Cyclodepsipeptide Alveolaride C: Total Synthesis and Structural Assignment

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Supporting Information

1. General Experimental Procedure:

All moisture sensitive reactions were performed in oven or flame-dried glassware with Teflon coated magnetic stirring bar under argon atmosphere using dry, freshly distilled solvents, unless otherwise noted. Air- and moisture-sensitive liquids were transferred via a gastight syringe and a stainless-steel needle. Reactions were monitored by thin layer chromatography (TLC, Silica gel 60 F254) plates with UV light, ethanolic anisaldehyde (with 1% AcOH and 3.3% conc. H_2SO_4)-heat and aqueous $KMnO_4$ (with K_2CO_3 and 10% aqueous NaOH solution) as developing agents. All workup and purification procedures were carried out with reagent-grade solvents under ambient atmosphere unless otherwise stated. Column chromatography was performed using silica gel 60-120 mesh, 100-200 mesh and 230-400 mesh. Yields mentioned as chromatographically and spectroscopically homogeneous materials unless otherwise stated. Optical rotations were measured using sodium (589, D line) lamp and are reported as follows: $[\alpha]_D^{25}$ (c = mg/100 mL, solvent). Melting points of solids were measured in melting point apparatus. IR spectra were recorded as thin films (for liquids) or KBr matrix (for solids). HRMS were taken using QuadrupleTOF (Q-TOF) micro MS system using electrospray ionisation (ESI) technique. ^{1}H NMR spectra were recorded on 300, 400 and 500 MHz spectrometers in appropriate solvents and calibrated using residual undeuterated solvent as an internal reference, and the chemical shifts are shown in δ ppm scales. Multiplicities of NMR signals are designated as s (singlet), d (doublet), t (triplet), q (quartet), br (broad), m (multiplet, for unresolved lines) etc. ^{13}C and 2D NMR spectra were recorded on 75, 100 and 125 MHz spectrometers.

2. Comparison Table of ^{1}H And ^{13}C NMR of Isolated 2,3-Dihydroxy-4-Methyltetradecanoic Acid (DHMTDA) With Synthetic DHMTDA Fragments.

2.1 Table ST1: ^{1}H and ^{13}C NMR Comparison of Isolated 2,3-Dihydroxy-4-Methyltetra-decanoic Acid (DHMTDA) with Synthetic DHMTDA 7a.

Position	**^{1}H**		**^{13}C**	
	Reported (MeOD-d_4, 600 MHz)	Synthesized (MeOD-d_4, 300 MHz)	Reported (MeOD-d_4, 125 MHz)	Synthesized (MeOD-d_4, 75 MHz)
1			175.6	175.71
2	4.24 (d, J = 2.8 Hz)	4.25 (d, J = 1.9 Hz)	71.5	71.20
3	3.59 (dd, J = 7.8, 2.8 Hz)	3.54 (d, J = 9.0 Hz)	76.1	76.51
4	1.77 (m)	1.77-1.69 (m)	35.1	35.28
4-CH_3	1.02 (d, J = 6.7 Hz)	0.95 – 0.87 (m)	14.3	14.71
5	1.50 (m); 1.19 (m)	1.49 – 1.40 (m); 1.22-1.16 (m)	32.8	32.39
6	1.25-1.45 (m)	1.30 (brs)	31.7	31.71
7	1.25-1.45 (m)	1.30 (brs)	29.6	29.81
8	1.25-1.45 (m)	1.30 (brs)	29.4	29.44
9	1.25-1.45 (m)	1.30 (brs)	29.4	29.44
10	1.25-1.45 (m)	1.30 (brs)	29.3	29.39
11	1.25-1.45 (m)	1.30 (brs)	29.1	29.11
12	1.25-1.45 (m)	1.30 (brs)	26.4	26.48
13	1.25-1.45 (m)	1.30 (brs)	22.3	22.36
14	0.93 (t, J = 7.0 Hz)	0.95 – 0.87 (m)	13.0	13.08

2.2 Table ST2: ^{1}H and ^{13}C NMR Comparison of Isolated 2,3-Dihydroxy-4-Methyltetra-decanoic Acid (DHMTDA) with Synthetic DHMTDA 7b.

Position	**^{1}H**		**^{13}C**	
	Reported (MeOD-d_4, 600 MHz)	Synthesized (MeOD-d_4, 300 MHz)	Reported (MeOD-d_4, 125 MHz)	Synthesized (MeOD-d_4, 75 MHz)
1			175.6	175.06
2	4.24 (d, J = 2.8 Hz)	4.11 (d, J = 5.2 Hz)	71.5	72.35
3	3.59 (dd, J = 7.8, 2.8 Hz)	3.48 (t, J = 5.9 Hz)	76.1	77.26
4	1.77 (m)	1.77 (dt, J = 13.8, 5.2 Hz)	35.1	34.53
4-CH_3	1.02 (d, J = 6.7 Hz)	0.90 (d, J = 6.8 Hz)	14.3	15.15
5	1.50 (m); 1.19 (m)	1.37-1.34 (m); 1.22-1.10 (m)	32.8	31.69
6	1.25-1.45 (m)	1.24 (brs)	31.7	31.10
7	1.25-1.45 (m)	1.24 (brs)	29.6	29.79
8	1.25-1.45 (m)	1.24 (brs)	29.4	29.44
9	1.25-1.45 (m)	1.24 (brs)	29.4	29.44
10	1.25-1.45 (m)	1.24 (brs)	29.3	29.38
11	1.25-1.45 (m)	1.24 (brs)	29.1	29.10
12	1.25-1.45 (m)	1.24 (brs)	26.4	26.68
13	1.25-1.45 (m)	1.24 (brs)	22.3	22.35
14	0.93 (t, J = 7.0 Hz)	0.84 (t, J = 6.4 Hz)	13.0	13.09

2.3 Table ST3: ^{1}H and ^{13}C NMR Comparison of Isolated 2,3-Dihydroxy-4-Methyltetra-decanoic Acid (DHMTDA) with Synthetic DHMTDA 7c.

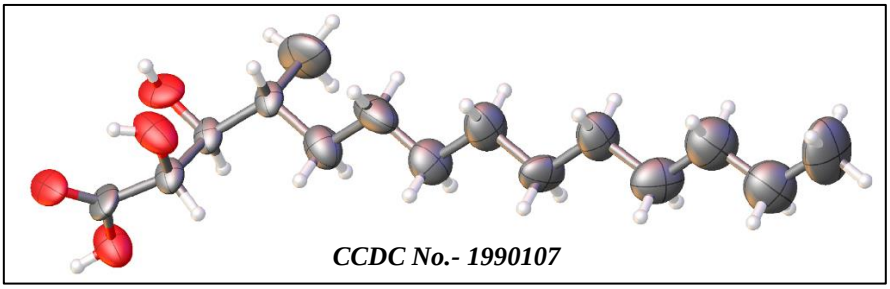
Position	^{1}H		^{13}C	
	Reported (MeOD-d_4, 600 MHz)	Synthesized (MeOD-d_4, 300 MHz)	Reported (MeOD-d_4, 125 MHz)	Synthesized (MeOD-d_4, 75 MHz)
1			175.6	175.51
2	4.24 (d, J = 2.8 Hz)	4.04 (d, J = 7.0 Hz)	71.5	72.17
3	3.59 (dd, J = 7.8, 2.8 Hz)	3.60 (dd, J = 7.0, 4.1 Hz)	76.1	75.08
4	1.77 (m)	1.81 (dt, J = 12.8, 4.3 Hz)	35.1	33.66
4-CH_3	1.02 (d, J = 6.7 Hz)	0.89-0.87 (m)	14.3	13.06
5	1.50 (m); 1.19 (m)	1.48 – 1.39 (m); 1.22-1.15 (m)	32.8	33.48
6	1.25-1.45 (m)	1.29 – 1.24 (m)	31.7	31.66
7	1.25-1.45 (m)	1.29 – 1.24 (m)	29.6	29.58
8	1.25-1.45 (m)	1.29 – 1.24 (m)	29.4	29.39
9	1.25-1.45 (m)	1.29 – 1.24 (m)	29.4	29.39
10	1.25-1.45 (m)	1.29 – 1.24 (m)	29.3	29.36
11	1.25-1.45 (m)	1.29 – 1.24 (m)	29.1	29.07
12	1.25-1.45 (m)	1.29 – 1.24 (m)	26.4	26.81
13	1.25-1.45 (m)	1.29 – 1.24 (m)	22.3	22.32
14	0.93 (t, J = 7.0 Hz)	0.89 – 0.87 (m)	13.0	12.44

2.4 Table ST4: ^{1}H and ^{13}C NMR Comparison of Isolated 2,3-Dihydroxy-4-Methyltetra-decanoic Acid (DHMTDA) with Synthetic DHMTDA 7d.

Position	^{1}H		^{13}C	
	Reported (MeOD-d_4, 600 MHz)	Synthesized (MeOD-d_4, 300 MHz)	Reported (MeOD-d_4, 125 MHz)	Synthesized (MeOD-d_4, 75 MHz)
1			175.6	175.61
2	4.24 (d, J = 2.8 Hz)	4.21 (d, J = 2.8 Hz)	71.5	71.44
3	3.59 (dd, J = 7.8, 2.8 Hz)	3.56 (dd, J = 7.8, 2.7 Hz)	76.1	76.17
4	1.77 (m)	1.78 – 1.69 (m)	35.1	35.15
4-CH_3	1.02 (d, J = 6.7 Hz)	0.99 (d, J = 6.7 Hz)	14.3	14.38
5	1.50 (m); 1.19 (m)	1.49 – 1.44 (m); 1.19 – 1.14 (m)	32.8	32.85
6	1.25-1.45 (m)	1.29 (brs)	31.7	31.70
7	1.25-1.45 (m)	1.29 (brs)	29.6	29.66
8	1.25-1.45 (m)	1.29 (brs)	29.4	29.42
9	1.25-1.45 (m)	1.29 (brs)	29.4	29.38
10	1.25-1.45 (m)	1.29 (brs)	29.3	29.37
11	1.25-1.45 (m)	1.29 (brs)	29.1	29.11
12	1.25-1.45 (m)	1.29 (brs)	26.4	26.45
13	1.25-1.45 (m)	1.29 (brs)	22.3	22.37
14	0.93 (t, J = 7.0 Hz)	0.89 (t, J = 6.9 Hz)	13.0	13.08

3. X-Ray Crystallographic Data for ent-7d.

3.1 Figure SF1: *Molecular structure of* ***ent-7d****, shown with 50% probability thermal ellipsoids (carbon, grey; oxygen, red; hydrogen, white).*

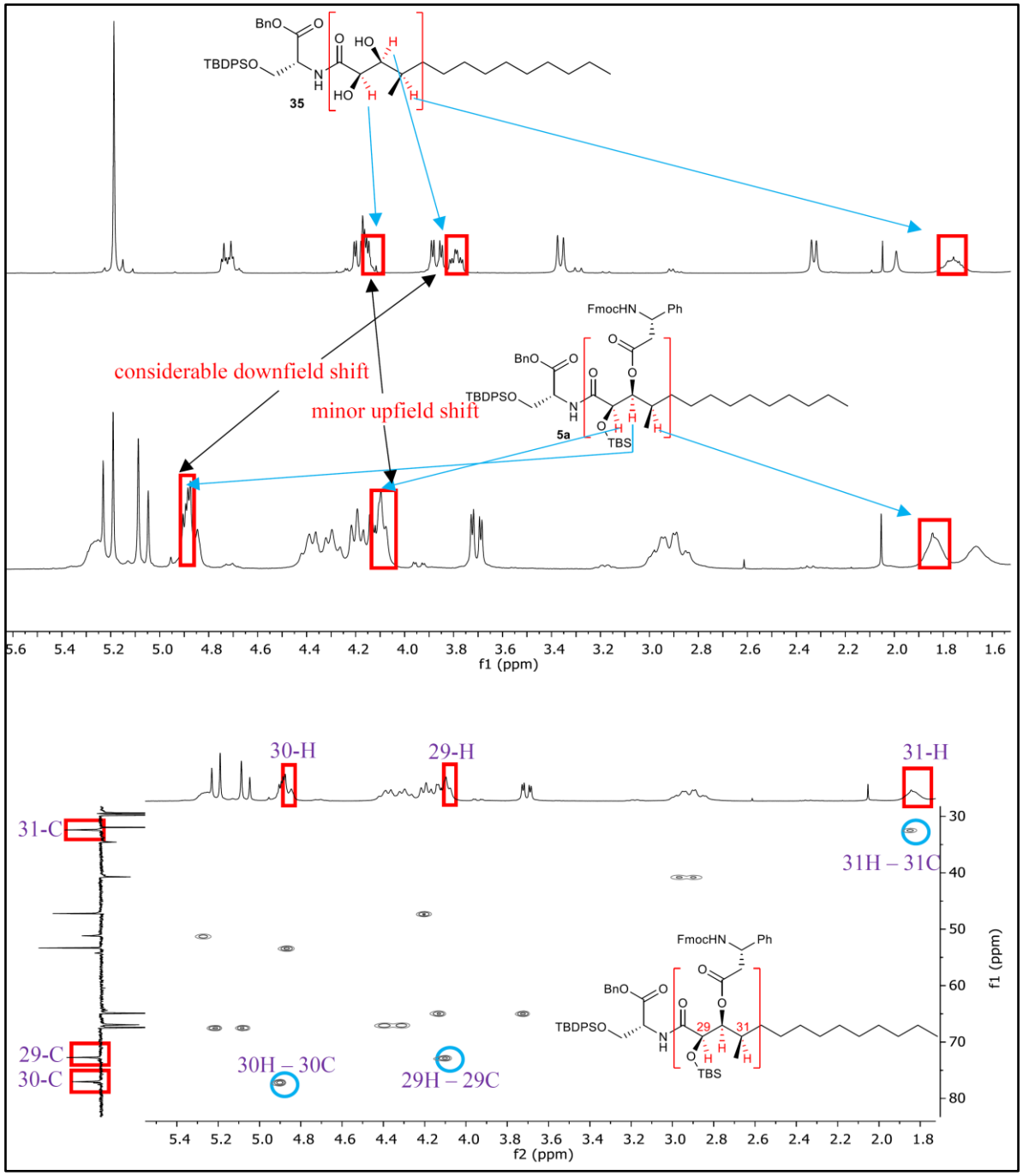


CCDC No.- 1990107

3.2 Table ST5: *X-ray crystallographic data for compound* ***ent-7d*** *at 301 K.*

Empirical formula	$C_{15}H_{30}O_4$
Formula weight	274.39
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.380(12)
b/Å	5.067(7)
c/Å	19.58(3)
α/°	90
β/°	94.25(4)
γ/°	90
Volume/Å^3	829(2)
Z	2
ρ_{calc}g/cm^3	1.099
μ/mm^{-1}	0.077
F(000)	304.0
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.874 to 49.994
Index ranges	$-9 \le h \le 9$, $-6 \le k \le 5$, $-17 \le l \le 23$
Reflections collected	4883
Independent reflections	2666 [R_{int} = 0.1653, R_{sigma} = 0.3293]
Data/restraints/parameters	2666/6/153
Goodness-of-fit on F^2	0.938
Final R indexes [I>=2σ (I)]	R_1 = 0.1285, wR_2 = 0.2632
Final R indexes [all data]	R_1 = 0.3111, wR_2 = 0.3464
Largest diff. peak/hole / e Å^{-3}	0.27/-0.29
Flack parameter	-3.3(10)

4. Figure SF2: NMR Comparison for the Confirmation of C-3 OH Esterification of Compound 35.



5. Comparison Table of ^{1}H and ^{13}C NMR of Isolated Alveolaride C with Synthetic Alveolarides.

5.1. Table ST6: ^{1}H and ^{13}C NMR Comparison of Isolated Alveolaride C with Diastereomer of Alveolaride C (3a).

Residue	Position	^{1}H		^{13}C	
		Reported (DMSO-d_6, 600 MHz)	Synthesized (DMSO-d_6, 300 MHz)	Reported (DMSO-d_6, 600 MHz)	Synthesized (DMSO-d_6, 75 MHz)
Phe	1			170.1	**168.72**
	2	3.15 (m); 2.87 (dd, *J* = 15.7, 4.4 Hz)	2.99 (d, *J* = 7.8 Hz); 2.83 – 2.77 (m)	38.5	**merged with DMSO**
	3	4.82 (m)	**5.12 (q, *J* = 7.6 Hz)**	49.9	49.70
	3-NH	7.61 (d, *J* = 7.4 Hz)	**7.46 (d, *J* = 7.4 Hz)**		
	4			141.5	**143.00**
	5	7.25 (m)	**7.32 – 7.28 (m)**	126.4	126.36
	6	7.25 (m)	**7.32 – 7.28 (m)**	126.4	128.80
	7	7.16 (m)	**7.21 – 7.18 (m)**	126.8	127.36
	8	7.25 (m)	**7.32 – 7.28 (m)**	126.4	128.80
	9	7.25 (m)	**7.32 – 7.28 (m)**	126.4	126.36
Gln	10			171.9	**170.88**
	11	3.93 (ddd, *J* = 9.6, 7.6, 5.5 Hz)	4.08 – 4.00 (m)	55.0	**54.10**
	11-NH	8.20 (d, *J* = 7.6 Hz)			
	12	1.95; 1.83 (m)	2.13 – 2.07 (m); 1.92 – 1.87 (m)	27.1	27.38
	13	2.04 (m)	2.13 – 2.07 (m); **2.32 – 2.26 (m)**	32.2	**33.17**
	14			174.2	**175.15**
	14-NH_2	7.24 (brs), 6.78 (brs)	7.26 – 7.23 (m); 6.55 (brs),		
Ser	25			171.7	**169.78**
	26	4.47 (m)	**4.68 – 4.60 (m)**	54.7	**53.12**
	26-NH	7.55 (d, *J* = 6.9 Hz)	**7.37 – 7.35 (m)**		

	27	3.59 (dd, *J* = 11.0, 5.4 Hz); 3.46 (dd, *J* = 11.0, 5.4 Hz)	3.62 (d, *J* = 5.4 Hz); 3.49 – 7.46 (m, 1H)	62.6	62.91
	27-OH		4.87 (t, *J* = 5.9 Hz)		
DHMTDA	28				172.20
	29	4.06	4.08 – 4.00 (m)	71.1	**72.51**
	29-OH		4.87 (t, *J* = 5.9 Hz)		
	30	4.71 (d, *J* = 8.2 Hz)	**4.99 (d, *J* = 4.7 Hz)**	76.8	**77.18**
	31	1.83 (m)	1.74-1.82 (m)	34.1	**34.90**
	31-CH_3	0.68 (d, *J* = 6.8 Hz)	**0.90 – 0.84 (m)**	15.7	**15.12**
	32	1.26 (m), 1.02 (m)	1.24 (brs)	32.7	**31.78**
	33	1.25 (m)	1.24 (brs)	22.5	22.59
	34	1.25 (m)	1.24 (brs)	26.5	26.31
	35	1.25 (m)	1.24 (brs)	29.2	29.21
	36	1.25 (m)	1.24 (brs)	29.4	29.38
	37	1.25 (m)	1.24 (brs)	29.49	29.50
	38	1.25 (m)	1.24 (brs)	29.52	29.52
	39	1.25 (m)	1.24 (brs)	29.7	29.64
	40	1.25 (m)	1.24 (brs)	31.8	31.62
	41	0.86 (t, *J* = 7.1 Hz)	**0.90 – 0.84 (m)**	14.4	14.45
Trp	CO			172. 7	172.60
	NH	8.62 (d, *J* = 6.0 Hz)	8.66 (d, *J* = 6.2 Hz)		
	H_α	4.22 (d, *J* = 9.1, 5.5 Hz)	4.22 – 4.28 (m, 1H),	56.4	**57.41**
	H_β	3.16 (m)	3.14 – 3.12 (m)	27.3	**26.67**
	NH	10.91(d, *J* = 2.6 Hz)	10.90 (brs)		
	2	7.27 (d, *J* = 2.6 Hz)	7.26 – 7.23 (m)	124.1	124.14
	3			110.2	110.12
	3a			127.6	127.66
	4	7.54 (brd, *J* = 7.7 Hz)	7.54 (d, *J* = 7.9 Hz)	118.5	118.49
	5	7.01 (ddd, *J* = 7.7, 6.9, 1.0 Hz)	7.01 (t, *J* = 7.3 Hz)	118. 8	118.87
	6	7.08 (ddd, *J* = 8.2, 6.9, 1.2 Hz)	7.09 (t, *J* = 7.5 Hz)	121.4	121.50
	7	7.35 (brd, *J* = 8.2 Hz)	7.37 – 7.35 (m)	111.8	111.90
	8a			136.6	136.61

5.2. Table ST7: ^{1}H and ^{13}C NMR Comparison of Isolated Alveolaride C with Diastereomer of Alveolaride C (3b).

Residue	Position	^{1}H		^{13}C	
		Reported (DMSO-d_6, 600 MHz)	Synthesized (DMSO-d_6, 300 MHz)	Reported (DMSO-d_6, 600 MHz)	Synthesized (DMSO-d_6, 100 MHz)
Phe	1			170.1	170.07
	2	3.15 (m); 2.87 (dd, *J* = 15.7, 4.4 Hz)	**2.83 (d, *J* = 8.0 Hz)**	38.5	**40.00**
	3	4.82 (m)	**5.16 (q, *J* = 7.9 Hz)**	49.9	**49.11**
	3-NH	7.61 (d, *J* = 7.4 Hz)	**7.32 – 7.30 (m)**		
	4			141.5	**142.76**
	5	7.25 (m)	**7.32 – 7.30 (m)**	126.4	126.55
	6	7.25 (m)	**7.32 – 7.30 (m)**	126.4	128.68
	7	7.16 (m)	7.16-7.19 (m)	126.8	**127.20**
	8	7.25 (m)	**7.32 – 7.30 (m)**	126.4	128.68
	9	7.25 (m)	**7.32 – 7.30 (m)**	126.4	126.55
Gln	10			171.9	**172.03**
	11	3.93 (ddd, *J* = 9.6, 7.6, 5.5 Hz)	3.98 – 3.92 (m)	55.0	**54.10**
	11-NH	8.20 (d, *J* = 7.6 Hz)	7.59 (d, *J* = 6.9 Hz)		
	12	1.95; 1.83 (m)	1.99 – 1.93 (m); 1.89 – 1.80 (m)	27.1	**26.31**
	13	2.04 (m)	2.09 (t, *J* = 7.5 Hz)	32.2	**31.56**
	14			174.2	174.47
	14-NH_2	7.24 (brs), 6.78 (brs)	7.24 – 7.22 (m); 6.77 (s)		
Ser	25			171.7	**170.65**
	26	4.47 (m)	4.42 (q, *J* = 6.5, 5.7 Hz)	54.7	**55.44**
	26-NH	7.55 (d, *J* = 6.9 Hz)	**7.85 (d, *J* = 5.5 Hz)**		
	27	3.59 (dd, *J* = 11.0, 5.4 Hz); 3.46 (dd, *J* = 11.0, 5.4 Hz)	3.63 – 3.57 (m); 3.49 – 3.48 (m)	62.6	**62.13**
	27-OH		5.30 (t, *J* = 5.6 Hz)		
DHMTDA	28				172.91
	29	4.06	**4.24 – 4.17 (m)**	71.1	**71.56**
	29-0H		6.20 (d, *J* = 6.8 Hz)		

	30	4.71 (d, *J* = 8.2 Hz)	**4.91 (dd, *J* = 9.1, 1.9 Hz)**	76.8	**77.72**
	31	1.83 (m)	1.89 – 1.80 (m)	34.1	**33.44**
	31-CH_3	0.68 (d, *J* = 6.8 Hz)	**0.82 (d, *J* = 6.8 Hz)**	15.7	15.90
	32	1.26 (m), 1.02 (m)	1.19 (m)	32.7	**32.33**
	33	1.25 (m)	1.25 (brs)	22.5	22.55
	34	1.25 (m)	1.25 (brs)	26.5	26.66
	35	1.25 (m)	1.25 (brs)	29.2	29.17
	36	1.25 (m)	1.25 (brs)	29.4	29.46
	37	1.25 (m)	1.25 (brs)	29.49	29.48
	38	1.25 (m)	1.25 (brs)	29.52	29.55
	39	1.25 (m)	1.25 (brs)	29.7	29.78
	40	1.25 (m)	1.25 (brs)	31.8	31.77
	41	0.86 (t, *J* = 7.1 Hz)	0.87 (t, *J* = 6.4 Hz)	14.4	14.42
Trp	CO			172. 7	172.98
	NH	8.62 (d, *J* = 6.0 Hz)	8.70 (d, *J* = 5.0 Hz)		
	H_α	4.22 (d, *J* = 9.1, 5.5 Hz)	4.24 – 4.17 (m)	56.4	56.43
	H_β	3.16 (m)	3.15 – 3.07 (m)	27.3	**26.77**
	NH	10.91(d, *J* = 2.6 Hz)	10.91 (d, *J* = 2.4 Hz)		
	2	7.27 (d, *J* = 2.6 Hz)	7.29 (d, *J* = 2.7 Hz)	124.1	123.95
	3			110.2	110.40
	3a			127.6	127.56
	4	7.54 (brd, *J* = 7.7 Hz)	7.54 (d, *J* = 7.8 Hz)	118.5	118.46
	5	7.01 (ddd, *J* = 7.7, 6.9, 1.0 Hz)	7.05 – 6.99 (m)	118. 8	118.89
	6	7.08 (ddd, *J* = 8.2, 6.9, 1.2 Hz)	7.14 – 7.08 (m)	121.4	121.55
	7	7.35 (brd, *J* = 8.2 Hz)	7.37 (brd, *J* = 8.1 Hz)	111.8	111.90
	8a			136.6	136.65

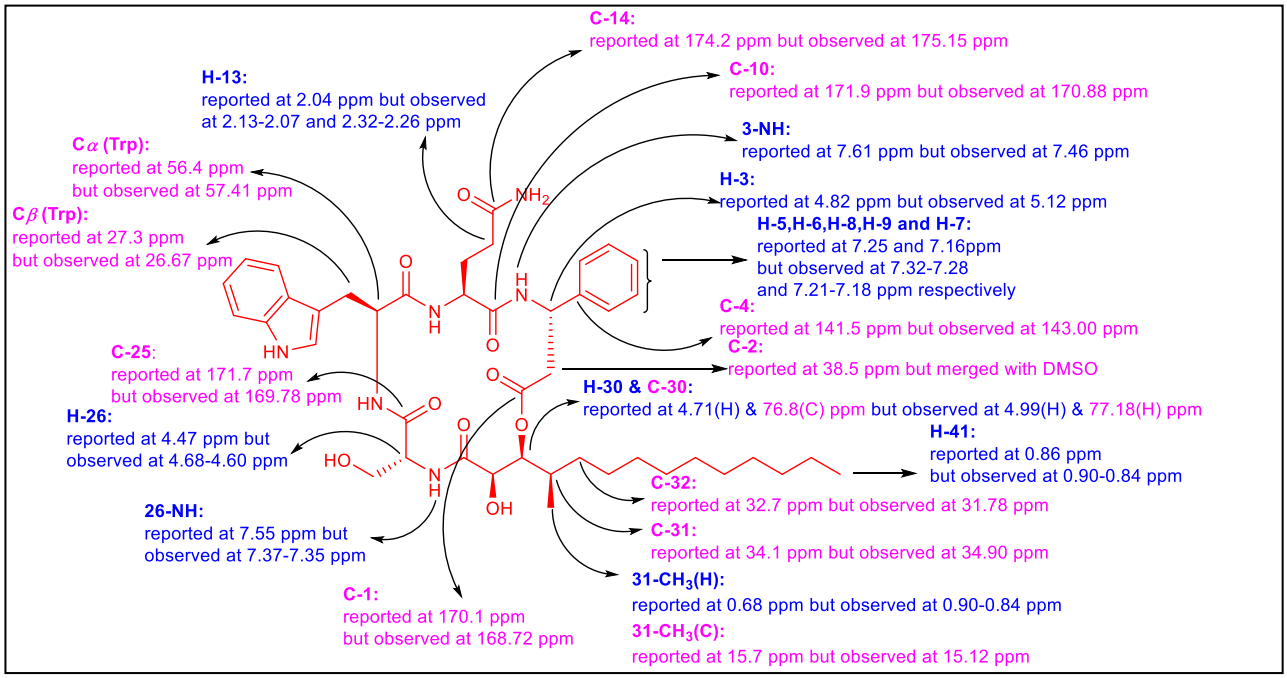
5.3. Table ST8: ^{1}H and ^{13}C NMR Comparison of Isolated Alveolaride C with Synthetic Alveolaride C (epi-3b).

Residue	Position	^{1}H		^{13}C	
		Reported (DMSO-d_6, 600 MHz)	Synthesized (DMSO-d_6, 300 MHz)	Reported (DMSO-d_6, 125 MHz)	Synthesized (DMSO-d_6, 75 MHz)
Phe	1			170.1	170.13
	2	3.15 (m); 2.87 (dd, *J* = 15.7, 4.4 Hz)	3.18 – 3.11 (m); 2.88 (d, *J* = 11.5 Hz)	38.5	38.50
	3	4.82 (m)	4.83 (q, *J* = 6.4 Hz)	49.9	49.89
	3-NH	7.61 (d, *J* = 7.4 Hz)	7.61 (d, *J* = 7.4 Hz)		
	4			141.5	141.50
	5	7.25 (m)	7.27 – 7.22 (m)	126.4	126.42
	6	7.25 (m)	7.27 – 7.22 (m)	126.4	128.27
	7	7.16 (m)	7.19 – 7.16 (m)	126.8	126.81
	8	7.25 (m)	7.27 – 7.22 (m)	126.4	128.27
	9	7.25 (m)	7.27 – 7.22 (m)	126.4	126.42
Gln	10			171.9	171.98
	11	3.93 (ddd, *J* = 9.6, 7.6, 5.5 Hz)	3.98 – 3.89 (m)	55.0	55.00
	11-NH	8.20 (d, *J* = 7.6 Hz)	**8.10 (d, *J* = 7.8 Hz)**		
	12	1.95 (m); 1.83 (m)	1.97 – 1.92 (m); 1.88 – 1.78 (m)	27.1	27.05
	13	2.04 (m)	2.09 – 2.01 (m)	32.2	32.16
	14			174.2	174.20
	14-NH_2	7.24 (brs), 6.78 (brs)	7.27 – 7.22 (m); 6.78 (s)		
Ser	25			171.7	171.74
	26	4.47 (m)	4.50 – 4.44 (m)	54.7	54.69
	26-NH	7.55 (d, *J* = 6.9 Hz)	7.57 – 7.50 (m), merged		
	27	3.59 (dd, *J* = 11.0, 5.4 Hz); 3.46 (dd, *J* = 11.0, 5.4 Hz)	3.58 (dd, *J* = 10.5, 5.4 Hz, 1H); 3.47 (d, *J* = 5.5 Hz)	62.6	62.60
	27-OH		5.13 (t, *J* = 5.4 Hz)		
DHMTDA	28				172.44
	29	4.06	4.06 (d, *J* = 6.6 Hz)	71.1	71.18

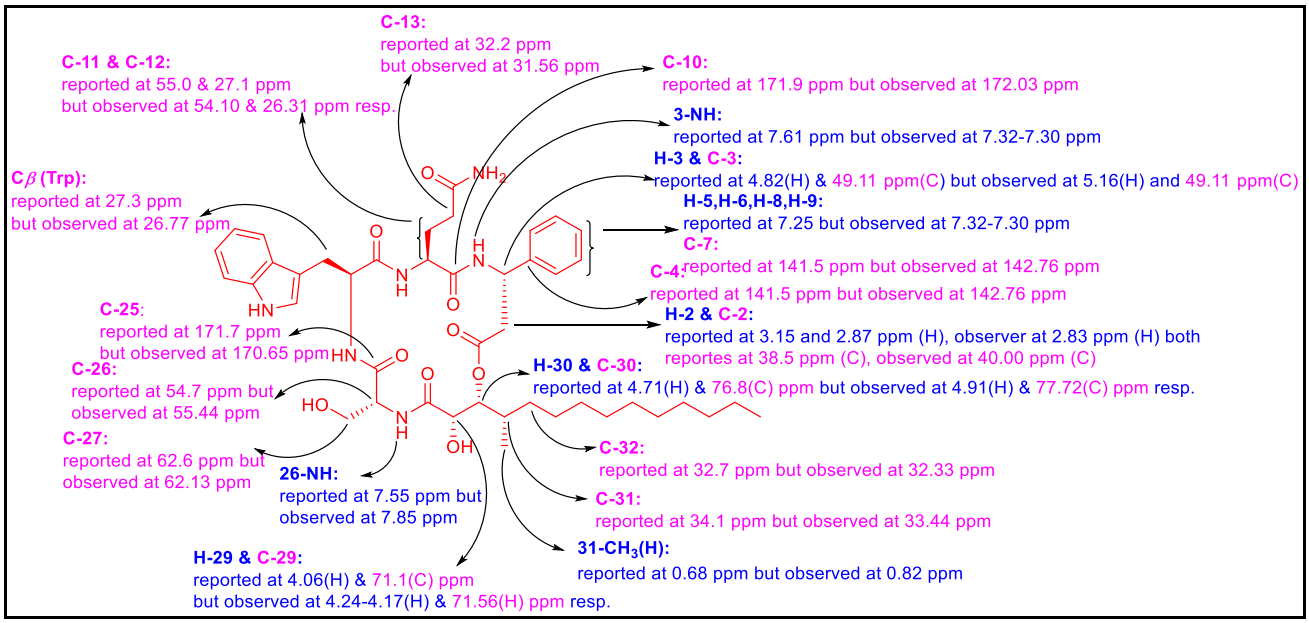
	29-0H		6.01 (d, *J* = 6.8 Hz)		
	30	4.71 (d, *J* = 8.2 Hz)	4.70 (d, *J* = 8.1 Hz)	76.8	76.82
	31	1.83 (m)	1.78-1.88 (m)	34.1	34.26
	31-CH_3	0.68 (d, *J* = 6.8 Hz)	0.67 (d, *J* = 6.7 Hz)	15.7	15.75
	32	1.26 (m), 1.02 (m)	1.28 (brs); 1.04 – 1.01 (m)	32.7	32.71
	33	1.25 (m)	1.24 (brs)	22.5	22.62
	34	1.25 (m)	1.24 (brs)	26.5	26.58
	35	1.25 (m)	1.24 (brs)	29.2	29.23
	36	1.25 (m)	1.24 (brs)	29.4	29.48
	37	1.25 (m)	1.24 (brs)	29.49	29.53
	38	1.25 (m)	1.24 (brs)	29.52	29.56
	39	1.25 (m)	1.24 (brs)	29.7	29.76
	40	1.25 (m)	1.24 (brs)	31.8	31.82
	41	0.86 (t, *J* = 7.1)	0.86 (t, *J* = 6.9 Hz)	14.4	14.49
Trp	CO			172. 7	172.63
	NH	8.62 (d, *J* = 6.0 Hz)	**8.36 (d, *J* = 5.9 Hz)**		
	H_α	4.22 (d, *J* = 9.1, 5.5 Hz)	4.26 – 4.20 (m)	56.4	56.39
	H_β	3.16 (m)	3.18 – 3.11 (m)	27.3	27.39
	NH	10.91(d, *J* = 2.6 Hz)	10.89 (brs)		
	2	7.27 (d, *J* = 2.6 Hz)	7.27 – 7.22 (m)	124.1	124.11
	3			110.2	110.19
	3a			127.6	127.68
	4	7.54 (brd, *J* = 7.7 Hz)	7.57 – 7.50 (m), merged	118.5	118.59
	5	7.01 (ddd, *J* = 7.7, 6.9, 1.0 Hz)	7.01 (t, *J* = 7.3 Hz)	118. 8	118.90
	6	7.08 (ddd, *J* = 8.2, 6.9, 1.2 Hz)	7.09 (t, *J* = 7.3 Hz)	121.4	121.52
	7	7.35 (brd, *J* = 8.2 Hz)	7.36 (brd, *J* = 8.1 Hz)	111.8	111.90
	8a			136.6	136.62

6. Figure Representing the Anomalies in ^{1}H (represented by blue) and ^{13}C (represented by pink) NMR of Compound 3a and 3b with respect to Naturally Occurring Alveolaride C.

6.1 Figure SF3: Major Mismatches in Compound 3a.

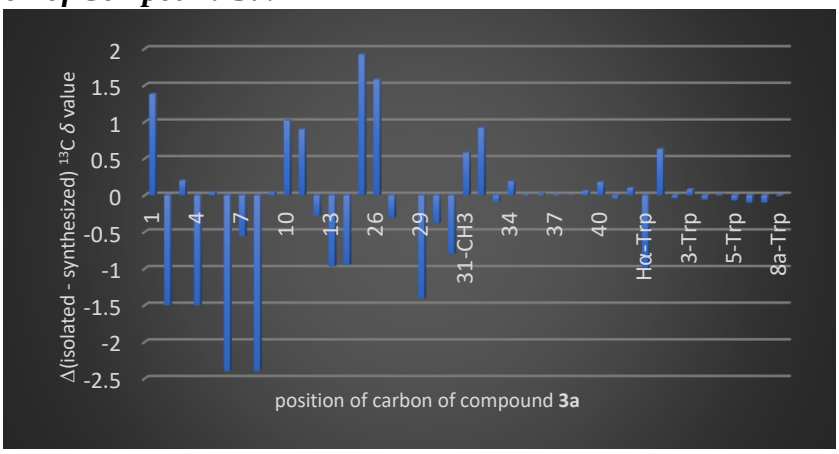


6.2 Figure SF4: Major Mismatches in Compound 3b.

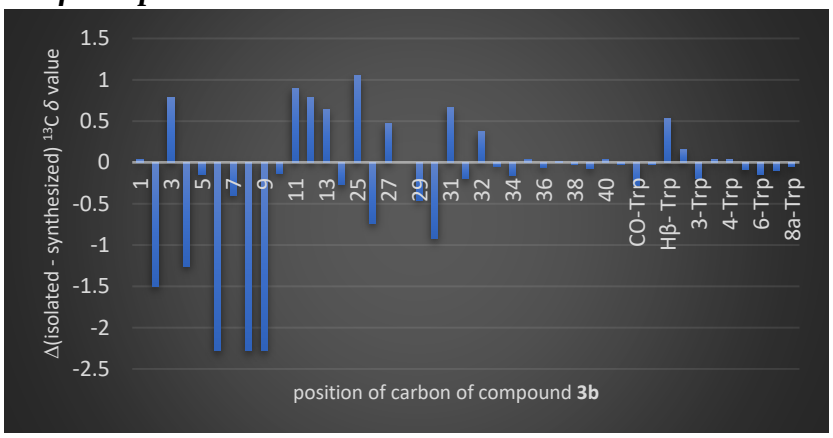


7. A Graphical Comparison: ^{13}C Values of Isolated and Synthesized Compounds.

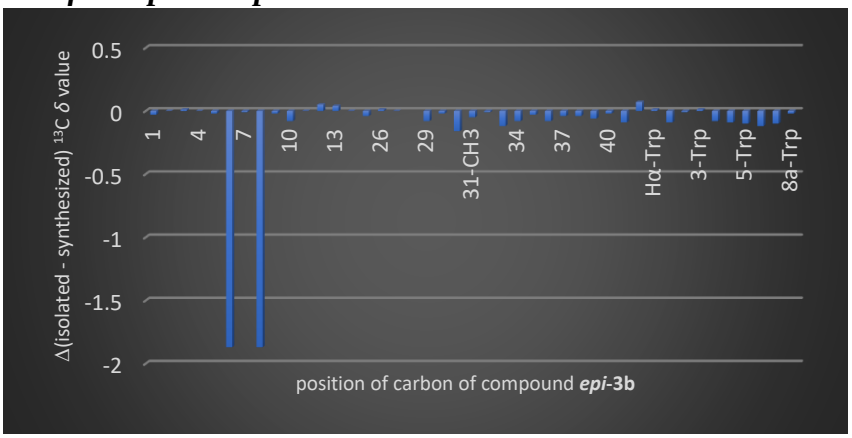
7.1 Fig SF5: Plot of Δ(Isolated - Synthesized) ^{13}C δ Value vs Position of Carbon of Compound 3a.



7.2 Fig SF6: Plot of Δ(Isolated - Synthesized) ^{13}C δ Value vs Position of Carbon of Compound 3b.



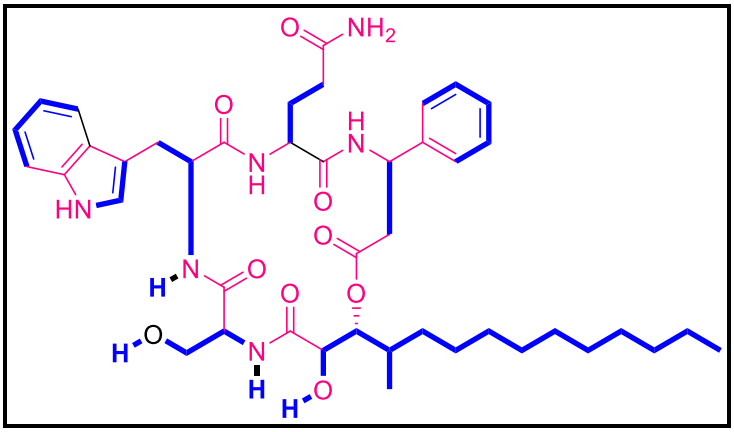
7.3 Fig SF7: Plot of Δ(Isolated - Synthesized) ^{13}C δ Value vs Position of Carbon of Compound epi-3b.



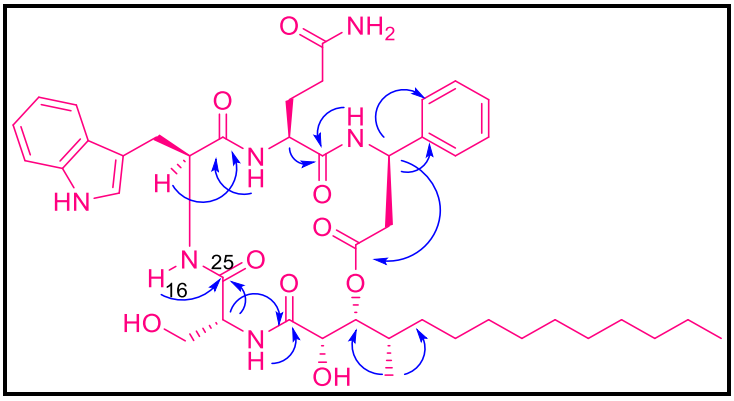
(**Note:** *Anomaly in Figure SF7 is most likely due to typographic mistakes. No spectra of alveolaride C were made available by the isolation group to recheck.*)

8. Key 2D-NMR Correlations and Structure Conformation of Actual Structure of Alveolaride C.

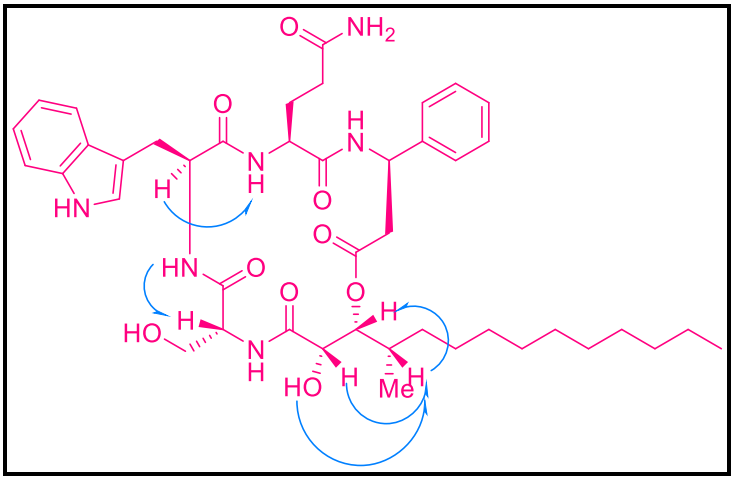
8.1 Figure SF8: *Selected COSY Correlations in Compound* ***epi-3b****.*



8.2 Figure SF9*: Selected HMBC Correlations in Compound* ***epi-3b****.*

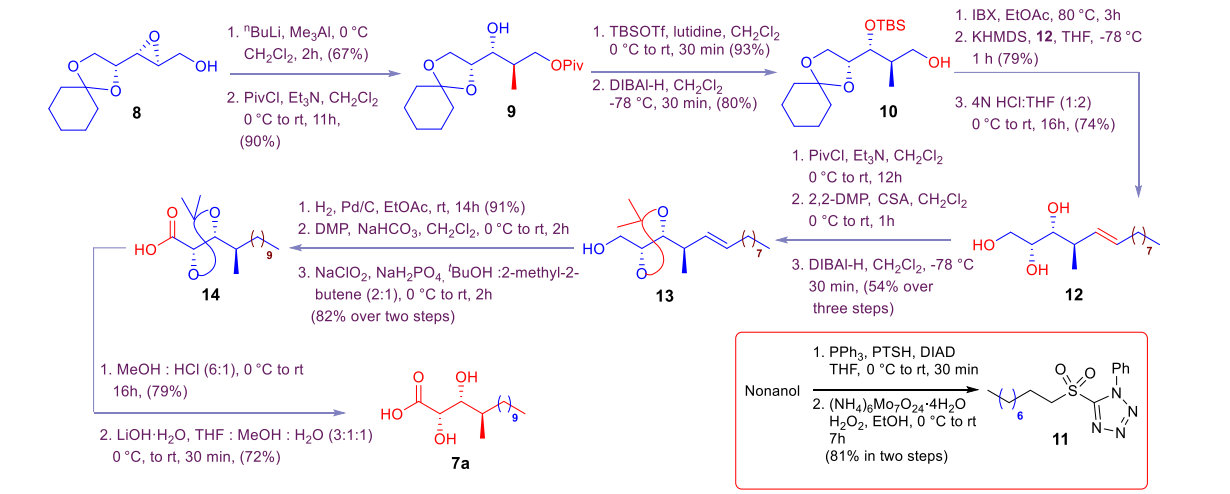


8.3 Figure SF10: *Selected NOESY Correlations in Compound* ***epi-3b****.*

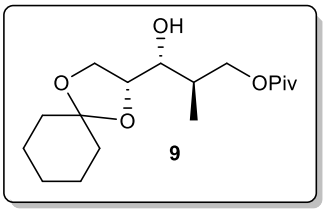


9. Experimental Procedure:

Scheme S1: *Synthesis of Acid* ***7a***.



(2*R*,3*R*)-3-Hydroxy-2-methyl-3-((*R*)-1,4-dioxaspiro[4.5]decan-2-yl)propyl pivalate (9):

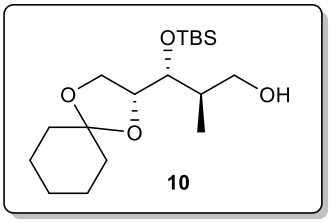


To a solution of epoxy alcohol **8** (1.07 g, 4.99 mmol) in anhydrous CH_2Cl_2 (30 mL), *n*-buLi (3.7 mL, 5.99 mmol, 1.6 M in hexane) was added at 0 °C under argon. After being stirred for 20 min at the same temperature, Me_3Al (7.5 mL, 14.97 mmol, 2 M in toluene) was added and the mixture was stirred for 2 h. Water (10 mL) followed by aqueous 3 N HCl (20 mL) were added cautiously and the organic layers were separated. The aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated under reduced pressure to provide the corresponding mixture of regioisomers. The mixture was then treated with $NaHCO_3$ (419 mg, 4.99 mmol) and $NaIO_4$ (1.07 g, 4.99 mmol) in THF:water (2:1, 30 mL) and stirred for 1 h at the room temperature. The reaction mixture was passed through Celite and the filtrated was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), concentrated in *vacuo*. Crude residue was purified using column chromatography (SiO_2, 100-200 mesh, 30-50% EtOAc in hexane as eluent) to afford the corresponding 1,3-diol (769 mg, 67%) as colourless oil. (R_f = 0.31, 40% EtOAc in hexane); $[\alpha]_D^{25}$ = -38.7 (*c* 0.49, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.26 – 4.21 (m, 1H), 4.05 (dd, *J* = 7.5, 6.5 Hz, 1H), 3.85 – 3.81 (m, 1H), 3.68 – 3.65

(m, 2H), 3.45 (q, *J* = 5.1 Hz, 1H), 2.88 (s, 1H), 2.55 (d, *J* = 6.6 Hz, 1H), 1.84 (dt, *J* = 12.3, 6.4 Hz, 1H), 1.62 (dt, *J* = 11.8, 7.6 Hz, 8H), 1.41 (q, *J* = 6.2 Hz, 2H), 0.97 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 110.23, 76.65, 75.79, 66.22, 66.14, 38.83, 36.24, 34.90, 25.23, 24.16, 23.96, 14.61; IR (neat) ν_{max} 3389, 2925, 2857, 1257, 1062 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{22}O_4Na$ $[M+Na]^+$ 253.1416, found 253.1415.

To an ice-cold solution of the above diol (702 mg, 3.05 mmol) in anhydrous CH_2Cl_2 (20 mL) under argon, Et_3N (0.86 mL, 6.096 mmol) was added and the mixture was stirred for 5 min. PivCl (0.38 mL, 3.048 mmol) was then added. The reaction was continued for 30 min at the same temperature and stirred further at room temperature for 11 h. The reaction was subsequently quenched with a saturated solution of NH_4Cl (10 mL), diluted with water. The resultant mixture was extracted with CH_2Cl_2 (3 × 15 mL), washed with solution of brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO_2, 100−200 mesh, 10-30% EtOAc in hexane as eluent) gave pivaloyl protected alcohol **9** (862 mg, 90%) as a colorless oil. R_f = 0.67 (25% EtOAc in hexane); $[\alpha]_D^{25}$ = -58.2 (*c* 0.32, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.27 – 4.18 (m, 2H), 4.13 – 4.00 (m, 2H), 3.82 (dd, *J* = 8.0, 6.9 Hz, 1H), 3.35 (q, *J* = 5.6 Hz, 1H), 2.30 (d, *J* = 7.1 Hz, 1H), 1.95 (tdd, *J* = 7.0, 6.1, 4.8 Hz, 1H), 1.60 (dd, *J* = 11.7, 3.1 Hz, 8H), 1.40 – 1.38 (m, 2H), 1.19 (s, 9H), 1.02 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.64, 110.03, 75.90, 73.06, 66.15, 66.07, 38.98, 36.91, 36.28, 34.91, 27.36, 25.26, 24.14, 23.93, 14.35; IR (neat) ν_{max} 3495, 2929, 2851, 1785, 1274, 1101 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{30}O_5Na$ $[M+Na]^+$ 337.1191, found 337.1193.

(2*R*,3*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-2-methyl-3-((R)-1,4-dioxaspiro[4.5]decan-2-yl)-propan-1-ol (10): To an ice-cold solution of alcohol **9** (812 mg, 2.58 mmol) in anhydrous

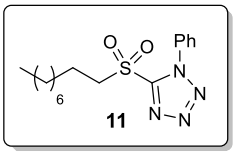


CH_2Cl_2 (20 mL) under argon, 2,6-lutidine (1.2 mL, 10.33 mmol) was added and the mixture was stirred for 5 min prior to addition of TBSOTf (1.5 mL, 6.45 mmol). The reaction was continued for 30 min at the same temperature and then quenched with a saturated solution of $NaHCO_3$ (10 mL), diluted with water. The resultant mixture was extracted with CH_2Cl_2 (3 × 15 mL), washed with aqueous solution of $CuSO_4$, water, brine, dried (Na_2SO_4), filtered, and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO_2, 100−200 mesh, 5% EtOAc in hexane as eluent) gave the corresponding TBS protected alcohol (1.03 g, 93%) as a colorless oil; R_f = 0.61 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -26.7 (*c* 0.58, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.22 – 4.09 (m, 2H), 4.02 (dd, *J* = 7.8, 6.2 Hz, 1H), 3.84 (dd, *J* = 11.1, 6.7 Hz, 1H), 3.58 (dd, *J* = 7.7, 2.2 Hz, 1H), 3.49 (t, *J* = 8.1 Hz, 1H), 1.77 – 1.71 (m, 1H), 1.57 (dt, *J* = 11.9, 4.1 Hz, 8H), 1.43 – 1.31 (m, 2H), 1.18 (s, 9H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.54, 109.90, 78.43, 77.46, 66.03, 65.46, 38.84, 36.63, 36.17, 35.20, 27.34, 26.20, 25.34, 24.01, 23.88, 18.59, 16.11, -3.67, -4.74; IR (neat) ν_{max} 2932, 2857, 1718, 1271, 1091 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{44}O_5SiNa$ $[M+Na]^+$ 451.2856, found 451.2858.

To a solution of the above pivaloyl ester (800 mg, 1.87 mmol) in anhydrous CH_2Cl_2 (20 mL) at -78 °C under argon, DIBAL-H (2.9 mL, 4.66 mmol, 1.6 M in toluene) was added slowly. The reaction was continued for 30 min at the same temperature and quenched carefully with MeOH (1 mL). A saturated solution of sodium potassium tartrate (40 mL) was added into the mixture. The resulting mixture was warmed to the room temperature and stirred vigorous for 2 h. Finally, the mixture was extracted with EtOAc (3 × 15 mL), washed with water, brine, dried (Na_2SO_4) and concentrated in *vacuo*. Purification of residue by a flash column

chromatography (SiO_2, 100−200 mesh, 10% EtOAc in hexane as eluent) produced pure alcohol **10** (515 mg, 80%) as a colorless liquid; R_f = 0.45 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -57.9 (*c* 0.37, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.30 – 4.20 (m, 1H), 3.99 (dd, *J* = 8.0, 6.3 Hz, 1H), 3.76 – 3.65 (m, 2H), 3.61 (q, *J* = 5.8 Hz, 1H), 3.53 (t, *J* = 8.2 Hz, 1H), 2.75 (d, *J* = 5.1 Hz, 1H), 1.63 – 1.56 (m, 8H), 1.42-1.37 (m, 2H), 1.08 (d, *J* = 7.1 Hz, 3H), 0.92 (s, 9H), 0.17 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 110.15, 79.62, 78.88, 65.96, 64.77, 37.46, 36.56, 35.09, 26.19, 25.32, 24.04, 23.90, 18.55, 16.43, -3.73, -4.70; IR (neat) ν_{max} 3429, 2938, 2854, 1253, 1081 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{36}O_4SiNa$ $[M+Na]^+$ 367.2281, found 367.2283.

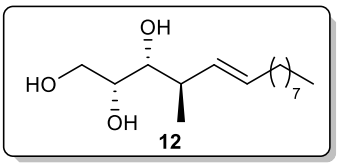
5-(Nonylsulfonyl)-1-phenyl-1H-tetrazole (11): To a mixture of nonanol (2.0 g, 13.86 mmol) in anhydrous THF (50 mL mL) at 0 °C under argon, Ph_3P (5.4 g, 20.79 mmol), 1-phenyl-1*H*-tetrazol-5-thiol (3.7 g, 20.79 mmol) and DIAD (4.1 mL, 20.79 mmol) were added sequentially and stirred for 2 h at the ambient temperature. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ (15 mL), extracted with EtOAc (3×30 mL), washed with brine, dried (Na_2SO_4) and concentrated under vacuum. The residue was purified by column chromatography (SiO_2, 100-200 mesh, 5% EtOAc in hexane as eluent) to afford the corresponding sulfide (3.9 g, 92%) as a thick oil. R_f = 0.49 in 10% EtOAc in hexane; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 – 7.48 (m, 5H), 3.43 (t, *J* = 7.5 Hz, 2H), 1.86-1.76 (m, 2H), 1.51-1.47 (m, 2H), 1.34 – 1.23 (m, 10H), 0.84 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.65, 133.93, 130.22, 129.91, 124.01, 33.53, 31.86, 29.01, 28.93, 28.65, 22.06, 14.17; IR (neat) ν_{max} 2957, 2927, 2853, 1499, 1374 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{24}N_4SNa$ $[M+Na]^+$ 327.1619, found 327.1616.



To an ice cold ethanolic solution (40 mL) of the above sulfide (3.5 g, 11.50 mmol), $(NH_4)_6Mo_7O_{24}.4H_2O$ (711 mg, 0.575 mmol) and 30% (w/w) aqueous H_2O_2 solution (12 mL) were added sequentially. The reaction mixture was stirred for 7 h at the room temperature. The

reaction mixture was then diluted with distilled water solution and the ethanol was evaporated in *vacuo*. The resultant mixture was extracted with EtOAc (3 × 25 mL), washed with saturated aqueous solution of $Na_2S_2O_3$, brine, dried over Na_2SO_4, filtered and concentrated. The crude material was purified by column chromatography (SiO_2, 100-200 mesh, 5% EtOAc in hexane as eluent) to get sulfone **11** (3.4 g, 88 %) as a white solid. R_f = 0.53 (10% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.66 (m, 2H), 7.61 (d, *J* = 7.0 Hz, 3H), 3.78 – 3.68 (m, 2H), 1.95 (p, *J* = 7.7 Hz, 2H), 1.51 (dd, *J* = 15.8, 8.5 Hz, 2H), 1.38 – 1.22 (m, 10H), 0.92 – 0.84 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.64, 133.21, 131.59, 129.85, 125.22, 56.17, 31.90, 29.28, 29.04, 28.29, 22.77, 22.10, 14.22; IR (neat) ν_{max} 2961, 2925, 2857, 1502, 1341, 1152 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{24}N_4O_2SNa$ $[M+Na]^+$ 359.1518, found 359.1519.

(2*R*,3*R*,4*R*,*E*)-4-Methyltetradec-5-ene-1,2,3-triol (12):To a stirred solution of alcohol **10**



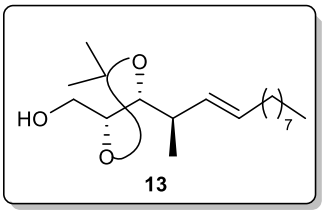
(313 mg, 0.91 mmol) in distilled EtOAc (5 mL), IBX (640 mg, 2.3 mmol) was added and refluxed (80 °C) for 3 h. The reaction mixture was then cooled to the room temperature, filtered through a Celite pad, washed with EtOAc (3×10 mL) and concentrated in *vacuo*. The crude aldehyde (R_f = 0.77, 25% EtOAc in hexane) was subjected to flash chromatography and used for the next reaction without further characterizations.

To a stirred solution of sulfone **11** (368 mg, 1.09 mmol) in anhydrous THF (5 mL) at -78 °C under argon, KHMDS (2.4 mL, 1.00 mmol, 0.5 M in toluene) was added and the reaction mixture was stirred for 30 min at the same temperature. A solution of the above aldehyde dissolved in anhydrous THF (2 mL) was cannulated to the reaction mixture and stirred for another 2 h at the same temperature before quenching it with saturated aqueous NH_4Cl solution (2 mL). The resultant mixture was extracted with EtOAc (3 × 20 mL), washed with brine, dried (Na_2SO_4), filtered and concentrated in *vacuo*. Purification by column chromatography (SiO_2, 100-200 mesh, 2% EtOAc in hexane as eluent) furnished exclusively the corresponding *E*-

olefin (382 mg, 79%, over two steps) as a colorless liquid; R_f = 0.51 (5% EtOAc in hexane); $[\alpha]_D^{25}$ = -87.4 (*c* 0.26, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.51 – 5.39 (m, 1H), 5.38 – 5.27 (m, 1H), 3.97 – 3.87 (m, 2H), 3.53 – 3.39 (m, 2H), 1.97 (q, *J* = 6.1, 5.6 Hz, 3H), 1.62-1.52 (m, 10H), 1.29 – 1.25 (m, 12H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 0.88 (t, *J* = 6.0 Hz, 3H), 0.14 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.99, 109.52, 79.16, 78.67, 65.71, 41.06, 36.72, 35.31, 32.72, 32.07, 29.86, 29.63, 29.51, 29.31, 26.27, 25.40, 24.05, 23.97, 22.84, 19.16, 18.68, 14.27, -3.58, -4.66; IR (neat) ν_{max} 2961, 2927, 2855,1735, 1462, 1235, 1085 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{52}O_3SiNa$ $[M+Na]^+$ 475.3583, found 475.3584.

To an ice-cold solution of above olefin (253 mg, 0.56 mmol) in THF (10 mL), 4N HCl solution (5 mL) was added dropwise over a period of 15 min. Then the mixture was stirred for 1 h at the same temperature and further at the room temperature for 16 h. The reaction was quenched with saturated aqueous solution of $NaHCO_3$ (10 mL) and finally extracted with EtOAc (3 × 10 mL), washed with water, brine, dried (Na_2SO_4) and concentrated in *vacuo*. Purification of the crude residue by a flash column chromatography (SiO_2, 100−200 mesh, 70% EtOAc in hexane as eluent) produced pure triol **12** (108 mg, 74%) as a yellow oil; R_f = 0.28 (60% EtOAc in hexane); $[\alpha]_D^{25}$ = -103.4 (*c* 0.13, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.59 (dt, *J* = 15.4, 6.7 Hz, 1H), 5.30 (ddt, *J* = 15.3, 9.0, 1.4 Hz, 1H), 3.76-3.70 (m, 3H), 3.33 (dt, *J* = 7.6, 2.3 Hz, 1H), 2.58 (s, 1H), 2.48 – 2.32 (m, 2H), 2.21 (s, 1H), 2.03 (q, *J* = 6.7 Hz, 2H), 1.36-1.25 (m, 12H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.91 – 0.85 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.45, 131.32, 76.02, 70.63, 65.64, 40.52, 32.73, 32.03, 29.56, 29.41, 29.33, 22.81, 17.23, 14.26; IR (neat) ν_{max} 3385, 2958, 2921, 2854, 1459, 1238, 1071 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}O_3SiNa$ $[M+Na]^+$ 281.2093, found 281.1914.

((4*R*)-5-((*R*,*E*)-Dodec-3-en-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (13): To an ice-cold solution of the alcohol **12** (91 mg, 0.35 mmol) in anhydrous CH_2Cl_2 (5 mL) under argon, Et_3N (0.1 mL, 0.71 mmol) was added and the mixture was stirred for 5 min followed by addition of PivCl (43 µL, 0.35 mmol). The reaction was continued for 30 min at the same temperature and then allowed to stir at the room temperature for 12 h and subsequently quenched with a saturated solution of NH_4Cl (5 mL), diluted with water. The resultant mixture was extracted with CH_2Cl_2 (3 × 10 mL), washed with solution of brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. Crude residue was passed through short silica pad (SiO_2, 100−200 mesh, 5-30% EtOAc in hexane as eluent) to give the corresponding pivaloyl protected alcohol as a colorless oil; R_f = 0.54 (25% EtOAc in hexane) which was directly used in next step.



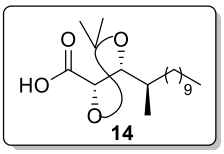
13

To an ice-cold solution of the above diol (87 mg, 0.254 mmol) in anhydrous CH_2Cl_2 (5 mL) under argon, 2,2- DMP (62 µL, 0.508 mmol) and CSA (3 mg, 0.013 mmol) were added sequentially. The reaction mixture was stirred for 1 h at the room temperature prior to quench with Et_3N (1 mL). The mixture was filtered using a short silica pad (60-120 mesh), washed with EtOAc (3 × 20 mL) and concentrated under vacuum. The crude product was then used directly for the next step without further characterization.

To a solution of the above acetonide protected pivaloyl ester (95 mg, 0.248 mmol) in anhydrous CH_2Cl_2 (5 mL) at -78 °C under argon, DIBAL-H (1.6 M in toluene, 0.4 mL, 0.621 mmol) was added slowly. The reaction was continued for 30 min at the same temperature and quenched carefully with MeOH (1 mL). A saturated solution of sodium potassium tartrate (10 mL) was added to the reaction mixture. The resulting mixture was warmed to the room temperature and stirred vigorous for 2 h and then diluted with water. Finally, the mixture was extracted with EtOAc (3 × 10 mL), washed with water, brine, dried (Na_2SO_4) and concentrated in *vacuo*. Purification of the residue by a flash column chromatography (SiO_2, 100−200 mesh,

2-10% EtOAc in hexane as eluent) produced pure alcohol **13** (56 mg, 54% over three steps) as a colorless liquid. R_f = 0.73 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -42.7 (*c* 0.42, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.50 – 5.36 (m, 2H), 3.88 (ddd, *J* = 8.0, 4.7, 3.0 Hz, 1H), 3.83 – 3.71 (m, 2H), 3.61 – 3.53 (m, 1H), 2.36 – 2.26 (m, 1H), 2.03 – 1.97 (m, 2H), 1.39 (d, *J* = 4.0 Hz, 6H), 1.25-1.30 (s, 12H), 1.07 (d, *J* = 7.0 Hz, 3H), 0.87 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.08, 130.64, 108.71, 80.50, 79.01, 62.88, 38.75, 32.75, 32.03, 29.59, 29.43, 29.32, 27.36, 27.27, 22.81, 17.19, 14.25; IR (neat) ν_{max} 3456, 2923, 2853, 1458, 1078 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{34}O_3Na$ $[M+Na]^+$ 321.2406, found 321.2409.

(4*S*)-5-((*R*)-Dodecan-2-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylic acid (14): To a stirred solution of compound **13** (45 mg, 0.151 mmol) in distilled EtOAc (2 mL) fitted a hydrogen balloon at the room temperature, 10% Pd/C (5 mg) was added and the mixture was stirred for 14 h. The reaction mixture was filtered using a short Celite pad and washed with EtOAc (3 × 15 mL). The saturated product was then purified by a flash column chromatography (SiO_2, 100−200 mesh, 2-10% EtOAc in hexane as eluent) to produce corresponding saturated pure alcohol (41 mg, 91%) as a yellow oil; R_f = 0.81 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -21.4 (*c* 0.62, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.91 (ddd, *J* = 7.9, 5.4, 2.8 Hz, 1H), 3.78 (dd, *J* = 11.9, 2.8 Hz, 1H), 3.67 (t, *J* = 7.3 Hz, 1H), 3.59 (dd, *J* = 11.8, 5.3 Hz, 1H), 1.70 – 1.64 (m, 1H), 1.61-1.52 (m, 1H) 1.40 (s, 6H), 1.30-1.12 (m, 18H), 0.90-0.85 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.58, 81.10, 79.75, 63.81, 36.37, 32.99, 32.06, 29.98, 29.81, 29.78, 29.49, 27.41, 27.02, 22.84, 15.32, 14.27; IR (neat) ν_{max} 3468, 2961, 2931, 2858, 1472, 1241, 1058 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{36}O_3SiNa$ $[M+Na]^+$ 323.2562, found 323.2564.



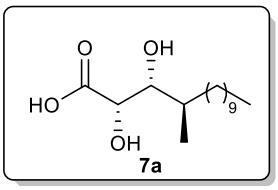
14

To an ice-cold solution of the above alcohol (31 mg, 0.105 mmol) in anhydrous CH_2Cl_2 (5 mL), $NaHCO_3$ (26 mg, 0.314 mmol) and DMP (89 mg, 0.210 mmol) were added sequentially in presence of argon. The reaction mixture was warmed gradually to the room temperature and

stirred further for 2 h. The reaction was then quenched with saturated aqueous solution of $Na_2S_2O_3$ (5 mL) and $NaHCO_3$ (5 mL), then diluted with CH_2Cl_2 (10 mL) and stirred until the two phases were separated. The resultant mixture was extracted with CH_2Cl_2 (3 × 7 mL), washed with water, brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude residue was subjected to flash column chromatography (using a short pad of 60-120 silica and EtOAc as eluent) to get the corresponding aldehyde (quantitative) as a colorless liquid which was taken for the next reaction without further characterizations.

To a stirred solution of the above aldehyde in ^{t}BuOH/2-methyl-2-butene (2:1, 4 mL) at the room temperature, a freshly prepared mixture of aqueous solution of $NaClO_2$ (38 mg, 0.420 mmol) and $NaH_2PO_4.2H_2O$ (66 mg, 0.420 mmol) was added. The reaction was continued for 2 h at the room temperature. ^{t}BuOH was evaporated and the mixture was extracted with EtOAc (3 × 15 mL). The combined organic layer was washed with brine, dried (Na_2SO_4), filtered, and concentrated in *vacuo*. Purification of the crude residue by column chromatography (SiO_2, 100-200 mesh, 20-50% EtOAc in hexane as eluent) provided carboxylic acid **14** (27 mg, 82%) as a colorless oil; R_f = 0.19 (40% EtOAc in hexane). $[\alpha]_D^{25}$ = -54.2 (*c* 0.57, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.27 (d, *J* = 6.4 Hz, 1H), 4.12-4.07 (m, 1H), 1.84 – 1.75 (m, 1H), 1.46 (d, *J* = 10.4 Hz, 6H), 1.26 (brs, 18H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.88 (t, *J* = 5.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 111.25, 83.66, 77.36, 36.32, 32.07, 31.91, 29.98, 29.79, 29.50, 27.16, 27.09, 25.81, 22.84, 15.70, 14.27; IR (neat) ν_{max} 2955, 2921, 2858, 1723, 1465, 1272, 1081 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{35}O_4$ $[M+H]^+$ 315.2535, found 315.2531.

(2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-methyltetradecanoic acid (7a): To an ice-cold solution of acid



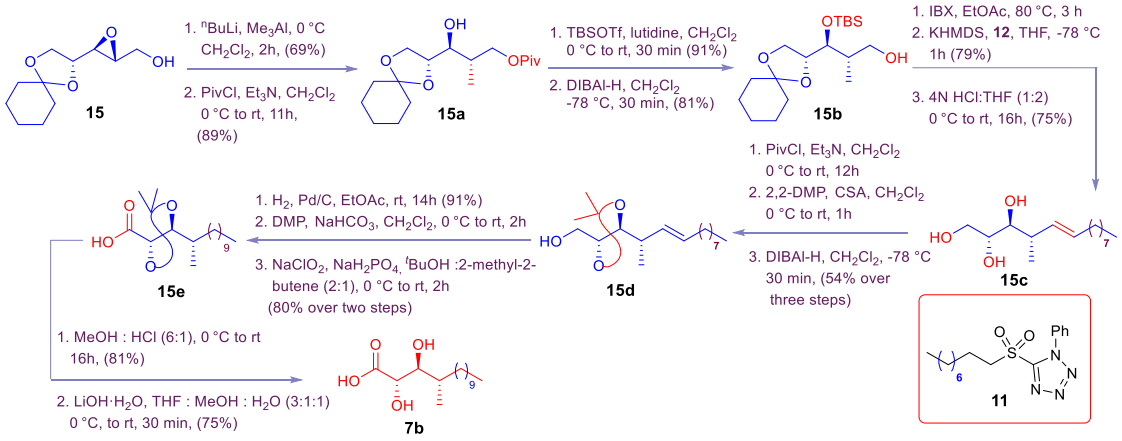
7a

14 (25 mg, 0.079 mmol) in distilled MeOH (3 mL) conc. HCl (0.5 mL) was added dropwise. The reaction mixture was gradually warmed to the room temperature and allowed further to stir for 16 h. Then the reaction was quenched with saturated $NaHCO_3$ solution (5 mL) and the solvent was evaporated

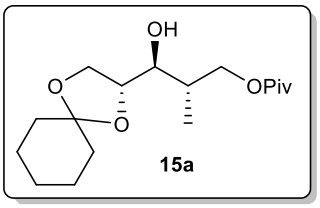
in *vacuo*. The resultant mixture was finally extracted with EtOAc (3 × 10 mL), washed with water, brine, dried (Na_2SO_4) and concentrated in *vacuo*. Purification of residue by a flash column chromatography (SiO_2, 100−200 mesh, 20-40% EtOAc in hexane as eluent) produced the corresponding methyl eater (18 mg, 79%) as pale yellow oil; R_f = 0.61 (40% EtOAc in hexane). $[\alpha]_D^{25}$ = -20.2 (*c* 0.12, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.30 (d, *J* = 4.8 Hz, 1H), 3.83 (s, 3H), 3.57 (t, *J* = 9.1 Hz, 1H), 3.06 (d, *J* = 5.0 Hz, 1H), 1.94 (d, *J* = 9.7 Hz, 1H), 1.74 − 1.66 (m, 1H), 1.37 − 1.42 (m, 1H), 1.26 (s, 17H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.87 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.83, 76.66, 71.31, 53.01, 36.21, 32.71, 32.06, 30.11, 29.82, 29.78, 29.49, 26.78, 22.83, 15.77, 14.26. IR (neat) ν_{max} 3459, 2962, 2924, 2860, 1736, 1456, 1122 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{32}O_4SiNa$ $[M+Na]^+$ 311.2198, found 311.2197.

To an ice-cold solution of the above methyl ester (15 mg, 0.052 mmol) in distilled THF (3 mL), a solution of $LiOH.H_2O$ (9 mg, 0.208 mmol) dissolved in mixture of distilled water and MeOH (1:1, 2 mL) was added. After 30 min of stirring, 0.5 M $KHSO_4$ (3 mL) was added into the resulting mixture. The mixture was warmed to the room temperature and diluted with distilled water and extracted with Et_2O (4 × 5 mL), washed with brine, dried (Na_2SO_4) and evaporated in *vacuo*. Purification of the crude residue by column chromatography (SiO_2, 100−200 mesh, 70-100% EtOAc in hexane as eluent) yielded acid **7a** (10.2 mg, 72%) as off white solid; R_f = 0.21 (80% EtOAc in hexane). $[\alpha]_D^{25}$ = -38.1 (*c* 0.21, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ 4.25 (d, *J* = 1.9 Hz, 1H), 3.54 (d, *J* = 9.0 Hz, 1H), 1.77 – 1.69 (m, 1H), 1.49 – 1.40 (m, 1H), 1.30 (brs, 16H), 1.22 – 1.16 (m, 1H), 0.95 – 0.87 (m, 6H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.71, 76.51, 71.20, 35.28, 32.39, 31.71, 29.81, 29.44, 29.44, 29.39, 29.11, 26.48, 22.36, 14.71, 13.08. IR (neat) ν_{max} 3502, 3389, 2915, 2854, 1723, 1652, 1464, 1250, 1135 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}O_4SiNa$ $[M+Na]^+$ 297.2042, found 297.2043.

