

Supplementary Materials

Novel oligonucleotides with enhanced cellular uptake

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CONTENT

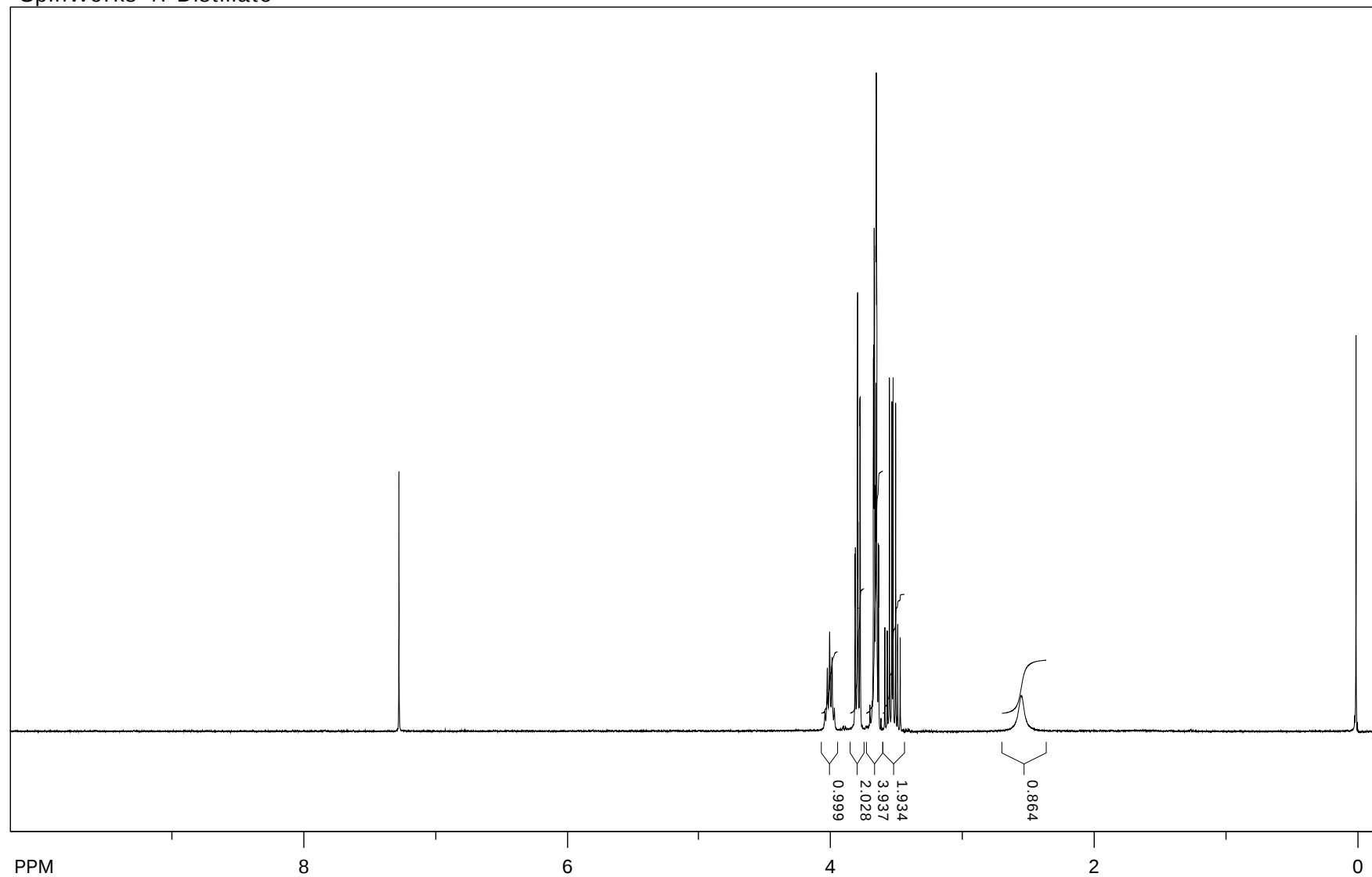
NMR Spectra

Differential Melting Curves of oligonucleotide duplexes

Fluorescent Images of incubation of oligonucleotides with A172 cells

^1H NMR of Bromo-3-(2-chloroethoxy)propan-2-ol (**1**) in CDCl_3

SpinWorks 4: Distillate

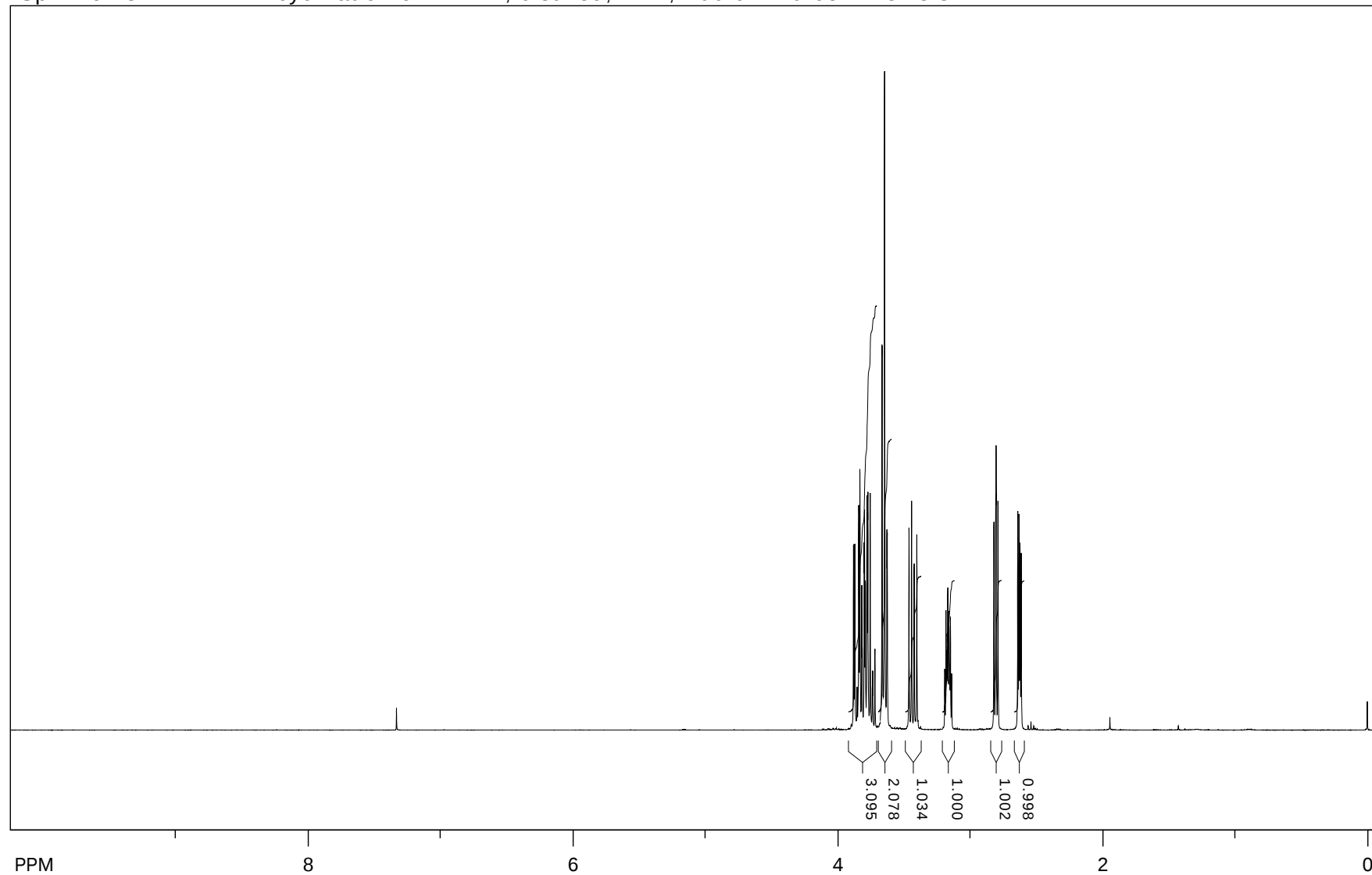


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number of scans: 8

freq. of 0 ppm: 299.393400 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

^1H NMR of 2-((2-chloroethoxy)methyl)oxirane (**2**) in CDCl_3

SpinWorks 4: MY X 14 cyclization of MYX12, distilled, fr. 2, 100 ul in 0.65 ml CDCl_3

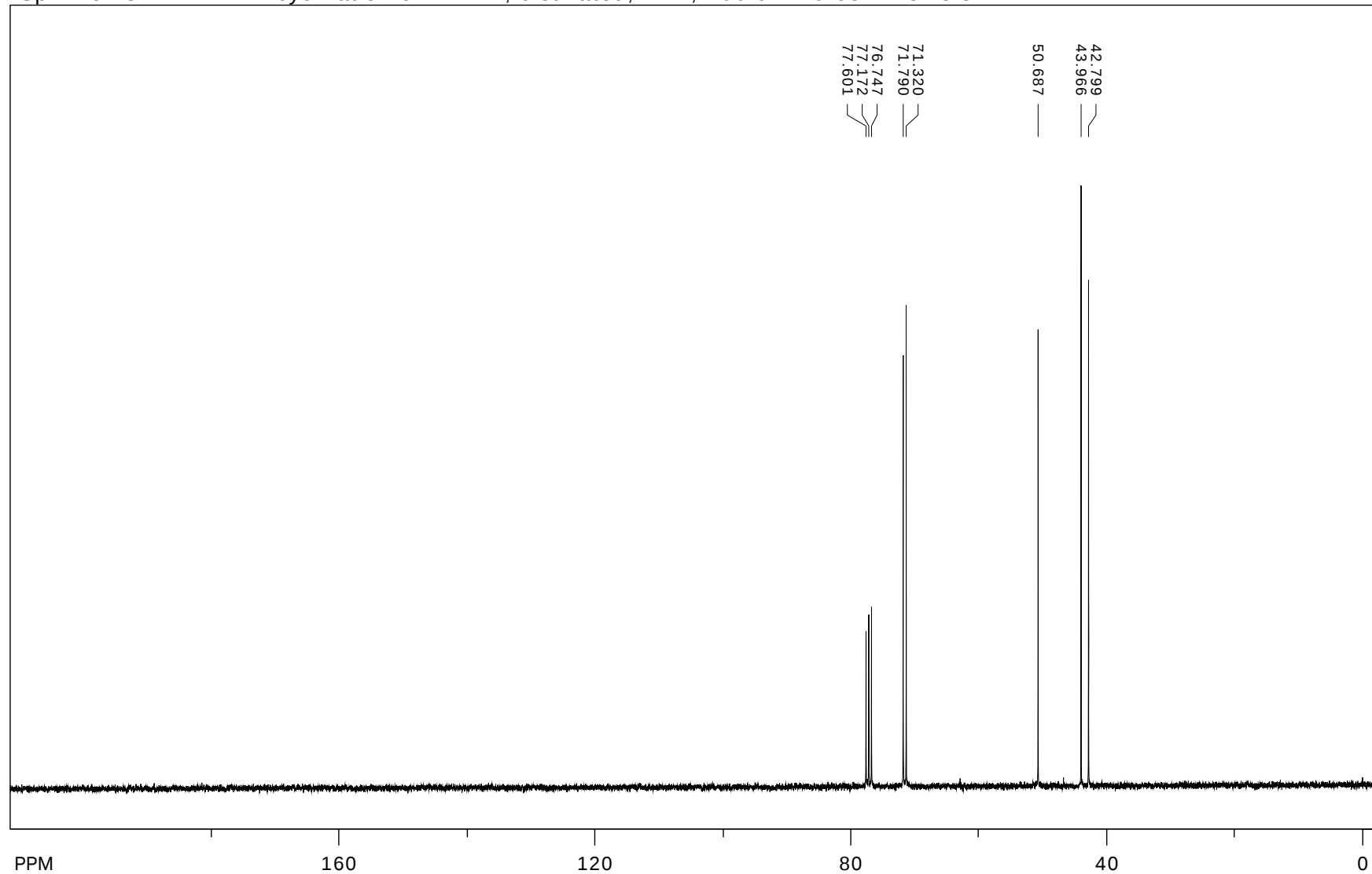


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number of scans: 19

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LB: 0.300 GF: 0.0000

^{13}C NMR of 2-((2-chloroethoxy)methyl)oxirane (**2**) in CDCl_3

SpinWorks 4: MY X 14 cyclization of MYX12, distilled, fr. 2, 100 ul in 0.65 ml CDCl_3

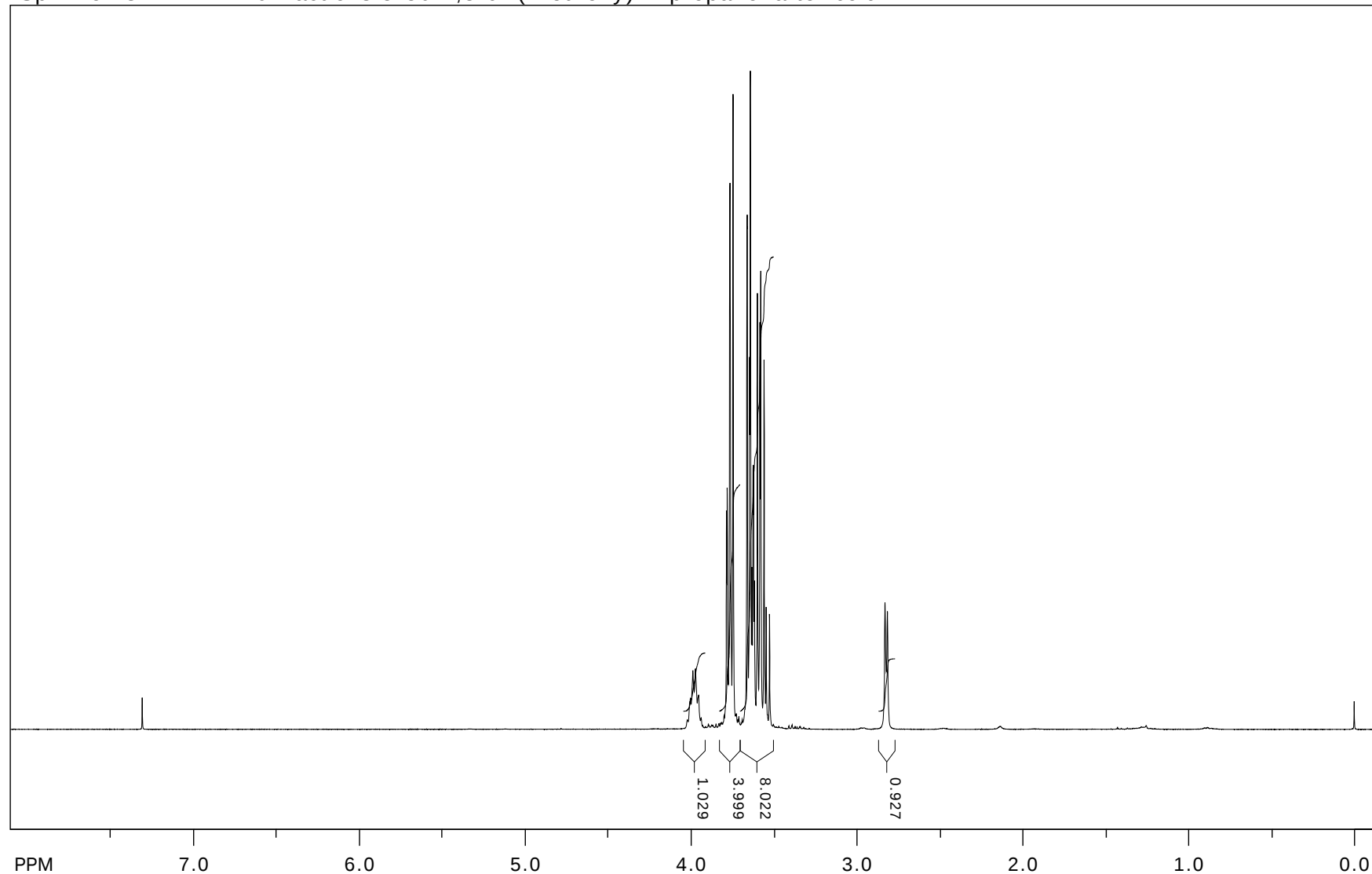


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width: 17985.61 Hz = 238.8843 ppm = 0.166672 Hz/pt
number of scans: 129

