ/mol) was found     1 times
 Conformation      61 (   -13.67810     kJ/mol) was found     1 times
 Conformation      62 (   -13.64260     kJ/mol) was found     2 times
 Conformation      63 (   -13.59640     kJ/mol) was found     1 times
 Conformation      64 (   -13.54574     kJ/mol) was found     4 times
 Conformation      65 (   -13.34747     kJ/mol) was found     3 times
          *** MC Statistics ***
 Percent of minimized structures within energetic window:   19.40000
 Average number of duplicates:     2.984615
 Duplication standard deviation:   2.381520
       2119  structures generated
        887  rejected by ring closure
        233  rejected by van der Waals
        181  duplicate minimised structures
             Time in Monte Carlo generation loop:       6.0 CPU sec
                    Time in energy minimizations:    1382.0 CPU sec
                   Time in geometry optimisation:       0.0 CPU sec

BatchMin: normal termination                          02-Sep-2012 15:38:57

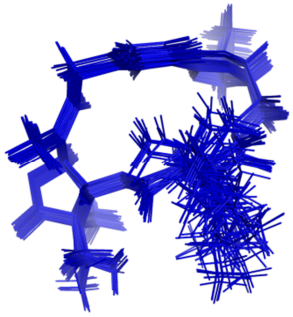
real   23m14.684s
user   23m6.199s
sys    0m3.567s
```

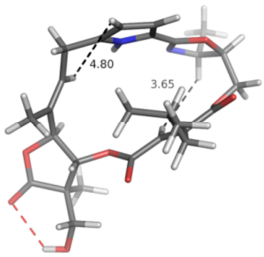
Analyses and Clustering

Table S 3 Structure Ensemble for each Cluster with identical conformations of the macrocycle. All conformers were superimposed and identical conformations of the macrocycle were clustered. This results in two to five families of macrocylic conformations (eg. *N*,*N*-*syn*-MC1_1, *N*,*N*-*syn*-MC1_2, *N*,*N*-*syn*-MC1_3 etc.). The conformer with lowest energy of each family was taken as "cluster representative".

name	Structure Ensemble	Representative
N,*N*-*syn*-MC1_1		
N,*N*-*syn*-MC1_2		
N,*N*-*syn*-MC1_3		
N,*N*-*syn*-MC2_1		

N,*N*-*syn*-MC2_2





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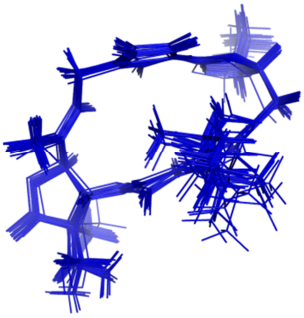
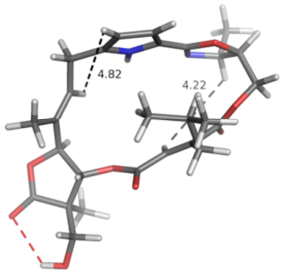
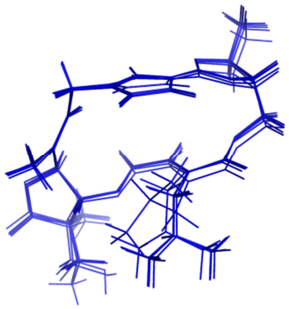
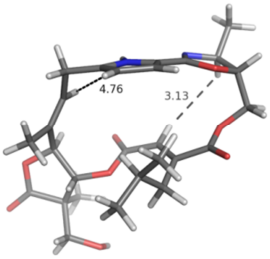


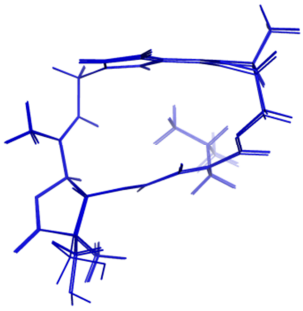


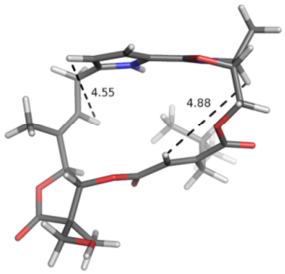
N,*N*-*syn*-MC2_4



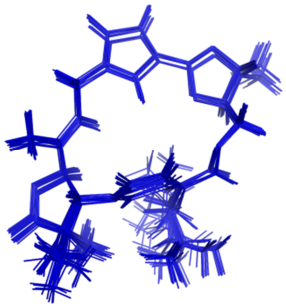


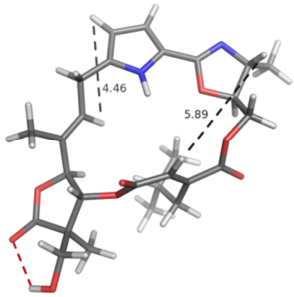
N,*N*-*syn*-MC2_5



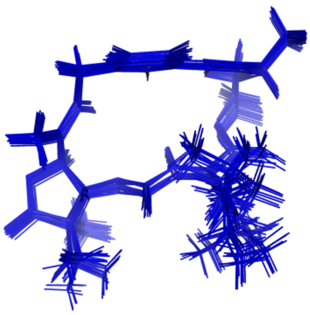


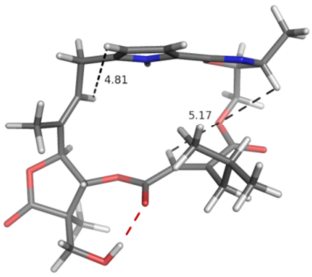
N,*N*-*anti*-MC1_1



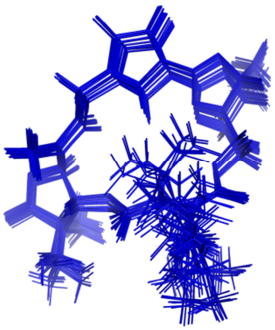


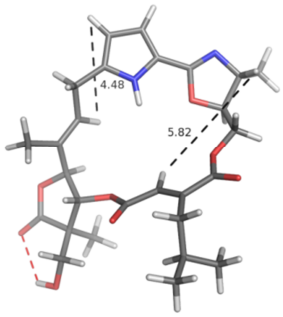
N,*N*-*anti*-MC1_2



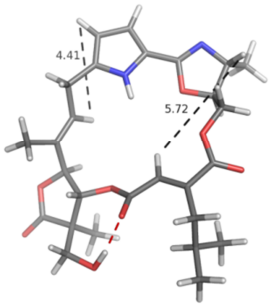


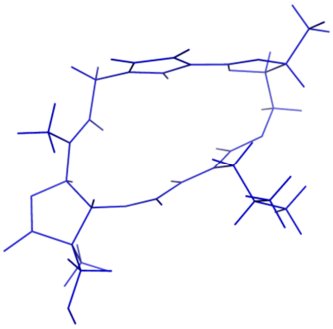
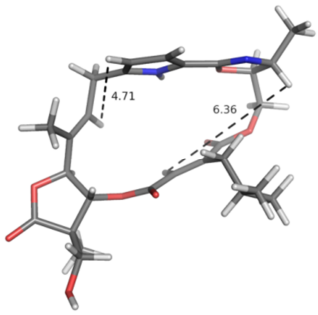
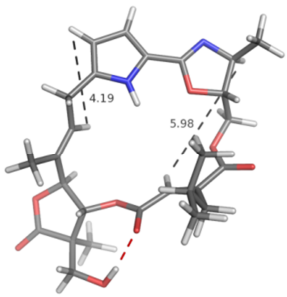
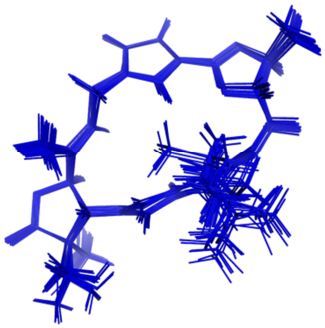
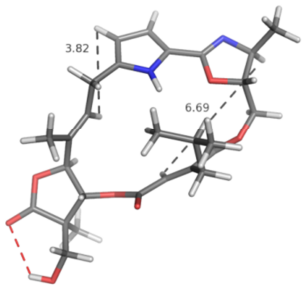
N,*N*-anti-MC1_3





N,*N*-anti-MC1_4



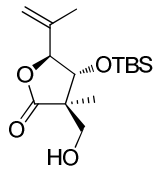
N,*N*-anti-MC1_5		
N,*N*-anti-MC2_1		
N,*N*-anti-MC2_2		

3 Experimental Procedures and Characterization Data

Acid **9**,[14] lactol **11**,[15] alkyne **16**[16] and propargylic alcohol **17**[17] were prepared according to literature procedures.

3.1 Synthesis of Butyrolactone 7

(3*R*,4*R*,5*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-(hydroxymethyl)-3-methyl-5-(prop-1-en-2-yl)dihydrofuran-2(3*H*)-one (14)



14

$C_{15}H_{28}O_4Si$, M = 300.5 g/mol

To a solution of **11** (59.2 mg, 194 µmol, 1.0 eq) in dry toluene (4 mL) at 45 °C was added a solution *iso*propenylmagnesium bromide (0.80 mL, 400 µmol, 2.06 eq, 0.5 M in THF) dropwise over 40 minutes. The reaction mixture was stirred at 40 °C for 11 hours before it was quenched with saturated solution of NH_4Cl (4 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 5 mL) and EtOAc (2 × 5 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the obtained crude product was performed by column chromatography (SiO_2, cyclohexane/EtOAc, 6:1) to give **14** (43.3 mg, 144 µmol, 74%) as a colorless liquid.

R_f = 0.33 (cyclohexane/EtOAc = 4/1); $[\alpha]_D^{20}$ = –11.4 (c = 1.00, EtOH); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 5.15 (s, 1H), 5.11 (s, 1H), 4.53–4.47 (m, 2H), 3.86 (d, *J* = 11.4 Hz, 1H), 3.46 (d, *J* = 11.4 Hz, 1H), 1.86 (s, 1H), 1.76 (s, 3H), 1.11 (s, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.02 (s, 3H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = 178.8, 139.5,

[14] (a) Andruszkiewicz, R.; Franklin, L. C.; Schwindt, M. A.; Silverman, R. B.; Sobieray, D. M.; Yuen, P. W.; *Pat. WO1993023383 A1*, **1993**, (b) Hoekstra, M. S.; Sobieray, D. M.; Schwindt, M. A.; Mulhern, T. A.; Grote, T. M.; Huckabee, B. K.; Hendrickson, V. S.; Franklin, L. C.; Granger, E. J.; Karrick, G. L. *Org. Process Res. Dev.* **1997**, *1*, 26.

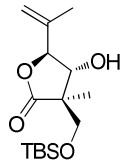
[15] Fronza, G.; Fuganti, C.; Grasselli, P.; Malpezzi, L.; Mele, A. *J. Org. Chem.* **1994**, *59*, 3487.

[16] (a) Debnar, T.; Wang, T.; Menche, D. *Org. Lett.* **2013**, *15*, 2774. (b) Debnar, T.; Dreisigacker, S.; Menche, D. *Chem. Commun.* **2013**, *49*, 725.

[17] Katukojvala, S.; Barlett, K. N.; Lotesta, S. D. Williams, L. J. *J. Am. Chem. Soc.* **2004**, *126*, 15348.

117.8, 86.1, 71.5, 64.2, 50.6, 25.8, 18.1, 16.3, 13.4, -4.3, -4.3; **HRMS** (ESI+) calculated for $C_{15}H_{28}O_4SiNa^+$ $[M+Na]^+$: 323.1665, found: 323.1662.

(3*R*,4*R*,5*S*)-3-(((*tert*-Butyldimethylsilyl)oxy)methyl)-4-hydroxy-3-methyl-5-(prop-1-en-2-yl)dihydrofuran-2(3*H*)-one (14a)



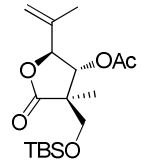
14a

$C_{15}H_{28}O_4Si$, M = 300.5 g/mol

To a solution of **14** (850 mg, 2.83 mmol, 1.0 eq) in dry THF (45 mL) at room temperature was added a solution of TBAF (5.94 mL, 5.94 mmol, 2.1 eq, 1.0 M in THF) dropwise over 2 minutes. The reaction mixture was stirred at room temperature for 15 minutes before it was diluted with EtOAc (50 mL) and quenched with brine (50 mL). After extraction with EtOAc (3 × 80 mL), the combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was dissolved in DMF (5.6 mL), Imidazol (385 mg, 5.66 mmol, 2.0 eq) and TBSCl (469 mg, 3.11 mmol, 1.1 eq) were added subsequently and the mixture was stirred at room temperature for 75 minutes and concentrated *in vacuo*. Purification of the obtained crude product was performed by column chromatography (SiO_2, cyclohexane/EtOAc, 4:1) to give **14a** (771 mg, 2.57 mmol, 91%) as a colorless liquid.

R_f = 0.35 (cyclohexane/EtOAc = 4/1); $[\alpha]_D^{20}$ = –19.2 (c = 1.00, EtOH); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 5.16 (s, 1H), 5.05 (s, 1H), 4.52–4.45 (m, 2H), 3.82 (d, *J* = 9.8 Hz, 1H), 3.57 (d, *J* = 9.8 Hz, 1H), 1.79 (s, 3H), 1.16 (s, 3H), 0.87 (s, 9H), 0.07 (s, 6H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = 177.6, 140.5, 115.0, 84.3, 73.0, 65.6, 49.8, 25.9, 18.3, 17.2, 13.2, -5.5; **HRMS** (ESI+) calculated for $C_{15}H_{28}O_4SiNa^+$ $[M+Na]^+$: 323.1665, found: 323.1652.

(2*S*,3*R*,4*R*)-4-(((*tert*-Butyldimethylsilyl)oxy)methyl)-4-methyl-5-oxo-2-(prop-1-en-2-yl)tetrahydrofuran-3-yl acetate (15)



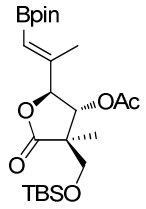
15

$C_{17}H_{30}O_5Si$, M = 342.5 g/mol

To a solution of **14a** (702 mg, 2.34 mmol, 1.0 eq) in dry CH_2Cl_2 (15 mL) at room temperature, DMAP (29.0 mg, 237 µmol, 0.1 eq), pyridine (12.0 mL, 149 mmol, 64 eq) and Ac_2O (1.10 mL, 11.6 mmol, 5.0 eq) were added subsequently. The reaction mixture was stirred at room temperature for 45 minutes before it was quenched with a saturated solution of $NaHCO_3$ (25 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the obtained crude product was performed by column chromatography (SiO_2, cyclohexane/EtOAc, 8:1) to give **15** (784 mg, 2.29 mmol, 98%) as a colorless liquid.

R_f = 0.44 (cyclohexane/EtOAc = 4/1); $[\alpha]_D^{20}$ = –42.5 (c = 1.00, CH_3Cl); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 5.68 (d, *J* = 7.5 Hz, 1H), 5.10 (s, 1H), 5.01 (s, 1H), 4.61 (d, *J* = 7.5 Hz, 1H), 3.81 (d, *J* = 9.4 Hz, 1H), 3.60 (d, *J* = 9.4 Hz, 1H), 2.10 (s, 3H), 1.78 (s, 3H), 1.07 (s, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = 177.4, 169.9, 140.0, 115.4, 82.4, 73.2, 65.8, 50.1, 25.9, 20.7, 18.4, 17.0, 14.0, -5.5, -5.5 ; **HRMS** (ESI+) calculated for $C_{17}H_{30}O_5SiNa^+$ $[M+Na]^+$: 365.1755, found: 365.1745.

(2*S*,3*R*,4*R*)-4-(((*tert*-Butyldimethylsilyl)oxy)methyl)-4-methyl-5-oxo-2-((*E*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-2-yl)tetrahydrofuran-3-yl acetate (7)



7

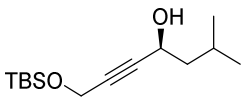
$C_{23}H_{41}BO_7Si$, M = 468.5 g/mol

A mixture of **15** (71.0 mg, 207 µmol, 1.0 eq) and Hoveyda-Grubbs^{2nd} catalyst (23.0 mg, 45.1 µmol, 0.22 eq) was dissolved in toluene (0.5 mL). 2,2-dimethylethenylboronic acid pinacol ester (110 µL, 538 µmol, 2.6 eq) was added and the mixture was boiled for 19 hours. After removal of the solvent *in vacuo* purification of the obtained crude product was performed by column chromatography (SiO_2, cyclohexane/EtOAc, 20:1→6:1) to give **7** (74.1 mg, 173 µmol, 84%, *E*/*Z* 9:1) as a colorless liquid.

R_f = 0.22 (cyclohexane/EtOAc = 7/1); $[\alpha]_D^{20}$ = –40.0 (c = 1.00, CH_3Cl); **^{1}H-NMR** (300 MHz, $CDCl_3$): δ [ppm] = 5.63 (d, *J* = 7.2 Hz, 1H), 5.46 (quin, *J* = 0.9 Hz, 1H), 4.60 (dd, *J* = 7.2, 0.9 Hz, 1H), 3.80 (d, *J* = 9.3 Hz, 1H), 3.63 (d, *J* = 9.3 Hz, 1H), 2.10 (s, 3H), 2.00 (d, *J* = 0.9 Hz, 3H), 1.27 (s, 12H), 1.05 (s, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); **^{13}C-NMR** (75 MHz, $CDCl_3$): δ [ppm] = 177.5, 170.0, 154.3, 84.5, 83.3, 74.0, 66.1, 50.2, 25.9, 25.0, 25.0, 20.8, 18.5, 15.8, 14.0, -5.5, -5.5; **HRMS** (ESI+) calculated for $C_{23}H_{41}BO_7SiNa^+$ $[M+Na]^+$: 491.2607, found: 491.2622.

3.2 Synthesis of Dihydrofuran 10

(*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-6-methylhept-2-yn-4-ol (17)



17

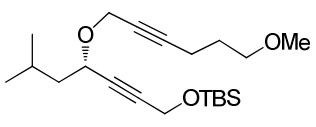
$C_{14}H_{28}O_2Si$, M = 256.5 g/mol

To a mixture of activated $Zn(OTf)_2$ (9.50 g, 26.1 mmol, 1.1 eq) and (−)-*N*-methylephedrine (5.11 g, 28.5 mmol, 1.2 eq) in dry toluene (65 ml) Et_3N (3.95 mL, 28.5 mmol, 1.2 eq) was added dropwise and stirred under argon atmosphere at room temperature for 2 hours. To the resulting milky–white slurry a solution of TBS protected propargyl ether (5.78 mL, 28.5 mmol, 1.2 eq) in dry toluene (20 ml) was added dropwise and it was stirred for 15 min. Afterwards, freshly distilled isovaleraldehyde (2.55 mL, 23.8 mmol, 1.0 eq) was added dropwise and it was stirred at rt overnight before the reaction mixture was diluted with toluene (660 mL) and washed with saturated aqueous NH_4Cl solution (3 × 120 mL) and dried over $MgSO_4$. Evaporation of solvent gave a crude product that was purified by column chromatography (SiO_2, petroleum ether/EtOAc, 95:5) to yield **17** (5.13 g, 20.0 mmol, 84%) as a colourless liquid in an enantiomeric excess of 94% as determined by Mosher ester analysis.[18]

$\mathbf{R_f}$ = 0.30 (petroleum ether/EtOAc = 95/5); $[\alpha]_D^{20}$ = –10.0 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.13 (s, 6H), 0.92 (s, 9H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.4 Hz, 3H), 1.51-1.59 (m, 1H), 1.60-1.67 (m, 1H), 1.73 (d, *J* = 5.6 Hz, 1H), 1.80-1.91 (m, 1H), 4.35 (d, *J* = 1.6 Hz, 2H), 4.45 (tdt, *J* = 7.2, 5.6, 1.6 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = -5.1, 18.3, 22.4, 22.5, 24.7, 25.8, 46.7, 51.7, 61.1, 83.5, 86.0; **HRMS** (ESI+): calculated for $C_{14}H_{28}NaO_2Si^+$ $[M+Na]^+$: 279.1751, found: 279.1745.

Spectral data match those previously reported.[18]

(*S*)-10-*iso*-Butyl-15,15,16,16-tetramethyl-2,9,14-trioxa-15-silaheptadeca-6,11-diyne (16a)



16a

$C_{21}H_{38}O_3Si$, M = 366.6 g/mol

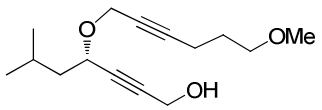
To a cold (0 °C) suspension of sodium hydride (60% in mineral oil, 935 mg, 23.4 mmol, 1.6 eq) in MeCN (170 mL) a solution of alcohol **16** (3.75 g, 14.6 mmol, 1.0 eq) in MeCN

[18] Katukojvala, S.; Barlett, K. N.; Lotesta, S. D. Williams, L. J. *J. Am. Chem. Soc.* **2004**, *126*, 15348.

(20 ml) was slowly added. The resulting mixture was warmed to room temperature and stirred for 1 hour. Afterwards a solution of **17** (4.13 g, 14.6 mmol, 1.0 eq) in MeCN (20 mL) was added. The mixture was stirred over night before it was quenched with a saturated solution of NH_4Cl (80 mL) and extracted with Et_2O (3 × 200 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (SiO_2, petroleum ether/EtOAc, 95:5) gave **16a** (4.55 g, 12.4 mmol, 85%) as a colorless oil.

R_f = 0.24 (petroleum ether/EtOAc = 95/5); $[\alpha]_D^{20}$ = –137.0 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.13 (s, 6H), 0.92 (s, 9H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 1.54 (ddd, *J* = 13.6, 7.3, 6.3 Hz, 1H), 1.68 (ddd, *J* = 13.6, 8.0, 6.8 Hz, 1H), 1.77 (tt, *J* = 7.1, 6.2 Hz, 2H), 1.88 (virt. spt, *J* = 6.7 Hz, 1H), 2.31 (tt, *J* = 7.1, 2.2 Hz, 2H), 3.34 (s, 3H), 3.46 (t, *J* = 6.2 Hz, 2H), 4.21 (dt, *J* = 15.2, 2.2 Hz, 1H), 4.31 (dt, *J* = 15.2, 2.2 Hz, 1H), 4.34-4.41 (m, 3H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = -5.1, 15.5, 18.3, 22.3, 22.6, 24.5, 25.8, 28.6, 44.4, 51.7, 56.2, 58.6, 66.4, 71.2, 76.0, 83.5, 84.5, 86.1; **HRMS** (ESI+) calculated for $C_{21}H_{38}NaO_3Si^+$ $[M+Na]^+$: 389.2482, found: 389.2468.

(*S*)-4-((6-Methoxyhex-2-yn-1-yl)oxy)-6-methylhept-2-yn-1-ol (16b)



16b

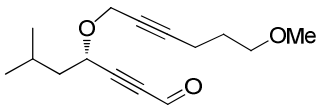
$C_{15}H_{24}O_3$, M = 252.3 g/mol

A stirred solution of TBS protected alcohol **16a** (5.18 g, 14.1 mmol, 1.0 eq) in MeOH (140 mL) was treated with CSA (984 mg, 4.24 mmol, 0.3 eq) at room temperature. After 10 minutes, TLC indicated complete conversion and a saturated solution of $NaHCO_3$ (400 mL) and EtOAc (1400 mL) were added. The layers were separated and the organic layer was washed with $NaHCO_3$ (400 ml) and with brine (400 mL) before it was dried over $MgSO_4$ and the solvent was evaporated *in vacuo* to give alcohol **16b** (3.52 g, 14.0 mmol, 99%).

R_f = 0.27 (petroleum ether/EtOAc = 70/30); $[\alpha]_D^{20}$ = –139.5 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.93 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 1.55

(ddd, *J* = 13.6, 7.3, 6.4 Hz, 1H), 1.70 (ddd, *J* = 13.6, 7.8, 6.7 Hz, 1H), 1.78 (tt, *J* = 7.1, 6.2 Hz, 2H), 1.87 (virt. spt, *J* = 6.7 Hz, 1H), 2.32 (tt, *J* = 7.1, 2.2 Hz, 2H), 3.34 (s, 3H), 3.47 (t, *J* = 6.2 Hz, 2H), 4.22 (dt, *J* = 15.2, 2.2 Hz, 1H), 4.28-4.39 (m, 4H); **^{13}C-NMR** (75 MHz, $CDCl_3$): δ [ppm] = 15.5, 22.2, 22.6, 24.6, 28.5, 44.5, 51.1, 56.4, 58.6, 66.5, 71.2, 76.0, 84.0, 84.6, 86.3; **HR-MS** (ESI+) calculated for $C_{15}H_{24}NaO_3^+$ $[M+Na]^+$: 275.1618, found: 275.1620.

(*S*)-4-((6-Methoxyhex-2-yn-1-yl)oxy)-6-methylhept-2-ynal (18)



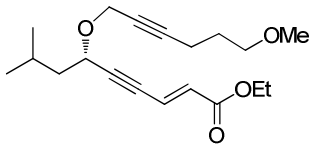
18

$C_{15}H_{22}O_3$, M = 250.3 g/mol

To a solution of alcohol **16b** (3.15 g, 12.6 mmol, 1.0 eq) in DMSO (80 mL) IBX (8.80 g, 31.4 mmol, 2.5 eq) was added and the reaction mixture was stirred at room temperature for 2 hours before TLC indicated complete formation of the aldehyde and CH_2Cl_2 (800 mL) was added. After stirring for 30 minutes, a white precipitate had formed which was removed by filtration. The remaining clear solution was washed with H_2O (2 × 700 mL) and dried over $MgSO_4$. Removal of the solvent under reduced pressure afforded a crude product that was purified by column chromatography (SiO_2, petroleum ether/EtOAc, 93:7) to give **18** (2.93 g, 11.7 mmol, 93%) as a colorless oil.

R_f = 0.24 (petroleum ether/EtOAc = 93/7); $[\alpha]_D^{20}$ = –217.2 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.95 (d, *J* = 6.6 Hz, 3H), 0.96 (d, *J* = 6.6 Hz, 3H), 1.61 (ddd, *J* = 13.6, 7.5, 6.0 Hz, 1H), 1.74-1.82 (m, 3H), 1.83-1.95 (m, 1H), 2.33 (tt, *J* = 7.1, 2.2 Hz, 2H), 3.34 (s, 3H), 3.45 (t, *J* = 6.2 Hz, 2H), 4.23 (dt, *J* = 15.4, 2.2 Hz, 1H), 4.34 (dt, *J* = 15.4, 2.2 Hz, 1H), 4.54 (dd, *J* = 8.1, 6.0 Hz, 1H), 9.25 (d, *J* = 0.4 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = 15.5, 22.0, 22.6, 24.5, 28.5, 43.6, 57.0, 58.6, 66.0, 71.1, 75.2, 85.0, 87.2, 95.1, 176.3; **HRMS** (ESI+) calculated for $C_{15}H_{22}NaO_3^+$ $[M+Na]^+$: 273.1461, found: 273.1472.

(*S*,*E*)-Ethyl 6-((6-methoxyhex-2-yn-1-yl)oxy)-8-methylnon-2-en-4-ynoate (18a)



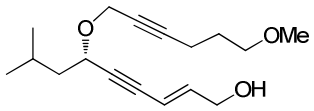
18a

$C_{19}H_{28}O_4$, M = 320.4 g/mol

Triethyl phosphonoacetate **19** (5.7 mL, 11.5 mol, 2.5 eq) was dissolved in dry THF (180 ml). After cooling to -78 °C, NaHMDS (1.0 M in THF, 23.0 ml, 23.0 mmol, 2.0 eq) was added dropwise over a period of 15 minutes. Stirring was continued for 1 hour at -78 °C. Afterwards, a solution of aldehyde **18** (2.89 g, 11.5 mmol, 1.0 eq) in THF (15 mL) was added over a period of 20 minutes. The reaction mixture was stirred for 2 hours at -78 °C before it was quenched by addition of buffer (pH 7, 150 ml). Et_2O (150 mL) was added and the organic layer was separated. The aqueous layer was extracted with Et_2O (2 × 150 mL) and the combined organic extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and after purification by column chromatography (SiO_2, petroleum ether/EtOAc, 93:7) **18a** was yielded (3.43 g, 10.7 mmol, 93%) as a colorless liquid.

R_f = 0.26 (petroleum ether/EtOAc = 93/7); $[\alpha]_D^{20}$ = –216.3 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.94 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.58 (ddd, *J* = 13.6, 7.3, 6.4 Hz, 1H), 1.69-1.82 (m, 3H), 1.87 (virt. spt, *J* = 6.6 Hz, 1H), 2.33 (tt, *J* = 7.1, 2.1 Hz, 2H), 3.34 (s, 3H), 3.46 (t, *J* = 6.2 Hz, 2H), 4.18-4.26 (m, 3H), 4.32 (dt, *J* = 15.3, 2.1 Hz, 1H), 4.49 (ddd, *J* = 7.9, 6.4, 1.7 Hz, 1H), 6.23 (d, *J* = 15.9 Hz, 1H), 6.78 (dd, *J* = 15.9, 1.7 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = 14.2, 15.5, 22.2, 22.6, 24.6, 28.6, 44.2, 56.5, 58.6, 60.8, 66.8, 71.1, 75.7, 82.6, 86.6, 97.4, 124.5, 130.8, 165.7; **HRMS** (ESI+): calculated for $C_{19}H_{28}NaO_4^+$ $[M+Na]^+$: 343.1880, found: 343.1887.

(*S*,*E*)-6-((6-Methoxyhex-2-yn-1-yl)oxy)-8-methylnon-2-en-4-yn-1-ol (18b)

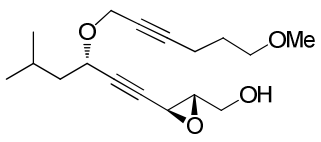


18b

$C_{17}H_{26}O_3$, M = 278.4 g/mol

To a cold (-78 °C) solution of ester **18a** (3.33 g, 10.4 mmol, 1.0 eq) in CH_2Cl_2 (110 mL) a solution of DIBAL-H (1 M in CH_2Cl_2, 31 mL, 31.0 mmol, 3.0 eq) was added over a period of 20 minutes. The resulting solution was stirred at -78 °C for 20 hours before it was warmed to 0 °C. The solution was diluted with CH_2Cl_2 (100 mL) and H_2O (1.3 mL) was slowly added followed by slow addition of an aqueous NaOH solution (15%, 1.3 mL) and finally H_2O (3.1 mL). The mixture was allowed to warm to room temperature and it was stirred for additional 30 minutes. Then it was dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo* to give **18b** (2.87 g, 10.3 mmol, 99%) as a colorless liquid.
R_f = 0.28 (petroleum ether/EtOAc = 70/30); $[\alpha]_D^{20}$ = –258.8 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.92-0.96 (m, 6H), 1.52-1.61 (m, 2H), 1.71 (ddd, *J* = 13.6, 7.5, 6.7 Hz, 1H), 1.78 (tt, *J* = 7.0, 6.3 Hz, 2H), 1.87 (virt. spt, *J* = 6.9 Hz, 1H), 2.32 (tt, *J* = 7.0, 2.1 Hz, 2H), 3.34 (s, 3H), 3.46 (t, *J* = 6.3 Hz, 2H), 4.19-4.26 (m, 3H), 4.31 (dt, *J* = 15.3, 2.1 Hz, 1H), 4.40-4.46 (m, 1H), 5.78 (dq, *J* = 15.9, 1.8 Hz, 1H), 6.26 (dt, *J* = 15.9, 5.2 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = 15.5, 22.3, 22.6, 24.6, 28.6, 44.5, 56.3, 58.6, 62.8, 67.0, 71.2, 76.1, 83.6, 86.2, 88.7, 109.9, 142.1; **HRMS** (ESI+): calculated for $C_{17}H_{26}NaO_3^+$ $[M+Na]^+$: 301.1774, found: 301.1770.

((2*S*,3*S*)-3-((*S*)-3-((6-Methoxyhex-2-yn-1-yl)oxy)-5-methylhex-1-yn-1-yl)oxiran-2-yl)methanol (20)



20

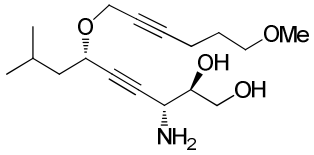
$C_{17}H_{26}O_4$, M = 294.4 g/mol

To a flask containing freshly activated MS (4 Å) and CH_2Cl_2 (25 mL) L-(+)-di-*iso*-propyl tartrate (187 mg, 168 µL, 0.797 mmol, 0.15 eq) was added and the mixture was cooled to -23 °C before Ti(O*i*Pr)$_4$ (227 mg, 236 µL, 0.797 mmol, 0.15 eq) and *t*-BuOOH (~5.5 M in decane, 1.93 mL, 10.6 mmol, 2.0 eq) were added successively. The mixture was stirred for 30 minutes before a solution of alcohol **18b** (1.48 g, 5.32 mmol) in CH_2Cl_2 (15 mL), which had been pre-dried over MS (4 Å) for 3 hours, was slowly added. The reaction mixture was stirred at -23 °C overnight.

When TLC indicated complete conversion, the reaction mixture was filtered and an aqueous solution of $FeSO_4$ (3.60 g) and citric acid (1.35 g) in H_2O (25 mL) was added. After it was stirred for 30 minutes it was cooled to 0 °C and treated with 1 M NaOH (12.5 mL) for 1 hour before it was diluted with H_2O (20 mL) and the phases were separated and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and evaporated *in vacuo*. The crude product was purified by flash column chromatography (SiO_2, petroleum ether/EtOAc, 6:4) to afford epoxyalcohol **20** as a colorless oil (1.46 g, 4.94 mmol, *dr* > 15:1, 93%).

R_f = 0.24 (petroleum ether/EtOAc = 70/30); $[\alpha]_D^{20}$ = –138.9 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.92 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 1.53 (ddd, *J* = 13.7, 7.4, 6.3 Hz, 1H), 1.69 (ddd, *J* = 13.7, 7.8, 6.7 Hz, 1H), 1.77 (tt, *J* = 7.1, 6.2 Hz, 2H), 1.80-1.91 (m, 2H), 2.31 (tt, *J* = 7.1, 2.2 Hz, 2H), 3.30 (dt, *J* = 3.3, 2.3 Hz, 1H), 3.33 (s, 3H), 3.45 (t, *J* = 6.2 Hz, 2H), 3.47-3.48 (m, 1H), 3.72 (ddd, *J* = 13.0, 8.1, 3.3 Hz, 1H), 3.93 (ddd, *J* = 13.0, 4.8, 2.3 Hz, 1H), 4.18 (dt, *J* = 15.3, 2.2 Hz, 1H), 4.29 (dt, *J* = 15.3, 2.2 Hz, 1H), 4.33 (ddd, *J* = 7.8, 6.3, 1.1 Hz, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = 15.5, 22.2, 22.6, 24.5, 28.5, 42.5, 44.3, 56.4, 58.6, 60.0, 60.1, 66.3, 71.2, 75.8, 81.6, 83.3, 86.4; **HRMS** (ESI+): calculated for $C_{17}H_{26}NaO_4^+$ $[M+Na]^+$: 317.1723, found: 317.1726.

(2*R*,3*R*,6*S*)-3-Amino-6-((6-methoxyhex-2-yn-1-yl)oxy)-8-methylnon-4-yne-1,2-diol (20a)



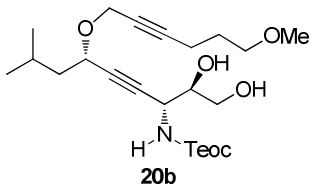
20a

$C_{17}H_{29}NO_4$, M = 311.4 g/mol

Epoxyalcohol **20** (2.00 g, 6.79 mmol) was shared in portions of 70 to 80 mg in high pressure microwave tubes equipped with a magnetic stirring bar. To each tube NH_4OH (25% in H_2O, 1 mL per 10 mg of **20** was added and the resulting mixture was dispersed by magnetic stirring and in an ultrasonic bath until a milky white emulsion was obtained. The tube was immediately placed into a microwave reactor (Cem Discover) were it was irradiated for 10 minutes between 20 and 30 W at 110 °C. Afterwards the solvent was removed *in vacuo* to give crude **20a** (2.03 g, max. 6.52 mmol) that was used without further purification. An analytical sample was purified by flash column chromatography (SiO_2, EtOAc/MeOH/*i*$PrNH_2$, 100:5:5) to afford **20a** as an orange gum.

R_f = 0.22 (EtOAc/MeOH/*i*$PrNH_2$ = 100/4/4); $[\alpha]_D^{20}$ = –131.9 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (500 MHz, CD_3OD): δ [ppm] = 0.96 (virt. t, *J* = 6.8 Hz, 6H), 1.54 (ddd, *J* = 13.6, 7.5, 6.2 Hz, 1H), 1.67 (ddd, *J* = 13.6, 7.9, 6.7 Hz, 1H), 1.76 (tt, *J* = 7.1, 6.2 Hz, 2H), 1.90 (virt. spt, *J* = 6.8 Hz, 1H), 2.32 (tt, *J* = 7.1, 2.1 Hz, 2H), 3.35 (s, 3H), 3.50 (t, *J* = 6.2 Hz, 2H), 3.64-3.69 (m, 3H), 3.76-3.78 (m, 1H), 4.30 (t, *J* = 2.1 Hz, 2H), 4.42 (ddd, *J* = 7.9, 6.2, 1.9 Hz, 1H); **^{13}C-NMR** (125 MHz, CD_3OD): δ [ppm] = 16.2, 22.8, 23.3, 25.9, 29.9, 46.0, 47.3, 57.0, 59.0, 64.9, 67.6, 72.3, 75.6, 77.3, 84.0, 86.5, 87.1; **HRMS** (ESI+): calculated for $C_{17}H_{30}NO_4^+$ $[M+H]^+$: 312.2169 found: 312.2165.

2-(Trimethylsilyl)ethyl ((2*R*,3*R*,6*S*)-1,2-dihydroxy-6-((6-methoxyhex-2-yn-1-yl)oxy)-8-methylnon-4-yn-3-yl)carbamate (20b)



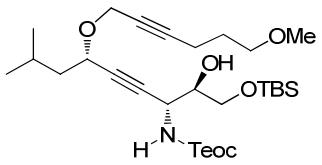
20b

$C_{23}H_{41}NO_6Si$, M = 455.7 g/mol

Crude amine **20a** (2.03 g, max. 6.52 mmol, 1.0 eq) was dissolved in a mixture of acetone and H_2O (2:1 *v*/*v*, 30 mL). $NaHCO_3$ (1.64 g, 19.6 mmol, 3.0 eq) was added followed by TeocOSuc (2.20 g, 8.48 mmol, 1.3 eq). The resulting solution was stirred at room temperature for 2 hours before H_2O (30 mL) was added followed by EtOAc (75 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. Purification by column chromatography (SiO_2, petroleum ether/EtOAc, 1:1) yielded **20b** (2.51 g, 5.50 mmol, 81% over 2 steps) as a yellow gum.

R_f = 0.23 (petroleum ether/EtOAc = 60/40); $[\alpha]_D^{20}$ = –131.8 (*c* = 2.0 in $CHCl_3$); **^{1}H-NMR** (500 MHz, $CDCl_3$): δ [ppm] = 0.02 (s, 9H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.94-1.01 (m, 2H), 1.50 (ddd, *J* = 13.6, 7.4, 6.3 Hz, 1H), 1.67 (ddd, *J* = 13.6, 7.9, 6.6 Hz, 1H), 1.75 (tt, *J* = 7.1, 6.2 Hz, 2H), 1.82 (virt. spt, *J* = 6.6 Hz, 1H), 2.29 (tt, *J* = 7.1, 2.1 Hz, 2H), 3.10 (br. s, 1H), 3.31 (s, 3H), 3.34 (br. s, 1H), 3.44 (t, *J* = 6.2 Hz, 2H), 3.65-3.77 (m, 3H), 4.11-4.22 (m, 3H), 4.26 (dt, *J* = 15.4, 2.1 Hz, 1H), 4.31 (ddd, *J* = 7.9, 6.3, 1.5 Hz, 1H), 4.56-4.64 (m, 1H), 5.43-5.52 (m, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$): δ [ppm] = −1.6, 15.4, 17.6, 22.1, 22.6, 24.5, 28.4, 44.3, 46.1, 56.3, 58.5, 63.3, 63.8, 66.4, 71.1, 73.4, 75.8, 81.8, 83.9, 86.4, 156.5; **HRMS** (ESI+): calculated for $C_{23}H_{41}NNaO_6Si^+$ $[M+Na]^+$: 478.2595, found: 478.2597.

2-(Trimethylsilyl)ethyl ((10*S*,13*R*,14*R*)-14-hydroxy-10-isobutyl-17,17,18,18-tetramethyl-2,9,16-trioxa-17-silanonadeca-6,11-diyn-13-yl)carbamate (20c)



20c

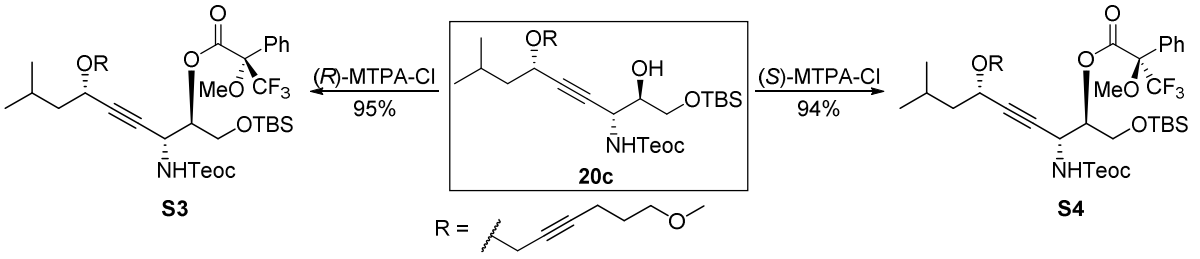
$C_{29}H_{55}NO_6Si_2$, M = 569.9 g/mol

A solution of diol **20b** (8.08 g, 17.7 mmol, 1.0 eq) in DMF (27 mL) was treated at room temperature with imidazole (3.02 g, 44.3 mmol, 2.5 eq). When the solution had turned clear, it was cooled to 0 °C and TBSCl (2.80 g, 18.6 mmol, 1.05 eq) was added. The mixture was warmed to ambient temperature again and stirred for 1 hour.

The reaction was quenched by addition of H_2O (100 mL) and Et_2O (200 mL). The layers were separated and the product was extracted into Et_2O (3 × 200 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, petroleum ether/EtOAc, 9:1 → 8:2) yielded **20c** (9.38 g, 16.5 mmol, 93%) as a yellow oil.

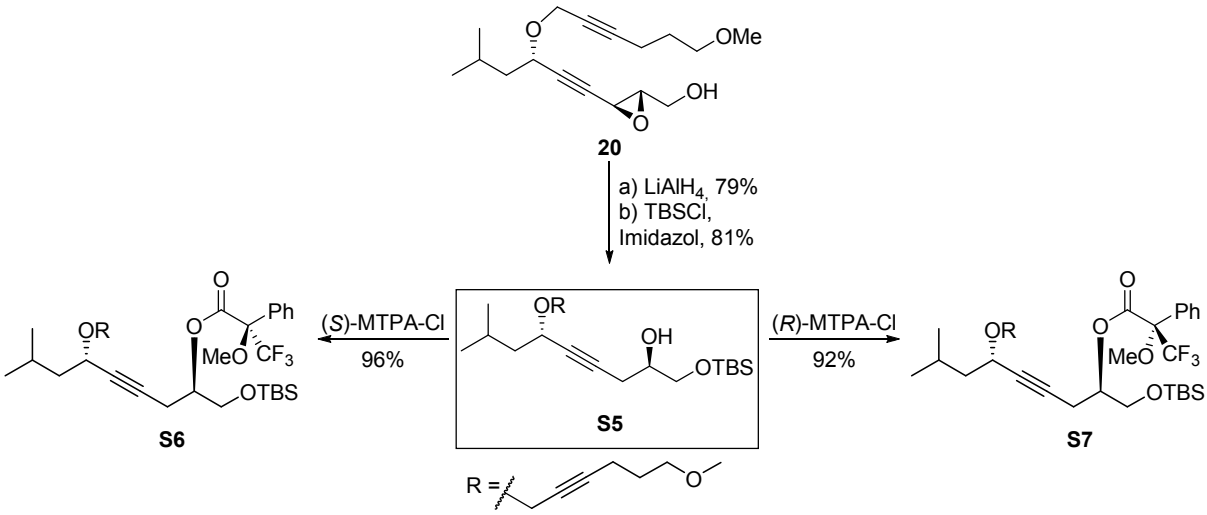
R_f = 0.33 (petroleum ether/EtOAc = 80/20); $[\alpha]_D^{20}$ = –115.9 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.04 (s, 9H), 0.10 (s, 6H), 0.89-0.95 (m, 6H), 0.92 (s, 9H) 0.95-1.03 (m, 2H), 1.52 (ddd, *J* = 13.7, 7.4, 6.5 Hz, 1H), 1.68 (ddd, *J* = 13.7, 7.8, 6.7 Hz, 1H), 1.73-1.81 (m, 2H), 1.85 (virt. spt, *J* = 6.7 Hz, 1H), 2.31 (tt, *J* = 7.1, 2.1 Hz, 2H), 2.55 (br. s, 1H), 3.34 (s, 3H), 3.45 (t, *J* = 6.2 Hz, 2H), 3.69 (dd, *J* = 9.9, 4.8 Hz, 1H), 3.73-3.81 (m, 1H), 3.85 (dd, *J* = 9.9, 5.1 Hz, 1H), 4.14-4.22 (m, 3H), 4.29 (dt, *J* = 15.3, 2.1 Hz, 1H), 4.33 (ddd, *J* = 7.8, 6.5, 1.5 Hz, 1H), 4.65-4.76 (m, 1H), 5.38-5.49 (m, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = -5.5, -1.5, 15.5, 17.7, 18.2, 22.2, 22.6, 24.6, 25.8, 28.6, 44.5, 46.5, 56.3, 58.6, 63.5, 64.4, 66.4, 71.2, 72.5, 75.9, 81.8, 83.8, 86.3, 156.1; **HRMS** (ESI+): calculated for $C_{29}H_{55}NNaO_6Si_2^+$ $[M+Na]^+$: 592.3460, found: 592.3462.

To confirm the absolute configuration at C13, alcohol **20c** was converted to the corresponding Mosher esters **S3** and **S4** (Scheme S 2)



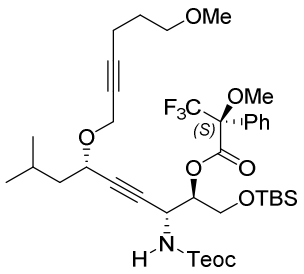
Scheme S 2: Attempts to determine the absolute configuration of **20c** at C13

Since determination of the absolute configuration at C13 using **S3** and **S4**, led to ambiguous results, **20** was reductively opened in a regioselective fashion to give **S5** after TBS-protection. Mosher ester analysis thereof clearly showed the indicated configuration (Scheme S 3).



Scheme S 3: Determination of the absolute configuration at C13 using alcohol **S5**.

(8*R*,9*R*)-8-((*S*)-3-((6-Methoxyhex-2-yn-1-yl)oxy)-5-methylhex-1-yn-1-yl)-2,2,12,12,13,13-hexamethyl-6-oxo-5,11-dioxa-7-aza-2,12-disilatetradecan-9-yl (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (S3)



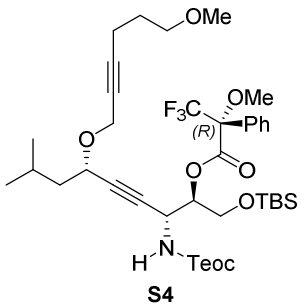
S3

$C_{39}H_{62}F_3NO_8Si_2$, M = 786.1 g/mol

Alcohol **20c** (6.8 mg, 11.9 µmol, 1.0 eq) was dissolved in CH_2Cl_2 (200 µL) before pyridine (8 µL, 99.3 µmol, 8.3 eq) and (*R*)-MTPA-Cl (9 µL, 48.1 µmol, 4.0 eq) were added successively. The solution was stirred for 1 hour at room temperature before further (*R*)-MTPA-Cl (9 µL, 48.1 µmol, 4.0 eq) was added. After 3 hours, when TLC indicated complete consumption of the starting material, a saturated solution of $NaHCO_3$ (1 mL) was added and the reaction mixture was extracted with Et_2O (3 × 2 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (SiO_2, petroleum ether/EtOAc, 88:12) gave **S3** (8.9 mg, 11.3 µmol, 95%) as a colorless oil.

R_f = 0.25 (petroleum ether/EtOAc = 90/10); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.03 (s, 3H), 0.04 (s, 9H), 0.05 (s, 3H), 0.88 (s, 9H), 0.90-0.93 (m, 6H), 0.94-1.00 (m, 2H), 1.49 (ddd, *J* = 13.7, 7.3, 6.5 Hz, 1H), 1.66 (ddd, *J* = 13.7, 7.8, 7.0 Hz, 1H), 1.72-1.89 (m, 3H), 2.31 (tt, *J* = 7.1, 2.1 Hz, 2H), 3.34 (s, 3H), 3.45 (t, *J* = 6.2 Hz, 2H), 3.52-3.55 (m, 3H), 3.76 (dd, *J* = 10.8, 4.9 Hz, 1H), 4.00-4.06 (m, 1H), 4.07-4.21 (m, 3H), 4.24 (dt, *J* = 15.3, 2.1 Hz, 1H), 4.31 (ddd, *J* = 7.8, 6.5, 1.4 Hz, 1H), 4.98-5.07 (m, 1H), 5.14-5.23 (m, 1H), 5.33-5.43 (m, 1H), 7.36-7.46 (m, 3H), 7.52-7.60 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = -5.9, -5.8, -1.5, 15.5, 17.6, 18.1, 22.2, 22.5, 24.5, 25.7, 28.6, 44.3, 44.5, 55.3, 56.3, 58.6, 61.8, 63.5, 66.2, 71.1, 75.8, 75.8, 80.6, 84.1, 84.9, 86.3, 123.1 (q, *J* = 288.2 Hz), 127.5, 128.5, 129.7, 131.7, 155.6, 165.9; **^{19}F-NMR** (282 MHz, $CDCl_3$): δ [ppm] = −71.9.

