Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Paleo-Soraphens: Chemical Total Syntheses and Biological Studies

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1. General Methods

All reactions were performed under inert atmosphere and stirred magnetically with the help of a Teflon coated stir bar. The used glassware was heated under high vacuum und flushed with inert gas (N_2) prior to use. Dry solvents were obtained by heating under reflux over CaH_2 and subsequent distillation (methylene chloride), by filtration through drying columns on a M. Braun solvent purification system (diethyl ether) or by heating under reflux over sodium and subsequent distillation (THF). Petroleum ether and ethyl acetate for flash column chromatography were distilled before use.

Flash chromatography was performed on Merck silica (grain size 40-63 m). Thin layer chromatography was performed on silica gel coated aluminium sheets Macherey-Nagel Alugram® Xtra SIL G/UV_{254} (0.20 mm layer). Indication was achieved with UV light (λ 254 nm) or common dip stains (cerium, potassium permanganate or vanillin). ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker DPX-200, DPX-400 or DPX-500 instruments with the residual proton signals of the solvents given as internal standard (in ppm: $CDCl_3$ 7.26 for ^{1}H and 77.16 for ^{13}C). Chemical shifts are given in ppm, coupling constants *J* are given in Hz. The used abbreviations for the multiplicities are as follows: s = singulet, d = dublet, t = triplett, q = quartet, quint = quintet, hex = hextet, hept = heptet, brs = broad singulet. Electron spray ionisation mass spectra (ESI-HRMS) were obtained from a Waters Micromass LCT instrument. The probes were injected in a loops mode of a Waters Alliance 2695 HPLC system. Optical rotations were measured on a polarimeter Perkin-Elmer 341 at 20 °C at a wavelength of λ 589.3 nm in a 1 mL quartz cell (1 dm length). The concentration is given in g/100 mL.

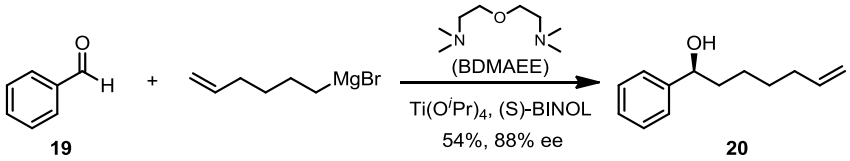
Abbreviations:

BDMAEE = cis(2-dimethylaminoethyl) ether
BINOL = 1,1'-bi-2-naphthol
DMAP = 4-dimethylaminopyridine
IBX = 2-iodoxybenzoic acid
DMP = Dess-Martin periodinane
MOMCl = chloromethyl methyl ether
MNBA = 2-methyl-6-nitrobenzoic anhydride
DIAD = diisopropyl azodicarboxylate

2. Experimental Procedures and Characterizations

2.1 Synthesis of the New Western Segments

(*S*)-1-Phenylhept-6-en-1-ol (20)[1]



19 20

$Ti(OiPr)_4$ (1.34 g, 4.70 mmol) was added dropwise to a solution of of (*S*)-BINOL (572 mg 2.0 mmol) in 10 mL of THF under argon at 0 °C, and the mixture was stirred for a further 0.5 h at room temperature. In the second flask, 5-hexen-1-ylmagnesium bromide (12.5 mL, 1.0 M in THF) was added slowly to of BDMAEE (2.45 mL, 12.5 mmol) in 20 mL of THF at 0 °C under argon and the mixture was stirred for 30 min. Then the catalyst solution was added via canula. The combined mixture was stirred for 1.0 h at room temperature. The solution was then cooled to -10 °C, and benzaldehyde (530 mg, 5 mmol) was added dropwise. The mixture was allowed to warm to room temperature and stirred until the aldehyde was consumed. The reaction mixture was quenched with 5% cold aqueous HCl (30 mL) and extracted three times with ether (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated *in vacuo*. The residue was purified by flash column chromatography to give the product **20** as yellow oil (513 mg, 54%, 88% ee). The enantioselectivity was determined to be 88% *ee* by chiral GC (method: hydrodex β-6-TBDM, 5 °C /min, 50→200 °C, holds 5 min), and the absolute configuration of the alcohol was assigned by Mosher's Method.[2] (*It is worth to note that larger scales will cause drop in yields but high ee maintained.*)

R_f 0.30 (PE/EtOAc 9:1, $KMnO_4$)

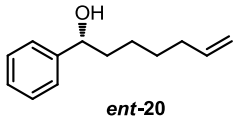
Opt. Rot. $[\alpha]^{20}_D$ = -22.9 (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.38-7.33 (m, 4H), 7.31-7.25 (m, 1H), 5.79 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 4.98 (ddd, *J* = 17.1, 3.6, 1.6 Hz, 1H), 4.93 (ddt, *J* = 10.2, 2.2, 1.2 Hz, 1H), 4.67 (dd, *J* = 7.4, 5.9 Hz, 1H), 2.04 (td, *J* = 6.8, 1.3 Hz, 2H), 1.88-1.66 (m, 3H), 1.47-1.37 (m, 2H), 1.35-1.24 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 145.0, 139.0, 128.6, 127.7, 126.0, 114.5, 74.8, 39.1, 33.8, 28.9, 25.5.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 213.1255, found: 213.1254.

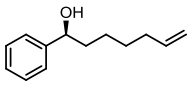
(*R*)-1-Phenylhept-6-en-1-ol (*ent*-20)



***ent*-20**

Prepared accordingly as described for **20** but in the prescence of catalyst $Ti(OiPr)_4$/(*R*)-BINOL.

(1) Liu, Y.; Da, C.-S.; Yu, S.-L.; Yin, X.-G.; Wang, J.-R.; Fan, X.-Y.; Li, W.-P.; Wang, R. *J. Org. Chem.* **2010**, *75*, 6869-6878.
(2) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092-4096.



20

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
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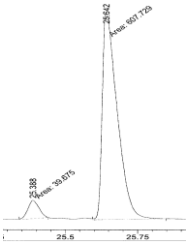

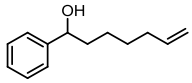

***rac*-20**

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
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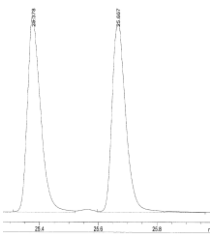

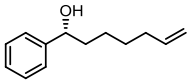

***ent*-20**

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
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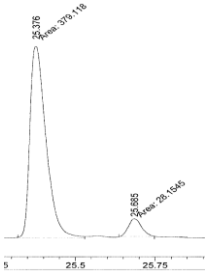
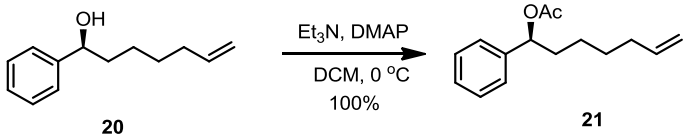


(*S*)-1-Phenylhept-6-en-1-yl acetate (21)



20 **21**

Triethylamine (0.44 mL, 3.16 mmol), 4-dimethylaminopyridine (19 mg, 0.16 mmol) and acetic anhydride (0.24 mL, 2.36 mmol) were sequentially added to a solution of (*S*)-1-phenylhept-6-en-1-ol (**20**) (300 mg, 1.58 mmol) in dichloromethane (10 mL) at 0 °C. The reaction was stirred at room temperature for 1 h. Then it was quenched with water (10 mL) and extracted with dichloromethane (2 × 10 mL). The combined organic extracts were dried over sodium sulfate, filtered and concentrated. The residue was purified by chromatography to afford the desired acetate as coloreless oil (368 mg, 100%).

R_f 0.65 (PE/EtOAc 9:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -46.0 (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

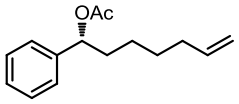
δ 7.36-7.27 (m, 5H), 5.82-5.71 (m, 2H), 5.00-4.91 (m, 2H), 2.07 (s, 3H), 2.06-2.00 (m, 2H), 1.96-1.87 (m, 1H), 1.82-1.73 (m, 1H), 1.44-1.21 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 170.4, 140.8, 138.6, 128.4, 127.8, 126.5, 114.5, 76.0, 36.1, 33.5, 28.6, 24.9, 21.3.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 255.1361, found: 255.1363.

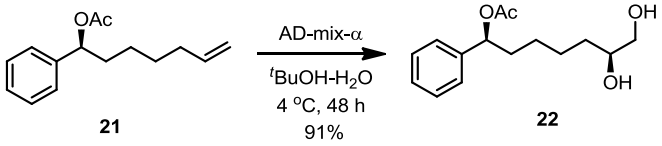
(*R*)-1-Phenylhept-6-en-1-yl acetate (*ent*-21)



***ent*-21**

Prepared accordingly as described above for **21** from (*R*)-1-phenylhept-6-en-1-ol **(*ent*-20)**.

(1*S*,6*S*)-6,7-Dihydroxy-1-phenylheptyl acetate (22)

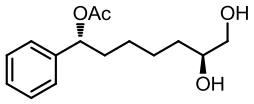


21 **22**

AD-mix-α (6 g) was added to a solution of (*S*)-1-Phenylhept-6-en-1-yl acetate (0.98 g, 4.2 mmol) in *t*-BuOH-H_2O (10 mL/10 mL) at 0 °C. The reaction was then stirred at 4 °C for 2 days and diluted with EtOAc (10 mL), quenched by Na_2SO_3 (5.0 g) in portions. The reaction was stirred for 30 minutes at 4 °C and 1 hour at room temperature. The organic phase was separated and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel chromatography (PE/EtOAc = 1:1) to give the desired product as a colorless oil (1.02 g, 91%).

R_f 0.25 (PE/EtOAc 1:2, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = -51.7 (c = 1.0, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
7.36-7.27 (m, 5H), 5.73 (q, *J* = 8.0 Hz, 1H), 3.73-3.54 (m, 2H), 3.41-3.38 (m, 1H), 2.06 (s, 3H), 1.93-1.89 (m, 1H), 1.82-1.74 (m, 1H), 1.46-1.26 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.5, 140.6, 128.4, 127.8, 126.5, 75.9, 72.0, 66.7, 36.2, 32.9, 25.4, 25.1, 21.3.
ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 289.1416, found: 289.1417.

(1*R*,6*S*)-6,7-Dihydroxy-1-phenylheptyl acetate (17-*epi*-22)

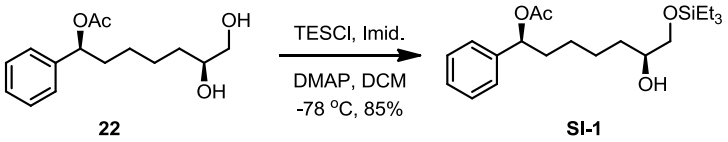


17-*epi*-22

Prepared accordingly as described above for **22** from (*R*)-1-phenylhept-6-en-1-yl acetate (***ent*-21**).

R_f 0.25 (PE/EtOAc 1:2, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = 51.9 (c = 1.3, $CHCl_3$)
^{1}H NMR (500 MHz, $CDCl_3$)
δ 7.35-7.26 (m, 5H), 5.72 (t, J = 4.0 Hz, 1H), 3.67-3.60 (m, 2H), 3.42-3.38 (m, 1H), 2.06 (s, 3H), 1.93-1.90 (m, 1H), 1.80-1.75 (m, 1H), 1.48-1.23 (m, 6H).
^{13}C NMR (125 MHz, $CDCl_3$)
δ 170.5, 140.6, 76.0, 72.0, 66.7, 36.1, 32.9, 26.1, 25.4, 25.2, 21.3.

(1*S*,6*S*)-6-Hydroxy-1-phenyl-7-((triethylsilyl)oxy)heptyl acetate (SI-1)

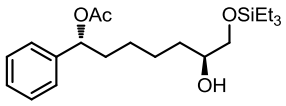


22 **SI-1**

To a solution of diol **22** (106.0 mg, 0.40 mmol), imidazole (82.0 mg, 1.2 mmol) and DMAP (2.44 mg, 0.02 mmol) in 5 mL dichloromethane was added chlorotriethylsilane (67 µL, 0.40 mmol, 1.0 eq) dropwise at –78 °C. After stirring at –78 °C for 2 h, the reaction was quenched with H_2O (5 mL) and extracted with MTBE (3 × 20 mL). The organic layers were combined and dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by silica gel chromatography (PE/EtOAc = 9:1) to give the desired product as a colorless oil (130 mg, 85%).

R_f 0.30 (PE/EtOAc 9:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = -62.0 (c = 0.35, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.35-7.26 (m, 5H), 5.72 (q, *J* = 8.0 Hz, 1H), 3.62-3.57 (m, 2H), 3.37-3.32 (m, 1H), 2.44 (br, 1H), 2.06 (s, 3H), 1.93-1.88 (m, 1H), 1.81-1.75 (m, 1H), 1.48-1.26 (m, 6H), 0.97-0.93 (m, 9H), 0.64-0.58 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.4, 140.7, 128.4, 127.8, 126.5, 76.0, 71.7, 66.9, 36.3, 32.6, 25.6, 25.3, 21.3, 6.70, 4.3.
ESI-HRMS calculated for $C_{28}H_{44}O_4Si$ $[M + Na]^+$: 403.2281, found: 403.2285.

(1*R*,6*S*)-6-Hydroxy-1-phenyl-7-((triethylsilyl)oxy)heptyl acetate (17-*epi*-SI-1)

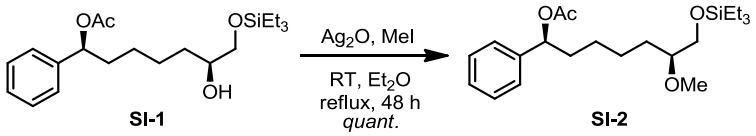


17-epi-SI-1

Prepared accordingly as described above for **SI-1** from (1*R*,6*S*)-6,7-dihydroxy-1-phenylheptyl acetate (**17-*epi*-22**).

R_f 0.30 (PE/EtOAc 9:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = 39.5 (c = 1.0, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.34-7.27 (m, 5H), 5.71 (q, *J* = 4.0 Hz, 1H), 3.61-3.57 (m, 2H), 3.37-3.32 (m, 1H), 2.44 (d, *J* = 4.0 Hz, 1H), 2.06 (s, 3H), 1.93-1.87 (m, 1H), 1.82-1.75 (m, 1H), 1.49-1.21 (m, 6H), 0.97-0.93 (m, 9H), 0.63-0.57 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.4, 140.7, 128.4, 127.8, 126.5, 126.4, 76.1, 71.6, 66.9, 36.2, 32.6, 25.6, 25.3, 21.3, 6.7, 4.3.

(1*S*,6*S*)-6-Methoxy-1-phenyl-7-((triethylsilyl)oxy)heptyl acetate (SI-2)



SI-1 SI-2

To a solution of alcohol (100 mg, 0.26 mmol) in diethyl ether (2 mL) were added silver oxide (301 mg, 1.30 mmol), 4 Å molecular sieves (400 mg) and iodomethane (0.16 mL, 2.6 mmol). The mixture was stirred at room temperature for 48 h in the absence of direct light. The reaction was then filtered throught a pad of celite and washed thoroghly with MTBE. The organic solution was concentrated. The residue was purified via flash column chromatography (PE/EtOAc = 15:1) to afford the desired product as colorless oil (106 mg, 100%).

R_f 0.20 (PE/EtOAc 15:1, $KMnO_4$)

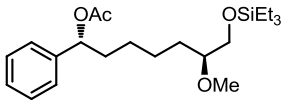
Opt. Rot. $[\alpha]^{20}_D$ = -48.3 (c = 0.74, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.38-7.29 (m, 5H), 5.74 (q, *J* = 8.0 Hz, 1H), 3.62 (dd, *J* =8.0 & 12.0 Hz, 1H), 3.54 (dd, *J* =8.0 & 12.0 Hz, 1H), 3.41 (s, 3H), 3.20-3.15 (m, 1H), 2.09 (s, 3H), 1.96-1.89 (m, 1H), 1.83-1.77 (m, 1H), 1.50-1.26 (m, 6H), 0.99-0.96 (m, 9H), 0.65-0.59 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.4, 140.8, 128.4, 127.8, 126.5, 81.9, 76.05, 64.8, 57.9, 36.3, 31.2, 25.7, 25.2, 21.3, 6.8, 4.4.

ESI-HRMS calculated for $C_{22}H_{30}O_4$ $[M + Na]^+$: 417.2437, found: 417.2439.

(1*R*,6*S*)-6-Methoxy-1-phenyl-7-((triethylsilyl)oxy)heptyl acetate (17-*epi*-SI-2)



17-epi-SI-2

Prepared accordingly as described above for **SI-2** from (1*R*,6*S*)-6-hydroxy-1-phenyl-7-((triethylsilyl)oxy)heptyl acetate (**17-*epi*-SI-1**).

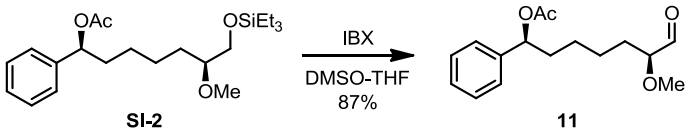
R_f 0.20 (PE/EtOAc 15:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = 28.4 (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.36-7.26 (m, 5H), 5.74 (q, *J* = 4.0 Hz, 1H), 3.60 (dd, *J* =4.0 & 12.0 Hz, 1H), 3.52 (dd, *J* =4.0 & 12.0 Hz, 1H), 3.39 (s, 3H), 3.17-3.12 (m, 1H), 2.06 (s, 3H), 1.92-1.87 (m, 1H), 1.82-1.73 (m, 1H), 1.50-1.20 (m, 6H), 0.97-0.93 (m, 9H), 0.62-0.56 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.4, 140.7, 128.4, 127.8, 126.6, 126.5, 81.8, 76.1, 64.8, 57.9, 36.2, 31.2, 25.6, 25.1, 21.3, 6.7, 4.4.

(1*S*,6*S*)-6-Methoxy-7-oxo-1-phenylheptyl acetate (11)



SI-2 **11**

(1*S*,6*S*)-6-Methoxy-1-phenyl-7-((triethylsilyl)oxy)heptyl acetate (106 mg, 0.26 mmol) was dissolved in DMSO-THF (10 mL/5 mL) and IBX[3] (271 mg, 0.97 mmol) was added at room temperature. The mixture was stirred overnight. Then, saturated aqueous $NaHCO_3$ (25 mL) was added and the mixture extracted with MTBE (3 × 25 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified via flash column chromatography (PE/EtOAc = 9:1) to afford the desired product as colorless oil (63 mg, 87%).

R_f 0.30 (PE/EtOAc 4:1, $KMnO_4$)

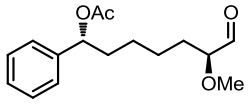
Opt. Rot. $[\alpha]^{20}_D$ = -103.3 (c = 1.5, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 9.62 (d, *J*= 4.0 Hz, 1H), 7.36-7.26 (m, 5H), 5.71 (q, *J* = 4.0 Hz, 1H), 3.54-3.50 (m, 1H), 3.42 (s, 3H), 2.06 (s, 3H), 1.94-1.86 (m, 1H), 1.79-1.73 (m, 1H), 1.63-1.59 (m, 6H), 1.45-1.21 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 203.9, 170.3, 140.6, 128.4, 127.9, 126.5, 85.6, 75.8, 58.2, 36.0, 29.6, 25.3, 24.4, 21.3.

ESI-HRMS calculated for $C_{22}H_{28}O_4$ $[M + Na]^+$: 301.1416, found: 301.1413.

(1*R*,6*S*)-6-Methoxy-7-oxo-1-phenylheptyl acetate (17-*epi*-11)



17-*epi*-11

Prepared accordingly as described above for **11** from (1*R*,6*S*)-6-methoxy-1-phenyl-7-((triethylsilyl)oxy)heptyl acetate (**17-*epi*-SI-2**).

R_f 0.30 (PE/EtOAc 4:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = 2.1 (c = 0.7, $CHCl_3$)

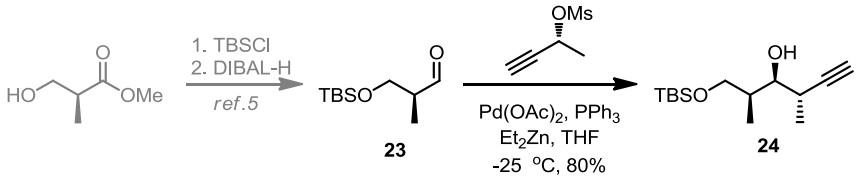
^{1}H NMR (400 MHz, $CDCl_3$)
δ 9.62 (d, *J* = 4.0 Hz, 1H), 7.36-7.27 (m, 5H), 5.71 (t, *J* = 8.0 Hz, 1H), 3.53-3.49 (m, 1H), 3.42 (s, 3H), 2.06 (s, 3H), 1.92-1.87 (m, 1H), 1.80-1.76 (m, 1H), 1.63-1.56 (m, 6H), 1.45-1.21 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 203.9, 170.3, 140.5, 128.4, 127.9, 126.5, 126.4, 85.5, 75.9, 58.2, 36.0, 29.6, 25.3, 24.3, 21.3.

(3) Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537.

2.2 Syntheses of the Eastern Segments (10 and 12)

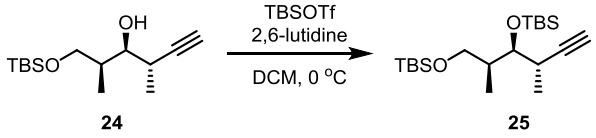
(2*S*,3*S*,4*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-2,4-dimethylhex-5-yn-3-ol (24)[4]



$Pd(OAc)_2$ (269 mg, 1.2 mmol) was dissolved in 120 mL of THF and cooled to -78 °C. PPh_3 (315 mg, 1.2 mmol) was added and the mixture was stirred for 10 min. A solution of aldehyde **23** (4.85 g, 24 mmol)[5] and mesylate (3.85 g, 26 mmol) in 15 mL of THF was added, followed by Et_2Zn (72 mL, 1.0 M in hexane) slowly. The mixture was stirred for 30 minutes, warmed to -25 °C and stirred at this temperature for 8 h. The dark reaction was then quenched by aqueous NH_4Cl. The organic phase was separated and the aqueous phase was extracted three times with Et_2O. The combined organic extracts were washed with brine and dried over $MgSO_4$ with activated charcoal. Filtration through Celite and concentration under reduced pressure, followed by flash chromatography on silica gel (5% EtOAc/ hexanes) afforded the desired product as yellow oil (4.90 g, 80%).

R_f 0.4 (PE/EtOAc 9:1, $KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 3.72-3.65 (m, 2H), 3.62-3.58 (m, 1H), 2.71 (d, *J* = 4.0 Hz, 1H), 2.70-2.62 (m, 1H), 2.13 (d, *J* = 4.0 Hz, 1H), 1.83-1.77 (m, 1H), 1.19 (d, *J* = 8.0 Hz, 3H), 0.96 (d, *J* = 8.0 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 86.5, 76.3, 70.1, 67.3, 37.4, 30.5, 25.9, 18.2, 17.6, 10.3, -5.3, -5.6.

(5*S*,6*S*)-5-((*S*)-But-3-yn-2-yl)-2,2,3,3,6,9,9,10,10-nonamethyl-4,8-dioxa-3,9-disilaundecane (25)



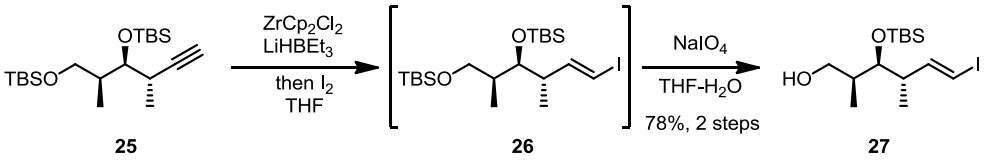
A solution of alcohol (3.6 g, 14 mmol) and 2,6-lutidine (2.5 mL, 21 mmol) in 50 mL of CH_2Cl_2 was cooled to 0 °C. TBSOTf (3.6 mL, 16 mmol) was added dropwise, and the mixture was stirred for 90 min at this temperature. It was then quenched with water. The organic phase was separated and the aqueous phase was extracted three times with CH_2Cl_2. The combined organic extracts were washed with brine and dried over $MgSO_4$. Filtration, concentration under reduced pressure followed by flash chromatography on silica gel (100% hexanes) afforded the desired product as yellow oil (4.88 g, 94% yield).

R_f 0.5 (PE/EtOAc 15:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = 6.6 (c = 1.4, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 3.79 (d, *J* = 4.0 Hz, 1H), 3.51 (dd, *J* = 8.0 & 12Hz, 1H), 3.42 (dd, *J* = 8.0 & 12Hz, 1H), 2.66-2.59 (m, 1H), 2.02 (d, *J* = 4.0 Hz, 1H), 1.96-1.88 (m, 1H), 1.18 (d, *J* = 8.0 Hz, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.86 (d, *J* = 8.0 Hz, 3H), 0.09 (s, 3H) , 0.07 (s, 3H), 0.04 (s, 9H).

(4) a) Marshall, J. A.; Keith, E. *Tetrahedron Lett.* **2004**, *45*, 1351; b) Marshall, J. A.; Bourbeau, M. P. *Org. Lett.* **2003**, *5*, 3197-3199.
(5) Urbanek, R. A.; Sabes, S. F.; Forsyth, C. J.; *J. Am. Chem. Soc.* **1998**, *120*, 2523-2533..

^{13}C NMR (100 MHz, $CDCl_3$)
δ 87.5, 73.8, 69.8, 65.8, 39.0, 31.8, 26.1, 25.9, 18.4, 18.2, 17.3, 11.4, -3.8, -4.2, -5. 29, -5.33.
ESI-HRMS calculated for $C_{29}H_{46}O_7$ [M + Na]$^+$: 393.2621, found: 393.2620.

(2*S*,3*S*,4*S*,*E*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-iodo-2,4-dimethylhex-5-en-1-ol (27)



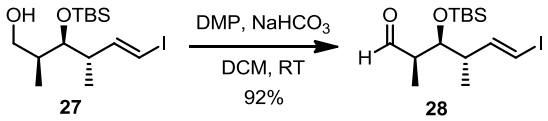
25 26 27

Super hydride (1.0 M, 15 mL) was added dropwise to a solution of zirconocene dichloride (4.38 g, 15 mmol) in THF (80 mL) at 0 °C. After further stirred 0.5 h at 0 °C and 0.5 h at room temperature, a solution of alkyne (3.70 g, 10 mmol) in THF (10 mL) was added dropwise over 10 min at 0 °C. The reaction mixture was allowed to stir at room temperature for 1 h, and a solution of I_2 (5.08 g, 20 mmmol) in THF (10 mL) was then added dropwise at 0 °C. After stirred for 5 h, it was warmed to room temperature and stirred for 2 h. The reaction was quenched with saturated $NaHCO_3$ (12 mL), saturated $Na_2S_2O_3$ (12 mL), filtered over Celite and extracted with MTBE (3 × 30 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated.

The residue was dissolved in THF (60 mL), H_2O (15 mL) and $NaIO_4$ (12.8 g, 60 mmol) were added. The suspension was stirred 2 days at room temperature, quenched with H_2O (40 mL) and extracted with MTBE (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification of the residue by flash column chromatography afforded the desired product as yellow oil (3.0 g, 78%).

R_f 0.3 (PE/EtOAc 9:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = - 15.8 (c = 1.0, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 6.52 (dd, *J* = 8.0 & 16.0 Hz, 1H), 6.02 (d, *J*= 16.0 Hz, 1H), 3.64 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.61-3.57 (m, 1H), 3.49-3.43 (m, 1H), 1.01 (d, *J* = 8.0 Hz, 3H), 0.91 (d, *J* = 8.0 Hz, 3H), 0.87 (d, *J* = 8.0 Hz, 3H), 0.07 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 149.5, 75.9, 75.2, 65.6, 44.8, 39.6, 26.0 (s), 18.3, 17.5, 11.6, -3.7, -4.0.
ESI-HRMS calculated for $C_{29}H_{46}O_7$ [M + Na]$^+$: 407.0879, found: 407.0878.

(2*R*,3*S*,4*S*,*E*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-iodo-2,4-dimethylhex-5-enal (28)

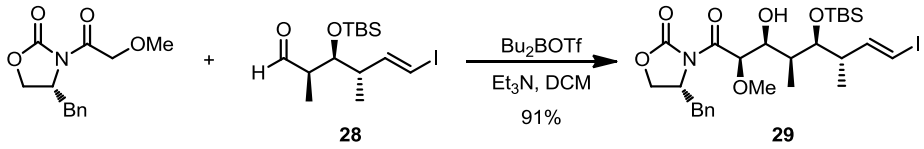


27 28

To a solution of the alcohol (1.68 g, 4.37 mmol) in DCM (70 mL) was added solid $NaHCO_3$ (2.90 g, 35 mmol) at room temperature. After stirred for 10 min, the reaction was cooled to 0 °C and Dess-Martin periodinane[6] (2.80 g, 6.55 mmol) was added. The mixture was stirred at room temperature for 1.5 h, quenched with 1 N Na_2SO_3 (35 mL) at 0 °C, further stirred for 1 h and diluted with water (10 mL). The mixture was then extracted with MTBE (3 × 60 mL). The combined organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified via flash column chromatography (PE/EtOAc = 15:1) to give the desired product as colorless oil (1.53 g, 92%).

R_f 0.5 (PE/EtOAc 9:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = - 102.3 (c = 0.7, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 9.73 (s, 1H), 6.45 (dd, *J* = 4.0 & 12.0 Hz, 1H), 6.06 (d, *J* = 12.0 Hz, 1H), 3.98 (t, *J* = 4.0 Hz, 1H), 2.50-2.39 (m, 2H), 1.10 (d, *J* = 8.0 Hz, 3H), 1.03 (d, *J* = 8.0 Hz, 3H), 0.89 (s, 9H), 0.09 (s, 3H) , 0.02 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 204.2, 147.8, 77.1, 74.5 (s), 50.9, 45.03, 25.9, 18.2, 17.2, 8.8, -4.0 , -4.1.
ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 405.0723, found: 405.0723.

(*R*)-4-Benzyl-3-((2*R*,3*S*,4*S*,5*S*,6*S*,*E*)-5-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-8-iodo-2-methoxy-4,6-dimethyloct-7-enoyl)oxazolidin-2-one (29)



28 29

To a solution of (*R*)-4-benzyl-3-(2-methoxyacetyl)oxazolidin-2-one (1.49 g, 6 mmol) in dichloromethane (20 mL) at -78 °C were sequentially added a 1 M solution of dibutylboron triflate in CH_2Cl_2 (6 mL, 6.0 mmol) and Et_3N (1.67 mL, 12 mmol). The mixture was stirred 45 min at 0 °C then cooled to -78 °C. A solution of aldehyde (1.53 g, 4 mmol) in 10 mL of CH_2Cl_2 was then added and the reaction was gradually warmed to 0 °C and stirred at this temperature overnight. The reaction mixture was then hydrolysed with 12 mL of a 2:1 mixture of methanol and phosphate buffer pH 7 and then 12 mL of a 2:1 mixture of methanol and 30% hydrogen peroxide were added at 0 °C. After stirring 1 h at 0 °C, the mixture was diluted with pH 7 buffer (12 mL) and extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (PE/ EtOAc, 1:1) and the desired product was obtained as colorless oil (2.30 g, 91%).

R_f 0.5 (PE/EtOAc 2:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = - 21.0 (c = 1.7, $CHCl_3$)

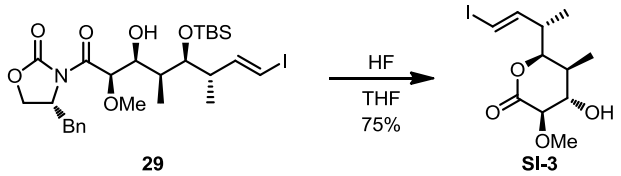
(6) a) Dess, D. B.; Martin, J. C. *J. Org.Chem.* **1983**, 48, 4155; *J. Am. Chem. Soc.* **1991**, 113, 7277. For two improved procedures for the preparation of DMP, see: Ireland, R. E.; Liu, J. *J. Org. Chem.* **1993**, *58*, 2899; Meyers, S. D.; Schreiber, S. L. *J. Org. Chem.* **1994**, *59*, 7459.

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.36-7.26 (m, 5H), 6.51 (dd, *J* = 8.0 & 16.0 Hz, 1H), 6.03 (d, *J* = 12.0 Hz, 1H), 5.05 (d, *J* = 4.0 Hz, 1H), 4.76-4.70 (m, 1H), 4.31-4.27 (m, 1H), 4.24-4.21 (m, 1H), 3.82-3.78 (m, 1H), 3.64 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.48 (s, 3H), 3.38 (dd, *J* = 4.0 & 16.0 Hz, 1H), 2.84 (dd, *J* = 4.0 & 12.0 Hz, 1H), 2.45-2.40 (m, 1H), 2.29 (d, *J* = 4.0 Hz, 1H), 1.79-1.77 (m, 1H), 1.58-1.56 (m, 1H), 1.04 (d, *J* = 4.0 Hz, 3H), 0.95 (d, *J* = 8.0 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 3H) , 0.05 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 171.0, 153.2, 148.4, 134.9, 129.5, 129.0, 127.5, 80.8, 75.7, 75.6, 72.9, 67.0, 58.5, 55.8, 45.8, 39.6, 37.7, 26.1, 18.4, 17.0, 10.7, -3.8, -4.0.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ [M + Na]$^+$: 654.1724, found: 654.1724.

(3*R*,4*S*,5*S*,6*S*)-4-Hydroxy-6-((*S*,*E*)-4-iodobut-3-en-2-yl)-3-methoxy-5-methyltetrahydro-*2H*-pyran-2-one (SI-3)



29 **SI-3**

A solution of alcohol (0.98 g, 1.5 mmol) in THF (20 mL) was treated dropwise with a solution of hydrogen fluoride in pyridine (~70 % hydrogen fluoride, 9 mL) at 0 °C. After addition, the reaction mixture was stirred overnight at room temperature and concentrated. The residue was purified by flash column chromatography (PE/EtOAc = 4:1) to afford the desired product as colorless oil (382 mg, 75%).

R_f 0.2 (PE/EtOAc 4:1, $KMnO_4$)

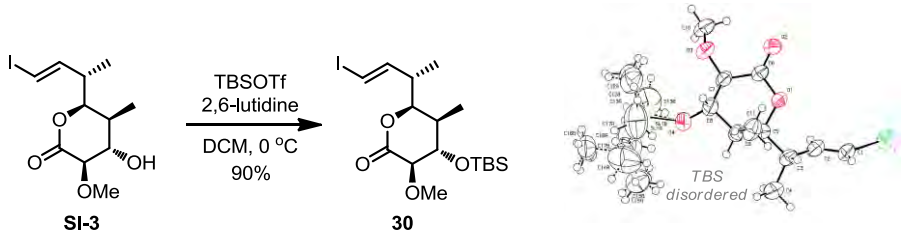
Opt. Rot. $[\alpha]^{20}_{D}$ = - 21.2 (c = 2.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 6.54 (dd, *J* = 4.0 & 16.0 Hz, 1H), 6.21 (d, *J* = 12.0 Hz, 1H), 4.20 (dd, *J* = 4.0 & 12.0 Hz, 1H), 3.87 (d, , *J* = 8.0 Hz, 1H), 3.63 (s, 3H), 3.59 (d, *J* = 8.0 Hz, 1H), 2.63 (br, 1H), 2.55-2.49 (m, 1H), 2.18-2.11 (m, 1H), 1.03 (d, *J* = 4.0 Hz, 3H), 1.01 (d, *J* = 4.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.0, 146.7, 81.7, 79.6, 77.3, 76.5, 59.7, 40.8, 38.1, 14.8, 12.5.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ [M + Na]$^+$: 363,0069, found: 363,0072.

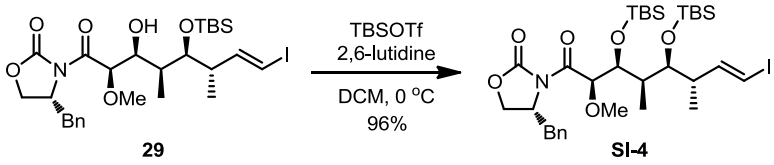
(3*R*,4*S*,5*R*,6*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-6-((*S*,*E*)-4-iodobut-3-en-2-yl)-3-methoxy-5-methyltetrahydro-*2H*-pyran-2-one (30)



A solution of alcohol (380 mg, 1.1 mmol) and 2,6-lutidine (0.25 mL, 2.2 mmol) in 10 mL of CH_2Cl_2 was cooled to 0 °C. TBSOTf (0.35 mL, 1.6 mmol) was added dropwise, and the mixture was stirred for 90 min at this temperature. It was then quenched with water. The organic phase was separated and the aqueous phase was extracted three times with CH_2Cl_2. The combined organic extracts were washed with brine and dried over $MgSO_4$. Filtration, concentration under reduced pressure followed by flash chromatography on silica gel (PE/EtOAc = 9:1) afforded the desired product as yellow oil (450 mg, 90%).

R_f 0.7 (PE/EtOAc 9:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = - 62.0 (c = 1.0, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 6.57 (dd, *J* = 8.0 & 16.0 Hz, 1H), 6.20 (d, *J* = 16.0 Hz, 1H), 4.21 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.75 (d, , *J* = 8.0 Hz, 1H), 3.58-3.56 (m, 4H), 2.54-2.45 (m, 1H), 2.01-1.95 (m, 1H), 0.99 (d, *J* = 8.0 Hz, 3H), 0.92-0.89 (m, 12H), 0.10 (s, 3H), 0.09 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.8, 146.9, 83.0, 79.5, 77.1, 59.8, 41.0, 40.2, 25.7, 17.9, 14.8, 11.3, -4.6, -4.9.
ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 477.0934, found: 477.0935.

(*R*)-4-Benzyl-3-((2*R*,3*S*,4*R*,5*S*,6*S*,*E*)-3,5-bis((*tert*-butyldimethylsilyl)oxy)-8-iodo-2-methoxy-4,6-dimethyloct-7-enoyl)oxazolidin-2-one (SI-4)

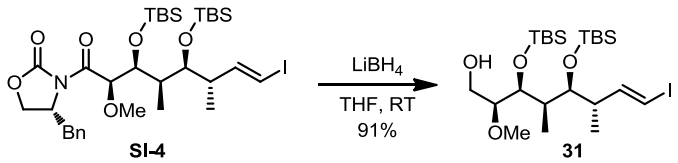


A solution of alcohol (6.20 g, 9.8 mmol) and 2,6-lutidine (2.1 mL, 18 mmol) in 50 mL of CH_2Cl_2 was cooled to 0 °C. TBSOTf (2.80 mL, 12 mmol) was added dropwise, and the mixture was stirred for 90 min at this temperature. It was then quenched with water. The organic phase was separated and the aqueous phase was extracted three times with CH_2Cl_2. The combined organic extracts were washed with brine and dried over $MgSO_4$. Filtration, concentration under reduced pressure followed by flash chromatography on silica gel (PE/EtOAc = 15:1) afforded the desired product as yellow oil (7.00 g, 96%).

R_f 0.5 (PE/EtOAc 9:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = - 55.3 (c = 0.3, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.39-7.26 (m, 5H), 6.44 (dd, *J* = 8.0 & 12.0 Hz, 1H), 6.06 (d, *J* = 16.0 Hz, 1H), 5.19 (br, 1H), 4.75-4.73 (m, 1H), 4.30-4.26 (m, 1H), 4.20 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.99 (d, *J* = 8.0 Hz, 1H), 3.54 (d, *J* = 8.0 Hz, 1H), 3.46-3.36 (m, 4H), 2.78 (dd, *J* = 8.0 & 12.0 Hz, 1H), 2.52-2.45 (m, 1H), 1.04 (d, *J* = 4.0 Hz, 3H), 0.92-0.85 (m, 21H), 0.12 (s, 3H), 0.10 (s, 3H) , 0.05 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 172.2, 153.0, 147.3, 135.0, 129.6, 129.0, 127.4, 76.3, 76.1, 73.7, 66.5, 58.1, 56.0, 44.1, 39.9, 37.7, 29.1, 26.3, 26.2, 22.6, 19.1, 18.5, 11.4, 11.3, -2.8, -3.5, -3.6, -4.7.
ESI-HRMS calculated for $C_{29}H_{46}O_7$ [M + Na]$^+$: 768.2589, found: 768.2587.

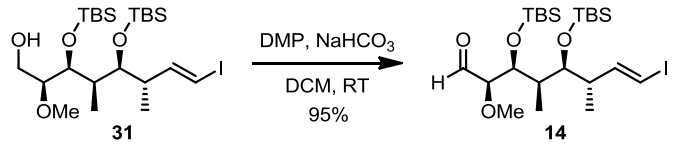
(2*S*,3*S*,4*R*,5*S*,6*S*,*E*)-3,5-Bis((*tert*-butyldimethylsilyl)oxy)-8-iodo-2-methoxy-4,6-dimethyloct-7-en-1-ol (31)



Lithium borohydride (4.0 M in THF, 8 mL, 32 mmol) was added to to a solution of **SI-4** (4.76 g, 6.4 mmol) in 50 mL of THF at 0 °C. The mixture was then stirred at room temperature for 6 h and quenched with slow addition of saturate aq. NH_4Cl (30 mL) at 0 °C. The mixture was extracted with EtOAc (3 × 30 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified via flash column chromatography (PE/EtOAc = 7:1) to afford the desired product as colorless oil (3.34 g, 91%).

R_f 0.2 (PE/EtOAc 9:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = - 6.4 (c = 1.0, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 6.54 (dd, *J* = 8.0 & 16.0 Hz, 1H), 6.02 (d, *J* = 12.0 Hz, 1H), 3.85-3.78 (m, 2H), 3.62 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.55-3.50 (m, 1H), 3.39 (s, 3H), 3.18-3.14 (m, 1H), 2.48-2.44 (m, 1H), 1.79-1.72 (m, 2H), 1.04 (d, *J* = 8.0 Hz, 3H), 0.93-0.85 (m, 21H), 0.09 (s, 3H), 0.06 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 148.0, 84.4, 76.0, 75.6, 72.0, 59.8, 57.9, 44.5, 39.0, 26.3, 26.1, 18.5, 18.4, 18.2, 11.0, -3.1, -3.5, -3.7, -4.5.
ESI-HRMS calculated for $C_{29}H_{46}O_7$ [M + Na]$^+$: 595.2112, found: 595.2112.

(2*R*,3*S*,4*R*,5*S*,6*S*,*E*)-3,5-Bis((*tert*-butyldimethylsilyl)oxy)-8-iodo-2-methoxy-4,6-dimethyloct-7-enal (14)



To a solution of the alcohol (458 mg, 0.8 mmol) in DCM (16 mL) was added solid $NaHCO_3$ (538 g, 6.4 mmol) at room temperature. After stirred for 10 min, the reaction was cooled to 0 °C and Dess-Martin periodinane (576 g, 1.36 mmol) was added. The mixture was stirred at room temperature for 1.5 h, quenched with 1 N Na_2SO_3 (10 mL) at 0 °C, further stirred for 1 h and diluted with water (10 mL). The mixture was then extracted with MTBE (3 × 25 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified via flash column chromatography (PE/EtOAc = 15:1) to give the desired product as colorless oil (435 mg, 95%).

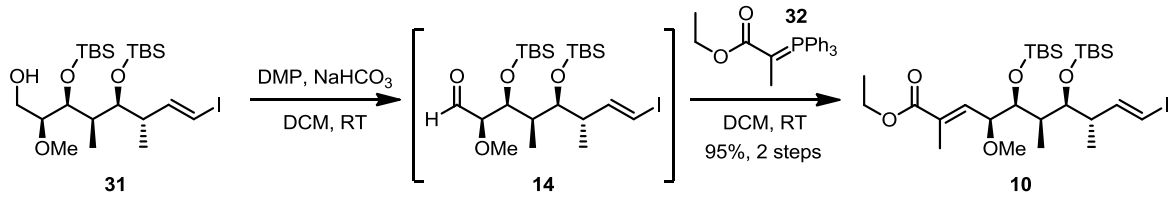
R_f 0.7 (PE/EtOAc 9:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D$ = 3.7(c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 9.64 (d, *J* = 4.0 Hz, 1H), 6.48 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.97 (d, *J* = 12.0 Hz, 1H), 3.93 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.62 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.56 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.38 (s, 3H), 2.43-2.38 (m, 1H), 1.70-1.66 (m, 1H), 0.99 (d, *J* = 4.0 Hz, 3H), 0.91-0.96 (m, 21H), 0.09 (s, 6H), 0.06 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 201.8, 148.4, 89.0, 75.2, 72.5, 58.6, 44.9, 39.6, 26.2, 26.0, 18.5, 18.4, 17.8, 10.9, -3.1, -3.5, -3.8, -4.6.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 593.1955, found: 593.1953.

Ethyl (2*E*,4*S*,5*S*,6*R*,7*S*,8*S*,9*E*)-5,7-bis((*tert*-butyldimethylsilyl)oxy)-10-iodo-4-methoxy-2,6,8-trimethyldeca-2,9-dienoate (10)



To a solution of the crude aldehyde prepared as described above (288 mg, 0.35 mmol) in DCM (10 mL) was added 1-carbethoxyethylidentriphenylphosphorane (1.28 mg, 3.5 mmol) at 0 °C and the mixture was stirred at room temperature for 16 h. Then the reaction was concentrated and the residue was purified by flash column chromatography (PE/Et_2O = 4:1) to afford the desired product as colorless oil (300 mg, 95%).

R_f 0.8 (PE/EtOAc 9:1, $KMnO_4$)

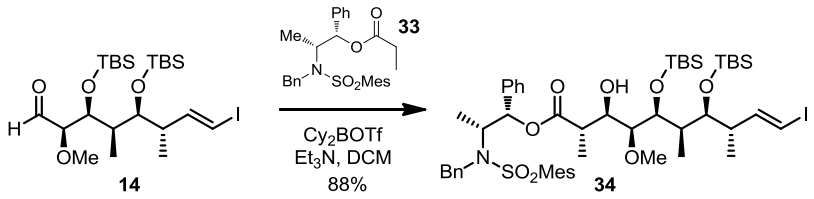
Opt. Rot. $[\alpha]^{20}_{D}$ = - 3.1 (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 6.50 (dd, *J* = 8.0 & 16.0 Hz, 1H), 6.30 (dd, *J* = 4.0 & 12.0 Hz, 1H), 5.96 (d, *J* = 16.0 Hz, 1H), 4.31-4.22 (m, 2H), 3.84 (d, *J* = 8.0 Hz, 1H), 3.68 (d, *J* = 4.0 Hz, 1H), 3.56 (d, *J* = 4.0 Hz, 1H), 3.17 (s, 3H), 2.46-2.39 (m, 1H), 1.95 (s, 3H), 1.34 (t, *J* = 8.0 Hz, 3H), 1.03 (d, *J* = 8.0 Hz, 3H), 0.91 (s, 18H), 0.82 (d, *J* = 8.0 Hz, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 167.4, 147.9, 136.3, 132.2, 80.9, 76.1, 74.9, 74.7, 61.1, 56.1, 44.2, 39.7, 26.3, 26.2, 18.7, 18.5, 14.4, 13.4, 11.0, -3.1, -3.4, -3.5, -4.9.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 677.2531, found: 677.2531.

(1*S*,2*R*)-2-((*N*-Benzyl-2,4,6-trimethylphenyl)sulfonamido)-1-phenylpropyl (2*S*,3*R*,4*S*,5*S*,6*R*,7*S*,8*S*,*E*)-5,7-bis ((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-10-iodo-4-methoxy-2,6,8-trimethyldec-9-enoate (34)



To (1*S*,2*R*)-2-((*N*-benzyl-2,4,6-trimethylphenyl)sulfonamido)-1-phenylpropyl propionate (1.92 g, 4 mmol) was added CH_2Cl_2 (25 mL) and triethylamine (2.00 mL, 14 mmol) via syringe under argon. The solution was cooled to -78 °C and dicyclohexylboron triflate[7] (1.0 M in hexane, 10 mL, 10 mmol) was added dropwise. The resulting solution was stirred at -78 °C for 2 h. Aldehyde **14** (2.28 g, 4 mmol) in CH_2Cl_2 (10 mL) was added dropwise to the enolate solution. The reaction mixture was stirred for 1 h at -78 °C and was allowed to warm to room temperature, stirred overnight, and then quenched by addition of pH 7 buffer solution (16 mL). The mixture was diluted with MeOH (80 mL) and 30% hydrogen peroxide (8 mL) was added carefully. The whole mixture was stirred vigorously for 3 h and then was diluted with water (40 mL) and extracted with CH_2Cl_2 (3 × 60 mL). The combined organic extracts were washed with water (3 × 40 mL) and dried with anhydrous sodium sulfate. The filtered organic layer was concentrated and the residue was purified via flash column chromatography (PE/EtOAc = 15:1→10:1) to give the desired product as colorless oil (3.70 g, 88%).

R_f 0.5 (PE/EtOAc 4:1, UV/$KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = - 26.1 (c = 1.5, $CHCl_3$)

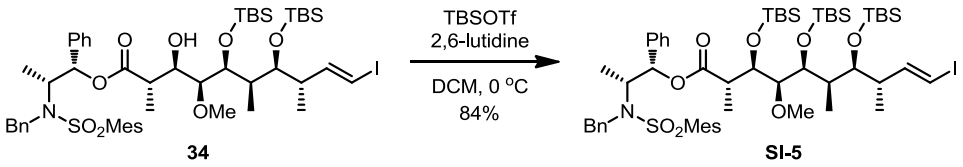
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.36-7.34 (m, 2H), 7.28-7.10 (m, 10H), 6.85 (s, 2H), 6.80 (d, *J* = 4.0 Hz, 1H), 6.52 (dd, *J* = 8.0 & 16.0 Hz, 1H), 6.02 (d, *J* = 12.0 Hz, 1H), 5.79 (d, *J* = 4.0 Hz, 1H), 4.82 (d, *J* = 16.0 Hz, 1H), 4.52 (d, *J* = 16.0 Hz, 1H), 4.15-4.10 (m, 1H), 3.82 (d, *J* = 8.0 Hz, 1H), 3.50-3.46 (m, 2H), 3.22 (s, 3H), 2.98 (d, *J* = 4.0 Hz, 1H), 2.62-2.56 (m, 1H), 2.51-2.42 (m, 6H), 2.29 (s, 3H), 1.23 (d, *J* = 4.0 Hz, 3H), 1.14 (d, *J* = 8.0 Hz, 3H), 1.02 (d, *J* = 8.0 Hz, 3H), 0.92-0.83 (m, 27H), 0.04 (s, 6H), 0.01 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 173.4, 147.8, 142.4, 140.4, 138.5, 138.0, 133.1, 132.1, 128.4, 128.3, 128.1, 128.0, 127.2, 126.7, 81.5, 77.7, 77.2, 76.0, 75.6, 72.7, 71.4, 60.8, 56.7, 48.1, 44.7, 44.5, 39.8, 26.3, 26.2, 22.9, 20.9, 18.8, 18.6, 18.2, 14.6, 14.5, 10.9, -2.9, -3.5, -3.6, -4.2.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 1072.4086, found: 1072.4086.

(7) a) Dess, D. B.; Martin, J. C. *J. Org.Chem.* **1983**, 48, 4155; *J. Am. Chem. Soc.* **1991**, 113, 7277. For two improved procedures for the preparation of DMP, see: Ireland, R. E.; Liu, J. *J. Org. Chem.* **1993**, *58*, 2899; Meyers, S. D.; Schreiber, S. L. *J. Org. Chem.* **1994**, *59*, 7549.

(1*S*,2*R*)-2-((*N*-Benzyl-2,4,6-trimethylphenyl)sulfonamido)-1-phenylpropyl (2*S*,3*R*,4*R*,5*S*,6*R*,7*S*,8*S*,*E*)-3,5,7-tris((*tert*-butyldimethylsilyl)oxy)-10-iodo-4-methoxy-2,6,8-trimethyldec-9-enoate (SI-5)



A solution of alcohol (568 mg, 0.54 mmol) and 2,6-lutidine (0.12 mL, 1.08 mmol) in 10 mL of CH_2Cl_2 was cooled to 0 °C. TBSOTf (0.19 mL, 0.81 mmol) was added dropwise, and the mixture was stirred for 2 h at this temperature. It was then quenched with water. The organic phase was separated and the aqueous phase was extracted three times with CH_2Cl_2 (10 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$. Filtration, concentration under reduced pressure followed by flash chromatography on silica gel (PE/EtOAc = 15:1) afforded the desired product as yellow oil (528 mg, 84%).

R_f 0.4 (PE/EtOAc 15:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = - 16.2 (c = 3.5, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

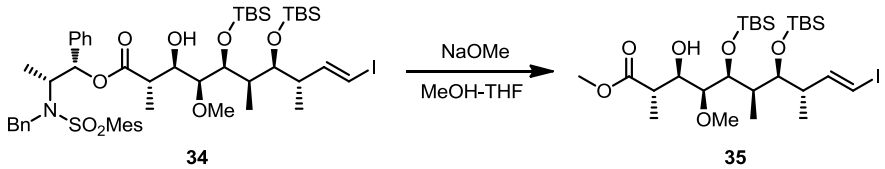
δ 7.39-7.37 (m, 1H), 7.31 (m, 4H), 7.19-7.15 (m, 1H), 7.03 (t, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.79 (s, 2H), 6.57 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.03 (d, *J* = 12.0 Hz, 1H), 5.71 (d, *J* = 8.0 Hz, 1H), 4.76 (d, *J* = 16.0 Hz, 1H), 4.38 (d, *J* = 16.0 Hz, 1H), 4.17-4.10 (m, 1H), 3.66 (br, 1H), 3.59 (d, *J* = 8.0 Hz, 1H), 3.21(d, *J* = 8.0 Hz, 1H), 3.15 (s, 3H), 2.64-2.59 (m, 1H), 2.40-2.36 (m, 1H), 2.99 (s, 9H), 1.67 (br, 1H), 1.27 (d, *J* = 8.0 Hz, 1H), 0.92 (s, 9H), 0.86 (s, 9H), 0.80 (s, 9H), 0.06-0.02 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 171.9, 148.0, 142.2, 140.5, 138.2, 137.5, 132.6, 132.1, 128.6, 128.5, 128.1, 127.9, 127.6, 127.5, 83.9, 77.5, 76.2, 75.1, 72.6, 59.5, 56.2, 47.8, 44.4, 39.6, 26.3, 26.1, 22.9, 20.9, 18.6, 18.5, 18.4, 18.3, 16.4, 15.1, 11.8, -3.0, -3.2, -3.3, -4.2, -4.6.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 1186.4953, found: 1186.4952.

Methyl (2*S*,3*R*,4*S*,5*S*,6*R*,7*S*,8*S*,*E*)-5,7-bis((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-10-iodo-4-methoxy-2,6,8-trimethyldec-9-enoate (35)



A solution of compound **34** (1.05 g, 1.0 mmol) in MeOH-THF (6/1 mL) at 0 °C, was treated with sodium methoxide (162 mg, 3.0 mmol). After stirred for another 2 h at room temperature, the reaction mixture was quenched with sat. NH_4Cl and extracted three times with MTBE (20 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$. Filtration, concentration under reduced pressure followed by flash chromatography on silica gel (PE/EtOAc = 15:1) afforded the desired product as colorless oil (581 mg, 88%).

R_f 0.55 (PE/EtOAc 4:1, $KMnO_4$)

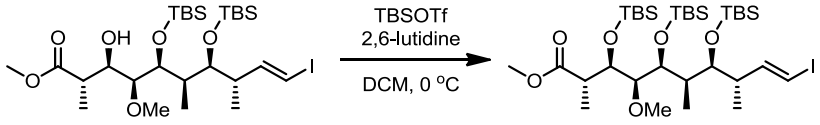
Opt. Rot. $[\alpha]^{20}_D$ = - 18 (c = 0.8, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 6.54 (dd, *J* = 8.0 & 16.0 Hz, 1H), 6.09 (d, *J* = 16.0 Hz, 1H), 3.90 (d, *J* = 8.0 Hz, 1H), 3.73 (s, 3H), 3.51 (d, *J* = 8.0 Hz, 1H), 3.47-3.42 (m, 4H), 3.99 (d, *J* = 8.0 Hz, 1H), 2.72 (d, *J* = 12.0 Hz, 1H), 2.65-2.58 (m, 1H), 2.54-2.50 (m, 1H), 1.57-1.50 (m, 2H), 1.22 (d, *J* = 4.0 Hz, 3H), 1.05 (d, *J* = 8.0 Hz, 3H), 0.93-0.88 (m, 21H), 0.09 (s, 3H), 0.07 (s, 6H), 0.03 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 175.5, 147.6, 81.6, 77.2, 76.1, 76.0, 72.9, 71.4, 61.2, 51.8, 44.4, 44.1, 40.0, 26.3, 26.2, 19.1, 18.6, 18.3, 14.7, 10.9, -2.8, -3.5, -3.6, -4.3.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 681.2480, found: 681.2480.

Methyl (2*S*,3*R*,4*R*,5*S*,6*R*,7*S*,8*S*,*E*)-3,5,7-tris((*tert*-butyldimethylsilyl)oxy)-10-iodo-4-methoxy-2,6,8-trimethyldec-9-enoate (12a)



35 **12a**

A solution of alcohol (581 mg, 0.88 mmol) and 2,6-lutidine (0.20 mL, 1.76 mmol) in 10 mL of CH_2Cl_2 was cooled to 0 °C. TBSOTf (0.30 mL, 1.32 mmol) was added dropwise, and the mixture was stirred for 2 h at this temperature. It was then quenched with water. The organic phase was separated and the aqueous phase was extracted three times with CH_2Cl_2 (20 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$. Filtration, concentration under reduced pressure followed by flash chromatography on silica gel (PE/EtOAc = 15:1) afforded the desired product as yellow oil (620 mg, 91%).

R_f 0.7 (PE/EtOAc 9:1, $KMnO_4$)

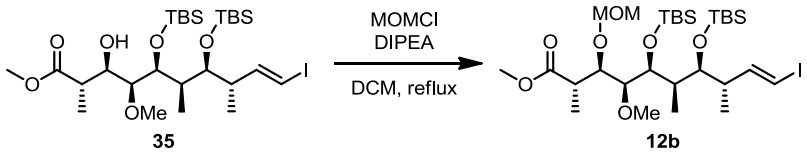
Opt. Rot. $[\alpha]^{20}_D$ = 2.0 (c = 0.6, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 6.67 (dd, *J* = 8.0 & 16.0 Hz, 1H), 6.09 (d, *J* = 16.0 Hz, 1H), 3.85 (t, *J* = 8.0 Hz, 1H), 3.72-3.68 (m, , 5H), 3.40-3.34 (m, 4H), 2.89-2.82 (m, 1H), 2.45-2.39 (m, 1H), 1.99-1.90 (m, 1H), 1.20 (d, *J* = 8.0 Hz, 3H), 1.09 (d, *J* = 8.0 Hz, 3H), 0.92-0.85 (m, 30H), 0.11-0.05 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 174.8, 147.9, 84.8, 77.2, 76.0, 75.7, 59.3, 51.5, 44.5, 43.0, 39.2, 26.3, 26.2, 25.9, 18.9, 18.6, 18.5, 18.0, 11.8, -3.0, -3.1, -3.4, -3.6, -4.3, -4.9.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 795.3344, found: 795.3346.

Methyl (2*S*,3*R*,4*S*,5*S*,6*R*,7*S*,8*S*,*E*)-5,7-bis((*tert*-butyldimethylsilyl)oxy)-10-iodo-4-methoxy-3-(methoxymethoxy)-2,6,8-trimethyldec-9-enoate (12b)



35 **12b**

To a solution of alcohol (1.88 g, 2.85 mmol) in DCM (5.0 mL) were sequentially added DIPEA (2.42 mL, 14.0 mmol) followed by MOMCl (1.44 mL, 14.0 mmol) at 0 °C. The mixture was then allowed to warm to room temperature and stirred overnight. The reaction was quenched by the addition of sat. NH_4Cl and extracted with DCM (10 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography to give the desired product as colorless oil (1.80 g, 90%).

R_f 0.55 (PE/EtOAc 4:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = - 2.7 (c = 1.0, $CHCl_3$)

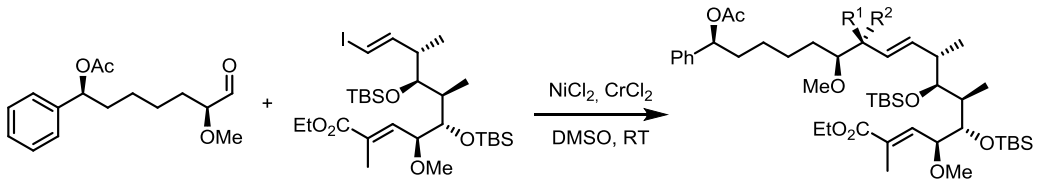
^{1}H NMR (400 MHz, $CDCl_3$)
δ 6.64 (dd, *J* = 8.0 & 16.0 Hz, 1H), 6.14 (d, *J* = 12.0 Hz, 1H), 4.68-4.46 (m, 2H), 3.76 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.71 (s, 3H), 3.64-3.60 (m, 2H), 3.42 (s, 3H), 3.40 (s, 3H), 3.26 (dd, *J* = 4.0 & 8.0 Hz, 1H), 2.95-2.88 (m, 1H), 2.58-2.51 (m, 1H), 1.62-1.55 (m, 1H), 1.23 (d, *J* = 8.0 Hz, 3H), 1.08 (d, *J* = 8.0 Hz, 3H), 0.93-0.88 (m, 21H), 0.13 (s, 3H), 0.07 (s, 6H), 0.05 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 147.8, 97.1, 81.9, 78.4, 77.2, 76.0, 75.9, 72.5, 60.2, 56.2, 51.6, 44.1, 42.4, 39.8, 26.3, 26.2, 19.2, 18.6, 18.4, -2.9, -3.4, -3.6, -4.4.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 725.2742, found: 725.2740.

2.3 Syntheses of paleo-soraphens A~E (1~5)

(2*E*,4*S*,5*S*,6*R*,7*S*,8*S*,9*E*,11*R*,12*S*,17*S*)-ethyl 17-acetoxy-5,7-bis((*tert*-butyldimethylsilyl)oxy)-11-hydroxy-4,12-dimethoxy-2,6,8-trimethyl-17-phenylheptadeca-2,9-dienoate (36) and (2*E*,4*S*,5*S*,6*R*,7*S*,8*S*,9*E*,11*S*,12*S*,17*S*)-ethyl 17-acetoxy-5,7-bis((*tert*-butyldimethylsilyl)oxy)-11-hydroxy-4,12-dimethoxy-2,6,8-trimethyl-17-phenylheptadeca-2,9-dienoate (37)



To aldehyde **11** (322 mg, 1.15 mmol) and vinyl iodide **10** (770 mg, 1.18 mmol) was added anhydrous DMSO (15 mL) via syringe under nitrogen atmosphere, followed by $CrCl_2$ (565 mg, 4.12 mmol) and $NiCl_2$ (6.0 mg, 0.46 mmol) at room temperature. After stirred overnight, saturated aqueous NH_4Cl (20 mL) was added and the mixture extracted with MTBE (4 × 20 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified via flash column chromatography (PE/EtOAc = 9:1) to afford compound **36** (444 mg, 47%) and **37** (304 mg, 32%).

*Data of the major isomer **36**:*

R_f 0.50 (PE/EtOAc 3:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -10.2 (c = 0.70, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.35-7.27 (m, 5H), 6.32 (dd, *J* = 4.0 & 8.0 Hz, 1H), 5.71 (d, *J* = 8.0 Hz, 1H), 5.59 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.50 (dd, *J* = 8.0 & 16.0 Hz, 1H), 4.22 (q, *J* = 8.0 Hz, 12H), 4.08-4.00 (m, 1H), 3.83-3.78 (m, 2H), 3.60-3.57 (m, 2H), 3.44-3.38 (m, 4H), 3.19-3.14 (m, 4H), 2.47-2.44 (m, 1H), 2.06 (s, 3H), 1.94-1.87 (m, 4H), 1.79-1.73 (m, 1H), 1.46-1.20 (m, 4H), 1.00 (d, *J* = 8.0 Hz, 3H), 0.90 (s, 18H), 0.78 (d, *J* = 8.0 Hz, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.04 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 170.3, 168.3, 140.8, 137.6, 134.8, 131.4, 130.3, 128.4, 128.3, 127.8, 126.5, 85.6, 84.5, 80.6, 76.3, 76.1, 74.5, 74.7, 61.4, 58.8, 55.9, 40.0, 39.9, 30.4, 26.4, 26.2, 25.7, 25.6, 21.3, 20.0, 18.7, 18.6, 14.2, 13.1, 10.9, -2.9, -3.2, -3.4, -5.0.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 829.5082, found: 829.5085.

*Data of the minor isomer **37**:*

R_f 0.45 (PE/EtOAc 3:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -23.2 (c = 1.5, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

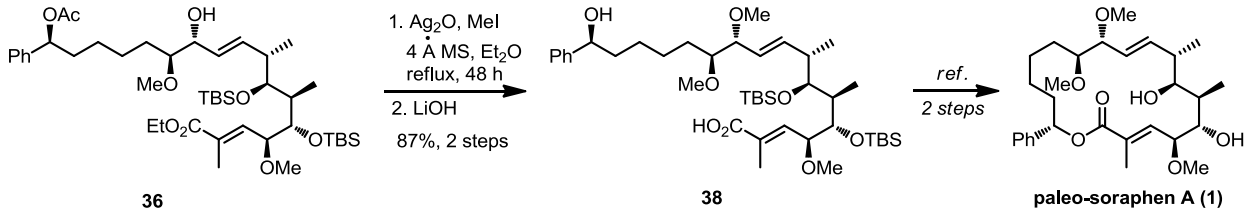
δ 7.35-7.25 (m, 5H), 6.34 (dd, *J* = 4.0 & 8.0 Hz, 1H), 5.72-5.66 (m, 2H), 5.36 (dd, *J* = 4.0 & 16.0 Hz, 1H), 4.24-4.18 (m, 2H), 4.00-3.96 (m, 1H), 3.83-3.79 (m, 1H), 3.73-3.71 (m, 1H), 3.60-3.58 (m, 1H), 3.37 (s, 3H), 3.15 (s, 3H), 3.21-2.95 (m, 1H), 2.59 (d, *J* = 4.0 Hz, 1H), 2.37-2.33 (m, 1H), 2.05 (s, 3H), 1.93-1.91 (m, 4H), 1.79-1.72 (m, 1H), 1.51-1.44 (m, 9H), 1.04 (d, *J* = 8.0 Hz, 3H), 0.90 (s, 18H), 0.75 (d, J = 8.0 Hz, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 170.2, 167.4, 140.7, 137.1, 134.4, 131.7, 130.0, 128.4, 127.8, 126.4, 83.8, 80.9, 76.6, 76.1, 74.8, 73.8, 61.0, 58.2, 56.0, 40.3, 39.5, 29.9, 26.3, 26.2, 25.9, 24.7, 21.2, 19.1, 18.6, 18.5, 14.2, 13.2, 10.8, -3.1, -3.4, -3.5, -4.7.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 829.5082, found: 829.5085.