***Scheme S2**: Synthesis of Acid **7b**.*



(2*S*,3*S*)-3-Hydroxy-2-methyl-3-((*R*)-1,4-dioxaspiro[4.5]decan-2-yl)propyl pivalate (15a):

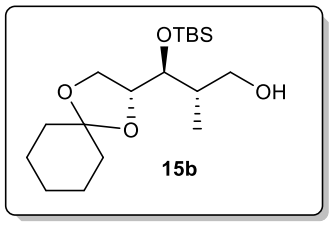


Following the same experimental procedure as described for the preparation of compound **9**, epoxy alcohol **15** (1.24 g, 5.79 mmol) was the treated with ^{n}BuLi (4.3 mL, 6.95 mmol, 1.6 M in hexane) and Me_3Al (8.7 mL, 17.37 mmol, 2.0 M in toluene) to produce 1,3-diol along with its regio-isomer. The crude product was reacted with $NaHCO_3$ (486 mg, 5.79 mmol) $NaIO_4$ (1.24 g, 5.79 mmol) and to furnish corresponding 1,3-diol (919 mg, 69%; purification: SiO_2, 100-200 mesh, 30-50% EtOAc in hexane as eluent) as coloueless oil; R_f = 0.25 (40% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.20 (td, J = 6.8, 4.5 Hz, 1H), 4.02 (dd, J = 8.1, 6.3 Hz, 1H), 3.97 – 3.91 (m, 1H), 3.71 (dq, J = 15.3, 4.8 Hz, 3H), 2.96 (s, 1H), 2.82 (s, 1H), 1.77 – 1.73 (m, 1H), 1.67- 1.55 (m, 8H), 1.40-1.33 (m, 2H), 0.94 (d, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.77, 76.46, 75.93, 67.50, 64.51, 37.17, 36.27, 34.96, 25.23, 24.08, 23.90, 13.54; IR (neat) ν_{max} 2961, 2927, 2855, 1462, 1252, 1096 cm^{-1}; IR (neat) ν_{max} 3391, 2928, 2858, 1447, 1259, 1067 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{22}O_4Na$ $[M+Na]^+$ 253.1416, found 253.0969.

Following the same experimental procedure as described for the preparation of compound **9**, the above diol (901 mg, 3.91 mmol) was reacted with Et_3N (1.1 mL, 7.82 mmol) and PivCl (0.53 mL, 4.30 mmol) to obtain pivaloyl ester **15a** (1.1 g, 89%; purification: SiO_2, 100−200 mesh, 10-30% EtOAc in hexane as eluent) as colorless oil; R_f = 0.72 (25% EtOAc in

hexane as eluent); $[\alpha]_D^{25}$ = +76.1 (*c* 0.21, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.20 – 4.10 (m, 3H), 4.00 (dd, *J* = 8.1, 6.3 Hz, 1H), 3.91 (dd, *J* = 8.1, 7.3 Hz, 1H), 3.68 (ddd, *J* = 7.4, 4.5, 2.6 Hz, 1H), 2.32 (d, *J* = 3.2 Hz, 1H), 1.87 (ddt, *J* = 9.6, 7.1, 3.6 Hz, 1H), 1.65 –1.57 (m, 8H), 1.43 –1.38 (m, 2H) 1.20 (s, 9H), 1.00 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.72, 109.72, 76.55, 72.24, 66.27, 64.50, 39.05, 36.32, 35.90, 35.08, 27.37, 25.27, 24.09, 23.94, 13.70; IR (neat) ν_{max} 3499, 2932, 1788, 1721, 1275, 1212, 1094 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{31}O_5$ $[M+H]^+$ 315.2171, found 315.2168.

(2*S*,3*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-2-methyl-3-((*R*)-1,4-dioxaspiro[4.5]decan-2-yl)-

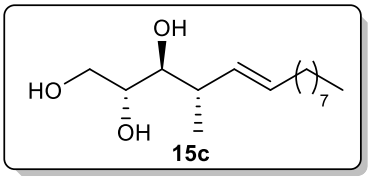


propan-1-ol (15b): Following the same protocol as used for the synthesis compound **10**, the TBS protected corresponding alcohol (1.13 g, 91%, Flash column chromatography; SiO_2, 100−200 mesh, 5% EtOAc in hexane as eluent) was prepared as colorless oil from compound **15a** (912 mg, 2.90 mmol) using 2,6-lutidine (1.4 mL, 11.60 mmol) and TBSOTf (1.6 mL, 7.25 mmol). R_f = 0.52 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = +39.3 (*c* 0.61, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.19 (dd, *J* = 10.9, 7.5 Hz, 1H), 4.10 – 3.95 (m, 3H), 3.80 – 3.73 (m, 2H), 2.09 (ddt, *J* = 10.3, 7.2, 3.2 Hz, 1H), 1.56 (d, *J* = 7.4 Hz, 8H), 1.38 (s, 2H), 1.21 (s, 9H), 0.99 (d, *J* = 7.1 Hz, 3H), 0.87 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.73, 75.75, 74.00, 67.61, 66.60, 38.92, 38.38, 36.50, 35.08, 27.41, 25.96, 25.32, 24.14, 24.05, 18.20, 12.14, -4.07, -4.32; IR (neat) ν_{max} 2961, 2927, 2855, 1721, 1462, 1270, 1095 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{44}O_5SiNa$ $[M+Na]^+$ 451.2856, found 451.2858.

Following the same procedure as used for preparation of compound **10**, alcohol **15b** (594 mg, 81%, Flash column chromatography; SiO_2, 100−200 mesh, 10% EtOAc in hexane as eluent) was prepared as colorless liquid from the above pivaloyl ester (912 mg, 2.13 mmol) using DIBAL-H (3.3 mL, 5.32 mmol, 1.6 M in toluene); R_f = 0.39 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = +71.3 (*c* 0.28, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.13 – 4.04 (m, 2H), 3.81 –

3.68 (m, 3H), 3.62 (t, *J* = 9.0 Hz, 1H), 2.88 (s, 1H), 1.98 (ddt, *J* = 10.5, 7.1, 3.5 Hz, 1H), 1.64 – 1.52 (m, 8H), 1.43 – 1.34 (m, 2H), 1.01 (d, *J* = 7.1 Hz, 3H), 0.87 (s, 9H), 0.08 (d, *J* = 1.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 110.24, 75.03, 68.23, 65.07, 40.41, 36.36, 35.08, 25.94, 25.20, 24.14, 24.03, 18.18, 11.32, -3.97, -4.46; IR (neat) ν_{max} 3431, 2934. 2858, 1472, 1252, 1095 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{36}O_4SiNa$ $[M+Na]^+$ 367.2281, found 367.2283.

(2*R*,3*S*,4*S*,*E*)-4-Methyltetradec-5-ene-1,2,3-triol (15c): Following the same experimental procedure as described for the preparation of compound **12**, the alcohol **15b** (506 mg, 1.47 mmol) was oxidised using IBX (1.03 g, 3.67 mmol) to corresponding aldehyde which was subjected to flash chromatography (SiO_2, 100-200 mesh, eluent 100% EtOAc) and used for the next reaction without further purification and characterizations.



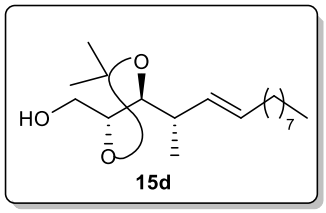
15c

Following the same experimental procedure as described for the preparation of compound **12**, the above aldehyde and sulfone **11** (593 mg, 1.76 mmol), was coupled with the help of KHMDS (3.9 mL, 1.94 mmol, 0.5 M in THF) to furnish corresponding *E*-olefin (525 mg, 79%; purification: SiO_2, 100-200 mesh, 2% EtOAc in hexane as eluent) as a colorless liquid; R_f = 0.43 (5% EtOAc in hexane).

Following the same experimental procedure as described for the preparation of compound **12**, the above olefin (321 mg, 0.709 mmol) was subjected to react with 4N HCl solution to result pure triol **15c** (137 mg, 75%; purification: SiO_2, 100−200 mesh, 70% EtOAc in hexane as eluent) as a yellow oil; R_f = 0.22 (60% EtOAc in hexane); $[\alpha]_D^{25}$ = +171.2 (*c* 0.07, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (dt, *J* = 15.2, 6.9 Hz, 1H), 5.35 (dd, *J* = 15.4, 8.3 Hz, 1H), 3.84 – 3.76 (m, 2H), 3.70 – 3.65 (m, 1H), 3.53 – 3.48 (m, 1H), 2.75 – 2.57 (m, 1H), 2.40 – 2.32 (m, 1H), 2.12 – 1.99 (m, 3H), 1.66 (s, 1H), 1.34 – 1.26 (m, 12H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.89 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.01, 130.88, 76.94, 71.91, 63.50, 39.82, 32.79, 32.02, 29.58, 29.42, 29.34, 22.81, 17.14, 14.26; IR (neat) ν_{max} 3383, 2956,

2923, 2853, 1459, 1070, 1028 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}O_3SiNa$ $[M+Na]^+$ 281.2093, found 281.2095.

((4*S*)-5-((*S*,*E*)-Dodec-3-en-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol(15d): Following



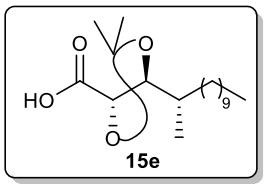
15d

the same experimental procedure as described for the preparation of compound **13**, the triol **15c** (121 mg, 0.468 mmol), was treated with Et_3N (0.13 mL, 0.936 mmol) and PivCl (63 µL, 0.515 mmol) to furnish pivaloyl protected alcohol as colorless oil (purification: SiO_2, 100−200 mesh, 5-30% EtOAc in hexane as eluent); R_f = 0.42 (25% EtOAc in hexane as eluent) which was used directly in next step.

Following the same experimental procedure as described for the preparation of compound **13**, the above pivaloyl ester (115 mg, 0.335 mmol) was allowed to react with 2,2-DMP (82 mL, 0.671 mmol) and CSA (4 mg, 0.017 mmol) to get the corresponding compound which was directly used for the next step without further characterization.

Following the same experimental procedure as described for the preparation of compound **13**, the above acetonide protected pivaloyl ester (124 mg, 0.324 mmol) was treated with DIBAL-H (0.5 mL, 0.81 mmol, 1.6 M in toluene) to afford pure alcohol **15d** (75 mg, 54%; purification: SiO_2, 100−200 mesh, 20-30% EtOAc in hexane as eluent) as colorless liquid; R_f = 0.61 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = +38.5 (*c* 0.23, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.54 – 5.44 (m, 2H), 4.13 (q, *J* = 5.9 Hz, 1H), 3.90 (dd, *J* = 9.2, 5.6 Hz, 1H), 3.63 (d, *J* = 7.0 Hz, 2H), 2.30 (qd, *J* = 6.2, 2.8 Hz, 1H), 2.03 – 1.98 (m, 2H), 1.65 (s, 1H), 1.47 (s, 3H), 1.36 (s, 3H), 1.26 (s, 12H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.14, 130.68, 108.42, 81.22, 78.07, 61.68, 35.53, 32.75, 32.04, 29.61, 29.54, 29.47, 29.25, 28.57, 25.88, 22.83, 18.05, 14.26; IR (neat) ν_{max} 3451, 2921, 2857, 1455, 1069 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{18}H_{34}O_3SiNa$ $[M+Na]^+$ 321.2406, found 321.2407.

(4*R*)-5-((*S*)-Dodecan-2-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylic acid (15e): Following



15e

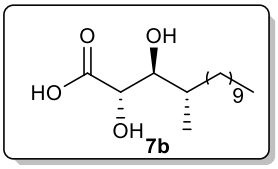
the same experimental procedure as described for the preparation of compound **14**, olefin **15d** (64 mg, 0.214 mmol) was hydrogenated in the presence of H_2 and 10 mol% Pd/C (7 mg) to give the corresponding saturated alcohol (59 mg, 91%; purification: SiO_2, 100−200 mesh, 2-10% EtOAc in hexane as eluent) as a yellow oil; R_f = 0.67 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = +22.3 (*c* 0.71, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.15 (q, *J* = 5.9 Hz, 1H), 3.81 (dd, *J* = 10.0, 5.5 Hz, 1H), 3.64 – 3.54 (m, 2H), 2.04-1.94 (m, 1H), 1.62 (s, 1H), 1.47 (s, 3H), 1.36 (s, 3H), 1.26 (s, 18H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.89 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.10, 81.85, 77.95, 61.85, 33.72, 32.34, 32.05, 29.97, 29.76, 29.48, 28.65, 26.82, 25.94, 22.83, 17.13, 14.26; IR (neat) ν_{max} 3458, 2961, 2928, 2858, 1469, 1061 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{36}O_3SiNa$ $[M+Na]^+$ 323.2562, found 323.2564.

Following the same experimental procedure as described for the preparation of compound **14**, the above alcohol (50 mg, 0.166 mmol) was oxidised using $NaHCO_3$ (56 mg, 0.664 mmol) and DMP (176 mg, 0.415 mmol) to get the corresponding aldehyde which was used subsequently for the next reaction without further purification characterization.

Following the same experimental procedure as described for the preparation of compound **14**, the above aldehyde was treated with $NaClO_2$ (60 mg, 0.664 mmol) and $NaH_2PO_4.2H_2O$ (104 mg, 0.664 mmol) to produce carboxylic acid **15e** (42 mg, 80%; purification: SiO_2, 100-200 mesh, 20-50% EtOAc in hexane as eluent) as colorless oil; R_f = 0.12 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = +72.5 (*c* 0.26, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.56 (d, *J* = 6.4 Hz, 1H), 4.03 (dd, *J* = 9.4, 6.4 Hz, 1H), 1.74 – 1.64 (m, 1H), 1.61 (s, 3H), 1.39 (s, 3H), 1.27 –1.66 (m, 18H), 1.00 (d, *J* = 6.4 Hz, 3H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 110.48, 83.09, 33.54, 33.49, 32.07, 30.10, 29.79, 29.50, 26.88, 26.23, 25.37,

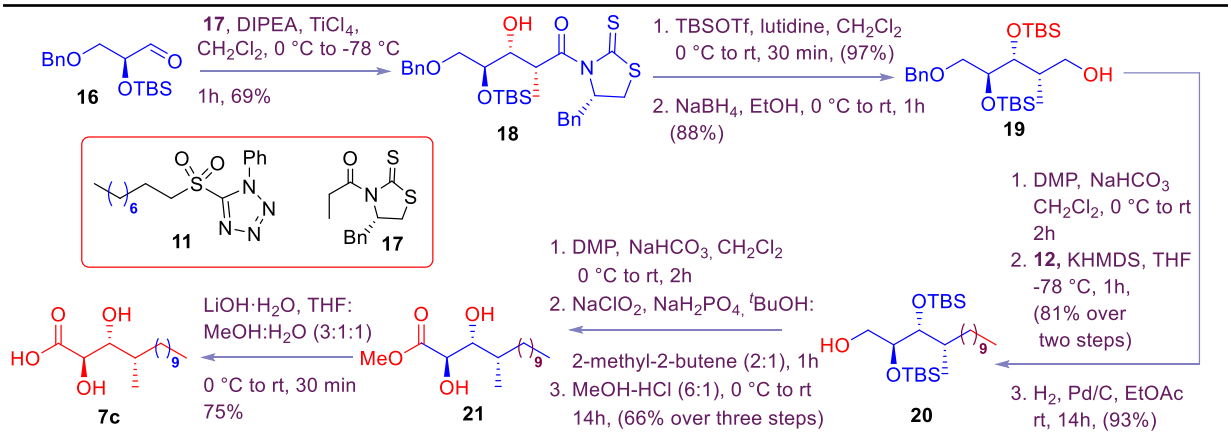
22.84, 16.34, 14.27; IR (neat) ν_{max} 3467, 2985, 2925, 2958, 2859, 1725, 1465 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{35}O_4$ $[M+H]^+$ 337.2355, found 337.2353.

(2*S*,3*S*,4*S*)-2,3-Dihydroxy-4-methyltetradecanoic acid (7b): Following the same experimental procedure as described for the preparation of compound **7a**, acid **15e** (35 mg, 0.111 mmol) was subjected to react with conc. HCl in MeOH (3 mL, 1:6) to furnish the corresponding ester (26 mg, 81%; purification: SiO_2, 100−200 mesh, 20-40% EtOAc in hexane as eluent) as a yellow oil; R_f = 0.53 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = +13.9 (c 0.24, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.31 (d, *J* = 3.8 Hz, 1H), 3.81 (s, 3H), 3.55 (dd, *J* = 8.1, 3.7 Hz, 1H), 3.24 (s, 1H), 2.43 (s, 1H), 1.72 – 1.63 (m, 1H), 1.42-1.36 (m, 1H), 1.25 (s, 16H), 1.19 –1.12 (m, 1H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.87 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.80, 78.24, 72.49, 52.70, 35.16, 32.34, 32.05, 30.15, 29.81, 29.78, 29.49, 26.74, 22.82, 15.85, 14.25 ppm; IR (neat) ν_{max} 3478, 2958, 2924, 2857, 1731, 1459, 1079 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{32}O_4SiNa$ $[M + Na]^+$ 311.2198, found 311.2197.



Following the same experimental procedure as described for the preparation of compound **7a**, the above ester (21 mg, 0.073 mmol) was treated with $LiOH.H_2O$ (12 mg, 0.292 mmol) to result acid **7b** (15 mg, 75%; purification: SiO_2, 100−200 mesh, 70-100% EtOAc in hexane as eluent) as off white solid; R_f = 0.12 (80% EtOAc in hexane); $[\alpha]_D^{25}$ = +34.7 (*c* 0.23, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ 4.11 (d, *J* = 5.2 Hz, 1H), 3.48 (t, *J* = 5.9 Hz, 1H), 1.77 (dt, *J* = 13.8, 5.2 Hz, 1H), 1.37 –1.34 (m, 1H), 1.24 (s, 16H), 1.22 –1.10 (m, 1H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.84 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.06, 77.26, 72.35, 34.53, 31.69, 31.10, 29.79, 29.44, 29.38, 29.10, 26.68, 22.35, 15.15, 13.09; IR (neat) ν_{max} 3424, 2944, 2920, 2852, 1710, 1466, 1220, 1075 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}O_4SiNa$ $[M+Na]^+$ 297.2042, found 297.2044.

***Scheme S3**: Synthesis of Acid **7c**.*

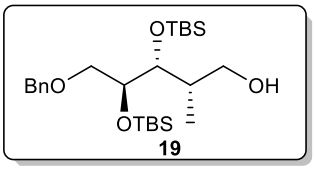


(2*R*,3*R*,4*S*)-1-((*S*)-4-Benzyl-2-thioxothiazolidin-3-yl)-5-(benzyloxy)-4-((tert-butyldimethylsilyl)oxy)-3-hydroxy-2-methylpentan-1-one (18): To the stirred solution of corresponding diol (1.15g, 3.52 mmol) in 2:1 THF/H_2O (40 mL) at 0 °C, $NaHCO_3$ (1.0 g, 12.33 mmol) and $NaIO_4$ (1.89 mg, 8.81 mmol) were added sequentially. The reaction mixture was warmed to room temperature and stirred further for 1h. The resultant mixture was filtered through a short pad of Celite, diluted with water, extracted with EtOAc (3 × 50 mL), washed with water, brine, dried (Na_2SO_4) and concentrated in *vacuo* to yield crude aldehyde **16** which was directly taken in Crimmins aldol without further purification and characterization.

To a stirred solution of thiazolidinethione **17** (1.03 g, 3.87 mmol) dissolved in anhydrous CH_2Cl_2 (20 mL), freshly distilled $TiCl_4$ (0.42 mL, 3.87 mmol) was added drop wise at 0 °C under argon and stirred for 5 min. DIPEA (0.68 mL, 3.87 mmol) was added drop wise into the reaction mixture and stirred for another 10 min. The reaction mixture was then cooled to −78 °C and aldehyde **16** from the previous step (dissolved in 10 mL anhydrous CH_2Cl_2) was cannulated into it. The reaction was continued further at −78 °C for 45 min prior to quench with saturated aqueous NH_4Cl solution (20 mL). The resulting mixture was warmed to the ambient temperature and extracted with CH_2Cl_2 (3 × 15 mL), washed with water, brine, dried (Na_2SO_4), filtered and concentrated in *vacuo*. Purification of residue by column

chromatography (SiO_2, 230−400 mesh, 5-15% EtOAc in hexane as eluent) resulted exclusively compound **18** (1.36 g, 69%) as yellow oil; R_f = 0.41 (15 % EtOAc in hexane); $[\alpha]_D^{25}$ = -22.3 (*c* 0.78, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.23 (m, 10H), 5.30 (dddd, *J* = 10.9, 7.2, 3.7, 1.0 Hz, 1H), 4.91 (qd, *J* = 7.0, 4.3 Hz, 1H), 4.57 – 4.45 (m, 2H), 4.13 (ddd, *J* = 6.8, 4.4, 2.5 Hz, 1H), 3.88 (dt, *J* = 6.6, 4.5 Hz, 1H), 3.69 (dd, *J* = 9.8, 4.6 Hz, 1H), 3.54 (dd, *J* = 9.8, 4.5 Hz, 1H), 3.31 (ddd, *J* = 11.5, 7.2, 1.0 Hz, 1H), 3.17 (dd, *J* = 13.2, 3.7 Hz, 1H), 3.10 (d, *J* = 2.6 Hz, 1H), 2.90 – 2.79 (m, 2H), 1.27 (d, *J* = 7.1 Hz, 3H), 0.90 (s, 9H), 0.11 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.62, 177.92, 138.18, 136.82, 129.52, 129.01, 128.44, 128.04, 127.69, 127.29, 73.75, 72.58, 72.40, 71.61, 69.16, 40.43, 36.86, 31.63, 26.05, 18.27, 12.25, -4.14, -4.63; IR (neat) ν_{max} 3371, 2928, 2853, 1684, 1456, 1259, 1101 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{29}H_{41}NO_4S_2SiNa$ $[M+Na]^+$ 582.2144, found 582.2147.

(2*S*,3*R*,4*S*)-5-(Benzyloxy)-3,4-bis((tert-butyldimethylsilyl)oxy)-2-methylpentan-1-ol (19):

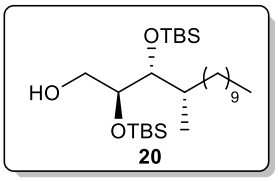


To an ice-cold solution of compound **18** (846 mg, 1.51 mmol) in anhydrous CH_2Cl_2 (20 mL) under argon, 2,6-lutidine (0.36 mL, 3.02 mmol) was added and the mixture was stirred for 5 min prior to addition of TBSOTf (0.51 mL, 2.27 mmol). The reaction was continued for 30 min at the same temperature and subsequently quenched with a saturated solution of $NaHCO_3$ (10 mL) and diluted with water. The resultant mixture was extracted with CH_2Cl_2 (3 × 20 mL), washed with aqueous solution of $CuSO_4$, water, brine, dried (Na_2SO_4), filtered and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO_2, 100−200 mesh, 5% EtOAc in hexane as eluent) gave the corresponding TBS ether (987 mg, 97%) as yellow oil. R_f = 0.68 (15% EtOAc in hexane); $[\alpha]_D^{25}$ = -34.1 (*c* 0.47, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 – 7.31 (m, 1H), 7.30 – 7.28 (m, 5H), 7.27 – 7.25 (m, 1H), 7.24 – 7.21 (m, 3H), 5.28 (ddd, *J* = 10.6, 7.1, 3.4 Hz, 1H), 4.92 (dt, *J* = 14.7, 7.1 Hz, 1H), 4.45 (d, *J* = 1.6 Hz, 2H), 4.24 (dd, *J* = 8.3, 1.6 Hz, 1H), 3.86 (td, *J* = 4.2, 2.1 Hz, 1H), 3.68 (dd, *J* = 9.9, 4.3 Hz, 1H), 3.37 (dd, *J* =

9.9, 6.0 Hz, 1H), 3.25 (dd, *J* = 11.5, 7.3 Hz, 1H), 3.10 (dd, *J* = 13.2, 3.3 Hz, 1H), 2.90 (dd, *J* = 13.2, 10.7 Hz, 1H), 2.75 (d, *J* = 11.5 Hz, 1H), 1.22 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.13 (s, 3H), 0.09 (d, *J* = 1.7 Hz, 6H), 0.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.58, 176.99, 138.61, 136.87, 129.49, 129.03, 128.33, 127.92, 127.44, 127.29, 77.22, 75.37, 73.54, 72.18, 69.13, 41.81, 37.10, 31.21, 26.31, 26.24, 25.84, 18.62, 18.46, 15.87, -2.80, -3.56, -4.26, -4.44, -4.62. IR (neat) ν_{max} 2957, 2931, 2854, 1686, 1466, 1253, 1098 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{35}H_{55}NO_4S_2Si_2$ $[M]^+$ 673.3111, found 673.3113.

To a solution of the above silyl ether (902 mg, 1.34 mmol) in anhydrous EtOH : THF (1 : 1, 20 mL), $NaBH_4$ (250 mg, 6.69 mmol) was added at 0 °C and stirred for 1 h at the same temperature under argon. The reaction was quenched with saturated aqueous NH_4Cl (15 mL). EtOH was removed under reduced pressure and diluted with water. The resultant mixture was extracted with EtOAc (3 × 30 mL), washed with brine, dried (Na_2SO_4) and concentrated in *vacuo*. Purification of the residue obtained by column chromatography (SiO_2, 100-200 mesh, 5-15% EtOAc in hexane eluent) afforded alcohol **19** (552 mg, 88%) as thick colorless oil; R_f = 0.33 in 10% EtOAc in hexane; $[\alpha]_D^{25}$ = -59.6 (*c* 0.67, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H), 4.59 – 4.47 (m, 2H), 3.99 – 3.94 (m, 1H), 3.82 (t, *J* = 3.8 Hz, 1H), 3.67 (dd, *J* = 9.9, 4.1 Hz, 1H), 3.54-3.51 (m, 2H), 3.45 (dd, *J* = 9.9, 6.2 Hz, 1H), 2.39 (t, *J* = 4.6 Hz, 1H), 2.01 (dq, *J* = 9.4, 3.4, 2.7 Hz, 1H), 0.96 – 0.90 (m, 21H), 0.13 (s, 3H), 0.10 (d, *J* = 2.2 Hz, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.31, 128.37, 127.82, 127.61, 76.13, 74.84, 73.43, 72.79, 65.47, 39.01, 26.18, 26.11, 18.42, 18.33, 12.60, -3.85, -4.24, -4.55, -4.68); IR (neat) ν_{max} 3440, 2954, 2928, 2856, 1471, 1252, 1095 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{49}O_4Si_2$ $[M+H]^+$ 469.3169, found 469.3163.

(2*S*,3*R*,4*S*)-2,3-bis((*tert*-Butyldimethylsilyl)oxy)-4-methyltetradecan-1-ol (20): To an ice-



20

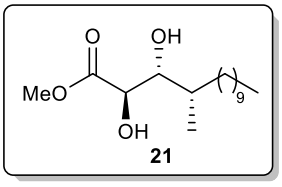
cold solution of alcohol **19** (522 mg, 1.11 mmol) in anhydrous CH_2Cl_2 (15 mL), $NaHCO_3$ (281 mg, 3.34 mmol) and DMP (944 mg, 2.23 mmol) were added sequentially. The reaction mixture was warmed gradually to the room temperature and stirred further for 2 h. The reaction was then quenched with saturated aqueous solution of $Na_2S_2O_3$ (8 mL) and $NaHCO_3$ (8 mL), and stirred until the two phases were separated. The resultant mixture was extracted with CH_2Cl_2 (3 × 10 mL), washed with water, brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude residue was purified using flash column chromatography (using a short pad of 60-120 silica and EtOAc as eluent) to get the corresponding aldehyde as pale yellow liquid which was taken for the next reaction without further purification and characterization.

To a stirred solution of sulfone **11** (412 mg, 1.22 mmol) in anhydrous THF (10 mL) at -78 ^{O}C under argon, KHMDS (2.7 mL, 1.35 mmol, 0.5 M in THF) was added and the reaction mixture was stirred for 30 min at the same temperature. A solution of the above aldehyde dissolved in anhydrous THF (5 mL) was cannulated to the reaction mixture and stirred for another 30 min at the same temperature before quenching it with saturated aqueous NH_4Cl solution (10 mL), diluted with water. The resultant mixture was extracted with EtOAc (3 × 15 mL), washed with brine, dried (Na_2SO_4), filtered and concentrated in *vacuo*. Purification by column chromatography (SiO_2, 100-200 mesh, 2% EtOAc in hexane as eluent) furnished the corresponding *E*-olefin (519 mg, 81%) as a colorless liquid; R_f = 0.53 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -49.9 (*c* 0.56, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, *J* = 4.3 Hz, 4H), 7.30 – 7.26 (m, 1H), 5.40 (dt, *J* = 15.4, 6.3 Hz, 1H), 5.28 (dd, *J* = 15.5, 7.9 Hz, 1H), 4.53-4.43 (m, 2H), 3.96 (dt, *J* = 6.2, 2.9 Hz, 1H), 3.63 (dd, *J* = 10.3, 3.2 Hz, 1H), 3.47 (dd, *J* = 7.2, 2.6 Hz, 1H), 3.43 – 3.37 (m, 1H), 2.33 (q, *J* = 7.1 Hz, 1H), 2.00 – 1.94 (m, 2H), 1.34 – 1.26 (m, 12H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 5.6 Hz, 21H), 0.07 – 0.03 (m, 12H); ^{13}C NMR (75 MHz,

$CDCl_3$) δ 138.90, 133.75, 130.86, 128.33, 127.68, 127.42, 80.37, 74.14, 73.29, 72.55, 40.49, 32.89, 32.08, 29.86, 29.68, 29.49, 29.44, 26.30, 26.22, 22.85, 18.60, 18.45, 17.13, 14.28, -3.62, -4.12, -4.40, -4.47; IR (neat) ν_{max} 2955, 2927, 2856, 1728, 1462 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{34}H_{64}O_3Si_2Na$ $[M+Na]^+$ 599.4292, found 599.4295.

To a stirred solution of the above olefin (481 mg, 0.832 mmol) in distilled EtOAc (5 mL) fitted with H_2 balloon, 10% Pd/C (50 mg) was added carefully at the room temperature and stirred for 14 h. The reaction mixture was filtered using a short Celite pad and washed with EtOAc (3 × 20 mL). Purification by column chromatography (SiO_2, 100-200 mesh, 5% EtOAc in hexane as eluent) furnished saturated alcohol **20** (380 mg, 93%) as colorless liquid; R_f = 0.53 (5% EtOAc in hexane); $[\alpha]_D^{25}$ = -110.2 (*c* 0.29, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 – 3.58 (m, 4H), 2.02 (dt, *J* = 13.2, 4.7 Hz, 1H), 1.73 – 1.64 (m, 1H), 1.26 (brs, 18H), 0.93 – 0.85 (m, 24H), 0.10 (dd, *J* = 10.2, 7.3 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 77.74, 74.22, 63.94, 35.63, 34.47, 32.08, 29.96, 29.82, 29.50, 27.78, 26.31, 26.06, 22.85, 18.62, 18.26, 14.27, -3.92, -4.07, -4.33; IR (neat) ν_{max} 3473, 2956, 2927, 2856, 1728, 1463, 1223 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{60}O_3Si_2Na$ $[M+Na]^+$ 511.3979, found 511.3978.

Methyl (2*R*,3*R*,4*S*)-2,3-dihydroxy-4-methyltetradecanoate (21): Following the same experimental procedure as described for the preparation of compound **14**, alcohol **20** (206 mg, 0.421 mmol) was oxidized to the corresponding aldehyde using $NaHCO_3$ (106 mg, 1.264 mmol) and DMP (357 mg, 0.842 mmol) which used for the next reaction without further purification and characterization.



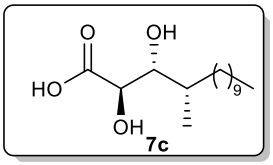
21

Following the same experimental procedure as described for the preparation of compound **14**, the above aldehyde was subjected to react with $NaClO_2$ (152 mg, 1.68 mmol) and $NaH_2PO_4.2H_2O$ (263 mg, 1.68 mmol) to furnish the corresponding carboxylic acid (167 mg, 79%; purification: SiO_2, 100-200 mesh, 20-50% EtOAc in hexane as eluent) as colorless

oil; R_f = 0.48 (5% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.24 (d, J = 3.2 Hz, 1H), 3.73 (dd, J = 5.6, 3.1 Hz, 1H), 1.82 – 1.75 (m, 1H), 1.25 (s, 18H), 0.91 (d, J = 6.1 Hz, 24H), 0.15 – 0.09 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.82, 79.42, 75.43, 35.76, 33.30, 32.07, 29.89, 29.78, 29.49, 27.39, 26.17, 26.07, 25.92, 22.84, 18.42, 18.35, 15.34, 14.27, -3.77, -4.33, -4.61, -5.00); IR (neat) ν_{max} 3525, 2959, 2926, 2855, 1721, 1463, 1262 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{58}O_4Si_2Na$ $[M+Na]^+$ 525.3771, found 525.3773.

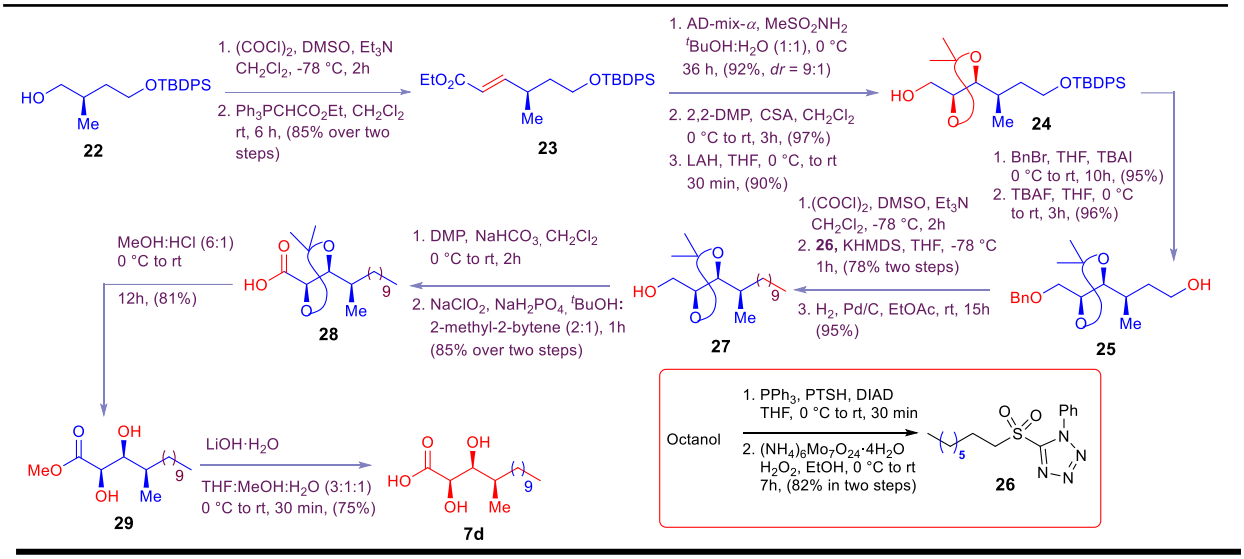
Following the same experimental procedure as described for the preparation of compound **7a**, the above acid (150 mg, 0.298 mmol) was treated with conc. HCl in MeOH (7 mL, 1:6) to obtain ester **21** (71 mg, 83%; purification: SiO_2, 100−200 mesh, 20-40% EtOAc in hexane as eluent) as pale yellow oil; R_f = 0.53 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = +3.6 (*c* 0.37, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.25 (t, J = 5.7 Hz, 1H), 3.82 (s, 3H), 3.63 (q, J = 5.4 Hz, 1H), 3.00 (d, J = 6.3 Hz, 1H), 2.32 (d, J = 5.7 Hz, 1H), 1.79 – 1.71 (m, 1H), 1.66 (s, 1H), 1.47 – 1.39 (m, 1H), 1.26 (s, 17H), 0.96 (d, J = 6.7 Hz, 3H), 0.87 (t, J = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.23, 76.49, 72.39, 52.79, 34.49, 33.47, 32.06, 29.92, 29.81, 29.77, 29.49, 26.96, 22.83, 14.30, 14.26; IR (neat) ν_{max} 3525, 2958, 2926, 2857, 1729, 1463, 1254, 1091 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{32}O_4Na$ $[M+Na]^+$ 311.2198, found 311.2196.

(2*R*,3*R*,4*S*)-2,3-Dihydroxy-4-methyltetradecanoic acid (7c): Following the same experimental procedure as described for the preparation of acid **7a**, ester **21** (60 mg, 0.208 mmol) was treated with LiOH.H_2O (35 mg, 0.832 mmol) to afford acid **7c** (43 mg, 75%; purification: SiO_2, 100-200 mesh, 70-100% EtOAc in hexane as eluent) as off white solid; R_f = 0.12 (80% EtOAc in hexane); $[\alpha]_D^{25}$ = +68.8 (*c* 0.46, MeOH); ^{1}H NMR (300 MHz, CD_3OD) δ 4.04 (d, J = 7.0 Hz, 1H), 3.60 (dd, J = 7.0, 4.1 Hz, 1H), 1.81 (dt, J = 12.8, 4.3 Hz, 1H), 1.48 – 1.39 (m, 1H), 1.29 – 1.24 (m, 16H), 1.15 – 1.22 (m, 1H), 0.87-0.89 (m, 6H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.51, 75.08, 72.17, 33.66, 33.48, 31.66, 29.58, 29.39, 29.39, 29.36, 29.07, 26.81, 22.32, 13.06, 12.44; IR (neat) ν_{max} 3421, 2958, 2926,

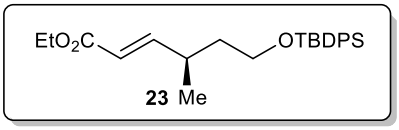


2855, 1729, 1465, 1221, 1074 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}O_4Na$ $[M+Na]^+$ 297.2042, found 297.2044.

***Scheme S4**: Synthesis of Acid **7d**.*



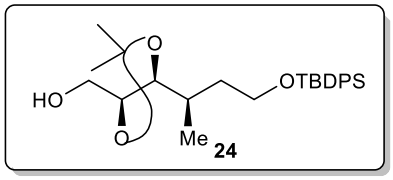
Ethyl (*R*,*E*)-6-((*tert*-butyldiphenylsilyl)oxy)-4-methylhex-2-enoate (23): To a stirred solution of $(COCl)_2$ (1.0 mL, 11.79 mmol) in anhydrous CH_2Cl_2 (20 mL) at -78 °C, DMSO (1.5 mL, 20.64 mmol) was added drop wise under argon atmosphere. After 15 min, alcohol **22** (2.02 g, 5.90 mmol, dissolved in 10 mL anhydrous CH_2Cl_2) was cannulated into the reaction mixture. After 30 min, Et_3N (2.9 mL, 20.64 mmol) was added and the reaction was continued further for 30 min at the same temperature. The reaction was then warmed slowly to 0 °C and stirred further for 15 min. The reaction mixture was then quenched with saturated aqueous NH_4Cl (20 mL), diluted with water and finally, extracted with EtOAc (3 × 30 mL), washed with saturated $NaHCO_3$, water, brine, dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (SiO_2, 100-200 mesh, 100% EtOAc in hexane as eluent) of the crude residue provided the corresponding aldehyde as colorless oil which was taken forward without further characterization.



To a solution of above aldehyde in anhydrous CH_2Cl_2 (40 mL) at the room temperature under argon, $Ph_3P{=}CHCO_2Et$ (4.1 g, 11.79 mmol) was added at once. The reaction was

continued for 6 h at the same temperature. The reaction mixture was then concentrated in *vacuo*. The residue obtained, was purified by flash chromatography (SiO_2, 100-200 mesh, 2% EtOAc in hexane as eluent) to afford the *α, β*-unsaturated olefin **23** (2.06 g, 85% over two steps) as colourless liquid; R_f= 0.79 (5% EtOAc in hexane); $[\alpha]_D^{25}$ = -18.1 (*c* 0.88, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.65 (ddt, *J* = 6.6, 2.0, 0.9 Hz, 4H), 7.43 – 7.35 (m, 6H), 6.86 (dd, *J* = 15.7, 7.8 Hz, 1H), 5.77 (dd, *J* = 15.7, 1.2 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.66 (dd, *J* = 6.7, 5.9 Hz, 2H), 2.58 (p, *J* = 7.0 Hz, 1H), 1.63 – 1.59 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 7.2 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 167.00, 154.30, 135.67, 133.93, 133.89, 129.73, 127.77, 119.93, 61.59, 60.30, 38.70, 33.13, 26.98, 19.40, 19.32, 14.44; IR (neat) ν_{max} 2959, 2930, 2858, 1717, 1652, 1261, 1104 cm^{-1}.

((4*S*)-5-((*R*)-4-((*tert*-Butyldiphenylsilyl)oxy)butan-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)-methanol (24): A stirred of AD mix-*α* (9.6 g, 2.0 g for 1 mmol of olefin) and $MeSO_2NH_2$ (1.15 g, 12.18 mmol) were dissolved in a mixture of ^{t}BuOH and distilled water (1:2, 30 mL) and stirred for 30 min at room temperature. The reaction mixture was cooled to 0 °C, and olefin **23** (2.0 g, 4.86 mmol, dissolved in 10 mL ^{t}BuOH) was added to it. The mixture was stirred vigorously for 36 h at the same temperature and finally quenched with $Na_2S_2O_3$ (4.8 g). The resulting mixture was stirred for another 1 h and ^{t}BuOH was removed. The residue was diluted with distilled water, extracted with EtOAc (3 × 25 mL). The organic layer was washed with water and brine, dried (Na_2SO_4), and concentrated in *vacuo*. Column chromatographic purification (SiO_2, 230−400 mesh, 10-13% EtOAc in hexane as eluent) of the resultant crude residue yielded the corresponding pure diol (1.99 g, *dr* = 9:1, 92%) colorless oil; R_f= 0.46 (20% EtOAc in hexane); $[\alpha]_D^{25}$ = -7.4 (*c* 0.54, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.70 – 7.67 (m, 4H), 7.44 – 7.36 (m, 6H), 4.32 – 4.19 (m, 3H), 3.82 – 3.67 (m, 3H), 3.13 (d, *J* = 5.4 Hz, 1H), 2.50 (d, *J* = 8.5 Hz, 1H), 2.01 – 1.92 (m, 1H), 1.83 – 1.76 (m, 1H), 1.53 – 1.43 (m, 1H),



24

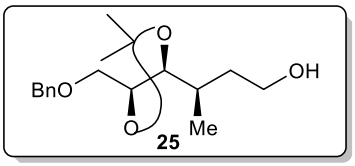
1.30 (t, *J* = 7.1 Hz, 3H), 1.06 (s, 9H), 1.00 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.11, 135.69, 133.81, 129.75, 127.78, 75.93, 71.77, 62.14, 61.91, 36.02, 33.65, 26.97, 19.28, 15.19, 14.29; IR (neat) ν_{max} 3473, 3068, 2957, 2931, 2857, 1732, 1427, 1260, 1105, 1021 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{36}O_5SiNa$ $[M+Na]^+$ 467.2230, found 467.2235.

To an ice-cold solution of the above diol (1.73 g, 3.89 mmol) in anhydrous CH_2Cl_2 (20 mL) under argon 2,2- DMP (1.9 mL, 15.56 mmol) and CSA (45 mg, 0.194 mmol) were added sequentially. The reaction mixture was stirred for 3 h at the room temperature prior to quenching it with Et_3N (2 mL). The residue was subsequently concentrated and purified by flash column chromatography (SiO_2, 100-200 mesh, 5-10% EtOAc in hexane as elutant) to obtain corresponding acetonide protected diol (1.83 g, 97%) as a colorless oil; R_f = 0.59 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -6.1 (*c* 0.66, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 – 7.61 (m, 4H), 7.46 – 7.34 (m, 6H), 4.28 – 4.17 (m, 3H), 4.12 (dd, *J* = 7.1, 4.6 Hz, 1H), 3.75 (td, *J* = 8.0, 7.4, 5.6 Hz, 2H), 2.10 – 2.00 (m, 1H), 1.80 (dtd, *J* = 14.1, 7.2, 4.5 Hz, 1H), 1.44 (d, *J* = 7.1 Hz, 6H), 1.30 –1.25 (m, 4H), 1.06 (s, 9H), 0.95 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.71, 135.69, 134.06, 129.72, 127.77, 110.97, 83.03, 77.12, 61.89, 61.39, 36.29, 32.13, 27.10, 27.01, 25.87, 19.34, 14.28, 14.11; IR (neat) ν_{max} 3071, 2959, 2934, 2861, 1755, 1259, 1091, 1015 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{40}O_5SiNa$ $[M+Na]^+$ 507.2543, found 507.2546.

To an ice-cold suspension of LAH (423 mg, 11.13 mmol) in anhydrous THF (10 mL), under argon the above ester (1.8 g, 3.71 mmol) was added dropwise (dissolving in 10 mL anhydrous THF) over a period of 15 min via cannula. The reaction was then allowed to stir at the same temperature for 30 min prior to quench with saturated aqueous Na_2SO_4 (8 mL). The organic part was filtered through sintered funnel and washed with EtOAc (3 × 25 mL) and evaporated in *vacuo.* Purification by column chromatography (SiO_2, 100-200 mesh, 5-10% EtOAc in hexane as eluent) furnished the corresponding alcohol **24** (1.48 g, 90%) as colorless

liquid; R_f = 0.33 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -67.8 (*c* 0.47, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.62 (m, 4H), 7.46 – 7.34 (m, 6H), 3.91 (ddd, *J* = 8.1, 5.3, 3.0 Hz, 1H), 3.80 – 3.69 (m, 4H), 3.57 (dd, *J* = 11.9, 5.4 Hz, 1H), 2.12 (s, 1H), 1.93 – 1.84 (m, 1H), 1.71 (ddt, *J* = 14.0, 7.1, 3.6 Hz, 1H), 1.40 (s, 6H), 1.06 (s, 9H), 0.94 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.68, 133.99, 129.73, 127.77, 108.70, 80.67, 79.42, 63.42, 61.73, 36.27, 31.84, 27.39, 27.32, 27.00, 19.32, 14.66; IR (neat) ν_{max} 3468, 2964, 2931, 2858, 1428, 1104, 1085, 1027 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{39}O_4Si$ $[M+H]^+$ 443.2618, found 443.2613.

(3*R*)-3-((5*S*)-5-((Benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)butan-1-ol (25): To an

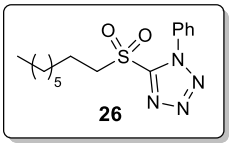


ice-cold solution of the alcohol **24** (1.34 g, 3.03 mmol) in anhydrous THF (20 mL) under argon, NaH (182 mg, 4.54 mmol) was added portion wise over a period of 15 min and the mixture was stirred for 5 min prior to addition of BnBr (0.43 mL, 3.64 mmol) followed by TBAI (56 mg, 0.152 mmol). The reaction was warmed gradually to the room temperature and continued further for 10 h at the same temperature. The reaction mixture was subsequently quenched with a saturated solution of NH_4Cl (10 mL) at 0 °C, diluted with water. The resultant mixture was extracted with EtOAc (2 × 15 mL), washed with brine, water, dried (Na_2SO_4), filtered, and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO_2, 100−200 mesh, 3% EtOAc in hexane as eluent) gave the corresponding benzyl protected alcohol (1.53 g, 95%) as colorless oil; R_f = 0.57 (5% EtOAc in hexane as eluent); $[\alpha]_D^{25}$ = -38.7 (*c* 0.62, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 – 7.68 (m, 4H), 7.43 – 7.37 (m, 6H), 7.36 – 7.35 (m, 5H), 4.62 (d, *J* = 3.0 Hz, 2H), 4.09 – 4.02 (m, 1H), 3.79 – 3.72 (m, 3H), 3.58 (s, 1H), 3.56 (d, *J* = 1.1 Hz, 1H), 1.92 (dtt, *J* = 9.1, 4.6, 2.4 Hz, 1H), 1.80 – 1.71 (m, 1H), 1.43 (d, *J* = 4.3 Hz, 7H), 1.08 (s, 9H), 0.95 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.14, 135.65, 134.01, 129.69, 128.47, 127.74, 108.84, 81.69, 78.00, 73.58, 71.67, 61.83, 36.55,

31.64, 27.32, 26.99, 19.31, 14.41; IR (neat) ν_{max} 3064, 2960, 2931, 2857, 1454, 1259, 1085, 1014 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{33}H_{44}NaO_4SiNa$ $[M+Na]^+$ 555.2907, found 555.2908.

To an ice-cold solution of the above benzyl ether (1.46 g, 2.74 mmol) in anhydrous THF (15 mL) under argon, TBAF (1M solution in THF, 3.3 mL, 3.29 mmol) was added. The reaction mixture was stirred further for 3 h at the room temperature prior to quench with saturated NH_4Cl solution (15 mL). The resultant mixture was extracted with EtOAc (3 × 10 mL), washed with water, brine, dried (Na_2SO_4), filtered and concentrated in *vacuo*. Purification by column chromatography (SiO_2, 100-200 mesh, 25% EtOAc in hexane as eluent) afforded alcohol **25** (777 mg, 96%) as a colorless oil; R_f = 0.61 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = -19.3 (*c* 0.62, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 5H), 4.58 (d, *J* = 1.3 Hz, 2H), 4.01 (dt, *J* = 8.1, 4.8 Hz, 1H), 3.81 (dd, *J* = 8.1, 3.8 Hz, 1H), 3.75 – 3.69 (m, 1H), 3.66 – 3.59 (m, 1H), 3.57 (d, *J* = 4.9 Hz, 2H), 2.32 (s, 1H), 1.87 (dtd, *J* = 8.9, 4.9, 4.2, 2.5 Hz, 1H), 1.76 – 1.66 (m, 1H), 1.57 – 1.46 (m, 1H), 1.40 (d, *J* = 3.5 Hz, 6H), 0.97 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.98, 128.44, 127.75, 108.85, 81.49, 77.61, 73.57, 71.35, 60.06, 36.71, 31.38, 27.15, 13.96; IR (neat) ν_{max} 3432, 2980, 2931, 2867, 1378, 1060, 1021 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{26}O_4Na$ $[M+Na]^+$ 317.1729, found 317.1727.

5-(Octylsulfonyl)-1-phenyl-1H-tetrazole (26): Following the same experimental procedure as described for the preparation of compound **11**, octanol (2 g, 13.86 mmol) was subjected to react with Ph_3P (5.4 g, 20.79 mmol), and 1-phenyl-1*H*-tetrazol-5-thiol (3.7 g, 20.79 mmol) and DIAD (4.1 mL, 20.79 mmol) to produce required sulfide (3.8 g, 94%; purification: SiO_2, 100−200 mesh, 5% EtOAc in hexane as eluent) as thick liquid; R_f = 0.41 (10% EtOAc in hexane)]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 – 7.49 (m, 5H), 3.39 (t, *J* = 7.2 Hz, 2H), 1.81 (p, *J* = 7.3 Hz, 2H), 1.49-1.39 (m, 2H), 1.34 – 1.23 (m, 8H), 0.87 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.66, 133.92, 130.18, 129.89, 124.01,

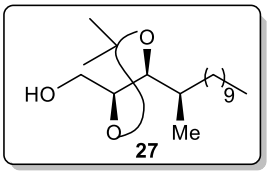


26

33.54, 31.88, 29.23, 29.13, 28.78, 22.75, 14.21; IR (neat) ν_{max} 2951, 2924, 2854, 1597, 1499, 1385 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{22}N_4SNa$ $[M+Na]^+$ 313.1463, found 313.1461.

Following the same experimental procedure as described for the preparation of compound **11**, the above sulfide (3.71 g, 12.77 mmol) was reacted with $(NH_4)_6Mo_7O_{24}.4H_2O$ (789 mg, 0.639 mmol) and 30% (w/w) aqueous H_2O_2 solution (13 mL) to afford sulfone **26** (3.6 g, 87%; purification: SiO_2, 100−200 mesh, 5% EtOAc in hexane as eluent) as white solid; R_f = 0.57 (10% EtOAc in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 – 7.65 (m, 2H), 7.63 – 7.56 (m, 3H), 3.77 – 3.69 (m, 2H), 2.01 – 1.89 (m, 2H), 1.48 (q, *J* = 7.2 Hz, 2H), 1.39 – 1.23 (m, 8H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.65, 133.21, 131.59, 129.85, 125.22, 56.17, 31.78, 28.99, 28.28, 22.70, 22.09, 14.18; IR (neat) ν_{max} 3068, 2948, 2926, 2857, 1498, 1339, 1150 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{22}N_4O_2SNa$ $[M+Na]^+$ 345.1361, found 345.1363.

((4*S*)-5-((*R*)-Dodecan-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (27): To a stirred solution of $(COCl)_2$ (0.44 mL, 5.14 mmol) in anhydrous CH_2Cl_2 (15 mL) at -78 °C under argon, DMSO (0.73 mL, 10.28 mmol) was added drop wise. After 15 min, alcohol **25** (758 mg, 2.57 mmol, dissolved in 5 mL anhydrous CH_2Cl_2) was cannulated into the reaction mixture. After 30 min, Et_3N (1.4 mL, 10.28 mmol) was added and the reaction was continued further for 15 min. The reaction was then warmed slowly to 0 °C and stirred further for 15 min. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL), diluted with water and extracted with EtOAc (3 × 30 mL), washed with NH_4Cl saturated, water, brine, dried (Na_2SO_4) and concentrated in *vacuo*. Flash column chromatography (SiO_2, 100-200 mesh, 50% EtOAc in hexane as eluent) of the crude residue provided the corresponding aldehyde as pale yellow oil which was taken forward immediately in the next step without further purification and characterization.



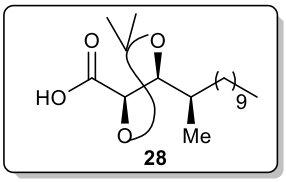
27

To a stirred solution of sulfone **26** (911 mg, 2.83 mmol) in anhydrous THF (10 mL) at -78 °C under argon, KHMDS (6.2 mL, 3.11 mmol, 0.5 M in toluene) was added and the reaction mixture was allowed to stir for 30 min at the same temperature. A solution of the above aldehyde dissolved in anhydrous THF (10 mL) was cannulated into the reaction mixture. The resultant mixture was stirred for another 30 min at the same temperature before quenching it with saturated aqueous NH_4Cl solution (10 mL). The mixture was then diluted with water and extracted with EtOAc (3 × 30 mL), washed with brine, dried (Na_2SO_4), filtered and concentrated in *vacuo*. Purification by column chromatography (SiO_2, 230-400 mesh, 3% EtOAc in hexane as eluent) furnished the corresponding *E*-olefin (781 mg, 78%) as colorless liquid; R_f = 0.76 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -41.1 (*c* 0.68, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.25 (m, 5H), 5.44 – 5.27 (m, 2H), 4.58 (d, *J* = 3.1 Hz, 2H), 4.01 (dt, *J* = 8.0, 4.8 Hz, 1H), 3.74 (dd, *J* = 7.9, 4.6 Hz, 1H), 3.55 (d, *J* = 4.8 Hz, 2H), 2.18 – 2.10 (m, 1H), 1.97 (d, *J* = 6.7 Hz, 2H), 1.90 – 1.80 (m, 1H), 1.68 – 1.59 (m, 1H), 1.39 (d, *J* = 3.7 Hz, 6H), 1.34 – 1.31 (m, 2H), 1.26 – 1.22 (m, 8H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.18, 132.73, 128.45, 127.90, 127.72, 108.78, 81.27, 78.03, 73.56, 71.60, 36.99, 35.55, 32.72, 31.98, 29.68, 29.29, 29.22, 27.31, 27.29, 22.78, 14.43, 14.22; IR (neat) ν_{max} 2991, 2958, 2924, 2855, 1726, 1459, 1378, 1368, 1244, 1091 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{40}O_3Na$ $[M+Na]^+$ 411.2875, found 411.2878.

To a stirred solution of the above olefin (770 mg, 1.42 mmol) in distilled EtOAc (5 mL) fitted with a H_2 balloon, 10% Pd/C (80 mg) was added carefully at the room temperature and allowed to stir for 15 h. The reaction mixture was filtered using a short Celite pad and washed with EtOAc (3 × 25 mL). Purification by column chromatography (SiO_2, 100-200 mesh, 10% EtOAc in hexane as eluent) furnished alcohol **27** (566 mg, 95%) as colorless liquid; R_f = 0.58 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -15.7 (*c* 0.65, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.90 (ddd, *J* = 8.1, 5.2, 2.9 Hz, 1H), 3.82 – 3.71 (m, 2H), 3.63 – 3.54 (m, 1H), 2.01 (t, *J* = 6.3 Hz,

1H), 1.64 – 1.57 (m, 1H), 1.40 (s, 6H), 1.33 (d, *J* = 3.5 Hz, 3H), 1.26 (s, 14H), 1.19 (s, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.63, 80.86, 79.54, 63.44, 35.52, 33.49, 32.06, 29.96, 29.80, 29.76, 29.48, 27.41, 27.24, 22.83, 14.93, 14.26; IR (neat) ν_{max} 3448, 2923, 2856, 1461, 1379, 1255, 1046 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{36}O_3Na$ $[M+Na]^+$ 323.2562, found 323.2563.

(4*R*)-5-((*R*)-Dodecan-2-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylic acid (28): Following

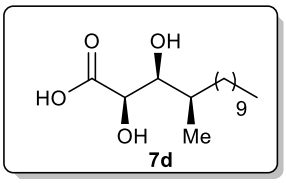


28

the same experimental procedure as described for the preparation of compound **14**, alcohol **27** (215 mg, 0.716 mmol) was oxidised using $NaHCO_3$ (180 mg, 2.148 mmol) and DMP (759 mg, 1.790 mmol) to the corresponding aldehyde which was used for the next reaction without further purification and characterization.

Following the same experimental procedure as described for the preparation of compound **14**, the above aldehyde was subjected to react with $NaClO_2$ (259 mg, 2.864 mmol) and $NaH_2PO_4.2H_2O$ (448 mg, 2.864 mmol) to provide carboxylic acid **28** (191 mg, 85%; purification: SiO_2, 100-200 mesh, 20-50% EtOAc in hexane as eluent) as colorless oil; R_f = 0.21 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = -17.8 (*c* 0.45, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.28 (d, *J* = 7.2 Hz, 1H), 4.13 (dd, *J* = 7.2, 4.3 Hz, 1H), 1.80 (p, *J* = 7.1, 6.6 Hz, 1H), 1.47 (s, 3H), 1.44 (s, 3H), 1.26 (s, 18H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.96, 111.33, 82.93, 76.57, 35.43, 33.64, 32.07, 29.91, 29.78, 29.49, 27.31, 27.06, 25.79, 22.84, 14.26, 13.89; IR (neat) ν_{max} 3189, 2993, 2957, 2924, 2855, 1731, 1464, 1381, 1214 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{35}O_4$ $[M+H]^+$ 315.2535, found 315.2531.

(2*R*,3*S*,4*R*)-2,3-Dihydroxy-4-methyltetradecanoic acid (7d): Following the same

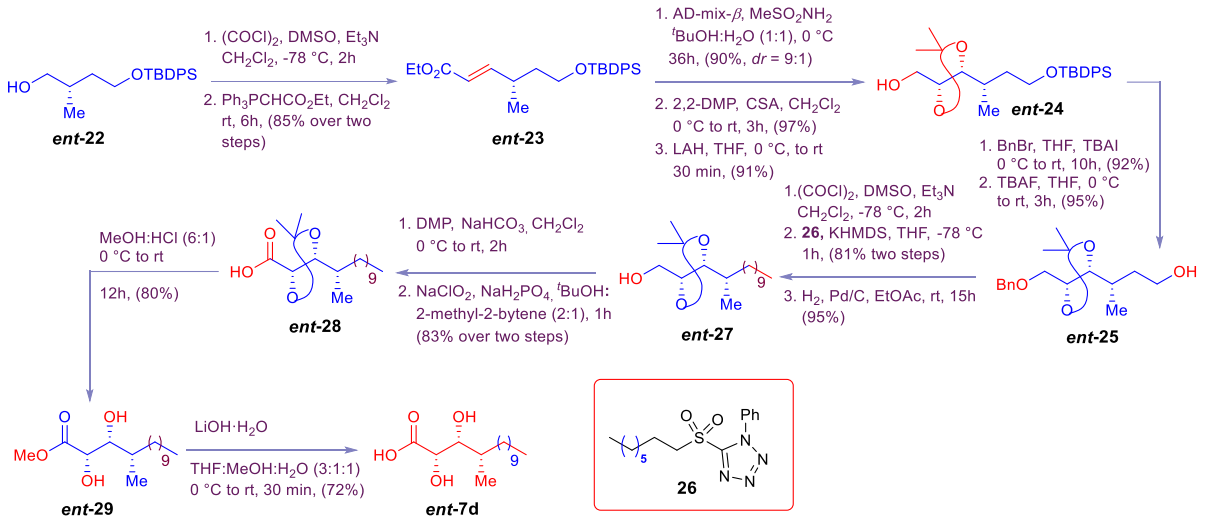


7d

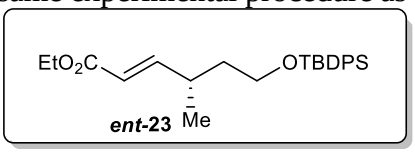
experimental procedure as described for the preparation of compound **21**, acid **28** (42 mg, 0.133 mmol) was treated with conc. HCl in MeOH (3 mL, 1:6) to produce methyl ester **29** (31 mg, 81%; purification: SiO_2, 100−200 mesh, 20-40% EtOAc in hexane as eluent) as pale yellow oil; R_f = 0.59 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = -10.8 (*c* 0.37, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.29 (d, *J* = 2.1 Hz, 1H), 3.82 (s, 3H), 3.60 (dd, *J* = 7.7, 2.1 Hz, 1H), 1.71 (qd, *J* = 7.3, 5.9, 3.3 Hz, 1H), 1.46 – 1.39 (m, 1H), 1.26 (s, 17H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.89 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.75, 76.43, 71.53, 52.99, 36.24, 33.18, 32.06, 30.06, 29.80, 29.76, 29.48, 26.90, 22.83, 15.34, 14.26; IR (neat) ν_{max} 3459, 2954, 2921, 2857, 1741, 1462, 1289, 1127, 1069 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{32}O_4Na$ $[M+Na]^+$ 311.2198, found 311.2195.

Following the same experimental procedure as described for the preparation of compound **7a**, methyl ester **29** (25 mg, 0.087 mmol) was reacted with $LiOH.H_2O$ (15 mg, 0.347 mmol) to yield acid **7d** (18 mg, 75%; purification: SiO_2, 100−200 mesh, 70-100% EtOAc in hexane as eluent) as off white solid; R_f = 0.22 (80% EtOAc in hexane; $[\alpha]_D^{25}$ = +79.2 (*c* 0.79, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD) δ 4.21 (d, *J* = 2.8 Hz, 1H), 3.56 (dd, *J* = 7.8, 2.7 Hz, 1H), 1.78 – 1.69 (m, 1H), 1.49 – 1.44 (m, 1H), 1.29 (s, 16H), 1.16 – 1.22 (m, 1H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.89 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.61, 76.17, 71.44, 35.15, 32.85, 31.70, 29.66, 29.42, 29.38, 29.37, 29.11, 26.45, 22.37, 14.38, 13.08; IR (neat) ν_{max} 3372, 2948, 2924, 2854, 1726, 1612, 1465 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}O_4Na$ $[M+Na]^+$ 297.2042, found 297.2040.

***Scheme S5**: Synthesis of Acid **ent-7d**.*

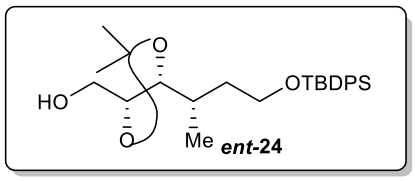


Ethyl (*S*,*E*)-6-((*tert*-butyldiphenylsilyl)oxy)-4-methylhex-2-enoate (*ent*-23): Following the same experimental procedure as described for the preparation of compound **23**, alcohol ***ent*-22**



(2.17 g, 6.34 mmol), was subjected to react with $(COCl)_2$ (1.1 mL, 12.67 mmol), DMSO (1.6 mL, 22.17 mmol) and Et_3N (3.1 mL, 22.17 mmol) to get the corresponding aldehyde which was reacted $Ph_3P{=}CHCO_2Et$ (4.5 g, 12.67 mmol) to afford α,β-unsaturated ester ***ent*-23** (2.20 g, 85% purification: SiO_2, 100-200 mesh, 2% EtOAc in hexane as eluent) as colourless liquid; R_f = 0.71 (5% EtOAc in hexane); $[\alpha]_D^{25}$ = +22.7 (*c* 1.23, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (ddt, *J* = 6.6, 2.0, 0.9 Hz, 4H), 7.43 – 7.36 (m, 6H), 6.86 (dd, *J* = 15.7, 7.8 Hz, 1H), 5.77 (dd, *J* = 15.7, 1.2 Hz, 1H), 4.24 – 4.16 (m, 2H), 3.66 (dd, *J* = 6.7, 5.9 Hz, 2H), 2.62 – 2.54 (m, 1H), 1.62 – 1.59 (m, 2H), 1.30 (d, *J* = 7.1 Hz, 3H), 1.05 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.30, 135.69, 129.74, 127.78, 119.95, 61.63, 60.30, 38.73, 33.15, 26.99, 19.40, 14.44; IR (neat) ν_{max} 2957, 2930, 2856, 1716, 1652, 1259, 1102 cm^{-1}.

((4*R*)-5-((*S*)-4-((*tert*-Butyldiphenylsilyl)oxy)butan-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)-methanol (*ent*-24): Following the same experimental procedure as described for the preparation of compound **24**, the *α,β*-unsaturated ester ***ent*-23** (2.0 g, 4.86 mmol) was treated with AD mix-*β* (9.6 g, 2.0 g/mmol of olefin) and $MeSO_2NH_2$ (1.15 g, 12.18 mmol) to furnish the corresponding diol (1.95 g, *dr*= 9:1, 90%; purification: SiO_2, 230−400 mesh, 10-13% EtOAc in hexane as eluent) as colorless oil; R_f=0.51 (20% EtOAc in hexane); $[\alpha]_D^{25}$ = +10.3 (*c* 0.46, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 – 7.66 (m, 4H), 7.44 – 7.36 (m, 6H), 4.31 – 4.23 (m, 2H), 4.21 (dd, *J* = 5.3, 2.5 Hz, 1H), 3.79 – 3.68 (m, 3H), 3.06 (d, *J* = 5.3 Hz, 1H), 2.46 – 2.39 (m, 1H), 2.02 – 1.92 (m, 1H), 1.85 – 1.76 (m, 1H), 1.50 (d, *J* = 2.0 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.05 (s, 9H), 1.00 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.11, 135.70, 133.83, 129.77, 127.79, 75.92, 71.76, 62.17, 61.94, 36.05, 33.71, 26.98, 19.30, 15.20, 14.30; IR (neat) ν_{max} 3479, 3059, 2954, 2929, 2857, 1731, 1255, 1101, 1015 cm^{-1} HRMS (ESI) *m/z* calcd for $C_{25}H_{37}O_5Si$ $[M+Na]^+$ 445.2410, found 445.2408.

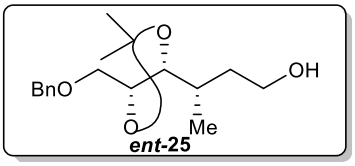


Following the same experimental procedure as described for the preparation of compound **24**, the above diol (1.61 g, 3.62 mmol) subjected to react with 2,2- DMP (1.78 mL, 14.48 mmol) and CSA (42 mg, 0.181 mmol) to get the corresponding acetonide protected alcohol (1.70 g, 97%; purification: SiO_2, 100-200 mesh, 5-10% EtOAc in hexane as eluent) as colorless oil; R_f = 0.52 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = +7.2 (*c* 0.87, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 – 7.61 (m, 4H), 7.46 – 7.34 (m, 6H), 4.29 – 4.16 (m, 3H), 4.11 (dd, *J* = 7.1, 4.5 Hz, 1H), 3.80 – 3.67 (m, 2H), 2.04 (ddd, *J* = 9.0, 4.6, 2.3 Hz, 1H), 1.84 – 1.74 (m, 1H), 1.45 (s, 3H), 1.45 (s, 3H), 1.30 – 1.25 (m, 4H), 1.05 (s, 9H), 0.94 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.71, 135.69, 134.06, 129.72, 127.77, 110.97, 83.03, 77.12, 61.89, 61.39, 36.29, 32.13, 27.10, 27.01, 25.87, 19.34, 14.28, 14.11; IR (neat) ν_{max} 3071, 2960, 2932 , 2858,

1757, 1259, 1088, 1016 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{40}O_5SiNa$ $[M+Na]^+$ 507.2543, found 507.2542.

Following the same experimental procedure as described for the preparation of compound **24**, the above acetonide protected compound (1.52 g, 3.14 mmol) was subjected to reduce by LAH (358 mg, 9.42 mmol) to furnish alcohol ***ent*-24** (1.26 g, 91%; purification; SiO_2, 100-200 mesh, 10% EtOAc in hexane as eluent) as colorless liquid; R_f = 0.26 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = +62.0 (*c* 0.82, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.62 (m, 4H), 7.46 – 7.34 (m, 6H), 3.91 (ddd, *J* = 8.1, 5.3, 3.0 Hz, 1H), 3.80 – 3.69 (m, 4H), 3.57 (dd, *J* = 11.9, 5.4 Hz, 1H), 2.12 (s, 1H), 1.93 – 1.84 (m, 1H), 1.71 (ddt, *J* = 14.0, 7.1, 3.6 Hz, 1H), 1.40 (s, 6H), 1.06 (s, 9H), 0.94 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.68, 133.99, 129.73, 127.77, 108.70, 80.67, 79.42, 63.42, 61.73, 36.27, 31.84, 27.39, 27.32, 27.00, 19.32, 14.66; IR (neat) ν_{max} 3469, 2963, 2929, 2858, 1427, 3468, 2964, 2931, 2858, 1428, 1109, 1086, 1031 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{38}NaO_4SiNa$ $[M+Na]^+$ 465.2437, found 465.2435.

(3*S*)-3-((5*R*)-5-((Benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)butan-1-ol (*ent*-25):



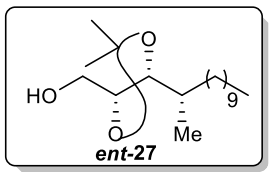
***ent*-25**

Following the same experimental procedure as described for the preparation of compound **25**, alcohol ***ent*-24** (1.13 g, 2.55 mmol) was treated with NaH (153 mg, 3.83 mmol) and BnBr (0.36 mL, 3.06 mmol) and TBAI (94 mg, 0.255 mmol) to obtain the corresponding benzyl ether (1.25 g, 92%); purification: SiO_2, 100−200 mesh, 3% EtOAc in hexane as eluent) as colorless oil; R_f = 0.63 (5% EtOAc in hexane); $[\alpha]_D^{25}$ = +43.4 (*c* 0.73, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.7, 1.8 Hz, 4H), 7.43 – 7.35 (m, 11H), 4.62 (d, *J* = 3.0 Hz, 2H), 4.09 – 4.02 (m, 1H), 3.79 – 3.72 (m, 3H), 3.58 (s, 1H), 3.56 (d, *J* = 1.1 Hz, 1H), 1.92 (dtt, *J* = 9.1, 4.6, 2.4 Hz, 1H), 1.80 – 1.71 (m, 1H), 1.43 (d, *J* = 4.3 Hz, 7H), 1.08 (s, 9H), 0.95 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.14, 135.65, 134.01, 129.69, 128.47, 127.74, 108.84, 81.69, 78.00, 73.58, 71.67, 61.83, 36.55, 31.64, 27.32, 26.99, 19.31, 14.41; IR (neat) ν_{max} 3070, 2931,

2857, 1427, 1378, 1259, 1085, 1018 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{33}H_{44}NaO_4SiNa$ $[M+Na]^+$ 555.2907, found 555.2906.

Following the same experimental procedure as described for the preparation of compound **25,** the above benzyl ether (1.19 g, 2.23 mmol) was treated with TBAF (1M solution in THF, 2.7 mL, 2.68 mmol) to afford alcohol ***ent*-25** (623 mg, 95%; purification: SiO_2, 100-200 mesh, 25% EtOAc in hexane as eluent) as colorless oil; R_f = 0.53 (40% EtOAc in hexane). $[\alpha]_D^{25}$ = +20.7 (*c* 0.69, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 4.58 (d, *J* = 1.1 Hz, 2H), 4.01 (dt, *J* = 8.1, 4.8 Hz, 1H), 3.80 (dd, *J* = 8.1, 3.8 Hz, 1H), 3.75 – 3.68 (m, 1H), 3.65 – 3.60 (m, 1H), 3.56 (d, *J* = 4.8 Hz, 2H), 2.30 (s, 1H), 1.91 – 1.84 (m, 1H), 1.74 – 1.65 (m, 1H), 1.52 (dt, *J* = 7.8, 6.2 Hz, 1H), 1.40 (d, *J* = 3.4 Hz, 6H), 0.96 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.98, 128.44, 127.75, 108.85, 81.49, 77.61, 73.57, 71.35, 60.06, 36.71, 31.38, 27.15, 13.96; IR (neat) ν_{max} 3428, 2978, 2931, 2867, 1369, 1212, 1062, 1027 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{26}NaO_4Na$ $[M+Na]^+$ 317.1729, found 317.1726.