(8*R*,9*R*)-8-((*S*)-3-((6-Methoxyhex-2-yn-1-yl)oxy)-5-methylhex-1-yn-1-yl)-2,2,12,12,13,13-hexamethyl-6-oxo-5,11-dioxa-7-aza-2,12-disilatetradecan-9-yl (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (S4)



S4

$C_{39}H_{62}F_3NO_8Si_2$, M = 786.1 g/mol

Alcohol **20c** (6.6 mg, 11.6 µmol, 1.0 eq) was dissolved in CH_2Cl_2 (200 µL) before pyridine (8 µL, 99.3 µmol, 8.6 eq) and (*S*)-MTPA-Cl (9 µL, 48.1 µmol, 4.2 eq) were added successively. The solution was stirred for 1 hour at room temperature before further (*S*)-MTPA-Cl (9 µL, 48.1 µmol, 4.2 eq) was added. After 3 hours, when TLC indicated complete consumption of the starting material, a saturated solution of $NaHCO_3$ (1 mL) was added and the reaction mixture was extracted with Et_2O (3 × 2 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (SiO_2, petroleum ether/EtOAc, 88:12) gave **S4** (8.6 mg, 10.9 µmol, 94%) as a colorless oil.

R_f = 0.25 (petroleum ether/EtOAc = 90/10); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.05 (s, 9H), 0.10 (s, 3H), 0.10 (s, 3H), 0.87-0.91 (m, 6H), 0.91 (s, 9H), 0.98 (dd, *J* = 9.8, 7.3 Hz, 2H), 1.46 (dt, *J* = 13.7, 7.0 Hz, 1H), 1.62 (ddd, *J* = 13.7, 7.5, 7.0 Hz, 1H), 1.73-1.84 (m, 3H), 2.31 (tt, *J* = 7.1, 2.1 Hz, 2H), 3.34 (s, 3H), 3.45 (t, *J* = 6.2 Hz, 2H), 3.56-3.58 (m, 3H), 3.84 (dd, *J* = 10.7, 5.1 Hz, 1H), 4.02 (dd, *J* = 10.7, 5.6 Hz, 1H), 4.10 (dt, *J* = 15.2, 2.1 Hz, 1H), 4.13-4.19 (m, 2H), 4.22 (dt, *J* = 15.2, 2.1 Hz, 1H), 4.28 (t, *J* = 7.0 Hz, 1H), 4.91-5.05 (m, 2H), 5.20-5.26 (m, 1H), 7.39-7.45 (m, 3H), 7.53-7.61 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = -5.7, -5.6, -1.5, 15.5, 17.7, 18.1, 22.3, 22.5, 24.5, 25.7, 28.6, 44.2, 44.3, 55.5, 56.2, 58.6, 61.9, 63.6, 66.2, 71.2, 75.8, 76.2, 80.3, 84.1, 84.8, 86.3, 123.3 (q, *J* = 288.2 Hz), 127.3, 128.5, 129.7, 132.2, 155.4, 165.9; **^{19}F-NMR** (282 MHz, $CDCl_3$): δ [ppm] = −71.8.

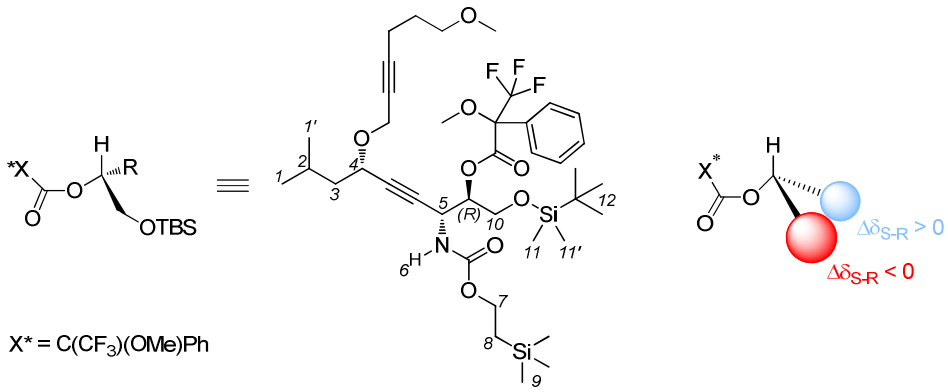
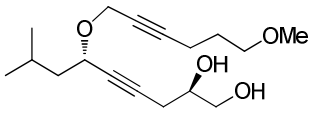


Table S 4: Mosher ester analysis of alcohol **20c**.[19]

# of H	δ_S	δ_R	$\Delta\delta_{S-R}$
1	0.90	0.88	+0.02
1’	0.92	0.90	+0.02
2	1.82	1.80	+0.02
3a	1.49	1.46	+0.03
3b	1.66	1.62	+0.04
4	4.31	4.28	+0.03
5	5.03	4.95	+0.08
6	5.38	4.98	+0.40
10a	3.76	3.84	−0.08
10b	4.03	4.02	+0.01[20]
11	0.03	0.10	−0.07
11‘	0.05	0.10	−0.05
12	0.88	0.91	−0.03

(2*R*,6*S*)-6-((6-Methoxyhex-2-yn-1-yl)oxy)-8-methylnon-4-yne-1,2-diol (20d)



20d

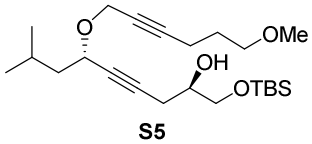
$C_{17}H_{28}O_4$, M = 296.4 g/mol

[19] Seco, J. M.; Quiñoa, E.; Riguera, R. *Chem. Rev*. **2004**, *104*, 17.
[20] not in accordance with the expected configuration

To a suspension of LAH (23.3 mg, 0.613 mmol, 2.0 eq) in dry THF (2.5 mL) a solution of epoxide **20** (90.2 mg, 0.306 mmol, 1.0 eq) in THF (2.5 mL) was added. The reaction mixture was stirred for 2 hours at room temperature before it was cooled down to 0 °C and H_2O (25 µL), NaOH (3 M, 25 µL) and further H_2O (75 µL) were added in this order with an interval of 5 minutes each to give a white precipitate. The mixture was filtered and the precipitate was washed with Et_2O (5 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo* to give crude **20d** (71.3 mg, 0.240 mmol, 79%) that was used without further purification.

R_f = 0.24 (petroleum ether/EtOAc = 50/50); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.93 (virt. t, *J* = 6.4 Hz, 6H), 1.52 (dt, *J* = 13.7, 7.1 Hz, 1H), 1.68 (dt, *J* = 13.7, 7.5 Hz, 1H), 1.78 (virt. quin, *J* = 6.7 Hz, 2H), 1.82-1.88 (m, 1H), 2.20 (br. s, 1H), 2.32 (tt, *J* = 7.1, 2.1 Hz, 2H), 2.45-2.51 (m, 2H), 2.56 (br. s, 1H), 3.34 (s, 3H), 3.46 (t, *J* = 6.2 Hz, 2H), 3.59 (dt, *J* = 11.0, 5.6 Hz, 1H), 3.71-3.79 (m, 1H), 3.83-3.91 (m, 1H), 4.21 (dt, *J* = 15.3, 2.1 Hz, 1H), 4.25-4.34 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = 15.5, 22.3, 22.6, 23.8, 24.6, 28.5, 44.7, 56.2, 58.6, 65.5, 66.7, 70.3, 71.2, 76.1, 81.7, 81.7, 86.2; **HRMS** (ESI+): calculated for $C_{17}H_{28}NaO_4^+$ $[M+Na]^+$: 319.1880, found: 319.1877.

(10*S*,14*R*)-10-*iso*-Butyl-17,17,18,18-tetramethyl-2,9,16-trioxa-17-silanonadeca-6,11-diyn-14-ol (S5)



S5

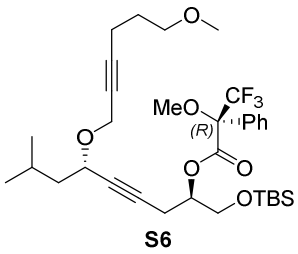
$C_{23}H_{42}O_4Si$, M = 410.7 g/mol

To a solution of diol **20d** (50.0 mg, 0.172 mmol, 1.0 eq) in DMF (0.35 mL) imidazole (25.8 mg, 0.378 mmol, 2.2 eq) was added followed by TBSCl (28.6 mg, 0.191 mmol, 1.1 eq). The reaction mixture was stirred at room temperature for 4 hours before it was quenched by addition of H_2O (1 mL). Et_2O (2 mL) was added, the organic layer was separated and the aqueous layer extracted with Et_2O (3 × 2 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed *in vacuo* to give a crude product

that was purified by column chromatography (SiO_2, petroleum ether/EtOAc, 85:15) to give **S5** (57.2 mg, 0.139 mmol, 81%) as a colorless oil.

R_f = 0.33 (petroleum ether/EtOAc = 85/15); $[\alpha]_D^{20}$ = –128.0 (*c* = 0.5 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.09 (s, 6H), 0.92 (s, 9H), 0.89-0.96 (m, 6H), 1.52 (ddd, *J* = 13.6, 7.2, 6.6 Hz, 1H), 1.67 (ddd, *J* = 13.6, 7.7, 7.0 Hz, 1H), 1.78 (tt, *J* = 7.1, 6.3 Hz, 2H), 1.86 (virt. spt, *J* = 6.7 Hz, 1H), 2.32 (tt, *J* = 7.1, 2.2 Hz, 2H), 2.40-2.53 (m, 3H), 3.34 (s, 3H), 3.46 (t, *J* = 6.3 Hz, 2H), 3.62 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.72 (dd, *J* = 9.9, 4.0 Hz, 1H), 3.75-3.84 (m, 1H), 4.20 (dt, *J* = 15.2, 2.2 Hz, 1H), 4.27-4.33 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = -5.4, -5.4, 15.6, 18.3, 22.3, 22.6, 23.4, 24.7, 25.9, 28.6, 44.8, 56.1, 58.6, 65.6, 66.7, 70.3, 71.2, 76.1, 81.0, 82.1, 86.1; **HRMS** (ESI+): calculated for $C_{23}H_{42}NaO_4Si^+$ $[M+Na]^+$: 433.2745, found: 433.2741.

(10*S*,14*R*)-10-*iso*-Butyl-17,17,18,18-tetramethyl-2,9,16-trioxa-17-silanonadeca-6,11-diyn-14-yl (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (S6)



S6

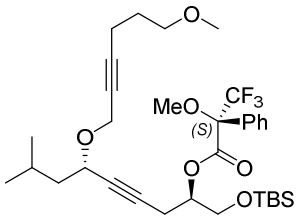
$C_{33}H_{49}F_3O_6Si$, M = 626.8 g/mol

Alcohol **S5** (16.4 mg, 39.9 µmol, 1.0 eq) was dissolved in CH_2Cl_2 (600 µL) before pyridine (26 µL, 322 µmol, 8.1 eq) and (*S*)-MTPA-Cl (30 µL, 160 µmol, 4.0 eq) were added successively. The solution was stirred for 3 hours at room temperature until TLC indicated complete consumption of the starting material. A saturated solution of $NaHCO_3$ (1.5 mL) was added and the reaction mixture was extracted with Et_2O (3 × 3 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (SiO_2, petroleum ether/EtOAc, 92:8) gave **S6** (23.9 mg, 38.1 µmol, 96%) as a colorless oil.

R_f = 0.24 (petroleum ether/EtOAc = 93/7); $[\alpha]_D^{20}$ = –43.9 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.07 (s, 3H), 0.08 (s, 3H), 0.90 (s, 9H), 0.87-0.94 (m, 6H),

1.46 (ddd, *J* = 13.7, 7.2, 6.6 Hz, 1H), 1.63 (ddd, *J* = 13.7, 7.7, 7.0 Hz, 1H), 1.77 (tt, *J* = 7.1, 6.3 Hz, 2H), 1.84 (virt. spt, *J* = 6.7 Hz, 1H), 2.31 (tt, *J* = 7.1, 2.1 Hz, 2H), 2.56 (ddd, *J* = 16.8, 5.4, 1.6 Hz, 1H), 2.64 (ddd, *J* = 16.8, 7.0, 2.0 Hz, 1H), 3.34 (s, 3H), 3.45 (t, *J* = 6.3 Hz, 2H), 3.57-3.59 (m, 3H), 3.84 (dd, *J* = 11.0, 5.8 Hz, 1H), 3.90 (dd, *J* = 11.0, 4.0 Hz, 1H), 4.14 (dt, *J* = 15.2, 2.1 Hz, 1H), 4.22-4.28 (m, 2H), 5.20 (dddd, *J* = 7.0, 5.8, 5.4, 4.0 Hz, 1H), 7.38-7.43 (m, 3H), 7.55-7.61 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = -5.6, 15.5, 18.2, 20.4, 22.3, 22.5, 24.6, 25.7, 28.6, 44.6, 55.4 (q, *J* = 1.2 Hz), 56.1, 58.6, 62.8, 66.5, 71.2, 75.1, 76.0, 80.4, 81.4, 84.7 (q, *J* = 27.8 Hz), 86.1, 123.3(q, *J* = 288.4 Hz), 127.4 (q, *J* = 1.0 Hz), 128.4, 129.6, 132.2, 166.0; **^{19}F-NMR** (282 MHz, $CDCl_3$): δ [ppm] = −72.0; **HRMS** (ESI+): calculated for $C_{33}H_{49}F_3NaO_6Si^+$ $[M+Na]^+$: 649.3143, found: 649.3147.

(10*S*,14*R*)-10- *iso*-Butyl-17,17,18,18-tetramethyl-2,9,16-trioxa-17-silanonadeca-6,11-diyn-14-yl (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (S7)



S7

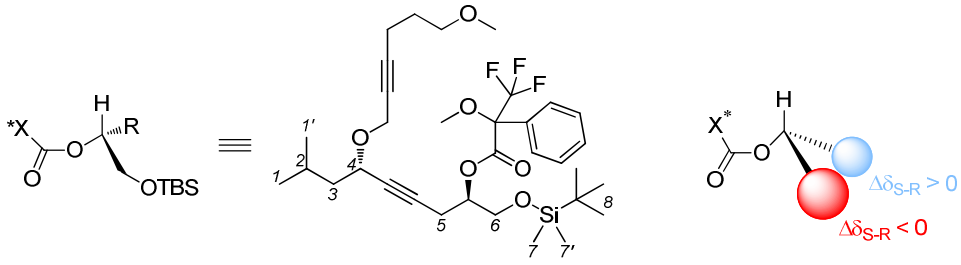
$C_{33}H_{49}F_3O_6Si$, M = 626.8 g/mol

Alcohol **S5** (18.9 mg, 46.2 µmol, 1.0 eq) was dissolved in CH_2Cl_2 (700 µL) before pyridine (30 µL, 372 µmol, 8.1 eq) and (*R*)-MTPA-Cl (35 µL, 185 µmol, 4.0 eq) were added successively. The solution was stirred for 3 hours at room temperature until TLC indicated complete consumption of the starting material. A saturated solution of $NaHCO_3$ (1.5 mL) was added and the reaction mixture was extracted with Et_2O (3 × 3 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (SiO_2, petroleum ether/EtOAc, 92:8) gave **S7** (26.5 mg, 42.3 µmol, 92%) as a colorless oil.

R_f = 0.24 (petroleum ether/EtOAc = 93/7); $[\alpha]_D^{20}$ = –91.2 (*c* = 1.0 in $CHCl_3$); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.01 (s, 3H), 0.01 (s, 3H), 0.86 (s, 9H), 0.89-0.94 (m, 6H),

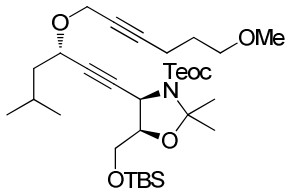
1.49 (ddd, *J* = 13.6, 7.2, 6.7 Hz, 1H), 1.65 (ddd, *J* = 13.6, 7.7, 7.0 Hz, 1H), 1.77 (tt, *J* = 7.1, 6.2 Hz, 2H), 1.84 (virt. spt, *J* = 6.7 Hz, 1H), 2.31 (tt, *J* = 7.1, 2.1 Hz, 2H), 2.64 (ddd, *J* = 17.0, 6.0, 1.7 Hz, 1H), 2.75 (ddd, *J* = 17.0, 6.0, 2.1 Hz, 1H), 3.33 (s, 3H), 3.45 (t, *J* = 6.2 Hz, 2H), 3.58-3.60 (m, 3H), 3.74 (dd, *J* = 10.9, 5.0 Hz, 1H), 3.77 (dd, *J* = 10.9, 5.0 Hz, 1H), 4.16 (dt, *J* = 15.3, 2.1 Hz, 1H), 4.23-4.32 (m, 2H), 5.20 (tt, *J* = 6.0, 5.0 Hz, 1H), 7.38-7.43 (m, 3H), 7.55-7.60 (m, 2H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = -5.7, -5.7, 15.5, 18.2, 20.7, 22.3, 22.5, 24.6, 25.7, 28.6, 44.6, 55.5 (q, *J* = 1.2 Hz), 56.1, 58.6, 62.6, 66.5, 71.2, 75.0, 76.0, 80.7 (q, *J* = 27.6 Hz), 81.4, 84.6, 86.1, 123.2(q, *J* = 288.6 Hz), 127.4 (q, *J* = 1.0 Hz), 128.4, 129.5, 132.2, 166.0; **^{19}F-NMR** (282 MHz, $CDCl_3$): δ [ppm] = −71.9; **HRMS** (ESI+): calculated for $C_{33}H_{49}F_3NaO_6Si^+$ $[M+Na]^+$: 649.3143, found: 649.3157.

Table S 5: Mosher ester analysis of alcohol **S5**.



# of H	δ_S	δ_R	$\Delta\delta_{S-R}$
1	0.90	0.89	+0.01
1’	0.92	0.91	+0.01
2	1.84	1.84	+0.00
3a	1.49	1.46	+0.03
3b	1.65	1.63	+0.02
4	4.29	4.26	+0.03
5a	2.64	2.56	+0.08
5b	2.75	2.64	+0.11
6a	3.74	3.84	−0.10
6b	3.77	3.90	−0.13
7	0.01	0.07	−0.06
7‘	0.01	0.08	−0.07
8	0.86	0.90	−0.04

2-(Trimethylsilyl)ethyl (4*R*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-4-((*S*)-3-((6-methoxyhex-2-yn-1-yl)oxy)-5-methylhex-1-yn-1-yl)-2,2-dimethyloxazolidine-3-carboxylate (21)



21

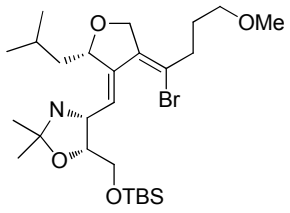
$C_{32}H_{59}NO_6Si_2$, M = 610.0 g/mol

To a solution of alcohol **20c** (950 mg, 1.67 mmol, 1.0 eq) in dry toluene (42 mL) PPTS (41 mg, 0.167 mmol, 0.1 eq) and 2-methoxypropene (6.3 mL, 67.3 mmol, 40 eq) were added and the mixture stirred at 110 °C overnight.

The next day, the reaction was quenched by addition of $NaHCO_3$ (40 mL). The organic layer was separated and the aqueous was extracted with Et_2O (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, petroleum ether/EtOAc, 93:7) yielded **21** (961 mg, 1.58 mmol, 95%) as a slightly yellow oil.

R_f = 0.25 (petroleum ether/EtOAc = 93/7); $[\alpha]_D^{20}$ = –105.4 (*c* = 1.0 in CH_2Cl_2); **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ [ppm] = 0.06 (s, 9H), 0.09 (s, 3H), 0.09 (s, 3H), 0.89-0.92 (m, 3H), 0.91 (s, 9H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.99-1.06 (m, 2H), 1.48-1.55 (m, 1H), 1.51 (s, 3H), 1.59 (s, 3H), 1.61-1.67 (m, 1H), 1.73 (tt, *J* = 7.1, 6.2 Hz, 2H), 1.80-1.89 (m, 1H), 2.28 (tt, *J* = 7.1, 2.2 Hz, 2H), 3.29 (s, 3H), 3.41 (t, *J* = 6.2 Hz, 2H), 3.84-3.91 (m, 2H), 4.09 (td, *J* = 6.1, 5.1 Hz, 1H), 4.14-4.22 (m, 3H), 4.26 (dt, *J* = 15.3, 2.2 Hz, 1H), 4.34 (t, *J* = 6.8 Hz, 1H), 4.61-4.72 (m, 1H); **^{13}C-NMR** (125 MHz, CD_2Cl_2): δ [ppm] = -5.1, -5.0, -1.3, 16.0, 18.4, 18.7, 22.7*, 22.8, 22.9, 22.9*, 24.8, 25.3, 25.8*, 26.2, 26.8, 27.9*, 29.3, 45.0, 51.5, 52.0*, 56.6, 58.9, 63.1, 63.8, 64.2*, 67.0, 71.6, 76.4, 77.0*, 77.3, 82.3*, 82.4, 83.8*, 84.0, 86.7, 95.0, 152.6 (*Note: extra signals due to amide resonance, distinguishable signals of the minor rotamer are denoted with an asterisk*); **HRMS** (ESI+): calculated for $C_{32}H_{59}NNaO_6Si_2^+$ $[M+Na]^+$: 632.3773, found: 632.3776.

2-(Trimethylsilyl)ethyl (4*R*,5*R*)-4-((*Z*)-((*S*,*E*)-4-(1-bromo-4-methoxybutylidene)-2-*iso*butyldihydrofuran-3(2*H*)-ylidene)methyl)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,2-dimethyloxazolidine-3-carboxylate (23)



23

$C_{32}H_{60}BrNO_6Si_2$, M = 690.9 g/mol

Zirconocene dichloride was heated under vacuum until sublimation started, then the heating was stopped and it was stored under vacuum overnight. Diyne **21** was co-evaporated with dry toluene (2 mL) under argon three times and it was stored under vacuum overnight. NBS was recrystallized from $CHCl_3$ prior to use.

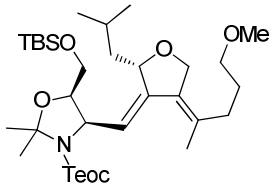
Zirconocene dichloride (98.6 mg, 0.337 mmol, 1.5 eq) was dissolved in dry THF (1.4 mL) and the mixture was cooled to -78 °C. Afterwards, *n*-BuLi (2.5 M in hexanes, 270 µL, 0.675 mmol, 3.0 eq) was added dropwise and the resulting light green solution was stirred at -78 °C for 30 minutes. Afterwards a solution of diyne (137 mg, 0.225 mmol, 1.0 eq) in THF (3.6 mL) was added. The mixture was allowed to warm up to room temperature and was stirred for 80 minutes. The resulting dark red solution was cooled again to -78 °C and NBS (80.1 mg, 0.450 mmol, 2.0 eq) was added in one portion (NOTE: *addition in one portion is crucial for regioselectivity!*). The mixture was stirred at -78 °C for 2 hours before further NBS (80.1 mg, 0.450 mmol, 2.0 eq) was added in one portion. After stirring for further 90 minutes at -78 °C the reaction mixture was quenched by addition of a saturated solution of NH_4Cl (4 mL). Afterwards the mixture was filtered and extracted with Et_2O (3 × 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, petroleum ether/EtOAc, 95:5) yielded **23** (107 mg, 0.155 mmol, 69%, regioisomeric ratio >20:1) as a slightly yellow oil.

R_f = 0.27 (petroleum ether/EtOAc = 93/7); $[\alpha]_D^{20}$ = –56.9 (*c* = 1.0 in CH_2Cl_2); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 0.04 (s, 9H), 0.06 (s, 3H), 0.06 (s, 3H), 0.90 (s, 9H), 0.93-1.04 (m, 9H), 1.45-1.56 (m, 1H), 1.60 (s, 3H), 1.69 (s, 3H), 1.79-1.94 (m, 3H), 2.43-2.57 (m, 2H), 3.33 (s, 3H), 3.34-3.39 (m, 2H), 3.65 (dd, *J* = 10.0, 8.5 Hz, 1H), 3.77 (dd, *J* =

10.0, 4.6 Hz, 1H), 4.12-4.25 (m, 3H), 4.45-4.52 (m, 3H), 4.92-4.98 (m, 1H), 6.44-6.58 (m, 1H); **HRMS** (ESI+): calculated for $C_{32}H_{60}BrNNaO_6Si_2^+$ $[M+Na]^+$: 712.3035, found: 712.3033.

NOTE: no ^{13}C-NMR-spectrum could be obtained for this compound due to line broadening caused by amide resonances.

2-(Trimethylsilyl)ethyl (4*R*,5*R*)-5-(((*tert*-butyldimethylsilyl)oxy)methyl)-4-((*Z*)-((*S*,*Z*)-2-*iso*butyl-4-(5-methoxypentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)methyl)-2,2-dimethyloxazolidine-3-carboxylate (23a)



23a

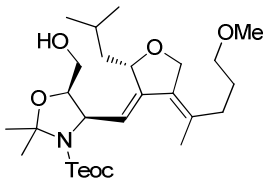
$C_{33}H_{63}NO_6Si_2$, M = 626.0 g/mol

To a solution of **23** (107 mg, 0.154 mmol, 1.0 eq) in dry THF (0.8 mL) at room temperature $Pd(P^tBu_3)_2$ (stored and weighed out in a glove box, 7.9 mg, 15.4 µmol, 0.1 eq) was added followed by slow addition of Me_2Zn (1.2 M in toluene, 1.0 mL, 1.2 mmol, 7.8 eq). The resulting yellow solution was stirred at room temperature for 18 h. Afterwards the reaction was quenched by slow addition of H_2O (1 mL) before a saturated solution of NH_4Cl (1 mL) was added dropwise. Phases were separated and the aqueous layer was extracted with Et_2O (3 × 3 mL). The organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the obtained crude product was performed by column chromatography (SiO_2, petroleum ether/EtOAc, 95:5) to give **23a** (74.6 mg, 0.119 mmol, 78%) as a colorless oil.

R_f = 0.26 (petroleum ether/EtOAc = 93/7); $[\alpha]_D^{20}$ = –131.3 (*c* = 0.5 in CH_2Cl_2); **^{1}H-NMR** (500 MHz, $CDCl_3$): δ [ppm] = 0.02 (s, 9H), 0.06 (s, 3H), 0.06 (s, 3H), 0.89 (s, 9H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.99-1.04 (m, 2H), 1.36-1.46 (m, 1H), 1.46-1.55 (m, 1H), 1.59 (s, 3H), 1.66 (s, 3H), 1.65-1.77 (m, 2H), 1.80-1.87 (m, 1H), 1.86 (s, 3H), 1.97-2.12 (m, 2H), 3.30-3.38 (m, 2H), 3.33 (s, 3H), 3.67 (dd, *J* = 10.2, 7.7 Hz, 1H), 3.74 (dd, *J* = 10.2, 4.9 Hz, 1H), 4.11-4.20 (m, 3H), 4.41 (m, 1H), 4.44-4.57 (m, 2H), 4.83

(d, *J* = 10.9 Hz, 1H), 5.31 (d, *J* = 9.9 Hz, 1H); **^{13}C-NMR** (125 MHz, $CDCl_3$): δ [ppm] = -5.6, -5.6, -1.6, 17.8*, 18.4, 18.8, 19.7, 21.4, 24.0 (2C), 24.7, 25.1*, 26.0, 27.3, 27.4, 28.3*, 29.7*, 33.9, 41.1, 41.9*, 58.5, 58.5, 59.0*, 61.7, 62.9, 63.2*, 68.9, 71.9, 77.7*, 78.1, 78.4, 79.1*, 93.8, 118.3*, 118.8, 130.8, 130.9, 143.5, 144.1*, 152.6 (*Note: extra signals due to amide resonance, distinguishable signals of the minor rotamer are denoted with an asterisk*); **HRMS** (ESI+): calculated for $C_{33}H_{63}NNaO_6Si_2^+$ $[M+Na]^+$: 648.4086, found: 648.4094.

(4*R*,5*R*)-2-(Trimethylsilyl)ethyl 5-(hydroxymethyl)-4-((*Z*)-((*S*,*Z*)-2-*iso*butyl-4-(5-methoxy-pentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)methyl)-2,2-dimethyloxazolidine-3-carboxylate (10)



10

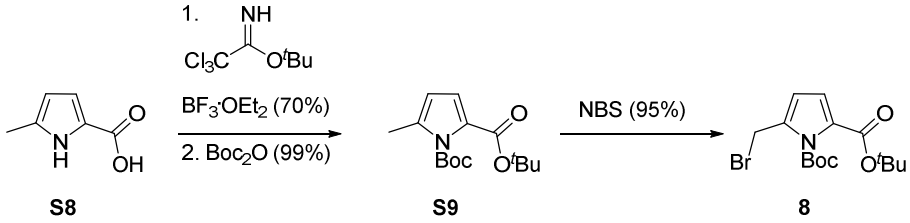
$C_{27}H_{49}NO_6Si$, M = 511.8 g/mol

23a (51.7 mg, 82.6 µmol, 1.0 eq) was dissolved in dry MeOH (1.6 mL). After cooling to 0 °C acetyl chloride (1:10 *v*/*v* in CH_2Cl_2, 32 µL, 40.7 µmol, 0.5 eq) was added dropwise. After complete addition the reaction mixture was warmed to room temperature and stirred for 45 minutes. The reaction mixture was diluted with toluene (5 mL) and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO_2, cyclohexane/EtOAc, 2:1) yielding **10** (39.5 mg, 77.2 µmol, 93%) as a white foam.
R_f (cyclohexane/EtOAc = 1/1) = 0.51; $[\alpha]_D^{20}$ = -151.2 (c = 1.0, $CHCl_3$); **^{1}H-NMR** (500 MHz, 339 K, CD_3CN): δ [ppm] = 0.01-0.07 (m, 9H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.99-1.03 (m, 2H), 1.42 (ddd, *J* = 14.3, 11.0, 4.4 Hz, 1H), 1.55 (s, 3H), 1.64 (s, 3H), 1.65-1.72 (m, 3H), 1.78-1.86 (m, 1H), 1.86-1.89 (m, 3H), 2.01-2.12 (m, 2H), 3.28 (s, 3H), 3.33 (t, *J* = 6.3 Hz, 2H), 3.52-3.61 (m, 2H), 4.10-4.19 (m, 2H), 4.22 (dt, *J* = 6.4, 5.4 Hz, 1H), 4.34-4.47 (m, 2H), 4.49 (dd, *J* = 10.0, 5.5 Hz, 1H), 4.78 (ddd, *J* = 10.8, 2.4, 1.5 Hz, 1H), 5.37 (d, *J* = 10.3 Hz, 1H); **^{13}C-NMR** (125 MHz, 339 K, CD_3CN) δ [ppm] = -1.5, 19.5, 20.0, 21.8, 24.2, 24.4, 25.8, 27.8, 28.1, 34.6, 42.2, 58.7,

59.2, 61.8, 63.4, 69.3, 72.5, 79.1, 79.4, 94.5, 120.5, 131.5, 132.4, 144.1, 153.4; **HRMS** (ESI+): calculated for $C_{27}H_{49}NNaO_6Si$ $[M+Na]^+$: 534.3221, found 534.3217.

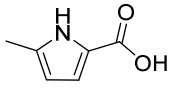
3.3 Synthesis of Pyrrole 8

The synthesis of **8**, started from pyrrole **S8** (Scheme S 4)[21,22] and involved conversion of the acid function to the corresponding *tert*-butyl-ester and Boc-protection of the nitrogen, before bromination of the sidechain was achieved by means of NBS.



Scheme S 4: Synthesis of pyrrole **8**.

5-Methyl-1*H*-pyrrole-2-carboxylic acid (S8)



S8

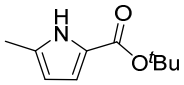
$C_6H_7NO_2$, M = 125.1 g/mol

To a solution of ethyl 5-methyl-1*H*-pyrrole-2-carboxylate (2.7 g, 17.6 mmol, 1.0 eq) in MeOH (120 mL) were added H_2O (70 mL) and NaOH (1 M in H_2O, 50.0 mL, 50.0 mmol, 2.8 eq) and the solution was stirred at 50 °C for 24 hours. The solution was concentrated to ca. 100 mL *in vacuo*, saturated with NH_4Cl (ca. 37 g) and acidified with solid $KHSO_4$ to pH = 3. The aqueous phase was extracted with EtOAc (3 × 100 mL) and the combined organic extracts were dried over $MgSO_4$. The solvent was removed *in vacuo* and **S8** was yielded (2.15 g, 17.2 mmol, 98 %) as a white solid.

[21] Olson, S.; Slossberg, L. H. *Tetrahedron Lett.* **2003**, 44, 61.
[22] Ashkenazi, T.; Pinkert, D.; Nudelman, A.; Widberg, A.; Wexler, B.; Wittenbach, V.; Flint, D. *Pest. Manag. Sci.* **2007**, *63*, 974.

R_f = 0.12 (cyclohexane/EtOAc = 2/1); **^{1}H-NMR** (300 MHz, $CDCl_3$): δ [ppm] = 2.33 (s, 3H), 5.97-6.04 (m, 1H), 6.94-7.01 (m, 1H), 9.14 (br. s., 1H); **^{13}C-NMR** (75 MHz, $CDCl_3$) δ [ppm] = 13.4, 109.9, 118.6, 120.3, 135.5, 165.8; **HRMS** (ESI-): calculated for $C_6H_6NO_2$ $[M-H]^+$: 124.0404, found 124.0402.

tert-Butyl 5-methyl-1_H_-pyrrole-2-carboxylate (S8a)



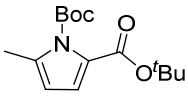
S8a

$C_{10}H_{15}NO_2$, M = 181.2 g/mol

To a solution of **S8** (2.15 g, 17.2 mmol, 1.0 eq) in dry CH_2Cl_2 (35 mL) was added *tert*-butyl 2,2,2-trichloroacetimidate (11.5 g, 52.6 mmol, 3.0 eq) in dry cyclohexane (35 mL). The resulting mixture was cooled to 0 °C and boron trifluoride etherate (48% BF_3, 350 µL, cat.) was added dropwise. Afterwards the reaction mixture was warmed to room temperature and stirred overnight. The reaction was quenched by the addition of solid $NaHCO_3$ (4.5 g, 53.5 mmol, 3.1 eq), filtered and finally the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, cyclohexane/EtOAc, 9:1) yielded **S8a** (2.18 g, 12.0 mmol, 70%) as a white solid.

R_f = 0.25 (cyclohexane/EtOAc = 9/1); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 1.55 (s, 9H), 2.30 (s, 3H), 5.89-5.94 (m, 1H), 6.71-6.76 (m, 1H), 8.88-9.22 (m, 1H); **^{13}C-NMR** (100 MHz, $CDCl_3$) δ [ppm] = 13.4, 28.6, 80.5, 108.7, 115.7, 123.0, 133.2, 160.9; **HRMS** (ESI+): calculated for $C_{10}H_{15}NO_2$ $[M]^+$: 181.1103, found 181.1104.

Di-_tert_-butyl 5-methyl-1_H_-pyrrole-1,2-dicarboxylate (S9)



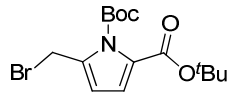
S9

$C_{15}H_{23}NO_4$, M = 281.3 g/mol

To a solution of **S8a** (906 mg, 5.00 mmol, 1.0 eq) in dry CH_2Cl_2 (25 mL) was added NEt_3 (7.0 mL, 50.0 mmol, 10.0 eq), di-*tert*-butyl dicarbonate (8.70 g, 40.0 mmol, 8.0 eq) and DMAP (305 mg, 2.50 mmol, 0.5 eq) and the resulting mixture was stirred at room temperature overnight. The reaction was quenched by the addition of H_2O (30 mL) and stirring was continued for additional 30 minutes. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO_2, cyclohexane/EtOAc, 30:1) yielding **S9** (1.39 g, 4.95 mmol, 99%) as a colorless oil.

$\mathbf{R_f}$ = 0.53 (cyclohexane/EtOAc = 9/1); [4-anisaldehyde, color: yellow]; **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 1.54 (s, 9H), 1.58 (s, 9H), 2.34 (s, 3H), 5.83-5.87 (m, 1H), 6.66 (d, *J* = 3.5 Hz, 1H); **^{13}C-NMR** (75 MHz, $CDCl_3$) δ [ppm] = 14.2, 27.7, 28.4, 80.7, 84.6, 109.4, 118.8, 126.4, 136.7, 149.8, 160.0; **HRMS** (EI+): calculated for $C_{15}H_{23}NO_4$ $[M]^+$: 281.1627, found 281.1630.

Di-*tert*-butyl 5-(bromomethyl)-1*H*-pyrrole-1,2-dicarboxylate (8)



8

$C_{15}H_{22}BrNO_4$, M = 360.2 g/mol

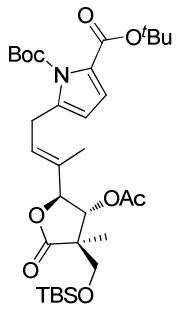
A solution of **S9** (272 mg, 964 μmol, 1.0 eq) in CCl_4 (10 mL) was irradiated with a 300 W daylight-lamp in approximately ten centimeter distance to the reaction vessel. After the solution started refluxing, AIBN (10 mg, cat.) and NBS (209 mg, 1.17 mmol, 1.2 eq) were added in one portion and the solution was irradiated to reflux for additional 2 hours. After cooling to room temperature the solution was filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (SiO_2, cyclohexane/EtOAc, 30:1) yielding **8** (330 mg, 916 μmol, 95%) as a white solid.

$\mathbf{R_f}$ = 0.53 (cyclohexane/EtOAc = 9/1); [4-anisaldehyde, color: green-grey]; **^{1}H-NMR** (400 MHz, CD_2Cl_2): δ [ppm] = 1.54 (s, 9H) 1.61 (s, 9H) 4.71 (s, 2H) 6.23 (d, *J* = 3.6 Hz,

1H) 6.63 (d, *J* = 3.6 Hz, 1H); **^{13}C-NMR** (100 MHz, CD_2Cl_2) δ [ppm] = 24.7, 27.8, 28.5, 81.9, 86.2, 113.0, 117.8, 129.6, 135.1, 149.3, 160.0; **HRMS** (EI+): calculated for $C_{15}H_{22}BrNO_4$ $[M]^+$: 359.0732, found 359.0734.

3.4 Completion of the Total Synthesis

Di-*tert*-butyl 5-((*E*)-3-((2*S*,3*R*,4*R*)-3-acetoxy-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-4-methyl-5-oxotetrahydrofuran-2-yl)but-2-en-1-yl)-1*H*-pyrrole-1,2-dicarboxylate (7a)



7a

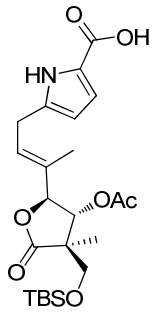
$C_{32}H_{51}NO_9Si$, M = 621.8 g/mol

To a mixture of **7** (54.0 mg, 115 µmol, 1.0 eq), $Pd(P^tBu_3)_2$ (14.7 mg, 28.8 µmol, 0.25 eq) and Cs_2CO_3 (60.1 mg, 184 µmol, 1.6 eq) was added a solution of **8** (82.8 mg, 330 µmol, 2.87 eq) in a THF-H_2O mixture (11:1, 770 µmL). The reaction mixture was stirred at room temperature for 16 hours before it was quenched with saturated solution of NH_4Cl (2 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 3 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification of the obtained crude product was performed by column chromatography (SiO_2, cyclohexane/EtOAc, 97:3 → 6:1) to give **7a** (51.1 mg, 82.1 µmol, 71 %) as a colorless liquid.

R_f = 0.26 (cyclohexane/EtOAc = 9/1); $[\alpha]_D^{20}$ = –14.5 (c = 1.00, CH_3Cl); **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 6.66 (d, *J* = 3.6 Hz, 1H), 5.83 (d, *J* = 3.6 Hz, 1H), 5.73 (d, *J* = 7.9 Hz, 1H), 5.71-5.76 (m, 1H), 4.57 (d, *J* = 7.9 Hz, 1H), 3.83 (d, *J* = 9.4 Hz, 1H), 3.60 (d, *J* = 9.4 Hz, 1H), 3.54 (dd, *J* = 17.1 Hz, *J* = 7.1 Hz, 1H), 3.48 (dd, *J* = 17.1 Hz, *J* =

7.1 Hz, 1H), 2.08 (s, 3H), 1.71 (s, 3H), 1.57 (s, 9H), 1.57 (s, 9H), 1.06 (s, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); **^{13}C-NMR** (100 MHz, $CDCl_3$): δ [ppm] = 177.2, 169.7, 159.8, 149.6, 138.1, 132.4, 127.1, 126.8, 118.4, 108.7, 84.8, 83.9, 80.7, 72.5, 65.7, 49.8, 28.4, 27.6, 26.5, 25.8, 20.6, 18.3, 13.8, 11.1, -5.6, -5.6; **HRMS** (ESI+) calculated for $C_{32}H_{51}NO_9SiNa^+$ $[M+Na]^+$: 644,3225, found: 644,3223.

5-((*E*)-3-((2*S*,3*R*,4*R*)-3-Acetoxy-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-4-methyl-5-oxotetrahydrofuran-2-yl)but-2-en-1-yl)-1*H*-pyrrole-2-carboxylic acid (24)



24

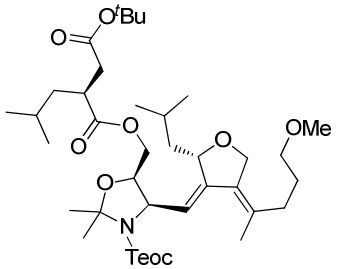
$C_{23}H_{35}NO_7Si$, M = 465.6 g/mol

To a mixture of ester **7a** (88.0 mg, 0.142 mmol, 1.0 eq) and 2,6-lutidine (330 µL, 2.84 mmol, 20 eq) in dry CH_2Cl_2 (1.4 mL) at 0 °C TMSOTf (256 µL, 1.42 mmol, 10 eq) was added. After 1 hour the mixture was allowed to warm up to room temperature and it was stirred over night. It was diluted with EtOAc (4 mL) and quenched by addition of a saturated solution of NH_4Cl (4 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 4 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by preparative TLC (SiO_2, petroleum ether/EtOAc/HOAc, 5:5:1) followed by co-evaporation with toluene to remove residual acetic acid yielded **24** (60.1 mg, 0.129 mmol, 91%).

R_f = 0.23 (cyclohexane/EtOAc/HOAc = 10/10/1); $[\alpha]_D^{20}$ = –9.3 (c = 0.3, CH_3Cl); **^{1}H-NMR** (500 MHz, CD_3OD) δ [ppm] = 6.77 (d, *J* = 3.7 Hz, 1H), 5.90 (d, *J* = 3.7 Hz, 1H), 5.84-5.77 (m, 2H), 4.72 (d, *J* = 8.3 Hz, 1H), 3.81 (d, *J* = 9.6 Hz, 1H), 3.59 (d, *J* = 9.6 Hz, 1H), 3.43 (d, *J* = 7.2 Hz, 2H), 2.06 (s, 3H), 1.76 (s, 2H), 1.10 (s, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). **^{13}C-NMR** (125 MHz, CD_3OD) δ [ppm] = 179.1, 171.6, 164.5,

137.5, 132.7, 129.3, 123.1, 117.4, 108.7, 85.2, 73.0, 66.4, 51.2, 27.0, 26.3, 20.4, 19.1, 13.8, 11.3, -5.5, -5.6. **HRMS** (ESI-): calculated for $C_{23}H_{34}NO_7Si^+$ $[M-H]^+$: 464.2110, found: 464.2114.

(*S*)-4-*tert*-Butyl 1-(((4*R*,5*R*)-4-((*Z*)-((*S*,*Z*)-2-isobutyl-4-(5-methoxypentan-2-ylidene)-dihydrofuran-3(2*H*)-ylidene)methyl)-2,2-dimethyl-3-((2-(trimethylsilyl)ethoxy)-carbonyl)oxazolidin-5-yl)methyl) 2-*iso*butylsuccinate (9a)



9a

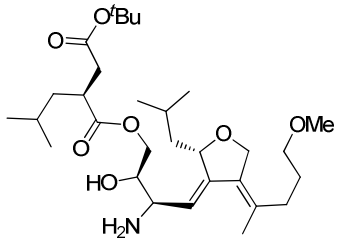
$C_{39}H_{69}NO_9Si$, M = 724.1 g/mol

To a solution of **9** (357 mg, 1.55 mmol, 2.2 eq) in dry CH_2Cl_2 (16 mL) was added NEt_3 (850 µL, 6.09 mmol, 8.8 eq), MNBA (530 mg, 1.10 mmol, 1.6 eq) and DMAP (140 mg, 1.15 mmol, 1.6 eq) and the resulting mixture was stirred at room temperature for 10 minutes. **10** (378 mg, 739 µmol, 1.0 eq) was dissolved in dry CH_2Cl_2 (21 mL), added to the reaction mixture and stirred for 60 minutes at room temperature. The reaction was quenched by the addition of saturated $NaHCO_3$ solution (30 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO_2, cyclohexane/EtOAc, 9:1) yielding **9a** (528 mg, 0.729 mmol, 99%) as a colorless oil.

R_f = 0.73 (cyclohexane/EtOAc = 2/1); $[\alpha]_D^{20}$ = -109.9 (c = 1.0, $CHCl_3$); **^{1}H-NMR** (500 MHz, 339 K, CD_3CN): δ [ppm] = 0.03-0.06 (m, 9H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.96-1.04 (m, 2H), 1.30-1.36 (m, 1H), 1.43 (s, 9H), 1.40-1.47 (m, 2H), 1.55 (s, 3H), 1.56-1.63 (m, 2H), 1.64 (s, 3H), 1.65-1.70 (m, 1H), 1.67-1.72 (m, 2H), 1.82-1.87 (m, 1H), 1.88 (m, 3H), 2.02-2.11 (m, 2H), 2.35 (dd, *J* = 16.2, 5.9 Hz, 1H), 2.54 (dd, *J* = 16.2, 8.4 Hz, 1H), 2.82 (tt, *J* = 8.3,

6.1 Hz, 1H), 3.28 (s, 3H), 3.33 (t, *J* = 6.3 Hz, 2H), 4.04-4.13 (m, 2H), 4.12-4.23 (m, 2H), 4.32-4.36 (m, 1H), 4.36-4.48 (m, 2H), 4.55 (dd, *J* = 10.1, 5.6 Hz, 1H), 4.76 (dt, *J* = 10.9, 2.0 Hz, 1H), 5.39 (d, *J* = 10.1 Hz, 1H); **^{13}C-NMR** (125 MHz, 339 K, CD_3CN) δ [ppm] = -1.2, 19.7, 20.2, 22.5, 22.8, 23.3, 24.5, 25.0, 26.3, 27.0, 28.4, 28.5, 28.7 (3C), 34.9, 39.0, 41.2, 42.2, 42.7, 58.9, 59.6, 63.9, 63.9, 69.7, 73.0, 76.5, 80.0, 81.6, 95.1, 120.4, 131.8, 133.1, 145.2, 153.7, 172.0, 175.9; **HRMS** (ESI+): $C_{39}H_{69}NNaO_9Si$ $[M+Na]^+$: 746.4634, found 746.4646.

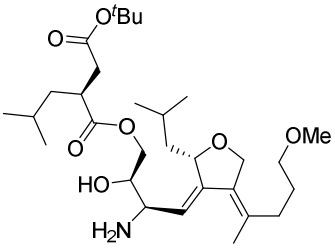
(*S*)-1-((2*R*,3*R*,*Z*)-3-amino-2-hydroxy-4-((*S*,*Z*)-2-isobutyl-4-(5-methoxypentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)butyl) 4-*tert*-butyl 2-*iso*butylsuccinate (25)



25

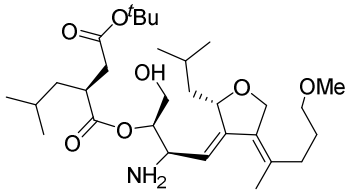
$C_{30}H_{53}NO_7$, M = 539.7 g/mol

TAS-F (90%, 230 mg, 0.75 mmol, 2.0 eq) was dissolved in dry MeCN (2.3 mL) and added dropwise to a solution of **9a** (268 mg, 0.37 mmol, 1.0 eq) in dry MeCN (3 mL) at 0 °C. The ice bath was removed and the reaction mixture was slowly heated to 45 °C over 30 minutes. After stirring for 2 hours at this temperature the reaction was quenched by the addition of saturated NH_4Cl solution (25 mL) and diethyl ether (20 mL). The organic phase was separated and the aqueous phase was extracted with Et_2O (2 × 25 mL) and EtOAc (25 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was filtered over a small pad of silica, eluating with cyclohexane/EtOAc/*i*$PrNH_2$ 85/15/3. The solvent was removed *in vacuo* yielding **25** (200 mg, 0.37 mmol, 100%) as yellow oil which was directly used without further purification. NMR analysis showed a purity of about 80%. (NOTE: slow column chromatography or purification by preparative TLC gave rise to small quantities of the more polar byproduct **S11** by migration of the acyl group to the amine).



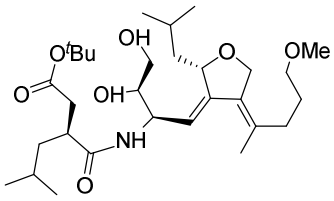
80%

25



20%

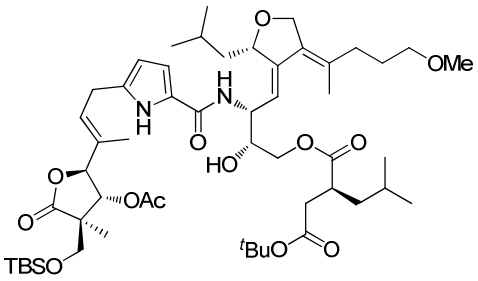
S10



S11

$\mathbf{R_f}$ (cyclohexane/EtOAc/*i*PrNH$_2$, 85/15/3) = 0.26.

