Electronic Supplementary Information

Amide rotation trajectories probed by symmetry

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Table S1. Activation energies for *N*-acetylated compounds as function of temperature (in deuterium oxide solution)

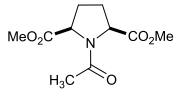
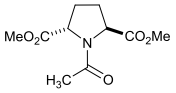
T, K	compound **2a** 		compound **3a** 		compound **4a** 	
	k, s^{-1}	$E^{\neq}$, kJ mol^{-1}	k, s^{-1}	$E^{\neq}$, kJ mol^{-1}	k, s^{-1}	$E^{\neq}$, kJ mol^{-1}
297.9	0.017 ± 0.002	83.06 ± 0.29	-	-	-	-
303.3	0.032 ± 0.003	83.0 ± 0.24	-	-	-	-
309.7	-	-	0.0015 ± 0.0008	92.68 ± 1.53	0.010 ± 0.002	87.79 ± 0.52
313.9	0.109 ± 0.003	82.80 ± 0.07	0.0025 ± 0.0010	92.66 ± 1.11	0.018 ± 0.002	87.50 ± 0.29
319.3	0.190 ± 0.007	82.78 ± 0.10	0.0055 ± 0.0013	92.18 ± 0.64	0.032 ± 0.001	87.51 ± 0.08
324.6	-	-	0.011 ± 0.002	91.89 ± 0.50	0.057 ± 0.002	87.46 ± 0.09
329.9	0.569 ± 0.010	82.63 ± 0.05	0.019 ± 0.002	91.95 ± 0.29	0.098 ± 0.002	87.45 ± 0.06
335.3	0.949 ± 0.026	82.58 ± 0.08	0.032 ± 0.002	92.03 ± 0.17	0.165 ± 0.003	87.46 ± 0.05

Table S2. Activation energies for *N*-aceturylated compounds as function of temperature (in buffered deuterium oxide solution)

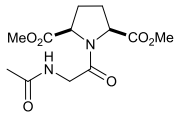
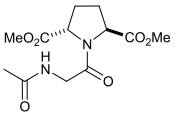
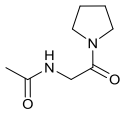
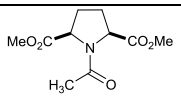
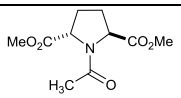
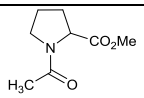
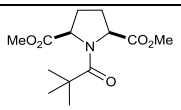
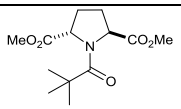
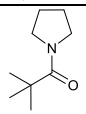
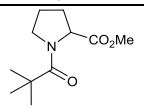
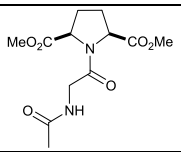
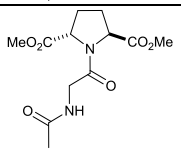
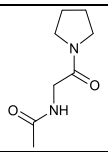
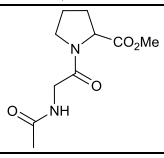
T, K	compound **2c** 		compound **3c** 		compound **4c** 	
	k, s^{-1}	$E^{\neq}$, kJ mol^{-1}	k, s^{-1}	$E^{\neq}$, kJ mol^{-1}	k, s^{-1}	$E^{\neq}$, kJ mol^{-1}
297.9	0.083 ± 0.006	79.13 ± 0.18	-	-	-	-
303.3	0.145 ± 0.009	79.18 ± 0.16	-	-	0.013 ± 0.002	85.26 ± 0.39
309.7	0.294 ± 0.015	79.09 ± 0.13	0.012 ± 0.002	87.32 ± 0.43	0.028 ± 0.004	85.14 ± 0.37
313.9	0.452 ± 0.019	79.09 ± 0.11	0.022 ± 0.004	86.98 ± 0.48	0.044 ± 0.005	85.17 ± 0.30
319.3	0.781 ± 0.076	79.03 ± 0.26	0.036 ± 0.004	87.19 ± 0.30	0.077 ± 0.005	85.18 ± 0.17
324.6	1.278 ± 0.058	79.06 ± 0.12	0.063 ± 0.005	87.18 ± 0.21	0.131 ± 0.010	85.21 ± 0.21
329.9	2.127 ± 0.135	79.01 ± 0.17	0.111 ± 0.007	87.11 ± 0.17	0.219 ± 0.009	85.24 ± 0.11
335.3	3.467 ± 0.238	78.97 ± 0.19	0.184 ± 0.007	87.15 ± 0.11	0.352 ± 0.019	85.34 ± 0.15

Table S3. Energetic terms for the amide rotation in *N*-acyl compounds in aqueous medium

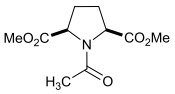
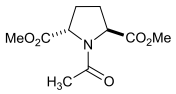
compound	ΔH, kJ mol^{-1}	ΔS, J mol^{-1} K^{-1}
2a	+ 86.5 ± 0.3	+ 11.9 ± 0.9
3a	+ 94.5 ± 3.0	+ 7.6 ± 9.0
4a	+ 88.5 ± 0.6	+ 3.2 ± 1.8
2c	+ 80.5 ± 0.3	+ 4.7 ± 0.9
3c	+ 87.8 ± 1.1	+ 2.0 ± 3.4
4c	+ 83.4 ± 0.7	– 5.7 ± 2.2

Table S4. Amide rotation kinetics for the examined substances measured in deuterium oxide solution

compound	structure	T, K	k, s^{-1}		$E^{\neq}$, kJ mol^{-1}	
N-acetyl compounds						
2a		298	0.019 ± 0.002		82.8 ± 0.3	
3a		310	0.0015 ± 0.0008		92.8 ± 1.9	
4a		310	0.009 ± 0.001		88.2 ± 0.3	
5a		310	*trans→cis*	*cis→trans*	*trans→cis*	*cis→trans*
			0.0070 ± 0.0005	0.033 ± 0.002	88.8 ± 0.2	84.8 ± 0.2
N-pivaloyl compounds						
2b		298	20.0 ± 0.2		65.6 ± 0.1	
3b		298	0.431 ± 0.018		75.1 ± 0.1	
4b		298	14.2 ± 0.9		66.4 ± 0.2	
5b		298	*trans→cis*	*cis→trans*	*trans→cis*	*cis→trans*
			0.622 ± 0.043	36.5 ± 2.0	74.2 ± 0.1	64.1 ± 0.1
2c		310	0.292 ± 0.029		79.2 ± 0.3	
3c		310	0.012 ± 0.002		87.4 ± 0.5	
4c		310	0.029 ± 0.005		85.1 ± 0.5	
5c		310	*trans→cis*	*cis→trans*	*trans→cis*	*cis→trans*
			0.020 ± 0.001	0.123 ± 0.006	86.1 ± 0.1	81.4 ± 0.2