((4*R*)-5-((*S*)-Dodecan-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (*ent*-27): Following

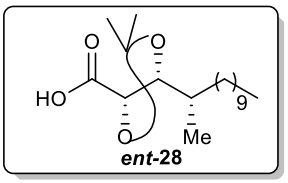


the same experimental procedure as described for the preparation of compound **27**, sulfone **26** (720 mg, 2.23 mmol) and aldehyde, prepared quantitatively from alcohol ***ent*-25** (598 mg, 2.03 mmol) following Swern oxidation as described in the synthesis of compound **27**, was subjected to react with KHMDS (5.4 mL, 2.68 mmol, 0.5 M in toluene) to result the corresponding *E*-olefin (639 mg, 81%; purification: SiO_2, 230-400 mesh, 3% EtOAc in hexane as eluent) as colorless liquid; R_f = 0.69 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = +38.4 (*c* 0.52, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.41 – 7.25 (m, 5H), 5.44 – 5.27 (m, 2H), 4.58 (d, *J* = 3.1 Hz, 2H), 4.01 (dt, *J* = 8.0, 4.8 Hz, 1H), 3.74 (dd, *J* = 7.9, 4.6 Hz, 1H), 3.55 (d, *J* = 4.8 Hz, 2H), 2.18 – 2.10 (m, 1H), 1.97 (d, *J* = 6.7 Hz, 2H), 1.90 – 1.80 (m, 1H), 1.68 – 1.59 (m, 1H), 1.39 (d, *J* = 3.7 Hz, 6H), 1.34 – 1.31 (m, 2H), 1.28 (d, *J* = 6.5 Hz, 8H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.89 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 138.18, 132.73, 128.45, 127.90, 127.72, 108.78, 81.27, 78.03, 73.56, 71.61, 36.99, 35.55, 32.72, 31.98, 29.68, 29.29, 29.22, 27.31, 27.29, 22.78, 14.43, 14.21; IR (neat) ν_{max} 2986, 2957, 2921, 2857, 1721, 1454, 1378, 1365, 1247, 1089 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{40}O_3Na$ $[M+Na]^+$ 411.2875, found 411.2876.

Following the same experimental procedure as described for the preparation of compound **27**, the above olefin (652 mg, 1.68 mmol) was subjected to hydrogenation in presence of Pd/C (70 mg) to furnished alcohol ***ent*-27** (479 mg, 95%; purification: SiO_2, 100-200 mesh, 10% EtOAc in hexane as eluent) as a colorless liquid; R_f = 0.48 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = +12.5 (*c* 0.32, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 3.90 (ddd, *J* = 8.1, 5.2, 2.9 Hz, 1H), 3.82 – 3.71 (m, 2H), 3.63 – 3.54 (m, 1H), 2.01 (t, *J* = 6.3 Hz, 1H), 1.64 – 1.57 (m, 1H), 1.40 (s, 6H), 1.33 (d, *J* = 3.5 Hz, 3H), 1.26 (s, 14H), 1.19 (s, 1H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.63, 80.86, 79.54, 63.44, 35.52, 33.49, 32.06, 29.96, 29.80, 29.76, 29.48, 27.41, 27.24, 22.83, 14.93, 14.26; IR (neat) ν_{max} 3449, 2923, 2854, 1457, 1378, 1257, 1046 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{36}O_3Na$ $[M+Na]^+$ 323.2562, found 323.2564.

(4*S*)-5-((*S*)-Dodecan-2-yl)-2,2-dimethyl-1,3-dioxolane-4-carboxylicacid (*ent*-28): Following the same experimental procedure as described for the preparation of compound **28**, alcohol ***ent*-27** (450 mg, 1.50 mmol) was oxidised to the corresponding aldehyde using $NaHCO_3$ (378 mg, 4.50 mmol) and DMP (1.59 g, 3.75 mmol). The crude aldehyde was subjected to flash chromatography (SiO_2, 60-120 mesh, EtOAc as eluent) and used for the next reaction without further purification and characterization.

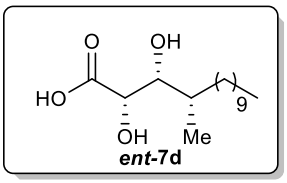


***ent*-28**

Following the same experimental procedure as described for the preparation of compound **28**, above aldehyde was treated with $NaClO_2$ (541 mg, 5.99 mmol) and $NaH_2PO_4.2H_2O$ (937 mg, 5.99 mmol) to provide carboxylic acid ***ent*-28** (392 mg, 83%;

purification: SiO_2, 100-200 mesh, 20-50% EtOAc in hexane as eluent) as colorless oil; R_f = 0.17 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = -13.6 (*c* 0.39, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.28 (d, *J* = 7.2 Hz, 1H), 4.13 (dd, *J* = 7.2, 4.3 Hz, 1H), 1.80 (p, *J* = 7.1, 6.6 Hz, 1H), 1.47 (s, 3H), 1.44 (s, 3H), 1.26 (s, 18H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.96, 111.33, 82.93, 76.57, 35.43, 33.64, 32.07, 29.91, 29.78, 29.49, 27.31, 27.06, 25.79, 22.84, 14.26, 13.89; IR (neat) ν_{max} 3189, 2995, 2951, 2924, 2857, 1725, 1464, 1381, 1214 cm^{-1}. HRMS (ESI) *m/z* calcd for $C_{18}H_{35}O_4$ $[M+Na]^+$ 315.2535, found 315.2532.

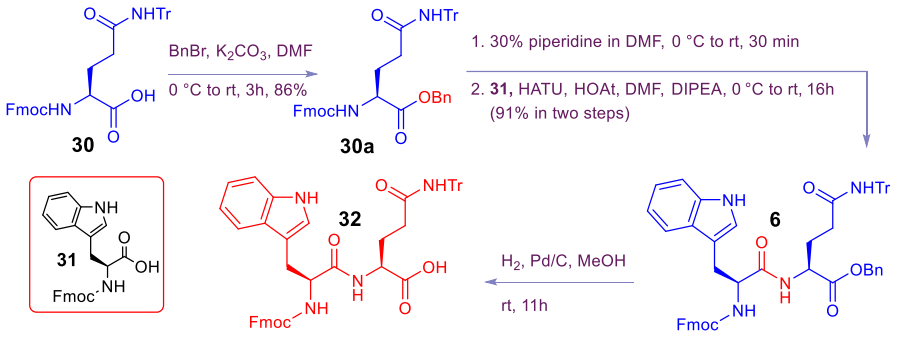
(2*S*,3*R*,4*S*)-2,3-Dihydroxy-4-methyltetradecanoic acid (*ent*-7d): Following the same experimental procedure as described for the preparation of compound **29**, acid ***ent*-28** (38 mg, 0.121 mmol) was treated with conc. HCl in MeOH (3 mL, 1:6) to result methyl ester ***ent*-29** (28 mg, 80%; purification: SiO_2, 100−200 mesh, 20-40% EtOAc in hexane as eluent) as pale yellow oil; R_f = 0.53 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = +12.4 (*c* 0.29, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.29 (d, *J* = 2.1 Hz, 1H), 3.82 (s, 3H), 3.60 (dd, *J* = 7.7, 2.1 Hz, 1H), 1.71 (qd, *J* = 7.3, 5.9, 3.3 Hz, 1H), 1.46 – 1.39 (m, 1H), 1.26 (s, 17H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.89 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.75, 76.43, 71.53, 52.99, 36.24, 33.18, 32.06, 30.06, 29.80, 29.76, 29.48, 26.90, 22.83, 15.34, 14.26; IR (neat) ν_{max} 3456, 2961, 2923, 2853, 1740, 1458, 1285, 1122, 1072 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{32}O_4Na$ $[M+Na]^+$ 311.2198, found 311.2196.



Following the same experimental procedure as described for the preparation of compound **7d**, ester ***ent*-29** (22 mg, 0.076 mmol) was subjected to react with $LiOH.H_2O$ (13 mg, 0.305 mmol) to furnish acid ***ent*-7d** (15 mg, 72%, purification: SiO_2, 100−200 mesh, 70-100% EtOAc in hexane as eluent) as off white crystalline solid; R_f = 0.19 (80% EtOAc in hexane); mp: 103 – 107 °C; $[\alpha]_D^{25}$ = -81.6 (*c* 0.11, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ

4.24 (d, *J* = 2.8 Hz, 1H), 3.59 (dd, *J* = 7.8, 2.7 Hz, 1H), 1.76 (dt, *J* = 13.4, 7.5 Hz, 1H), 1.52-1.47 (m, 1H), 1.32 (s, 16H), 1.20 – 1.15 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.93 – 0.90 (m, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.61, 76.17, 71.44, 35.15, 32.85, 31.71, 29.66, 29.42, 29.38, 29.11, 26.45, 22.37, 14.38, 13.09; IR (neat) ν_{max} 3373, 2944, 2924, 2852, 1725, 1610, 1466 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{30}O_4Na$ $[M+Na]^+$ 297.2042, found 297.2045.

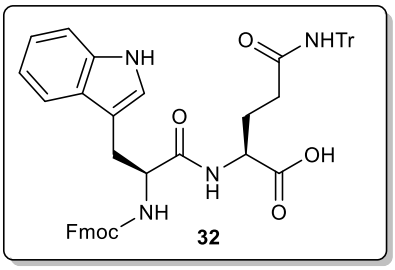
Scheme S6: *Synthesis of Dipeptide **32***.



(*S*)-Benzyl 2-(((9H-fluoren-9-yl)methoxy)carbonylamino)-5-oxo-5-(tritylamino)pentanoate (30a): To an ice-cold solution of the acid **30** (612 mg, 1.00 mmol) in anhydrous DMF (20 mL) under argon, K_2CO_3 (277 mg, 2.00 mmol) followed by BnBr (0.18 mL, 1.50 mmol) were added. The reaction was gradually warmed to the room temperature and continued for 3 h at the same temperature. The resultant mixture was concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO_2, 100−200 mesh, 10-30% EtOAc in hexane as eluent) gave benzyl protected ester **30a** (604 mg, 86%) as a white powder; R_f = 0.55 (40% EtOAc in hexane as eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.59 (d, *J* = 7.5 Hz, 2H), 7.41 (d, *J* = 6.6 Hz, 2H), 7.32 (d, *J* = 6.1 Hz, 6H), 7.29 (s, 3H), 7.26 (s, 6H), 7.21 (d, *J* = 7.5 Hz, 7H), 6.85 (s, 1H), 5.63 (d, *J* = 7.9 Hz, 1H), 5.17 (d, *J* = 3.9 Hz, 2H), 4.43 (dt, *J* = 16.8, 8.9 Hz, 3H), 4.22 (t, *J* = 7.0 Hz, 1H), 2.34 – 2.19 (m, 3H), 2.02 – 1.91 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.92, 170.82, 156.42, 144.67, 144.00, 143.76, 141.39, 135.29, 128.79, 128.72, 128.62, 128.53, 128.03, 127.81, 127.19, 127.13,

125.23, 120.07, 77.36, 70.75, 67.43, 67.12, 53.73, 47.30, 33.35, 28.39; IR (neat) ν_{max} 3317, 3061, 3029, 2935, 2857, 1719, 1703, 1681, 1508, 1491, 1453, 1346, 1246 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{46}H_{40}N_2O_5Na$ $[M+Na]^+$ 723.2835, found 723.2833.

N^2-((((9H-Fluoren-9-yl)methoxy)carbonyl)-*L*-trypto-phyl)-N^5-trityl-*L*-glutamine (32): To



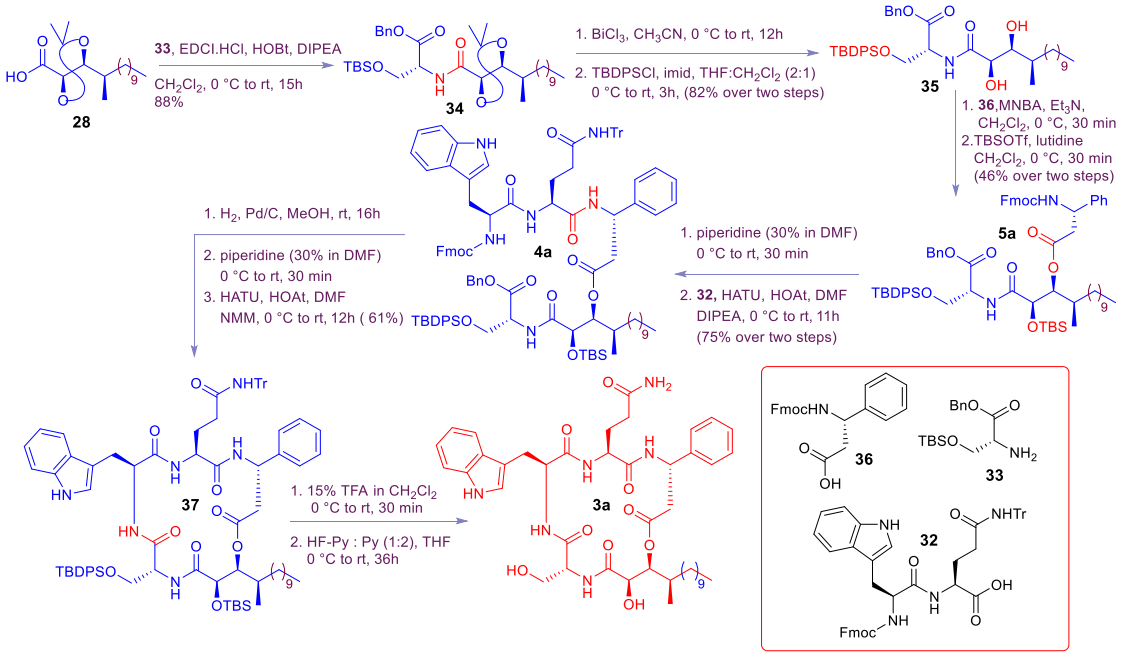
32

a solution of compound **30a** (507 mg, 0.723 mmol) in anhydrous DMF (7 mL) under argon, piperidine (3 mL) was added. After being stirred at the room temperature for 30 min, the reaction mixture was concentrated in *vacuo*. The residue was azeotroped with anhydrous toluene (2 × 5 mL), dissolved in anhydrous DMF (10 mL) and transferred via cannula under argon atmosphere into a stirred mixture of acid **31** (370 mg, 0.868 mmol), DIPEA (0.36 mL, 2.084 mmol), HOAt (142 mg, 1.042 mmol) and HATU (396 mg, 1.042 mmol) in anhydrous DMF (5 mL) at the room temperature. After being stirred for 16h at the same temperature, the reaction mixture was concentrated in *vacuo*. The residue was purified by flash chromatography (SiO_2, 60-120 mesh, 10-50% EtOAc in hexane as eluent) to give dipeptide **6** (583 mg, 91%) as white solid; R_f = 0.46 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = +94.0 (*c* 0.17, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.76 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.30 (s, 7H), 7.27 – 7.26 (m, 4H), 7.24 (s, 5H), 7.22 (s, 1H), 7.20 – 7.19 (m, 4H), 7.17 – 7.16 (m, 2H), 7.10 (q, *J* = 8.6, 7.1 Hz, 2H), 6.89 (d, *J* = 15.1 Hz, 2H), 6.68 (d, *J* = 7.4 Hz, 1H), 5.49 (d, *J* = 7.8 Hz, 1H), 5.05 (q, *J* = 12.2 Hz, 2H), 4.52 (td, *J* = 8.0, 3.8 Hz, 2H), 4.37 (t, *J* = 8.8 Hz, 1H), 4.26 (t, *J* = 8.7 Hz, 1H), 4.17 (d, *J* = 7.1 Hz, 1H), 3.30 (dd, *J* = 15.0, 5.3 Hz, 1H), 3.13 (dd, *J* = 14.5, 6.9 Hz, 1H), 2.14 (d, *J* = 8.9 Hz, 1H), 1.99 (dt, *J* = 7.7, 3.3 Hz, 1H), 1.84 (dd, *J* = 12.1, 7.7 Hz, 1H), 1.77 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.65, 171.20, 171.06, 156.03, 144.59, 143.96, 143.79, 141.36, 136.20, 135.31, 128.78, 128.73, 128.65, 128.56, 128.03, 127.81, 127.61, 127.19, 127.14, 125.23, 123.79, 122.19, 120.06, 119.84, 118.61, 111.45, 109.80, 77.36, 70.65,

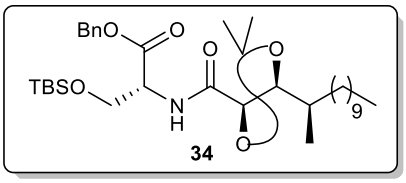
67.37, 67.17, 55.92, 52.00, 47.17, 32.96, 28.33; IR (neat) ν_{max} 3311, 3058, 2970, 2941, 1722, 1650, 1522, 1492, 1453, 1174 cm^{-1}; HRMS (ESI) m/z calcd for $C_{57}H_{50}N_4O_6Na$ $[M + Na]^+$ 909.3628, found 909.3626.

A solution of compound above benzyl ester **6** (553 mg, 0.623 mmol) and 10% Pd/C (55 mg) in distilled MeOH (2 mL) was stirred under H_2 atmosphere (hydrogen balloon) at room temperature for 11 h. The reaction mixture was filtered using a short Celite bed followed by silica pad (60-120 mesh) using CH_2Cl_2-MeOH (7:3) (3 × 50 mL). This acid was directly used in next required step without further purification.

***Scheme S7**: Completion of Total Synthesis of Compound **3a**.*



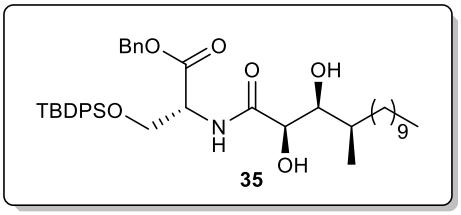
Benzyl O-(*tert*-butyldimethylsilyl)-N-((4*R*)-5-((*R*)-dodecan-2-yl)-2,2-dimethyl-1,3-di-oxo-lane-4-carbonyl)-*D*-serinate (34): To a stirred solution of acid **28** (132 mg, 0.420 mmol) in



anhydrous CH_2Cl_2 (5 mL), DIPEA (0.22 mL, 1.259 mmol) and HOBt (85 mg, 0.630 mmol) and EDCI (137 mg, 0.630 mmol) were added sequentially under an argon atmosphere at 0 °C and the reaction mixture was stirred for 15 min at the same temperature. Amine **33** (118 mg, 0.504 mmol), dissolved in anhydrous CH_2Cl_2 (5 mL) was then added into reaction mixture

via cannula. After being stirred for 15 h at the room temperature, the reaction mixture was concentrated in *vacuo*. The residue was purified by flash chromatography (SiO_2, 100-200 mesh, 5-15% EtOAc in hexane as eluent) to give amide **34** (224 mg, 88%) as colorless oil; R_f = 0.54 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = +13.1 (*c* 0.61, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.4 Hz, 1H), 7.37 – 7.32 (m, 5H), 5.23 – 5.14 (m, 2H), 4.68 (dt, *J* = 8.3, 2.8 Hz, 1H), 4.19 (d, *J* = 7.5 Hz, 1H), 4.10 (dd, *J* = 10.1, 2.6 Hz, 1H), 4.01 (dd, *J* = 7.5, 3.7 Hz, 1H), 3.84 (dd, *J* = 10.1, 3.0 Hz, 1H), 1.89 – 1.79 (m, 1H), 1.45 (s, 3H), 1.41 (s, 3H), 1.25 (s, 18H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.91 – 0.83 (m, 12H), -0.02 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.41, 169.94, 135.43, 128.74, 128.56, 128.44, 110.20, 83.26, 67.43, 63.55, 53.96, 35.38, 34.17, 32.07, 29.97, 29.80, 29.50, 27.47, 27.15, 26.26, 25.82, 22.84, 18.26, 14.27, 13.54, -5.47, -5.55; IR (neat): ν_{max} 3427, 2954, 2926, 2855, 1748, 1683, 1512, 1464, 1378, 1256, 1107 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{34}H_{60}NO_6Si$ $[M+H]^+$ 606.4190, found 606.4186.

Benzyl O-(*tert*-butyldiphenylsilyl)-N-((2*R*,3*S*,4*R*)-2,3-dihydroxy-4-methyltetradecanoyl)-*D*-serinate (35): To a stirred solution of acetonide **34** (221 mg, 0.365 mmol) in distilled MeCN



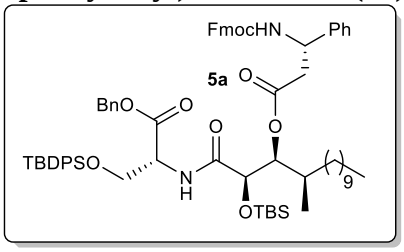
35

(10 mL) bismuth trichloride (6 mg, 0.018) and two drops of water were added 0 °C. The reaction mixture was then warmed slowly to room temperature and stirred for 12h at same temperature. After completion of the reaction, $NaHCO_3$ (5 mL) was added and the solvent was removed in *vacuo*. The reaction mixture was diluted with water and extracted with EtOAc (3 × 20 mL), washed with brine, dried over anhydrous Na_2SO_4 and concentrated and filtered through short celite pad (EtOAc as eluent) to give the crude triol as white solid [R_f = 0.22 (40% EtOAc in hexane)] that was directly used in the next step without further purification and characterization.

To an ice-cold stirred solution of imidazole (37 mg, 0.548 mmol) in anhydrous CH_2Cl_2 (5 mL) under argon, the above triol dissolved in anhydrous THF (10 mL) was added via

cannula. TBDPSCl (0.11 mL, 0.438 mmol) was then added. The reaction mixture was stirred for 30 min at the same temperature. The resulting mixture was then warmed slowly to the room temperature and stirred for 3 h before quenching with saturated solution of NH_4Cl (5 mL), diluted with water. The aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, 100-200 mesh, 10-30% EtOAc in hexane as eluent) to afford TBDPS ether **35** (206 mg, 82% over two step) as colorless oil; R_f = 0.34 (20% EtOAc in hexane); $[\alpha]_D^{25}$ = -57.1 (*c* 0.07, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.60 (m, 1H), 7.59 – 7.58 (m, 1H), 7.57 – 7.56 (m, 1H), 7.54 – 7.53 (m, 1H), 7.42 (d, *J* = 1.5 Hz, 1H), 7.40 – 7.38 (m, 1H), 7.38 (s, 1H), 7.37 – 7.35 (m, 2H), 7.34 – 7.32 (m, 6H), 7.31 – 7.29 (m, 1H), 5.19 (s, 2H), 4.72 (dt, *J* = 8.6, 2.9 Hz, 1H), 4.21 – 4.14 (m, 2H), 3.87 (dd, *J* = 10.5, 3.3 Hz, 1H), 3.79 (ddd, *J* = 9.0, 6.4, 2.7 Hz, 1H), 3.36 (d, *J* = 7.2 Hz, 1H), 2.33 (d, *J* = 6.0 Hz, 1H), 1.80 – 1.72 (m, 1H), 1.47 – 1.38 (m, 2H), 1.32 – 1.24 (m, 16H), 1.03 – 0.98 (m, 12H), 0.92 – 0.87 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.20, 170.22, 135.66, 135.62, 135.60, 135.25, 132.72, 130.09, 130.04, 128.77, 128.74, 128.57, 128.52, 128.46, 127.99, 127.91, 75.55, 72.50, 67.58, 64.39, 54.15, 35.59, 33.37, 32.04, 30.08, 29.81, 29.77, 29.47, 27.05, 26.81, 22.81, 19.37, 15.03, 14.25; IR (neat) ν_{max} 3414, 2959, 2928, 2855, 1736, 1660, 1453, 1259, 1111 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{41}H_{59}NO_6SiNa$ [M+Na]+ 712.4009, found 712.4008.

Benzyl N-((2*R*,3*S*,4*R*)-3-(((*S*)-3-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-phenyl-propanoyl)oxy)-2-((tert-butyldimethylsilyl)-oxy)-4-methyltetradecan-oyl)-O-(tert-butyl-diphenyl-silyl)-*D*-serinate (5a): To a stirred mixture of carboxylic acid **36** (43 mg, 0.111 mmol) and alcohol **35** (51 mg, 0.074 mmol) in anhydrous CH_2Cl_2 (5 mL) at room temperature under argon atmosphere, MNBA (38 mg, 0.111 mmol), Et_3N (0.09 mL,



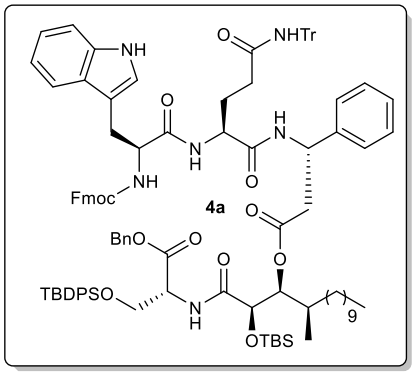
0.666 mmol) and DMAP (1.5 mg, 0.011 mmol) were added sequentially at room temperature. Stirring was continued at same temperature for 30 min. The reaction mixture was then diluted with water and extracted with EtOAc (3 × 10 mL), washed with brine, dried over Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was passed thorugh silica gel (60-120 mesh) and washed with EtOAc (3 × 20 mL) to get corresponding ester as a yellow oil which was immediately used in next step without further characterisation.

Note: *152 mg of alcohol **35** was converted batchwise to the corresponding ester (as on scaling up the undesired product was formed in exclusive amount).*

To an ice-cold solution of the above ester in anhydrous CH_2Cl_2 (10 mL) under argon, 2,6-lutidine (0.05 mL, 0.44 mmol) was added and the mixture was stirred for 5 min prior to addition of TBSOTf (0.07 mL, 0.33 mmol). The reaction was continued for 30 min at the same temperature and subsequently quenched with a saturated solution of $NaHCO_3$ (5 mL) and diluted with distilled water. The resultant mixture was extracted with CH_2Cl_2 (3 × 10 mL), washed with aqueous solution of $CuSO_4$, water, brine, dried (Na_2SO_4), filtered, and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO_2, 100−200 mesh, 3-12% EtOAc in hexane as eluent) gave TBS protected alcohol **5a** (119 mg, 46%) as colorless oil; R_f = 0.61 (20% EtOAc in hexane as eluent); $[\alpha]_D^{25}$ = +24.2 (*c* 0.37, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.5 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.59 – 7.48 (m, 4H), 7.44 – 7.39 (m, 2H), 7.37 – 7.31 (m, 11H), 7.29 – 7.25 (m, 4H), 7.24 – 7.20 (m, 3H), 7.18 – 7.16 (m, 1H), 7.09 (d, J = 9.3 Hz, 1H), 5.29 – 5.16 (m, 2H), 5.06 (d, *J* = 12.2 Hz, 1H), 4.96 – 4.85 (m, 2H), 4.39 – 4.30 (m, 2H), 4.19 (t, *J* = 5.7 Hz, 1H), 4.15 – 4.06 (m, 2H), 3.71 (dd, *J* = 10.2, 3.0 Hz, 1H), 2.97 (dd, *J* = 14.4, 5.7 Hz, 1H), 2.87 (dd, *J* = 15.3, 4.8 Hz, 1H), 1.87 – 1.82 (m, 1H), 1.27 – 1.14 (m, 18H), 1.02 (s, 9H), 0.93 (s, 9H), 0.90 – 0.87 (m, 3H), 0.75 (d, *J* = 6.7 Hz, 3H), 0.09 (d, *J* = 8.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.12, 170.48, 169.89, 144.26, 141.37, 135.63, 135.16, 132.66, 132.59, 130.08, 130.03, 128.76,

128.70, 128.63, 128.57, 128.49, 128.44, 127.98, 127.89, 127.84, 127.72, 127.53, 127.13, 127.08, 126.21, 125.41, 125.33, 119.99, 100.10, 77.37, 72.87, 67.56, 67.07, 65.03, 53.45, 47.34, 40.87, 34.52, 32.52, 32.06, 29.91, 29.86, 29.78, 29.49, 27.10, 27.01, 26.93, 25.85, 22.83, 19.40, 18.03, 14.48, 14.27, -4.97, -5.10, -5.15, -5.21 ppm; IR (neat) ν_{max} 3455, 2954, 2925, 2854, 1721, 1719, 1452, 1274, 1114 cm^{-1}; HRMS (ESI) m/z calcd for $C_{71}H_{93}N_2O_9Si_2$ $[M+H]^+$ 1173.6420, found 1173.6423.

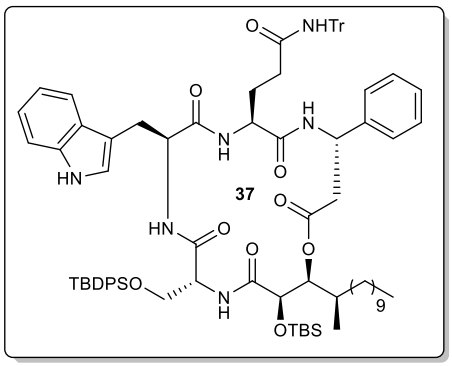
Benzyl N-((2*R*,3*S*,4*R*)-3-(((*S*)-3-((*S*)-2-((*S*)-2-((((9H-fluoren-9-yl)-methoxy)carbonyl)-amino)-3-(1H-indol-3-yl)propanamido)-5-oxo-5-(tritylamino)pentanamido)-3-phenyl-propanoyl)oxy)-2-((*tert*-butyldimethylsilyl)oxy)-4-methyltetradecanoyl)-O-(tert-butyl-diphenylsilyl)-*D*-serinate (4a): To a solution of amine **5a** (82 mg, 0.070 mmol) in anhydrous



DMF (3.5 mL) under argon, piperidine (1.5 mL) was added. After being stirred at the room temperature for 30 min, the reaction mixture was concentrated in *vacuo*. The residue was azeotroped with anhydrous toluene (2 × 5 mL) and dissolved in anhydrous DMF (5 mL).in which acid **32** (69 mg, 0.084 mmol, dissolved in 5 mL anhydrous DMF), DIPEA (35 µL, 0.202 mmol), HOAt (14 mg, 0.101 mmol) and HATU (38 mg, 0.101 mmol) were added sequentially under an argon. After being stirred for 11 h at room temperature, the reaction mixture was concentrated in *vacuo*. The residue was purified by flash chromatography (SiO_2, 100-200 mesh, 10-30% EtOAc in hexane as eluent) to give the protected cyclic precursor depsipeptide **4a** (91 mg, 75% over two steps) as colorless oil; R_f = 0.46 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = +21.8 (*c* 0.55, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.07 – 8.01 (m, 1H), 7.76 – 7.60 (m, 4H), 7.56 – 7.48 (m, 7H), 7.43 – 7.33 (m, 4H), 7.34 (s, 1H), 7.34 – 7.32 (m, 2H), 7.30 (d, *J* = 3.2 Hz, 3H), 7.28 – 7.27 (m, 3H), 7.25 (s, 3H), 7.23 – 7.19 (m, 11H), 7.17 (s, 6H), 7.15 (s, 3H), 7.12 – 6.99 (m, 3H), 6.91 – 6.77 (m, 3H), 5.37 (dt, *J* = 13.6, 6.8 Hz, 2H),

5.16 – 5.01 (m, 2H), 4.88 – 4.75 (m, 2H), 4.51 – 4.45 (m, 1H), 4.39 – 4.31 (m, 1H), 4.24 – 4.20 (m, 2H), 4.16 – 4.14 (m, 1H), 4.09 – 3.97 (m, 1H), 3.85 – 3.73 (m, 1H), 3.28 (td, *J* = 14.4, 5.1 Hz, 1H), 3.11 (q, *J* = 7.0, 6.3 Hz, 1H), 2.81 (dt, *J* = 10.2, 5.2 Hz, 2H), 2.05 (td, *J* = 12.9, 11.6, 5.3 Hz, 3H), 1.90 – 1.83 (m, 2H), 1.29 – 1.10 (m, 18H), 1.02 (s, 9H), 0.89 – 0.86 (m, 12H), 0.69 (t, *J* = 7.2 Hz, 3H), 0.08 (d, *J* = 3.9 Hz, 2H), 0.05 (d, *J* = 4.2 Hz, 2H), -0.00 (d, *J* = 5.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.83, 171.45, 171.29, 170.99, 170.21, 170.10, 169.91, 144.69, 144.10, 143.87, 141.40, 140.03, 136.28, 135.67, 135.60, 135.19, 132.69, 132.62, 130.07, 128.83, 128.73, 128.67, 128.51, 128.06, 127.98, 127.91, 127.80, 127.72, 127.64, 127.22, 127.12, 126.45, 126.33, 125.35, 123.95, 123.57, 122.27, 122.16, 120.06, 119.84, 118.54, 111.61, 111.50, 110.19, 109.64, 72.96, 72.36, 70.58, 67.61, 67.23, 67.12, 64.98, 64.87, 56.02, 53.71, 53.59, 52.51, 49.44, 47.24, 40.61, 34.89, 34.57, 33.00, 32.51, 32.06, 29.91, 29.79, 29.50, 29.19, 28.28, 27.10, 26.98, 25.86, 22.83, 19.42, 18.07, 18.00, 14.66, 14.28, 0.15, -5.07, -5.15; IR (neat) ν_{max} 3497, 3311, 2964, 2926, 2854, 1735, 1665, 1508, 1260, 1104, 1029 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{106}H_{124}N_6O_{12}Si_2Na$ $[M+Na]^+$ 1751.8713, found 1751.8715.

3-((4*S*,7*S*,10*S*,13*R*,16*R*,17*S*)-10-((1H-Indol-3-yl)methyl)-16-((*tert*-butyldimethylsilyl)oxy)-13-(((*tert*-butyldiphenylsilyl)oxy)methyl)-17-((*R*)-dodecan-2-yl)-2,6,9,12,15-penta-oxo-4-phenyl-1-oxa-5,8,11,14-tetraazacycloheptadecan-7-yl)-N-tritylpropanamide (37): A

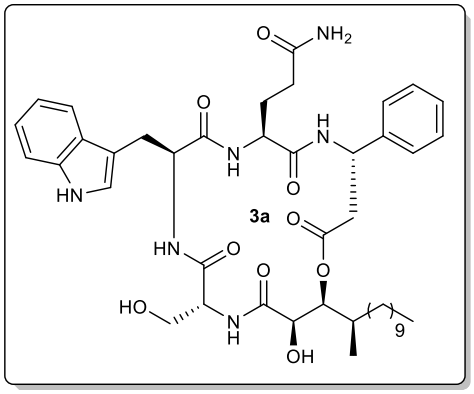


solution of compound **4a** (36 mg, 0.021 mmol) and 10% Pd/C (4 mg) in distilled MeOH (2 mL) was stirred under H_2 atmosphere (hydrogen balloon) at room temperature for 16 h. The reaction mixture was filtered using a short pad of Celite followed by a silica bed (60-120 mesh) and washed with mixture of CH_2Cl_2 and MeOH (7:3) (3 × 30 mL). The crude acid was then directly used in next step without further purification and characterization.

To the solution of the above acid (quantitative, 0.021 mmol) in anhydrous DMF (1.4 mL) under argon, piperidine (0.6 mL) was added at room temperature. The reaction was stirred at the same temperature for 30 min and then concentrated in *vacuo*. The residue was azeotroped with anhydrous toluene (2 × 3 mL) and dissolved again in anhydrous DMF (10 mL) in which NMM (1 µL, 0.051 mmol) was added followed by addition a mixture of HOAt (4 mg, 0.025 mmol) and HATU (10 mg, 0.025 mmol) in DMF (10 mL) under an argon atmosphere over a period of 30 min via cannula, so as to maintain the overall concentration at 0.001M. After being stirred for 12 h at the room temperature, the reaction mixture was concentrated in *vacuo*. The residue was purified by flash chromatography (SiO_2, 100-200 mesh, 20-40% EtOAc in hexane as eluent) to give protected cyclic depsipeptide **37** (18 mg, 61%) as a colorless oil; R_f = 0.32 (40% EtOAc in hexane); $[\alpha]_D^{25}$ = -4.6 (*c* 0.51, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (d, *J* = 9.8 Hz, 1H), 8.21 (s, 1H), 7.97 (d, *J* = 9.5 Hz, 1H), 7.63 – 7.58 (m, 4H), 7.49 – 7.39 (m, 6H), 7.36 – 7.34 (m, 3H), 7.32 (s, 4H), 7.30 (s, 4H), 7.24 – 7.23 (m, 6H), 7.21 – 7.11 (m, 7H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.89 (t, *J* = 7.7 Hz, 1H), 6.66 (d, *J* = 2.4 Hz, 1H), 6.12 (d, *J* = 9.5 Hz, 1H), 5.66 – 5.59 (m, 1H), 4.97 – 4.90 (m, 1H), 4.63 (dd, *J* = 16.8, 7.5 Hz, 1H), 4.49 (dd, *J* = 8.2, 3.4 Hz, 1H), 3.84 – 3.81 (m, 2H), 3.74 – 3.65 (m, 2H), 3.50 (dd, *J* = 14.7, 5.1 Hz, 1H), 3.34 (d, *J* = 3.4 Hz, 1H), 3.03 (dd, *J* = 14.4, 5.1 Hz, 1H), 2.78 (dd, *J* = 14.2, 3.0 Hz, 1H), 2.10 (t, *J* = 7.3 Hz, 2H), 1.93 – 1.86 (m, 1H), 1.80 – 1.72 (m, 2H), 1.28 (d, *J* = 0.7 Hz, 2H), 1.28 – 1.06 (m, 18H), 1.06 (s, 9H), 0.86 (t, J = 6.7 Hz, 3H), 0.80 (s, 9H), 0.70 (d, *J* = 6.6 Hz, 3H), -0.15 (d, *J* = 5.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.79, 171.68, 171.58, 170.89, 169.82, 167.64, 144.69, 138.35, 136.09, 135.68, 135.59, 132.56, 130.39, 130.33, 129.02, 128.88, 128.19, 128.15, 128.03, 127.45, 127.19, 125.83, 124.03, 122.11, 119.90, 118.49, 111.54, 109.60, 77.37, 73.41, 70.74, 63.30, 58.34, 54.59, 53.51, 48.03, 41.05, 34.21, 33.33, 33.18, 32.04, 30.28, 29.86, 29.80, 29.47, 27.06, 26.67, 25.86, 22.82, 19.29, 18.03, 15.96, 14.27, 0.15,

-5.10, -5.55; IR (neat) ν_{max} 3343, 2958, 2925, 2854, 1728, 1722, 1657, 1544, 1459 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{84}H_{107}N_6O_9Si_2$ $[M+H]^+$ 1399.7638, found 1399.7635.

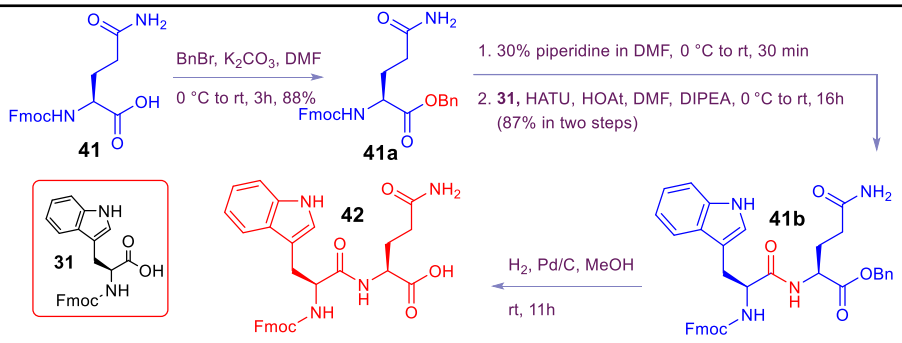
Diastereomer of alveolaride C (3a): To a stirred solution of compound **37** (15 mg, 0.011 mmol) in anhydrous CH_2Cl_2 (1.9 mL) under argon, TFA (0.1 mL) was added at room temperature. The reaction was then stirred for 1h at the same temperature. The resultant mixture was then concentrated in *vacuo* to afford a crude trityl deprotected product. The crude product was filtered through short silica bed (60-120 mesh) using CH_2Cl_2-MeOH (9:1) (3 × 30 mL), azeotrope with distilled EtOAc (3 × 5 mL) and subsequently taken for the next step without further purification and characterization.



To a solution of above trityl deprotected compound in THF (1 mL) under argon, a fresh solution of HF-Py (0.1 mL), Py (0.2 mL) in anhydrous THF (2 mL) was added at room temperature. After 36 h of stirring at the same temperature, the reaction mixture was diluted with Et_2O (5 mL) and washed with aqueous HCl solution (1N, 2 × 5 mL) and distilled water. The organic layer dried over anhydrous Na_2SO_4 and was concentrated in *vacuo* (*the temperature should not exceed more than 35 °C, as at high temperature undesired spot my appear*). The resulting residue was purified by column chromatography (neutral Al_2O_3, eluent: 60% EtOAc in hexane followed by 10% MeOH in CH_2Cl_2, **Note**: *compound may decompose on passing through silica or keeping for long time in alumina also*) to get white solid compound **3a** (6 mg, 68%); R_f = 0.32 (5% MeOH in CH_2Cl_2); $[\alpha]_D^{25}$ = -26.6 (*c* 0.07, MeOH). ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.90 (s, 1H), 8.66 (d, *J* = 6.2 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.37 – 7.35 (m, 2H), 7.32 – 7.28 (m, 4H), 7.26 – 7.23 (m, 1H), 7.21 – 7.18 (m, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.01 (t, *J* = 7.3 Hz, 1H), 6.55 (s, 1H), 5.12 (q, *J* = 7.6 Hz, 1H), 4.99 (d, *J* = 4.7 Hz, 1H), 4.87 (t, *J* = 5.9 Hz, 1H), 4.68 – 4.60 (m, 1H), 4.28 – 4.22 (m,

1H), 4.08-4.00 (m, 2H), 3.62 (d, *J* = 5.4 Hz, 1H), 3.49-3.46 (m, 1H), 3.14-3.12 (m, 2H), 2.99 (d, *J* = 7.8 Hz, 1H), 2.83 – 2.77 (m, 1H), 2.31 – 2.27 (m, 1H), 2.13 – 2.07 (m, 2H), 1.92 – 1.87 (m, 1H), 1.82 – 1.74 (m, 1H), 1.24 (s, 18H), 0.90 – 0.84 (m, 6H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.15, 172.60, 172.20, 170.88, 169.78, 168.72, 143.00, 136.61, 128.80, 128.80, 127.66, 127.36, 126.36 , 126.36, 124.14, 121.50, 118.87, 118.49, 111.90, 110.12, 77.18, 72.51, 62.91, 57.41, 54.10, 53.12, 49.70, 34.90, 33.17, 31.78, 31.62, 29.64, 29.52, 29.50, 29.38, 29.21, 27.38, 26.67, 26.31, 22.59, 15.12, 14.45; IR (neat) ν_{max} 3327, 2964, 2925, 2860, 1719, 1716, 1654, 1459, 1178 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{43}H_{60}N_6O_9Na$ $[M+Na]^+$ 827.4319, found 827.4315.

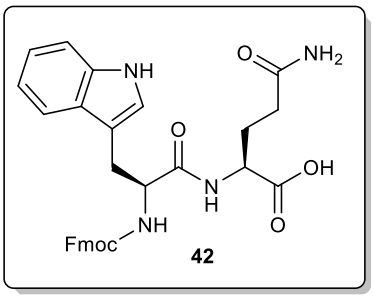
Scheme S8: *Synthesis of Dipeptide **42**.*



(*S*)-Benzyl-2-(((9H-fluoren-9-yl)methoxy)carbonylamino)-5-amino-5-oxopentanoate (41a): Following the same experimental procedure as described for the preparation of compound **30a**, acid **41** (678 mg, 1.84 mmol) was reacted with K_2CO_3 (509 mg, 3.68 mmol) and BnBr (0.33 mL, 2.76 mmol) to obtain benzyl ester **41a** (742 mg, 88%; purification: SiO_2, 100-200 mesh, 1-4% MeOH in CH_2Cl_2 as eluent) as white solid; R_f = 0.52 (EtOAc); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.89 (d, *J* = 6.0 Hz, 2H), 7.72 (d, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.37 – 7.28 (m, 7H), 5.13 (s, 2H), 4.33 – 4.19 (m, 3H), 4.10 (dd, *J* = 9.5, 4.6 Hz, 1H), 2.18 (t, *J* = 7.4 Hz, 2H), 2.05 – 1.96 (m, 1H), 1.80 (ddd, *J* = 13.5, 8.1, 4.5 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.23, 173.11, 172.10, 156.15, 156.08, 143.74, 140.68, 135.92,

128.36, 127.97, 127.69, 127.62, 127.06, 125.21, 120.09, 65.87, 65.72, 53.61, 53.51, 46.59, 31.10, 31.03, 26.28; IR (neat) ν_{max} 3334, 3061, 2945, 1722, 1668, 1533, 1408 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{27}N_2O_5$ $[M+H]^+$ 459.1920, found 459.1922.

(((9H-Fluoren-9-yl)methoxy)carbonyl)-*L*-tryptophyl-*L*-glutamine (42): Following the same experimental procedure as described for the preparation of compound **32**, amine **41a** (526 mg, 1.15 mmol) was treated with piperidine (10 mL, 30% in DMF) which was then coupled with acid **31** (587 mg, 1.38 mmol) in the presence DIPEA (0.78 mL), HOAt (226 mg, 1.66 mmol), HATU (630 mg, 1.66 mmol) to result dipeptide **41b** (645 mg, 87%; purification: SiO_2, 60-120 mesh, 40-80% EtOAc in hexane as eluent) as a white solid; R_f = 0.44 (60% EtOAc in hexane); $[\alpha]_D^{25}$ = +99.9 (*c* 0.08, MeOH); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.81 (s, 1H), 8.57 (d, *J* = 7.3 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 2H), 7.70 – 7.59 (m, 3H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.43 – 7.40 (m, 1H), 7.40 – 7.34 (m, 5H), 7.32 (dt, *J* = 2.8, 1.3 Hz, 3H), 7.29 – 7.22 (m, 2H), 7.18 (d, *J* = 2.3 Hz, 1H), 7.10 – 7.03 (m, 1H), 7.02 – 6.95 (m, 1H), 6.79 (s, 1H), 5.14 (s, 2H), 4.45 – 4.31 (m, 2H), 4.21 – 3.97 (m, 3H), 3.08 (dd, *J* = 14.7, 3.9 Hz, 1H), 2.91 (dd, *J* = 14.7, 10.3 Hz, 1H), 2.18 (t, *J* = 7.6 Hz, 2H), 2.08 – 1.96 (m, 1H), 1.95 – 1.83 (m, 1H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.25, 172.41, 171.65, 155.76, 143.76, 143.70, 140.59, 136.04, 135.91, 128.36, 127.98, 127.73, 127.56, 127.20, 127.02, 125.35, 125.25, 123.82, 120.79, 120.02, 118.56, 118.11, 111.24, 110.20, 99.49, 65.90, 65.62, 55.12, 51.87, 46.53, 31.12, 27.78, 26.50. IR (neat) ν_{max} 3314, 3068, 2974, 1735, 1658, 1544 cm^{-1}; HRMS (ESI) m/z calcd for $C_{38}H_{36}N_4O_6Na$ $[M + Na]^+$ 667.2533, found 667.2535.

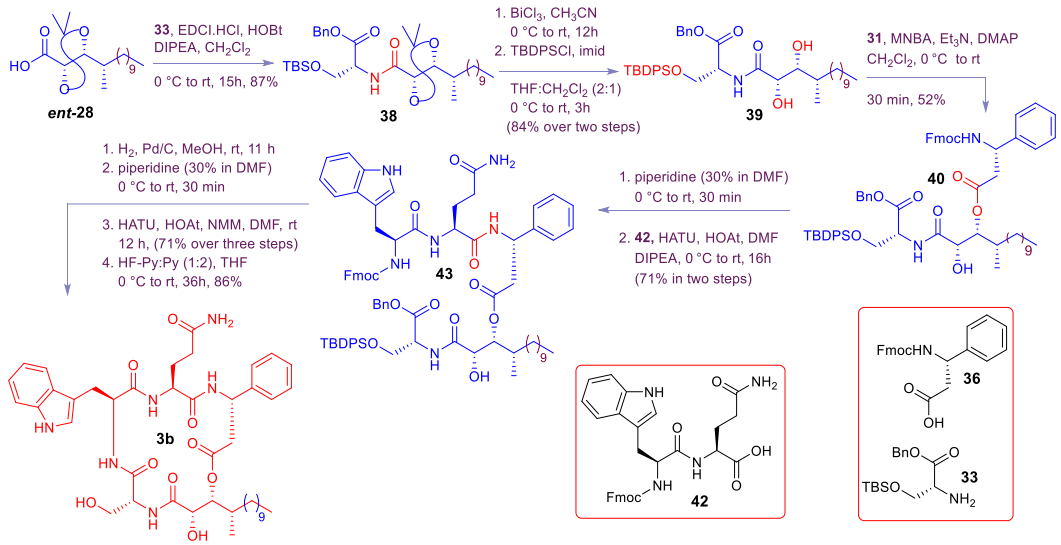


42

Following the same experimental procedure as described for the preparation of compound **32**, the above dipeptide **41b** (617 mg, 0.492 mmol) was subjected to react with H_2 in presence of

Pd/C (70 mg) to furnish acid **42** which was subsequently taken for the next required step without further purification and characterization.

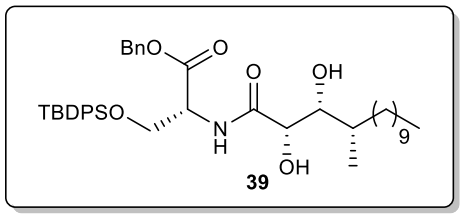
Scheme S9: *Completion of Total Synthesis of Compound **3b**.*



Benzyl O-(*tert*-butyldimethylsilyl)-N-((4*S*)-5-((*S*)-dodecan-2-yl)-2,2-dimethyl-1,3-dioxolane-4-carbonyl)-*D*-serinate (38): Following the same experimental procedure as described for the preparation of compound **34**, acid ***ent*-28** (328 mg, 1.04 mmol) and amine **33** (387 mg, 1.25 mmol) were subjected to react with DIPEA (0.65 mL, 3.76 mmol), HOBt (254 mg, 1.88 mmol) and EDC (410 mg, 1.88 mmol) to furnish the corresponding amide **38** (548 mg, 87%; purification: SiO_2, 100-200 mesh, 5-15% EtOAc in hexane as eluent) as colorless oil; R_f = 0.54 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -69.6 (*c* 0.31, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.7 Hz, 1H), 7.37 – 7.31 (m, 5H), 5.16 (d, *J* = 3.3 Hz, 2H), 4.70 – 4.64 (m, 1H), 4.19 – 4.14 (m, 2H), 4.03 (dd, *J* = 7.5, 3.4 Hz, 1H), 3.81 (dd, *J* = 10.1, 3.1 Hz, 1H), 1.83 (brs, 1H), 1.44 (s, 3H), 1.37 (s, 3H), 1.26 (s, 18H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.88 – 0.83 (m, 12H), 0.03 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.51, 170.08, 135.35, 128.73, 128.60, 128.53, 110.36, 83.13, 77.49, 67.47, 63.47, 53.64, 35.28, 34.21, 32.07, 29.99, 29.79, 29.50, 27.49, 27.14, 25.87, 25.80, 22.84, 18.23, 14.27, 13.35, -5.46, -5.53; IR

(neat): ν_{max} 3424, 2922, 2859, 1748, 1684, 1508 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{34}H_{59}NO_6SiNa$ $[M+Na]^+$ 628.4009, found 628.4012.

Benzyl O-(*tert*-butyldiphenylsilyl)-N-((2*S*,3*R*,4*S*)-2,3-dihydroxy-4-methyltetradecanoyl)-*D*-serinate (39): Following the same experimental procedure as described for the preparation

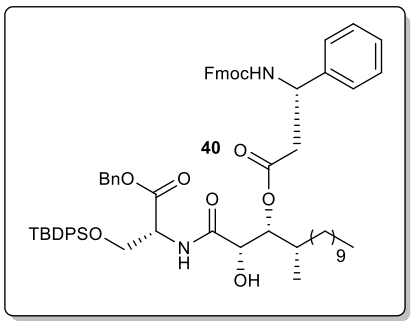


39

of compound **35**, the protected alcohol **38** (513 mg, 0.709 mmol) was treated with $BiCl_3$ (13 mg, 0.042 mmol) and two drops of water to furnish the corresponding triol. Which was subsequently used for the next step without further characterization.

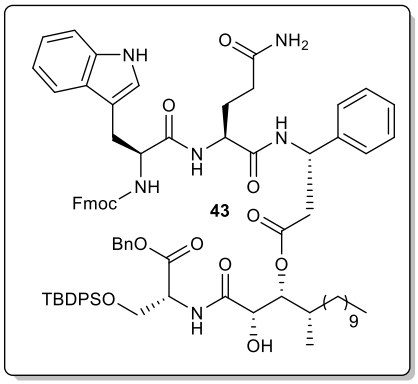
Following the same experimental procedure as described for the preparation of compound **35**, above triol (0.709 mmol, quantitative) was subjected to react with imidazole (86 mg, 1.27 mmol) and TBDPSCl (0.26 mL, 1.02 mmol) to obtain the TBDPS ether **39** (490 mg, 84%; purification: SiO_2, 100-200 mesh, 10-30% EtOAc in hexane as eluent) as a colorless oil; R_f = 0.34 (20% EtOAc in hexane); $[\alpha]_D^{25}$ = +9.7 (*c* 0.82, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 – 7.59 (m, 2H), 7.58 (d, *J* = 1.7 Hz, 1H), 7.55 (d, *J* = 1.5 Hz, 1H), 7.52 (d, *J* = 1.5 Hz, 1H), 7.42 (dd, *J* = 4.9, 2.2 Hz, 2H), 7.39 (d, *J* = 1.6 Hz, 1H), 7.37 (d, *J* = 1.6 Hz, 1H), 7.34 (dd, *J* = 2.4, 1.5 Hz, 2H), 7.33 (s, 2H), 7.32 – 7.31 (m, 2H), 7.30 – 7.29 (m, 1H), 5.16 (dd, *J* = 18.0, 12.0 Hz, 2H), 4.68 (dt, *J* = 8.8, 2.8 Hz, 1H), 4.22 (dd, *J* = 10.4, 2.5 Hz, 1H), 4.16 – 4.12 (m, 1H), 3.91 – 3.82 (m, 2H), 3.19 – 3.10 (m, 1H), 2.72 (brs, 1H), 1.78 – 1.71 (m, 1H), 1.67 – 1.61 (m, 2H), 1.44 – 1.27 (s, 16H), 1.03 – 1.00 (m, 12H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.16, 170.88, 135.69, 135.64, 135.14, 132.63, 130.14, 130.07, 128.79, 128.68, 128.55, 128.03, 127.95, 75.93, 72.84, 67.87, 63.92, 54.37, 35.63, 33.15, 32.06, 30.10, 29.82, 29.78, 29.49, 27.00, 26.84, 22.83, 19.39, 15.46, 14.25; IR (neat) ν_{max} 3414, 2964, 2926, 2855, 1742, 1662, 1519, 1453, 1260, 1105 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{41}H_{59}NO_6SiNa$ $[M+Na]^+$ 712.4009, found 712.4008.

Benzyl N-((2*S*,3*R*,4*S*)-3-(((*S*)-3-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-phenylpropanoyl)oxy)-2-hydroxy-4-methyltetradecanoyl)-O-(*tert*-butyldiphenylsilyl)-*D*-serinate (40): Following the same experimental procedure as described for Shiina esterification for the synthesis of compound **5a**, carboxylic acid **36** (138 mg, 0.357 mmol) and alcohol **39** (164 mg, 0.238 mmol; **note:** *the reaction was performed batch wise*) was subjected to react with MNBA (123 mg, 0.357 mmol), Et_3N (0.29 mL, 2.142 mmol) and DMAP (5 mg, 0.036 mmol) to result required ester **40** (131 mg, 52%; purification: SiO_2, 230-400 mesh, 10-16% EtOAc in hexane as eluent) as colorless oil; R_f = 0.43 (20% EtOAc in hexane as eluent); $[\alpha]_D^{25}$ = -332.9 (*c* 0.06, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 2H), 7.62 – 7.53 (m, 7H), 7.43 – 7.39 (m, 5H), 7.35 – 7.32 (m, 6H), 7.28 – 7.26 (m, 6H), 7.25 – 7.22 (m, 2H), 7.19 – 7.17 (m, 1H), 5.79 (d, *J* = 8.9 Hz, 1H), 5.43 – 5.29 (m, 1H), 5.25 (d, *J* = 8.4 Hz, 1H), 5.16 – 5.14 (m, 1H), 5.07 (d, *J* = 12.3 Hz, 1H), 4.68 (d, *J* = 8.5 Hz, 1H), 4.36 (d, *J* = 7.0 Hz, 2H), 4.26 – 4.12 (m, 3H), 3.84 (dd, *J* = 10.2, 3.0 Hz, 1H), 2.97 – 2.82 (m, 2H), 1.94 – 1.92 (m, 1H), 1.34 – 1.18 (m, 18H), 1.02 (d, *J* = 5.4 Hz, 9H), 0.91 – 0.83 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.82, 170.29, 169.60, 156.25, 144.01, 143.94, 141.39, 135.70, 135.61, 135.24, 132.75, 132.67, 130.11, 130.02, 128.86, 128.78, 128.69, 128.55, 128.49, 128.41, 128.00, 127.91, 127.78, 127.24, 127.18, 126.35, 126.26, 125.25, 125.17, 120.04, 78.45, 77.36, 72.27, 71.57, 67.59, 67.22, 64.16, 53.98, 51.35, 47.32, 40.72, 34.06, 32.82, 32.05, 29.97, 29.77, 29.48, 26.86, 22.83, 19.39, 15.48, 14.87, 14.26; IR (neat): ν_{max} 3413, 2957, 2927, 2855, 1732, 1703, 1677, 1519, 1255, 1112, 1041 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{65}H_{79}N_2O_9Si$ $[M+H]^+$ 1059.5555, found 1059.5552.



Benzyl N-((2*S*,3*R*,4*S*)-3-(((*S*)-3-((*S*)-2-((*S*)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(1H-indol-3-yl)propanamido)-5-amino-5-oxopentanamido)-3-phenylpropanoyl)-

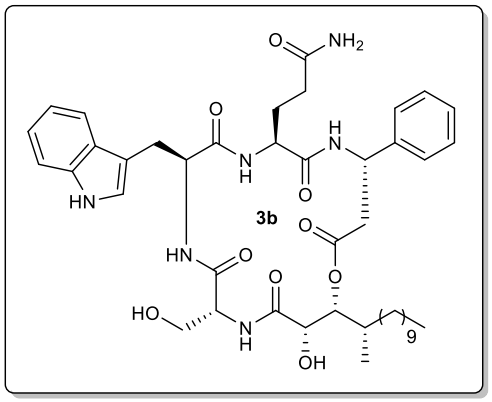
oxy)-2-hydroxy-4-methyltetradecanoyl)-O-(*tert*-butyldiphenylsilyl)-*D*-serinate (43): To a



solution of amine **40** (43 mg, 0.037 mmol) in anhydrous DMF (3.5 mL) under argon, piperidine (1.5 mL) was added. After being stirred at the room temperature for 30 min, the reaction mixture was concentrated in *vacuo*. The residue was azeotrope with anhydrous toluene (2 × 3 mL) and dissolved again in anhydrous DMF (5 mL). To this N-deprotected amine, acid **42** (21 mg, 0.037), DIPEA (15 µL, 0.088 mmol), HOAt (6 mg, 0.044 mmol) and HATU (17 mg, 0.044 mmol) were added sequentially under an argon. After being stirred for 16 h at room temperature, the reaction mixture was concentrated in *vacuo*. The residue was purified by flash chromatography (SiO_2, 60-120 mesh, 1-3% MeOH in CH_2Cl_2 as eluent) to give compound **43** (39.6 mg, 71%) as a white solid; R_f = 0.58 (100% EtOAc in hexane); $[\alpha]_D^{25}$ = +79.9 (*c* 0.05, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.74 (d, *J* = 7.5 Hz, 3H), 7.59 – 7.51 (m, 8H), 7.42 – 7.34 (m, 6H), 7.32 (d, *J* = 3.7 Hz, 3H), 7.28 (d, *J* = 3.9 Hz, 8H), 7.24 – 7.19 (m, 5H), 7.15 – 7.06 (m, 2H), 7.01 (s, 1H), 6.04 (s, 1H), 5.66 (d, *J* = 6.8 Hz, 1H), 5.52 (s, 1H), 5.40 (s, 1H), 5.15 – 5.01 (m, 3H), 4.69 (d, *J* = 8.2 Hz, 1H), 4.49 (d, *J* = 6.5 Hz, 1H), 4.39 (d, *J* = 7.6 Hz, 2H), 4.30 (d, *J* = 6.8 Hz, 1H), 4.17 (dd, *J* = 14.0, 8.0 Hz, 3H), 3.87 (dd, *J* = 10.4, 3.3 Hz, 1H), 3.22 (h, *J* = 7.4, 6.1 Hz, 2H), 2.95 (dd, *J* = 16.7, 8.5 Hz, 1H), 2.81 (dd, *J* = 17.1, 4.8 Hz, 1H), 2.35 – 2.29 (m, 1H), 2.20 – 2.12 (m, 1H), 2.03 – 1.96 (m, 2H), 1.91 – 1.84 (m, 1H), 1.29 – 1.22 (m, 18H), 1.00 – 0.96 (m, 9H), 0.88 (t, *J* = 6.3 Hz, 3H), 0.69 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.06, 171.93, 170.45, 170.00, 156.51, 143.94, 143.83, 141.39, 141.05, 136.46, 135.68, 135.62, 135.14, 132.72, 130.11, 128.85, 128.74, 128.57, 128.48, 128.38, 128.01, 127.94, 127.87, 127.54, 127.25, 126.53, 126.36, 125.27, 123.87, 122.28, 120.10, 119.81, 118.77, 111.63, 109.77, 78.20, 77.36, 71.98, 67.71, 67.37, 64.15, 63.82, 56.13, 54.23, 52.77, 49.69, 47.20, 40.46, 33.79, 33.18, 32.06, 31.66,

30.03, 29.83, 29.78, 29.50, 26.87, 26.81, 22.83, 19.39, 14.96, 14.27, 0.15; IR (neat) ν_{max} 3414, 3064, 2957, 2921, 2857, 1739, 1674, 1538, 1466, 1261, 1101 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{81}H_{97}N_6O_{12}Si$ $[M+H]^+$ 1373.6934, found 1373.6936.

Diastereomer of alveolaride C (3b): Following the same experimental procedure as described for the preparation of compound **37**, compounds **43** (32 mg, 0.023 mmol) was hydrogenated in presence of H_2 and 10% Pd/C (4 mg) was added at the room temperature and allowed to stir for 11 h. The reaction mixture was filtered using a short Celite pad followed by short silica bed (60-120) washing with CH_2Cl_2-MeOH (7:3) (3 × 30 mL). This crude acid was directly used in the next step without further purification.



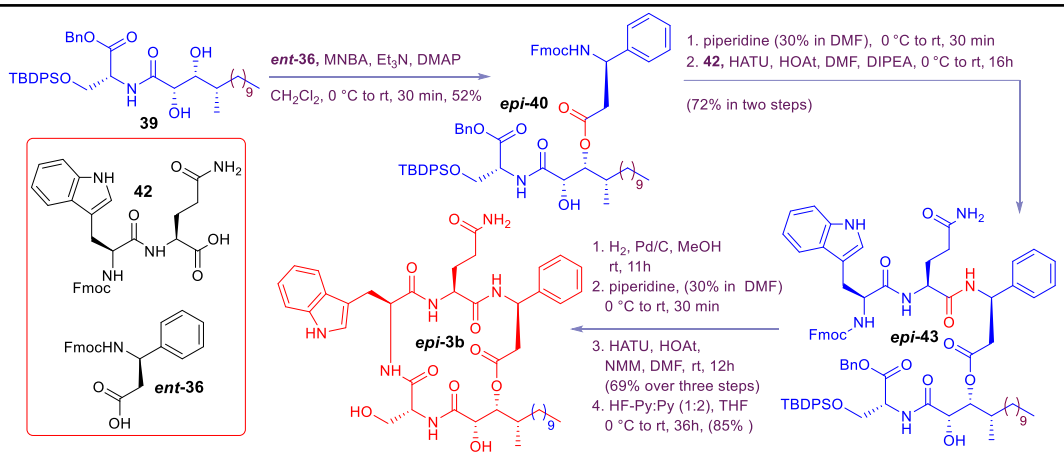
To a solution of the above N-Fmoc protected acid (quantitative, 0.023 mmol) in anhydrous DMF (1.4 mL) under argon, piperidine (0.6 mL) was added. After being stirred at room temperature for 30 min, the reaction mixture was concentrated in *vacuo*. The residue was azeotrope with anhydrous toluene (2 × 3 mL) and dissolved in anhydrous DMF (10 mL) followed by addition of NMM (1 µL, 0.056 mmol). Then a mixture of HOAt (4 mg, 0.028 mmol) and HATU (11 mg, 0.028 mmol) in dry DMF (10 mL) were added to the reaction mixture under an argon atmosphere using cannula over a period of 30 min, so that the overall concentration was maintained at 0.001M. After being stirred for 12 h at the room temperature, the reaction mixture was concentrated in *vacuo*. The residue was purified by flash chromatography (SiO_2, 60-120 mesh, 1-3% MeOH in CH_2Cl_2 as eluent) to give corresponding protected cyclic depsipeptide (17 mg, 71%) as a colorless oil; R_f = 0.23 (5% MeOH in CH_2Cl_2); $[\alpha]_D^{25}$ = -9.9 (*c* 0.37, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.00 (s, 1H), 7.60 (d, *J* = 7.1 Hz, 4H), 7.53 – 7.50 (m, 1H), 7.49 – 7.47 (m, 1H), 7.47 – 7.42 (m, 3H), 7.42 – 7.39 (m, 2H), 7.37 – 7.35(m, 1H), 7.33 – 7.31 (m, 4H), 7.29 – 7.27 (m,

1H), 7.25 – 7.24 (m, 1H), 7.23 – 7.19 (m, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.80 – 6.61 (m, 2H), 6.39 (s, 1H), 5.61 (s, 1H), 5.23 – 5.15 (m, 1H), 5.10 – 5.02 (m, 2H), 4.47 (q, *J* = 5.2 Hz, 1H), 4.28 – 4.22 (m, 2H), 3.85 – 3.73 (m, 2H), 3.30 (dd, *J* = 8.7, 6.3 Hz, 1H), 3.20 – 3.10 (m, 1H), 2.78 – 2.59 (m, 2H), 2.17 – 2.08 (m, 2H), 1.96 – 1.84 (m, 3H), 1.42 – 1.39 (m, 2H), 1.29 – 1.24 (m, 16H), 1.03 (s, 9H), 0.89 – 0.85 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.09, 172.03, 171.61, 170.53, 169.55, 141.89, 136.39, 135.75, 132.97, 132.80, 130.42, 130.32, 128.84, 128.51, 128.20, 128.14, 127.38, 126.27, 123.12, 122.58, 119.96, 118.70, 111.50, 109.38, 77.36, 72.29, 65.51, 56.06, 53.59, 53.39, 49.79, 40.22, 34.52, 32.66, 32.05, 30.94, 29.96, 29.85, 29.78, 29.72, 29.48, 26.94, 26.90, 26.71, 24.21, 22.83, 19.44, 15.67, 14.27, 0.15; IR (neat): ν_{max} 3327, 2961, 2921, 2857, 1739, 1663, 1537, 1463, 1265, 1122, 1035 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{59}H_{79}N_6O_9Si$ $[M+H]^+$ 1043.5678, found 1043.5675.

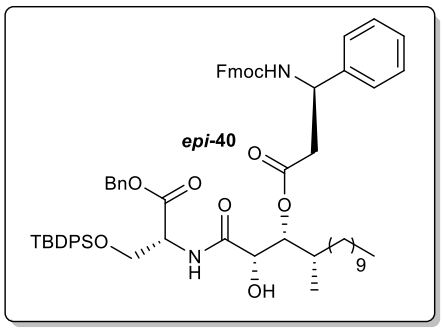
To an ice-cold fresh solution of HF-Py (0.1mL), Py (0.2 mL) in anhydrous THF (1 mL) a solution of the above cyclic depsipeptide (14 mg, 0.013 mmol) in anhydrous THF (2 mL) was added under argon. After 36 h the reaction mixture was diluted with Et_2O (10 mL) and washed with aqueous HCl solution (1N, 2 × 5 mL), distilled water. The organic layer dried over anhydrous Na_2SO_4 and concentrated in *vacuo* (*the temperature should not exceed more than 35 °C, as at high temperature undesired spot my appear*). The resultant residue was purified by column chromatography (neutral Al_2O_3, eluent: 60% EtOAc in hexane followed by 10% MeOH in CH_2Cl_2, **Note**: *compound may decompose on passing through silica or keeping for long time in alumina also*) to get white solid compound **3b** (9 mg, 86%); R_f= 0.31 (10% MeOH in CH_2Cl_2); $[\alpha]_D^{25}$ = -5.1 (*c* 0.17, MeOH); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.91 (d, *J* = 2.4 Hz, 1H), 8.70 (d, *J* = 5.0 Hz, 1H), 7.85 (d, *J* = 5.5 Hz, 1H), 7.59 (d, *J* = 6.9 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.37 (brd, *J* = 8.1 Hz, 1H), 7.32 – 7.30 (m, 5H), 7.29 (d, *J* = 2.7 Hz, 1H), 7.24 – 7.22 (m, 1H), 7.19 – 7.16 (m, 1H), 7.14 – 7.08 (m, 1H), 7.05 – 6.99 (m, 1H), 6.77 (s, 1H), 6.20 (d, *J* = 6.8 Hz, 1H), 5.30 (t, *J* = 5.6 Hz, 1H), 5.16 (q, *J* = 7.9 Hz, 1H), 4.91 (dd, *J*

= 9.1, 1.9 Hz, 1H), 4.42 (q, *J* = 6.5, 5.7 Hz, 1H), 4.17 – 4.24 (m, 2H), 3.98 – 3.92 (m, 1H), 3.57 – 3.63 (m, 1H), 3.49 – 3.48 (m, 1H), 3.15 – 3.07 (m, 2H), 2.83 (d, *J* = 8.0 Hz, 2H), 2.09 (t, *J* = 7.5 Hz, 2H), 1.99 – 1.93 (m, 1H), 1.89 – 1.80 (m, 2H), 1.25 (s, 16H), 1.19 (m 2H), 0.87 (t, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.47, 172.98, 172.91, 172.03, 170.65, 170.07, 142.76, 136.65, 128.68, 127.56, 127.20, 126.55, 123.95, 121.55, 118.89, 118.46, 111.90, 110.40, 77.72, 71.56, 62.13, 56.43, 55.44, 54.10, 49.11, 40.00, 33.44, 32.33, 31.77, 31.56, 29.78, 29.55, 29.48, 29.46, 29.17, 26.77, 26.66, 26.31, 22.55, 15.90, 14.42; IR (neat): ν_{max} 3295, 2954, 2922, 2851, 1736, 1651, 1530, 1427, 1328, 1256, 1167, 1105 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{43}H_{60}N_6O_9Na$ $[M+Na]^+$ 827.4319, found 827.4316.

