

Alternative Synthesis of the Colorado Potato Beetle (CPB) Pheromone

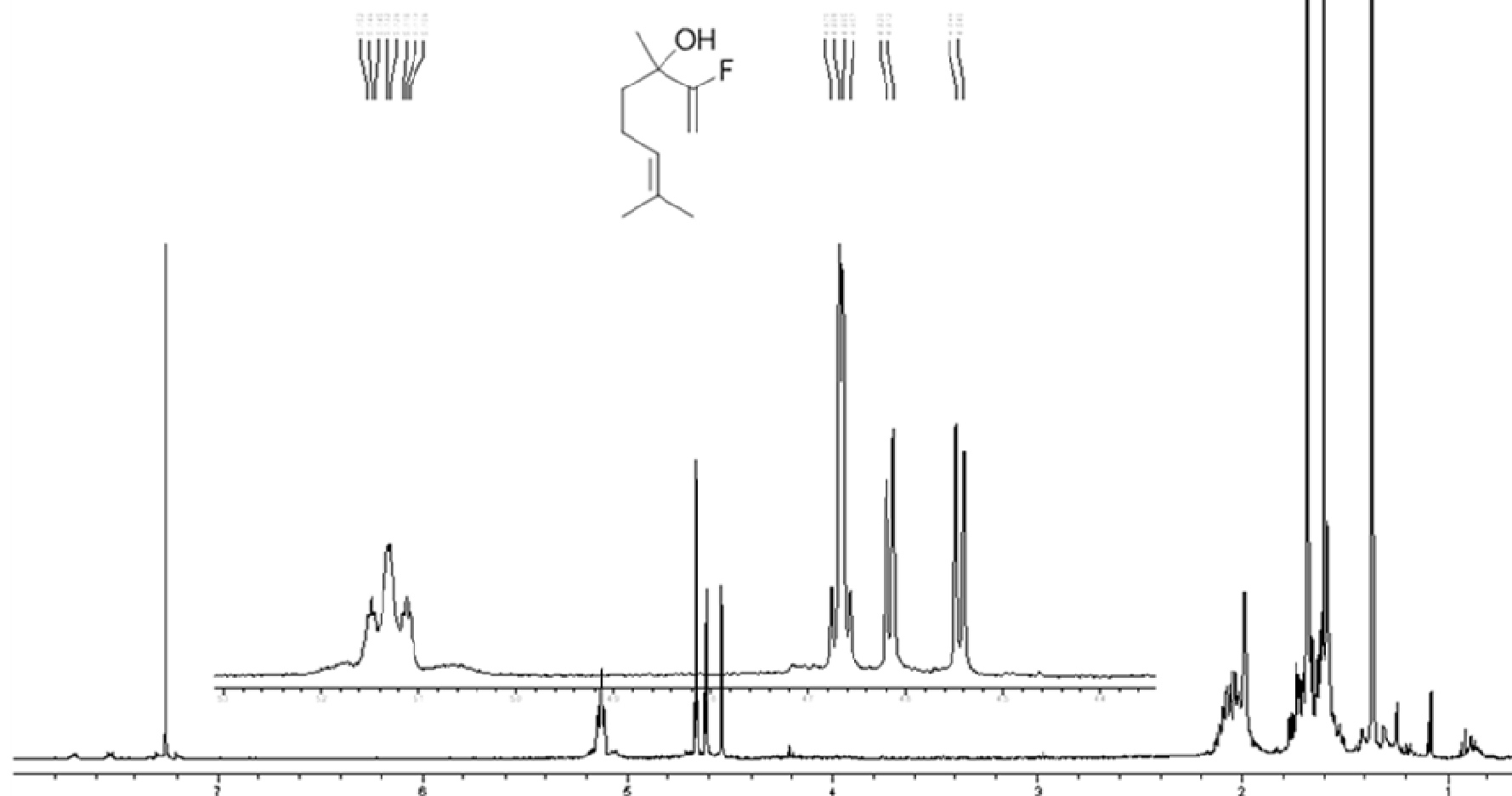
Juan A. Faraldos,* Robert M. Coates and José-L. Giner

Supporting Information

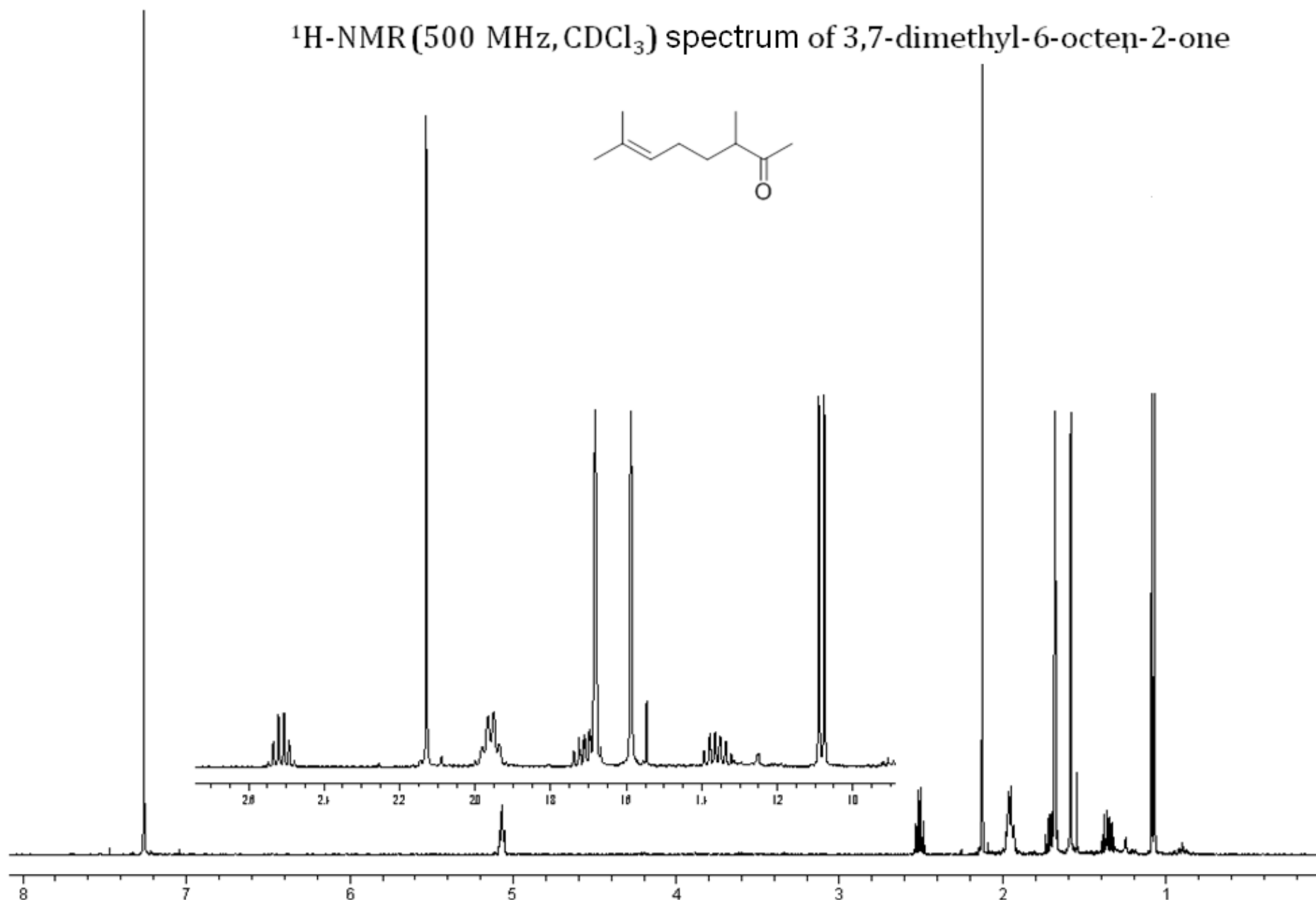
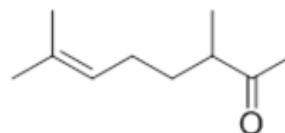
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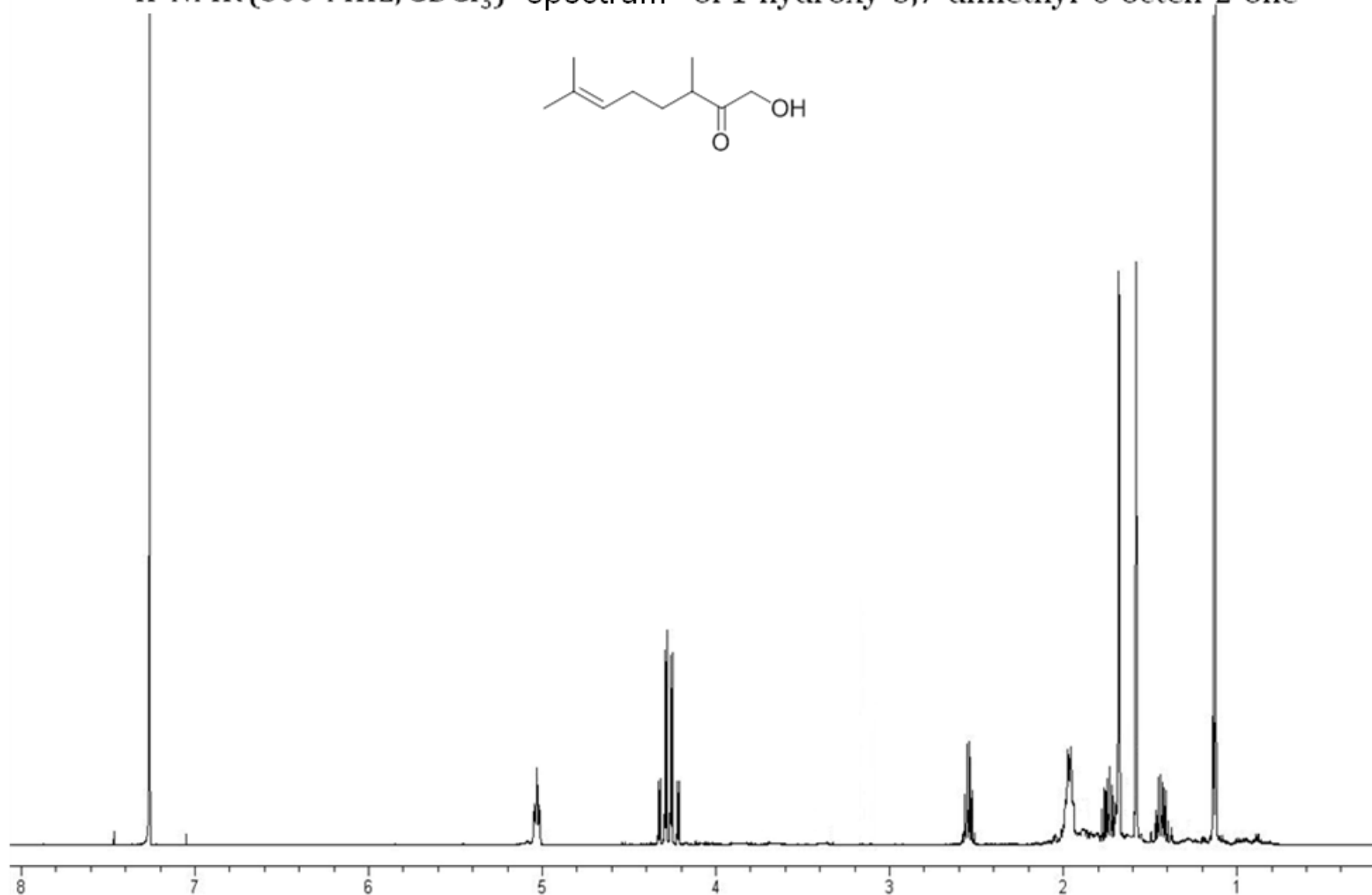
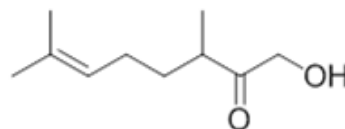
^1H NMR (500 MHz, CDCl_3) spectrum of racemic 2F-Linalool
(2-fluoro-3,7-dimethylocta-1,6-dien-3-ol)



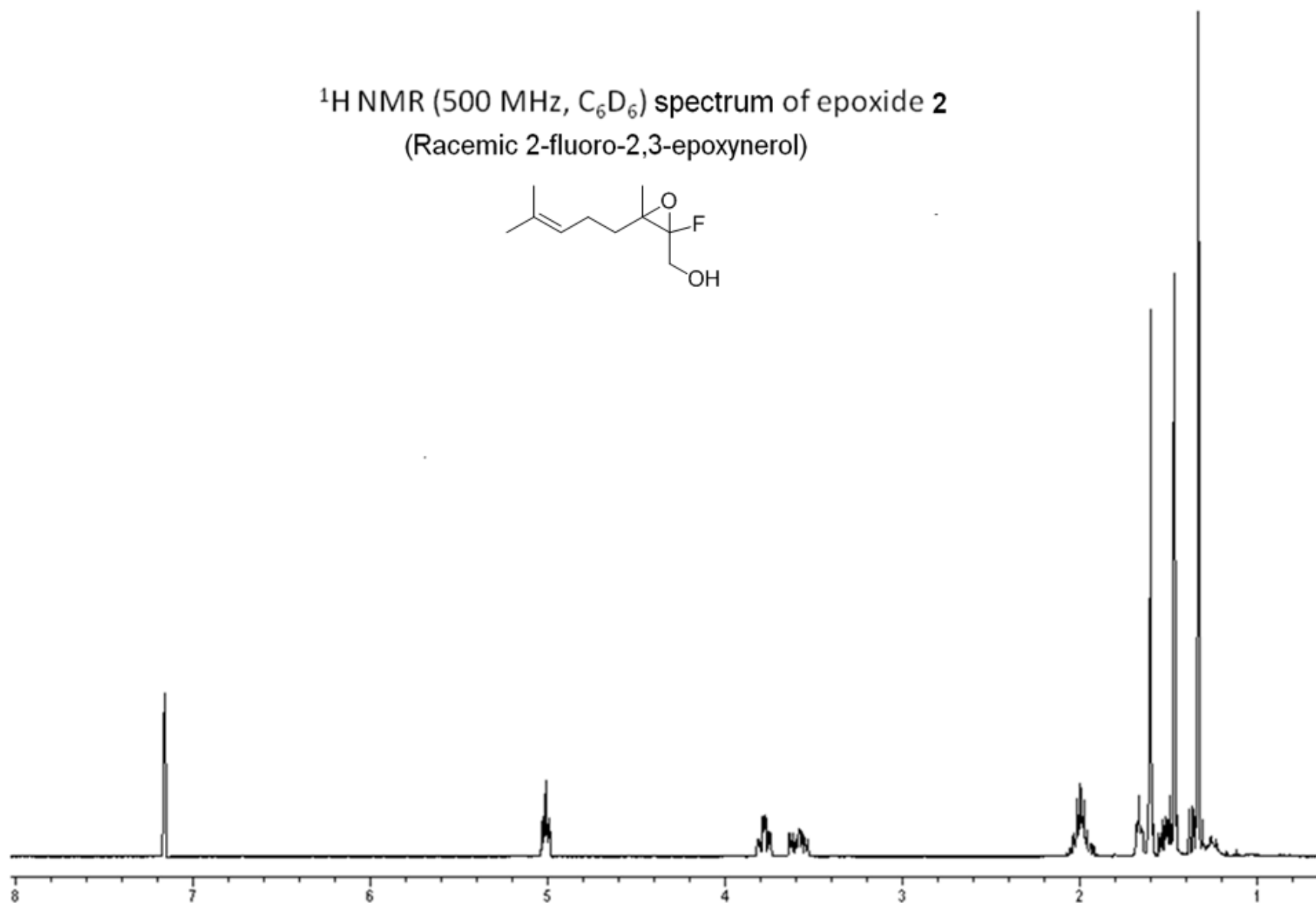
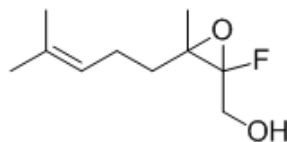
^1H -NMR (500 MHz, CDCl_3) spectrum of 3,7-dimethyl-6-octen-2-one



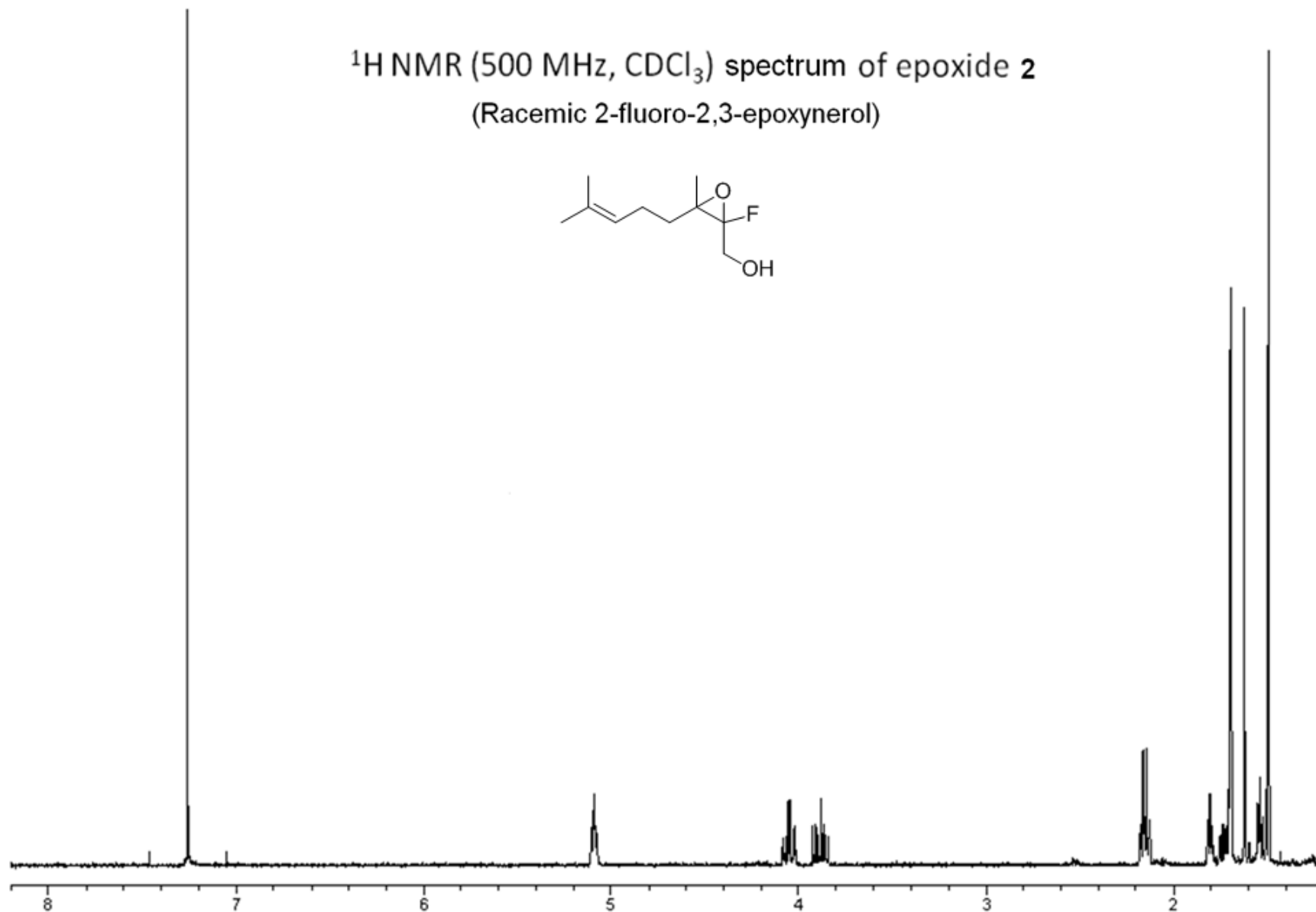
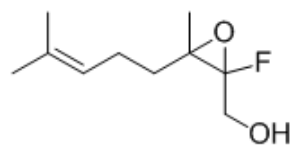
^1H -NMR (500 MHz, CDCl_3) spectrum of 1-hydroxy-3,7-dimethyl-6-octen-2-one

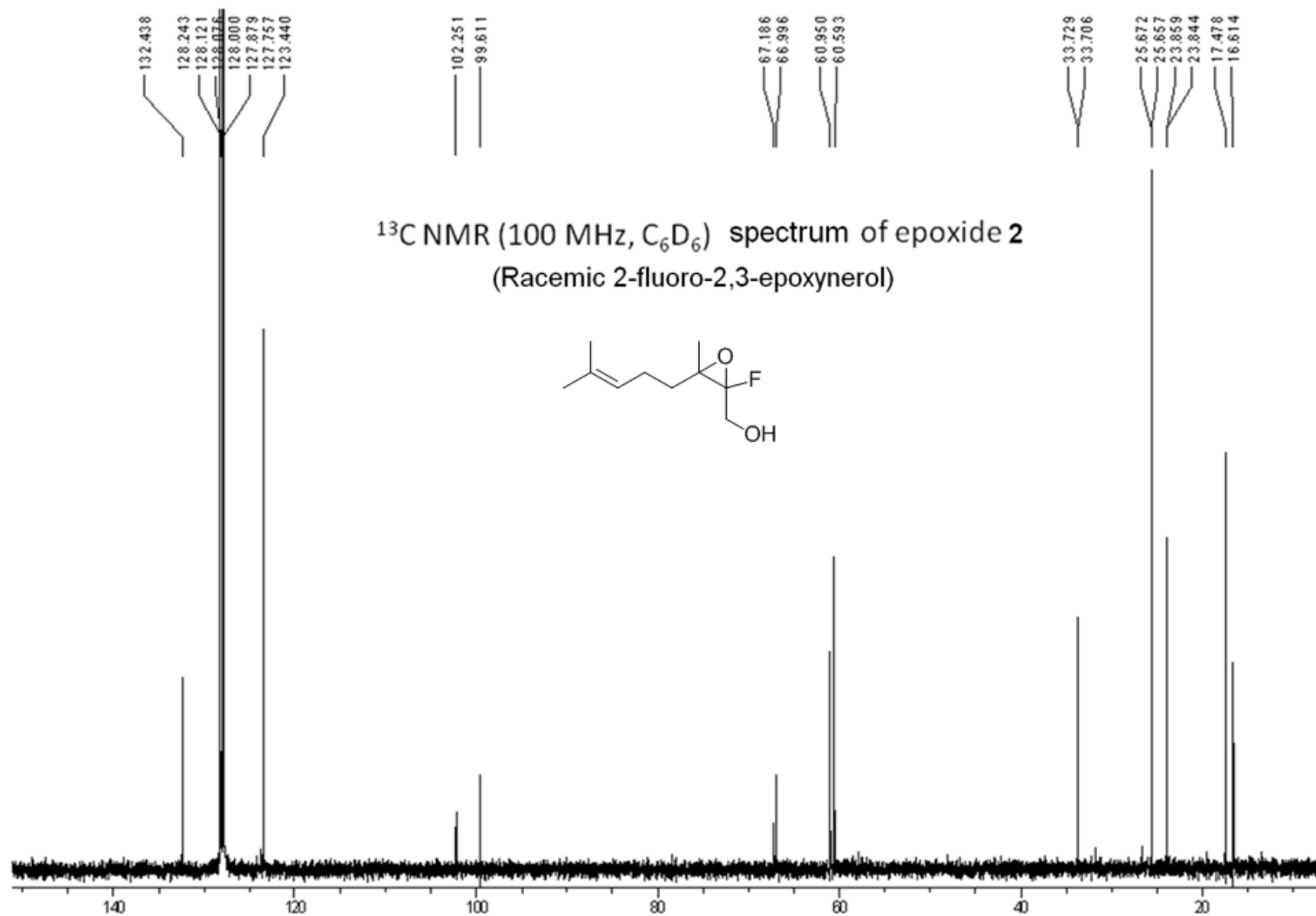


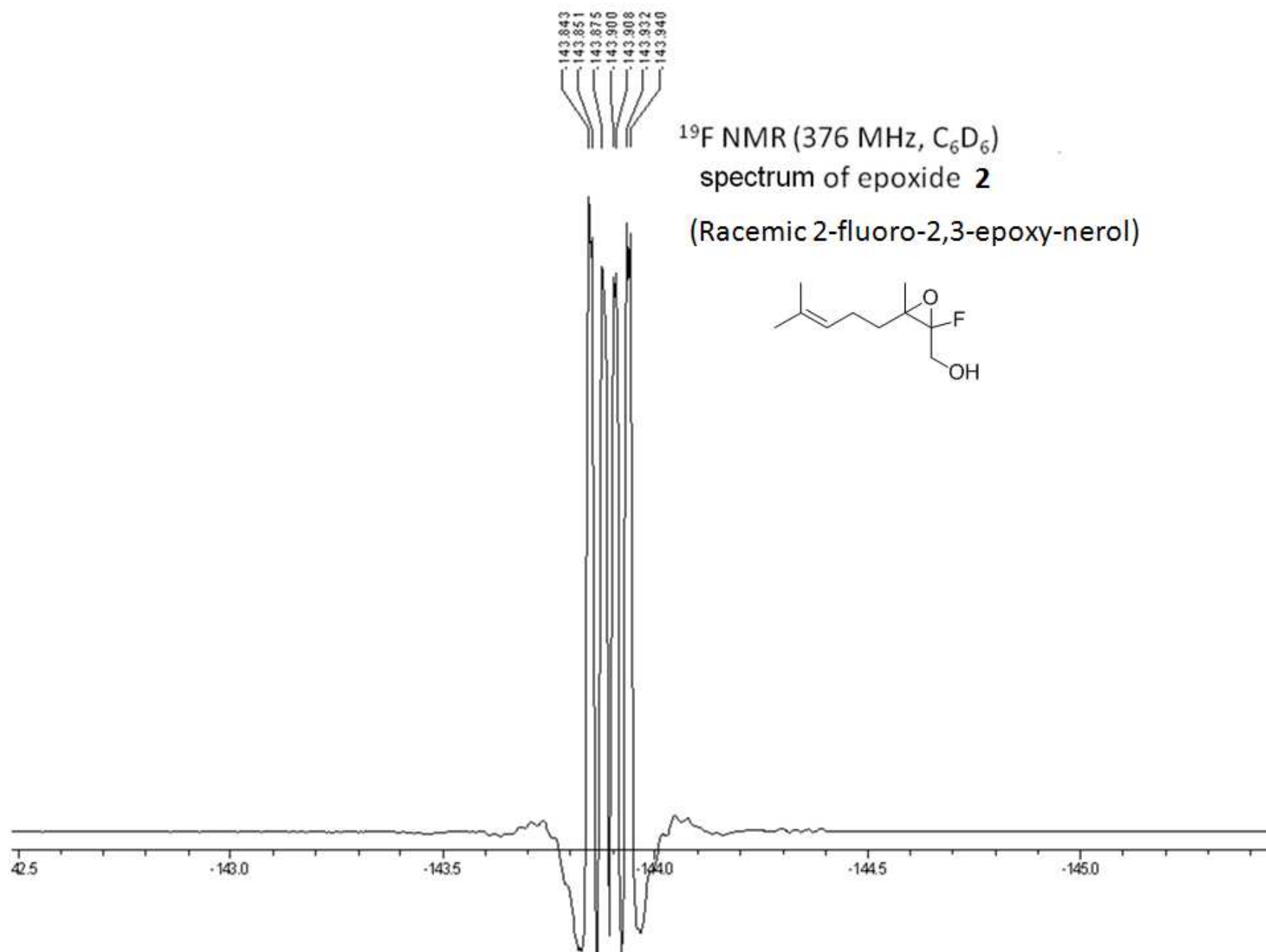
^1H NMR (500 MHz, C_6D_6) spectrum of epoxide **2**
(Racemic 2-fluoro-2,3-epoxyneryl)



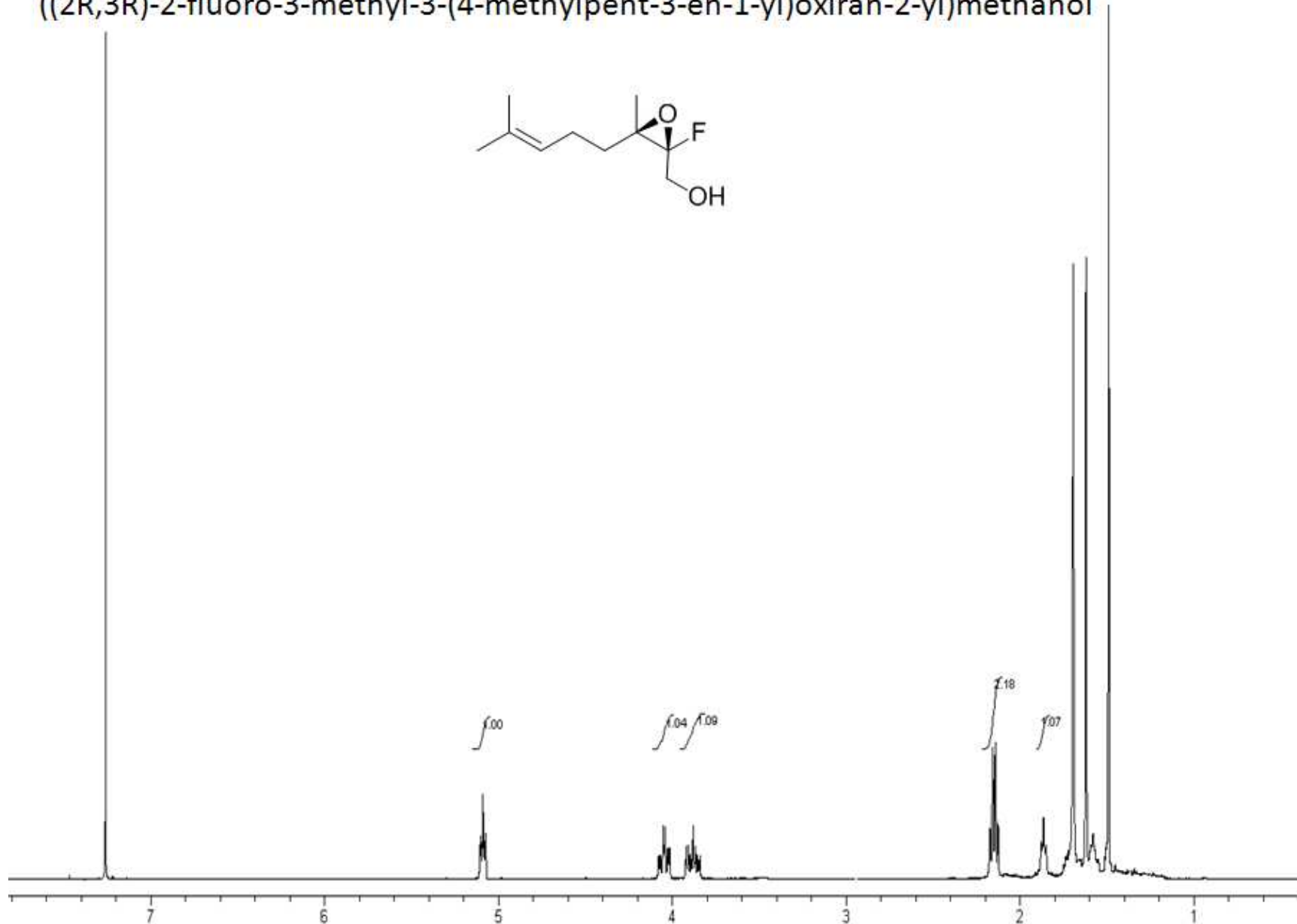
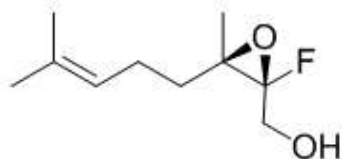
^1H NMR (500 MHz, CDCl_3) spectrum of epoxide **2**
(Racemic 2-fluoro-2,3-epoxynol)