freq. of 0 ppm: 75.282530 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

^1H NMR of 1,3-Bis(2-chloroethoxy)propan-2-ol (**3**) in CDCl_3

SpinWorks 4: MY X 20 fractions 5-50 1,3-di-(2-ethoxy)-2-propanol after column

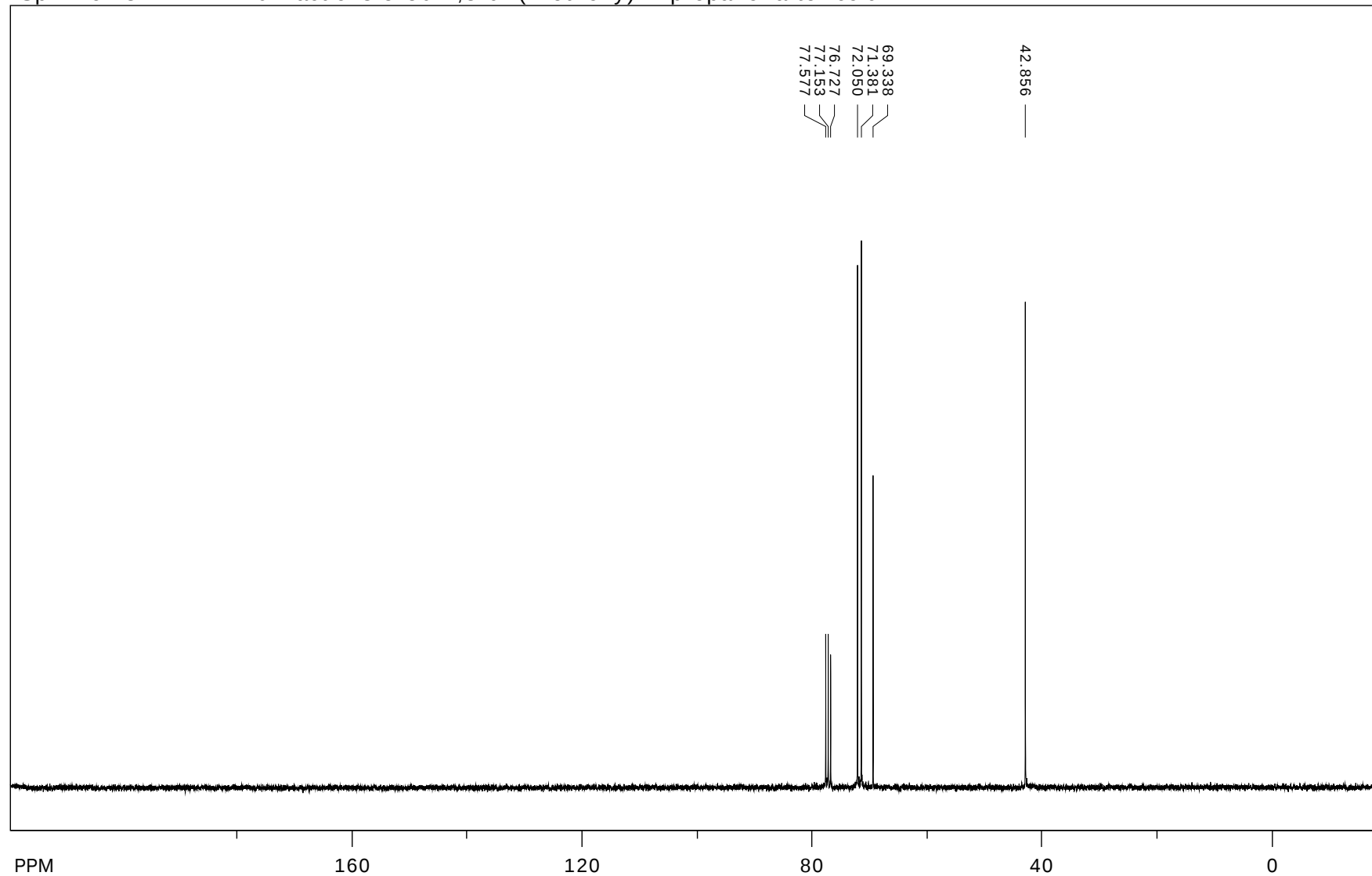


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number of scans: 8

freq. of 0 ppm: 299.393389 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

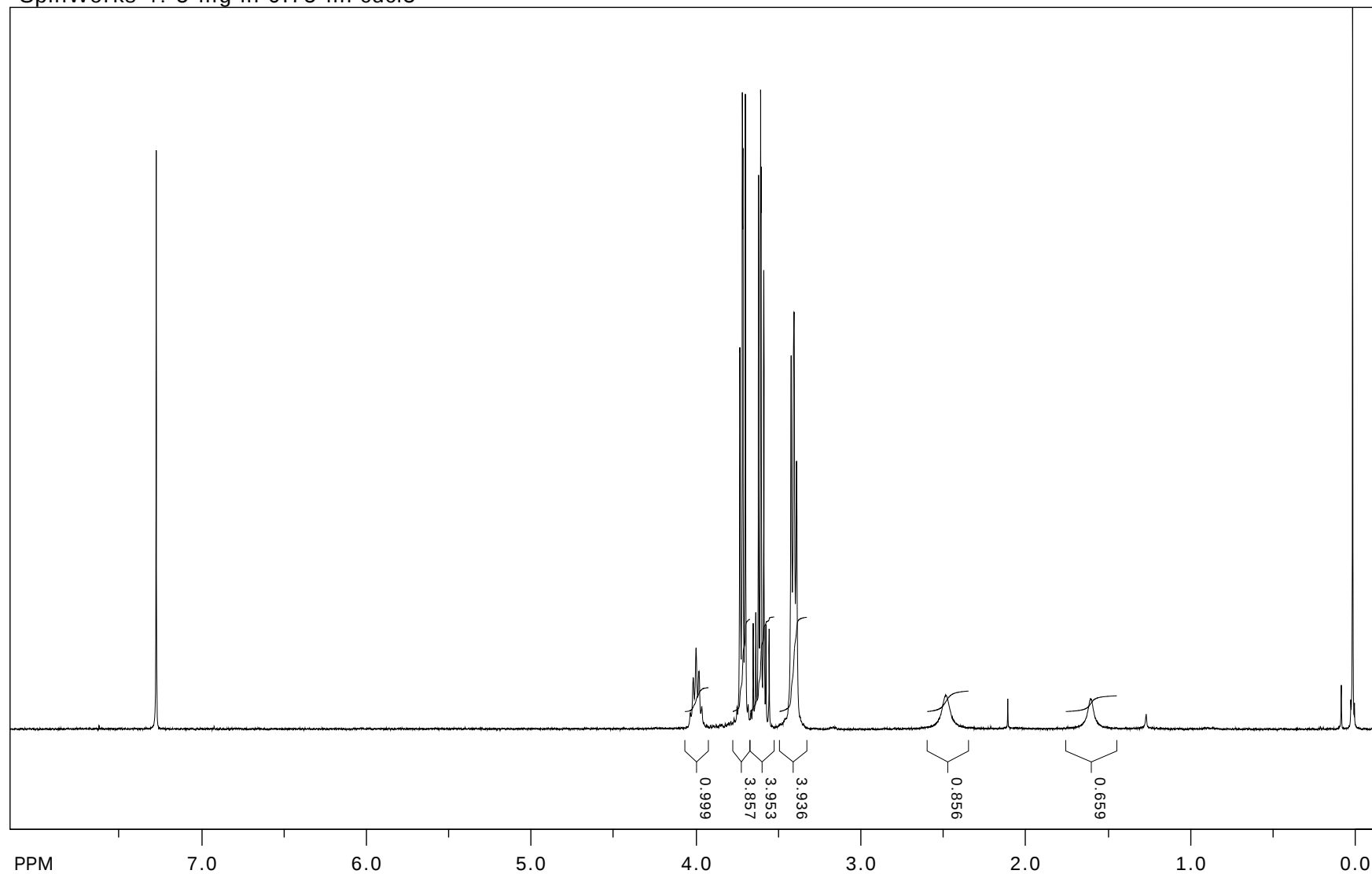
^{13}C NMR of 1,3-Bis(2-chloroethoxy)propan-2-ol (**3**) in CDCl_3

SpinWorks 4: MY X 20 fractions 5-50 1,3-di-(2-ethoxy)-2-propanol after column



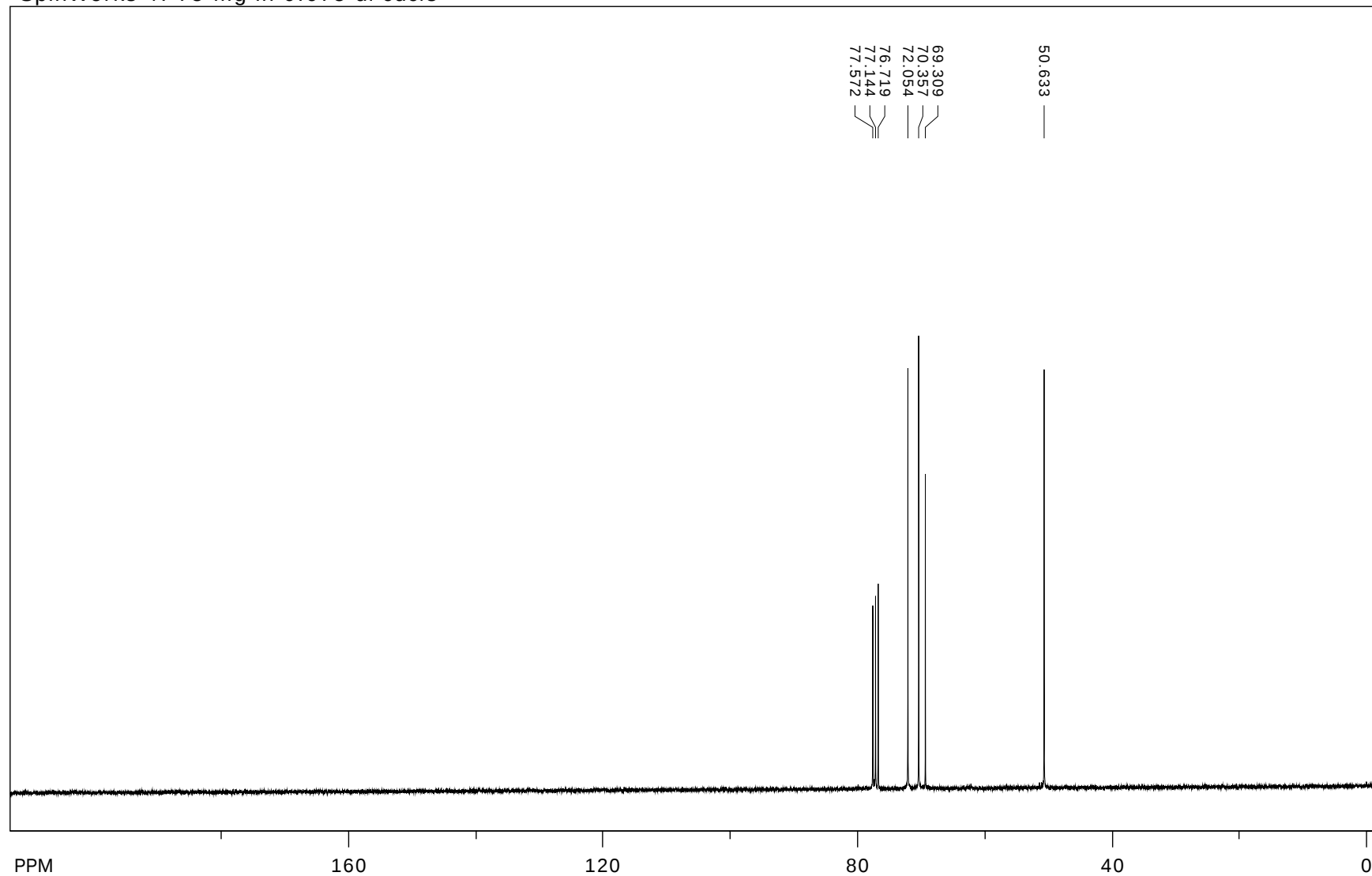
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number of scans: 120

freq. of 0 ppm: 75.282530 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

¹H NMR of 1,3-Bis(2-azidoethoxy)propan-2-ol (5)SpinWorks 4: 5 mg in 0.75 ml cdcl₃

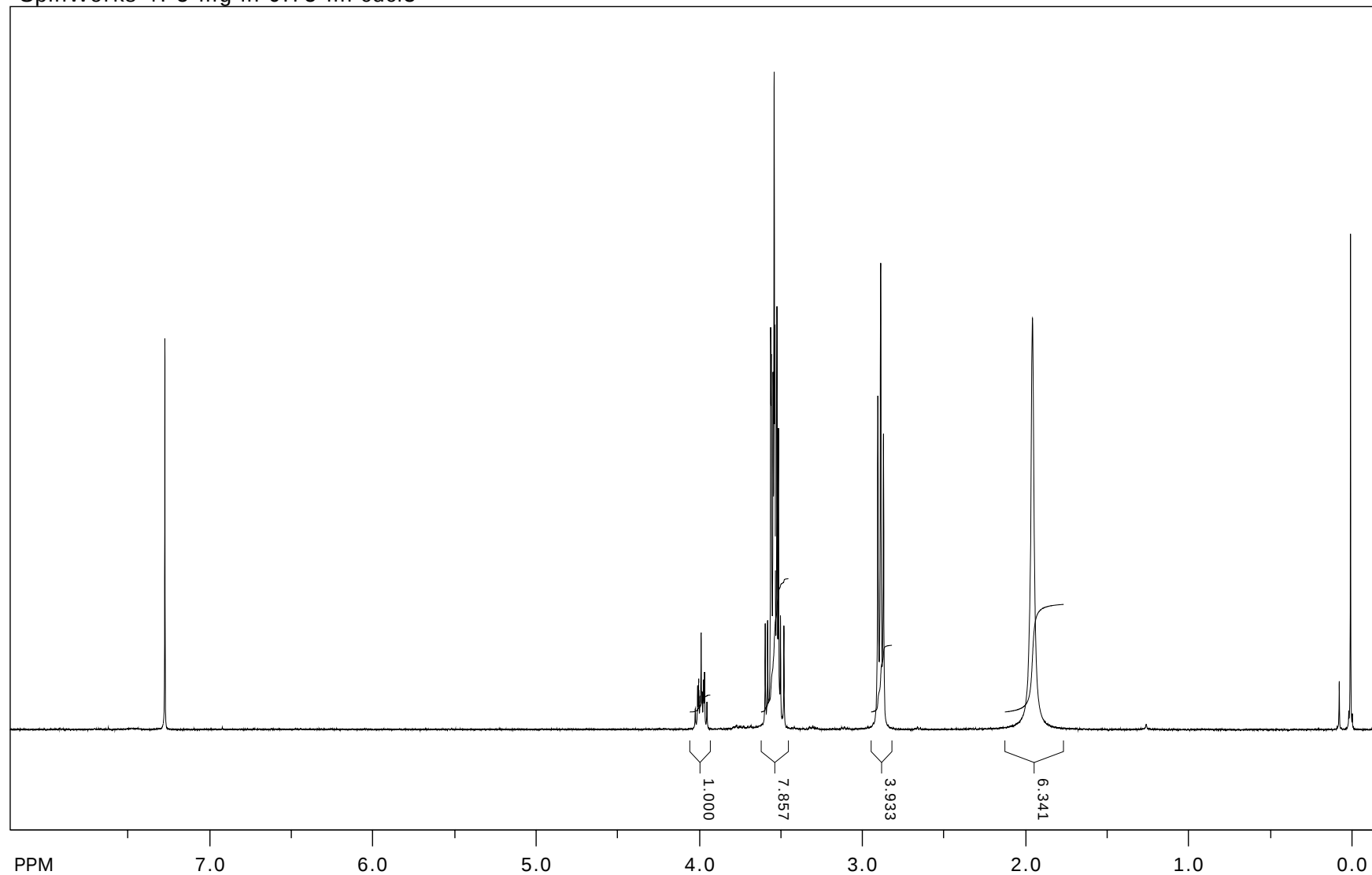
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number of scans: 32

freq. of 0 ppm: 299.393400 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

^{13}C NMR of 1,3-Bis(2-azidoethoxy)propan-2-ol (5)SpinWorks 4: 75 mg in 0.675 ul cdCl_3 

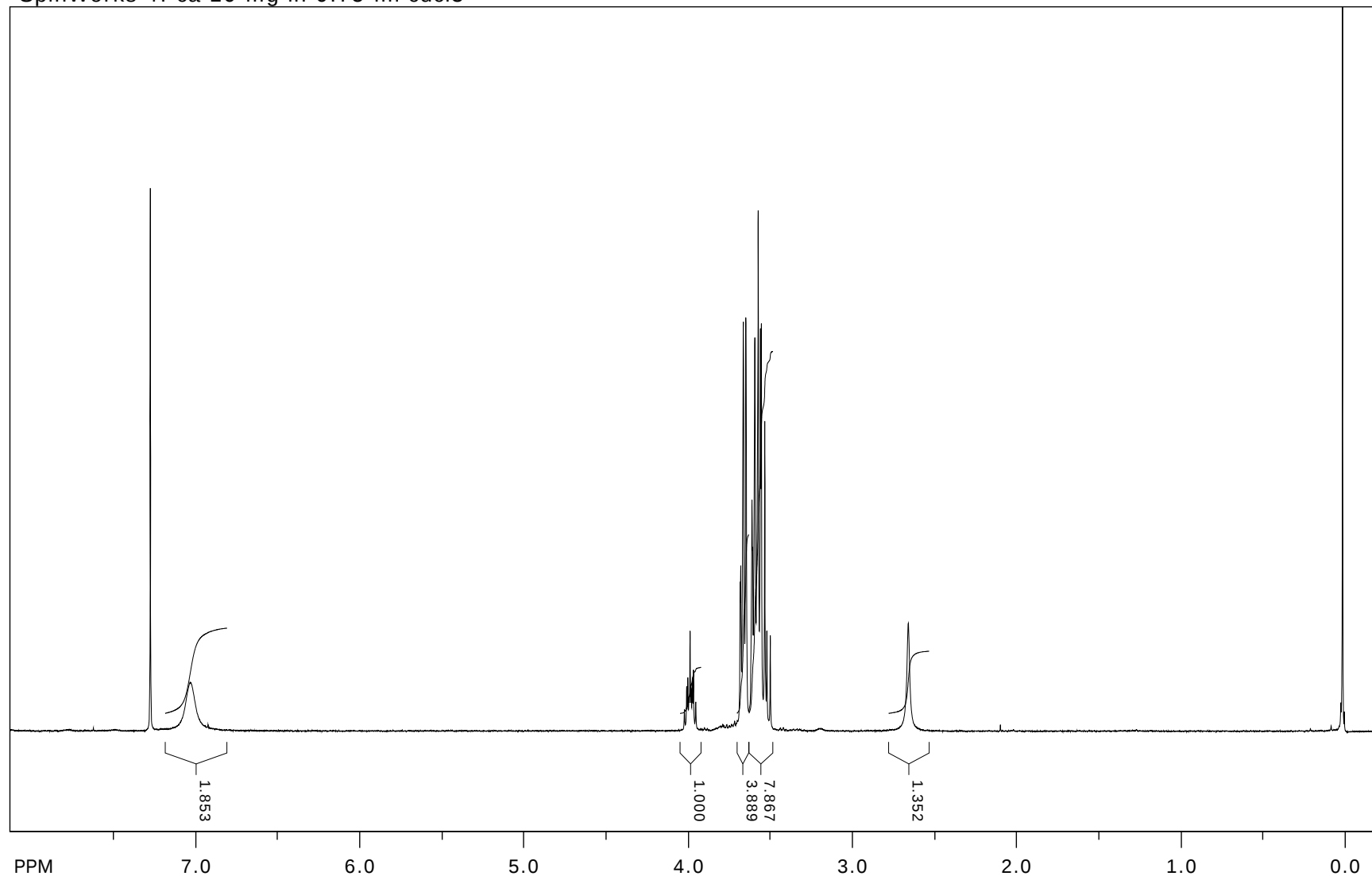
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width: 17985.61 Hz = 238.8843 ppm = 0.166672 Hz/pt
number of scans: 657

freq. of 0 ppm: 75.282530 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

¹H NMR of 1,3-Bis(2-aminoethoxy)propan-2-ol (**6**)SpinWorks 4: 5 mg in 0.75 ml cdcl₃

