

## SUPPORTING INFORMATION

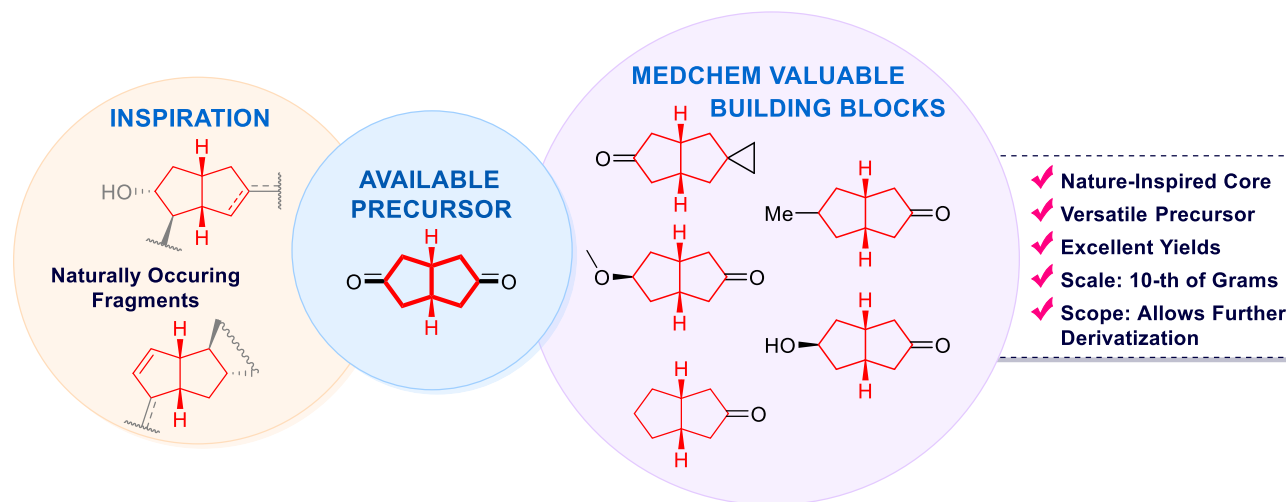
### Nature-Inspired Tetrahydropentalene Building Blocks: Scalable Synthesis for Medicinal Chemistry

Oleh K. Smyrnov,<sup>1,2</sup> Olexandr Ye. Pashenko,<sup>1,2,3</sup>

<sup>a</sup>*Enamine Ltd, 78 Winston Churchill str., 02094 Kyiv, Ukraine*

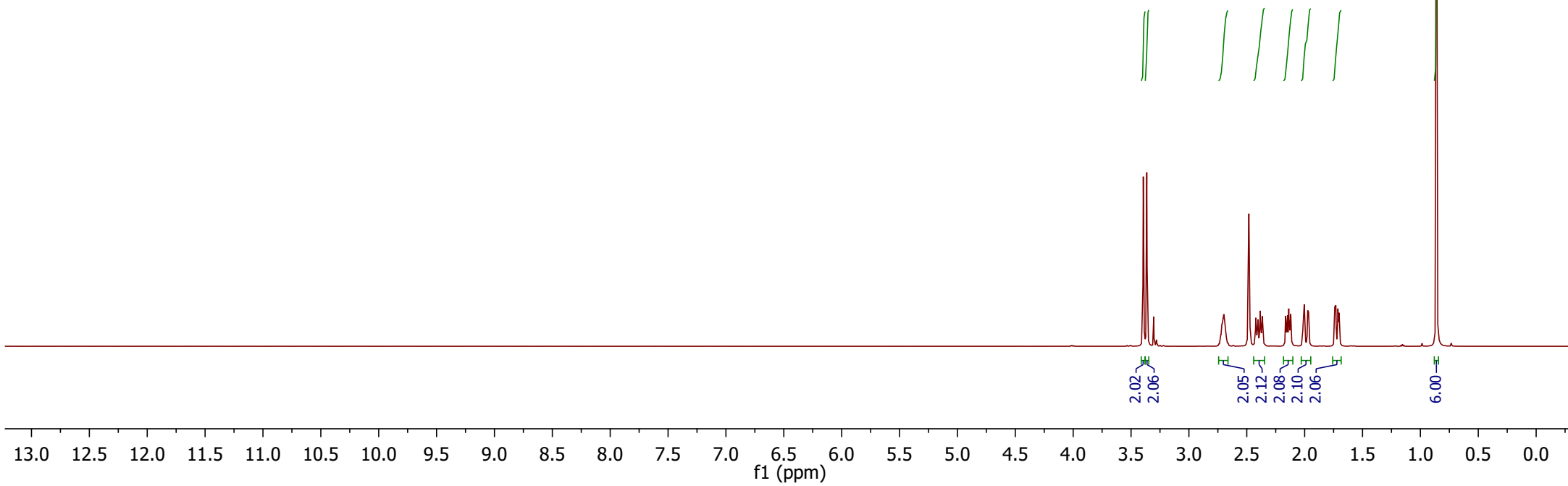
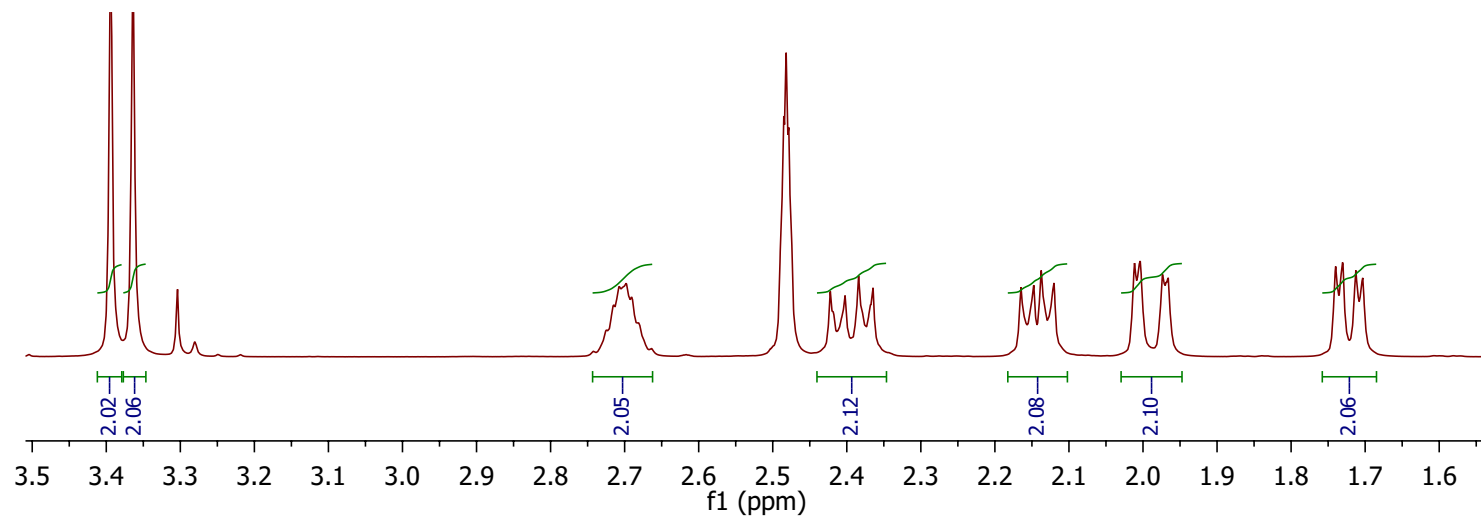
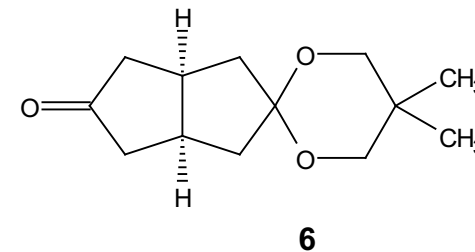
<sup>b</sup>*Taras Shevchenko National University of Kyiv, 60 Volodymyrska str., 01601 Kyiv, Ukraine*

<sup>c</sup>*Institute of Organic Chemistry, National Academy of Sciences of Ukraine, 5 Akademik Kuhar str., 02660 Kyiv, Ukraine*

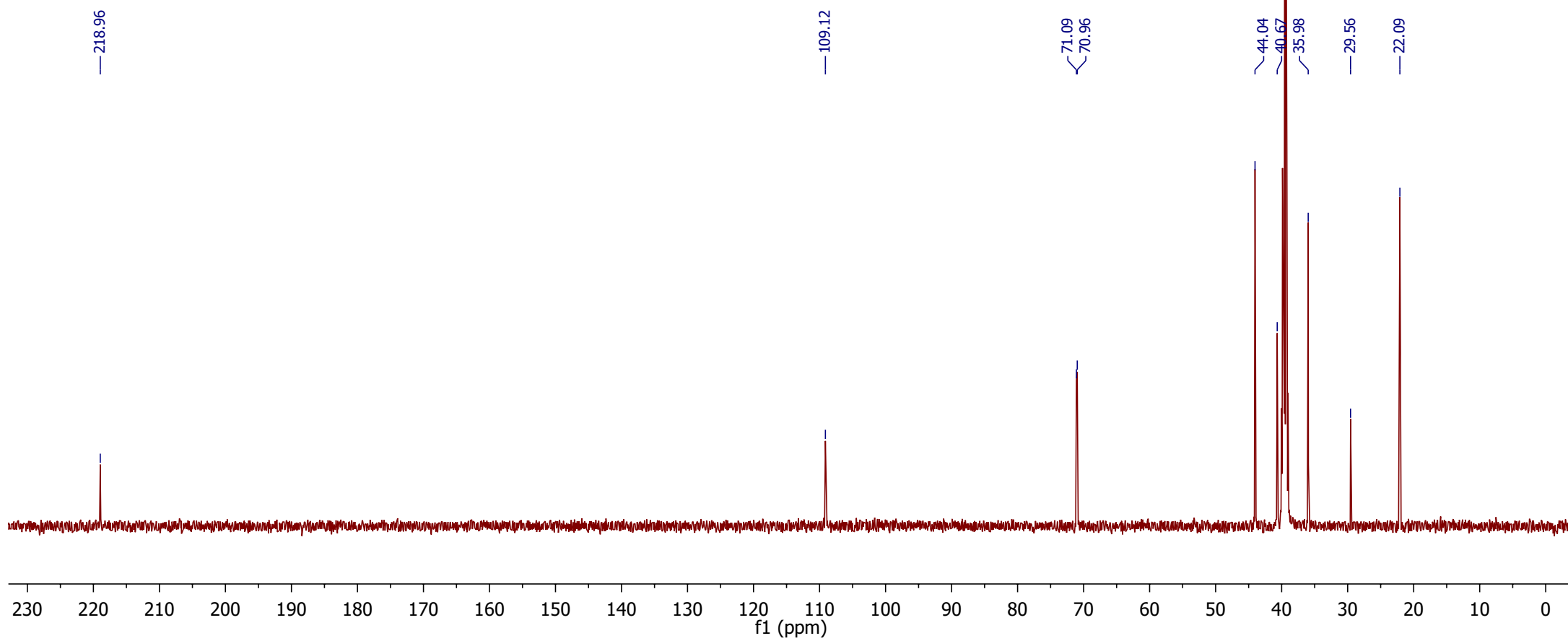
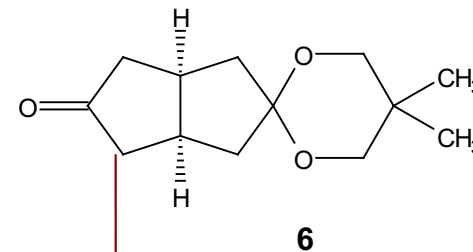


<https://doi.org/10.24959/ophcj.23.299612>

$^1\text{H}$  NMR (DMSO- $d_6$ , 500 MHz)  $\delta$  0.86 (6H, s), 1.68 – 1.76 (2H, m), 1.95 – 2.03 (2H, m), 2.10 – 2.18 (2H, m), 2.33 – 2.44 (2H, m), 2.70 (2H, td,  $J=8.7, 4.7$  Hz), 3.36 (2H, s), 3.39 (2H, s)



$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 126 MHz)  $\delta$  22.1, 29.6, 36.0, 40.7, 44.0, 71.0, 71.1, 109.1, 219.0.

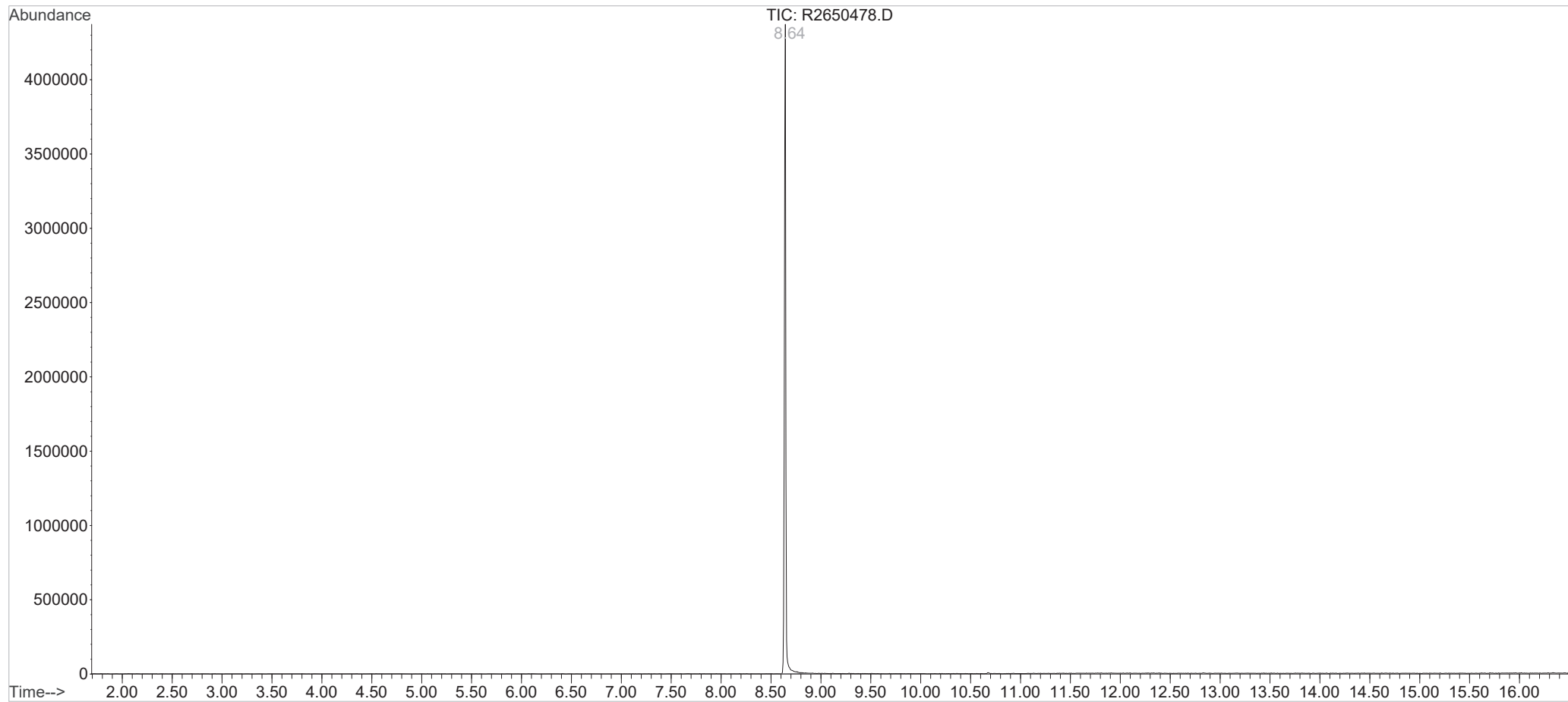
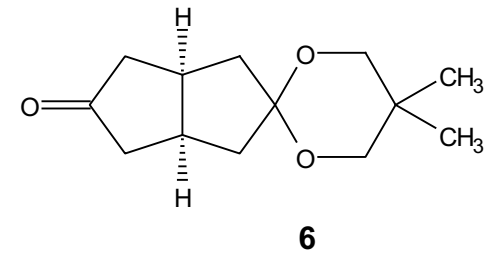


Library Search Report

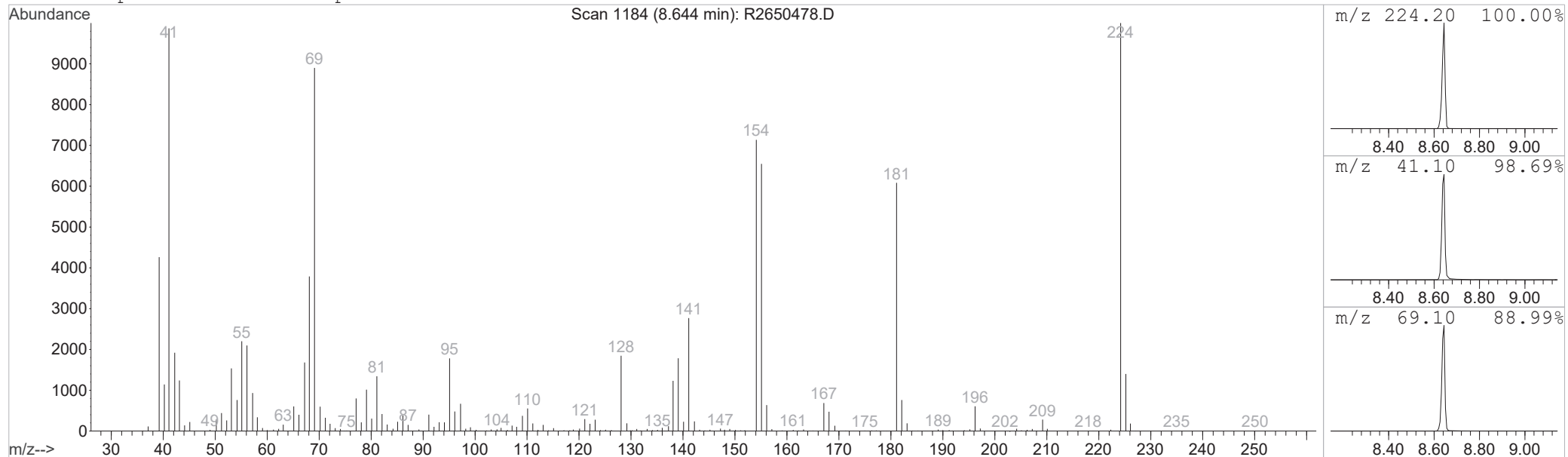
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MS Integration Params: autoint1.e  
Method  
Title :