1-((2*R*,3*R*,*Z*)-3-(5-((*E*)-3-((2*S*,3*R*,4*R*)-3-Acetoxy-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-4-methyl-5-oxotetrahydrofuran-2-yl)but-2-en-1-yl)-1*H*-pyrrole-2-carboxamido)-2-hydroxy-4-((*S*,*Z*)-2-isobutyl-4-(5-methoxypentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)butyl) 4-(*tert*-butyl) (*S*)-2-isobutylsuccinate (24a)



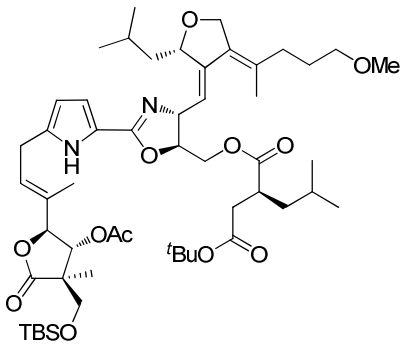
24a

$C_{53}H_{86}N_2O_{13}$, M = 987.4 g/mol

To a solution of **25** (40.2 mg, 74.5 µmol, 1.0 eq) and crude acid **24** (max. 96.8 µmol, 1.3 eq) in dry MeCN (2.6 mL) at room temperature NEt_3 (31 µL, 0.224 mmol, 3.0 eq) and HATU (56.7 mg, 0.149 mmol, 2.0 eq) were added. The resulting solution was stirred for 2 hours at 40 °C before it was quenched by addition of a saturated solution of $NaHCO_3$ (4 mL). The layers were separated and it was extracted with EtOAc (3 × 4 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, petroleum ether/EtOAc, 65:35) gave **24a** (51.5 mg, 52.1 µmol, 70%) as a colorless gum.

$\mathbf{R_f}$ = 0.21 (petroleum ether/EtOAc = 70/30); $[\alpha]_D^{20}$ = –128.4 (*c* = 0.5 in CH_2Cl_2); **^{1}H-NMR** (400 MHz, CD_2Cl_2): δ [ppm] = 0.06 (s, 3H), 0.08 (s, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.91 (d, *J* = 6.2 Hz, 3H), 0.93 (d, *J* = 6.2 Hz, 3H), 1.08 (s, 3H), 1.22-1.31 (m, 2H), 1.41 (s, 9H), 1.42-1.45 (m, 1H), 1.48-1.60 (m, 2H), 1.62-1.72 (m, 2H), 1.75 (s, 3H), 1.77-1.81 (m, 1H), 1.92 (s, 3H), 1.99-2.06 (m, 2H), 2.07 (s, 3H), 2.39 (dd, *J* = 16.4, 4.4 Hz, 1H), 2.58 (dd, *J* = 16.4, 10.0 Hz, 1H), 2.73-2.83 (m, 1H), 3.29 (s, 3H), 3.32 (t, *J* = 6.2 Hz, 2H), 3.40 (dd, *J* = 16.4, 6.7 Hz, 1H), 3.46 (dd, *J* = 16.4, 7.7 Hz, 1H), 3.56 (d, *J* = 9.6 Hz, 1H), 3.81 (d, *J* = 9.6 Hz, 1H), 3.96-4.06 (m, 2H), 4.24-4.29 (m, 1H), 4.38-4.44 (m, 1H), 4.44-4.50 (m, 1H), 4.56 (d, *J* = 8.1 Hz, 1H), 4.68-4.74 (m, 1H), 4.84 (dt, *J* = 10.6, 1.8 Hz, 1H), 5.67-5.76 (m, 3H), 5.92 (t, *J* = 3.1 Hz, 1H), 6.35 (d, *J* = 7.8 Hz, 1H), 6.50-6.54 (m, 1H), 9.14 (br. s, 1H); **^{13}C-NMR** (100 MHz, CD_2Cl_2): δ [ppm] = -5.4, -5.4, 11.4, 14.1, 18.7, 20.4, 20.9, 21.9, 22.5, 22.9, 24.1, 25.6, 26.1, 26.3, 26.9, 27.9, 28.3, 34.6, 38.6, 40.4, 41.7, 43.1, 50.1, 52.6, 58.8, 66.0, 66.3, 69.7, 72.5, 72.5, 72.7, 80.0, 81.8, 84.5, 108.2, 110.7, 118.1, 125.3, 127.7, 131.0, 132.9, 133.3, 134.9, 146.4, 161.0, 170.8, 172.6, 175.8, 177.3; **HRMS** (ESI+): calculated for $C_{53}H_{86}N_2O_{13}Si^+$ $[M+Na]^+$: 1009.5791, found: 1009.5788.

1-(((4*R*,5*S*)-2-(5-((*E*)-3-((2*S*,3*R*,4*R*)-3-Acetoxy-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-4-methyl-5-oxotetrahydrofuran-2-yl)but-2-en-1-yl)-1*H*-pyrrol-2-yl)-4-((*Z*)-((*S*,*Z*)-2-isobutyl-4-(5-methoxypentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)methyl)-4,5-dihydrooxazol-5-yl)methyl) 4-(*tert*-butyl) (*S*)-2-isobutylsuccinate (26)



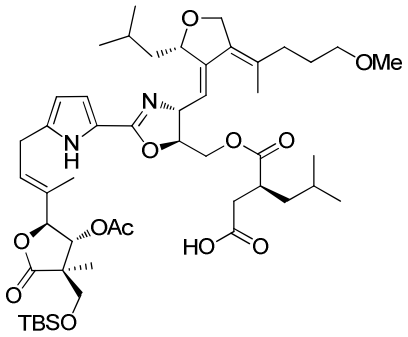
26

$C_{53}H_{84}N_2O_{12}Si$, M = 969.3 g/mol

To a solution of **24a** (94.0 mg, 95.2 µmol, 1.0 eq) in dry CH_2Cl_2 (1.8 mL) at -78 °C a solution of DAST (19 µL, 0.143 mmol, 1.5 eq) in dry CH_2Cl_2 (0.57 mL) was added. The resulting solution was stirred for 1 hour at the indicated temperature before further DAST (10 µL, 75.3 µmol, 0.8 eq) in CH_2Cl_2 (0.30 mL) was added. After an additional hour at -78 °C anhydrous K_2CO_3 (19.7 mg, 0.143 mmol, 1.5 eq) was added. The mixture was allowed to warm up to -10 °C before it was quenched by addition of a saturated solution of $NaHCO_3$ (2 mL). The layers were separated and it was extracted with Et_2O (3 × 3 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by HPLC (System C, column: Daicel Chiralpak IB, 5 µm; 250 × 20 mm, *n*-heptane/*i*PrOH = 98:2, flow rate 18 mL/min, total running time: 22 min, detection at 280 nm) gave **26** (74.4 mg, 76.8 µmol, 81%) as a colorless gum.

R_f = 0.30 (petroleum ether/EtOAc = 70/30); $[\alpha]_D^{20}$ = –42.5 (*c* = 0.5 in CH_2Cl_2); **^{1}H-NMR** (400 MHz, CD_2Cl_2): δ [ppm] = 0.06 (s, 3H), 0.07 (s, 3H), 0.81 (d, *J* = 6.3 Hz, 3H), 0.84 (d, *J* = 6.3 Hz, 3H), 0.88 (s, 9H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 1.07 (s, 3H), 1.18-1.26 (m, 1H), 1.35 (ddd, *J* = 14.1, 9.4, 2.8 Hz, 1H), 1.41 (s, 9H), 1.46-1.60 (m, 3H), 1.62-1.70 (m, 2H), 1.75 (s, 3H), 1.81-1.88 (m, 1H), 1.90 (s, 3H), 1.97-2.06 (m, 2H), 2.07 (s, 3H), 2.32 (dd, *J* = 16.3, 5.4 Hz, 1H), 2.54 (dd, *J* = 16.3, 9.0 Hz, 1H), 2.78-2.87 (m, 1H), 3.29 (s, 3H), 3.31 (t, *J* = 6.2 Hz, 2H), 3.41 (dd, *J* = 16.6, 6.6 Hz, 1H), 3.46 (dd, *J* = 16.6, 7.4 Hz, 1H), 3.56 (d, *J* = 9.5 Hz, 1H), 3.81 (d, *J* = 9.5 Hz, 1H), 4.17 (dd, *J* = 12.0, 5.4 Hz, 1H), 4.38-4.45 (m, 2H), 4.45-4.55 (m, 3H), 4.56 (d, *J* = 7.9 Hz, 1H), 4.89 (dt, *J* = 10.7, 2.0 Hz, 1H), 5.46 (d, *J* = 9.3 Hz, 1H), 5.69-5.72 (m, 1H), 5.72 (d, *J* = 7.9 Hz, 1H), 5.94 (d, *J* = 3.5 Hz, 1H), 6.60 (d, *J* = 3.5 Hz, 1H), 9.07 (br. s, 1H); **^{13}C-NMR** (100 MHz, CD_2Cl_2): δ [ppm] = -5.4, -5.4, 11.4, 14.1, 18.7, 20.4, 21.0, 22.0, 22.4, 22.9, 24.1, 25.5, 26.1, 26.3, 26.9, 27.9, 28.3, 34.7, 38.3, 40.2, 41.7, 44.0, 50.2, 58.8, 64.7, 66.0, 68.6, 69.8, 72.4, 72.6, 79.8, 81.1, 83.6, 84.4, 108.3, 113.9, 119.6, 122.4, 127.7, 130.7, 133.1 (2C), 135.2, 144.7, 158.3, 170.6, 171.4, 175.5, 177.3; **HRMS** (ESI+): calculated for $C_{53}H_{84}N_2NaO_{12}Si^+$ $[M+Na]^+$: 991.5686, found: 991.5686.

(*S*)-3-((((4*R*,5*S*)-2-(5-((*E*)-3-((2*S*,3*R*,4*R*)-3-Acetoxy-4-(((*tert*-butyldimethylsilyl)oxy)-methyl)-4-methyl-5-oxotetrahydrofuran-2-yl)but-2-en-1-yl)-1*H*-pyrrol-2-yl)-4-((*Z*)-((*S*,*Z*)-2-isobutyl-4-(5-methoxypentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)methyl)-4,5-dihydrooxazol-5-yl)methoxy)carbonyl)-5-methylhexanoic acid (26a)



26a

$C_{49}H_{76}N_2O_{12}Si$, M = 913.2 g/mol

To a solution of **26** (27.8 mg, 28.7 µmol, 1.0 eq) and 2,6-lutidine (97 µL, 0.831 mmol, 30 eq) in dry CH_2Cl_2 (640 µL) at 0 °C TMSOTf (78 µL, 0.431 mmol, 15 eq) was added. The resulting solution was stirred for 30 minutes at 0 °C before it was allowed to warm up to room temperature. After further 30 minutes the reaction was quenched by addition of a saturated solution of NH_4Cl (1 mL). The layers were separated and the aqueous layer was extracted with EtOAc (4 × 2 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo* to give crude **26a** as a yellow oil that was used without further purification.

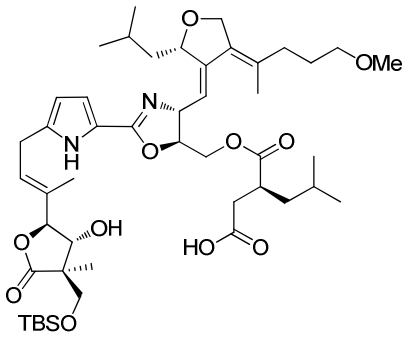
An analytical sample was purified by preparative TLC (SiO_2, cyclohexane/EtOAc/HOAc, 5:5:0.2) followed by co-evaporation with toluene to remove residual acetic acid.

R_f = 0.38 (petroleum ether/EtOAc/HOAc = 50/50/3); **^{1}H-NMR** (400 MHz, CD_3OD) δ [ppm] = 0.07 (d, *J* = 6.6 Hz, 6H), 0.74 (d, *J* = 6.4 Hz, 3H), 0.79 (d, *J* = 6.4 Hz, 3H), 0.89 (s, 9H), 0.98 (d, *J* = 6.7 Hz, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 1.09 (s, 3H), 1.18-1.26 (m, 1H), 1.31-1.36 (m, 1H), 1.36-1.43 (m, 1H), 1.44-1.53 (m, 2H), 1.55–1.64 (m, 1H), 1.65-1.75 (m, 2H), 1.76 (s, 3H), 1.83-1.91 (m, 1H), 1.95 (s, 3H), 2.07 (s, 3H), 2.04-2.22 (m, 2H), 2.38 (dd, *J* = 16.6, 5.3 Hz, 1H), 2.58 (dd, *J* = 16.7, 9.4 Hz, 1H), 2.82-2.91 (m, 1H), 3.32 (s, 3H), 3.35-3.38 (m, 2H), 3.44 (d, *J* = 7.3 Hz, 2H), 3.60 (d, *J* = 9.5 Hz, 1H), 3.81 (d, *J* = 9.5 Hz, 1H), 4.19 (dd, *J* = 12.4, 3.3 Hz, 1H), 4.42-4.56 (m, 2H), 4.56-4.60 (m,

1H), 4.66 (dd, *J* = 12.4, 3.3 Hz, 1H), 4.70-4.73 (m, 1H), 4.72-4.75 (m, 1H), 4.96-5.01 (m, 1H), 5.54 (d, *J* = 10.1 Hz, 1H), 5.79 (d, *J* = 8.2 Hz, 1H), 5.81 (d, *J* = 6.4 Hz, 1H), 5.93 (d, *J* = 3.6 Hz, 1H), 6.73 (d, *J* = 3.8 Hz, 1H); **^{13}C-NMR** (100 MHz, CD_3OD) δ [ppm] = -5.4, -5.3, 11.5, 14.0, 19.3, 20.4, 20.6, 22.3, 22.5, 23.3, 24.3, 26.3, 26.4, 27.1, 27.2, 28.5, 35.1, 38.2, 41.2, 42.7, 44.9, 51.3, 58.9, 64.5, 66.6, 68.3, 70.4, 73.0, 73.2, 80.7, 84.5, 85.3, 108.9, 115.9, 119.1, 123.4, 129.3, 131.4, 133.0, 134.1, 137.0, 145.4, 161.0, 171.6, 176.1, 177.1, 179.3;

HRMS (ESI+): calculated for $C_{49}H_{77}N_2NaO_{12}Si^+$ $[M+H]^+$: 913.5240, found: 913.5247.

(*S*)-3-((((4*R*,5*S*)-2-(5-((*E*)-3-((2*S*,3*R*,4*R*)-4-(((*tert*-Butyldimethylsilyl)oxy)methyl)-3-hydroxy-4-methyl-5-oxotetrahydrofuran-2-yl)but-2-en-1-yl)-1*H*-pyrrol-2-yl)-4-((*Z*)-((*S*,*Z*)-2-isobutyl-4-(5-methoxypentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)methyl)-4,5-dihydrooxazol-5-yl)methoxy)carbonyl)-5-methylhexanoic acid (27)



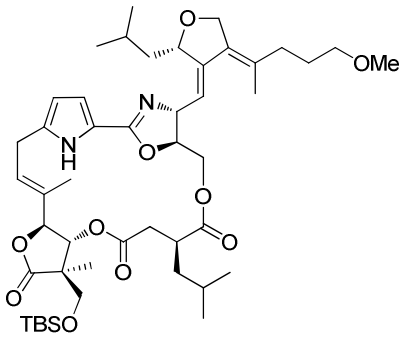
27

$C_{47}H_{74}N_2O_{11}Si$, M = 871.2 g/mol

Crude **26a** (max. 28.7 µmol) was dissolved in THF (1.7 mL) at room temperature. Then MeOH (1.7 mL) was added followed by 1 M aqueous K_2CO_3-solution (1.7 mL). The resulting mixture was stirred at room temperature for 2 hours before it was quenched by addition of a saturated solution of NH_4Cl (2 mL) and Et_2O (3 mL). The layers were separated and the aqueous layer was extracted with EtOAc (4 × 4 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by preparative TLC (SiO_2, petroleum ether/EtOAc/HOAc, 50:50:2) followed by co-evaporation with toluene to remove residual acetic acid gave **27** (21.0 mg, 24.1 µmol, 84% over 2 steps) as a colorless gum.

R_f = 0.32 (petroleum ether/EtOAc/HOAc = 50/50/3); $[\alpha]_D^{20}$ = –41.2 (*c* = 0.5 in CH_2Cl_2); **^{1}H-NMR** (500 MHz, CD_3OD): δ [ppm] = 0.07 (s, 3H), 0.08 (s, 3H), 0.73 (d, *J* = 6.5 Hz, 3H), 0.79 (d, *J* = 6.4 Hz, 3H), 0.88 (s, 9H), 0.98 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.5 Hz, 3H), 1.04 (s, 3H), 1.21 (ddd, *J* = 13.4, 7.9, 5.9 Hz, 1H), 1.40 (ddd, *J* = 14.3, 9.4, 2.7 Hz, 1H), 1.42-1.47 (m, 1H), 1.47-1.54 (m, 1H), 1.60 (ddd, *J* = 14.3, 10.5, 4.4 Hz, 1H), 1.64-1.74 (m, 2H), 1.75 (s, 3H), 1.83-1.90 (m, 1H), 1.92-1.97 (m, 3H), 2.02-2.09 (m, 1H), 2.09-2.16 (m, 1H), 2.38 (dd, *J* = 16.6, 5.2 Hz, 1H), 2.58 (dd, *J* = 16.6, 9.4 Hz, 1H), 2.82-2.90 (m, 1H), 3.32 (s, 3H), 3.36 (t, *J* = 6.2 Hz, 2H), 3.48 (d, *J* = 7.2 Hz, 2H), 3.51 (d, *J* = 9.9 Hz, 1H), 3.80 (d, *J* = 9.9 Hz, 1H), 4.19 (dd, *J* = 12.5, 3.3 Hz, 1H), 4.42-4.48 (m, 1H), 4.50 (d, *J* = 8.5 Hz, 1H), 4.52-4.57 (m, 1H), 4.57-4.59 (m, 1H), 4.58 (d, *J* = 8.5 Hz, 1H), 4.67 (dd, *J* = 12.5, 3.2 Hz, 1H), 4.73 (dd, *J* = 9.9, 7.4 Hz, 1H), 4.96-5.01 (m, 1H), 5.55 (d, *J* = 9.9 Hz, 1H), 5.81 (t, *J* = 7.2 Hz, 1H), 5.98 (d, *J* = 3.7 Hz, 1H), 6.72 (d, *J* = 3.7 Hz, 1H); **^{13}C NMR** (125 MHz, CD_3OD): δ [ppm] = -5.4, -5.3, 11.6, 13.4, 19.2, 20.4, 22.3, 22.6, 23.3, 24.3, 26.3, 26.4, 27.2, 27.2, 28.5, 35.1, 39.5, 41.6, 42.8, 45.0, 51.6, 58.9, 64.4, 65.7, 68.3, 70.4, 71.5, 73.0, 80.7, 84.6, 88.0, 109.0, 116.0, 119.1, 123.4, 128.4, 131.4, 133.7, 134.1, 137.3, 145.5, 161.1, 177.4, 177.5, 180.7; **HRMS** (ESI+): calculated for $C_{47}H_{73}N_2O_{11}Si^-$ [M-H$^+$]$^-$: 869.4989, found: 869.4994.

(1^4*R*,1^5*S*,6^2*S*,6^3*R*,6^4*R*,10*S*,*E*)-6^4-(((*tert*-Butyldimethylsilyl)oxy)methyl)-10-isobutyl-1^4-((Z)-((*S*,*Z*)-2-isobutyl-4-(5-methoxypentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)methyl)-6^4,5-dimethyl-1^4,1^5,6^2,6^3,6^4,6^5-hexahydro-2^1*H*-7,12-dioxa-1(2,5)-oxazola-2(2,5)-pyrrola-6(2,3)-furanacyclotridecaphan-4-ene-6^5,8,11-trione (28)



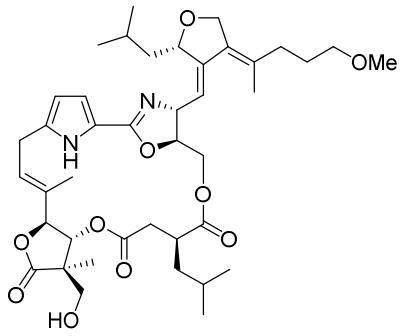
28

$C_{47}H_{72}N_2O_{10}Si$, M = 853.2 g/mol

2-Methyl-6-nitrobenzoic anhydride (15.8 mg 45.9 µmol, 5 eq), DMAP (9.0 mg, 73.4 µmol, 8 eq) and molecular sieves (4 Å) were dried under vacuum for 4 hours before CH_2Cl_2 (4.6 mL) was added. To this, a solution of **27** (8.0 mg, 9.18 µmol, 1.0 eq) in CH_2Cl_2 (4.6 mL) was added over a period of 16 hours by a syringe pump. After 4 more hours at room temperature, the reaction mixture was filtered and an aqueous solution of $NaHCO_3$ (2 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 3 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by preparative TLC (SiO_2, petroleum ether/EtOAc, 65:35) gave **28** (7.2 mg, 8.40 µmol, 92%) as a colorless gum.

R_f = 0.29 (petroleum ether/EtOAc = 70/30); $[\alpha]_D^{20}$ = +17.6 (*c* = 0.5 in CH_2Cl_2); **^{1}H-NMR** (500 MHz, CD_2Cl_2): δ [ppm] = -0.02 (s, 3H), -0.01 (s, 3H), 0.78 (s, 9H), 0.89 (d, *J* = 6.2 Hz, 3H), 0.92 (d, *J* = 6.2 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 1.12 (s, 3H), 1.25-1.31 (m, 1H), 1.36 (ddd, *J* = 14.3, 9.4, 2.7 Hz, 1H), 1.57 (ddd, *J* = 14.3, 10.8, 4.3 Hz, 1H), 1.59-1.65 (m, 2H), 1.65-1.72 (m, 2H), 1.75-1.77 (m, 3H), 1.80-1.88 (m, 1H), 1.91 (t, *J* = 1.6 Hz, 3H), 1.99-2.09 (m, 2H), 2.68 (dd, *J* = 16.6, 5.4 Hz, 1H), 2.76 (dd, *J* = 16.6, 8.1 Hz, 1H), 2.81-2.88 (m, 1H), 3.29 (s, 3H), 3.31 (t, *J* = 6.3 Hz, 2H), 3.48 (d, *J* = 7.5 Hz, 2H), 3.49 (d, *J* = 9.8 Hz, 1H), 3.80 (d, *J* = 9.8 Hz, 1H), 3.96 (dd, *J* = 11.7, 2.0 Hz, 1H), 4.38 (dd, *J* = 9.7, 6.7 Hz, 1H), 4.42 (dq, *J* = 12.2, 1.6 Hz, 1H), 4.46-4.50 (m, 1H), 4.50 (d, *J* = 7.4 Hz, 1H), 4.55 (ddd, *J* = 8.7, 6.7, 2.0 Hz, 1H), 4.63 (dd, *J* = 11.7, 8.7 Hz, 1H), 4.82 (dt, *J* = 10.5, 2.2 Hz, 1H), 5.48 (d, *J* = 9.7 Hz, 1H), 5.55 (d, *J* = 7.4 Hz, 1H), 5.73-5.78 (m, 1H), 6.00-6.03 (m, 1H), 6.73 (dd, *J* = 3.3, 1.7 Hz, 1H), 9.07 (br. s, 1H); **^{13}C-NMR** (125 MHz, CD_2Cl_2): δ [ppm] = -5.5, 13.9, 14.6, 18.6, 20.4, 21.9, 22.7, 22.8, 24.0, 25.6, 26.0, 26.4, 26.9, 27.9, 34.7, 36.9, 39.4, 40.6, 43.7, 50.4, 58.8, 65.6, 65.8, 68.3, 69.8, 72.4, 75.5, 79.9, 83.7, 84.1, 109.0, 114.0, 119.7, 122.0, 126.9, 130.6, 133.3, 134.5, 135.1, 144.7, 158.3, 171.7, 174.9, 177.0; **HRMS** (ESI+): calculated for $C_{47}H_{72}N_2NaO_{10}Si^+$ $[M+H]^+$: 875.4848, found: 875.4861.

Leupyrrin A_1 (5)



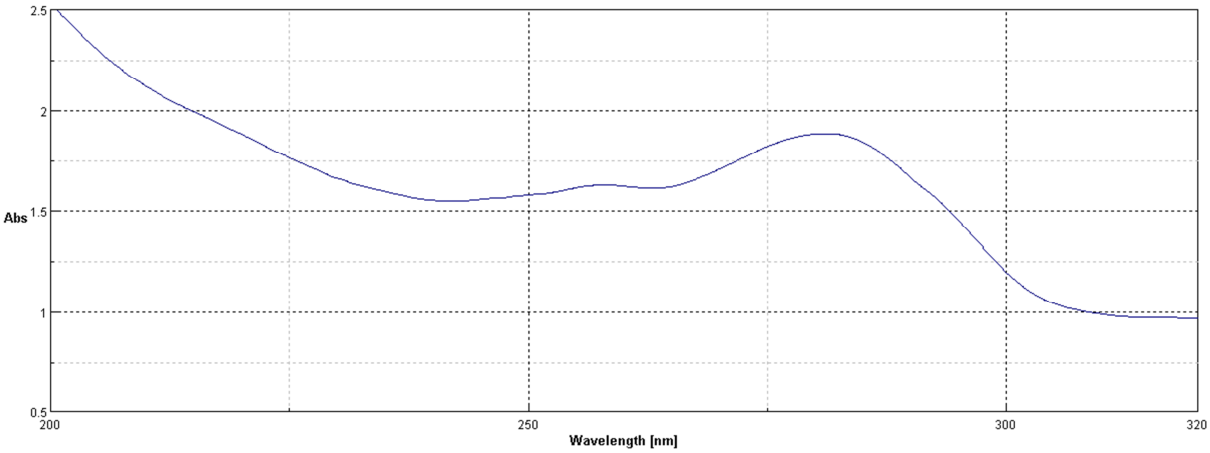
5

$C_{41}H_{58}N_2O_{10}$, M = 738.4 g/mol

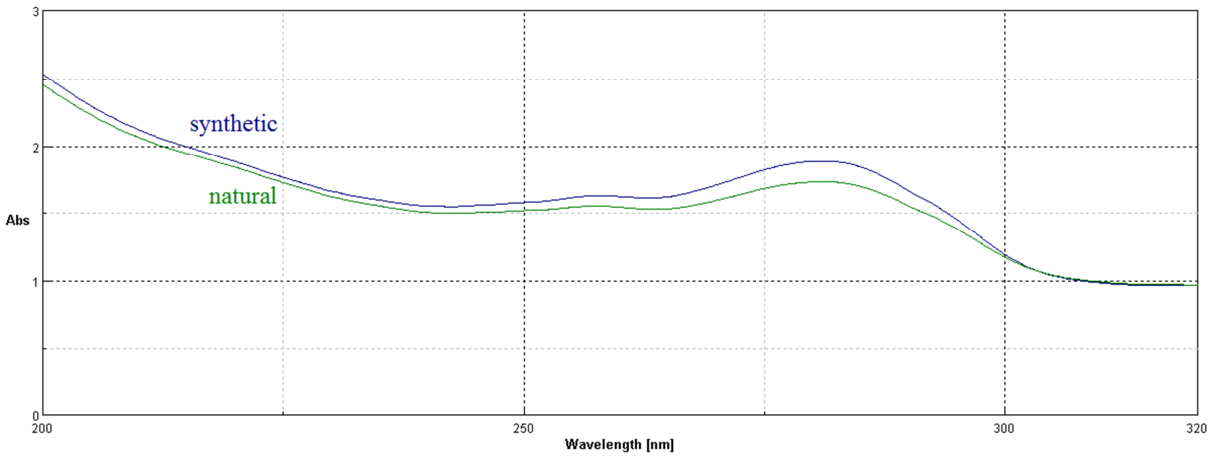
To a solution of TBS protected alcohol **28** (6.2 mg, 7.27 µmol, 1.0 eq) in MeCN (125 µL) at 0 °C a solution of TASF (90%, 8.9 mg, 29.1 µmol, 4.0 eq) in MeCN (25 µL) was added. The resulting mixture was stirred at this temperature for 1 hour before it was allowed to warm up to room temperature. After 2.5 hours further TASF (90%, 4.4 mg, 15.5 µmol, 2.0 eq) in MeCN (12 µL) was added. After 2 hours, when TLC indicated complete consumption of starting material **28** the reaction mixture was diluted with EtOAc (1 mL) and it was quenched by addition of a saturated solution of $NaHCO_3$ (1 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 1.5 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by preparative TLC (SiO_2, petroleum ether/EtOAc, 50:50) gave leupyrrin A_1 (**5)** (4.1 mg, 5.55 µmol, 76%).

R_f = 0.31 (petroleum ether/EtOAc = 50/50); $[\alpha]_D^{20}$ = +11.0 (*c* = 0.313 in MeOH); **^{1}H-NMR** (500 MHz, CD_3OD): δ [ppm] = 0.88 (d, *J* = 6.5 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.99 (d, *J* = 6.6 Hz, 3H), 1.03 (d, *J* = 6.6 Hz, 3H), 1.06 (s, 3H), 1.27-1.31 (m, 1H), 1.41 (ddd, *J* = 14.3, 9.5, 2.5 Hz, 1H), 1.57 (ddd, *J* = 14.3, 10.8, 4.1 Hz, 1H), 1.58-1.69 (m, 3H), 1.69-1.76 (m, 1H), 1.73 (d, *J* = 1.0 Hz, 3H), 1.83-1.90 (m, 1H), 1.93 (t, *J* = 1.5 Hz, 3H), 2.02-2.08 (m, 1H), 2.11 (ddd, J = 13.5, 8.0, 7.0 Hz, 1H), 2.61-2.68 (m, 1H), 2.73-2.82 (m, 2H), 3.32 (s, 3H), 3.34 (m, 1H), 3.36 (t, *J* = 6.0 Hz, 2H), 3.58 (d, *J* = 11.0 Hz, 1H), 3.59 (dd, *J* = 15.5, 9.0 Hz, 1H), 3.73 (d, *J* = 11.0 Hz, 1H), 4.16 (dd, *J* = 12.0, 2.5 Hz, 1H), 4.45 (dq, *J* = 12.0, 1.5 Hz, 1H), 4.52 (dd, *J* = 10.1, 5.5 Hz, 1H), 4.53-4.54 (m, 1H), 4.54 (dd, *J* = 12.0, 5.5 Hz, 1H), 4.67 (td, *J* = 5.5, 2.5 Hz, 1H), 4.73 (dd, *J* = 7.7, 0.4 Hz, 1H), 4.96 (ddd, *J* = 10.8, 2.5, 1.7 Hz, 1H), 5.51 (d, *J* = 10.1 Hz, 1H), 5.54 (d, *J* = 7.7 Hz,

1H), 5.85 (m, 1H), 6.03 (d, J = 3.6 Hz, 1H), 6.75 (d, J = 3.6 Hz, 1H); **^{13}C-NMR** (125 MHz, CD_2Cl_2): δ [ppm] = 11.5, 14.7, 20.3, 22.2, 22.8, 23.0, 24.3, 26.2, 27.0, 27.0, 28.5, 35.0, 36.5, 39.9, 40.1, 44.4, 51.2, 58.9, 65.9, 66.1, 68.2, 70.3, 73.0, 75.3, 80.6, 84.6, 85.5, 109.7, 115.3, 119.5, 123.2, 128.6, 131.4, 134.1, 135.3, 136.6, 145.0, 160.8, 172.3, 175.6, 179.5; **HRMS** (ESI+): calculated for $C_{41}H_{59}N_2O_{10}^+$ $[M+H]^+$: 739.4164, found: 739.4165.



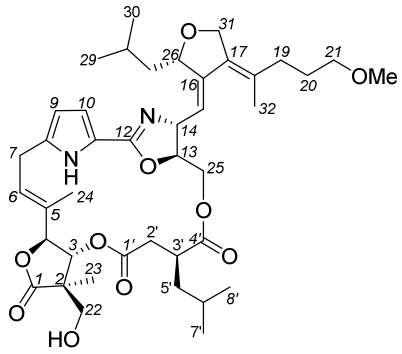
Scheme S 5: CD-Spectrum of synthetic leupyrrin A_1 (c = 10^{-4} mol/L, MeCN).



Scheme S 6: CD-Spectra-overlay of synthetic and natural leupyrrin A_1 (c = 10^{-4} mol/L, MeCN).

Natural Leupyrrin: CD_3OD, 400 MHz (^{1}H-NMR), 100 MHz (^{13}C-NMR);[23]

Synthetic Leupyrrin: CD_3OD, 500 MHz (^{1}H-NMR), 125 MHz (^{13}C-NMR).



Position	Natural leupyrrin A_1[24]		Synthetic leupyrrin A_1	
	H [δ (mult, *J* / Hz]	C	H [δ (mult, *J* / Hz]	C
1	---	179.3	---	179.5
2	---	51.1	---	51.2
3	5.58 (d, 8.0), 1H	75.4	5.54 (d, 7.7), 1H	75.3
4	4.76 (dd, 8.0, 1.0), 1H	85.5	4.73 (dd, 7.7, 0.4), 1H	85.5
5	---	135.1	---	135.3
6	5.89 (td, 7.5, 1.5), 1H	128.4	5.85 (m), 1H	128.6
7a	3.38 (m), 1H	26.9	3.34 (m), 1H	27.0
7b	3.62 (dd, 15.5, 9.0), 1H		3.59 (dd, 15.5, 9.0), 1H	
8	---	136.5	---	136.6
9	6.07 (d, 3.5), 1H	109.6	6.03 (d, 3.6), 1H	109.7
10	6.79 (d, 3.5), 1H	115.2	6.75 (d, 3.6), 1H	115.3
11	---	119.3	---	119.5
12	---	160.6	---	160.8
13	4.70 (td, 5.5, 2.5), 1H	84.5	4.67 (td, 5.5, 2.5), 1H	84.6
14	4.56 (dd, 10.0, 5.5), 1H	68.8[25]	4.52 (dd, 10.1, 5.5), 1H	68.2
15	5.55 (dd, 10.0, 1.5), 1H	123.0	5.51 (d, 10.1), 1H	123.2
16	---	144.9	---	145.0
17	---	131.2	---	131.4
18	---	134.0	---	134.1

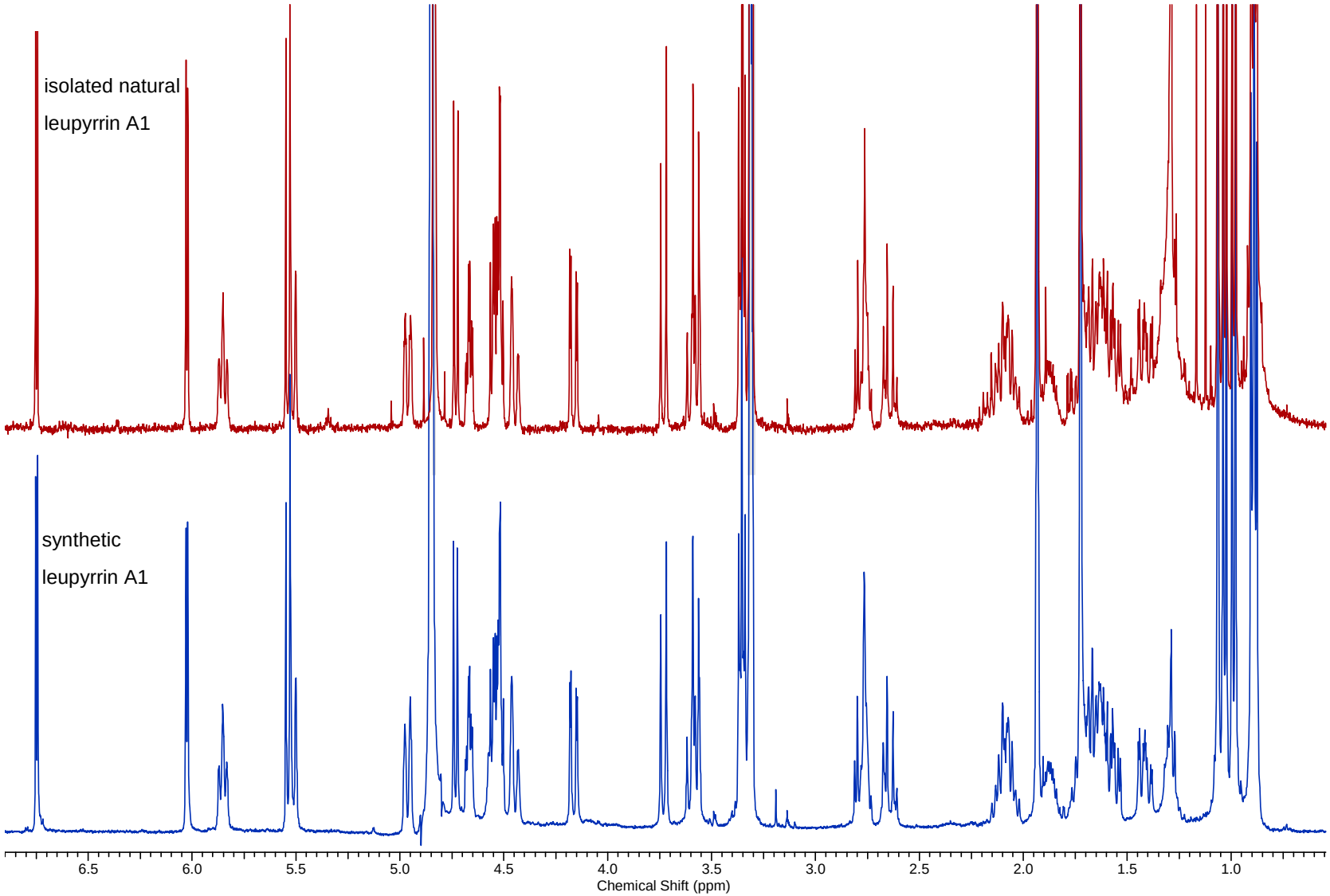
[23] Bode, H. B.; Irschik, H.; Wenzel, S. C.; Reichenbach, H.; R. Müller, R.; Höfle, G. *J. Nat. Prod.* **2003**, *66*, 1203-1206.

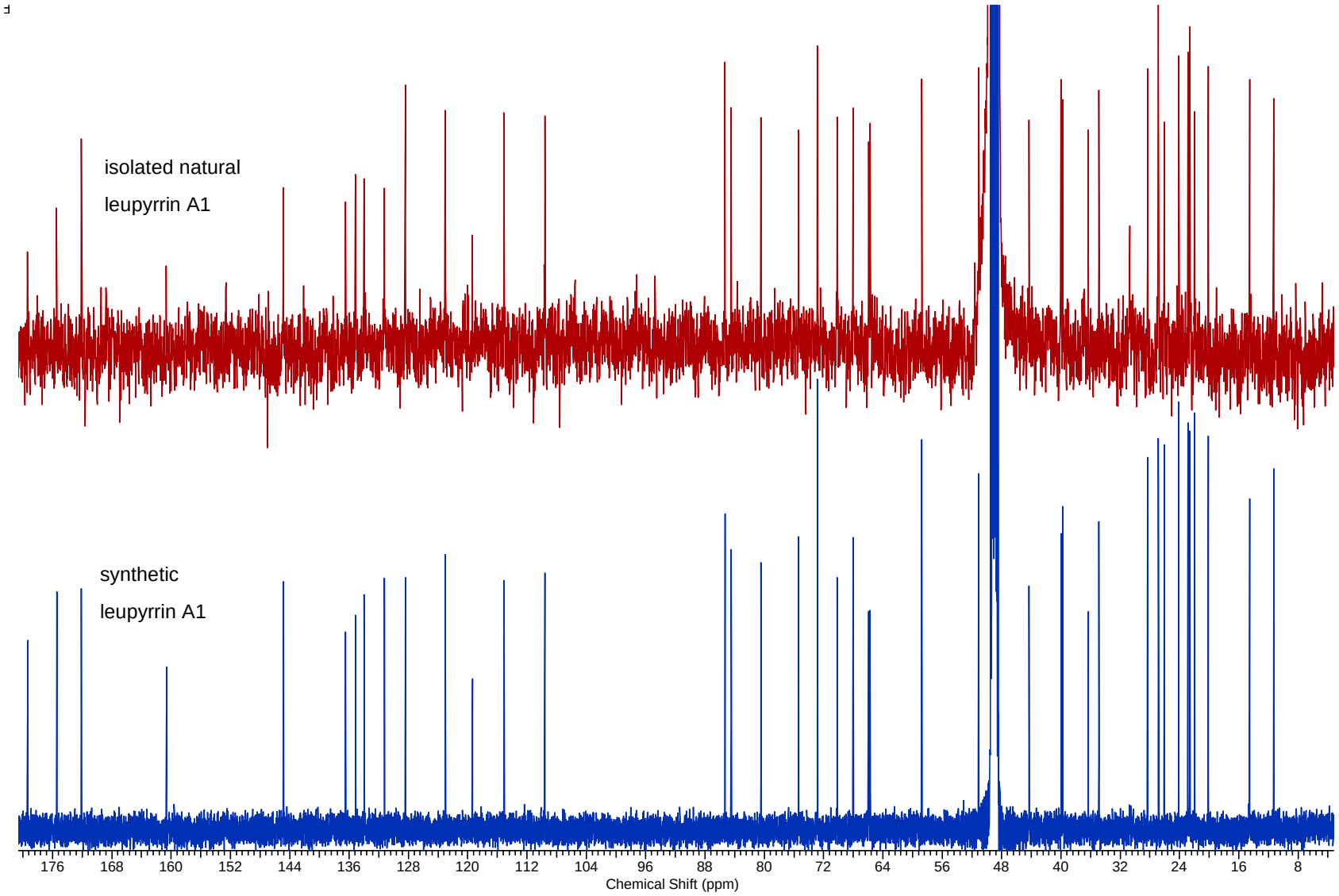
[24] The observed ^{1}H-NMR chemical shifts values of synthetic leupyrrin A_1 were systematically 0.03-0.05 ppm lower as compared to the reported data for natural leupyrrin A_1. They were however identical to the data for reisolated leupyrin A_1. This discrepancy may be explained by a difference of the calibtration. An overlay of the spectra of natural and synthetic leupyrrin A_1 recorded in our group confirmed this observation (see below).

[25] For reisolated leupyrrin A_1 a value of 68.1 ppm was found.

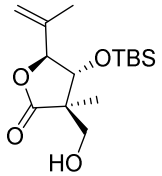
19a	2.11 (ddd, 13.5, 8.0, 7.0), 1H	34.9	2.06 (m), 1H	35.0
19b	2.14 (ddd, 13.5, 8.0, 7.0), 1H		2.11 (ddd, 13.5, 8.0, 7.0), 1H	
20a	1.70 (m), 1H	28.3	1.68 (m), 1H	28.5
20b	1.76 (m), 1H		1.73 (m), 1H	
21	3.39 (t, 6.0), 2H	72.8	3.36 (t, 6.0), 2H	73.0
21-OMe	3.35 (s), 3H	58.8	3.32 (s), 3H	58.9
22a	3.63 (d, 11.0), 1H	65.7	3.58 (d, 11.0), 1H	65.9
22b	3.77 (d, 11.0), 1H		3.73 (d, 11.0), 1H	
23	1.10 (s), 3H	14.6	1.06 (s), 3H	14.7
24	1.77 (d, 2.0), 1H[26]	11.4	1.72 (d, 1.0), 3H	11.5
25a	4.19 (dd, 12.0, 2.5), 1H	65.9	4.16 (dd, 12.0, 2.5), 1H	66.1
25b	4.59 (dd, 12.5, 5.5), 1H		4.54 (dd, 12.0, 5.5), 1H	
26	5.00 (ddd, 11.0, 3.0, 1.5), 1H	80.5	4.96 (ddd, 10.8, 2.5, 1.7), 1H	80.6
27a	1.45 (ddd, 14.0, 9.5, 2.5), 1H	44.3	1.41 (ddd, 14.3, 9.5, 2.5), 1H	44.4
27b	1.60 (m), 1H		1.57 (ddd, 14.3, 10.8, 4.1), 1H	
28	1.91 (m), 1H	26.1	1.87 (m), 1H	26.2
29	1.03 (d, 6.5), 3H	24.1	0.99 (d, 6.6), 3H	24.3
30	1.07 (d, 6.5), 3H	22.0	1.03 (d, 6.6), 3H	22.2
31a	4.49 (m), 1H	70.1	4.45 (dq, 12.0, 1.5), 1H	70.3
31b	4.57 (d, 10.0), 1H		4.54 (m), 1H	
32	1.97 (t, 2.0), 3H	20.2	1.93 (t, 1.5), 3H	20.3
1‘	---	172.1	---	172.3
2‘a	2.69 (m), 1H	36.4	2.64 (m), 1H	36.5
2‘b	2.83 (m), 1H		2.79 (m), 1H	
3‘	2.79 (m), 1H	39.8	2.75 (m), 1H	39.9
4‘	---	175.4	---	175.6
5‘a	1.33 (m), 1H	40.1	1.29 (m), 1H	40.1
5‘b	1.68 (m), 1H		1.65 (m), 1H	
6‘	1.65 (m), 1H	26.9	1.61 (m), 1H	27.0
7‘	0.94 (d, 6.5), 3H	22.9	0.90 (d, 6.5), 3H	23.0
8‘	0.92 (d, 6.5), 3H	22.7	0.88 (d, 6.5), 3H	22.8

[26] Integral value does not match the expected amount of protons.