Scheme S10: *Completion of Total Synthesis of the Actual Structure of Alveolaride C (**epi**-**3b**)*



Benzyl N-((2*S*,3*R*,4*S*)-3-(((*R*)-3-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-phenylpropanoyl)oxy)-2-hydroxy-4-methyltetradecanoyl)-O-(*tert*-butyldiphenylsilyl)-*D*-serinate (*epi*-40): Following the same experimental procedure as described for the preparation of

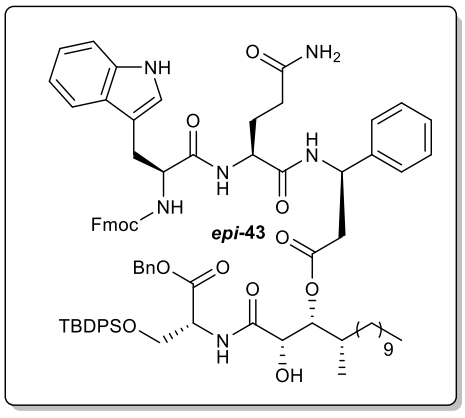


compound **40**, carboxylic acid ***ent*-36** (90 mg, 0.232 mmol) and alcohol **39** (107 mg, 0.155 mmol, **note:** *the reaction was carried out batch wise*) was treated with MNBA (80 mg, 0.232 mmol), Et_3N (0.19 mL, 1.395 mmol) and DMAP (3 mg, 0.023 mmol) to get ester ***epi*-40**

(131 mg, 52%; purification: SiO_2, 230-400 mesh, 10-16% EtOAc in hexane as eluent) as a white solid; R_f = 0.37 (20% EtOAc in hexane); $[\alpha]_D^{25}$ = -699.1 (*c* 0.04, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.5 Hz, 2H), 7.59 – 7.49 (m, 6H), 7.40 – 7.36 (m, 4H), 7.34 – 7.33 (m, 3H), 7.32 – 7.28 (m, 12H), 7.25 – 7.24 (m, 1H), 6.08 (d, *J* = 8.7 Hz, 1H), 5.21 – 5.09 (m, 4H), 4.68 (d, *J* = 8.4 Hz, 1H), 4.35 – 4.30 (m, 2H), 4.22 – 4.09 (m, 3H), 3.82 (dd, *J* = 10.6, 3.3 Hz, 1H), 3.29 – 3.08 (m, 1H), 2.94 – 2.78 (m, 2H), 1.90 (q, *J* = 7.3 Hz, 1H), 1.26 (s, 18H), 1.00 (s, 9H), 0.89 (t, *J* = 6.7 Hz, 3H), 0.74 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.18, 170.51, 170.36, 170.21, 170.04, 156.01, 144.02, 143.93, 141.40, 135.70, 135.62, 135.50, 135.24, 132.78, 130.16, 130.07, 128.99, 128.84, 128.75, 128.57, 128.42, 127.96, 127.77, 127.19, 126.28, 125.23, 120.05, 77.36, 71.56, 67.61, 67.08, 64.40, 64.26, 54.45, 54.32, 54.02, 51.55, 47.32, 40.74, 40.41, 34.95, 33.88, 33.63, 33.45, 32.99, 32.06, 29.97, 29.79, 29.49, 26.85, 22.84, 19.38, 15.10, 14.27 ppm; IR (neat): ν_{max} 3408, 2961, 2924, 2854, 1735, 1658, 1515, 1456, 1259, 1105, 1038 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{65}H_{78}N_2O_9SiNa$ $[M+Na]^+$ 1081.5374, found 1081.5378.

Benzyl N-((2*S*,3*R*,4*S*)-3-(((*R*)-3-((*S*)-2-((*S*)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(1H-indol-3-yl)propanamido)-5-amino-5-oxopentanamido)-3-phenylpropanoyl)oxy)-2-hydroxy-4-methyltetradecanoyl)-O-(*tert*-butyldiphenylsilyl)-*D*-serinate(*epi*-43):

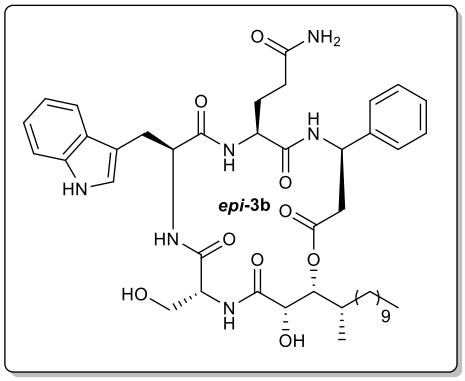
Following the same experimental procedure as described for the preparation of compound **43**,



Fmoc protected amine ***epi*-40** (57 mg, 0.054 mmol) was subjected to react with piperidine (1.5 mL in 3.5 mL DMF) to deprotect Fmoc. The corresponding Fmoc deprotected compound was reacted with acid **42** (30 mg, 0.054 mmol), DIPEA (20 µL, 0.116 mmol), HOAt (8 mg, 0.058 mmol) and HATU (22 mg, 0.058 mmol) to result the corresponding cyclic precursor ***epi*-43** (53 mg, 72%, purification: SiO_2, 60-120 mesh,

1-3% MeOH in CH_2Cl_2 as eluent) as a white solid. to give acyclic depsipeptide; R_f = 0.54 (100% EtOAc); $[\alpha]_D^{25}$ = +54.2 (*c* 0.16, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 – 7.59 (m, 2H), 7.74 (d, *J* = 7.1 Hz, 2H), 7.55 (dd, *J* = 13.2, 7.0 Hz, 6H), 7.39 – 7.34 (m, 5H), 7.32 – 7.27 (m, 10H), 7.25 – 7.18 (m, 8H), 7.13- 7.69 (m, 3H), 6.89 – 6.80 (m, 1H), 6.36 (s, 1H), 5.68 (s, 1H), 5.39 (s, 1H), 5.16 – 5.08 (m, 3H), 4.71 (d, *J* = 8.5 Hz, 1H), 4.46 (s, 1H), 4.30 (tt, *J* = 13.4, 8.2 Hz, 4H), 4.18 – 4.00 (m, 3H), 3.83 (dd, *J* = 10.2, 2.7 Hz, 1H), 3.26 (d, *J* = 14.7 Hz, 1H), 3.09 (d, *J* = 10.0 Hz, 1H), 2.95 – 2.80 (m, 2H), 2.03 – 1.81 (m, 5H), 1.52 (d, J = 5.7 Hz, 1H), 1.43 (d, *J* = 5.9 Hz, 1H), 1.26 – 1.22 (m, 16H), 0.99 (d, *J* = 3.1 Hz, 8H), 0.94 – 0.85 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.31, 172.24, 171.44, 171.40, 170.54, 170.42, 170.41, 143.84, 141.37, 136.36, 135.70, 135.63, 135.24, 132.79, 130.04, 130.04, 129.63, 129.63, 129.14, 129.14, 128.82, 128.82, 128.74, 128.74, 128.54, 128.54, 128.40, 128.40, 128.04, 127.95, 127.89, 127.81, 127.38, 127.25, 126.69, 125.46, 125.32, 125.32, 122.26, 120.09, 119.82, 118.62, 111.62, 77.36, 77.36, 72.27, 67.62, 64.29, 56.21, 56.21, 54.24, 54.24, 54.17, 54.17, 53.32, 53.32, 53.13, 50.16, 50.16, 47.14, 33.92, 33.92, 33.53, 33.53, 32.06, 30.01, 29.83, 29.77, 29.49, 26.97, 26.84, 24.57, 22.83, 22.44, 22.09, 19.35, 18.84, 17.57, 14.80, 14.26, 12.27, 0.14, 0.14; IR (neat) ν_{max} 3319, 2952, 2926, 2855, 1736, 1662, 1531, 1246, 1029 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{81}H_{97}N_6O_{12}Si$ $[M+H]^+$ 1373.6934, found 1373.6936.

Actual alveolaride C (*epi*-3b): Following the same experimental procedure as described for the preparation of compound **3b**, compound ***epi*-43** (48 mg, 0.032 mmol) was treated with H_2 in presence of Pd/C (5 mg) to obtain the corresponding acid which was subsequently taken in next step without further purification.



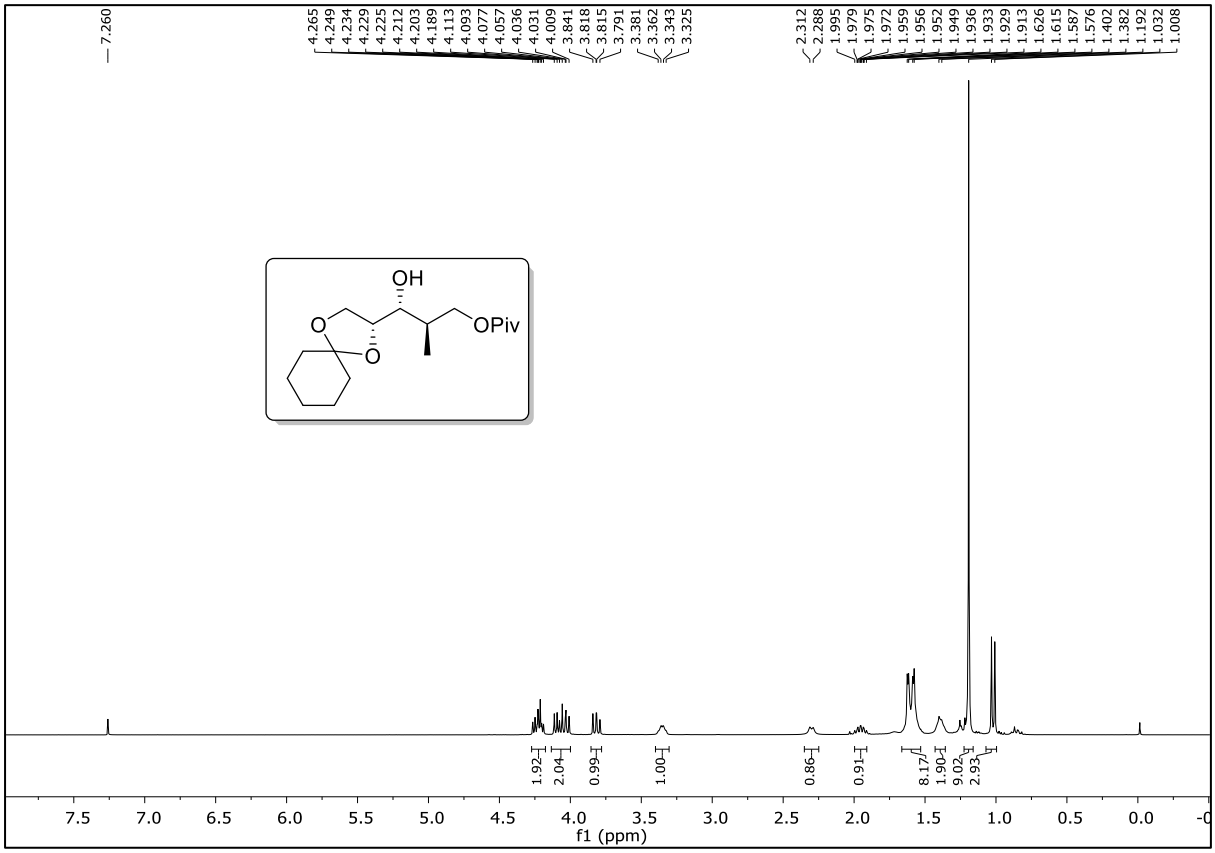
Following the same experimental procedure as described for the preparation of compound **3b**, the above acid was subjected to react with piperidine (0.6 mL in 1.4 mL DMF)

to deprotect Fmoc. To this resultant compound, NMM (1 µL, 0.076 mmol), HOAt (5 mg, 0.038 mmol) and HATU (15 mg, 0.038 mmol) was added to afford the corresponding cyclic depsipeptide (23 mg, 69%; purification: SiO_2, 60-120 mesh, 1-3% MeOH in CH_2Cl_2 as eluent) as a colorless oil; R_f = 0.49 (10% MeOH in CH_2Cl_2); $[\alpha]_D^{25}$ = -12.9 (*c* 0.48, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (d, *J* = 2.5 Hz, 1H), 7.95 (d, *J* = 6.9 Hz, 1H), 7.67 – 7.58 (m, 6H), 7.47 (td, *J* = 6.5, 5.3, 3.4 Hz, 3H), 7.43 – 7.36 (m, 5H), 7.32 – 7.28 (m, 4H), 7.22 – 7.18 (m, 1H), 7.13 (td, *J* = 7.7 , 0.8 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 5.4 Hz, 1H), 6.73 (d, *J* = 2.3 Hz, 1H), 5.90 (s, 1H), 5.85 (s, 1H), 5.08 (d, *J* = 7.6 Hz, 1H), 4.80 (ddt, *J* = 12.8, 8.7, 4.0 Hz, 2H), 4.54 (q, *J* = 5.6 Hz, 1H), 4.20 – 4.13 (m, 2H), 3.88 (dd, *J* = 10.3, 4.0 Hz, 1H), 3.80 (dd, *J* = 10.3, 5.1 Hz, 1H), 3.56 (dd, J = 13.8, 10.2 Hz, 1H), 3.35 (dd, *J* = 15.1, 6.3 Hz, 1H), 3.17 – 3.06 (m, 2H), 2.95 (dd, *J* = 13.7, 3.1 Hz, 1H), 2.33 – 2.27 (m, 1H), 2.17 – 2.07 (m, 1H), 1.99 (t, *J* = 5.3 Hz, 1H), 1.92 – 1.87 (m, 1H), 1.60 – 1.47 (m, 1H), 1.38 – 1.32 (m, 2H), 1.29 – 1.19 (m, 16H), 1.05 (s, 9H), 0.89 – 0.82 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.57, 172.07, 171.87, 171.68, 171.64, 171.02, 139.80, 136.42, 135.72, 133.03, 132.89, 130.32, 130.25, 128.50, 128.19, 128.15, 128.10, 127.59, 127.39, 126.72, 123.44, 123.37, 122.52, 119.95, 118.61, 111.58, 109.35, 109.28, 77.36, 71.84, 64.93, 63.86, 56.27, 53.96, 38.05, 35.56, 32.80, 32.05, 31.18, 29.95, 29.85, 29.77, 29.70, 29.48, 27.06, 26.98, 26.44, 22.82, 19.46, 15.50, 14.25, 0.14; IR (neat) ν_{max} 3300, 2933, 2855, 1736, 1664, 1546, 1478, 1439, 1279, 1111, 1019 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{59}H_{79}N_6O_9Si$ $[M+H]^+$ 1043.5678, found 1043.5675.

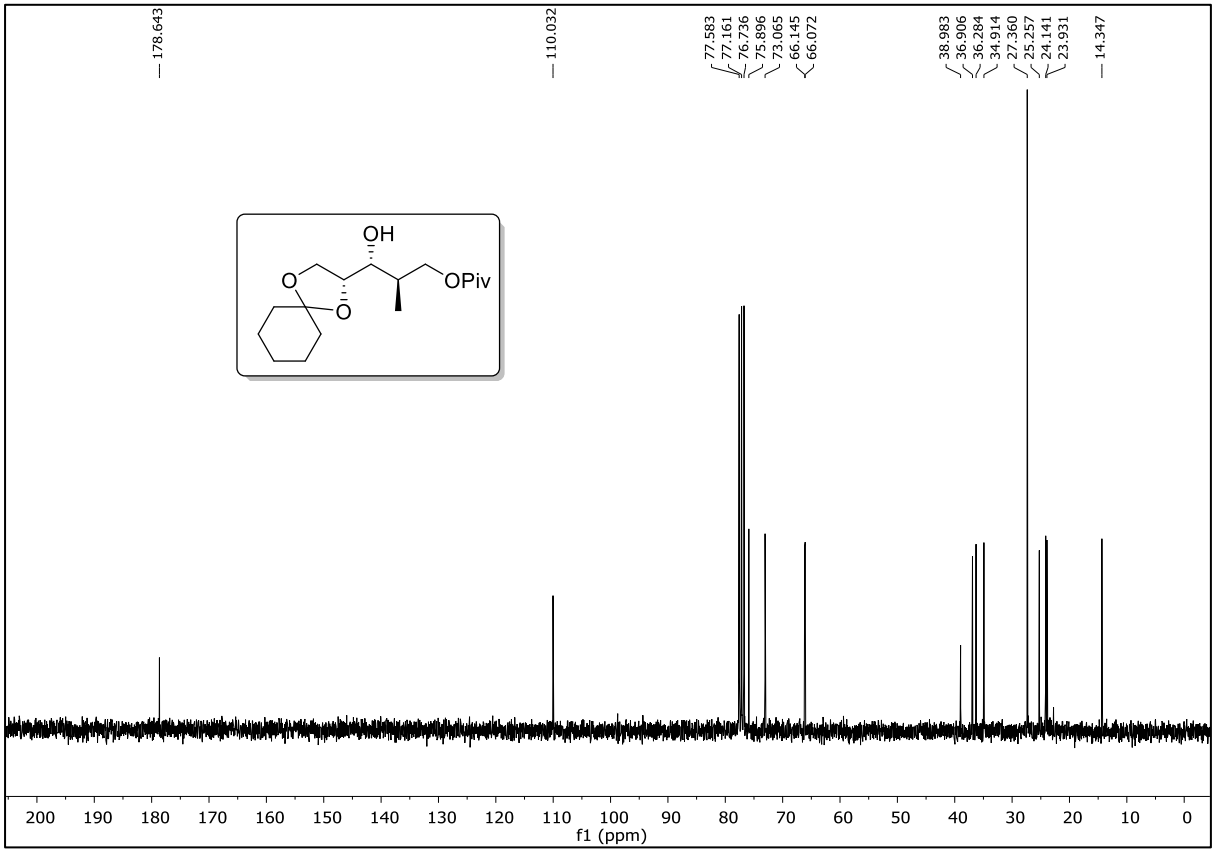
Following the same experimental procedure as described for the preparation of compound **3b**, the above silyl protected cyclic compound was treated with HF-Py (0.1 mL) and Py (0.2 mL) to furnish compound ***epi*-3b** as white solid (13 mg, 85%; purification: neutral Al_2O_3, eluent: 60% EtOAc in hexane followed by 10% MeOH in CH_2Cl_2, **Note**: *compound may decompose on passing through silica or keeping for long time in alumina also. Temperature should be maintained below 35 °C throughout the course of purification*); R_f =

0.28 (10% MeOH in CH_2Cl_2). $[\alpha]_D^{25}$ = -15.8 (*c* 0.21, MeOH). ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.89 (brs, 1H), 8.36 (d, *J* = 5.9 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 7.4 Hz, 1H), 7.57 – 7.50 (m, 2H), 7.36 (brd, *J* = 8.1 Hz, 1H), 7.27 – 7.22 (m, 6H), 7.19 – 7.16 (m, 1H), 7.09 (t, *J* = 7.3 Hz, 1H), 7.01 (t, *J* = 7.3 Hz, 1H), 6.78 (s, 1H), 6.01 (d, *J* = 6.8 Hz, 1H), 5.13 (t, *J* = 5.4 Hz, 1H), 4.83 (q, *J* = 6.4 Hz, 1H), 4.70 (d, *J* = 8.1 Hz, 1H), 4.50 – 4.44 (m, 1H), 4.20-4.26 (m, 1H), 4.06 (d, *J* = 6.6 Hz, 1H), 3.98 – 3.89 (m, 1H), 3.58 (dd, *J* = 10.5, 5.4 Hz, 1H), 3.47 (d, *J* = 5.5 Hz, 1H), 3.18 – 3.11 (m, 3H), 2.88 (d, *J* = 11.5 Hz, 1H), 2.09 – 2.01 (m, 2H), 1.97 – 1.92 (m, 1H), 1.88 – 1.78 (m, 2H), 1.28 (brs, 1H) 1.24 (brs, 16H) 1.04 – 1.01 (m, 1H), 0.86 (t, *J* = 6.9 Hz, 3H), 0.67 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.20, 172.63, 172.44, 171.98, 171.74, 170.13, 141.50, 136.62, 128.73, 128.27, 127.68, 126.81, 126.42, 124.11, 121.52, 118.90, 118.59, 111.90, 110.19, 76.82, 71.18, 62.60, 56.39, 55.00, 54.69, 49.89, 38.50, 34.26, 32.71, 32.16, 31.82, 29.76, 29.56, 29.53, 29.48, 29.23, 27.39, 27.05, 26.58, 22.62, 15.75, 14.49; IR (neat) ν_{max} 3267, 2933, 2852, 1731, 1658, 1530, 1461, 1427, 1212, 1186, 1016 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{43}H_{61}N_6O_9$ $[M+H]^+$ 805.4500, found 805.4502.

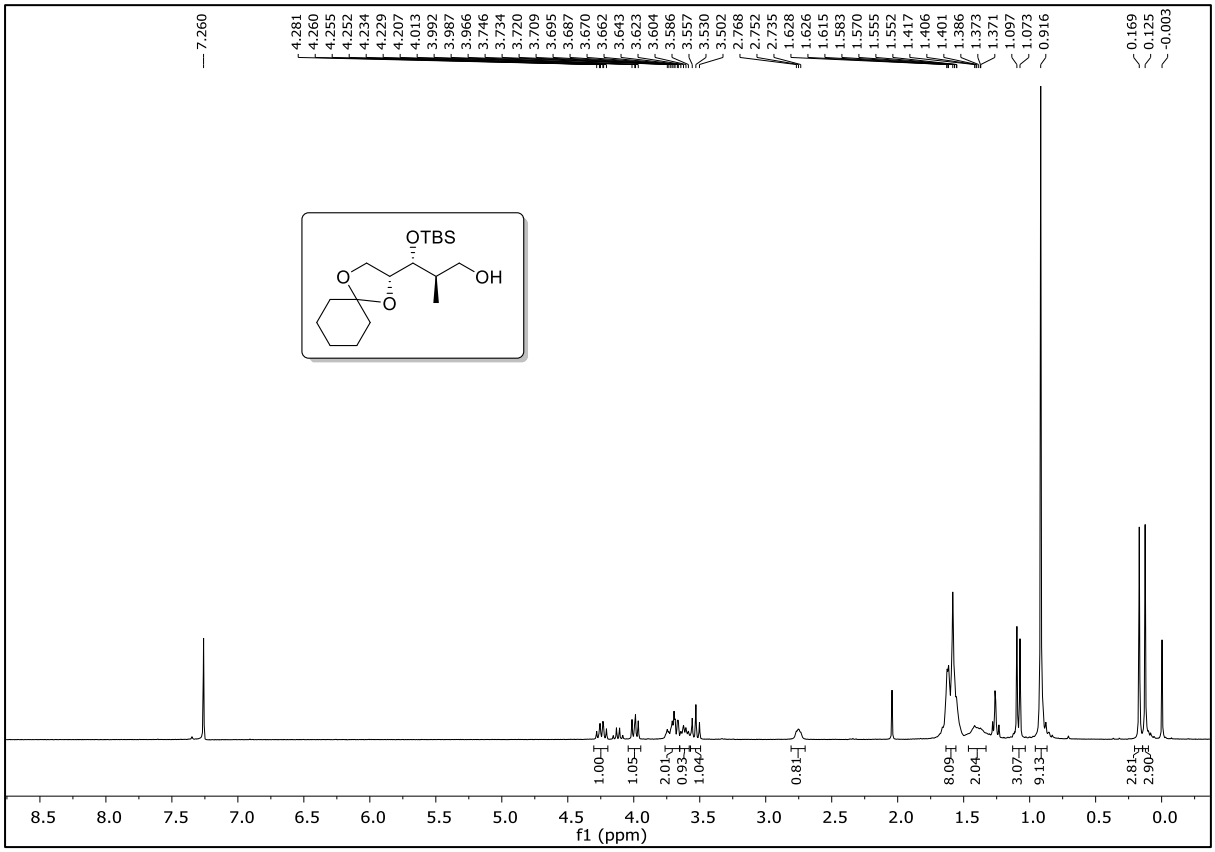
^{1}H-NMR spectrum of compound 9 (300 MHz, $CDCl_3$):



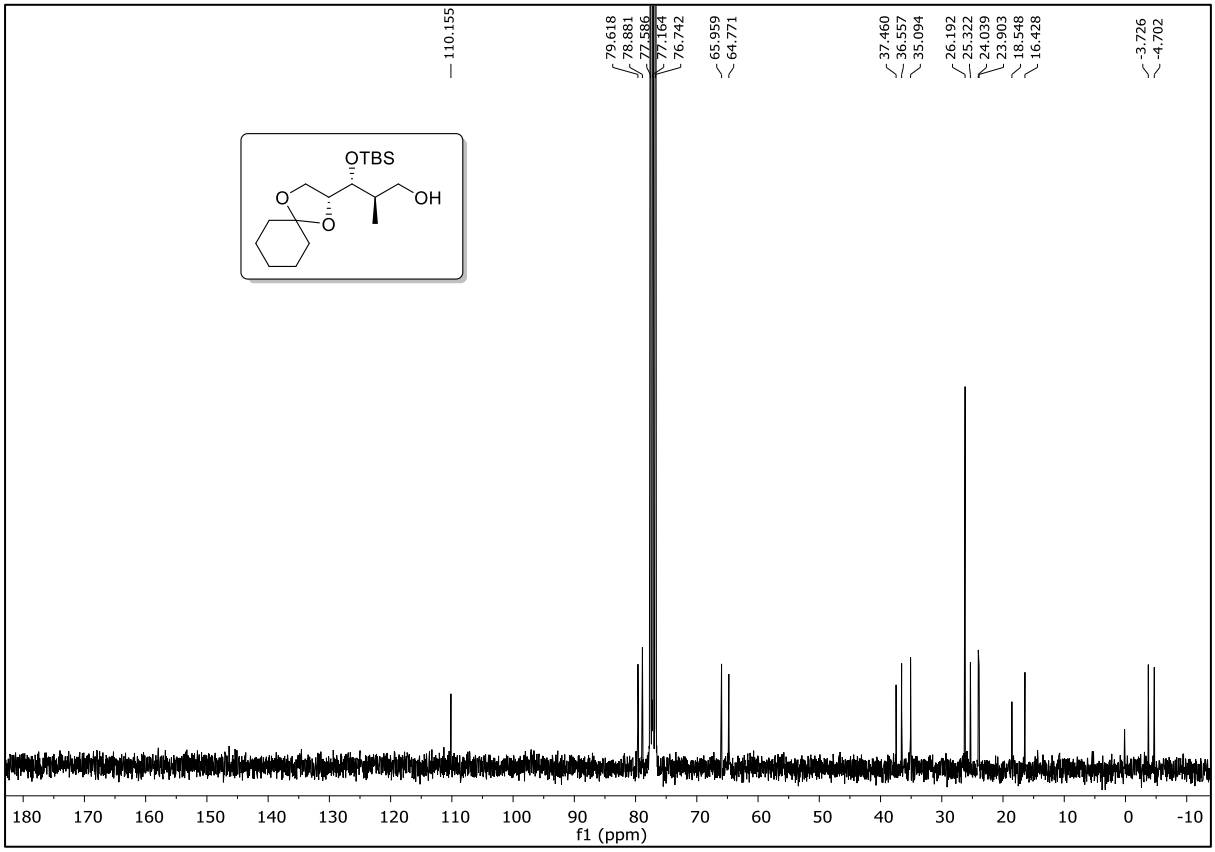
^{13}C-NMR spectrum of compound 9 (75 MHz, $CDCl_3$):



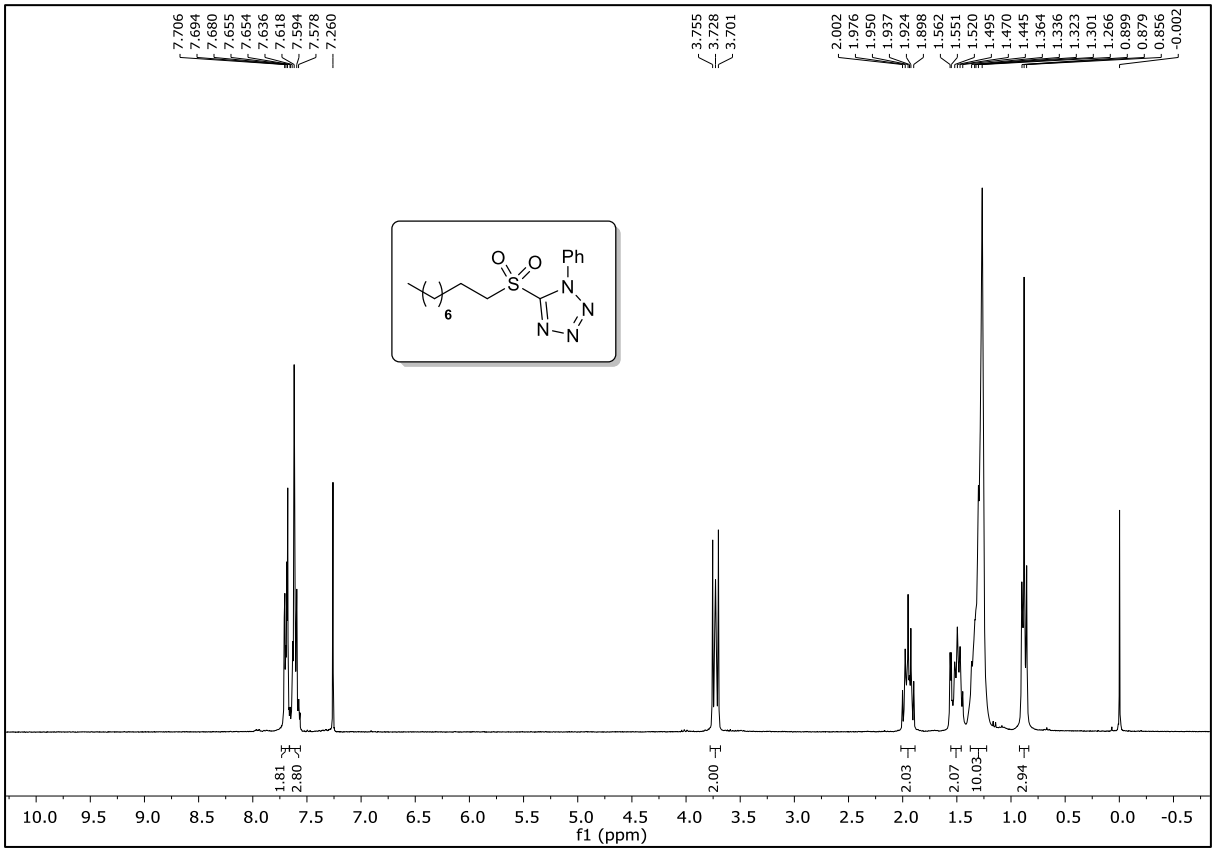
^{1}H-NMR spectrum of compound 10 (300 MHz, $CDCl_3$):



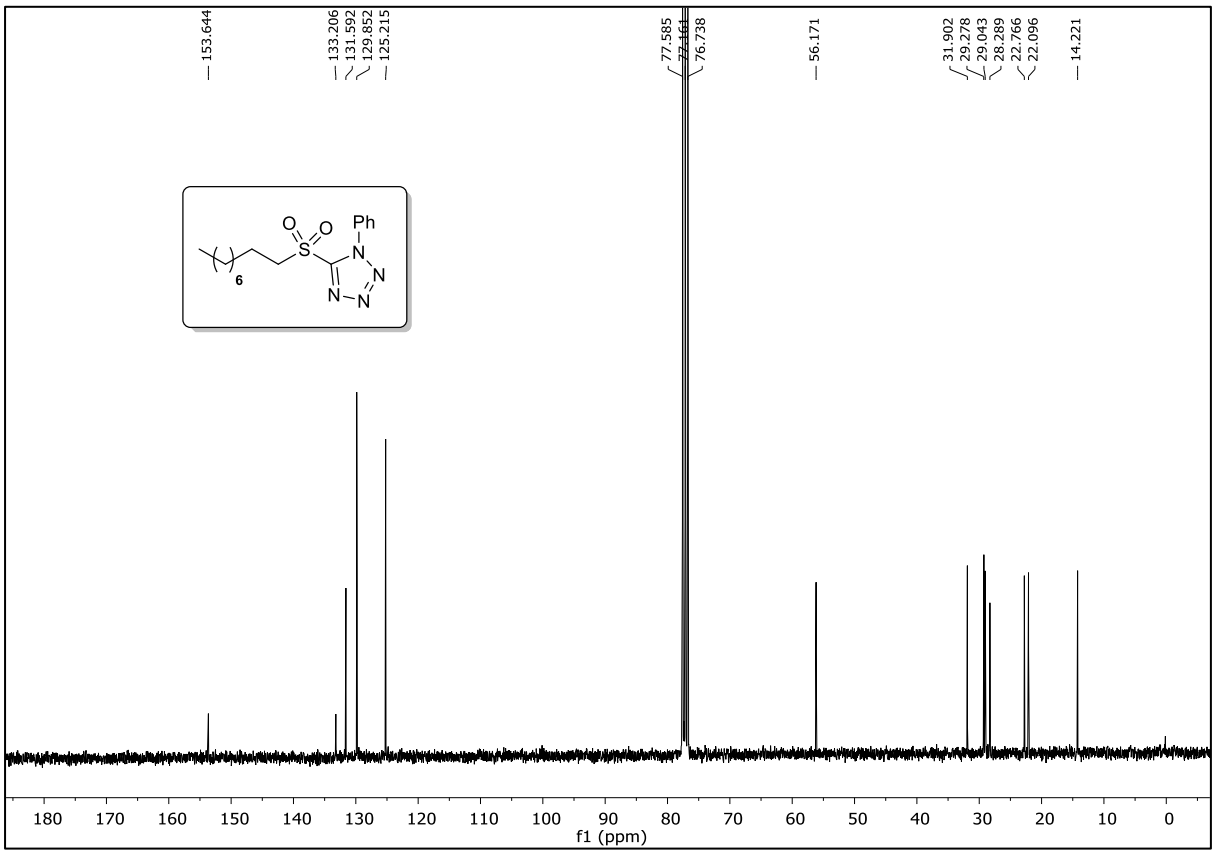
^{13}C-NMR spectrum of compound 10 (75 MHz, $CDCl_3$):



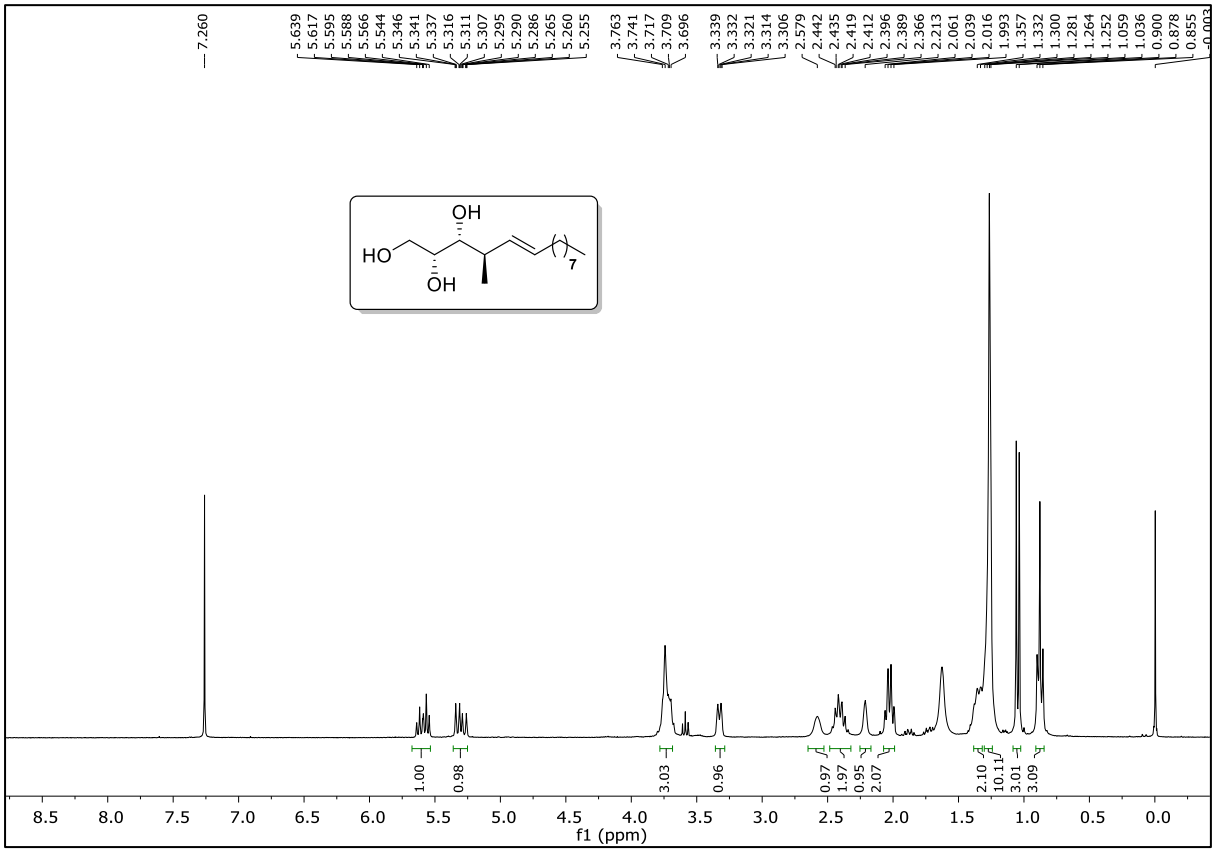
^{1}H-NMR spectrum of compound 11 (300 MHz, $CDCl_3$):



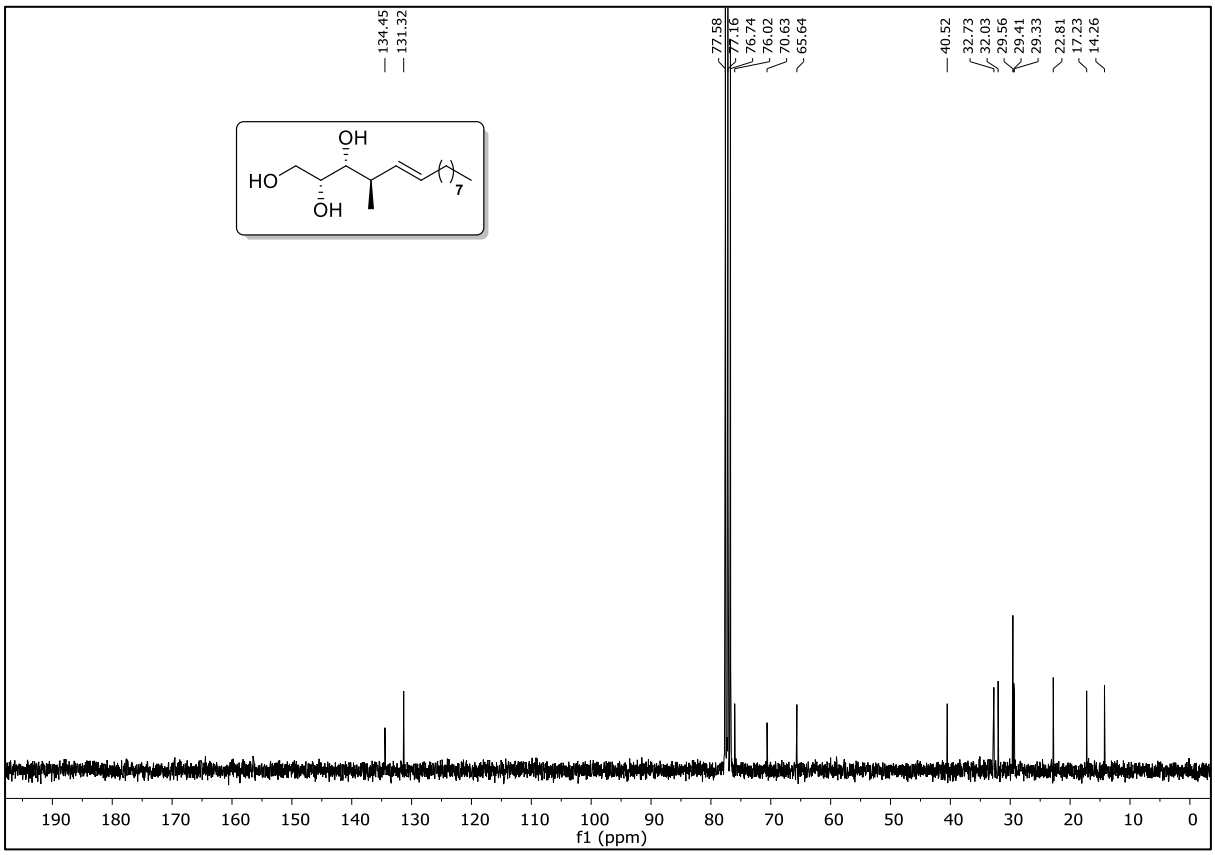
^{13}C-NMR spectrum of compound 11 (75 MHz, $CDCl_3$):



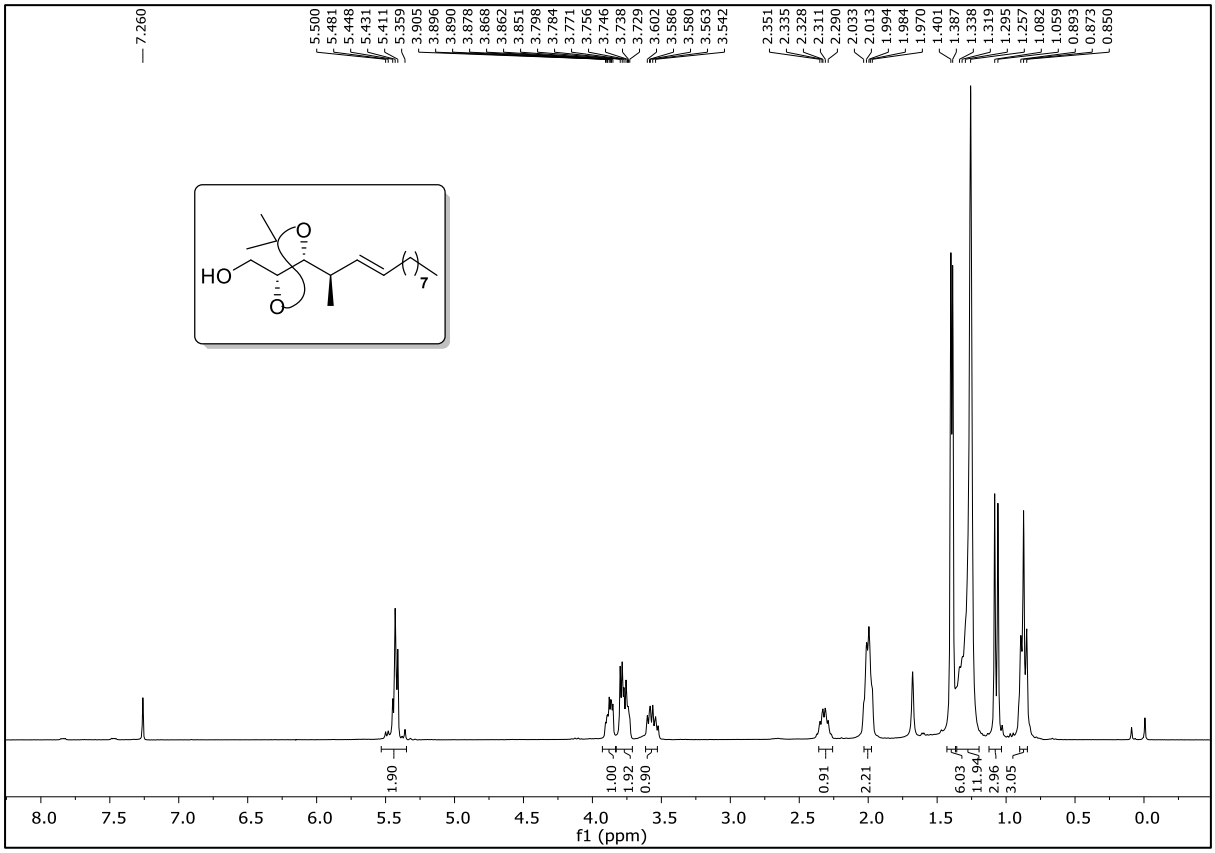
^{1}H-NMR spectrum of compound 12 (300 MHz, $CDCl_3$):



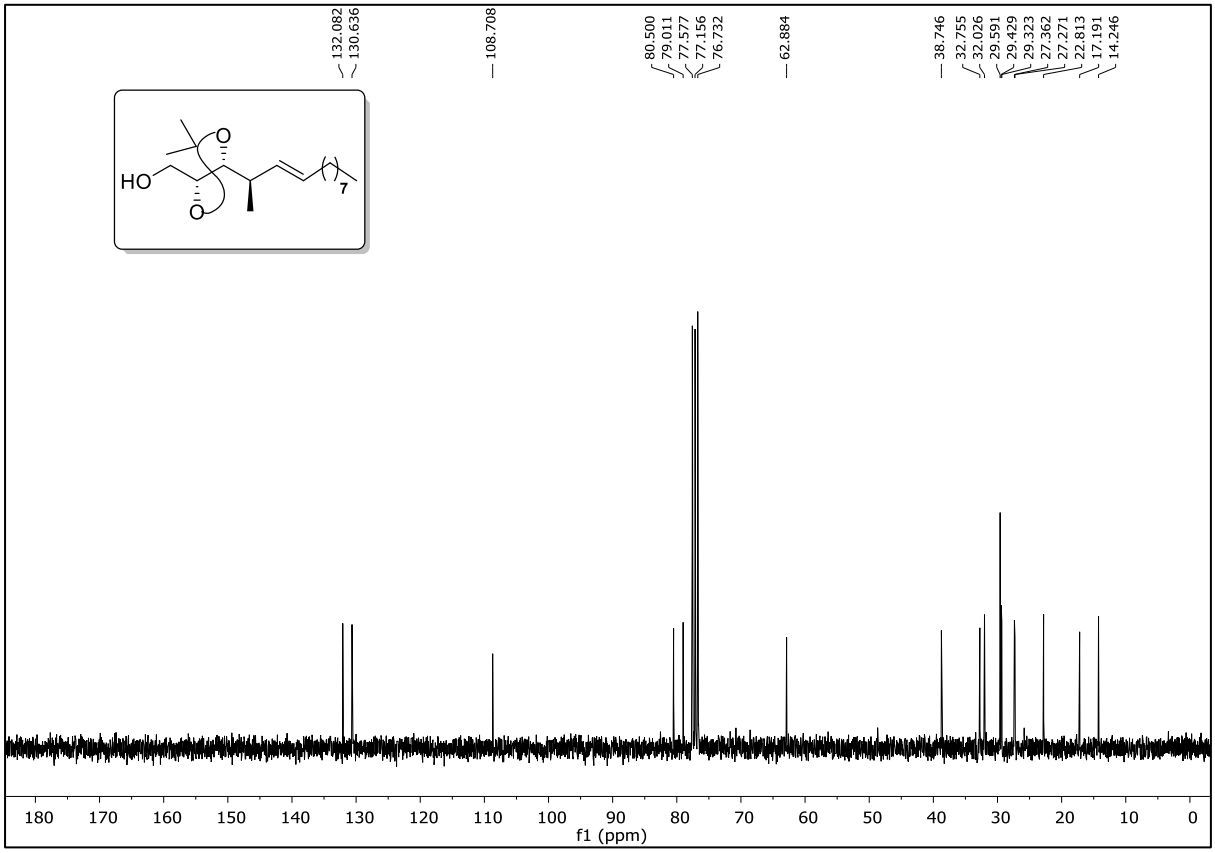
^{13}C-NMR spectrum of compound 12 (75 MHz, $CDCl_3$):



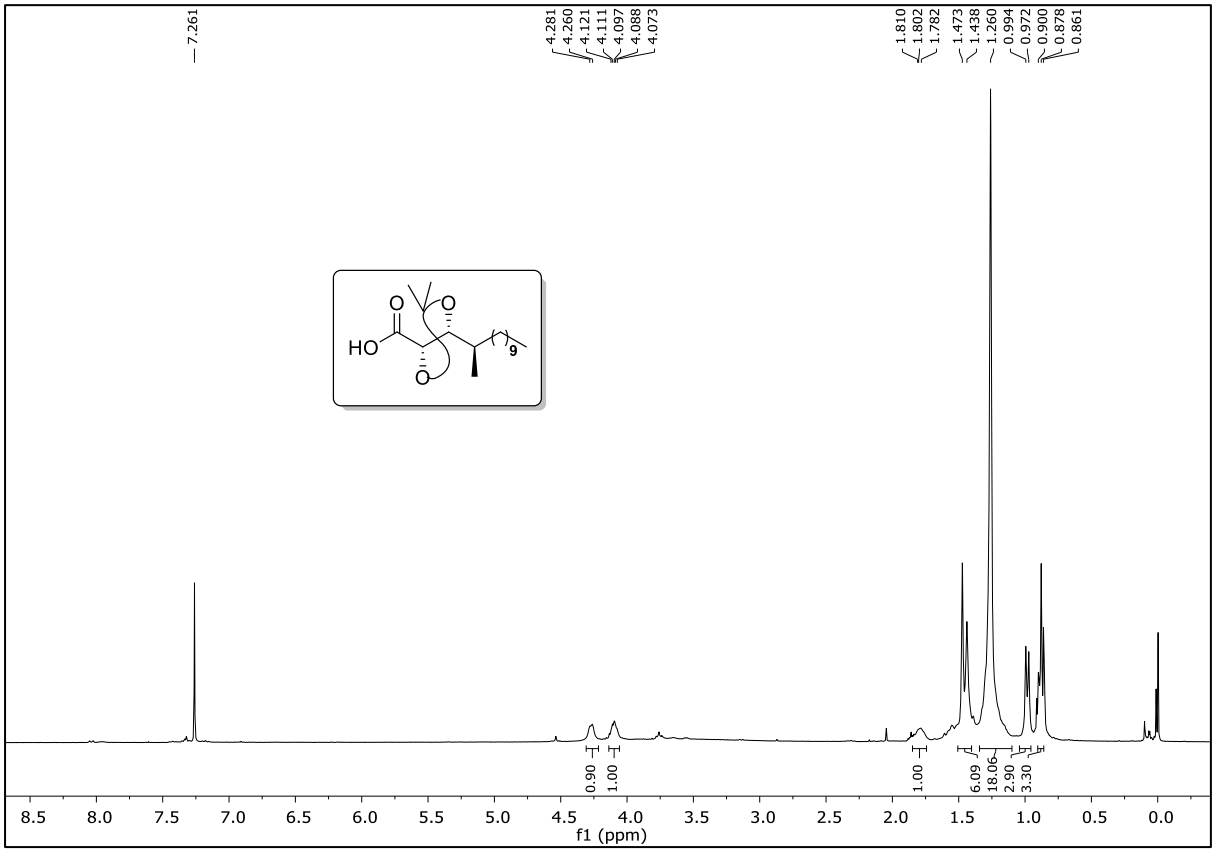
^{1}H-NMR spectrum of compound 13 (300 MHz, $CDCl_3$):



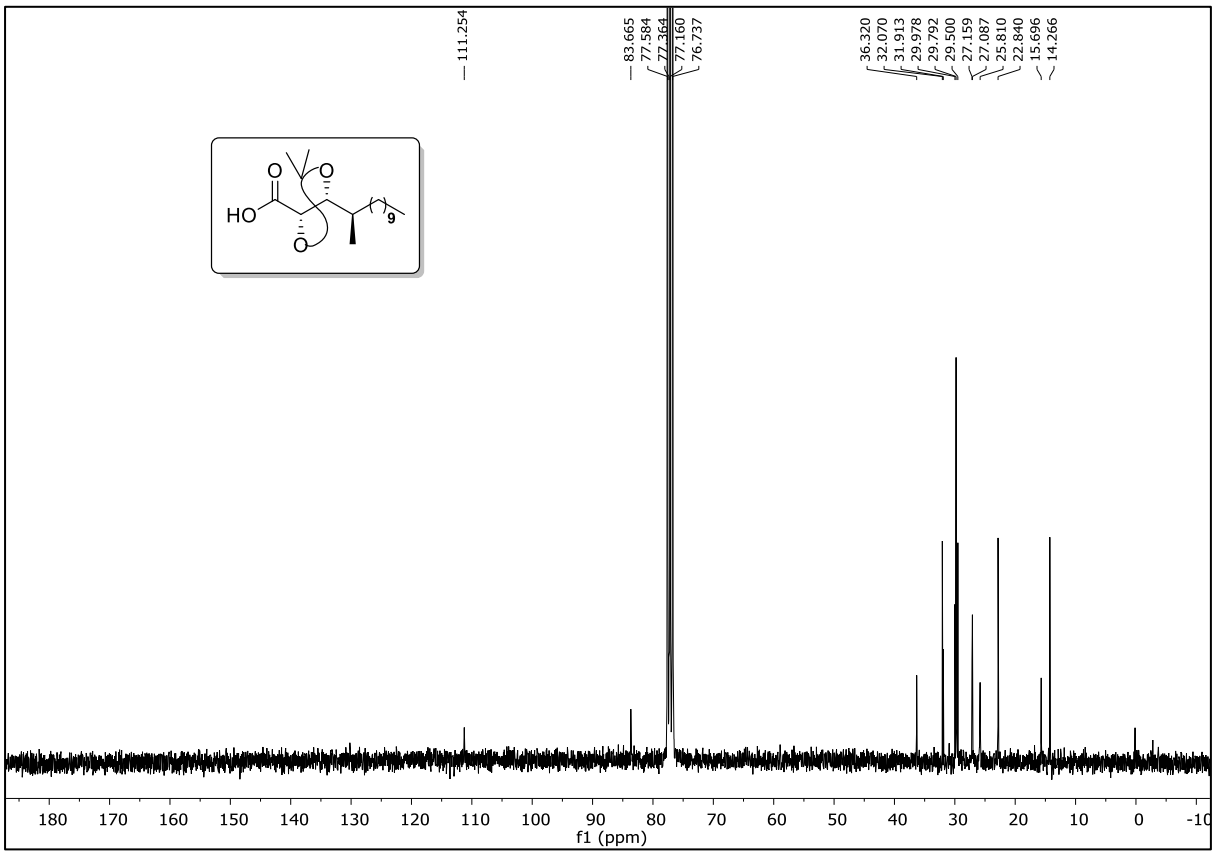
^{13}C-NMR spectrum of compound 13 (75 MHz, $CDCl_3$):



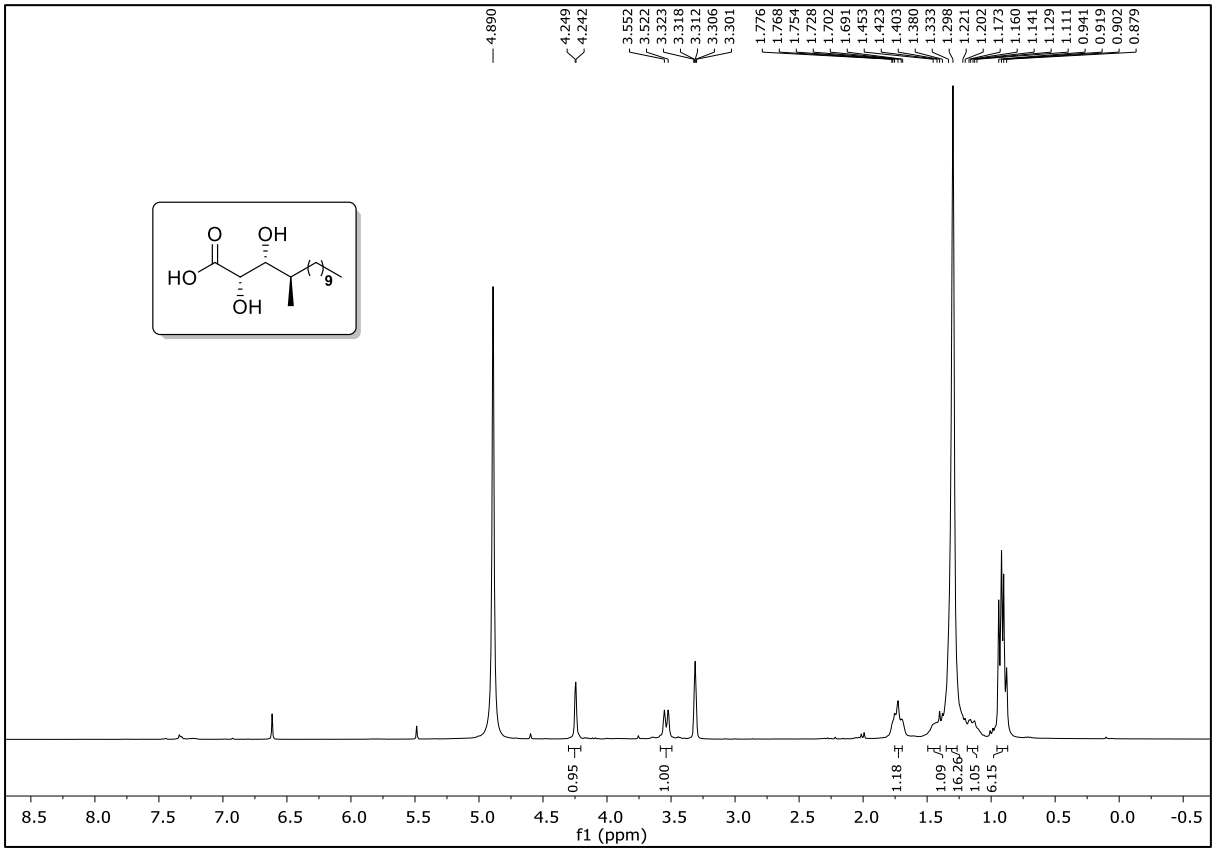
^{1}H-NMR spectrum of compound 14 (300 MHz, $CDCl_3$):



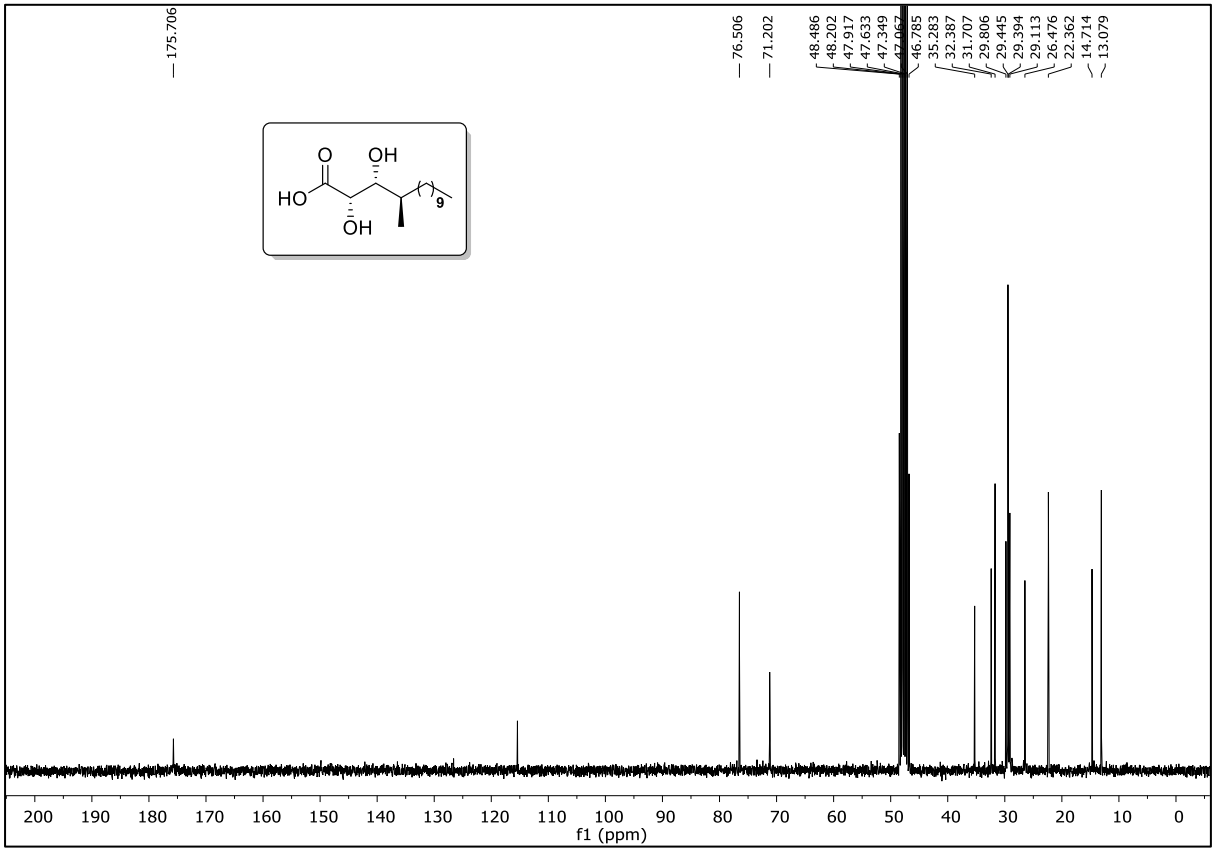
^{13}C-NMR spectrum of compound 14 (75 MHz, $CDCl_3$):



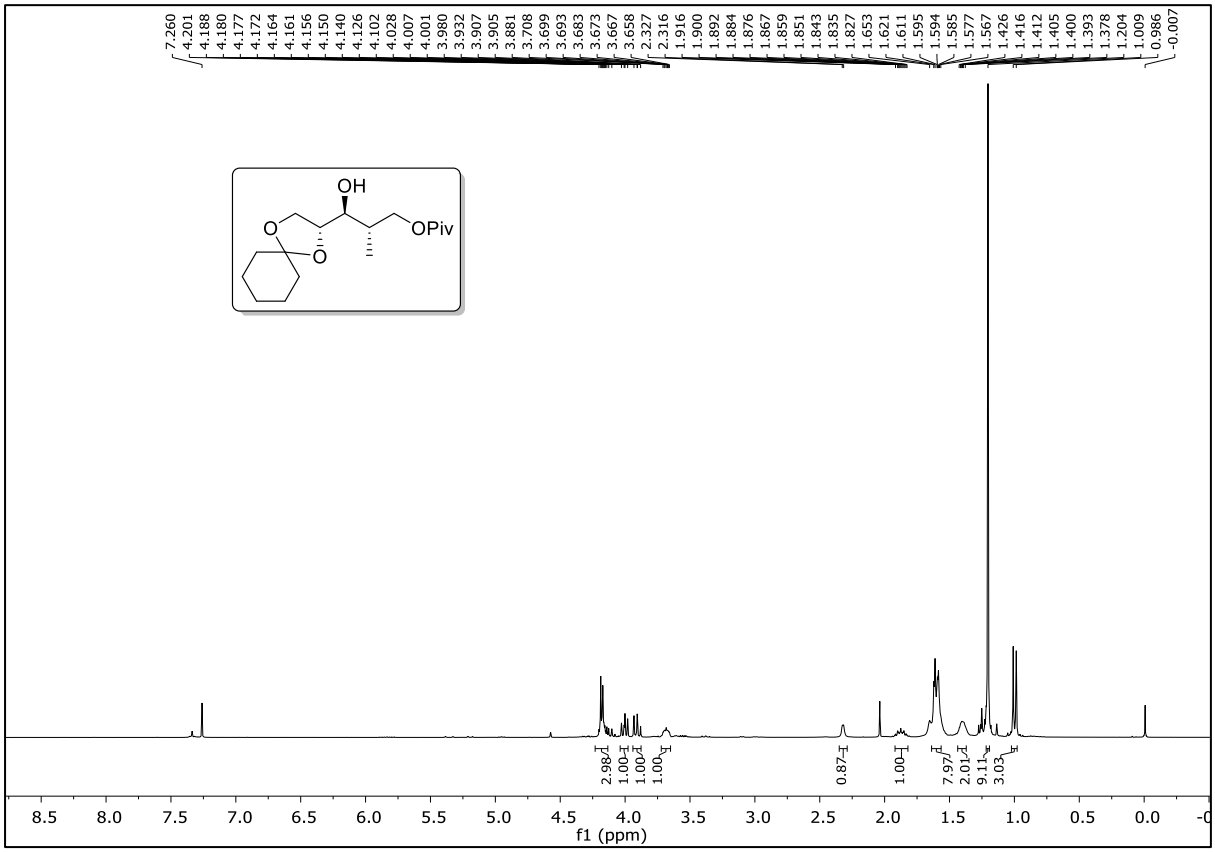
^{1}H-NMR spectrum of compound 7a (300 MHz, CD_3OD):



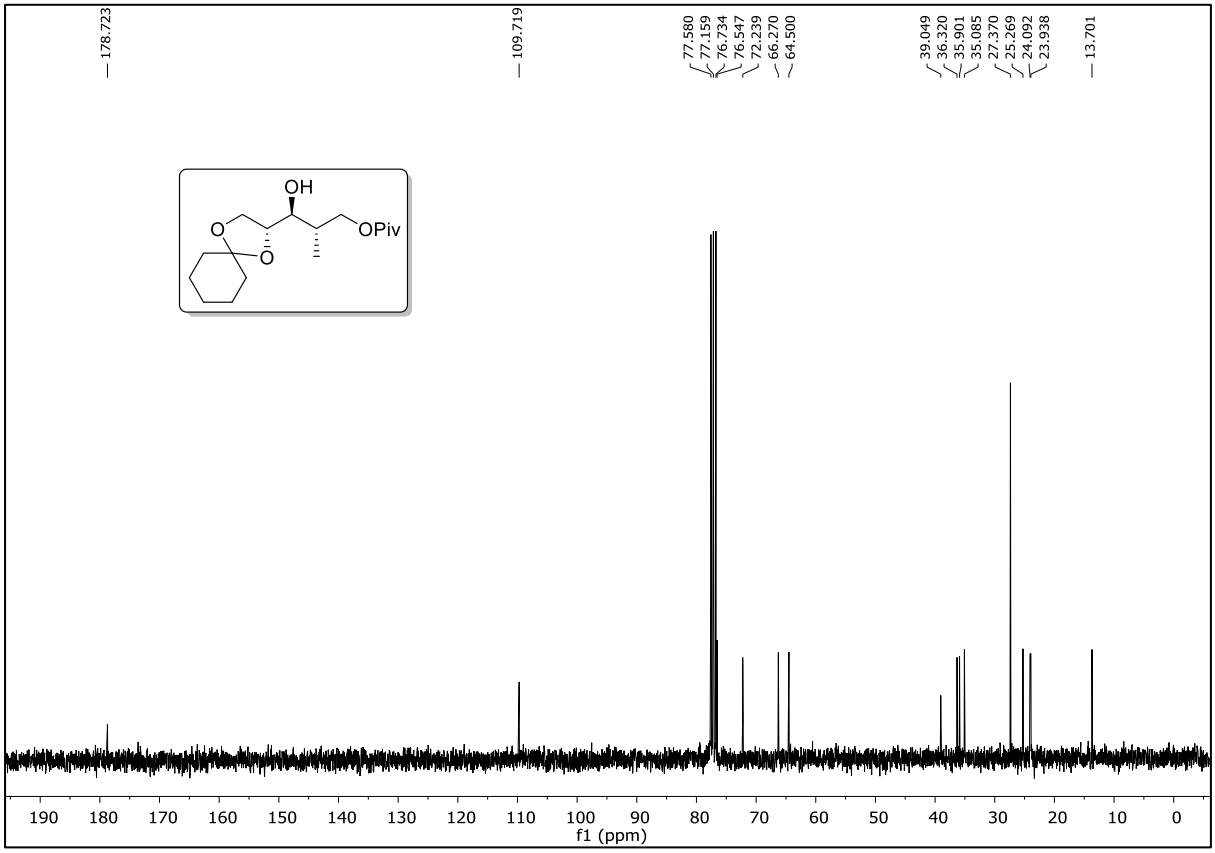
^{13}C-NMR spectrum of compound 7a (75 MHz, CD_3OD):



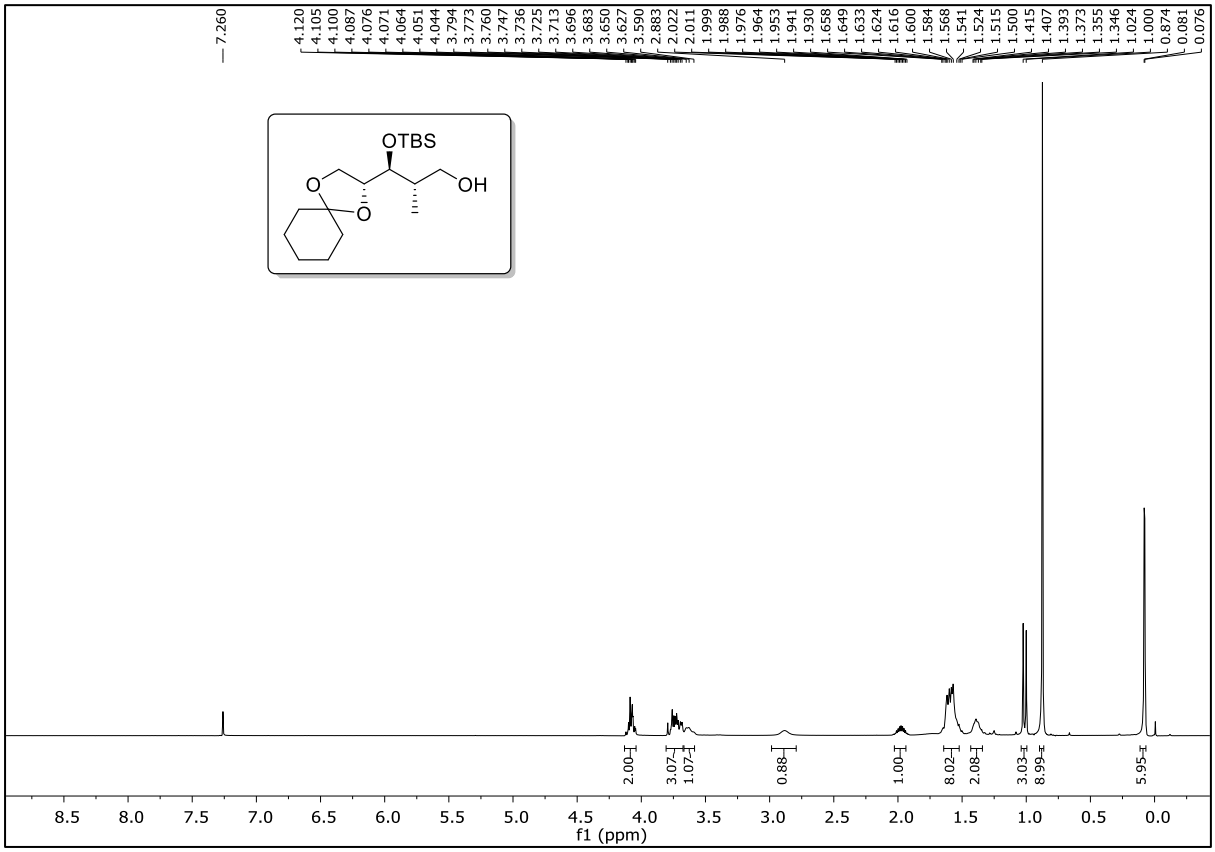
^{1}H-NMR spectrum of compound 15a (300 MHz, $CDCl_3$):



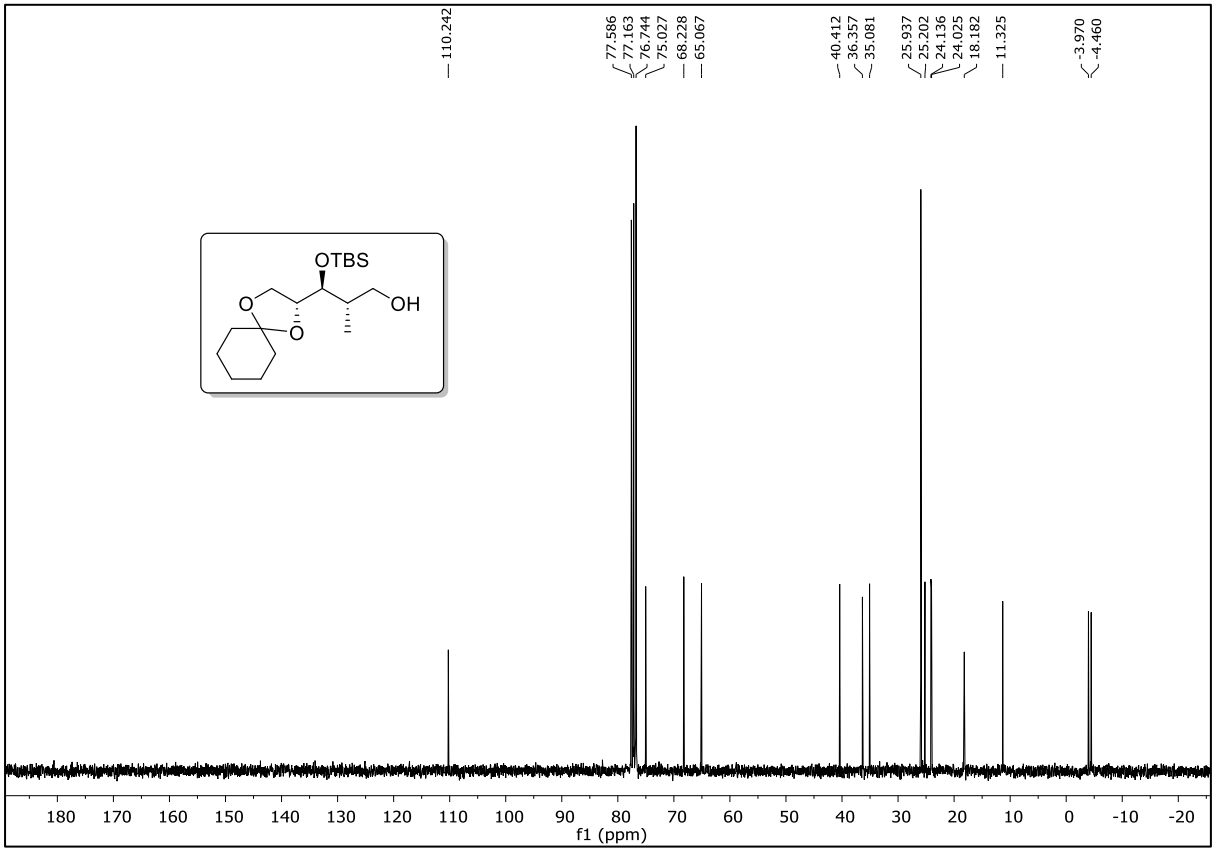
^{13}C-NMR spectrum of compound 15a (75 MHz, $CDCl_3$):