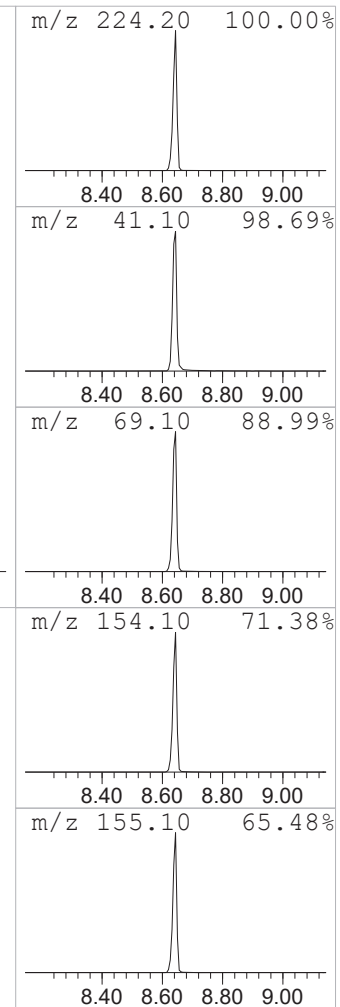


Unknown Spectrum based on Apex

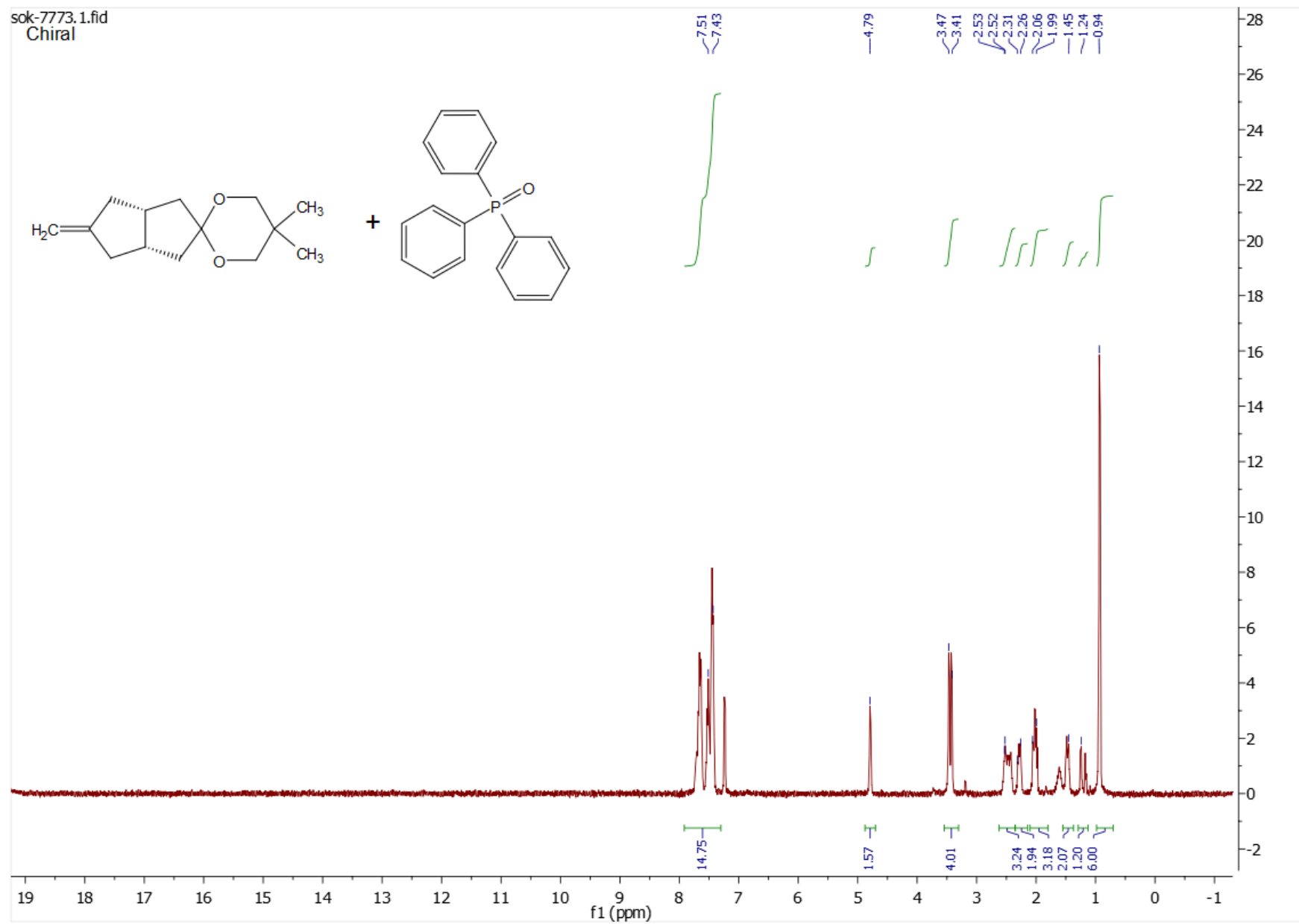


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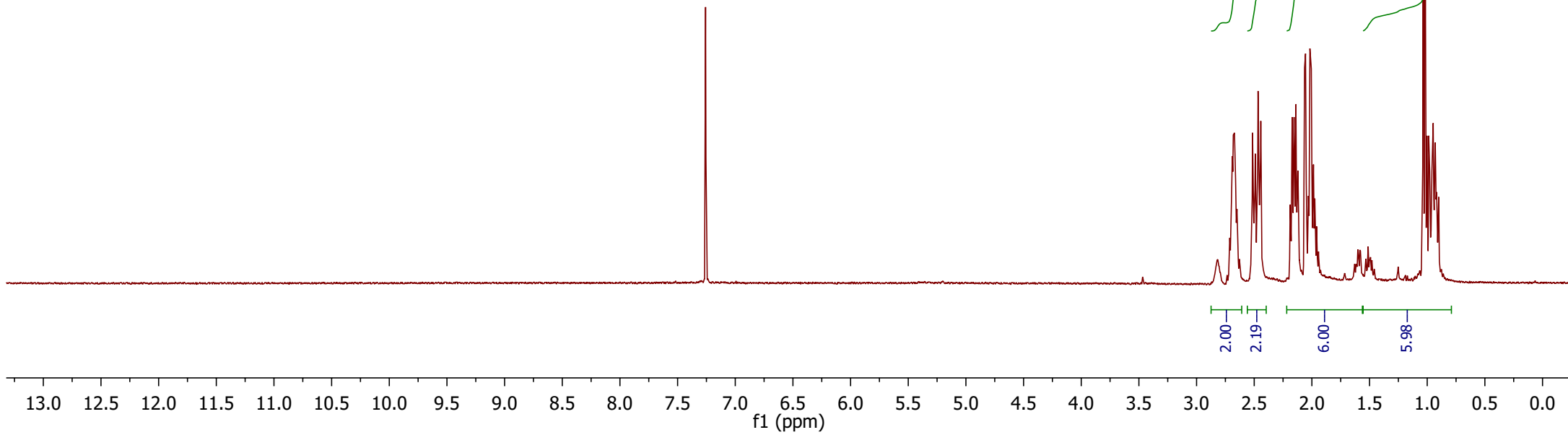
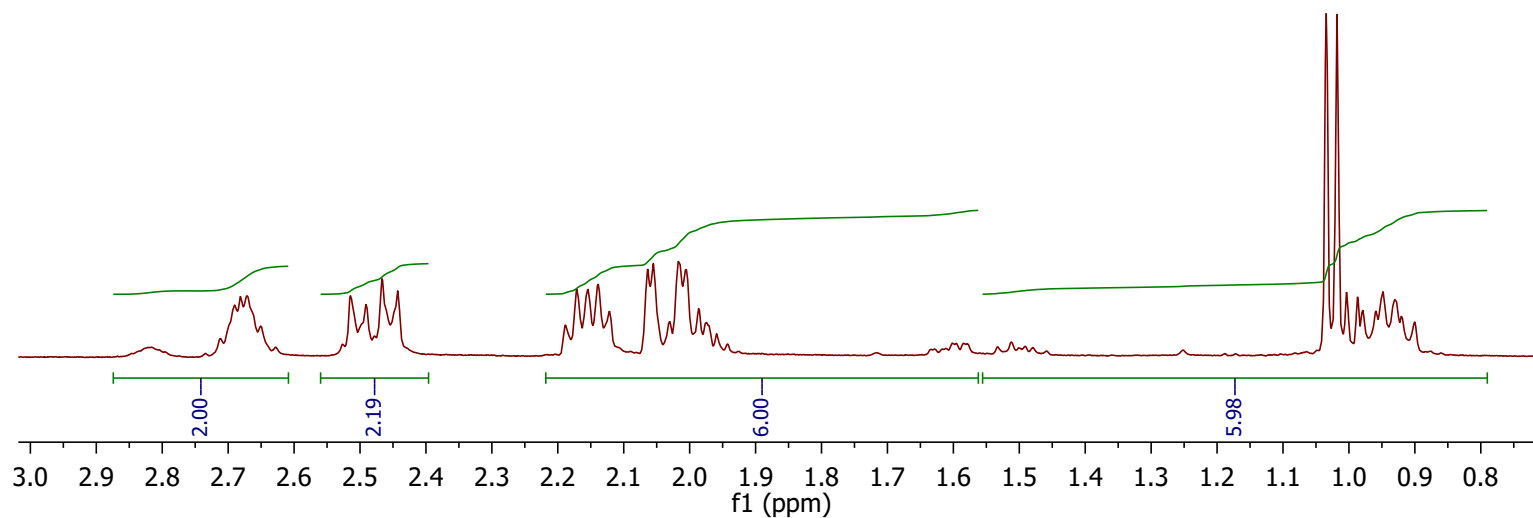
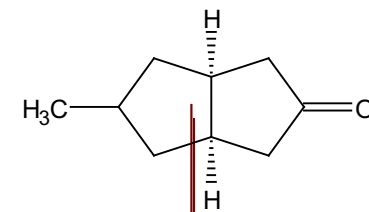
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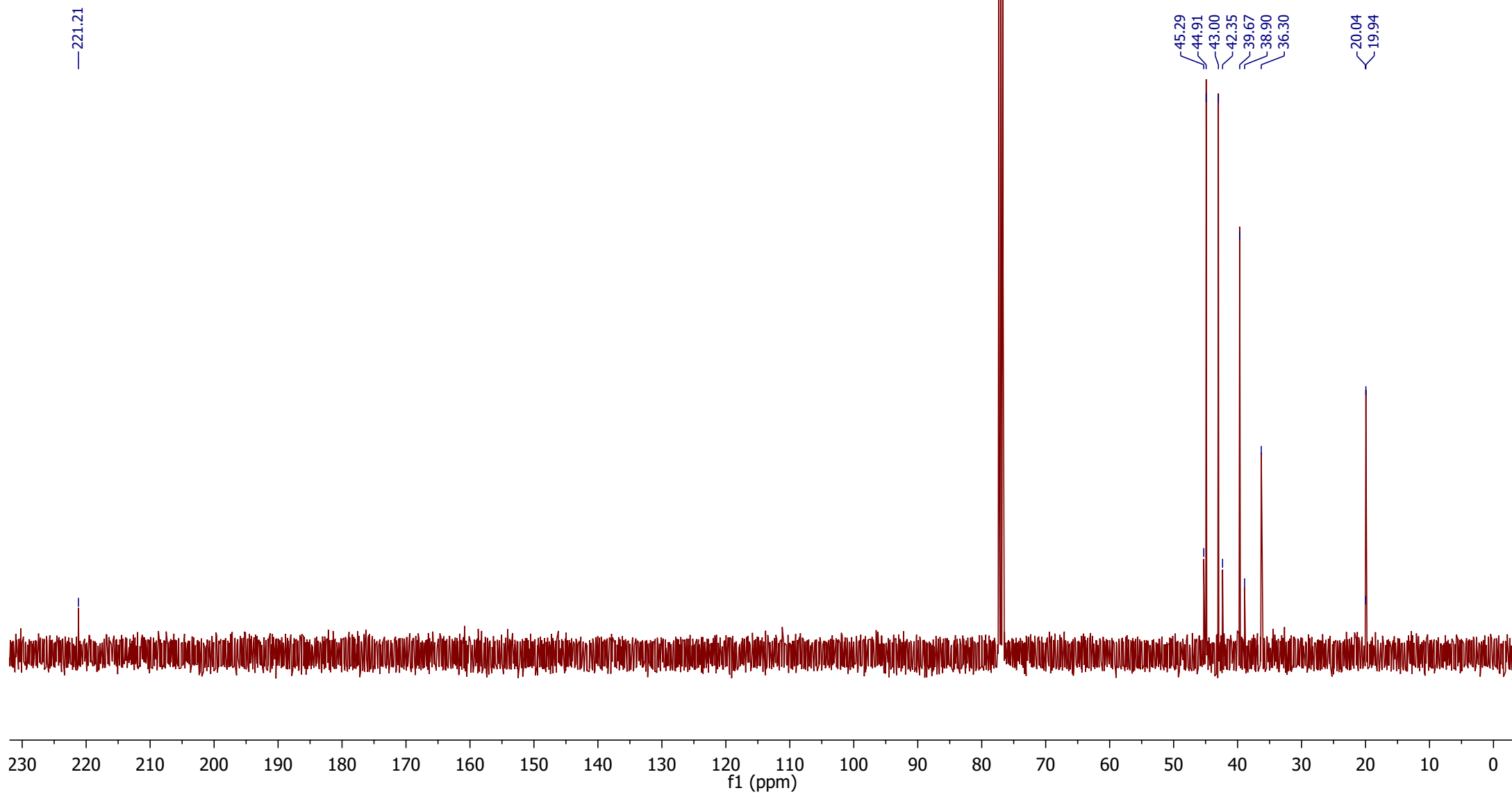
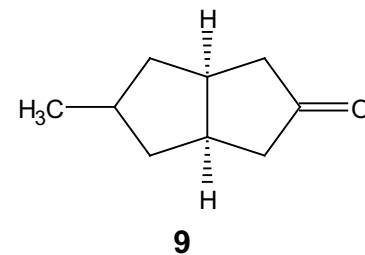
# <sup>1</sup>H NMR spectra of impure 7



$^1\text{H}$  NMR (Chloroform-*d*, 400 MHz)  $\delta$  0.79 – 1.56 (6H, m), 1.56 – 2.22 (6H, m), 2.40 – 2.56 (2H, m), 2.61 – 2.87 (2H, m)



$^{13}\text{C}$  NMR ( $\text{cdCl}_3$ , 101 MHz)  $\delta$  19.9, 20.0, 36.3, 38.9, 39.7, 42.4, 43.0, 44.9, 45.3, 221.2.



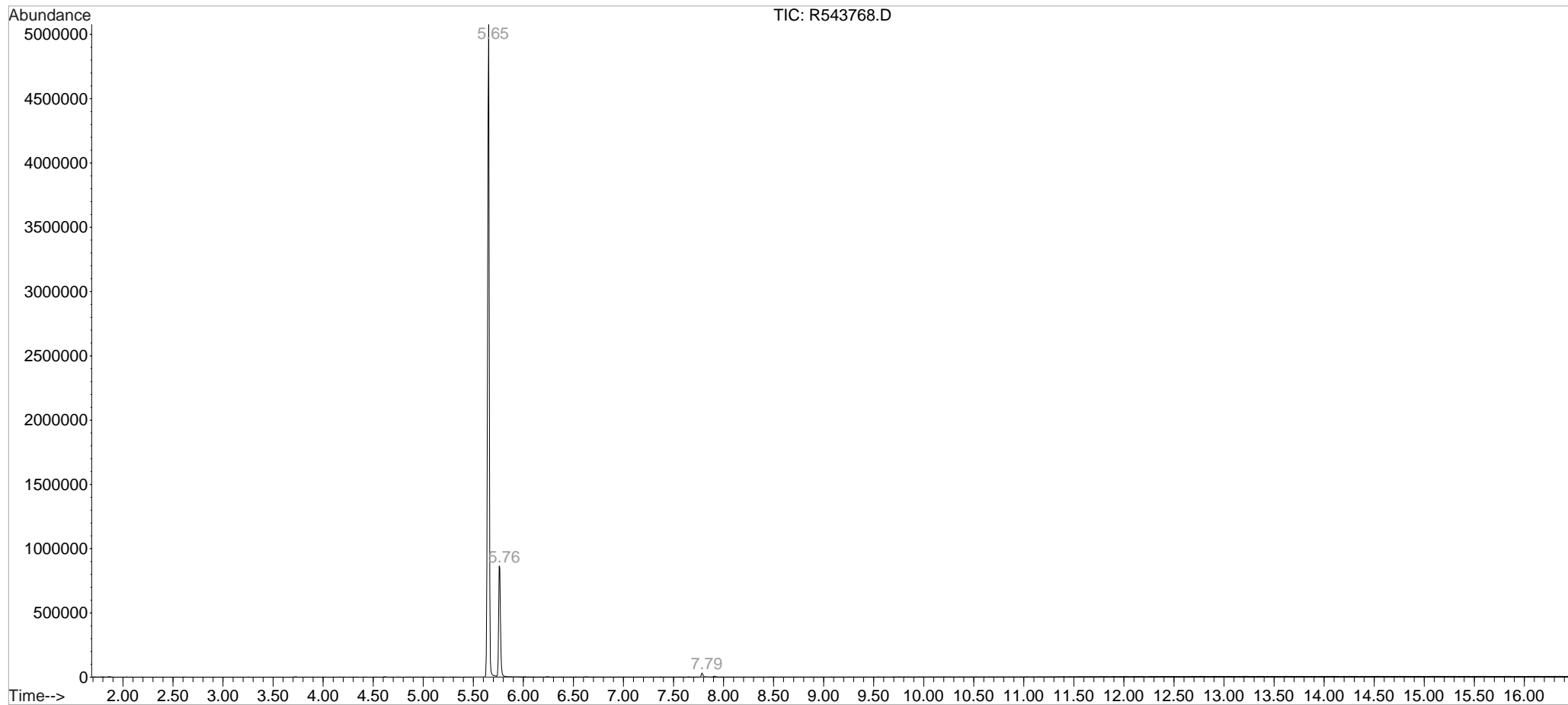
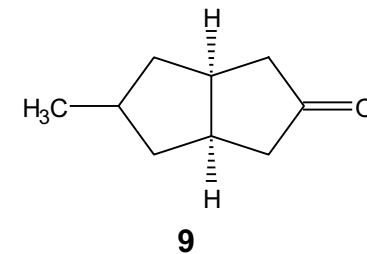


Library Search Report

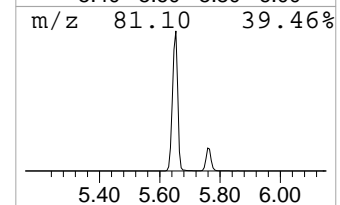
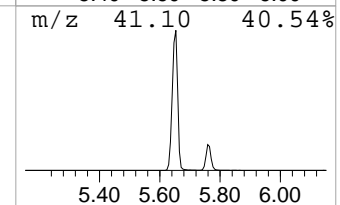
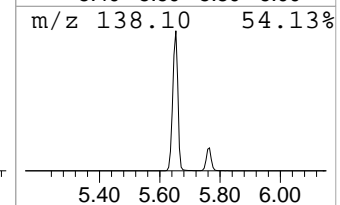
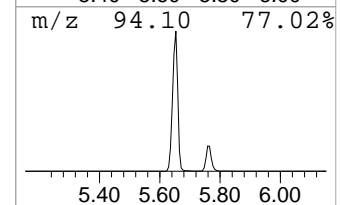
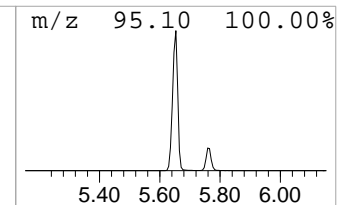
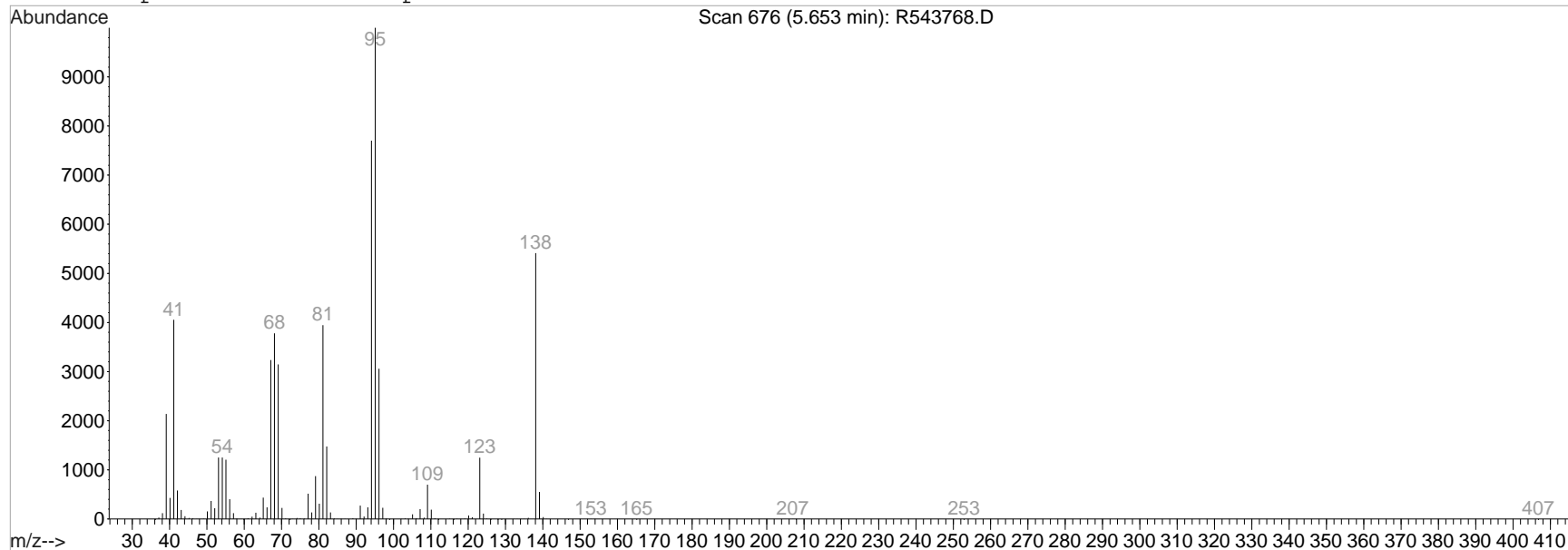
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Sample  
Misc : CH3OH

Vial: 6  
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Inst : Instrumen  
Multiplr: 1.00  
Sample Amount: 0.00

MS Integration Params: autoint1.e  
Method  
Title :



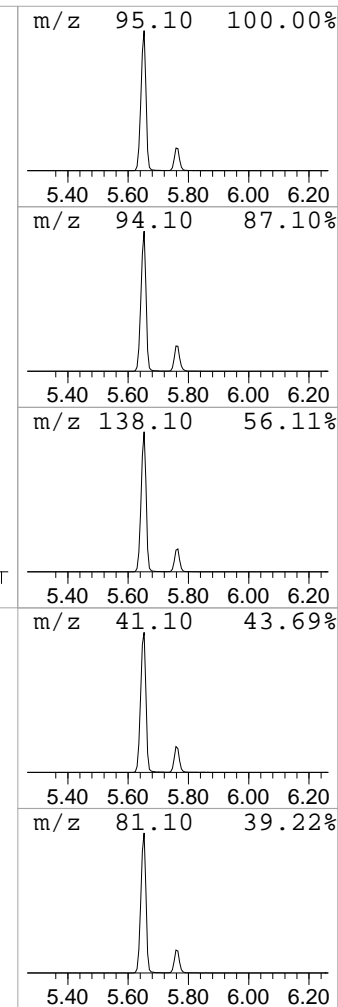
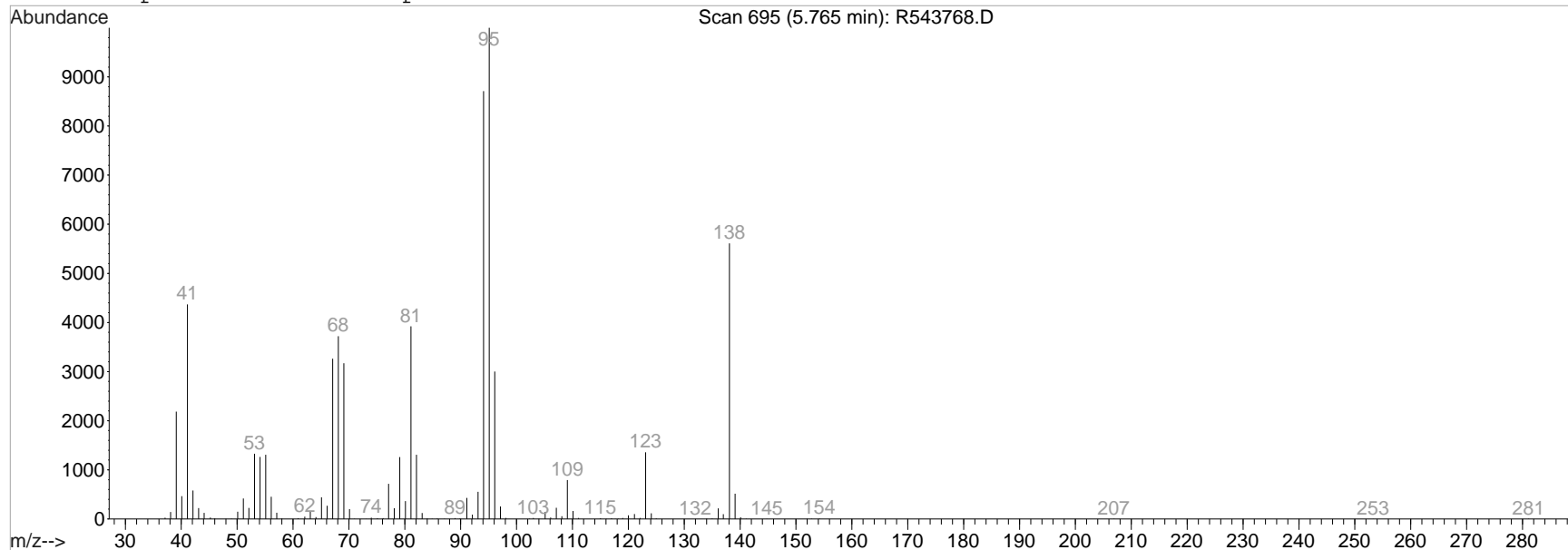
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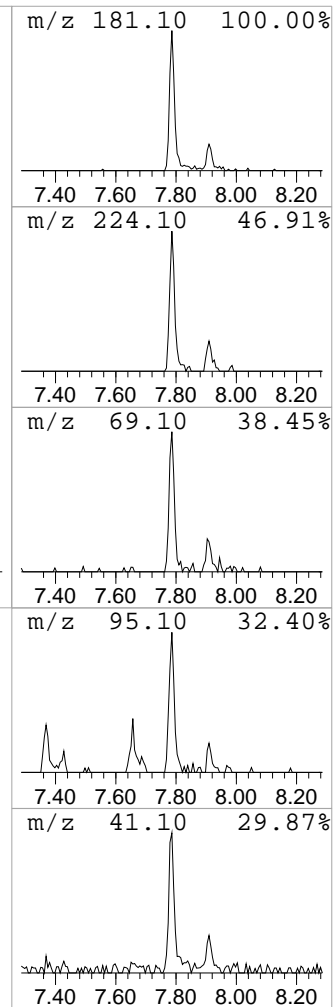
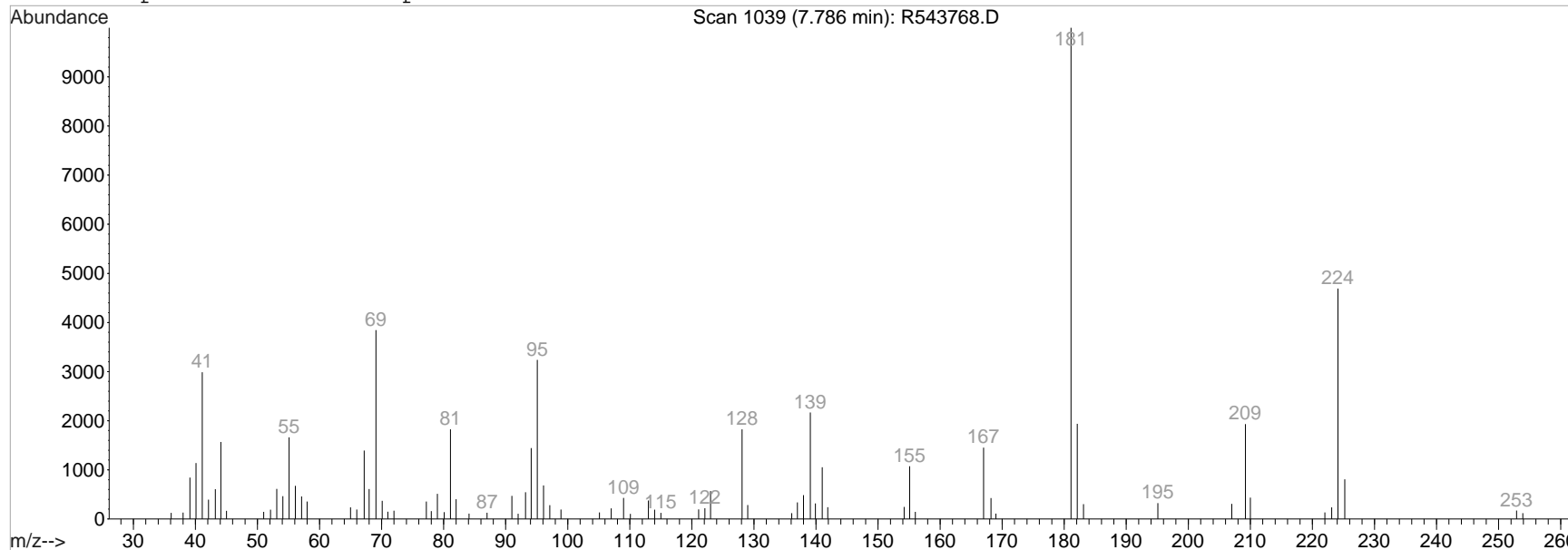
Unknown Spectrum based on Apex



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 Cmp# Ref# CAS# Qual

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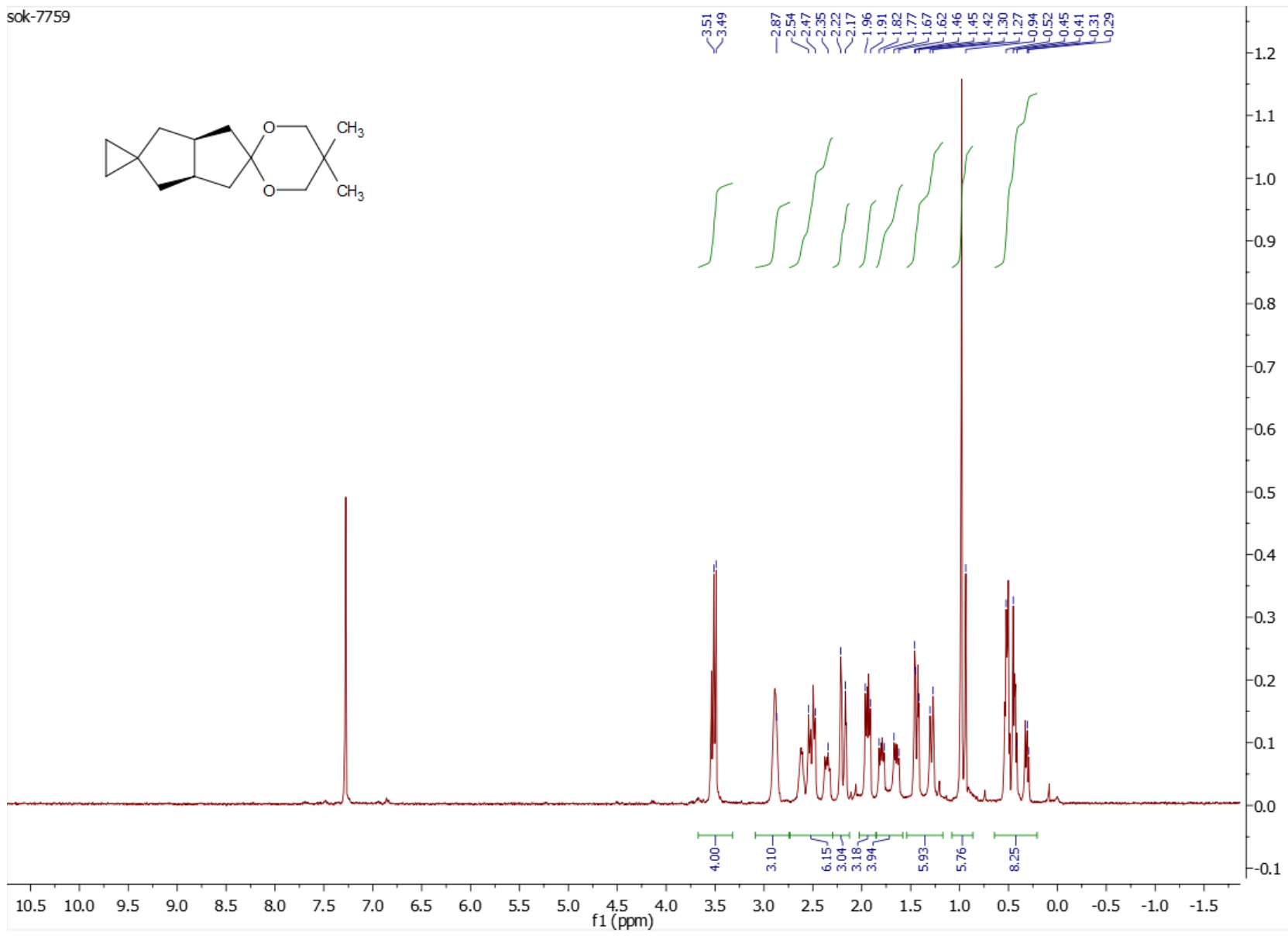


