Total Synthesis and Stereochemical Assignment of Bipolamide A Acetate

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1. Comparison Tables of ^{1}H And ^{13}C NMR of Reported Bipolamide A Acetaete With Synthetic Compounds 3a and 3b:

Table S1. ^{1}H NMR Comparison of Reported Bipolamide A Acetate With Synthetic Compounds 3a and 3b.

^{1}H			
Position	Reported	Synthetic Compound **3a**	Synthetic Compound **3b**
2	5.74 (d, *J* = 15.0 Hz)	5.74 (d, *J* = 14.7 Hz)	5.74 (d, *J* = 15.0 Hz)
3	7.22 (dd, *J* = 11.4, 15.0Hz)	7.23 (dd, *J* = 11.1, 15.0Hz)	7.23 (dd, *J* = 11.1, 15.0Hz)
4	6.17 (dd, *J* = 11.4, 15.6Hz)	6.17 (dd, *J* = 15.3, 11.1 Hz)	6.17 (dd, *J* = 15.0, 11.1 Hz)
5	6.53 (d, *J* = 15.6 Hz)	6.54 (d, *J* = 15.3 Hz)	6.54 (d, *J* = 15.3 Hz)
7	5.45 (d, *J* = 10.2 Hz)	5.45 (d, *J* = 9.7 Hz)	5.45 (d, *J* = 9.8 Hz)
8	2.40 (m)	2.43(m)	2.43(m)
9	1.29, 1.38 (m)	1.29, 1.38 (m)	1.29, 1.38 (m)
10	0.83 (t, *J* = 7.5 Hz)	0.83(t, *J*=7.5Hz)	0.83 (t, *J* = 7.4 Hz).
11	0.96 (d, *J* = 6.6 Hz)	0.97(d, *J* = 6.6 Hz)	0.97 (d, *J* = 6.6 Hz)
12	1.77 (s)	1.77(d, *J*=0.9Hz)	1.77(d, *J*=0.9Hz)
NH	5.70 (d, *J* = 9.6 Hz)	5.66(d, *J* = 9.9 Hz)	5.65 (d, *J* = 9.9 Hz)
1’	4.26, 4.43 (dd, *J* = 8.4, 11.4; dd, *J* = 4.2, 11.4Hz)	4.27, 4.44 (dd, *J* = 8.4, 11.4; dd, *J* = 4.2, 11.4Hz)	4.27, 4.44 (dd, *J* = 8.4, 11.4; dd, *J* = 4.2, 11.4Hz)
2’	4.77 (ddd, *J* = 4.2, 8.4, 9.6Hz)	4.76 (ddd, *J* = 9.9, 8.3, 4.2 Hz)	4.76 (ddd, *J* = 9.9, 8.4, 4.2 Hz)
5’	2.28 (s)	2.28(s)	2.28(s)
6’	1.41 (s)	1.42(s)	1.42(s)
3’-OH	4.31 (s, br)	–	4.31(s)
1’-OCO**C**H_3	2.03 (s)	2.03 (s)	2.03 (s)

Table S2. ^{13}C NMR Comparison of Reported Bipolamide A Acetate With Synthetic Compounds 3a and 3b.

^{13}C			
Position	Reported	Synthetic Compound **3a**	Synthetic Compound **3b**
1	166.2	166.2	166.2
2	121.0	121.0	121.0
3	142.9	142.9	142.9
4	123.4	123.4	123.4
5	145.9	145.9	145.9
6	132.4	132.4	132.4
7	144.6	144.6	144.6
8	34.7	34.7	34.7
9	30.1	30.2	30.2
10	11.9	11.9	11.9
11	20.3	20.3	20.3
12	12.5	12.5	12.5
NH			
1’	62.7	62.6	62.6
2’	52.5	52.5	52.5
3’	79.4	79.4	79.4
4’	210.4	210.3	210.3
5’	23.5	23.5	23.5
6’	22.6	22.6	22.6
3’-OH			
1’-O**C**OCH$_3$	171.1	171.1	171.1
1’-OCO**C**H$_3$	20.8	20.9	20.9

2. X-Ray Crystallographic Data of Compound 9.

Fig S1: *Molecular Structure of Compound* ***9****, shown with 50% probability thermal ellipsoids (carbon, blue; oxygen, red; nitrogen, purple).*

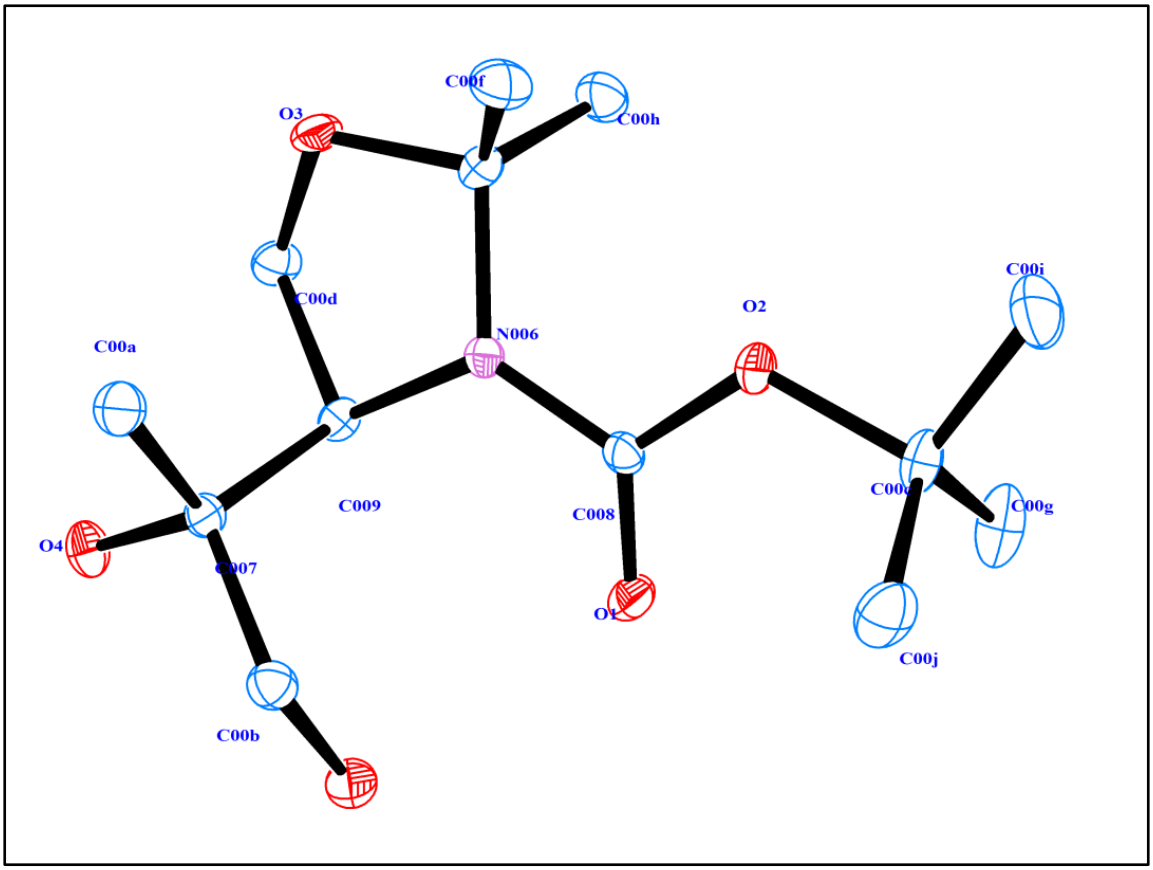


Fig S2: *Molecular Structure of Compound **13**, shown with 50% probability thermal ellipsoids (carbon, blue; oxygen, red; nitrogen, purple).*

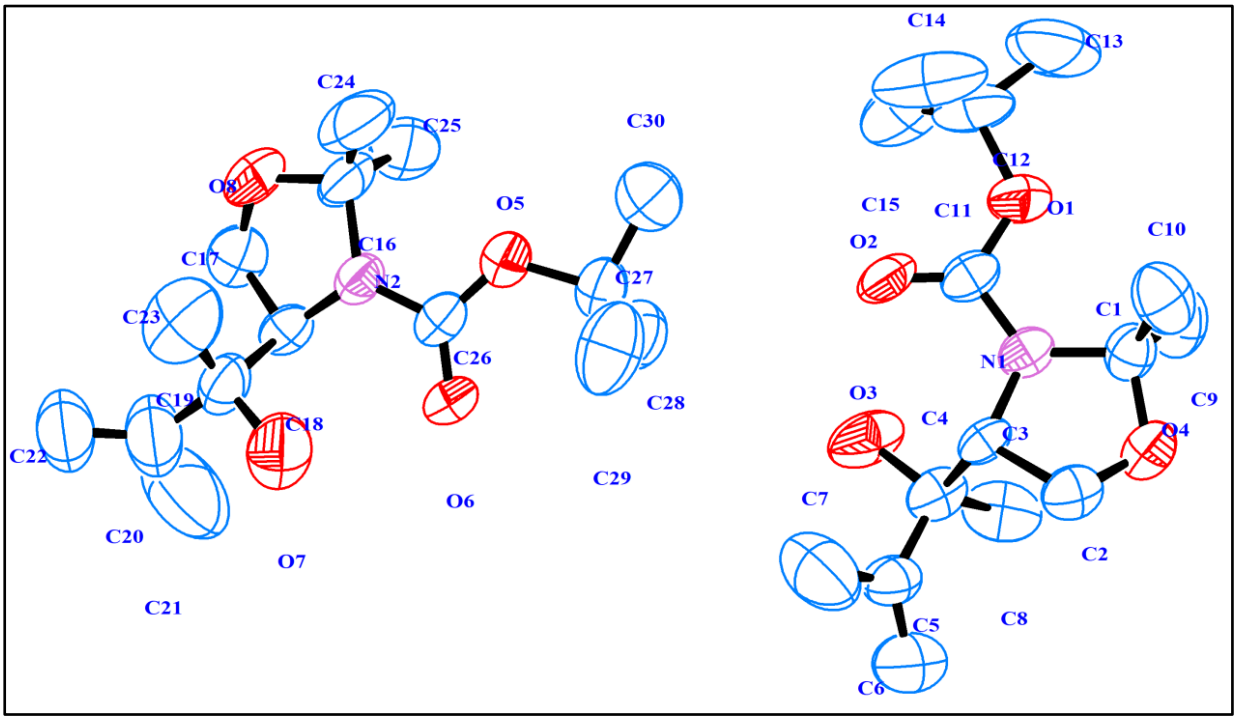


Fig S3: *Molecular Structure of Compound **16**, shown with 50% probability thermal ellipsoids (carbon, blue; oxygen, red; nitrogen, purple).*

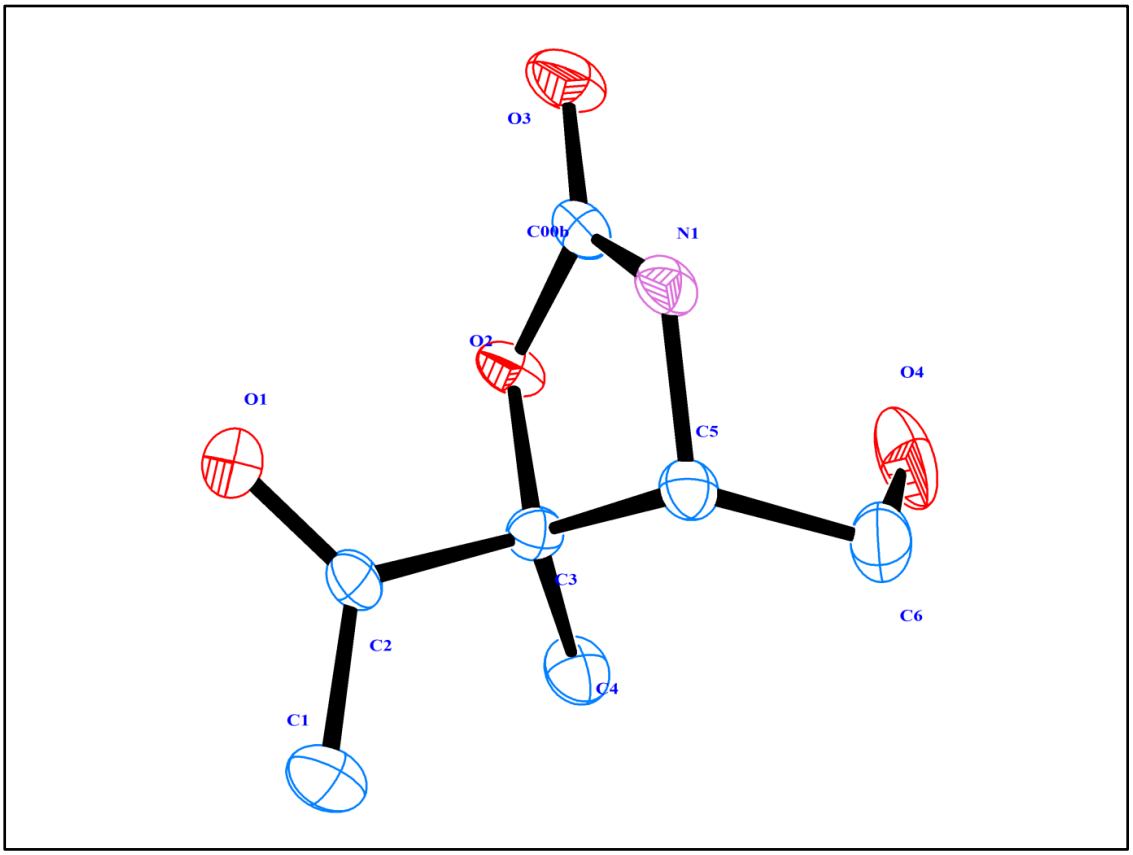
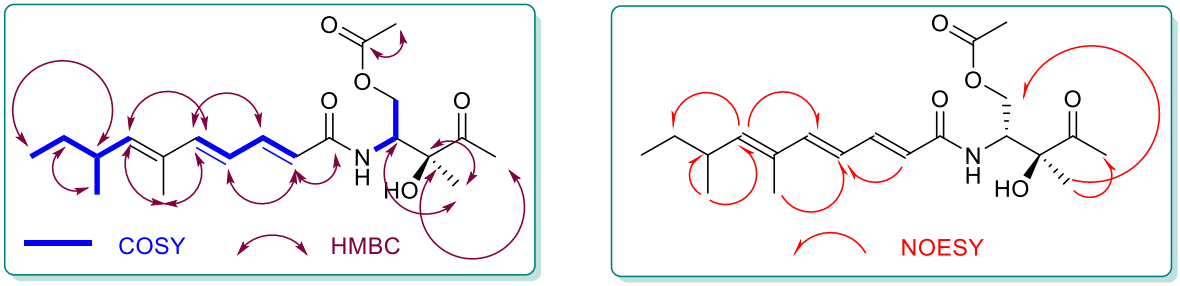


Table S3: X-ray Crystallographic Data of Compounds **9**, **13** and **16** at 301 K.

Identification code	**9**	**13**	**16**
Empirical formula	$C_{13}H_{25}NO_5$	$C_{15}H_{27}NO_4$	$C_7H_{11}NO_4$
Formula weight	275.34	285.37	173.17
Temperature/K	126.44	302.81	146.15
Crystal system	monoclinic	monoclinic	orthorhombic
Space group	$P2_1$	$P2_1$	$P2_12_12_1$
a/Å	10.7002(11)	10.537(6)	5.4660(12)
b/Å	6.0652(7)	10.802(6)	10.025(2)
c/Å	11.8500(12)	15.329(8)	15.193(4)
α/°	90	90	90
β/°	99.659(3)	94.978(15)	90
γ/°	90	90	90
Volume/Å^3	758.15(14)	1738.2(16)	832.5(3)
Z	2	4	4
ρ_{calc}g/cm^3	1.206	1.091	1.382
μ/mm^{-1}	0.092	0.078	0.114
F(000)	300.0	624.0	368.0
Crystal size/mm^3	0.56 × 0.1 × 0.09	0.45 × 0.1 × 0.09	0.52 × 0.1 × 0.1
Radiation	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)
2Θ range for data collection/°	7.726 to 50.014	4.62 to 50.782	5.362 to 50.28
Index ranges	-12 ≤ h ≤ 12, -7 ≤ k ≤ 7, -13 ≤ l ≤ 14	-12 ≤ h ≤ 12, -12 ≤ k ≤ 12, -18 ≤ l ≤ 18	-6 ≤ h ≤ 6, -11 ≤ k ≤ 11, -18 ≤ l ≤ 18
Reflections collected	6668	16934	7535
Independent reflections	2586 [R_{int} = 0.0540, R_{sigma} = 0.0591]	5685 [R_{int} = 0.1172, R_{sigma} = 0.1326]	1488 [R_{int} = 0.0906, R_{sigma} = 0.0618]
Data/restraints/parameters	2586/1/180	5685/1/374	1488/0/111
Goodness-of-fit on F^2	1.157	1.045	1.079
Final R indexes [I>=2σ (I)]	R_1 = 0.0525, wR_2 = 0.1359	R_1 = 0.0933, wR_2 = 0.1758	R_1 = 0.0419, wR_2 = 0.0963
Final R indexes [all data]	R_1 = 0.0540, wR_2 = 0.1366	R_1 = 0.1727, wR_2 = 0.2079	R_1 = 0.0505, wR_2 = 0.1026
Largest diff. peak/hole / e Å^{-3}	0.35/-0.21	0.27/-0.24	0.18/-0.19
Flack parameter	0.0(6)	-0.5(10)	0.1(10)

3. Key 2D-NMR Correlations and Structure Conformation of Compounds 3a and 3b.



4. Graphical Comparison of Compounds 3a and 3b with Reported Bipolamide A Acetate.

Fig S4. Plot of Δ(reported-synthesised) ^{13}C Values vs Position of Carbon of Compound **3a**.

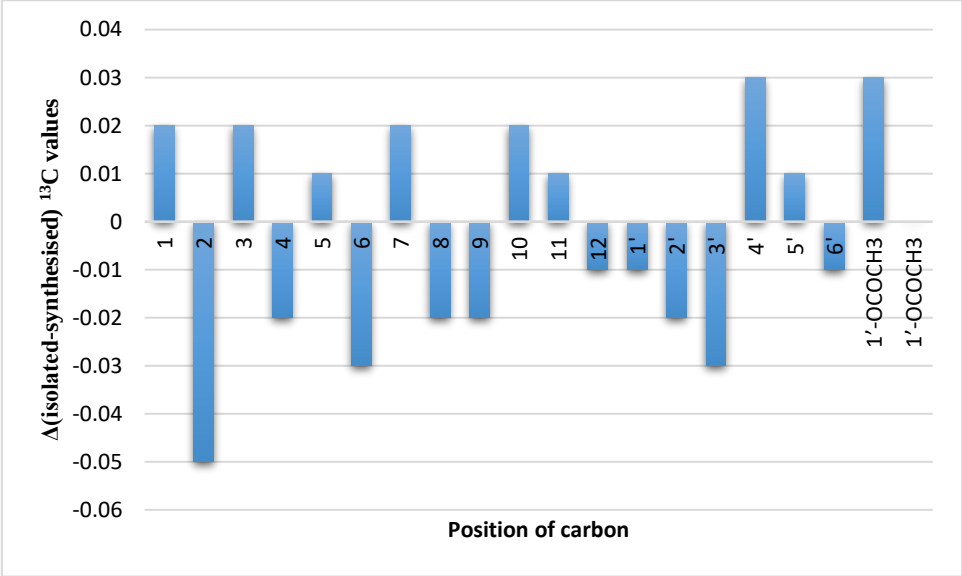
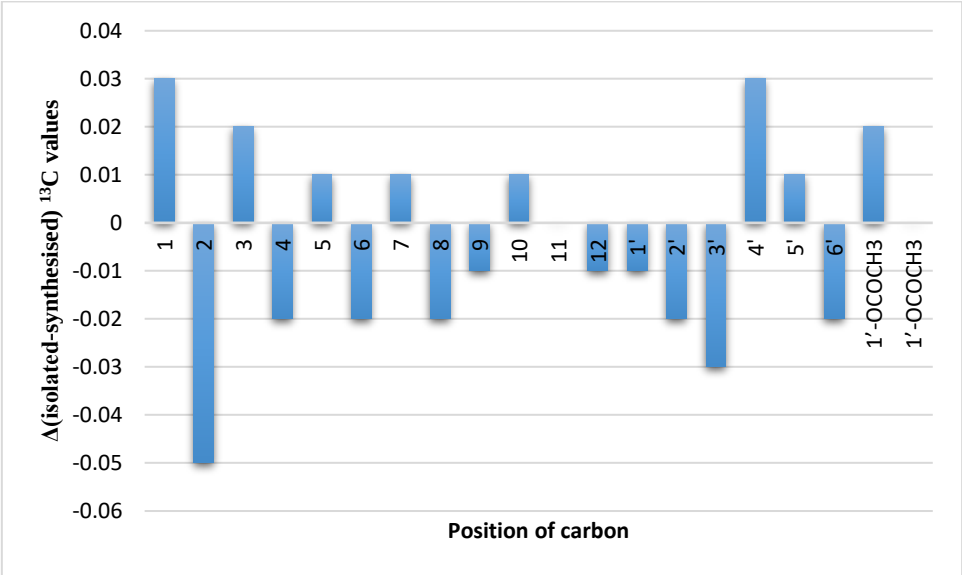
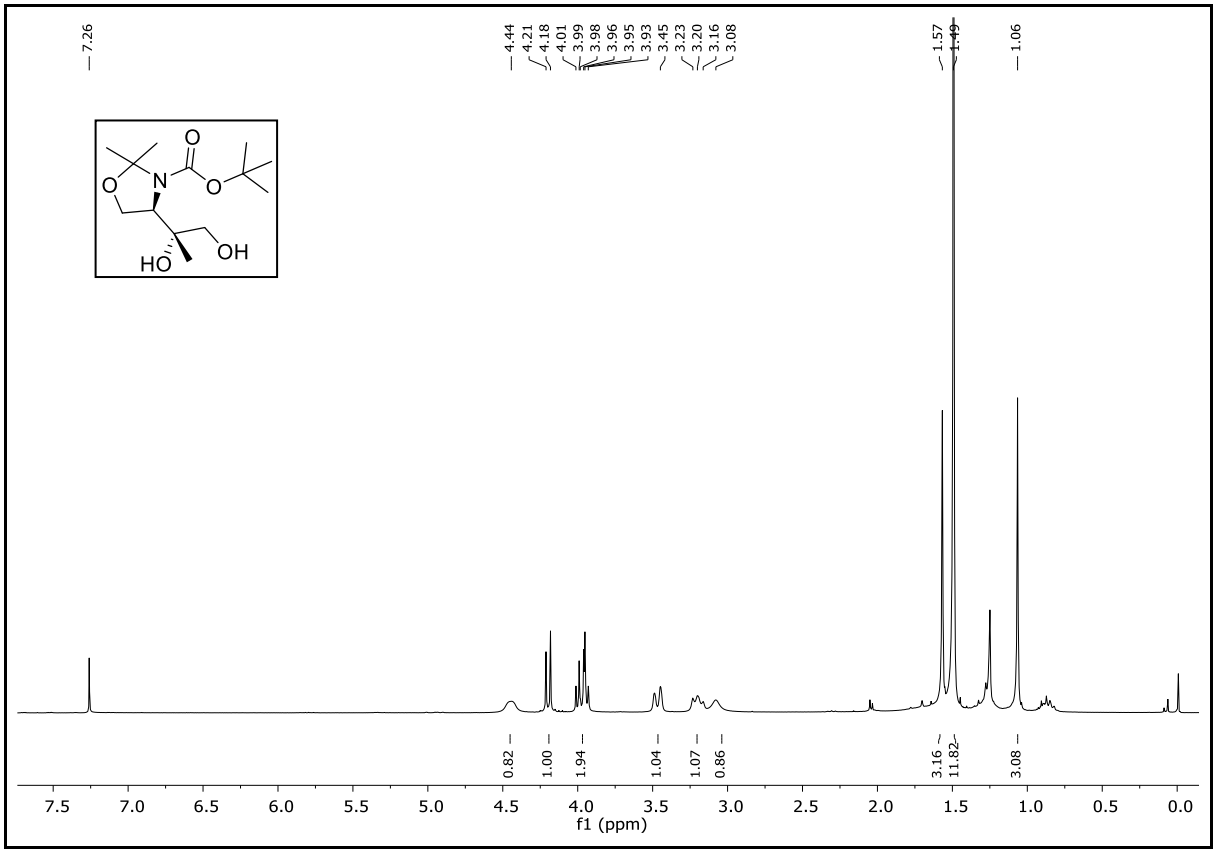


Fig S5. Plot of Δ(reported-synthesised) ^{13}C Values vs Position of Carbon of Compound **3b**.