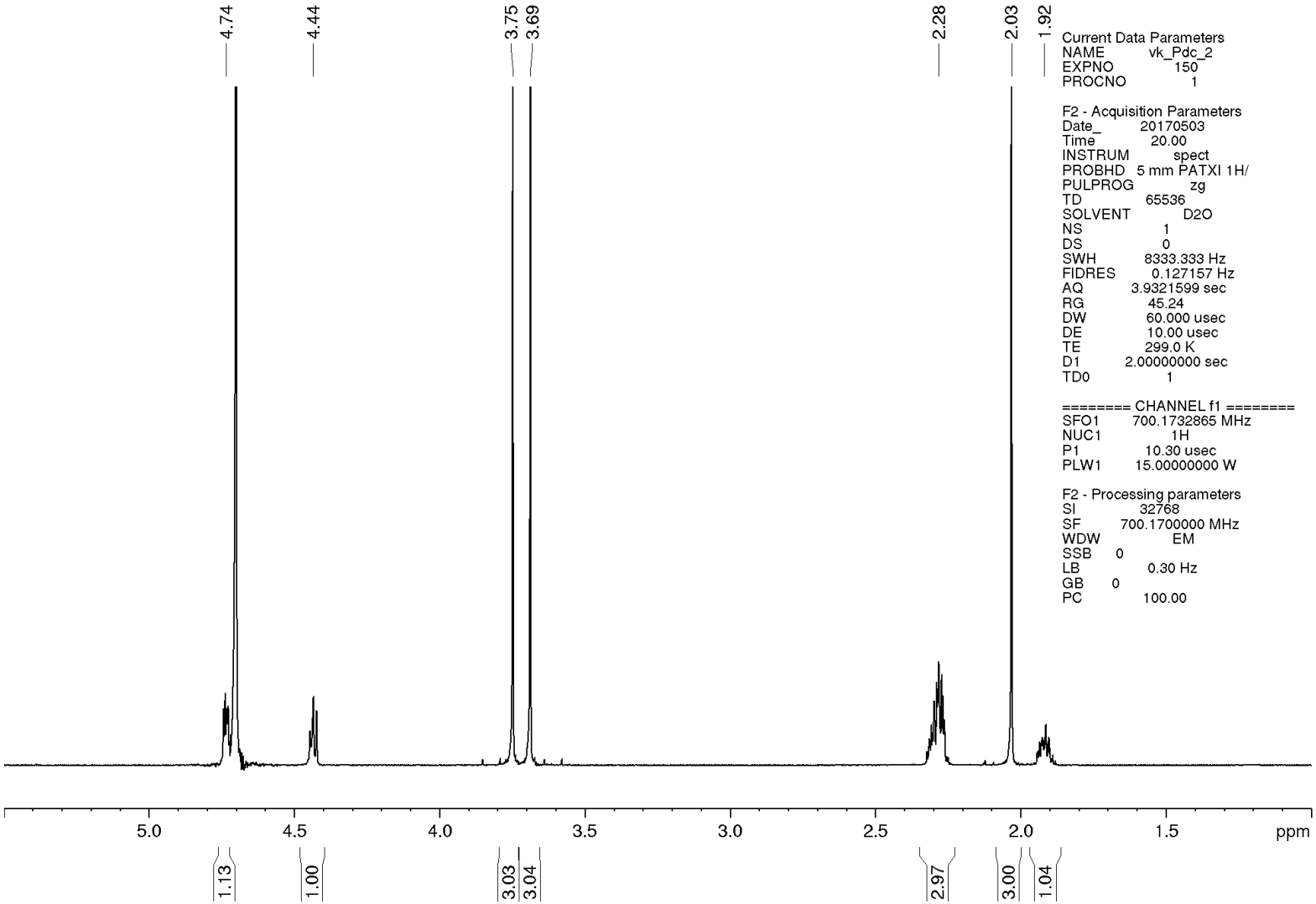
Note: for the *N*-aceturyl compounds **2c**-**5c** the measurements were conducted in buffered deuterium oxide (potassium phosphate buffer, 70 mM, pH 7)

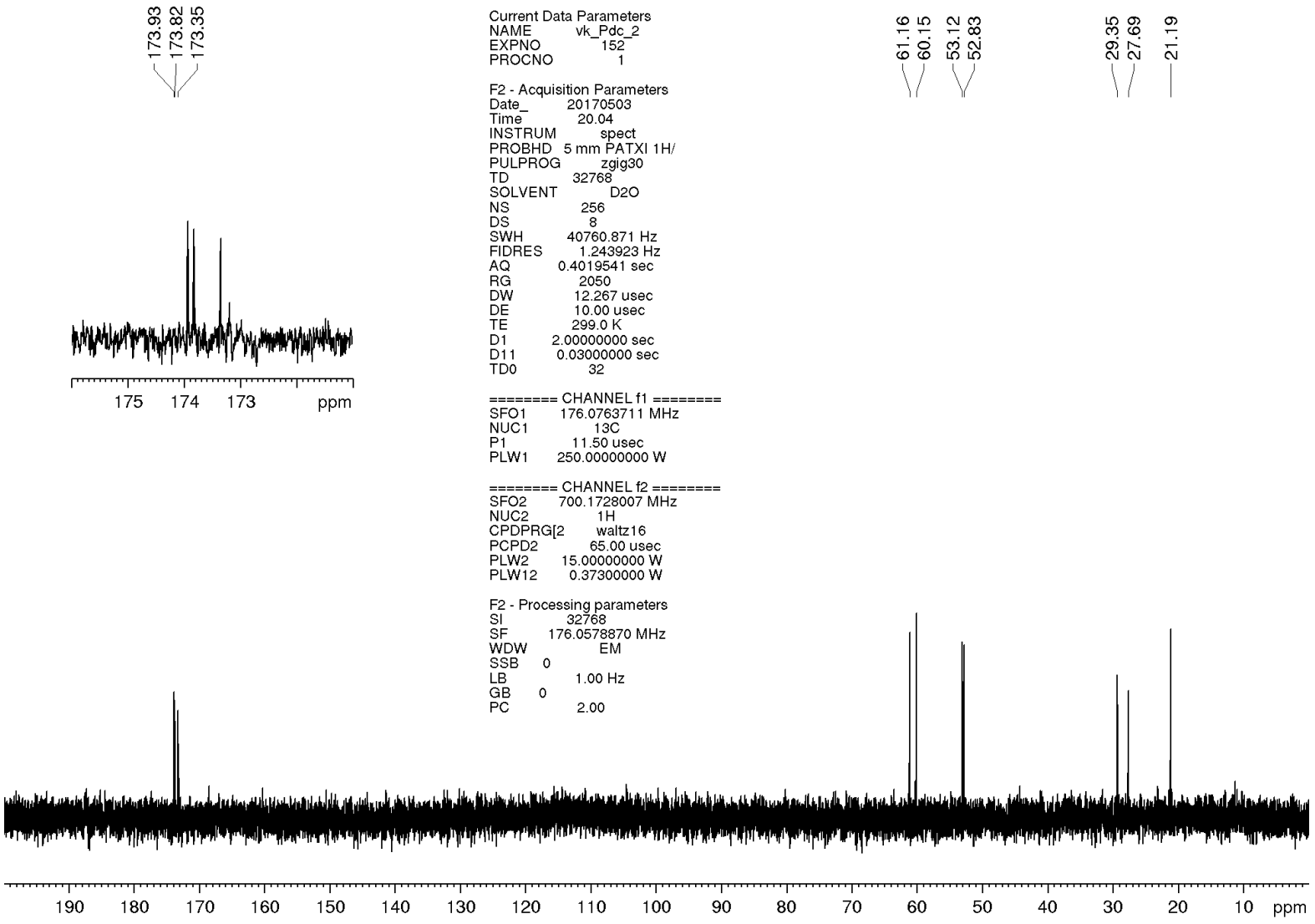
Table S5. Amide rotation kinetics for the *N*-acetyl compounds measured in different solvents