(2*E*,4*S*,5*S*,6*R*,7*S*,8*S*,9*E*,11*R*,12*S*,17*S*)-5,7-Bis((*tert*-butyldimethylsilyl)oxy)-17-hydroxy-4,11,12-trimethoxy-2,6,8-trimethyl-17-phenylheptadeca-2,9-dienoic acid (38)[8]

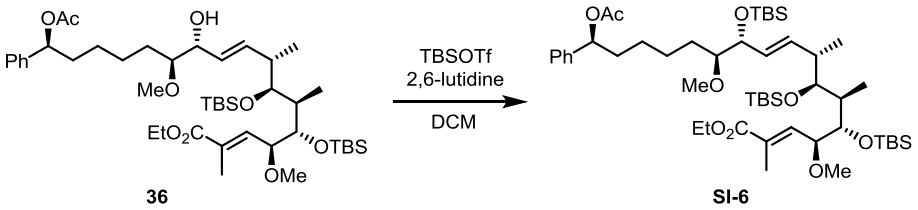


36 **38** **paleo-soraphen A (1)**

To a solution of alcohol (81 mg, 0.10 mmol) in diethyl ether (1 mL) were added silver oxide (165 mg, 0.50 mmol), 4 Å molecular sieves (600 mg) and iodomethane (0.10 mL, 1.2 mmol). The mixture was heated at reflux for 48 h in the absence of direct light. The reaction was then filtered throught a pad of celite and washed thoroghly with MTBE. The organic solution was concentrated.

The residue was dissolved in THF/MeOH/H_2O (1 mL/1 mL/0.5 mL) and LiOH (54 mg, 2.0 mmol) was added at room temperature. The mixture was stirred overnight at the same temperature. Then the reaction was quenched with 10% citric acid (4 mL) extracted with EtOAc (4 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EtOAc = 2:1) to afford the desired product as waxy solid (65 mg, 87%). The corresponding data matches our reported ones.[8]

Ethyl (2*E*,4*S*,5*S*,6*R*,7*S*,8*S*,9*E*,11*R*,12*S*,17*S*)-17-acetoxy-5,7,11-tris((*tert*-butyldimethylsilyl)oxy)-4,12-dimethoxy-2,6,8-trimethyl-17-phenylheptadeca-2,9-dienoate (SI-6)



36 **SI-6**

A solution of **36** (160 mg, 0.2 mmol) and 2,6-lutidine (46 µL, 0.4 mmol) in CH_2Cl_2 (10 mL) was cooled to 0 °C. TBSOTf (55 µL, 0.24 mmol) was added dropwise. After stirring for 2 h at 0 °C water was added. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$. Filtration and concentration under reduced pressure followed by flash chromatography on silica gel (PE/EtOAc = 15:1) afforded **SI-6** as yellow oil (150 mg, 83%).

R_f 0.60 (PE/EtOAc 9:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -23.4 (c = 1.0, $CHCl_3$)

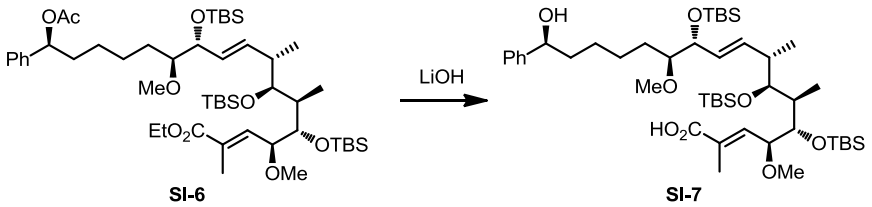
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.34-7.24 (m, 5H), 6.39 (d, *J* = 8.0 Hz, 1H), 5.71-5.59 (m, 2H), 5.35 (dd, *J* = 4.0 & 12.0 Hz, 1H), 4.20 (q, *J* = 8.0 Hz, 2H), 4.10-4.08 (m, 1H), 3.87-3.83 (m, 1H), 3.72-3.70 (m, 1H), 3.58 (q, *J* = 8.0 Hz, 1H), 3.35 (s, 3H), 3.15 (s, 3H), 2.92-2.89 (m, 1H), 2.36-2.29 (m, 1H), 2.05 (s, 3H), 1.93-1.89 (m, 4H), 1.79-1.72 (m, 1H), 1.61-1.58 (m, 1H), 1.42-1.16 (m, 8H), 1.04 (d, *J* = 8.0 Hz, 3H), 0.90-0.86 (s, 27H), 0.76 (d, *J* = 4.0 Hz, 3H), 0.09-0.01 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.3, 167.2, 140.8, 137.0, 133.5, 131.8, 130.5, 128.3, 127.7, 126.5, 60.7, 58.2, 56.0, 40.0, 39.6, 36.4, 26.3, 26.2, 21.3, 21.2, 19.3, 18.6, 18.5, 18.2, 14.3, 13.3, -3.2, -3.4, -3.5, -4.2, -4.5, -4.8.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 943.5947, found: 943.5947.

(8) Lu, H.-H.; Raja, A.; Franke, R.; Landsberg, D.; Sasse, F.; Kalesse, M. *Angew. Chem. Int. Ed.* **2013**, *52*, 13579-13552.

(2*E*,4*S*,5*S*,6*R*,7*S*,8*S*,9*E*,11*R*,12*S*,17*S*)-5,7,11-Tris((*tert*-butyldimethylsilyl)oxy)-17-hydroxy-4,12-dimethoxy-2,6,8-trimethyl-17-phenylheptadeca-2,9-dienoic acid (SI-7)



To a solution of **SI-6** (150 mg, 0.17 mmol) in THF/MeOH/H_2O (4 mL/4 mL/2 mL) was added LiOH (78 mg, 3.25 mmol) at room temperature. The mixture was stirred overnight at the same temperature. Then the reaction was quenched with 10% citric acid (10 mL) extracted with EtOAc (4 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EtOAc = 2:1) to afford the desired product as colorless oil (100 mg, 83%).

R_f 0.20 (PE/DCM/EtOAc 1:1:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -15.4 (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

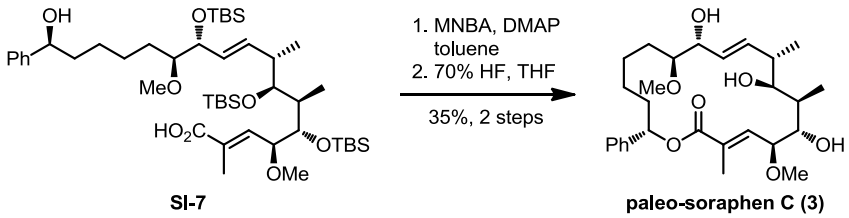
δ 7.33-7.25 (m, 5H), 6.46 (d, *J* = 8.0 Hz, 1H), 5.65 (dd, *J* = 4.0 & 12.0 Hz, 1H), 5.45 (dd, *J* = 4.0 & 16.0 Hz, 1H), 4.70 (dd, *J* = 4.0 & 8.0 Hz, 1H), 4.08 (t, *J* =8.0 Hz, 1H), 3.87-3.82 (m, 1H), 3.75 (d, *J* = 4.0 Hz, 1H), 3.59 (d, *J* = 8.0 Hz, 1H), 3.38 (s, 3H), 3.14 (s, 3H), 3.01-2.99 (m, 1H), 2.63 (s, 1H), 2.40-2.37 (m, 1H), 2.17 (s, 1H), 1.93 (s, 3H), 1.83-1.79 (m, 1H), 1.72-1.65 (m, 1H), 1.58-1.33 (m, 6H), 1.04 (d, *J* = 8.0 Hz, 3H), 0.90-0.86 (m, 27H), 0.76 (d, *J* = 4.0 Hz, 3H), 0.09-0.02 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 144.6, 138.3, 132.9, 131.3, 130.8, 128.4, 127.5, 125.8, 85.0, 81.1, 77.1, 75.1, 74.9, 74.5, 58.4, 55.9, 53.8, 39.7, 39.6, 38.8, 31.7, 29.8, 29.2, 26.3, 26.2, 26.0, 25.5, 19.6, 18.7, 18.6, 18.2, 13.1, 10.9, -3.2, -3.3, -3.4, -4.1, -4.7, -4.8.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 873.5528, found: 873.5531.

(3*E*,5*S*,6*S*,7*R*,8*S*,9*S*,10*E*,12*R*,13*S*,18*S*)-6,8,12-Trihydroxy-5,13-dimethoxy-3,7,9-trimethyl-18-phenyloxacyclooctadeca-3,10-dien-2-one (paleo-soraphen C, 3)



SI-7 **paleo-soraphen C (3)**

A solution of **SI-7** (43 mg, 0.05 mmol) in toluene (8 mL) was added over a period of 7 h through a syringe pump to a solution of MNBA (26 mg, 0.075 mmol), DMAP (36 mg, 0.30 mmol), and 4 Å molecular sieves (600 mg) in toluene (15 mL) under nitrogen atmosphere at room temperature. After the completion of the addition, the stirring was continued for another 16 h. The reaction mixture was then filtered over Celite. The filtrate was diluted with EtOAc (50 mL), washed with aqueous saturated $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo.

The residue was dissolved in THF (1 mL) and cooled cooled to 0 °C. The solution was treated dropwise with a solution of hydrogen fluoride pyridine (~70 % hydrogen fluoride, 0.2 mL). After addition, the reaction mixture was stirred overnight at room temperature and concentrated. The residue was purified by flash column chromatography (PE/EtOAc = 3:2) to afford the desired product as colorless oil (8.6 mg, 35%).

R_f 0.30 (DCM/actone 4:1, $KMnO_4$)

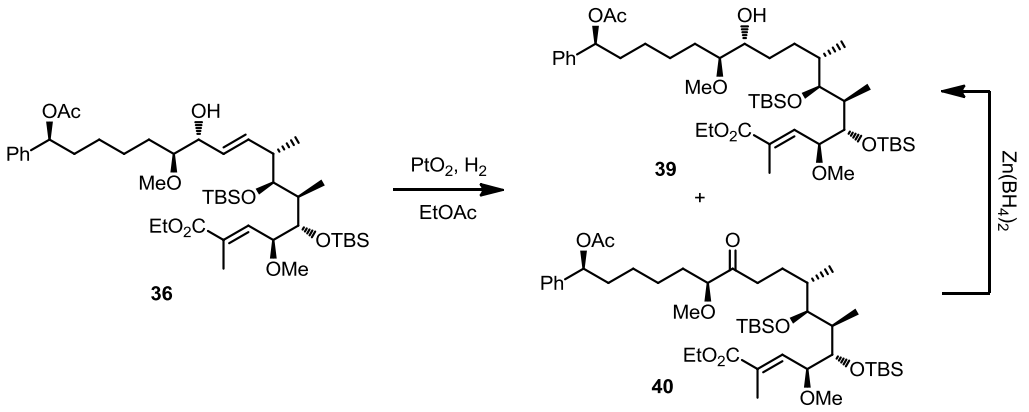
Opt. Rot. $[\alpha]^{20}_D$ = -17.4 (c = 0.086, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.38-7.27 (m, 5H), 6.51 (d, *J* = 8.0 Hz, 1H), 6.03 (dd, *J* = 4.0 & 12.0 Hz, 1H), 5.68 (dd, *J* = 4.0 & 16.0 Hz, 1H), 5.50 (dd, *J* = 4.0 & 16.0 Hz, 1H), 4.22-4.20 (m, 1H), 3.95 (t, *J* = 8.0 Hz, 1H), 3.76 (d, *J* = 8.0 Hz, 1H), 3.61 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.41 (s, 3H), 3.29 (s, 3H), 3.20-3.16 (m, 1H), 2.85 (br, 1H), 2.70-2.67 (m, 1H), 2.05-1.99 (m, 4H), 1.82-1.77 (m, 1H), 1.60-1.24 (m, 6H), 1.15 (d, *J* = 8.0 Hz, 3H), 1.02 (d, *J* = 4.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 166.6, 140.9, 136.7, 133.7, 132.8, 129.8, 128.5, 127.9, 126.1, 83.9, 79.5, 77.2, 74.9, 73.1, 57.6, 56.8, 38.1, 37.6, 36.3, 28.9, 25.8, 24.3, 16.1, 13.5, 9.5.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 513.2828, found: 513.2825.

Ethyl (4*S*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*S*,*E*)-17-acetoxy-5,7-bis((*tert*-butyldimethylsilyl)oxy)-11-hydroxy-4,12-dimethoxy-2,6,8-trimethyl-17-phenylheptadec-2-enoate (39) and (4*S*,5*S*,6*R*,7*S*,8*S*,12*S*,17*S*,*E*)-ethyl 17-acetoxy-5,7-bis((*tert*-butyldimethylsilyl)oxy)-4,12-dimethoxy-2,6,8-trimethyl-11-oxo-17-phenylheptadec-2-enoate (40)



Compound **36** (190 mg, 0.24 mmol) was dissolved in 20 mL of EtOAc. To this solution was then added 20 mg of platinum (IV) oxide hydrate, and the heterogenous mixture was stirred under hydrogen atomosphere for 1 h. The reaction was subsequently filtered through a plug of Celite, washed with EtOAc, and concentrated under reduced pressure. Purification of the resulting oil by silica gel chromatography (PE/EtOAc = 9:1) afforded alcohol **39** (137 mg, 72%) and ketone **40** (41 mg, 21%) both as colorless oils.

*Data of the alcohol **39**:*

R_f 0.30 (PE/EtOAc 4:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -21.8 (c = 0.6, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.33-7.27 (m, 5H), 6.42 (d, *J* = 8.0 Hz, 1H), 5.72 (t, *J* = 8.0 Hz, 1H), 4.20 (q, *J* = 8.0 Hz, 1H), 3.89-3.84 (m, 1H), 3.70 (d, *J* = 8.0 Hz, 1H), 3.60-3.53 (m, 2H), 3.38 (s, 3H), 3.17 (s, 3H), 3.03-3.00 (m, 1H), 2.06 (s, 3H), 1.95-1.87 (m, 4H), 1.82-1.75 (m, 1H), 1.64-1.24 (m, 15H), 1.00 (d, *J* = 8.0 Hz, 3H), 0.94 (d, *J* = 8.0 Hz, 3H), 0.90-0.88 (m, 18H), 0.83 (d, *J* = 8.0 Hz, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.03 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.3, 167.8, 140.8, 137.7, 131.8, 128.4, 127.8, 126.5, 84.5, 80.8, 77.9, 76.1, 75.2, 72.3, 61.0, 57.8, 56.1, 38.6, 36.4, 36.3, 30.9, 28.7, 26.4, 26.3, 26.2, 25.8, 25.7, 21.3, 18.6, 18.2, 14.3, 13.2, 11.4, -3.1, -3.4, -3.5, -4.8.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 831.5239, found: 831.5243.

*Data of the ketone **40**:*

R_f 0.50 (PE/EtOAc 4:1, $KMnO_4$)

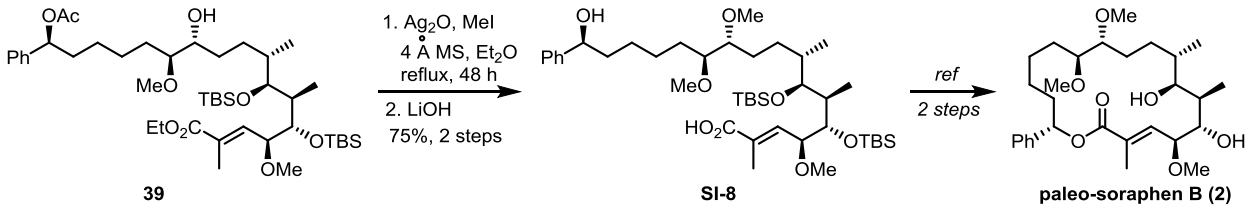
Opt. Rot. $[\alpha]^{20}_D$ = -18.4 (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.35-7.25 (m, 5H), 6.48 (d, *J* = 8.0 Hz, 1H), 5.71 (t, *J* = 8.0 Hz, 1H), 4.18 (q, *J* = 8.0 Hz, 1H), 3.90-3.85 (m, 1H), 3.74-3.72 (m, 1H), 3.58-3.50 (m, 2H), 3.31 (s, 3H), 3.17 (s, 3H), 2.52-2.38 (m, 2H), 2.06 (s, 3H), 1.95-1.87 (m, 4H), 1.67-1.55 (m, 6H), 1.35-1.15 (m, 10H), 0.92-0.83 (m, 24H), 0.07-0.03 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 212.6, 170.3, 167.4, 140.6, 137.0, 131.9, 128.4, 127.8, 126.5, 126.4, 87.1, 80.9, 77.8, 75.9, 75.2, 60.8, 58.1, 56.1, 38.8, 36.1, 35.5, 35.3, 31.8, 26.3, 26.2, 25.3, 25.0, 21.3, 18.6, 18.5, 17.8, 14.2, 13.3, 11.3, -3.1, -3.4, -3.5, -4.8.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 829.5082, found: 829.5085.

(4*S*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*S*,*E*)-5,7-Bis((*tert*-butyldimethylsilyl)oxy)-17-hydroxy-4,11,12-trimethoxy-2,6,8-trimethyl-17-phenylheptadec-2-enoic acid (SI-8)[8]

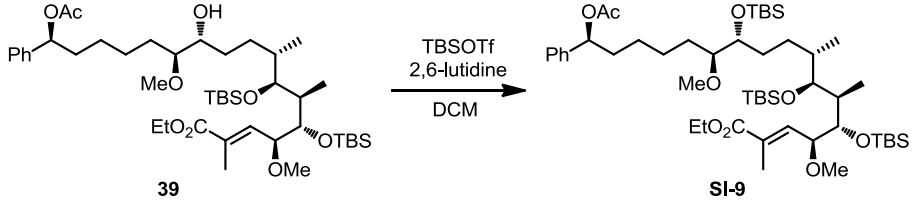


39 **SI-8** **paleo-soraphen B (2)**

To a solution of alcohol **39** (40 mg, 0.05 mmol) in diethyl ether (1 mL) were added silver oxide (165 mg, 0.50 mmol), 4 Å molecular sieves (600 mg) and iodomethane (0.10 mL, 1.2 mmol). The mixture was heated at reflux for 48 h in the absence of direct light. The reaction was then filtered throught a pad of celite and washed thoroughly with MTBE. The organic solution was concentrated.

The residue was dissolved in THF/MeOH/H_2O (1 mL/1 mL/0.5 mL) and LiOH (27 mg, 1.0 mmol) was added at room temperature. The mixture was stirred overnight at the same temperature. Then the reaction was quenched with 10% citric acid (4 mL) extracted with EtOAc (4 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EtOAc = 2:1) to afford the desired product as waxy solid (28 mg, 75%). The corresponding data matched its reported ones.[8]

Ethyl (4*S*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*S*,*E*)-17-acetoxy-5,7,11-tris((*tert*-butyldimethylsilyl)oxy)-4,12-dimethoxy-2,6,8-trimethyl-17-phenylheptadec-2-enoate (SI-9)



39 **SI-9**

A solution of alcohol **39** (116 mg, 0.14 mmol) and 2,6-lutidine (32 µL, 0.28 mmol) in 5 mL of CH_2Cl_2 was cooled to 0 °C. TBSOTf (39 µL, 0.17 mmol) was added dropwise, and the mixture was stirred for 2 h at this temperature. It was then quenched with water. The organic phase was separated and the aqueous phase was extracted three times with CH_2Cl_2 (20 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$. Filtration and concentration under reduced pressure followed by flash chromatography on silica gel (PE/EtOAc = 15:1) afforded the desired product as yellow oil (120 mg, 93%).

R_f 0.60 (PE/EtOAc 9:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -25.0 (c = 0.8, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

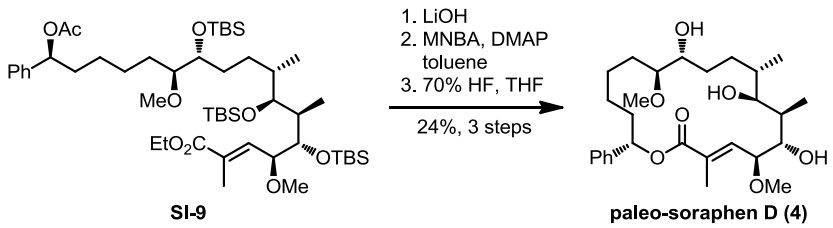
δ 7.36-7.25 (m, 5H), 6.42 (d, *J* = 8.0 Hz, 1H), 5.72 (t, *J* = 8.0 Hz, 1H), 4.20 (q, *J* = 8.0 Hz, 1H), 3.90-3.85 (m, 1H), 3.70-3.64 (m, 2H), 3.57-3.54 (m, 1H), 3.33 (s, 3H), 3.16 (s, 3H), 3.00-2.95 (m, 1H), 2.06 (s, 3H), 1.95-1.87 (m, 4H), 1.80-1.78 (m, 1H), 1.66-1.62 (m, 1H), 1.49-1.24 (m, 13H), 0.94-0.82 (m, 33H), 0.08- 0.03 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 170.3, 167.3, 140.9, 137.0, 131.8, 128.4, 127.8, 126.5, 126.4, 84.2, 80.9, 77.8, 76.7, 76.1, 75.4, 73.8, 60.7, 58.0, 56.0, 39.1, 37.0, 36.4, 31.9, 29.8, 26.3, 26.2, 25.9, 21.3, 18.6, 18.5, 18.2, 18.1, 14.3, 13.3, 11.3, -3.2, -3.5, -4.3, -4.5, -4.6.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 945.6103, found: 945.6100.

(5*S*,6*S*,7*R*,8*S*,9*S*,12*R*,13*S*,18*S*,*E*)-6,8,12-Trihydroxy-5,13-dimethoxy-3,7,9-trimethyl-18-phenyloxacyclooctadec-3-en-2-one (paleo-soraphen D, 4)



To a solution of **SI-9** (110 mg, 0.12 mmol) in THF/MeOH/H_2O (4 mL/4 mL/2 mL) was added LiOH (57 mg, 2.4 mmol) at room temperature. The mixture was stirred overnight at the same temperature. Then the reaction was quenched with 10% citric acid (10 mL) extracted with EtOAc (4 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo.

Half of the residue was dissolved in toluene (8 mL) and was added over a period of 7 h through a syringe pump to a solution of MNBA (26 mg, 0.075 mmol), DMAP (36 mg, 0.30 mmol), and 4 Å molecular sieves (600 mg) in toluene (15 mL) under nitrogen atmosphere at room temperature. After the completion of the addition, the stirring was continued for another 16 h. The reaction mixture was then filtered over Celite. The filtrate was diluted with EtOAc (50 mL), washed with aqueous saturated $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo.

The residue was dissolved in THF (1 mL) and cooled to 0 °C. The solution was treated dropwise with a solution of hydrogen fluoride pyridine (~70 % hydrogen fluoride, 0.2 mL). After addition, the reaction mixture was stirred overnight at room temperature and concentrated. The residue was purified by flash column chromatography (PE/EtOAc = 3:2) to afford the desired product as colorless oil (7.6 mg, 24%).

R_f 0.30 (DCM/actone 4:1, $KMnO_4$)

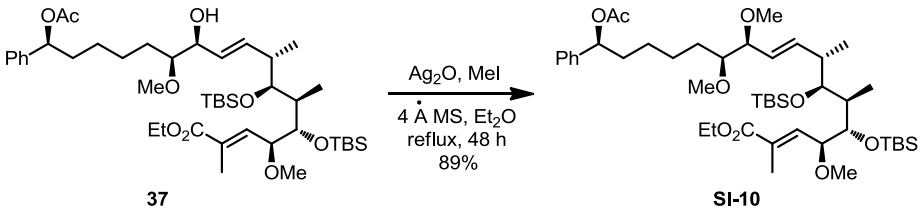
Opt. Rot. $[\alpha]^{20}_D$ = -65.7 (c = 0.07, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.38-7.27 (m, 5H), 6.51 (d, *J* = 8.0 Hz, 1H), 6.02 (dd, *J* = 4.0 & 12.0 Hz, 1H), 3.98-3.91 (m, 2H), 3.68-3.63 (m, 2H), 3.42 (s, 3H), 3.29 (s, 3H), 3.19-3.15 (m, 1H), 2.02-1.76 (m, 4H), 1.65-1.54 (m, 13H), 1.30 (d, *J* = 8.0 Hz, 3H), 1.01 (d, *J* = 4.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 166.6, 140.9, 137.3, 133.7, 128.5, 127.9, 126.0, 80.9, 79.2, 78.7, 77.2, 76.8, 75.8, 69.4, 57.3, 56.8, 36.8, 36.3, 35.3, 29.1, 26.6, 25.3, 24.1, 15.2, 13.5, 8.8.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 515.2985, found: 515.2987.

Ethyl (2*E*,4*S*,5*S*,6*R*,7*S*,8*S*,9*E*,11*S*,12*S*,17*S*)-17-acetoxy-5,7-bis((*tert*-butyldimethylsilyl)oxy)-4,11,12-trimethoxy-2,6,8-trimethyl-17-phenylheptadeca-2,9-dienoate (SI-10)



37 **SI-10**

To a solution of alcohol **37** (300 mg, 0.37 mmol) in diethyl ether (3 mL) were added silver oxide (428 mg, 1.30 mmol), 4 Å molecular sieves (600 mg) and iodomethane (0.23 mL, 2.6 mmol). The mixture was heated at reflux for 48 h in the absence of direct light. The reaction was then filtered throught a pad of celite and washed thoroughly with MTBE. The organic solution was concentrated. The residue was purified via flash column chromatography (PE/EtOAc = 9:1) to afford the desired product as colorless oil (270 mg, 89%).

R_f 0.40 (PE/EtOAc 9:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -9.4 (c = 1.7, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

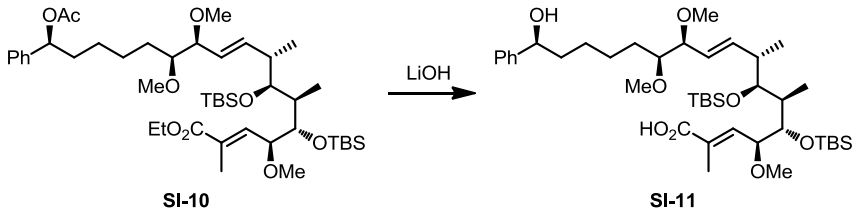
δ 7.34-7.24 (m, 5H), 6.35 (dd, *J* = 4.0 & 8.0 Hz, 1H), 5.70-5.61 (m, 2H), 5.21 (dd, *J* = 8.0 & 16.0 Hz, 1H), 4.26-4.16 (m, 2H), 3.83-3.79 (m, 1H), 3.75-3.73 (m, 1H), 3.60-3.58 (m, 1H), 3.53-3.50 (m, 1H), 3.40 (s, 3H), 3.21 (s, 3H), 3.15 (s, 3H), 3.05-2.95 (m, 1H), 2.41-2.37 (m, 1H), 2.05 (s, 3H), 1.93-1.87 (m, 4H), 1.77-1.71 (m, 1H), 1.51-1.26 (m, 9H), 1.06 (d, *J* = 8.0 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.77 (d, *J* = 8.0 Hz, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 170.3, 167.2, 140.8, 136.8, 136.0, 131.9, 128.3, 127.7, 127.2, 126.5, 84.4, 83.1, 81.0, 76.7, 76.1, 74.9, 60.9, 58.6, 56.4, 56.0, 39.9, 39.8, 36.4, 30.5, 26.3, 26.2, 25.8, 25.0, 21.3, 19.4, 18.7, 18.5, 14.2, 13.3, 10.9, -3.1, -3.4, -3.5, -4.7.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 843.5239, found: 843.5239.

(2*E*,4*S*,5*S*,6*R*,7*S*,8*S*,9*E*,11*S*,12*S*,17*S*)-5,7-Bis((*tert*-butyldimethylsilyl)oxy)-17-hydroxy-4,11,12-trimethoxy-2,6,8-trimethyl-17-phenylheptadeca-2,9-dienoic acid (SI-11)



SI-10 **SI-11**

To a solution of **SI-10** (270 mg, 0.33 mmol) in THF/MeOH/H_2O (3 mL/3 mL/1.5 mL) was added LiOH (80 mg, 3.3 mmol) at room temperature. The mixture was stirred overnight at the same temperature. Then the reaction was quenched with 10% citric acid (10 mL) extracted with EtOAc (4 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EtOAc = 2:1) to afford the desired product as waxy solid (226 mg, 91%).

R_f 0.50 (PE/EtOAc 1:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -4.5 (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.33-7.23 (m, 5H), 6.42 (d, *J* = 12.0 Hz, 1H), 5.72-5.66 (m, 1H), 5.33 (dd, *J* = 4.0 & 12.0 Hz, 1H), 4.74-4.70 (m, 1H), 3.86-3.77 (m, 2H), 3.60-3.40 (m, 2H), 3.21 (s, 3H), 3.20-3.14 (m, 4H), 2.46-2.42 (m, 1H), 1.92 (s, 3H), 1.88-1.78 (m, 1H), 1.72-1.66 (m, 1H), 1.48-1.26 (m, 6H), 1.07 (d, *J* = 8.0 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.79 (d, *J* = 8.0 Hz, 3H), 0.09 (s, 6H), 0.06 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.4, 144.5, 138.1, 135.9, 131.3, 128.4, 127.5, 127.4, 125.8, 125.7, 84.0, 82.9, 81.2, 76.7, 74.9, 58.6, 56.3, 56.0, 40.0, 39.6, 38.8, 30.0, 29.7, 26.3, 26.2, 25.7, 24.8, 20.1, 18.7, 18.6, 13.0, 10.9, -3.0, -3.3, -3.4, -4.9.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 773.4820, found: 773.4819.

(3*E*,5*S*,6*S*,7*R*,8*S*,9*S*,10*E*,12*S*,13*S*,18*S*)-6,8-Dihydroxy-5,12,13-trimethoxy-3,7,9-trimethyl-18-phenyloxacyclooctadeca-3,10-dien-2-one (paleo-soraphen E, 5)

SI-11 **paleo-soraphen E (5)**

A solution of **SI-11** (38 mg, 0.05 mmol) in toluene (8 mL) was added over a period of 7 h through a syringe pump to a solution of MNBA (26 mg, 0.075 mmol), DMAP (36 mg, 0.30 mmol), and 4 Å molecular sieves (600 mg) in toluene (15 mL) under nitrogen atmosphere at room temperature. After the completion of the addition, the stirring was continued for another 16 h. The reaction mixture was then filtered over Celite. The filtrate was diluted with EtOAc (50 mL), washed with aqueous saturated $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo.

The residue was dissolved in THF (1 mL) and cooled to 0 °C. The solution was treated dropwise with a solution of hydrogen fluoride pyridine (~70 % hydrogen fluoride, 0.2 mL). After addition, the reaction mixture was stirred overnight at room temperature and concentrated. The residue was purified by flash column chromatography (PE/EtOAc = 3:2) to afford the desired product as colorless oil (7.6 mg, 30%).

R_f 0.20 (PE/EtOAc 2:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_{D}$ = -16.1 (c = 0.062, $CHCl_3$)

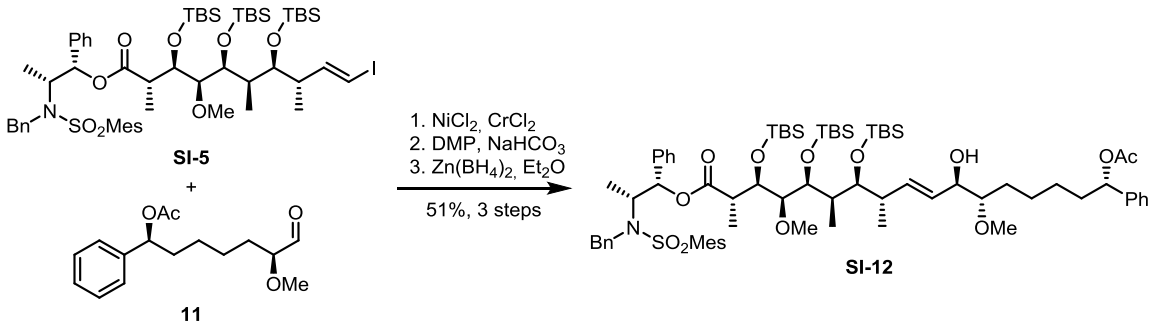
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.38-7.28 (m, 5H), 6.4 (d, *J* = 8.0 Hz, 1H), 5.91 (t, *J* = 8.0 Hz, 1H), 5.75 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.48 (dd, *J* = 8.0 & 16.0 Hz, 1H), 3.93 (t, *J* = 8.0 Hz, 1H), 3.76 (d, *J* = 8.0 Hz, 1H), 3.45 (dd, *J* = 8.0 & 16.0 Hz, 1H), 3.42 (s, 3H), 3.25 (s, 3H), 3.25 (s, 3H), 3.22-3.14 (m, 1H), 2.63-2.57 (m, 1H), 2.02 (s, 3H), 1.87-1.82 (m, 2H), 1.60-1.45 (m, 6H), 1.18 (d, *J* = 8.0 Hz, 3H), 0.98 (d, *J* = 4.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 166.8, 140.8, 136.1, 135.1, 134.0, 129.0, 127.7, 125.8, 84.4, 82.4, 79.6, 77.2, 76.2, 74.9, 58.9, 56.6, 56.2, 40.3, 37.8, 35.7, 29.7, 29.5, 24.3, 24.2, 19.2, 13.6, 9.3

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 527.2985, found: 527.2987.

2.4 Towards Paleo-Soraphens F (6) by the Mitsunobu Approach and Completion of 17-*epi*-Paleo-Soraphen F (46)

(1*S*,2*R*)-2-((*N*-Benzyl-2,4,6-trimethylphenyl)sulfonamido)-1-phenylpropyl (2*S*,3*R*,4*R*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*S*,*E*)-17-acetoxy-3,5,7-tris((*tert*-butyldimethylsilyl)oxy)-11-hydroxy-4,12-dimethoxy-2,6,8-trimethyl-17-phenylheptadec-9-enoate (SI-12)



To aldehyde **11** (140 mg, 0.50 mmol) and vinyl iodide **SI-5** (600 mg, 0.52 mmol) was added anhydrous DMSO-THF (6 mL/1 mL) via syringe under nitrogen atmosphere, followed by $CrCl_2$ (300 mg, 2.5 mmol) and $NiCl_2$ (2.60 mg, 0.02 mmol) at room temperature. After stirring overnight, saturated aqueous NH_4Cl (20 mL) was added and the mixture extracted with MTBE (4 × 20 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure.

The residue was dissolved in DCM (10 mL) and $NaHCO_3$ (336 mg, 4.00 mmol) was added at room temperature. After stirred for 10 min, the reaction was cooled to 0 °C and Dess-Martin periodinane[9] (320 mg, 0.75 mmol) was added. The mixture was stirred at room temperature for 1.5 h, quenched with 1 N Na_2SO_3 (3 mL) at 0 °C and diluted with water (10 mL). The mixture was extracted with MTBE (3 × 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure.

The crude enone was dissolved in anhydrous ether (20 mL) and cooled to -55 °C. Then a solution of zinc borohydride (12.7 mL, 0.13 M in ether, 1.65 mmol) was added. The mixture was allowed to warm to -10 °C slowly, stirred at this temperature for 3 h, and quenched with saturated aqueous NH_4Cl (15 mL). The mixture was extracted with MTBE (4 × 20 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified via flash column chromatography (PE/EtOAc = 4:1) to afford the desired product as colorless oil (336 mg, 51%).

R_f 0.30 (PE/EtOAc 4:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -28.1 (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.38-7.24 (m, 10H), 7.16 (t, *J* = 8.0 Hz, 1H), 7.02 (t, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.78 (s, 2H), 5.78 (d, *J* = 8.0 Hz, 2H), 5.71 (t, *J* = 8.0 Hz, 2H), 5.60 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.34 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.74 (d, *J* = 8.0 Hz, 2H), 4.37 (d, *J* = 8.0 Hz, 2H), 4.17-4.11 (m, 1H), 3.57-3.53 (m, 4H), 3.36 (s, 3H), 3.24 (s, 3H), 3.13 (t, *J* = 4.0 Hz, 1H), 3.02-2.97 (m, 1H), 2.54-2.50 (m, 1H), 2.27 (s, 9H), 2.06 (s, 3H), 1.92-1.87 (m, 1H), 1.78-1.72 (m, 1H), 1.58-1.22 (m, 5H), 1.09 (d, *J* = 8.0 Hz, 3H), 0.99 (d, *J* = 8.0 Hz, 3H), 0.92-0.79 (m, 33H), 0.08-0.01 (m, 18H).

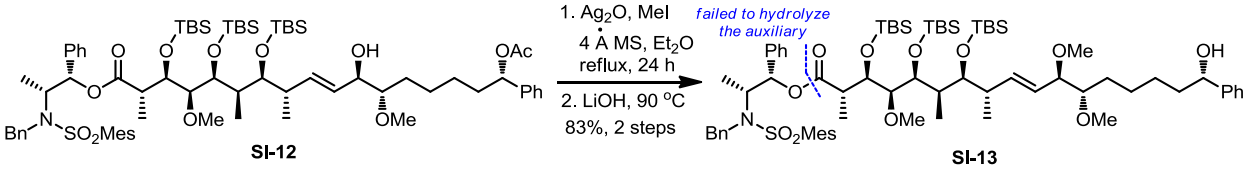
^{13}C NMR (100 MHz, $CDCl_3$)

δ 172.1, 140.7, 140.4, 138.1, 137.4, 134.6, 132.6, 132.0, 129.9, 128.6, 128.5, 128.3, 128.1, 128.0, 127.8, 127.5, 126.5, 126.4, 84.2, 77.1, 76.1, 74.3, 72.4, 59.6, 58.5, 56.1, 47.7, 43.0, 40.3, 40.0, 36.3, 30.0, 26.4, 26.2, 26.1, 25.7, 22.8, 21.2, 18.6, 18.3, 16.4, 11.2, -2.8, -3.2, -3.3, -3.8, -4.5, -4.8.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 1338.7502, found: 1338.7502.

(9) a) Dess, D. B.; Martin, J. C. *J. Org.Chem.* **1983**, 48, 4155; *J. Am. Chem. Soc.* **1991**, 113, 7277. For two improved procedures for the preparation of DMP, see: Ireland, R. E.; Liu, J. *J. Org. Chem.* **1993**, *58*, 2899; Meyers, S. D.; Schreiber, S. L. *J. Org. Chem.* **1994**, *59*, 7459.

(1*S*,2*R*)-2-((*N*-Benzyl-2,4,6-trimethylphenyl)sulfonamido)-1-phenylpropyl (2*S*,3*R*,4*R*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*S*,*E*)-3,5,7-tris((*tert*-butyldimethylsilyl)oxy)-17-hydroxy-4,11,12-trimethoxy-2,6,8-trimethyl-17-phenylheptadec-9-enoate (SI-13)



To a solution of alcohol **SI-12** (132 mg, 0.10 mmol) in diethyl ether (1 mL) were added silver oxide (165 mg, 0.50 mmol), 4 Å molecular sieves (600 mg) and iodomethane (0.10 mL, 1.2 mmol). The mixture was stirred at room temperature for 48 h in the absence of direct light. The reaction was then filtered throught a pad of Celite and washed thoroughly with MTBE. The organic solution was concentrated.

The residue was dissolved in THF/MeOH/H_2O (1 mL/1 mL/0.5 mL) and LiOH (54 mg, 2.0 mmol) was added at room temperature. The mixture was heated at 90 °C for 24 h. Then the reaction was quenched with 10% citric acid (4 mL) and extracted with EtOAc (4 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EtOAc = 2:1) to afford compound **SI-13** as waxy solid (107 mg, 83%).

R_f 0.25 (PE/EtOAc 4:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -17.0 (c = 1.5, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

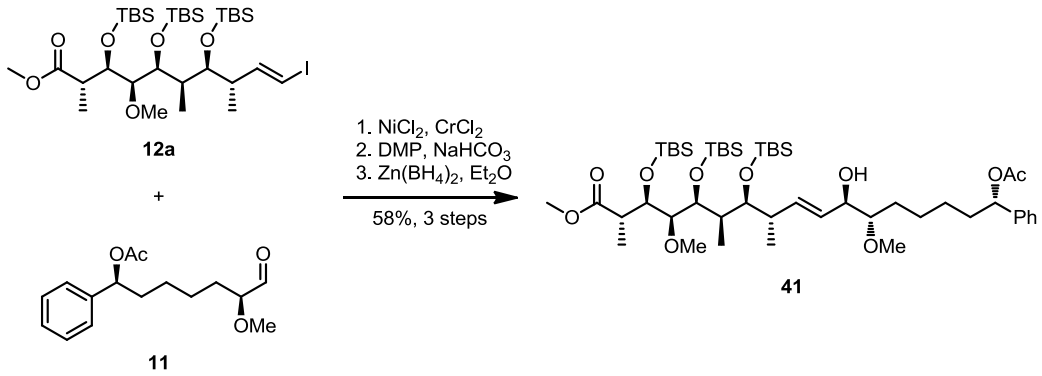
δ 7.40-7.24 (m, 10H), 7.16 (t, *J* = 8.0 Hz, 1H), 7.00 (t, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 6.79 (s, 2H), 5.79 (d, *J* = 8.0 Hz, 2H), 5.65 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.25 (dd, *J* = 8.0 & 16.0 Hz, 1H), 4.78 (d, *J* = 16.0 Hz, 1H), 4.65 (t, *J* = 8.0 Hz, 1H), 4.34 (d, *J* = 16.0 Hz, 1H), 4.13-4.08 (m, 1H), 3.64 (d, *J* = 4.0 Hz, 1H), 3.60-3.58 (m, 1H), 3.50 (d, *J* = 8.0 Hz, 1H), 3.35-3.32 (m, 4H), 3.28-3.21 (m, 1H), 3.16 (s, 3H), 3.09-3.06 (m, 1H), 2.95 (s, 3H), 2.67-2.65 (m, 1H), 2.29-2.26 (m, 10H), 1.81-1.64 (m, 4H), 1.41-1.24 (m, 10 H), 1.12 (d, *J* = 8.0 Hz, 3H), 1.02 (d, *J* = 8.0 Hz, 3H), 0.91-0.76 (m, 33H), 0.10-0.00 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 171.2, 144.8, 142.2, 140.5, 138.2, 137.5, 136.9, 132.6, 132.1, 128.6, 128.5, 128.4, 128.1, 127.9, 127.5, 127.4, 127.0, 125.8, 84.5, 83.5, 77.1, 76.1, 75.8, 74.5, 72.8, 59.8, 58.4, 56.1, 47.8, 42.4, 40.6, 40.4, 39.0, 30.5, 26.3, 26.2, 26.1, 22.9, 20.9, 20.2, 18.6, 18.4, 18.2, 16.6, 15.4, 11.7, -2.8, -3.1, -3.5, -4.0, -4.3, -4.7.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 1310.7553, found: 1310.7561.

Methyl (2*S*,3*R*,4*R*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*S*,*E*)-17-acetoxy-3,5,7-tris((*tert*-butyldimethylsilyl)oxy)-11-hydroxy-4,12-dimethoxy-2,6,8-trimethyl-17-phenylheptadec-9-enoate (41)



To aldehyde **11** (180 mg, 0.65 mmol) and vinyl iodide **12a** (617 mg, 0.80 mmol) was added anhydrous DMSO-THF (10 mL/2 mL) via syringe under nitrogen atmosphere, followed by $CrCl_2$ (500 mg, 3.3 mmol) and $NiCl_2$ (3.40 mg, 0.026 mmol) at room temperature. After stirring overnight, saturated aqueous NH_4Cl (20 mL) was added and the mixture extracted with MTBE (4 × 20 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure.

The residue was dissolved in DCM (10 mL) and $NaHCO_3$ (349 mg, 4.08 mmol) was added at room temperature. After being stirred for 10 min, the reaction was cooled to 0 °C and Dess-Martin periodinane (425 mg, 1.04 mmol) was added. The mixture was stirred at room temperature for 1.5 h, quenched with 1 N Na_2SO_3 (5 mL) at 0 °C and diluted with water (10 mL). The mixture was extracted with MTBE (3 × 15 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure.

The crude enone was dissolved in anhydrous ether (20 mL) and cooled to -55 °C, where a solution of zinc borohydride (15.0 mL, 0.13 M in ether) was added. The mixture was allowed to warm slowly to -10 °C, stirred at this temperature for 3 h, and quenched with saturated aqueous NH_4Cl (15 mL). The mixture was extracted with MTBE (4 × 20 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified via flash column chromatography (PE/EtOAc = 4:1) to afford the desired product as colorless oil (348 mg, 58%).

R_f 0.40 (PE/EtOAc 4:1, $KMnO_4$)

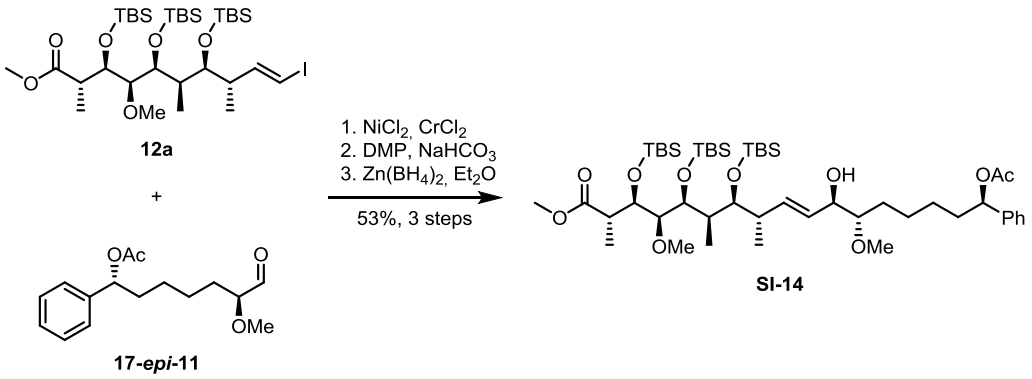
Opt. Rot. $[\alpha]^{20}_D$ = -9.2 (c = 0.50, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.35-7.25 (m, 5H), 5.93 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.71 (t, *J* = 8.0 Hz, 1H), 5.57 (dd, *J* = 8.0 & 16.0 Hz, 1H), 4.09 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.99 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.76 (d, *J* = 8.0 Hz, 1H), 3.66-3.62 (m, 4H), 3.41 (s, 3H), 3.36 (s, 3H), 3.24-3.21 (m, 1H), 3.16-3.12 (m, 1H), 2.88-2.81 (m, 1H), 2.48-2.44 (m, 1H), 2.06 (s, 3H), 1.99-1.88 (m, 2H), 1.79-1.73 (m, 1H), 1.44-1.24 (m, 6H), 1.18 (d, *J* = 8.0 Hz, 3H), 1.08 (d, *J* = 8.0 Hz, 3H), 0.91-0.83 (m, 30H), 0.12-0.04 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 175.4, 170.3, 140.8, 135.2, 130.0, 128.4, 127.8, 126.5, 85.0, 84.5, 76.7, 76.1, 74.9, 72.5, 72.2, 58.9, 58.7, 51.7, 44.1, 39.3, 36.4, 30.3, 26.3, 25.7, 21.3, 21.1, 18.6, 17.9, 14.4, 12.1, -2.9, -3.2, -3.4, -4.5, -5.3.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 947.5896, found: 947.5898.

Methyl (2*S*,3*R*,4*R*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*R*,*E*)-17-acetoxy-3,5,7-tris((*tert*-butyldimethylsilyl)oxy)-11-hydroxy-4,12-dimethoxy-2,6,8-trimethyl-17-phenylheptadec-9-enoate (SI-14)



Prepared accordingly as described above for **41** from **17-*epi*-11**.

$\underline{R_f}$ 0.40 (PE/EtOAc 4:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = 24.3 (c = 0.6, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

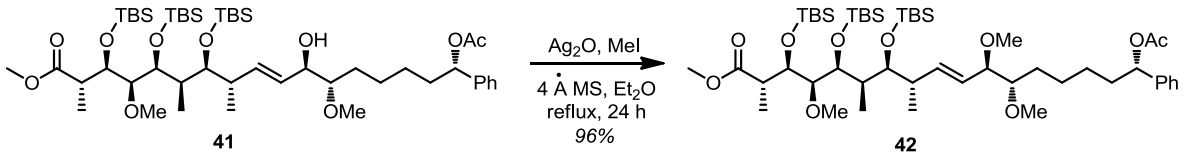
δ 7.35-7.25 (m, 5H), 5.93 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.71 (t, *J* = 8.0 Hz, 1H), 5.57 (dd, *J* = 8.0 & 16.0 Hz, 1H), 4.09 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.99 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.76 (d, *J* = 8.0 Hz, 1H), 3.66-3.64 (m, 4H), 3.42 (s, 3H), 3.37 (s, 3H), 3.24-3.21 (m, 1H), 3.16-3.12 (m, 1H), 2.88-2.81 (m, 1H), 2.48-2.44 (m, 1H), 2.06 (s, 3H), 1.99-1.86 (m, 2H), 1.79-1.72 (m, 1H), 1.44-1.24 (m, 6H), 1.18 (d, *J* = 8.0 Hz, 3H), 1.08 (d, *J* = 8.0 Hz, 3H), 0.92-0.82 (m, 30H), 0.12-0.03 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 175.4, 170.3, 140.8, 135.2, 130.0, 128.4, 127.8, 126.5, 85.0, 84.5, 76.7, 76.1, 74.9, 72.5, 72.2, 58.9, 58.7, 51.7, 44.1, 39.3, 36.4, 30.3, 26.3, 25.7, 21.3, 21.1, 18.6, 17.9, 14.4, 12.1, -2.9, -3.2, -3.4, -4.5, -5.3.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 947.5896, found: 947.5897.

Methyl (2*S*,3*R*,4*R*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*S*,*E*)-17-acetoxy-3,5,7-tris((*tert*-butyldimethylsilyl)oxy)-4,11,12-trimethoxy-2,6,8-trimethyl-17-phenylheptadec-9-enoate (42)



To a solution of alcohol **41** (348 mg, 0.38 mmol) in diethyl ether (3 mL) were added silver oxide (497 mg, 2.15 mmol), 4 Å molecular sieves (700 mg) and iodomethane (0.27 mL, 4.3 mmol). The mixture was heated at reflux for 48 h in the absence of direct light. The reaction was then filtered throught a pad of Celite and washed thoroughly with MTBE. The organic solution was concentrated. The residue was purified via flash column chromatography (PE/EtOAc = 9:1) to afford the desired product as colorless oil (388 mg, 96%).

$\underline{R_f}$ 0.40 (PE/EtOAc 9:1, $KMnO_4$)

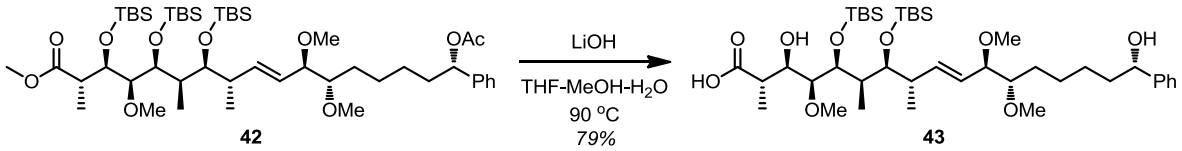
Opt. Rot. $[\alpha]^{20}_D$ = -23.2 (c = 4.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.35-7.25 (m, 5H), 5.83 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.71 (t, *J* = 4.0 Hz, 1H), 5.36 (dd, *J* = 8.0 & 16.0 Hz, 1H), 3.79-3.73 (m, 3H), 3.64 (s, 3H), 3.57 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.46 (t, *J* = 8.0 Hz, 1H), 3.38 (s, 6H), 3.24 (s, 3H), 3.14-3.11 (m, 1H), 3.02-2.99 (m, 1H), 2.41-2.36 (m, 1H), 2.05 (s, 3H), 1.91-1.86 (m, 2H), 1.79-1.76 (m, 1H), 1.47-1.24 (m, 6H), 1.19 (d, *J* = 8.0 Hz, 3H), 1.09 (d, *J* = 8.0 Hz, 3H), 0.92-0.83 (m, 30H), 0.13-0.05 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 174.1, 170.3, 140.8, 137.2, 128.4, 127.8, 126.8, 126.5, 84.9, 84.5, 83.8, 76.1, 75.9, 74.6, 72.8, 59.5, 58.3, 56.4, 51.1, 42.4, 41.0, 39.9, 36.3, 30.3, 26.3, 26.2, 25.9, 25.8, 21.3, 19.8, 18.6, 18.3, 18.1, 15.1, 12.1, -3.0, -3.3, -3.5, -3.9, -4.3, -4.7.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 961.6052, found: 961.6053.

(2*S*,3*R*,4*S*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*S*,*E*)-5,7-Bis((*tert*-butyldimethylsilyl)oxy)-3,17-dihydroxy-4,11,12-trimethoxy-2,6,8-trimethyl-17-phenylheptadec-9-enoic acid (43)



To a solution of ester **42** (160 mg, 0.17 mmol) in THF/MeOH/H_2O (1 mL/1 mL/0.5 mL) was added LiOH (54 mg, 2.0 mmol) at room temperature. The mixture was heated at 90 °C for 24 h. Then the reaction was quenched with 10% citric acid (4 mL) and extracted with EtOAc (4 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (DCM/MeOH = 30:1) to afford **43** as waxy solid (103 mg, 79%).

R_f 0.30 (DCM/MeOH 25:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -15.6 (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.33-7.15 (m, 5H), 5.72 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.39 (dd, *J* = 8.0 & 16.0 Hz, 1H), 4.68 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.95 (d, *J* = 8.0 Hz, 1H), 3.60-3.56 (m, 2H), 3.50 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.44 (s, 3H), 3.40-3.37 (m, 4H), 3.28-3.19 (m, 5H), 3.08 (d, *J* = 8.0 Hz, 1H), 2.70-2.64 (m, 1H), 2.52-2.45 (m, 1H), 2.35 (s, 1H), 1.83-1.77 (m, 1H), 1.71-1.64 (m, 2H), 1.43-1.24 (m, 6H), 1.21 (d, *J* = 8.0 Hz, 3H), 1.07 (d, *J* = 8.0 Hz, 3H), 0.92-0.83 (m, 21H), 0.11-0.06 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 178.3, 144.6, 137.8, 136.8, 129.0, 128.4, 128.2, 127.4, 126.8, 125.8, 125.3, 84.5, 82.9, 82.3, 76.4, 74.5, 72.6, 72.0, 61.4, 58.3, 56.3, 43.9, 40.1, 39.8, 30.3, 26.3, 25.7, 25.6, 21.4, 19.9, 18.6, 18.3, 14.3, 10.6, -2.9, -3.5, -3.6, -4.1.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 791.4926, found: 791.4927.

(2*S*,3*R*,4*S*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*R*,*E*)-5,7-Bis((*tert*-butyldimethylsilyl)oxy)-3,17-dihydroxy-4,11,12-trimethoxy-2,6,8-trimethyl-17-phenylheptadec-9-enoic acid (47)

SI-14 **47**

Prepared accordingly as described above for **43** from **SI-14**.

R_f 0.30 (DCM/MeOH 25:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -8.3 (c = 1.2, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

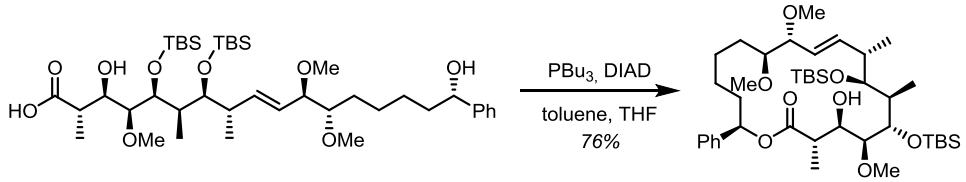
δ 7.35-7.25 (m, 5H), 5.74 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.41 (dd, *J* = 8.0 & 16.0 Hz, 1H), 4.70 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.97 (d, *J* = 8.0 Hz, 1H), 3.62-3.59 (m, 2H), 3.53 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.47 (s, 3H), 3.42-3.39 (m, 4H), 3.28-3.19 (m, 5H), 3.10 (d, *J* = 8.0 Hz, 1H), 2.73-2.66 (m, 1H), 2.55-2.47 (m, 1H), 2.35 (s, 1H), 1.84-1.79 (m, 1H), 1.72-1.68 (m, 2H), 1.47-1.24 (m, 6H), 1.23 (d, *J* = 8.0 Hz, 3H), 1.09 (d, *J* = 8.0 Hz, 3H), 0.96-0.90 (m, 21H), 0.13-0.09 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 178.4, 144.6, 136.8, 128.4, 128.3, 127.4, 126.8, 125.9, 84.6, 83.0, 82.4, 76.4, 74.5, 72.6, 72.0, 61.3, 58.3, 56.3, 43.9, 40.1, 39.8, 38.8, 30.4, 26.3, 26.1, 25.7, 25.6, 19.9, 18.6, 18.3, 14.4, 10.6, -2.9, -3.5, -3.6, -4.1.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 791.4926, found: 791.4925.

(3*S*,4*R*,5*S*,6*S*,7*R*,8*S*,9*S*,12*R*,13*S*,18*R*,*E*)-6,8-Bis((*tert*-butyldimethylsilyl)oxy)-4-hydroxy-5,12,13-trimethoxy-3,7,9-trimethyl-18-phenyloxacyclooctadec-10-en-2-one (45)



43 **45**

To a solution of tributylphosphine (0.16 mL, 0.65 mmol, 5.0 equiv) in anhydrous toluene (10 mL) was added diisopropyl azodicarboxylate (0.10 mL, 0.52 mmol, 4.0 equiv) at 0 °C. A solution of acid **43** (103 mg, 0.13 mmol, 1.0 equiv) in THF (10 mL) was then added via syringe pump over 1 h. After 50 min, the mixture was concentrated in vacuo and the crude oil was purified by flash chromatography (PE/EtOAc = 15:1) to provide the desired compound as colorless oil (74 mg, 76%).

R_f 0.30 (PE/EtOAc 15:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = 25.7 (c = 2.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

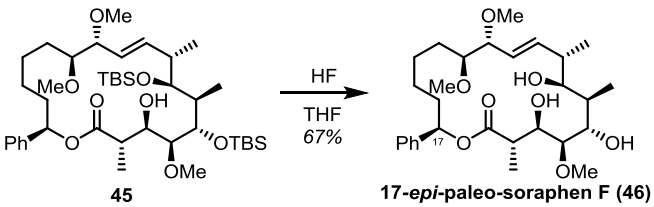
δ 7.37-7.24 (m, 5H), 6.15 (dd, *J* = 4.0 & 12.0 Hz, 1H), 5.90 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.34 (dd, *J* = 4.0 & 16.0 Hz, 1H), 4.05 (dd, *J* = 4.0 & 8.0 Hz, 2H), 3.76-3.70 (m, 2H), 3.58-3.56 (m, 1H), 3.50 (s, 3H), 3.42 (s, 3H), 3.36-3.20 (m, 7H), 2.98-2.90 (m, 1H), 2.63-2.55 (m, 1H), 1.97-1.92 (m, 1H), 1.77-1.17 (m, 12H), 1.12-1.00 (m, 6H), 0.94-0.82 (m, 21H), 0.15 (s, 3H), 0.09 (s, 6H), 0.07 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 175.7, 141.7, 128.3, 127.4, 126.1, 84.6, 84.0, 82.8, 76.4, 73.7, 73.2, 73.0, 61.3, 58.5, 56.8, 44.2, 39.5, 39.3, 30.7, 26.4, 26.3, 26.2, 25.6, 23.0, 18.6, 18.5, 14.3, 10.8, -2.9, -3.2, -3.3, -3.9.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 773.4820, found: 773.4819.

(3*S*,4*R*,5*R*,6*S*,7*R*,8*S*,9*S*,12*R*,13*S*,18*R*,*E*)-4,6,8-Trihydroxy-5,12,13-trimethoxy-3,7,9-trimethyl-18-phenyloxacyclooctadec-10-en-2-one (17-*epi*-paleo-soraphen F, 46)



Compound **45** (12 mg, 0.016 mmol) was dissolved in THF (1 mL) and cooled to 0 °C. The solution was treated dropwise with a solution of hydrogen fluoride pyridine (~70 % hydrogen fluoride, 0.2 mL). After addition, the reaction mixture was stirred overnight at room temperature and concentrated. The residue was purified by flash column chromatography (PE/EtOAc = 3:2) to afford the desired product as colorless oil (6.5 mg, 67%).

R_f 0.20 (PE/EtOAc 1:1, $KMnO_4$)

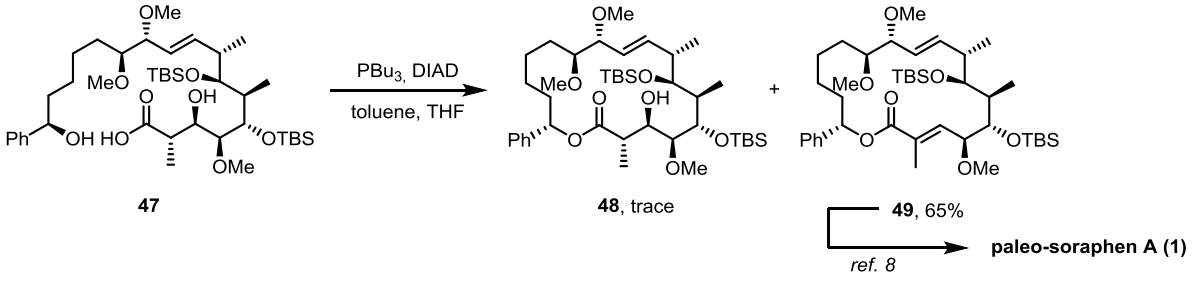
Opt. Rot. $[\alpha]^{20}_D$ = -80.0 (c = 0.04, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.36-7.18 (m, 5H), 6.40-6.18 (m, 1H), 5.56-5.52 (m, 2H), 4.64 (dd, *J* = 4.0 & 8.0 Hz, 1H), 4.27-4.25 (m, 1H), 3.69-3.68 (m, 1H), 3.63-3.61 (m, 1H), 3.45 (s, 3H), 3.45 (s, 3H), 3.40-3.27 (m, 6H), 2.85-2.82 (m, 1H), 2.37-2.34 (m, 1H), 2.25-2.21 (m, 3H), 1.68-1.41 (m, 10H), 1.34 (d, *J* = 8.0 Hz, 3H), 1.08 (d, *J* = 8.0 Hz, 3H), 0.98 (d, *J* = 8.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 173.1, 137.7, 137.1, 130.5, 130.1, 129.0, 128.5, 126.9, 125.9, 83.9, 83.1, 81.0, 77.2, 75.1, 73.1, 67.7, 58.6, 57.5, 56.9, 41.4, 36.0, 35.3, 33.0, 30.5, 25.6, 16.7, 11.8, 8.7.

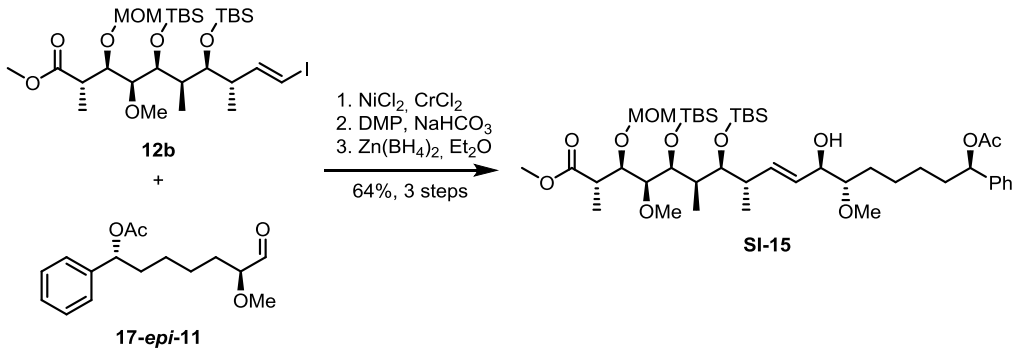
ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 545.3090, found: 545.3091.

(3*E*,5*S*,6*S*,7*R*,8*S*,9*S*,10*E*,12*R*,13*S*,18*S*)-6,8-Bis((*tert*-butyldimethylsilyl)oxy)-5,12,13-trimethoxy-3,7,9-trimethyl-18-phenyloxacyclooctadeca-3,10-dien-2-one (49)[8]



To a solution of tributylphosphine (0.16 mL, 0.65 mmol, 5.0 equiv) in anhydrous toluene (10 mL) was added diisopropyl azodicarboxylate (0.10 mL, 0.52 mmol, 4.0 equiv) at 0 °C. A solution of acid **47** (103 mg, 0.13 mmol, 1.0 equiv) in THF (10 mL) was then added via syringe pump over 1 h. After 50 min, the mixture was concentrated in vacuo and the crude oil was purified by flash chromatography (PE/EtOAc = 15:1) to provide the title compound as colorless oil (62 mg, 65%).[8]

Methyl (2*S*,3*R*,4*S*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*R*,*E*)-17-acetoxy-5,7-bis((*tert*-butyldimethylsilyl)oxy)-11-hydroxy-4,12-dimethoxy-3-(methoxymethoxy)-2,6,8-trimethyl-17-phenylheptadec-9-enoate (SI-15)



Prepared accordingly as described above for **41** but starting from aldehyde **17-*epi*-11** and vinyliodide **12b**.