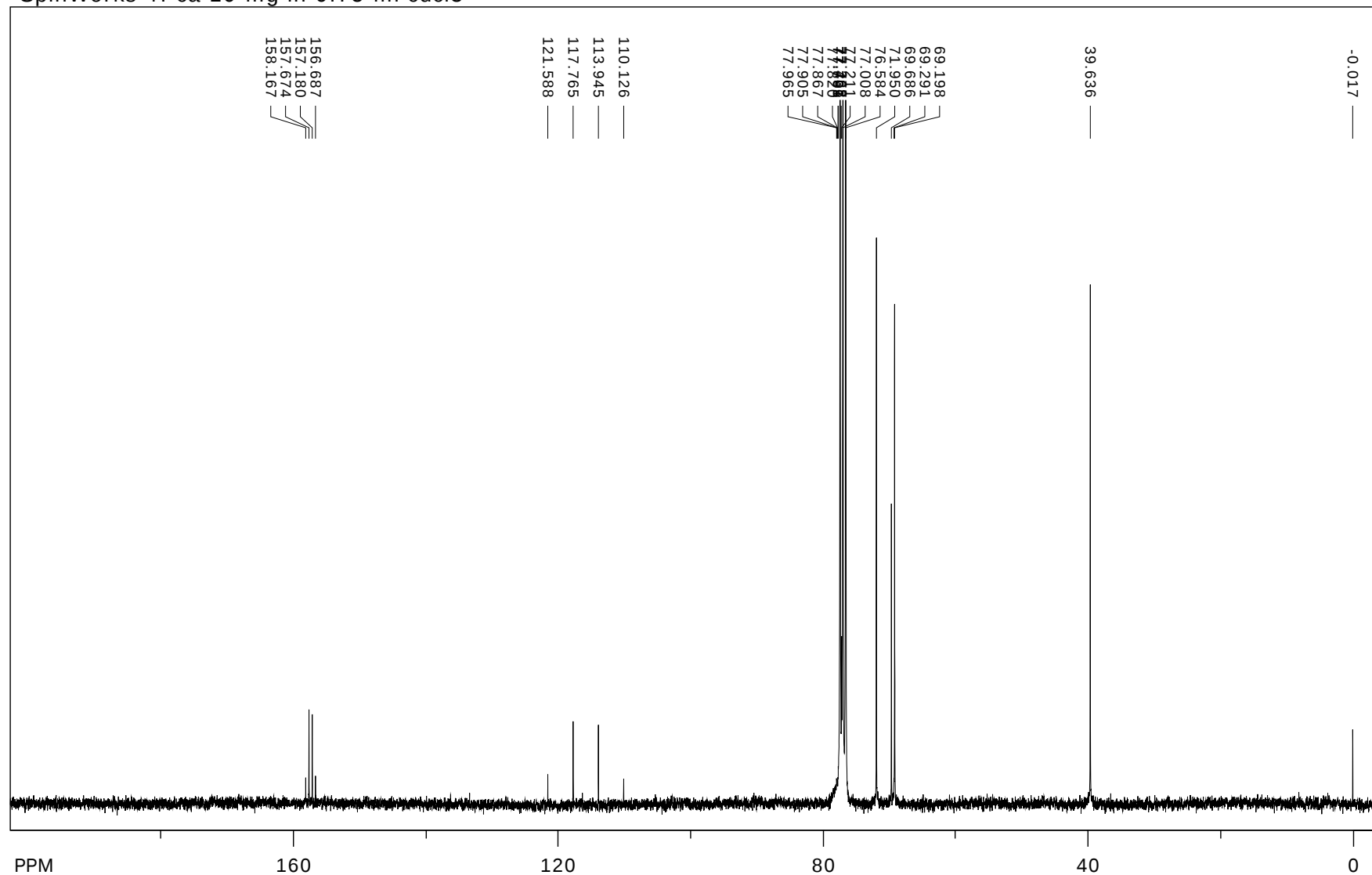
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transmitter freq.: 299.395419 MHz
time domain size: 31474 points
width: 4496.40 Hz = 15.0183 ppm = 0.142861 Hz/pt
number of scans: 17

freq. of 0 ppm: 299.393400 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

¹H NMR of 1,3-Bis(2-((trifluoroacetyl)amino)ethoxy)propan-2-ol (7)SpinWorks 4: ca 10 mg in 0.75 ml cdcl₃

file: ...Y141126_Sleeve1_diTFA_rm48h\10\fid expt: <zg30>
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time domain size: 31474 points
width: 4496.40 Hz = 15.0183 ppm = 0.142861 Hz/pt
number of scans: 73

freq. of 0 ppm: 299.393400 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

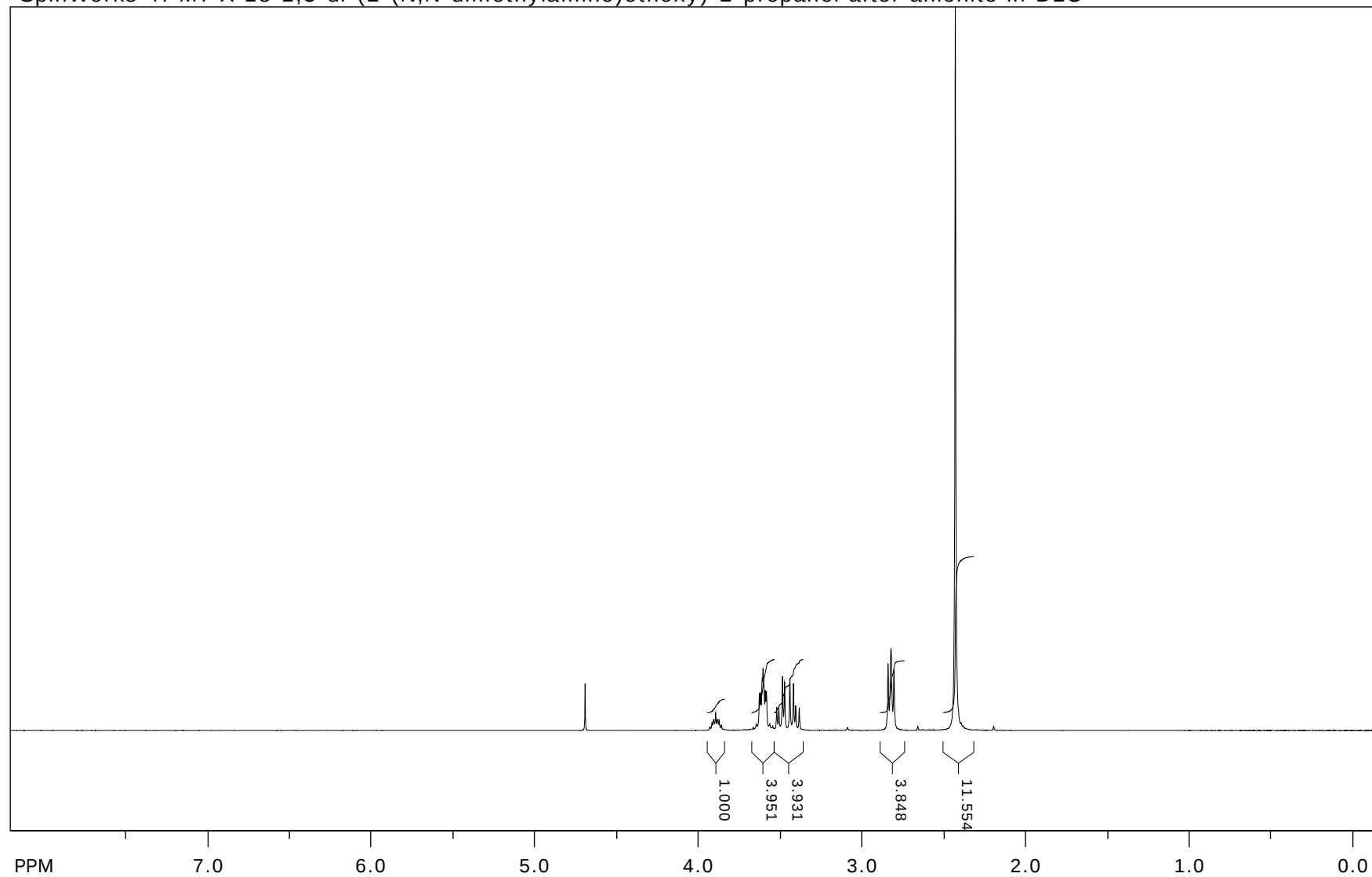
^{13}C NMR of 1,3-Bis(2-((trifluoroacetyl)amino)ethoxy)propan-2-ol (7)SpinWorks 4: ca 10 mg in 0.75 ml cdCl_3 

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number of scans: 20993

freq. of 0 ppm: 75.282530 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

¹H NMR of 1,3-Bis(2-(dimethylamino)ethoxy)propan-2-ol (**8**)

SpinWorks 4: MY X 18 1,3-di-(2-(N,N-dimethylamino)ethoxy)-2-propanol after anionite in D2O

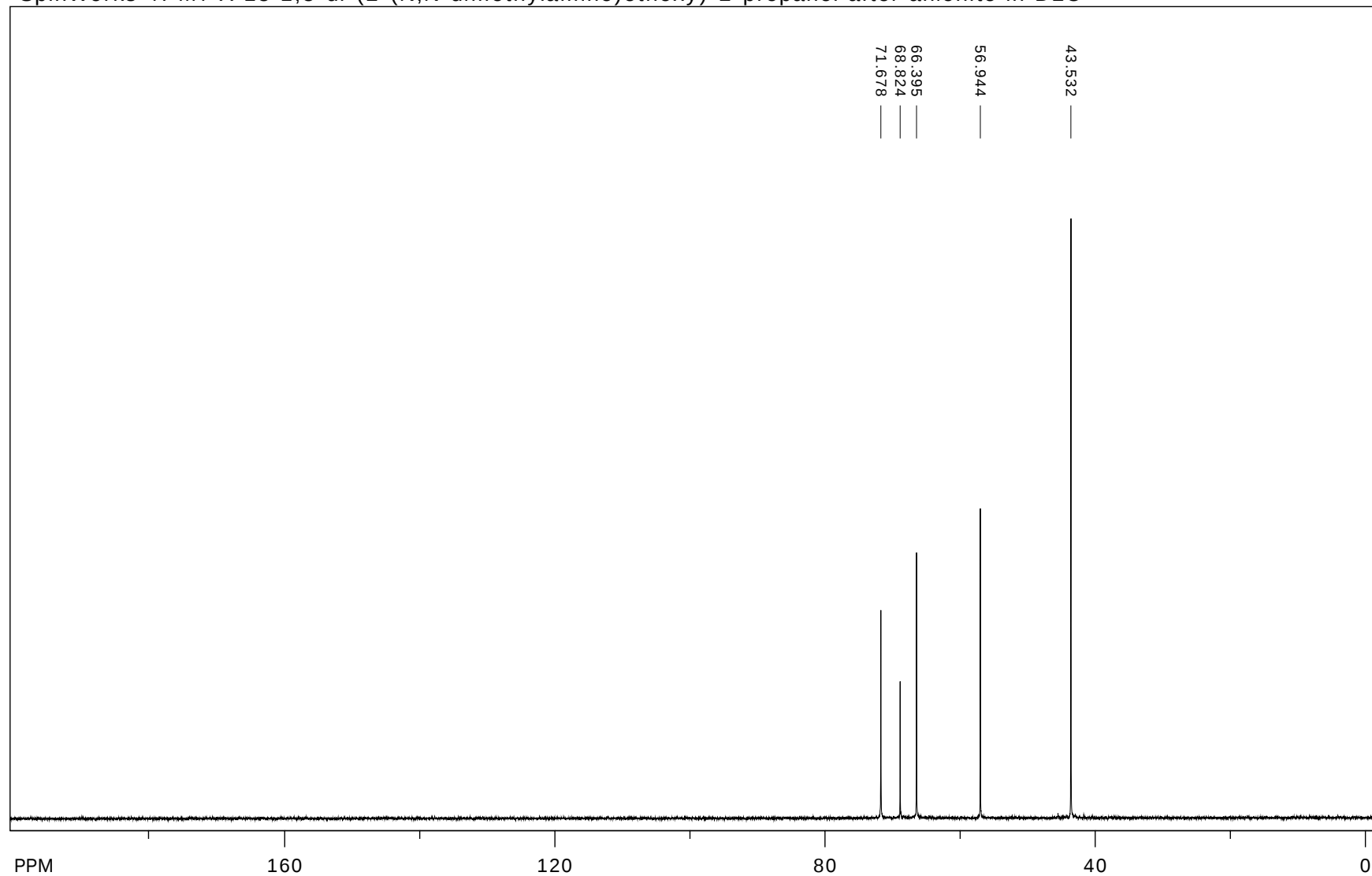


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number of scans: 16

freq. of 0 ppm: 299.393400 MHz
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

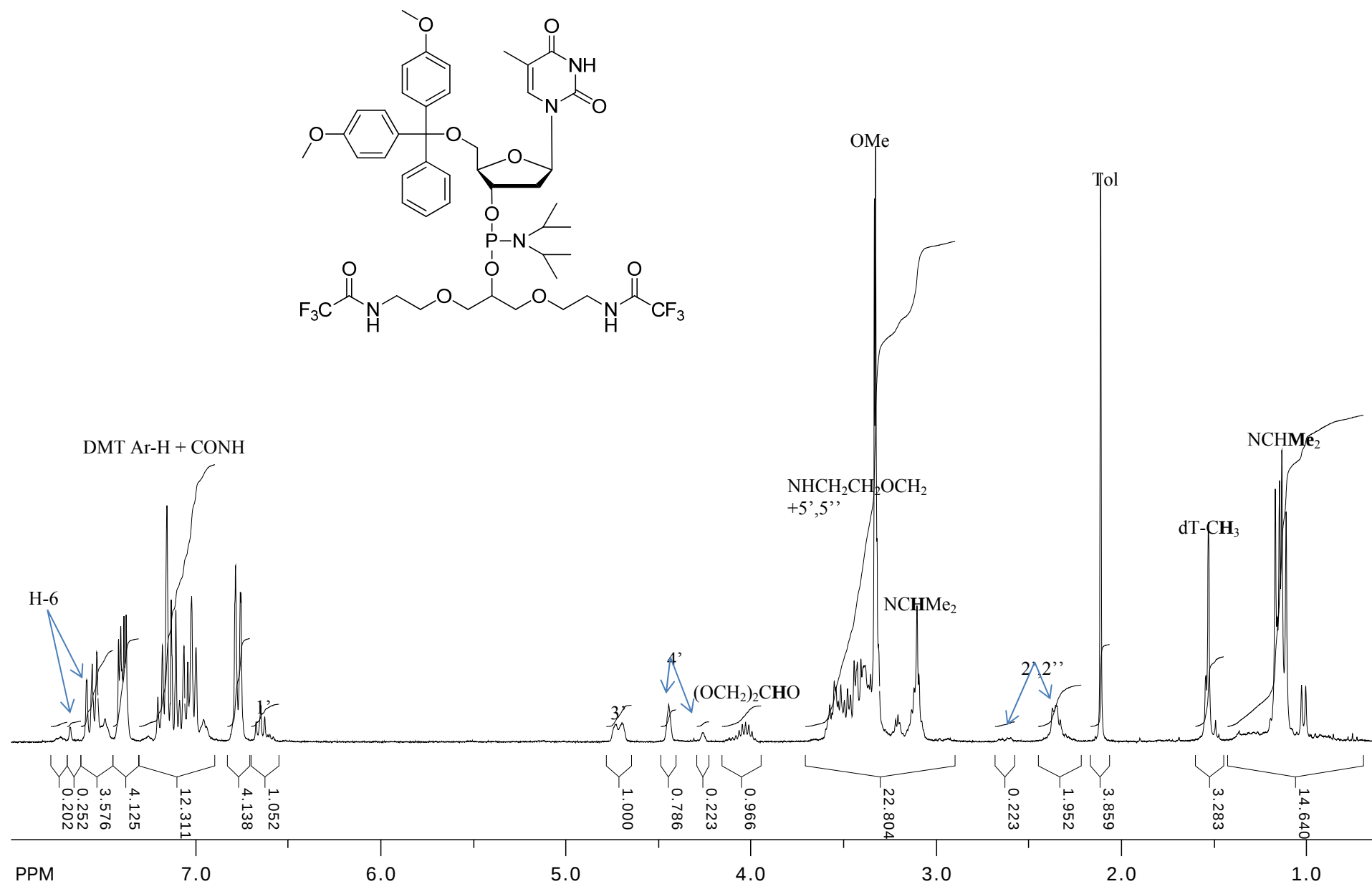
^{13}C NMR of 1,3-Bis(2-(dimethylamino)ethoxy)propan-2-ol (**8**)

