Supplementary Information

Borylated 5-membered Ring Iminosugars: Synthesis and Biological Evaluation for Glycosidase Inhibition and Anticancer Properties for Application in Boron Neutron Capture Therapy (BNCT) – Part 2

Kate Prichard [1], Kosuke Yoshimura [2], Suzuka Yamamoto [2], Atsumi Taguchi [2], Barbara Bartholomew [3], Jayne Gilbert [4], Jennette Sakoff [4], Robert Nash [3], Atsushi Kato [2], Michela Simone [1,*,†]

Index

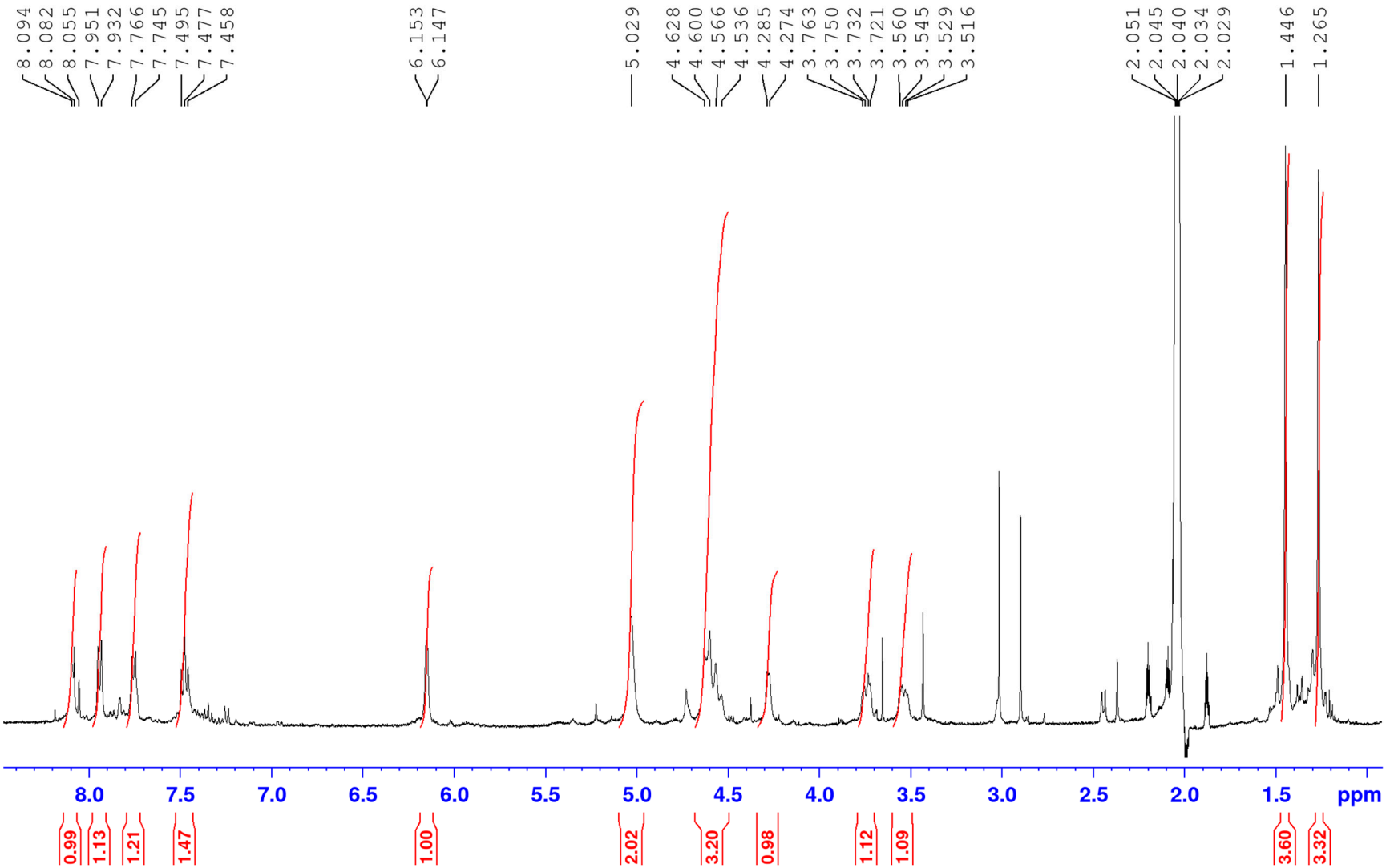
Figure S1. ^{1}H- (400 MHz), ^{13}C-NMR (100 MHz), DEPT, COSY and HSQC spectra of *N*-(3-hydroxyphenyl)-3,6-dideoxy-3,6-imino-1,2-*O*-isopropylidene-α-D-gulofuranose **meta 6** in *Acetic acid-d*^{6}. **2**

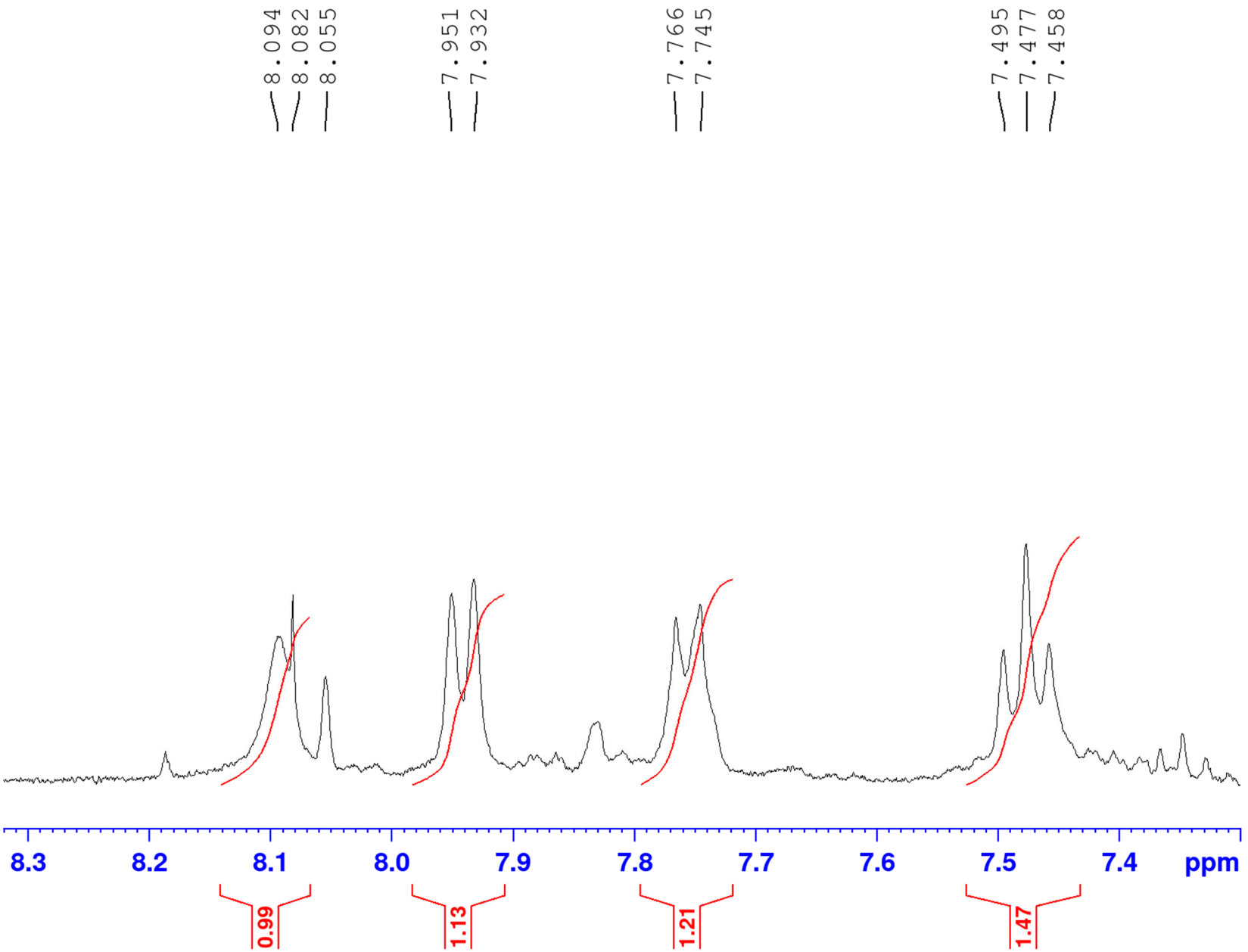
Figure S2. ^{1}H- (400 MHz), ^{13}C-NMR (100 MHz), DEPT, COSY, HSQC and HMBC spectra of *N*-(3-hydroxyphenyl)-1,4-dideoxy-1,4-imino-L-gulitol **meta 7** in *Acetic acid-d*^{6}. **12**

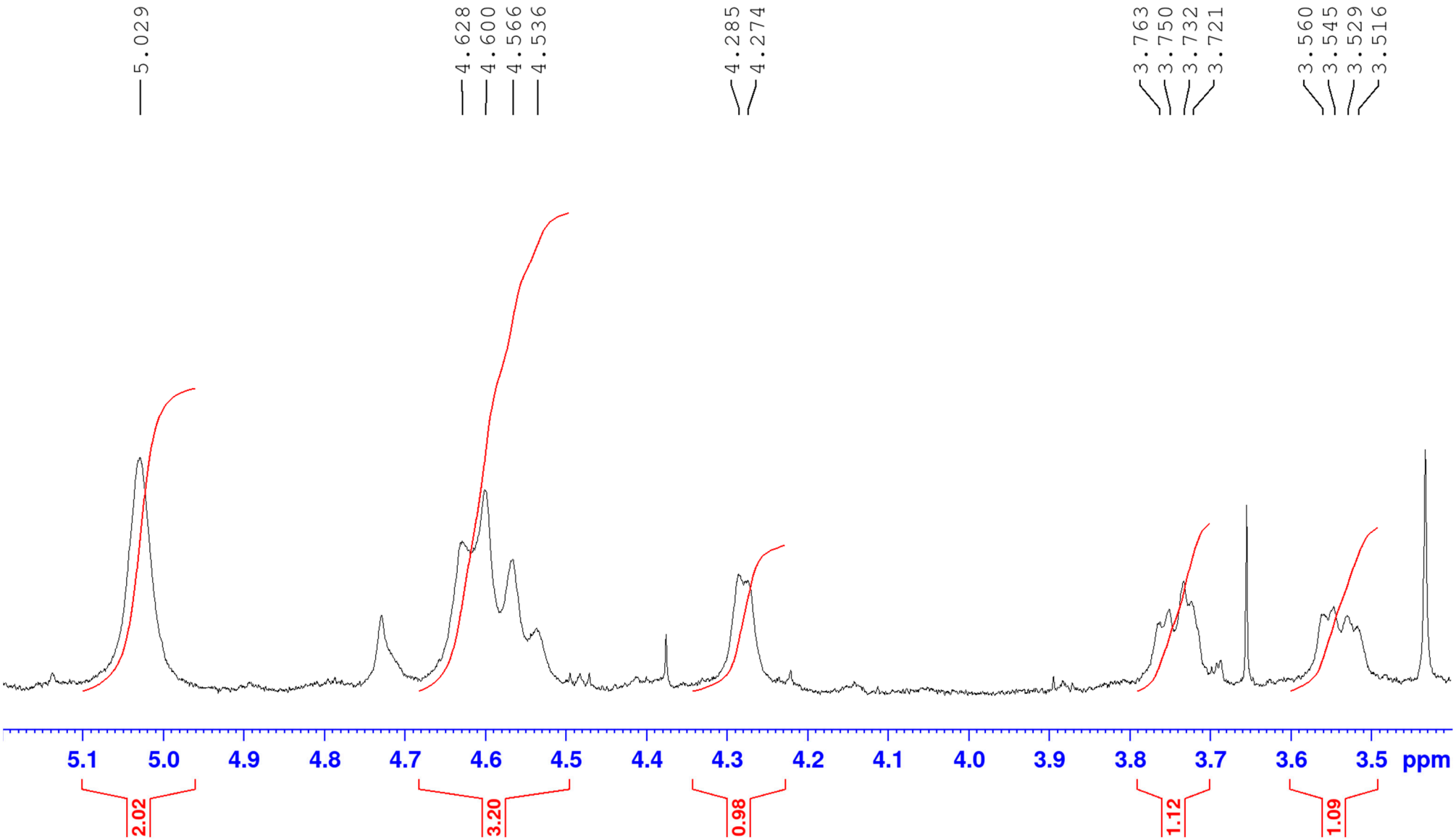
NMR Experimental details (*Acetic acid-d*^{6}). **25**