isolated natural
leupyrrin A1
synthetic
leupyrrin A1
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


isolated natural
leupyrrin A1
synthetic
leupyrrin A1
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

3.5 Copies of NMR spectra



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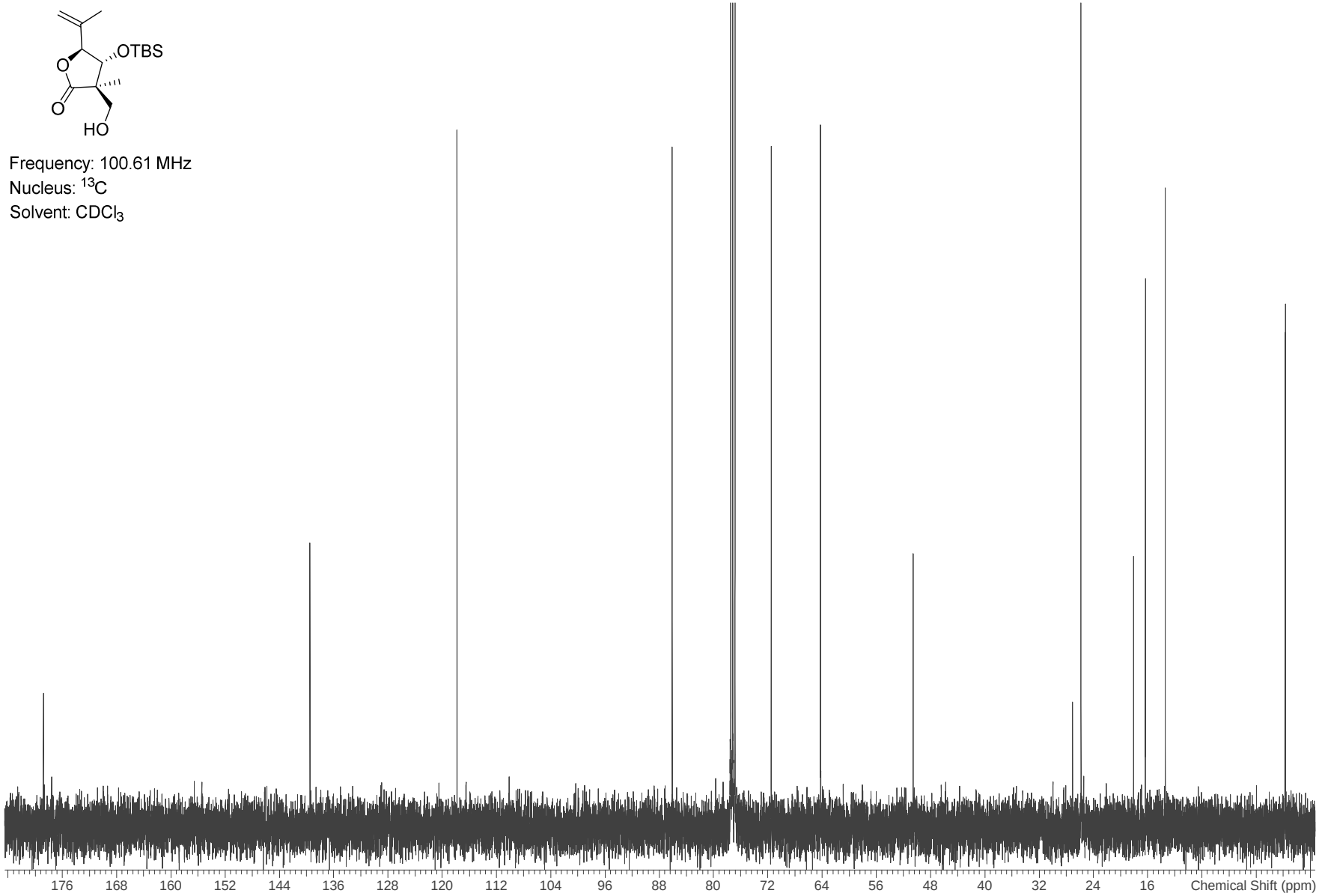
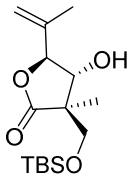
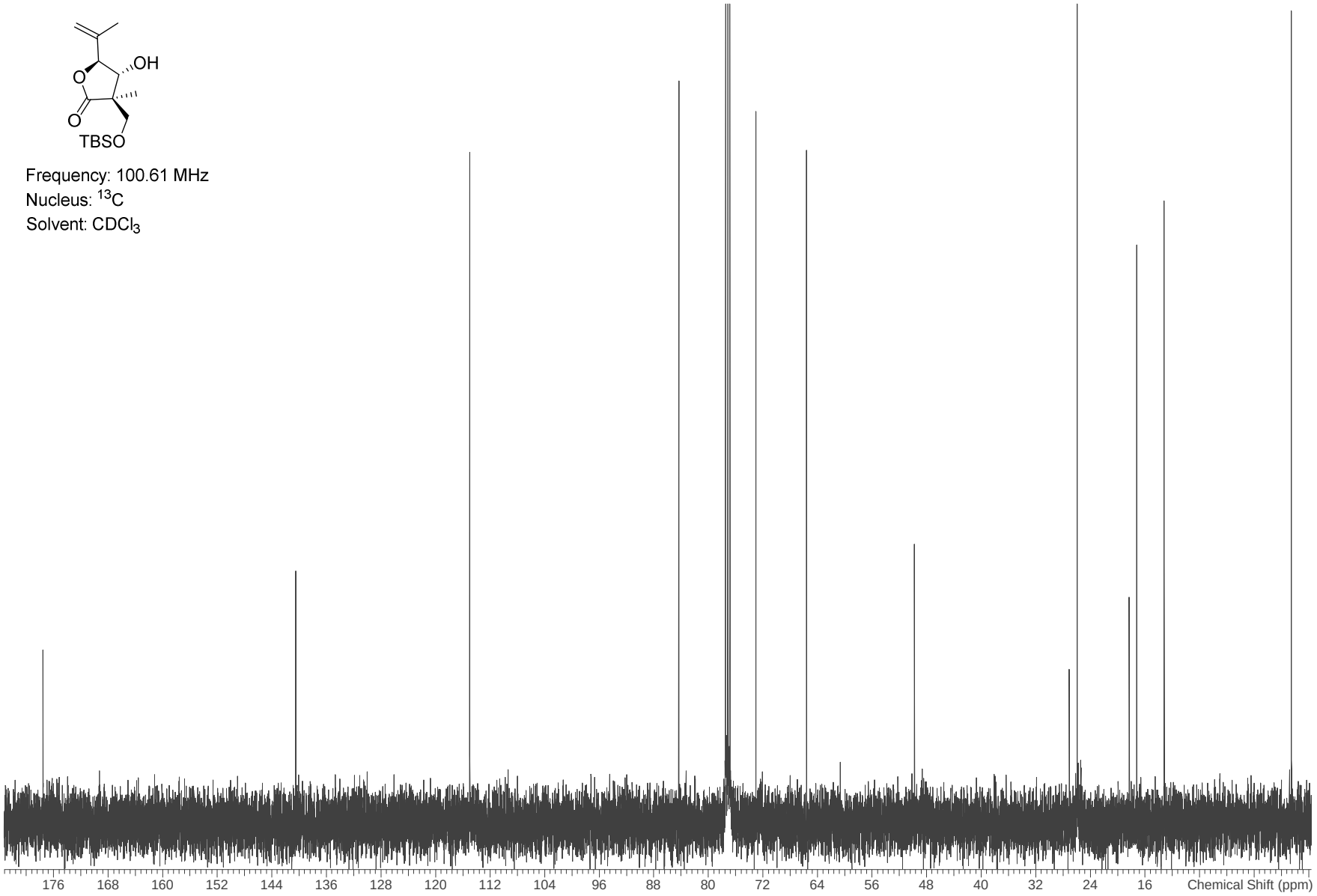
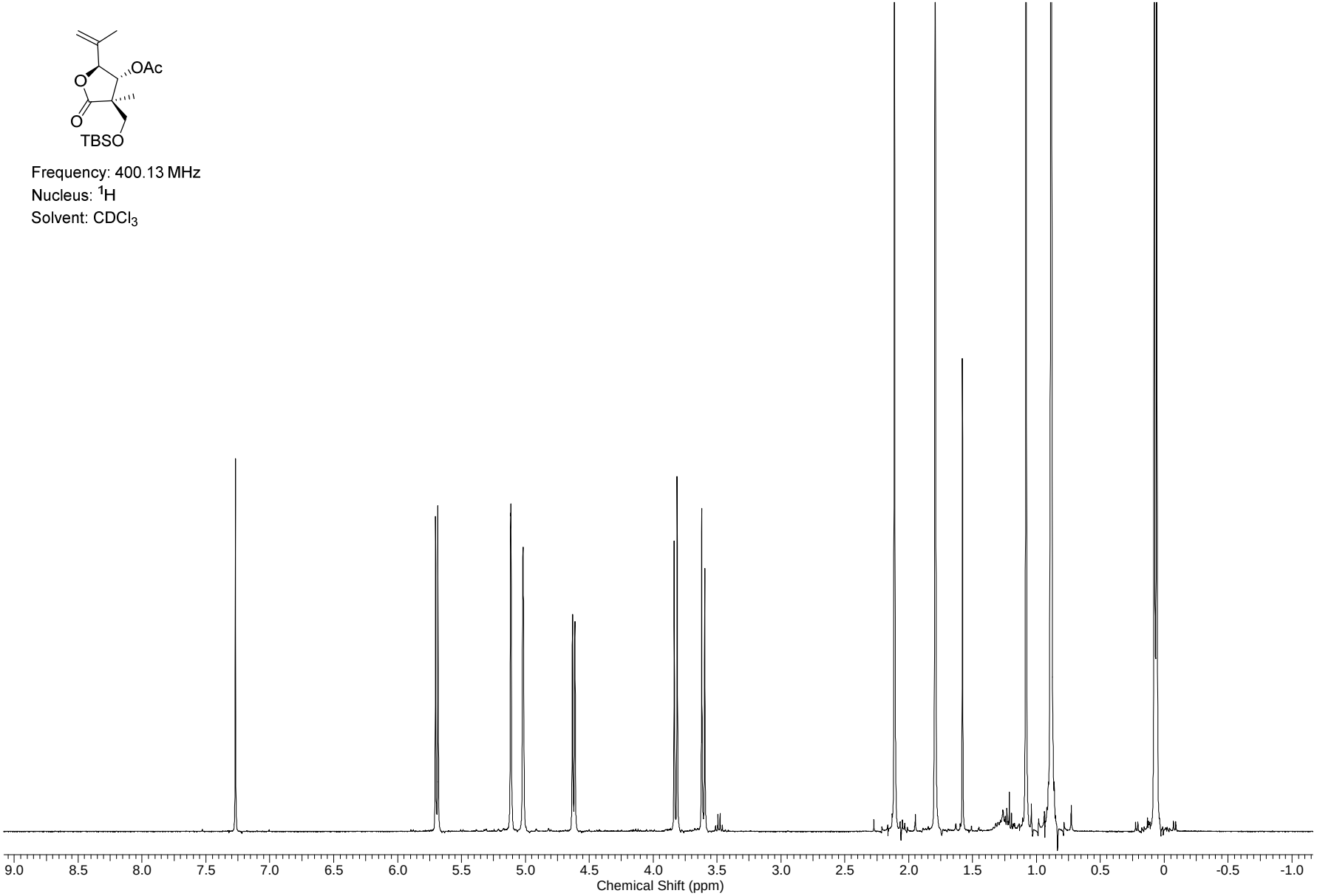
Nucleus: ^{1}H
Solvent: $CDCl_3$


OTBS
O
O
HO
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)



Frequency: 400.13 MHz
Nucleus: ^{1}H
Solvent: $CDCl_3$


OH
O
O
TBSO
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)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O
O
TBSO
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Solvent: CDCl3
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7.5
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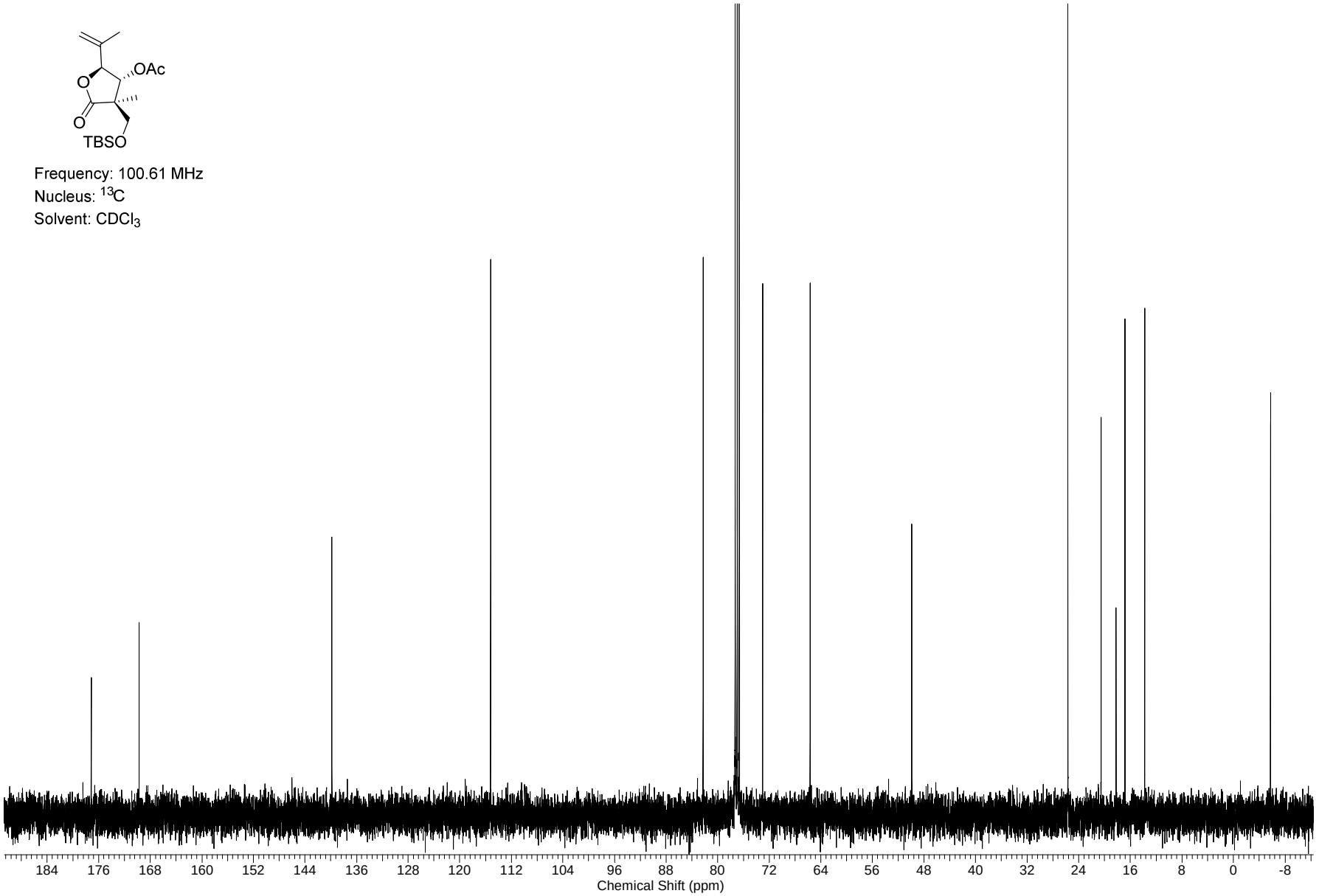
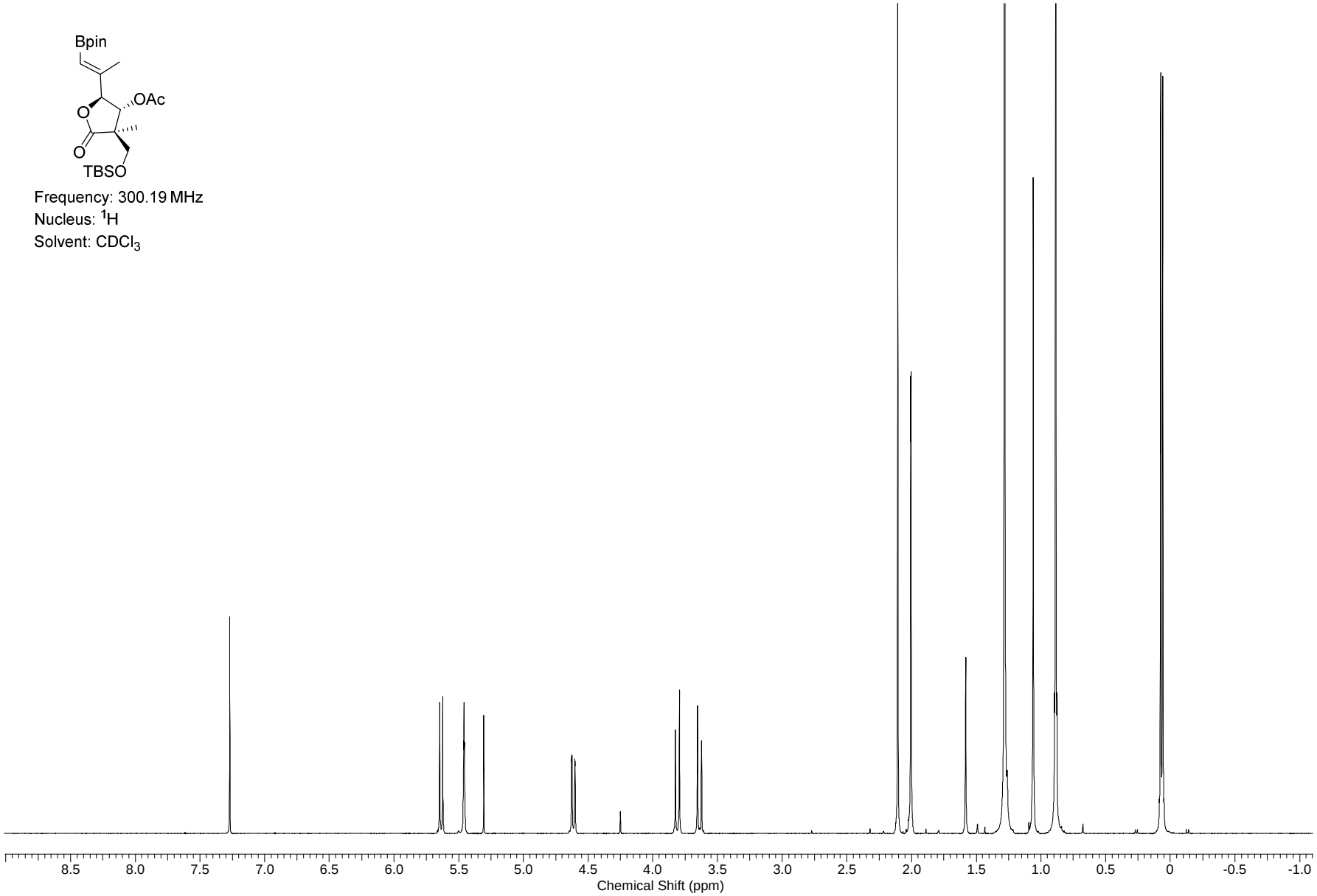
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)


OAc
O
O
TBSO
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)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O
O
TBSO
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Nucleus: 1H
Solvent: CDCl3
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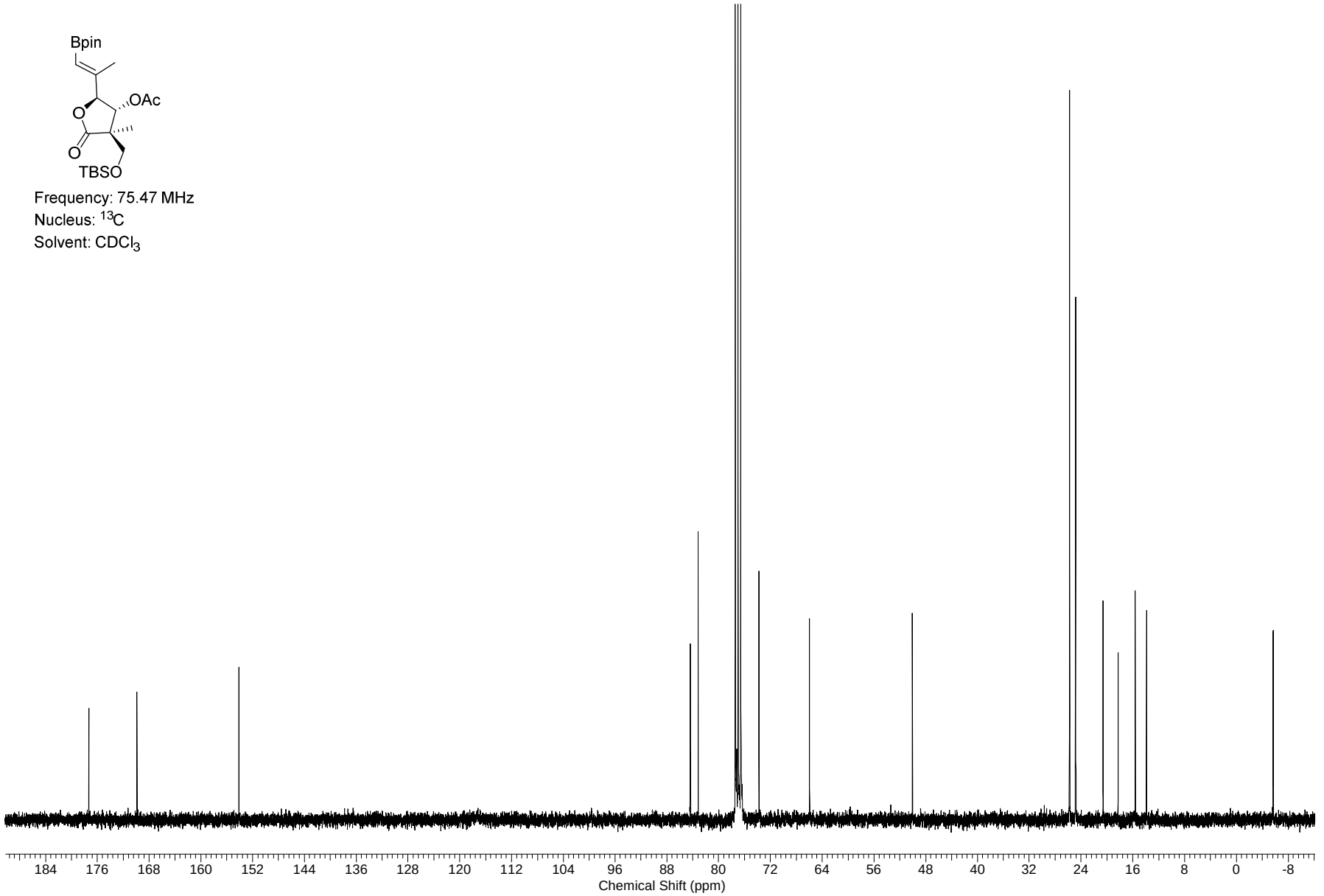
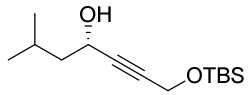
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)


Bpin
OAc
O
O
TBSO
Frequency: 75.47 MHz
Nucleus: 13C
Solvent: CDCl3
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)



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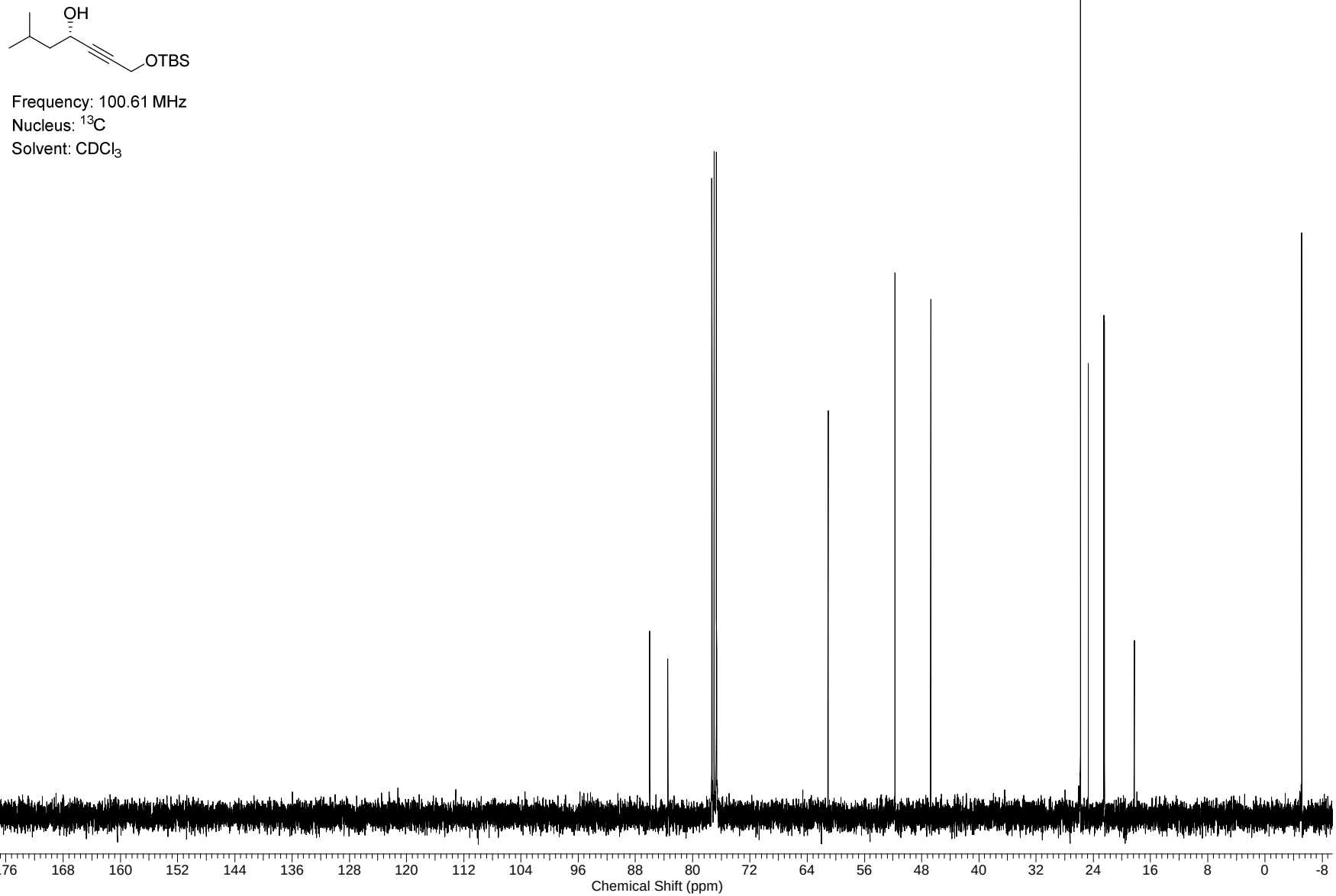
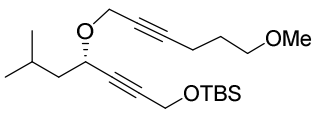
Nucleus: ^{1}H
Solvent: $CDCl_3$


OH
OTBS
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)



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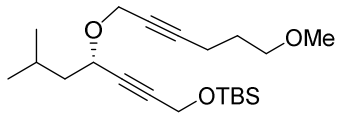
Nucleus: ^{1}H
Solvent: $CDCl_3$



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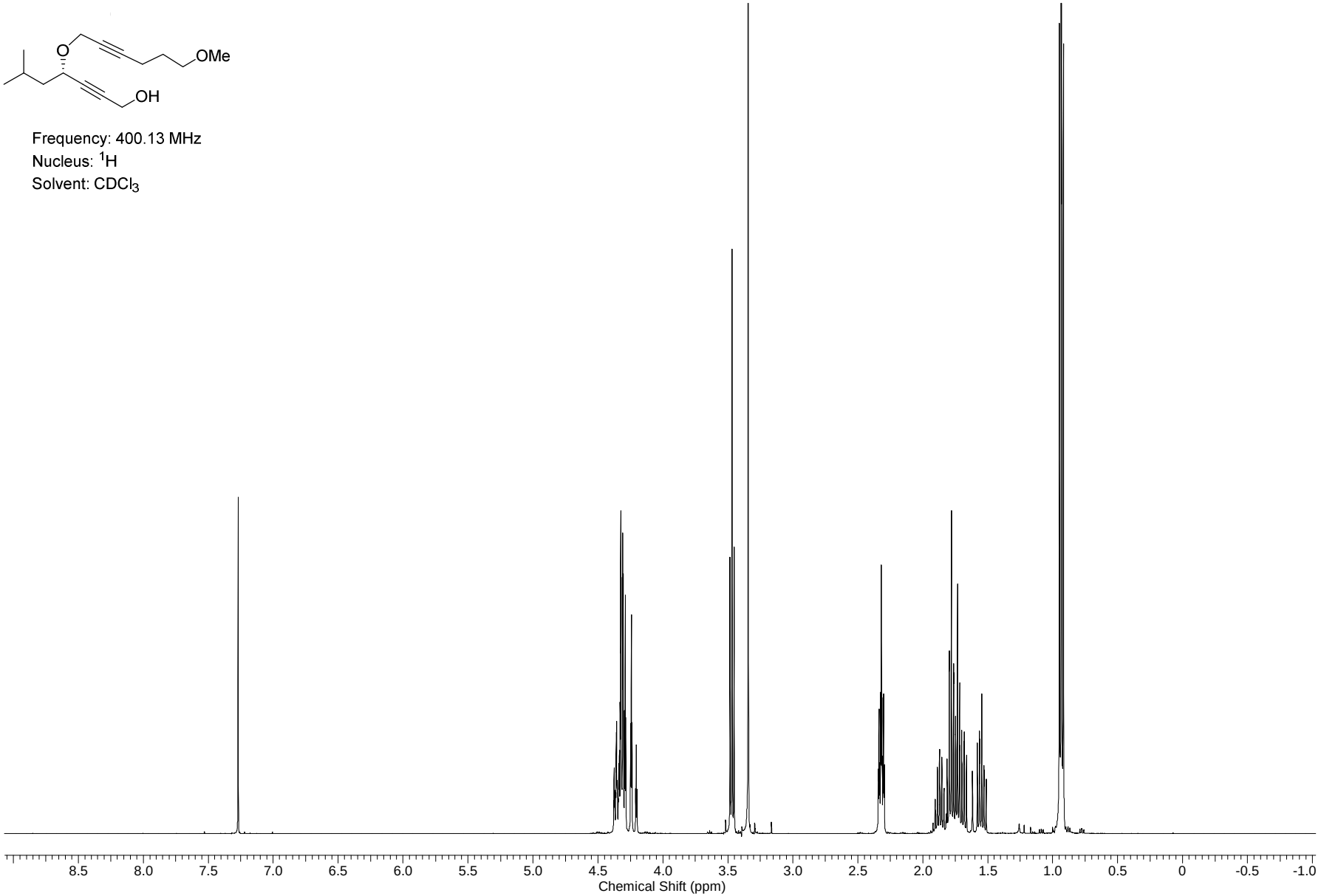
Nucleus: ^{13}C
Solvent: $CDCl_3$


O
OMe
OH
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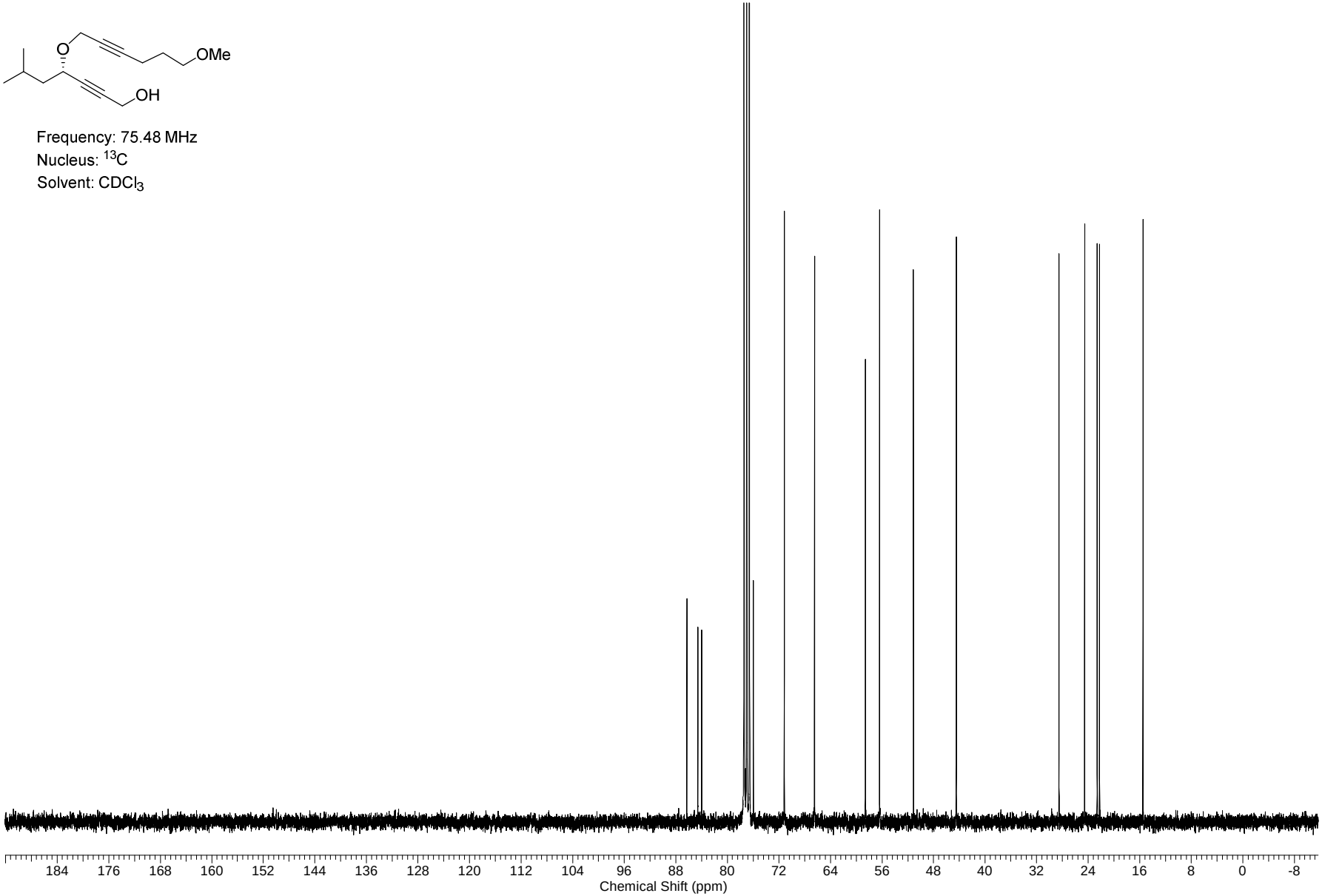
Nucleus: 1H
Solvent: CDCl3
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)


O
OMe
OH
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Nucleus: 13C
Solvent: CDCl3
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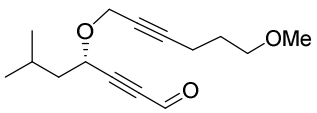
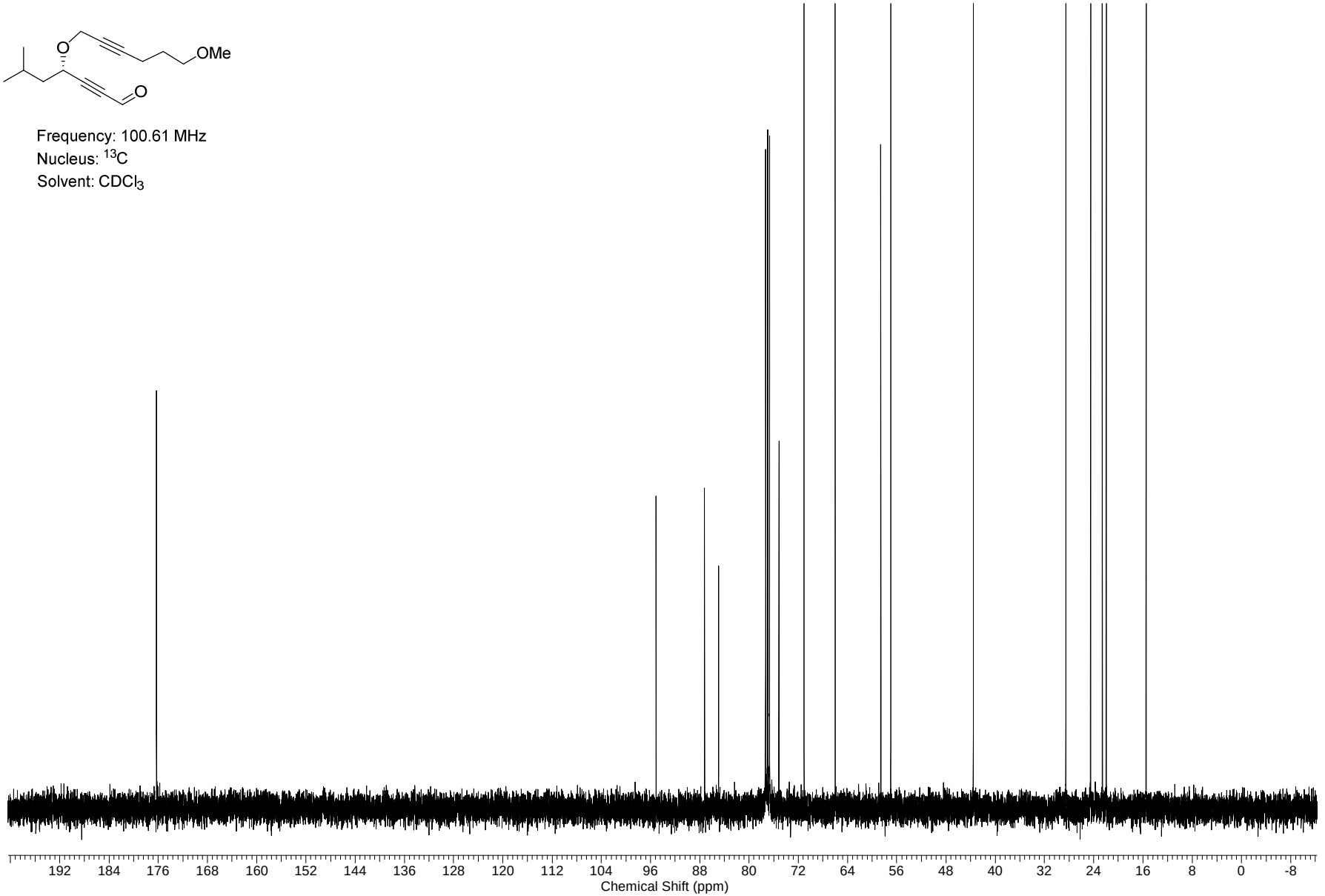
Chemical Shift (ppm)



Frequency: 400.13 MHz
Nucleus: ^{1}H
Solvent: $CDCl_3$


OMe
O
O
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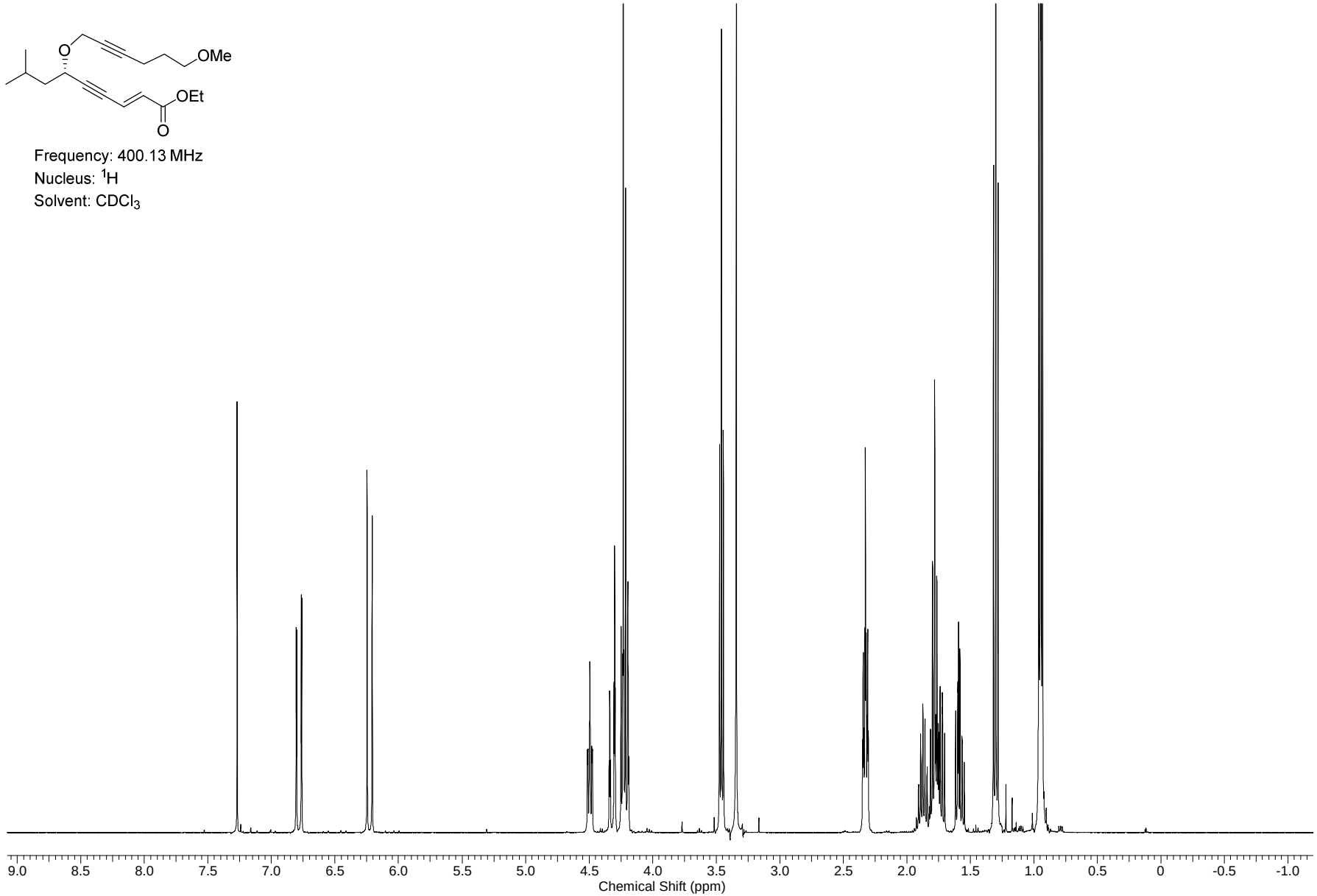
Nucleus: 13C
Solvent: CDCl3
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)


OMe
OEt
O
O
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Nucleus: 1H
Solvent: CDCl3
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8.5