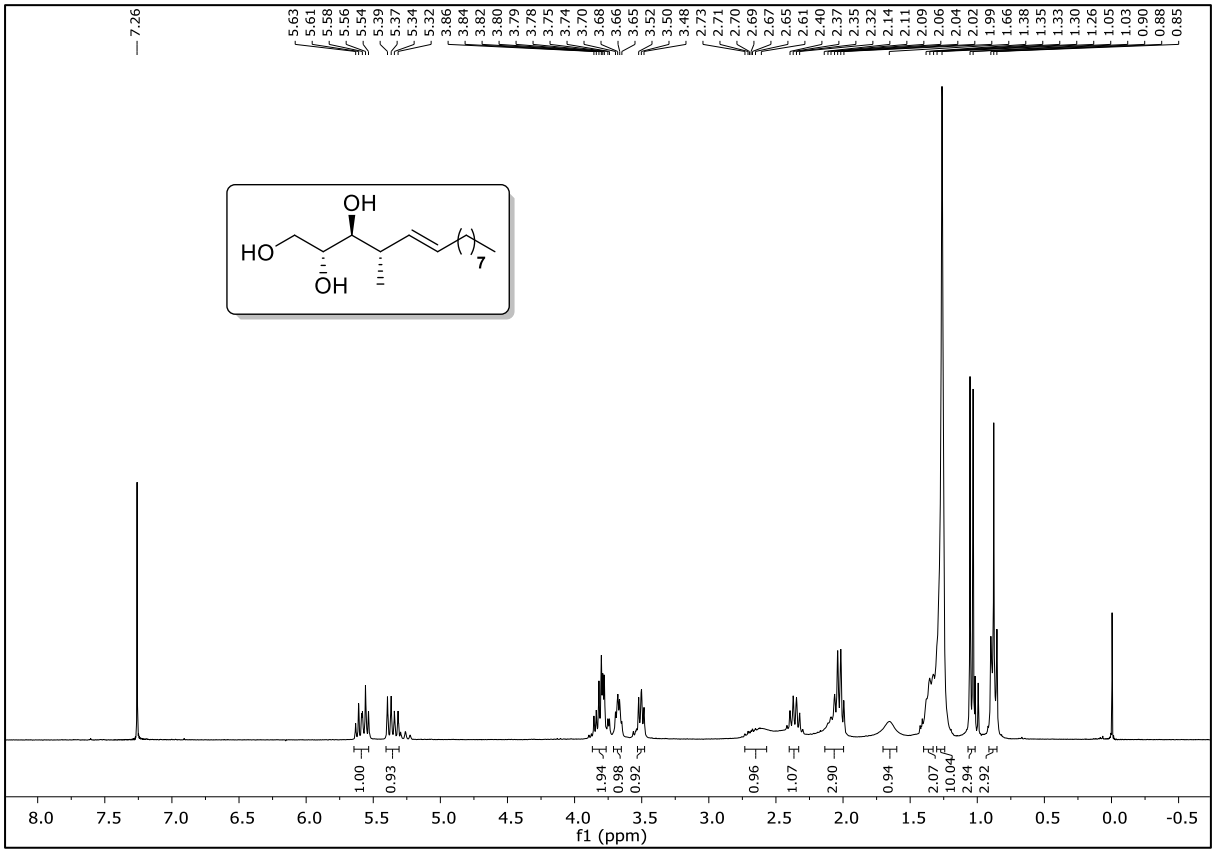
^{1}H-NMR spectrum of compound 15b (300 MHz, $CDCl_3$):



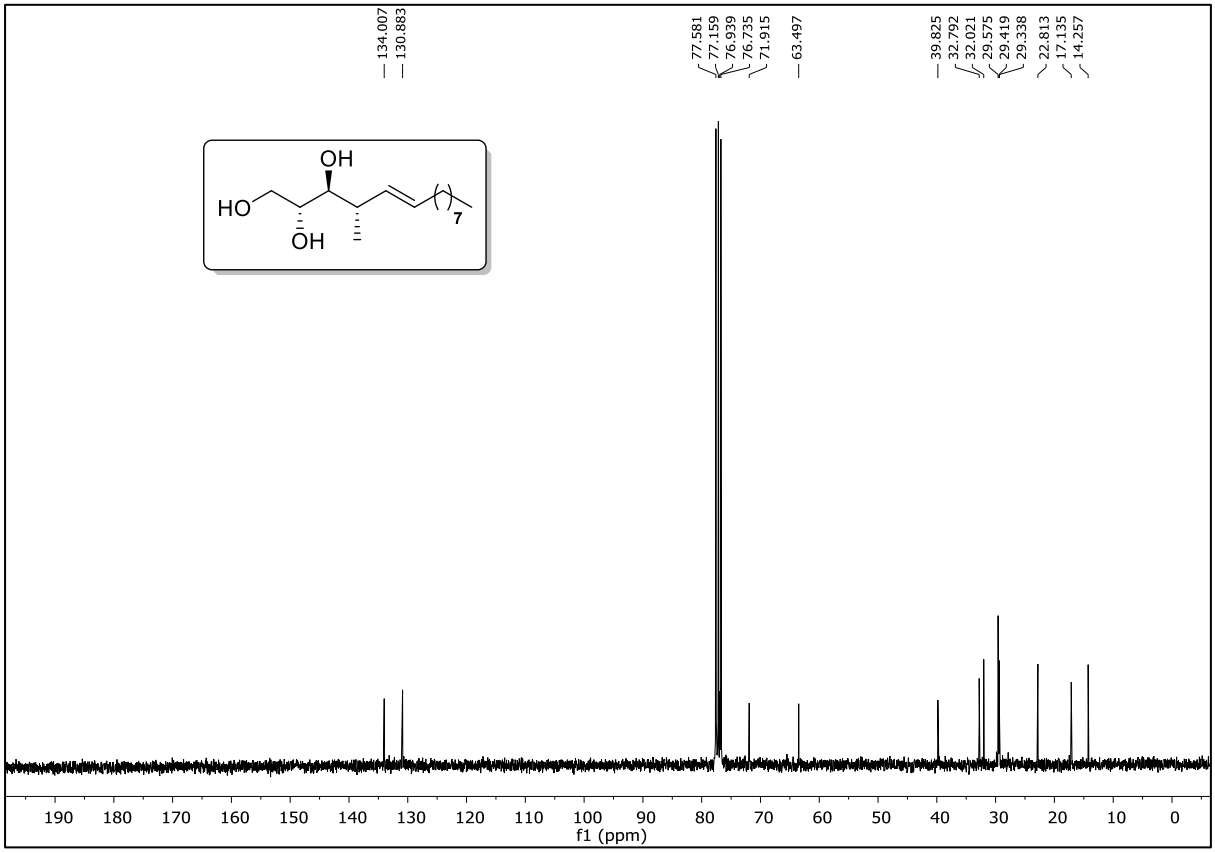
^{13}C-NMR spectrum of compound 15b (75 MHz, $CDCl_3$):



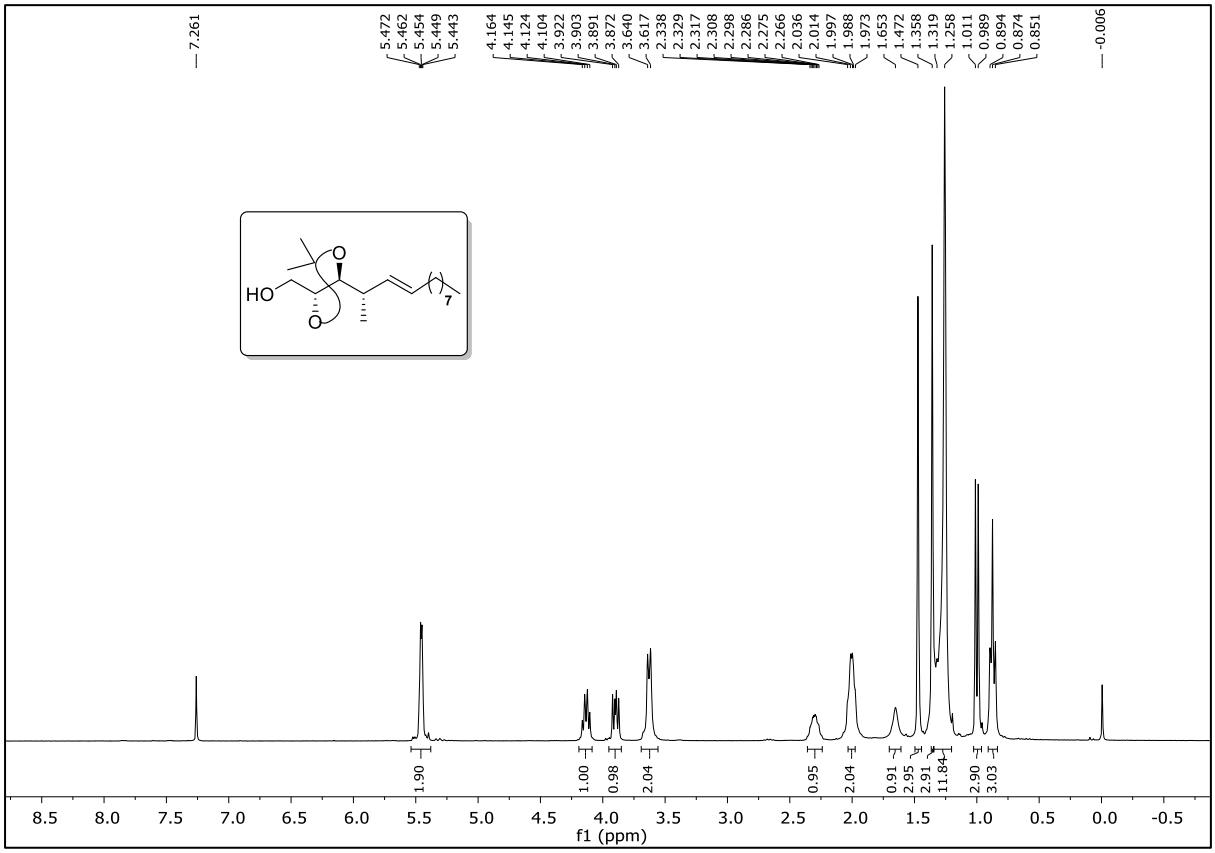
^{1}H-NMR spectrum of compound 15c (300 MHz, $CDCl_3$):



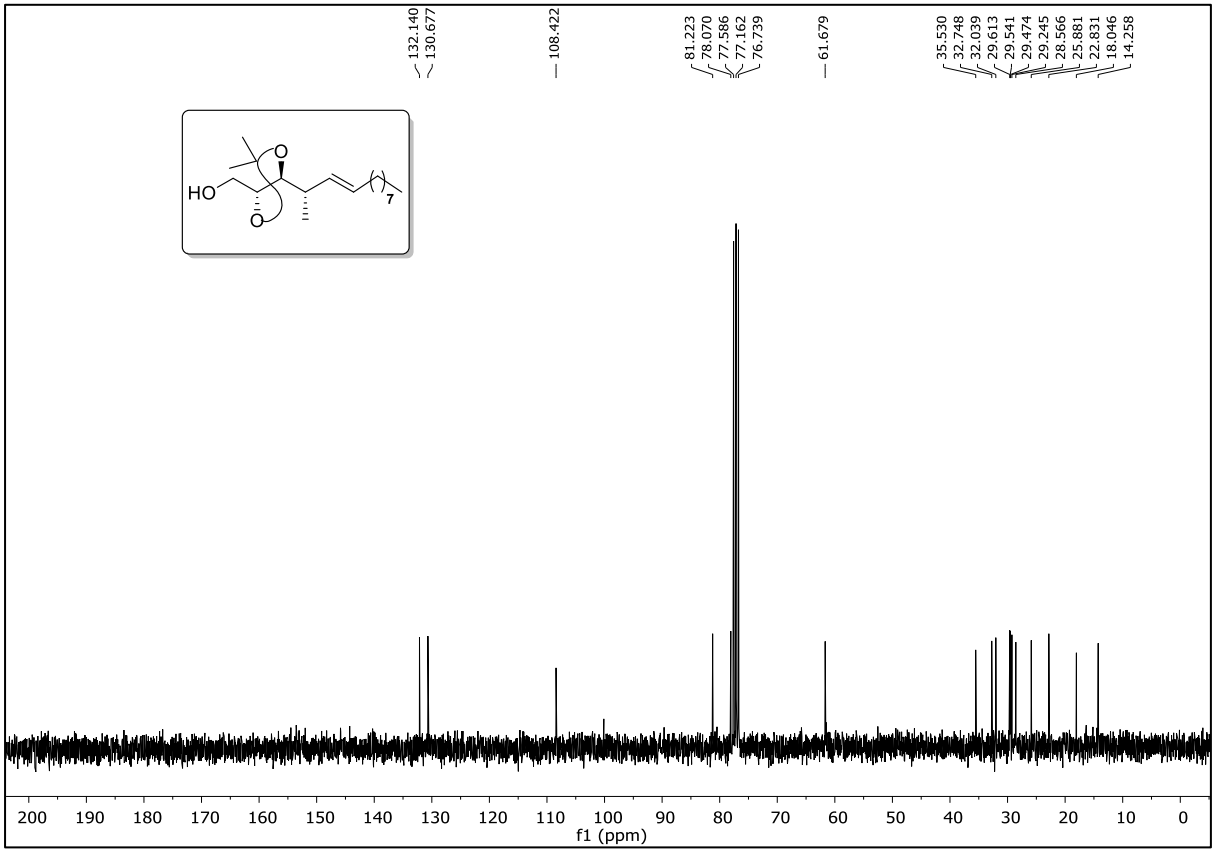
^{13}C-NMR spectrum of compound 15c (75 MHz, $CDCl_3$):



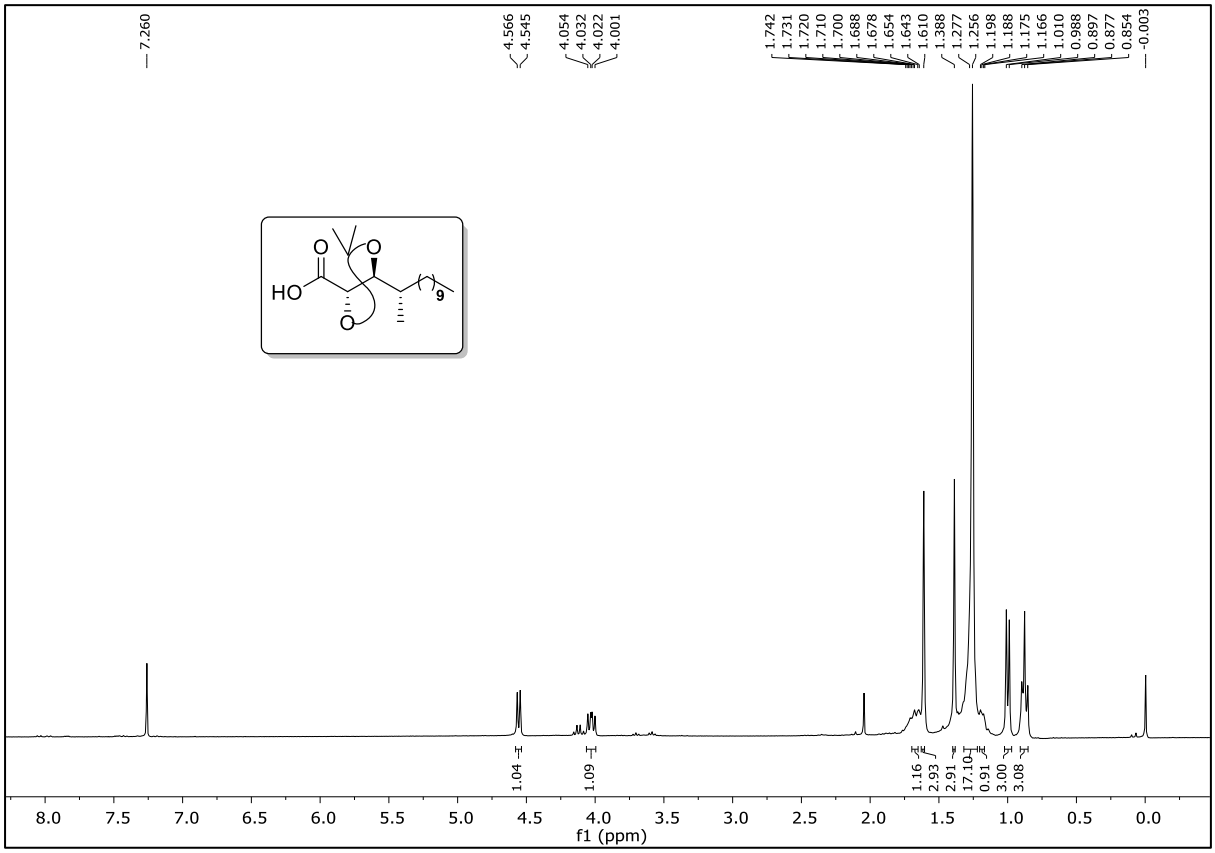
^{1}H-NMR spectrum of compound 15d (300 MHz, $CDCl_3$):



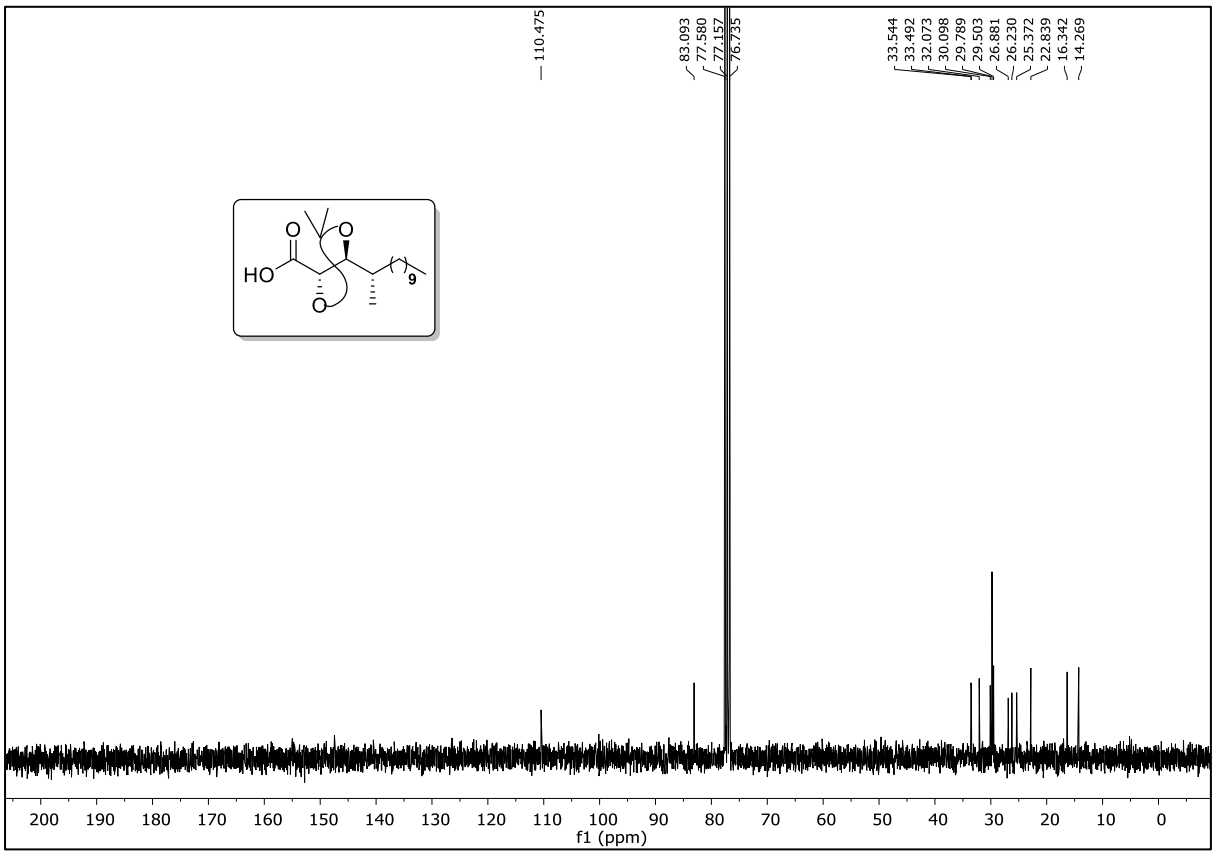
^{13}C-NMR spectrum of compound 15d (75 MHz, $CDCl_3$):



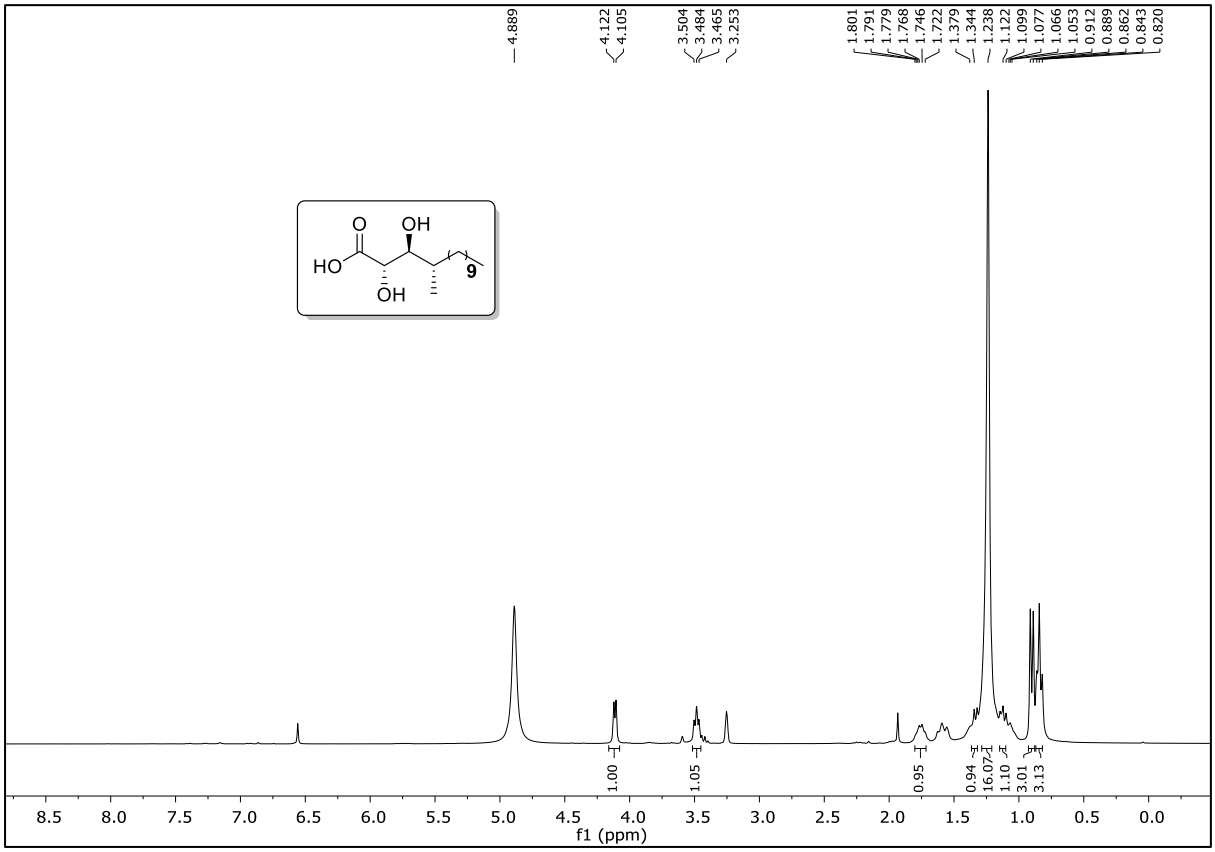
^{1}H-NMR spectrum of compound 15e (300 MHz, $CDCl_3$):



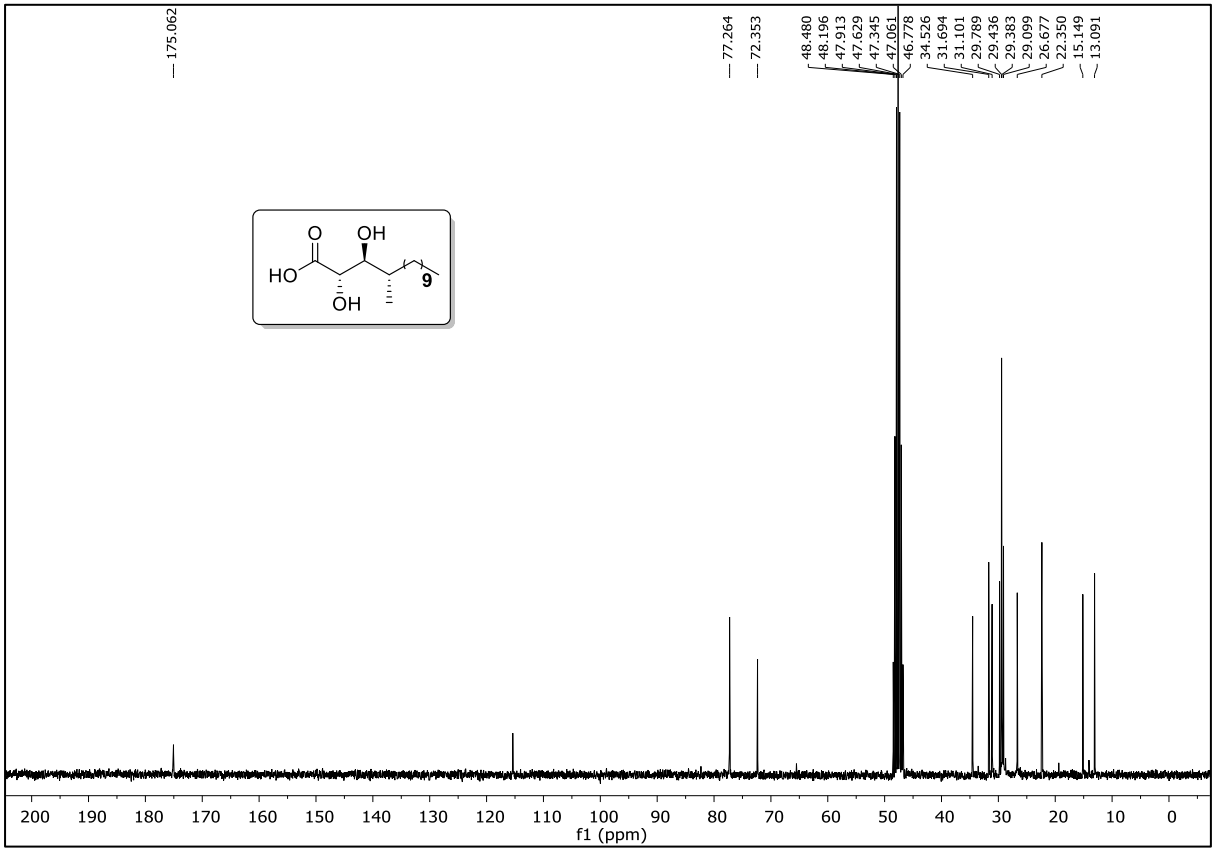
^{13}C-NMR spectrum of compound 15e (75 MHz, $CDCl_3$):



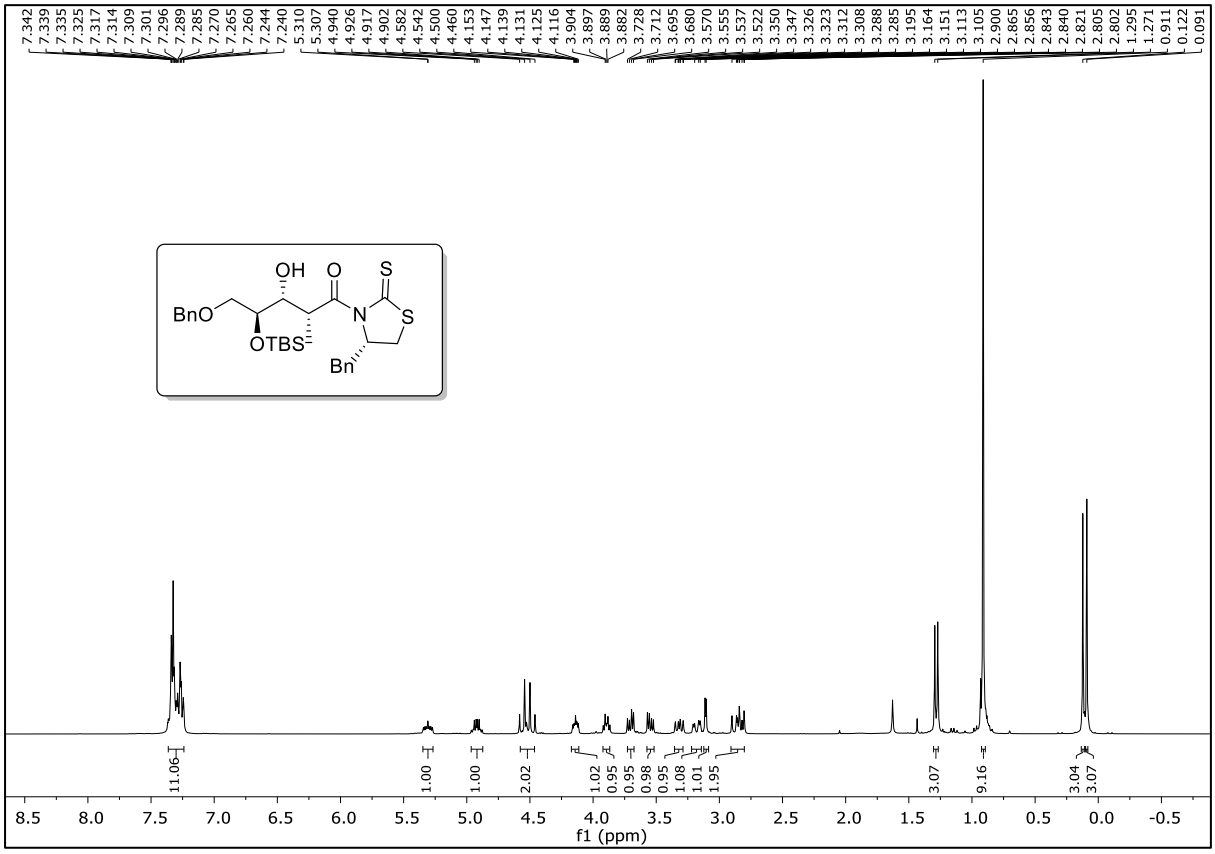
^{1}H-NMR spectrum of compound 7b (300 MHz, CD_3OD):



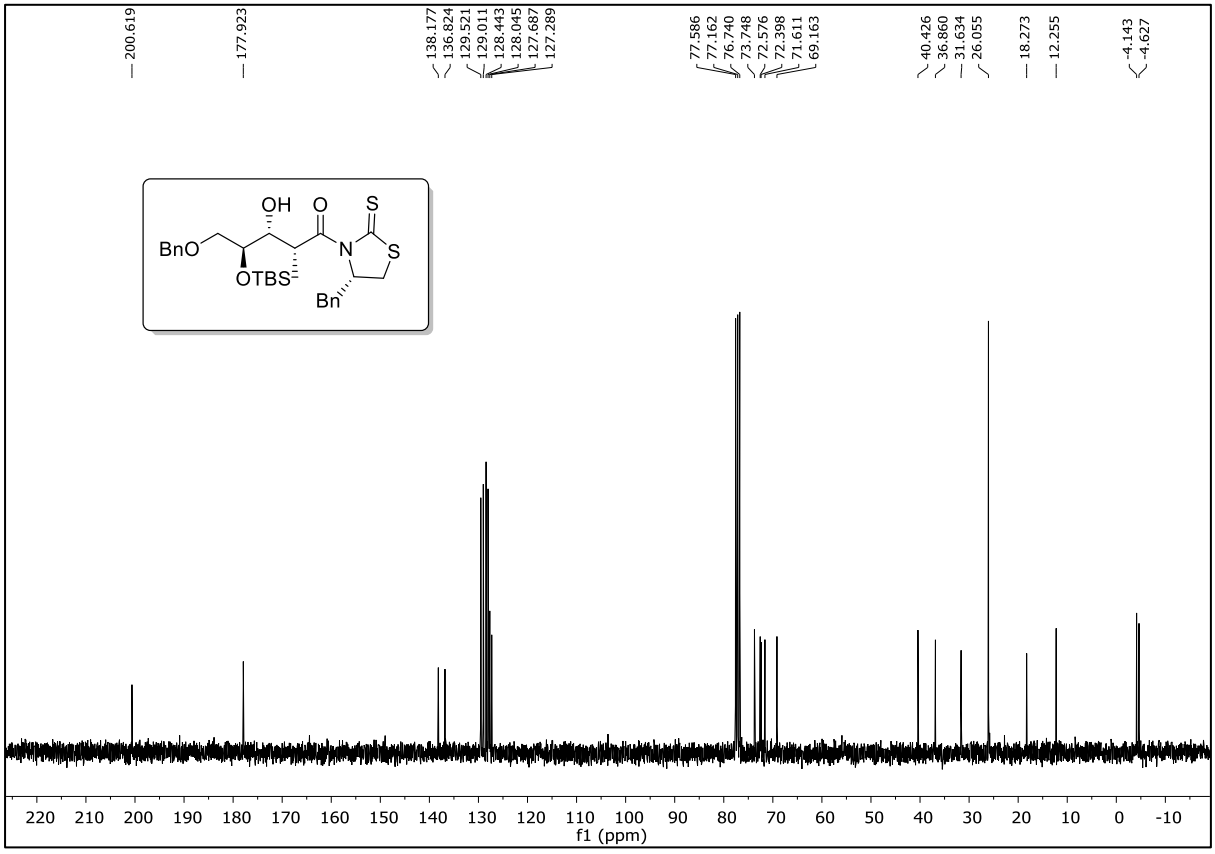
^{13}C-NMR spectrum of compound 7b (75 MHz, CD_3OD):



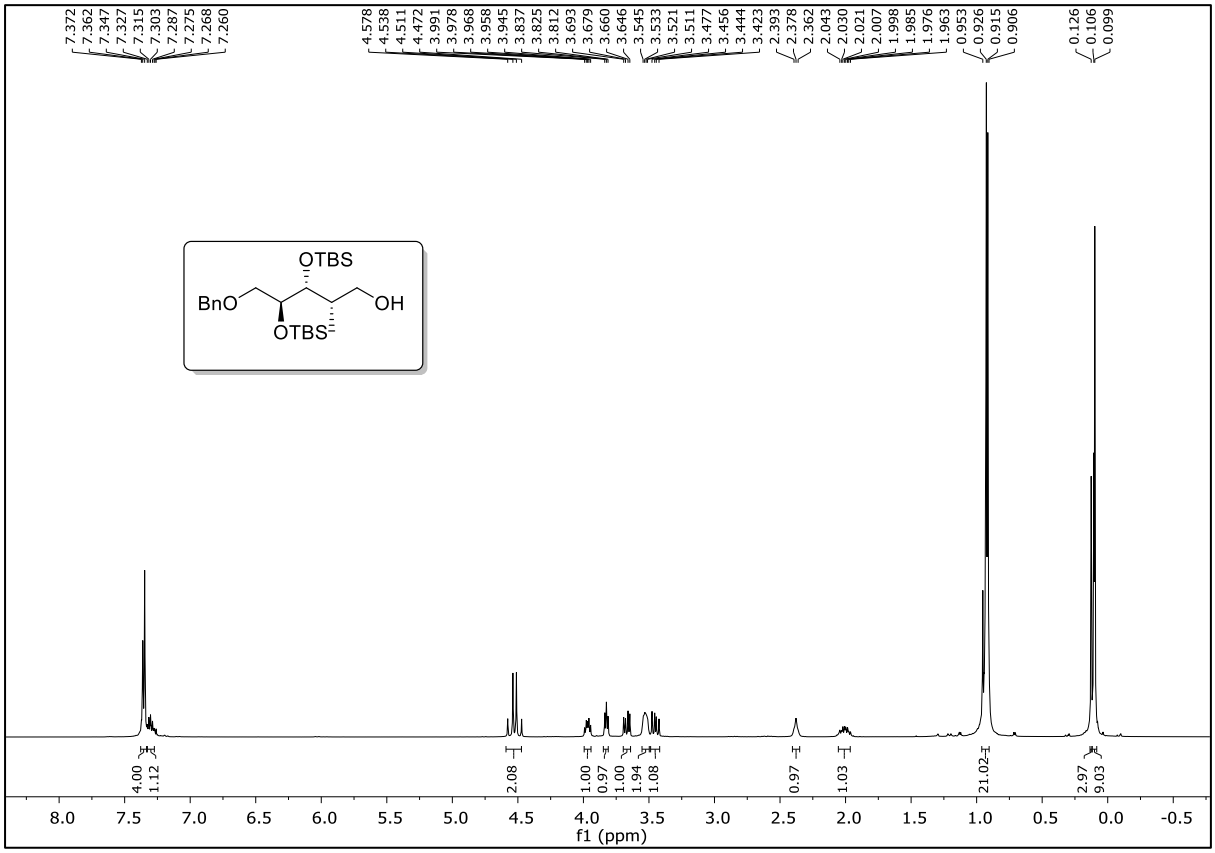
^{1}H-NMR spectrum of compound 18 (300 MHz, $CDCl_3$):



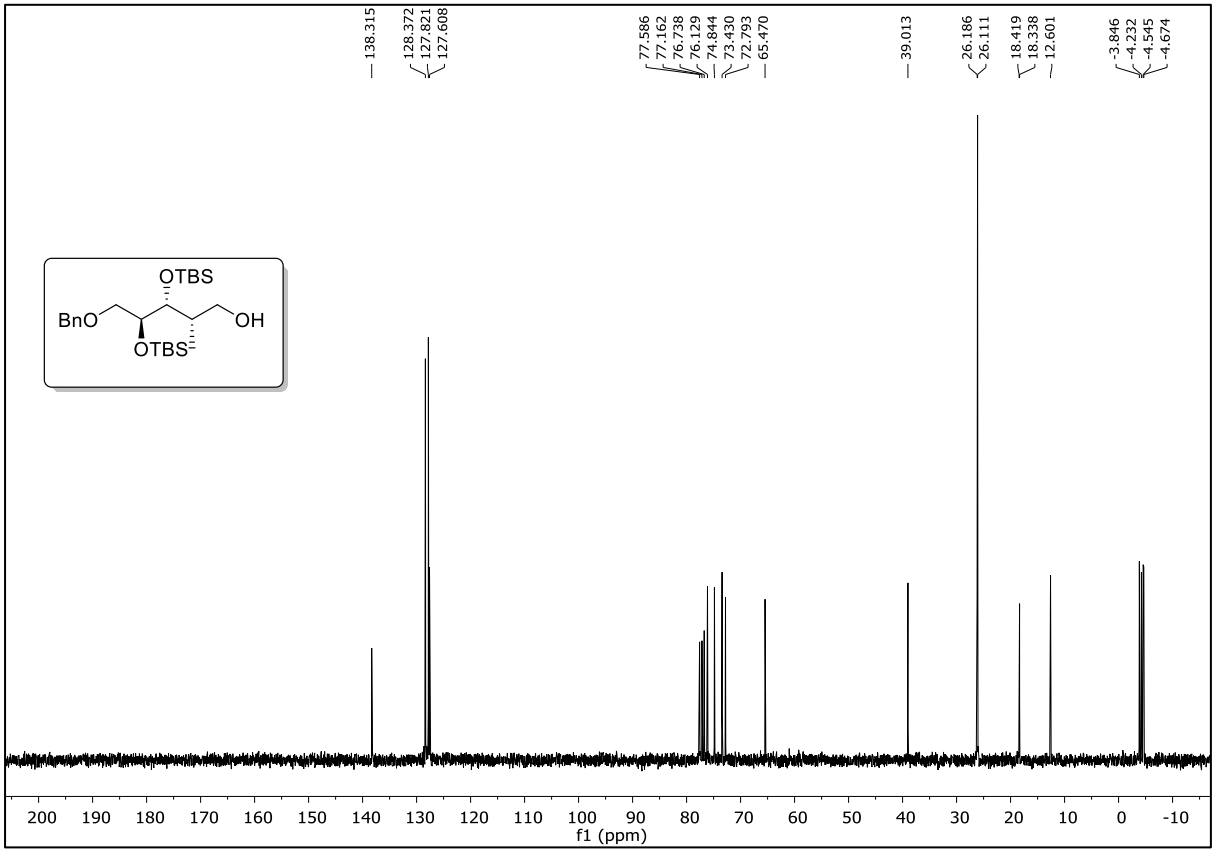
^{13}C-NMR spectrum of compound 18 (75 MHz, $CDCl_3$):



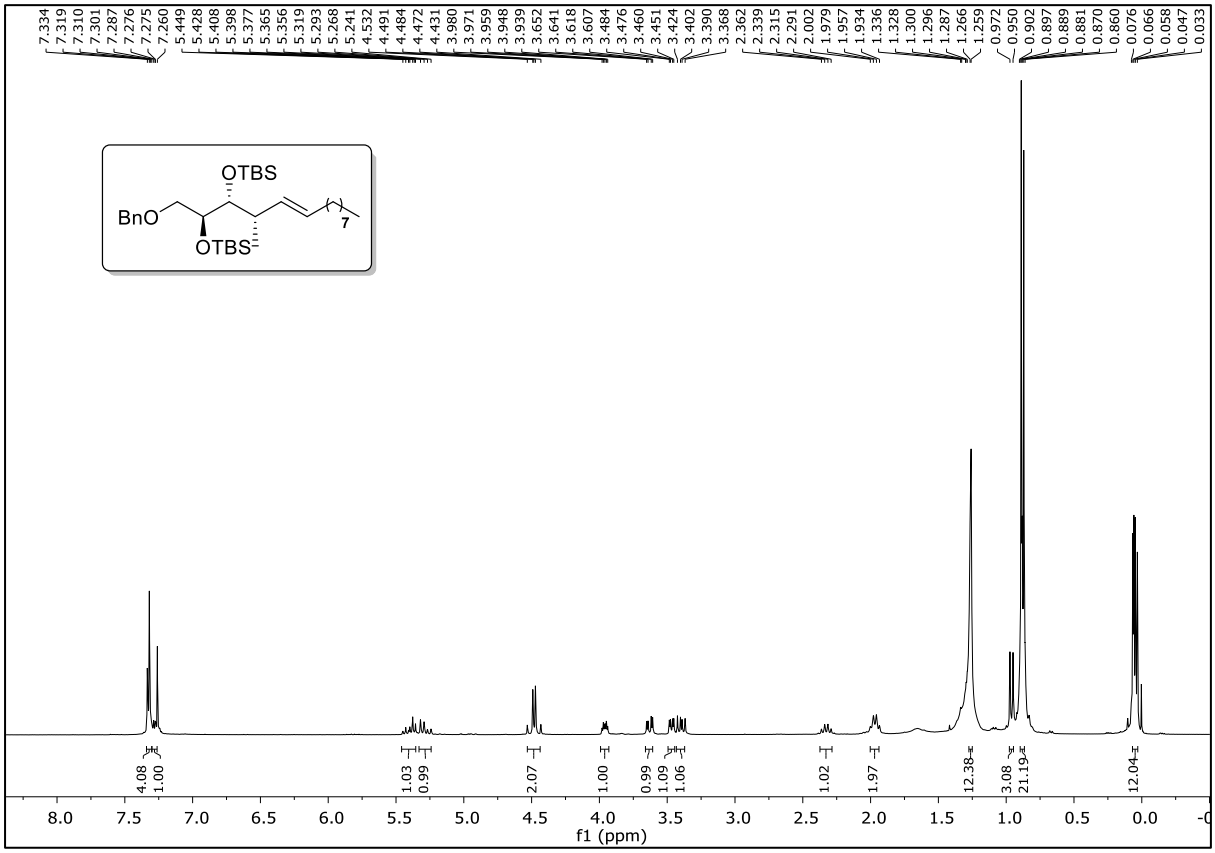
^{1}H-NMR spectrum of compound 19 (300 MHz, $CDCl_3$):



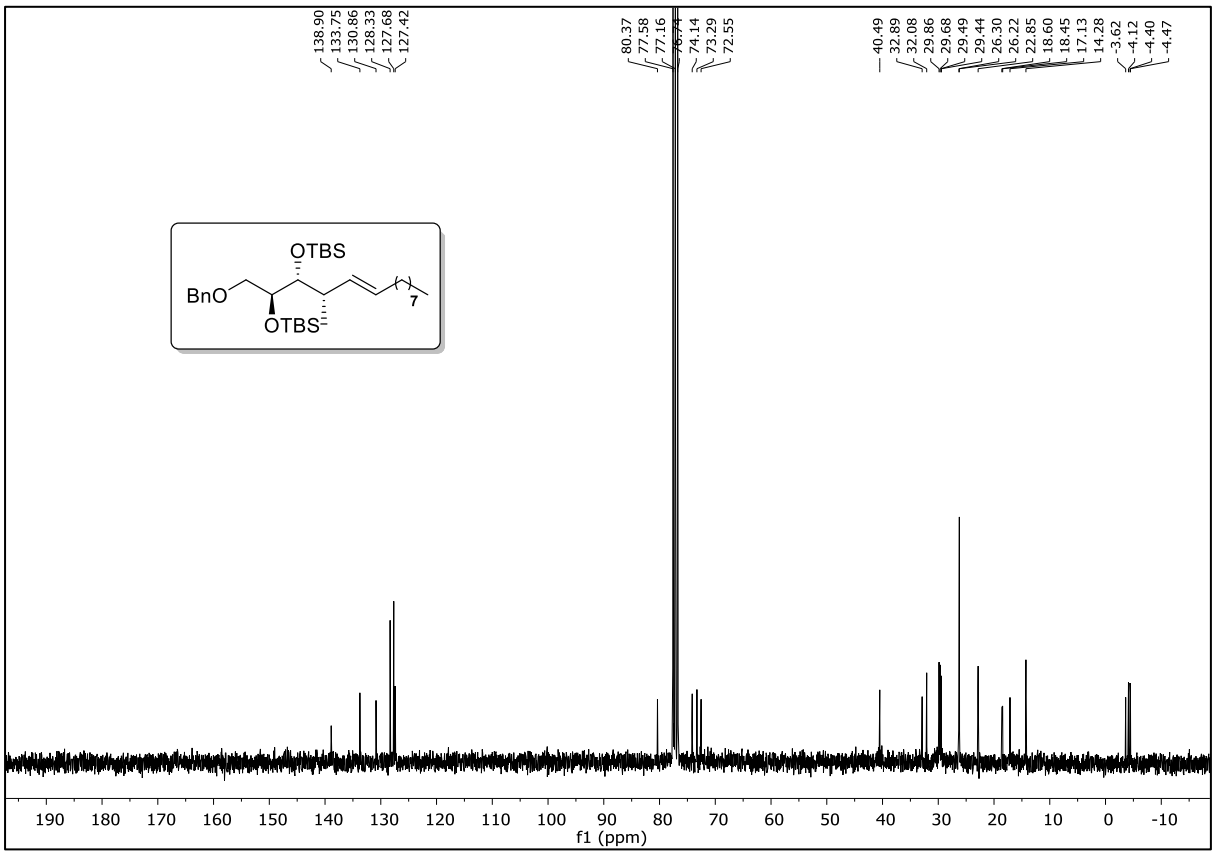
^{13}C-NMR spectrum of compound 19 (75 MHz, $CDCl_3$):



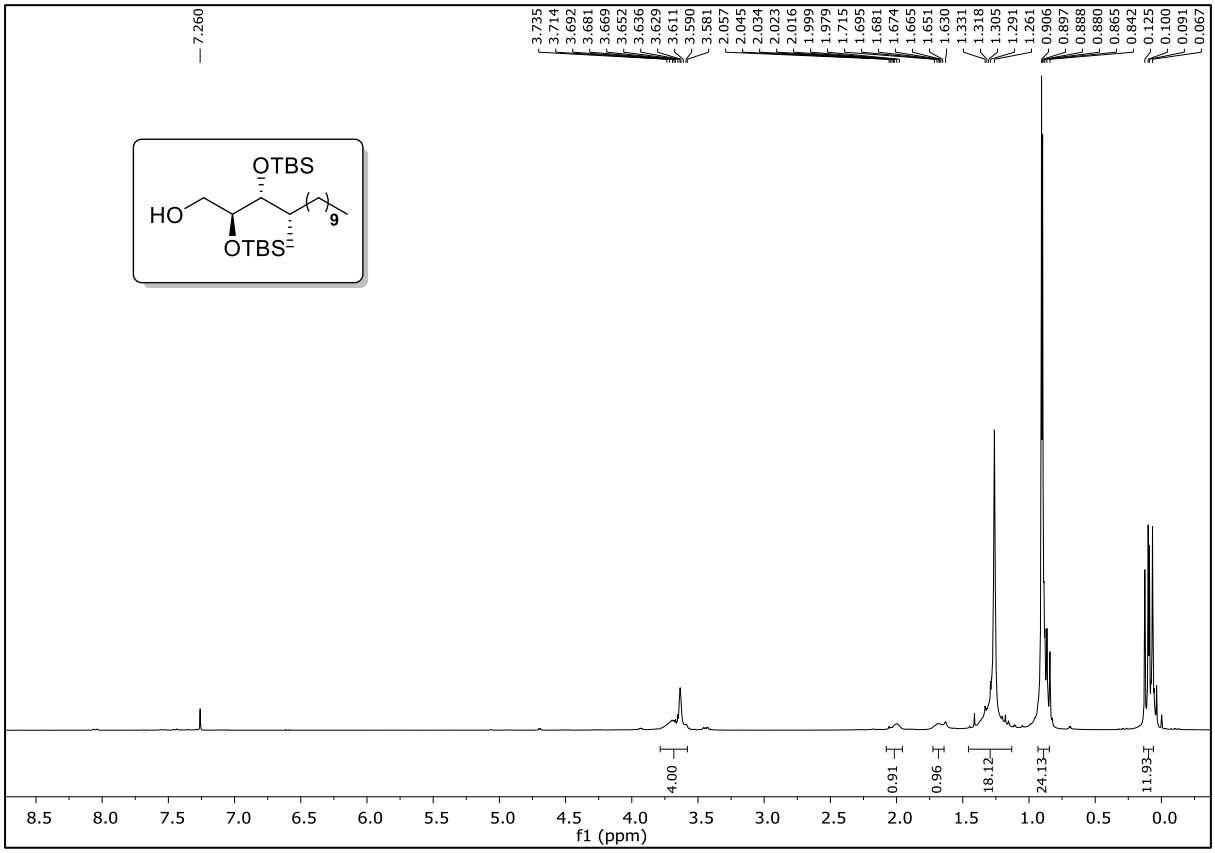
^{1}H-NMR spectrum of intermediate of compound 20 (300 MHz, $CDCl_3$):



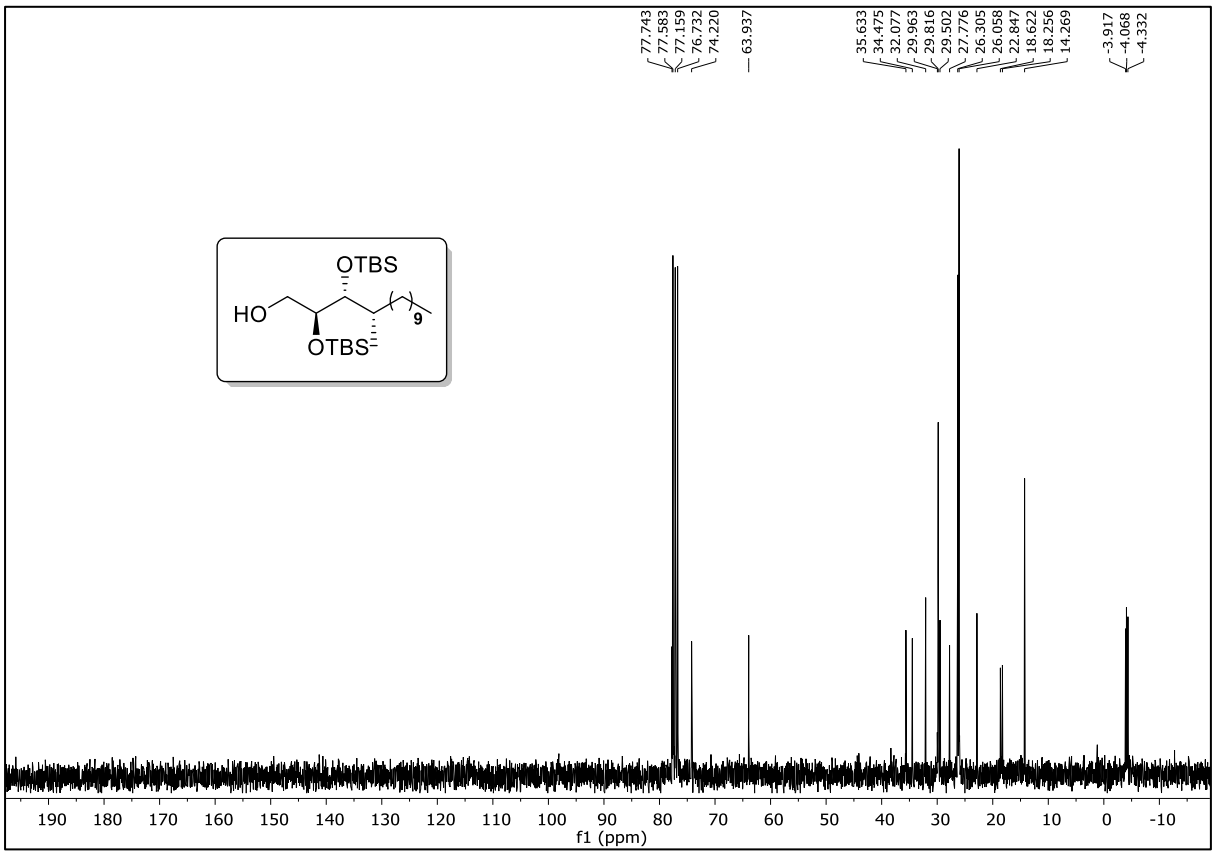
^{13}C-NMR spectrum of intermediate of compound 20 (75 MHz, $CDCl_3$):



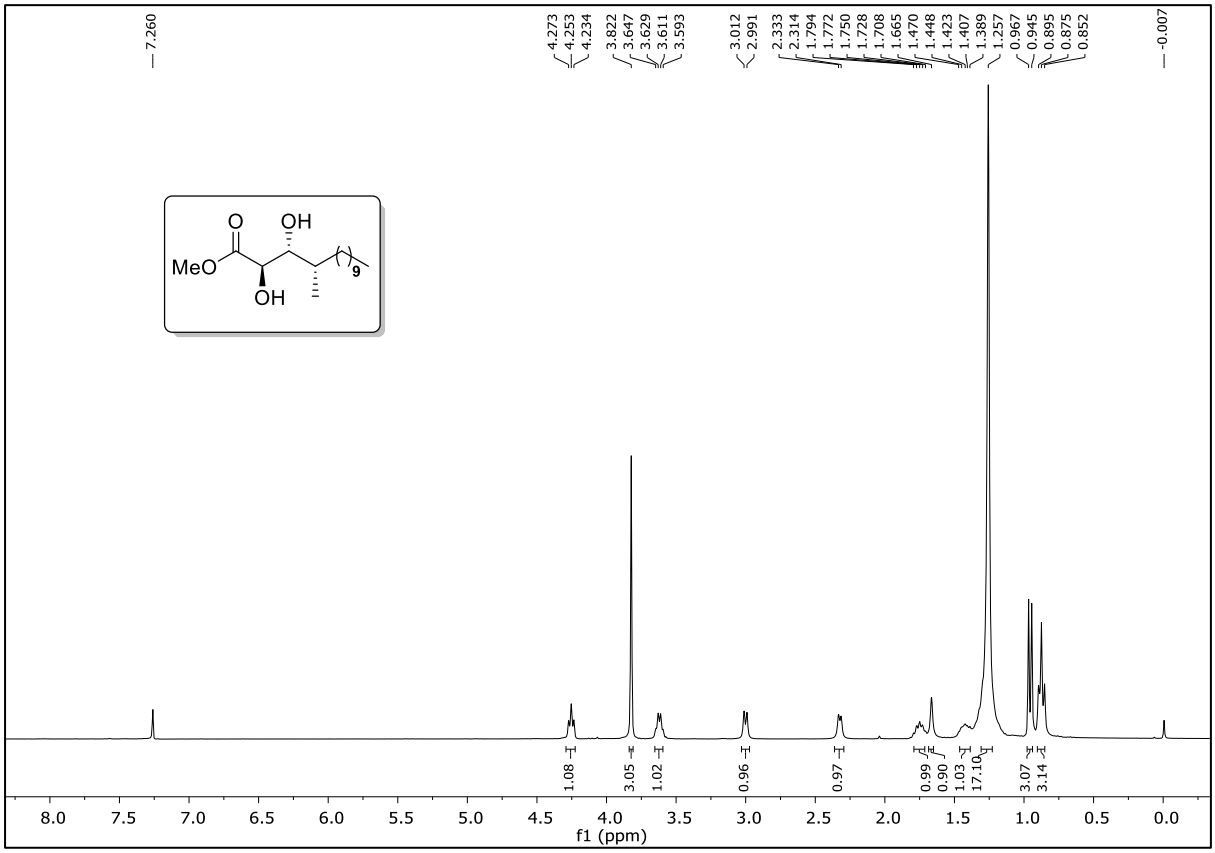
^{1}H-NMR spectrum of compound 20 (300 MHz, $CDCl_3$):



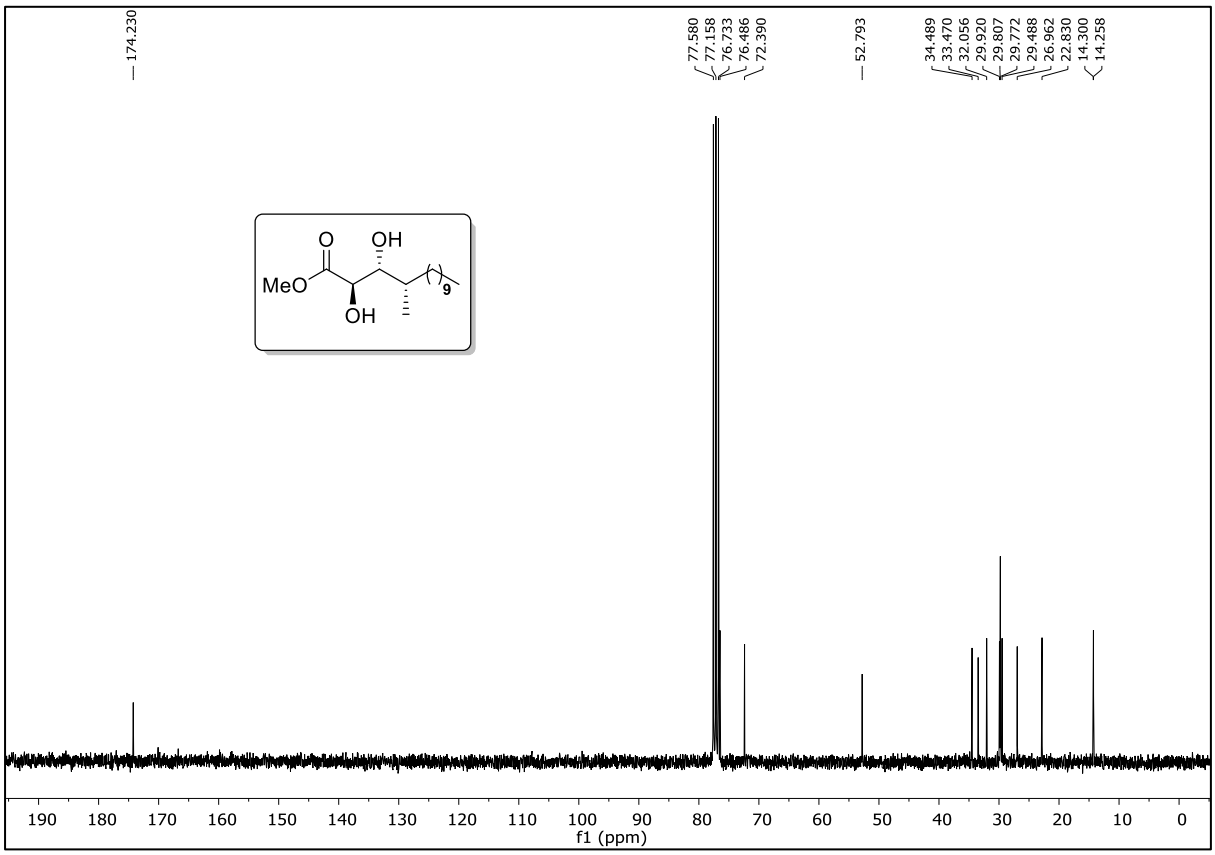
^{13}C-NMR spectrum of compound 20 (75 MHz, $CDCl_3$):



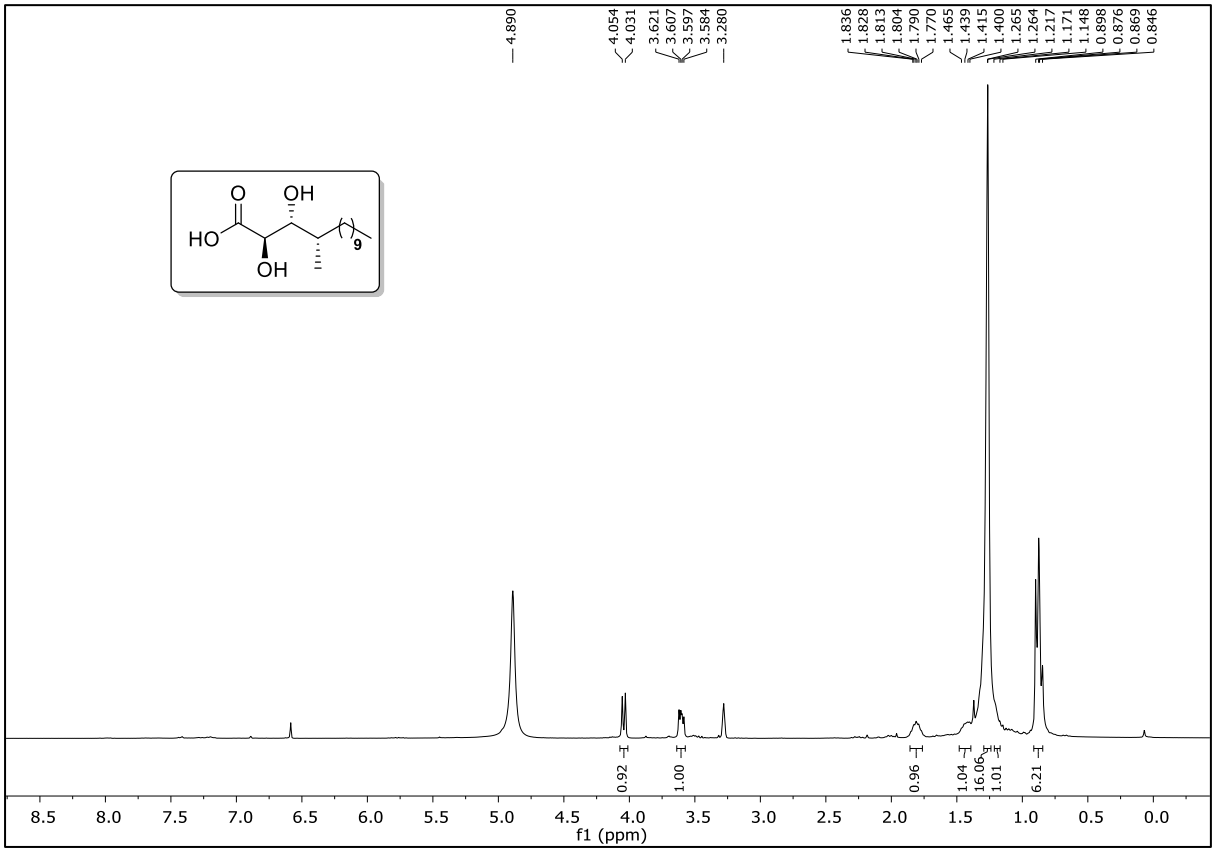
^{1}H-NMR spectrum of compound 21 (300 MHz, $CDCl_3$):



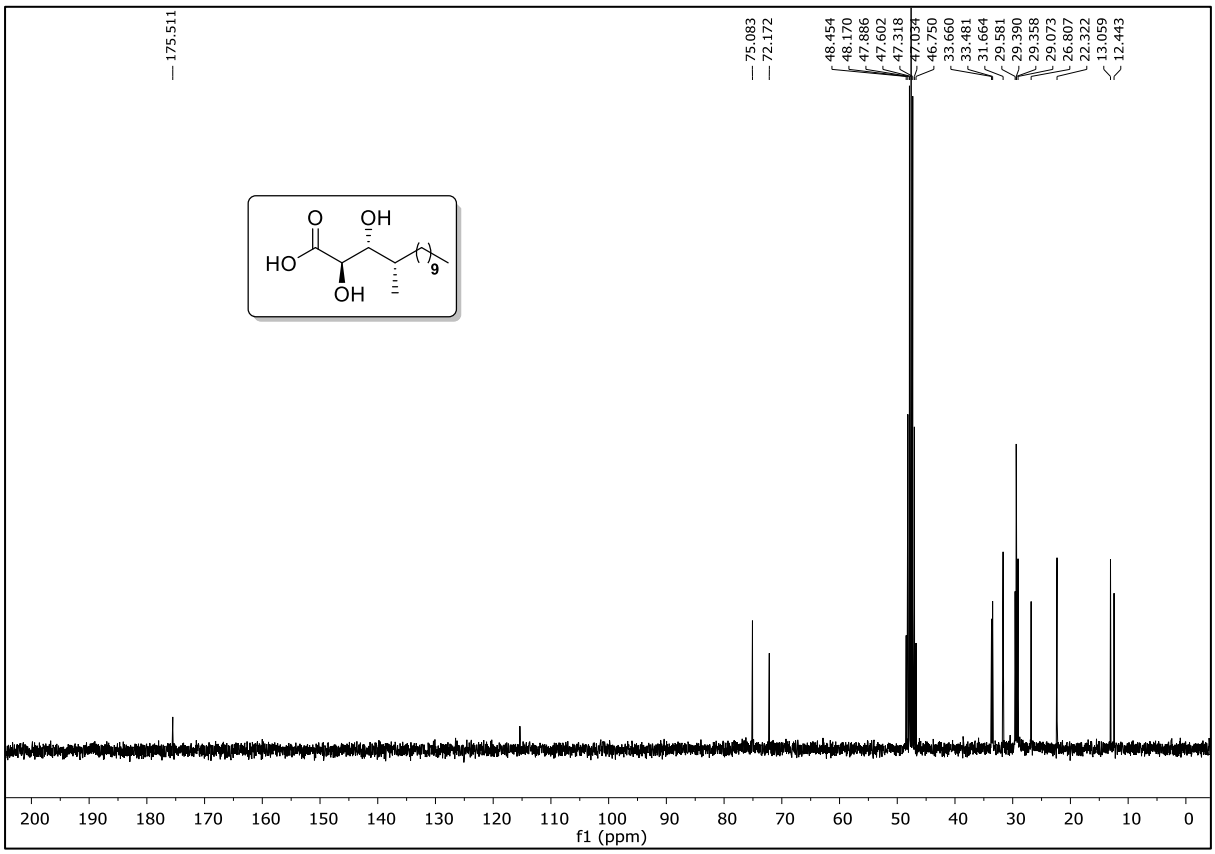
^{13}C-NMR spectrum of compound 21 (75 MHz, $CDCl_3$):



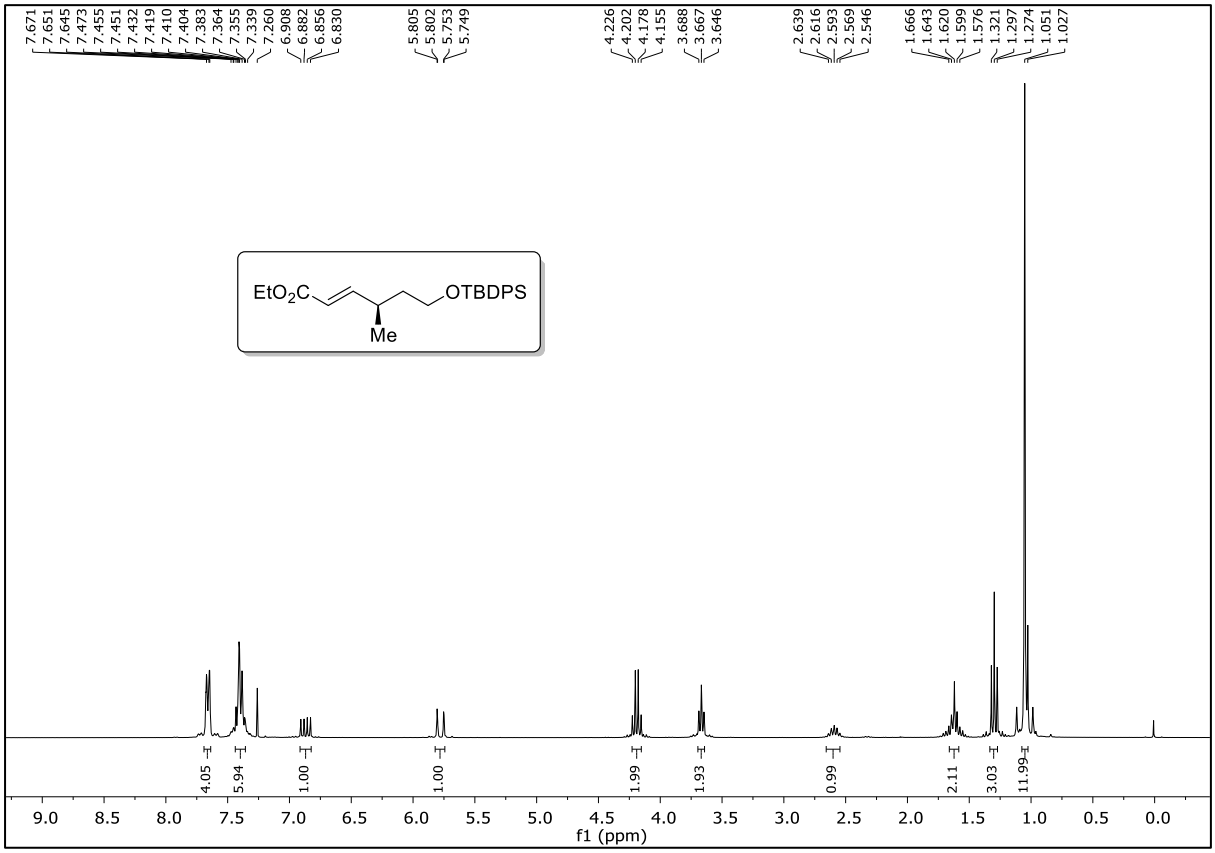
^{1}H-NMR spectrum of compound 7c (300 MHz, CD_3OD):



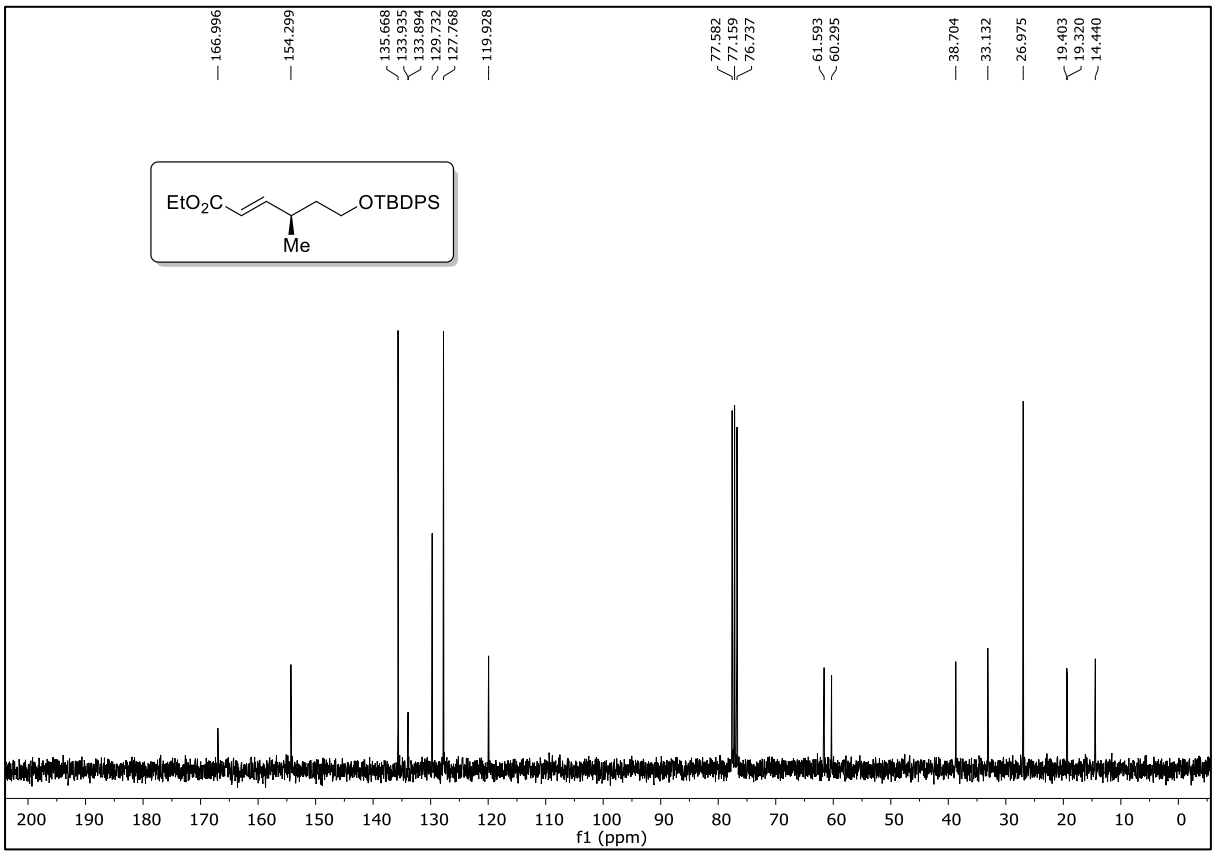
^{13}C-NMR spectrum of compound 7c (75 MHz, CD_3OD):