solvent	ET, kJ mol^{-1}	compound **2a** 			compound **3a** 			compound **4a** 		
		T, K	k, s^{-1}	$E^{\neq}$, kJ mol^{-1}	T, K	k, s^{-1}	$E^{\neq}$, kJ mol^{-1}	T, K	k, s^{-1}	$E^{\neq}$, kJ mol^{-1}
toluene-d_8	141.8	298	2.81 ± 0.25	70.4 ± 0.3	298	0.024 ± 0.005	82.2 ± 0.6	298	0.090 ± 0.005	79.0 ± 0.1
benzene-d_6	143.5	298	2.42 ± 0.05	70.8 ± 0.1	298	0.024 ± 0.002	82.2 ± 0.2	298	0.073 ± 0.005	79.5 ± 0.2
THF-d_8	156.5	298	2.55 ± 0.03	70.7 ± 0.1	298	0.019 ± 0.002	82.8 ± 0.3	298	0.103 ± 0.005	78.6 ± 0.1
CD_2Cl_2	171.9	298	0.742 ± 0.010	73.7 ± 0.1	298	0.0067 ± 0.0010	85.4 ± 0.4	298	0.028 ± 0.014	81.8 ± 1.8
acetone-d_6	176.5	298	1.07 ± 0.03	72.8 ± 0.1	310	0.037 ± 0.002	84.5 ± 0.2	310	0.197 ± 0.005	80.2 ± 0.1
CD_3CN	190.8	298	0.469 ± 0.011	74.9 ± 0.1	310	0.019 ± 0.001	86.2 ± 0.2	298	0.029 ± 0.001	81.8 ± 0.1
ethanol-d_6	217.1	310	0.787 ± 0.022	76.6 ± 0.1	310	0.011 ± 0.002	87.6 ± 0.6	310	0.027 ± 0.002	85.3 ±0.2