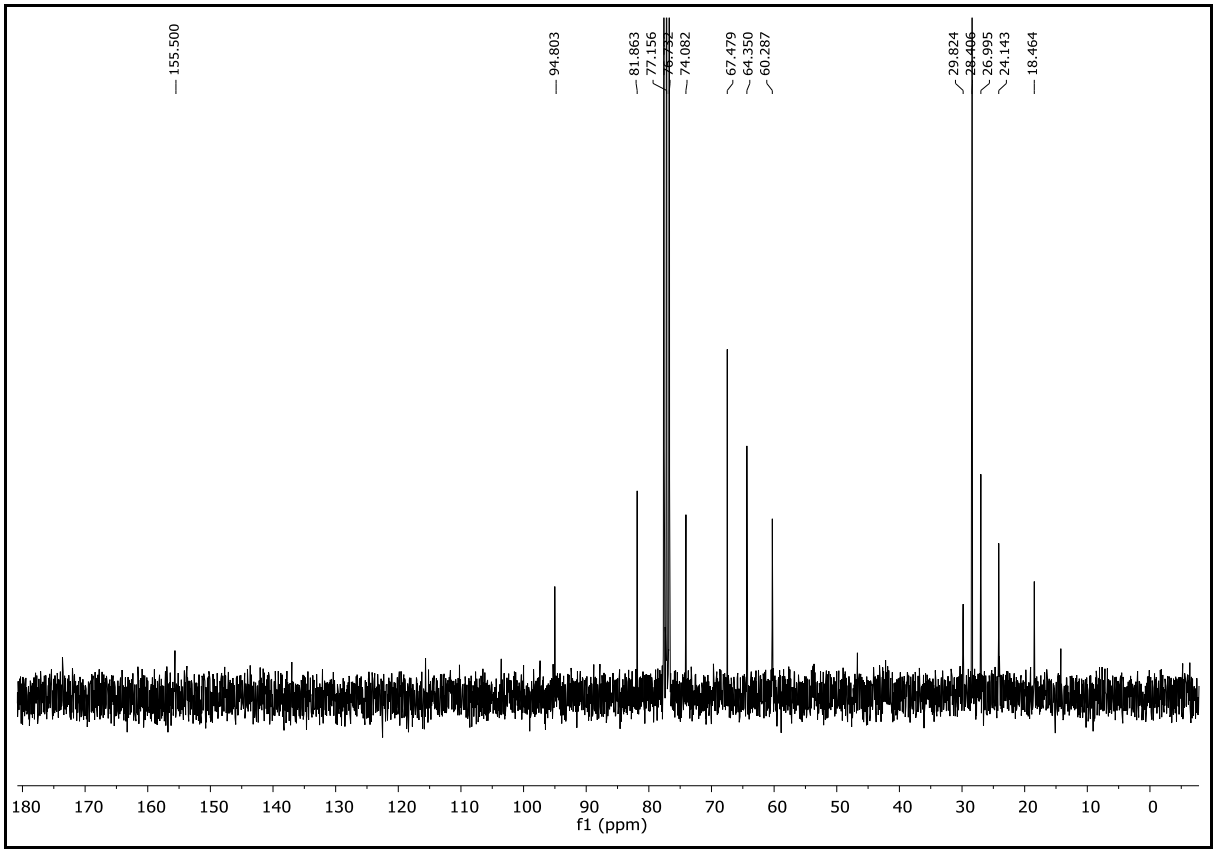


Copies of ^{1}H NMR, ^{13}C NMR, 2D NMR and HRMS Spectra

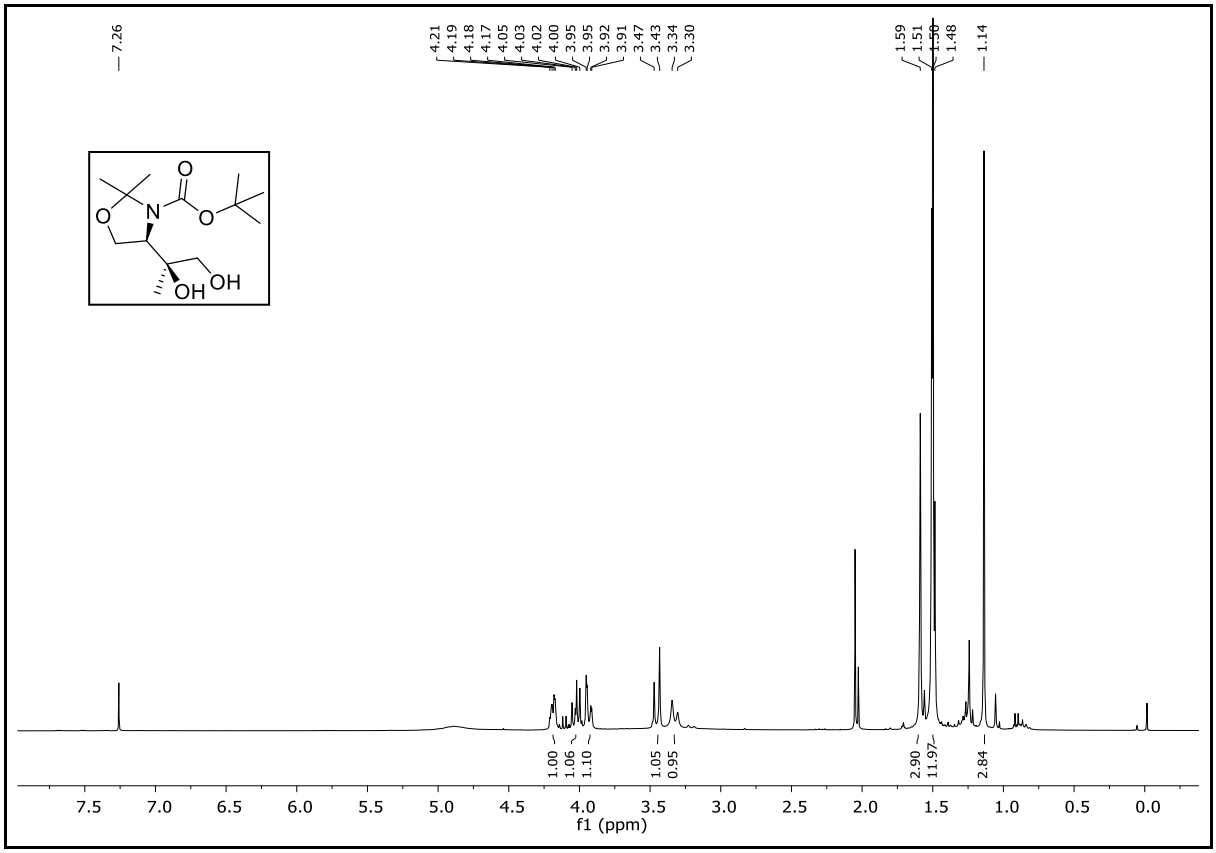
^{1}H-NMR Spectrum of Compound of 9 (300 MHz, $CDCl_3$):



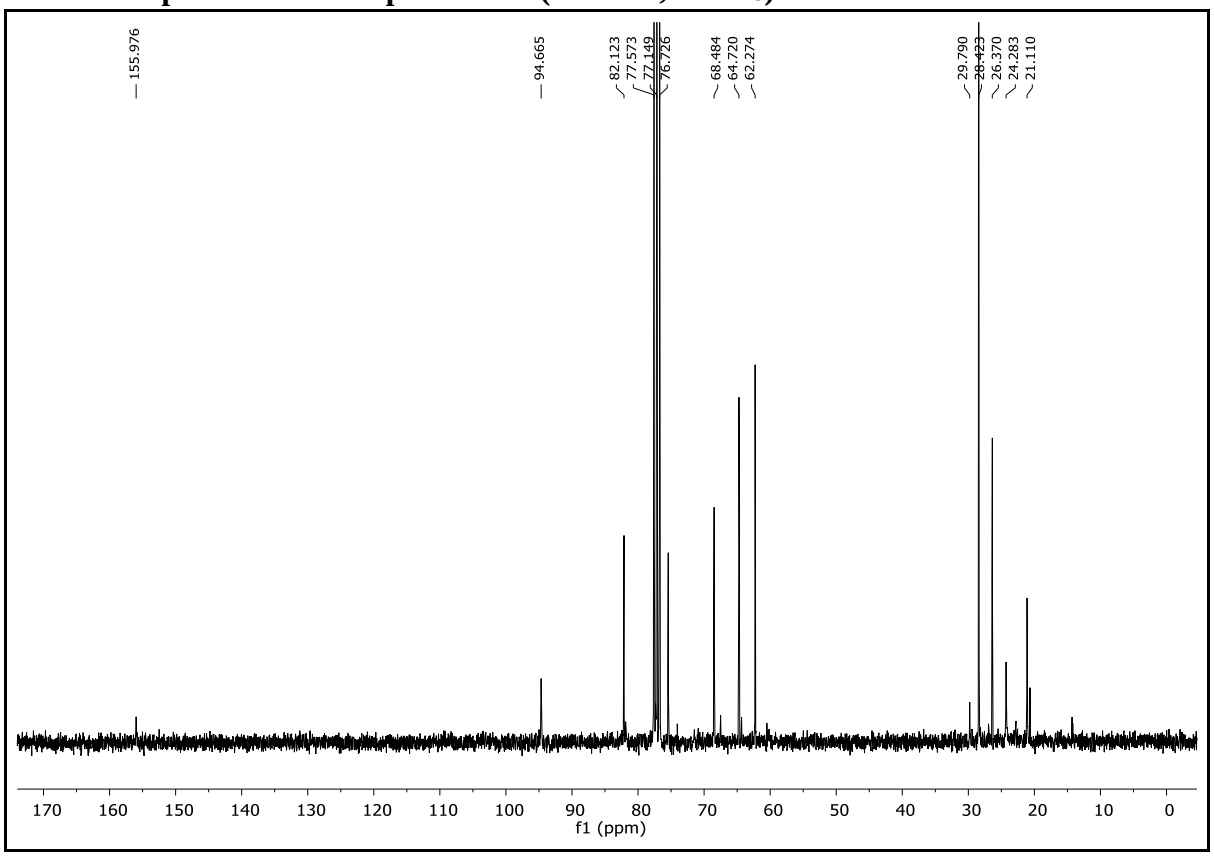
^{13}C-NMR Spectrum of Compound of 9 (75 MHz, $CDCl_3$):



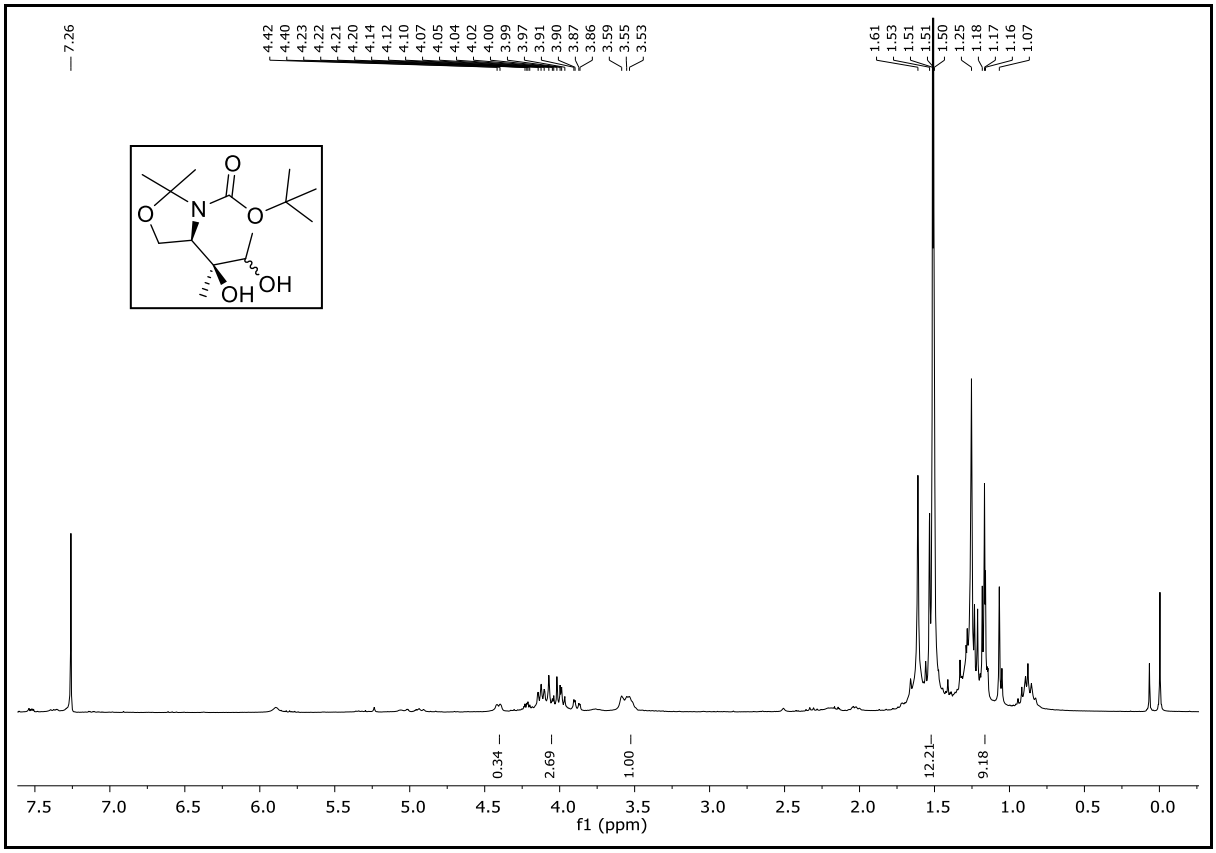
^{1}H-NMR Spectrum of Compound of 8 (300 MHz, $CDCl_3$):



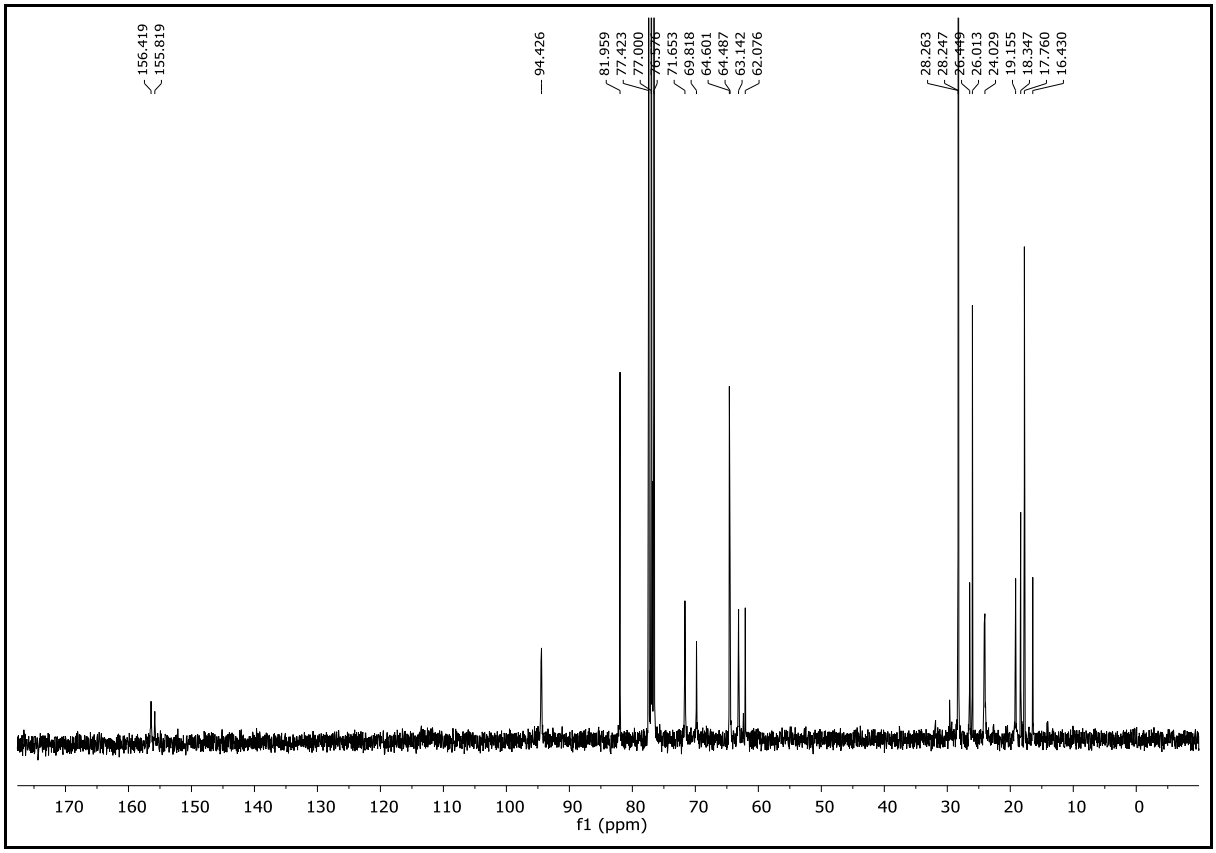
^{13}C-NMR Spectrum of Compound of 8 (75 MHz, $CDCl_3$):



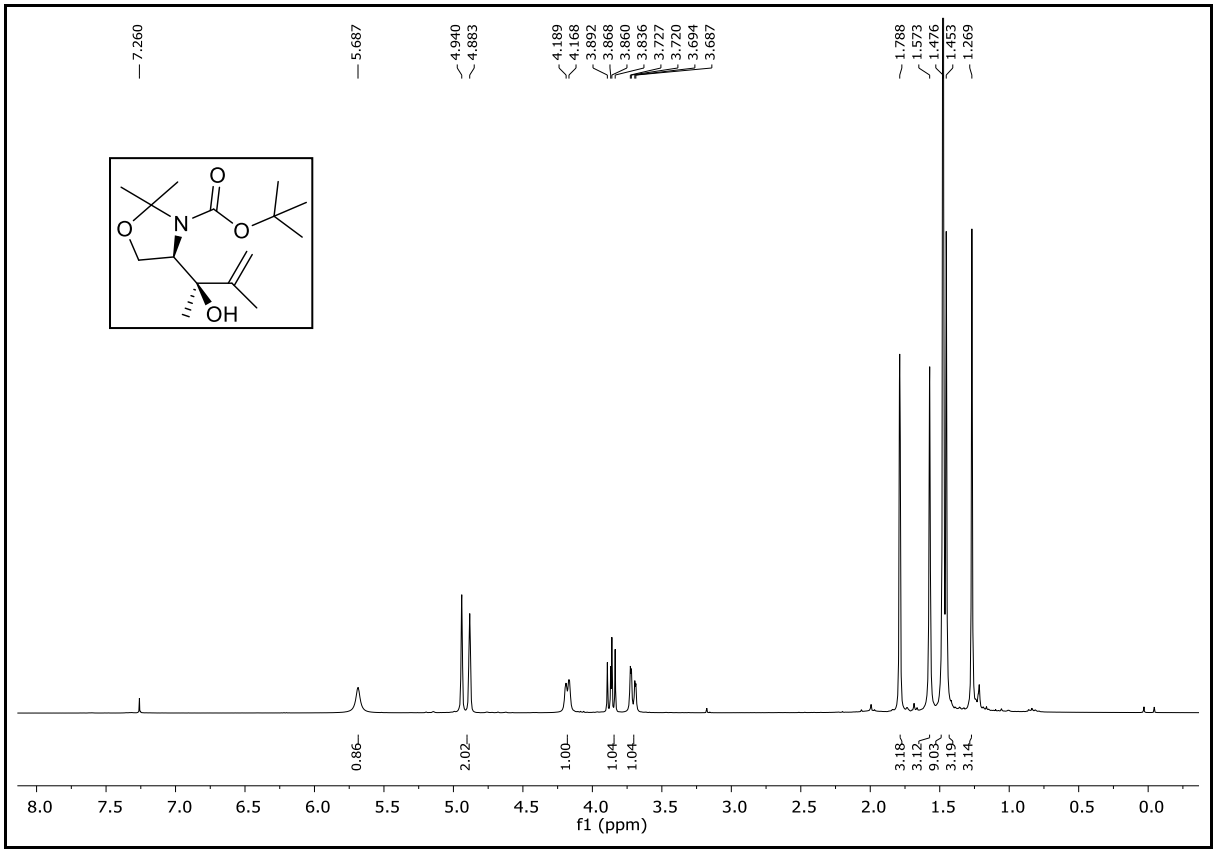
^{1}H-NMR Spectrum of Compound of 10(a-b) (300 MHz, $CDCl_3$):



