Total Synthesis of Tiacumicin A. Total Synthesis, Relay Synthesis, and Degradation Studies of Fidaxomicin (Tiacumicin B, Lipiarmycin A3)

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1. Positional Numbering System: The carbon numbering system and ring assignment as outlined below is utilized through the Supplementary Materials file for ^{1}H and ^{13}C NMR assignments.
Assignments were performed with the aid of 2D homonuclear (COSY, TOCSY and NOESY) and heteronuclear (HSQC and HMBC) NMR spectra.

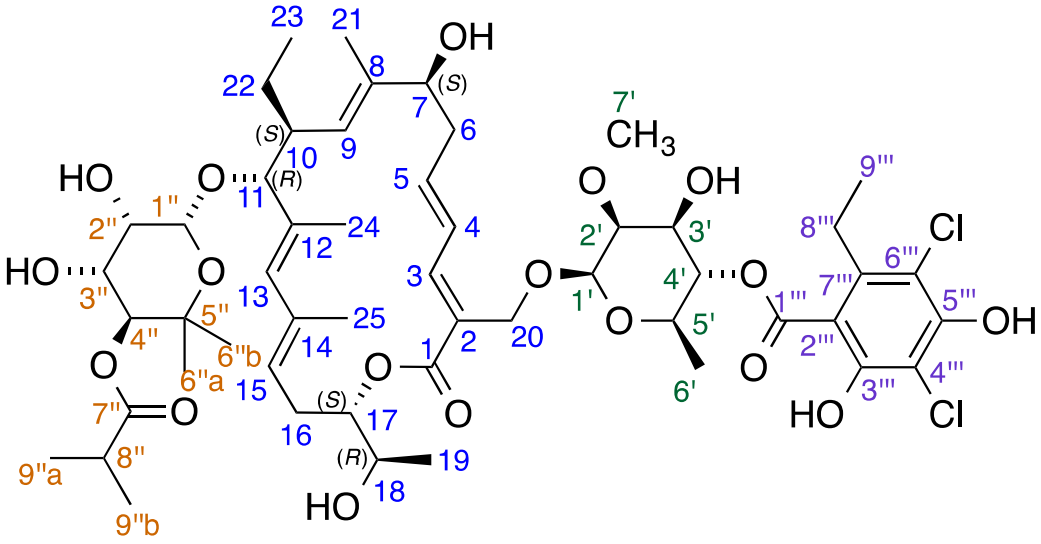


Figure S1. Positional numbering system of fidaxomicin.

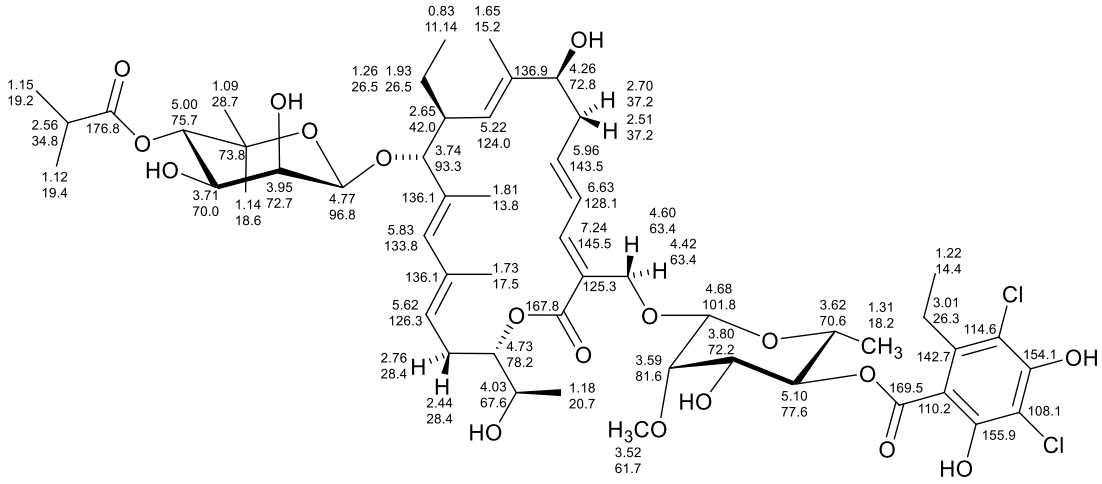


Figure S2. ^{1}H and ^{13}C NMR chemical shift of natural fidaxomicin.

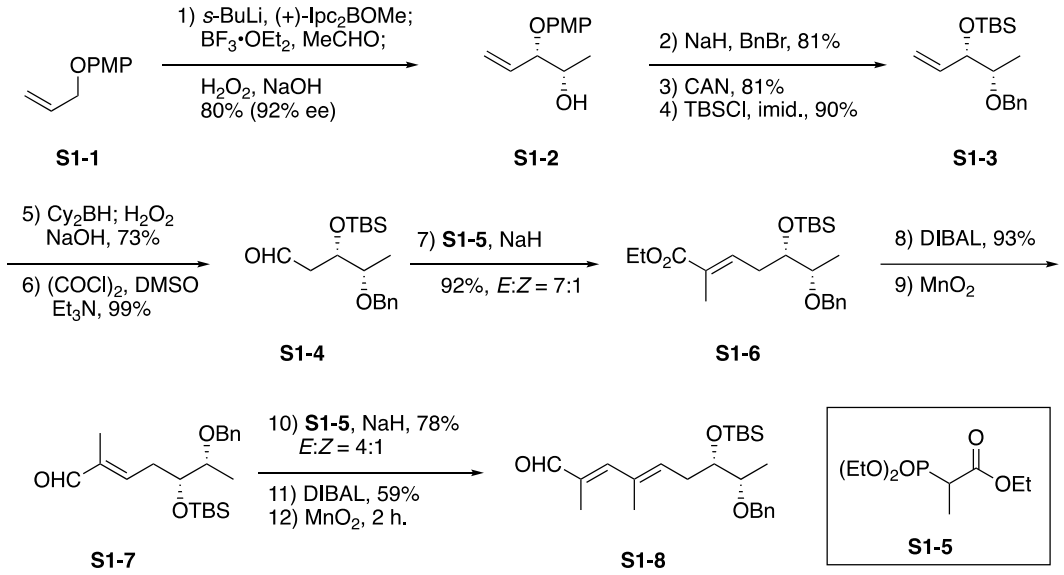
^{1}H NMR (500 MHz, acetone-d_6) δ 7.24 (dd, J = 11.5, 0.8 Hz, 1H, H3), 6.63 (dddd, J = 14.8, 11.6, 2.0, 1.0 Hz, 1H, H4), 5.96 (ddd, J = 14.6, 9.3, 4.6 Hz, 1H, H5), 5.83 (s, 1H, H13), 5.71 – 5.54 (m, 1H, H15), 5.22 (dt, J = 10.6, 1.5 Hz, 1H, H9), 5.10 (t, J = 9.8 Hz, 1H, H4'), 5.00 (d, J = 10.1 Hz, 1H, H4''), 4.77 (d, J = 1.3 Hz, 1H, H1''), 4.75 – 4.71 (m, 1H, H17), 4.68 (d, J = 0.8 Hz, 1H, H1'), 4.60 (d, J = 11.5 Hz, 1H, H20a), 4.42 (d, J = 11.5 Hz, 1H, H20b), 4.26 (s, 1H, H7), 4.05 – 3.99 (m, 1H, H18), 3.95 (dd, J = 3.4, 1.2 Hz, 1H, H2''), 3.80 (dd, J = 9.9, 3.4 Hz, 1H, H3'), 3.75 – 3.73 (m, 1H, H11), 3.73 – 3.70 (m, 1H, H3''), 3.65 – 3.60 (m, 1H, H5'), 3.59 (d, J = 2.5 Hz, 1H, H2'), 3.52 (s, 3H, H7'), 3.01 (qd, J = 7.4, 2.0 Hz, 2H, H8'''), 2.76 (dd, J = 14.4, 7.2 Hz, 1H, H16a, down), 2.72 – 2.67 (m, 1H, H6a), 2.67 – 2.60 (m, 1H, H10), 2.56 (sept, J = 7.0 Hz, 1H, H8''), 2.53 – 2.46 (m, 1H, H6b), 2.46 – 2.38 (m, 1H, H16b, up), 1.93 (qdd, J = 10.5, 6.3, 1.9 Hz, 1H, H22a), 1.81 (d, J = 1.3 Hz, 3H, H24), 1.73 (d, J = 1.5 Hz, 3H, H25), 1.65 (dd, J = 1.4, 0.7 Hz, 3H, H21), 1.31 (d, J = 6.2 Hz, 3H, H6'), 1.29 – 1.24 (m, 1H,

H22b), 1.22 (t, J = 7.4 Hz, 3H, H9’’’), 1.18 (d, J = 6.3 Hz, 3H, H19), 1.16 – 1.12 (m, 9H, H9’’a, H9’’b, H6’’a, axial), 1.09 (s, 3H, H6’’b, equatorial), 0.83 (t, J = 7.5 Hz, 3H, H23).

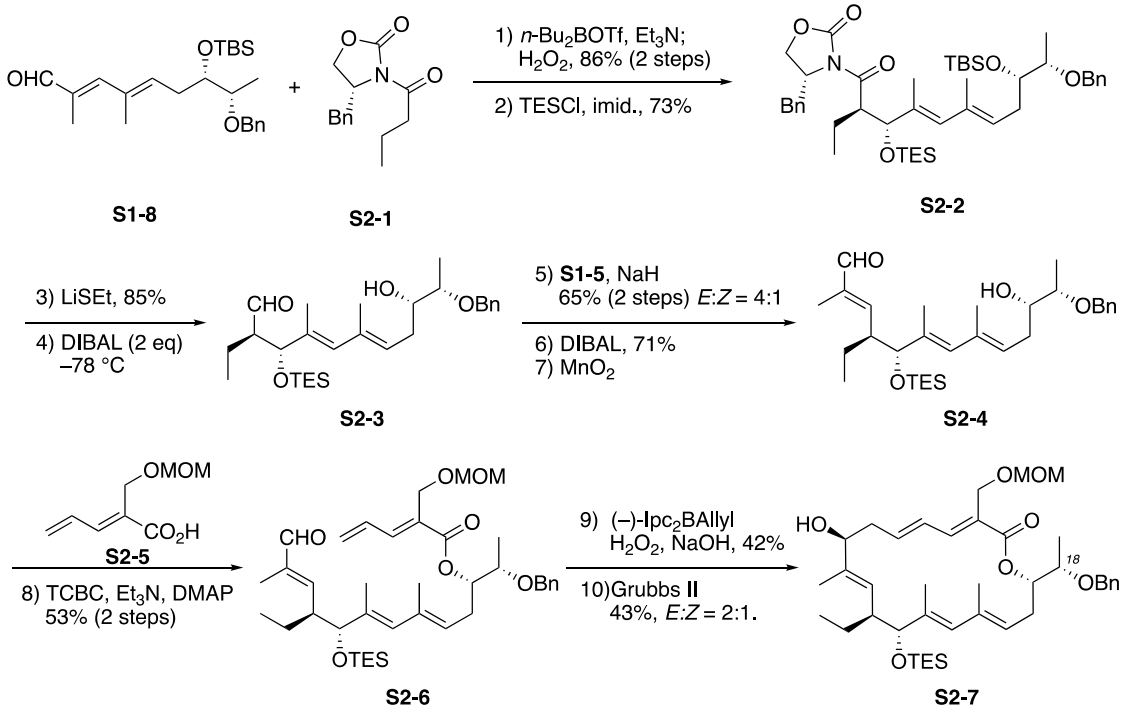
^{13}C NMR (126 MHz, acetone-d_6) δ 176.8 (C7’’), 169.5 (C1’’’), 167.8 (C1), 155.9 (C3’’’), 154.1 (C5’’’), 145.5 (C3), 143.5 (C5), 142.7 (C7’’’), 136.9 (C8), 136.1 (C12 or C14), 136.1 (C12 or C14), 133.8 (C13), 128.1 (C4), 126.3 (C15), 125.3 (C2), 124.0 (C9), 114.64 (C6’’’), 110.2 (C2’’’), 108.1 (C4’’’), 101.8 (C1’), 96.8 (C1’’), 93.3 (C11), 81.6 (C2’), 78.2 (C17), 77.6 (C4’), 75.7 (C4’’), 73.8 (C5’’), 72.8 (C7), 72.7 (C2’’), 72.2 (C3’), 70.6 (C5’), 70.0 (C3’’), 67.6 (C18), 63.4 (C20), 61.7 (C7’), 42.0 (C10), 37.2 (C6), 34.8 (C8’’), 28.7 (C6’’b, equatorial), 28.4 (C16), 26.5 (C22), 26.3 (C8’’’), 20.7 (C19), 19.4 (C9’’b), 19.2 (C9’’a), 18.6 (C6’’a, axial) , 18.2 (C6’), 17.5 (C25), 15.2 (C21), 14.4 (C9’’’), 13.8 (C24), 11.14 (C23).

Retention Factor
R_f = 0.19 (acetone/pentane 2/3)
R_f = 0.32 (CH_2Cl_2/MeOH 12/1)
R_f = 0.67 (acetone/pentane 2/1)

2. Synthetic study of macrocycle reported by Zhu and co-workers.[1]



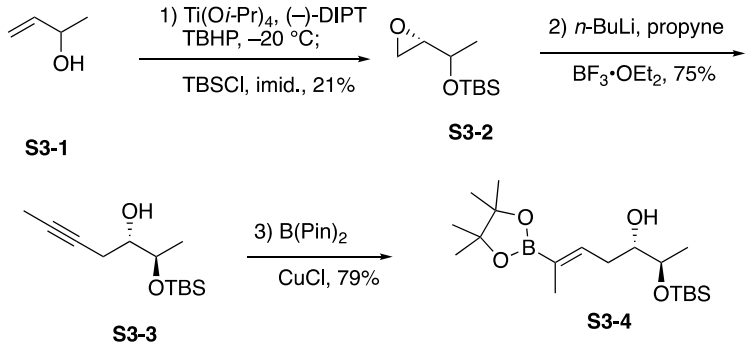
Scheme S1. Synthesis of aldehyde **S1-8** reported by Zhu and co-workers. Reagents and conditions: 1) *s*-BuLi, THF, –78 °C, 30 min; (+)-Ipc$_2$BOMe, –78 °C, 60 min; $BF_3 \cdot OEt_2$, –78 °C; MeCHO, –78 °C, 3 h; H_2O_2, NaOH, –78 °C to rt, 18 h, 80%, 92% ee; 2) NaH, DMF, 0 °C, 1 h; BnBr, 0 °C to rt, 18 h, 81%; 3) CAN, MeCN, H_2O, 0 °C, 15 min, 81%; 4) TBSCl, imid., DMF, rt, 18 h, 90%; 5) Cy_2BH, THF, 0 °C, 2 h; H_2O_2, *aq*. NaOH, 0 °C, 4 h, 73%; 6) $(COCl)_2$, DMSO, CH_2Cl_2, –78 °C, 1 h; Et_3N, –78 °C to rt, 1 h, 99%; 7) phosphate **S1-5**, NaH, THF, 0 °C, 20 min; **S1-4**, 0 °C, 2 h, 92%, *E*:*Z* = 7:1; 8) DIBAL, PhMe, –78 °C, 1 h, 93%; 9) MnO_2, THF, rt, 2 h; 10) phosphate **S1-5**, NaH, THF, 0 °C, 20 min; **S1-7**, 0 °C, 2 h, 78%, *E*:*Z* = 4:1; 11) DIBAL, PhMe, –78 °C, 1 h, 59%; 12) MnO_2, THF, rt, 2 h, CAN= ceric ammonium nitrate, TBSCl = *tert*-butyldimethylchlorosilane, imid. = imidazole, DIBAL = diisobutylaluminum hydride.



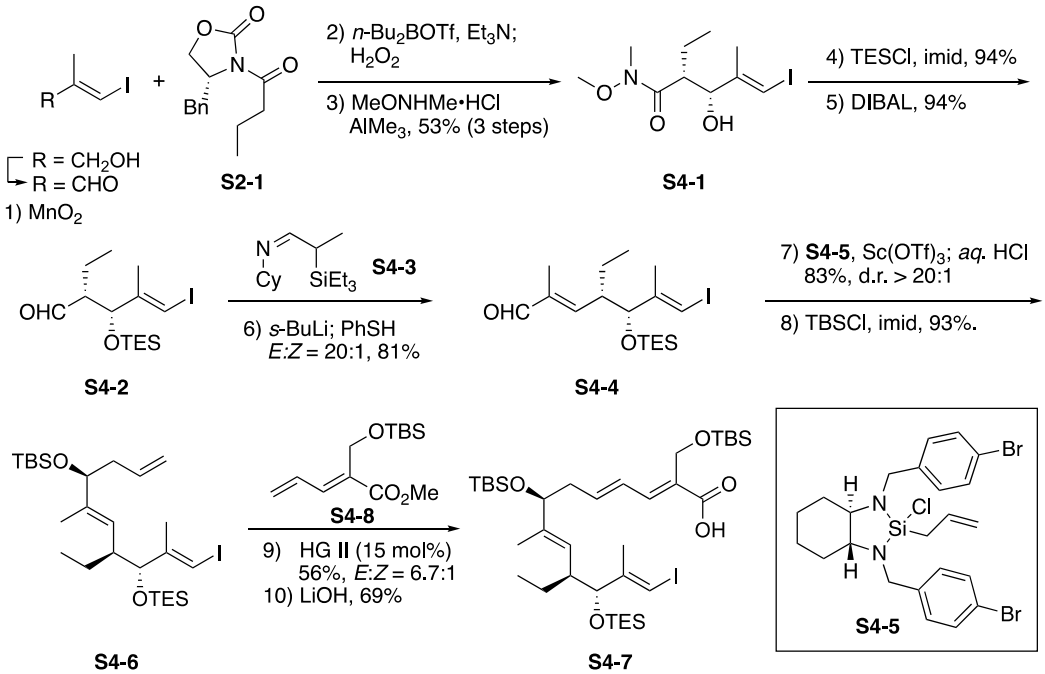
[1] Erb, W.; Grassot, J. M.; Linder, D.; Neuville, L.; Zhu, J. *Angew. Chem. Int. Ed.* **2015**, *54*, 1929.

Scheme S2. Synthesis of macrocycle **S2-7** reported by Zhu and co-workers. Reagents and conditions: 1) *n*-Bu_2BOTf, Et_3N, CH_2Cl_2, 0 °C, 30 min; **S1-7**, –78 °C to rt; H_2O_2, MeOH, buffer pH 7.0, 10 °C to rt, 1 h, 86% (2 steps); 2) TESCl, imid., DMF, 0 °C, 20 min, 73%; 3) EtSH, *n*-BuLi, THF, 0 °C, 5 min; **S2-2**, THF, rt, 10 min, 85%; 4) DIBAL (2 eq), PhMe, –78 °C, 20 min; 5) phosphate **S1-5**, NaH, THF, 0 °C, 2 h; **S2-3**, 0 °C, 2 h, 65% (2 steps), *E*:*Z* = 4:1; 6) DIBAL (5 eq), CH_2Cl_2, –78 °C, 1 h, 71%; 7) MnO_2, THF, rt, 2 h; 8) carboxylic acid **S2-5**, 1,3,5-trichloro-benzoyl chloride, Et_3N, PhMe, rt, 1 h; **S2-4**, DMAP, rt, 4 h, 53% (2 steps); 9) (–)-Ipc_2Ballyl, THF, –78 °C, 1 h; H_2O_2, NaOH, –78 °C to rt, 3 h, 42%; 10) Grubbs II (20 mol%), PhMe, 100 °C, 43%, *E*:*Z* = 2:1, TESCl = chlorotriethylsilane, TCBC = 1,3,5-trichloro-benzoyl chloride, DMAP = 4-dimethylaminopyridine, Ipc_2 = diisopinocampheyl.

Synthetic study of macrocycle reported by Altmann and co-workers.[2]

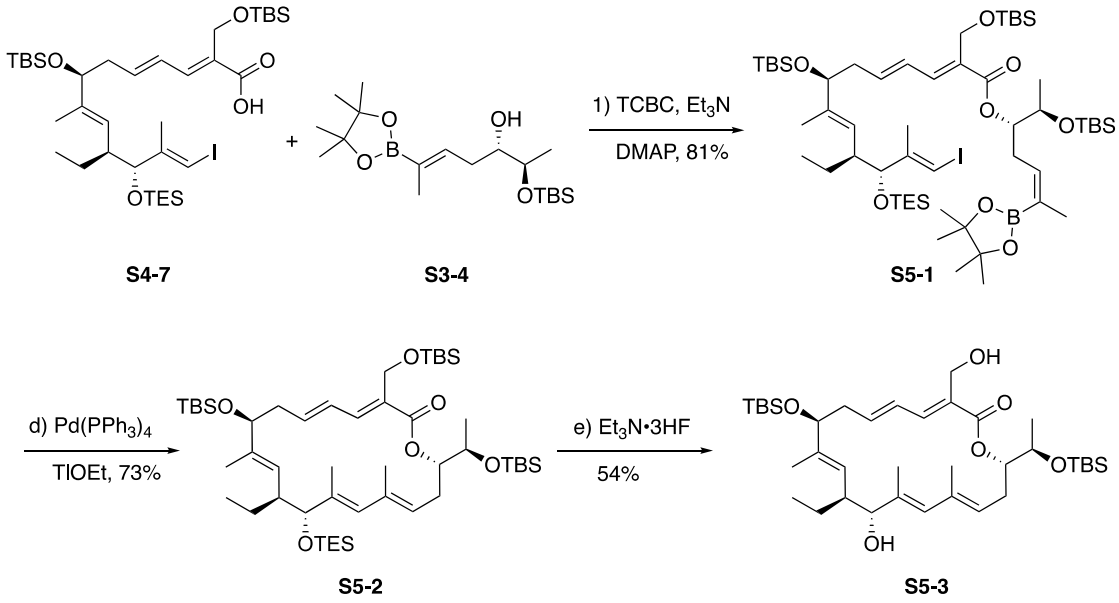


Scheme S3. Synthesis of boronate **S3-4** reported by Altmann and co-workers. Reagents and conditions: 1) Ti(O*i*-Pr)$_4$, (–)-DIPT, TBHP (0.45 eq), MS 3Å, CH_2Cl_2, –20 °C, 39 h; TBSCl, imid., CH_2Cl_2, –20 °C to rt, 16 h, 21%; 2) *n*-BuLi, propyne, $BF_3 \cdot OEt_2$, THF, –78 °C, 3.5 h, 75%; 3) bis(pinacolato)diboron, CuCl (5 mol%), KO*t*-Bu (20 mol%), PPh_3 (6 mol%), MeOH, THF, rt, 3.5 h, 79%, (–)-DIPT = (−)-diisopropyl D-tartrate, TBHP = *tert*-butyl hydroperoxide.



[2] Glaus, F.; Altmann, K. H. *Angew. Chem. Int. Ed*. **2015**, *54*, 1937.

Scheme S4. Synthesis of carboxylic acid **S4-7** reported by Altmann and co-workers. Reagents and conditions: 1) MnO_2, MS 3Å, CH_2Cl_2, rt, 75 min; 2) *n*-Bu_2BOTf, Et_3N, CH_2Cl_2, –78 °C, 2.5 h; 0 °C, 1.5 h; pH 7 buffer, MeOH, H_2O_2, 0 °C, 1 h; 3) MeONHMe·HCl, $AlMe_3$, THF, 0 °C, 2 h, 53% (3 steps); 4) TESCl, imid., CH_2Cl_2, rt, 30 min, 94%; 5) DIBAL, THF, –30 °C, 1 h; –20 °C, 1 h, 94%; 6) **S4-3**, *s*-BuLi, THF, –20 °C, 2 h; PhSH, –20 °C, 2 h; sat. *aq*. NaH_2PO_4, rt, 4 h, *E*:*Z* = 20:1, 81%; 7) **S4-5**, $Sc(OTf)_3$, CH_2Cl_2, –35 °C to –20 °C, 30 min; –20 °C, 2.5 h; 1M HCl, rt, 7 min, 83%, *d.r.* > 20:1; 8) TBSCl, imid., CH_2Cl_2, rt, 22 h, 93%; 9) Hoveyda–Grubbs II (15 mol%), EtOAc, rt, 3.5 h, 56%, *E:Z* 6.7:1; 10) LiOH, *t*-BuOH/H_2O 3:1, 33 °C, 48 h, 69%.

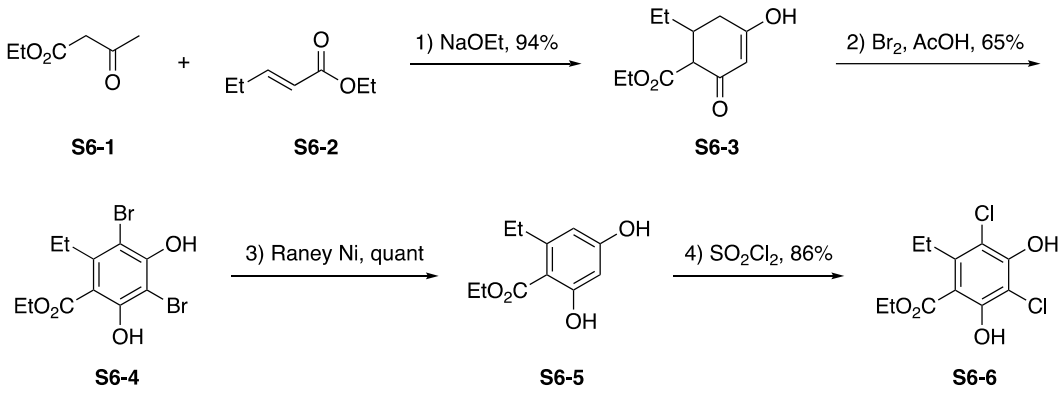


S4-7 **S3-4** **S5-1**

S5-2 **S5-3**

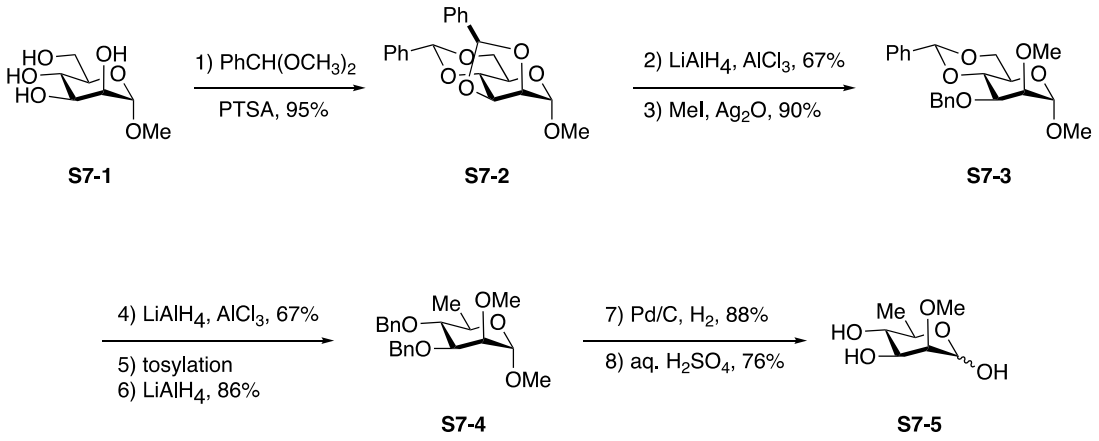
Scheme S5. Synthesis of macrocycle **S5-3** reported by Altmann and co-workers. Reagents and conditions: 1) 2,4,6-$Cl_3H_2C_6COCl$, Et_3N, DMAP, PhMe, rt, 5.5 h, 81%; 2) $Pd(PPh_3)_4$ (20 mol%), TlOEt, THF/H_2O 3:1, rt, 25 min, 73%; f) $Et_3N·3HF$, MeCN/THF 6:4, –15 °C to 5 °C, 2 h; 5 °C, 5 h; 15 °C, 27 h, 54%.

Synthetic study of resorcylate unit reported by Scharf and co-workers.[3]



Scheme S6. Synthesis of resorcylate **S6-6** reported by Scharf and co-workers. Reagents and conditions: 1) Na, EtOH, 94%; 2) Br_2, AcOH, 40 °C, 16 h, 65%; 3) Raney Nickel, 1M NaOH, 0 to 5 °C, 4 h, quant.; 4) SO_2Cl_2, Et_2O, reflux, 10 min, 86%.

Synthetic study of rhamnose unit reported by Liptak and co-workers.[4]



Scheme S7. Synthesis of rhamnose **S7-5** reported by Liptak and co-workers. Reagents and conditions: 1) $PhCH(OCH_3)_2$, PTSA, DMF, 95%; 2) $LiAlH_4$, $AlCl_3$, Et_2O, CH_2Cl_2, 67%; 3) MeI, Ag_2O, DMF, 90%; 4) $LiAlH_4$, $AlCl_3$, Et_2O, CH_2Cl_2, reflux, 67%; 5) tosylation (not described); 6) $LiAlH_4$, PhH, Et_2O, reflux, 86%; 7) Pd/C, H_2, AcOH, EtOH, 88%; 8) *aq*. H_2SO_4, 100 °C, 6 h, 76%, PTSA = *p*-toluenesulfonic acid.

[3] (a) Dornhagen, J.; Scharf, H. D. *Tetrahedron* **1985**, *41*, 173–175. (b) Alexy, M.; Scharf, H.-D. *Liebigs Ann. Chem.* **1991**, *1991*, 1363–1364.
[4] Lipták, A. *Carbohydr. Res.* **1982**, *107*, 300–302.

3. Degradation study of fidaxomicin

Determination of Fidaxomicin's pK_a Value and Degradation in Alkaline Media
Fidaxomicin was weighed into a glass vial (26.8 mg, 0.025 mmol) and dissolved in a MeOH/H_2O mixture (4.5 mL MeOH, 0.5 mL H_2O). A freshly prepared aqueous solution of NaOH (0.01 M) was added portionwise and the pH was determined after each addition.

Table S1. Determination of pK_a value of fidaxomicin.

V(NaOH)	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8
pH	5.33	5.63	5.89	6.05	6.17	6.25	6.32	6.39	6.44

V(NaOH)	0.90	1.00	1.10	1.20	1.30	1.40	1.50	1.60	1.70
pH	6.49	6.58	6.59	6.64	6.69	6.74	6.80	6.86	6.93

V(NaOH)	1.80	1.85	1.90	1.95	2.00	2.05	2.10	2.15	2.20
pH	7.00	7.05	7.09	7.14	7.21	7.34	7.41	7.52	7.67

V(NaOH)	2.25	2.30	2.35	2.40	2.45	2.50	2.55	2.60	2.65
pH	7.82	8.11	8.54	8.95	9.29	9.51	9.65	9.73	9.83

V(NaOH)	2.70	2.75	2.80	2.85	2.90	2.95	3.00	3.10	3.20
pH	9.91	9.98	10.04	10.10	10.16	10.18	10.22	10.28	10.34

V(NaOH)	3.30	3.40	3.50	3.60	3.60	3.80	3.90	4.00	4.20
pH	10.40	10.45	10.49	10.54	10.58	10.62	10.66	10.69	10.76

V(NaOH)	4.40	4.60	4.80	5.00	5.20	5.40	5.60	5.80	6.00
pH	10.82	10.90	10.96	11.03	11.08	11.13	11.18	11.22	11.26

V(NaOH)	6.20	6.40	6.60	6.80	7.00	7.20	7.40	7.60	7.80
pH	11.27	11.30	11.33	11.36	11.38	11.41	11.46	11.48	11.50

V(NaOH)	8.00	8.50	9.00	9.50	10.00	10.50	11.00	11.50	12.00
pH	11.52	11.53	11.54	11.56	11.59	11.62	11.63	11.65	11.66

V(NaOH)	12.50	13.00	14.00	15.00	16.00	17.00
pH	11.66	11.66	12.67	12.95	13.21	13.50

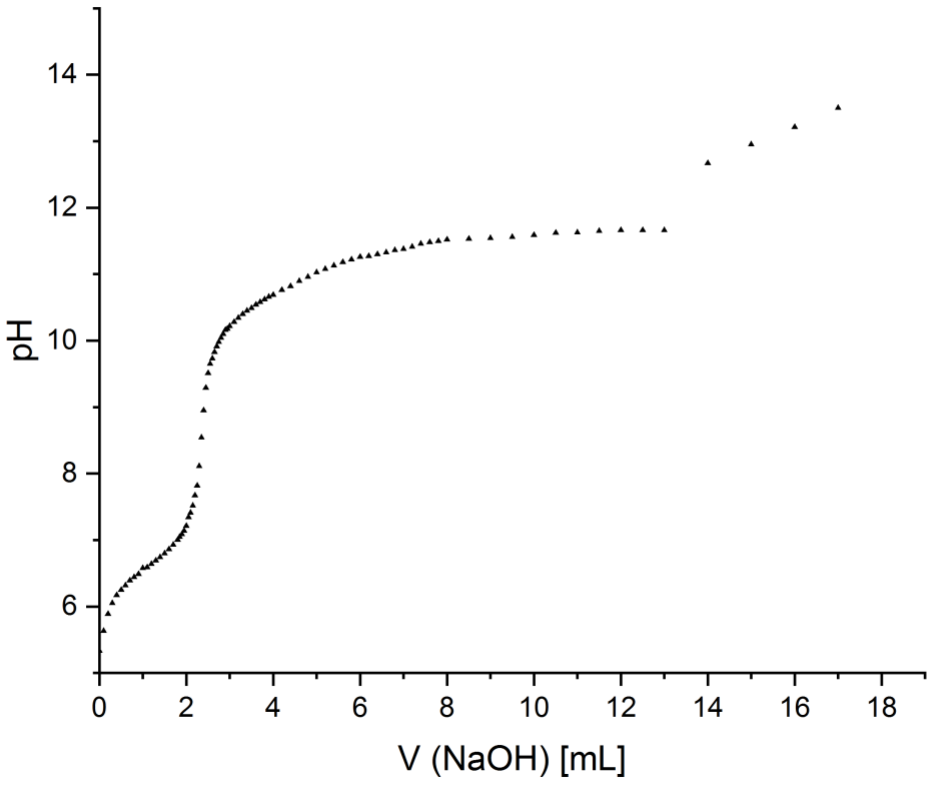


Figure S3. Titration curve of fidaxomicin (**1**) for titration with NaOH (0.01 M).

The point with the largest slope was determined (both analytically and graphically) and identified as the equivalence point of the titration (at 2.4 mL of titrant added). The mid-point was identified as the point with half the volume of titrant added (1.2 mL). At the mid-point, the equation pH = $^{s}_{w}pK_a$ holds true. The pK_a of fidaxomicin in a MeOH-H_2O mixture of 4.5 mL/1.7 mL (2.6/1) is thus $^{s}_{w}pK_a$ = 6.6. This is in accordance with the value given in the literature ($^{s}_{w}pK_a$ = 6.8 in a solvent mixture 2-methoxyethanol/H_2O 4/1).[5] However, the pK_a in pure H_2O, which was not experimentally determined due to the low solubility of fidaxomicin in H_2O, is of higher interest for reasons of comparability. With the help of empirical parameters specific for phenols as acids, the corresponding value was calculated to be $^{w}_{w}pK_a$ = 5.6.[6] In the course of the above described experiment for pK_a determination, aliquot samples of the mixture were analyzed by reversed-phase LC-MS. Analyses were performed on a Shimadzu LC system with a Reprospher column (Dr. Maisch, 100 Å C18-Aqua, 5 µm, 125 mm x 2 mm) and an amaZon X Bruker mass spectrometer. The solvents used were: H_2O + 0.01 % HCOOH (A), MeCN + 0.01 % HCOOH (B) at a flow rate of 0.5 mL min^{-1}. The following LC time program (min – % B) was applied: 0.0 – 10 %, 2.0 – 10 %; 12.0 – 95 %, 15.0 – 95 %; 16.0 – 10 %; 18.0 – 10 %. Integration of the peak areas in the UV spectrum gave the following results.

Table S2. Degradation of fidaxomicin by hydrolysis to OP-1118 in basic medium.

V(NaOH)	0.50	1.00	1.50	2.00	2.30
pH	6.25	6.58	6.80	7.21	8.11
peak area fidaxomicin [%][a]	100	100	100	100	100

[5] B. Cavalleri, A. Arnone, E. d. Modugno, G. Nasini, B. P. Goldstein, *J. Antibiot.* **1988**, *41*, 308.
[6] X. Subirats, M. Roses, E. Bosch, *Sep. Purif. Rev.* **2007**, *36*, 231.

V(NaOH)	2.50	3.00	4.00	5.00	6.00
pH	9.51	10.22	10.69	11.03	11.26
peak area fidaxomicin [%][a]	100	98.5	98.7	97.8	91.5

V(NaOH)	13.00	14.00	15.00	16.00	17.00
pH	11.66	12.67	12.95	13.21	13.50
peak area fidaxomicin [%][a]	46.8	3.3	0	0	0

[a] Peak shapes in the basic medium indicate that there are in fact at least two peaks, as regioisomers are formed by transacylation (not resolved).

Degradation in Acidic Media

HPLC-MS experiments were performed on an Agilent 1200 Infinity system equipped with a high-performance autosampler model HiP-ALS SL+, a G1315D photodiode array (DAD) detector and a 6120 Quadrupole LC/MS detector with electrospray ionization using a reversed-phase column (*LiChroCART 250-4*, LiChrospher 100, RP18e, 5 µm, sorbent lot No. L58138033; *Merck*) for analytical HPLC with the following solvents: H_2O + 0.1 % HCOOH (A), MeCN + 0.1 % HCOOH (B). The flow was 1 mL/min, injection volume was 10 µL and the following LC time program (min – % B) was applied: 0.0 – 45 %, 2.0 – 45 %, 14.0 – 95 %, 15.0 – 95 %, 15.1 – 100 %, 16.0 – 100 %, 16.1 – 45 %, 18.0 – 45 %. Peaks were integrated in the UV spectrum at λ = 270 nm using the *LC/MSD ChemStation* Software Rev. B. 04.03 [16] by Agilent technologies. Fidaxomicin was observed at t_R = 10.9 min and the two isomeric degradation products with m/z = 863 at t_R = 12.6–13.1 min.

Calibration by HPLC-MS

A calibration curve for fidaxomicin quantification by integration of the UV peaks at λ = 242 nm was obtained with mass concentrations ß = 1000, 750, 500, 250, 100, 50 and 25 µg/mL in methanol using acetanilide as an internal standard (IS, 0.1 mg/mL).

1) *Preparation of acetanilide stock solution (ß = 1.00 mg/mL)*: A flask was charged with acetanilide (10.0 mg, 74.0 µmol) and the solid dissolved in methanol (10.0 mL).

2) *Preparation of fidaxomicin stock solution (ß = 1.25 mg/mL)*: In a vial, fidaxomicin (3.01 mg, 2.84 µmol) was dissolved in methanol (2.408 mL).

3) *Pipet scheme for the preparation of calibration samples 1–8.*

Table S3.

vial	ß (fidaxomicin) [µg/mL]	V (fidaxomicin stock solution) [µL]	V (IS stock solution) [µL]	V (MeOH) [µL]
1	1000	800	100	100
2	750	600	100	300
3	500	400	100	500
4	250	200	100	700
5	100	80	100	820
6	75	60	100	840
7	50	40	100	860
8	25	20	100	880

Table S4.

ß (fidaxomicin) [µg/mL]	ß(fidaxomicin)/ß(IS)	integral(fidaxomicin)/integral(IS) (mean of three runs)	S.D.
1000	10.00	3.2141	0.02658
750	7.50	2.3416	0.00597

500	5.00	1.4960	0.00239
250	2.50	0.7817	0.00065
100	1.00	0.2546	0.00023
75	0.75	0.2133	0.00102
50	0.50	0.1413	0.00035
25	0.25	0.0700	0.00004

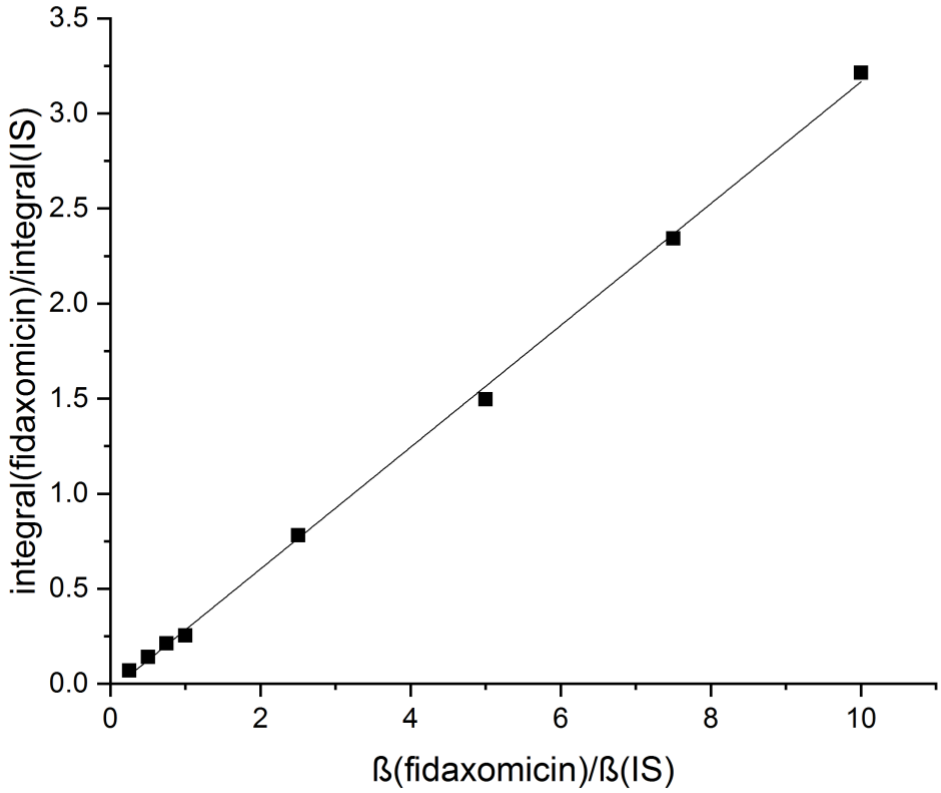


Figure S4. Calibration curve for degradation study of fidaxomicin

Result from linear fit (as calculated by Origin Pro 2018G):
y = 0.32029 x – 0.03694; R² (kor.) = 0.99882
with x = ß(fidaxomicin)/ß(IS) and y = integral(fidaxomicin)/integral(IS)

Degradation of fidaxomicin with HCl in methanol (100, 50, 10 equiv.)

1) *Preparation of MeOH·HCl stock solution (c = 0.5 mmol/mL)*: A sealed MeOH-HCl (3 N) vial was opened and MeOH·HCl solution (1.0 mL) transferred to a flask filled with MeOH (5.0 mL).

2) *Preparation of acetanilide stock solution (ß = 1.00 mg/mL)*: A flask was charged with acetanilide (10.0 mg, 74.0 µmol) and the solid diluted in methanol (10 mL).

3) *Preparation of fidaxomicin+IS stock solution* (*c (fidaxomicin) = 0.01 mmol/mL; c(IS) = 1.0 mg/mL*): Fidaxomicin (7.41 mg, 7.0 µmol) was weighed into a vial and acetanilide stock solution (0.7 mL) was added.

4*) Pipet scheme for preparation of samples:*

Table S5.

vial	equivalents HCl	V (fidaxomicin+IS stock solution)	V (MeOH·HCl stock solution)	V (MeOH)

		[µL]	[µL]	[µL]
1	100	100	200	700
2	50	100	100	800
3	10	100	20	880

Results from HPLC-MS analyses of samples

Table S6. Degradation of fidaxomicin with 100 equivalents of HCl, **vial 1**

run	time [min]	integral IS peak[a]	integral fidaxomicin peak	integral(fidaxomicin)/ integral(IS)	concentration ß of fidaxomicin [µg/mL]
0	0				1059
1	1	3477.00	9840.35	2.830127	895
2	40	3505.63	3007.32	0.857854	279
3	78	3472.16	947.55	0.272899	97
4	117	3399.76	284.91	0.083804	38
5	155	3362.95	91.63	0.027246	20
6	194	3321.87	24.94	0.007507	14
7	232	3275.43	0.00	0.000000	0[b]

[a] We also observed slight degradation of acetanilide under these conditions. However, setting the integral of the IS peak on a constant value, *e.g.* 3477.00, which is a good approximation as injection volumes on our HPLC system have been shown to be very constant, we did only see extremely slight and negligible differences in the calculated fidaxomicin concentrations. We thus use the values as measured as an approximation. [b] This concentration value was set to 0 as no more peak was observed, i.e. fidaxomicin concentration was beneath the detection limit.

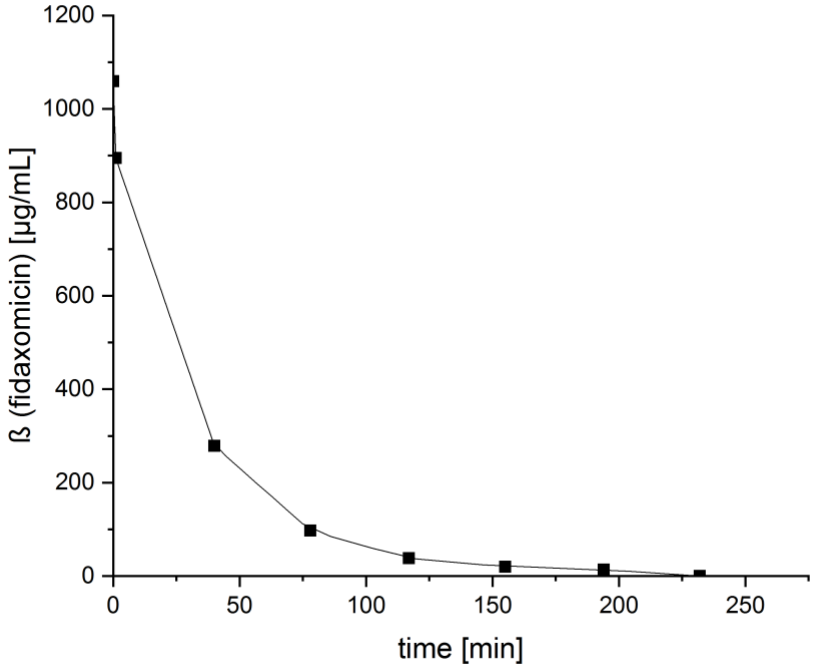


Figure S5. Degradation of fidaxomicin with 100 equivalents of HCl

Table S7. Degradation of fidaxomicin with 50 equivalents of HCl, **vial 2**

run	time [min]	integral IS peak[a]	integral fidaxomicin peak	integral(fidaxomicin)/ integral(IS)	concentration ß of fidaxomicin [µg/mL]
0	0				1059
1	1	4015.90	11400.20	2.838766	898
2	40	3970.71	6706.85	1.689081	539
3	79	3923.16	3880.60	0.989152	320
4	117	3908.42	2235.64	0.572006	190
5	156	3903.48	1318.58	0.337796	117
6	194	3859.18	770.85	0.199744	74
7	233	3845.53	471.86	0.122703	50
8	271	3821.73	281.41	0.073633	35
9	310	3798.32	178.86	0.047088	26
10	348	3768.61	108.28	0.028732	20
11	387	3744.25	67.02	0.017899	17
12	425	3737.78	0.00	0.000000	0[b]

[a] We also observed slight degradation of acetanilide under these conditions. However, setting the integral of the IS peak on a constant value, *e.g.* 4015.90, which is a good approximation as injection volumes on our HPLC system have been shown to be very constant, we did only see extremely slight and negligible differences in the calculated fidaxomicin concentrations. We thus use the values as measured as an approximation. [b] This concentration value was set to 0 as no more peak was observed, i.e. fidaxomicin concentration was beneath the detection limit.

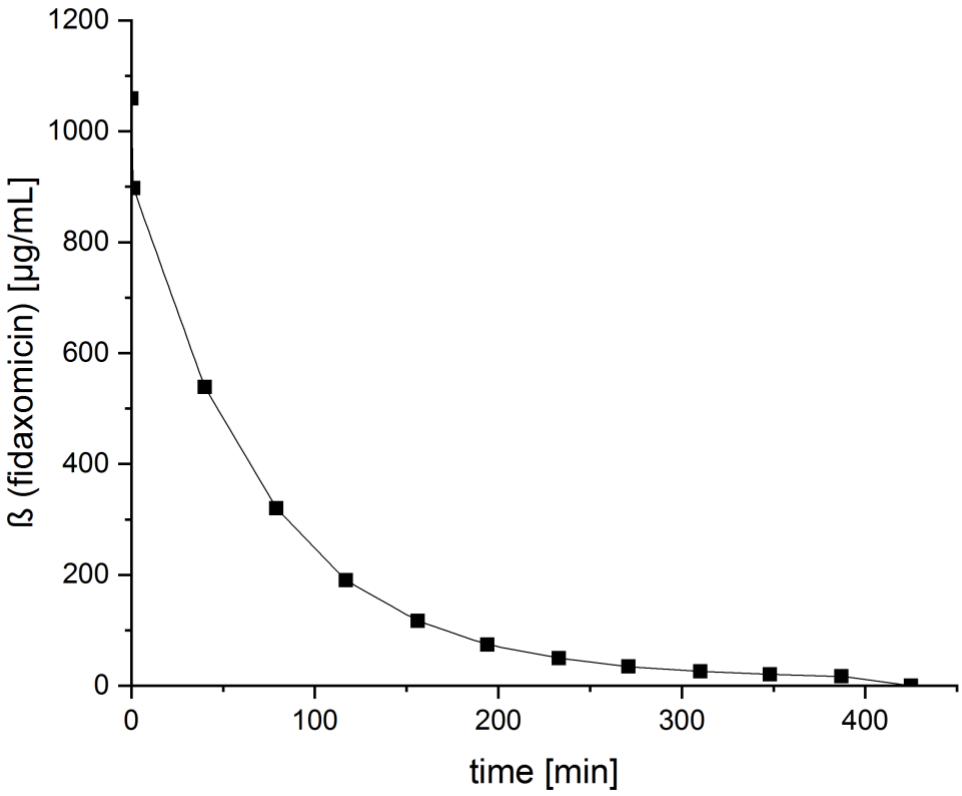


Figure S6. Degradation of fidaxomicin with 50 equivalents of HCl

Table S8. Degradation of fidaxomicin with 10 equivalents of HCl, **vial 3**

run	time [min]	integral IS peak[a]	integral fidaxomicin peak	integral(fidaxomicin)/ integral(IS)	concentration ß of fidaxomicin [µg/mL]
0	0				
1	1	3490.23	9889.74	2.833550	896
2	39	3529.53	9315.72	2.639366	836
3	78	3513.81	8222.87	2.340158	742
4	116	3513.87	7346.68	2.090766	664
5	155	3514.98	6477.27	1.842762	587
6	194	3496.18	5783.49	1.654231	528
7	232	3495.66	5185.27	1.483345	475
8	271	3494.91	4646.08	1.329385	427
9	309	3479.24	4182.63	1.202168	387
10	348	3489.21	3759.65	1.077508	348
11	386	3484.84	3375.15	0.968524	314
12	425	3477.66	3045.62	0.875767	285
13	463	3473.68	2754.18	0.792871	259
14	502	3466.66	2496.77	0.720224	236
15	540	3461.59	2258.96	0.652579	215
16	579	3460.90	2045.00	0.590887	196
17	618	3452.60	1850.79	0.536057	179
18	656	3438.28	1675.86	0.487412	164
19	695	3434.74	1512.45	0.440339	149
20	733	3436.68	1376.87	0.400640	137
21	772	3432.69	1244.86	0.362649	125
22	810	3420.36	1128.73	0.330003	115
23	849	3424.78	1035.74	0.302425	106
24	887	3416.45	928.05	0.271643	96
25	926	3414.00	836.02	0.244880	88
26	964	3411.92	751.75	0.220331	80
27	1003	3395.18	676.01	0.199108	74
28	1041	3402.07	609.71	0.179216	67
29	1080	3389.66	539.51	0.159164	61
30	1119	3387.07	479.30	0.141508	56
31	1157	3383.20	431.74	0.127614	51
32	1196	3384.34	385.89	0.114021	47
33	1234	3363.80	348.15	0.103500	44
34	1273	3369.93	313.52	0.093035	41
35	1311	3362.38	274.77	0.081719	37
36	1349	3346.61	252.52	0.075454	35
37	1387	3334.40	221.21	0.066342	32
38	1425	3345.80	204.19	0.061028	31
39	1463	3350.28	178.55	0.053295	28
40	1501	3324.28	163.86	0.049292	27
41	1539	3330.00	145.96	0.043833	25

[a] We also observed slight degradation of acetanilide under these conditions. However, setting the integral of the IS peak on a constant value, *e.g.* 3490.23, which is a good approximation as injection volumes on our HPLC system have been shown to be very constant, we did only see extremely slight and negligible differences in the calculated fidaxomicin concentrations. We thus use the values as measured as an approximation.

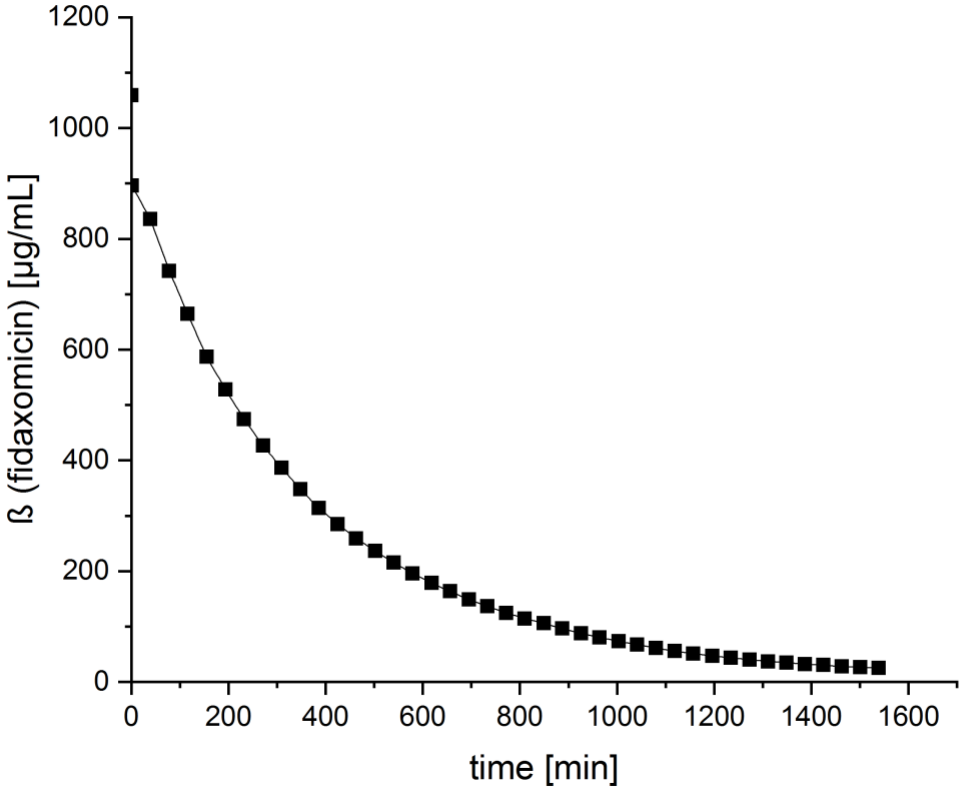
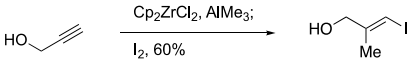


Figure S7. Degradation of fidaxomicin with 10 equivalents of HCl

4. Synthesis of known compounds.

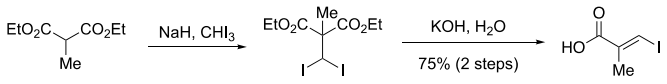
Compound **36a**



36 **36a**

To a solution of Cp_2ZrCl_2 (8,62 g, 29.5 mmol, 0.25 eq) in CH_2Cl_2 (250 mL) under Ar, Me_3Al (2 M in hexane or heptane, 175 mL, 354 mmol, 3.0 eq) were added by cannula and the resulting mixture was then cooled to 0 °C by ice-salt bath. At this temperature, a solution of propargyl alcohol (7.00 mL, 118 mmol) in CH_2Cl_2 (60 mL) was added dropwise over 20 min using a dropping funnel. After stirring for 17 h under warming to room temperature (the solution became redish-brown from yellow overnight) and continued stirring 1 more overnight, the mixture was cooled to –30 °C and a solution of iodine (36 g, 142 mmol, 1.2 eq) in THF (175 mL) was added slowly. Stirring was continued and gradually heated up to –5 °C and cooled again to –40 °C before quenching with sat. Rochelle (200 mL) and sat. $NaHCO_3$ (100 mL). (heavy-gas and heat development. The cooling bath was removed and stirred vigorously for more than 3 h. Then aqueous layer was extracted with Et_2O and combined organic layers were washed with sat. $Na_2S_2O_3$ (50 mL) solution, dried with $MgSO_4$, filtered, and concentrated. Purification by silica gel column chromatography (hexane/Et_2O = 1/5 - 1/4) gave desired product iodide (14.0 g, 60%) as a pale yellow oil; The obtained data matched to those reported.[7] R_f = 0.3 (Et_2O/pentane = 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (q, *J* = 1.3 Hz, 1H), 4.13 (d, *J* = 5.4 Hz, 2H), 1.85 (s, 3H), 1.58 (t, *J* = 3.1 Hz, 1H).

Compound **37a**



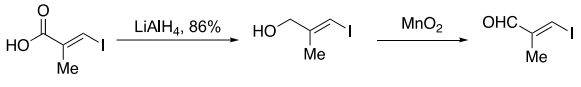
37 **37a** **37b**

To a suspension of NaH (1.65 g, 69.0 mmol, 1.2 eq) in Et_2O (100 mL) was added a solution of diethyl methylmalonate **37** (9.81 mL, 57.0 mmol) in Et_2O (20 mL) over 30 min. (Reaction mixture reached reflux temperature during the addition of malonate. Vigorous hydrogen gas evolution was observed.) Once the addition was complete, the mixture was stirred under reflux for 1.5 h before solid CHI_3 (22.6 g, 57.0 mmol, 1.0 eq) was added. The reaction mixture was heated at reflux temperature for 12 h and excess NaH was carefully quenched with aqueous HCl (1 M, 100 mL) after cooling to 0 °C. After stirring the heterogeneous mixture for 20 min, the layers were separated and the aqueous phase was extracted with Et_2O (4 x 50 mL). The combined organic layers were washed with brine (80 mL), dried over Na_2SO_4 and concentrated to give the diester **37a** as a pale brown oil, which was used in the next without further purification; The obtained crude data matched to those reported.[9] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.77 (d, *J* = 0.7 Hz, 1H), 4.22 (qd, *J* = 7.1, 1.5 Hz, 4H), 1.80 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 6H).

Compound **37b**

To a solution of crude malonate **37a** (crude, 24.8 g, 56.9 mmol) in EtOH (180 mL) was added a solution of KOH (15.9 g, 283 mmol, 5.0 eq) in water (60 mL). The resulting red solution was stirred at 90 °C for 4 h. After cooling and evaporation of EtOH, the residue was added K_2CO_3 (12 g, 85 mmol, 1.5 eq) in water (150 mL), which was then carefully acidified with conc. HCl at 0 °C. Extraction with CH_2Cl_2 (8 x 50 mL) was followed by drying of the combined organic layers over Na_2SO_4 and evaporation of the solvent. The residue was purified by column chromatography (hexanes/AcOEt, 9:1 + 0.5% HOAc) to yield the desired carboxylic acid **37b** as a pale yellow solid (9.03 g, 75%, two steps); The obtained data matched to those reported.[9] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 2.06 (d, *J* = 1.3 Hz, 3H).

Compound **36a**



37b **36a** **16**

A solution of acid **37a** (9.03 g, 42 mmol) in Et_2O (25 mL) was added over 20 min to a suspension of $LiAlH_4$ (1.78 g, 47 mmol, 1.1 eq) in Et_2O (60 mL) at 0 °C (in the ice bath). After stirring additional 30 min at this temperature, the ice bath was removed and the reaction mixture was stirred at room temperature for 2.5 h. The excess $LiAlH_4$ was carefully quenched with water (20 mL) and the mixture diluted with 3N HCl (50 mL, after addition and stirring, pH was checked). The mixture was stirred for 1 h at room temperature gave a good separation of water layer and yellowish organic layer. Then the aqueous layer was extracted with Et_2O (3 x 40 mL), the combined

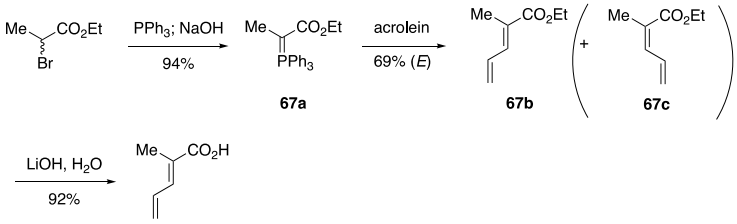
[7] (a) Baker, R.; Castro, J. L. *J. Chem. Soc. Perkin Trans. 1* **1990**, *112*, 47. (b) Menche, D.; Hassfeld, J.; Li, J.; Mayer, K.; Rudolph, S. *J. Org. Chem.* **2009**, *74*, 7220.

organic phases were washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by column chromatography (pentane/Et_2O = 5/1 - 4/1 - 3/1) and removal of the solvent by evaporation under 100 mbar at 40 °C gave desired alcohol **36a** as a colorless oil (7.27 g, 86%). R_f = 0.3 (Et_2O/pentane = 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (q, *J* = 1.3 Hz, 1H), 4.13 (d, *J* = 5.4 Hz, 2H), 1.85 (s, 3H), 1.58 (t, *J* = 3.1 Hz, 1H). The obtained data matched to those reported.[9]

Compound **16**

To a stirred solution of alcohol **36a** (1.0 g, 5.05 mmol) in CH_2Cl_2 (25 mL), MnO_2 (4.8 g, 56 mmol, 11 eq) was added at room temperature and stirred for 5 h. The reaction mixture was filtered through a pad of Celite and the solvent was dried over $MgSO_4$, filtered, and evaporated to give desired aldehyde **16** as a CH_2Cl_2 (ca. 5 mL) solution. This was used in the following step without purification; The obtained data matched to those reported.[9] R_f = 0.9 (Et_2O/pentane = 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.81 (q, *J* = 1.2 Hz, 1H), 1.92 (d, *J* = 1.2 Hz, 3H).

Compound **67**



A mixture of triphenylphosphine (2.11 g, 8.06 mmol, 1.0 eq) and ethyl bromopropionate (1.2 mL, 8.85 mmol) in water (9.0 mL) was stirred for 24 h at 65 to 85 °C under Ar. The reaction mixture was cooled to room temperature and added a water (10 mL) solution of NaOH (740 mg, 18.5 mmol, 2.3 eq). Rapid precipitation of ylide was observed. The resulting mixture was stirred for 5 min at room temperature and then CH_2Cl_2 was added to dissolve the solid that formed. The organic layer was separated and aqueous layer was extracted with CH_2Cl_2 2 times. Combined organics were washed with brine, dried over Na_2SO_4, filtered and concentrated. The obtained residue was triturated with pentane and filtered. The resulting solid was dried to give Ethyl (triphenylphosphoranylidene)propionate **67a** (2.84 g, 94%) as a yellow solid. The obtained data matched to those reported.

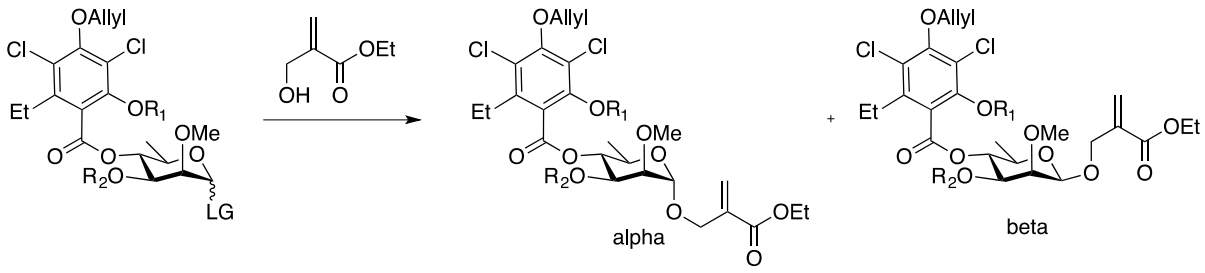
To a solution of ylid **67a** (2.8 g, 7.4 mmol) in CH_2Cl_2 (10 mL) was slowly added freshly distilled acrolein (540 µL, 9.62 mmol, 1.3 eq) at room temperature. After the reaction mixture was stirred at room temperature for 1 h, it was heated to 40 °C for 1 h. At this point, full conversion of the reaction was confirmed by ^{1}H NMR analysis of reaction mixture. (TLC monitoring did not work). The reaction mixture was partially concentrated so that 1/5 of CH_2Cl_2 left in the flask and it was added excess pentane. Precipitate (PPh_3O) formed was it was filtered off and washed with pentane. After concentration precipitate again formed was filtered off and washed with excess pentane. The filtrate obtained was concentrated to give rather volatile ester. Distillation at 50 to 60 °C under 8 mbar (oil bath 80 °C) provided ca. 698 mg of desired ester as a *E*/*Z* mixture (ca. 10:1 determined by ^{1}H NMR). This mixture was further purified by column chromatography (Et_2O/pentane = 1/100 – 1.5/100 - 2/100 - 3/100) to give desired (*E*)-ester **67b** (719 mg, 69%) and (*Z*)-ester **67c** as a rather volatile oil. R_f = 0.6 (Et_2O/pentane = 1/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 11.4 Hz, 1H), 6.66 (ddd, *J* = 16.9, 11.4, 10.1 Hz, 1H), 5.56 (d, *J* = 16.9 Hz, 1H), 5.44 (d, *J* = 10.0 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 1.95 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 138.4, 132.4, 128.3, 124.2, 60.8, 14.5, 12.8. The obtained data matched to those reported.

To a solution of ethyl ester (*E*)-**67b** (650 mg, 4.63 mmol) in THF (30 mL) was added LiOH H_2O (1.68 g, 40 mmol, 8.5 eq) in water (15 mL) and stirred at room temperature for 6 h. Reaction mixture was cooled down to 0 °C and acidified with 3N HCl and the aqueous phase was extracted with Et_2O 3 times. Combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, filtered and concentrated. This mixture was dissolved in Et_2O and crystalized from pentane to give desired carboxylic acid **67** (478 mg, 92%) as a white solid. This product could further be purified by column chromatography (CH_2Cl_2/MeOH = 100/1 - 100/2 - 100/5) to give a white solid (ca. 70% after chromatography); The obtained data matched to those reported.[8] R_f = 0.5 (CH_2Cl_2/MeOH = 1/50); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.03 (s, 1H), 7.22 (dd, *J* = 11.4, 1.4 Hz, 1H), 6.61 (ddd, *J* = 16.8, 11.4, 10.1 Hz, 1H), 5.55 (d, *J* = 16.8 Hz, 1H), 5.44 (d, *J* = 10.0 Hz, 1H), 1.89 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 140.8, 132.2, 127.4, 125.6, 12.4.

[8] Bond, F. T.; Ho, C.-Y. *J. Org. Chem*. **1976**, *41*, 1421.

5. Screening of rhamnosylation

Table S9. Screening of rhamnosylations.



Screening of beta selective Rhamnosylation

Entry	R1	R2	LG	Promoter, conditions	Yield	alpha beta
1	H	H	SPh	NIS, AgOEt (cat.), DCM, -78 °C to rt	58%	1:2
2a	TBS	TBS	SPh	NBS, DCM, 0 °C to rt	full conv.	1.7:1
3a	TBS	TBS	SPh	NIS, AgOEt (cat.), DCM, -78 to -30 °C	68%	4:1
4a	TBS	TBS	S(=O)Ph	Tf2O, 2,6-(t-Bu)Py.,DCM, -78 °C	full conv.	3:1
5	SEM	SEM	SPh	NIS, AgOEt (1 eq.), 2,6-(t-Bu)Py.,DCM, rt	full conv.	3:2
6	Allyl	H	SPh	NIS, AgOEt (1 eq.), 2,6-(t-Bu)Py.,DCM, 0 °C	77%	5:6
7	Allyl	H	S(=O)Ph	Tf2O, 2,6-(t-Bu)Py.,DCM, -78 °C then ROH	full conv.	1:2
8	Allyl	H	OC(=N-Ph)CF3	TBSOTf, DCM, -78 to -55 °C	full conv.	1:3

7. Comparison of natural (semisynthetic) and synthetic samples

Comparison of ^{1}H NMR of synthetic and semisynthetic 7

Figure S8. Comparison of ^{1}H NMR chemical shifts and coupling constants in acetone-d_6 of synthetic (up) and semisynthetic (down) **7** (500 MHz).

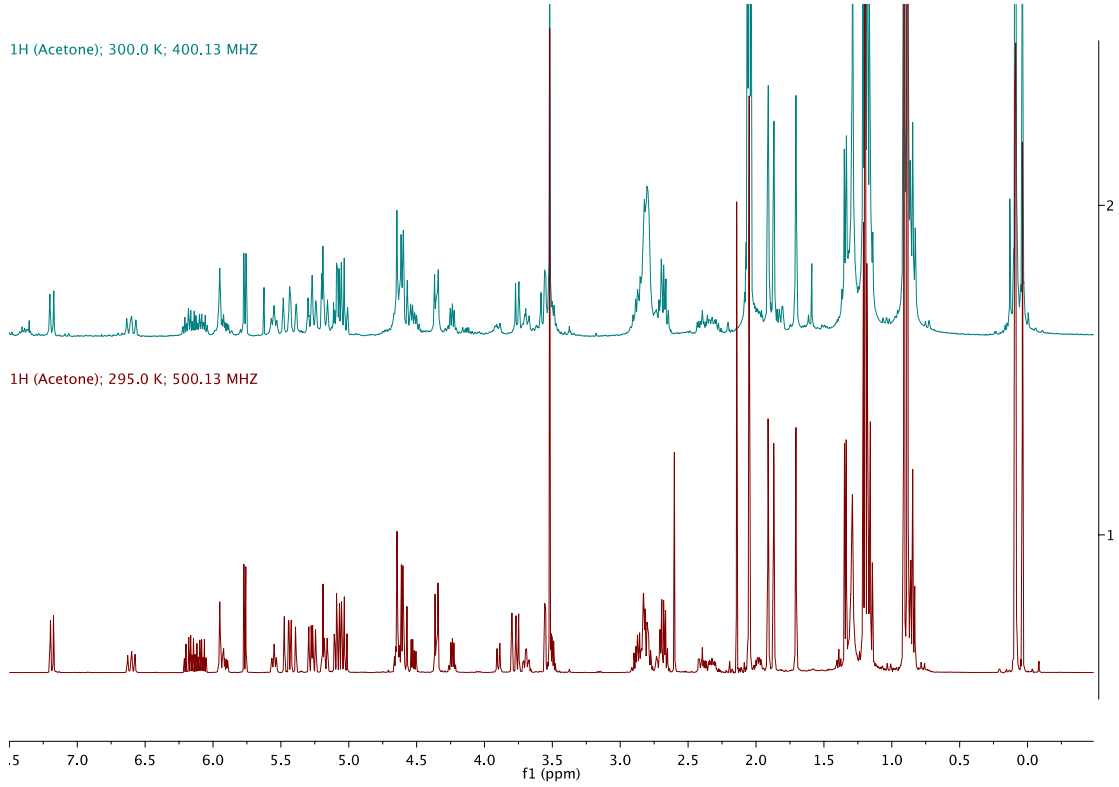
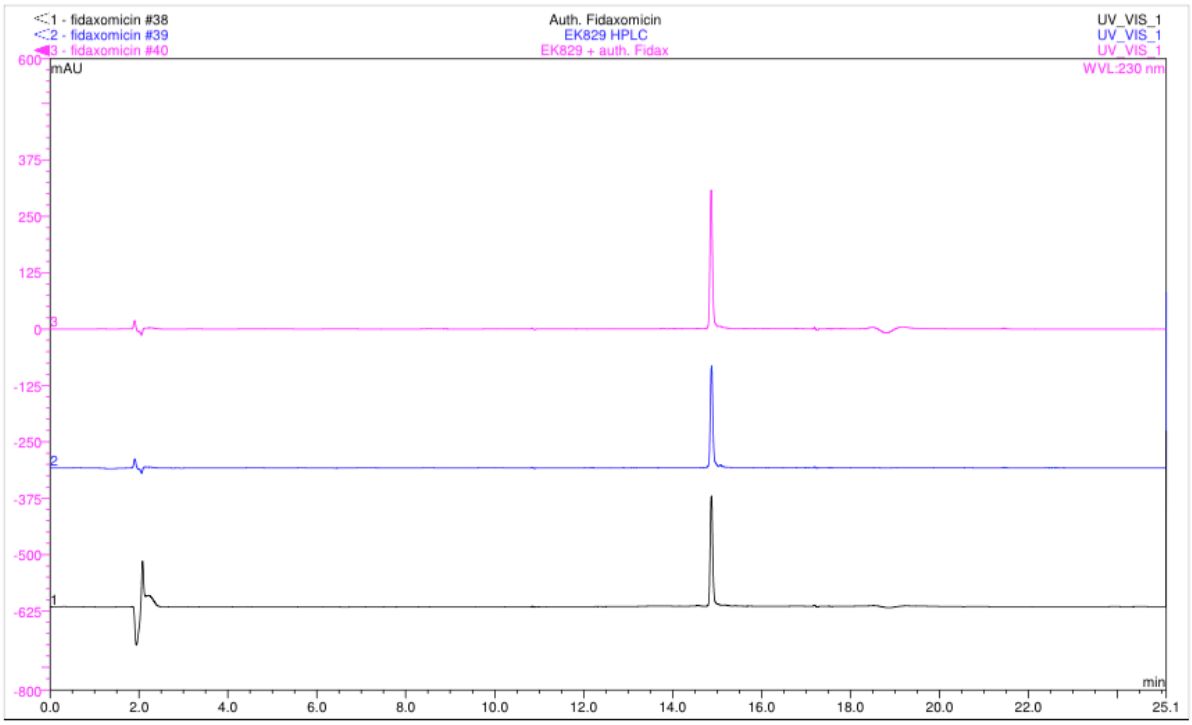


Table S10. Comparison of ^{1}H NMR chemical shifts and coupling constants in acetone-d_6 of of synthetic and semisynthetic **7** (500 MHz).

Semisynthetic **7**[a]				Totally Synthetic **7**[b]				Δ^c = **7**^{semi} - **7**^{total}
ppm	H		*J*	ppm	H		*J*	ppm
7.19	1	d	11.4	7.19	1	d	11.5	0.00
6.63	1	dd	14.9, 11.6	6.60	1	t	12	0.03
6.17	1	ddt	17.1, 10.4, 5.8	6.18	1	m		-0.01
6.09	1	ddt	17.1, 10.4, 5.8	6.09	1	m		0.00
5.95	1	s		5.95	1	s		0.00
5.92	1	ddd	14.8, 10.3, 4.5	5.90	1	m		0.02
5.77	1	d	7.0	5.76	1	d	6.8	0.01
5.55	1	t	8.3	5.55	1	t	8.3	0.00
5.46	1	dq	17.2, 1.6	5.46	1	dt	17.3, 1.7	0.00
5.41	1	dq	17.2, 1.6	5.40	1	dt	17.3, 1.7	0.01
5.29	1	dq	10.4, 1.2	5.29	1	dt	1.3	0.00
5.26	1	dq	10.4, 1.2	5.27	1	dt	1.3	-0.01
5.19	1	d	3.2	5.19	1	d	3.1	0.00
5.17	1	dt	10.6, 1.3	5.17	1	d	11	0.00
5.10	1	dd	8.9, 3.2	5.10	1	dd	8.8, 3.2	0.00
5.05	1	dd	8.7, 7.2	5.06	1	d	6.6	-0.01
5.03	1	t	9.6	5.04	1	t	9.5	-0.01
4.64	4	m		4.64	4	m		0.00
4.61	2	d	5.7	4.61	2	d	6.0	0.00
4.58	1	d	11.2	4.58	1	d	11.5	0.00
4.52	1	ddt	11.8, 5.8, 1.3	4.52	1	ddt	11.7, 5.9, 1.4	0.00
4.36	1	d	11.0	4.35	1	d	11	0.01
4.35	1	m		4.35	1	m		0.00
4.24	1	m		4.24	1	m		0.00
3.90	1	d	10.1	3.90				0.00
3.76	1	d	9.8	3.76	1	d	9.8	0.00
3.69	1	dt	9.7, 3.3	3.69	1	dd	9.8, 3.4	0.00
3.55	1	d	3.5	3.55	1	d	3.5	0.00
3.52	3	s		3.52	3	s		0.00
3.50	1	m		3.51	1	m		-0.01
2.83	5	m		2.82	5	m		0.01
2.73	2	m		2.68	2	m		0.05
2.40	1	ddd	14.8, 10.3, 4.5	2.40	1	td	10.2, 10.1, 5.1	0.00
2.32	1	ddd	13.8, 7.6, 4.1	2.30	1	m		0.02
1.98	1	m		1.98	1	m		0.00
1.91	3	s		1.91	3	s		0.00
1.87	3	s		1.87	3	s		0.00
1.71	3	s		1.71	3	s		0.00
1.34	3	d	6.2	1.34	2	d	6.2	0.00
1.21	3	d	7.2	1.21	3	m		0.00
1.20	3	d	6.9	1.20	3	m		0.00
1.19	3	d	6.9	1.19	3	m		0.00
1.17	3	d	6.3	1.17	3	m		0.00
1.16	3	t	7.4	1.16	3	m		0.00
0.91	9	s		0.91	9	s		0.00
0.88	9	s		0.89	9	s		-0.01
0.85	3	t	7.4	0.85	3	t	7.6	0.00
0.09	3	s		0.09	3	s		0.00
0.09	3	s		0.09	3	s		0.00
0.08	3	s		0.09	3	s		-0.01
0.04	3	s		0.04	3	s		0.00

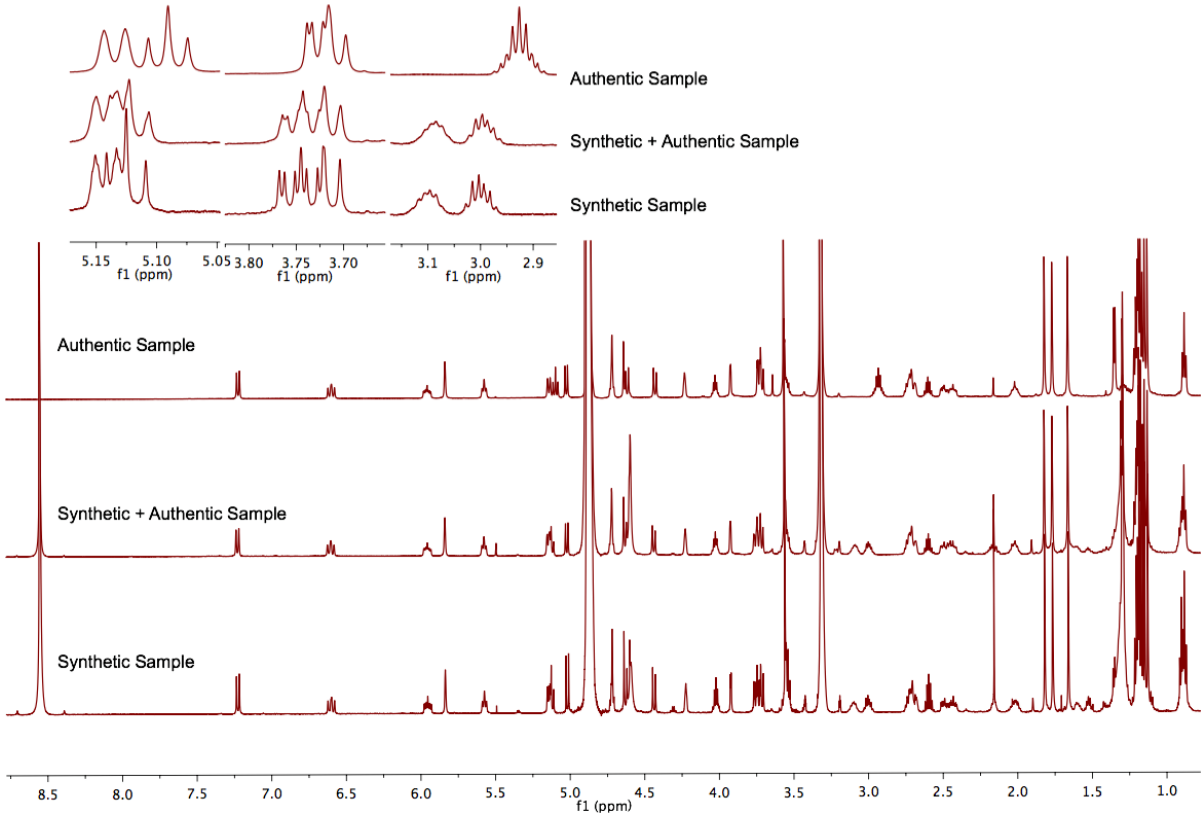
a) ^{1}H NMR of Semisynthetic fidaxomicin **7** acquired in 500 MHz spectrometer with BBI probe; b) ^{1}H NMR of totally synthetic sample **7** acquired in 500 MHz spectrometer with BBI probe; c) chemical shift difference.