R_f 0.30 (PE/EtOAc 9:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D = 16.5$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)

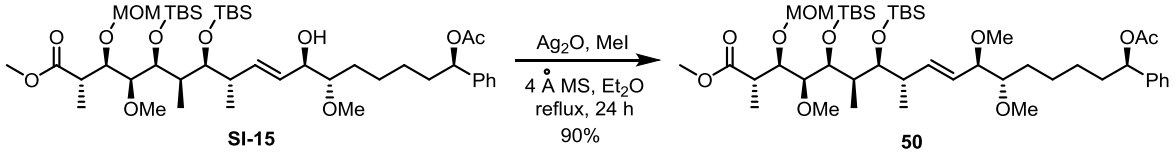
δ 7.35-7.25 (m, 5H), 5.80 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.71 (t, *J* = 4.0 Hz, 1H), 5.59 (dd, *J* = 8.0 & 16.0 Hz, 1H), 4.67 (s, 2H), 4.05-4.01 (m, 1H), 3.81-3.78 (m, 1H), 3.69-3.65 (m, 4H), 3.47 (d, *J* = 4.0 Hz, 1H), 3.42 (s, 3H), 3.41 (s, 3H), 3.37 (s, 3H), 3.24 (dd, *J* = 4.0 & 8.0 Hz, 1H),3.28-3.14 (m, 1H), 2.99-2.92 (m, 1H), 2.56-2.48 (m, 1H), 2.06 (s, 3H), 1.91-1.87 (m, 1H), 1.79-1.75 (m, 1H), 1.65-1.18 (m, 7H), 1.05 (d, *J* = 8.0 Hz, 1H), 0.92-0.88 (m, 21H), 0.12 (s, 3H), 0.06 (s, 3H), 0.05 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 175.4, 170.3, 140.7, 135.2, 130.7, 128.4, 127.8, 126.5, 96.7, 84.5, 82.1, 78.3, 77.2, 76.1, 75.8, 75.0, 72.5, 60.1, 58.8, 56.1, 51.8, 42.5, 40.2, 39.5, 30.5, 26.3, 26.2, 25.7, 25.6, 21.3, 20.3, 18.6, 18.4, 14.2, 11.2, -3.0, -3.4, -3.6, -4.6.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ $[M + Na]^+$: 877.5293, found: 877.5291.

Methyl (2*S*,3*R*,4*S*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,17*R*,*E*)-17-acetoxy-5,7-bis((*tert*-butyldimethylsilyl)oxy)-4,11,12-trimethoxy-3-(methoxymethoxy)-2,6,8-trimethyl-17-phenylheptadec-9-enoate (50)



To a solution of alcohol **SI-15** (367 mg, 0.43 mmol) in diethyl ether (3 mL) were added silver oxide (497 mg, 2.15 mmol), 4 Å molecular sieves (700 mg) and iodomethane (0.27 mL, 4.3 mmol). The mixture was heated at reflux for 24 h in the absence of direct light. The reaction was then filtered throught a pad of Celite and washed thoroughly with MTBE. The organic solution was concentrated. The residue was purified via flash column chromatography (PE/EtOAc = 9:1) to afford the desired product as colorless oil (336 mg, 90%).

R_f 0.20 (PE/EtOAc 9:1, $KMnO_4$)

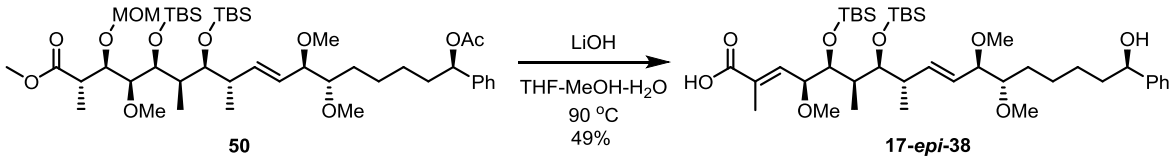
Opt. Rot. $[\alpha]^{20}_D = 6.3$ (c = 0.6, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.35-7.25 (m, 5H), 5.80 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.70 (t, *J* = 8.0 Hz, 1H), 5.40 (dd, *J* = 8.0 & 16.0 Hz, 1H), 4.64 (s, 2H), 3.82 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.67-3.63 (m, 4H), 3.59 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.52 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.43 (s, 3H), 3.39-3.31 (m, 7H), 3.24 (s, 3H), 3.14-3.11 (m, 1H), 3.00-2.93 (m, 1H), 2.55-2.47 (m, 1H), 2.05 (s, 3H), 1.91-1.86 (m, 1H), 1.80-1.69 (m, 2H), 1.43-1.23 (m, 5H), 1.20 (d, *J* = 8.0 Hz, 1H), 1.08 (d, *J* = 8.0 Hz, 1H), 0.92-0.85 (m, 21H), 0.14 (s, 3H), 0.07 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 174.5, 170.3, 140.8, 137.2, 128.4, 127.8, 127.4, 126.5, 97.7, 84.7, 83.7, 82.3, 79.6, 76.3, 76.1, 72.3, 60.4, 58.3, 56.2, 56.1, 51.4.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ [M + Na]$^+$: 891.5450, found: 891.5449.

(2*E*,4*S*,5*S*,6*R*,7*S*,8*S*,9*E*,11*R*,12*S*,17*R*)-5,7-Bis((*tert*-butyldimethylsilyl)oxy)-17-hydroxy-4,11,12-trimethoxy-2,6,8-trimethyl-17-phenylheptadeca-2,9-dienoic acid (17-*epi*-38)



50 **17-*epi*-38**

To a solution of ester **50** (128 mg, 0.15 mmol) in THF/MeOH/H_2O (1 mL/1 mL/0.5 mL) was added LiOH (54 mg, 2.0 mmol) at room temperature. The mixture was heated at 90 °C for 24 h. Then the reaction was quenched with 10% citric acid (4 mL) and extracted with EtOAc (4 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (DCM/MeOH = 50:1) to afford **17-*epi*-38** as yellow oil (55 mg, 49%).

R_f 0.15 (PE/EA 2:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = -6.0 (c = 0.4, $CHCl_3$)

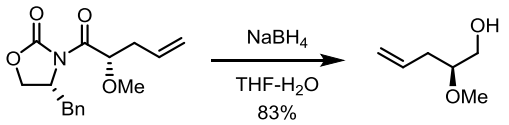
^{1}H NMR δ 7.34-7.25 (m, 5H), 6.34 (dd, *J* = 10.0, 1.6 Hz, 1H), 5.68 (dd, *J* = 15.6, 8.0 Hz, 1H), 5.27 (dd, *J* = 16.0, 8.4 Hz, 1H), 4.66 (t, *J* = 6.6 Hz, 1H), 4.28-4.10 (m, 2H), 3.88-3.80 (m, 1H), 3.76 (dd, *J* = 7.6, 1.6 Hz, 1H), 3.61 (d, *J* = 9.2 Hz, 1H), 3.48 (dd, *J* = 8.4, 3.6 Hz, 1H), 3.38 (s, 3H), 3.18 (s, 3H), 3.15 (s, 3H), 3.14 - 3.10 (m, 1H), 2.48-2.40 (m, 1H), 1.93 (d, *J* = 1.2 Hz, 3H), 1.88 (brs, 1H), 1.83 - 1.75 (m, 1H), 1.74-1.66 (m, 1H), 1.58 - 1.49 (m, 1H), 1.49-1.36 (m, 5H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.80 (d, *J* = 6.8 Hz, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 170.6, 144.7, 138.3, 137.2, 131.5, 128.4, 127.5, 127.1, 125.8,
84.5, 83.4, 81.2, 76.8, 75.0, 74.6, 58.2, 56.2, 56.0, 39.8, 39.7, 38.9, 30.2, 26.3, 26.2, 25.8, 25.5, 19.5, 18.7, 18.5, 13.0, 10.9, -3.1, -3.4, -3.5, -4.8.

ESI-HRMS calculated for $C_{20}H_{36}O_3Si$ [M + Na]$^+$: 773.4820, found: 773.4823.

2.5 Towards Paleo-Soraphen F (6) by the RCM Approach

(*S*)-2-Methoxypent-4-en-1-ol (SI-16)

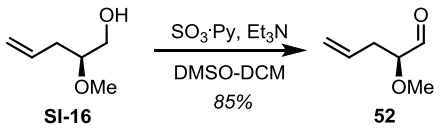


51 **SI-16**

A solution of sodium borohydride (2.27 g, 60 mmol) in water (15 mL) was added dropwise to a mixture of (*R*)-4-benzyl-3-((*S*)-2-methoxypent-4-enoyl)oxazolidin-2-one[10] (4.34 g, 15 mmol) in THF (45 mL). The mixture was stirred at room temperature for 8 h, and quenched with sat. NH_4Cl. The reaction mixture was extracted with ethyl acetate (3 × 60 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (PE/EtOAc = 4:1) to afford the desired product as colorless liquid (1.45 g, 83%).

R_f 0.20 (PE/EtOAc 4:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D = 30.1$ (c = 1.0, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 5.84-5.73 (m, 1H), 5.13-5.05 (m, 2H), 3.66 (dd, *J* = 8.0 & 12.0 Hz, 1H), 3.56 (dd, *J* = 8.0 & 12.0 Hz, 1H), 3.42 (s, 3H), 3.36-3.32 (m, 1H), 2.39-2.32 (m, 1H), 2.28-2.20 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 134.0,117.5, 80.9, 63.7, 57.1, 34.7.
ESI-HRMS calculated for $C_{22}H_{28}O_4$ $[M + Na]^+$: 139.0735, found: 139.0736.

(*S*)-2-Methoxypent-4-enal (52)



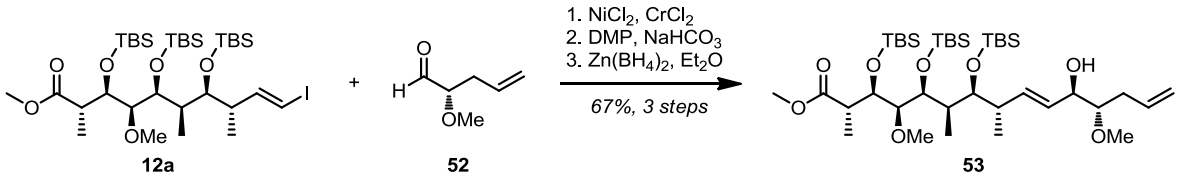
SI-16 **52**

Sulfur trioxide pyridine complex (8.8 g, 56 mmol) was added to a solution of alcohol **SI-16** (2.15 g, 18.5 mmol), DMSO (13 mL, 185 mmol) and diisopropylethylamine (17 mL, 92.5 mmol) in dichloromethane (100 mL) at 0 °C under an argon atmosphere. After 45 min, the reaction mixture was diluted with diethyl ether (200 mL) and water (80 mL), and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 100 mL). The combined organic layers were washed sequentially with 1.0 M aqueous HCl (50 mL), sat. $NaHCO_3$ (50 mL) and brine (50 mL). The organics were then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting oil was purified by distillation under reduced pressure to afford aldehyde **52** as colorless liquid (b.p. 62 °C /68 mbar, 1.80 g, 85%).

R_f 0.45 (PE/EtOAc 4:1, $KMnO_4$)
Opt. Rot. $[\alpha]^{20}_D = -107.8$ (c = 1.6, $CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$)
δ 9.66 (d, *J* = 4.0 Hz, 1H), 5.83-5.74 (m, 1H), 5.17-5.11 (m, 2H), 3.66-3.62 (m, 1H), 3.46 (s, 3H), 2.51-2.41 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$)
δ 203.2, 132.2, 118.4, 85.0, 58.2, 34.3.
ESI-HRMS calculated for $C_{22}H_{28}O_4$ $[M + Na]^+$: 137.0578, found: 137.0576.

(10) Crimmins, M. T.; Emmitte, K.A.; Katz, J. D. *Org. Lett.* **2000**, *2*, 2165.

Methyl (2*S*,3*R*,4*R*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,*E*)-3,5,7-tris((*tert*-butyldimethylsilyl)oxy)-11-hydroxy-4,12-dimethoxy-2,6,8-trimethylpentadeca-9,14-dienoate (53)



Prepared accordingly as described above for **41** but from (*S*)-2-methoxypent-4-enal.

R_f 0.2 (PE/EtOAc 9:1, $KMnO_4$)

Opt. Rot. $[\alpha]^{20}_D$ = 12.0 (c = 0.5, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 5.96 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.89-5.79 (m, 1H), 5.60 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.11-5.02 (m, 2H), 4.15-4.13 (m, 1H), 4.00 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.77 (d, *J* = 4.0 Hz, 1H), 3.68-3.65 (m, 4H), 3.45 (s, 3H), 3.37 (s, 3H), 3.29-3.23 (m, 2H), 3.22 (br, 1H), 2.90-2.83 (m, 1H), 2.50-2.45 (m, 2H), 2.30-2.18 (m, 2H), 2.00-1.95 (m, 1H), 1.19 d, *J* = 8.0 Hz, 1H), 1.11 (d, *J* = 8.0 Hz, 1H), 0.91-0.83 (m, 30H), 0.13-0.05 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 175.4, 135.5, 135.4, 129.6, 116.7, 85.1, 84.1, 77.2, 76.7, 58.9, 58.5, 51.7, 44.0, 39.4, 34.9, 26.3, 25.8, 21.1, 18.6, 18.5, 17.9, 14.5, 12.1, -2.9, -3.2, -3.4, -5.2.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 783.5059, found: 783.5058.

Methyl (2*S*,3*R*,4*R*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,*E*)-3,5,7-tris((*tert*-butyldimethylsilyl)oxy)-4,11,12-trimethoxy-2,6,8-trimethylpentadeca-9,14-dienoate (SI-17)

To a solution of alcohol **53** (360 mg, 0.47 mmol) in diethyl ether (3 mL) were added silver oxide (1.09 g, 4.70 mmol), 4 Å molecular sieves (800 mg) and iodomethane (1.00 mL, 14.2 mmol). The mixture was heated at reflux for 24 h in the absence of direct light. The reaction was then filtered throught a pad of Celite and washed thoroughly with MTBE. The organic solution was concentrated. The residue was purified via flash column chromatography (PE/EtOAc = 9:1) to afford the desired product as colorless oil (353 mg, 97%).

R_f 0.4 (PE/EtOAc 9:1, $KMnO_4$)

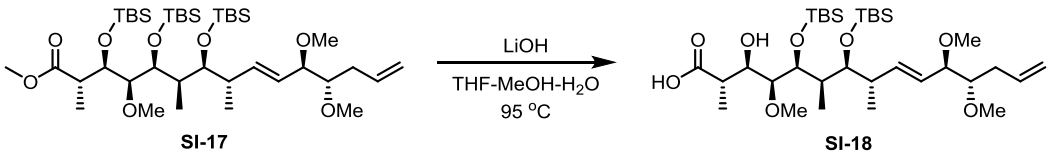
Opt. Rot. $[\alpha]^{20}_D$ = - 12.8 (c = 0.35, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 5.89-5.78 (m, 2H), 5.42 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.10-5.02 (m, 2H), 3.81-3.74 (m, 3H), 3.65 (s, 3H), 3.62 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.48 (t, *J* = 4.0 Hz, 1H), 3.38 (s, 3H), 3.36 (s, 3H), 3.30-3.27 (m, 4H), 3.06-3.01 (m, 1H), 2.41-2.17 (m, 3H), 1.89-1.85 (m, 1H), 1.21 (d, *J* = 8.0 Hz, 1H), 1.11 (d, *J* = 8.0 Hz, 1H), 0.91-0.83 (m, 30H), 0.14-0.07 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 174.1, 137.5, 135.4, 126.5, 116.7, 85.0, 84.1, 83.3, 77.2, 75.9, 72.9, 59.5, 58.3, 56.4, 51.1, 42.4, 40.0, 34.9, 26.3, 26.2, 25.9, 19.9, 18.7, 18.3, 18.1, 15.1, 12.2, -3.0, -3.3, -3.5, -3.8, -4.2, -4.7.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 797.5215, found: 797.5215.

(2*S*,3*R*,4*S*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,*E*)-5,7-Bis((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-4,11,12-trimethoxy-2,6,8-trimethylpentadeca-9,14-dienoic acid (SI-18)



SI-17 SI-18

To a solution of **SI-17** (270 mg, 0.35 mmol) in THF/MeOH/H_2O (6 mL/6 mL/3 mL) was added LiOH·H_2O (117 mg, 2.8 mmol) at room temperature. The mixture was heated at 90 °C for 24 h. Then the reaction was quenched with 10% citric acid (4 mL) and extracted with EtOAc (4 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (DCM/MeOH = 50:1) to afford the desired product as yellow oil (183 mg, 81%).

R_f 0.2 (DCM/MeOH 25:1, $KMnO_4$)

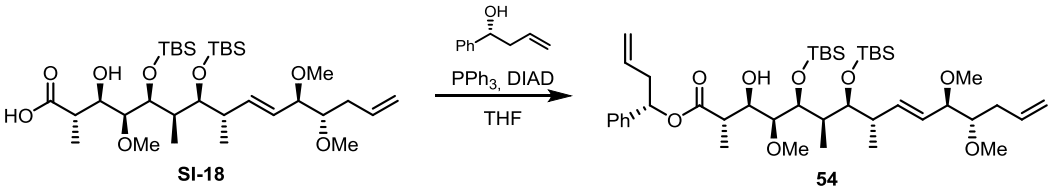
Opt. Rot. $[\alpha]^{20}_D$ = - 11.2 (c = 0.50, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$)
δ 5.83-5.71 (m, 2H), 5.45 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.10-5.04 (m, 2H), 3.94 (d, *J* = 4.0 Hz, 1H), 3.60-3.51 (m, 3H), 3.45 (s, 3H), 3.41 (s, 3H), 3.38-3.34 (m, 1H), 3.29 (s, 3H), 3.09 (d, *J* = 8.0 Hz, 1H), 2.70-2.63 (m, 1H), 2.54-2.49 (m, 1H), 2.31-2.04 (m, 2H), 1.65-1.57 (m, 1H), 1.25 (d, *J* = 8.0 Hz, 1H), 1.09 (d, *J* = 8.0 Hz, 1H), 0.94-0.89 (m, 21H), 0.12-0.07 (m, 12H).

^{13}C NMR (100 MHz, $CDCl_3$)
δ 176.6, 137.3, 134.8, 126.5, 117.1, 84.2, 82.6, 82.1, 77.2, 76.4, 72.6, 72.0, 61.4, 58.5, 56.4, 43.8, 40.3, 36.2, 26.3, 20.0, 18.6, 18.3, 14.4, 10.6, -2.8, -3.4, -3.5, -4.1.

ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 669.4194, found: 669.4191.

(*S*)-1-Phenylbut-3-en-1-yl (2*S*,3*R*,4*S*,5*S*,6*R*,7*S*,8*S*,11*R*,12*S*,*E*)-5,7-bis((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-4,11,12-trimethoxy-2,6,8-trimethylpentadeca-9,14-dienoate (54)



SI-18 54

To a solution of tributylphosphine (0.16 mL, 0.65 mmol) in anhydrous toluene (10 mL) was added diisopropyl azodicarboxylate (0.12 mL, 0.56 mmol) at 0 °C. A solution of acid **SI-18** (183 mg, 0.28 mmol, 1.0 equiv.) and (*R*)-1-phenylbut-3-en-1-ol (83 mg, 0.56 mmol) in THF (10 mL) was then added dropwise. After 50 min, the mixture was concentrated in vacuo and the crude oil was purified by flash chromatography (PE/EtOAc = 15:1) to provide the desired compound as colorless oil (174 mg, 80%).

R_f 0.4 (PE/EtOAc 9:1, $KMnO_4$)

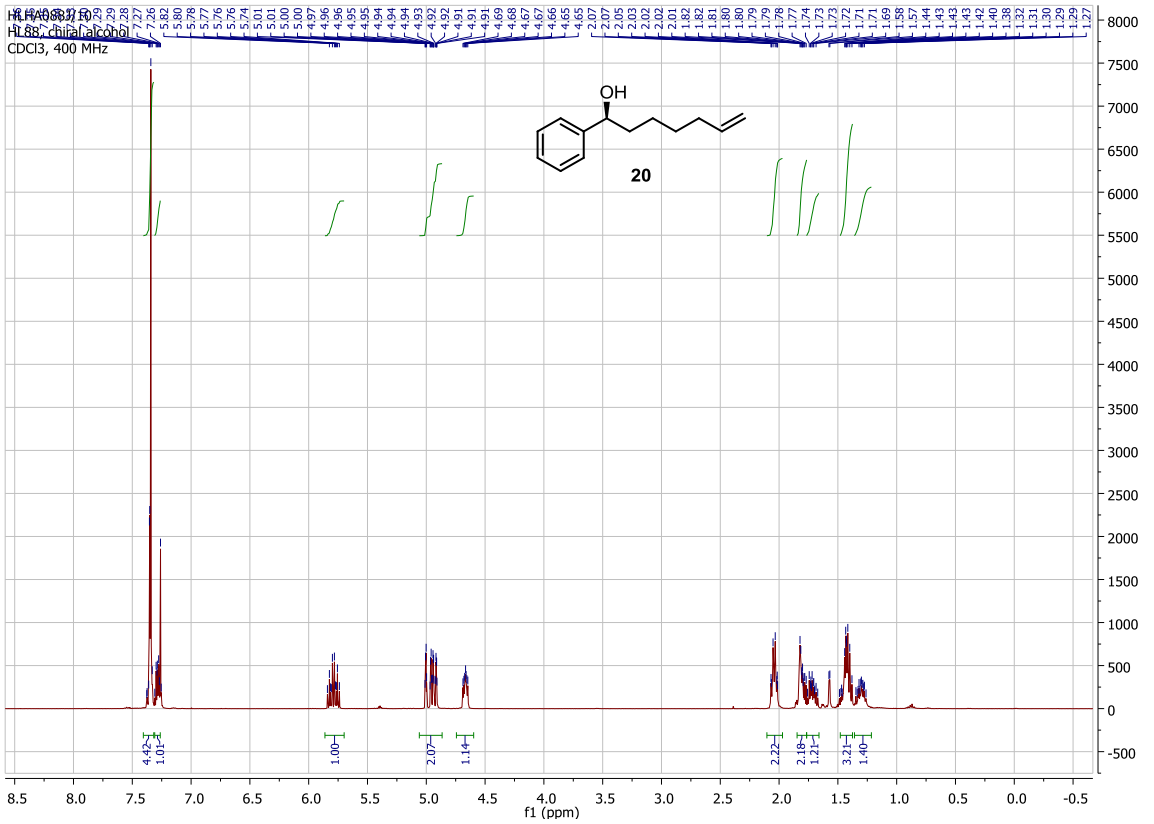
Opt. Rot. $[\alpha]^{20}_D$ = - 43.5 (c = 0.4, $CHCl_3$)

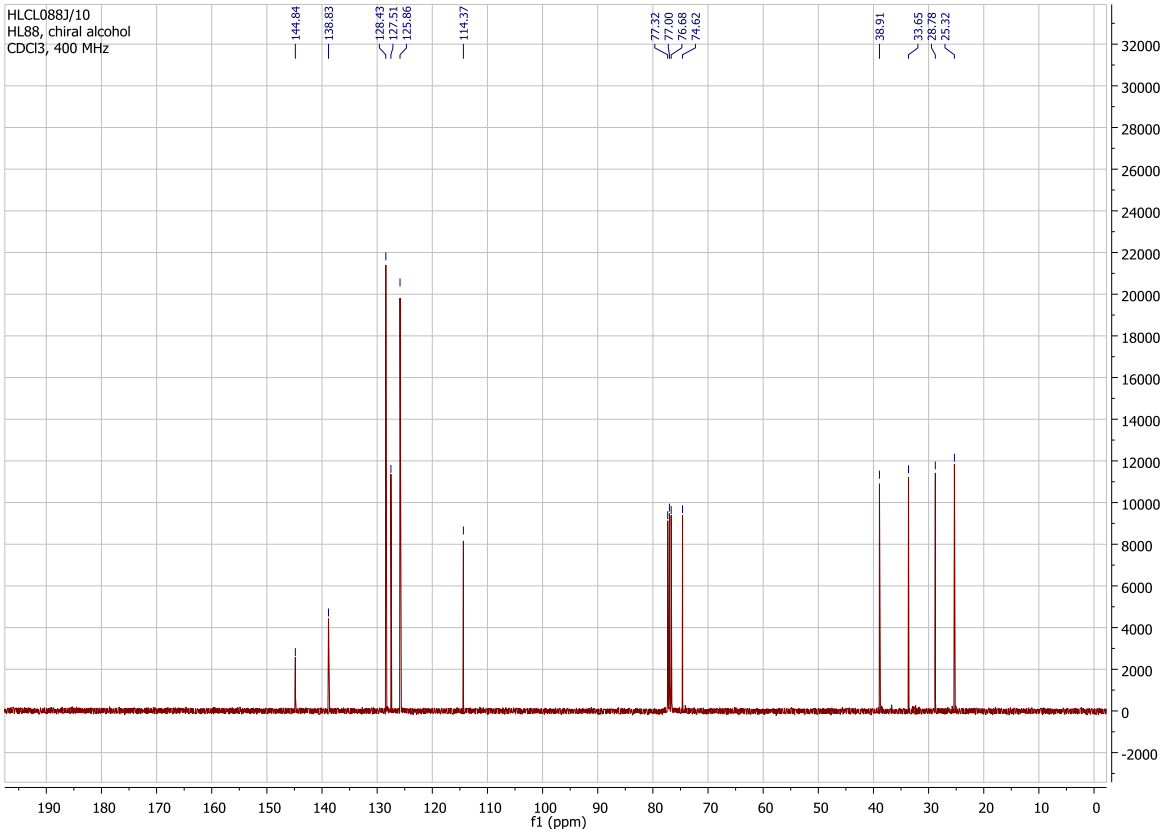
^{1}H NMR (400 MHz, $CDCl_3$)
δ 7.35-7.24 (m, 5H), 5.84-5.66 (m, 4H), 5.39 (dd, *J* = 8.0 & 16.0 Hz, 1H), 5.12-5.00 (m, 4H), 3.97 (d, *J* = 8.0 Hz, 1H),3.60-3.55 (m, 2H), 3.49 (dd, *J* = 4.0 & 8.0 Hz, 1H), 3.39 (s, 3H), 3.28-3.24 (m, 1H), 3.15 (s, 3H), 2.70-2.47 (m, 4H), 2.25-2.14 (m, 4H), 1.70-1.66 (m, 1H), 1.24 (d, *J* = 8.0 Hz, 1H), 1.06 (d, *J* = 8.0 Hz, 1H), 0.93 (s, 18H), 0.88 (d, *J* = 8.0 Hz, 1H), 0.11-0.06 (m, 12H).

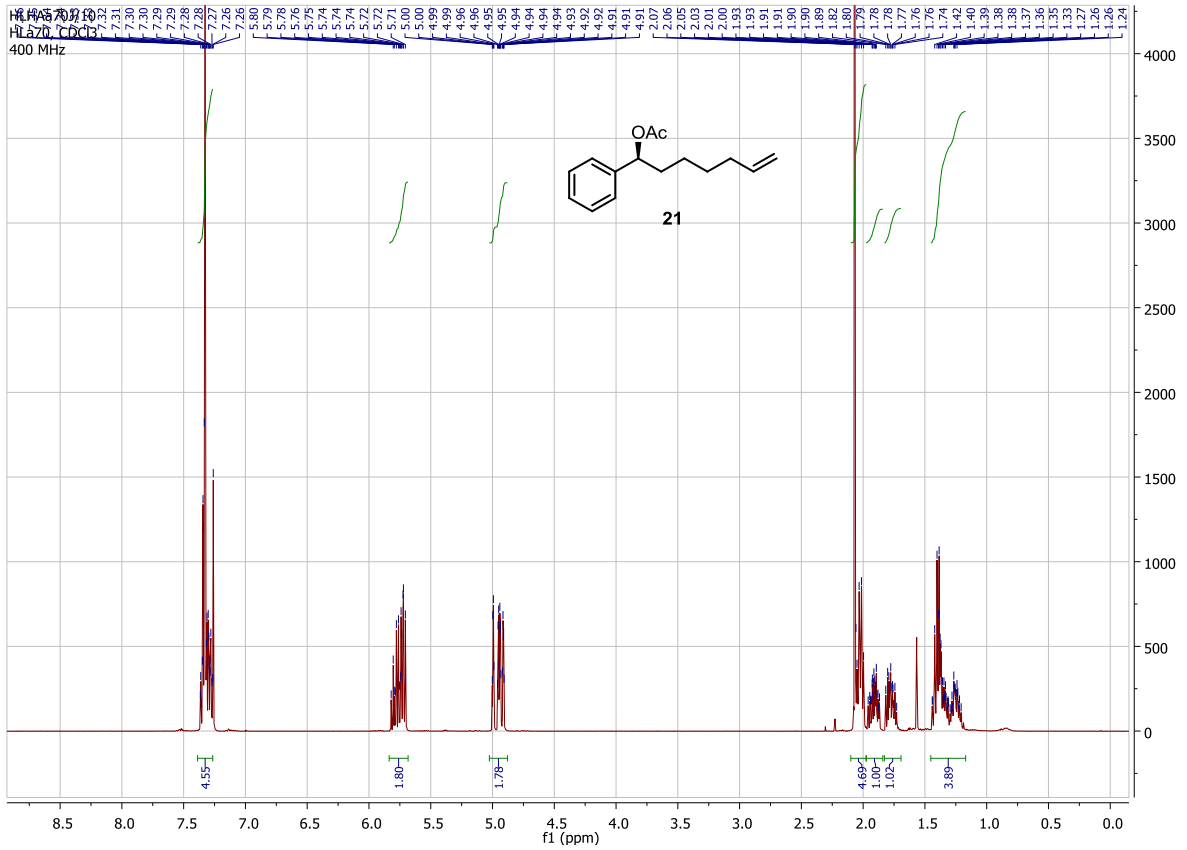
^{13}C NMR (100 MHz, $CDCl_3$)
δ 174.5, 140.1, 137.2, 135.4, 133.5, 128.3, 127.8, 127.1, 126.4, 118.0, 116.6, 84.2, 82.6, 82.3, 77.2, 76.5, 75.0, 72.5, 72.0, 61.1, 58.4, 56.1, 44.5, 40.9, 40.2, 39.9, 35.1, 26.3, 20.0, 18.6, 18.3, 14.9, 10.7, -2.9, -3.4, -3.5, -4.1.

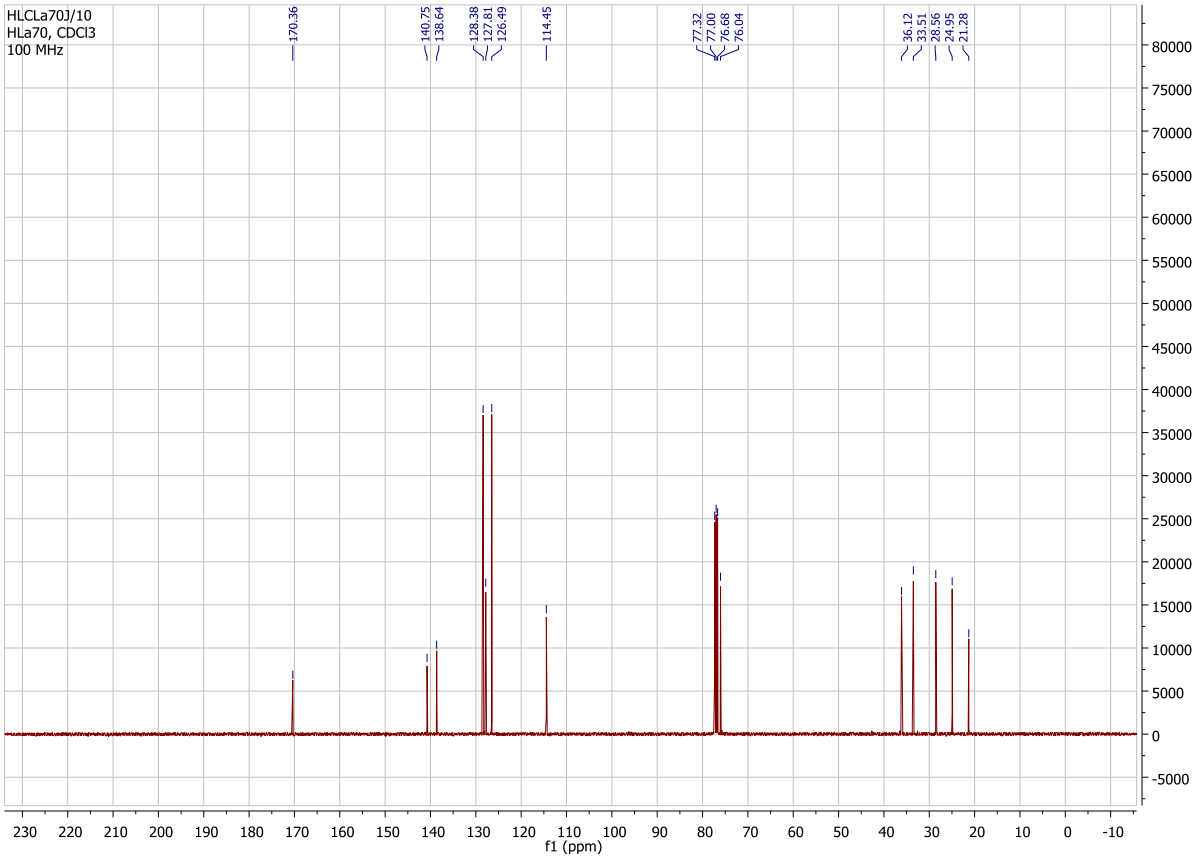
ESI-HRMS calculated for $C_{29}H_{46}O_7$ $[M + Na]^+$: 799.4976, found: 799.4973.

3. NMR Spectra






HLCLa70J/10
HLa70, CDCl3
400 MHz
OAc
21
4.55
1.80
1.78
4.69
1.00
1.02
3.89
f1 (ppm)


HLCLa70J/10
HLa70, CDCl3
100 MHz
170.36
140.75
138.64
128.38
127.81
126.49
114.45
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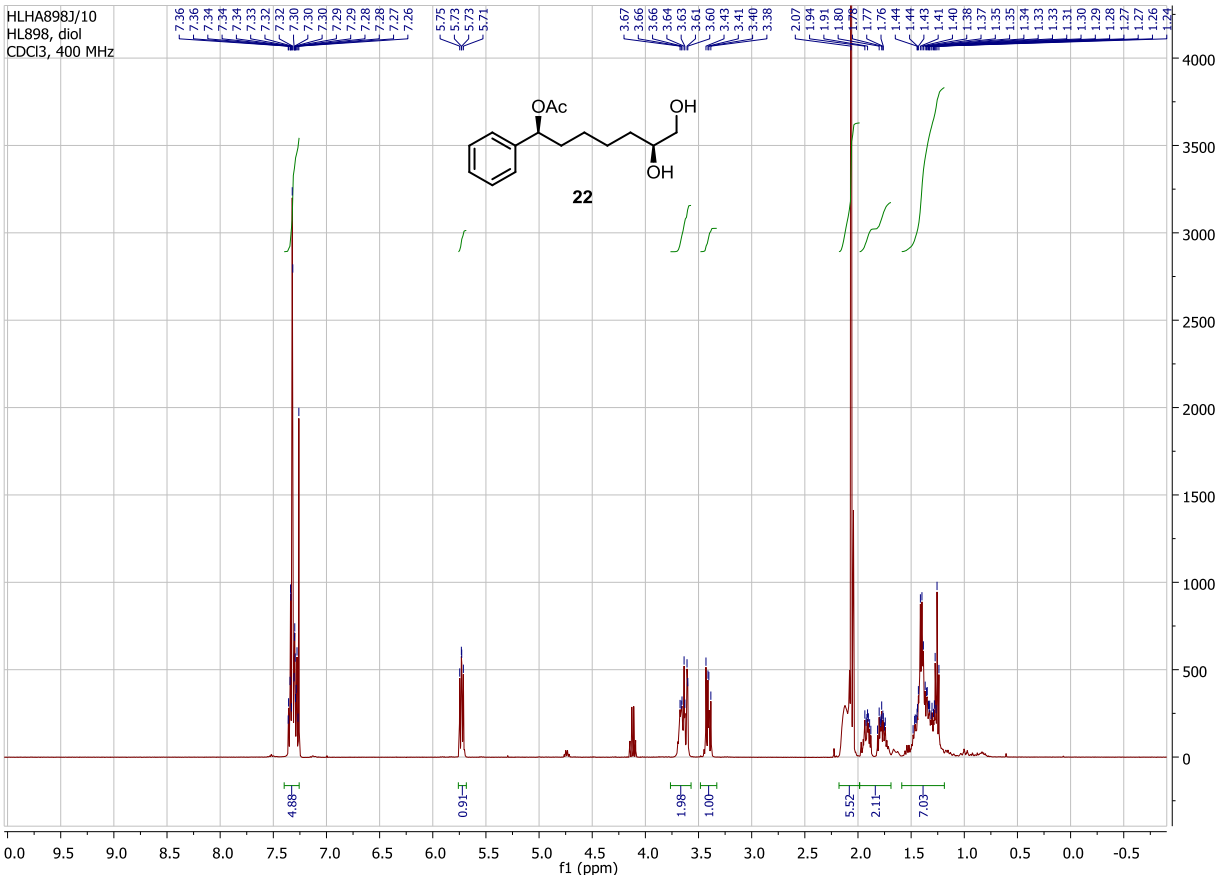
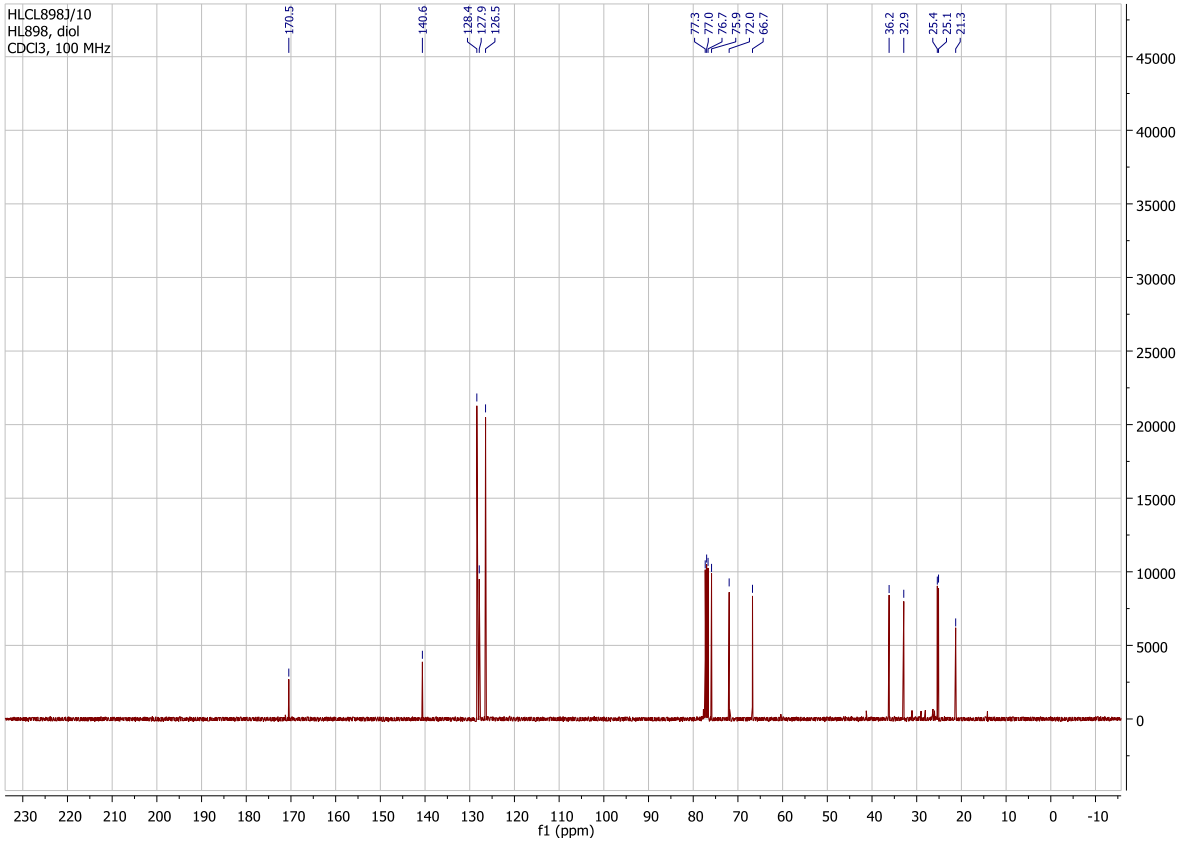
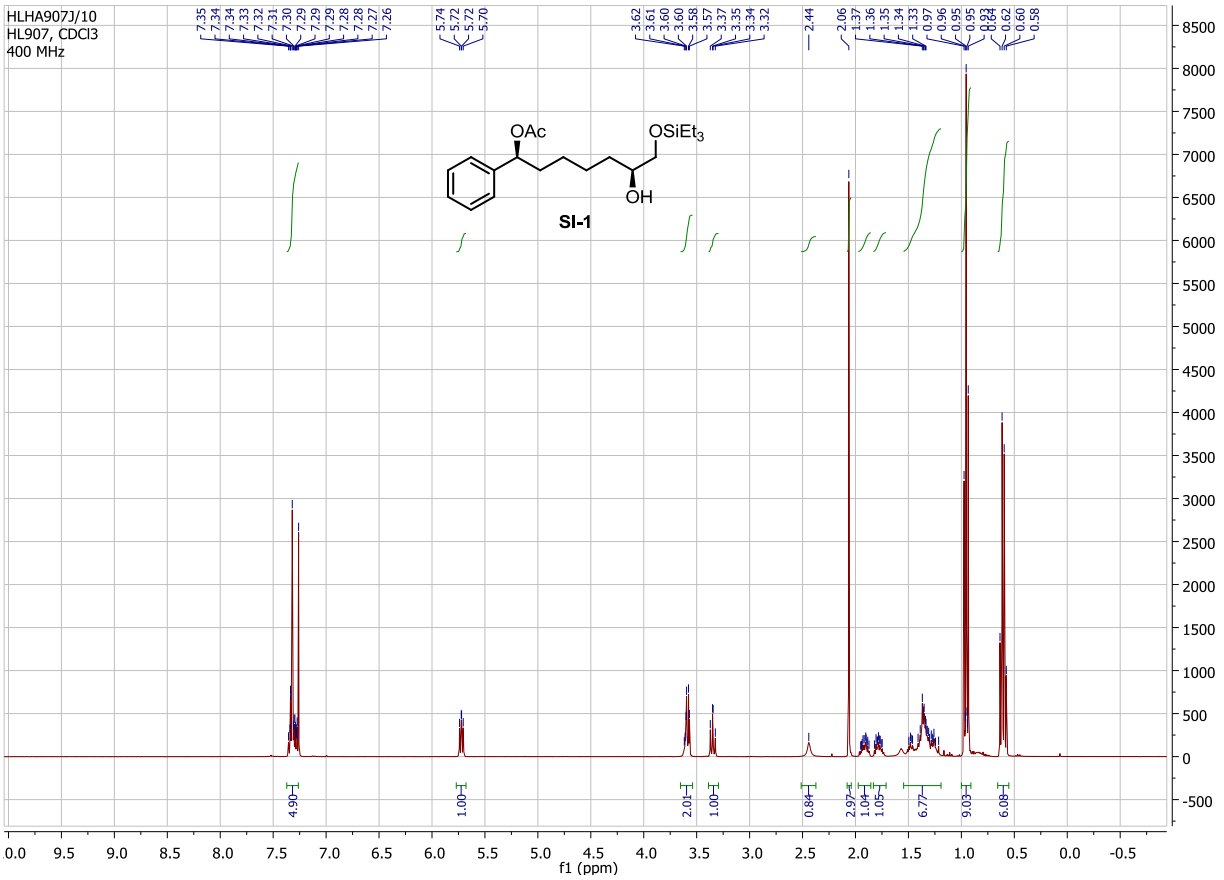
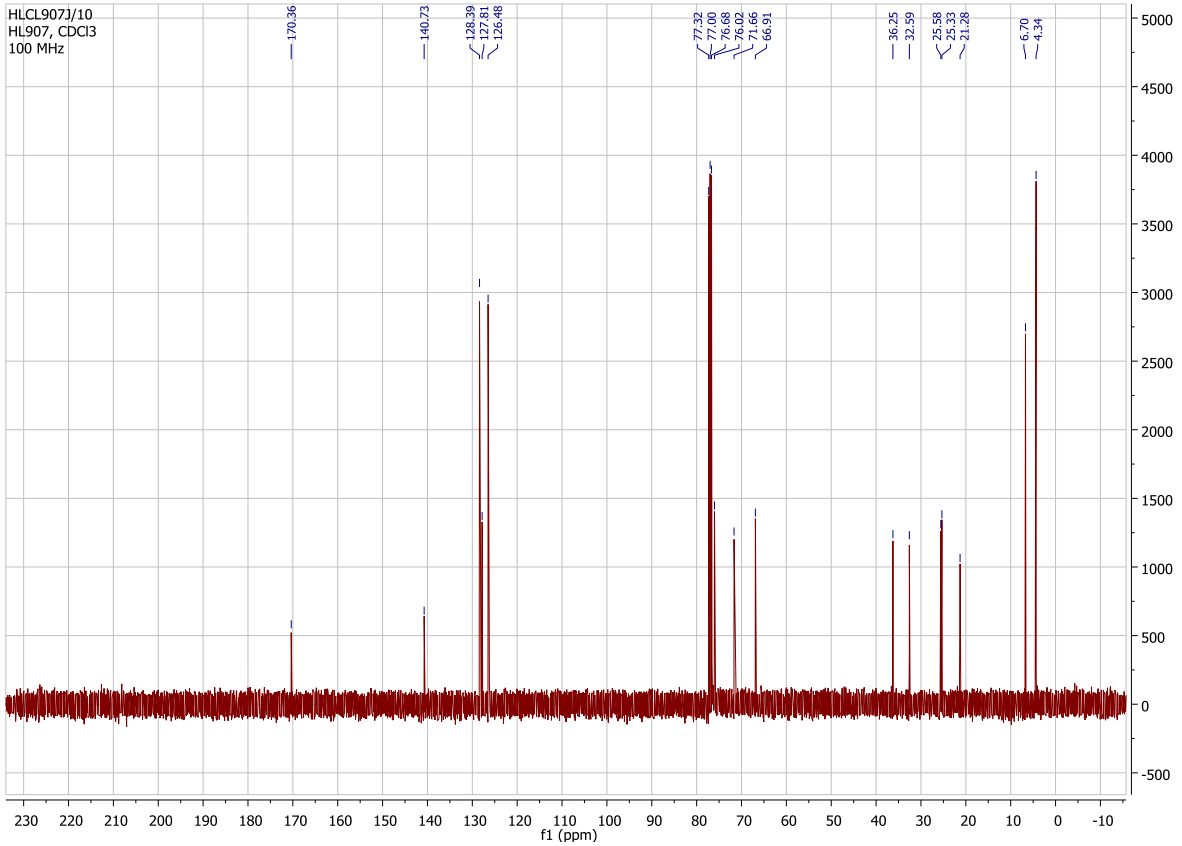
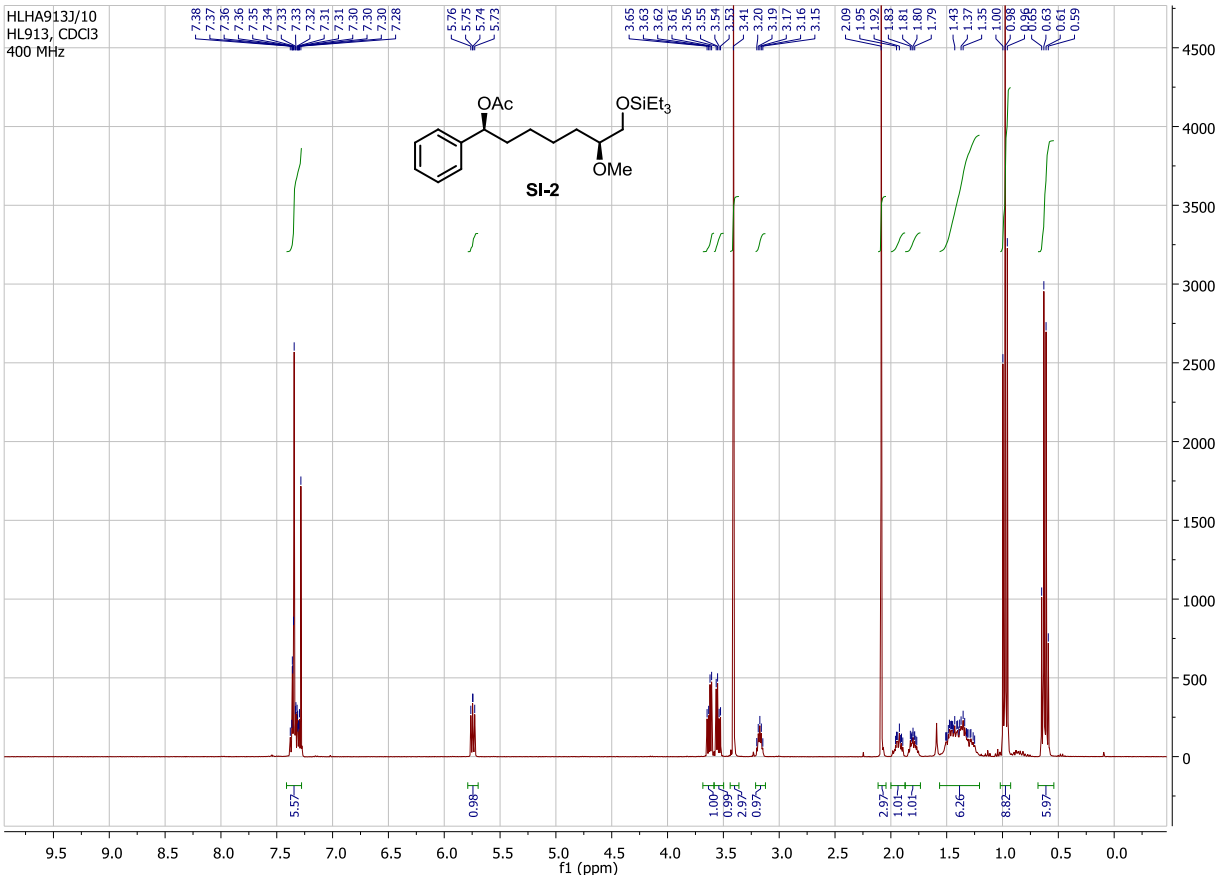
76.68
76.04
36.12
33.51
28.56
24.95
21.28
f1 (ppm)

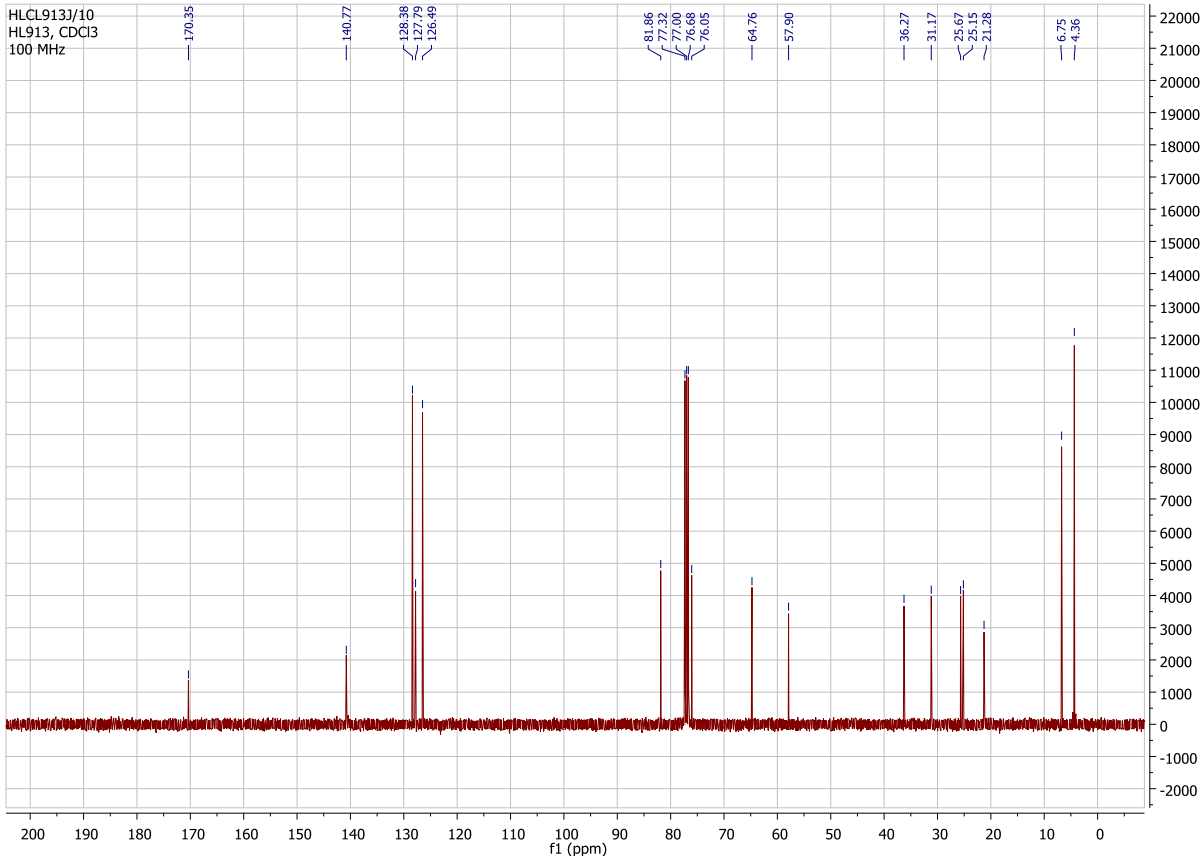

HLHA898J/10
HL898, diol
CDCl3, 400 MHz
OAc
OH
OH
22
f1 (ppm)


HLCL898J/10
HL898, diol
CDCl3, 100 MHz
f1 (ppm)


HLHA907J/10
HL907, CDCl3
400 MHz
OAc
OSiEt3
OH
SI-1
f1 (ppm)


HLCL907J/10
HL907, CDCl3
100 MHz
f1 (ppm)


HLHA913J/10
HL913, CDCl3
400 MHz
OAc
OSiEt3
OMe
SI-2
f1 (ppm)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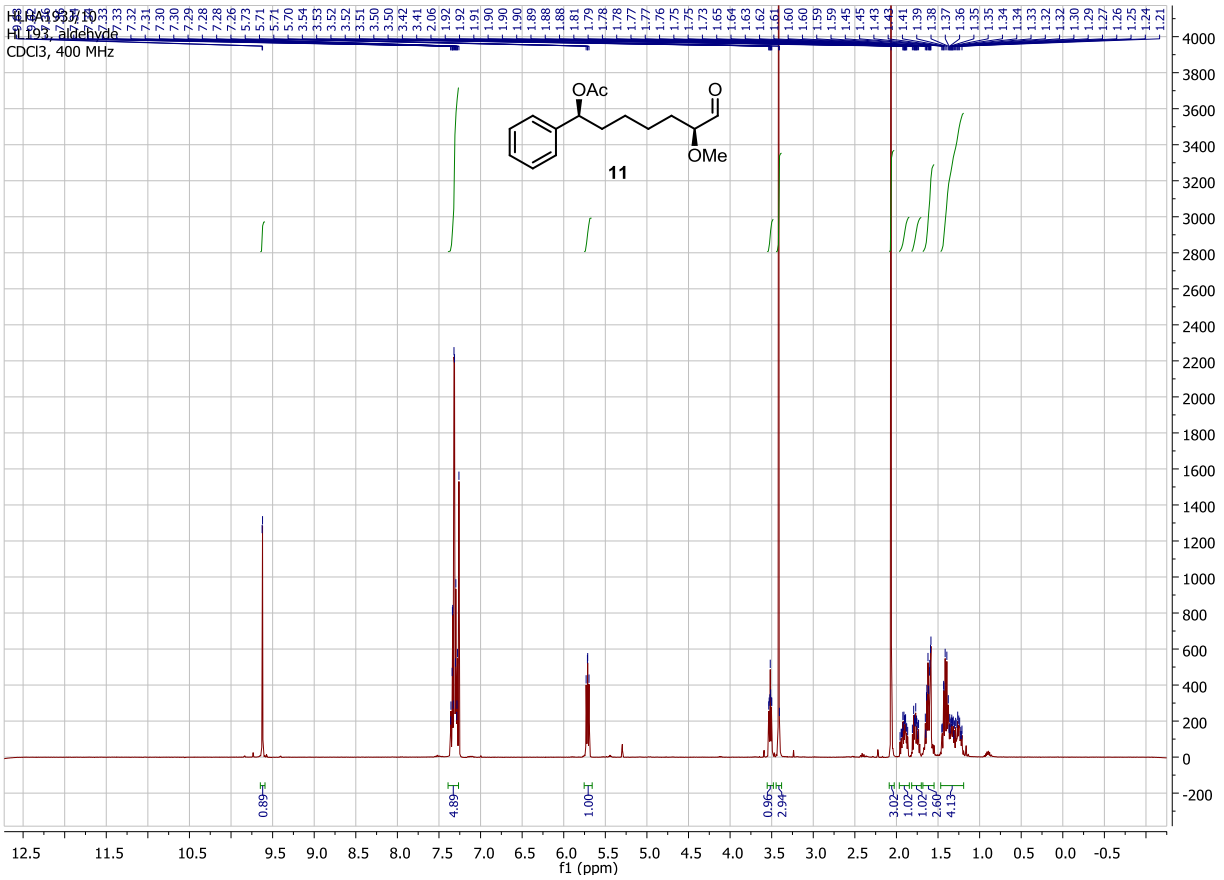
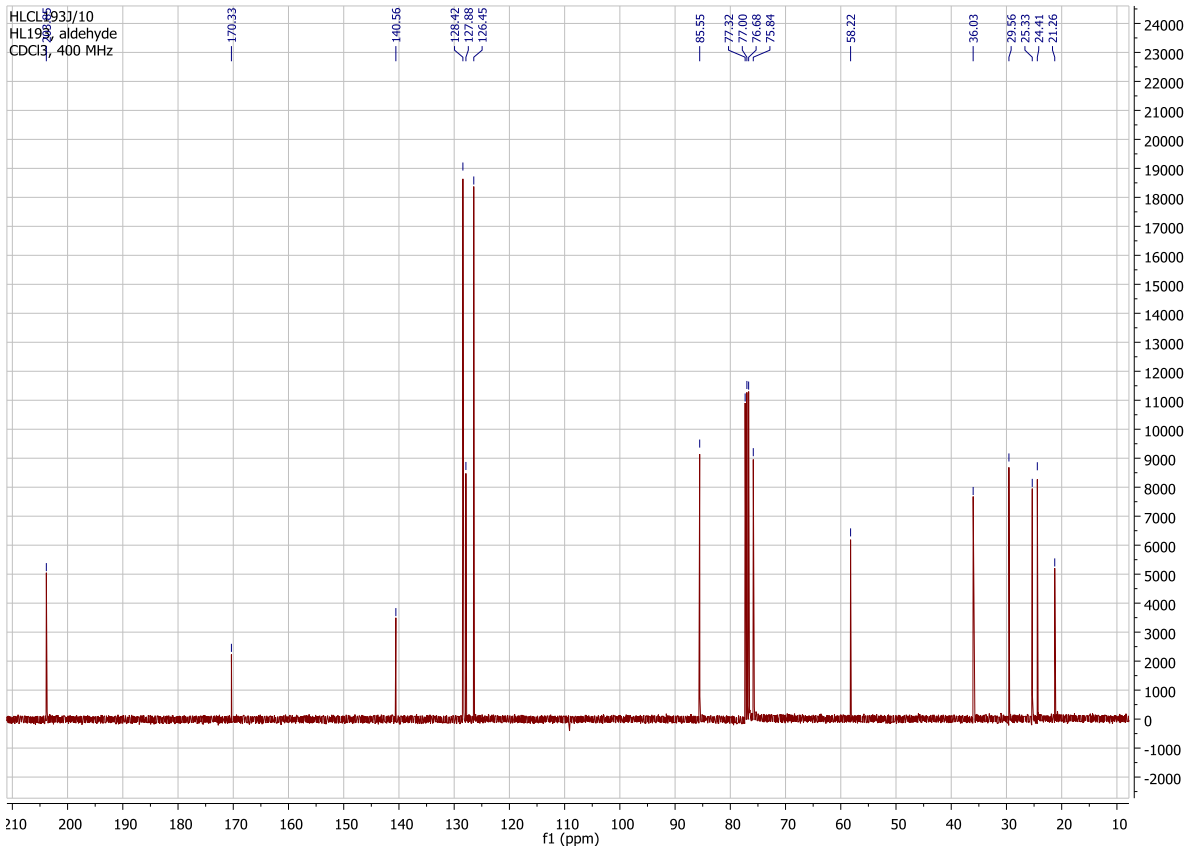
HL913, CDCl3
100 MHz
f1 (ppm)


HLCL193J/10
HL193, aldehyde
CDCl3, 400 MHz
OAc
O
OMe
11
f1 (ppm)