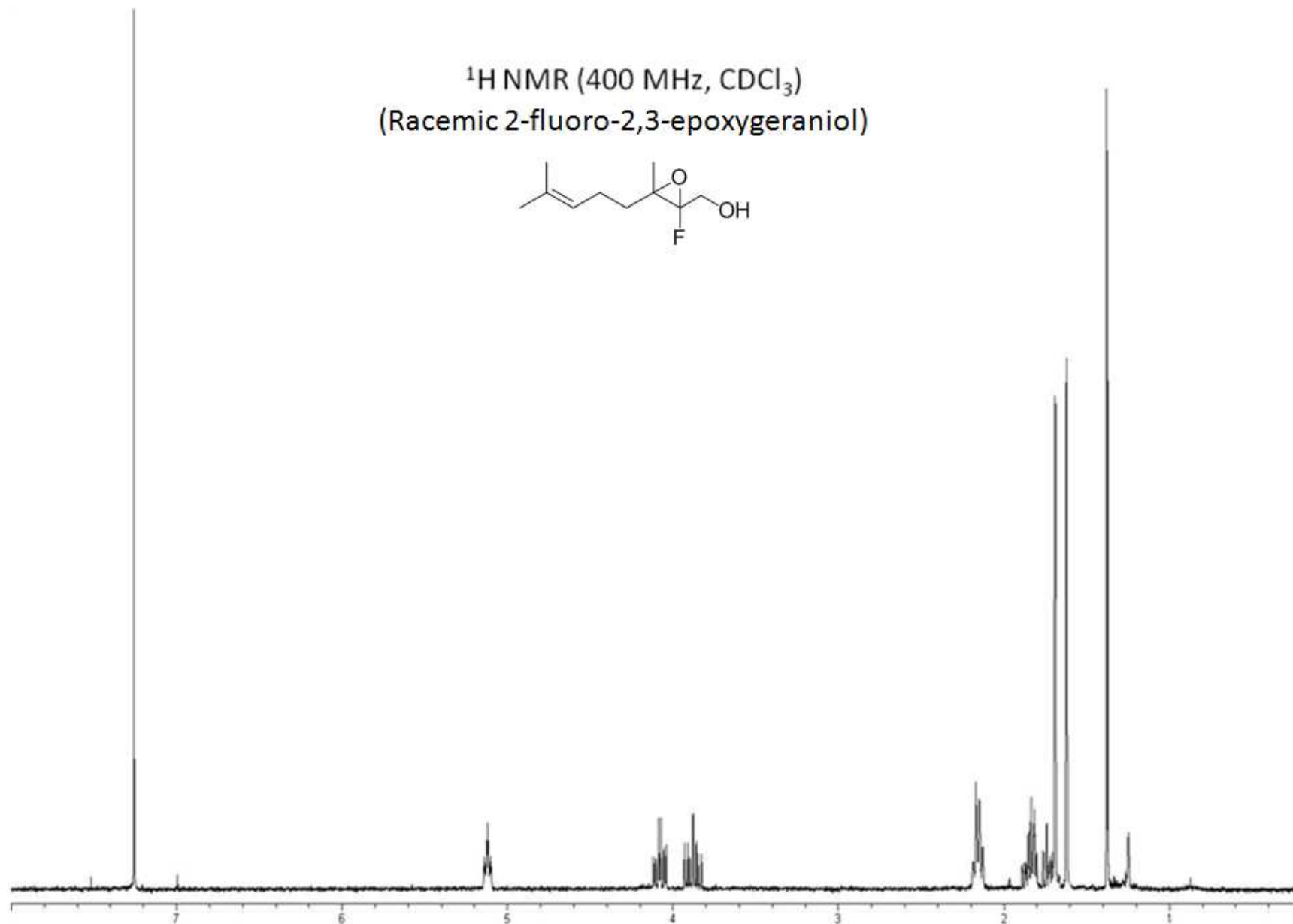
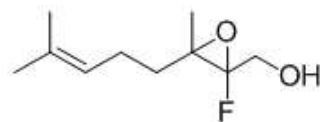


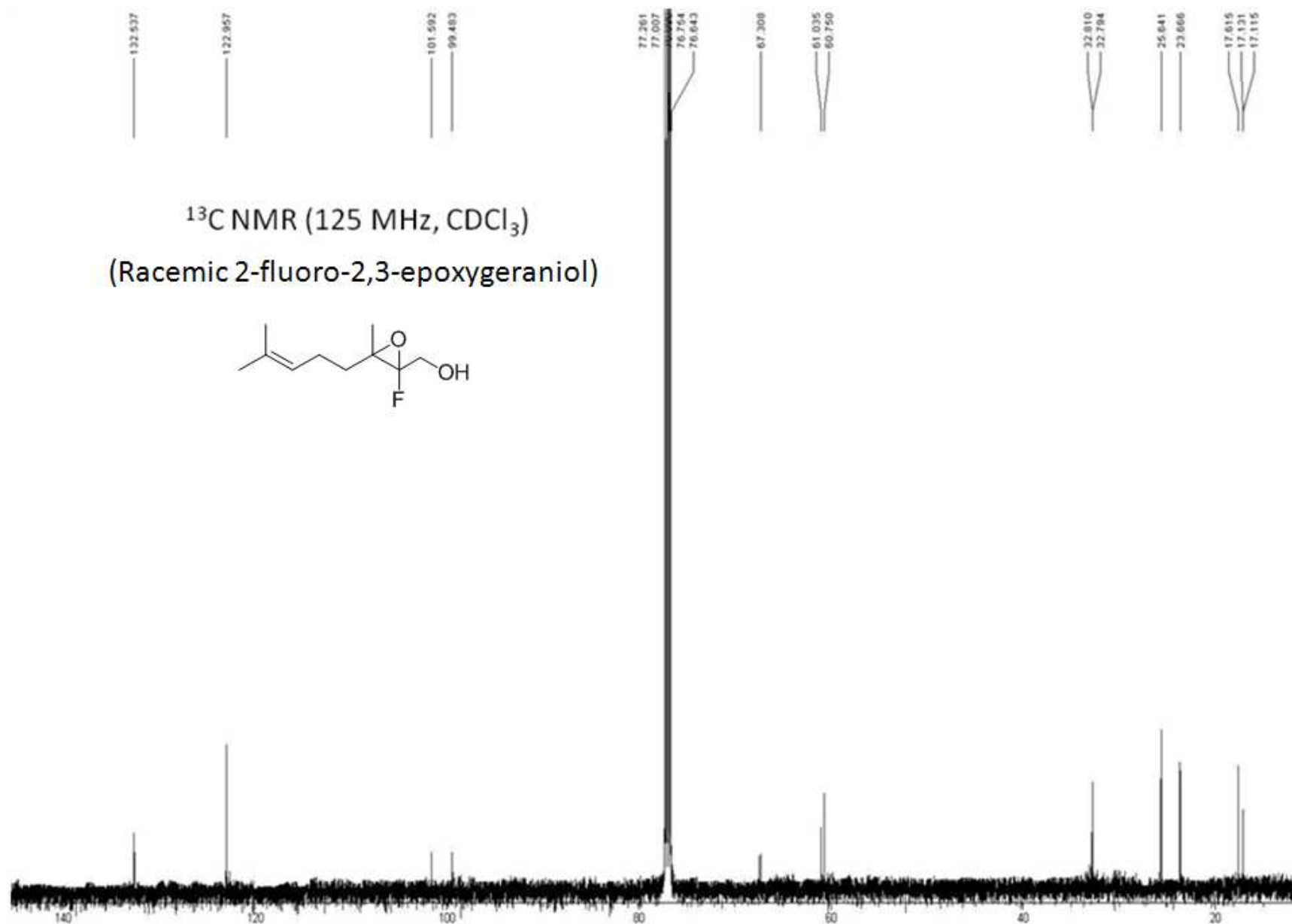


^1H NMR (CDCl_3 , 500 MHz) of (2R,3R)-2
((2R,3R)-2-fluoro-3-methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)methanol



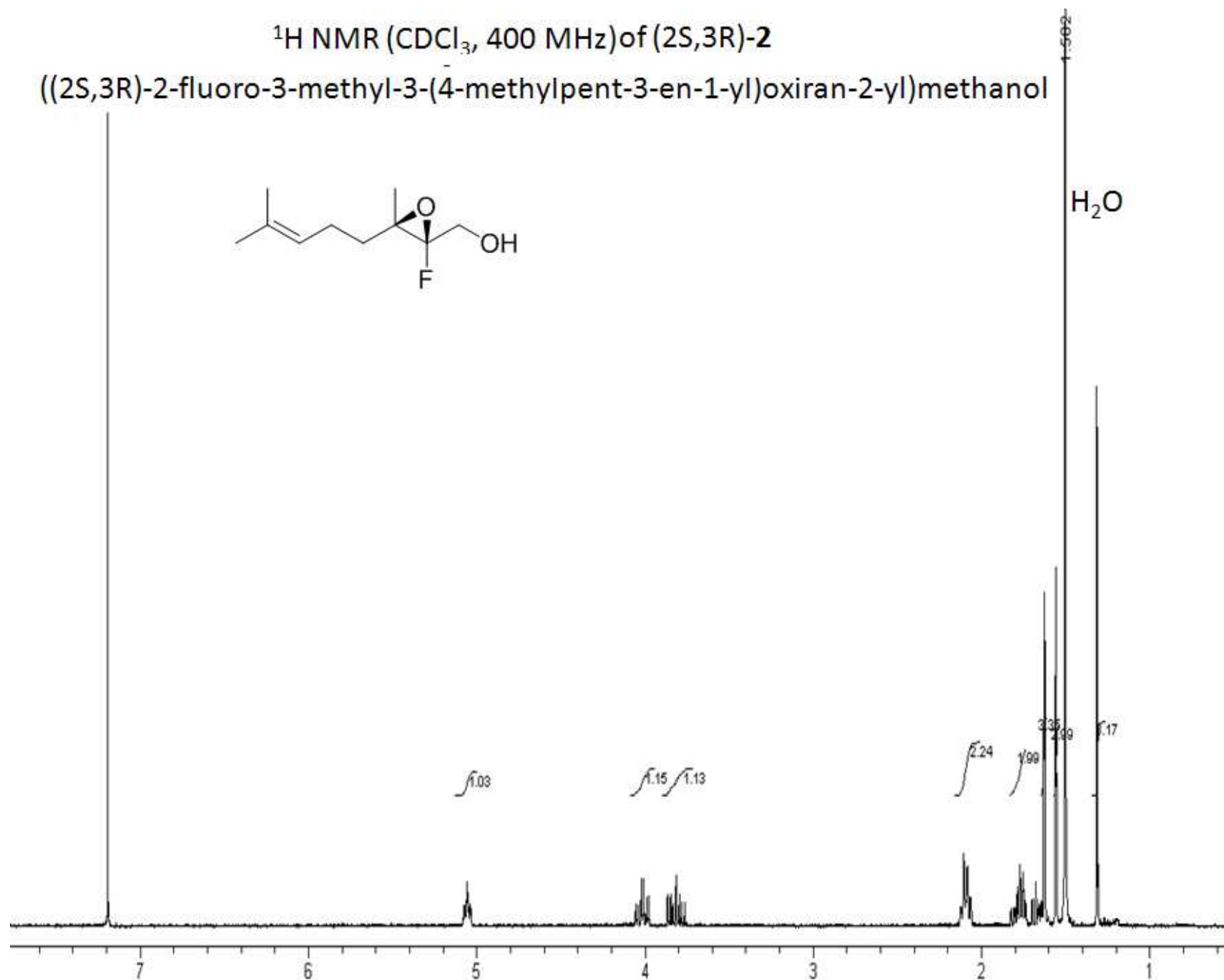
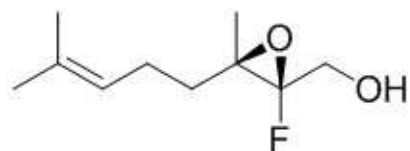
^1H NMR (400 MHz, CDCl_3)
(Racemic 2-fluoro-2,3-epoxygeraniol)



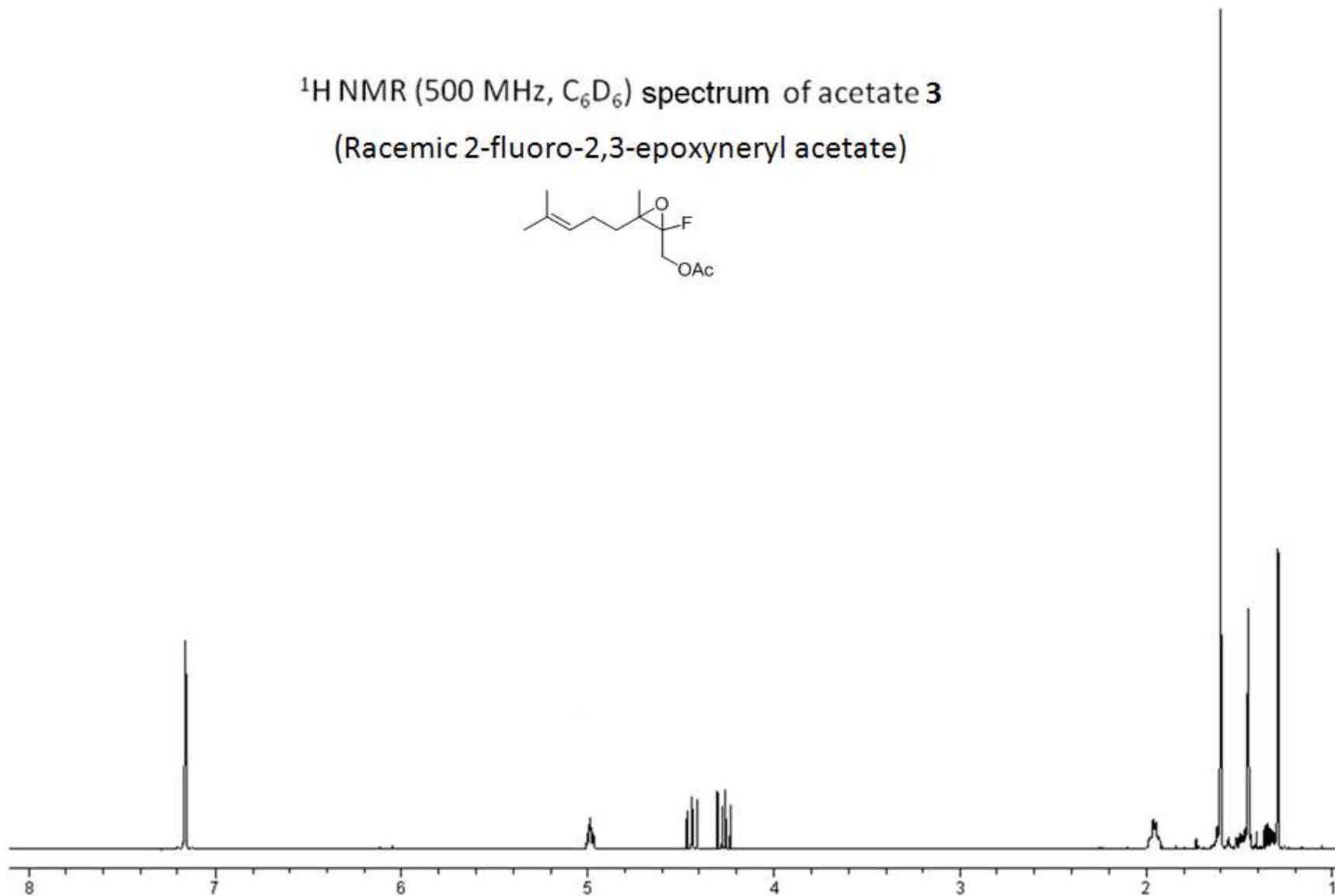
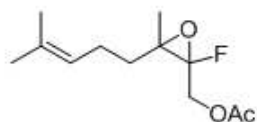


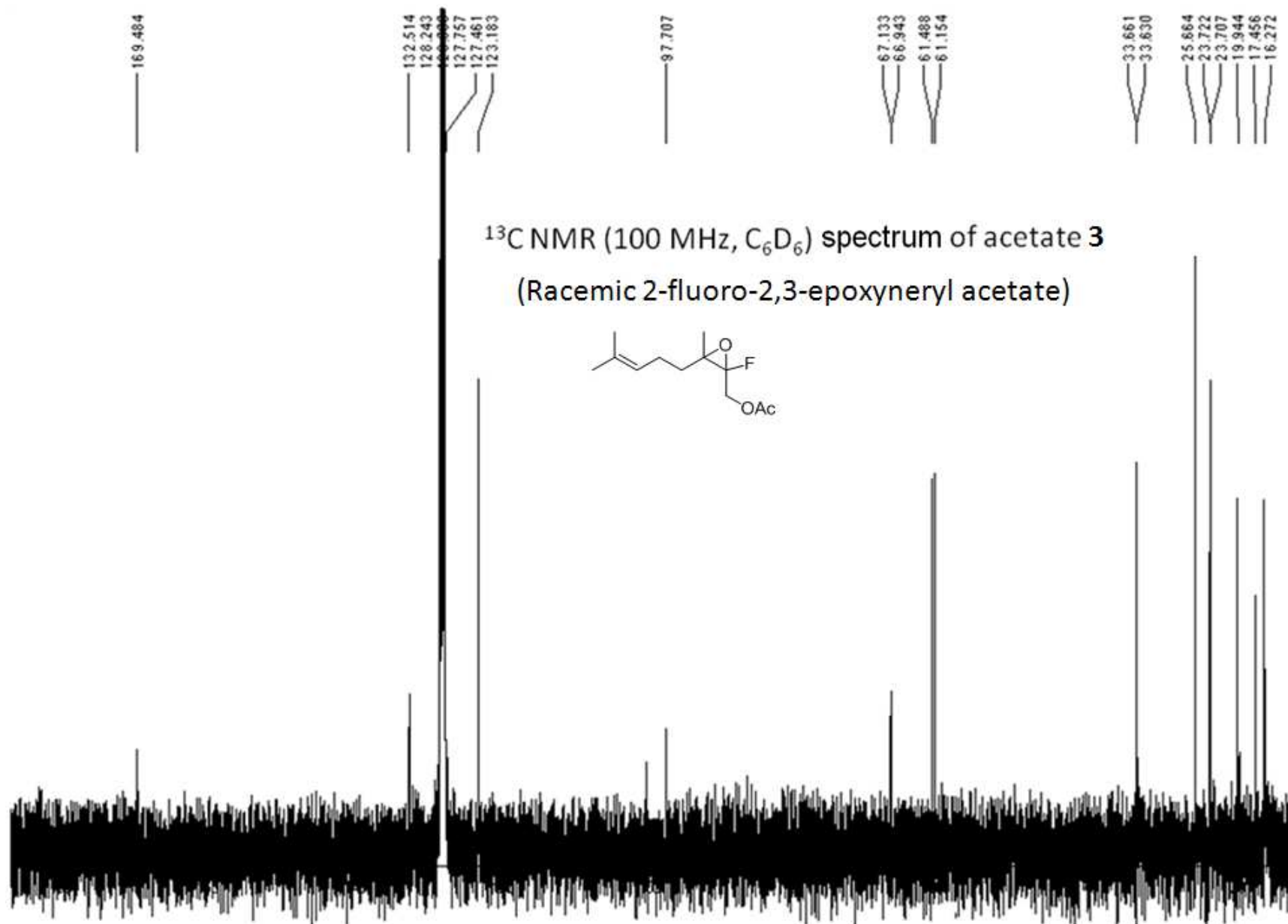
^1H NMR (CDCl_3 , 400 MHz) of (2S,3R)-2

((2S,3R)-2-fluoro-3-methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)methanol

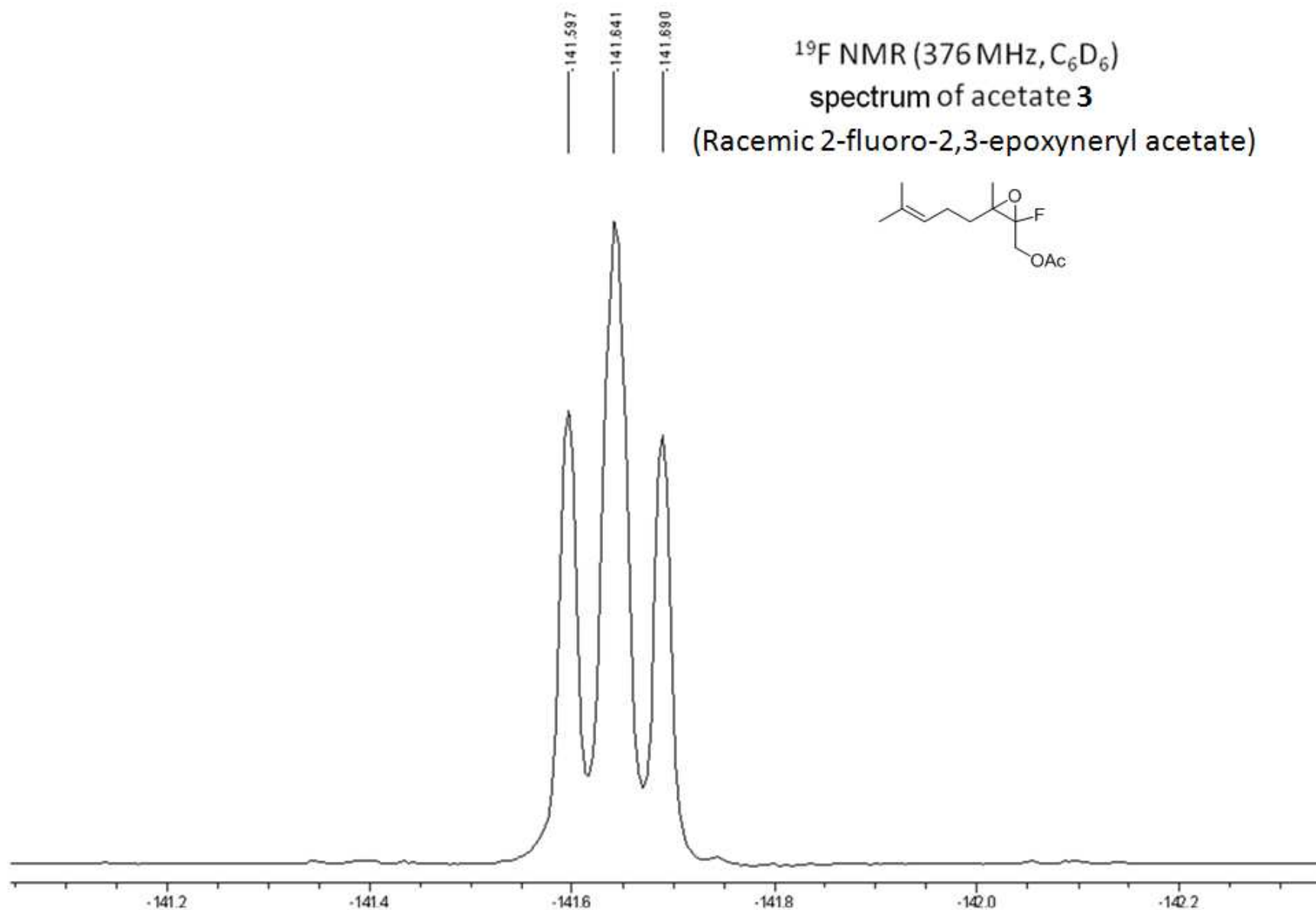
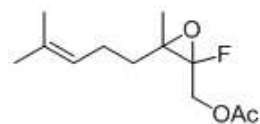


^1H NMR (500 MHz, C_6D_6) spectrum of acetate **3**
(Racemic 2-fluoro-2,3-epoxyneryl acetate)

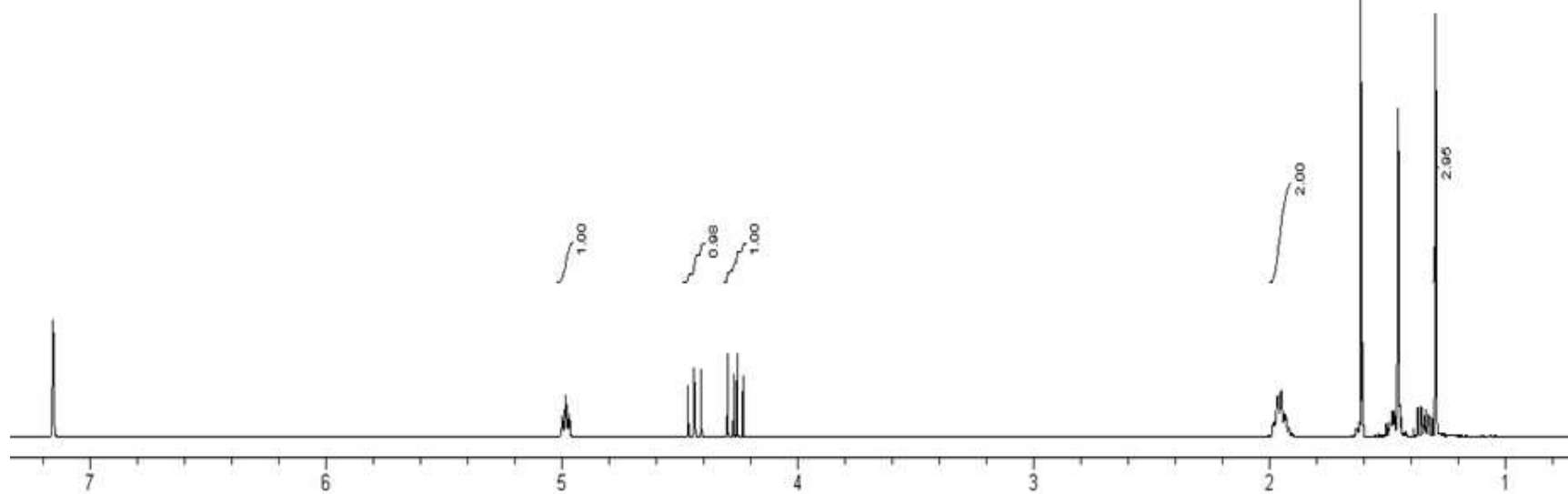
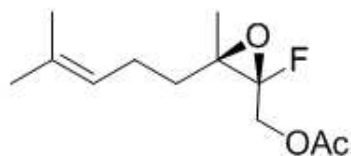




^{19}F NMR (376 MHz, C_6D_6)
spectrum of acetate **3**
(Racemic 2-fluoro-2,3-epoxyneryl acetate)

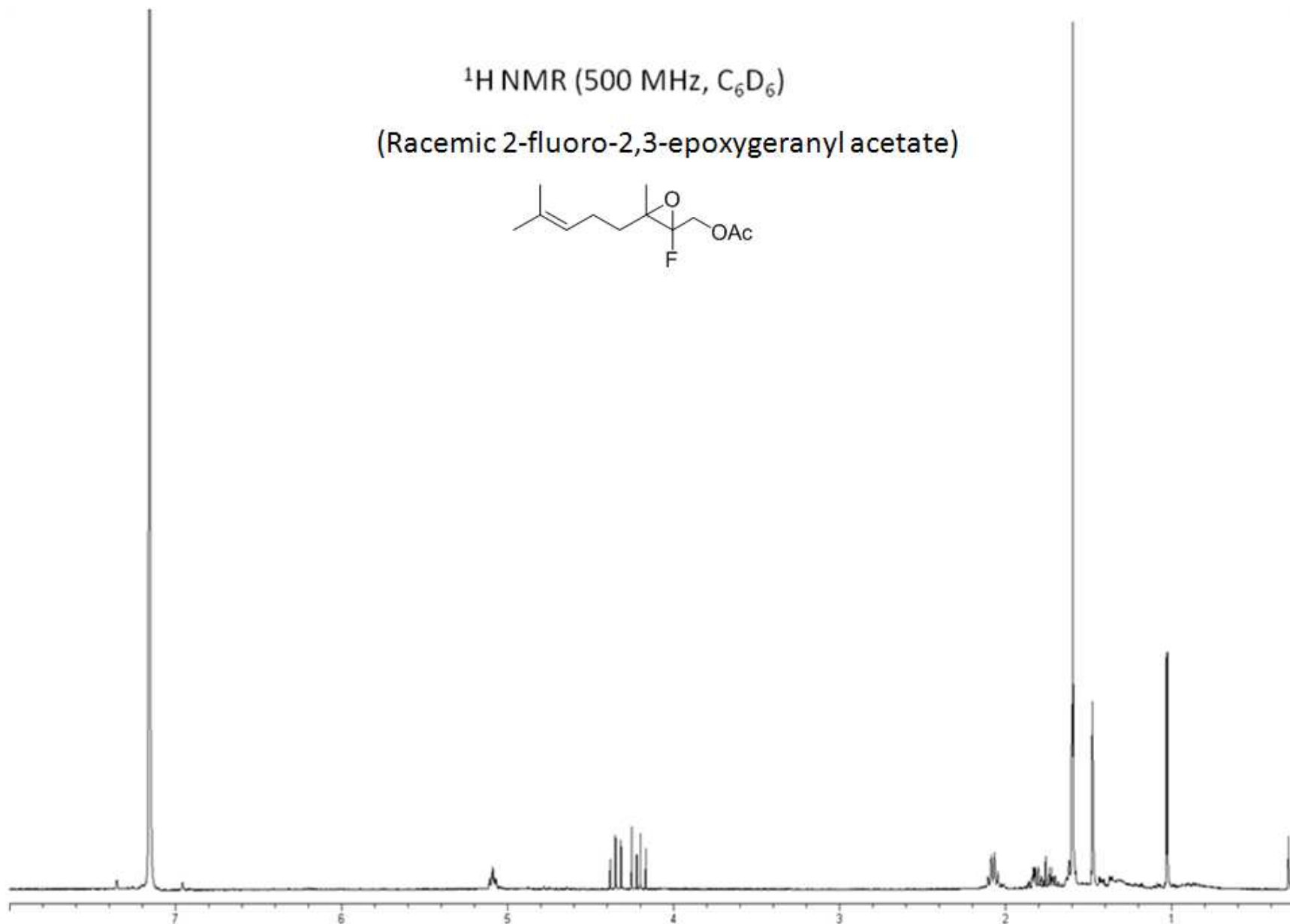
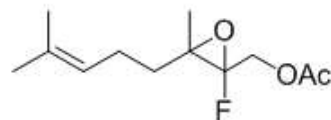


^1H NMR (C_6D_6 , 500 MHz) of (2R,3R)-3
 ((2R,3R)-2-fluoro-3-methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)methyl acetate

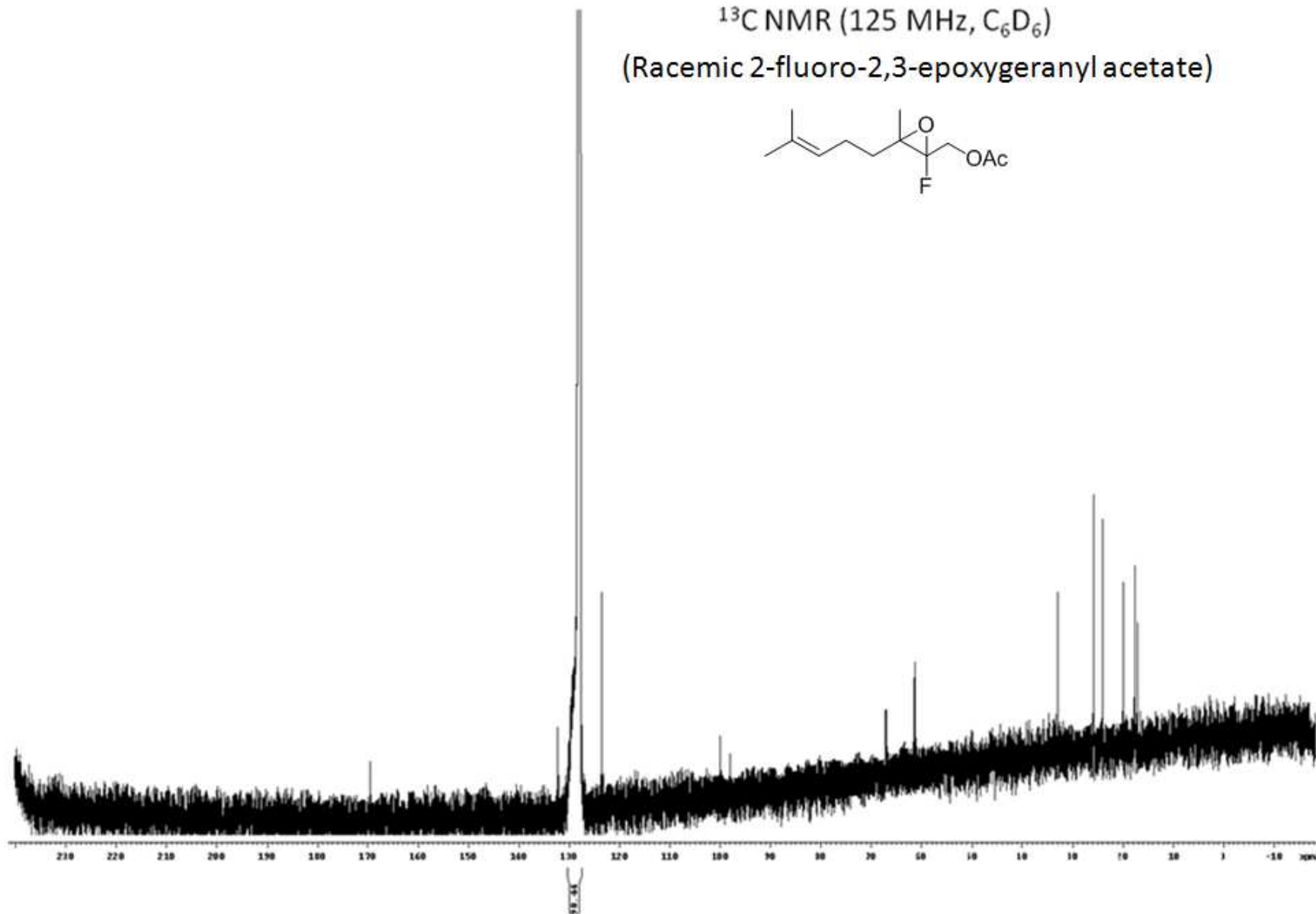
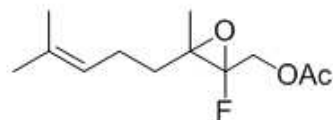