Figure S9. Comparison of RP-HPLC of synthetic **1** and natural **1**[a]



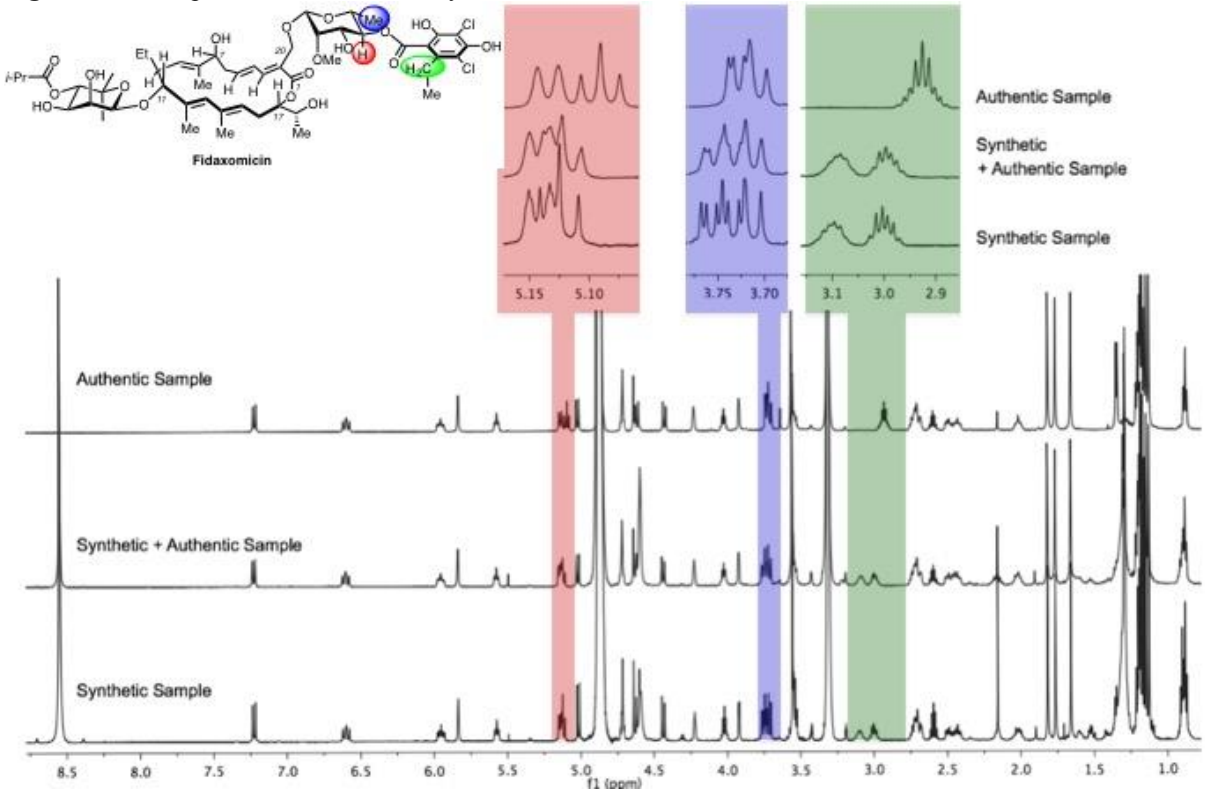
[a]RP-HPLC co-injection of the authentic and synthetic compound. Black = authentic sample; blue = fully synthetic sample; pink = mixture of authentic and fully synthetic sample.

Figure S10. Comparison of ^{1}H NMR of synthetic and natural **1**[a]



[a]Proof of co-identity of the natural **1** and fully synthetic (containing formate) **1** in CD_3OD.

Figure S11. Comparison of ^{1}H NMR of synthetic and natural **1**[a]



[a]As mentioned in the experimental section, the ^{1}H NMR of synthetic **1** and natural **1** did not match completely. The signals of the resorcylate-rhamnosyl part were shifted, whereas the signals from the macrolide and the novioside were identical with the corresponding signals of the natural **1**. Depicted regions are highlighted: red, δ 5.10 ppm: C4'H triplett of rhamnosyl part; green, δ 2.92 ppm methlyene substituent at resorcylate; blue, δ 1.35 ppm C6'H methyl group of rhamnosyl part.

Figure S12. Comparison of ^{1}H NMR chemical shifts and coupling constants in $CDCl_3$ of natural (up)[9] and synthetic (down) tiacumicin A (**2**) (500 MHz).

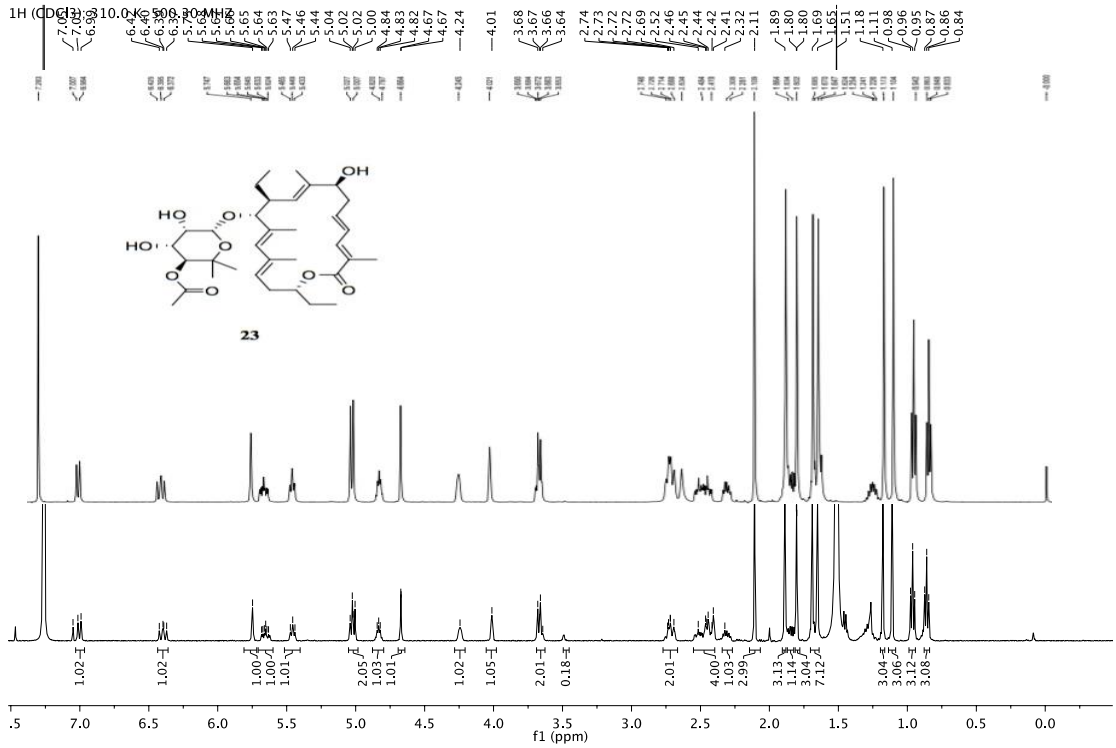
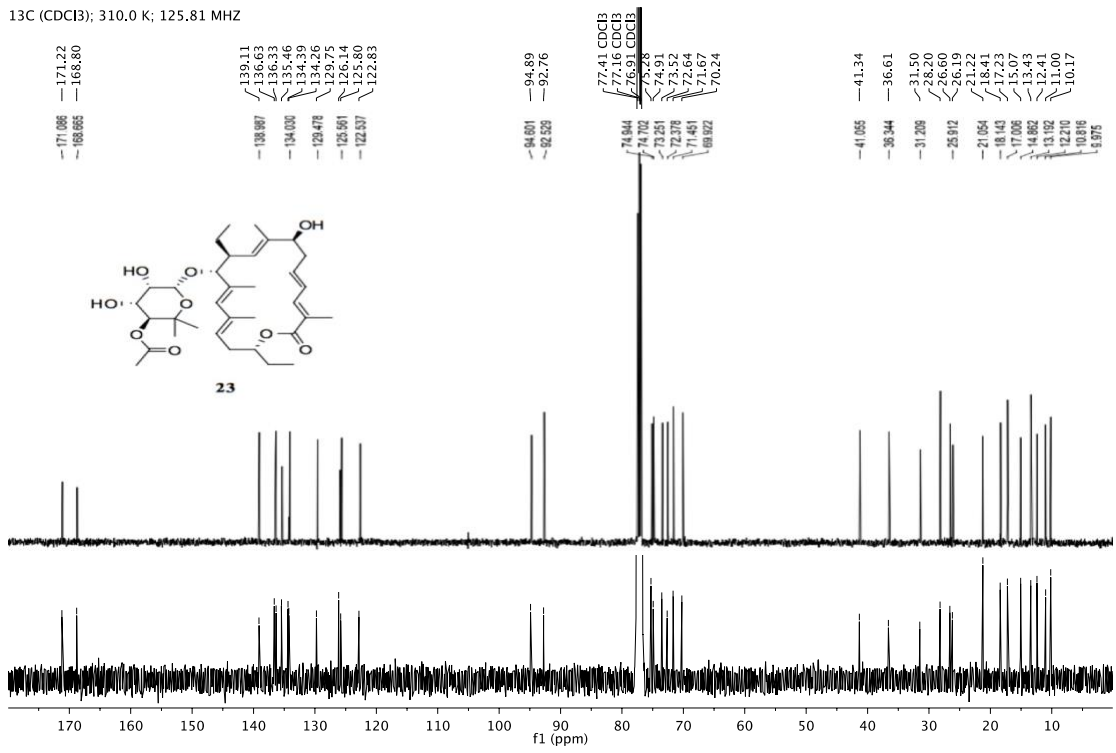


Figure S13. Comparison of ^{13}C NMR chemical shifts and coupling constants in $CDCl_3$ of natural[9] (up) and synthetic (down) tiacumicin A (**2**) (125 MHz).



[9] (a) Hochlowski, J. E.; Swanson, S. J.; Ranfranz, L. M.; Whittern, D. N.; Buko, A. M.; McAlpine, J. B. *J. Antibiot. (Tokyo)*. **1987**, *40*, 575. (b) Xiao, Y.; Li, S.; Niu, S.; Ma, L.; Zhang, G.; Zhang, H.; Zhang, G.; Ju, J.; Zhang, C. *J. Am. Chem. Soc*. **2011**, *133*, 1092.

Table S11. Comparison of ^{1}H NMR chemical shifts and coupling constants in $CDCl_3$ of natural and synthetic tiacumicin A (**2**) (500 MHz).

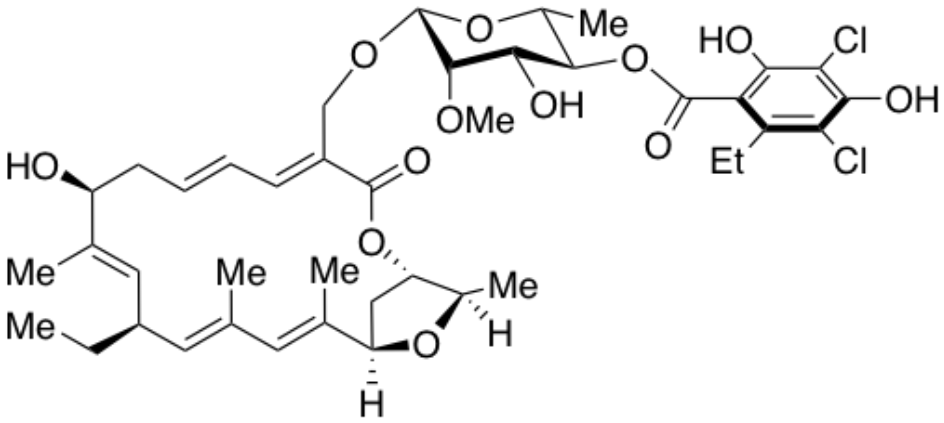
Natural Tiacumicin A (**2**) J Antibiotics[9a]		Natural Tiacumicin A (**2**) JACS[9b, a]		Synthetic Tiacumicin A (**2**)[b]			Δ^c = **2**$^{nat(JACS)}$ - **2**$^{syn(d)}$
ppm	*J*	ppm	*J*	ppm[d]	ppm[e]	*J*	ppm
7.25	(d, 1H, J=11.3)	6.98	(d, 11.0)	6.97	7.00	(d, J = 11.3 Hz, 1H)	-0.01
6.25	(ddd, 1H, J=14.5, 11.4)	6.38	(t, 13.3)	6.37	6.40	(dd, J = 14.7, 11.8 Hz, 1H)	-0.01
5.67	(ddd, 1H, J=15.1, 10.3, 4.7)	5.73	s	5.72	5.75	(s, 1H)	-0.01
5.58	(br s, 1H)	5.63	m	5.62	5.65	(ddd, J = 14.8, 10.2, 4.5 Hz, 1H)	-0.01
5.53	(br t, 1H, J=8.2)	5.43	(t. 8.0)	5.43	5.46	(t, J = 8.3 Hz, 1H)	0.00
5.40	(d, 1H, J=10.5)	4.99	(d, 10.0)	5.00	5.03	(d, J = 10.6 Hz, 1H)	0.01
5.21	(br d, 1H, J=10.3)	4.99	(d, 10.0)	4.98	5.01	(d, J = 10.0 Hz, 1H)	-0.01
4.99	(m, 1H)	4.80	m	4.80	4.83	(p, J = 6.2 Hz, 1H)	0.00
4.26	(d, 1H, J=1.3)	4.65	s	4.64	4.67	(s, 1H)	-0.01
3.97	(m, 1H)	4.23	br	4.21	4.24	(br s, 1H)	-0.02
3.81	(br d, 1H, J=2.9)	4.00	s	3.98	4.01	(s, 1H)	-0.02
3.58	(br dd, 1H, J=10.5, 2.9)	3.65	m	3.64	3.67	(d, J = 9.8 Hz, 1H)	-0.01
3.45	(d, 1H, J=9.7)	3.65	m	3.63	3.66	(br m, J = 9.3 Hz, 1H)	-0.02
2.66	(ddd, 1H, J=10.3, 9.7, 5.7)	2.71	s	2.69	2.72	(m, 2H)	-0.02
2.48	(ddd, 1H, J=11.1, 8.2, 4.5)	2.62	br	2.49	2.52	(ddd, J = 13.8, 9.0, 4.3 Hz, 1H)	-0.13
2.34	(m, 1H)	2.47	m	2.41	2.44	(m, 3H)	-0.06
2.18	(m, 1H)	2.43	m				-2.46
2.15	(m, 1H)	2.29	m	2.28	2.31	(dt, J = 13.7, 6.5 Hz, 1H)	-0.01
1.95	(br s, 3H)	2.09	s	2.08	2.11	(s, 3H)	-0.01
1.90	(br s, 3H)	1.86	s	1.86	1.89	(s, 3H)	0.00
1.85	(m, 1H)	1.83	(dd, 7.0, 14.0)	1.81	1.84	(m, J = 14.1, 7.0 Hz, 1H)	-0.02
1.85	(m, 1H)	1.81	m	-0.03			-1.84
1.75	(s, 3H)	1.78	s	1.77	1.80	(s, 3H)	-0.01
1.70	(br s, 3H)	1.67	s	1.66	1.69	(s, 3H)	-0.01
		1.63	s	1.62	1.65	(s, 3H)	-0.01
1.58	(m, 1H)	1.62	m	1.57	1.60	(m, 1H)	-0.05
1.36	(br s, 3H)	not reported		not observed			
1.30	(m, 1H)	1.23	m	1.27	1.30	(m, 1H)	0.04
1.20	(s, 3H)	1.15	s	1.15	1.18	(s, 3H)	0.00
1.02	(s, 3H)	1.08	s	1.08	1.11	(s, 3H)	0.00
0.95	(t, 3H, J=7.4)	0.94	(t, 7.5)	0.93	0.96	(t, J = 7.5 Hz, 3H)	-0.01
0.82	(t, 3H, J=7.4)	0.83	(t, 7.5)	0.83	0.86	(t, J = 7.4 Hz, 3H)	0.00

a) ^{1}H NMR of natural tiacumicin A (**2**) acquired in 500 MHz spectrometer in $CDCl_3$; b) ^{1}H NMR of synthetic tiacumicin A (**2**) acquired in 500 MHz spectrometer with BBI probe; c) chemical shift difference; d) chemical shift of synthetic tiacumicin A (**2**); e) chemical shift corrected based on the chloroform peak at 7.26.

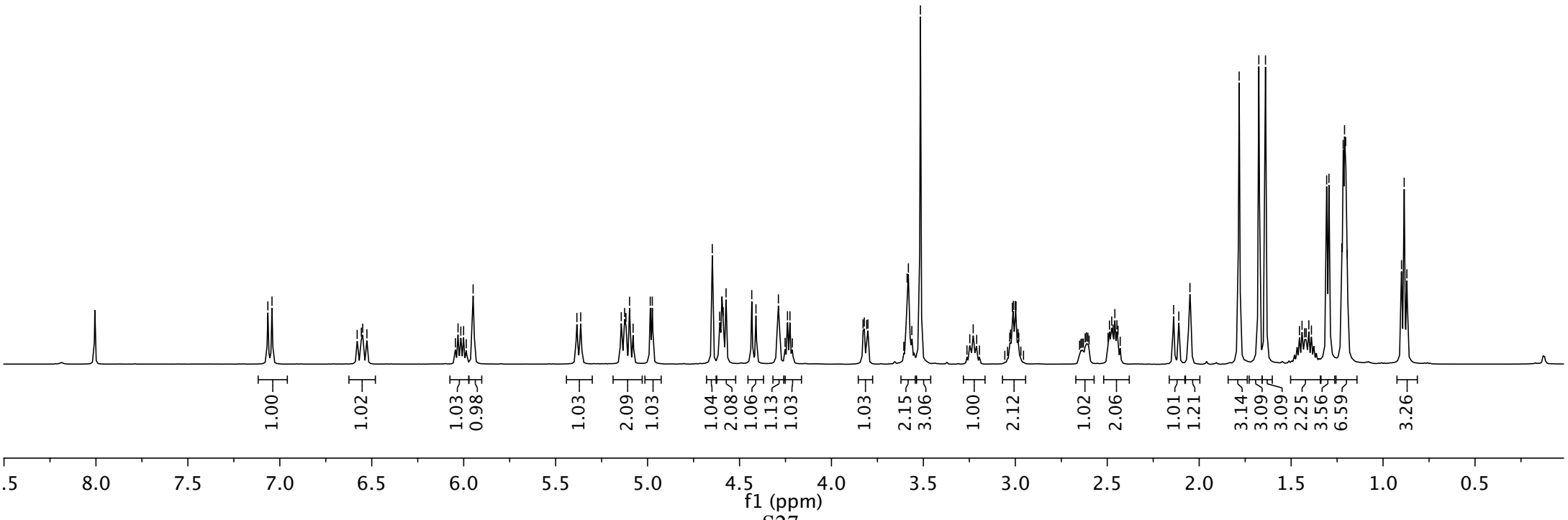
Table S12. Comparison of ^{13}C NMR chemical shifts and coupling constants in $CDCl_3$ of natural and synthetic tiacumicin A (**2**) (125 MHz).

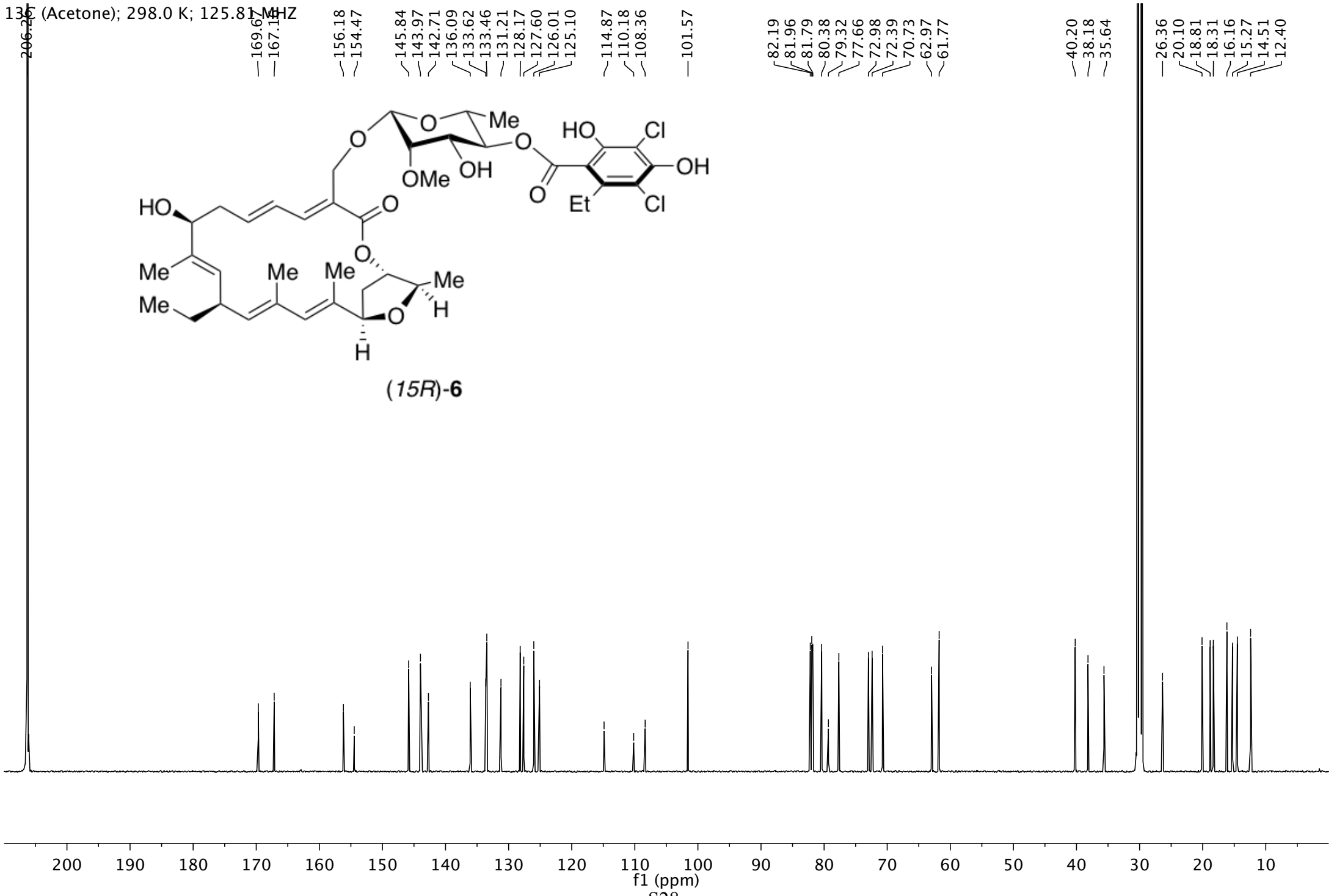
	Natural Tiacumicin A (**2**)[9a, a]				synthetic Tiacumicin A (**2**)[b]	
	J Antibiotics		JACS		synthetic	Δ^c = **2**^{nat}(JACS) – **2**^{syn}
position	ppm	^{13}C	ppm	^{13}C	ppm	ppm
1""	171.3	Q	171.1	s	171.22	-0.12
1	169.1	Q	168.7	s	168.80	-0.10
3	139.7	CH	139.0	d	139.11	-0.11
8	137.4	CH	136.4	s	136.63	-0.23
5	135.8	Q	136.3	d	136.33	-0.03
14	135.2	Q	135.3	s	135.46	-0.16
12	134.3	Q	134.1	s	134.39	-0.29
13	133.6	CH	134.0	d	134.26	-0.26
4	128.3	CH	129.5	d	129.75	-0.25
2	125.1	CH	125.8		126.14	-0.34
15	124.8	Q	125.5	d	125.80	-0.30
9	122.6	CH	122.5	d	122.83	-0.33
1´´	94.9	CH	94.6	d	94.89	-0.29
11	92.6	CH	92.5	d	92.76	-0.26
CDCl3					77.41	
CDCl3					77.16	
CDCl3					76.91	
4´´	74.8	CH	74.9	d	75.28	-0.38
17	74.8	CH	74.7	d	74.91	-0.21
5´´	73.1	Q	73.3	s	73.52	-0.22
7	71.3	CH	72.4	d	72.64	-0.24
2´´	71.2	CH	71.5	d	71.67	-0.17
3´´	69.4	CH	69.9	d	70.24	-0.34
10	40.9	Q	41.1	d	41.34	-0.24
6	35.9	CH2	36.3	t	36.61	-0.31
16	31.0	CH2	31.2	t	31.50	-0.30
6´´	27.7	CH3	27.9	d	28.20	-0.30
18	26.1	CH2	26.3	t	26.60	-0.30
22	25.6	CH2	25.9	t	26.19	-0.29
2""	20.6	CH3	21.1	q	21.22	-0.12
7´´	17.8	CH3	18.1	q	18.41	-0.31
25	16.7	CH3	17.0	q	17.23	-0.23
21	14.6	CH3	14.9	q	15.07	-0.17
24	12.9	CH3	13.2	q	13.43	-0.23
20	11.7	CH3	12.2	q	12.41	-0.21
23	10.4	CH3	10.8	q	11.00	-0.20
19	9.6	CH3	10.0	q	10.17	-0.17

a) ^{13}C NMR of natural tiacumicin A (**2**) acquired in 125 MHz spectrometer in $CDCl_3$; b) ^{13}C NMR of synthetic tiacumicin A (**2**) acquired in 125 MHz spectrometer with cryo-BBO probe; c) chemical shift difference.


HO
O
O
Me
OMe
OH
O
HO
Cl
OH
O
Et
Cl
O
Me
Me
Me
Me
Me
O
H
H

(*15R*)-**6**


1.00
1.02
1.03
0.98
1.03
2.09
1.03
1.04
2.08
1.06
1.13
1.03
1.03
2.15
3.06
1.00
2.12
1.02
2.06
1.01
1.21
3.14
3.09
3.09
2.25
3.56
6.59
3.26
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


13C (Acetone); 298.0 K; 125.81 MHZ
206.26
169.67
167.14
156.18
154.47
145.84
143.97
142.71
136.09
133.62
133.46
131.21
128.17
127.60
126.01
125.10
114.87
110.18
108.36
101.57
82.19
81.96
81.79
80.38
79.32
77.66
72.98
72.39
70.73
62.97
61.77
40.20
38.18
35.64
26.36
20.10
18.81
18.31
16.16
15.27
14.51
12.40
HO
Cl
OH
Cl
Et
O
Me
OMe
OH
Me
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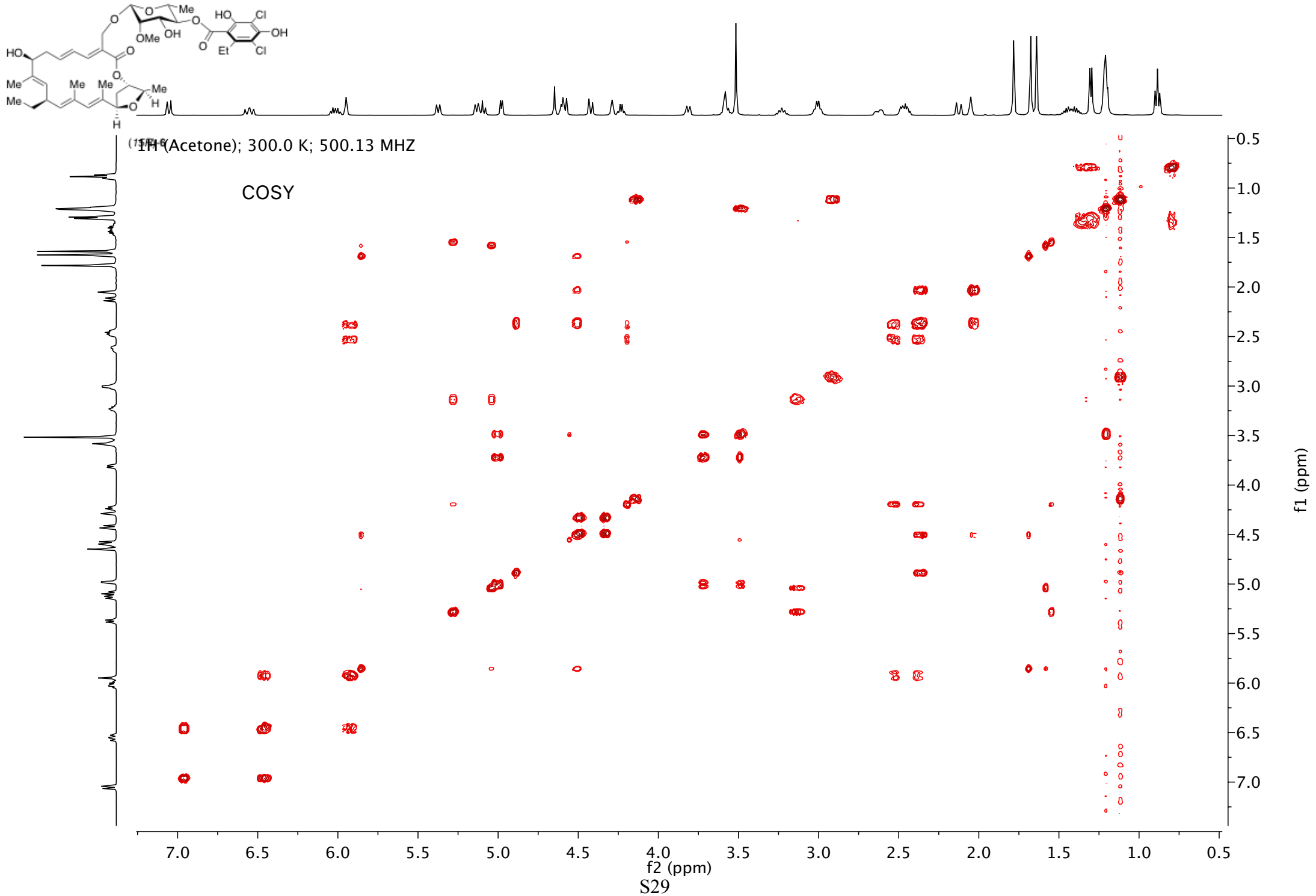
Me
Me
Me
H
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

(*15R*)-**6**


1H (Acetone); 300.0 K; 500.13 MHZ
COSY
f2 (ppm)
f1 (ppm)
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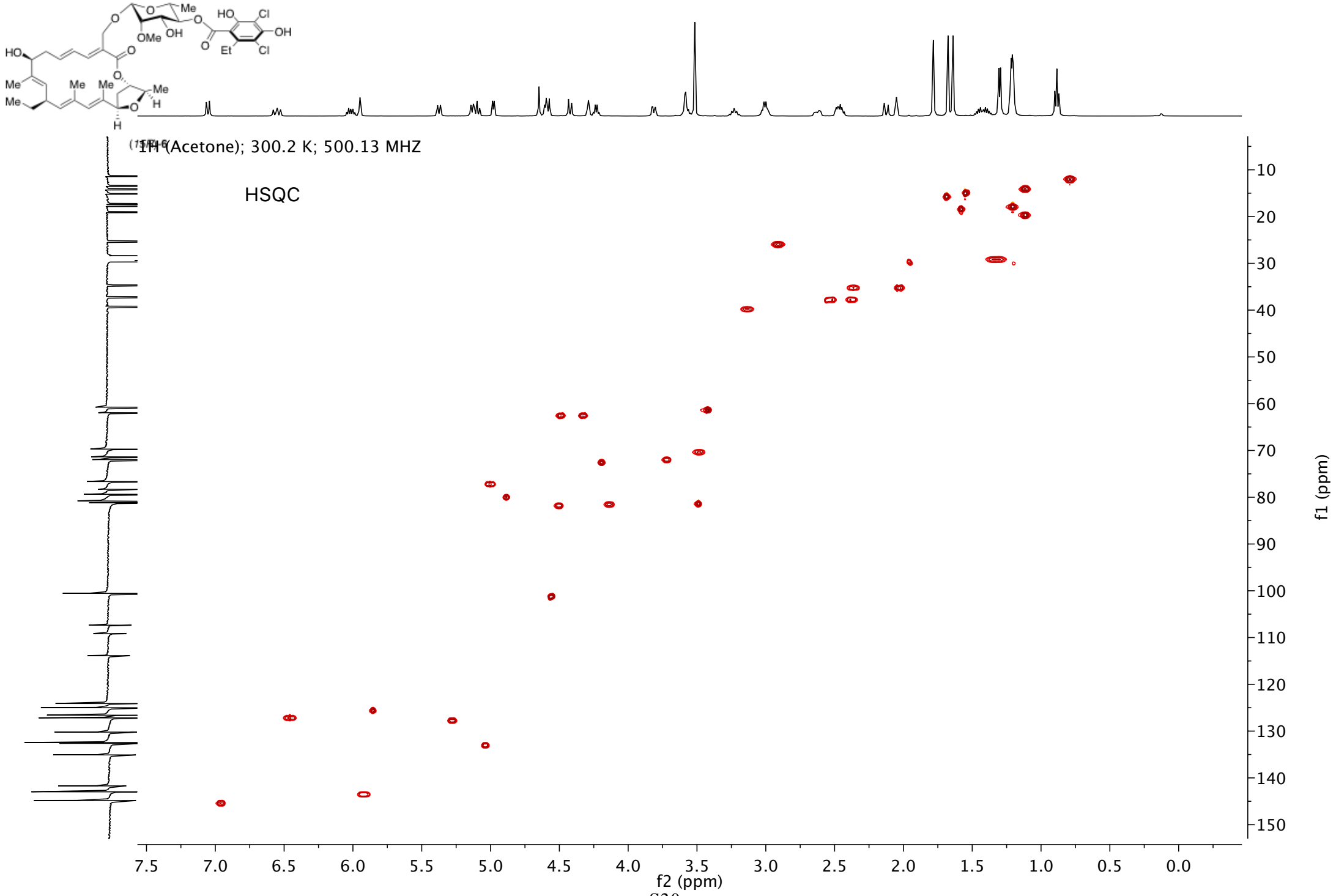
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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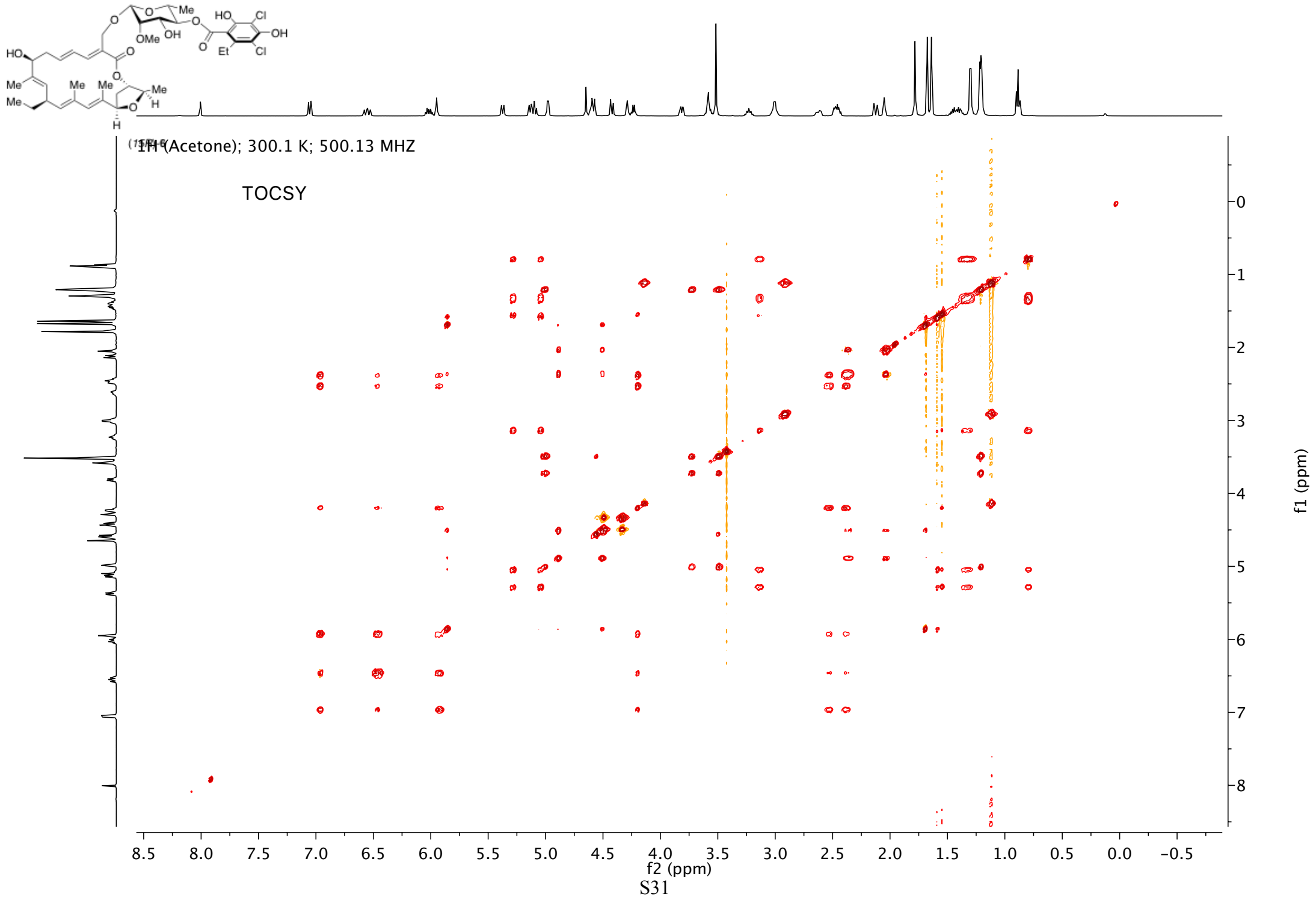
f2 (ppm)
f1 (ppm)


1H (Acetone); 300.1 K; 500.13 MHZ
TOCSY
f2 (ppm)
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
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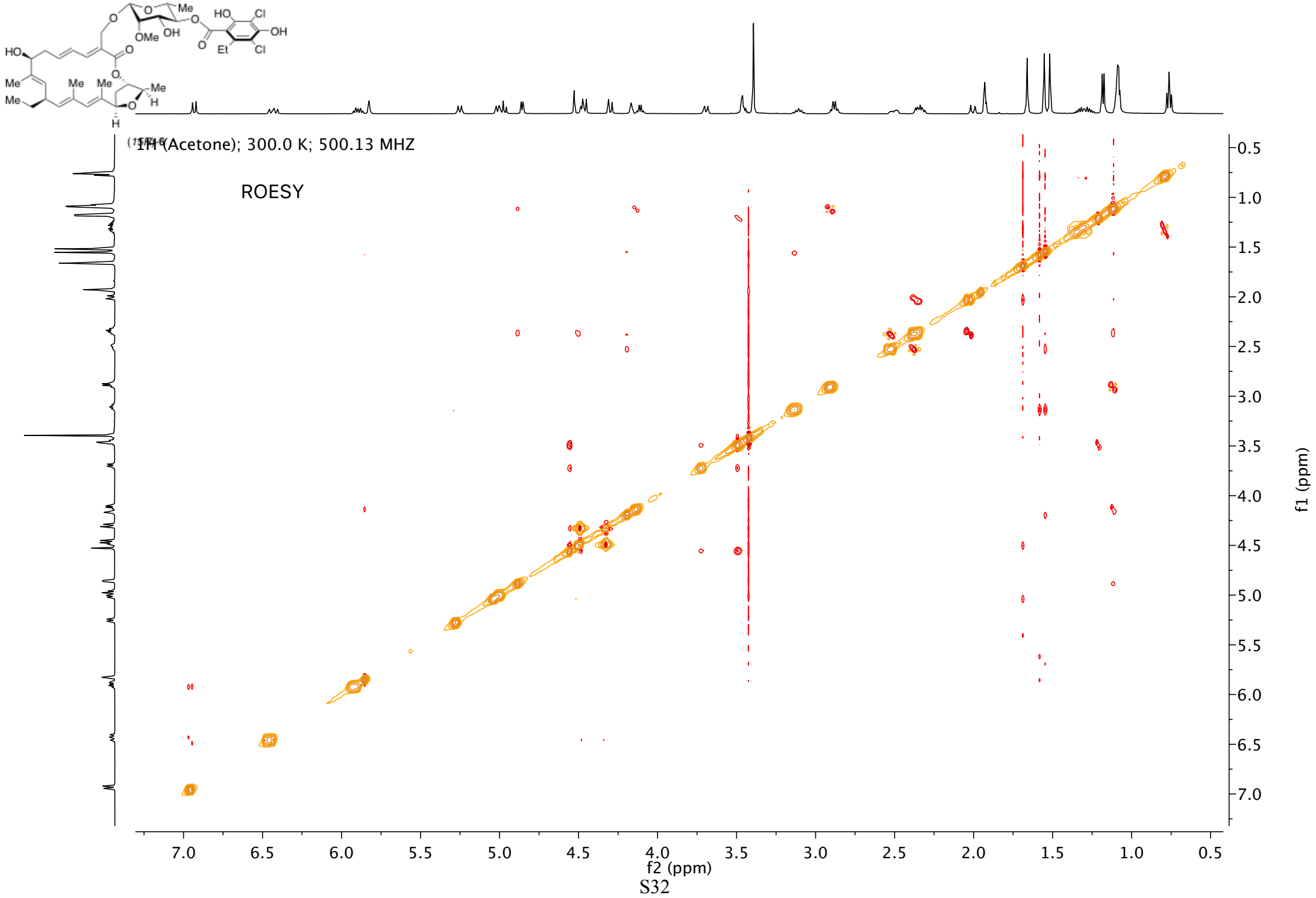
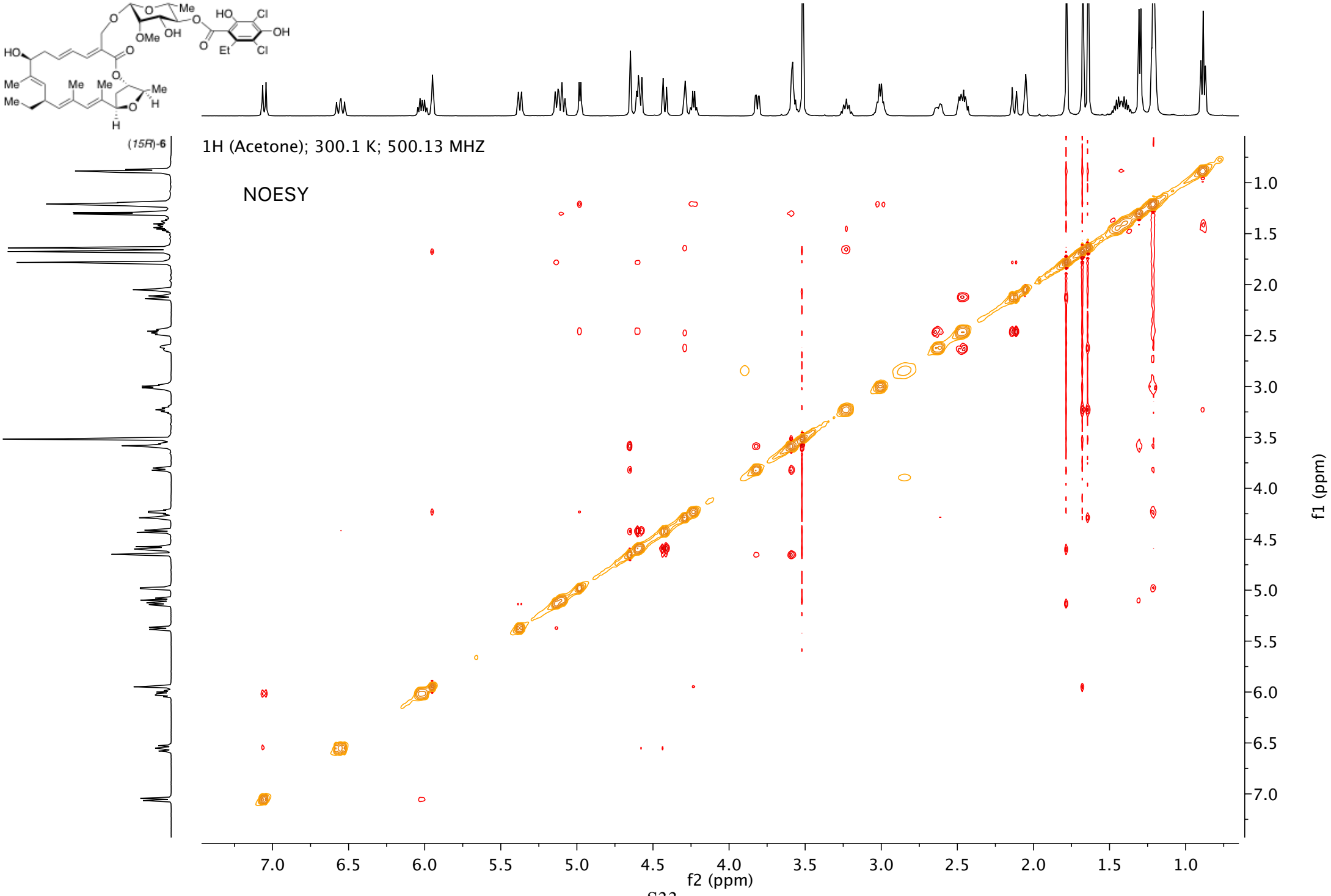
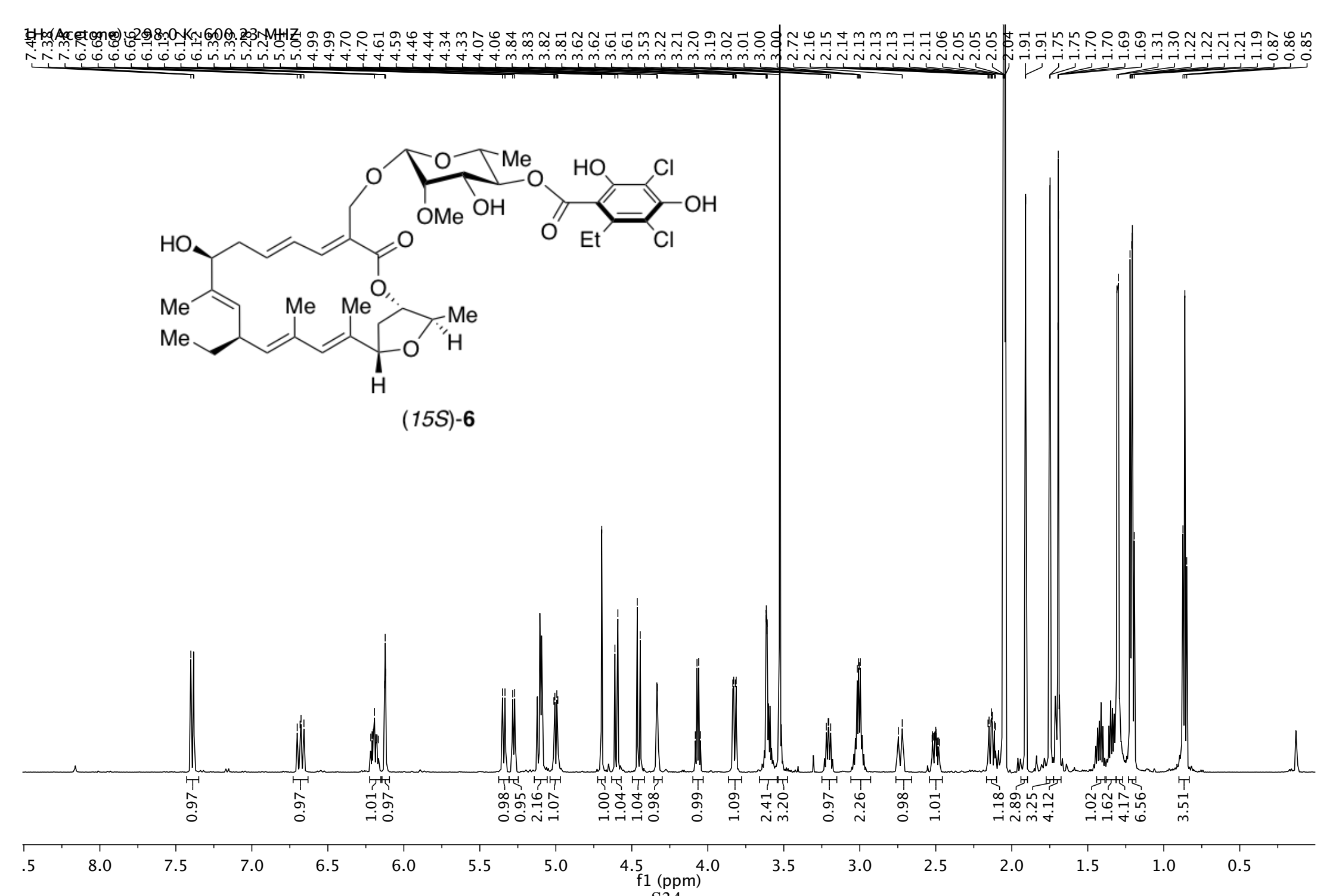
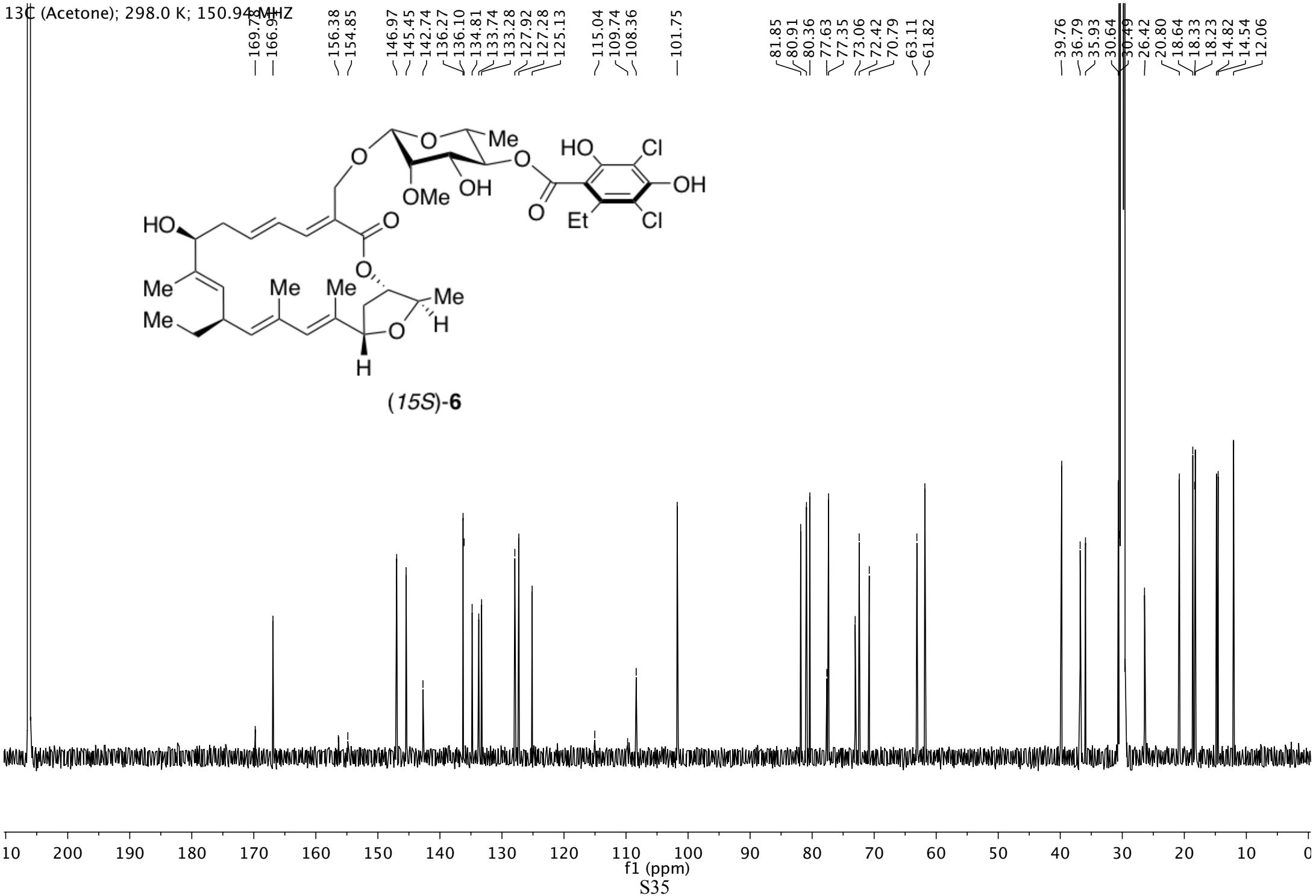
0
1
2
3
4
5
6
7
8


1H (Acetone); 300.0 K; 500.13 MHZ
ROESY
f2 (ppm)
f1 (ppm)
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


(15R)-6
1H (Acetone); 300.1 K; 500.13 MHZ
NOESY
f2 (ppm)
f1 (ppm)


1H (Acetone) 298.0 K, 600.23 MHz
HO
O
Me
O
HO
Cl
OH
OMe
OH
O
Et
Cl
HO
O
O
Me
Me
Me
Me
Me
O
H
H
(15S)-6
f1 (ppm)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146.97
145.45
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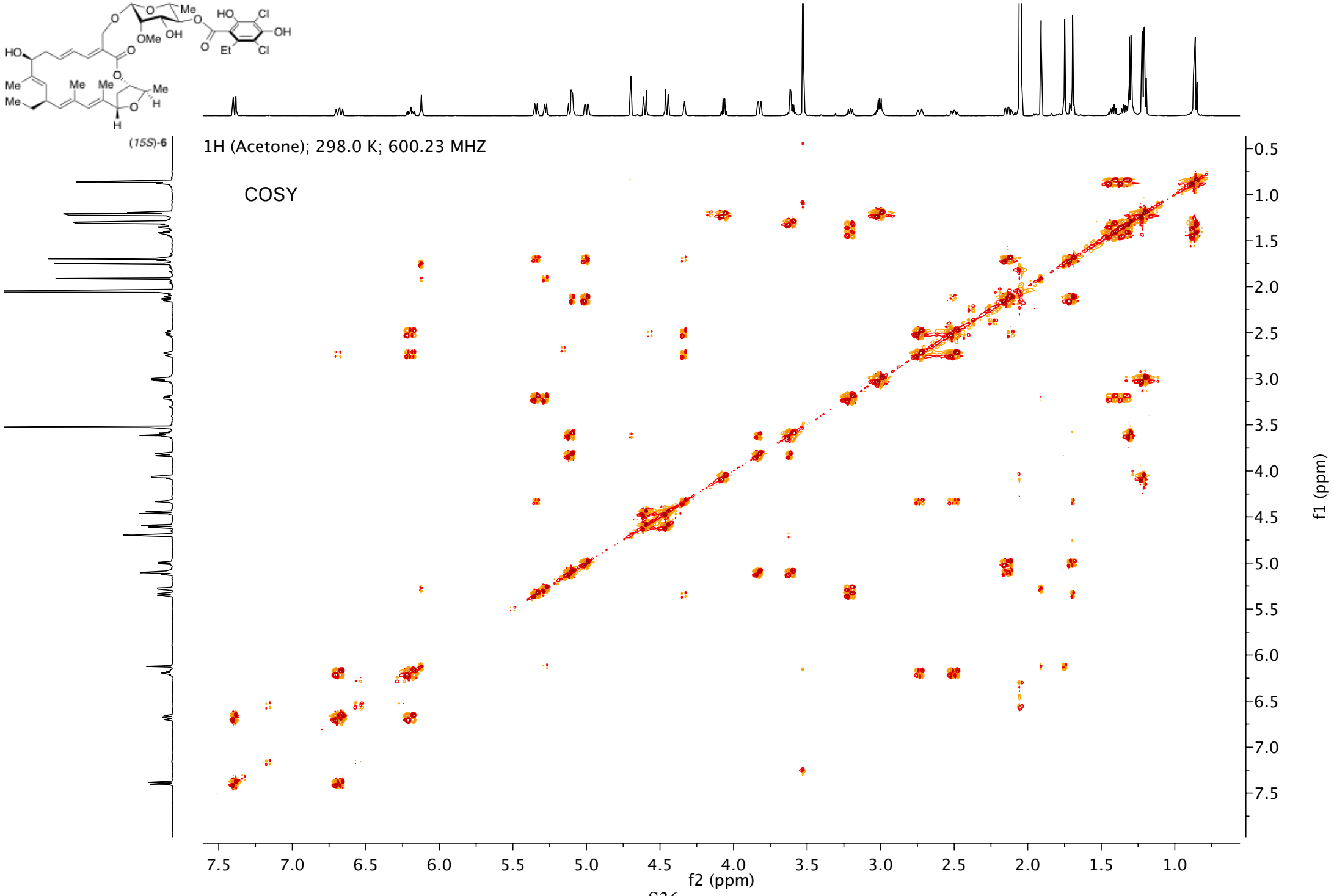
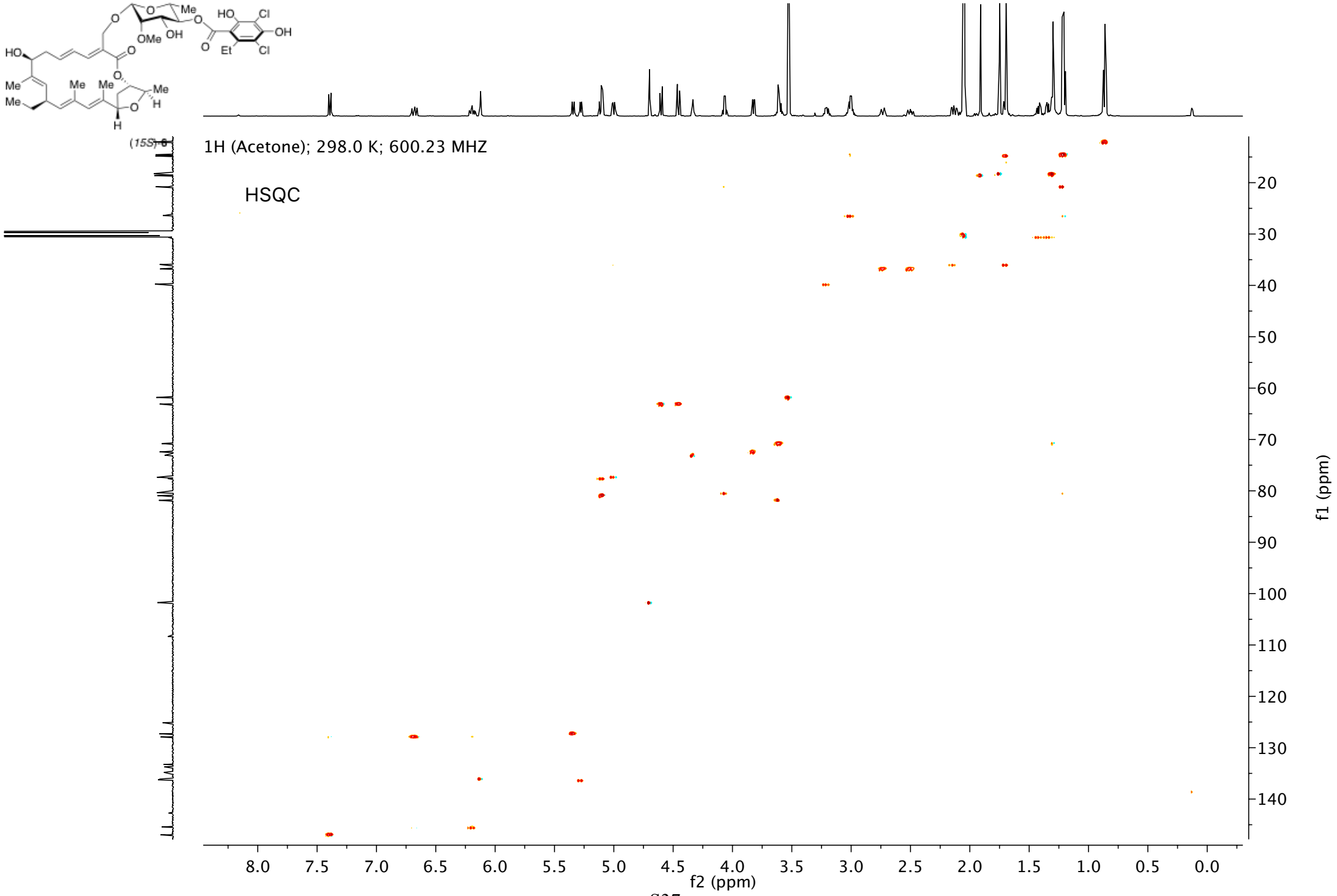
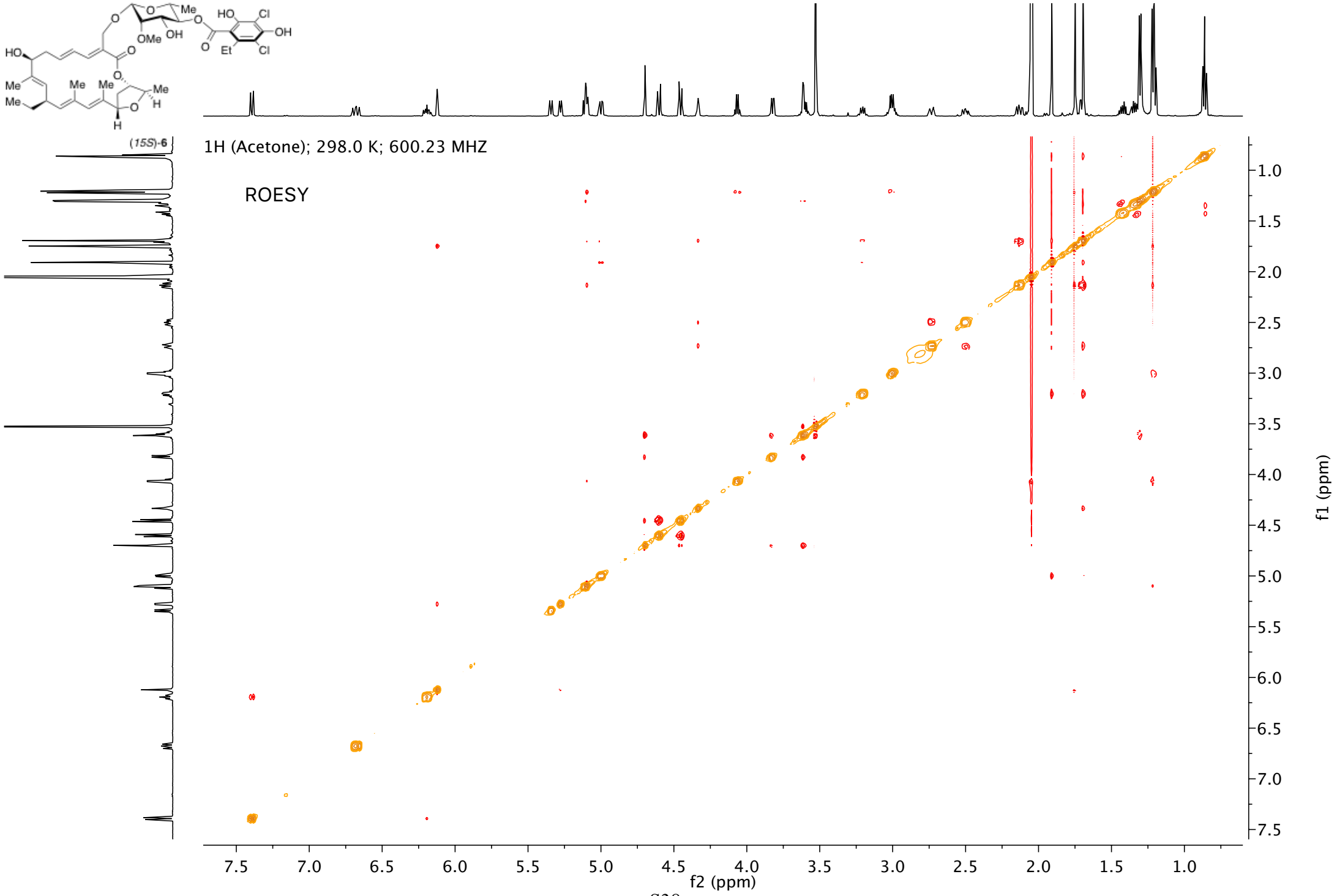
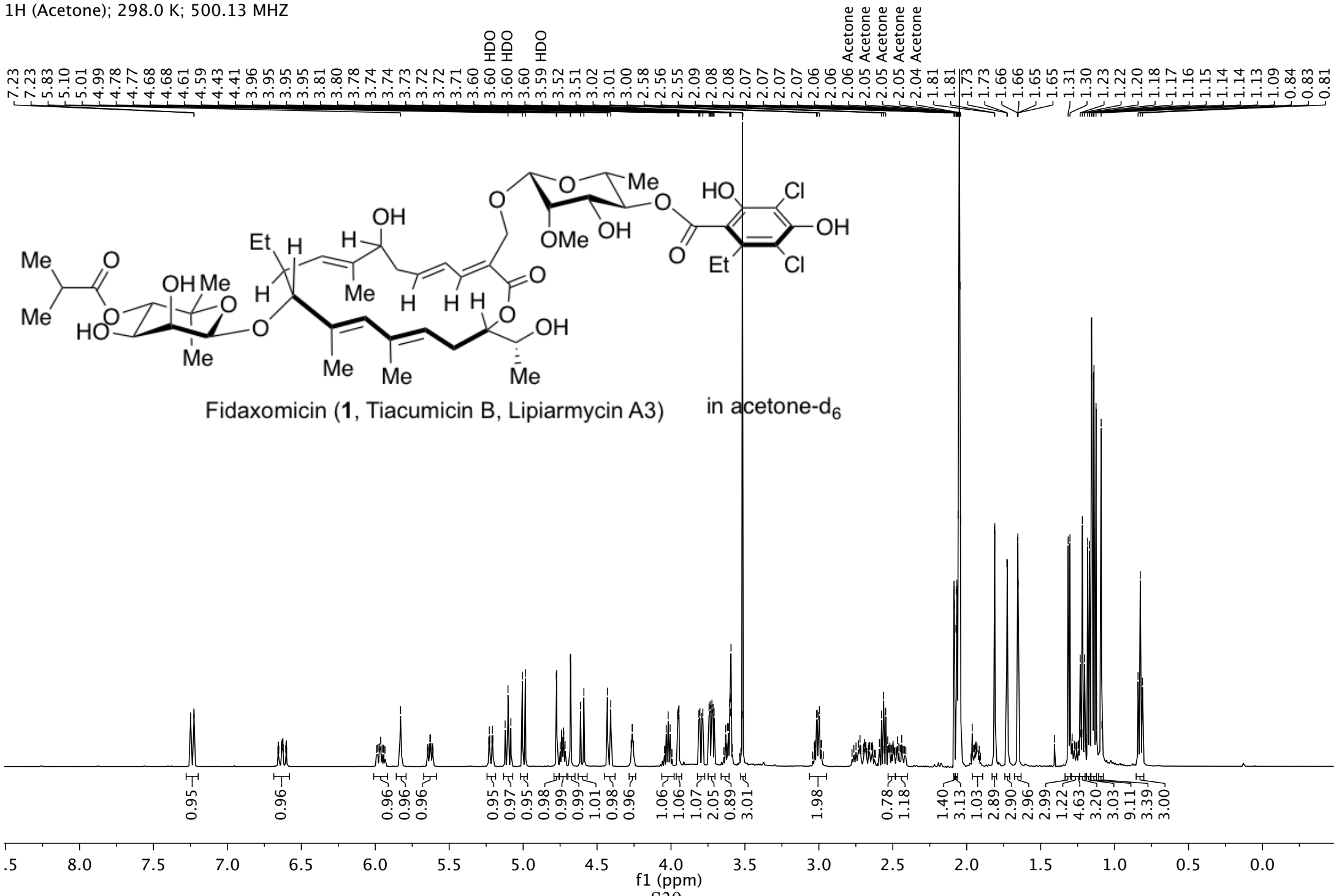
136.27
136.10
134.81
133.74
133.28
127.92
127.28
125.13
115.04
109.74
108.36
101.75
81.85
80.91
80.36
77.63
77.35
73.06
72.42
70.79
63.11
61.82
39.76
36.79
35.93
30.64
30.49
26.42
20.80
18.64
18.33
18.23
14.82
14.54
12.06
HO
Me
Me
Me
Me
O
O
O
O
OMe
OH
O
HO
Cl
OH
Et
Cl
Me
O
H
H
f1 (ppm)

(*15S*)-**6**

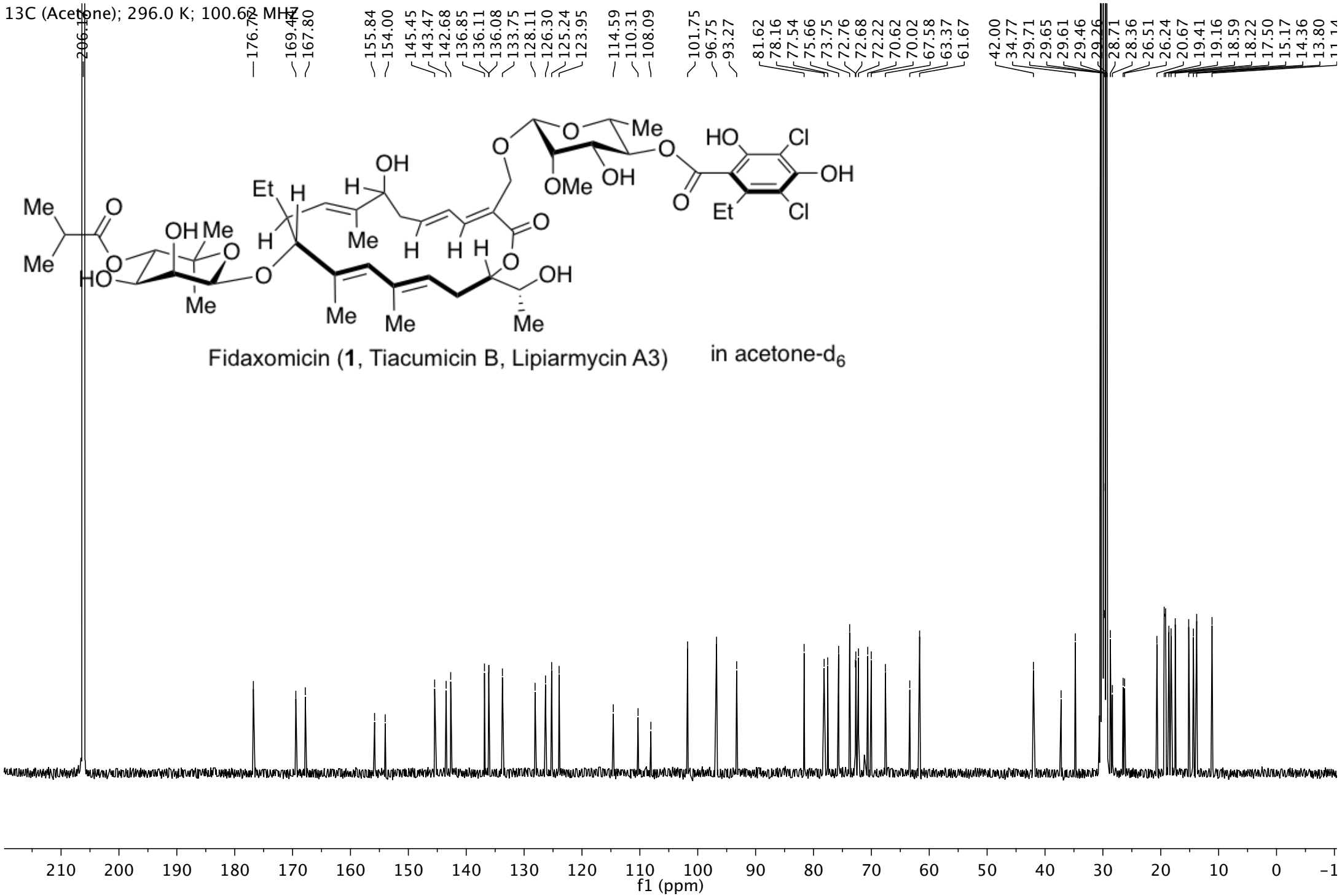

(15S)-6
1H (Acetone); 298.0 K; 600.23 MHZ
COSY
f2 (ppm)
f1 (ppm)

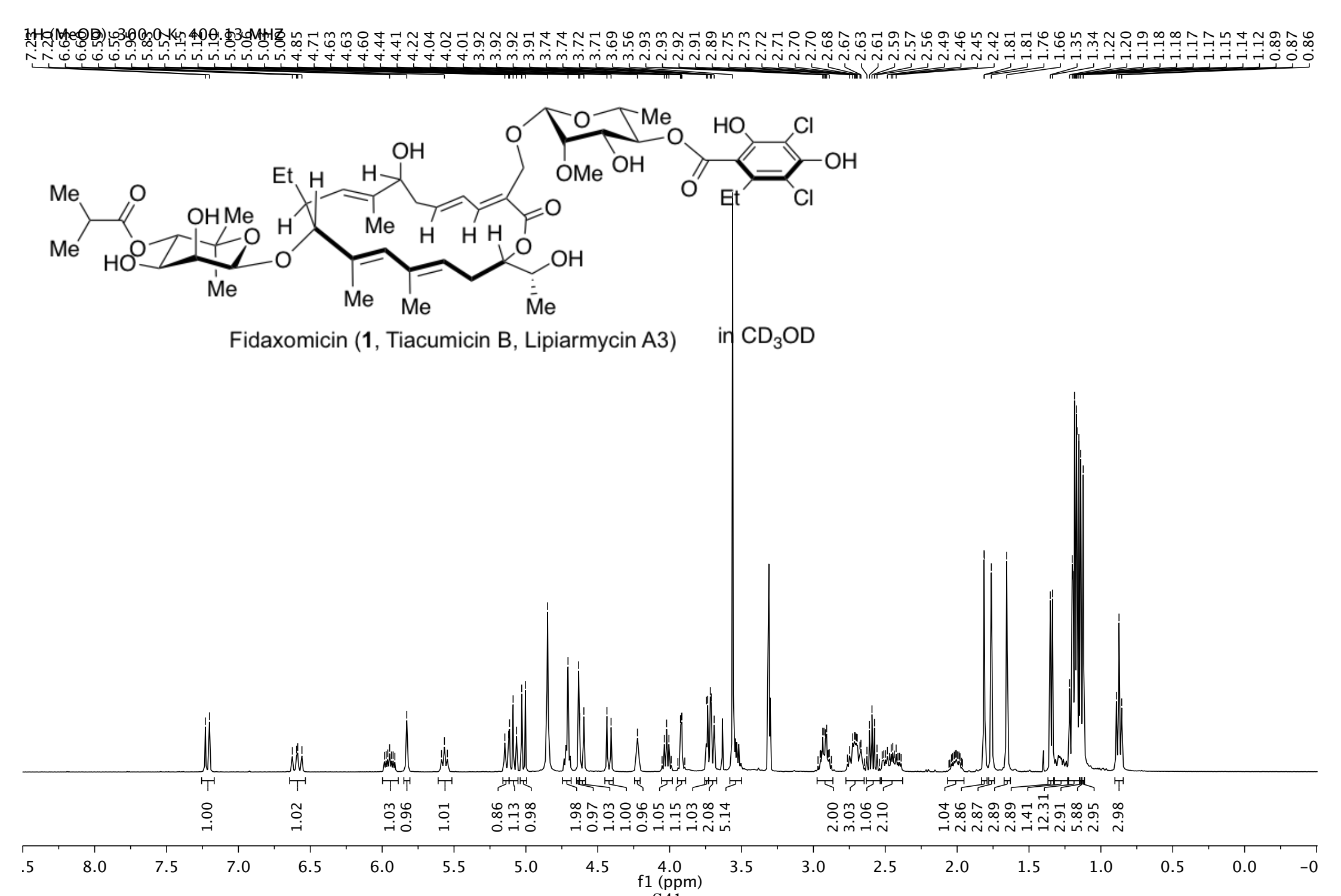

(15S)-6
1H (Acetone); 298.0 K; 600.23 MHZ
HSQC
f2 (ppm)
f1 (ppm)