methanol-d_4	232.2	310	0.575 ± 0.035	77.4 ± 0.2	310	0.0085 ± 0.0011	88.3 ± 0.4	310	0.025 ± 0.004	85.5 ± 0.5
D_2O	264.0	298	0.019 ± 0.002	82.8 ± 0.3	310	0.0015 ± 0.0008	92.8 ± 1.9	310	0.009 ± 0.001	88.2 ± 0.3

Copies of the NMR spectra for the Pdc derivatives

Compound **2a** in deuterium oxide:





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FIDRES 1.243923 Hz
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RG 2050
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DE 10.00 usec
TE 299.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 32

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NUC1 13C
P1 11.50 usec
PLW1 250.00000000 W

======== CHANNEL f2 ========
SFO2 700.1728007 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 15.00000000 W
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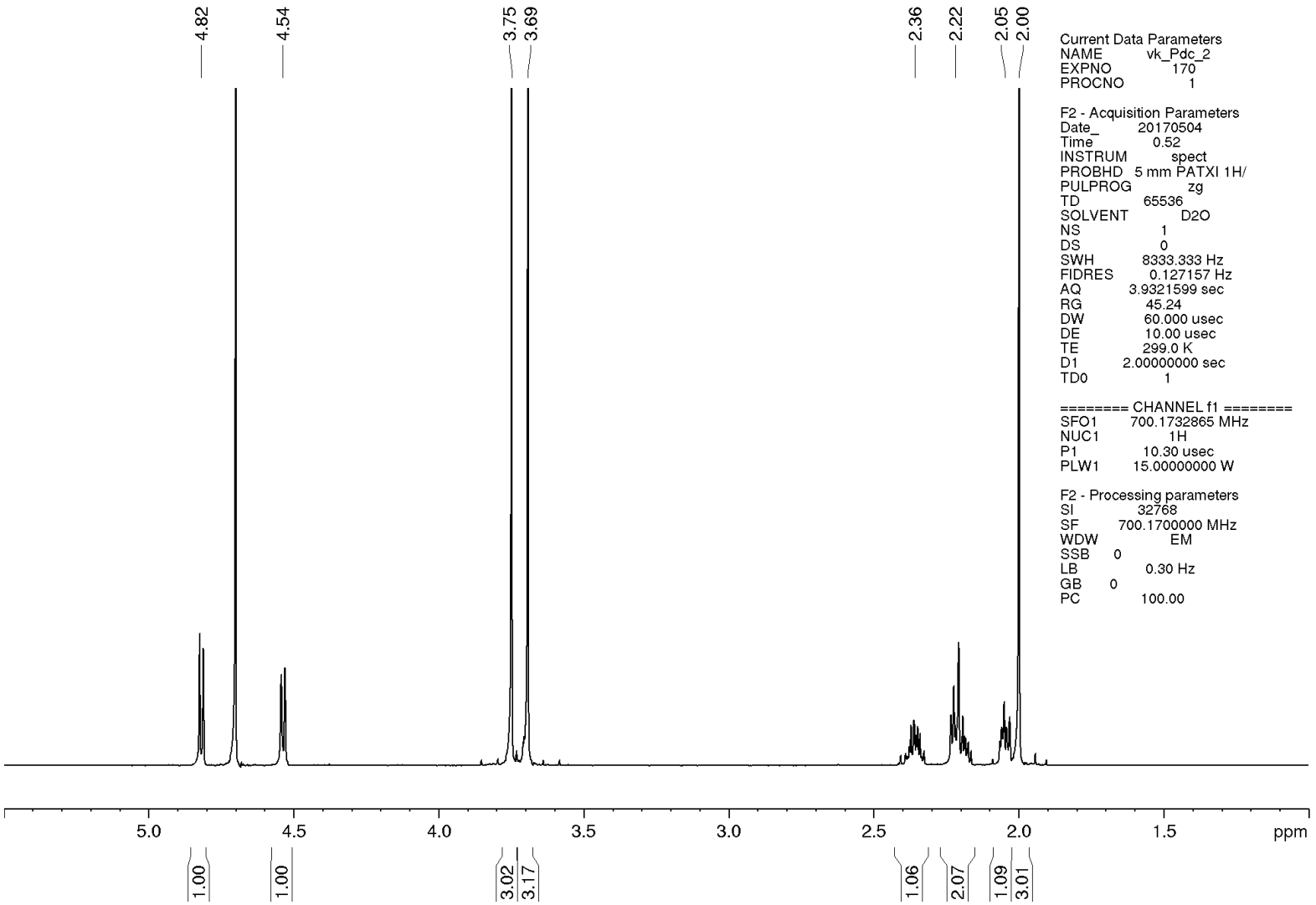
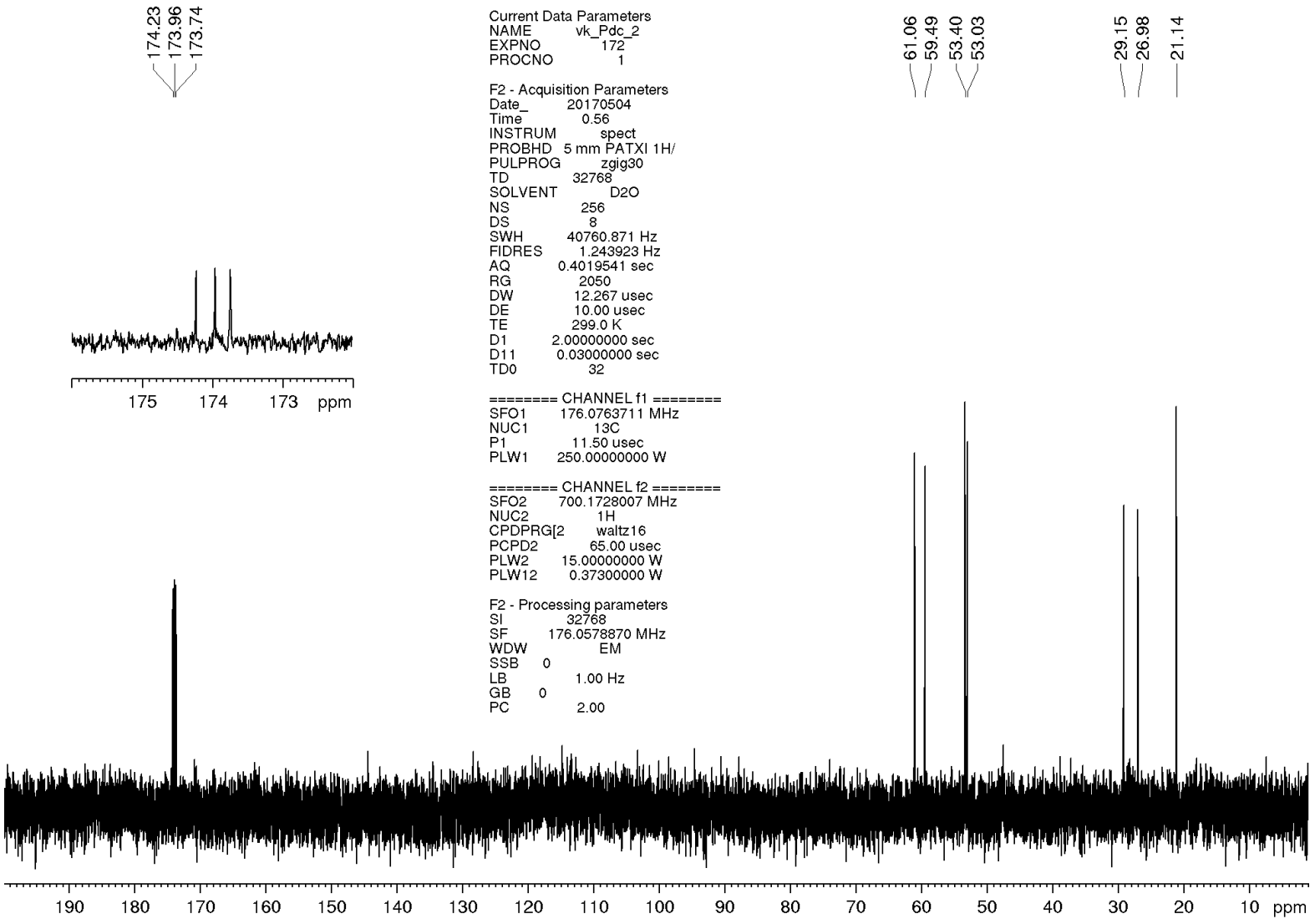
Compound **3a** in deuterium oxide