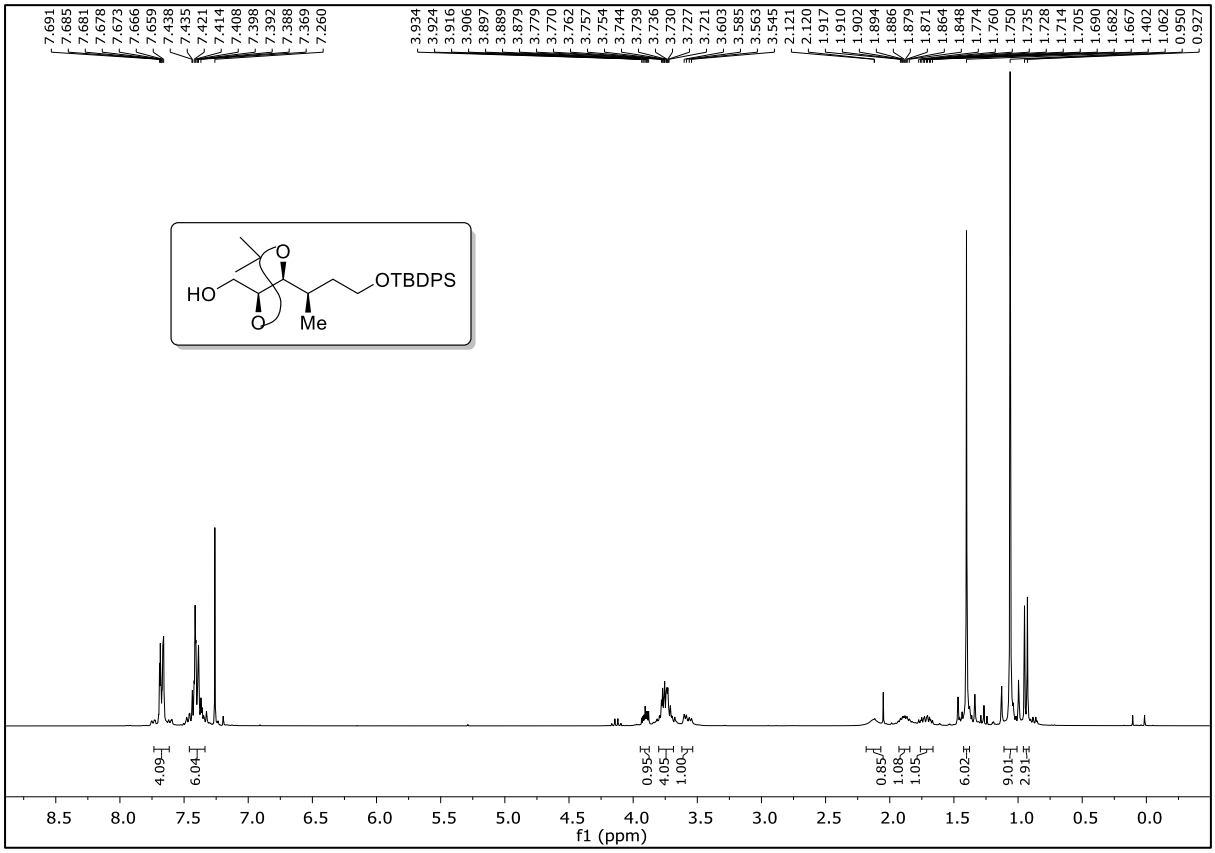
^{1}H-NMR spectrum of compound 23 (300 MHz, $CDCl_3$):



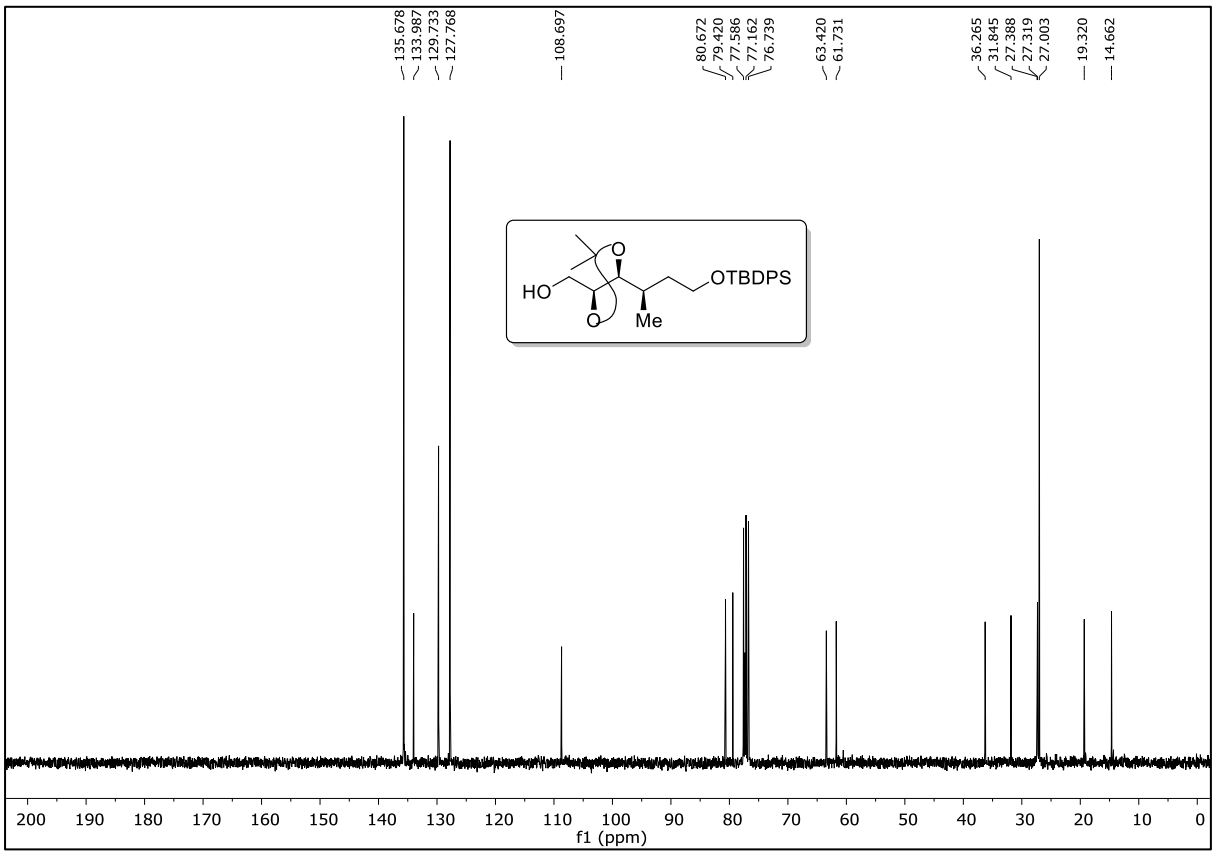
^{13}C-NMR spectrum of compound 23 (75 MHz, $CDCl_3$):



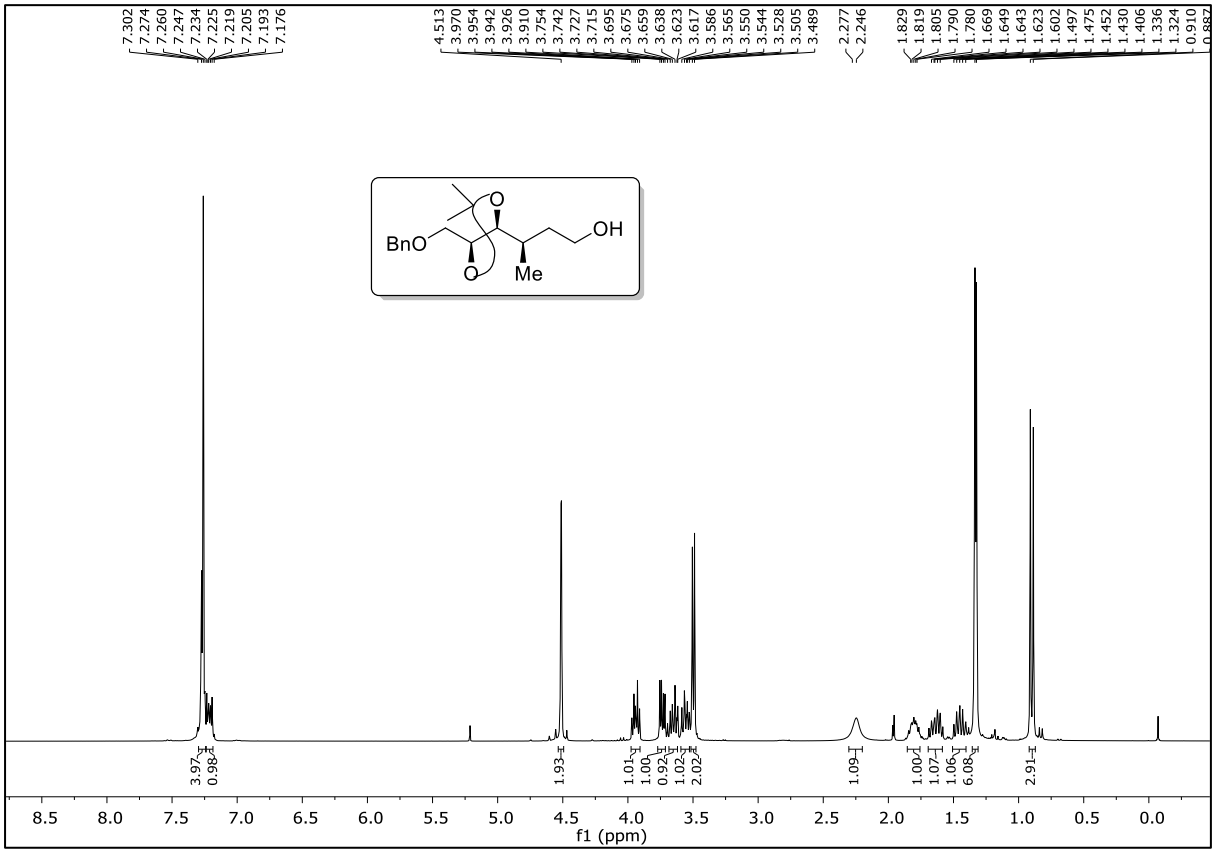
^{1}H-NMR spectrum of compound 24 (300 MHz, $CDCl_3$):



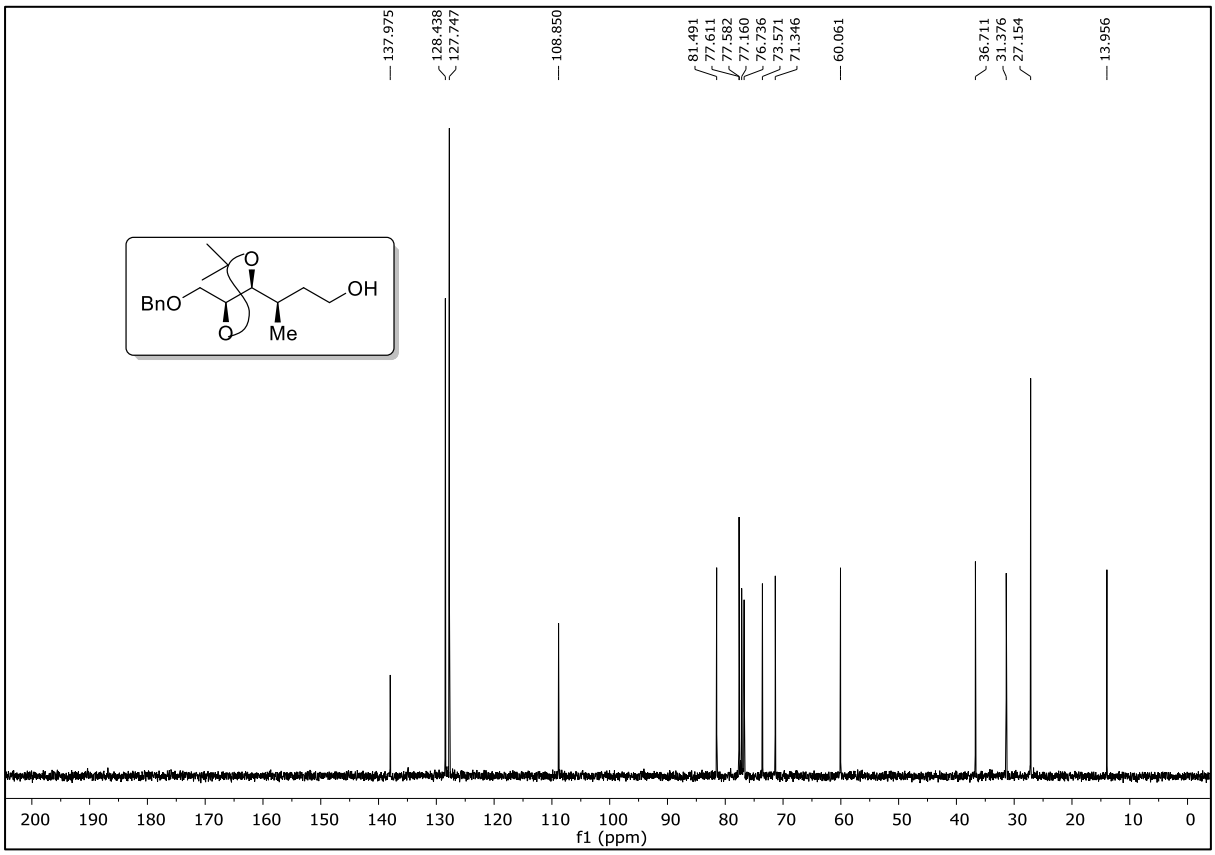
^{13}C-NMR spectrum of compound 24 (75 MHz, $CDCl_3$):



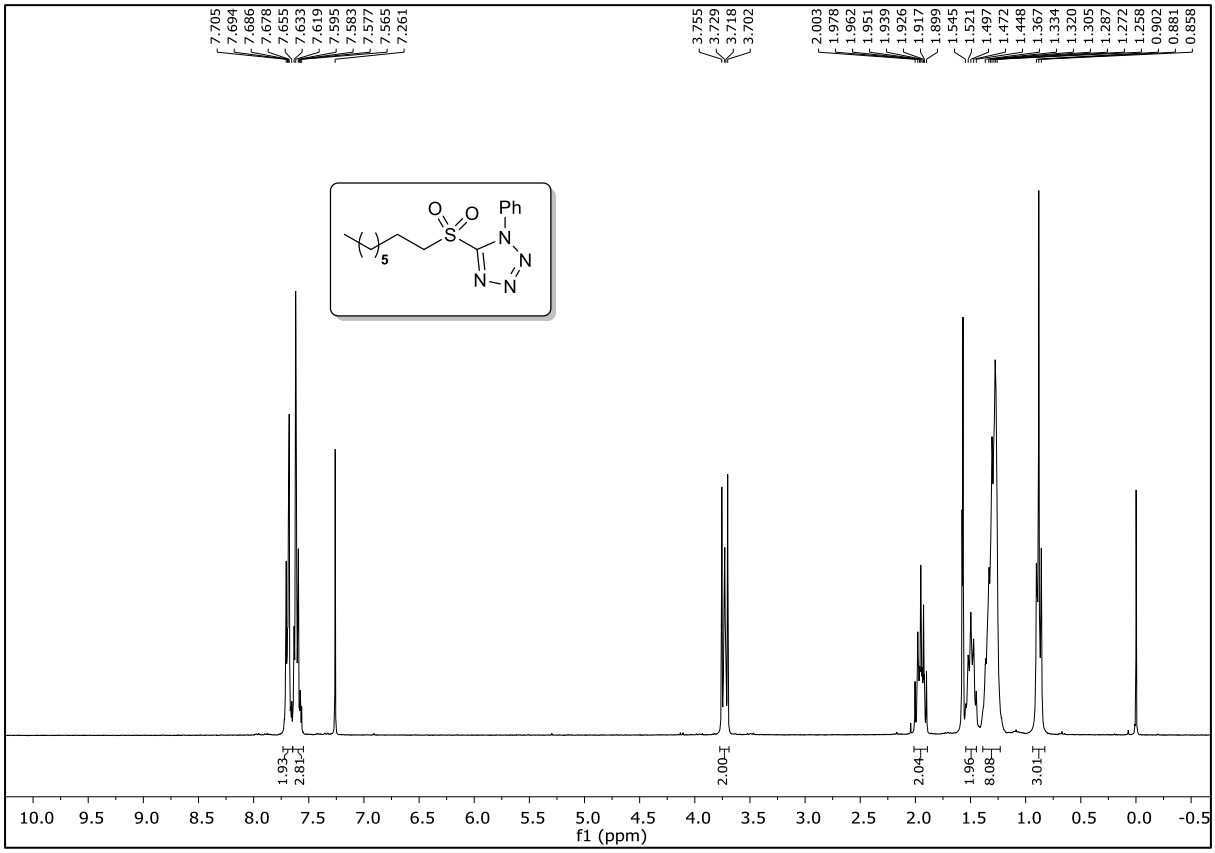
^{1}H-NMR spectrum of compound 25 (300 MHz, $CDCl_3$):



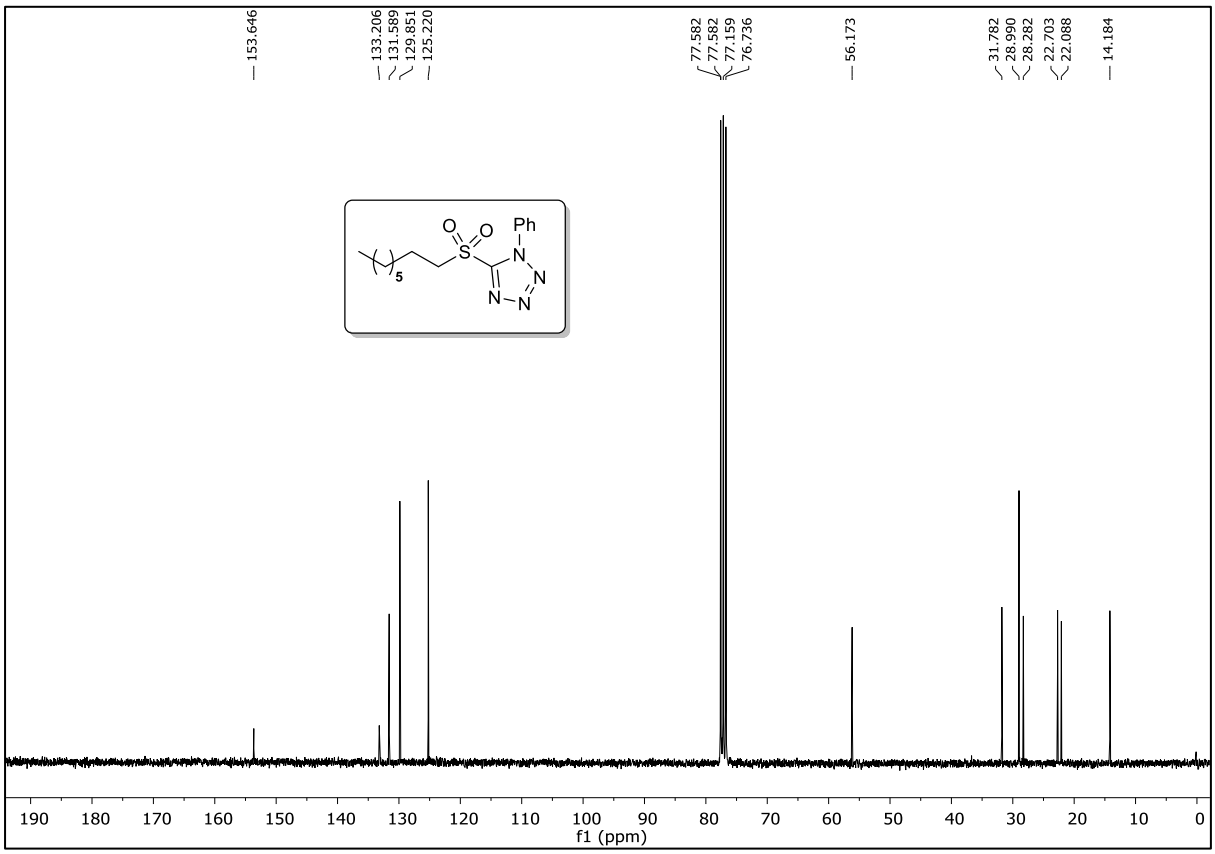
^{13}C-NMR spectrum of compound 25 (75 MHz, $CDCl_3$):



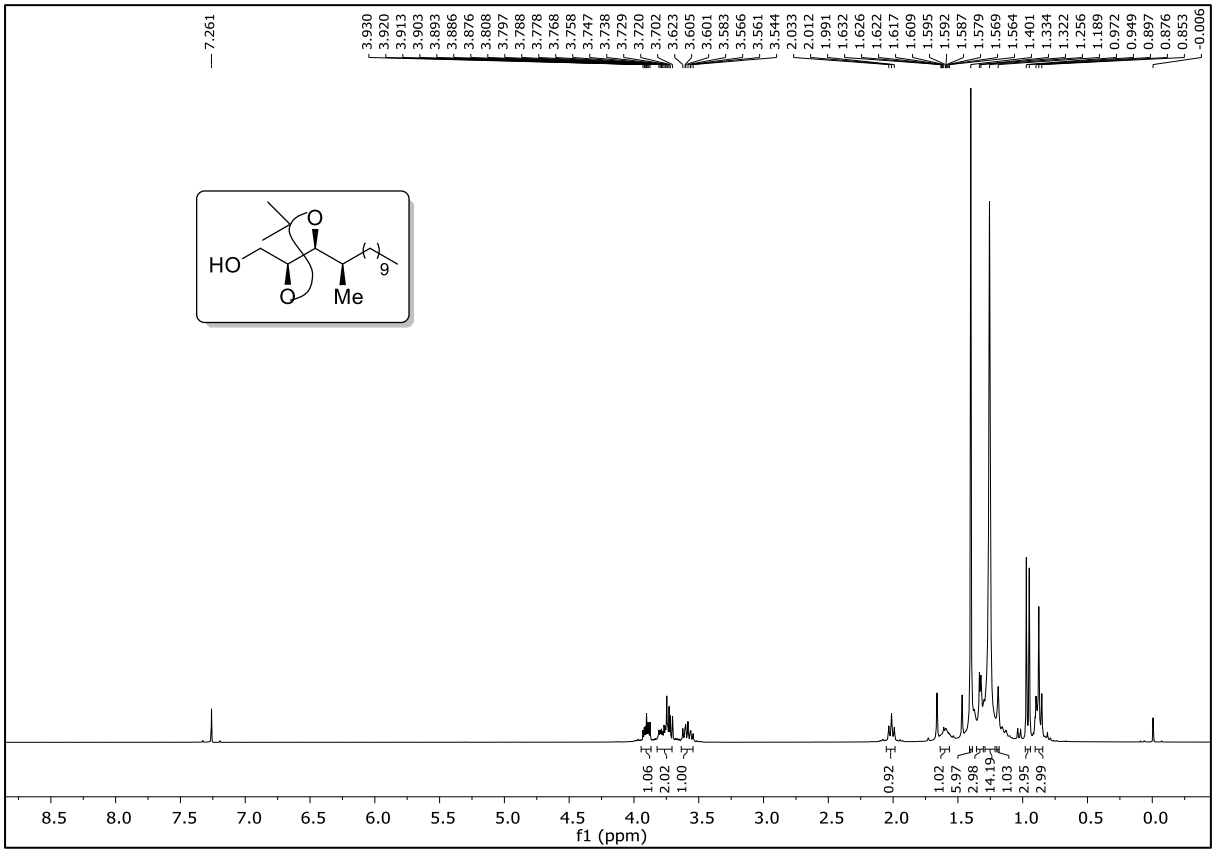
^{1}H-NMR spectrum of compound 26 (300 MHz, $CDCl_3$):



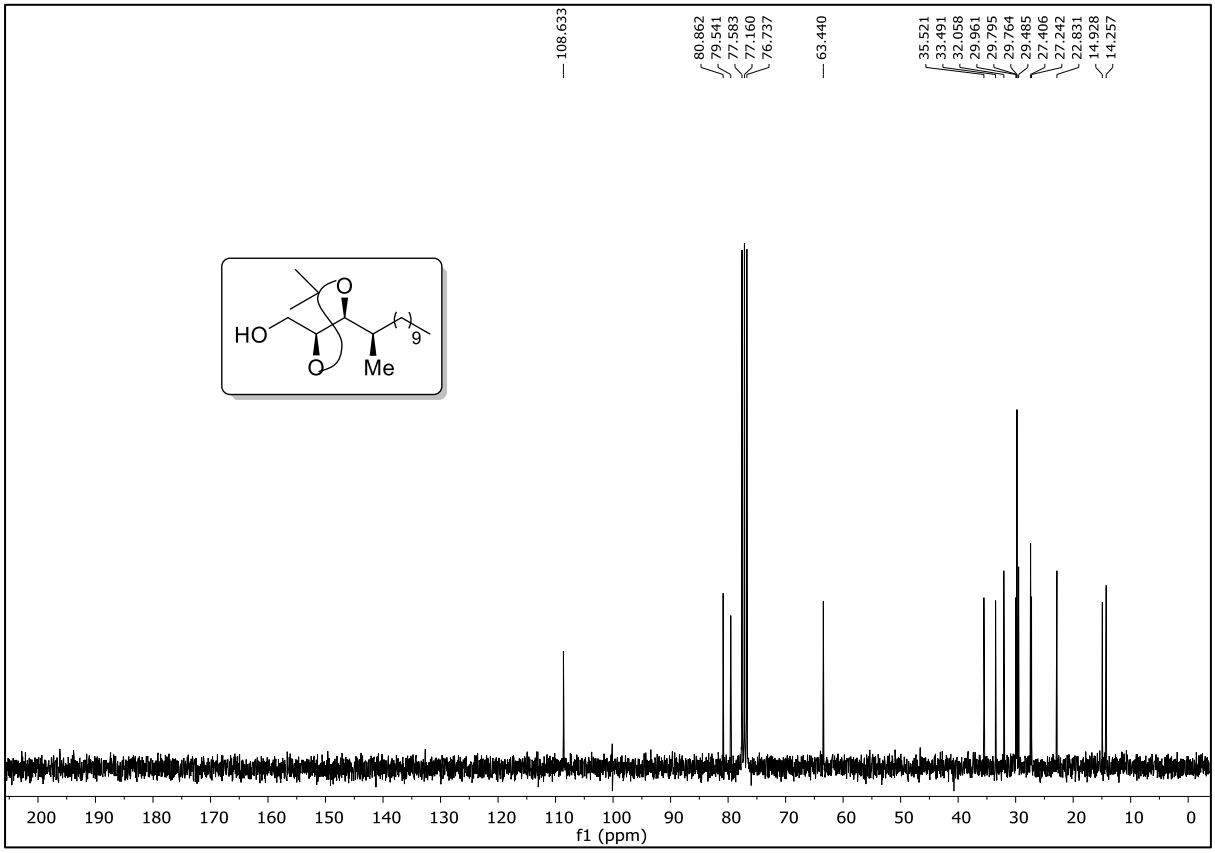
^{13}C-NMR spectrum of compound 26 (75 MHz, $CDCl_3$):



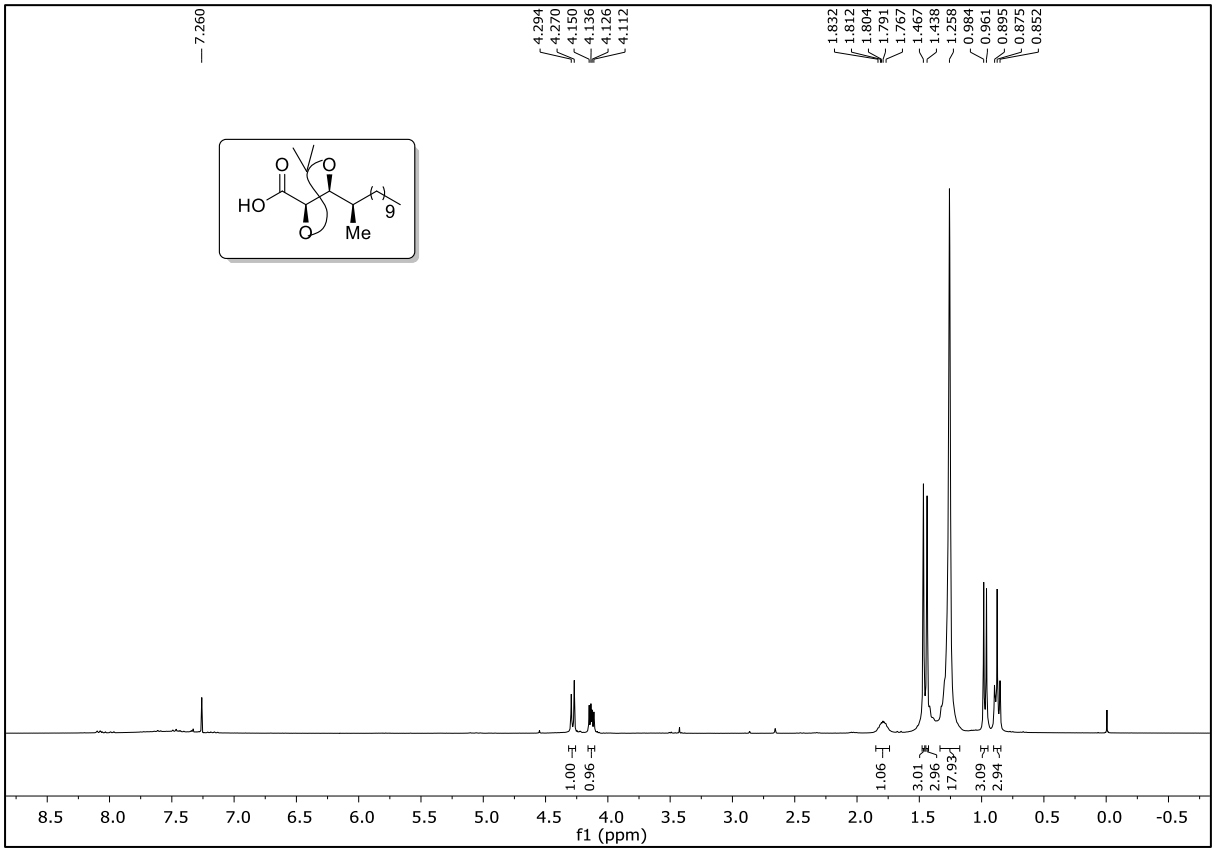
^{1}H-NMR spectrum of compound 27 (300 MHz, $CDCl_3$):



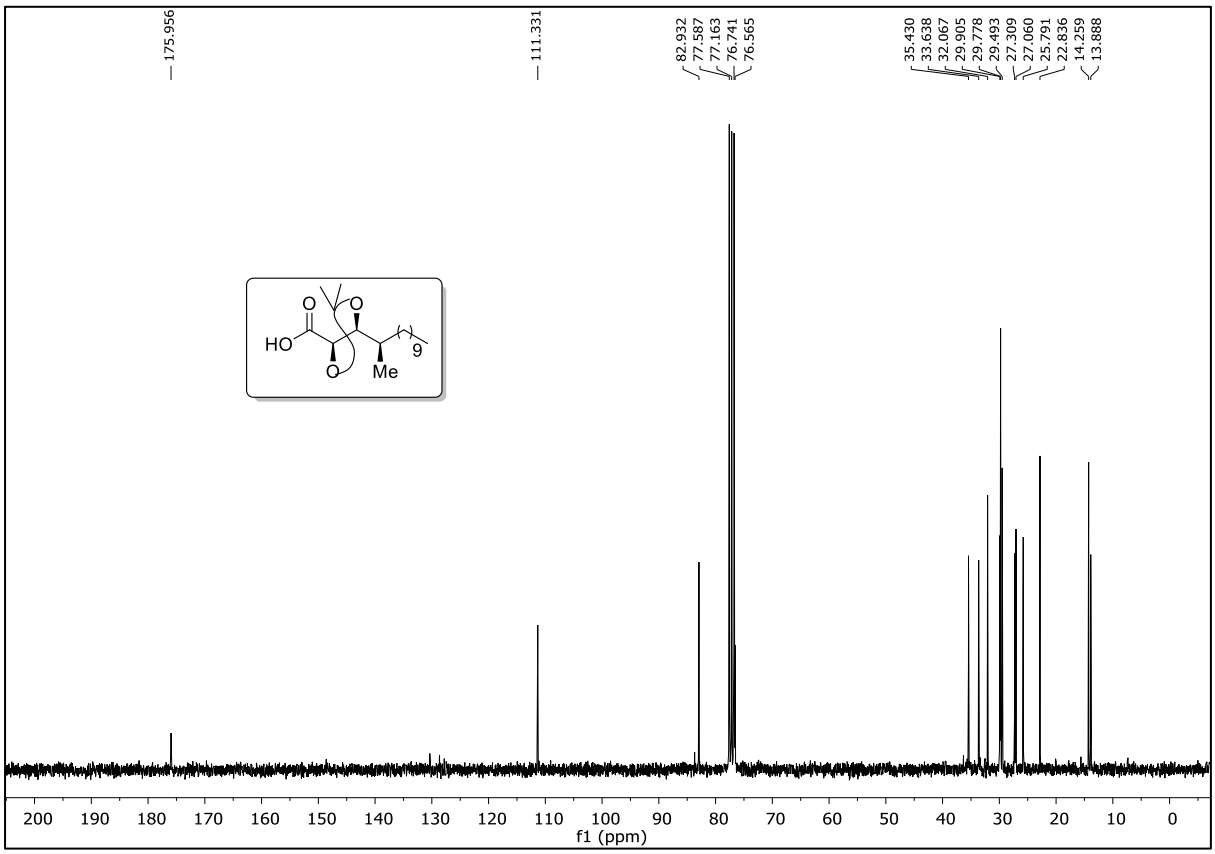
^{13}C-NMR spectrum of compound 27 (75 MHz, $CDCl_3$):



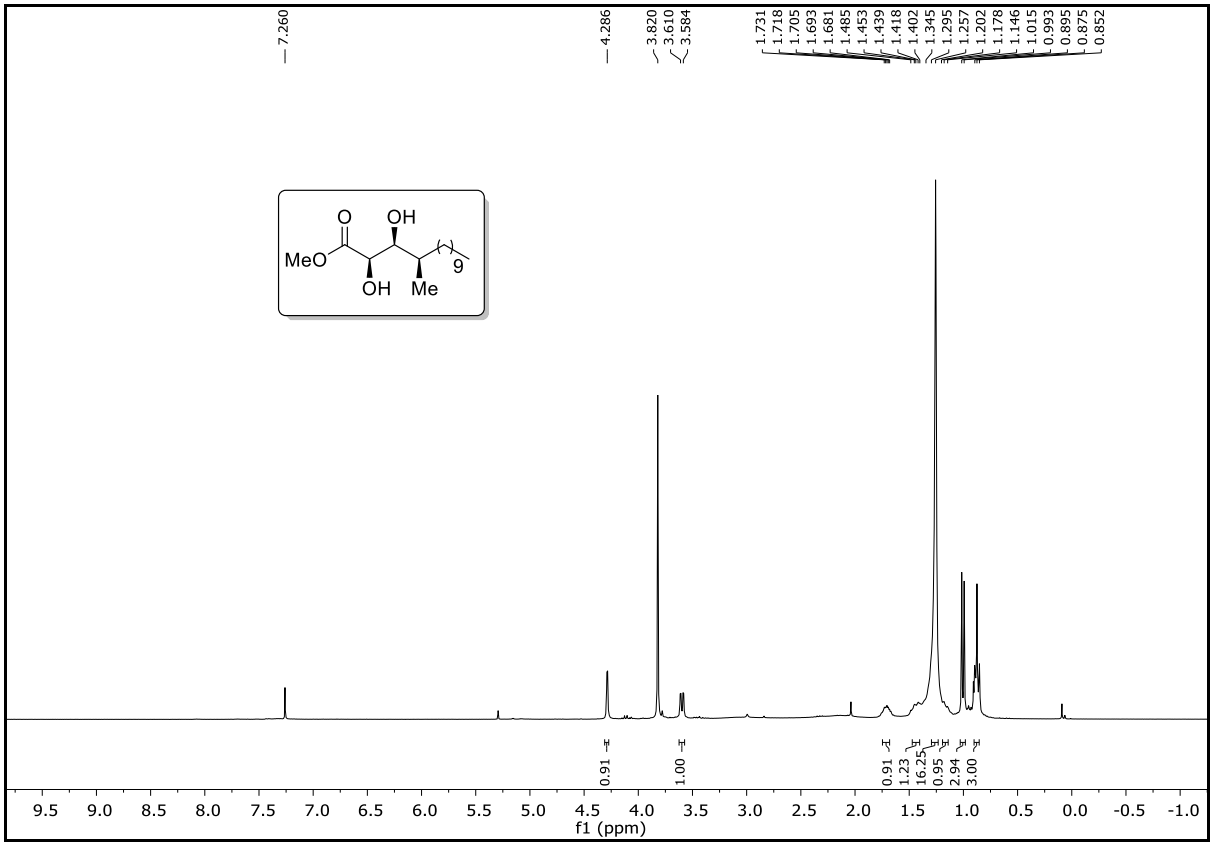
^{1}H-NMR spectrum of compound 28 (300 MHz, $CDCl_3$):



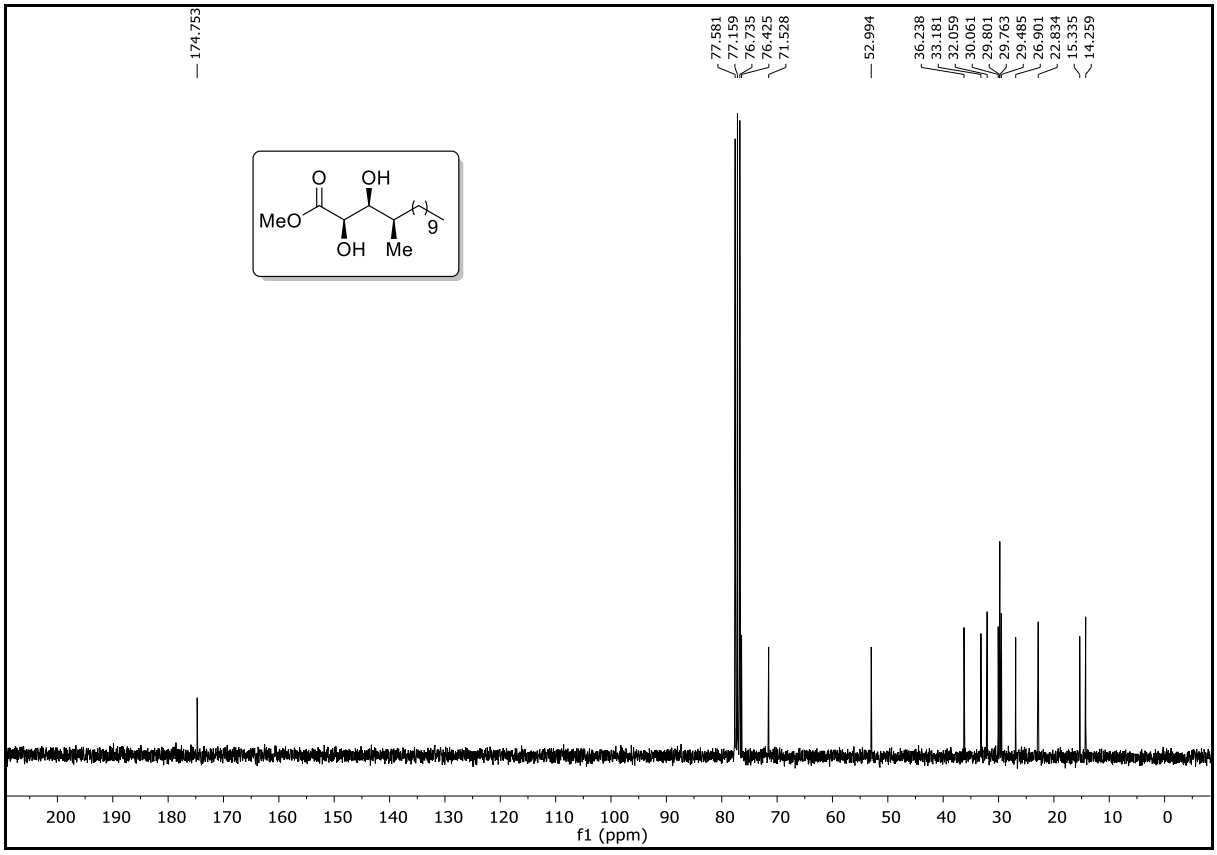
^{13}C-NMR spectrum of compound 28 (75 MHz, $CDCl_3$):



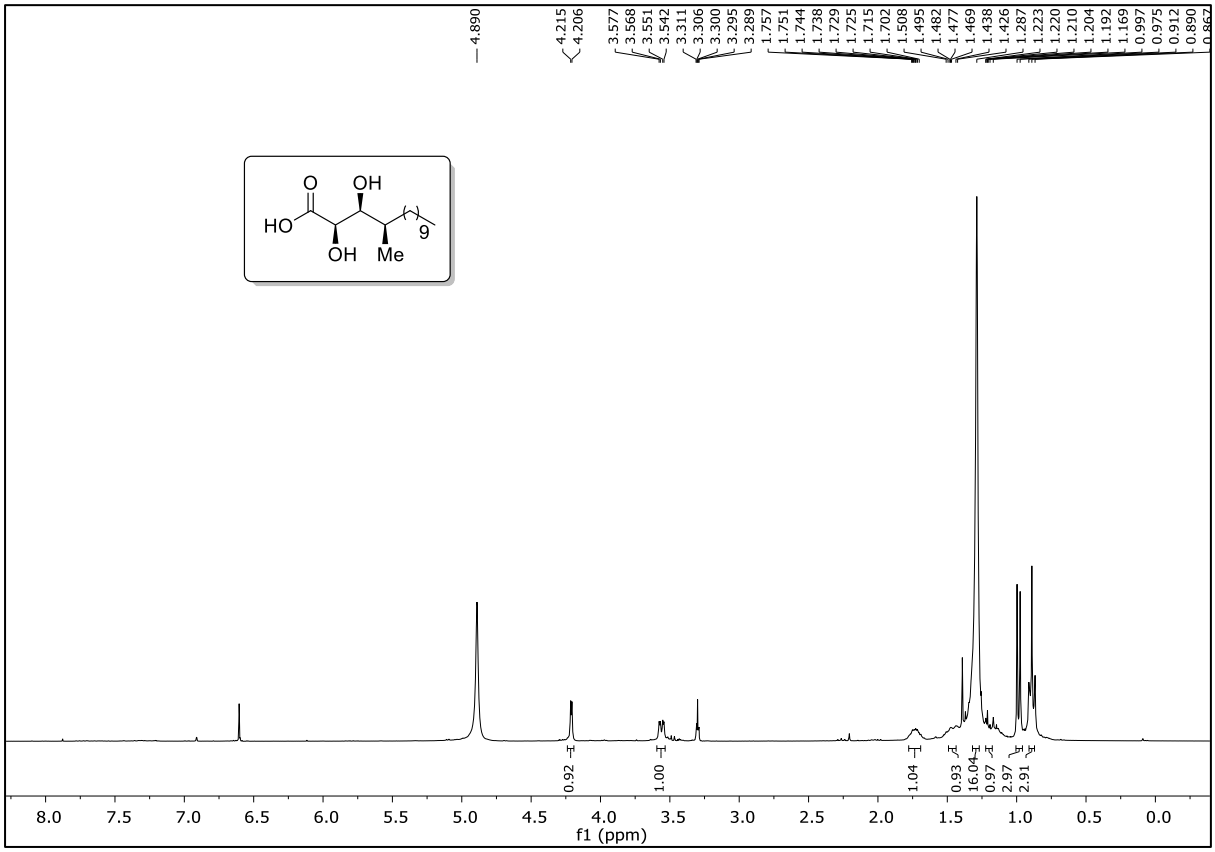
^{1}H-NMR spectrum of compound 29 (300 MHz, $CDCl_3$):



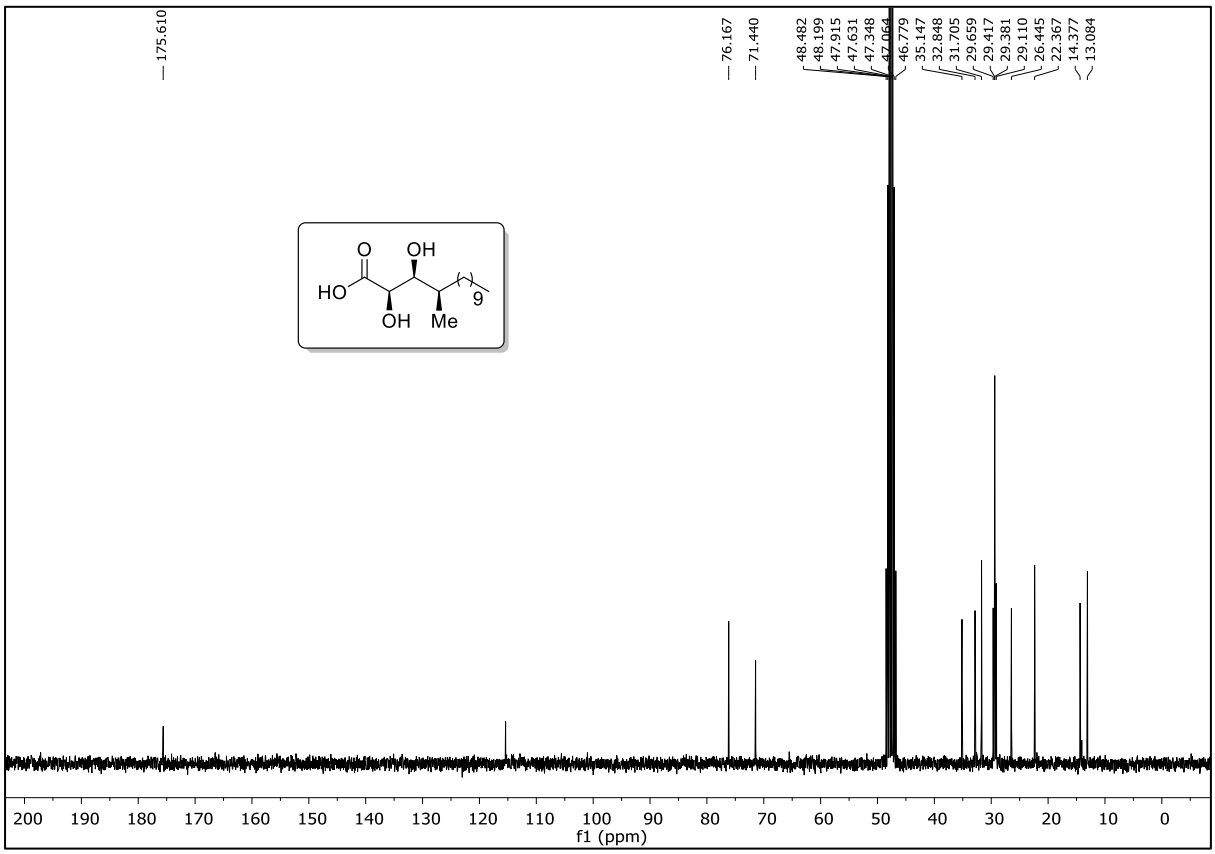
^{13}C-NMR spectrum of compound 29 (75 MHz, $CDCl_3$):



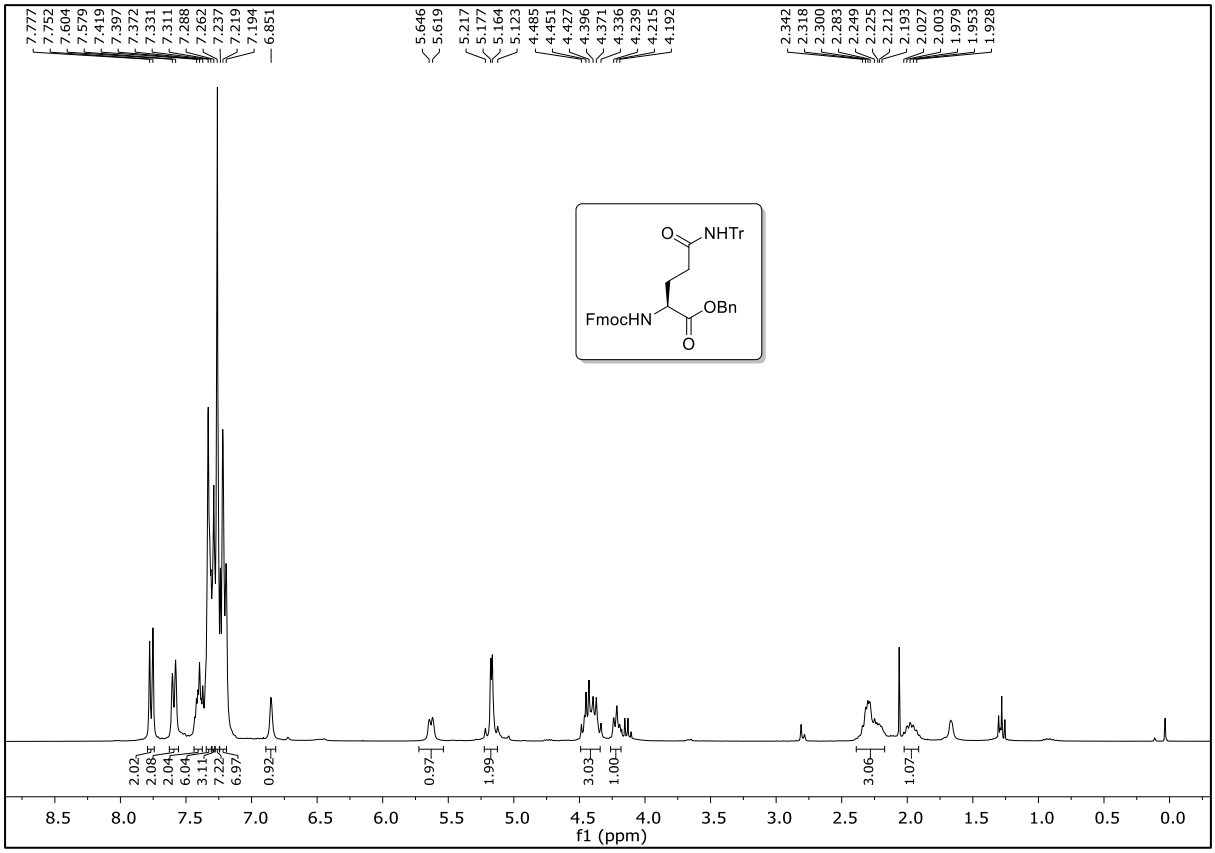
^{1}H-NMR spectrum of compound 7d (300 MHz, CD_3OD):



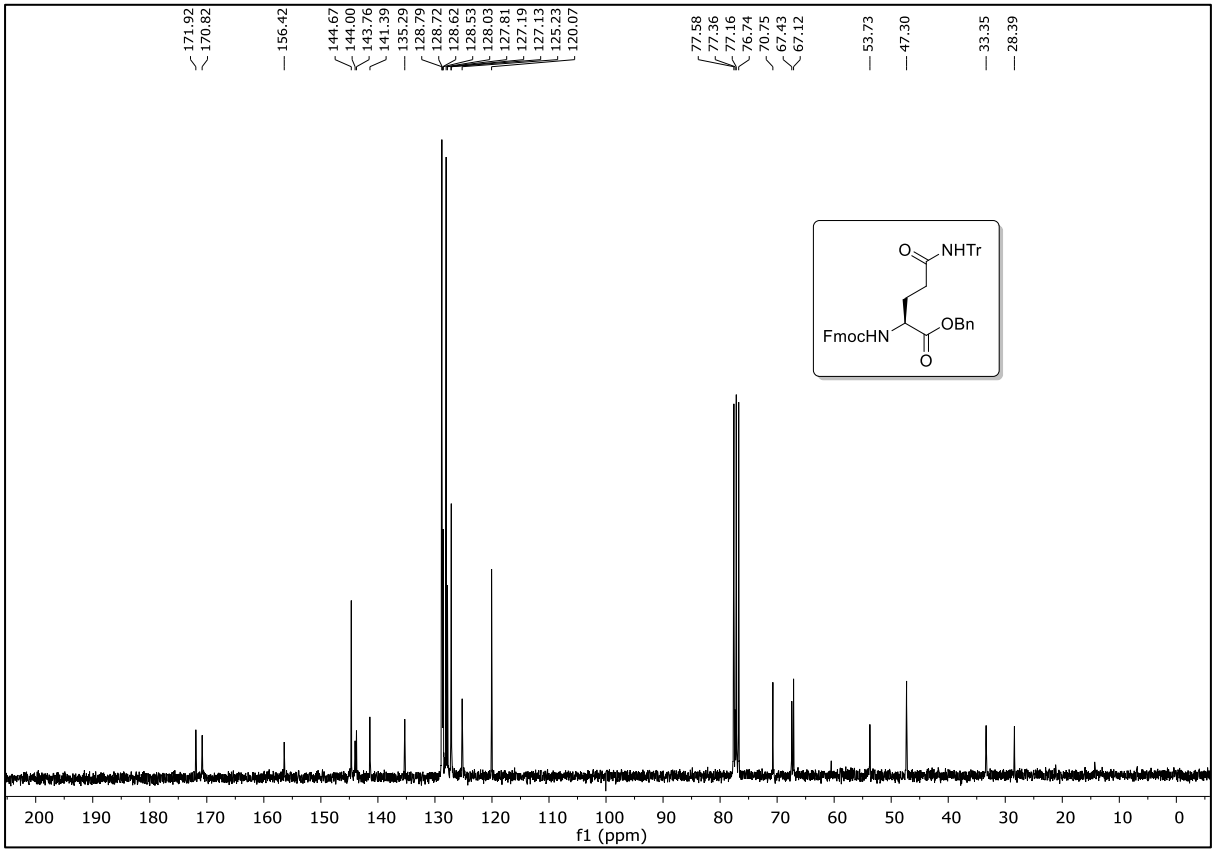
^{13}C-NMR spectrum of compound 7d (75 MHz, CD_3OD):



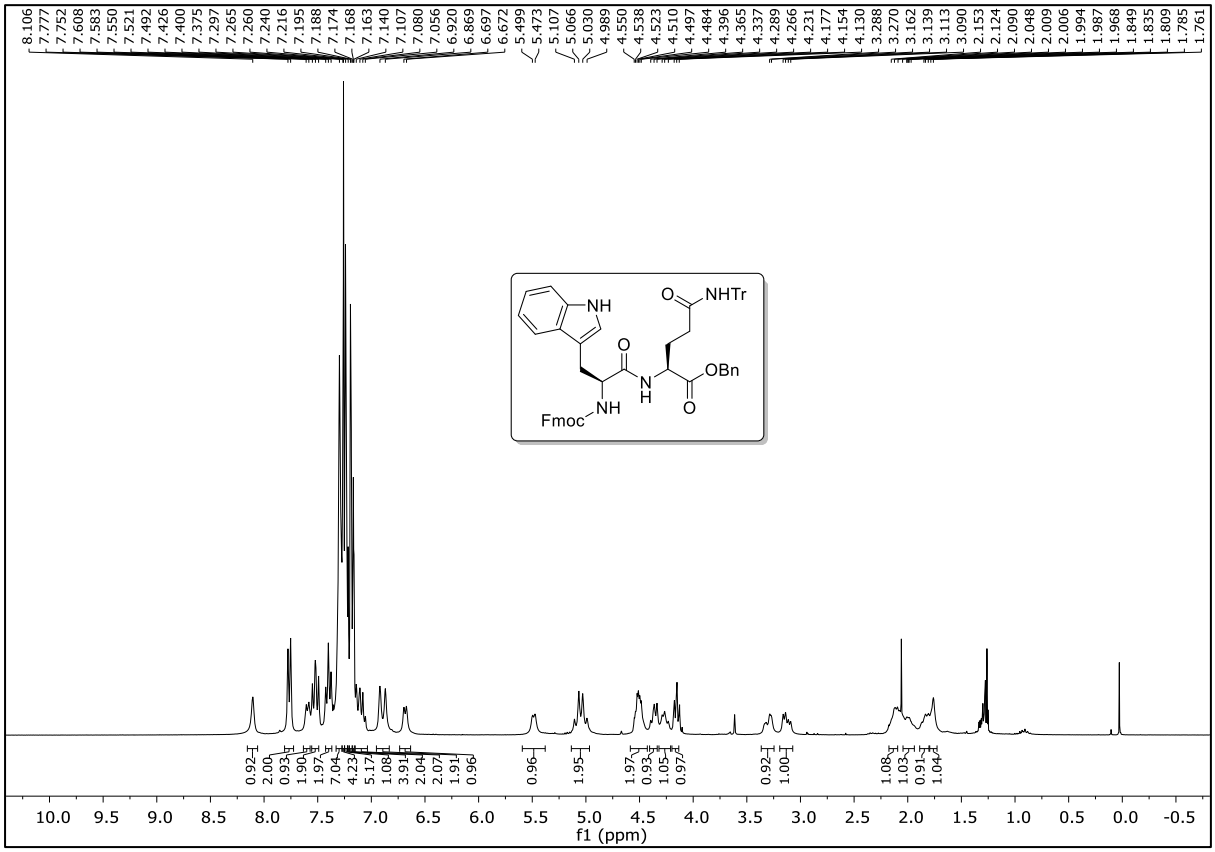
^{1}H-NMR spectrum of compound 30a (300 MHz, $CDCl_3$):



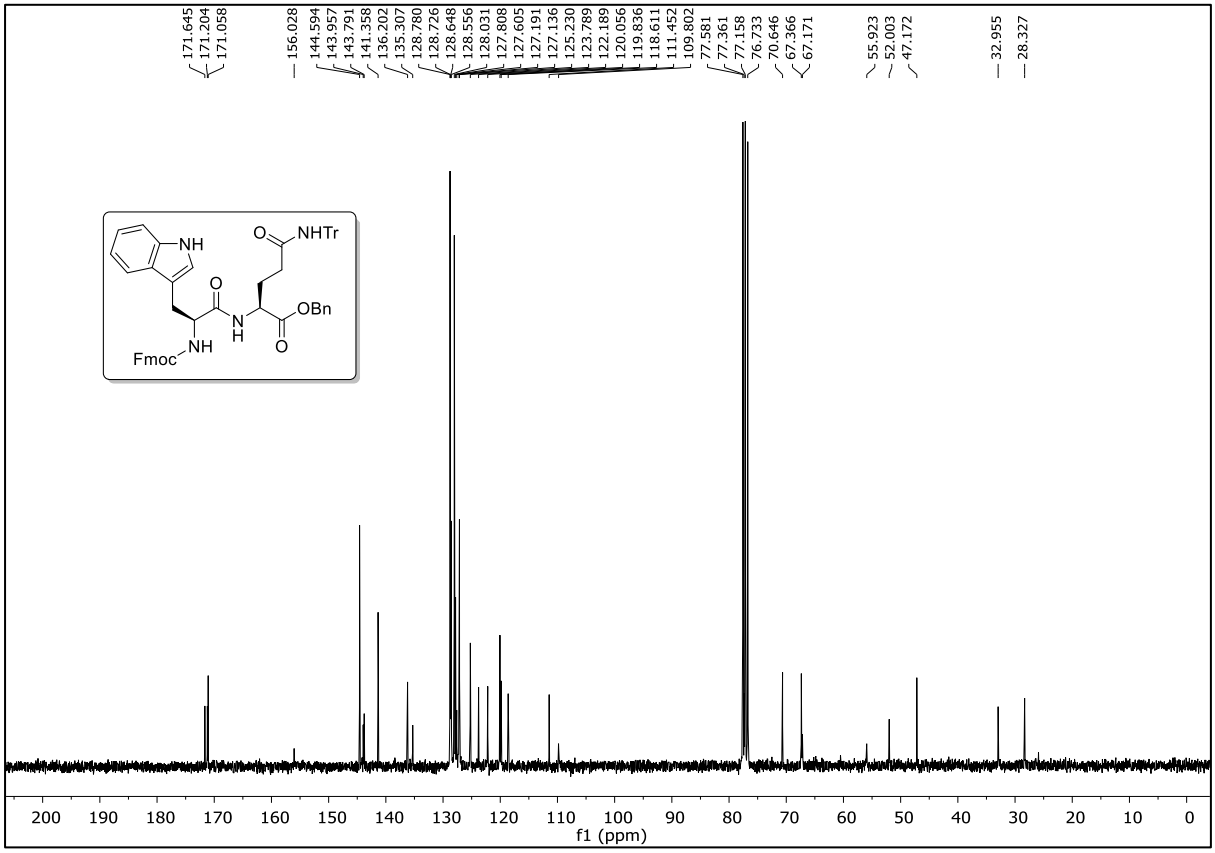
^{13}C-NMR spectrum of compound 30a (75 MHz, $CDCl_3$):



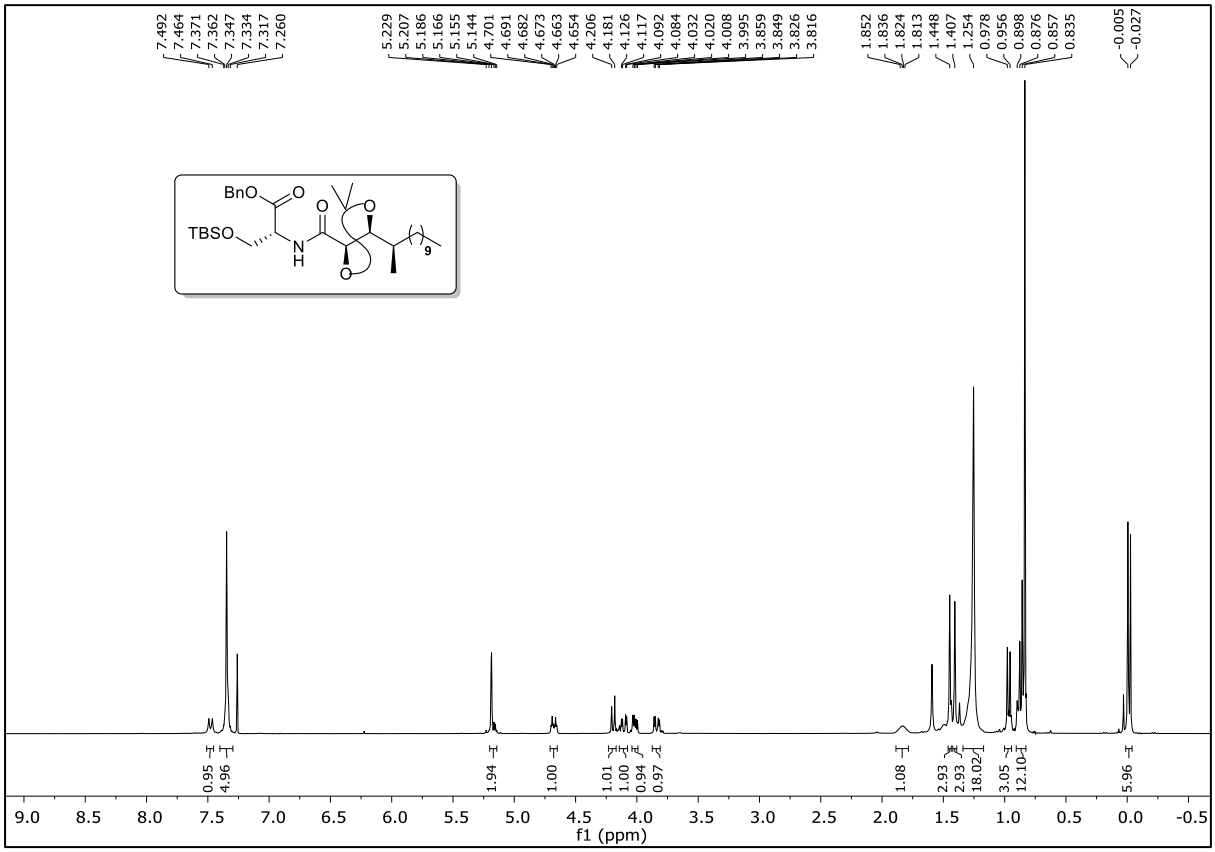
^{1}H-NMR spectrum of compound 6 (300 MHz, $CDCl_3$):



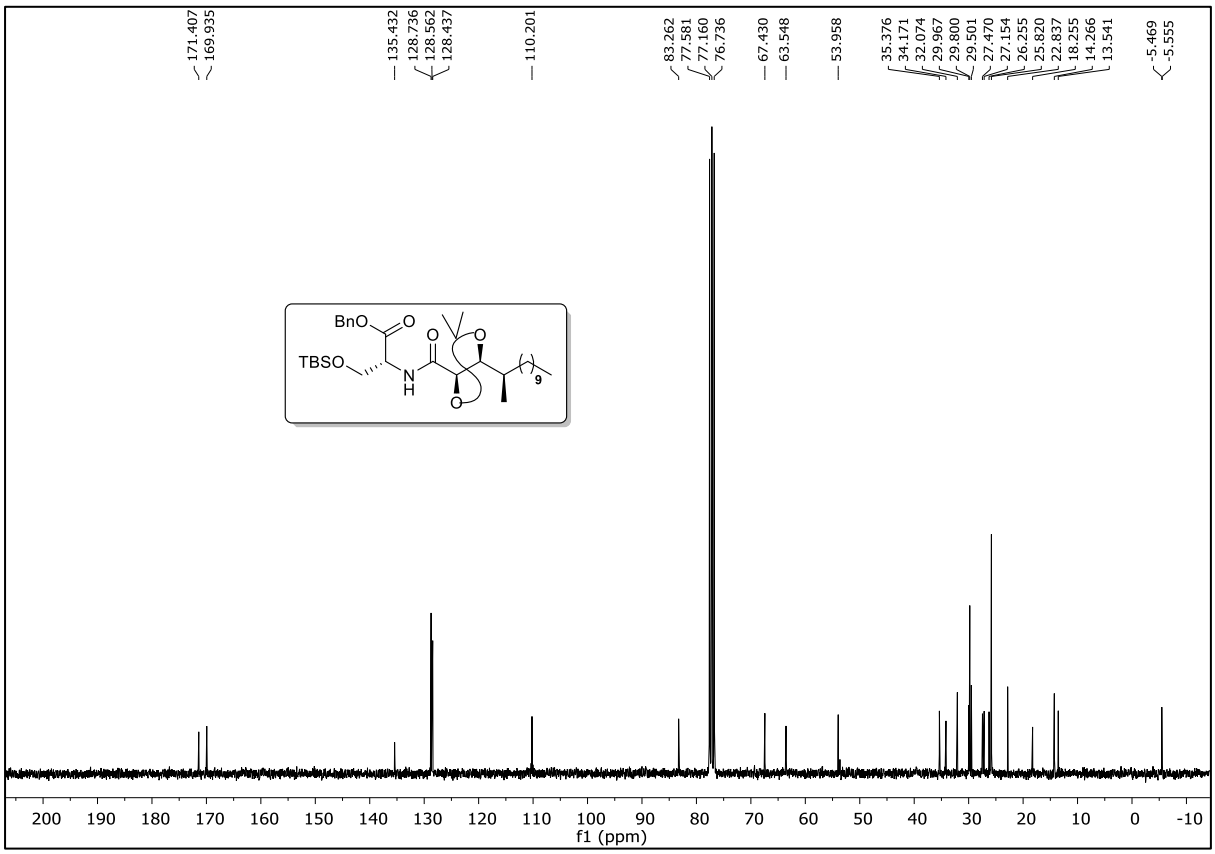
^{13}C-NMR spectrum of compound 6 (75 MHz, $CDCl_3$):



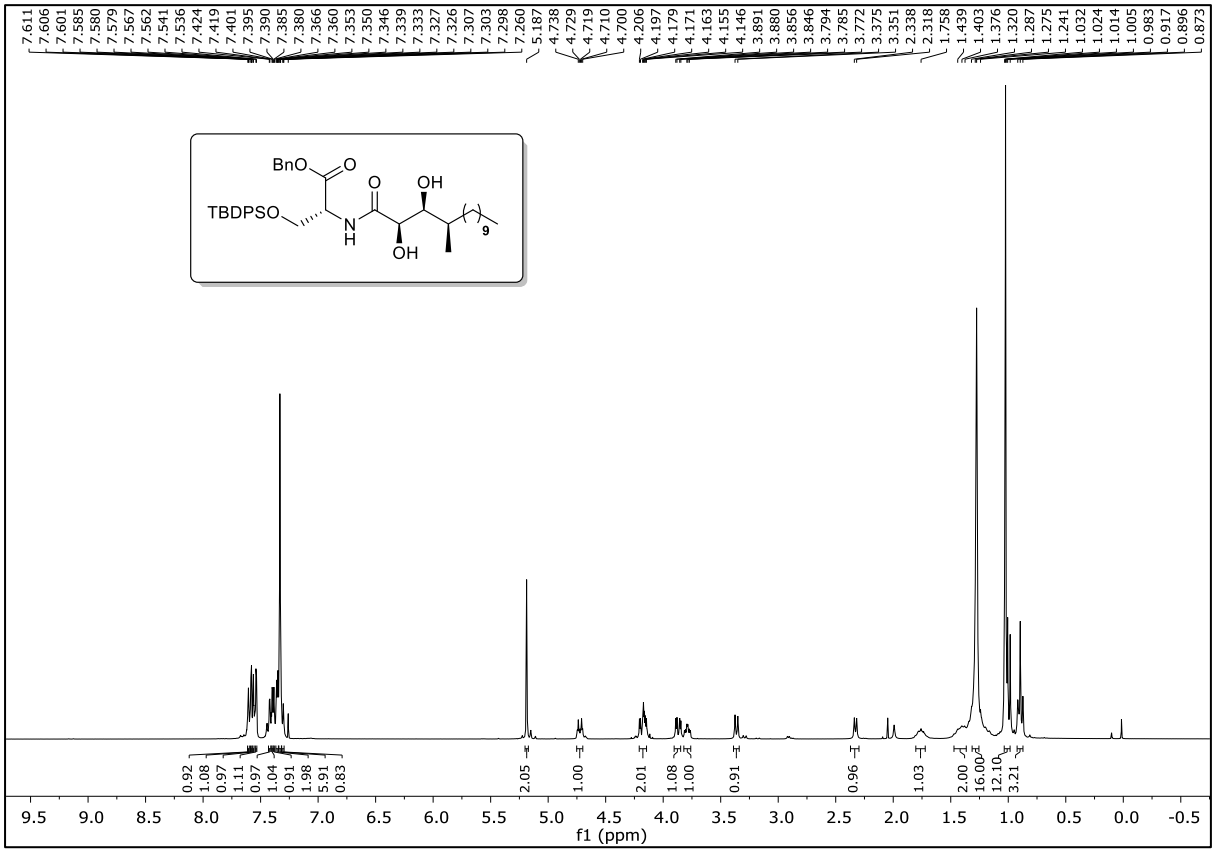
^{1}H-NMR spectrum of compound 34 (300 MHz, $CDCl_3$):



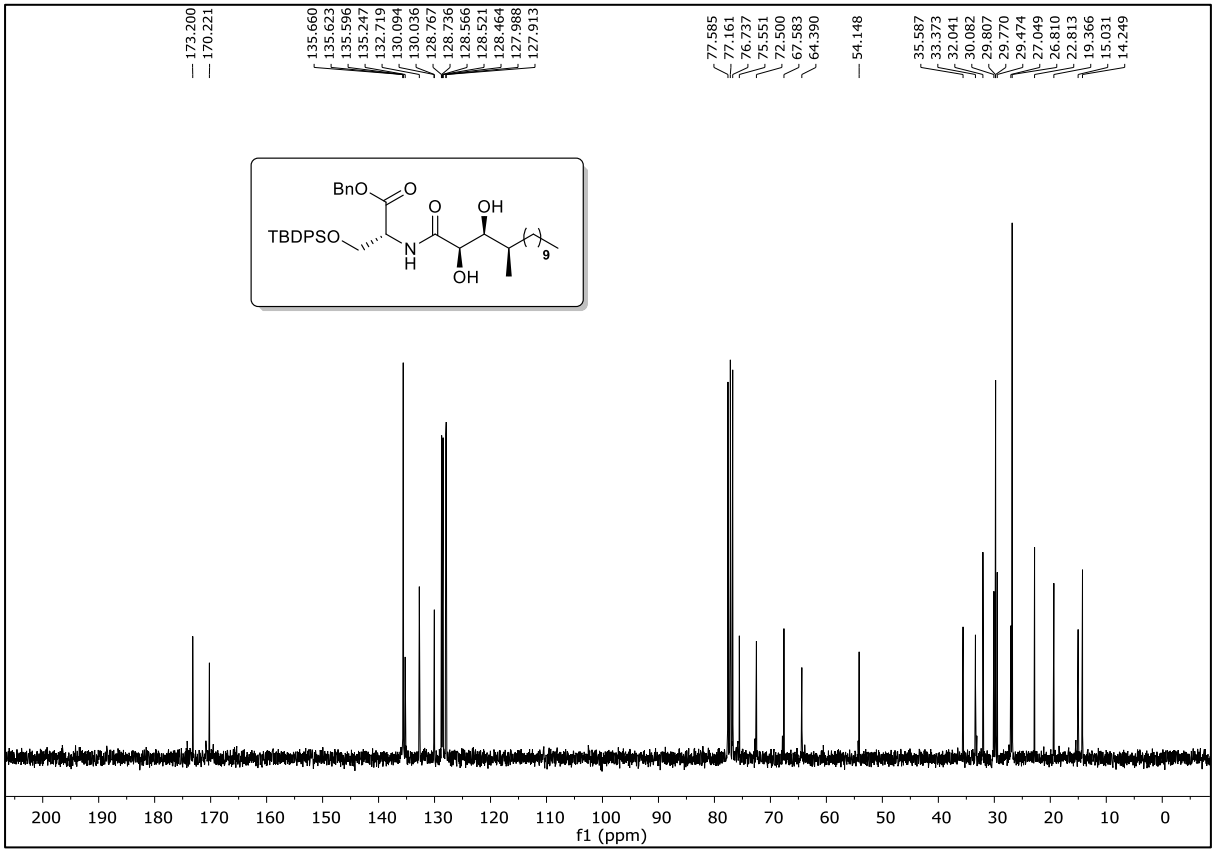
^{13}C-NMR spectrum of compound 34 (75 MHz, $CDCl_3$):