^1H NMR (500 MHz, C_6D_6)

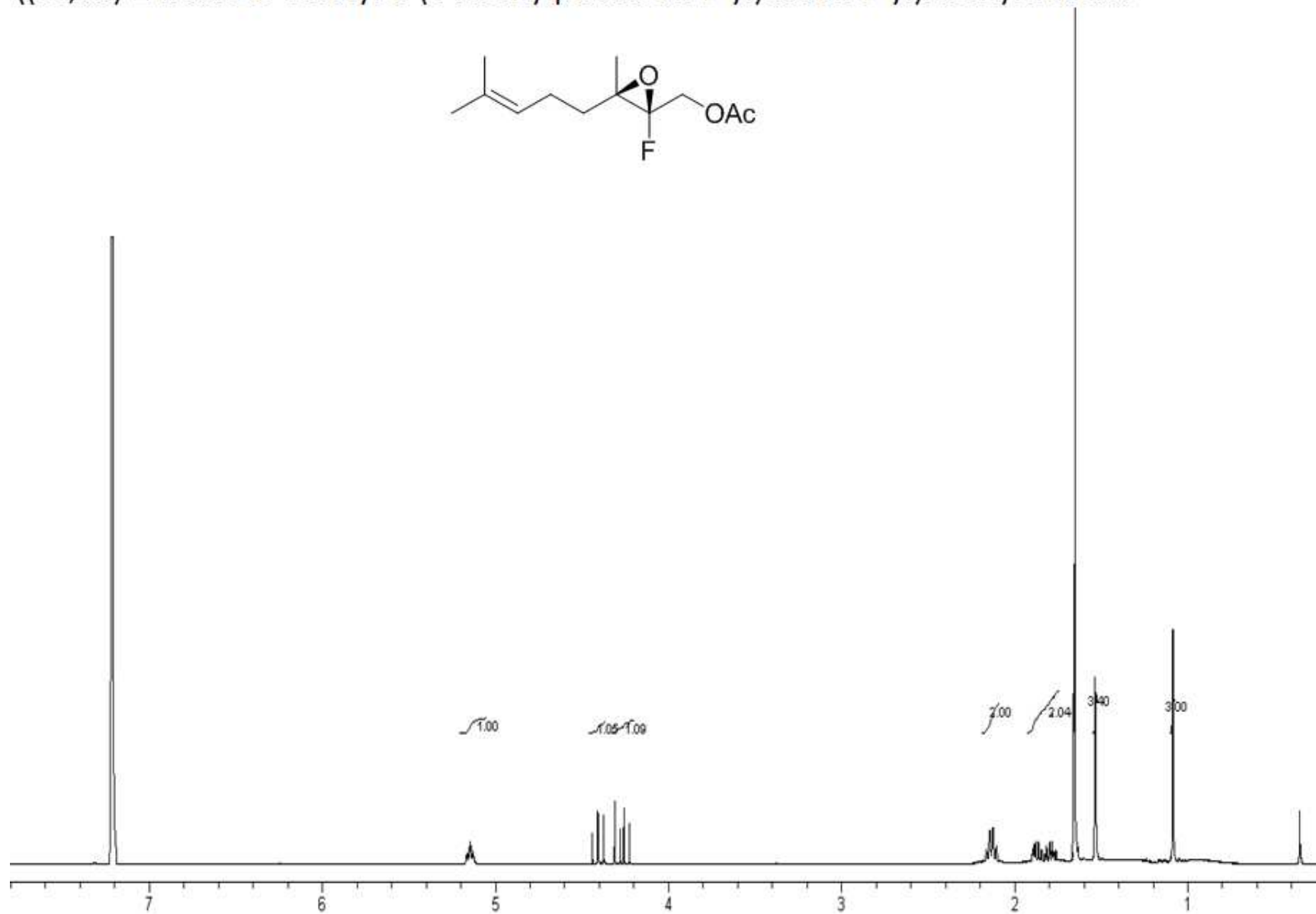
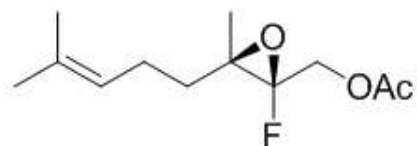
(Racemic 2-fluoro-2,3-epoxygeranyl acetate)



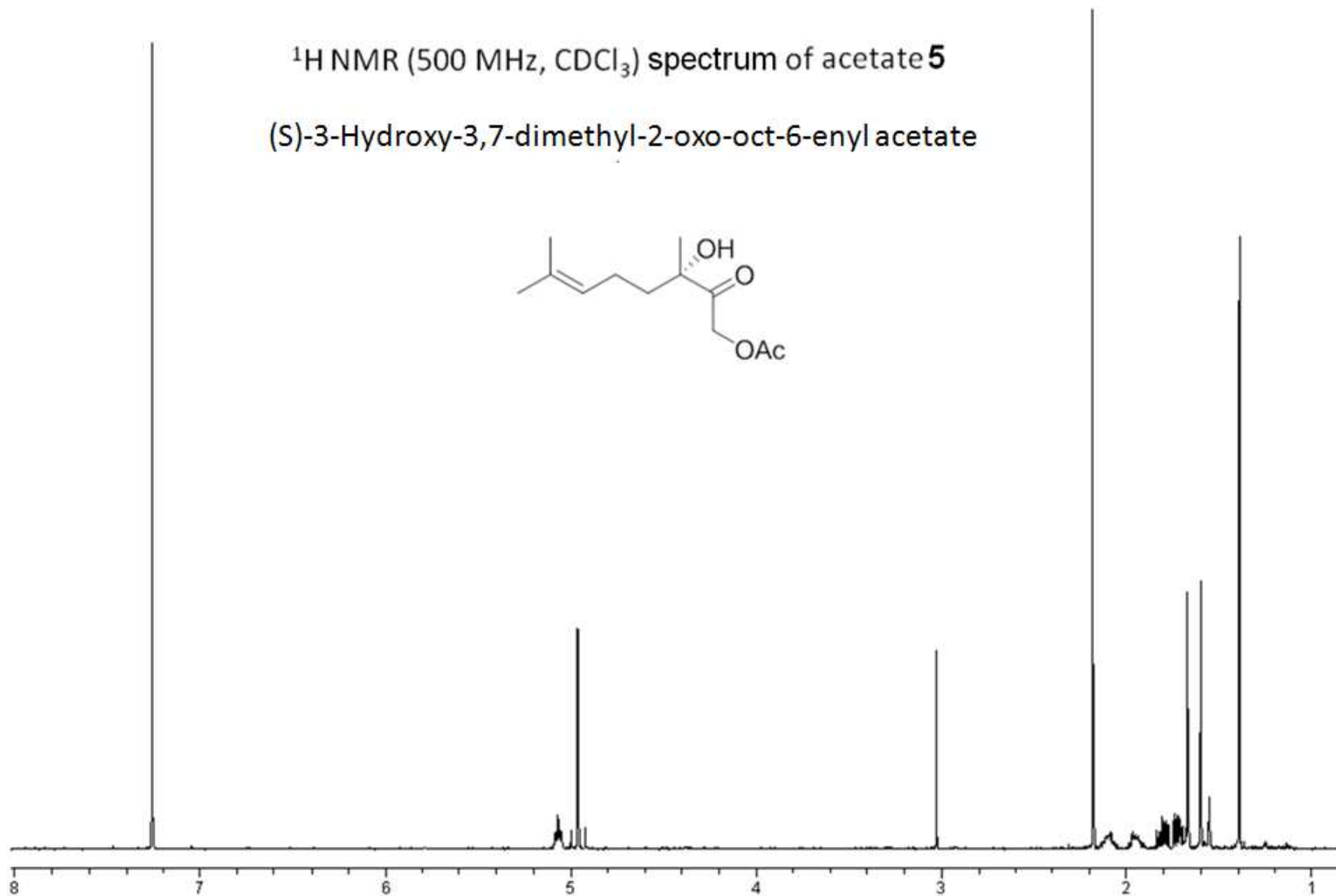
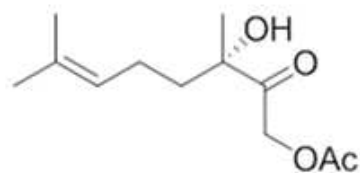
^{13}C NMR (125 MHz, C_6D_6)
(Racemic 2-fluoro-2,3-epoxygeranyl acetate)



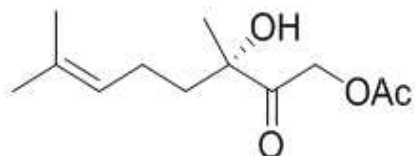
^1H NMR (C_6D_6 , 500 MHz) of (2S,3R)-3-
 ((2S,3R)-2-fluoro-3-methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)methyl acetate



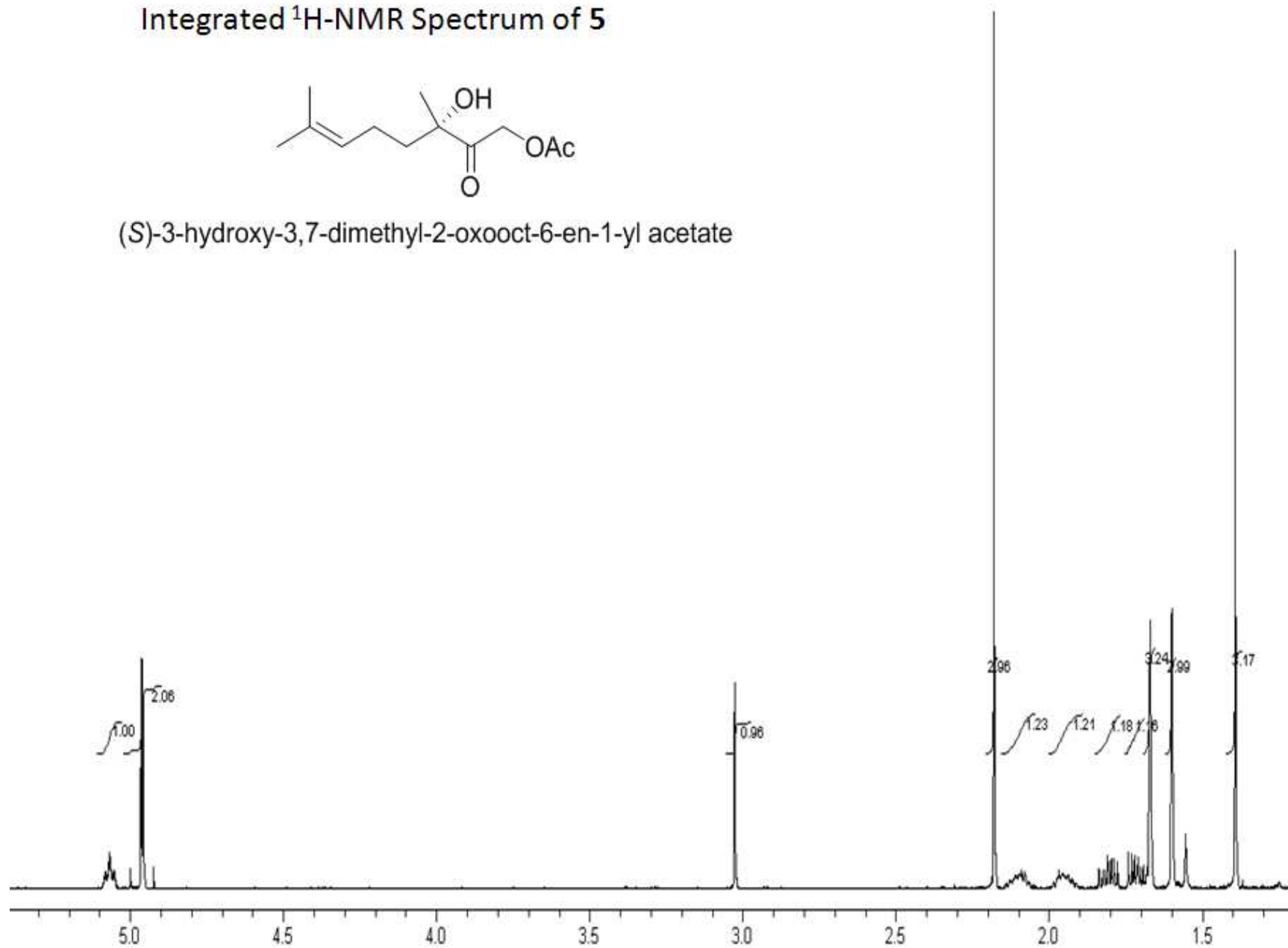
^1H NMR (500 MHz, CDCl_3) spectrum of acetate **5**
(S)-3-Hydroxy-3,7-dimethyl-2-oxo-oct-6-enyl acetate

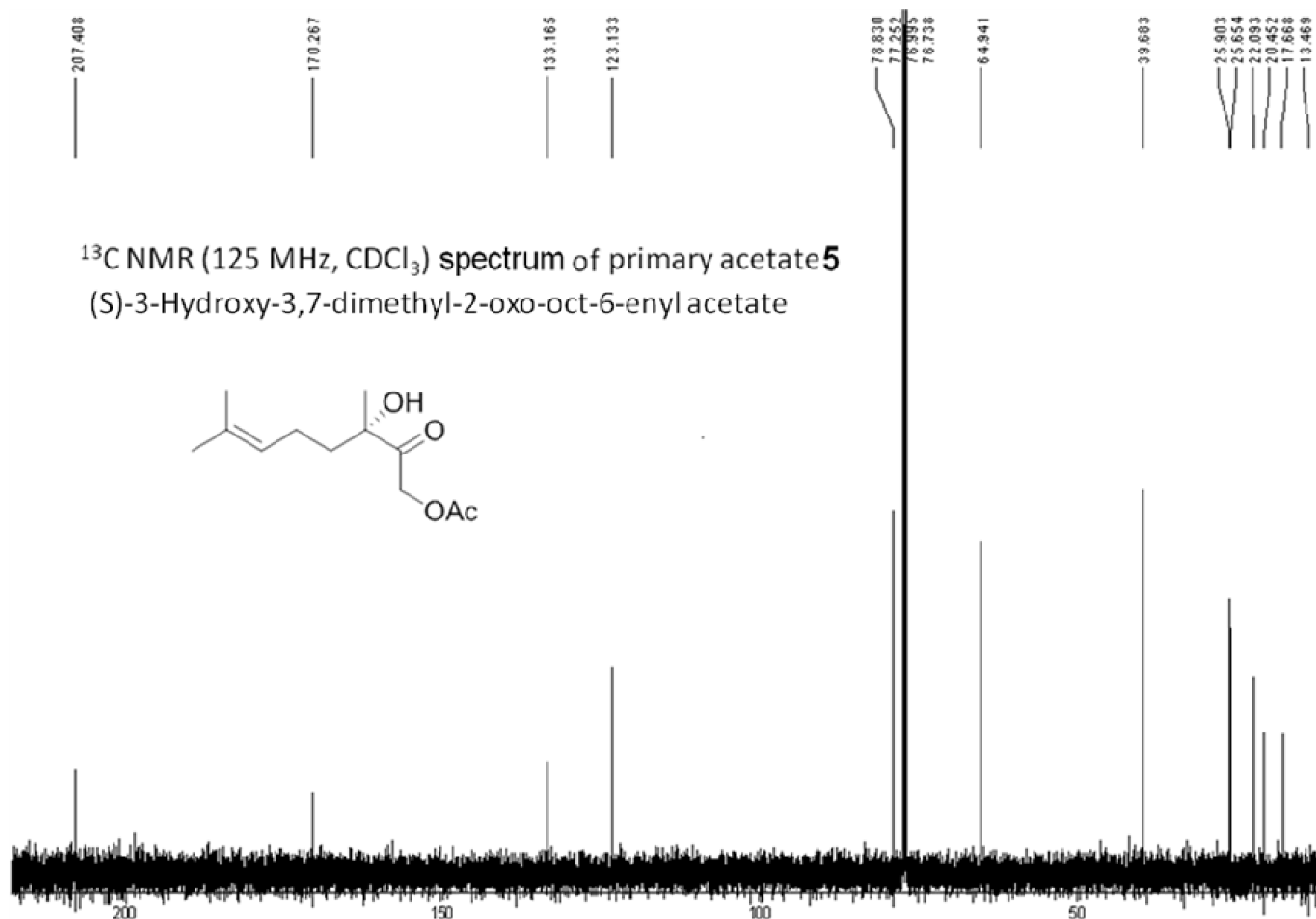


Integrated ^1H -NMR Spectrum of 5

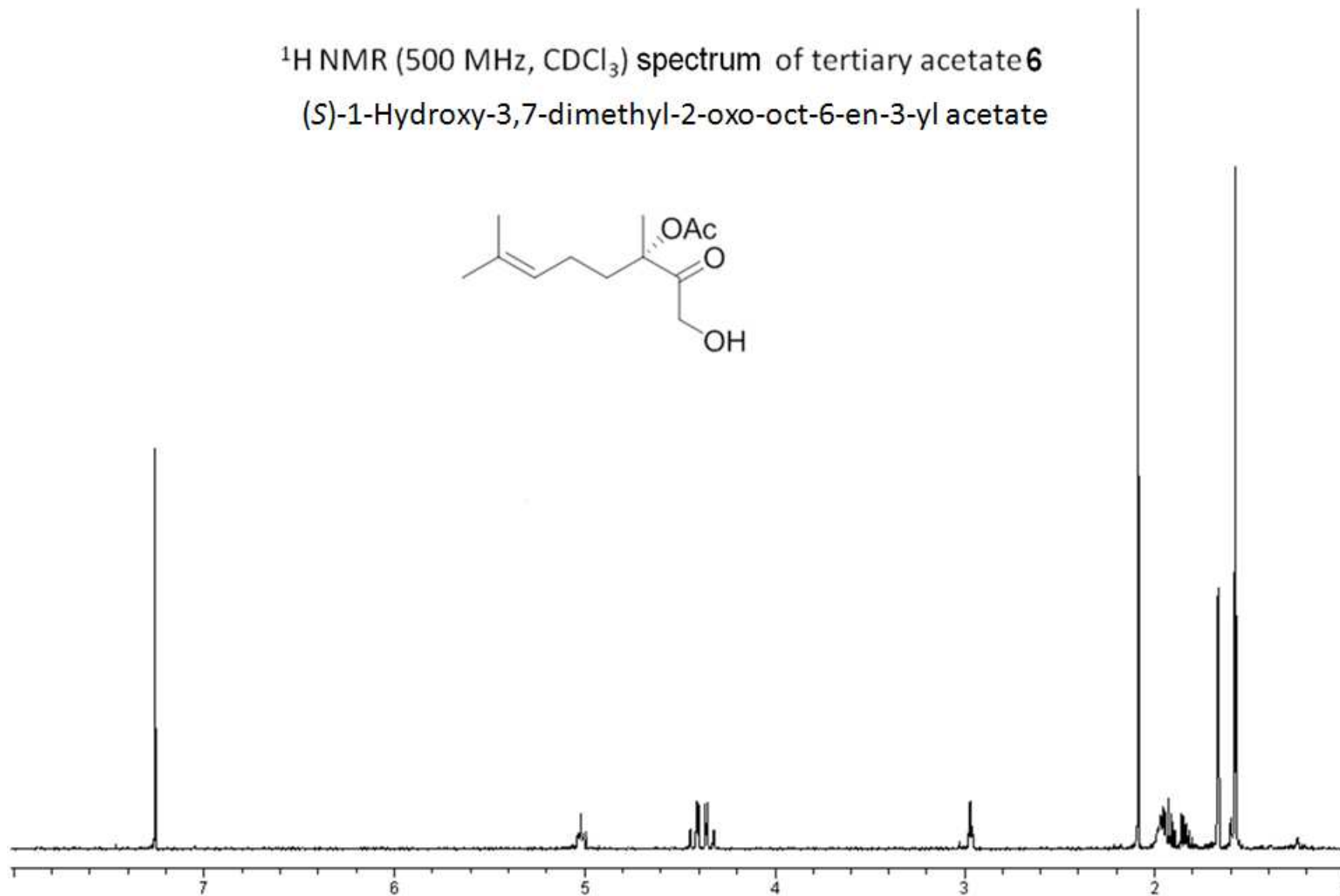
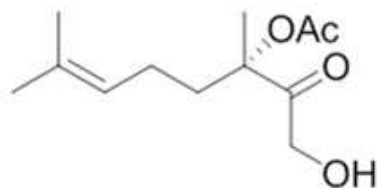


(*S*)-3-hydroxy-3,7-dimethyl-2-oxooct-6-en-1-yl acetate

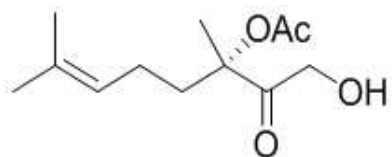




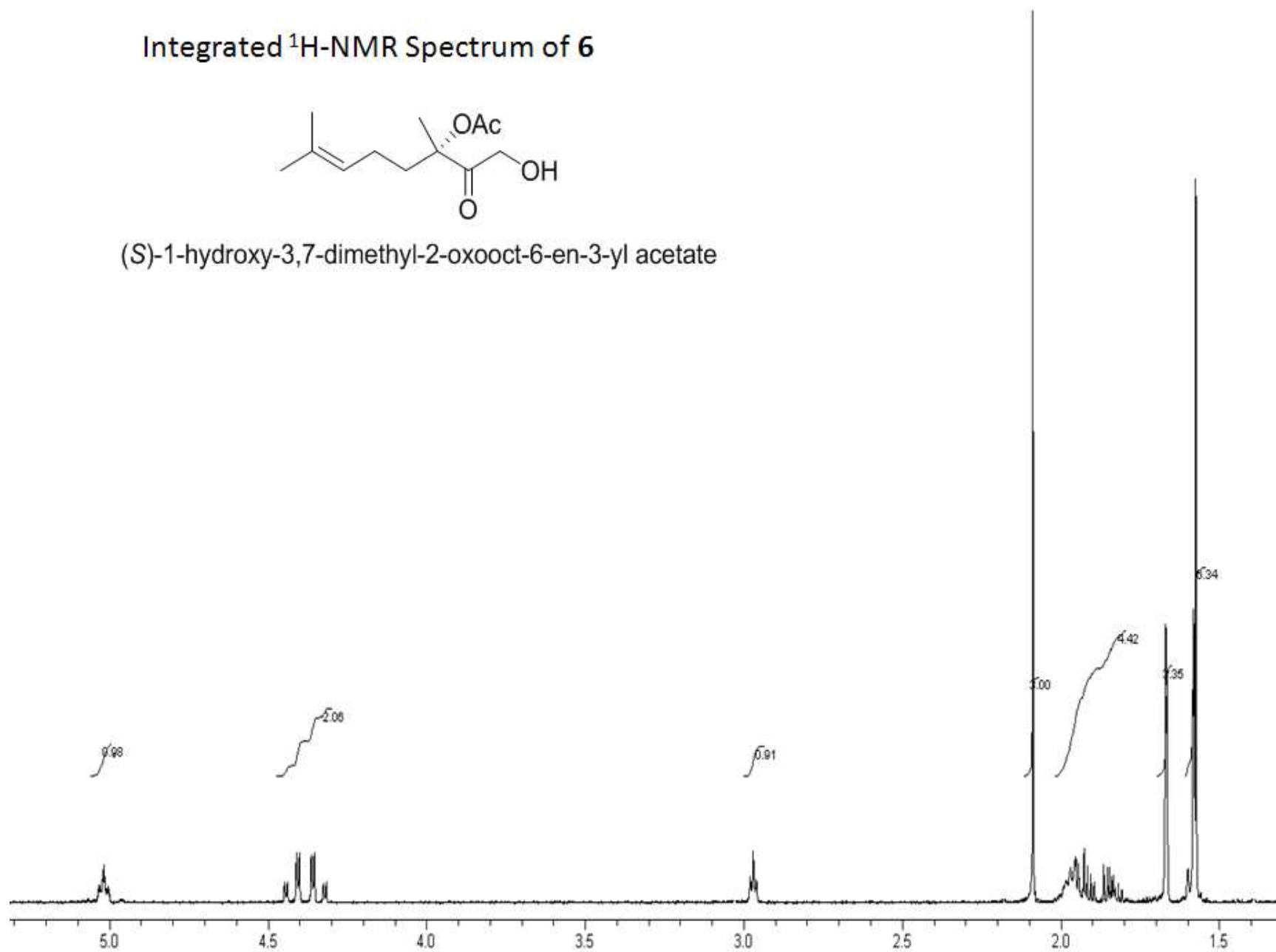
^1H NMR (500 MHz, CDCl_3) spectrum of tertiary acetate **6**
(S)-1-Hydroxy-3,7-dimethyl-2-oxo-oct-6-en-3-yl acetate



Integrated ^1H -NMR Spectrum of 6



(S)-1-hydroxy-3,7-dimethyl-2-oxooct-6-en-3-yl acetate



208.940

170.080

133.002

122.535

84.678

77.252

77.197

76.995

76.746

64.716

37.016

25.623

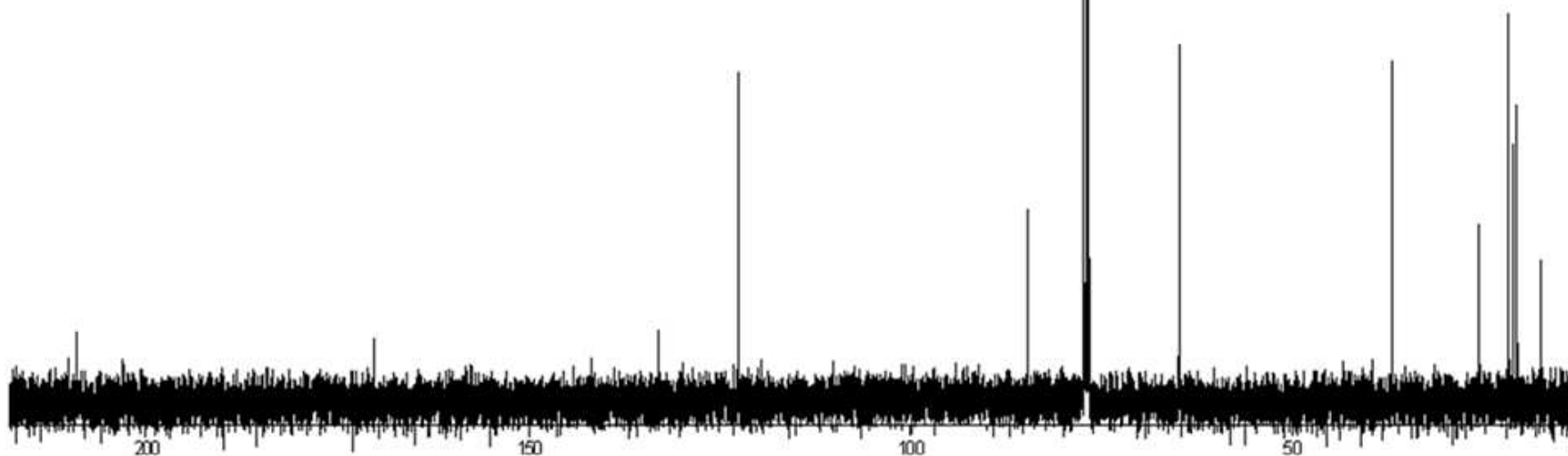
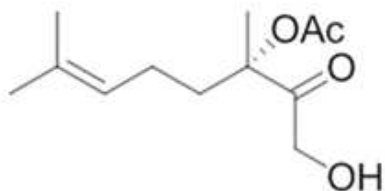
21.805

21.183

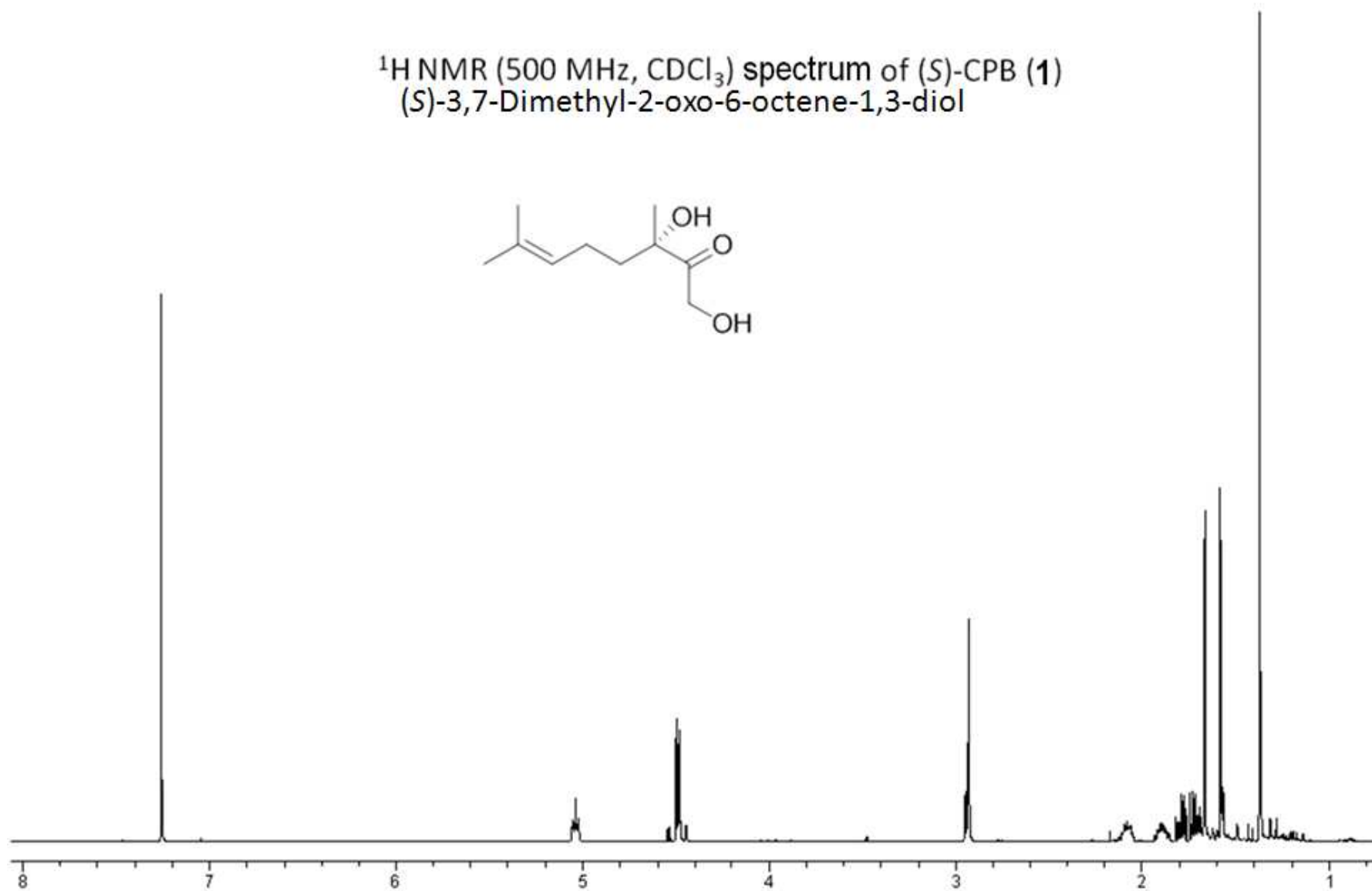
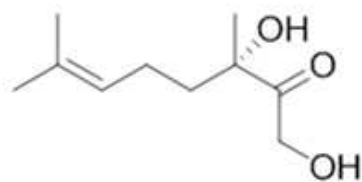
20.724