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DE 10.00 usec
TE 299.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 32
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NUC1 13C
P1 11.50 usec
PLW1 250.00000000 W
======== CHANNEL f2 ========
SFO2 700.1728007 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 15.00000000 W
PLW12 0.37300000 W
F2 - Processing parameters
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SF 176.0578870 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
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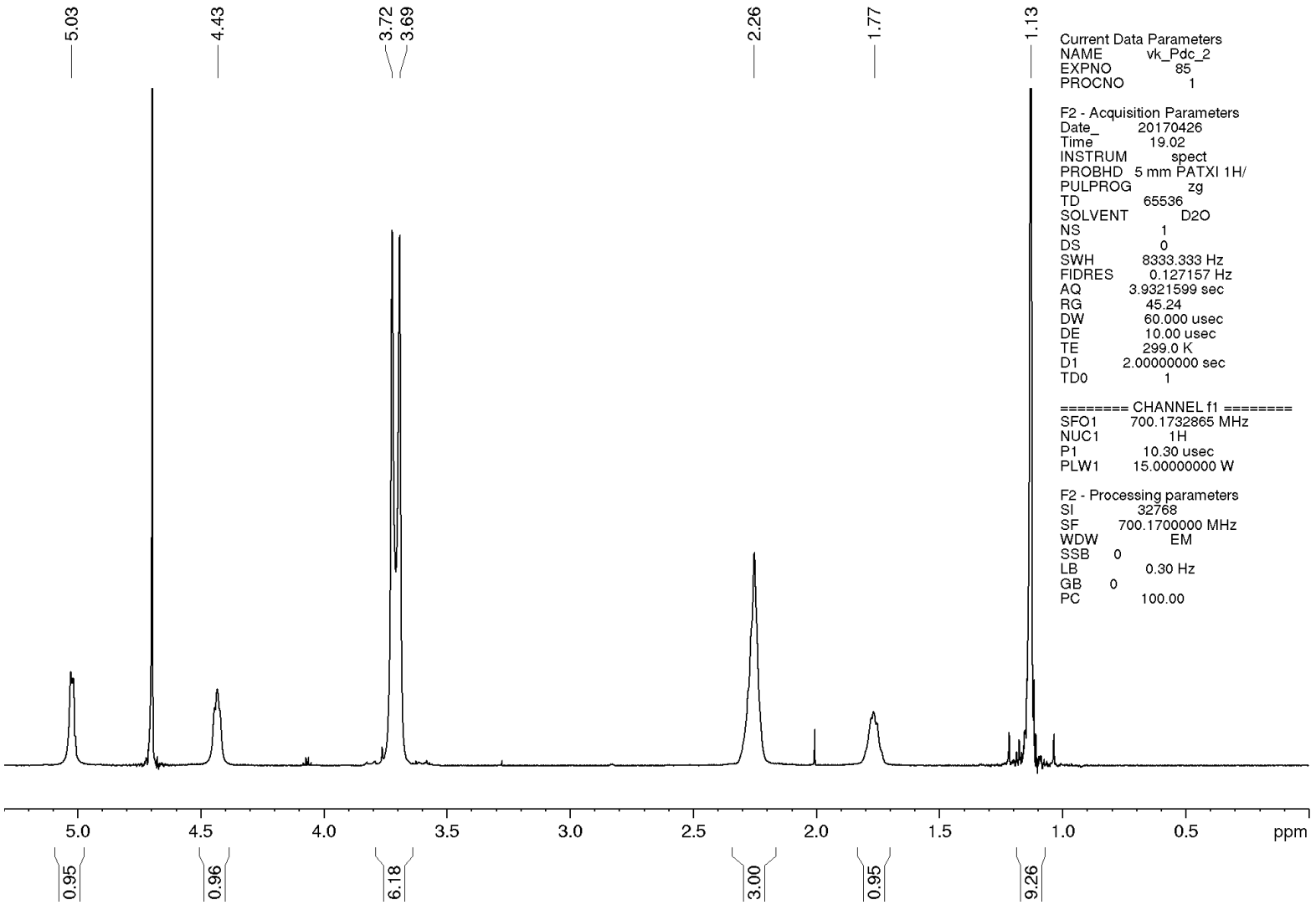
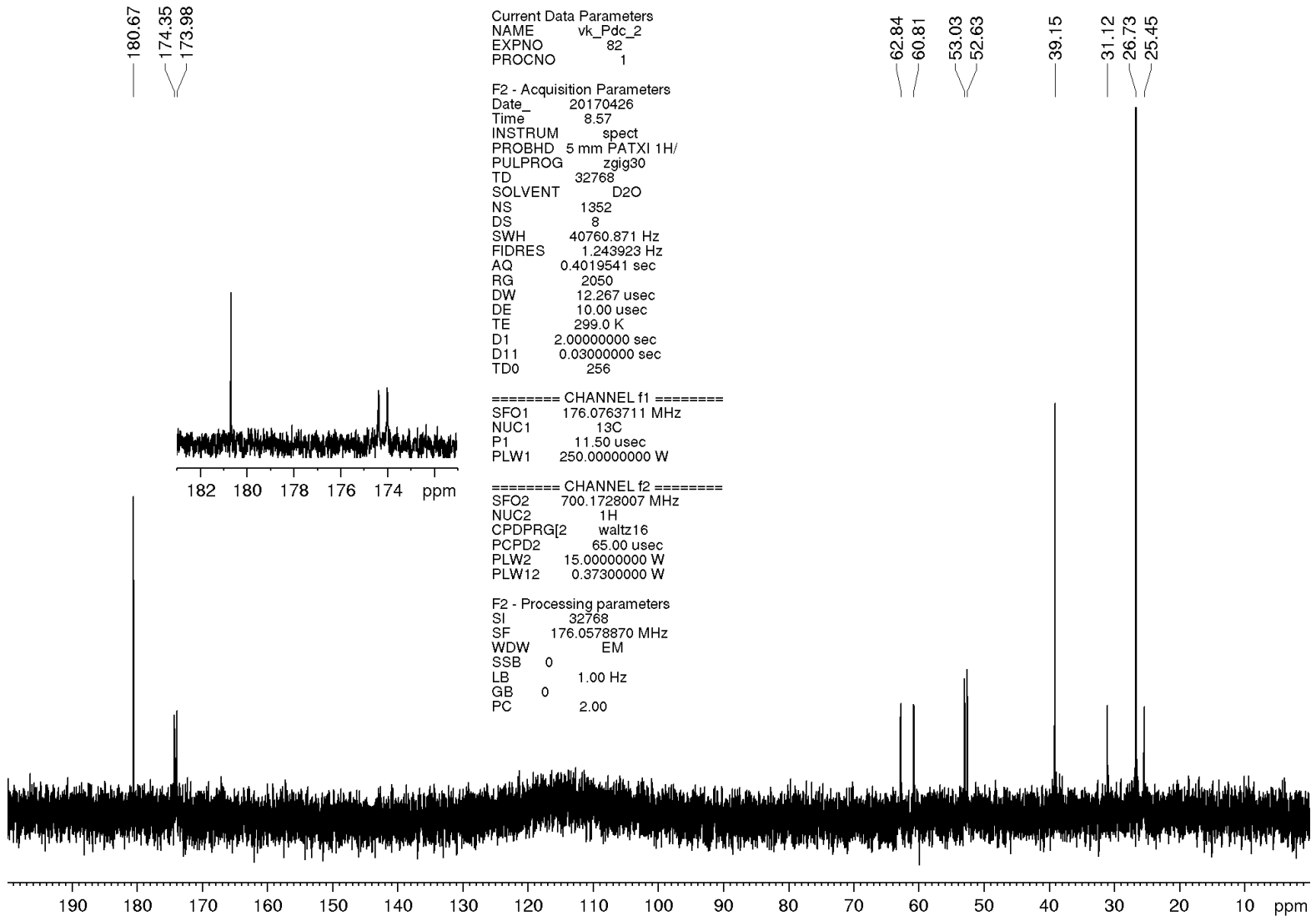
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Compound **2b** in deuterium oxide