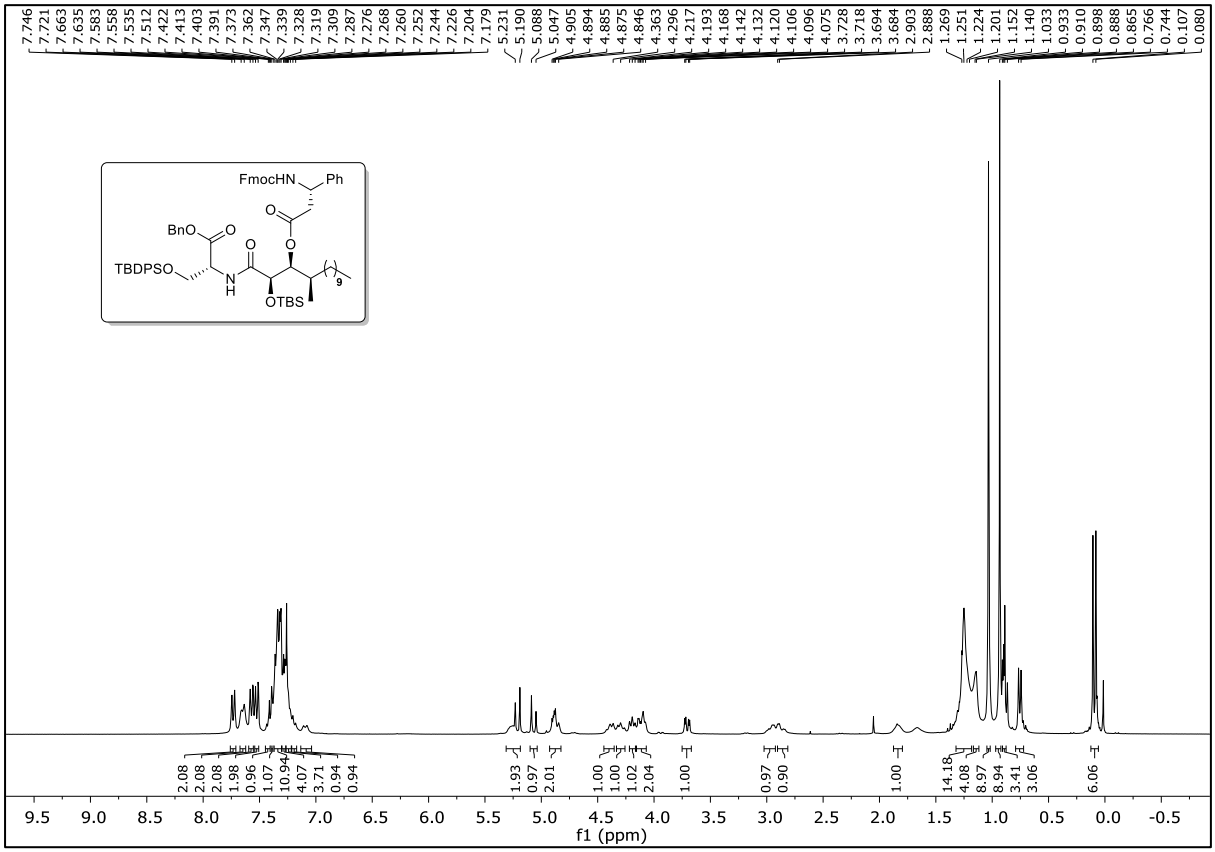
^{1}H-NMR spectrum of compound 35 (300 MHz, $CDCl_3$):



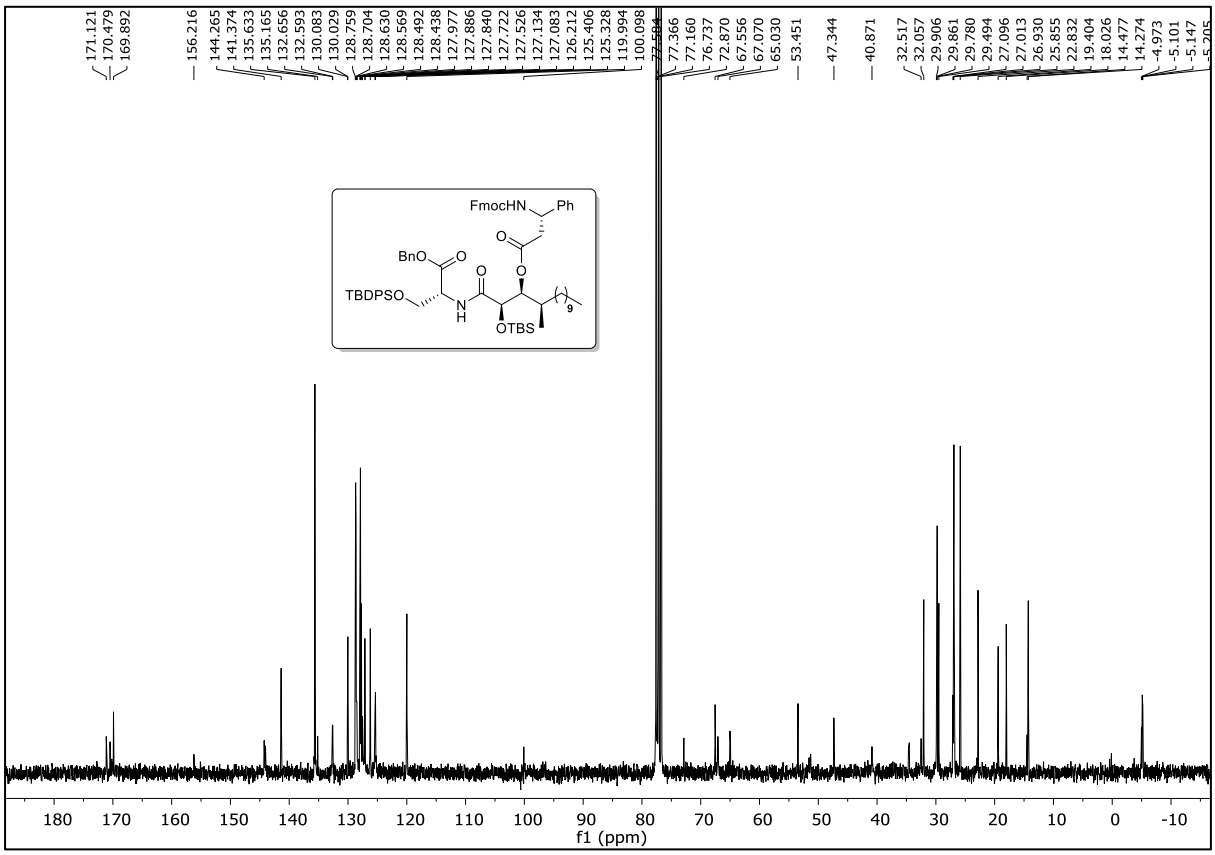
^{13}C-NMR spectrum of compound 35 (75 MHz, $CDCl_3$):

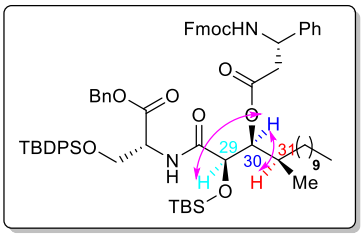


^{1}H-NMR spectrum of compound 5a (300 MHz, $CDCl_3$):

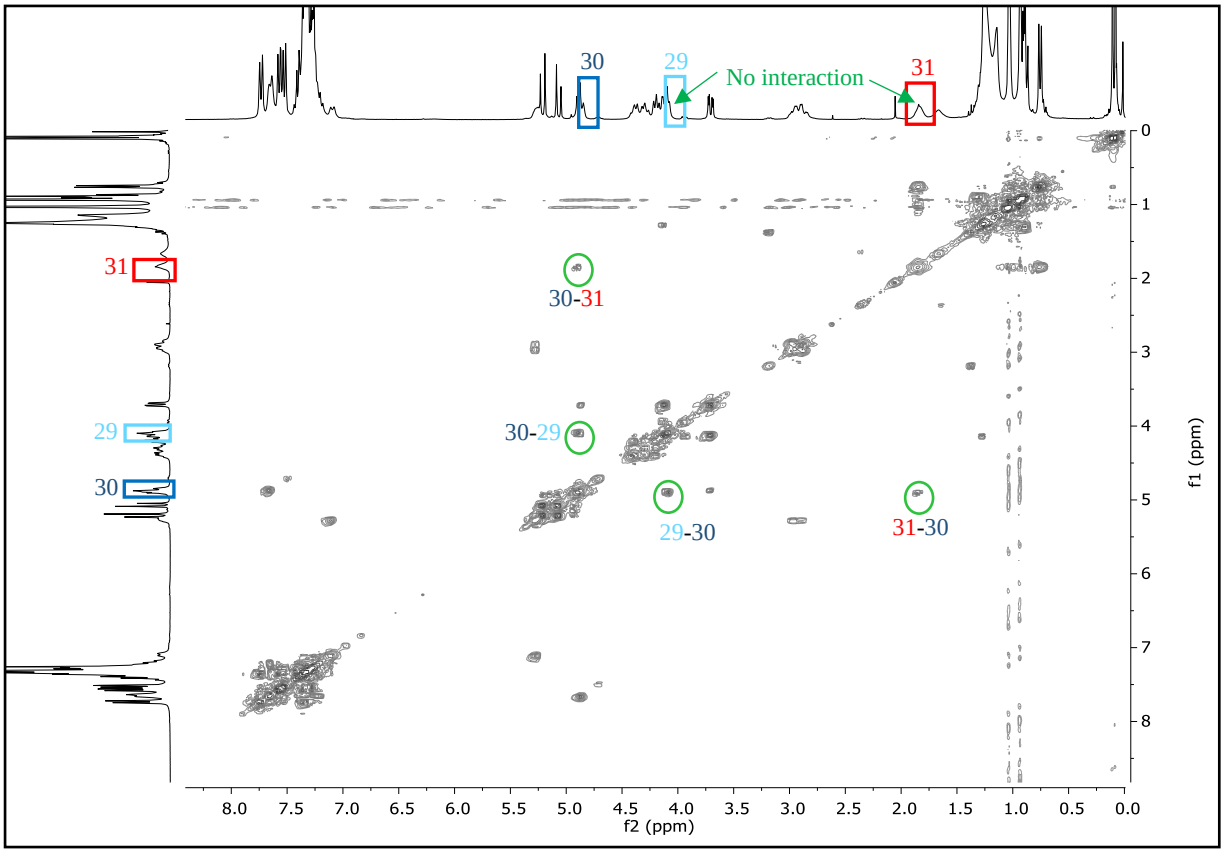


^{13}C-NMR spectrum of compound 5a (75 MHz, $CDCl_3$):

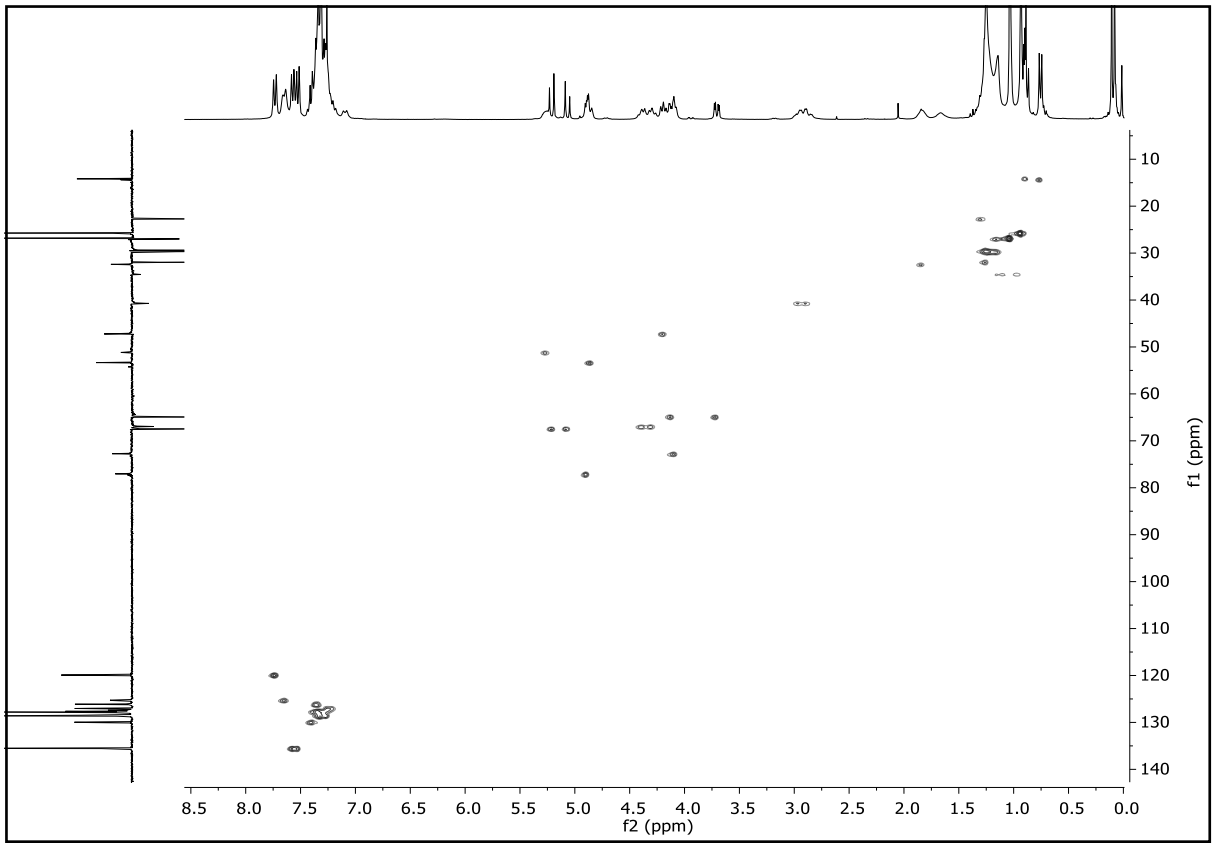




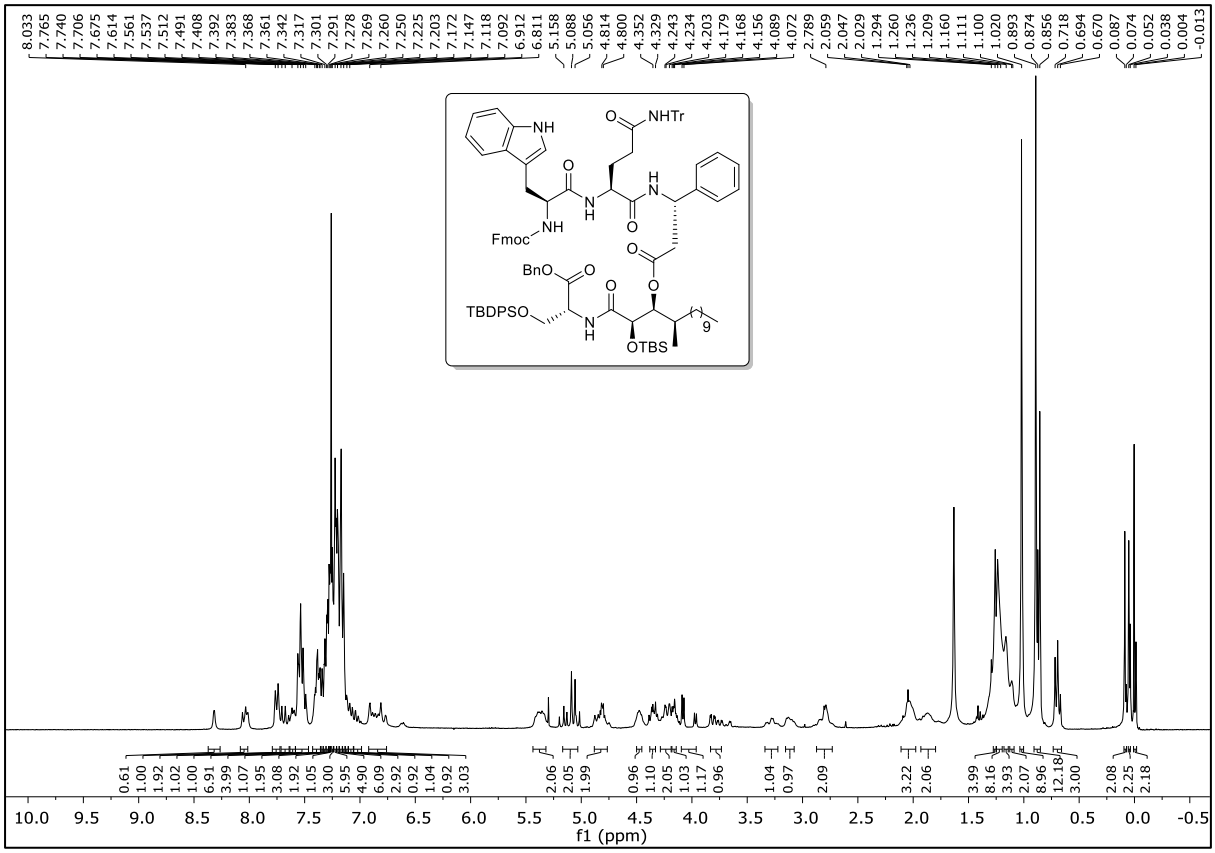
COSY spectrum of compound 5a (125 MHz, DMSO-*d*$_6$):



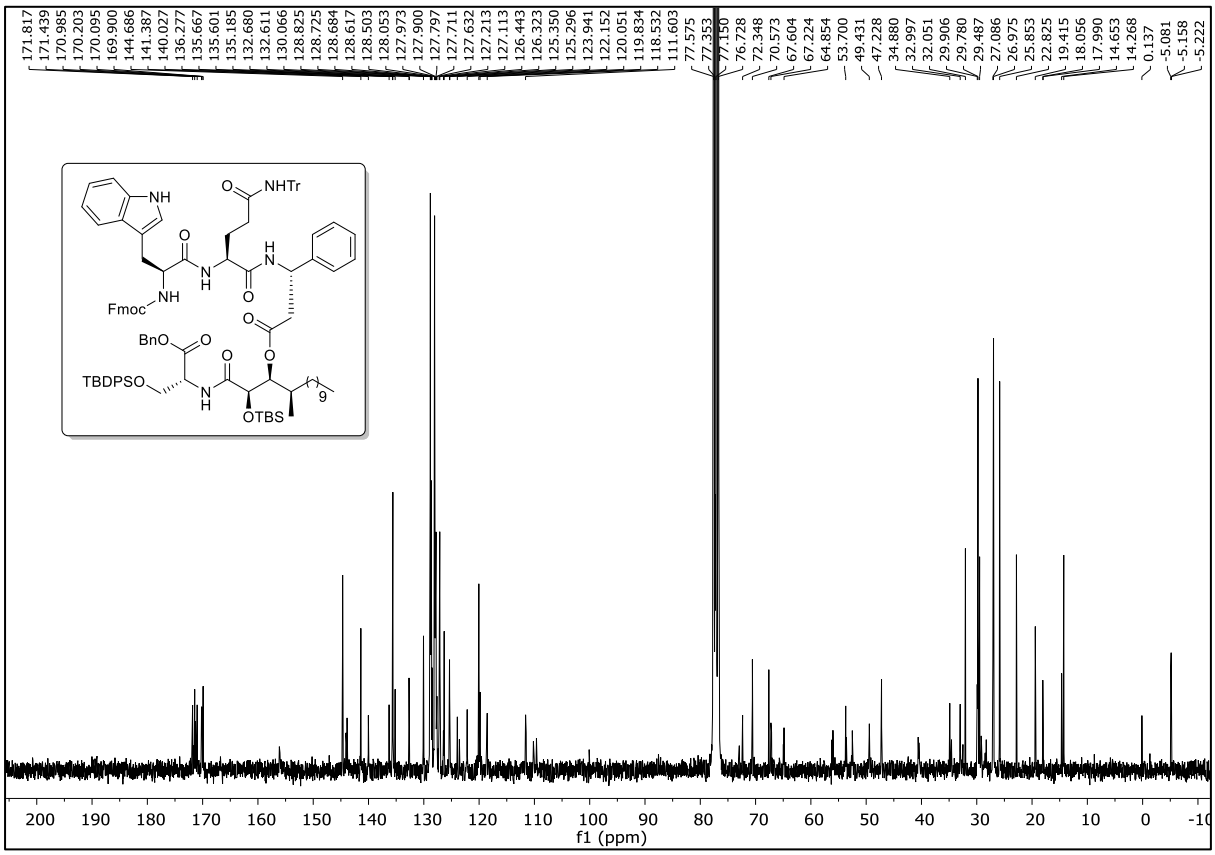
HSQC spectrum of compound 5a (125 MHz, DMSO-*d*$_6$):



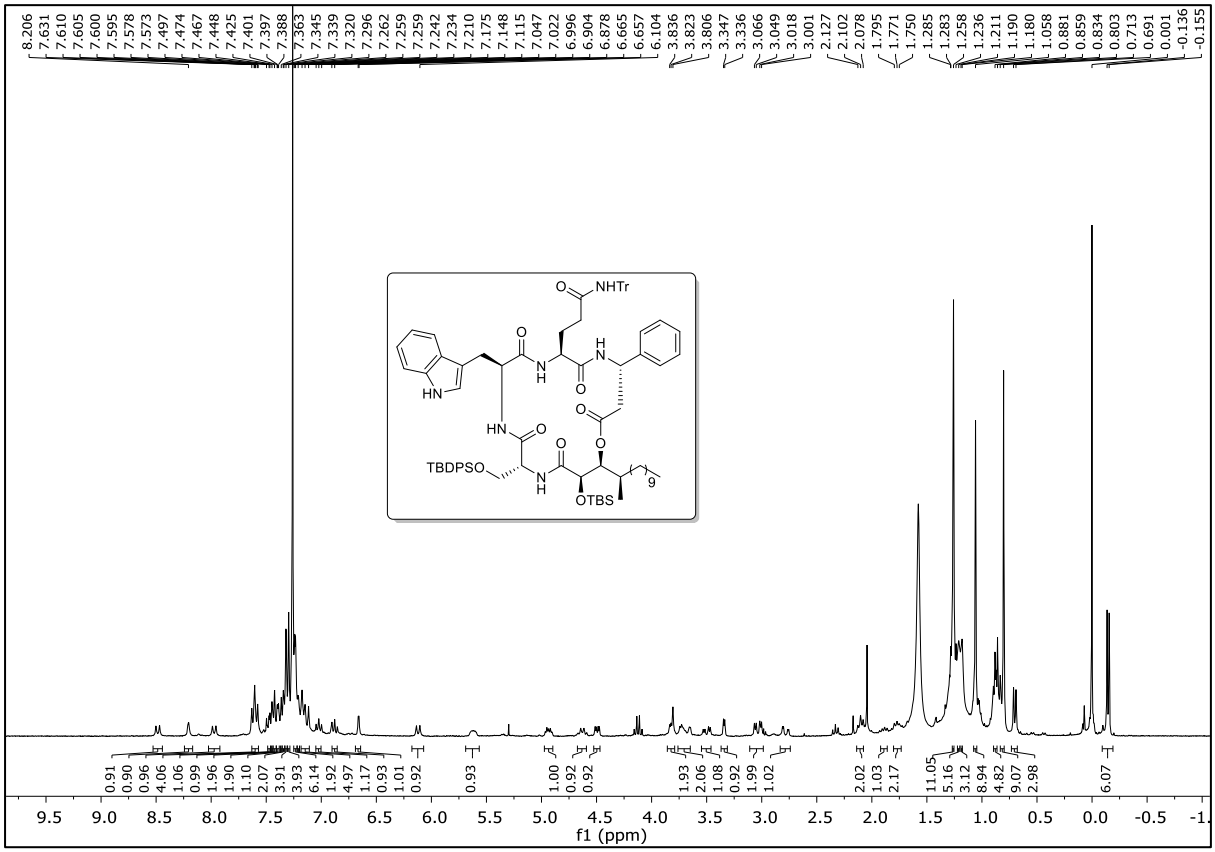
^{1}H-NMR spectrum of compound 4a (300 MHz, $CDCl_3$):



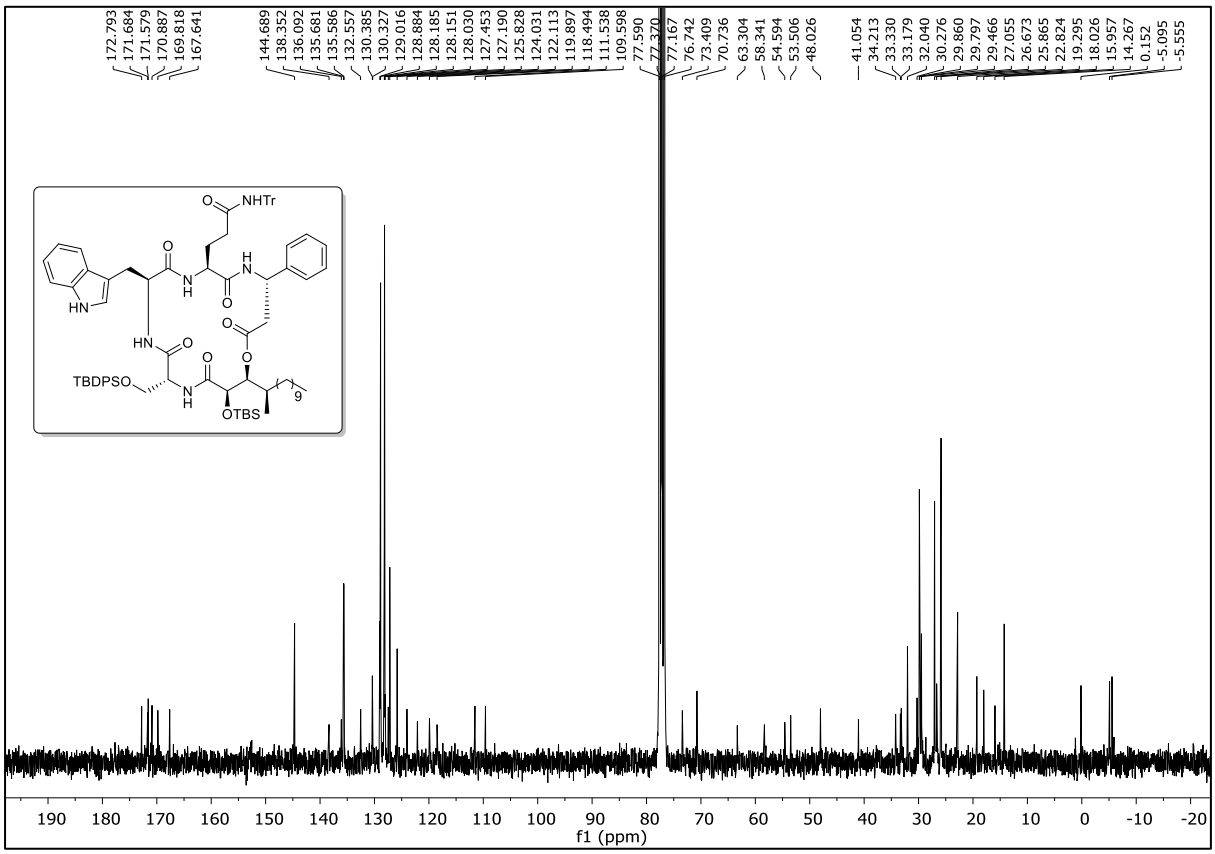
^{13}C-NMR spectrum of compound 4a (75 MHz, $CDCl_3$):



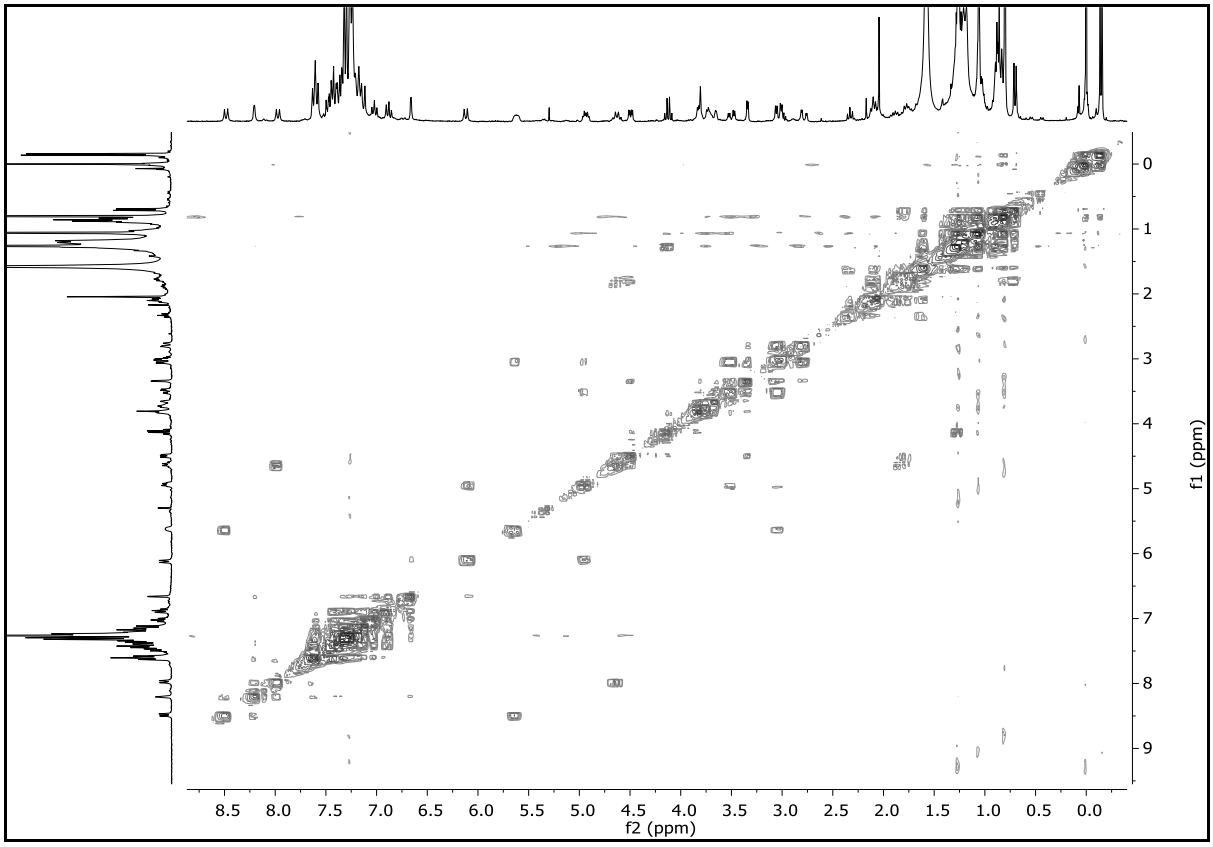
^{1}H-NMR spectrum of compound 37 (300 MHz, $CDCl_3$):



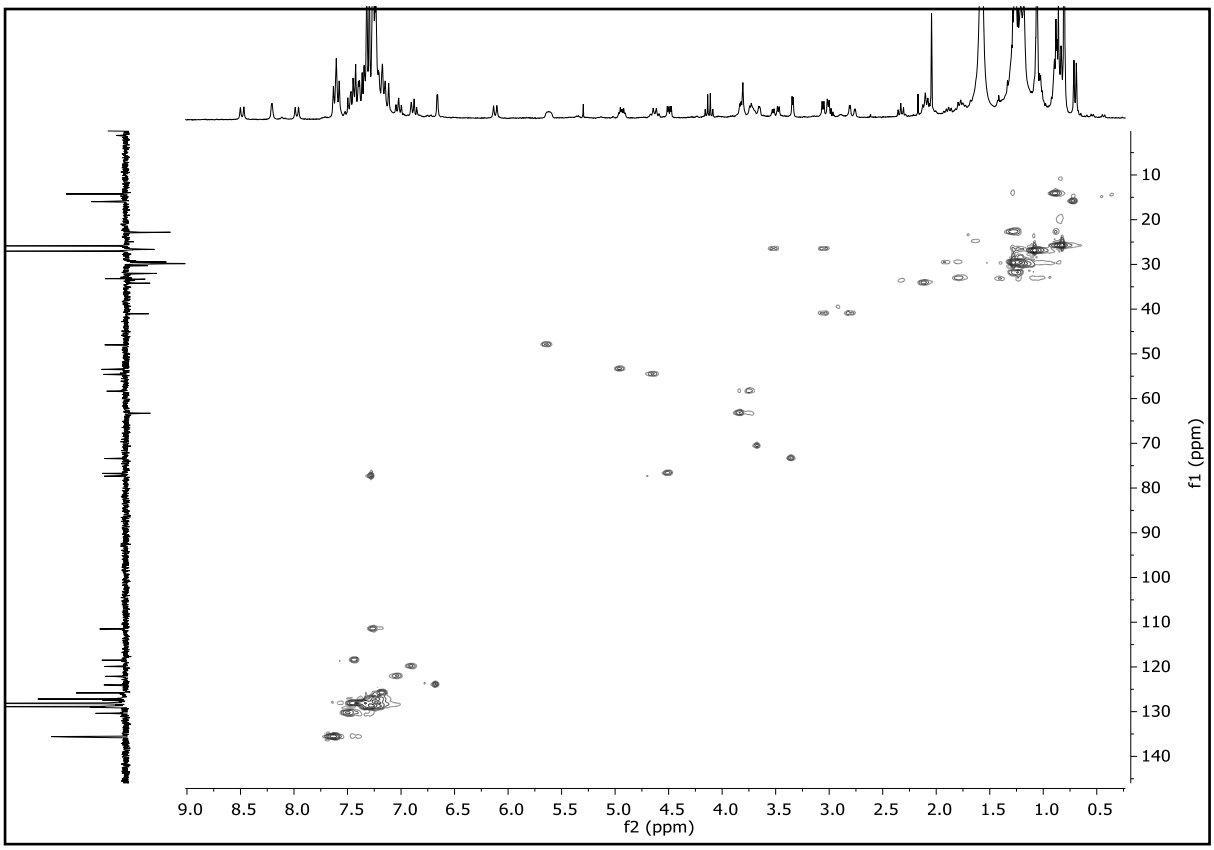
^{13}C-NMR spectrum of compound 37 (75 MHz, $CDCl_3$):



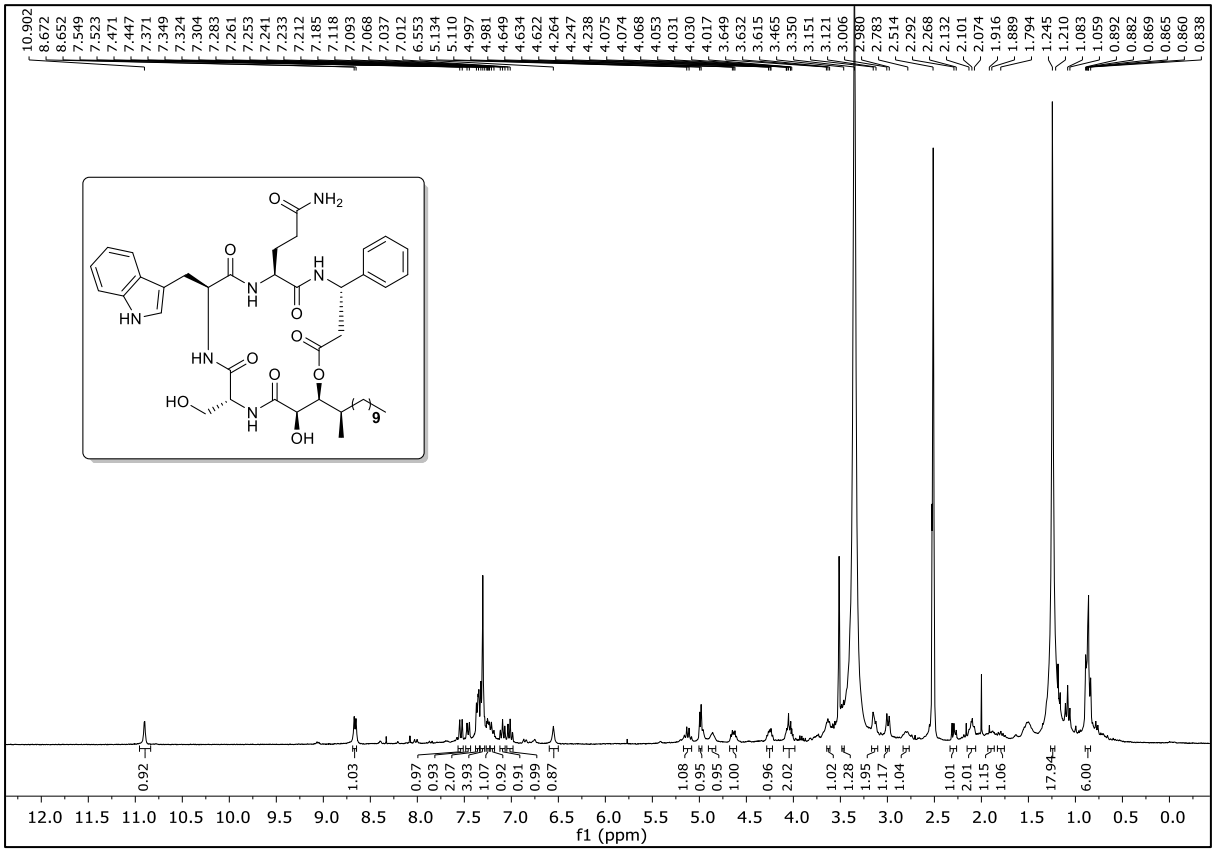
COSY spectrum of compound 37 (75 MHz, $CDCl_3$):



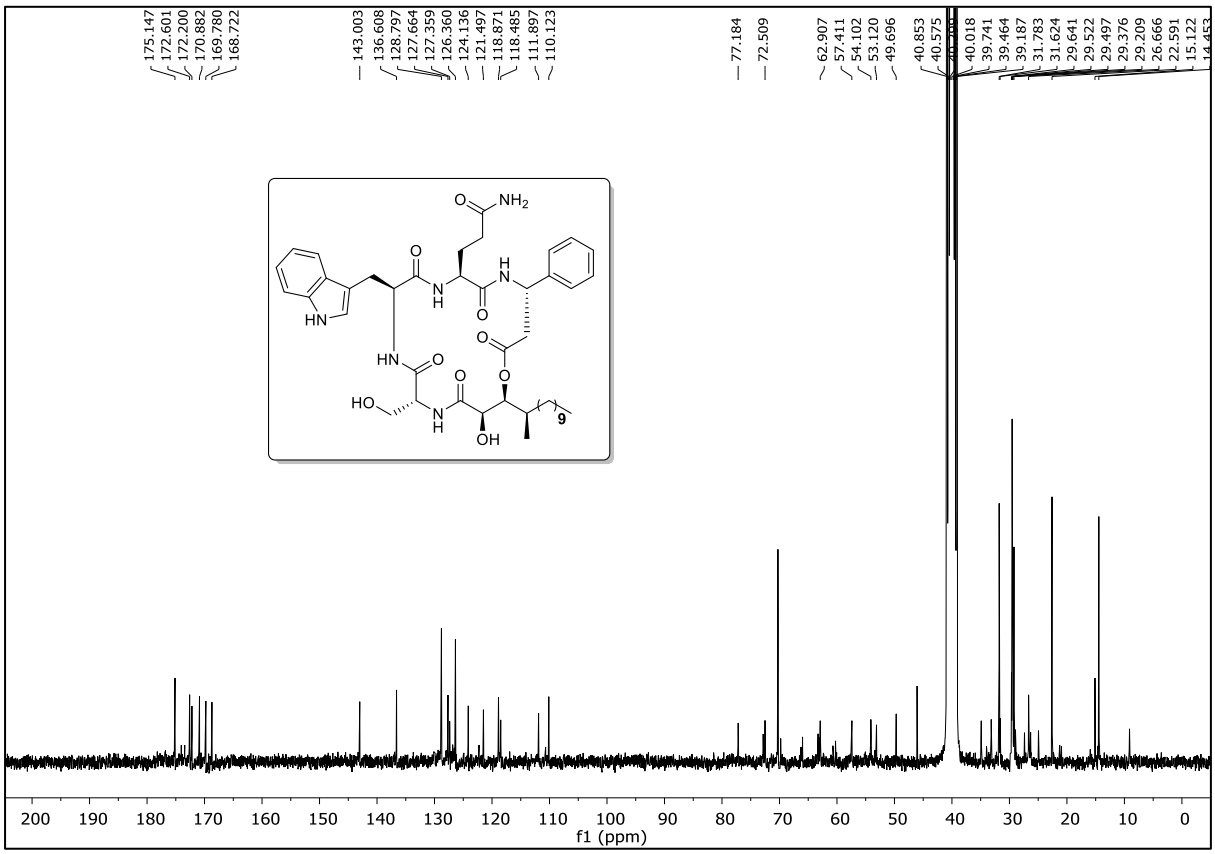
HSQC spectrum of compound 37 (75 MHz, $CDCl_3$):



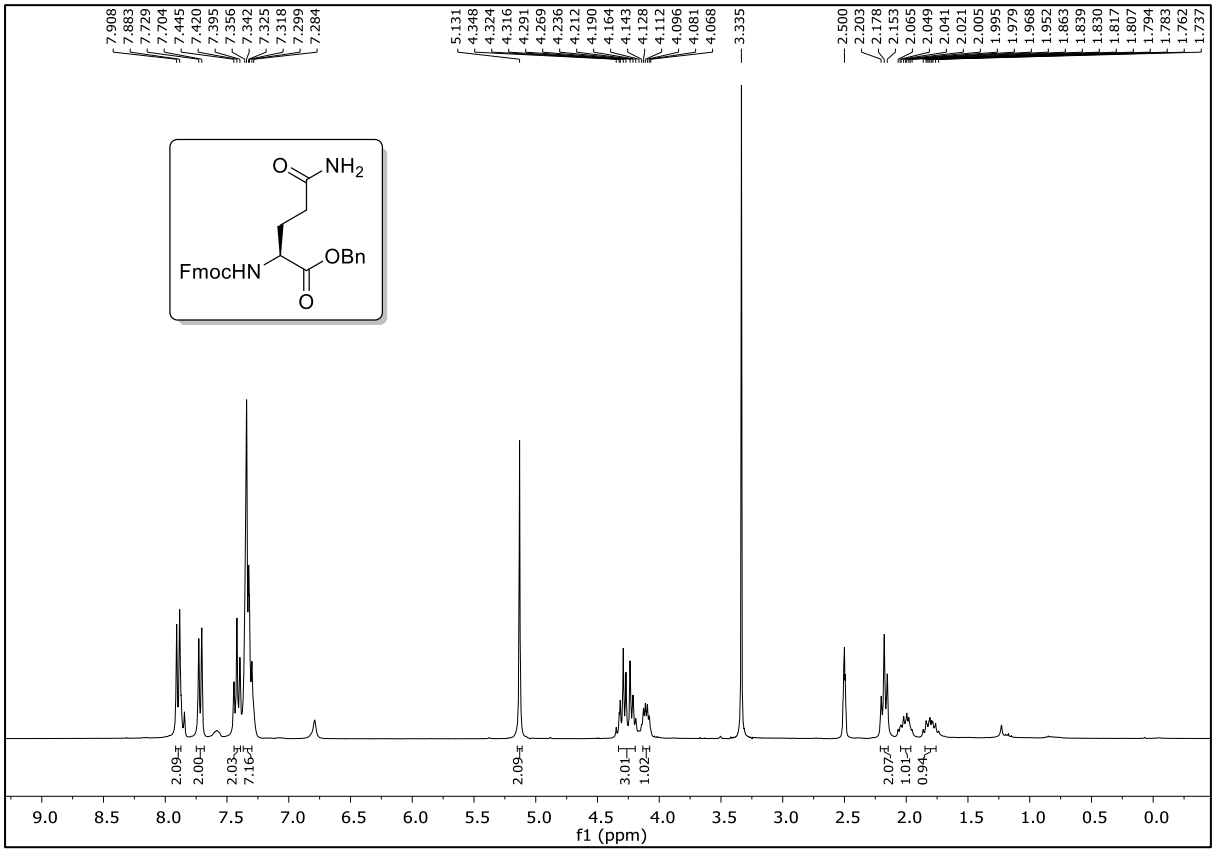
[1]H-NMR spectrum of diastereomer of alveolaride C (3a) [300 MHz, DMSO-*d*6]:



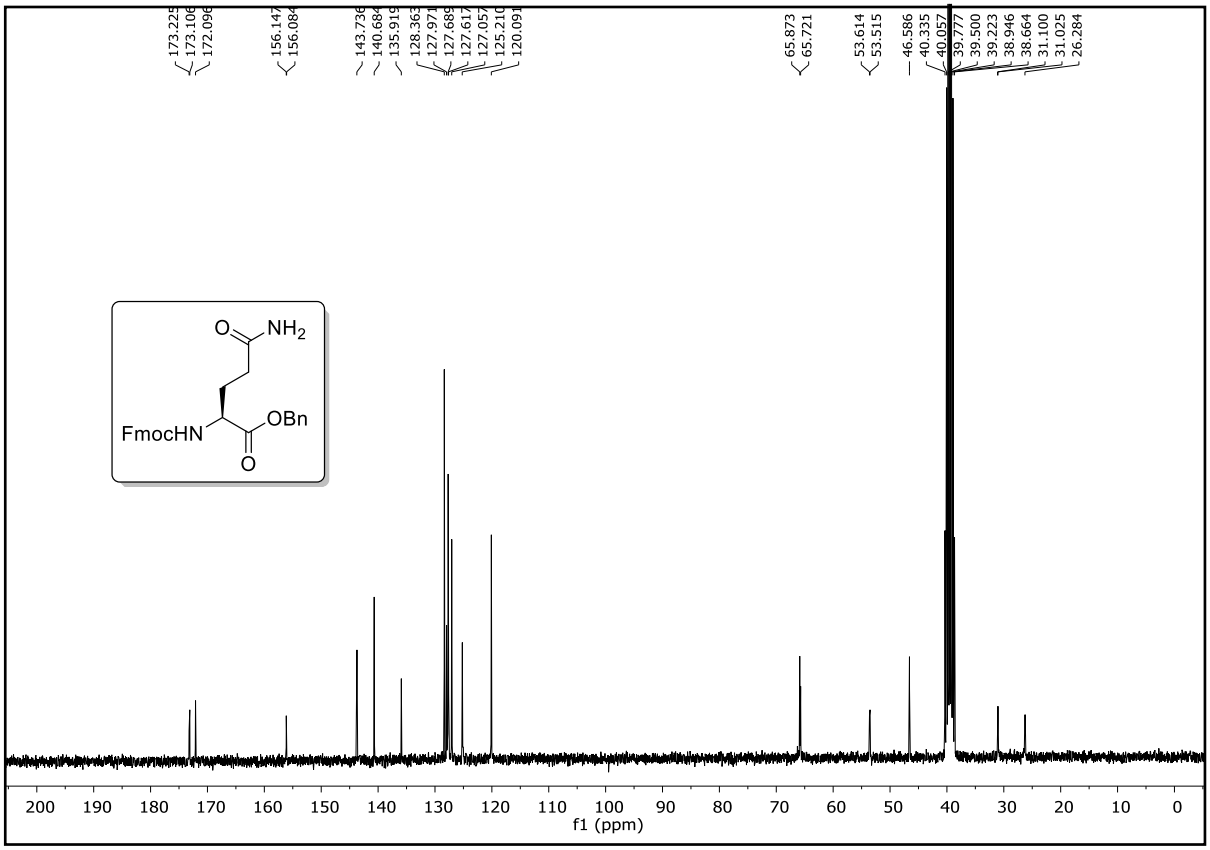
[13]C-NMR spectrum of diastereomer of alveolaride C (3a) (75 MHz, DMSO-*d*6):



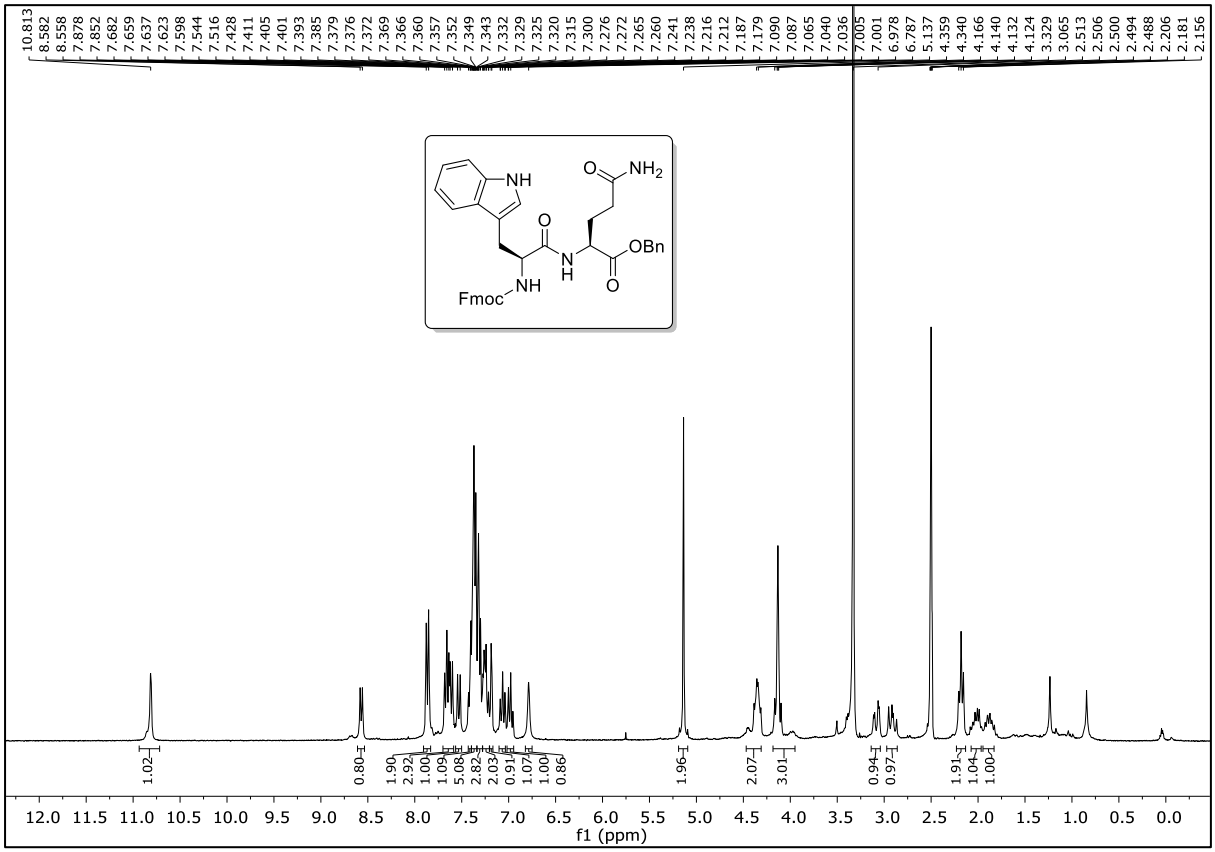
^{1}H-NMR spectrum of compound 41a (300 MHz, DMSO-*d*$_6$):



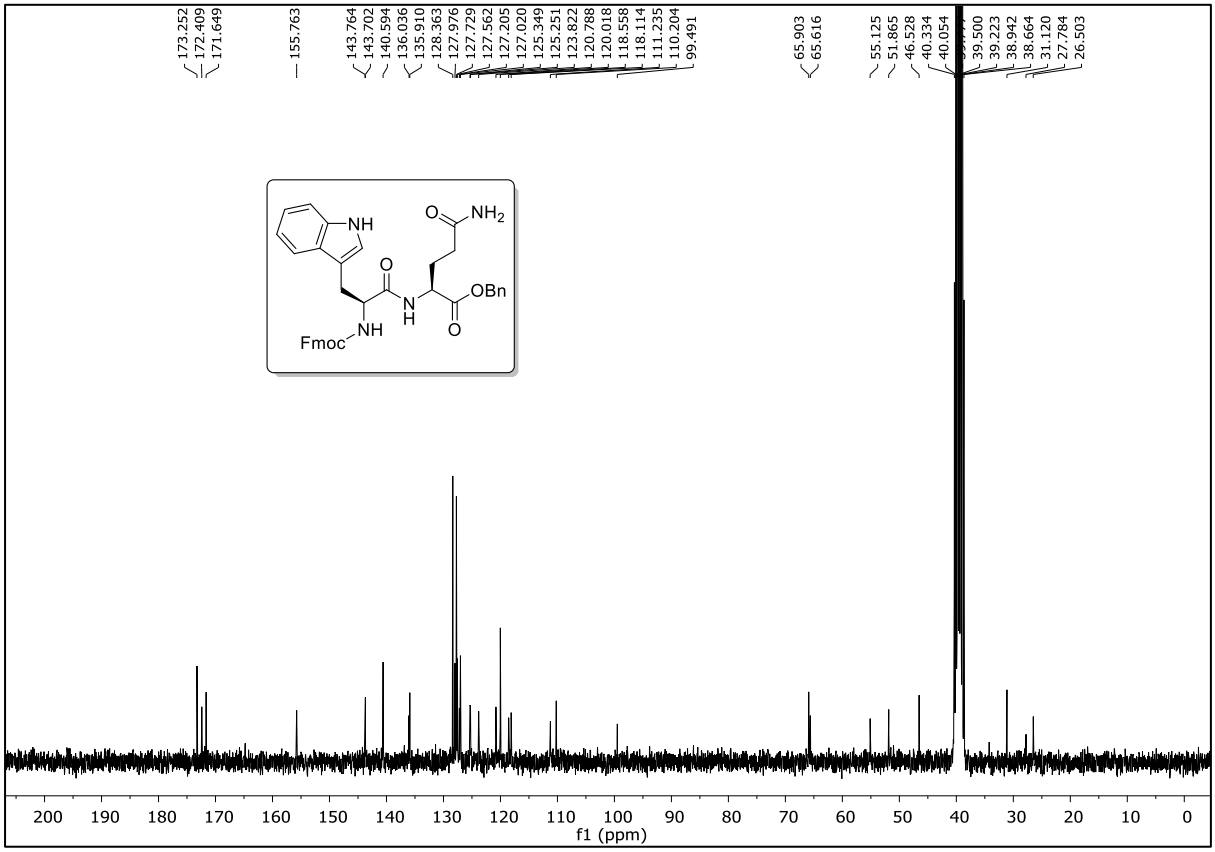
^{13}C-NMR spectrum of compound 41a (75 MHz, DMSO-*d*$_6$):



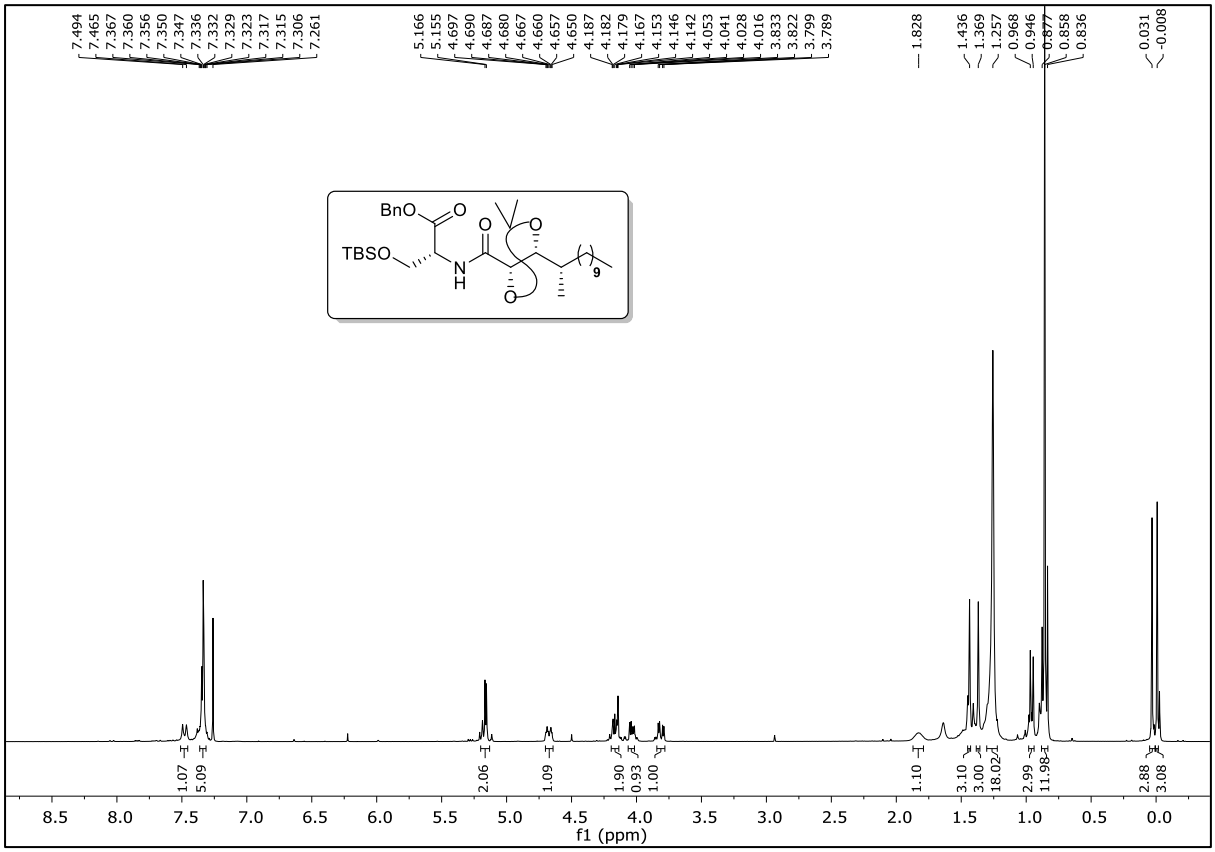
^{1}H-NMR spectrum of intermediate of compound 42 (300 MHz, DMSO-d_6):



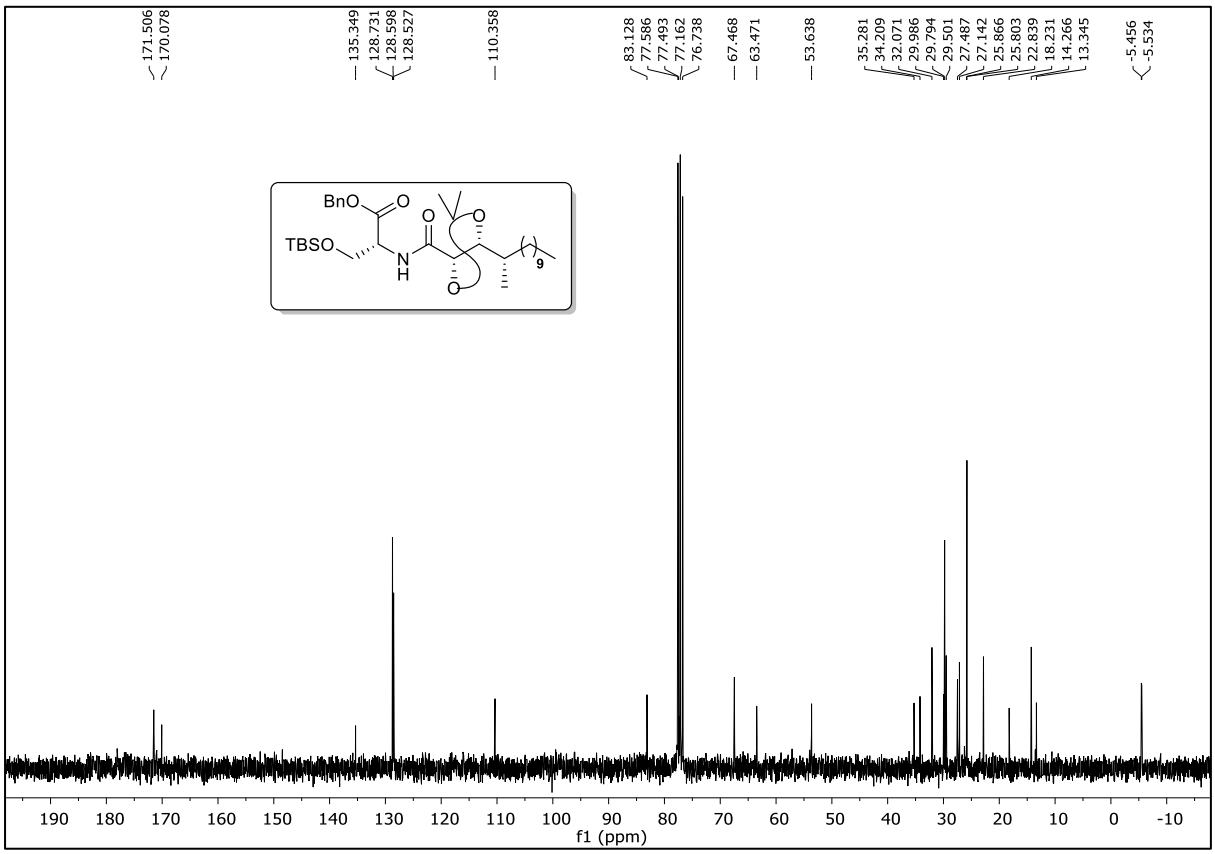
^{13}C-NMR spectrum of intermediate of compound 42 (75 MHz, DMSO-d_6):



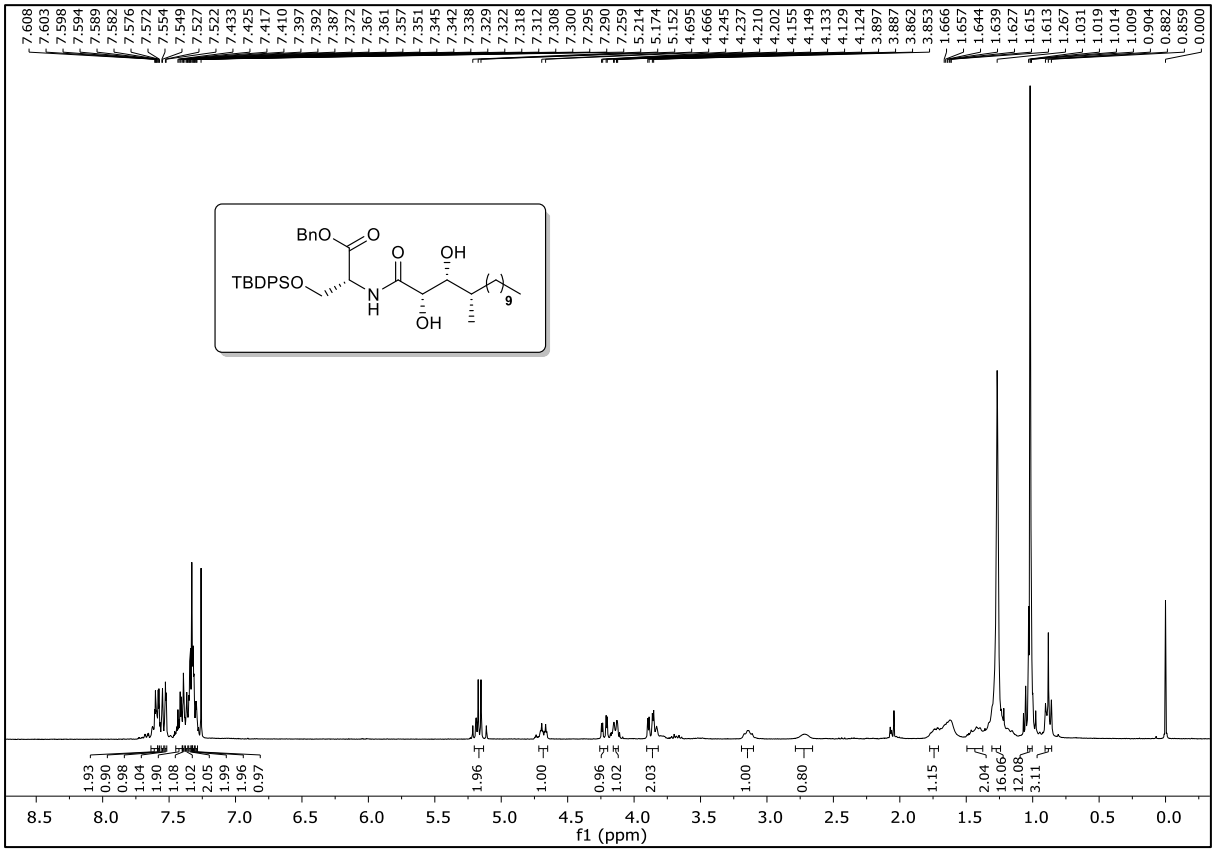
^{1}H-NMR spectrum of compound 38 (300 MHz, $CDCl_3$):



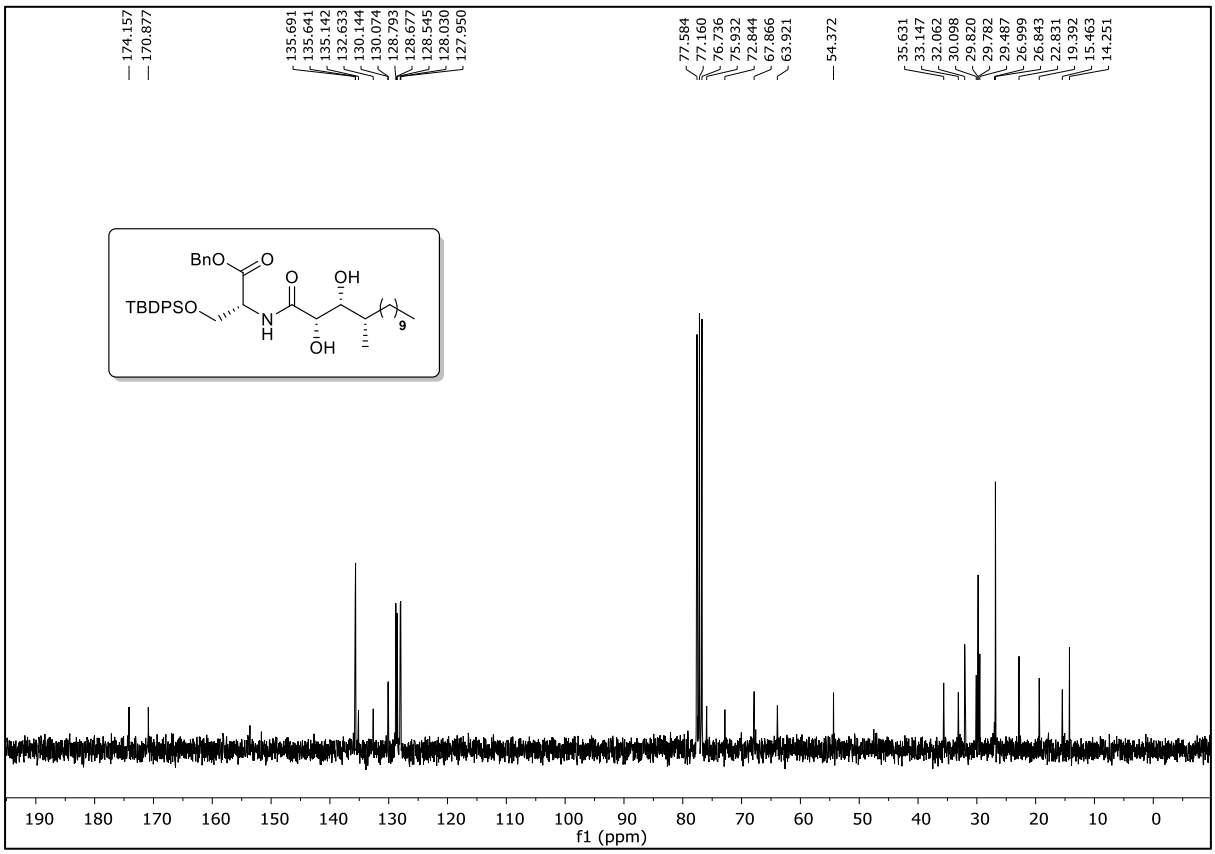
^{13}C-NMR spectrum of compound 38 (75 MHz, $CDCl_3$):



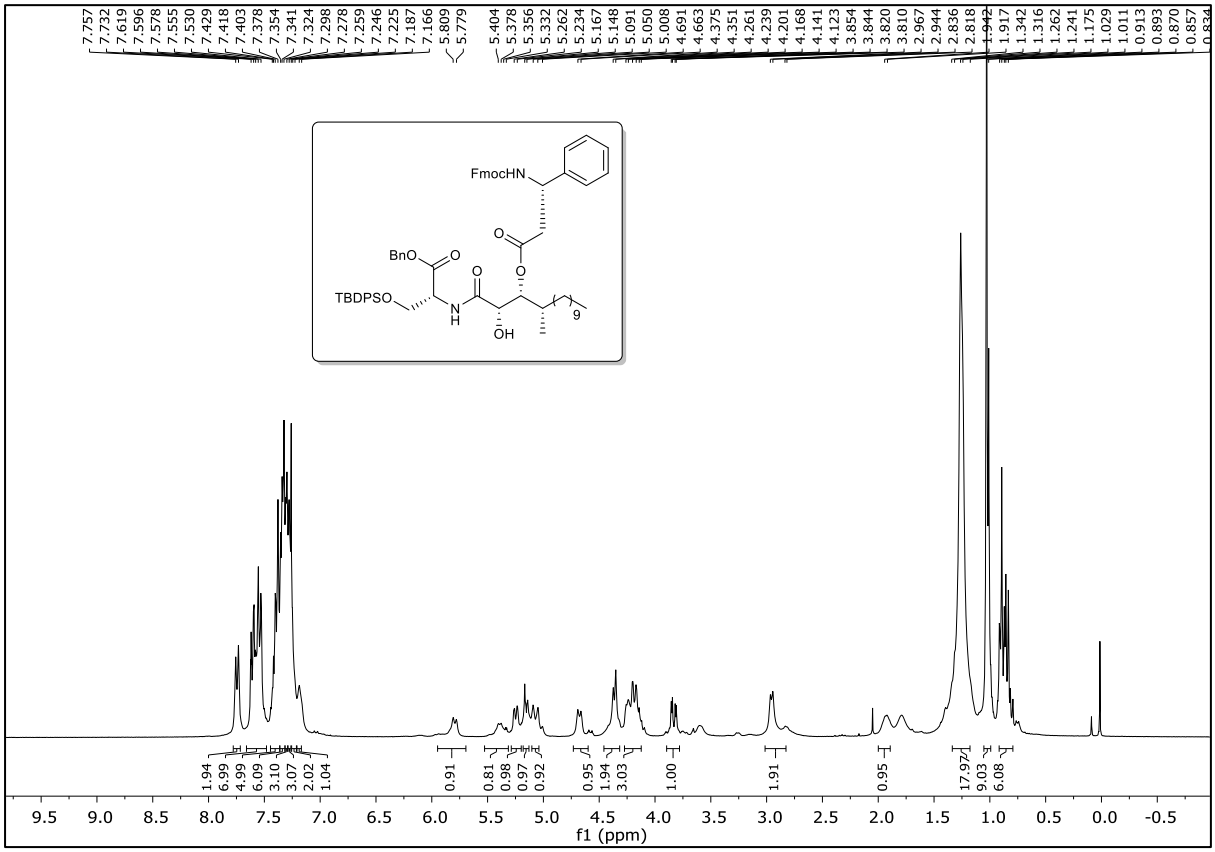
^{1}H-NMR spectrum of compound 39 (300 MHz, $CDCl_3$):