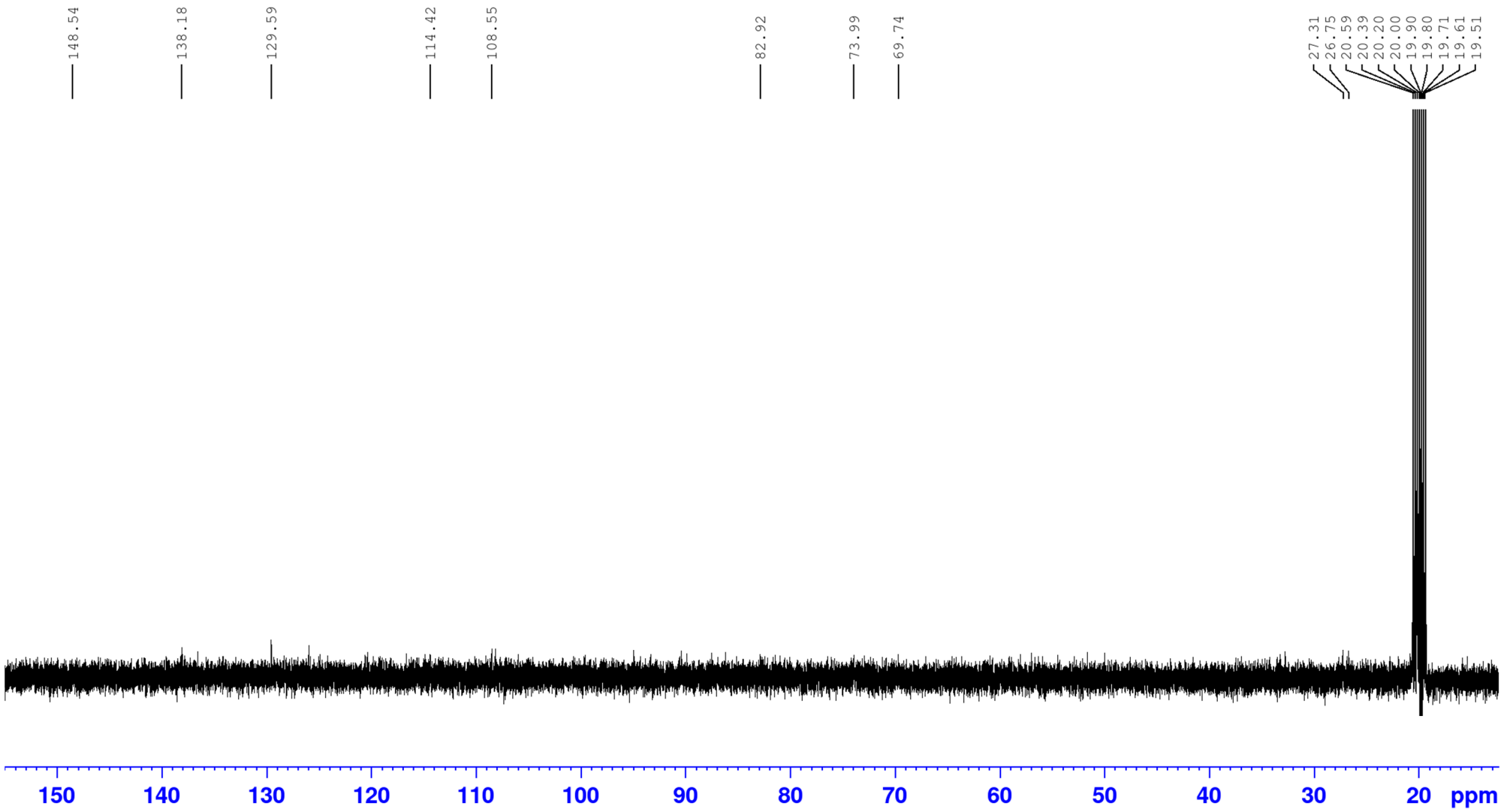
Figure S1. ^{1}H- (400 MHz), ^{13}C-NMR (100 MHz), DEPT, COSY and HSQC spectra of *N*-(3-hydroxyphenyl)-3,6-dideoxy-3,6-imino-1,2-*O*-isopropylidene-*α*-D-gulofuranose **meta 6** in *Acetic acid-d*^{6}.

^{1}H-NMR

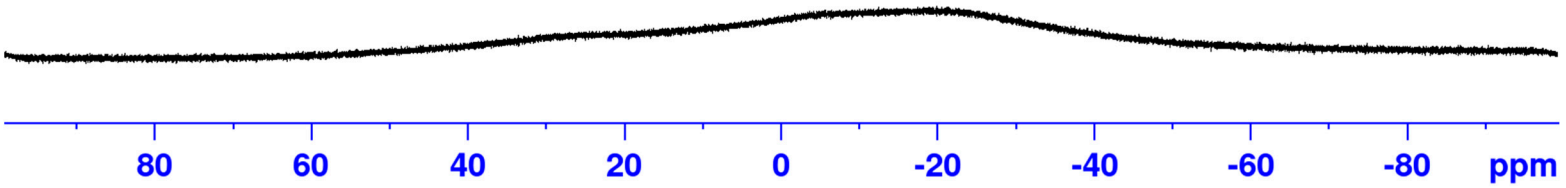



8.094
8.082
8.055
7.951
7.932
7.766
7.745
7.495
7.477
7.458
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
ppm
0.99
1.13
1.21
1.47

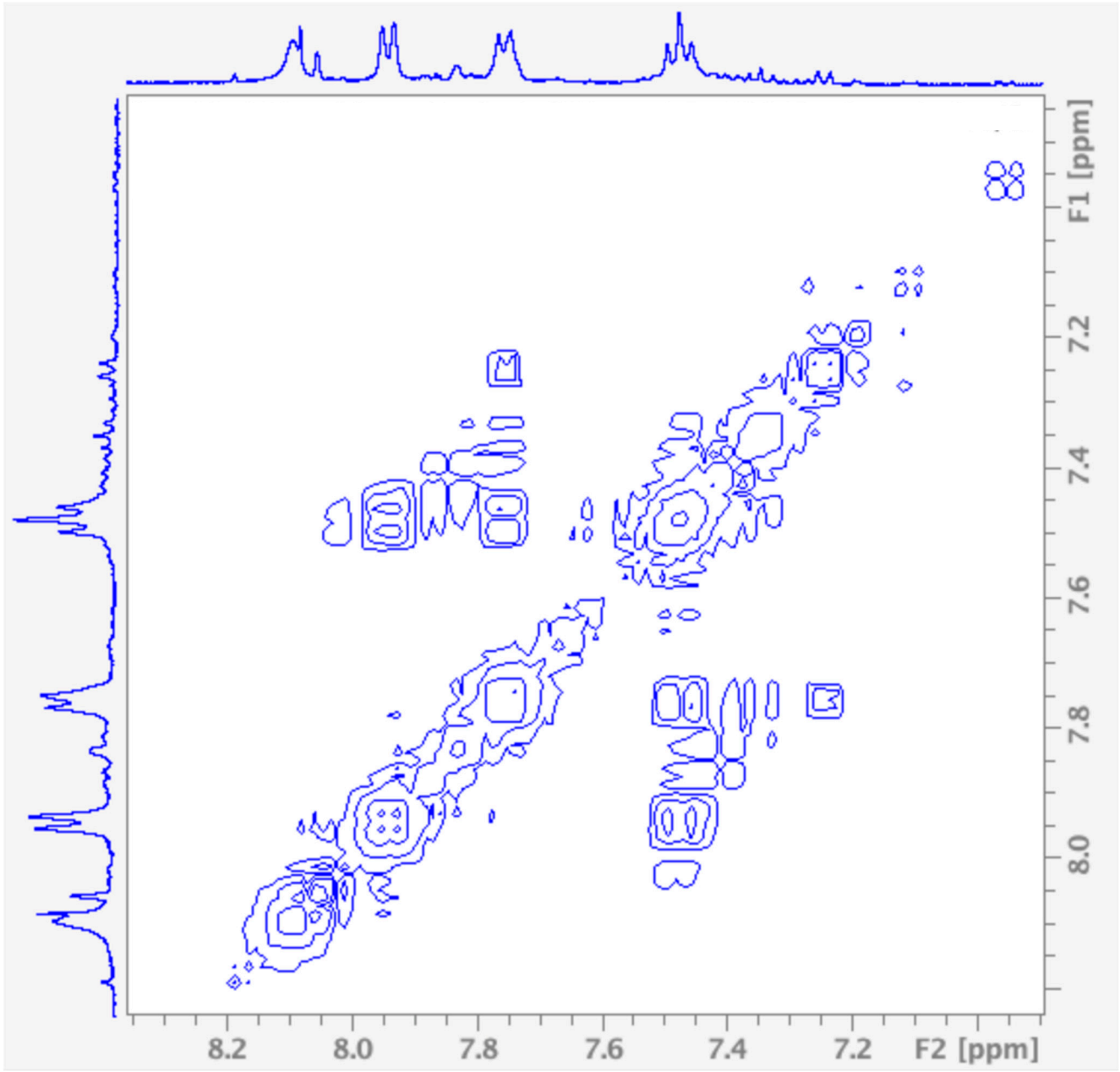

5.029
4.628
4.600
4.566
4.536
4.285
4.274
3.763
3.750
3.732
3.721
3.560
3.545
3.529
3.516
5.1
5.0
4.9
4.8
4.7
4.6
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
ppm
2.02
3.20
0.98
1.12
1.09