(15S)-6
1H (Acetone); 298.0 K; 600.23 MHZ
ROESY
f2 (ppm)
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0



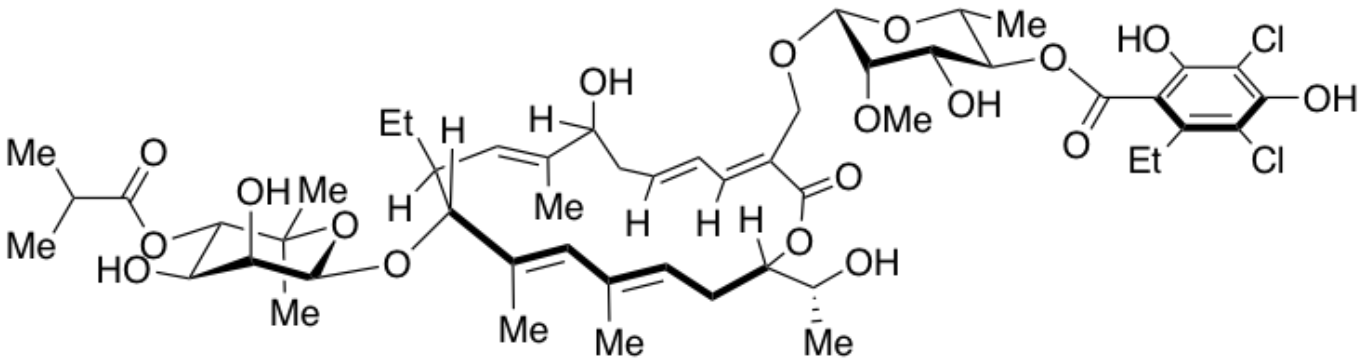
Fidaxomicin (**1**, Tiacumicin B, Lipiarmycin A3) in acetone-d_6


13C (Acetone); 296.0 K; 100.62 MHz
206.15
176.72
169.47
167.80
155.84
154.00
145.45
143.47
142.68
136.85
136.11
136.08
133.75
128.11
126.30
125.24
123.95
114.59
110.31
108.09
101.75
96.75
93.27
81.62
78.16
77.54
75.66
73.75
72.76
72.68
72.22
70.62
70.02
67.58
63.37
61.67
42.00
34.77
29.71
29.65
29.61
29.46
29.26
28.71
28.36
26.51
26.24
20.67
19.41
19.16
18.59
18.22
17.50
15.17
14.36
13.80
Fidaxomicin (1, Tiacumicin B, Lipiarmycin A3)
in acetone-d6
f1 (ppm)

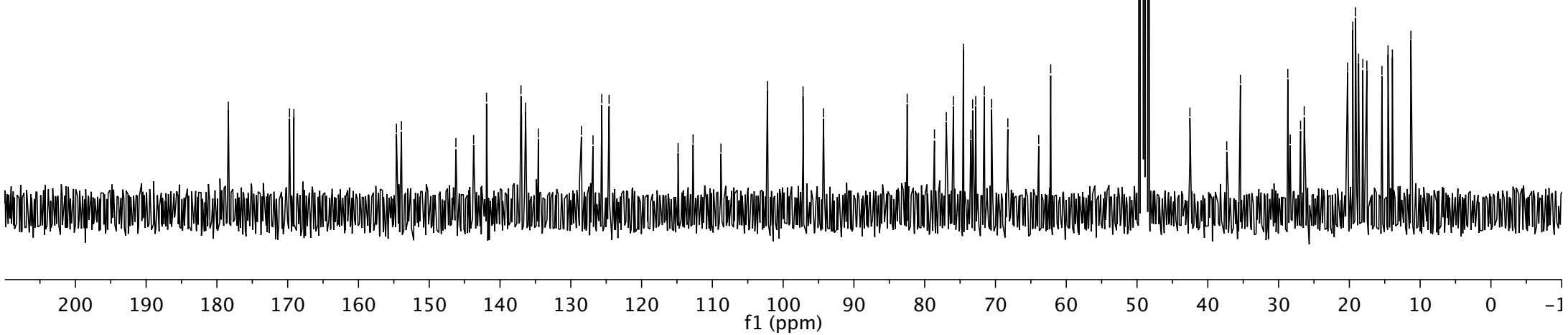

1H (MeOD, 300.0 K, 400.13 MHz)
Fidaxomicin (1, Tiacumicin B, Lipiarmycin A3) in CD3OD
f1 (ppm)

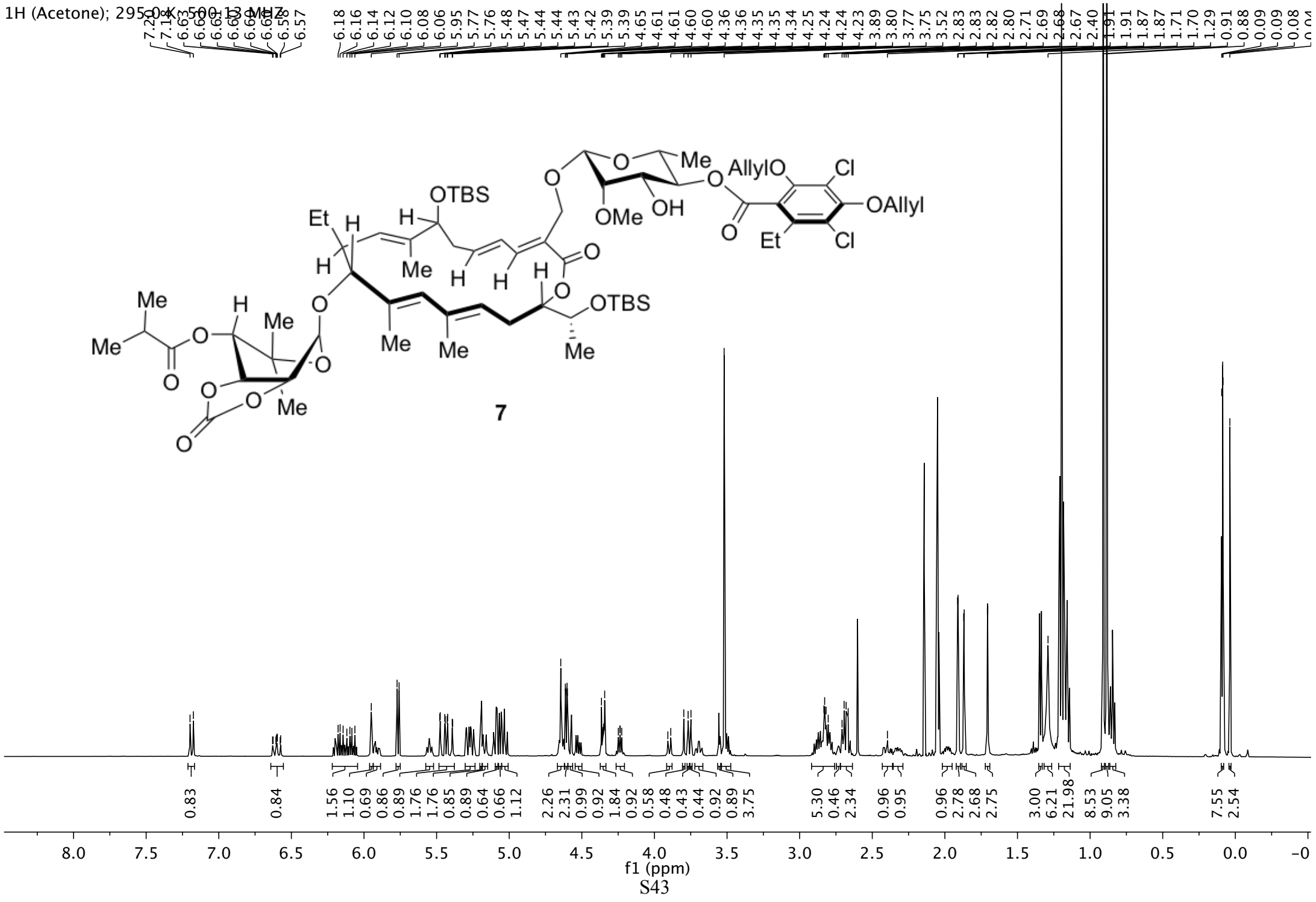
13C (MeOD); 300.0 K; 100.61 MHZ

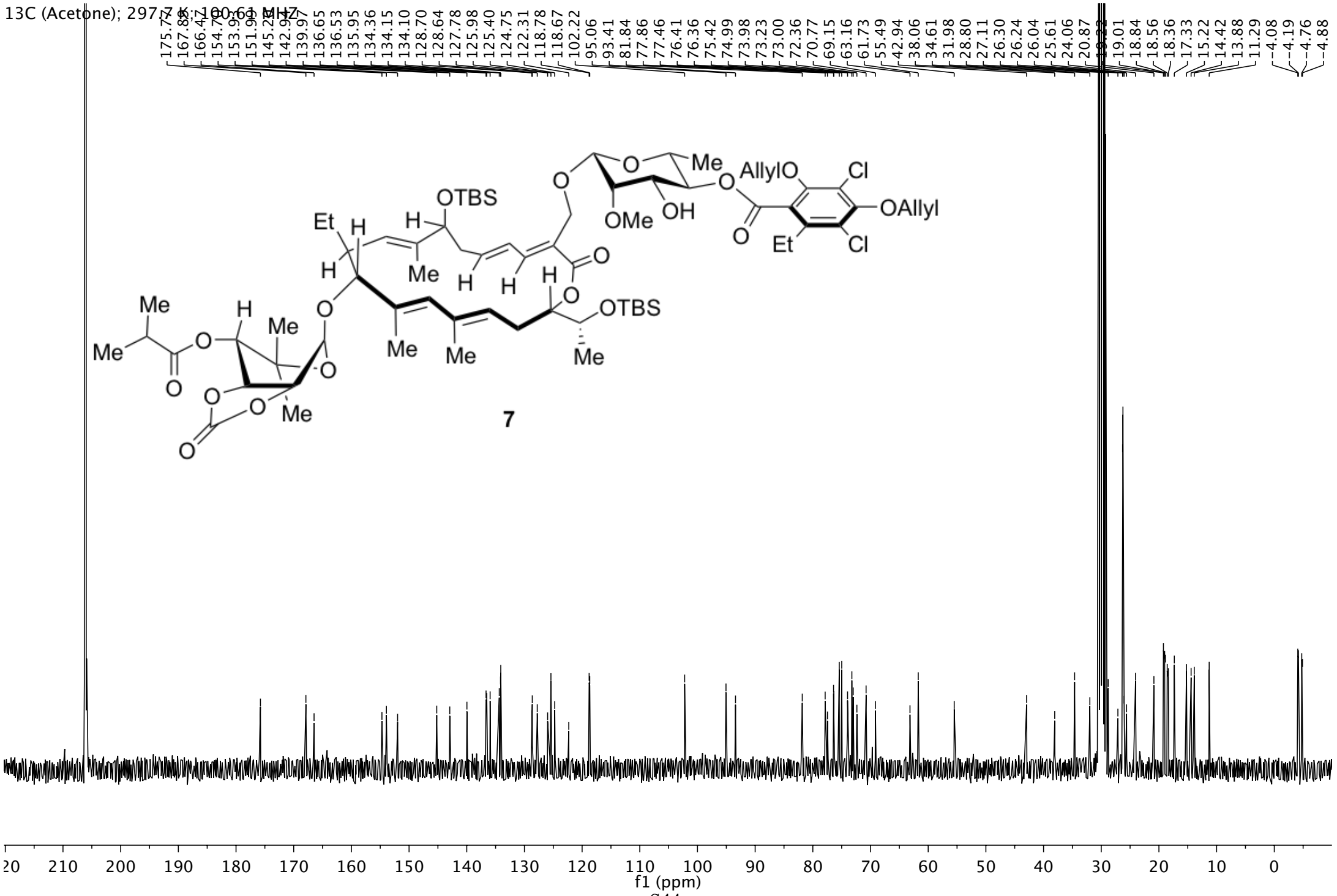
178.30
169.74
169.14
154.63
153.93
146.24
143.73
141.91
137.04
136.96
136.38
134.59
128.50
126.86
125.62
124.59
114.84
112.72
108.79
102.22
97.19
94.30
82.47
78.62
76.94
75.94
74.53
73.48
73.23
72.78
71.58
70.55
68.26
63.89
62.20
42.53
37.32
35.39
28.70
28.35
26.89
26.38
20.26
19.52
19.12
18.70
18.10
17.53
15.40
14.54
13.92
11.31

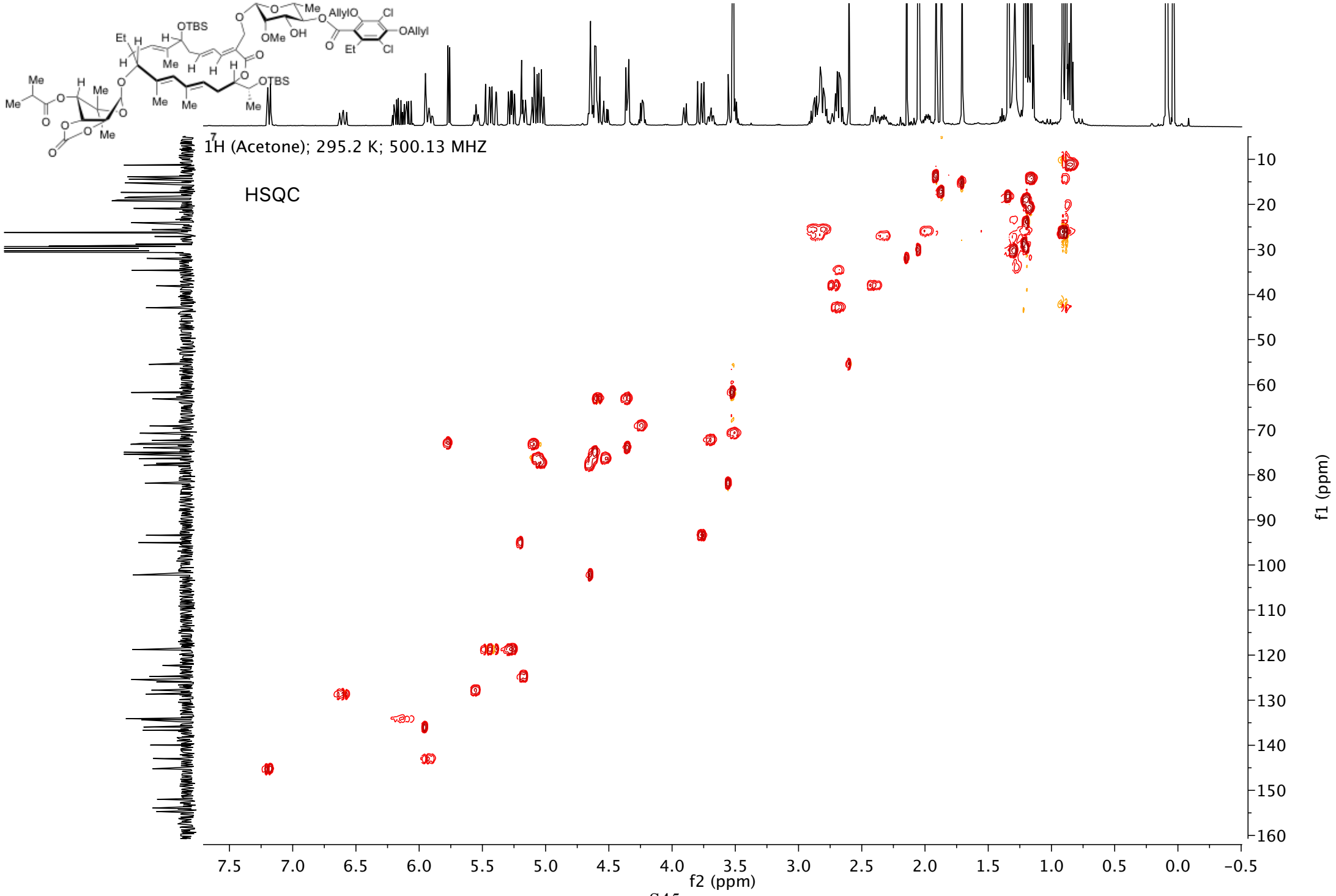


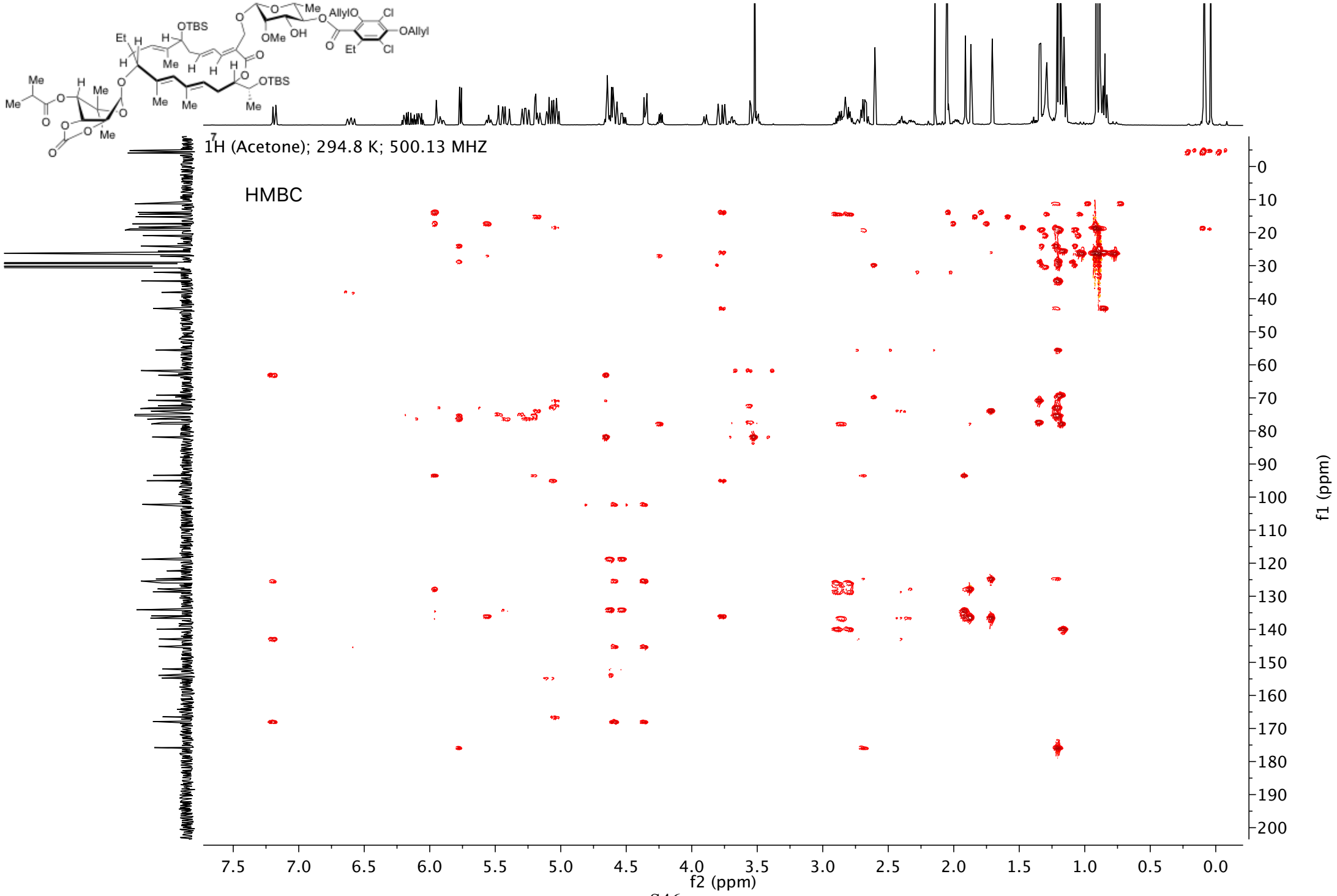
Fidaxomicin (**1**, Tiacumicin B, Lipiarmycin A3) in CD_3OD

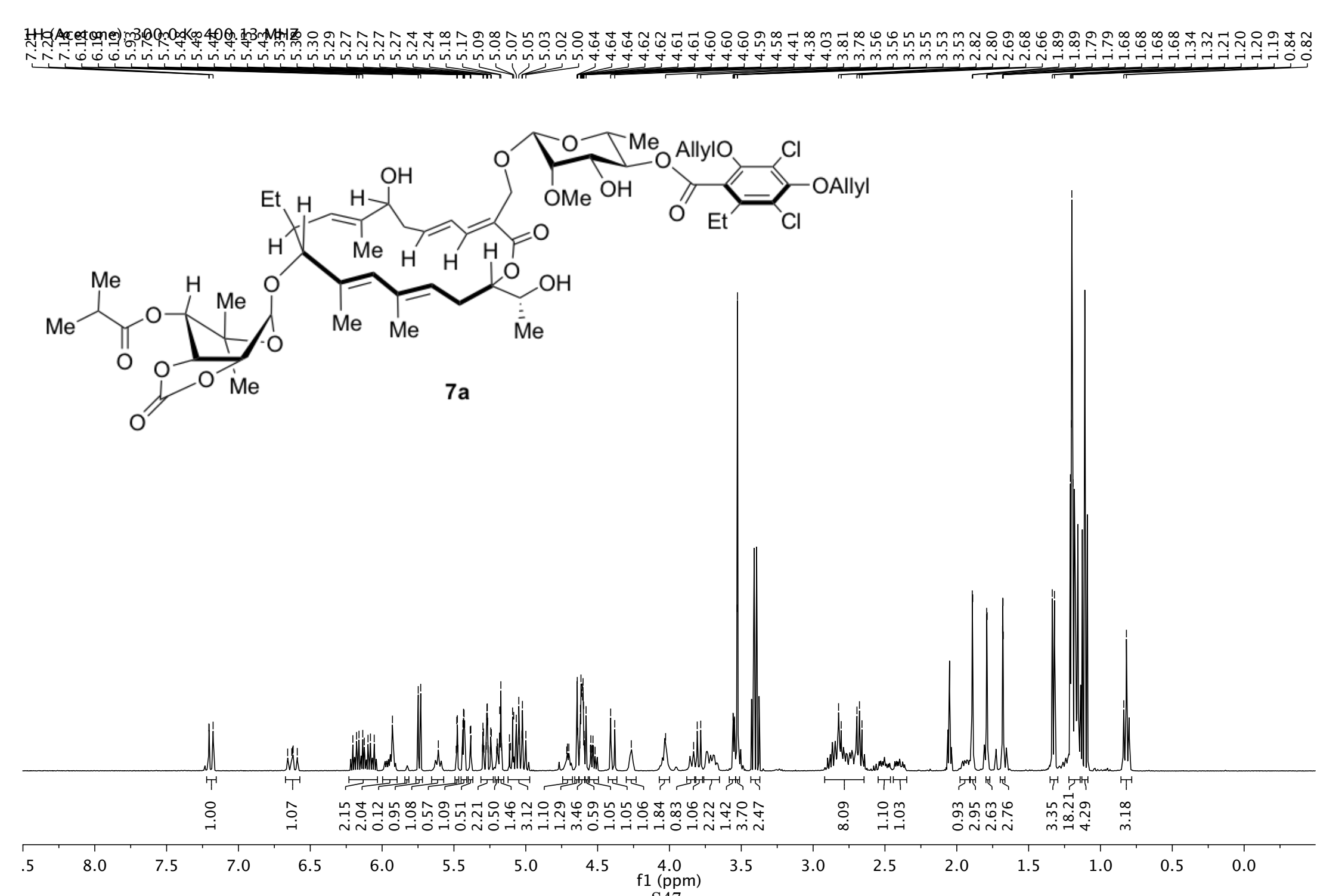


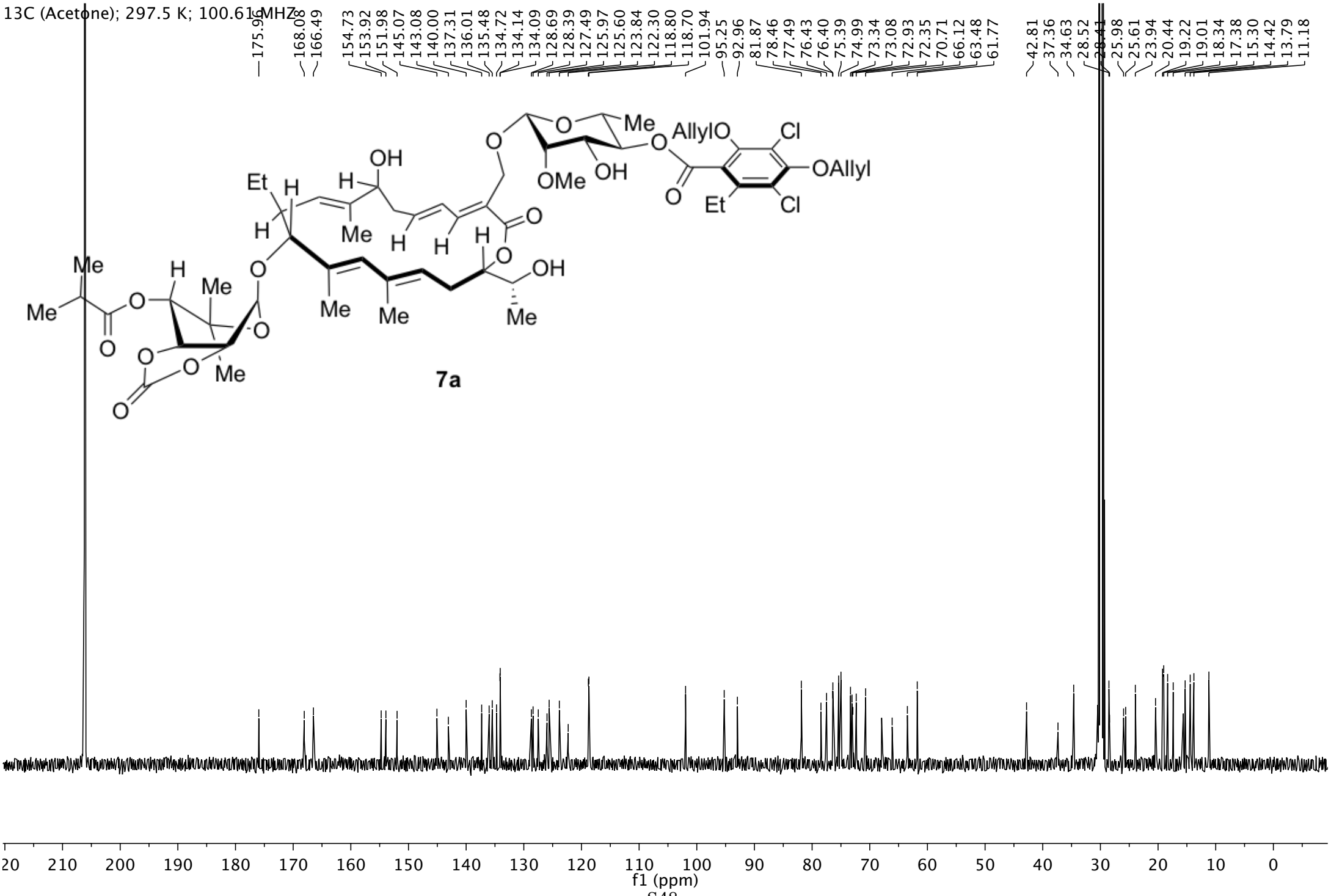

1H (Acetone); 295.0 K; 500.13 MHz
7.20 7.14 6.63 6.62 6.61 6.60 6.59 6.58 6.57
6.18 6.16 6.14 6.12 6.10 6.08 6.06 5.95 5.77 5.76 5.48 5.47 5.44 5.44 5.43 5.42 5.39 5.39 4.65 4.61 4.61 4.60 4.60 4.36 4.36 4.35 4.35 4.34 4.25 4.24 4.24 4.23 3.89 3.80 3.77 3.75 3.52 2.83 2.83 2.82 2.80 2.71 2.69 2.68 2.67 2.40 1.91 1.91 1.87 1.87 1.71 1.70 1.29 0.91 0.88 0.09 0.09 0.08
Me
Me
O
O
H
Me
O
O
O
Me
O
O
Et
H
H
OTBS
Me
H
H
H
O
O
Me
OMe
OH
O
AllylO
Cl
OAllyl
Et
Cl
O
OTBS
Me
Me
Me
7
0.83 0.84 1.56 1.10 0.69 0.86 0.89 1.76 1.76 0.85 0.89 0.64 0.66 1.12 2.26 2.31 0.99 0.92 1.84 0.92 0.58 0.48 0.43 0.44 0.92 0.89 3.75 5.30 0.46 2.34 0.96 0.95 0.96 2.78 2.68 2.75 3.00 6.21 21.98 8.53 9.05 3.38 7.55 2.54
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0
f1 (ppm)

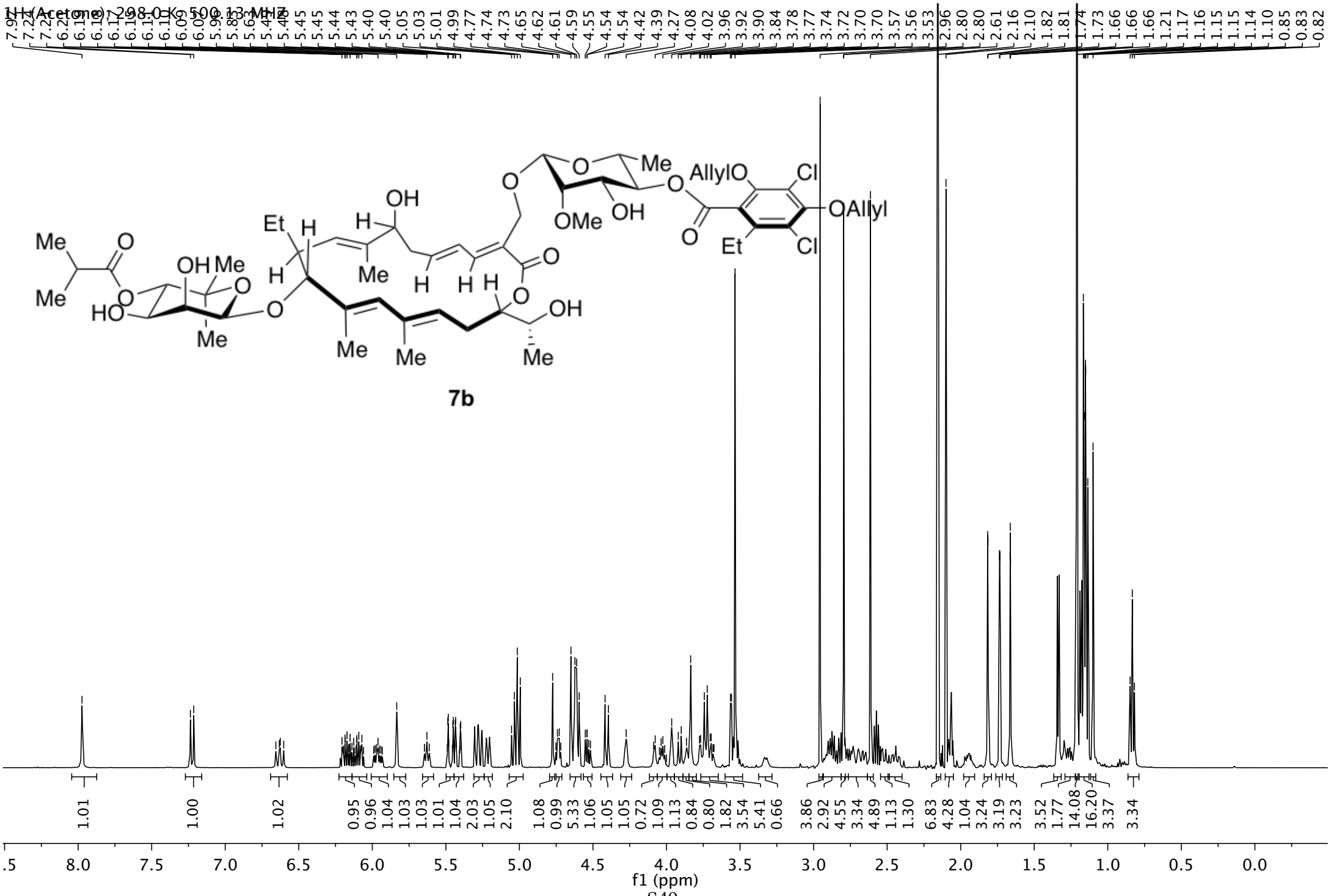

13C (Acetone); 297.7 K; 100.61 MHz
175.77
167.88
166.47
154.70
153.99
151.91
145.24
142.97
139.97
136.65
136.53
135.95
134.36
134.15
134.10
128.70
128.64
127.78
125.98
125.40
124.75
122.31
118.78
118.67
102.22
95.06
93.41
81.84
77.86
77.46
76.41
76.36
75.42
74.99
73.98
73.23
73.00
72.36
70.77
69.15
63.16
61.73
55.49
42.94
38.06
34.61
31.98
28.80
27.11
26.30
26.24
26.04
25.61
24.06
20.87
19.22
19.01
18.84
18.56
18.36
17.33
15.22
14.42
13.88
11.29
-4.08
-4.19
-4.76
-4.88
OTBS
Et
H
H
Me
H
H
H
O
OTBS
Me
Me
Me
Me
H
Me
O
O
O
O
O
O
Me
Me
O
O
Me
O
Me
OMe
OH
AllylO
Cl
OAllyl
Et
Cl
7
f1 (ppm)


1H (Acetone); 295.2 K; 500.13 MHZ
HSQC
f2 (ppm)
f1 (ppm)

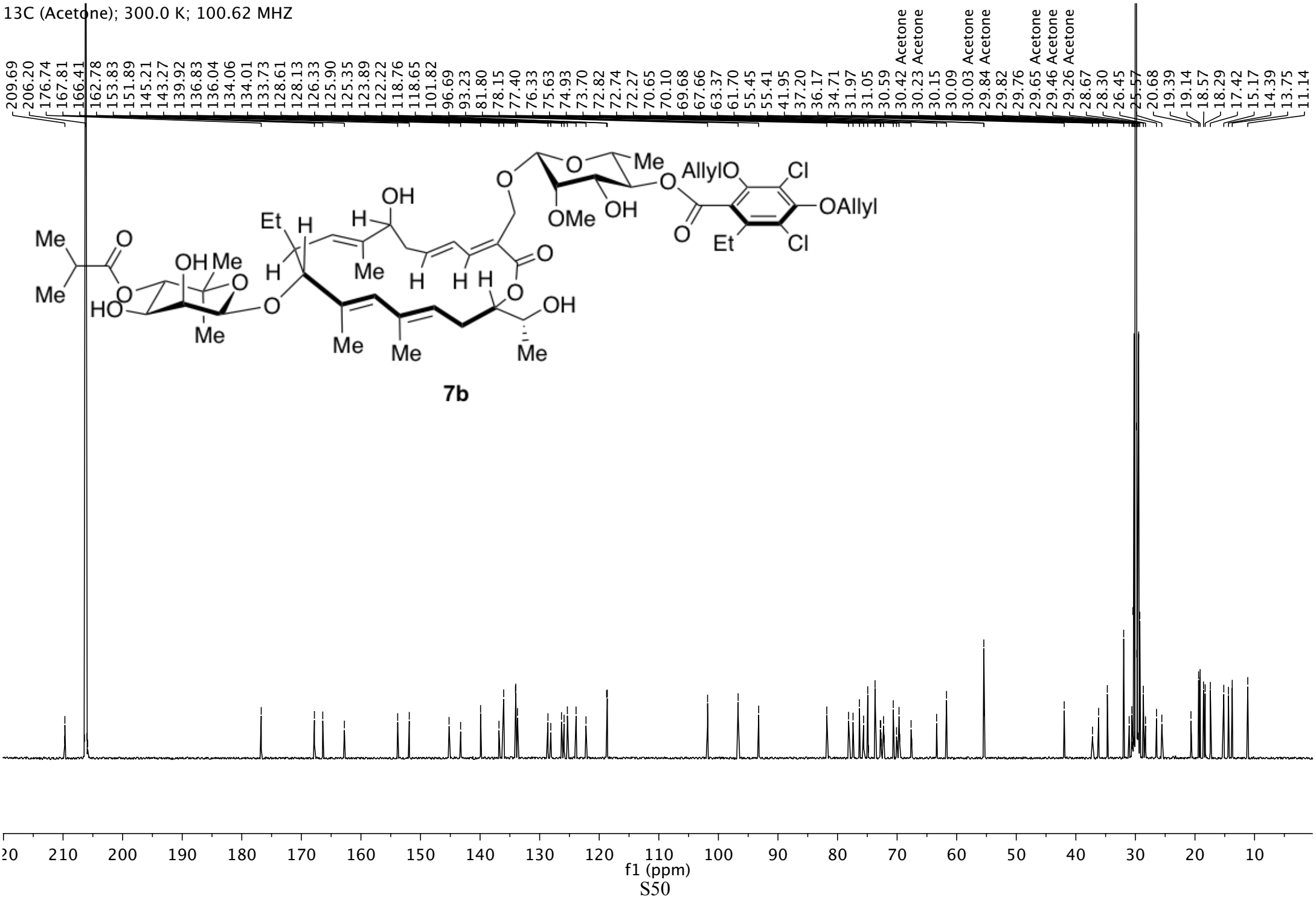

1H (Acetone); 294.8 K; 500.13 MHZ
HMBC
f2 (ppm)
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200

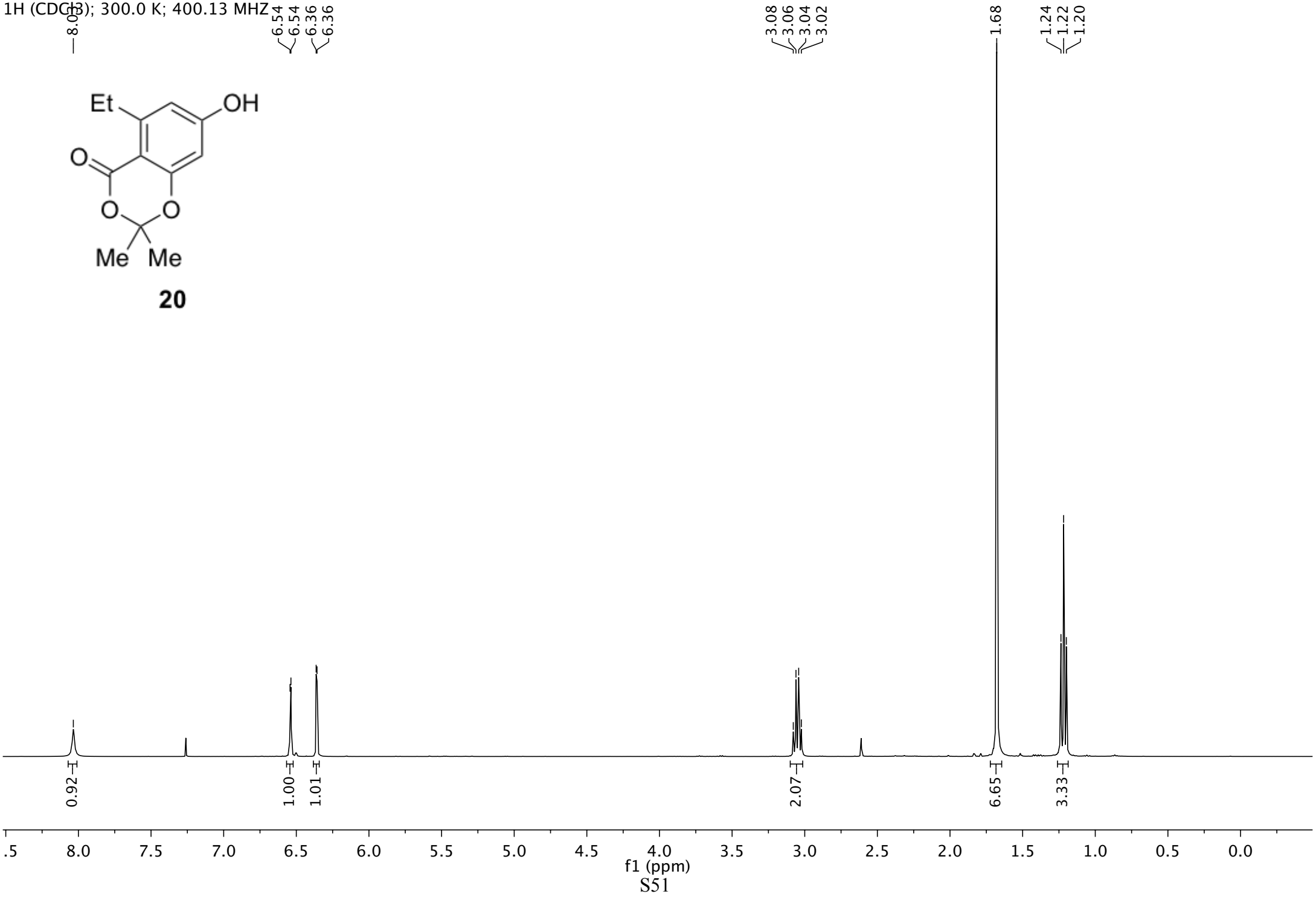

1H (Acetone) - 300.0K - 400.13 MHz
7.24 7.24 7.16 6.19 6.19 6.19 6.19 5.93 5.78 5.78 5.45 5.45 5.45 5.45 5.45 5.43 5.43 5.43 5.43 5.38 5.38 5.30 5.29 5.27 5.27 5.27 5.27 5.24 5.24 5.18 5.17 5.09 5.08 5.07 5.05 5.03 5.02 5.00 4.64 4.64 4.64 4.62 4.62 4.61 4.61 4.60 4.60 4.60 4.59 4.58 4.41 4.38 4.03 3.81 3.78 3.56 3.56 3.55 3.55 3.53 3.53 2.82 2.80 2.69 2.68 2.66 1.89 1.89 1.79 1.79 1.68 1.68 1.68 1.68 1.34 1.32 1.21 1.20 1.20 1.19 0.84 0.82
Me
O
H
Me
O
Me
O
O
O
O
Me
O
O
Me
Et
H
H
OH
H
Me
H
H
H
O
OH
Me
Me
Me
Me
O
O
Me
OMe
OH
AllylO
Cl
OAllyl
O
Et
Cl
7a
1.00 1.07 2.15 2.04 0.12 0.95 1.08 0.57 1.09 0.51 2.21 0.50 1.46 3.12 1.10 1.29 3.46 0.59 1.05 1.05 1.06 1.84 0.83 1.06 2.22 1.42 3.70 2.47 8.09 1.10 1.03 0.93 2.95 2.63 2.76 3.35 18.21 4.29 3.18
.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


13C (Acetone); 297.5 K; 100.61 MHz
175.99
168.08
166.49
154.73
153.92
151.98
145.07
143.08
140.00
137.31
136.01
135.48
134.72
134.14
134.09
128.69
128.39
127.49
125.97
125.60
123.84
122.30
118.80
118.70
101.94
95.25
92.96
81.87
78.46
77.49
76.43
76.40
75.39
74.99
73.34
73.08
72.93
72.35
70.71
66.12
63.48
61.77
42.81
37.36
34.63
28.52
28.41
25.98
25.61
23.94
20.44
19.22
19.01
18.34
17.38
15.30
14.42
13.79
11.18
AllylO
Cl
OAllyl
Et
Cl
OMe
OH
Me
OH
Et
H
H
Me
H
H
H
O
OH
Me
Me
Me
Me
Me
Me
Me
O
O
O
O
O
O
O
O
7a
f1 (ppm)



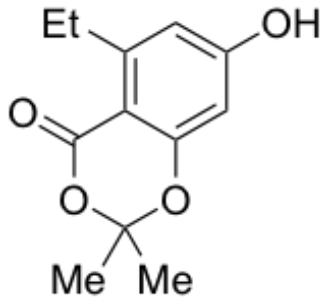
7b


13C (Acetone); 300.0 K; 100.62 MHZ
209.69 206.20 176.74 167.81 166.41 162.78 153.83 151.89 145.21 143.27 139.92 136.83 136.04 134.06 134.01 133.73 128.61 128.13 126.33 125.90 125.35 123.89 122.22 118.76 118.65 101.82 96.69 93.23 81.80 78.15 77.40 76.33 75.63 74.93 73.70 72.82 72.74 72.27 70.65 70.10 69.68 67.66 63.37 61.70 55.45 55.41 41.95 37.20 36.17 34.71 31.97 31.05 30.59 30.42 Acetone 30.23 Acetone 30.15 30.09 30.03 Acetone 29.84 Acetone 29.82 29.76 29.65 Acetone 29.46 Acetone 29.26 Acetone 28.67 28.30 26.45 25.57 20.68 19.39 19.14 18.57 18.29 17.42 15.17 14.39 13.75 11.14
Me
O
Me
OH
Me
O
HO
Me
O
Et
H
H
OH
H
Me
H
H
H
O
O
O
OMe
Me
O
OH
AllylO
Cl
OAllyl
O
Et
Cl
OH
Me
Me
Me
Me
7b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

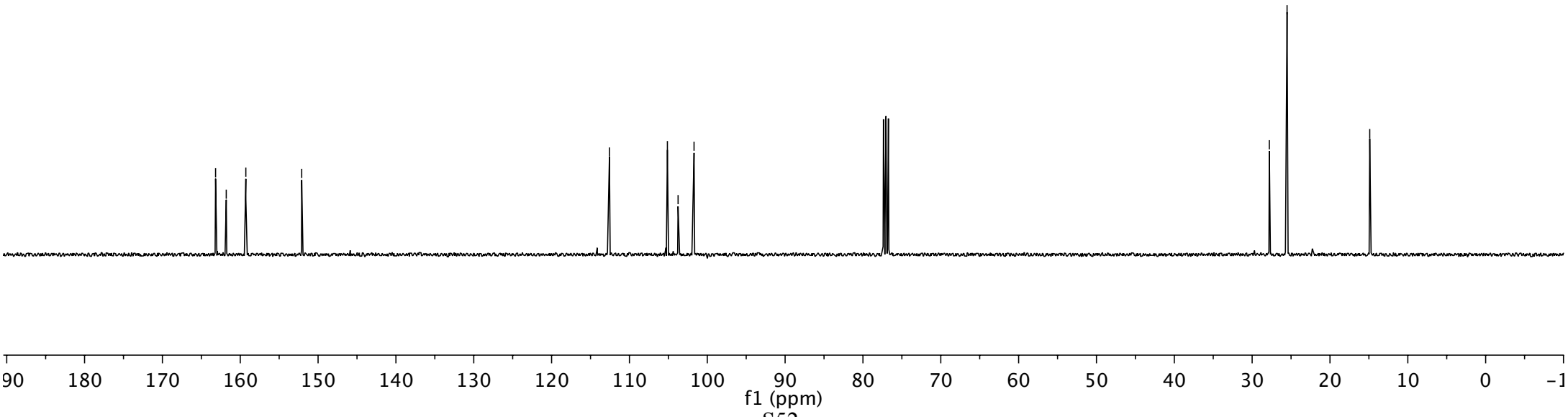

1H (CDCl3); 300.0 K; 400.13 MHZ
8.03
6.54
6.54
6.36
6.36
3.08
3.06
3.04
3.02
1.68
1.24
1.22
1.20
Et
OH
O
O
O
Me
Me
20
0.92
1.00
1.01
2.07
6.65
3.33
f1 (ppm)

13C (CDCl3); 300.0 K; 100.61 MHZ

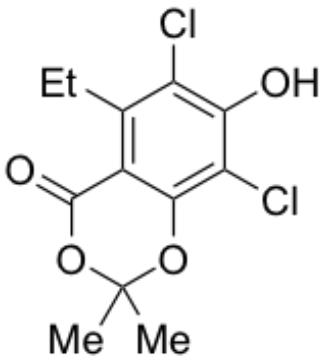
163.17
161.80
159.29
152.14
112.57
105.12
103.75
101.70
27.79
25.51
14.89



20



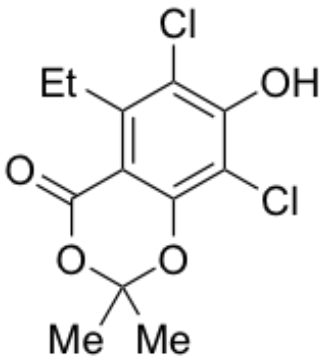
1H (CDCl3); 296.0 K; 400.13 MHZ



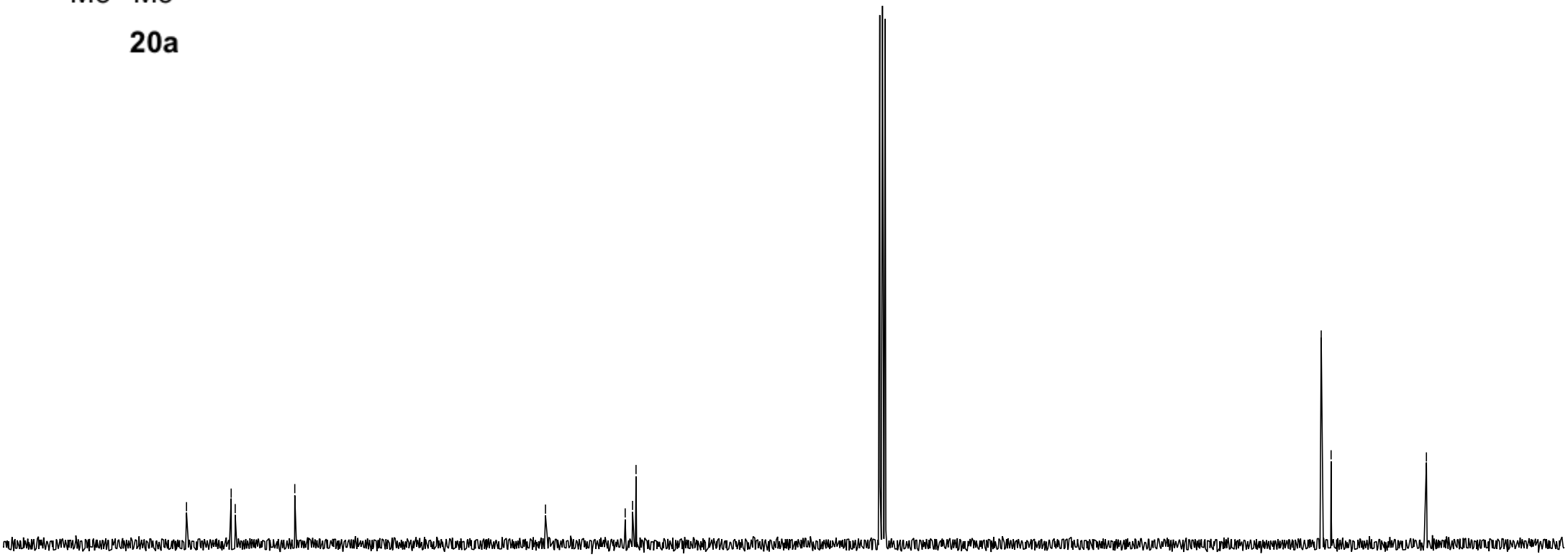
20a

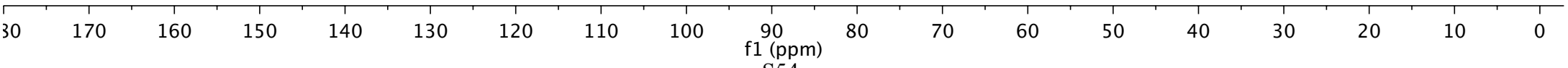
13C (CDCl3); 300.0 K; 100.61 MHZ

158.59
153.34
152.88
145.89
116.51
107.17
106.31
105.90
25.62
24.46
13.29

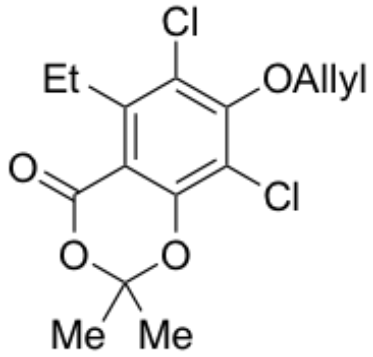


20a

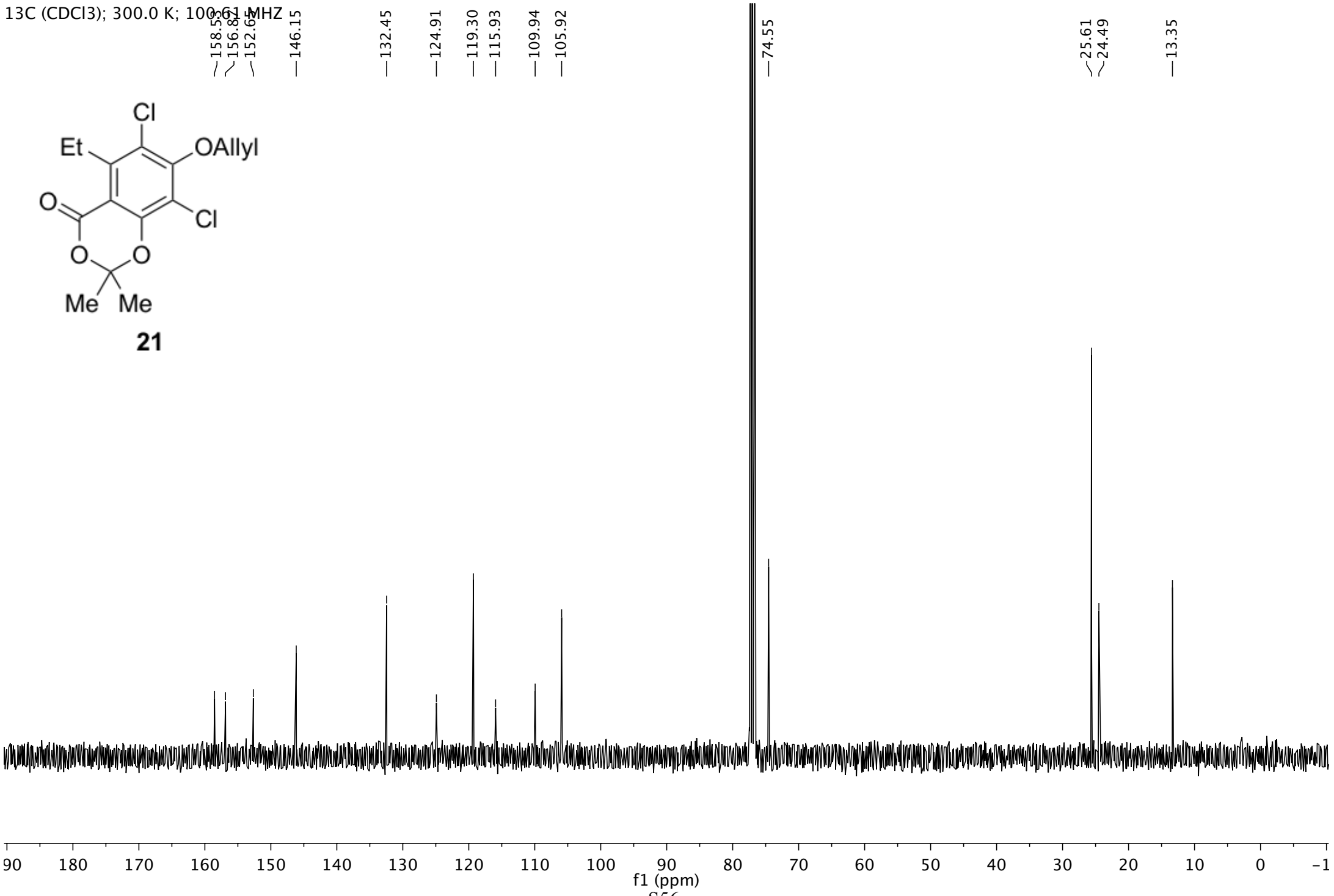




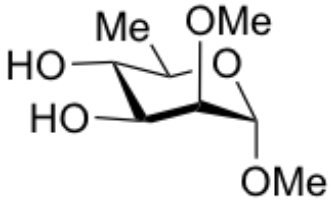
1H (CDCl3); 296.8 K; 400.13 MHZ



21


13C (CDCl3); 300.0 K; 100.61 MHZ
158.55
156.82
152.62
146.15
132.45
124.91
119.30
115.93
109.94
105.92
74.55
25.61
24.49
13.35
Cl
Et
OAllyl
O
Cl
O
O
Me
Me
21
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

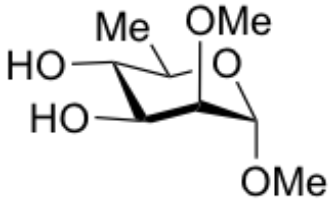
1H (CDCl3); 300.0 K; 400.13 MHZ



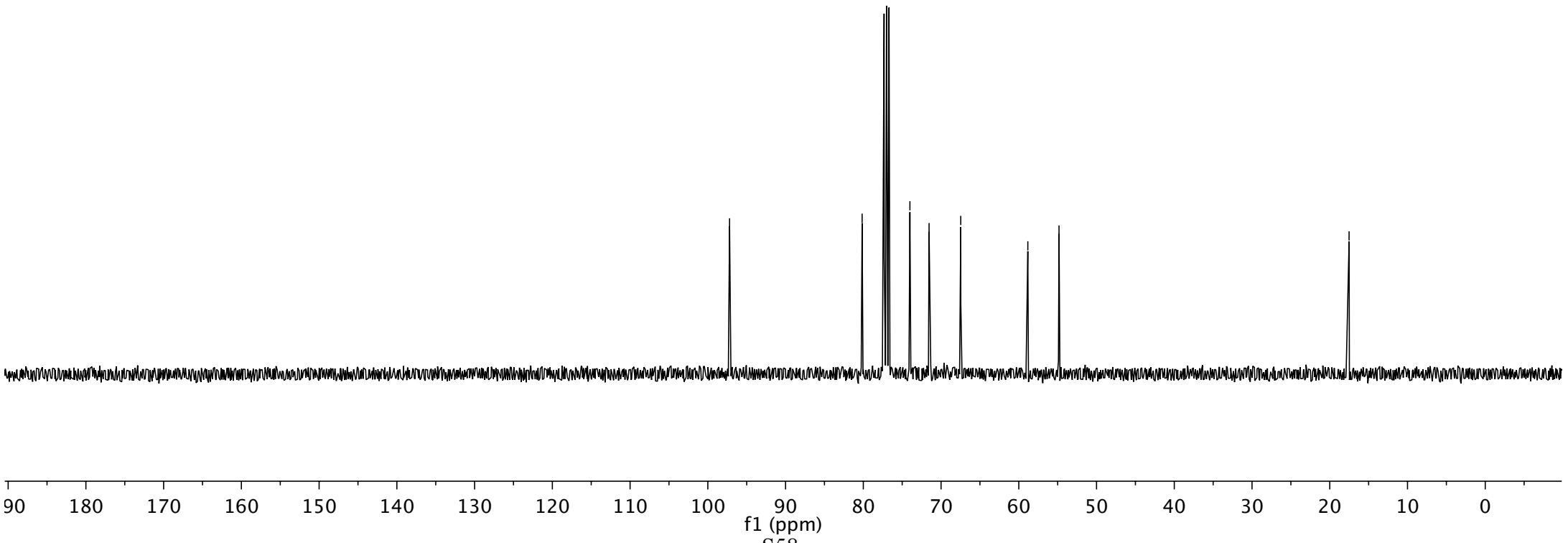
23

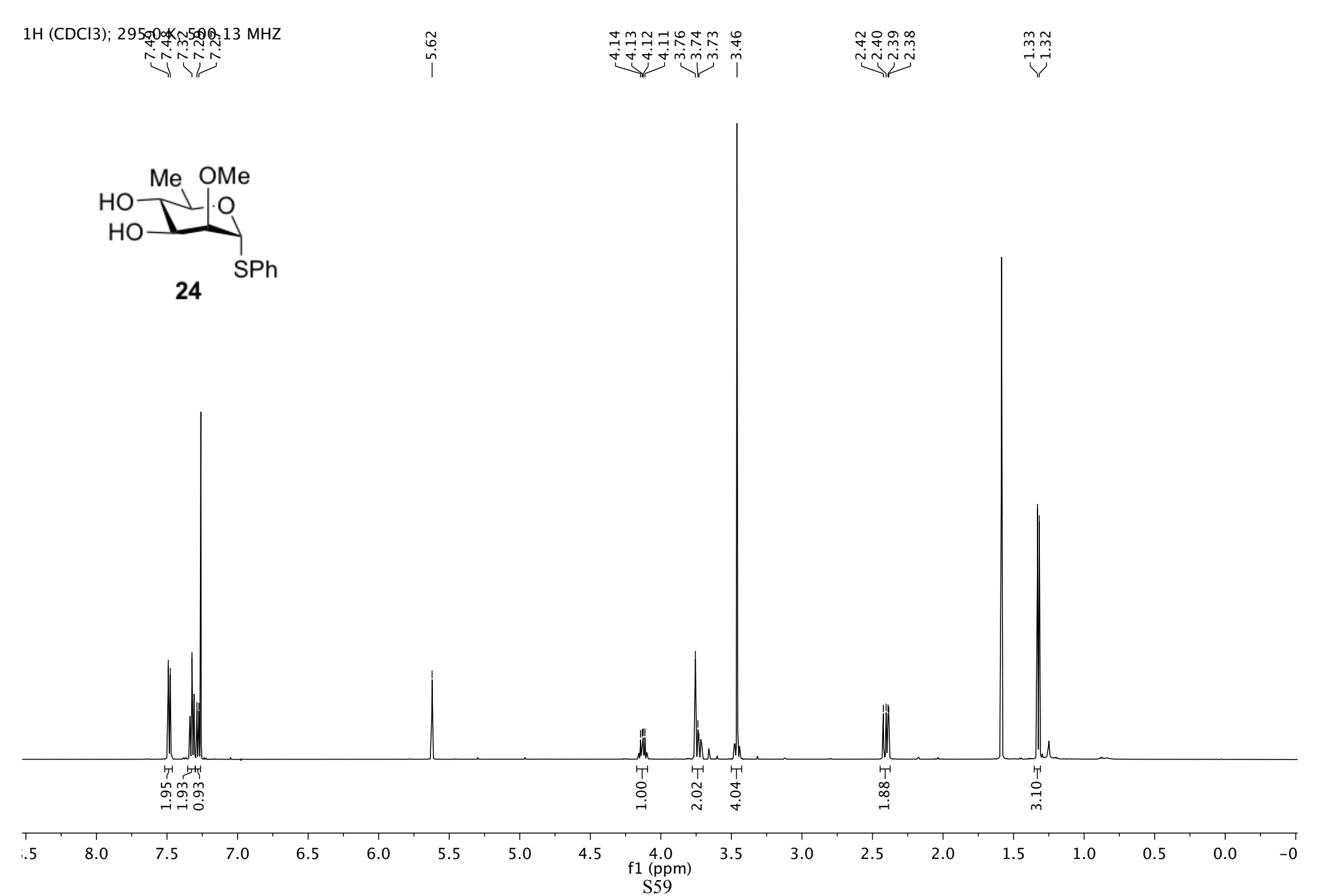
13C (CDCl3); 300.0 K; 100.61 MHZ

97.20
80.15
74.01
71.54
67.47
58.84
54.83
17.51



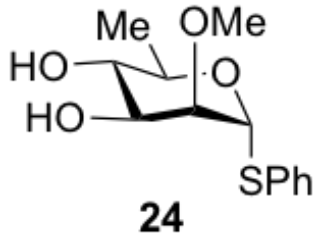
23




1H (CDCl3); 295.0K; 500.13 MHZ
7.49
7.48
7.32
7.20
7.20
5.62
4.14
4.13
4.12
4.11
3.76
3.74
3.73
3.46
2.42
2.40
2.39
2.38
1.33
1.32
Me
OMe
HO
O
HO
SPh
24
1.95
1.93
0.93
1.00
2.02
4.04
1.88
3.10
f1 (ppm)

13C (CDCl3); 300.0 K; 100.61 MHZ

134.38
131.32
129.10
127.44
84.02
81.66
74.31
72.05
68.90
58.06
17.42

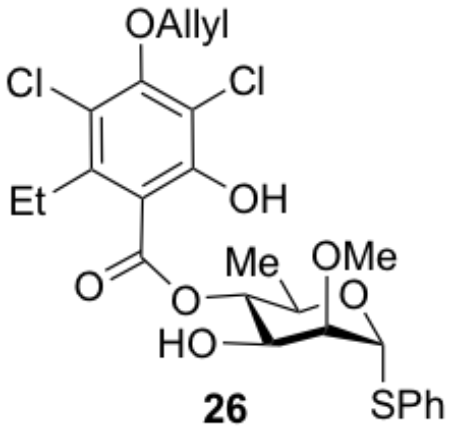


24

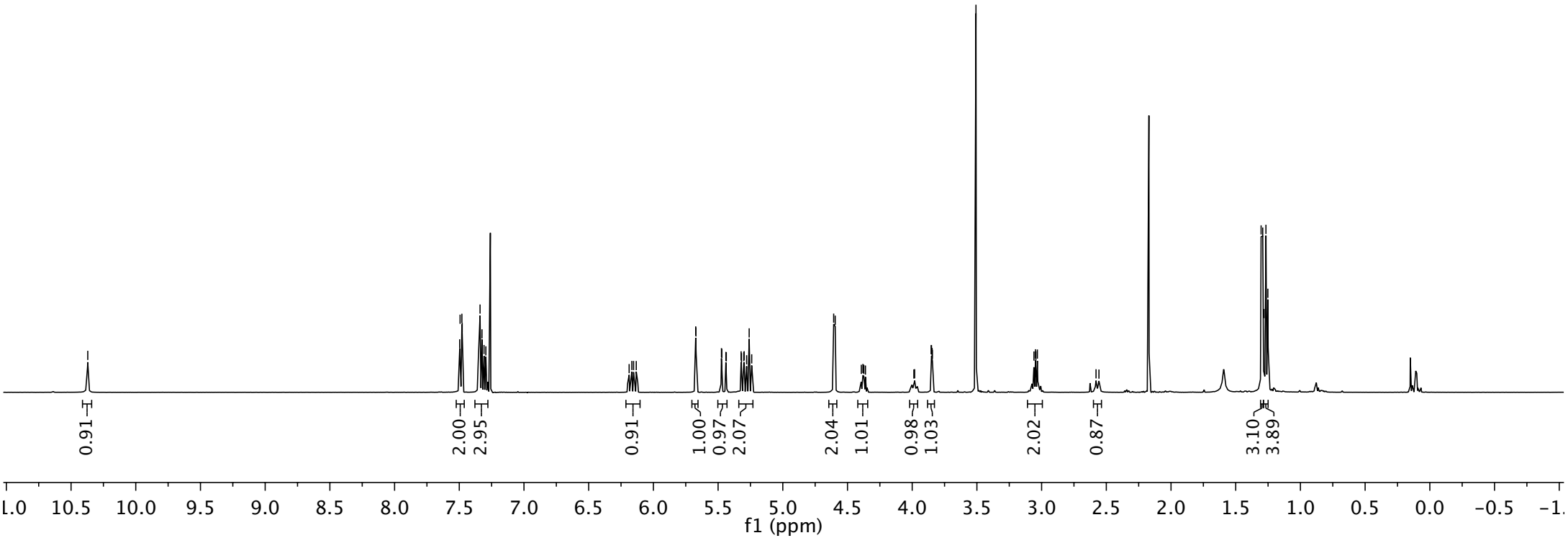
90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −1

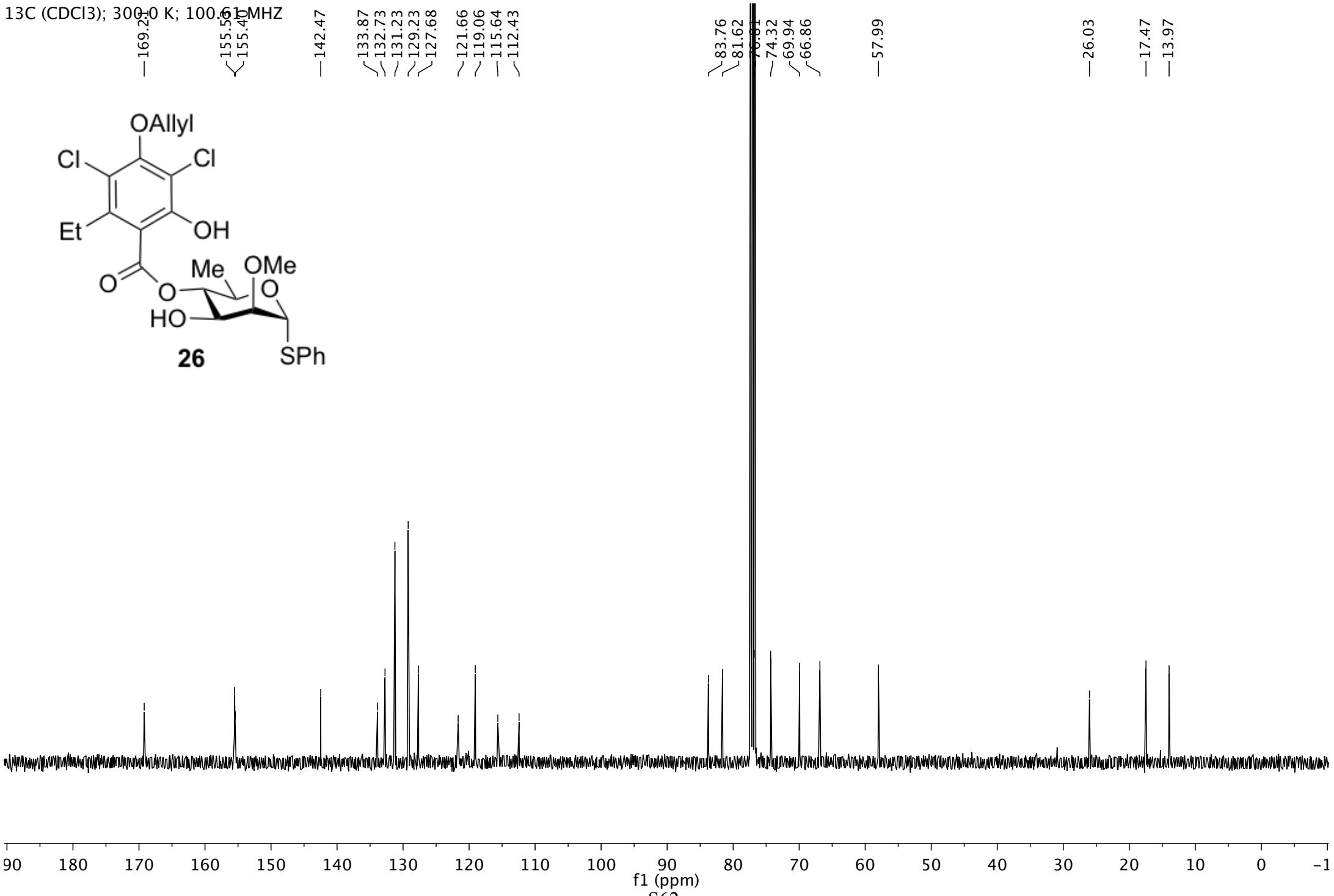
f1 (ppm)

1H (CDCl3); 295.0 K; 500.13 MHZ

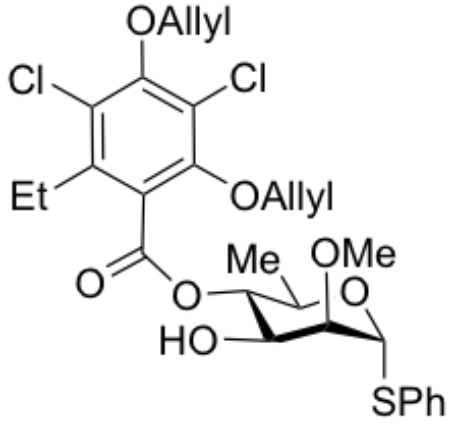


26

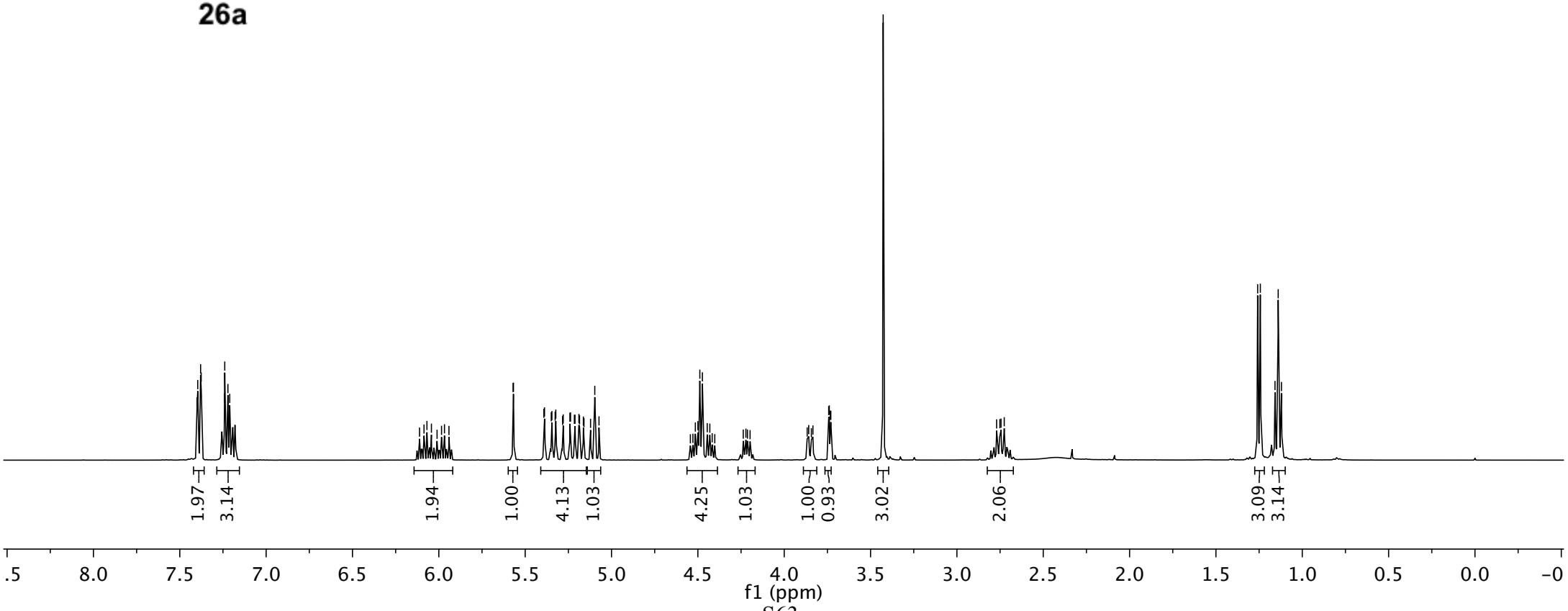



13C (CDCl3); 300.0 K; 100.61 MHZ
169.22
155.56
155.40
142.47
133.87
132.73
131.23
129.23
127.68
121.66
119.06
115.64
112.43
83.76
81.62
74.32
69.94
66.86
57.99
26.03
17.47
13.97
OAllyl
Cl
Cl
Et
OH
Me
OMe
O
O
HO
O
SPh
26
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)