17.598

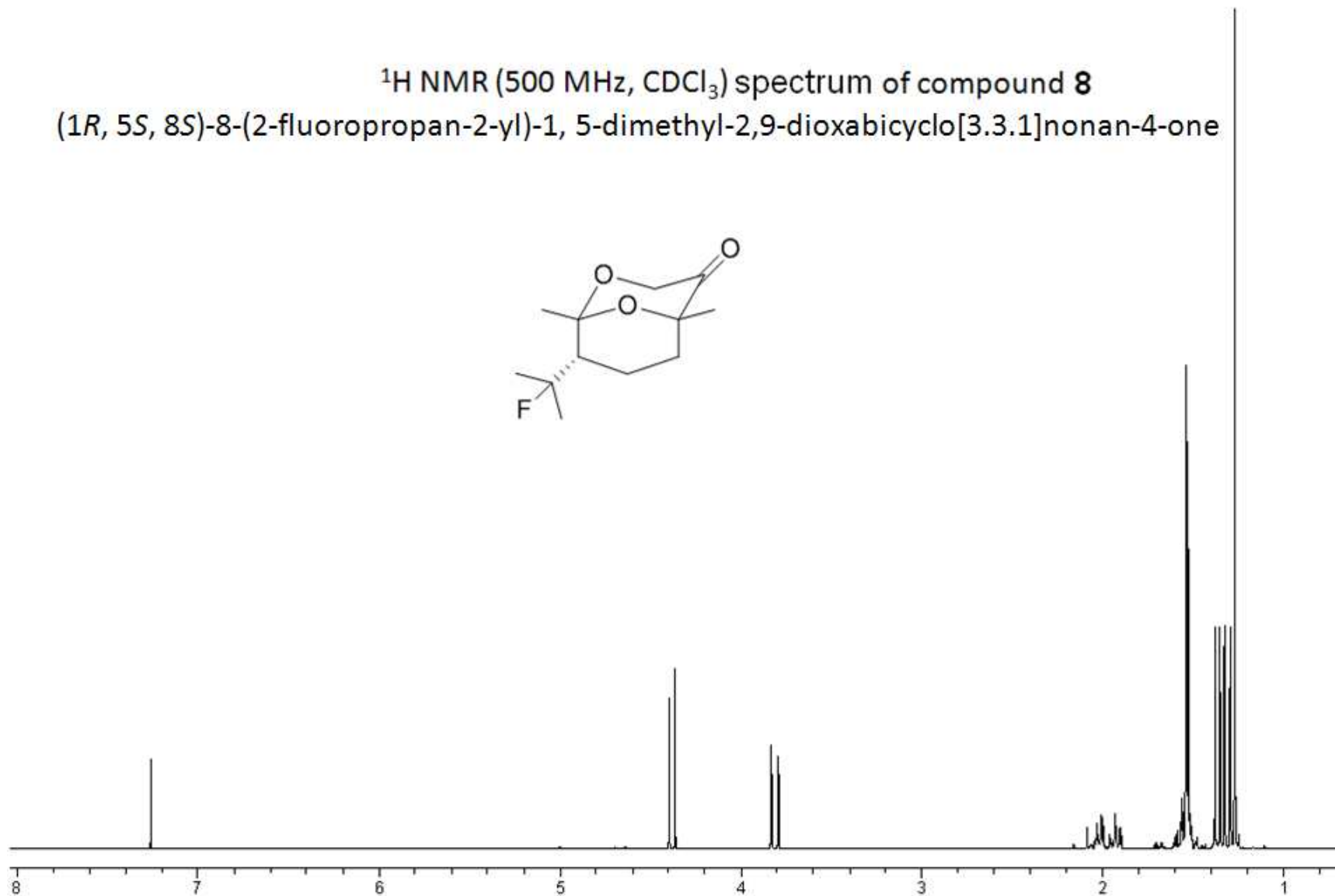
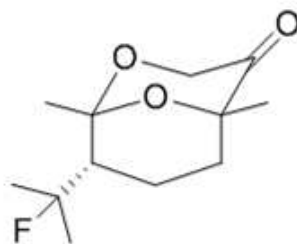
^{13}C NMR (125 MHz, CDCl_3) spectrum of tertiary acetate **6**
(*S*)-1-Hydroxy-3,7-dimethyl-2-oxo-oct-6-en-3-yl acetate



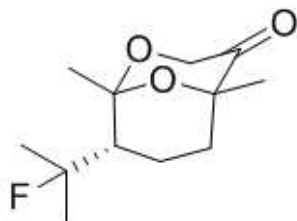
^1H NMR (500 MHz, CDCl_3) spectrum of (*S*)-CPB (**1**)
 (*S*)-3,7-Dimethyl-2-oxo-6-octene-1,3-diol



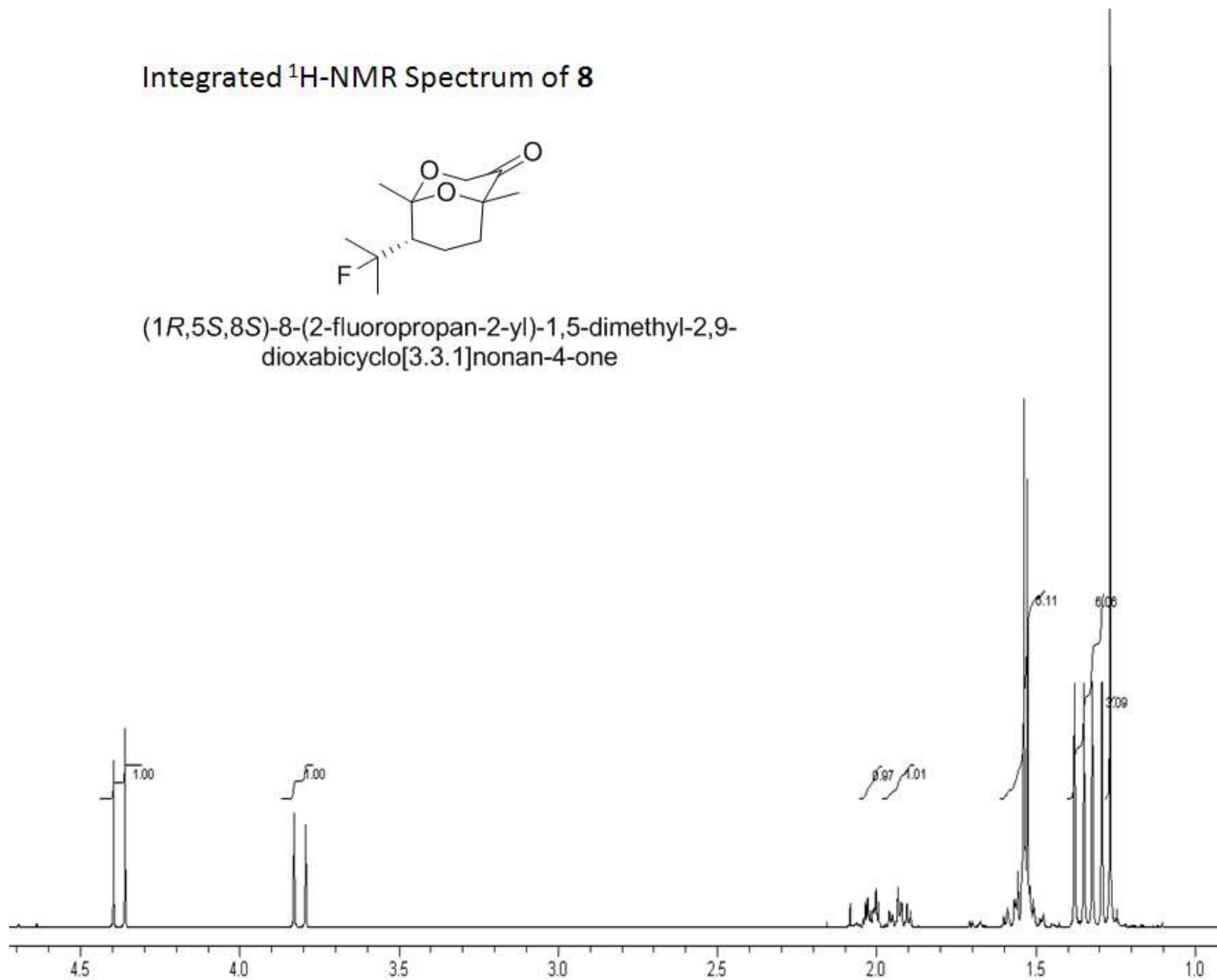
^1H NMR (500 MHz, CDCl_3) spectrum of compound **8**
(1*R*, 5*S*, 8*S*)-8-(2-fluoropropan-2-yl)-1, 5-dimethyl-2,9-dioxabicyclo[3.3.1]nonan-4-one



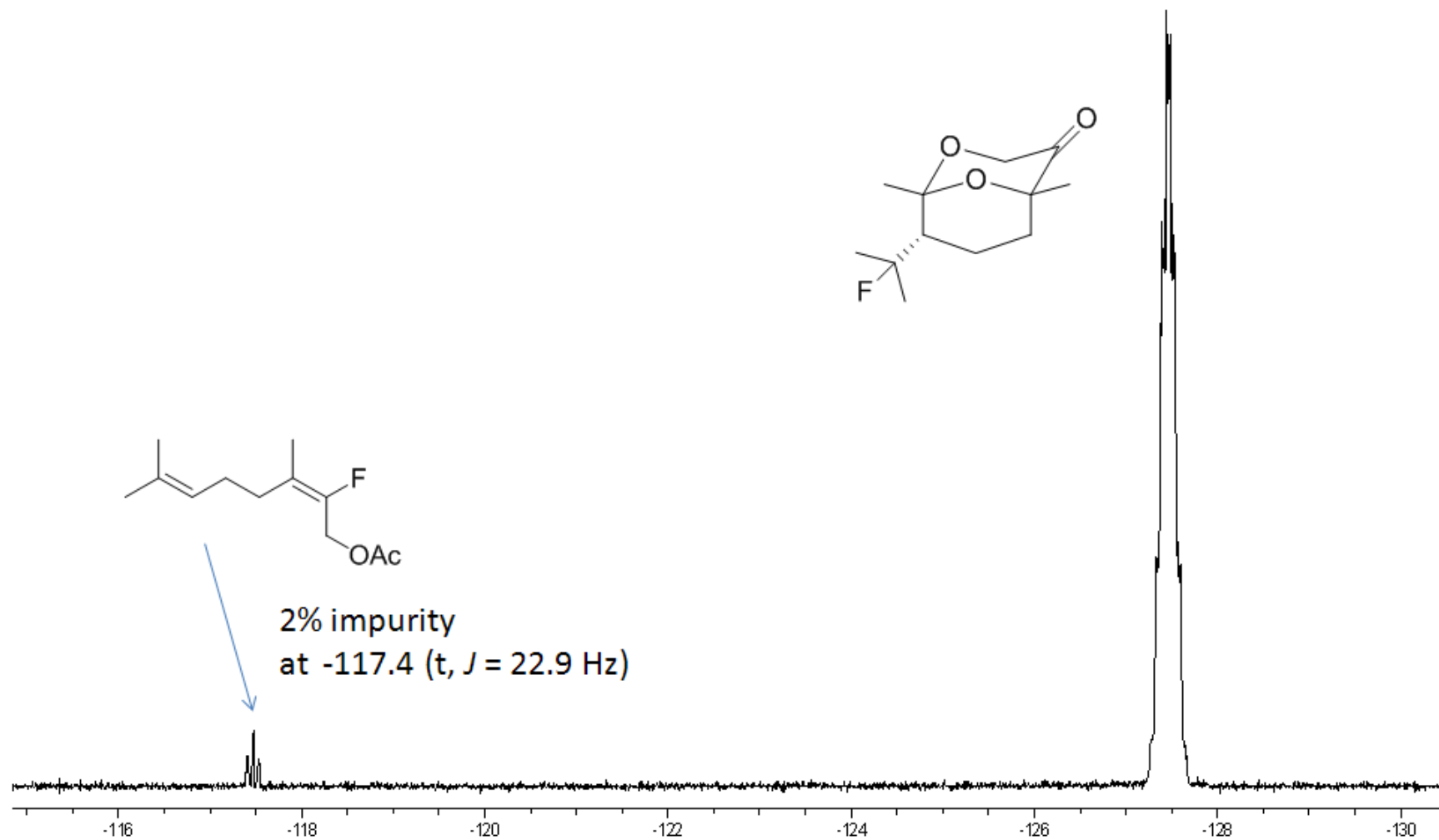
Integrated ^1H -NMR Spectrum of **8**

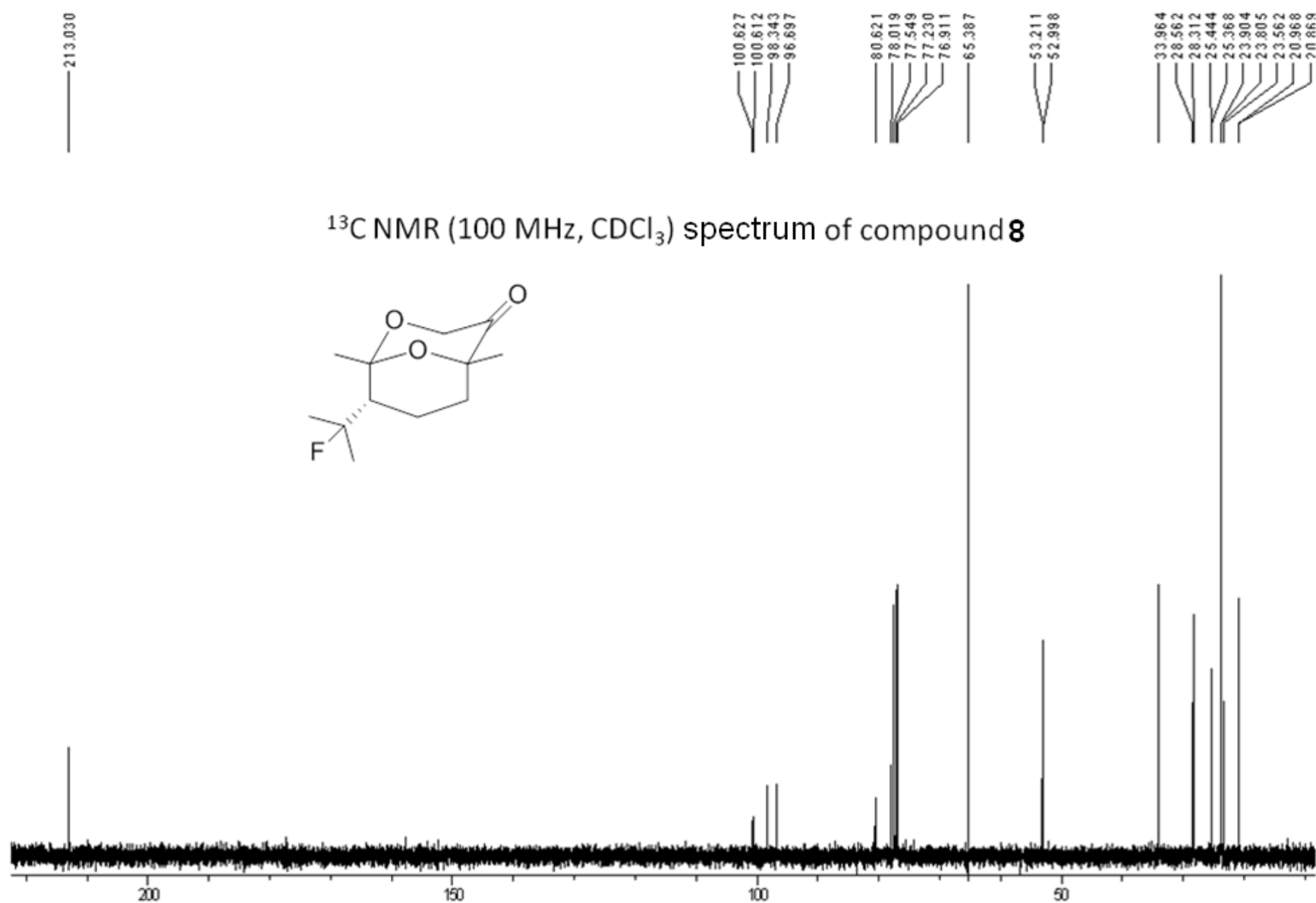


(1*R*,5*S*,8*S*)-8-(2-fluoropropan-2-yl)-1,5-dimethyl-2,9-dioxabicyclo[3.3.1]nonan-4-one

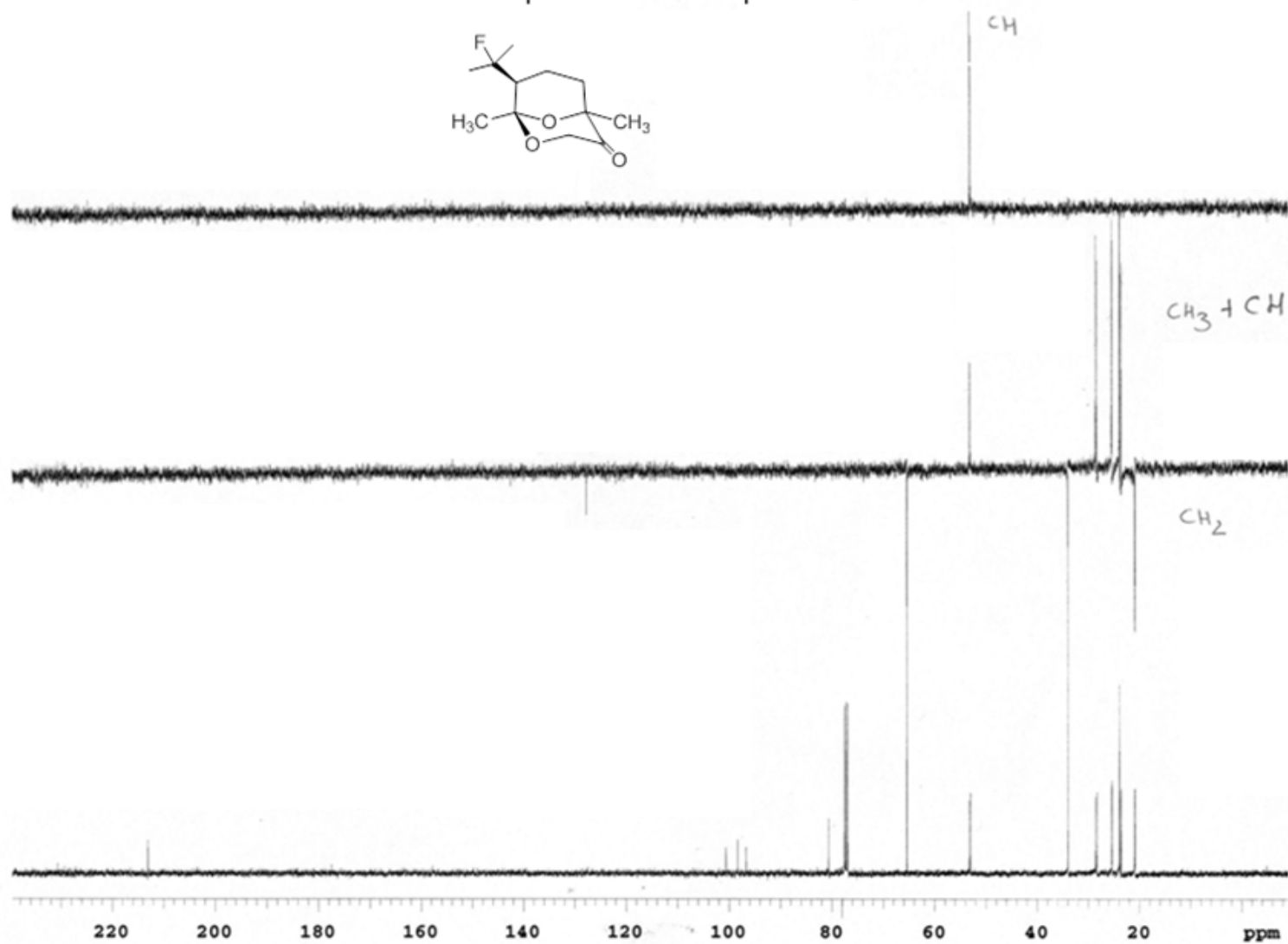


^{19}F NMR (376 MHz, CDCl_3) spectrum of compound **8**





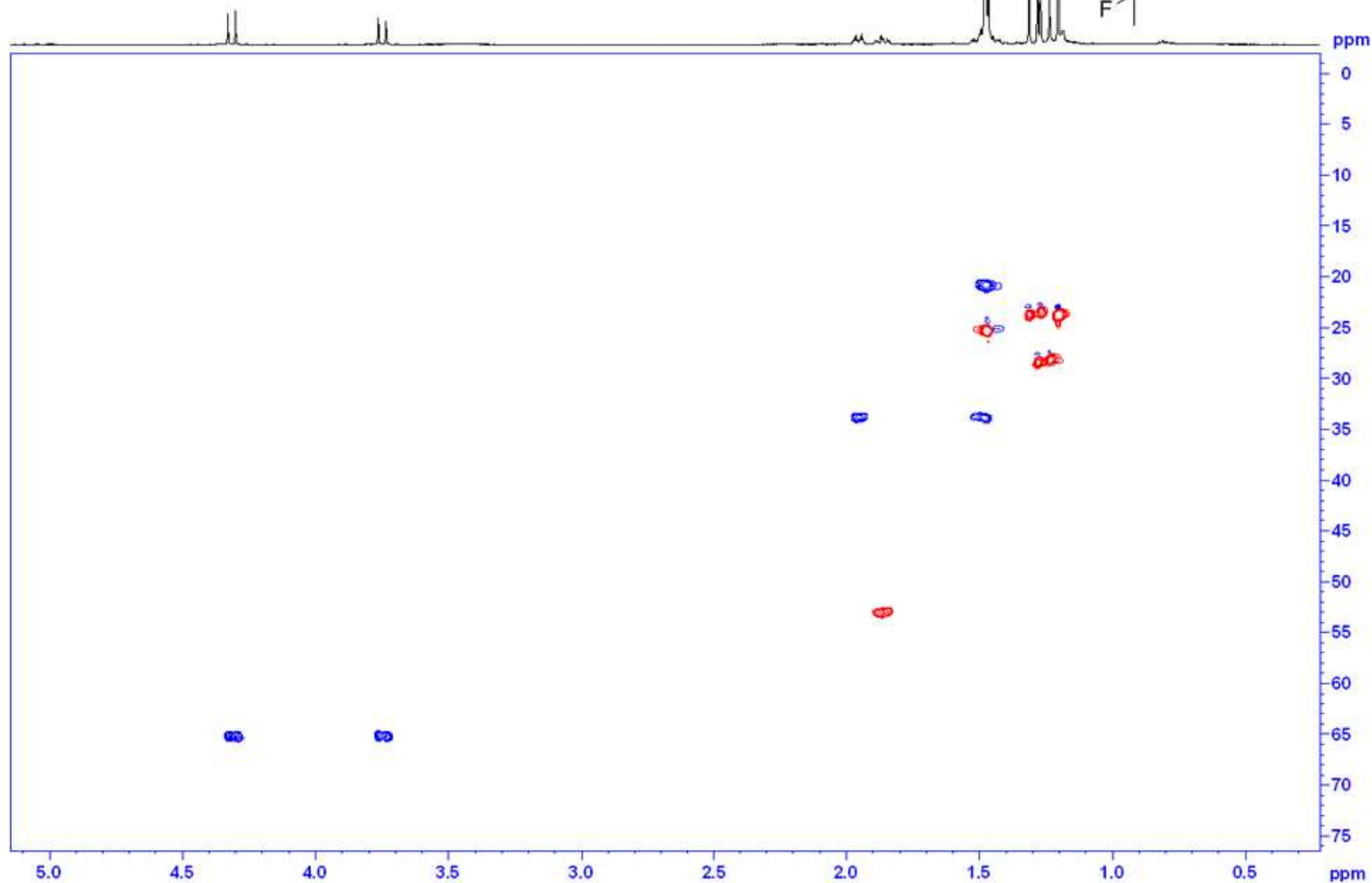
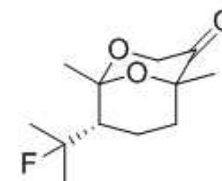
DEPT spectra for compound **8**

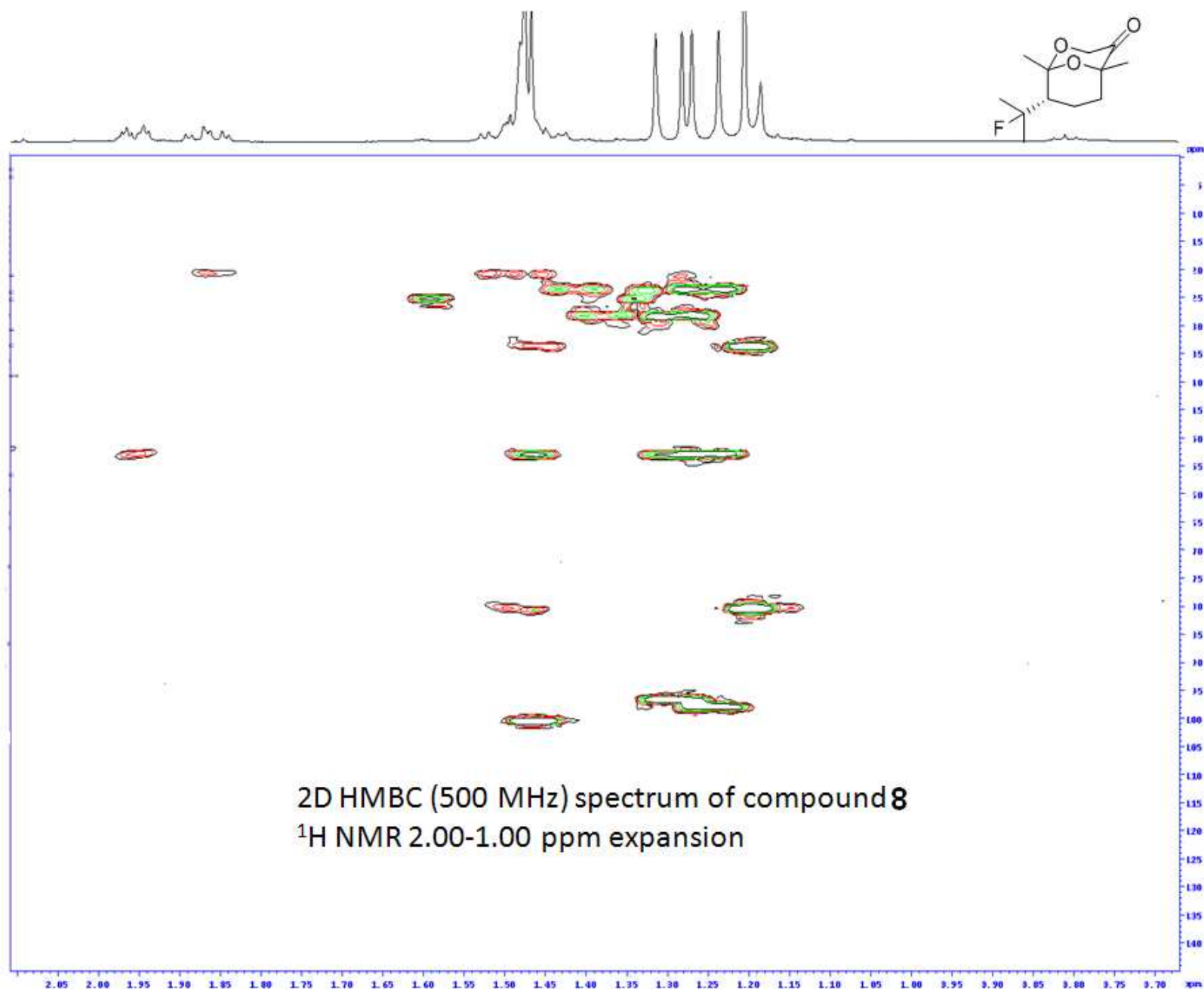


2D HSQC (500 MHz) spectrum of compound **8**

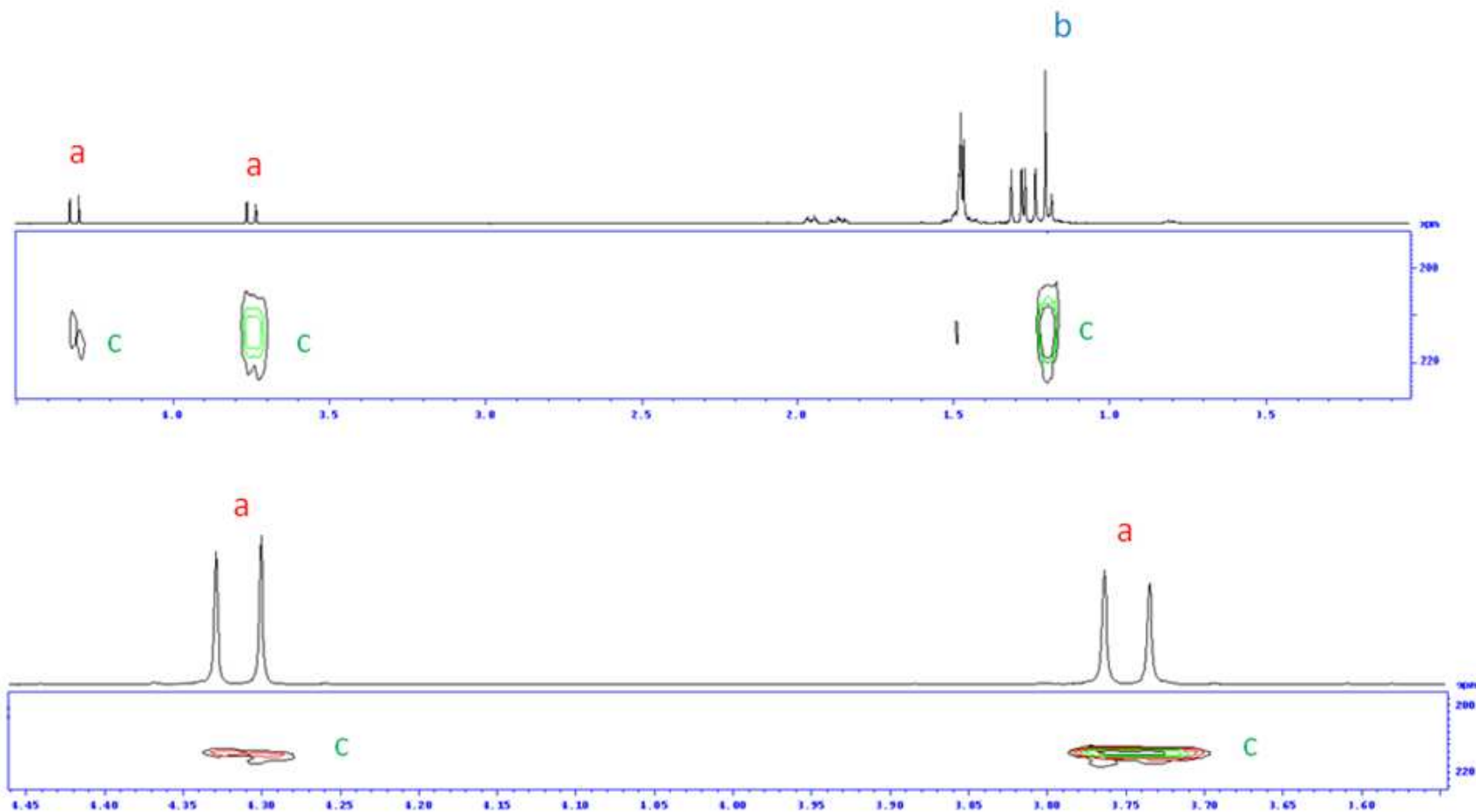
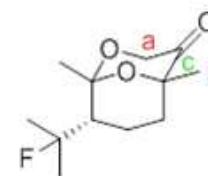
CH₂ (in Blue)