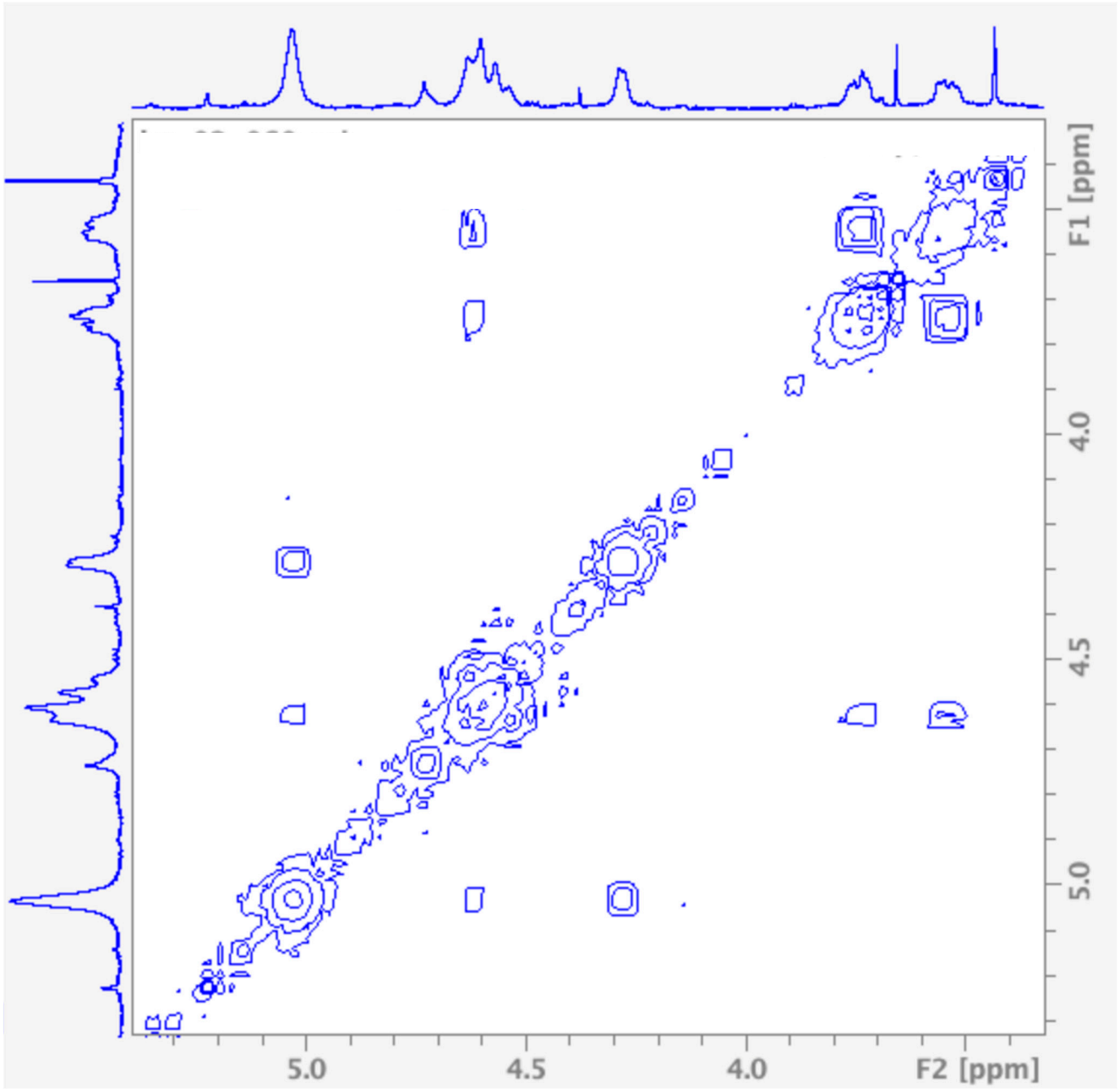

148.54
138.18
129.59
114.42
108.55
82.92
73.99
69.74
27.31
26.75
20.59
20.39
20.20
20.00
19.90
19.80
19.71
19.61
19.51
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

^{11}B-NMR

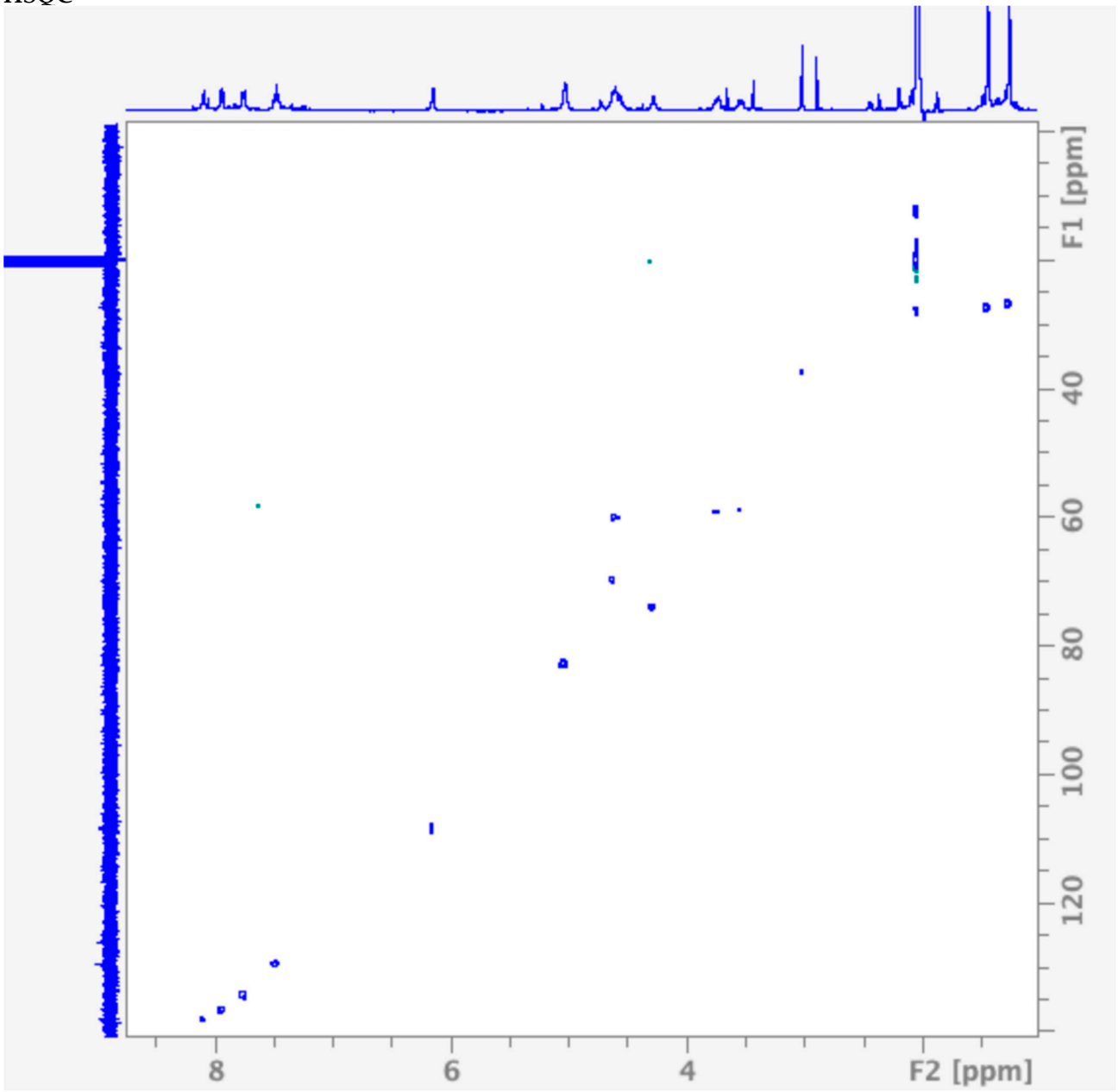


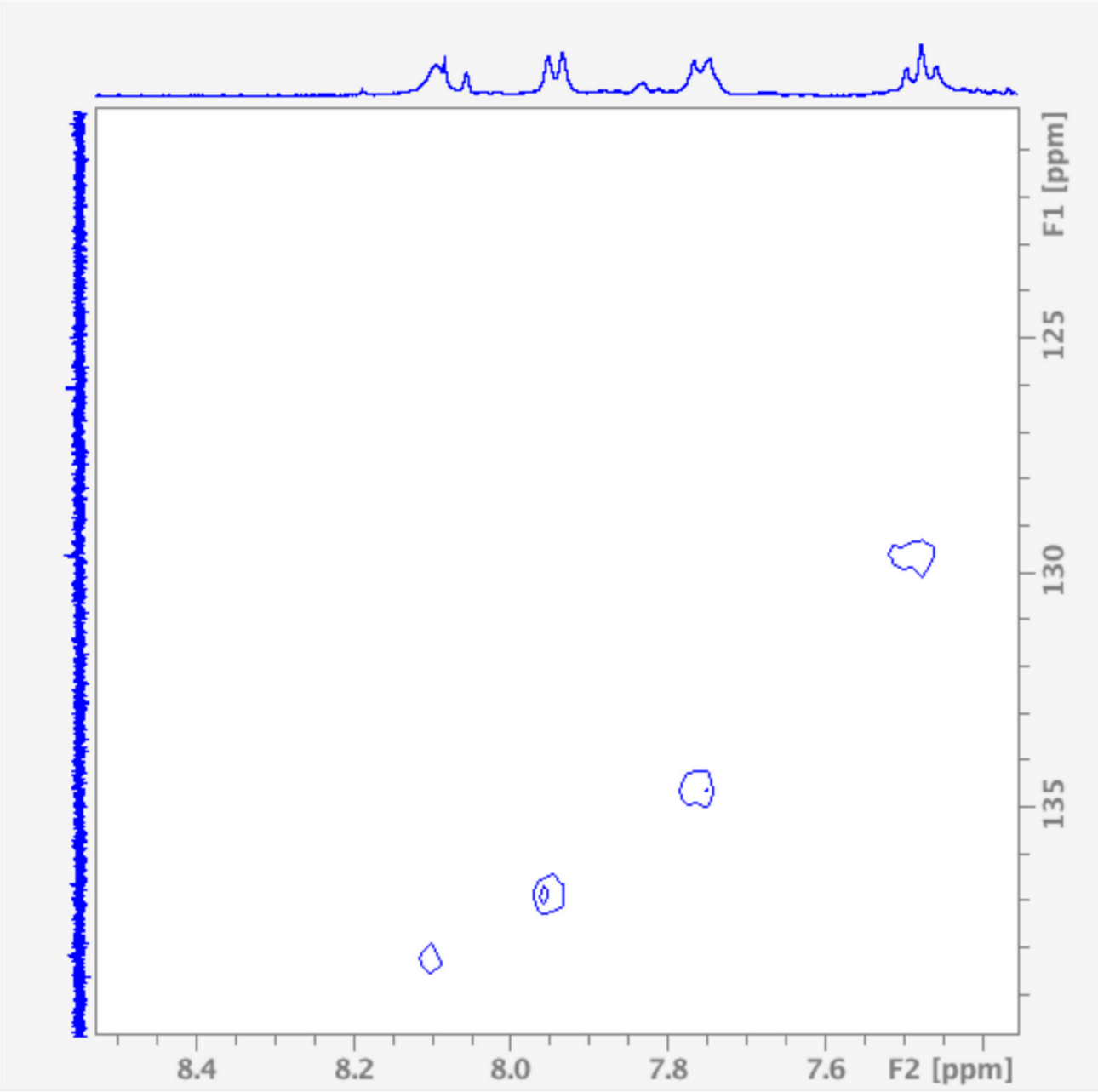
COSY




F1 [ppm]
4.0
4.5
5.0
5.0
4.5
4.0
F2 [ppm]

HSQC




F1 [ppm]
125
130
135
8.4
8.2
8.0
7.8
7.6
F2 [ppm]