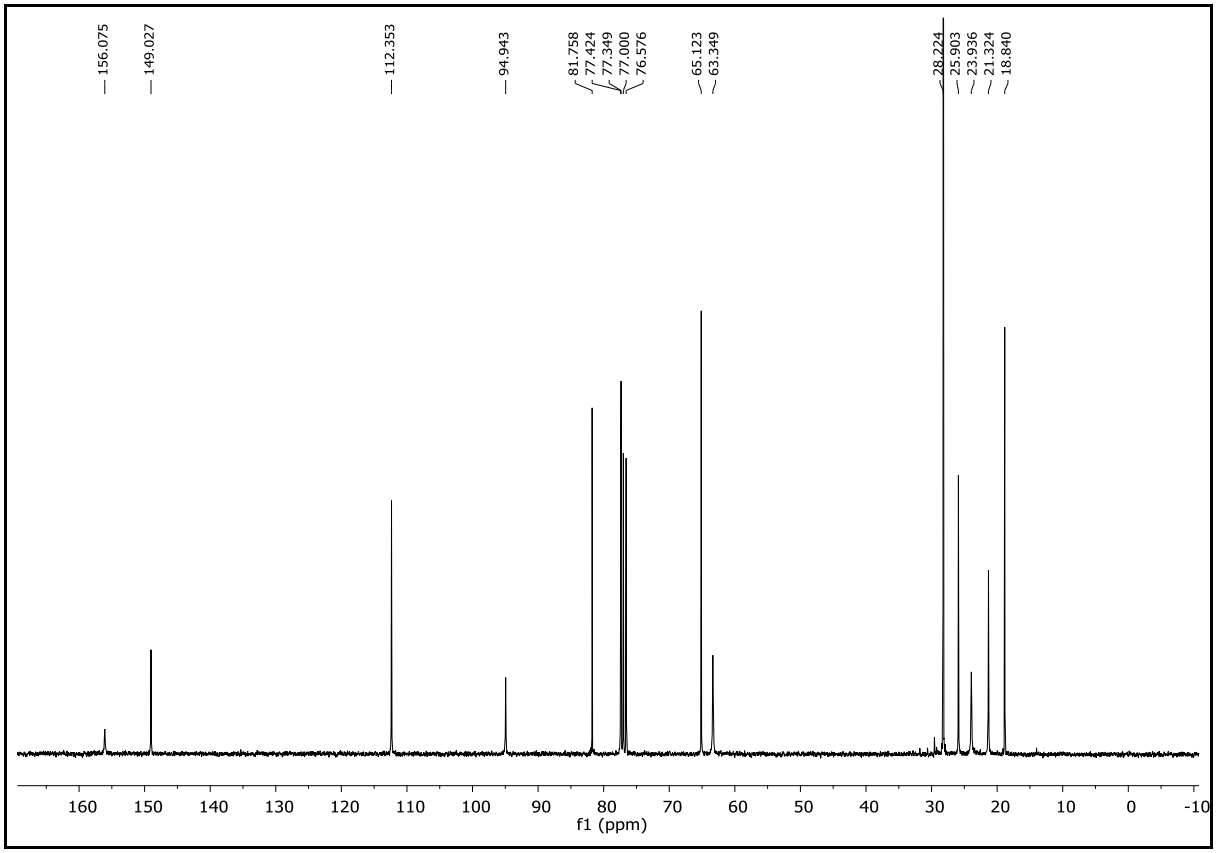
^{13}C-NMR Spectrum of Compound of 10(a-b) (75 MHz, $CDCl_3$):



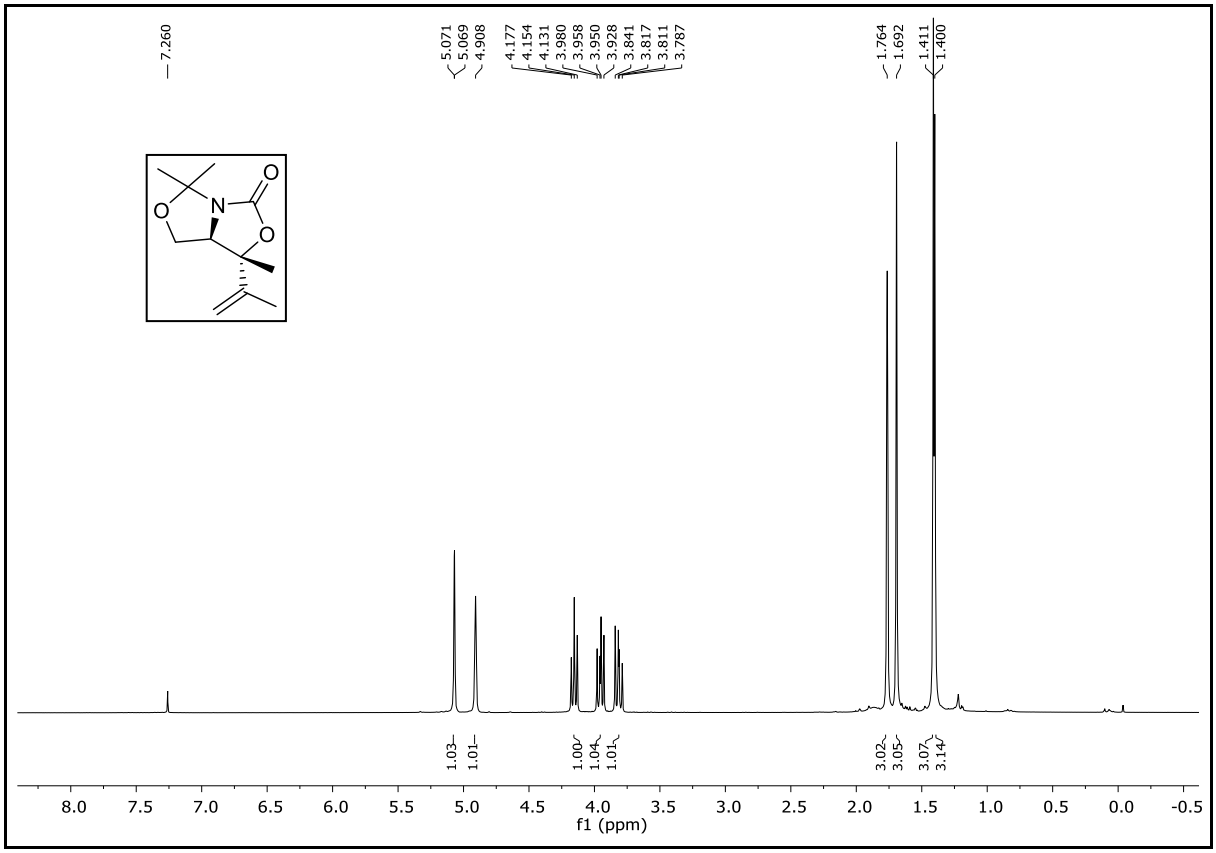
^{1}H-NMR Spectrum of Compound of 13 (300 MHz, $CDCl_3$):



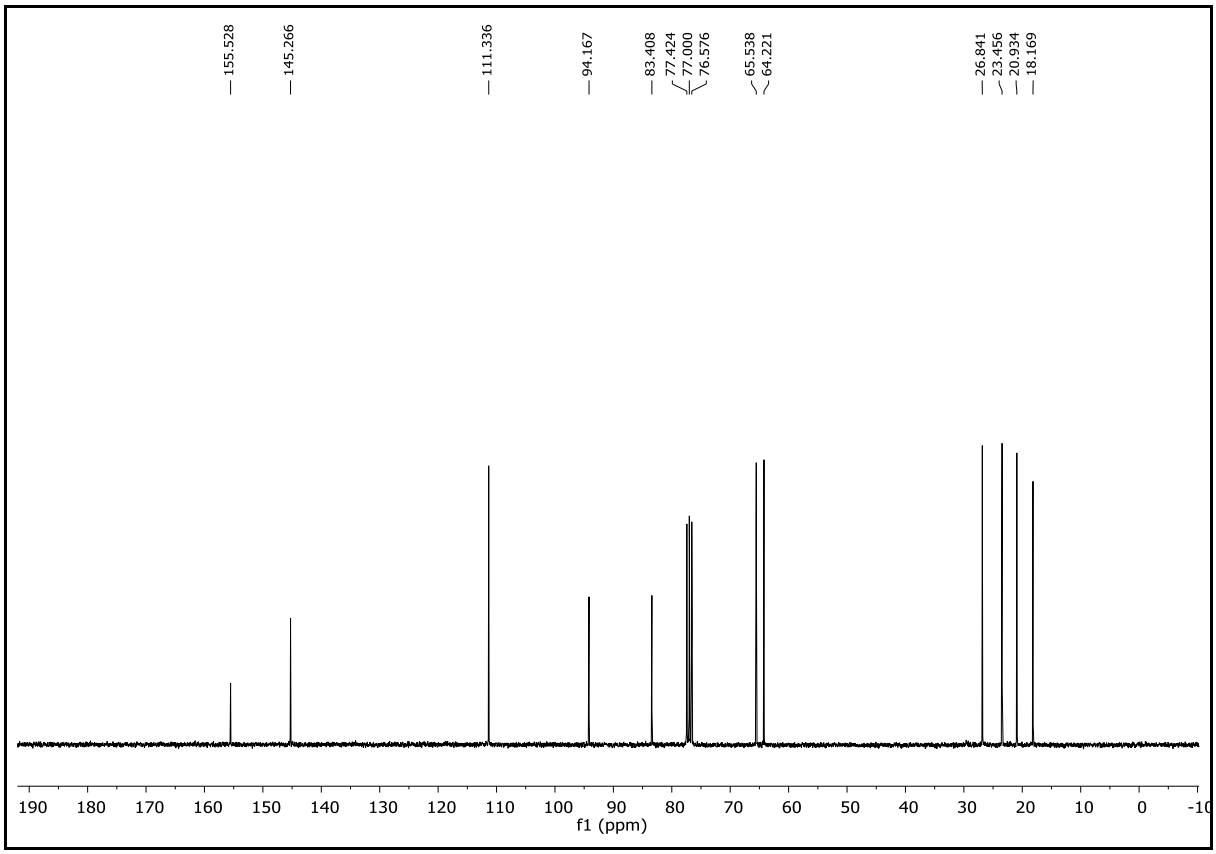
^{13}C-NMR Spectrum of Compound of 13 (75 MHz, $CDCl_3$):



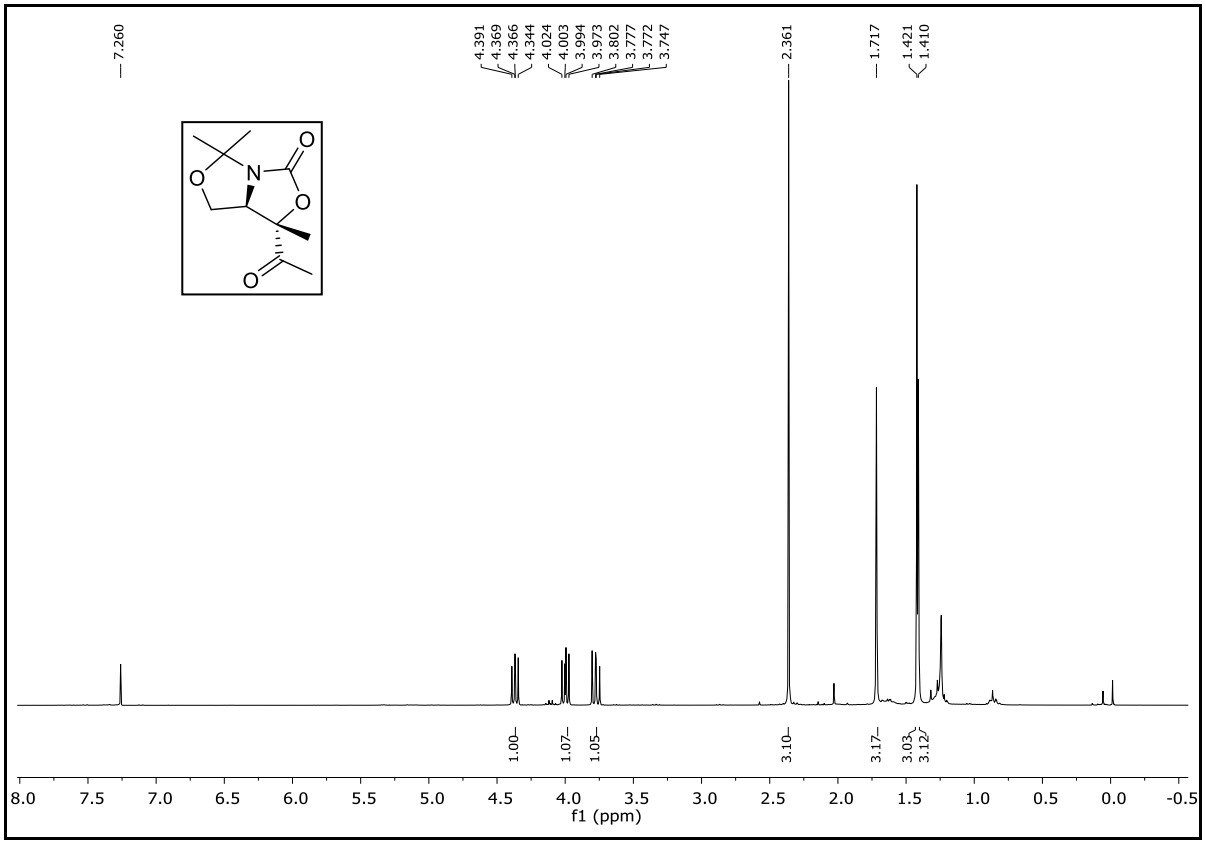
^{1}H-NMR Spectrum of Compound of 14 (300 MHz, $CDCl_3$):



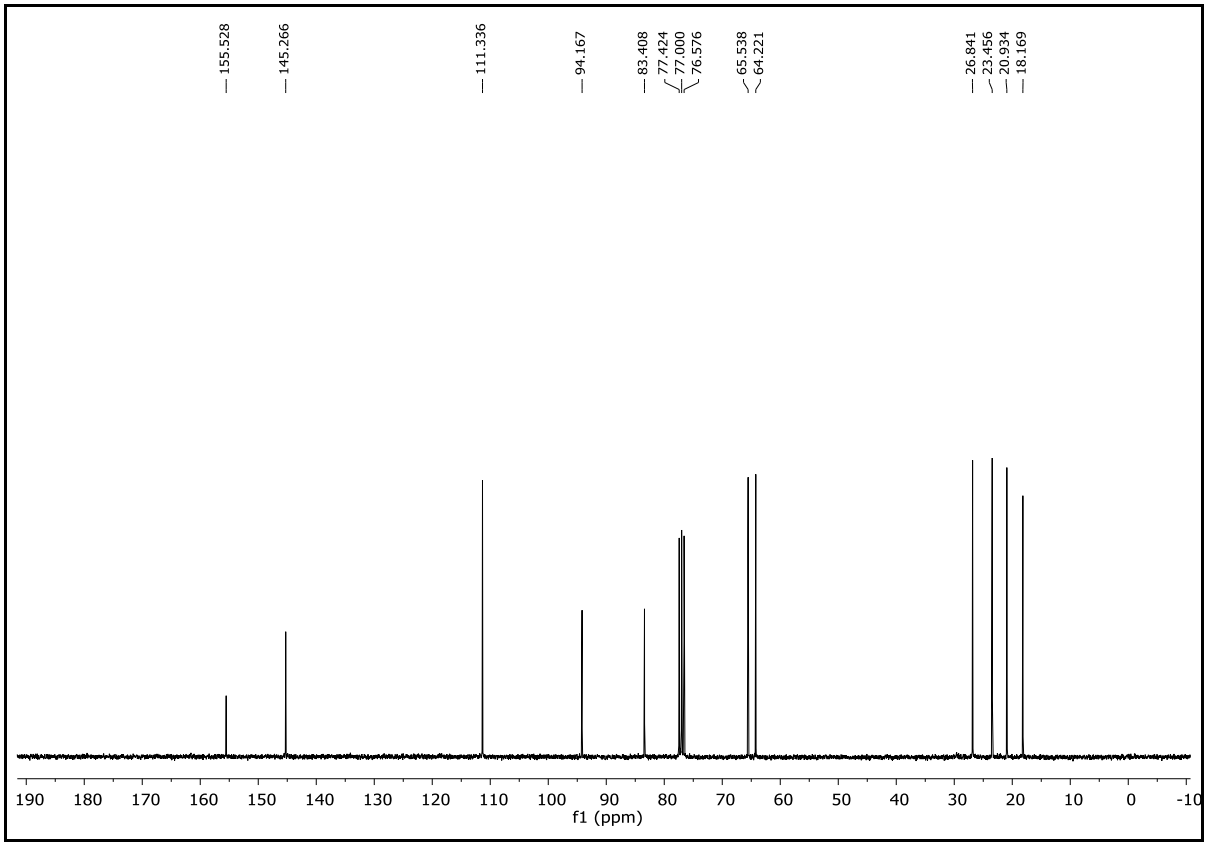
^{13}C-NMR Spectrum of Compound of 14 (75 MHz, $CDCl_3$):



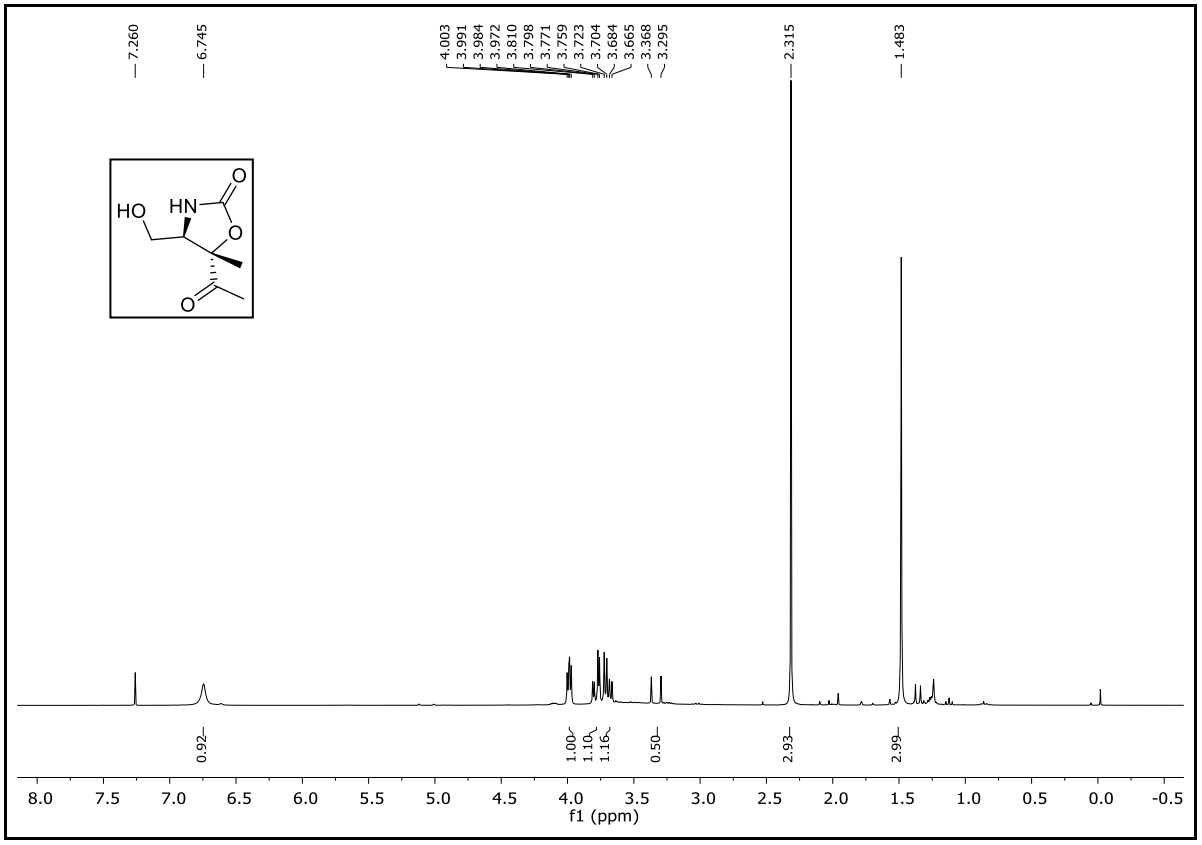
^{1}H-NMR Spectrum of Compound of 15 (300 MHz, $CDCl_3$):