CH and CH₃ (in RED)

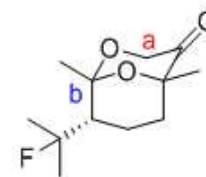




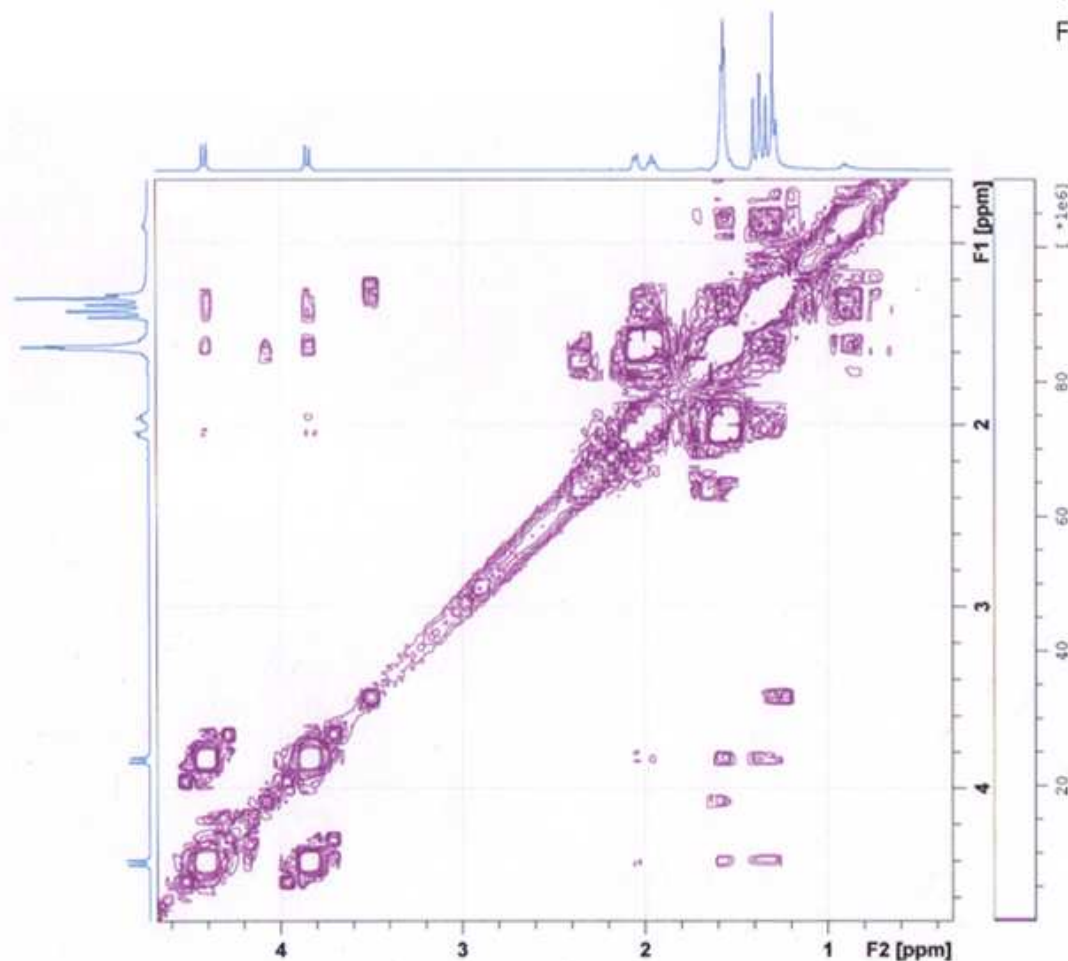
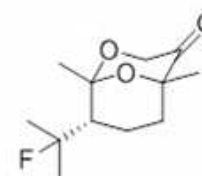
2D HMBC (500 MHz) spectrum of compound **8**
 ^{13}C NMR 200-220 ppm expansion



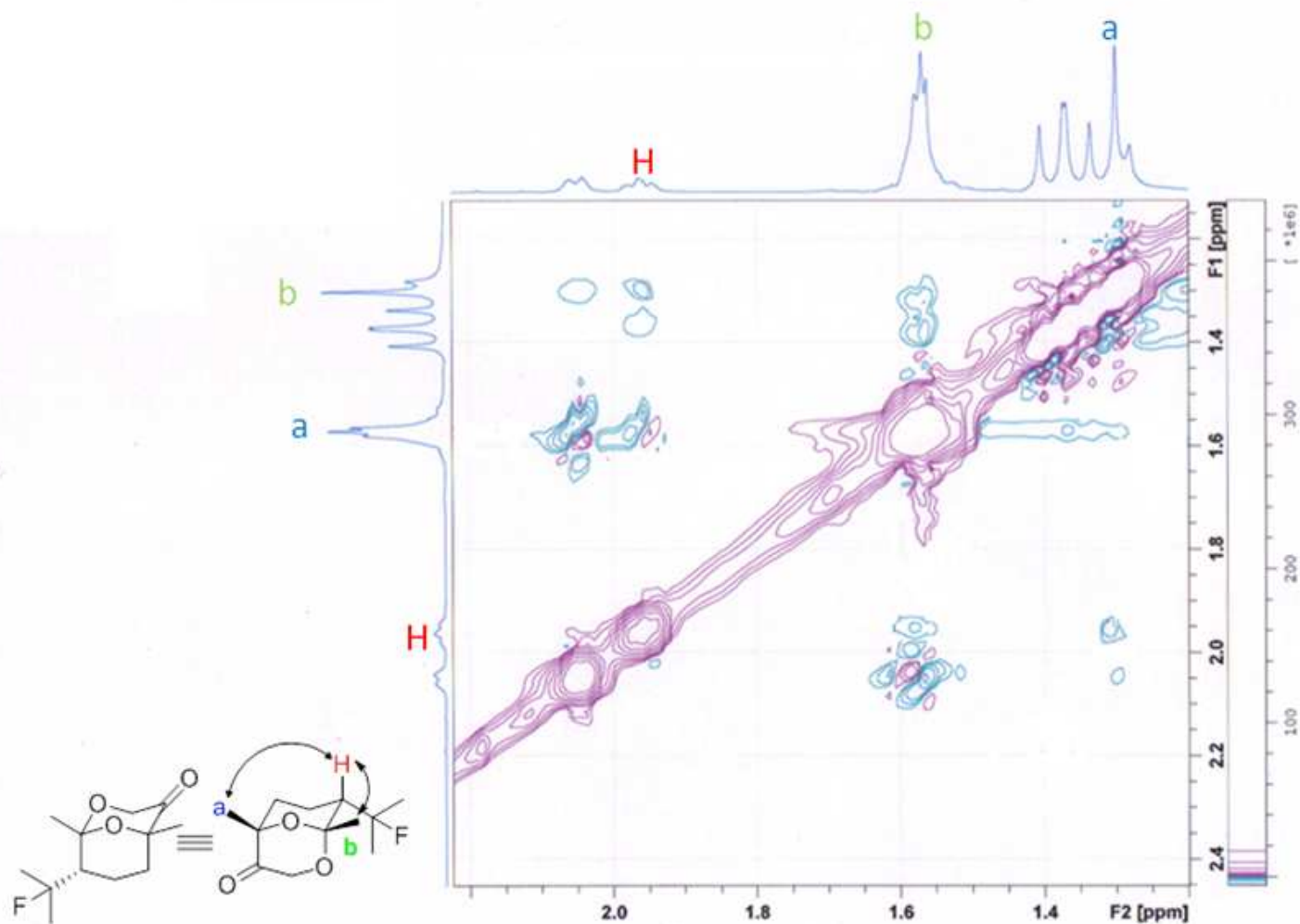
2D HMBC (500 MHz) spectrum of compound **8**
 ^{13}C NMR 100 ppm expansion



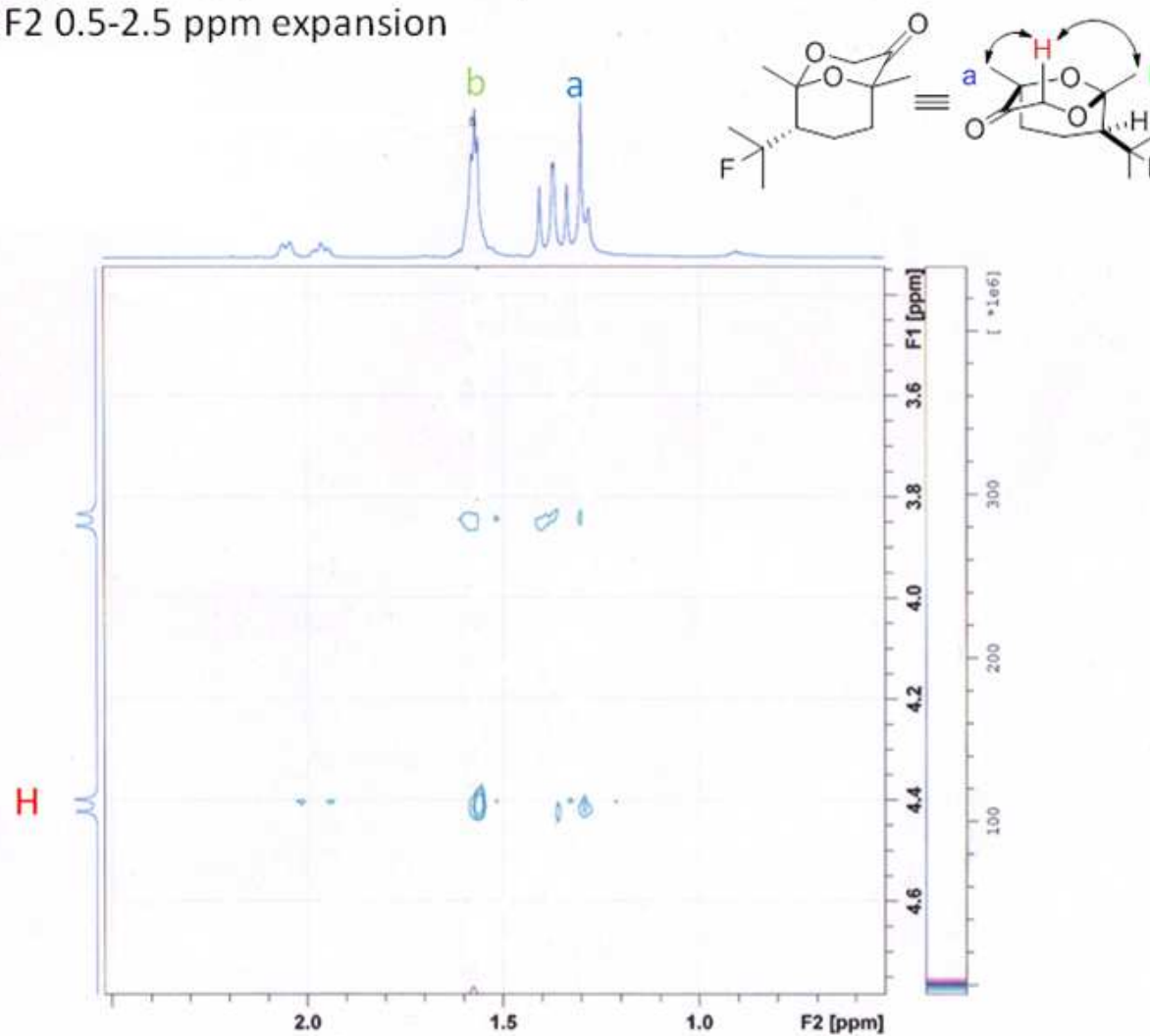
2D COSY (600 MHz) spectrum of compound **8**



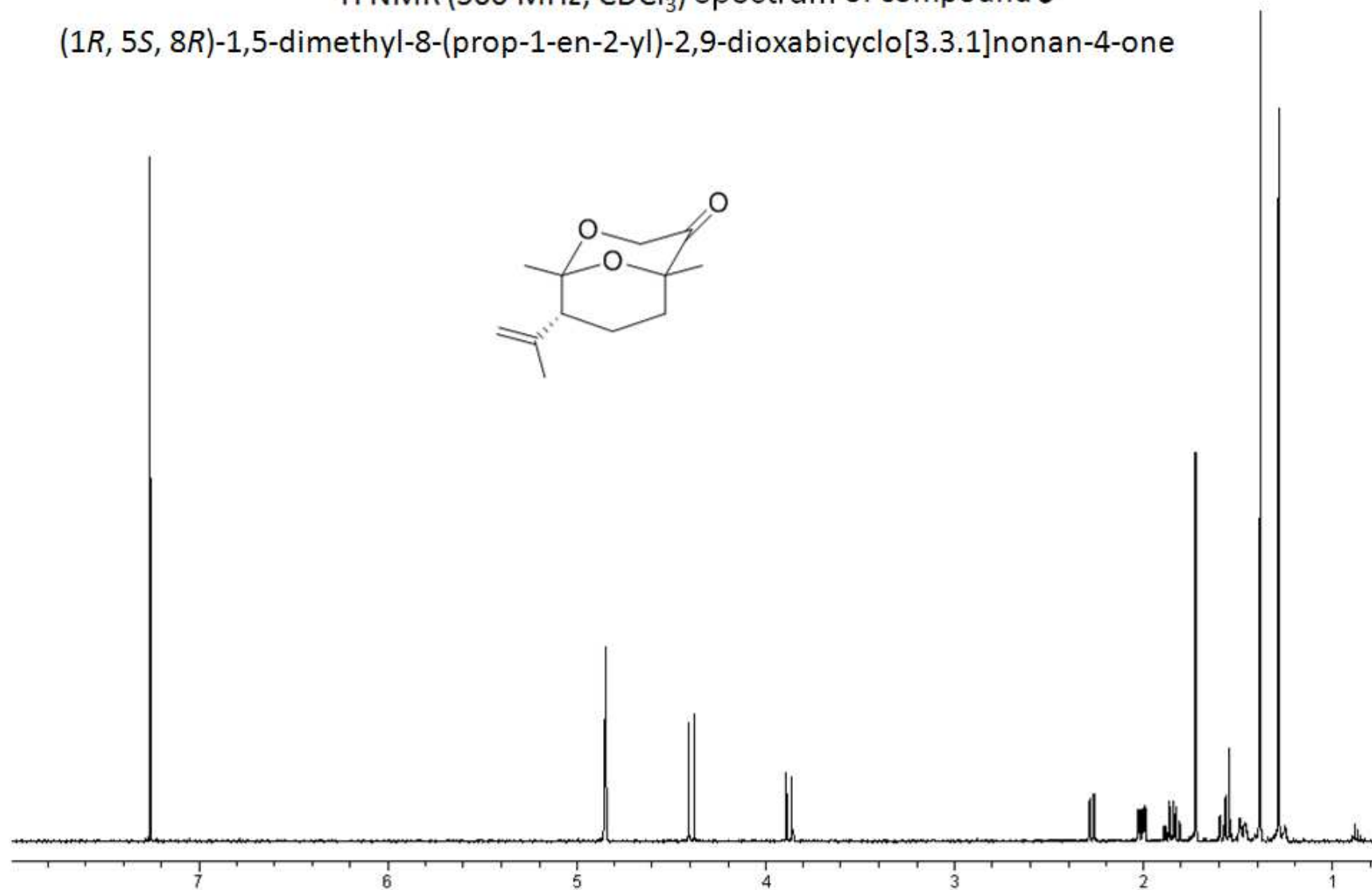
2D NOESY (600 MHz) spectrum of compound **8**
 ^1H NMR F1/F2 1.2-2.2 ppm expansion



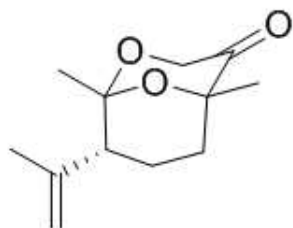
2D NOESY (600 MHz) spectrum of compound **8**
 ^1H NMR F2 0.5-2.5 ppm expansion



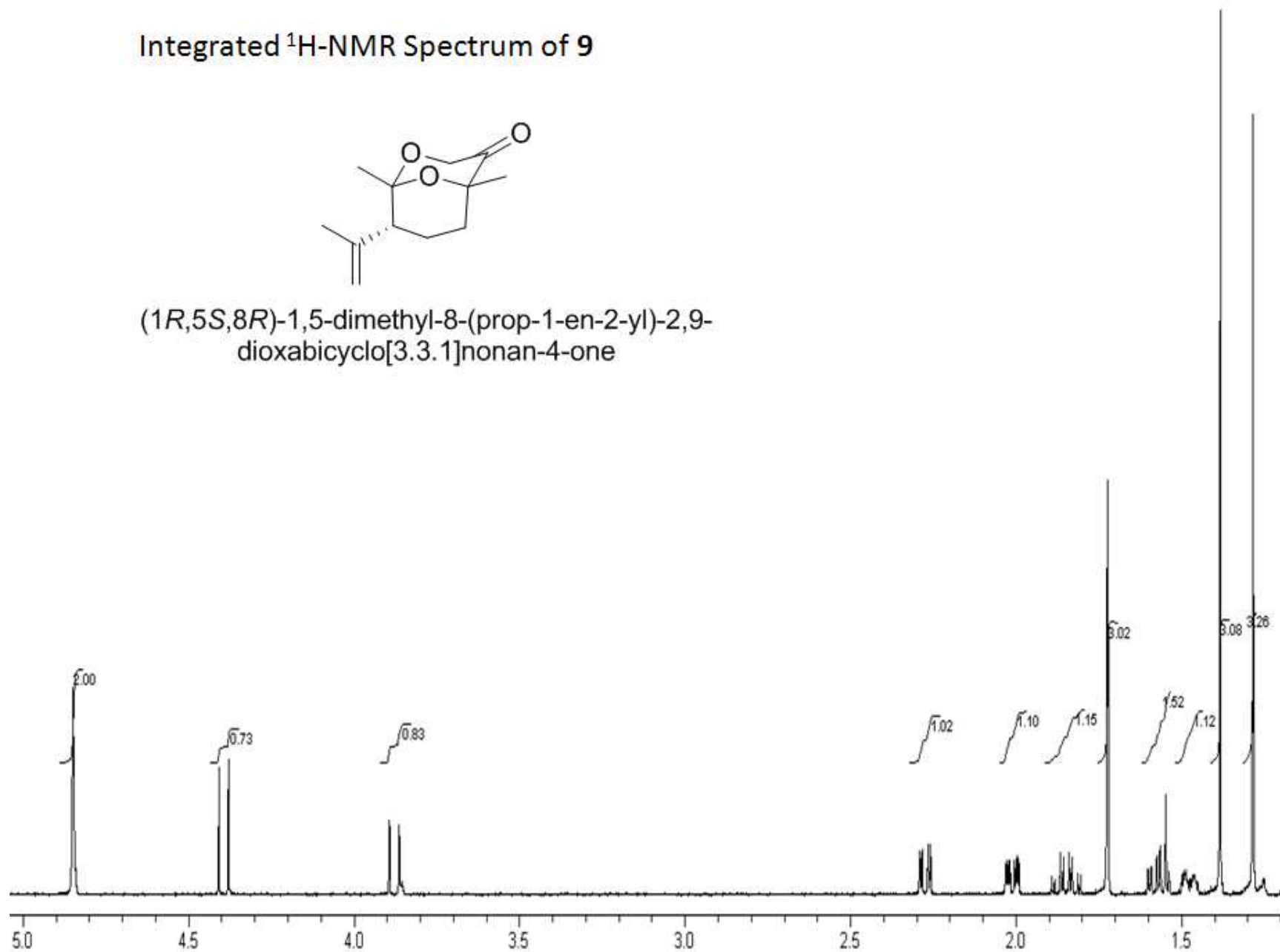
^1H NMR (500 MHz, CDCl_3) spectrum of compound **9**
(1*R*, 5*S*, 8*R*)-1,5-dimethyl-8-(prop-1-en-2-yl)-2,9-dioxabicyclo[3.3.1]nonan-4-one

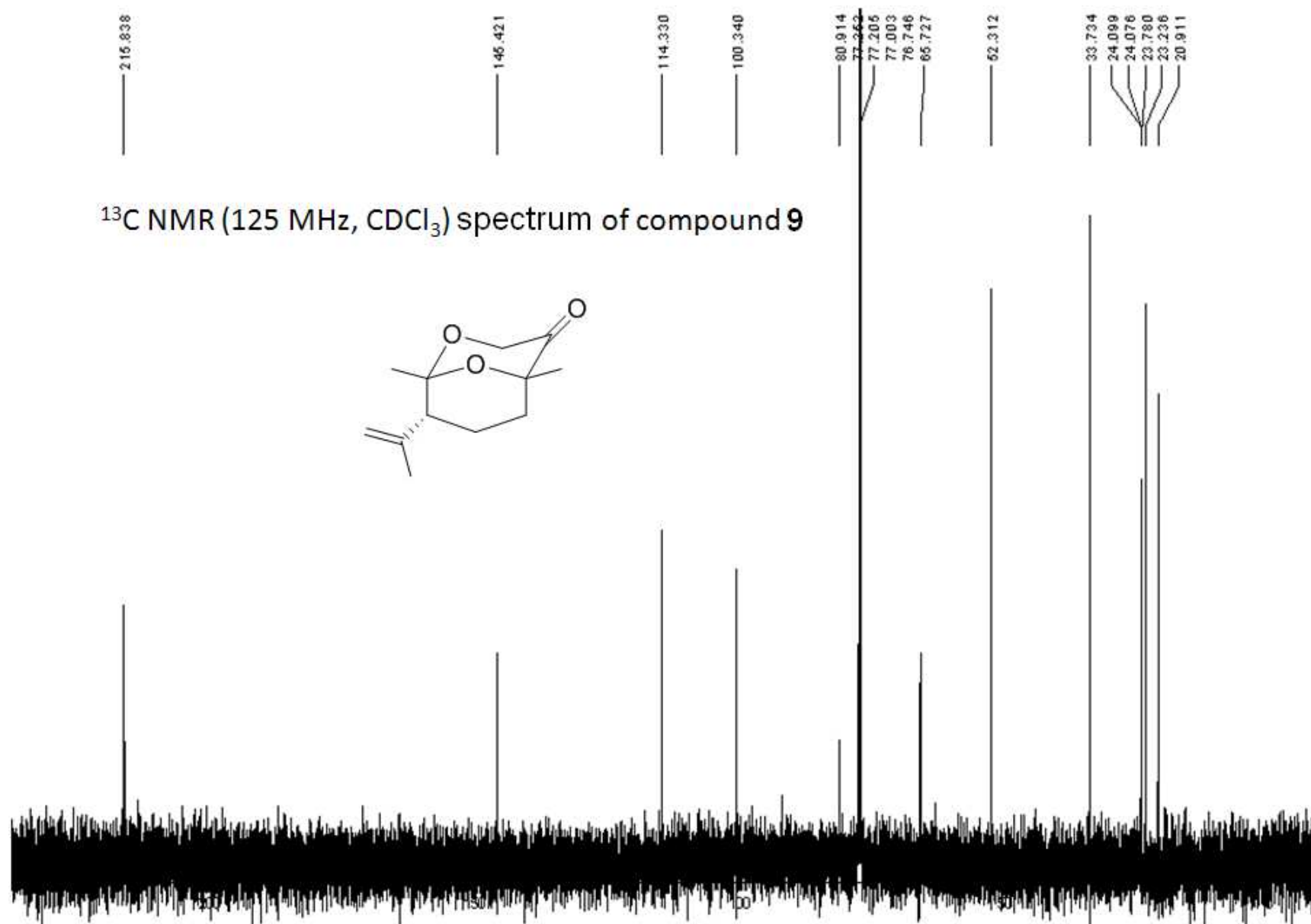


Integrated ^1H -NMR Spectrum of 9



(1*R*,5*S*,8*R*)-1,5-dimethyl-8-(prop-1-en-2-yl)-2,9-dioxabicyclo[3.3.1]nonan-4-one

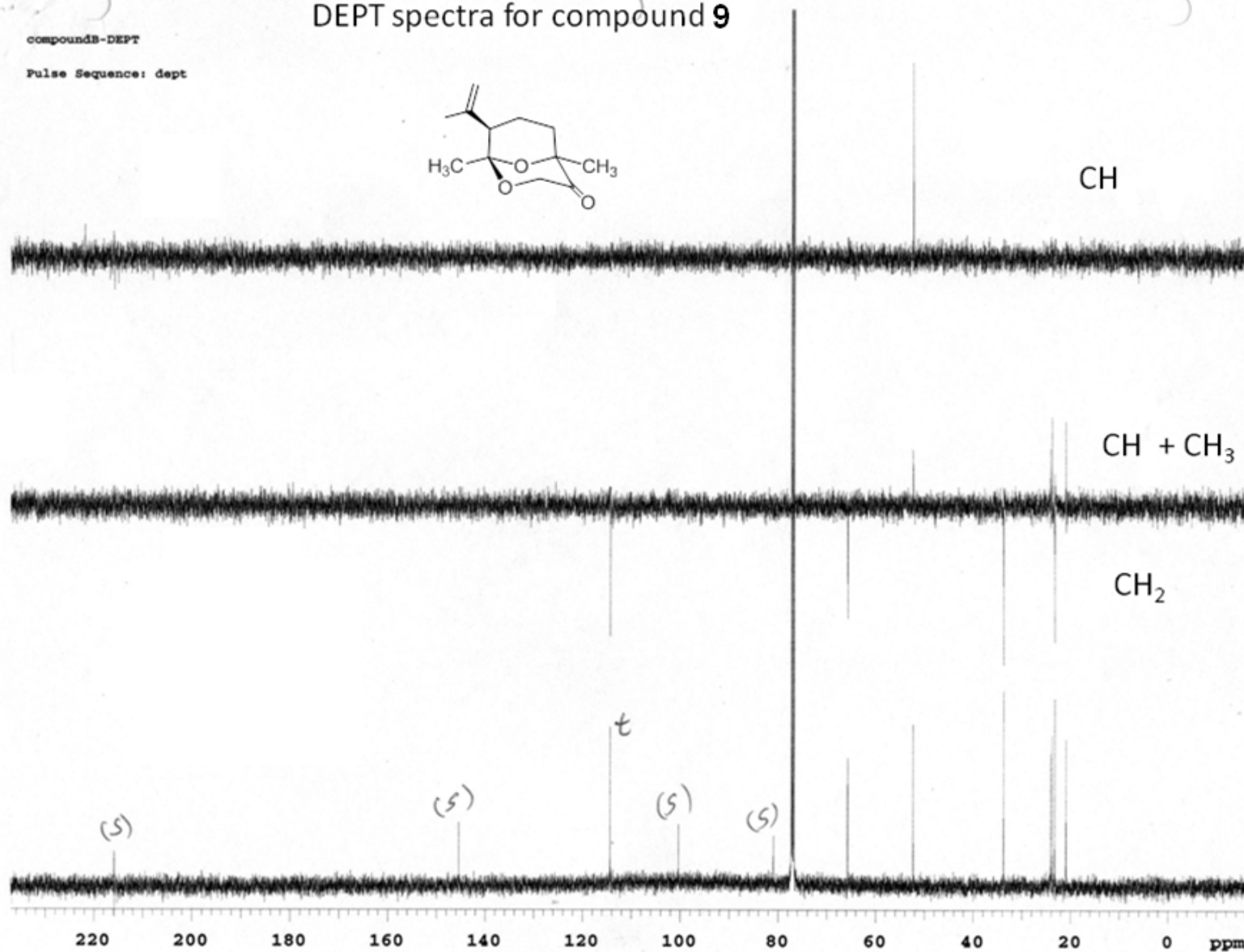
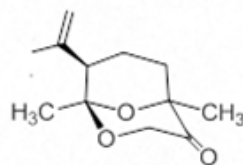