SpinWorks 4: MY X 18 1,3-di-(2-(N,N-dimethylamino)ethoxy)-2-propanol after anionite in D2O



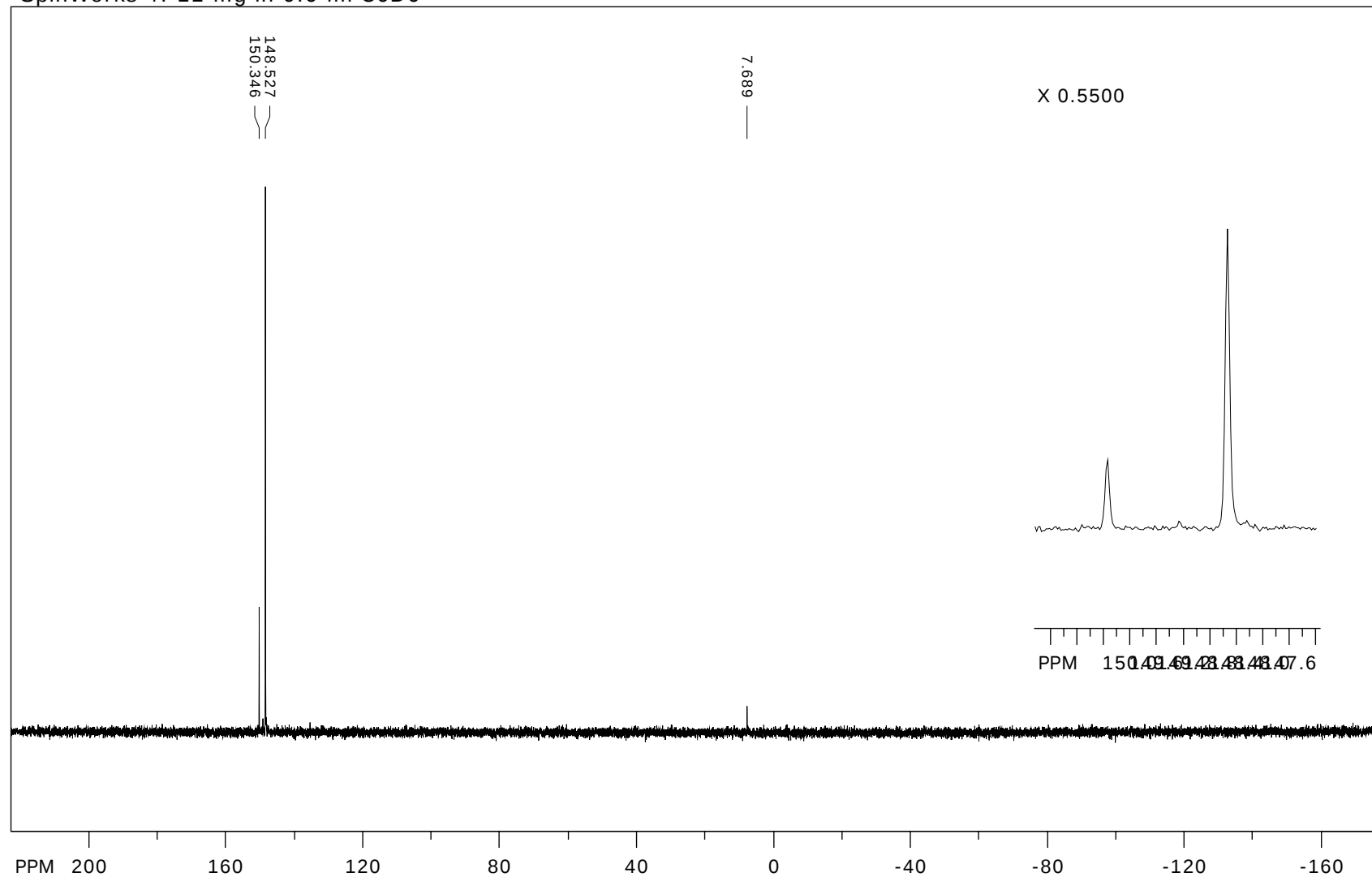
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transmitter freq.: 75.290059 MHz
time domain size: 107910 points
width: 17985.61 Hz = 238.8843 ppm = 0.166672 Hz/pt
number of scans: 660

freq. of 0 ppm: 75.282530 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

¹H NMR with assignments of Phosphoroamidite **12**

^{31}P (^1H decoupled) of Phosphoroamidite **12**

SpinWorks 4: 11 mg in 0.6 ml C₆D₆

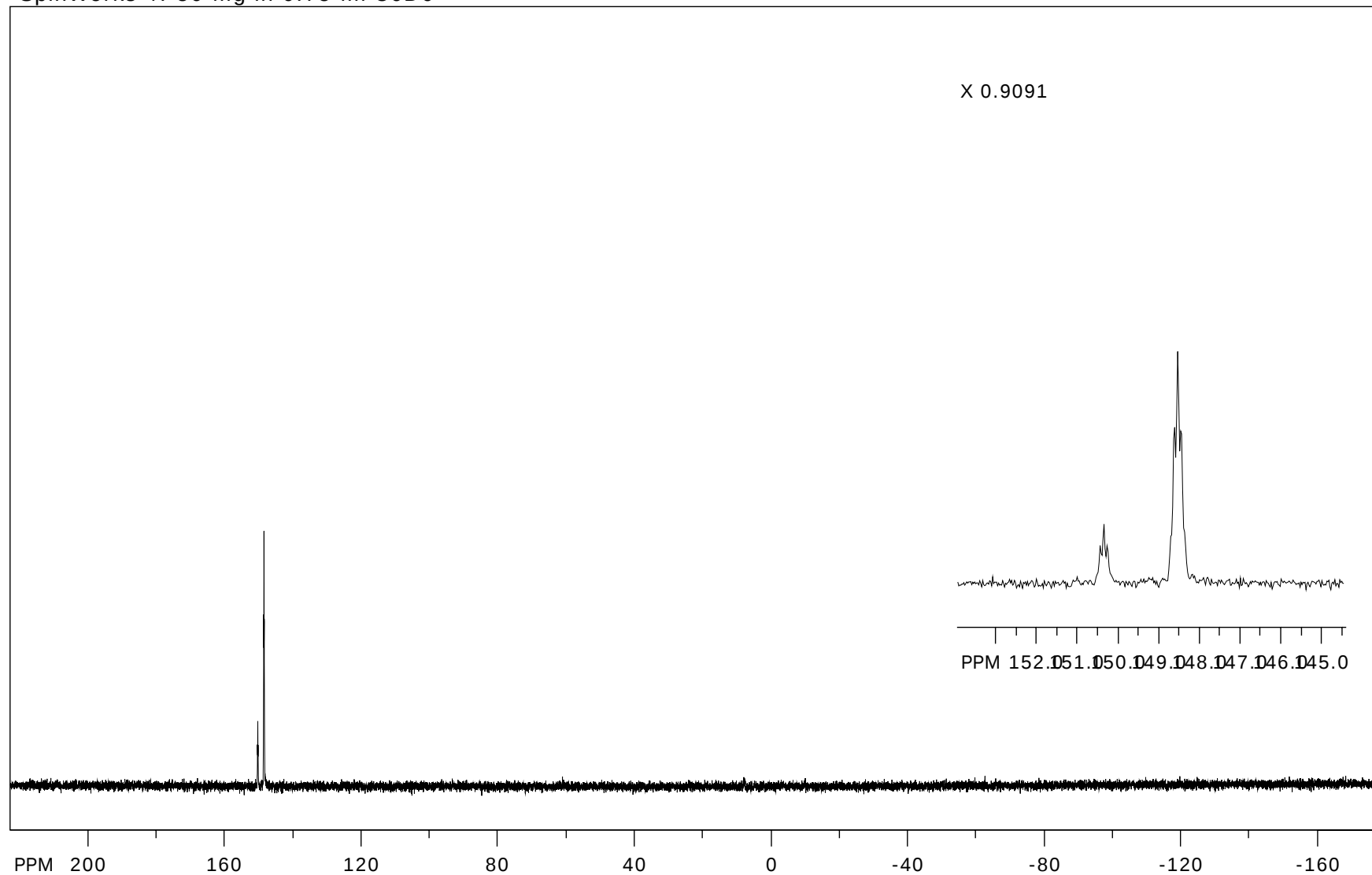


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transmitter freq.: 121.199081 MHz
time domain size: 136248 points
width: 48661.80 Hz = 401.5030 ppm = 0.357156 Hz/pt
number of scans: 365

freq. of 0 ppm: 121.196394 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

^{31}P , (^1H coupled) of Phosphoroamidite **12**

SpinWorks 4: 50 mg in 0.75 ml C₆D₆

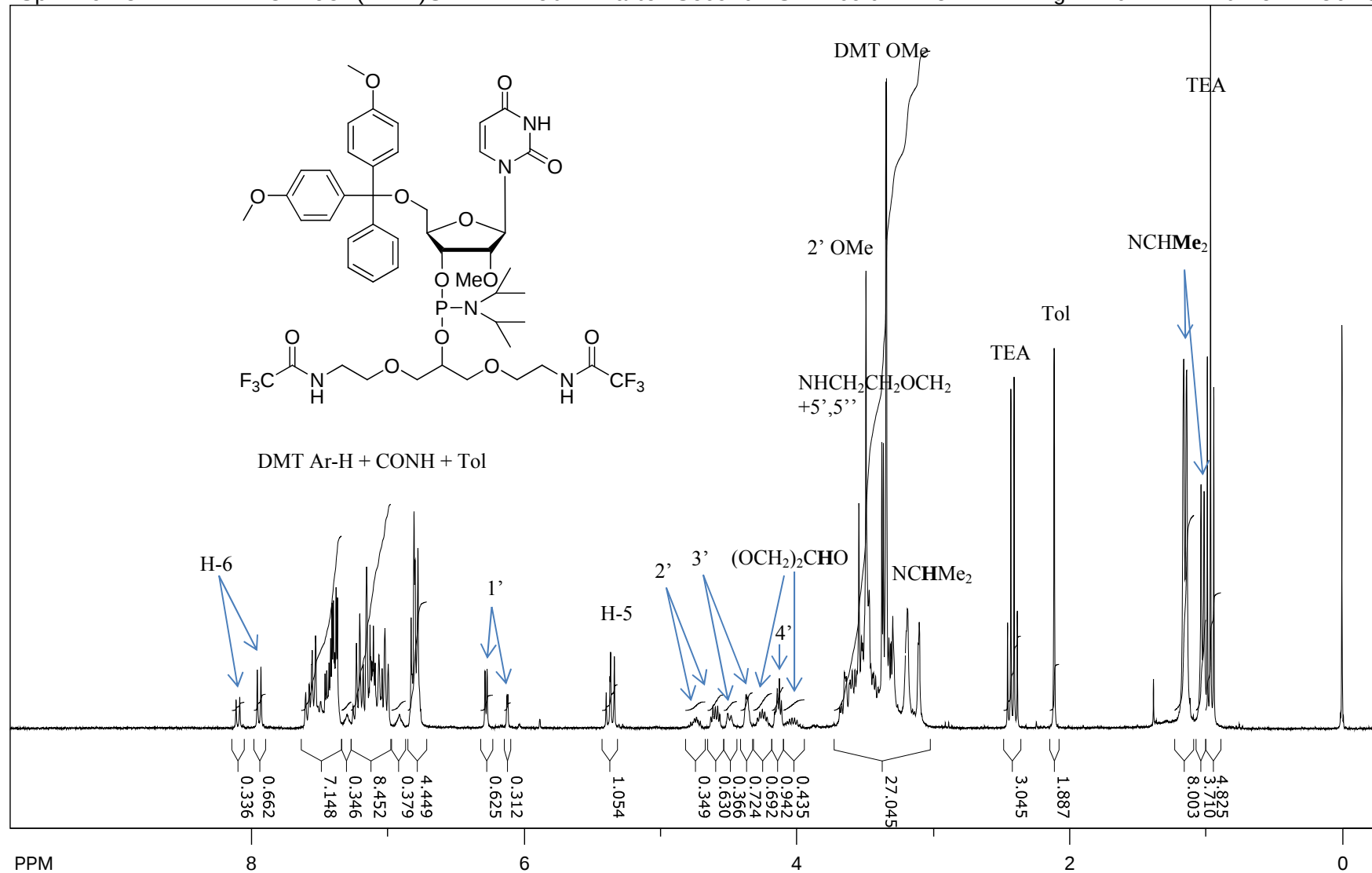


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time domain size: 136248 points
width: 48661.80 Hz = 401.5030 ppm = 0.357156 Hz/pt
number of scans: 625

freq. of 0 ppm: 121.196394 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

¹H NMR with assignments of Phosphoroamidite **14**

SpinWorks 4: DMT-2'-O-MeUP(IP2N)Siv1 IBY150122 after Second LS RP column f8-11 21 mg + 1ul TEA in 0.75 ml C6D6

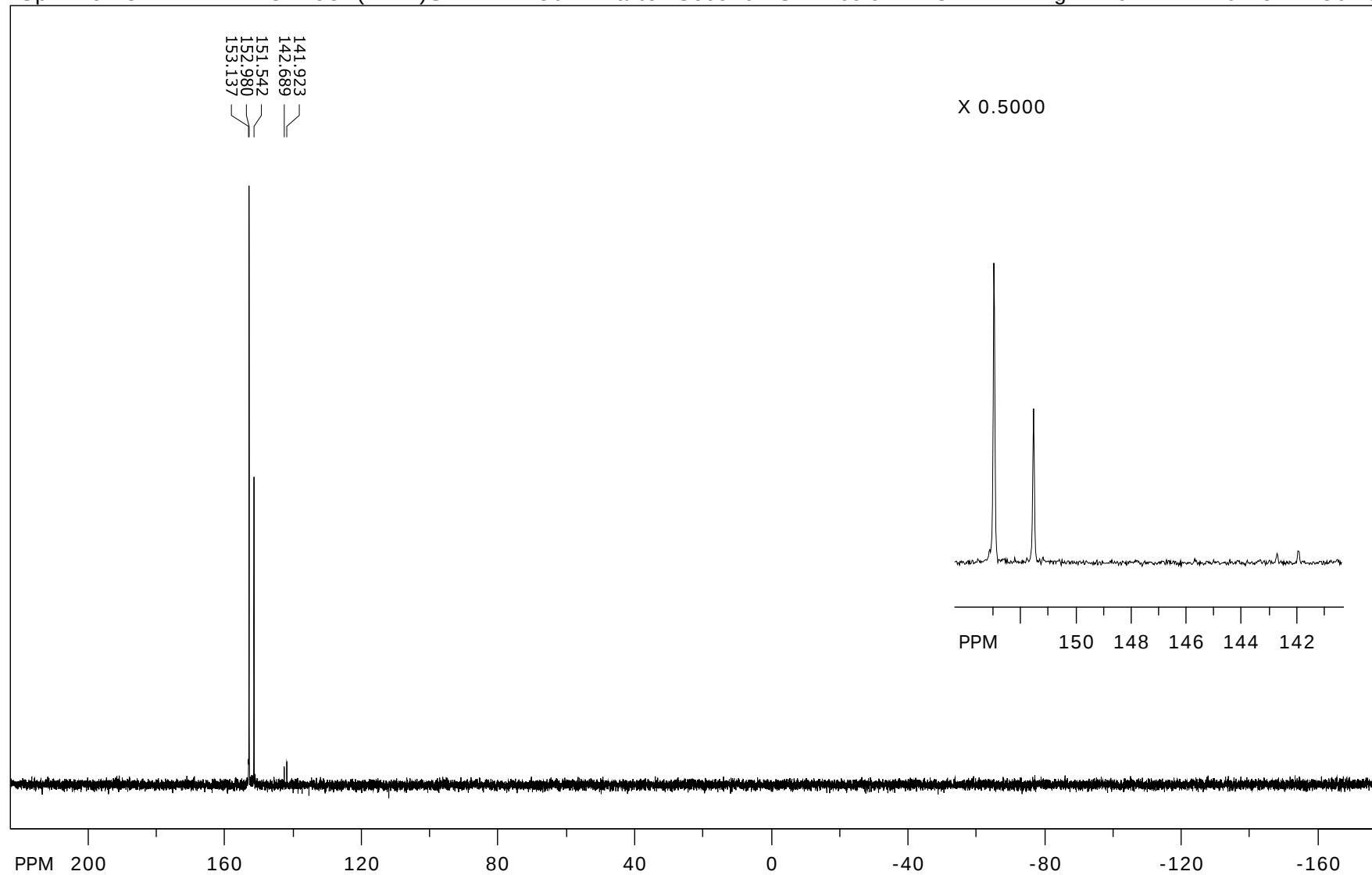


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 number of scans: 32

freq. of 0 ppm: 299.393431 MHz
 processed size: 32768 complex points
 LB: 0.300 GF: 0.0000

³¹P NMR (¹H decoupled) of Phosphoroamidite **14**

SpinWorks 4: DMT-2'-O-MeUP(IP2N)Slv1 IBY150122 after Second LS RP column f8-11 21 mg + 1ul TEA in 0.75 ml C6D6