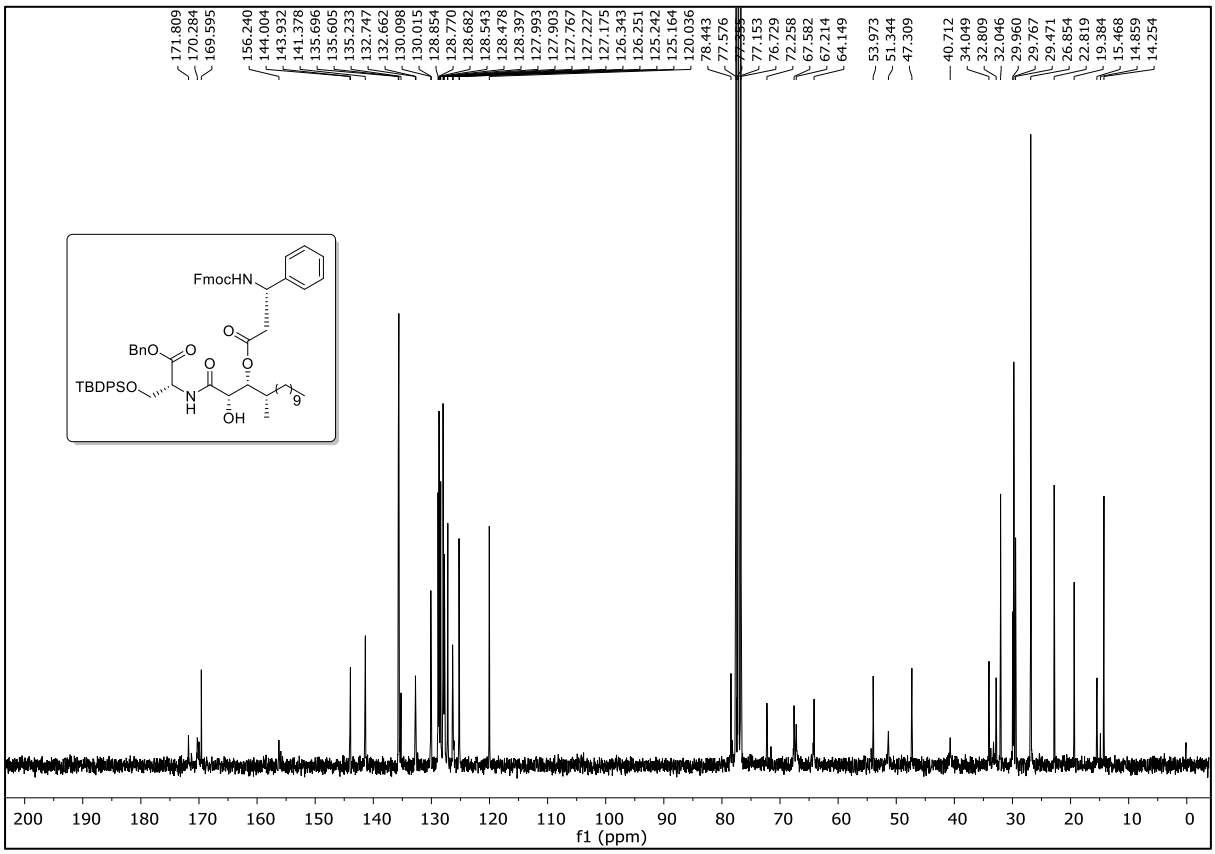
^{13}C-NMR spectrum of compound 39 (75 MHz, $CDCl_3$):



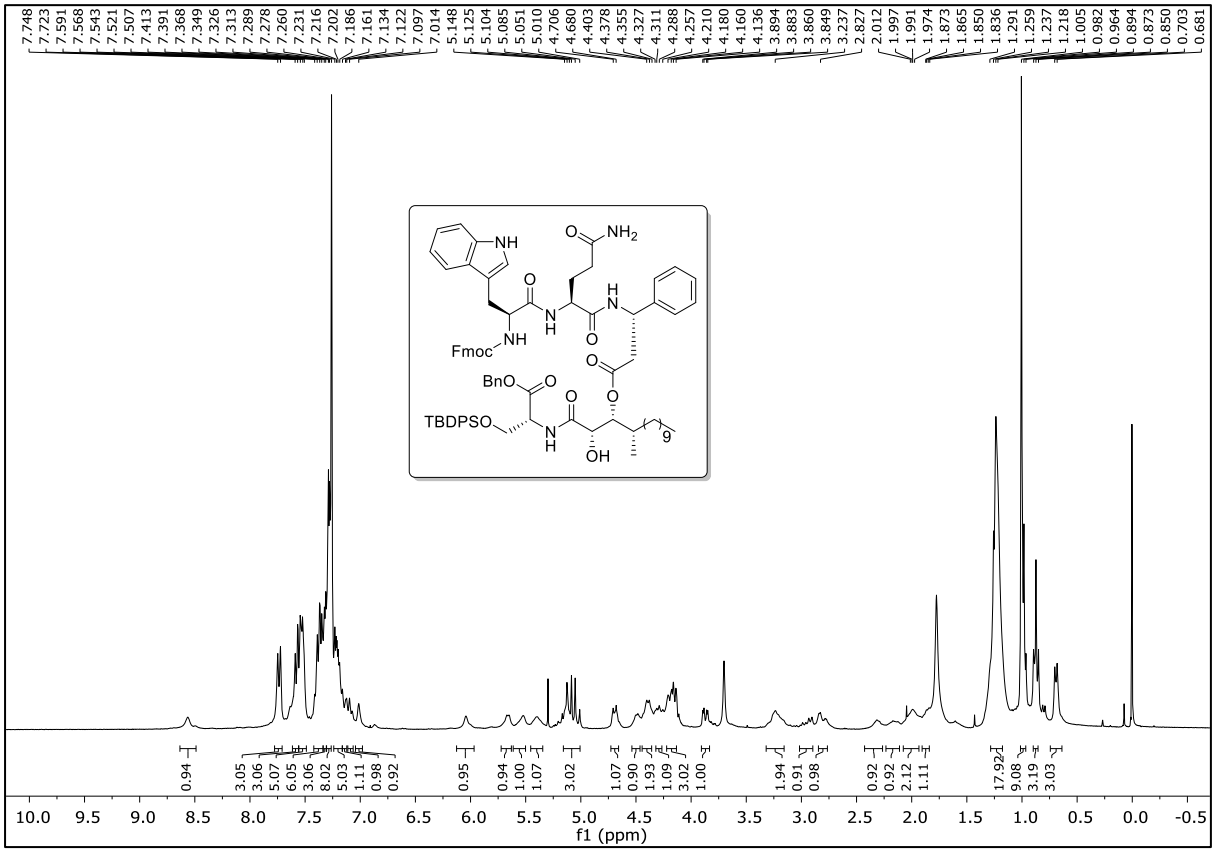
^{1}H-NMR spectrum of compound 40 (300 MHz, $CDCl_3$):



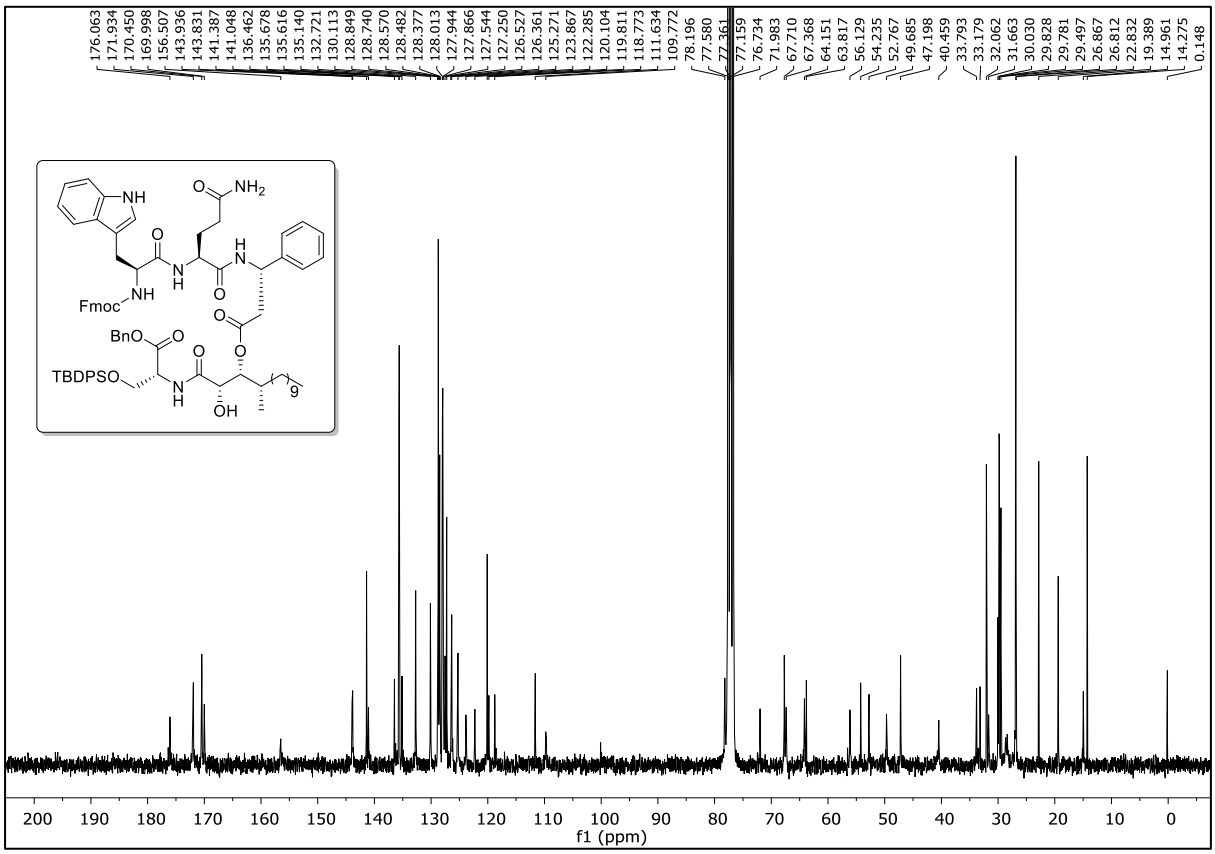
^{13}C-NMR spectrum of compound 40 (75 MHz, $CDCl_3$):



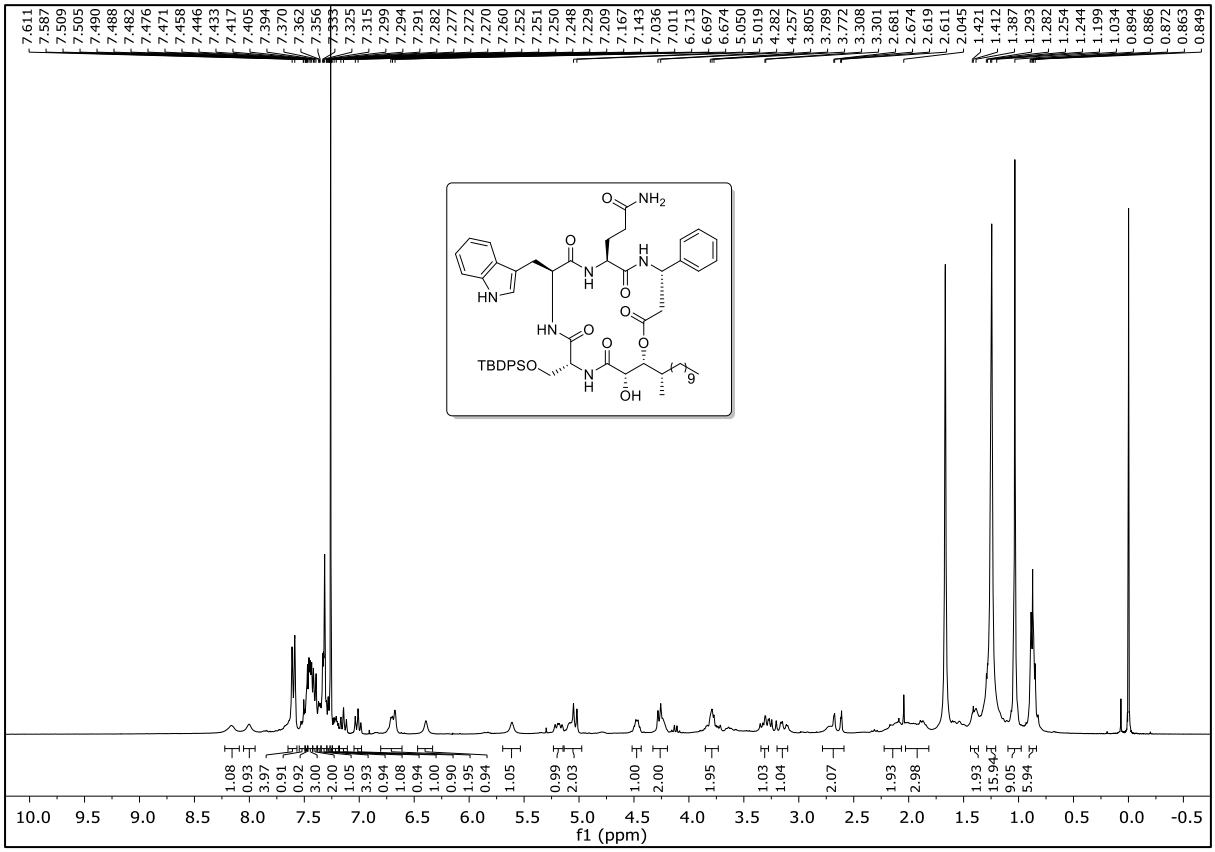
^{1}H-NMR spectrum of compound 43 (300 MHz, $CDCl_3$):



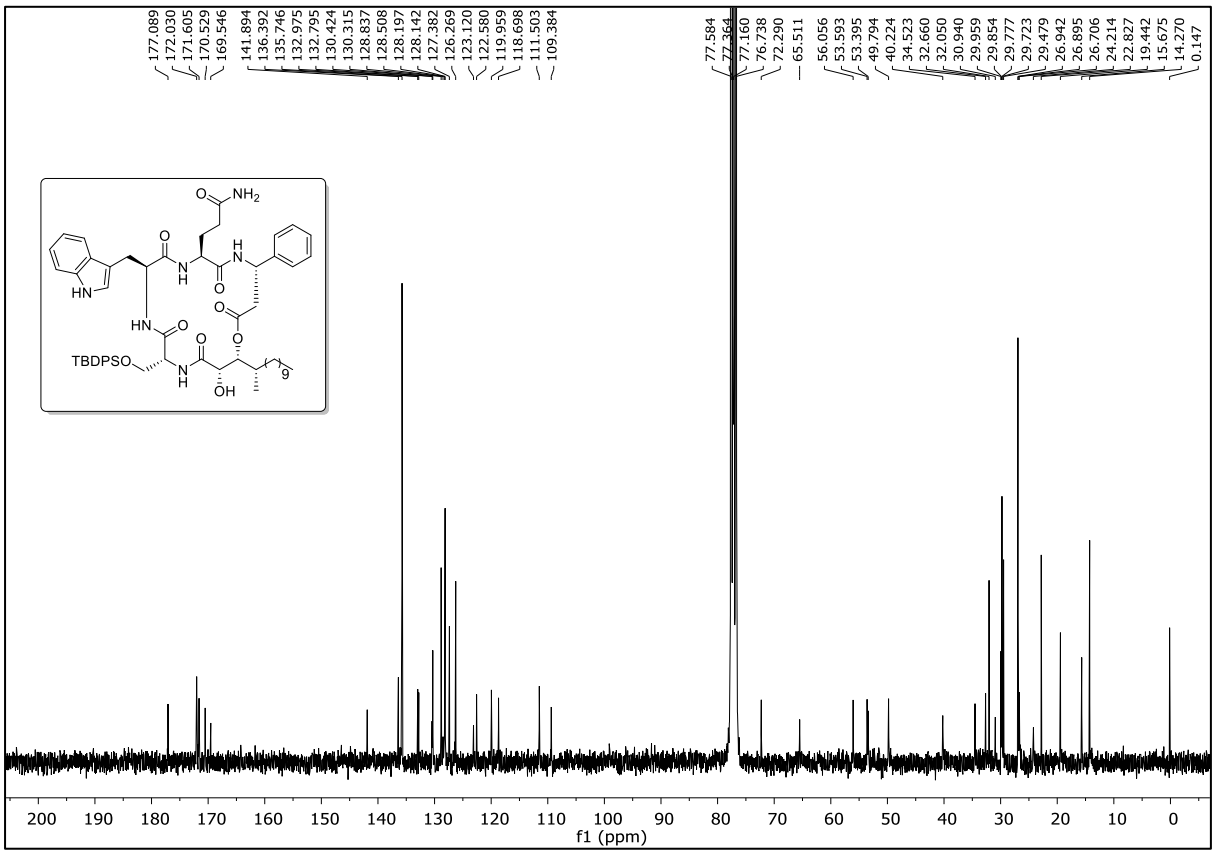
^{13}C-NMR spectrum of compound 43 (75 MHz, $CDCl_3$):



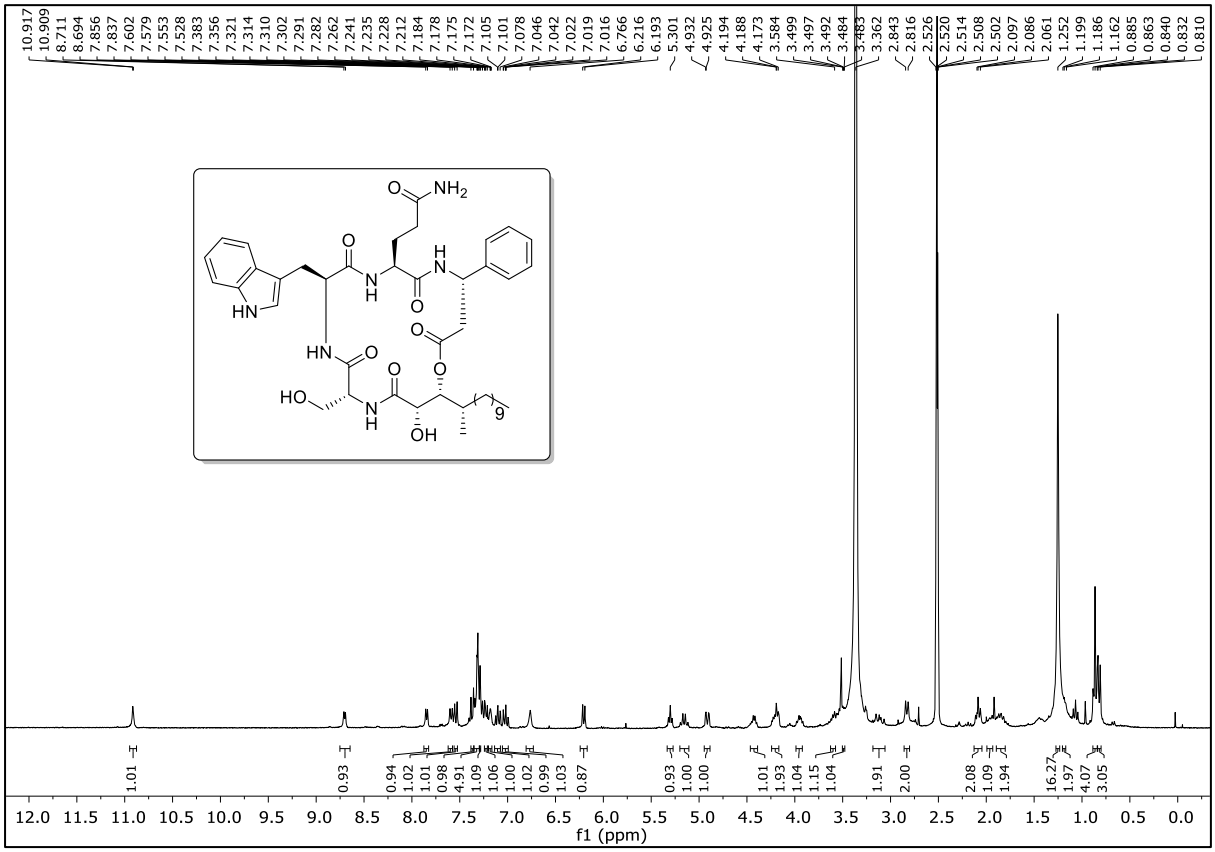
^{1}H-NMR spectrum of intermediate of compound 3b (300 MHz, $CDCl_3$):



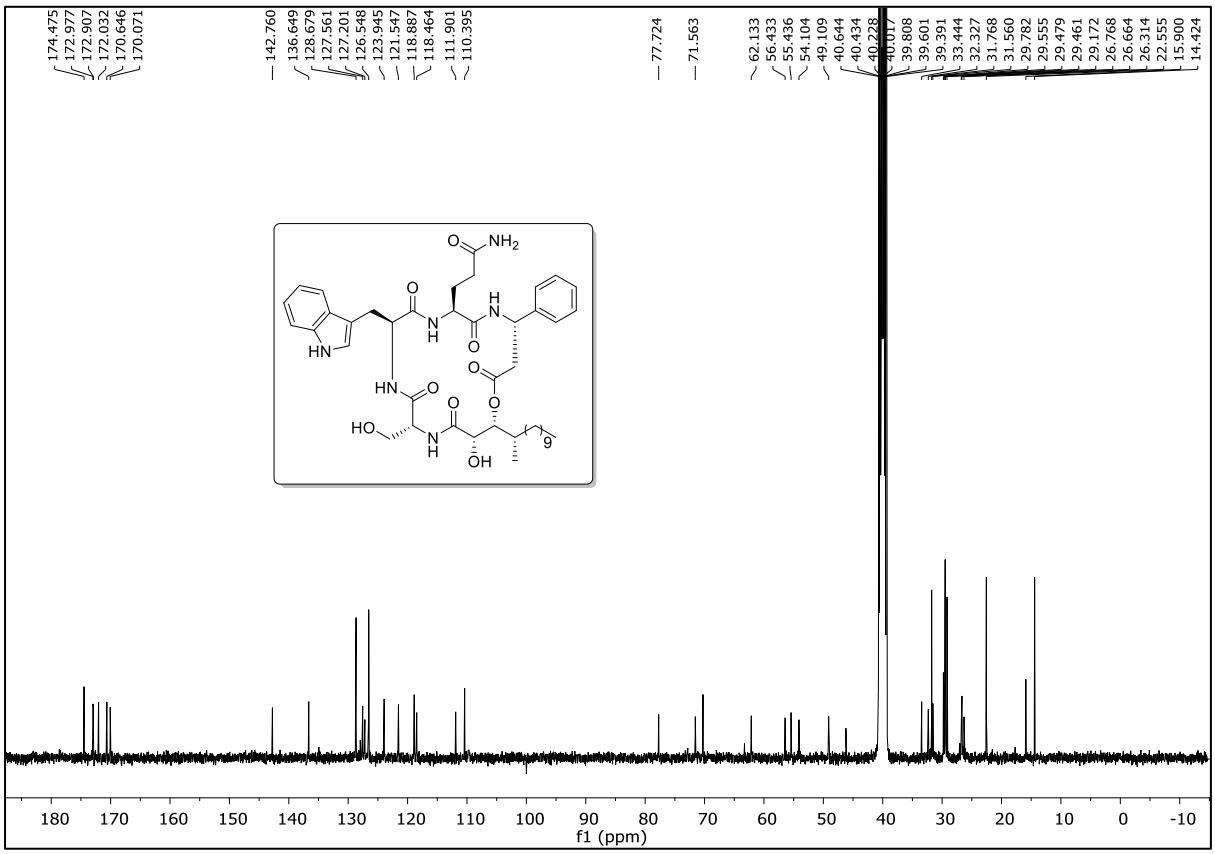
^{13}C-NMR spectrum of intermediate of compound 3b (75 MHz, $CDCl_3$):



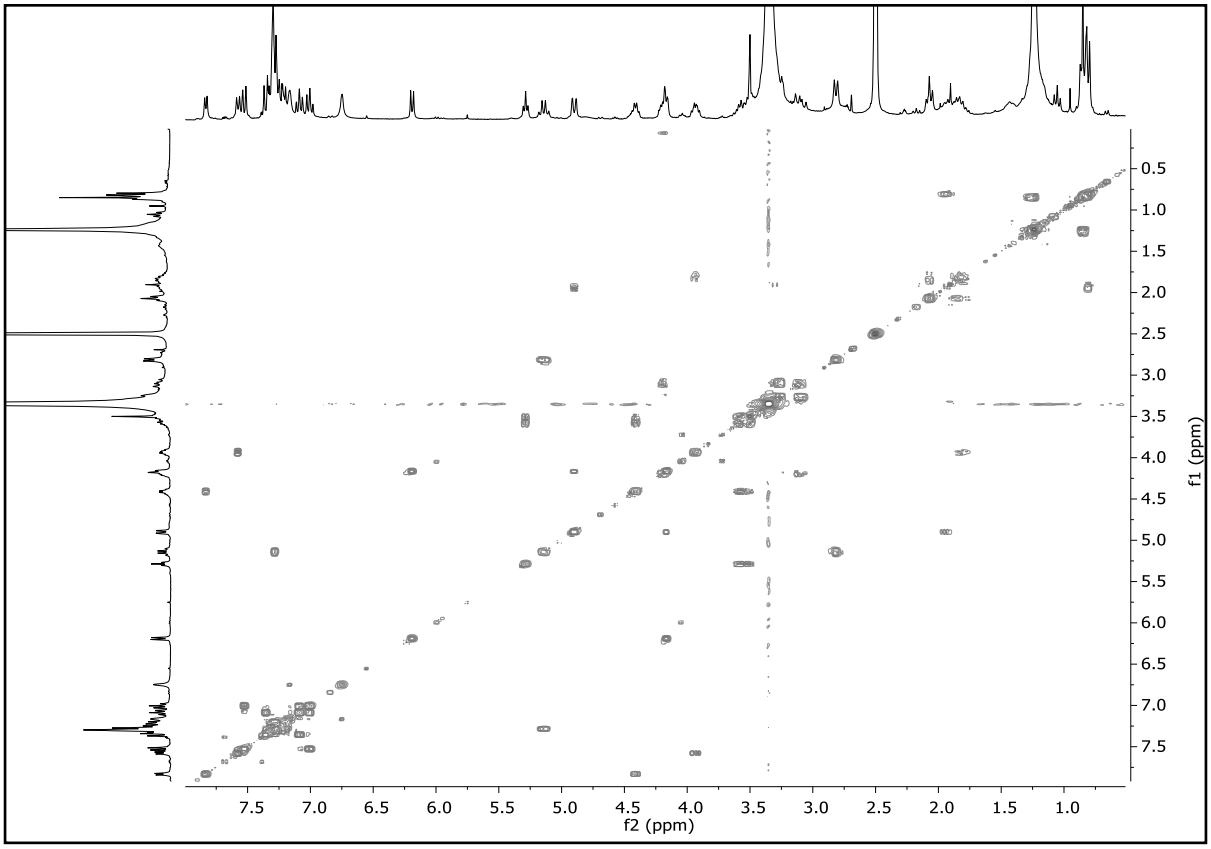
^{1}H-NMR spectrum of diastereomer of alveolaride C (3b) (300 MHz, DMSO-d_6):



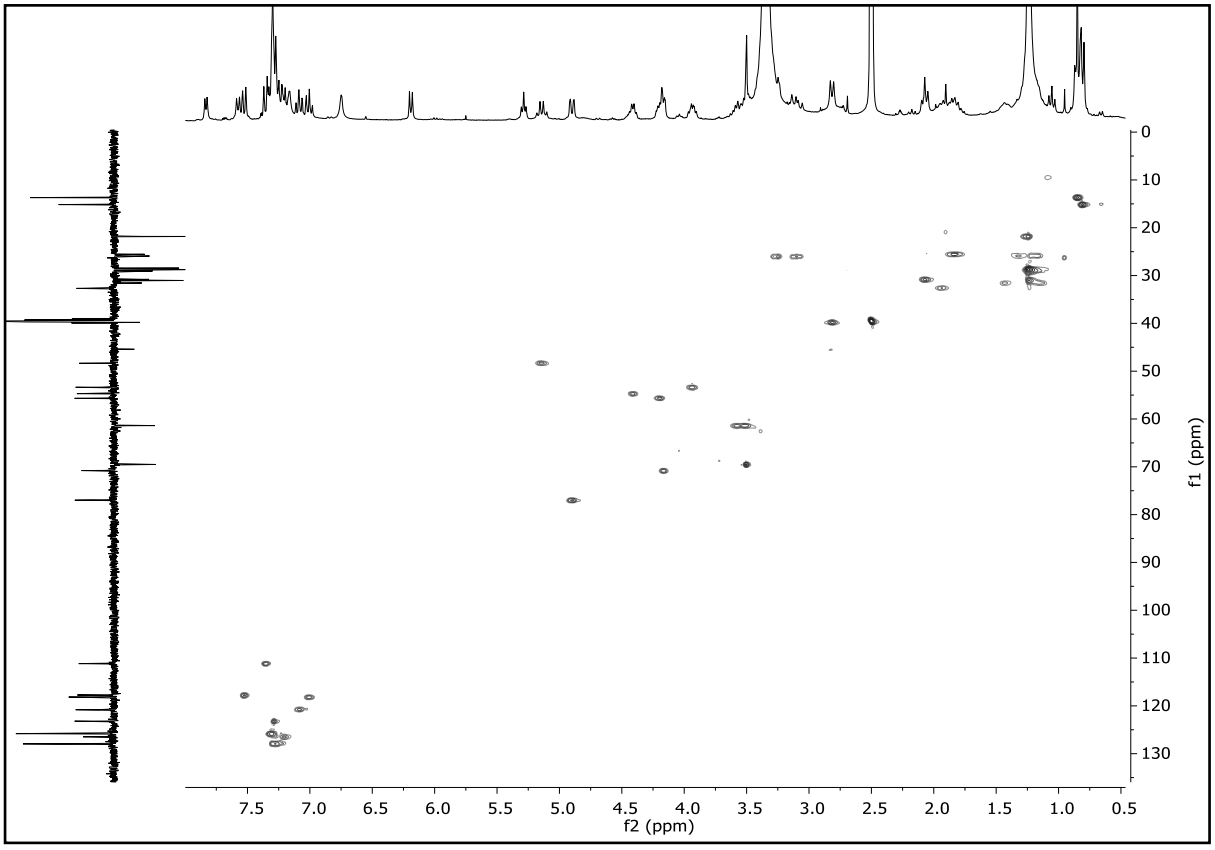
^{13}C-NMR spectrum of diastereomer of alveolaride C (3b) (75 MHz, DMSO-d_6):



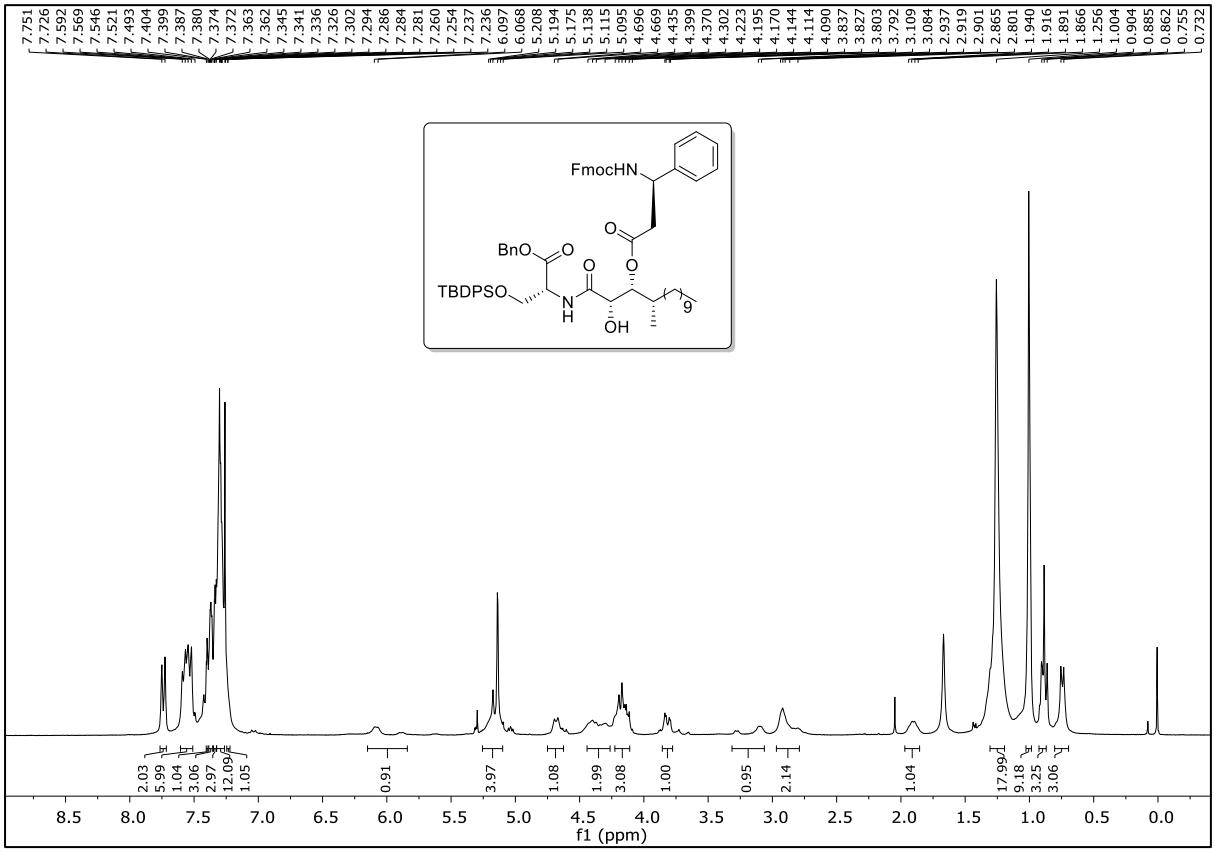
COSY spectrum of diastereomer of alveolaride C (3b) (100 MHz, DMSO-d_6):



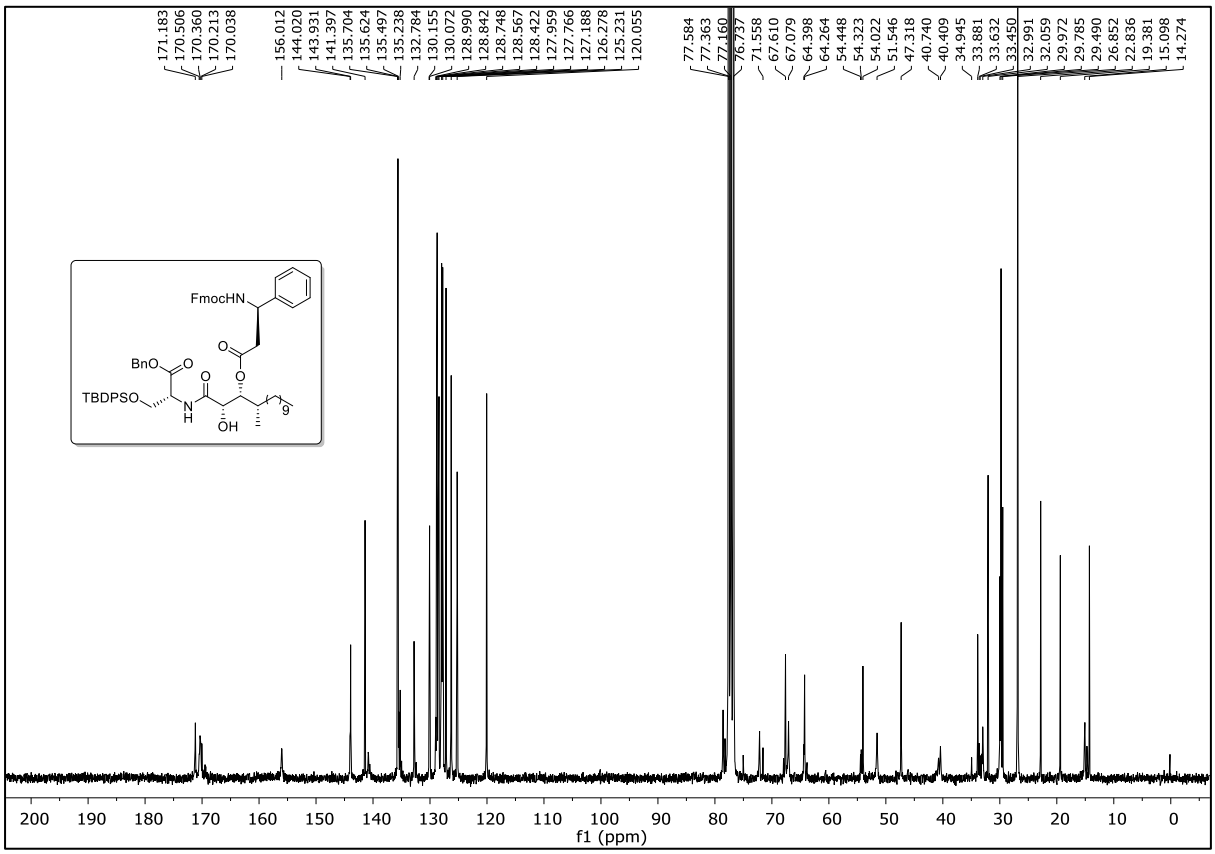
HSQC spectrum of diastereomer of alveolaride C (3b) (100 MHz, DMSO-d_6):



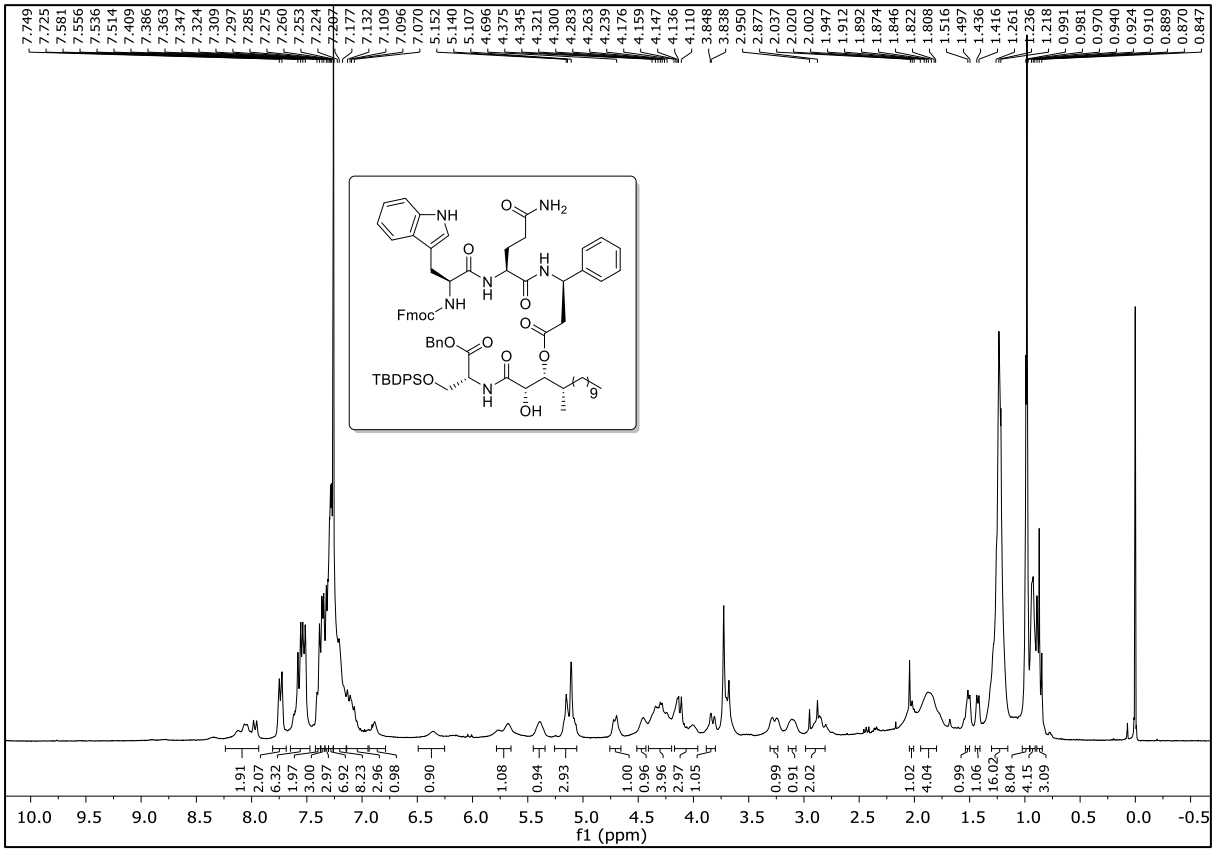
^{1}H-NMR spectrum of compound *epi*-40 (300 MHz, $CDCl_3$):



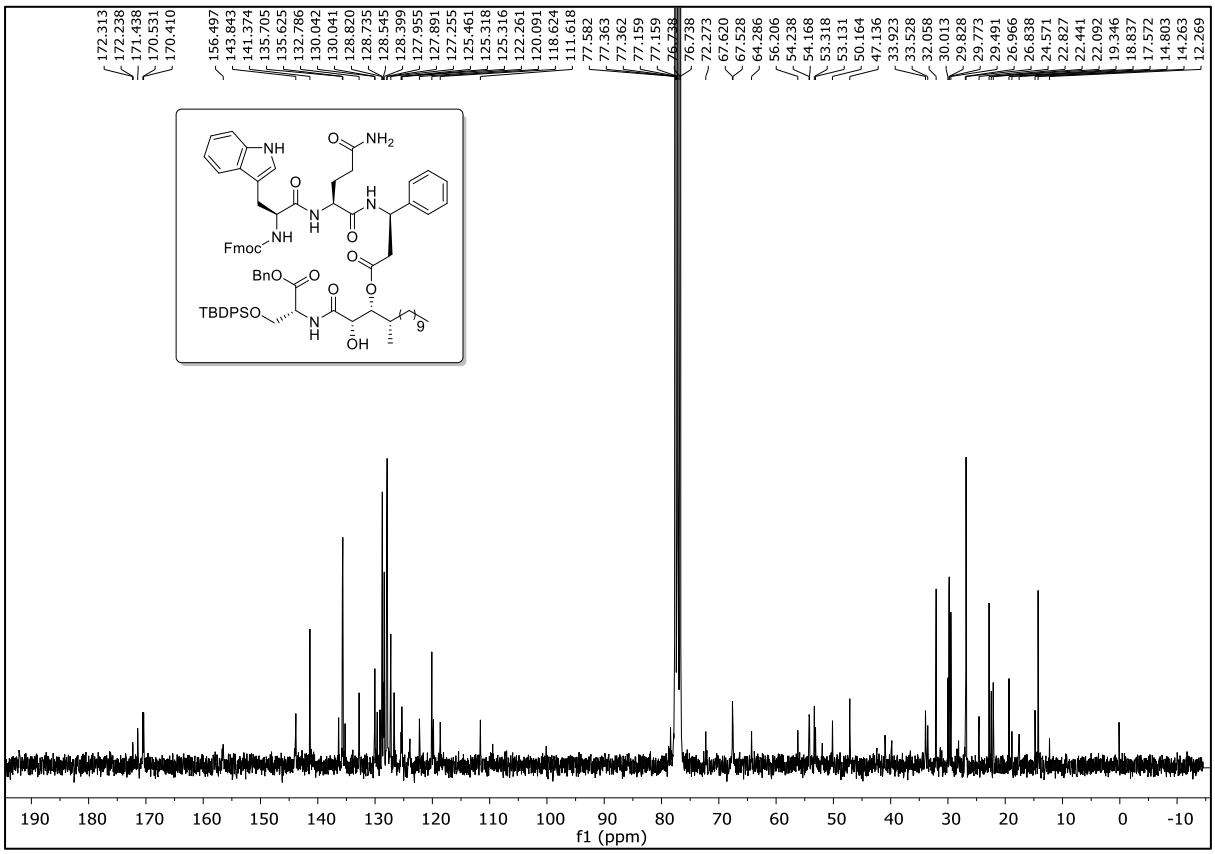
^{13}C-NMR spectrum of compound *epi*-40 (75 MHz, $CDCl_3$):



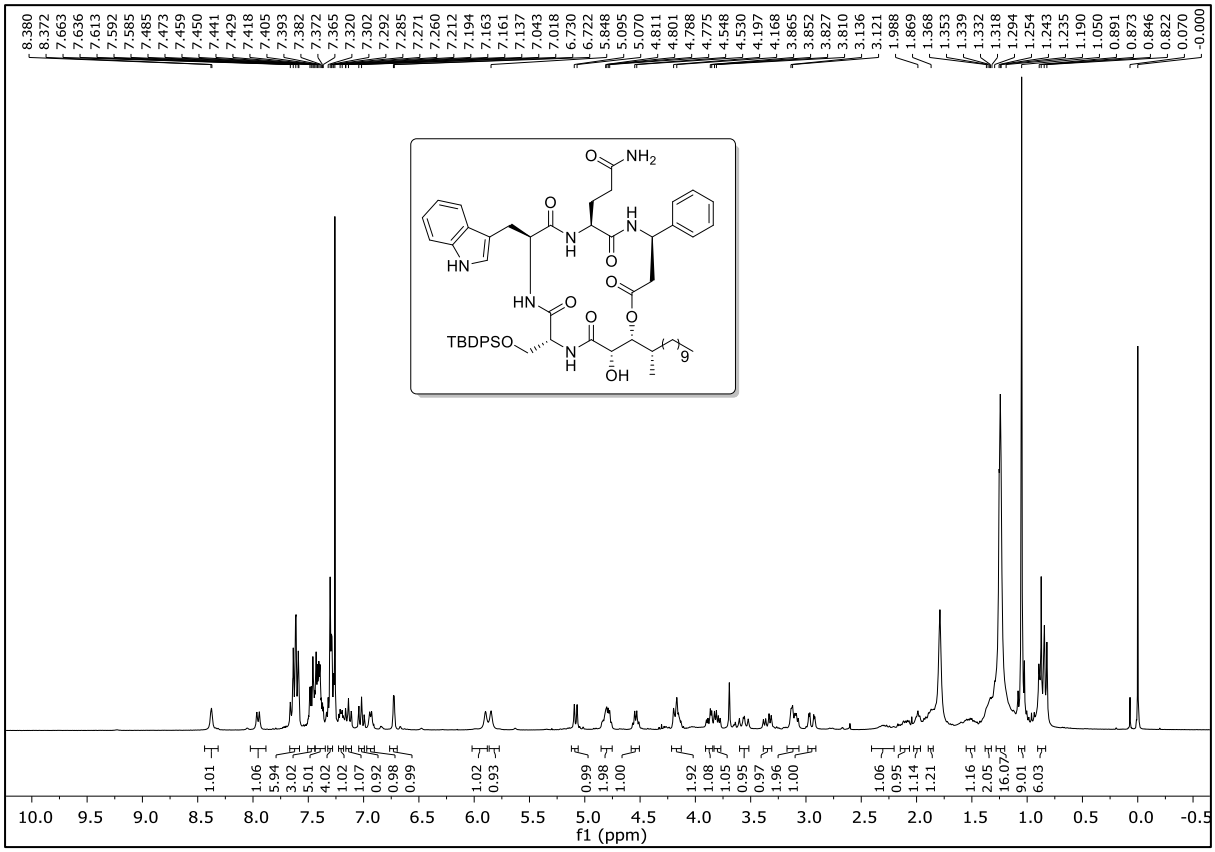
^{1}H-NMR spectrum of compound *epi*-43 (300 MHz, $CDCl_3$):



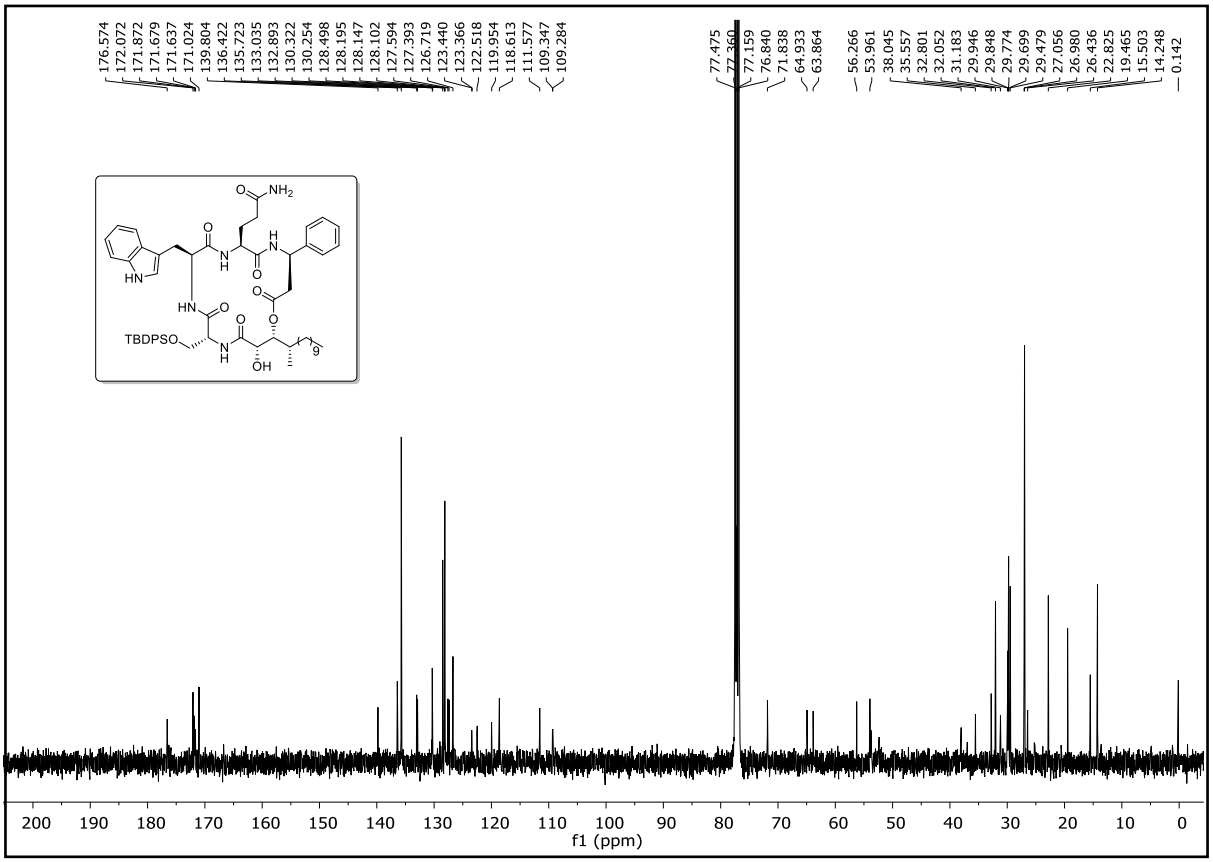
^{13}C-NMR spectrum of compound *epi*-43 (75 MHz, $CDCl_3$):



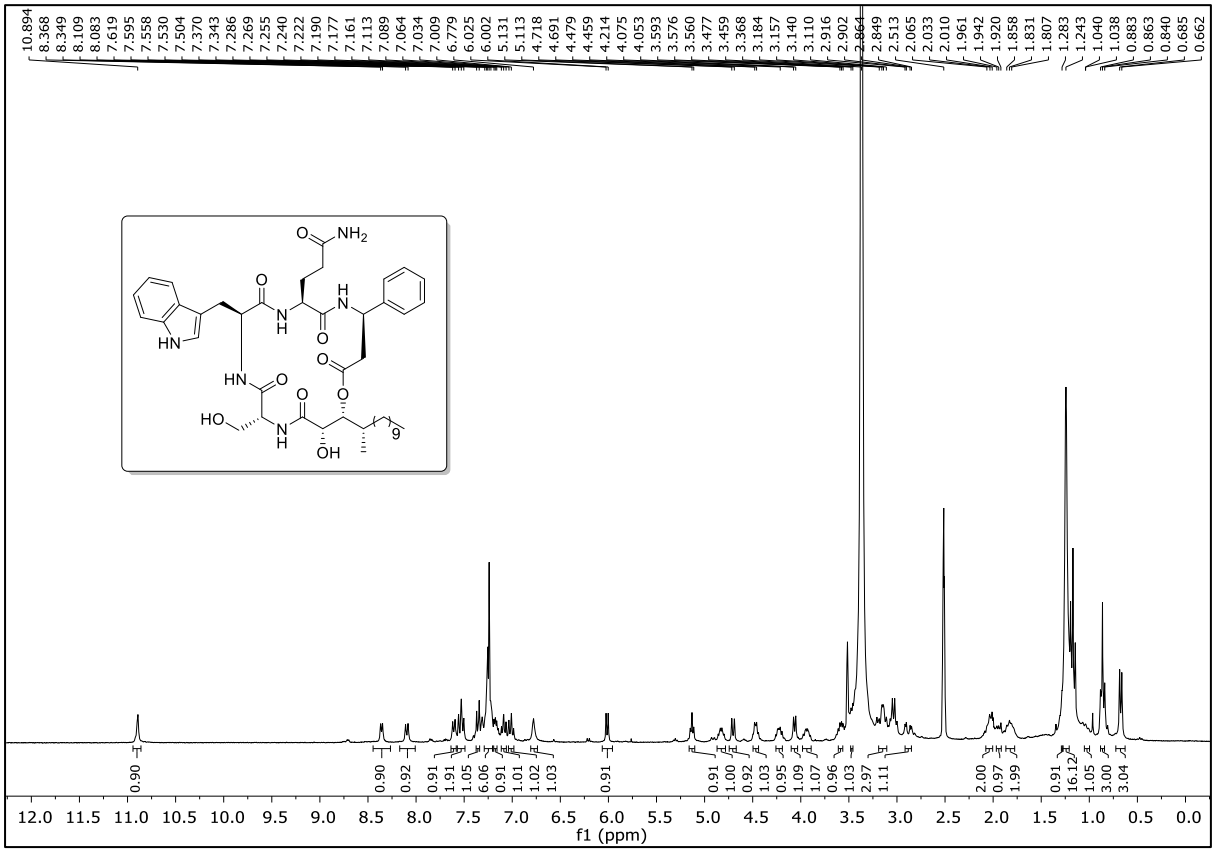
^{1}H-NMR spectrum of intermediate of compound *epi*-3b (300 MHz, $CDCl_3$):



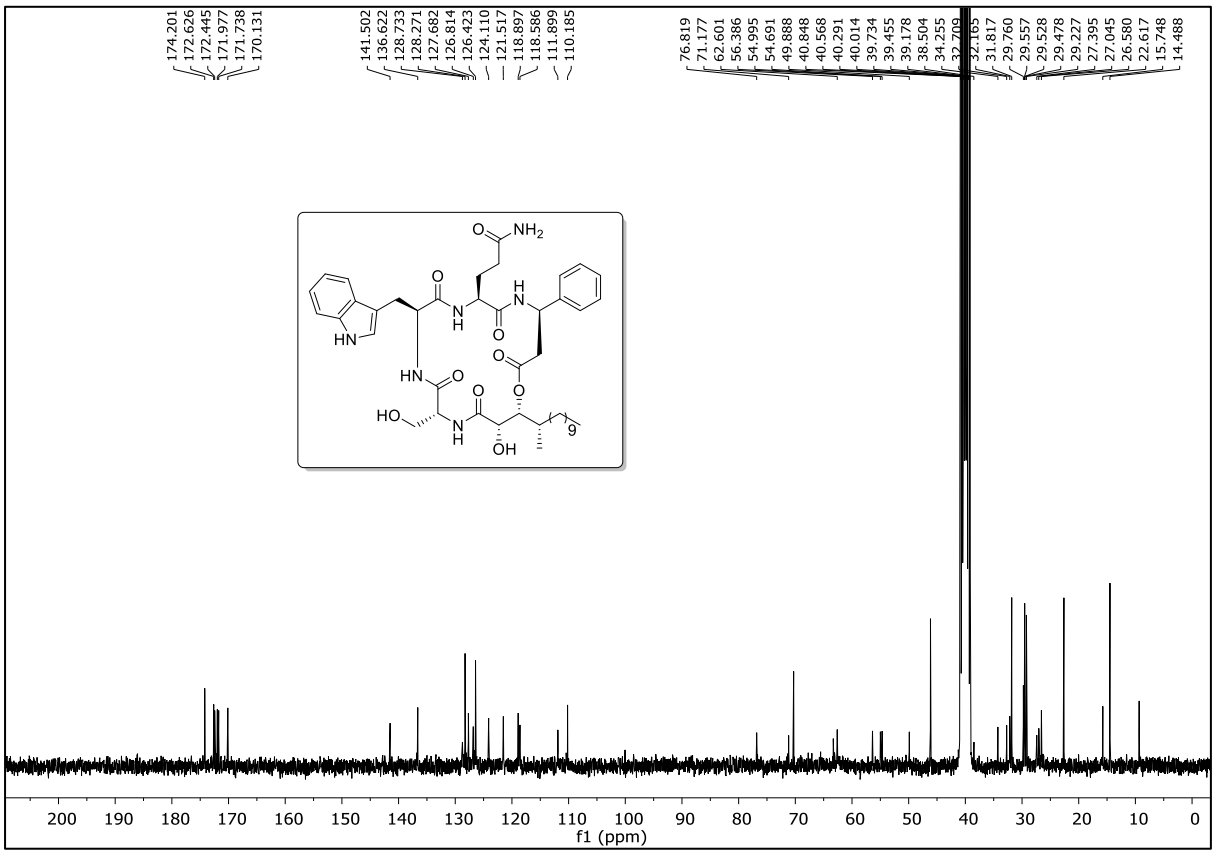
^{13}C-NMR spectrum of intermediate of compound *epi*-3b (100 MHz, $CDCl_3$):

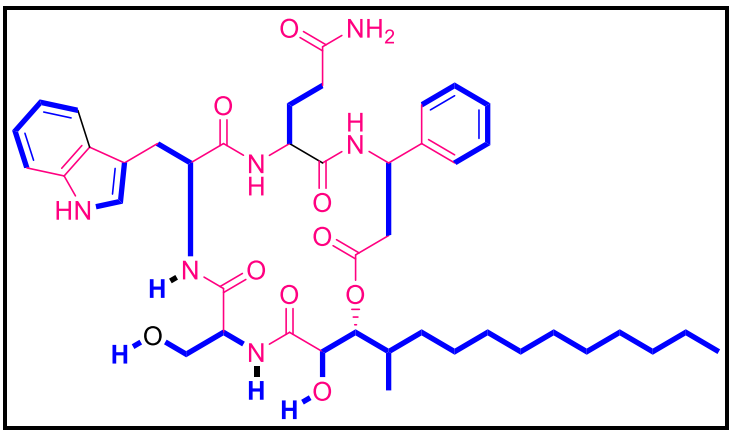


^{1}H-NMR spectrum of actual alveolaride C (*epi*-3b) (300 MHz, DMSO-d_6):



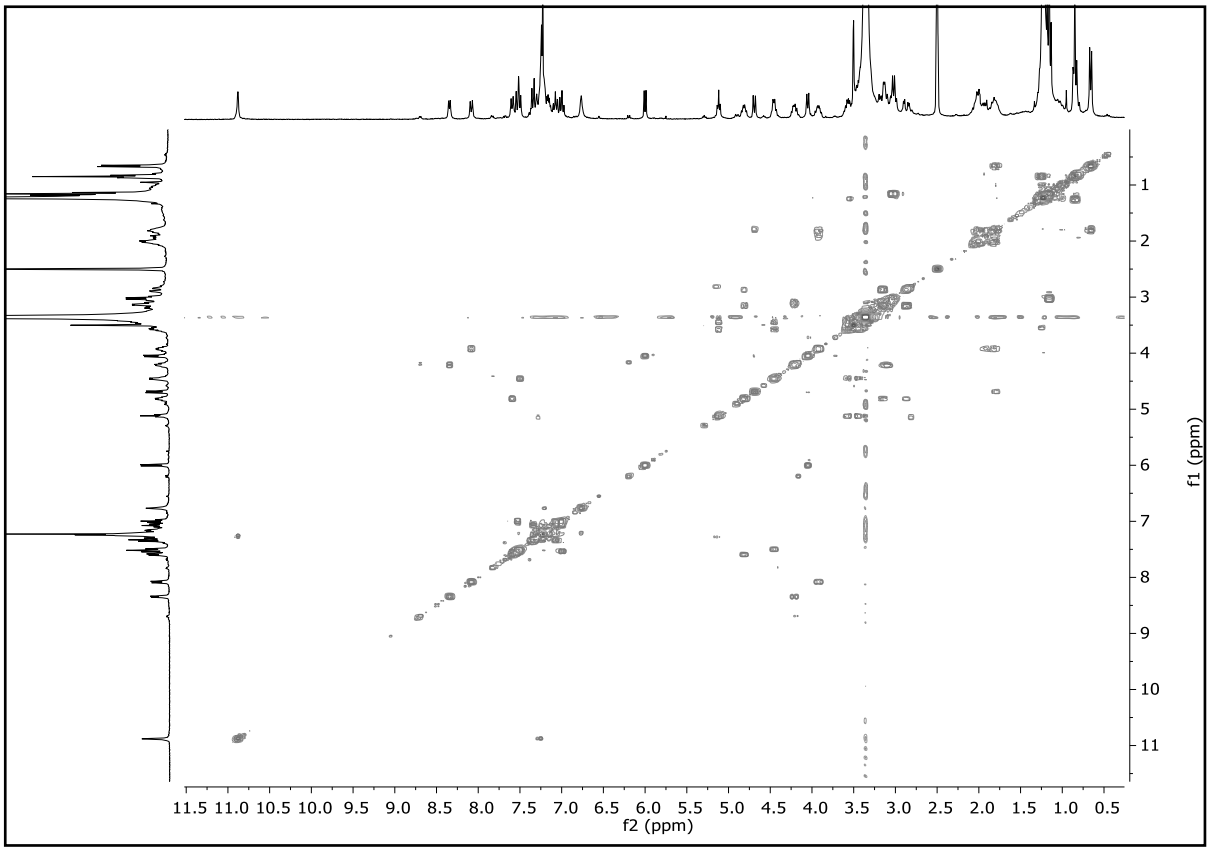
^{13}C-NMR spectrum of actual alveolaride C (*epi*-3b) (100 MHz, DMSO-d_6):



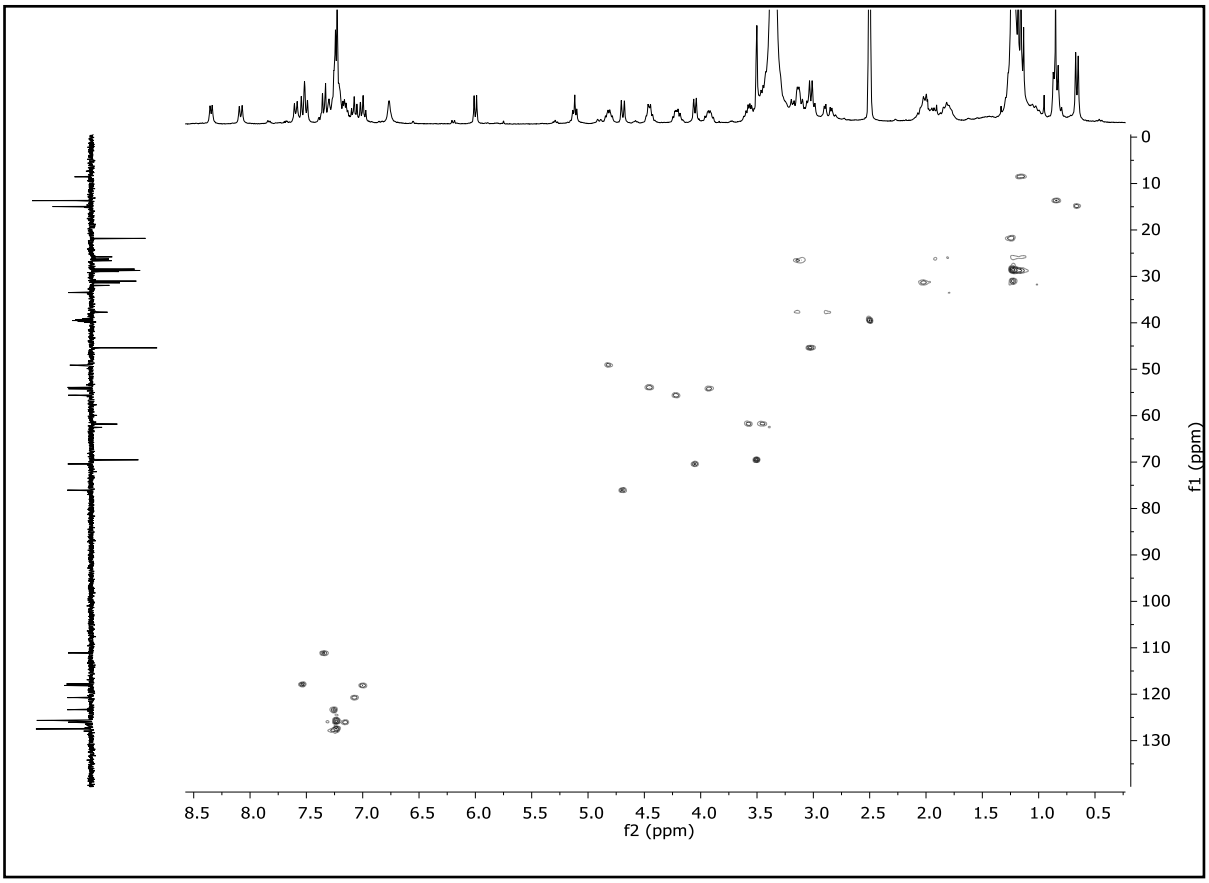


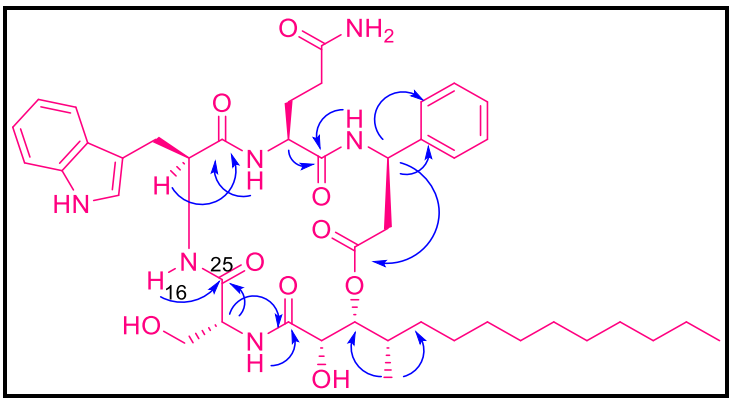
Selected COSY correlations in compound ***epi*-3b**.

COSY spectrum of actual alveolaride C (*epi*-3b) (100 MHz, DMSO-d_6):



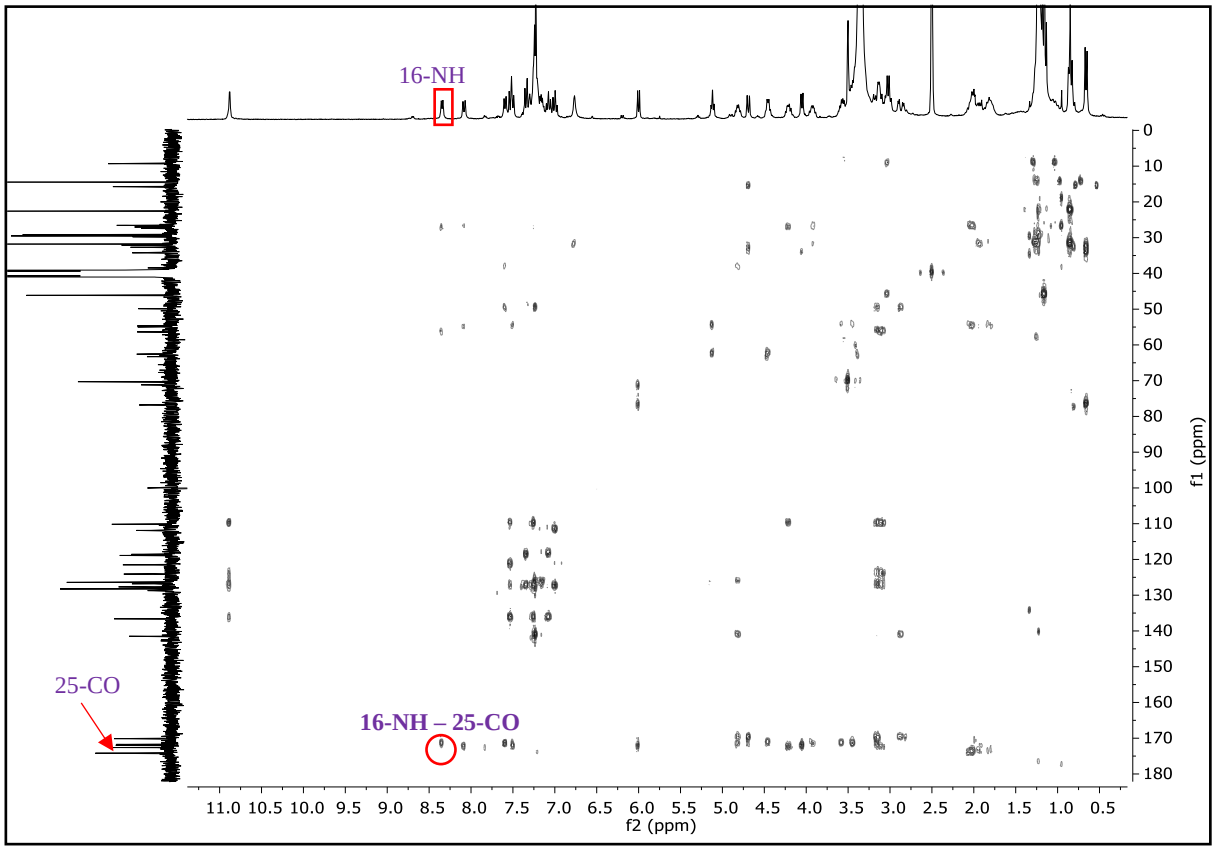
HSQC spectrum of actual alveolaride C (*epi*-3b) (100 MHz, DMSO-d_6):

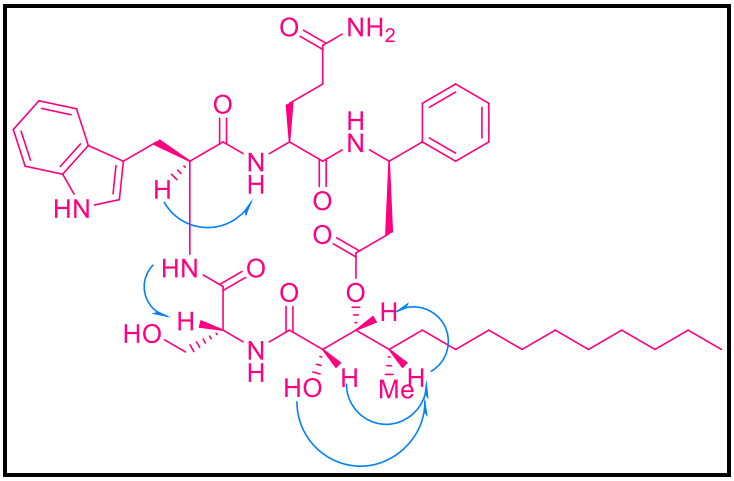




Selected HMBC correlations in compound ***epi*-3b**.

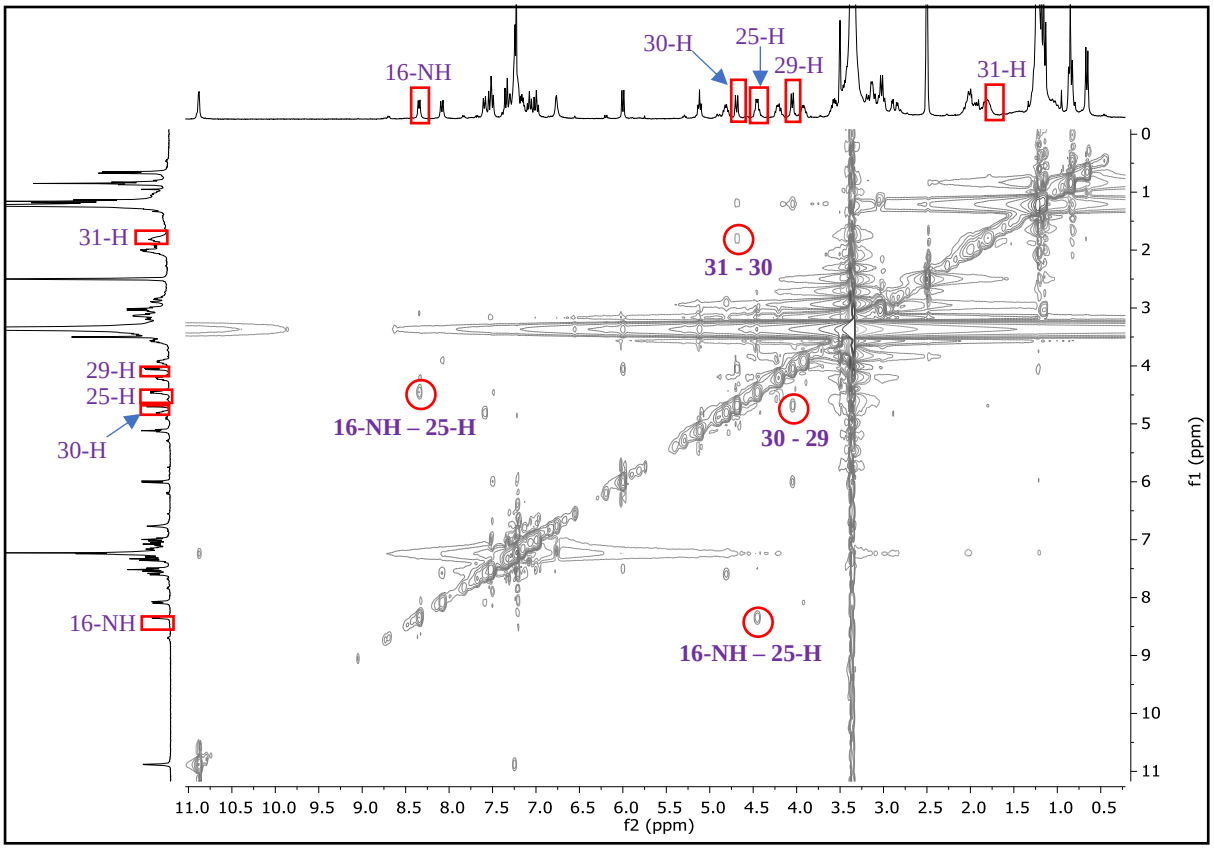
HMBC spectrum of actual alveolaride C (*epi*-3b) (125 MHz, DMSO-d_6):





Selected NOESY correlations in compound ***epi*-3b**.

NOESY spectrum of actual alveolaride C (*epi*-3b) (75 MHz, DMSO-d_6):



HRMS spectrum of actual alveolaride C (*epi*-3b):