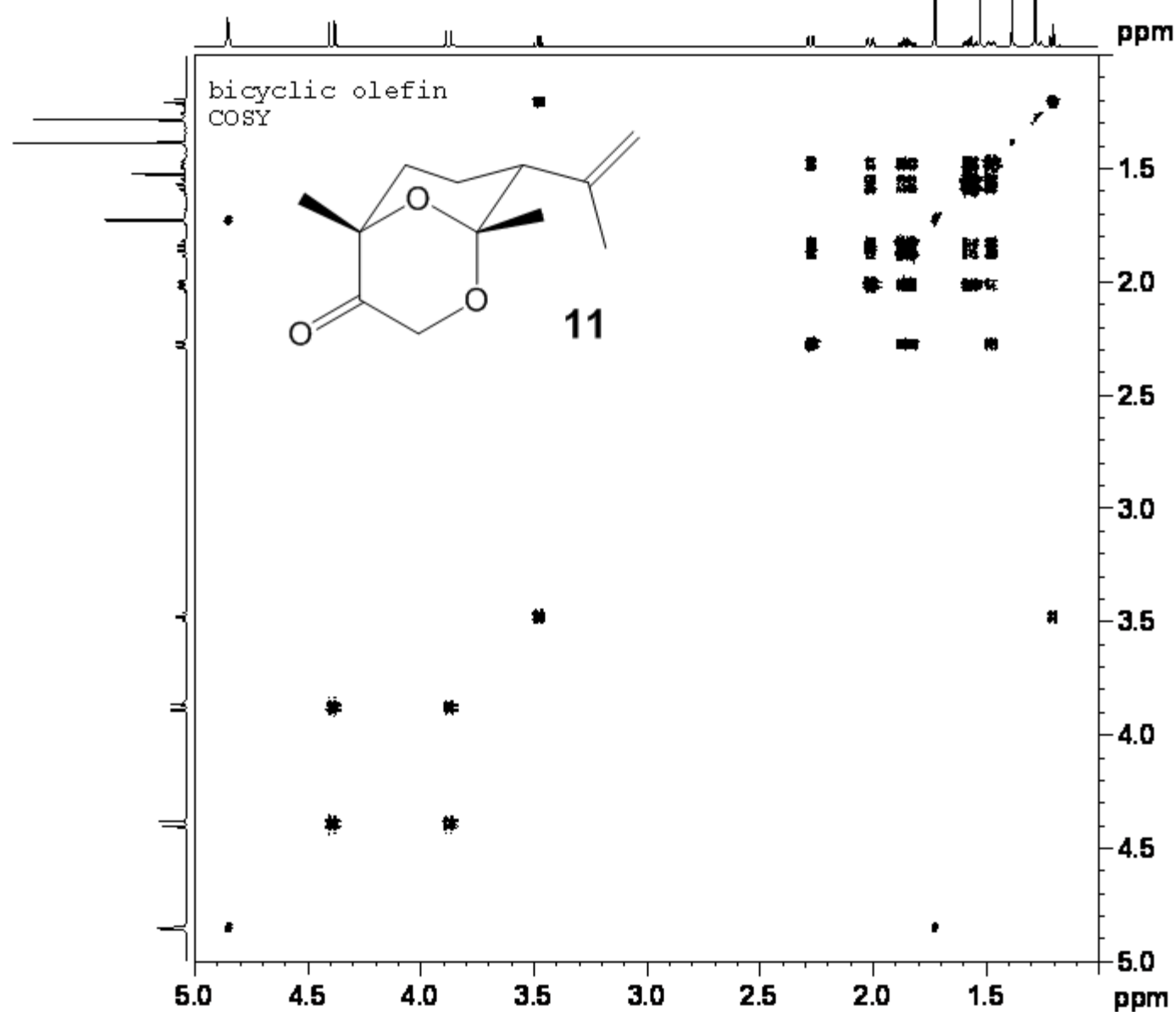
DEPT spectra for compound 9

compoundB-DEPT

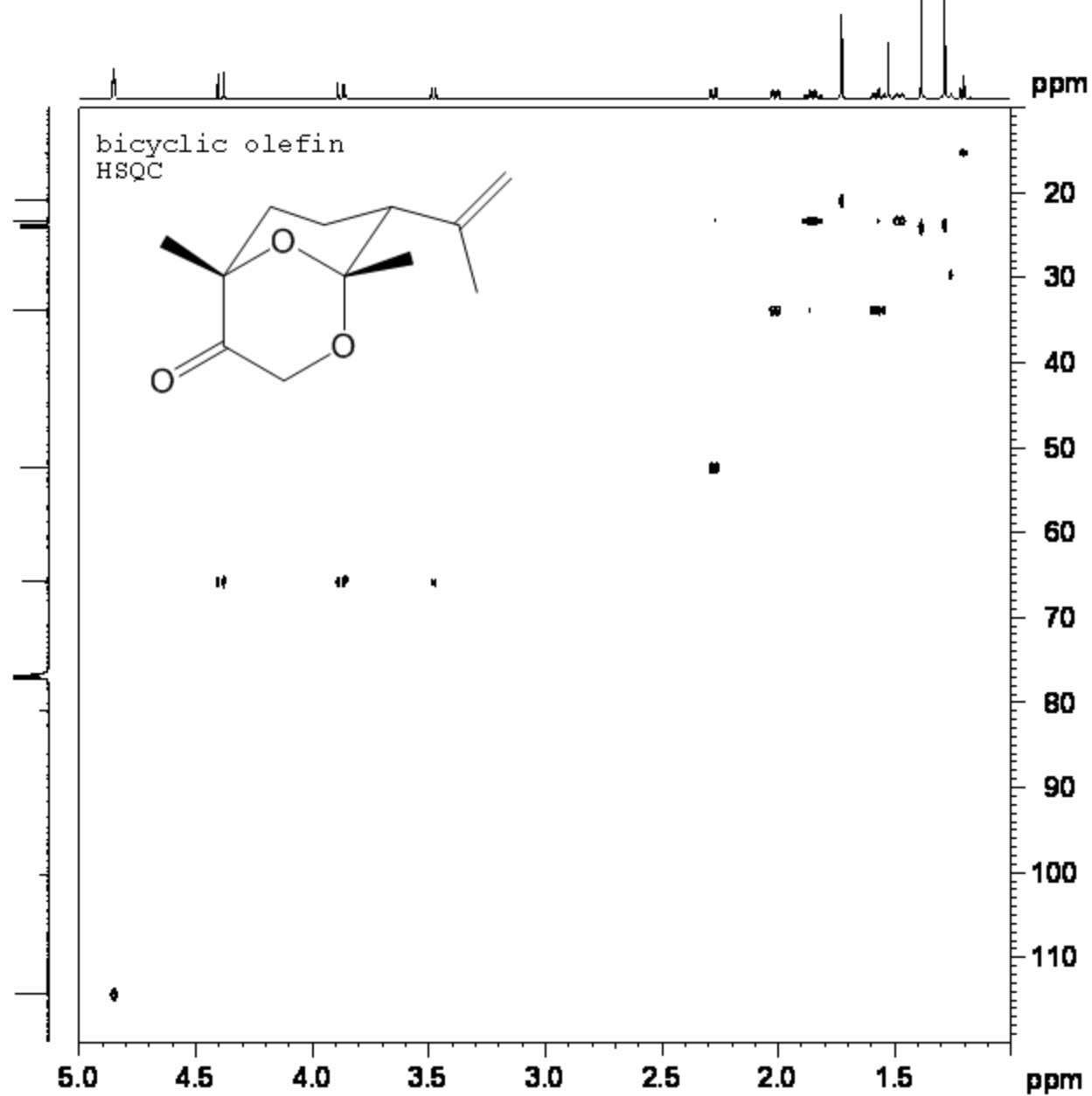
Pulse Sequence: dept



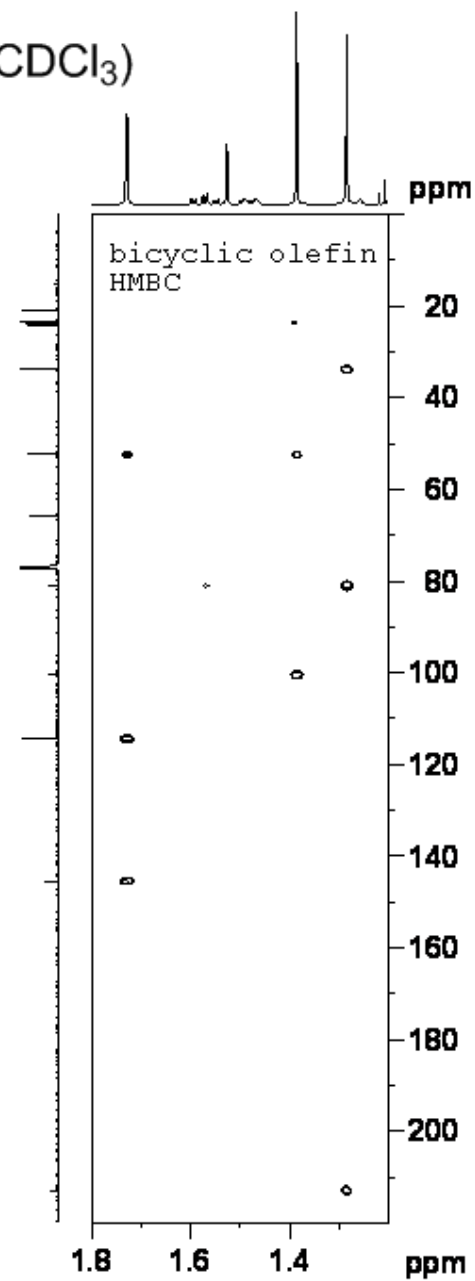
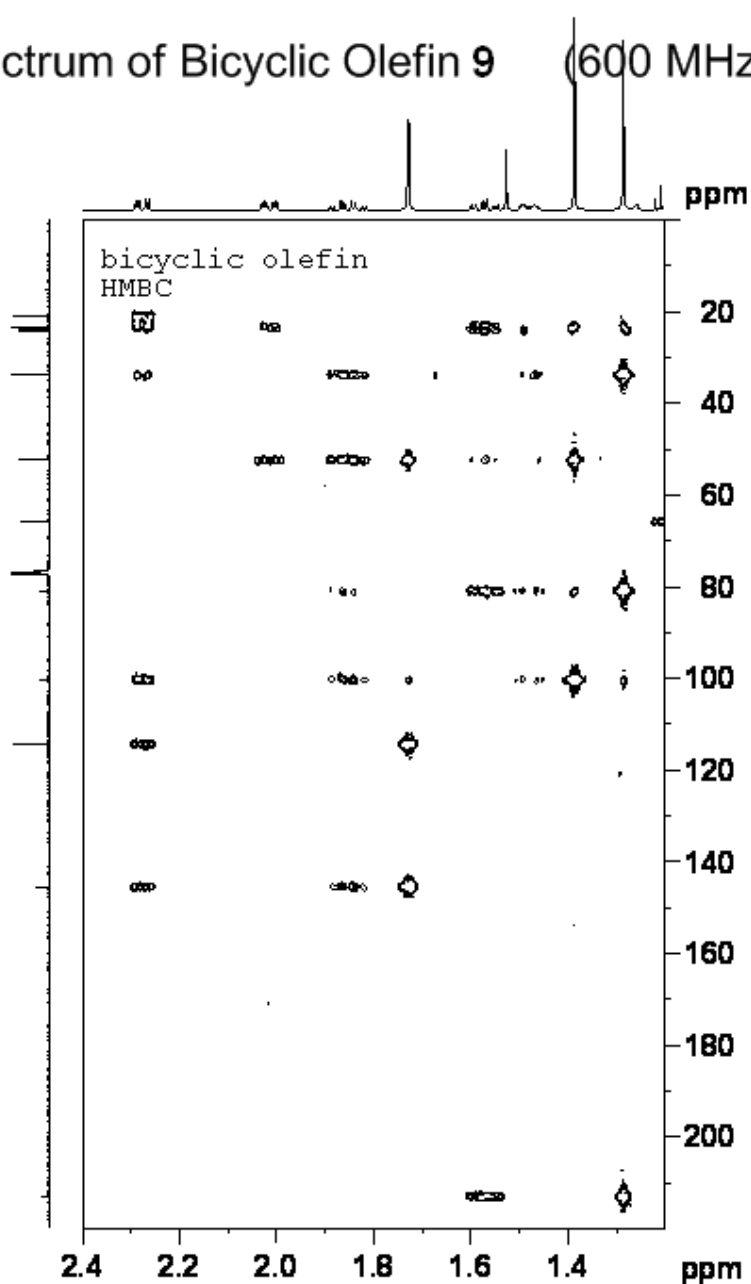
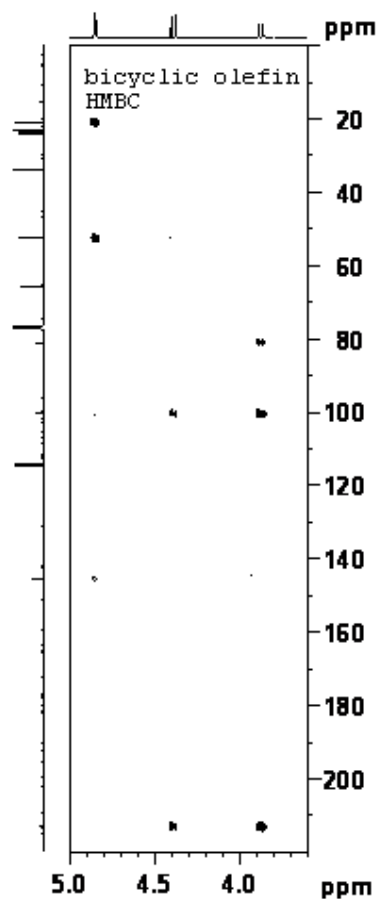
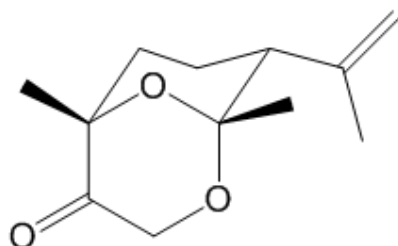
COSY Spectrum of Bicyclic Olefin 9 (600 MHz, CDCl₃)

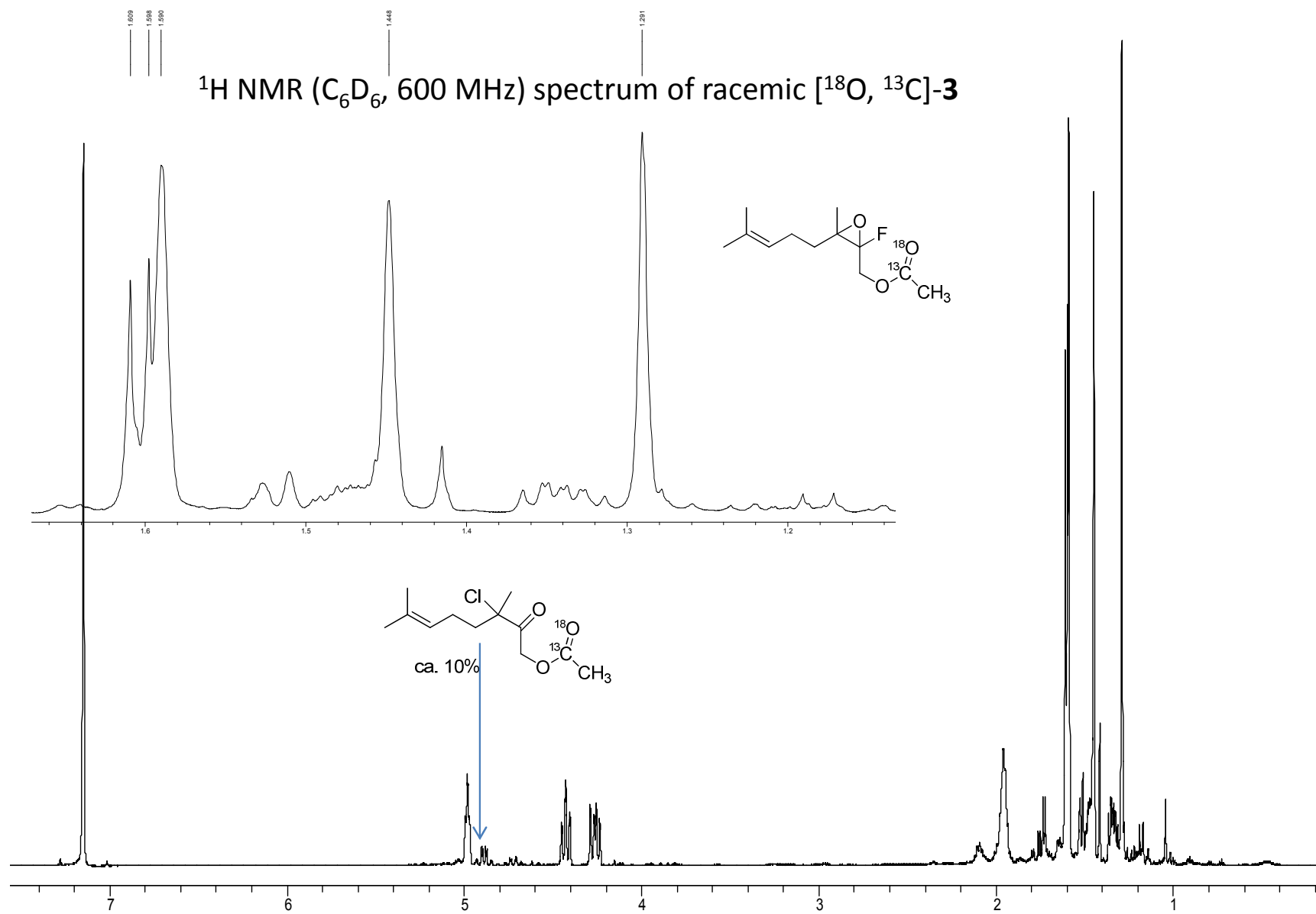


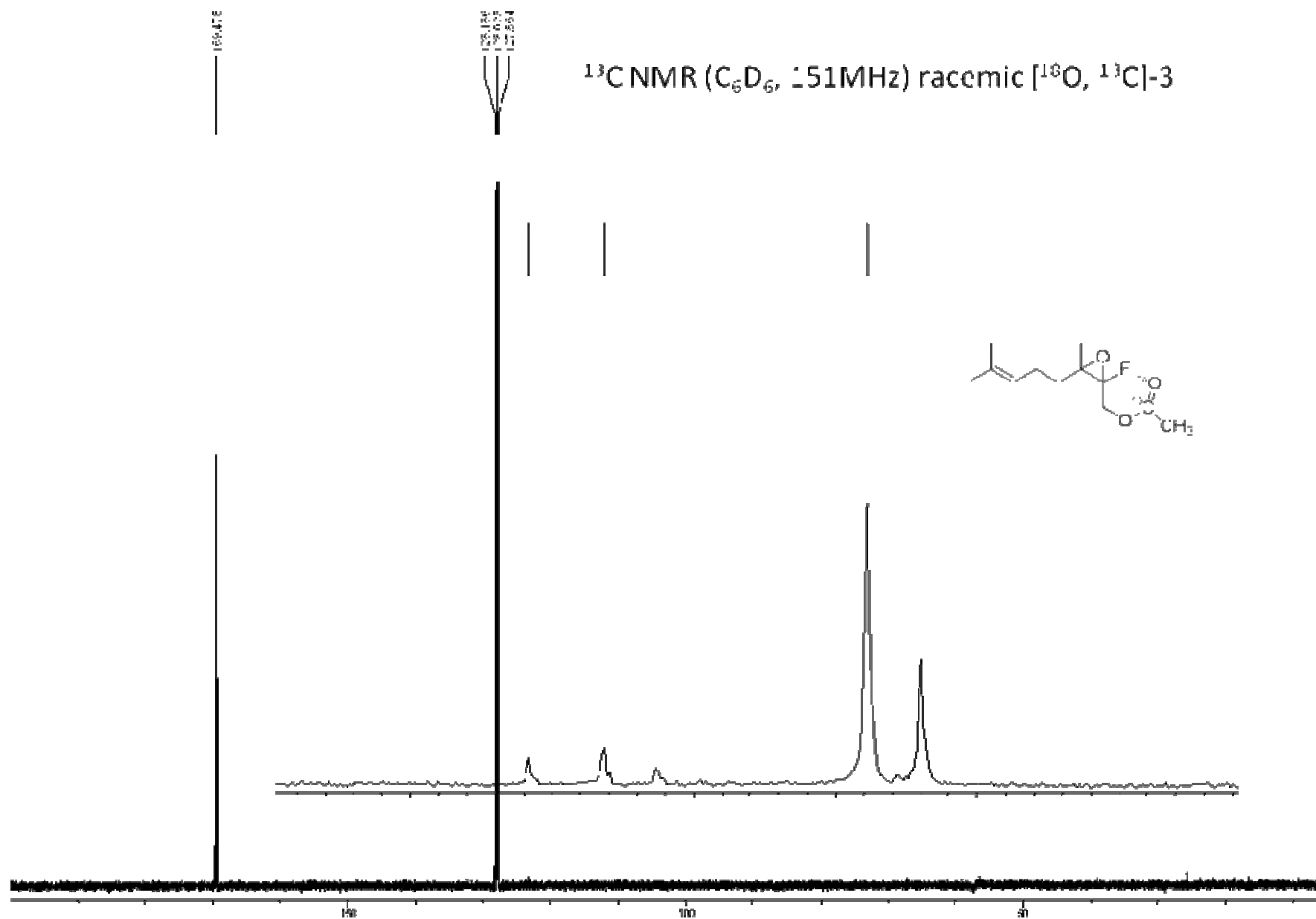
HSQC Spectrum of Bicyclic Olefin 9 (600 MHz, CDCl₃)



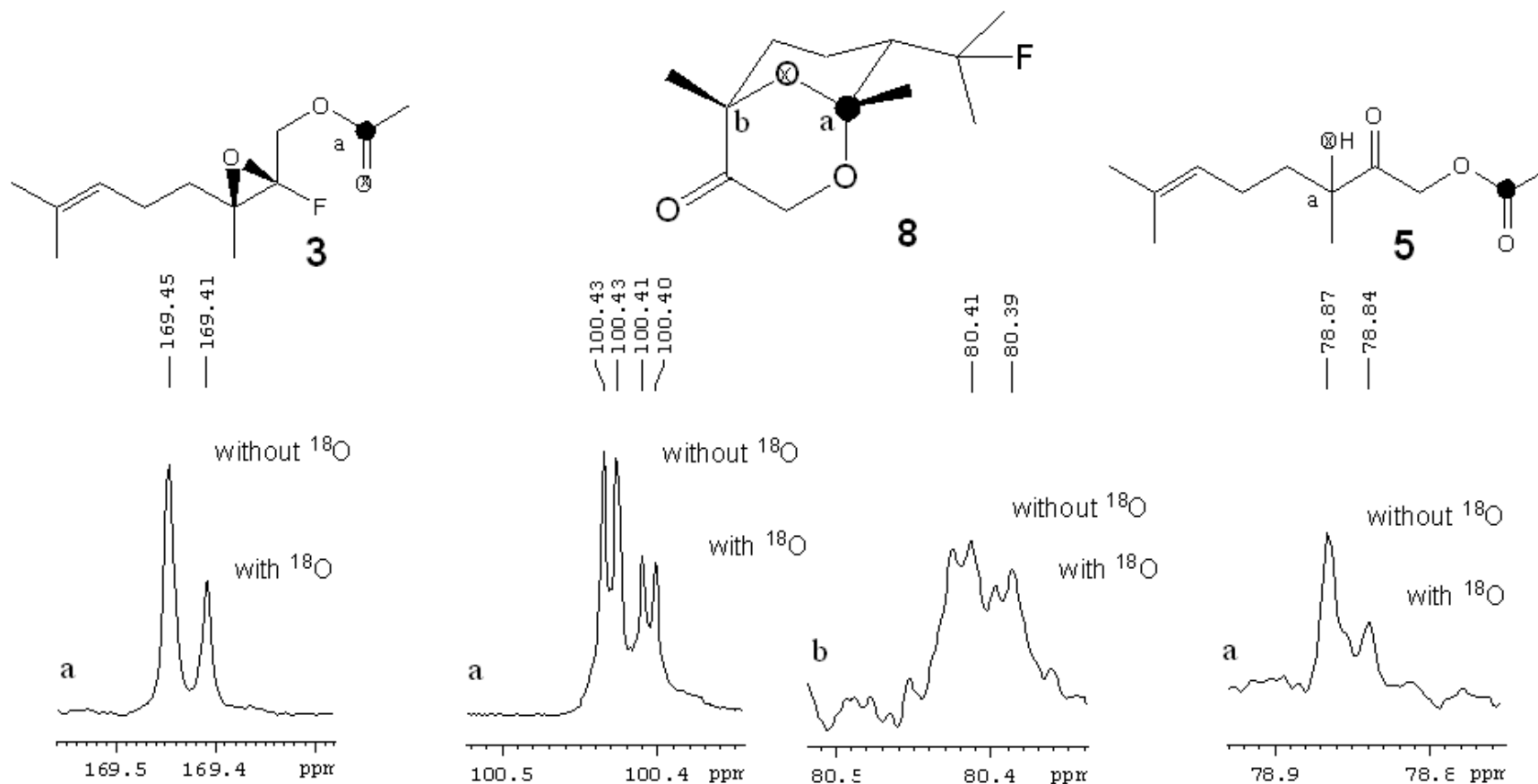
HMBC Spectrum of Bicyclic Olefin 9 (600 MHz, CDCl₃)



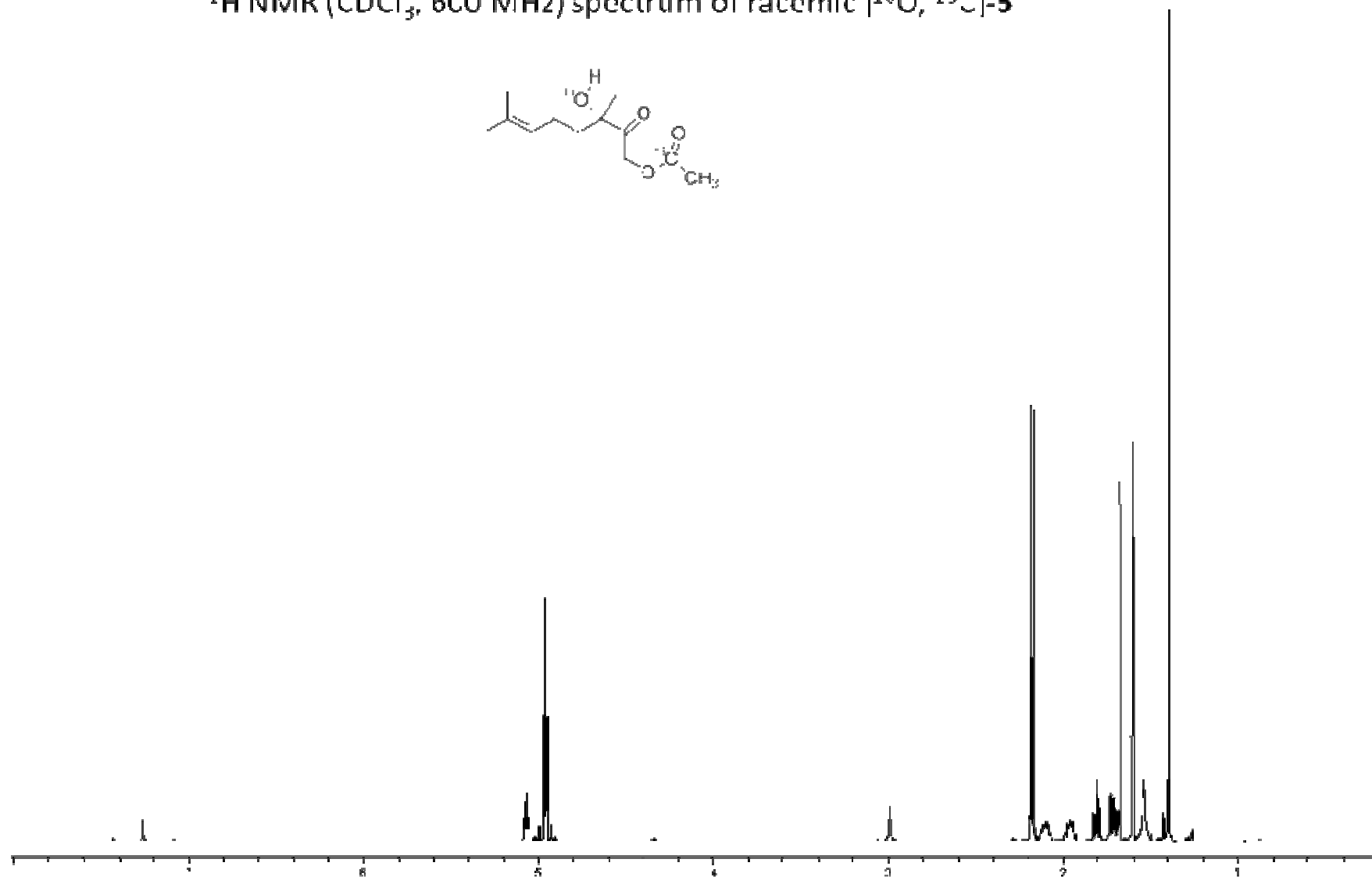
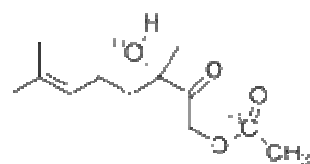




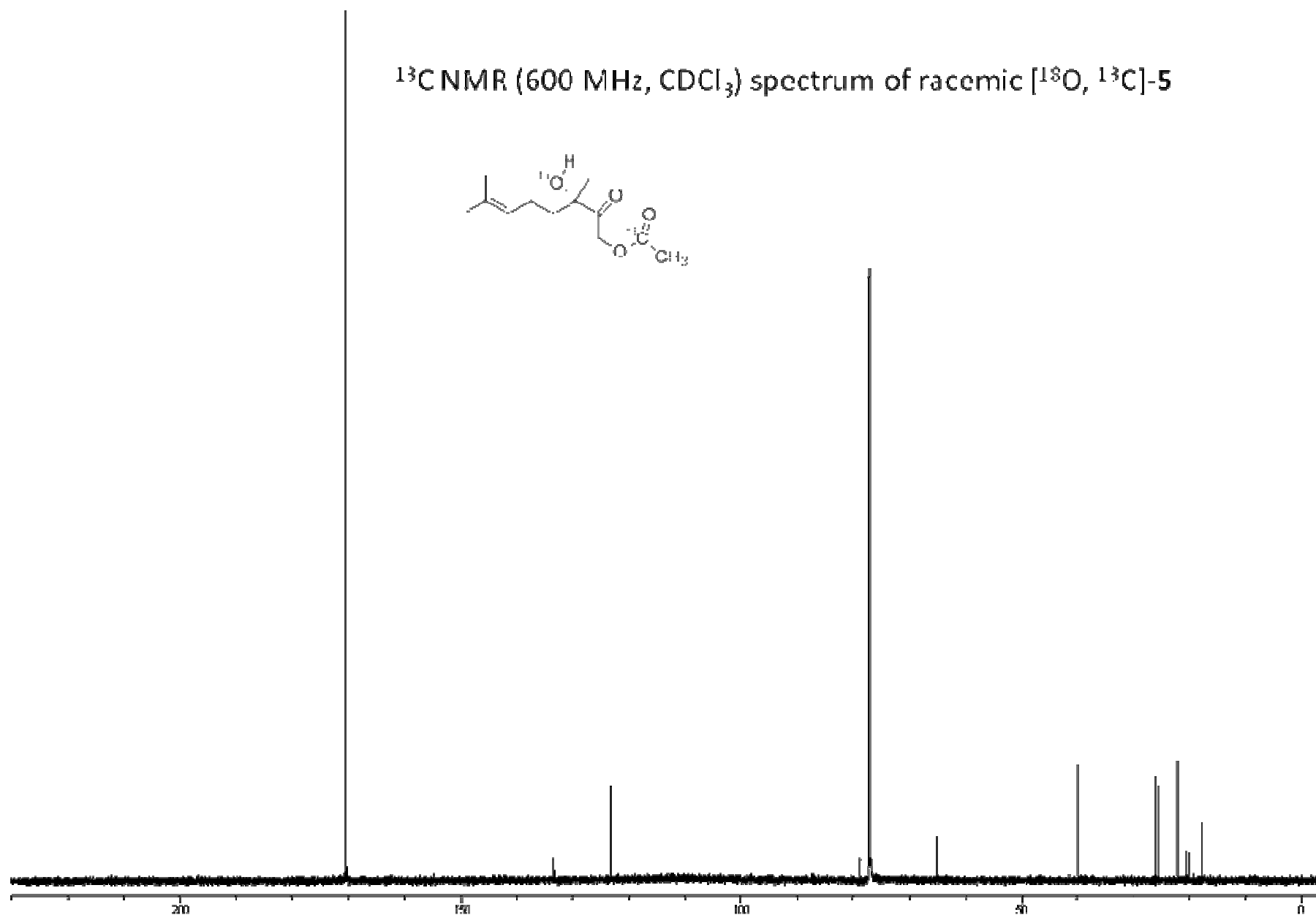
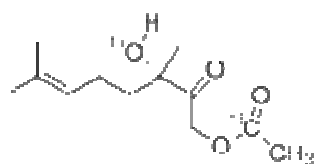
^{13}C -NMR Spectrum of ^{13}C , ^{18}O -Labeled Compounds 151MHz, CDCl_3)



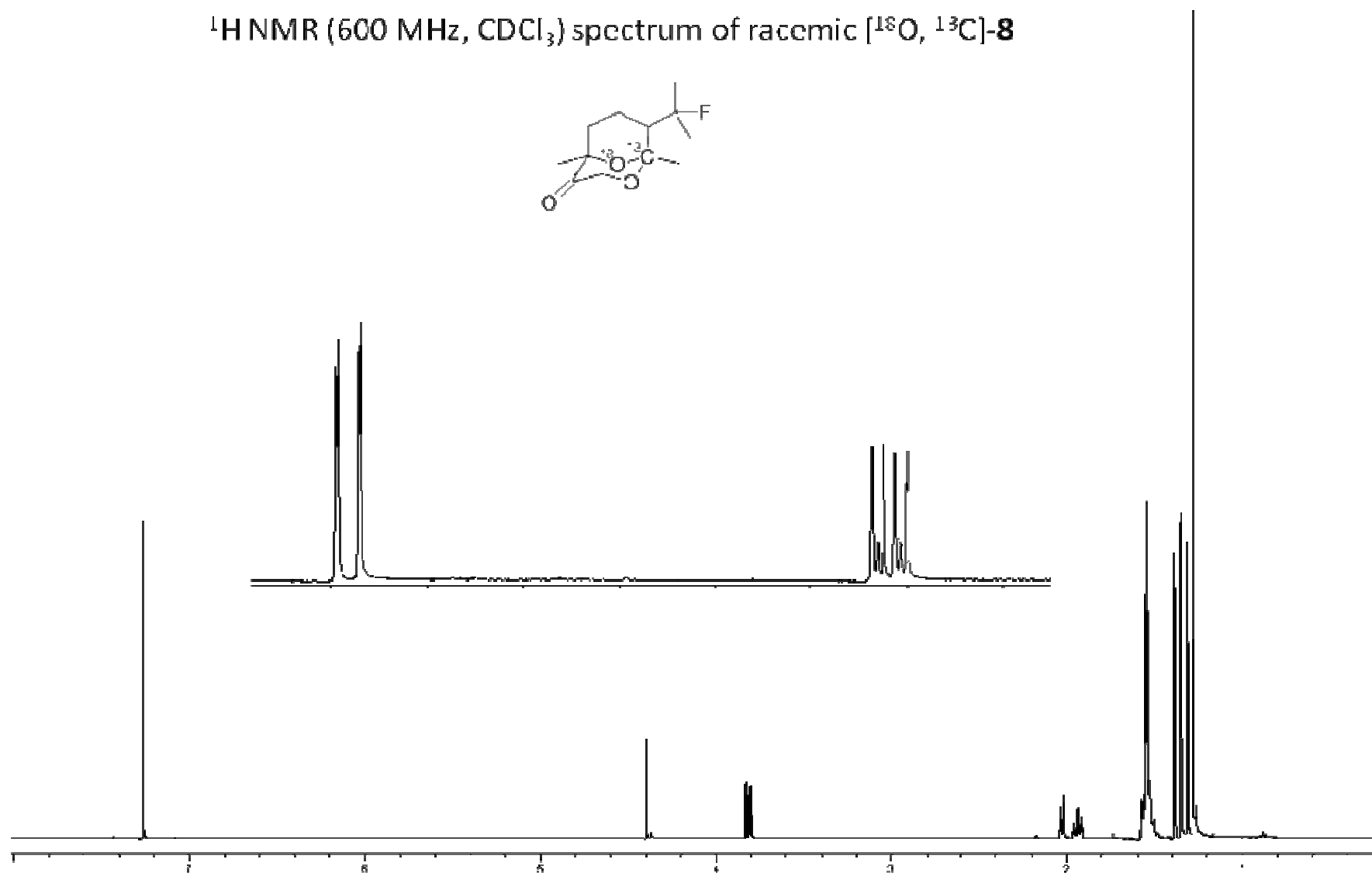
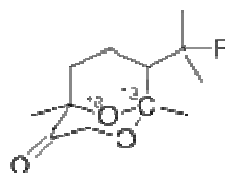
^1H NMR (CDCl_3 , 600 MHz) spectrum of racemic [^{18}O , ^{13}C]-5