1H (CDCl3); 300.0 K; 400.13 MHZ

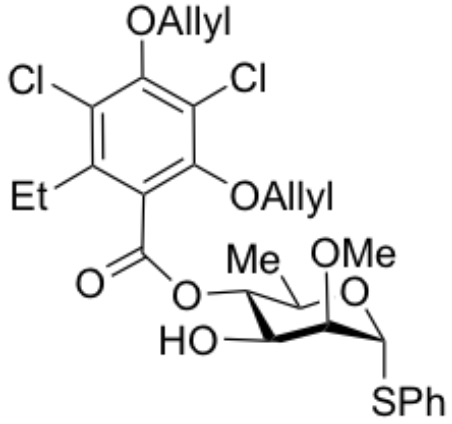


26a

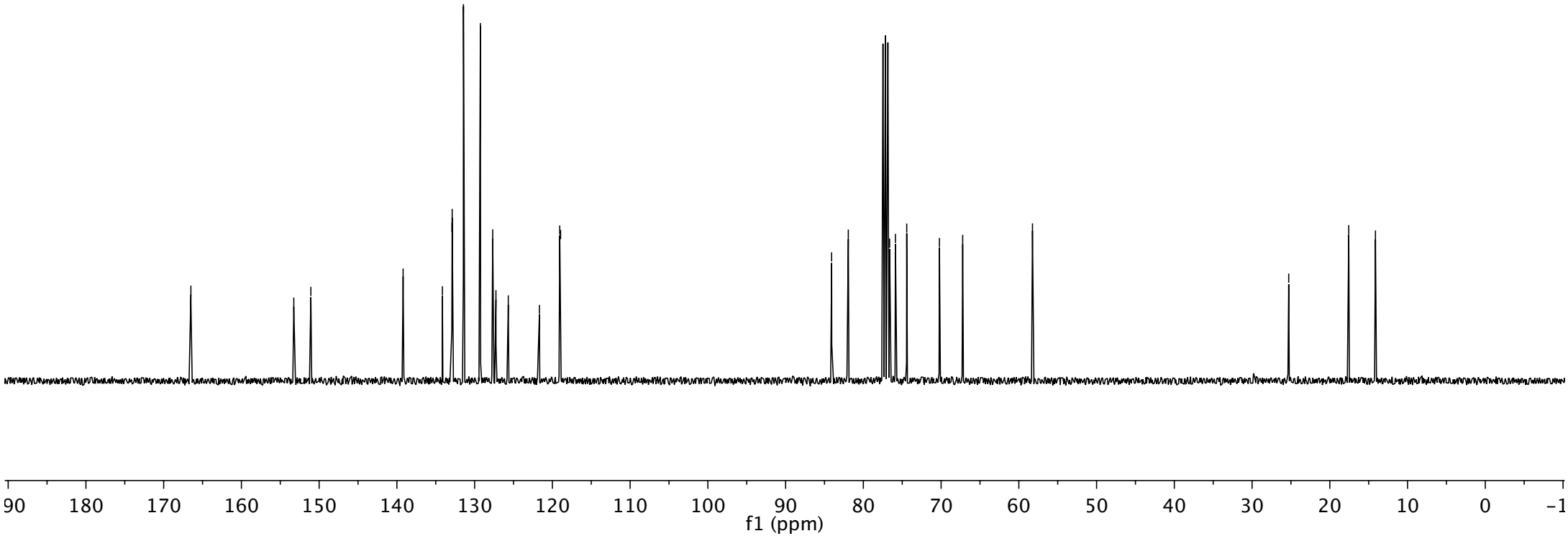


13C (CDCl3); 300.0 K; 100.614 MHZ

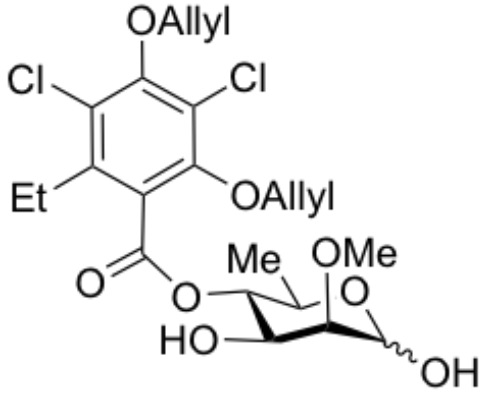
166.58
153.24
151.05
139.20
134.14
132.92
132.89
131.44
129.26
127.67
127.26
125.67
121.67
119.05
118.95
84.08
81.94
76.62
75.87
74.42
70.21
67.22
58.25
25.29
17.56
14.13



26a



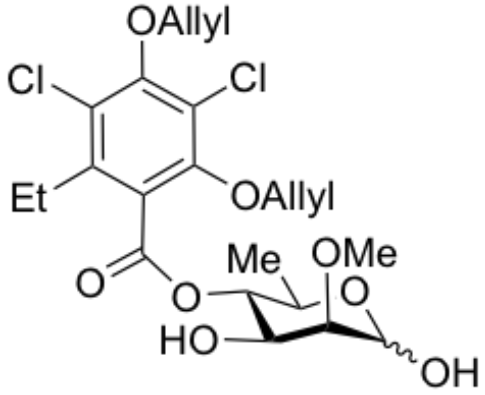
1H (CDCl3); 300.0 K; 400.13 MHz



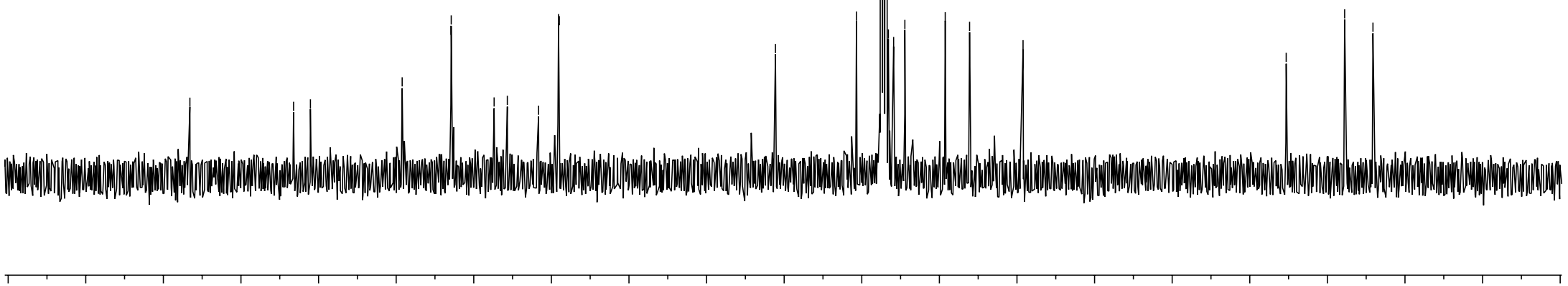
26b

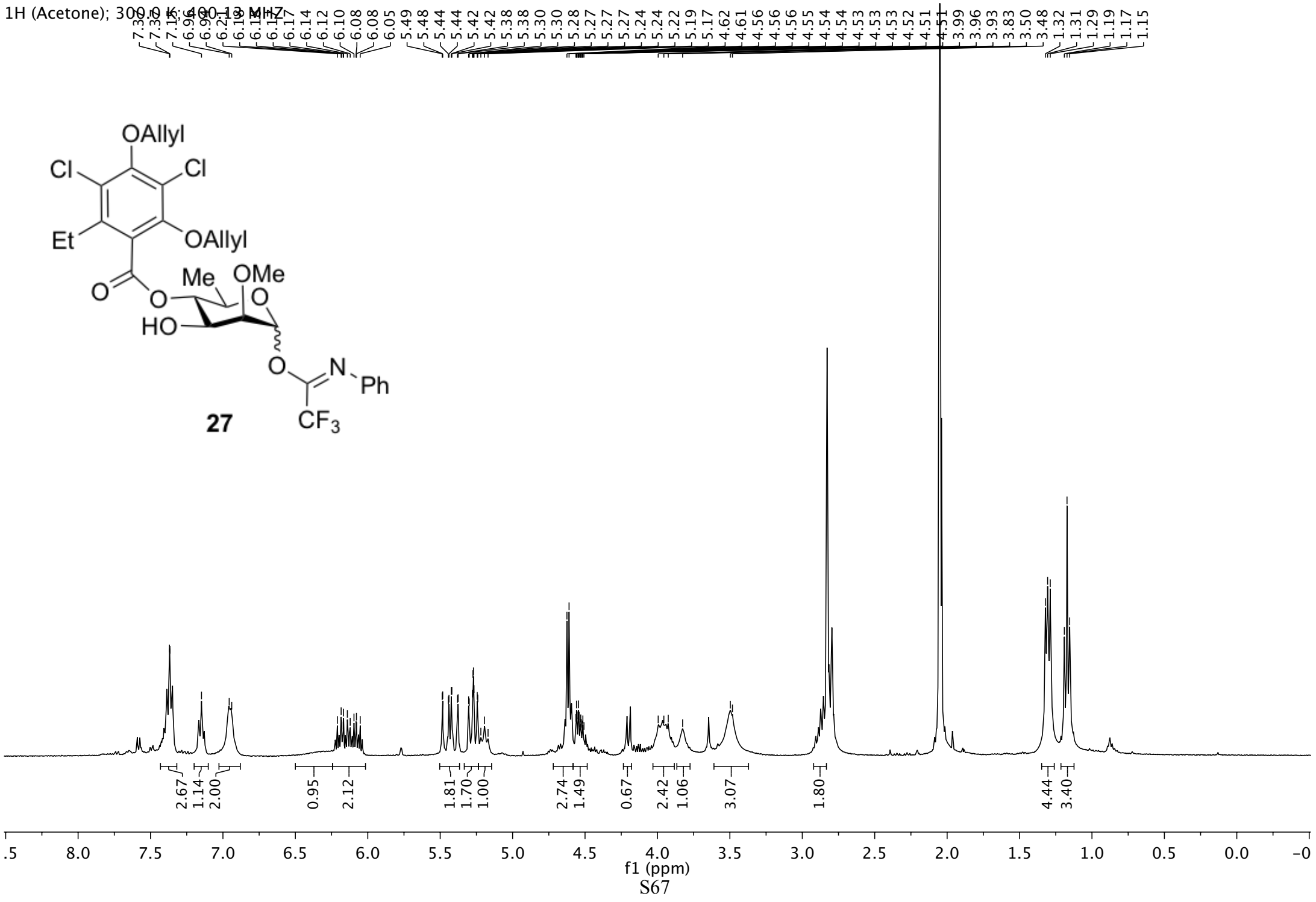
13C (CDCl3); 300.0 K; 100.62 MHZ

166.55
153.22
151.05
139.23
132.94
132.90
127.38
125.68
121.65
119.08
118.98
91.12
80.68
76.57
75.90
74.45
69.25
66.11
59.22
25.31
17.77
14.13

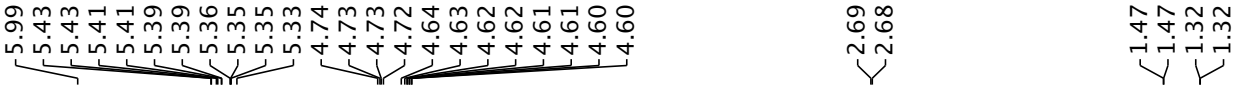


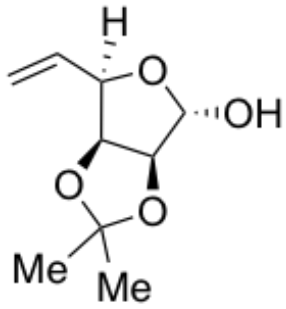
26b



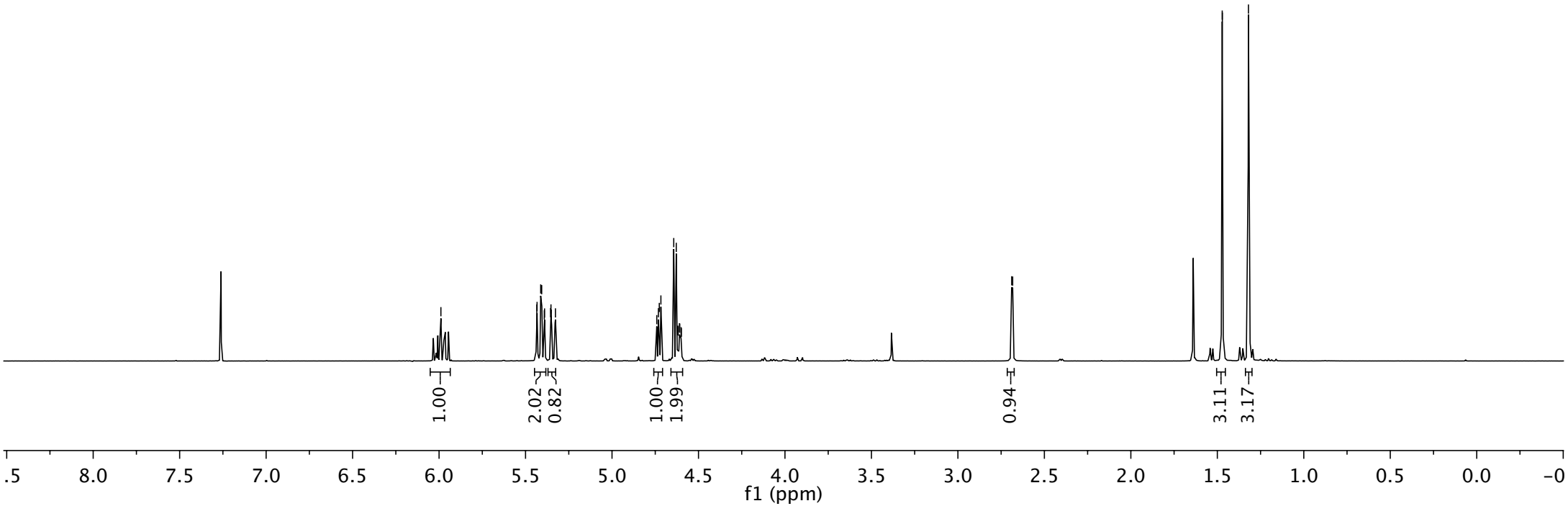

1H (Acetone); 300.0 K; 400.13 MHz
OAllyl
Cl
Cl
Et
OAllyl
Me
OMe
O
O
HO
O
O
N
Ph
CF3
27
f1 (ppm)

1H (CDCl3); 300.0 K; 400.13 MHZ



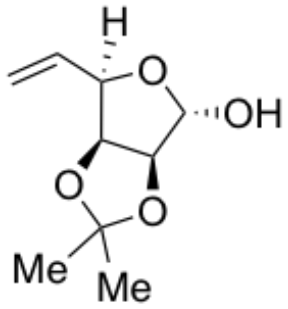


28a

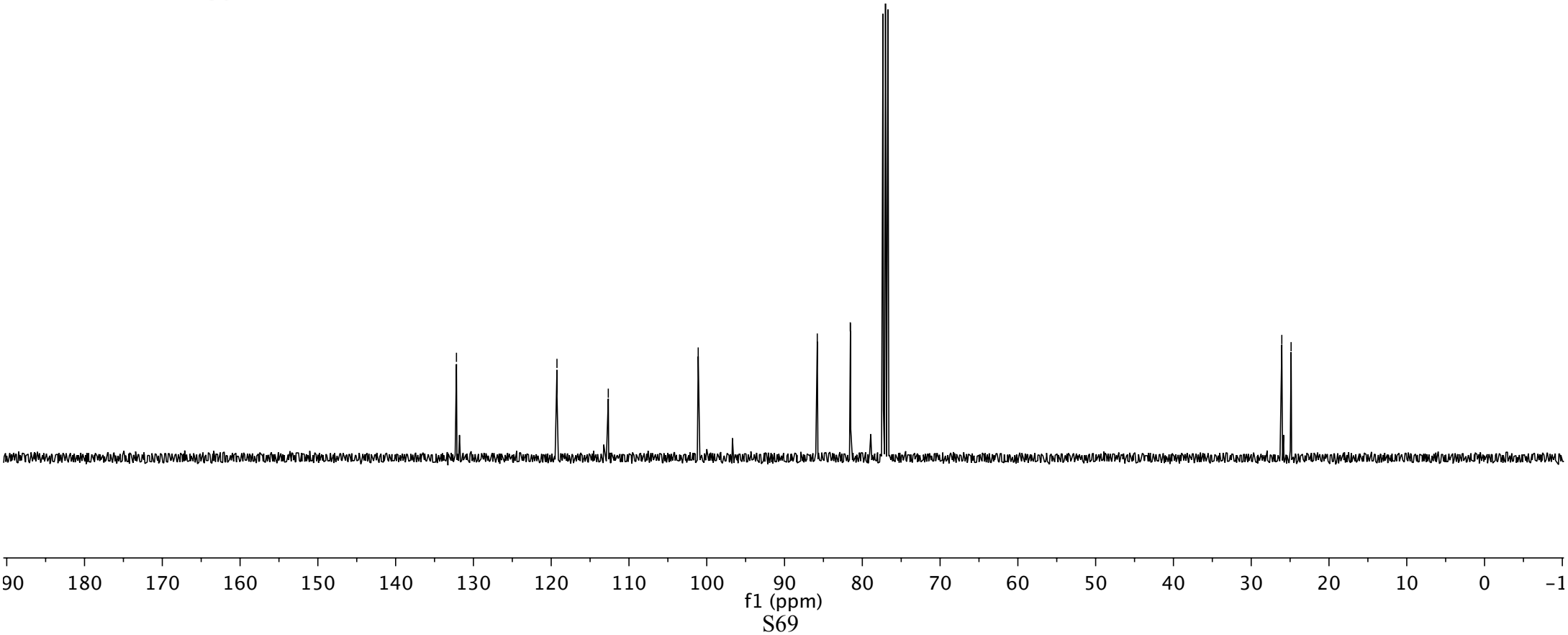


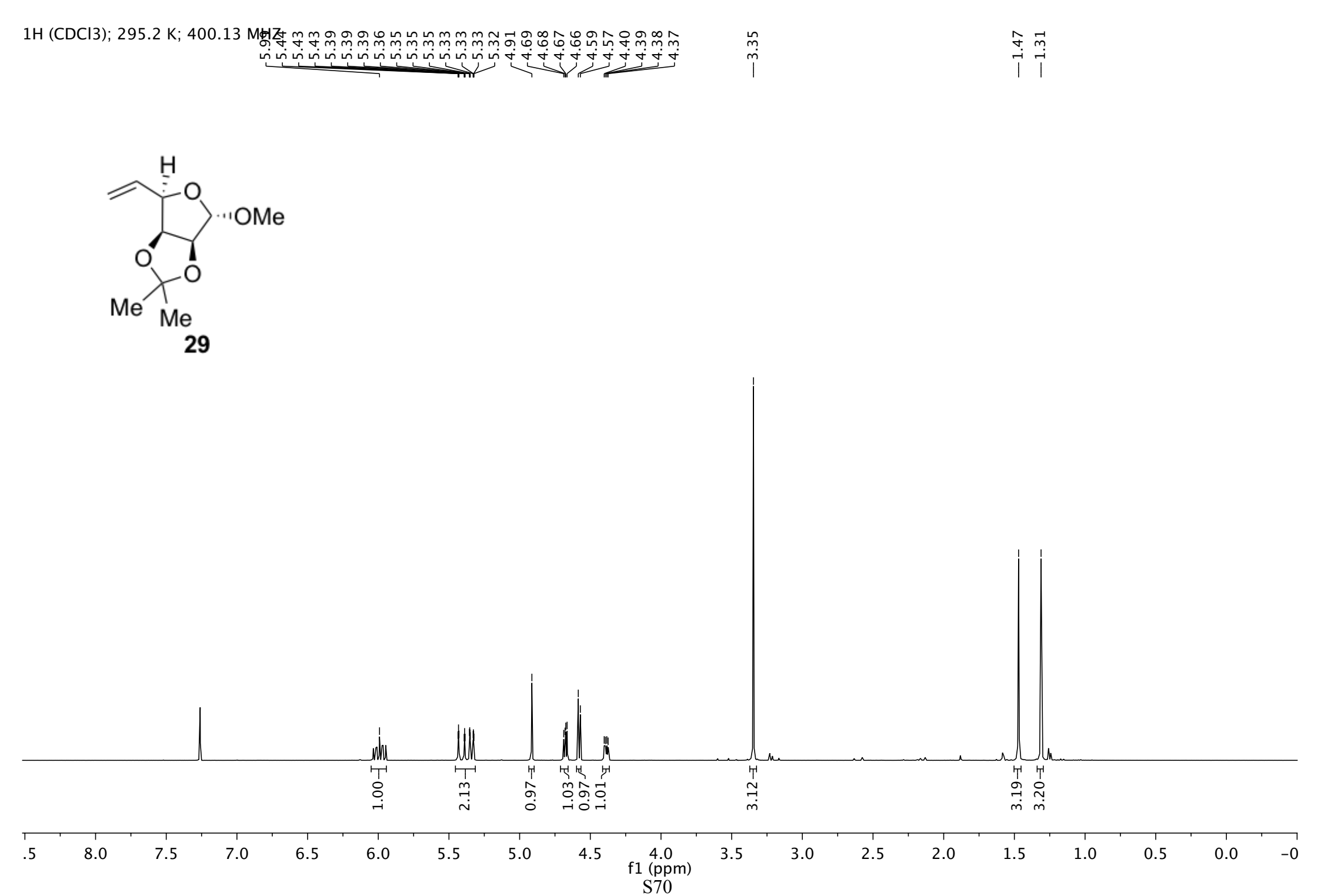
13C (CDCl3); 297.1 K; 100.61 MHZ

132.18
119.26
112.66
101.10
85.79
81.55
81.53
26.07
24.87



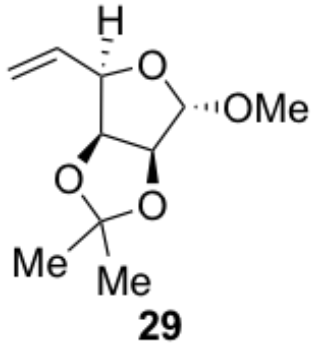
28a



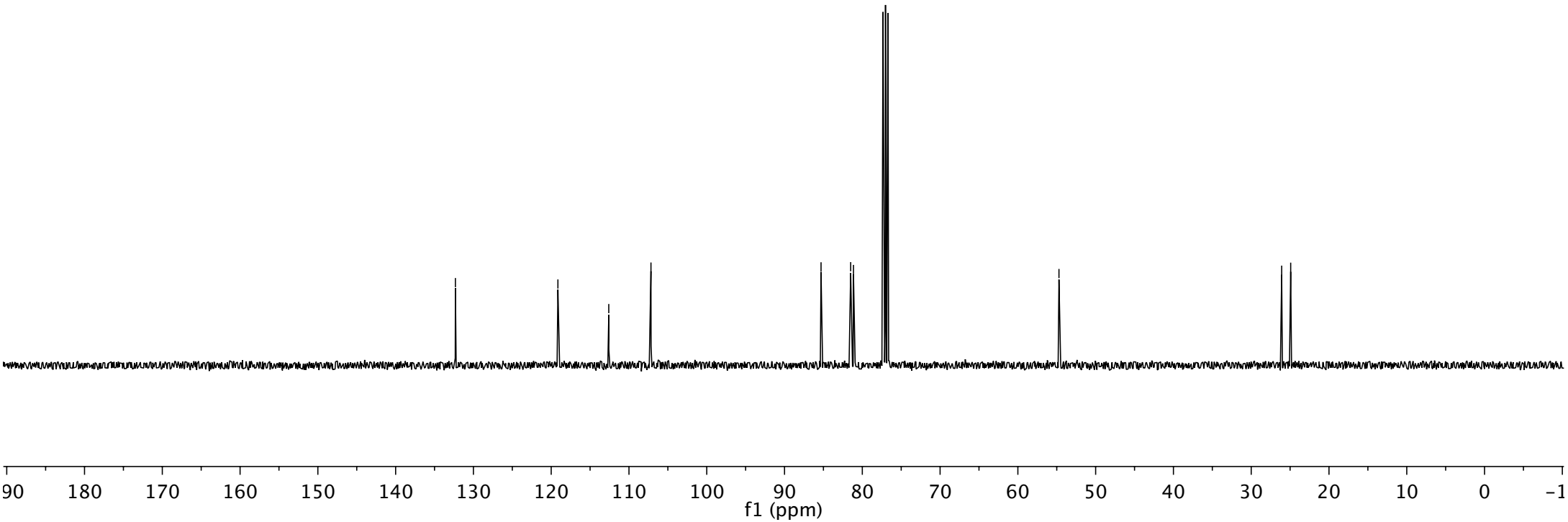

1H (CDCl3); 295.2 K; 400.13 MHZ
5.94
5.44
5.43
5.43
5.39
5.39
5.39
5.36
5.35
5.35
5.35
5.33
5.33
5.33
5.32
4.91
4.69
4.68
4.67
4.66
4.59
4.57
4.40
4.39
4.38
4.37
3.35
1.47
1.31
H
O
OMe
O
O
Me
Me
29
1.00
2.13
0.97
1.03
0.97
1.01
3.12
3.19
3.20
.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0
f1 (ppm)

13C (CDCl3); 300.0 K; 100.61 MHZ

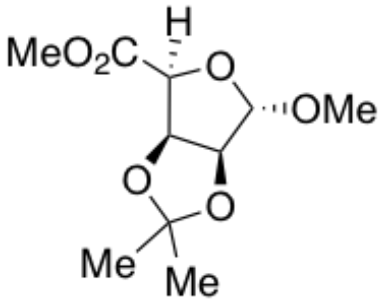
132.31
119.14
112.60
107.17
85.31
81.50
81.14
54.72
26.08
24.92



29



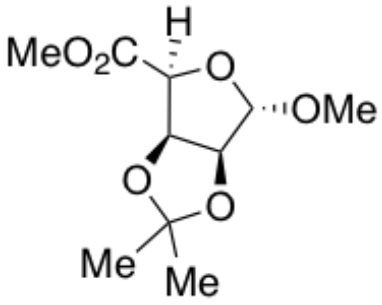
1H (CDCl3); 300.0 K; 400.13 MHZ



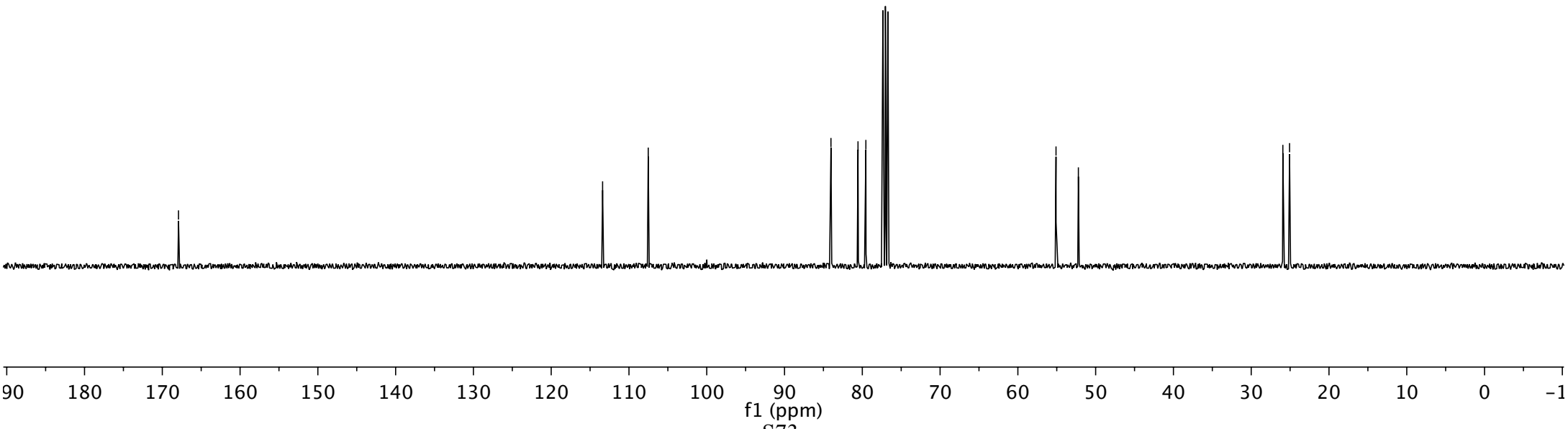
30

13C (CDCl3); 300.0 K; 100.61 MHZ

167.92
113.39
107.52
84.03
80.55
79.54
55.10
52.22
25.93
25.07

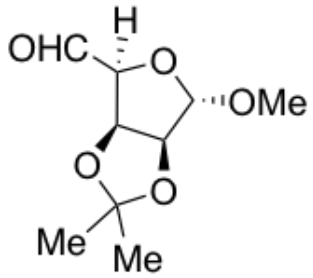


30

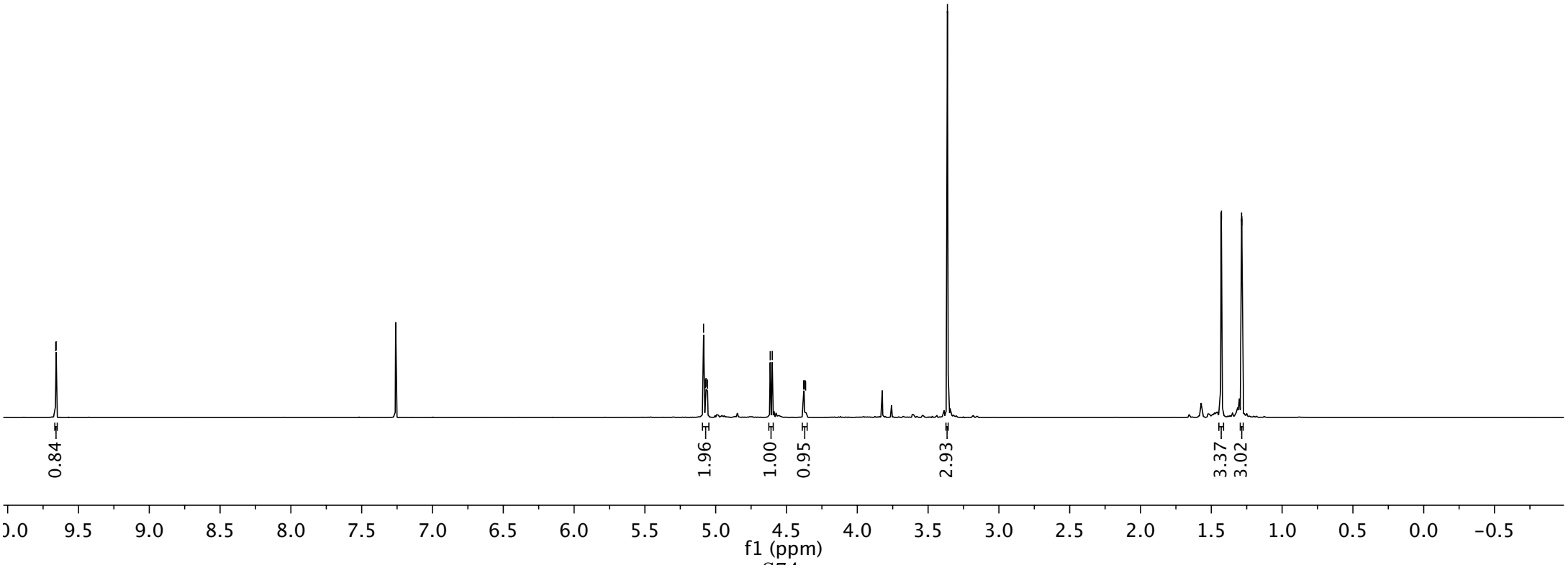


1H (CDCl3); 300.0 K; 400.13 MHZ

9.66
9.65
5.09
5.08
5.07
5.07
5.06
4.62
4.60
4.38
4.38
4.37
4.37
3.36
1.43
1.43
1.29
1.28

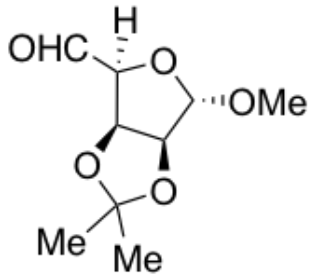


31



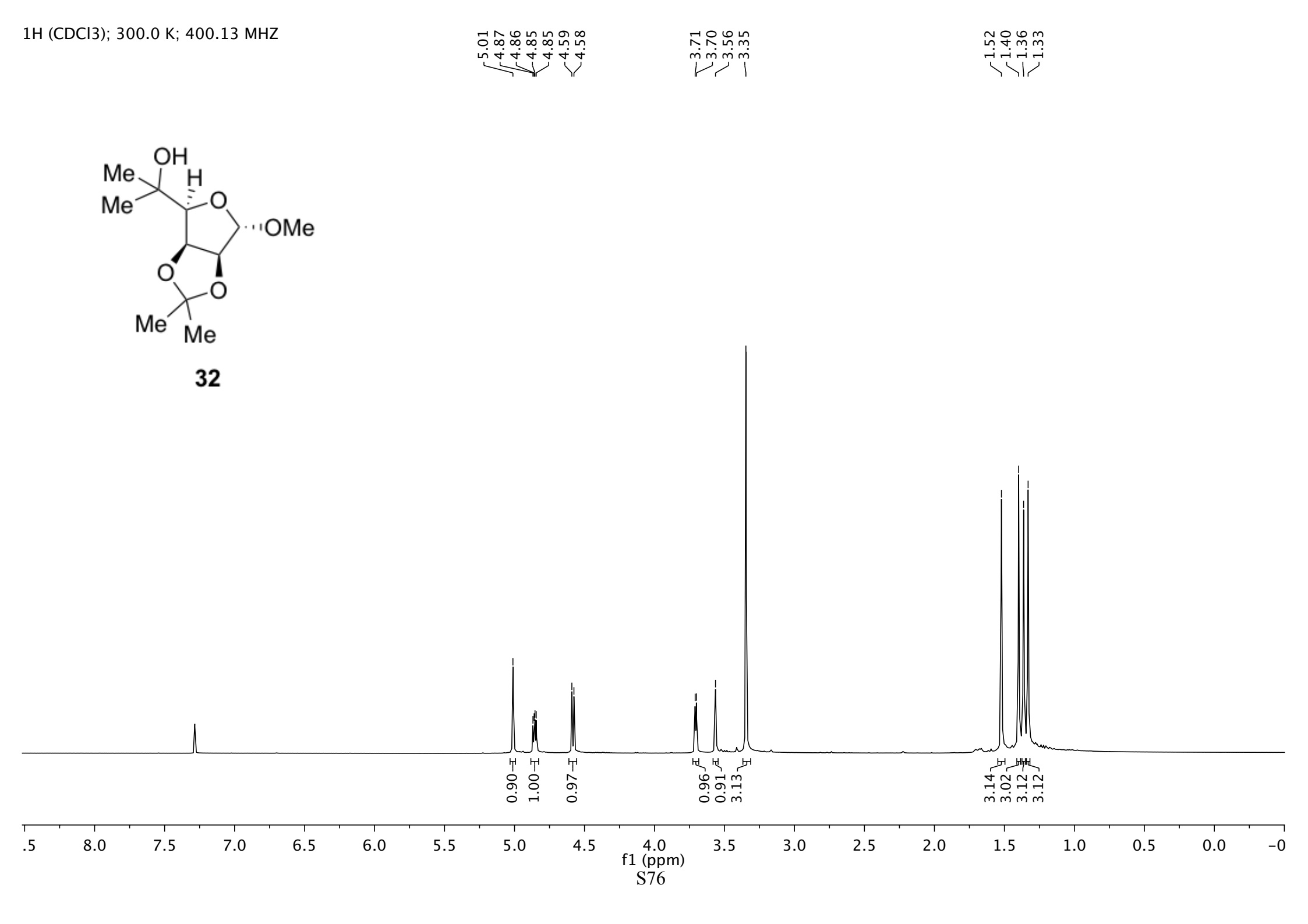
13C (CDCl3); 300.0 K; 100.61 MHZ

197.80
113.54
107.86
84.55
83.97
80.86
55.07
25.87
24.60



31

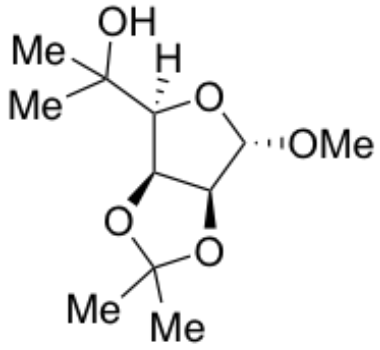
1H (CDCl3); 300.0 K; 400.13 MHZ



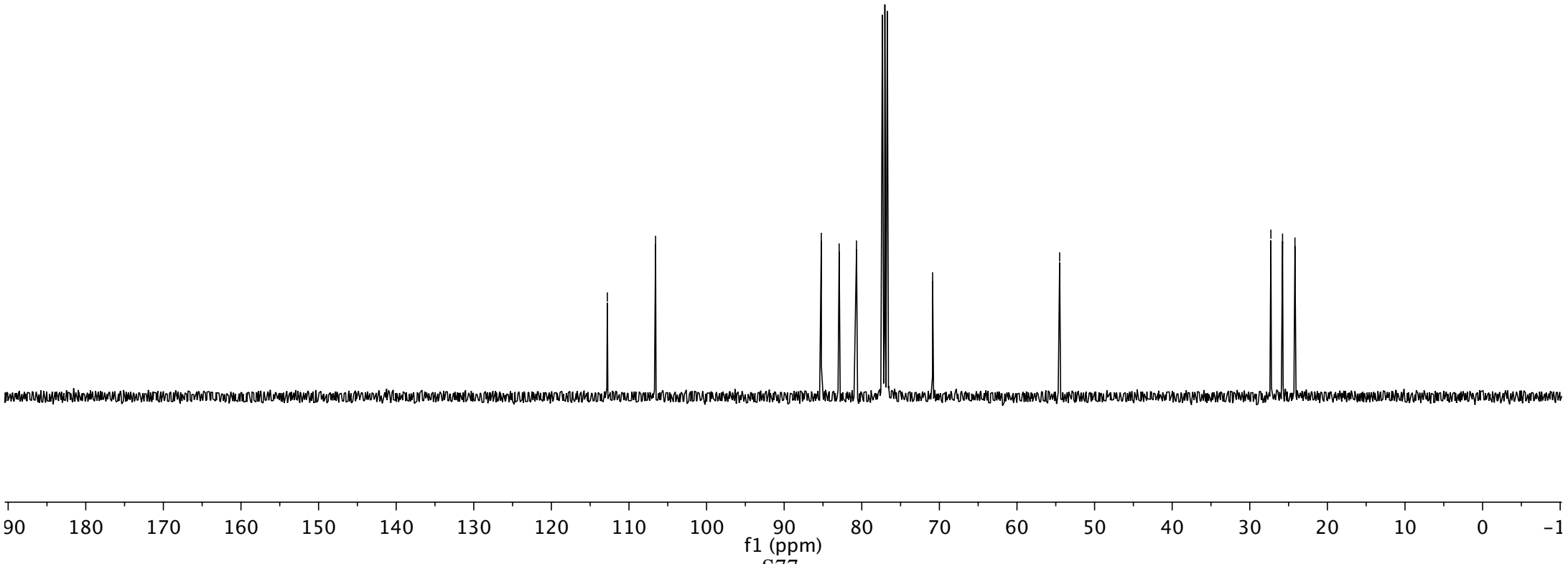
32

13C (CDCl3); 300.0 K; 100.61 MHZ

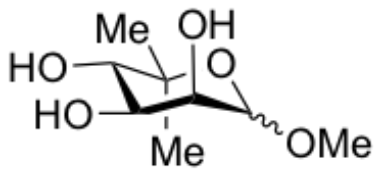
112.79
106.57
85.21
82.91
80.68
70.87
54.50
27.31
27.28
25.78
24.18



32

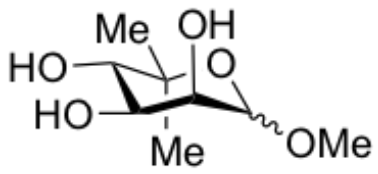


1H (MeOD); 295.5 K; 400.13 MHZ

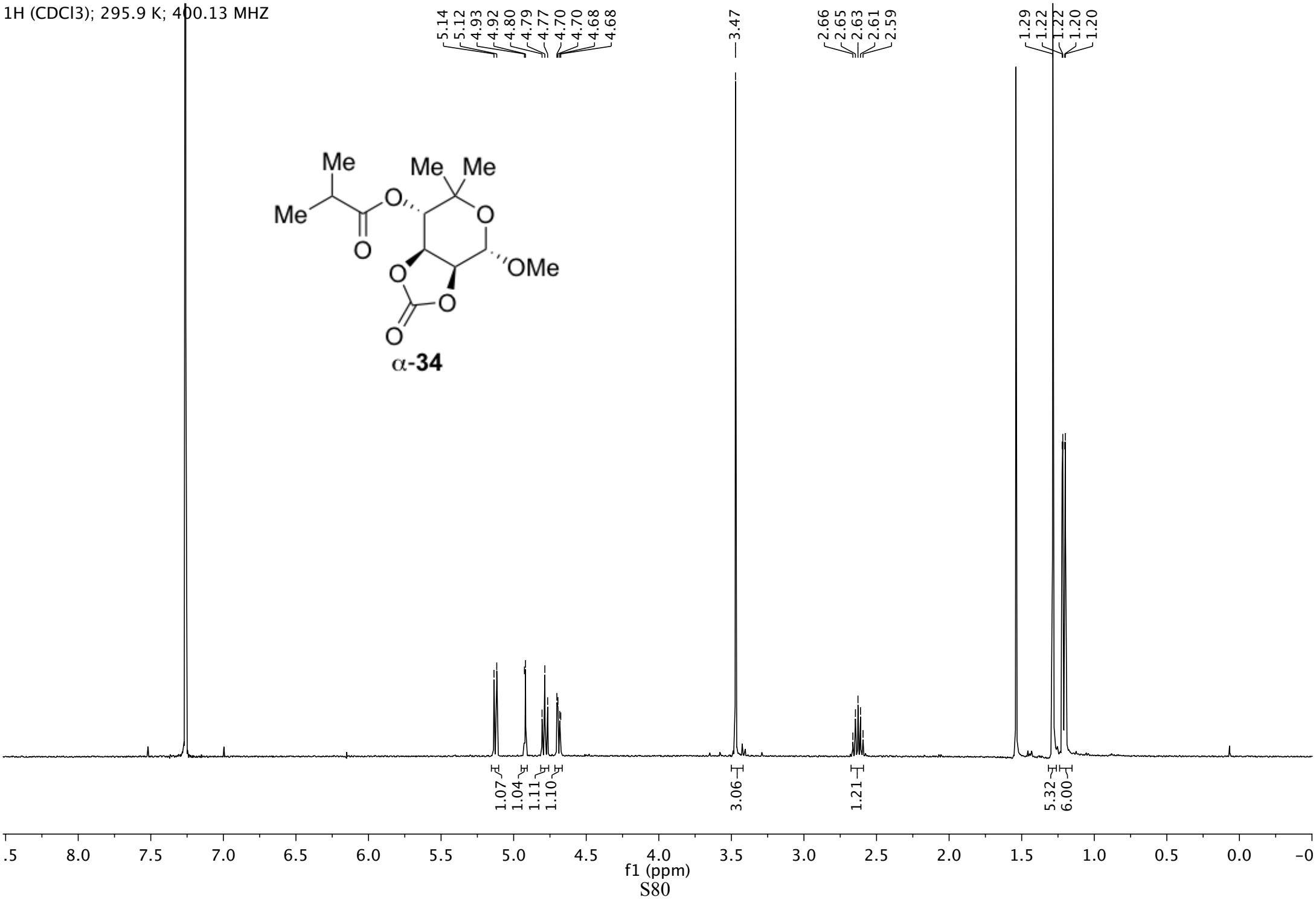


33

13C (MeOD); 300.0 K; 100.61 MHZ



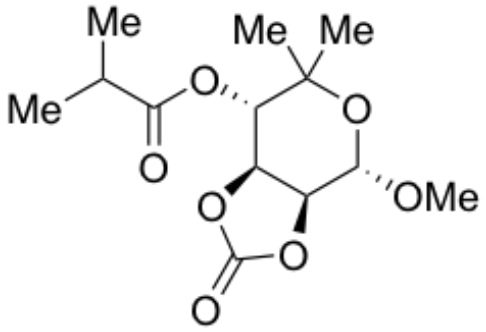
33


1H (CDCl3); 295.9 K; 400.13 MHZ
5.14
5.12
4.93
4.92
4.80
4.79
4.77
4.70
4.70
4.68
4.68
3.47
2.66
2.65
2.63
2.61
2.59
1.29
1.22
1.22
1.20
1.20
Me
Me
Me
Me
O
O
O
O
O
O
O
OMe
1.07
1.04
1.11
1.10
3.06
1.21
5.32
6.00
f1 (ppm)

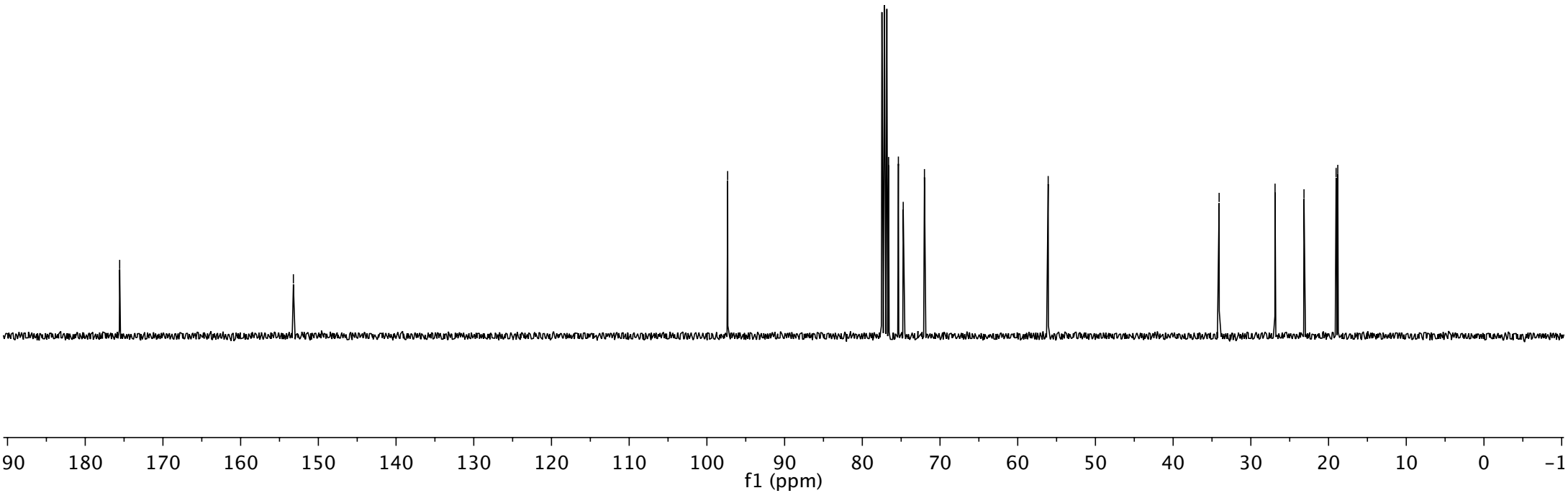
α-**34**

13C (CDCl3); 300.0 K; 100.61 MHZ

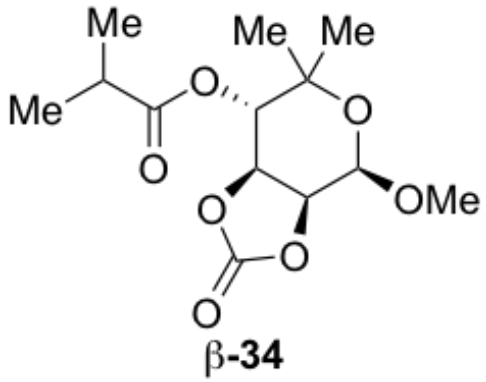
175.57
153.24
97.33
76.62
75.36
74.74
72.00
56.08
34.08
26.89
23.16
19.03
18.81



α-**34**



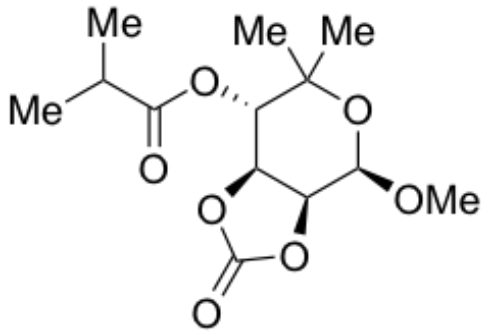
1H (CDCl3); 300.0 K; 400.13 MHZ



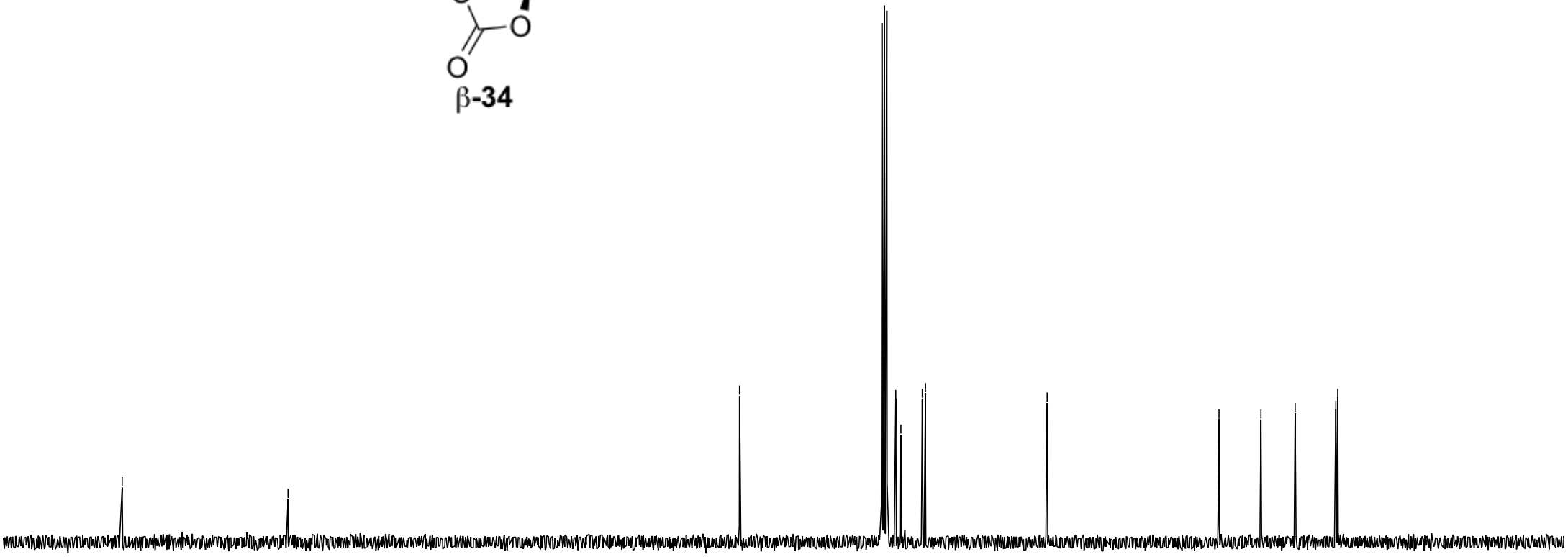
β-34

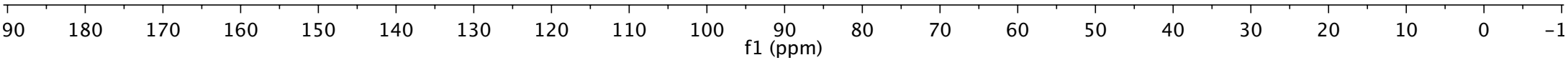
13C (CDCl3); 300.0 K; 100.61 MHZ

175.25
153.90
95.80
75.70
75.04
72.28
71.87
56.21
34.10
28.70
24.30
19.06
18.82

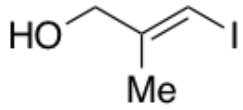


β-34

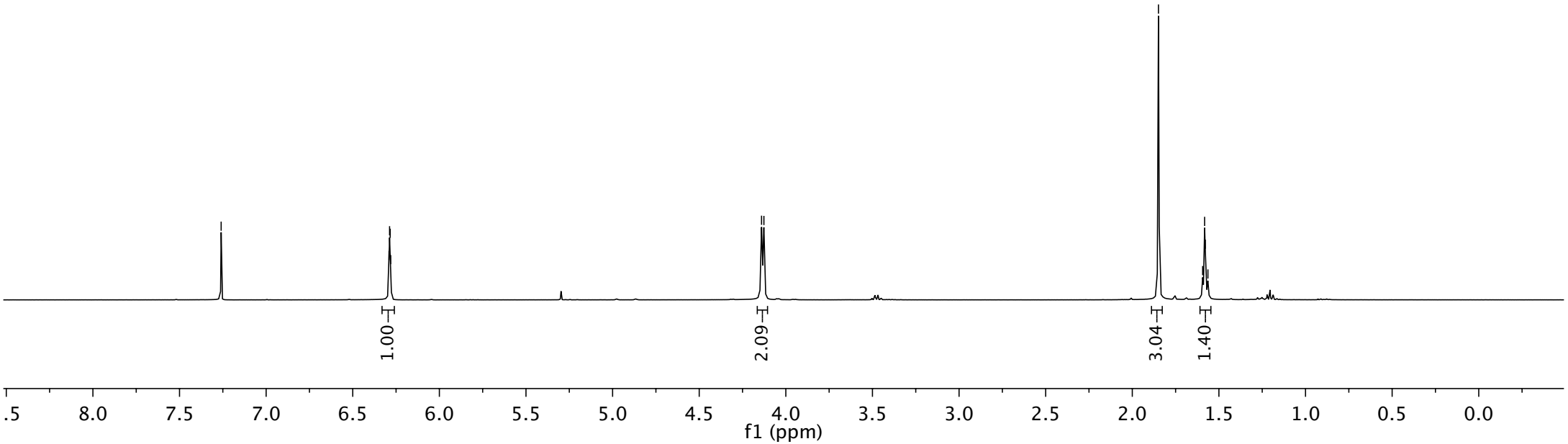




1H (CDCl3); 300.0 K; 400.13 MHZ

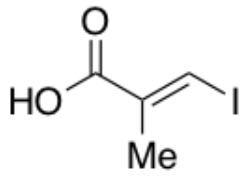


36a

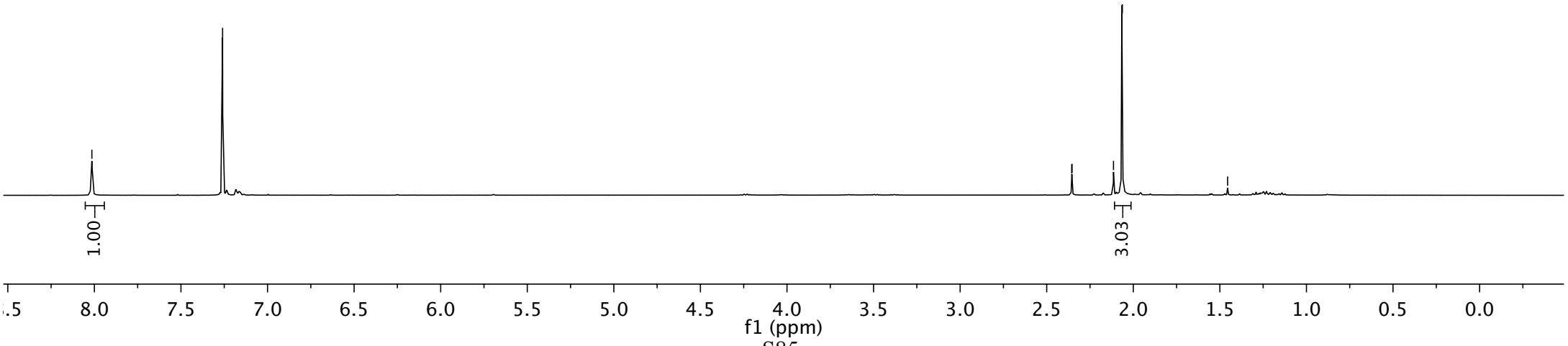


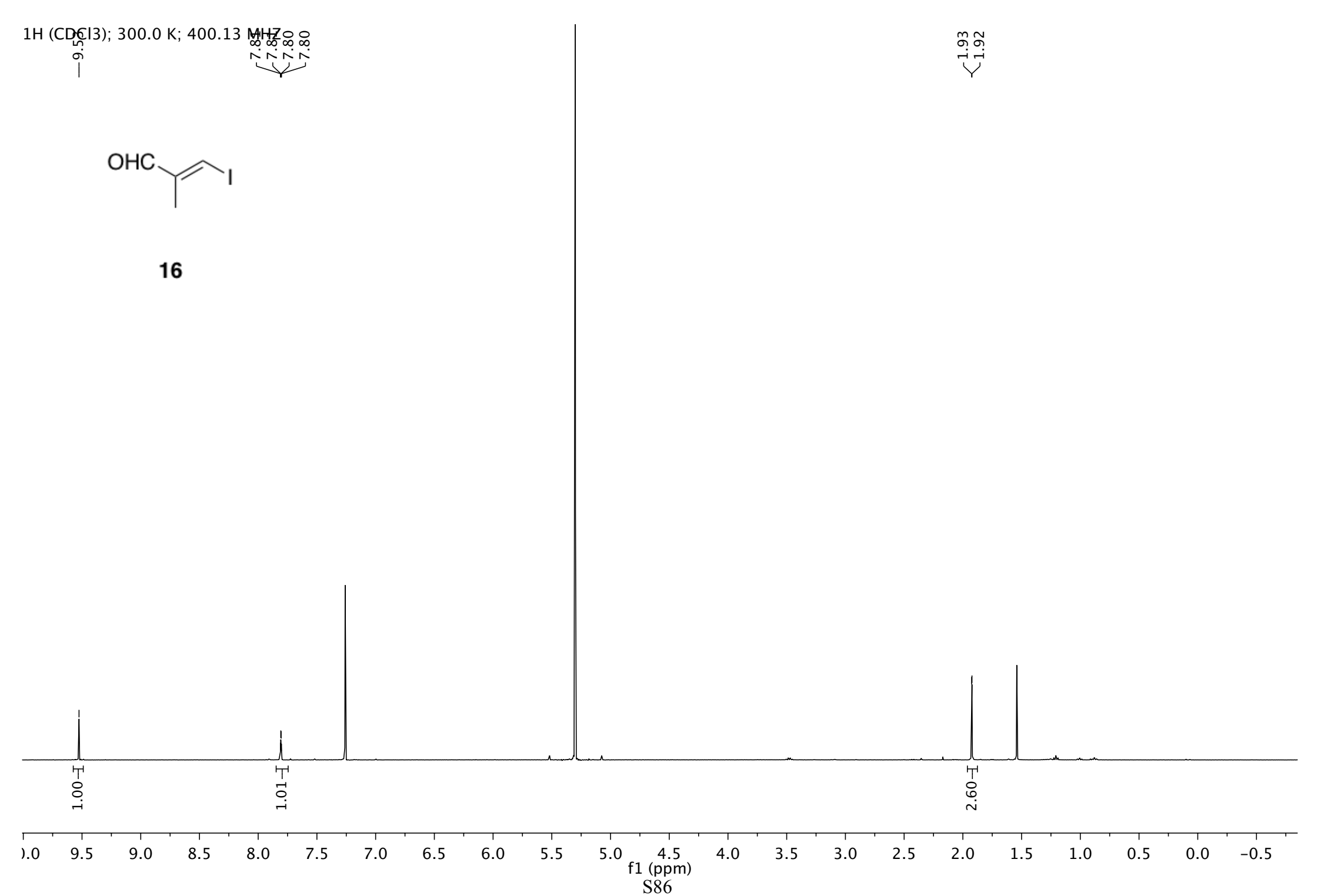
1H (CDCl3); 300.0 K; 400.13 MHZ

8.01
7.26
2.36
2.35
2.11
2.07
2.06
1.46

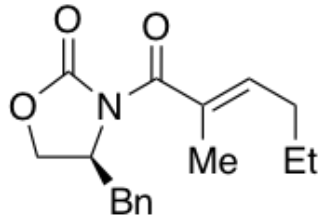


37a

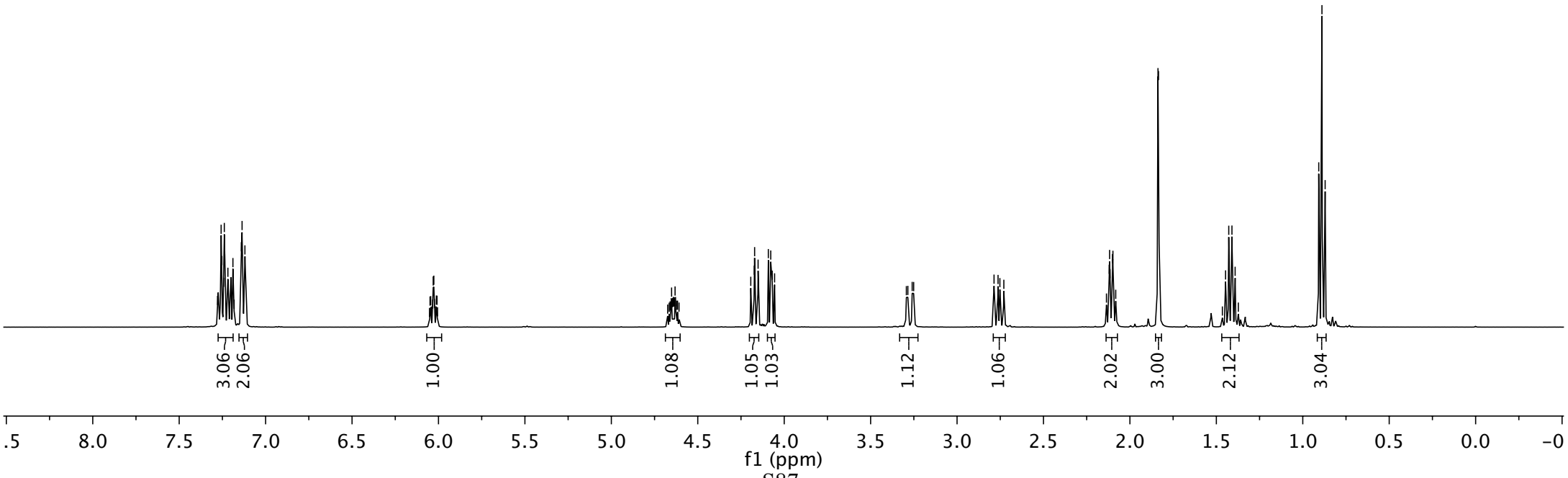



1H (CDCl3); 300.0 K; 400.13 MHz
9.56
7.82
7.82
7.80
7.80
1.93
1.92
OHC
I
16
1.00
1.01
2.60
f1 (ppm)

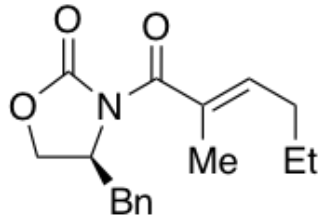
1H (CDCl3, 300.0 K, 400.13 MHz)



38

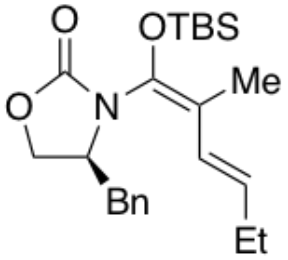


13C (CDCl3); 300.0 K; 100.62 MHZ



38

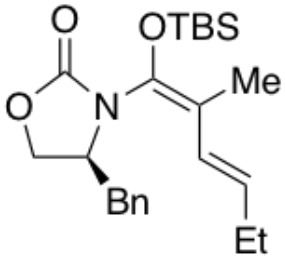
1H (CDCl3) ; 295.0 K ; 500.13 MHz



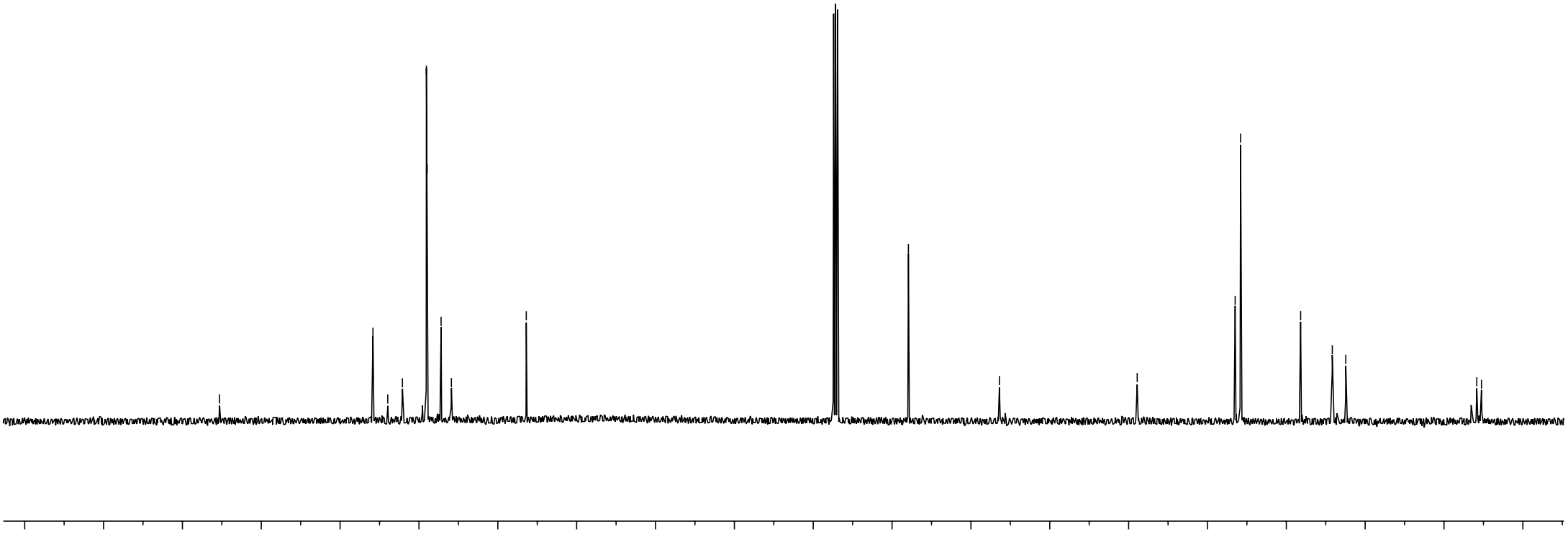
15

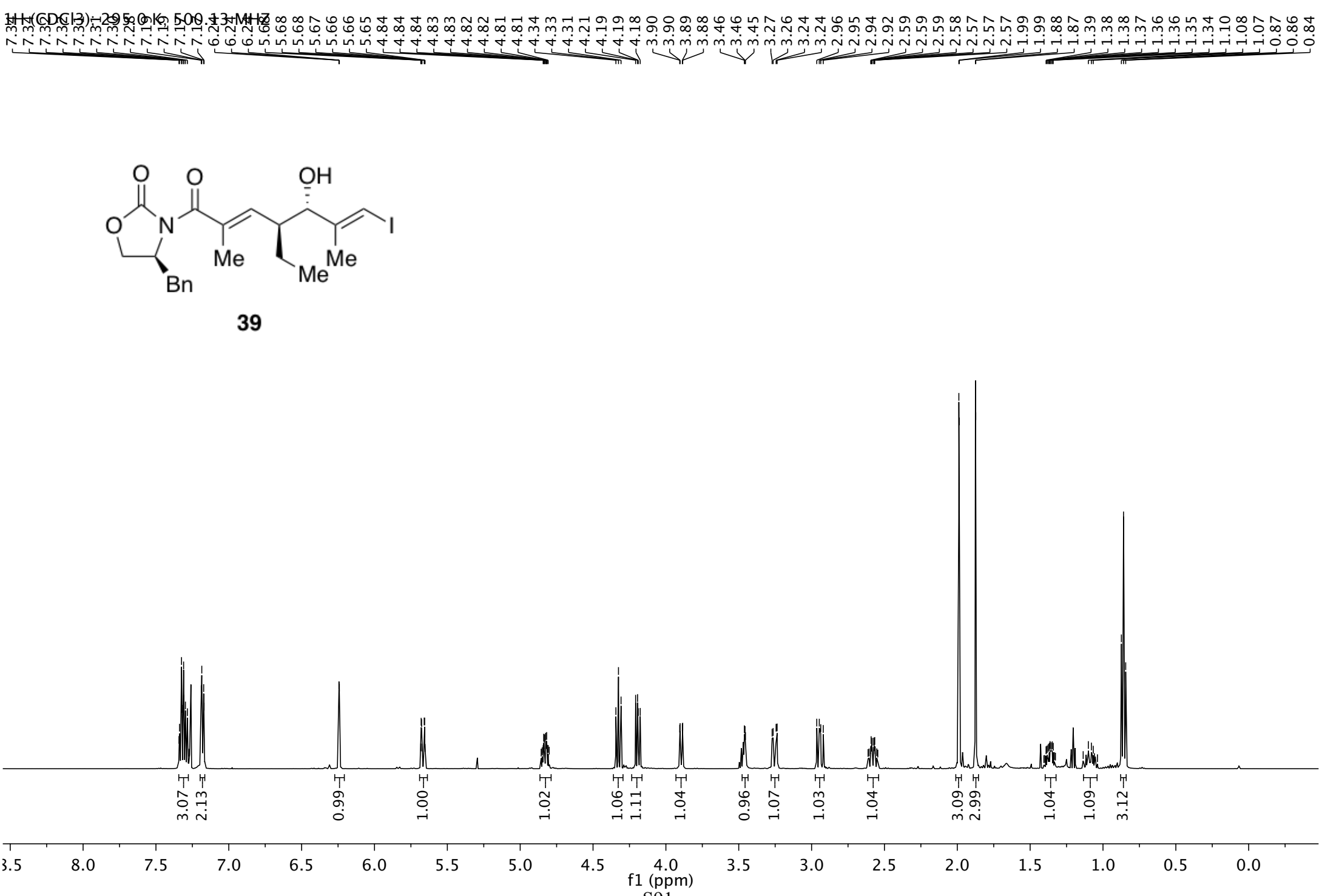
13C (CDCl3); 298.1 K; 125.77 MHZ

155.29
135.84
133.96
132.10
129.06
128.96
127.19
125.89
116.39
67.93
56.39
38.91
26.49
25.80
18.18
14.17
12.46
-4.16
-4.75



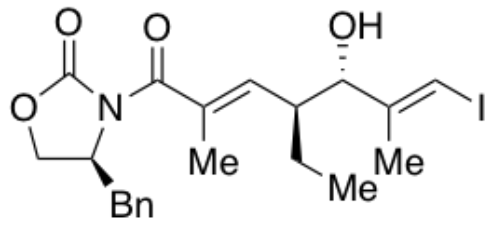
15



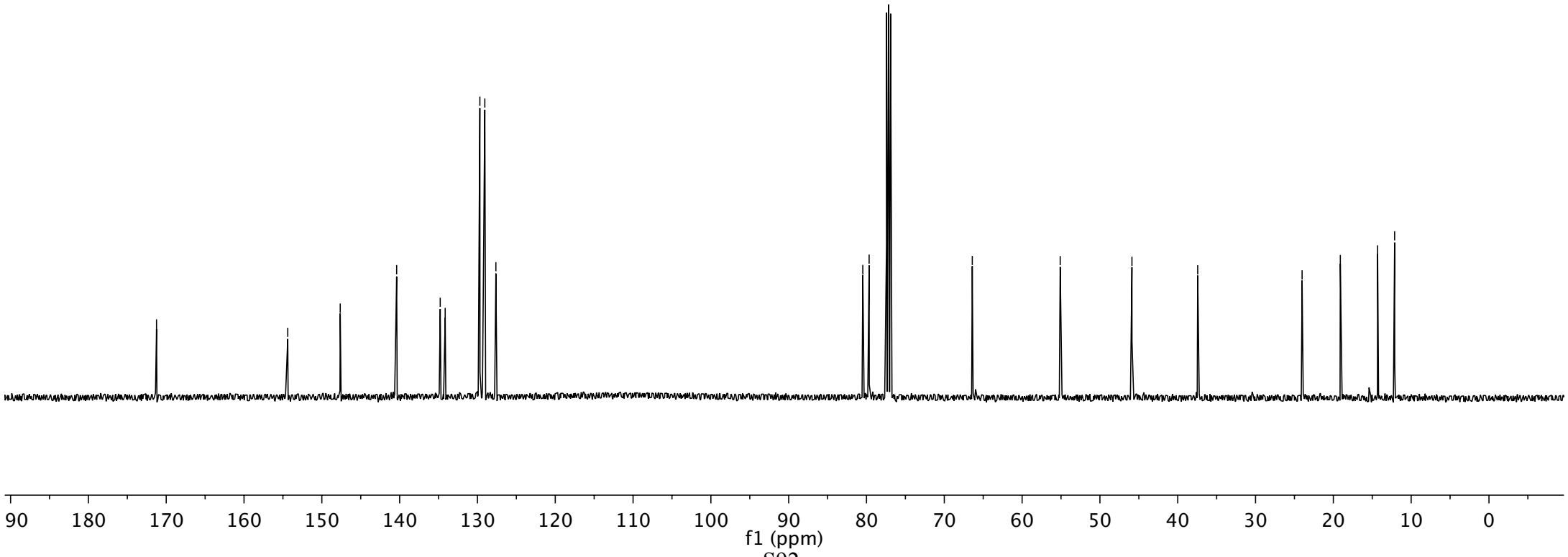

1H (CDCl3, 295.0 K, 500.13 MHz)
7.34 7.32 7.32 7.31 7.31 7.30 7.29 7.19 7.19 7.16 7.16 6.24 6.24 6.23 5.68 5.68 5.67 5.66 5.66 5.65 4.84 4.84 4.84 4.83 4.83 4.82 4.82 4.81 4.81 4.34 4.33 4.31 4.21 4.19 4.19 4.18 3.90 3.90 3.89 3.88 3.46 3.46 3.45 3.27 3.26 3.24 3.24 2.96 2.95 2.94 2.92 2.59 2.59 2.59 2.58 2.57 2.57 2.57 1.99 1.99 1.88 1.87 1.39 1.38 1.38 1.37 1.36 1.36 1.35 1.34 1.10 1.08 1.07 0.87 0.86 0.84
O
O
OH
O
N
I
Me
Me
Me
Bn
39
3.07
2.13
0.99
1.00
1.02
1.06
1.11
1.04
0.96
1.07
1.03
1.04
3.09
2.99
1.04
1.09
3.12
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

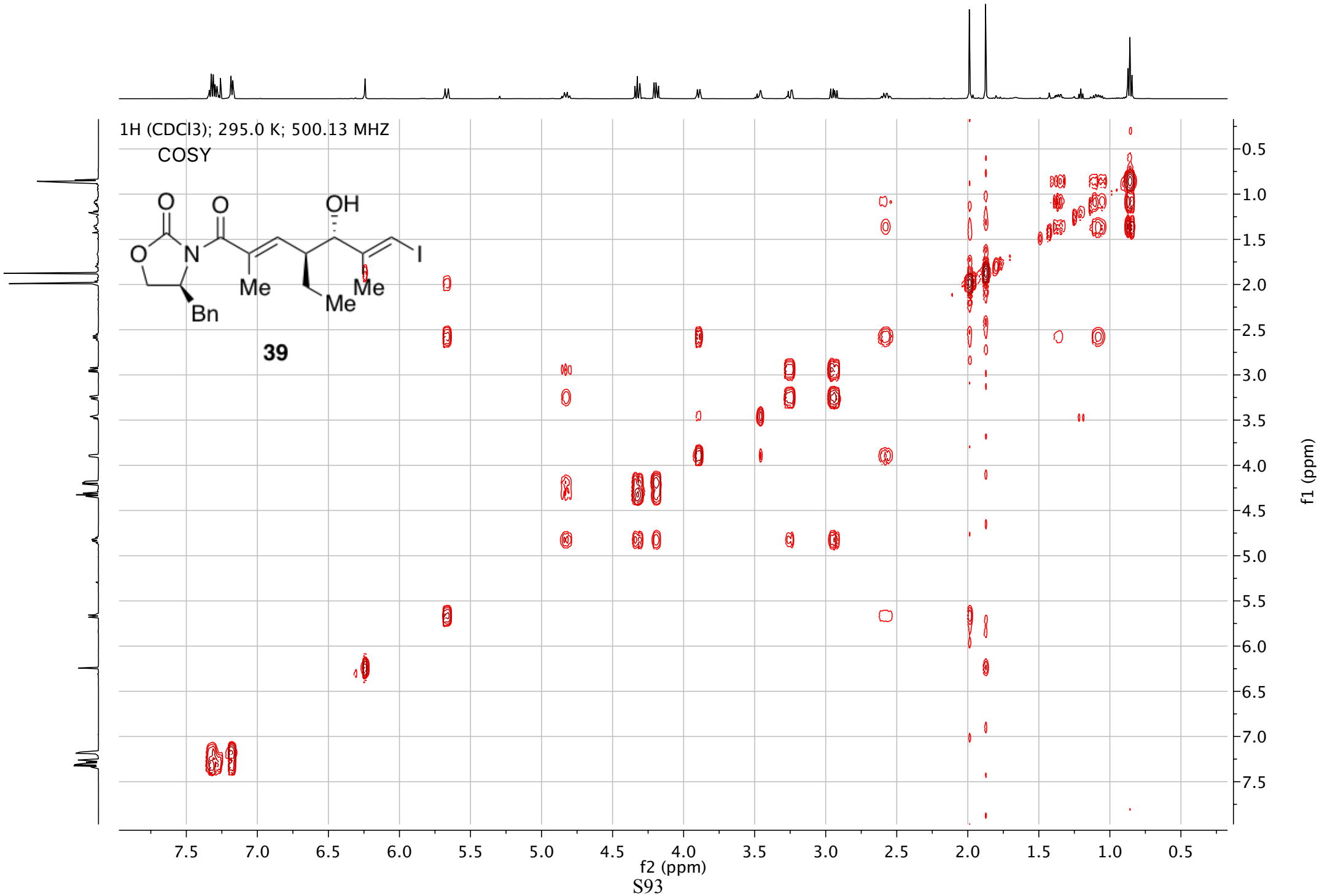
13C (CDCl3); 295.0 K; 125.77 MHZ

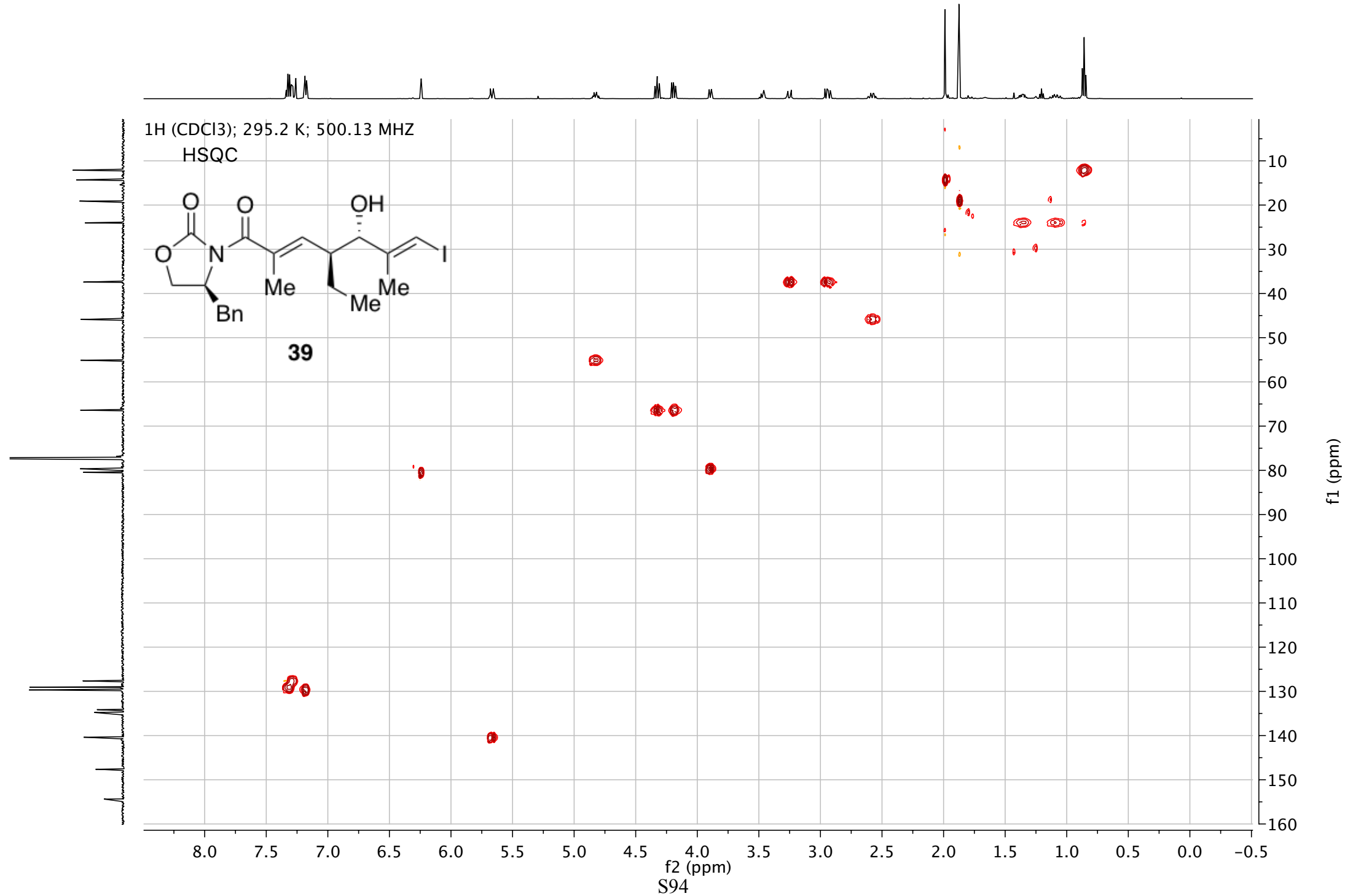
171.25
154.38
147.64
140.38
134.78
134.15
129.69
129.05
127.63
80.48
79.66
66.40
55.10
45.88
37.43
24.02
19.10
14.31
12.12