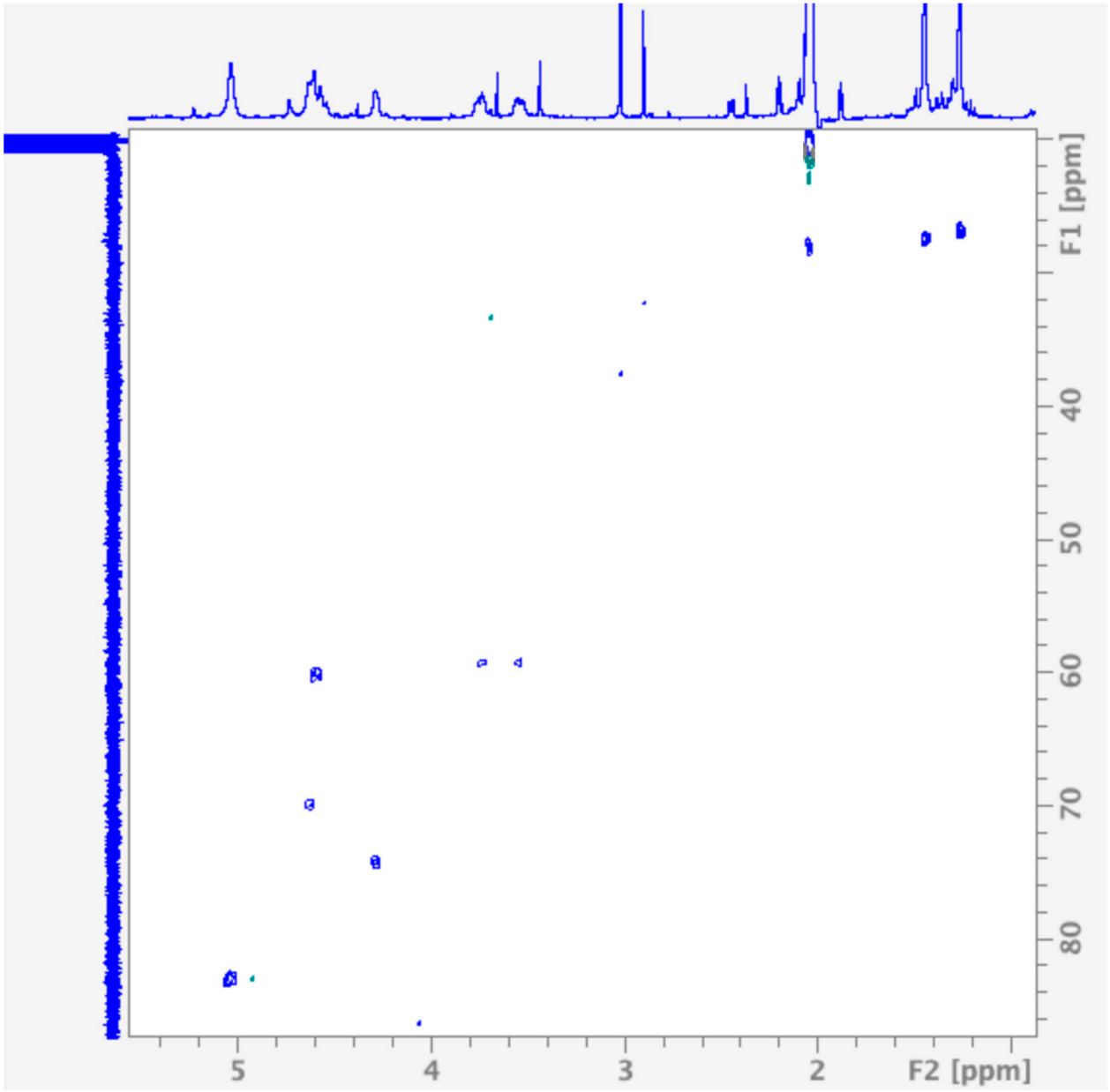
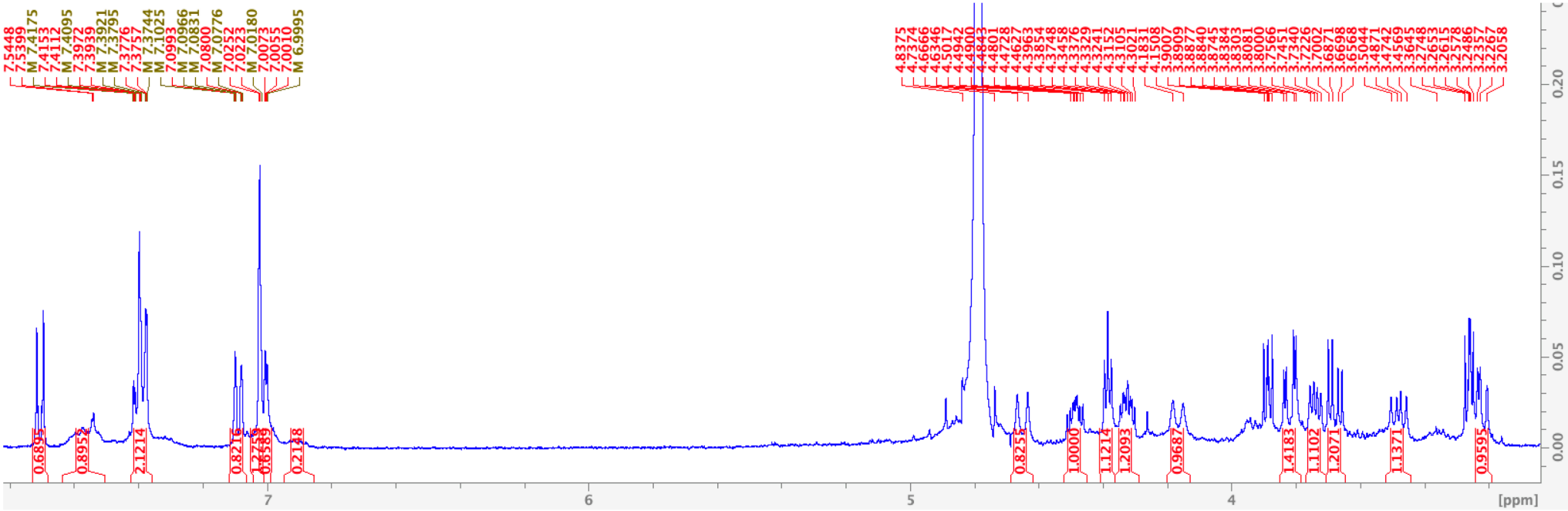
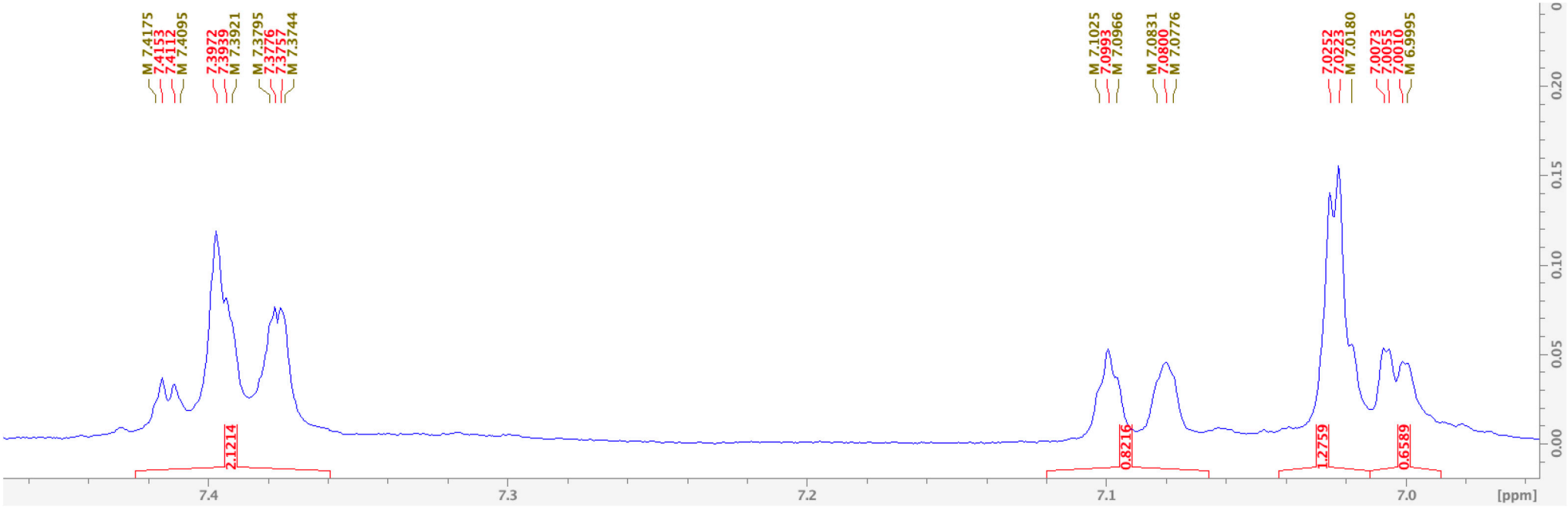
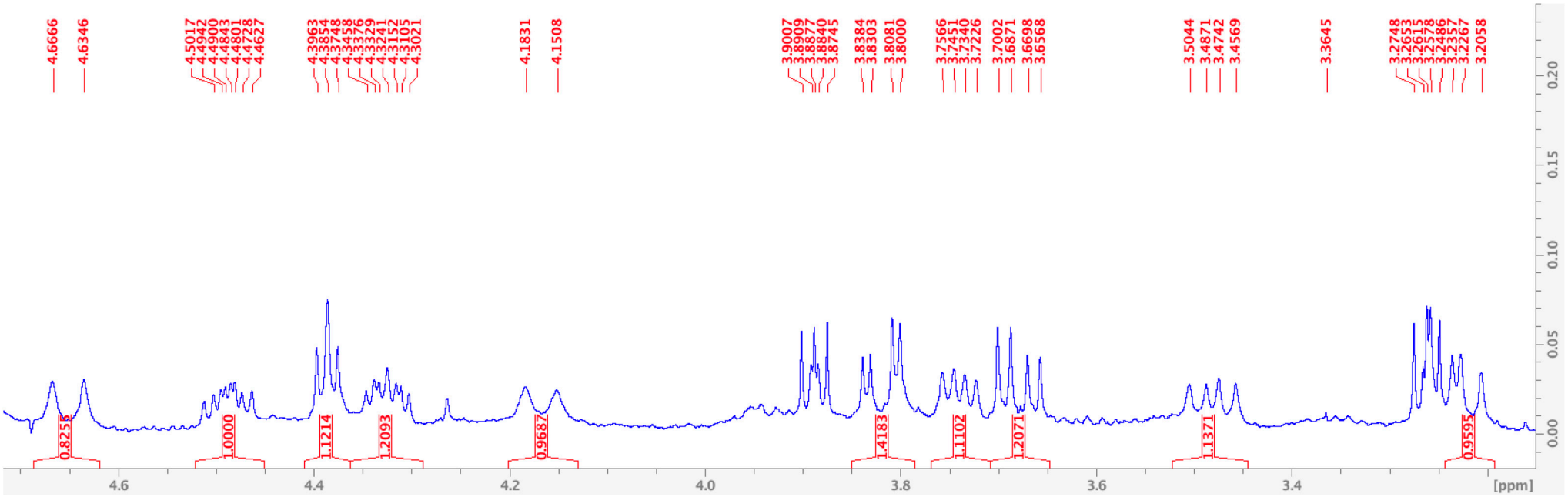

F1 [ppm]
40
50
60
70
80
5
4
3
2
F2 [ppm]

Figure S2. ^{1}H- (400 MHz), ^{13}C-NMR (100 MHz), DEPT, ^{11}B-NMR (128 MHz), COSY and HSQC spectra of *N*-(3-hydroxyphenyl)-1,4-dideoxy-1,4-imino-L-gulitol **meta 7** in *Acetic acid-d*^{6}.