8.0
7.5
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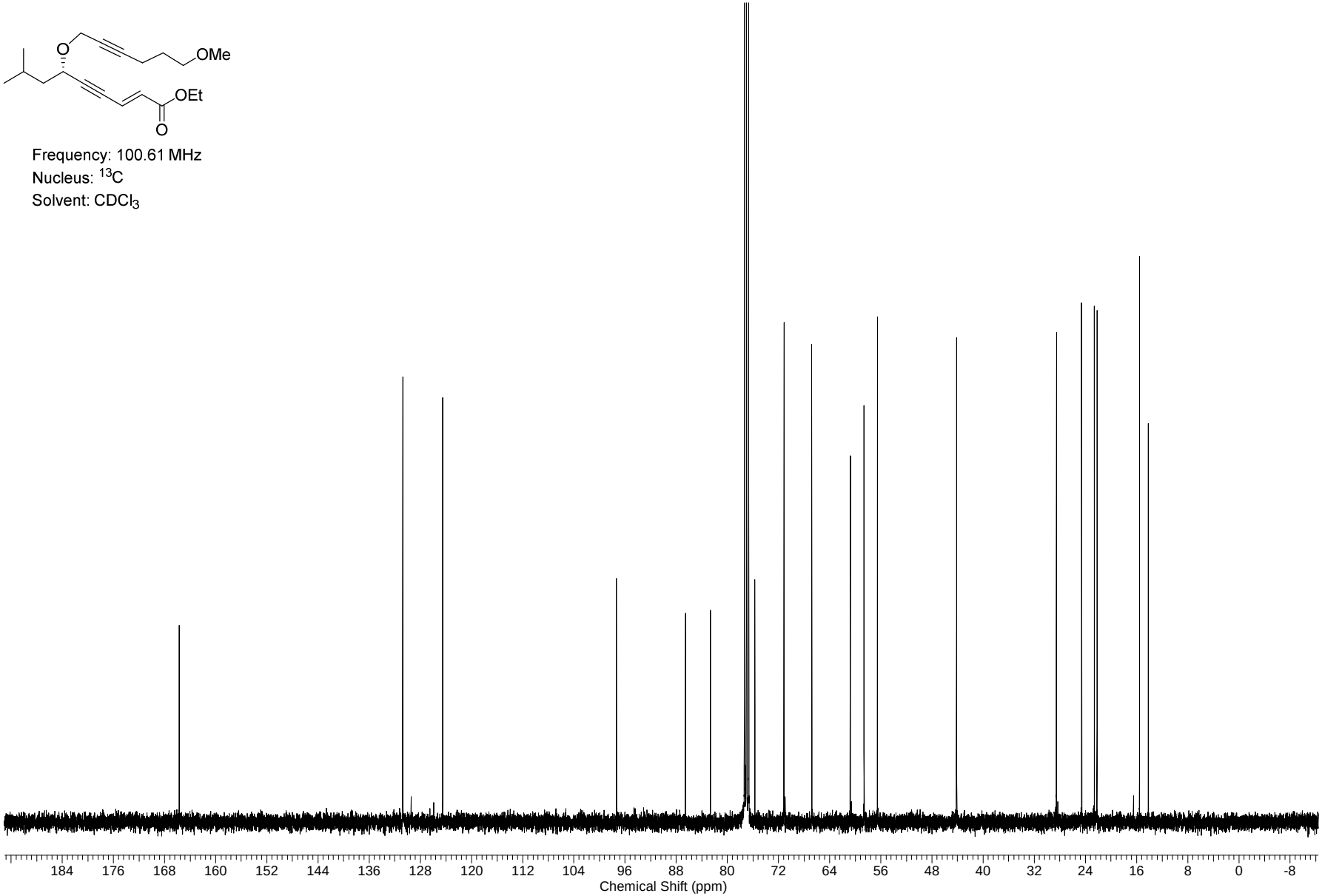
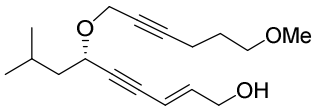
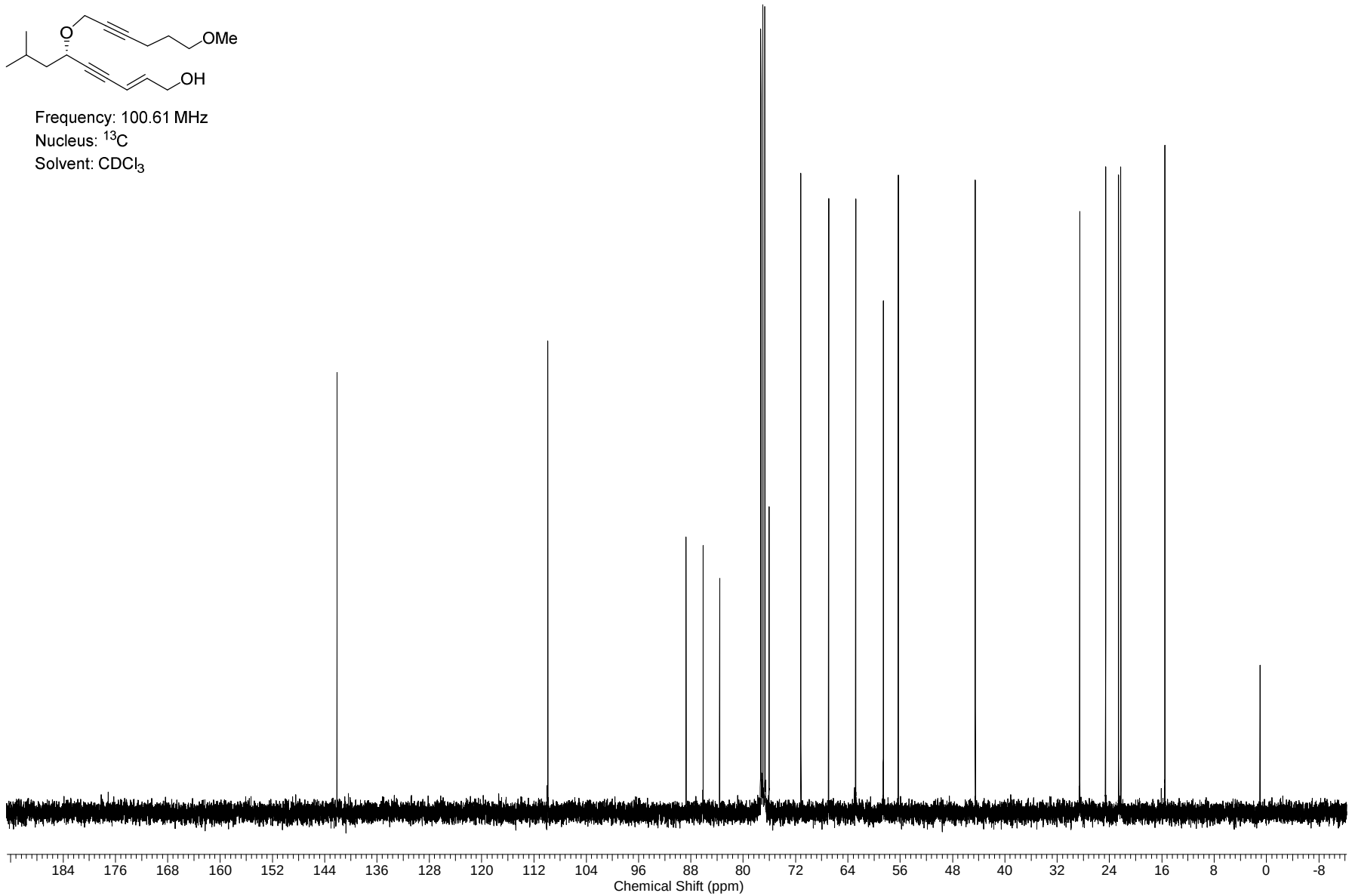
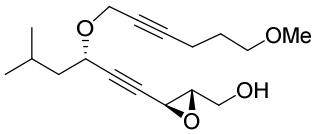
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)


OMe
OEt
O
O
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

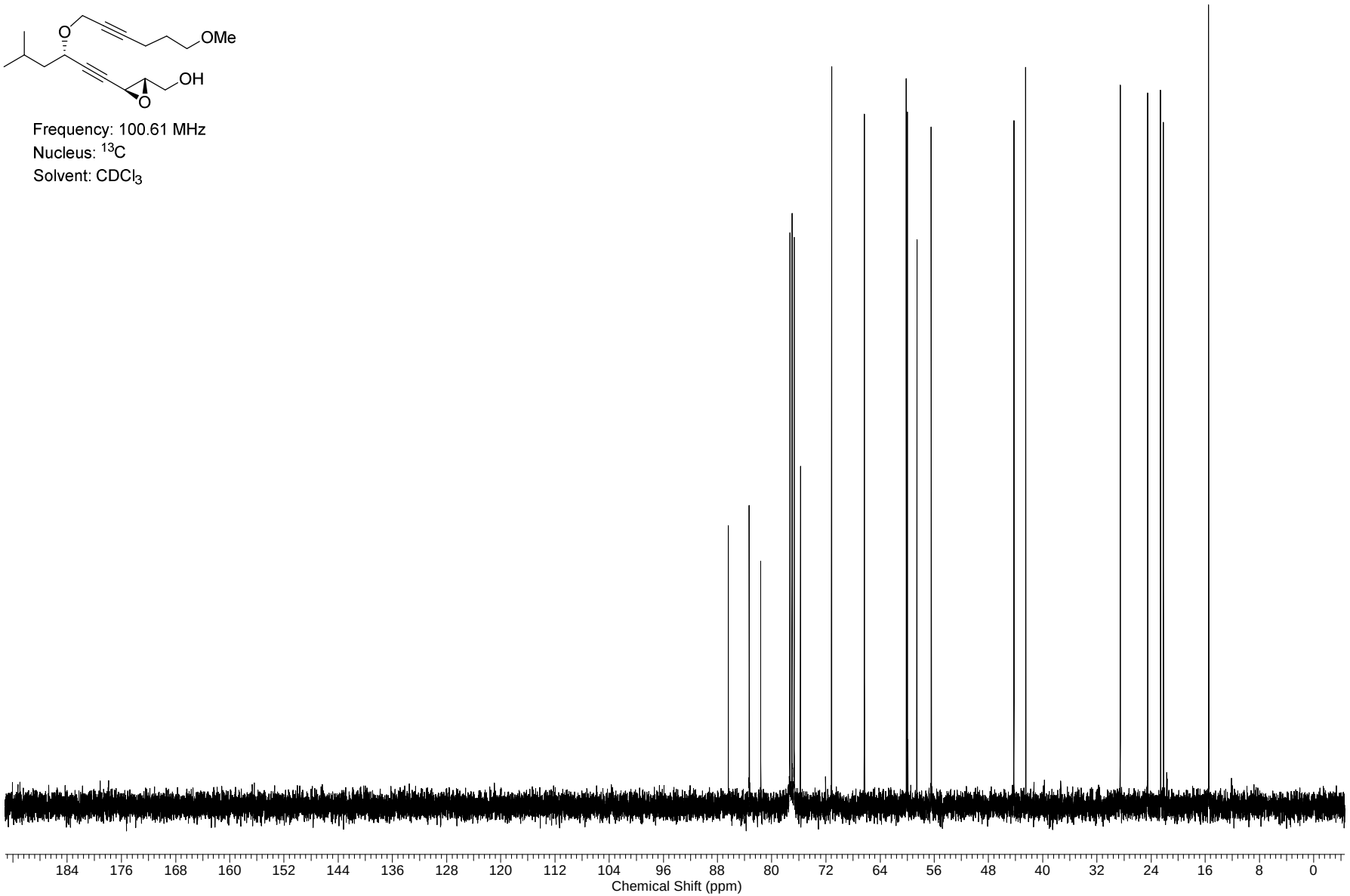


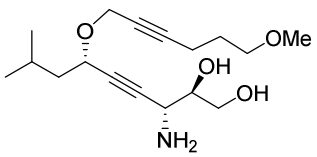
Frequency: 100.61 MHz
Nucleus: ^{13}C
Solvent: $CDCl_3$


O
OMe
OH
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

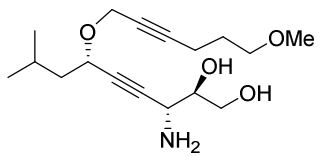


Frequency: 400.13 MHz
Nucleus: ^{1}H
Solvent: $CDCl_3$

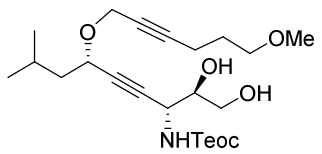

OMe
OH
O
O
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
Chemical Shift (ppm)



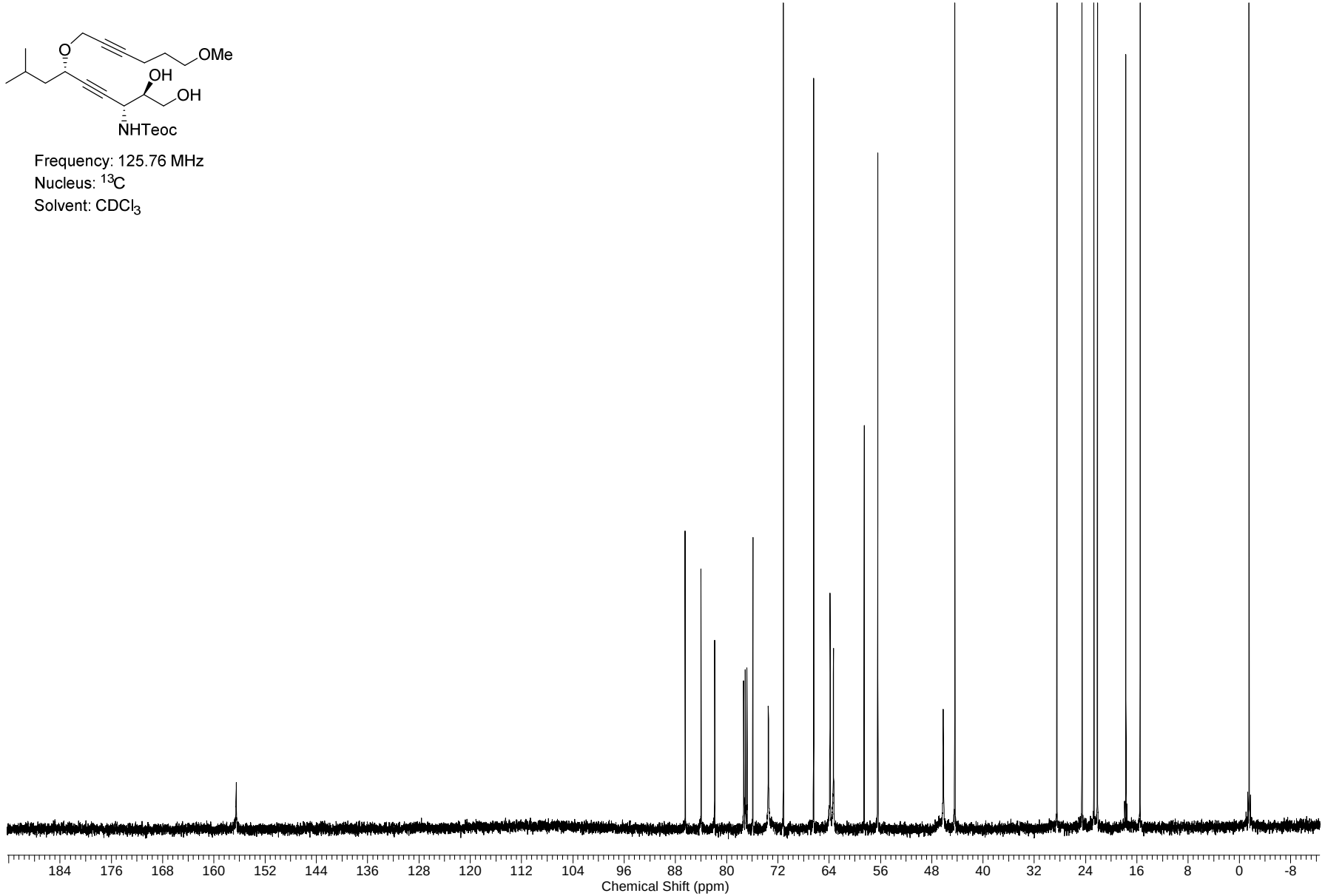
Frequency: 125.76 MHz
Nucleus: ^{13}C
Solvent: CD_3OD

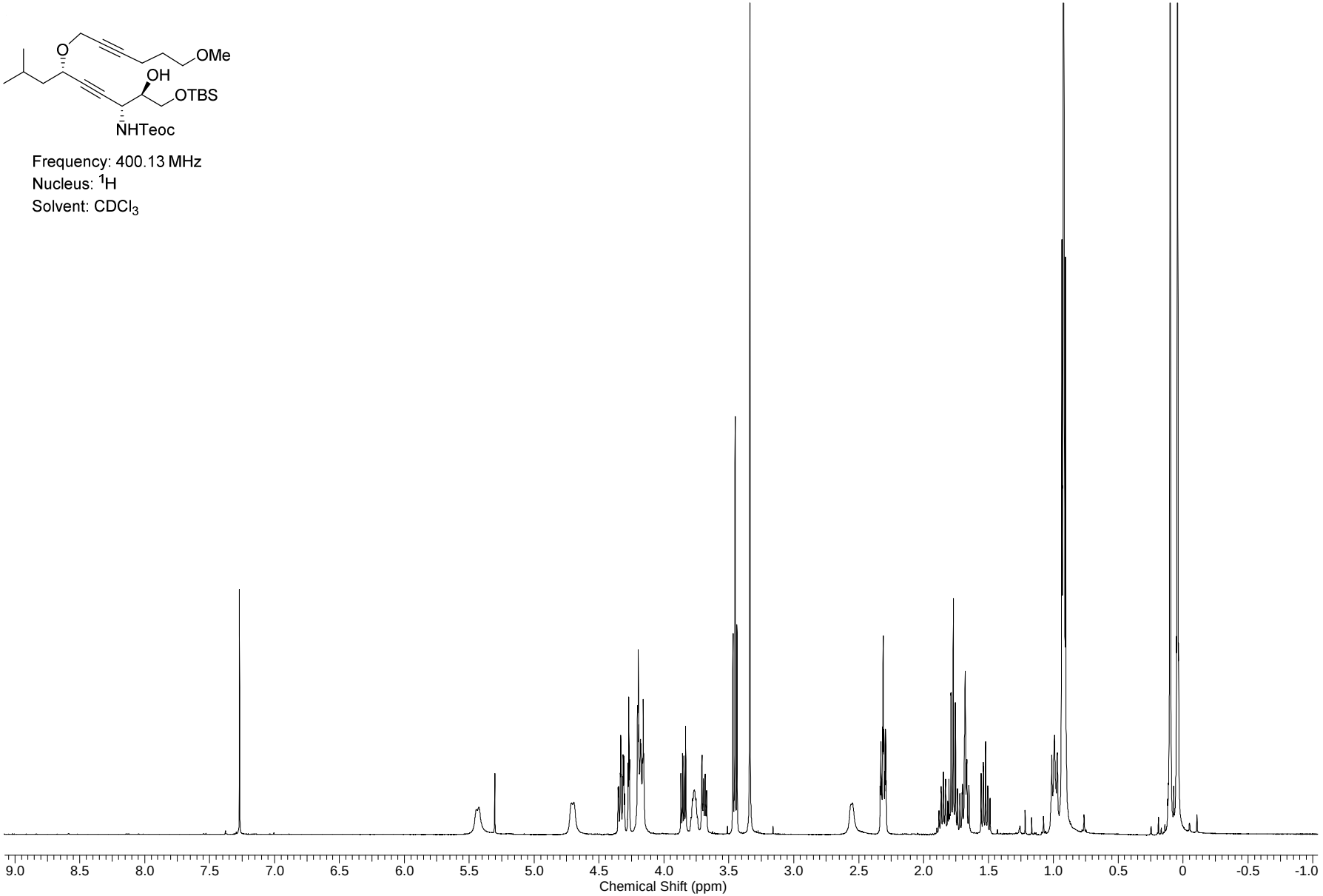


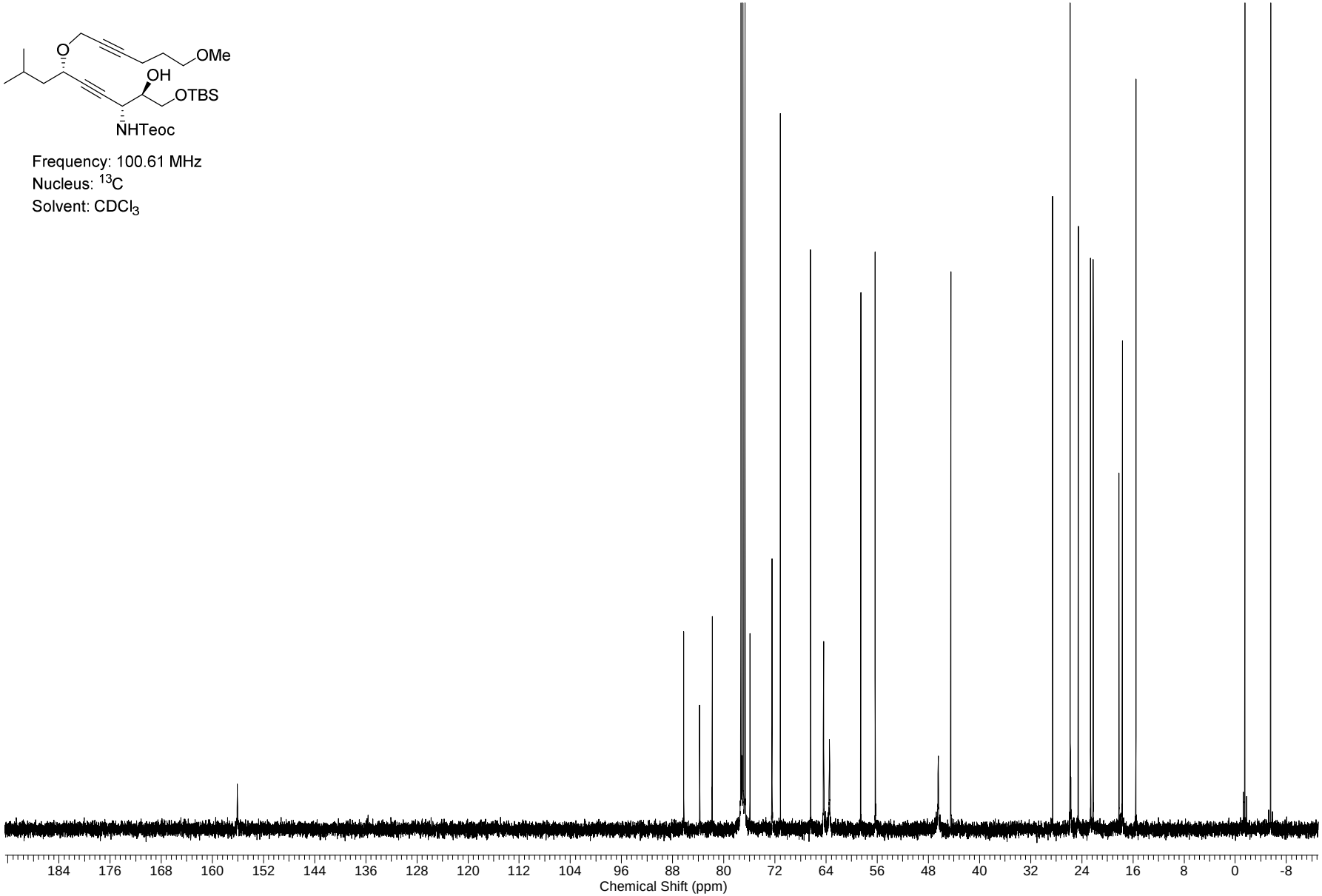
Frequency: 500.13 MHz
Nucleus: ^{1}H
Solvent: CD_3OD

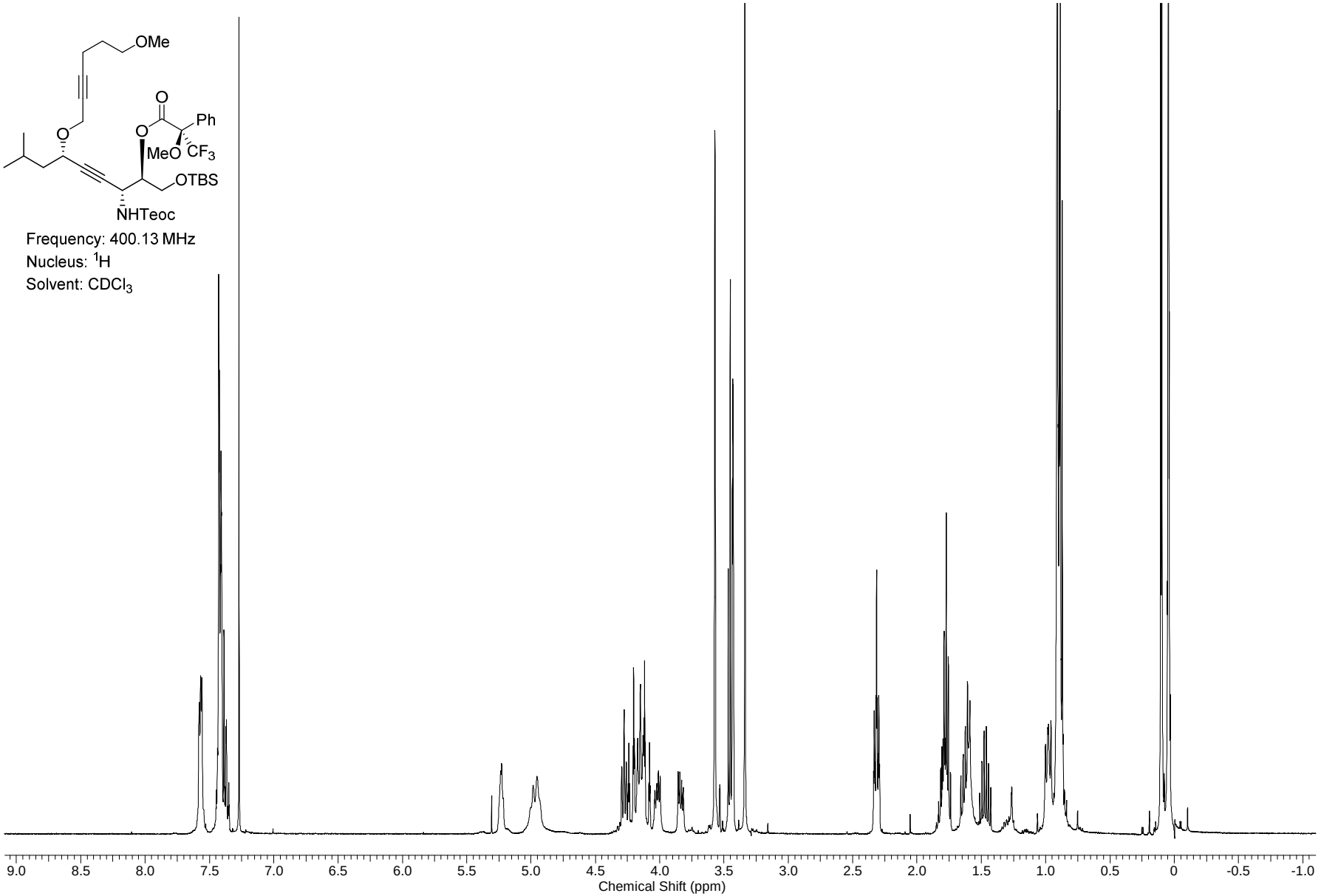


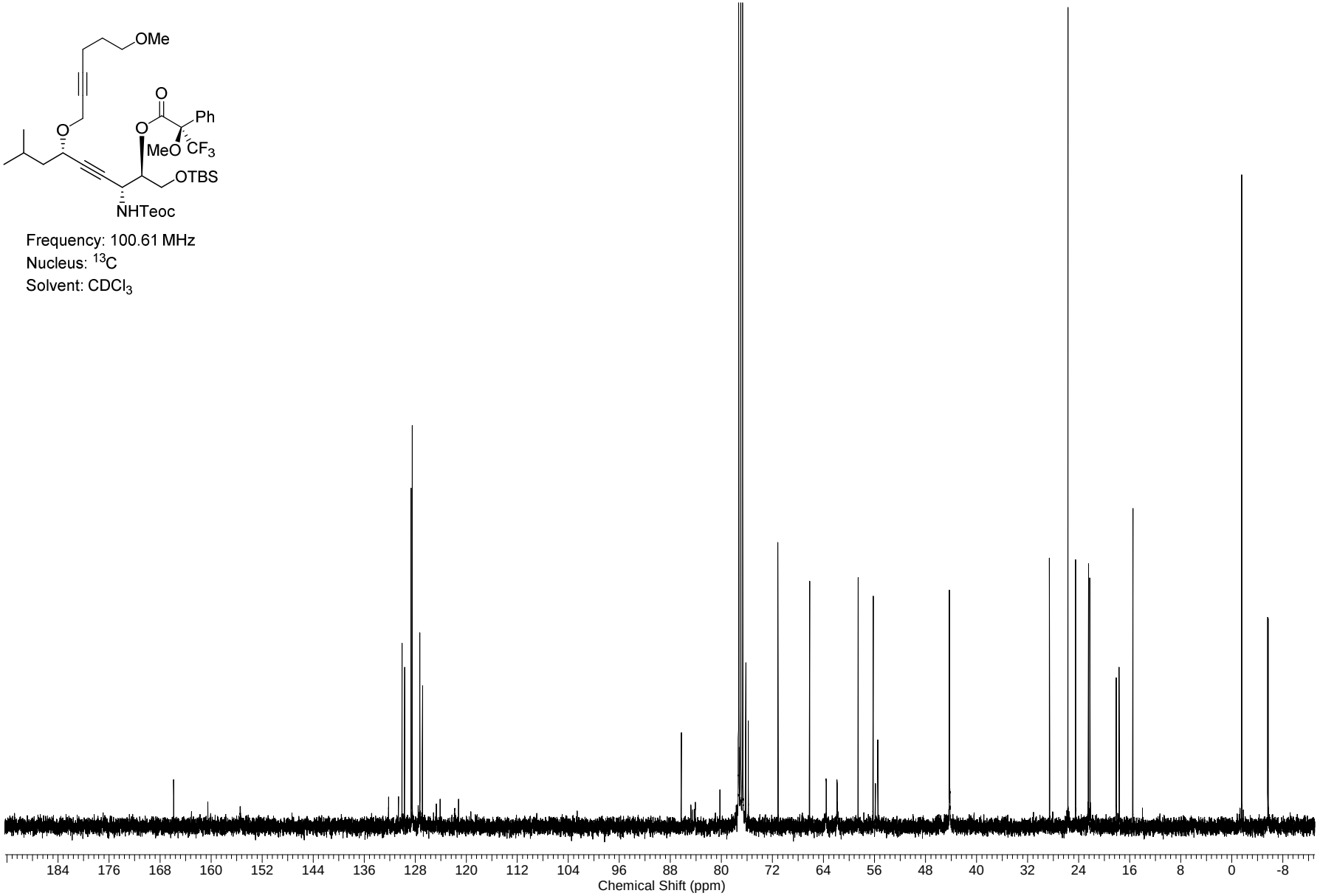
Frequency: 500.13 MHz
Nucleus: ^{1}H
Solvent: $CDCl_3$

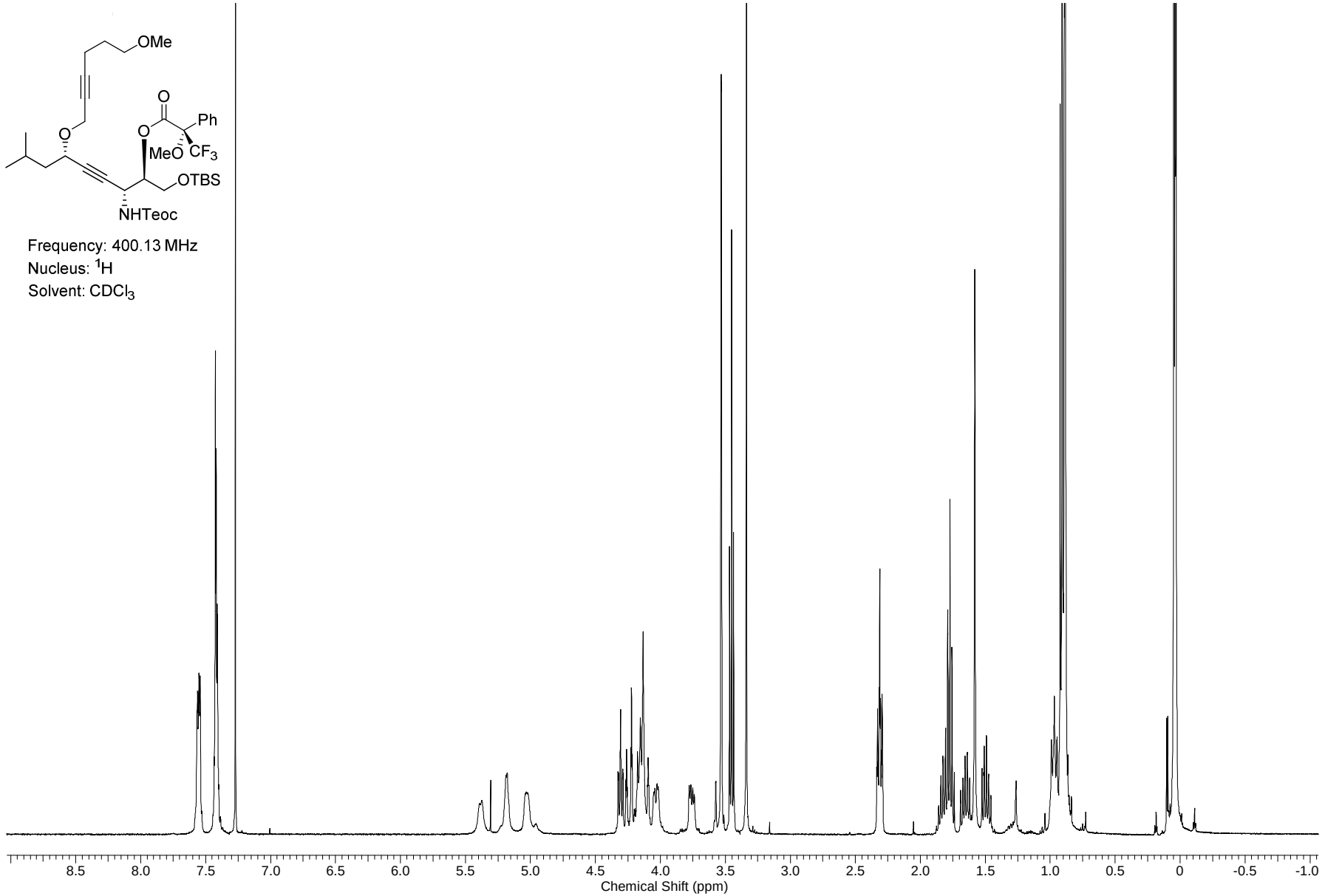

O
OMe
OH
OH
NHTeoc
Frequency: 125.76 MHz
Nucleus: 13C
Solvent: CDCl3
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

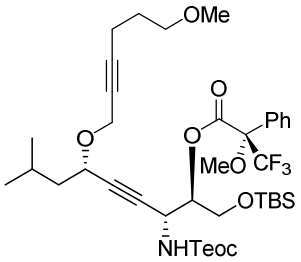

OMe
O
OH
OTBS
NHTeoc
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CDCl3
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)


OMe
OH
OTBS
NHTeoc
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

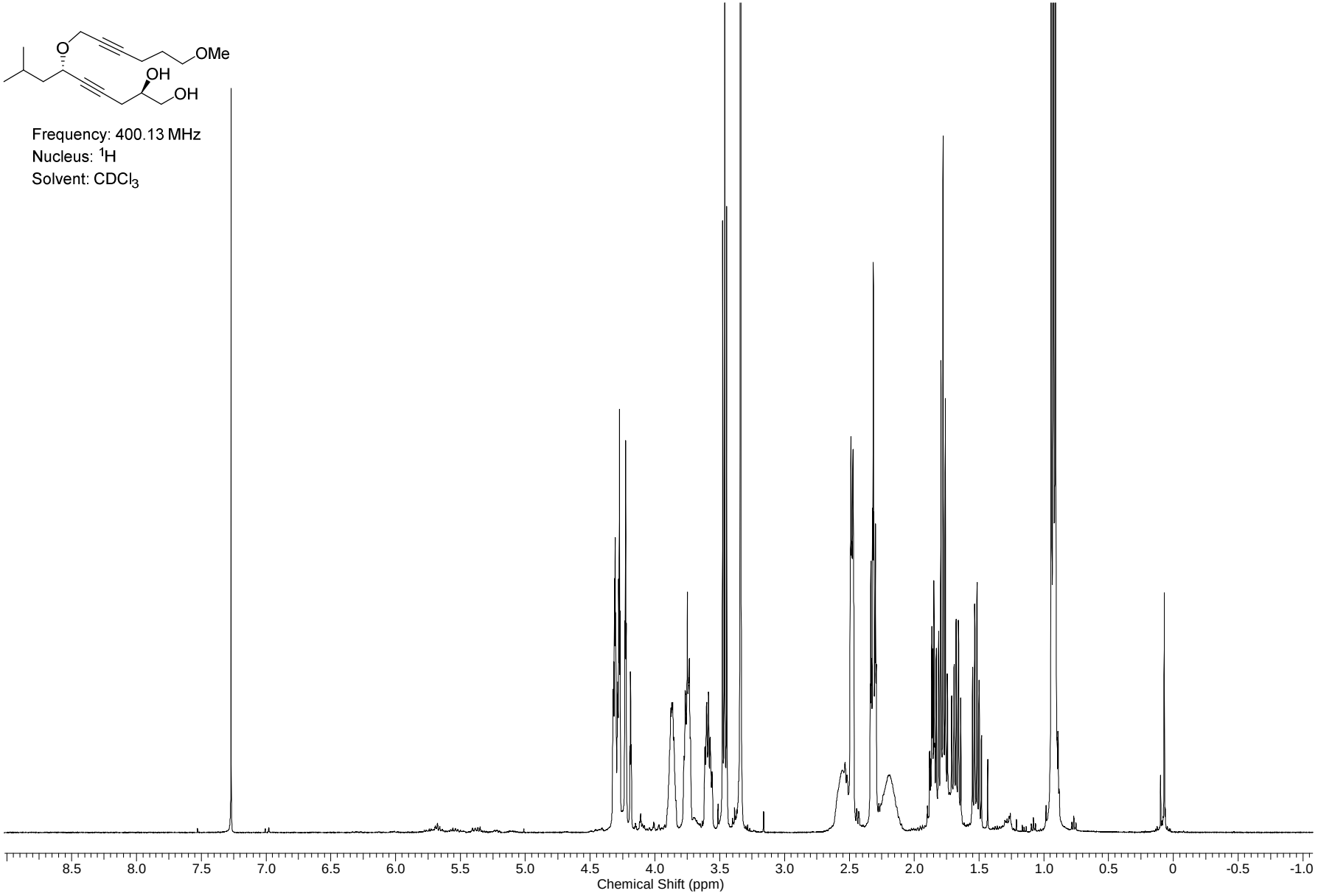

OMe
O
O
Ph
O
MeO
CF3
OTBS
NHTeoc
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CDCl3
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)

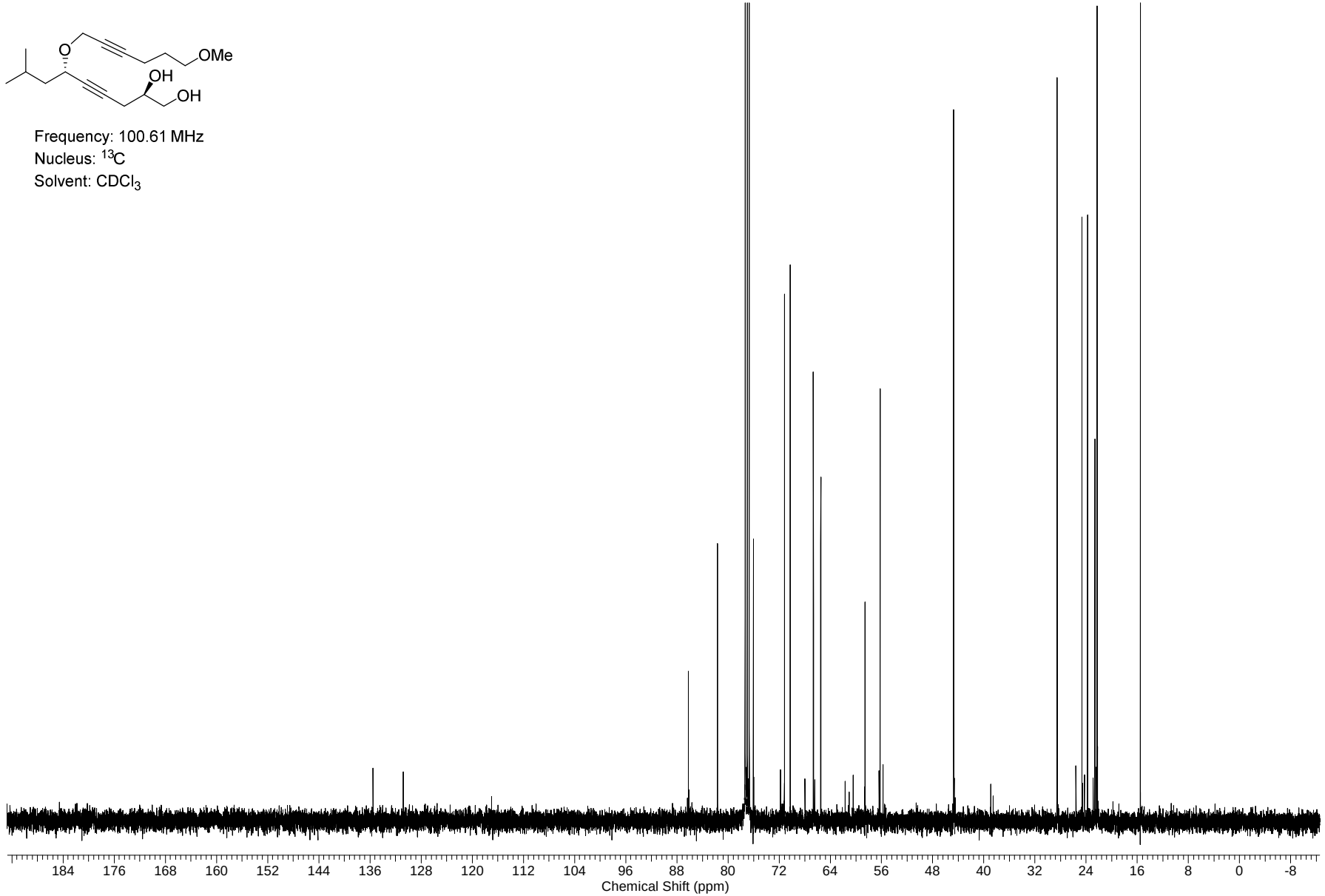

OMe
O
O
Ph
O
MeO
CF3
OTBS
NHTeoc
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)

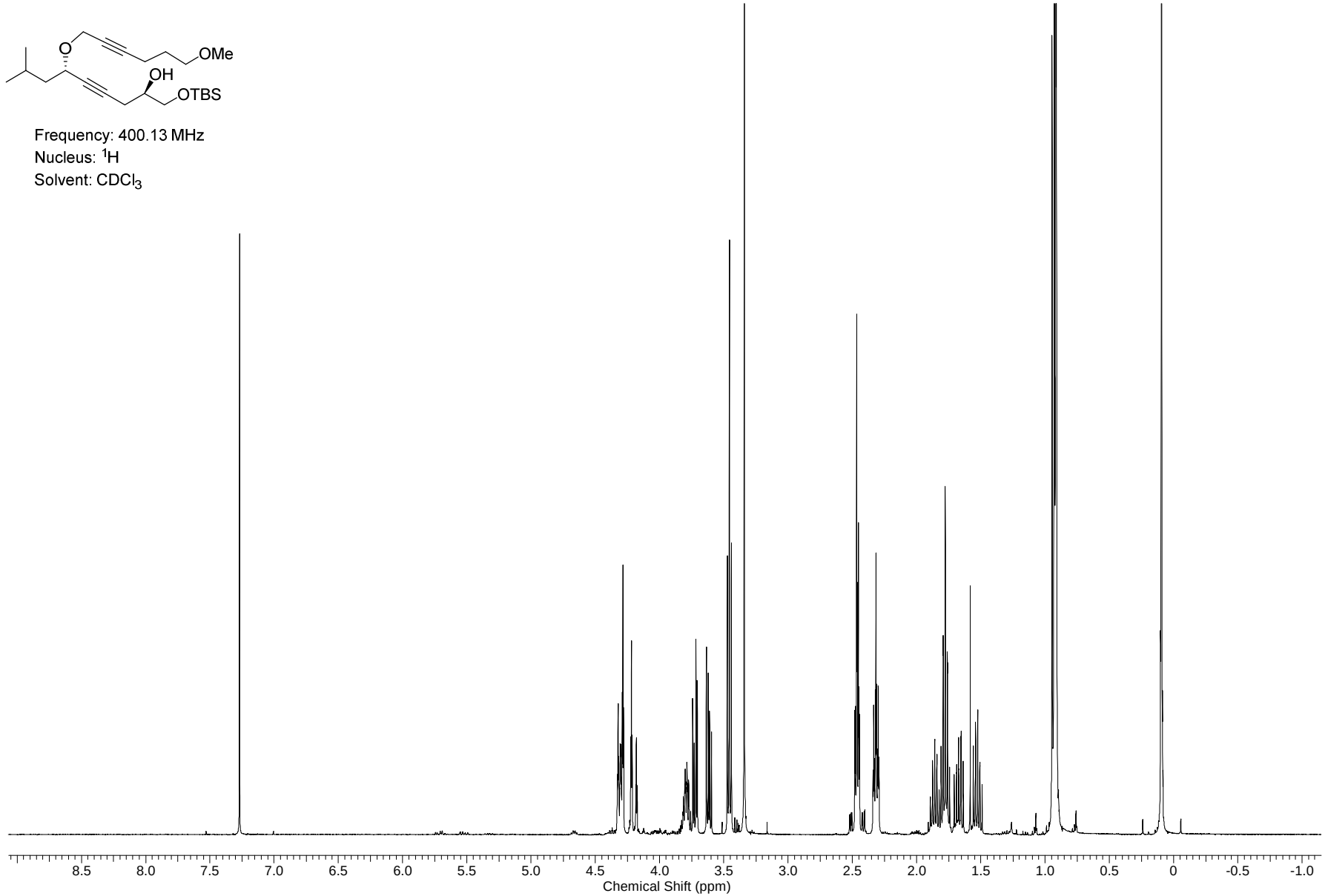

OMe
O
O
Ph
O
MeO
CF3
OTBS
NHTeoc
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CDCl3
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)

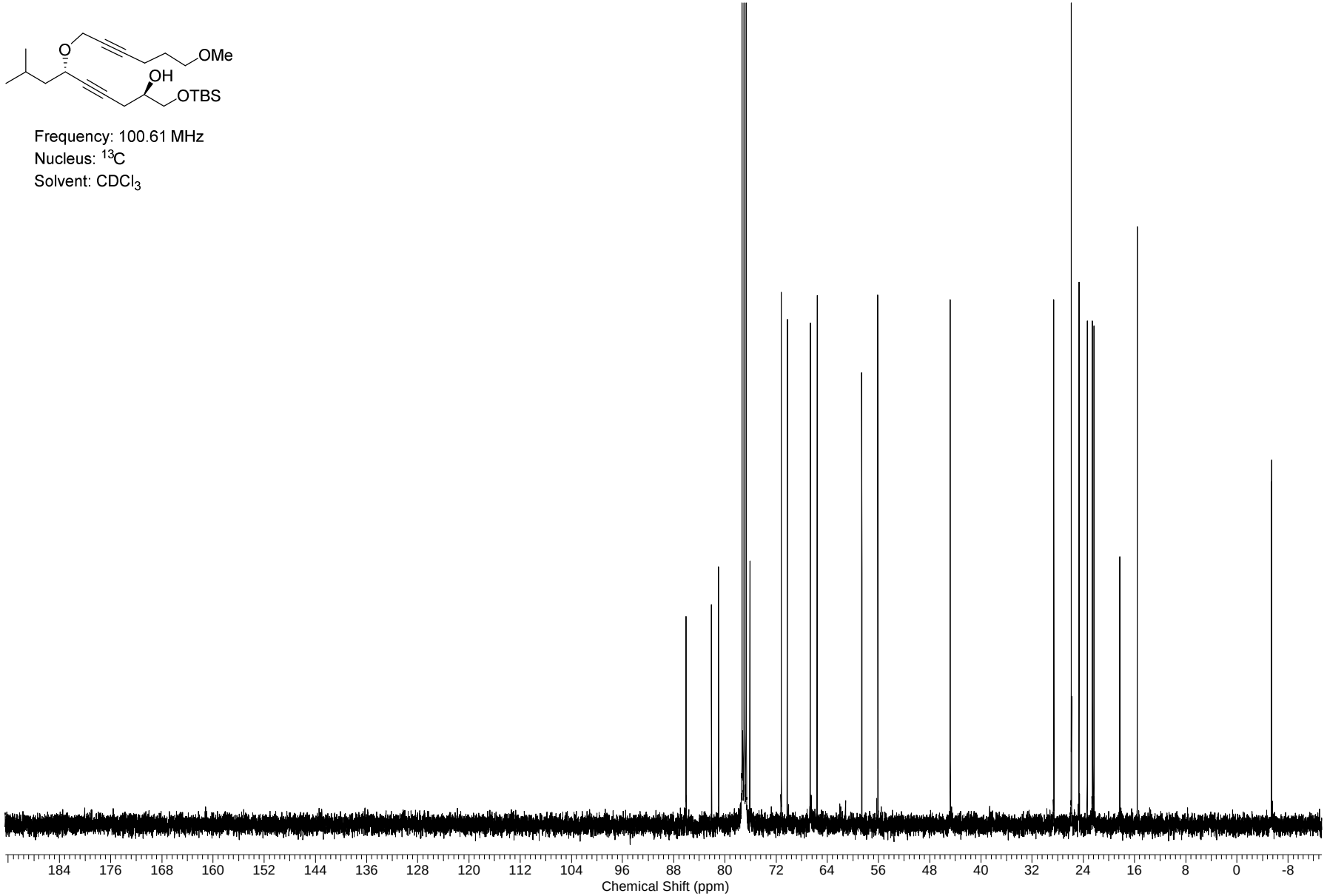


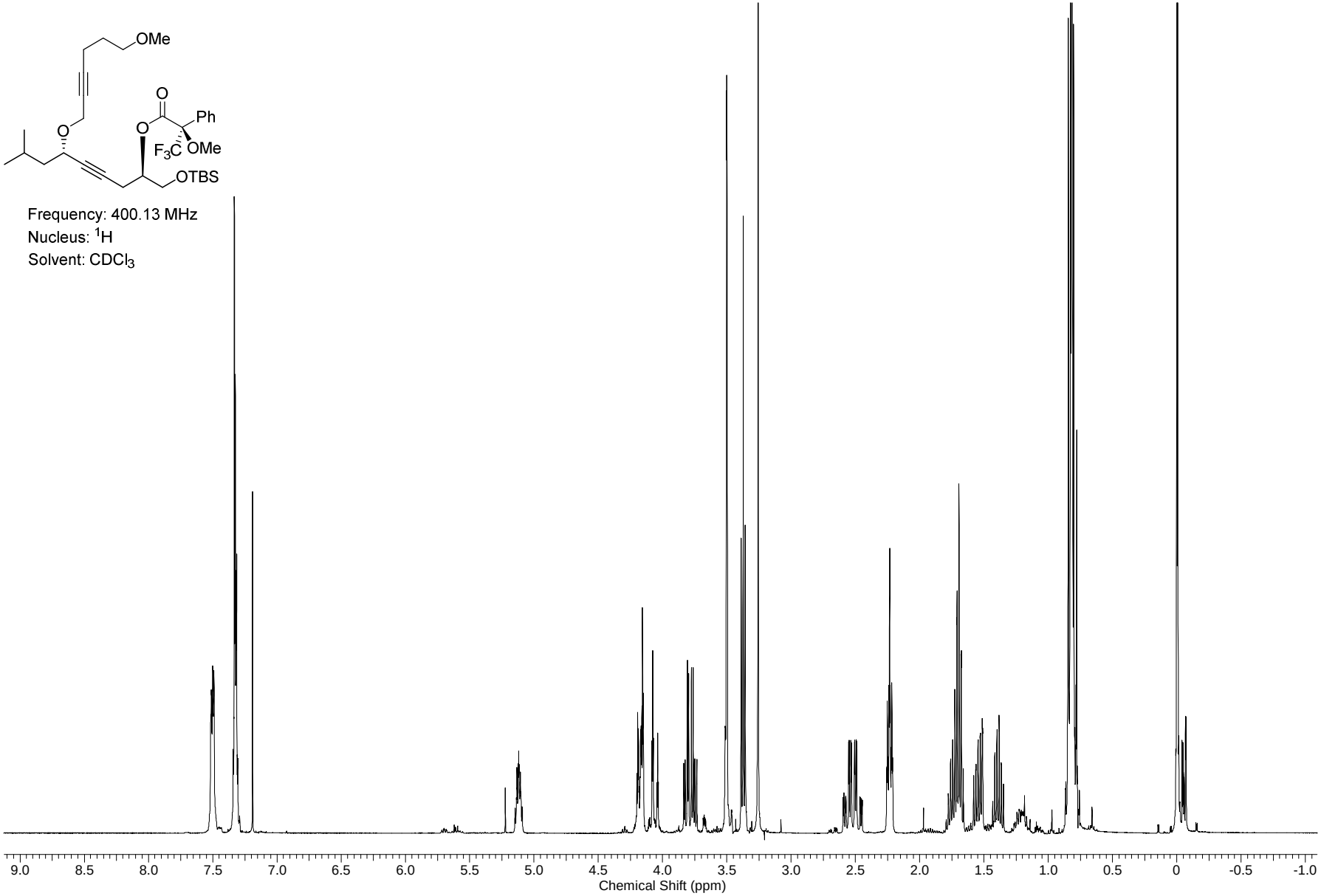
Frequency: 100.61 MHz
Nucleus: ^{13}C
Solvent: $CDCl_3$

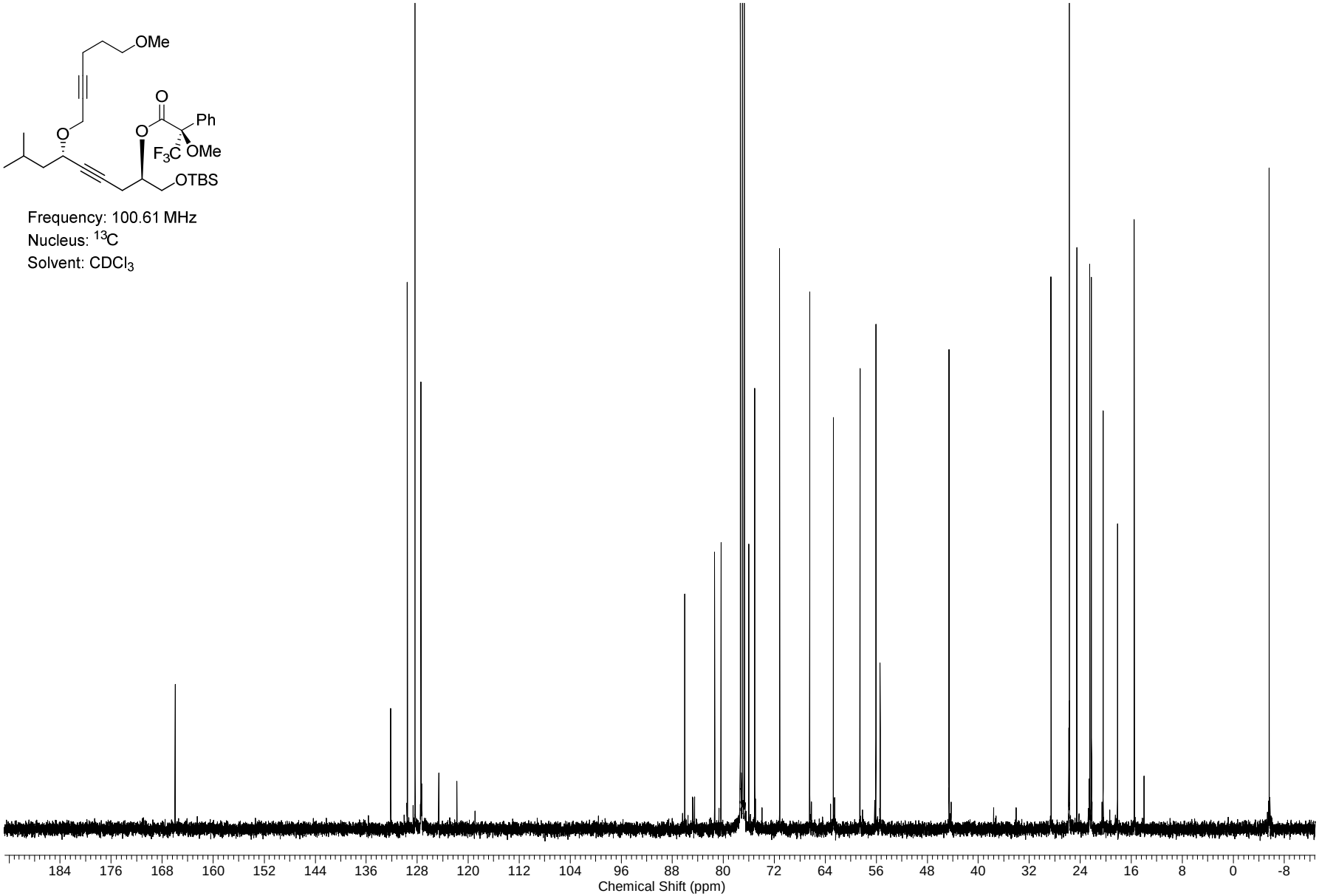

OMe
OH
OH
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CDCl3
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)

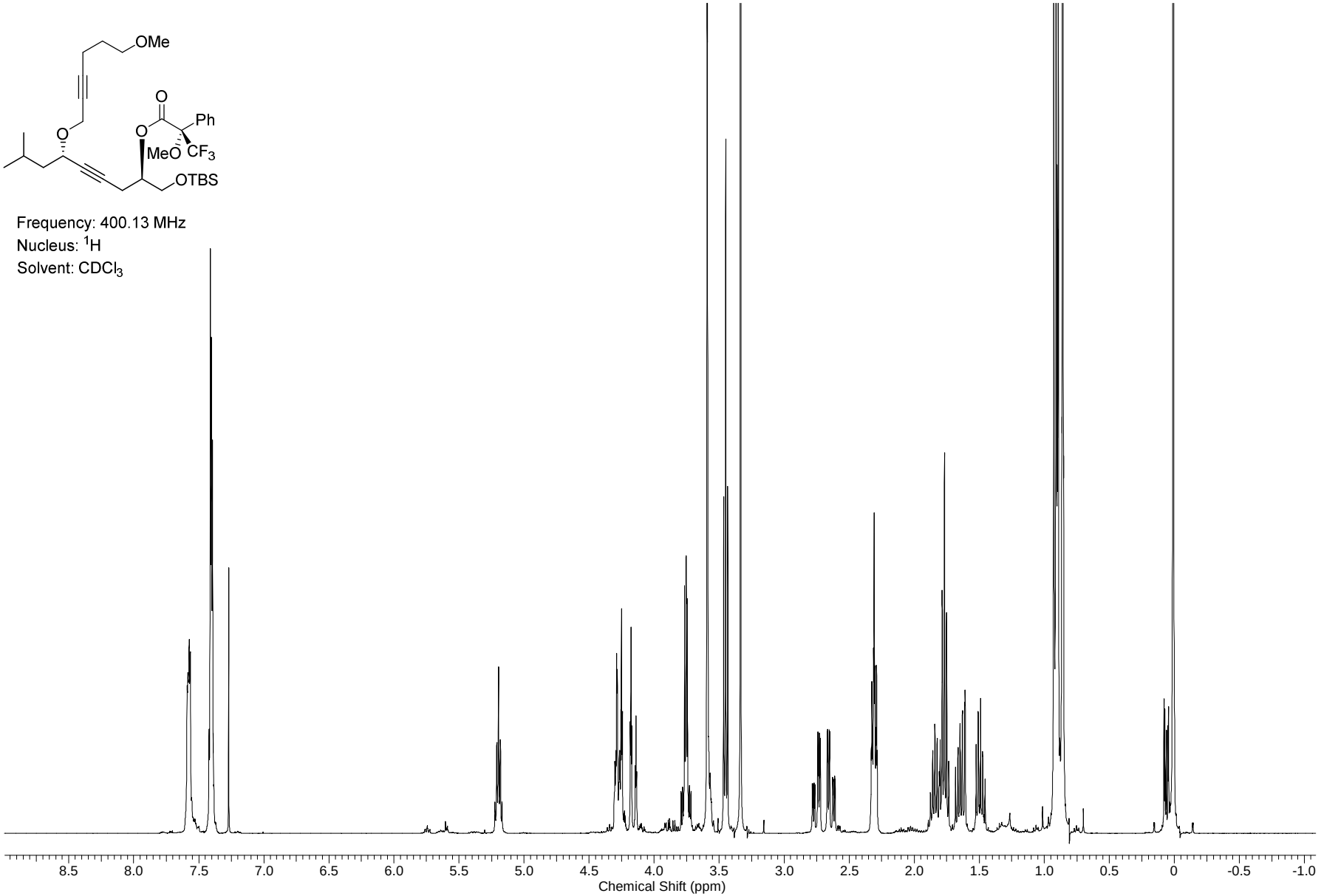

O
OMe
OH
OH
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

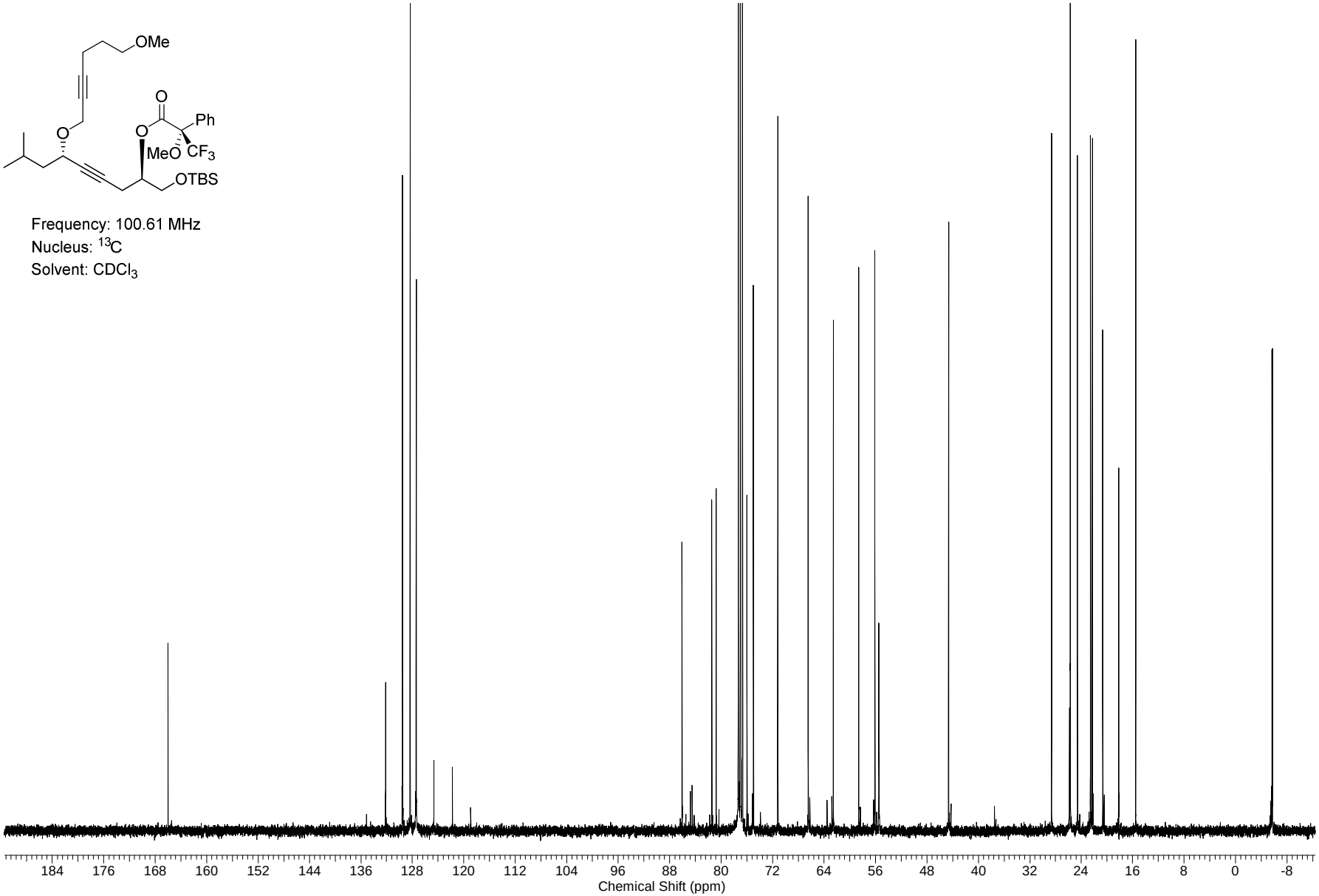

OMe
OH
OTBS
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CDCl3
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)

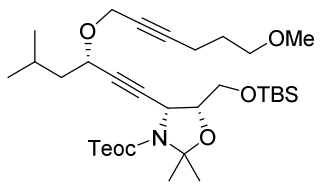

OMe
OH
OTBS
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)


OMe
O
Ph
O
O
F3C OMe
OTBS
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CDCl3