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53.03
52.63
39.15
31.12
26.73
25.45
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PROCNO 1
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FIDRES 1.243923 Hz
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RG 2050
DW 12.267 usec
DE 10.00 usec
TE 299.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 256
======== CHANNEL f1 ========
SFO1 176.0763711 MHz
NUC1 13C
P1 11.50 usec
PLW1 250.00000000 W
======== CHANNEL f2 ========
SFO2 700.1728007 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 15.00000000 W
PLW12 0.37300000 W
F2 - Processing parameters
SI 32768
SF 176.0578870 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 2.00
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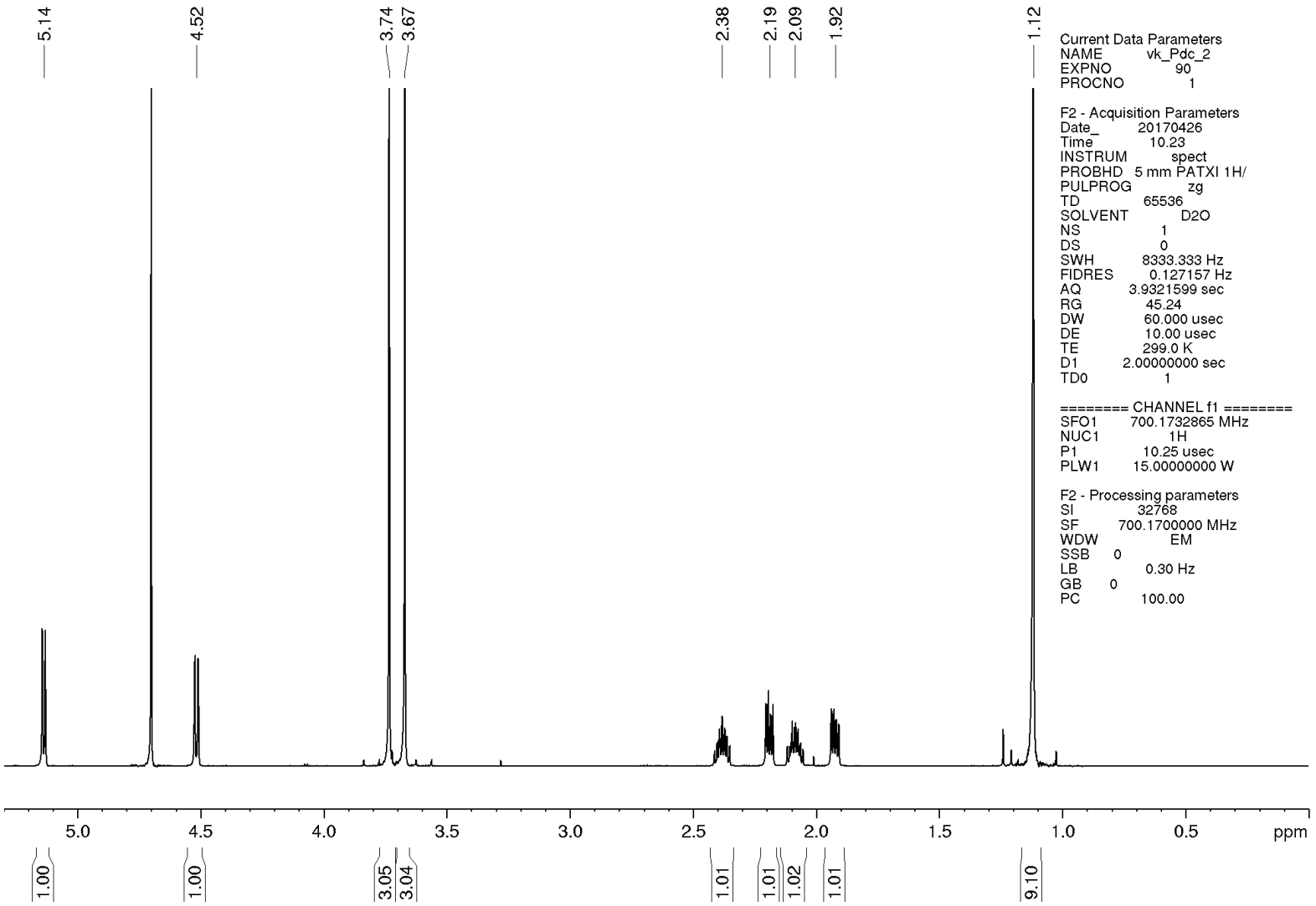
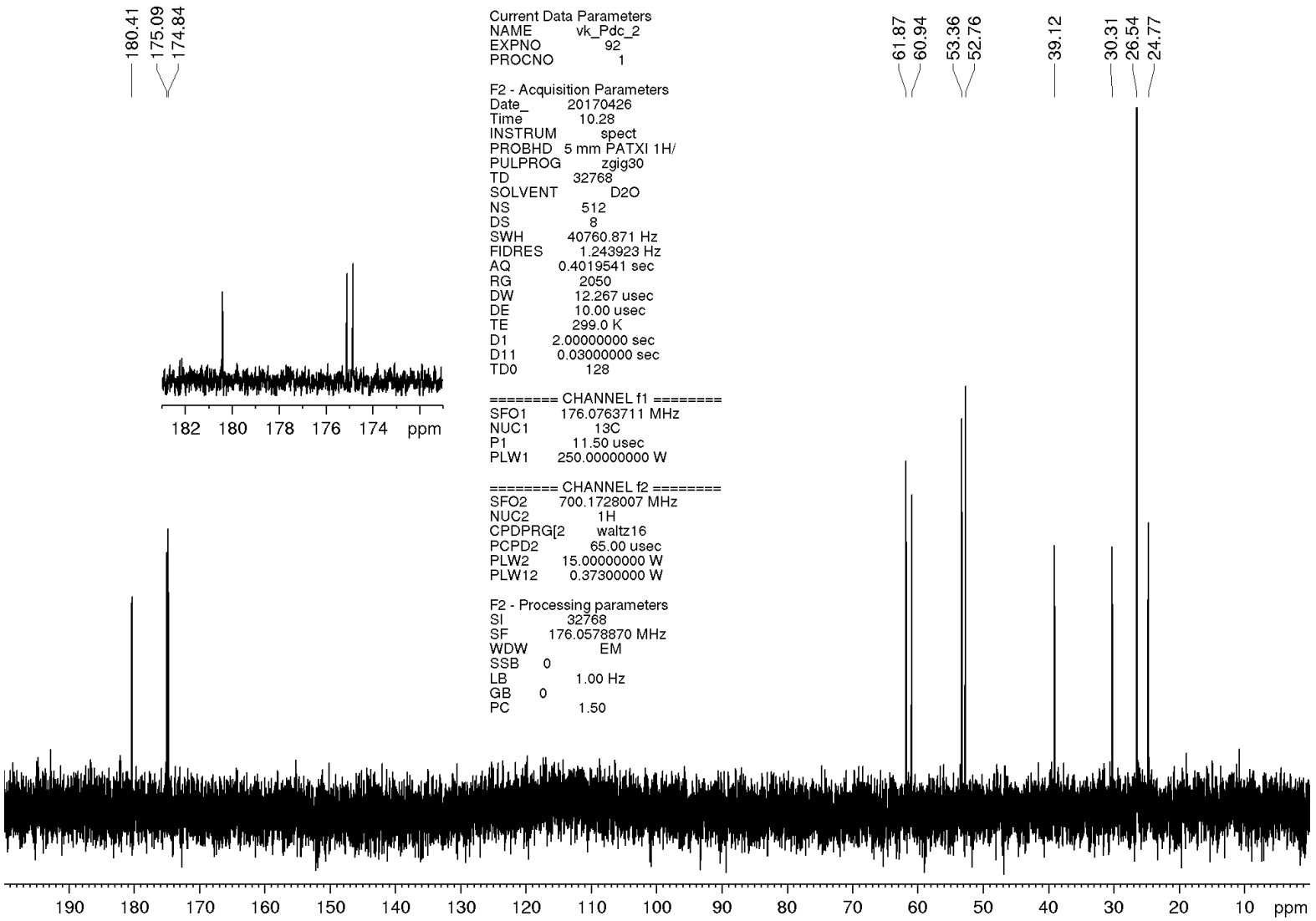
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Compound **3b** in deuterium oxide