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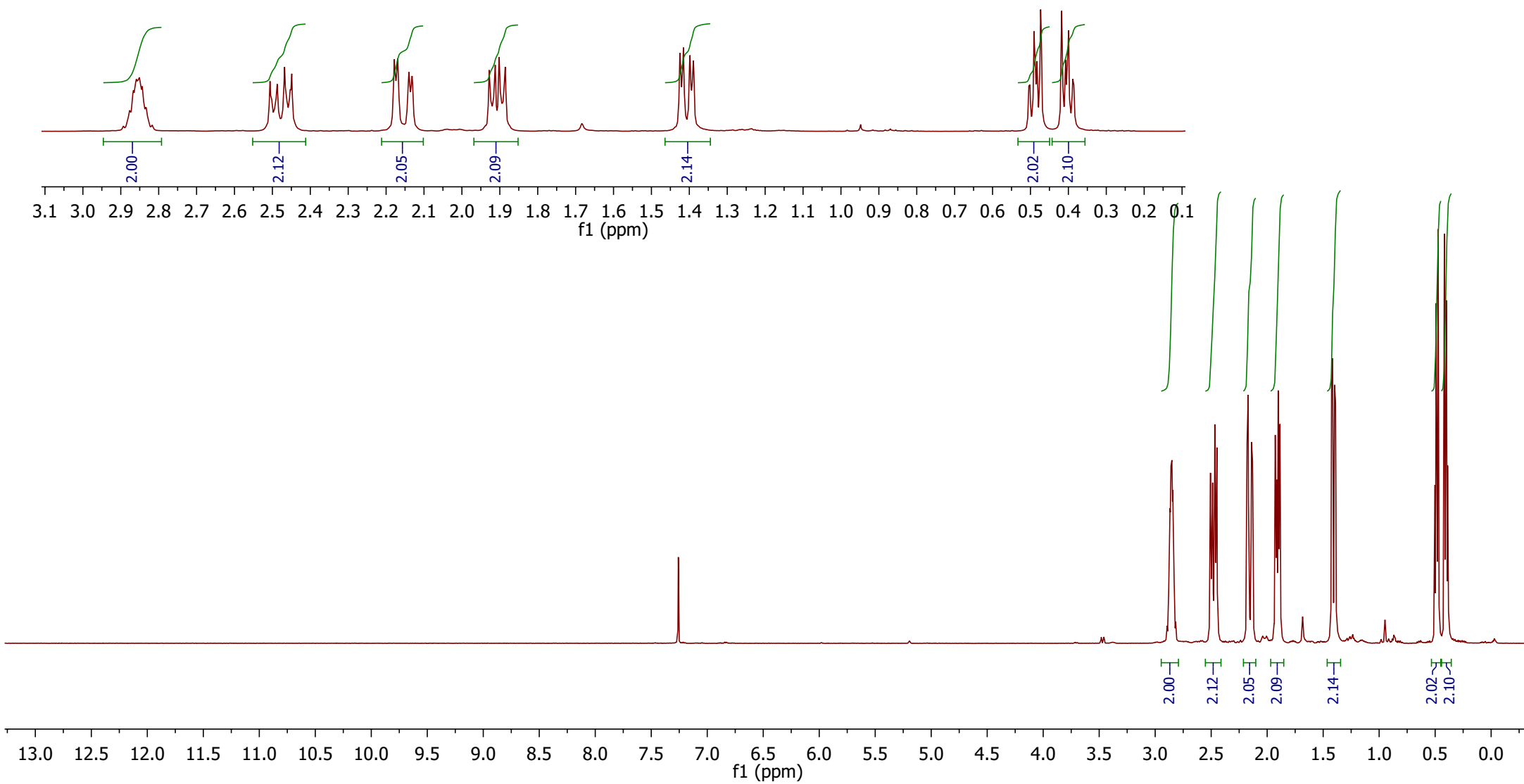
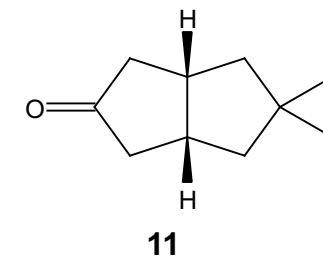
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Ref#	CAS#	Qual
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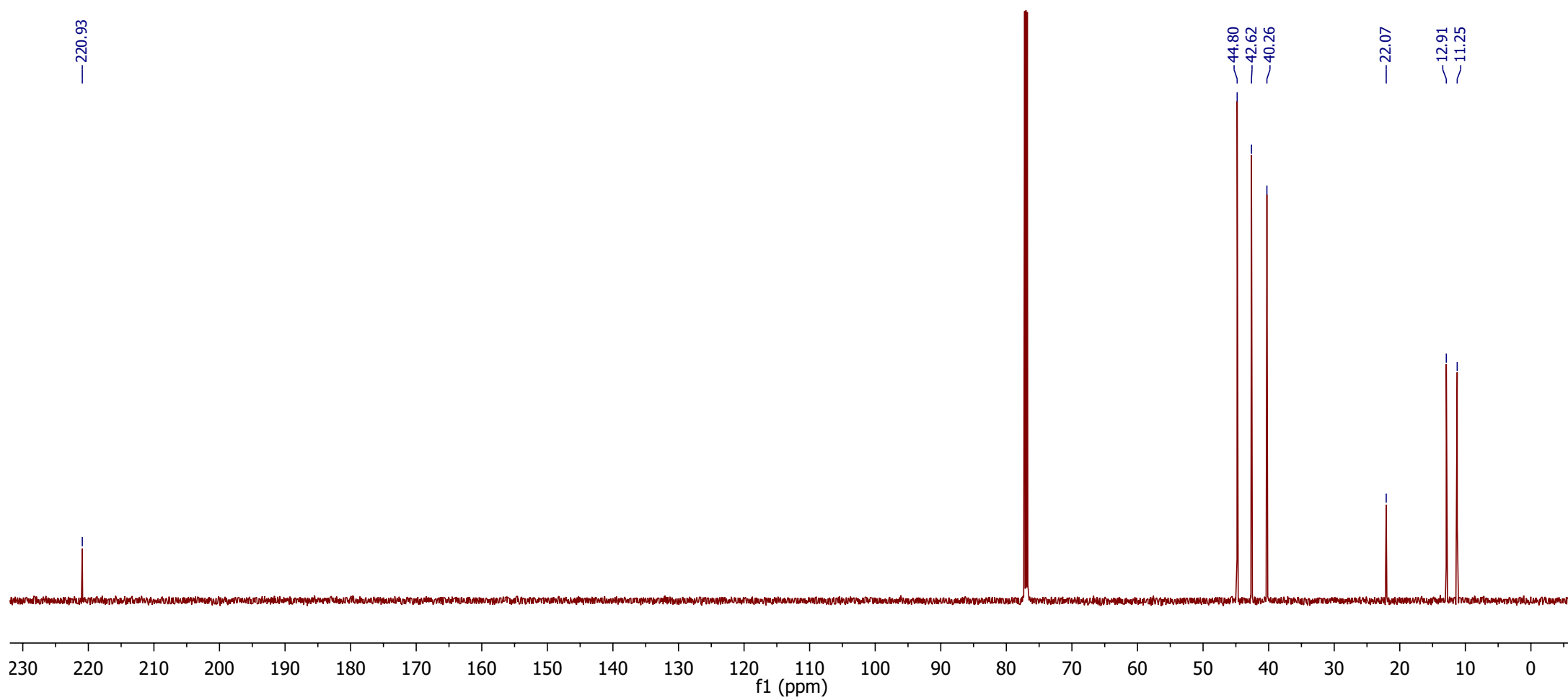
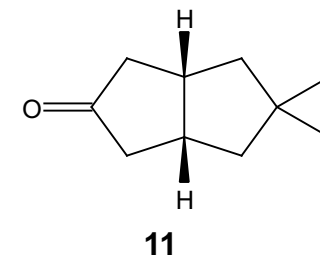
# <sup>1</sup>H NMR spectra of impure 10



$^1\text{H}$  NMR (Chloroform-*d*, 500 MHz)  $\delta$  0.36 – 0.44 (2H, m), 0.45 – 0.53 (2H, m), 1.41 (2H, dd,  $J=13.1$ , 4.4 Hz), 1.91 (2H, dd,  $J=13.1$ , 7.8 Hz), 2.10 – 2.21 (2H, m), 2.48 (2H, ddd,  $J=19.2$ , 7.3, 2.2 Hz), 2.86 (2H, tt,  $J=8.7$ , 4.7 Hz)



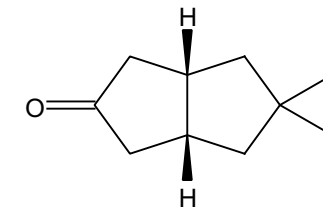
$^{13}\text{C}$  NMR ( $\text{cdCl}_3$ , 151 MHz)  $\delta$  11.2, 12.9, 22.1, 40.3, 42.6, 44.8, 220.9.



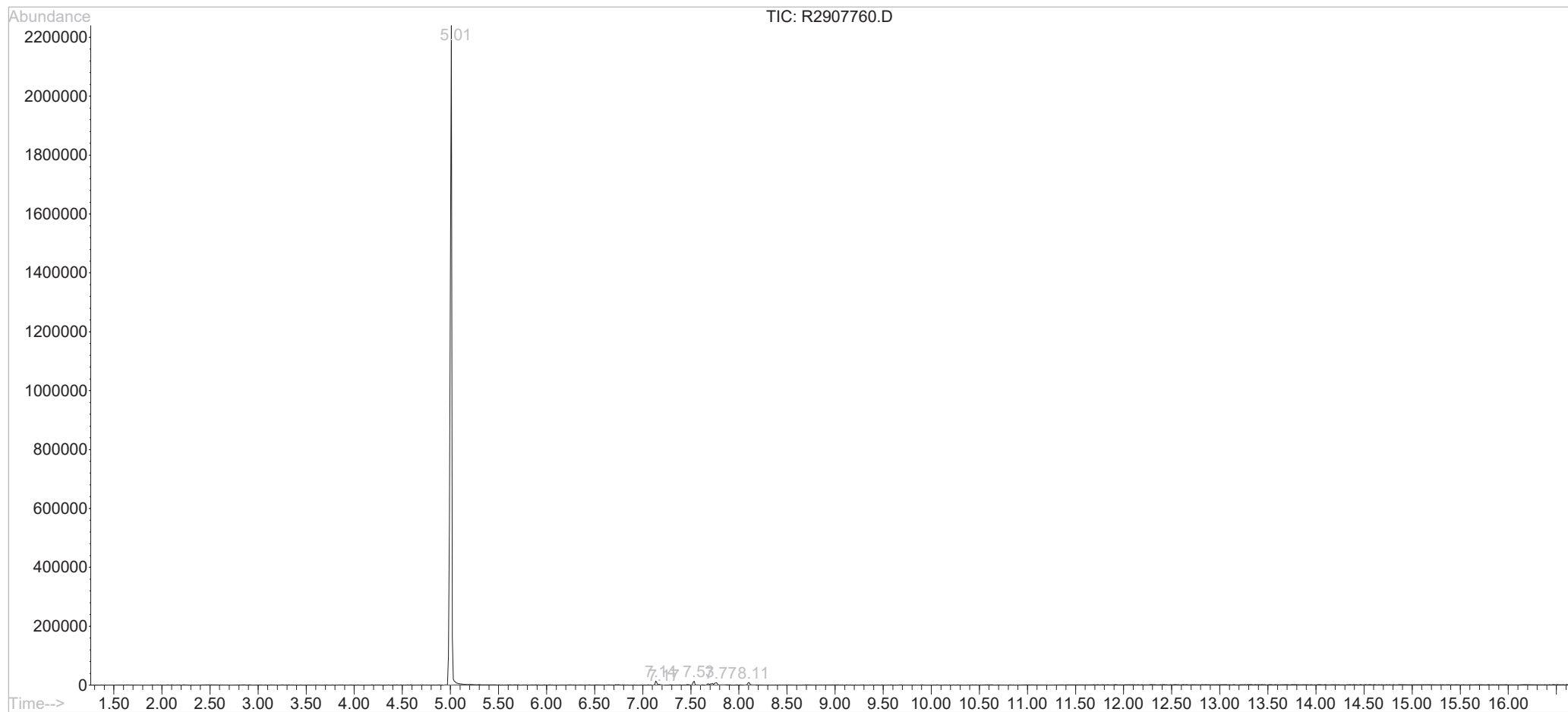
Library Search Report

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Operator:  
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Multiplr: 1.00  
Sample Amount: 0.00



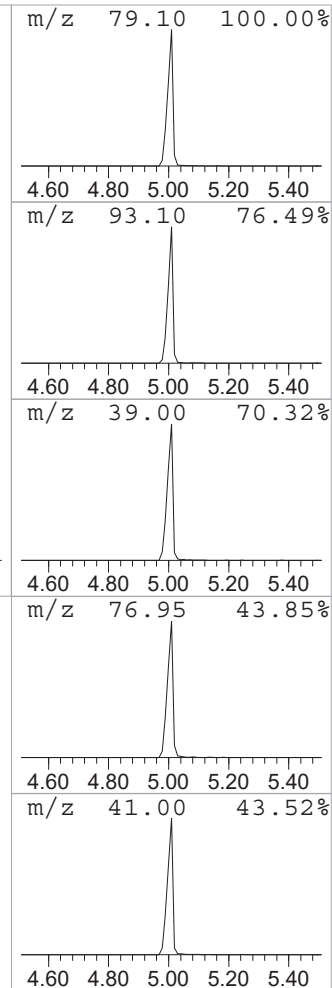
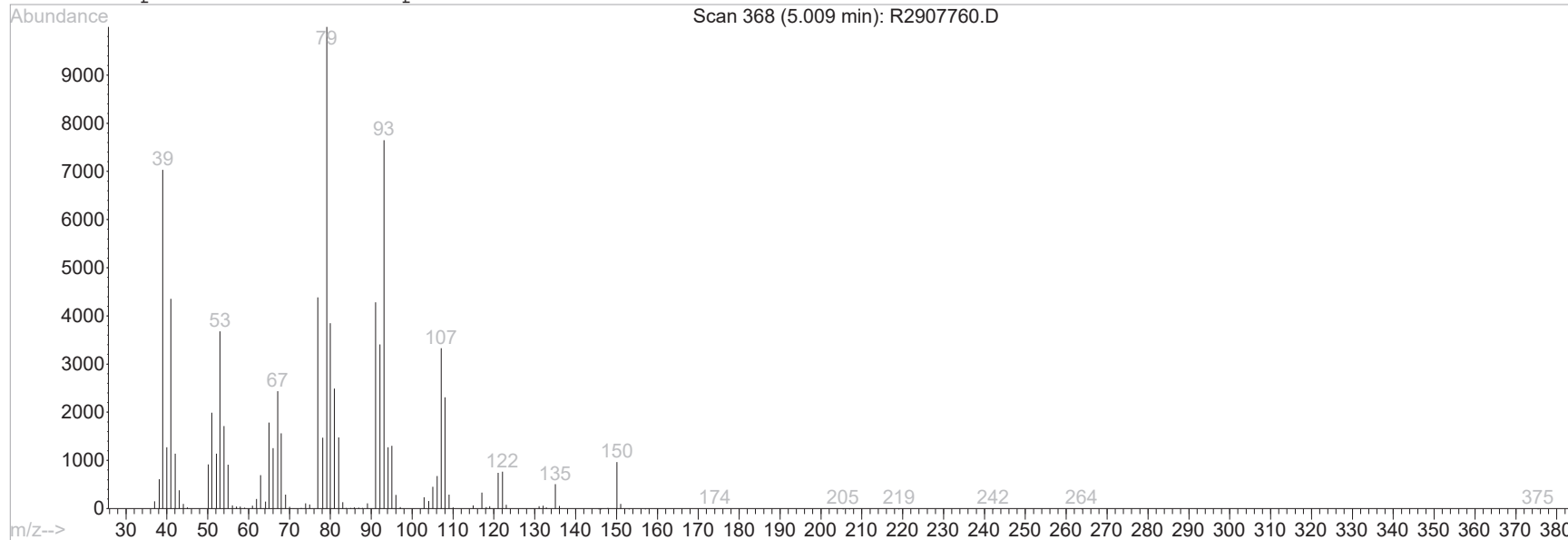
11





Unknown Spectrum based on Apex

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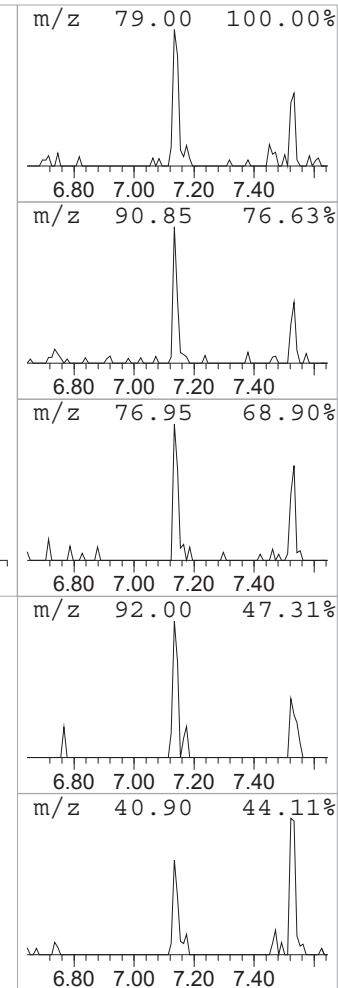
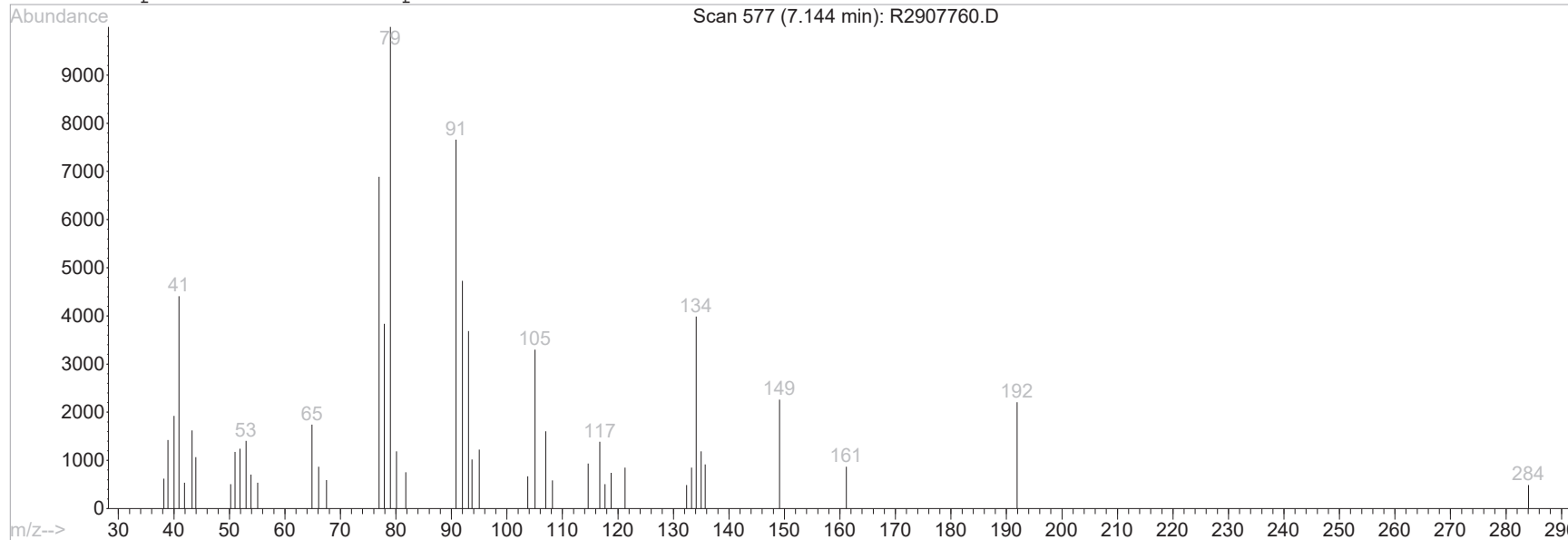


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The 3 best hits from each library. Ref# CAS# Qual

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Unknown Spectrum based on Apex

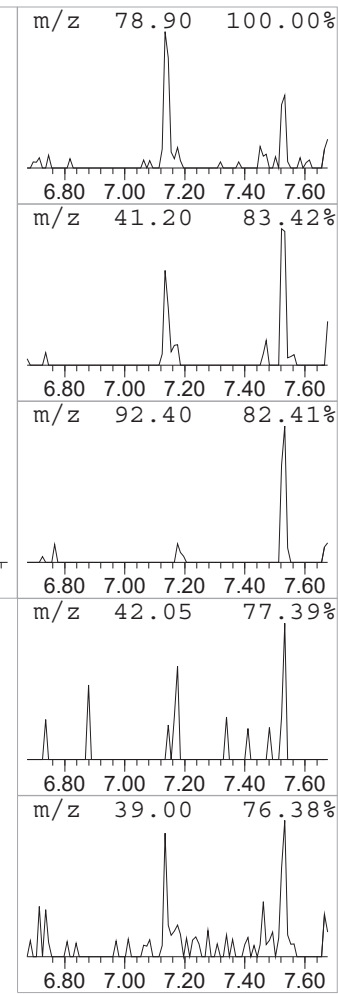
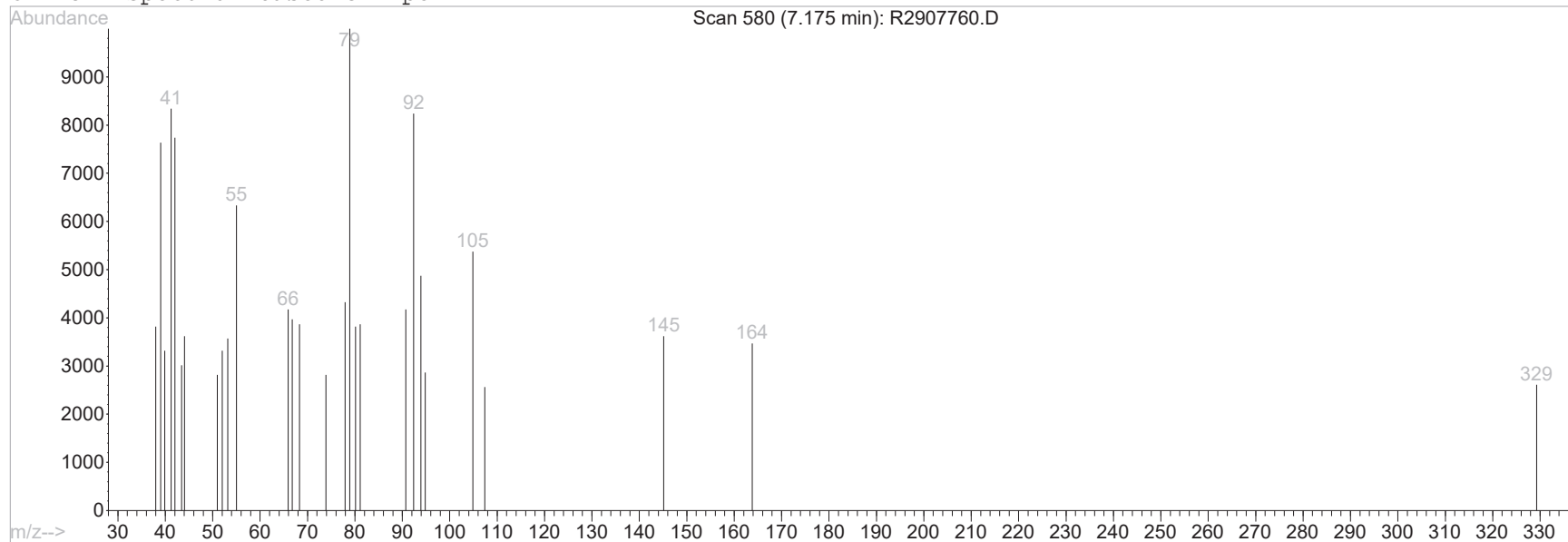


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Unknown Spectrum based on Apex



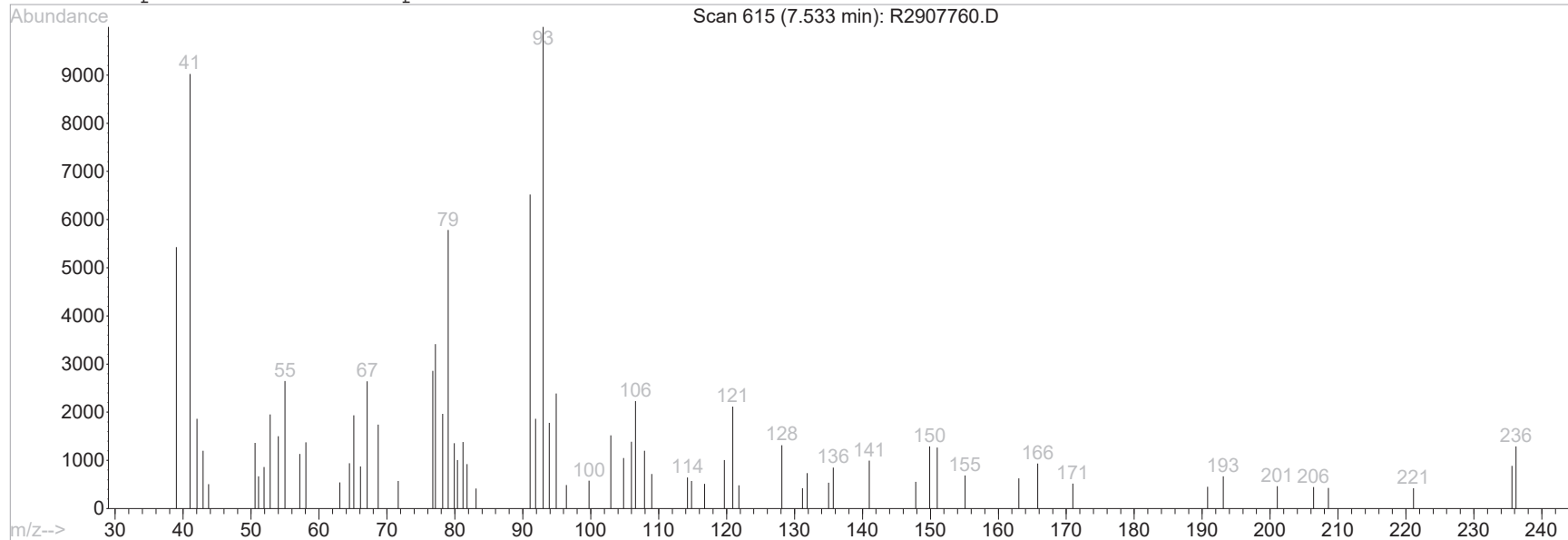
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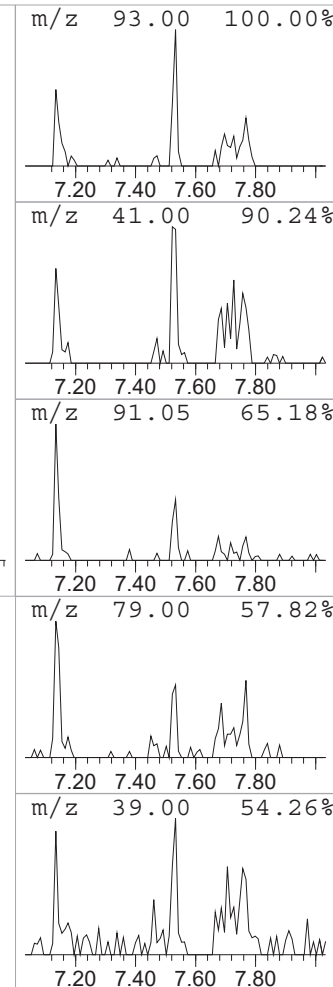
Unknown Spectrum based on Apex



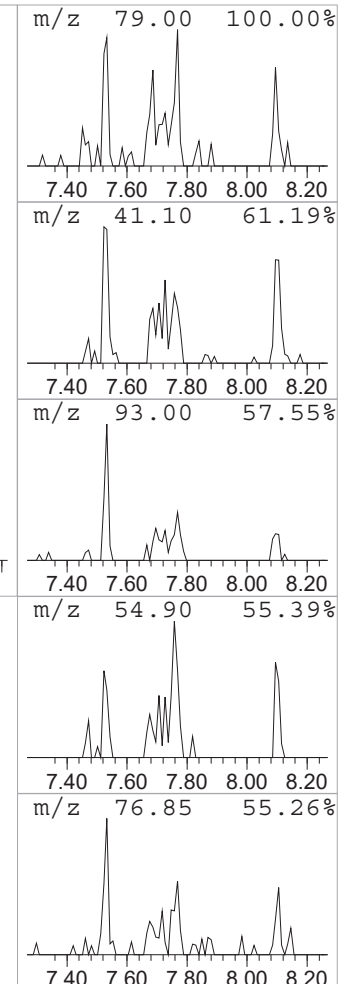
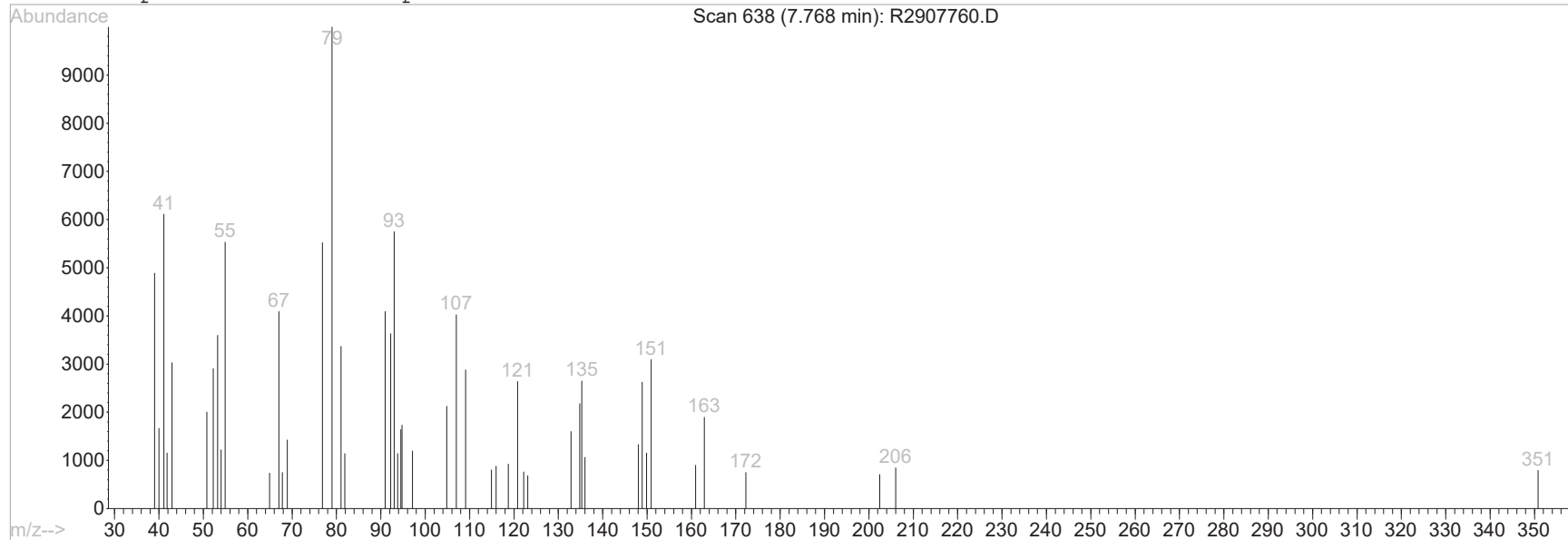
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Unknown Spectrum based on Apex

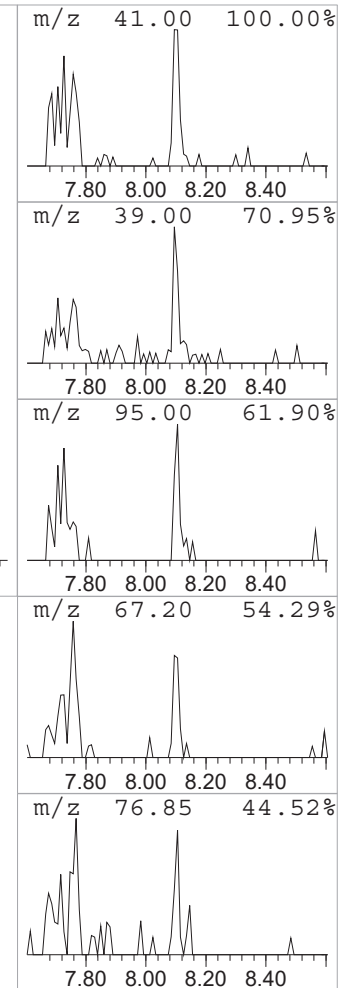
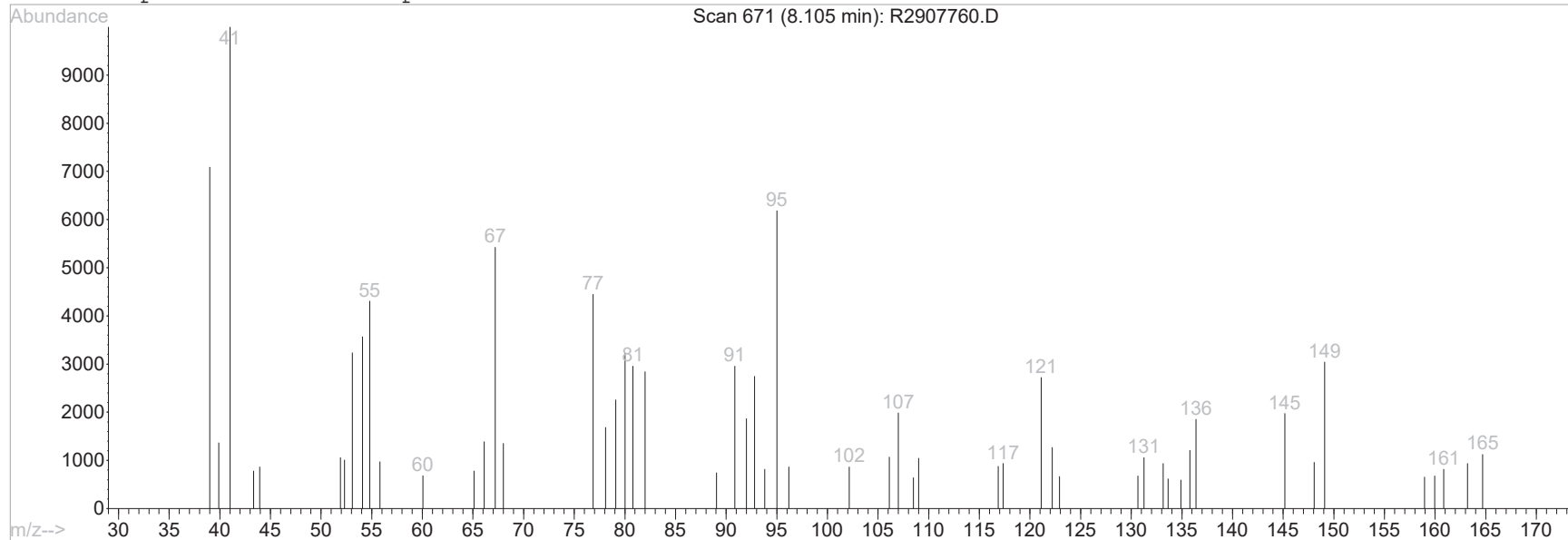


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Unknown Spectrum based on Apex

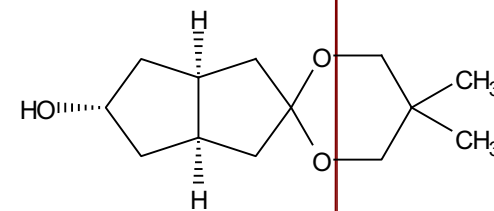


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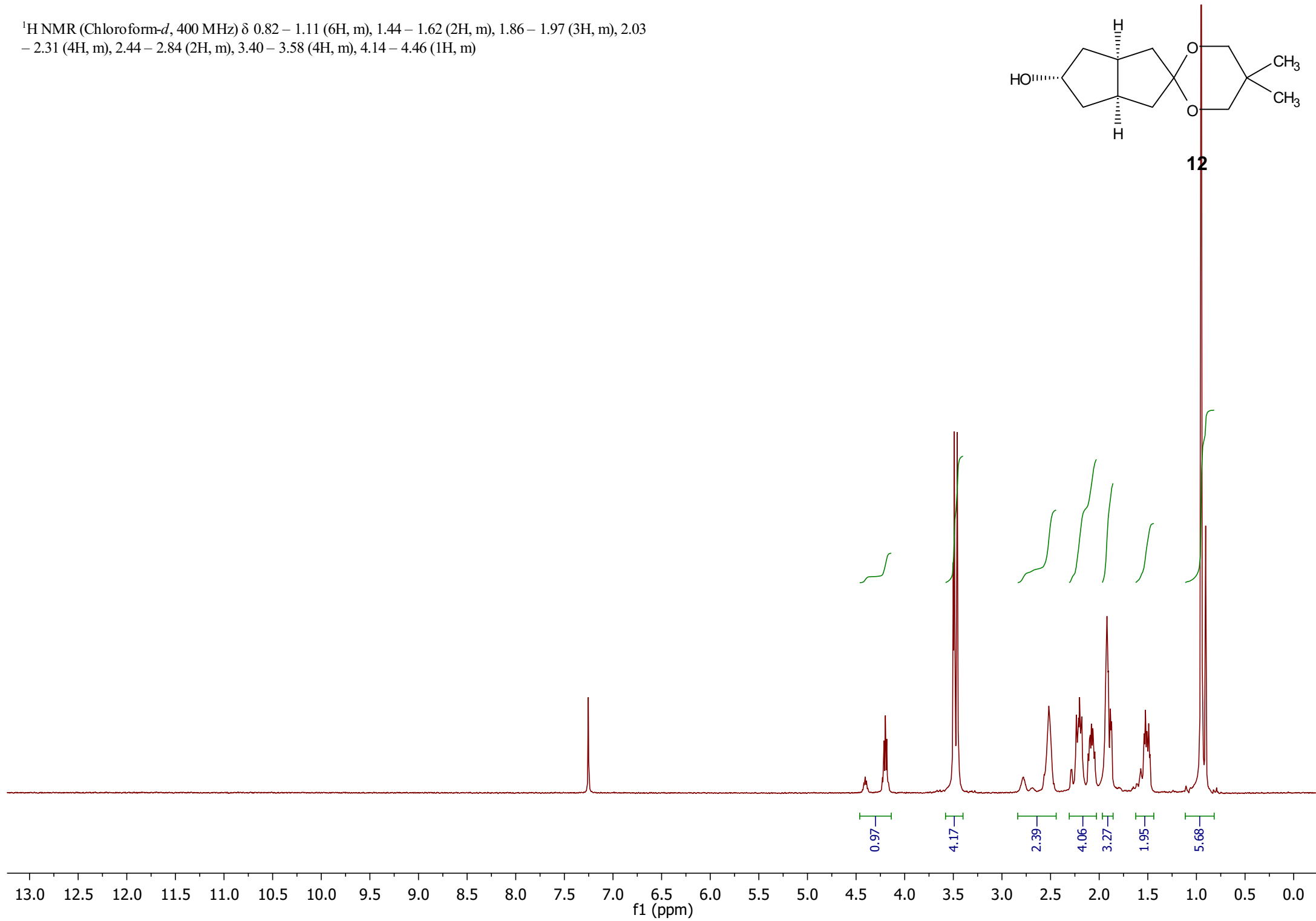
The 3 best hits from each library. Ref# CAS# Qual

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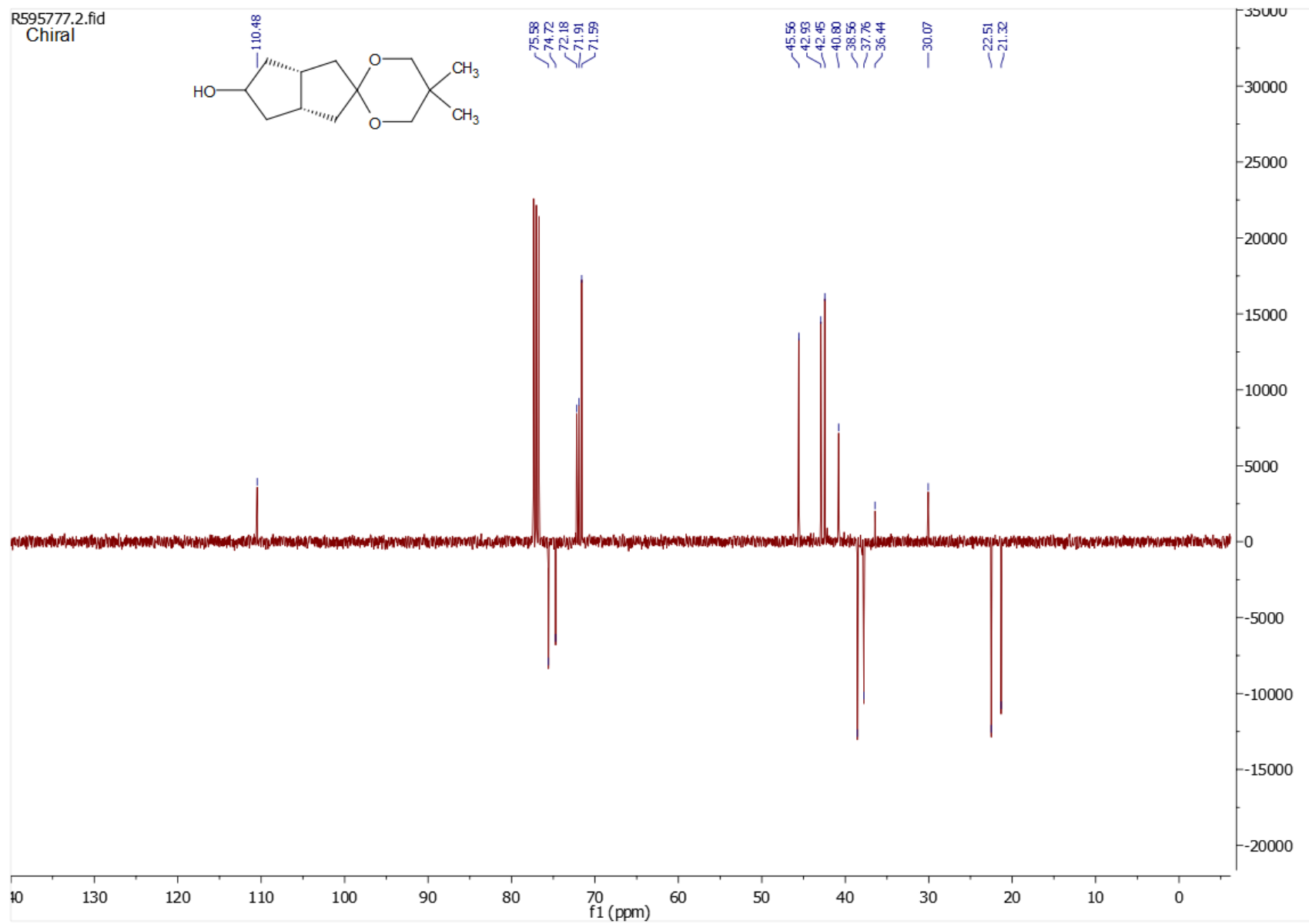
$^1\text{H}$  NMR (Chloroform-*d*, 400 MHz)  $\delta$  0.82 – 1.11 (6H, m), 1.44 – 1.62 (2H, m), 1.86 – 1.97 (3H, m), 2.03 – 2.31 (4H, m), 2.44 – 2.84 (2H, m), 3.40 – 3.58 (4H, m), 4.14 – 4.46 (1H, m)



12

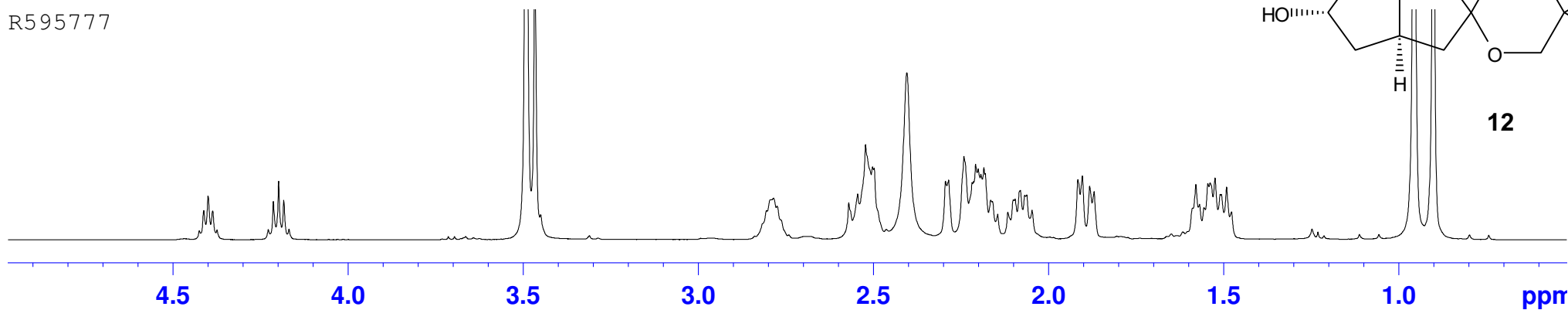
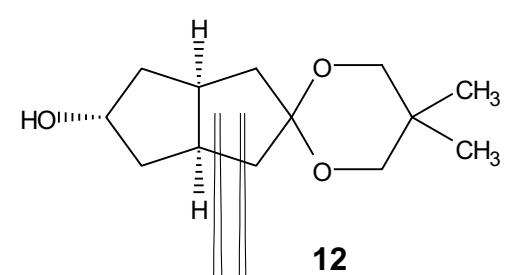


# <sup>13</sup>C NMR spectrum of 12

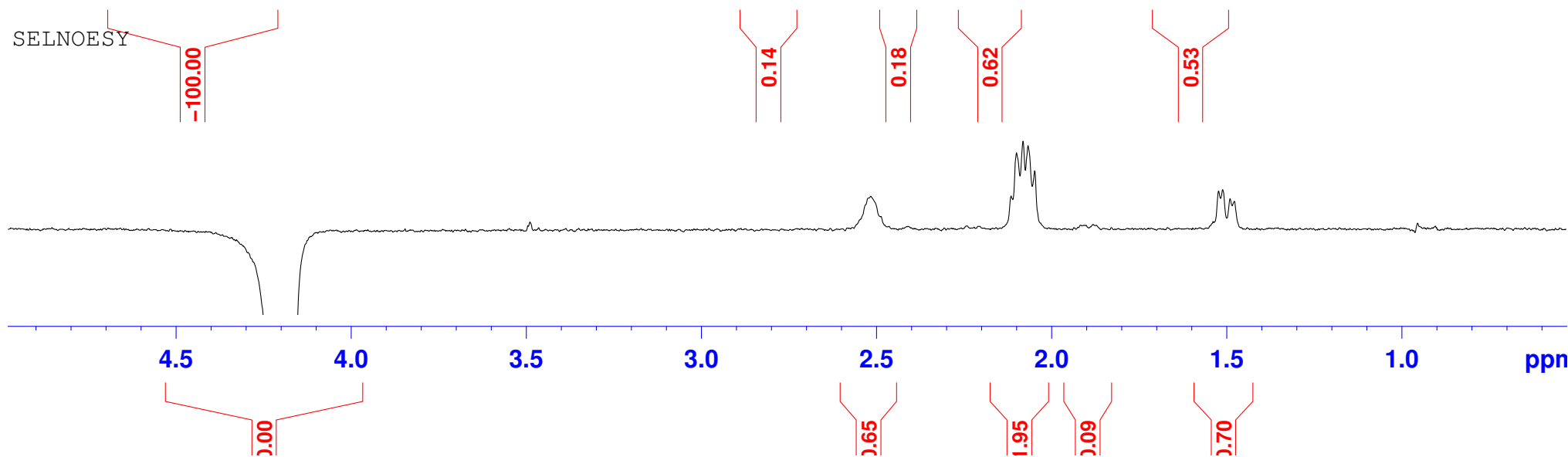
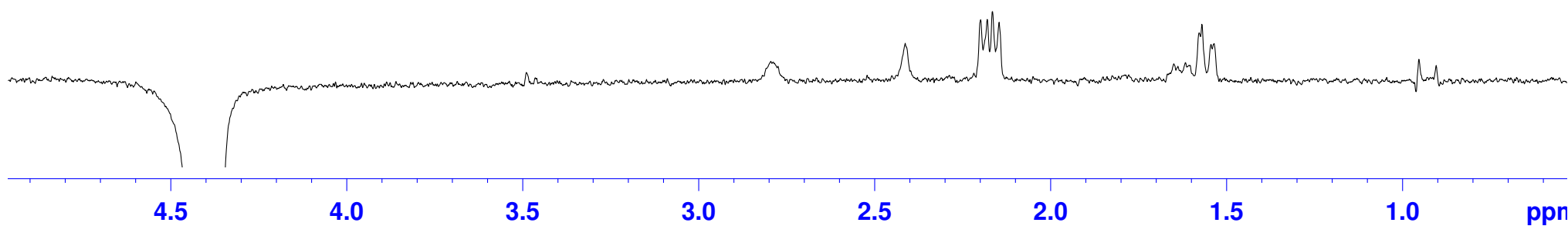




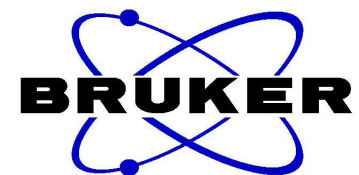
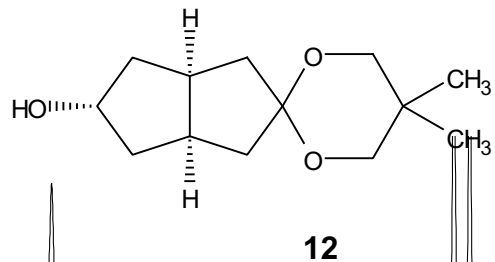
R595777



SELNOESY

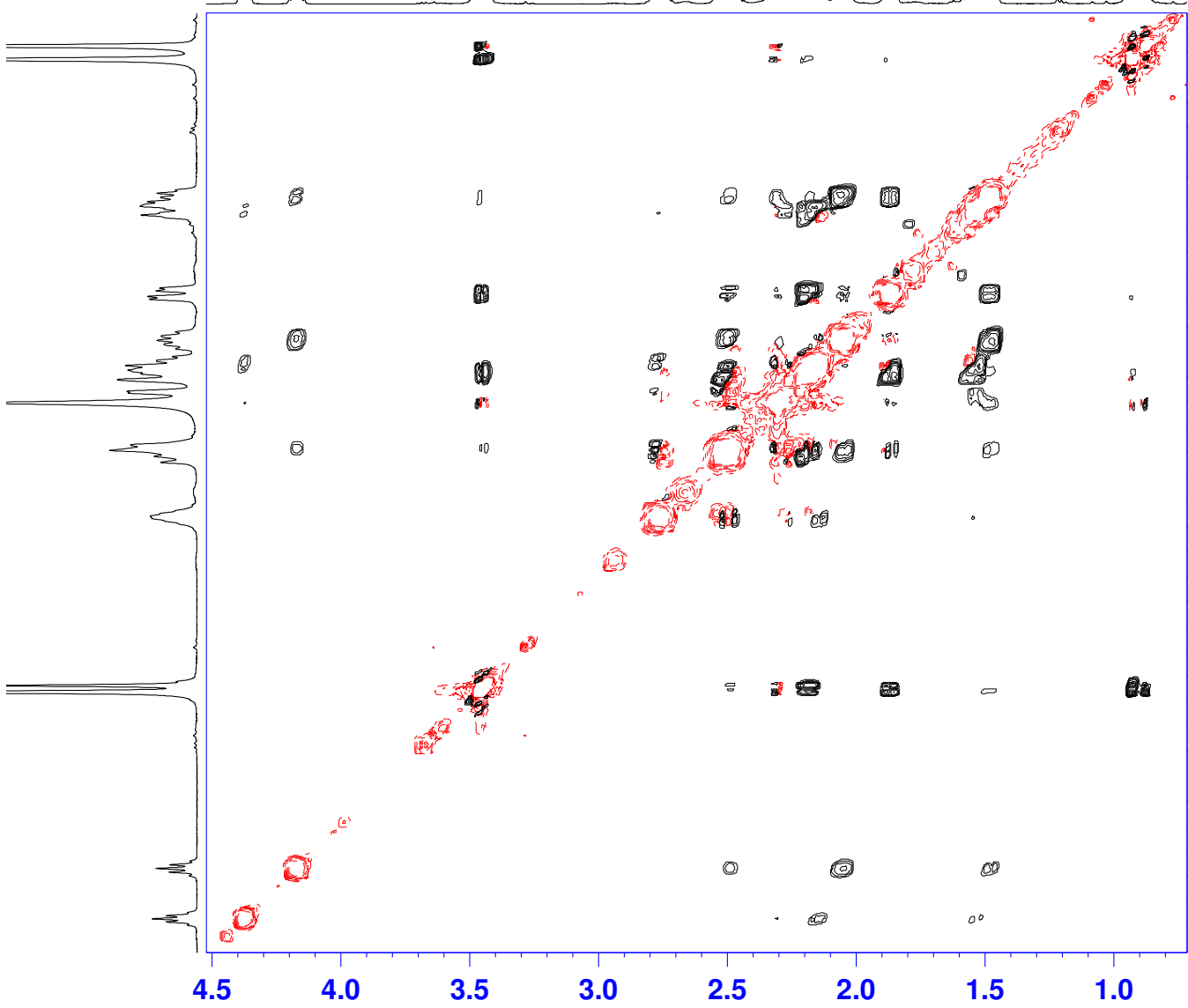


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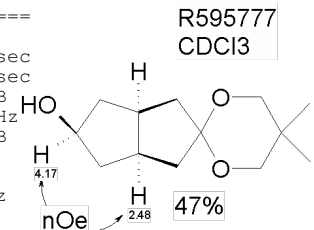


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SWH 2000.000 Hz  
FIDRES 1.953125 Hz  
AQ 0.2560500 sec  
RG 32  
DW 250.000 usec  
DE 6.50 usec  
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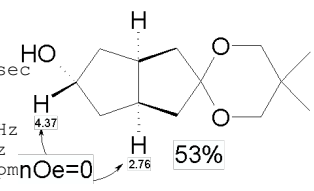
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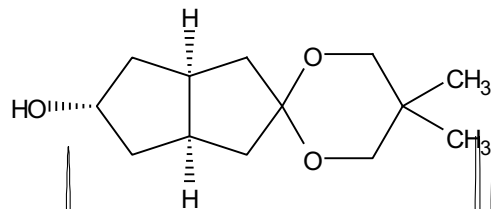
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SP29 28.00 dB  
SPNAM29 Crp40,20,20.10  
SPOAL29 0.500  
SPOFFS29 0.00 Hz



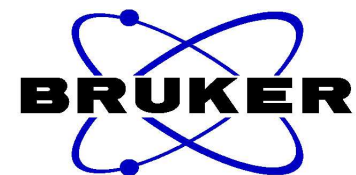
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FIDRES 15.630117 Hz  
SW 5.000 ppm  
FnMODE States-TPPI  
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SF 400.1300129 MHz  
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SSB 2  
LB 0.00 Hz  
GB 0  
PC 1.40  
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HSQC



12

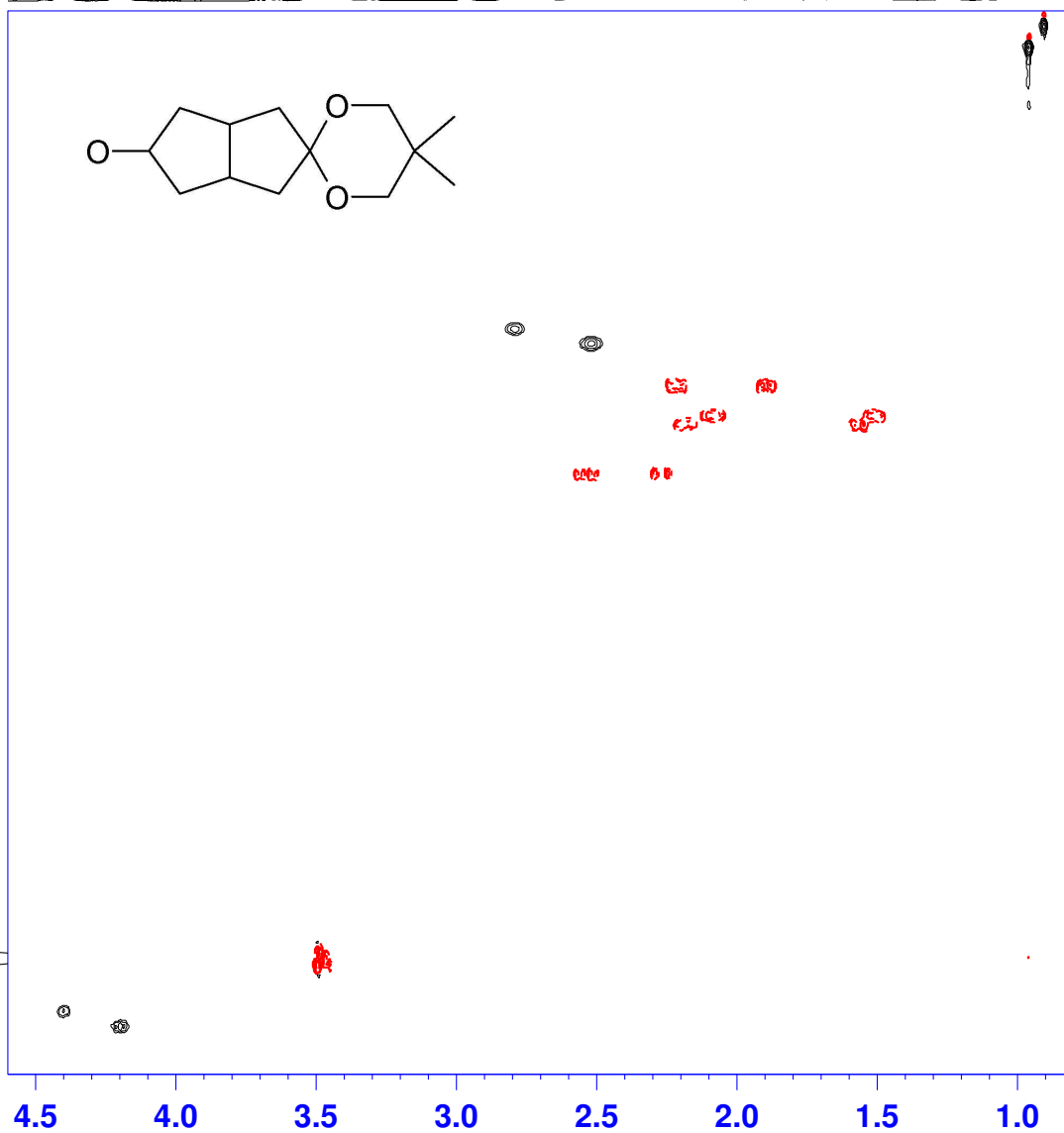
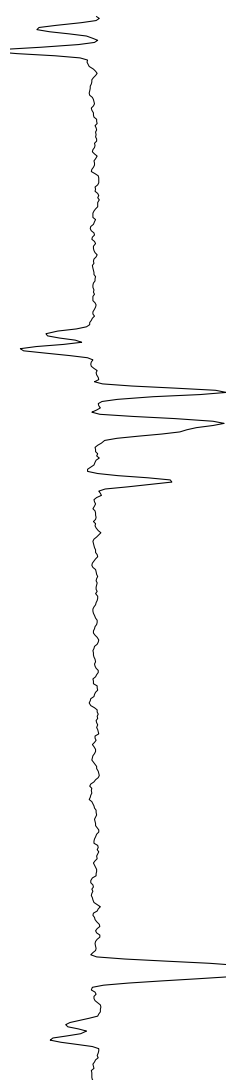


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D1 2.00000000 sec  
D4 0.00172414 sec  
D11 0.03000000 sec  
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D16 0.00020000 sec  
D21 0.00344830 sec  
INO 0.00008280 sec  
ZGPTNS

===== CHANNEL f1 =====  
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P2 20.60 usec  
P28 1000.00 usec  
PL1 0.00 dB  
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===== CHANNEL f2 =====  
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NUC2 13C  
P3 10.00 usec  
P4 20.00 usec  
PCPD2 60.00 usec  
PL2 6.30 dB  
PL12 25.30 dB  
SFO2 100.6177996 MHz

===== GRADIENT CHANNEL =====  
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GPNAM2 SINE.100  
GPZ1 80.00 %  
GPZ2 20.10 %  
P16 1000.00 usec  
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FIDRES 47.164593 Hz  
SW 60.000 ppm  
FnMODE Echo-Antiecho  
SI 1024  
SF 400.1300000 MHz  
WDW QSINE  
SSB 2  
LB 0.00 Hz  
GB 0  
PC 1.40  
SI 512  
MC2 echo-antiecho  
SF 100.6127690 MHz  
WDW QSINE  
SSB 2  
LB 0.00 Hz  
GB 0



ppm

25

30

35

40

45

50

55

60

65

70

75

4.5

4.0

3.5

3.0

2.5

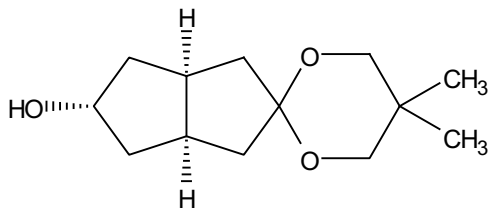
2.0

1.5

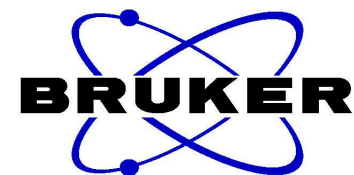
1.0

ppm

COSY-45



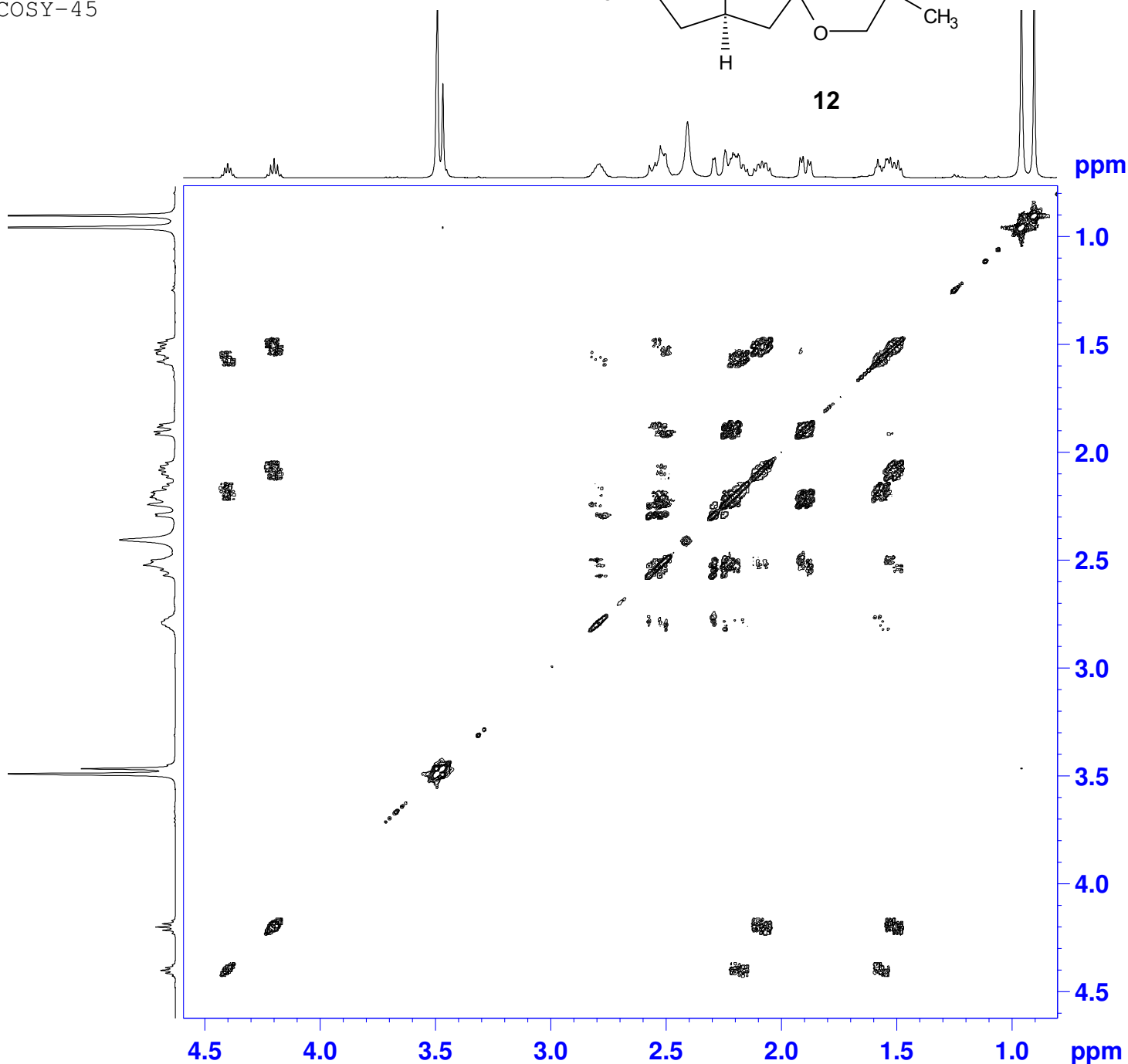
12



NAME R595777  
EXPNO 3  
PROCNO 1  
Date\_ 20180328  
Time 1.56  
INSTRUM spect  
PROBHD 5 mm QNP 1H/15  
PULPROG cosygpgf  
TD 2048  
SOLVENT CDC13  
NS 1  
DS 8  
SWH 1802.451 Hz  
FIDRES 0.880103 Hz  
AQ 0.5681652 sec  
RG 406  
DW 277.400 usec  
DE 6.50 usec  
TE 297.4 K  
D0 0.00000300 sec  
D1 1.48689198 sec  
D13 0.00000400 sec  
D16 0.00020000 sec  
IN0 0.00055535 sec

===== CHANNEL f1 =====  
NUC1 1H  
P0 5.15 usec  
P1 10.30 usec  
PL1 0.00 dB  
SFO1 400.1311004 MHz

===== GRADIENT CHANNEL =====  
GPNAM1 SINE.100  
GPZ1 10.00 %  
P16 1000.00 usec  
ND0 1  
TD 256  
SFO1 400.1311 MHz  
FIDRES 7.033555 Hz  
SW 4.500 ppm  
FnMODE QF  
SI 2048  
SF 400.1300000 MHz  
WDW SINE  
SSB 0  
LB 0.00 Hz  
GB 0  
PC 1.40  
SI 2048  
MC2 QF  
SF 400.1300000 MHz  
WDW SINE  
SSB 0  
LB 0.00 Hz  
GB 0

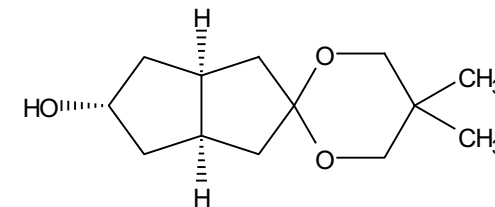


Library Search Report

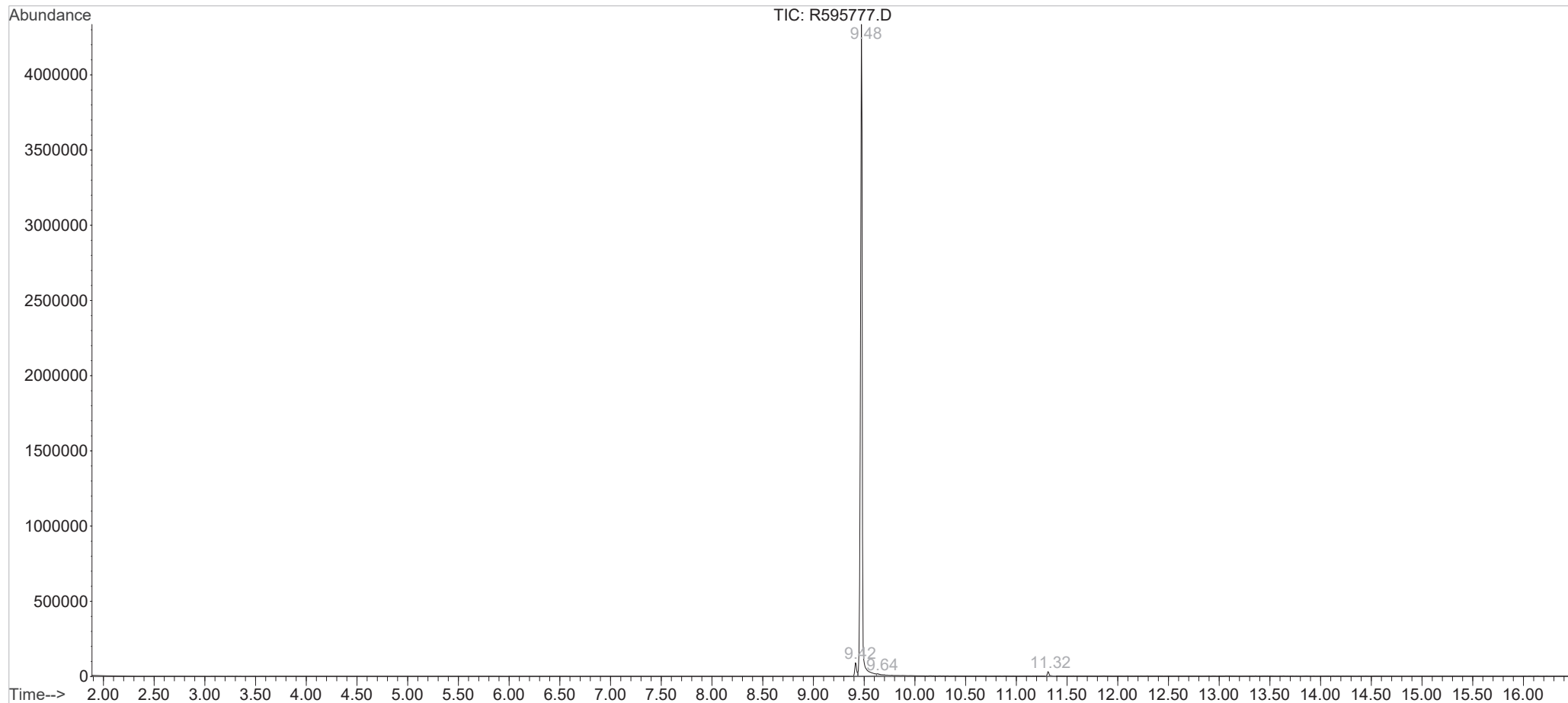
Acq On  
Sample  
Misc : CH2CL2

Vial: 99  
Operator:  
Inst : Instrumen  
Multiplr: 1.00  
Sample Amount: 0.00

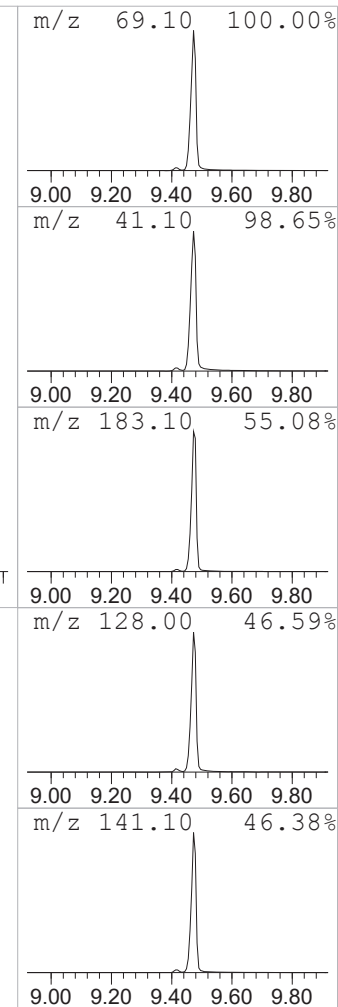
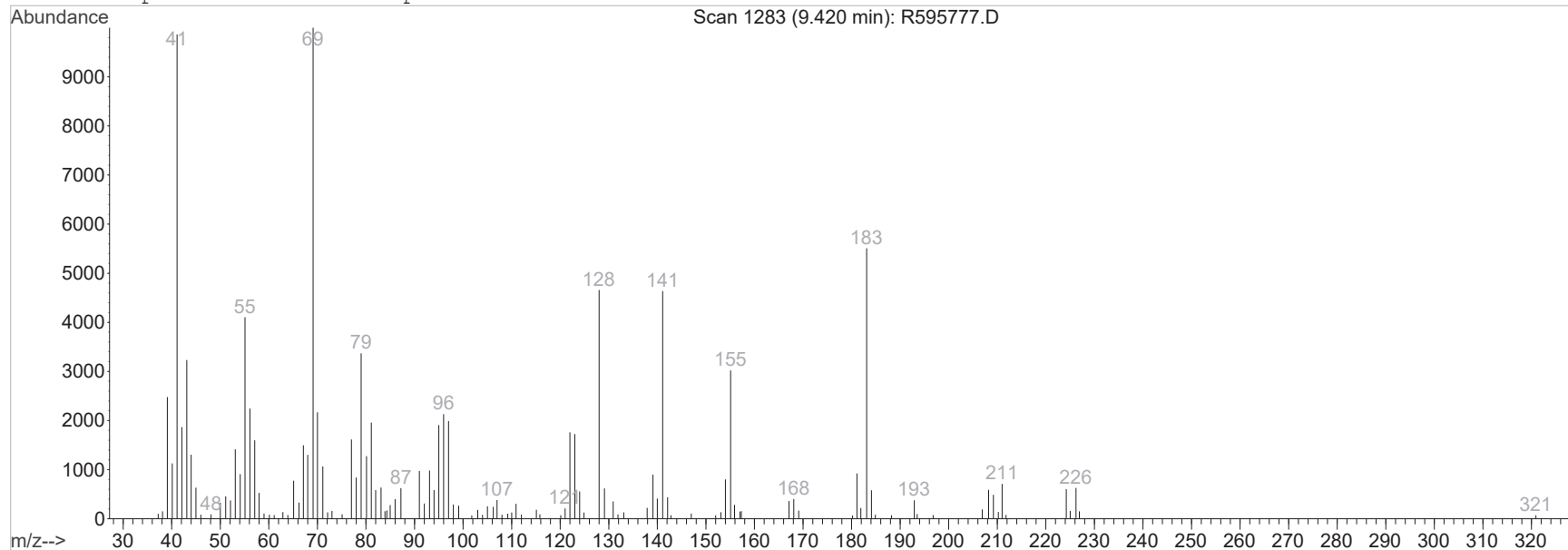
MS Integration Params: autoint1.e  
Method  
Title :



**12**



Unknown Spectrum based on Apex

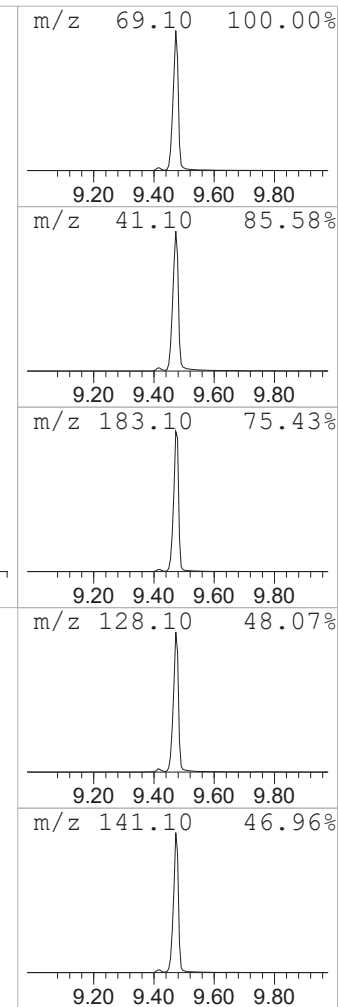
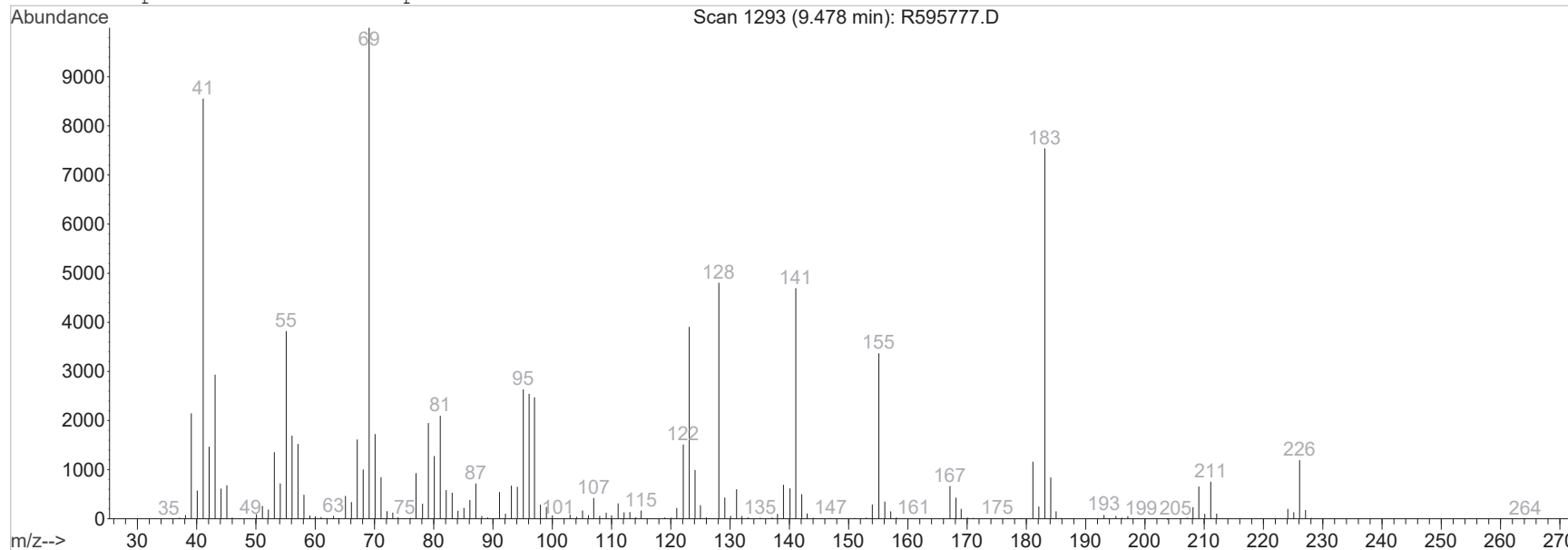


Peak Number: 1 at 9.42 min Area: 1070343 Area % 1.94

-----  
 The database \MSDCHEM from eanb library were retrieved  
 -----

Ref#	CAS#	Qual

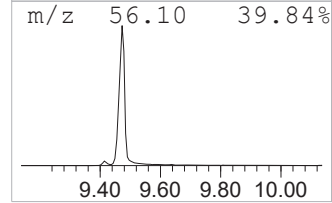
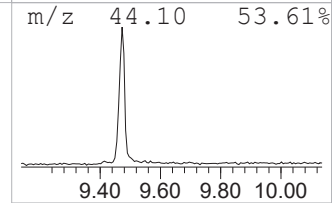
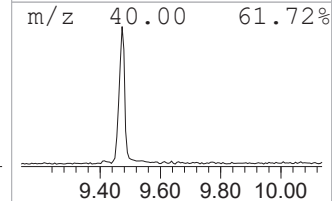
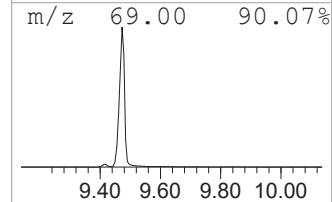
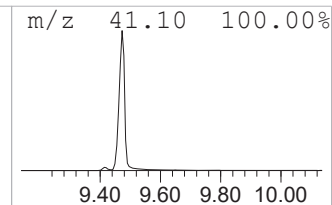
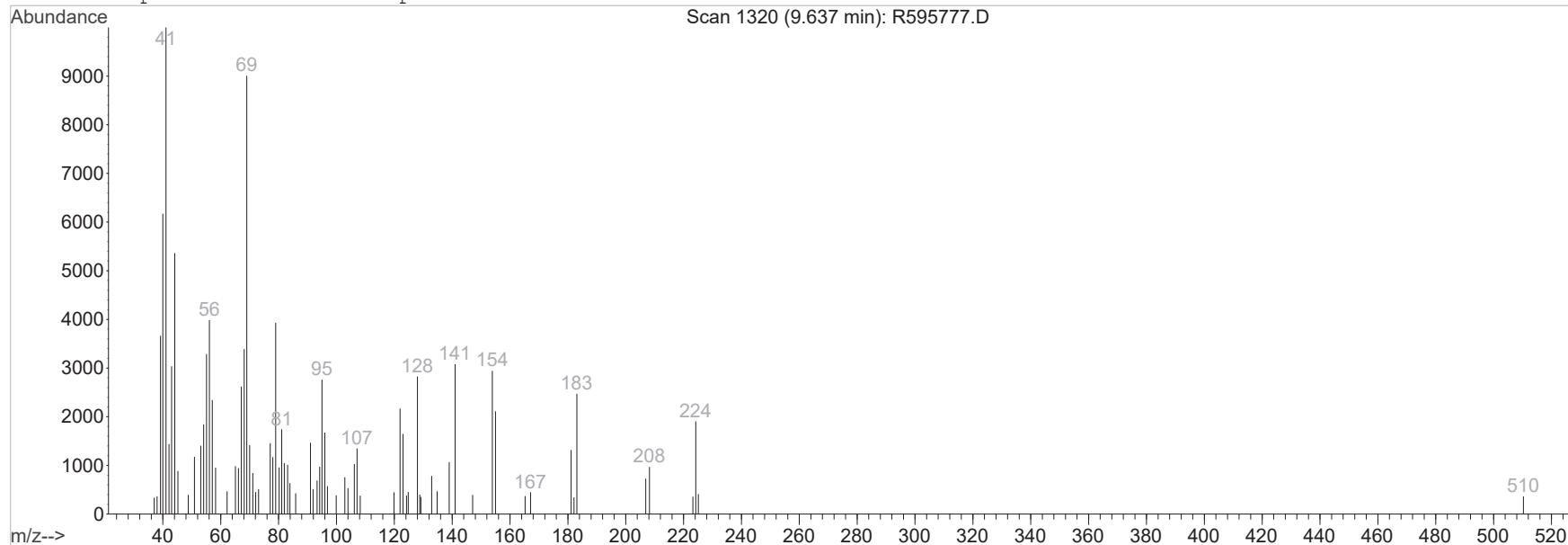
Unknown Spectrum based on Apex



Peak Number: 2 at 9.48 min Area: 53352240 Area % 96.60

-----  
 The database(s) searched from each library were retrieved Ref# CAS# Qual  
 -----

Unknown Spectrum based on Apex

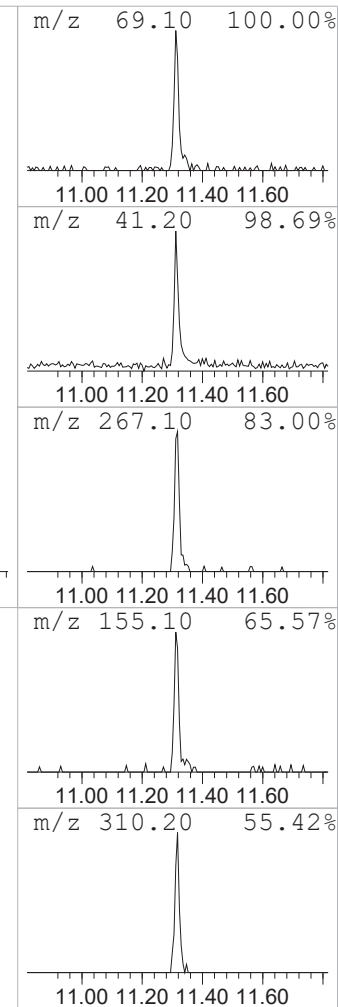
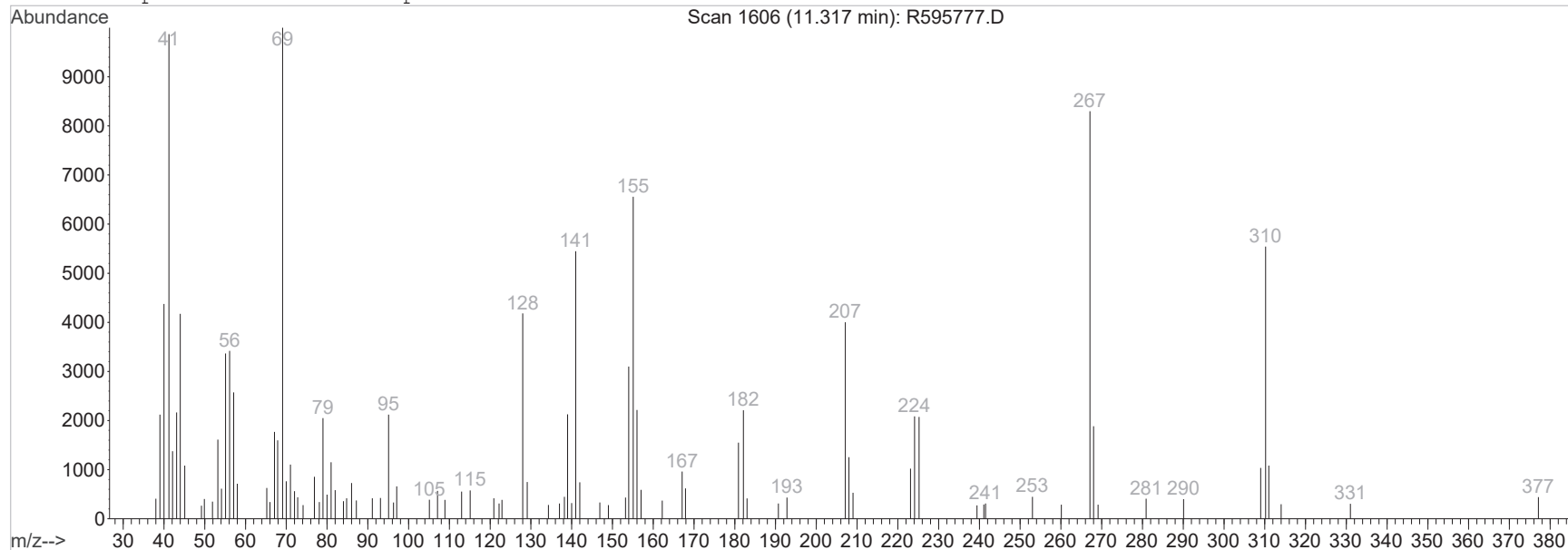


Peak Number: 3 at 9.64 min Area: 448767 Area % 0.81

-----  
 The database \MSDCHEM\MSDCHEM was searched and no hits were retrieved.  
 -----



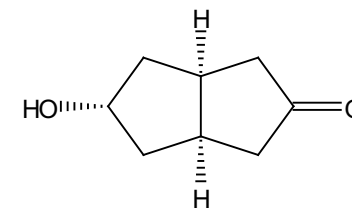
Unknown Spectrum based on Apex



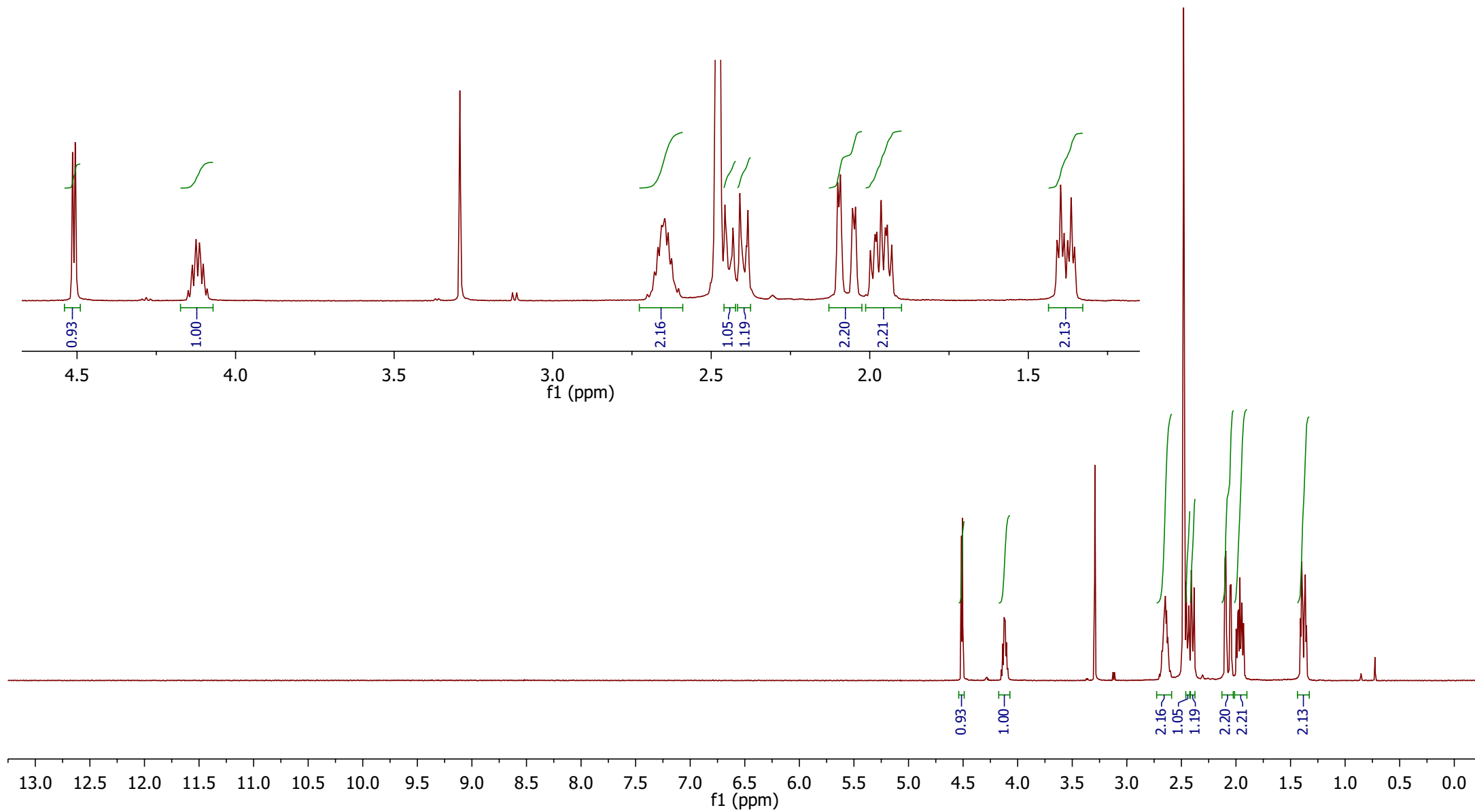
Peak Number: 4 at 11.32 min Area: 360710 Area % 0.65

-----  
 The database \MSDCHEM\Library was used to retrieve the following information:  
 Name CAS# Qual  
 -----

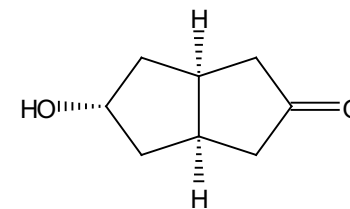
$^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  1.38 (2H, dt,  $J=13.2, 4.4$  Hz), 1.96 (2H, ddd,  $J=13.4, 8.2, 5.6$  Hz), 2.07 (2H, dd,  $J=18.9, 3.4$  Hz), 2.38 – 2.42 (1H, m), 2.42 – 2.46 (1H, m), 2.59 – 2.73 (2H, m), 4.07 – 4.17 (1H, m), 4.51 (1H, d,  $J=3.4$  Hz)



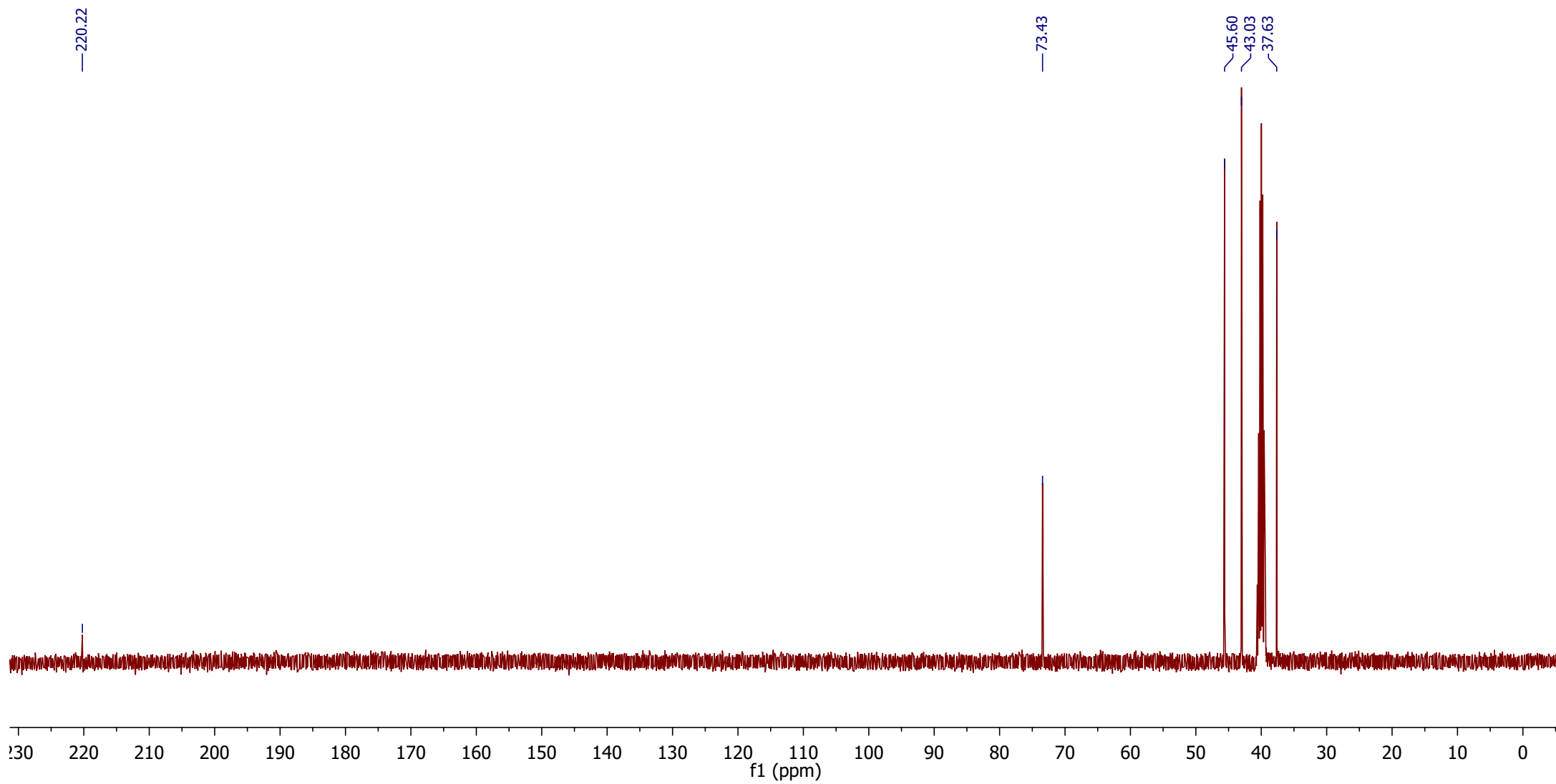
**13**



$^{13}\text{C}$  NMR (dmsO, 101 MHz)  $\delta$  37.6, 43.0, 45.6, 73.4, 220.2.



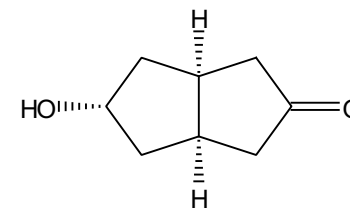
**13**



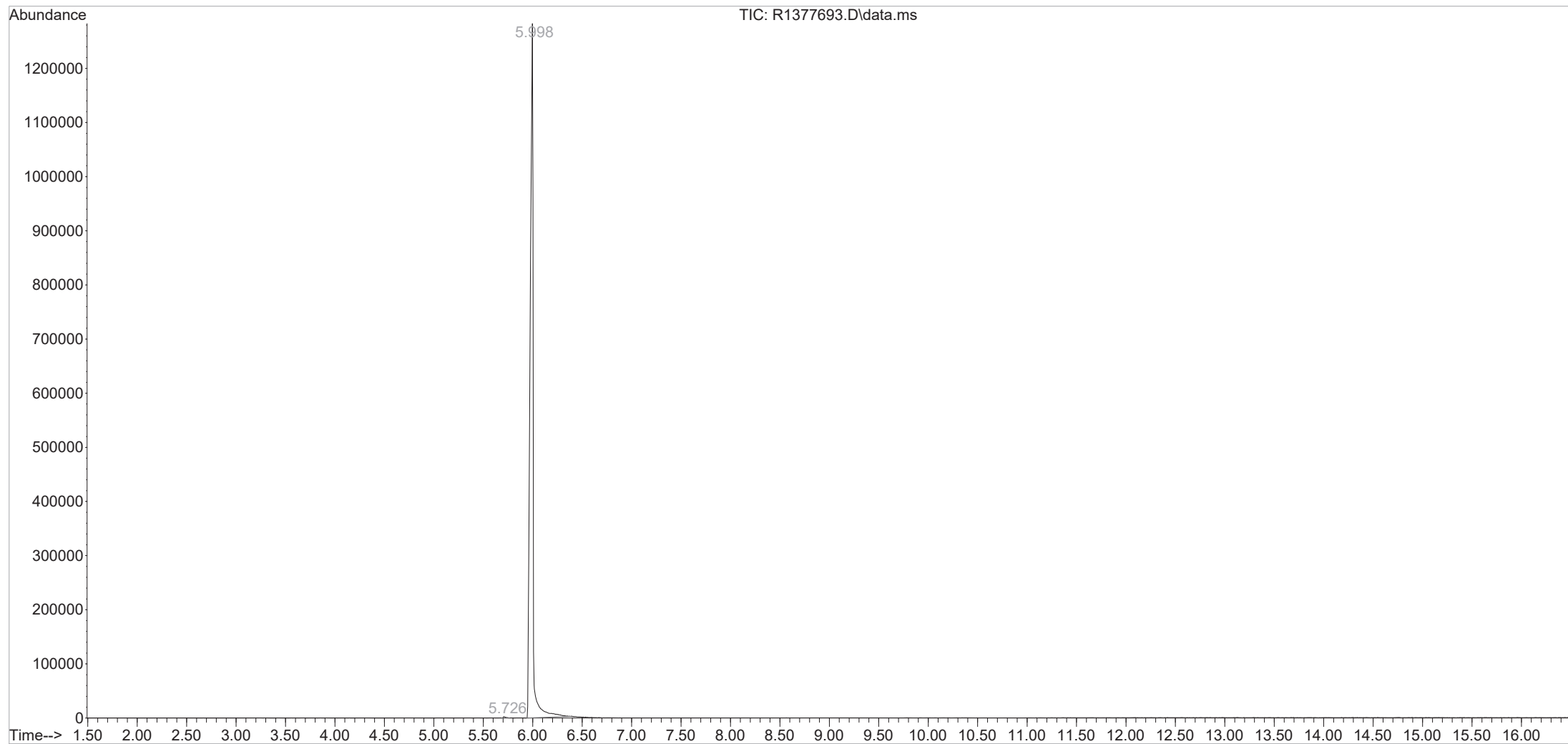
Acq On  
Operator :  
Sample  
Misc : CH3OH  
ALS Vial : 117 Sample Multiplier: 1

Search Libraries: Minimum Quality: 0

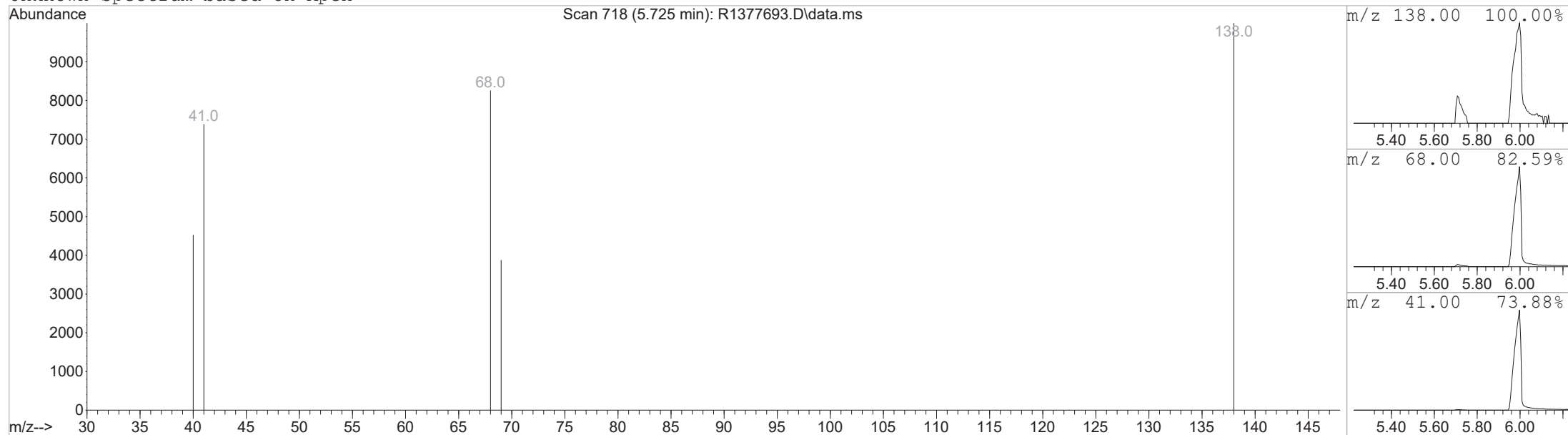
Unknown Spectrum: Apex  
Integration Events: ChemStation Integrator - autoint1.e



**13**



## Unknown Spectrum based on Apex



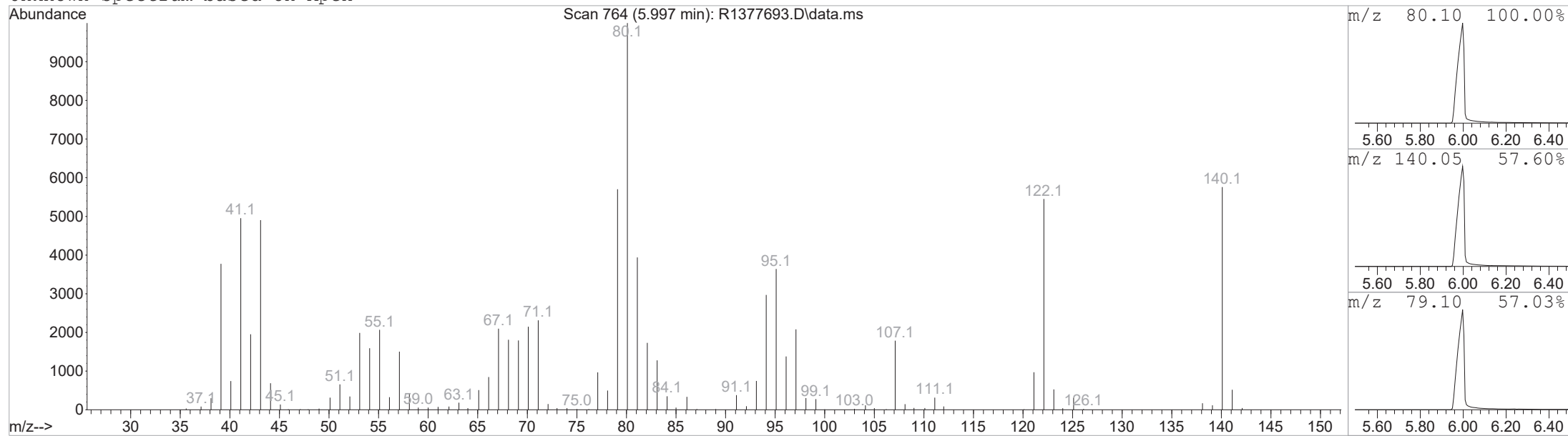
Sample

Peak Number: 1 at 5.726 min Area: 48566 Area % 0.17

The 3 best hits from each library. Ref\# CAS\# Qual

-----  
No hits were retrieved.

## Unknown Spectrum based on Apex



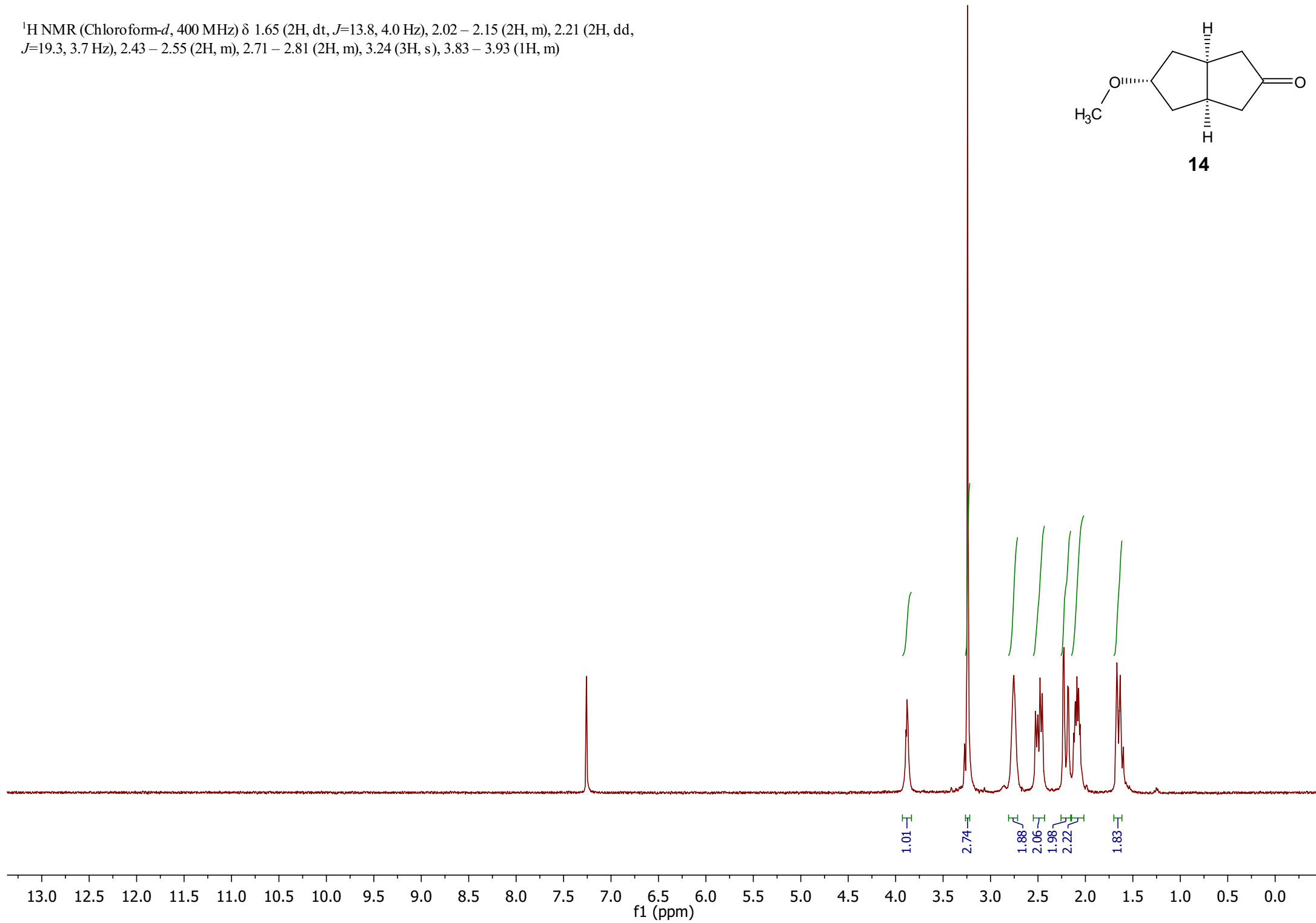
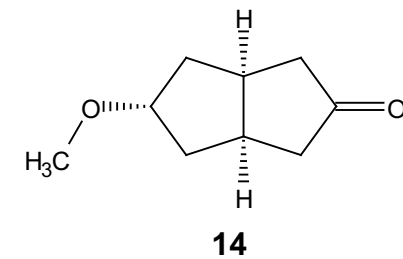
Sample

Peak Number: 2 at 5.998 min Area: 27848050 Area % 99.83

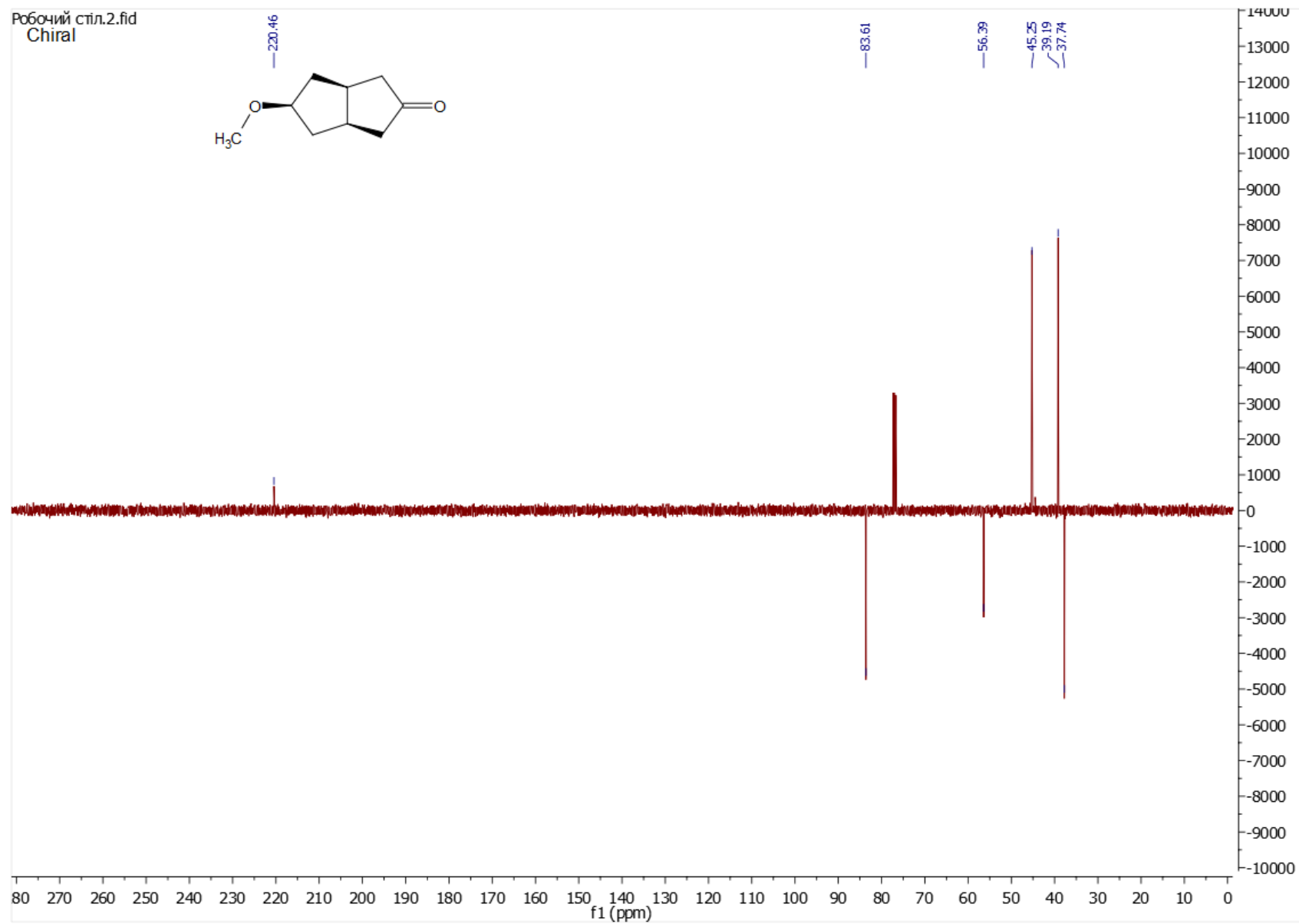
The 3 best hits from each library. Ref\# CAS\# Qual

-----  
No hits were retrieved.

$^1\text{H NMR}$  (Chloroform-*d*, 400 MHz)  $\delta$  1.65 (2H, dt,  $J=13.8, 4.0$  Hz), 2.02 – 2.15 (2H, m), 2.21 (2H, dd,  $J=19.3, 3.7$  Hz), 2.43 – 2.55 (2H, m), 2.71 – 2.81 (2H, m), 3.24 (3H, s), 3.83 – 3.93 (1H, m)

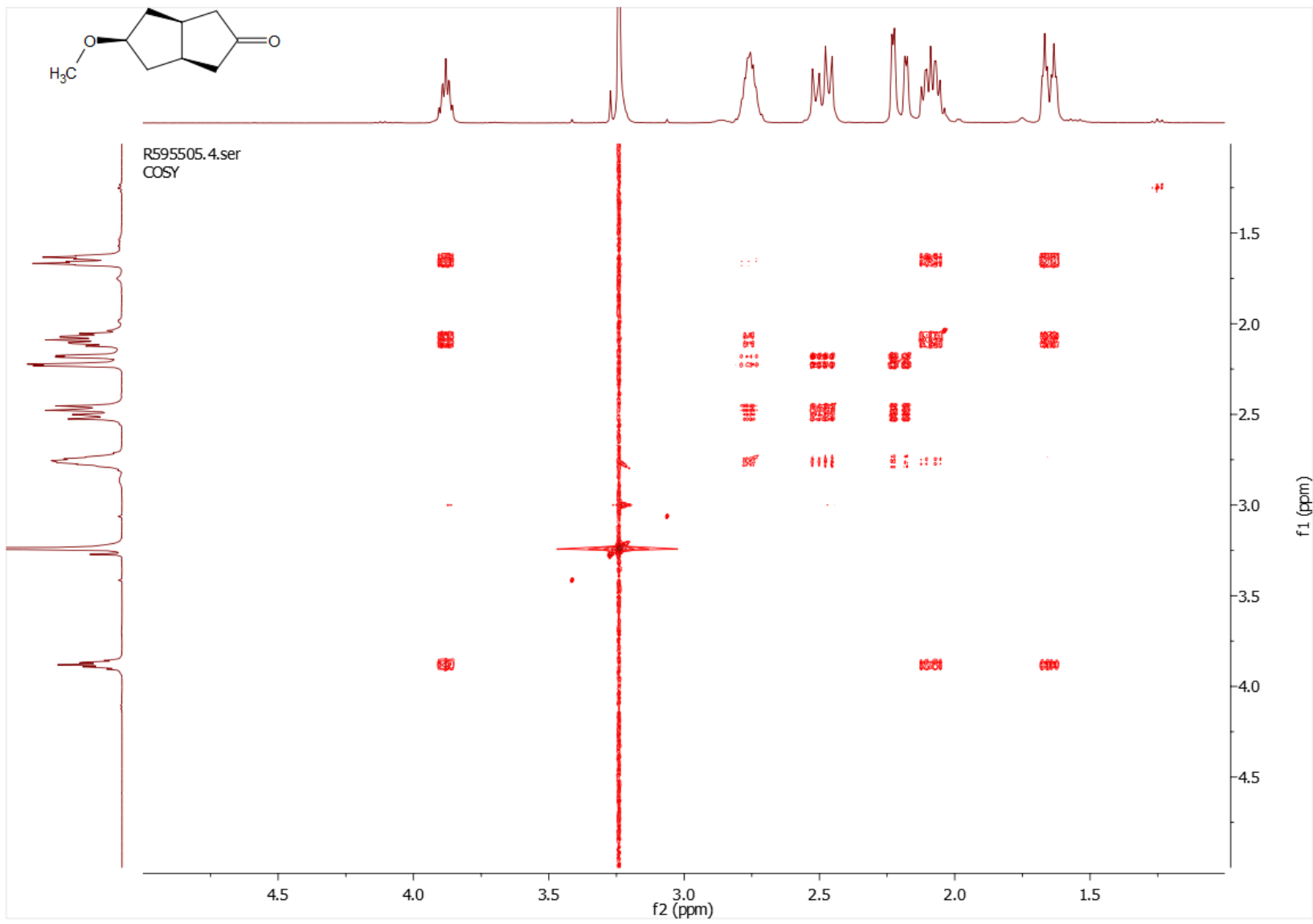


# <sup>13</sup>C NMR spectrum of 14

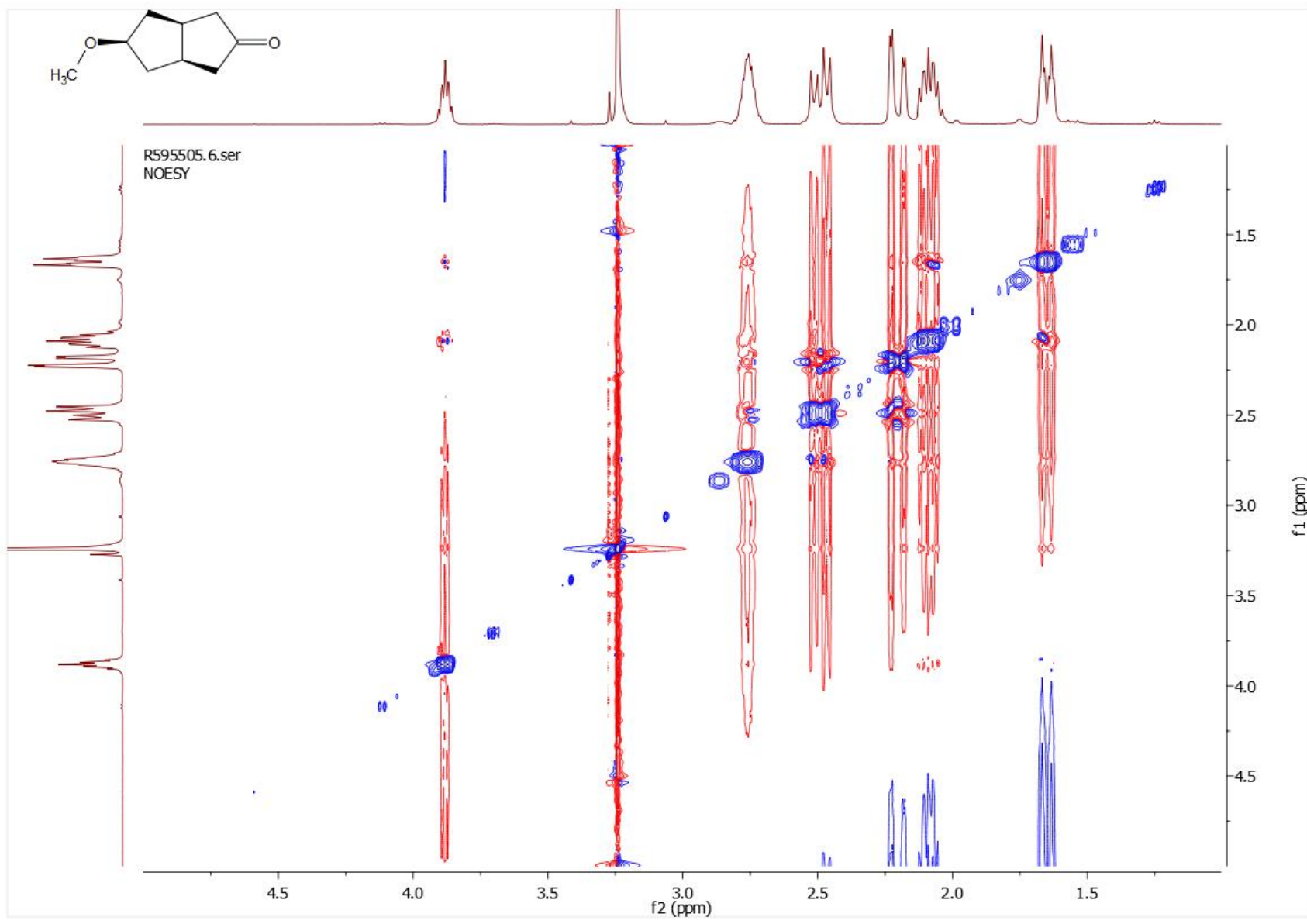


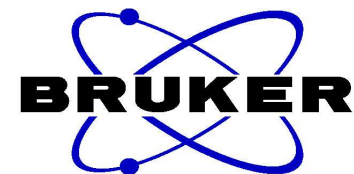
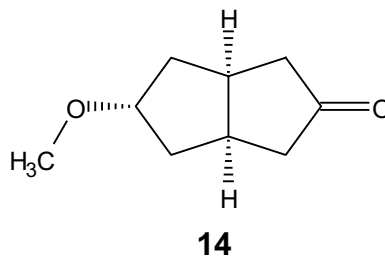


# COSY spectrum of 14

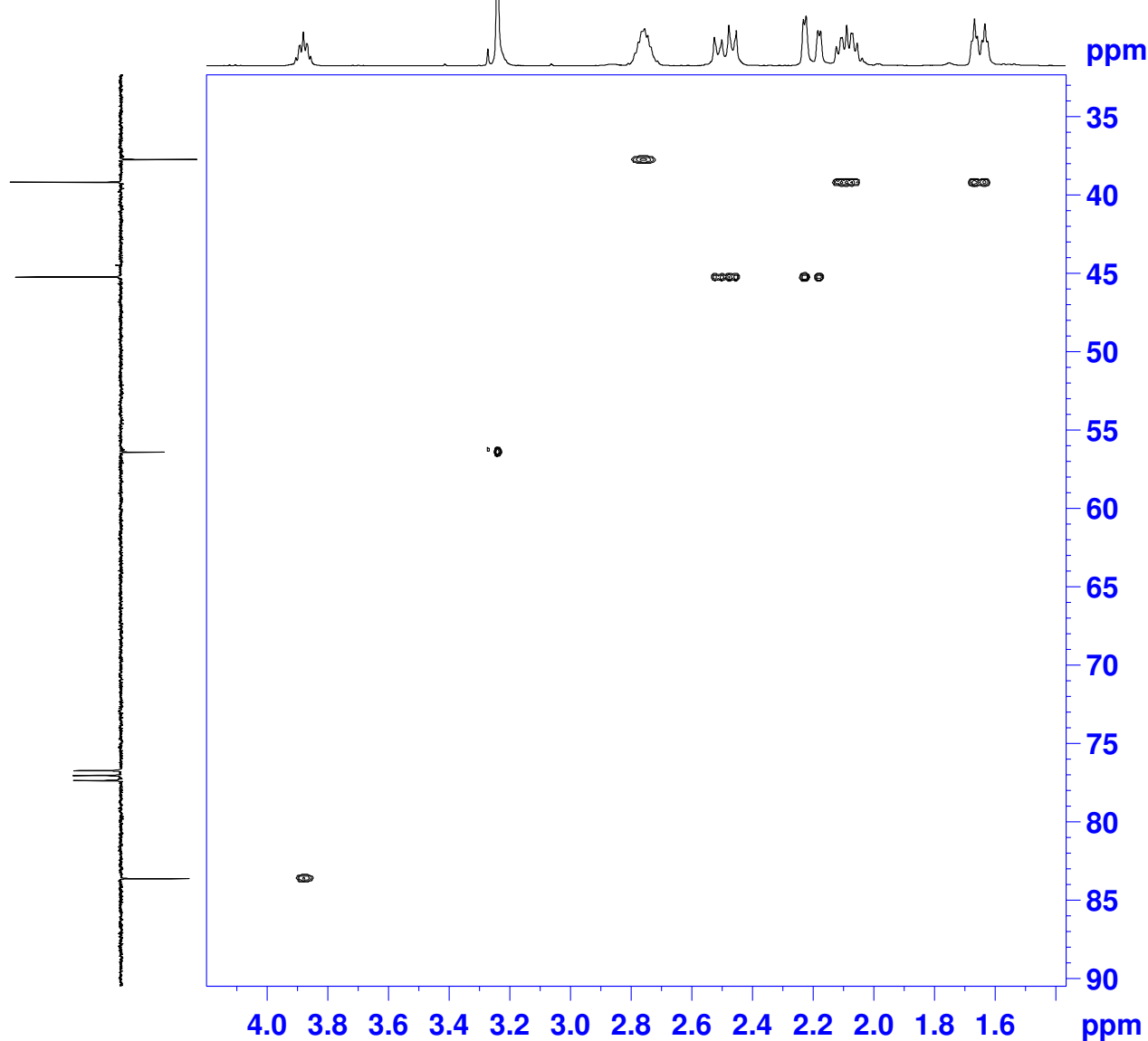


# NOESY spectrum of 14





HSQC



```

NAME R595505
EXPNO 5
PROCNO 1
Date_ 20151225
Time 2.30
INSTRUM spect
PROBHD 5 mm QNP 1H/15
PULPROG hsqcetgpsi2
TD 1024
SOLVENT CDCl3
NS 2
DS 16
SWH 1600.512 Hz
FIDRES 1.563000 Hz
AQ 0.3199476 sec
RG 2050
DW 312.400 usec
DE 6.50 usec
TE 297.4 K
CNST2 145.0000000
D0 0.00000300 sec
D1 1.50000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
D24 0.00086207 sec
IN0 0.00006210 sec
ZGPTNS

```

```

===== CHANNEL f1 =====
NUC1 1H
P1 10.30 usec
P2 20.60 usec
P28 1000.00 usec
PL1 0.00 dB
SFO1 400.1312004 MHz

```

```

===== CHANNEL f2 =====
CPDPRG2 garp
NUC2 13C
P3 10.00 usec
P4 20.00 usec
PCPD2 60.00 usec
PL2 6.30 dB
PL12 25.30 dB
SFO2 100.6188058 MHz

```

```

===== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPNAM3 SINE.100
GPNAM4 SINE.100
GPZ1 80.00 %
GPZ2 20.10 %
GPZ3 11.00 %
GPZ4 -5.00 %
P16 1000.00 usec
P19 600.00 usec
ND0 2
TD 256
SFO1 100.6188 MHz
FIDRES 31.443377 Hz
SW 80.000 ppm
FnMODE Echo-Antiecho
SI 1024
SF 400.1300000 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.40
SI 1024
MC2 echo-antiecho
SF 100.6127690 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0

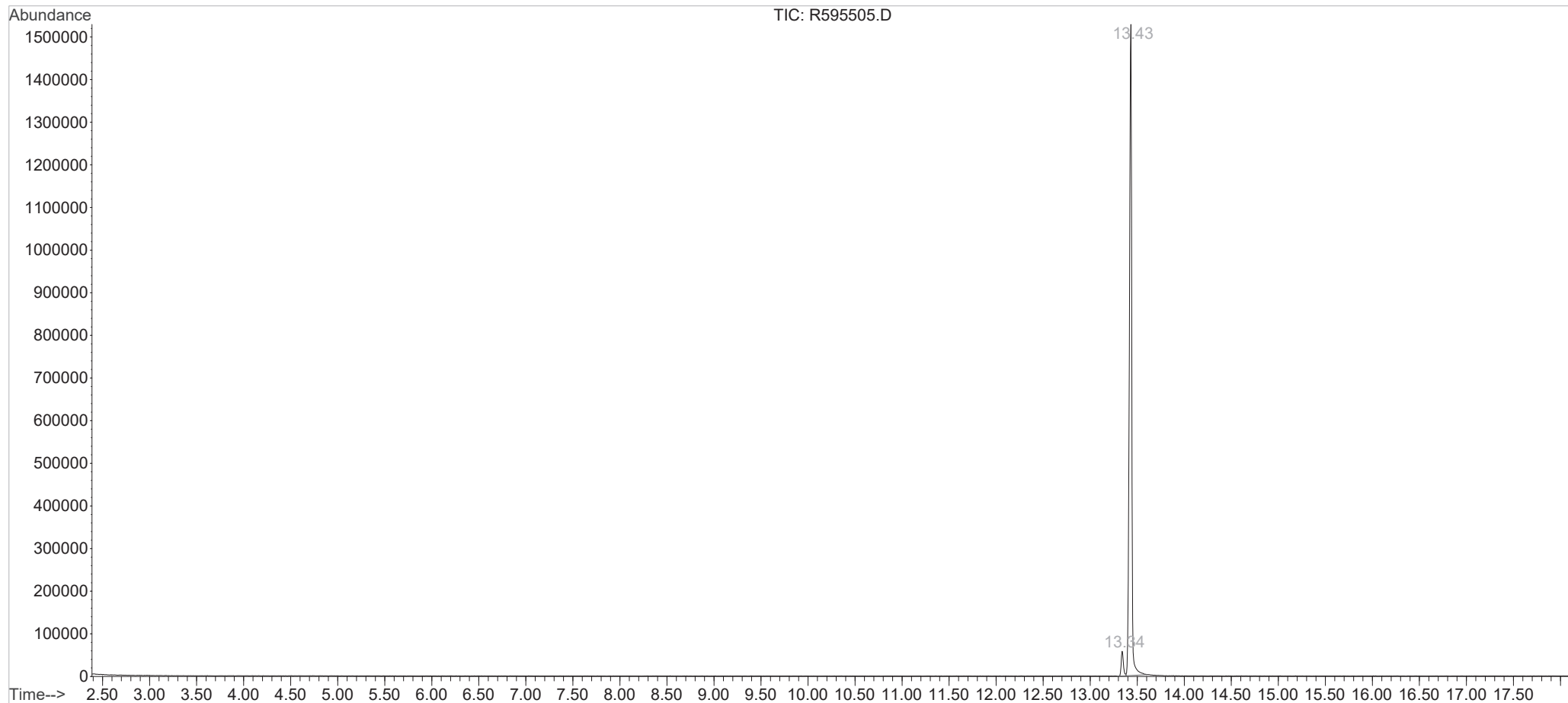
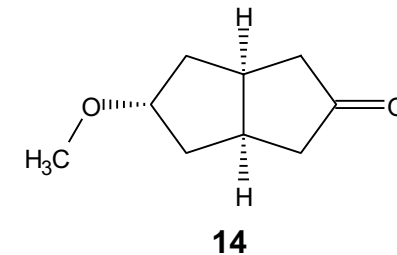
```

Library Search Report

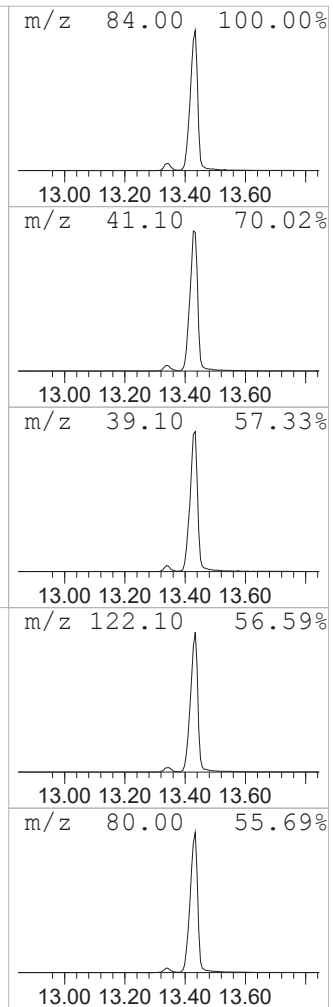
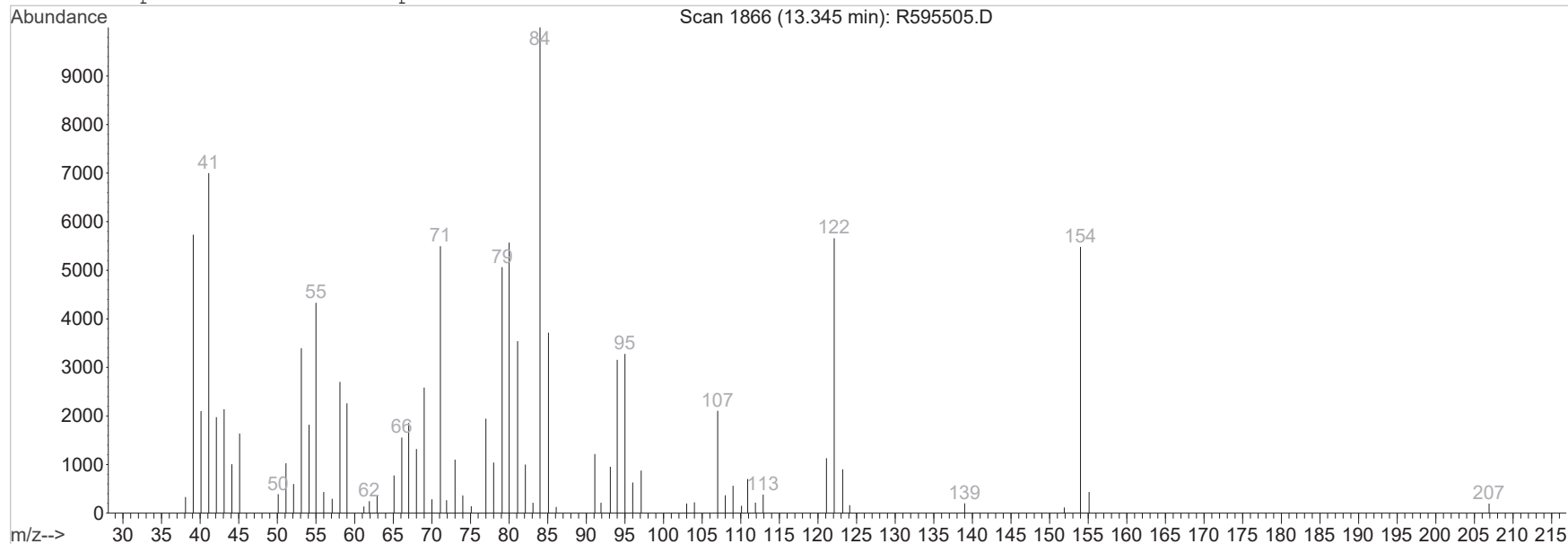
Acq On  
Sample  
Misc : CH3CN

Vial: 29  
Operator:  
Inst : Instrumen  
Multiplr: 1.00  
Sample Amount: 0.00

MS Integration Params: autoint1.e  
Method  
Title :



Unknown Spectrum based on Apex

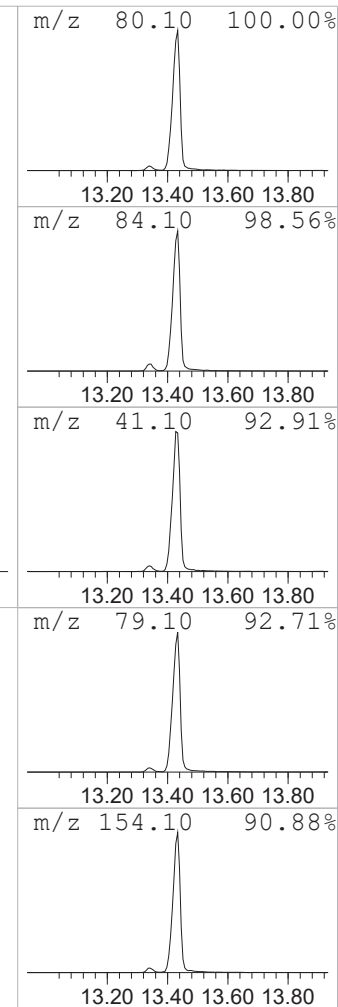
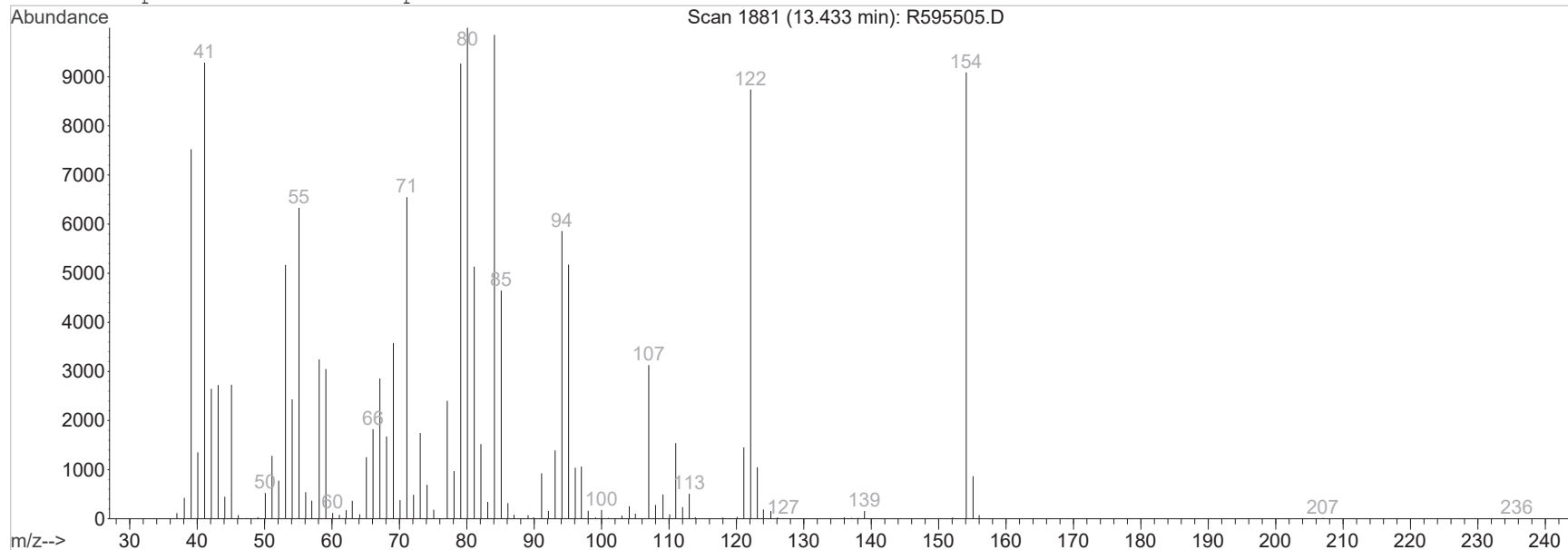


Peak Number: 1 at 13.35 min Area: 933618 Area % 3.36

-----  
 The database \MSDCHEM\ from each library were retrieved  
 -----

Ref#	CAS#	Qual

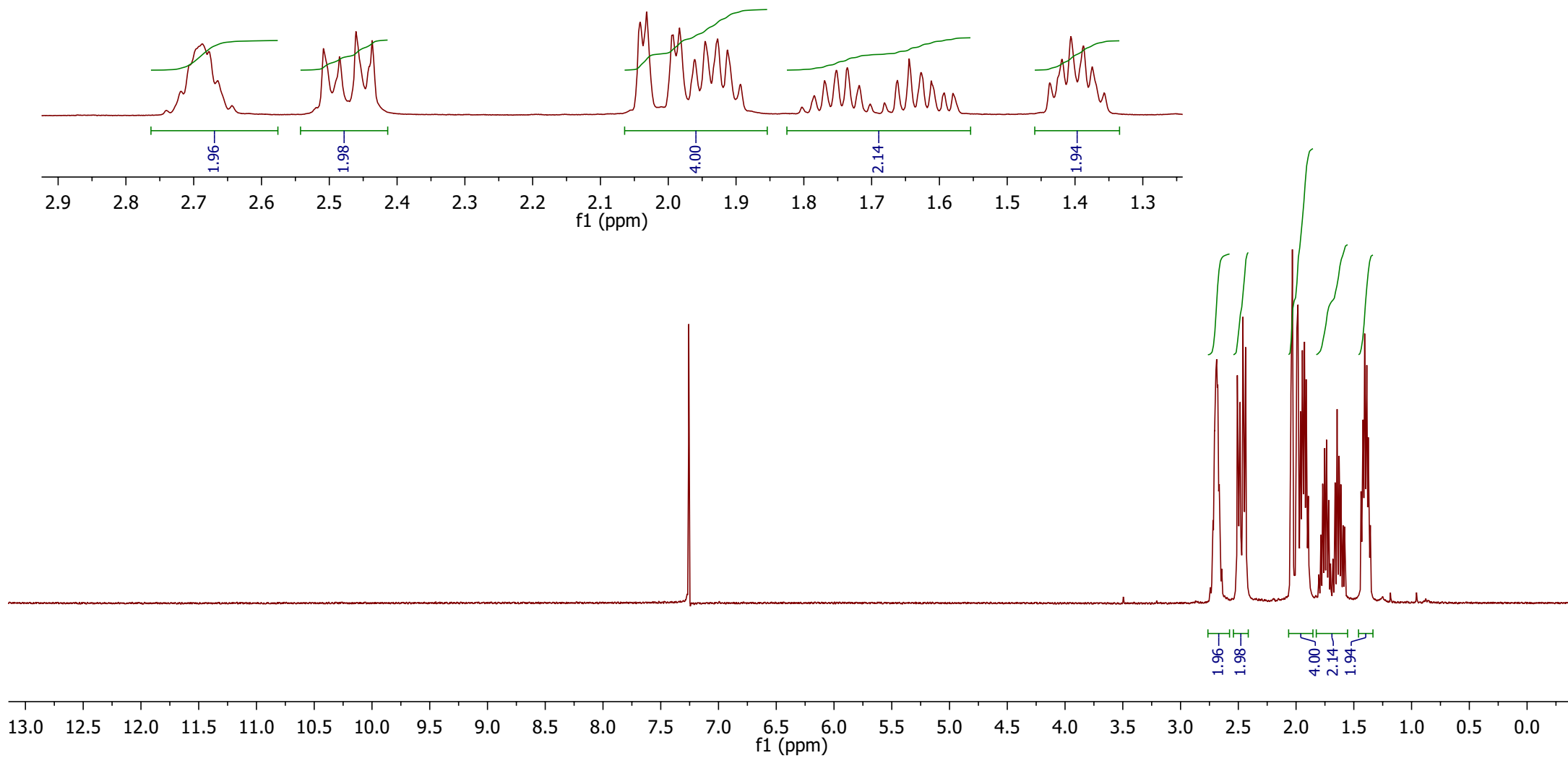
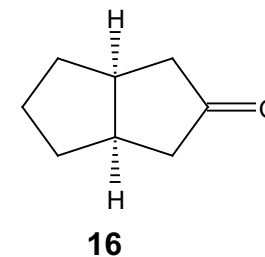
Unknown Spectrum based on Apex



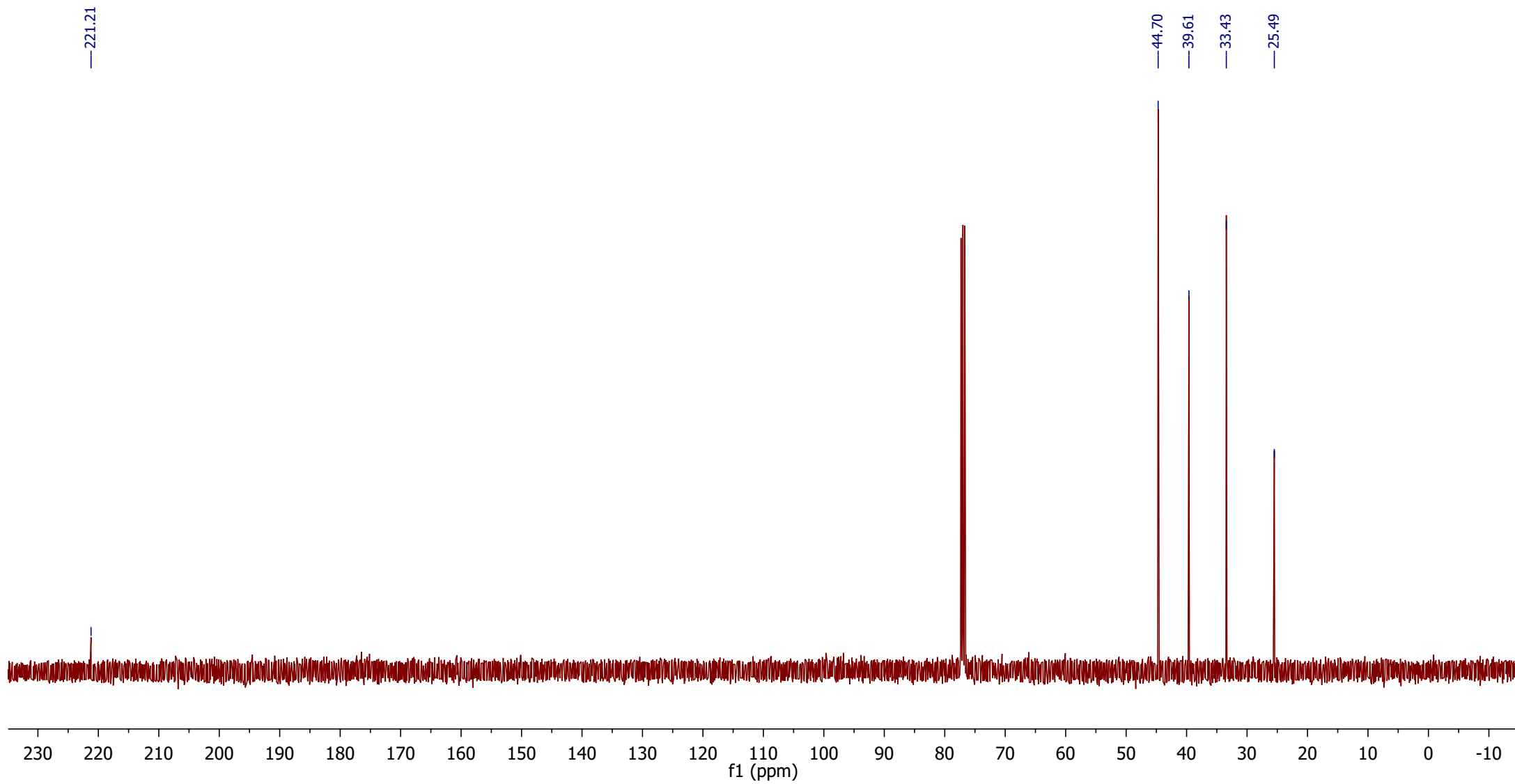
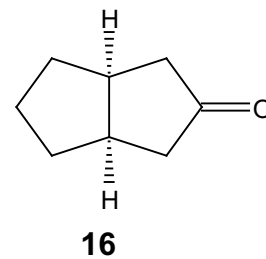
Peak Number: 2 at 13.43 min Area: 26875652 Area % 96.64

-----  
 The database \MSDCHEM\ from each library were retrieved  
 -----  
 Ref# CAS# Qual

$^1\text{H}$  NMR (Chloroform-*d*, 400 MHz)  $\delta$  1.33 – 1.46 (2H, m), 1.55 – 1.82 (2H, m), 1.85 – 2.06 (4H, m), 2.41 – 2.54 (2H, m), 2.58 – 2.76 (2H, m)



$^{13}\text{C}$  NMR (cdcl<sub>3</sub>, 101 MHz)  $\delta$  25.5, 33.4, 39.6, 44.7, 221.2.

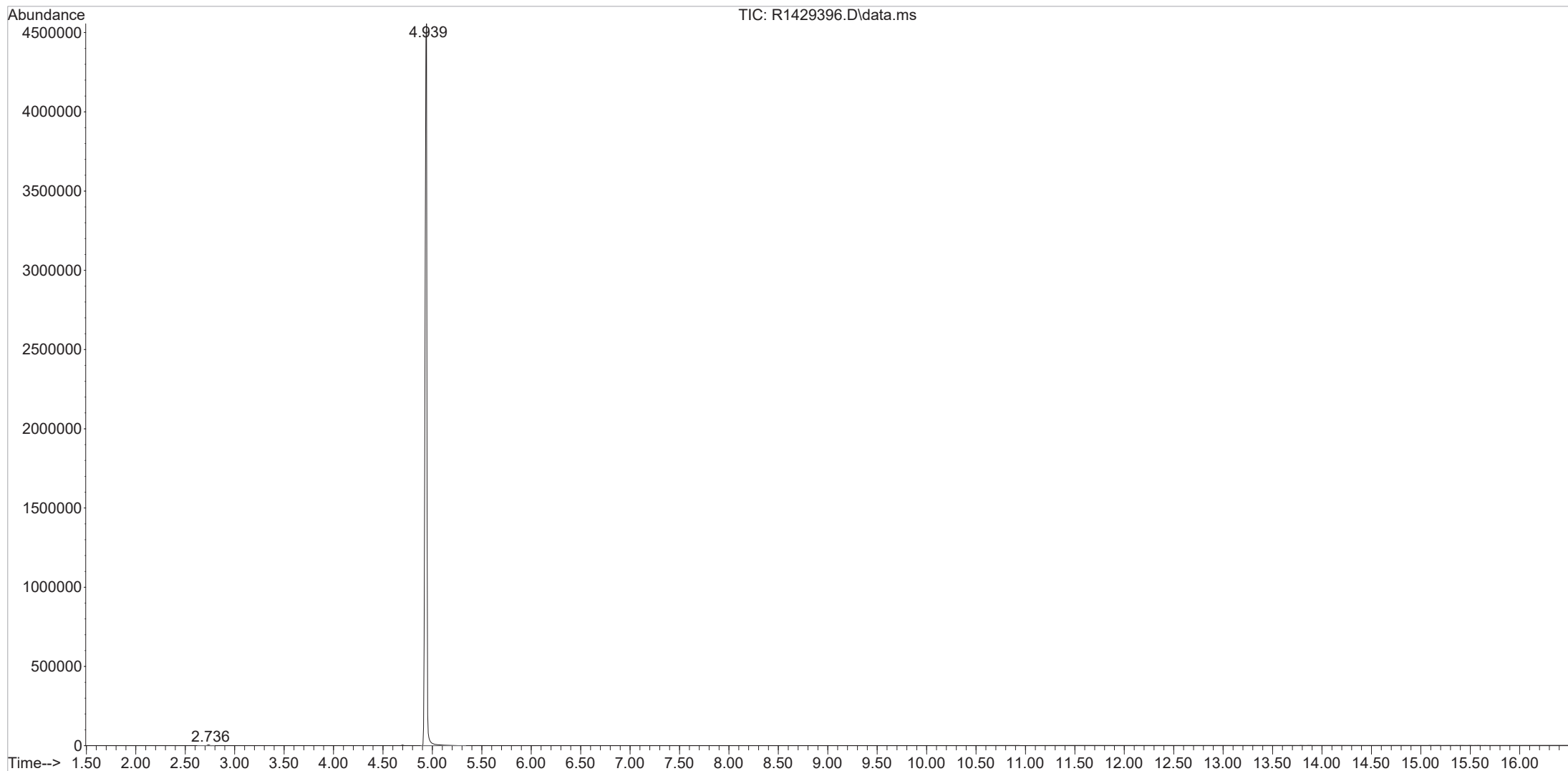
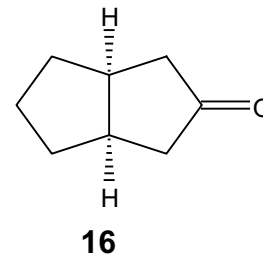




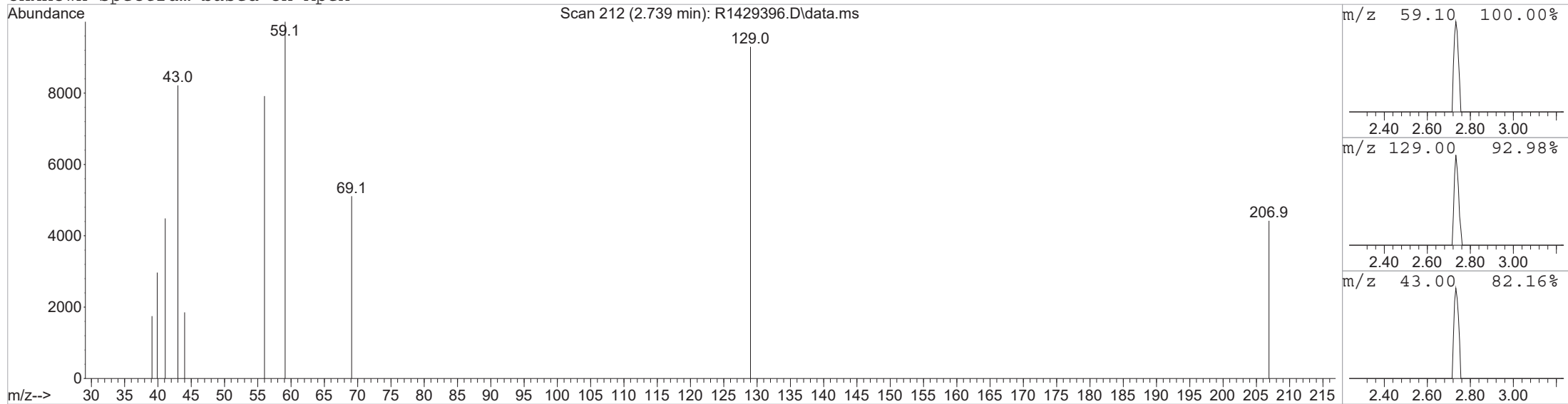
Acq On  
Operator :  
Sample  
Misc : CH3OH  
ALS Vial : 57 Sample Multiplier: 1

Search Libraries: C:\Database\EMPTY.L Minimum Quality: 0

Unknown Spectrum: Apex  
Integration Events: ChemStation Integrator - autoint1.e



## Unknown Spectrum based on Apex



Sample

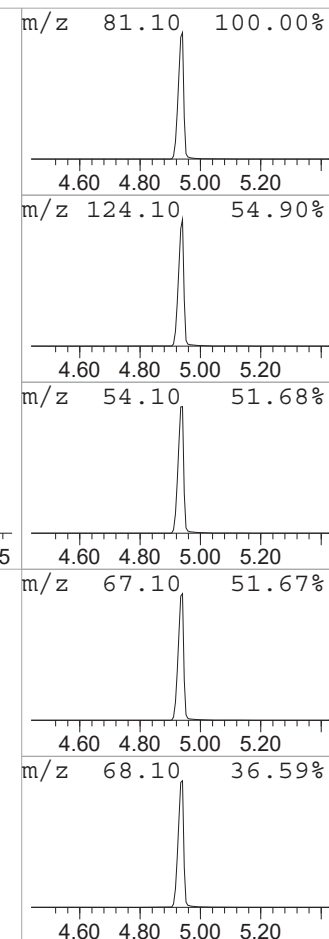
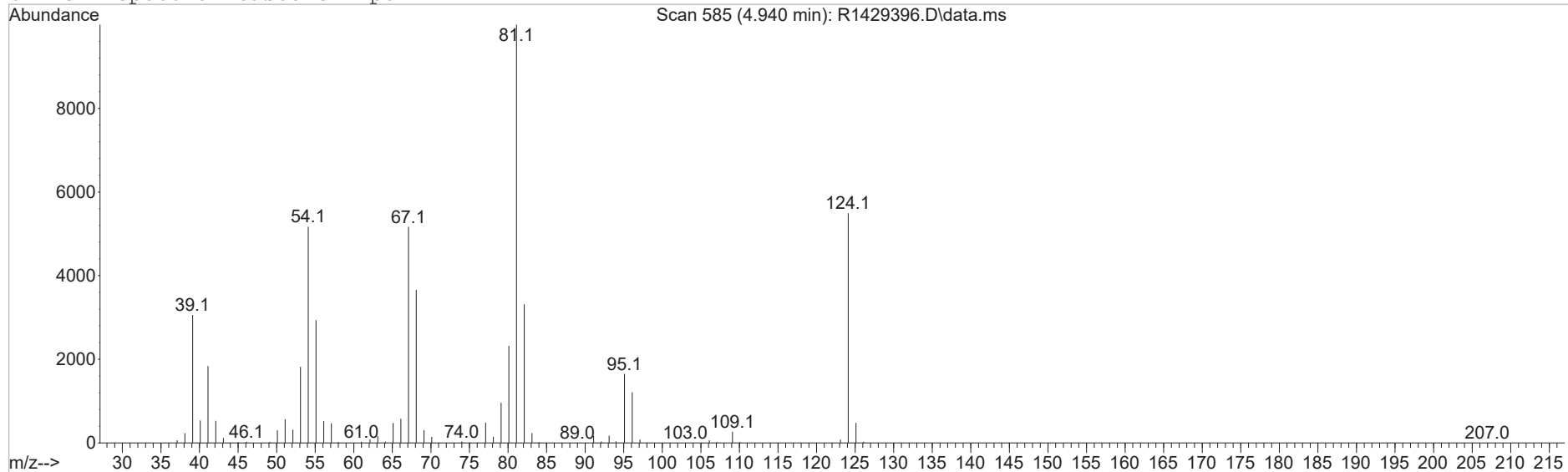
Peak Number: 1 at 2.736 min Area: 87688 Area % 0.15

The 3 best hits from each library. Ref\# CAS\# Qual

-----  
No hits were retrieved.

## Unknown Spectrum based on Apex

Scan 585 (4.940 min): R1429396.D\data.ms



Sample

Peak Number: 2 at 4.939 min Area: 59369715 Area % 99.85

The 3 best hits from each library. Ref\# CAS\# Qual

-----  
No hits were retrieved.