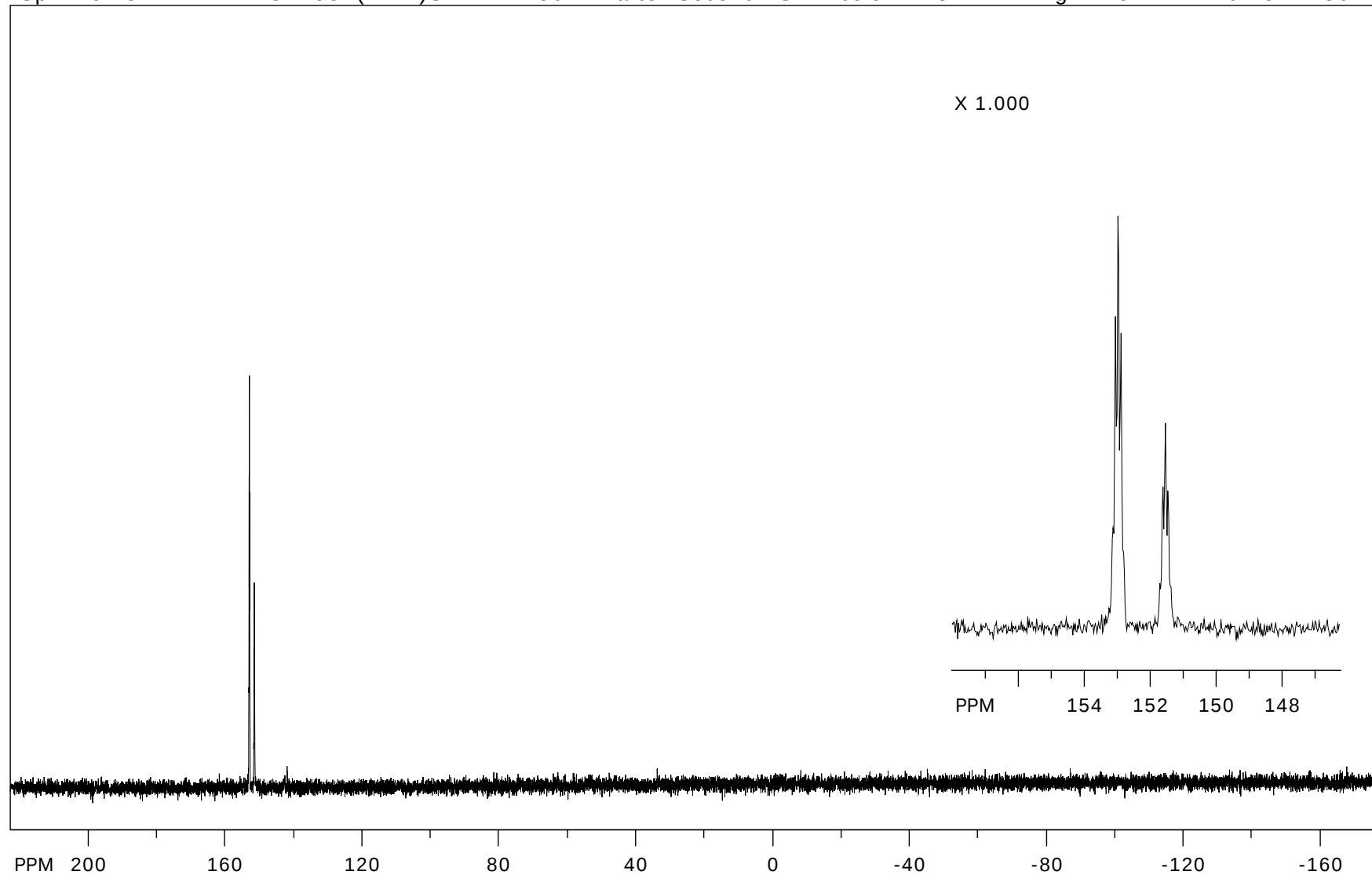


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number of scans: 257

freq. of 0 ppm: 121.196394 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

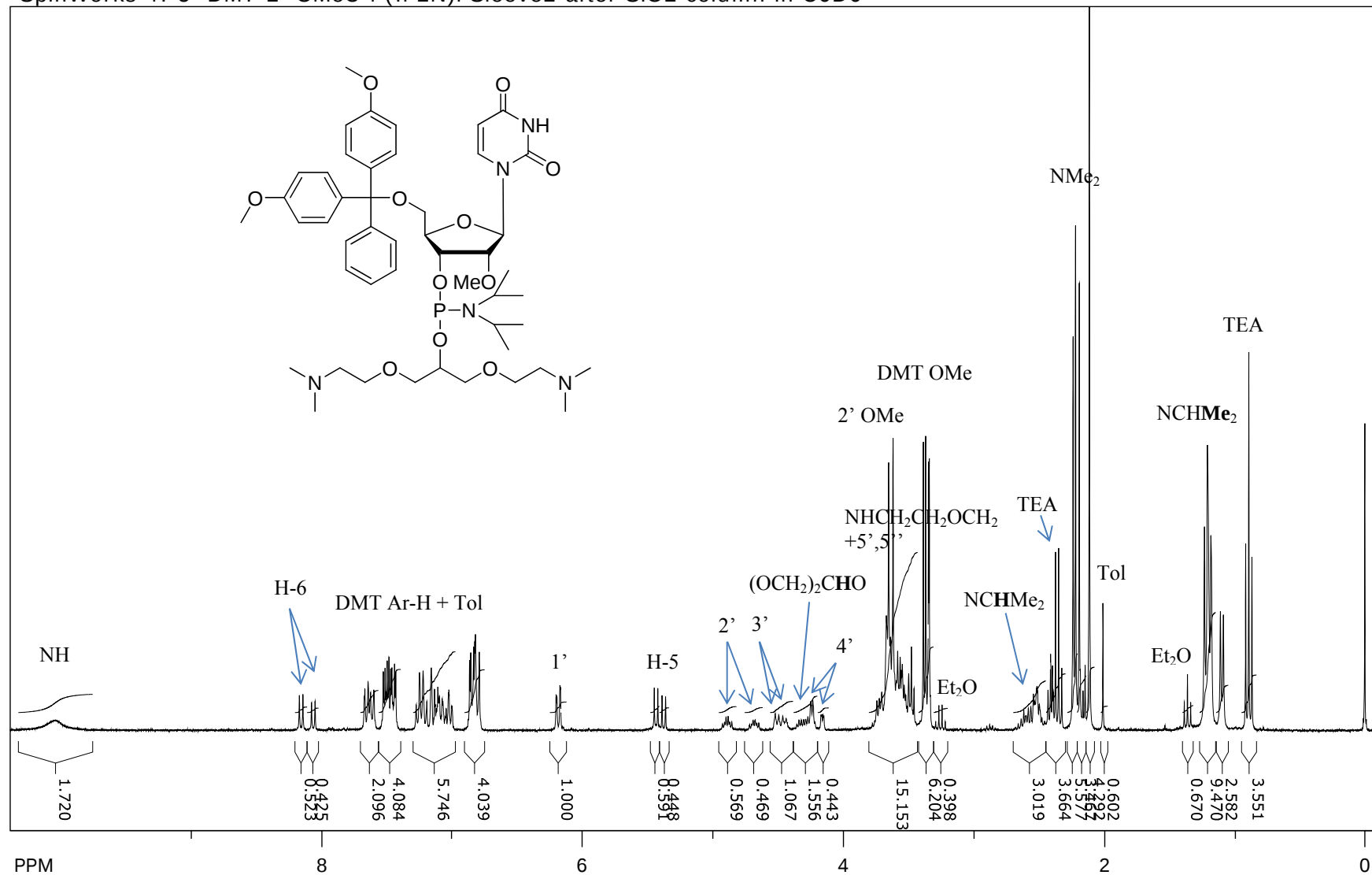
³¹P NMR (¹H coupled) of Phosphoroamidite **14**

SpinWorks 4: DMT-2'-O-MeUP(IP2N)Siv1 IBY150122 after Second LS RP column f8-11 21 mg + 1ul TEA in 0.75 ml C6D6



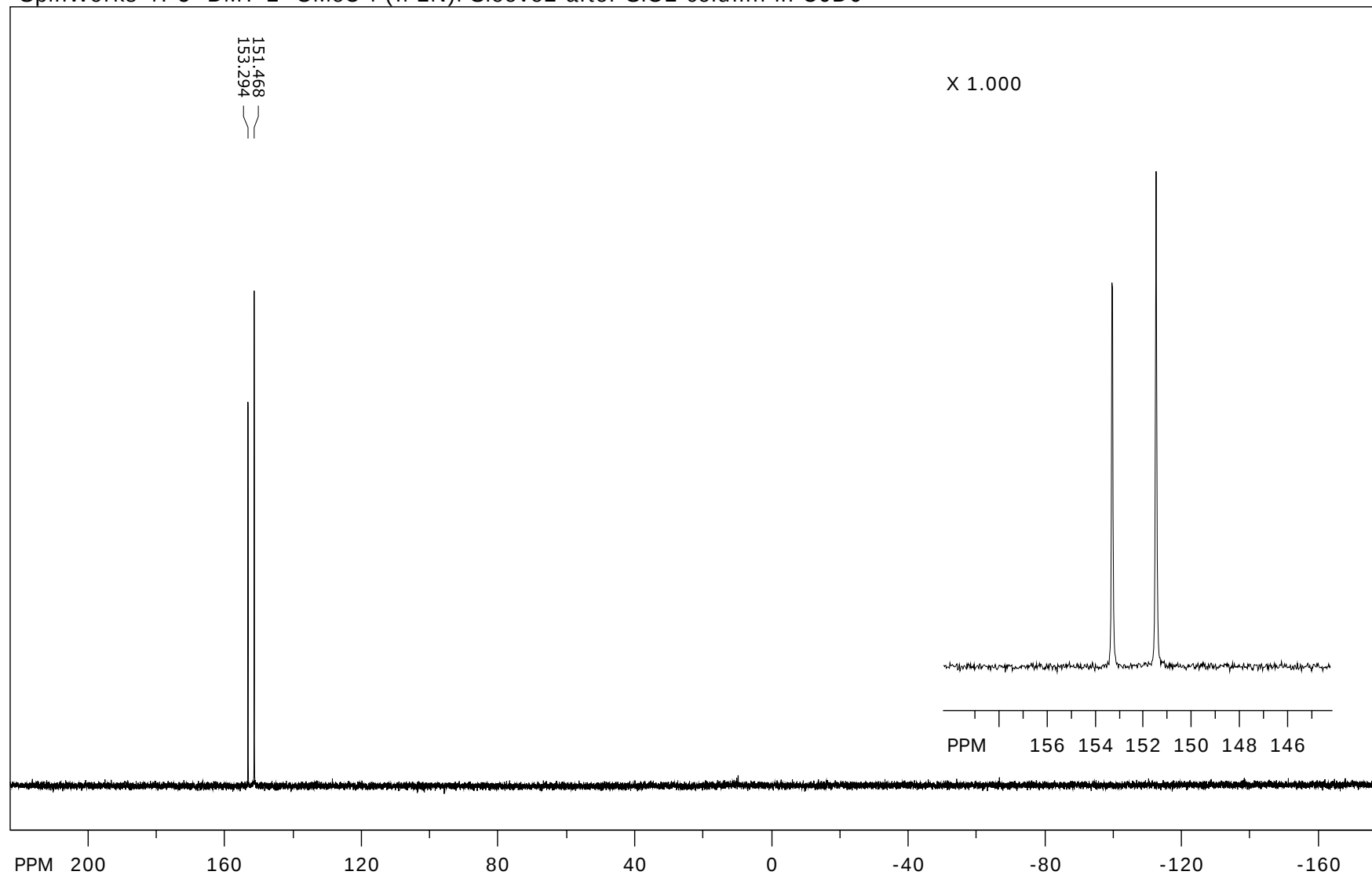
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time domain size: 136248 points
width: 48661.80 Hz = 401.5030 ppm = 0.357156 Hz/pt
number of scans: 344

freq. of 0 ppm: 121.196394 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

¹H NMR with assignments of Phosphoroamidite **16**SpinWorks 4: 5'-DMT-2'-OMeU-P(IP2N)PSleeve2 after SiO₂ column in C₆D₆

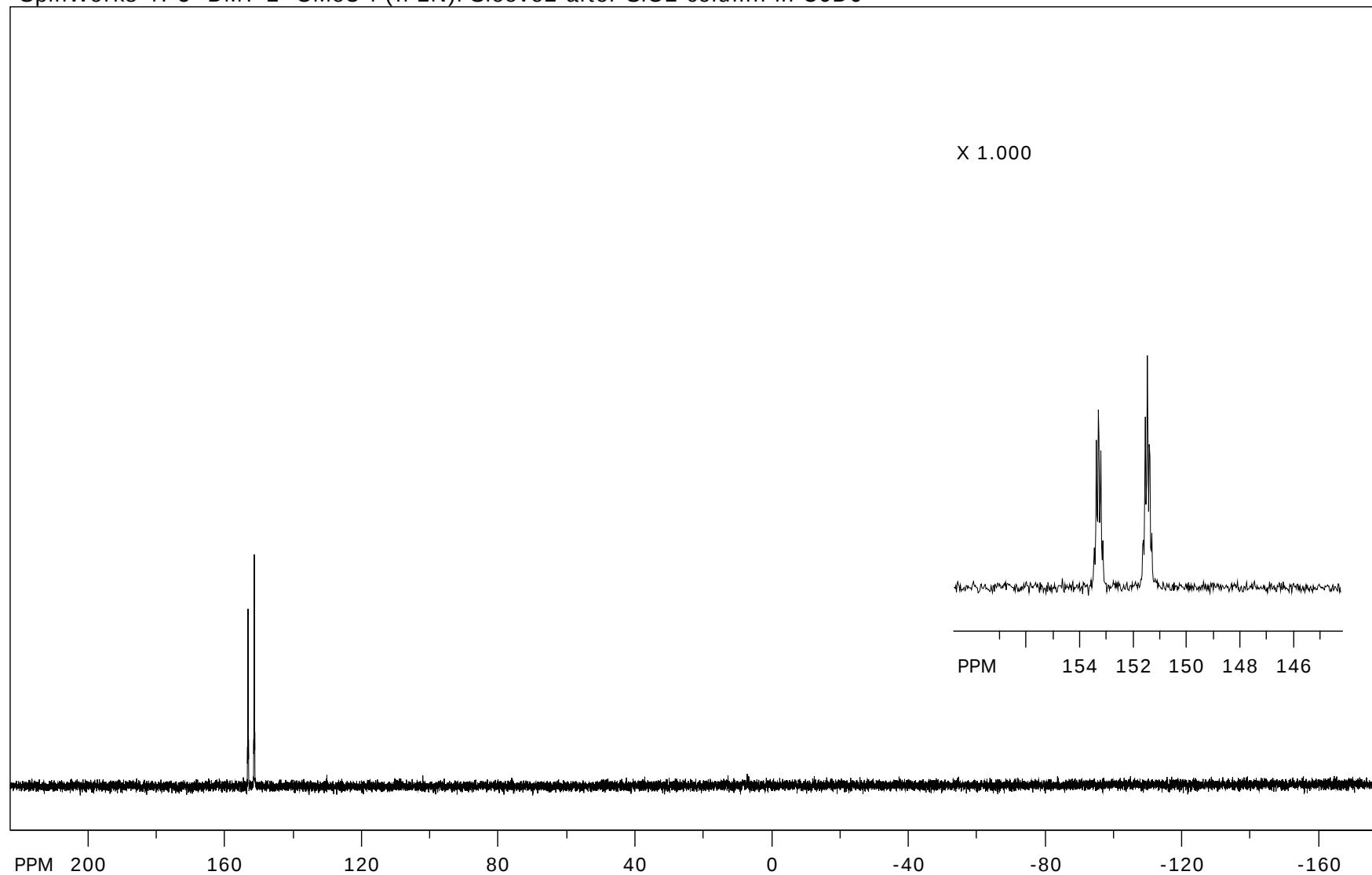
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 transmitter freq.: 299.395419 MHz
 time domain size: 31474 points
 width: 4496.40 Hz = 15.0183 ppm = 0.142861 Hz/pt
 number of scans: 16

freq. of 0 ppm: 299.393431 MHz
 processed size: 32768 complex points
 LB: 0.300 GF: 0.0000

^{31}P NMR (^1H decoupled) of Phosphoroamidite **16**SpinWorks 4: 5'-DMT-2'-OMeU-P(IP2N)PSleeve2 after SiO₂ column in C₆D₆

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time domain size: 136248 points
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number of scans: 605

freq. of 0 ppm: 121.196394 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

³¹P NMR (¹H coupled) of Phosphoroamidite **16**SpinWorks 4: 5'-DMT-2'-OMeU-P(IP2N)PSleeve2 after SiO₂ column in C₆D₆

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time domain size: 136248 points
width: 48661.80 Hz = 401.5030 ppm = 0.357156 Hz/pt
number of scans: 519

freq. of 0 ppm: 121.196394 MHz
processed size: 16384 complex points
LB: 1.000 GF: 0.0000

¹H NMR of 1,9-Dichlorononan-5-one (18)1,9-dichloro-5-nonanone batch MYX28 dist. fr. 3, 60 ul in 0.6 ml cdcl₃