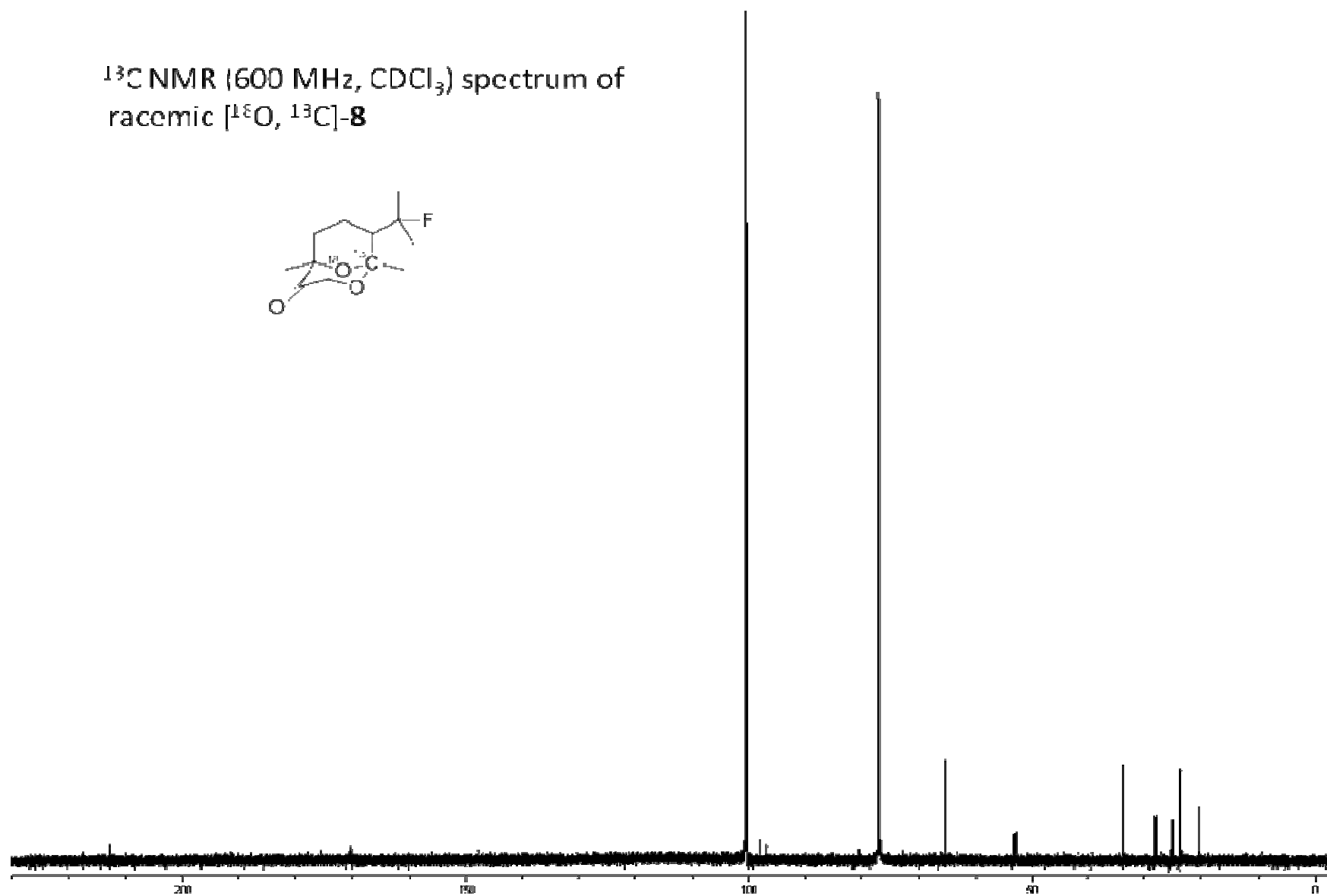
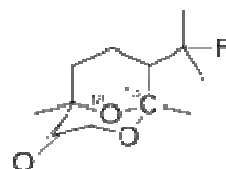
^{13}C NMR (600 MHz, CDCl_3) spectrum of racemic [^{18}O , ^{13}C]-5



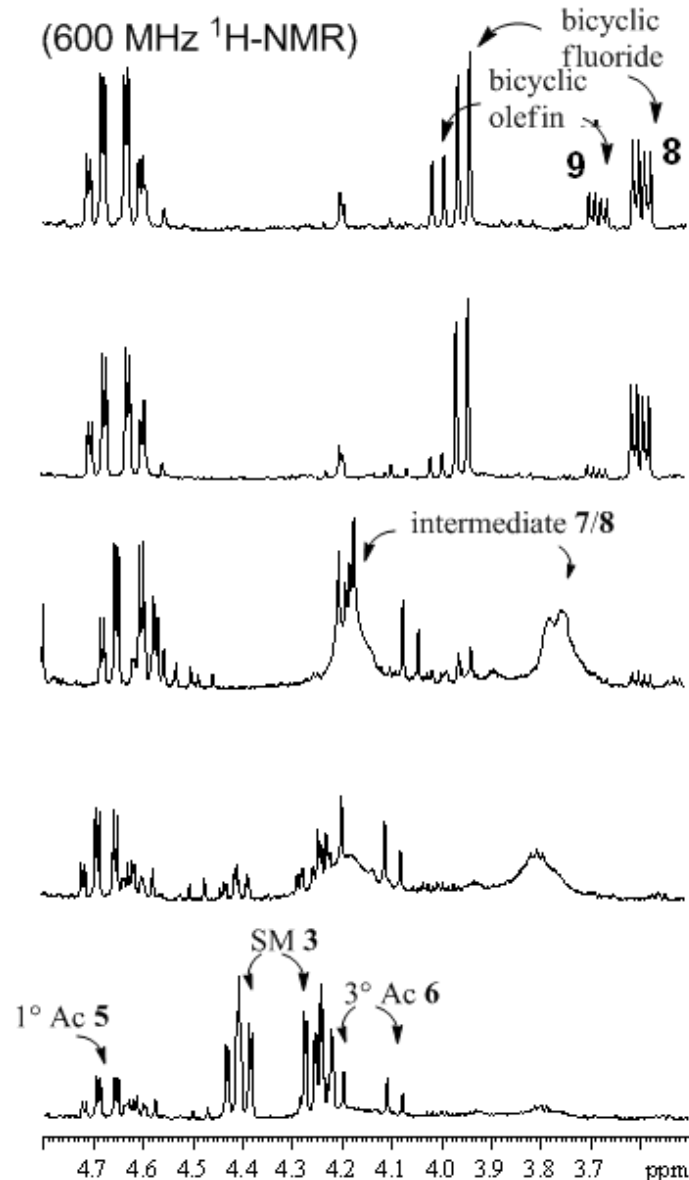
^1H NMR (600 MHz, CDCl_3) spectrum of racemic [^{18}O , ^{13}C]-**8**



^{13}C NMR (600 MHz, CDCl_3) spectrum of
racemic $[^{18}\text{O}, ^{13}\text{C}]$ -**8**



NMR Kinetics of Reaction of ^{13}C , ^{18}O -Labeled Epoxy Acetate **3**



10 mM TFA/ C_6D_6
2 hr 30 °C + 2 hr 50 °C
(measured at 10 °C)

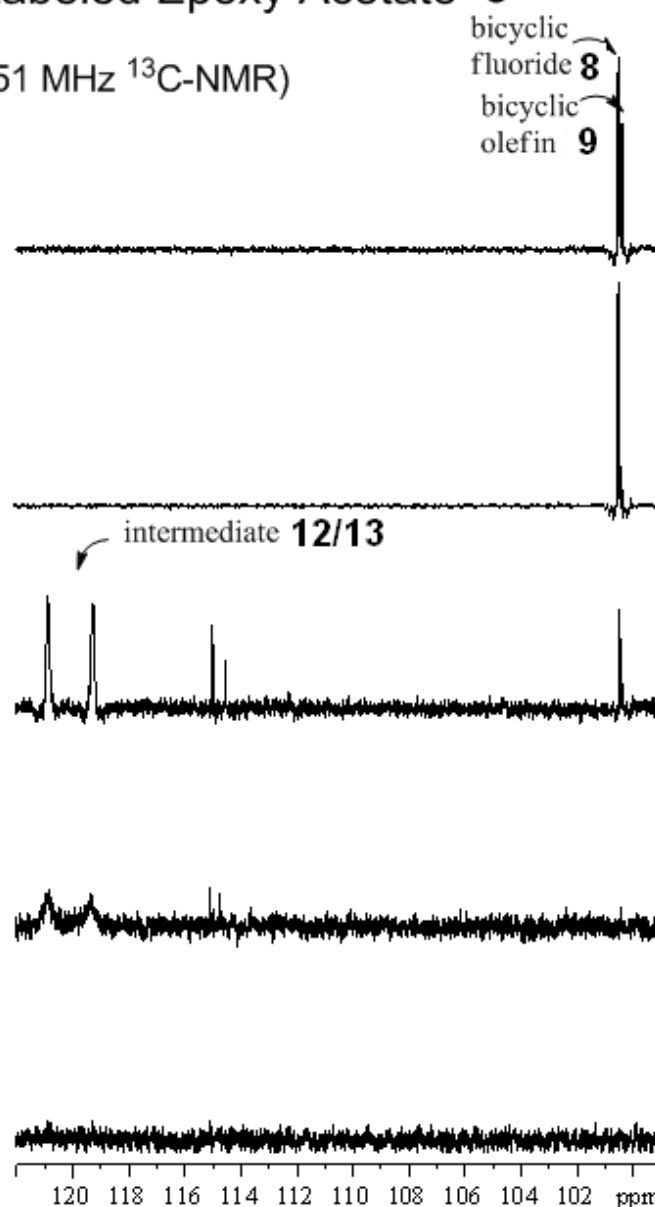
10 mM TFA/ C_6D_6
2 hr 30 °C + 1 hr 50 °C
(measured at 10 °C)

10 mM TFA/ C_6D_6
50 min 30 °C
(measured at 10 °C)

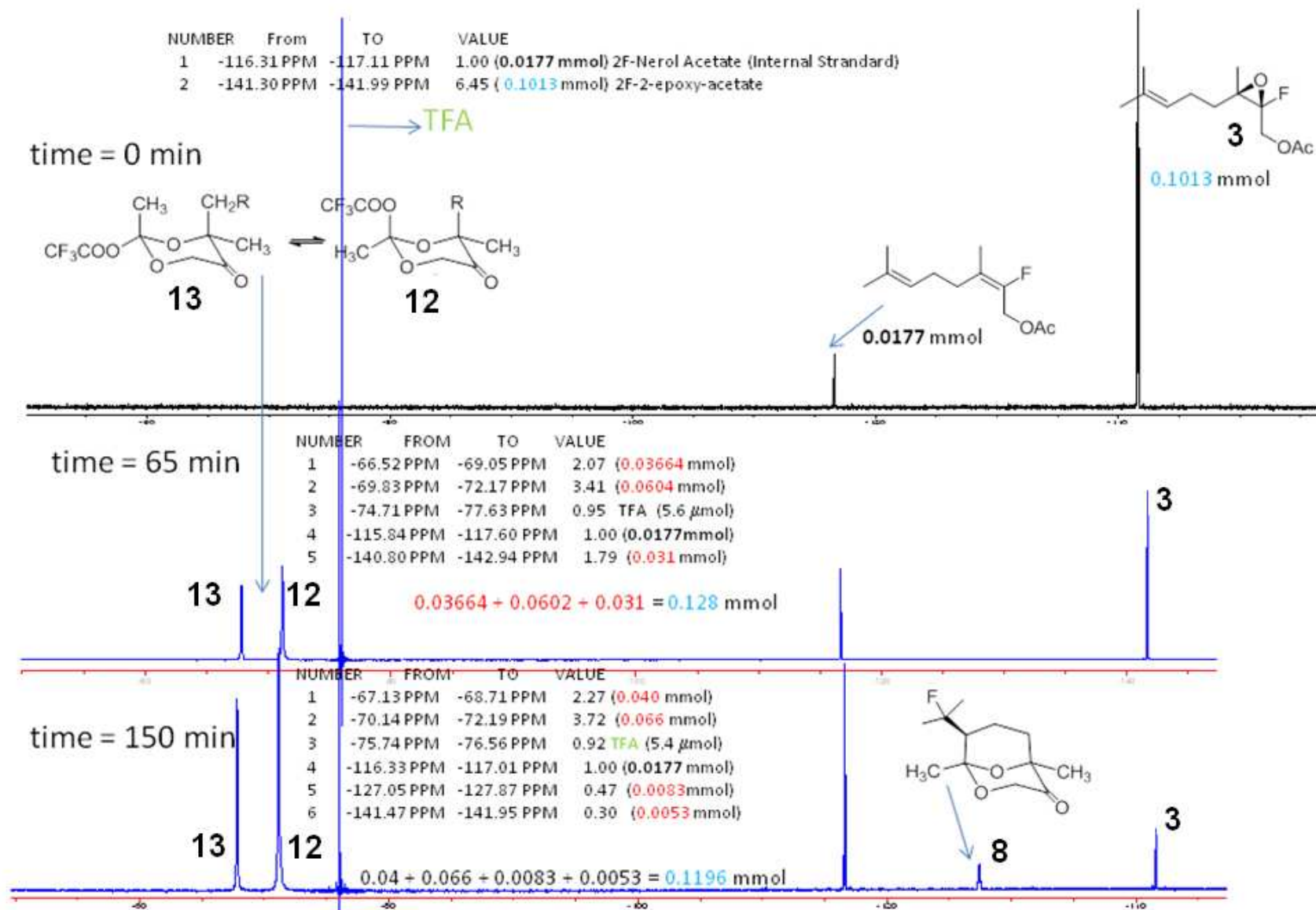
10 mM TFA/ C_6D_6
20 min 30 °C

10 mM TFA/ C_6D_6
3 min 30 °C

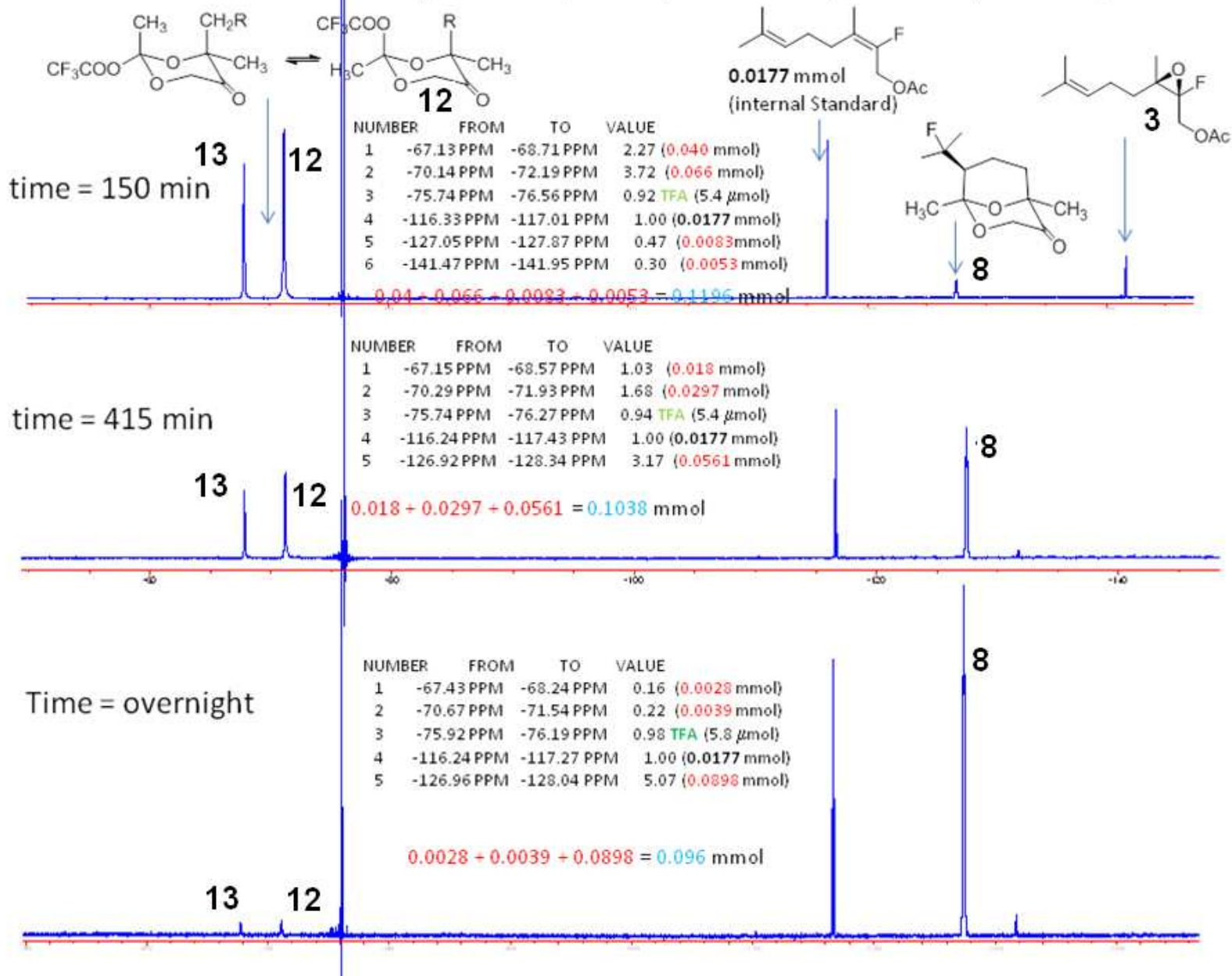
(151 MHz ^{13}C -NMR)



Conversion of acetate **3** to compound **8** (and **9**) via **12** + **13** followed by ^{19}F -NMR (376 MHz)



Conversion of acetate **3** to compound **8** (and **9**) followed by ^{19}F -NMR (376 MHz). Continuation



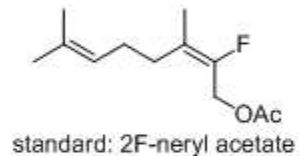
F19 OBSERVE

exp2 s2pul

Conversion of **3** to **8** monitored by ^{19}F NMR (376 MHz, CD_3CN)

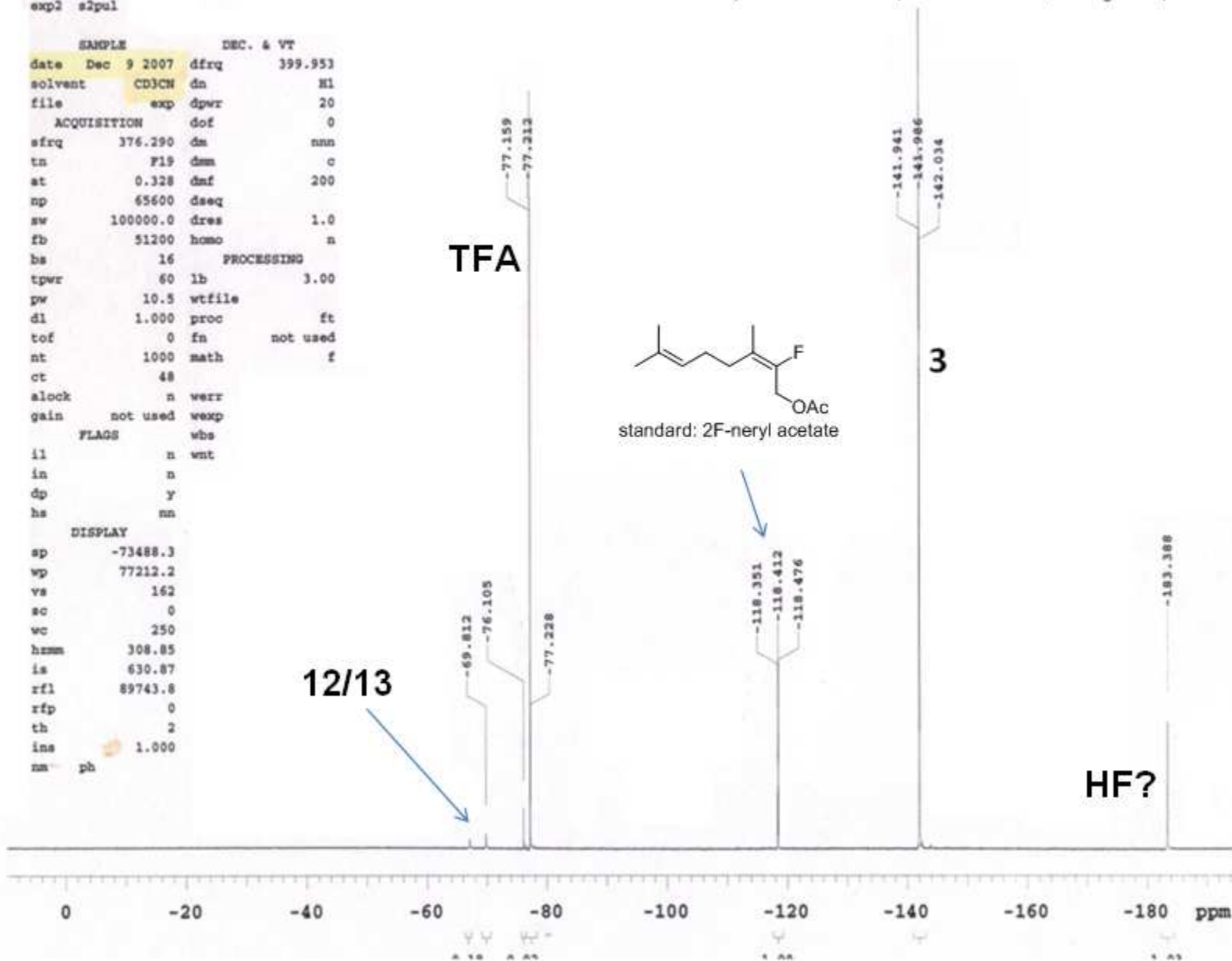
SAMPLE		DEC. & VT	
date	Dec 9 2007	dfrq	399.953
solvent	CD_3CN	dn	H1
file	exp	dpwr	20
ACQUISITION		dof	0
sfrq	376.290	dm	nnn
tn	F19	dsm	c
at	0.328	dntf	200
np	65600	dseq	
sv	100000.0	dres	1.0
fb	51200	homo	n
bs	16	PROCESSING	
tpwr	60	lb	3.00
pw	10.5	wtfile	
dl	1.000	proc	ft
tof	0	fn	not used
nt	1000	math	f
ct	48		
alock	n	werr	
gain	not used	wexp	
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-73488.3		
wp	77212.2		
vs	162		
sc	0		
vc	250		
hzm	308.85		
is	630.87		
rfl	89743.8		
rflp	0		
th	2		
ins	1.000		
nm	ph		

TFA

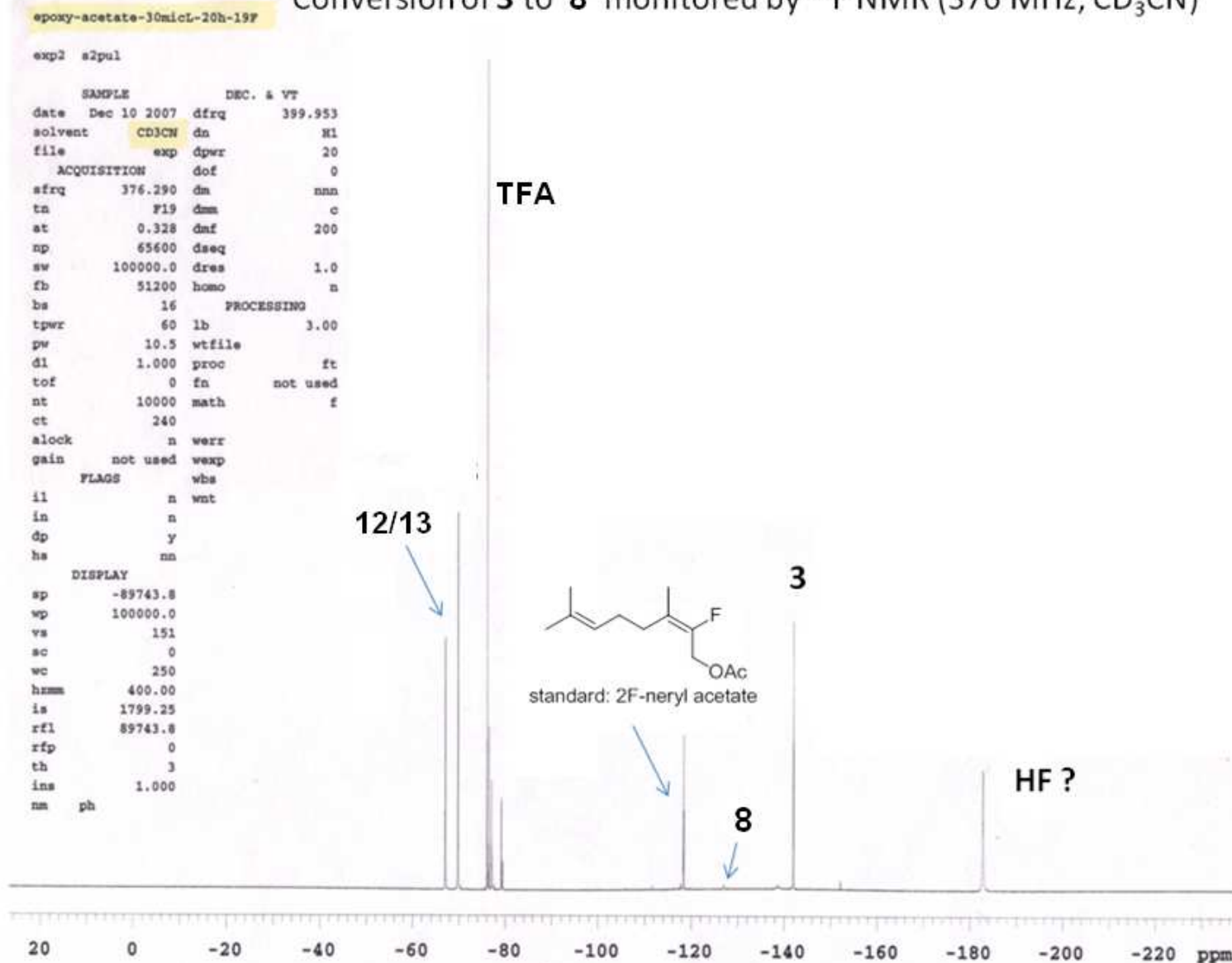
3

12/13

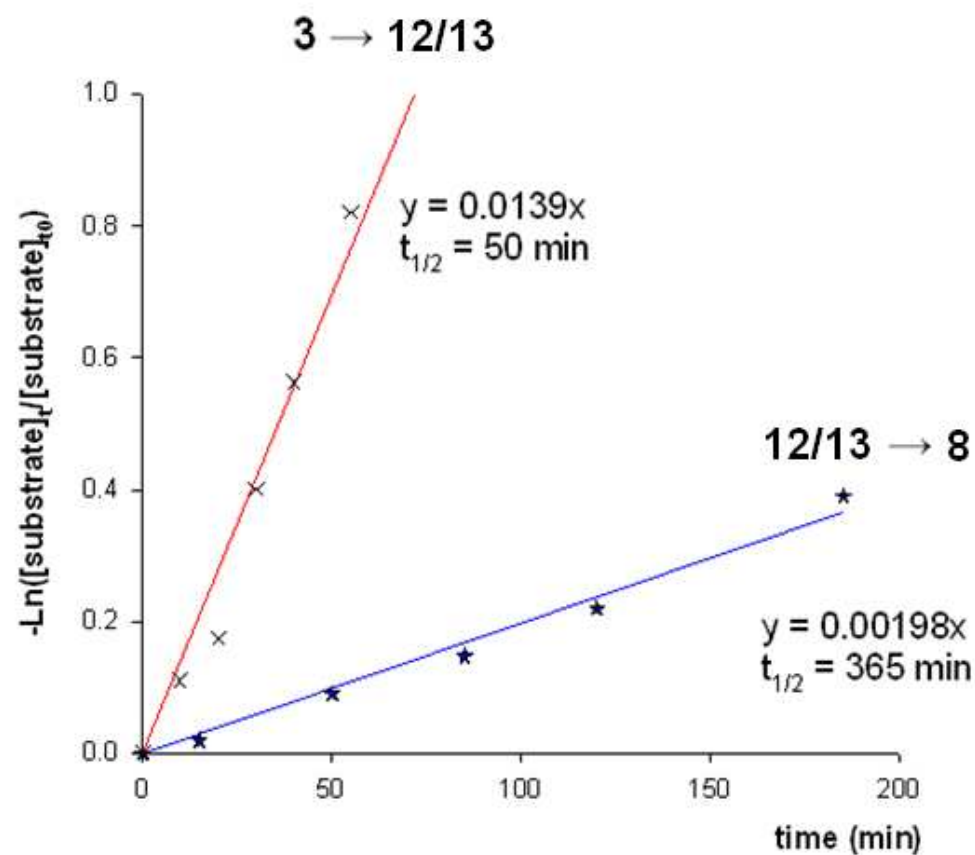
HF?