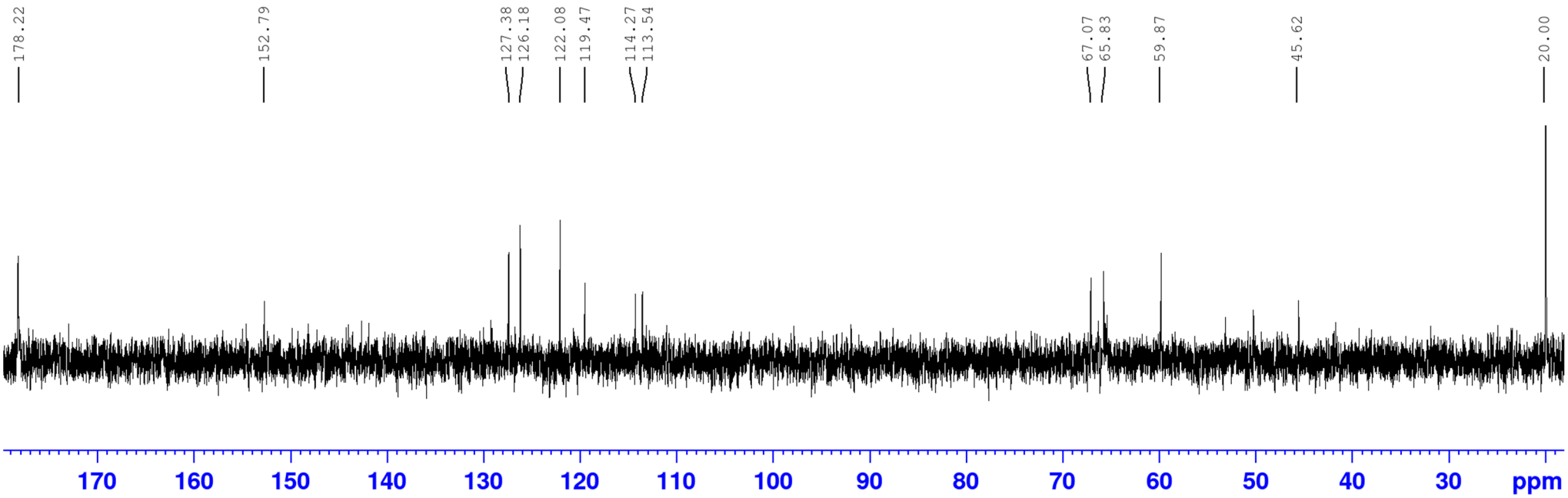
^{1}H-NMR

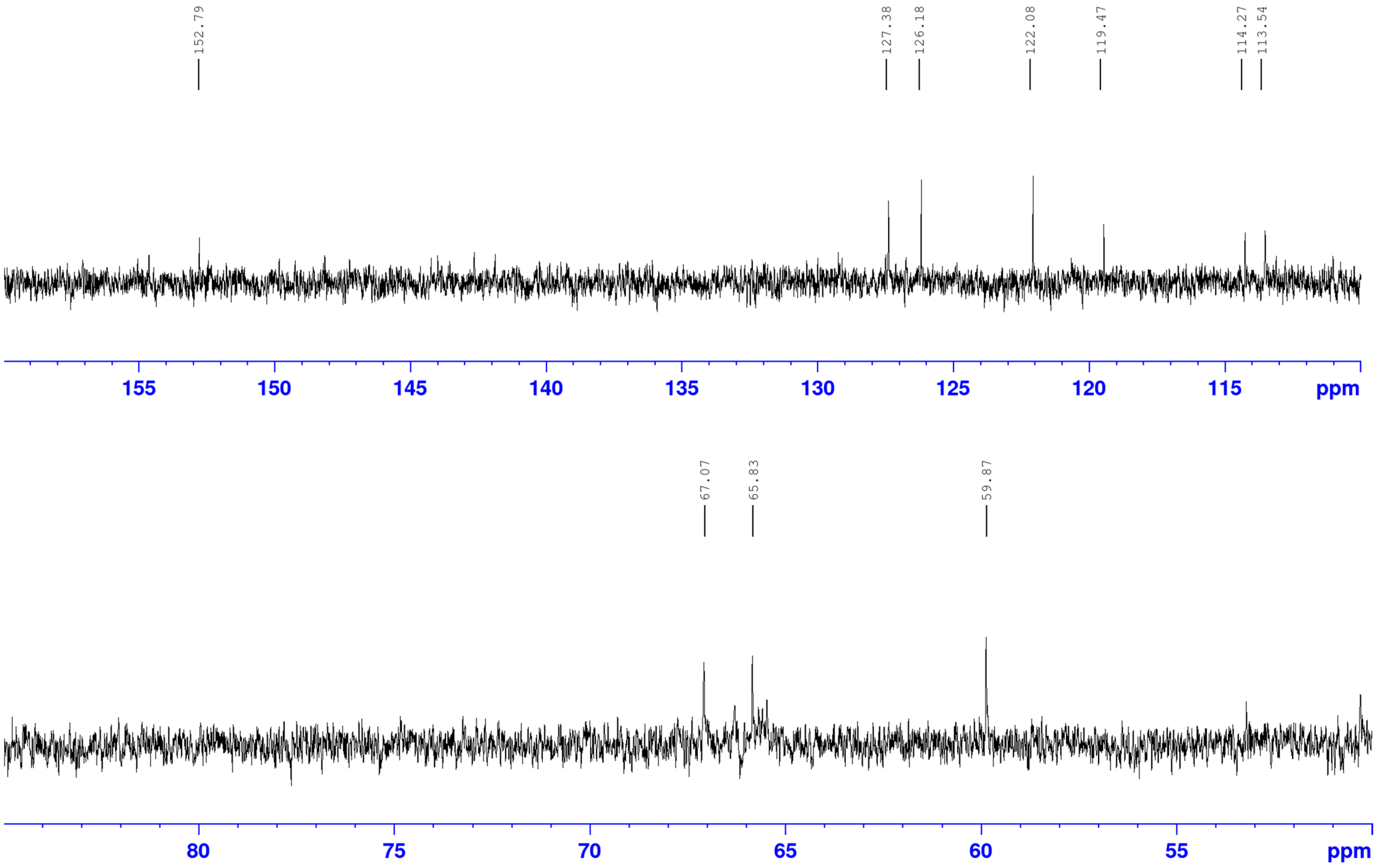


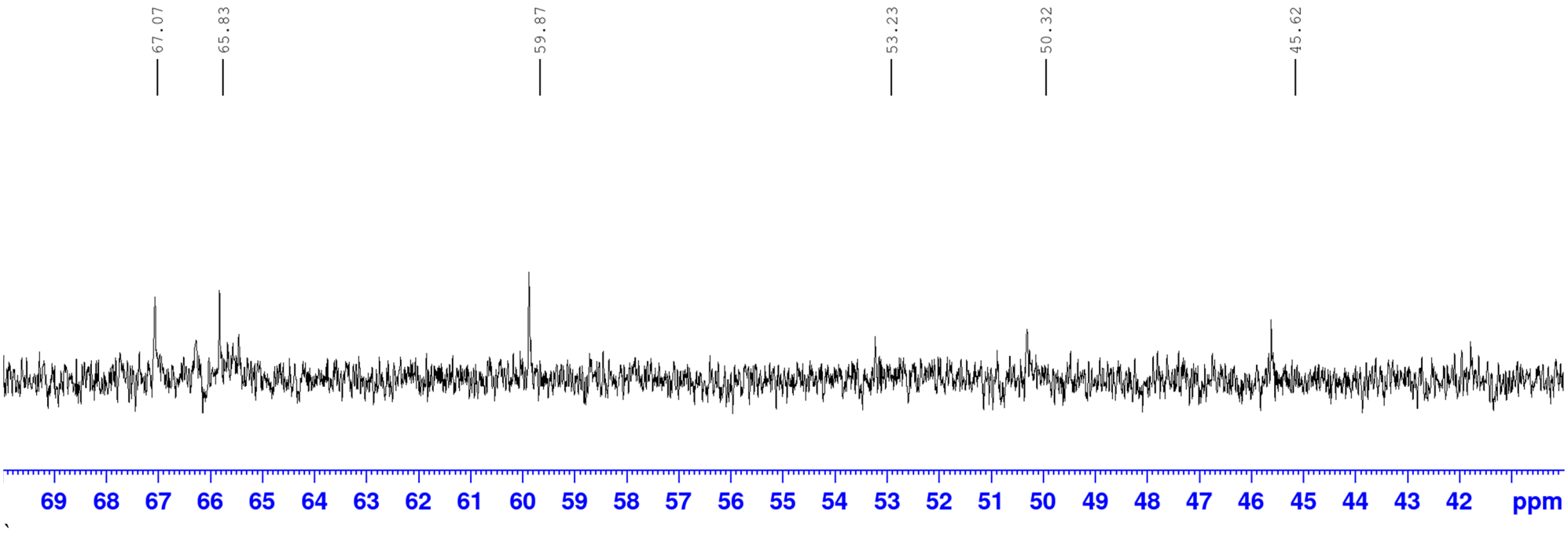

M 7.4175
7.4153
7.4112
M 7.4095
7.3972
7.3939
M 7.3921
M 7.3795
7.3776
7.3757
M 7.3744
M 7.1025
7.0993
M 7.0966
M 7.0831
7.0800
M 7.0776
7.0252
7.0223
M 7.0180
7.0073
7.0055
7.0010
M 6.9995
2.1214
0.8216
1.2759
0.6589
7.4
7.3
7.2
7.1
7.0
[ppm]
0.20
0.15
0.10
0.05
0.00


4.6666
4.6346
4.5017
4.4942
4.4900
4.4843
4.4801
4.4728
4.4627
4.3963
4.3854
4.3748
4.3458
4.3376
4.3329
4.3241
4.3152
4.3105
4.3021
4.1831
4.1508
3.9007
3.8909
3.8877
3.8840
3.8745
3.8384
3.8303
3.8081
3.8000
3.7566
3.7451
3.7340
3.7226
3.7002
3.6871
3.6698
3.6568
3.5044
3.4871
3.4742
3.4569
3.3645
3.2748
3.2653
3.2615
3.2578
3.2486
3.2357
3.2267
3.2058
0.8256
1.0000
1.1214
1.2093
0.9687
1.4183
1.1102
1.2071
1.1371
0.9595
4.6
4.4
4.2
4.0
3.8
3.6
3.4
[ppm]
0.20
0.15
0.10
0.05
0.00

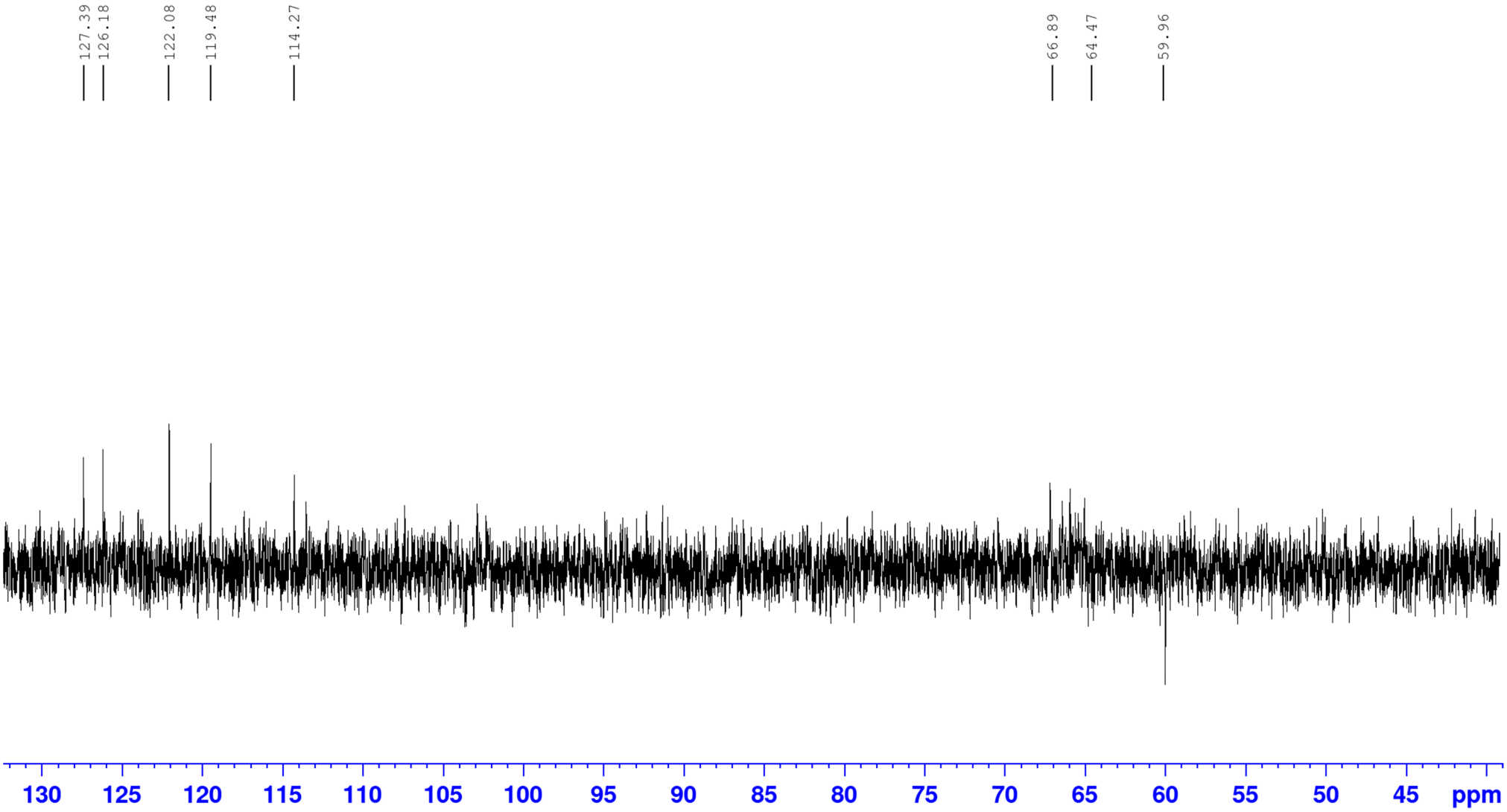
^{13}C-NMR


178.22
152.79
127.38
126.18
122.08
119.47
114.27
113.54
67.07
65.83
59.87
45.62
20.00
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