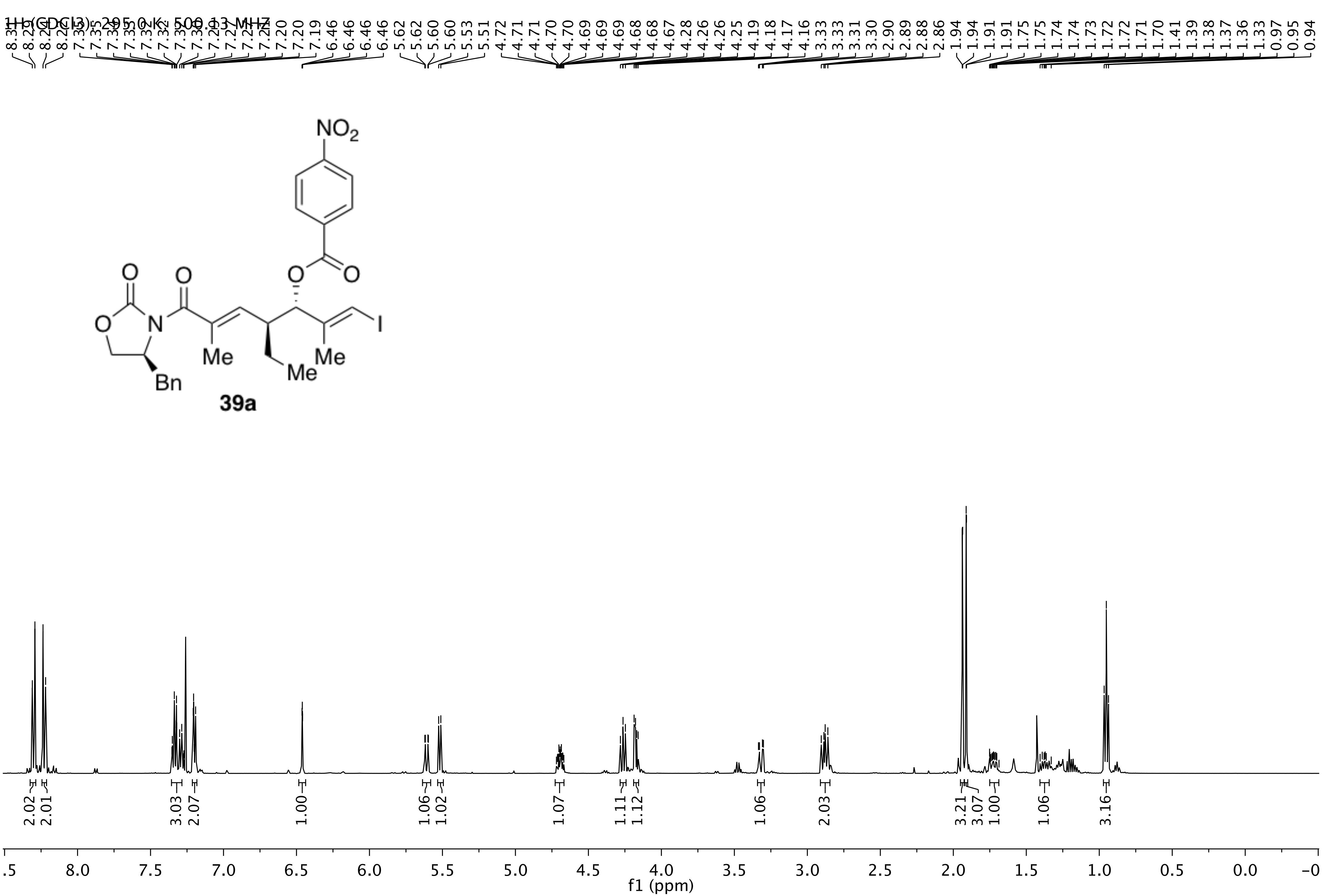


39

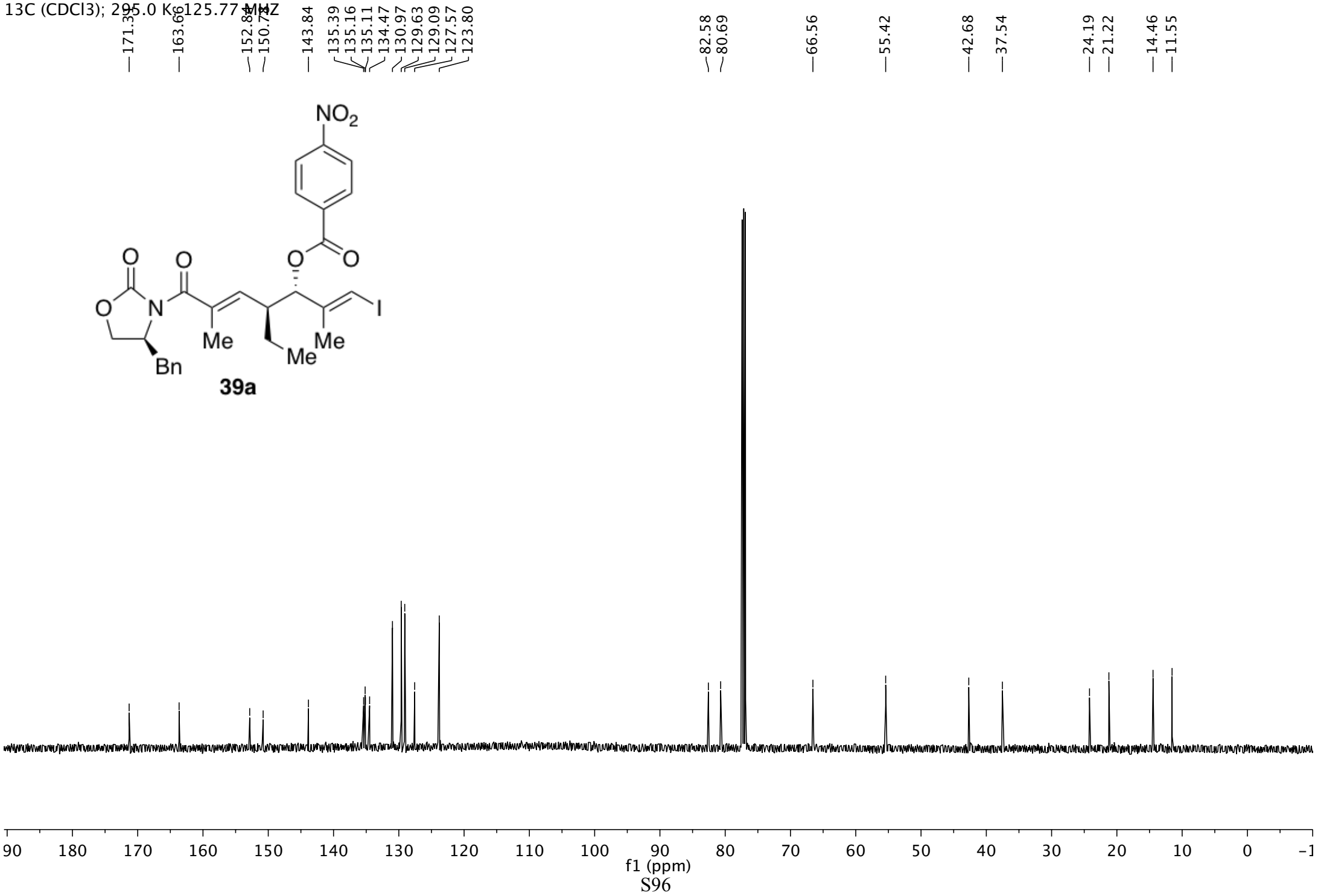


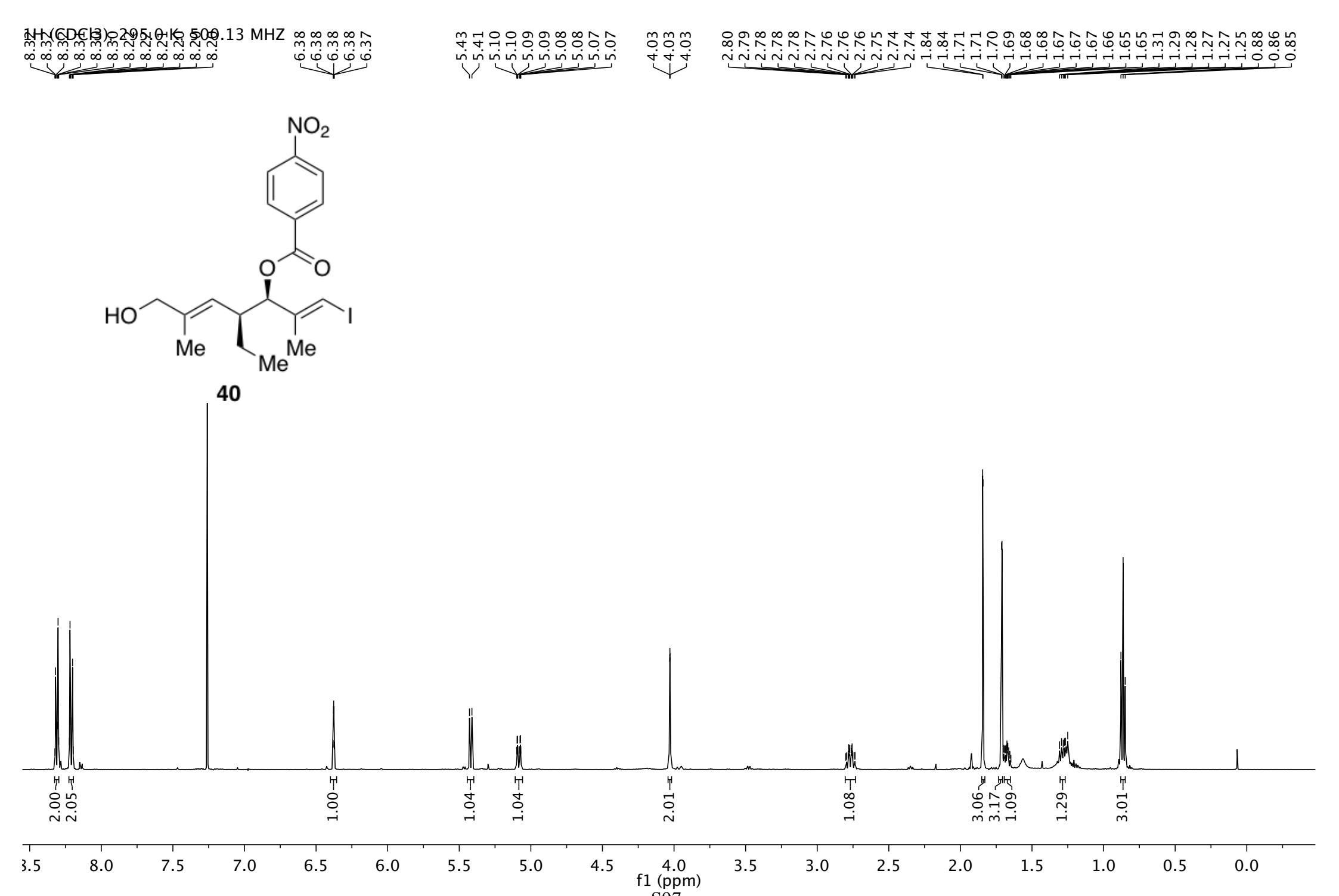

1H (CDCl3); 295.0 K; 500.13 MHZ
COSY
O
O
OH
O
N
I
Me
Me
Me
Bn
39
f2 (ppm)
f1 (ppm)

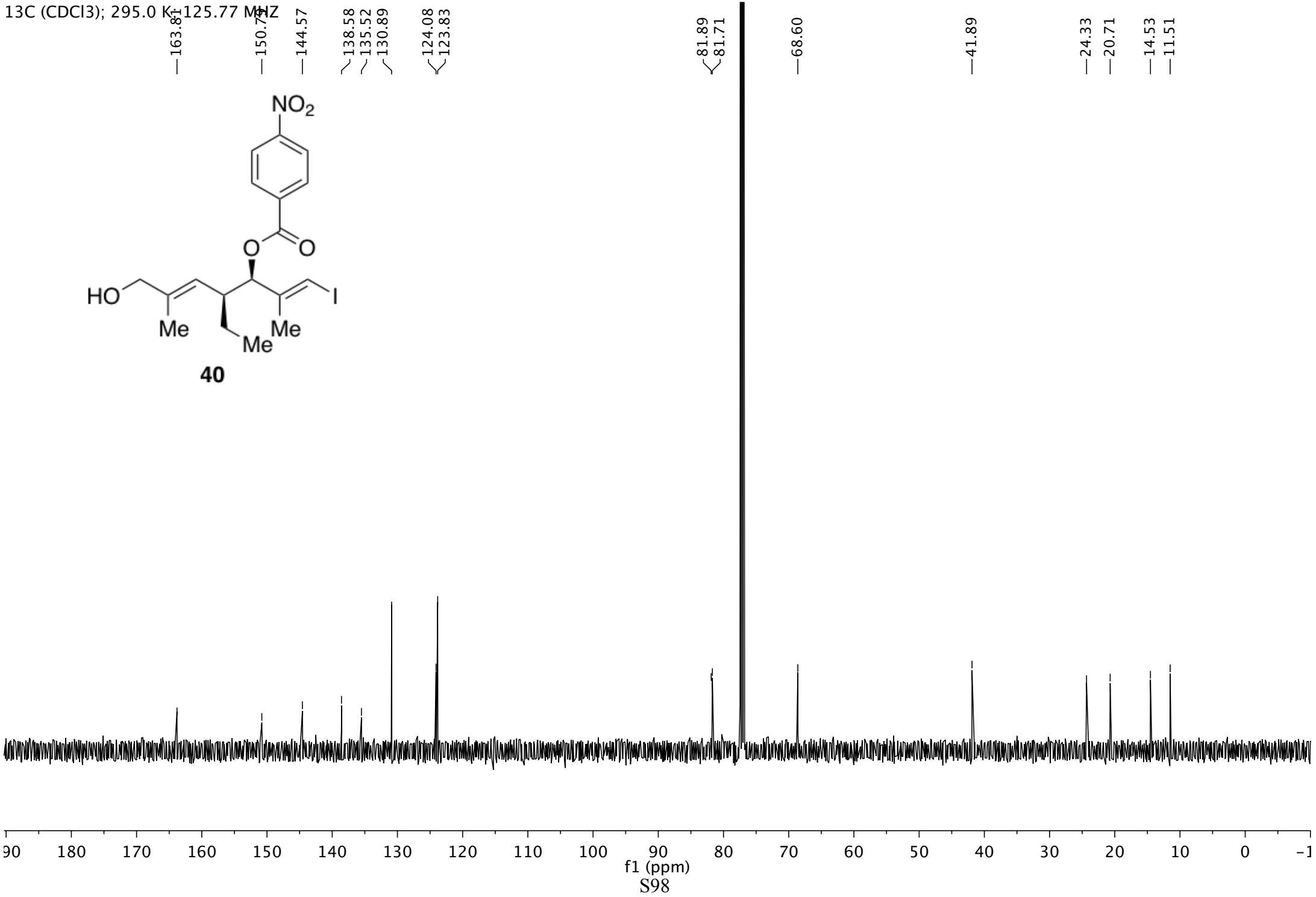

1H (CDCl3); 295.2 K; 500.13 MHZ
HSQC
O
O
OH
O
N
I
Me
Me
Me
Bn
39
f2 (ppm)
f1 (ppm)

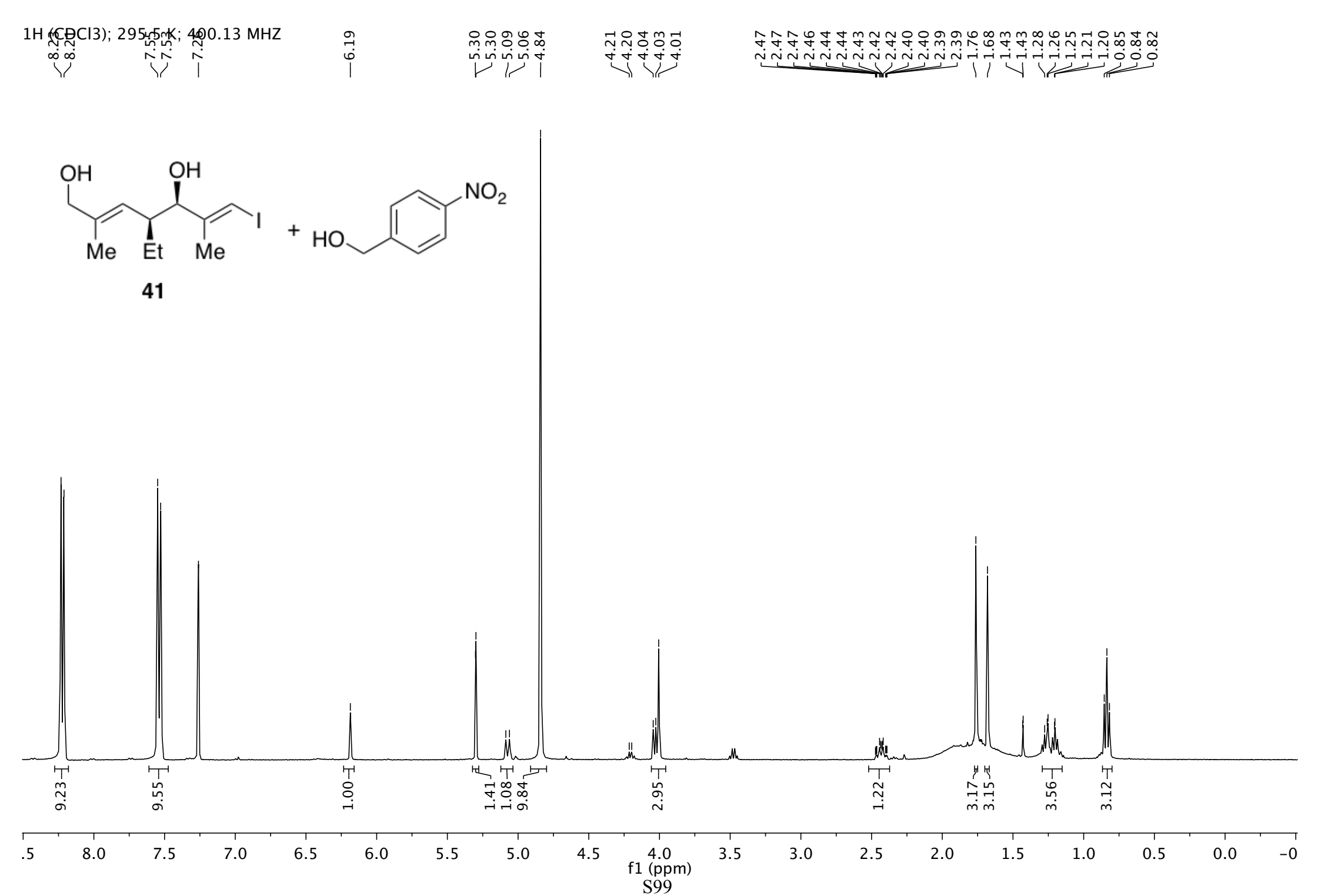


39a

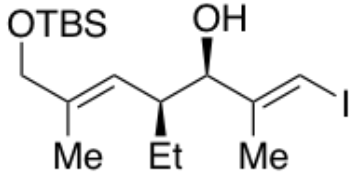

13C (CDCl3); 295.0 K; 125.77 MHZ
171.39
163.66
152.84
150.78
143.84
135.39
135.16
135.11
134.47
130.97
129.63
129.09
127.57
123.80
82.58
80.69
66.56
55.42
42.68
37.54
24.19
21.22
14.46
11.55
NO2
O
O
O
O
O
N
I
Me
Me
Me
Bn
39a
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


1H (CDCl3, 295.0 K, 500.13 MHZ
8.32 8.32 8.31 8.31 8.31 8.31 8.29 8.29 8.29 8.29 8.28 8.28
6.38 6.38 6.38 6.38 6.37
5.43 5.41 5.10 5.10 5.09 5.09 5.08 5.08 5.07 5.07
4.03 4.03 4.03
2.80 2.79 2.78 2.78 2.78 2.77 2.76 2.76 2.76 2.75 2.74 2.74
1.84 1.84 1.71 1.71 1.70 1.69 1.68 1.68 1.67 1.67 1.67 1.66 1.65 1.65 1.31 1.29 1.28 1.27 1.27 1.25 0.88 0.86 0.85
NO2
O
O
HO
I
Me
Me
Me
40
2.00
2.05
1.00
1.04
1.04
2.01
1.08
3.06
3.17
1.09
1.29
3.01
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


13C (CDCl3); 295.0 K; 125.77 MHZ
163.81
150.74
144.57
138.58
135.52
130.89
124.08
123.83
81.89
81.71
68.60
41.89
24.33
20.71
14.53
11.51
NO2
O
O
HO
I
Me
Me
Me
40
f1 (ppm)

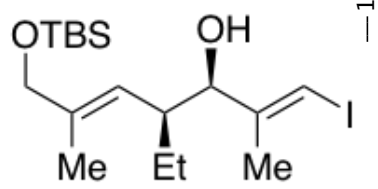

1H (CDCl3); 295.5 K; 400.13 MHZ
8.23
8.22
7.53
7.51
7.26
6.19
5.30
5.30
5.09
5.06
4.84
4.21
4.20
4.04
4.03
4.01
2.47
2.47
2.47
2.46
2.44
2.44
2.43
2.42
2.42
2.40
2.40
2.39
2.39
1.76
1.68
1.43
1.43
1.28
1.26
1.25
1.21
1.20
0.85
0.84
0.82
OH
OH
I
Me
Et
Me
+
HO
NO2
41
9.23
9.55
1.00
1.41
1.08
9.84
2.95
1.22
3.17
3.15
3.56
3.12
f1 (ppm)

1H (CDCl3); 300.0 K; 400.13 MHz



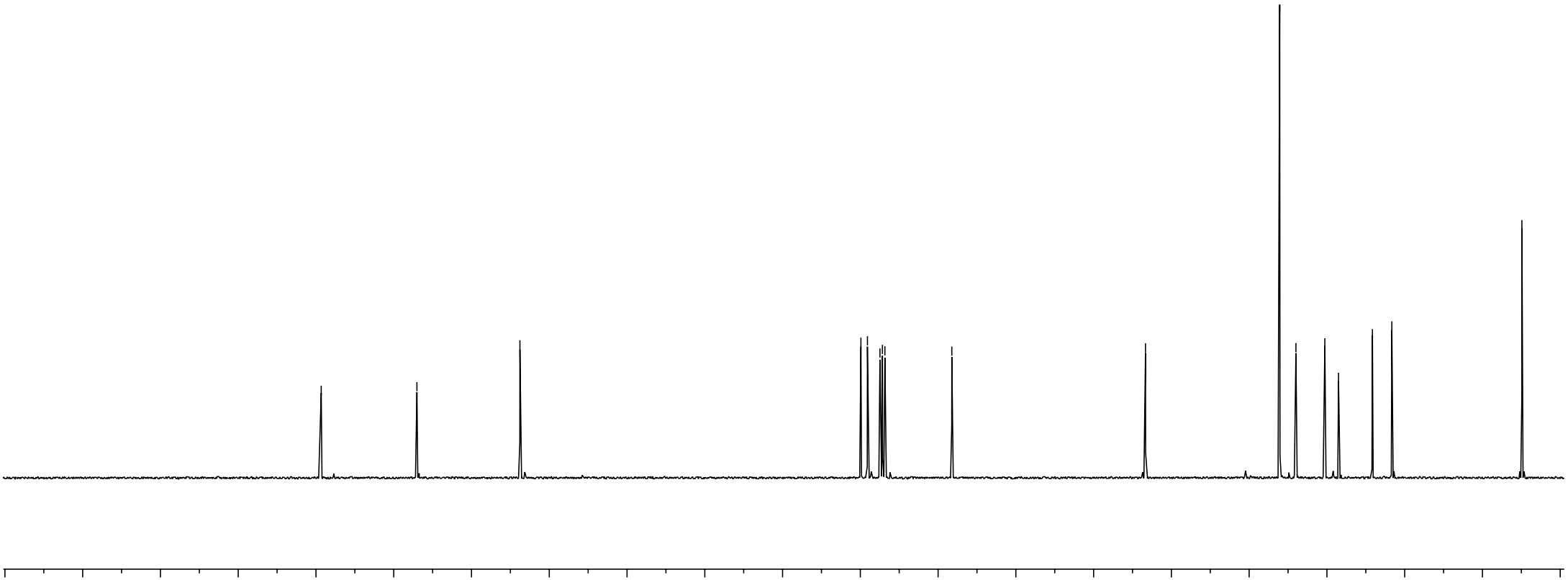
41a

13C (CDCl3); 300.0 K; 100.62 MHZ

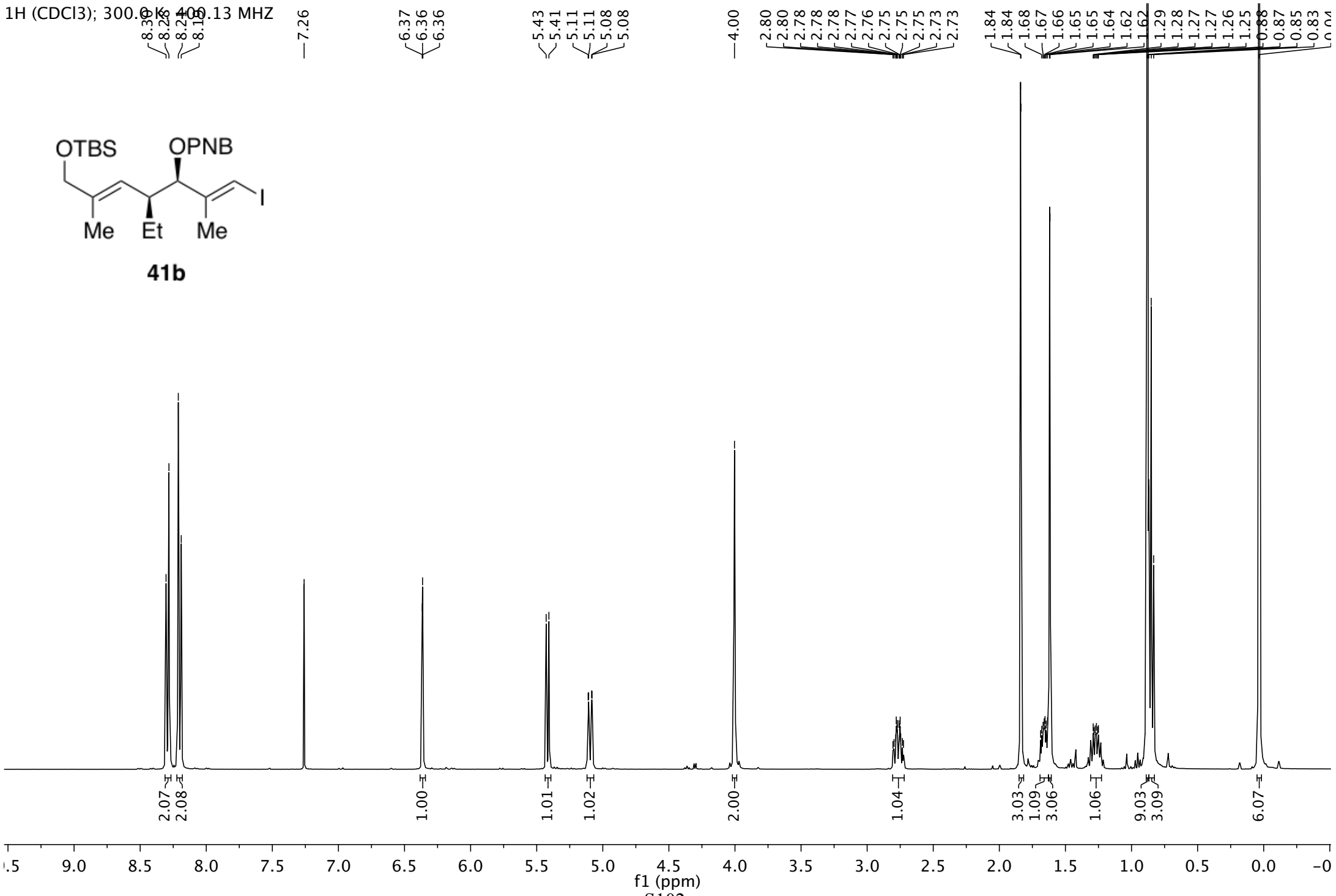


41a

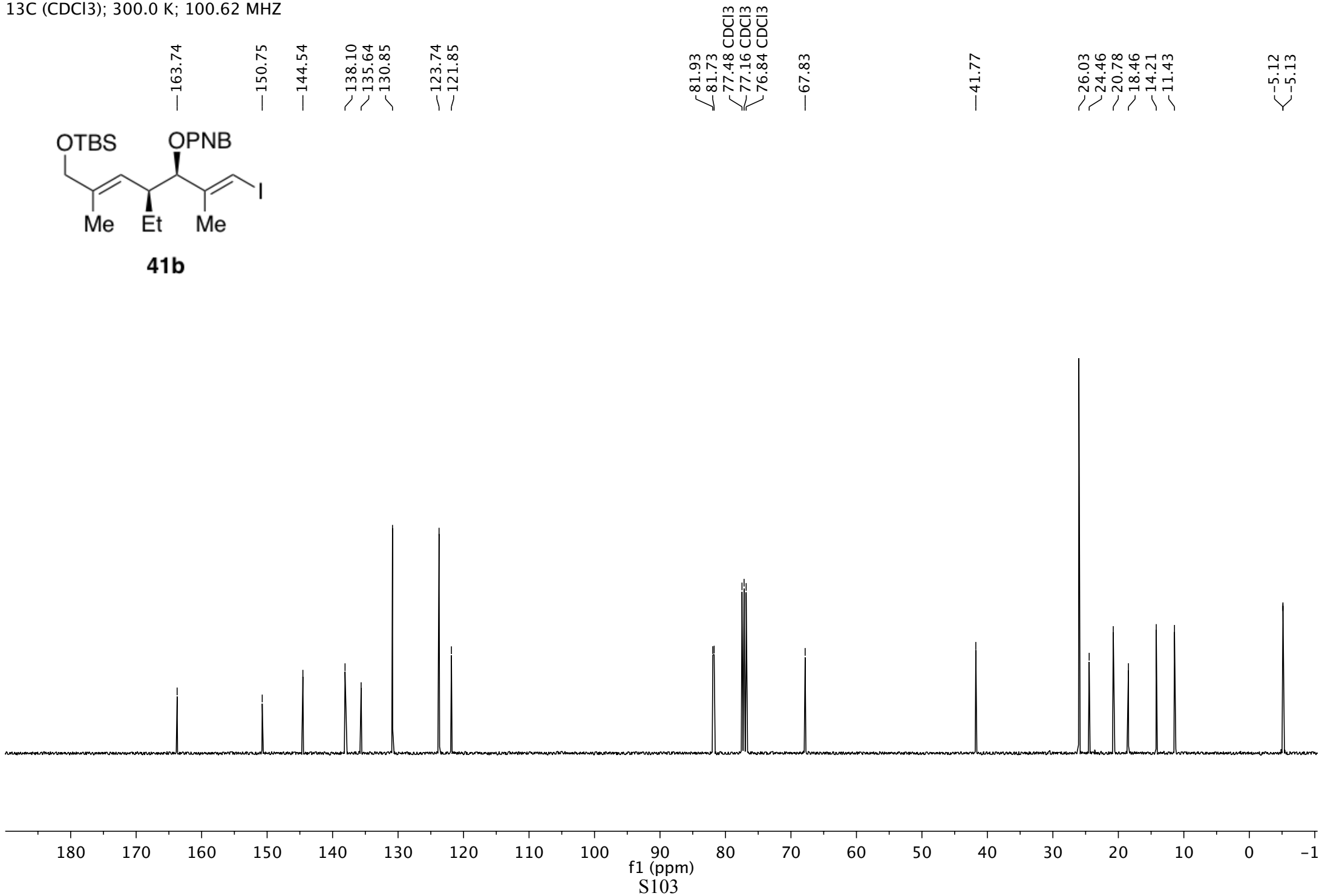
149.33
137.02
123.77
79.92
79.09
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.24
43.33
26.07
23.98
20.27
18.51
14.15
11.65
-5.07



f1 (ppm)

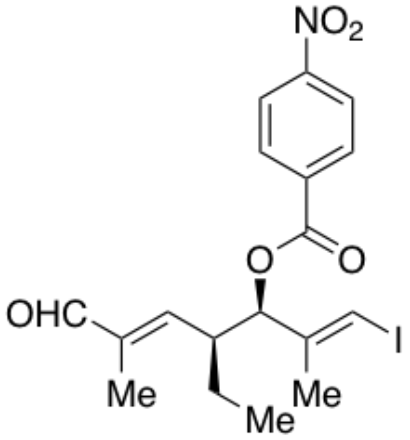

1H (CDCl3); 300.0 K; 400.13 MHZ
OTBS
OPNB
I
Me
Et
Me
41b
f1 (ppm)

13C (CDCl3); 300.0 K; 100.62 MHZ

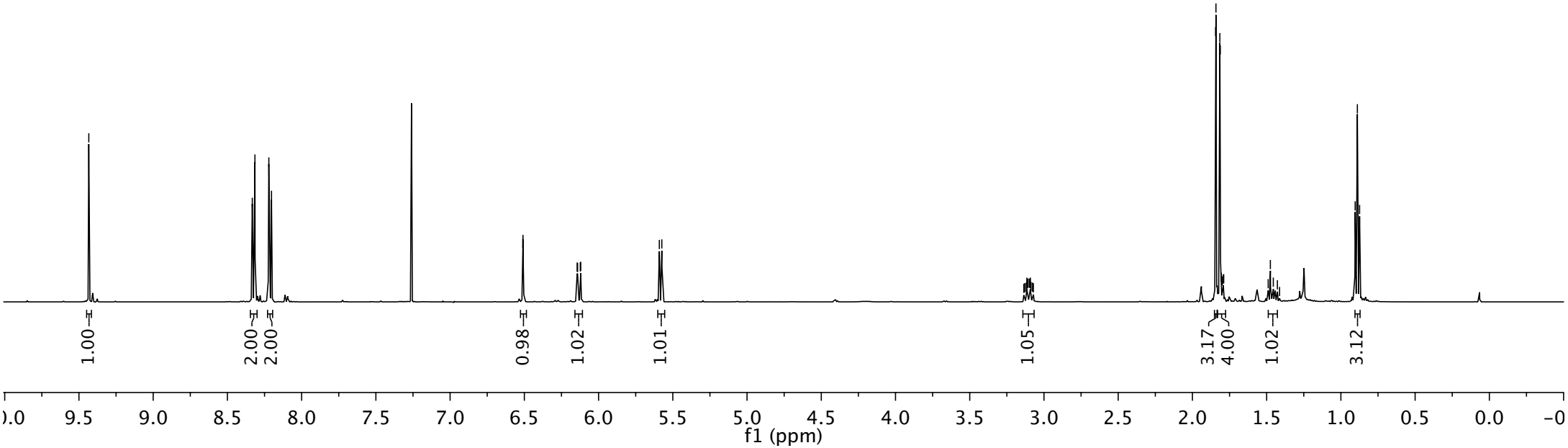


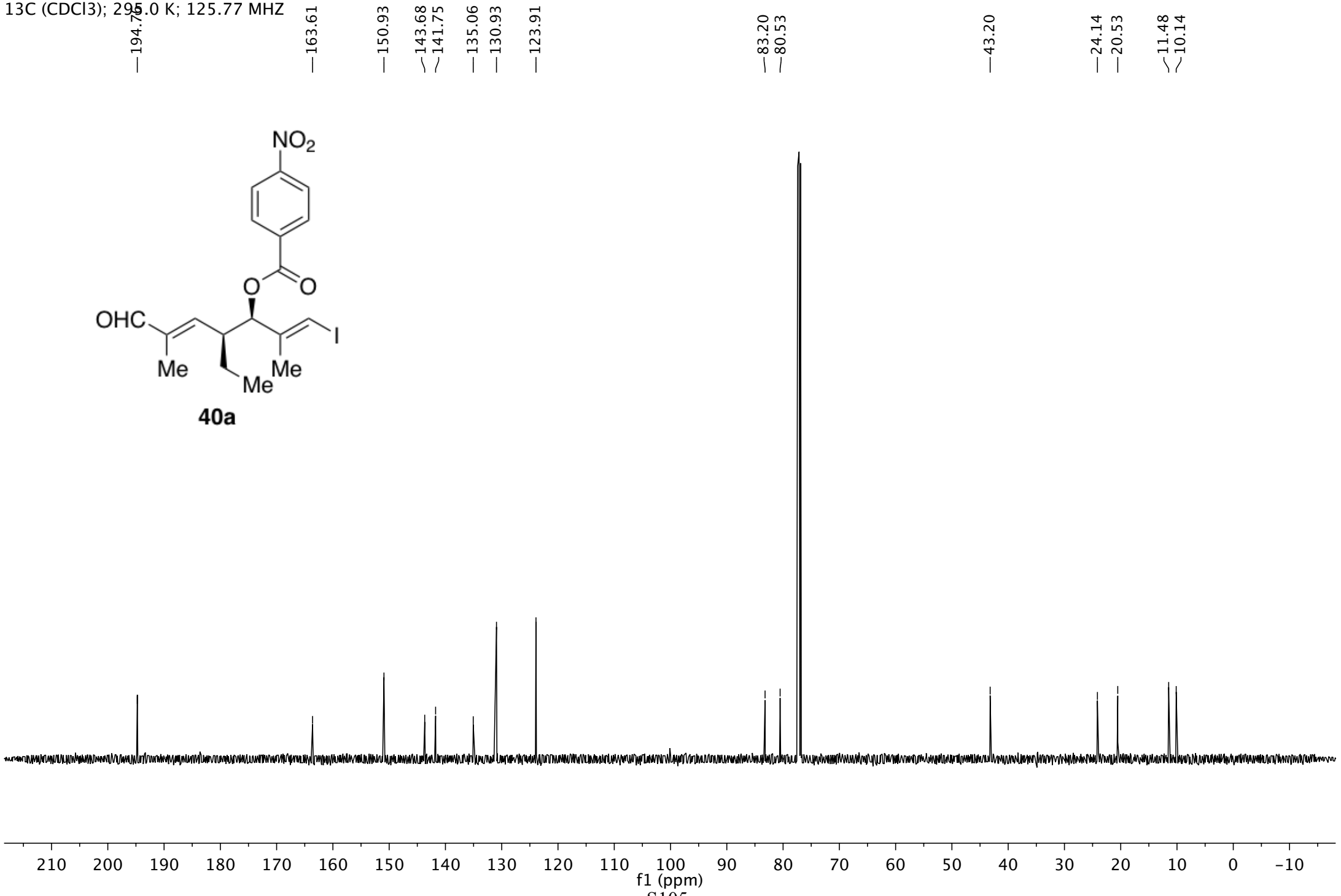
1H (CDCl3); 295.0 K; 500.13 MHZ

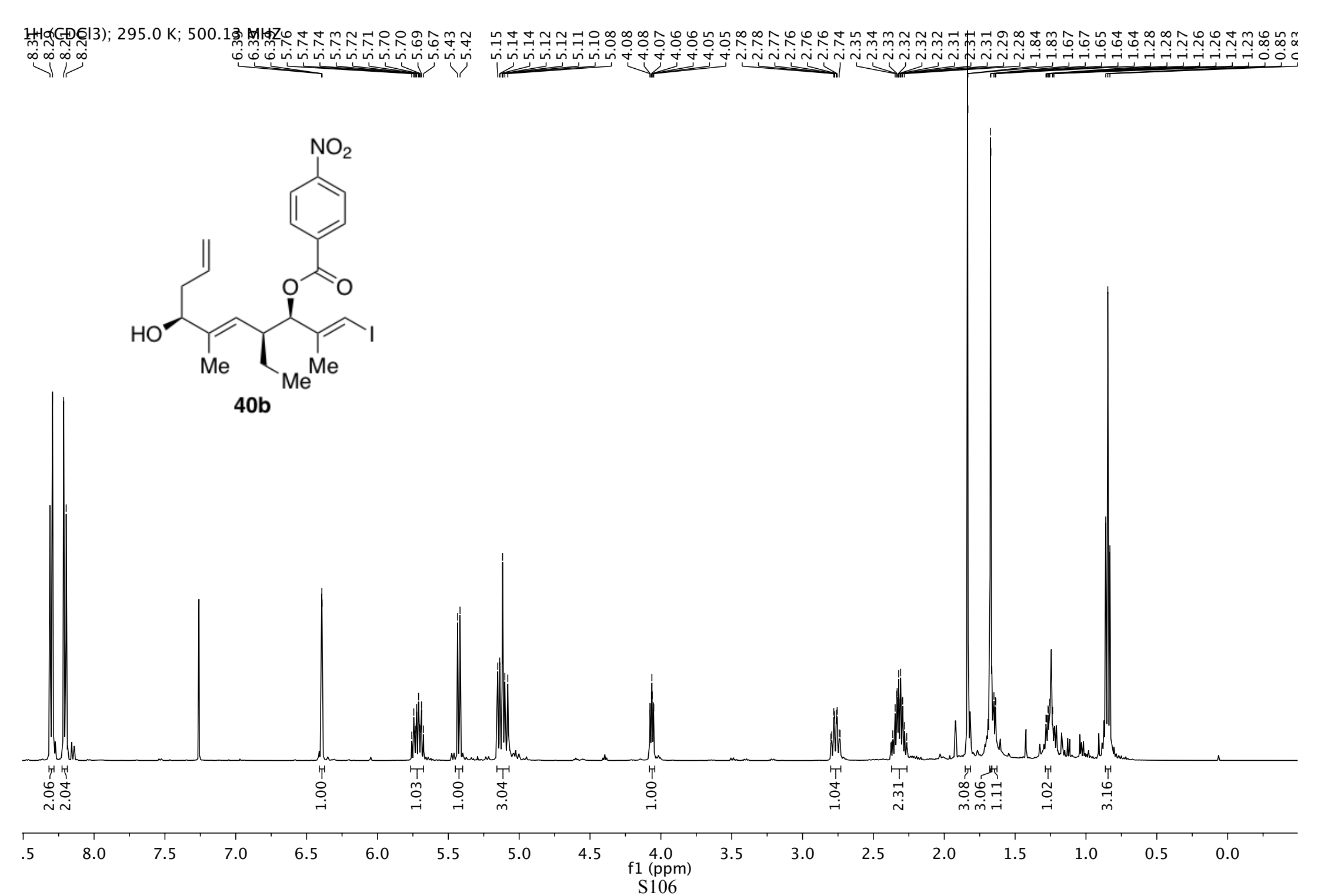
9.43
8.31
8.31
8.22
8.22
6.51
6.51
6.51
6.14
6.14
6.12
6.12
5.59
5.57
3.14
3.13
3.12
3.12
3.11
3.11
3.10
3.09
3.09
3.09
3.08
3.07
1.84
1.84
1.82
1.81
1.81
1.80
1.79
1.79
1.49
1.48
1.46
1.43
1.41
0.90
0.89
0.87



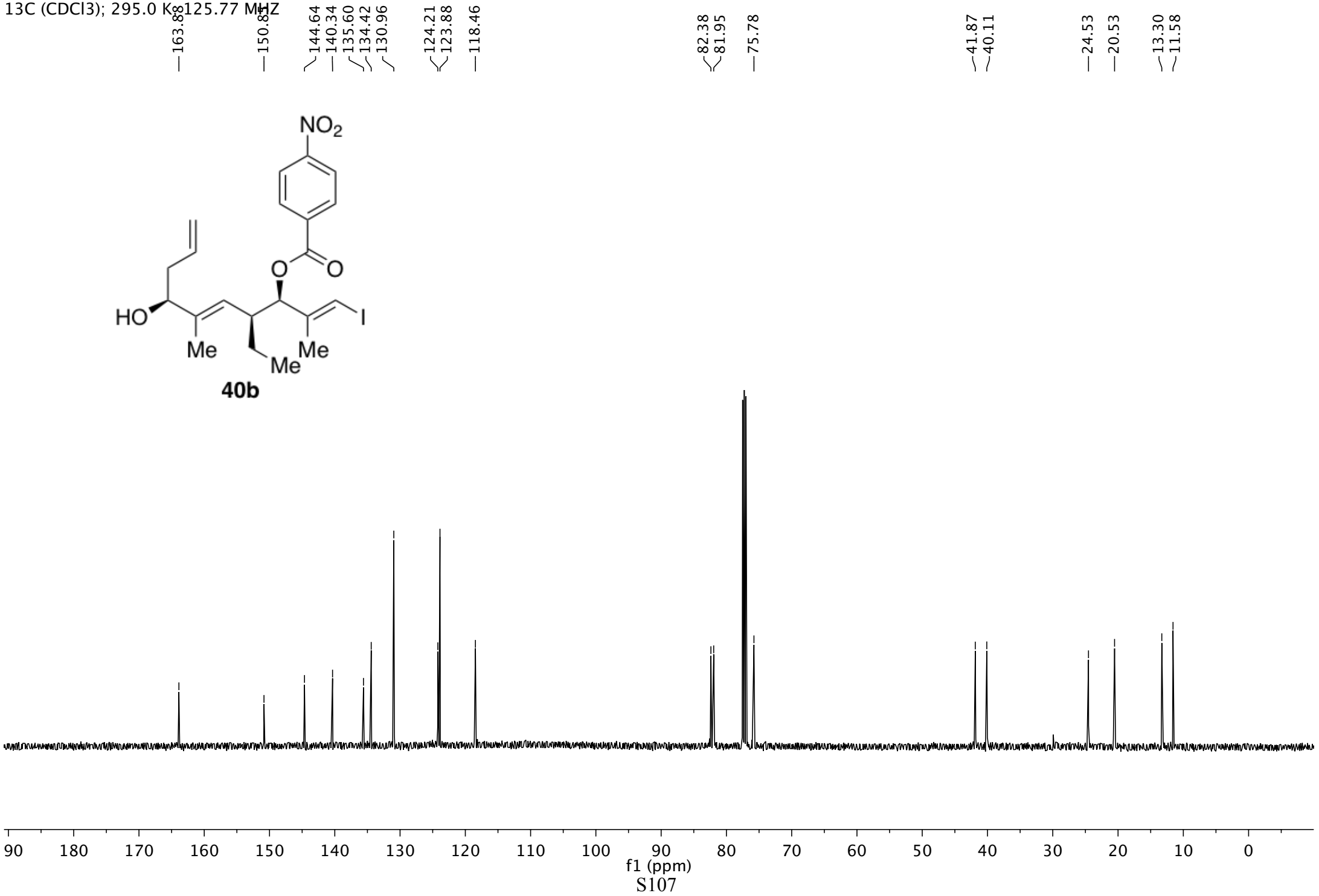
40a

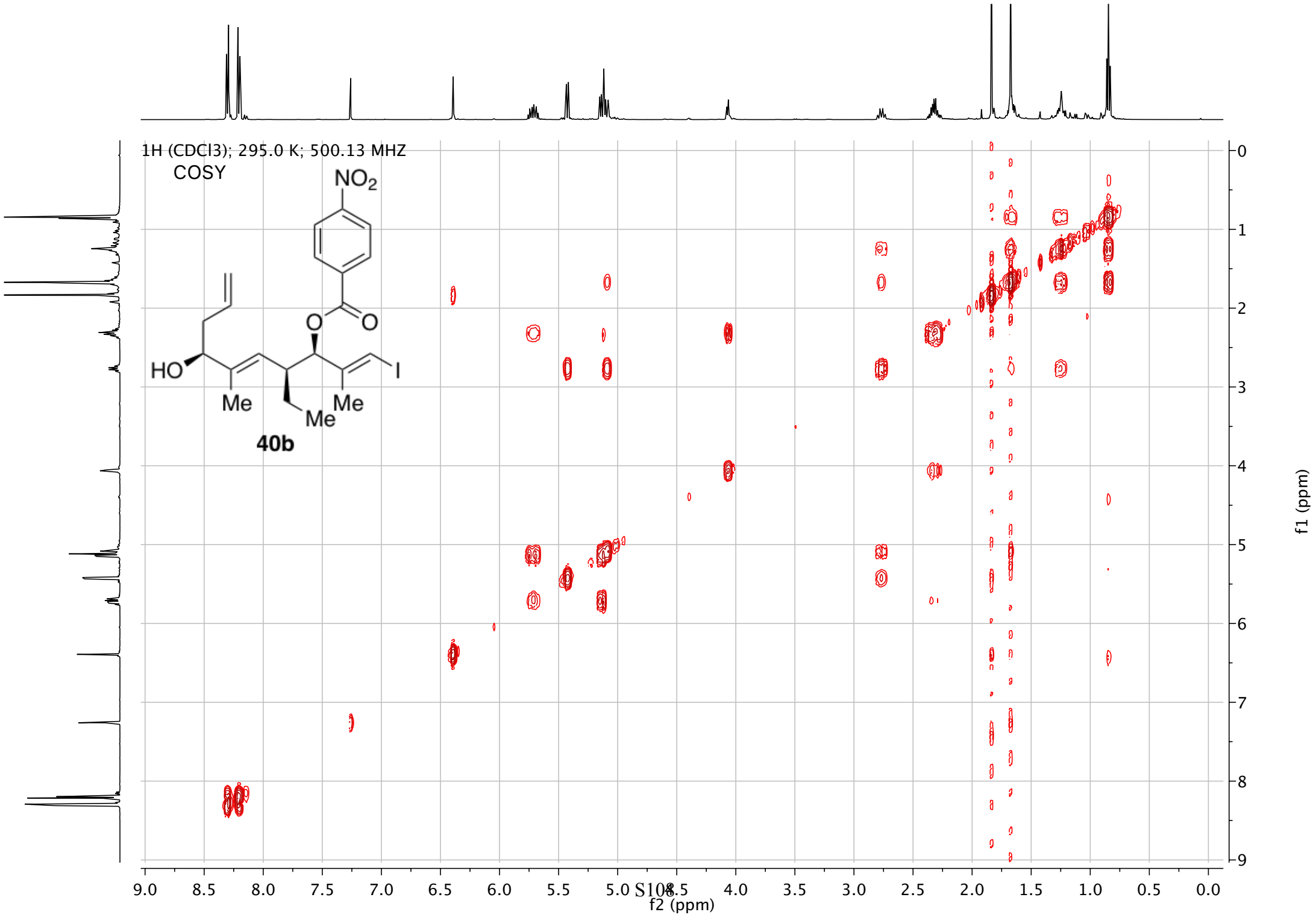


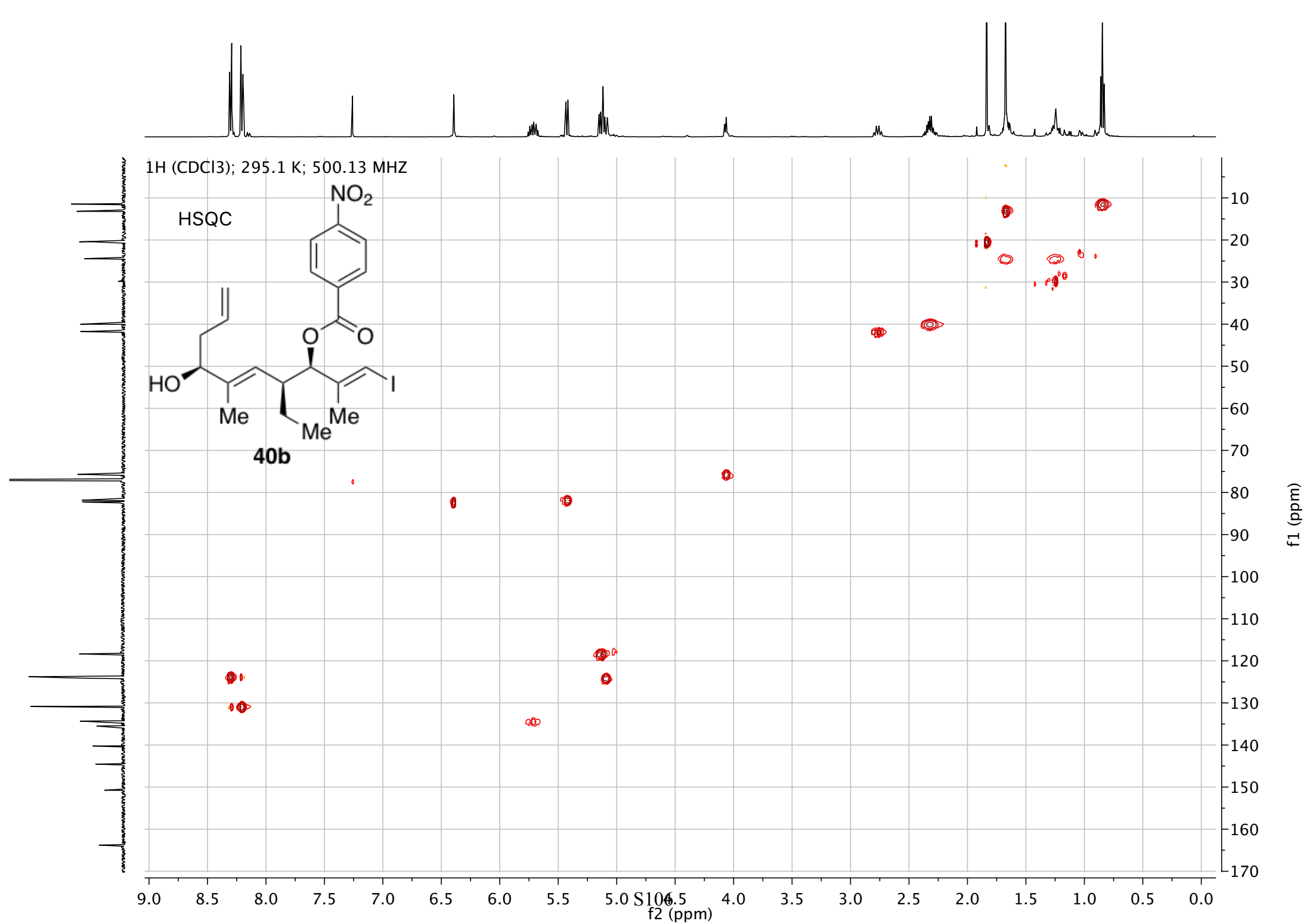

13C (CDCl3); 295.0 K; 125.77 MHZ
194.75
163.61
150.93
143.68
141.75
135.06
130.93
123.91
83.20
80.53
43.20
24.14
20.53
11.48
10.14
NO2
O
O
OHC
I
Me
Me
Me
40a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

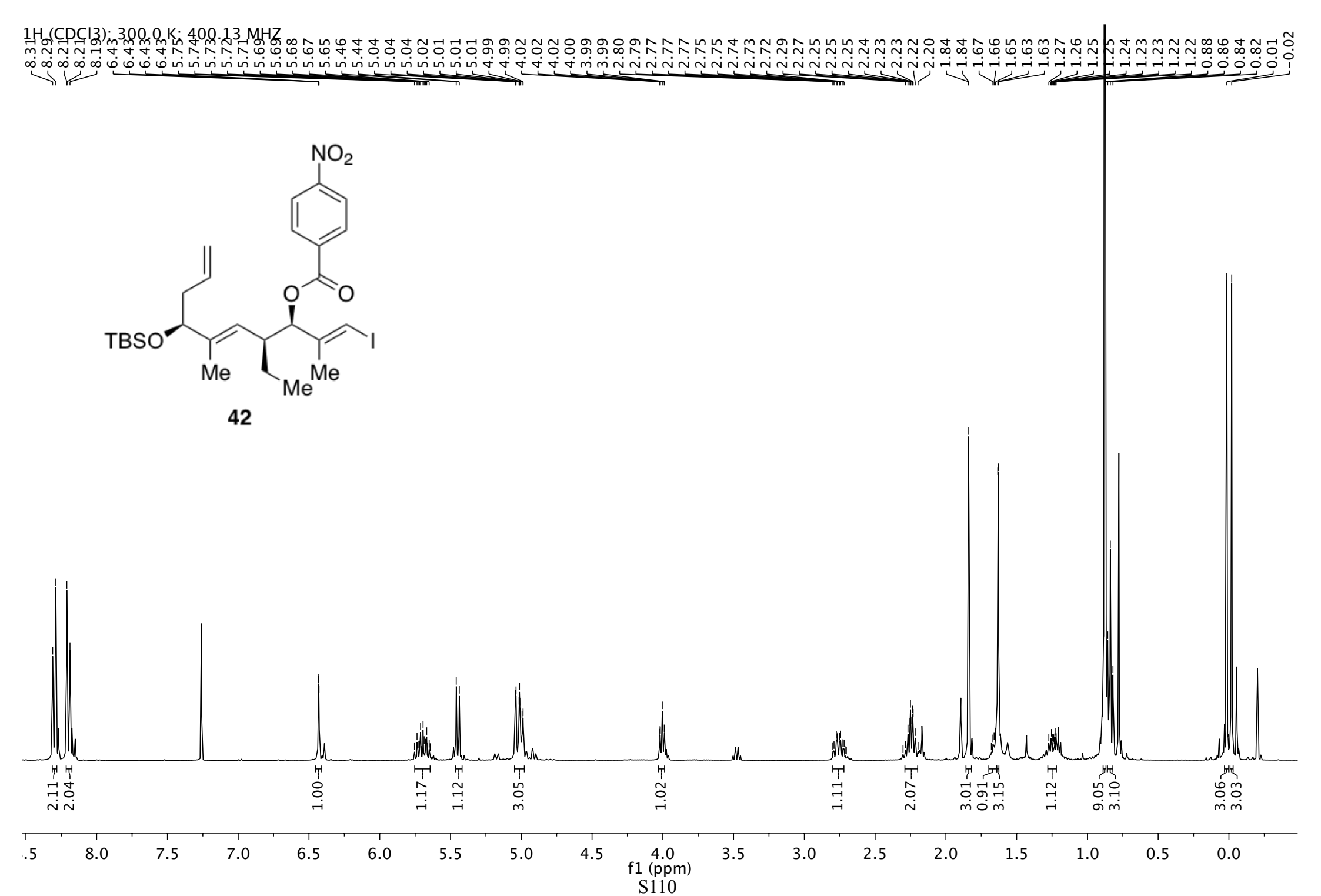

1H (CDCl3); 295.0 K; 500.13 MHz
NO2
O
O
HO
I
Me
Me
Me
40b
f1 (ppm)

13C (CDCl3); 295.0 K; 125.77 MHZ



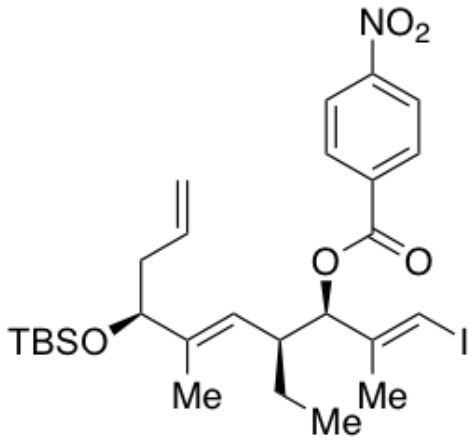

1H (CDCl3); 295.0 K; 500.13 MHZ
COSY
NO2
O
O
HO
I
Me
Me
Me
40b
f2 (ppm)
f1 (ppm)


1H (CDCl3); 295.1 K; 500.13 MHZ
HSQC
NO2
O
O
HO
I
Me
Me
Me
40b
f2 (ppm)
f1 (ppm)


1H (CDCl3); 300.0 K; 400.13 MHZ
NO2
O
O
TBSO
I
Me
Me
Me
42
f1 (ppm)

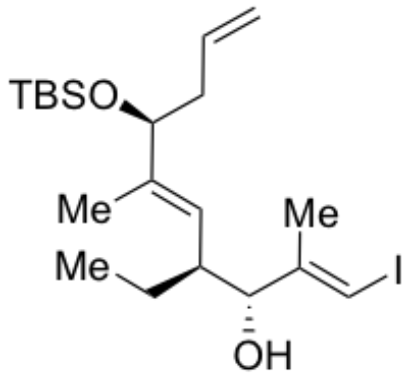
13C (CDCl3); 300.0 K; 100.62 MHZ

163.77
150.74
144.40
140.97
135.66
135.34
130.87
123.77
123.24
116.72
82.84
81.77
77.54
41.74
41.61
25.98
24.69
20.43
18.33
12.68
11.30
-4.26
-4.69



42

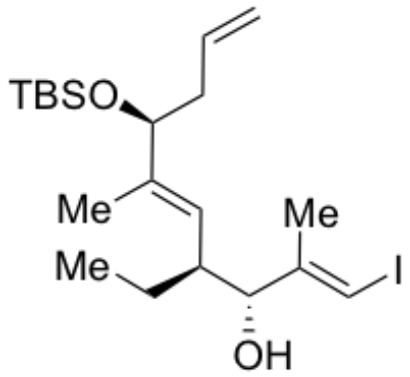
1H (CDCl3); 298.0 K; 500.13 MHZ



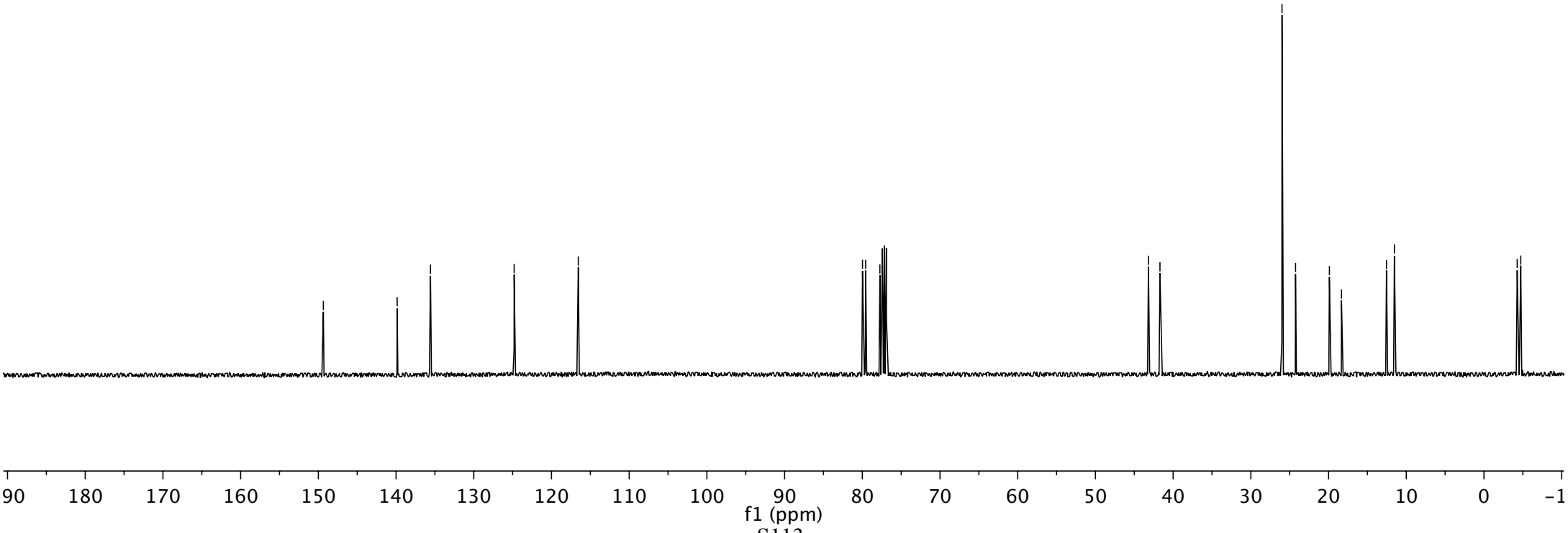
43

13C (CDCl3); 298.0 K; 125.77 MHz

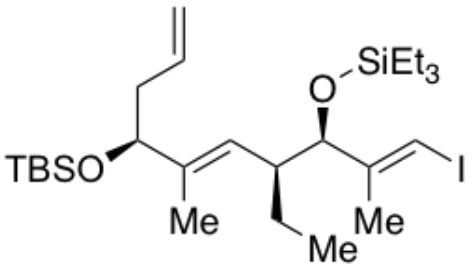
149.36
139.86
135.57
124.80
116.55
79.98
79.57
77.74
43.18
41.70
25.99
24.25
19.89
18.34
12.55
11.53
-4.28
-4.73



43

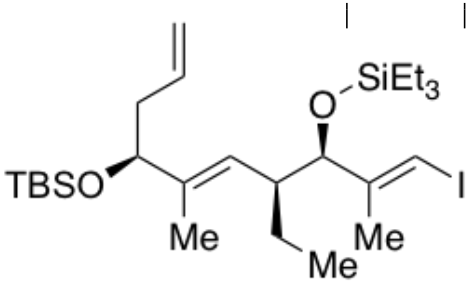


1H (CDCl3); 295.0 K; 500.13 MHZ



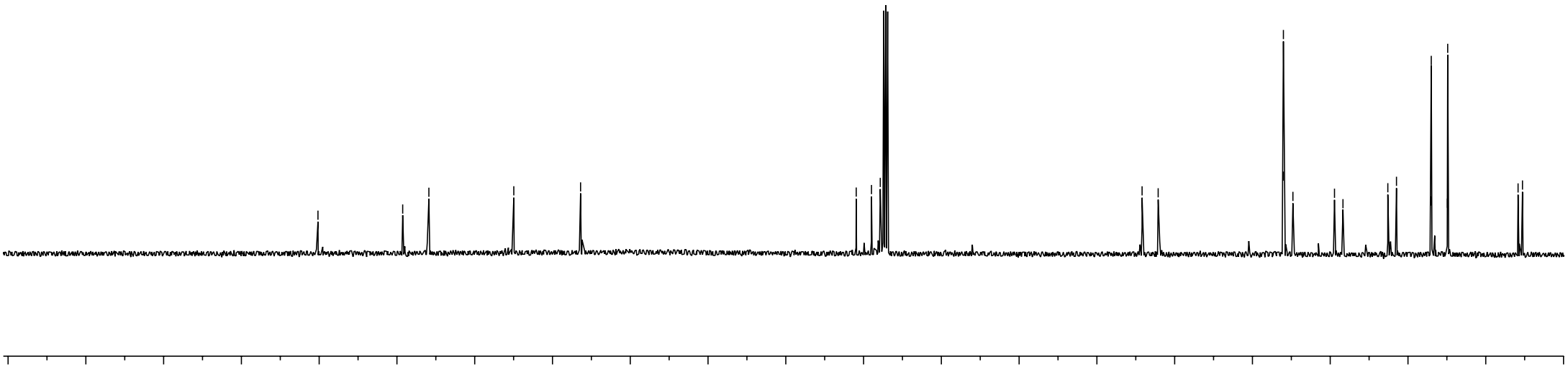
44

13C (CDCl3); 295.0 K; 125.77 MHZ



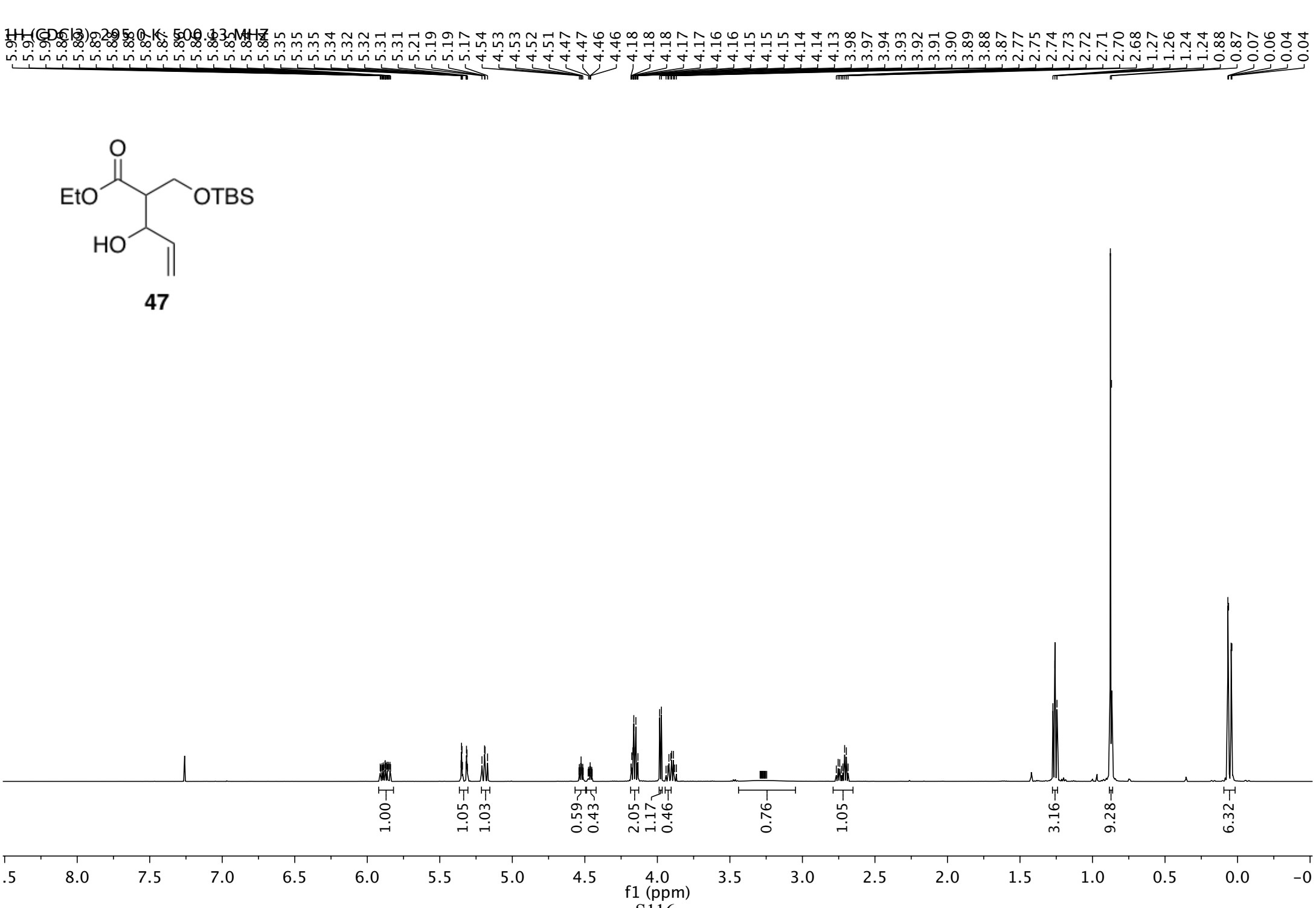
44

150.12
139.26
135.89
124.97
116.39
80.95
78.98
77.85
44.19
42.12
26.03
26.02
24.80
19.45
18.36
12.59
11.48
7.04
7.01
4.93
4.89
-4.16
-4.72



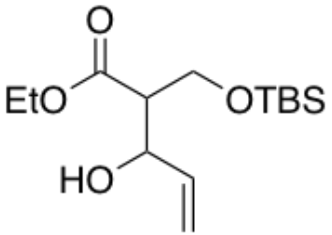
90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

f1 (ppm)

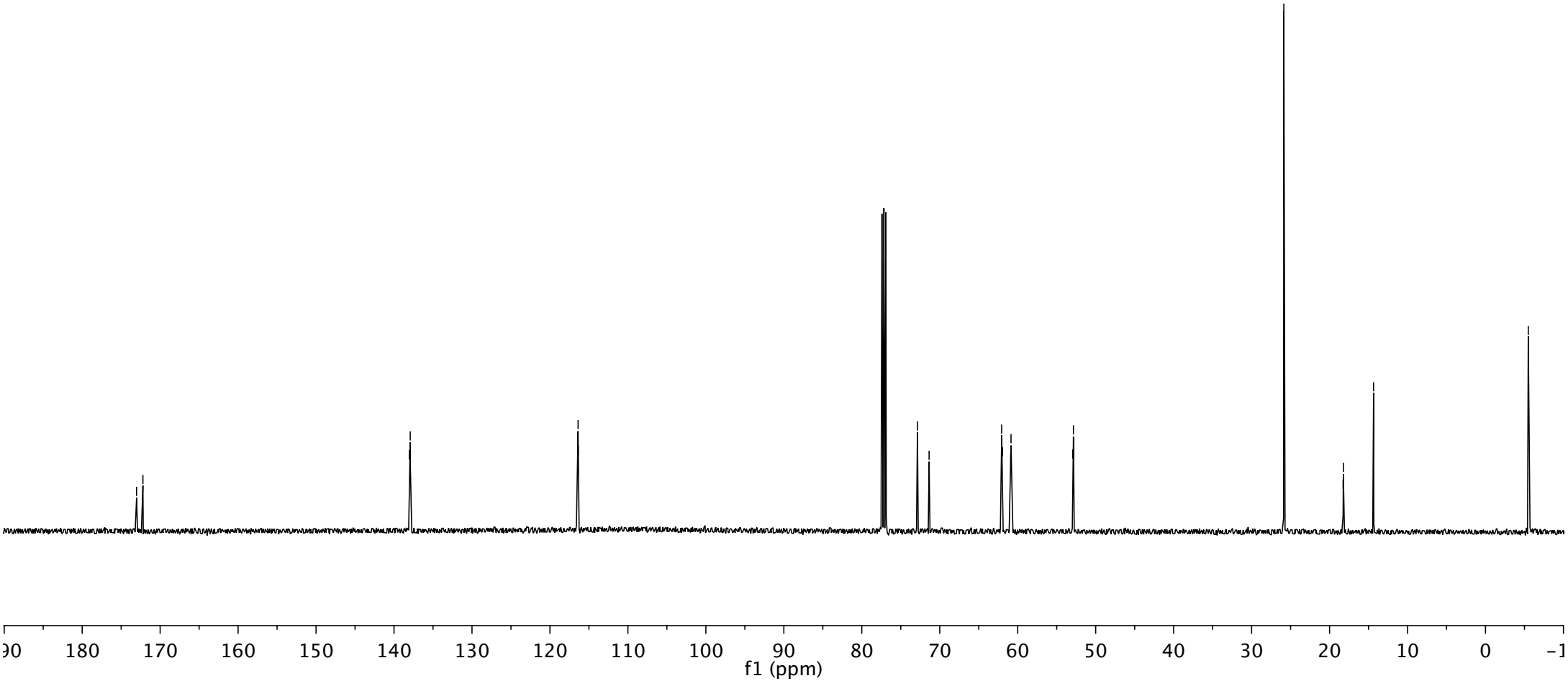

1H (CDCl3, 295.0 K, 500.13 MHz)
5.90 5.90 5.90 5.88 5.88 5.88 5.88 5.88 5.88 5.88 5.88 5.88 5.88 5.88 5.88 5.88 5.35 5.35 5.35 5.34 5.32 5.32 5.31 5.31 5.21 5.19 5.19 5.17 4.54 4.53 4.53 4.52 4.51 4.47 4.47 4.46 4.46 4.18 4.18 4.18 4.17 4.17 4.16 4.16 4.15 4.15 4.15 4.14 4.14 4.13 3.98 3.97 3.94 3.93 3.92 3.91 3.90 3.89 3.88 3.87 2.77 2.75 2.74 2.73 2.72 2.71 2.70 2.68 1.27 1.26 1.24 1.24 0.88 0.87 0.07 0.06 0.04 0.04
O
EtO
OTBS
HO
47
1.00
1.05
1.03
0.59
0.43
2.05
1.17
0.46
0.76
1.05
3.16
9.28
6.32
.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0
f1 (ppm)

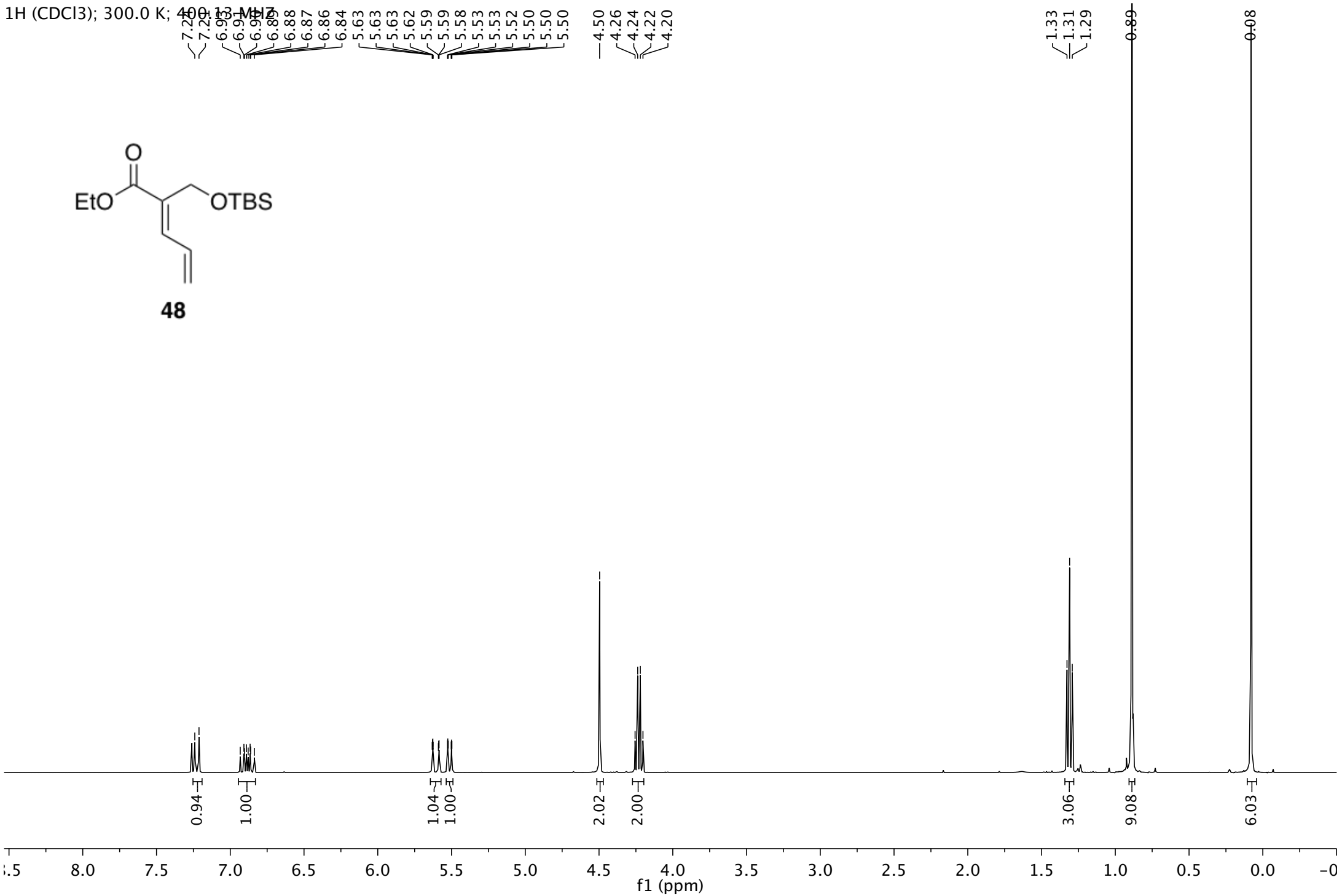
13C (CDCl3); 295.0 K; 125.77 MHZ

173.07
172.29
138.04
137.92
116.39
116.36
72.86
71.37
62.06
61.96
60.90
60.86
52.94
52.85
25.87
18.26
18.23
14.35
-5.49
-5.50



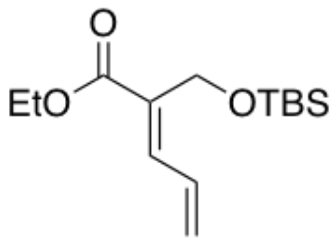
47



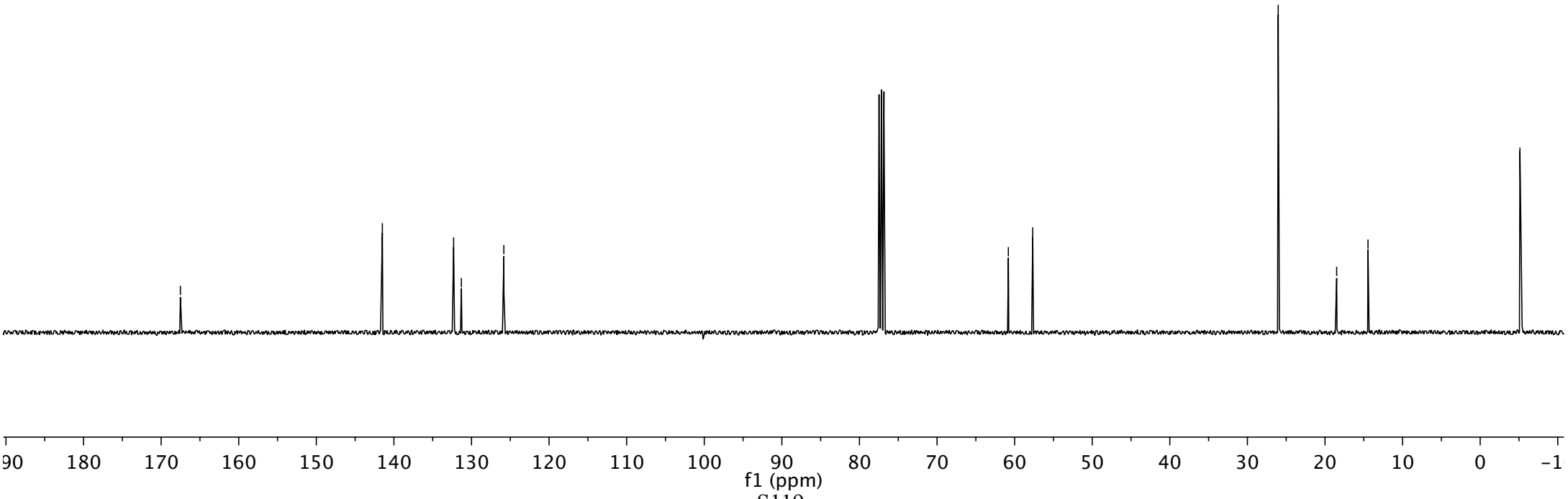

1H (CDCl3); 300.0 K; 400.13 MHz
7.26
7.25
6.93
6.91
6.90
6.89
6.88
6.87
6.86
6.84
5.63
5.63
5.63
5.62
5.59
5.59
5.58
5.53
5.53
5.52
5.50
5.50
5.50
4.50
4.26
4.24
4.22
4.20
1.33
1.31
1.29
0.89
0.08
O
EtO
OTBS
48
0.94
1.00
1.04
1.00
2.02
2.00
3.06
9.08
6.03
f1 (ppm)

13C (CDCl3); 300.0 K; 100.62 MHZ

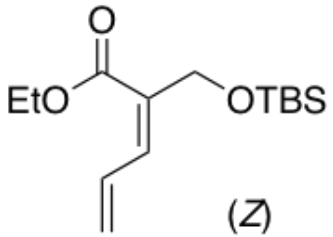
167.52
141.49
132.31
131.31
125.83
60.81
57.67
26.03
18.50
14.46
-5.13



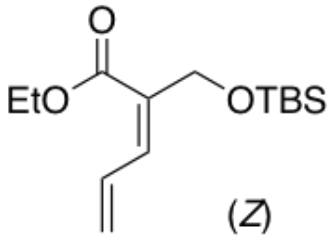
48



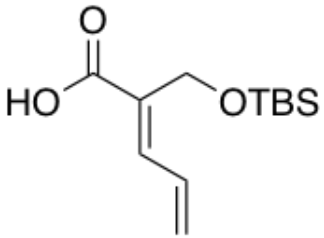
1H (CDCl3); 300.0 K; 400.13 MHz



13C (CDCl3); 300.0 K; 100.62 MHZ



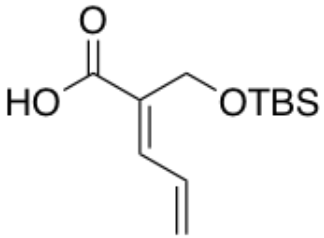
1H (CDCl3); 300.0 K; 400.13 MHZ



49

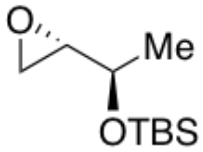
13C (CDCl3); 300.0 K; 100.62 MHZ

^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.94, 143.36, 131.78, 129.65, 127.35, 57.78, 25.98, 18.45, -5.17.