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
-0.5
-1.0
Chemical Shift (ppm)

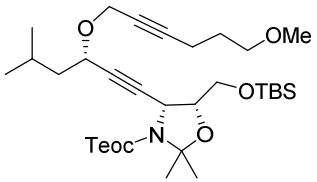

OMe
O
Ph
O
O
F3C OMe
OTBS
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)


OMe
O
O
Ph
O
MeO
CF3
OTBS
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CDCl3
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
-0.5
-1.0
Chemical Shift (ppm)

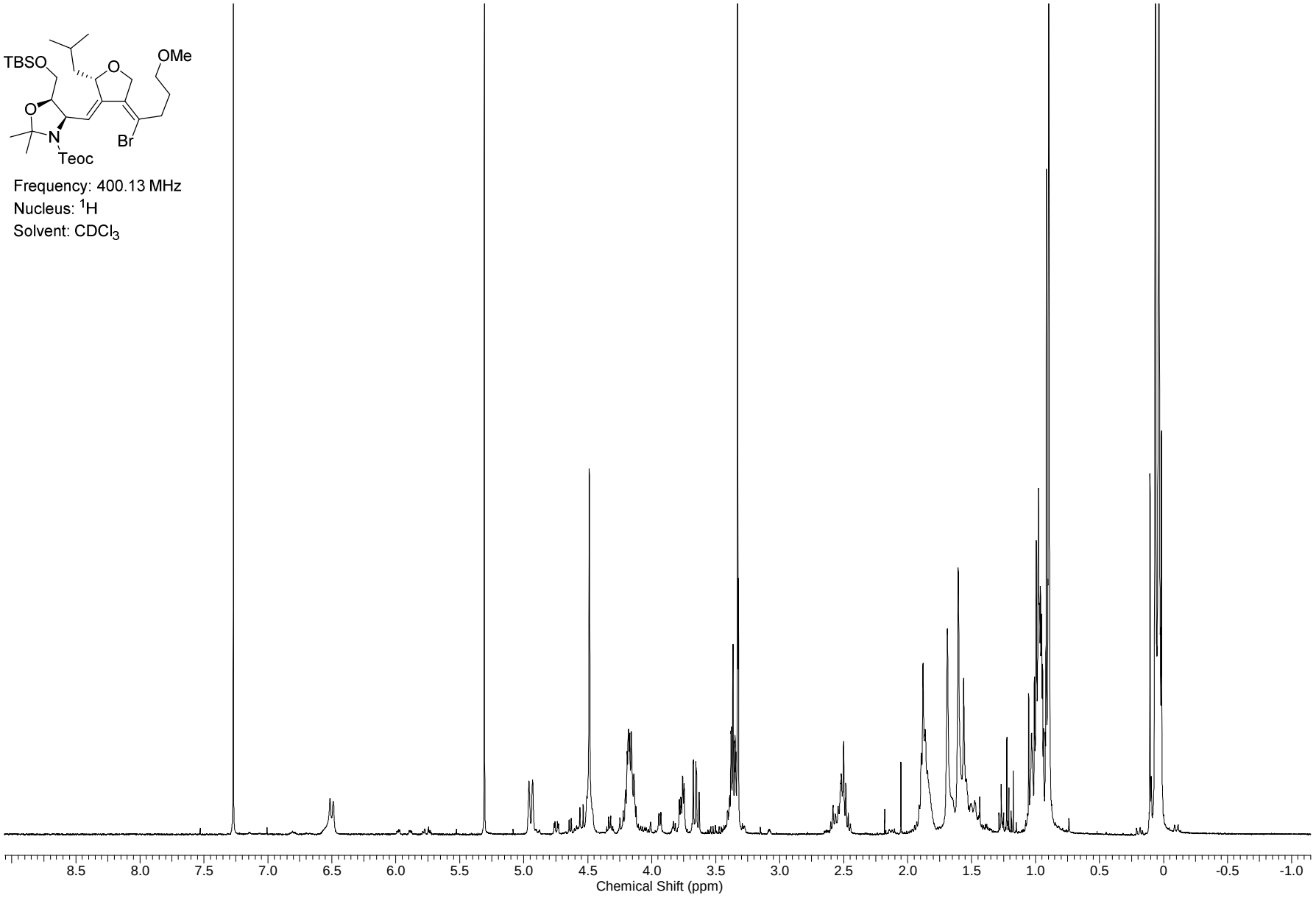

OMe
O
Ph
O
O
MeO
CF3
OTBS
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

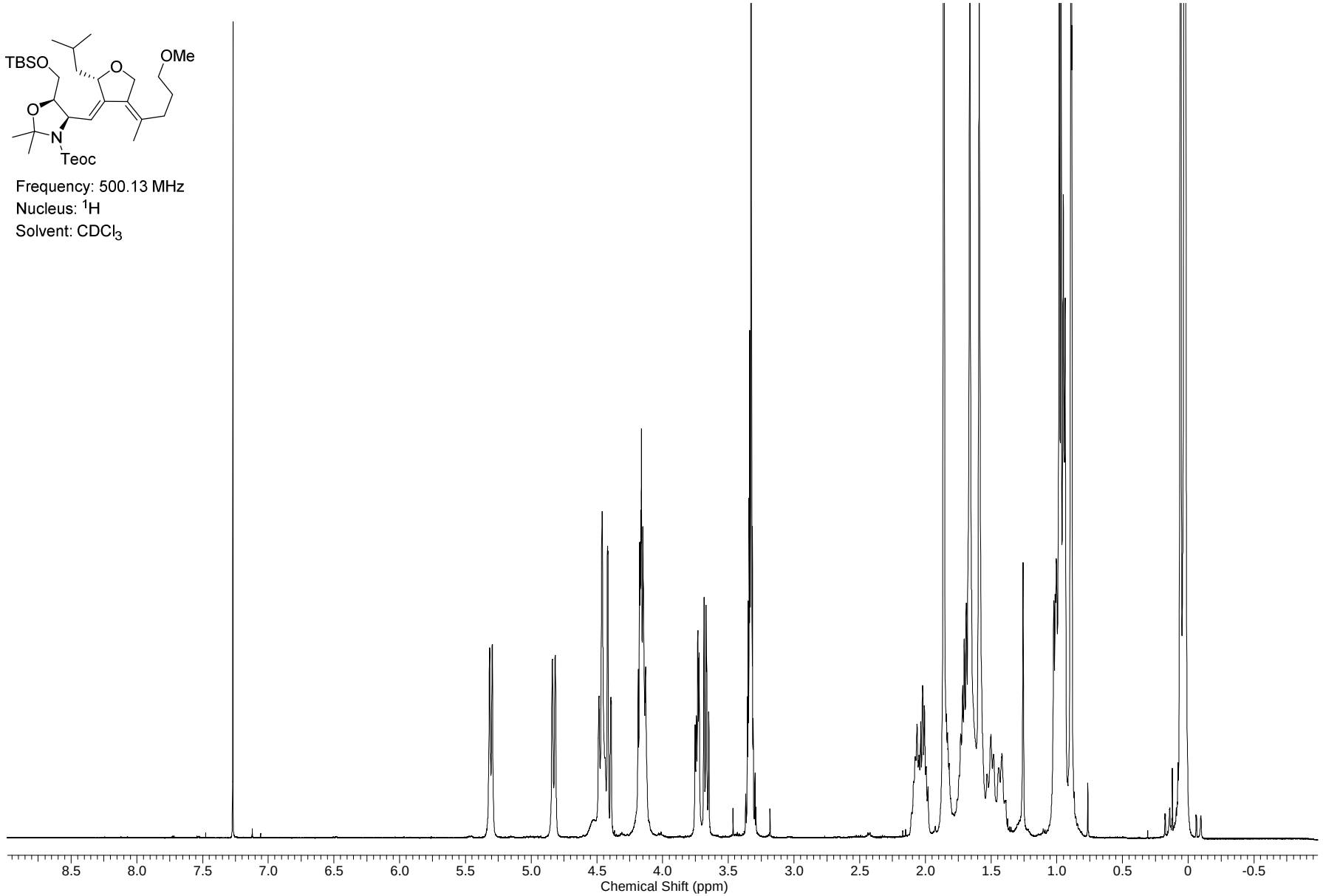


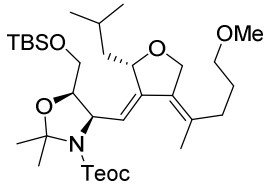
Frequency: 500.13 MHz
Nucleus: ^{1}H
Solvent: CD_2Cl_2



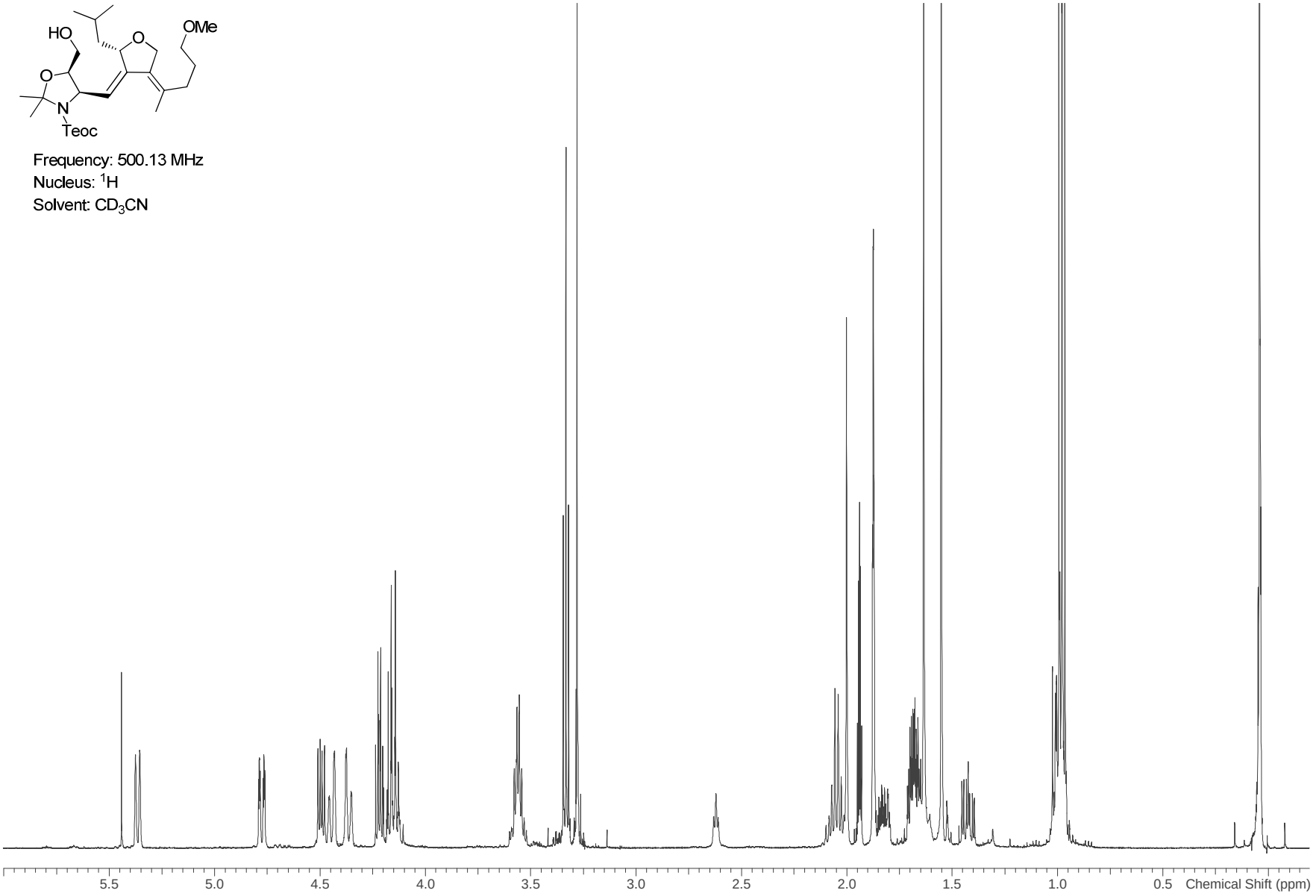
Frequency: 125.76 MHz
Nucleus: ^{13}C
Solvent: CD_2Cl_2

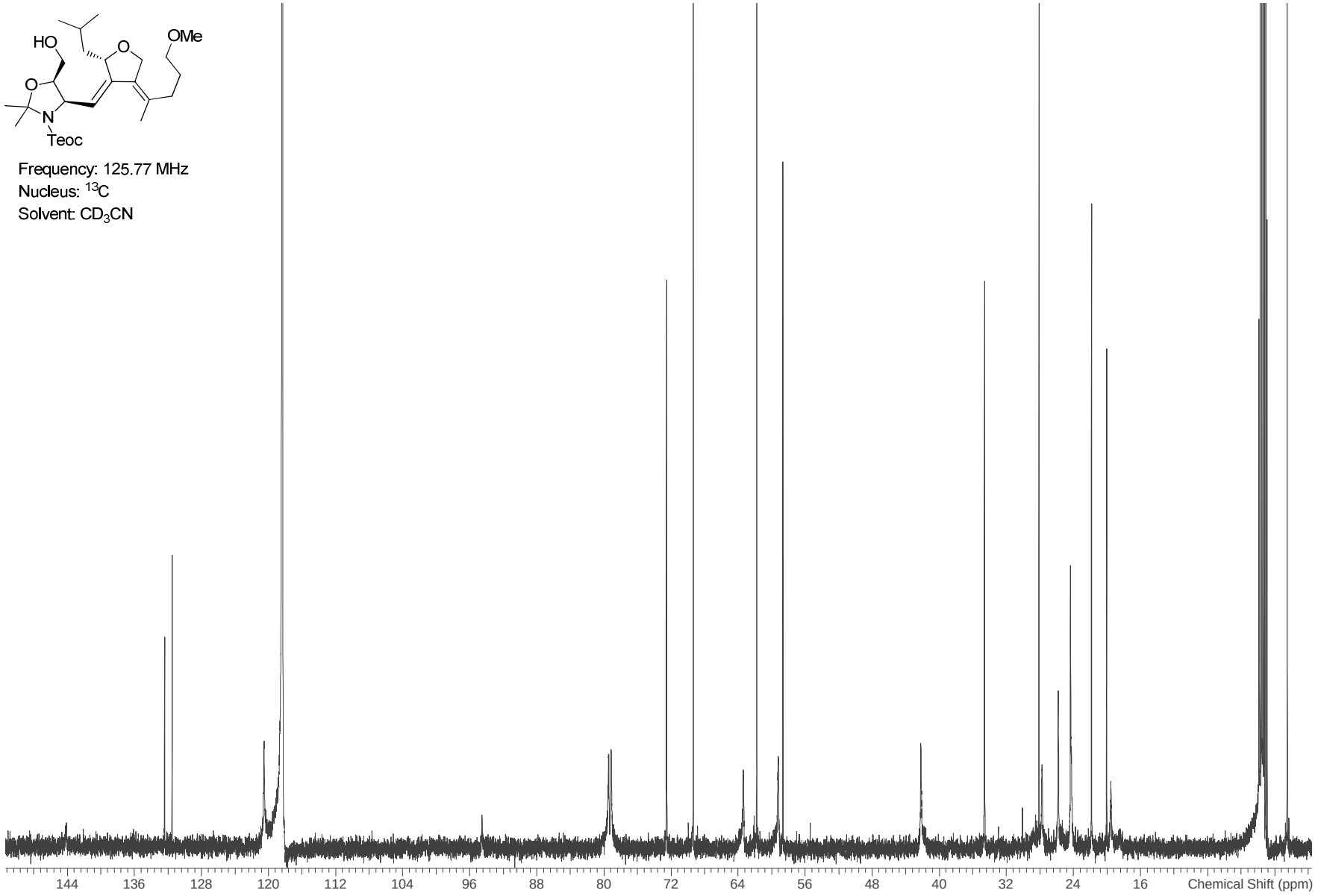

TBSO
O
OMe
O
N
Br
Teoc
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CDCl3
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)

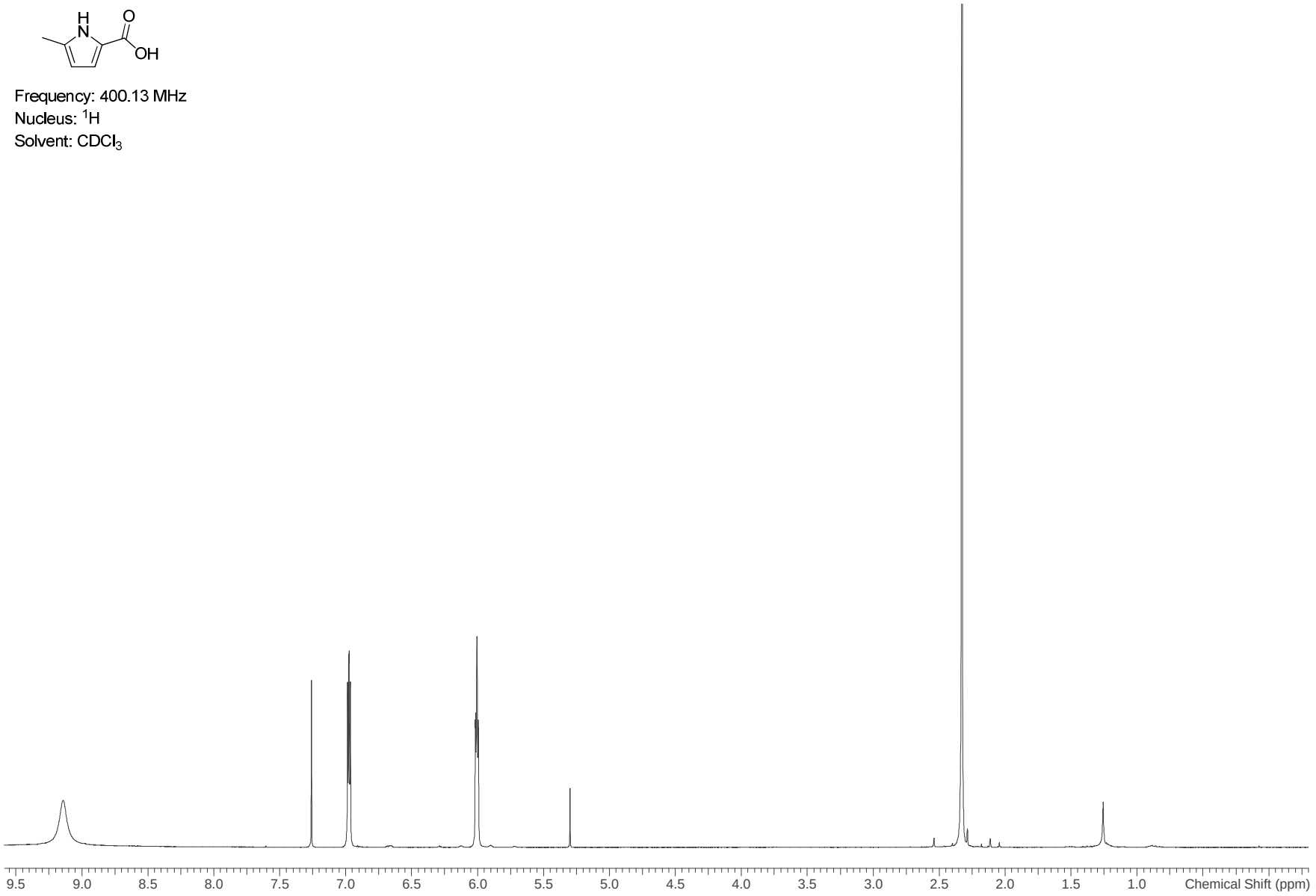

TBSO
O
OMe
O
N
Teoc
Frequency: 500.13 MHz
Nucleus: 1H
Solvent: CDCl3
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
Chemical Shift (ppm)

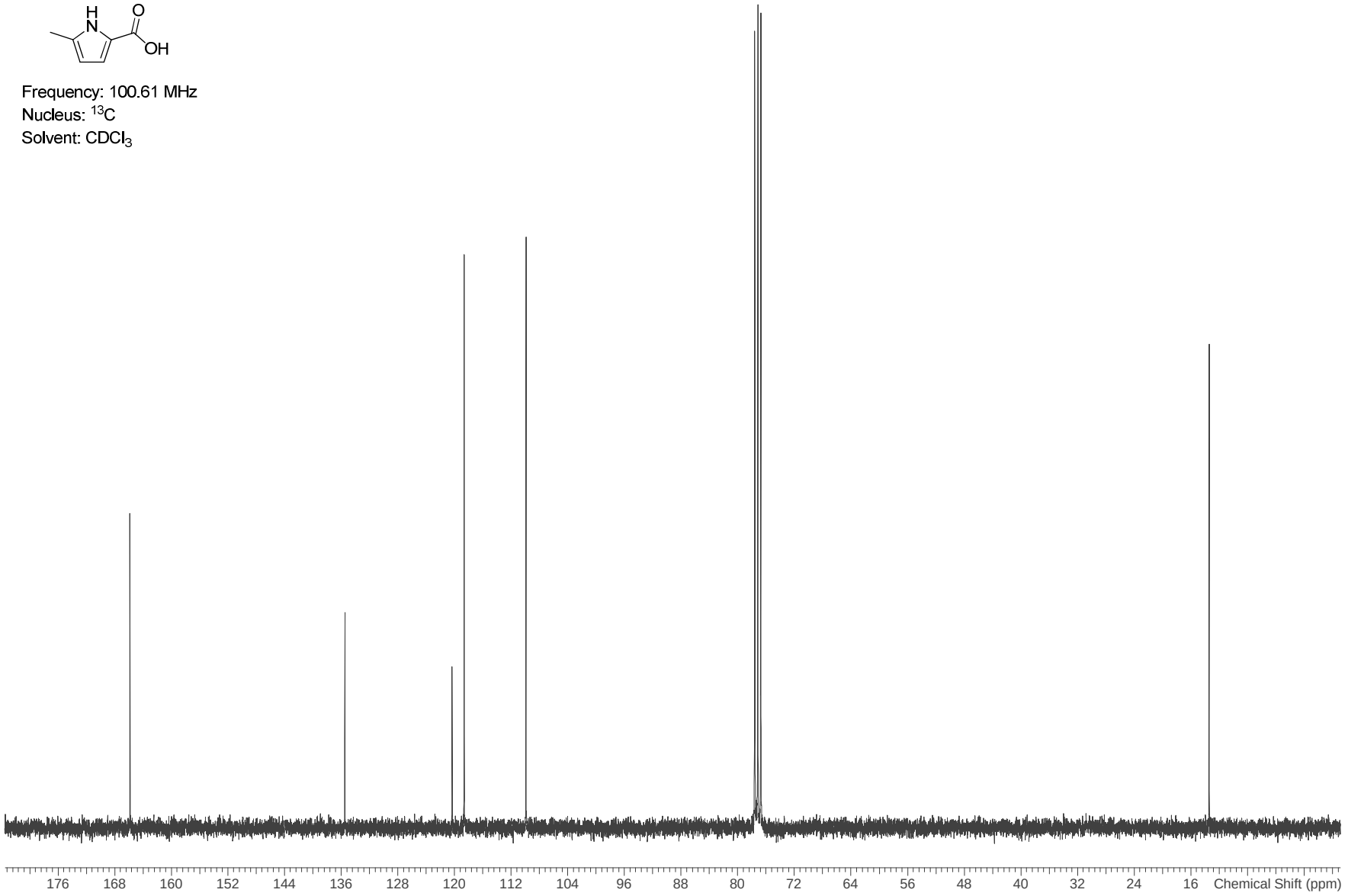


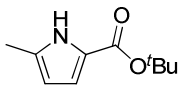
Frequency: 125.76 MHz
Nucleus: ^{13}C
Solvent: $CDCl_3$


HO
O
OMe
O
N
Teoc
Frequency: 500.13 MHz
Nucleus: 1H
Solvent: CD3CN
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

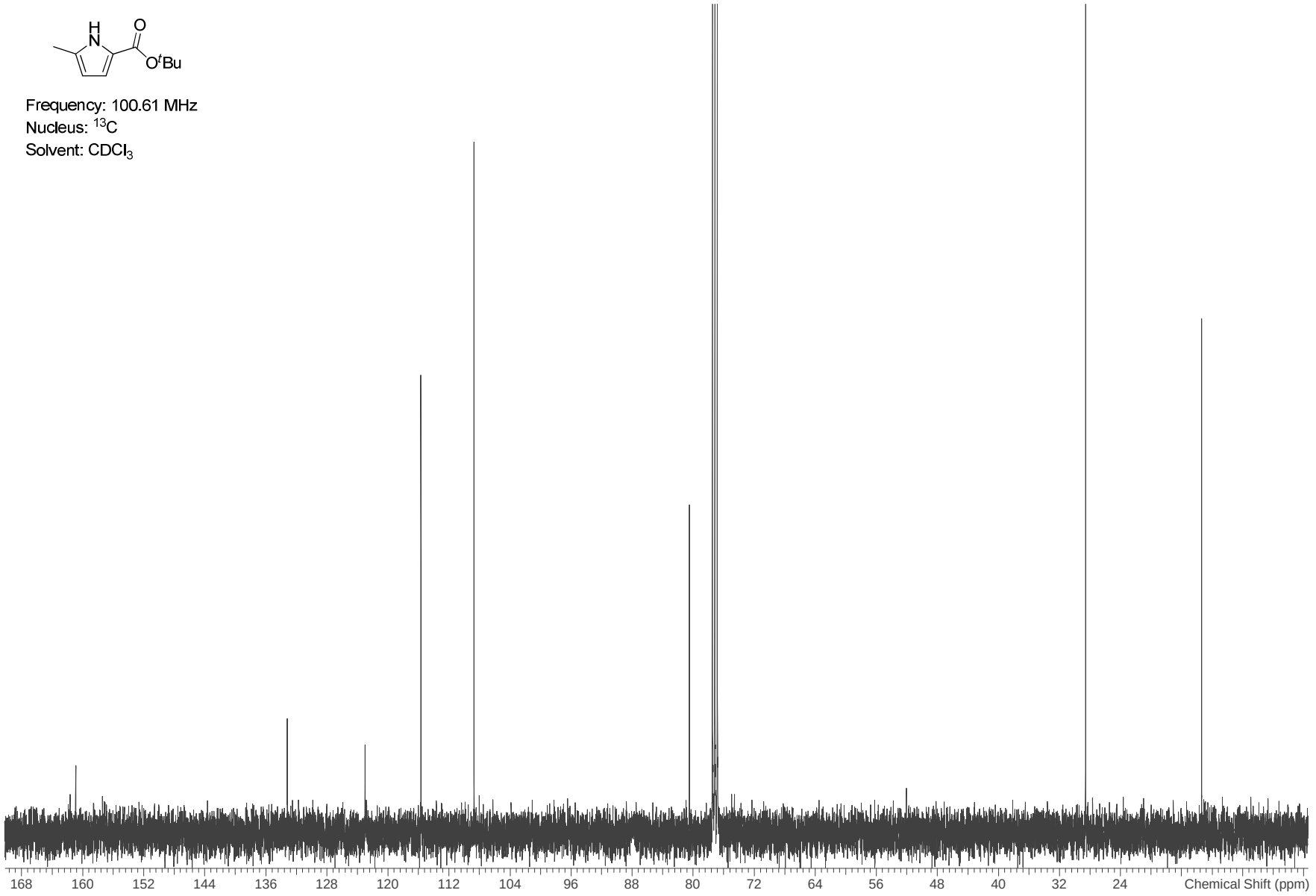

HO
O
OMe
O
N
Teoc
Frequency: 125.77 MHz
Nucleus: 13C
Solvent: CD3CN
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)

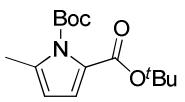

H
N
O
OH
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CDCl3
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


H
N
O
OH
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)

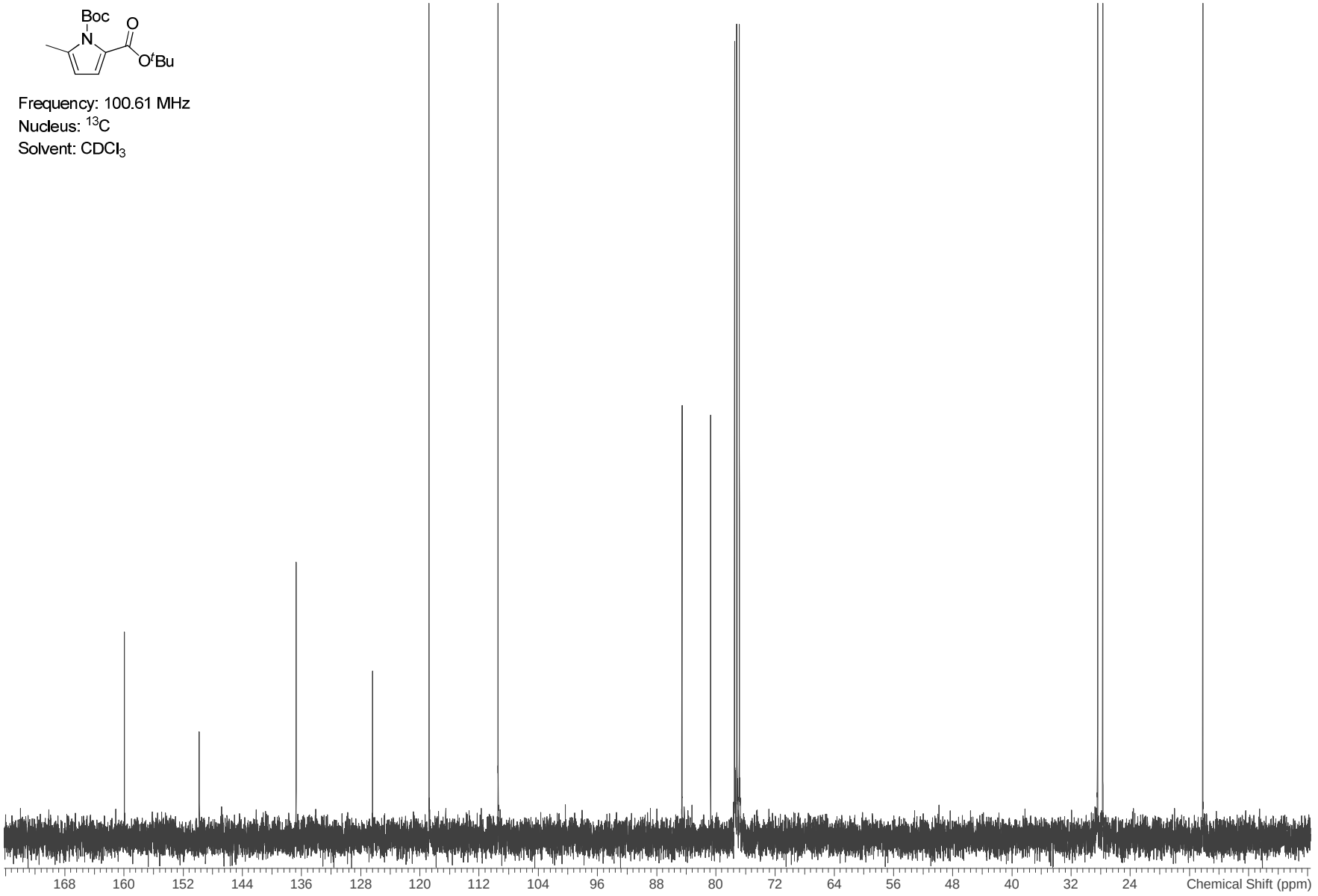


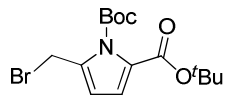
Frequency: 400.13 MHz
Nucleus: ^{1}H
Solvent: $CDCl_3$


H
N
O
O^{t}Bu
Frequency: 100.61 MHz
Nucleus: ^{13}C
Solvent: $CDCl_3$
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)

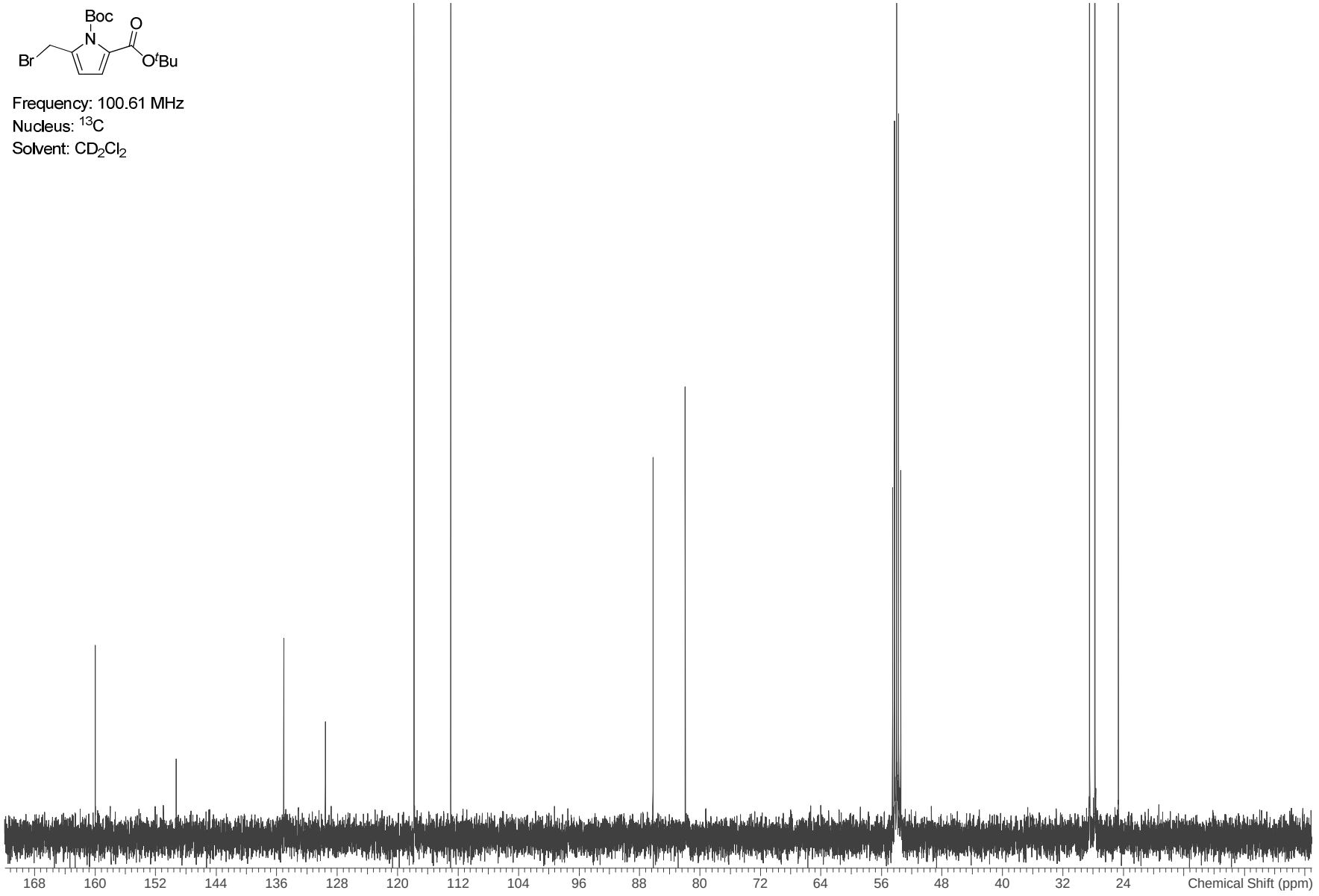


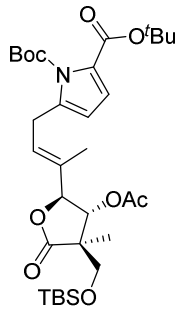
Frequency: 400.13 MHz
Nucleus: ^{1}H
Solvent: $CDCl_3$


Boc
N
O
O^{t}Bu
Frequency: 100.61 MHz
Nucleus: ^{13}C
Solvent: $CDCl_3$
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)

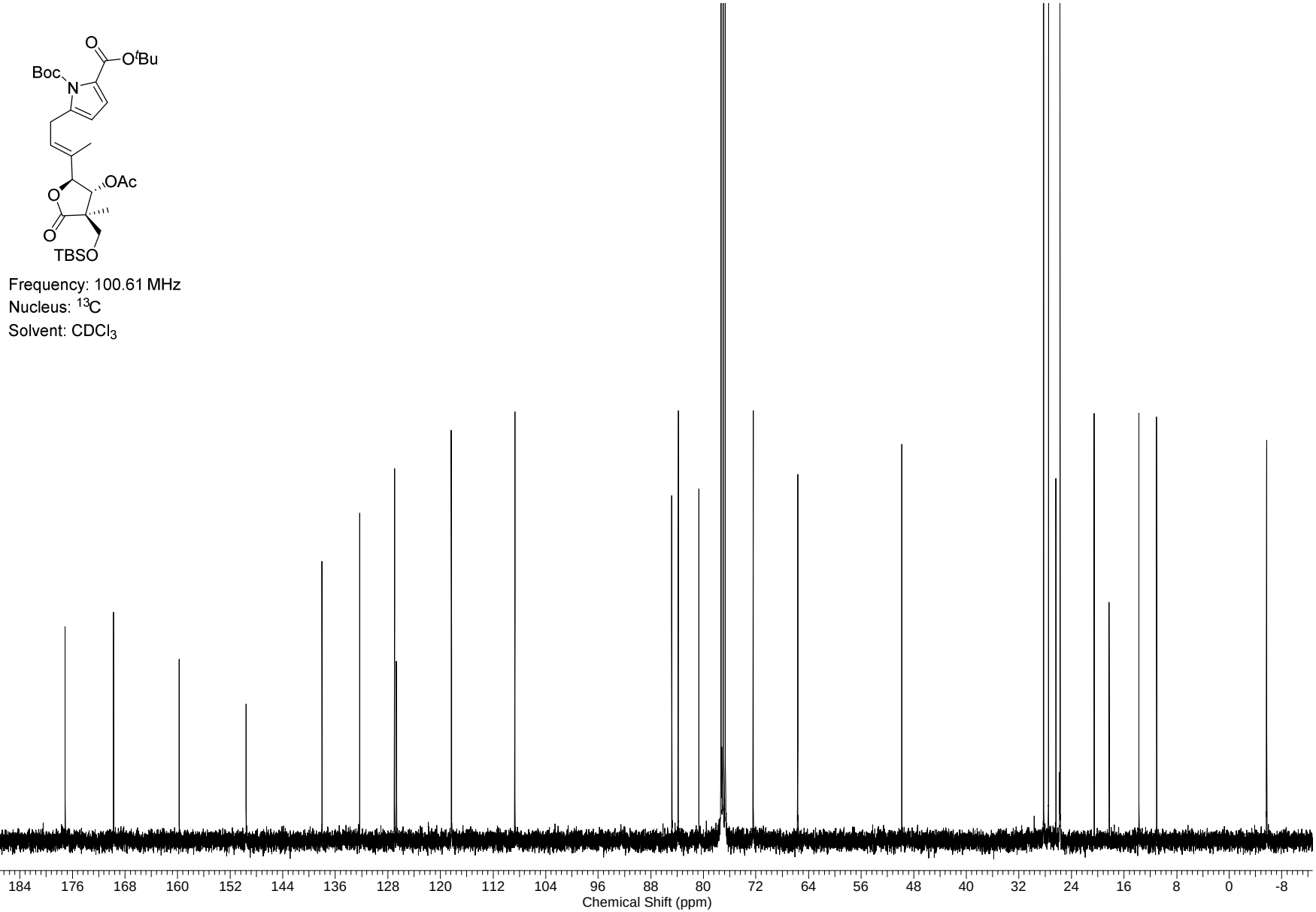


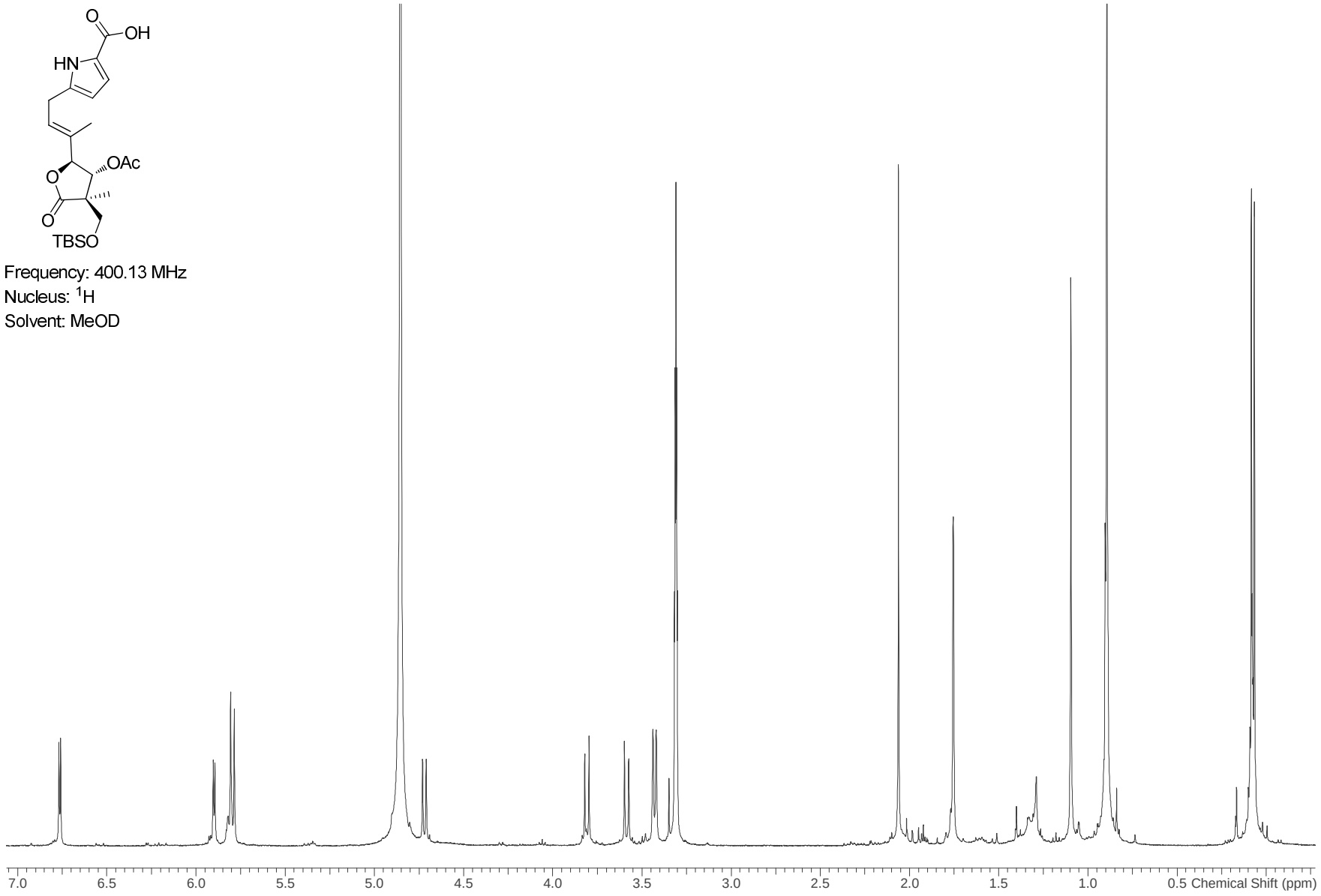
Frequency: 400.13 MHz
Nucleus: ^{1}H
Solvent: CD_2Cl_2

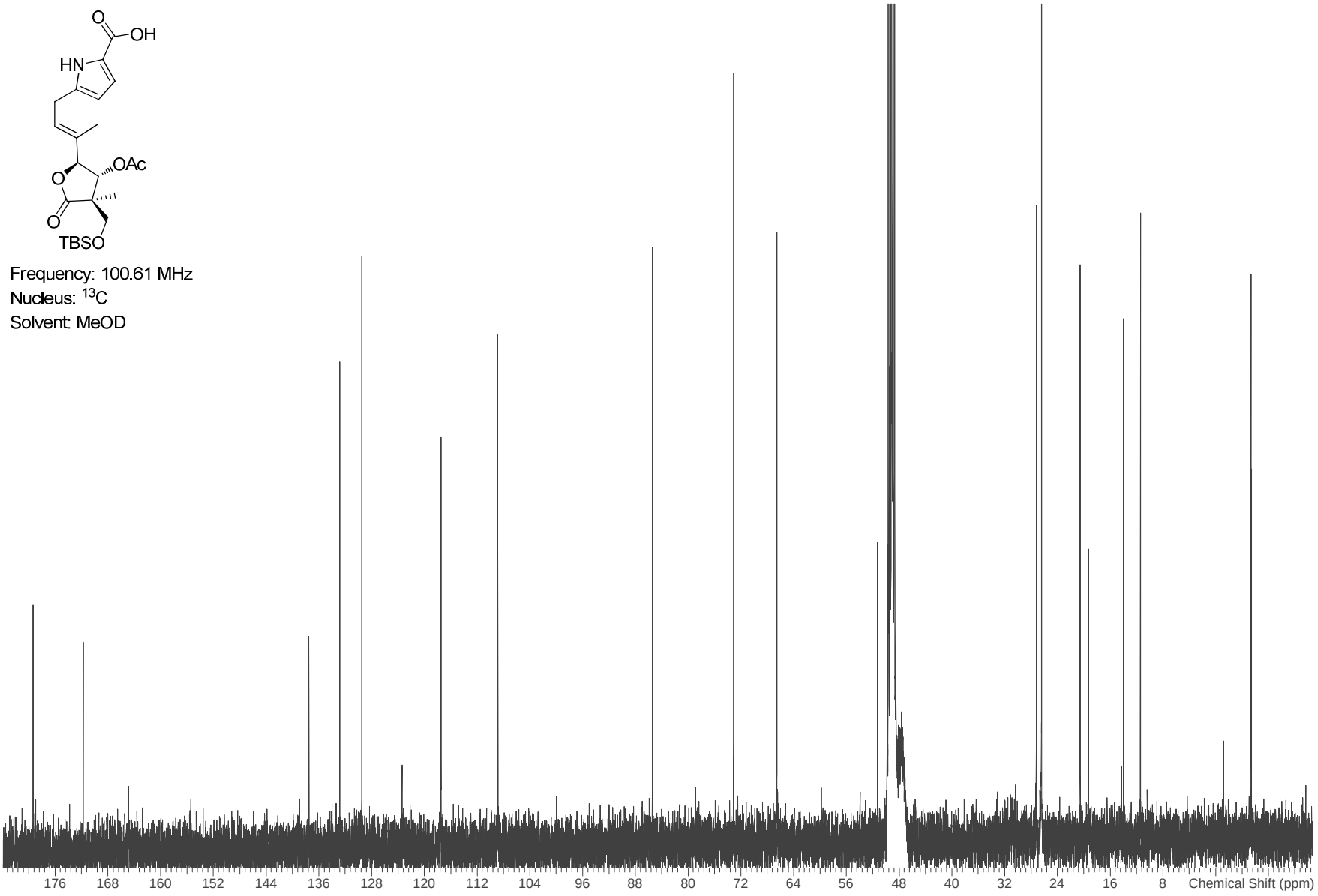

Boc
O
N
Br
O^{t}Bu
Frequency: 100.61 MHz
Nucleus: ^{13}C
Solvent: CD_2Cl_2
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)

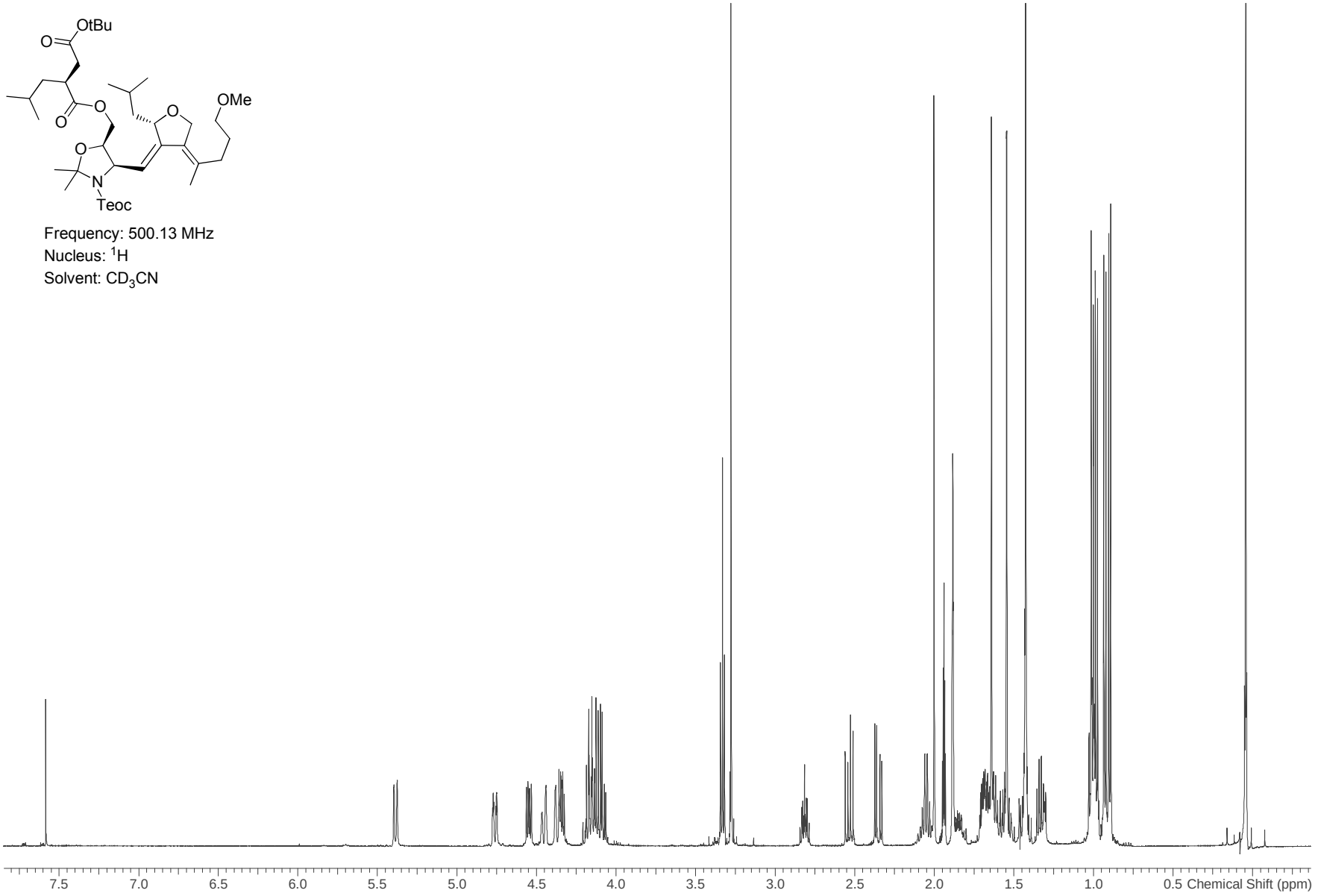


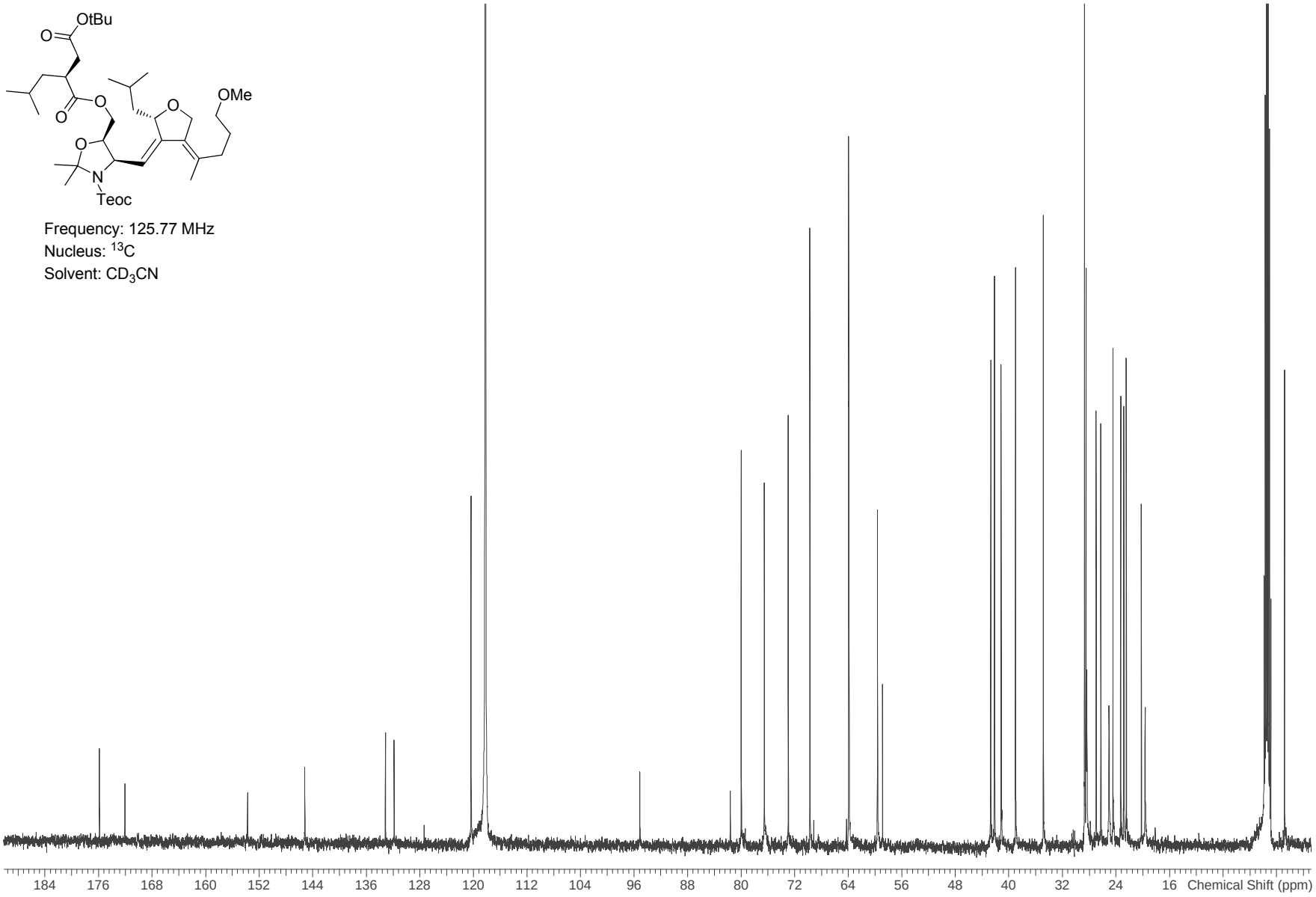
Frequency: 400.13 MHz
Nucleus: ^{1}H
Solvent: $CDCl_3$

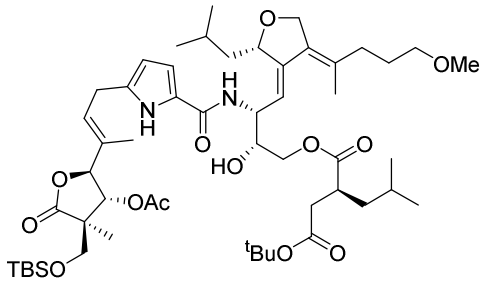

Boc
N
O
O
tBu
OAc
O
O
TBSO
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CDCl3
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)