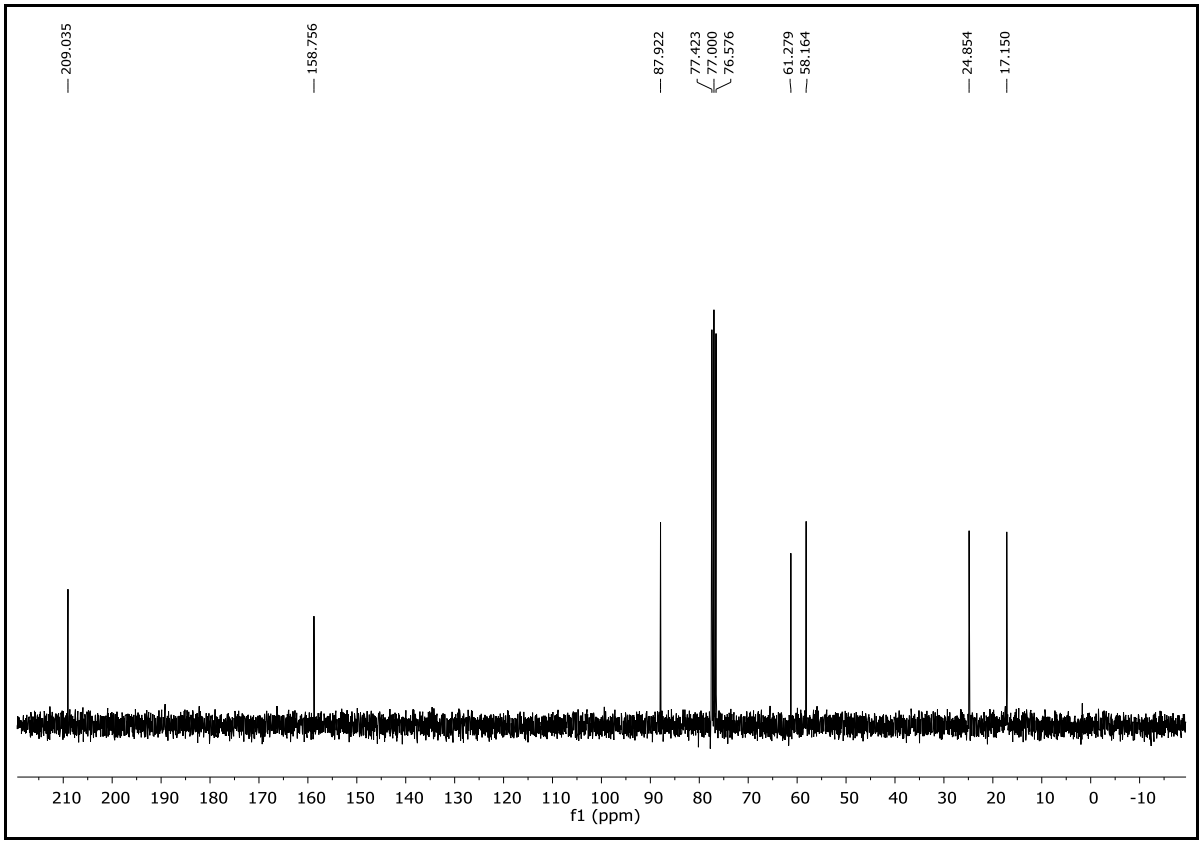
^{13}C NMR Spectrum of Compound of 15 (75 MHz, $CDCl_3$):



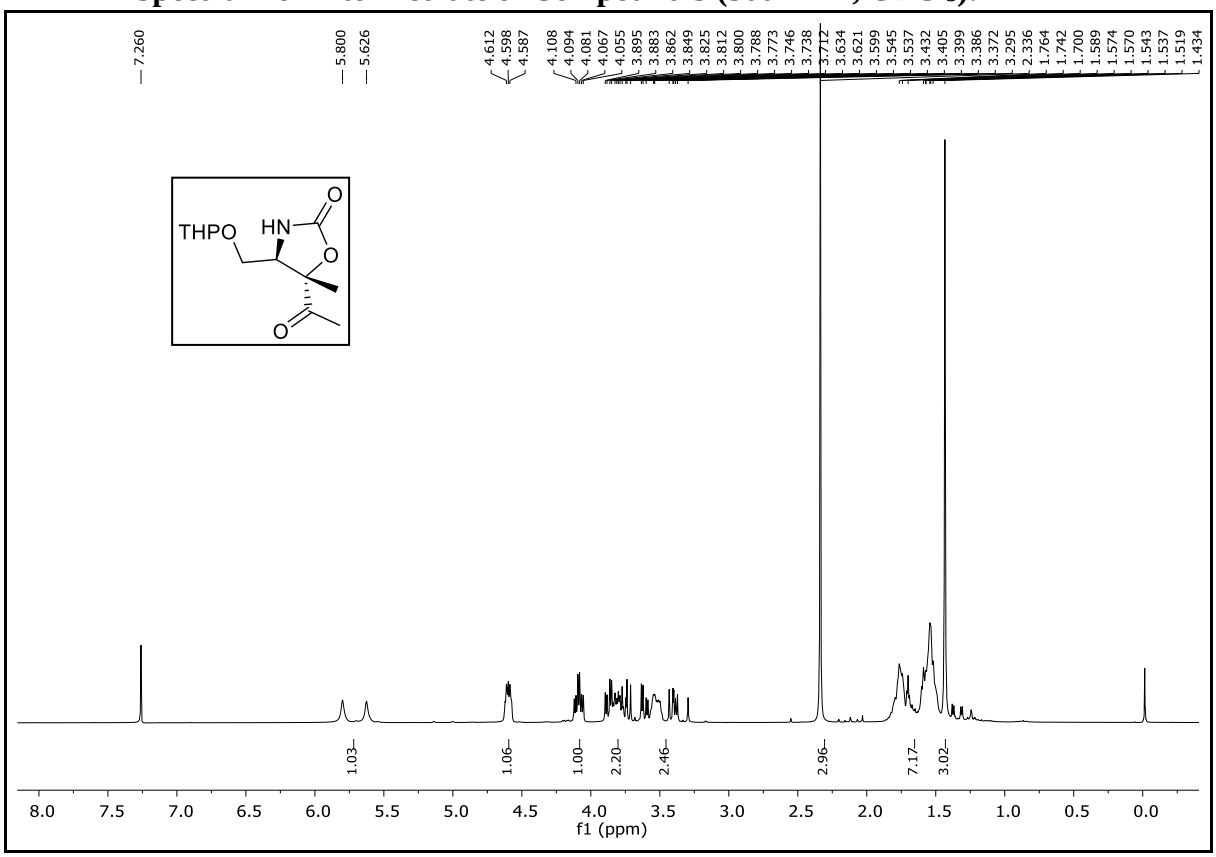
^{1}H-NMR Spectrum of Compound of 16 (300 MHz, $CDCl_3$):



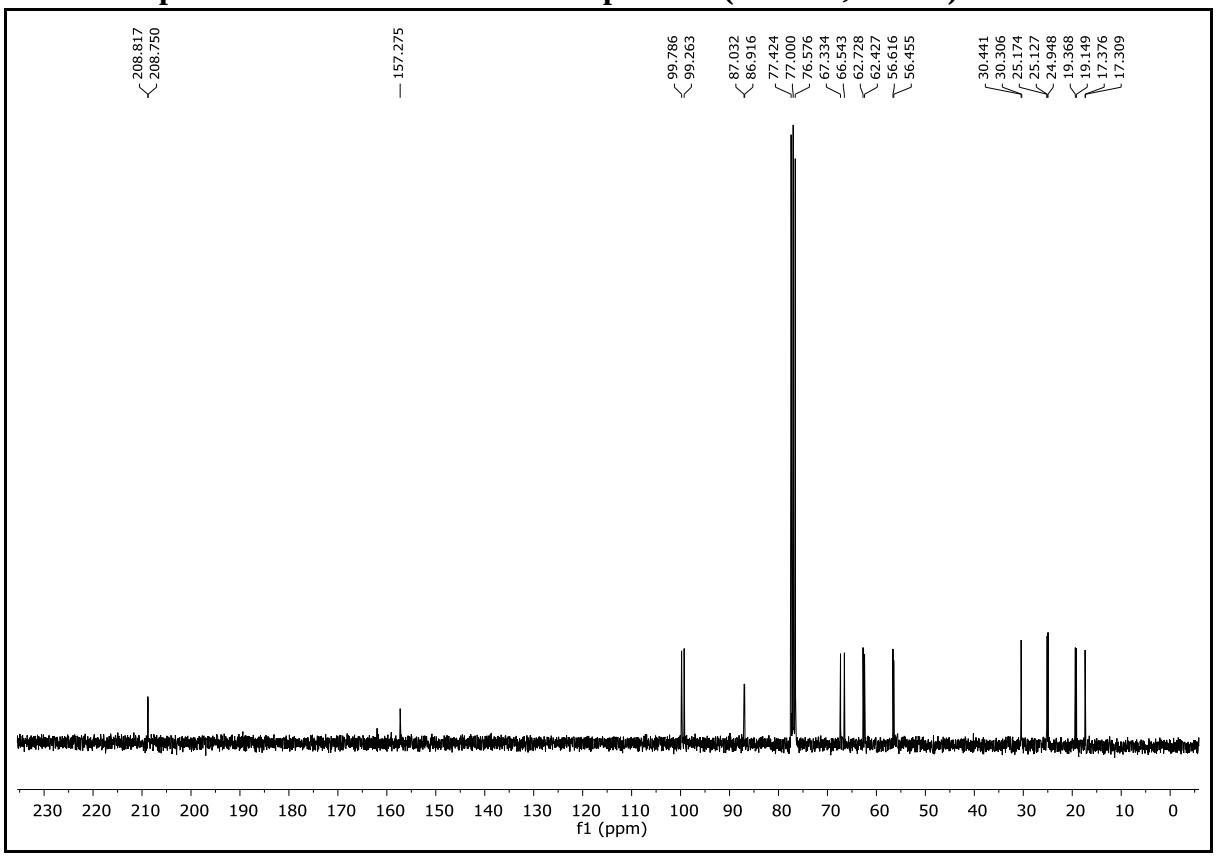
^{13}C NMR Spectrum of Compound of 16 (75 MHz, $CDCl_3$):



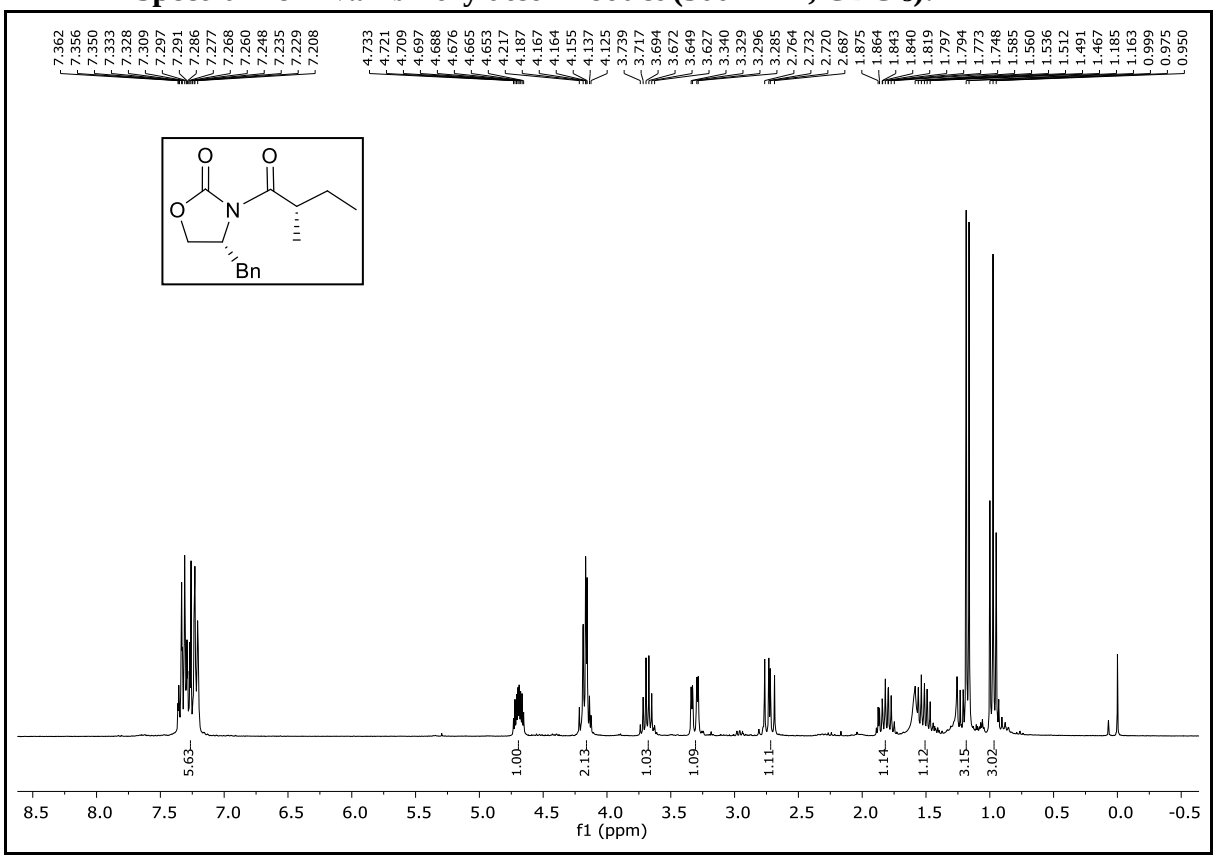
^{1}H-NMR Spectrum of Intermediate of Compound 5 (300 MHz, $CDCl_3$):



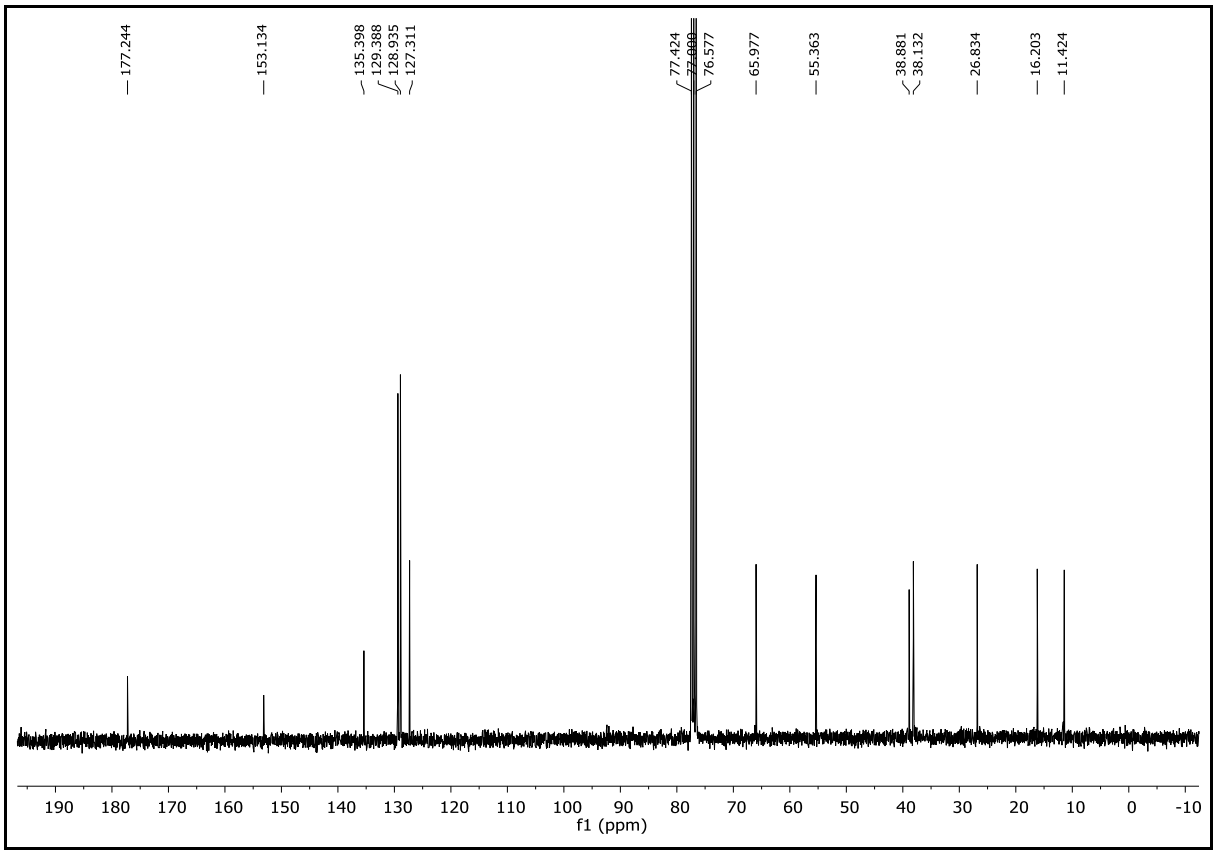
^{13}C NMR Spectrum of Intermediate of Compound 5 (75 MHz, $CDCl_3$):



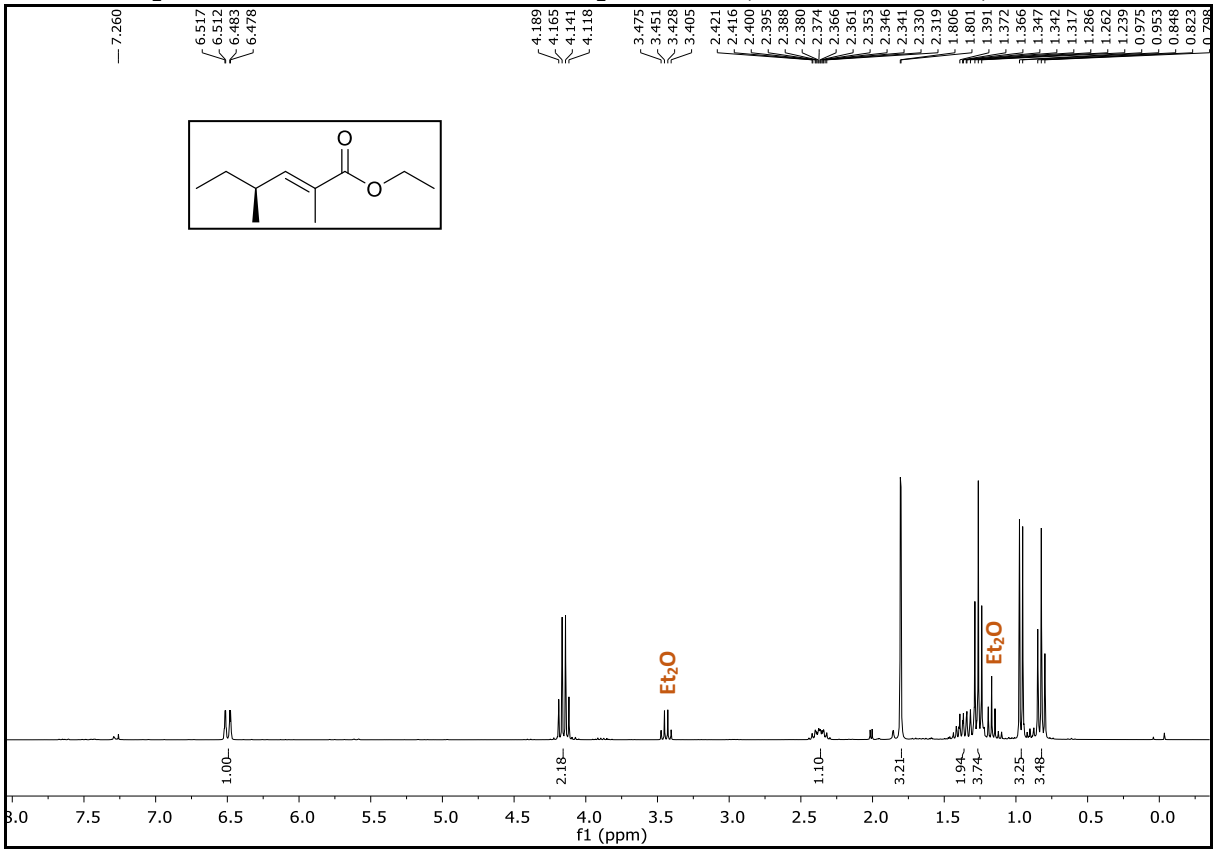
^{1}H-NMR Spectrum of Evan's Ethylated Product (300 MHz, $CDCl_3$):



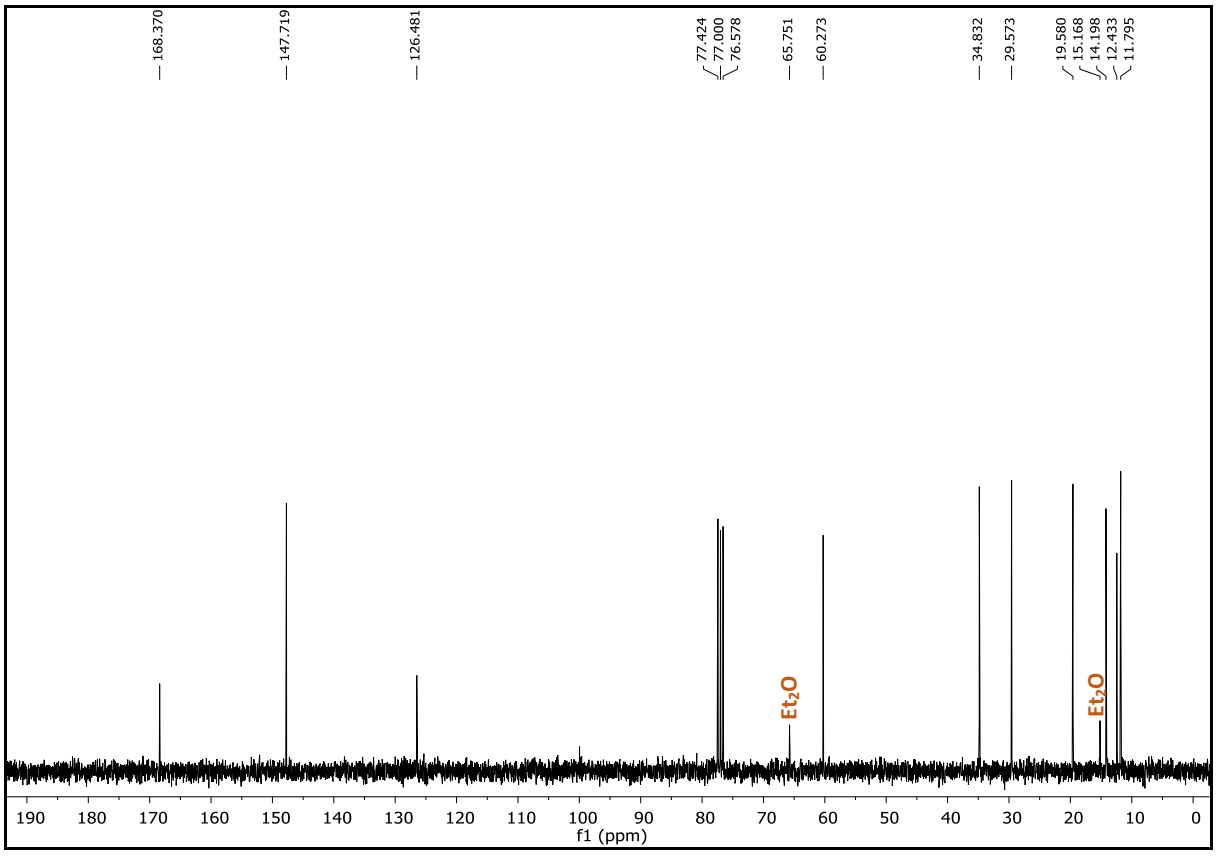
^{13}C NMR Spectrum of Evan's Ethylated Product (75 MHz, $CDCl_3$):