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FIDRES 1.243923 Hz
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RG 2050
DW 12.267 usec
DE 10.00 usec
TE 299.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 128

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NUC1 13C
P1 11.50 usec
PLW1 250.00000000 W

======== CHANNEL f2 ========
SFO2 700.1728007 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 15.00000000 W
PLW12 0.37300000 W

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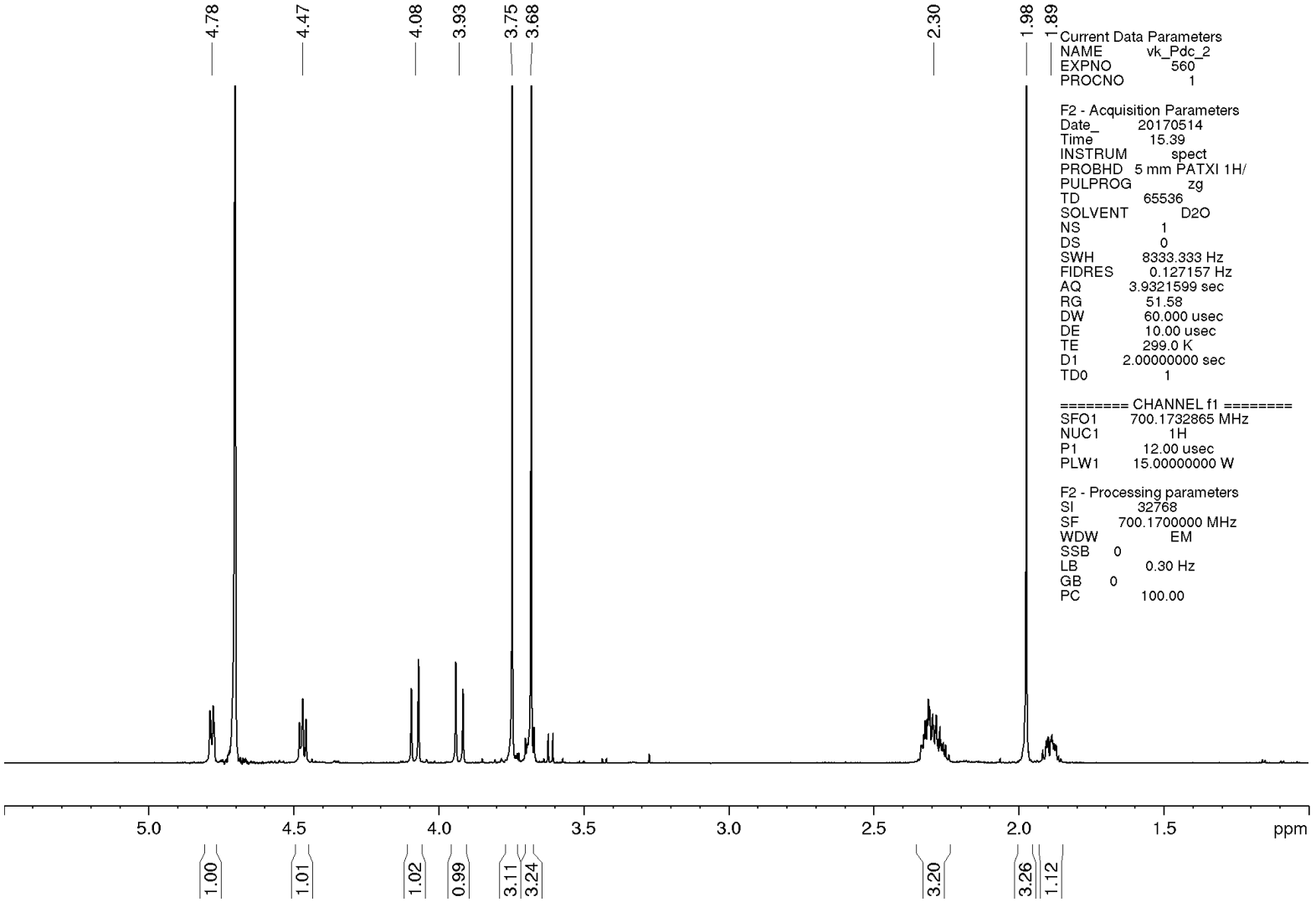
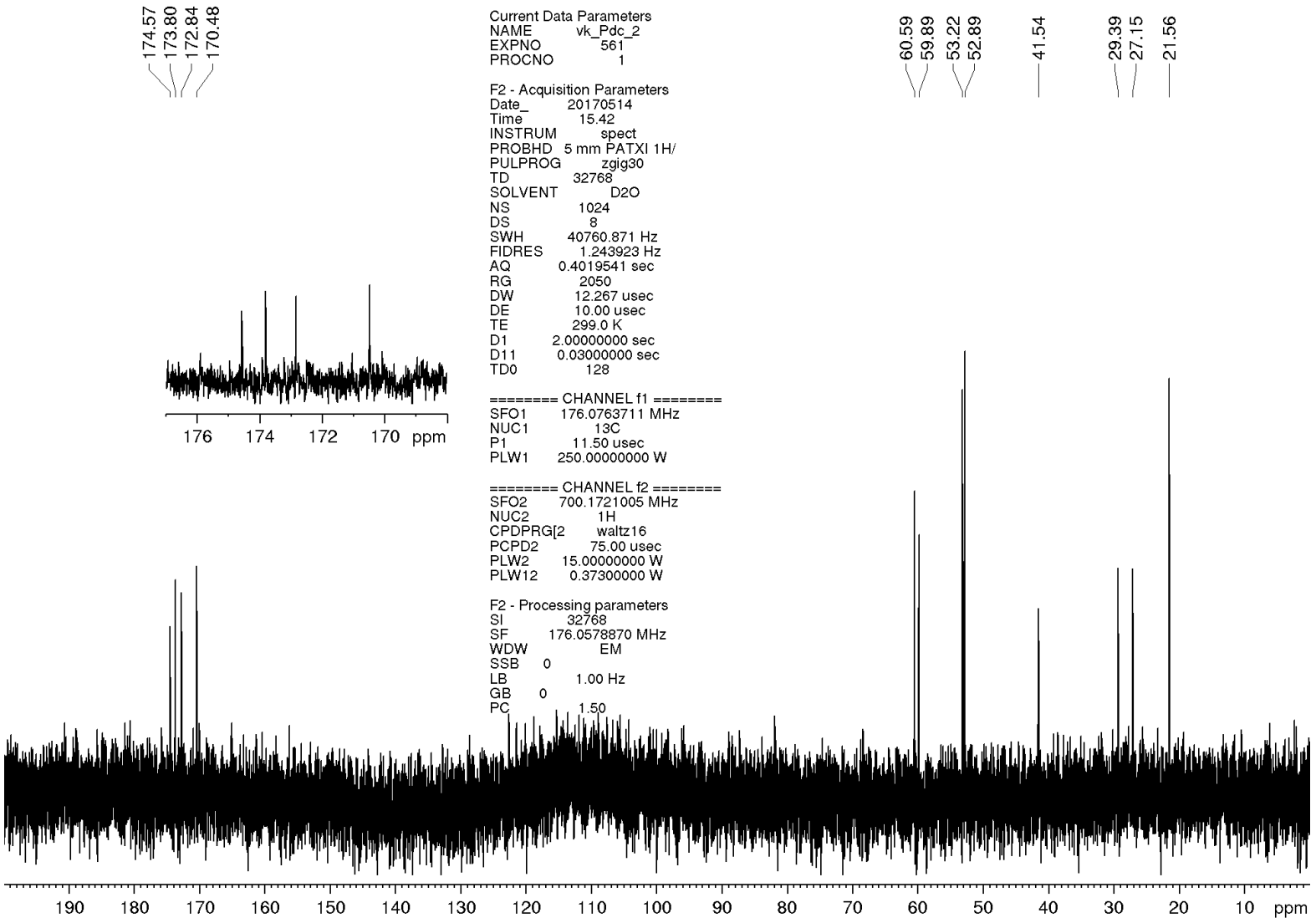
SF 176.0578870 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.50