O
OH
HN
OAc
O
O
TBSO
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: MeOD
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 Chemical Shift (ppm)

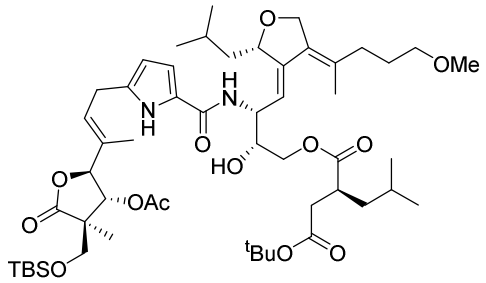

O
OH
HN
OAc
O
O
TBSO
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: MeOD
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)


OtBu
O
O
O
O
O
O
OMe
N
Teoc
Frequency: 500.13 MHz
Nucleus: 1H
Solvent: CD3CN
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 Chemical Shift (ppm)

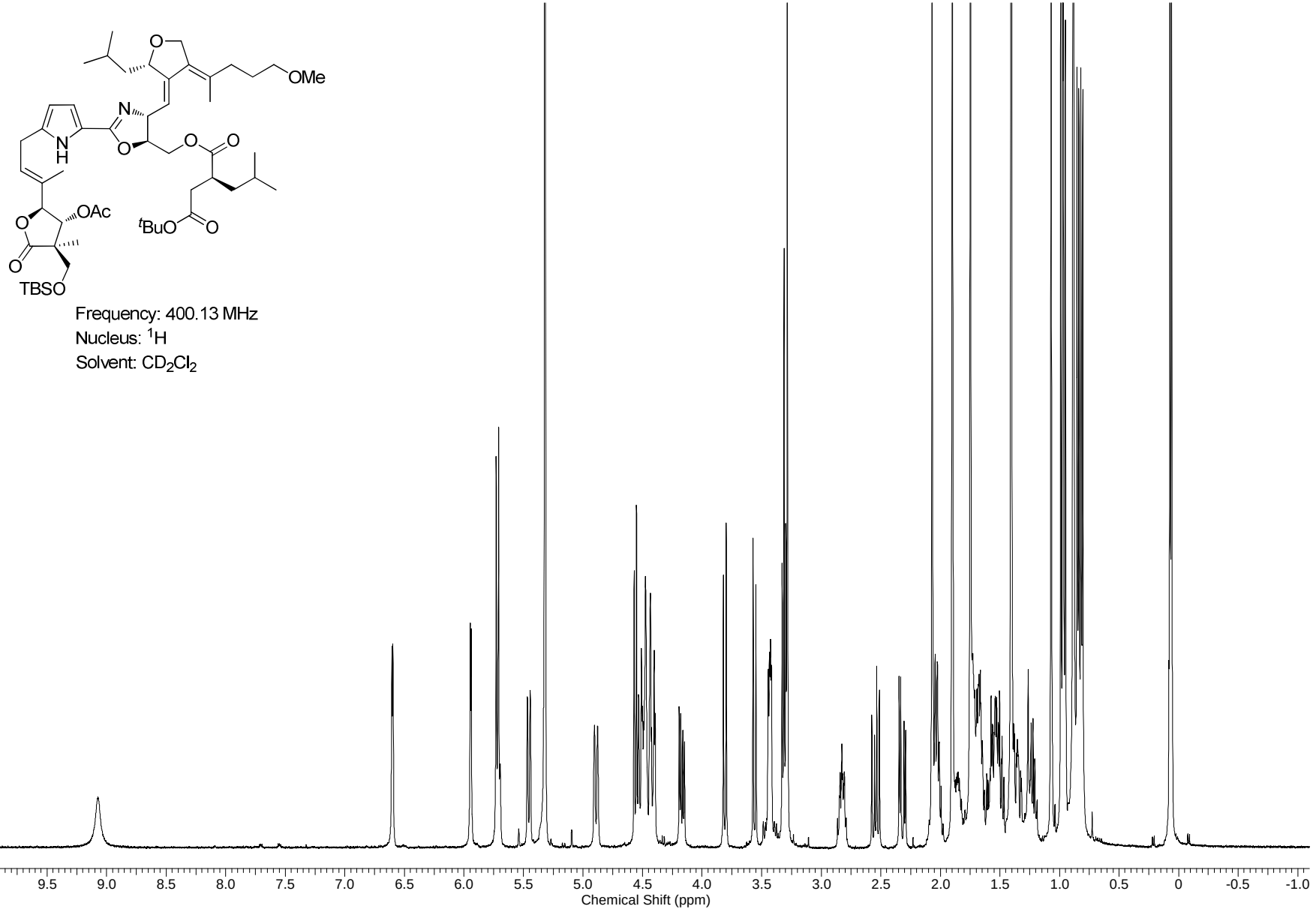

OtBu
O
O
O
O
O
OMe
N
Teoc
Frequency: 125.77 MHz
Nucleus: 13C
Solvent: CD3CN
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)

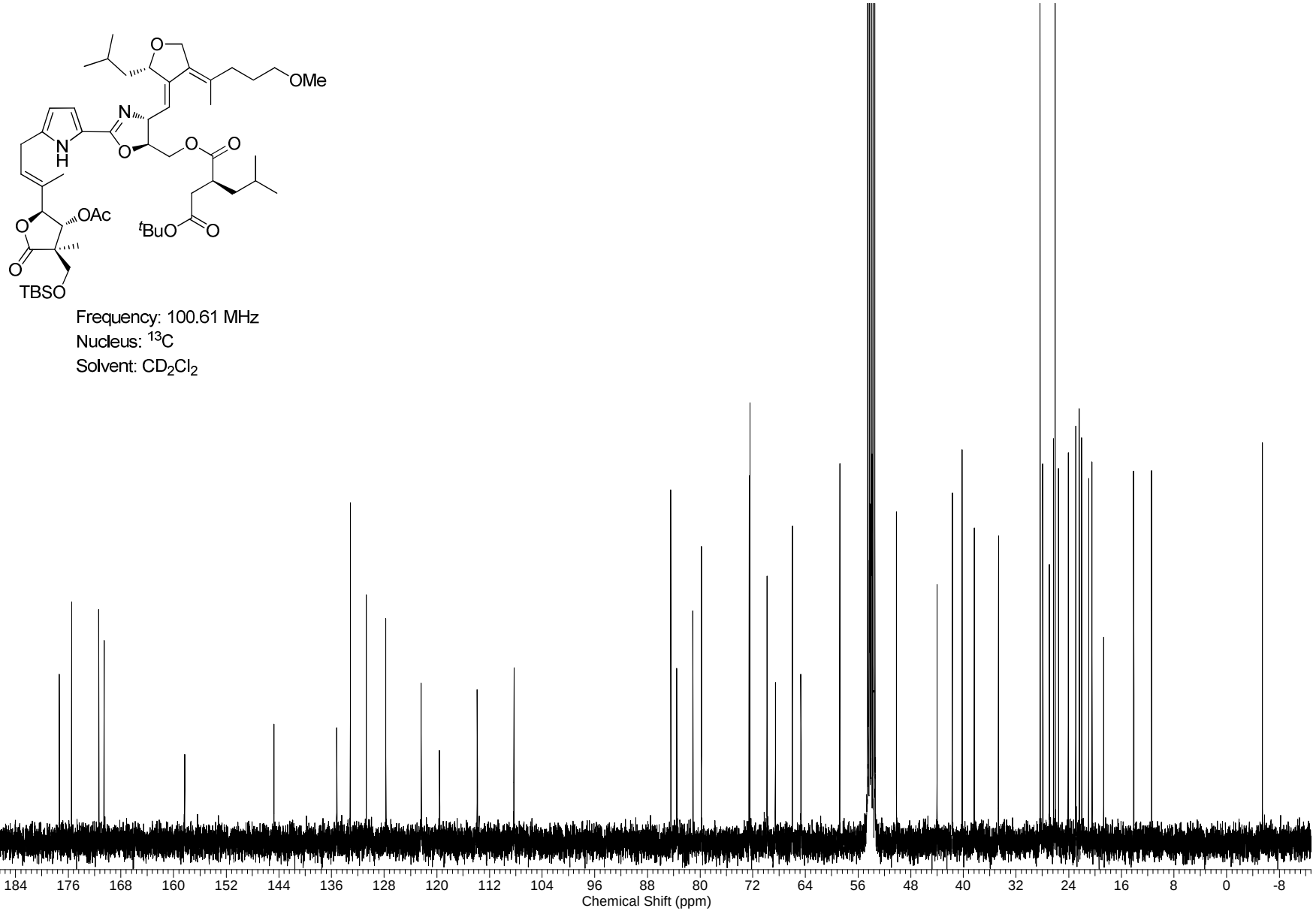


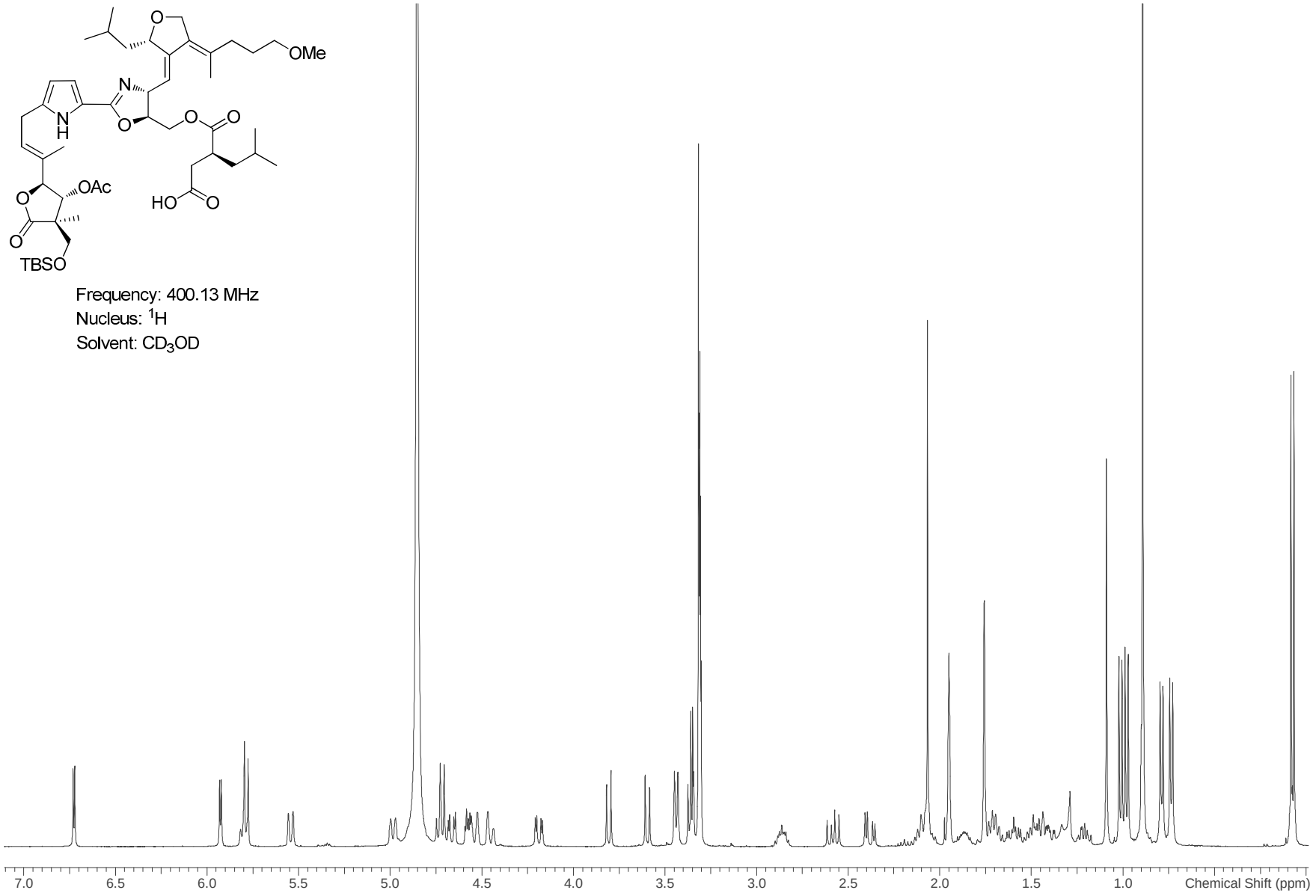
Frequency: 400.13 MHz
Nucleus: ^{1}H
Solvent: CD_2Cl_2

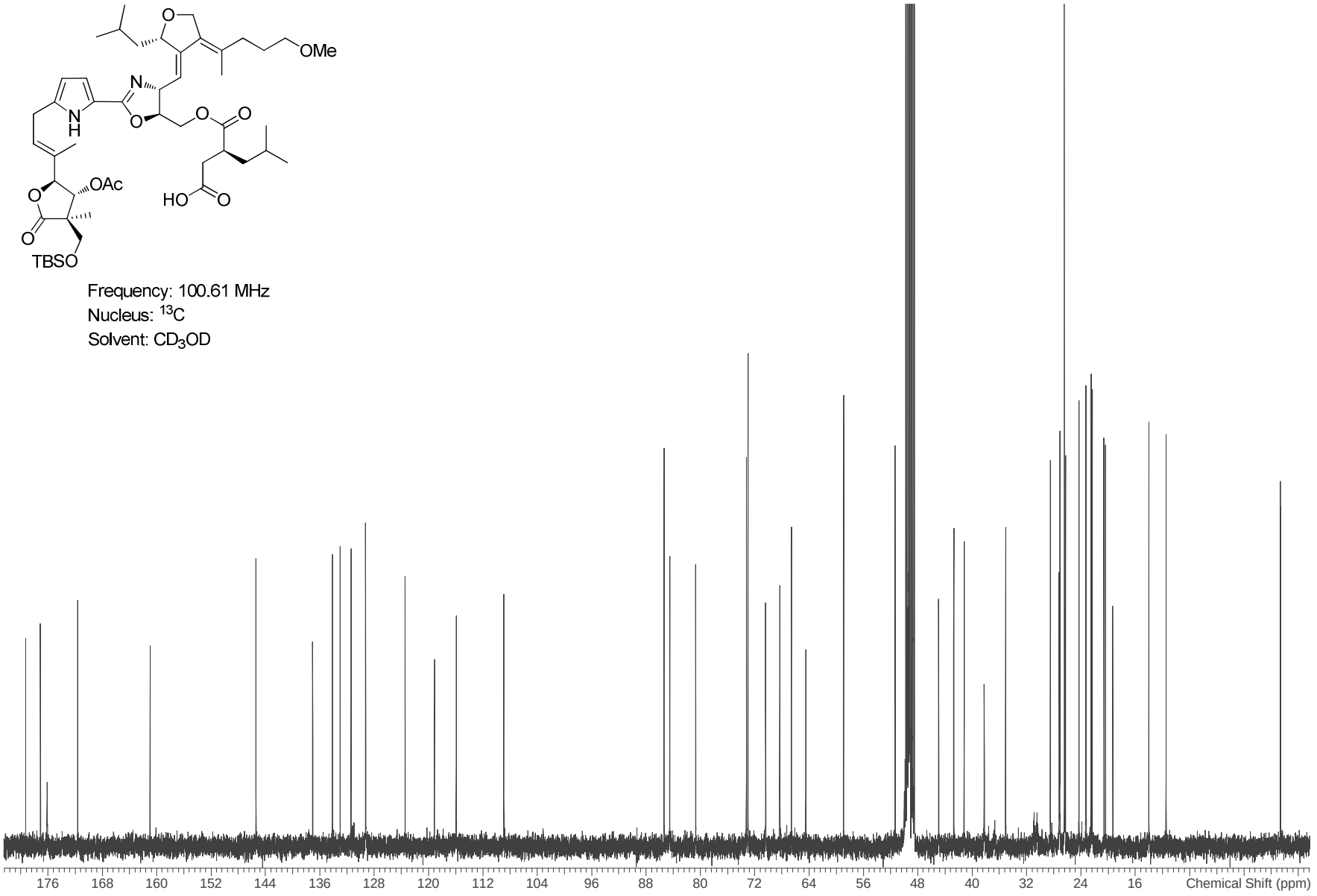


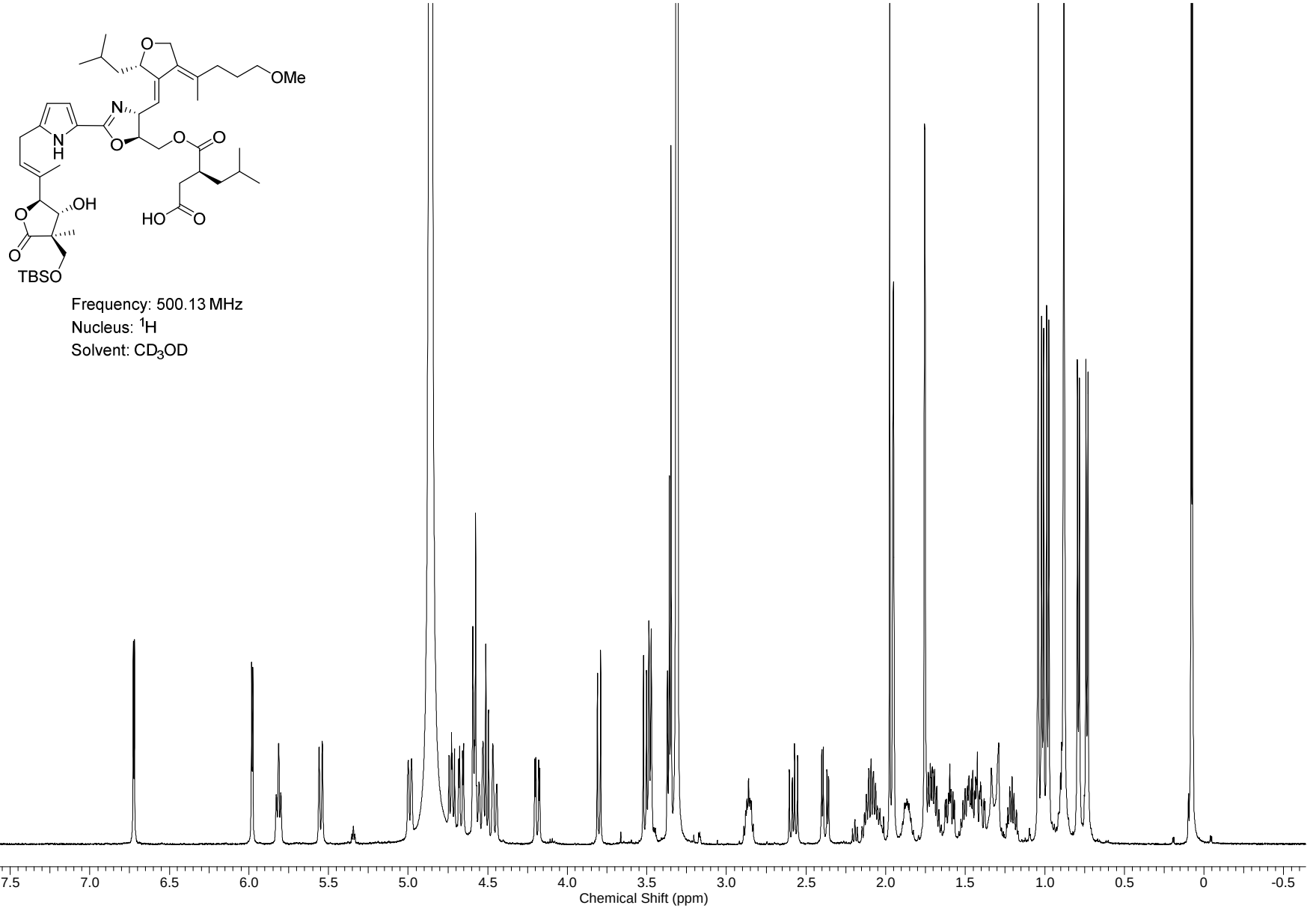
Frequency: 100.61 MHz
Nucleus: ^{13}C
Solvent: CD_2Cl_2

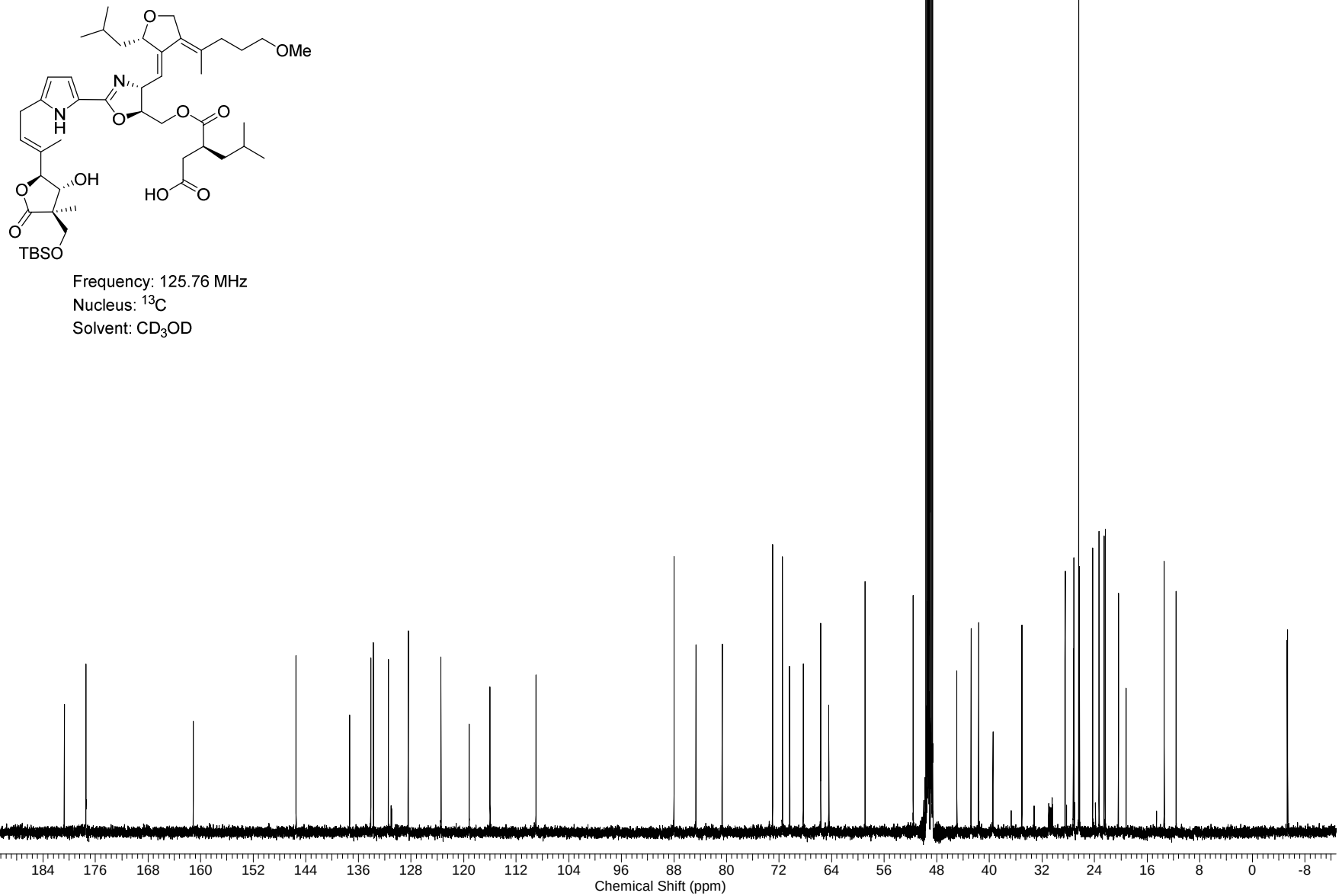

OMe
N
H
O
O
O
O
OAc
tBuO
O
O
TBSO
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CD2Cl2
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
-0.5
-1.0
Chemical Shift (ppm)

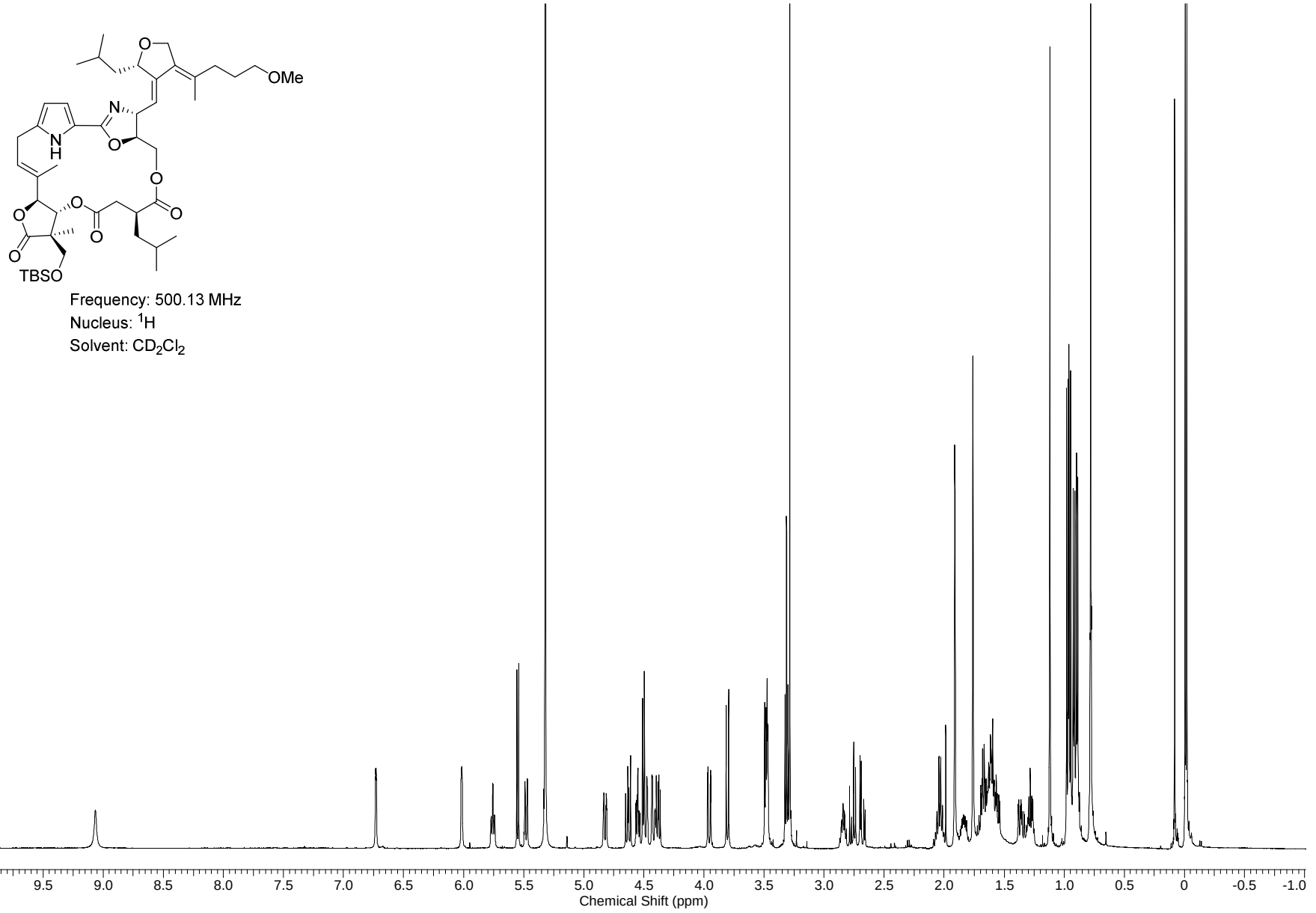

OMe
N
H
O
N
O
O
O
OAc
O
O
tBuO
O
O
TBSO
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CD2Cl2
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)

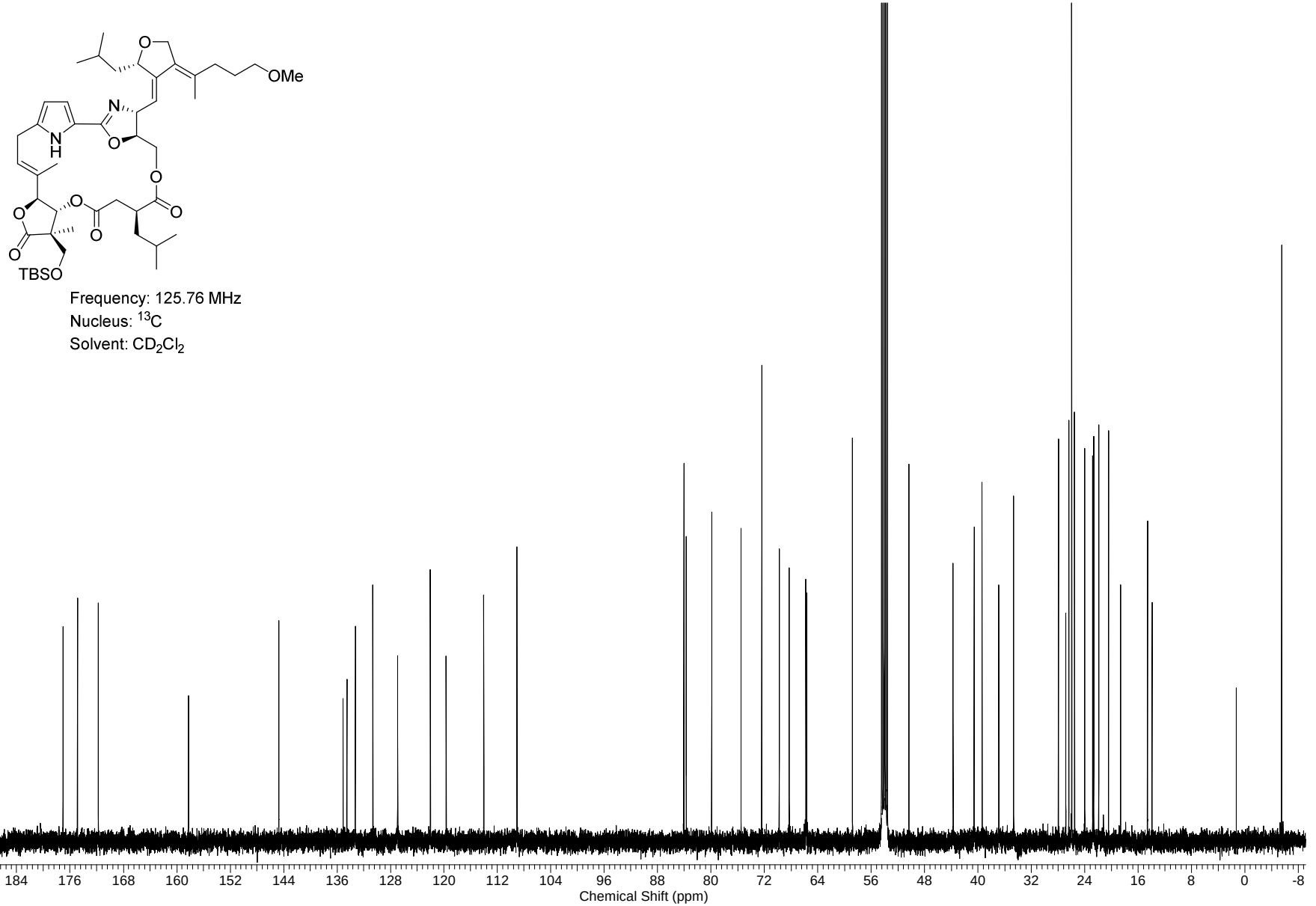

OMe
N
H
O
O
O
O
OAc
HO
O
O
O
TBSO
Frequency: 400.13 MHz
Nucleus: 1H
Solvent: CD3OD
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

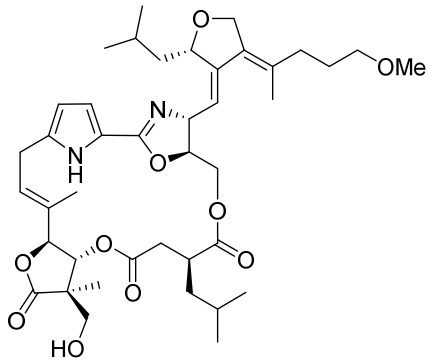

OMe
N
H
O
O
O
O
OAc
HO
O
O
TBSO
Frequency: 100.61 MHz
Nucleus: 13C
Solvent: CD3OD
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


OMe
N
H
O
N
O
O
O
HO
O
O
OH
O
TBSO
Frequency: 500.13 MHz
Nucleus: 1H
Solvent: CD3OD
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
-0.5
Chemical Shift (ppm)

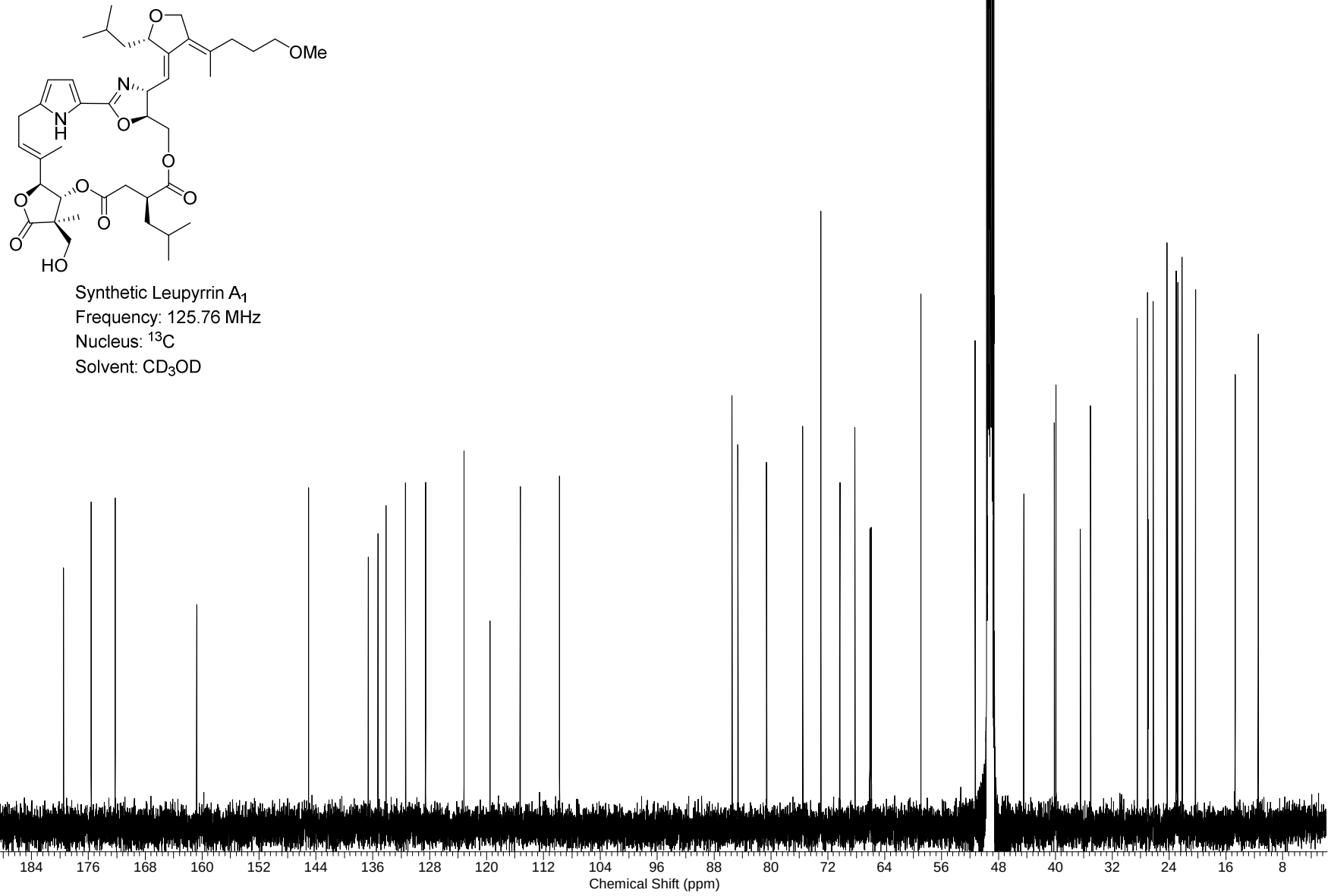

OMe
N
H
O
OH
HO
TBSO
Frequency: 125.76 MHz
Nucleus: 13C
Solvent: CD3OD
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)


OMe
N
H
TBSO
Frequency: 500.13 MHz
Nucleus: 1H
Solvent: CD2Cl2
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
-0.5
-1.0
Chemical Shift (ppm)


OMe
N
H
N
O
O
O
O
O
O
O
O
O
TBSO
Frequency: 125.76 MHz
Nucleus: 13C
Solvent: CD2Cl2
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)



Synthetic Leupyrrin A_1
Frequency: 500.13 MHz
Nucleus: ^1H
Solvent: CD_3OD


OMe
N
H
O
HO
Synthetic Leupyrrin A1
Frequency: 125.76 MHz
Nucleus: 13C
Solvent: CD3OD
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

4 X-Ray Crystal Structure Analysis of Leupyrrin B_1

Suitable crystals could be obtained from a biphasic mixture of diethyl ether and methanol (90:10) at 8 °C

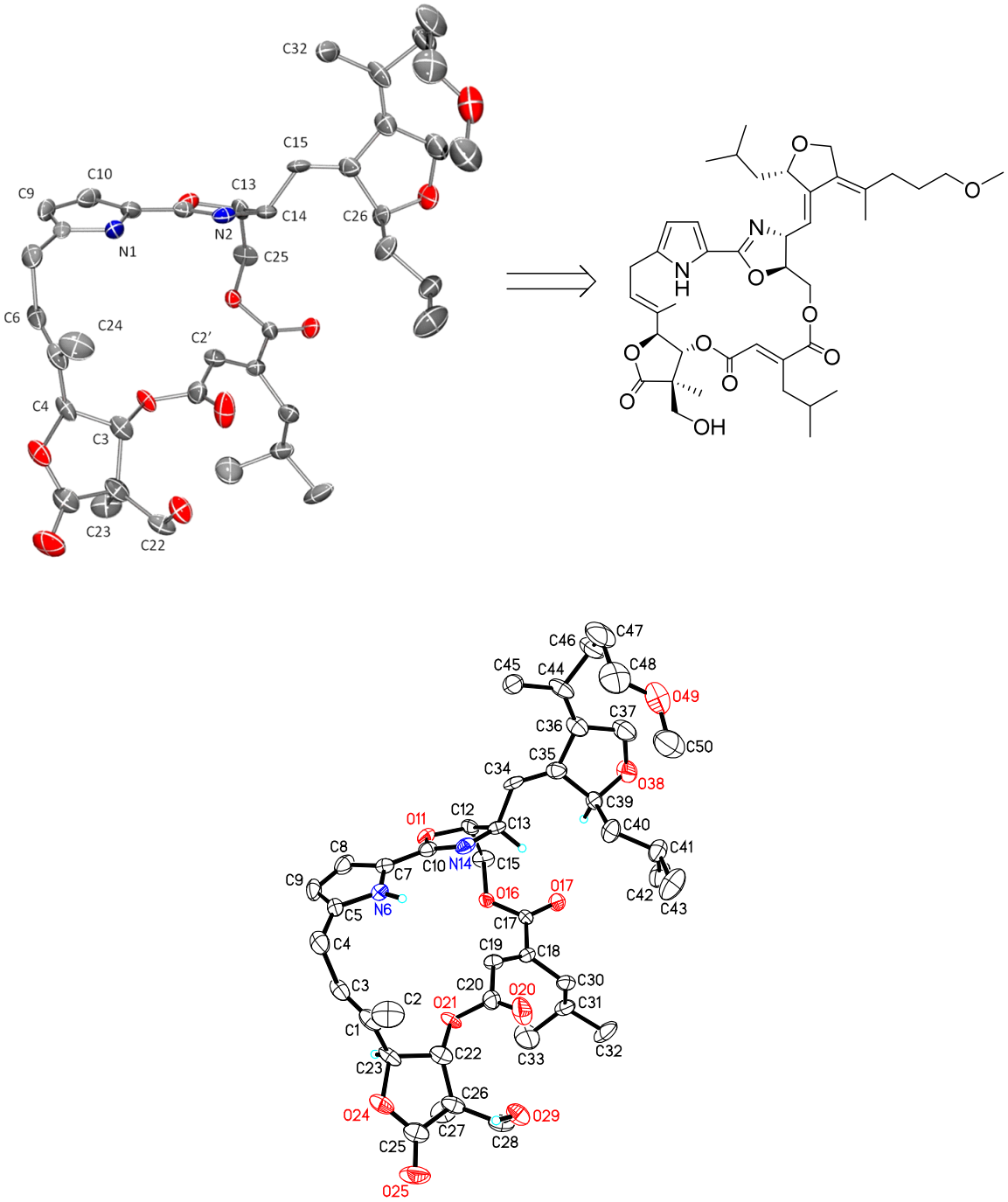


Figure S 2: Crystal structure of leupyrrin B_1 (**2**).

Table S 6 Crystal data for leupyrrin B_1 (**2**).