Current Data Parameters

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EXPNO 10
PROCNO 1

F2 - Acquisition Parameters

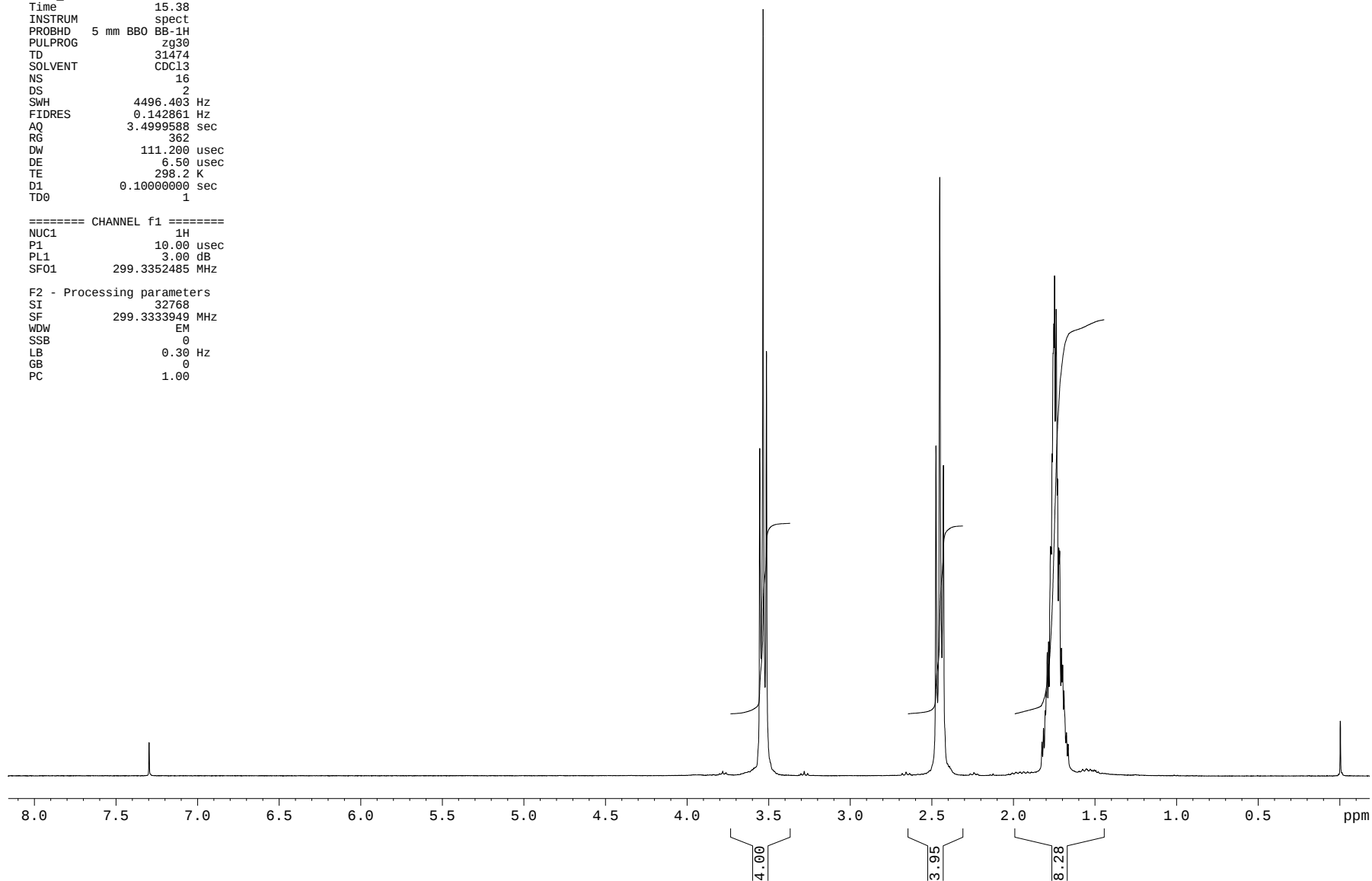
Date_ 20150720
Time_ 15.38
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PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 31474
SOLVENT CDCl₃
NS 16
DS 2
SWH 4496.403 Hz
FIDRES 0.142861 Hz
AQ 3.4999588 sec
RG 362
DW 111.200 usec
DE 6.50 usec
TE 298.2 K
D1 0.10000000 sec
TD0 1

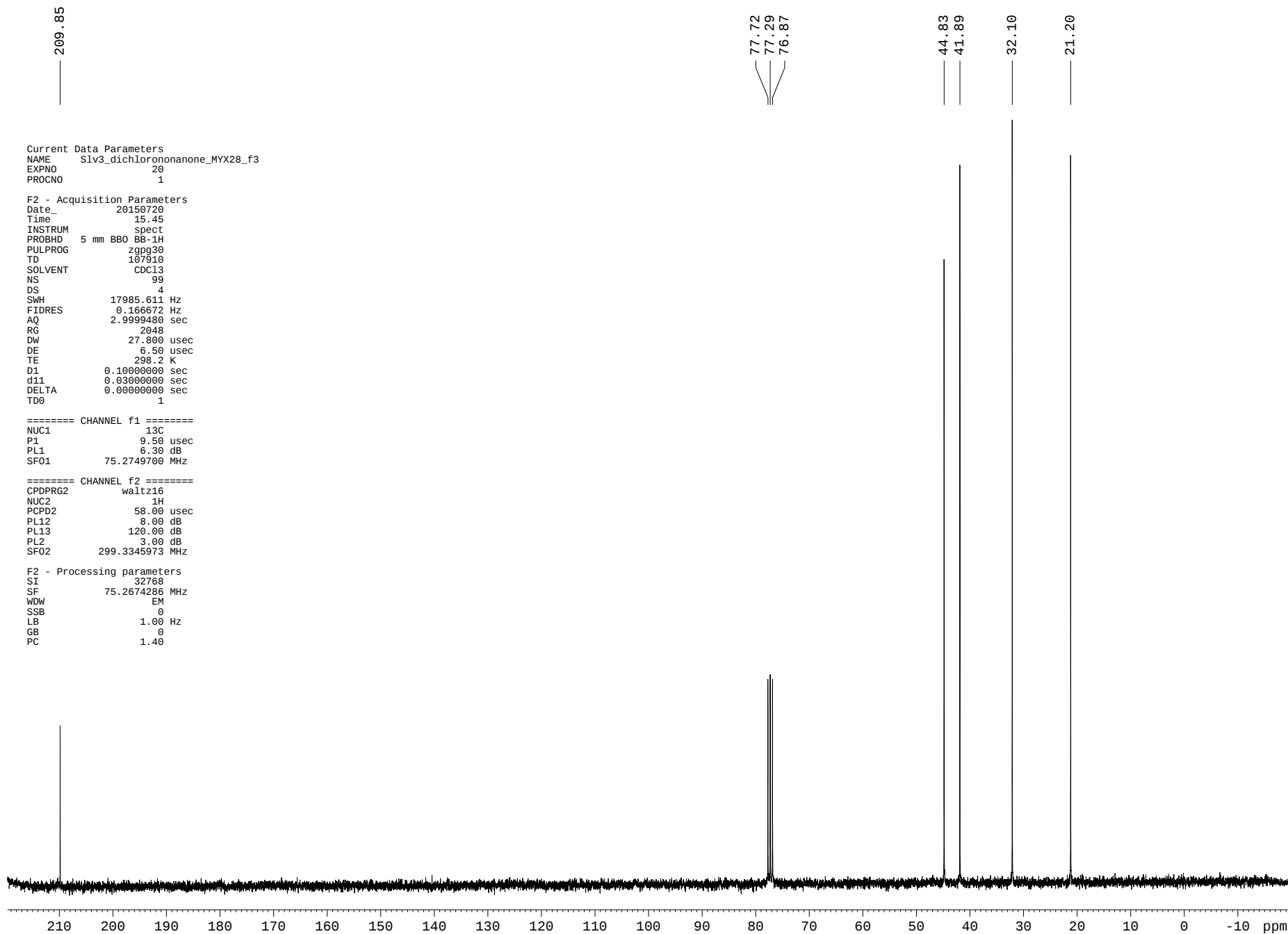
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PL1 3.00 dB
SF01 299.3352485 MHz

F2 - Processing parameters

SI 32768
SF 299.3333949 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



¹H NMR of 1,9-Dichlorononan-5-one (18)1,9-dichloro-5-nonanone batch MYX28 dist. fr. 3, 60 ul in 0.6 ml cdcl₃

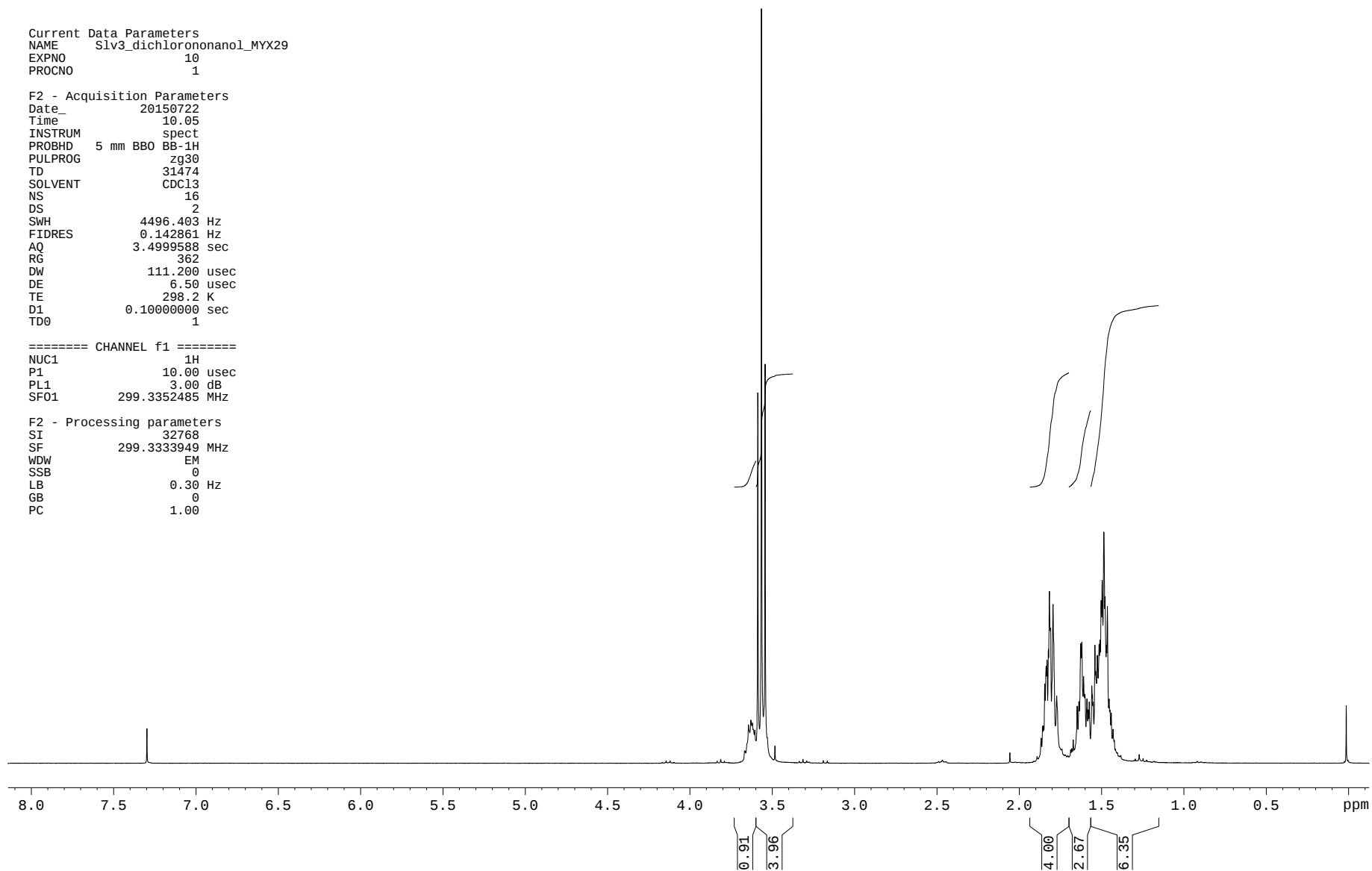
¹H NMR of 1,9-Dichloro-5-nonanol (19)1,9-dichloro-5-nonanol batch MYX29, 50 μ l in 0.6 ml cdcl_3

Current Data Parameters
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EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150722
Time 10.05
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 31474
SOLVENT CDCl_3
NS 16
DS 2
SWH 4496.403 Hz
FIDRES 0.142861 Hz
AQ 3.4999588 sec
RG 362
DW 111.200 μ sec
DE 6.50 μ sec
TE 298.2 K
D1 0.10000000 sec
TD0 1

===== CHANNEL f1 =====
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P1 10.00 μ sec
PL1 3.00 dB
SF01 299.3352485 MHz

F2 - Processing parameters
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SF 299.3333949 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



¹³C NMR of 1,9-Dichloro-5-nonanol (**19**)

1,9-dichloro-5-nonanol batch MYX29, 50 ul in 0.6 ml cdcl₃

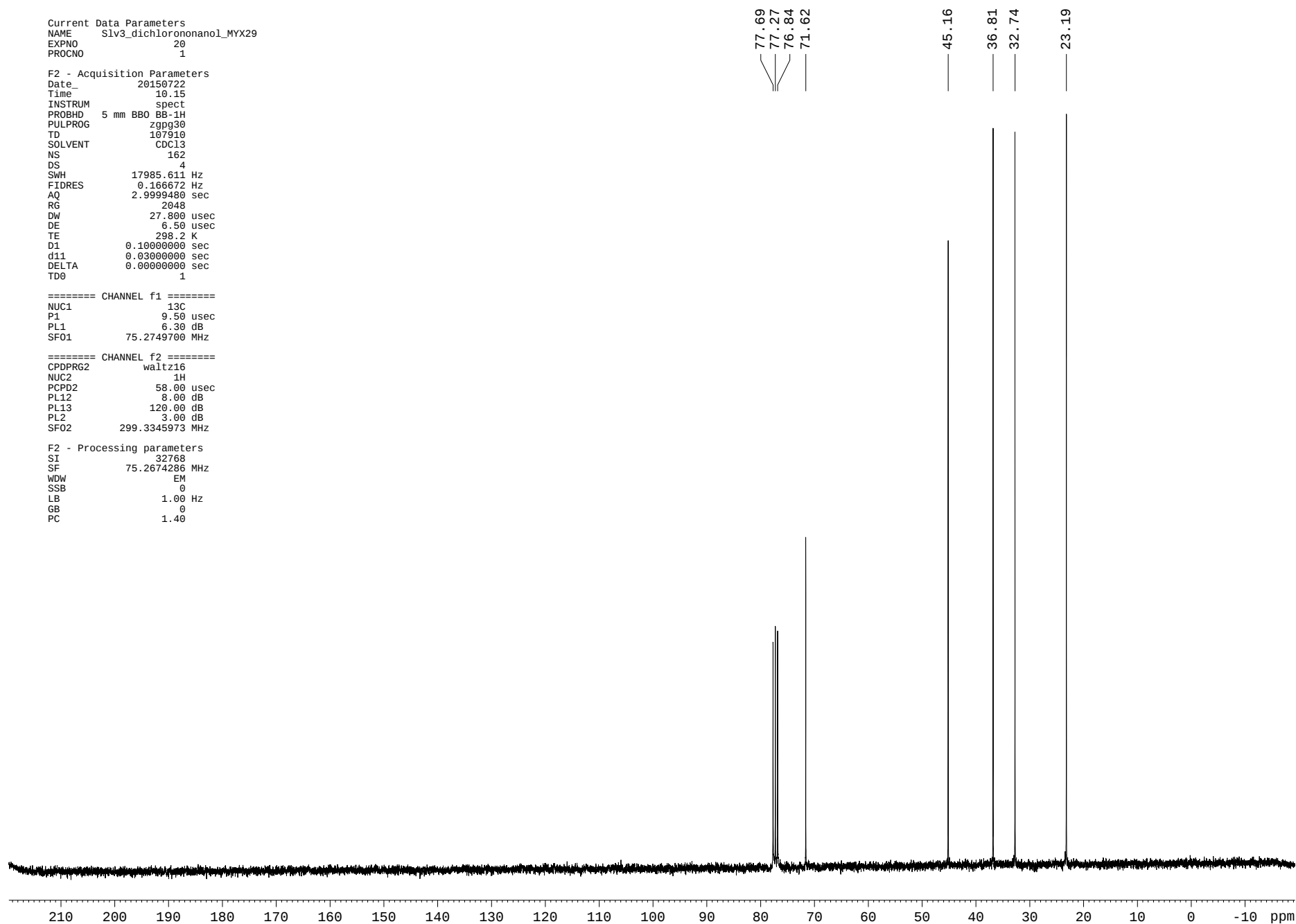
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 EXPNO 20
 PROCNO 1