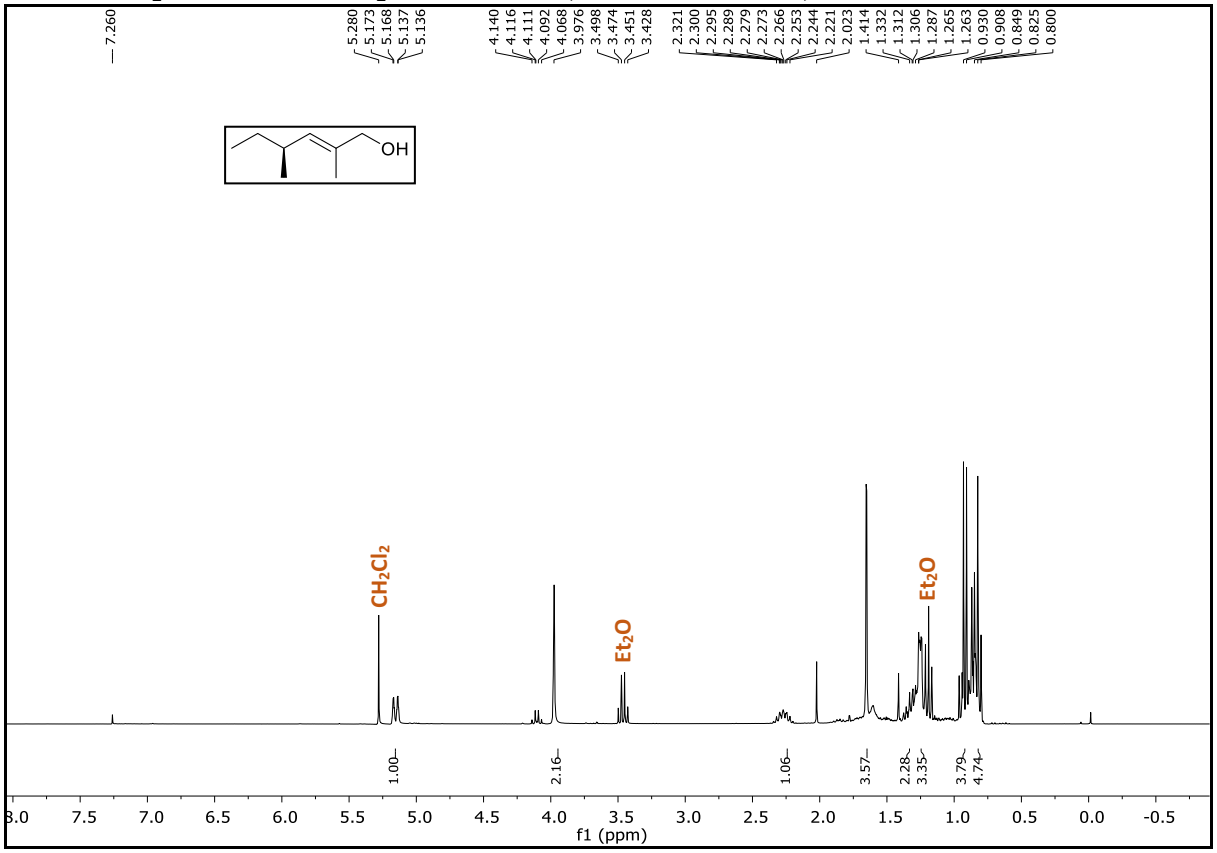
^{1}H-NMR Spectrum of Intermediate of Compound19a (300 MHz, $CDCl_3$):



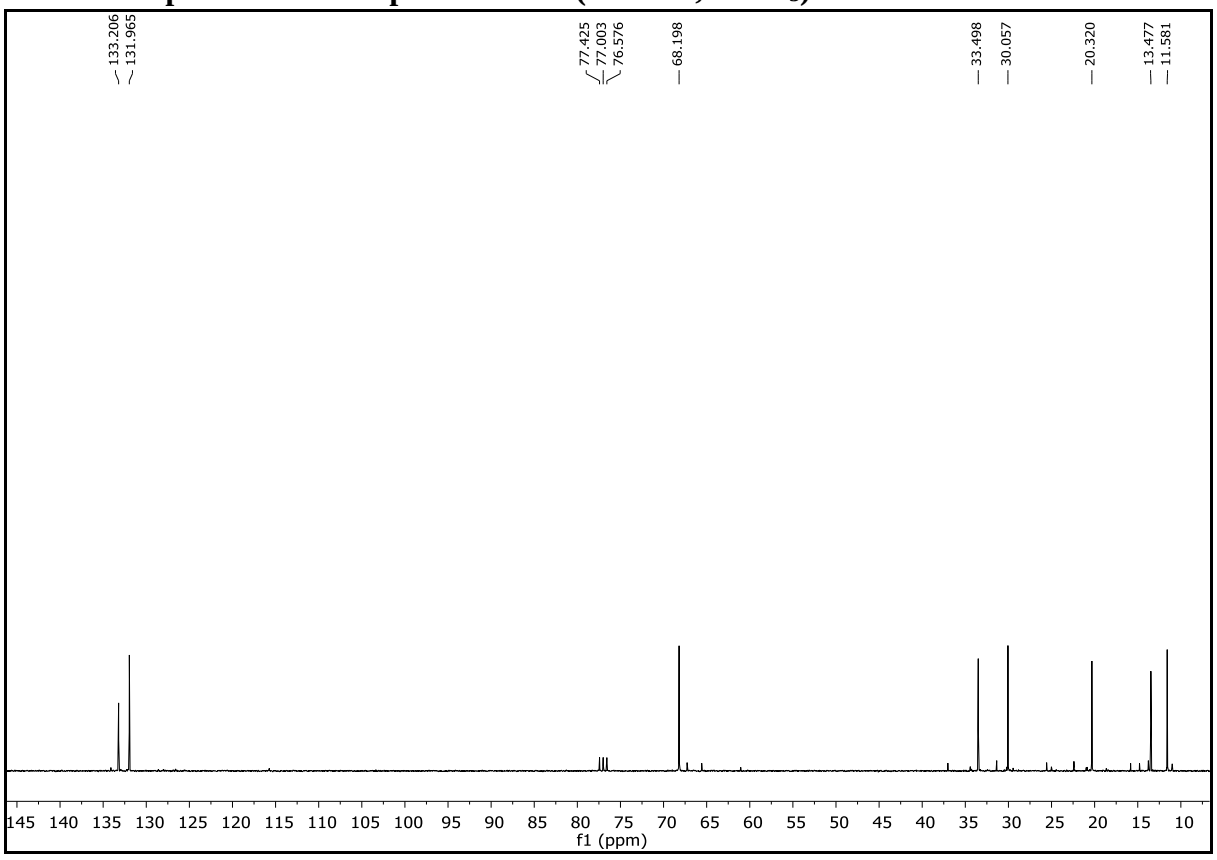
^{13}C NMR spectrum of intermediate of Compound 19a (75 MHz, $CDCl_3$):



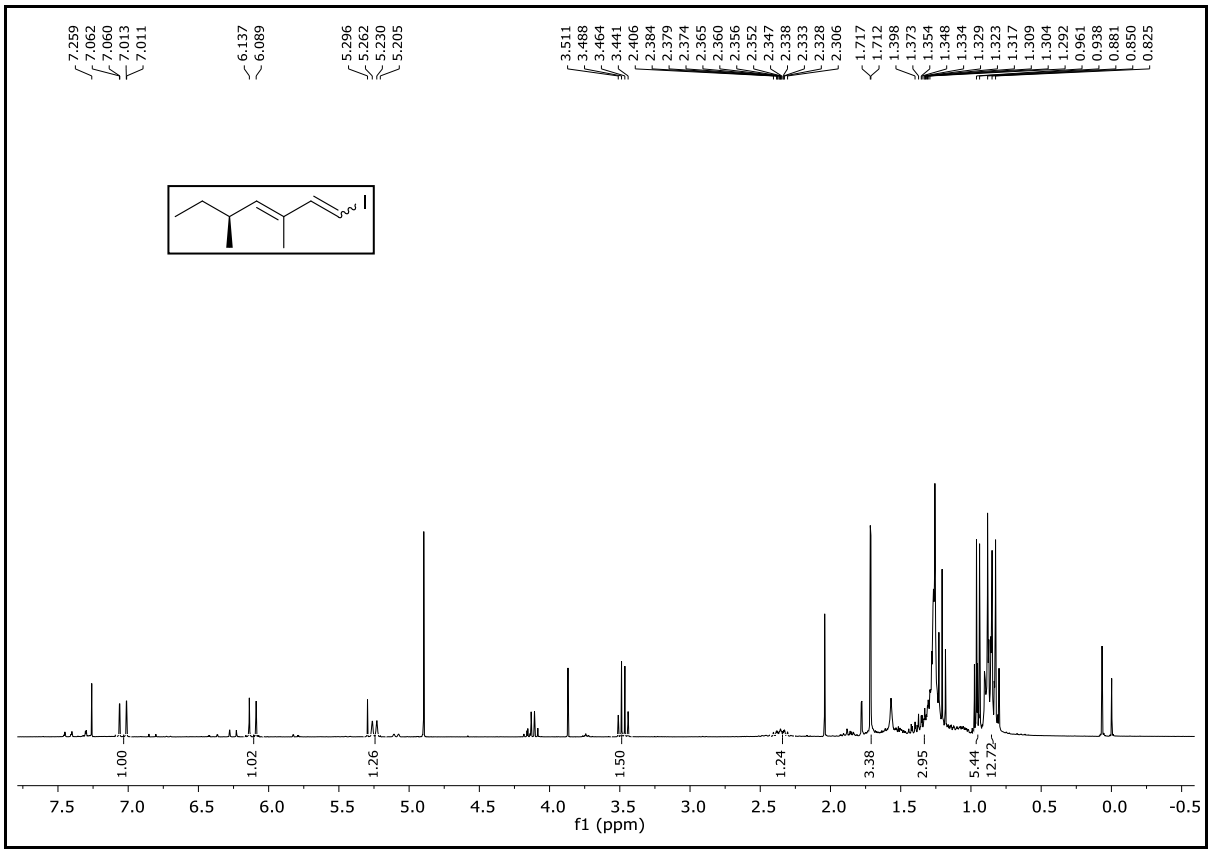
^{1}H-NMR Spectrum of Compound of 19a (300 MHz, $CDCl_3$):



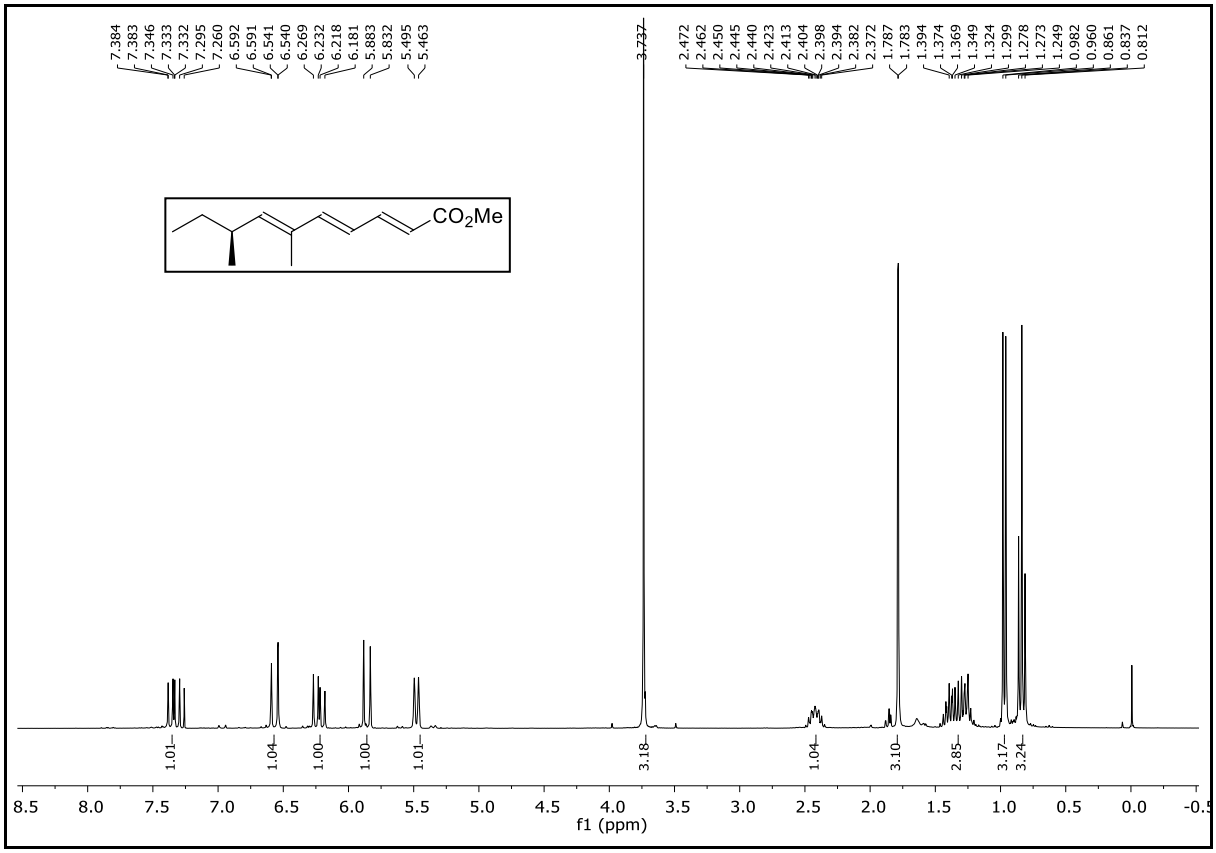
^{13}C NMR Spectrum of Compound of 19a (75 MHz, $CDCl_3$):



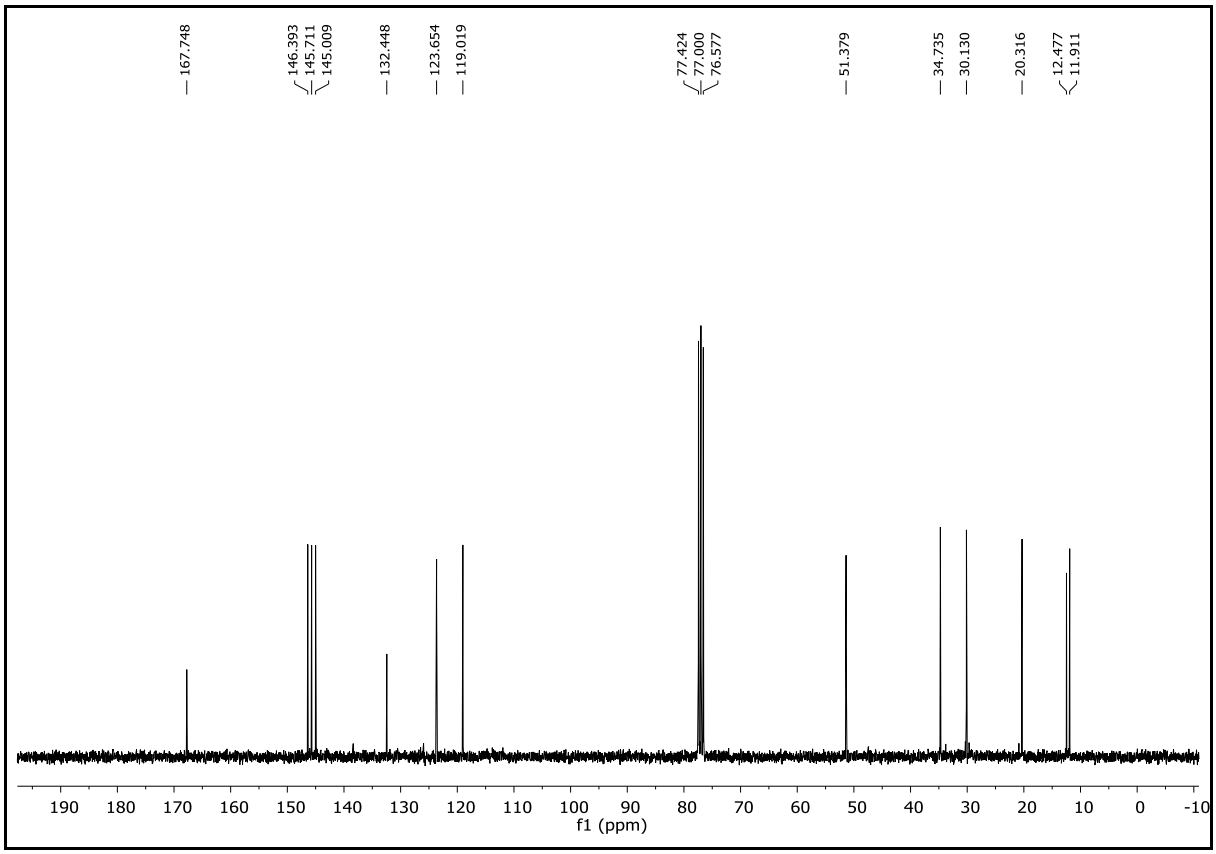
^{1}H-NMR Spectrum of Compound of 6a (300 MHz, $CDCl_3$):



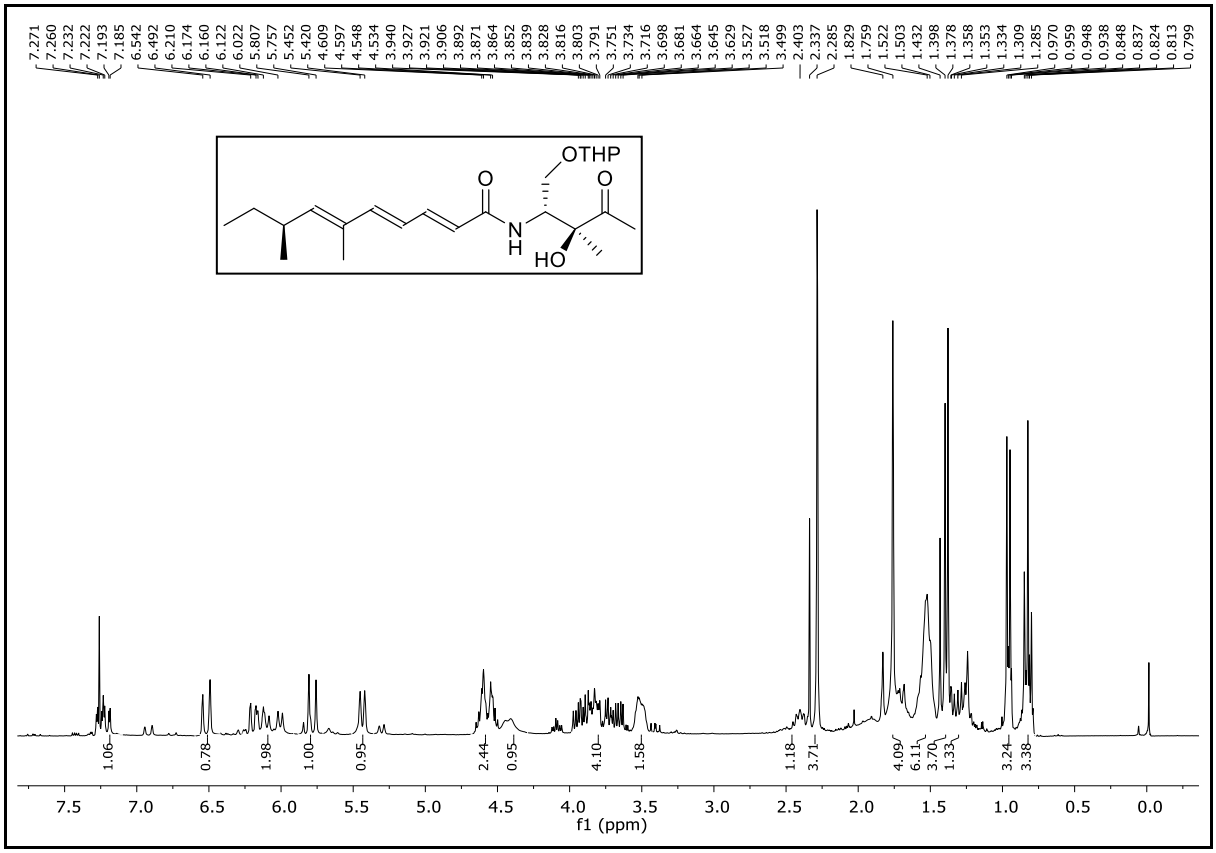
^{1}H-NMR Spectrum of Intermediate of Compound 4a (300 MHz, $CDCl_3$):