49

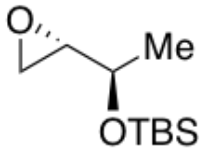
1H (CDCl3); 300.0 K; 400.13 MHZ



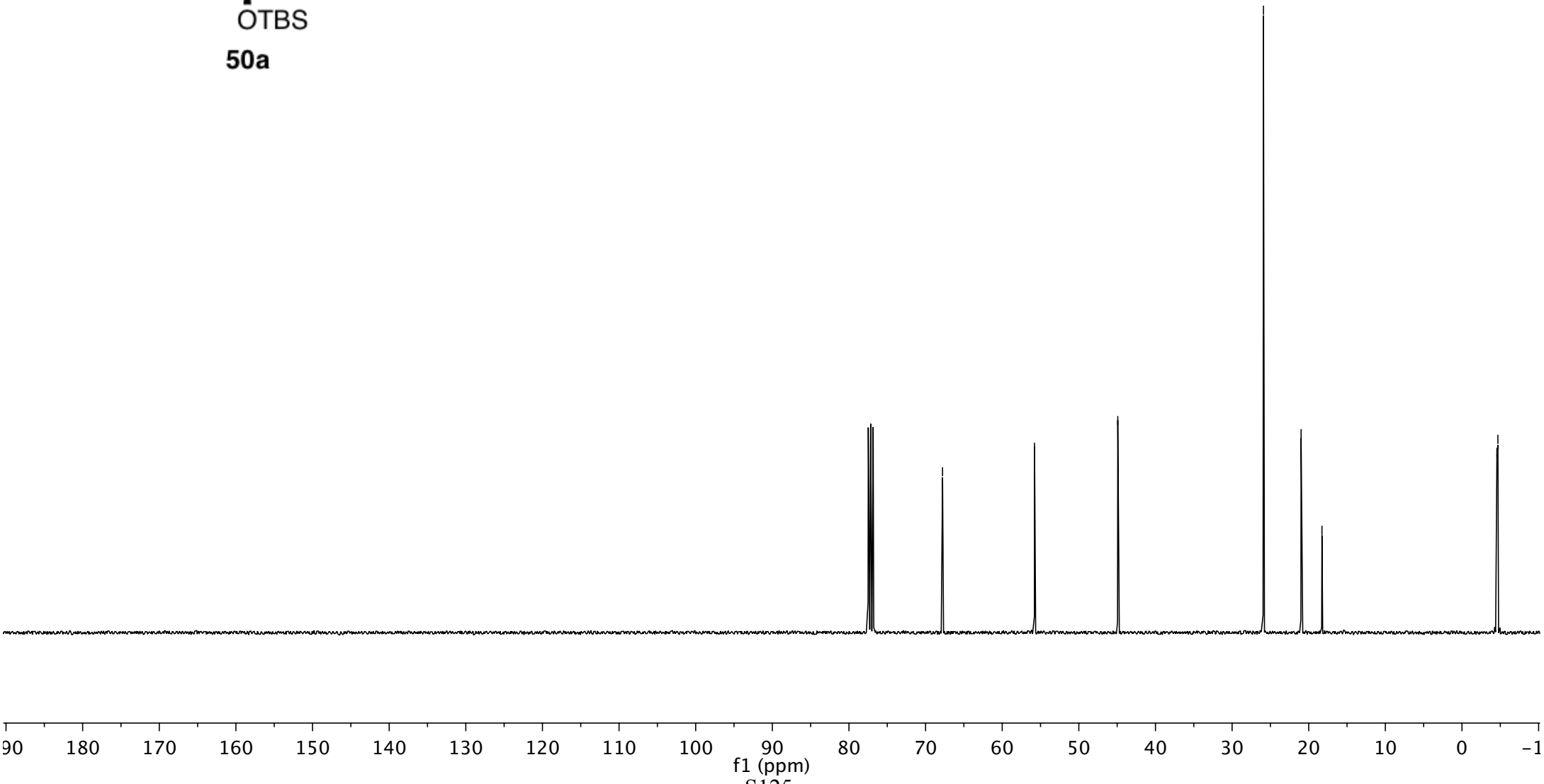
50a

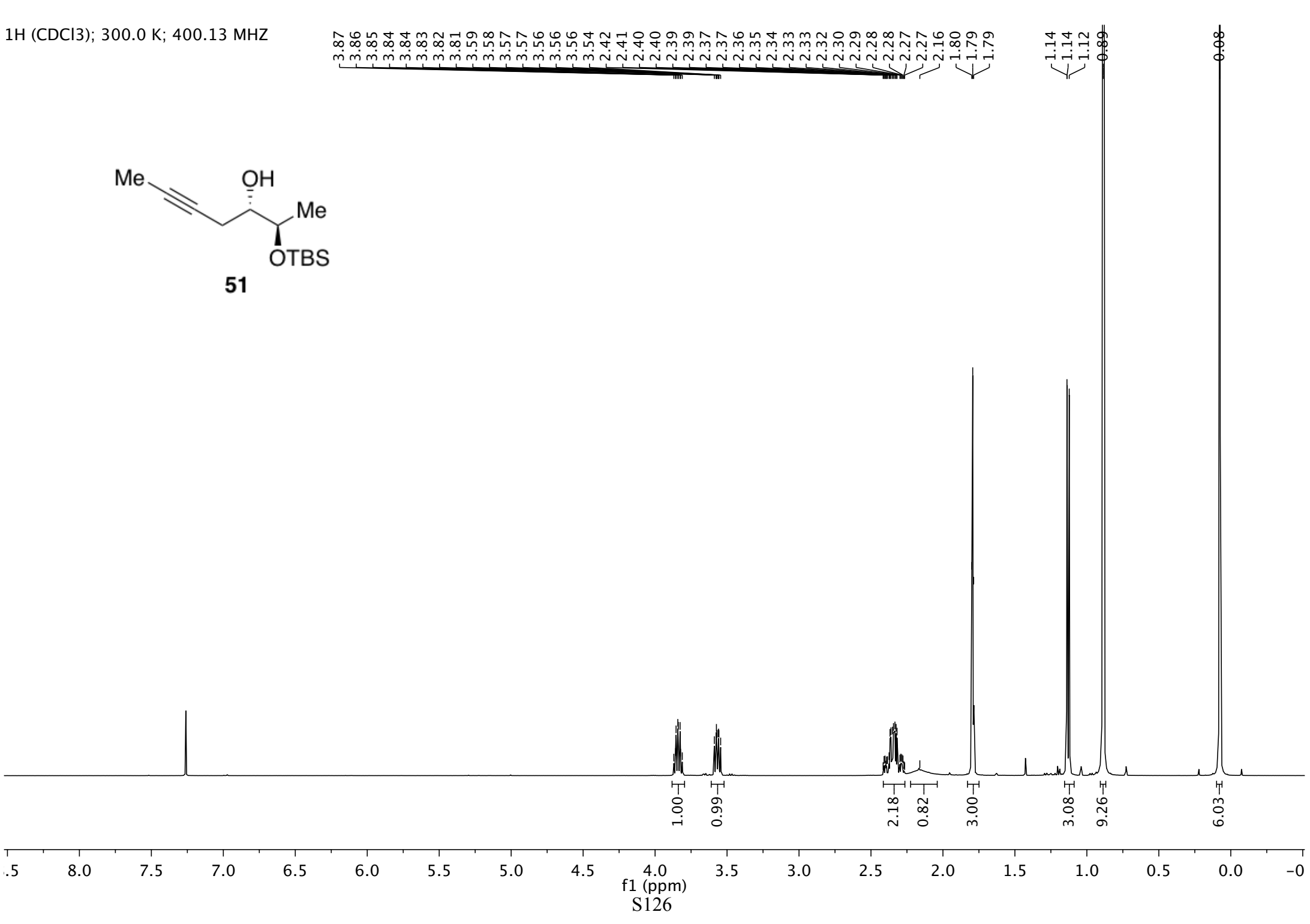
13C (CDCl3); 296.9 K; 100.62 MHZ

67.79
55.78
44.92
25.91
20.99
18.27
4.56
-4.69



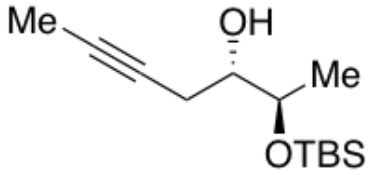
50a



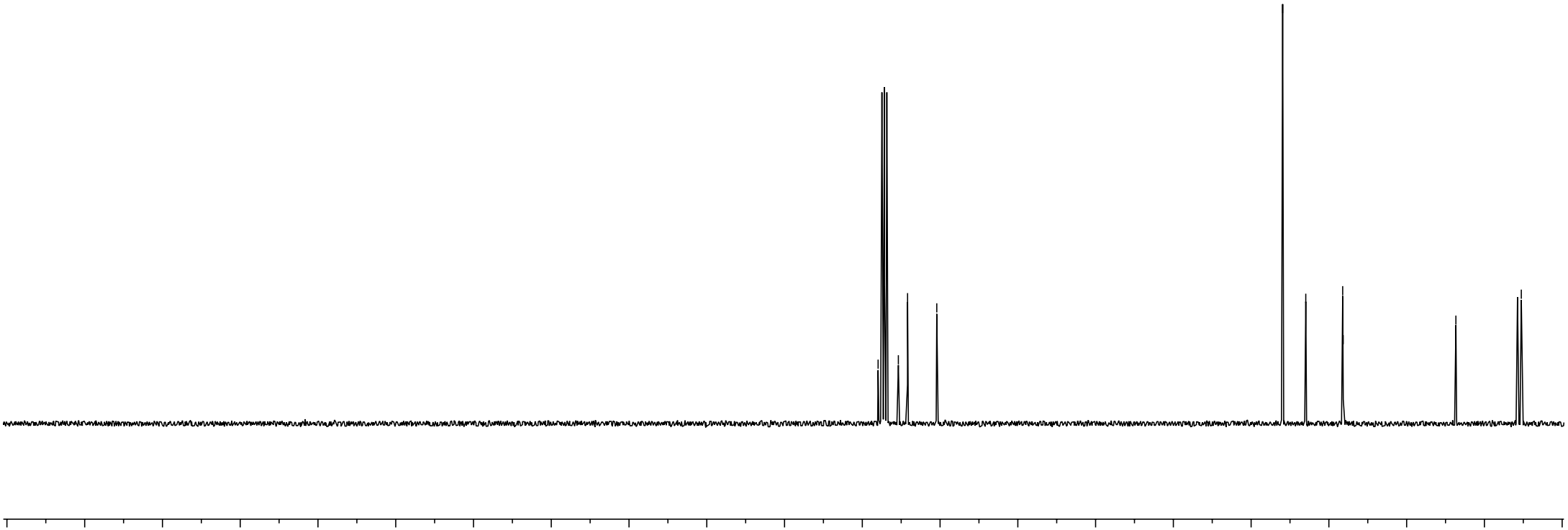

1H (CDCl3); 300.0 K; 400.13 MHZ
3.87 3.86 3.85 3.84 3.84 3.83 3.82 3.81 3.59 3.58 3.57 3.57 3.56 3.56 3.56 3.54 2.42 2.41 2.40 2.40 2.39 2.39 2.37 2.37 2.36 2.35 2.34 2.33 2.33 2.32 2.30 2.29 2.28 2.28 2.27 2.27 2.16 1.80 1.79 1.79 1.14 1.14 1.12 0.89 0.08
Me
OH
Me
OTBS
51
1.00 0.99 2.18 0.82 3.00 3.08 9.26 6.03
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

13C (CDCl3); 300.0 K; 100.62 MHZ

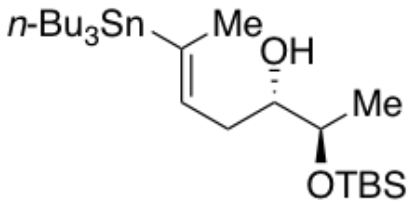
77.97
75.36
74.18
70.42
25.94
22.97
18.22
18.16
3.67
-4.26
-4.75



51

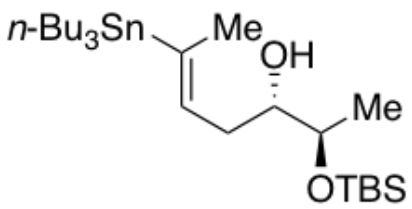


1H (CDCl3); 296.5 K; 400.13 MHZ



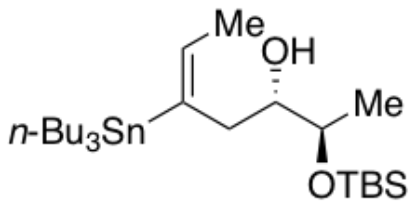
52

13C (CDCl3); 297.1 K; 100.62 MHZ



52

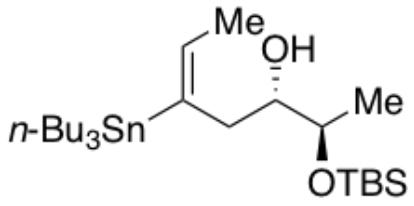
1H (CDCl3); 300.0 K; 400.13 MHz



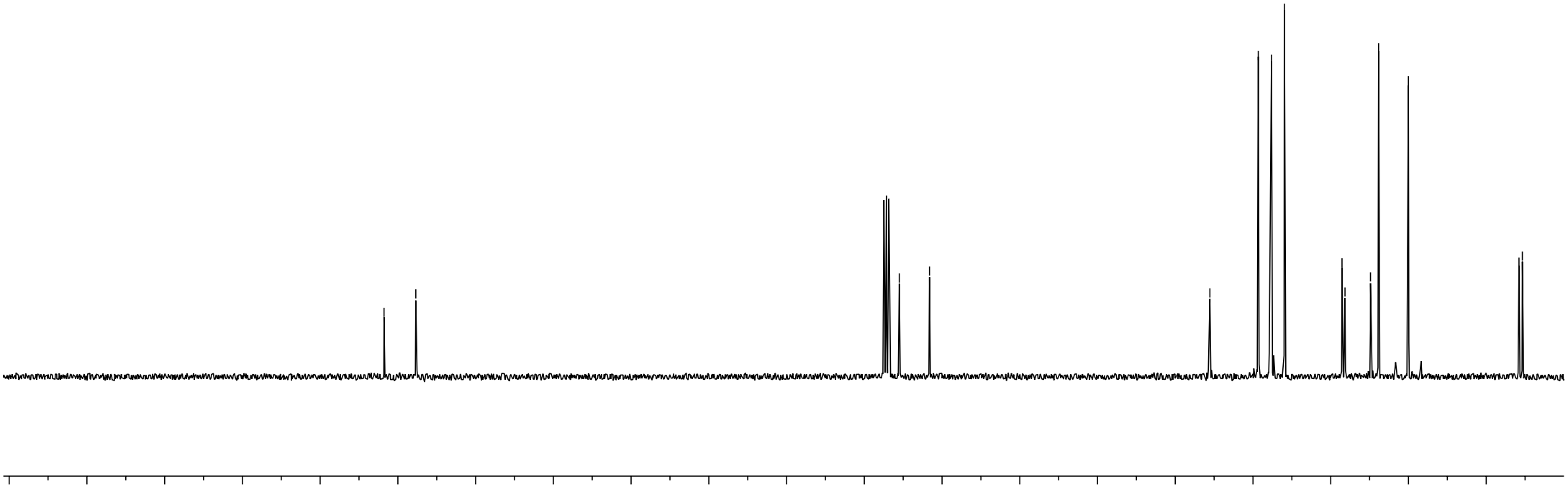
53

13C (CDCl3); 300.0 K; 100.62 MHZ

141.78
137.69
75.50
71.61
35.55
29.32
27.62
25.97
18.55
18.16
14.89
13.84
10.01
4.22
-4.65

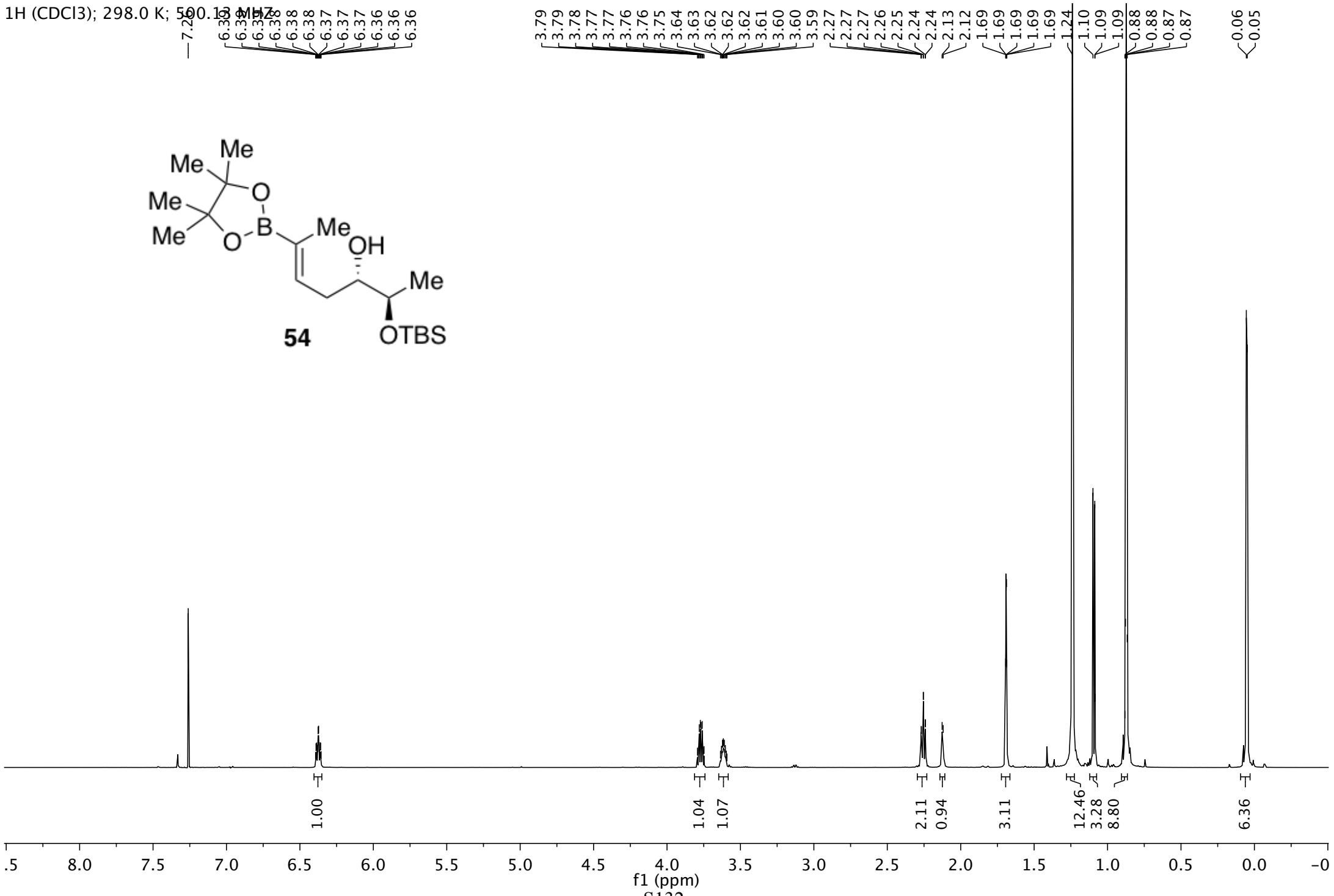


53



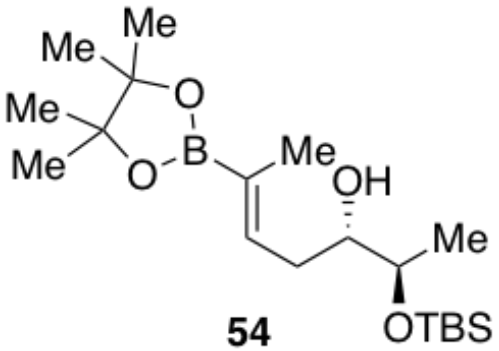
90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

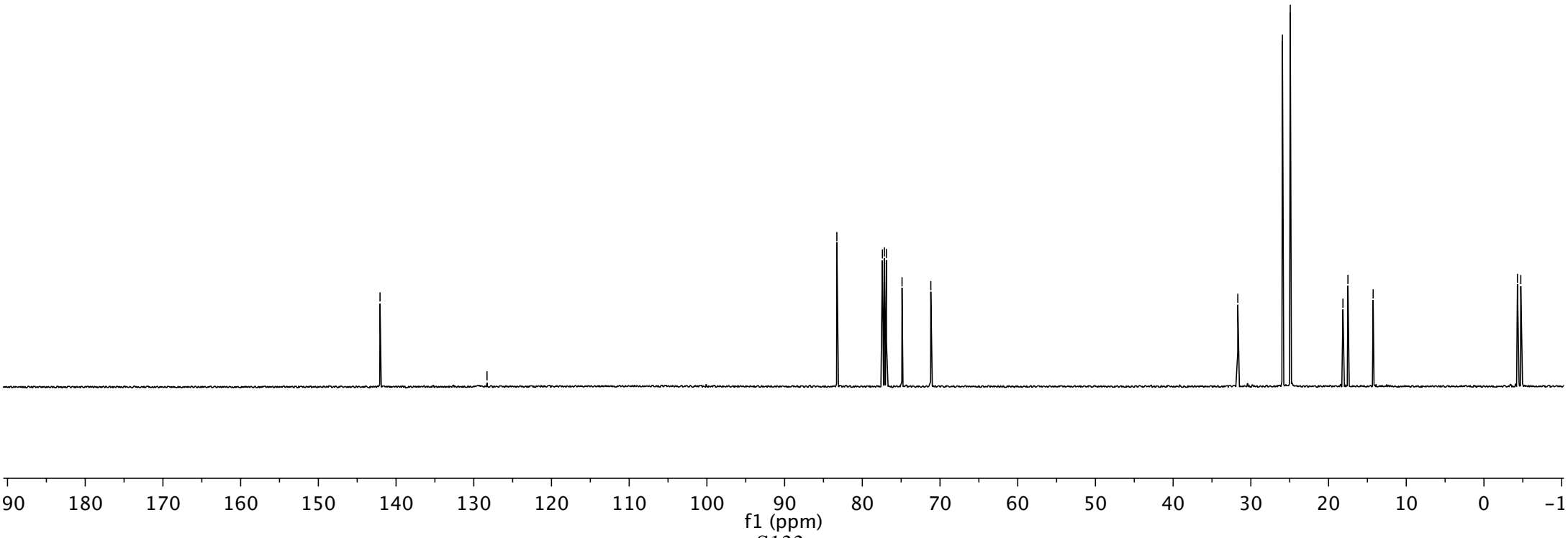

1H (CDCl3); 298.0 K; 500.13 MHz
Me
Me
Me
Me
O
B
O
Me
OH
Me
OTBS
54
f1 (ppm)

13C (CDCl3); 298.0 K; 125.77 MHZ

142.06
128.30
83.27
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
74.89
71.18
31.68
25.94
24.93
18.15
17.51
14.26
-4.31
-4.74

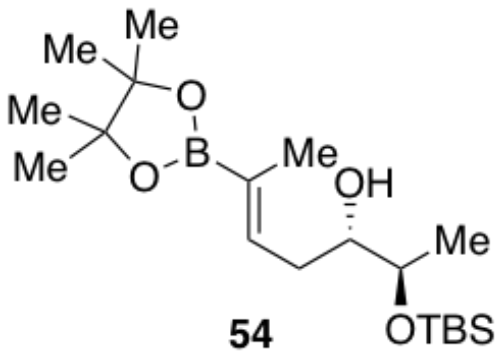


54

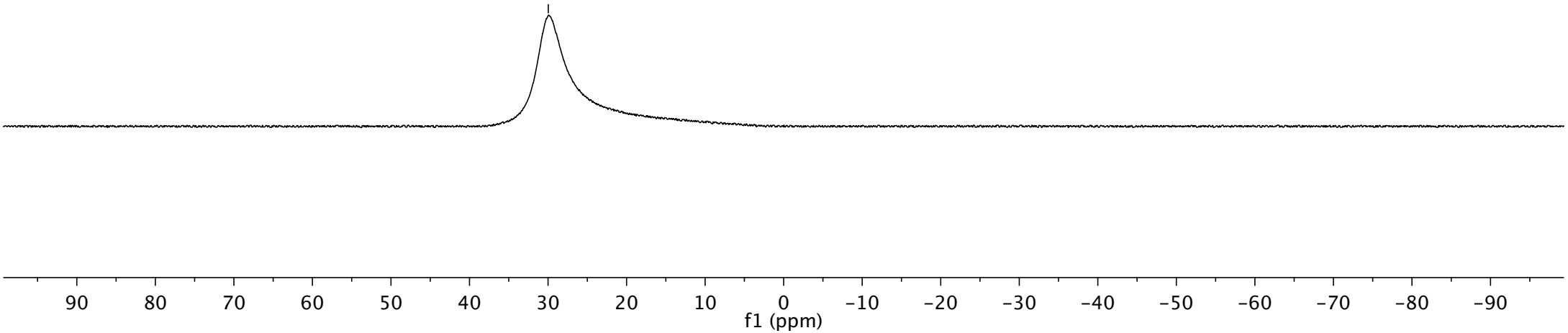


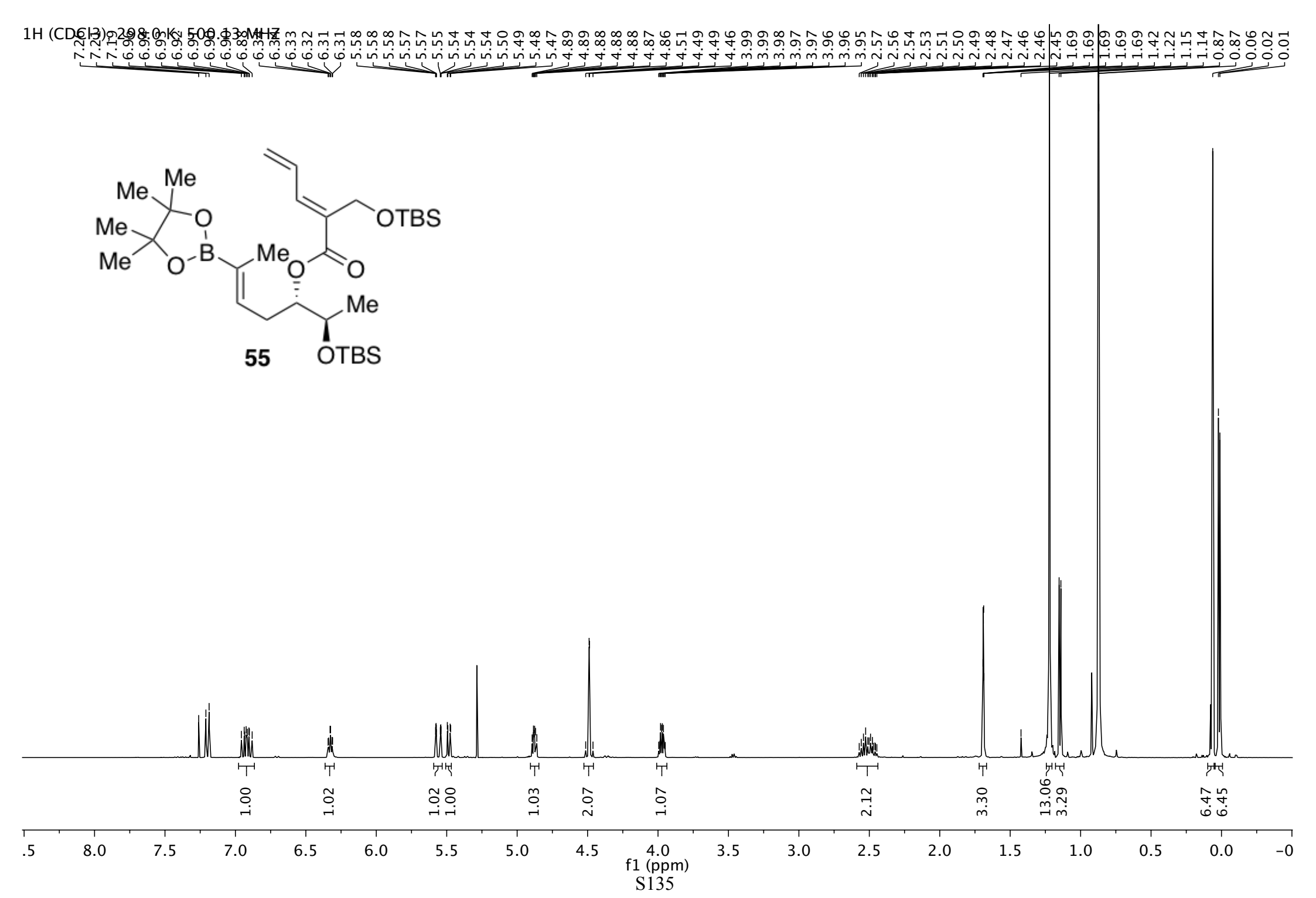
11B (CDCl3); 300.0 K; 128.38 MHZ

29.97

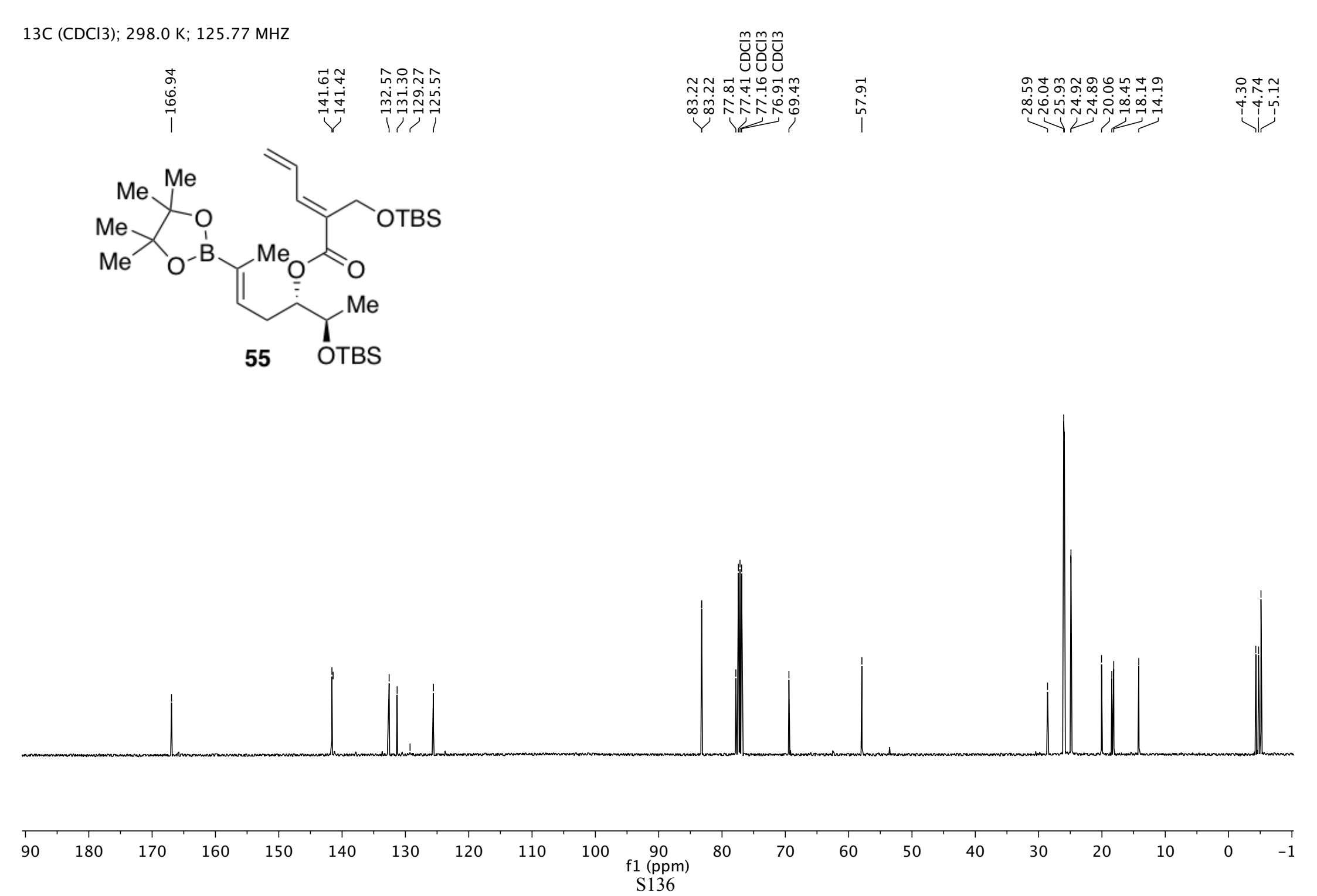


54



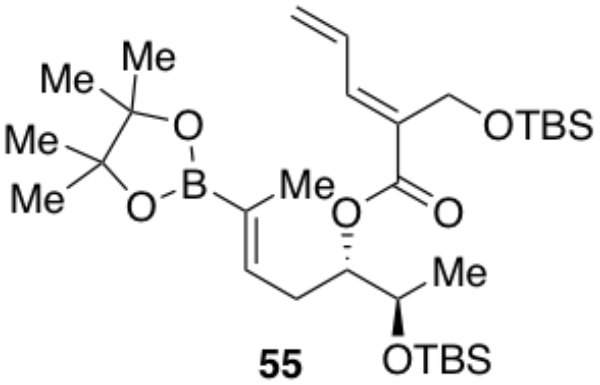

1H (CDCl3, 298.0 K, 500.13 MHz)
Me
Me
Me
Me
O
B
O
Me
O
O
OTBS
Me
OTBS
55
f1 (ppm)

13C (CDCl3); 298.0 K; 125.77 MHZ

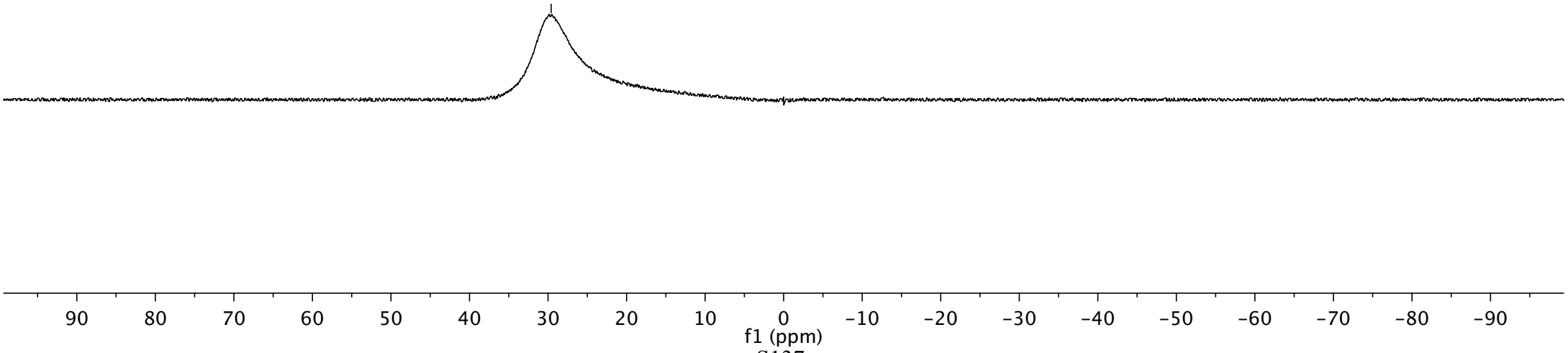


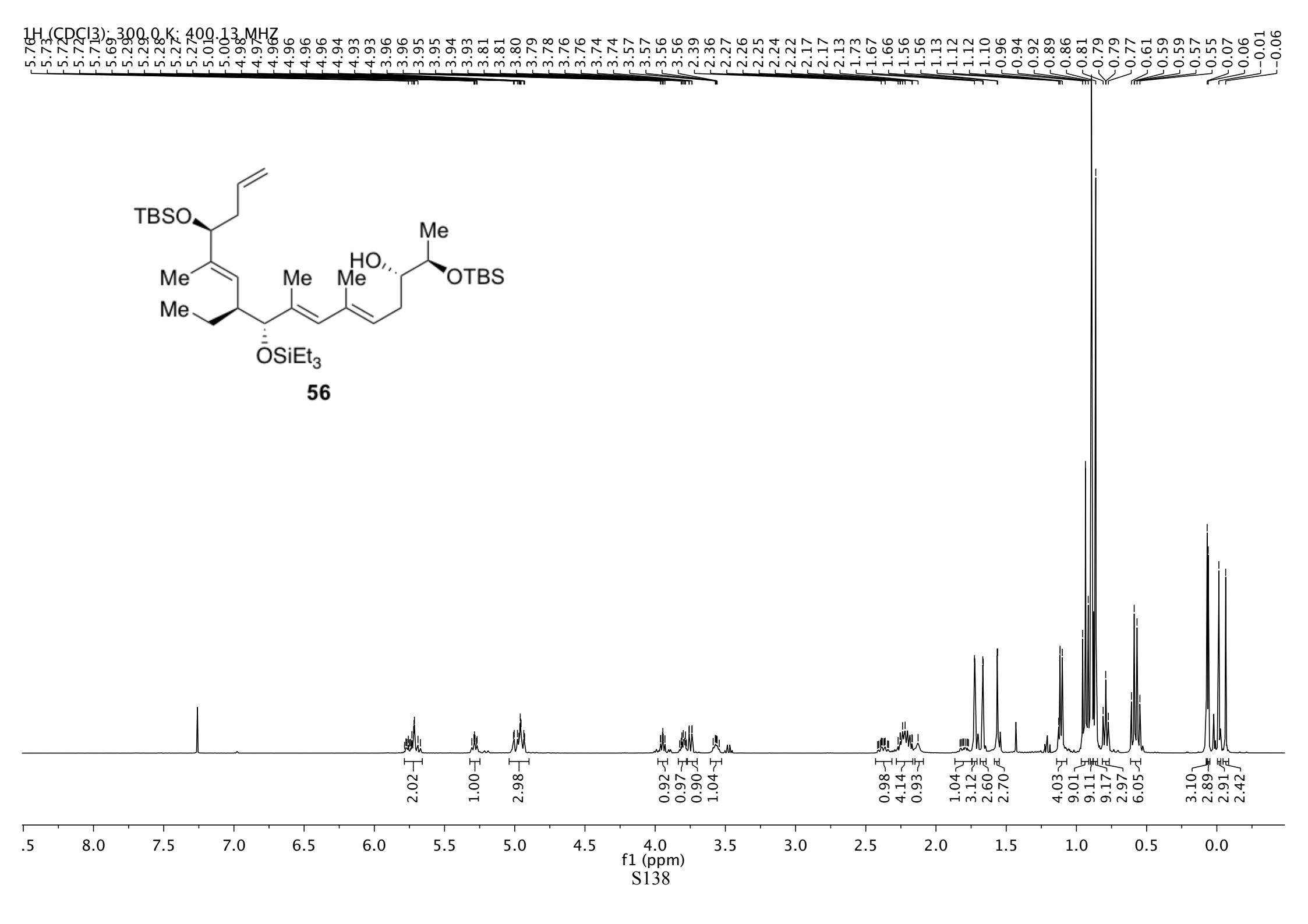
11B (CDCl3); 300.0 K; 128.38 MHZ

29.60

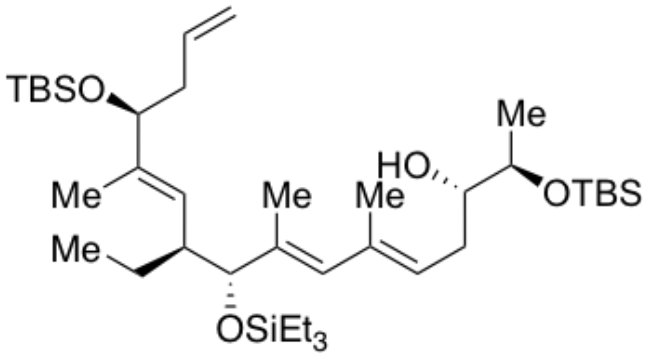


55

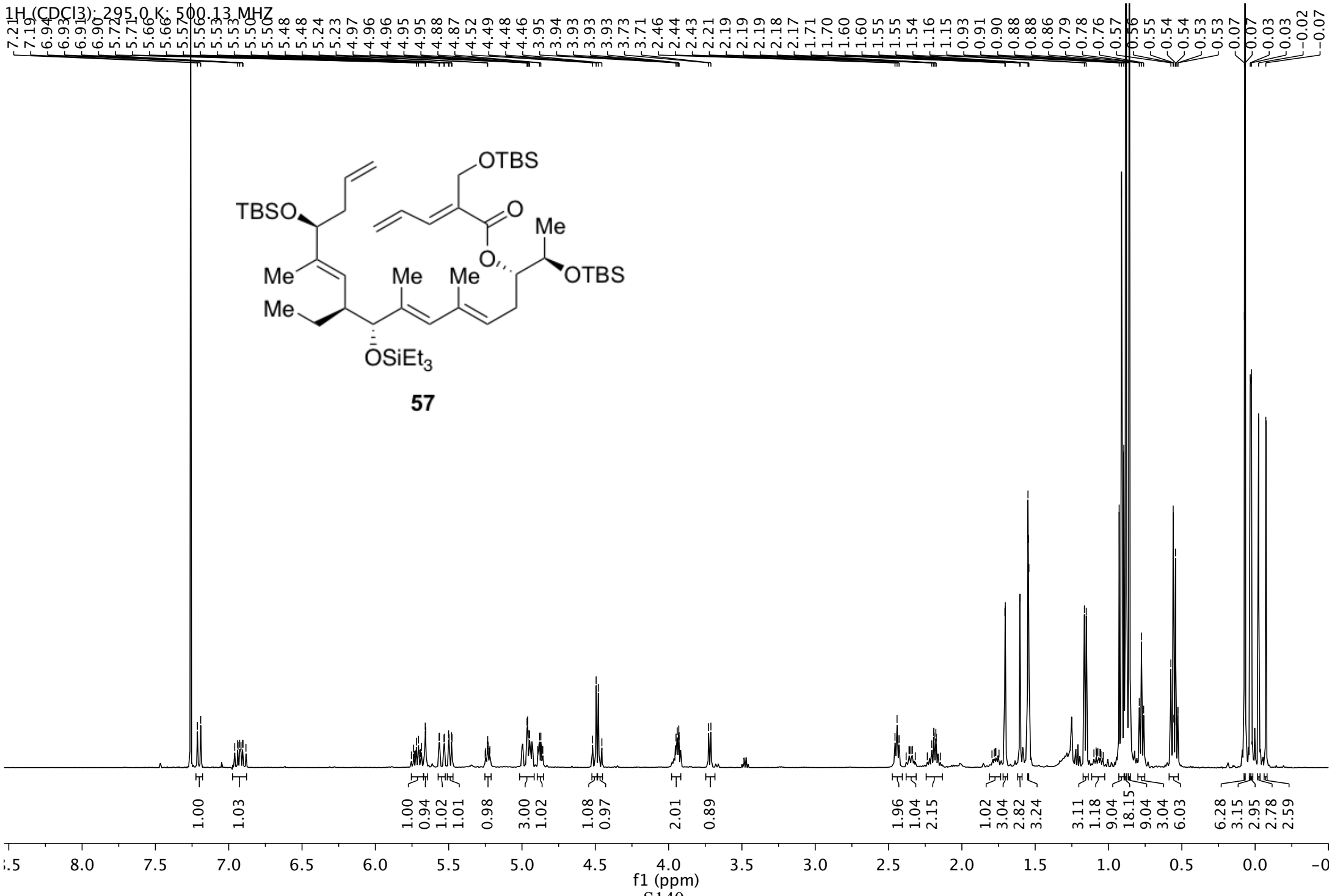


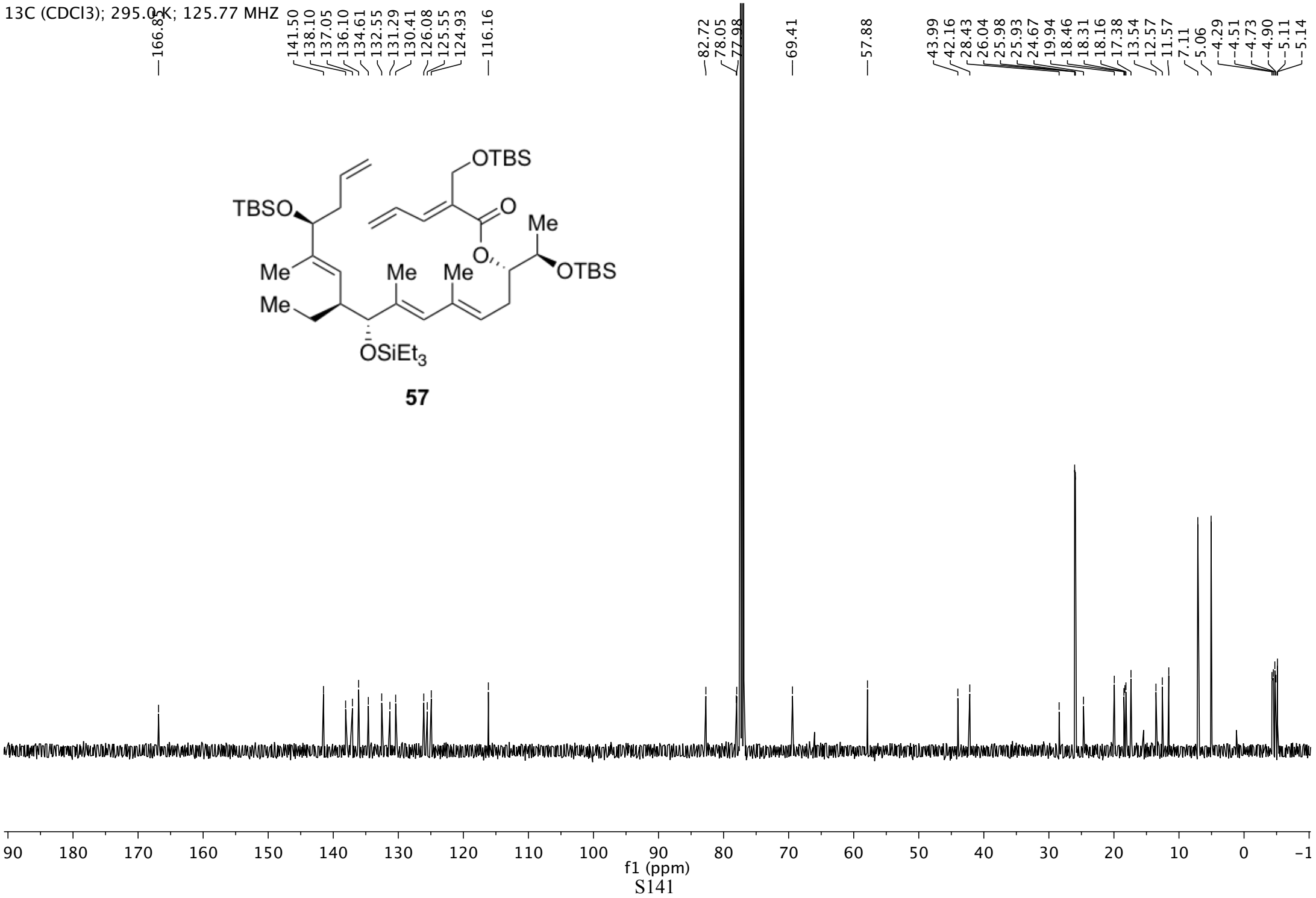

1H (CDCl3): 300.0 K: 400.13 MHZ
TBSO
Me
Me
Me
Me
HO
Me
OTBS
OSiEt3
56
f1 (ppm)

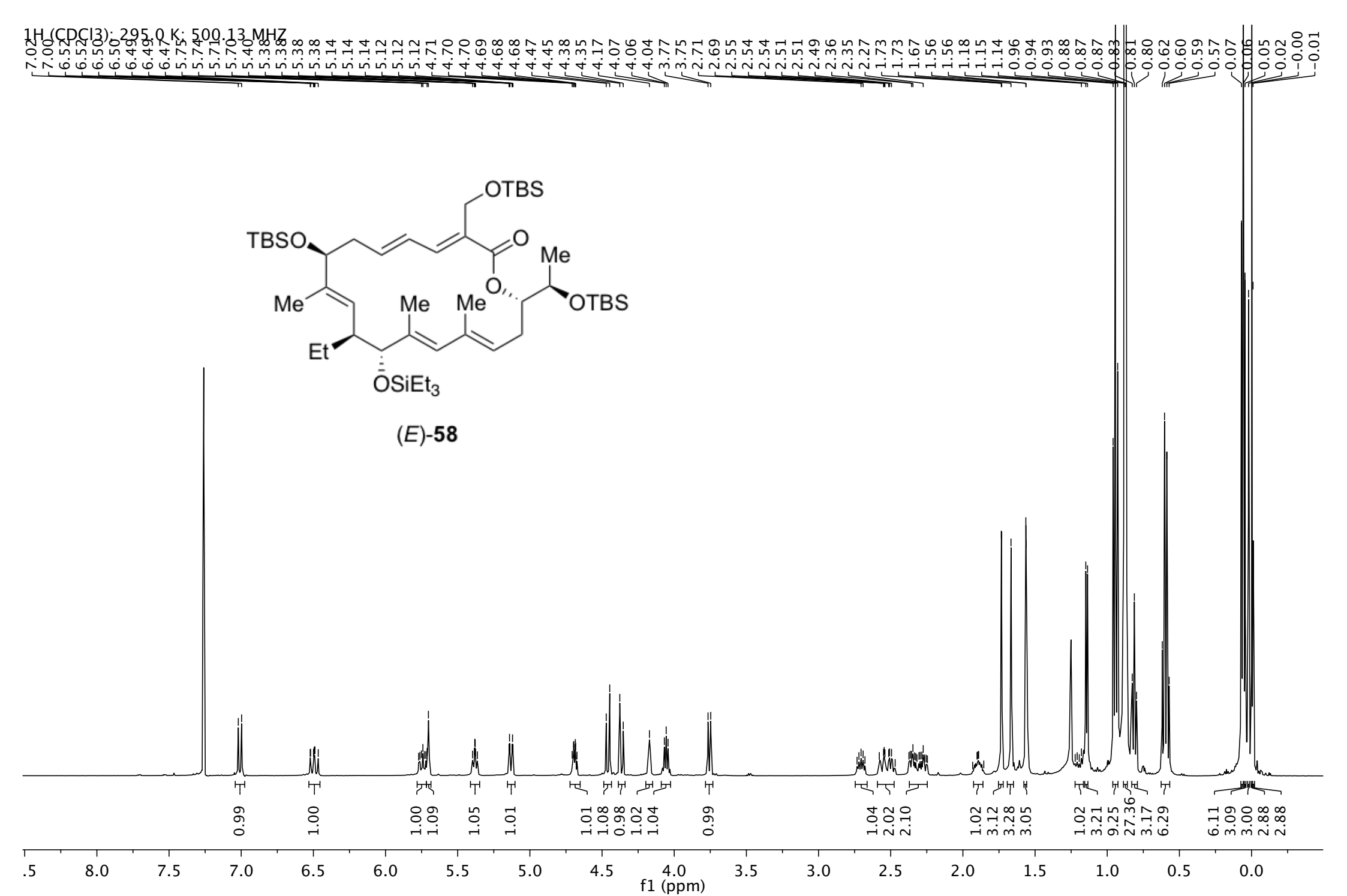
13C (CDCl3); 300.0 K; 100.62 MHZ

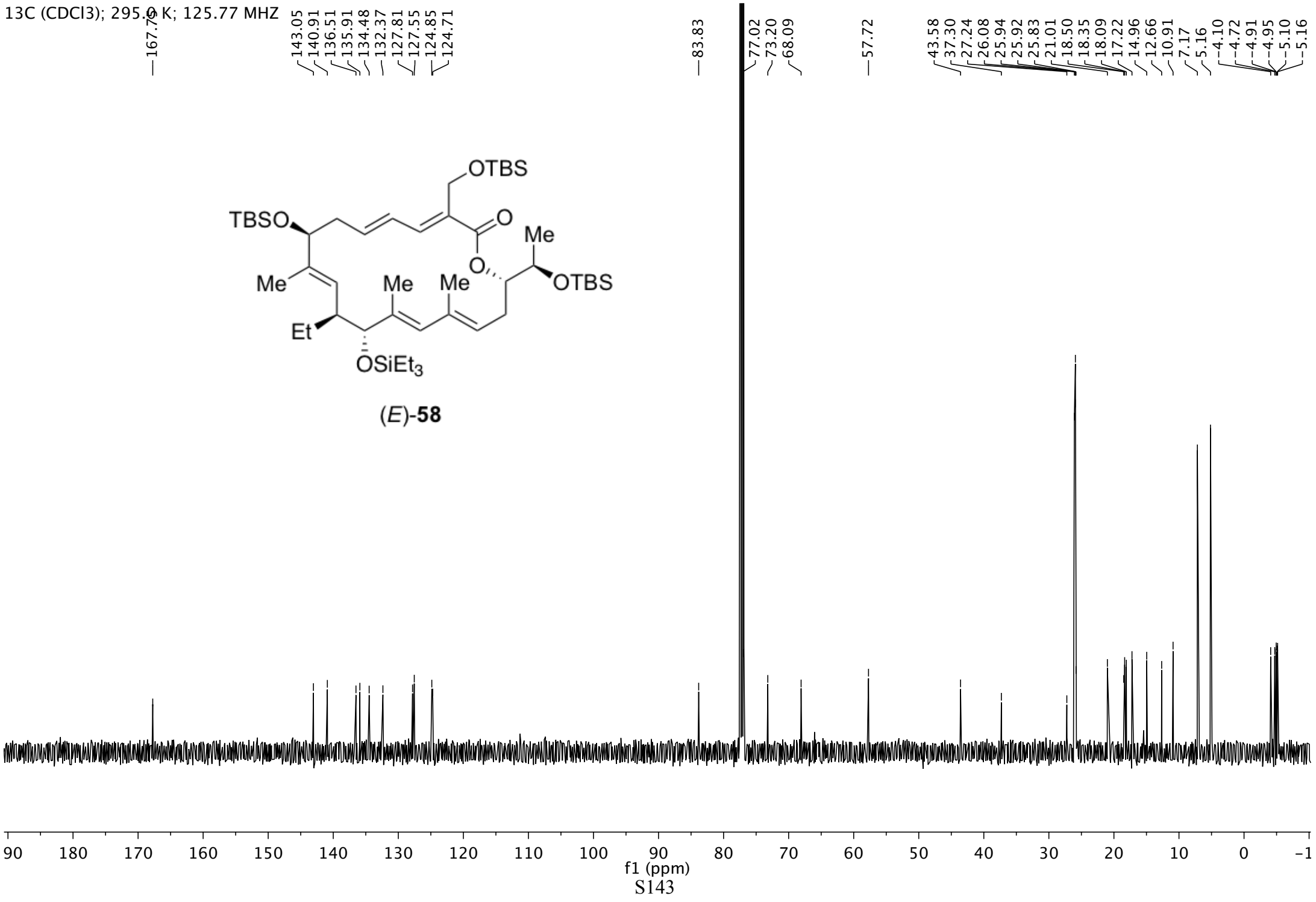


56


1H (CDCl3; 295.0 K; 500.13 MHZ
OTBS
TBSO
O
Me
O
Me
Me
Me
Me
OTBS
OSiEt3
57
f1 (ppm)

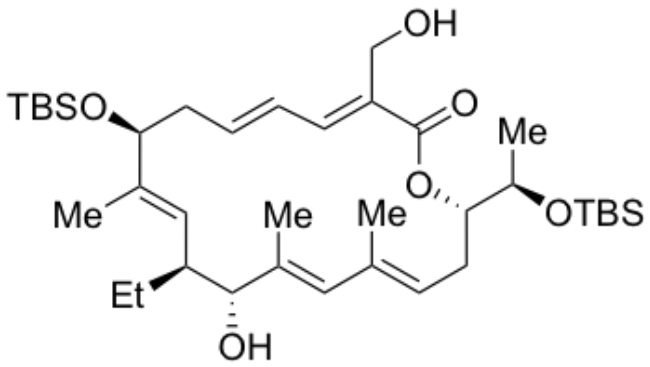

13C (CDCl3); 295.0 K; 125.77 MHZ
166.85
141.50
138.10
137.05
136.10
134.61
132.55
131.29
130.41
126.08
125.55
124.93
116.16
82.72
78.05
77.98
69.41
57.88
43.99
42.16
28.43
26.04
25.98
25.93
24.67
19.94
18.46
18.31
18.16
17.38
13.54
12.57
11.57
7.11
5.06
-4.29
-4.51
-4.73
-4.90
-5.11
-5.14
OTBS
TBSO
O
Me
O
Me
Me
Me
OTBS
Me
OSiEt3
57
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


1H (CDCl3): 295.0 K: 500.13 MHZ
OTBS
TBSO
O
Me
O
Me
Me
Me
OTBS
Et
OSiEt3
(E)-58
f1 (ppm)


13C (CDCl3); 295.0 K; 125.77 MHZ
167.79
143.05
140.91
136.51
135.91
134.48
132.37
127.81
127.55
124.85
124.71
83.83
77.02
73.20
68.09
57.72
43.58
37.30
27.24
26.08
25.94
25.92
25.83
21.01
18.50
18.35
18.09
17.22
14.96
12.66
10.91
7.17
5.16
-4.10
-4.72
-4.91
-4.95
-5.10
-5.16
OTBS
TBSO
O
Me
O
Me
Me
Me
OTBS
Et
OSiEt3
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

(*E*)-**58**

1H (CDCl3); 295.0 K; 500.13 MHZ

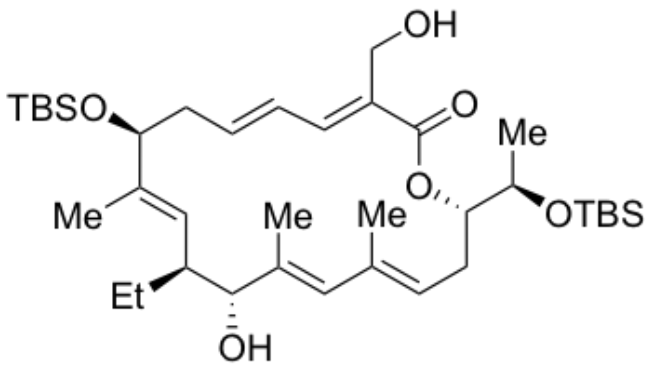


10

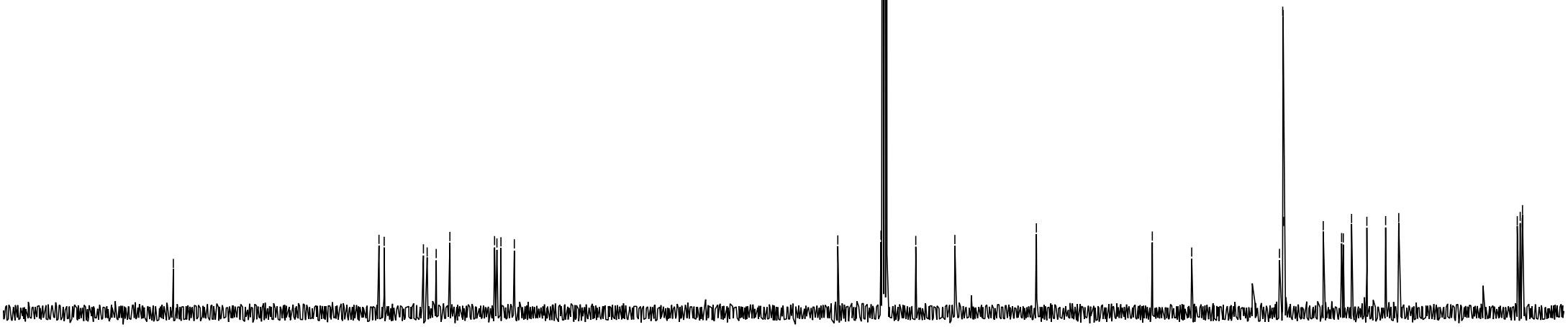
f1 (ppm)

13C (CDCl3); 295.0 K; 125.77 MHZ

168.72
142.26
141.58
136.53
136.05
134.89
133.13
127.38
127.07
126.56
124.83
83.20
77.64
73.16
68.13
57.64
42.72
37.64
26.35
25.93
25.88
25.81
20.71
18.35
18.13
17.07
15.10
12.68
11.00
-4.26
-4.64
-4.91
-4.93

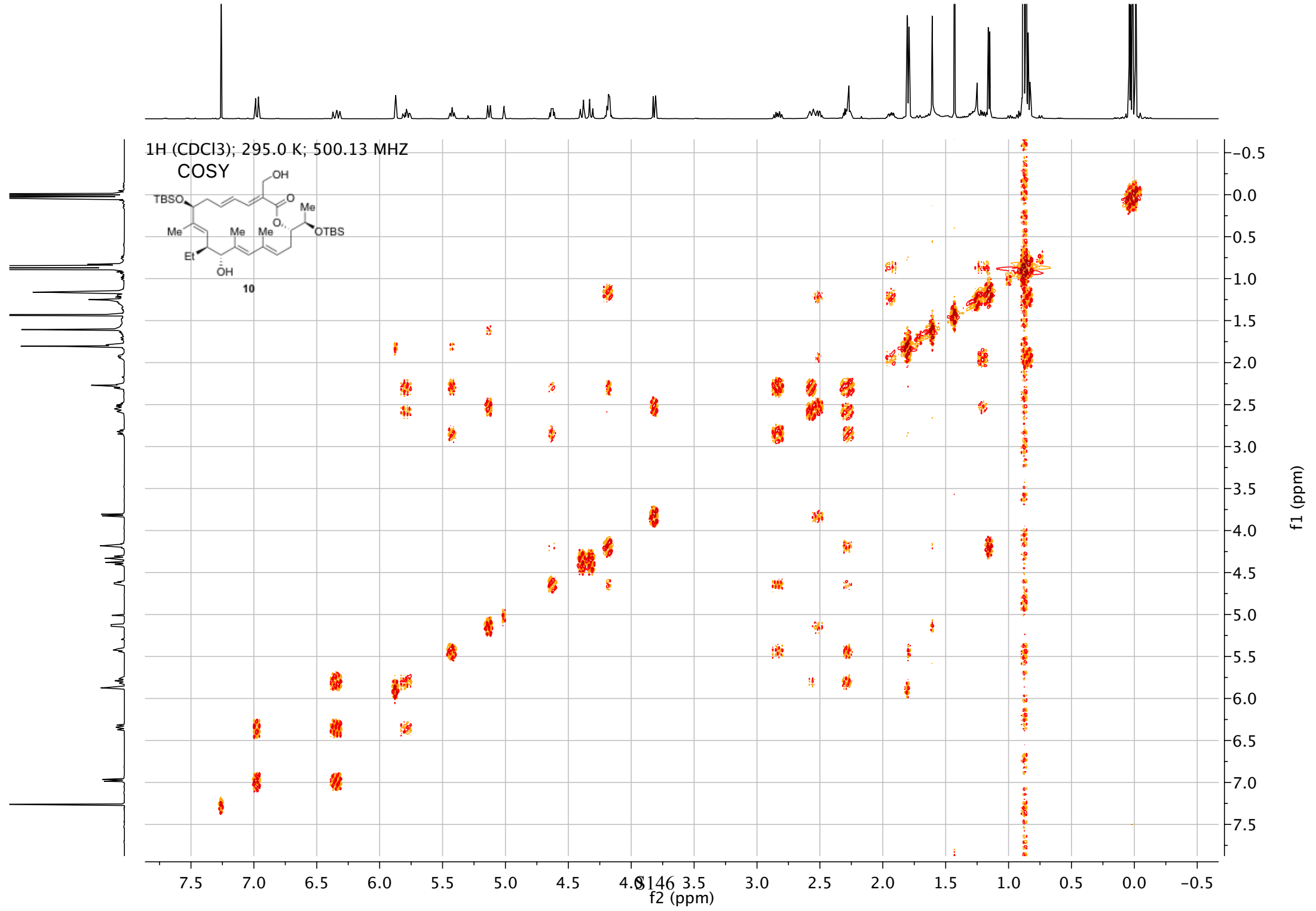


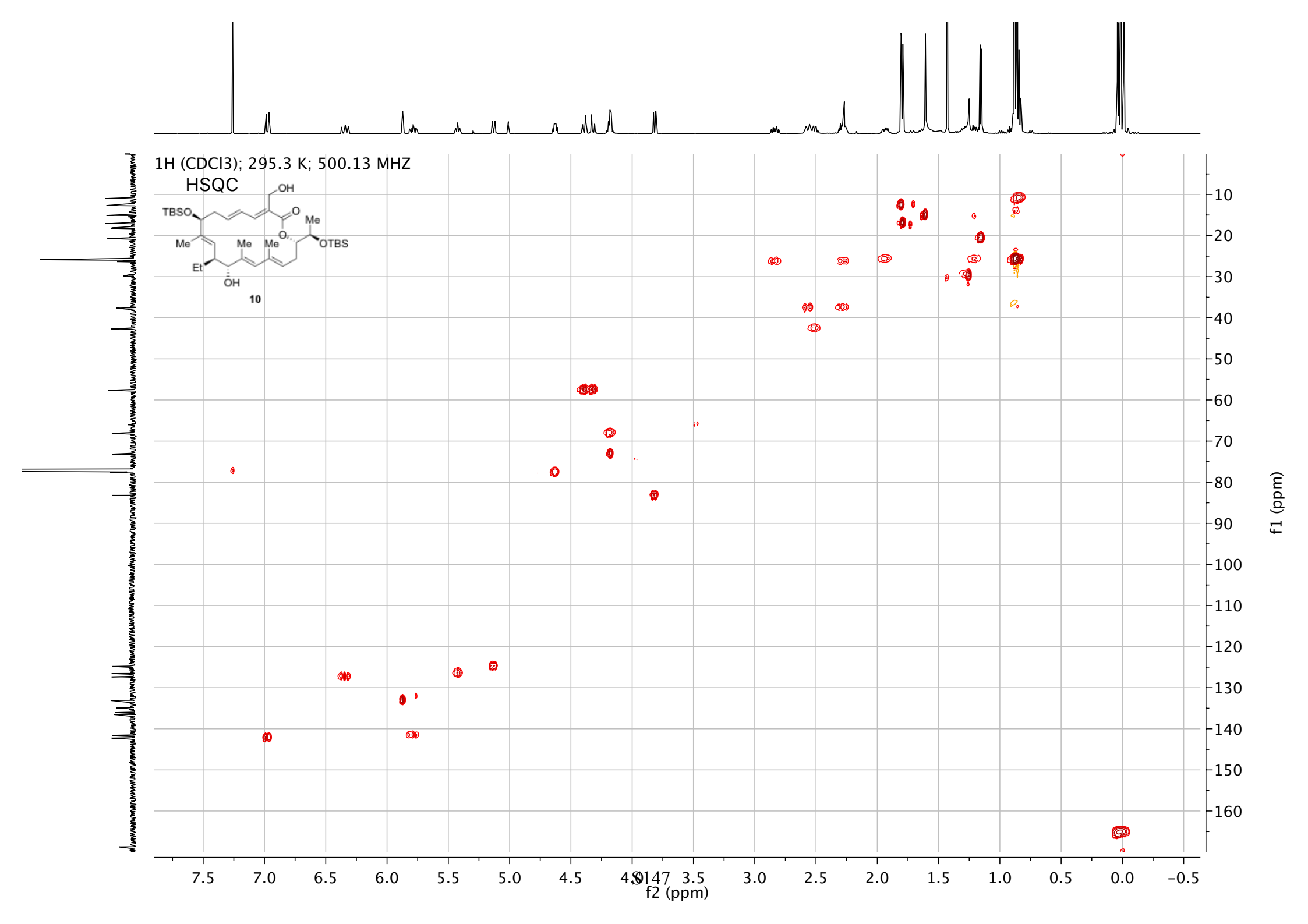
10

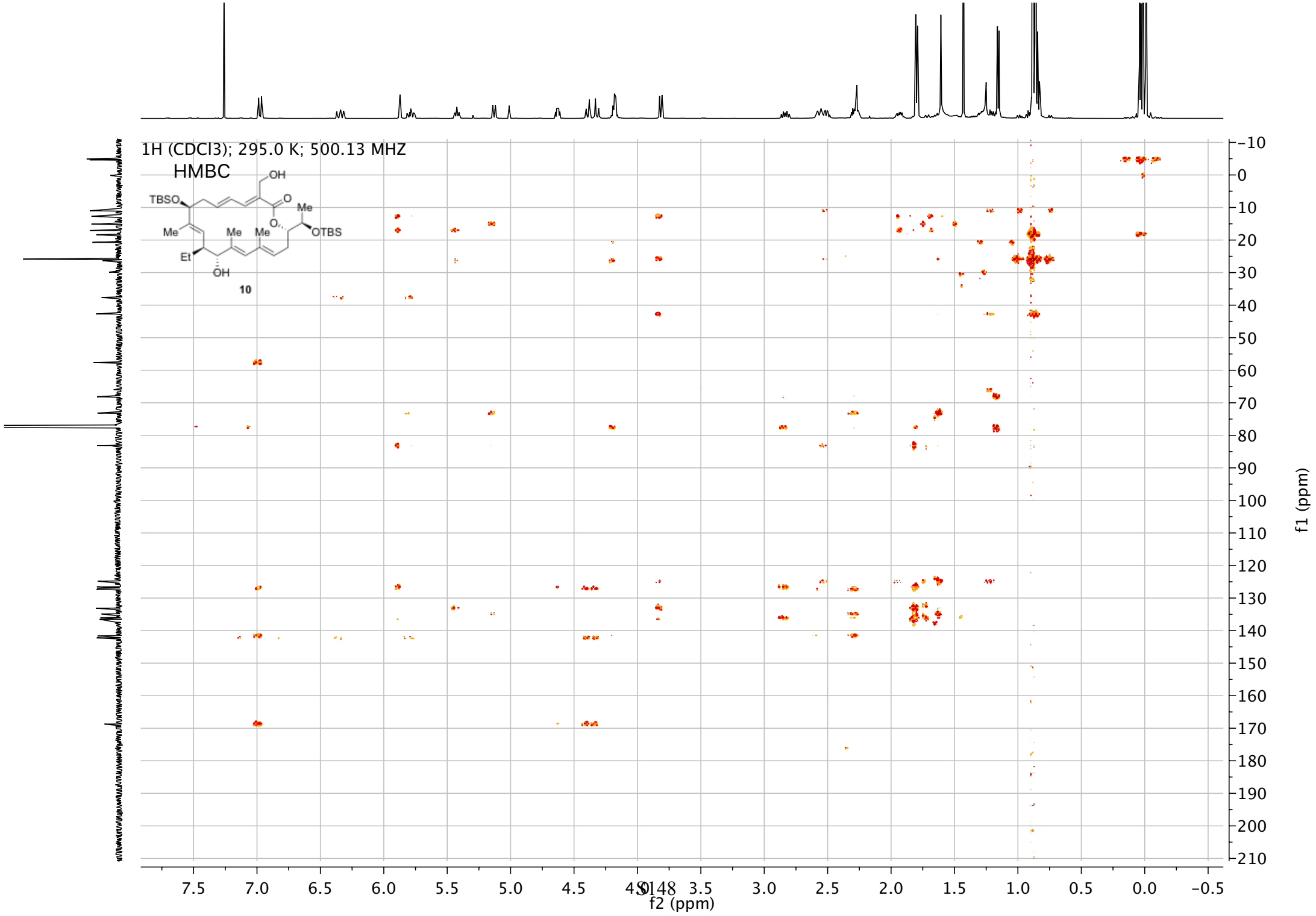


90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

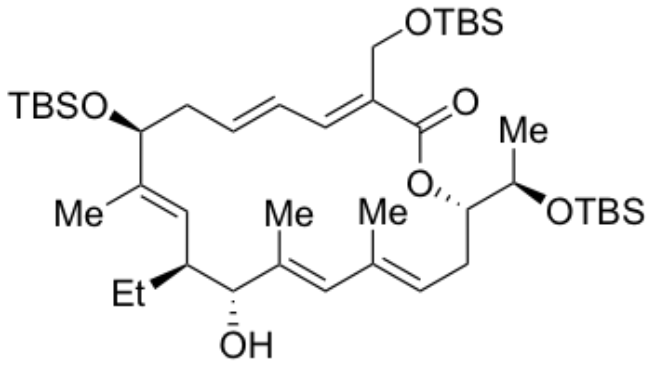
f1 (ppm)