HLCL193J/10
HL193, aldehyde
CDCl3, 400 MHz
170.33
140.56
128.42
127.88
126.45
85.55
77.32
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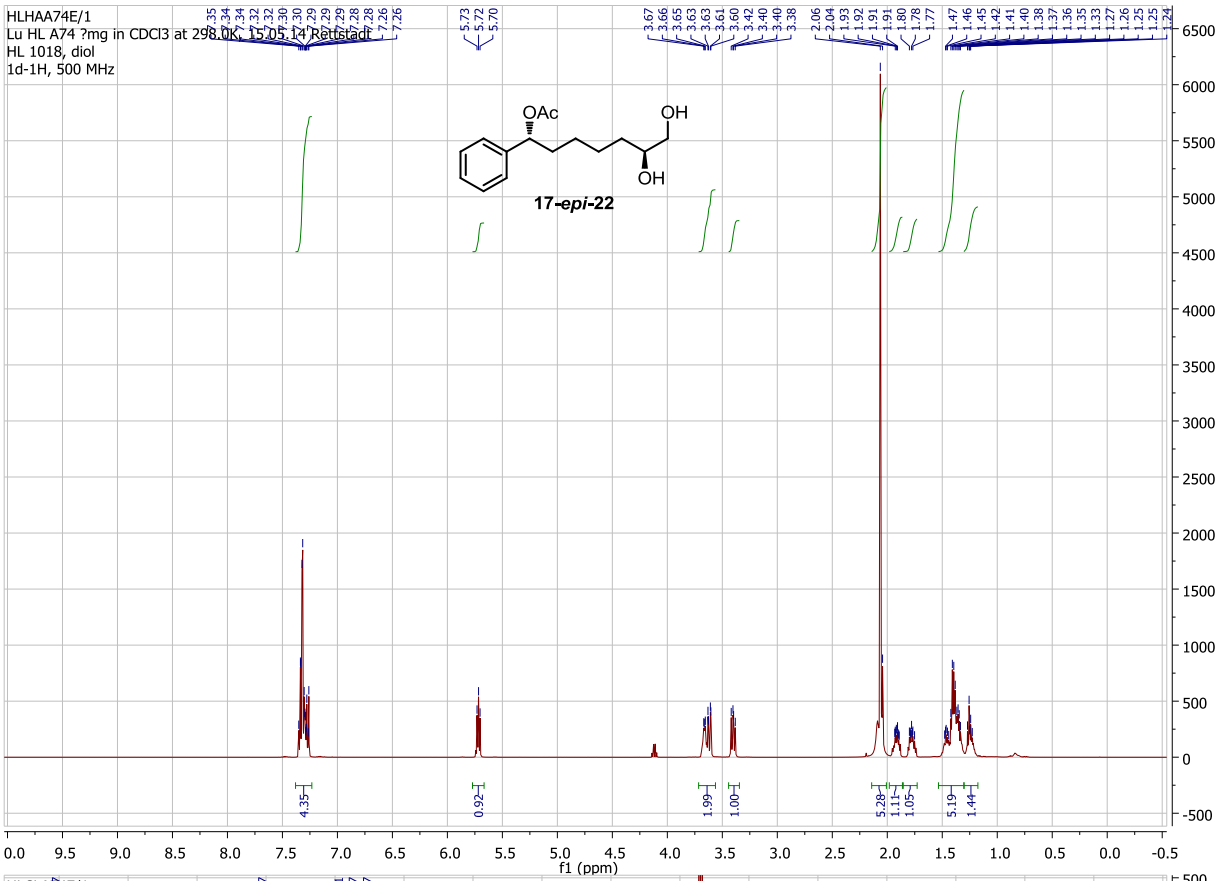
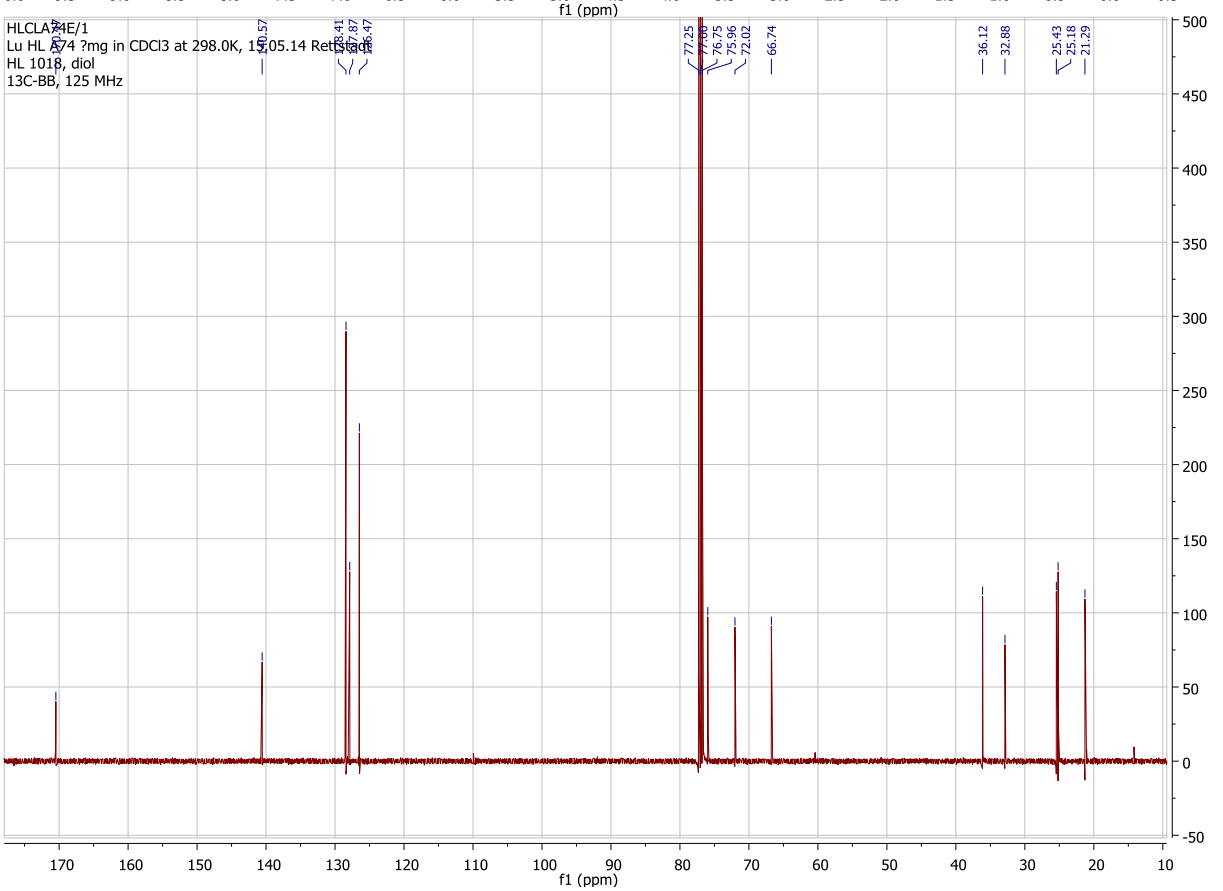
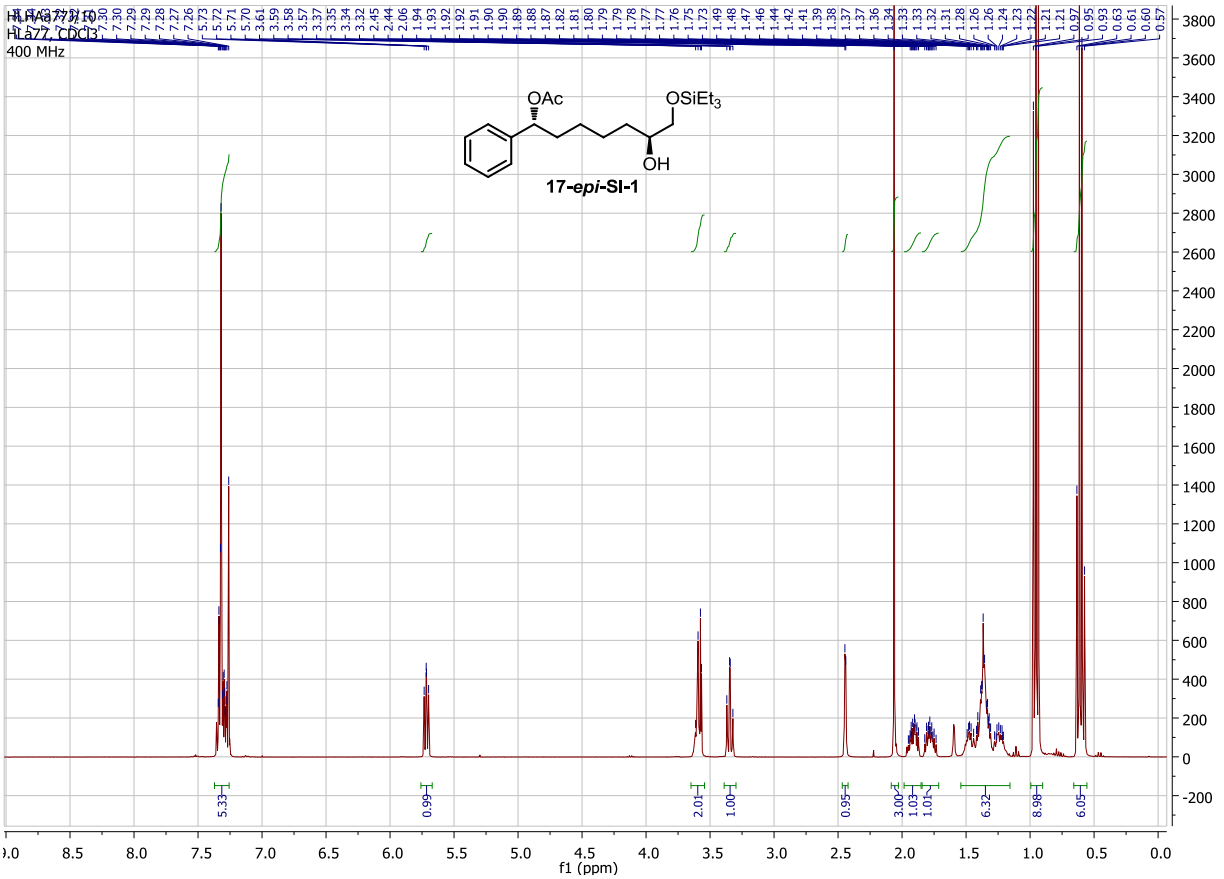
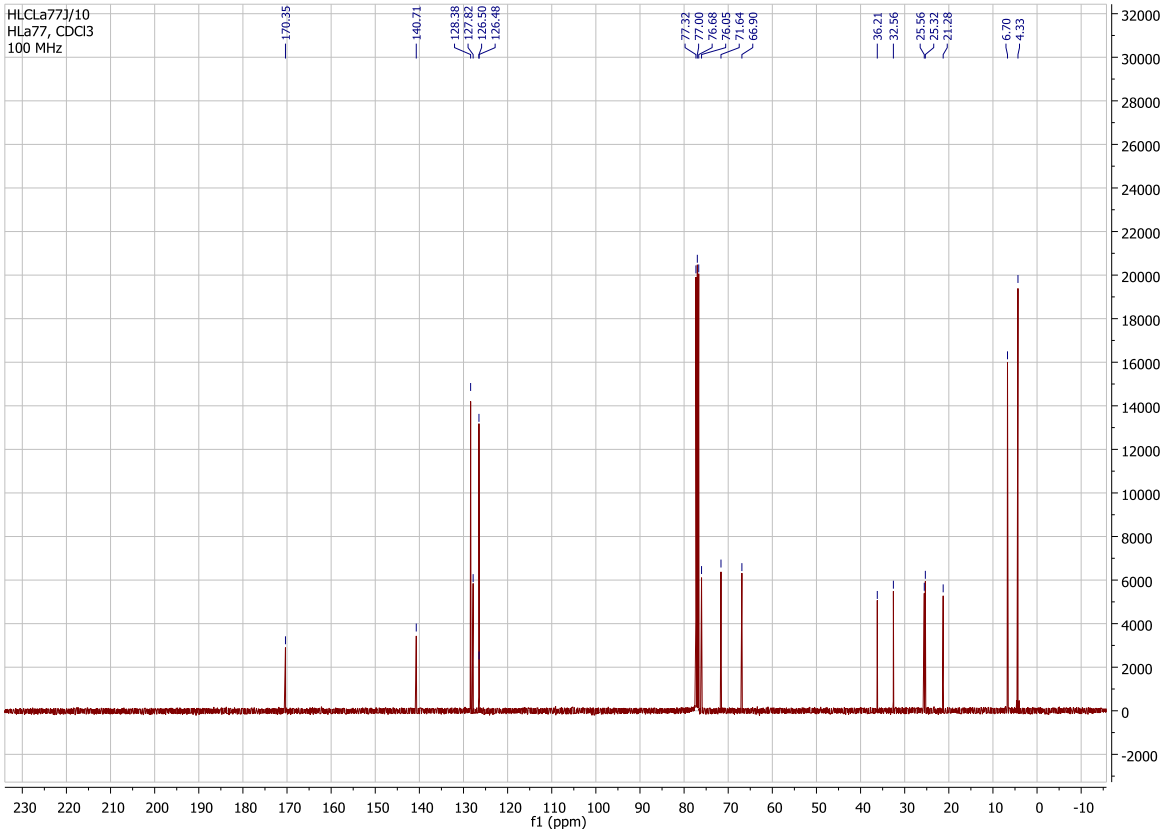
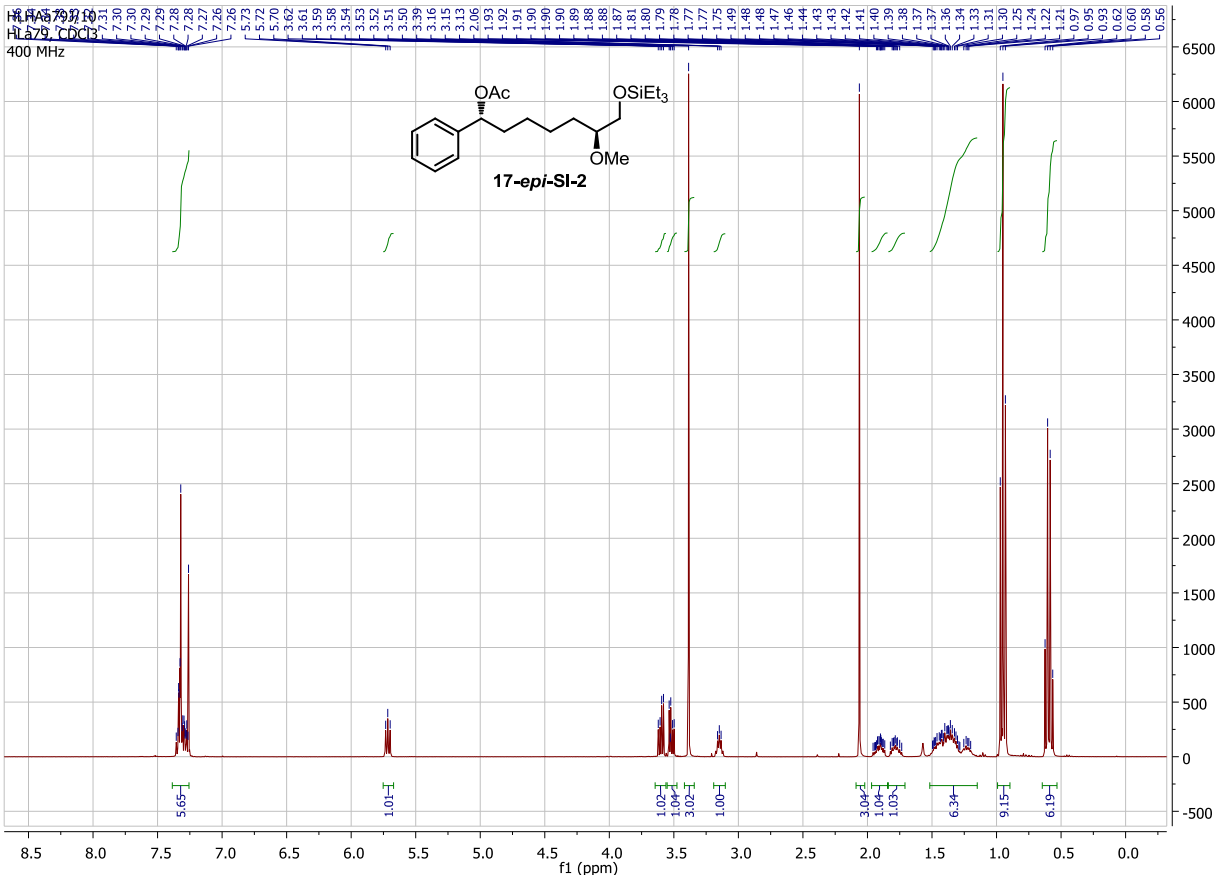
76.68
75.84
58.22
36.03
29.56
25.33
24.41
21.26
f1 (ppm)

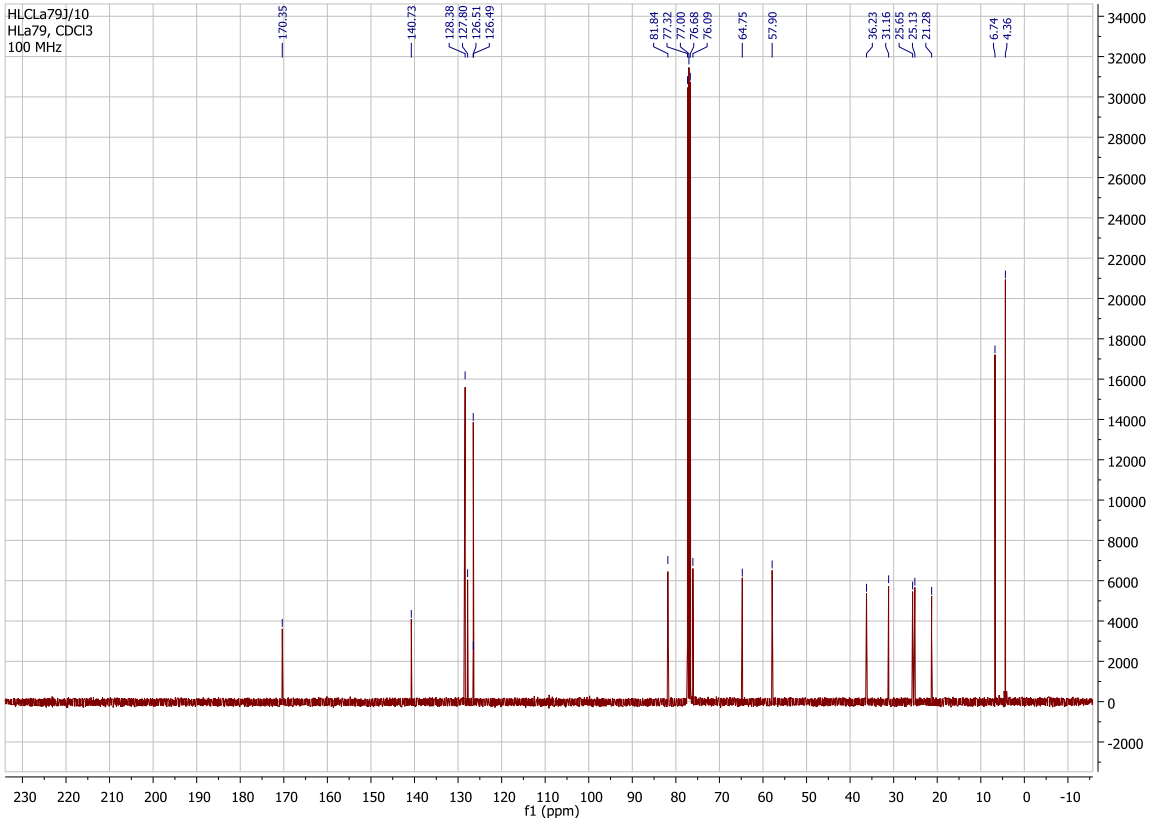

HLHAA74E/1
Lu HL A74 ?mg in CDCl3 at 298.0K, 15.05.14 Rettstadt
HL 1018, diol
1d-1H, 500 MHz
OAc
OH
OH
17-epi-22
f1 (ppm)

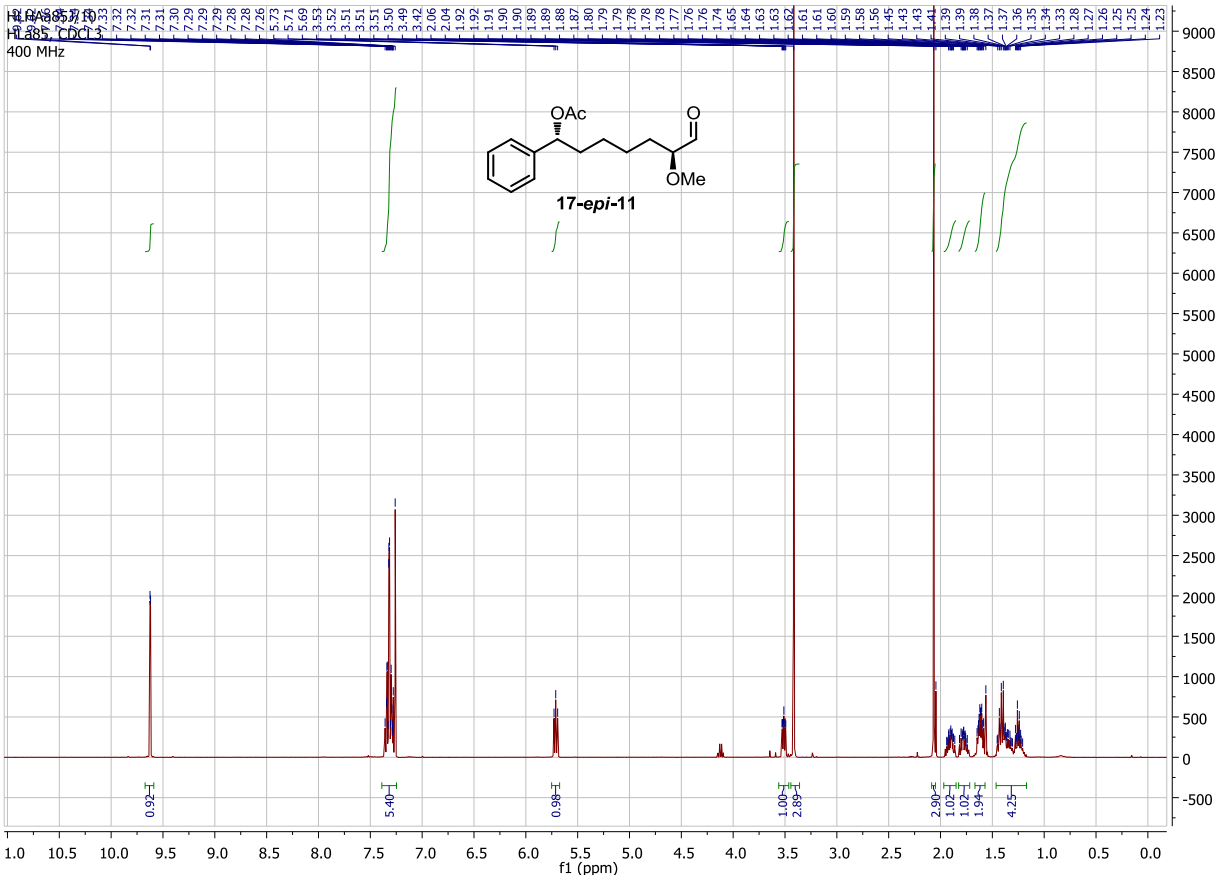

HLCLA74E/1
Lu HL A74 ?mg in CDCl3 at 298.0K, 15.05.14 Rettstadt
HL 1018, diol
13C-BB, 125 MHz
f1 (ppm)

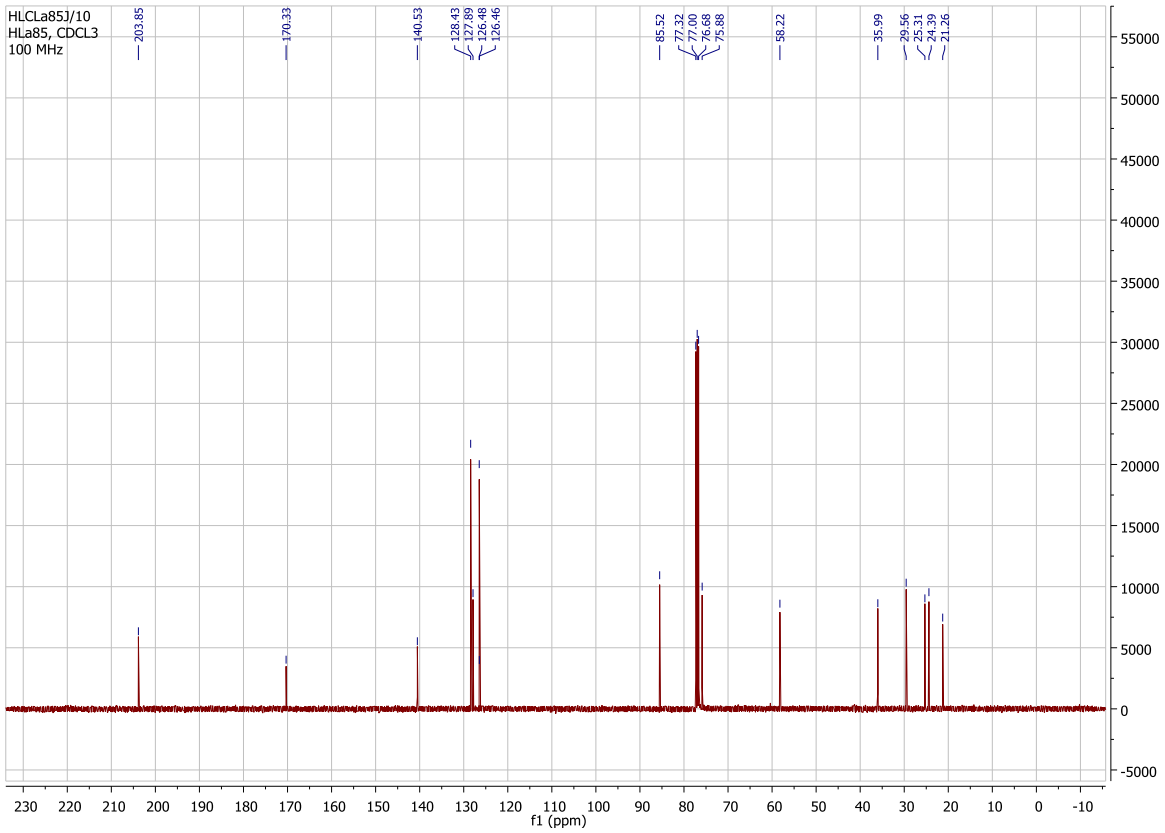

HLCLa77J/10
HLa77, CDCl3
400 MHz
OAc
OSiEt3
OH
17-epi-SI-1
f1 (ppm)

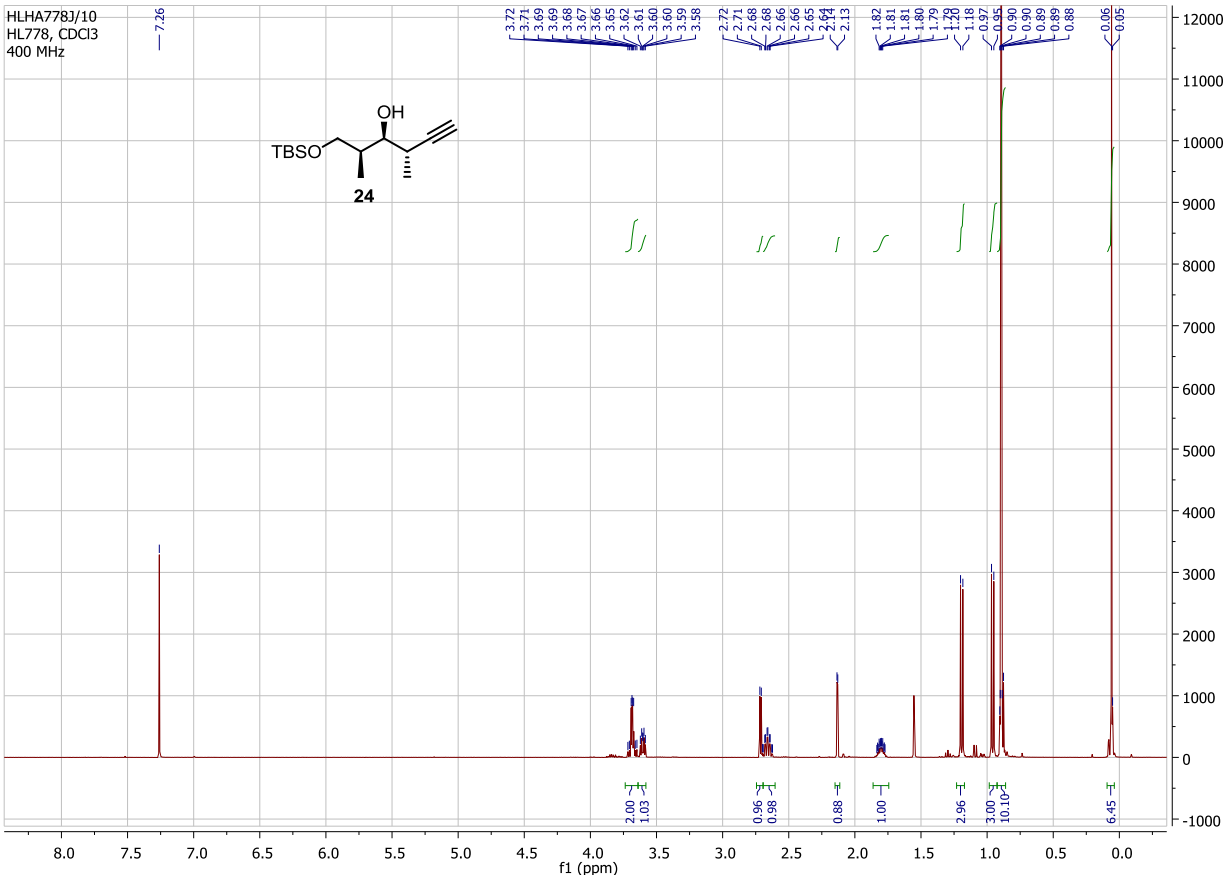

HLCLa77J/10
HLa77, CDCl3
100 MHz
170.35
140.71
128.38
127.82
126.50
126.48
77.32
77.00
76.68
76.05
71.64
66.90
36.21
32.56
25.56
25.32
21.28
6.70
4.33
f1 (ppm)

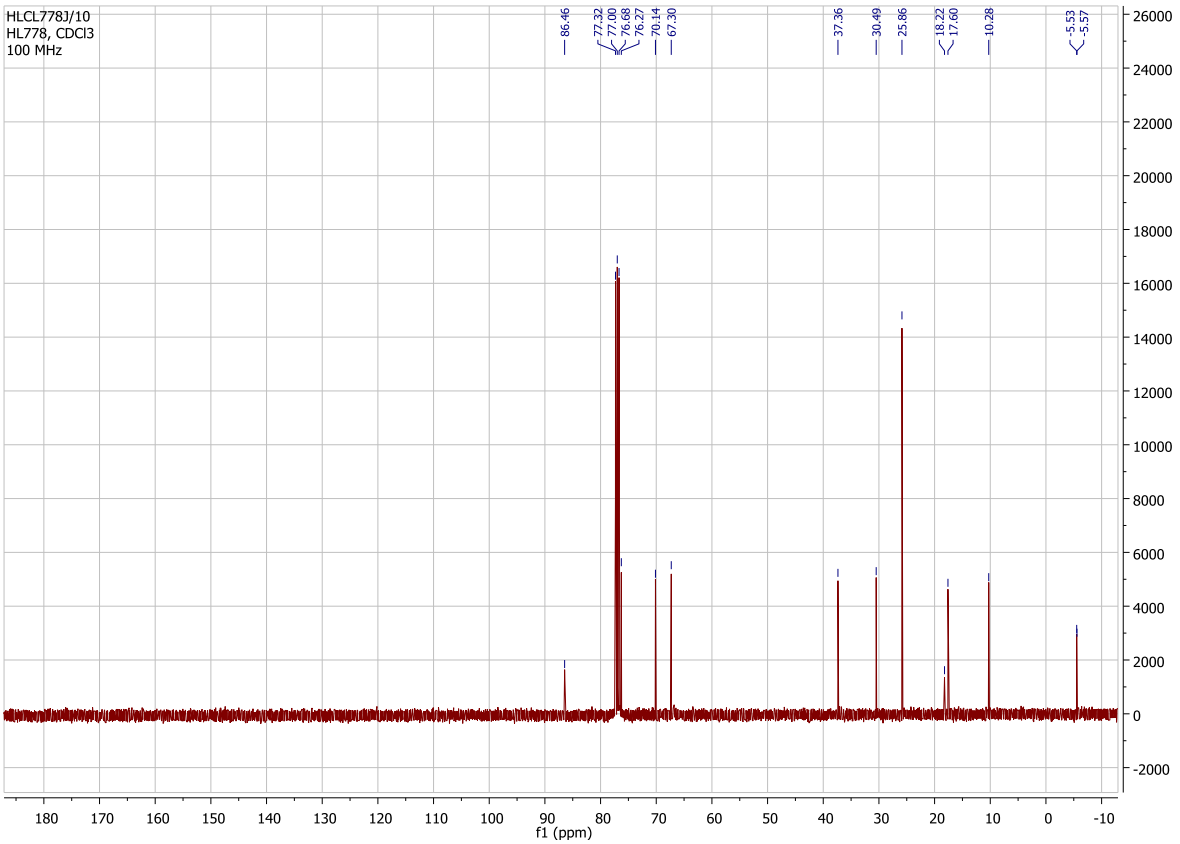

HLCLa79J/10
HLa79, CDCl3
400 MHz
OAc
OSiEt3
OMe
17-epi-SI-2
f1 (ppm)

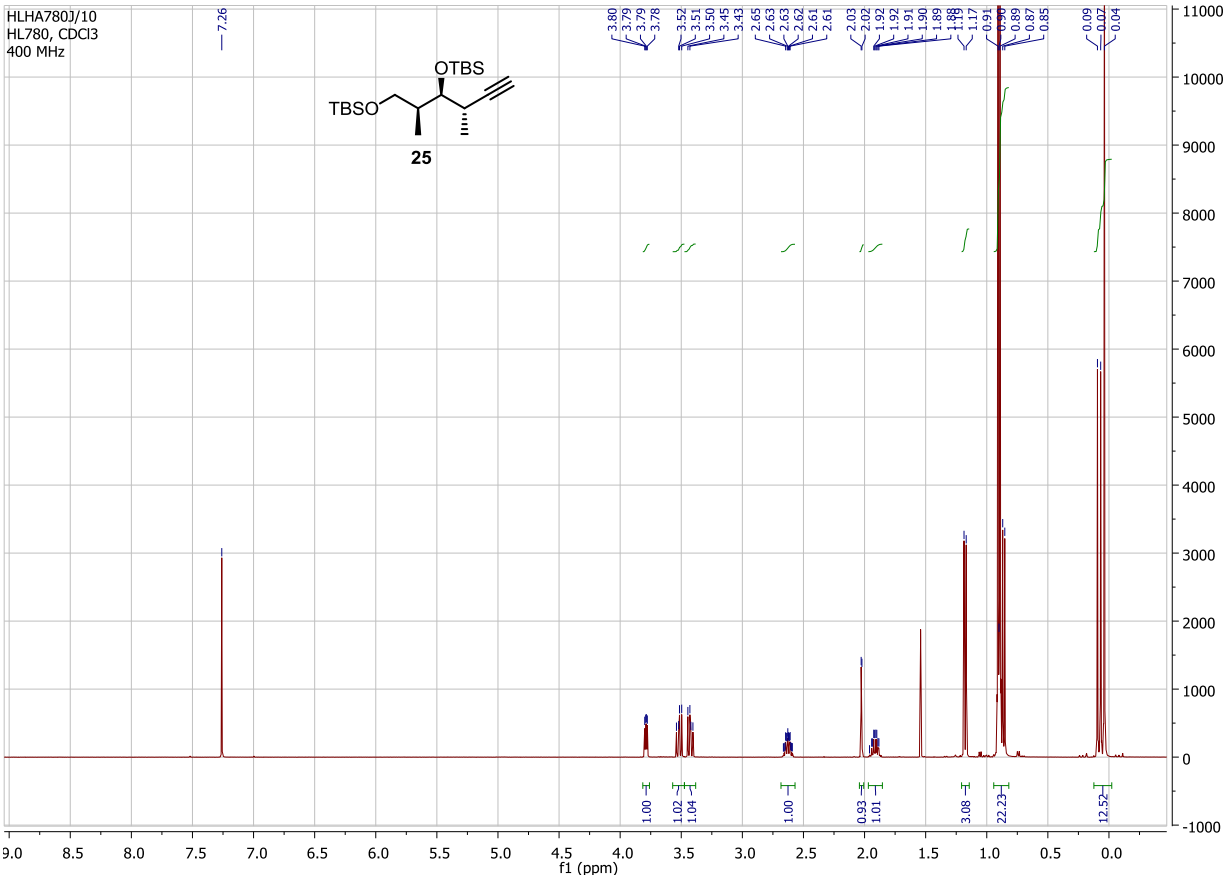

HLCLa79J/10
HLa79, CDCl3
100 MHz
f1 (ppm)

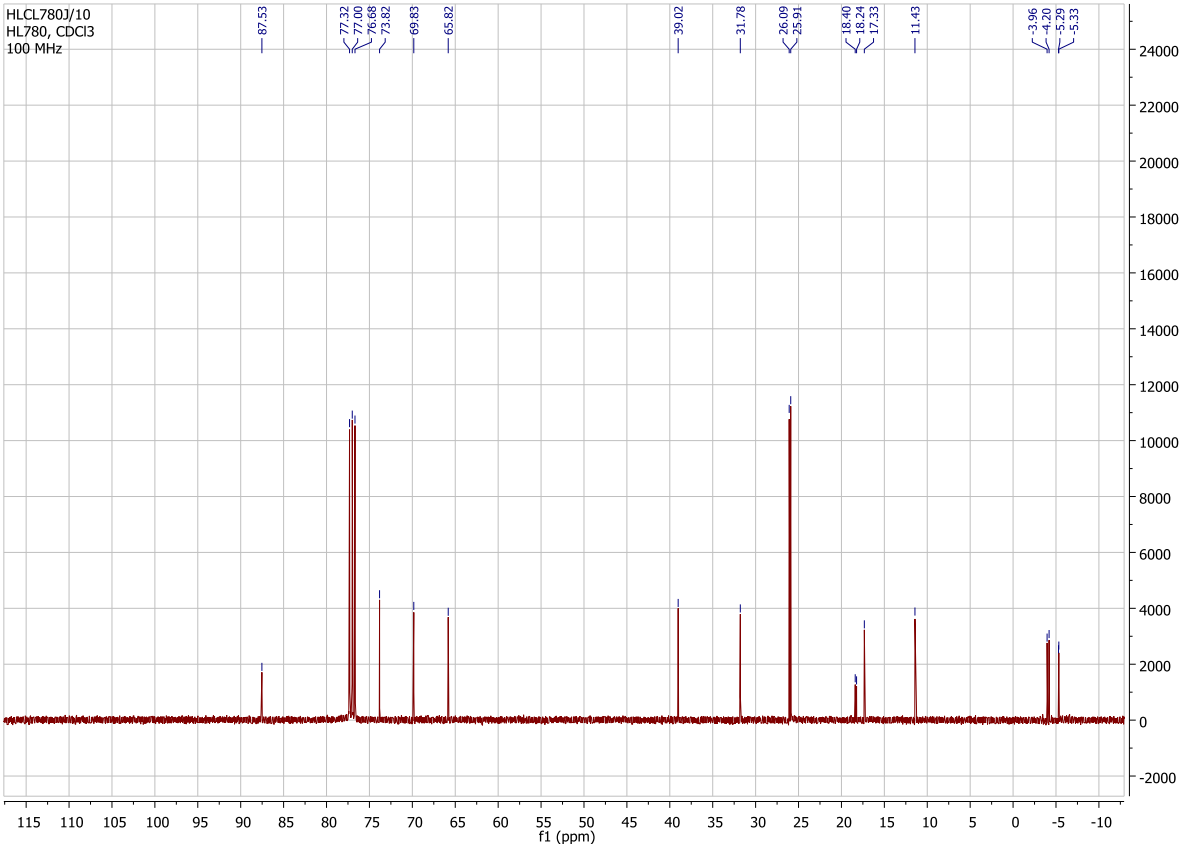

HLCLa85J/10
HLa85, CDCL3
400 MHz
OAc
O
OMe
17-epi-11
f1 (ppm)

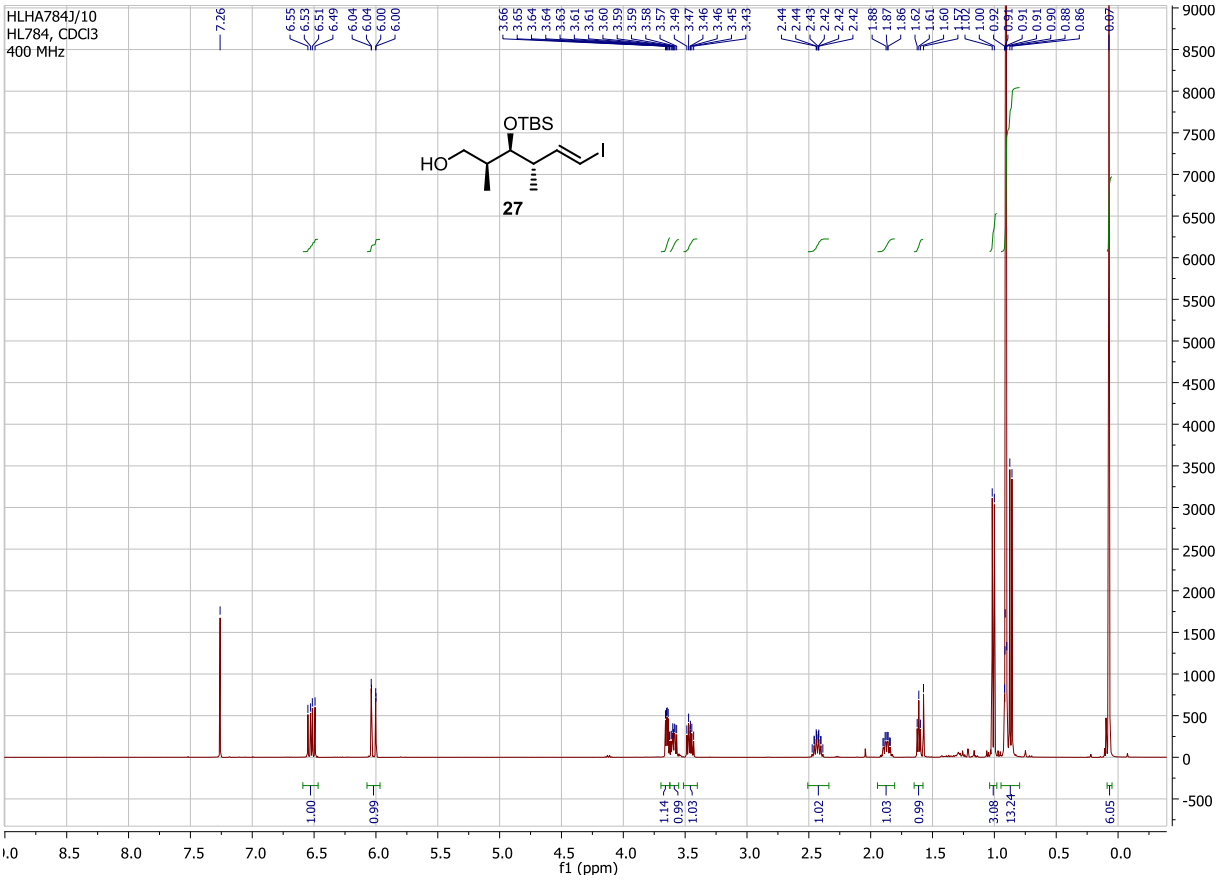

HLCLa85J/10
HLa85, CDCL3
100 MHz
f1 (ppm)

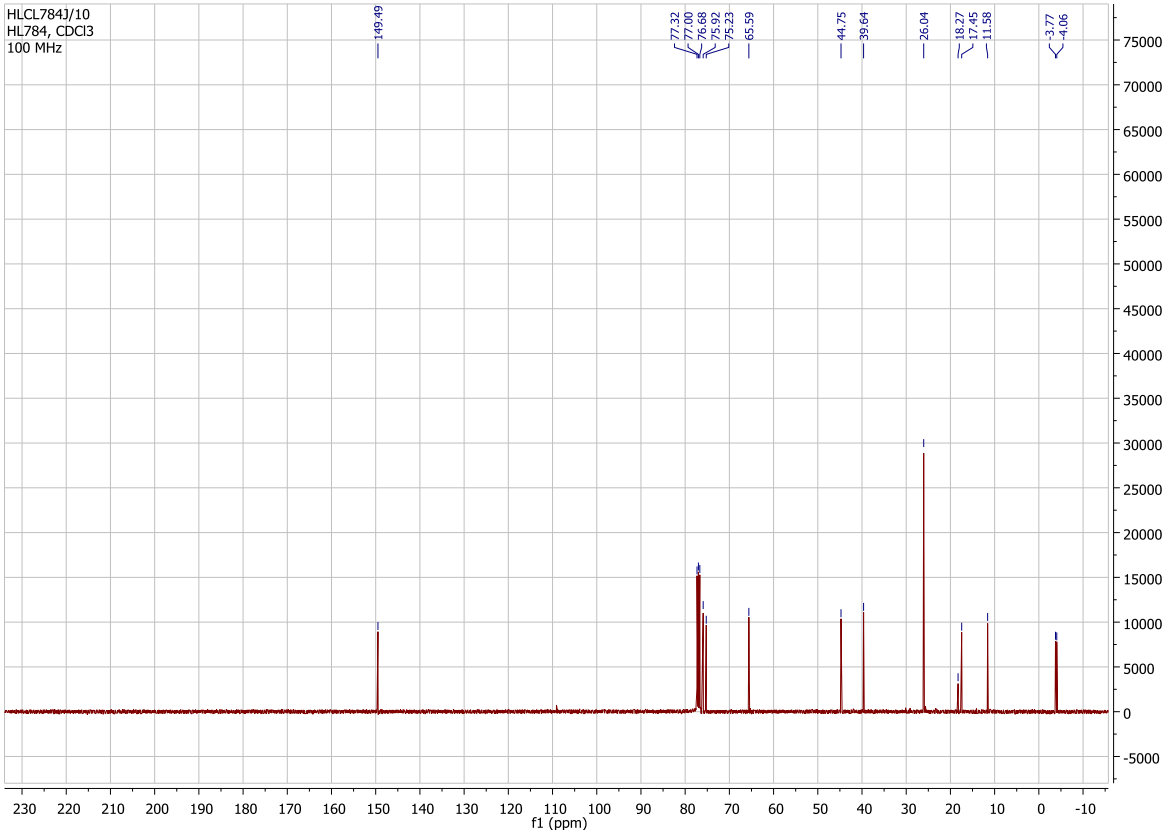

HLHA778J/10
HL778, CDCl3
400 MHz
OH
TBSO
24
f1 (ppm)

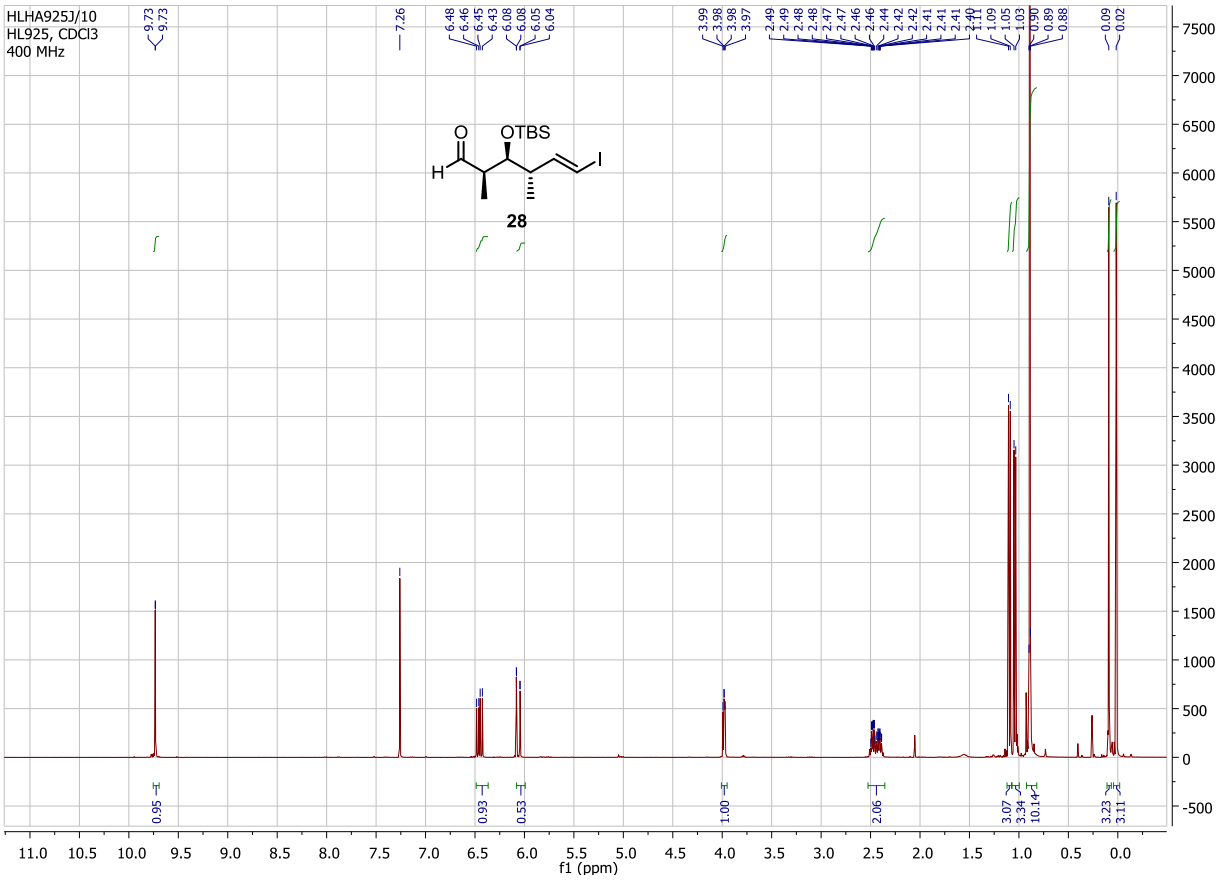

HLCL778J/10
HL778, CDCl3
100 MHz
f1 (ppm)

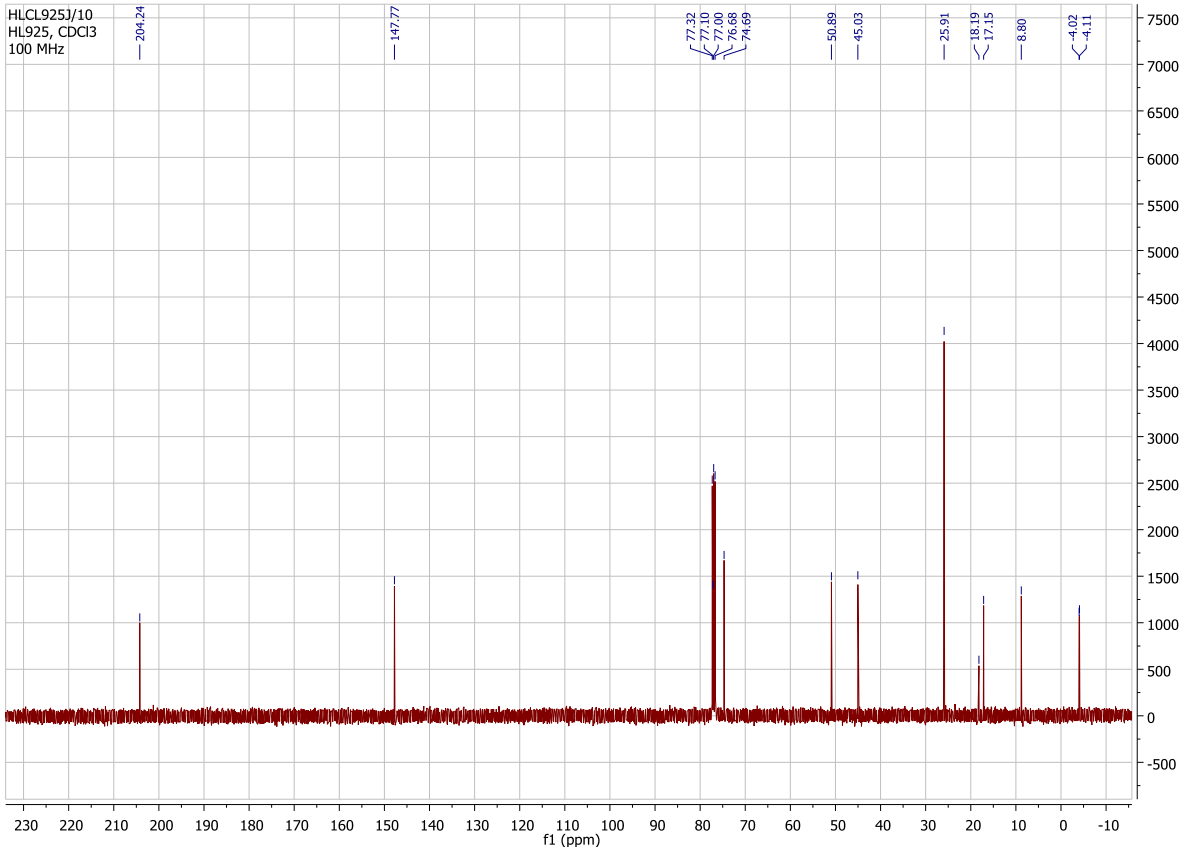

HLHA780J/10
HL780, CDCl3
400 MHz
OTBS
TBSO
25
f1 (ppm)

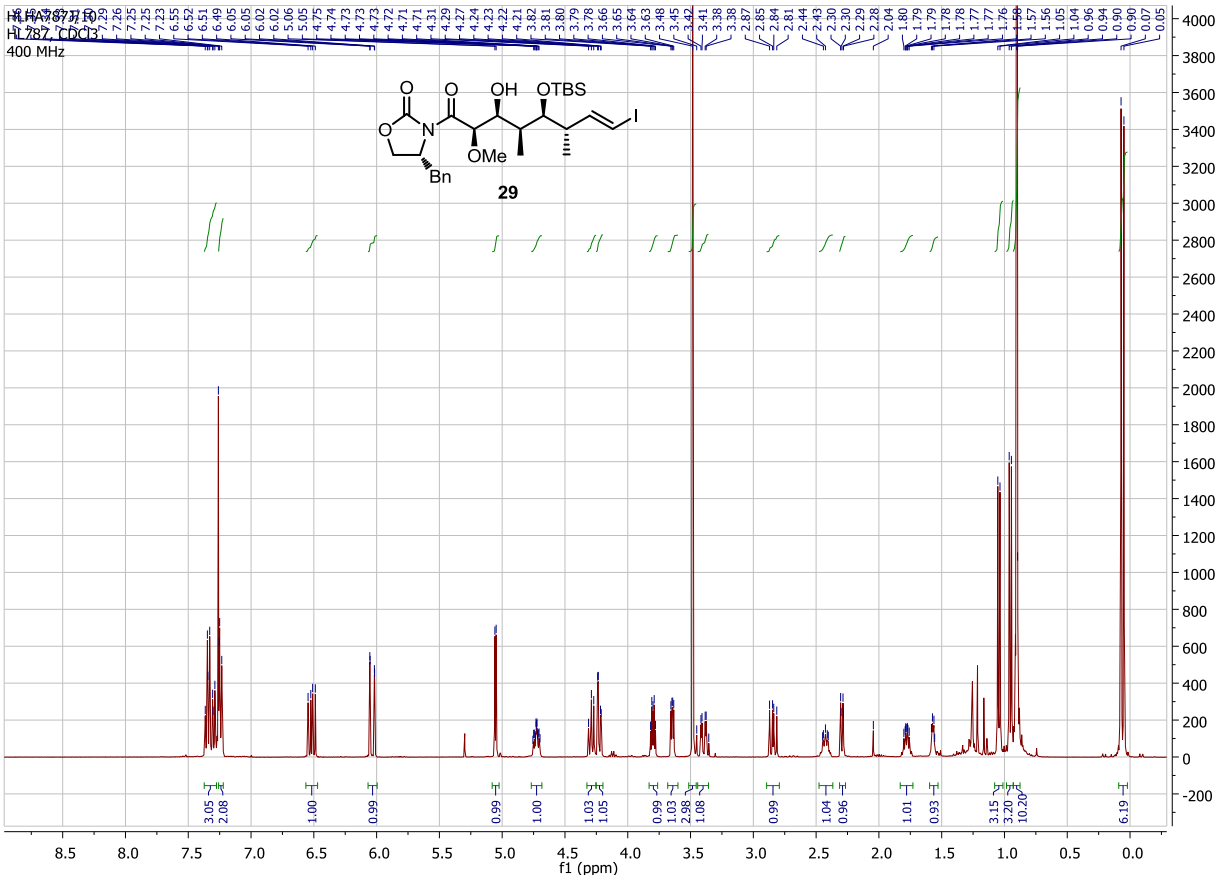

HLCL780J/10
HL780, CDCl3
100 MHz
f1 (ppm)

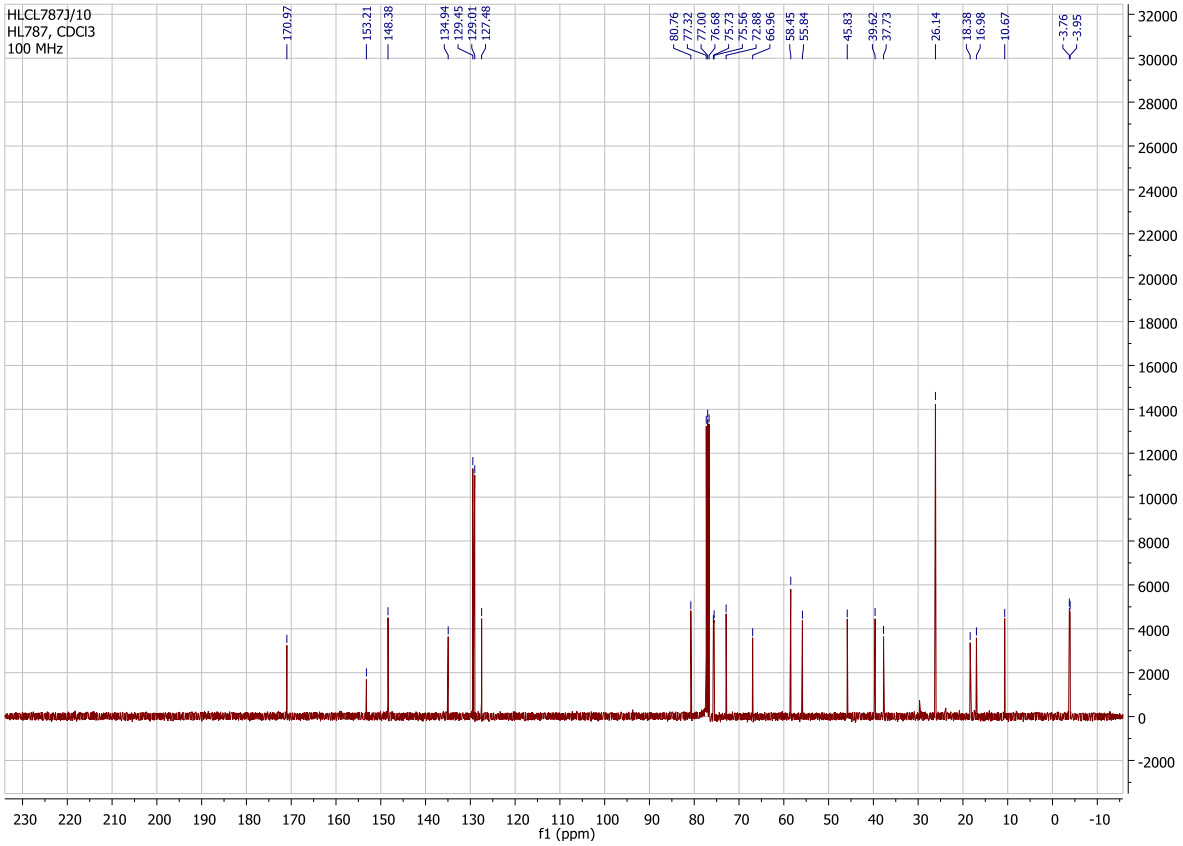

HLHA784J/10
HL784, CDCl3
400 MHz
OTBS
HO
I
27
f1 (ppm)

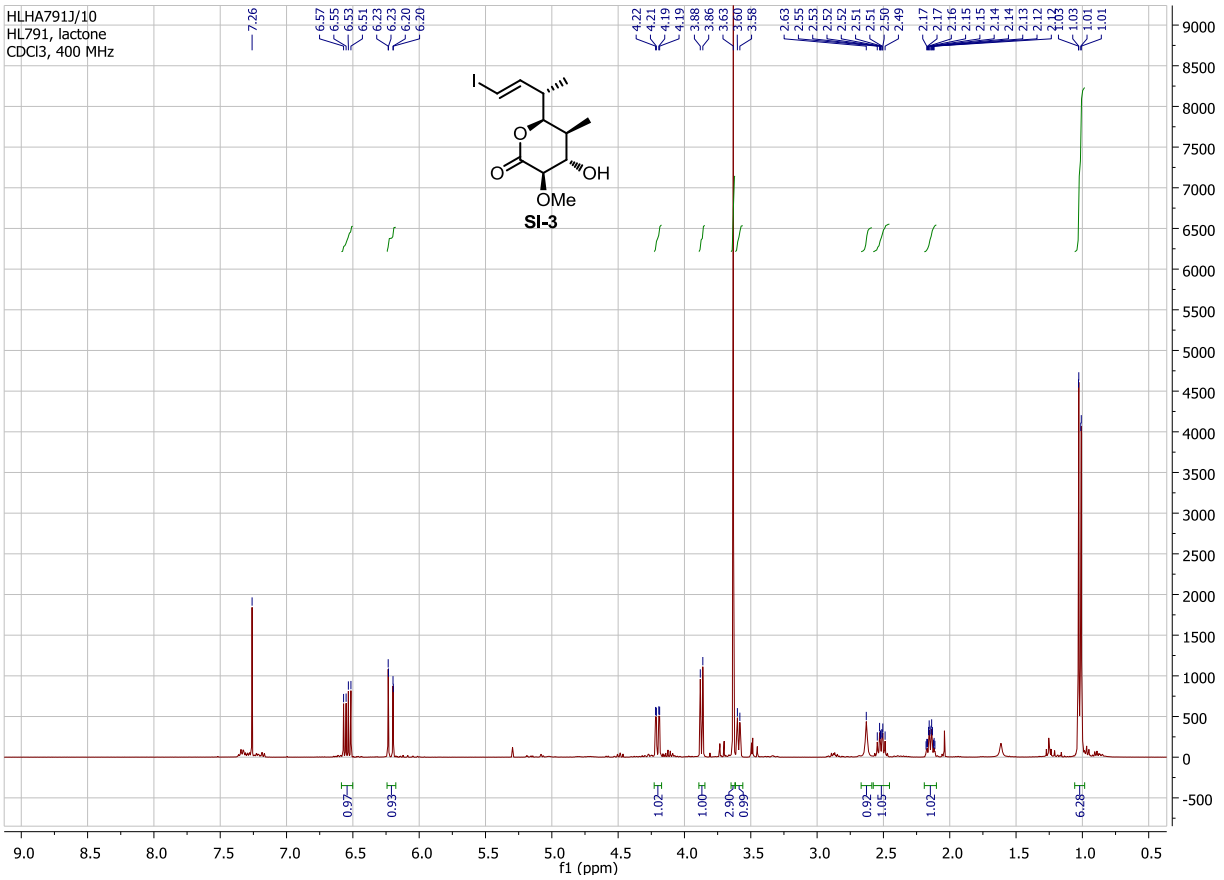

HLCL784J/10
HL784, CDCl3
100 MHz
f1 (ppm)

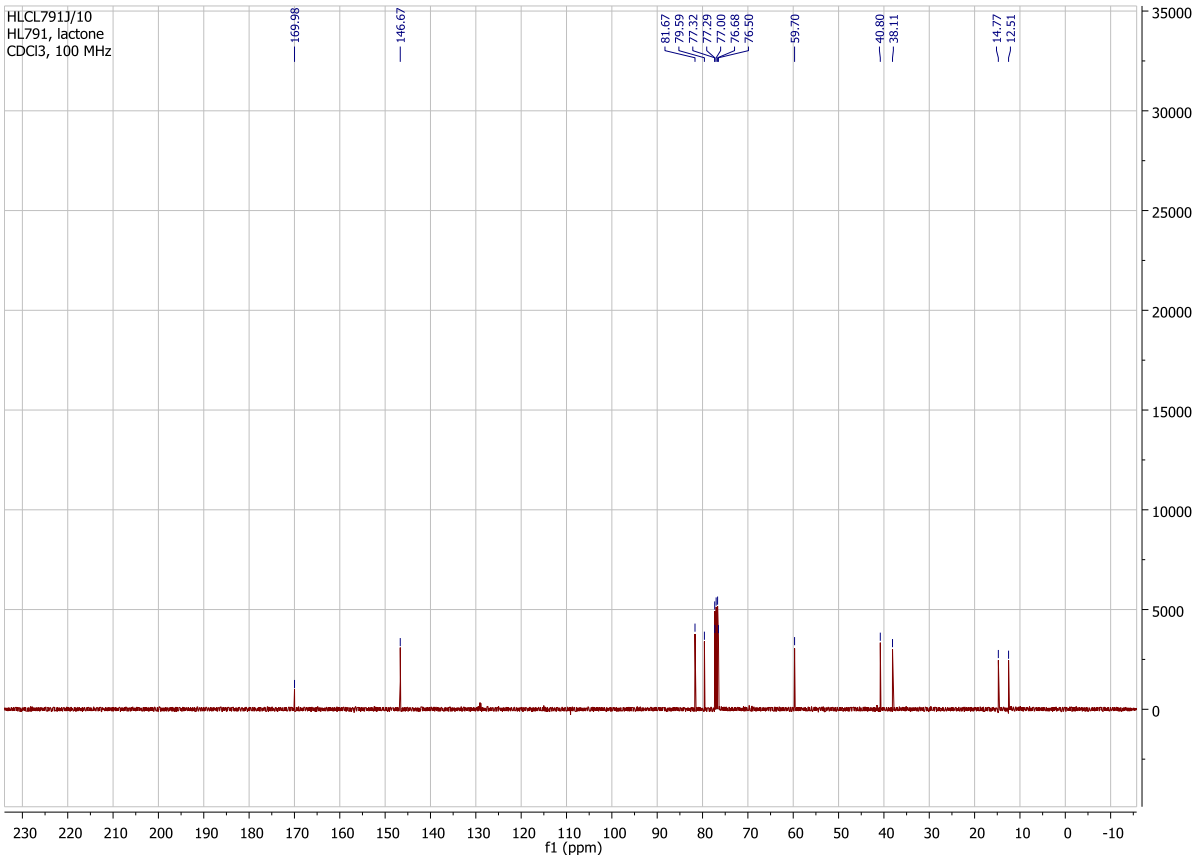

HLHA925J/10
HL925, CDCl3
400 MHz
O
OTBS
H
I
28
f1 (ppm)

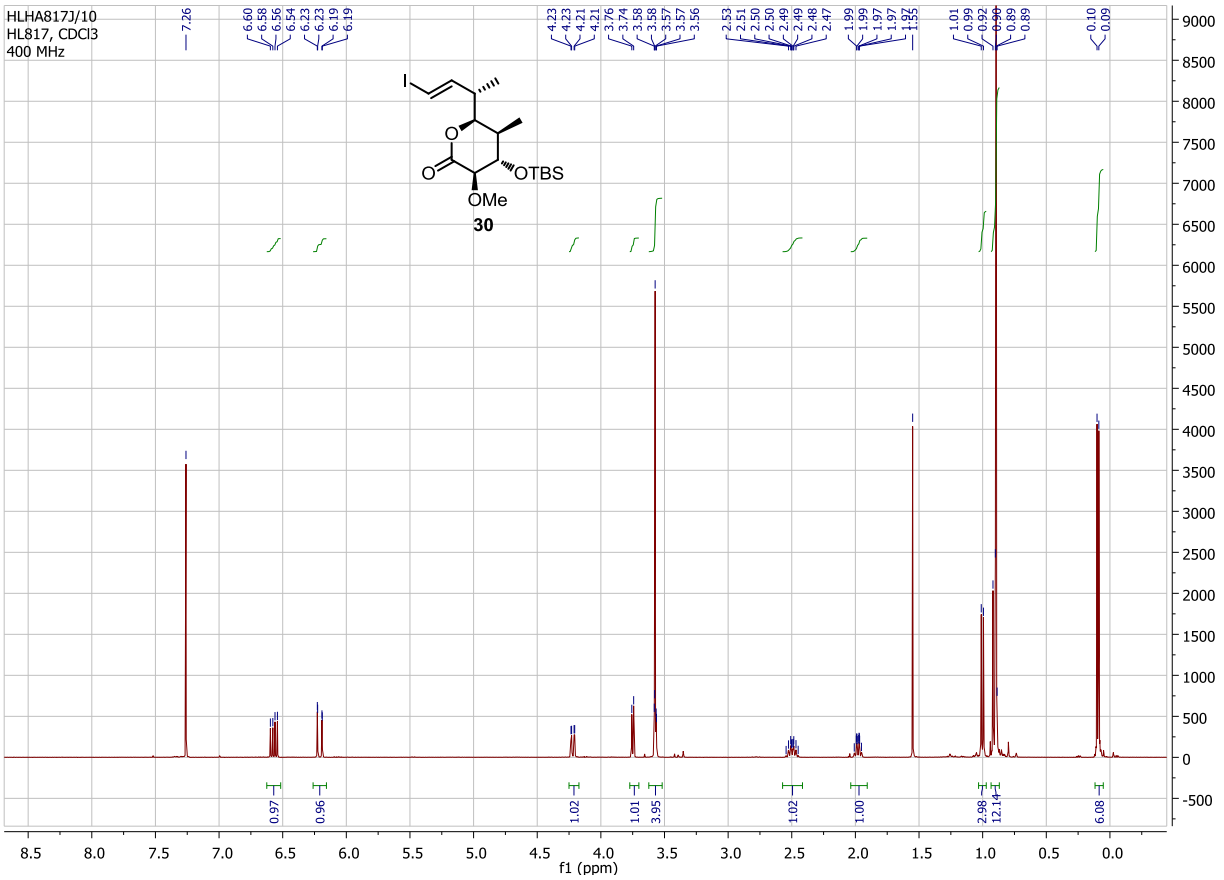

HLCL925J/10
HL925, CDCl3
100 MHz
f1 (ppm)