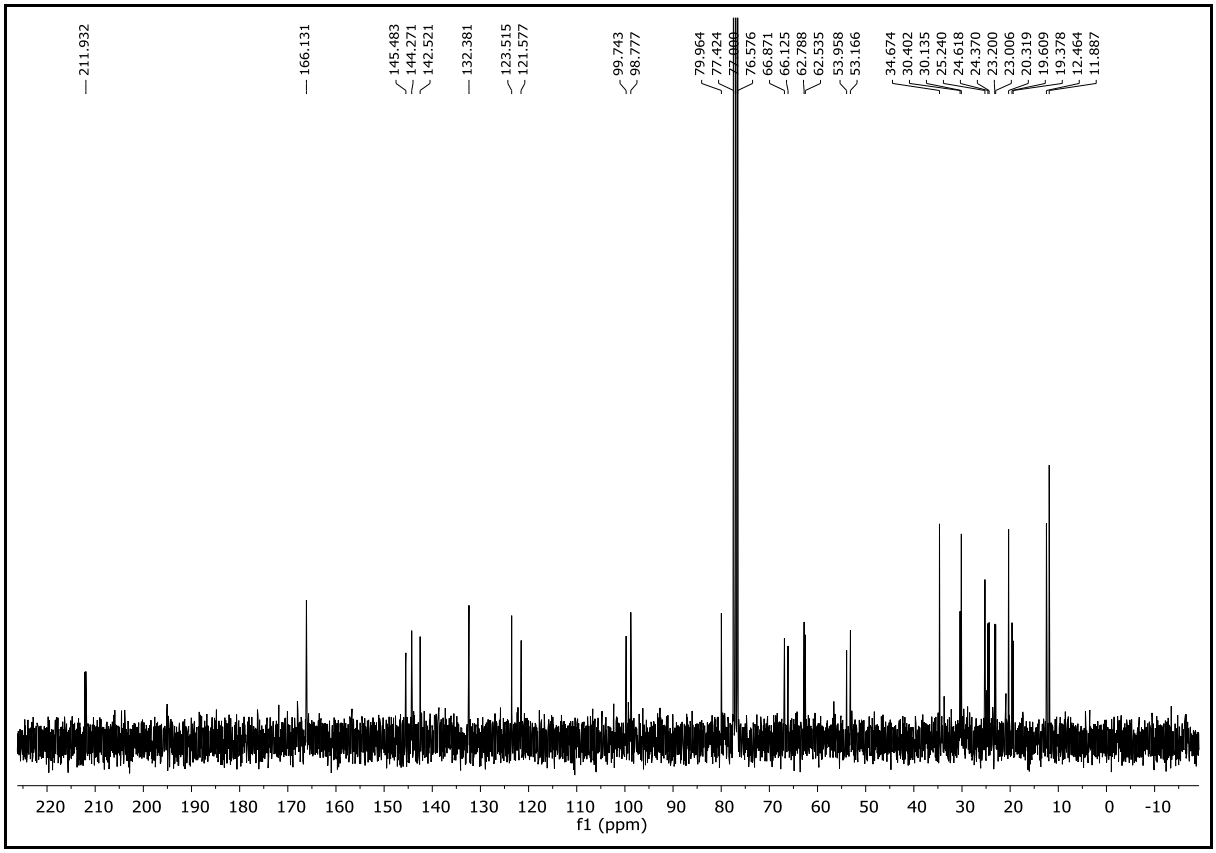
^{13}C-NMR spectrum of Intermediate of Compound 4a (75 MHz, $CDCl_3$):



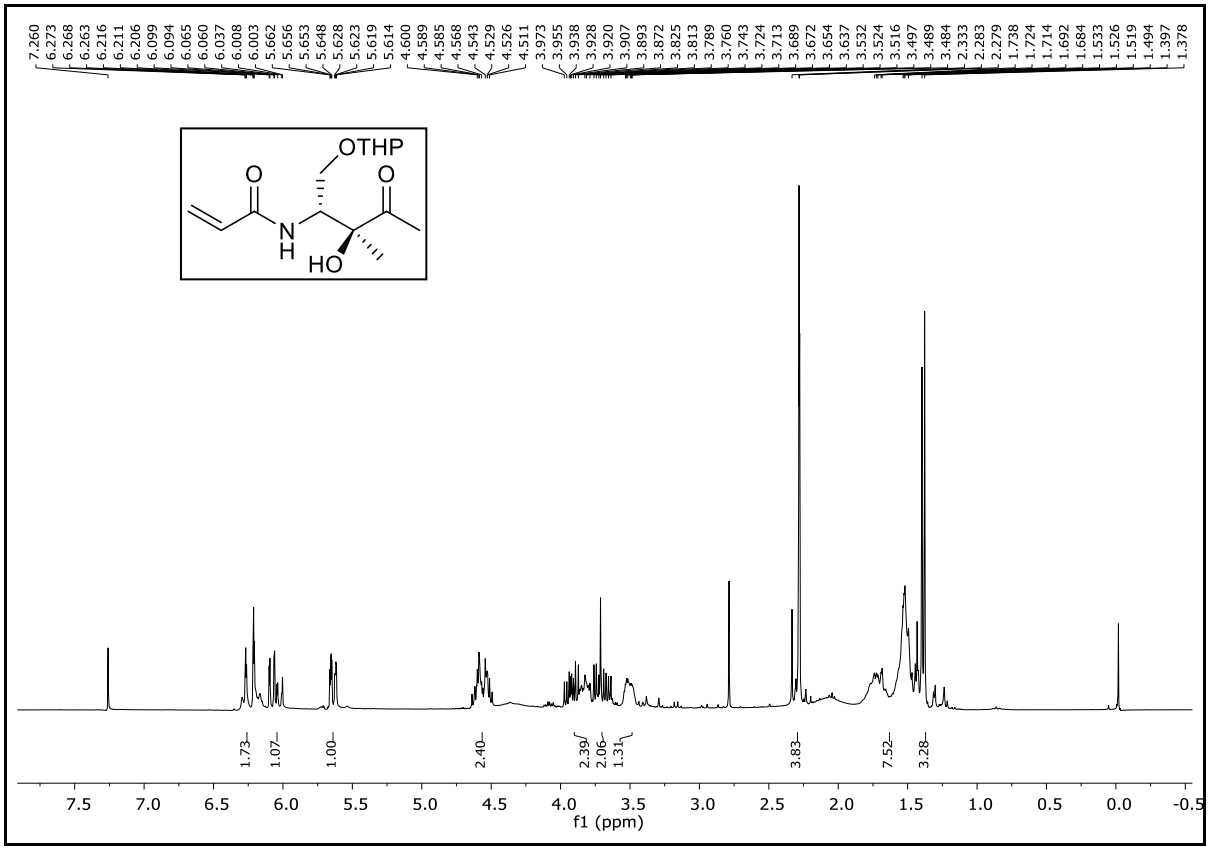
^{1}H-NMR Spectrum of Compound of 20 (300 MHz, $CDCl_3$):



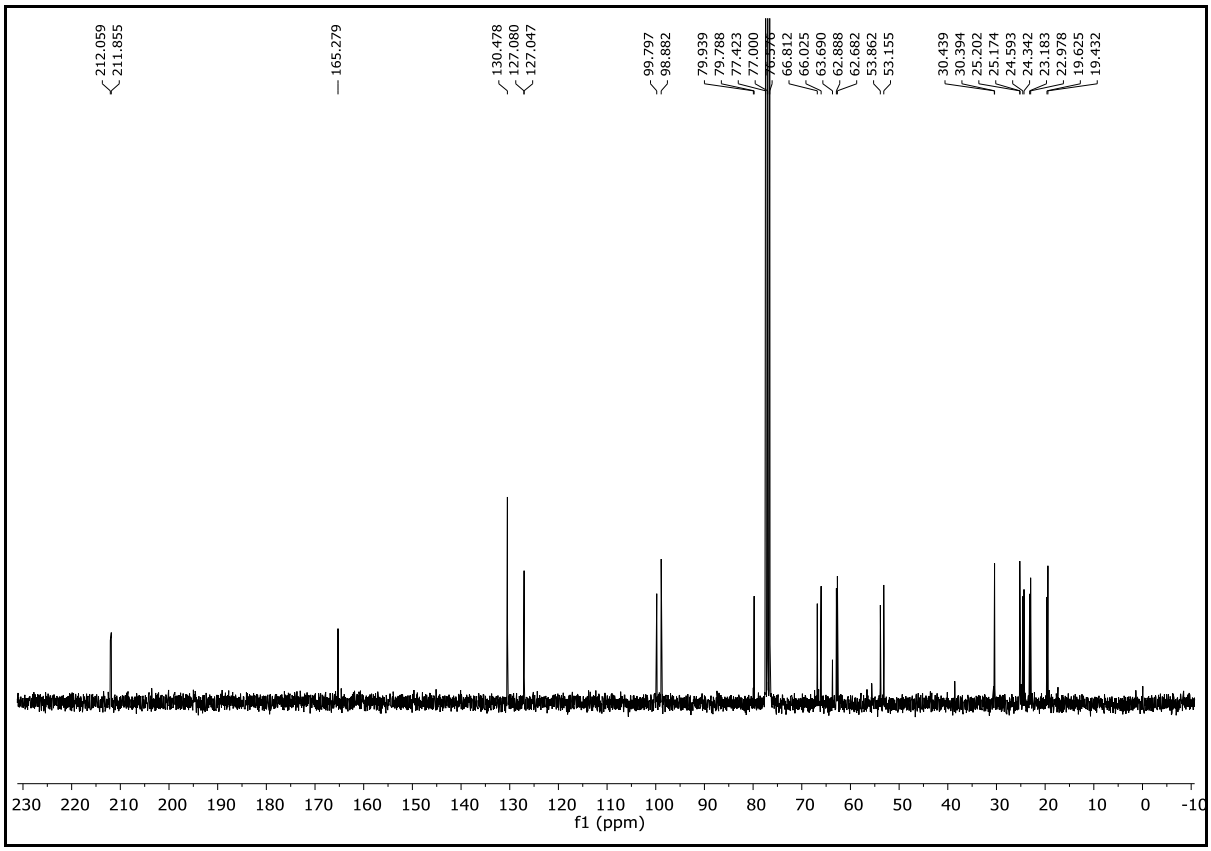
^{13}C-NMR Spectrum of Compound of 20 (75 MHz, $CDCl_3$):



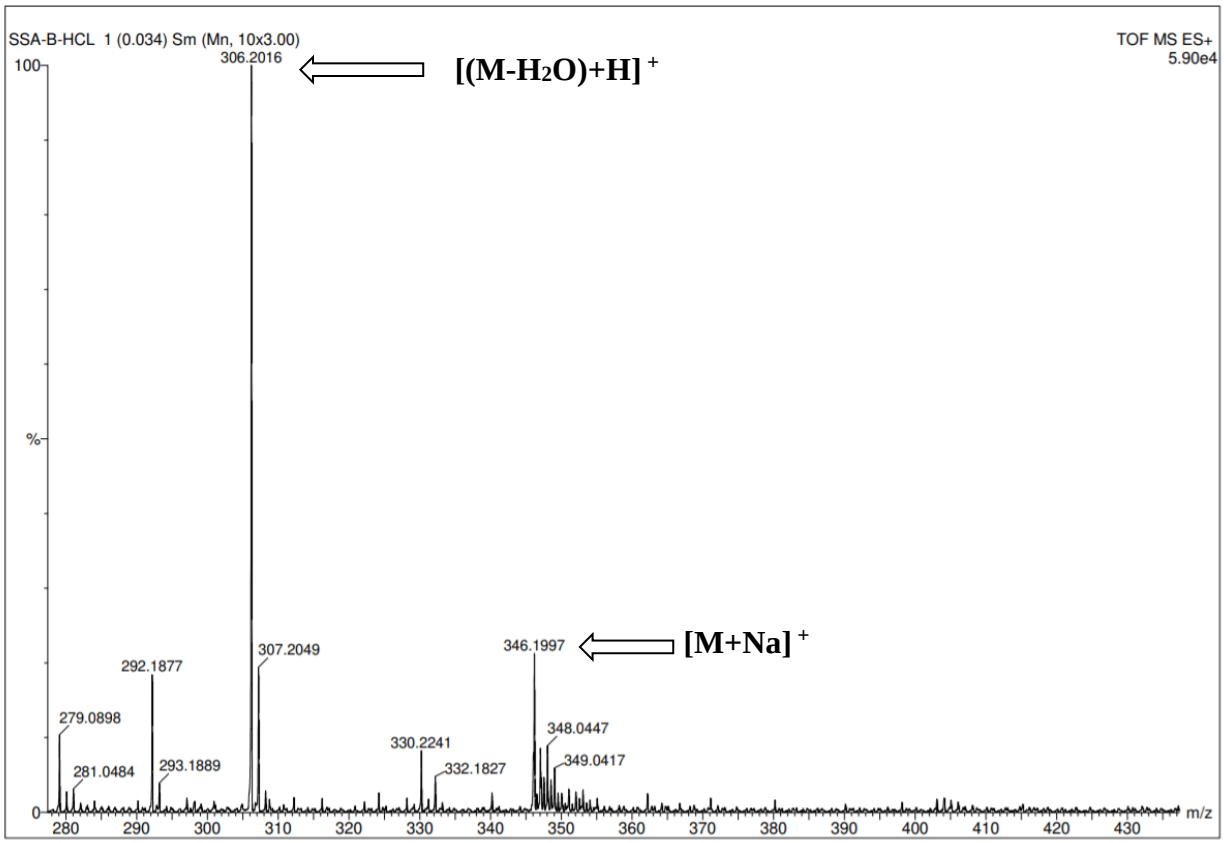
^{1}H-NMR Spectrum of Compound of 21 (300 MHz, $CDCl_3$):



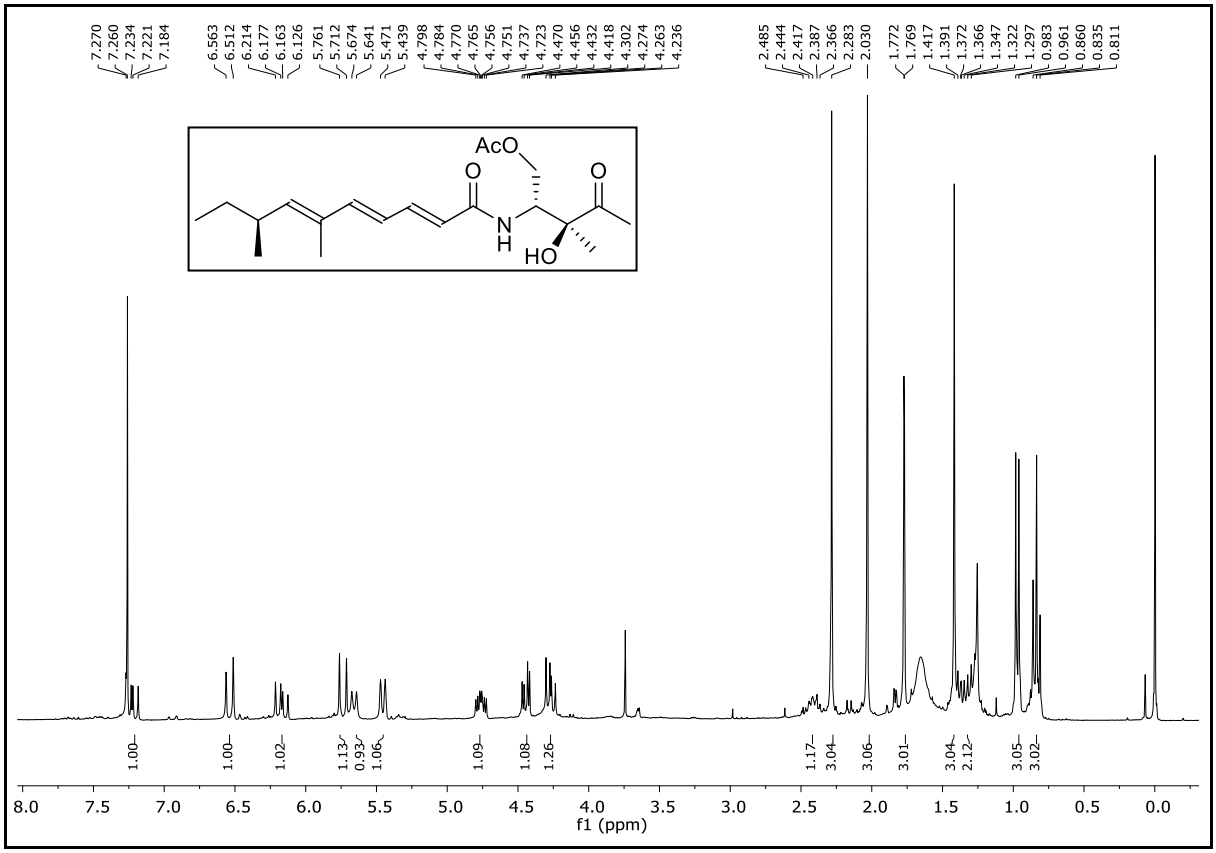
^{13}C-NMR Spectrum of Compound of 21 (75 MHz, $CDCl_3$):



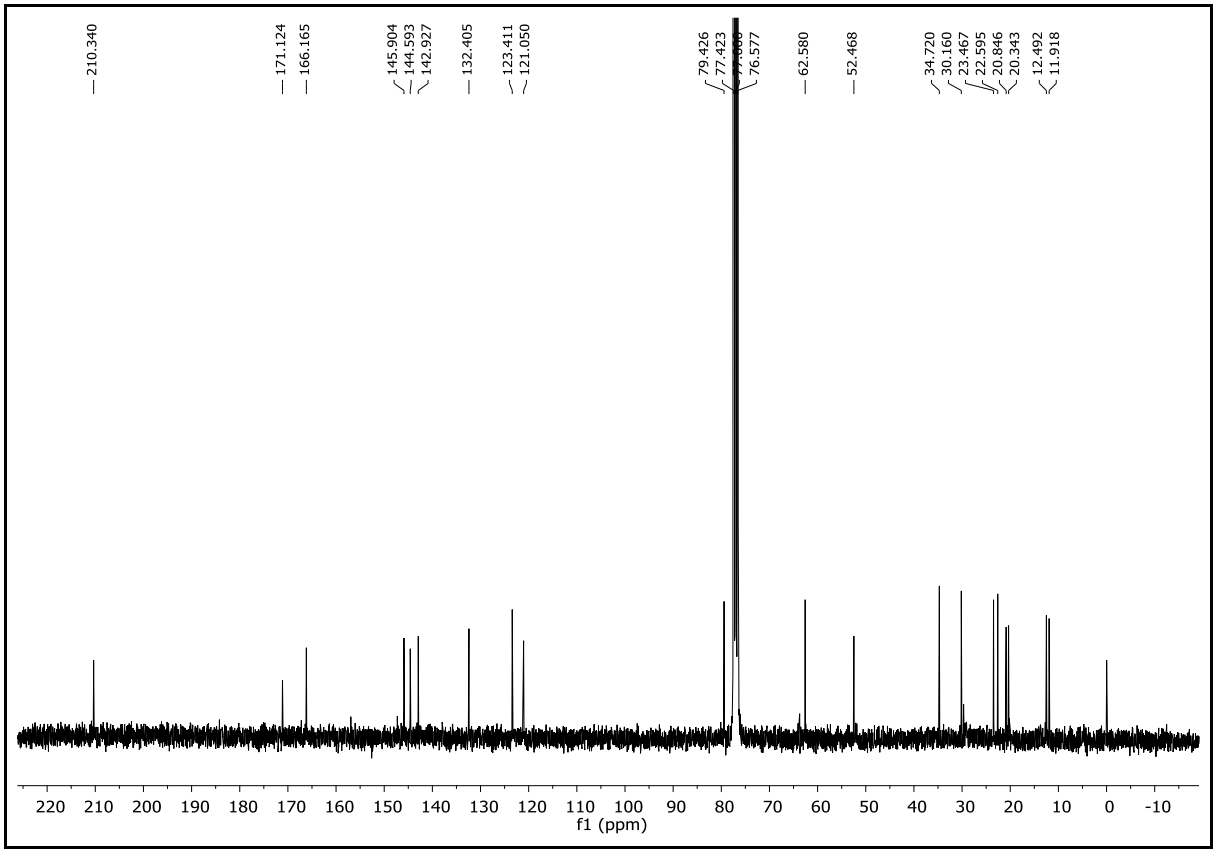
HRMS Spectrum of Compound 22:



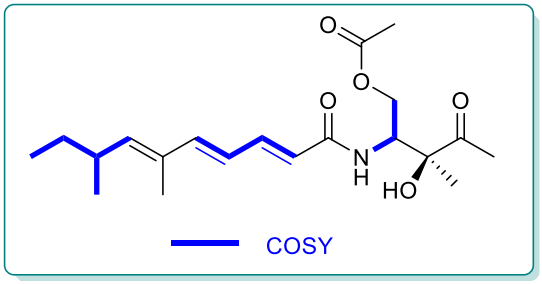
^{1}H-NMR Spectrum of Compound of 3a (300 MHz, $CDCl_3$):

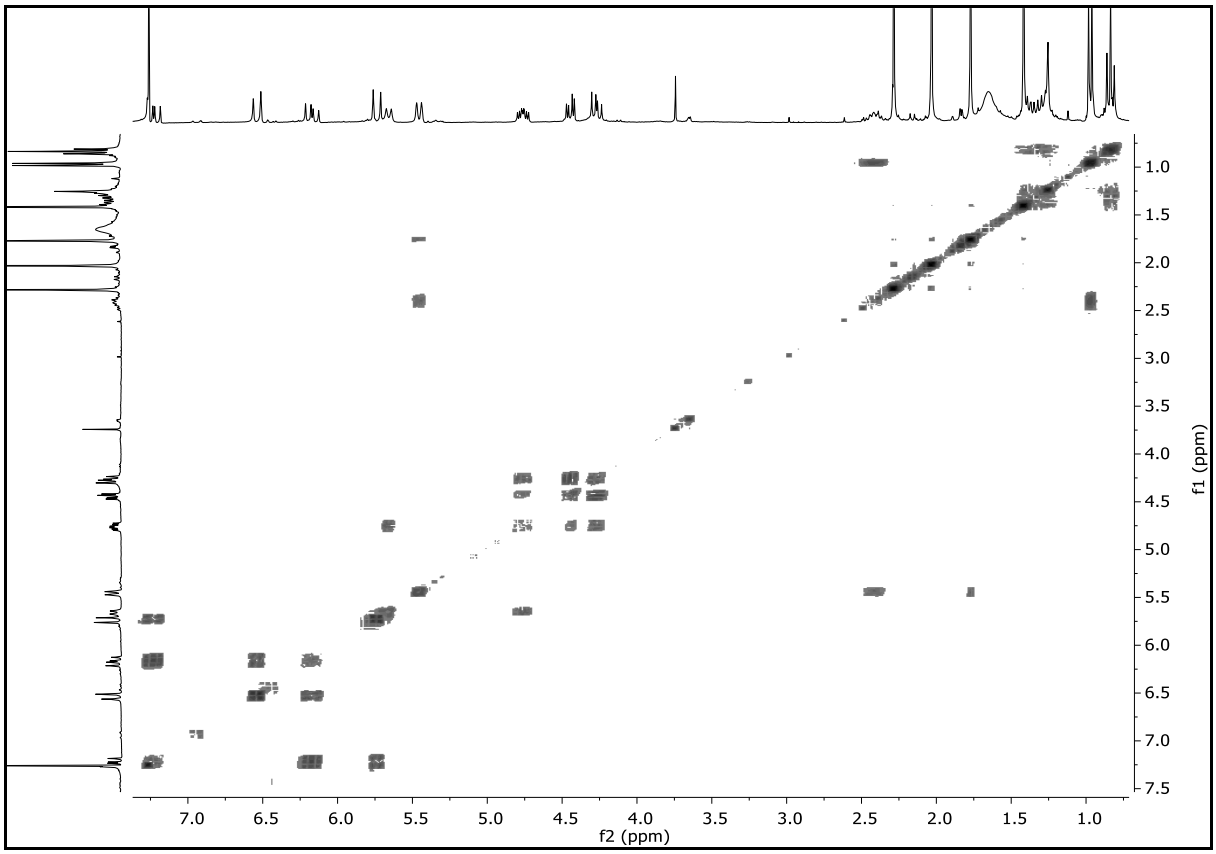


^{13}C-NMR Spectrum of Compound of 3a (75 MHz, $CDCl_3$):