Conversion of **3** to **8** monitored by ^{19}F NMR (376 MHz, CD_3CN)



Pseudo first-order kinetic plots ($t_{1/2} - \ln(2)/k$) for the TFA-mediated conversion of acetate **3** to compounds **12/13** (RED) and the further conversion of the latter(s) to compound **8** (BLUE) by ^{19}F NMR integrations

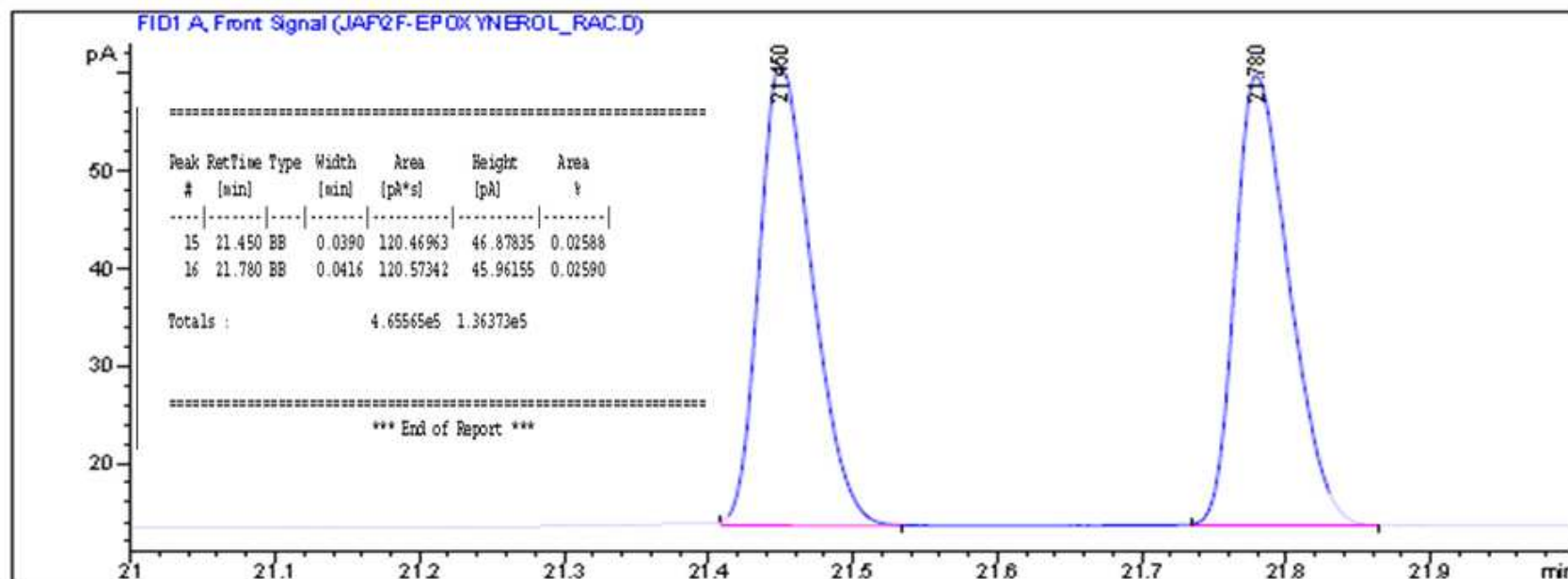
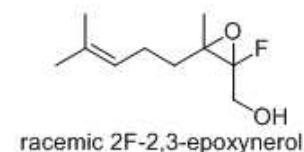


Data File C:\CHEM32\1\DATA\JAF\2F-EPOXYNEROL_RAC.D

=====

Acq. Operator	: JUAN	Location	: Vial 1
Acq. Instrument	: Instrument 1	Inj Volume	: Manually
Injection Date	: 2/6/2013 4:42:58 PM		
Acq. Method	: C:\CHEM32\1\METHODS\JUAN CHIRAL.M		
Last changed	: 2/6/2013 4:10:03 PM by JUAN		
Analysis Method	: C:\CHEM32\1\METHODS\JUAN CHIRAL.M		
Last changed	: 2/18/2013 1:39:47 PM by JUAN		
	(modified after loading)		

=====



Column: CHIRALDEX B-DM

Area Percent Report

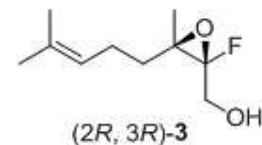
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

GC conditions
Injection port 220° C
Split 50:1
Program. 90° C hold 2 min then ramp at 5
5° C/min to 170° C hold 40 min

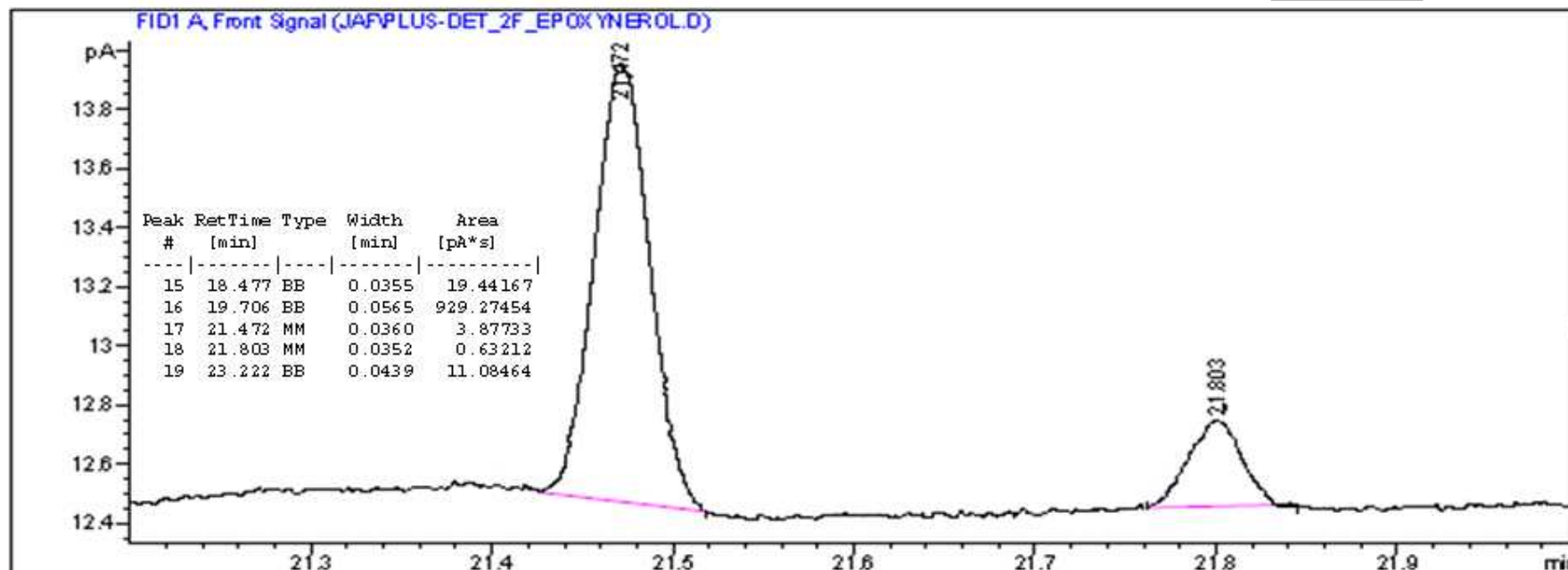
Data File C:\CHEM32\1\DATA\JAF\PLUS-DET_2F_EPOXYNEROL.D

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Acq. Operator   : JUAN
Acq. Instrument : Instrument 1
Injection Date  : 2/14/2013 10:21:32 AM
Location       : Vial 1
Inj Volume     : Manually

Acq. Method    : C:\CHEM32\1\METHODS\JUAN_CHIRAL.M
Last changed   : 2/14/2013 10:18:10 AM by JUAN
Analysis Method: C:\CHEM32\1\METHODS\TERPENE_CHIRAL.70.M
Last changed   : 7/8/2013 12:18:51 PM by JUAN
                (modified after loading)
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68 % ee



Area Percent Report

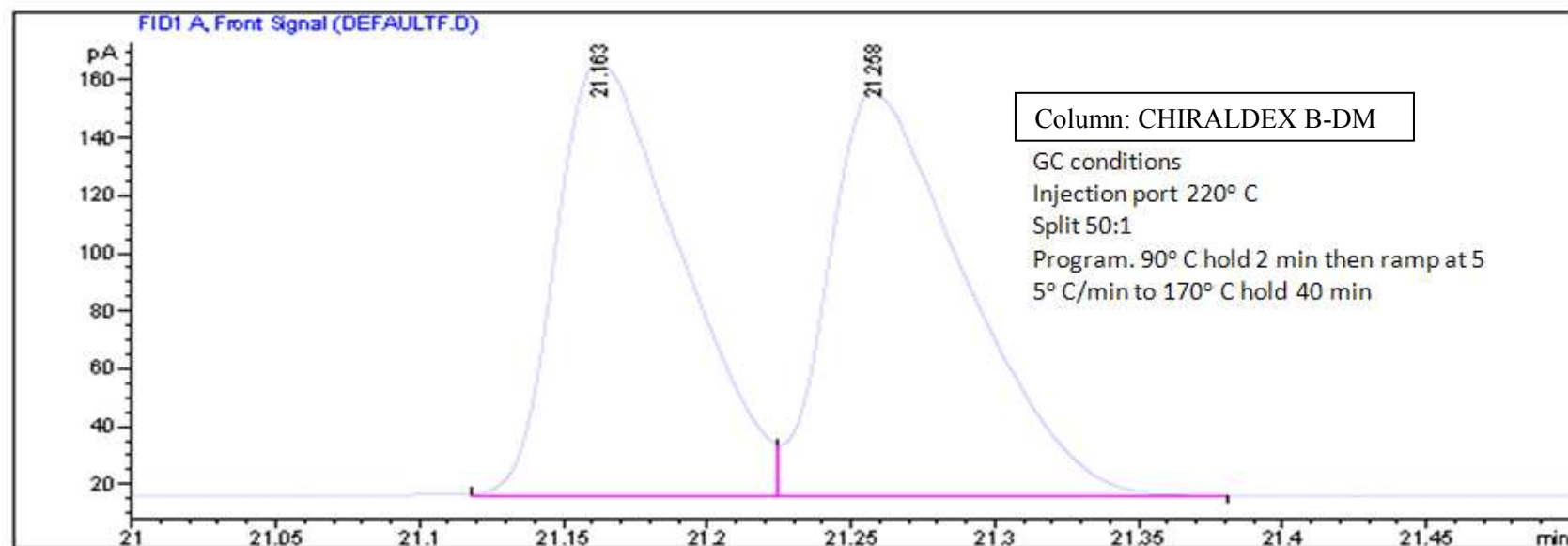
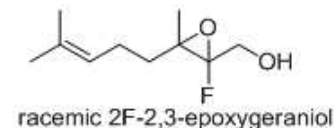
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=====
Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
=====
```

Column: CHIRALDEX B-DM

GC conditions
Injection port 220° C
Split 50:1
Program. 90° C hold 2 min then ramp at 5
5° C/min to 170° C hold 40 min

Data File C:\CHEM32\1\DATA\DEFAULTF.D

```
=====
Acq. Operator   :
Acq. Instrument : Instrument 1          Location : Vial 1
Injection Date  : 2/4/2013 11:25:52 AM
                                           Inj Volume : Manually
Acq. Method     : C:\CHEM32\1\METHODS\JUAN_CHIRAL.M
Last changed    : 2/4/2013 11:25:49 AM
                  (modified after loading)
Analysis Method : C:\CHEM32\1\METHODS\TERPENE_CHIRAL.70.M
Last changed    : 2/18/2013 1:34:40 PM by JUAN
                  (modified after loading)
=====
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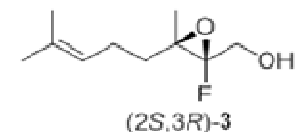


Area Percent Report							
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %	
1	2.916	BV	0.0241	2099.92480	1283.26697	2.30870	
2	3.037	VB	0.0246	11.31900	7.11024	0.01244	
3	3.157	BV	0.0222	42.60529	28.88835	0.04684	
4	3.241	VV	0.0240	124.69621	83.23972	0.13709	
5	3.269	VB S	0.1220	8.77457e4	1.19829e4	96.46947	
6	4.488	BB	0.0451	12.98585	4.57206	0.01428	
7	21.163	BV	0.0455	453.54565	148.93942	0.49864	
8	21.258	VB	0.0500	466.18405	139.47443	0.51253	
Totals :				9.09570e4	1.36784e4		

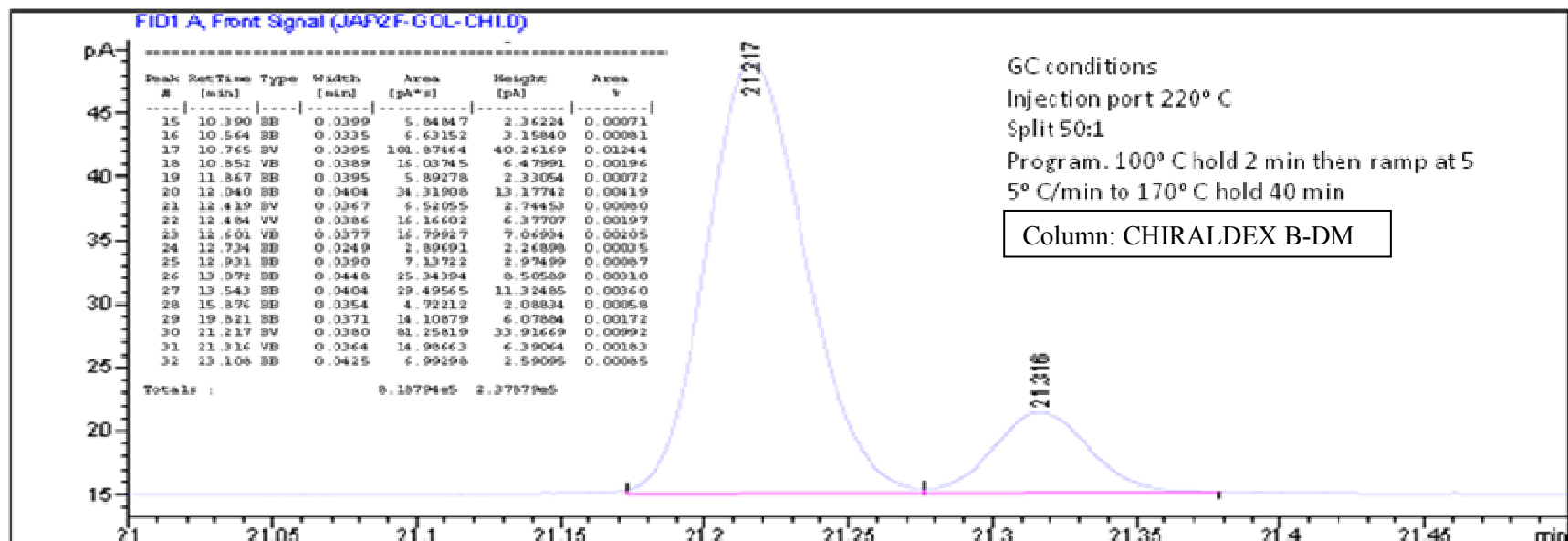
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Data File C:\CHEM32\1\DATA\JAF\2F-GOL-CHI.D

```
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Acq. Operator   : JUAN
Acq. Instrument : Instrument 1
Injection Date  : 2/4/2013 12:26:22 PM
Location       : Vial 1
Ing Volume     : Manually
Acq. Method    : C:\CHEM32\1\METHODS\JUAN_CHIRAL.M
Last changed   : 2/4/2013 12:18:42 PM
Analysis Method: C:\CHEM32\1\METHODS\TERPENE_CHIRAL.70.M
Last changed   : 2/18/2013 12:21:14 PM by JUAN
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=====
```



70 % ee

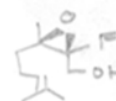
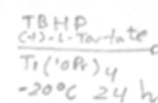
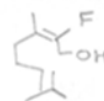


Area Percent Report

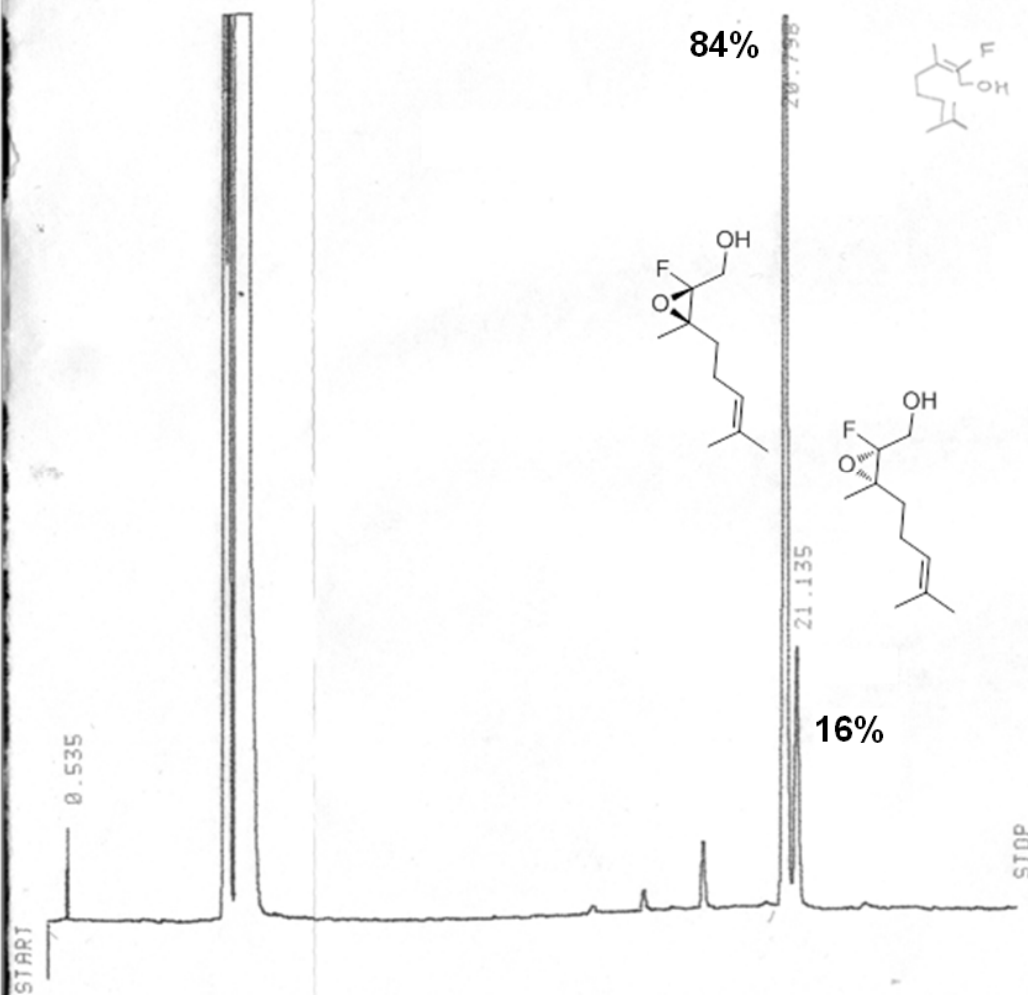
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Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs
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GC trace of epoxide **2** using a
CHIRALDEX B-DM column

T=90°C / 2 min
ramp 50°C to 160
by port 220°C



ee 68%



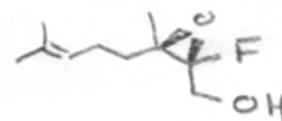
RUN# 153 OCT 7, 1901 23:51:03

AREA%	RT	AREA	TYPE	WIDTH	AREA%
.535	295	.00376	BB	.009	
5.017	194154	2.47543	BU	.062	
5.142	45788	.58379	UH	.068	
5.320	7551258	96.27715	SHB	.155	
20.798	42631	.54354	BU	.135	
21.135	8124	.11633	UB	.133	

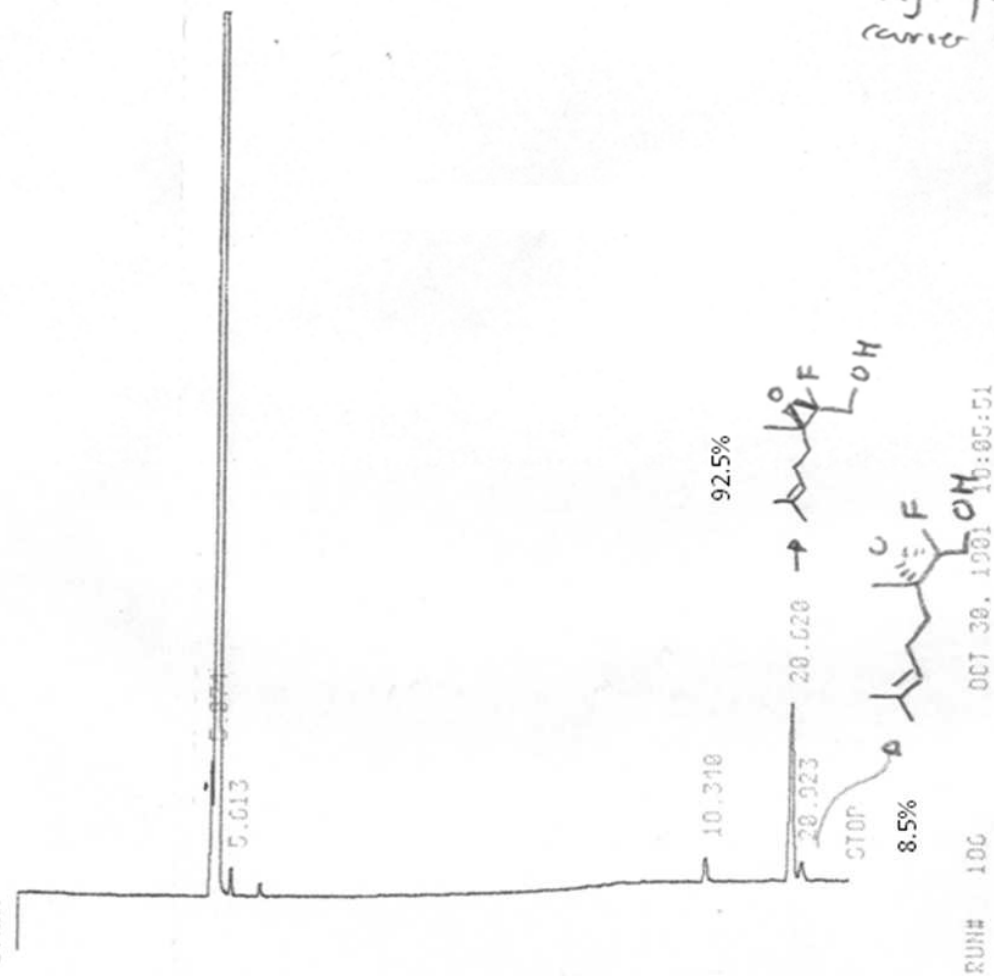
TOTAL AREA=7843248
MUL FACTOR=1.0000E+00

GC trace of epoxide 2 using a
CHIRALDEX B-DM column

CT 90°C / 2 min
ramp 5°C/min to 160°C
by part 220°C
carrier He.



3 RUN # 100 OCT 30, 1991 10:05:51
START



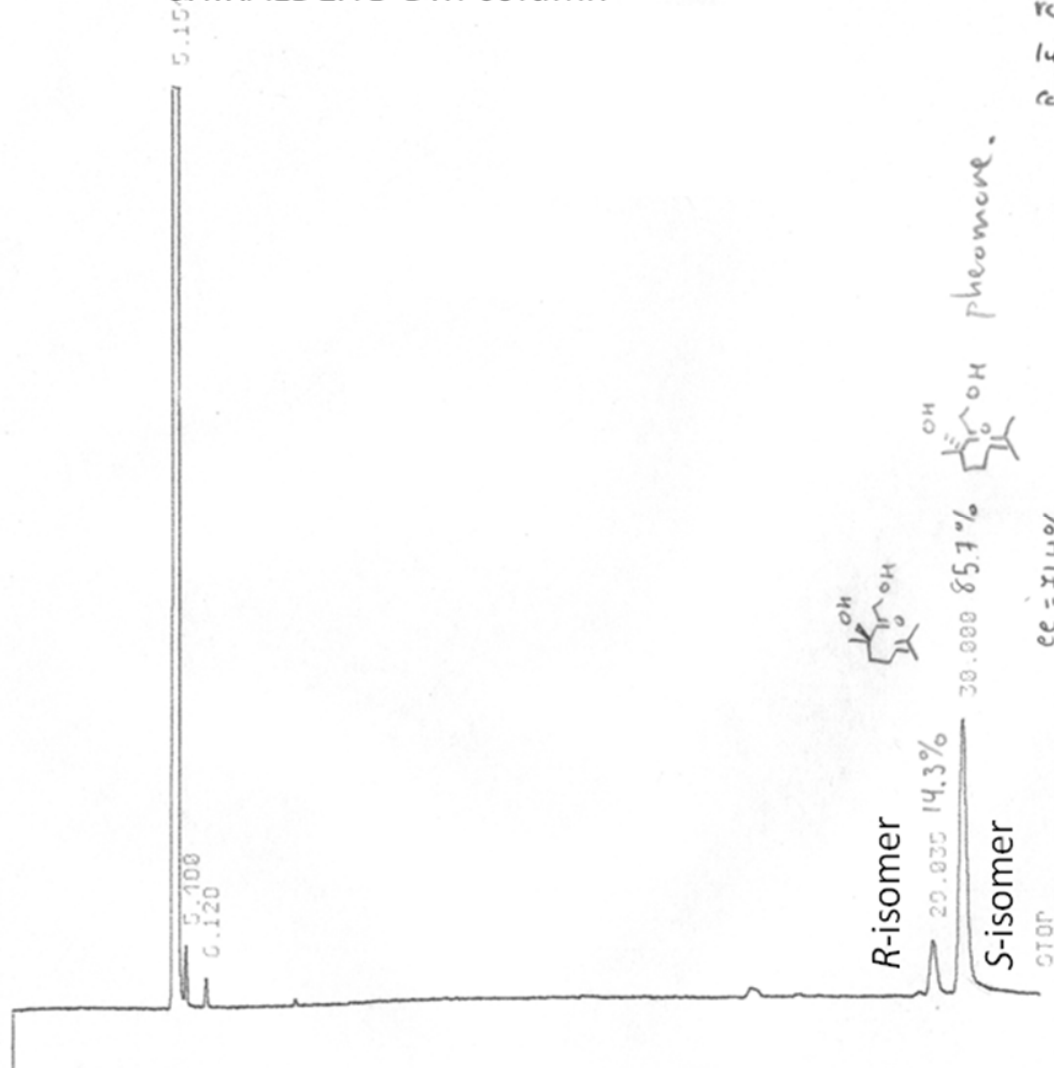
RT	AREA	TYPE	WIDTH	AREA
5.074	3017	PV	.055	.10057
5.203	950159	UD	.072	97.90100
5.613	1143	DU	.073	.11609
10.310	1570	FF	.115	.16137
20.620	11741	DU	.121	1.20060
20.923	1027	UU	.125	.13570

TOTAL AREA= 977065
MUL FACTOR=1.0000E+00

GC trace of **1** using a
CHIRALDEX B-DM column

T=100°C / 2 min
ramp 50°C/min to 150°C
by port 220°C
carrier He

* STOR # 100 OCT 30, 1981 20:07:57

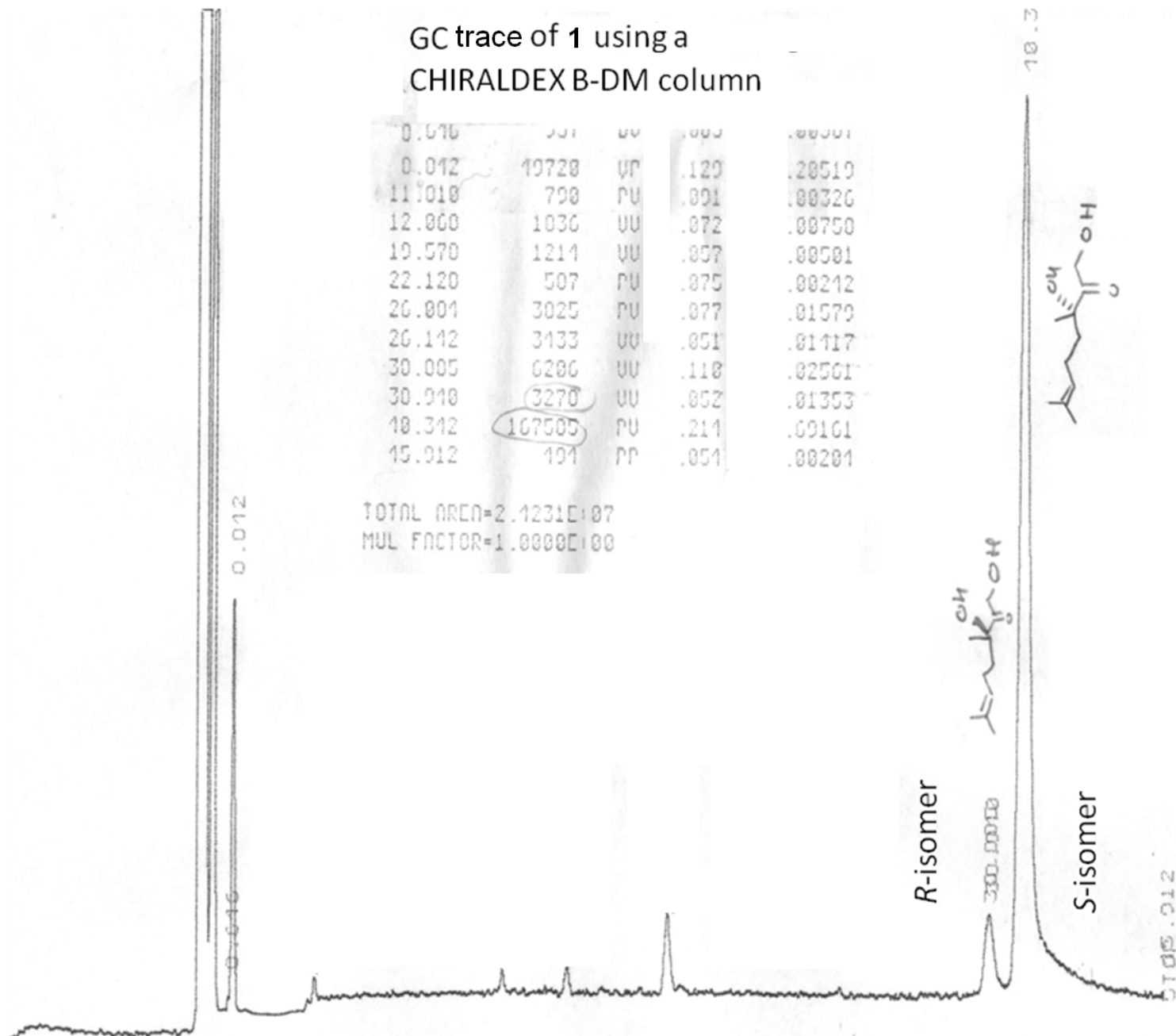


RUN# 100 OCT 30, 1981 20:07:57

AREA	RT	AREA	TYPE	WIDTH	AREA
5.154	3094609	PD	.077	90.50406	
5.400	2144	DF	.071	.00024	
6.120	1221	FF	.070	.03007	
20.035	6467	PU	.234	.20505	
30.000	37130	DU	.205	1.10200	

TOTAL AREA=3141037
MUL FACTOR=1.00000E+00

GC trace of **1** using a
CHIRALDEX B-DM column

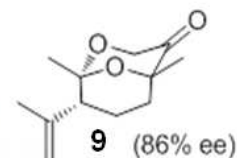
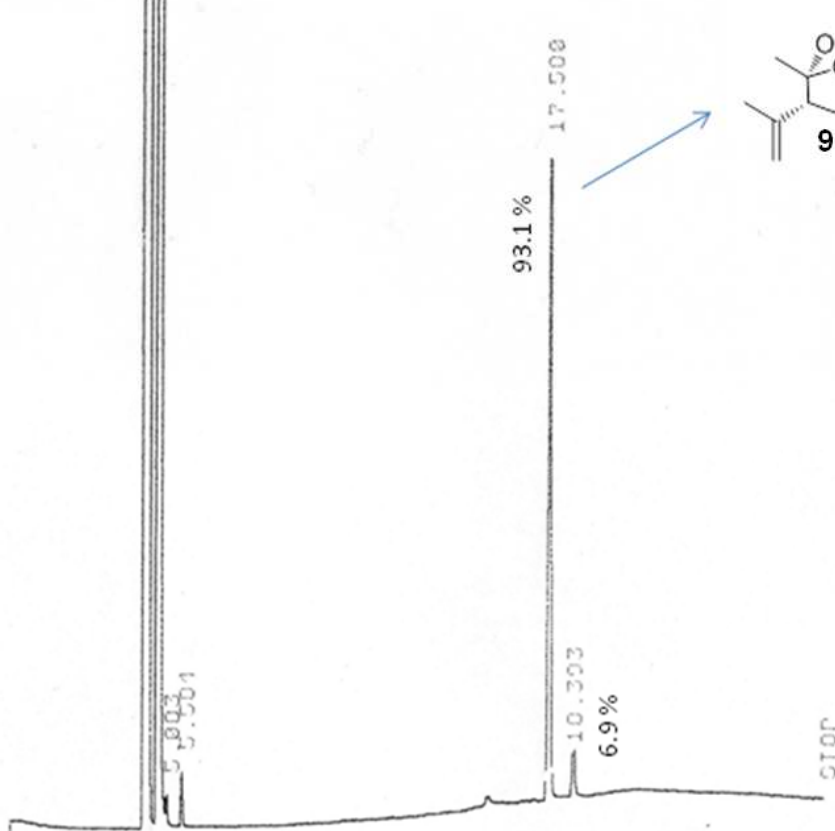


192 OCT 31, 1981 15:15:37

RT	Area	Type	Width	Area%
12	23707952	UU	.130	.97.04147
25	203142	UU	.133	1.16051

GC trace of **9** (from **2**) using a
CHIRALDEX B-DM column

* RUN # 200 NOV 7, 1991 21:32:53
START



RUN#	200	NOV	7. 1981	21:32:53	
AREA#	RT	AREA	TYPE	WIDTH	AREA#
1.330	1204730	PU	.810	57.01554	
1.450	1024652	UD	.857	13.08294	
1.710	2141147	DV	.870	20.12510	
5.003	2014	UP	.871	.02071	
5.504	3104	PV	.861	.01200	
17.500	00200	PD	.800	.00011	
10.393	0592	DV	.102	.00751	

TOTAL AREA=7532576
MUL FACTOR=1.0000E+00