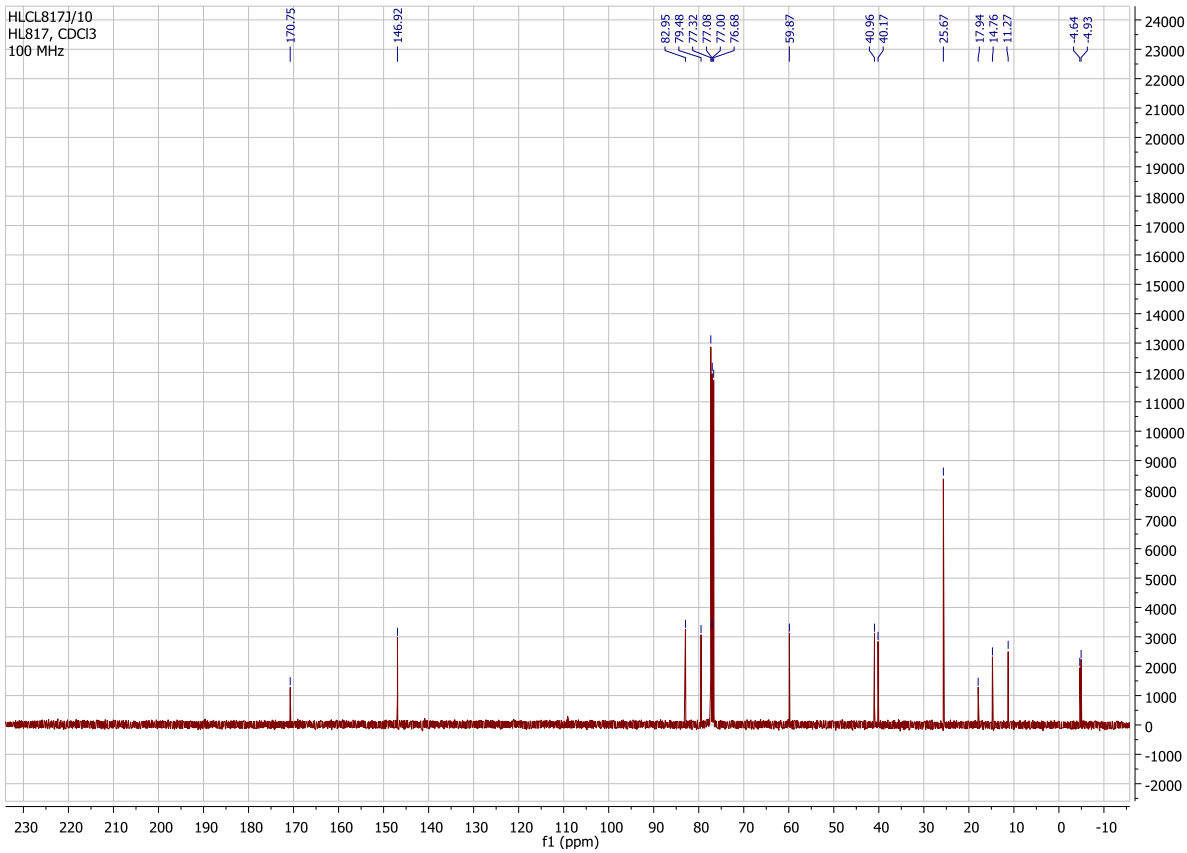

HLHA787J/10
HL787, CDCl3
400 MHz
O
O
OH
OTBS
N
O
OMe
Bn
I
29
f1 (ppm)

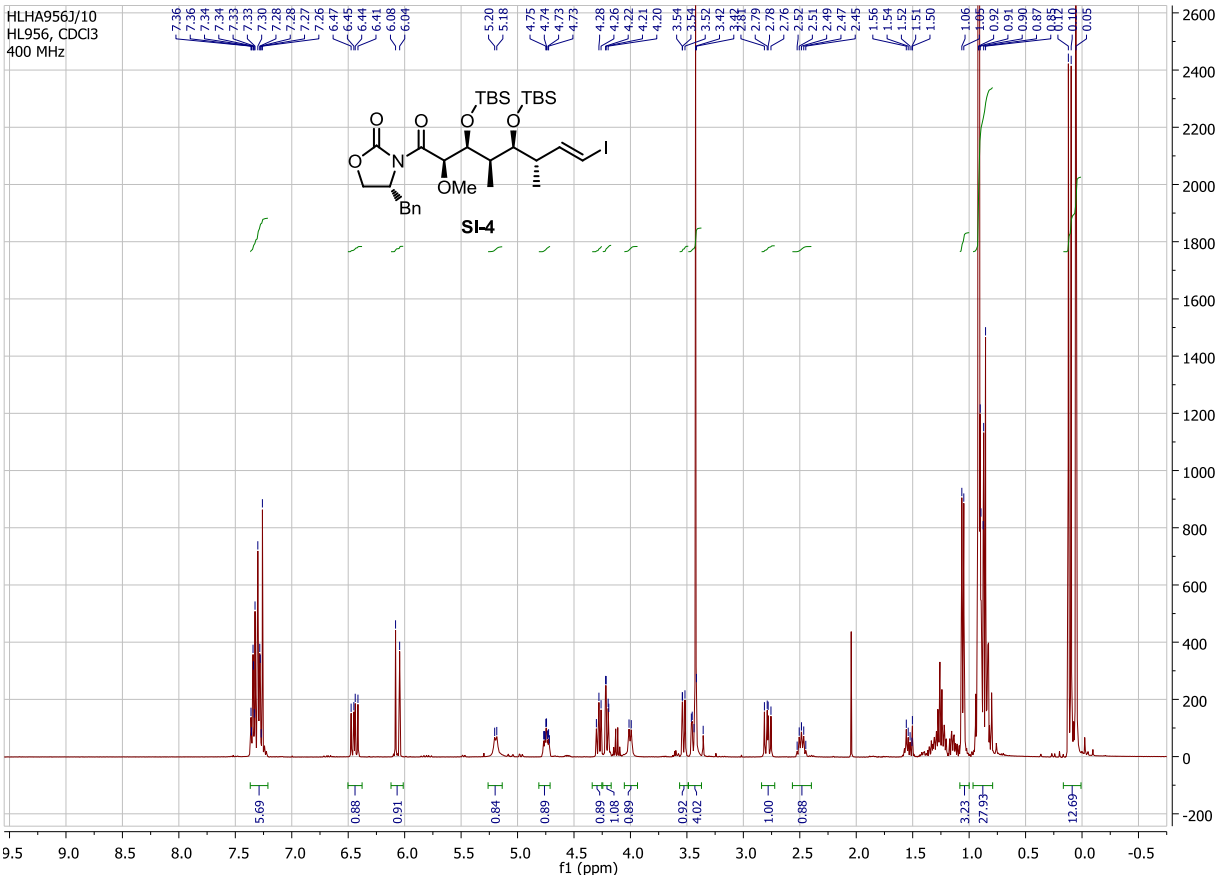

HLCL787J/10
HL787, CDCl3
100 MHz
f1 (ppm)

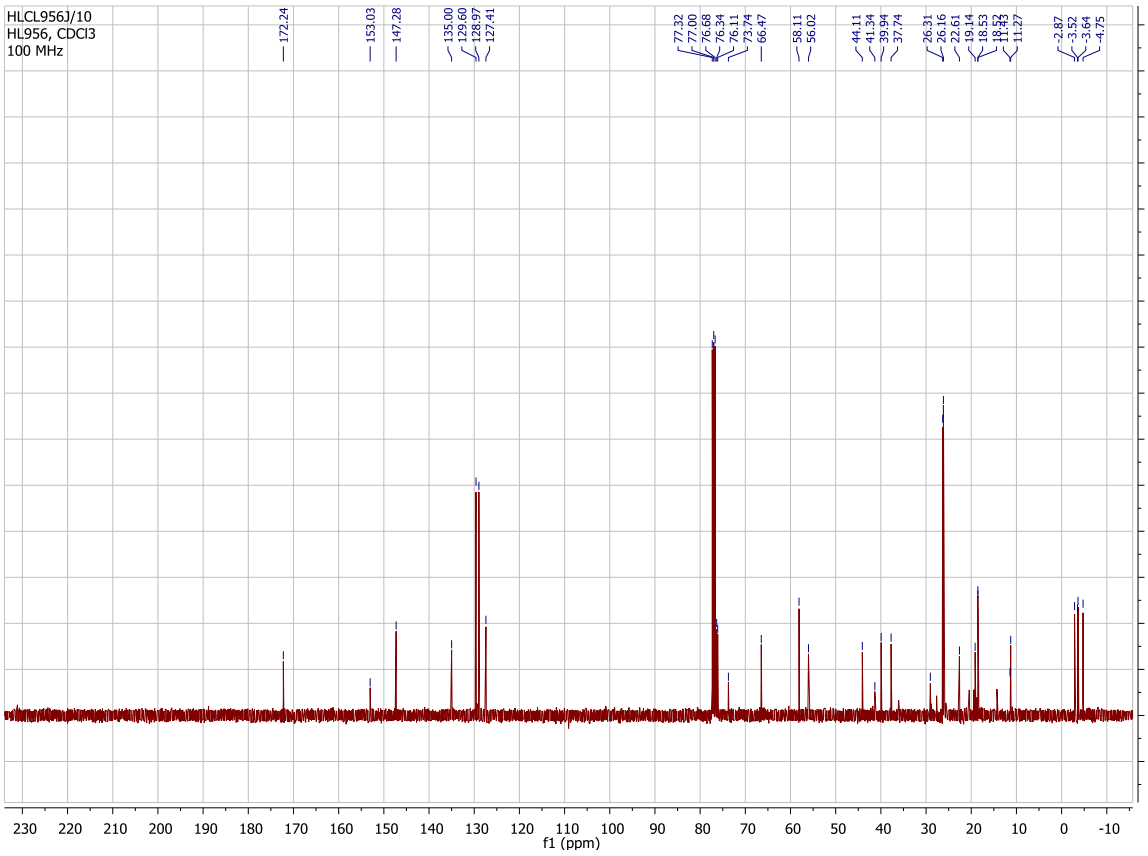

HLHA791J/10
HL791, lactone
CDCl3, 400 MHz
SI-3
f1 (ppm)

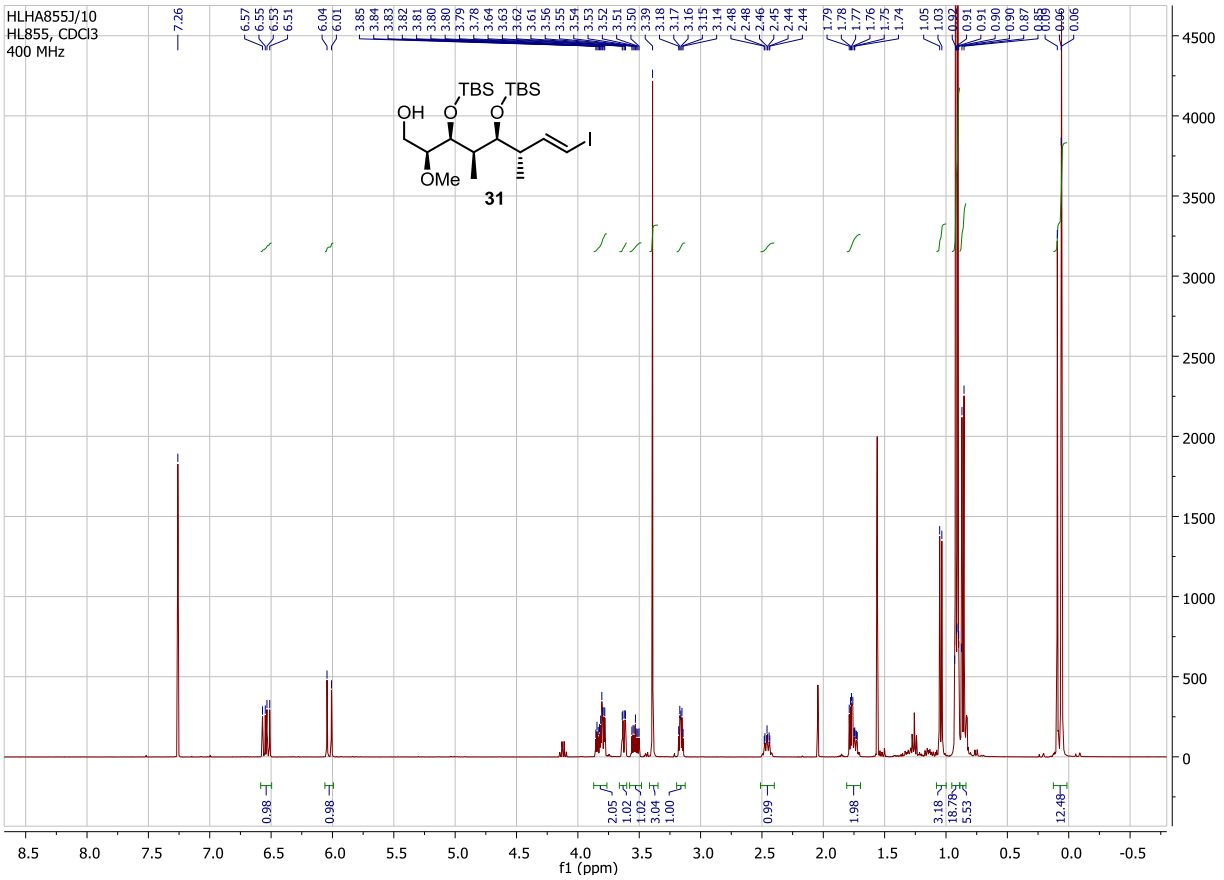

HLCL791J/10
HL791, lactone
CDCl3, 100 MHz
f1 (ppm)

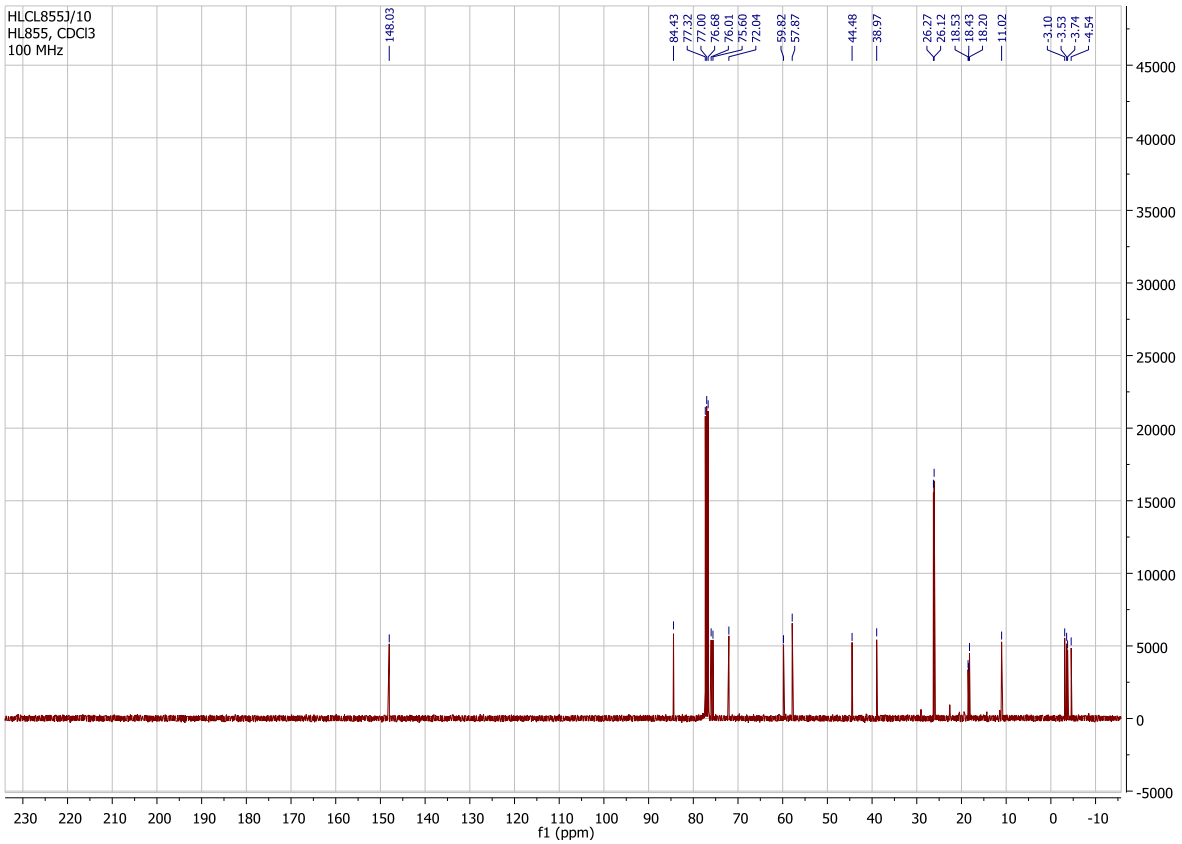

HLHA817J/10
HL817, CDCl3
400 MHz
OTBS
OMe
30
f1 (ppm)

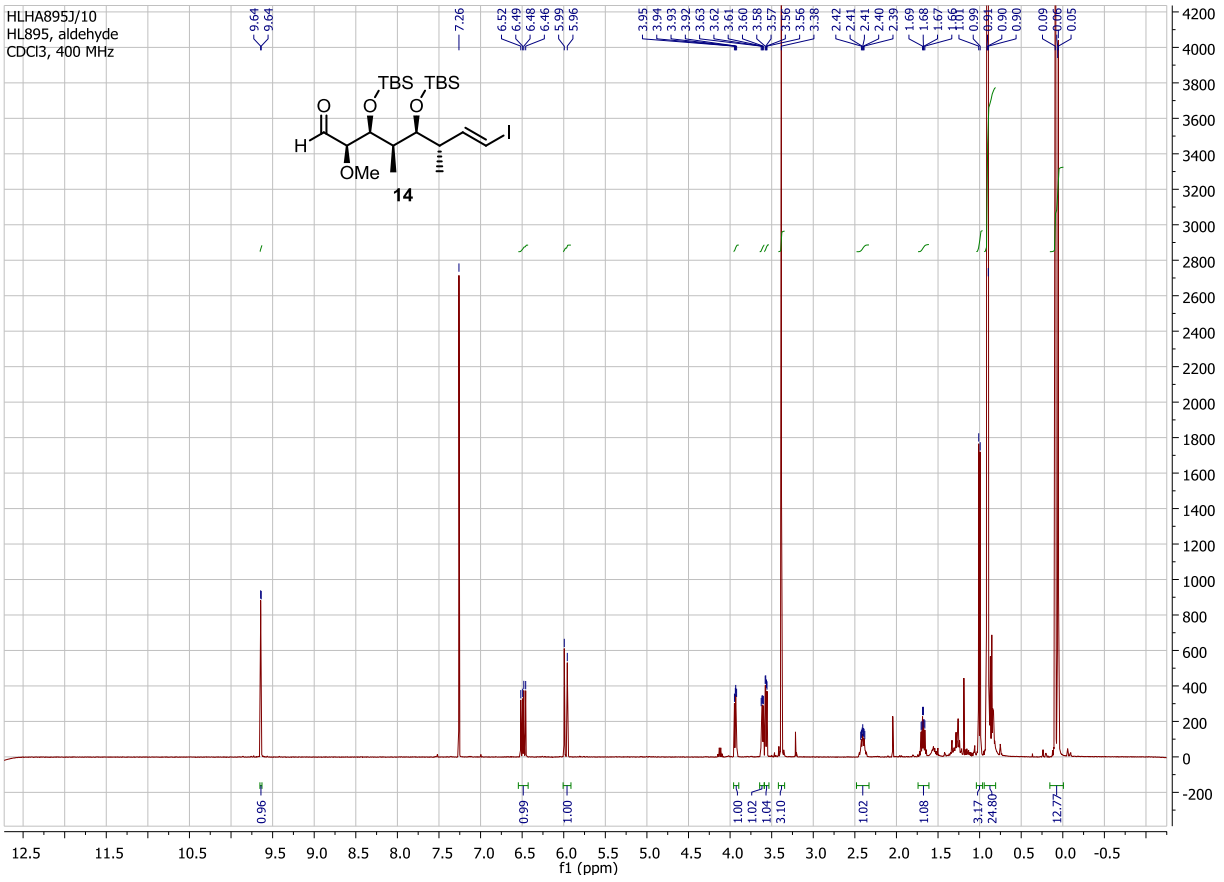

HLCL817J/10
HL817, CDCl3
100 MHz
f1 (ppm)

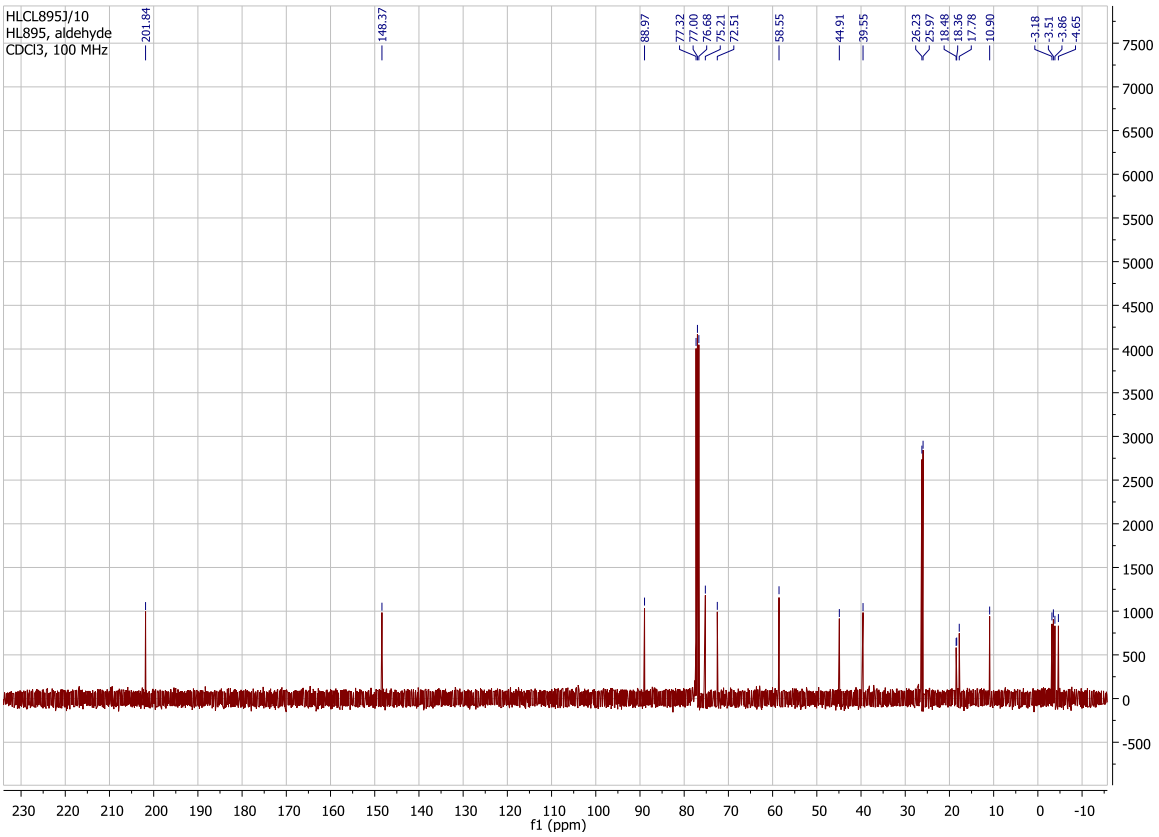

HLHA956J/10
HL956, CDCl3
400 MHz
TBS
TBS
OMe
Bn
I
SI-4
f1 (ppm)

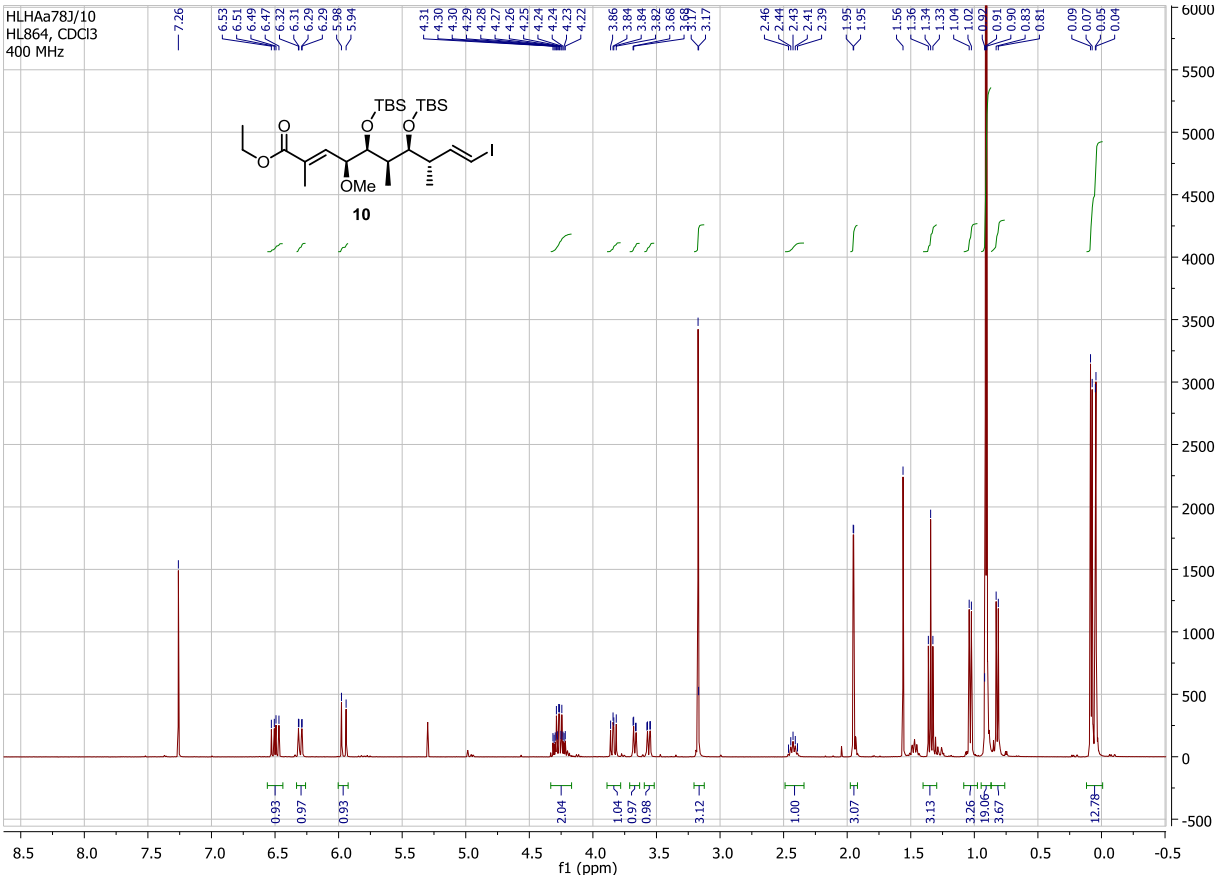

HLCL956J/10
HL956, CDCl3
100 MHz
f1 (ppm)

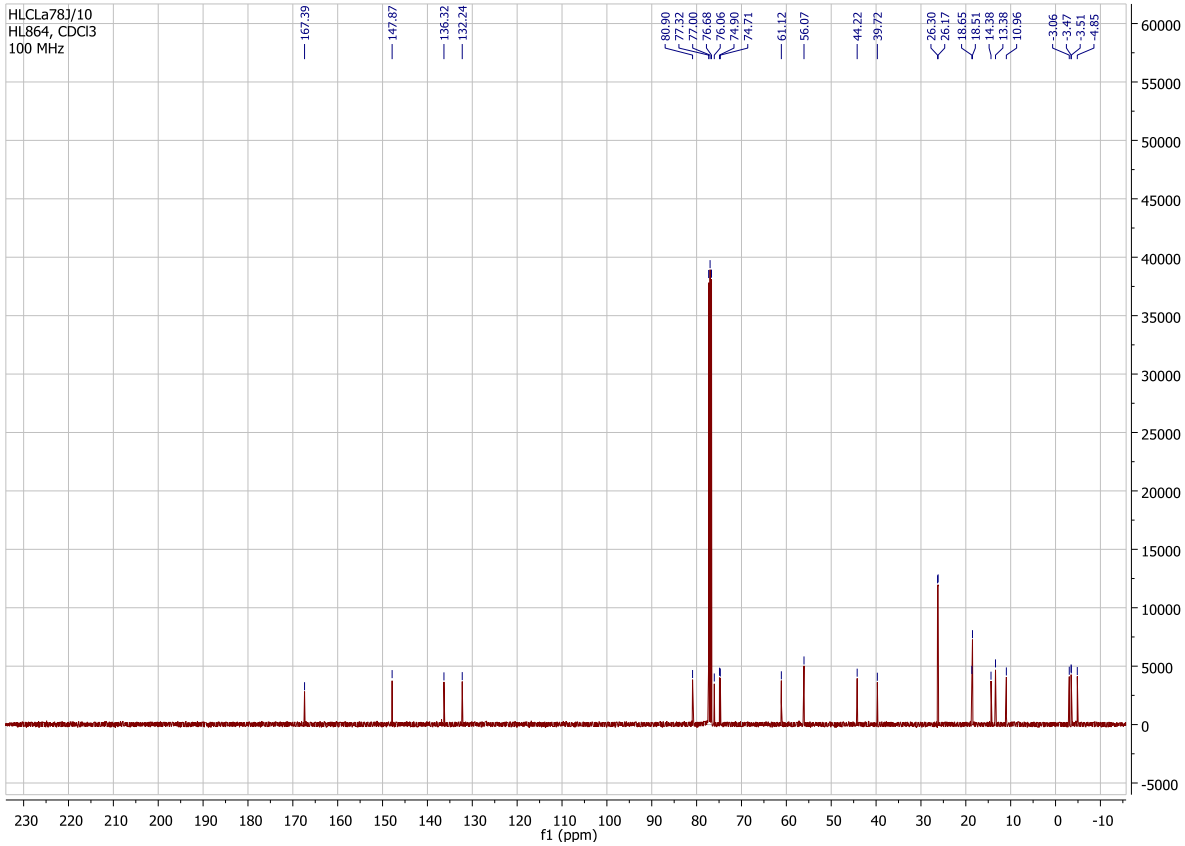

HLHA855J/10
HL855, CDCl3
400 MHz
TBS TBS
OH O O
OMe
I
31
f1 (ppm)

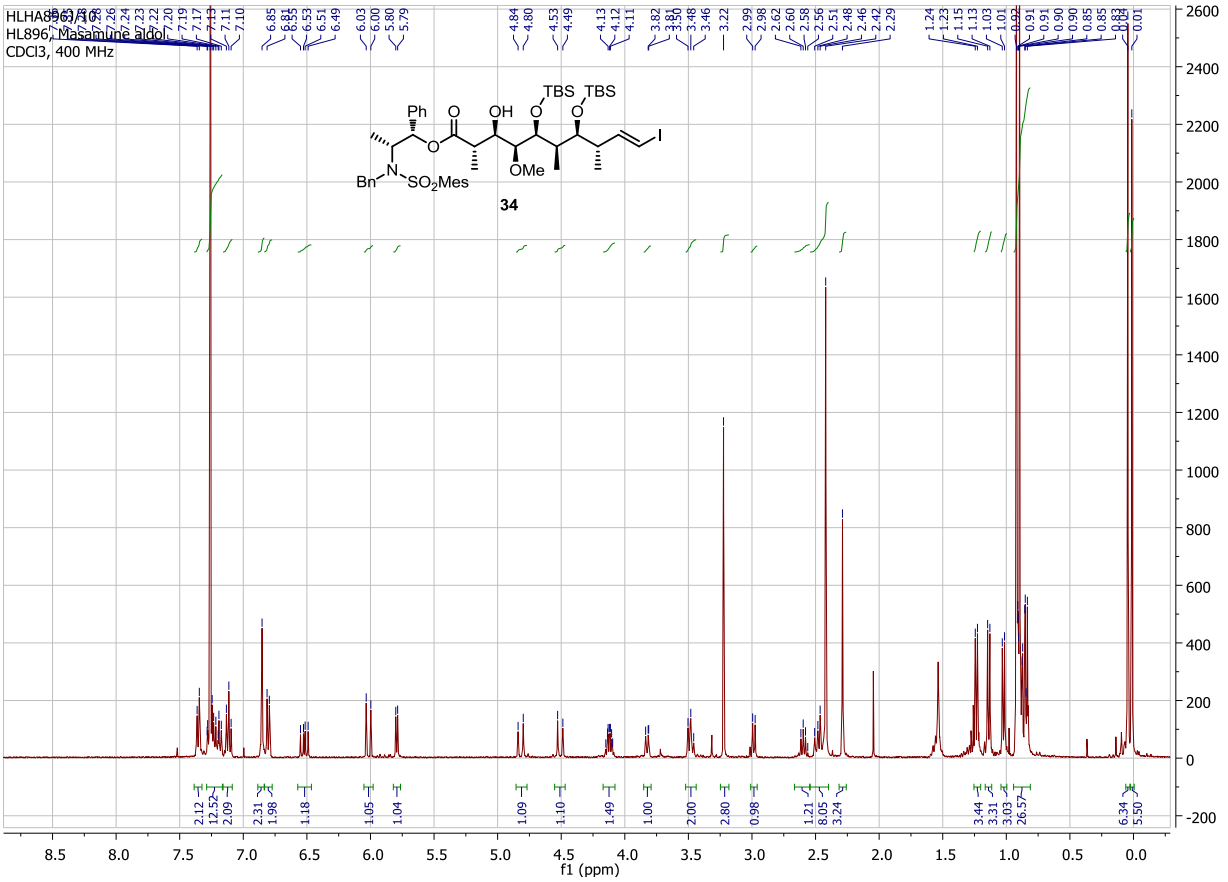

HLCL855J/10
HL855, CDCl3
100 MHz
f1 (ppm)

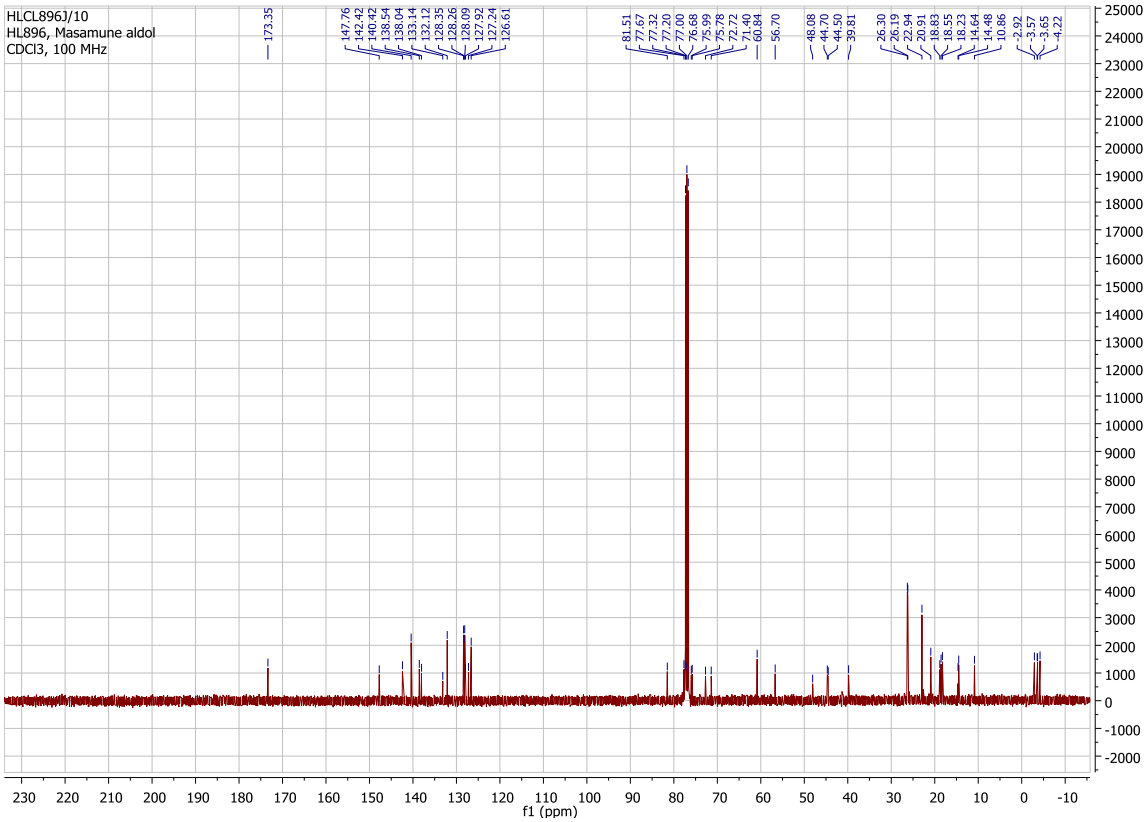

HLHA895J/10
HL895, aldehyde
CDCl3, 400 MHz
TBS
TBS
O
O
O
H
OMe
I
14
f1 (ppm)

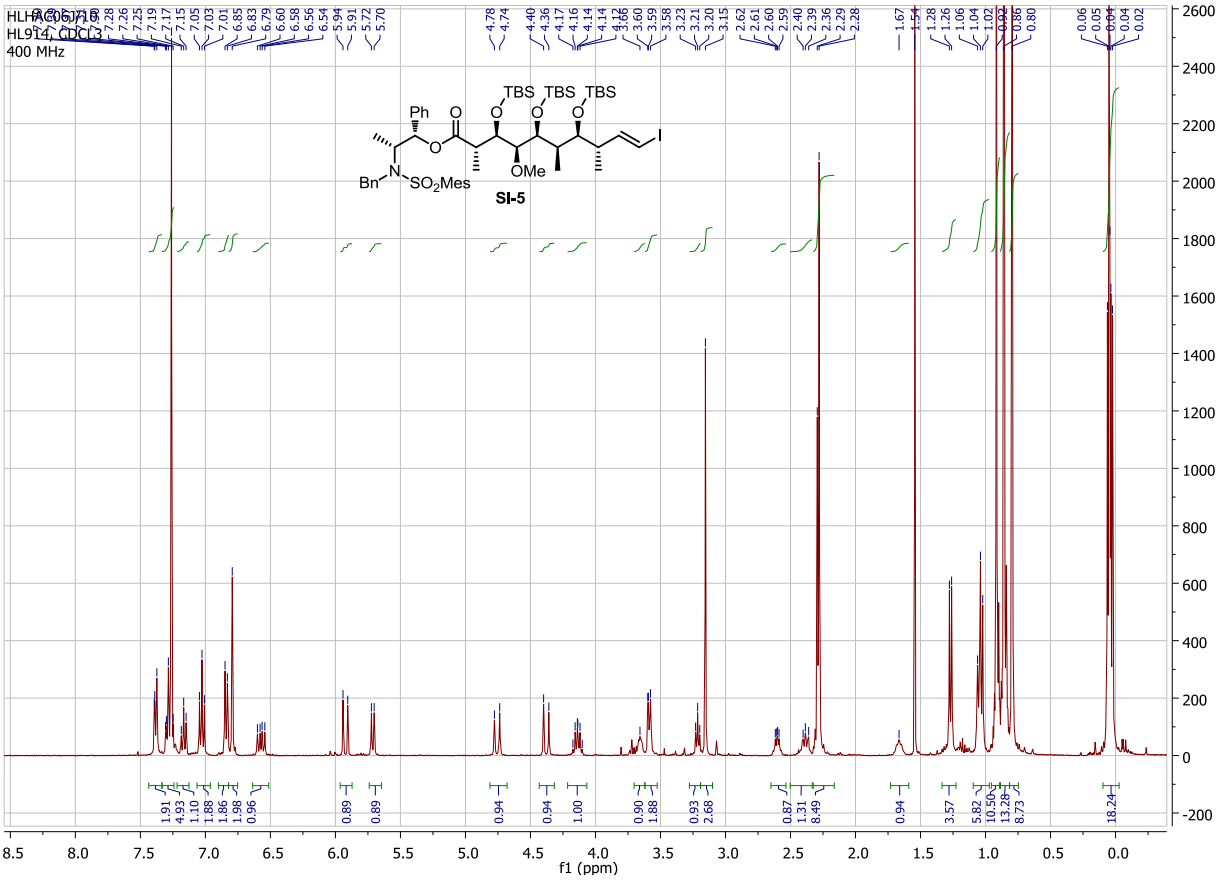

HLCL895J/10
HL895, aldehyde
CDCl3, 100 MHz
f1 (ppm)

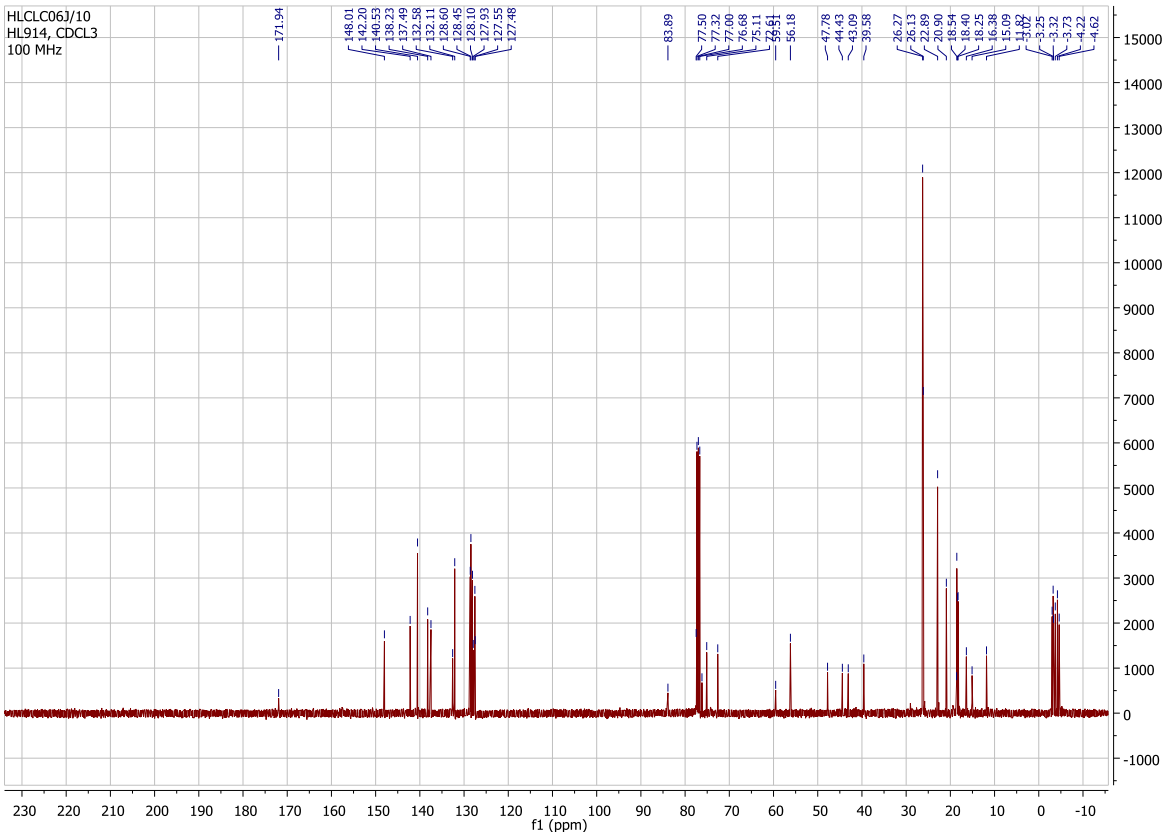

HLHAa78J/10
HL864, CDCl3
400 MHz
TBS TBS
OMe
10
f1 (ppm)

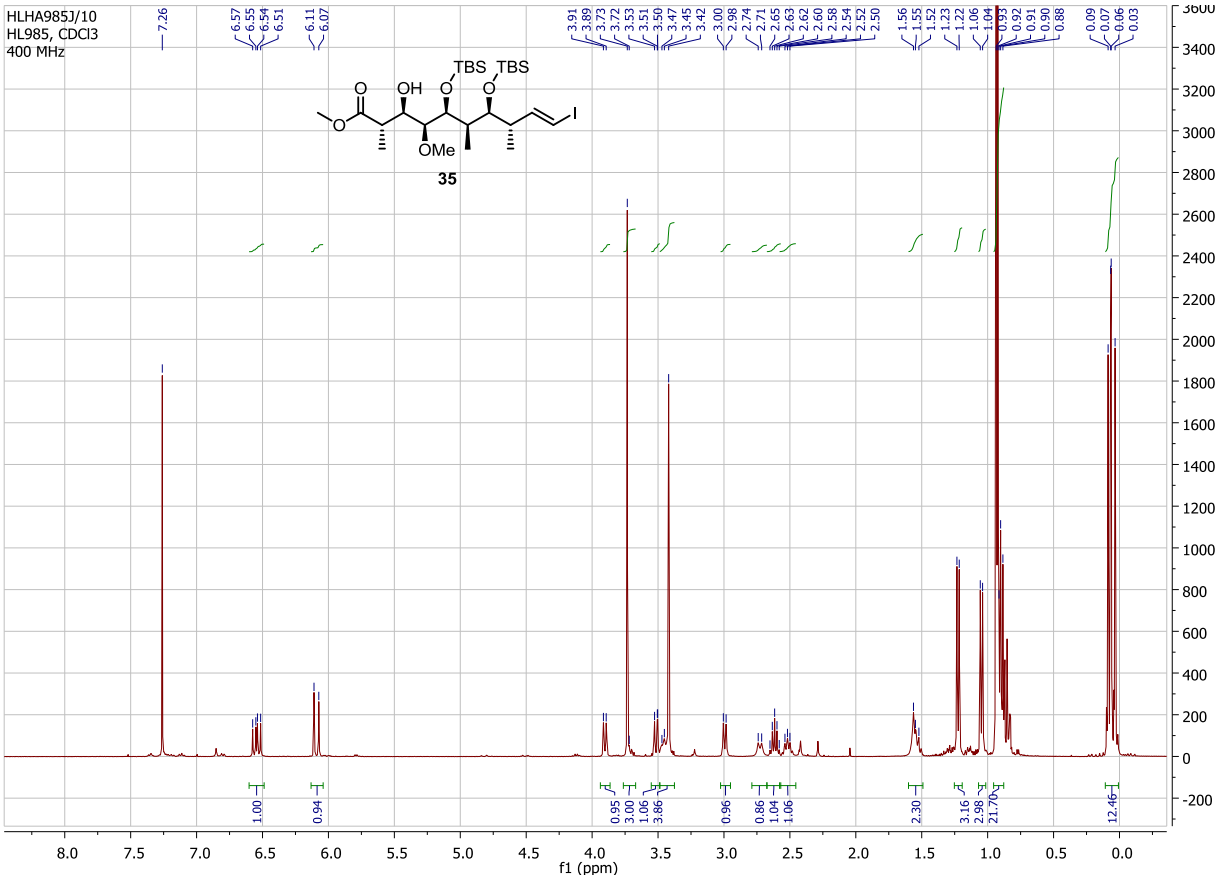

HLCLa78J/10
HL864, CDCl3
100 MHz
f1 (ppm)

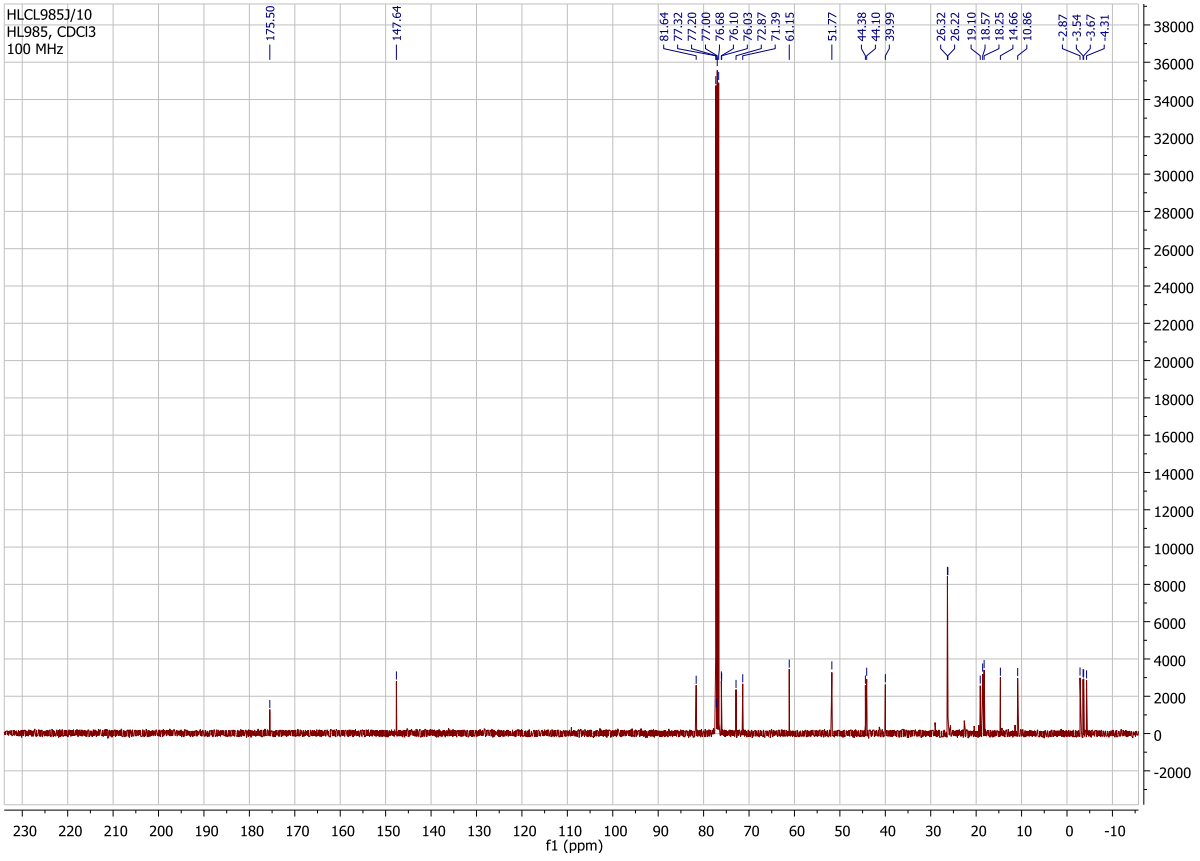

HLHA896J/10
HL896, Masamune aldol
CDCl3, 400 MHz
TBS TBS
Ph O OH O O
O I
N
Bn SO2Mes
OMe
34
f1 (ppm)

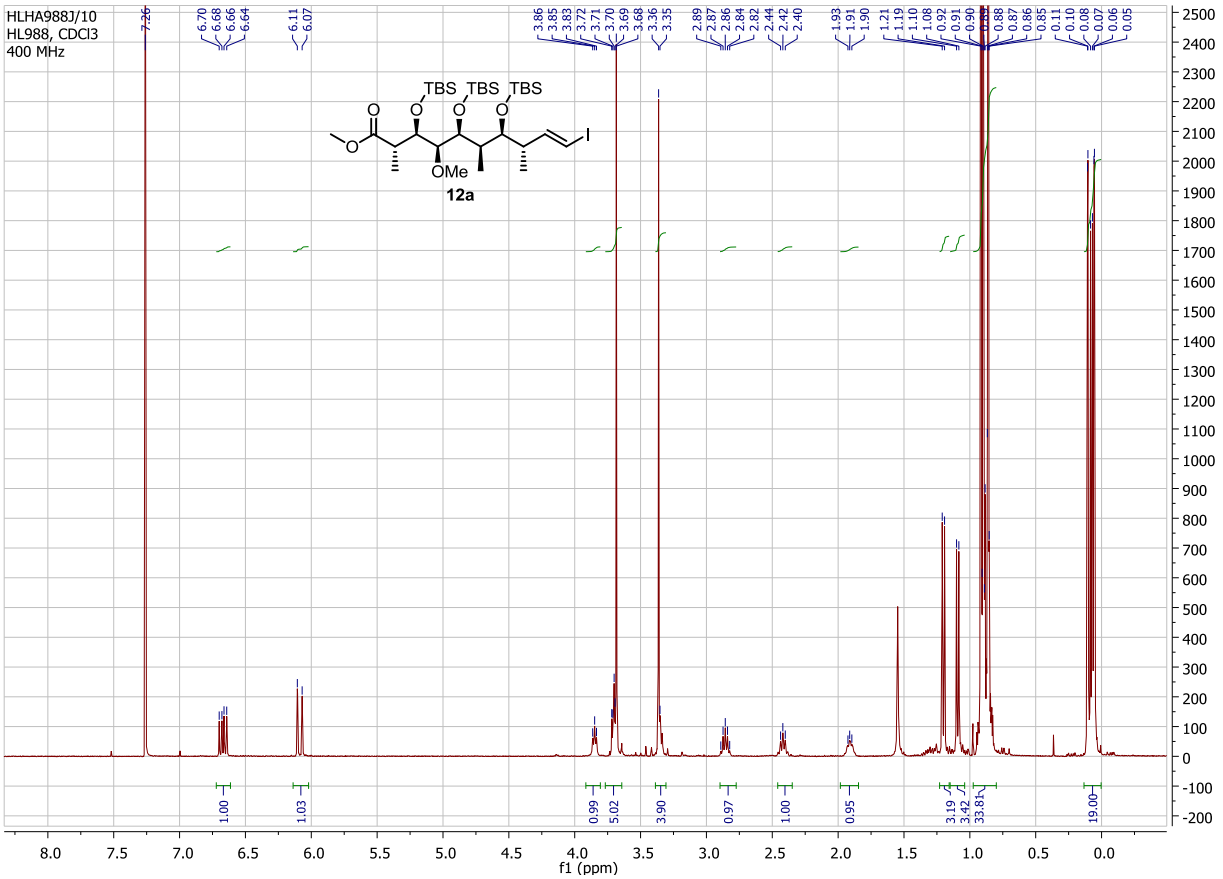

HLCL896J/10
HL896, Masamune aldol
CDCl3, 100 MHz
f1 (ppm)

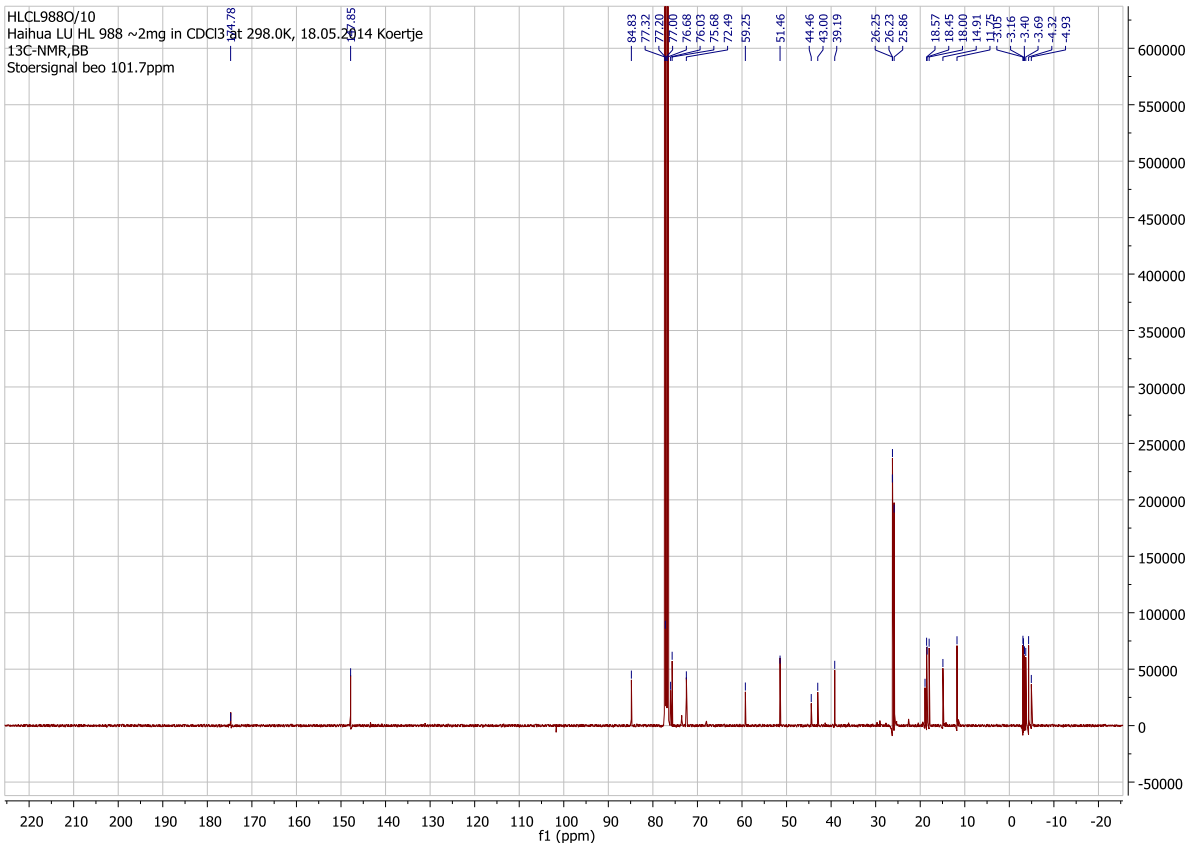

HLHAC06J/10
HL914, CDCL3
400 MHz
TBS TBS TBS
Ph
O
O
O
O
O
OMe
N
Bn
SO2Mes
SI-5
f1 (ppm)

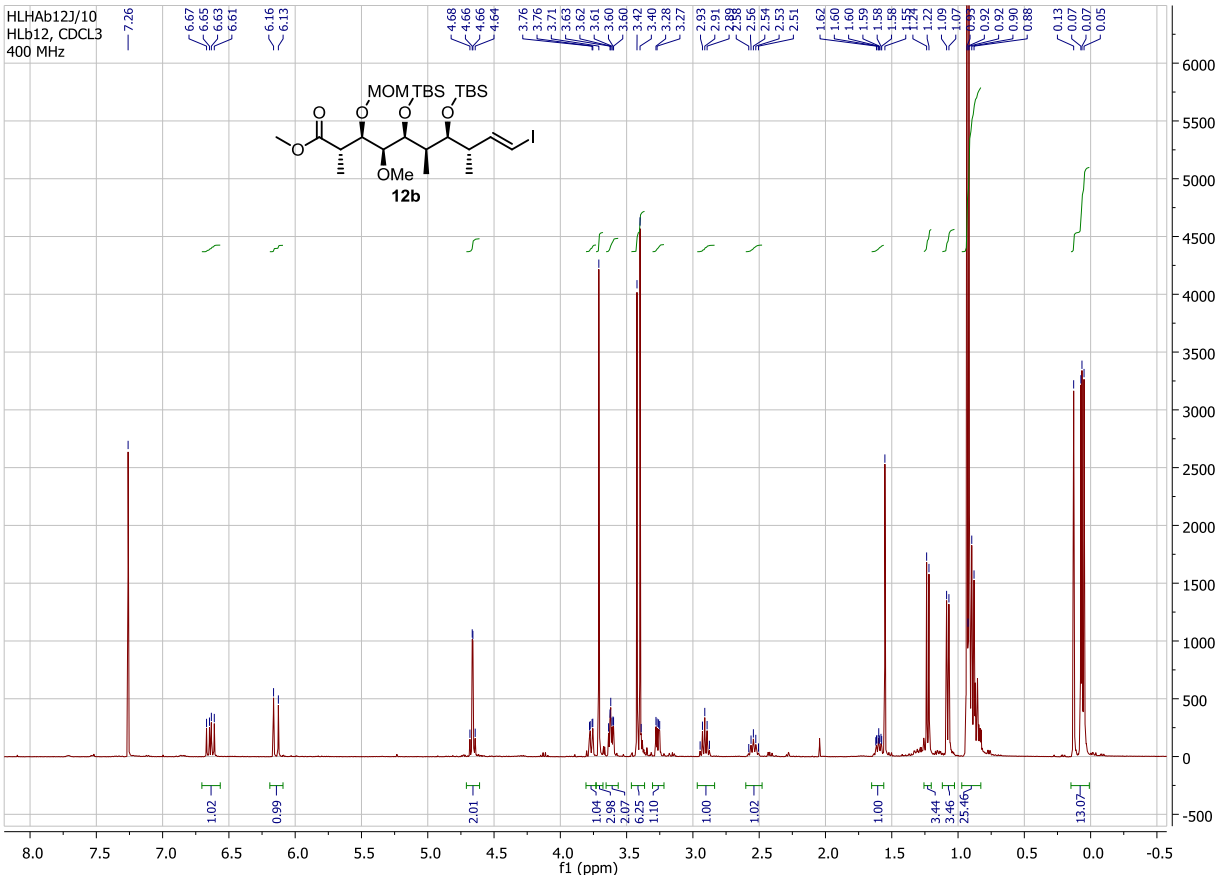

HLCLC06J/10
HL914, CDCL3
100 MHz
f1 (ppm)

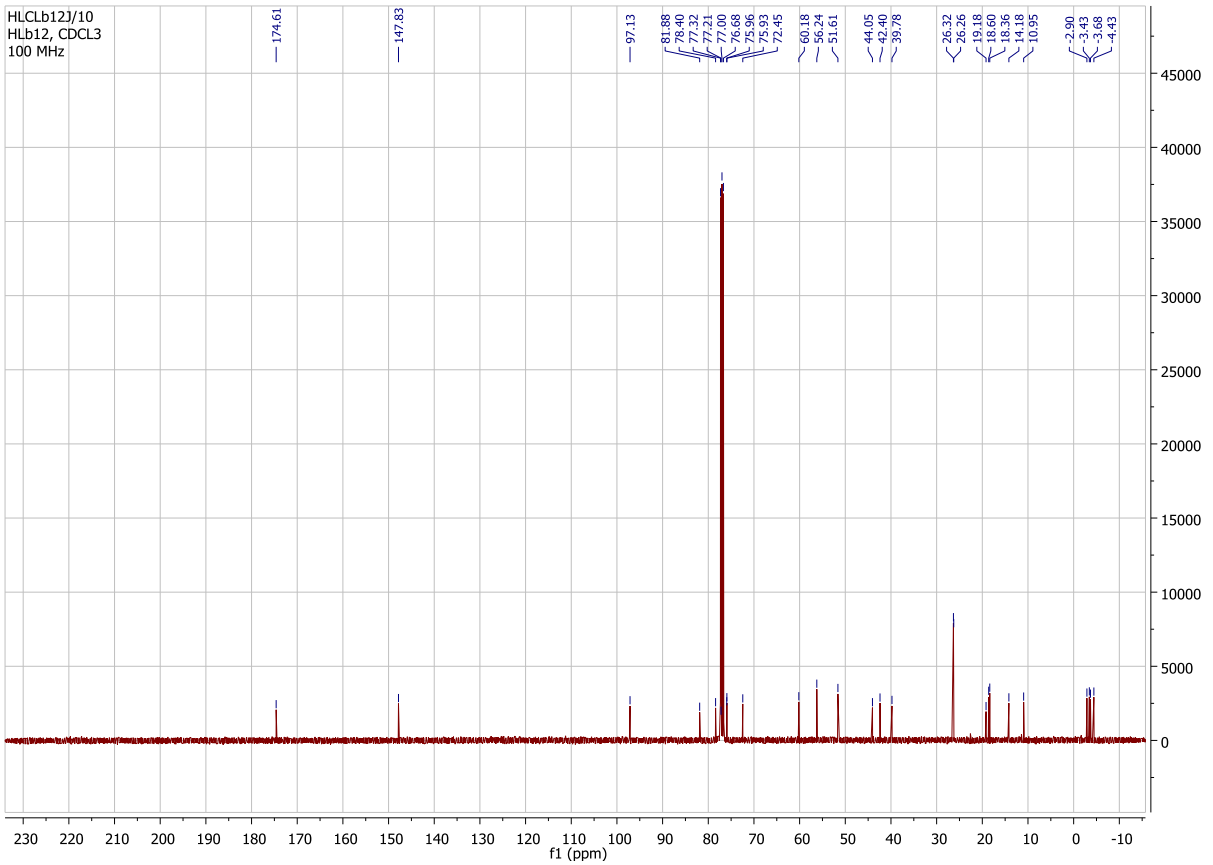

HLHA985J/10
HL985, CDCl3
400 MHz
TBS TBS
OH
OMe
35
f1 (ppm)

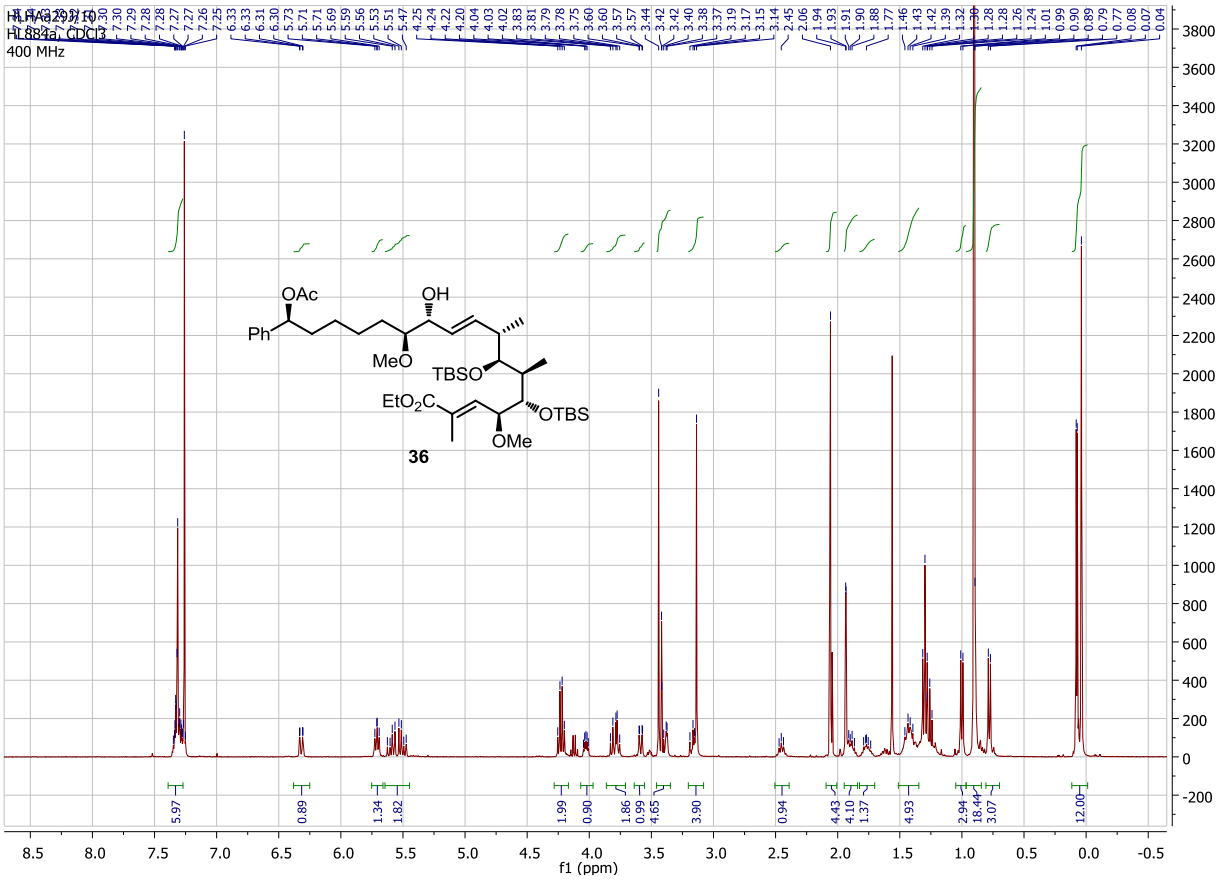

HLCL985J/10
HL985, CDCl3
100 MHz
f1 (ppm)