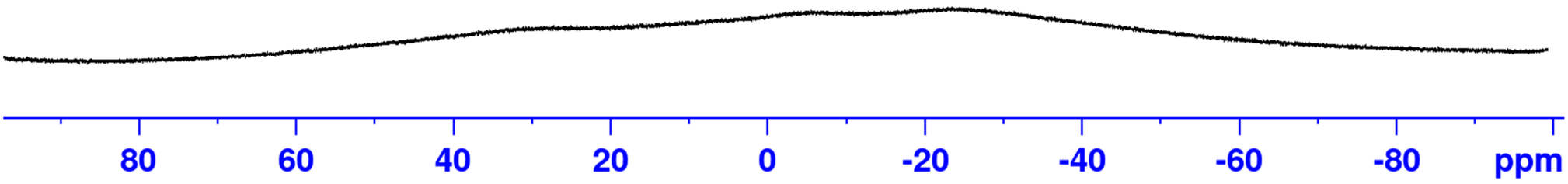

152.79
127.38
126.18
122.08
119.47
114.27
113.54
155
150
145
140
135
130
125
120
115
ppm
67.07
65.83
59.87
80
75
70
65
60
55
ppm


67.07
65.83
59.87
53.23
50.32
45.62
69 68 67 66 65 64 63 62 61 60 59 58 57 56 55 54 53 52 51 50 49 48 47 46 45 44 43 42 ppm

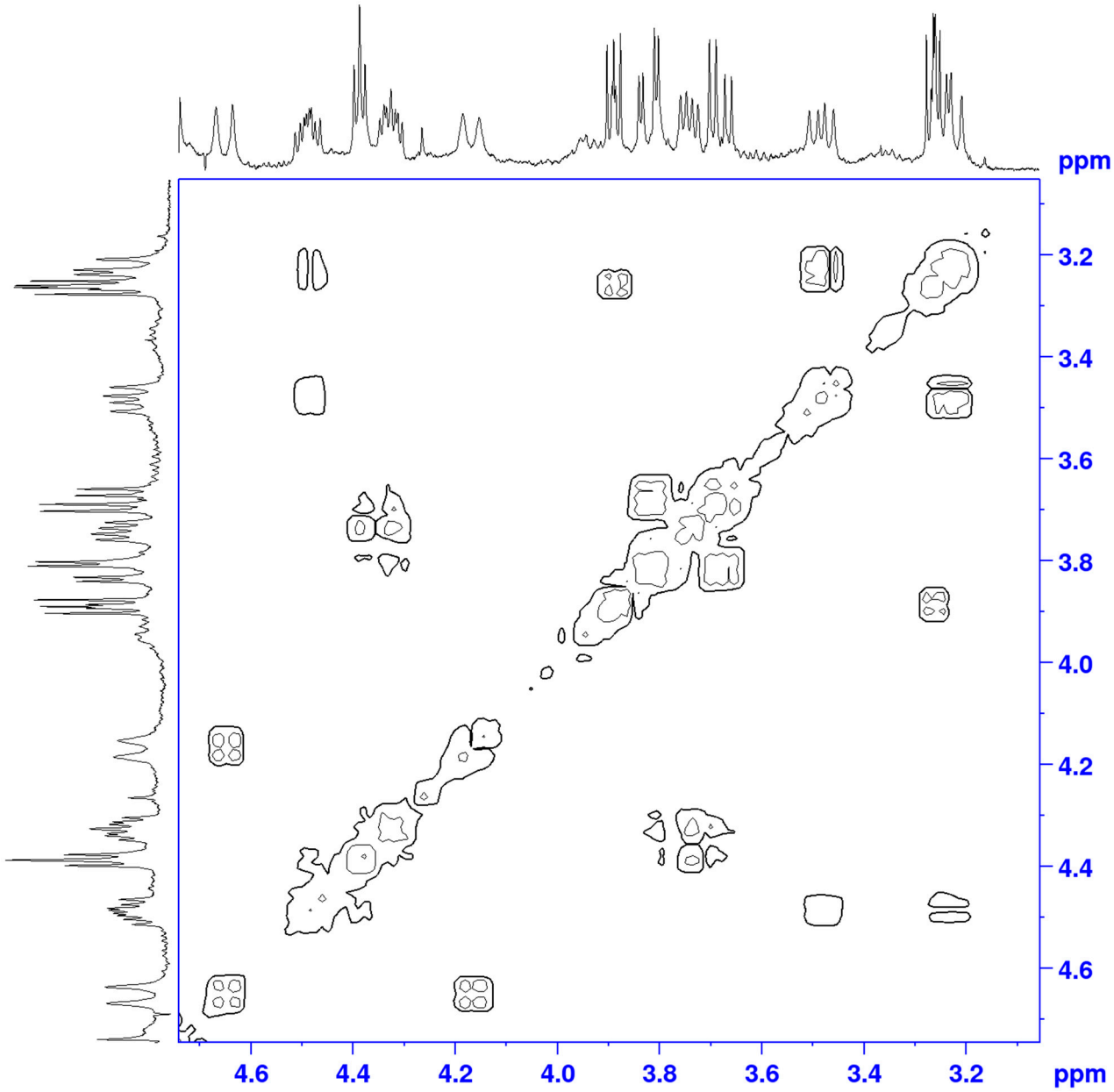
DEPT

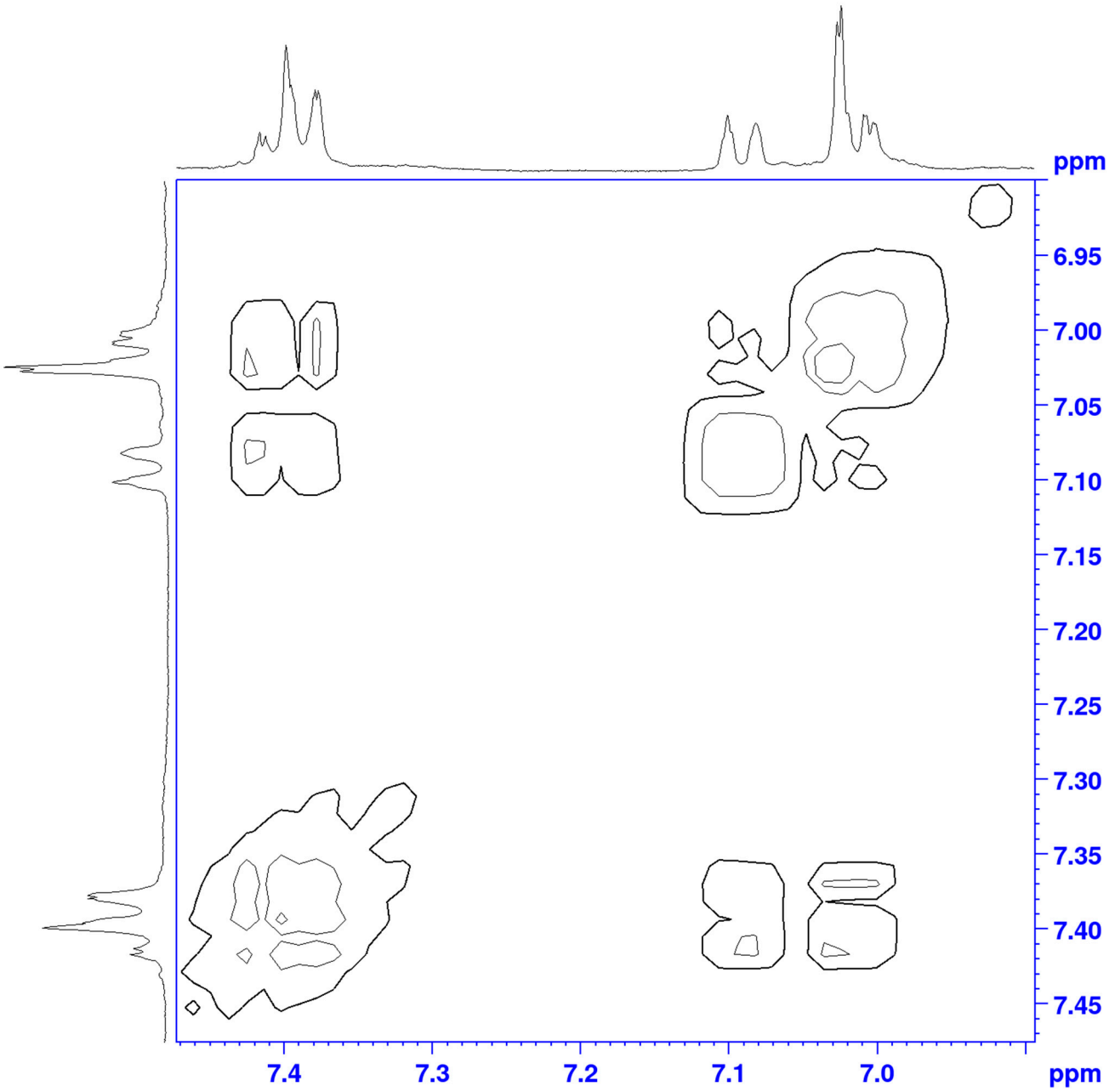

127.39
126.18
122.08
119.48
114.27
66.89
64.47
59.96
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
ppm

