Meroterpene-like α-glucosidase inhibitors based on biomimic reactions staring from β-caryophyllene

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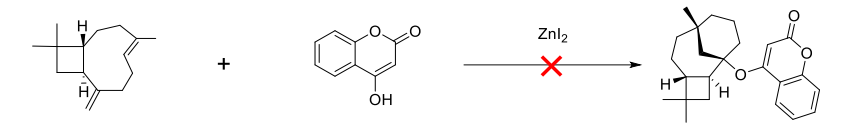
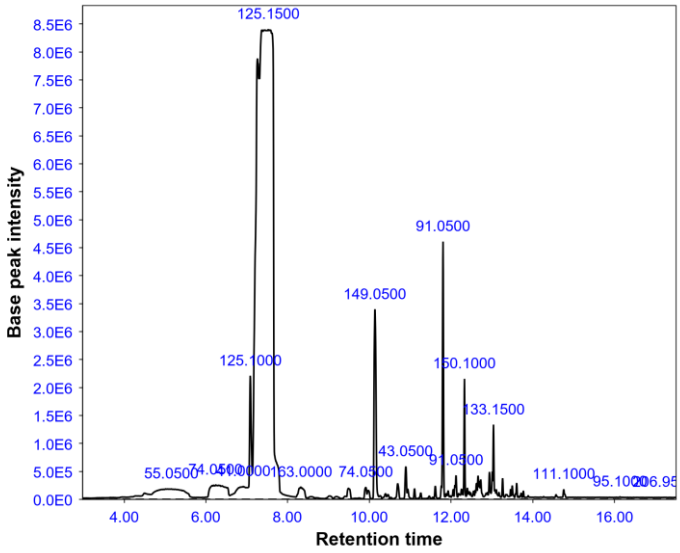
Content

Figure S1. GC-EI MS (a) and LC-ESI-MS/MS analysis

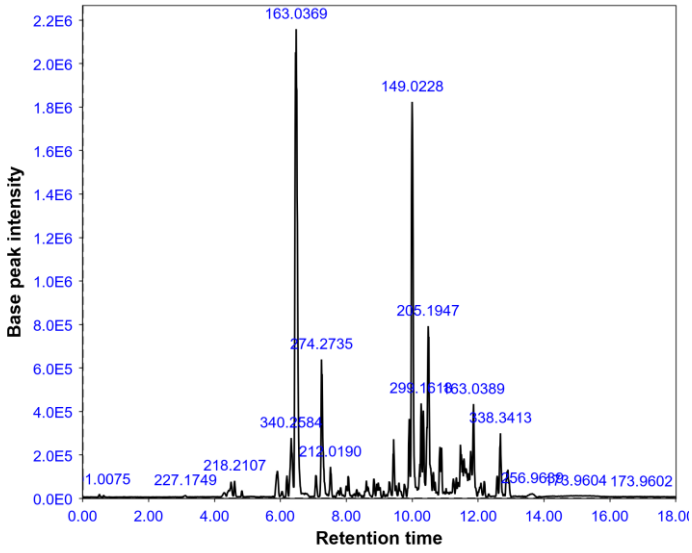


(a) GC-EI-MS analysis



The crude product was dissolved in MeOH (200 μg/ml) and was analyzed on a Shimadzu GCMS-QP2010 Ultra instrument equipped with a capillary column of Rxi® -5Sil MS (30 m × 0.25 mm i.d., 0.25 μm film thickness). Helium (He) gas was used as a mobile phase at a constant flow of 1.3 mL/min. The temperature was held at 150 °C for 5 min, then increased to 300 at 4 °C/min, maintaining the last temperature for 5 min. The temperature of the ion source was 250 °C. EI-MS spectra (*m/z* 35 ~ 500) were recorded with a scan event time of 0.3 s. Electron energy was 70 eV. The raw data was saved into netCDF format in the GCMS solution software and then was converted into mzXML format by ProteoWizard MSConvert 3. The TIC chromatography was extracted using MZMine2.

(b) LC-QTOF-MS/MS analysis

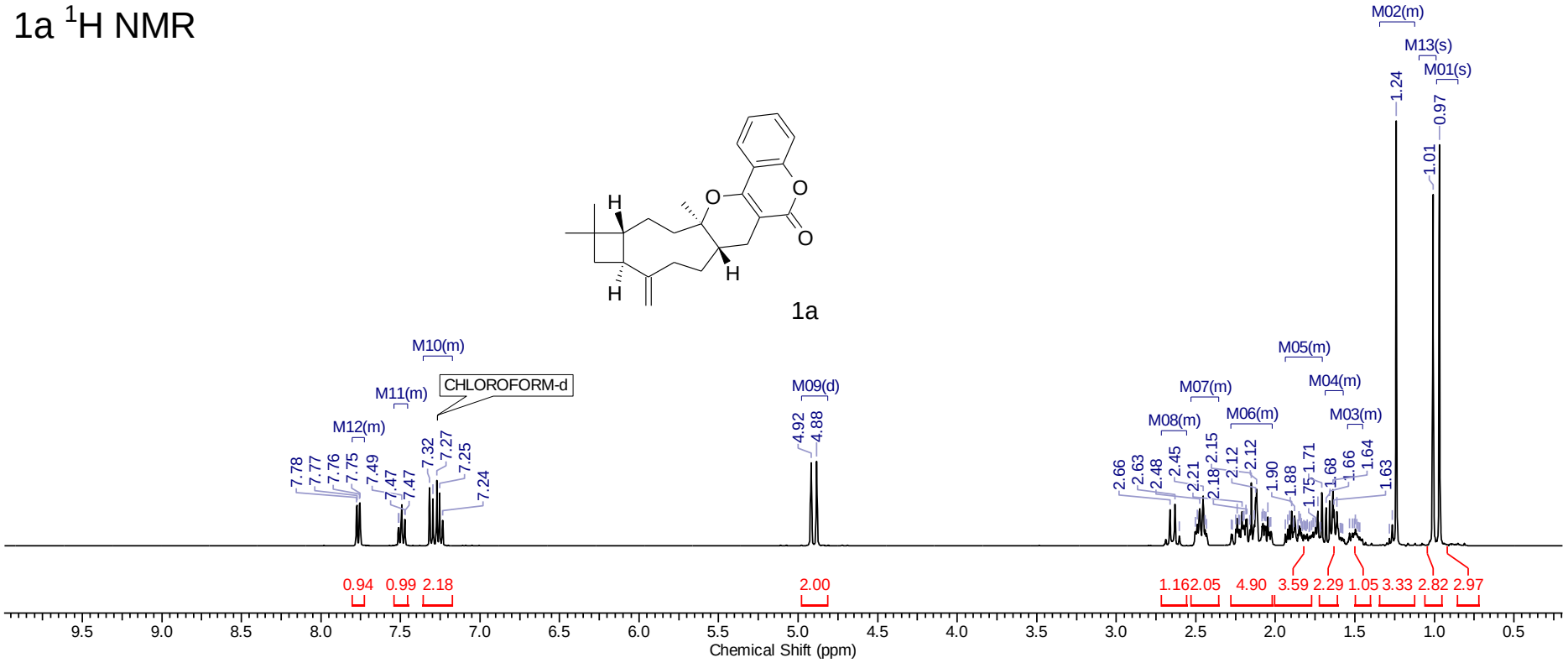


The crude product was analyzed by AB SCIEX TripleTOF5600+ equipped with a Shimadzu UPLC (LC-30A）Shim-pack XR-ODS (100 mm × 2.1 mm, 1.7 μ m) column. The temperature was maintained at 30 ° C. Mixtures of H_2O (A), and MeOH (B) were eluted at the flow rate of 0.3 mL/min with a linear gradient of 10 ~ 100% B (0 − 17 min). The samples (200 μg/mL in MeOH, 2 μ L portions were injected) were analyzed in data-dependent acquisition (DDA) mode. The full MS survey scan was performed for 150 ms in the range of *m/z* 100 ~ 2000; The collision energy was set as 40 eV. The raw data were converted to the mzXML format with MSConvert 3.0. The TIC chromatography was extracted using MZMine2 with *m/z* range 100~1500.

Figure S2: NMR and HR-MS spectra

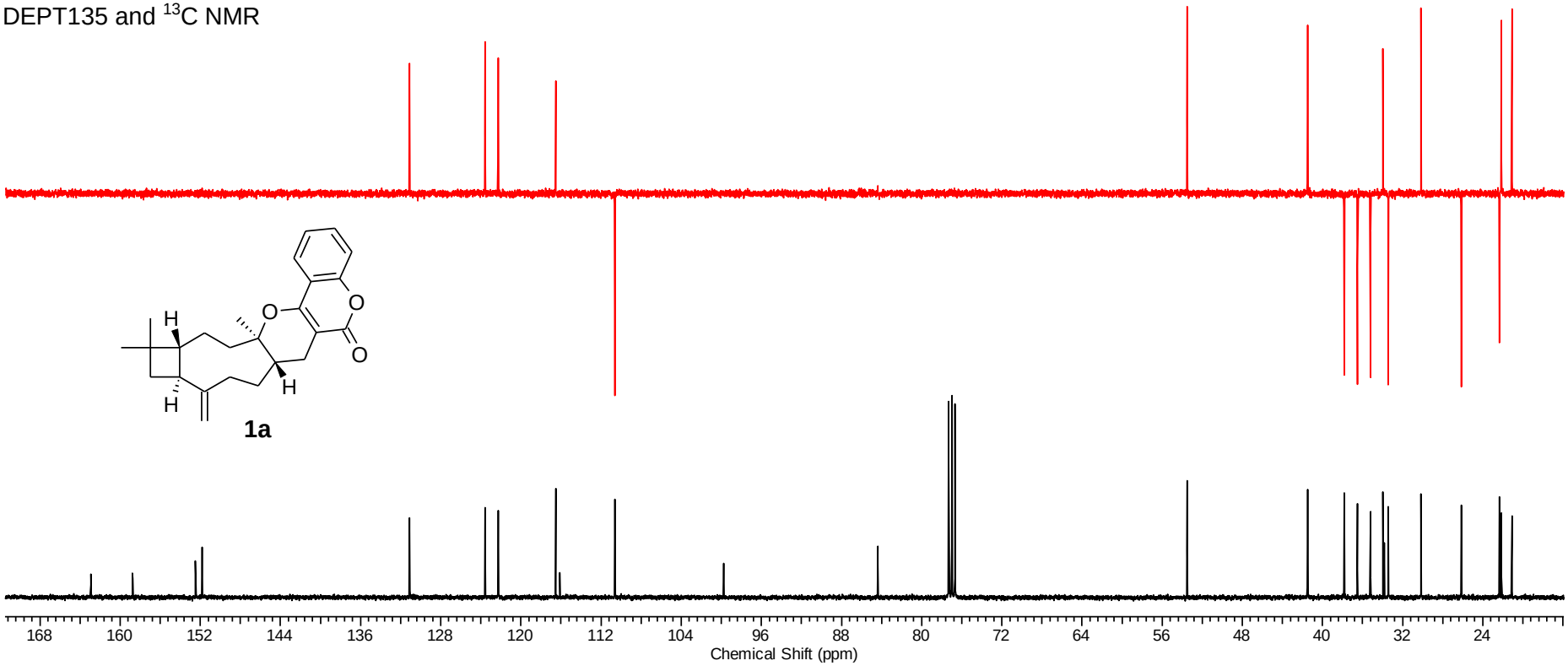
Compound 1a

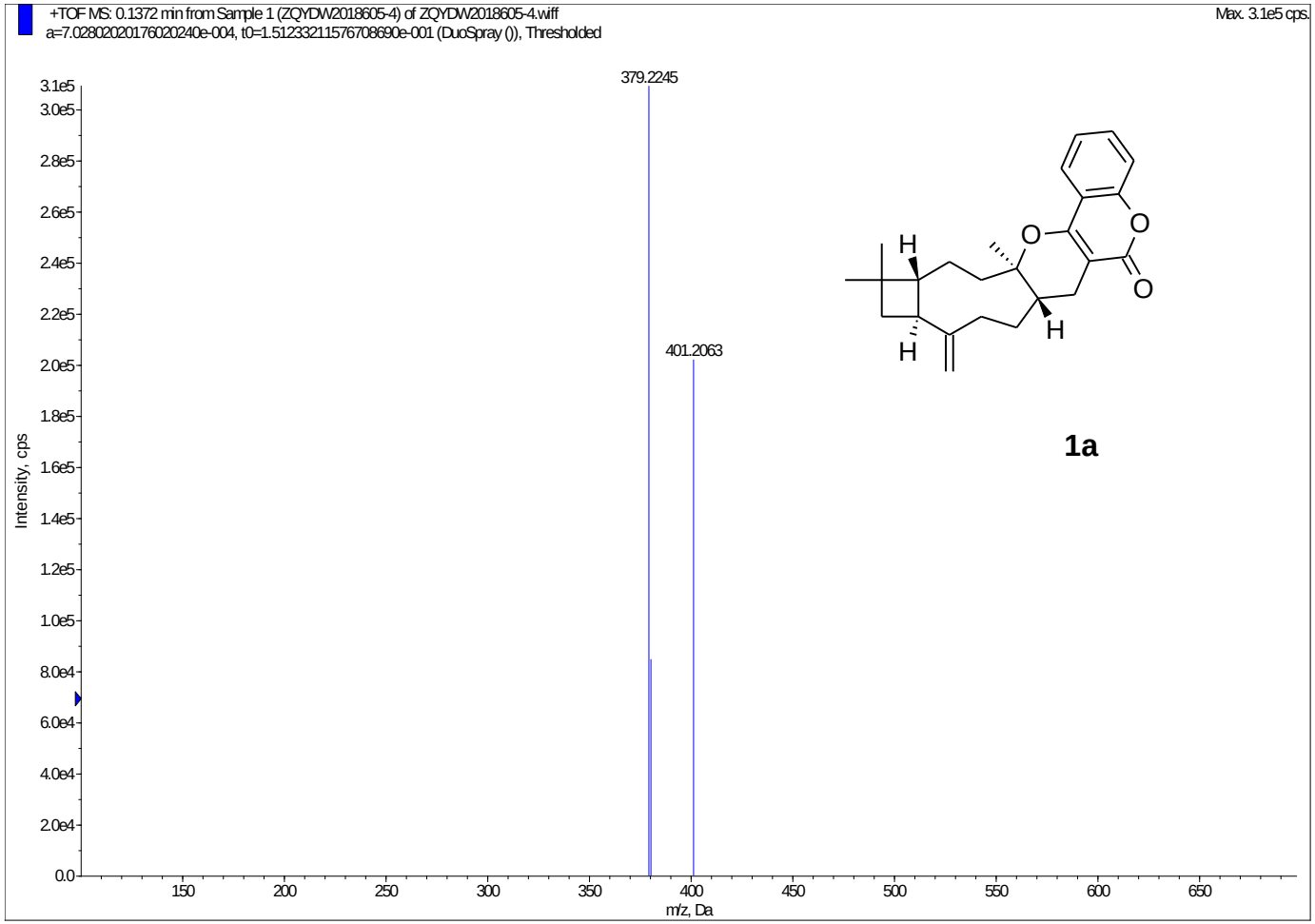
1a ^{1}H NMR



1a

DEPT135 and ^{13}C NMR

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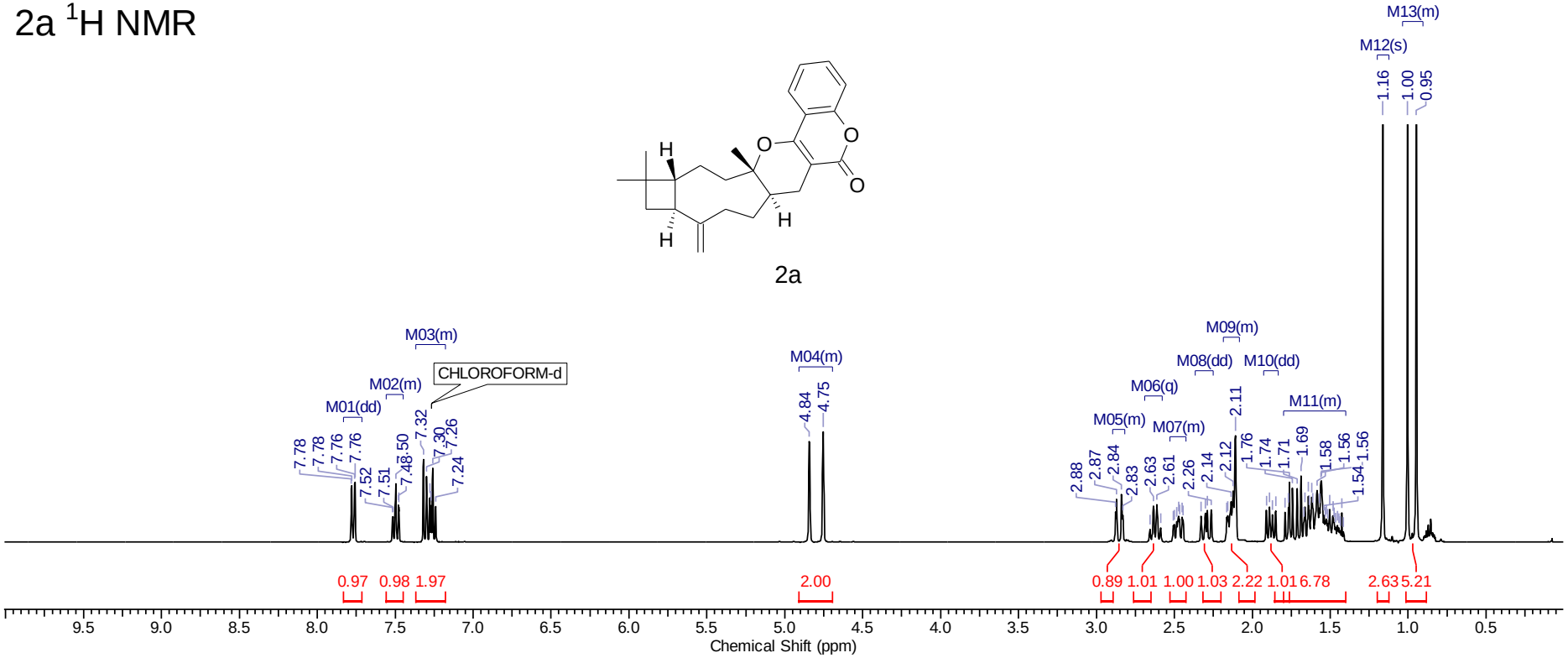
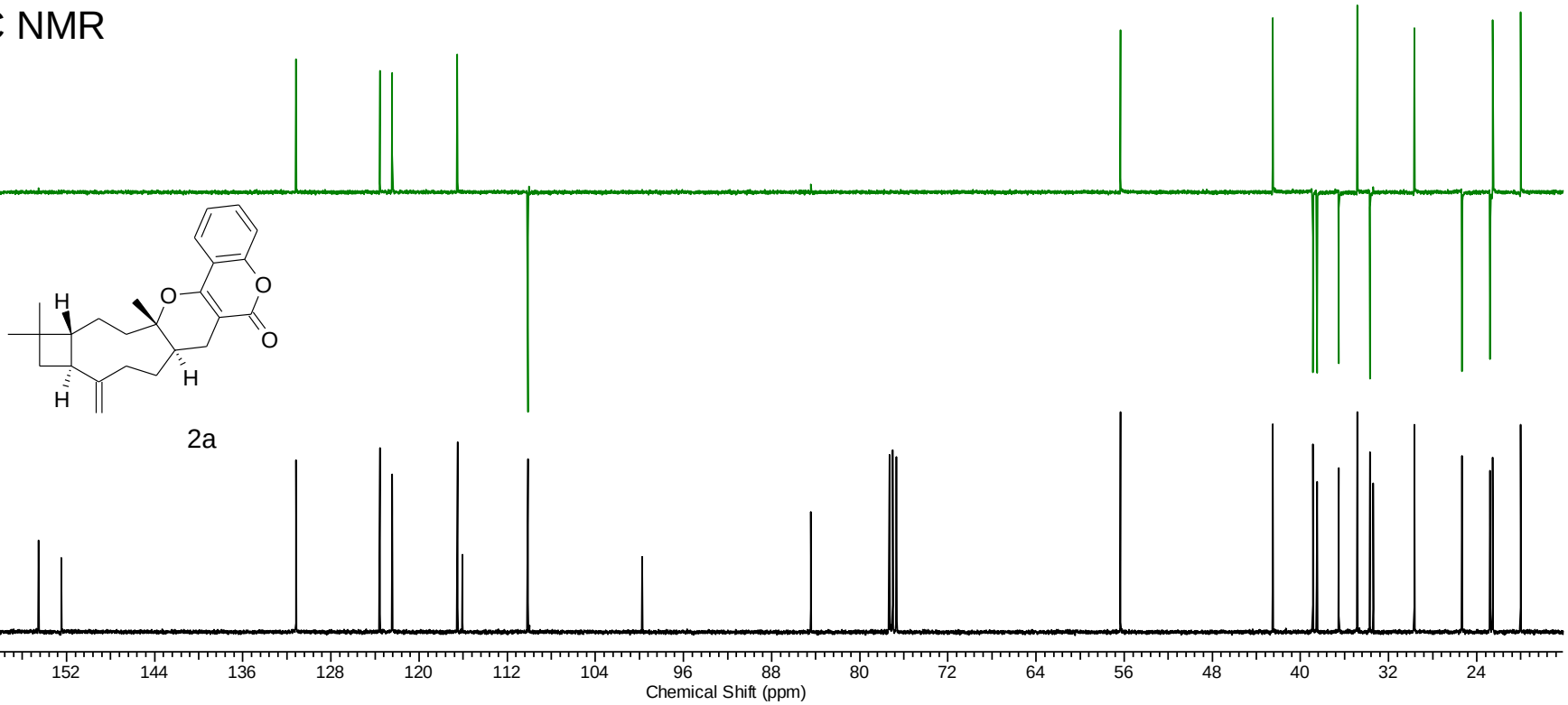
a=7.02802020176020240e-004, t0=1.51233211576708690e-001 (DuoSpray ()), Thresholded
Max. 3.1e5 cps.
379.2245
401.2063
Intensity, cps
m/z, Da
3.1e5
3.0e5
2.8e5
2.6e5
2.4e5
2.2e5
2.0e5
1.8e5
1.6e5
1.4e5
1.2e5
1.0e5
8.0e4
6.0e4
4.0e4
2.0e4
0.0
150
200
250
300
350
400
450
500
550
600
650
H
O
O
O
H
H
1a

Compound 2a

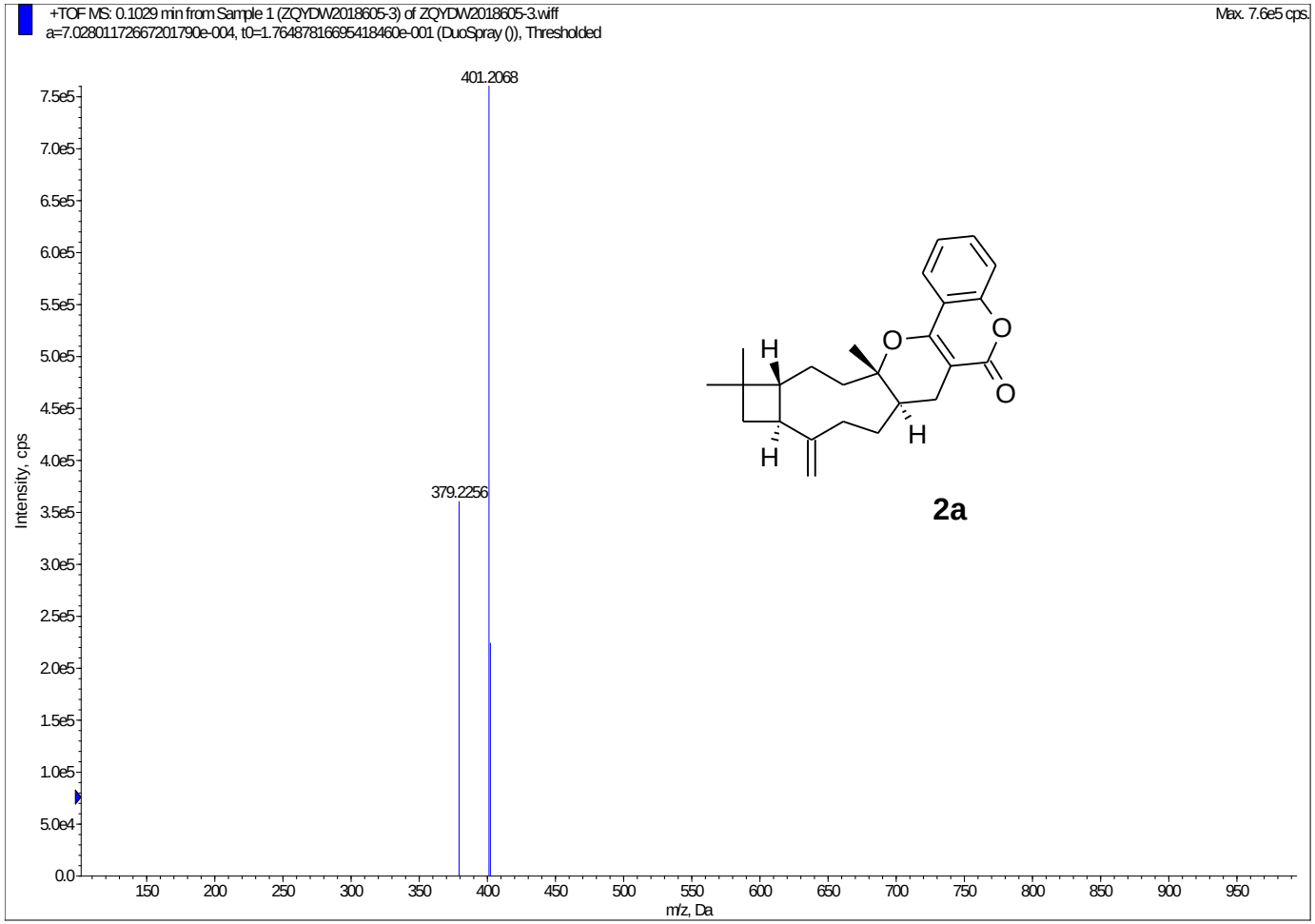
2a ^{1}H NMR



2a ^{13}C NMR


H
O
O
O
H
H
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)

2a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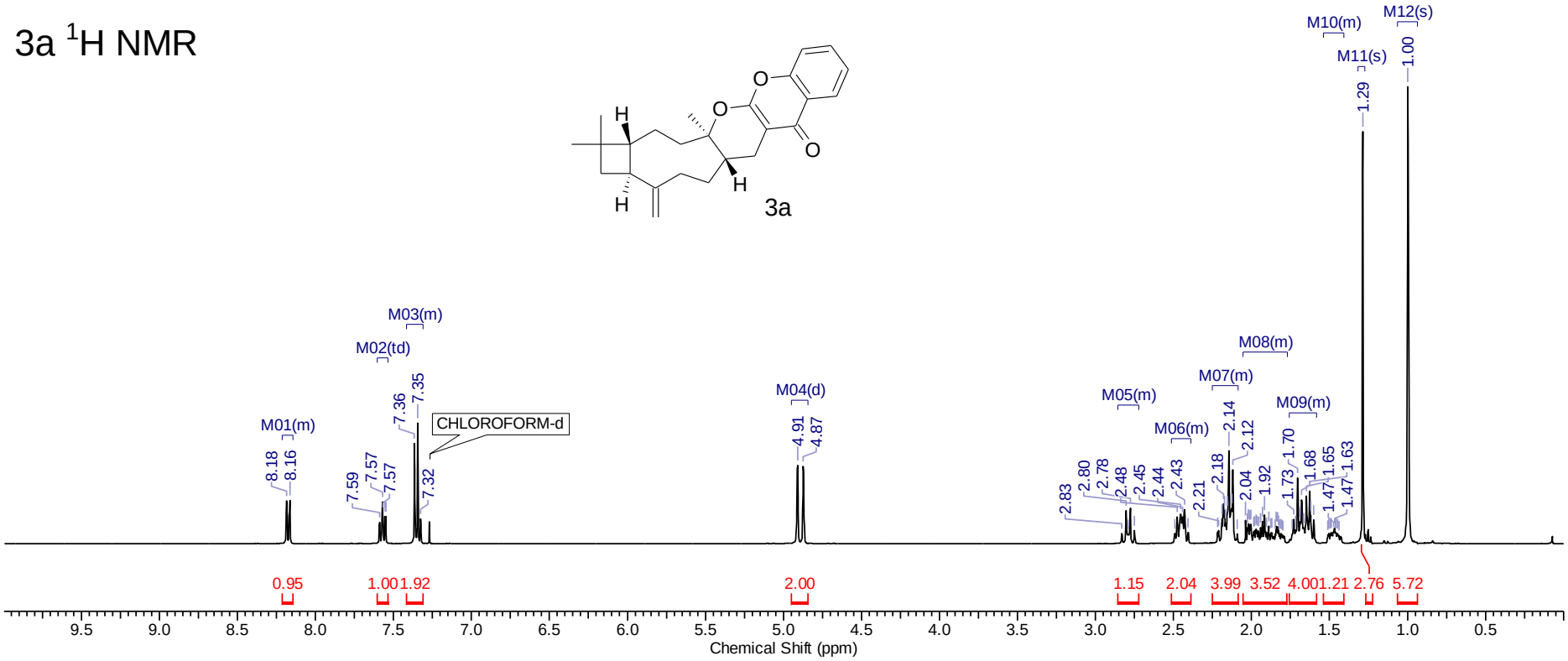
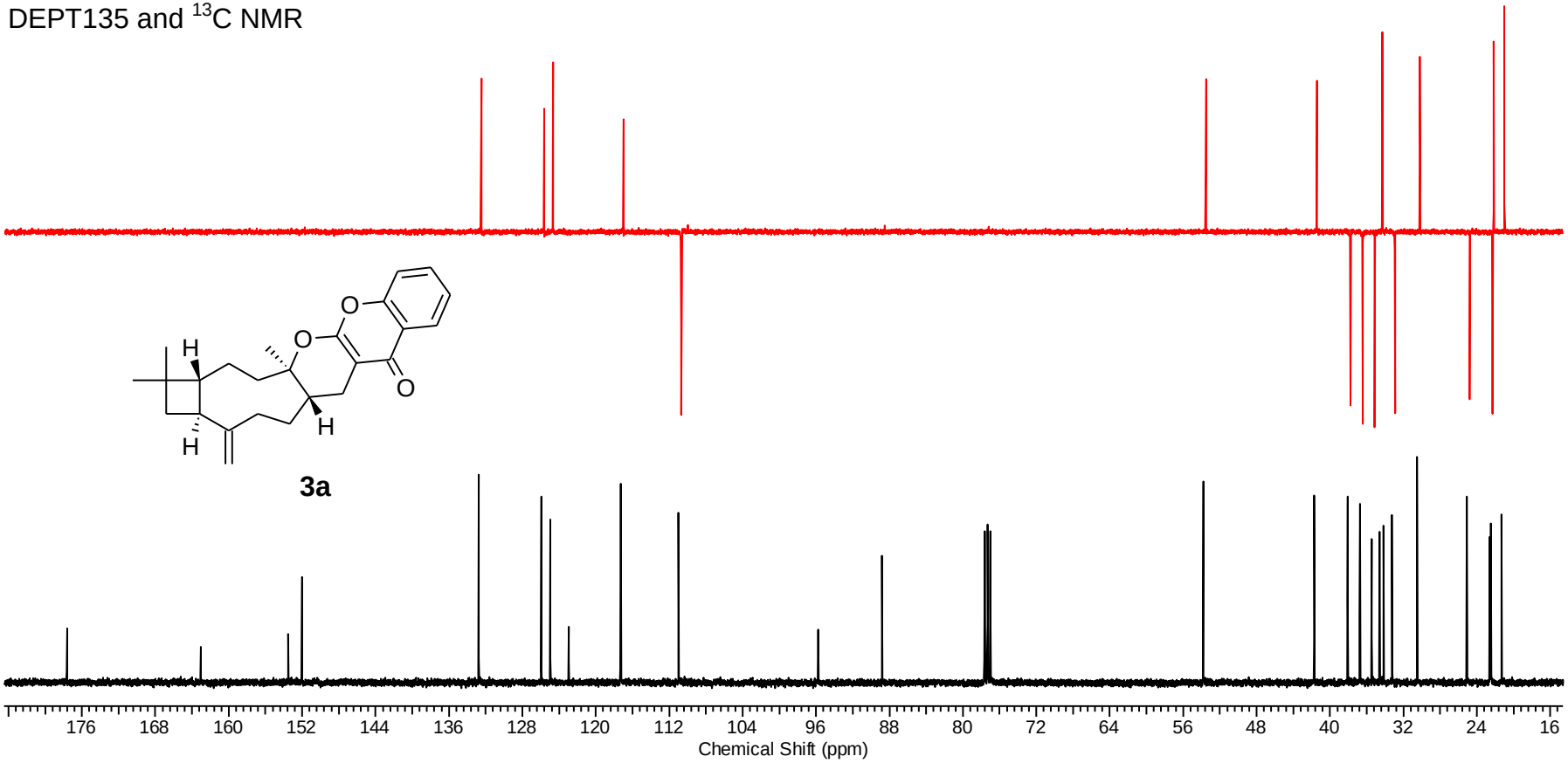
Max. 7.6e5 cps.
401.2068
379.2256
Intensity, cps
m/z, Da
2a

Compound 3a

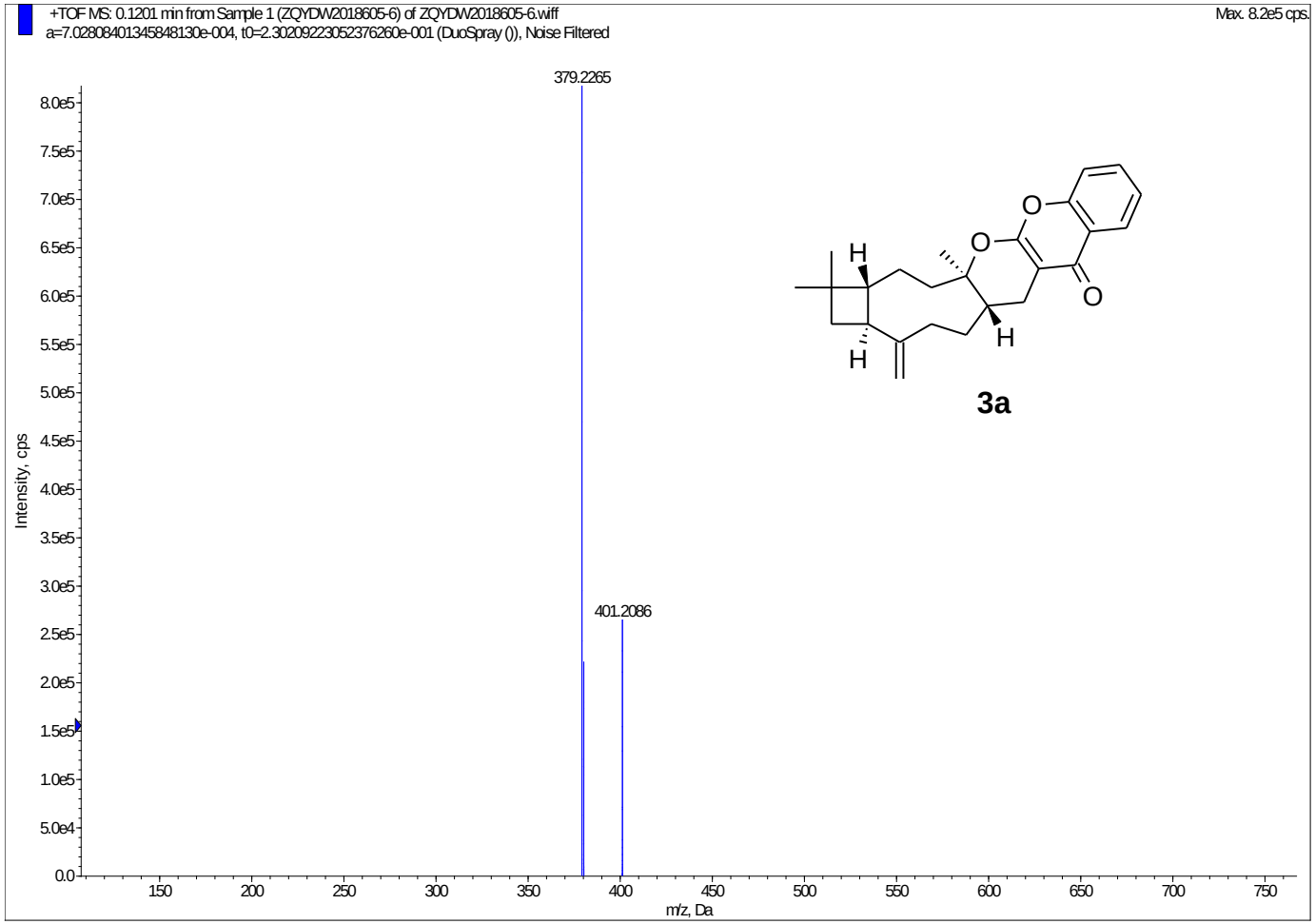
3a ^{1}H NMR



DEPT135 and ^{13}C NMR



3a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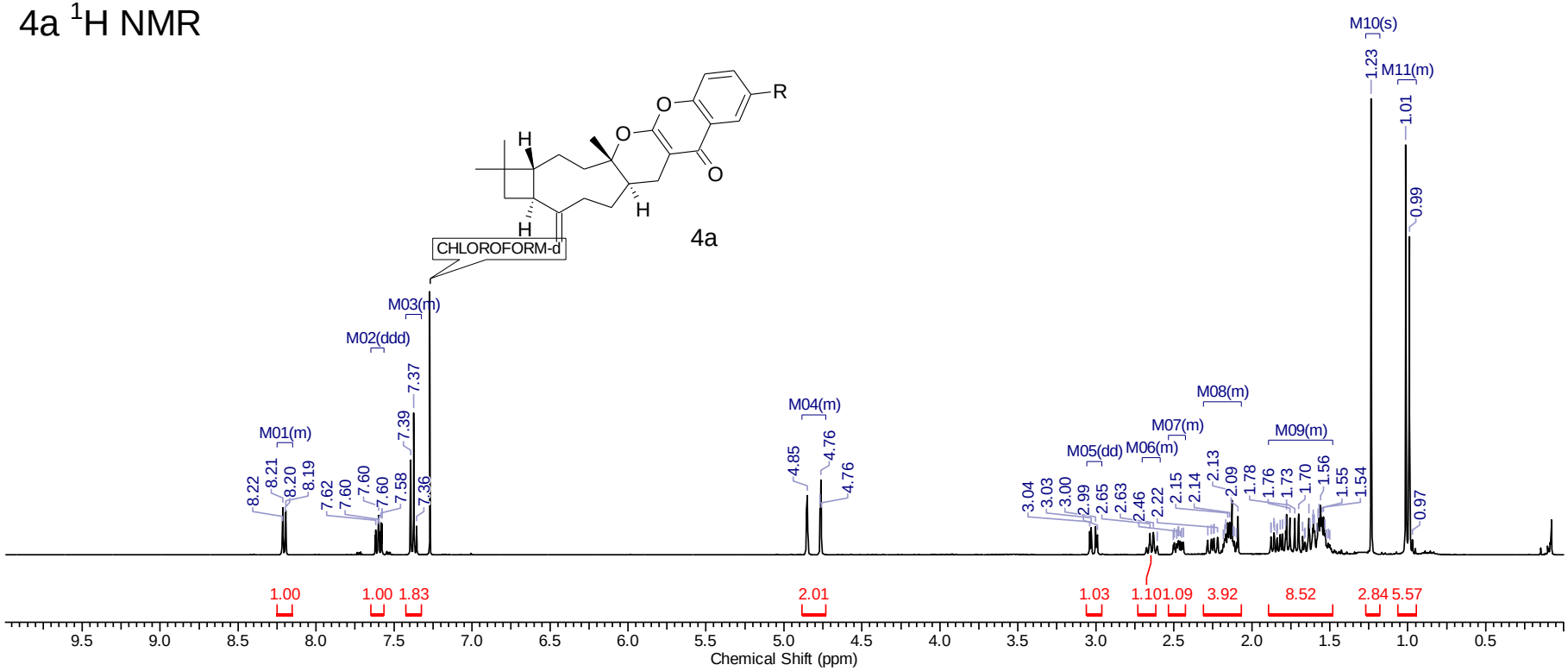
Max. 8.2e5 cps.
379.2265
401.2086
Intensity, cps
m/z, Da
8.0e5
7.5e5
7.0e5
6.5e5
6.0e5
5.5e5
5.0e5
4.5e5
4.0e5
3.5e5
3.0e5
2.5e5
2.0e5
1.5e5
1.0e5
5.0e4
0.0
150
200
250
300
350
400
450
500
550
600
650
700
750
O
O
O
H
H
H

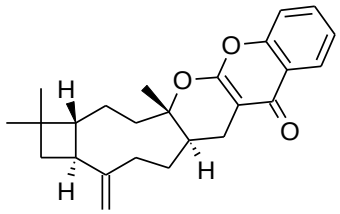
3a

Compound 4a

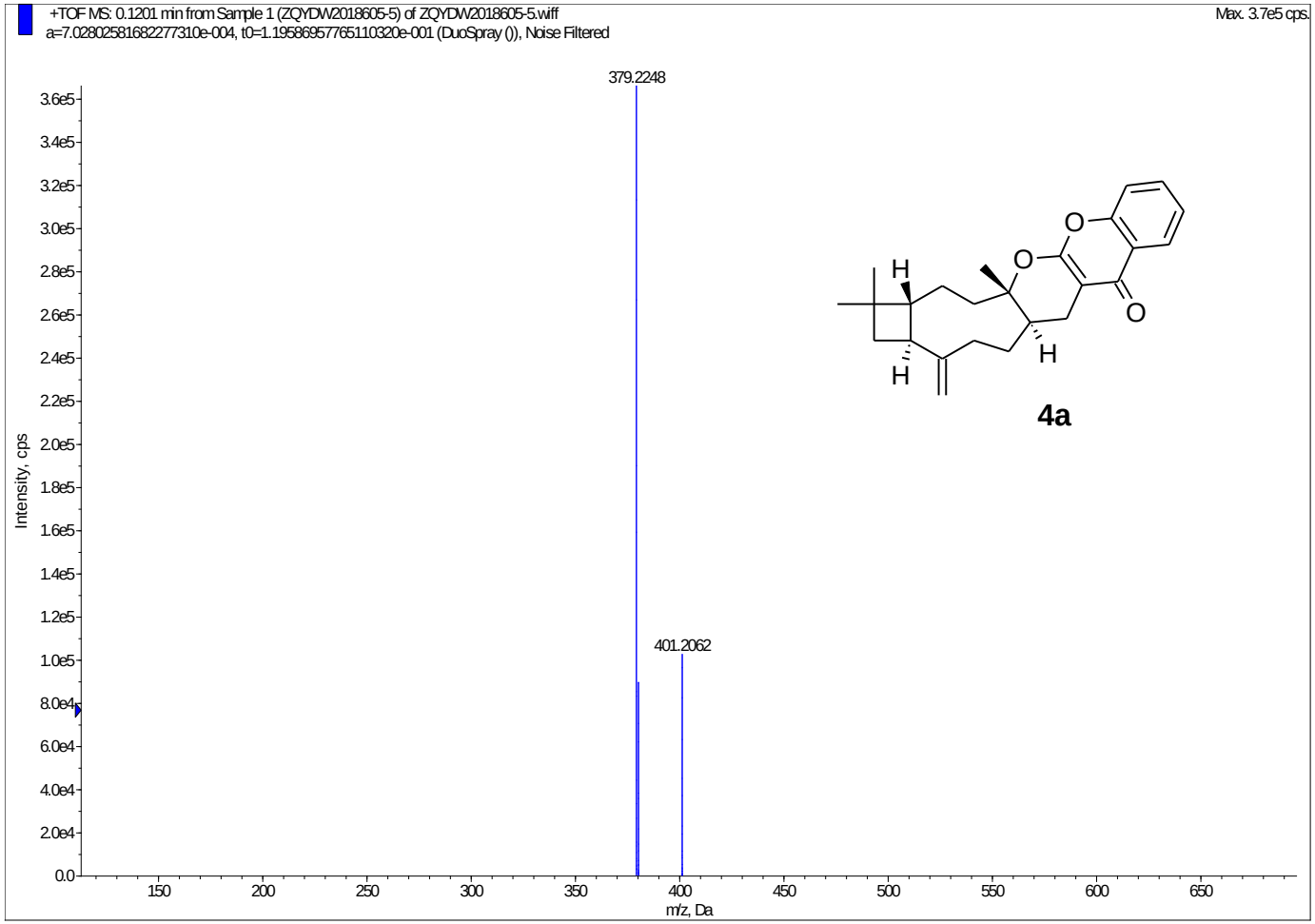
4a ^{1}H NMR



DEPT135 and ^{13}C NMR



4a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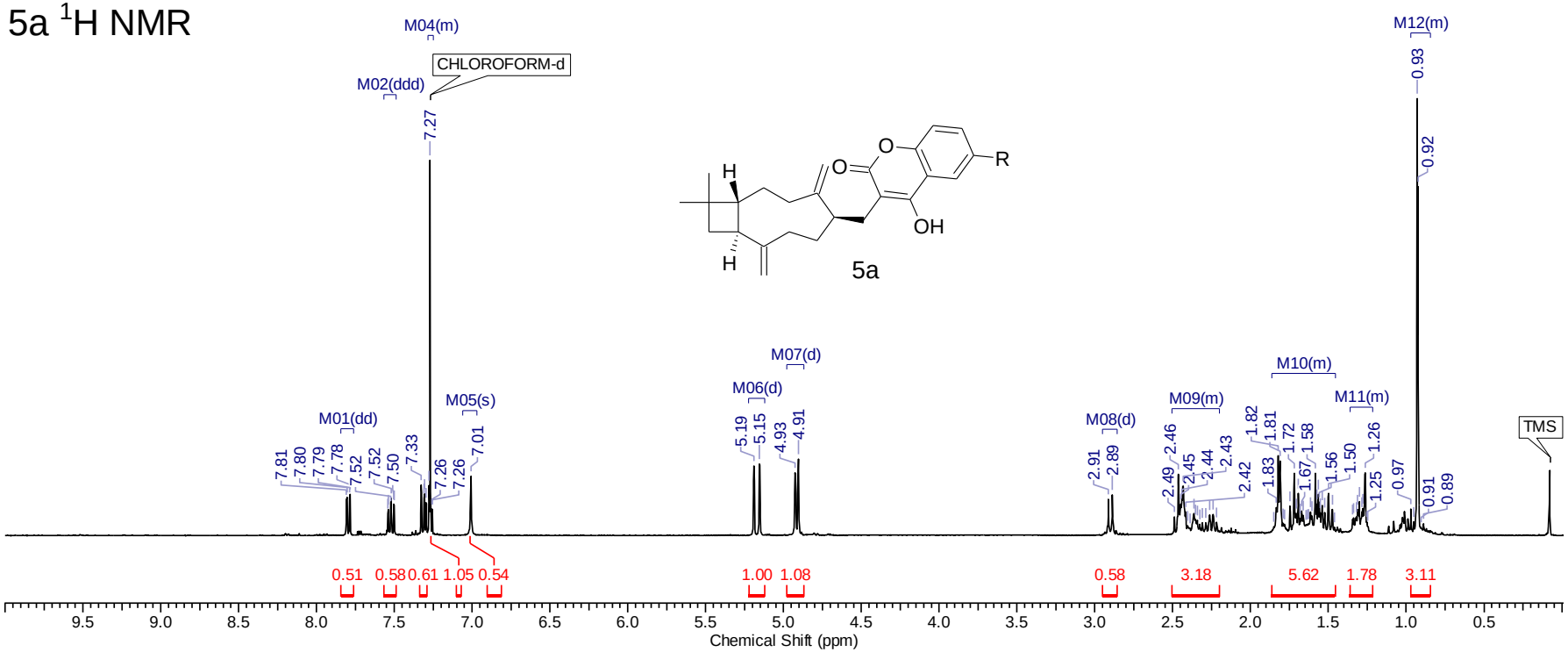
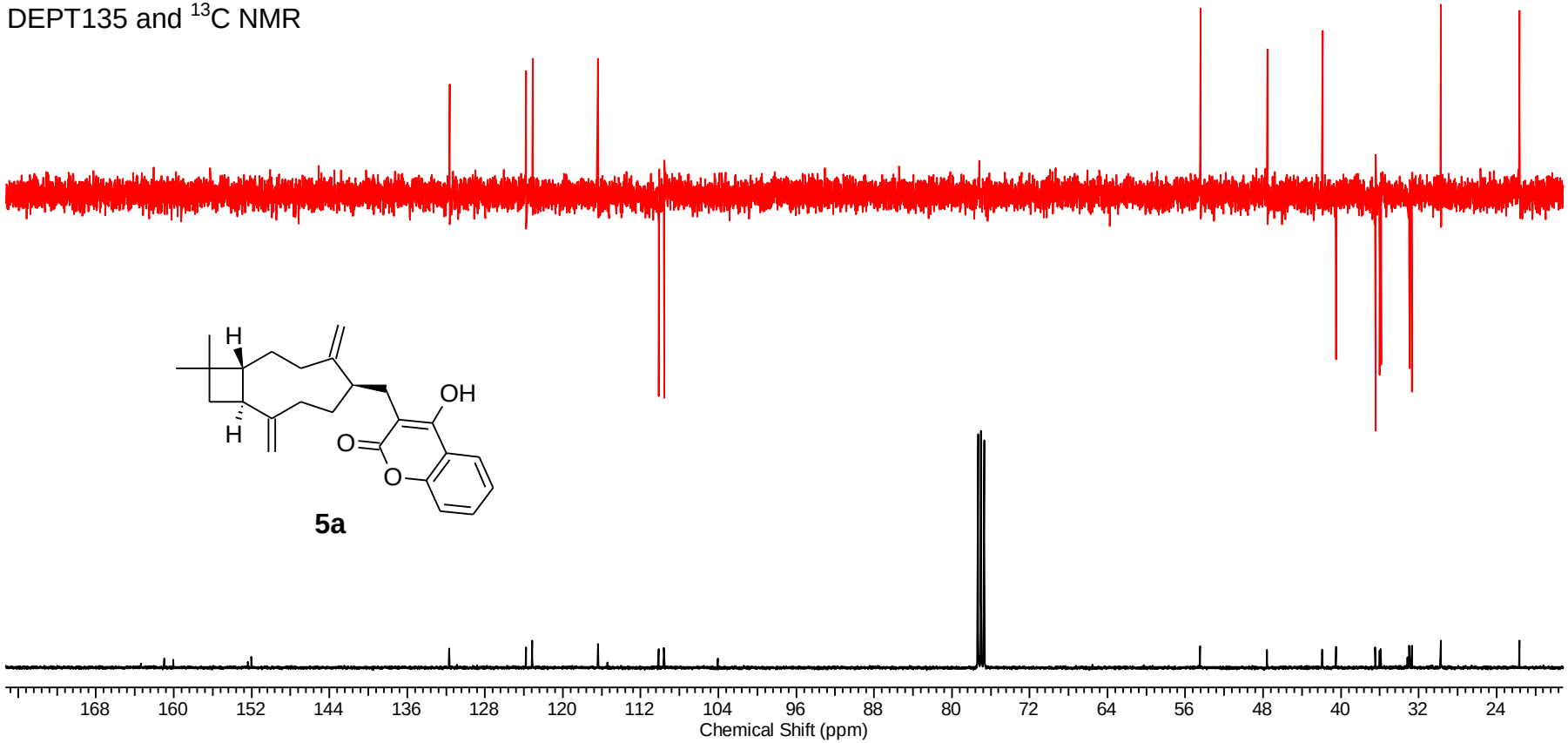
a=7.0280258168227731 0e-004, t0=1.1958695776511032 0e-001 (DuoSpray ()), Noise Filtered
Max. 3.7e5 cps.
379.2248
401.2062
Intensity, cps
m/z, Da
4a

Compound 5a

5a ^{1}H NMR

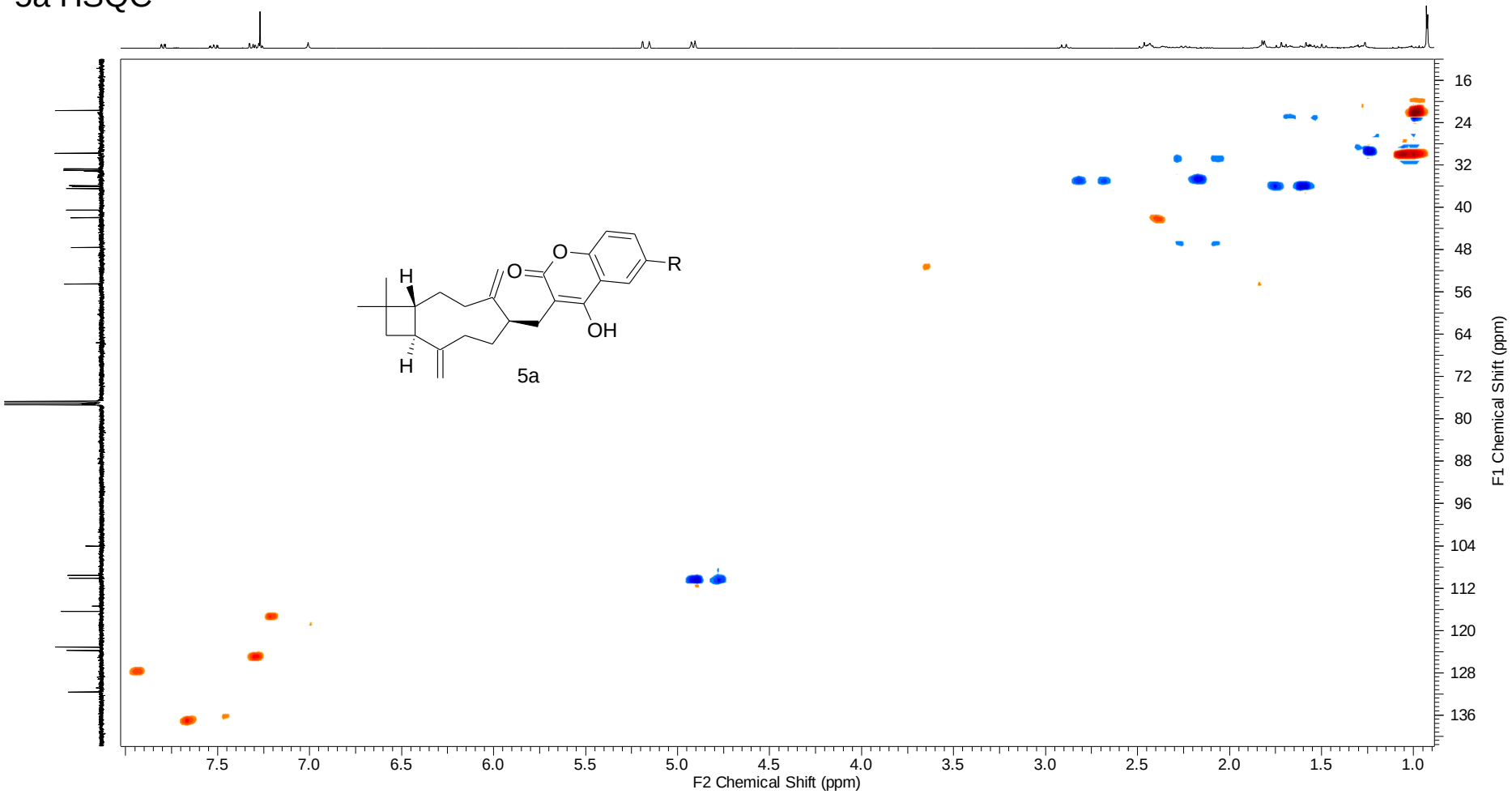


DEPT135 and ^{13}C NMR

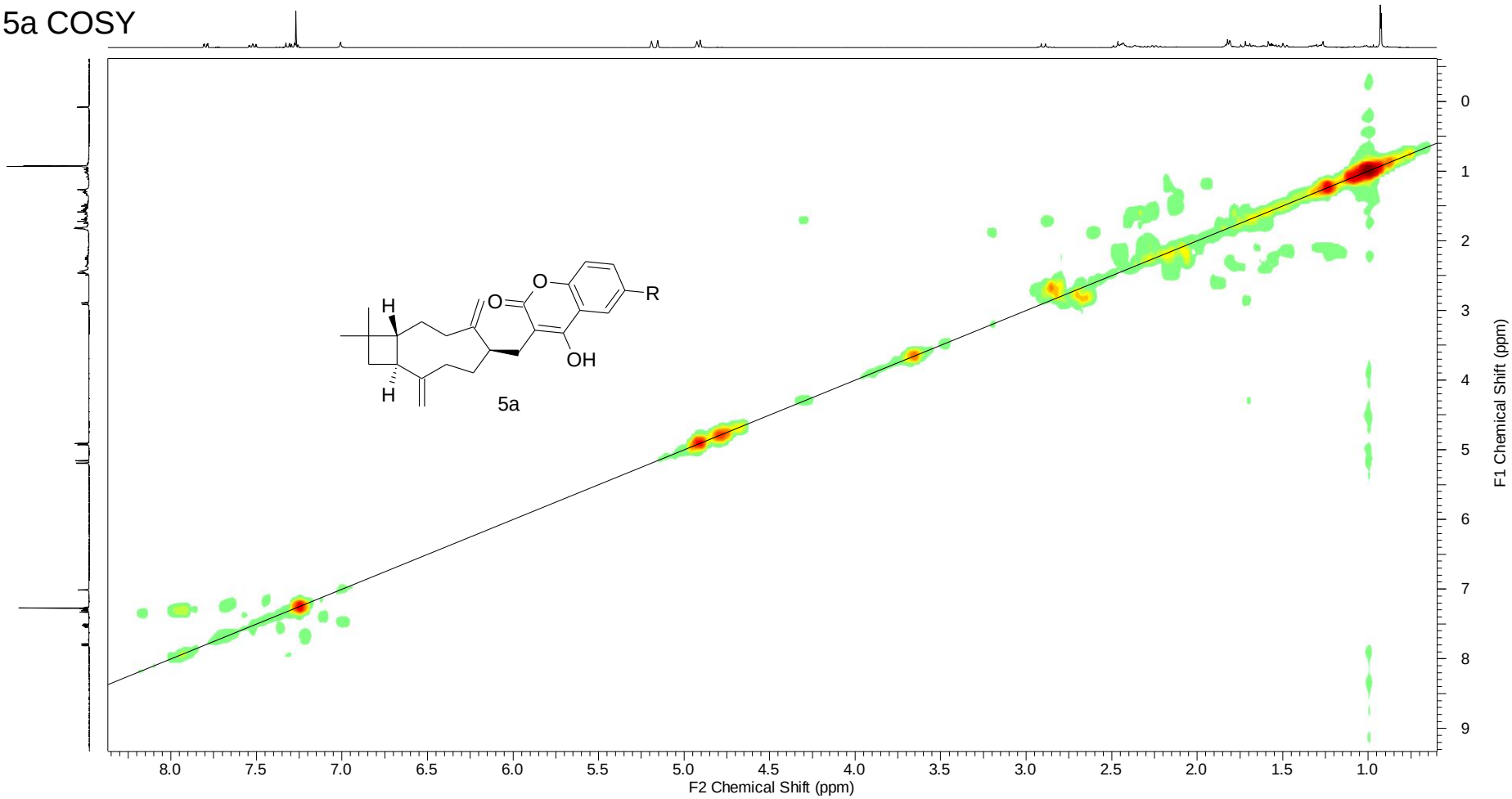


5a

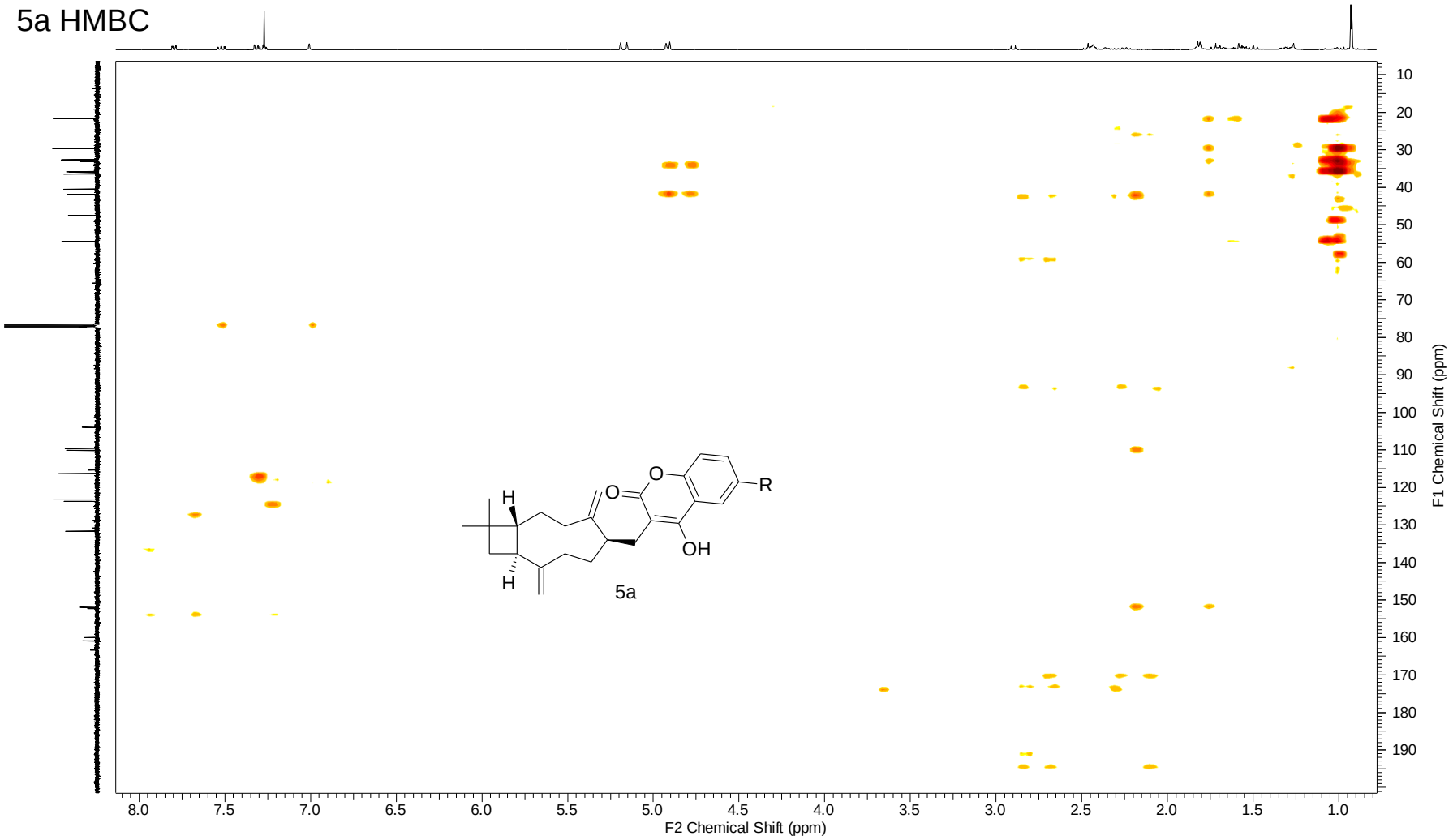
5a HSQC



5a COSY

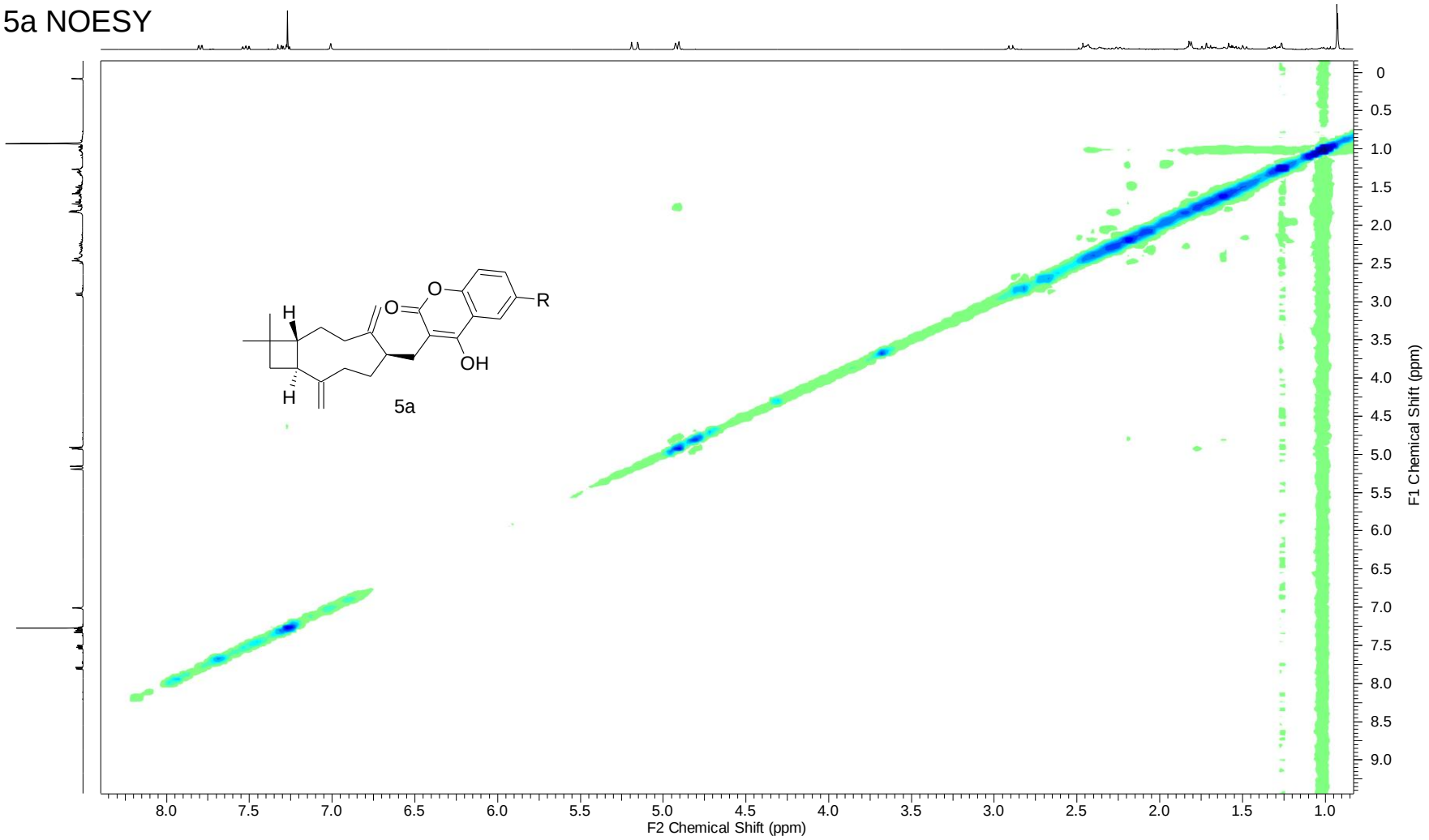

H
O
O
R
OH
H
5a
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
F2 Chemical Shift (ppm)
0
1
2
3
4
5
6
7
8
9
F1 Chemical Shift (ppm)

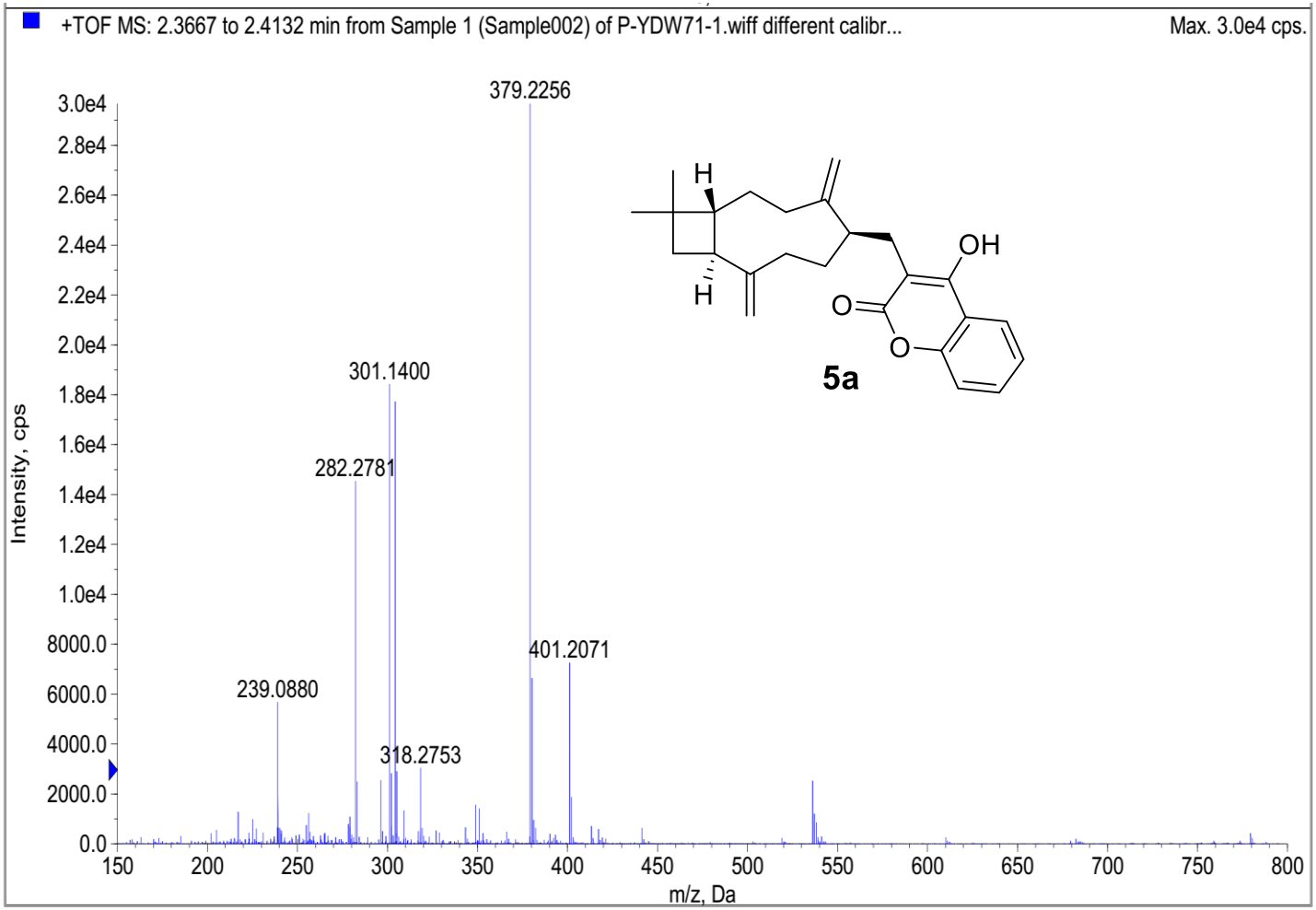
5a HMBC


F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
H
H
O
O
R
OH

5a

5a NOESY

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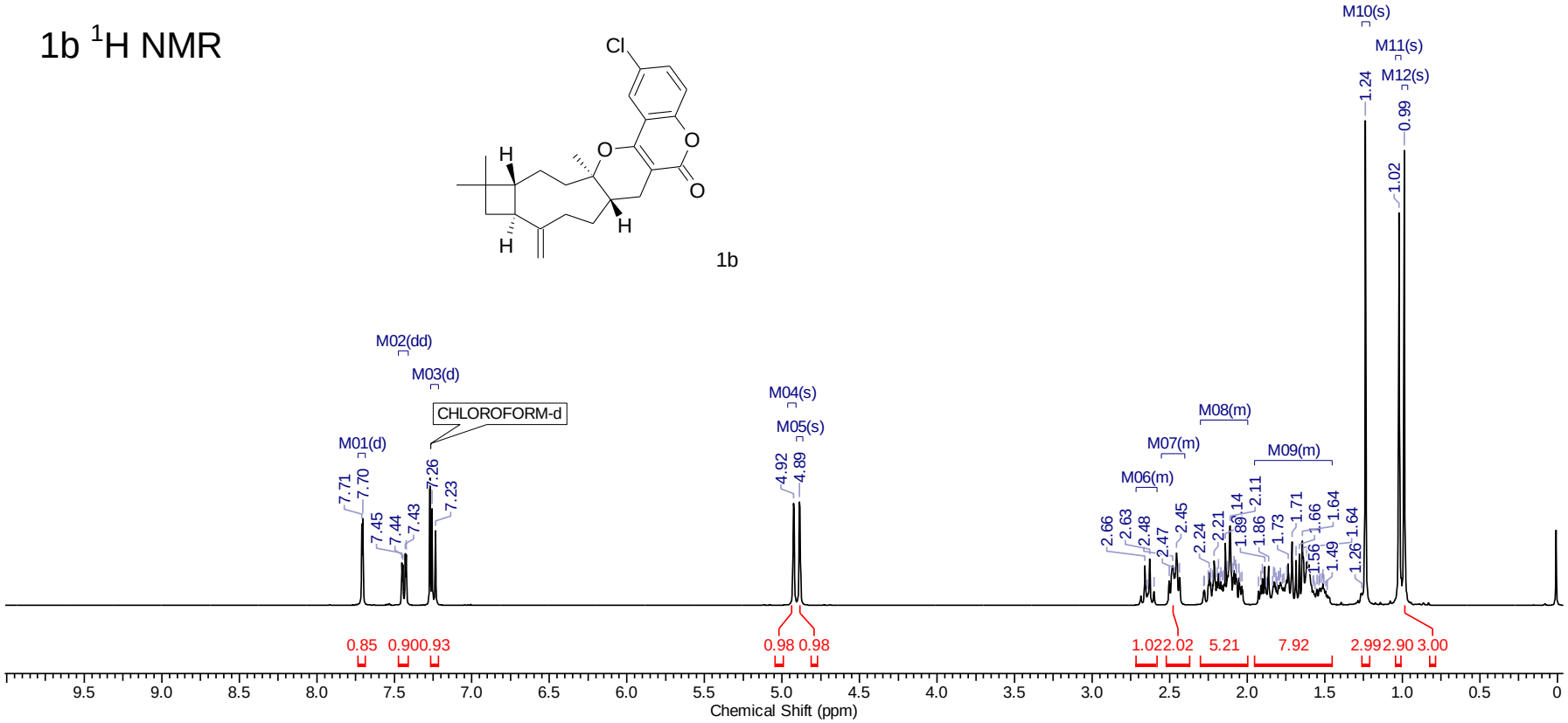
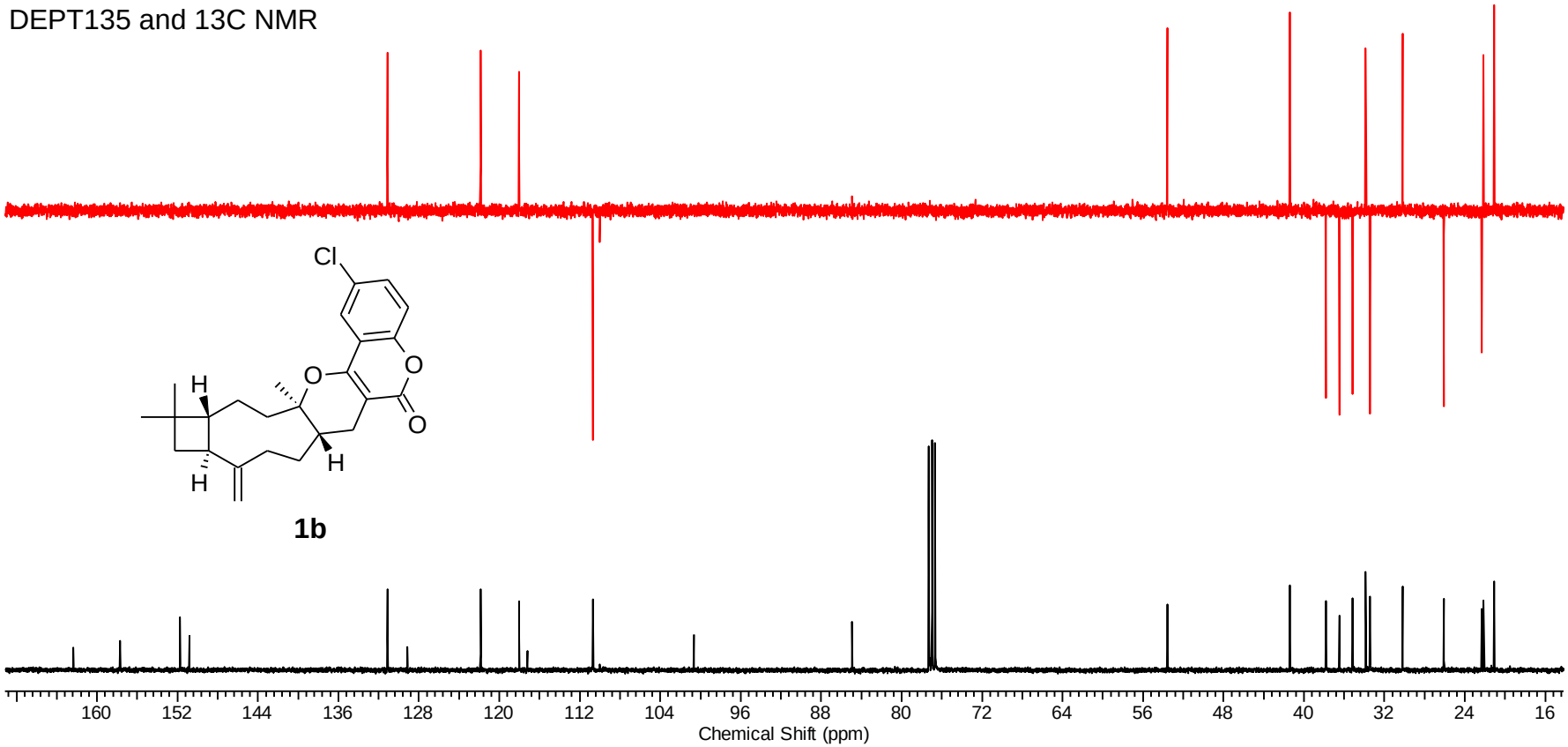
Max. 3.0e4 cps.
379.2256
301.1400
282.2781
401.2071
239.0880
318.2753
Intensity, cps
m/z, Da
H
H
OH
O
O
5a

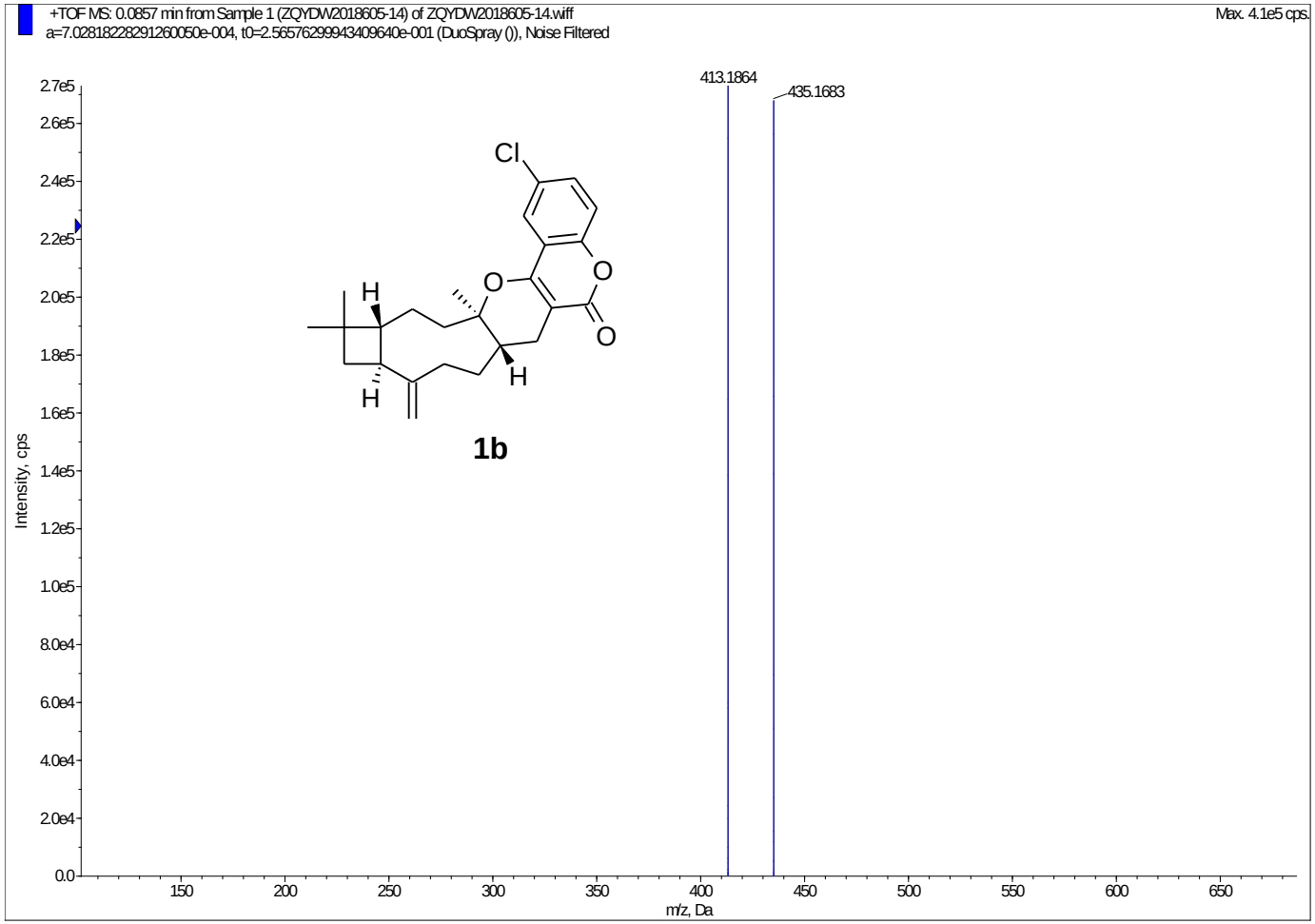
Compound 1b


1b ^{1}H NMR
Cl
H
O
O
O
H
H
1b
M10(s)
M11(s)
M12(s)
1.24
0.99
1.02
M02(dd)
M03(d)
M04(s)
M05(s)
M08(m)
M07(m)
M09(m)
M06(m)
CHLOROFORM-d
M01(d)
7.71
7.70
7.45
7.44
7.43
7.26
7.23
4.92
4.89
2.66
2.63
2.48
2.47
2.45
2.24
2.21
2.14
2.11
1.89
1.86
1.73
1.71
1.66
1.64
1.64
1.56
1.49
1.26
0.85
0.90
0.93
0.98
0.98
1.02
2.02
5.21
7.92
2.99
2.90
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

DEPT135 and 13C NMR



1b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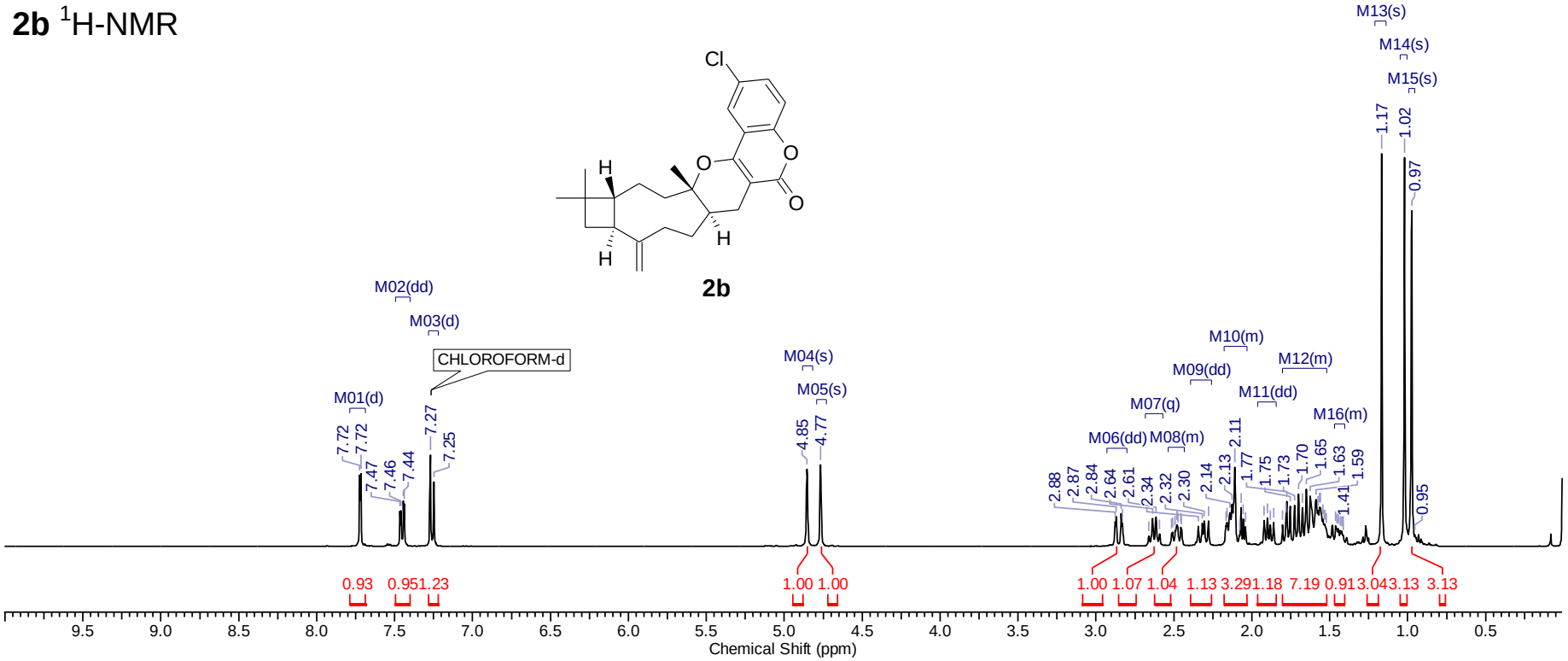
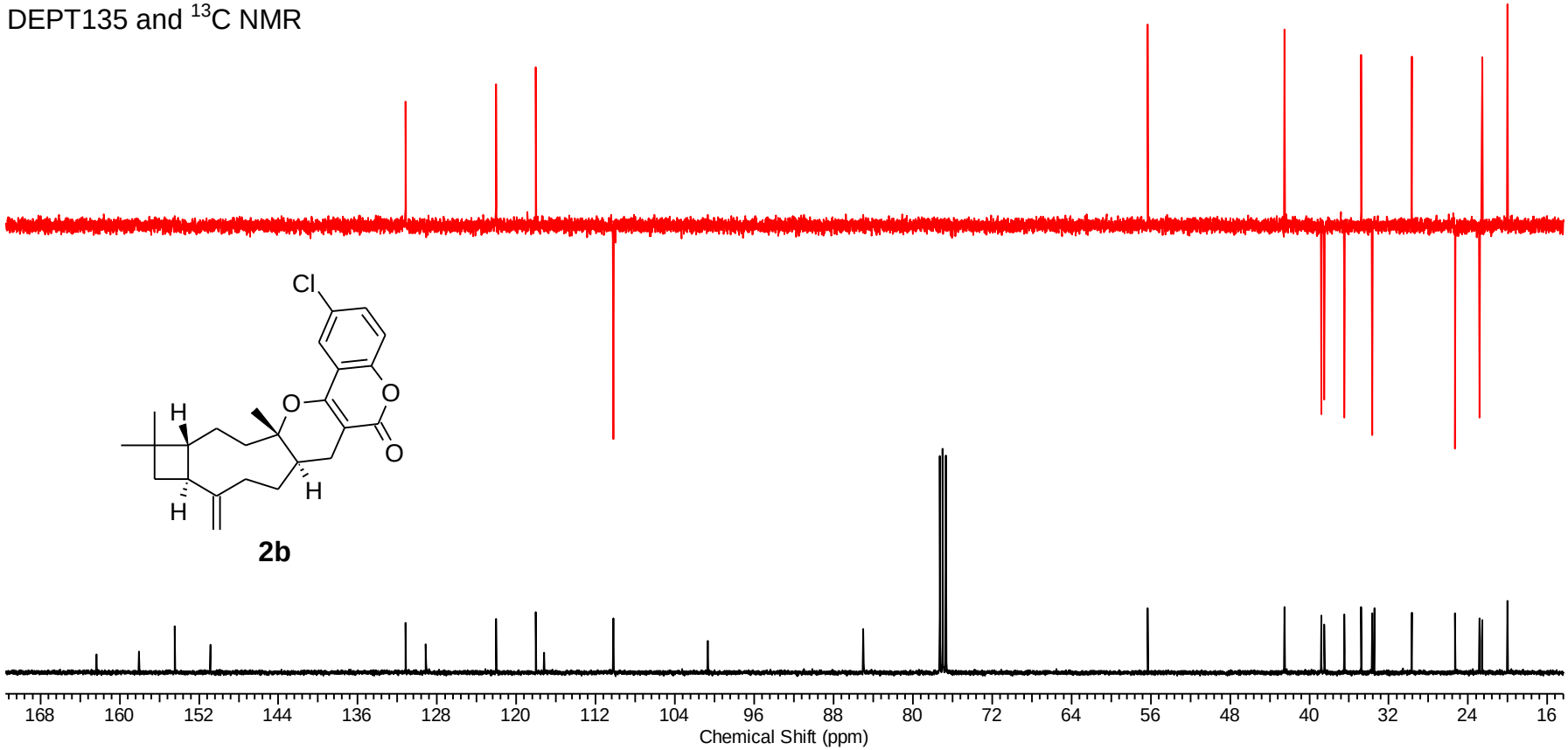
Max. 4.1e5 cps.
413.1864
435.1683
Cl
O
O
O
H
H
H
1b
Intensity, cps
2.7e5
2.6e5
2.4e5
2.2e5
2.0e5
1.8e5
1.6e5
1.4e5
1.2e5
1.0e5
8.0e4
6.0e4
4.0e4
2.0e4
0.0
150
200
250
300
350
400
450
500
550
600
650
m/z, Da

Compound 2b

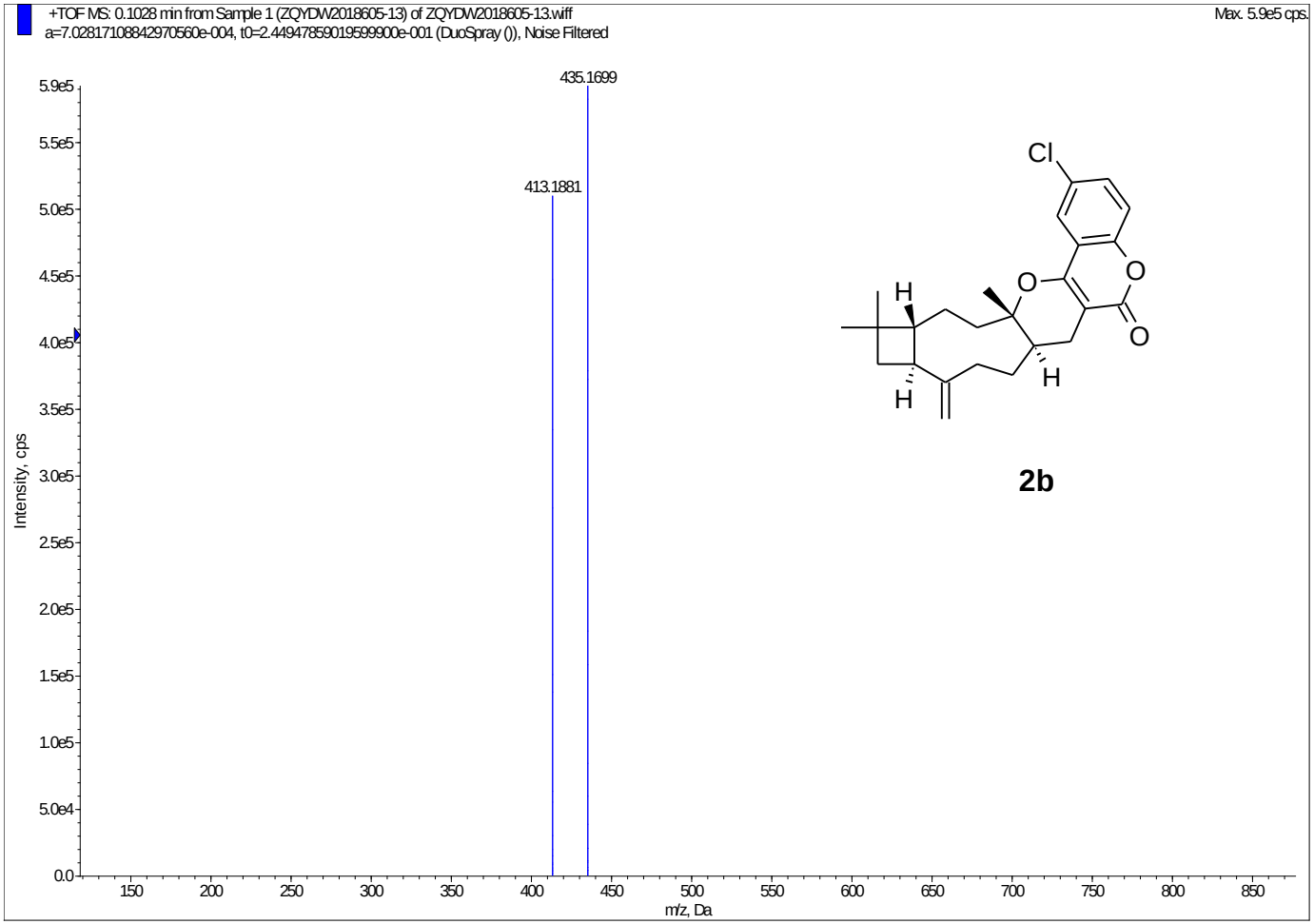
2b ^{1}H-NMR



DEPT135 and ^{13}C NMR



2b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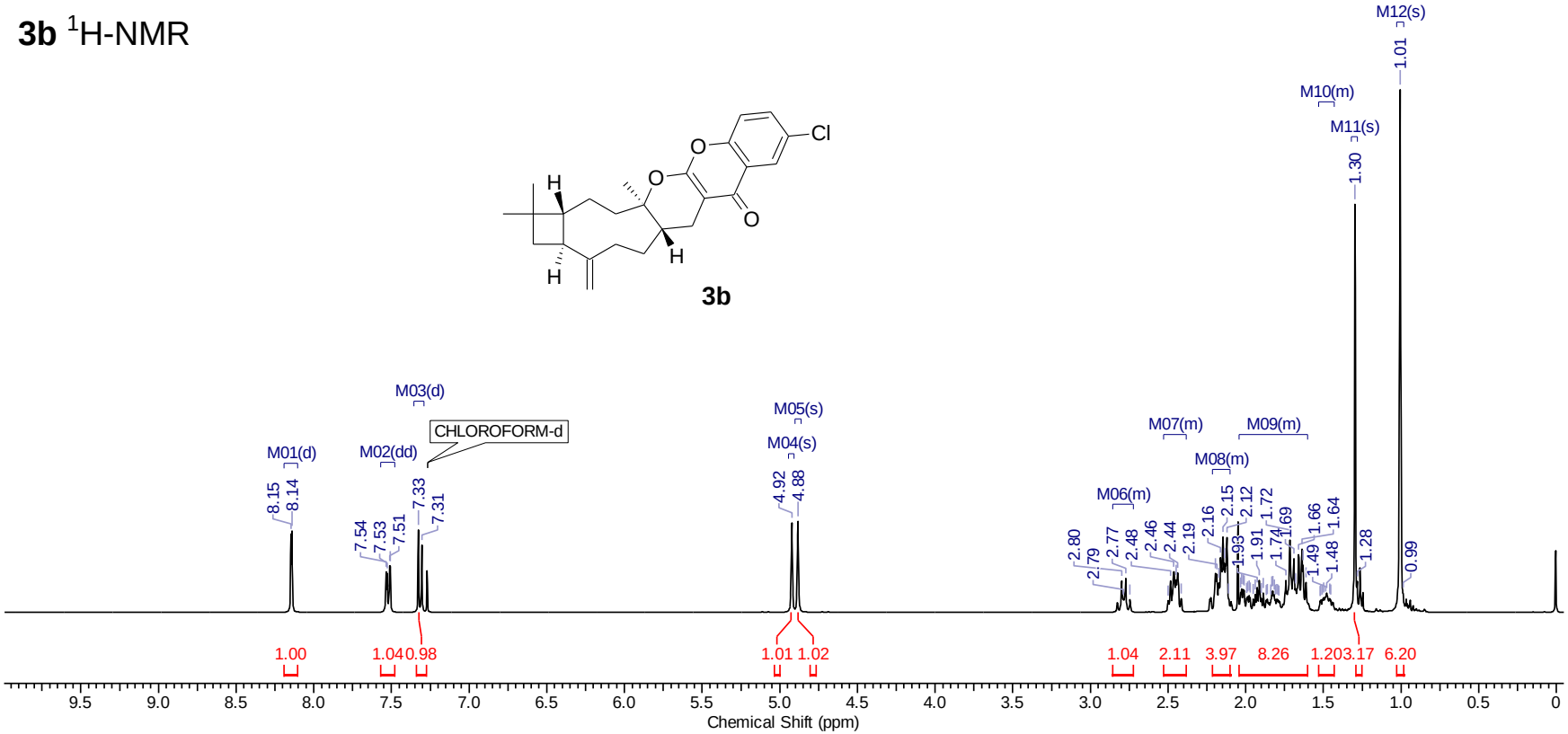
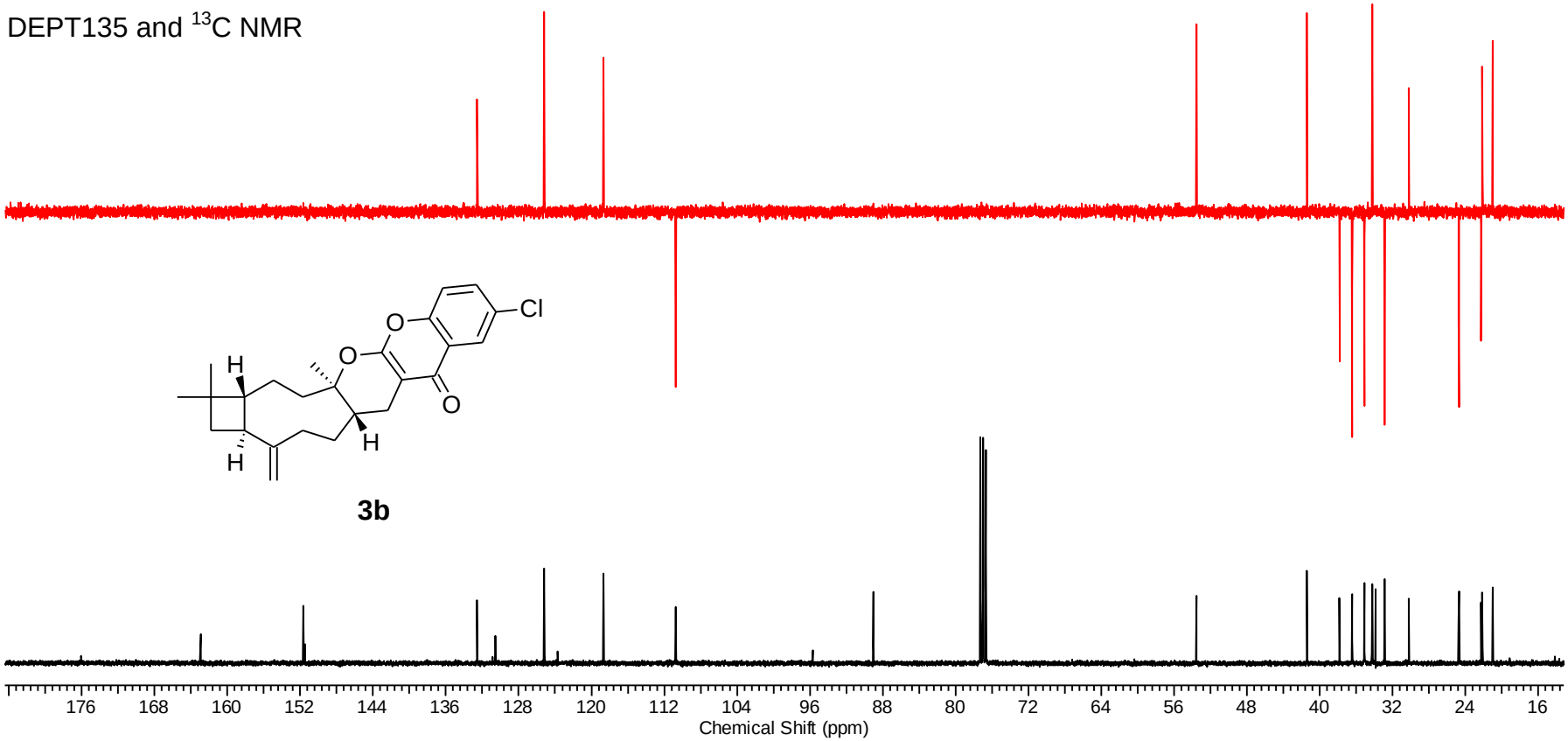
Max. 5.9e5 cps.
435.1699
413.1881
Intensity, cps
m/z, Da
Cl
O
O
O
H
H
H
2b

Compound 3b

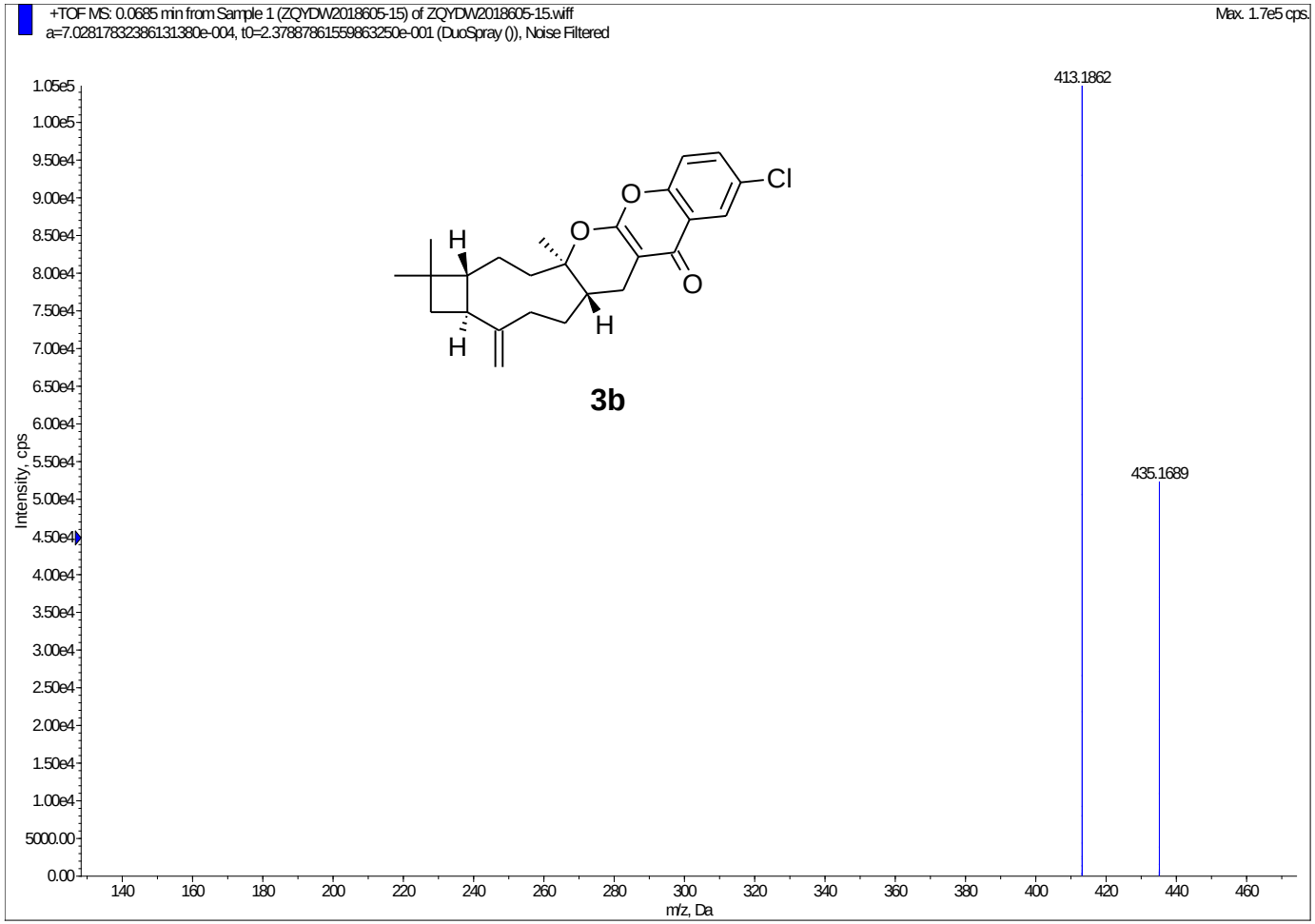
3b ^{1}H-NMR



DEPT135 and ^{13}C NMR



3b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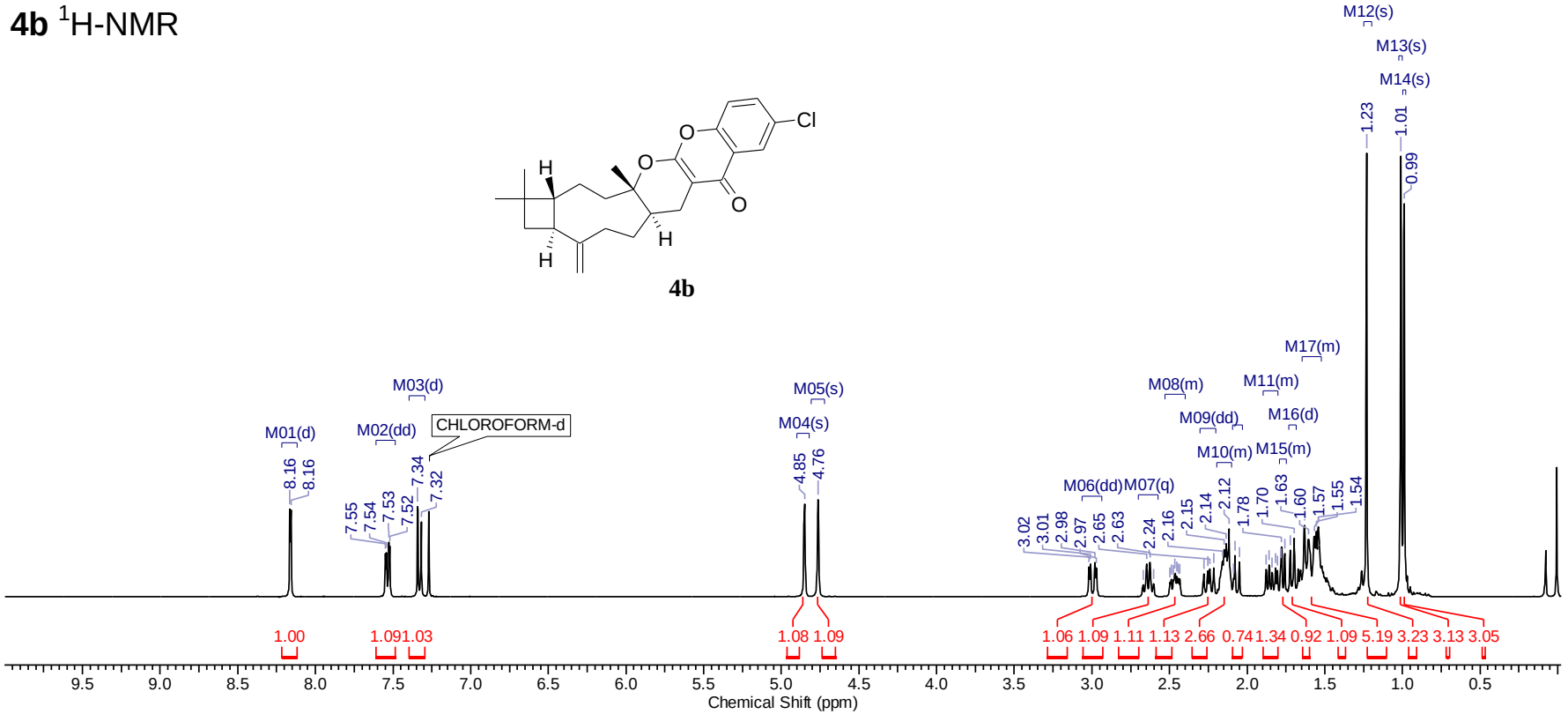
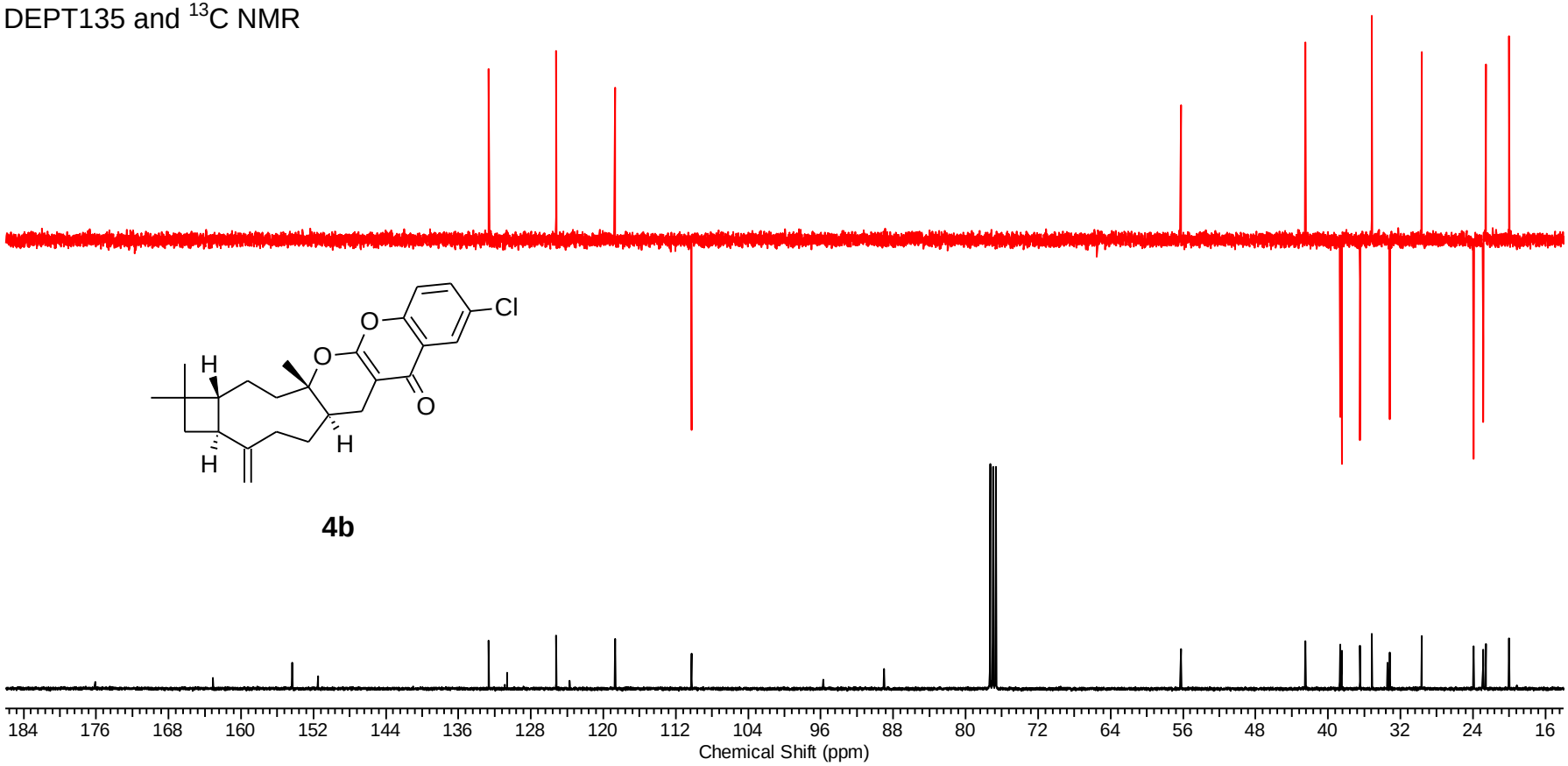
Max. 1.7e5 cps.
413.1862
435.1689
Cl
O
O
O
H
H
H
3b
Intensity, cps
m/z, Da

Compound 4b

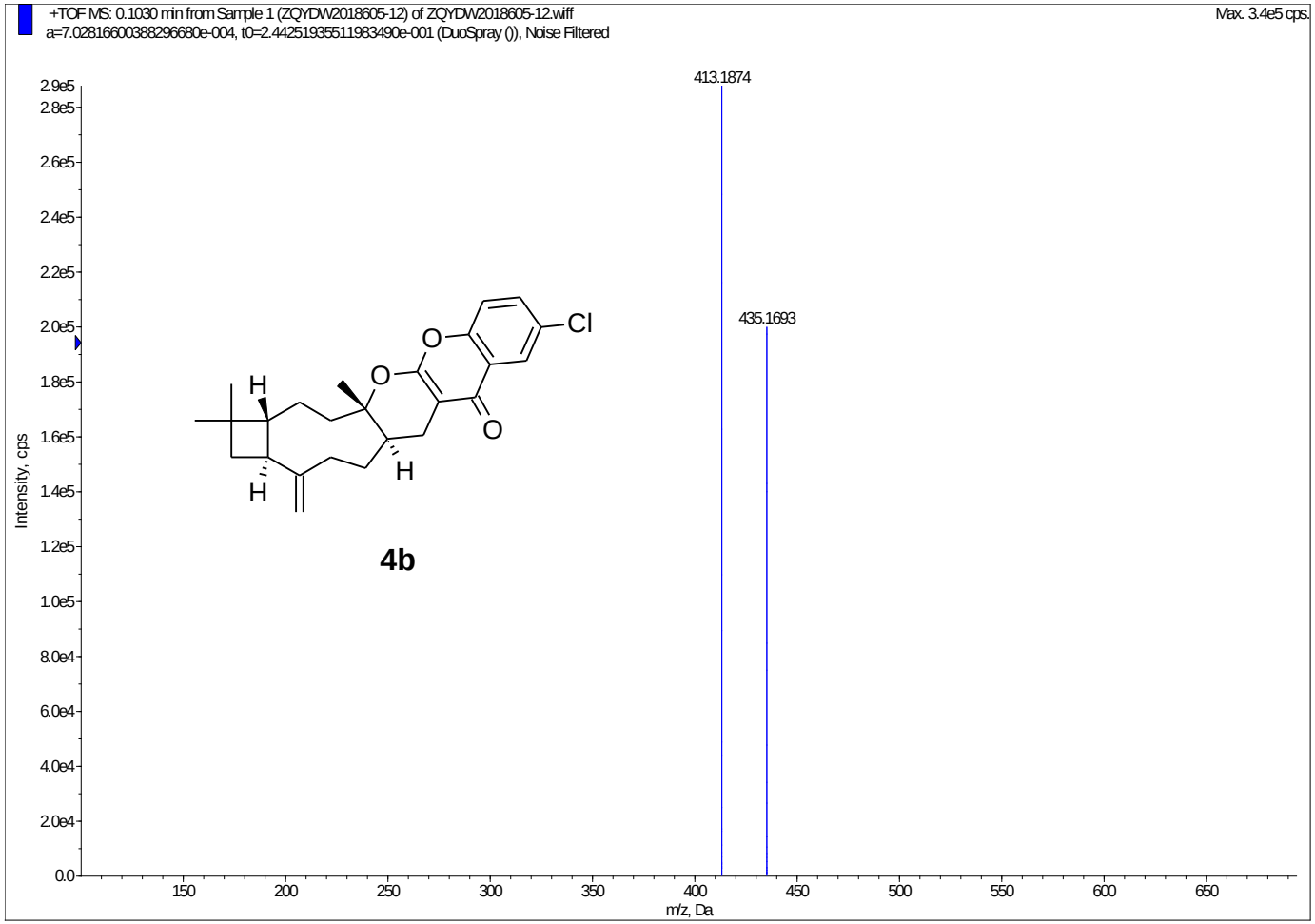
4b ^{1}H-NMR



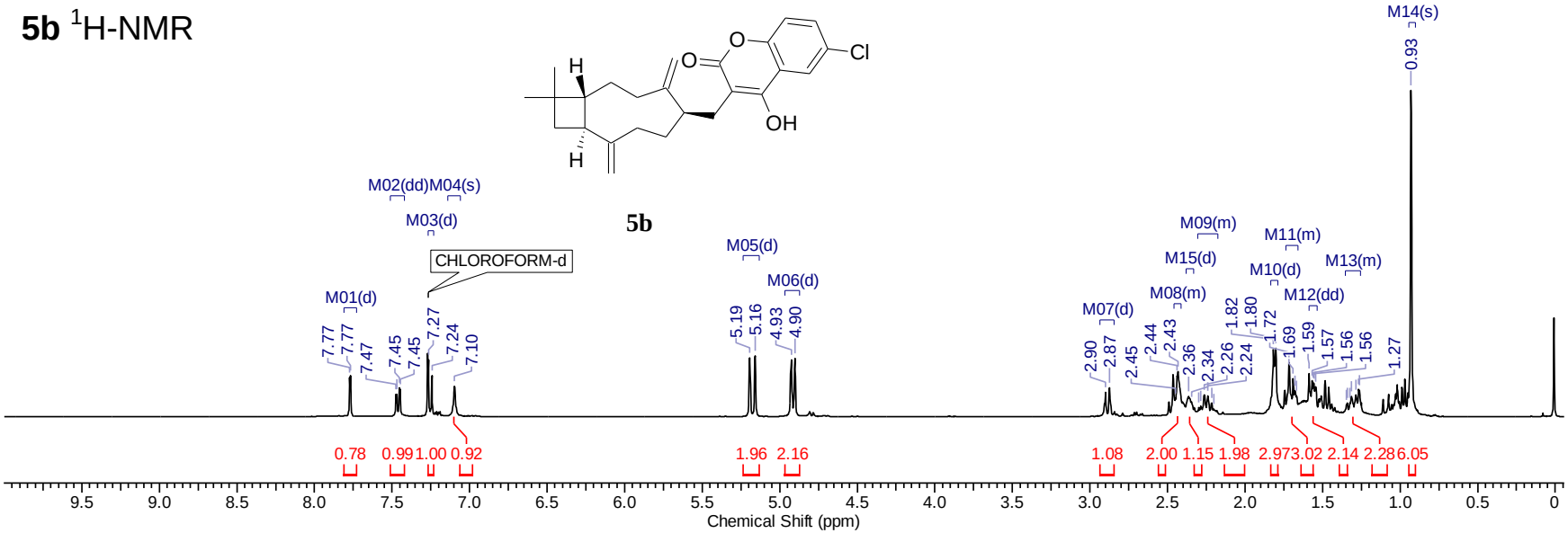
DEPT135 and ^{13}C NMR



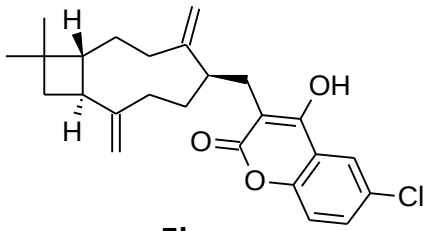
4b


+TOF MS: 0.1030 min from Sample 1 (ZQYDW2018605-12) of ZQYDW2018605-12.wiff
a=7.028166003882966800e-004, t0=2.442519355119834900e-001 (DuoSpray ()), Noise Filtered
Max. 3.4e5 cps.
413.1874
435.1693
Intensity, cps
m/z, Da
4b

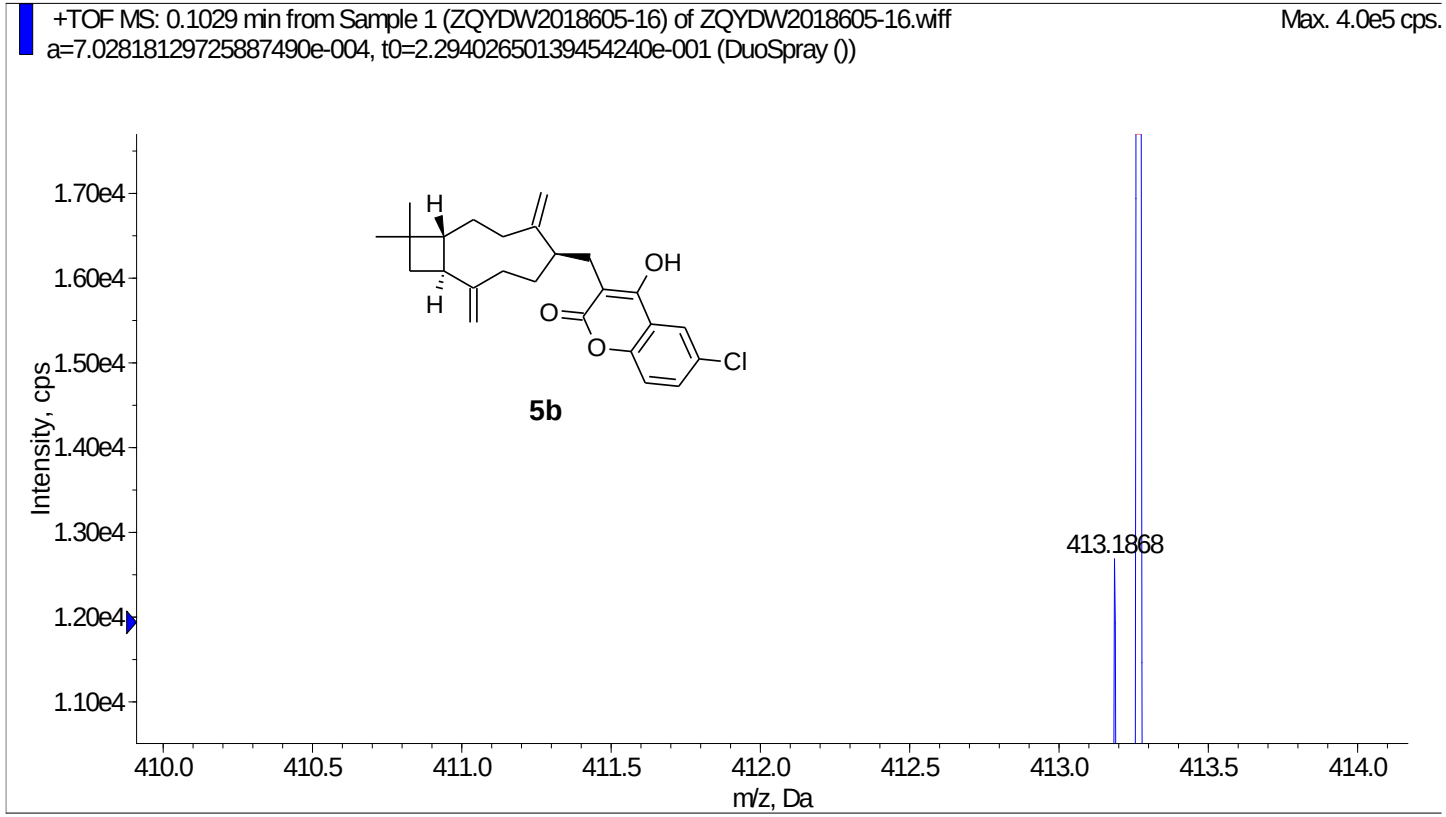
Compound 5b


5b ^{1}H-NMR
5b
M14(s)
0.93
M02(dd)M04(s)
M03(d)
CHLOROFORM-d
M01(d)
M05(d)
M06(d)
M09(m)
M11(m)
M15(d)
M10(d)
M13(m)
M08(m)
M12(dd)
M07(d)
7.77
7.77
7.47
7.45
7.45
7.27
7.24
7.10
5.19
5.16
4.93
4.90
2.90
2.87
2.45
2.44
2.43
2.36
2.34
2.26
2.24
1.82
1.80
1.72
1.69
1.59
1.57
1.56
1.56
1.27
0.78
0.99
1.00
0.92
1.96
2.16
1.08
2.00
1.15
1.98
2.97
3.02
2.14
2.28
6.05
Chemical Shift (ppm)

DEPT135 and ^{13}C NMR



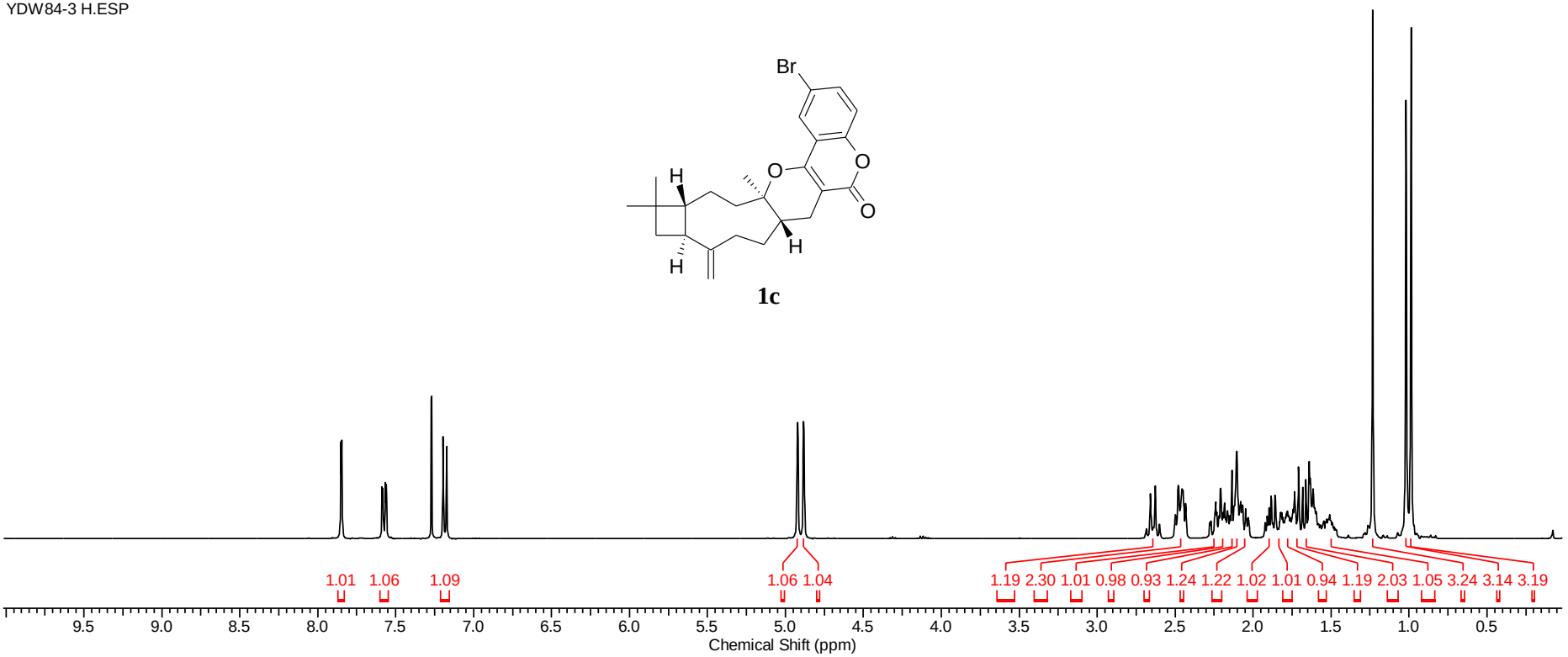
5b


+TOF MS: 0.1029 min from Sample 1 (ZQYDW2018605-16) of ZQYDW2018605-16.wiff
Max. 4.0e5 cps.
a=7.02818129725887490e-004, t0=2.29402650139454240e-001 (DuoSpray ())
Intensity, cps
1.70e4
1.60e4
1.50e4
1.40e4
1.30e4
1.20e4
1.10e4
410.0
410.5
411.0
411.5
412.0
412.5
413.0
413.5
414.0
m/z, Da
413.1868
H
H
OH
O
O
Cl
5b

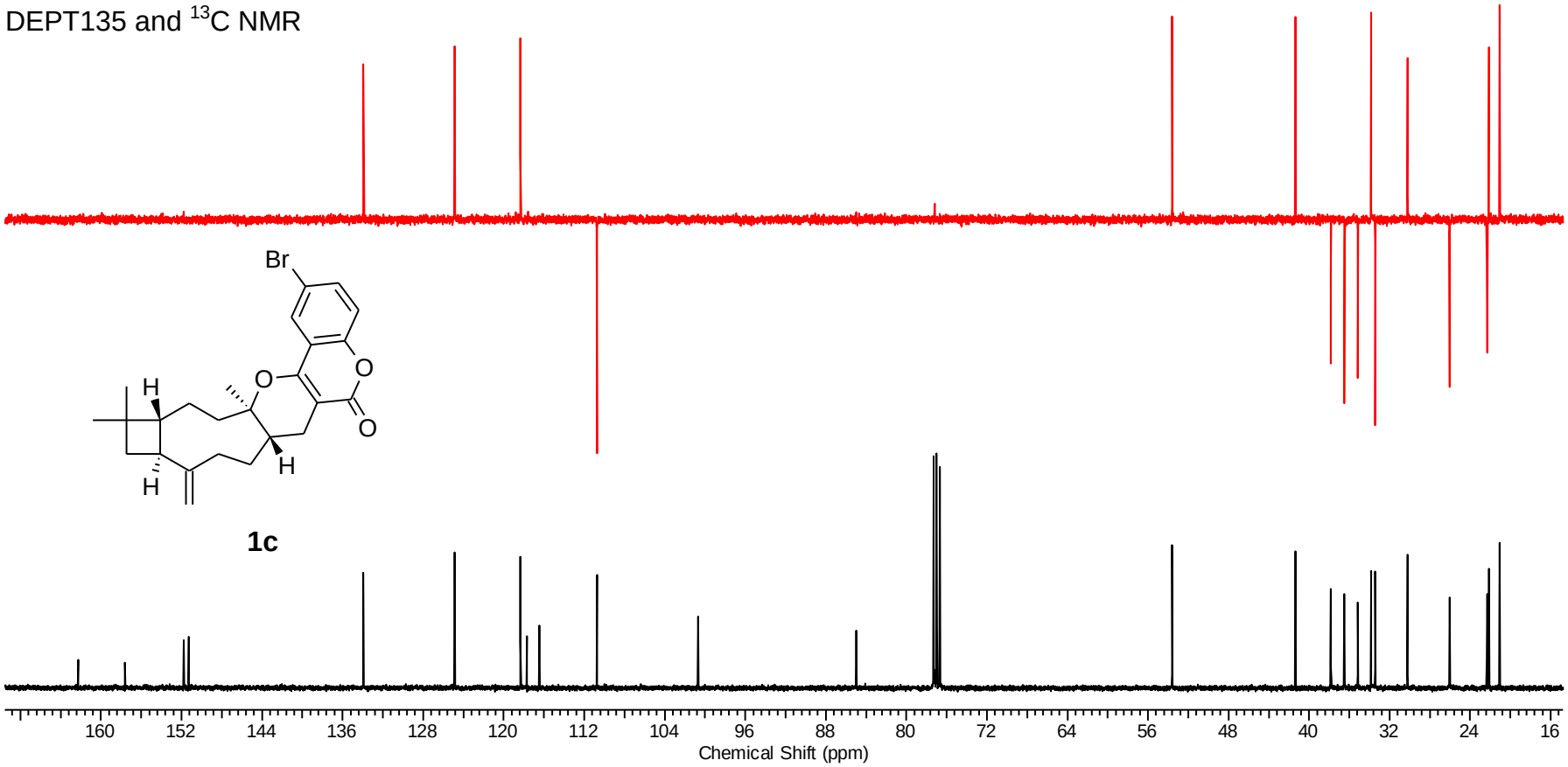
Compound 1c

1c ^{1}H-NMR

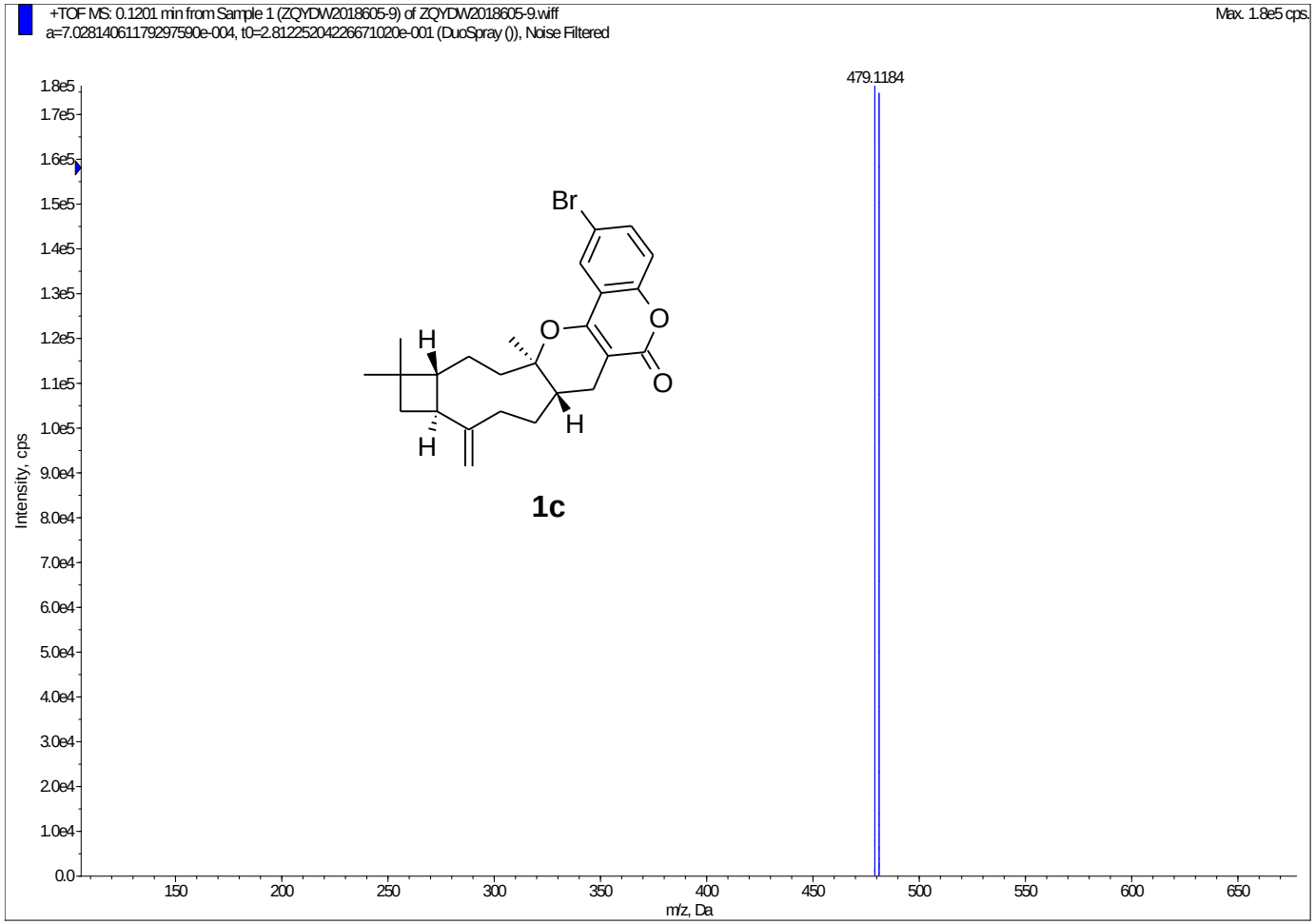
YDW84-3 H.ESP



DEPT135 and ^{13}C NMR

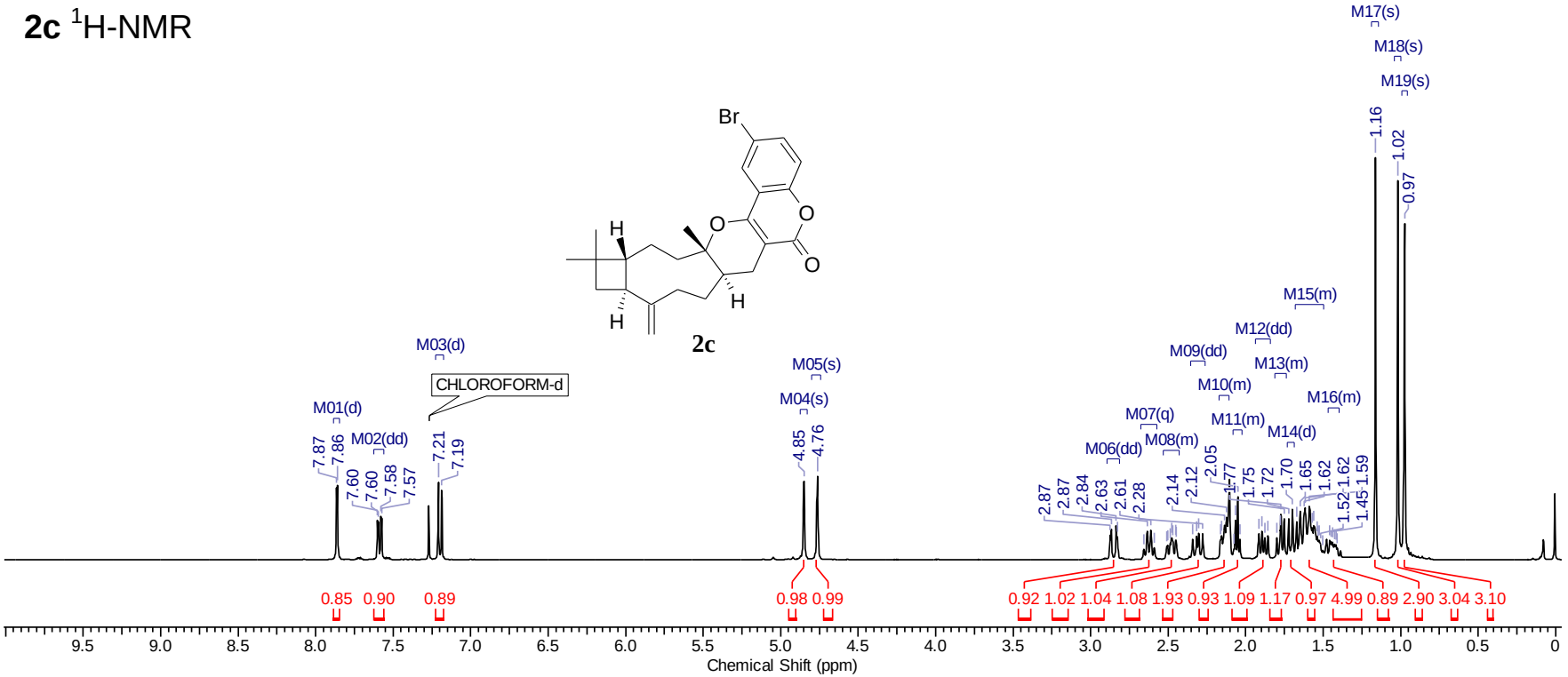


1c

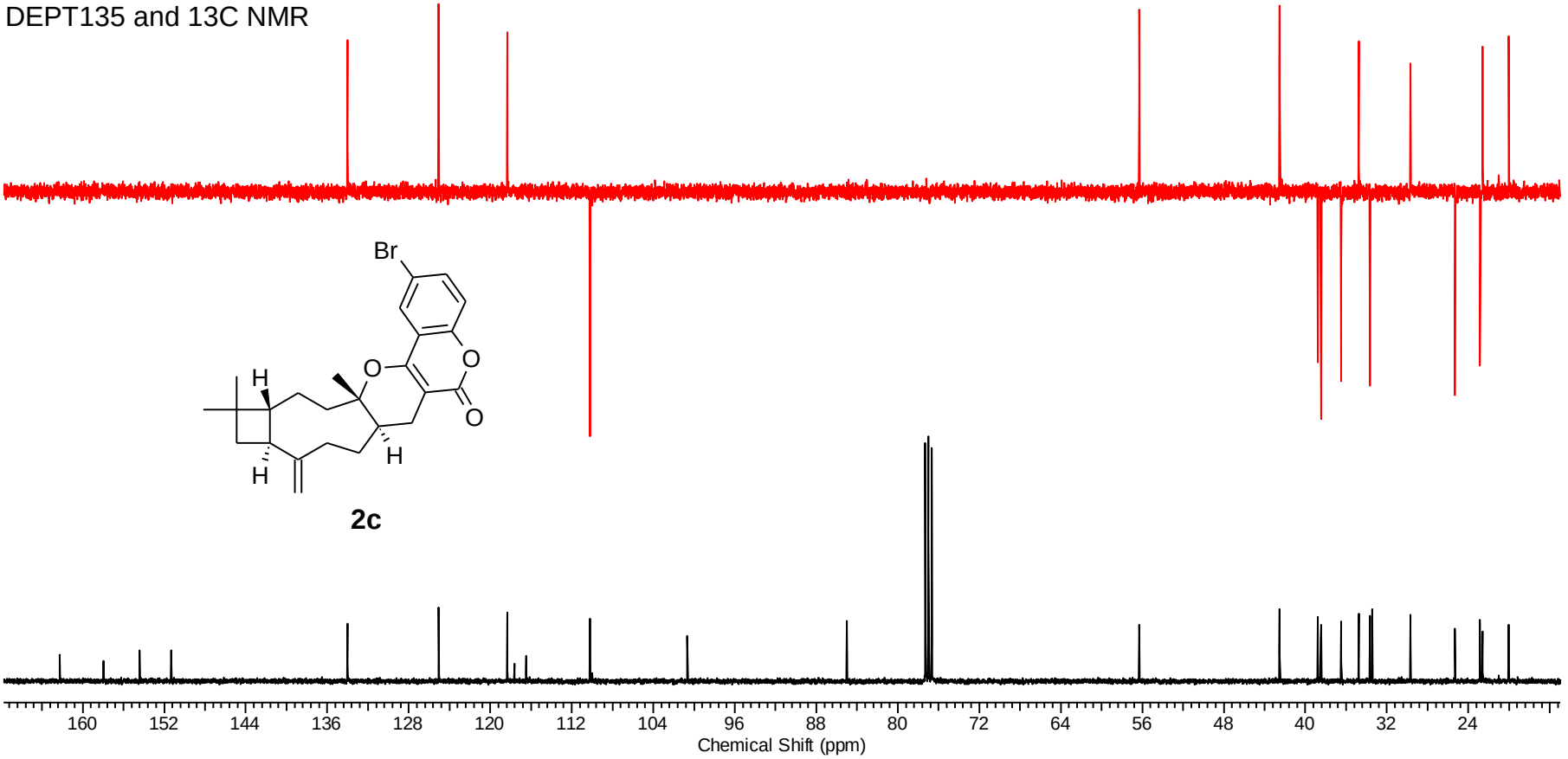

+TOF MS: 0.1201 min from Sample 1 (ZQYDW2018605-9) of ZQYDW2018605-9.wiff
a=7.028140611792975 90e-004, t0=2.8122520422667 1020e-001 (DuoSpray ()), Noise Filtered
Max. 1.8e5 cps.
479.1184
Intensity, cps
m/z, Da
Br
O
O
O
H
H
H
1c

Compound 2c

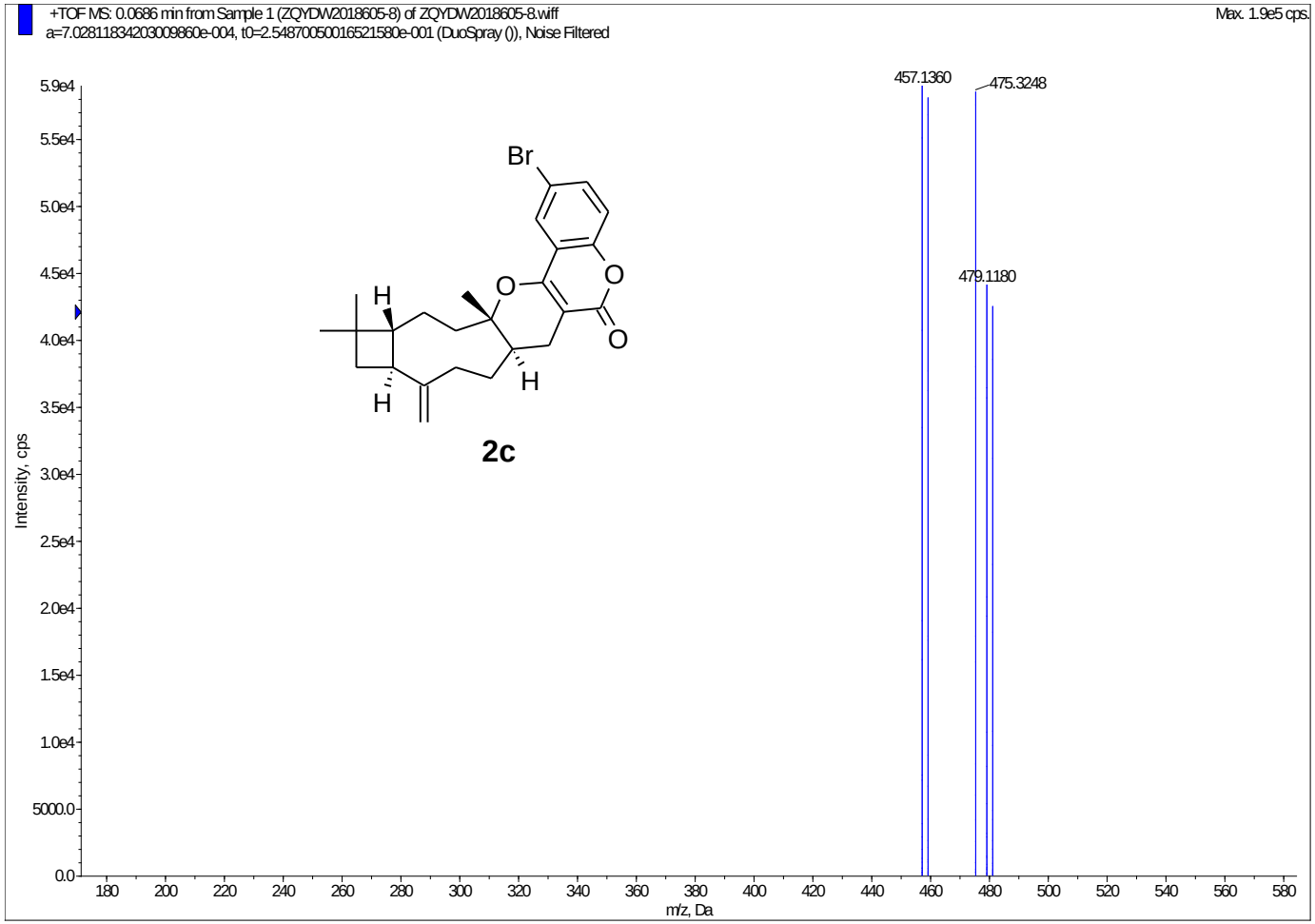
2c ^{1}H-NMR



DEPT135 and 13C NMR



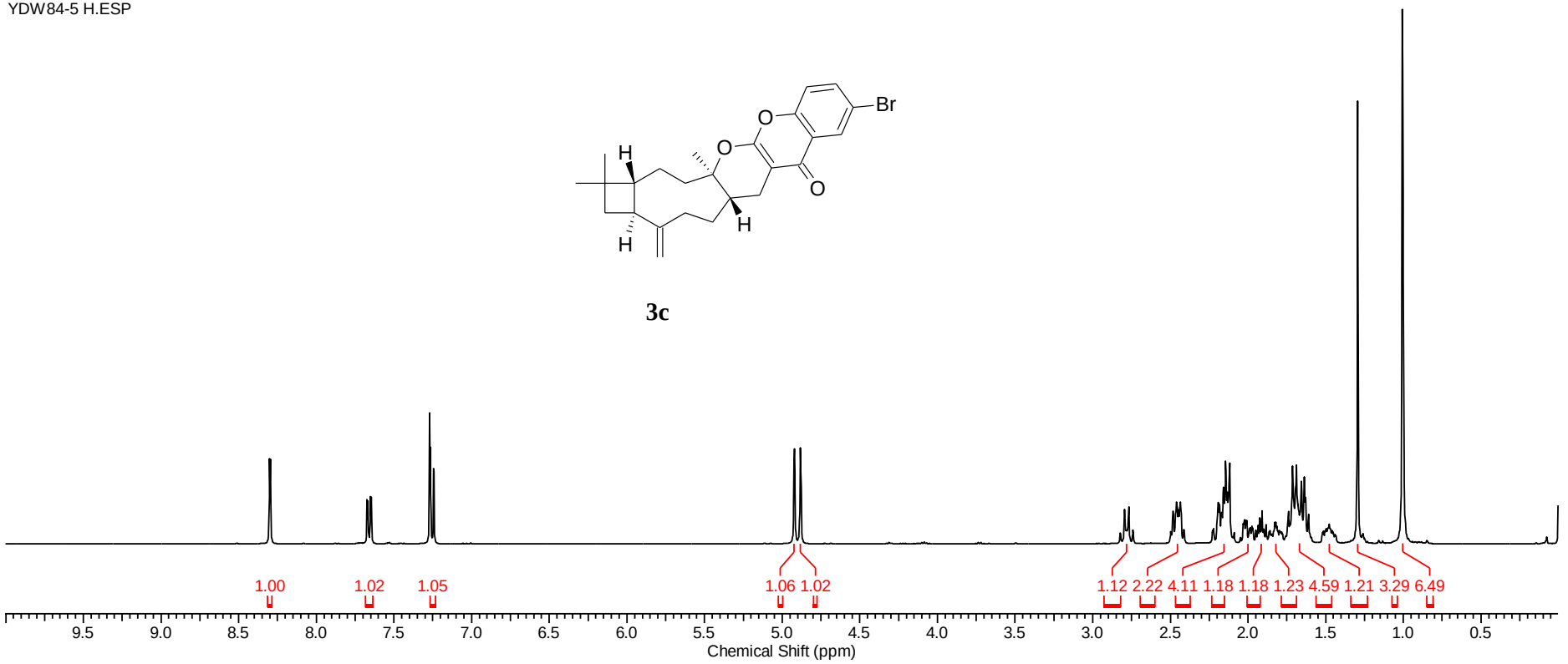
2c


+TOF MS: 0.0686 min from Sample 1 (ZQYDW2018605-8) of ZQYDW2018605-8.wiff
a=7.028118342030098 60e-004, t0=2.54870050016521580e-001 (DuoSpray ()), Noise Filtered
Max. 1.9e5 cps.
457.1360
475.3248
479.1180
Br
O
O
O
H
H
H
2c
Intensity, cps
m/z, Da

Compound 3c

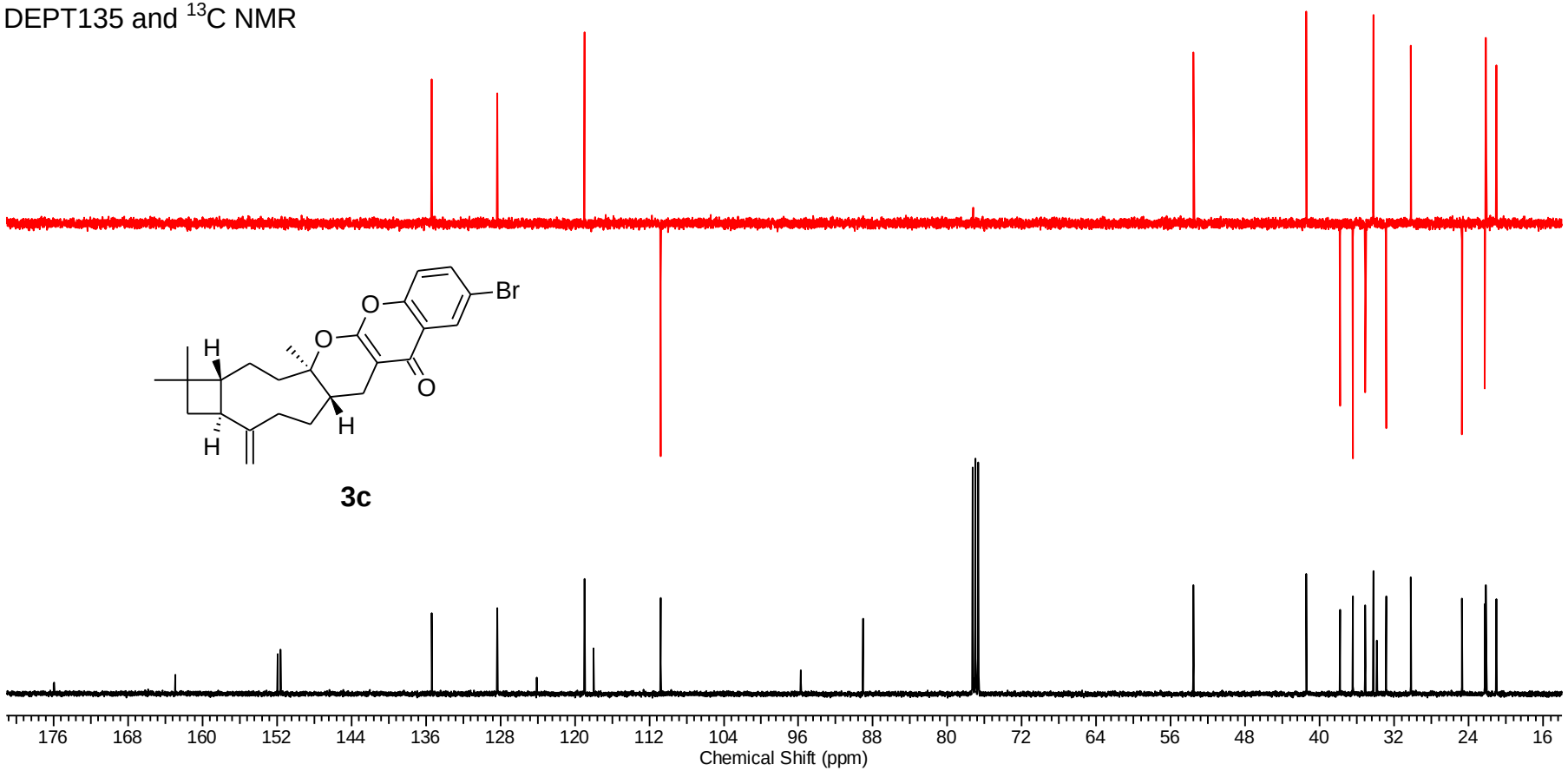
3c ^{1}H-NMR

YDW84-5 H.ESP

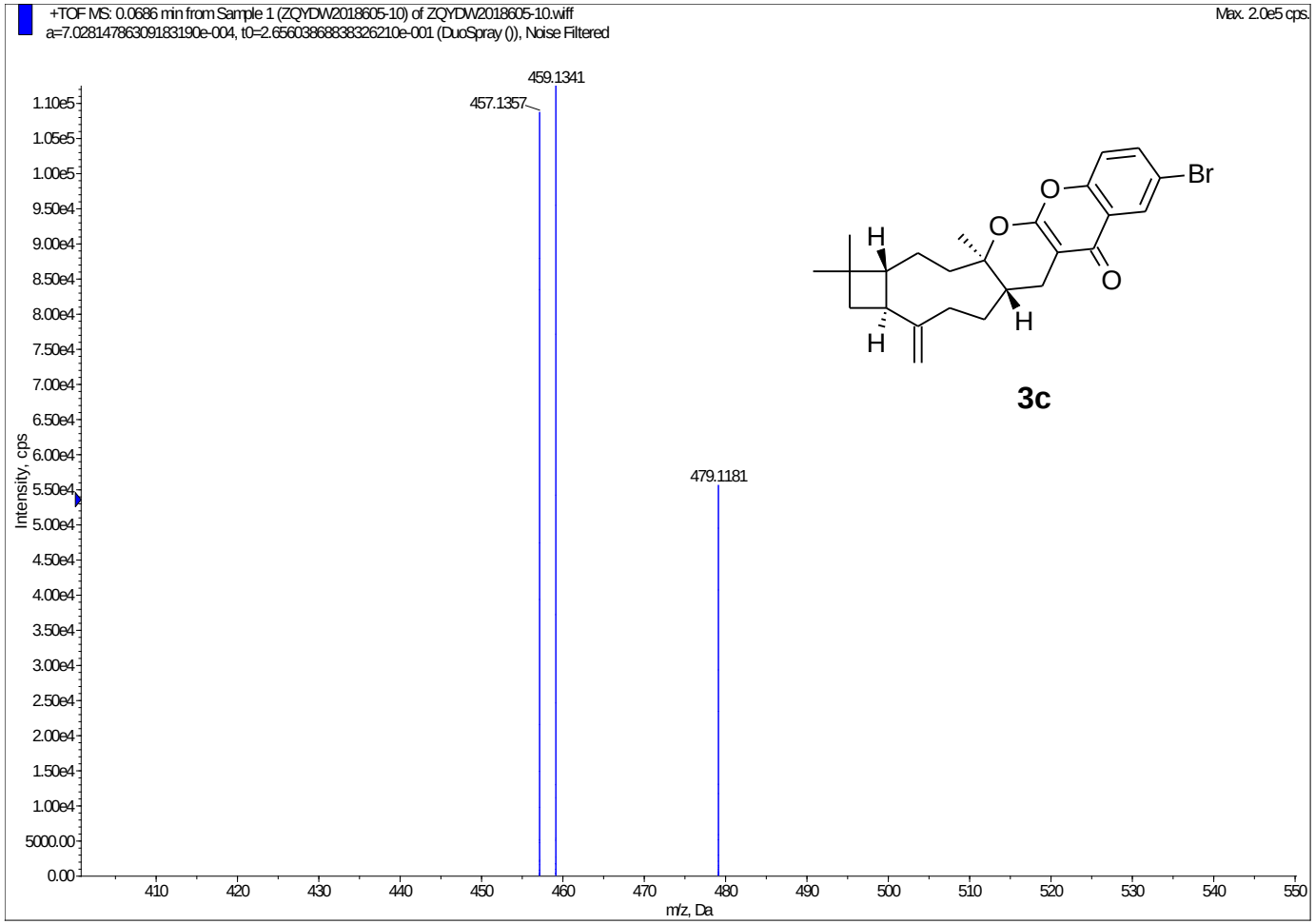


3c

DEPT135 and ^{13}C NMR

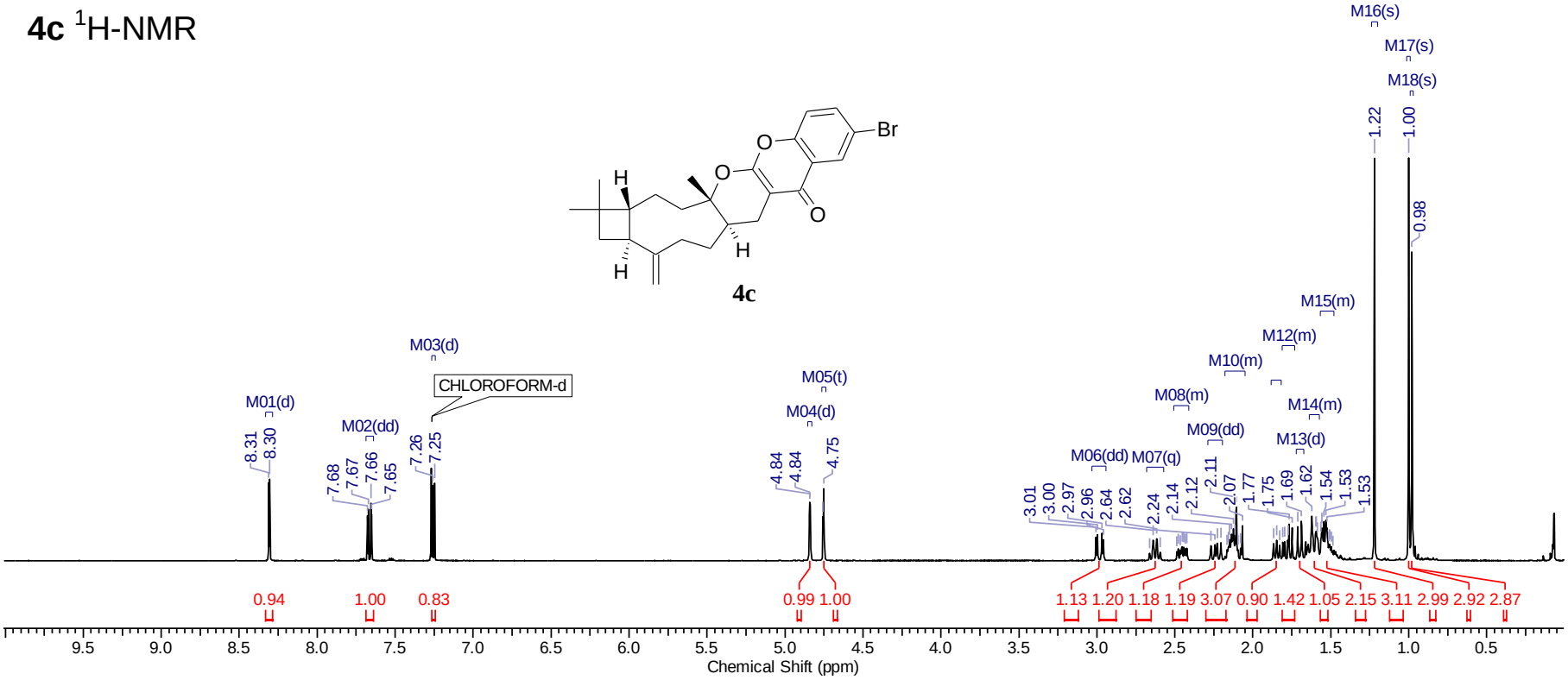


3c


+TOF MS: 0.0686 min from Sample 1 (ZQYDW2018605-10) of ZQYDW2018605-10.wiff
a=7.028147863091831 90e-004, t0=2.656038688383262 10e-001 (DuoSpray ()), Noise Filtered
Max. 2.0e5 cps.
459.1341
457.1357
479.1181
Intensity, cps
m/z, Da
Br
O
O
O
H
H
H
3c

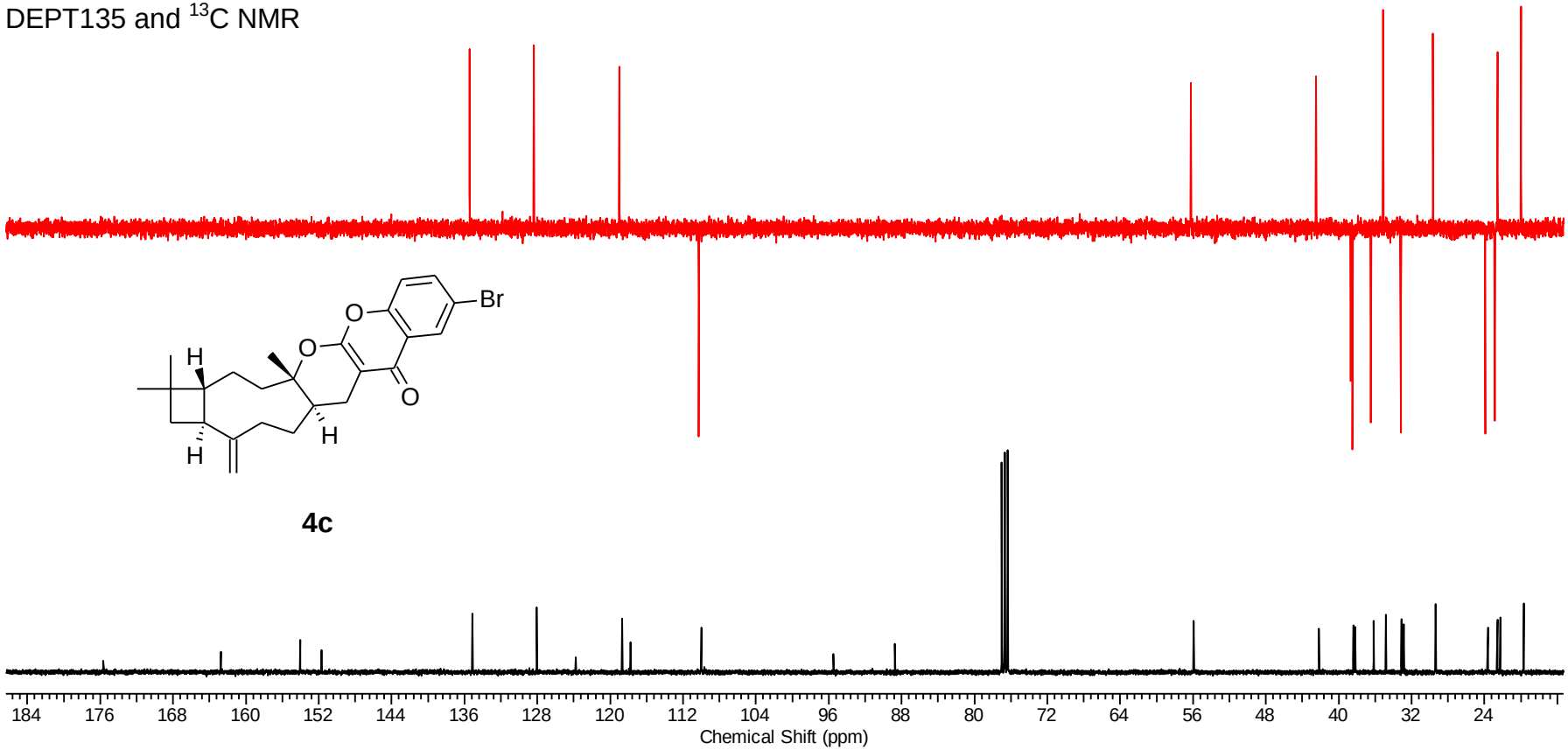
Compound 4c

4c ^{1}H-NMR

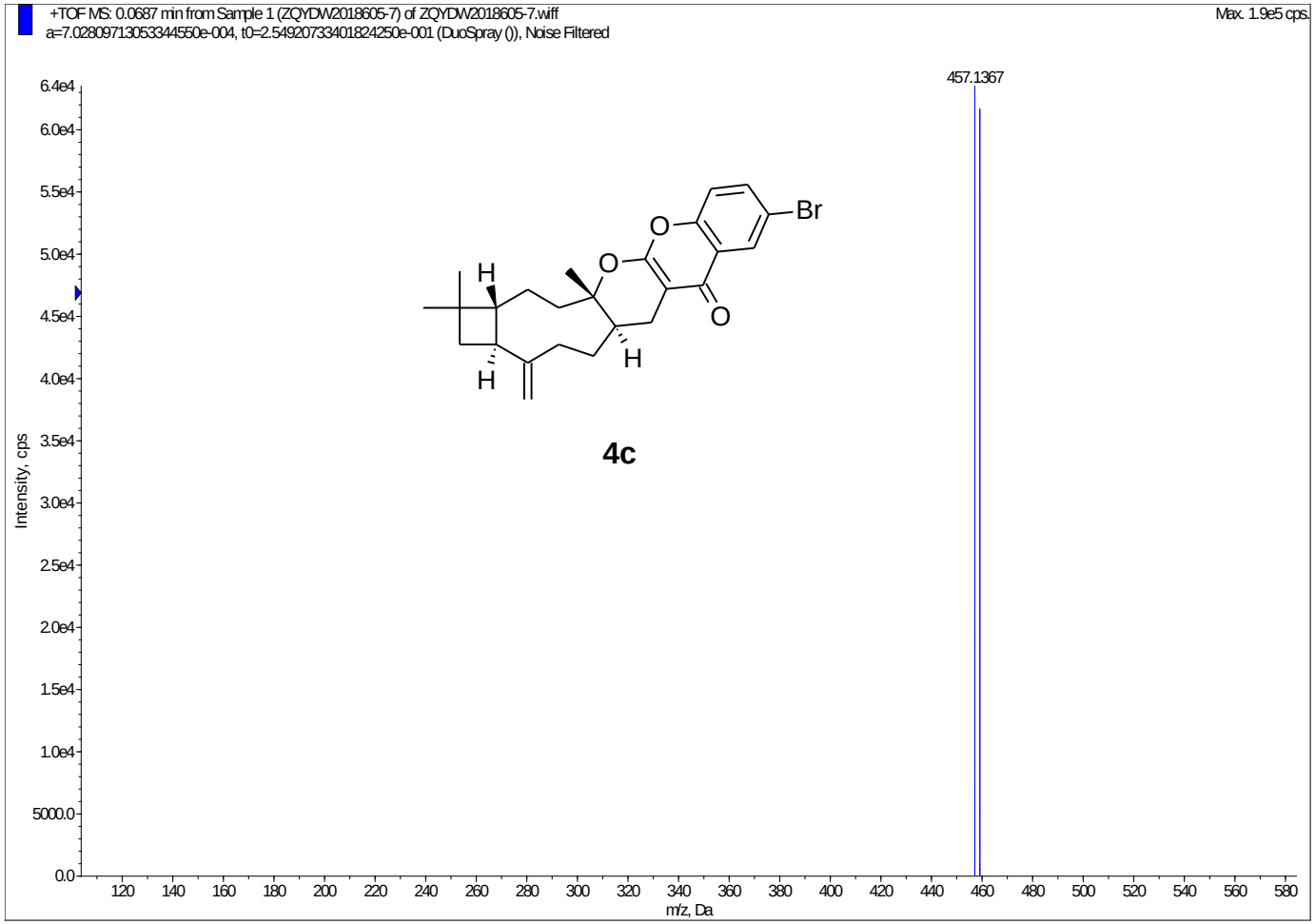


4c

DEPT135 and ^{13}C NMR

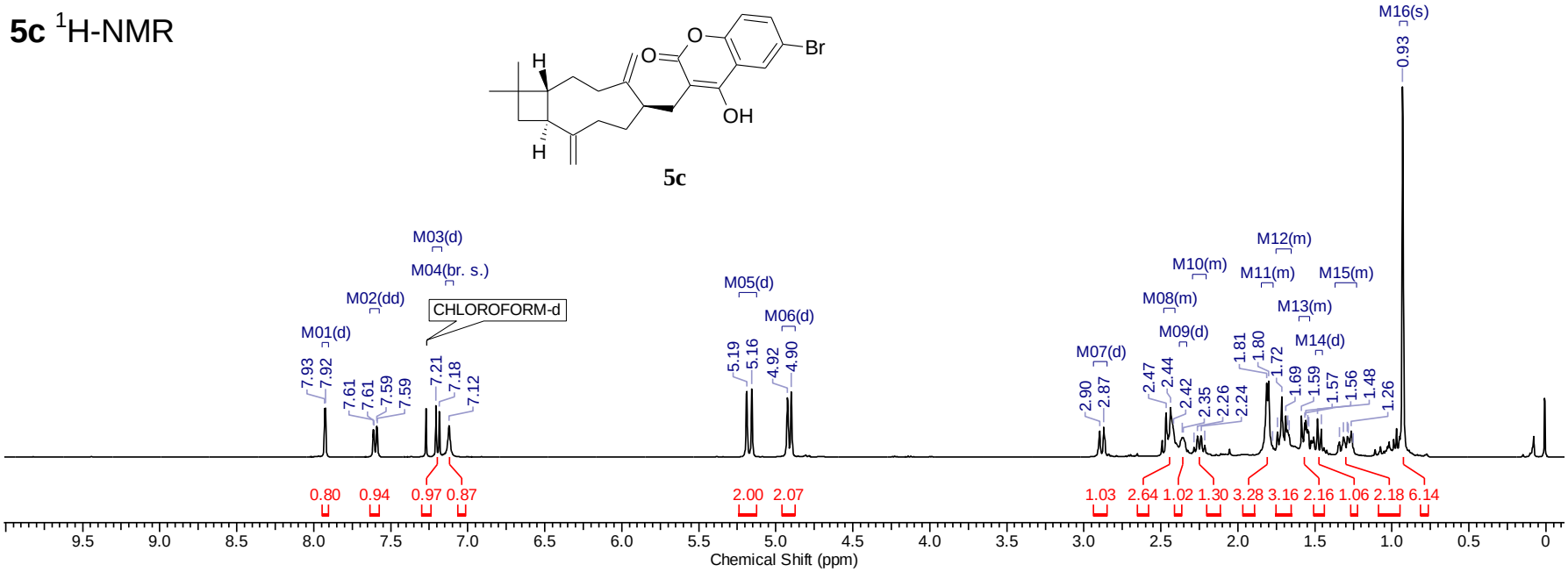


4c

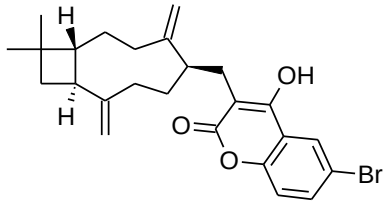

+TOF MS: 0.0687 min from Sample 1 (ZQYDW2018605-7) of ZQYDW2018605-7.wiff
a=7.028097130533445550e-004, t0=2.549207334018242 50e-001 (DuoSpray ()), Noise Filtered
Max. 1.9e5 cps.
457.1367
Intensity, cps
m/z, Da
Br
O
O
O
H
H
H
4c

Compound 5c

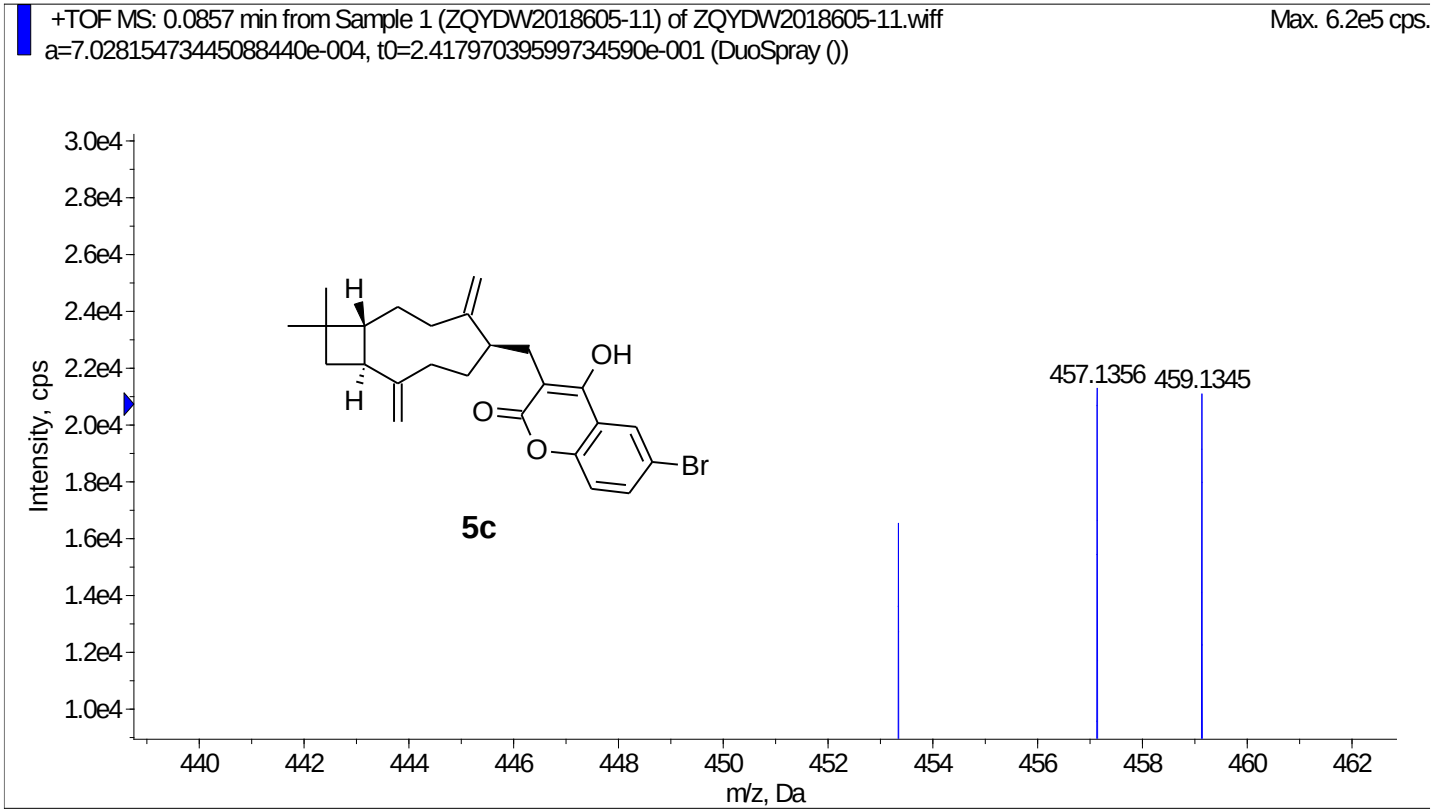
5c ^{1}H-NMR



DEPT135 and ^{13}C NMR



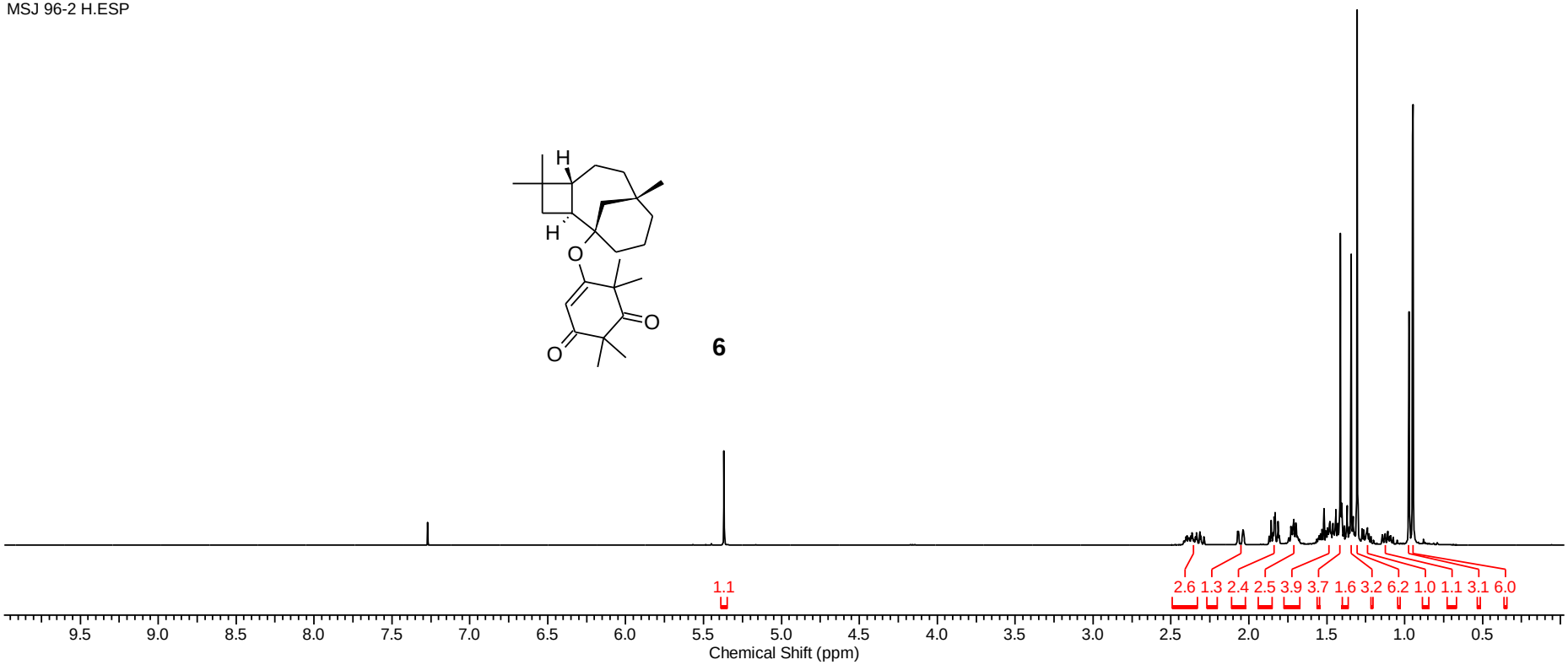
5c


+TOF MS: 0.0857 min from Sample 1 (ZQYDW2018605-11) of ZQYDW2018605-11.wiff
Max. 6.2e5 cps.
a=7.028154734450884 40e-004, t0=2.41797039599734590e-001 (DuoSpray ())
Intensity, cps
3.0e4
2.8e4
2.6e4
2.4e4
2.2e4
2.0e4
1.8e4
1.6e4
1.4e4
1.2e4
1.0e4
440
442
444
446
448
450
452
454
456
458
460
462
m/z, Da
457.1356
459.1345
H
H
OH
O
O
Br
5c

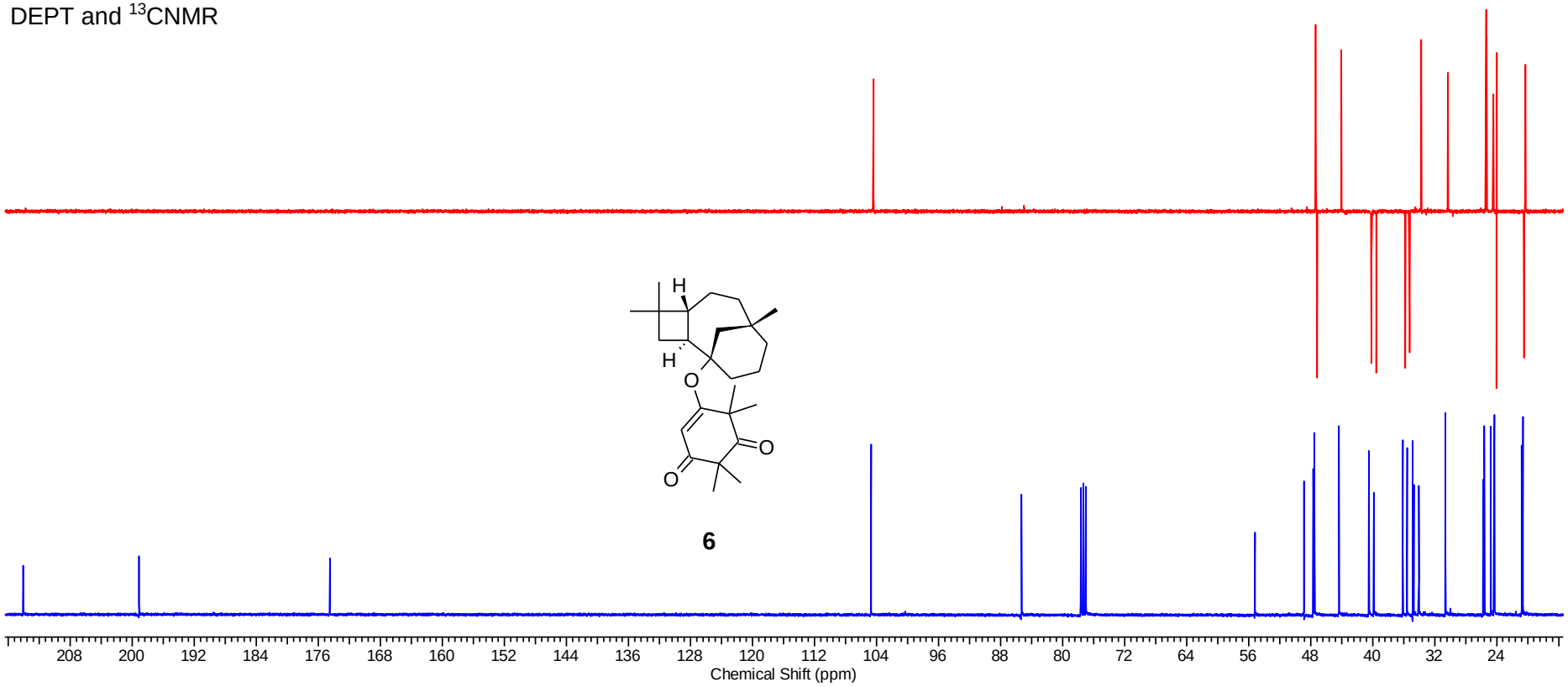
Compound 6

6 ^{1}H-NMR

MSJ 96-2 H.ESP

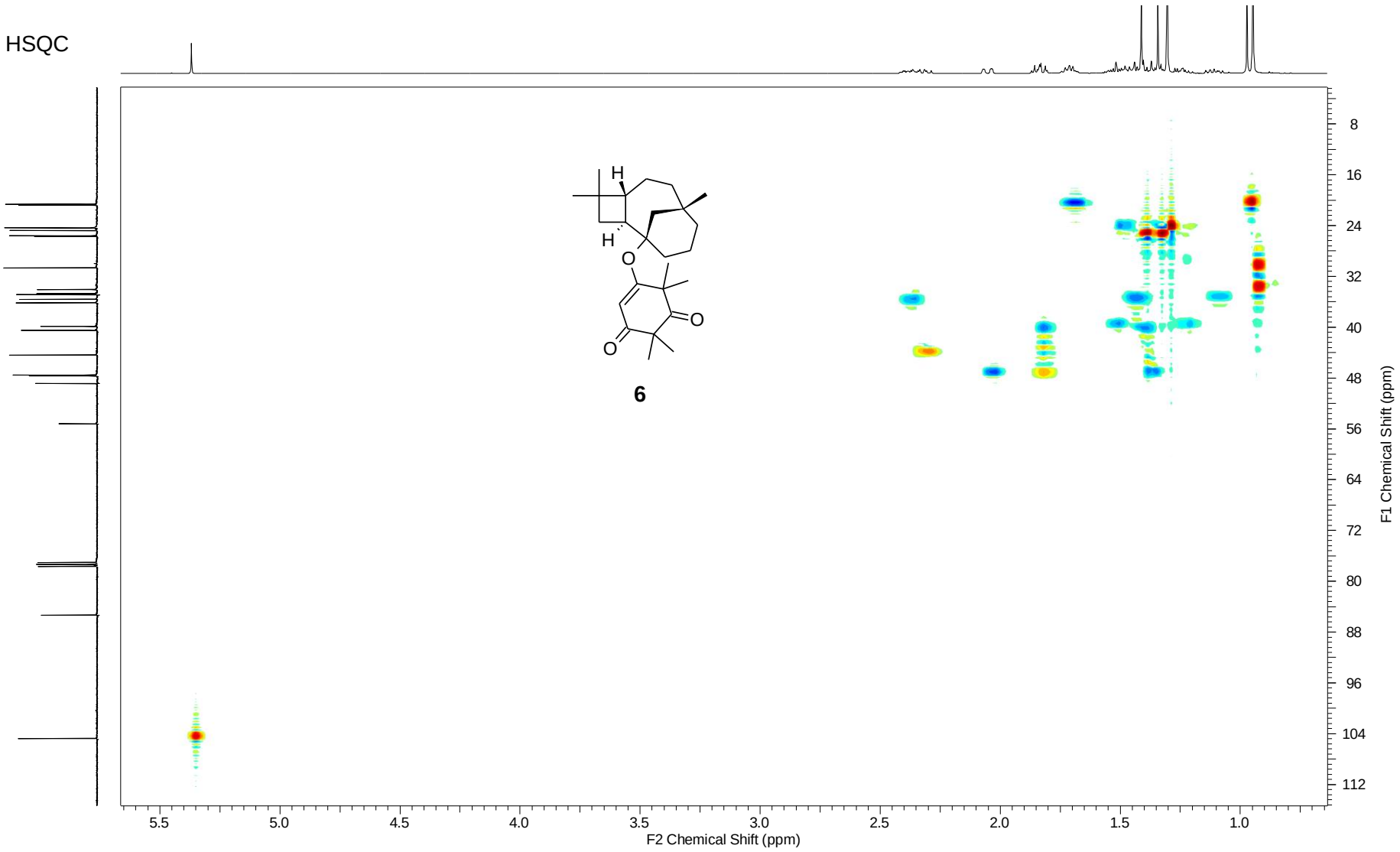


DEPT and ^{13}CNMR

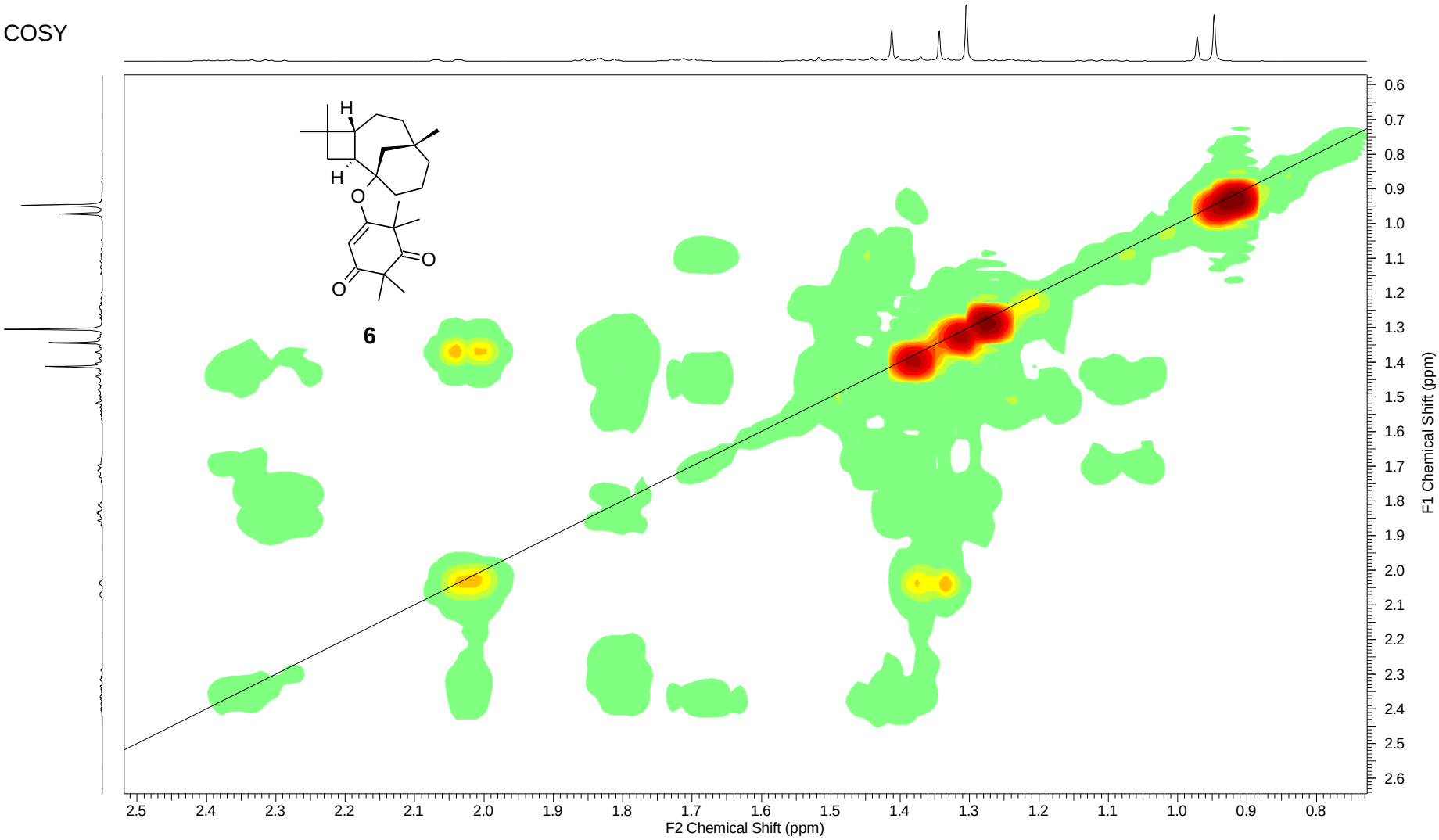


6

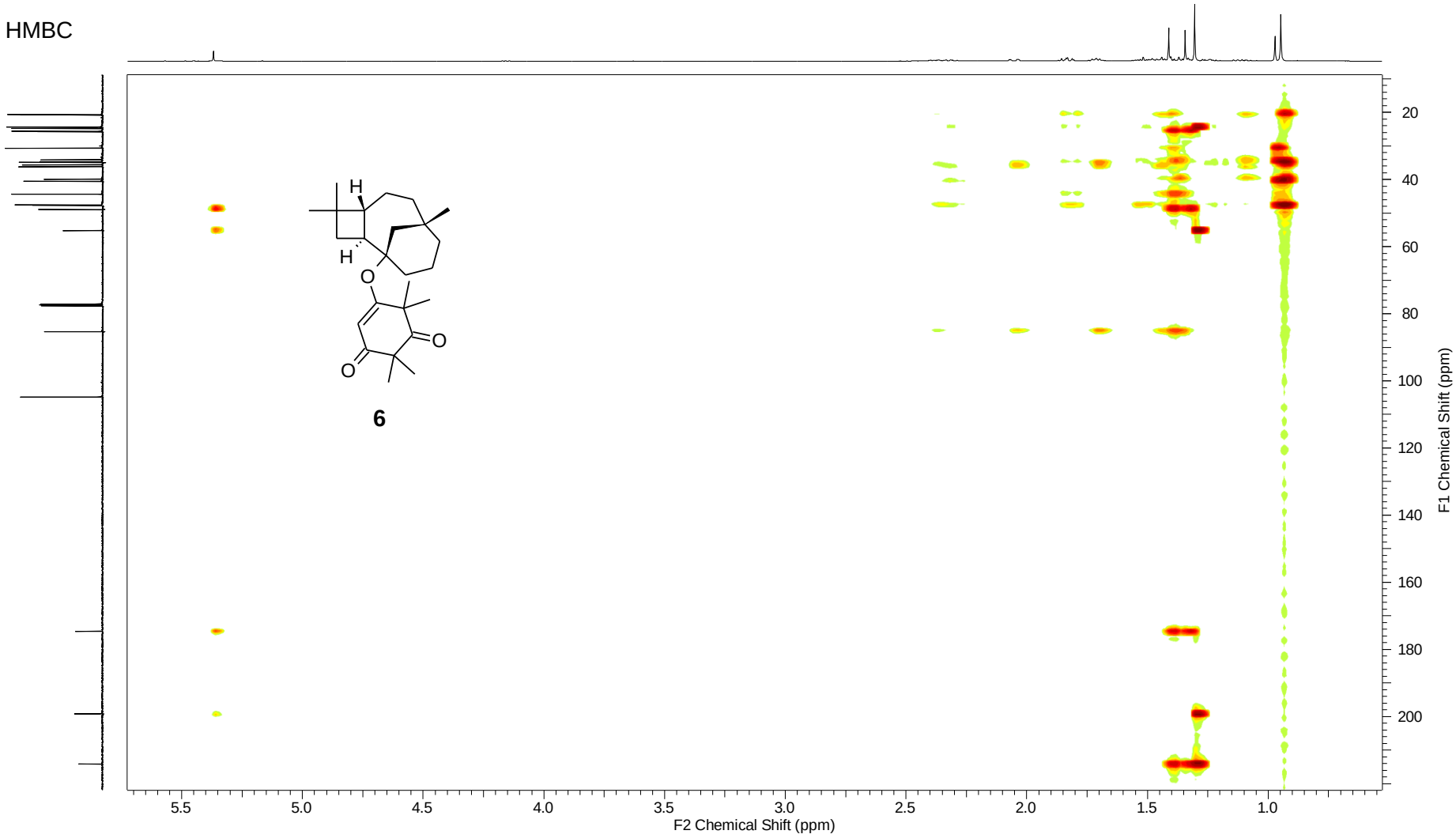
HSQC


H
H
O
O
O
6
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
F2 Chemical Shift (ppm)
8
16
24
32
40
48
56
64
72
80
88
96
104
112
F1 Chemical Shift (ppm)

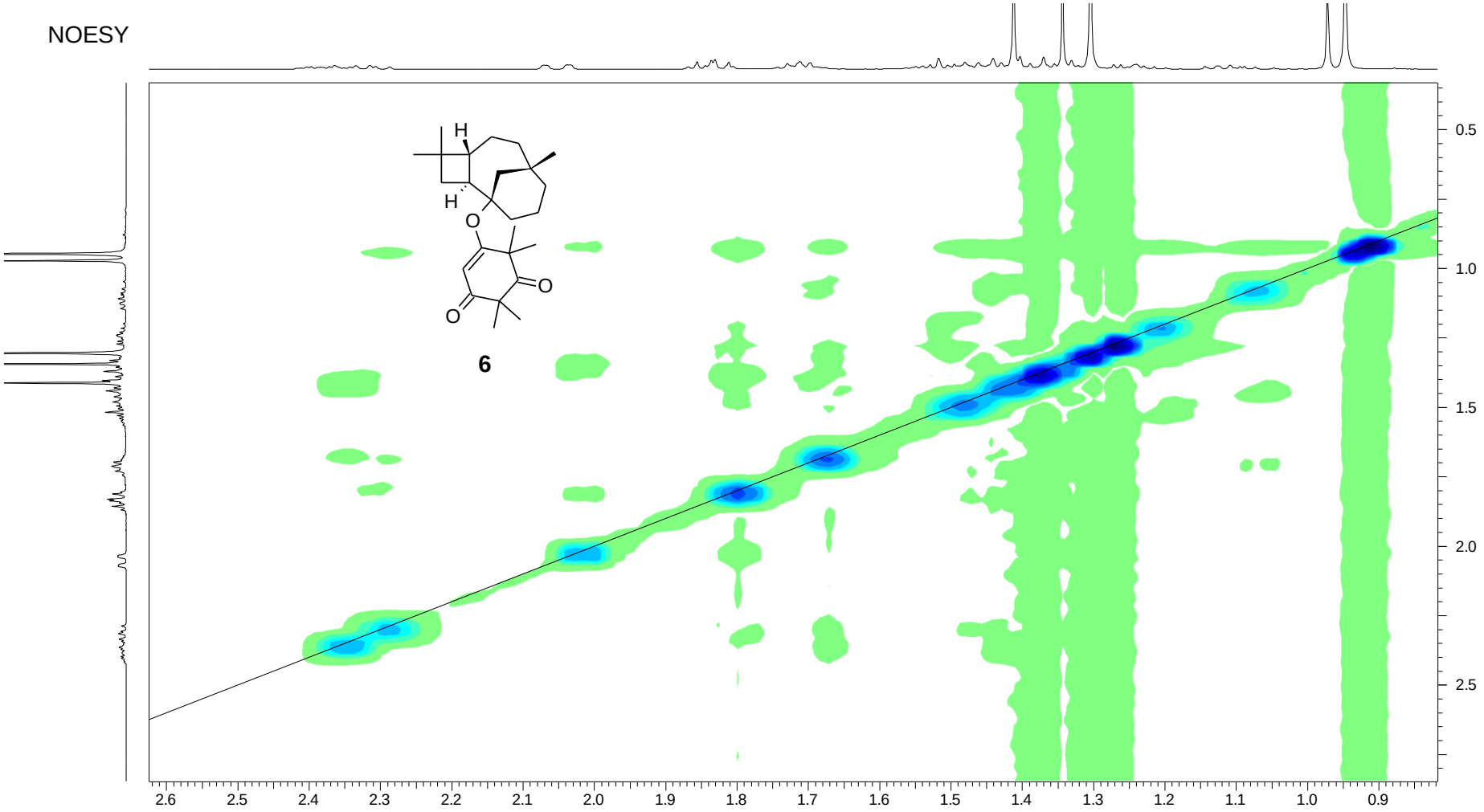
COSY



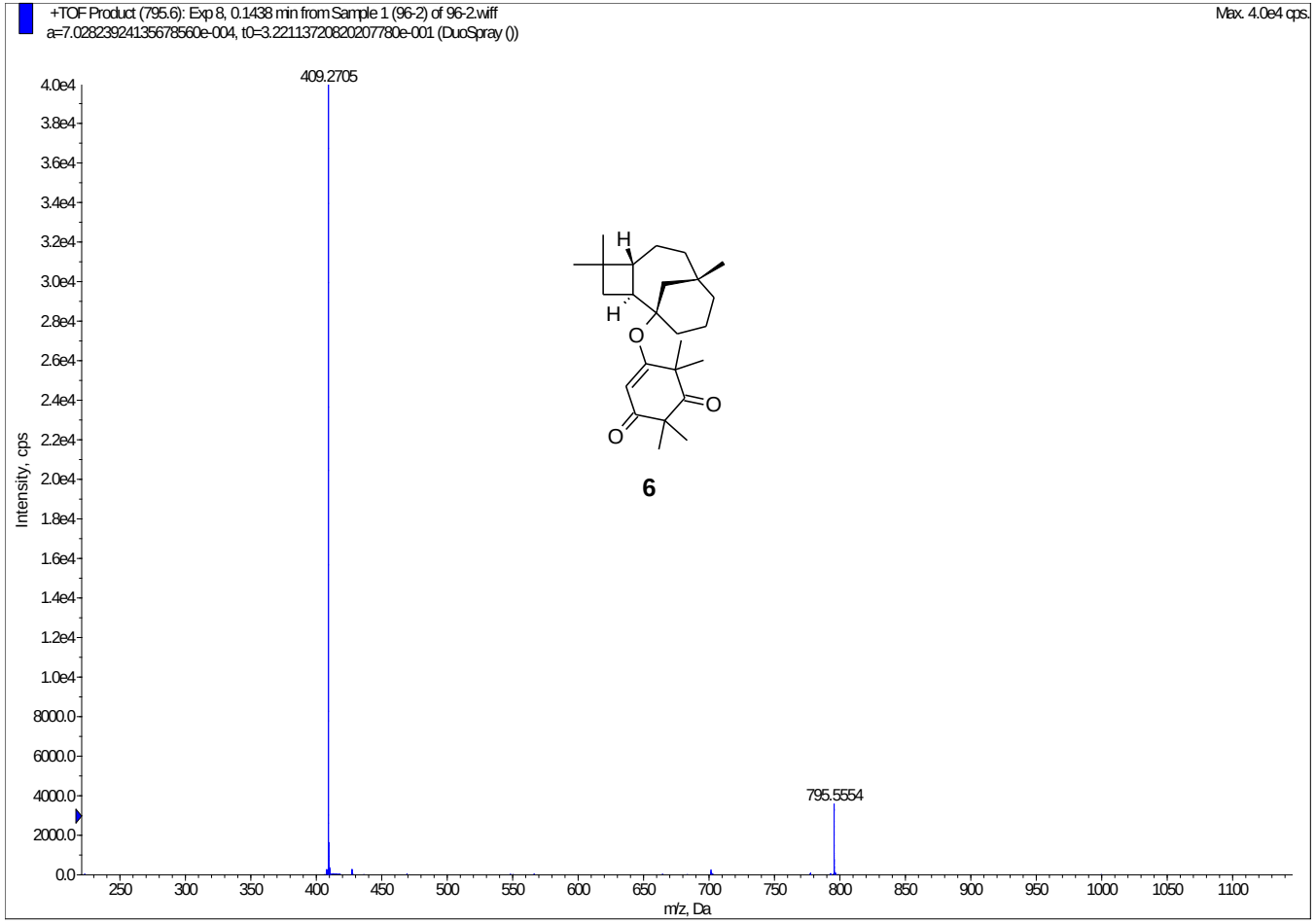
HMBC


H
H
O
O
O
6
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
F2 Chemical Shift (ppm)
20
40
60
80
100
120
140
160
180
200
F1 Chemical Shift (ppm)

NOESY

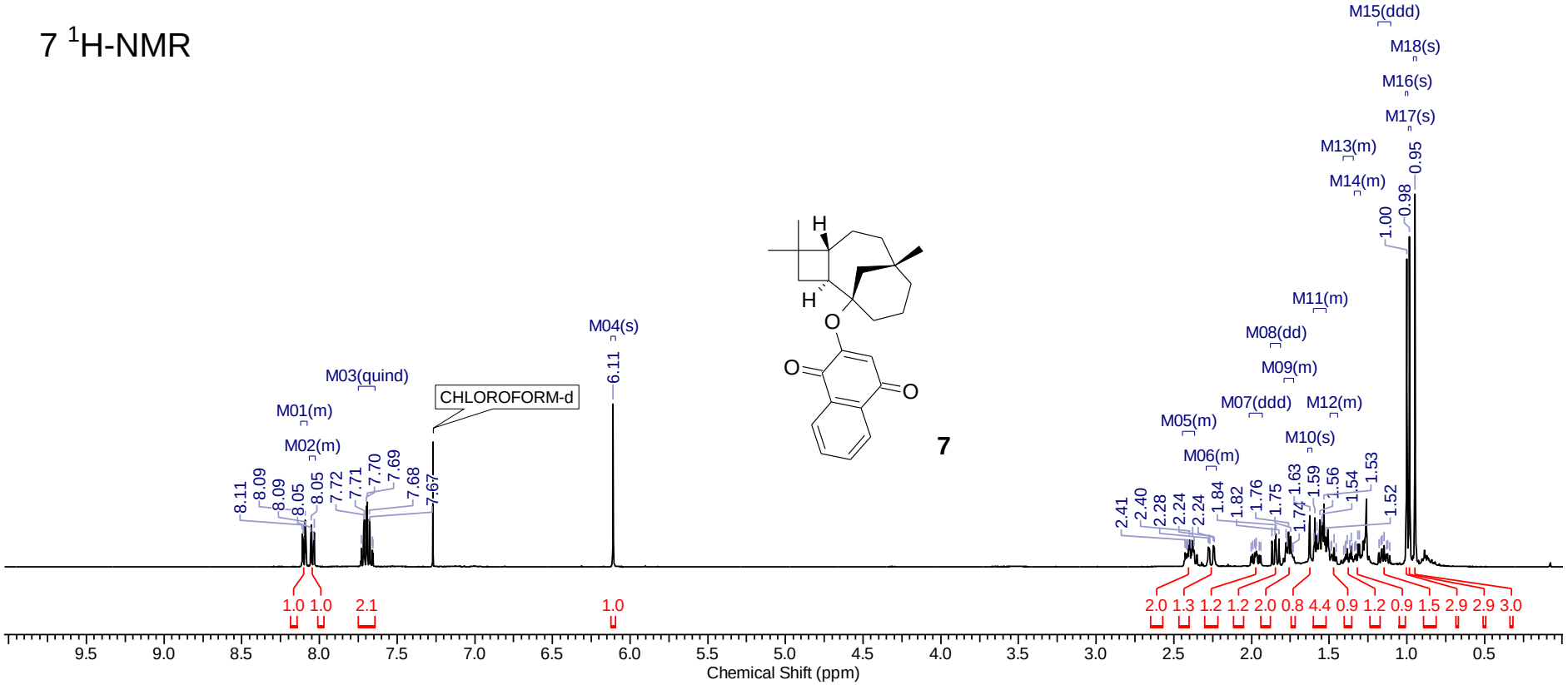

H
H
O
O
O
6
0.5
1.0
1.5
2.0
2.5
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9

HR-ESI-MS

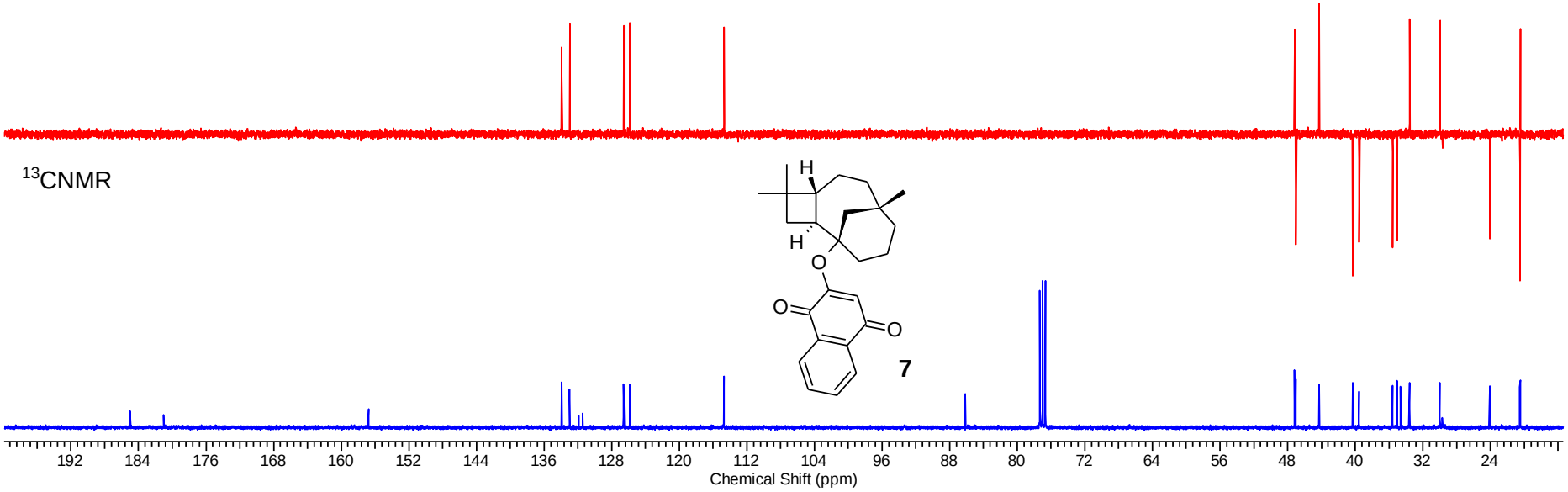

+TOF Product (795.6): Exp 8, 0.1438 min from Sample 1 (96-2) of 96-2.wiff
a=7.028239241356785 60e-004, t0=3.2211372082020778 0e-001 (DuoSpray ())
Max. 4.0e4 cps.
409.2705
795.5554
Intensity, cps
m/z, Da
H
H
O
O
O
6

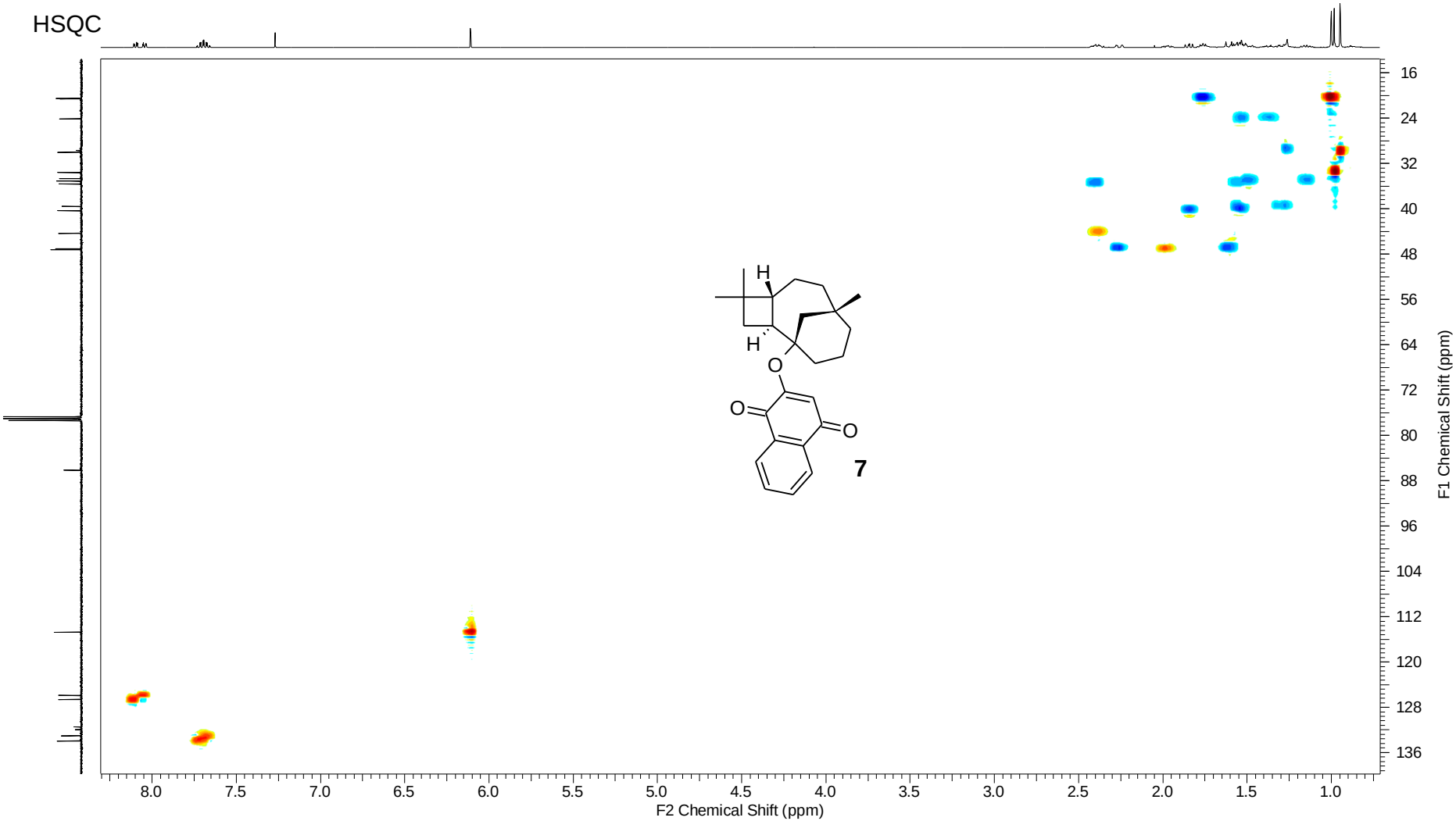
Compound 7

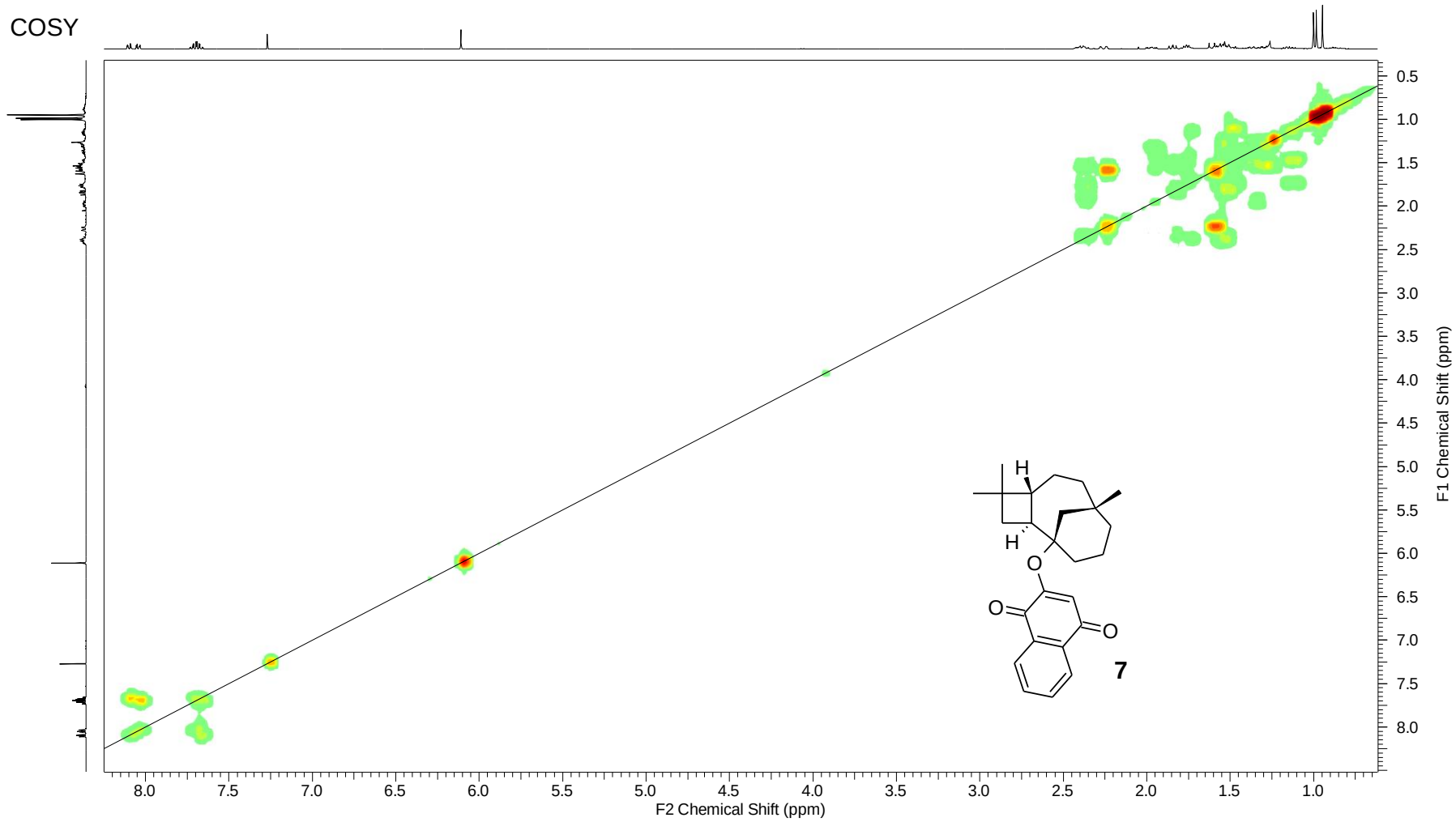
7 ^{1}H-NMR

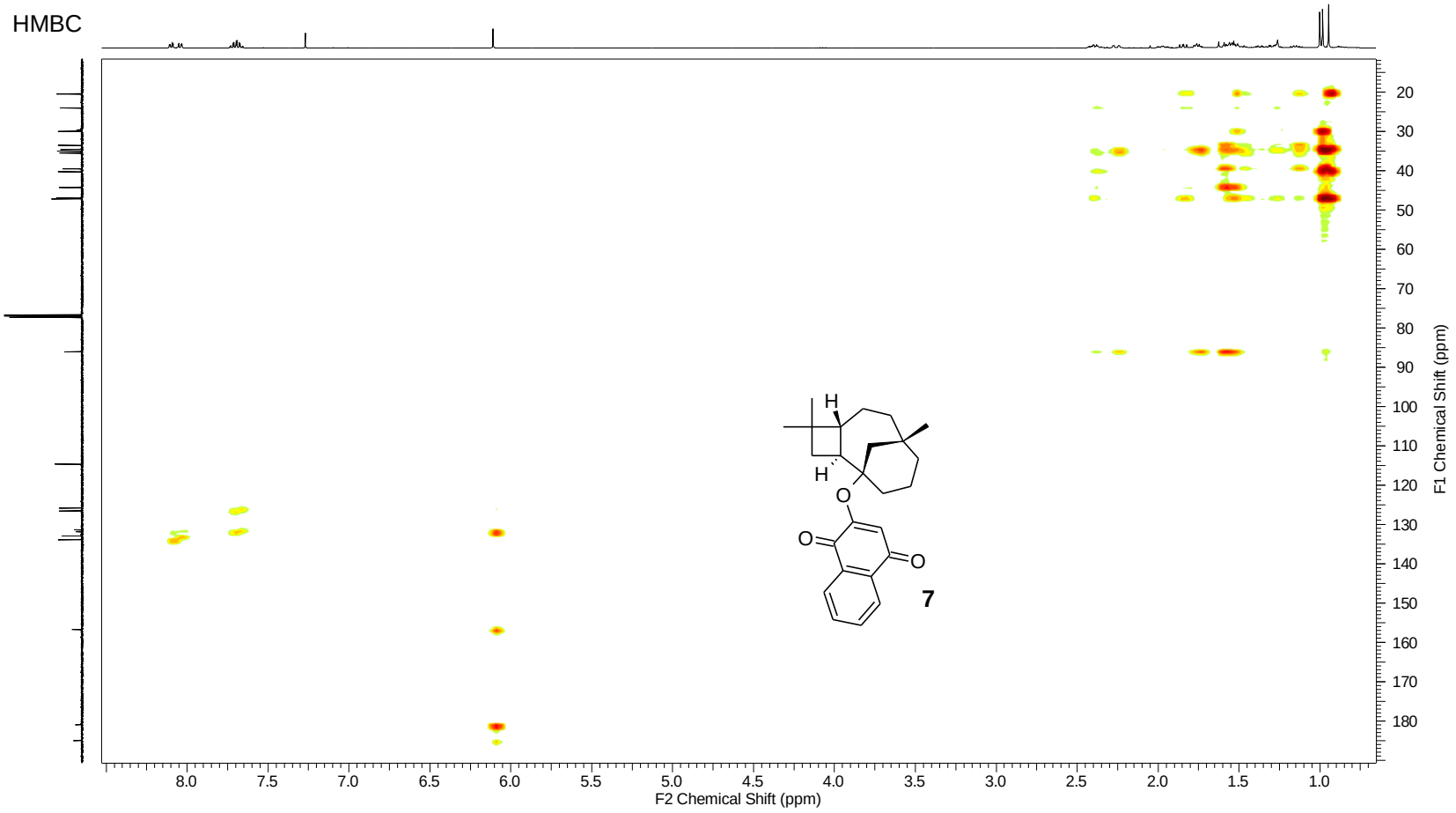


^{13}C-NMR and DEPT135

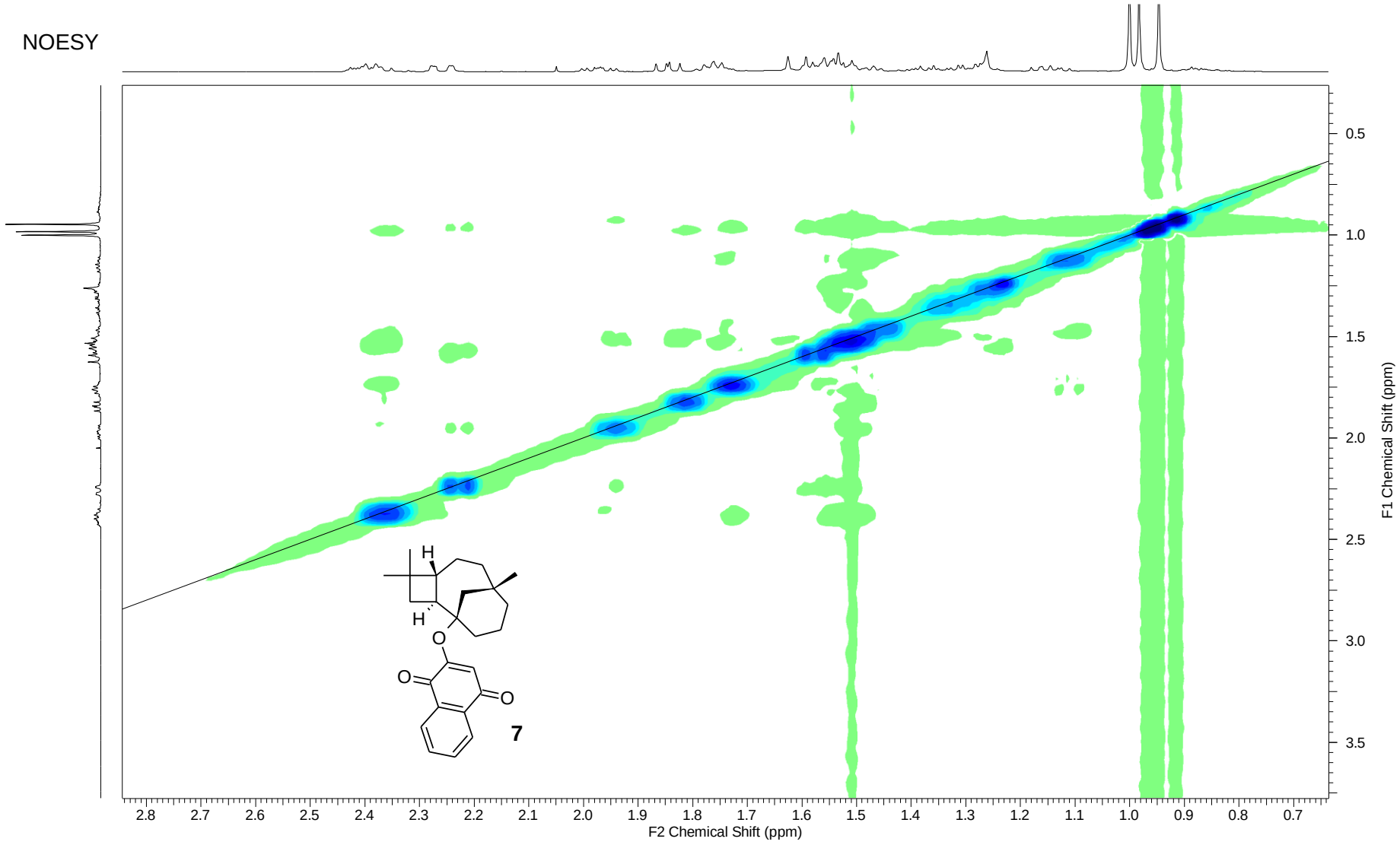



HSQC
H
H
O
O
O
7
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
16
24
32
40
48
56
64
72
80
88
96
104
112
120
128
136

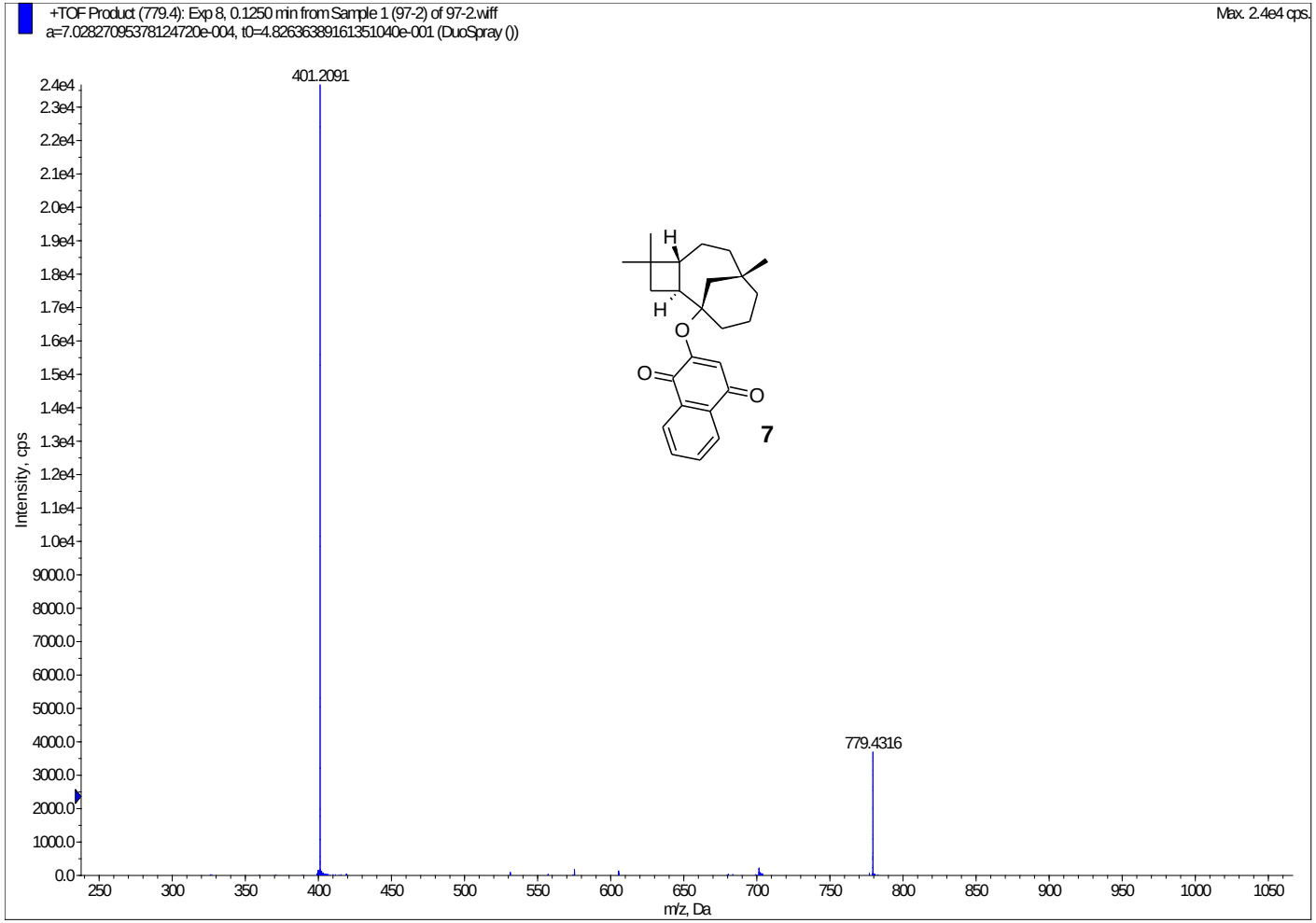

COSY
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)
H
H
O
O
O
7


HMBC
F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
H
H
O
O
O
7

NOESY


H
H
O
O
O
7
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
F2 Chemical Shift (ppm)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
F1 Chemical Shift (ppm)

HR-ESI-MS


+TOF Product (779.4): Exp 8, 0.1250 min from Sample 1 (97-2) of 97-2.wiff
a=7.028270953781247 20e-004, t0=4.826363891613510 40e-001 (DuoSpray ())
Max. 2.4e4 cps.
401.2091
779.4316
Intensity, cps
m/z, Da
7