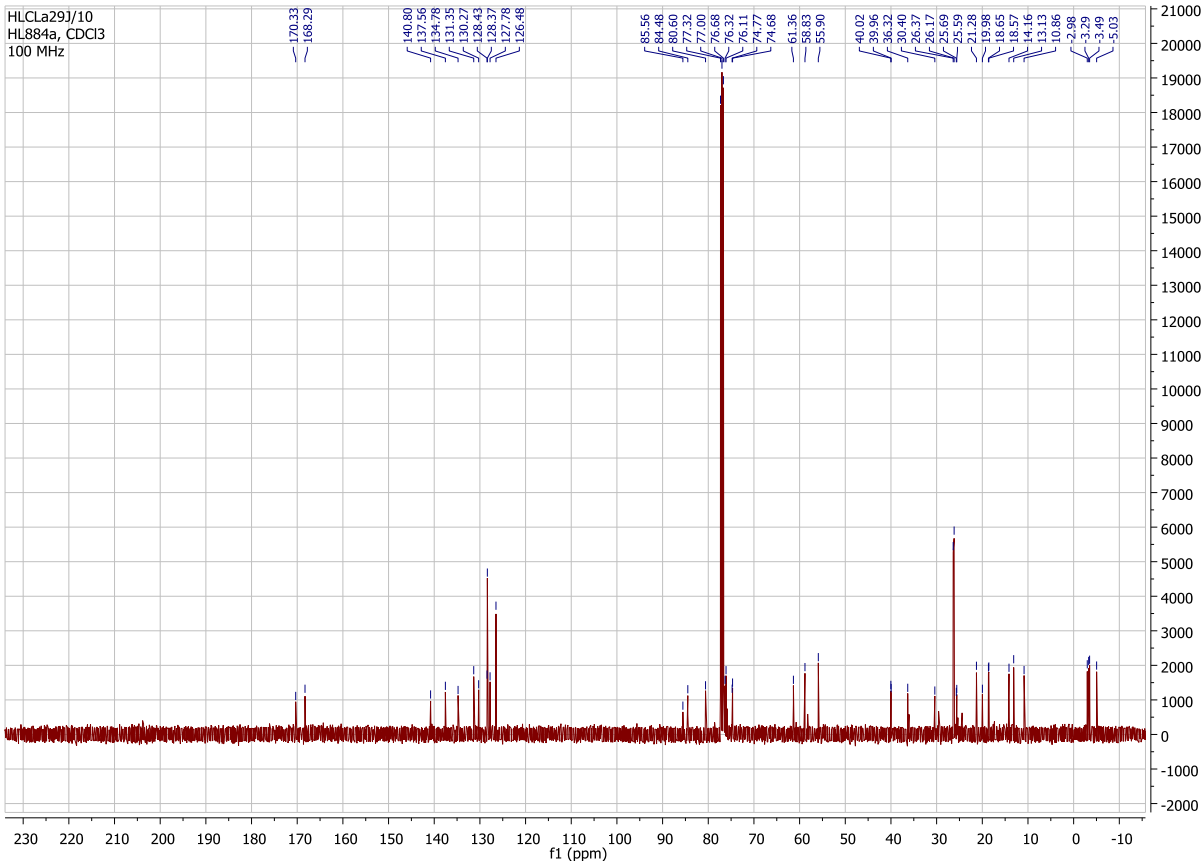

HLHA988J/10
HL988, CDCl3
400 MHz
TBS TBS TBS
OMe
12a
f1 (ppm)

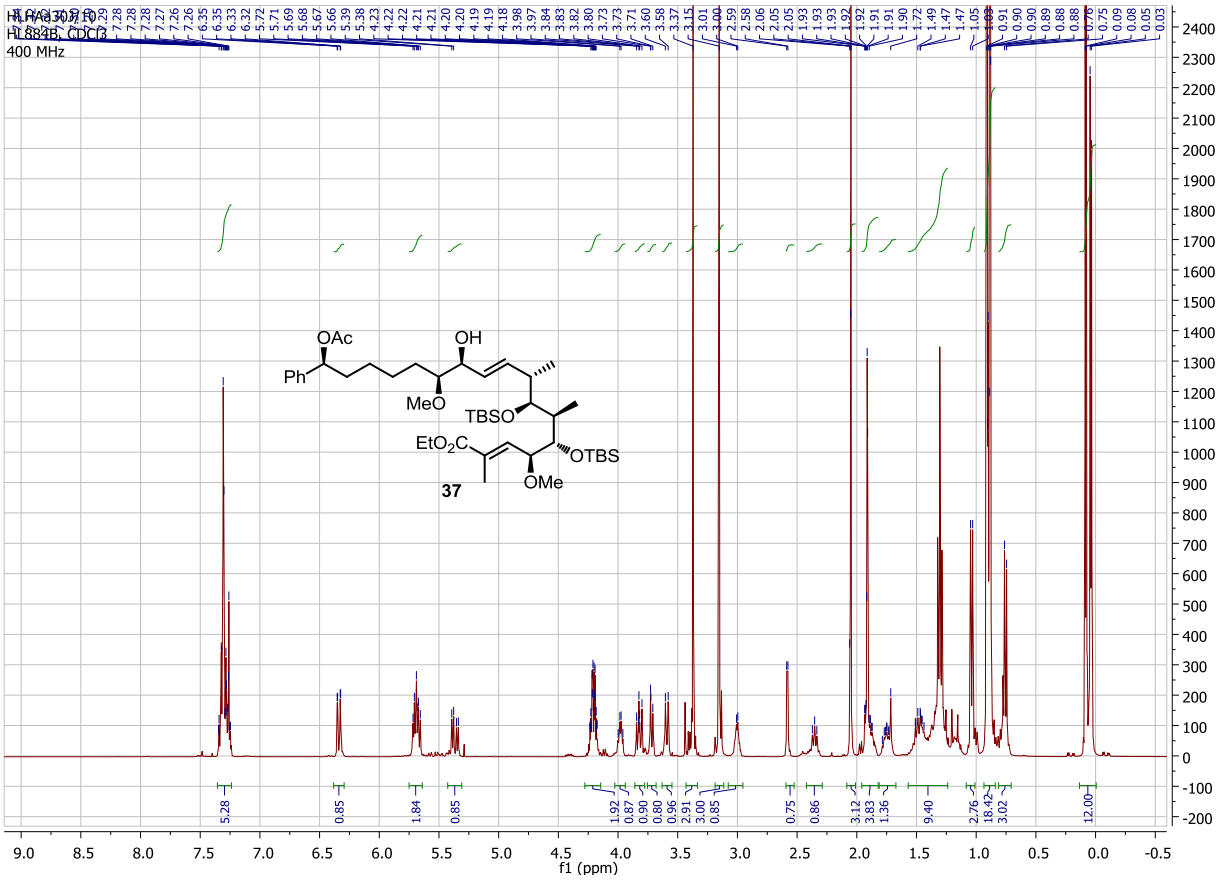

HLCL988O/10
Haihua LU HL 988 ~2mg in CDCl3 at 298.0K, 18.05.2014 Koertje
13C-NMR,BB
Stoersignal beo 101.7ppm
f1 (ppm)

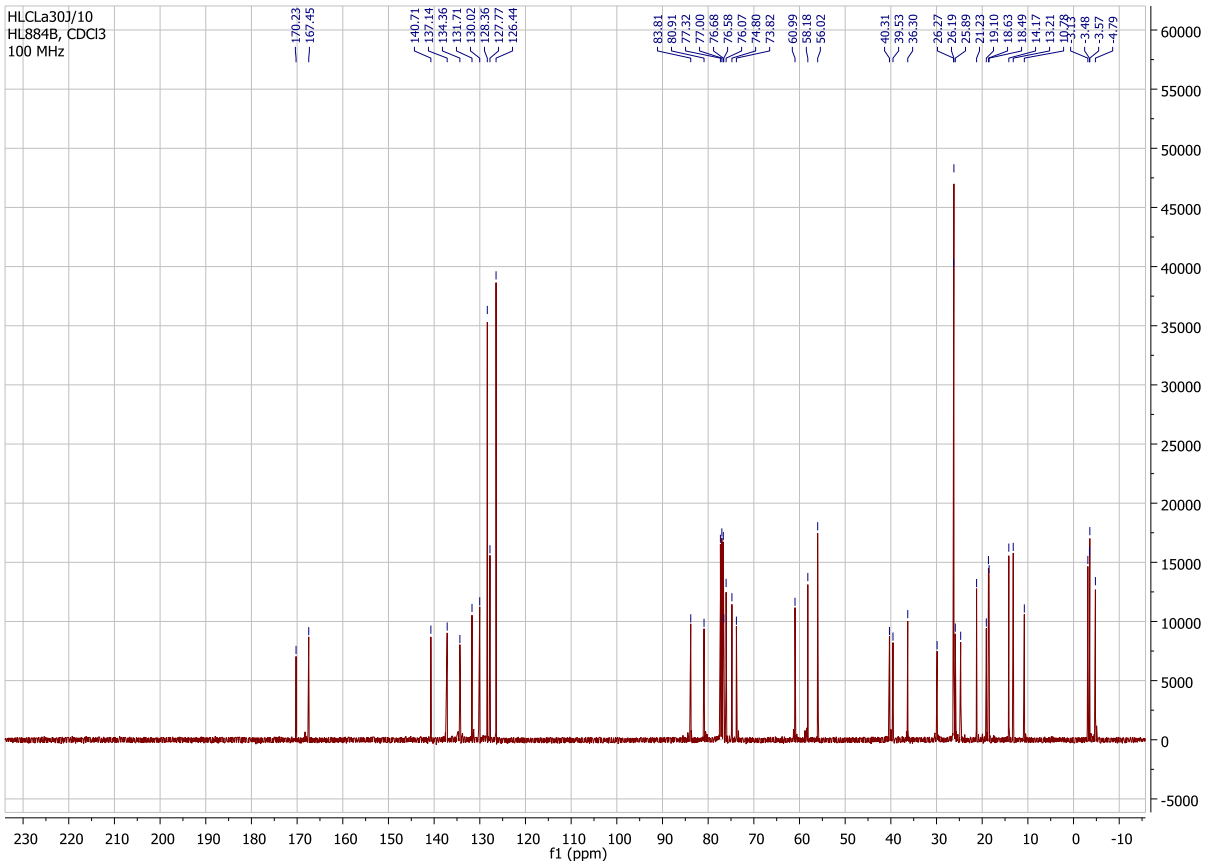

HLHAb12J/10
HLb12, CDCL3
400 MHz
MOM TBS TBS
OMe
12b
f1 (ppm)

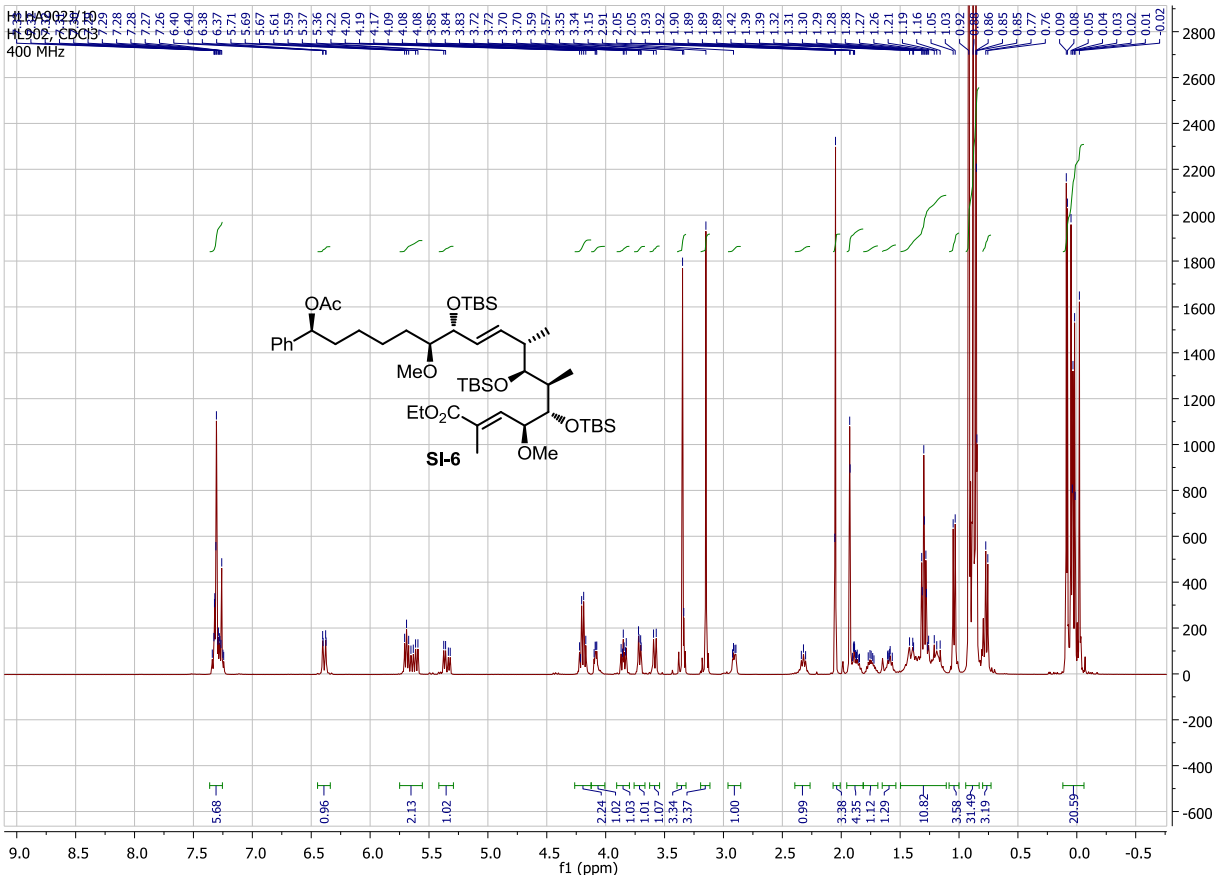

HLCLb12J/10
HLb12, CDCL3
100 MHz
f1 (ppm)

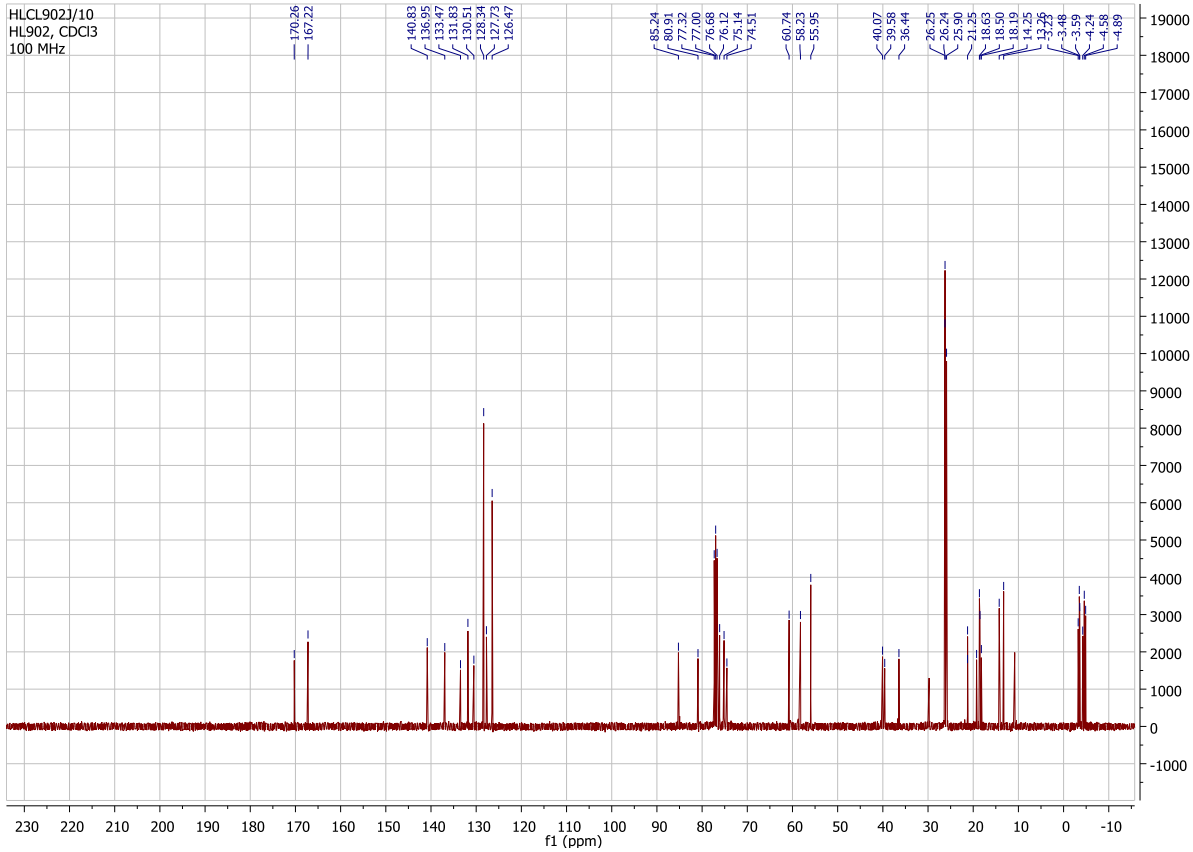

HLCLa29J/10
HL884a, CDCl3
400 MHz
OAc
OH
Ph
MeO
TBSO
EtO2C
OTBS
OMe
36
f1 (ppm)

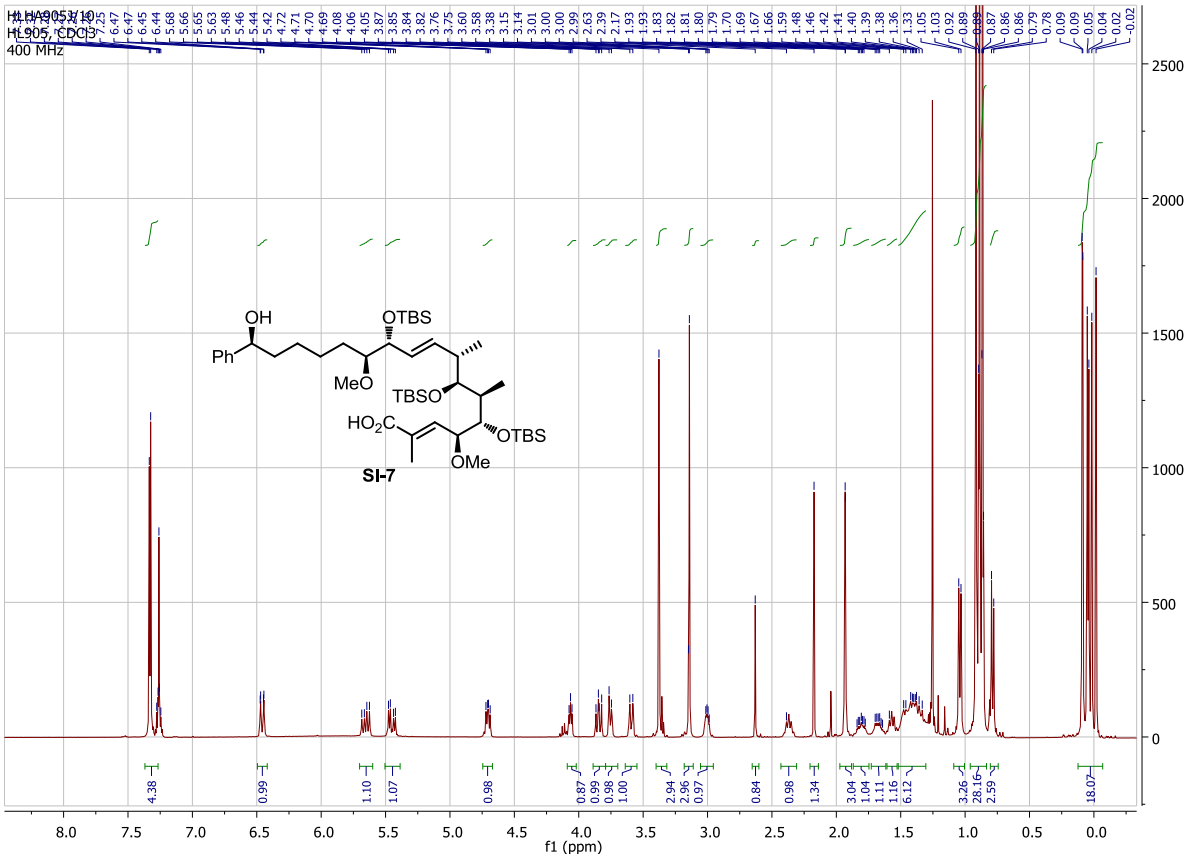

HLCLa29J/10
HL884a, CDCl3
100 MHz
f1 (ppm)

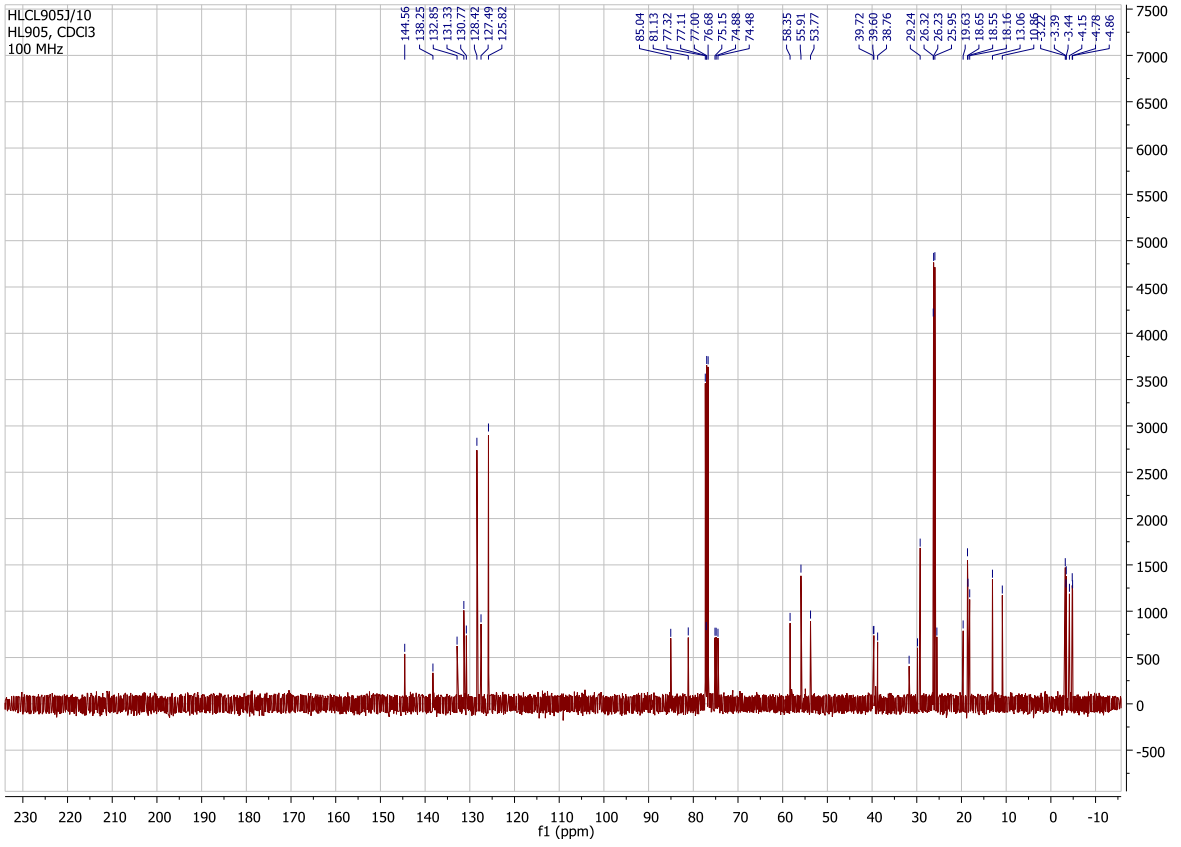

HLCLa30J/10
HL884B, CDCl3
400 MHz
OAc
OH
Ph
MeO
TBSO
EtO2C
OTBS
OMe
37
f1 (ppm)

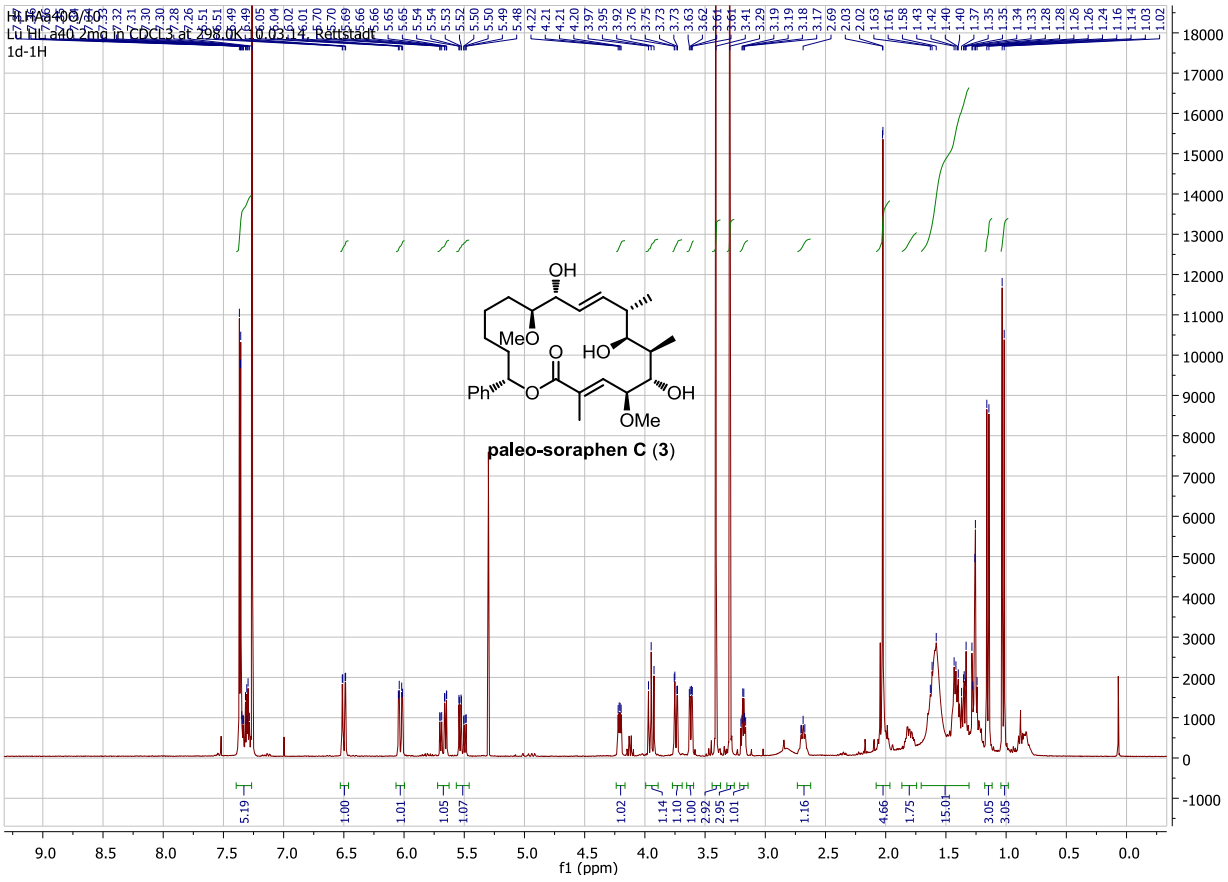

HLCLa30J/10
HL884B, CDCl3
100 MHz
f1 (ppm)

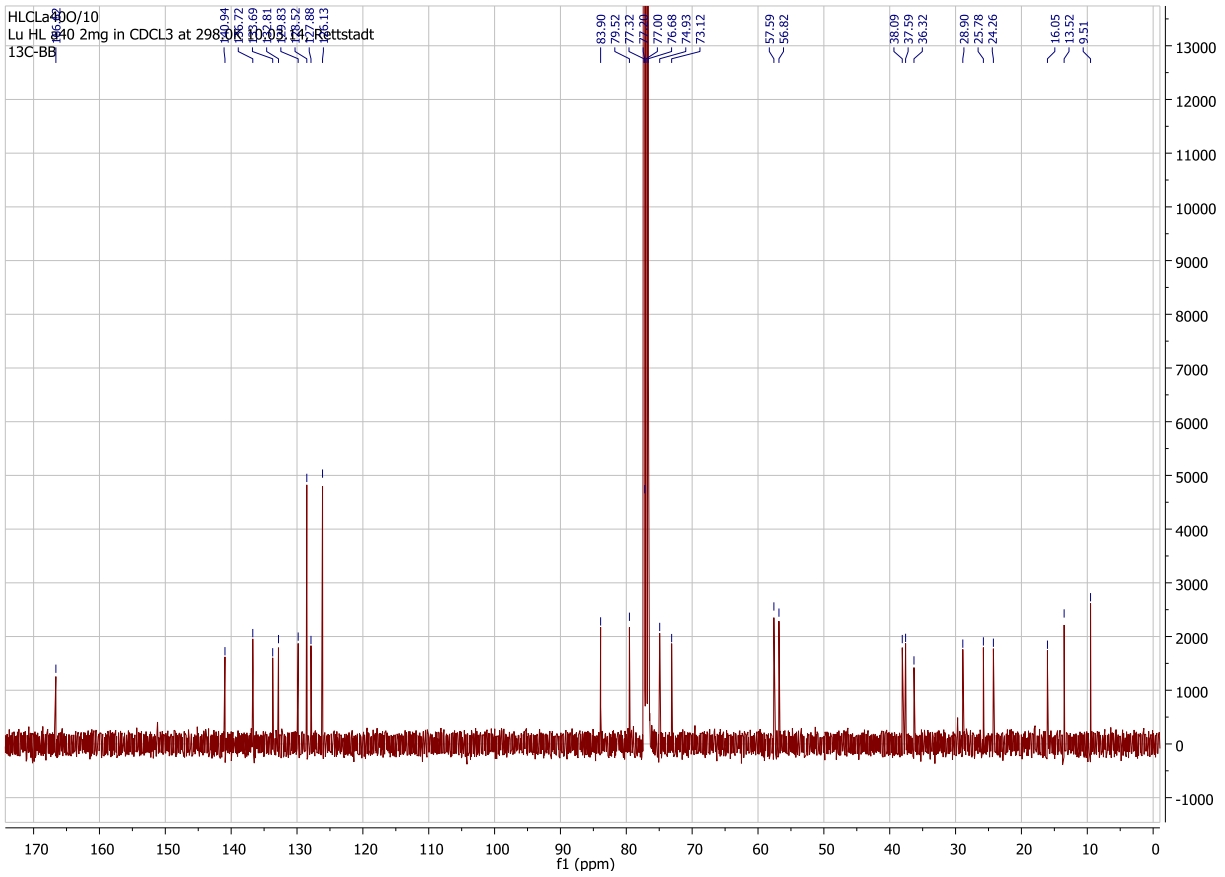

HLHA902J/10
HL902, CDCl3
400 MHz
OAc
OTBS
Ph
MeO
TBSO
EtO2C
OTBS
OMe
SI-6
f1 (ppm)

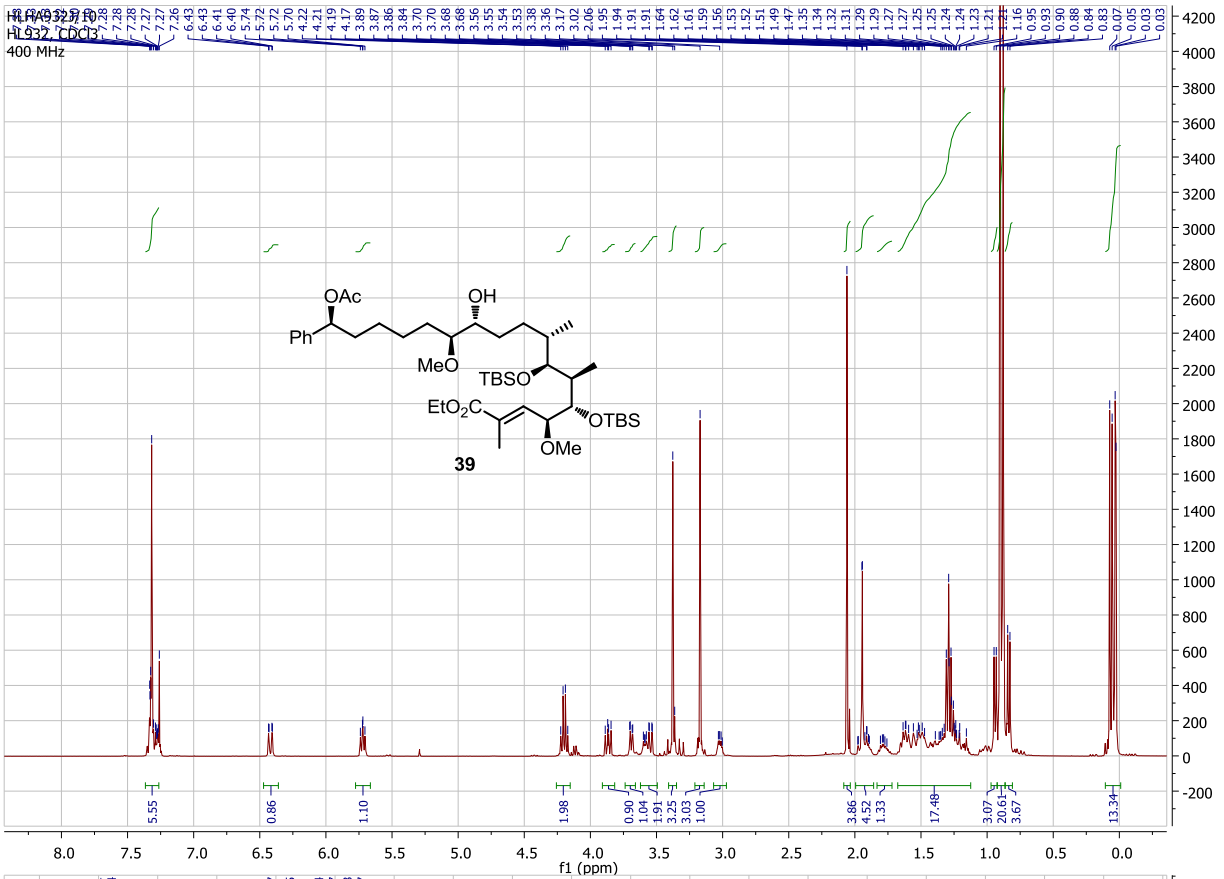

HLCL902J/10
HL902, CDCl3
100 MHz
f1 (ppm)

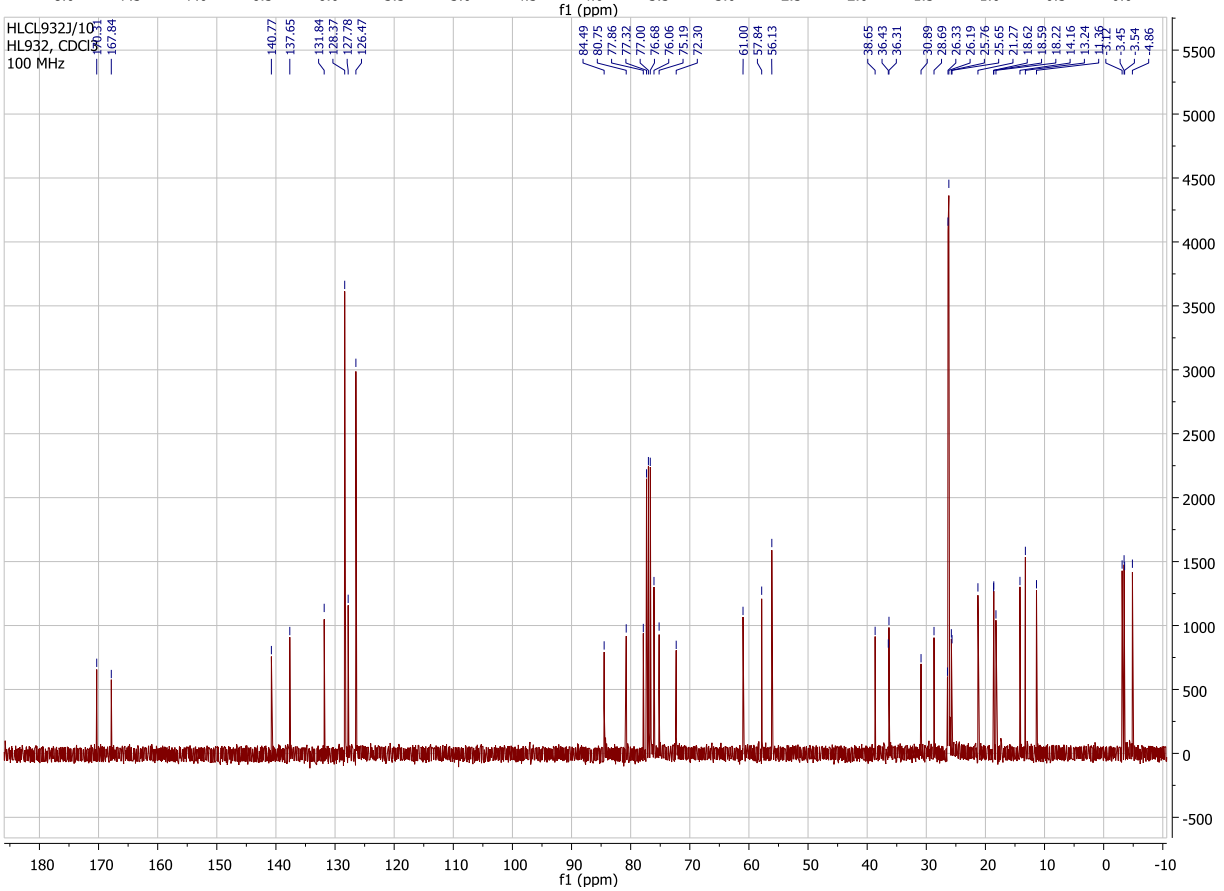

HLHA905J/10
HL905, CDCl3
400 MHz
OH
OTBS
Ph
MeO
TBSO
HO2C
OTBS
OMe
SI-7
f1 (ppm)

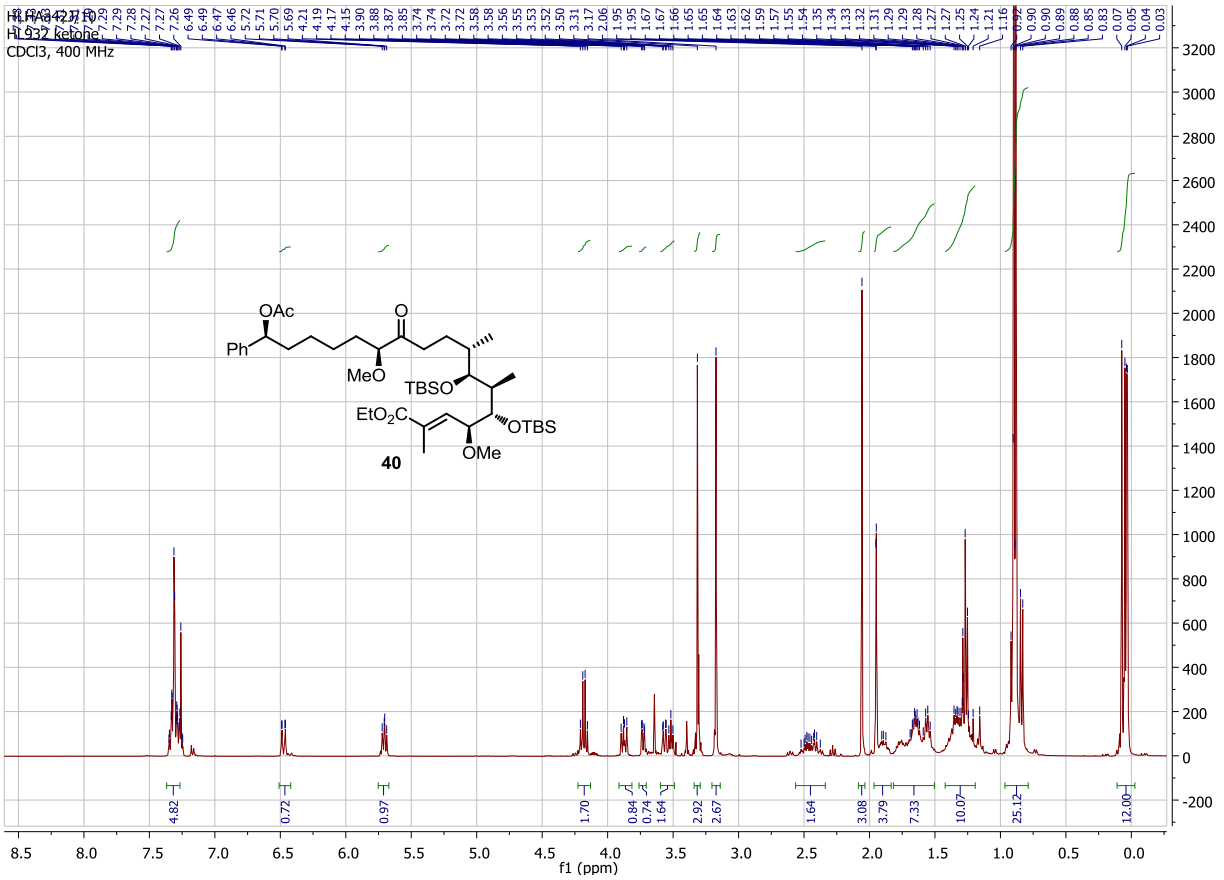

HLCL905J/10
HL905, CDCl3
100 MHz
f1 (ppm)

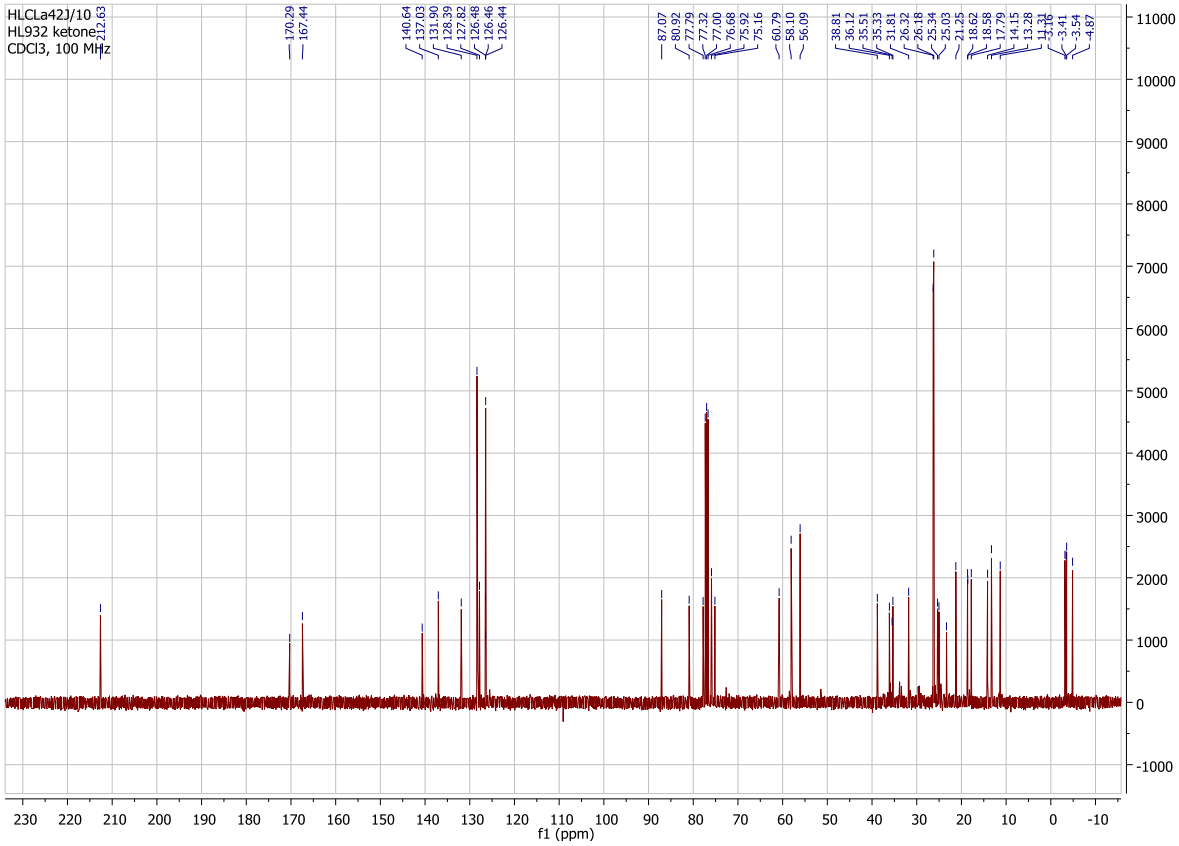

HLHA400/10
Lu HL a40 2mg in CDCL3 at 298.0K 10.03.14, Rettstadt
1d-1H
OH
MeO
O
HO
Ph
O
OH
OMe
paleo-soraphen C (3)
f1 (ppm)

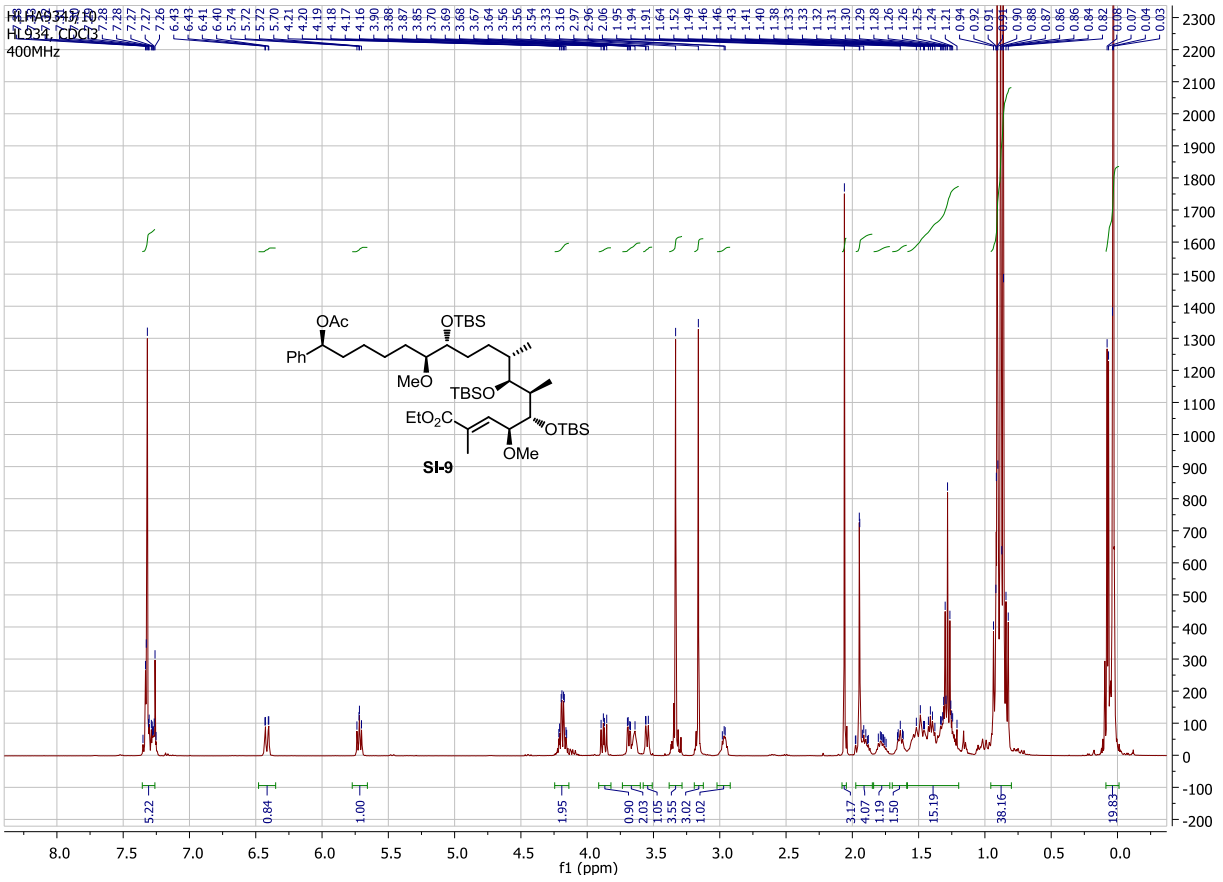

HLCLa400/10
Lu HL a40 2mg in CDCL3 at 298.0K 10.03.14, Rettstadt
13C-BB
f1 (ppm)

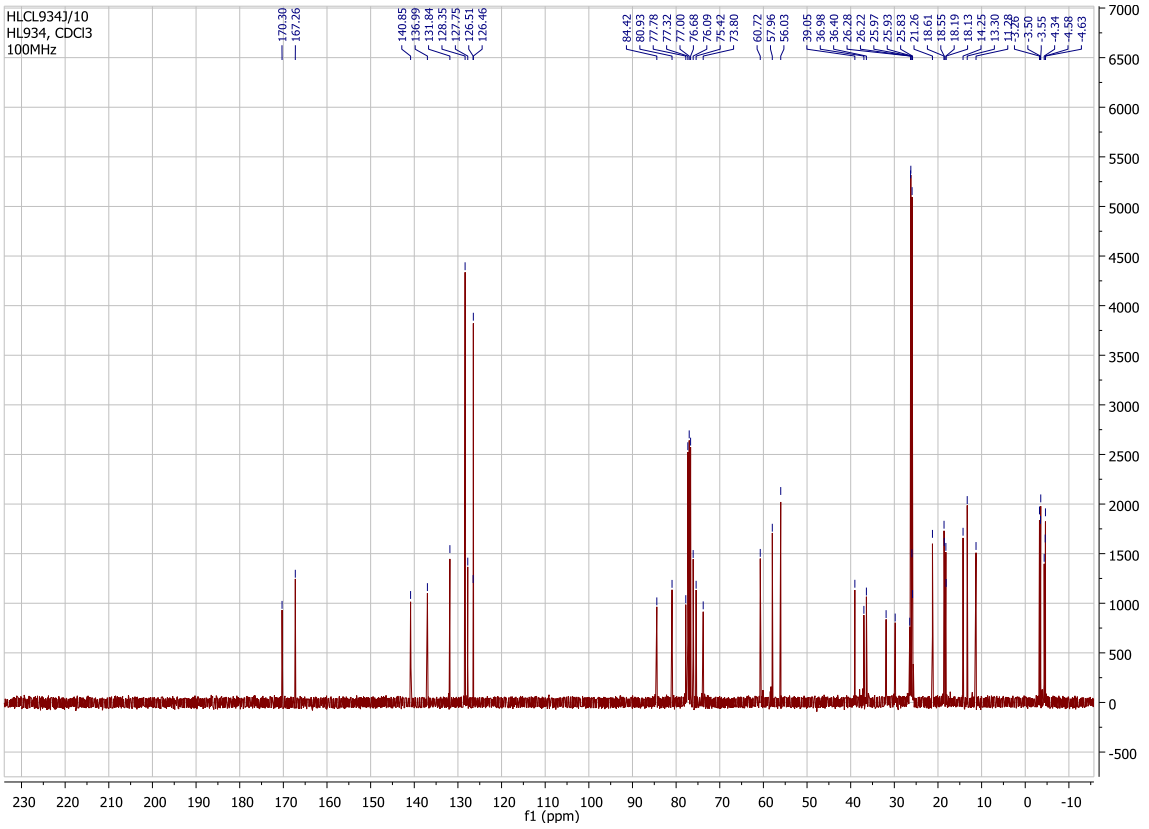

HLCL932J/10
HL932, CDCl3
400 MHz
OAc
OH
Ph
MeO
TBSO
EtO2C
OTBS
OMe
39
f1 (ppm)

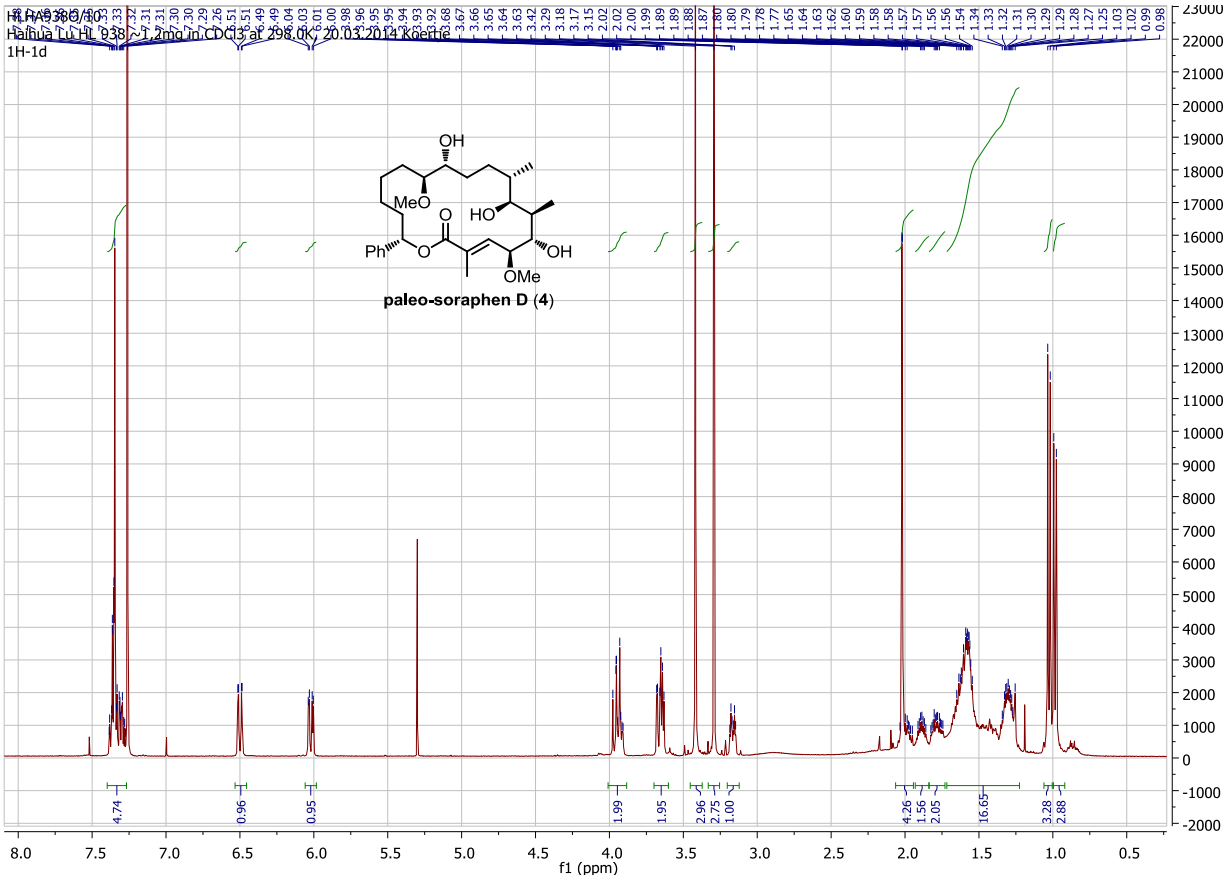

HLCL932J/10
HL932, CDCl3
100 MHz
f1 (ppm)

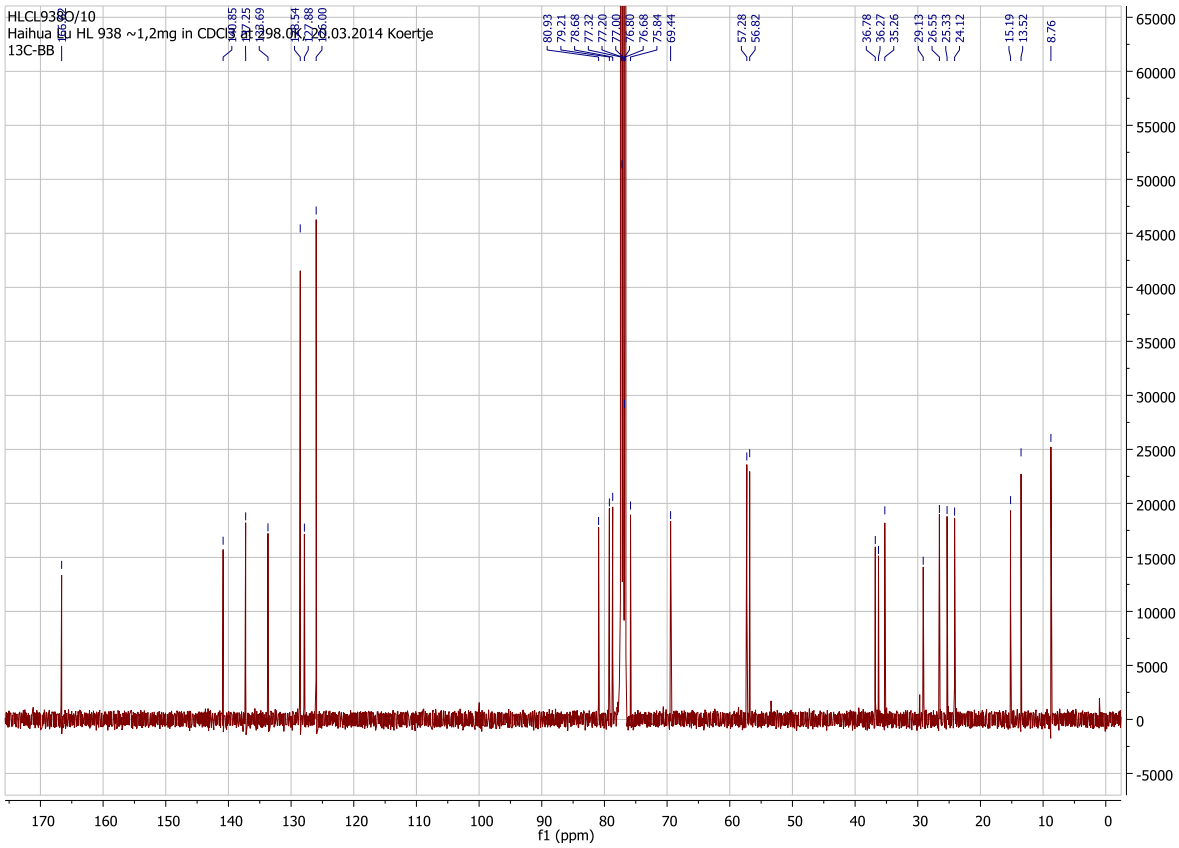

HLCLa42J/10
HL932 ketone
CDCl3, 400 MHz
OAc
O
Ph
MeO
TBSO
EtO2C
OTBS
OMe
40
f1 (ppm)

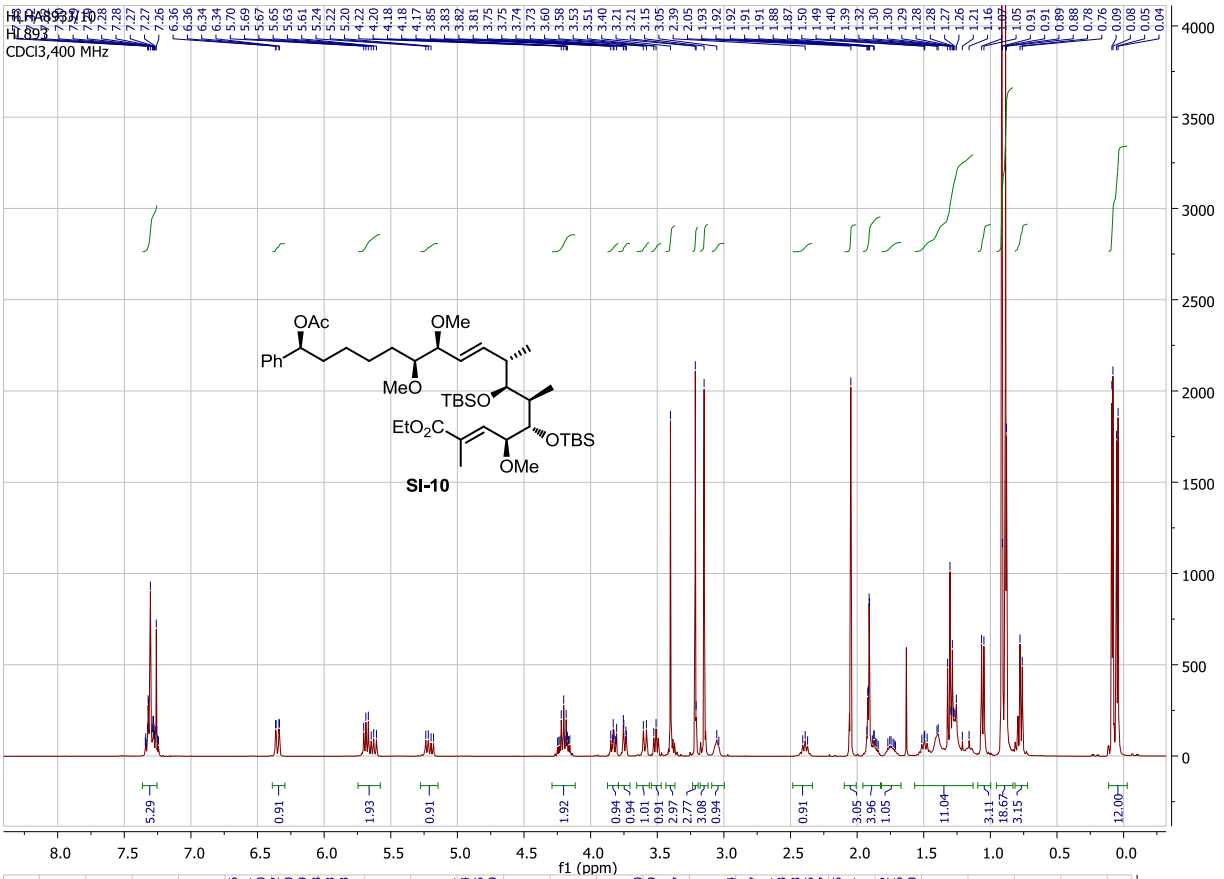

HLCLa42J/10
HL932 ketone
CDCl3, 100 MHz
f1 (ppm)

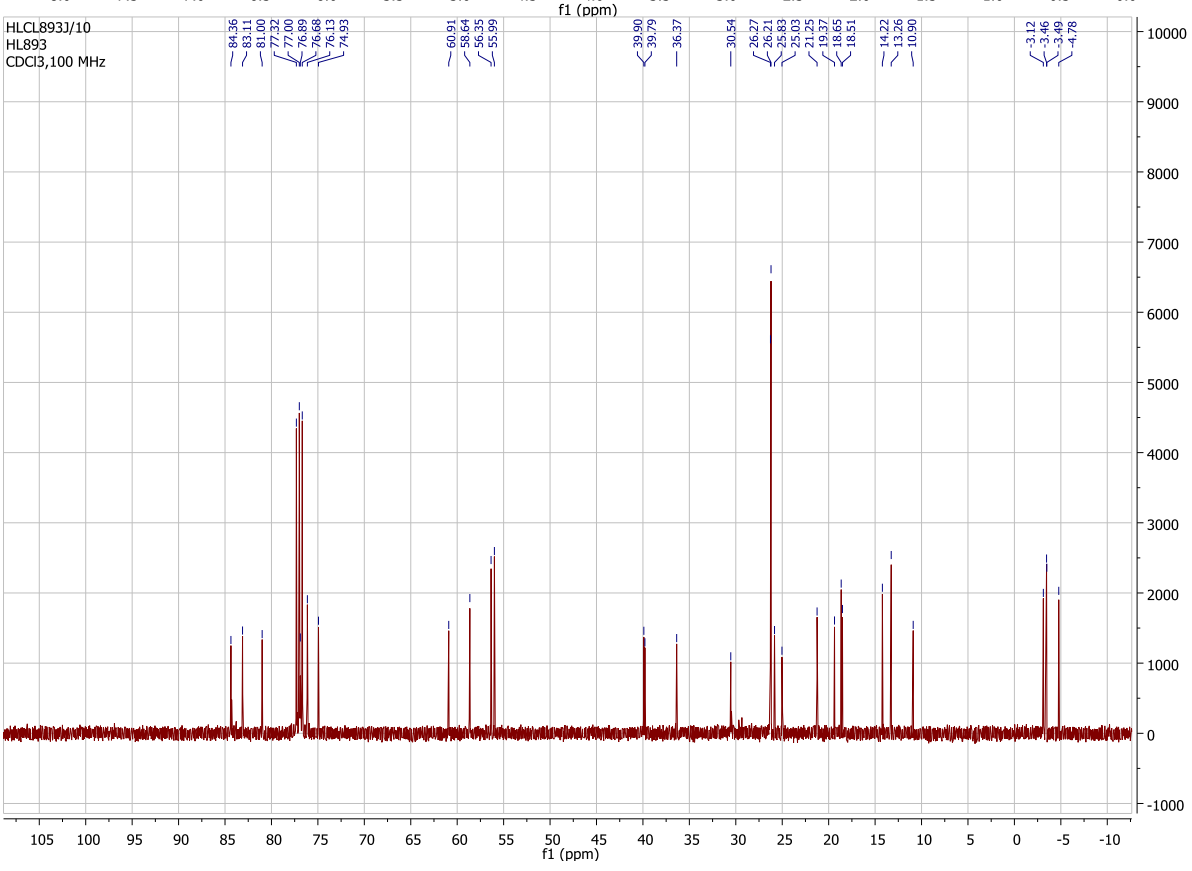

HLCL934J/10
HL934, CDCl3
400MHz
OAc
OTBS
Ph
MeO
TBSO
EtO2C
OTBS
OMe
SI-9
f1 (ppm)