^{11}B-NMR

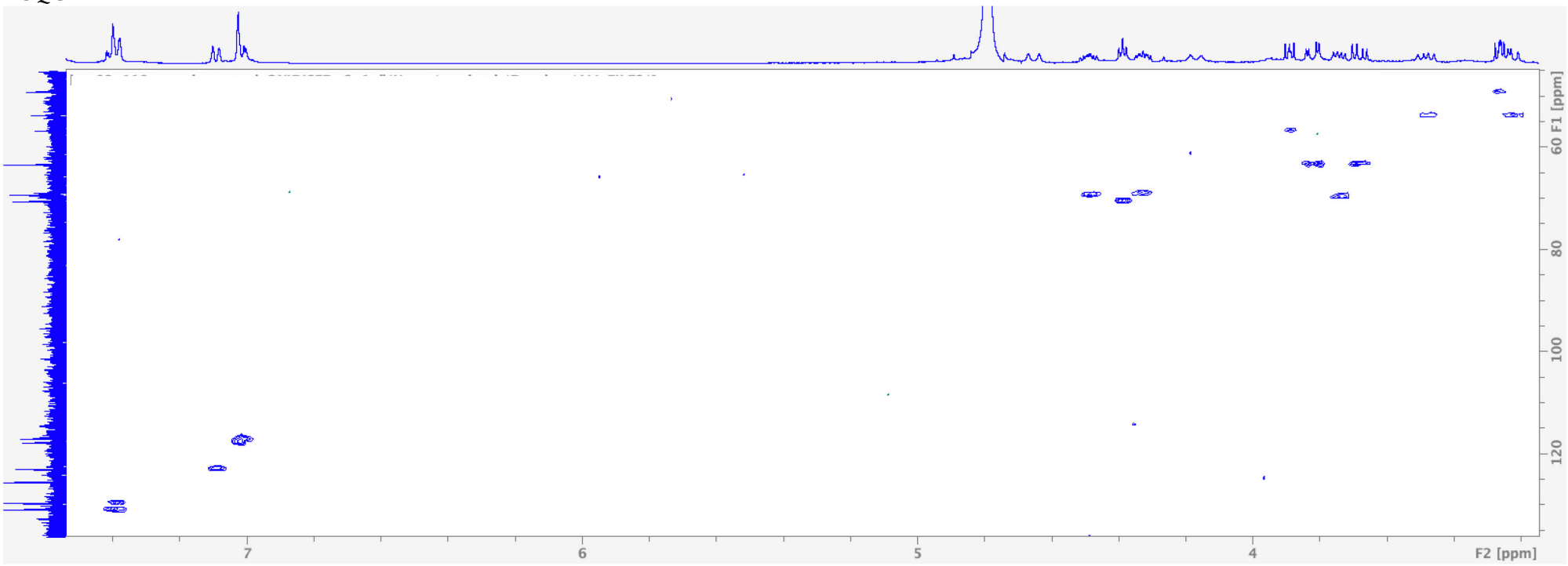


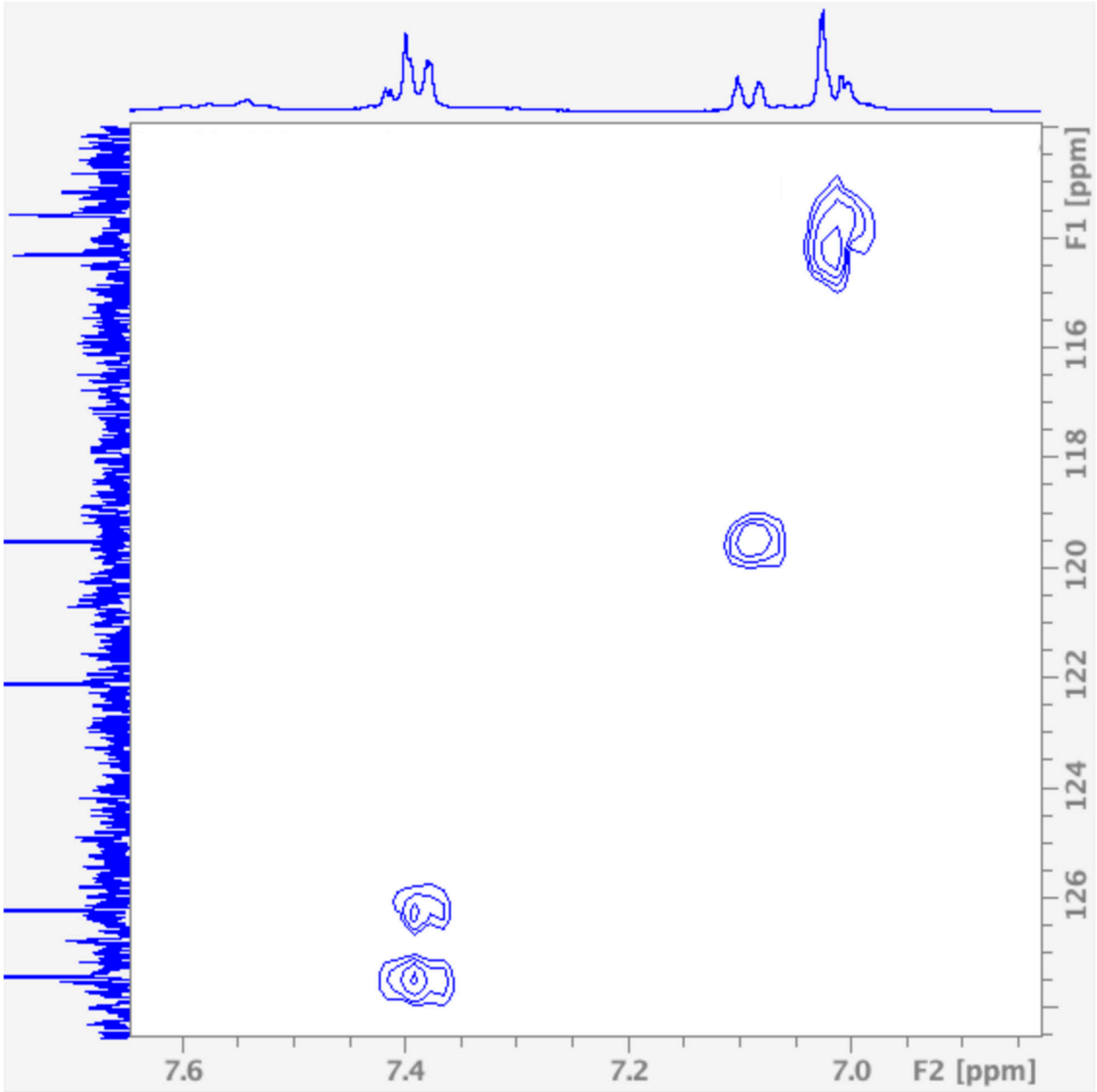
COSY

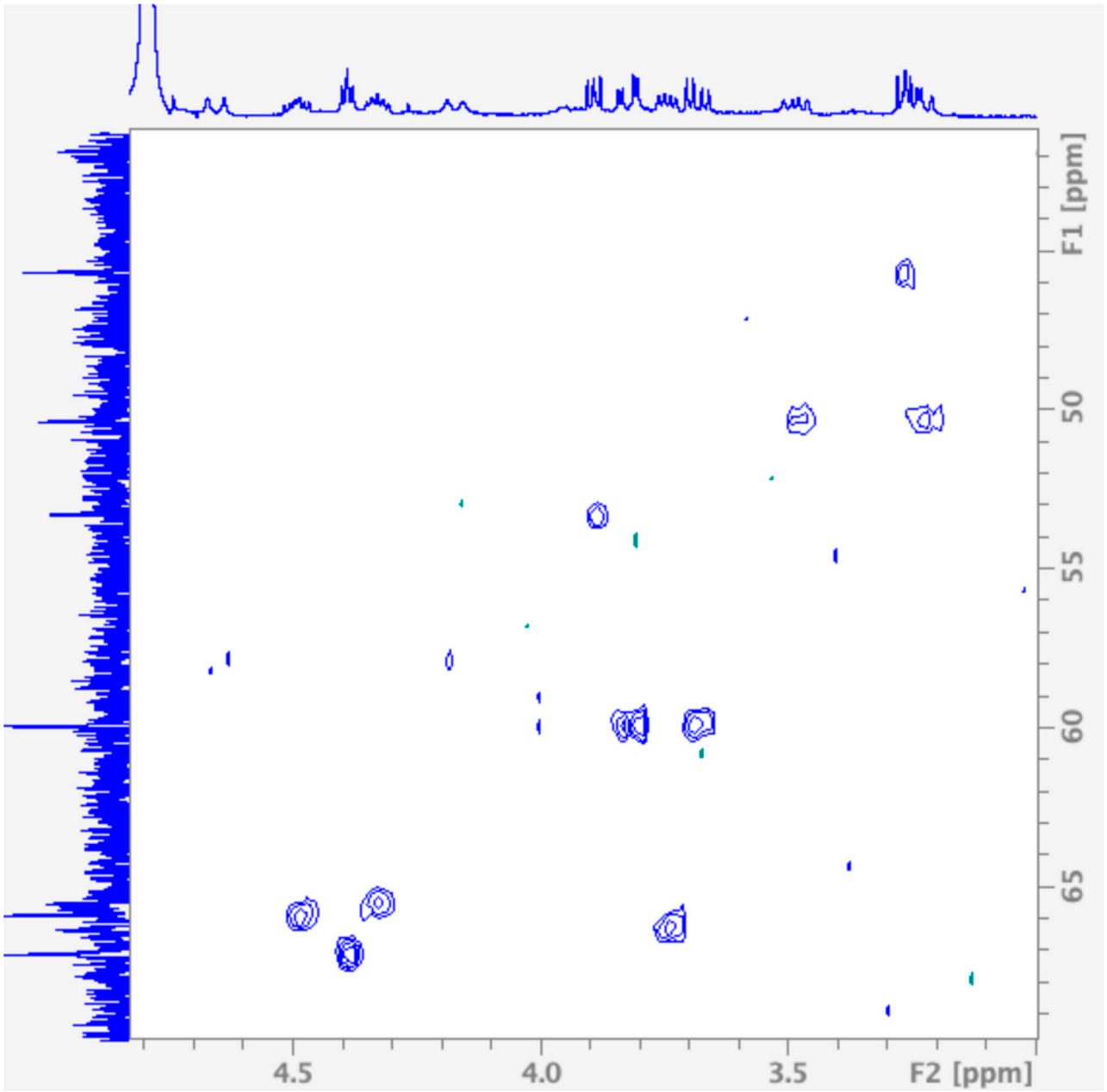



ppm
6.95
7.00
7.05
7.10
7.15
7.20
7.25
7.30
7.35
7.40
7.45
7.4
7.3
7.2
7.1
7.0
ppm

HSQC




F1 [ppm]
116
118
120
122
124
126
7.6
7.4
7.2
7.0
F2 [ppm]


F1 [ppm]
50
55
60
65
4.5
4.0
3.5
F2 [ppm]

NMR Experimental details (*Acetic acid-d*^{6})

	meta 6	**meta 7**
^{1}H	F2 - Acquisition Parameters Date_ 20171012 Time 12.13 INSTRUM spect PROBHD 5 mm PABBO BB- PULPROG zg TD 48076 SOLVENT Acetic NS 8 DS 2 SWH 6002.401 Hz FIDRES 0.124852 Hz AQ 4.0047307 sec RG 119.51 DW 83.300 usec DE 16.70 usec TE 298.1 K D1 5.00000000 sec TD0 1 ======== CHANNEL f1 ======== SFO1 400.1320007 MHz NUC1 1H P1 15.00 usec PLW1 12.50300026 W F2 - Processing parameters SI 32768 SF 400.1300097 MHz WDW EM SSB 0 LB 0.30 Hz GB 0 PC 1.00	F2 - Acquisition Parameters Date_ 20180427 Time 14.38 INSTRUM spect PROBHD 5 mm PABBO BB- PULPROG zg TD 48076 SOLVENT D2O NS 8 DS 2 SWH 6002.401 Hz FIDRES 0.124852 Hz AQ 4.0047307 sec RG 107 DW 83.300 usec DE 16.70 usec TE 298.2 K D1 5.00000000 sec TD0 1 ======== CHANNEL f1 ======== SFO1 400.1320007 MHz NUC1 1H P1 15.00 usec PLW1 12.50300026 W F2 - Processing parameters SI 32768 SF 400.1299645 MHz WDW EM SSB 0 LB 0.30 Hz GB 0 PC 1.00

^{13}C	F2 - Acquisition Parameters Date_ 20171015 Time 1.56 INSTRUM spect PROBHD 5 mm PABBO BB- PULPROG zgpg30 TD 65536 SOLVENT Acetic NS 4000 DS 4 SWH 22058.824 Hz FIDRES 0.336591 Hz AQ 1.4854827 sec RG 192.58 DW 22.667 usec DE 6.50 usec TE 298.2 K D1 2.00000000 sec D11 0.03000000 sec TD0 1 ======== CHANNEL f1 ======== SFO1 100.6223253 MHz NUC1 13C P1 9.80 usec PLW1 60.95399857 W ======== CHANNEL f2 ======== SFO2 400.1316005 MHz NUC2 1H CPDPRG[2 waltz16 PCPD2 90.00 usec PLW2 12.50300026 W PLW12 0.34731001 W PLW13 0.28132001 W F2 - Processing parameters SI 65536 SF 100.6126556 MHz WDW no SSB 0 LB 0 Hz GB 0 PC 1.40	F2 - Acquisition Parameters Date_ 20180428 Time 16.41 INSTRUM spect PROBHD 5 mm PABBO BB- PULPROG zgpg30 TD 65536 SOLVENT D2O NS 3000 DS 4 SWH 22058.824 Hz FIDRES 0.336591 Hz AQ 1.4854827 sec RG 42.64 DW 22.667 usec DE 6.50 usec TE 298.1 K D1 2.00000000 sec D11 0.03000000 sec TD0 1 ======== CHANNEL f1 ======== SFO1 100.6223253 MHz NUC1 13C P1 9.80 usec PLW1 60.95399857 W ======== CHANNEL f2 ======== SFO2 400.1316005 MHz NUC2 1H CPDPRG[2 waltz16 PCPD2 90.00 usec PLW2 12.50300026 W PLW12 0.34731001 W PLW13 0.28132001 W F2 - Processing parameters SI 65536 SF 100.6130962 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40