1H (CDCl3); 295.0 K; 500.13 MHZ
COSY
OH
TBSO
O
Me
O
Me
Me
Me
OTBS
Et
OH
10
f2 (ppm)
f1 (ppm)


1H (CDCl3); 295.3 K; 500.13 MHZ
HSQC
OH
TBSO
O
Me
O
Me
Me
Me
OTBS
Et
OH
10
f2 (ppm)
f1 (ppm)


1H (CDCl3); 295.0 K; 500.13 MHZ
HMBC
OH
TBSO
O
Me
O
Me
Me
Me
OTBS
Et
OH
10
f2 (ppm)
f1 (ppm)

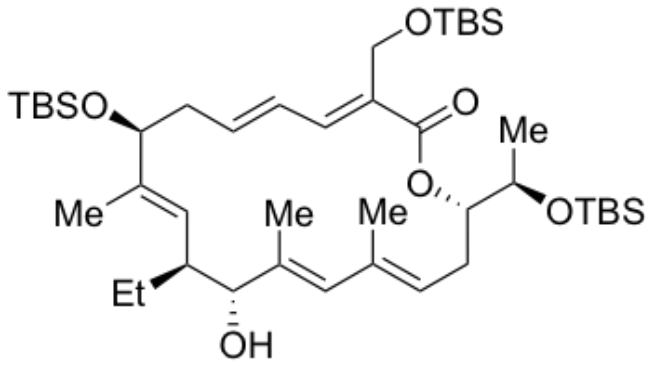
1H (CDCl3); 295.0 K; 500.13 MHZ



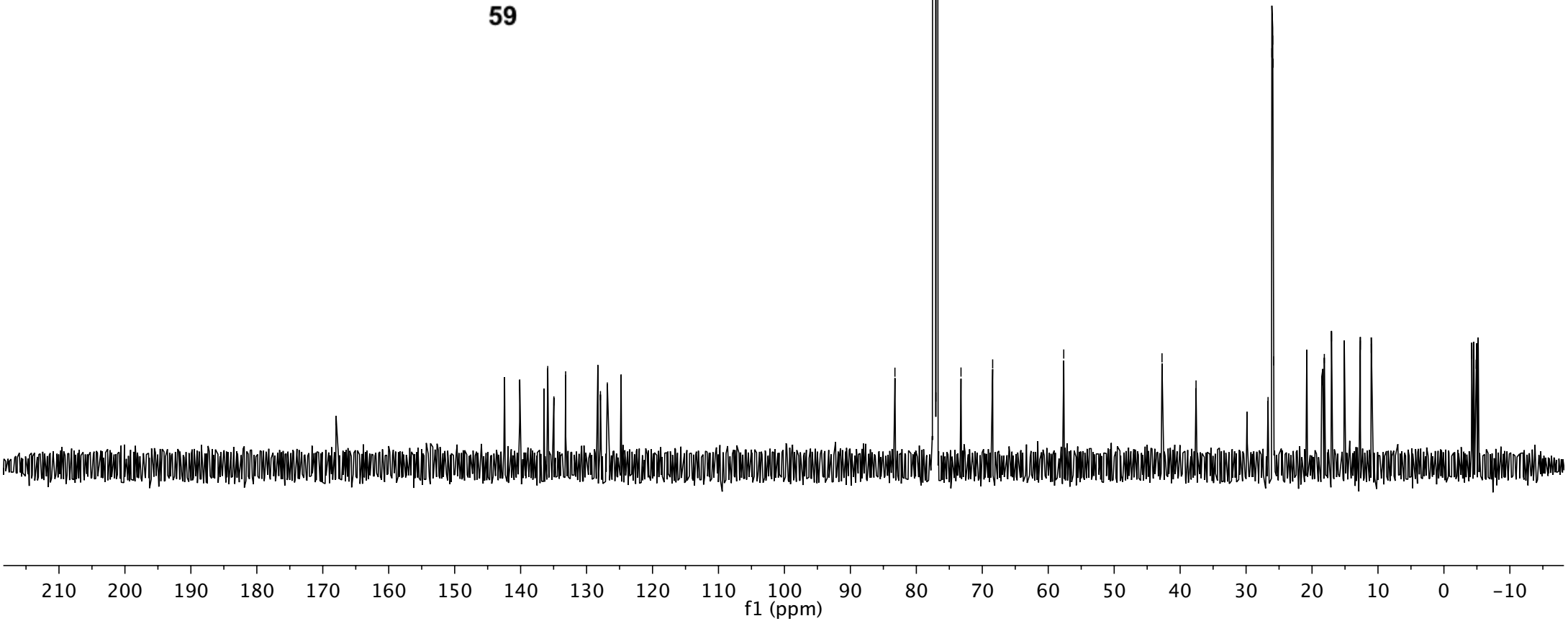
59

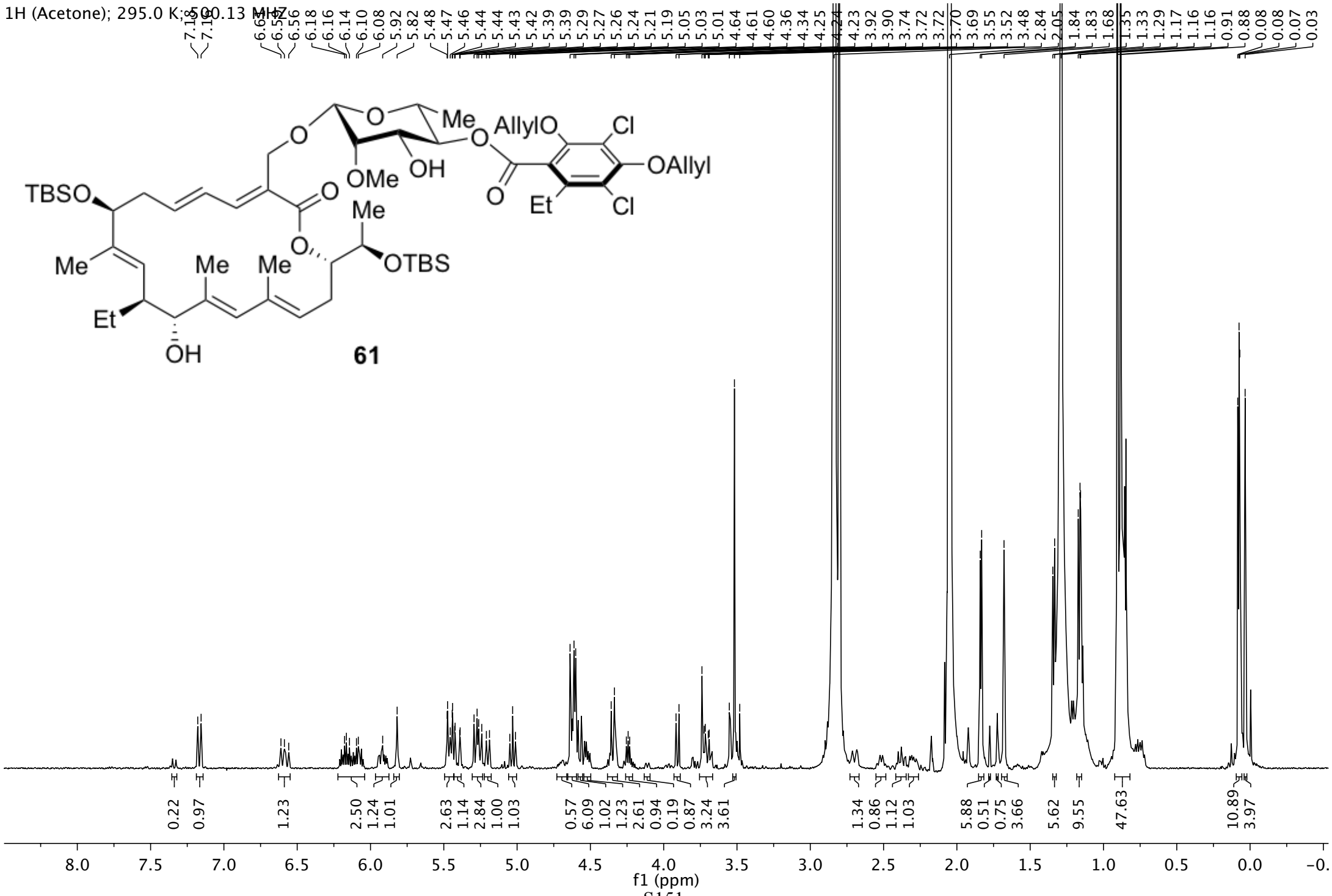
13C (CDCl3); 295.0 K; 125.77 MHZ

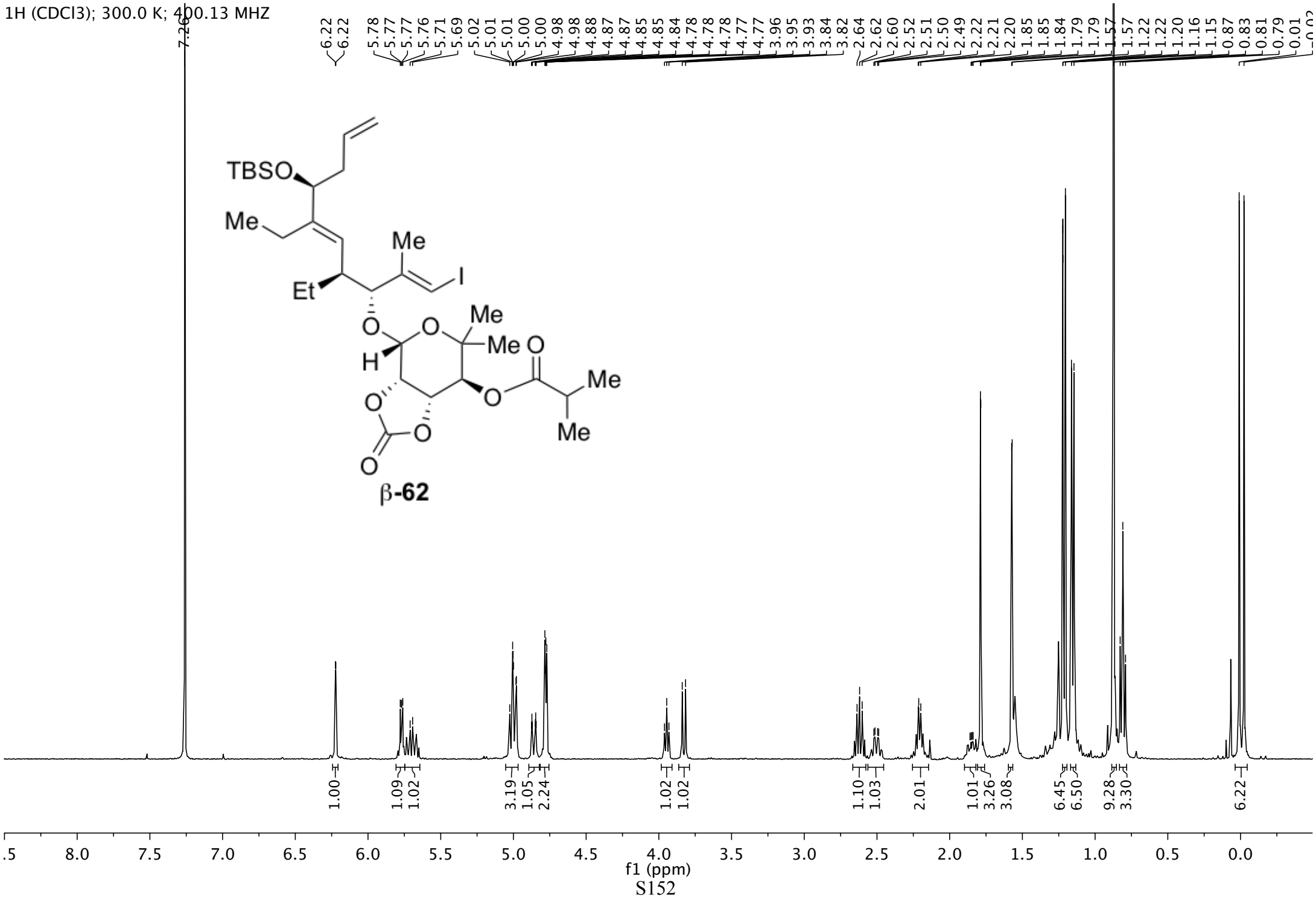
167.99
142.44
140.14
136.47
135.89
134.96
133.18
128.29
127.90
126.85
124.77
83.25
77.03
73.23
68.43
57.65
42.75
37.59
26.67
26.09
25.96
25.91
25.81
20.79
18.52
18.36
18.13
17.05
15.11
12.67
11.02
-4.23
-4.54
-4.89
-4.96
-5.11
-5.20

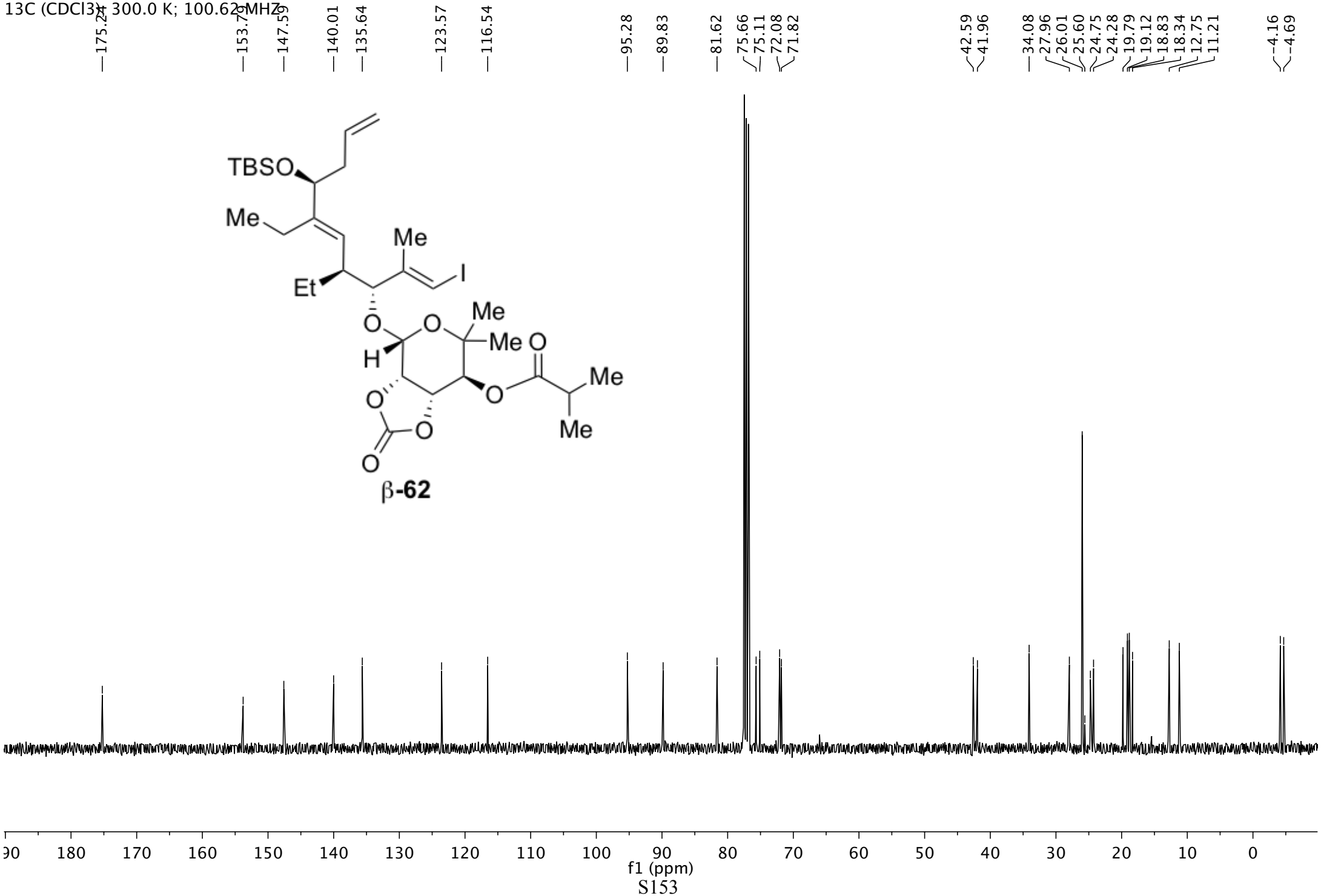


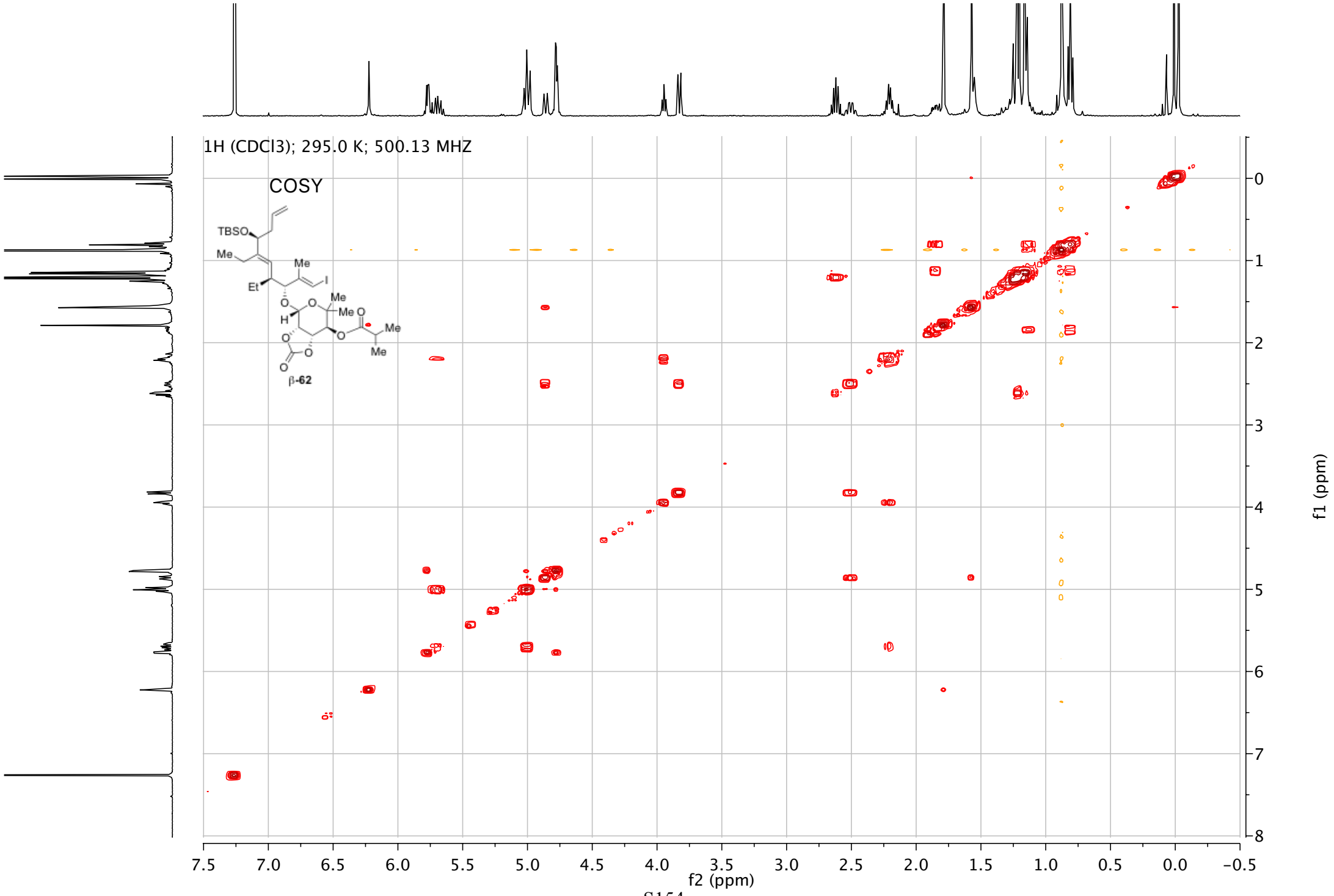
59

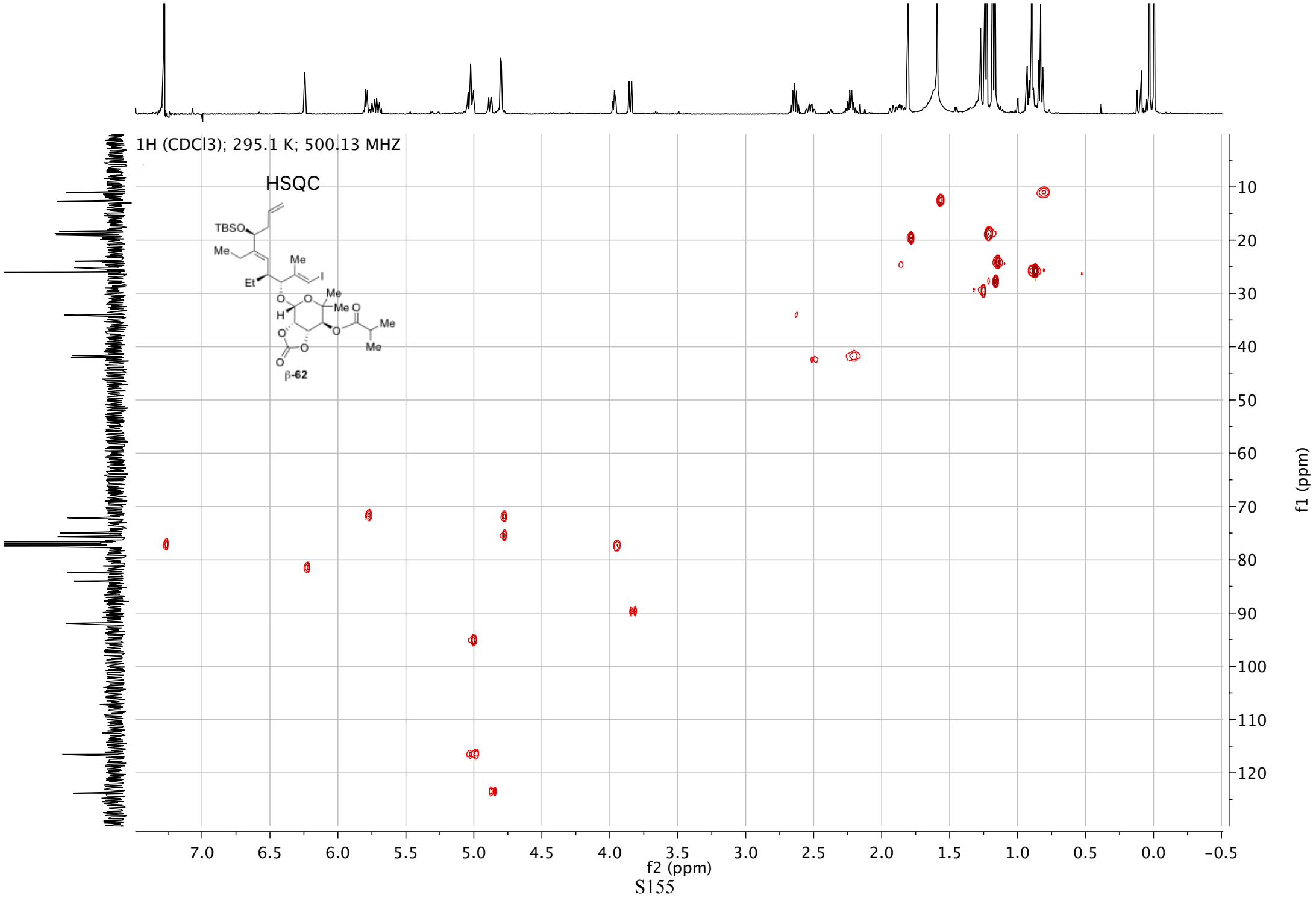


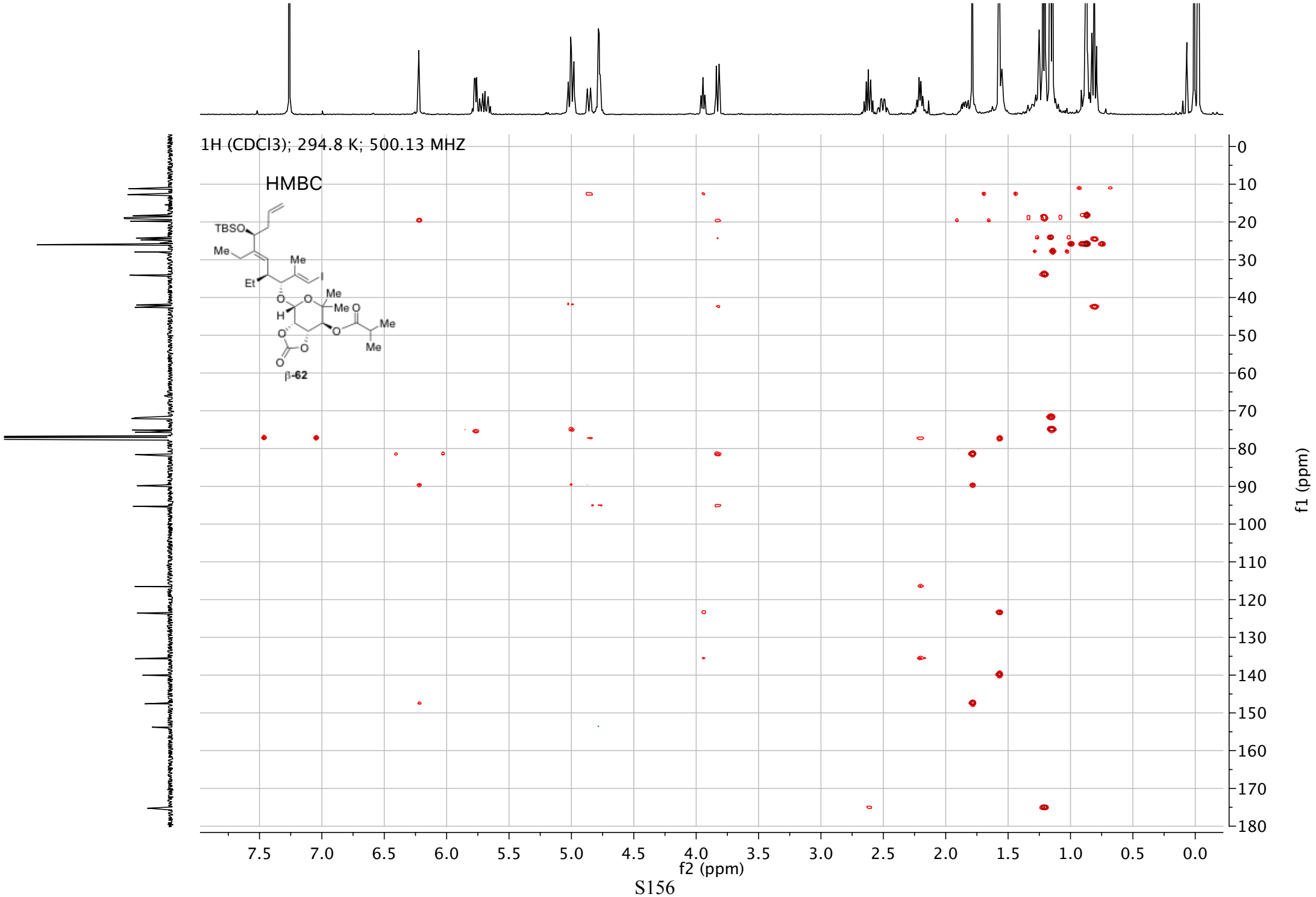

1H (Acetone); 295.0 K; 500.13 MHz
TBSO
OMe
OH
Me
AllylO
Cl
OAllyl
Et
Cl
Me
Me
Me
Me
OTBS
Et
OH
61
f1 (ppm)

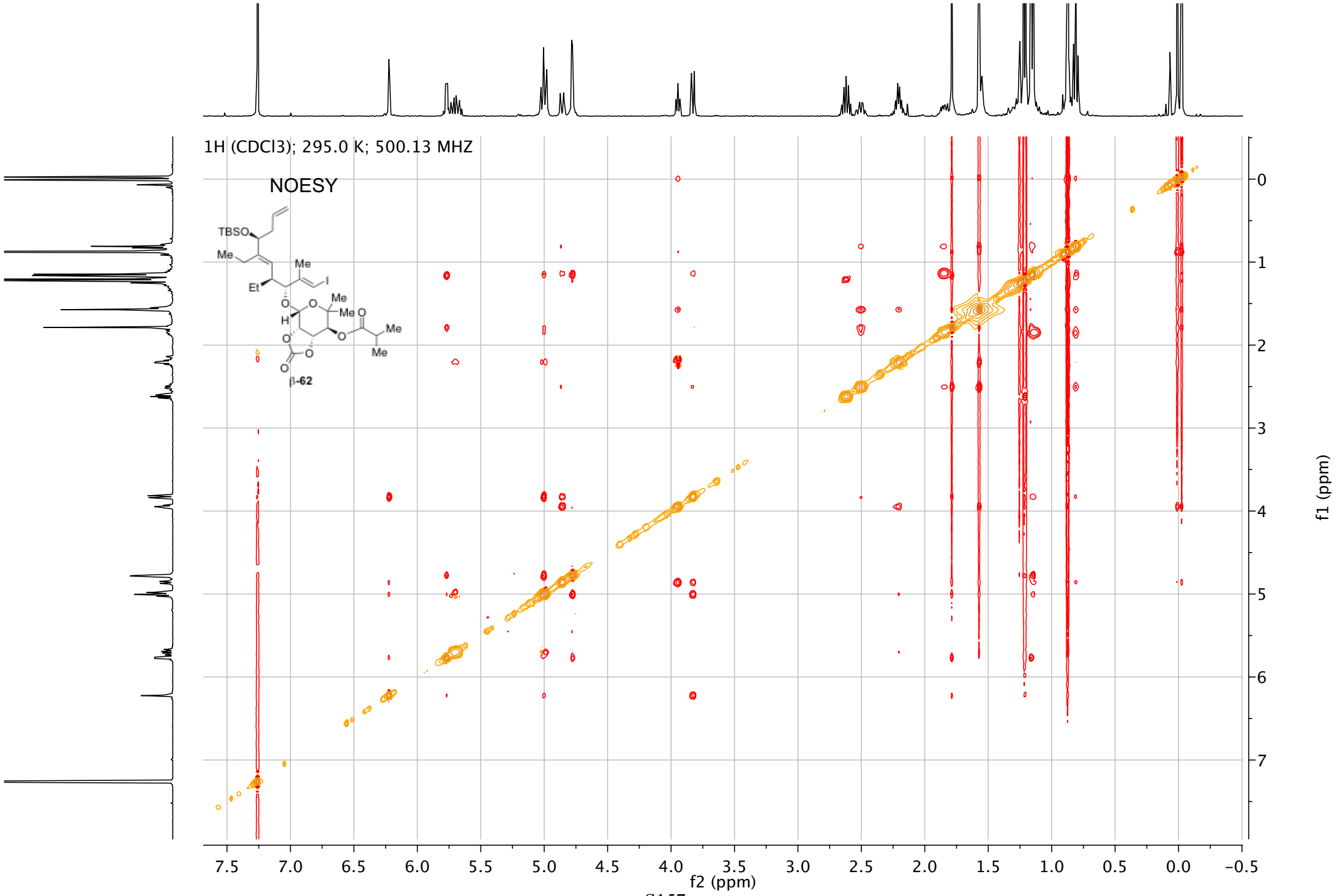

1H (CDCl3); 300.0 K; 400.13 MHZ
TBSO
Me
Et
Me
I
Me
Me
O
Me
H
O
O
O
O
O
Me
Me
β-62
f1 (ppm)


13C (CDCl3); 300.0 K; 100.62 MHZ
175.24
153.76
147.59
140.01
135.64
123.57
116.54
95.28
89.83
81.62
75.66
75.11
72.08
71.82
42.59
41.96
34.08
27.96
26.01
25.60
24.75
24.28
19.79
19.12
18.83
18.34
12.75
11.21
-4.16
-4.69
TBSO
Me
Et
Me
I
Me
Me
O
H
Me
Me
β-62
f1 (ppm)

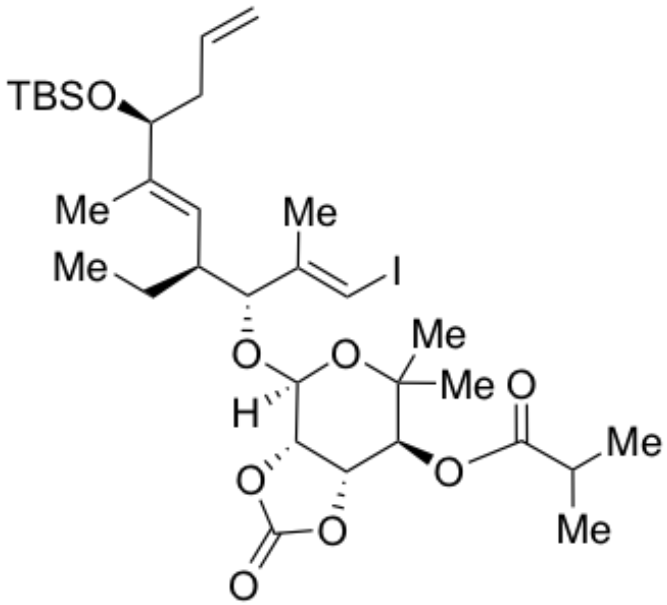

1H (CDCl3); 295.0 K; 500.13 MHZ
COSY
TBSO
Me
Me
Et
I
Me
Me O
Me
Me
β-62
f2 (ppm)
f1 (ppm)


1H (CDCl3); 295.1 K; 500.13 MHZ
HSQC
TBSO
Me
Me
Et
I
Me
Me
Me
H
O
O
O
O
O
O
O
Me
Me
β-62
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f2 (ppm)
10
20
30
40
50
60
70
80
90
100
110
120
f1 (ppm)

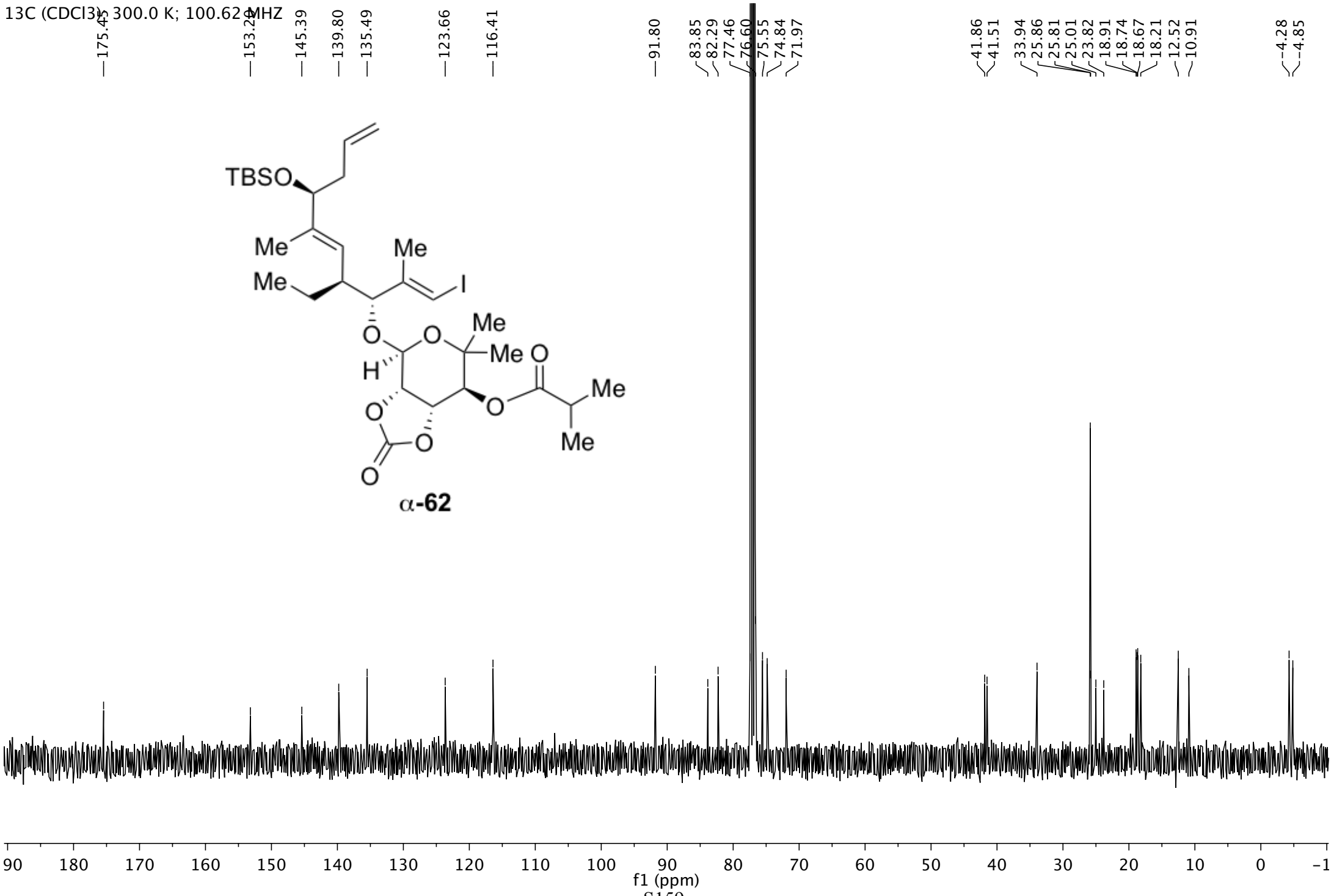

1H (CDCl3); 294.8 K; 500.13 MHZ
HMBC
TBSO
Me
Et
Me
I
Me
Me
O
Me
Me
β-62
f2 (ppm)
f1 (ppm)

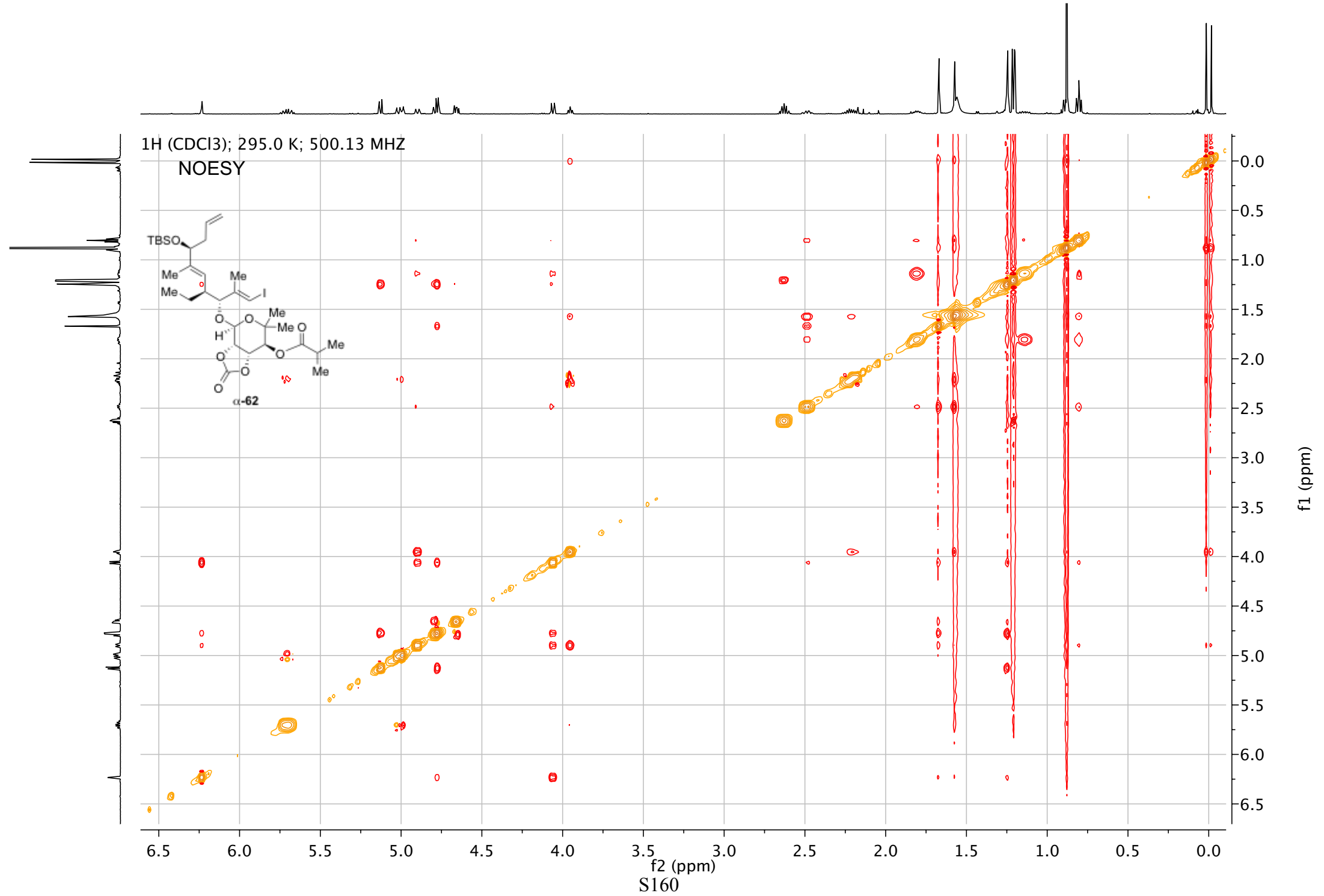

1H (CDCl3); 295.0 K; 500.13 MHZ
NOESY
TBSO
Me
Me
Et
I
Me
Me
Me
Me
H
β-62
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f2 (ppm)
0
1
2
3
4
5
6
7
f1 (ppm)

1H (CDCl3); 300.0 K; 400.13 MHZ

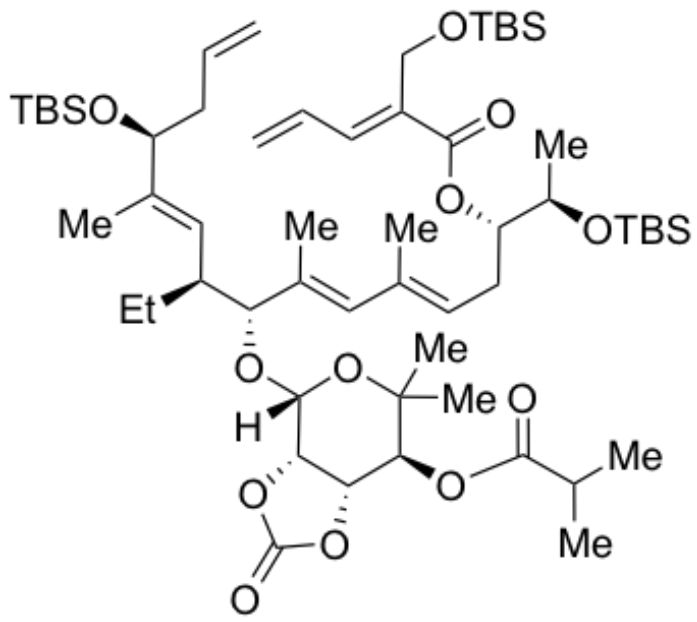


α-62

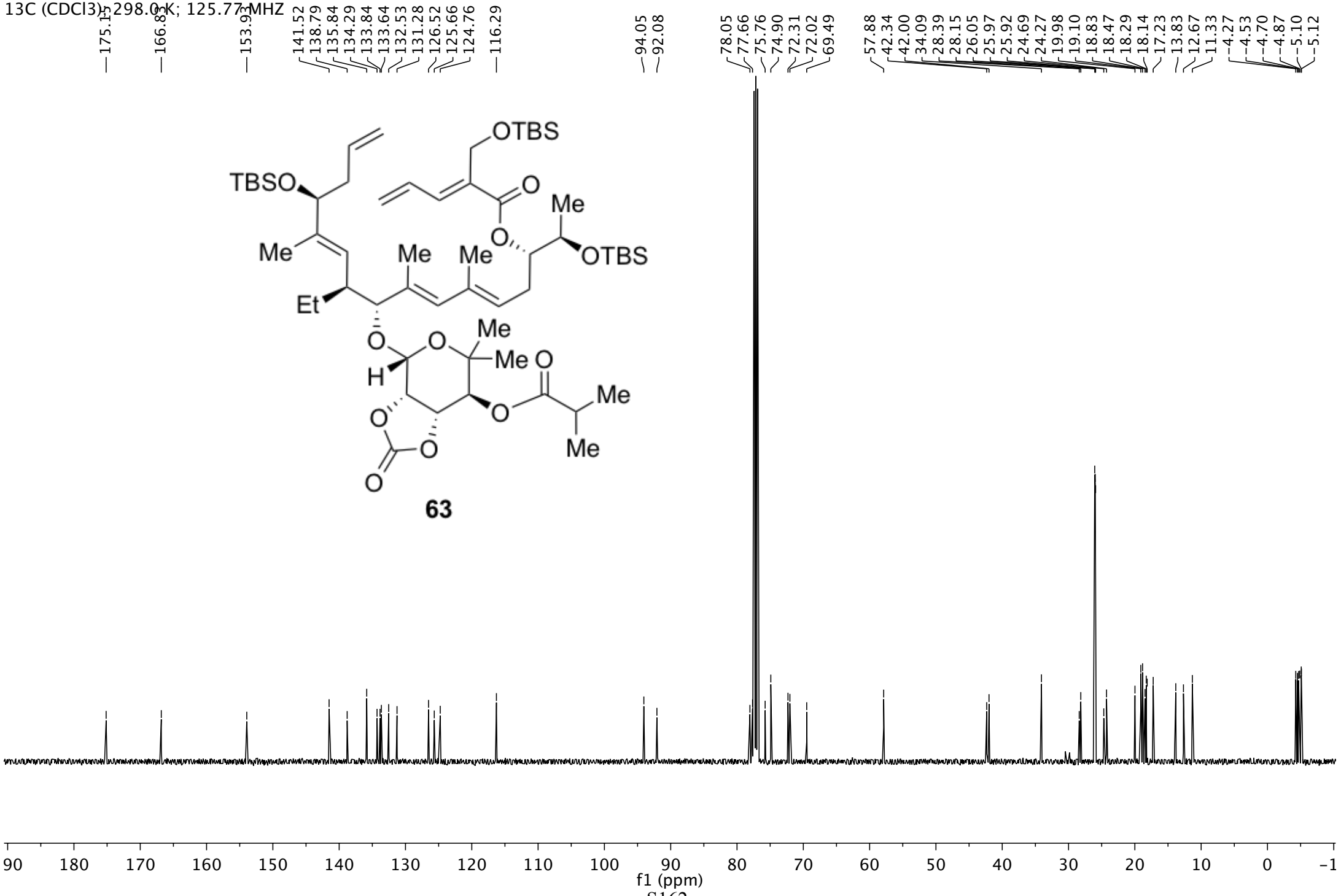

13C (CDCl3); 300.0 K; 100.62 MHZ
175.45
153.24
145.39
139.80
135.49
123.66
116.41
91.80
83.85
82.29
77.46
76.60
75.55
74.84
71.97
41.86
41.51
33.94
25.86
25.81
25.01
23.82
18.91
18.74
18.67
18.21
12.52
10.91
-4.28
-4.85
TBSO
Me
Me
Me
I
O
O
Me
Me
O
H
O
O
O
Me
O
O
Me
α-62
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


1H (CDCl3); 295.0 K; 500.13 MHZ
NOESY
TBSO
Me
Me
Me
I
Me
Me O
H
Me
Me
α-62
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
f1 (ppm)

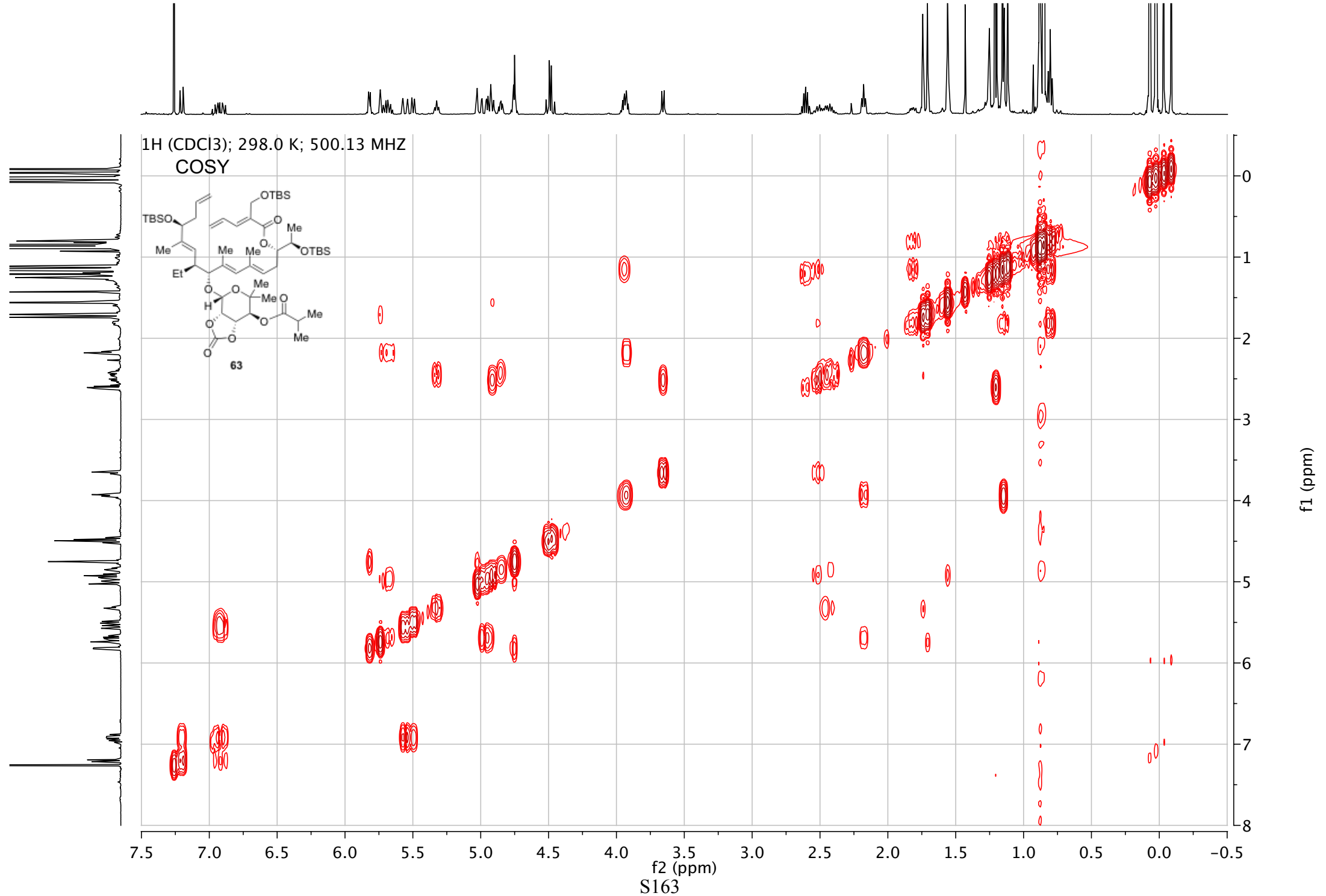
1H (CDCl3; 298.0 K; 500.13 MHZ

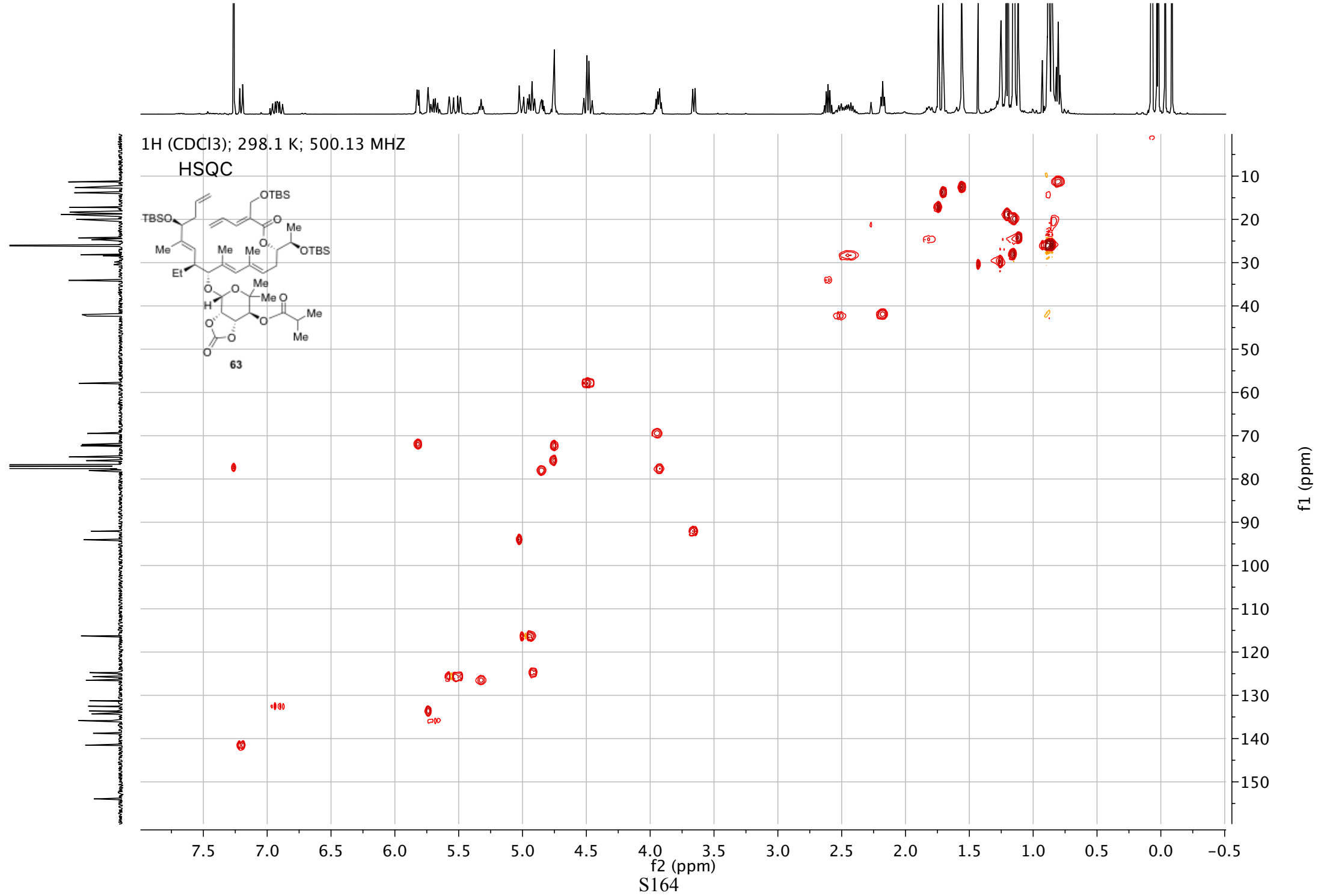


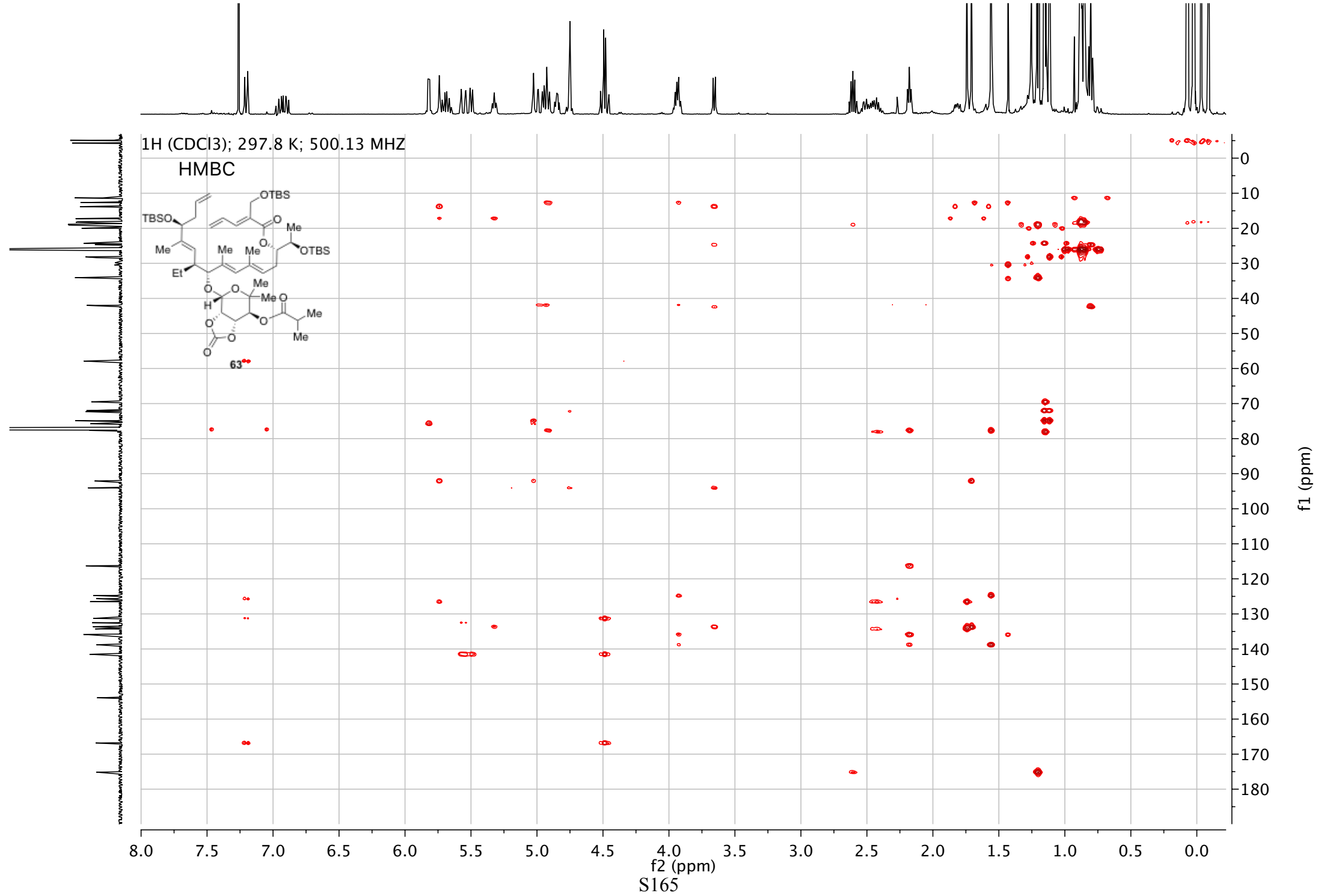
63


13C (CDCl3); 298.0 K; 125.77 MHZ
175.15
166.85
153.93
141.52
138.79
135.84
134.29
133.84
133.64
132.53
131.28
126.52
125.66
124.76
116.29
94.05
92.08
78.05
77.66
75.76
74.90
72.31
72.02
69.49
57.88
42.34
42.00
34.09
28.39
28.15
26.05
25.97
25.92
24.69
24.27
19.98
19.10
18.83
18.47
18.29
18.14
17.23
13.83
12.67
11.33
-4.27
-4.53
-4.70
-4.87
-5.10
-5.12
TBSO
OTBS
O
Me
Me
Me
Me
O
OTBS
Et
O
O
Me
Me
O
H
O
O
Me
O
O
O
Me
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

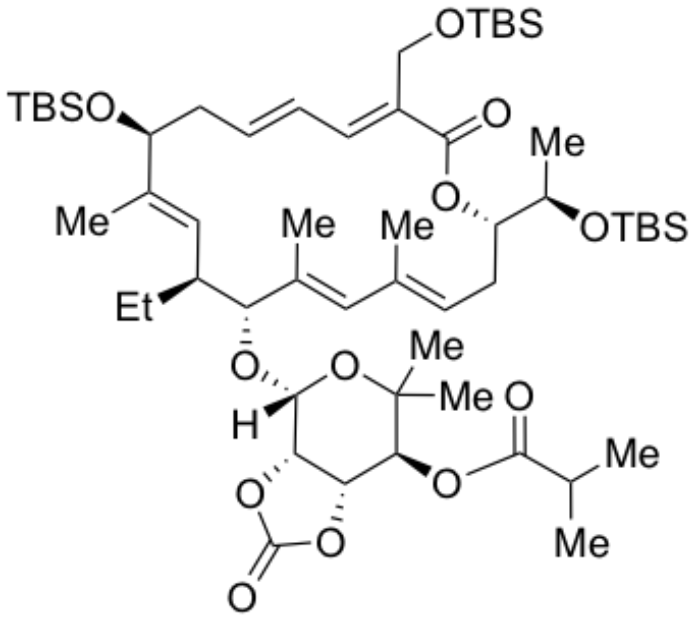
63


1H (CDCl3); 298.0 K; 500.13 MHZ
COSY
OTBS
TBSO
Me
Me
Me
Me
OTBS
Et
Me
Me
H
Me
Me
63
f2 (ppm)
f1 (ppm)


1H (CDCl3); 298.1 K; 500.13 MHZ
HSQC
OTBS
TBSO
Me
Me
Me
Me
OTBS
Et
Me
Me
Me
H
Me
Me
63
f2 (ppm)
f1 (ppm)

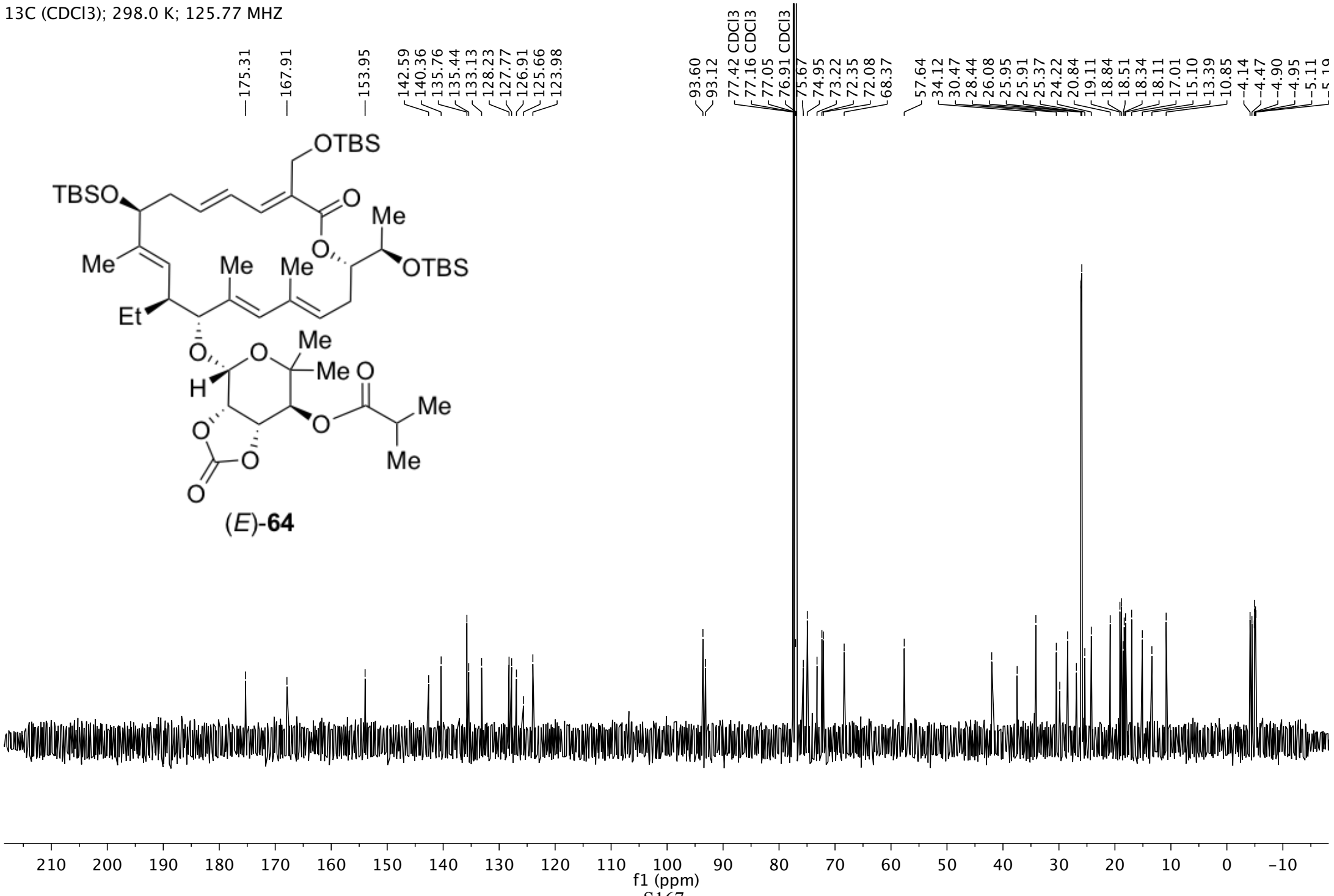

1H (CDCl3); 297.8 K; 500.13 MHZ
HMBC
OTBS
TBSO
Me
Me
Me
Me
OTBS
Et
Me
Me
H
Me
Me
63
f2 (ppm)
f1 (ppm)

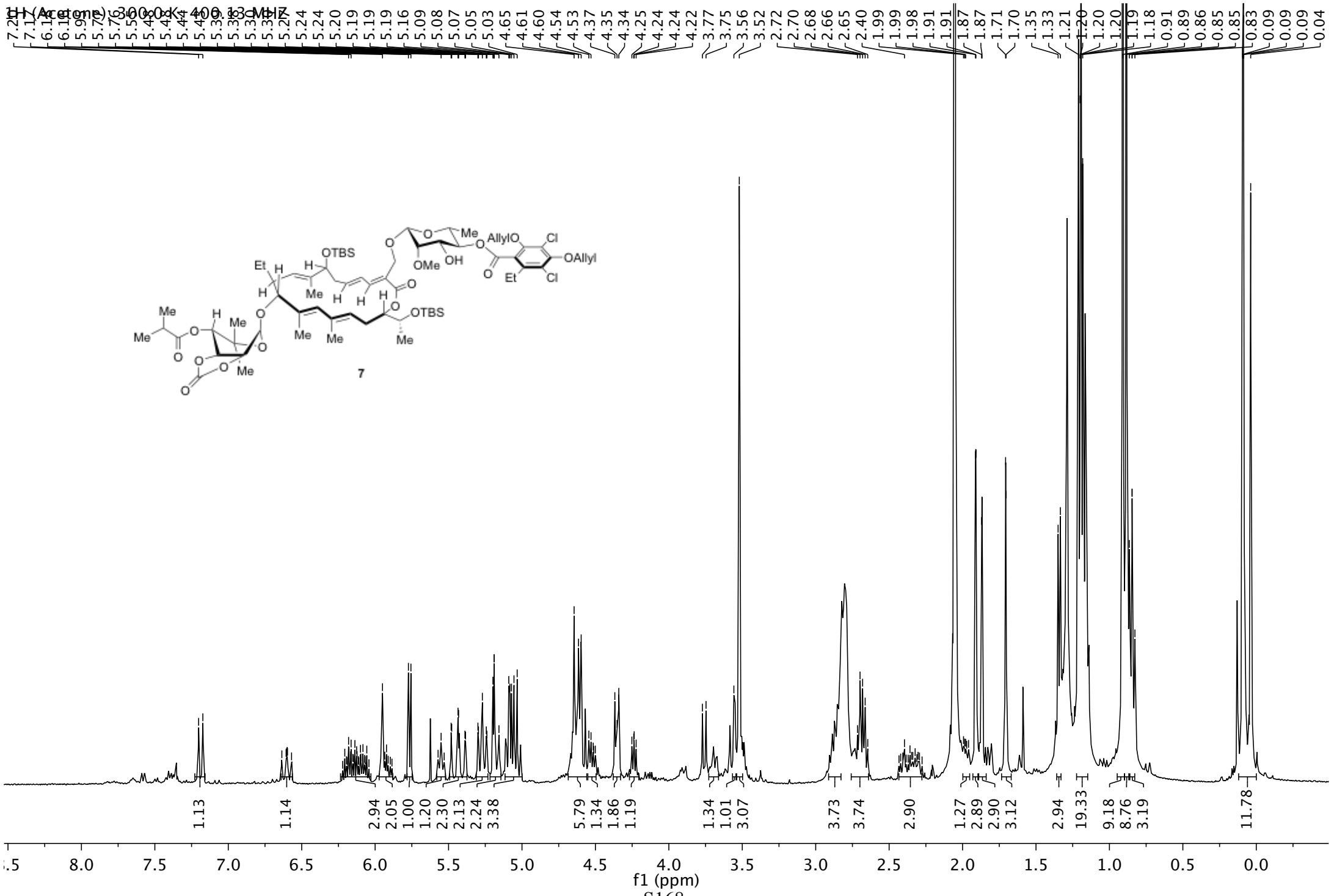
1H (CDCl3); 298.0 K; 500.13 MHZ

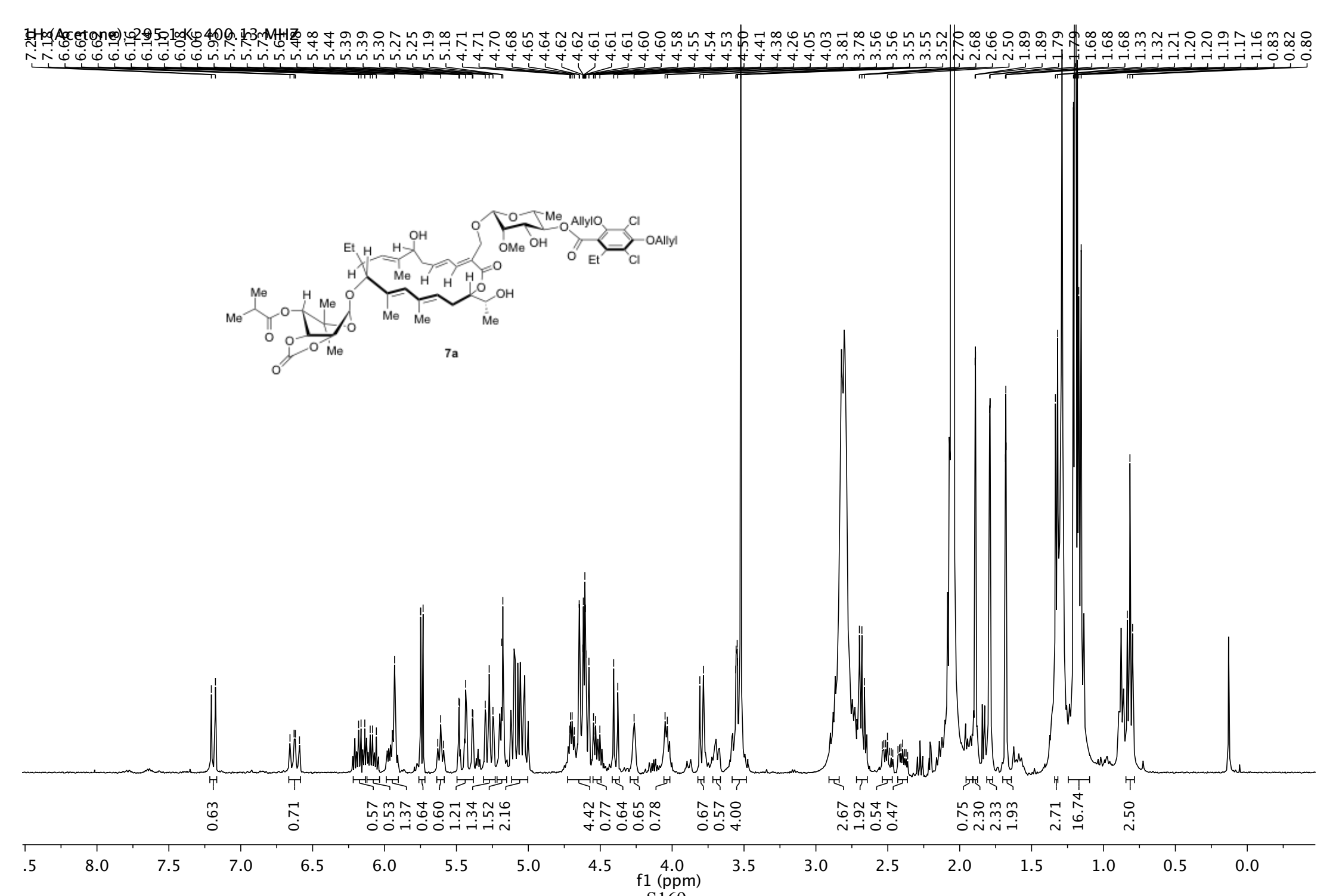


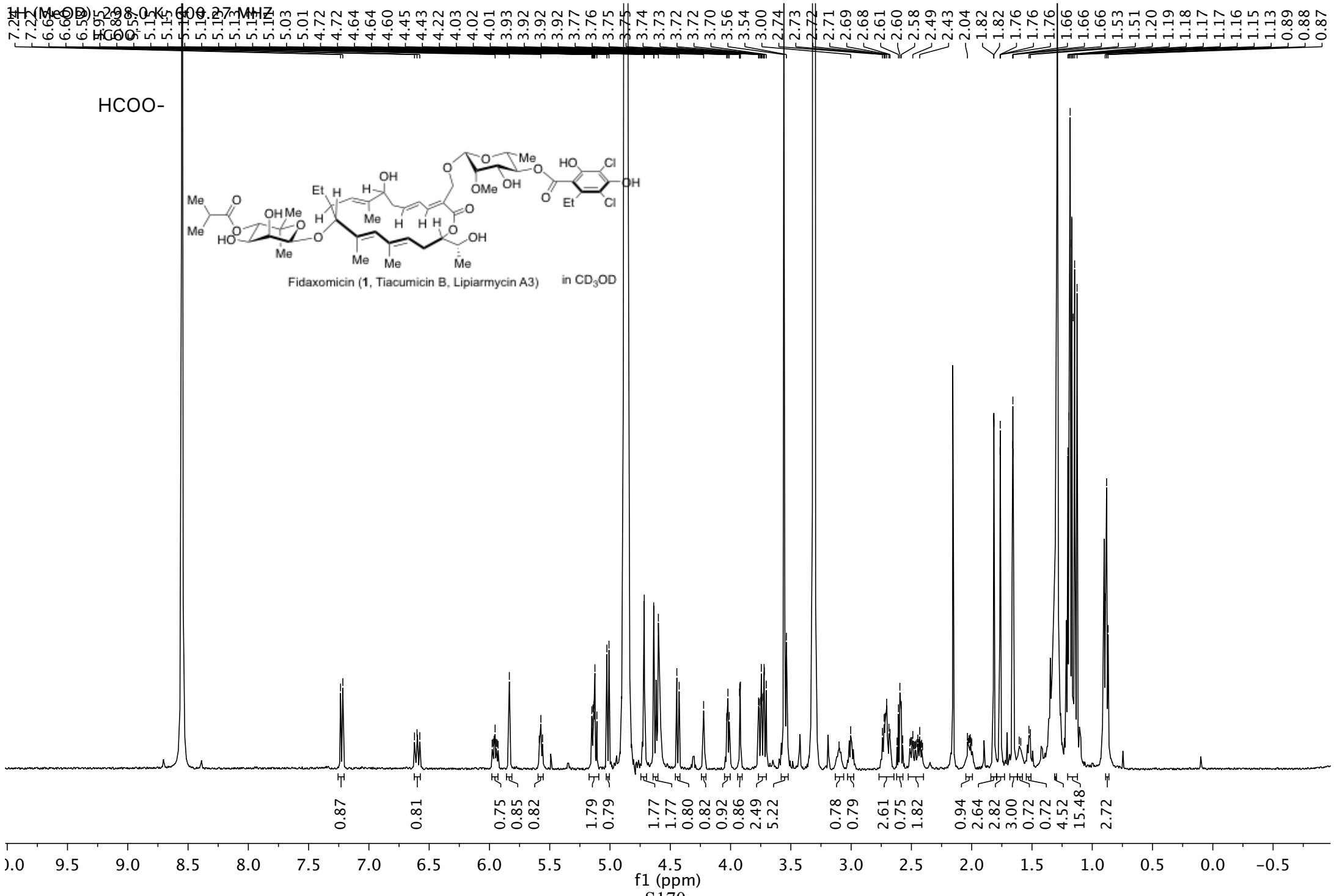
(*E*)-**64**

13C (CDCl3); 298.0 K; 125.77 MHZ

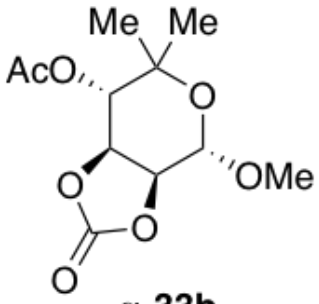



1H (Acetone) - 300.0K - 400.13 MHz
7.27 7.15 6.18 6.16 5.99 5.78 5.76 5.55 5.44 5.43 5.40 5.38 5.35 5.33 5.31 5.27 5.24 5.24 5.20 5.19 5.19 5.19 5.16 5.09 5.08 5.07 5.05 5.03 4.65 4.61 4.60 4.54 4.53 4.37 4.35 4.34 4.25 4.24 4.24 4.22 3.77 3.75 3.56 3.52 2.72 2.70 2.68 2.66 2.65 2.40 1.99 1.99 1.98 1.91 1.91 1.87 1.87 1.71 1.70 1.35 1.33 1.21 1.20 1.20 1.20 1.19 1.18 0.91 0.89 0.86 0.85 0.85 0.83 0.09 0.09 0.09 0.04
OTBS
Et
H
Me
OMe
OH
AllylO
Cl
OAllyl
Et
Cl
OTBS
Me
7
1.13 1.14 2.94 2.05 1.00 1.20 2.30 2.13 2.24 3.38 5.79 1.34 1.86 1.19 1.34 1.01 3.07 3.73 3.74 2.90 1.27 2.89 2.90 3.12 2.94 19.33 9.18 8.76 3.19 11.78
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