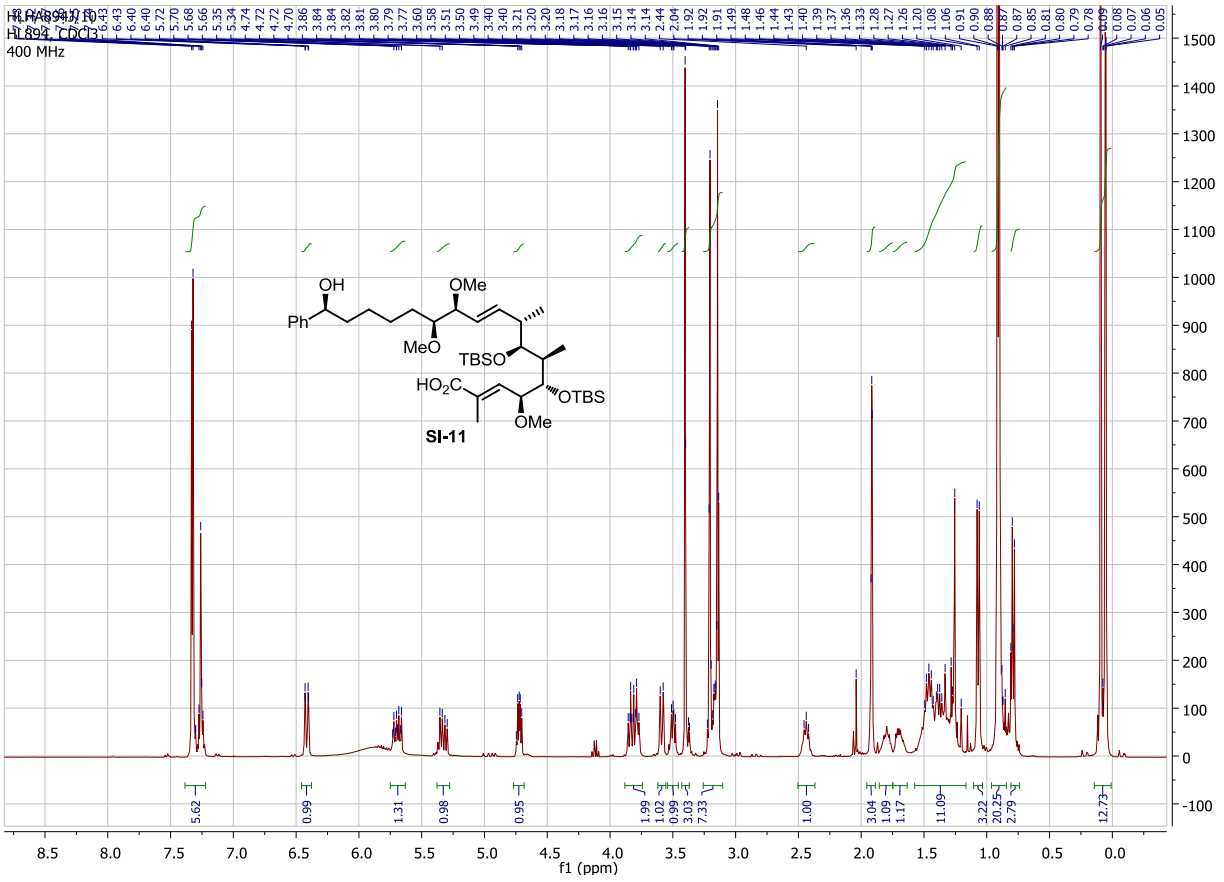

HLCL934J/10
HL934, CDCl3
100MHz
f1 (ppm)

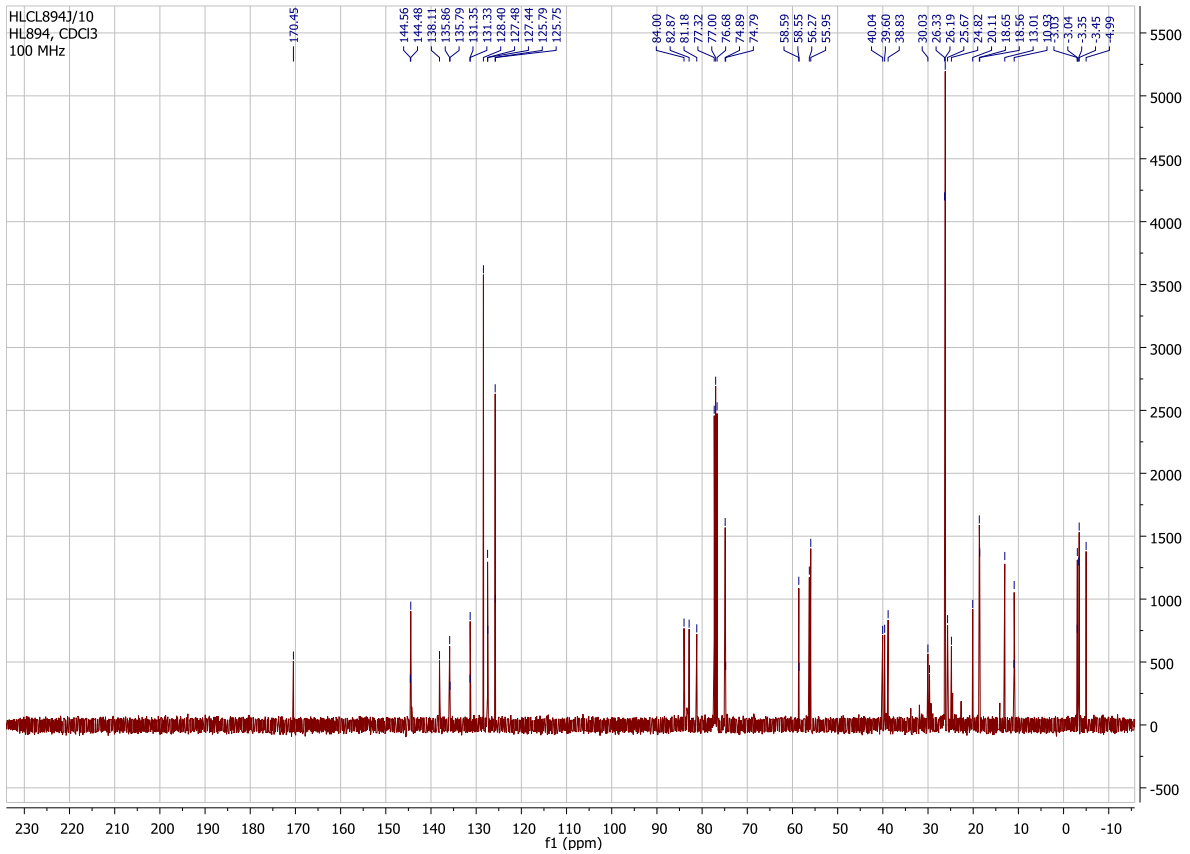

HLHA938/10
Haihua Lu HL 938 ~1,2mg in CDCl3 at 298.0K 20.03.2014 Koertje
1H-1d
OH
MeO
O
HO
Ph
O
OH
OMe
paleo-soraphen D (4)
4.74
0.96
0.95
1.99
1.95
2.96
2.75
1.00
4.26
1.56
2.05
16.65
3.28
2.88
f1 (ppm)

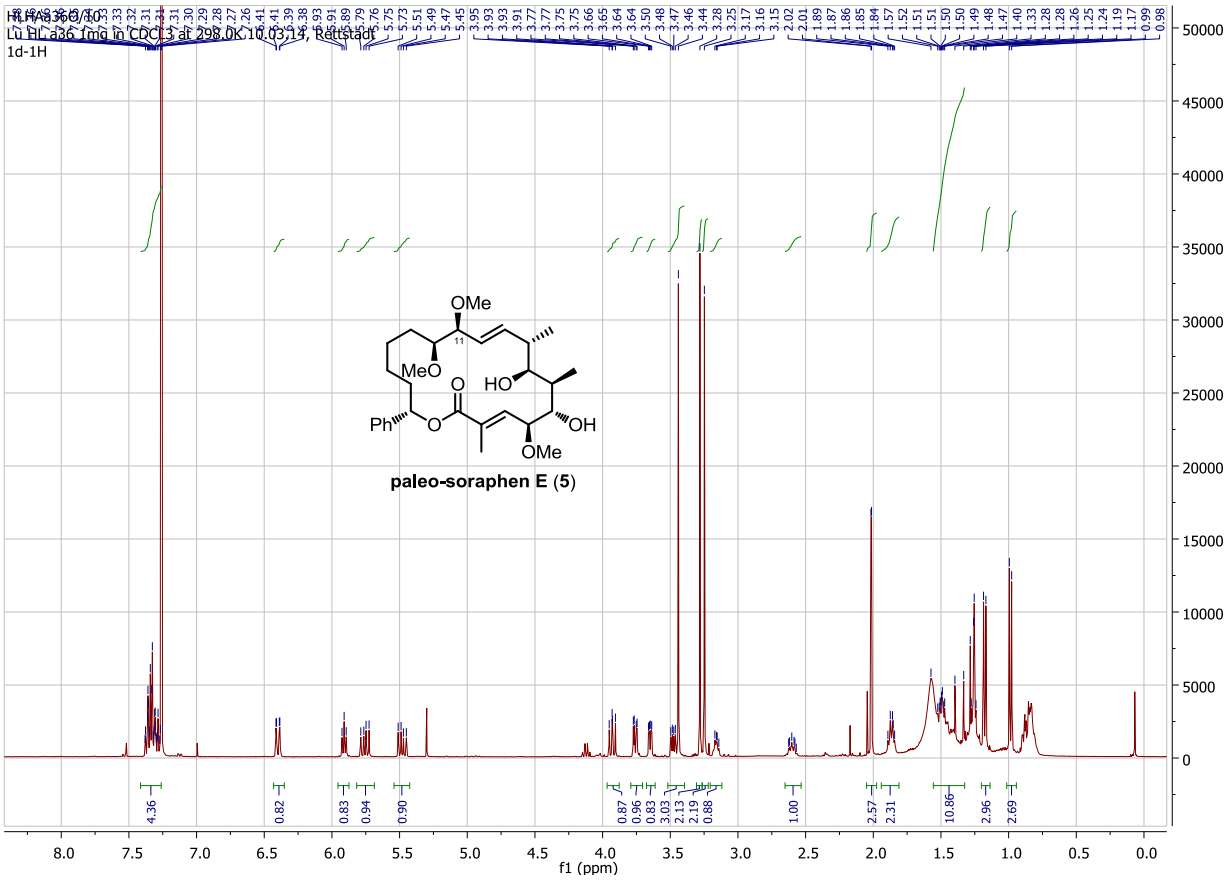

HLCL938D/10
Haihua Lu HL 938 ~1,2mg in CDCl3 at 298.0K 20.03.2014 Koertje
13C-BB
140.85
137.25
128.69
128.54
127.88
126.00
80.93
79.21
78.68
77.32
77.20
77.00
76.80
76.68
75.84
69.44
57.28
56.82
36.78
36.27
35.26
29.13
26.55
25.33
24.12
15.19
13.52
8.76
f1 (ppm)

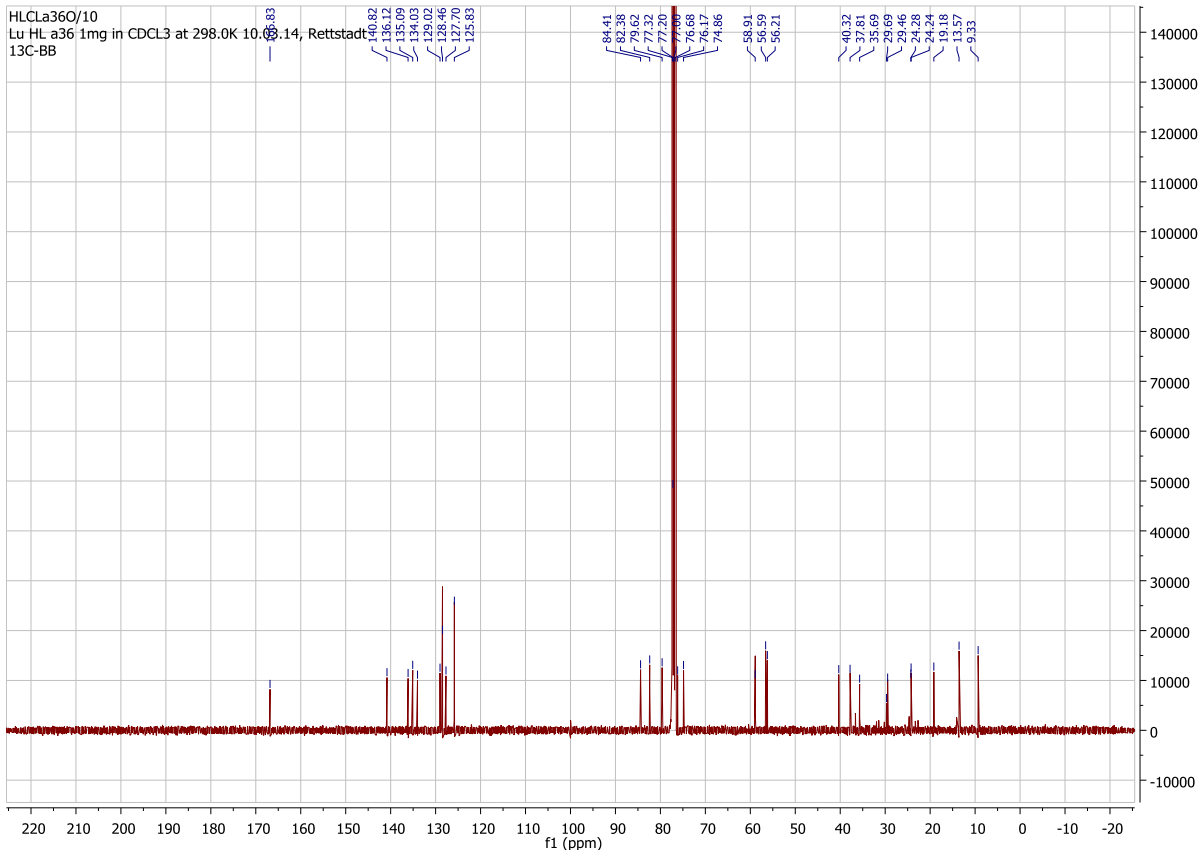

HLCL893J/10
HL893
CDCl3,400 MHz
OAc
OMe
Ph
MeO
TBSO
EtO2C
OTBS
OMe
SI-10
f1 (ppm)

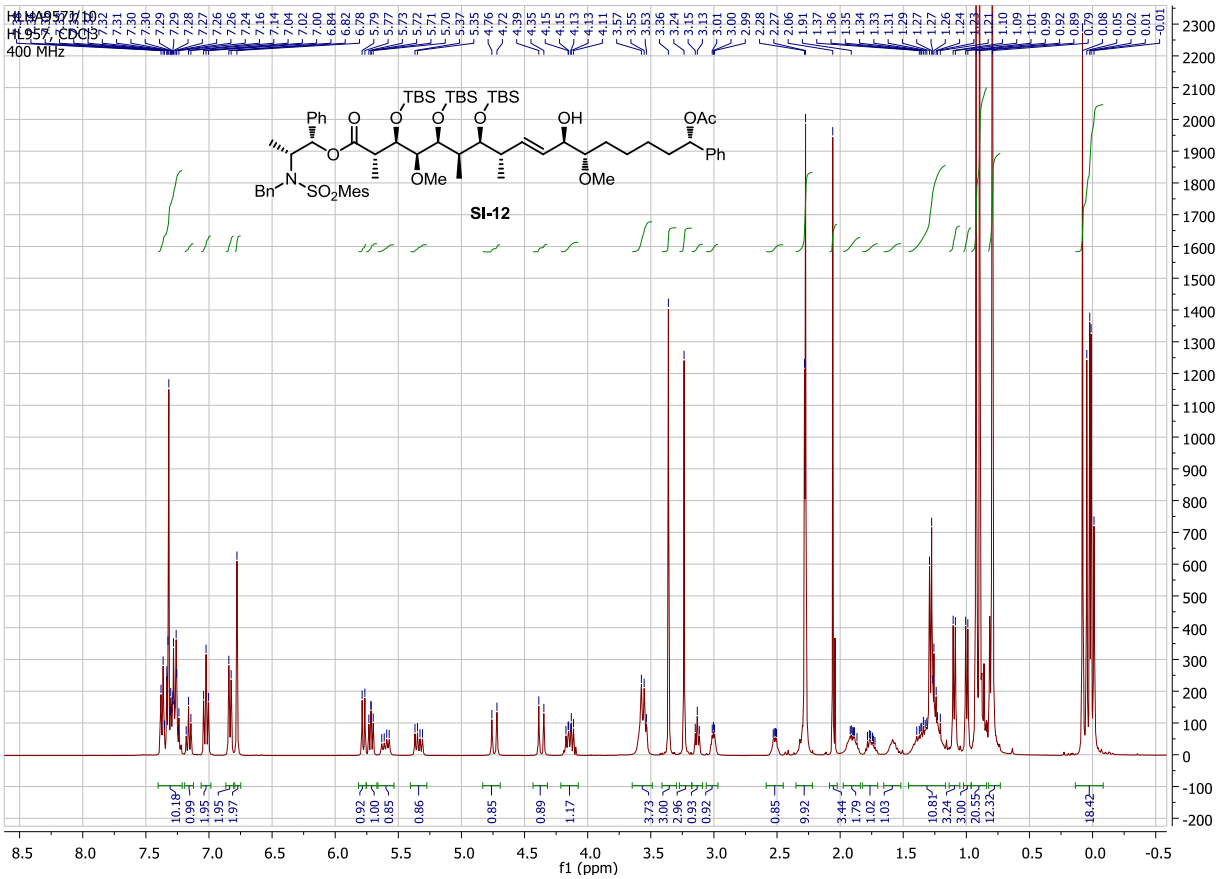

HLCL893J/10
HL893
CDCl3,100 MHz
f1 (ppm)

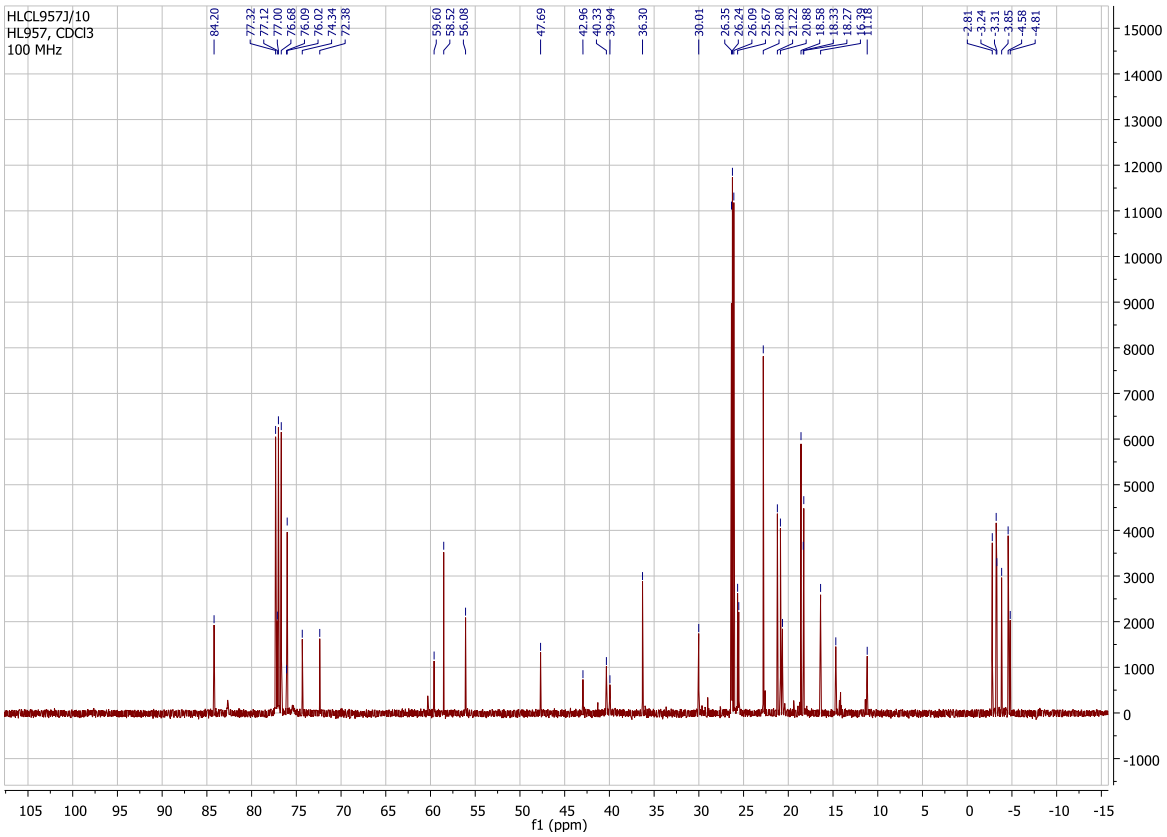

HLCL894J/10
HL894, CDCl3
400 MHz
OH
OMe
Ph
MeO
TBSO
HO2C
OTBS
OMe
SI-11
f1 (ppm)

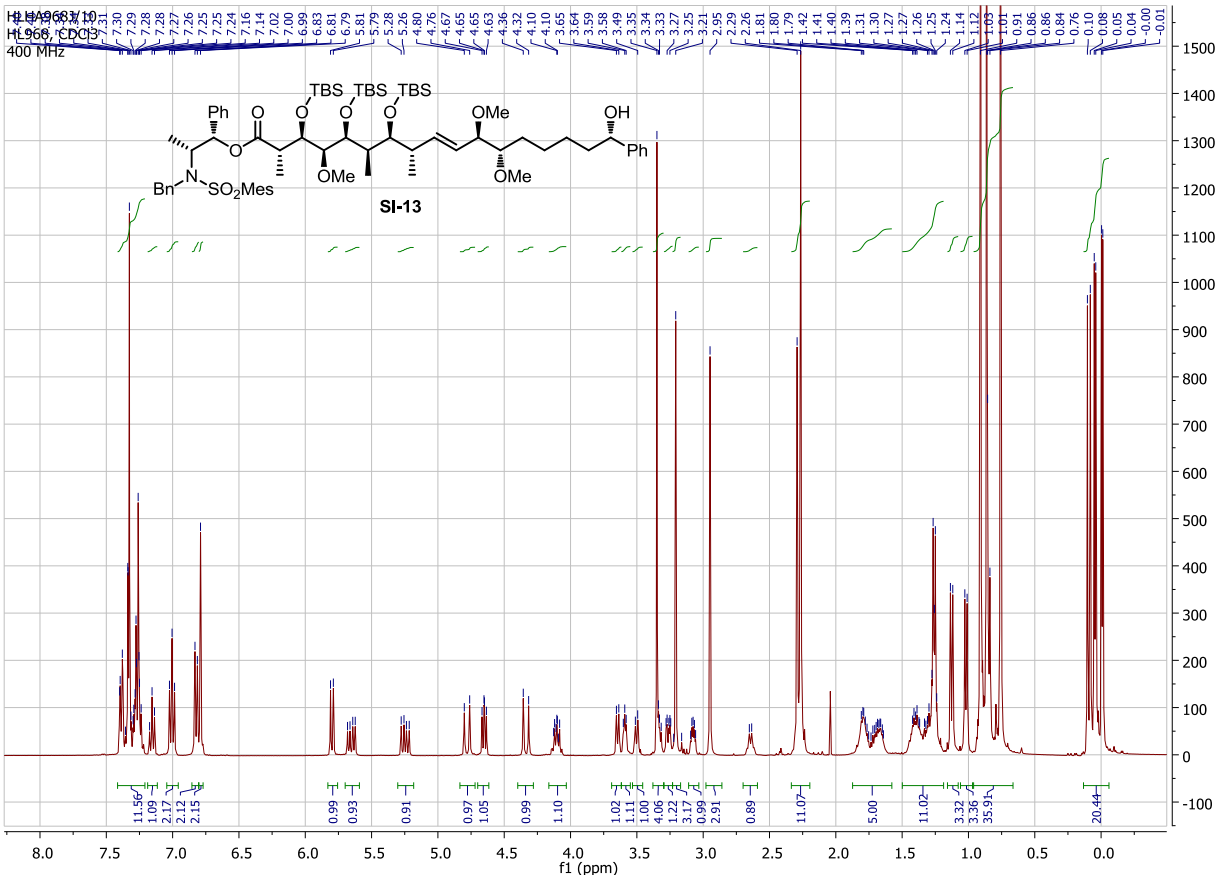

HLCL894J/10
HL894, CDCl3
100 MHz
f1 (ppm)

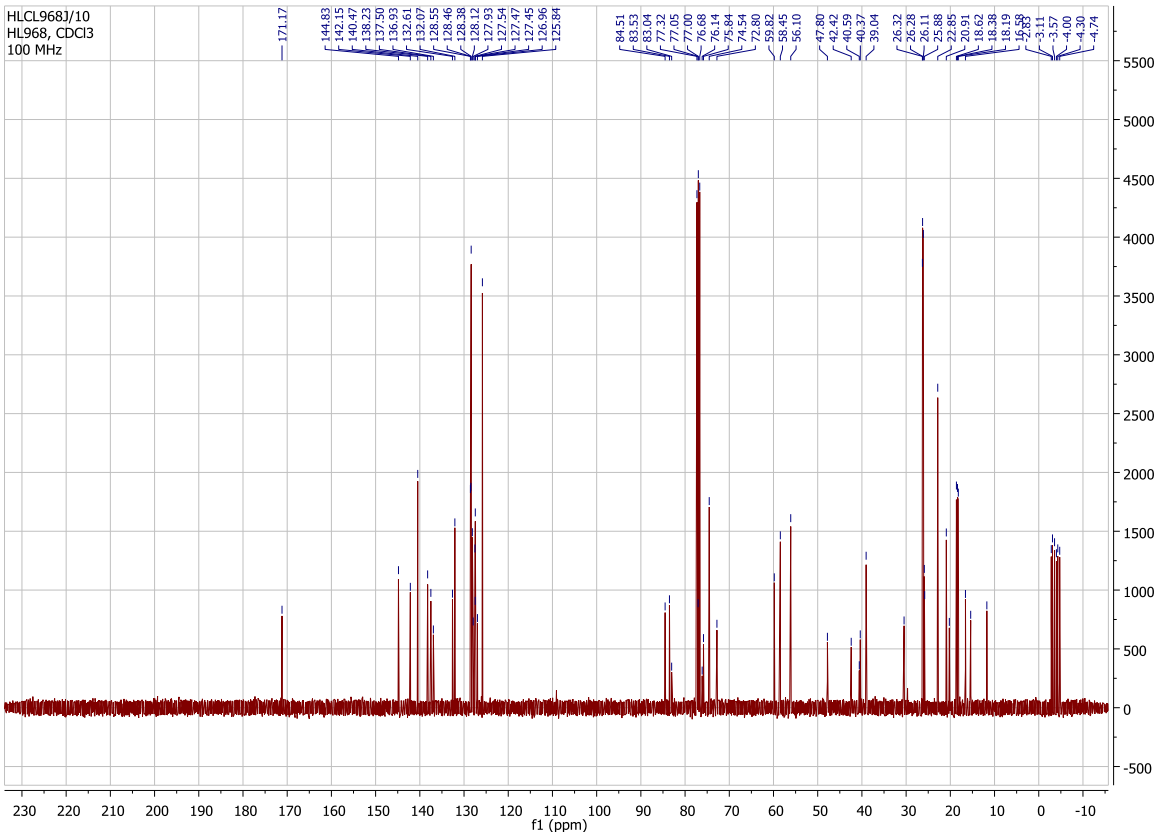

HLHa36O/10
Lu HL a36 1mg in CDCL3 at 298.0K 10.03.14, Rettstadt
1d-1H
OMe
MeO
HO
O
Ph
O
OH
OMe
paleo-soraphen E (5)
f1 (ppm)

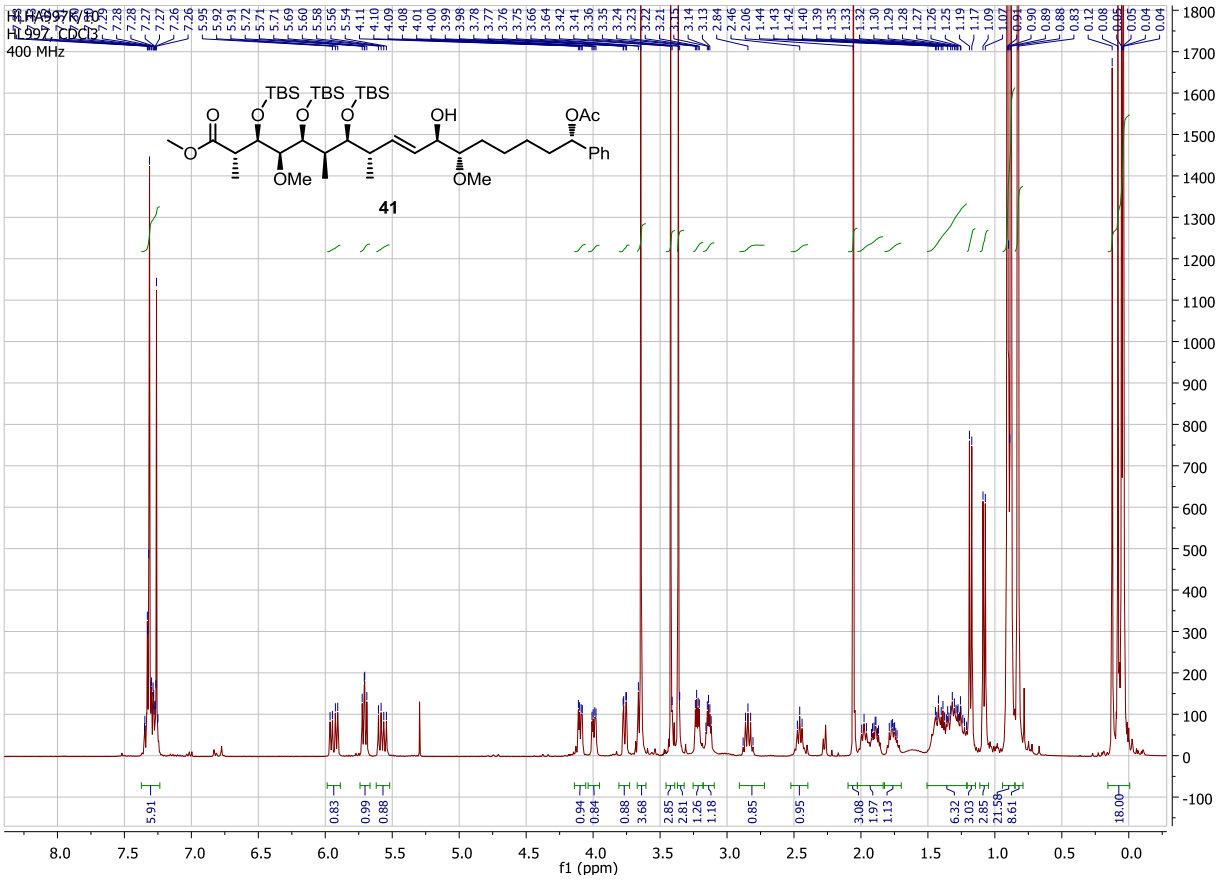

HLCLa36O/10
Lu HL a36 1mg in CDCL3 at 298.0K 10.03.14, Rettstadt
13C-BB
f1 (ppm)

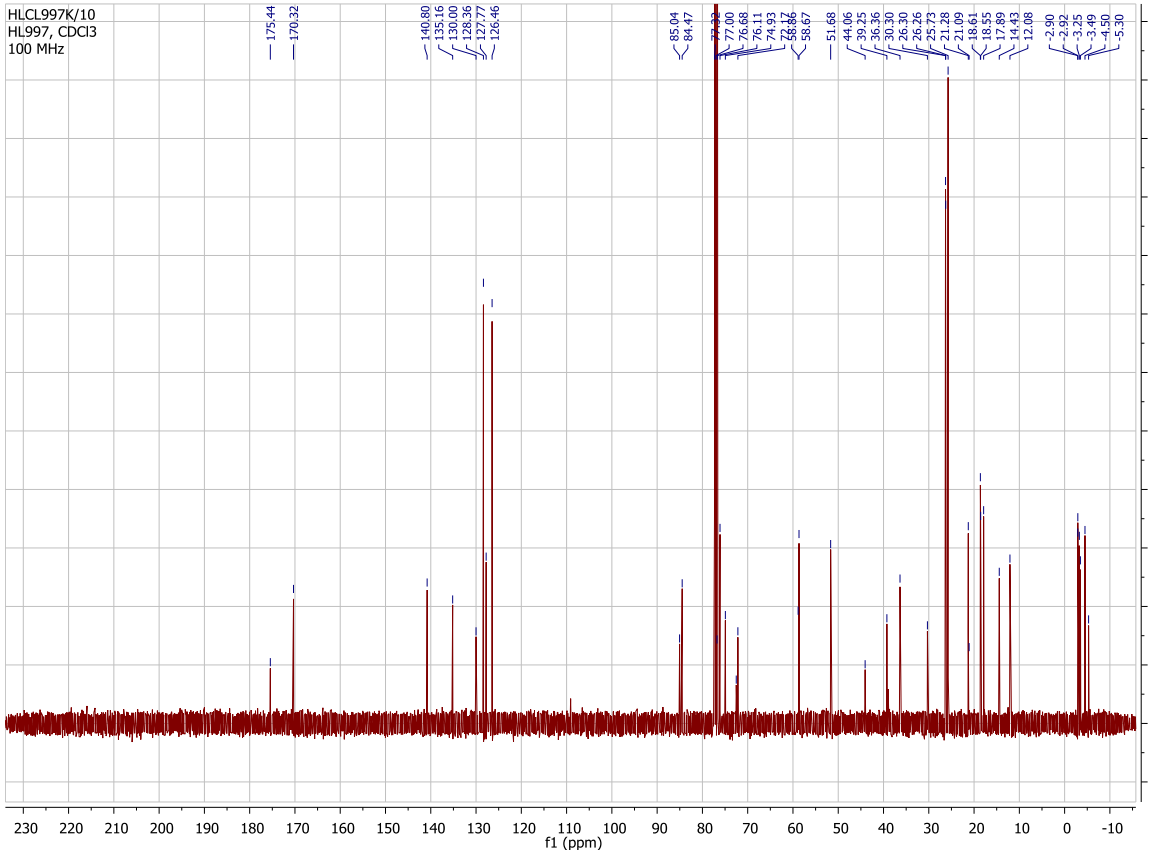

HLAA957J/10
HL957, CDCl3
400 MHz
TBS TBS TBS
Ph
O
O
O
O
O
OH
OAc
Ph
Bn
N
SO2Mes
OMe
OMe
SI-12
f1 (ppm)

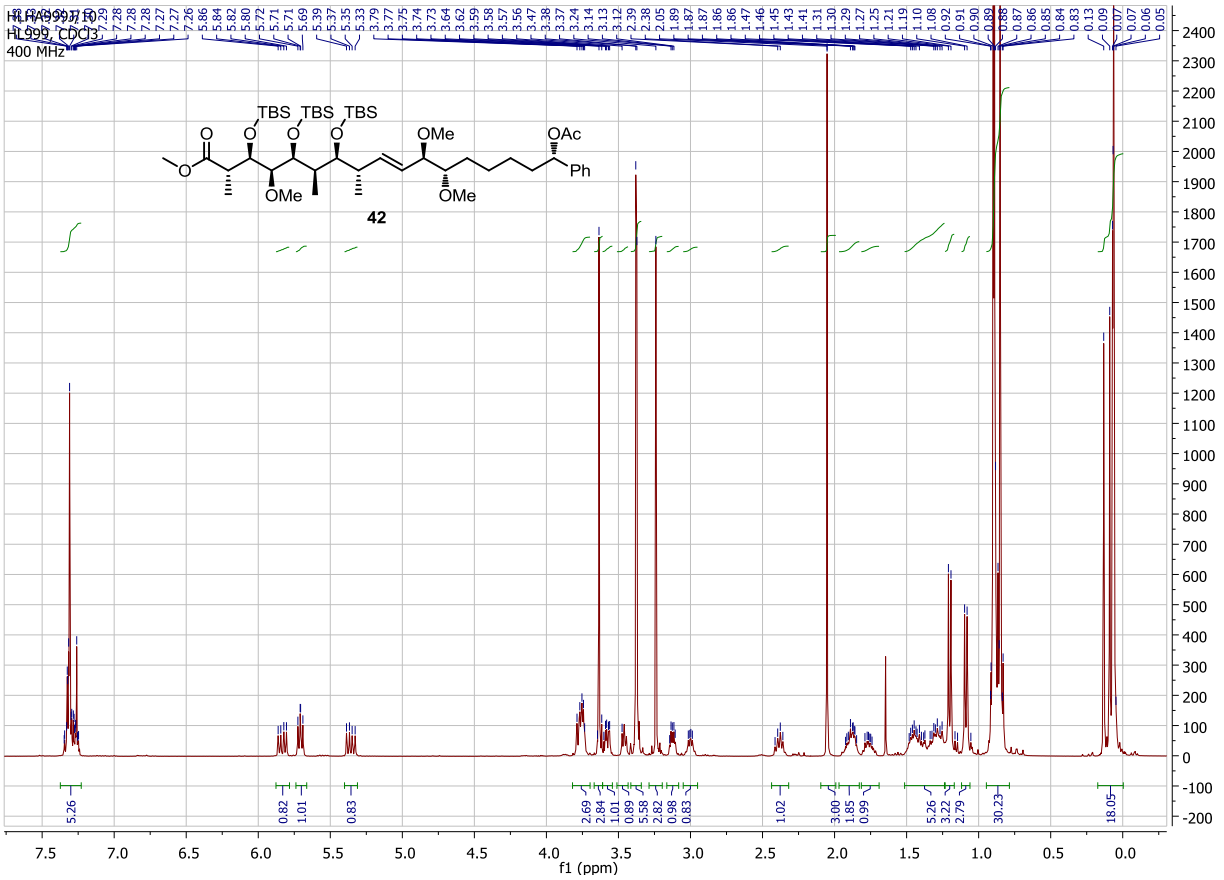

HLCL957J/10
HL957, CDCl3
100 MHz
f1 (ppm)

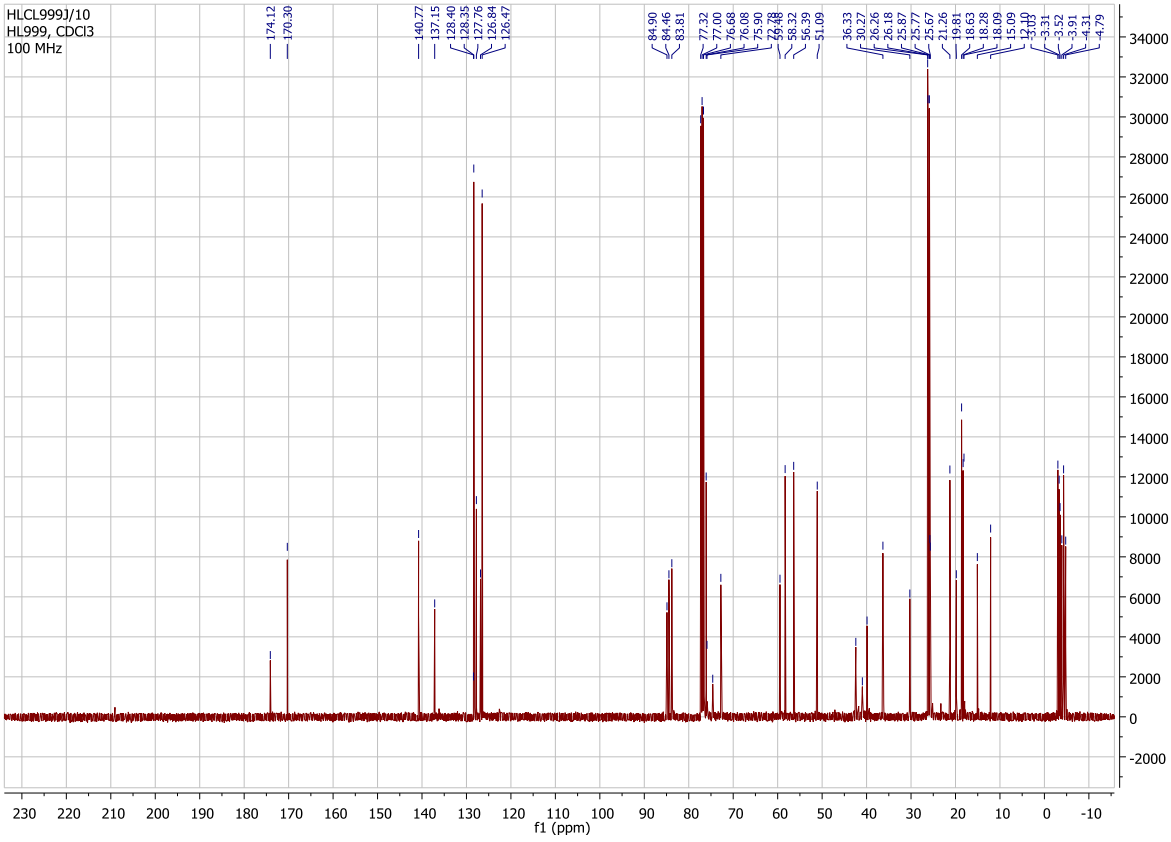

HLLA9683/10
HL968, CDCl3
400 MHz
TBS TBS TBS
Ph
O
O
O
O
OMe
OH
Ph
N
Bn
SO2Mes
OMe
OMe
SI-13
f1 (ppm)

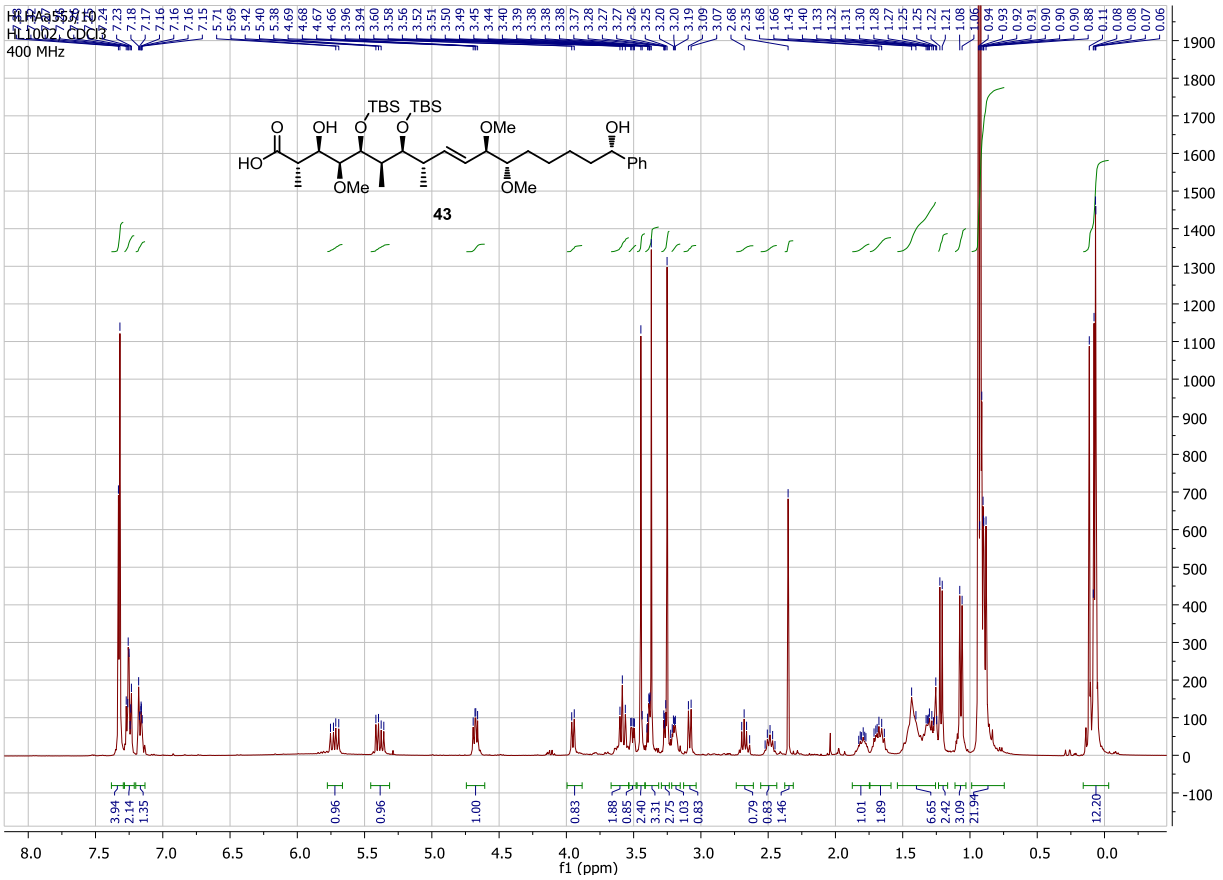

HLCL968J/10
HL968, CDCl3
100 MHz
f1 (ppm)

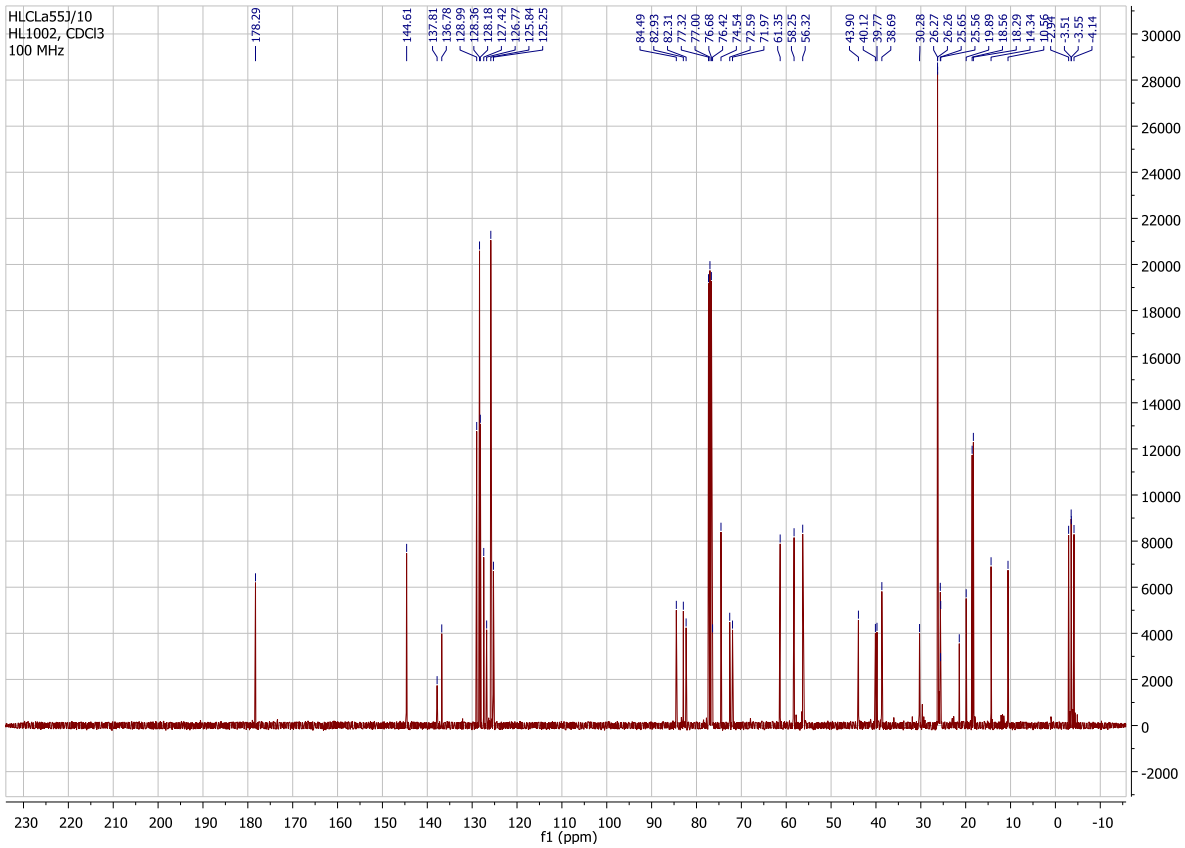

HLCL997K/10
HL997, CDCl3
400 MHz
TBS TBS TBS
OH
OAc
Ph
OMe
OMe
41
f1 (ppm)

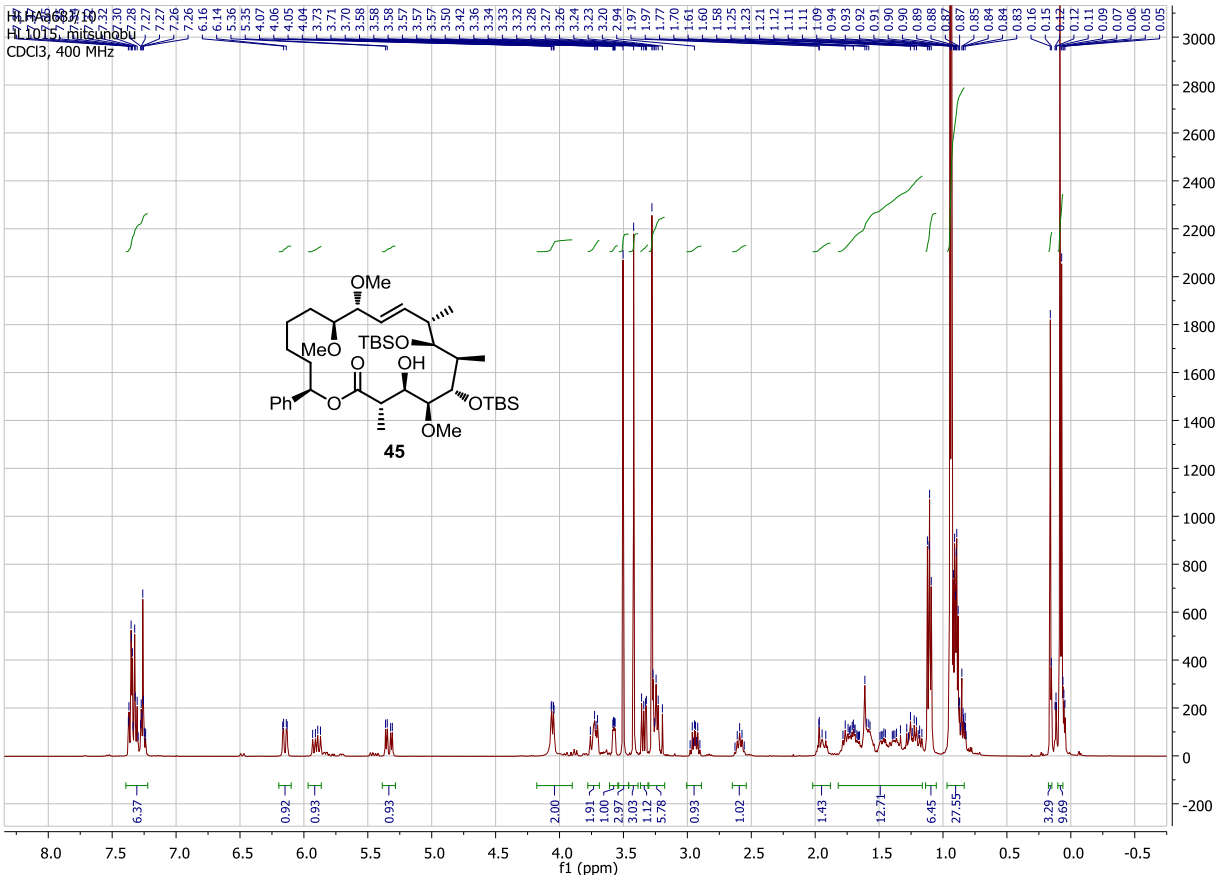

HLCL997K/10
HL997, CDCl3
100 MHz
f1 (ppm)

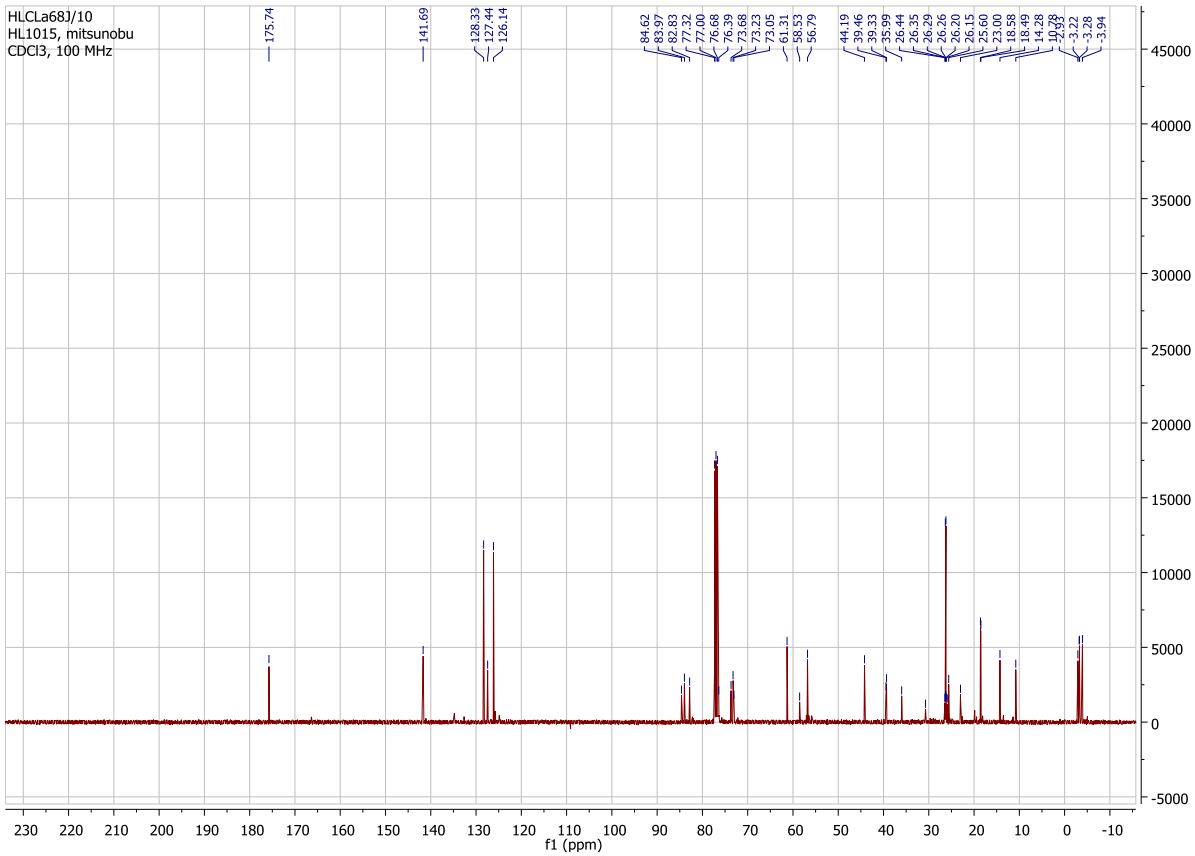

HLCL999J/10
HL999, CDCl3
400 MHz
TBS TBS TBS
OMe
OAc
Ph
OMe
OMe
42
f1 (ppm)

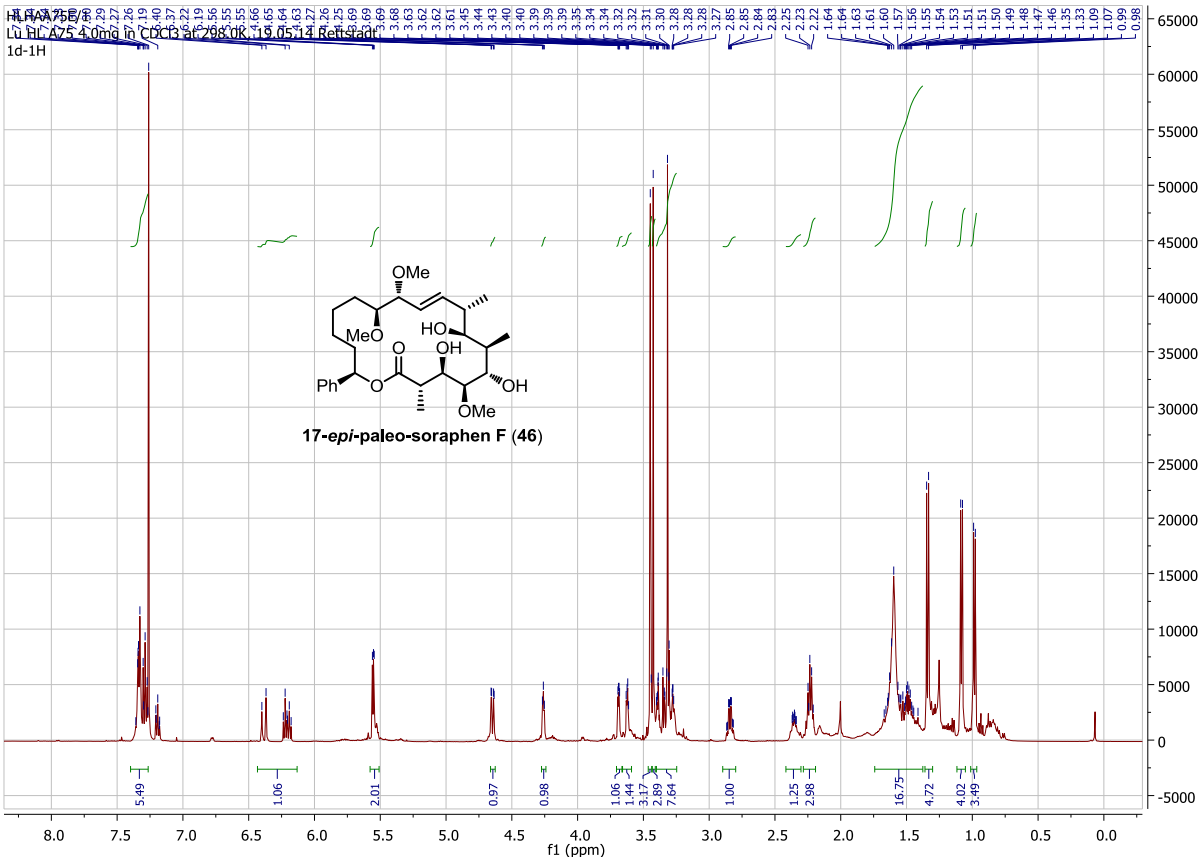

HLCL999J/10
HL999, CDCl3
100 MHz
f1 (ppm)

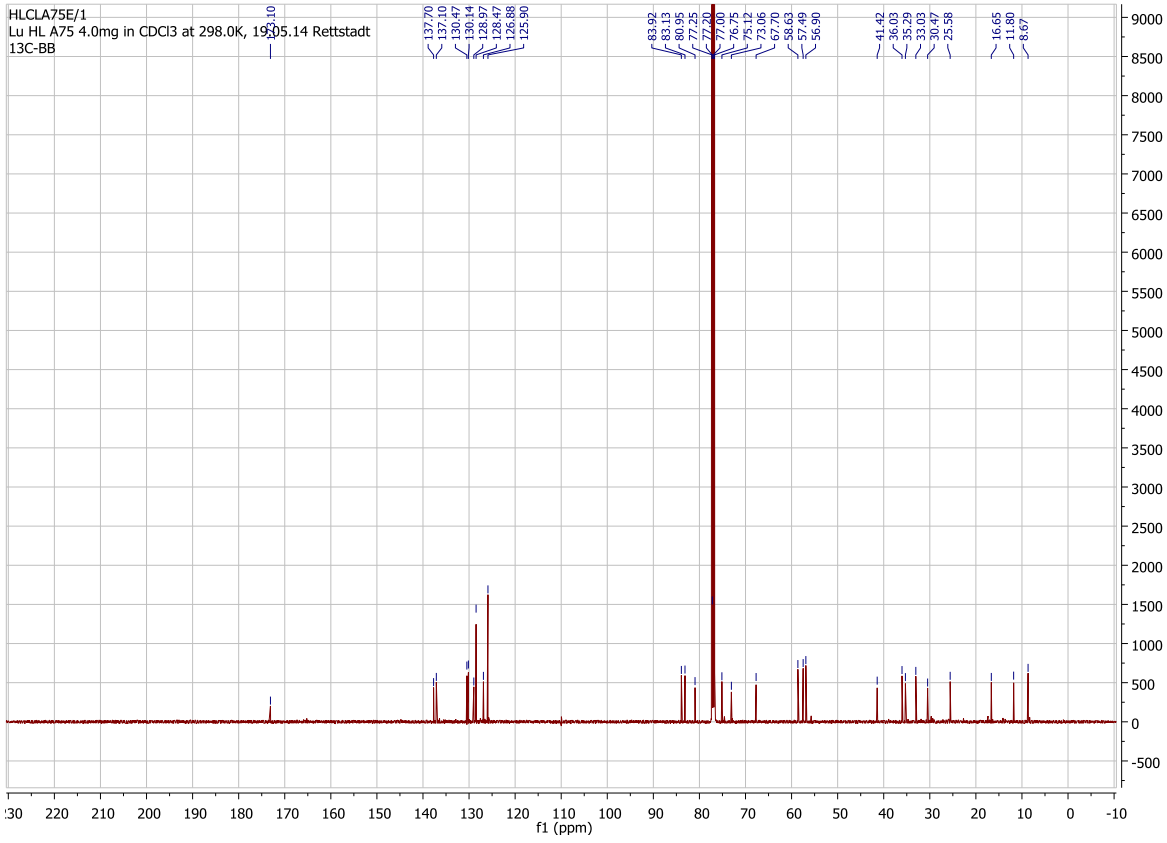

HLCLa55J/10
HL1002, CDCl3
400 MHz
TBS TBS
O
OH
O
O
OMe
OH
HO
Ph
OMe
OMe
43
f1 (ppm)

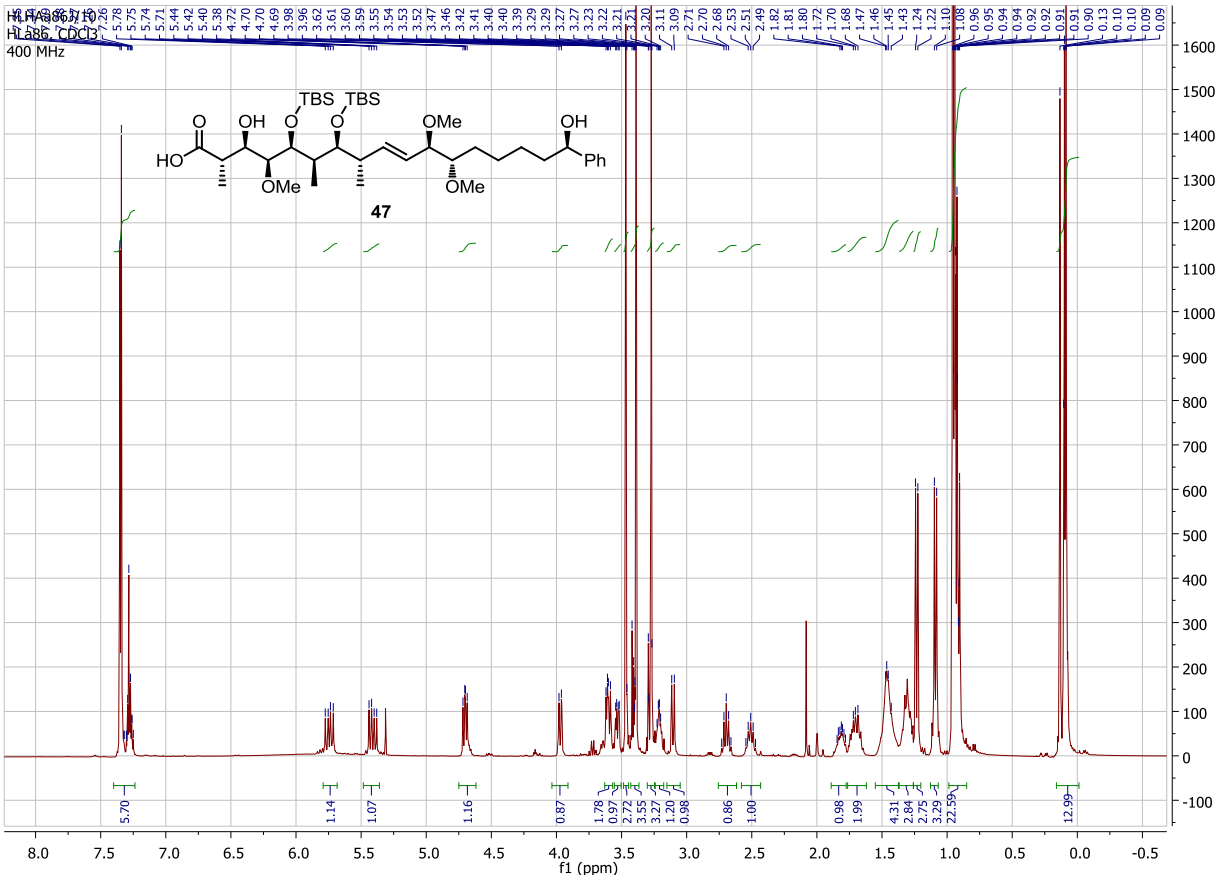

HLCLa55J/10
HL1002, CDCl3
100 MHz
f1 (ppm)