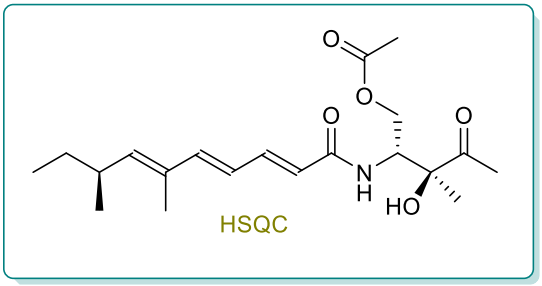


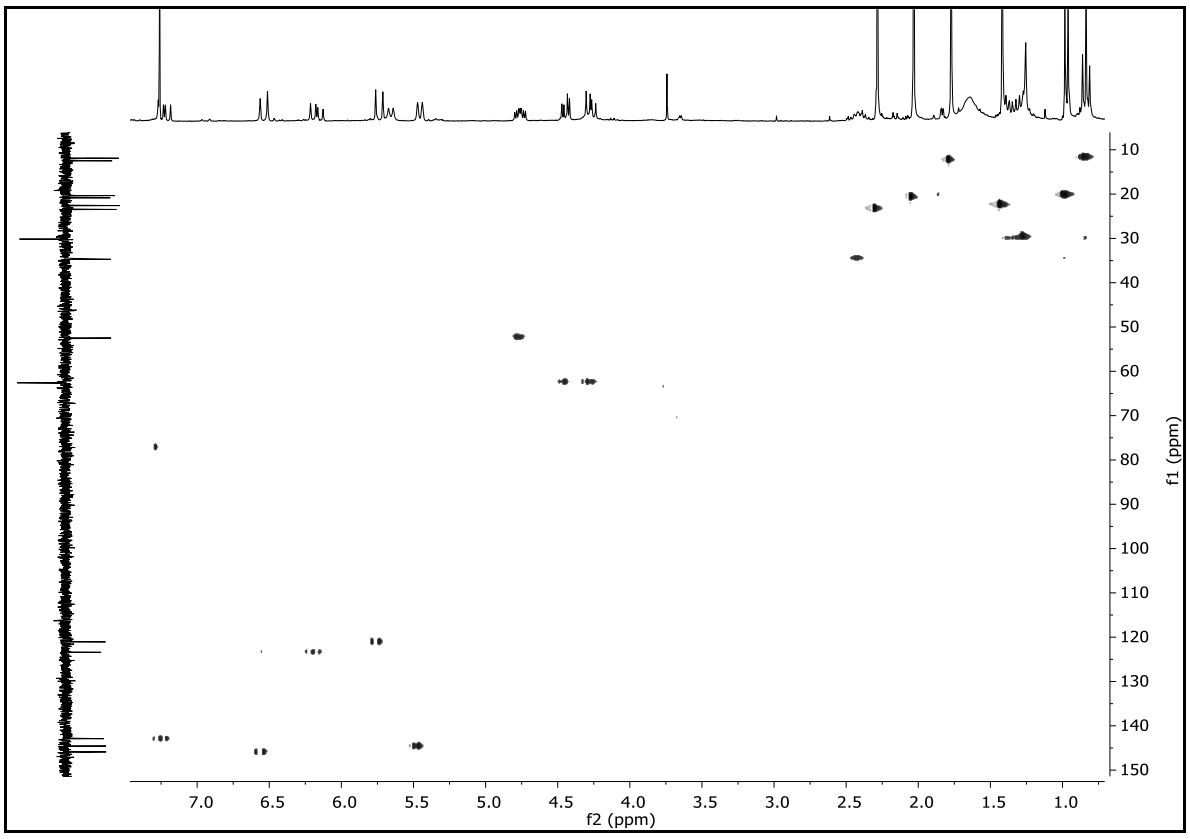
COSY Spectrum of Compound 3a (300 MHz, $CDCl_3$):



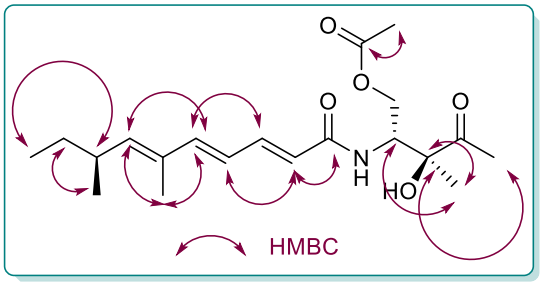


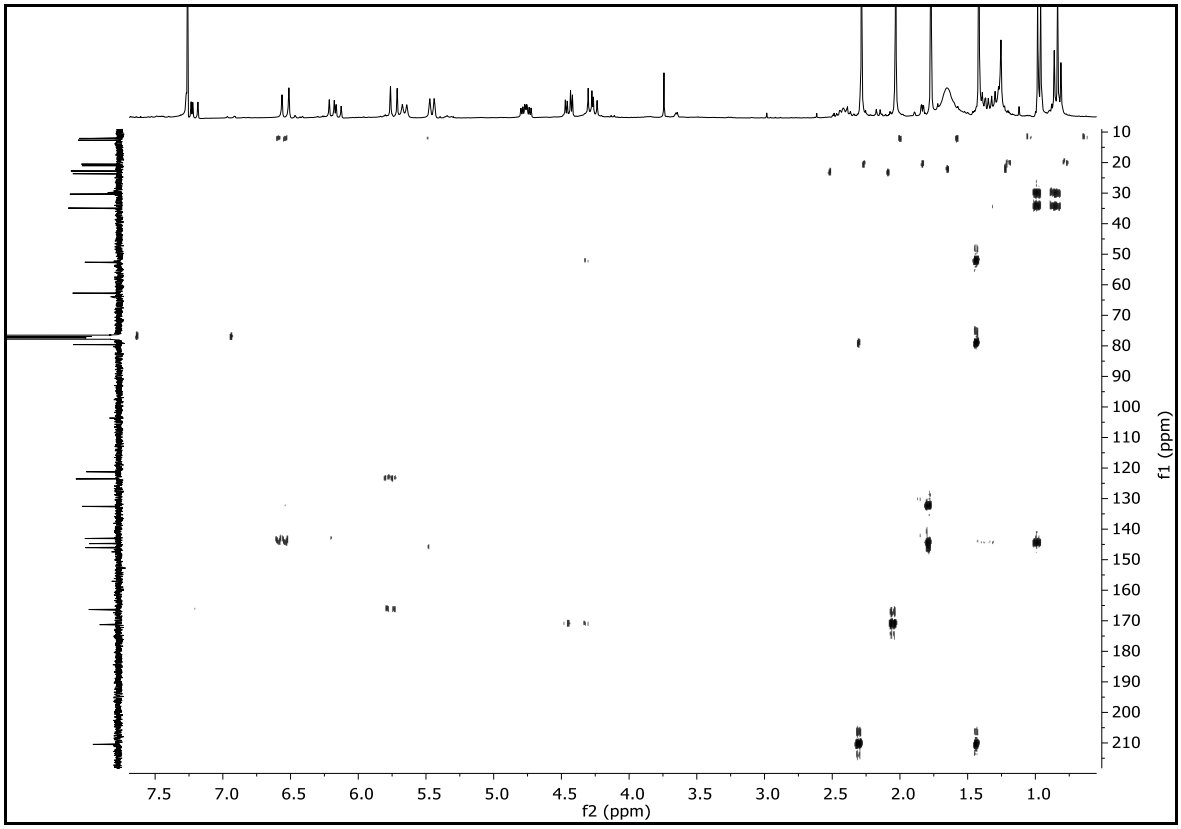
HSQC Spectrum of Compound 3a (75MHz, $CDCl_3$):



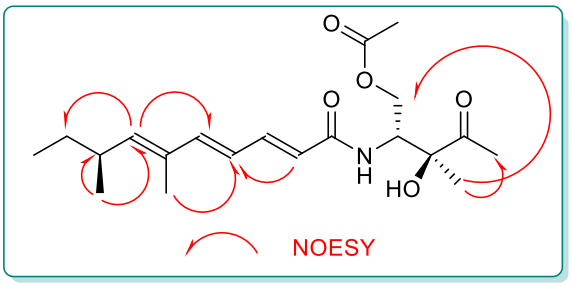


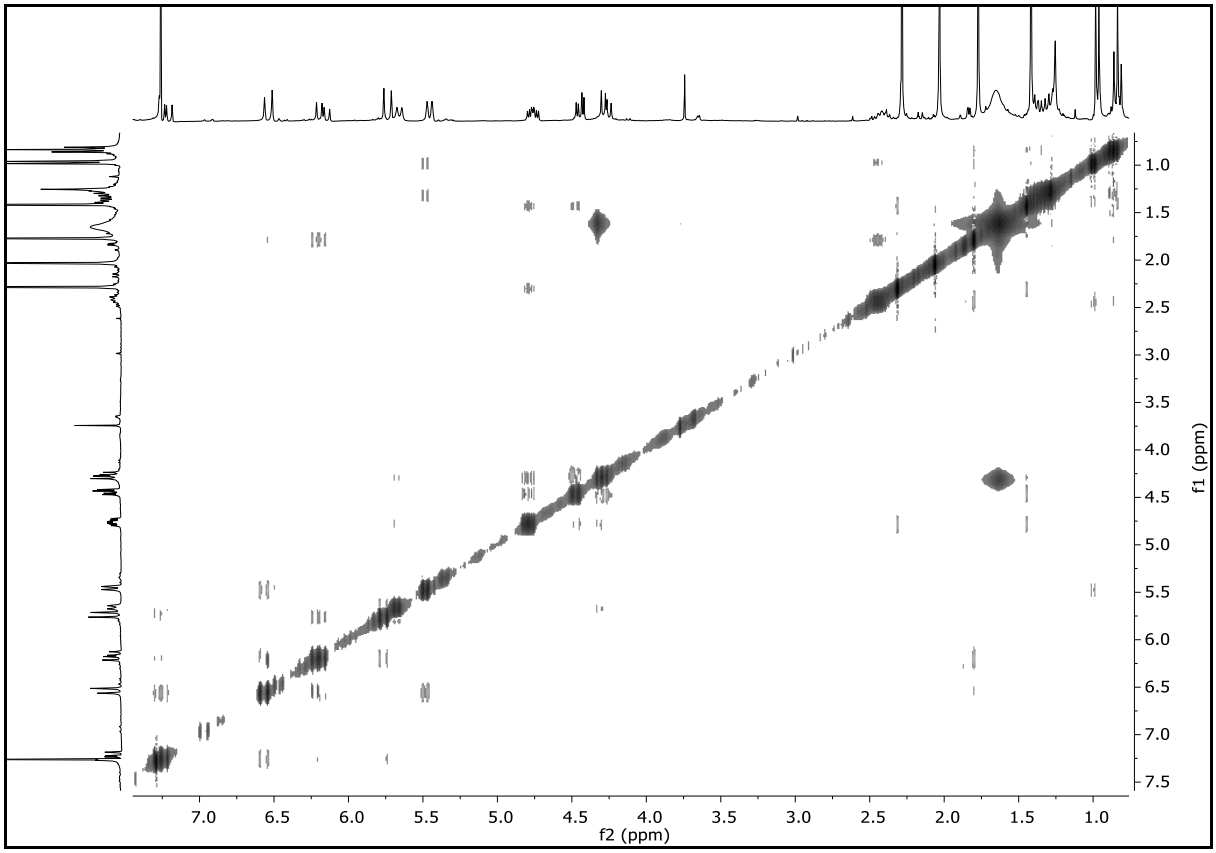
HMBC Spectrum of Compound 3a (300 MHz, $CDCl_3$):



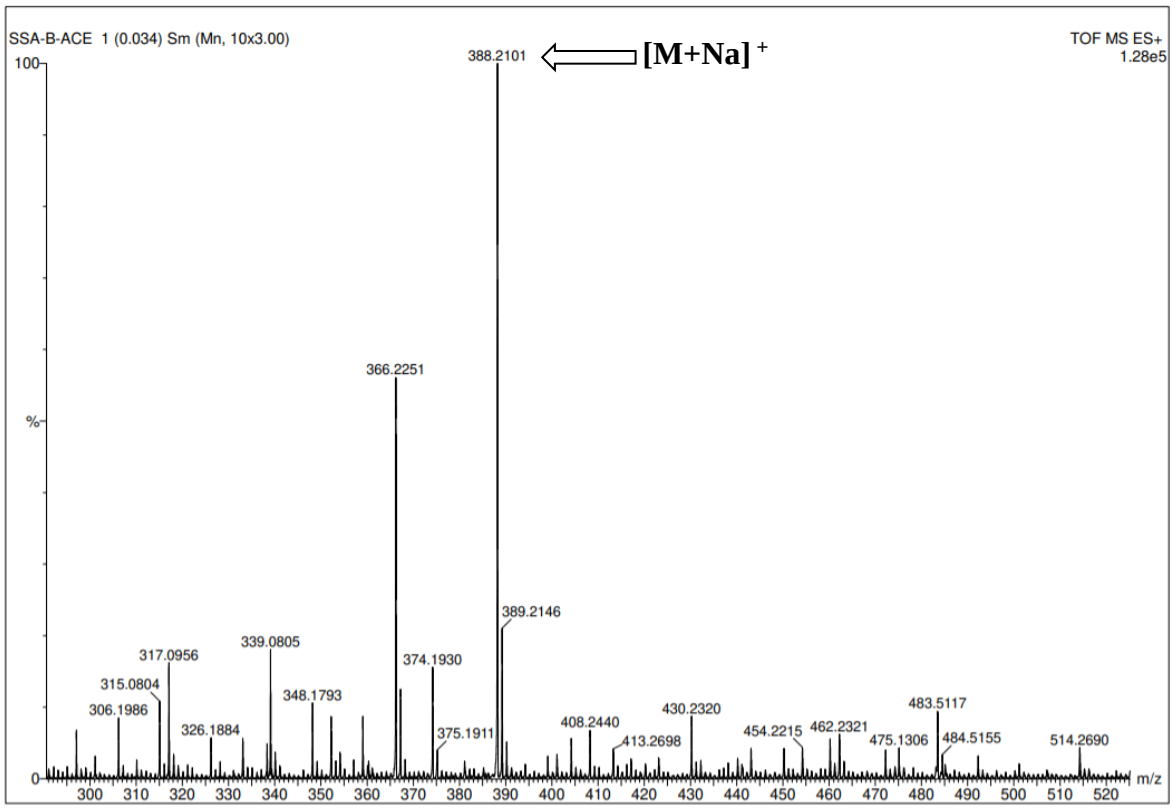


NOESY Spectrum of Compound 3a (300 MHz, $CDCl_3$):

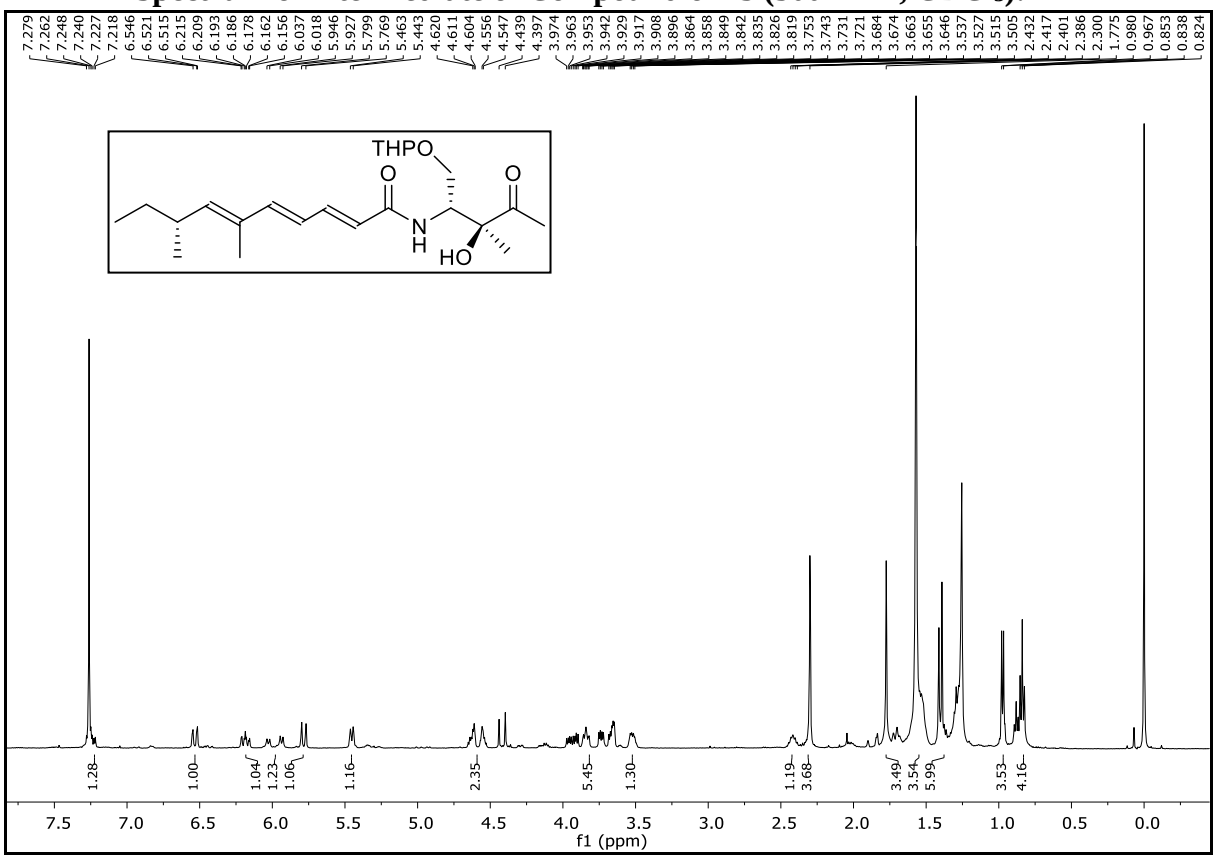




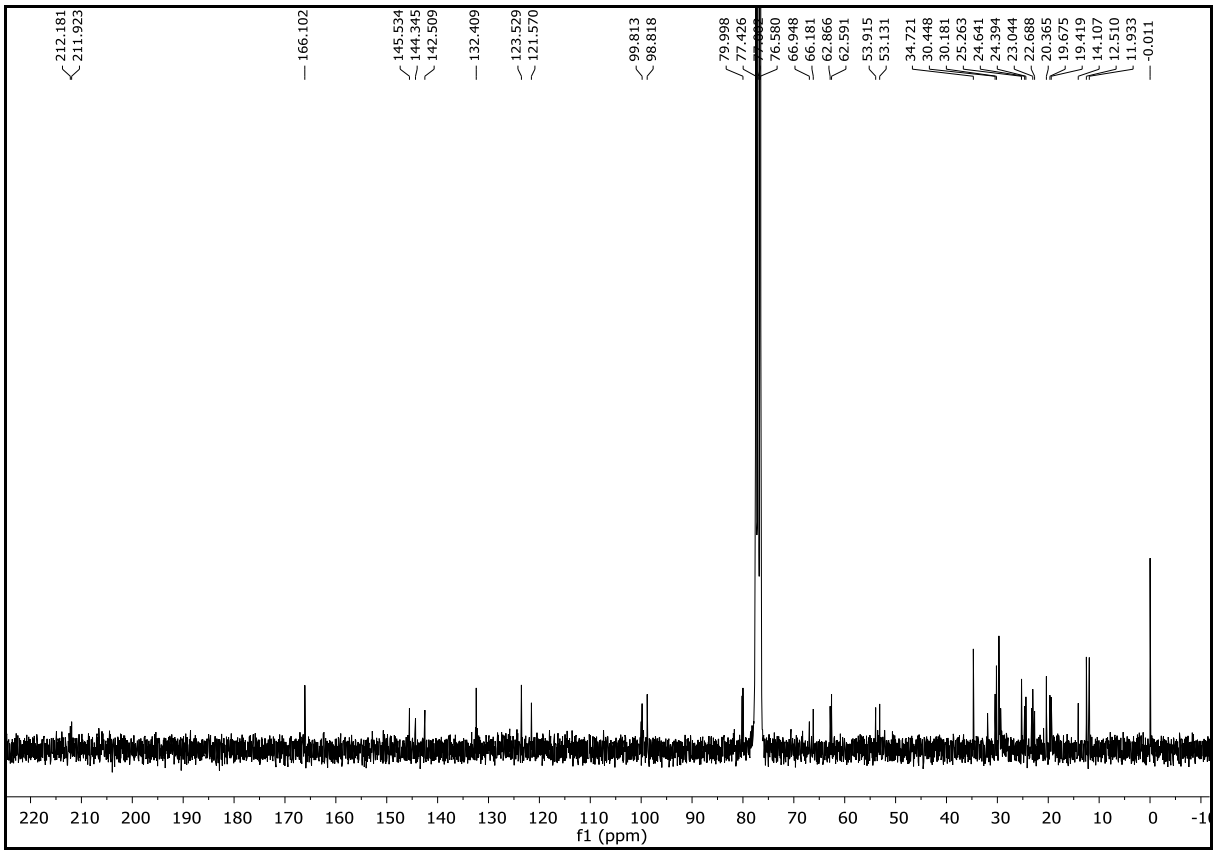
HRMS Spectrum of Compound 3a:



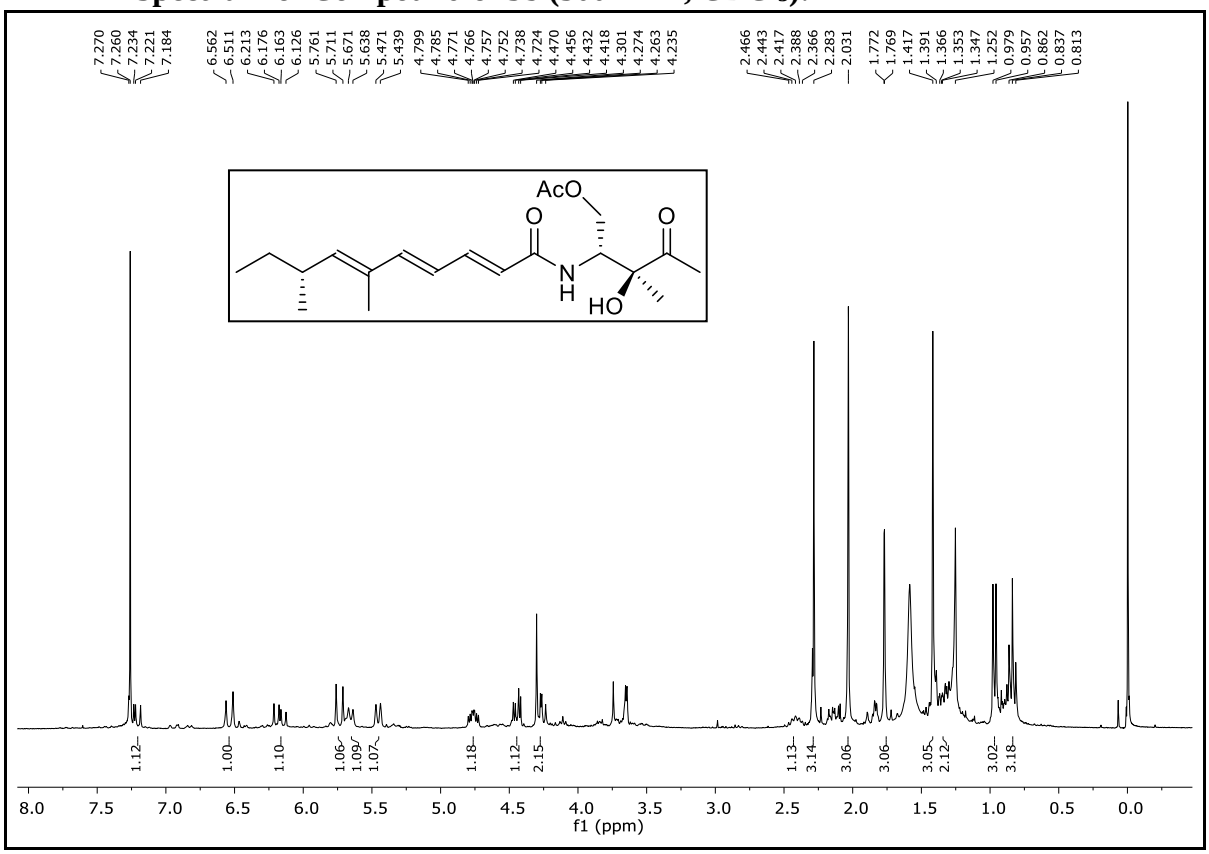
^{1}H-NMR Spectrum of intermediate of Compound of 23 (500 MHz, $CDCl_3$):



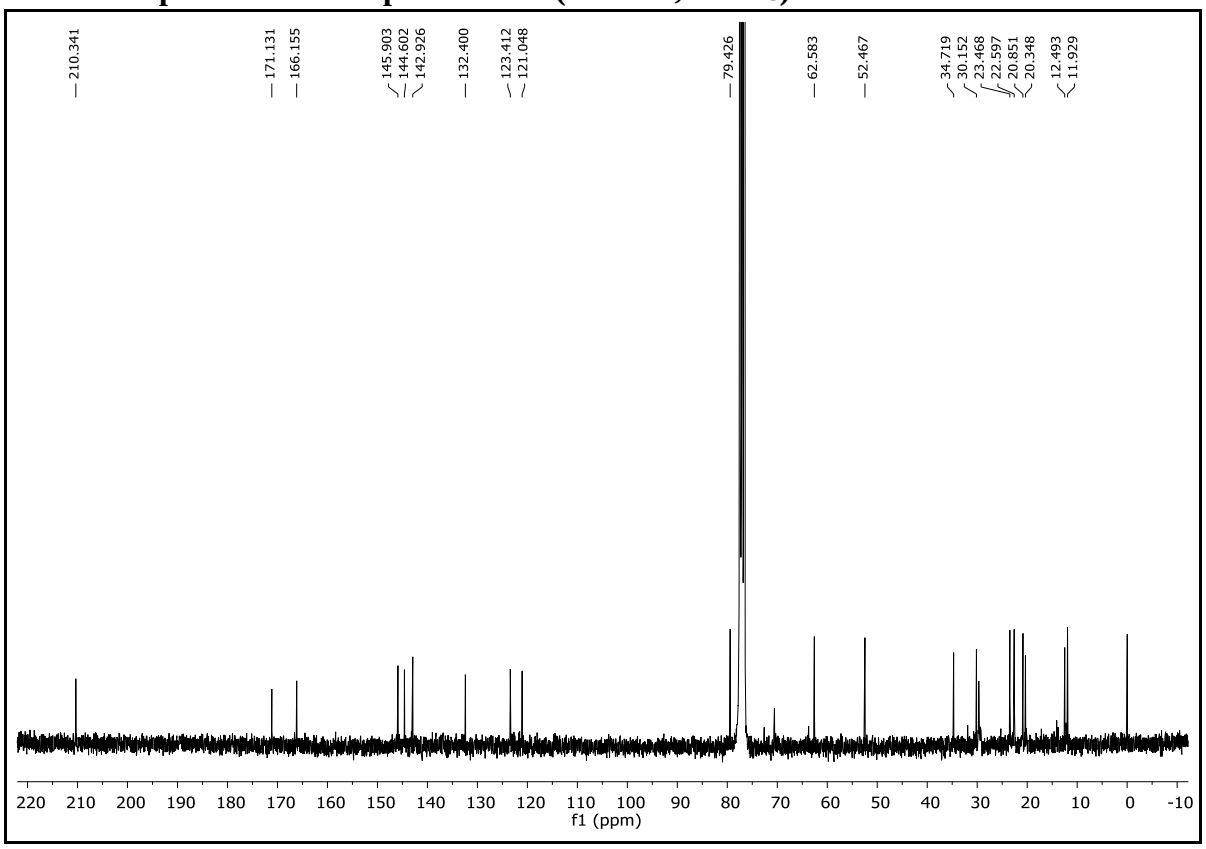
^{13}C-NMR Spectrum of intermediate of Compound of 23 (75 MHz, $CDCl_3$):



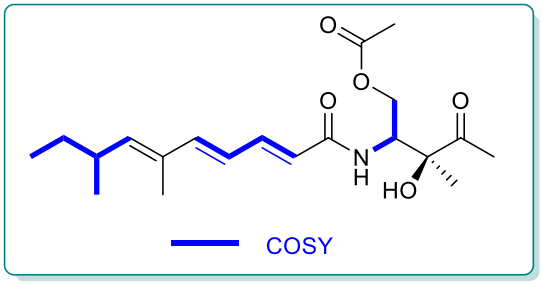
^{1}H-NMR Spectrum of Compound of 3b (300 MHz, $CDCl_3$):

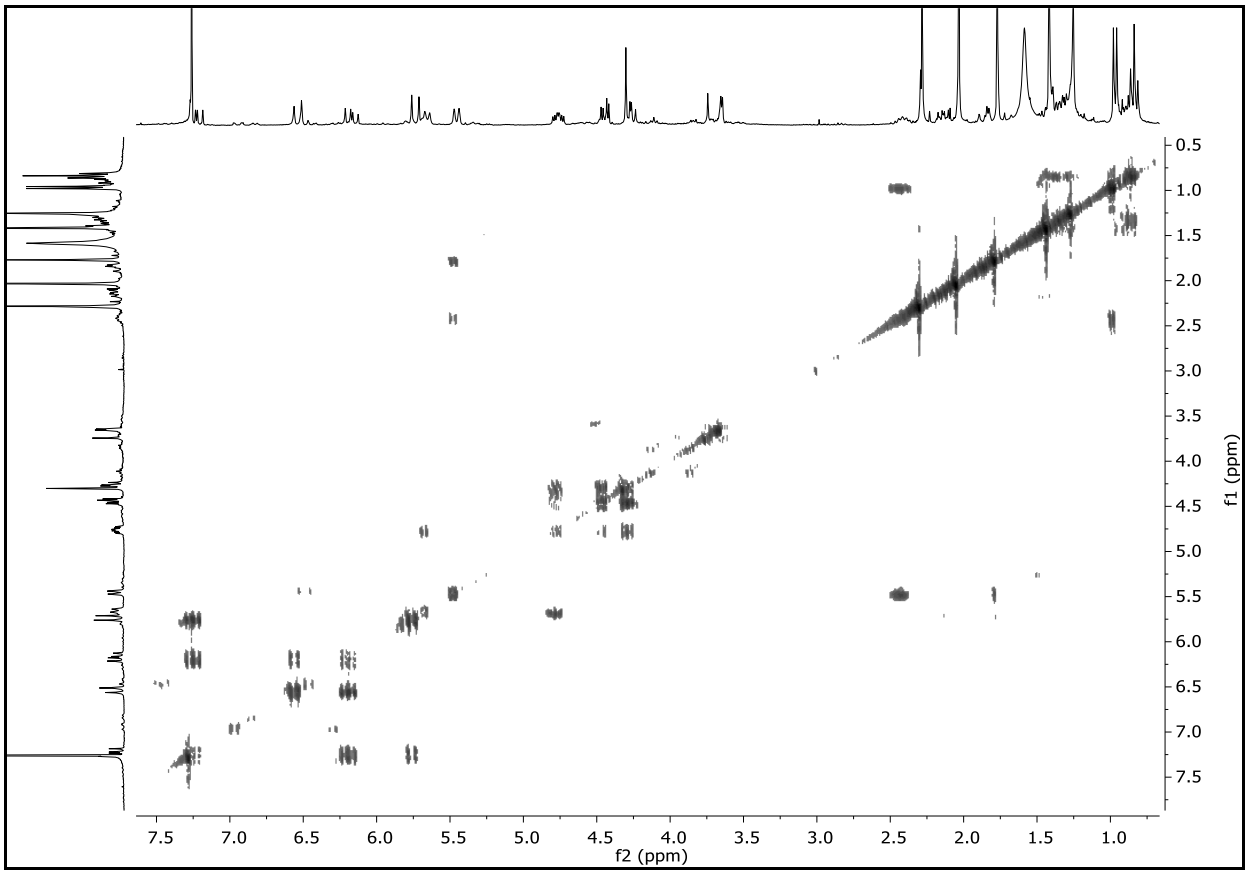


^{13}C NMR Spectrum of Compound of 3b (75 MHz, $CDCl_3$):

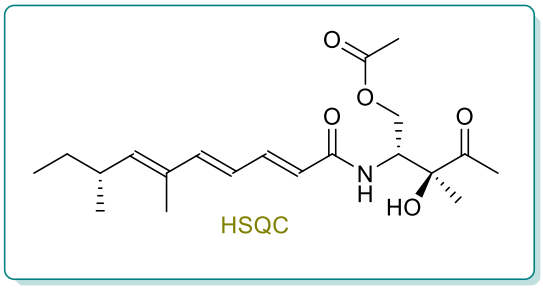


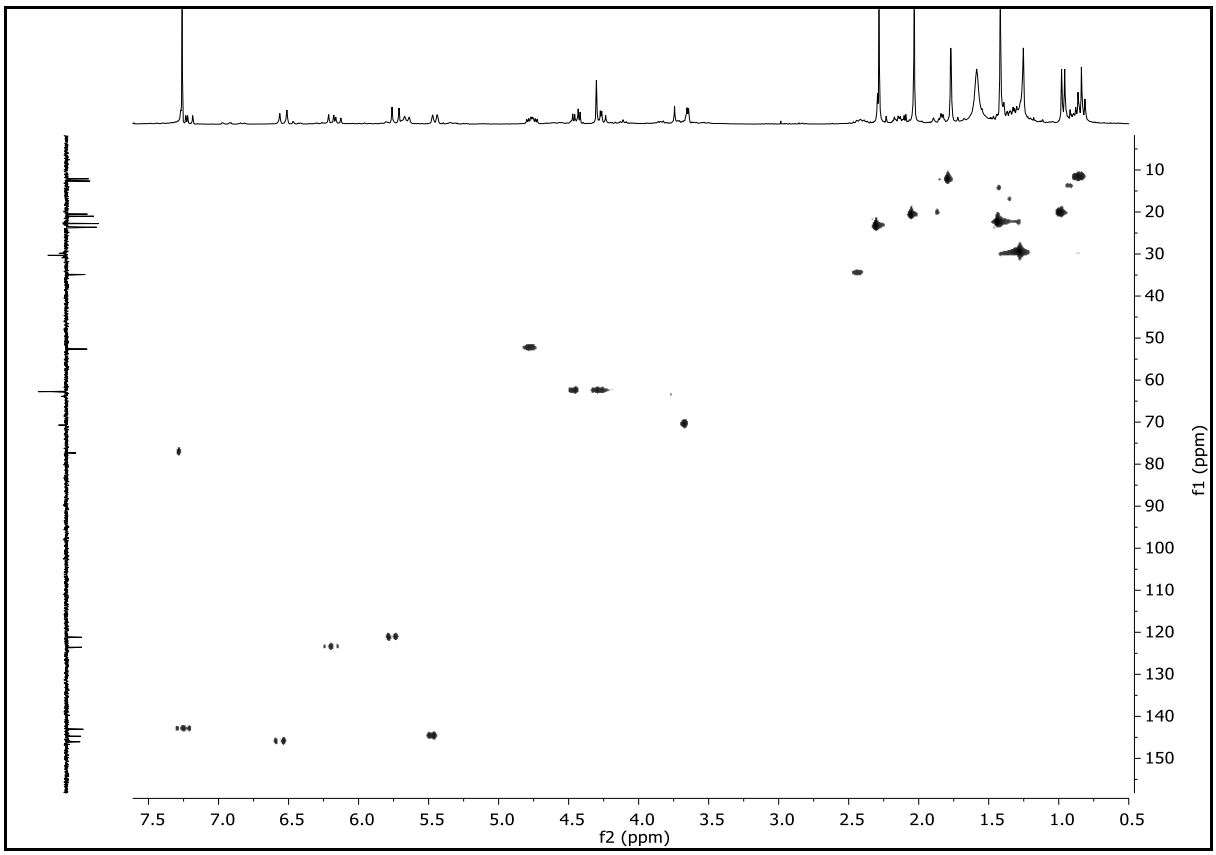
COSY Spectrum of Compound 3b (300 MHz, $CDCl_3$):



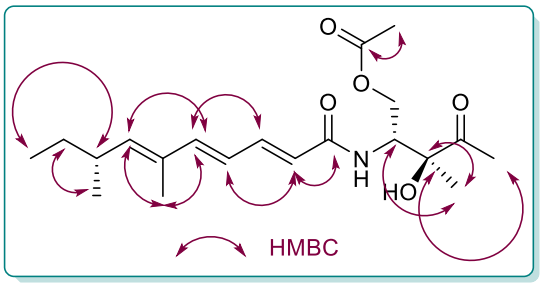


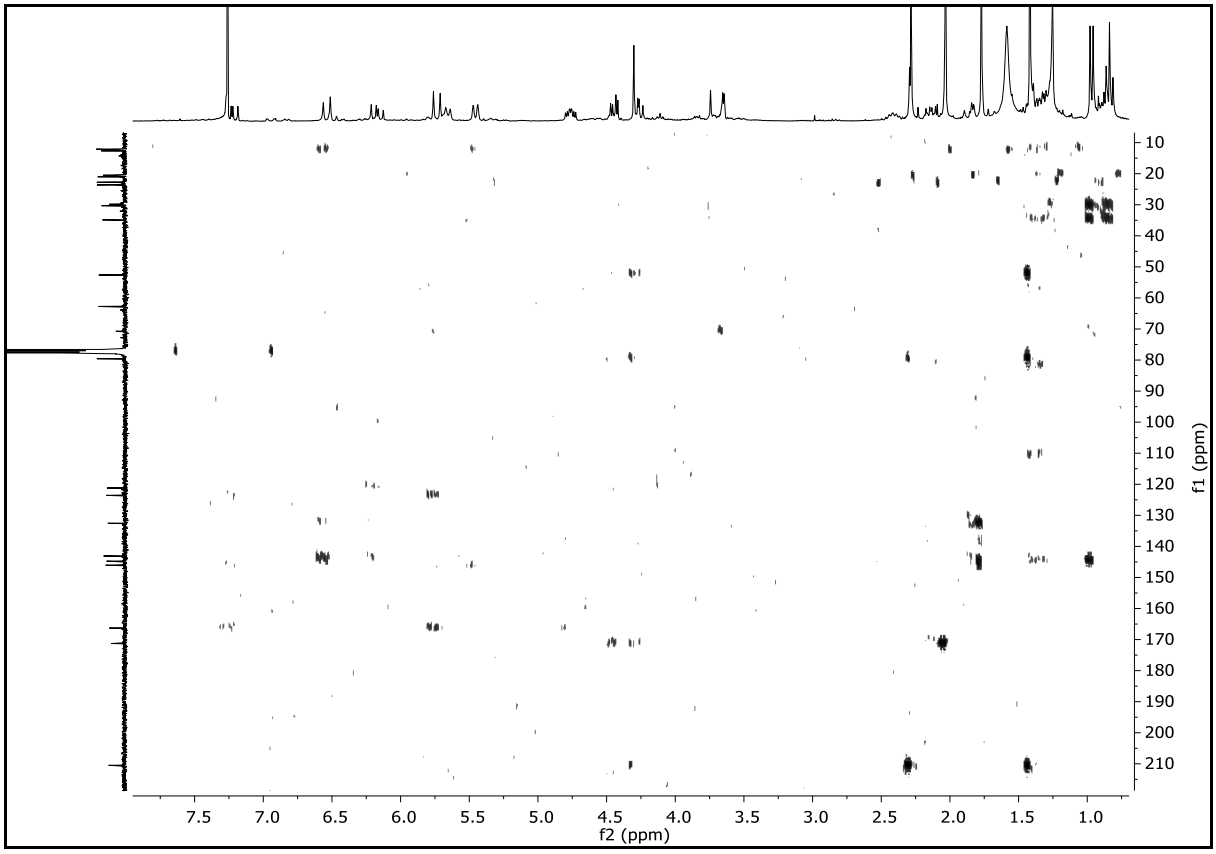
HSQC Spectrum of Compound 3b (75 MHz, $CDCl_3$):



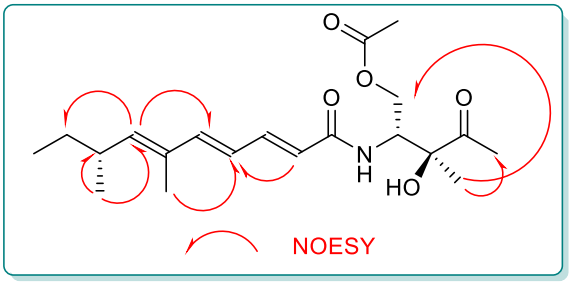


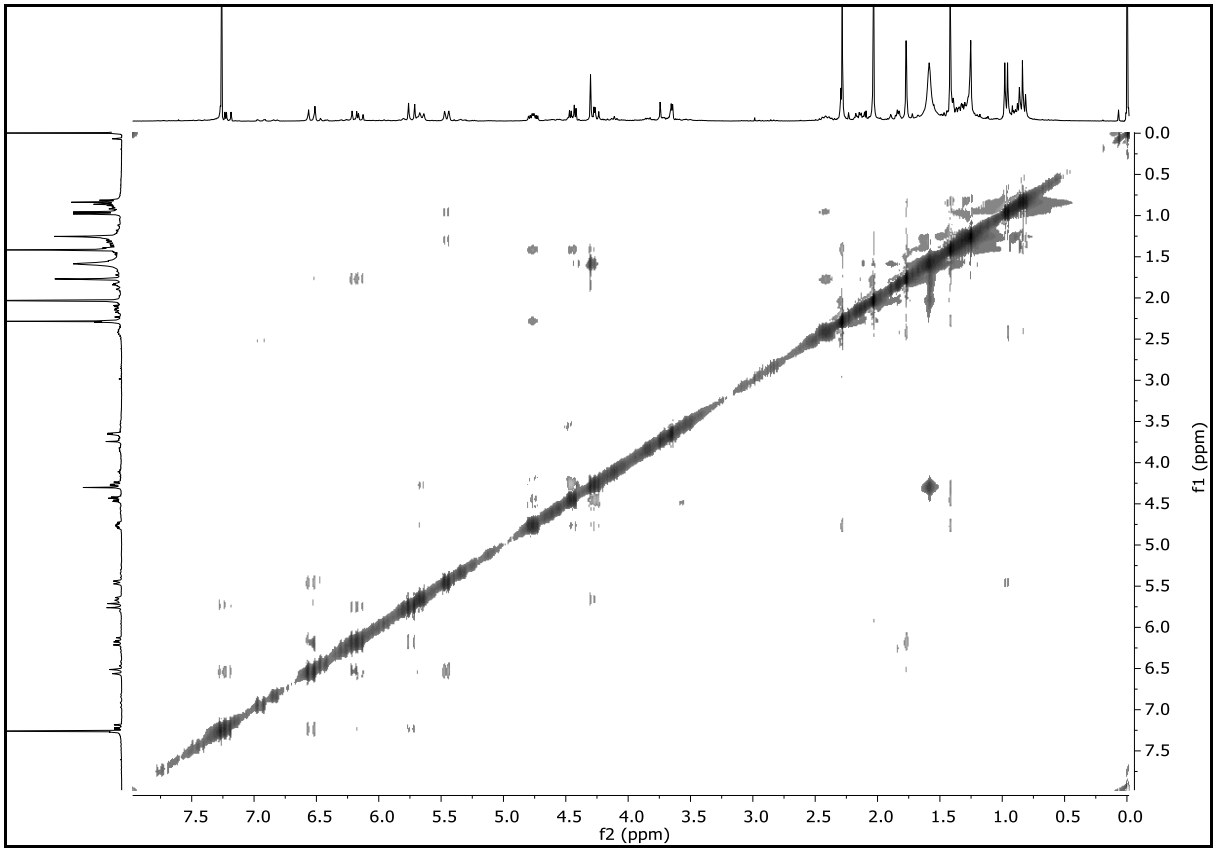
HMBC Spectrum of Compound 3b (75 MHz, $CDCl_3$):





NOESY Spectrum of Compound 3b (300 MHz, $CDCl_3$):





HRMS Spectrum of Compound 3b: