Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

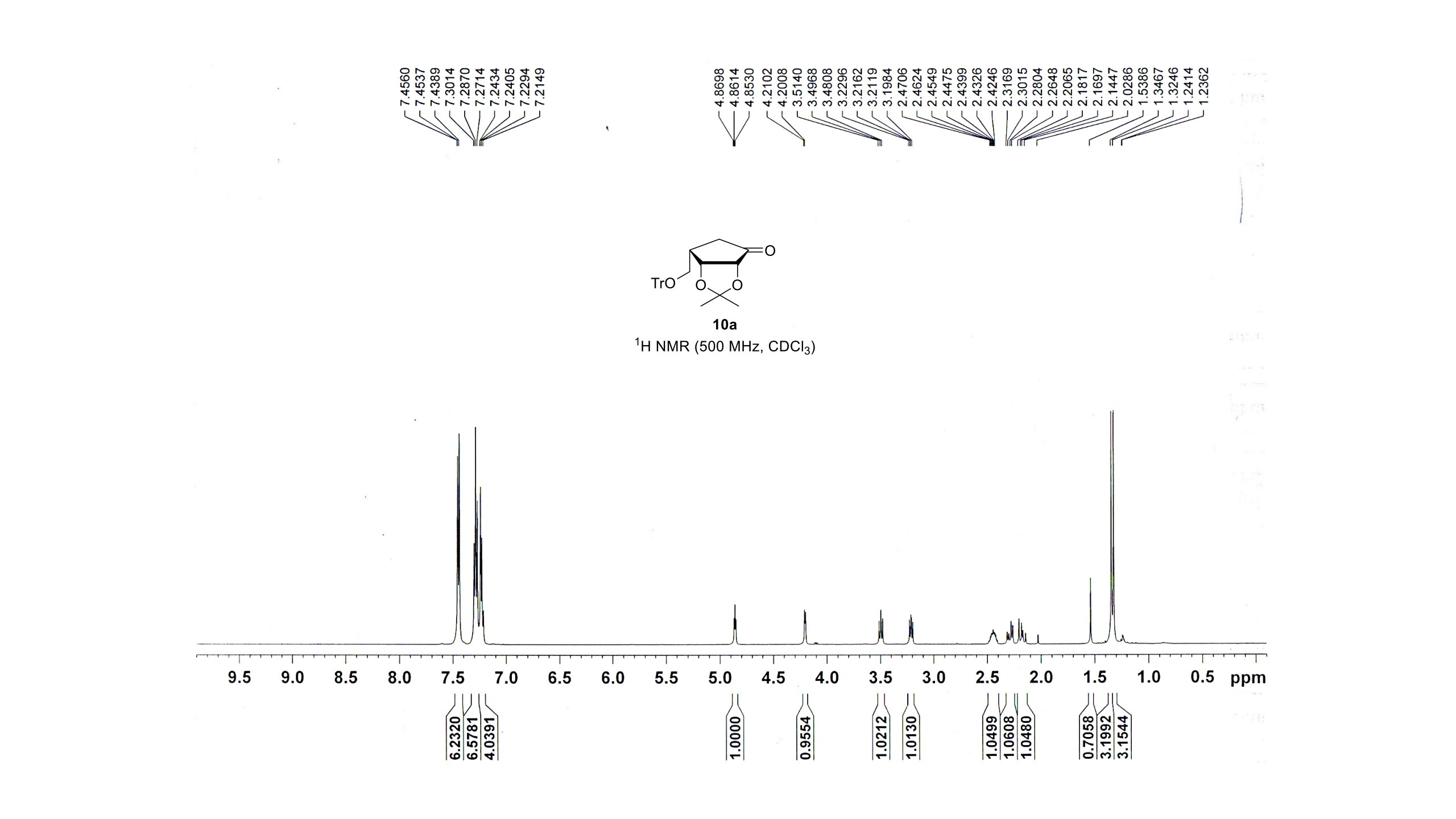
Supporting Information

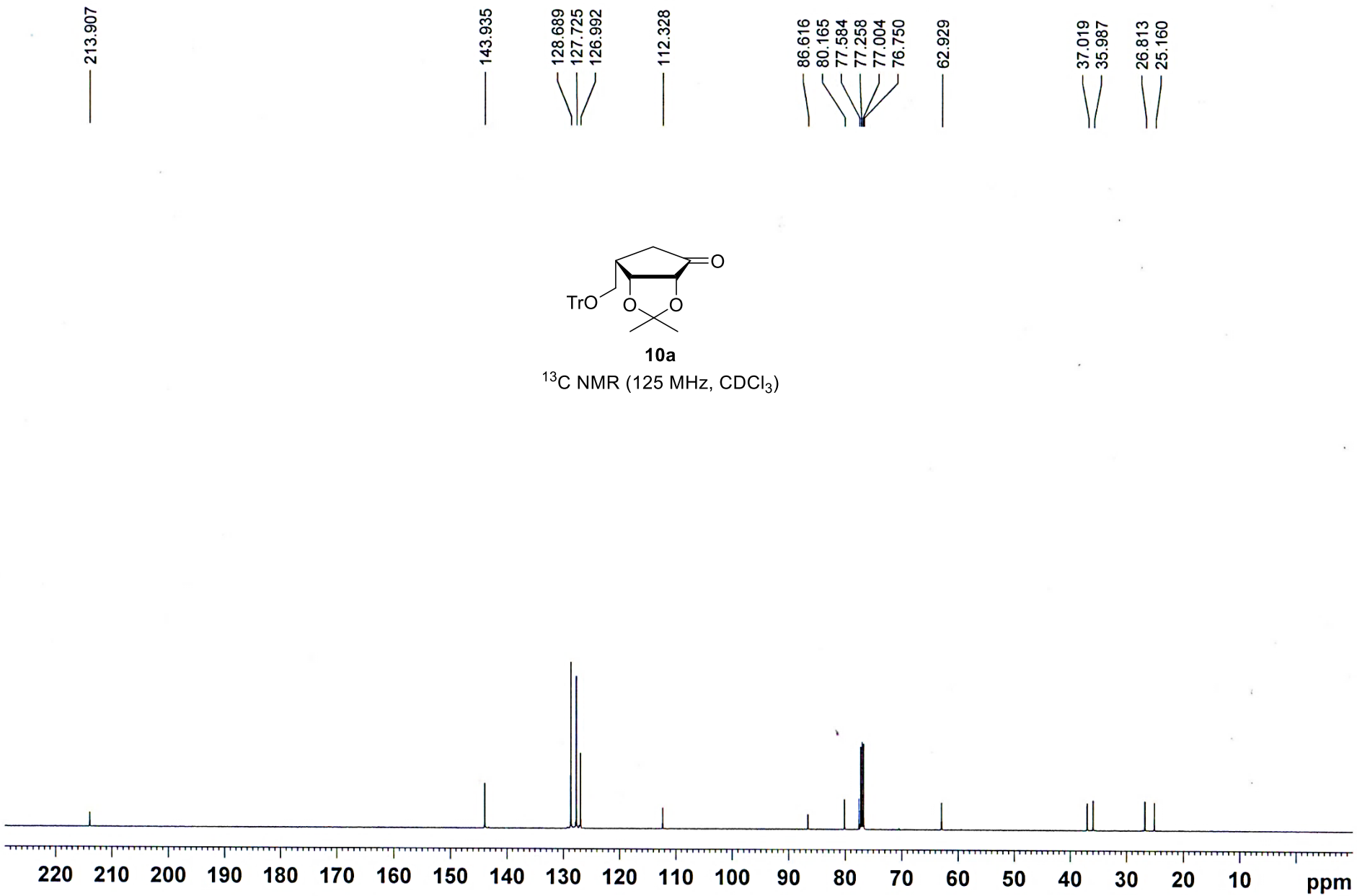
An Efficient Synthesis of Fluoro-neplanocin A Analogs Using Electrophilic Fluorination and Palladium-catalyzed Dehydrosilylation

Dnyandev B. Jarhad,[a] Min Hwan Jang,[a] Young Sup Shin,[a] Gyudong Kim,[a,b] Hong-Rae Kim,[a] Young Eum Hyun,[a] Ji-seong Yoon,[a] and Lak Shin Jeong*,[a]

[a]Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University, Seoul 08826, Korea, Tel: +82-2-880-7850; [b]College of Pharmacy and Research Institute of Drug Development, Chonnam National University, Gwangju 500-757, Korea.

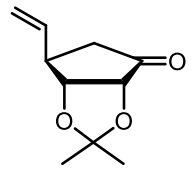
E-mail: lakjeong@snu.ac.kr


7.4560
7.4537
7.4389
7.3014
7.2870
7.2714
7.2434
7.2405
7.2294
7.2149
4.8698
4.8614
4.8530
4.2102
4.2008
3.5140
3.4968
3.4808
3.2296
3.2162
3.2119
3.1984
2.4706
2.4624
2.4549
2.4475
2.4399
2.4326
2.4246
2.3169
2.3015
2.2804
2.2648
2.2065
2.1817
2.1697
2.1447
2.0286
1.5386
1.3467
1.3246
1.2414
1.2362
TrO
O
O
O
10a
1H NMR (500 MHz, CDCl3)
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
ppm
6.2320
6.5781
4.0391
1.0000
0.9554
1.0212
1.0130
1.0499
1.0608
1.0480
0.7058
3.1992
3.1544



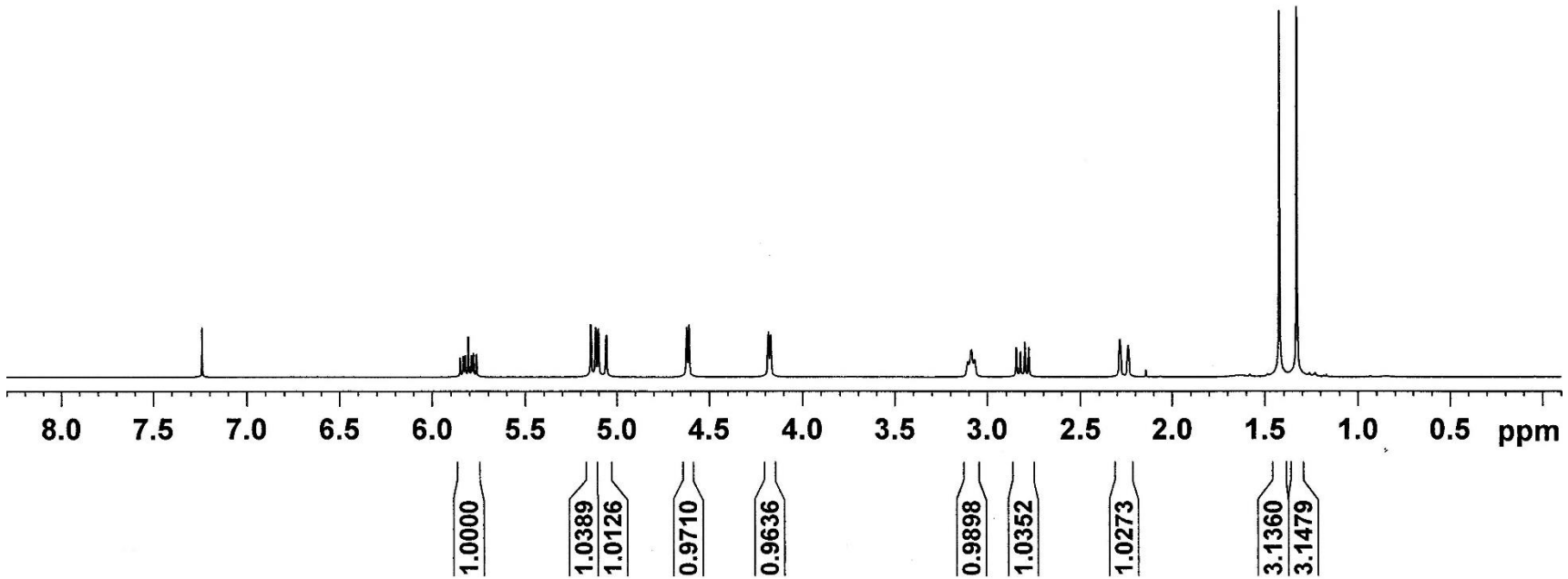
10a

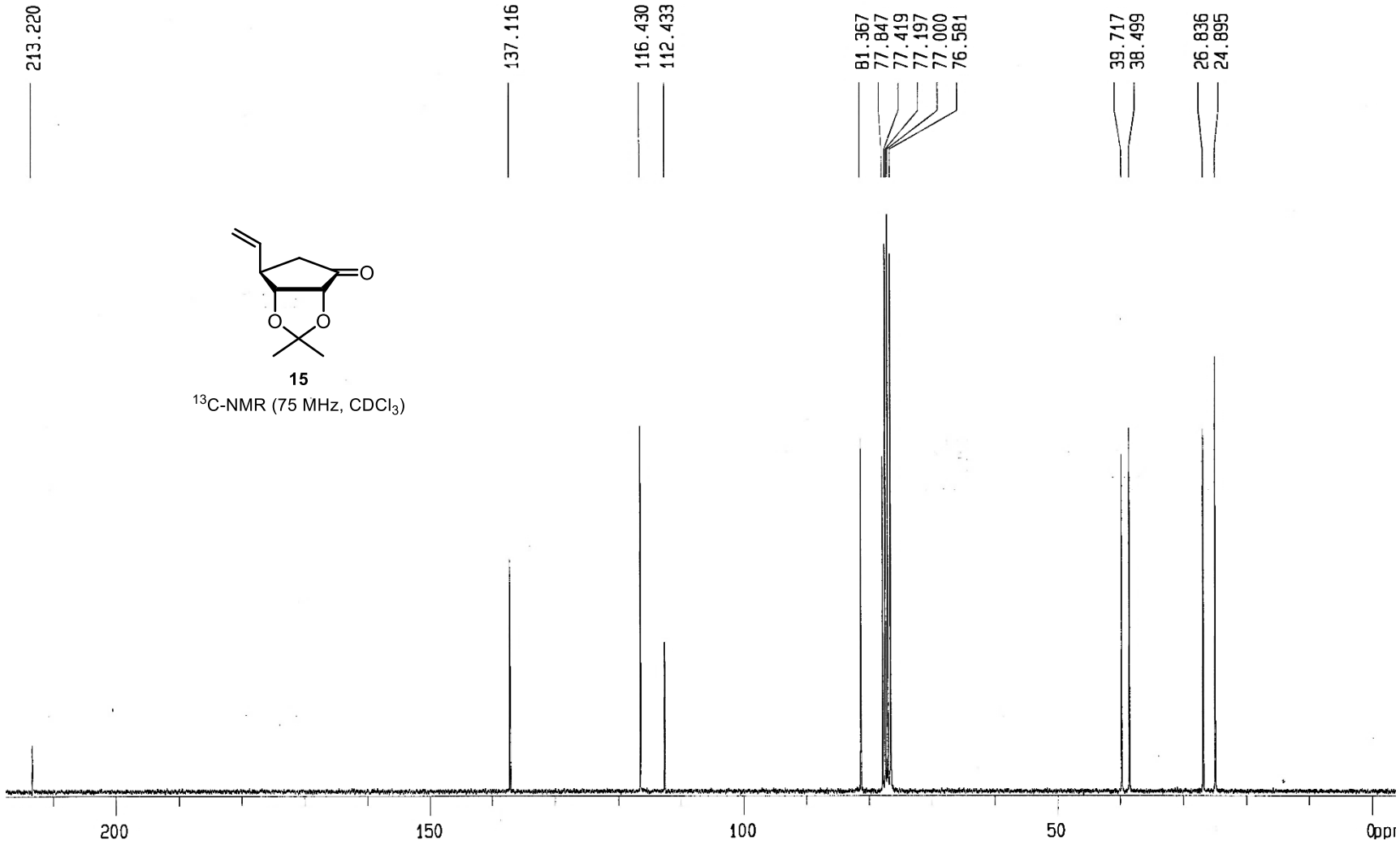
^{13}C NMR (125 MHz, $CDCl_3$)



15

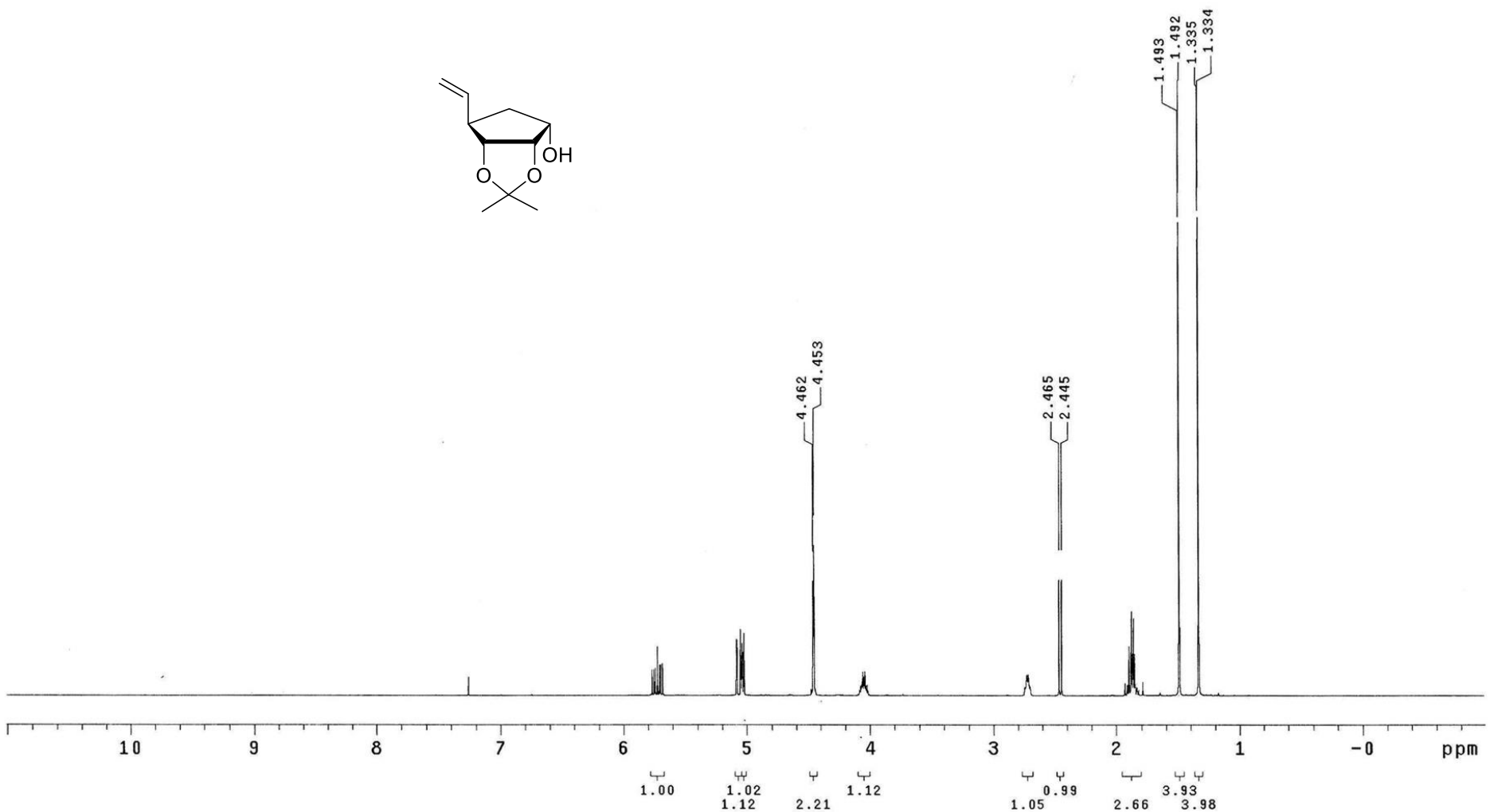
^{1}H-NMR (400 MHz, $CDCl_3$)

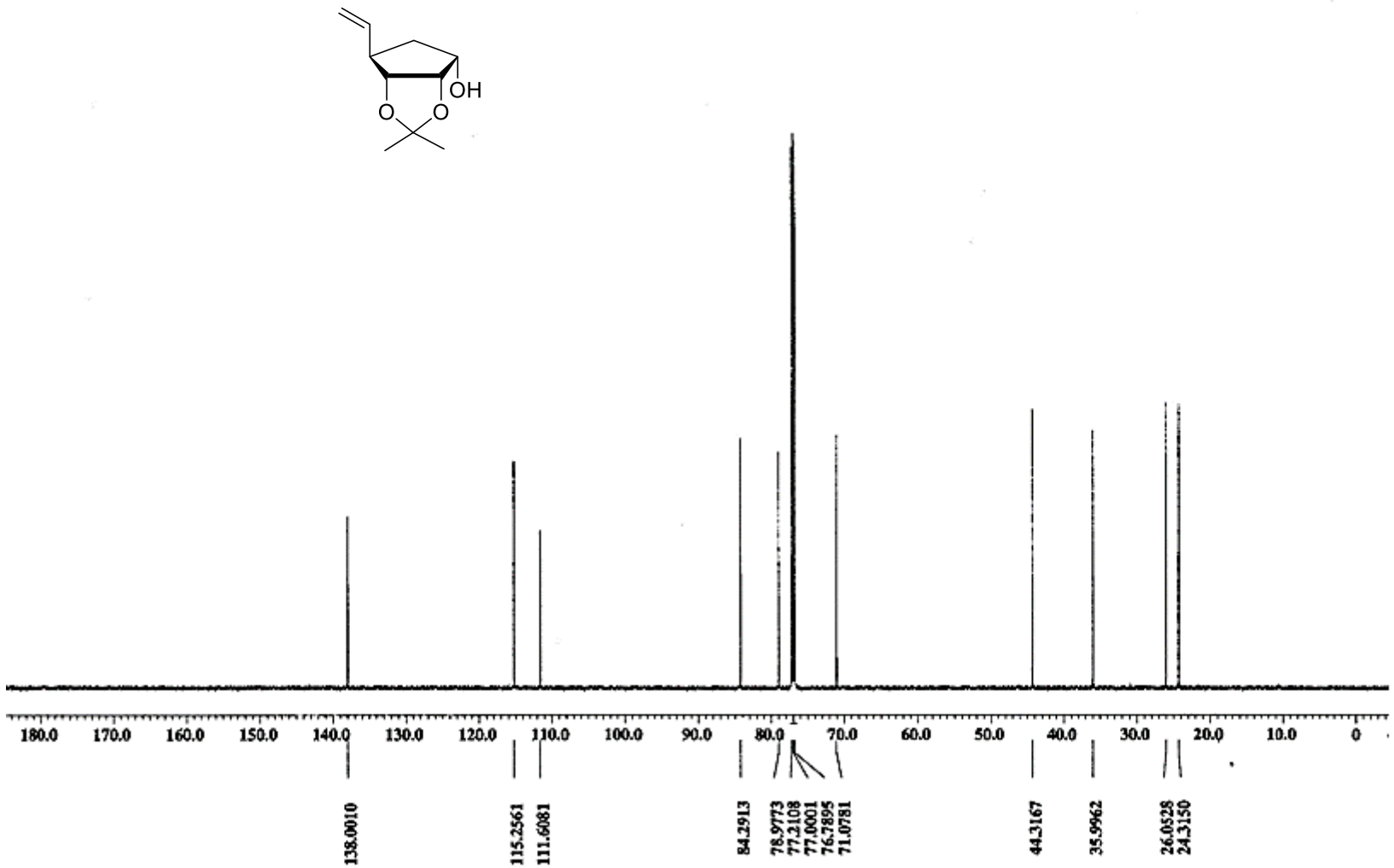


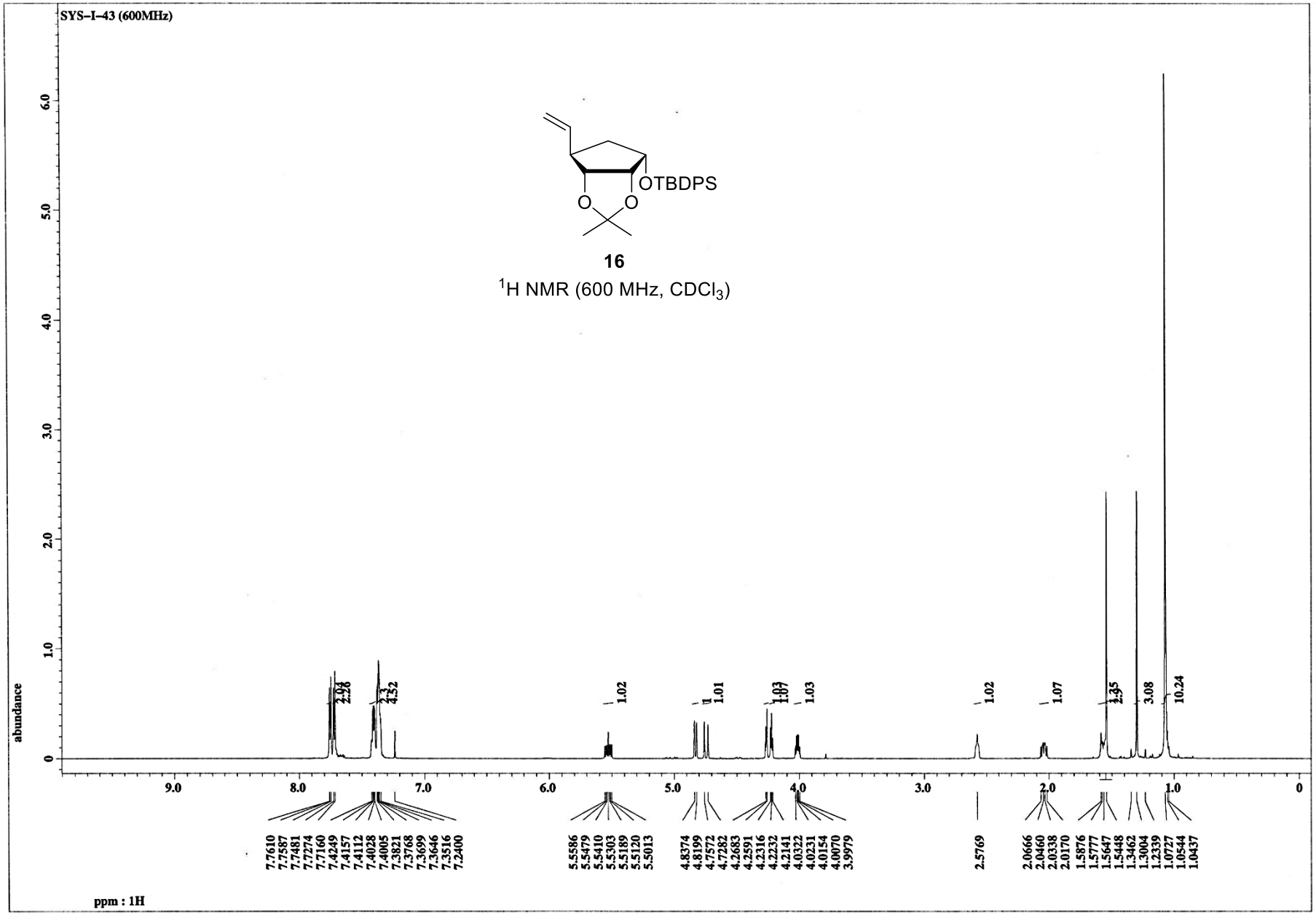


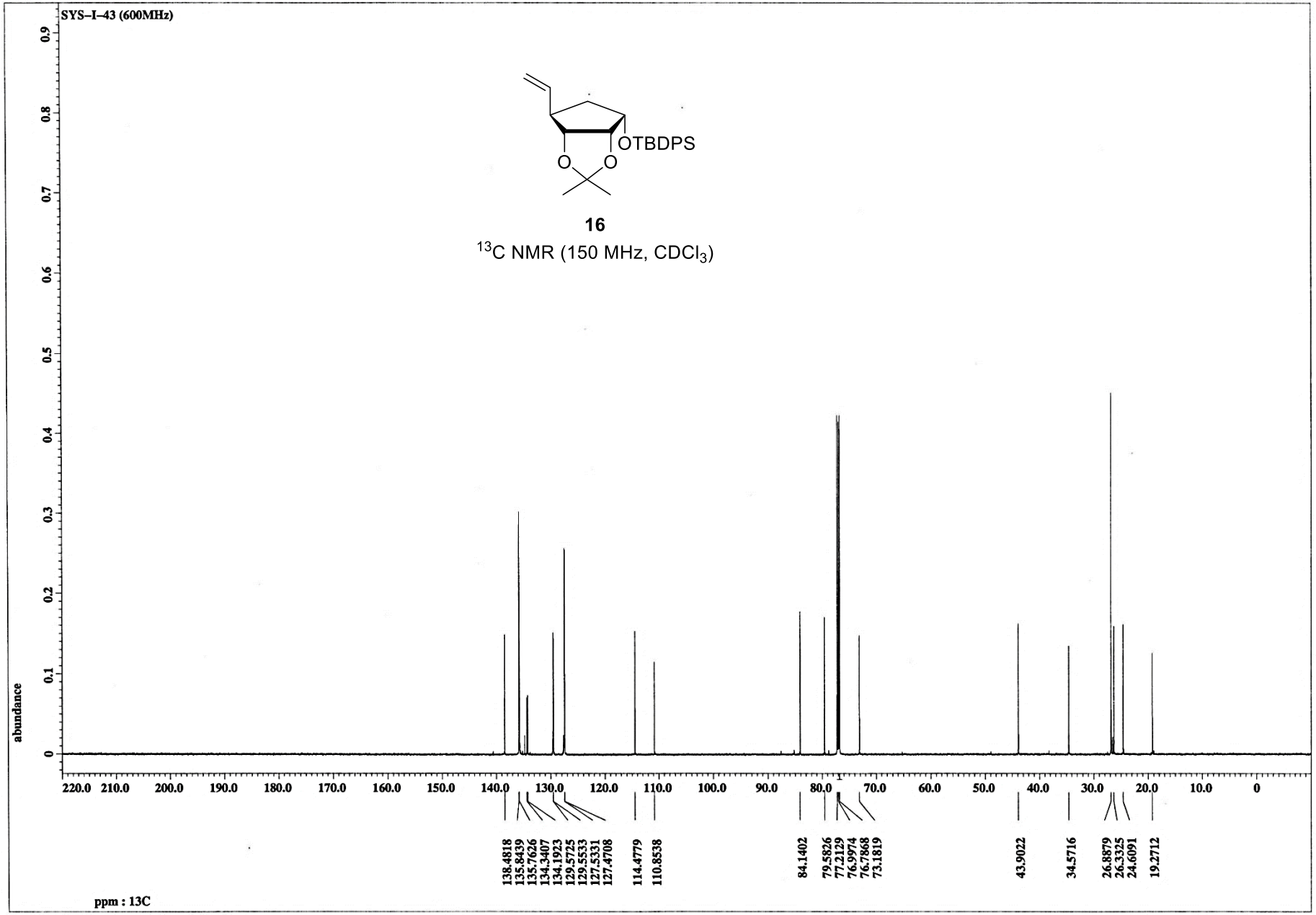
15

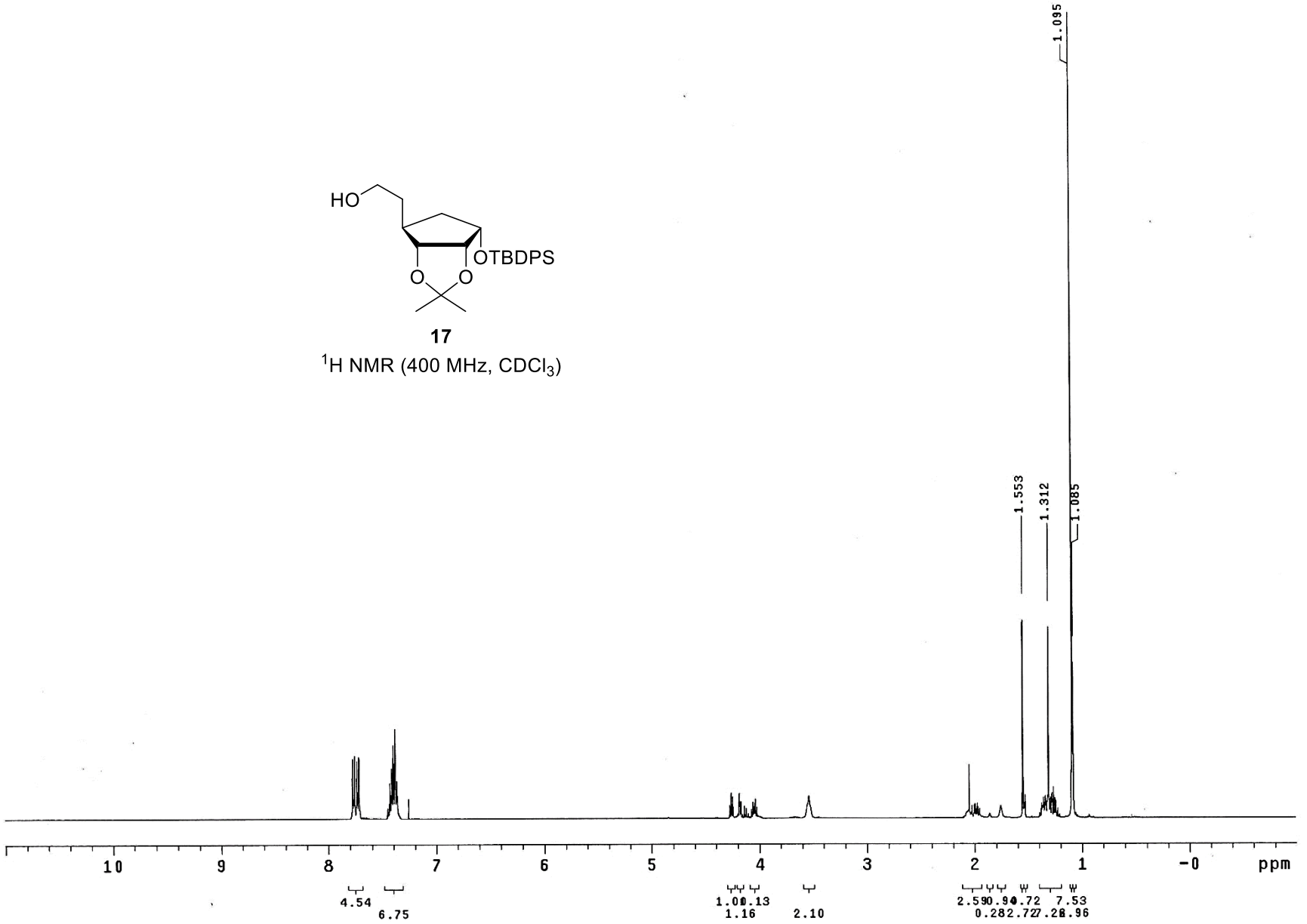
^{13}C-NMR (75 MHz, $CDCl_3$)


OH
O
O
1.493
1.492
1.335
1.334
4.462
4.453
2.465
2.445
10
9
8
7
6
5
4
3
2
1
-0
ppm
1.00
1.02
1.12
2.21
1.12
1.05
0.99
2.66
3.93
3.98


OH
O
O
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
138.0010
115.2561
111.6081
84.2913
78.9773
77.2108
77.0001
76.7895
71.0781
44.3167
35.9962
26.0528
24.3150

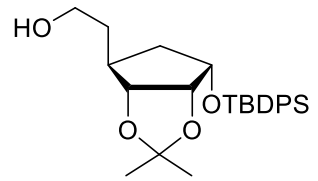

SYS–I–43 (600MHz)
OTBDPS
O
O
16
^{1}H NMR (600 MHz, $CDCl_3$)
abundance
ppm : 1H


SYS–I–43 (600MHz)
OTBDPS
O
O
16
^{13}C NMR (150 MHz, $CDCl_3$)
abundance
ppm : 13C
138.4818
135.8439
135.7626
134.3407
134.1923
129.5725
129.5533
127.5331
127.4708
114.4779
110.8538
84.1402
79.5826
77.2129
76.9974
76.7868
73.1819
43.9022
34.5716
26.8879
26.3325
24.6091
19.2712



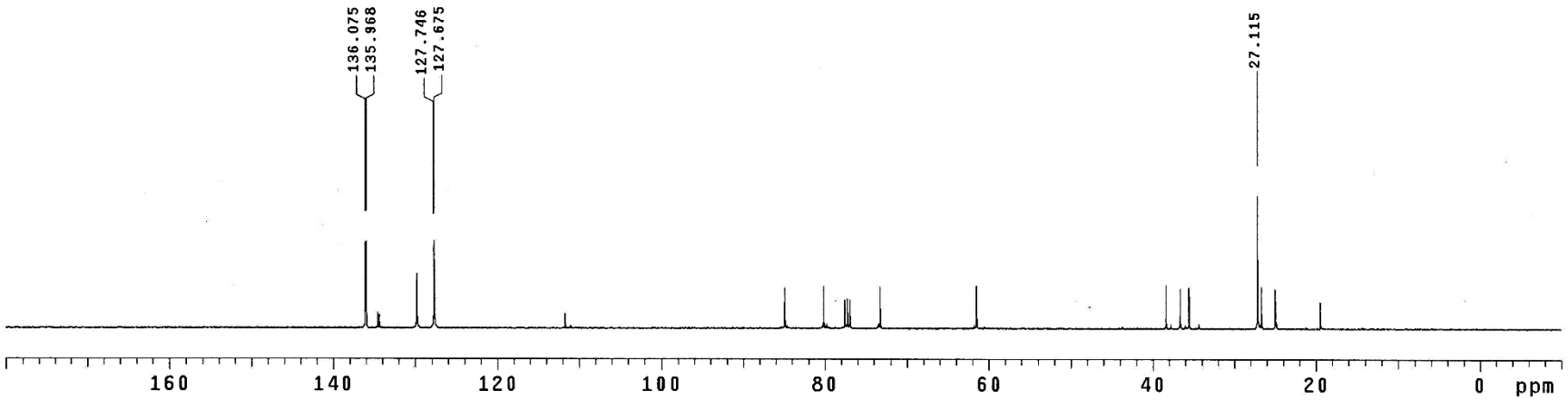
17

^{1}H NMR (400 MHz, $CDCl_3$)



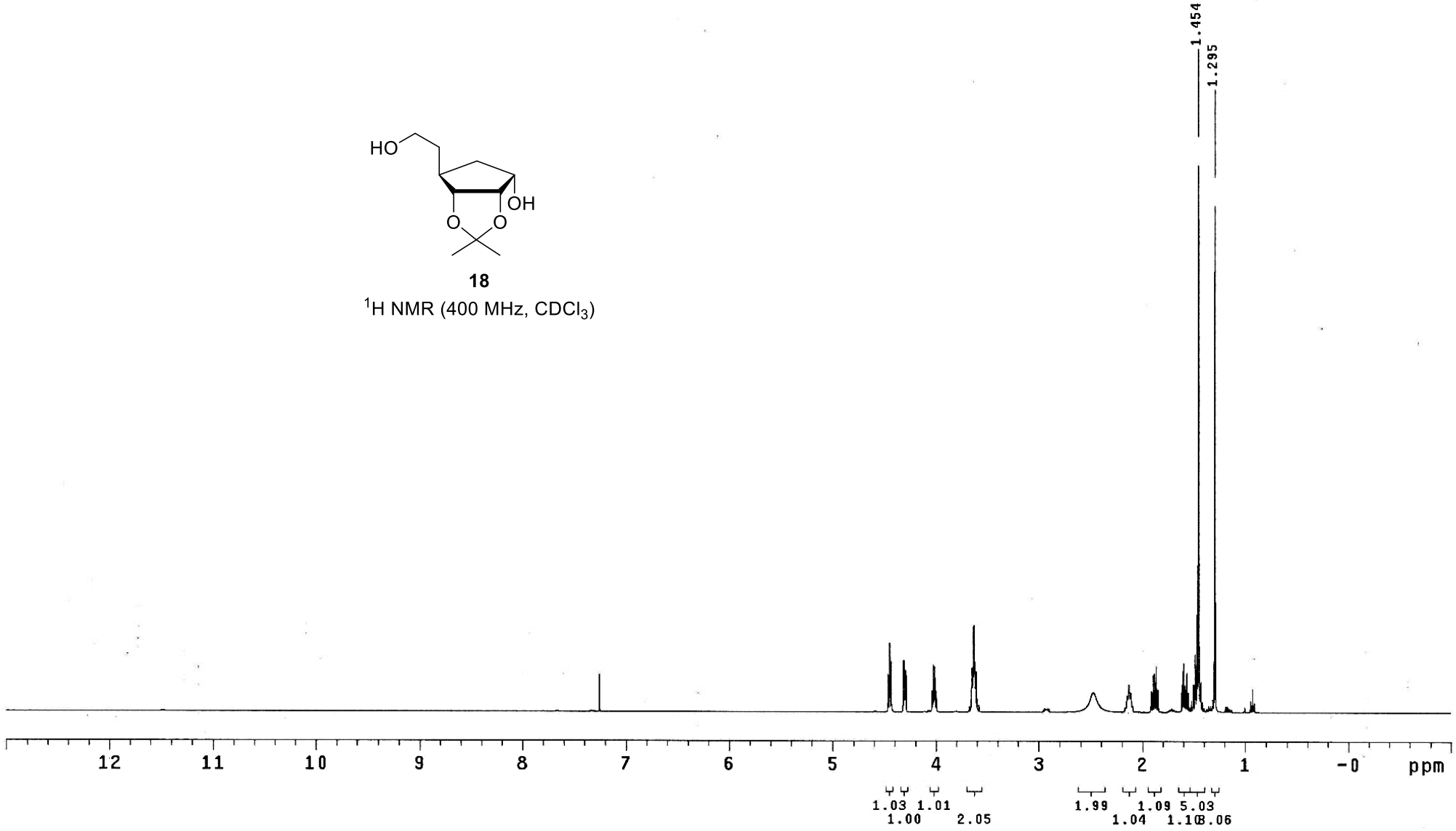
17

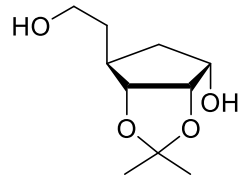
^{13}C NMR (100 MHz, $CDCl_3$)



18

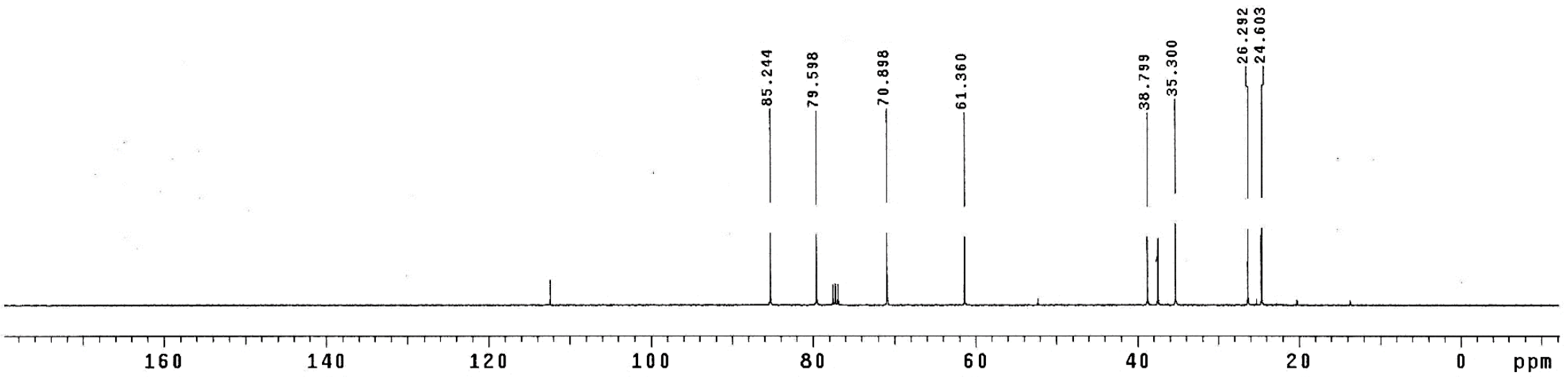
^{1}H NMR (400 MHz, $CDCl_3$)



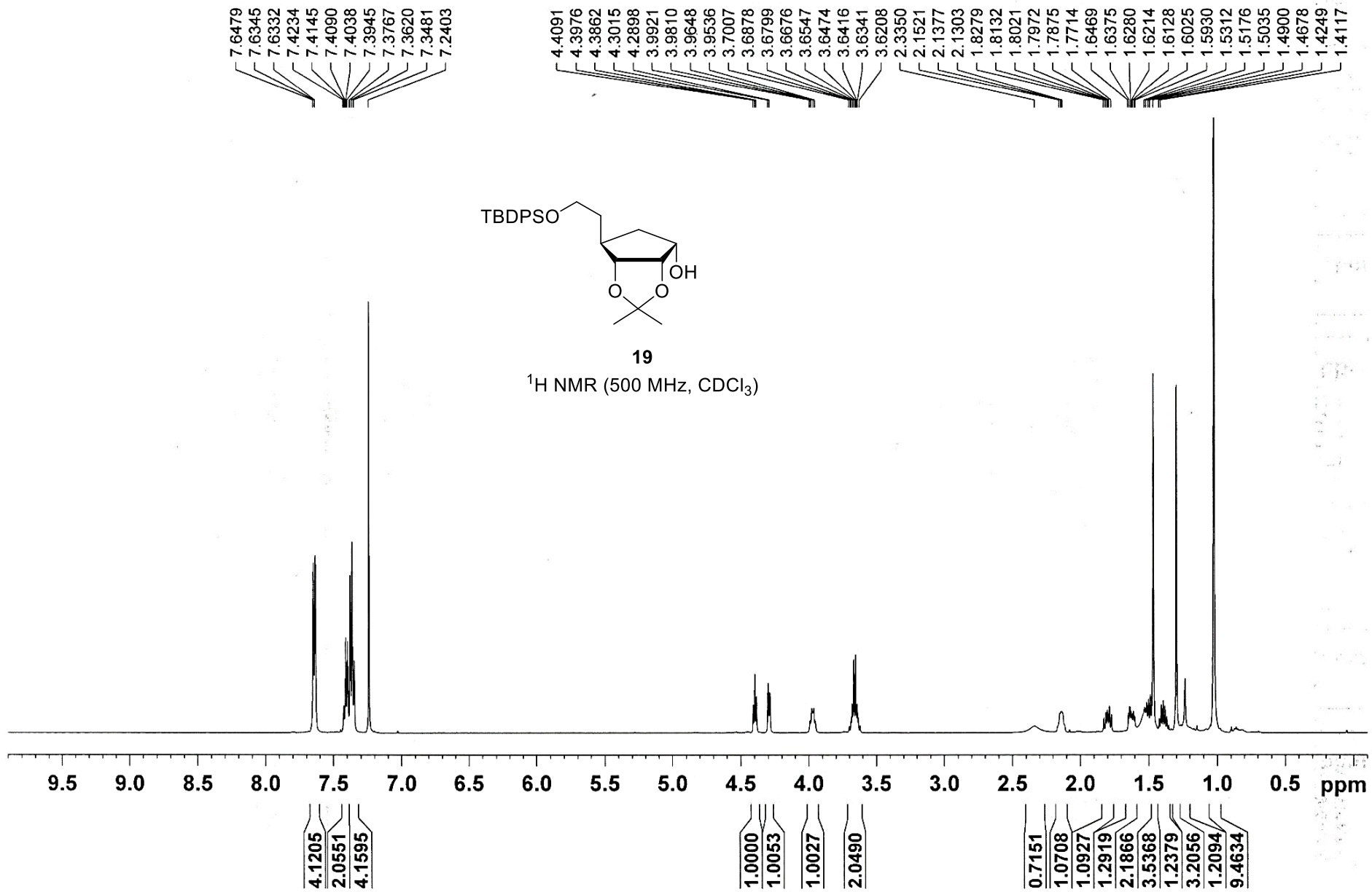


18

^{13}C NMR (100 MHz, $CDCl_3$)



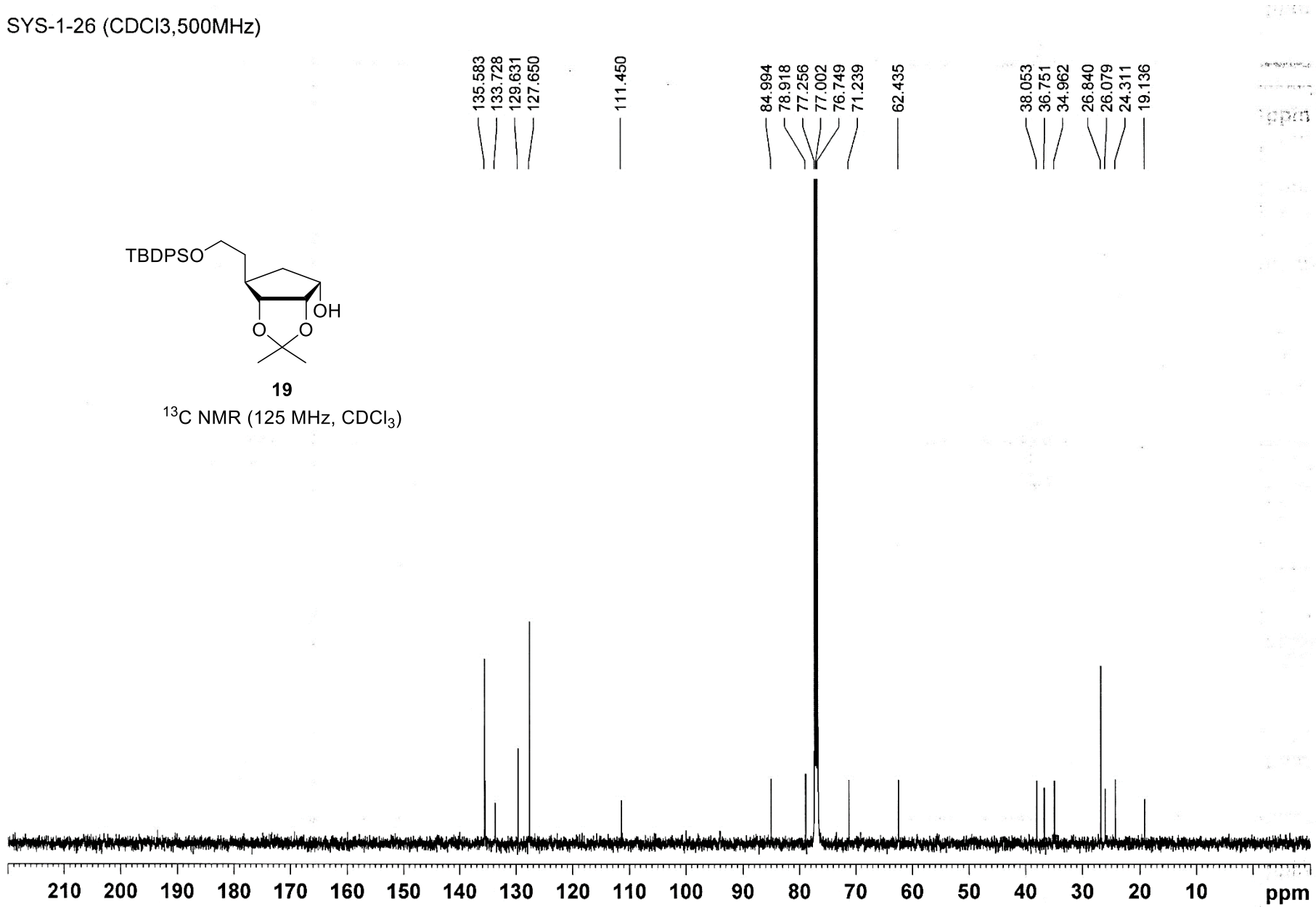
SYS-1-26 (CDCl3,500MHz)



19

^{1}H NMR (500 MHz, $CDCl_3$)

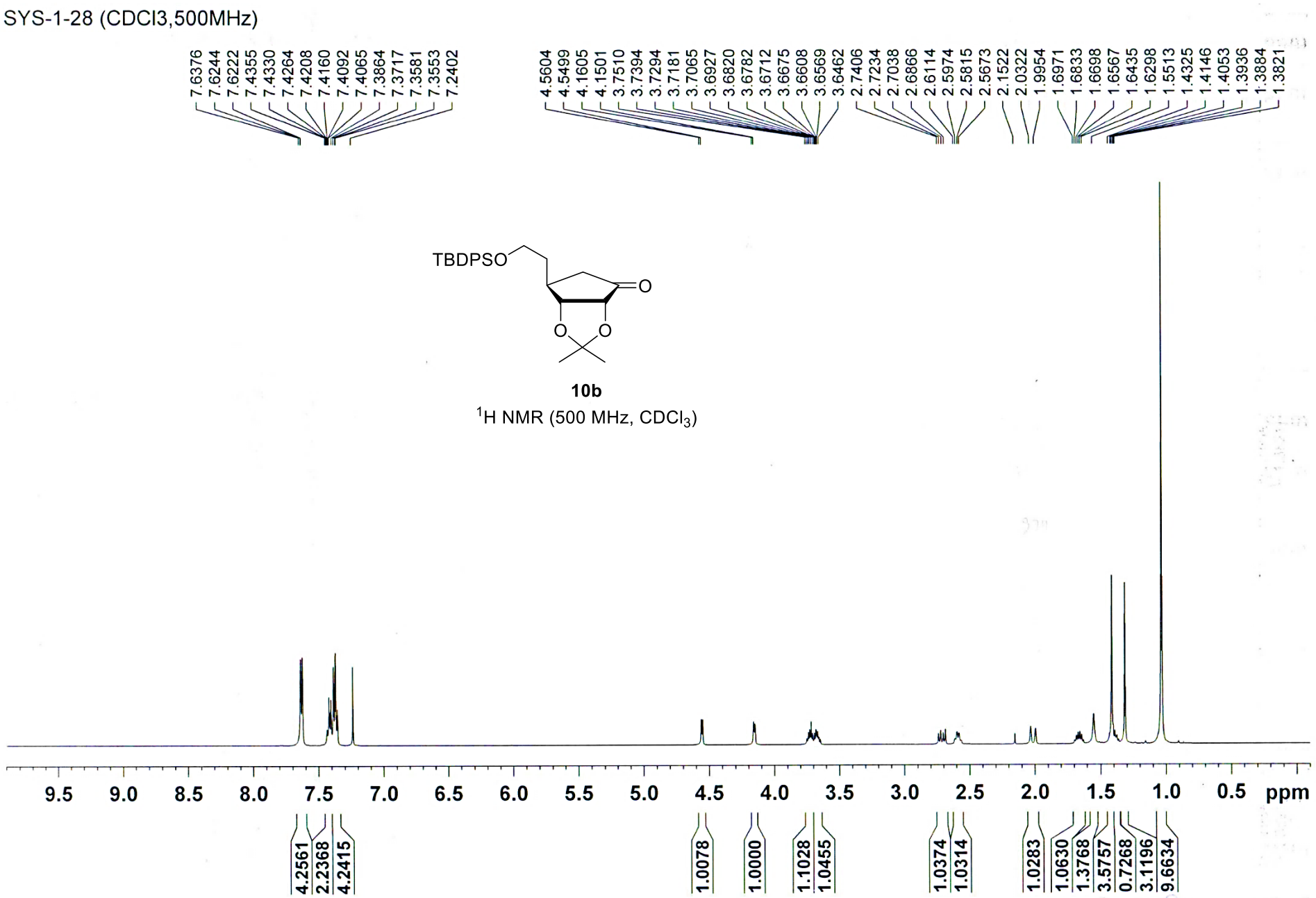
SYS-1-26 (CDCl3,500MHz)



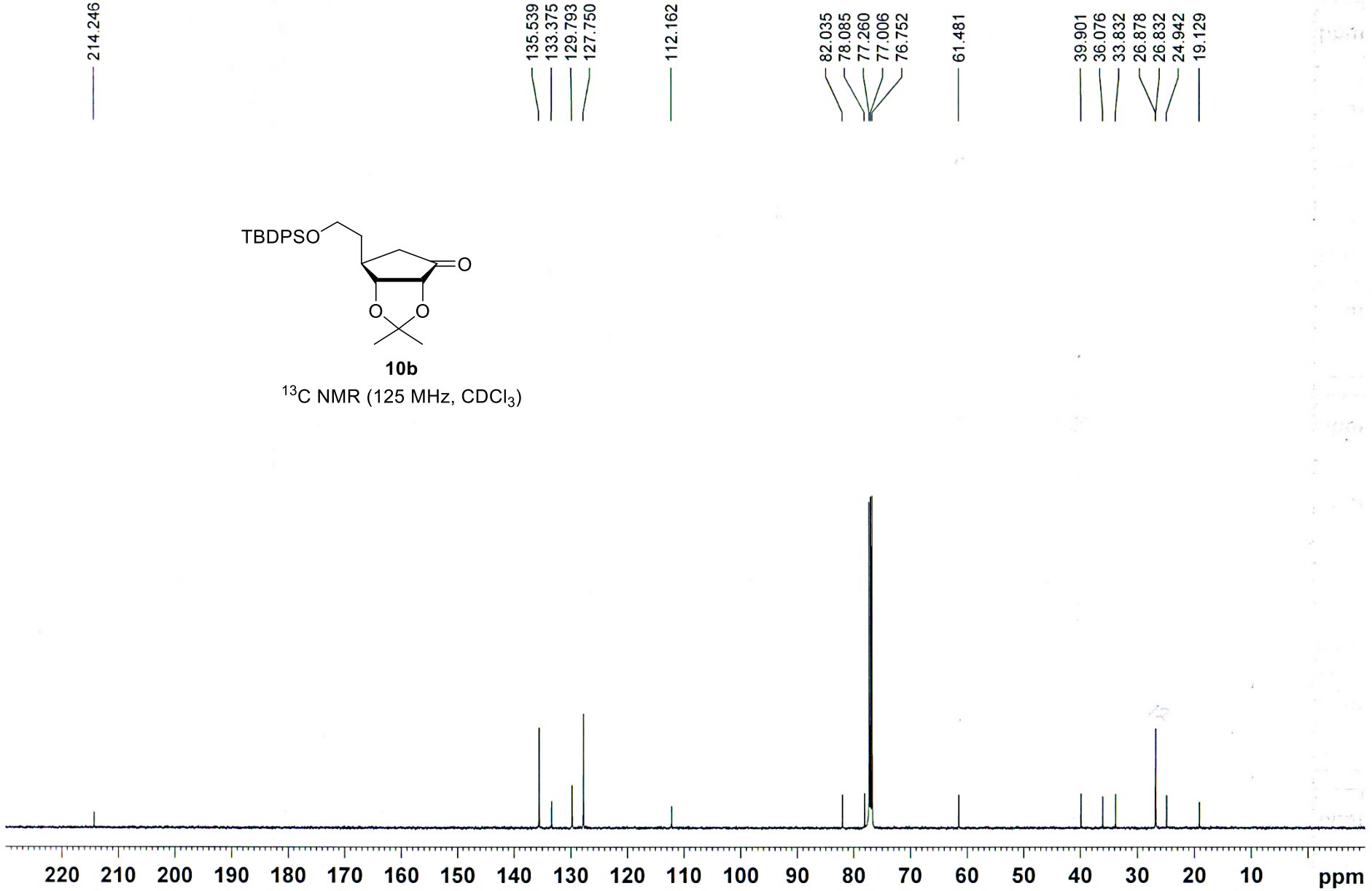
19

^{13}C NMR (125 MHz, $CDCl_3$)

SYS-1-28 (CDCl3,500MHz)

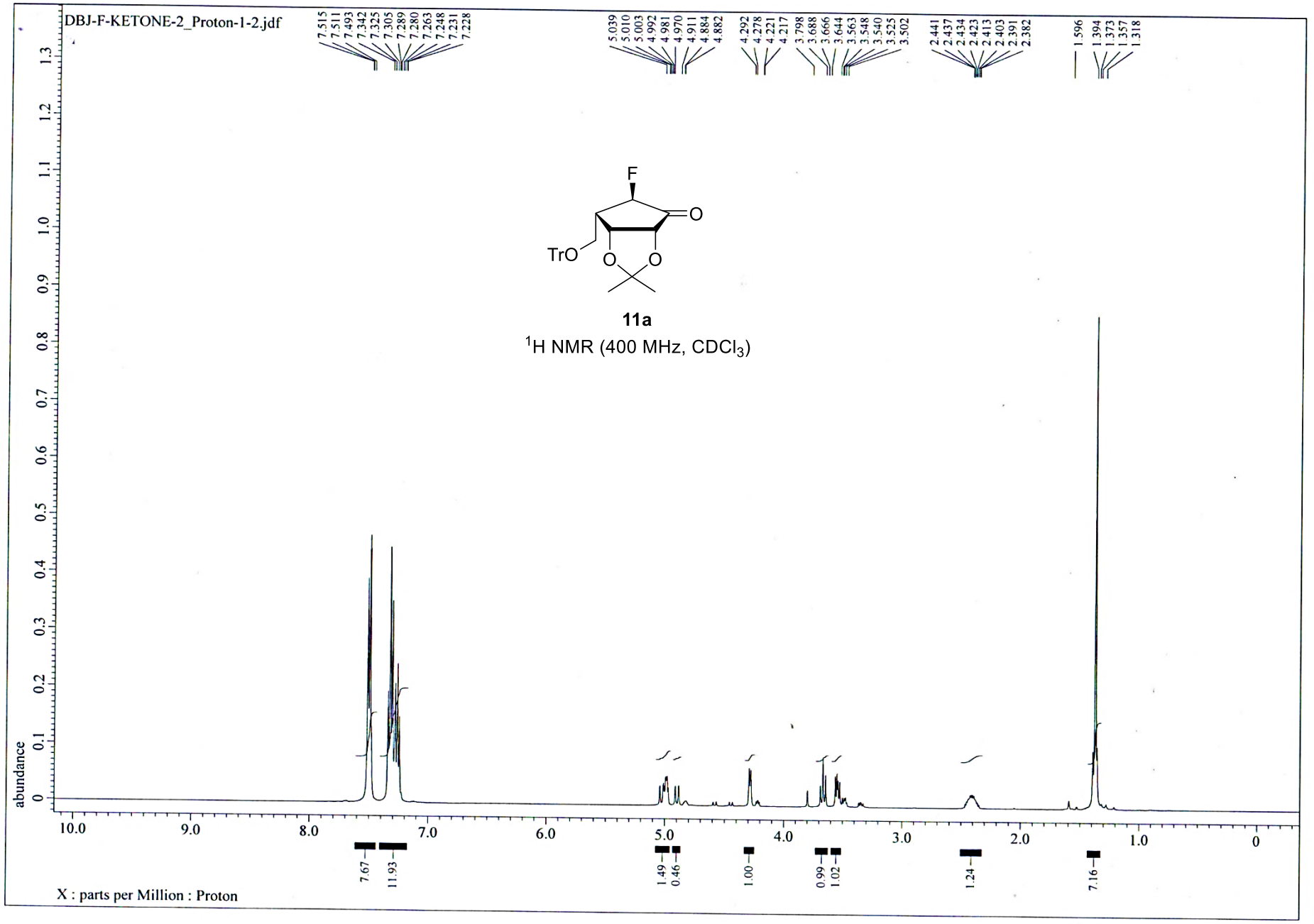


SYS-1-28 (CDCl3,500MHz)



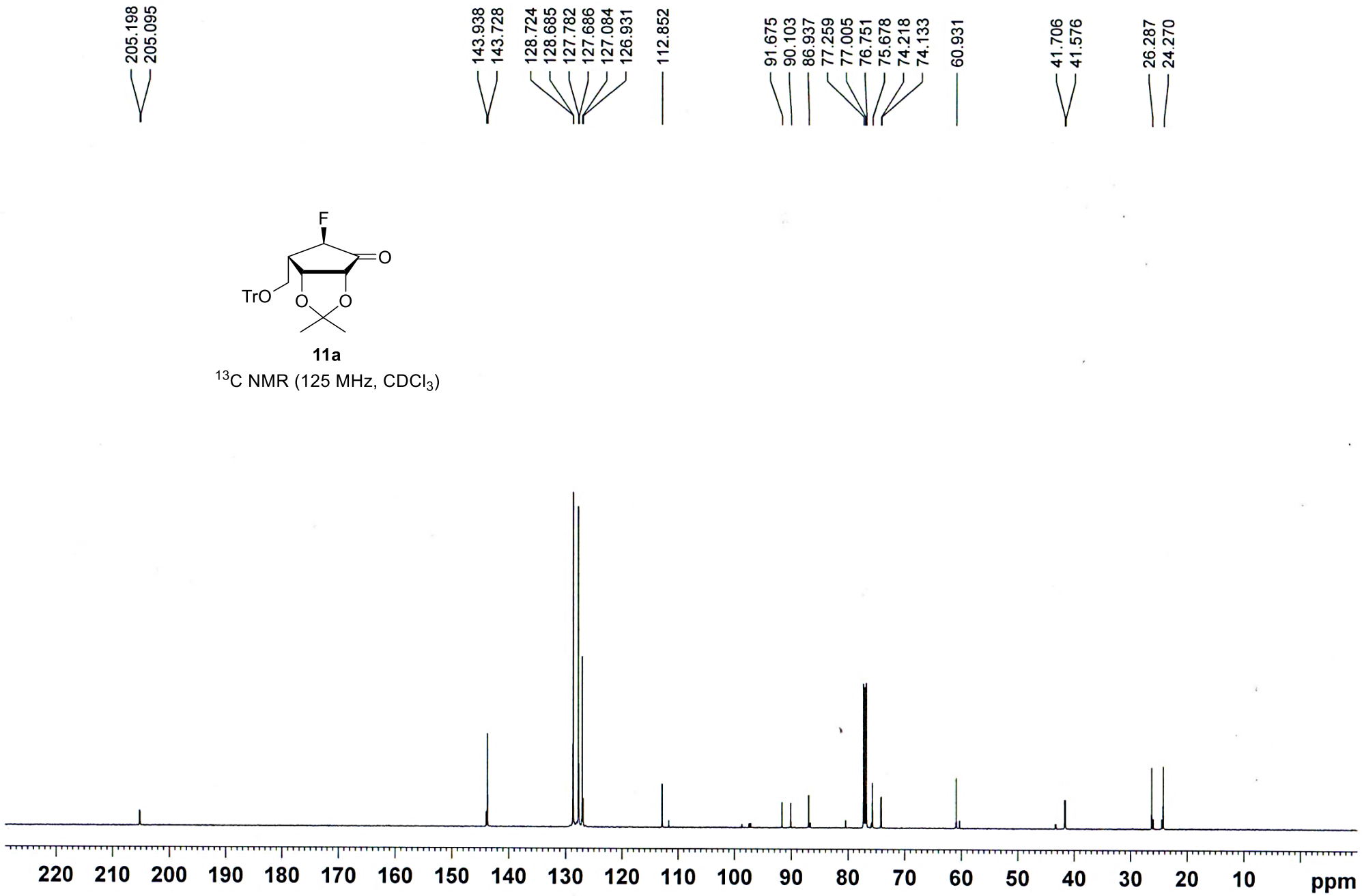
10b

^{13}C NMR (125 MHz, $CDCl_3$)



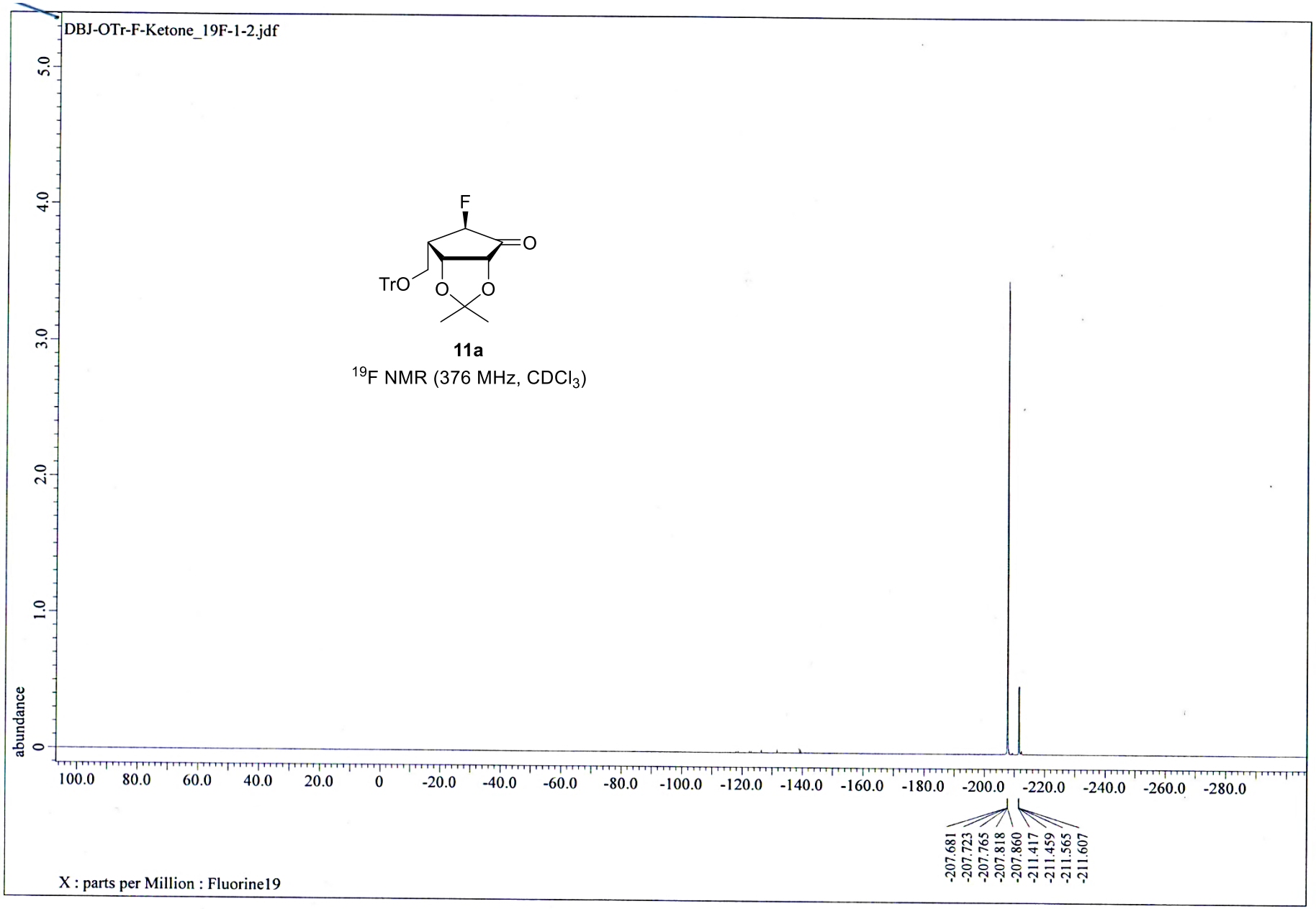
11a

^{1}H NMR (400 MHz, $CDCl_3$)



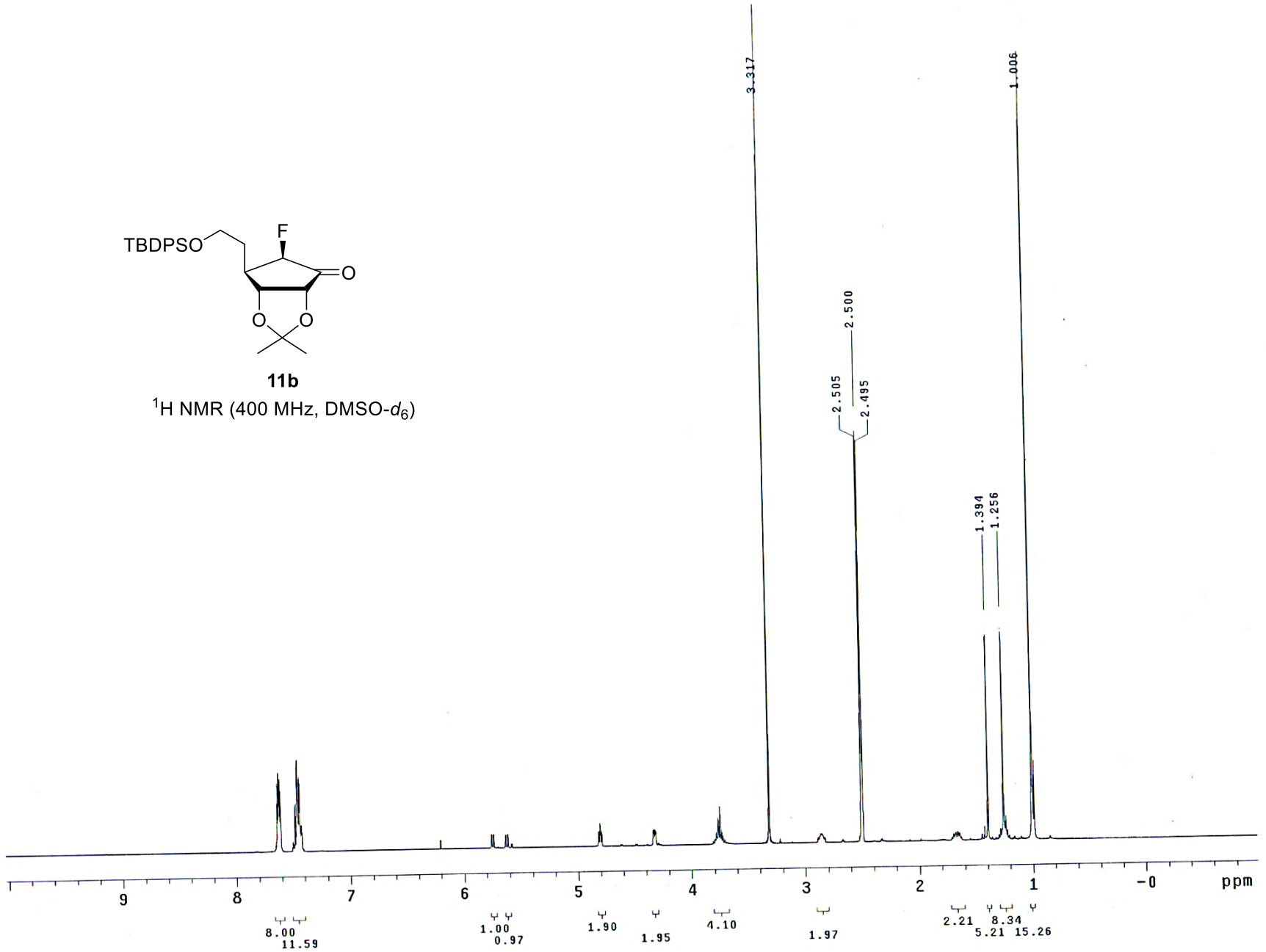
11a

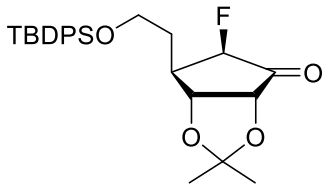
^{13}C NMR (125 MHz, $CDCl_3$)


DBJ-OTr-F-Ketone_19F-1-2.jdf
F
O
TrO
O
O
11a
^{19}F NMR (376 MHz, $CDCl_3$)
abundance
5.0
4.0
3.0
2.0
1.0
0
100.0 80.0 60.0 40.0 20.0 0 -20.0 -40.0 -60.0 -80.0 -100.0 -120.0 -140.0 -160.0 -180.0 -200.0 -220.0 -240.0 -260.0 -280.0
-207.681
-207.723
-207.765
-207.818
-207.860
-211.417
-211.459
-211.565
-211.607
X : parts per Million : Fluorine19

11b

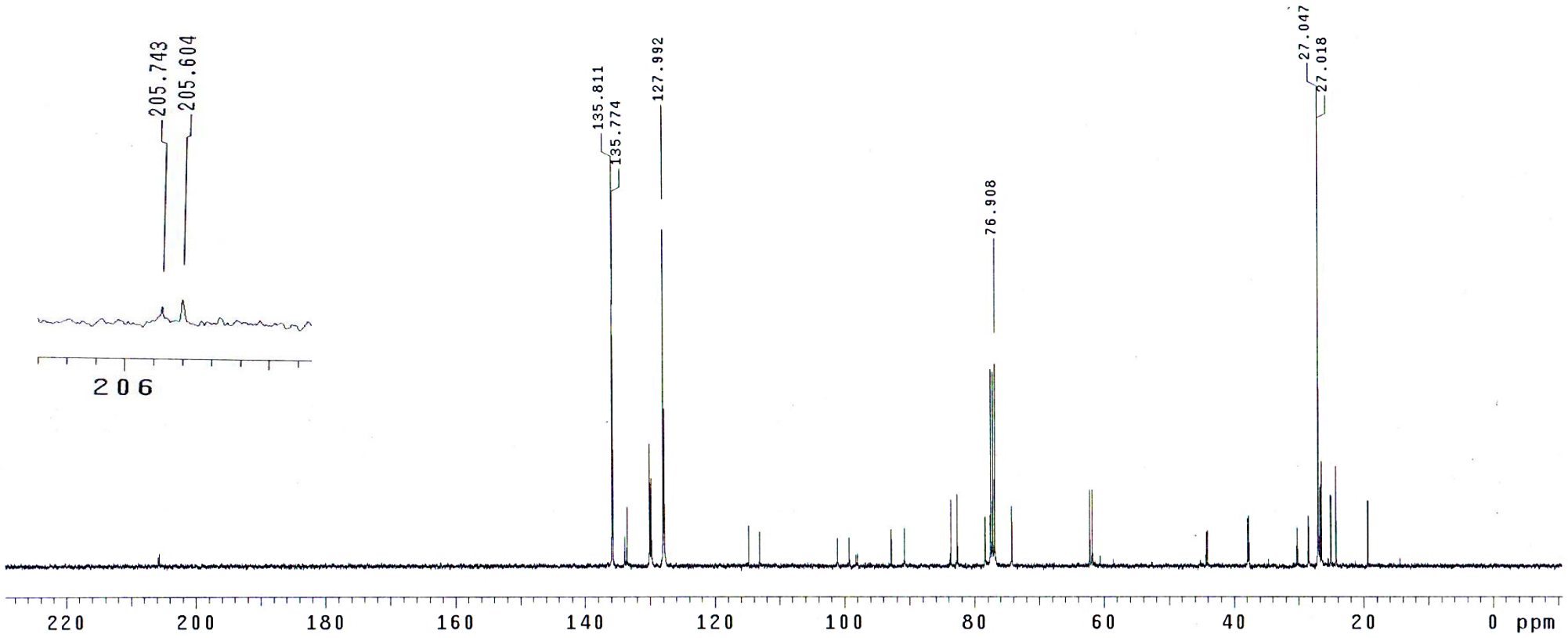
^{1}H NMR (400 MHz, DMSO-d_6)

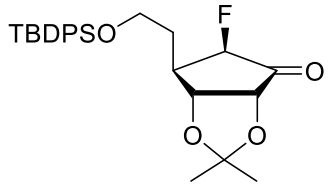




11b

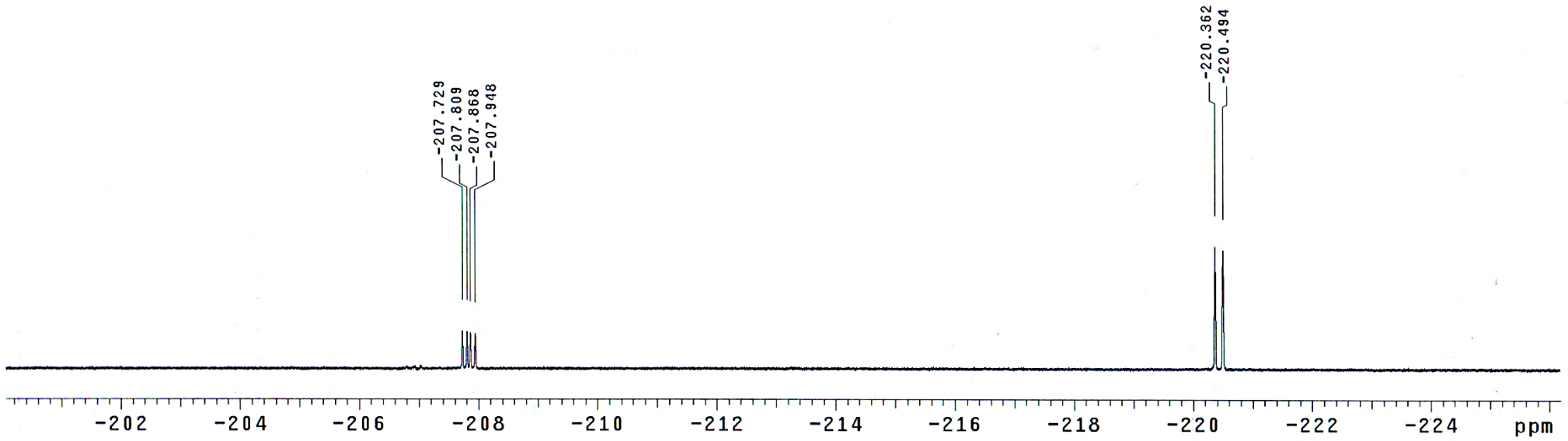
^{13}C NMR (100 MHz, $CDCl_3$)

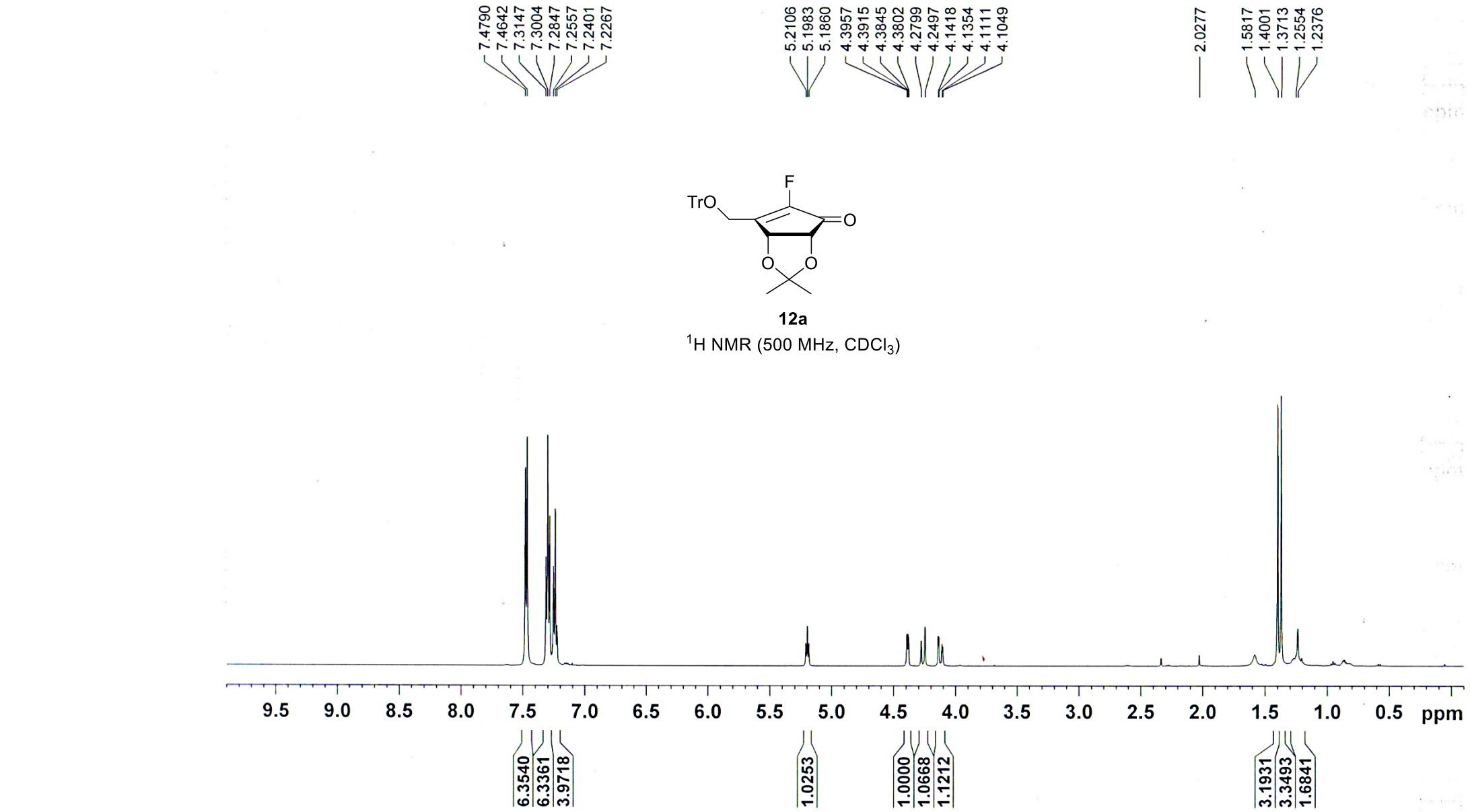


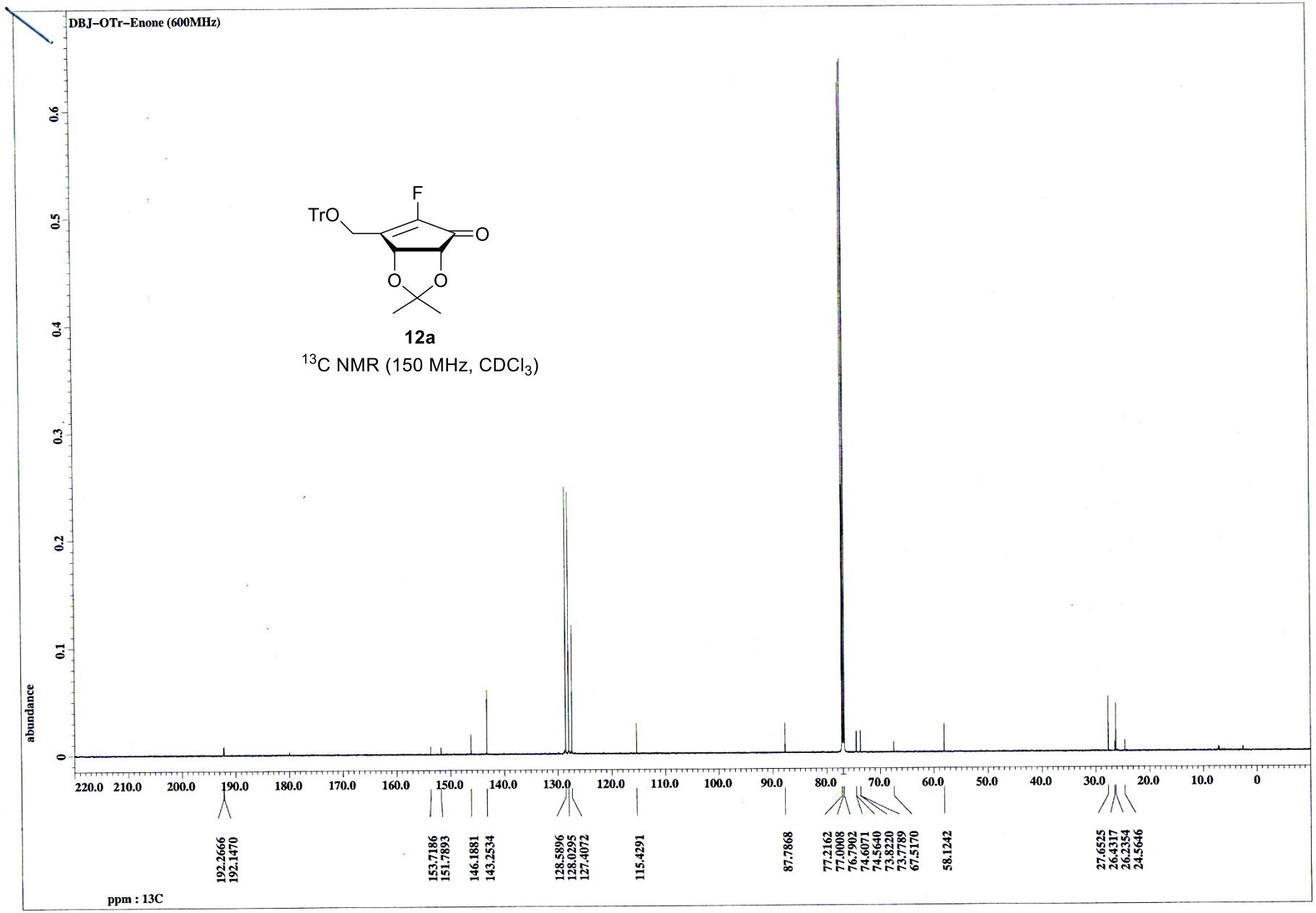


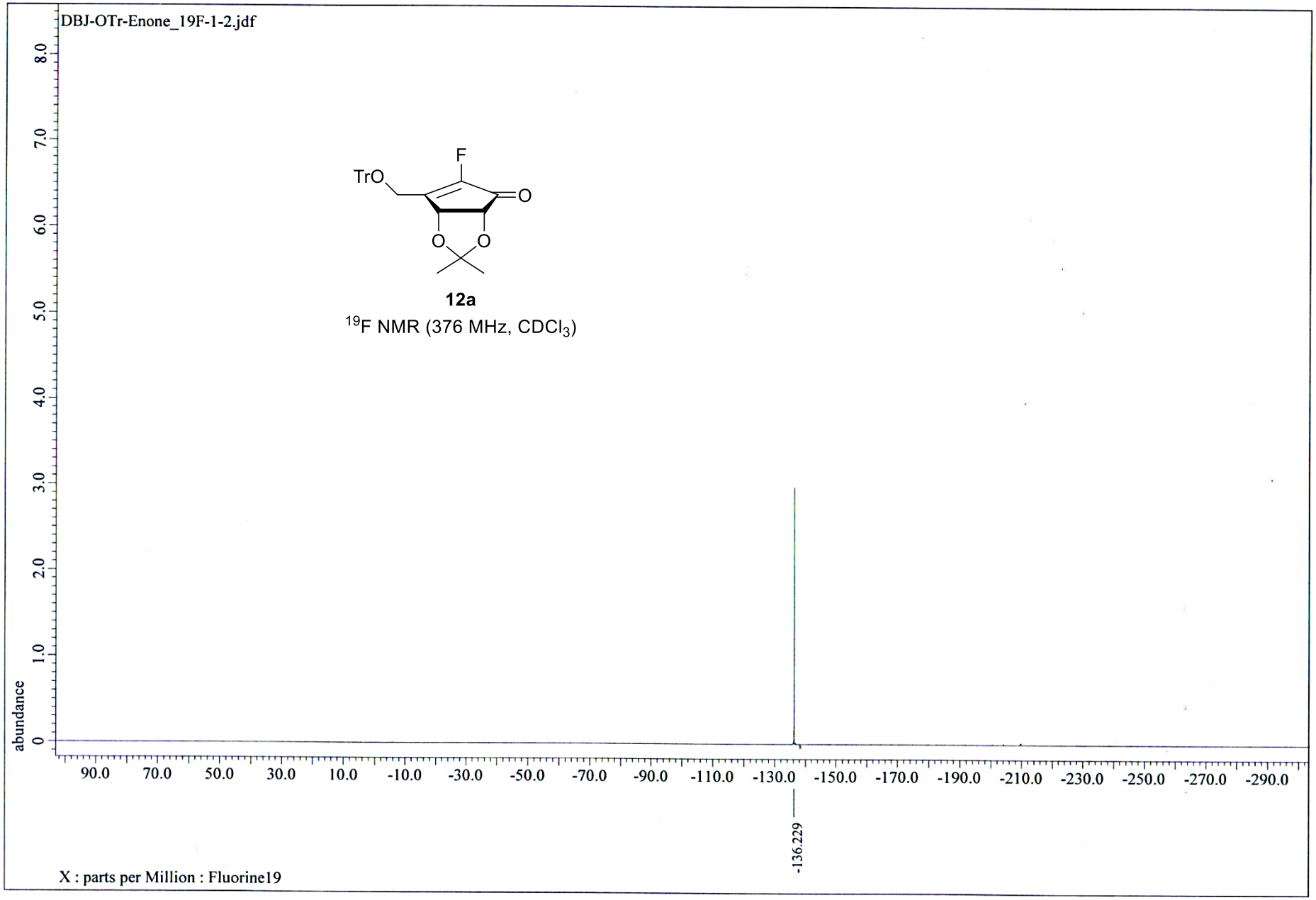
11b

^{19}F NMR (376 MHz, $CDCl_3$)

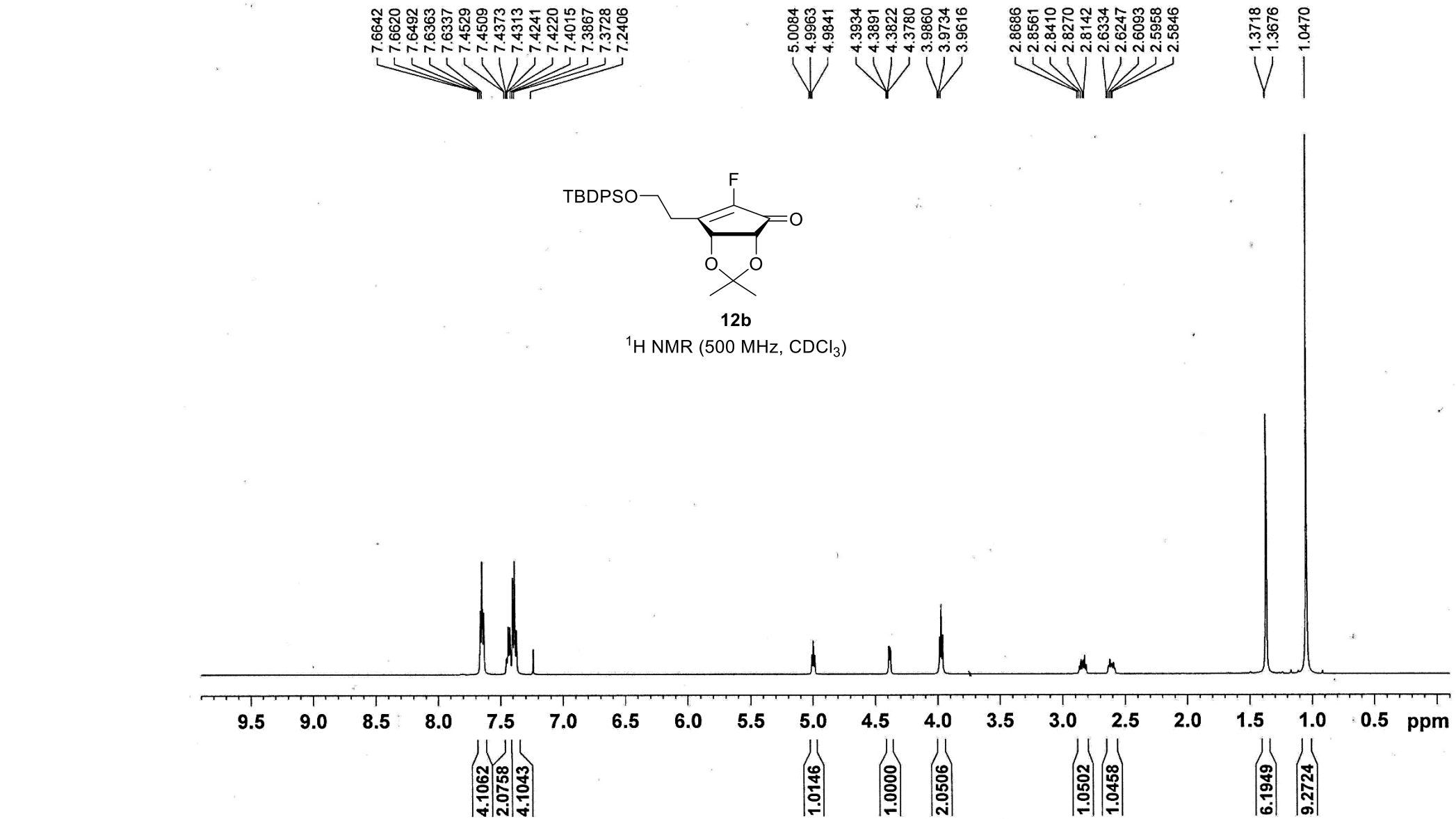



7.4790
7.4642
7.3147
7.3004
7.2847
7.2557
7.2401
7.2267
5.2106
5.1983
5.1860
4.3957
4.3915
4.3845
4.3802
4.2799
4.2497
4.1418
4.1354
4.1111
4.1049
2.0277
1.5817
1.4001
1.3713
1.2554
1.2376
F
TrO
O
O
O
12a
1H NMR (500 MHz, CDCl3)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
6.3540
6.3361
3.9718
1.0253
1.0000
1.0668
1.1212
3.1931
3.3493
1.6841


DBJ-OTr-Enone (600MHz)
F
TrO
O
O
O
12a
^{13}C NMR (150 MHz, $CDCl_3$)
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
192.2666
192.1470
153.7186
151.7893
146.1881
143.2534
128.5896
128.0295
127.4072
115.4291
87.7868
77.2162
77.0008
76.7902
74.6071
74.5640
73.8220
73.7789
67.5170
58.1242
27.6525
26.4317
26.2354
24.5646
ppm : 13C


DBJ-OTr-Enone_19F-1-2.jdf
F
TrO
O
O
O
12a
19F NMR (376 MHz, CDCl3)
abundance
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
90.0
70.0
50.0
30.0
10.0
-10.0
-30.0
-50.0
-70.0
-90.0
-110.0
-130.0
-150.0
-170.0
-190.0
-210.0
-230.0
-250.0
-270.0
-290.0
-136.229
X : parts per Million : Fluorine19

1) Isomerization 180123 (CDCl3,500MHz)

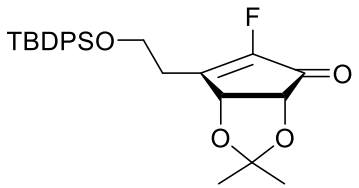


12b

^{1}H NMR (500 MHz, $CDCl_3$)

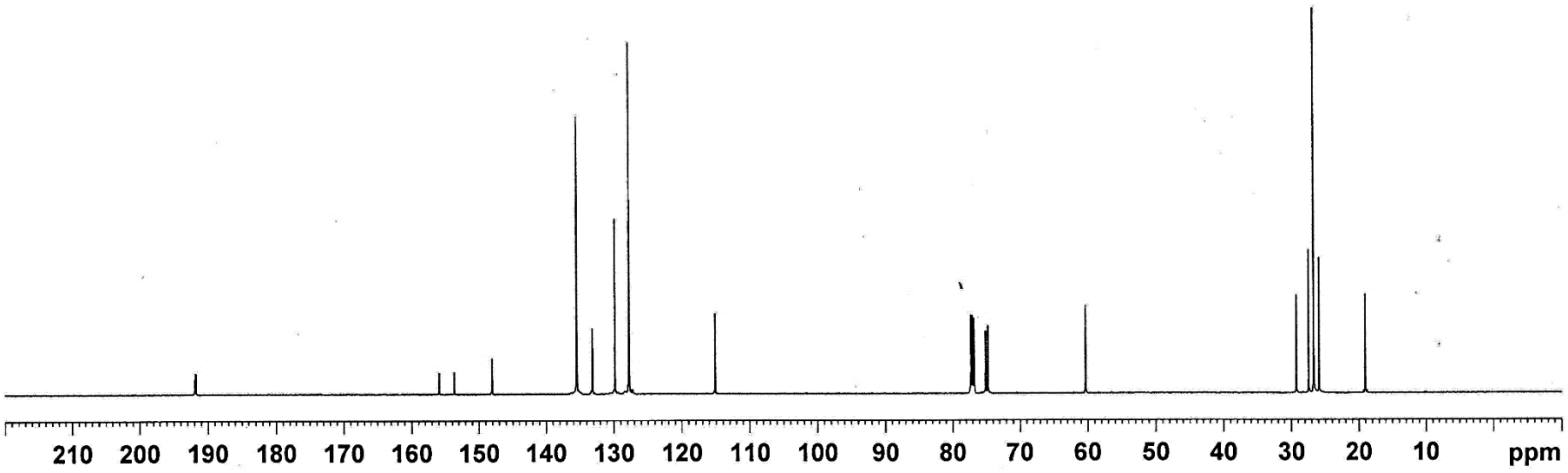
Isomerization (CDCl3,500MHz)

191.871
191.733
155.938
153.650
148.057
148.035
135.481
135.434
133.160
133.135
129.815
127.726
115.113
77.256
77.002
76.747
75.066
75.006
74.736
74.683
60.299
29.233
27.440
26.694
25.915
19.013



12b

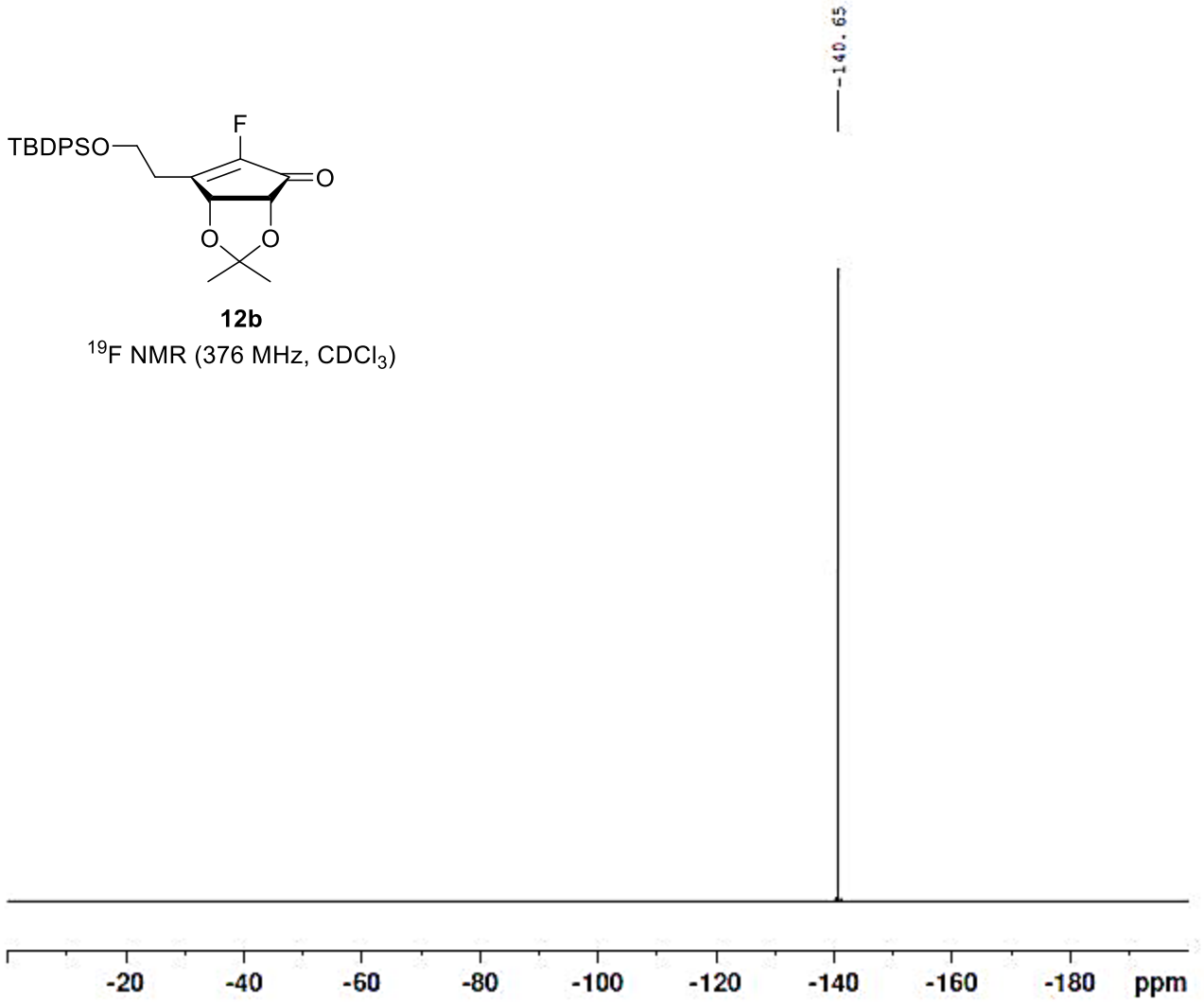
^{13}C NMR (125 MHz, $CDCl_3$)



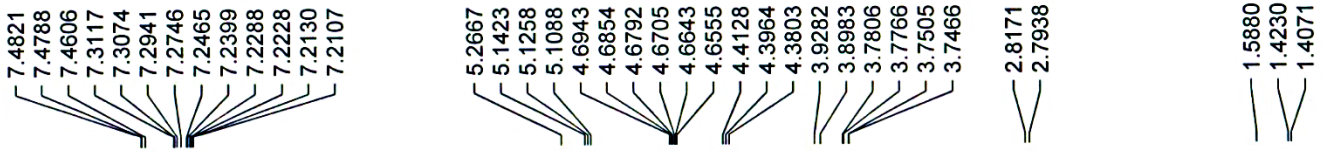
Isomerization-CDCl3 / 19F

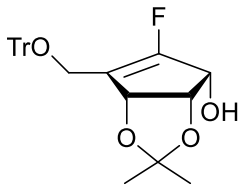
12b

^{19}F NMR (376 MHz, $CDCl_3$)



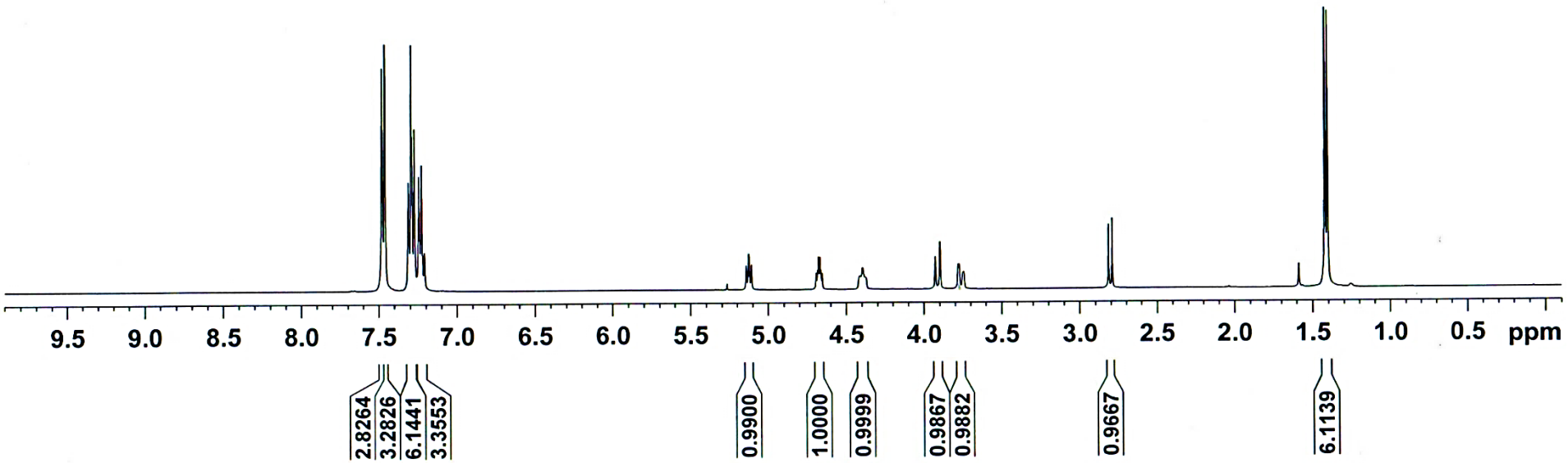

```
Current Data Parameters
NAME        feb22-ph-jmh
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameter
Date_          20180222
Time              10.16 h
INSTRUM           spect
PROBHD   Z3246_0288 (PH
PULPROG      zgfhigqn.2
TD               131072
SOLVENT            CDCl3
NS                    16
DS                     4
SWH            66964.289 H
FIDRES          1.021794 H
AQ              0.9786710 s
RG                201.38
DW                 7.467 u
DE                 6.50 u
TE                298.0 K
D1           2.00000000 s
D11          0.03000000 s
D12          0.00002000 s
TD0                    1
SFO1         282.3761146 M
NUC1                19F
P1                19.20 u
PLW1         21.00000000 W
SFO2         300.1312005 M
NUC2                1H
CPDPRG[2         waltz16
PCPD2              90.00 u
PLW2         10.00000000 W
PLW12         0.17778000 W

F2 - Processing parameter
SI                 65536
SF           282.4043552 M
WDW                  EM
SSB       0
LB                 1.00 H
GB        0
PC                 1.00
```

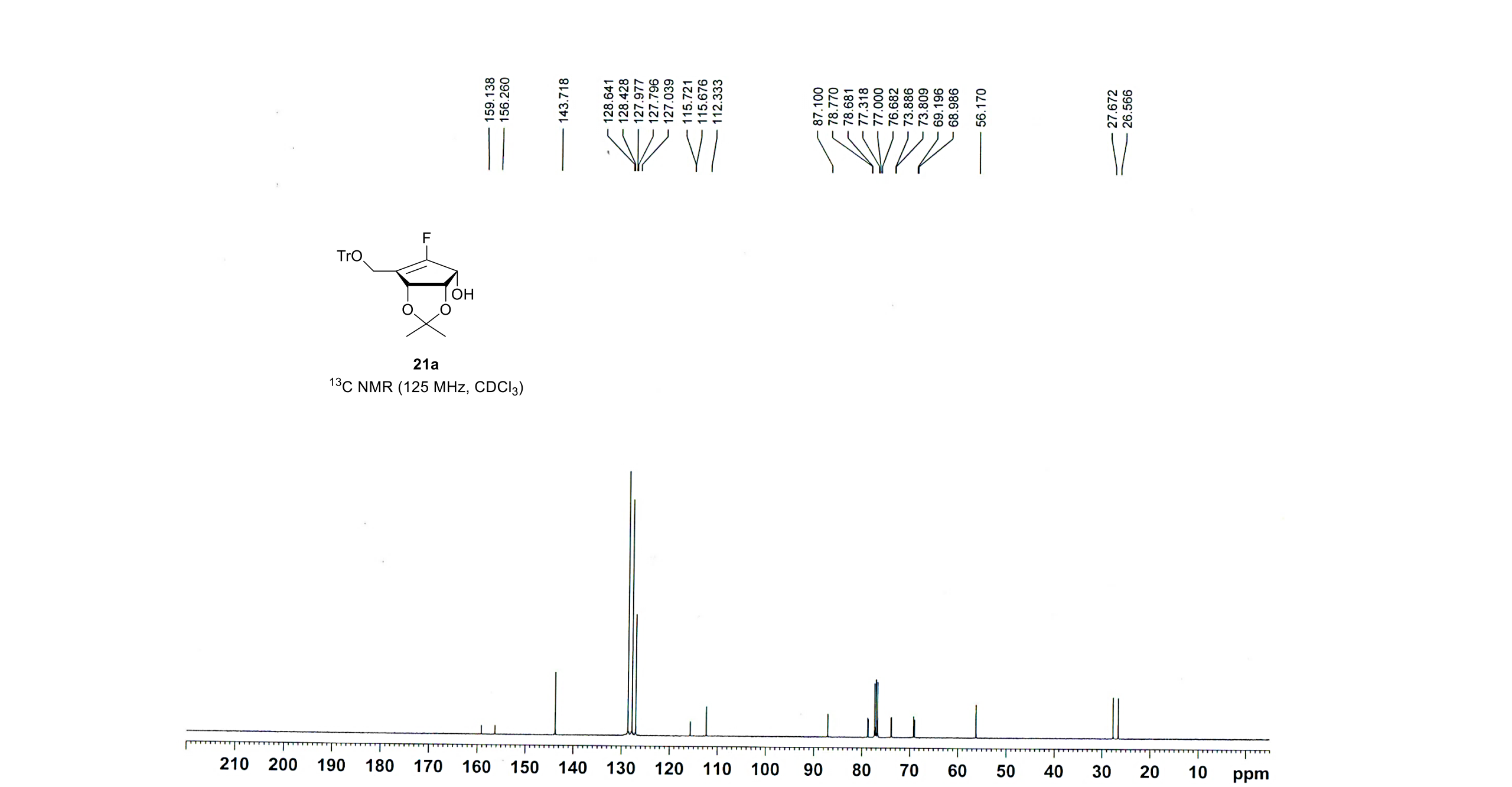




21a

^{1}H NMR (500 MHz, $CDCl_3$)



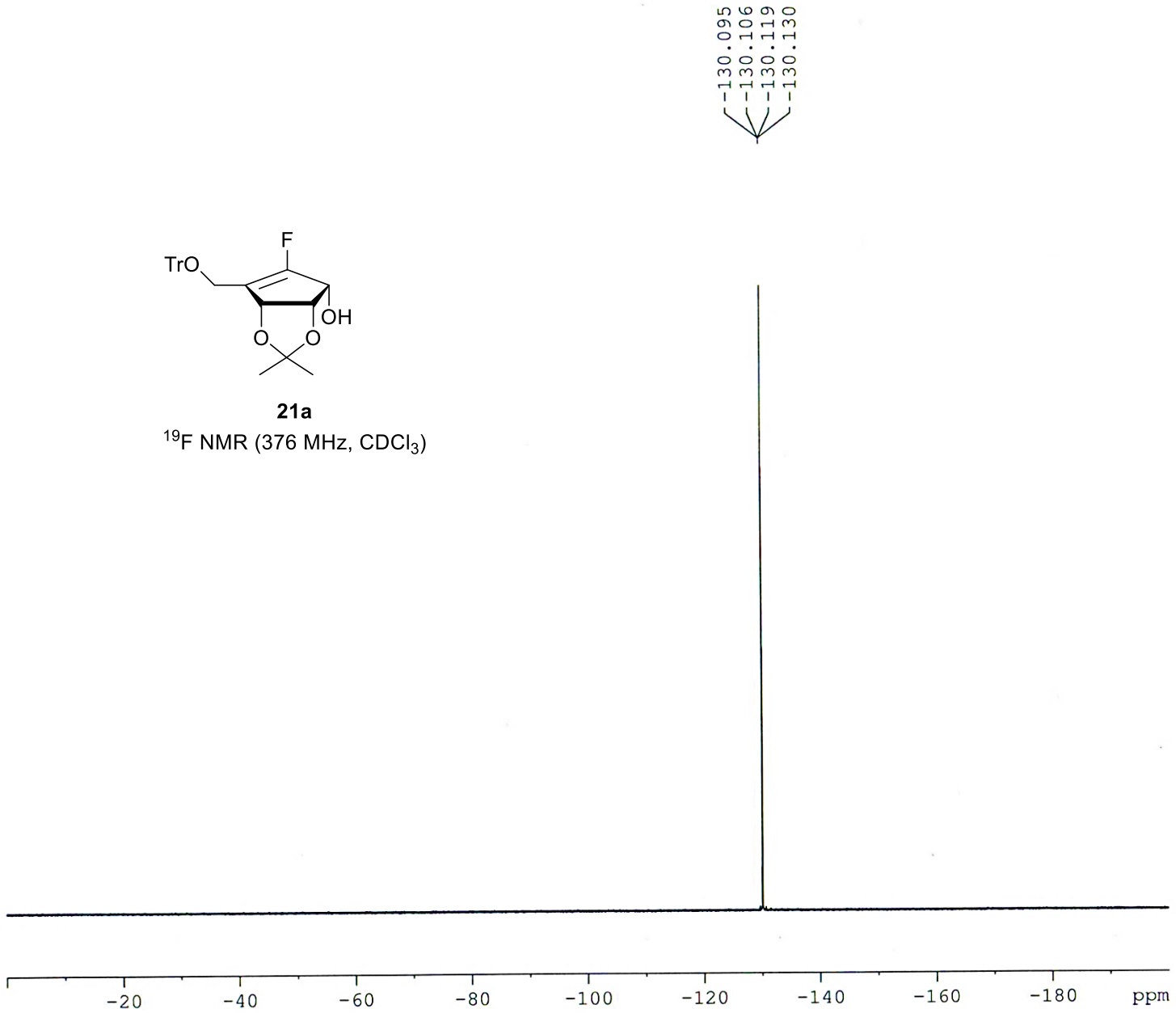


21a

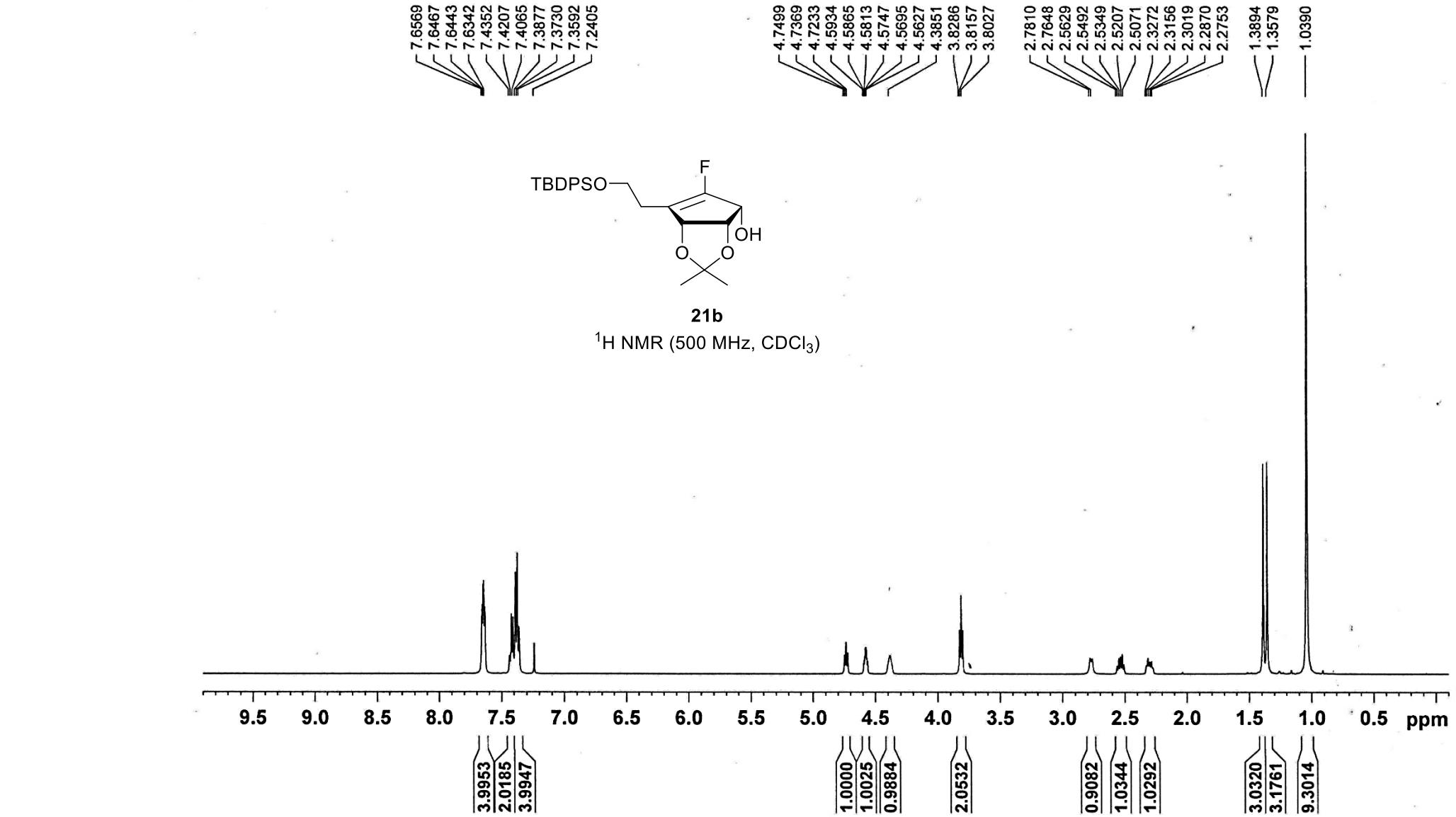
^{13}C NMR (125 MHz, $CDCl_3$)

21a

^{19}F NMR (376 MHz, $CDCl_3$)



1) Luche reduction 180126 (CDCl3,500MHz)

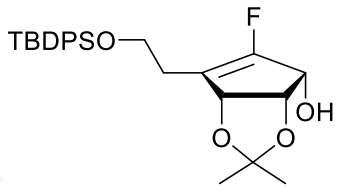


21b

^{1}H NMR (500 MHz, $CDCl_3$)

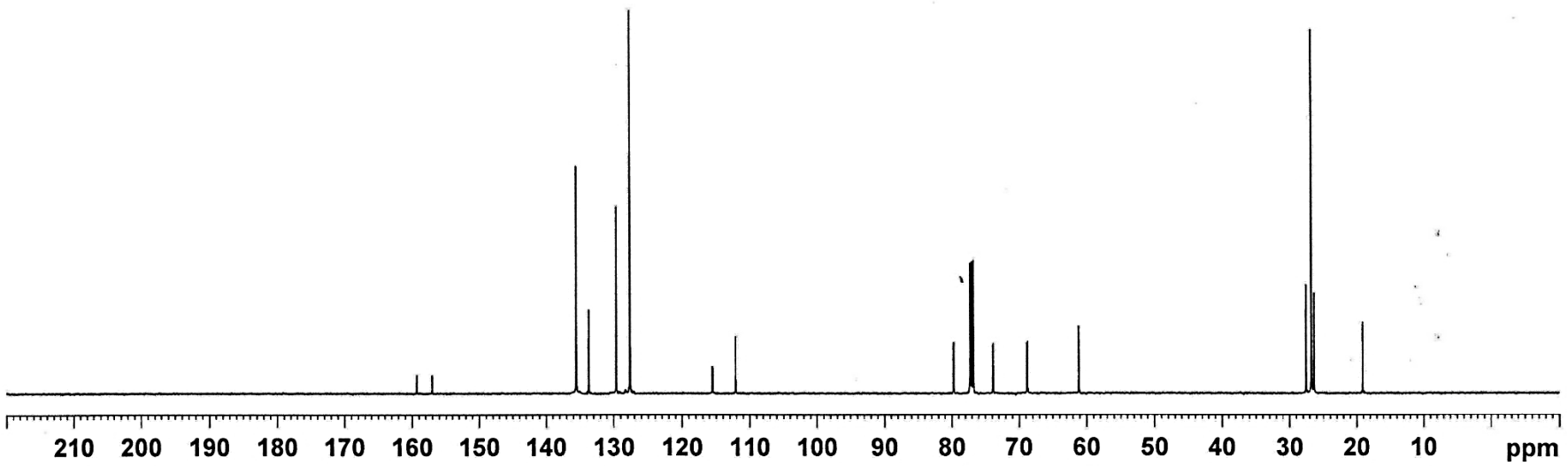
Reduction (CDCl3,500MHz)

159.301
157.033
135.540
135.511
133.686
129.627
127.626
115.569
115.515
112.131
79.815
79.733
77.259
77.005
76.751
73.877
73.815
68.899
68.730
61.142
27.546
26.767
26.373
19.108



21b

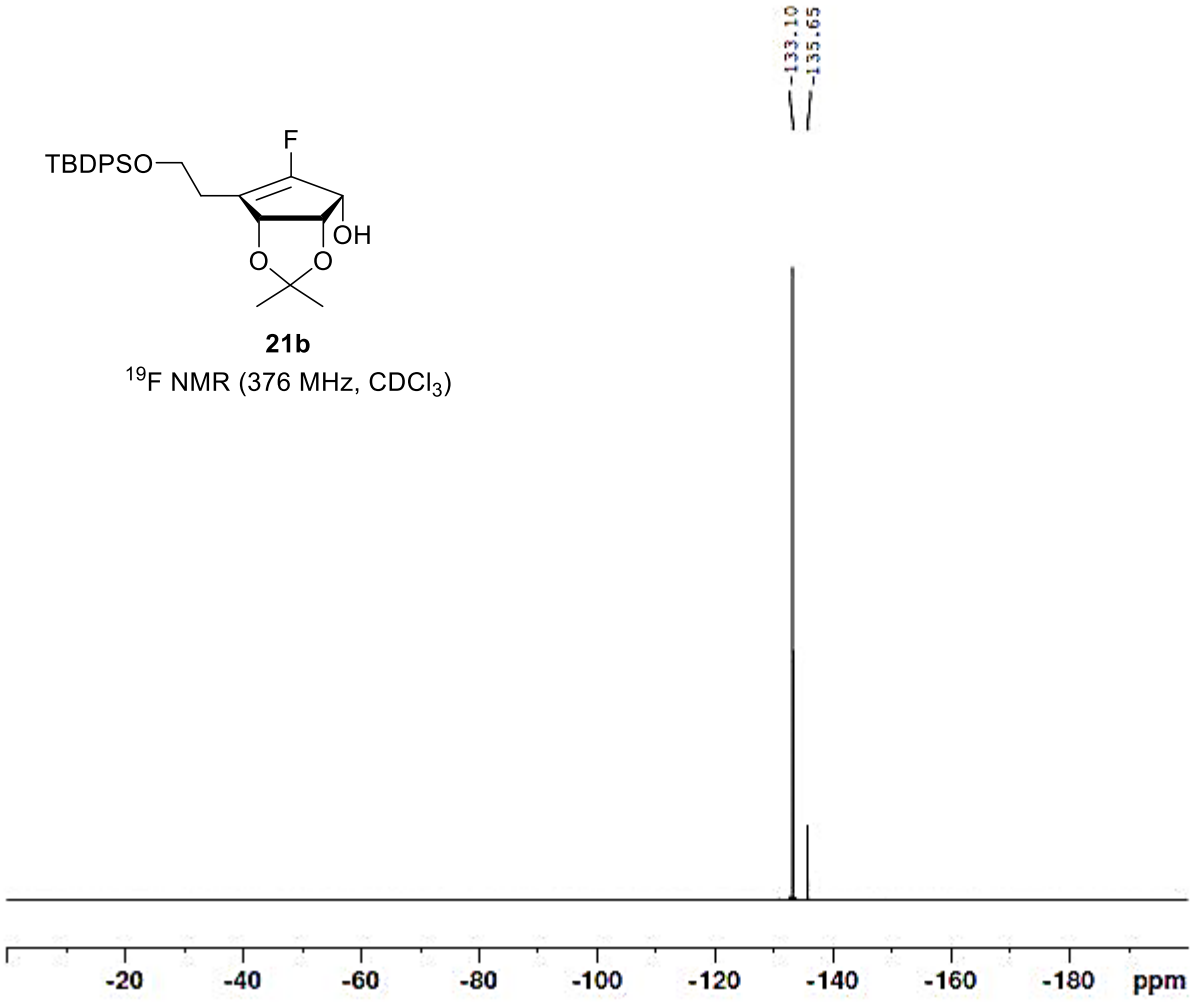
^{13}C NMR (125 MHz, $CDCl_3$)



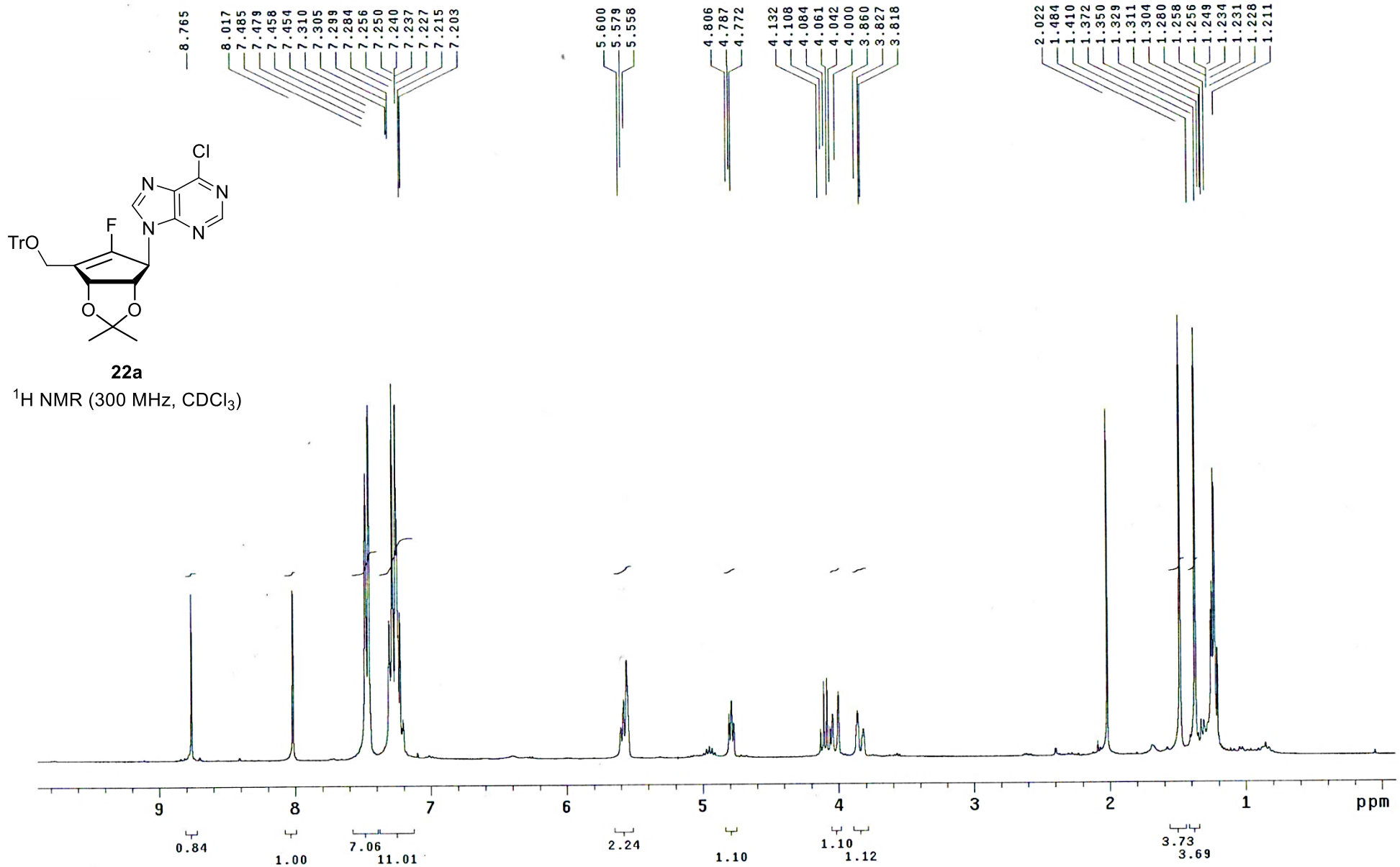
Reduction-CDCl3 / 19F

21b

^{19}F NMR (376 MHz, $CDCl_3$)

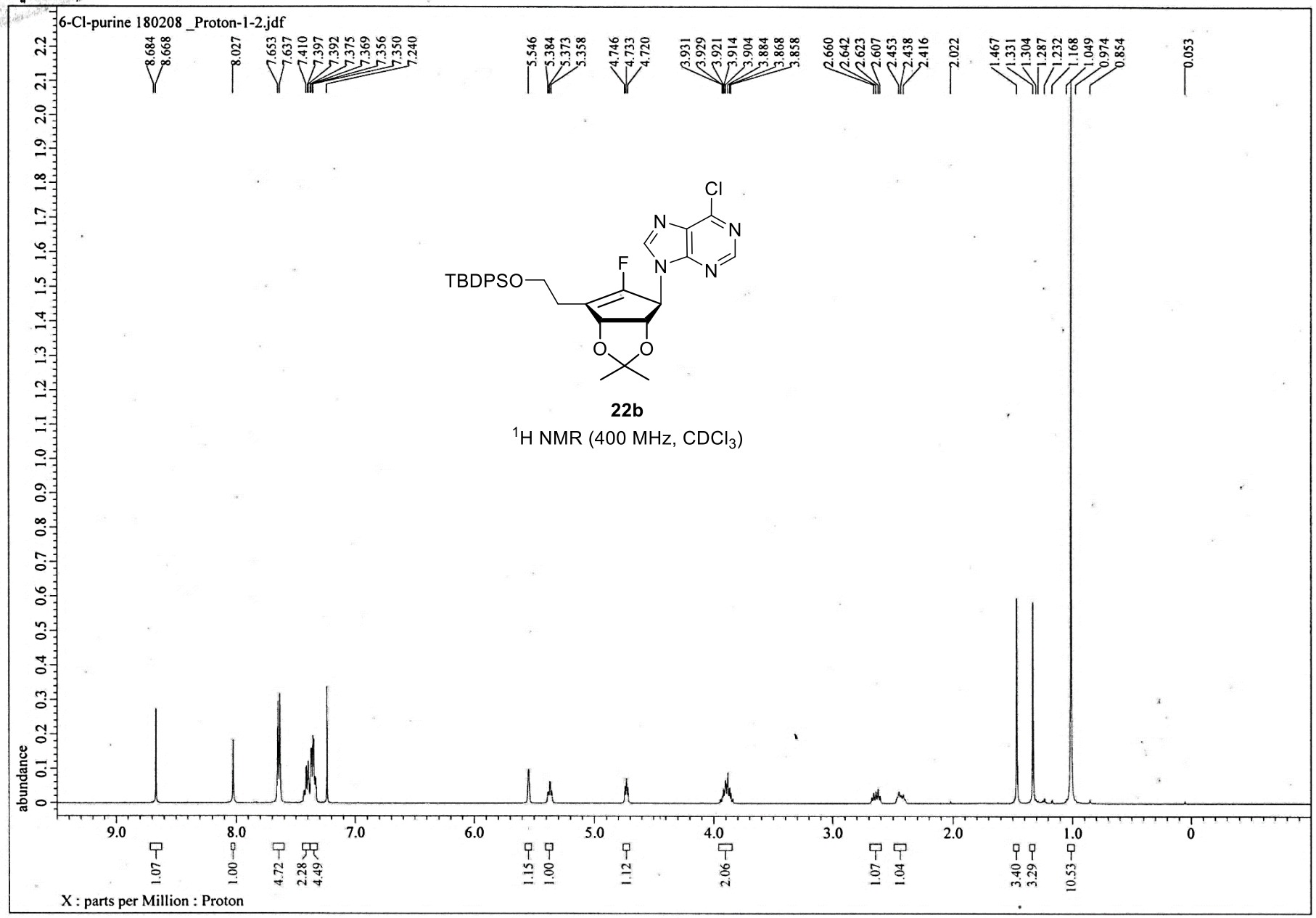



```
Current Data Parameters
NAME        feb22-ph-jmh
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180222
Time              10.23 h
INSTRUM             spect
PROBHD   Z3246_0288 (PH
PULPROG       zgfhigqn.2
TD                131072
SOLVENT             CDCl3
NS                    16
DS                     4
SWH            66964.289 Hz
FIDRES         1.021794 Hz
AQ             0.9786710 sec
RG                201.38
DW                 7.467 usec
DE                 6.50 usec
TE                298.0 K
D1             2.00000000 sec
D11            0.03000000 sec
D12            0.00002000 sec
TD0                    1
SFO1         282.3761146 MHz
NUC1                 19F
P1                19.20 usec
PLW1         21.00000000 W
SFO2         300.1312005 MHz
NUC2                 1H
CPDPRG[2          waltz16
PCPD2             90.00 usec
PLW2         10.00000000 W
PLW12         0.17778000 W

F2 - Processing parameters
SI                 65536
SF           282.4043552 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.00
```



22a

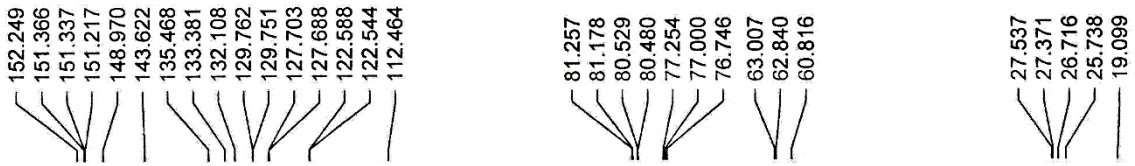
^{1}H NMR (300 MHz, $CDCl_3$)

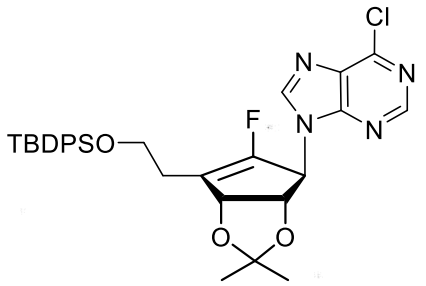


22b

^{1}H NMR (400 MHz, $CDCl_3$)

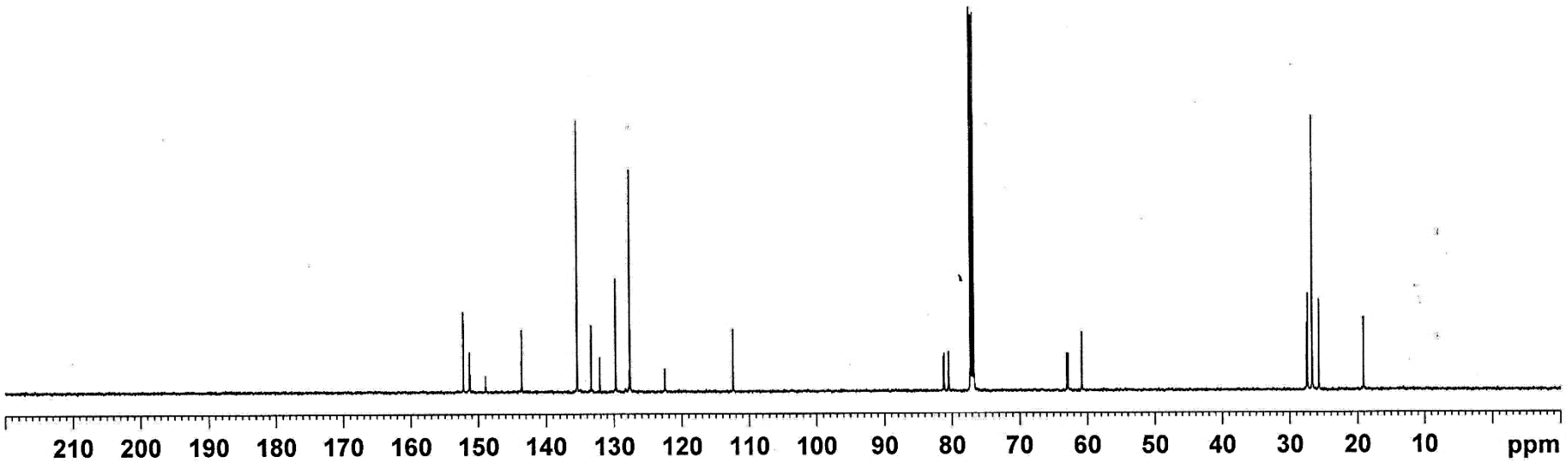
6-Cl-purine condensation (CDCl3,500MHz)





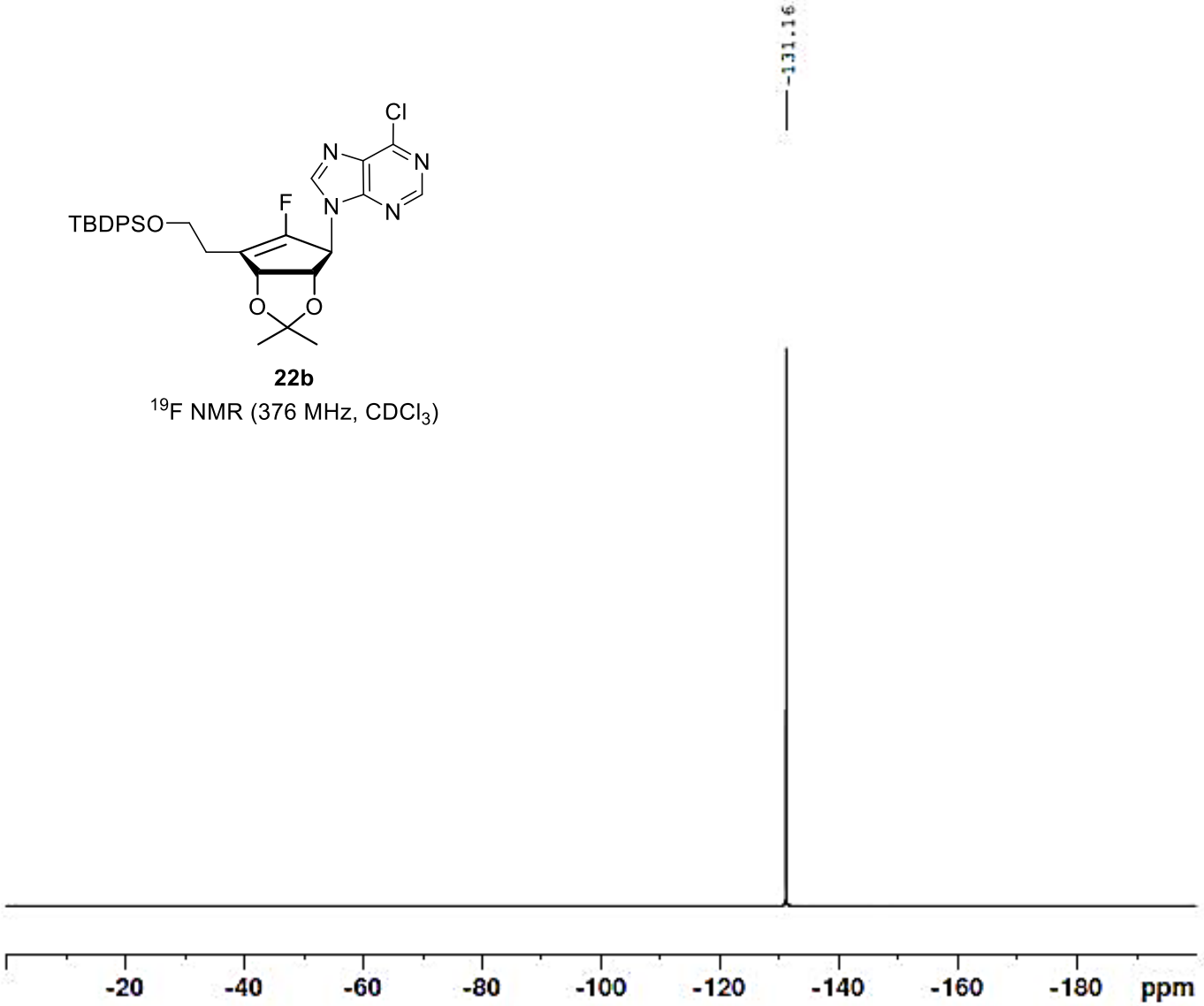
22b

^{13}C NMR (125 MHz, $CDCl_3$)

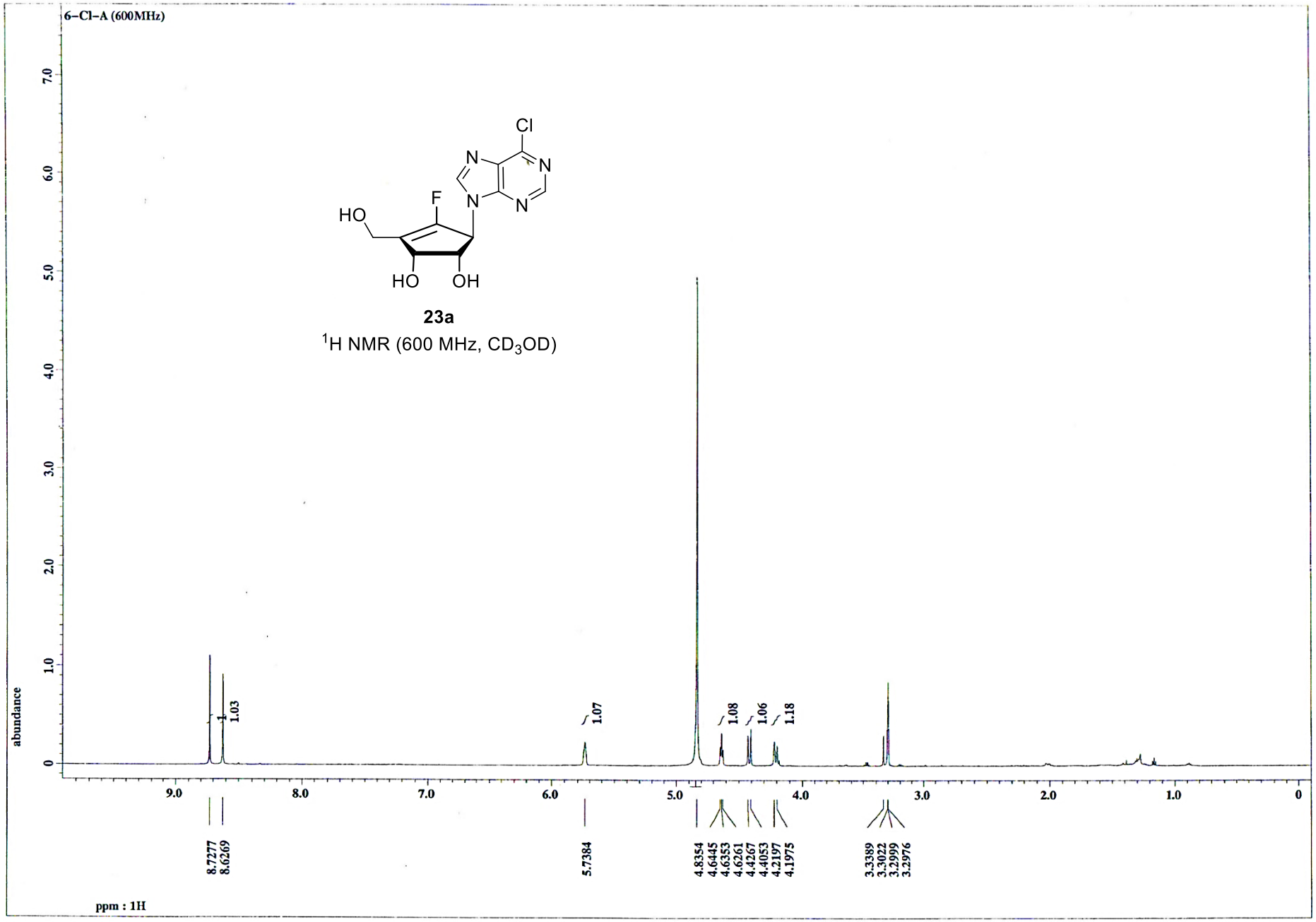


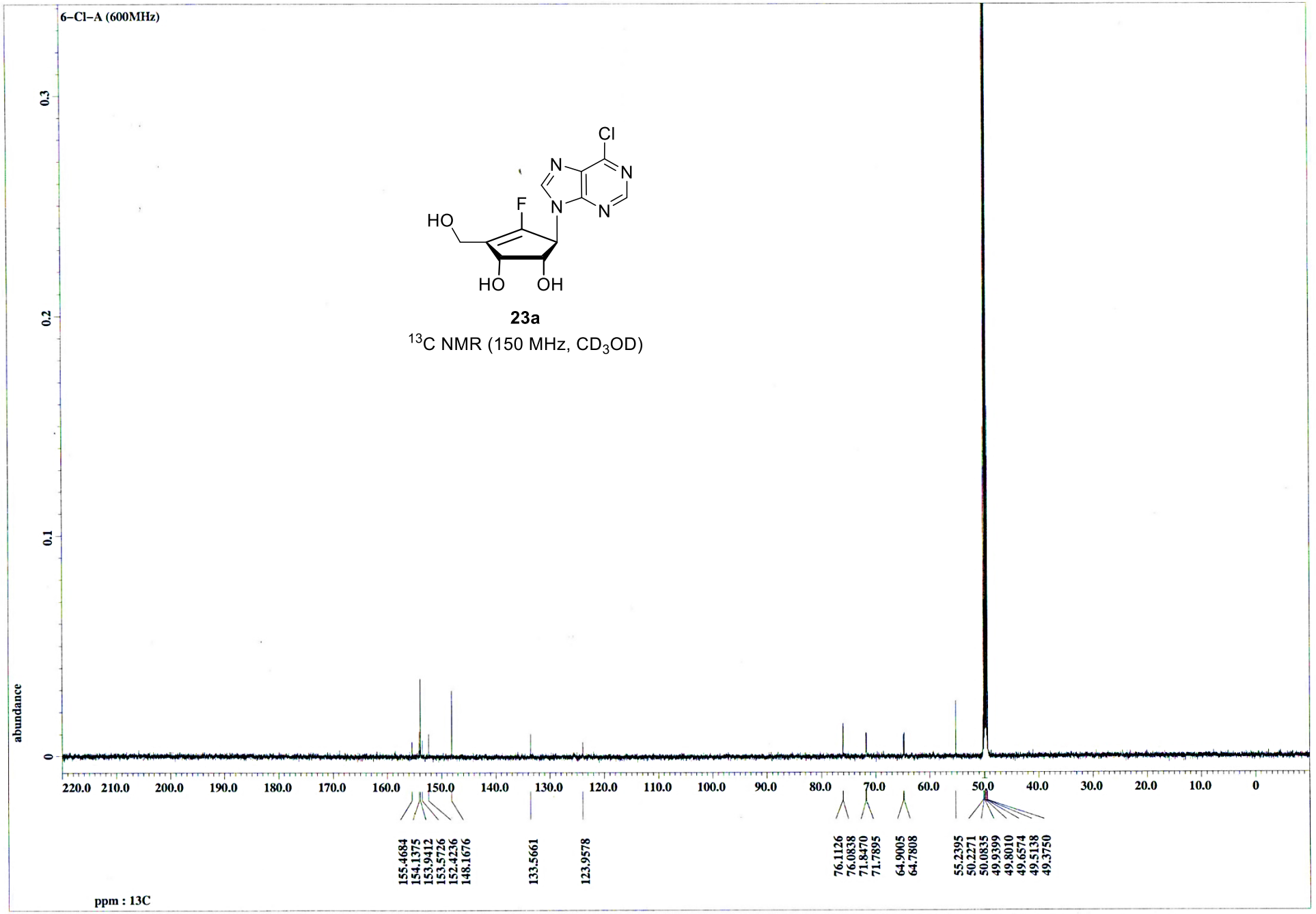
22b

^{19}F NMR (376 MHz, $CDCl_3$)




```
Current Data Parameters
NAME        mar12-ph-jmh
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180312
Time               15.01 h
INSTRUM             spect
PROBHD   Z3246_0288 (PH
PULPROG       zgfhigqn.2
TD                131072
SOLVENT             CDCl3
NS                     16
DS                      4
SWH            66964.289 Hz
FIDRES          1.021794 Hz
AQ              0.9786710 sec
RG                 201.38
DW                 7.467 usec
DE                  6.50 usec
TE                 298.0 K
D1             2.00000000 sec
D11            0.03000000 sec
D12            0.00002000 sec
TD0                    1
SFO1         282.3761146 MHz
NUC1                 19F
P1                19.20 usec
PLW1         21.00000000 W
SFO2         300.1312005 MHz
NUC2                 1H
CPDPRG[2          waltz16
PCPD2             90.00 usec
PLW2         10.00000000 W
PLW12         0.17778000 W

F2 - Processing parameters
SI                  65536
SF           282.4043552 MHz
WDW                    EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.00
```


6-Cl-A (600MHz)
Cl
N
N
N
N
F
HO
HO
OH
23a
1H NMR (600 MHz, CD3OD)
abundance
1.03
1.07
1.08
1.06
1.18
8.7277
8.6269
5.7384
4.8354
4.6445
4.6353
4.6261
4.4267
4.4053
4.2197
4.1975
3.3389
3.3022
3.2999
3.2976
ppm : 1H

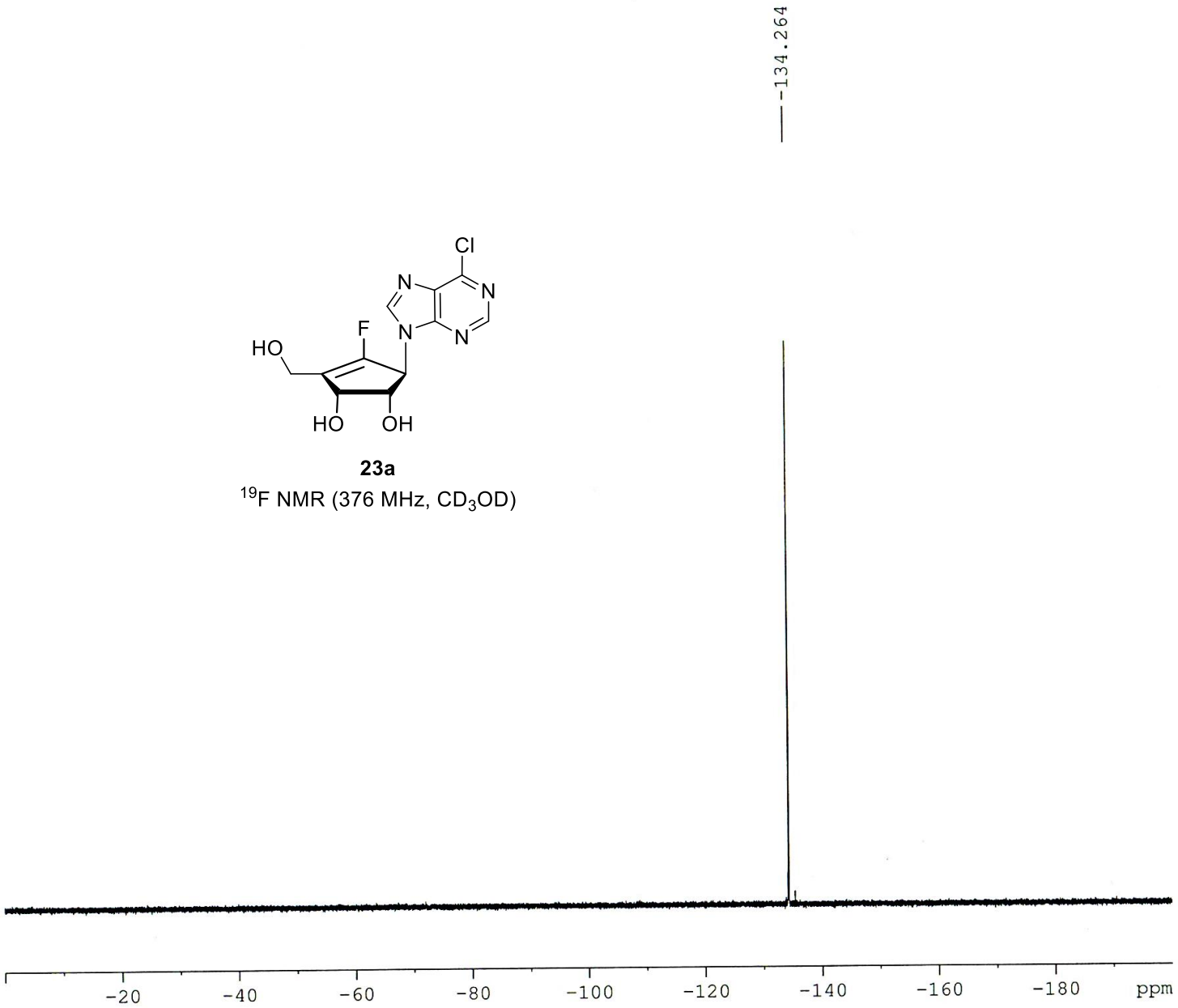


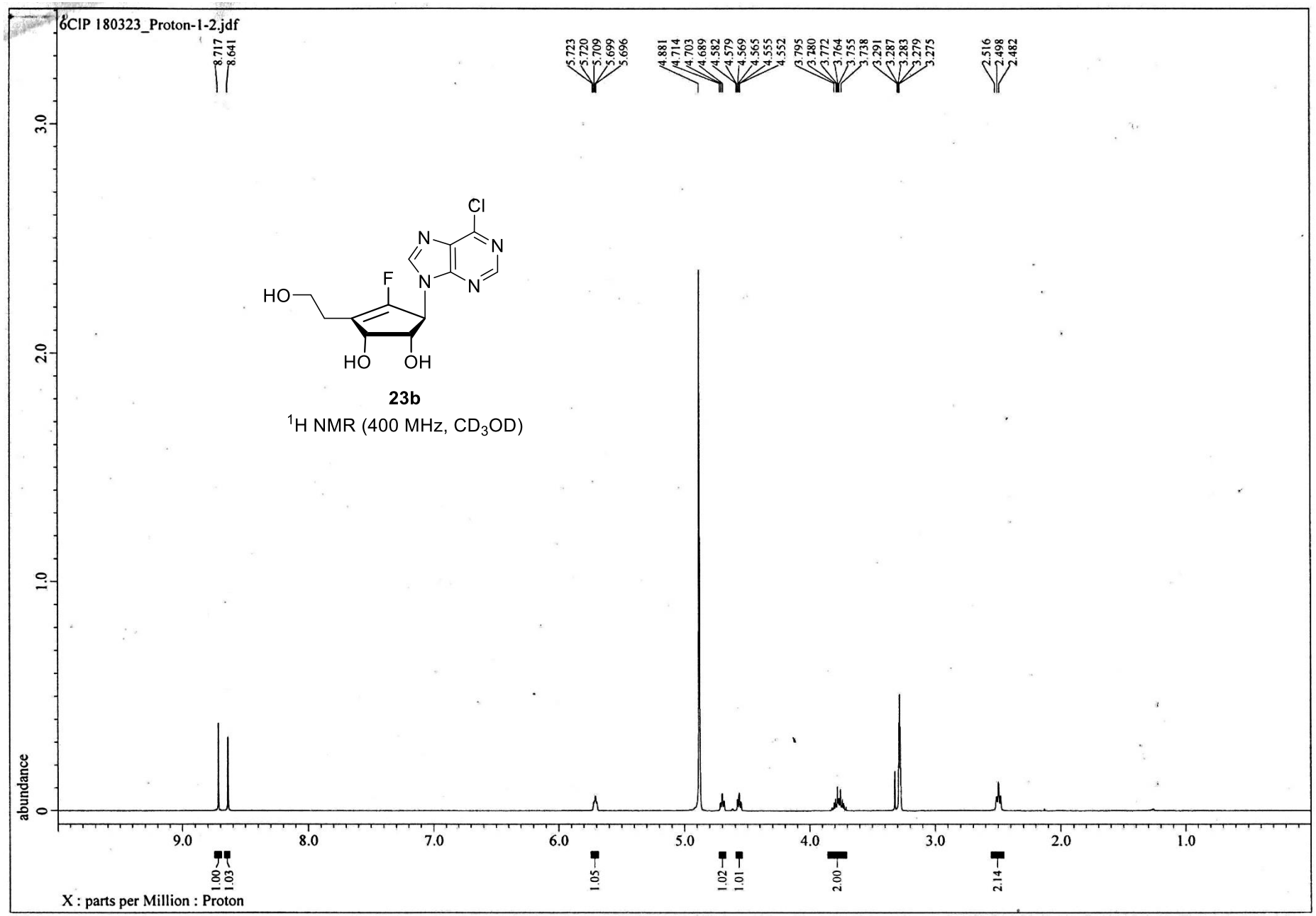
23a

^{13}C NMR (150 MHz, CD_3OD)

23a

^{19}F NMR (376 MHz, CD_3OD)

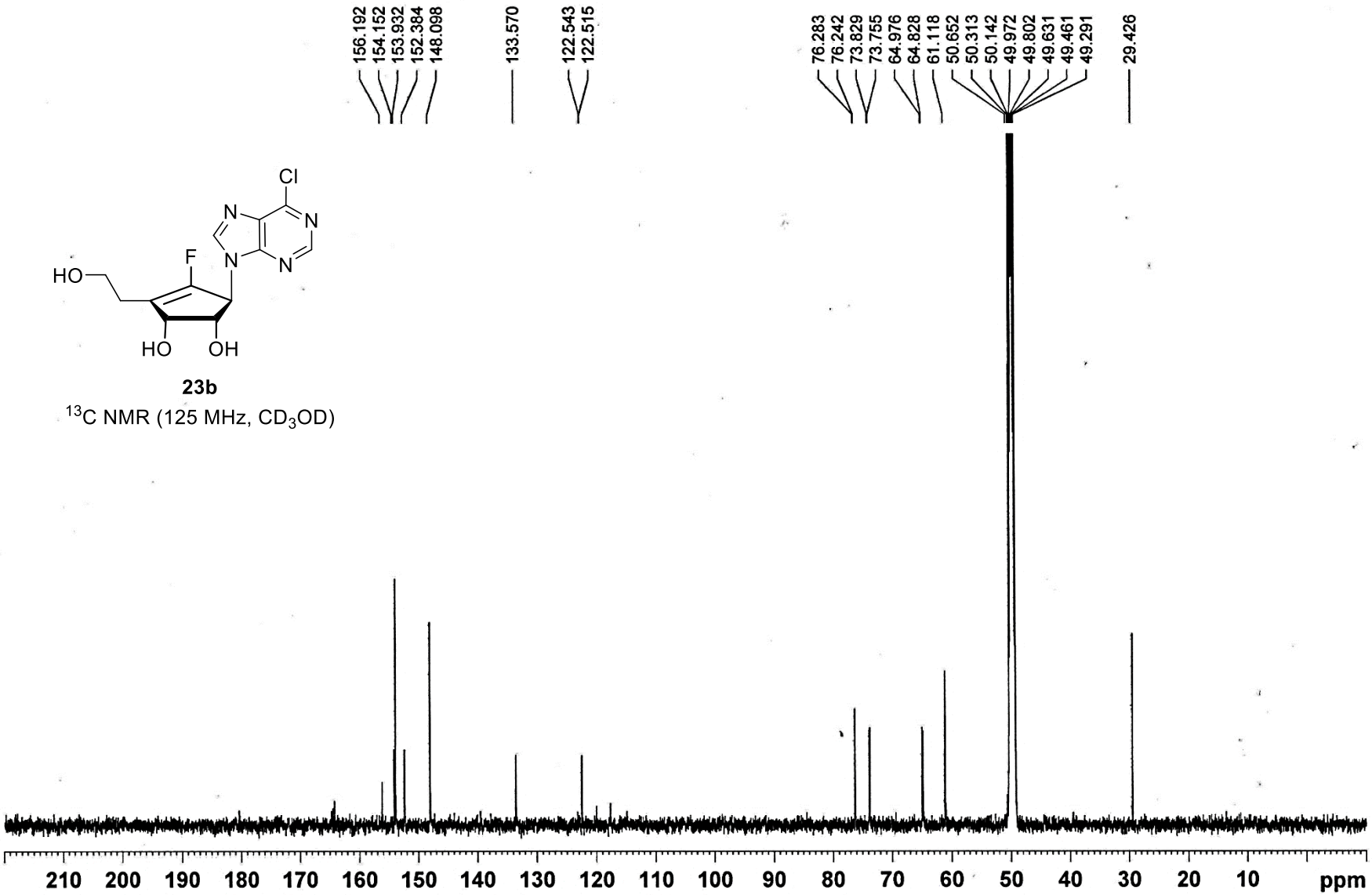



6CIP 180323_Proton-1-2.jdf
8.717
8.641
5.723
5.720
5.709
5.699
5.696
4.881
4.714
4.703
4.689
4.582
4.579
4.569
4.565
4.555
4.552
3.795
3.780
3.772
3.764
3.755
3.738
3.291
3.287
3.283
3.279
3.275
2.516
2.498
2.482
Cl
N
N
N
N
F
HO
HO
OH
23b
1H NMR (400 MHz, CD3OD)
abundance
3.0
2.0
1.0
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
1.00
1.03
1.05
1.02
1.01
2.00
2.14
X : parts per Million : Proton

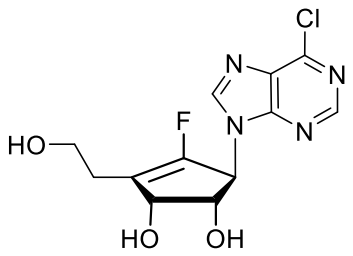
6-Cl purine (MeOD,500MHz)

23b

^{13}C NMR (125 MHz, CD_3OD)

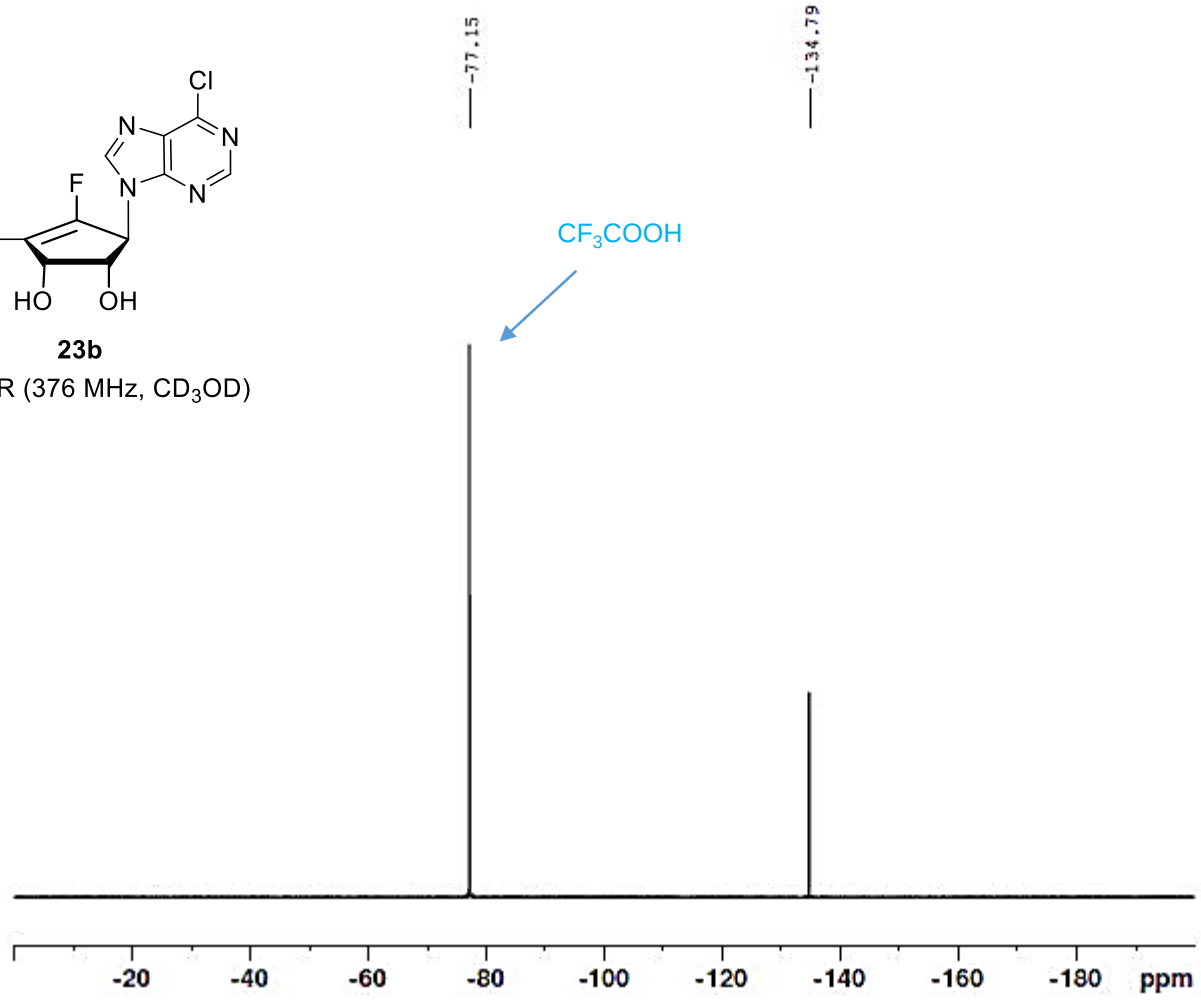


6CIP deprotection / 19F

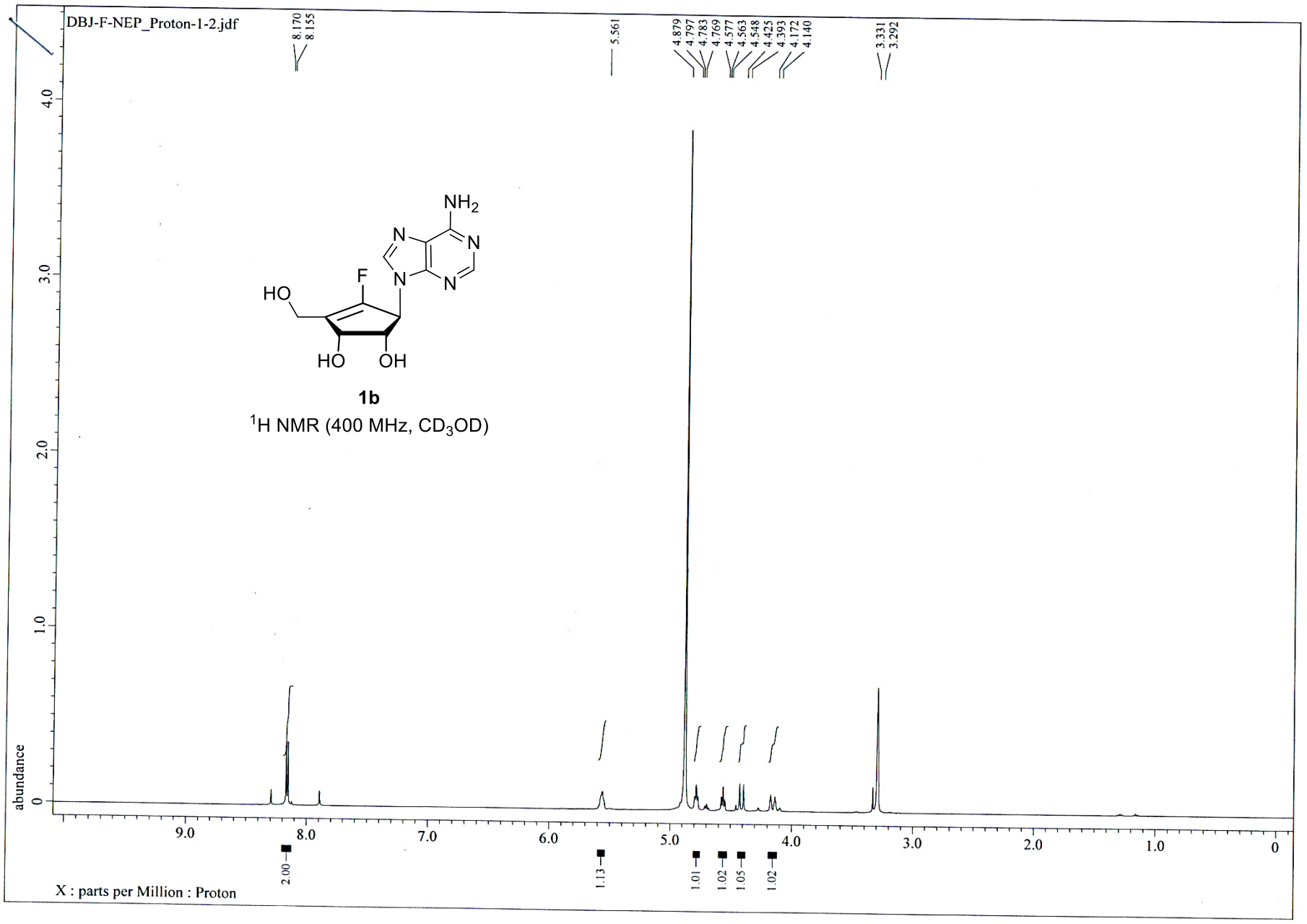


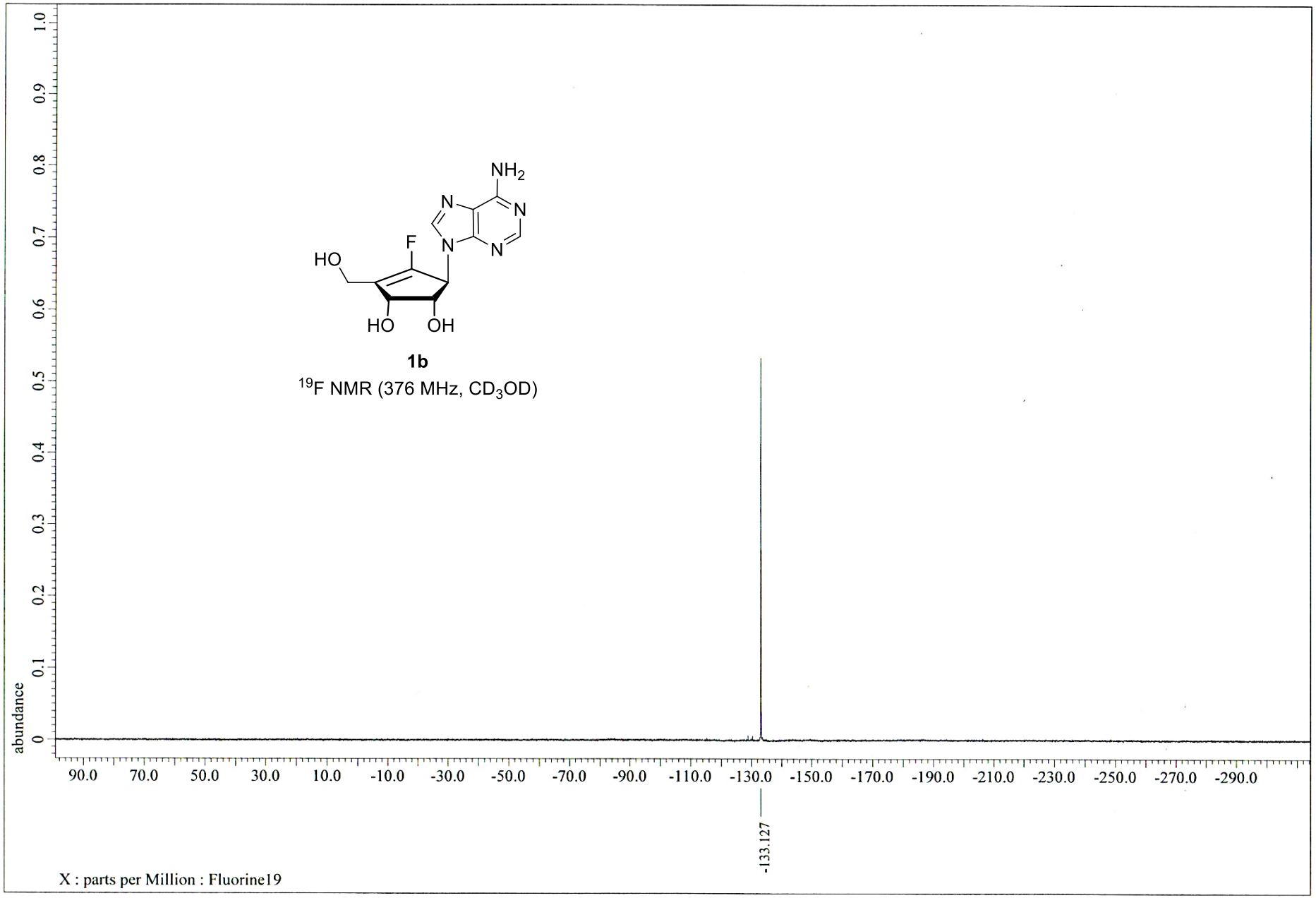
23b

^{19}F NMR (376 MHz, CD_3OD)

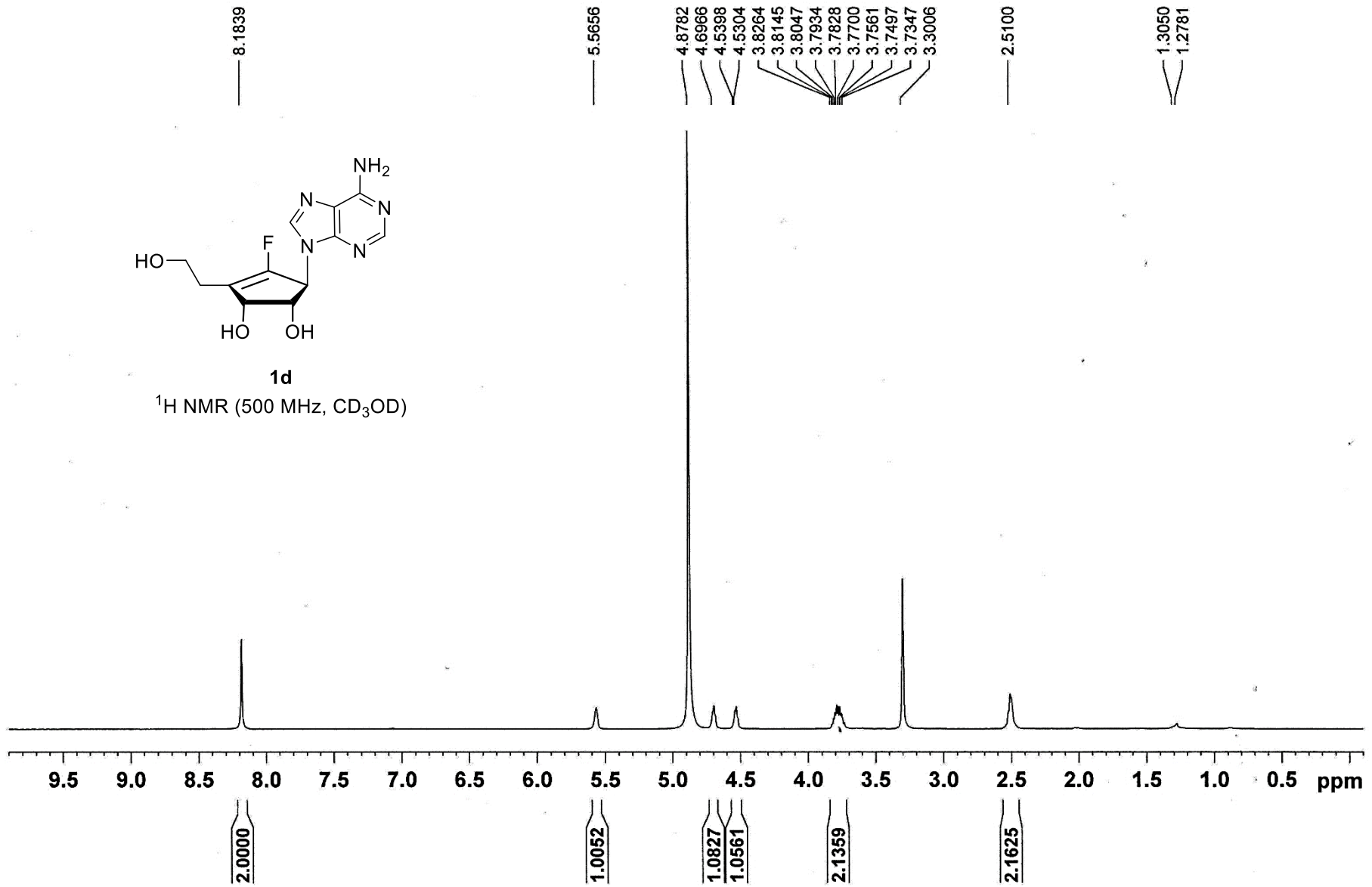



```
Current Data Parameters
NAME          mar27-ph-jmh
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_              20180327
Time                 13.58 h
INSTRUM              spect
PROBHD    Z3246_0288 (PH
PULPROG        zgfhigqn.2
TD                  131072
SOLVENT               MeOD
NS                      32
DS                       4
SWH              66964.289 Hz
FIDRES           1.021794 Hz
AQ               0.9786710 sec
RG                  201.38
DW                 7.467 usec
DE                  6.50 usec
TE                 298.0 K
D1              2.00000000 sec
D11             0.03000000 sec
D12             0.00002000 sec
TD0                      1
SFO1          282.3761146 MHz
NUC1                  19F
P1                 19.20 usec
PLW1            21.00000000 W
SFO2          300.1312005 MHz
NUC2                  1H
CPDPRG[2           waltz16
PCPD2              90.00 usec
PLW2            10.00000000 W
PLW12            0.17778000 W

F2 - Processing parameters
SI                    65536
SF            282.4043552 MHz
WDW                     EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.00
```


DBJ-F-NEP_Proton-1-2.jdf
8.170
8.155
5.561
4.879
4.797
4.783
4.769
4.577
4.563
4.548
4.425
4.393
4.172
4.140
3.331
3.292
NH2
N
N
N
N
F
HO
HO
OH
1b
1H NMR (400 MHz, CD3OD)
abundance
4.0
3.0
2.0
1.0
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
2.00
1.13
1.01
1.02
1.05
1.02
X : parts per Million : Proton

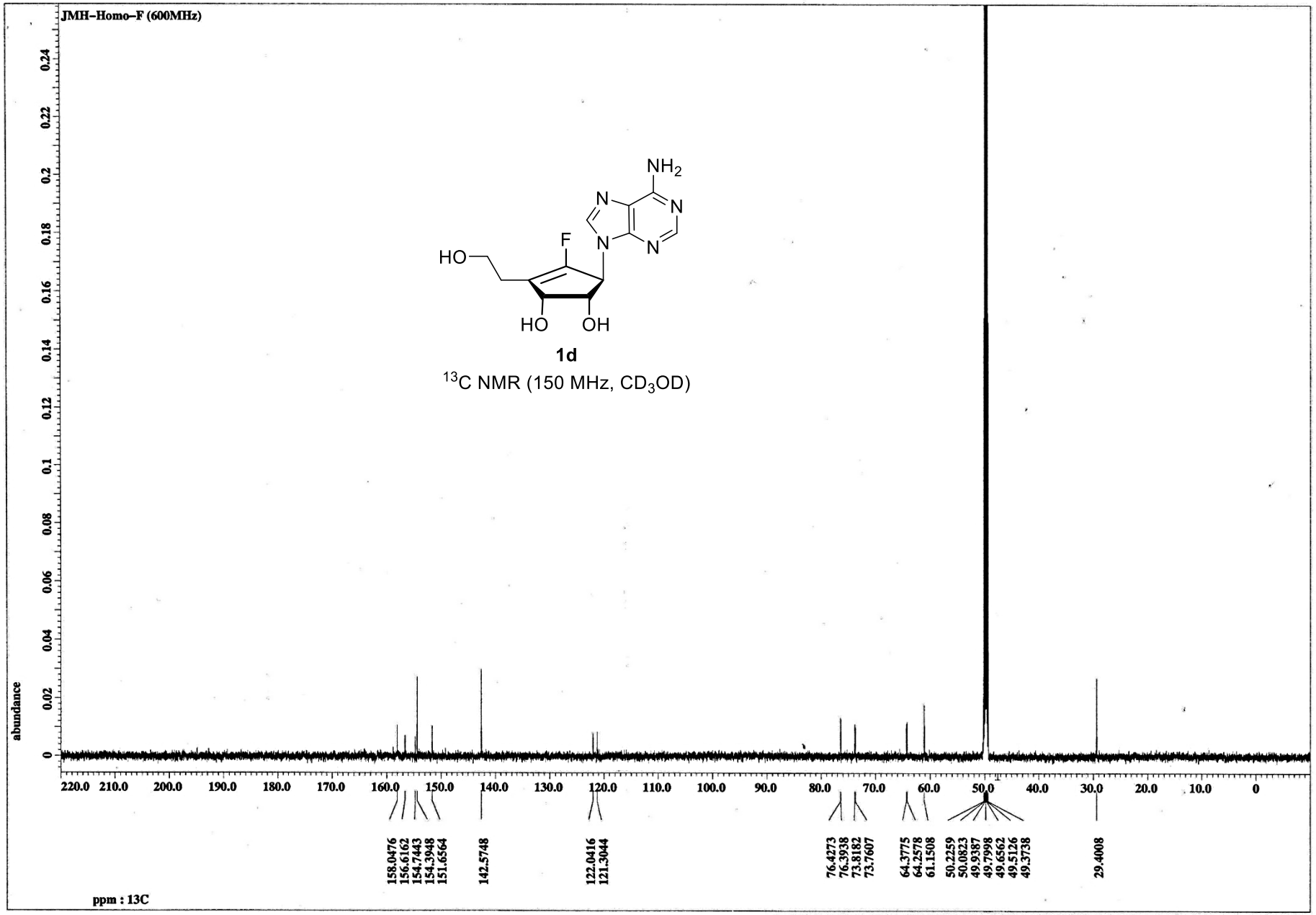

NH2
N
N
F
N
N
HO
HO
OH
1b
19F NMR (376 MHz, CD3OD)
abundance
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
90.0
70.0
50.0
30.0
10.0
-10.0
-30.0
-50.0
-70.0
-90.0
-110.0
-130.0
-150.0
-170.0
-190.0
-210.0
-230.0
-250.0
-270.0
-290.0
-133.127
X : parts per Million : Fluorine19

JMH-Homo-F (MeOD,500MHz)



1d

^{1}H NMR (500 MHz, CD_3OD)

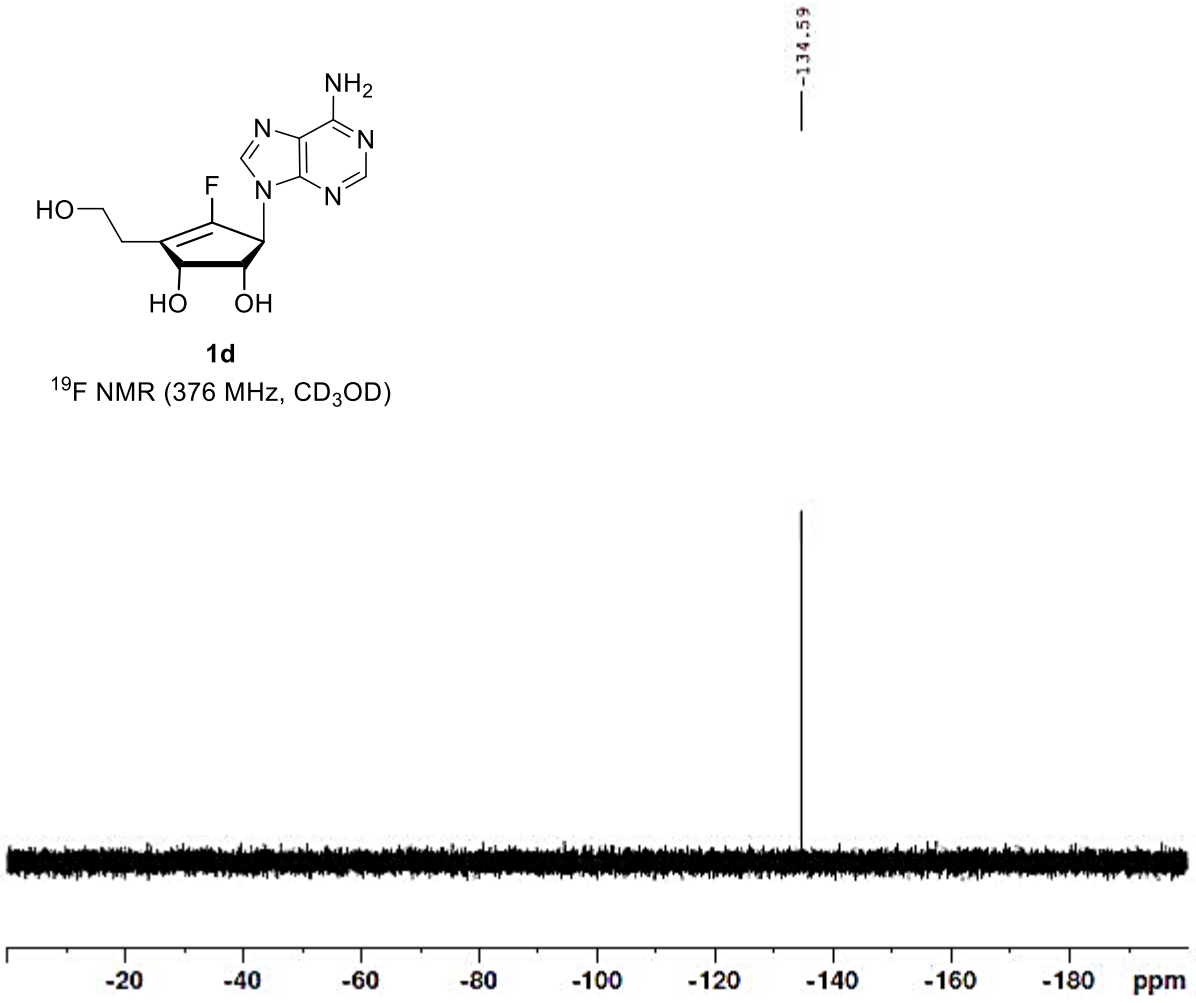


1d

^{13}C NMR (150 MHz, CD_3OD)

1d

^{19}F NMR (376 MHz, CD_3OD)




```
Current Data Parameters
NAME          mar23-ph-jmh
EXPNO                    2
PROCNO                   1

F2 - Acquisition Parameter
Date_             20180323
Time                11.13 h
INSTRUM              spect
PROBHD   Z3246_0288 (PH
PULPROG       zgfhigqn.2
TD                  131072
SOLVENT               MeOD
NS                     128
DS                       4
SWH              66964.289 Hz
FIDRES           1.021794 Hz
AQ               0.9786710 se
RG                  201.38
DW                   7.467 us
DE                   6.50 us
TE                  298.0 K
D1             2.00000000 se
D11            0.03000000 se
D12            0.00002000 se
TD0                      1
SFO1         282.3761146 MH
NUC1                  19F
P1                  19.20 us
PLW1         21.00000000 W
SFO2         300.1312005 MH
NUC2                  1H
CPDPRG[2          waltz16
PCPD2               90.00 us
PLW2         10.00000000 W
PLW12         0.17778000 W

F2 - Processing parameters
SI                   65536
SF           282.4043552 MH
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.00
```