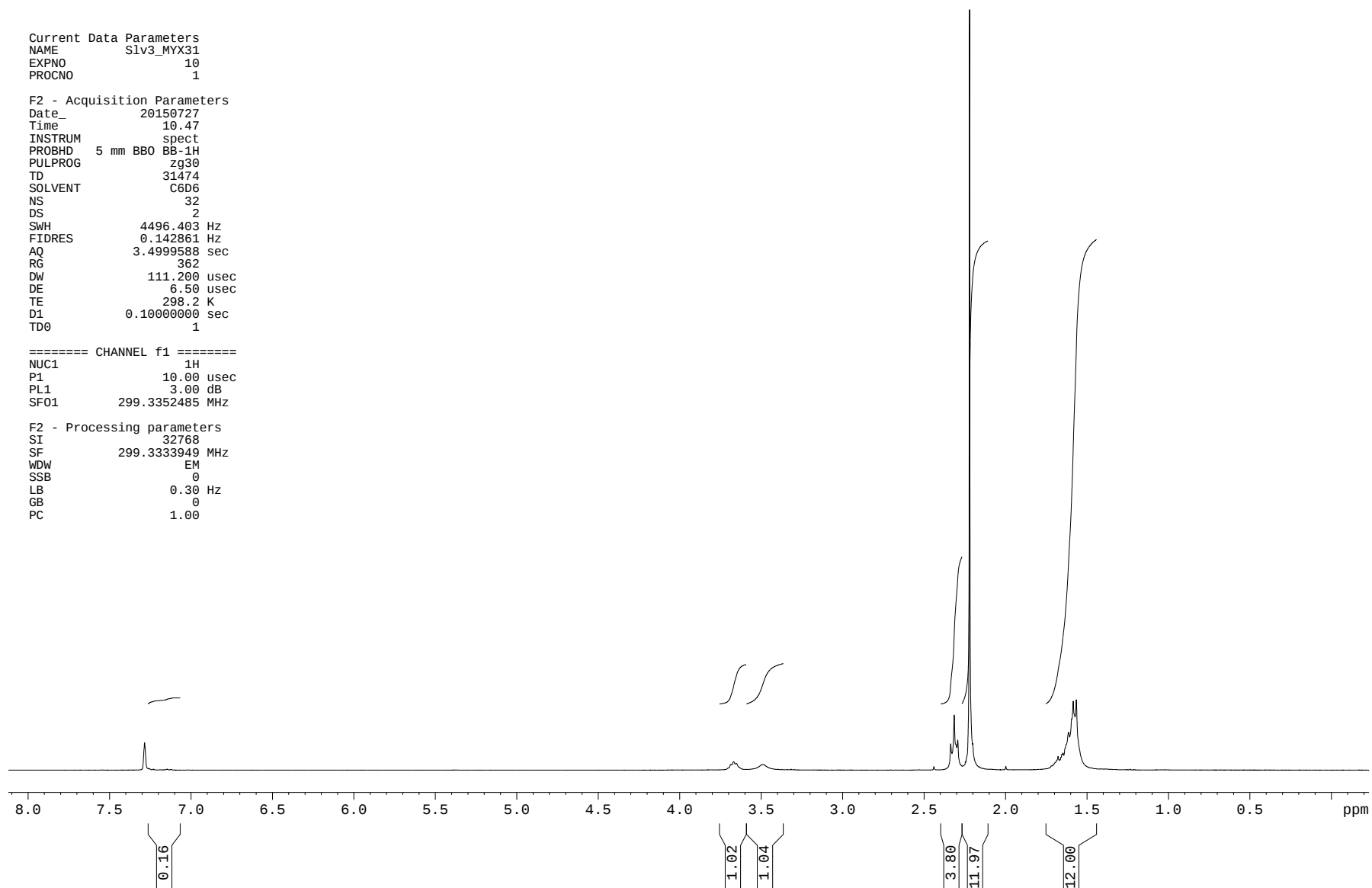
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 Time 10.15
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 PULPROG zgpg30
 TD 107910
 SOLVENT CDCl₃
 NS 162
 DS 4
 SWH 17985.611 Hz
 FIDRES 0.166672 Hz
 AQ 2.9999480 sec
 RG 2048
 DW 27.800 usec
 DE 6.50 usec
 TE 298.2 K
 D1 0.10000000 sec
 d11 0.03000000 sec
 DELTA 0.00000000 sec
 TD0 1

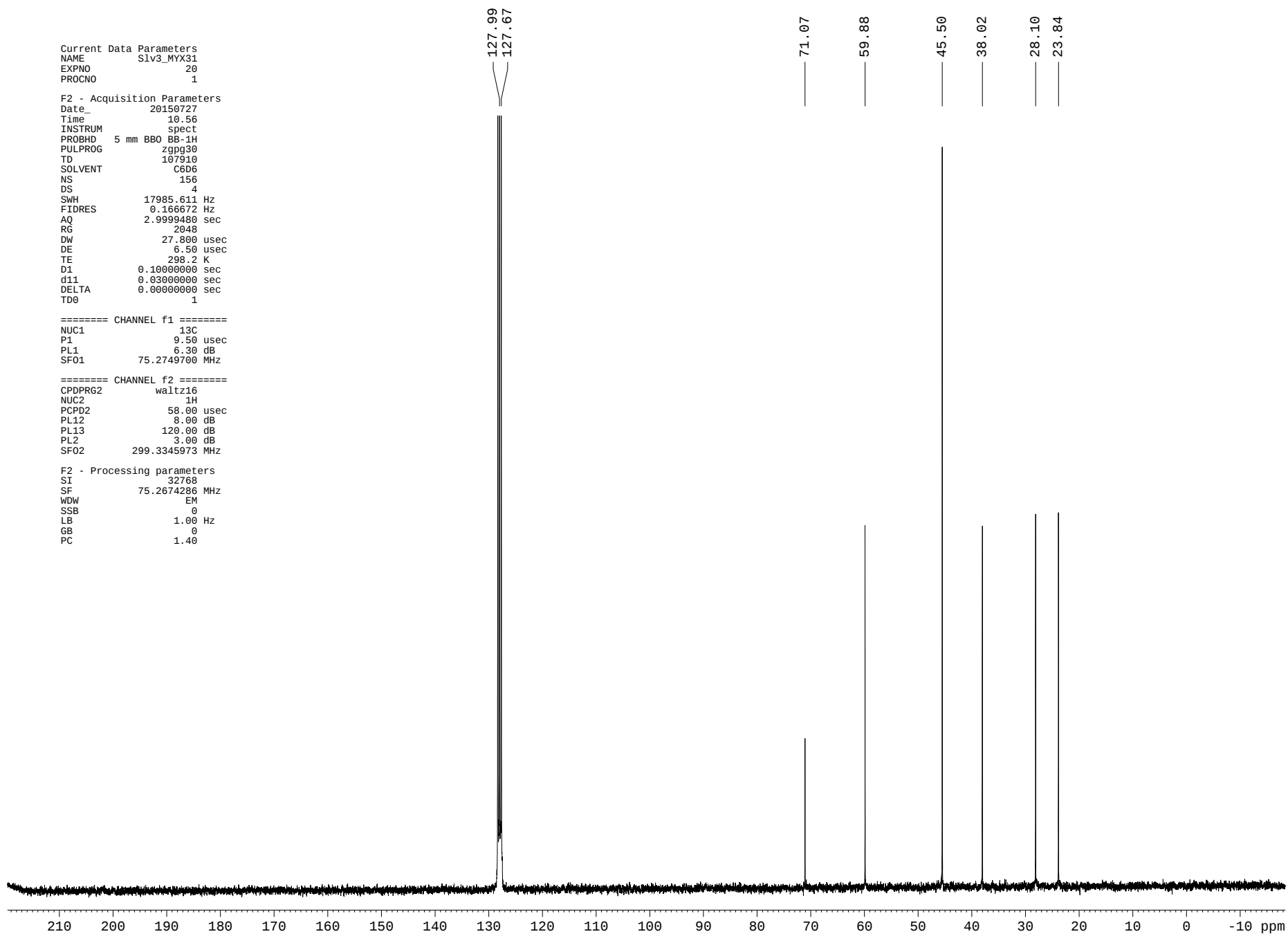
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 PL1 6.30 dB
 SF01 75.2749700 MHz

===== CHANNEL f2 =====
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 NUC2 1H
 PCPD2 58.00 usec
 PL12 8.00 dB
 PL13 120.00 dB
 PL2 3.00 dB
 SF02 299.3345973 MHz

F2 - Processing parameters
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 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

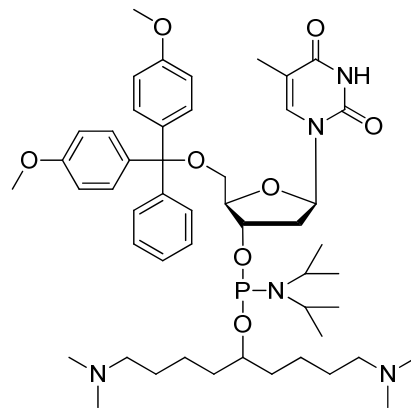


¹H NMR of 1,9-Bis(dimethylamino)-5-nonanol (20)Sleeve 3, 1,9-bis(dimethylamino)-5-nonanol, MYX31, ca. 50 mg in 0.7 ml CD₃CN

¹³CNMR of 1,9-Bis(dimethylamino)-5-nonanol (20)Sleeve 3, 1,9-bis(dimethylamino)-5-nonanol, MYX31, ca. 50 mg in 0.7 ml CD₃CN

¹H NMR of Phosphoroamidite **22**, two diastereomers in a ratio 4:1

1H of IBY150727 DMTdT(IP2N)Slv3 after sec. SiO2 col, fr.1, 15 mg in 0.7 ul c6d6+1 ul TEA

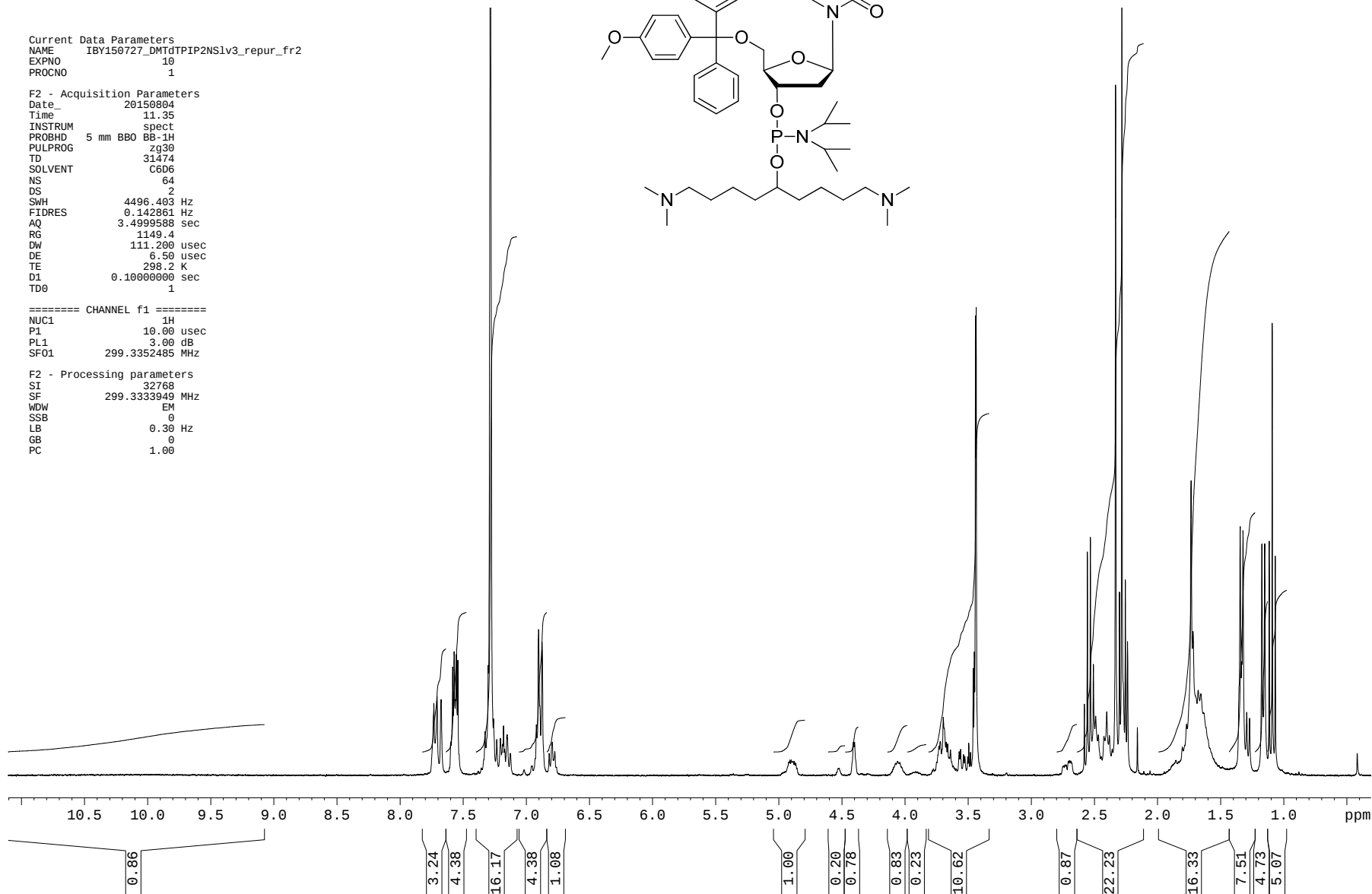


Current Data Parameters
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EXPNO 10
PROCNO 1

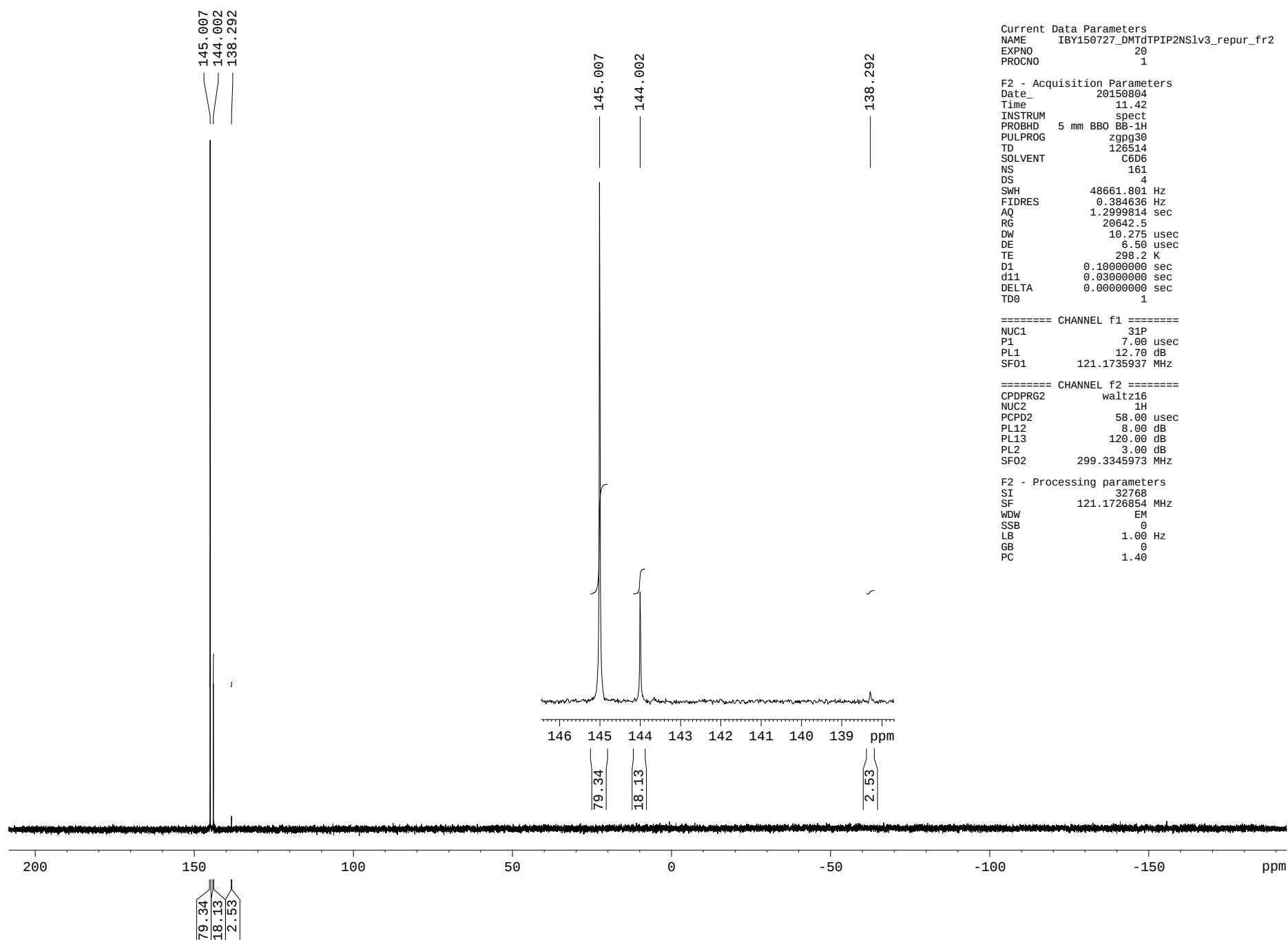
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Time 11.35
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TD 31474
SOLVENT C6D6
NS 64
DS 2
SWH 4496.403 Hz
FIDRES 0.142861 Hz
AQ 3.4999588 sec
RG 1149.4
DW 111.200 usec
DE 6.50 usec
TE 298.2 K
D1 0.10000000 sec
TD0 1

===== CHANNEL f1 =====
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PL1 3.00 dB
SF01 299.3352485 MHz