Empirical formula	$C_{41}H_{56}N_2O_{10}$	
Formula weight	736.88	
Temperature	200(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	$P2_1$	
Z	4	
Unit cell dimensions	a =15.112(5) Å	α = 90°
	b =11.463(4) Å	β = 99.302(6) °
	c =23.854(8) Å	γ = 90°
Volume	4078(2) $Å^3$	
Density (calculated)	1.200 g/cm^3	
Absorption coefficient	0.085 mm^{-1}	
Crystal shape	polyhedron	
Crystal size	0.18 x 0.15 x 0.04 mm^3	
Crystal colour	colourless	
Theta range for data collection	1.73 bis 19.86 °	
Index ranges	-14≤h≤14, -10≤k≤10, -22≤l≤22	
Reflections collected	18935	
Independent reflections	3965 (R(int) = 0.1261)	
Observed reflections	3240 (I >2s(I))	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00 und 0.98	
Refinement method	Full-matrix least-squares an F^2	
Data/restraints/parameters	3965 / 279 / 958	
Goodness-of-fit on F^2	1.08	
Final R indices (I>2σ(I))	R1 = 0.076, wR2 = 0.157	
Absolute structure parameter	-1(2)	
Extinction coefficient	0.047(3)	
Largest diff. peak and hole	0.49 und -0.40 $eÅ^{-3}$	

Table S 7 Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for leupyrrin B_1 (**2**). U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

atom	x	y	z	U_{eq}
C11	0.4450(7)	1.1053(11)	0.6175(4)	0.035(3)
C21	0.3789(8)	1.0975(12)	0.5644(5)	0.056(3)
C31	0.4855(7)	1.0100(10)	0.6446(5)	0.034(3)
C41	0.4816(8)	0.8823(10)	0.6255(5)	0.043(3)
C51	0.5717(7)	0.8453(9)	0.6197(4)	0.031(2)
N61	0.6131(6)	0.8823(7)	0.5763(3)	0.031(2)
C71	0.7012(7)	0.8481(9)	0.5855(4)	0.031(2)
C81	0.7171(8)	0.7890(10)	0.6365(4)	0.039(3)
C91	0.6350(8)	0.7877(10)	0.6566(5)	0.042(3)
C101	0.7643(7)	0.8843(9)	0.5490(4)	0.027(2)
O111	0.8512(4)	0.8681(6)	0.5737(3)	0.0329(17)
C121	0.9052(7)	0.9218(9)	0.5358(4)	0.031(2)
C131	0.8366(6)	0.9498(9)	0.4815(4)	0.030(2)
N141	0.7494(5)	0.9284(7)	0.4994(4)	0.030(2)
C151	0.9511(6)	1.0248(9)	0.5639(5)	0.034(3)
O161	0.8855(4)	1.1122(6)	0.5712(3)	0.0239(16)
C171	0.8808(7)	1.2091(9)	0.5385(4)	0.026(2)
O171	0.9365(4)	1.2345(6)	0.5102(3)	0.0347(19)
C181	0.7963(6)	1.2766(9)	0.5375(4)	0.024(2)
C191	0.7261(6)	1.2241(9)	0.5541(4)	0.025(2)
C201	0.6374(7)	1.2812(10)	0.5525(5)	0.035(3)
O201	0.5983(5)	1.3340(8)	0.5124(3)	0.056(2)
O211	0.6047(4)	1.2621(6)	0.6004(3)	0.0289(17)
C221	0.5130(6)	1.2972(10)	0.6007(4)	0.032(2)
C231	0.4745(7)	1.2191(10)	0.6405(4)	0.032(2)
O241	0.3983(4)	1.2886(7)	0.6536(3)	0.0382(19)
C251	0.4161(7)	1.4032(12)	0.6486(5)	0.039(3)
O251	0.3660(5)	1.4764(8)	0.6616(4)	0.060(2)
C261	0.5015(7)	1.4217(10)	0.6240(4)	0.035(2)
C271	0.5747(7)	1.4537(11)	0.6738(5)	0.046(3)
C281	0.4908(7)	1.5215(10)	0.5816(4)	0.038(3)
O291	0.4306(4)	1.4965(7)	0.5303(3)	0.0372(19)
C301	0.8013(7)	1.3989(9)	0.5186(4)	0.032(2)
C311	0.8591(7)	1.4785(9)	0.5622(5)	0.036(3)
C321	0.8633(8)	1.5987(10)	0.5372(6)	0.056(4)
C331	0.8235(10)	1.4828(12)	0.6184(5)	0.070(4)
C341	0.8478(7)	0.8772(9)	0.4313(4)	0.035(3)
C351	0.8767(7)	0.9167(9)	0.3847(5)	0.034(2)

C361	0.8892(7)	0.8524(11)	0.3328(4)	0.037(3)
C371	0.9352(8)	0.9373(11)	0.2993(5)	0.052(3)
O381	0.9598(5)	1.0370(7)	0.3345(3)	0.045(2)
C391	0.8999(6)	1.0429(9)	0.3743(5)	0.029(2)
C401	0.8166(7)	1.1154(10)	0.3535(5)	0.038(3)
C411	0.8335(7)	1.2294(10)	0.3242(5)	0.040(3)
C421	0.9012(8)	1.3071(10)	0.3608(5)	0.052(3)
C431	0.7471(8)	1.2987(12)	0.3078(6)	0.068(4)
C441	0.8654(7)	0.7455(11)	0.3145(4)	0.039(3)
C451	0.8172(8)	0.6615(10)	0.3469(5)	0.046(3)
C461	0.8788(8)	0.7060(12)	0.2568(5)	0.053(3)
C471	0.7929(9)	0.6811(14)	0.2166(5)	0.070(4)
C481	0.7237(9)	0.7790(13)	0.2129(6)	0.068(4)
O491	0.7622(6)	0.8836(9)	0.1951(3)	0.070(3)
C501	0.7058(10)	0.9821(14)	0.2000(6)	0.075(4)
C12	-0.1953(7)	0.6445(11)	0.0183(5)	0.041(3)
C22	-0.1534(10)	0.6241(13)	-0.0345(5)	0.072(4)
C32	-0.2146(7)	0.5649(10)	0.0542(5)	0.037(3)
C42	-0.1903(7)	0.4372(10)	0.0561(5)	0.042(3)
C52	-0.1324(7)	0.4143(9)	0.1104(5)	0.035(3)
N62	-0.0449(5)	0.4479(7)	0.1197(4)	0.032(2)
C72	-0.0107(6)	0.4373(9)	0.1758(4)	0.027(2)
C82	-0.0772(7)	0.3966(9)	0.2030(5)	0.035(3)
C92	-0.1536(7)	0.3788(10)	0.1626(5)	0.040(3)
C102	0.0800(7)	0.4751(9)	0.1980(4)	0.025(2)
O112	0.1000(5)	0.4726(6)	0.2561(3)	0.0363(18)
C122	0.1860(7)	0.5321(9)	0.2708(4)	0.033(2)
C132	0.2189(6)	0.5432(9)	0.2138(4)	0.027(2)
N142	0.1406(5)	0.5120(7)	0.1713(3)	0.027(2)
C152	0.1717(7)	0.6461(9)	0.2987(4)	0.034(3)
O162	0.1193(4)	0.7217(6)	0.2566(3)	0.0271(17)
C172	0.1634(8)	0.8098(9)	0.2385(4)	0.029(2)
O172	0.2359(5)	0.8451(6)	0.2602(3)	0.040(2)
C182	0.1132(6)	0.8652(9)	0.1854(4)	0.025(2)
C192	0.0503(6)	0.8050(9)	0.1521(4)	0.030(3)
C202	0.0048(7)	0.8442(10)	0.0951(5)	0.032(3)
O202	0.0434(5)	0.8708(9)	0.0570(3)	0.063(3)
O212	-0.0839(4)	0.8401(7)	0.0907(3)	0.0368(19)
C222	-0.1354(6)	0.8529(10)	0.0345(4)	0.032(2)
C232	-0.2141(7)	0.7696(10)	0.0308(5)	0.037(2)
O242	-0.2788(5)	0.8212(7)	-0.0149(3)	0.044(2)

C252	-0.2598(8)	0.9351(12)	-0.0199(5)	0.045(3)
O252	-0.3083(5)	0.9957(9)	-0.0535(4)	0.067(3)
C262	-0.1781(7)	0.9717(10)	0.0207(5)	0.035(2)
C272	-0.2074(8)	1.0330(11)	0.0713(5)	0.054(3)
C282	-0.1214(8)	1.0540(12)	-0.0079(5)	0.053(3)
O292	-0.0879(5)	1.0040(9)	-0.0545(3)	0.065(3)
C302	0.1454(7)	0.9867(9)	0.1741(5)	0.035(3)
C312	0.1058(7)	1.0789(9)	0.2111(5)	0.039(3)
C322	0.1611(9)	1.1892(11)	0.2142(6)	0.061(4)
C332	0.0080(8)	1.1045(12)	0.1873(6)	0.063(4)
C342	0.2983(6)	0.4695(10)	0.2067(4)	0.033(3)
C352	0.3788(7)	0.5136(9)	0.1994(4)	0.029(2)
C362	0.4610(6)	0.4537(10)	0.1917(4)	0.033(2)
C372	0.5350(7)	0.5443(11)	0.2006(5)	0.051(3)
O382	0.4956(5)	0.6467(7)	0.2185(3)	0.044(2)
C392	0.4007(7)	0.6428(9)	0.2010(4)	0.035(3)
C402	0.3708(8)	0.6984(10)	0.1433(5)	0.042(3)
C412	0.3766(8)	0.8309(11)	0.1423(5)	0.056(3)
C422	0.4688(10)	0.8799(13)	0.1532(7)	0.094(5)
C432	0.3239(10)	0.8804(13)	0.0857(6)	0.084(5)
C442	0.4735(7)	0.3415(11)	0.1749(5)	0.049(3)
C452	0.3998(8)	0.2529(11)	0.1637(6)	0.056(4)
C462	0.5645(8)	0.3008(13)	0.1642(6)	0.066(4)
C472	0.5647(9)	0.2611(14)	0.1030(6)	0.074(4)
C482	0.5273(9)	0.3526(15)	0.0597(6)	0.076(4)
O492	0.5813(6)	0.4540(10)	0.0674(4)	0.082(3)
C502	0.5442(10)	0.5428(16)	0.0304(7)	0.092(5)

Table S 8 Hydrogen coordinates and isotropic displacement parameters ($Å^2$) for leupyrrin B_1 (**2**).

atom	x	y	z	U_{eq}
H2A1	0.3593	1.1761	0.5519	0.084
H2B1	0.3269	1.0519	0.5714	0.084
H2C1	0.4067	1.0594	0.5349	0.084
H31	0.5211	1.0249	0.6805	0.04
H4A1	0.4582	0.833	0.6538	0.052
H4B1	0.4412	0.8743	0.5887	0.052
H61	0.5872	0.9223	0.5467	0.037
H81	0.7722	0.7559	0.6542	0.047
H91	0.625	0.752	0.691	0.05

H121	0.9506	0.8646	0.5264	0.037
H131	0.8413	1.0342	0.4717	0.036
H15A1	0.9851	1.0023	0.6014	0.04
H15B1	0.9939	1.0564	0.5405	0.04
H191	0.7332	1.1462	0.5676	0.03
H221	0.4778	1.2898	0.5616	0.038
H231	0.5192	1.2084	0.6759	0.038
H27A1	0.5834	1.3888	0.7009	0.07
H27B1	0.5567	1.5235	0.6928	0.07
H27C1	0.6309	1.469	0.6596	0.07
H28A1	0.4687	1.591	0.5997	0.045
H28B1	0.5503	1.5409	0.5719	0.045
H291	0.3848	1.4628	0.5383	0.045
H30A1	0.7397	1.4312	0.5106	0.038
H30B1	0.8261	1.4001	0.4827	0.038
H311	0.9213	1.4459	0.5695	0.043
H32A1	0.8998	1.6495	0.5648	0.084
H32B1	0.8025	1.6308	0.5281	0.084
H32C1	0.8901	1.5941	0.5026	0.084
H33A1	0.8629	1.532	0.6454	0.105
H33B1	0.8221	1.4038	0.6339	0.105
H33C1	0.7628	1.5155	0.6122	0.105
H341	0.8335	0.7967	0.4326	0.042
H37A1	0.9892	0.9011	0.2882	0.062
H37B1	0.8943	0.9607	0.2644	0.062
H391	0.9319	1.0771	0.4105	0.035
H40A1	0.7866	1.1335	0.3865	0.046
H40B1	0.7746	1.0675	0.3268	0.046
H411	0.8577	1.2102	0.2887	0.048
H42A1	0.9113	1.3777	0.3395	0.079
H42B1	0.9579	1.2648	0.371	0.079
H42C1	0.8781	1.3287	0.3954	0.079
H43A1	0.7601	1.3713	0.289	0.102
H43B1	0.7216	1.3171	0.342	0.102
H43C1	0.7041	1.2523	0.2818	0.102
H45A1	0.8068	0.5884	0.3256	0.069
H45B1	0.7595	0.6951	0.3523	0.069
H45C1	0.8536	0.6461	0.384	0.069
H46A1	0.9159	0.6343	0.2609	0.064
H46B1	0.9127	0.7668	0.2398	0.064
H47A1	0.766	0.6087	0.229	0.085

H47B1	0.8076	0.6669	0.1782	0.085
H48A1	0.6698	0.7578	0.1854	0.082
H48B1	0.7053	0.791	0.2505	0.082
H50A1	0.7341	1.0527	0.1879	0.112
H50B1	0.6972	0.9909	0.2397	0.112
H50C1	0.6476	0.9703	0.1759	0.112
H2A2	-0.1474	0.6987	-0.0536	0.108
H2B2	-0.1916	0.5715	-0.0603	0.108
H2C2	-0.094	0.5888	-0.0237	0.108
H32	-0.2479	0.591	0.0823	0.045
H4A2	-0.2451	0.3888	0.0527	0.05
H4B2	-0.1583	0.4177	0.0242	0.05
H62	-0.0149	0.4728	0.0934	0.038
H82	-0.0723	0.3827	0.2427	0.042
H92	-0.2094	0.3484	0.1694	0.048
H122	0.2283	0.4824	0.2972	0.039
H132	0.2342	0.6267	0.2081	0.033
H15A2	0.1393	0.6334	0.3311	0.041
H15B2	0.2302	0.6829	0.3133	0.041
H192	0.0331	0.7318	0.1656	0.036
H222	-0.0976	0.8317	0.0053	0.038
H232	-0.2392	0.7735	0.0671	0.044
H27A2	-0.2455	0.9806	0.0895	0.081
H27B2	-0.2411	1.1036	0.0583	0.081
H27C2	-0.1543	1.0543	0.0988	0.081
H28A2	-0.1578	1.1234	-0.0212	0.064
H28B2	-0.0702	1.0806	0.0205	0.064
H292	-0.1157	1.0316	-0.0849	0.078
H30A2	0.127	1.0059	0.1334	0.042
H30B2	0.2117	0.9891	0.1826	0.042
H312	0.1091	1.0469	0.2504	0.047
H32A2	0.2233	1.1715	0.2307	0.091
H32B2	0.1367	1.2467	0.238	0.091
H32C2	0.1592	1.221	0.1759	0.091
H33A2	-0.0275	1.0332	0.1879	0.094
H33B2	0.0034	1.1325	0.1481	0.094
H33C2	-0.0148	1.1645	0.2105	0.094
H342	0.2918	0.3871	0.2074	0.04
H37A2	0.585	0.5179	0.2299	0.061
H37B2	0.5585	0.5585	0.1648	0.061
H392	0.3702	0.6823	0.2301	0.042

H40A2	0.308	0.6752	0.1295	0.05
H40B2	0.4081	0.6665	0.1163	0.05
H412	0.3454	0.8599	0.1735	0.068
H42A2	0.4657	0.9653	0.1526	0.141
H42B2	0.5023	0.8531	0.1237	0.141
H42C2	0.4994	0.8538	0.1905	0.141
H43A2	0.3289	0.9657	0.0857	0.126
H43B2	0.2606	0.8582	0.0823	0.126
H43C2	0.349	0.8485	0.0535	0.126
H45A2	0.4242	0.1791	0.1522	0.084
H45B2	0.3532	0.281	0.1333	0.084
H45C2	0.3739	0.2406	0.1983	0.084
H46A2	0.5847	0.2354	0.1902	0.079
H46B2	0.6081	0.3653	0.1731	0.079
H47A2	0.6269	0.2422	0.098	0.088
H47B2	0.5285	0.189	0.0958	0.088
H48A2	0.5263	0.3217	0.0208	0.091
H48B2	0.4651	0.3722	0.0642	0.091
H50A2	0.5814	0.613	0.037	0.138
H50B2	0.4834	0.5603	0.0374	0.138
H50C2	0.5417	0.517	-0.009	0.138

Table S 9 Anisotropic displacement parameters ($Å^2$) for leupyrrin B_1 (**2**). The anisotropic displacement factor exponent takes the form: $-2\ pi^2\ (h^2\ a^{*2}\ U_{11} + ... + 2\ h\ k\ a^*\ b^*\ U_{12})$.

atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C11	0.027(7)	0.053(5)	0.025(6)	-0.013(5)	0.005(5)	-0.007(5)
C21	0.050(8)	0.059(9)	0.051(7)	-0.025(7)	-0.011(5)	-0.010(6)
C31	0.032(6)	0.044(6)	0.026(7)	-0.015(5)	0.011(5)	-0.020(5)
C41	0.053(6)	0.039(6)	0.042(7)	-0.014(6)	0.020(6)	-0.027(5)
C51	0.051(6)	0.021(6)	0.024(6)	-0.014(5)	0.014(5)	-0.023(5)
N61	0.042(5)	0.022(5)	0.031(5)	0.003(4)	0.011(4)	0.005(4)
C71	0.041(5)	0.023(7)	0.032(6)	-0.002(5)	0.010(5)	0.006(5)
C81	0.062(7)	0.026(7)	0.027(6)	0.003(5)	-0.003(5)	0.004(6)
C91	0.075(7)	0.032(7)	0.021(6)	-0.002(5)	0.015(5)	-0.017(6)
C101	0.034(5)	0.022(6)	0.024(6)	-0.004(5)	0.000(4)	0.003(5)
O111	0.038(4)	0.021(4)	0.041(4)	0.005(3)	0.009(3)	0.006(3)
C121	0.028(5)	0.035(6)	0.033(6)	0.002(5)	0.016(4)	0.011(5)
C131	0.042(6)	0.015(6)	0.034(5)	-0.006(4)	0.009(4)	-0.001(5)

N141	0.038(5)	0.019(5)	0.031(5)	-0.005(4)	-0.001(4)	-0.001(4)
C151	0.010(6)	0.041(6)	0.049(7)	-0.001(5)	0.001(5)	0.012(4)
O161	0.023(4)	0.027(4)	0.023(4)	0.003(3)	0.006(3)	0.006(3)
C171	0.030(6)	0.026(6)	0.024(6)	0.001(5)	0.011(5)	0.003(5)
O171	0.033(4)	0.029(4)	0.047(5)	0.003(4)	0.021(4)	-0.003(3)
C181	0.026(5)	0.019(5)	0.026(6)	0.000(5)	0.002(5)	0.003(4)
C191	0.017(5)	0.025(6)	0.032(6)	-0.004(5)	0.001(4)	0.003(4)
C201	0.034(6)	0.033(7)	0.042(7)	0.006(6)	0.014(5)	0.002(5)
O201	0.032(4)	0.085(7)	0.056(5)	0.033(5)	0.020(4)	0.024(4)
O211	0.018(4)	0.041(5)	0.029(4)	-0.008(4)	0.011(3)	0.004(3)
C221	0.015(5)	0.046(6)	0.032(6)	-0.006(5)	-0.001(4)	0.004(5)
C231	0.020(6)	0.050(5)	0.026(6)	-0.015(5)	0.008(5)	-0.005(5)
O241	0.023(4)	0.053(5)	0.041(5)	-0.013(4)	0.013(3)	0.000(4)
C251	0.026(6)	0.050(6)	0.040(7)	-0.010(6)	0.001(5)	0.005(5)
O251	0.043(5)	0.058(6)	0.082(6)	-0.010(5)	0.022(5)	0.022(4)
C261	0.026(6)	0.048(6)	0.029(6)	-0.011(5)	0.000(4)	0.007(5)
C271	0.034(6)	0.044(8)	0.056(7)	-0.008(6)	-0.009(5)	-0.003(6)
C281	0.036(7)	0.039(6)	0.037(6)	-0.018(5)	0.001(5)	0.005(5)
O291	0.026(4)	0.052(5)	0.033(4)	-0.007(4)	0.005(3)	-0.001(4)
C301	0.030(6)	0.028(5)	0.038(6)	-0.001(5)	0.011(5)	0.007(4)
C311	0.034(7)	0.024(6)	0.051(7)	-0.003(5)	0.009(5)	0.002(5)
C321	0.052(8)	0.021(6)	0.098(10)	0.011(6)	0.019(7)	-0.001(6)
C331	0.105(11)	0.054(9)	0.056(7)	-0.029(7)	0.025(8)	-0.034(9)
C341	0.051(7)	0.013(6)	0.043(6)	-0.005(5)	0.009(5)	0.004(5)
C351	0.030(6)	0.031(6)	0.045(6)	-0.007(5)	0.013(5)	-0.002(5)
C361	0.032(6)	0.047(6)	0.034(6)	-0.011(5)	0.007(5)	-0.010(5)
C371	0.053(8)	0.059(8)	0.048(7)	-0.013(6)	0.023(6)	-0.007(6)
O381	0.041(5)	0.046(5)	0.054(5)	-0.003(4)	0.025(4)	-0.015(4)
C391	0.022(6)	0.031(5)	0.037(7)	0.002(4)	0.015(5)	-0.002(5)
C401	0.030(6)	0.035(6)	0.049(7)	0.008(6)	0.007(5)	-0.009(4)
C411	0.050(7)	0.031(6)	0.037(7)	0.005(5)	0.000(5)	-0.007(5)
C421	0.075(8)	0.033(7)	0.044(8)	0.000(6)	-0.007(6)	-0.022(6)
C431	0.066(8)	0.051(9)	0.079(10)	0.023(8)	-0.013(7)	0.002(7)
C441	0.023(6)	0.061(7)	0.034(6)	-0.018(6)	0.010(5)	-0.004(6)
C451	0.074(9)	0.032(7)	0.030(7)	0.000(6)	0.005(6)	0.004(6)
C461	0.063(7)	0.061(9)	0.042(7)	-0.021(6)	0.023(5)	-0.014(7)
C471	0.090(9)	0.087(9)	0.032(7)	-0.020(7)	0.003(6)	0.006(8)
C481	0.063(8)	0.081(8)	0.054(9)	-0.013(8)	-0.011(7)	-0.018(6)
O491	0.074(6)	0.088(6)	0.050(5)	0.007(5)	0.020(5)	-0.004(5)
C501	0.080(10)	0.087(9)	0.057(9)	-0.010(9)	0.014(8)	0.010(8)
C12	0.031(7)	0.053(6)	0.041(7)	-0.012(5)	0.007(5)	0.006(5)

C22	0.097(11)	0.073(11)	0.054(8)	-0.023(8)	0.035(8)	-0.016(9)
C32	0.024(6)	0.046(6)	0.040(7)	-0.012(5)	0.000(5)	0.000(5)
C42	0.028(6)	0.048(6)	0.049(6)	-0.012(6)	0.002(5)	0.002(6)
C52	0.032(6)	0.029(7)	0.044(6)	-0.002(5)	0.009(5)	-0.005(5)
N62	0.027(5)	0.037(6)	0.033(5)	0.002(5)	0.008(4)	-0.009(4)
C72	0.024(5)	0.020(6)	0.039(6)	-0.004(5)	0.009(4)	0.001(5)
C82	0.044(6)	0.024(7)	0.040(6)	-0.001(5)	0.015(5)	-0.002(5)
C92	0.035(6)	0.038(7)	0.051(6)	-0.001(6)	0.014(5)	-0.008(6)
C102	0.028(5)	0.017(6)	0.029(6)	0.005(5)	0.001(4)	0.007(5)
O112	0.048(4)	0.034(4)	0.027(4)	0.000(4)	0.009(3)	-0.010(4)
C122	0.032(6)	0.029(6)	0.036(5)	0.016(5)	0.005(4)	0.000(5)
C132	0.032(5)	0.014(6)	0.034(6)	-0.002(5)	-0.001(4)	0.001(4)
N142	0.023(4)	0.024(5)	0.034(5)	-0.004(4)	0.009(4)	0.001(4)
C152	0.039(7)	0.038(6)	0.024(6)	0.010(4)	-0.002(5)	-0.001(5)
O162	0.031(4)	0.021(4)	0.027(4)	0.001(3)	0.000(3)	-0.004(3)
C172	0.036(6)	0.015(6)	0.035(6)	-0.008(4)	0.004(5)	0.003(5)
O172	0.042(5)	0.033(5)	0.041(5)	0.002(4)	-0.006(4)	-0.011(4)
C182	0.031(6)	0.027(5)	0.019(5)	-0.003(4)	0.008(4)	-0.001(5)
C192	0.026(6)	0.029(7)	0.036(6)	0.006(5)	0.003(4)	0.006(5)
C202	0.025(5)	0.033(7)	0.037(6)	-0.002(6)	0.003(4)	0.007(6)
O202	0.040(5)	0.112(8)	0.034(5)	0.025(5)	-0.001(4)	-0.014(5)
O212	0.032(4)	0.060(5)	0.018(4)	0.005(4)	0.002(3)	0.008(4)
C222	0.025(5)	0.059(6)	0.012(5)	-0.001(5)	0.007(4)	0.004(4)
C232	0.028(6)	0.049(5)	0.031(6)	0.005(5)	0.000(5)	0.006(5)
O242	0.037(4)	0.062(5)	0.030(4)	0.005(4)	-0.006(3)	0.005(4)
C252	0.037(6)	0.060(7)	0.038(7)	0.008(6)	0.010(5)	0.012(5)
O252	0.036(5)	0.087(7)	0.071(6)	0.034(5)	-0.009(4)	0.008(5)
C262	0.027(6)	0.043(6)	0.037(6)	0.005(5)	0.008(4)	0.015(4)
C272	0.064(9)	0.059(9)	0.040(7)	0.007(6)	0.014(6)	0.025(7)
C282	0.042(7)	0.067(8)	0.052(8)	0.011(6)	0.013(6)	0.005(6)
O292	0.037(5)	0.119(8)	0.041(5)	0.022(5)	0.013(4)	0.036(5)
C302	0.035(6)	0.031(5)	0.039(7)	0.001(5)	0.009(5)	-0.005(5)
C312	0.054(7)	0.022(6)	0.040(7)	-0.003(5)	0.008(6)	0.002(5)
C322	0.074(9)	0.039(7)	0.065(9)	-0.003(7)	-0.001(7)	-0.014(6)
C332	0.058(7)	0.050(9)	0.078(10)	-0.013(8)	0.001(7)	0.015(6)
C342	0.026(5)	0.023(6)	0.049(7)	-0.005(6)	0.001(5)	-0.004(4)
C352	0.033(5)	0.034(5)	0.021(6)	0.005(5)	0.003(5)	0.000(4)
C362	0.023(5)	0.050(6)	0.025(6)	0.002(6)	-0.004(5)	0.007(4)
C372	0.032(6)	0.064(7)	0.053(8)	-0.008(7)	-0.003(6)	0.002(5)
O382	0.034(4)	0.049(5)	0.045(5)	0.001(4)	-0.007(4)	-0.002(4)
C392	0.034(6)	0.039(6)	0.031(6)	0.002(5)	0.005(5)	-0.009(5)

C402	0.044(7)	0.038(6)	0.041(7)	0.002(5)	0.001(5)	-0.006(5)
C412	0.070(8)	0.045(7)	0.054(8)	0.020(6)	0.010(6)	-0.012(7)
C422	0.082(9)	0.048(9)	0.140(14)	0.014(10)	-0.015(9)	-0.026(8)
C432	0.093(10)	0.070(10)	0.083(10)	0.041(9)	-0.002(7)	-0.010(9)
C442	0.043(7)	0.053(7)	0.052(8)	-0.003(7)	0.015(6)	0.010(5)
C452	0.056(7)	0.036(7)	0.084(10)	-0.005(7)	0.035(7)	0.007(5)
C462	0.045(7)	0.076(10)	0.078(7)	-0.001(7)	0.015(7)	0.020(6)
C472	0.054(9)	0.085(10)	0.089(9)	-0.019(7)	0.030(8)	0.013(8)
C482	0.064(10)	0.108(11)	0.058(8)	-0.012(8)	0.020(7)	-0.002(8)
O492	0.046(6)	0.104(8)	0.100(8)	0.002(6)	0.021(6)	0.005(5)
C502	0.066(11)	0.115(12)	0.105(13)	0.012(9)	0.044(9)	0.009(9)

Table S 10 Bond lengths (Å) and angles (deg) for Leupyrrin B_1 (2).

atoms	bond length/angle
C11-C31	1.363(15)
C11-C231	1.457(15)
C11-C21	1.484(14)
C21-H2A1	0.98
C21-H2B1	0.98
C21-H2C1	0.98
C31-C41	1.532(16)
C31-H31	0.95
C41-C51	1.453(15)
C41-H4A1	0.99
C41-H4B1	0.99
C51-N61	1.361(12)
C51-C91	1.361(15)
N61-C71	1.371(12)
N61-H61	0.88
C71-C81	1.378(14)
C71-C101	1.452(14)
C81-C91	1.401(15)
C81-H81	0.95
C91-H91	0.95
C101-N141	1.272(12)
C101-O111	1.362(11)
O111-C121	1.450(12)
C121-C151	1.475(14)
C121-C131	1.557(14)
C121-H121	1
C131-N141	1.470(12)
C131-C341	1.489(14)
C131-H131	1
C151-O161	1.439(11)
C151-H15A1	0.99
C151-H15B1	0.99
O161-C171	1.352(12)
C171-O171	1.198(11)
C171-C181	1.489(14)
C181-C191	1.333(13)
C181-C301	1.479(14)
C191-C201	1.486(14)
C191-H191	0.95
C201-O201	1.202(12)
C201-O211	1.335(12)
O211-C221	1.443(11)
C221-C231	1.491(15)
C221-C261	1.552(15)
C221-H221	1
C231-O241	1.473(12)
C231-H231	1
O241-C251	1.350(14)
C251-O251	1.204(13)
C251-C261	1.516(15)
C261-C281	1.518(15)
C261-C271	1.532(14)
C271-H27A1	0.98
C271-H27B1	0.98
C271-H27C1	0.98
C281-O291	1.430(12)
C281-H28A1	0.99
C281-H28B1	0.99
O291-H291	0.84
C301-C311	1.542(15)
C301-H30A1	0.99
C301-H30B1	0.99
C311-C321	1.507(15)
C311-C331	1.525(15)
C311-H311	1
C321-H32A1	0.98
C321-H32B1	0.98
C321-H32C1	0.98
C331-H33A1	0.98
C331-H33B1	0.98
C331-H33C1	0.98
C341-C351	1.338(14)
C341-H341	0.95
C351-C361	1.478(15)
C351-C391	1.518(15)
C361-C441	1.331(16)
C361-C371	1.499(16)

C371-O381	1.431(13)	C22-H2C2	0.98
C371-H37A1	0.99	C32-C42	1.508(16)
C371-H37B1	0.99	C32-H32	0.95
O381-C391	1.416(12)	C42-C52	1.466(15)
C391-C401	1.523(14)	C42-H4A2	0.99
C391-H391	1	C42-H4B2	0.99
C401-C411	1.524(15)	C52-N62	1.361(12)
C401-H40A1	0.99	C52-C92	1.396(14)
C401-H40B1	0.99	N62-C72	1.358(12)
C411-C421	1.520(15)	N62-H62	0.88
C411-C431	1.524(16)	C72-C82	1.365(14)
C411-H411	1	C72-C102	1.454(14)
C421-H42A1	0.98	C82-C92	1.393(14)
C421-H42B1	0.98	C82-H82	0.95
C421-H42C1	0.98	C92-H92	0.95
C431-H43A1	0.98	C102-N142	1.271(12)
C431-H43B1	0.98	C102-O112	1.369(11)
C431-H43C1	0.98	O112-C122	1.459(12)
C441-C461	1.492(15)	C122-C152	1.499(15)
C441-C451	1.496(16)	C122-C132	1.527(14)
C451-H45A1	0.98	C122-H122	1
C451-H45B1	0.98	C132-N142	1.473(12)
C451-H45C1	0.98	C132-C342	1.499(14)
C461-C471	1.511(17)	C132-H132	1
C461-H46A1	0.99	C152-O162	1.459(12)
C461-H46B1	0.99	C152-H15A2	0.99
C471-C481	1.527(19)	C152-H15B2	0.99
C471-H47A1	0.99	O162-C172	1.322(12)
C471-H47B1	0.99	C172-O172	1.204(11)
C481-O491	1.428(16)	C172-C182	1.507(14)
C481-H48A1	0.99	C182-C192	1.330(14)
C481-H48B1	0.99	C182-C302	1.514(15)
O491-C501	1.431(16)	C192-C202	1.491(14)
C501-H50A1	0.98	C192-H192	0.95
C501-H50B1	0.98	C202-O202	1.196(11)
C501-H50C1	0.98	C202-O212	1.327(11)
C12-C32	1.316(15)	O212-C222	1.444(11)
C12-C232	1.502(16)	C222-C232	1.516(15)
C12-C22	1.517(16)	C222-C262	1.520(16)
C22-H2A2	0.98	C222-H222	1
C22-H2B2	0.98	C232-O242	1.468(12)

C232-H232	1	C252-O252	1.212(13)
O242-C252	1.346(14)	C252-C262	1.501(16)
C262-C282	1.510(16)	C422-H42A2	0.98
C262-C272	1.523(15)	C422-H42B2	0.98
C272-H27A2	0.98	C422-H42C2	0.98
C272-H27B2	0.98	C432-H43A2	0.98
C272-H27C2	0.98	C432-H43B2	0.98
C282-O292	1.417(13)	C432-H43C2	0.98
C282-H28A2	0.99	C442-C452	1.499(16)
C282-H28B2	0.99	C442-C462	1.513(16)
O292-H292	0.84	C452-H45A2	0.98
C302-C312	1.557(15)	C452-H45B2	0.98
C302-H30A2	0.99	C452-H45C2	0.98
C302-H30B2	0.99	C462-C472	1.530(17)
C312-C322	1.511(16)	C462-H46A2	0.99
C312-C332	1.524(15)	C462-H46B2	0.99
C312-H312	1	C472-C482	1.52(2)
C322-H32A2	0.98	C472-H47A2	0.99
C322-H32B2	0.98	C472-H47B2	0.99
C322-H32C2	0.98	C482-O492	1.415(17)
C332-H33A2	0.98	C482-H48A2	0.99
C332-H33B2	0.98	C482-H48B2	0.99
C332-H33C2	0.98	O492-C502	1.403(18)
C342-C352	1.355(13)	C502-H50A2	0.98
C342-H342	0.95	C502-H50B2	0.98
C352-C362	1.457(14)	C502-H50C2	0.98
C352-C392	1.517(15)	C31-C11-C231	116.9(9)
C362-C442	1.368(16)	C31-C11-C21	123.1(11)
C362-C372	1.516(16)	C231-C11-C21	119.9(11)
C372-O382	1.414(14)	C11-C21-H2A1	109.5
C372-H37A2	0.99	C11-C21-H2B1	109.5
C372-H37B2	0.99	H2A1-C21-H2B1	109.5
O382-C392	1.428(12)	C11-C21-H2C1	109.5
C392-C402	1.519(15)	H2A1-C21-H2C1	109.5
C392-H392	1	H2B1-C21-H2C1	109.5
C402-C412	1.522(16)	C11-C31-C41	129.2(10)
C402-H40A2	0.99	C11-C31-H31	115.4
C402-H40B2	0.99	C41-C31-H31	115.4
C412-C422	1.486(17)	C51-C41-C31	108.5(9)
C412-C432	1.560(17)	C51-C41-H4A1	110
C412-H412	1	C31-C41-H4A1	110

C51-C41-H4B1	110	C171-O161-C151	118.4(7)
C31-C41-H4B1	110	O171-C171-O161	123.3(9)
H4A1-C41-H4B1	108.4	O171-C171-C181	122.9(9)
N61-C51-C91	106.3(10)	O161-C171-C181	113.7(8)
N61-C51-C41	122.3(10)	C191-C181-C301	126.8(9)
C91-C51-C41	130.7(10)	C191-C181-C171	118.8(9)
C51-N61-C71	110.1(9)	C301-C181-C171	114.3(9)
C51-N61-H61	124.9	C181-C191-C201	123.5(10)
C71-N61-H61	124.9	C181-C191-H191	118.3
N61-C71-C81	107.9(9)	C201-C191-H191	118.3
N61-C71-C101	122.5(9)	O201-C201-O211	124.0(10)
C81-C71-C101	129.2(10)	O201-C201-C191	124.6(10)
C71-C81-C91	105.7(10)	O211-C201-C191	111.3(9)
C71-C81-H81	127.2	C201-O211-C221	116.6(8)
C91-C81-H81	127.2	O211-C221-C231	108.1(8)
C51-C91-C81	110.0(10)	O211-C221-C261	115.0(8)
C51-C91-H91	125	C231-C221-C261	104.2(8)
C81-C91-H91	125	O211-C221-H221	109.8
N141-C101-O111	118.0(9)	C231-C221-H221	109.8
N141-C101-C71	129.6(10)	C261-C221-H221	109.8
O111-C101-C71	112.4(9)	C11-C231-O241	111.2(8)
C101-O111-C121	105.8(7)	C11-C231-C221	115.2(9)
O111-C121-C151	109.1(8)	O241-C231-C221	102.1(8)
O111-C121-C131	103.9(7)	C11-C231-H231	109.4
C151-C121-C131	114.5(9)	O241-C231-H231	109.4
O111-C121-H121	109.7	C221-C231-H231	109.4
C151-C121-H121	109.7	C251-O241-C231	109.5(8)
C131-C121-H121	109.7	O251-C251-O241	120.8(10)
N141-C131-C341	111.4(8)	O251-C251-C261	127.7(11)
N141-C131-C121	103.3(8)	O241-C251-C261	111.4(9)
C341-C131-C121	114.0(8)	C251-C261-C281	111.0(9)
N141-C131-H131	109.3	C251-C261-C271	106.7(9)
C341-C131-H131	109.3	C281-C261-C271	108.8(9)
C121-C131-H131	109.3	C251-C261-C221	99.3(9)
C101-N141-C131	107.8(8)	C281-C261-C221	117.4(8)
O161-C151-C121	109.3(8)	C271-C261-C221	112.8(9)
O161-C151-H15A1	109.8	C261-C271-H27A1	109.5
C121-C151-H15A1	109.8	C261-C271-H27B1	109.5
O161-C151-H15B1	109.8	H27A1-C271-H27B1	109.5
C121-C151-H15B1	109.8	C261-C271-H27C1	109.5
H15A1-C151-H15B1	108.3	H27A1-C271-H27C1	109.5

H27B1-C271-H27C1	109.5	O381-C371-C361	107.8(8)
O291-C281-C261	113.8(9)	O381-C371-H37A1	110.1
O291-C281-H28A1	108.8	C361-C371-H37A1	110.1
C261-C281-H28A1	108.8	O381-C371-H37B1	110.1
O291-C281-H28B1	108.8	C361-C371-H37B1	110.1
C261-C281-H28B1	108.8	H37A1-C371-H37B1	108.5
H28A1-C281-H28B1	107.7	C391-O381-C371	107.3(8)
C281-O291-H291	109.5	O381-C391-C351	104.7(8)
C181-C301-C311	114.0(9)	O381-C391-C401	113.1(9)
C181-C301-H30A1	108.8	C351-C391-C401	111.8(8)
C311-C301-H30A1	108.8	O381-C391-H391	109
C181-C301-H30B1	108.8	C351-C391-H391	109
C311-C301-H30B1	108.8	C401-C391-H391	109
H30A1-C301-H30B1	107.7	C391-C401-C411	115.2(9)
C321-C311-C331	111.1(10)	C391-C401-H40A1	108.5
C321-C311-C301	109.3(10)	C411-C401-H40A1	108.5
C331-C311-C301	111.7(9)	C391-C401-H40B1	108.5
C321-C311-H311	108.2	C411-C401-H40B1	108.5
C331-C311-H311	108.2	H40A1-C401-H40B1	107.5
C301-C311-H311	108.2	C421-C411-C401	112.7(9)
C311-C321-H32A1	109.5	C421-C411-C431	108.2(10)
C311-C321-H32B1	109.5	C401-C411-C431	111.4(9)
H32A1-C321-H32B1	109.5	C421-C411-H411	108.1
C311-C321-H32C1	109.5	C401-C411-H411	108.1
H32A1-C321-H32C1	109.5	C431-C411-H411	108.1
H32B1-C321-H32C1	109.5	C411-C421-H42A1	109.5
C311-C331-H33A1	109.5	C411-C421-H42B1	109.5
C311-C331-H33B1	109.5	H42A1-C421-H42B1	109.5
H33A1-C331-H33B1	109.5	C411-C421-H42C1	109.5
C311-C331-H33C1	109.5	H42A1-C421-H42C1	109.5
H33A1-C331-H33C1	109.5	H42B1-C421-H42C1	109.5
H33B1-C331-H33C1	109.5	C411-C431-H43A1	109.5
C351-C341-C131	125.0(10)	C411-C431-H43B1	109.5
C351-C341-H341	117.5	H43A1-C431-H43B1	109.5
C131-C341-H341	117.5	C411-C431-H43C1	109.5
C341-C351-C361	129.1(10)	H43A1-C431-H43C1	109.5
C341-C351-C391	124.9(10)	H43B1-C431-H43C1	109.5
C361-C351-C391	106.0(9)	C361-C441-C461	120.9(11)
C441-C361-C351	132.1(10)	C361-C441-C451	123.4(10)
C441-C361-C371	123.1(10)	C461-C441-C451	115.5(10)
C351-C361-C371	104.8(9)	C441-C451-H45A1	109.5

C441-C451-H45B1	109.5	C42-C32-H32	116.1
H45A1-C451-H45B1	109.5	C52-C42-C32	108.0(9)
C441-C451-H45C1	109.5	C52-C42-H4A2	110.1
H45A1-C451-H45C1	109.5	C32-C42-H4A2	110.1
H45B1-C451-H45C1	109.5	C52-C42-H4B2	110.1
C441-C461-C471	114.4(10)	C32-C42-H4B2	110.1
C441-C461-H46A1	108.7	H4A2-C42-H4B2	108.4
C471-C461-H46A1	108.7	N62-C52-C92	107.1(9)
C441-C461-H46B1	108.7	N62-C52-C42	121.2(10)
C471-C461-H46B1	108.7	C92-C52-C42	130.7(10)
H46A1-C461-H46B1	107.6	C72-N62-C52	109.9(8)
C461-C471-C481	114.0(11)	C72-N62-H62	125.1
C461-C471-H47A1	108.7	C52-N62-H62	125.1
C481-C471-H47A1	108.7	N62-C72-C82	107.9(9)
C461-C471-H47B1	108.7	N62-C72-C102	121.3(9)
C481-C471-H47B1	108.7	C82-C72-C102	130.6(10)
H47A1-C471-H47B1	107.6	C72-C82-C92	108.2(9)
O491-C481-C471	109.0(11)	C72-C82-H82	125.9
O491-C481-H48A1	109.9	C92-C82-H82	125.9
C471-C481-H48A1	109.9	C82-C92-C52	106.9(9)
O491-C481-H48B1	109.9	C82-C92-H92	126.5
C471-C481-H48B1	109.9	C52-C92-H92	126.5
H48A1-C481-H48B1	108.3	N142-C102-O112	117.1(9)
C481-O491-C501	111.2(10)	N142-C102-C72	129.0(10)
O491-C501-H50A1	109.5	O112-C102-C72	113.9(9)
O491-C501-H50B1	109.5	C102-O112-C122	106.1(7)
H50A1-C501-H50B1	109.5	O112-C122-C152	109.2(8)
O491-C501-H50C1	109.5	O112-C122-C132	103.3(8)
H50A1-C501-H50C1	109.5	C152-C122-C132	114.4(8)
H50B1-C501-H50C1	109.5	O112-C122-H122	109.9
C32-C12-C232	117.6(10)	C152-C122-H122	109.9
C32-C12-C22	126.8(11)	C132-C122-H122	109.9
C232-C12-C22	115.5(11)	N142-C132-C342	110.7(8)
C12-C22-H2A2	109.5	N142-C132-C122	104.6(8)
C12-C22-H2B2	109.5	C342-C132-C122	115.8(8)
H2A2-C22-H2B2	109.5	N142-C132-H132	108.5
C12-C22-H2C2	109.5	C342-C132-H132	108.5
H2A2-C22-H2C2	109.5	C122-C132-H132	108.5
H2B2-C22-H2C2	109.5	C102-N142-C132	107.4(8)
C12-C32-C42	127.9(11)	O162-C152-C122	108.2(8)
C12-C32-H32	116.1	O162-C152-H15A2	110.1

C122-C152-H15A2	110.1	C262-C272-H27B2	109.5
O162-C152-H15B2	110.1	H27A2-C272-H27B2	109.5
C122-C152-H15B2	110.1	C262-C272-H27C2	109.5
H15A2-C152-H15B2	108.4	H27A2-C272-H27C2	109.5
C172-O162-C152	115.6(8)	H27B2-C272-H27C2	109.5
O172-C172-O162	126.0(10)	O292-C282-C262	113.8(11)
O172-C172-C182	121.4(10)	O292-C282-H28A2	108.8
O162-C172-C182	112.7(9)	C262-C282-H28A2	108.8
C192-C182-C172	119.8(9)	O292-C282-H28B2	108.8
C192-C182-C302	126.2(9)	C262-C282-H28B2	108.8
C172-C182-C302	113.9(9)	H28A2-C282-H28B2	107.7
C182-C192-C202	124.6(10)	C282-O292-H292	109.5
C182-C192-H192	117.7	C182-C302-C312	111.0(8)
C202-C192-H192	117.7	C182-C302-H30A2	109.4
O202-C202-O212	124.0(9)	C312-C302-H30A2	109.4
O202-C202-C192	124.0(10)	C182-C302-H30B2	109.4
O212-C202-C192	111.8(9)	C312-C302-H30B2	109.4
C202-O212-C222	117.1(8)	H30A2-C302-H30B2	108
O212-C222-C232	106.9(8)	C322-C312-C332	110.6(10)
O212-C222-C262	116.0(9)	C322-C312-C302	109.6(9)
C232-C222-C262	104.5(8)	C332-C312-C302	111.0(9)
O212-C222-H222	109.8	C322-C312-H312	108.5
C232-C222-H222	109.8	C332-C312-H312	108.5
C262-C222-H222	109.8	C302-C312-H312	108.5
O242-C232-C12	111.2(9)	C312-C322-H32A2	109.5
O242-C232-C222	102.2(8)	C312-C322-H32B2	109.5
C12-C232-C222	116.2(9)	H32A2-C322-H32B2	109.5
O242-C232-H232	109	C312-C322-H32C2	109.5
C12-C232-H232	109	H32A2-C322-H32C2	109.5
C222-C232-H232	109	H32B2-C322-H32C2	109.5
C252-O242-C232	109.3(9)	C312-C332-H33A2	109.5
O252-C252-O242	120.0(11)	C312-C332-H33B2	109.5
O252-C252-C262	127.7(12)	H33A2-C332-H33B2	109.5
O242-C252-C262	112.2(10)	C312-C332-H33C2	109.5
C252-C262-C282	110.5(9)	H33A2-C332-H33C2	109.5
C252-C262-C222	99.5(9)	H33B2-C332-H33C2	109.5
C282-C262-C222	113.9(9)	C352-C342-C132	123.8(10)
C252-C262-C272	109.1(9)	C352-C342-H342	118.1
C282-C262-C272	109.1(10)	C132-C342-H342	118.1
C222-C262-C272	114.2(9)	C342-C352-C362	129.9(10)
C262-C272-H27A2	109.5	C342-C352-C392	123.9(9)

C362-C352-C392	106.1(9)	C412-C432-H43C2	109.5
C442-C362-C352	129.9(10)	H43A2-C432-H43C2	109.5
C442-C362-C372	123.4(10)	H43B2-C432-H43C2	109.5
C352-C362-C372	106.5(9)	C362-C442-C452	123.7(10)
O382-C372-C362	105.9(8)	C362-C442-C462	120.8(11)
O382-C372-H37A2	110.6	C452-C442-C462	115.5(11)
C362-C372-H37A2	110.6	C442-C452-H45A2	109.5
O382-C372-H37B2	110.6	C442-C452-H45B2	109.5
C362-C372-H37B2	110.6	H45A2-C452-H45B2	109.5
H37A2-C372-H37B2	108.7	C442-C452-H45C2	109.5
C372-O382-C392	109.8(8)	H45A2-C452-H45C2	109.5
O382-C392-C352	104.0(8)	H45B2-C452-H45C2	109.5
O382-C392-C402	112.8(8)	C442-C462-C472	113.3(11)
C352-C392-C402	110.8(9)	C442-C462-H46A2	108.9
O382-C392-H392	109.7	C472-C462-H46A2	108.9
C352-C392-H392	109.7	C442-C462-H46B2	108.9
C402-C392-H392	109.7	C472-C462-H46B2	108.9
C392-C402-C412	115.0(10)	H46A2-C462-H46B2	107.7
C392-C402-H40A2	108.5	C482-C472-C462	112.7(12)
C412-C402-H40A2	108.5	C482-C472-H47A2	109
C392-C402-H40B2	108.5	C462-C472-H47A2	109
C412-C402-H40B2	108.5	C482-C472-H47B2	109
H40A2-C402-H40B2	107.5	C462-C472-H47B2	109
C422-C412-C402	115.5(11)	H47A2-C472-H47B2	107.8
C422-C412-C432	110.3(11)	O492-C482-C472	109.7(12)
C402-C412-C432	110.7(11)	O492-C482-H48A2	109.7
C422-C412-H412	106.6	C472-C482-H48A2	109.7
C402-C412-H412	106.6	O492-C482-H48B2	109.7
C432-C412-H412	106.6	C472-C482-H48B2	109.7
C412-C422-H42A2	109.5	H48A2-C482-H48B2	108.2
C412-C422-H42B2	109.5	C502-O492-C482	110.5(11)
H42A2-C422-H42B2	109.5	O492-C502-H50A2	109.5
C412-C422-H42C2	109.5	O492-C502-H50B2	109.5
H42A2-C422-H42C2	109.5	H50A2-C502-H50B2	109.5
H42B2-C422-H42C2	109.5	O492-C502-H50C2	109.5
C412-C432-H43A2	109.5	H50A2-C502-H50C2	109.5
C412-C432-H43B2	109.5	H50B2-C502-H50C2	109.5
H43A2-C432-H43B2	109.5		