^{11}**B**	F2 - Acquisition Parameters Date_ 20171013 Time 6.56 INSTRUM spect PROBHD 5 mm PABBO BB- PULPROG zg TD 65536 SOLVENT Acetic NS 128 DS 4 SWH 25510.203 Hz FIDRES 0.389255 Hz AQ 1.2845056 sec RG 192.58 DW 19.600 usec DE 6.50 usec TE 298.1 K D1 1.00000000 sec TD0 1 ======== CHANNEL f1 ======== SFO1 128.3776052 MHz NUC1 11B P1 17.05 usec PLW1 11.69499969 W F2 - Processing parameters SI 32768 SF 128.3776052 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	F2 - Acquisition Parameters Date_ 20180428 Time 17.05 INSTRUM spect PROBHD 5 mm PABBO BB- PULPROG zg TD 65536 SOLVENT D2O NS 128 DS 4 SWH 25510.203 Hz FIDRES 0.389255 Hz AQ 1.2845056 sec RG 192.58 DW 19.600 usec DE 6.50 usec TE 298.1 K D1 1.00000000 sec TD0 1 ======== CHANNEL f1 ======== SFO1 128.3776052 MHz NUC1 11B P1 17.05 usec PLW1 11.69499969 W F2 - Processing parameters SI 32768 SF 128.3776052 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40

DEPT		F2 - Acquisition Parameters Date_ 20180427 Time 14.56 INSTRUM spect PROBHD 5 mm PABBO BB- PULPROG deptqgpsp TD 65536 SOLVENT D2O NS 256 DS 4 SWH 22058.824 Hz FIDRES 0.336591 Hz AQ 1.4854827 sec RG 192.58 DW 22.667 usec DE 6.50 usec TE 298.2 K CNST2 145.0000000 CNST12 1.5000000 D1 2.00000000 sec D2 0.00344828 sec D12 0.00002000 sec D16 0.00020000 sec TD0 1 ======== CHANNEL f1 ======== SFO1 100.6223258 MHz NUC1 13C P1 9.80 usec P13 2000.00 usec PLW0 0 W PLW1 60.95399857 W SPNAM[5] Crp60comp.4 SPOAL5 0.500 SPOFFS5 0 Hz SPW5 8.94419956 W ======== CHANNEL f2 ======== SFO2 400.1316005 MHz NUC2 1H CPDPRG[2 waltz16 P0 22.50 usec P3 15.00 usec P4 30.00 usec PCPD2 90.00 usec PLW2 12.50300026 W PLW12 0.34731001 W ====== GRADIENT CHANNEL ===== GPNAM[1] SMSQ10.32 GPNAM[2] SMSQ10.32 GPNAM[3] SMSQ10.32 GPZ1 31.00 % GPZ2 31.00 % GPZ3 31.00 % P16 1000.00 usec F2 - Processing parameters SI 65536 SF 100.6127690 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40

COSY

```
F2 - Acquisition Parameters
Date_           20171012
Time               12.39
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG         cosygpqf
TD                 2048
SOLVENT          Acetic
NS                    1
DS                    8
SWH             4807.692 Hz
FIDRES          2.347506 Hz
AQ             0.2129920 sec
RG               192.58
DW              104.000 usec
DE                6.50 usec
TE               298.1 K
D0            0.00000300 sec
D1            1.48689198 sec
D13           0.00000400 sec
D16           0.00020000 sec
IN0           0.00020800 sec

======== CHANNEL f1 ========
SFO1         400.1322007 MHz
NUC1                  1H
P0                15.00 usec
P1                15.00 usec
PLW1         12.50300026 W

====== GRADIENT CHANNEL =====
GPNAM[1]     SMSQ10.100
GPZ1              10.00 %
P16             1000.00 usec

F1 - Acquisition parameters
TD                   128
SFO1            400.1322 MHz
FIDRES         75.120193 Hz
SW                12.015 ppm
FnMODE               QF

F2 - Processing parameters
SI                  1024
SF           400.1300096 MHz
WDW                 SINE
SSB                    0
LB                     0 Hz
GB                     0
PC                  1.40

F1 - Processing parameters
SI                  1024
MC2                   QF
SF           400.1300090 MHz
WDW                 SINE
SSB                    0
LB                     0 Hz
GB                     0
```

```
F2 - Acquisition Parameters
Date_           20180427
Time               14.58
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG         cosygpqf
TD                 2048
SOLVENT             D2O
NS                    1
DS                    8
SWH             4807.692 Hz
FIDRES          2.347506 Hz
AQ             0.2129920 sec
RG               192.58
DW              104.000 usec
DE                6.50 usec
TE               298.0 K
D0            0.00000300 sec
D1            1.48689198 sec
D13           0.00000400 sec
D16           0.00020000 sec
IN0           0.00020800 sec

======== CHANNEL f1 ========
SFO1         400.1322007 MHz
NUC1                  1H
P0                15.00 usec
P1                15.00 usec
PLW1         12.50300026 W

====== GRADIENT CHANNEL =====
GPNAM[1]     SMSQ10.100
GPZ1              10.00 %
P16             1000.00 usec

F1 - Acquisition parameters
TD                   128
SFO1            400.1322 MHz
FIDRES         75.120193 Hz
SW                12.015 ppm
FnMODE               QF

F2 - Processing parameters
SI                  1024
SF           400.1299640 MHz
WDW                 SINE
SSB                    0
LB                     0 Hz
GB                     0
PC                  1.40

F1 - Processing parameters
SI                  1024
MC2                   QF
SF           400.1299640 MHz
WDW                 SINE
SSB                    0
LB                     0 Hz
GB                     0
```

HSQC

```
F2 - Acquisition Parameters
Date_            20171012
Time                13.02
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG  hsqcetgpsisp2.2
TD                  2048
SOLVENT           Acetic
NS                     2
DS                    16
SWH             5341.880 Hz
FIDRES          2.608340 Hz
AQ             0.1916928 sec
RG                192.58
DW                93.600 usec
DE                 6.50 usec
TE                298.3 K
CNST2         145.0000000
CNST17         -0.5000000
D0             0.00000300 sec
D1             1.50000000 sec
D4             0.00172414 sec
D11            0.03000000 sec
D16            0.00020000 sec
D24            0.00086207 sec
IN0            0.00003000 sec

======== CHANNEL f1 ========
SFO1          400.1324057 MHz
NUC1                   1H
P1                  15.00 usec
P2                  30.00 usec
P28               1000.00 usec
PLW1          12.50300026 W

======== CHANNEL f2 ========
SFO2          100.6202713 MHz
NUC2                  13C
CPDPRG[2 bi_p5m4sp_4sp.2
P3                   9.80 usec
P14                500.00 usec
P24               2000.00 usec
P63               1500.00 usec
PLW0                    0 W
PLW2          60.95399857 W
PLW12          0.91469002 W
SPNAM[3] Crp60,0.5,20.1
SPOAL3               0.500
SPOFFS3                 0 Hz
SPW3           8.94419956 W
SPNAM[7]    Crp60comp.4
SPOAL7               0.500
SPOFFS7                 0 Hz
SPW7           8.94419956 W
SPNAM[14 Crp32,1.5,20.2
SPOAL14              0.500
SPOFFS14                0 Hz
SPW14          3.81620002 W
SPNAM[31 Crp32,1.5,20.2
SPOAL31              0.500
SPOFFS31                0 Hz
SPW31          0.95405000 W

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPNAM[2]      SMSQ10.100
GPNAM[3]      SMSQ10.100
GPNAM[4]      SMSQ10.100
GPZ1                80.00 %
GPZ2                20.10 %
GPZ3                11.00 %
GPZ4                -5.00 %
P16               1000.00 usec
P19                600.00 usec

F1 - Acquisition parameters
TD                    256
SFO1            100.6203 MHz
FIDRES        130.208328 Hz
SW               165.639 ppm
FnMODE    Echo-Antiecho

F2 - Processing parameters
SI                   1024
SF            400.1300087 MHz
WDW                 QSINE
SSB                     2
LB                      0 Hz
GB                      0
PC                   1.40

F1 - Processing parameters
SI                   1024
MC2        echo-antiecho
SF            100.6126505 MHz
WDW                 QSINE
SSB                     2
LB                      0 Hz
GB                      0
```

```
F2 - Acquisition Parameters
Date_            20180428
Time                16.44
INSTRUM             spect
PROBHD   5 mm PABBO BB-
PULPROG  hsqcetgpsisp2.2
TD                  2048
SOLVENT              D2O
NS                     2
DS                    16
SWH             5341.880 Hz
FIDRES          2.608340 Hz
AQ             0.1916928 sec
RG                192.58
DW                93.600 usec
DE                 6.50 usec
TE                298.0 K
CNST2         145.0000000
CNST17         -0.5000000
D0             0.00000300 sec
D1             1.50000000 sec
D4             0.00172414 sec
D11            0.03000000 sec
D16            0.00020000 sec
D24            0.00086207 sec
IN0            0.00003000 sec

======== CHANNEL f1 ========
SFO1          400.1324057 MHz
NUC1                   1H
P1                  15.00 usec
P2                  30.00 usec
P28               1000.00 usec
PLW1          12.50300026 W

======== CHANNEL f2 ========
SFO2          100.6202713 MHz
NUC2                  13C
CPDPRG[2 bi_p5m4sp_4sp.2
P3                   9.80 usec
P14                500.00 usec
P24               2000.00 usec
P63               1500.00 usec
PLW0                    0 W
PLW2          60.95399857 W
PLW12          0.91469002 W
SPNAM[3] Crp60,0.5,20.1
SPOAL3               0.500
SPOFFS3                 0 Hz
SPW3           8.94419956 W
SPNAM[7]    Crp60comp.4
SPOAL7               0.500
SPOFFS7                 0 Hz
SPW7           8.94419956 W
SPNAM[14 Crp32,1.5,20.2
SPOAL14              0.500
SPOFFS14                0 Hz
SPW14          3.81620002 W
SPNAM[31 Crp32,1.5,20.2
SPOAL31              0.500
SPOFFS31                0 Hz
SPW31          0.95405000 W

====== GRADIENT CHANNEL =====
GPNAM[1]      SMSQ10.100
GPNAM[2]      SMSQ10.100
GPNAM[3]      SMSQ10.100
GPNAM[4]      SMSQ10.100
GPZ1                80.00 %
GPZ2                20.10 %
GPZ3                11.00 %
GPZ4                -5.00 %
P16               1000.00 usec
P19                600.00 usec

F1 - Acquisition parameters
TD                    256
SFO1            100.6203 MHz
FIDRES        130.208328 Hz
SW               165.639 ppm
FnMODE    Echo-Antiecho

F2 - Processing parameters
SI                   1024
SF            400.1299646 MHz
WDW                 QSINE
SSB                     2
LB                      0 Hz
GB                      0
PC                   1.40

F1 - Processing parameters
SI                   1024
MC2        echo-antiecho
SF            100.6130928 MHz
WDW                 QSINE
SSB                     2
LB                      0 Hz
GB                      0
```