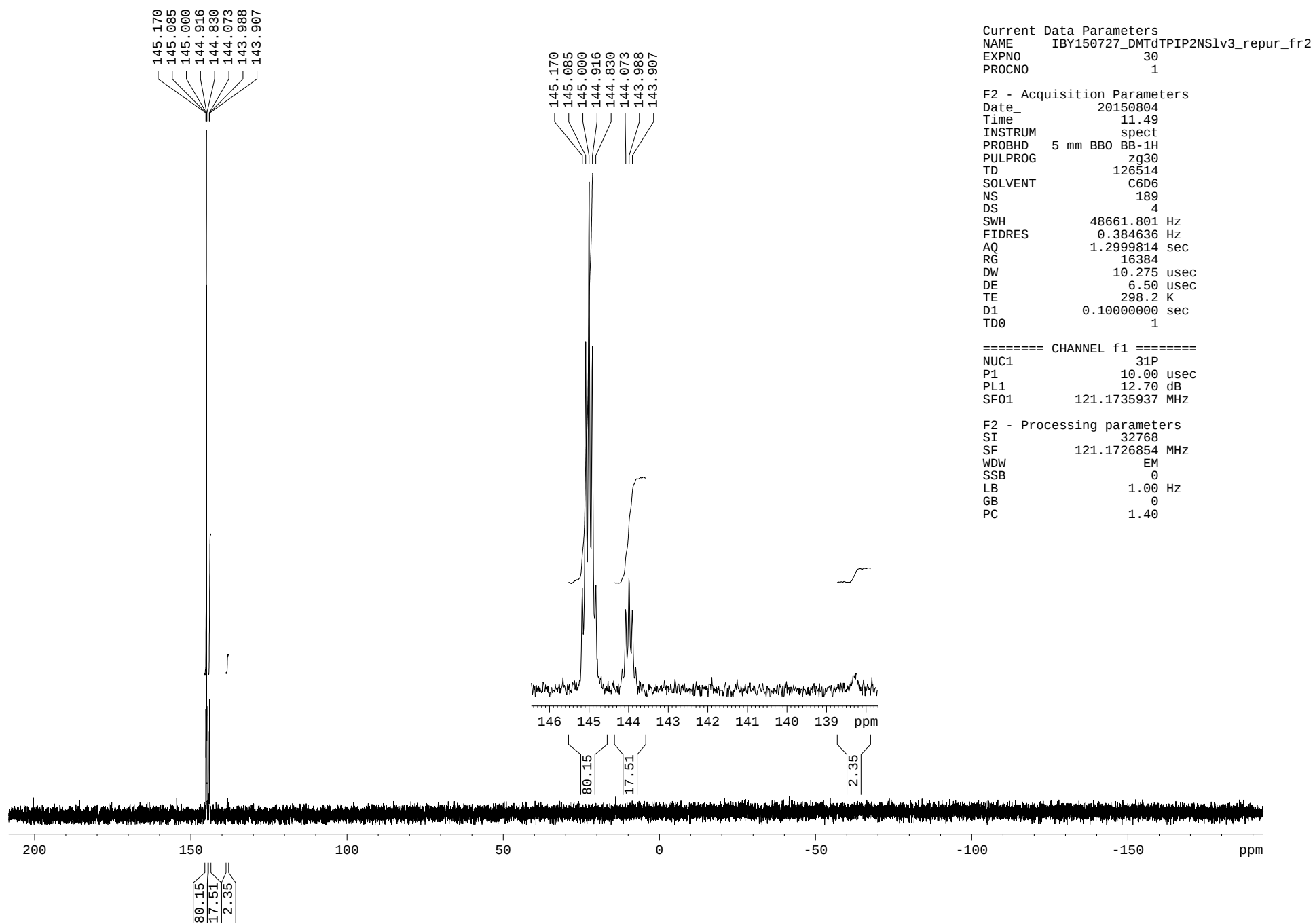
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GB 0
PC 1.00



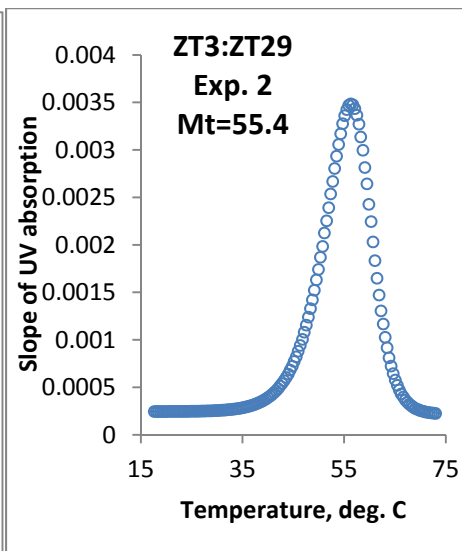
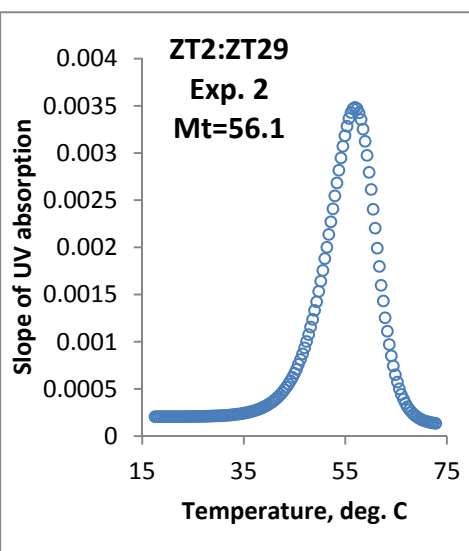
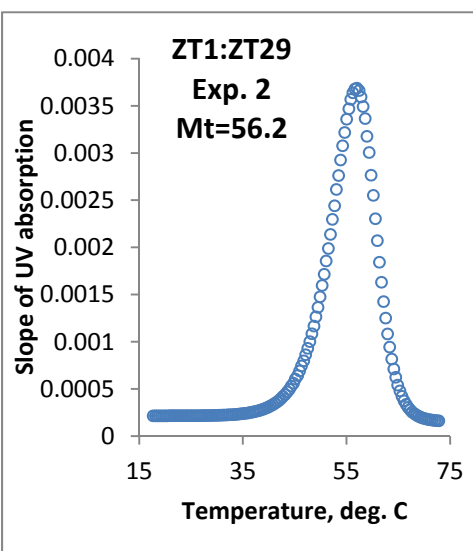
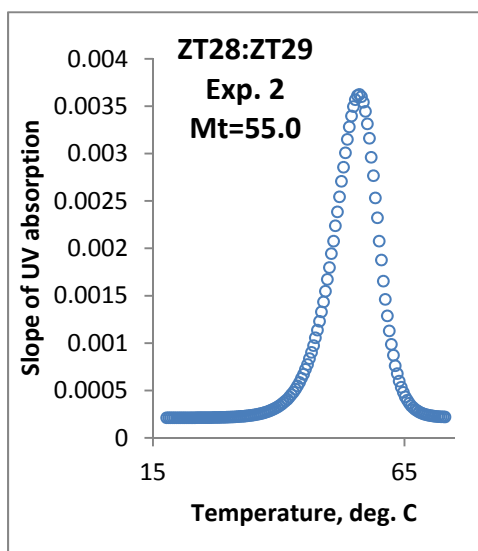
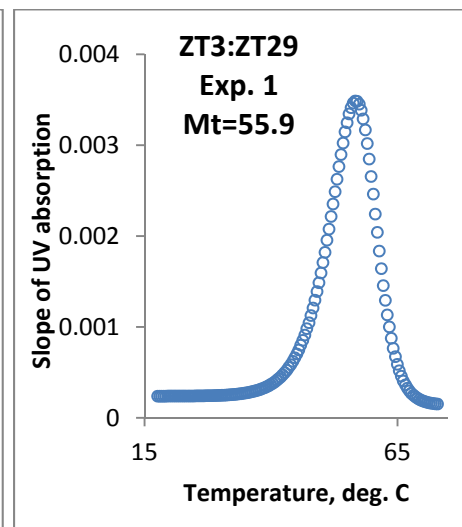
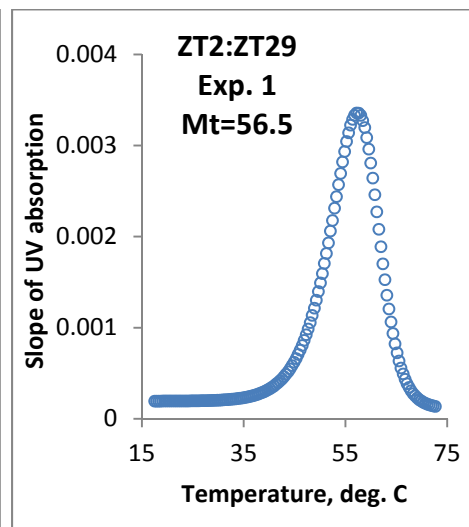
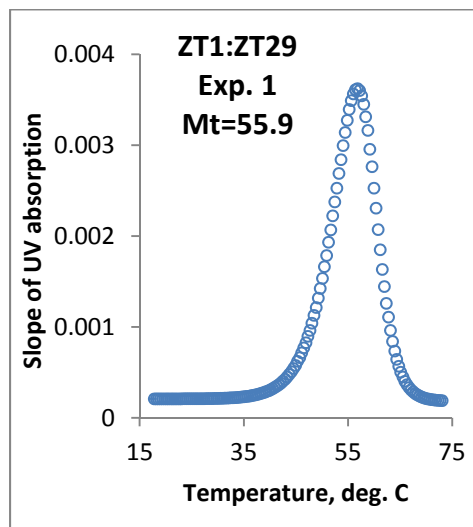
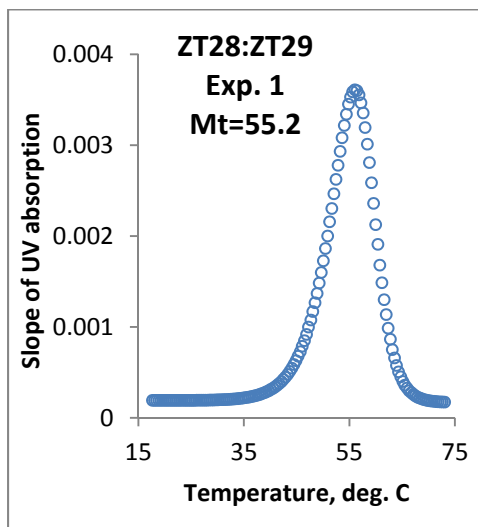
^{31}P (^1H decoupled) NMR of Phosphoroamidite **22**, two diastereomers in a ratio 4:1
of IBY150727 DMTdT(IP2N)Slv3 after sec. Si02 col, fr.2, 15 mg in 0.7 ul c6d6+1

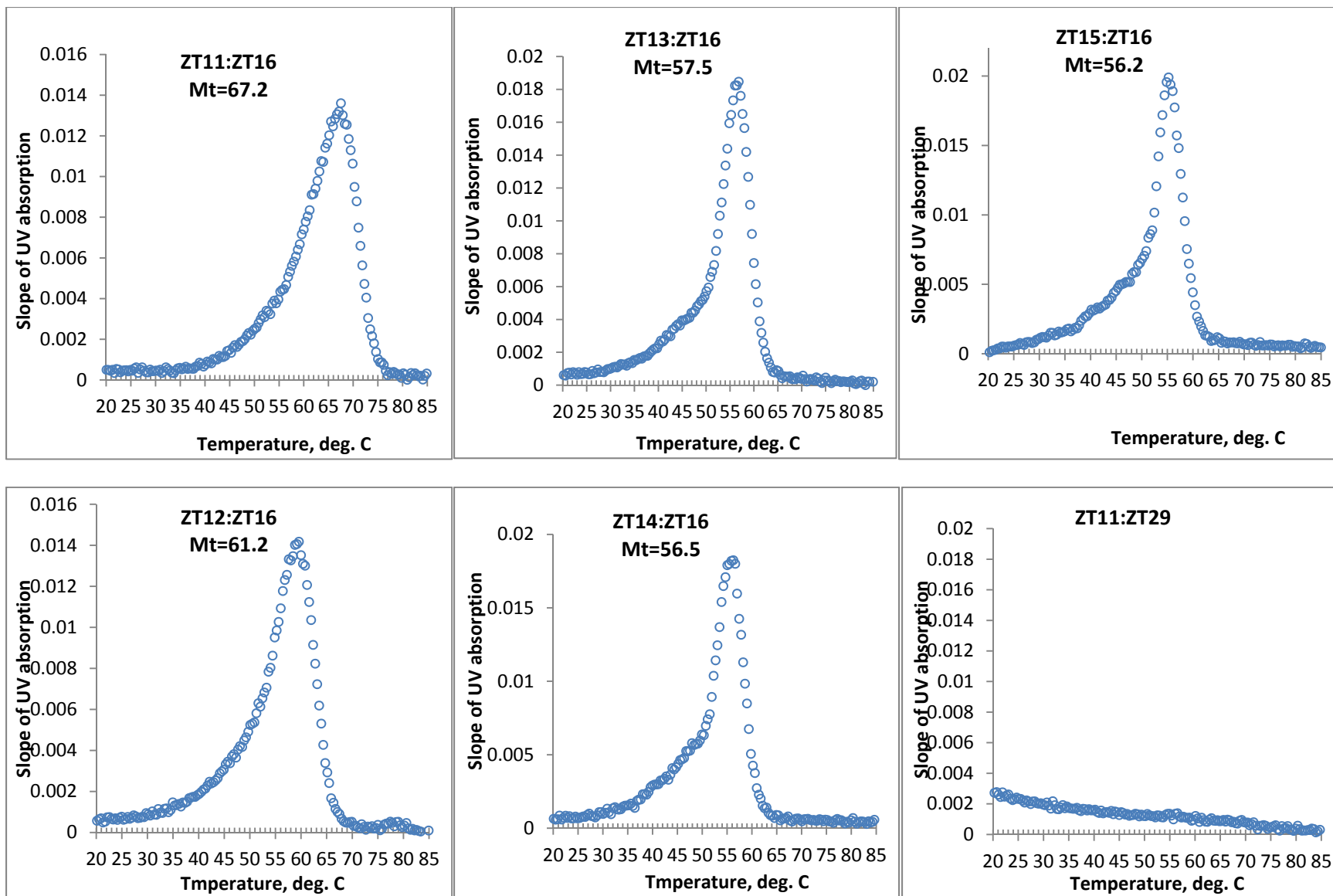


^{31}P (^1H decoupled) NMR of Phosphoroamidite **22**, two diastereomers in a ratio 4:1
 of IBY150727 DMTdT(IP2N)Slv3 after sec. SiO2 col, fr.2, 15 mg in 0.7 uL c6d6+1 uL

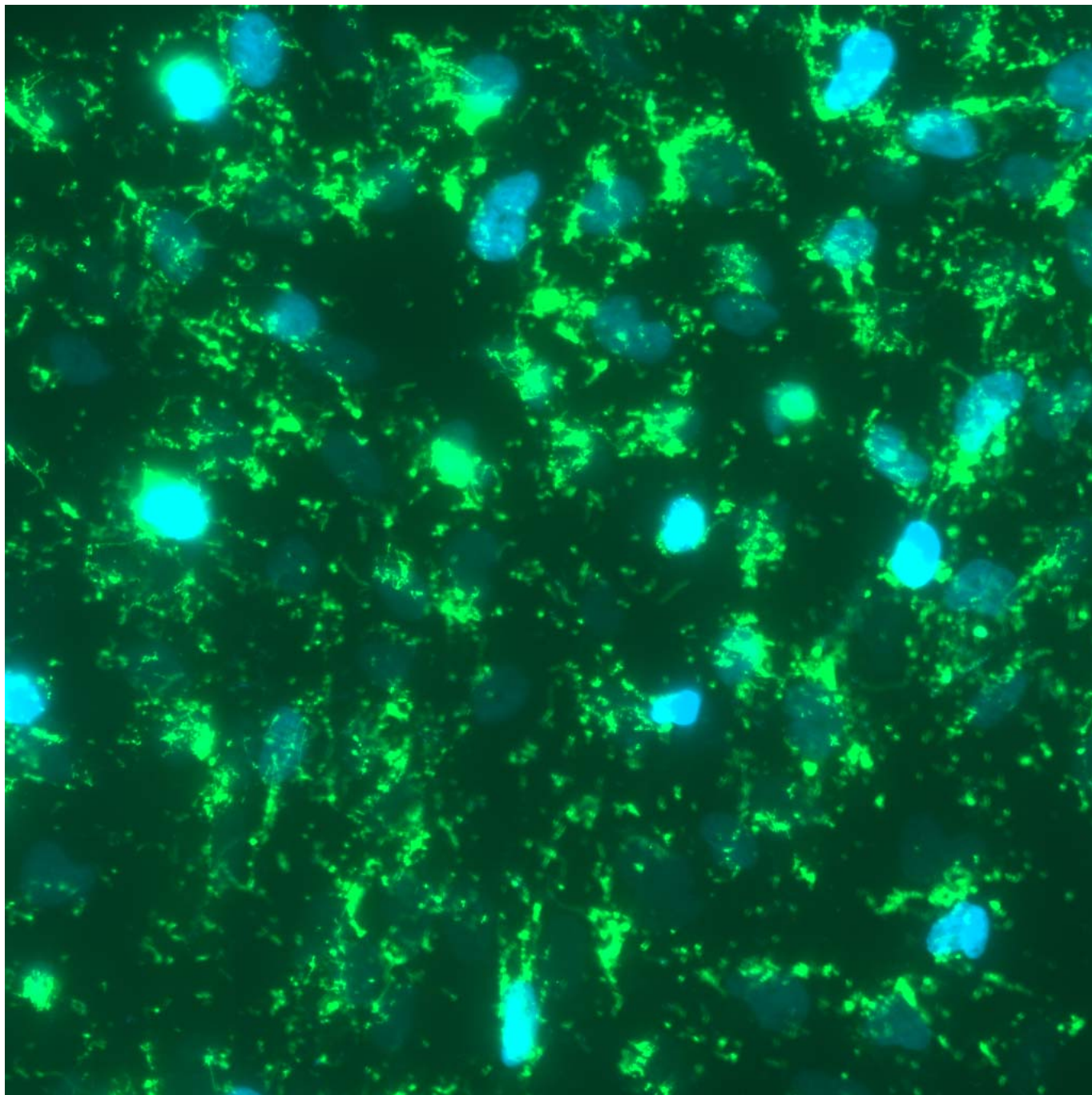


Differential Melting Curves of ON Duplexes. See Table 1 and Table 2 for sequences.





Fluorescent image of incubation of A172 cell culture with 1 μ M of ZT20. of manuscript. See experimental section and Fig. 10 for image details.



Fluorescent image of incubation of A172 cell culture with 1 μ M of ZT17. See experimental section and Fig. 10 for image details.