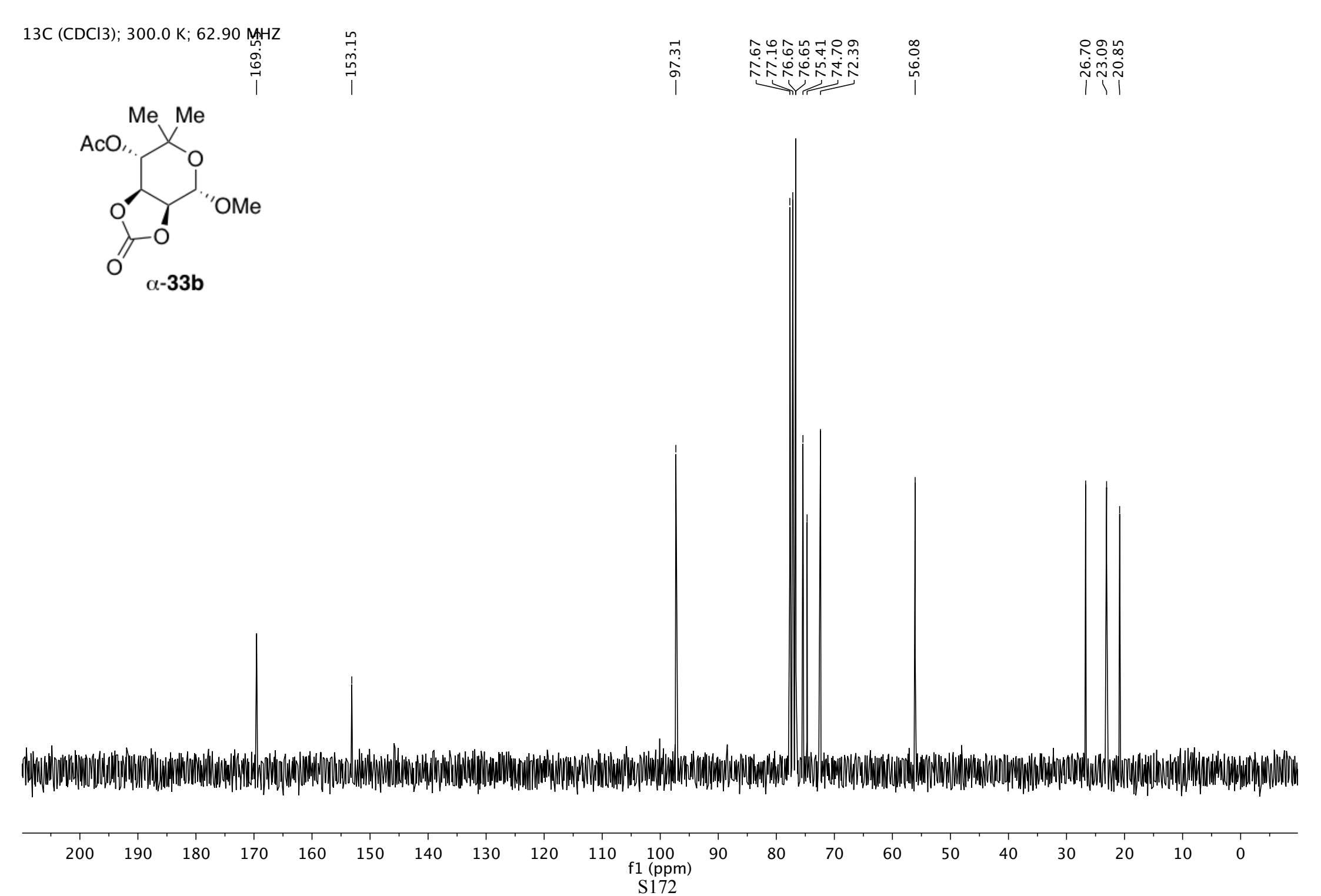

1H (Acetone) : 295.1 K : 400.13 MHz
7.24 7.15 6.66 6.66 6.66 6.16 6.16 6.15 6.15 6.06 6.06 5.99 5.78 5.78 5.67 5.48 5.44 5.39 5.39 5.30 5.27 5.25 5.19 5.18 4.71 4.71 4.70 4.68 4.65 4.64 4.62 4.62 4.61 4.61 4.61 4.60 4.60 4.58 4.55 4.54 4.53 4.50 4.41 4.38 4.26 4.05 4.03 3.81 3.78 3.56 3.56 3.55 3.55 3.52 2.70 2.68 2.66 2.50 1.89 1.89 1.79 1.79 1.68 1.68 1.68 1.33 1.32 1.21 1.20 1.20 1.19 1.17 1.16 0.83 0.82 0.80
7a
0.63 0.71 0.57 0.53 1.37 0.64 0.60 1.21 1.34 1.52 2.16 4.42 0.77 0.64 0.65 0.78 0.67 0.57 4.00 2.67 1.92 0.54 0.47 0.75 2.30 2.33 1.93 2.71 16.74 2.50
.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


1H (MeOD) 298.0K 600.27 MHz
HCOO-
HCOO-
Fidaxomicin (1, Tiacumicin B, Lipiarmycin A3) in CD3OD
0.87
0.81
0.75
0.85
0.82
1.79
0.79
1.77
1.77
0.80
0.82
0.92
0.86
2.49
5.22
0.78
0.79
2.61
0.75
1.82
0.94
2.64
2.82
3.00
0.72
0.72
4.52
15.48
2.72
f1 (ppm)

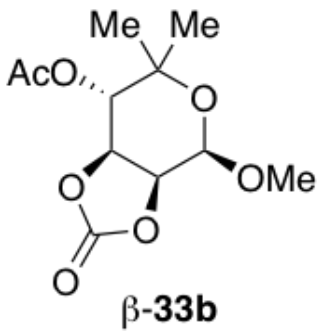
1H (CDCl3); 297.1 K; 400.13 MHZ



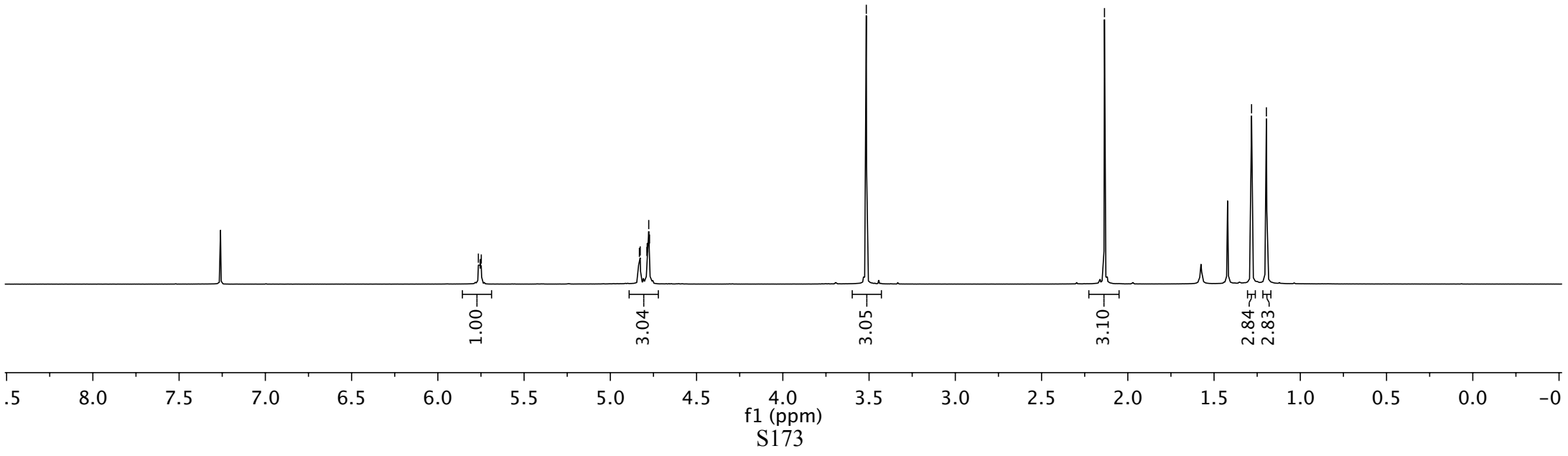
α-**33b**


13C (CDCl3); 300.0 K; 62.90 MHZ
169.51
153.15
97.31
77.67
77.16
76.67
76.65
75.41
74.70
72.39
56.08
26.70
23.09
20.85
Me
Me
AcO
O
OMe
O
O
O
O
α-33b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

1H (CDCl3); 300.0 K; 400.13 MHZ

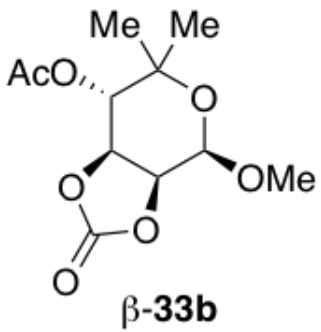


β-**33b**

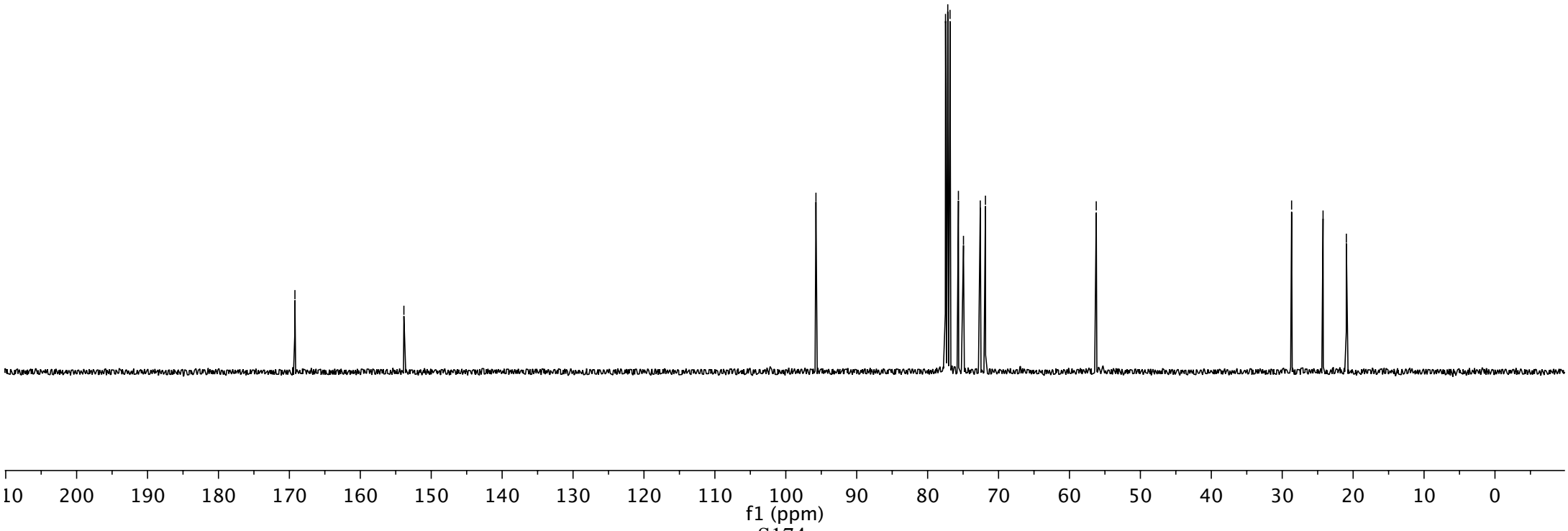


13C (CDCl3); 300.0 K; 100.62 MHZ

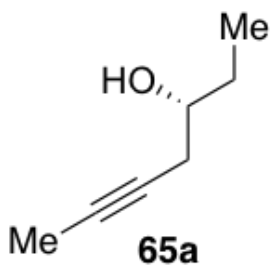
169.22
153.85
95.75
77.48
77.16
76.84
75.66
74.95
72.58
71.85
56.22
28.68
24.24
20.96



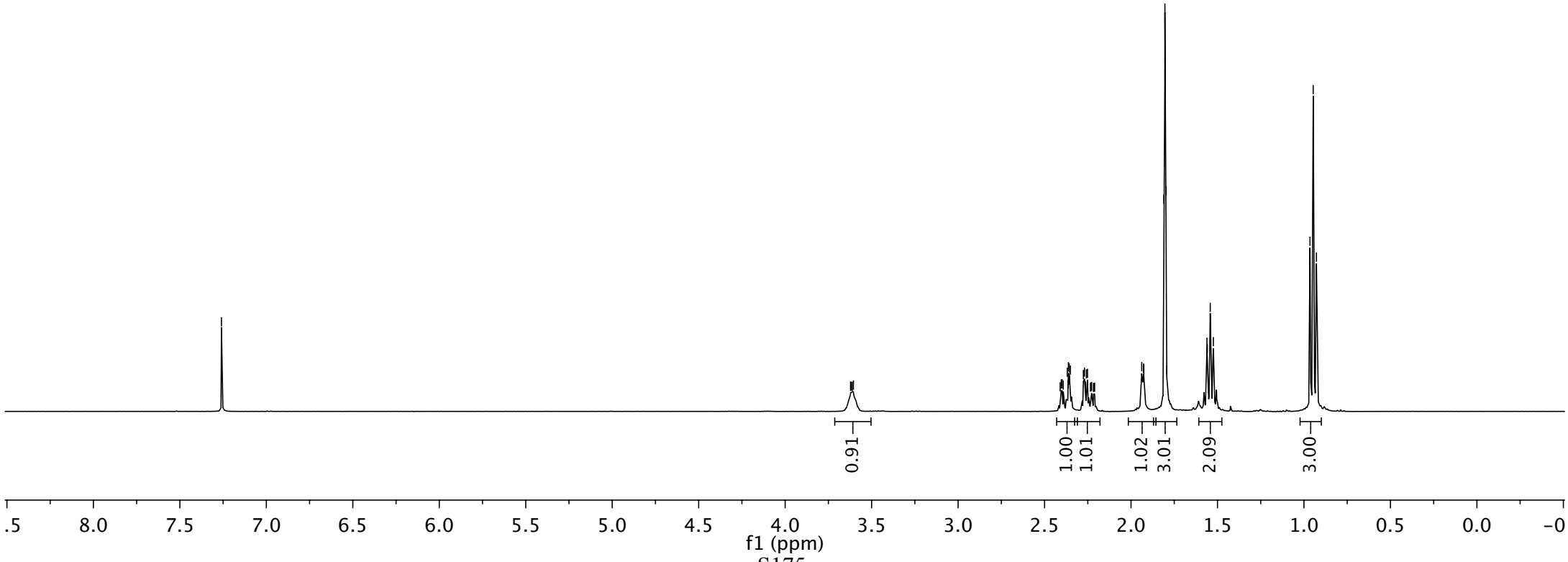
β-**33b**



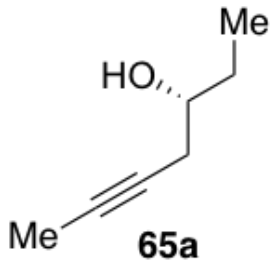
1H (CDCl3); 300.0 K; 400.13 MHZ



65a

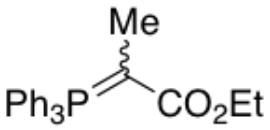


13C (CDCl3); 300.0 K; 100.62 MHZ

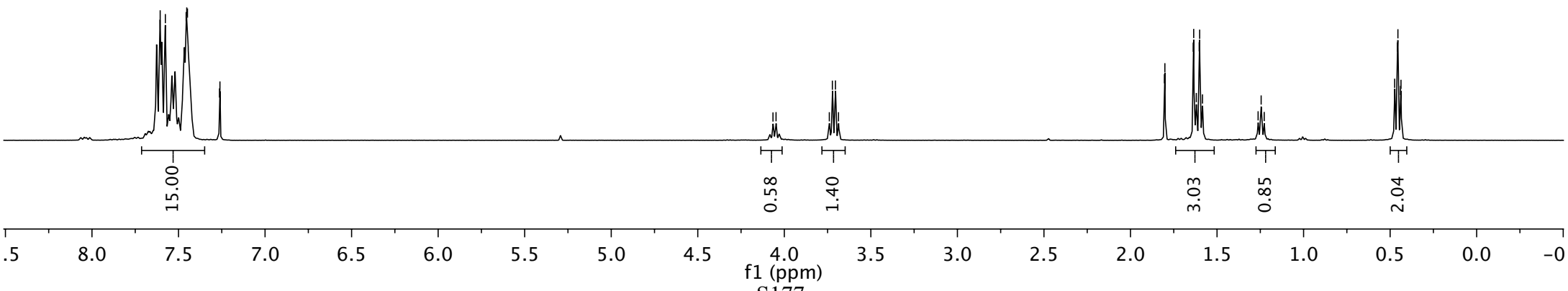


65a

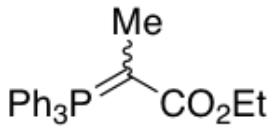
1H (CDCl3); 300.0 K; 400.13 MHZ



67a

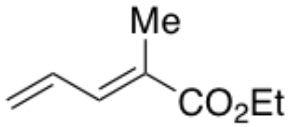


13C (CDCl3); 300.0 K; 100.62 MHZ

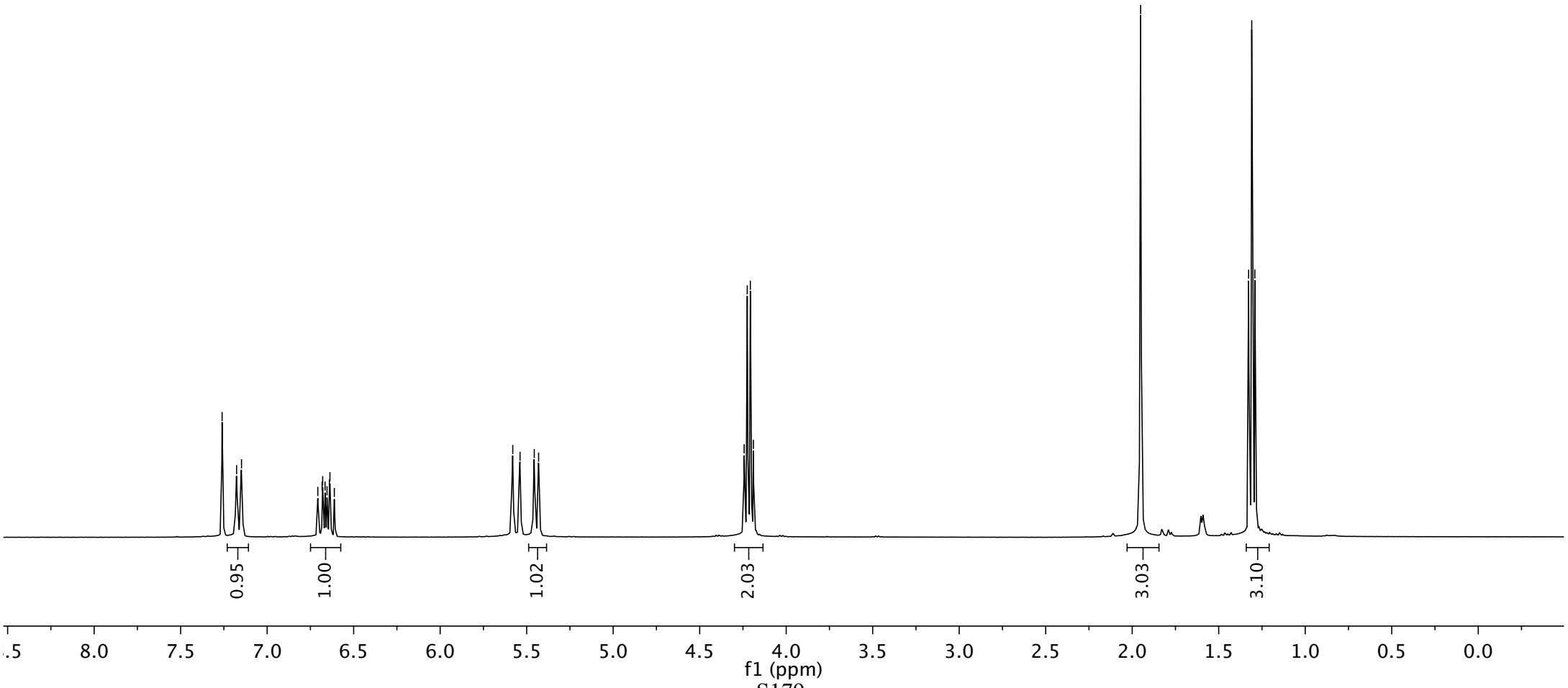


67a

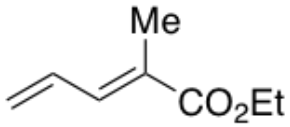
1H (CDCl3); 300.0 K; 400.13 MHz



67b

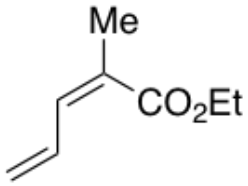


13C (CDCl3); 300.0 K; 100.62 MHZ



67b

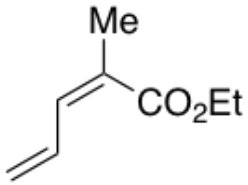
1H (CDCl3, 300.0 K, 400.13 MHz)



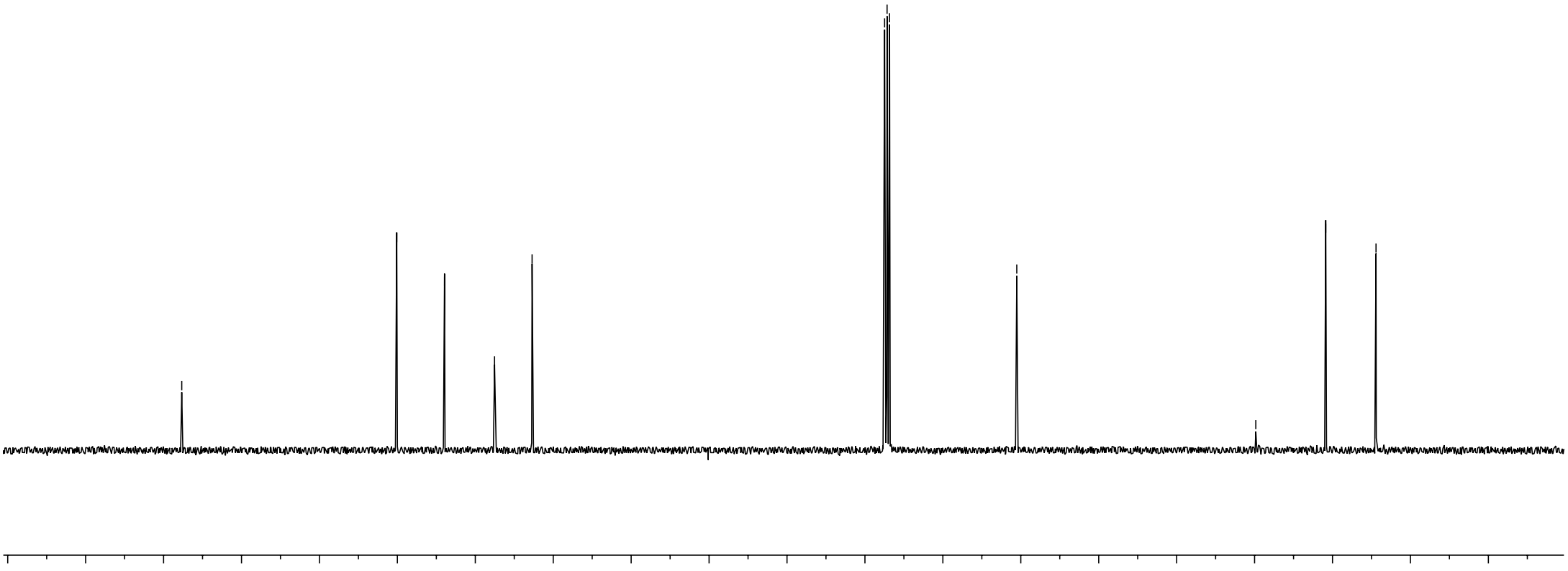
67c

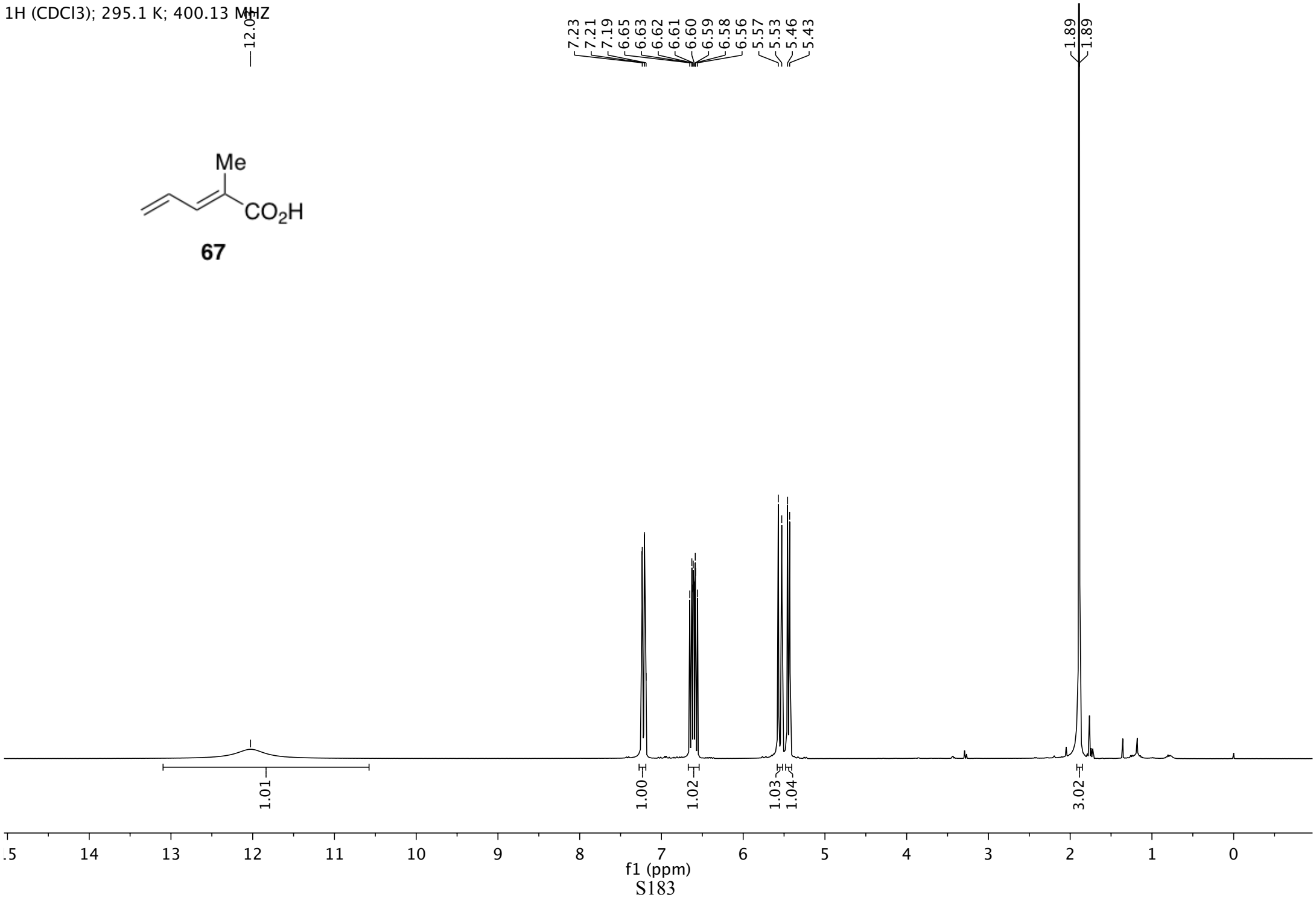
13C (CDCl3); 295.7 K; 100.62 MHZ

167.67
140.08
133.95
127.53
122.71
77.48
77.16
76.84
60.52
29.84
20.87
14.42



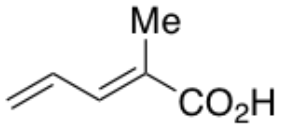
67c



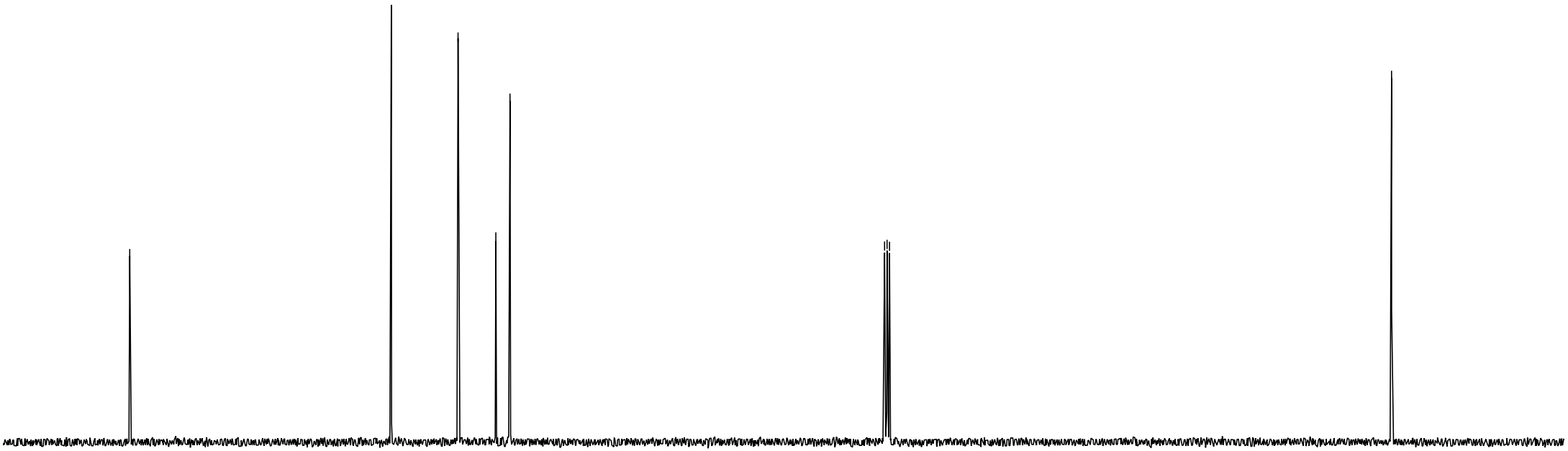

1H (CDCl3); 295.1 K; 400.13 MHZ
12.01
7.23
7.21
7.19
6.65
6.63
6.62
6.61
6.60
6.59
6.58
6.56
5.57
5.53
5.46
5.43
1.89
1.89
Me
CO2H
67
1.01
1.00
1.02
1.03
1.04
3.02
f1 (ppm)

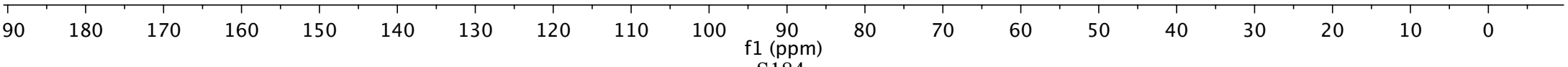
13C (CDCl3), 300.0 K; 100.62 MHZ

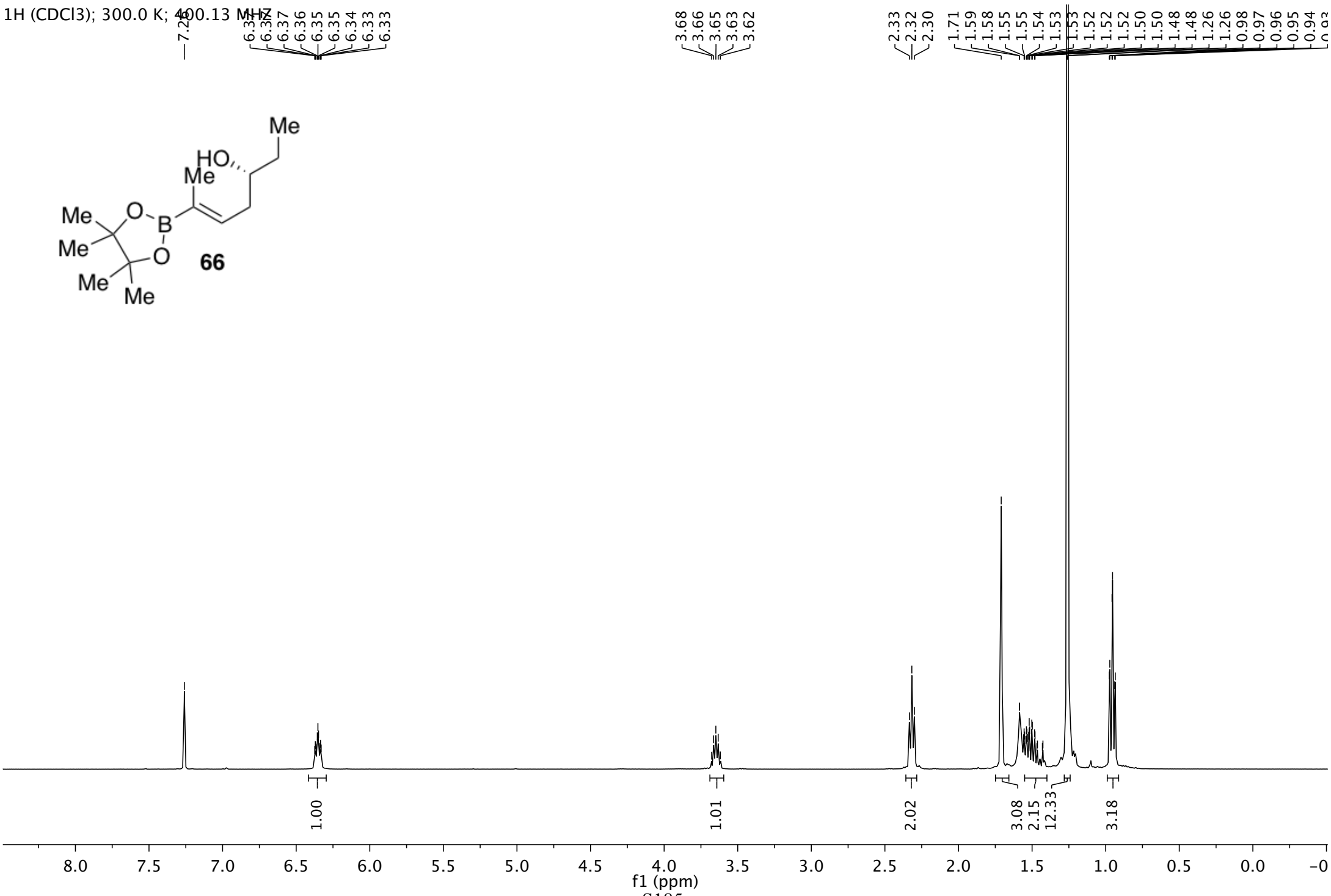
174.34
140.78
132.21
127.36
125.55
77.48
77.16
76.84
12.42



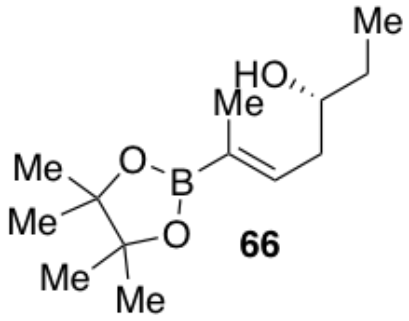
67



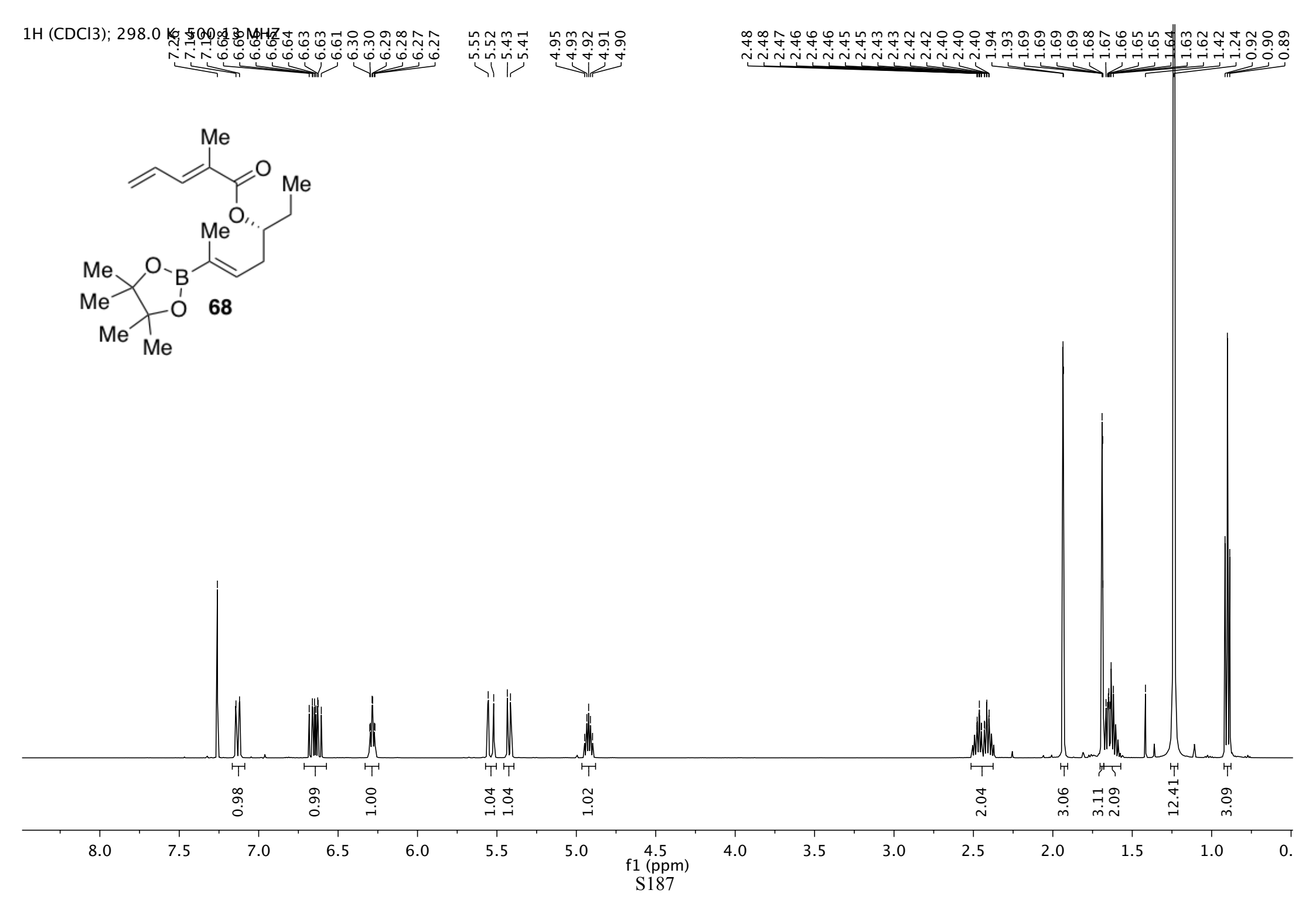



1H (CDCl3); 300.0 K; 400.13 MHz
7.26
6.38
6.38
6.37
6.36
6.35
6.35
6.34
6.33
6.33
3.68
3.66
3.65
3.63
3.62
2.33
2.32
2.30
1.71
1.59
1.58
1.55
1.55
1.54
1.53
1.53
1.52
1.52
1.52
1.50
1.50
1.48
1.48
1.26
1.26
0.98
0.97
0.96
0.95
0.94
Me
HO
Me
Me
O
B
Me
Me
O
Me
Me
66
1.00
1.01
2.02
3.08
2.15
12.33
3.18
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0
f1 (ppm)

13C (CDCl3); 300.0 K; 100.62 MHZ

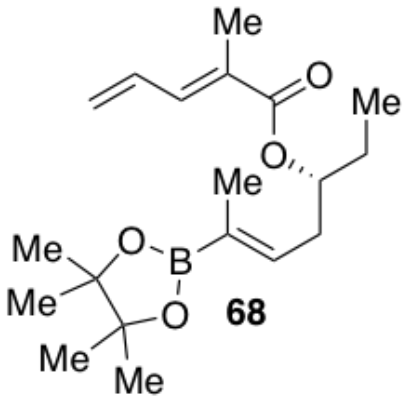


66

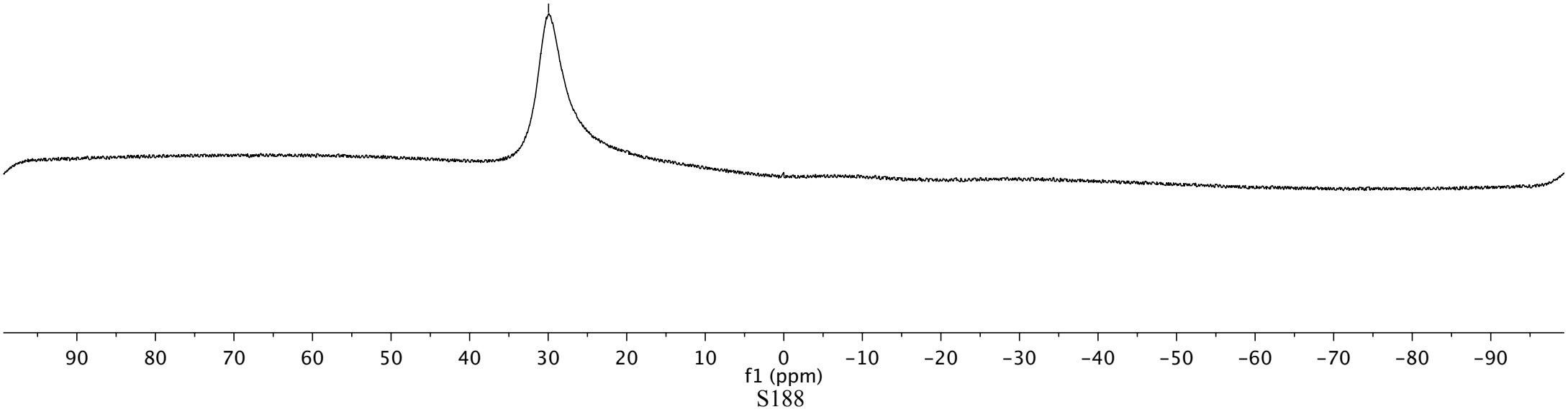

1H (CDCl3); 298.0 K; 500.13 MHz
Me
O
Me
O
Me
Me
O
B
Me
O
Me
Me
Me
68
f1 (ppm)

11B (CDCl3); 300.0 K; 128.38 MHZ

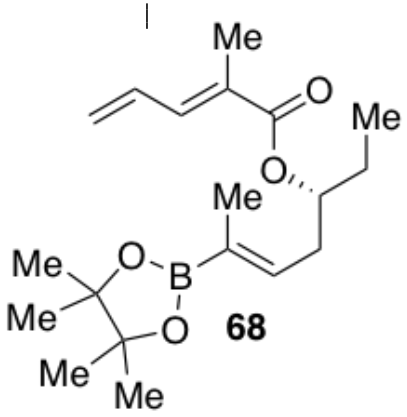
29.95



68

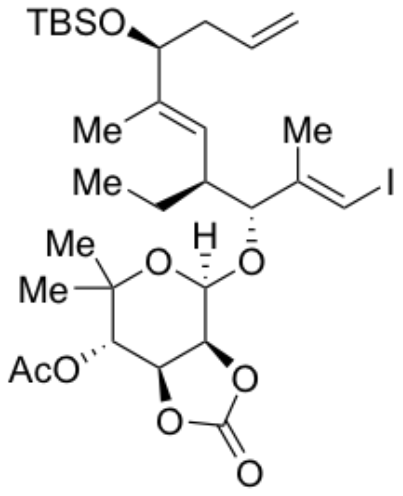


13C (CDCl3); 298.0 K; 125.77 MHZ



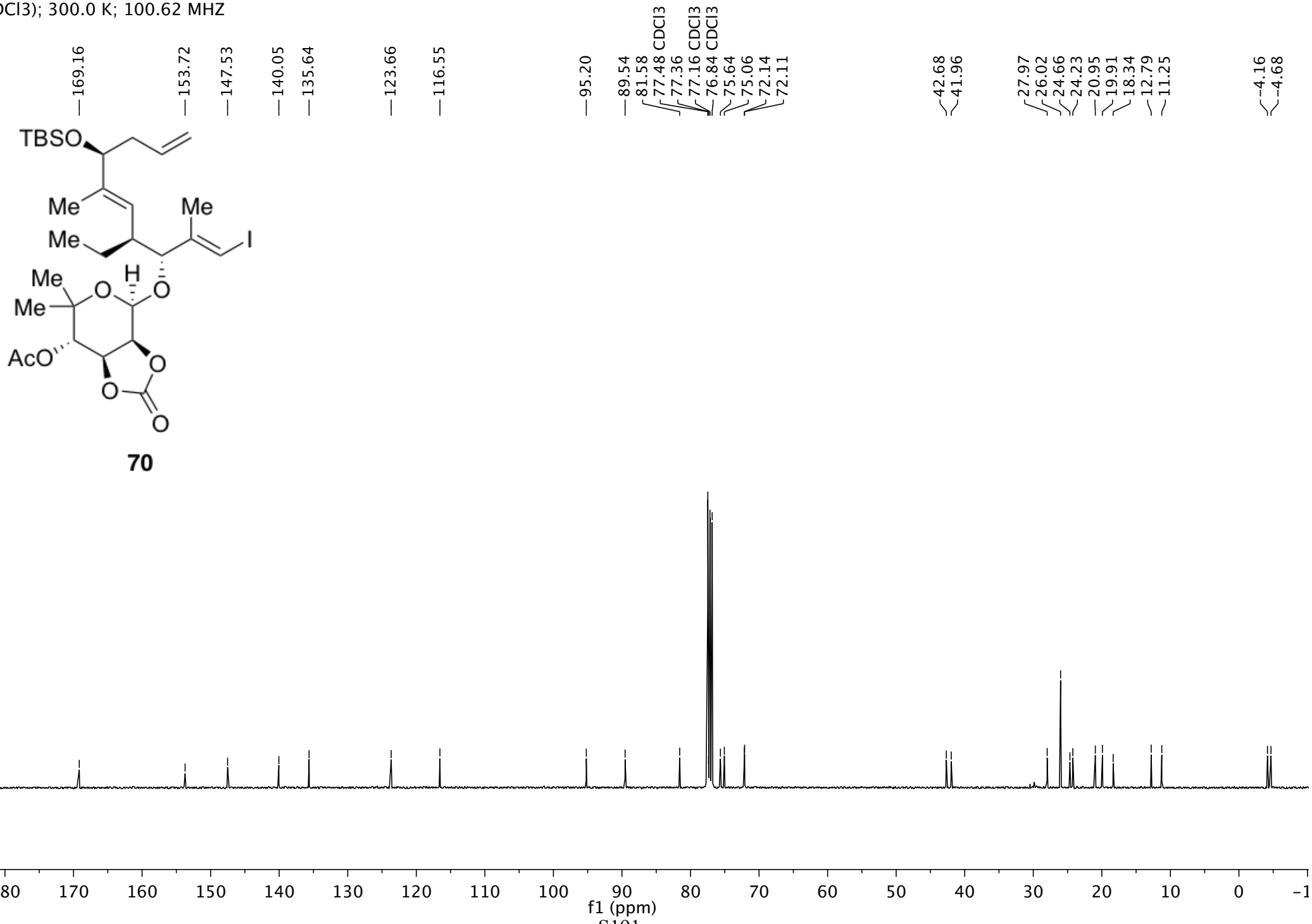
68

1H (CDCl3): 298.0 K: 500.13 MHZ

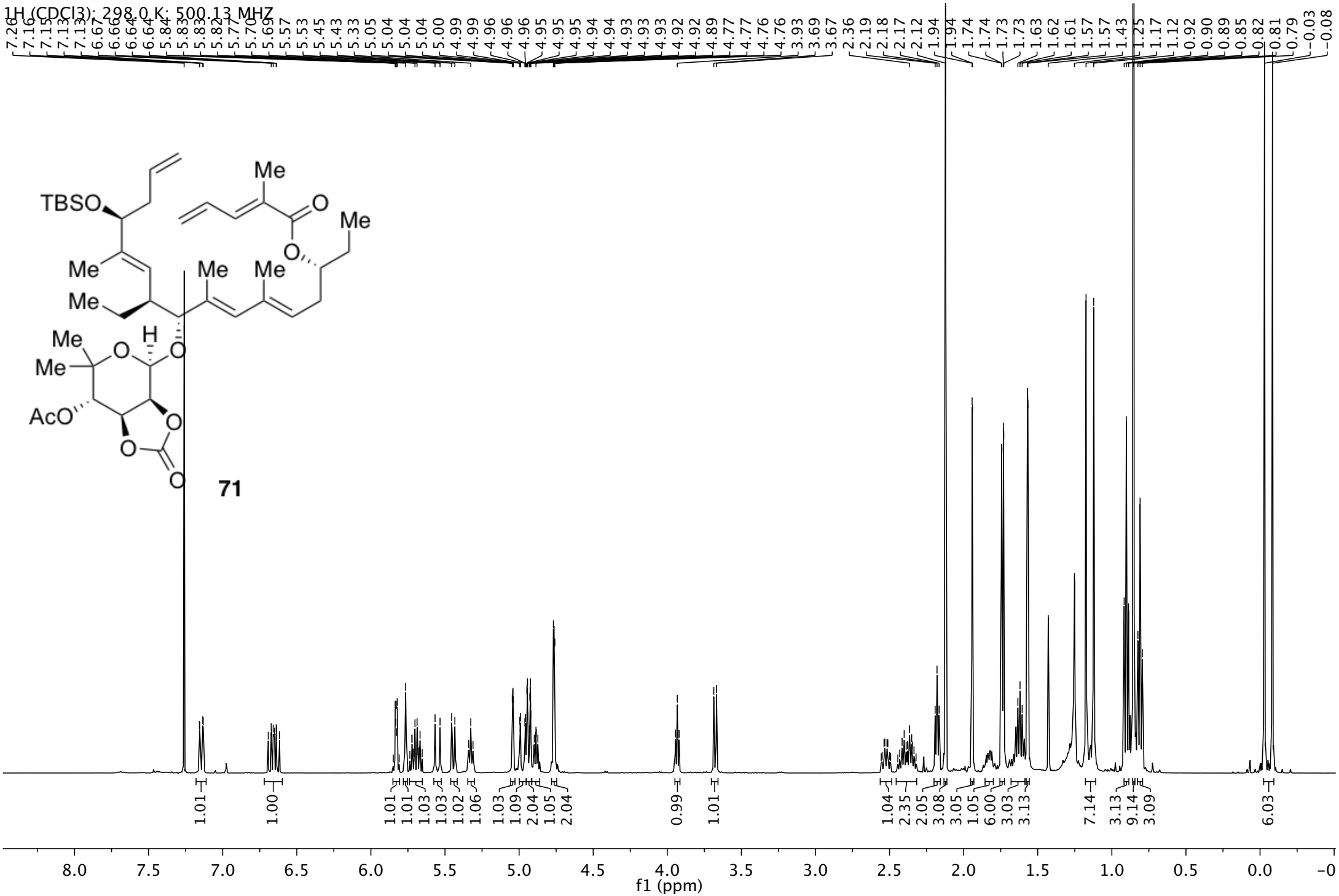


70

13C (CDCl3); 300.0 K; 100.62 MHZ

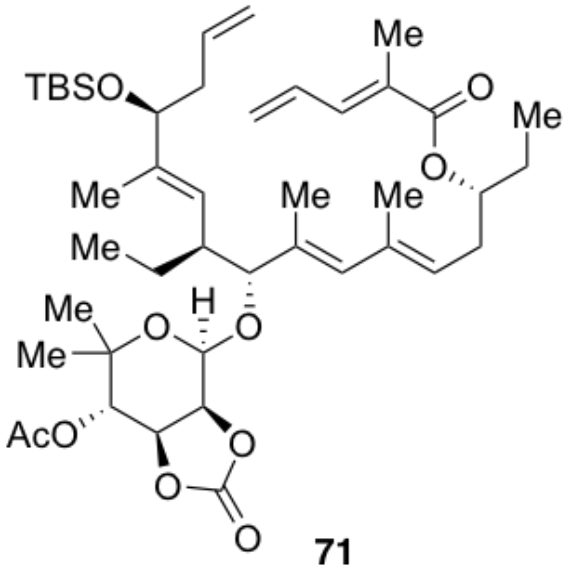


70


1H (CDCl3): 298.0 K: 500.13 MHZ
TBSO
Me
O
Me
O
Me
Me
Me
Me
Me
H
O
O
Me
O
AcO
O
O
O
71
f1 (ppm)

13C (CDCl3); 298.0 K; 125.77 MHZ

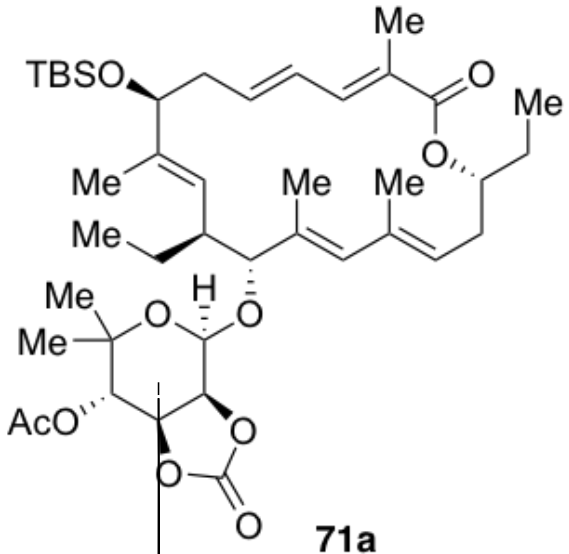
169.12
168.10
153.88
138.86
138.21
135.84
134.63
134.07
133.50
132.41
128.56
125.81
124.71
124.12
116.30
94.24
91.96
77.59
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
75.74
75.55
74.88
72.32
42.46
41.99
32.51
28.05
26.62
25.96
24.69
24.26
20.96
18.29
17.27
13.90
12.89
12.78
11.37
9.88
-4.53
-4.89



71

f1 (ppm)

1H (CDCl3); 300.0 K; 400.13 MHZ

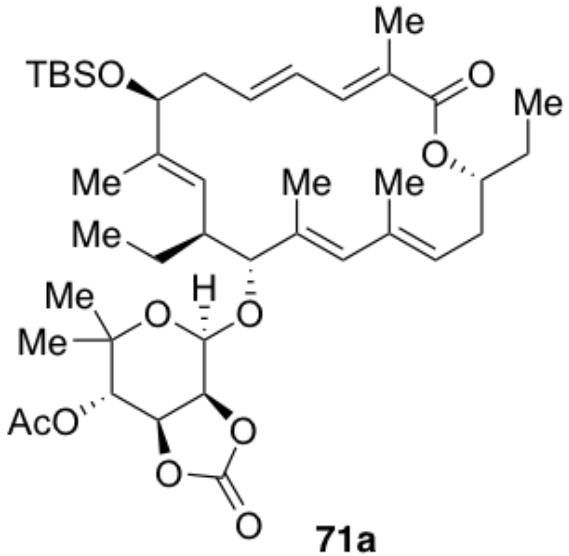


71a

f1 (ppm)

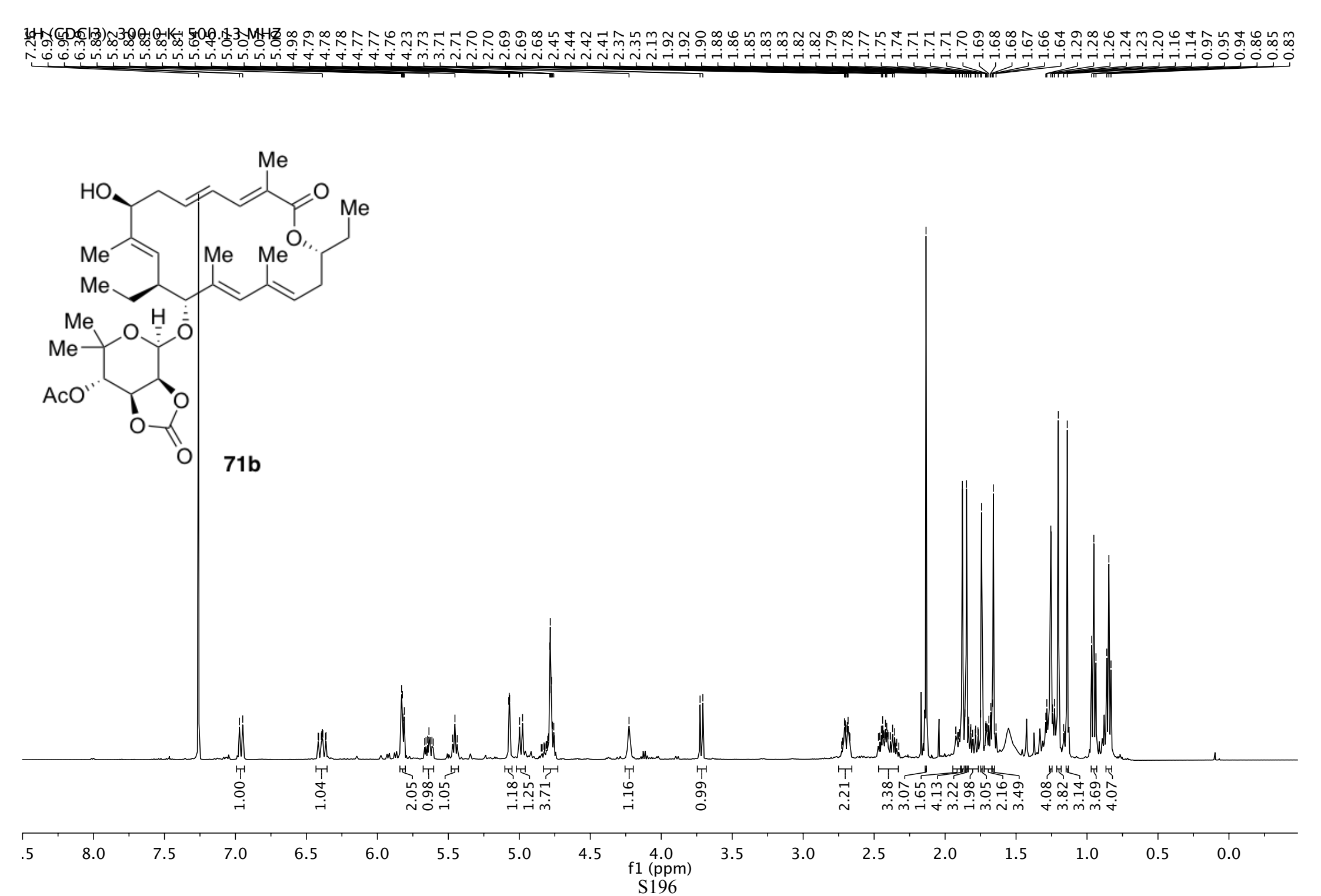
13C (CDCl3); 300.0 K; 100.62 MHZ

169.17
168.96
153.89
140.47
138.76
135.35
135.19
134.86
134.04
127.85
124.91
124.34
123.64
94.20
92.72
77.48 CDCl3
77.36
77.16 CDCl3
76.84 CDCl3
76.84
75.71
74.94
74.61
73.03
72.37
41.59
37.10
31.27
30.48
29.85
28.21
26.24
25.91
25.45
24.16
20.97
18.33
17.03
14.79
13.04
12.15
10.65
10.36
-4.90
-4.95



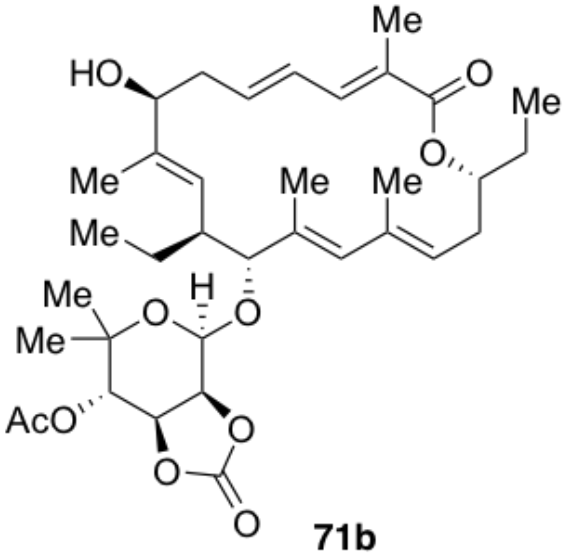
71a

f1 (ppm)


1H (CDCl3, 300.0 K, 500.13 MHz)
71b
f1 (ppm)

13C (CDCl3); 300.0 K; 100.65 MHZ

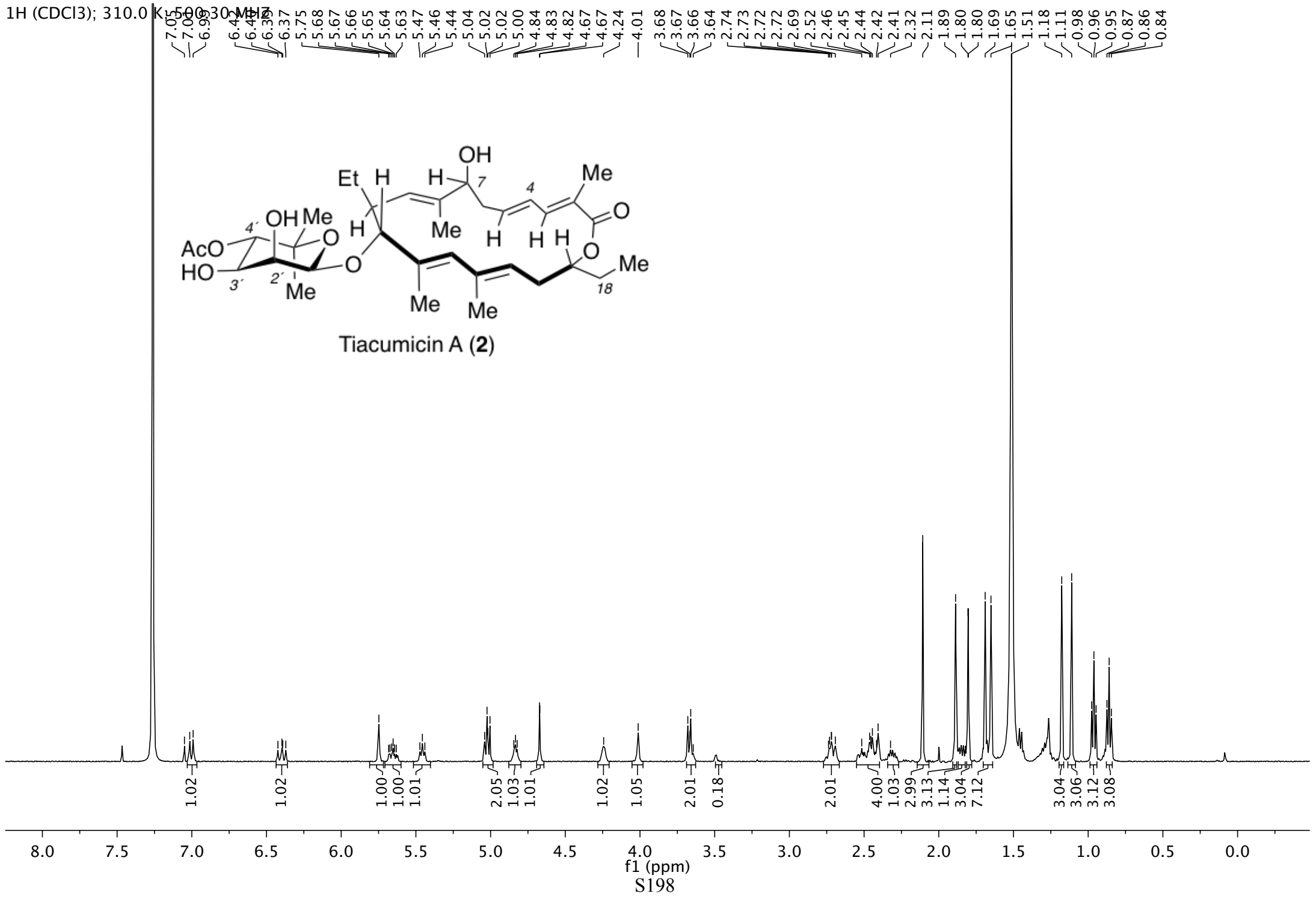
169.22
168.96
153.85
138.97
136.62
136.30
135.32
135.06
133.66
129.83
126.79
126.16
122.95
94.37
92.70
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
75.68
75.07
74.94
72.65
72.36
42.08
36.60
31.76
29.85
28.12
26.82
25.35
24.18
20.99
17.19
15.20
13.40
12.45
10.97
10.05



71b

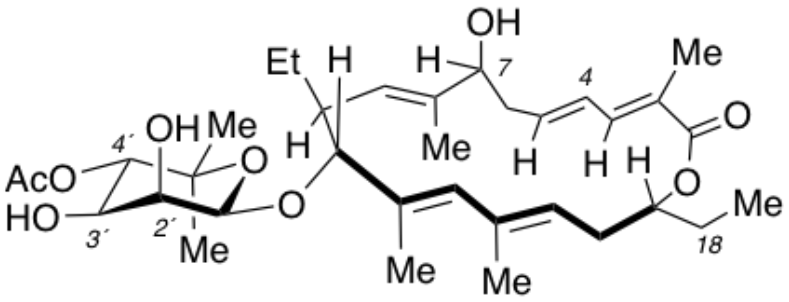
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)

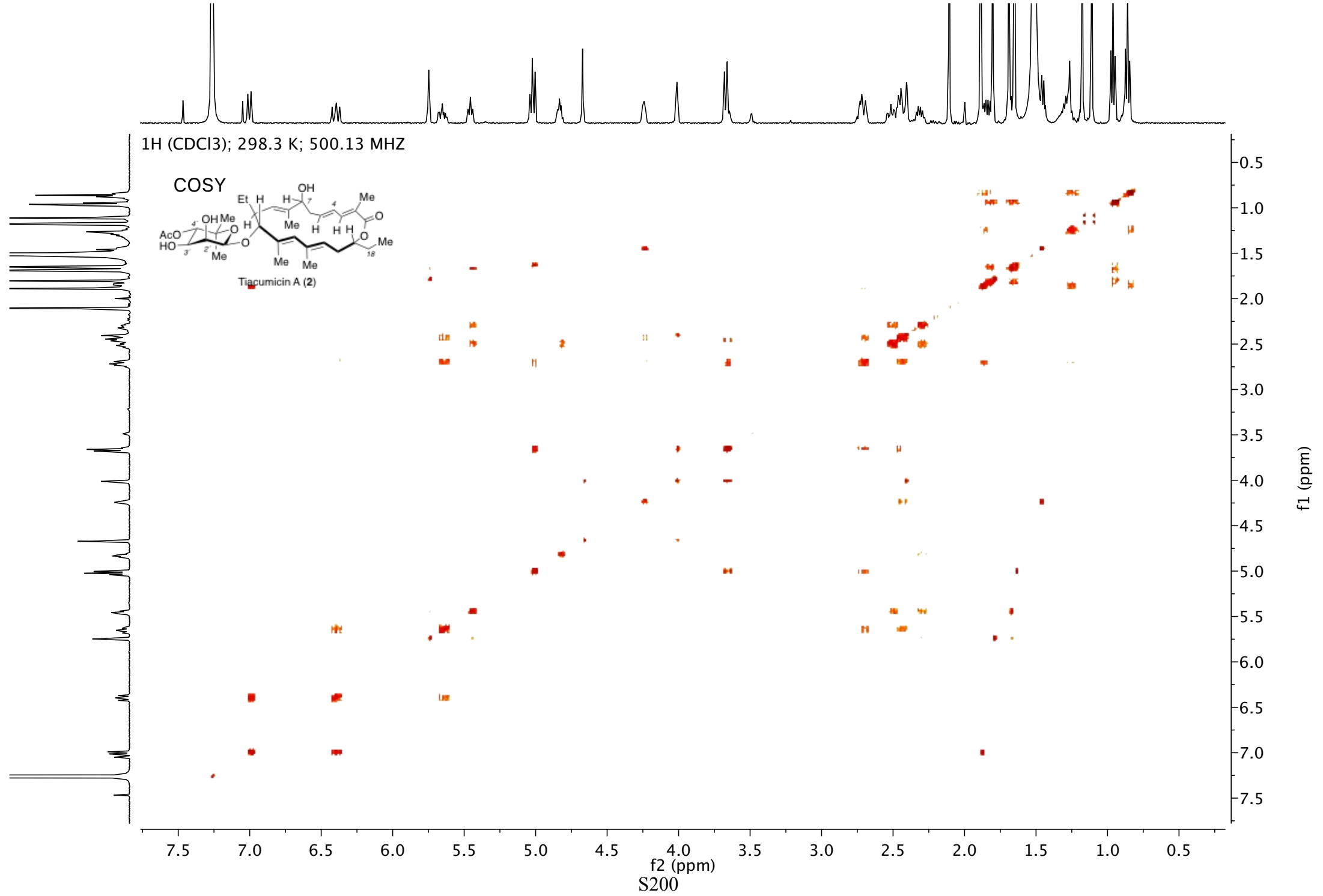

1H (CDCl3); 310.0 K; 500.30 MHz
7.05 7.04 6.99 6.43 6.42 6.39 6.37 5.75 5.68 5.67 5.66 5.65 5.64 5.63 5.47 5.46 5.44 5.04 5.02 5.02 5.00 4.84 4.83 4.82 4.67 4.67 4.24 4.01 3.68 3.67 3.66 3.64 2.74 2.73 2.72 2.72 2.69 2.52 2.46 2.45 2.44 2.42 2.41 2.32 2.11 1.89 1.80 1.80 1.69 1.65 1.51 1.18 1.11 0.98 0.96 0.95 0.87 0.86 0.84
OH
Et H H 7 4 Me
H Me H H H O
AcO 4´ OH Me O
HO 3´ 2´ Me O
Me
Me Me
18
Tiacumicin A (2)
1.02 1.02 1.00 1.00 1.01 2.05 1.03 1.01 1.02 1.05 2.01 0.18 2.01 4.00 1.03 2.99 3.13 1.14 3.04 7.12 3.04 3.06 3.12 3.08
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

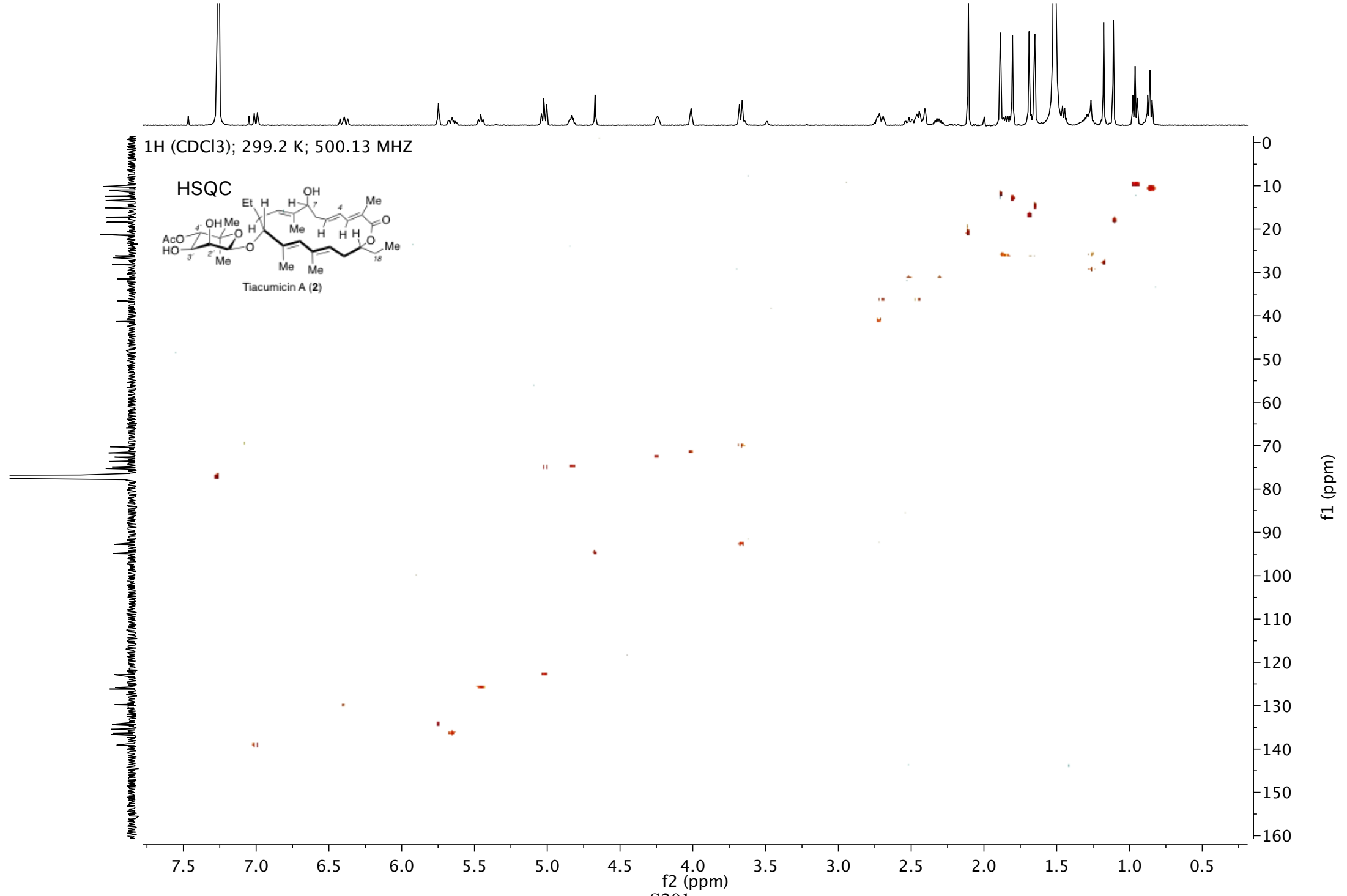
13C (CDCl3); 310.0 K; 125.81 MHZ

171.22
168.80
139.11
136.63
136.33
135.46
134.39
134.26
129.75
126.14
125.80
122.83
94.89
92.76
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
75.28
74.91
73.52
72.64
71.67
70.24
41.34
36.61
31.50
28.20
26.60
26.19
21.22
18.41
17.23
15.07
13.43
12.41
11.00
10.17



Tiacumicin A (**2**)


1H (CDCl3); 298.3 K; 500.13 MHZ
COSY
Tiacumicin A (2)
f2 (ppm)
f1 (ppm)


1H (CDCl3); 299.2 K; 500.13 MHZ
HSQC
Tiacumicin A (2)
f2 (ppm)
f1 (ppm)