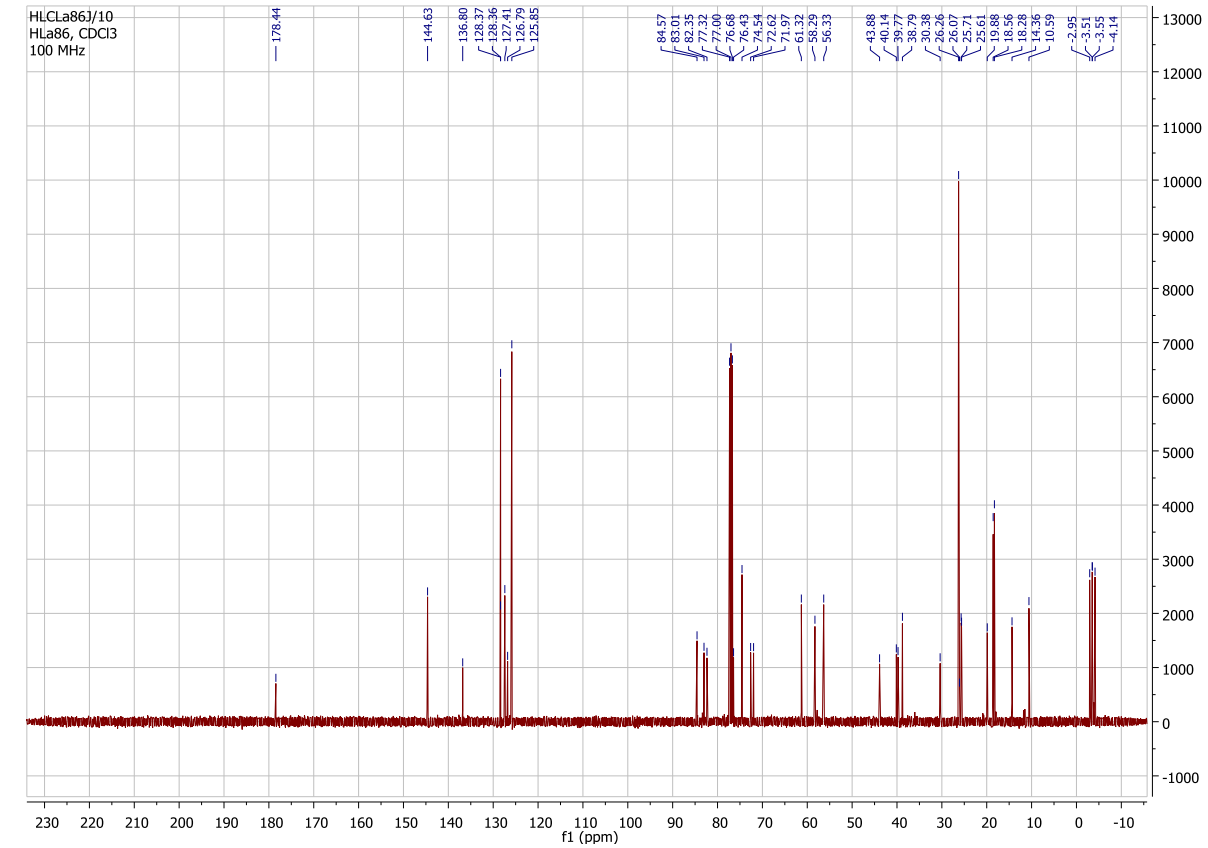

HLHA68J/10
HL1015, mitsunobu
CDCl3, 400 MHz
OMe
MeO
TBSO
O
OH
Ph
O
OTBS
OMe
45
f1 (ppm)

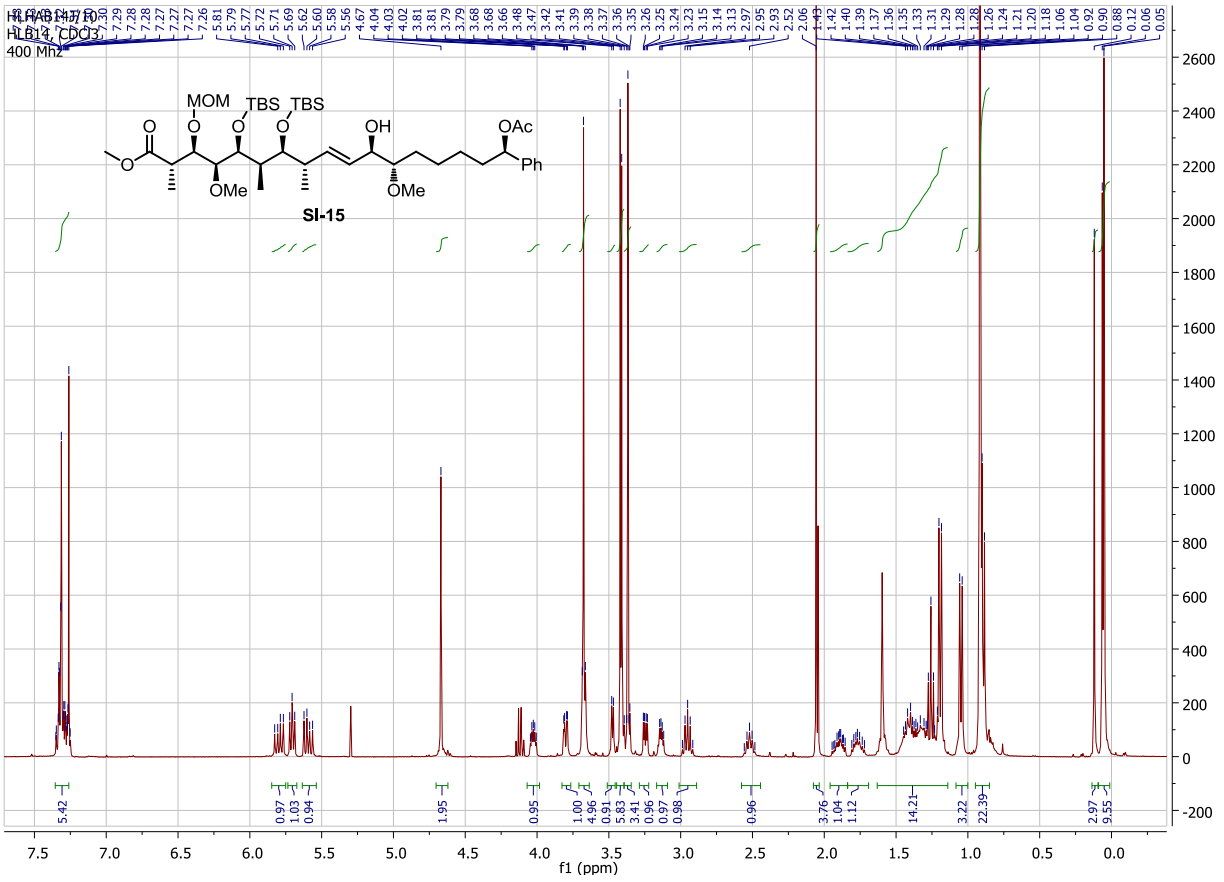

HLCLa68J/10
HL1015, mitsunobu
CDCl3, 100 MHz
f1 (ppm)

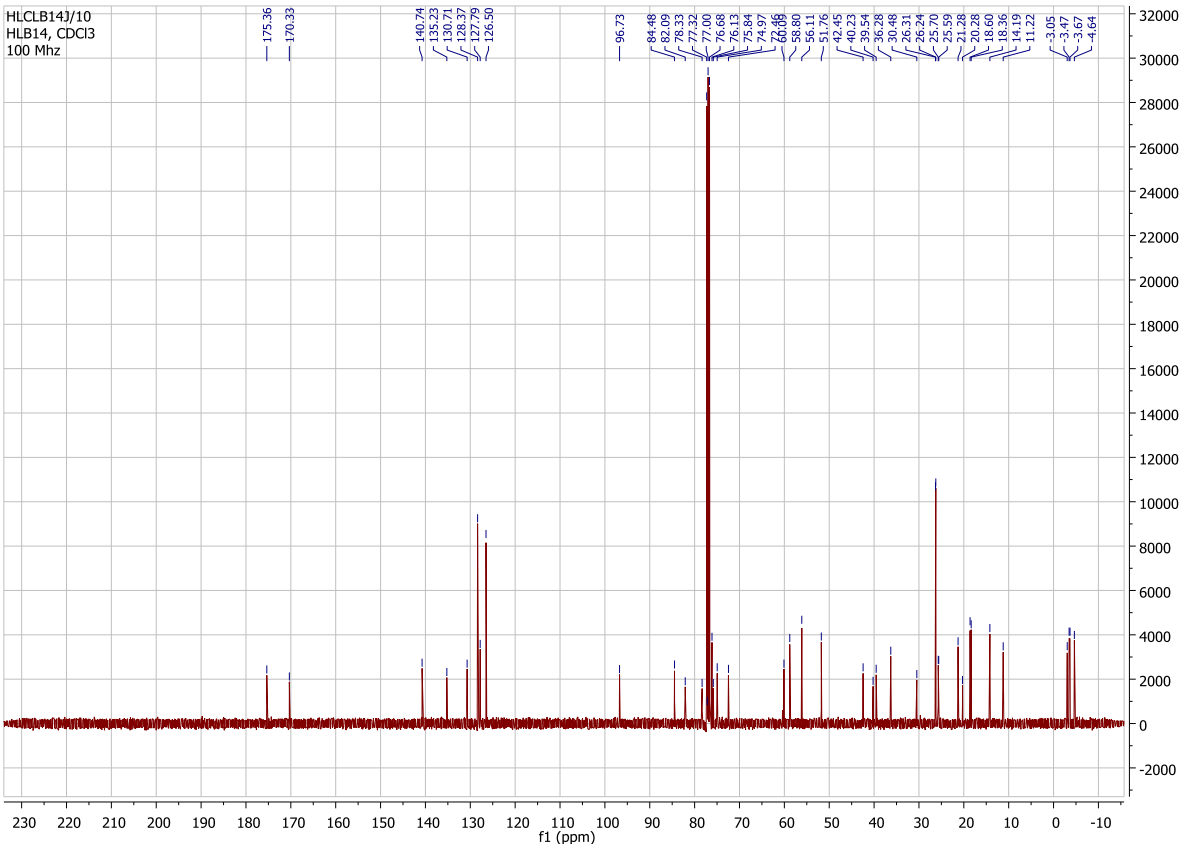

HLCLA75E/1
Lu HL A75 4.0mg in CDCl3 at 298.0K, 19.05.14 Rettstadt
1d-1H
OMe
MeO
HO
O
OH
Ph
O
OH
OMe
17-epi-paleo-soraphen F (46)
f1 (ppm)

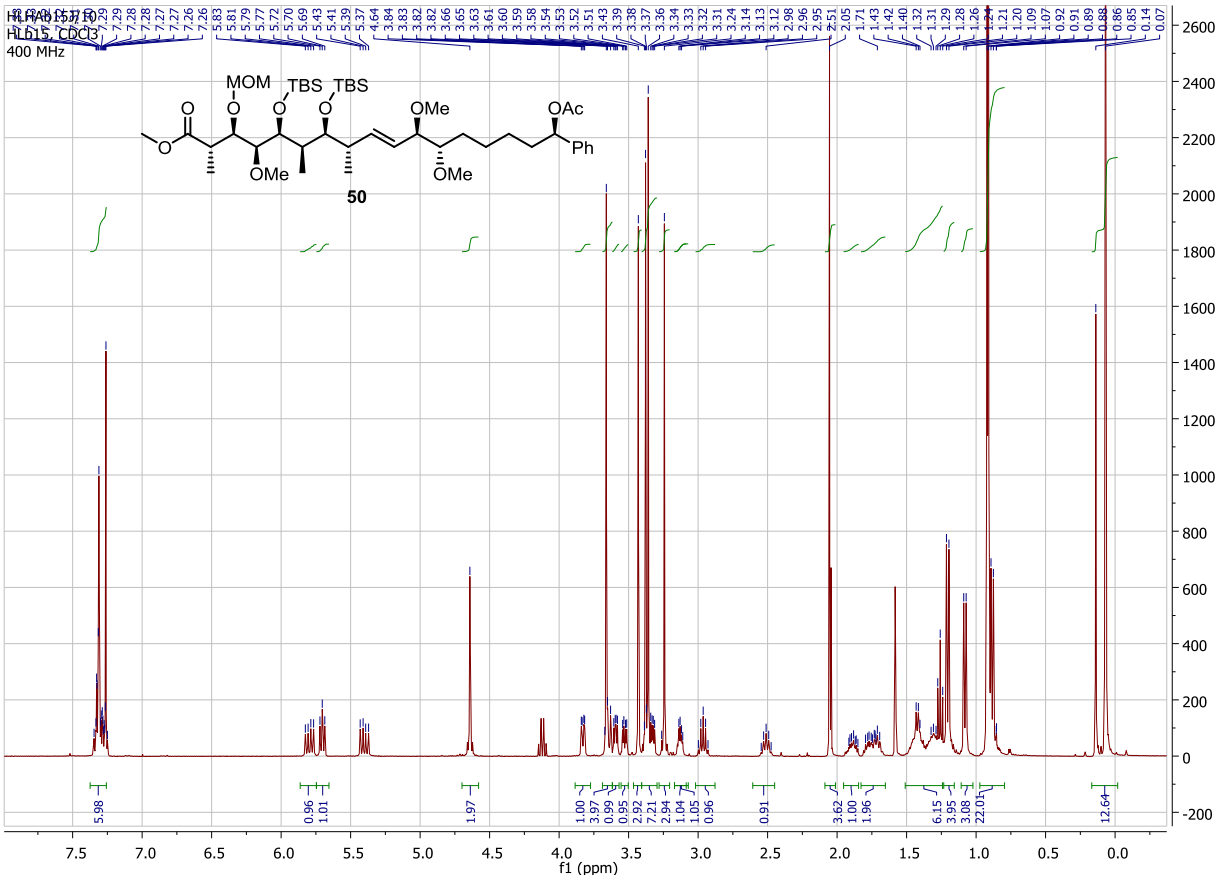

HLCLA75E/1
Lu HL A75 4.0mg in CDCl3 at 298.0K, 19.05.14 Rettstadt
13C-BB
f1 (ppm)

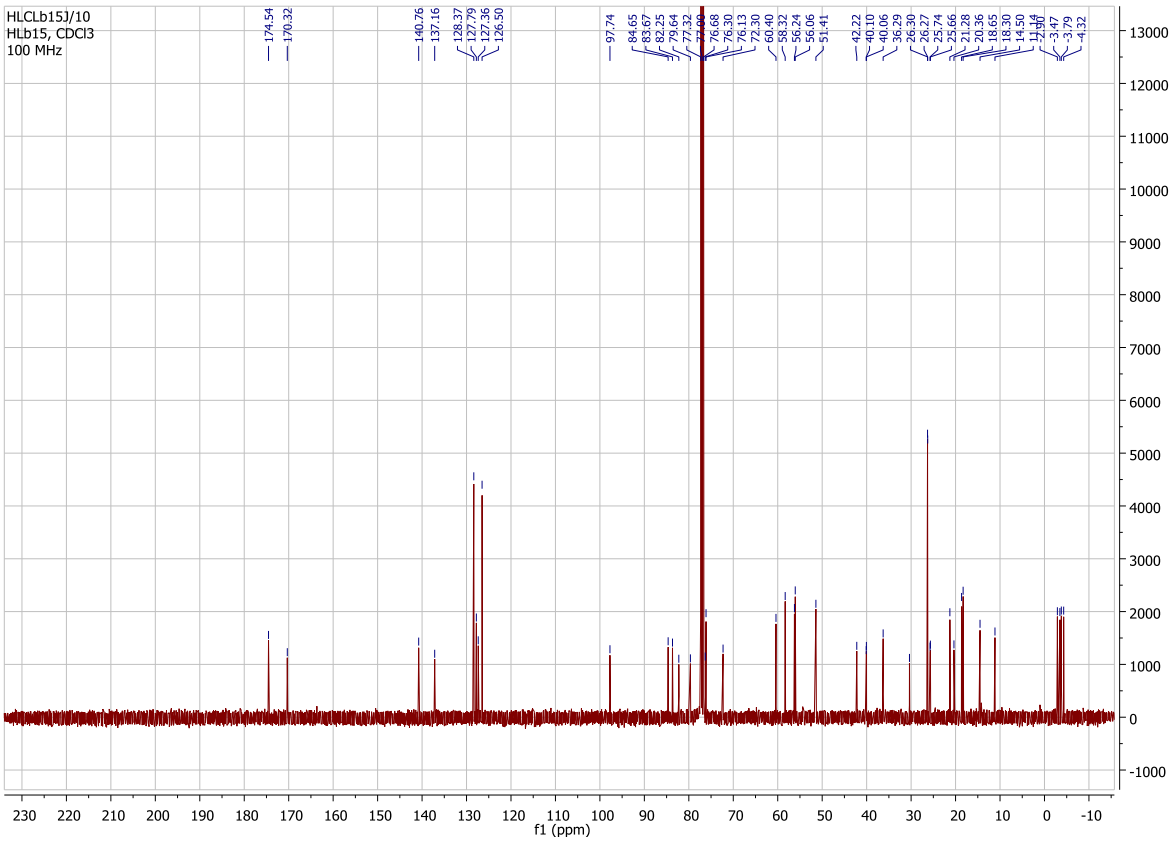

HLCLa86J/10
HLa86, CDCl3
400 MHz
TBS TBS
O
OH
O
O
OMe
OH
HO
Ph
OMe
OMe
47
f1 (ppm)

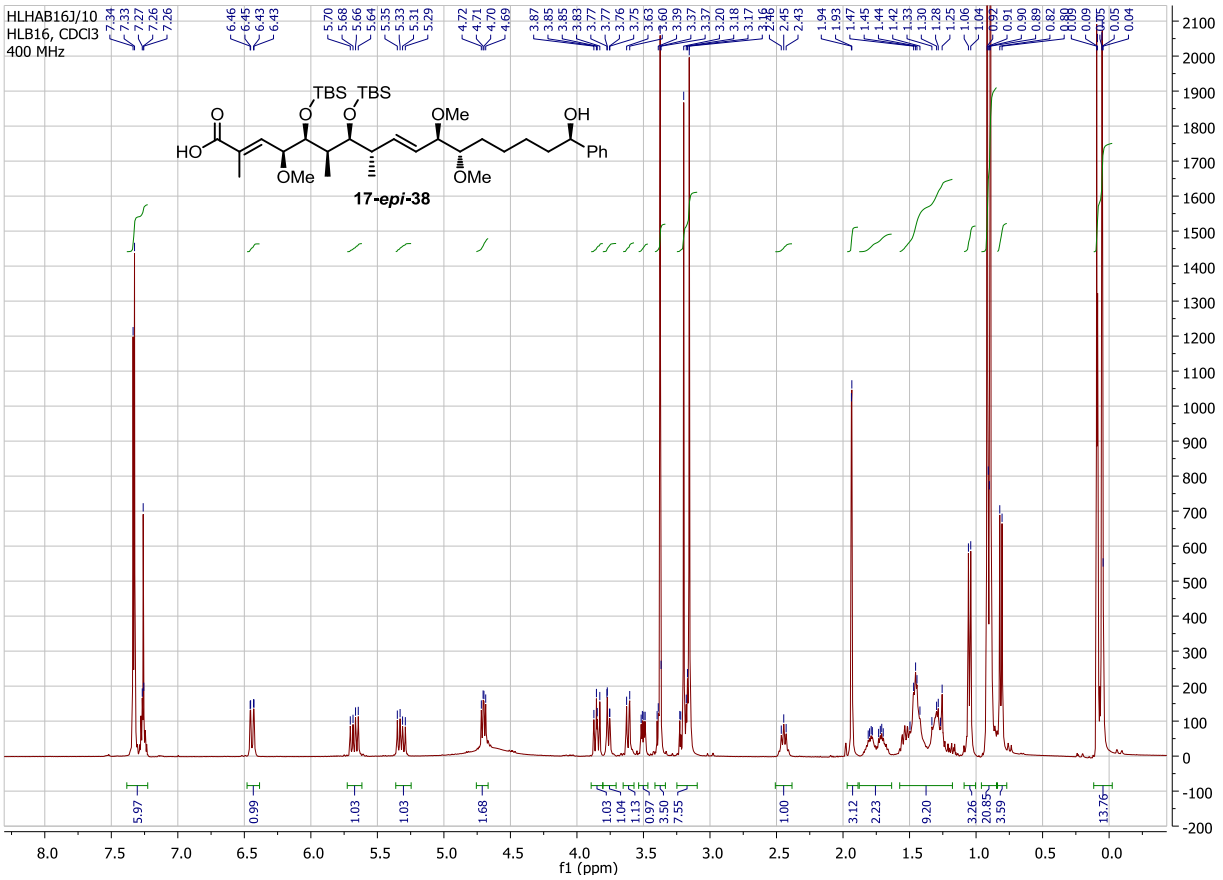

HLCLa86J/10
HLa86, CDCl3
100 MHz
f1 (ppm)

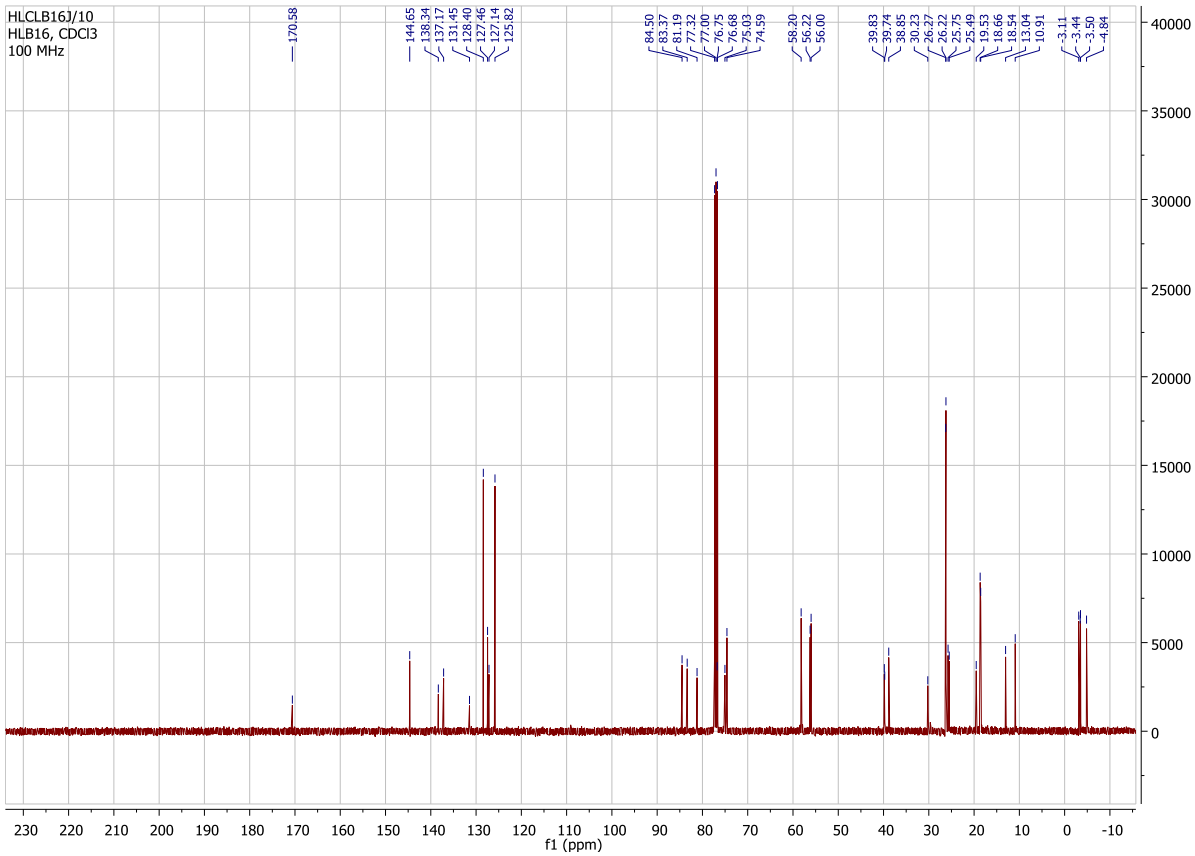

HLCLB14J/10
HLB14, CDCl3
400 Mhz
MOM
TBS
TBS
OH
OAc
Ph
OMe
OMe
SI-15
f1 (ppm)

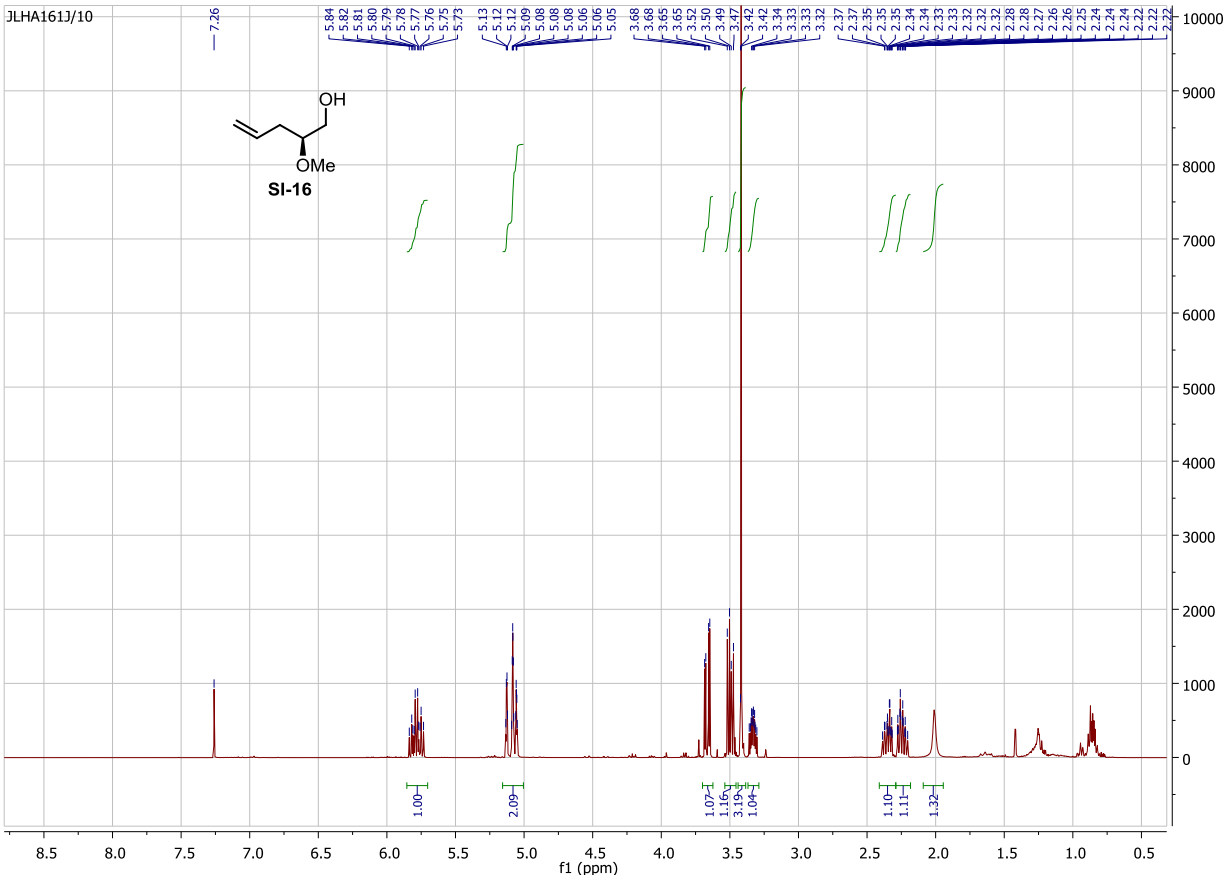

HLCLB14J/10
HLB14, CDCl3
100 Mhz
f1 (ppm)

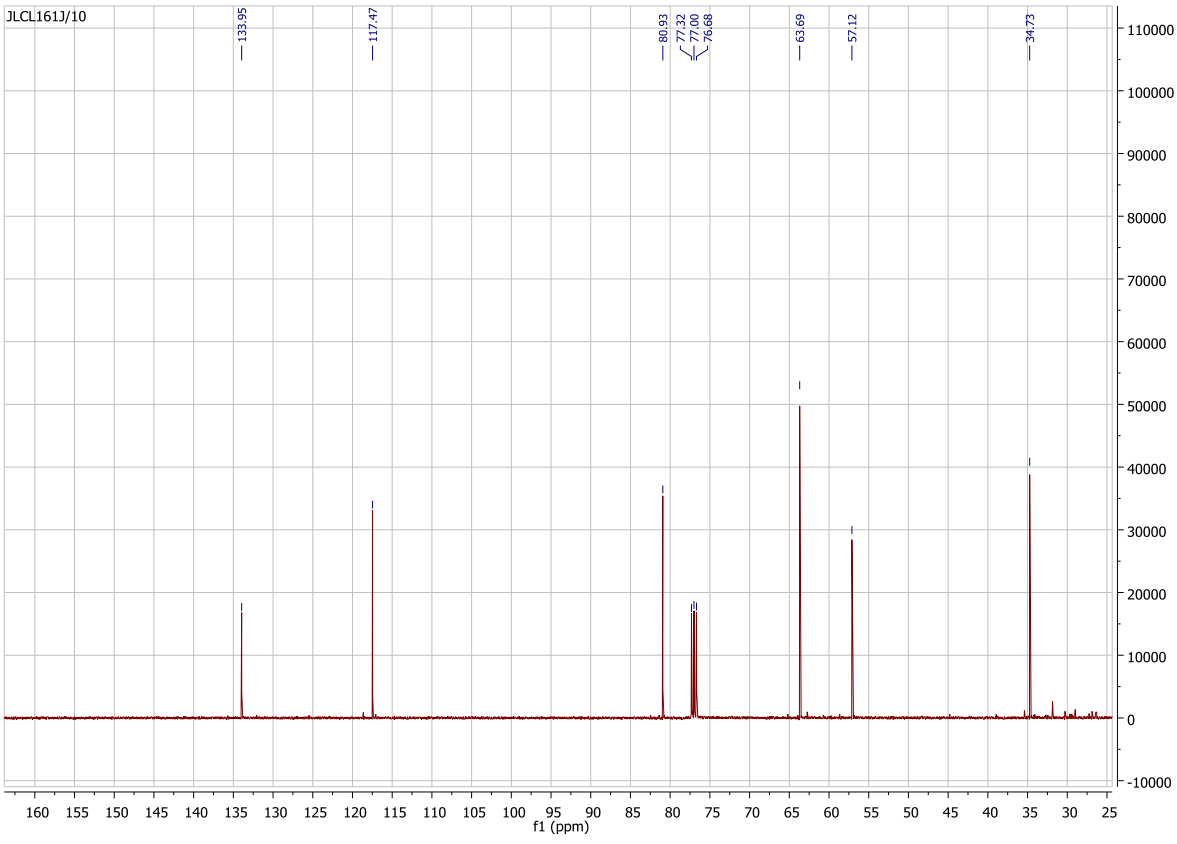

HLCLb15J/10
HLb15, CDCl3
400 MHz
MOM
TBS
TBS
OMe
OAc
Ph
OMe
OMe
50
f1 (ppm)

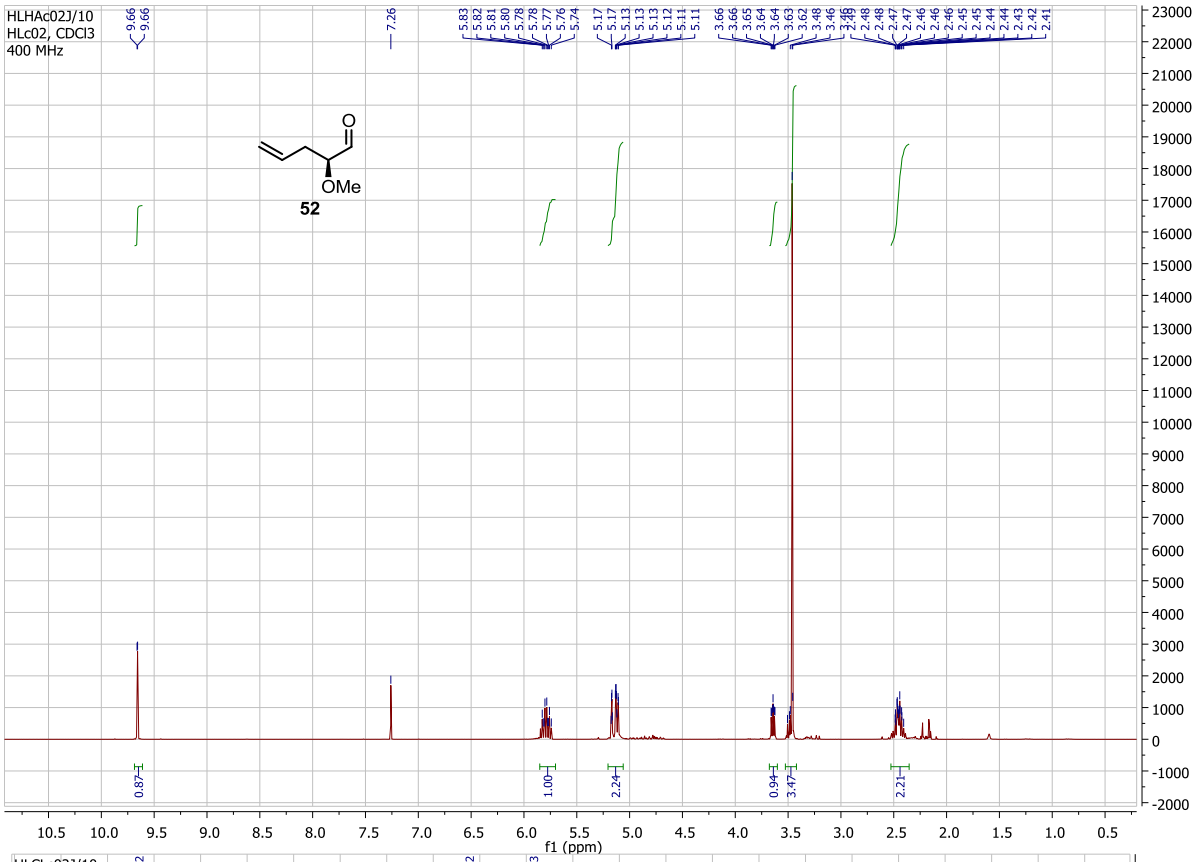

HLCLb15J/10
HLb15, CDCl3
100 MHz
f1 (ppm)

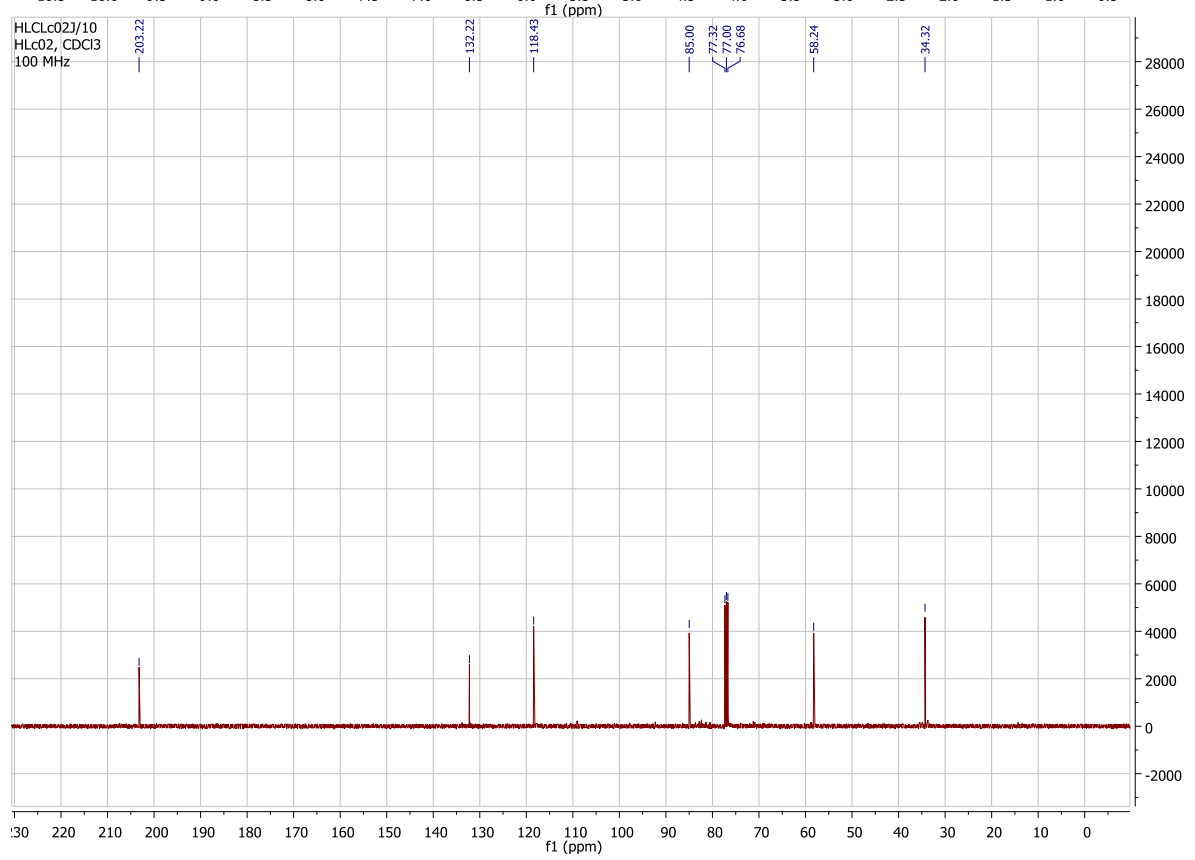

HLHAB16J/10
HLB16, CDCl3
400 MHz
TBS TBS
O
O
O
OMe
OH
HO
OMe
OMe
Ph
17-epi-38
f1 (ppm)

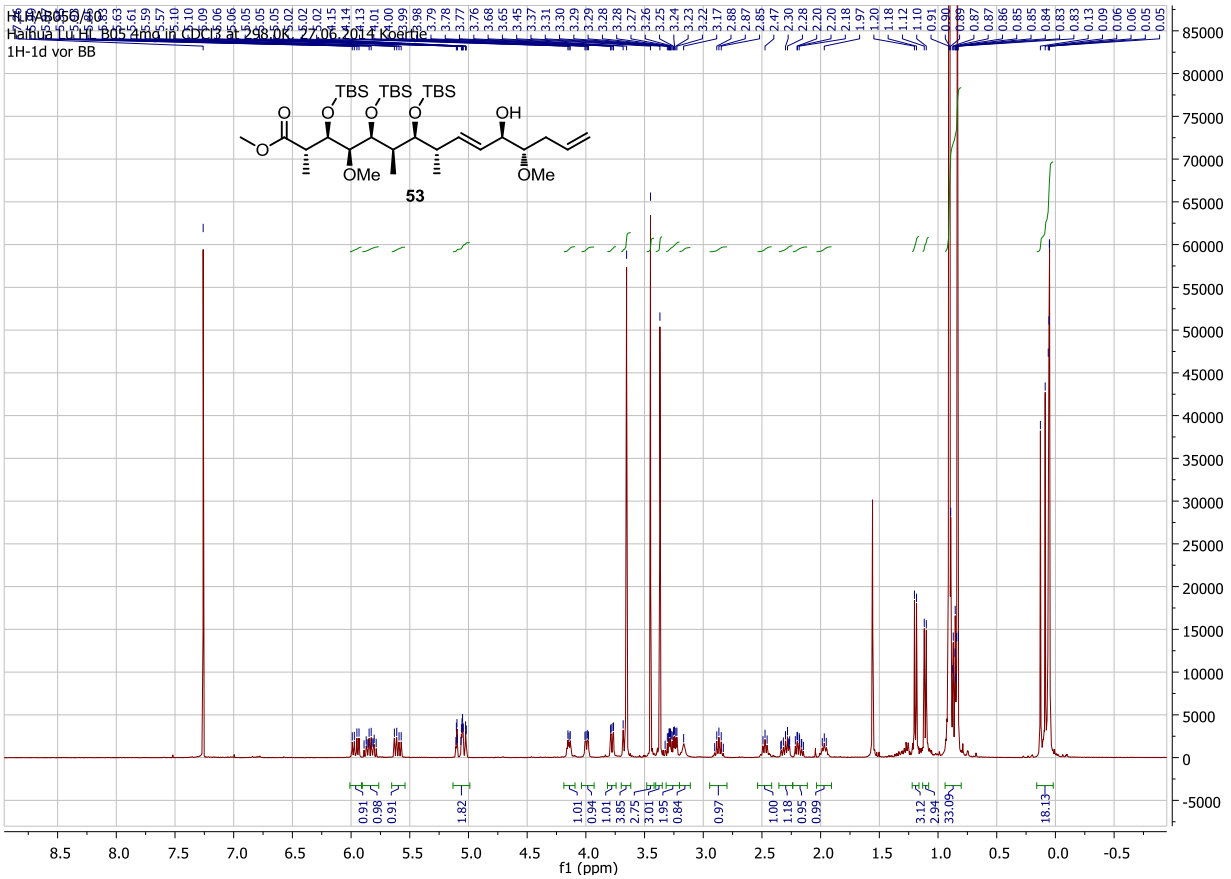

HLCLB16J/10
HLB16, CDCl3
100 MHz
f1 (ppm)

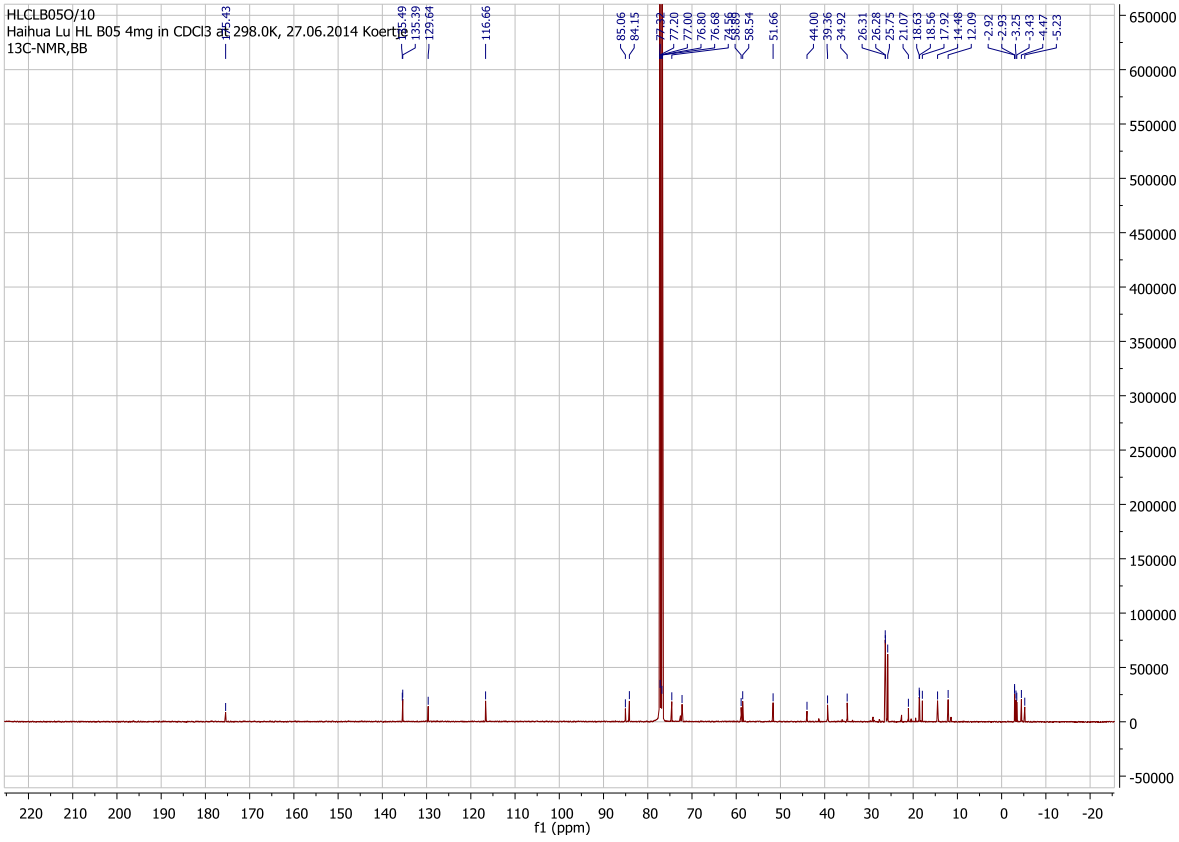

JLHA161J/10
OH
OMe
SI-16
f1 (ppm)

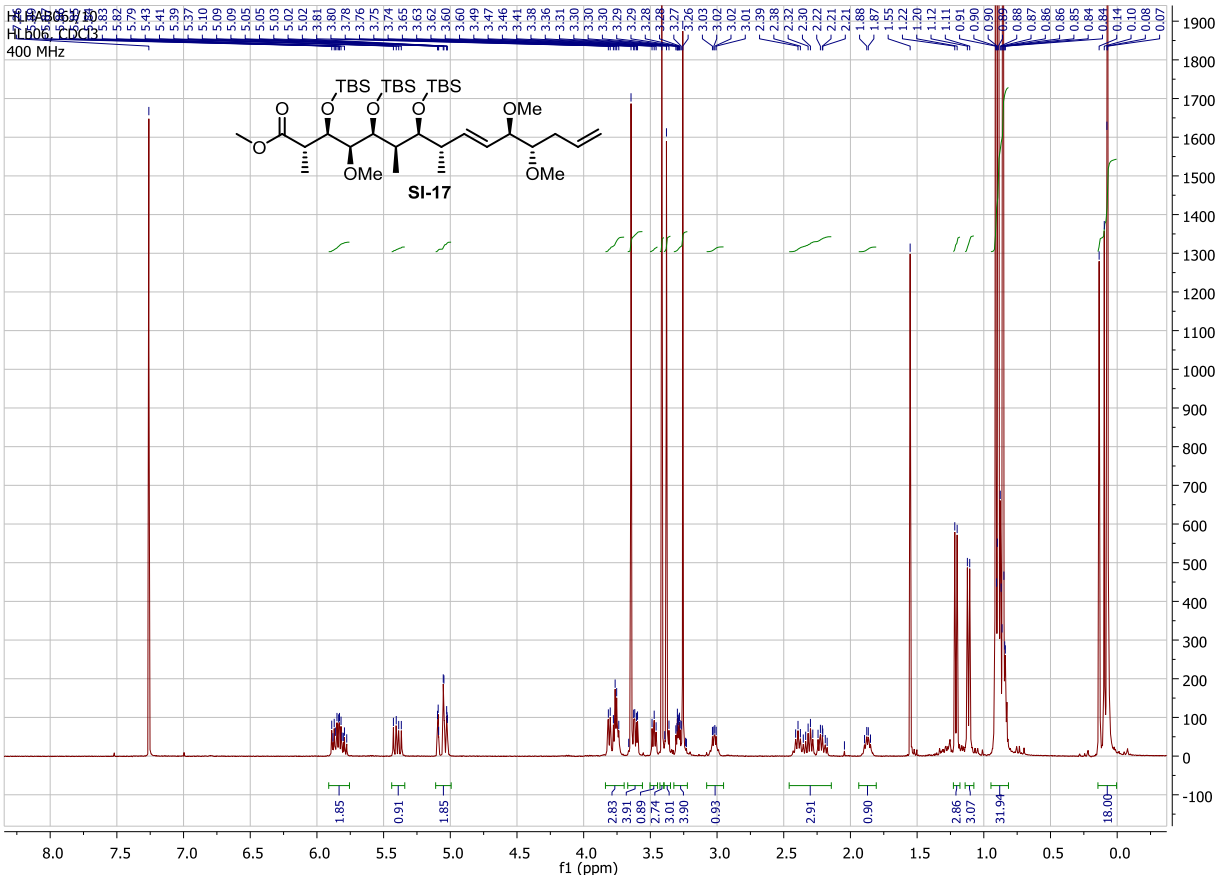

JLCL161J/10
f1 (ppm)

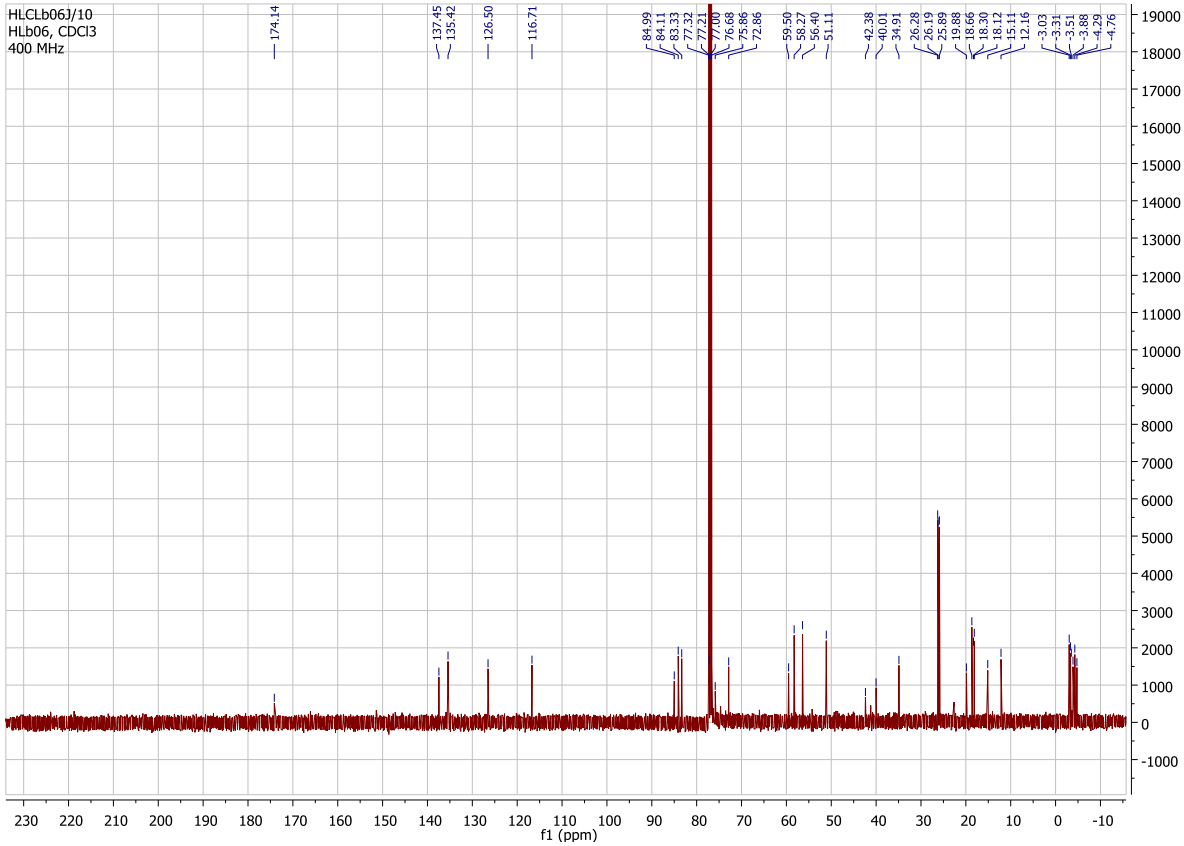

HLHAc02J/10
HLc02, CDCl3
400 MHz
OMe
52
f1 (ppm)

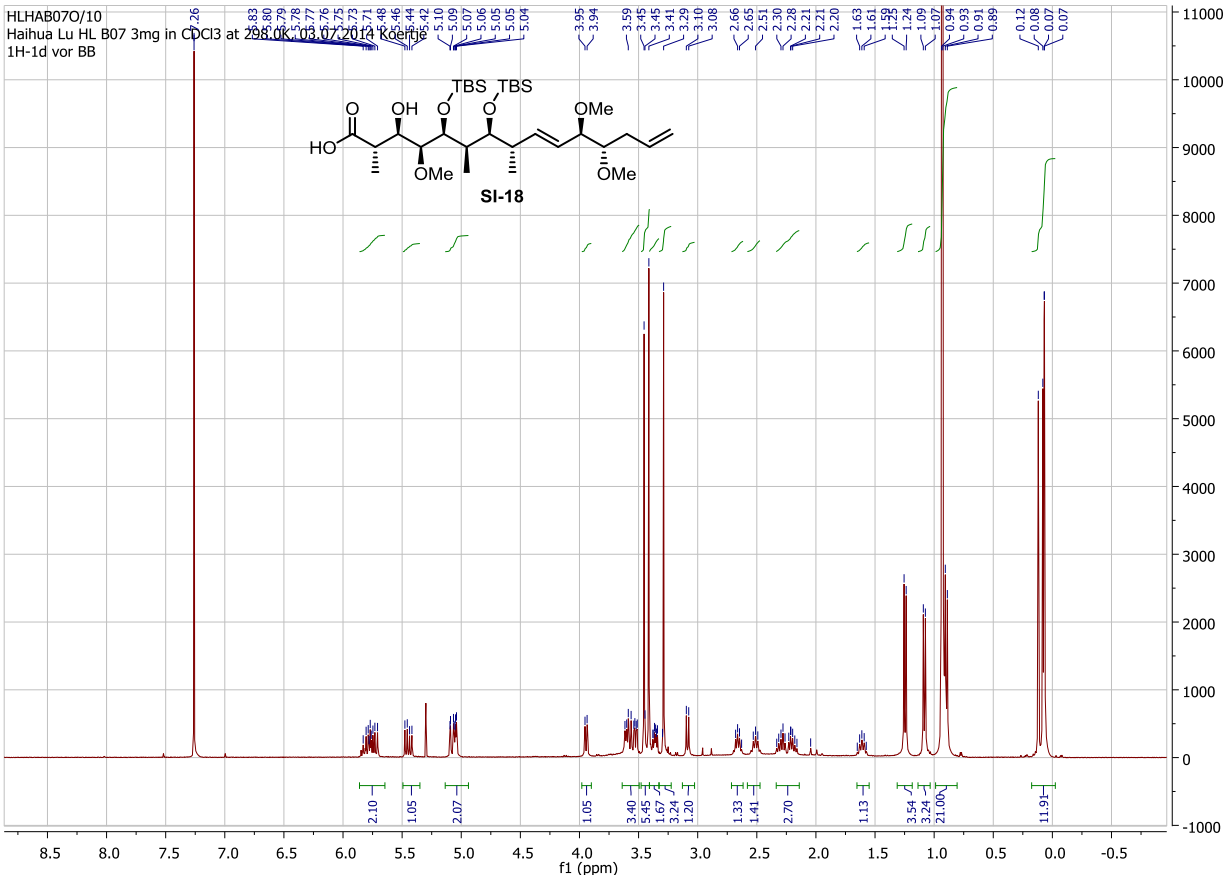

HLCLc02J/10
HLc02, CDCl3
100 MHz
f1 (ppm)

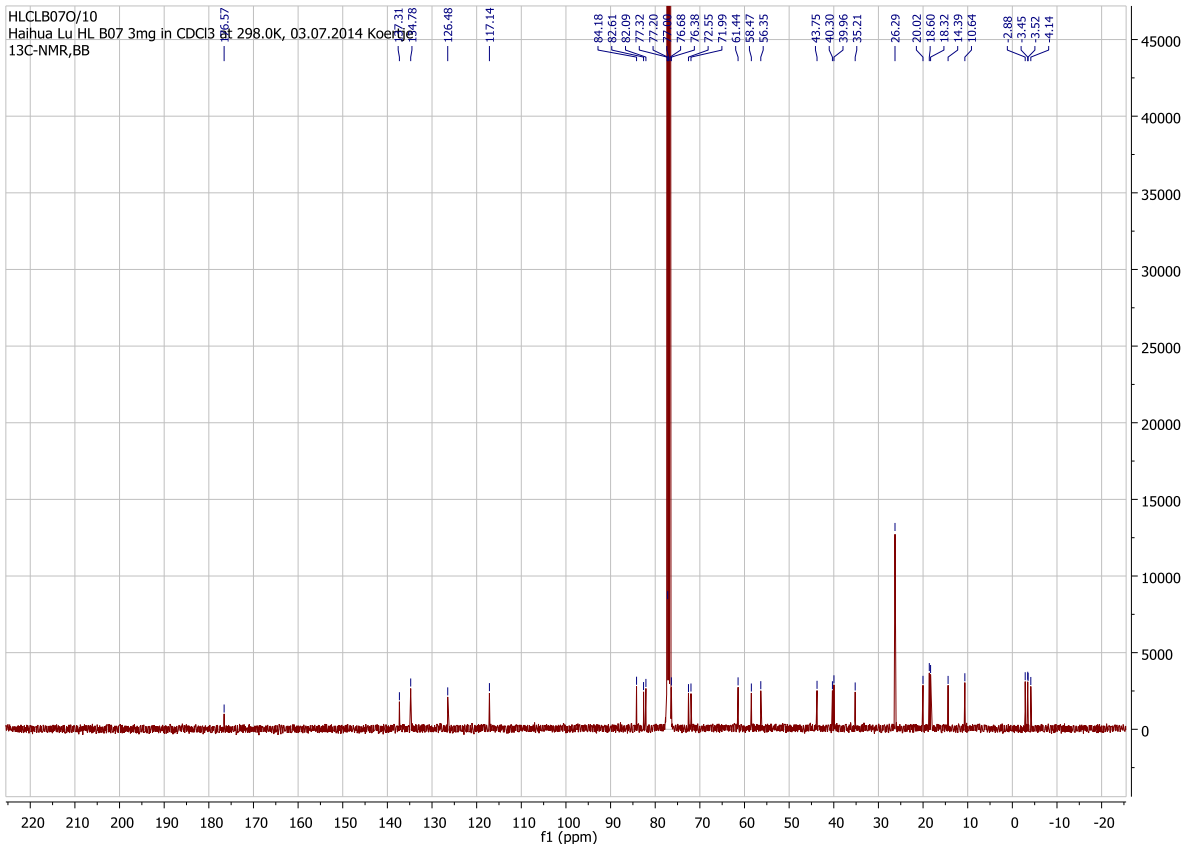

HLCLB05O/10
Haihua Lu HL B05 4mg in CDCl3 at 298.0K, 27.06.2014 Koertje
1H-1d vor BB
TBS TBS TBS
OH
OMe
OMe
53
f1 (ppm)

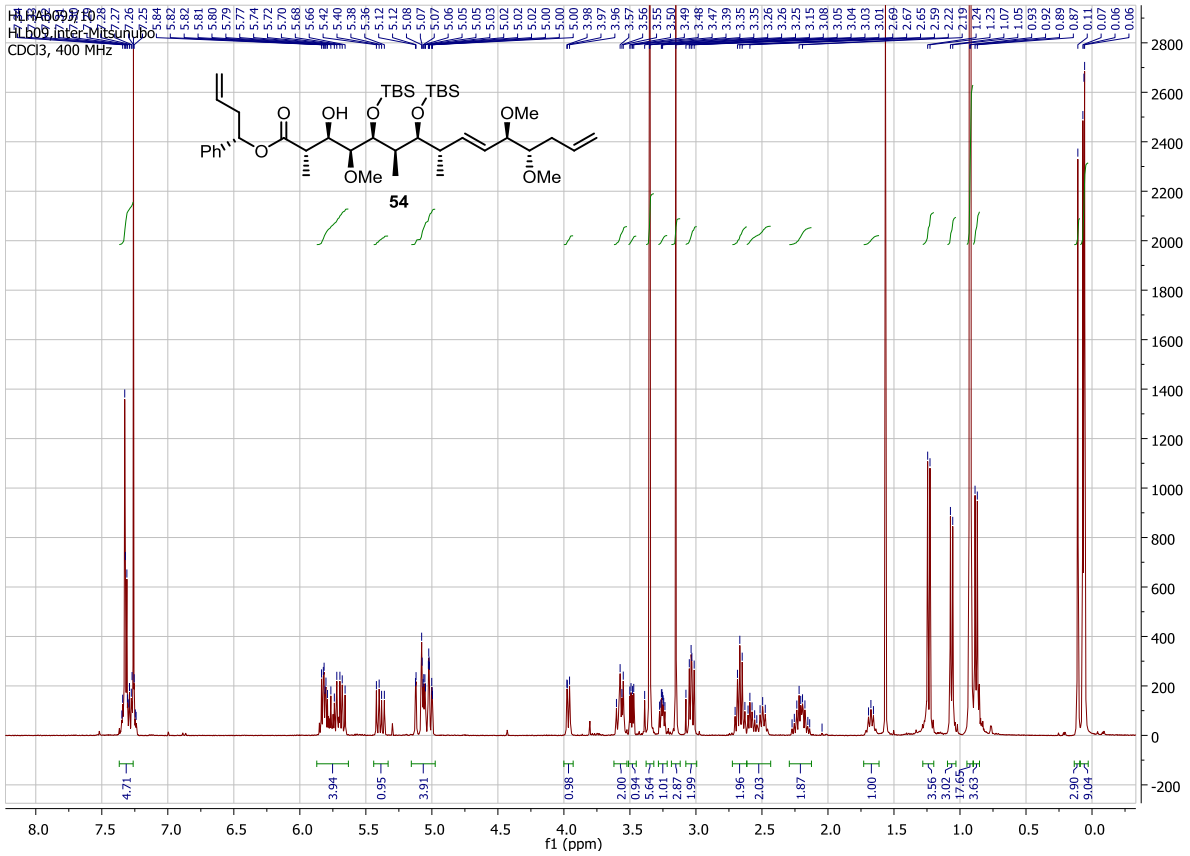

HLCLB05O/10
Haihua Lu HL B05 4mg in CDCl3 at 298.0K, 27.06.2014 Koertje
13C-NMR,BB
f1 (ppm)

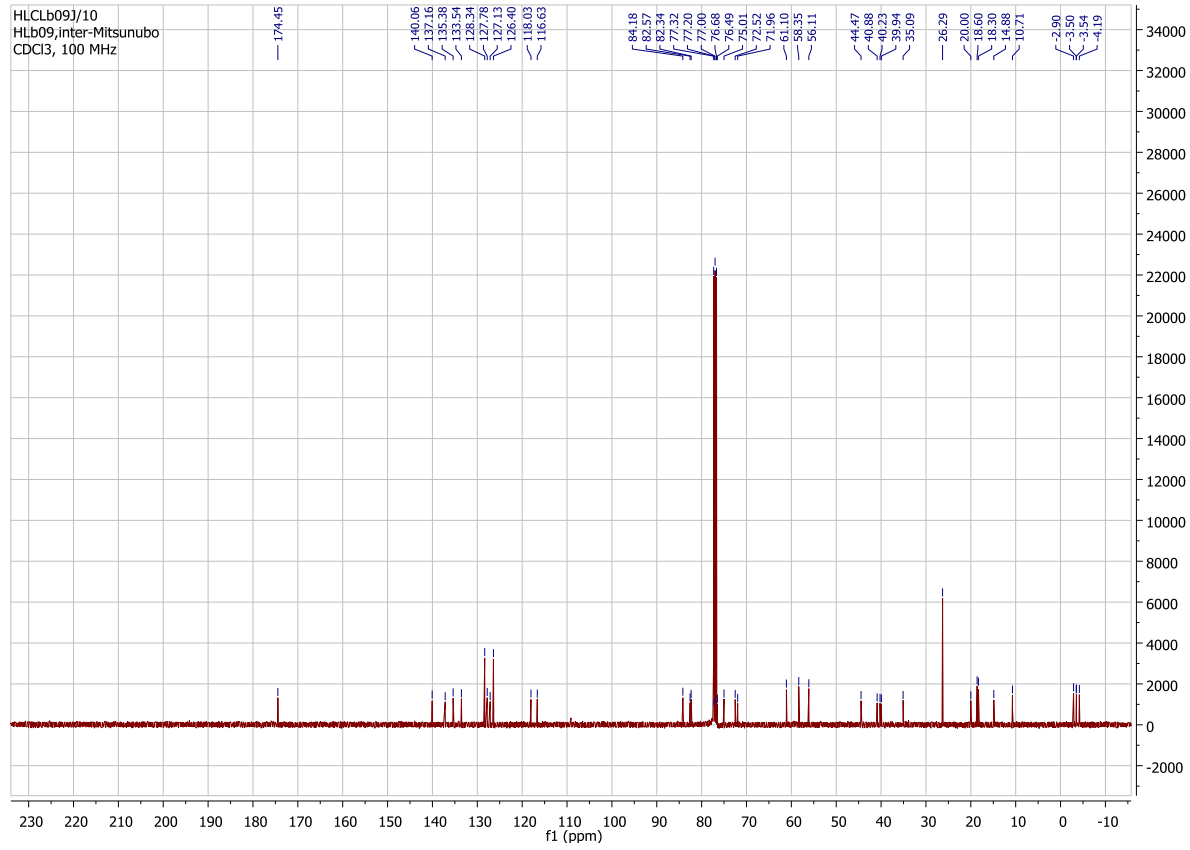

HLAB06J/10
HLb06, CDCl3
400 MHz
TBS TBS TBS
OMe
OMe
OMe
SI-17
1.85
0.91
1.85
2.83
3.91
0.89
2.74
3.01
3.90
0.93
2.91
0.90
2.86
3.07
31.94
18.00
f1 (ppm)


HLCLb06J/10
HLb06, CDCl3
400 MHz
174.14
137.45
135.42
126.50
116.71
84.99
84.11
83.33
77.32
77.21
77.00
76.68
75.86
72.86
59.50
58.27
56.40
51.11
42.38
40.01
34.91
26.28
26.19
25.89
19.88
18.66
18.30
18.12
15.11
12.16
-3.03
-3.31
-3.51
-3.88
-4.29
-4.76
f1 (ppm)


HLHAB07O/10
Haihua Lu HL B07 3mg in CDCl3 at 298.0K, 03.07.2014 Koenig
1H-1d vor BB
TBS TBS
O
OH
O
O
OMe
HO
OMe
OMe
SI-18
f1 (ppm)


HLCLB07O/10
Haihua Lu HL B07 3mg in CDCl3 at 298.0K, 03.07.2014 Koenig
13C-NMR,BB
f1 (ppm)


HLHA09J10
HLb09,inter-Mitsunubo
CDCl3, 400 MHz
TBS TBS
O
OH
O
O
OMe
Ph
O
OMe
OMe
54
f1 (ppm)


HLCLb09J/10
HLb09,inter-Mitsunubo
CDCl3, 100 MHz
f1 (ppm)