Compound **2c** in buffered deuterium oxide

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173.80
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59.89
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52.89
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29.39
27.15
21.56
Current Data Parameters
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PROCNO 1
F2 - Acquisition Parameters
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PULPROG zgig30
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FIDRES 1.243923 Hz
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D11 0.03000000 sec
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SFO2 700.1721005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 75.00 usec
PLW2 15.00000000 W
PLW12 0.37300000 W
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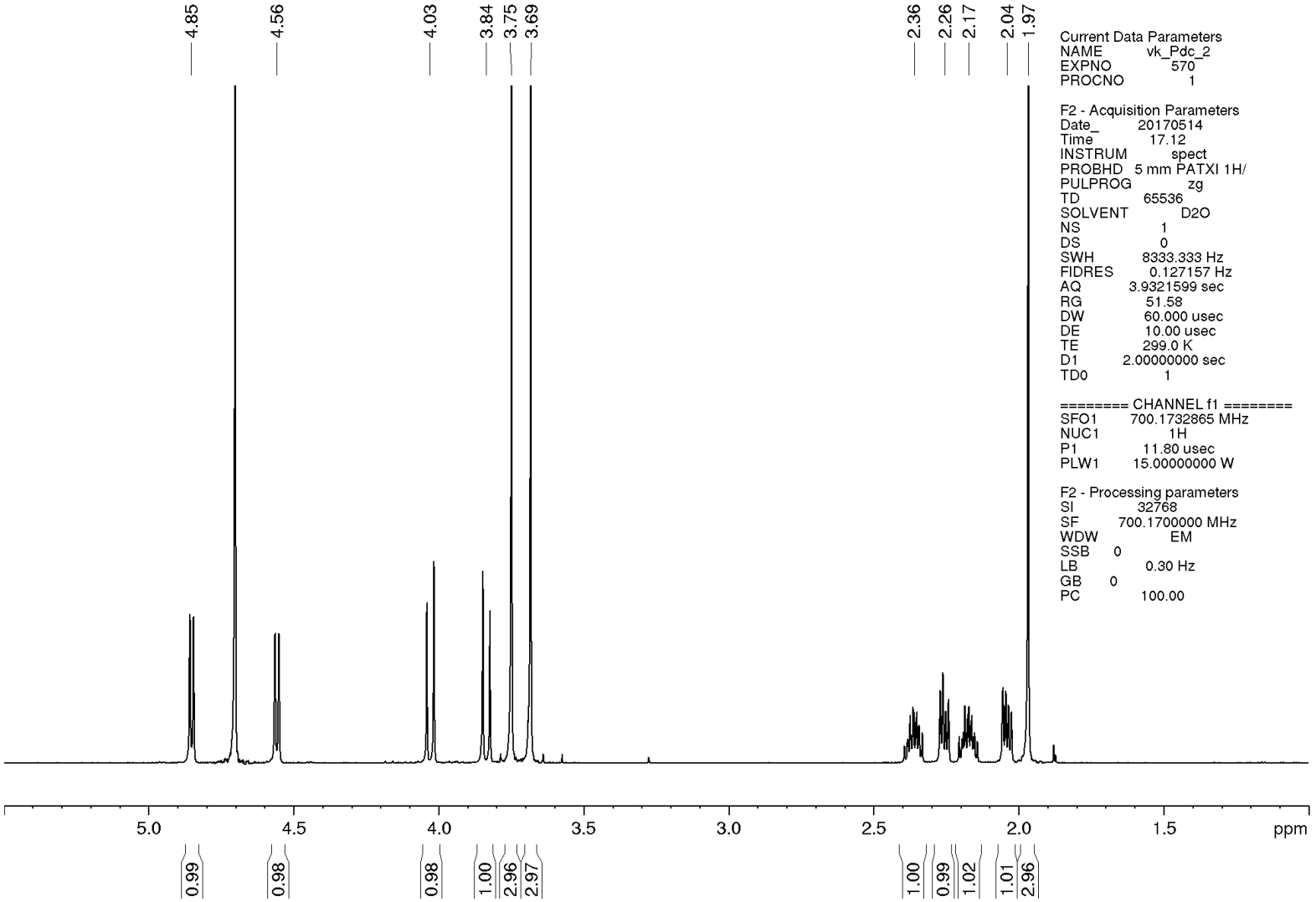
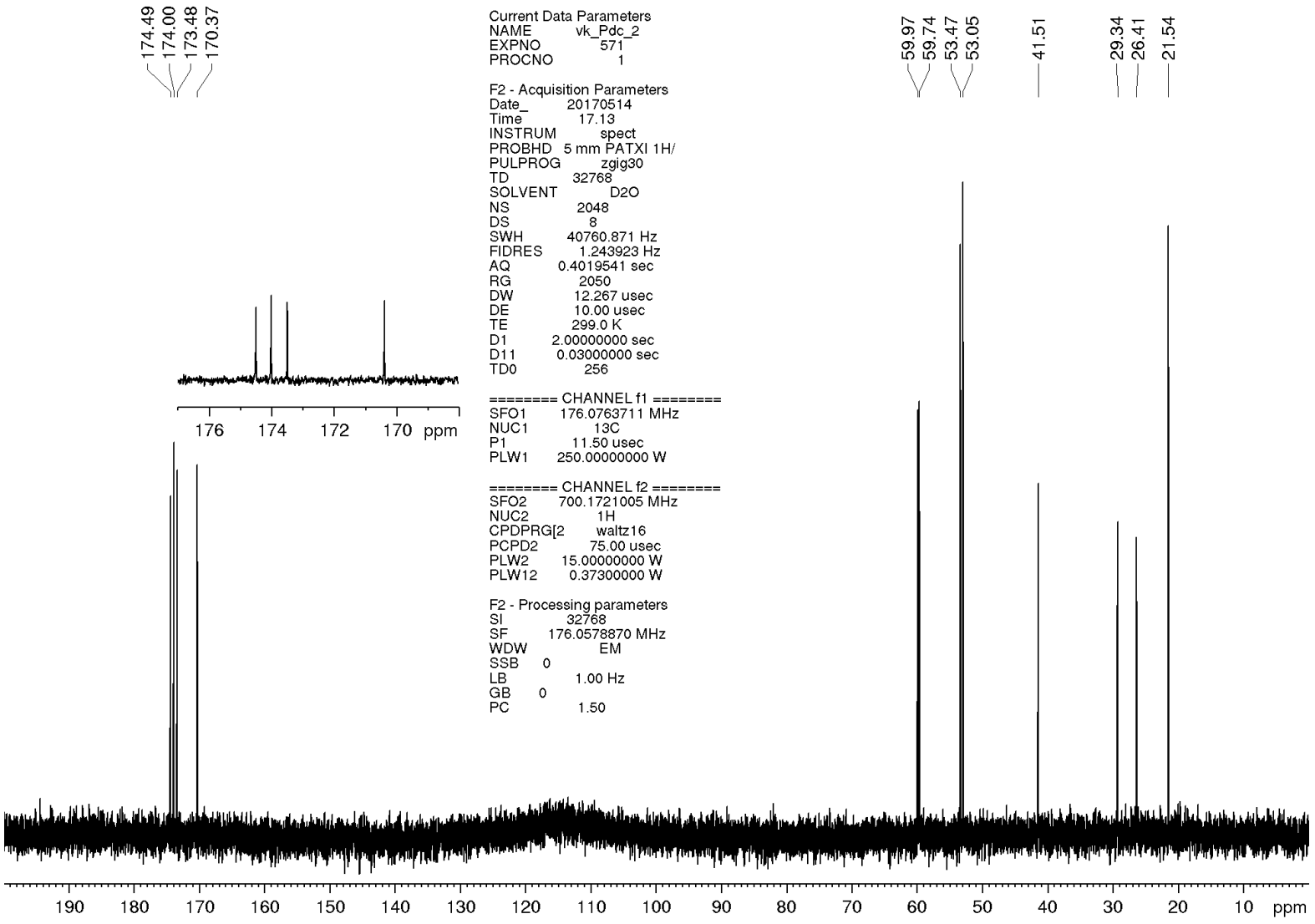
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.50
176
174
172
170 ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

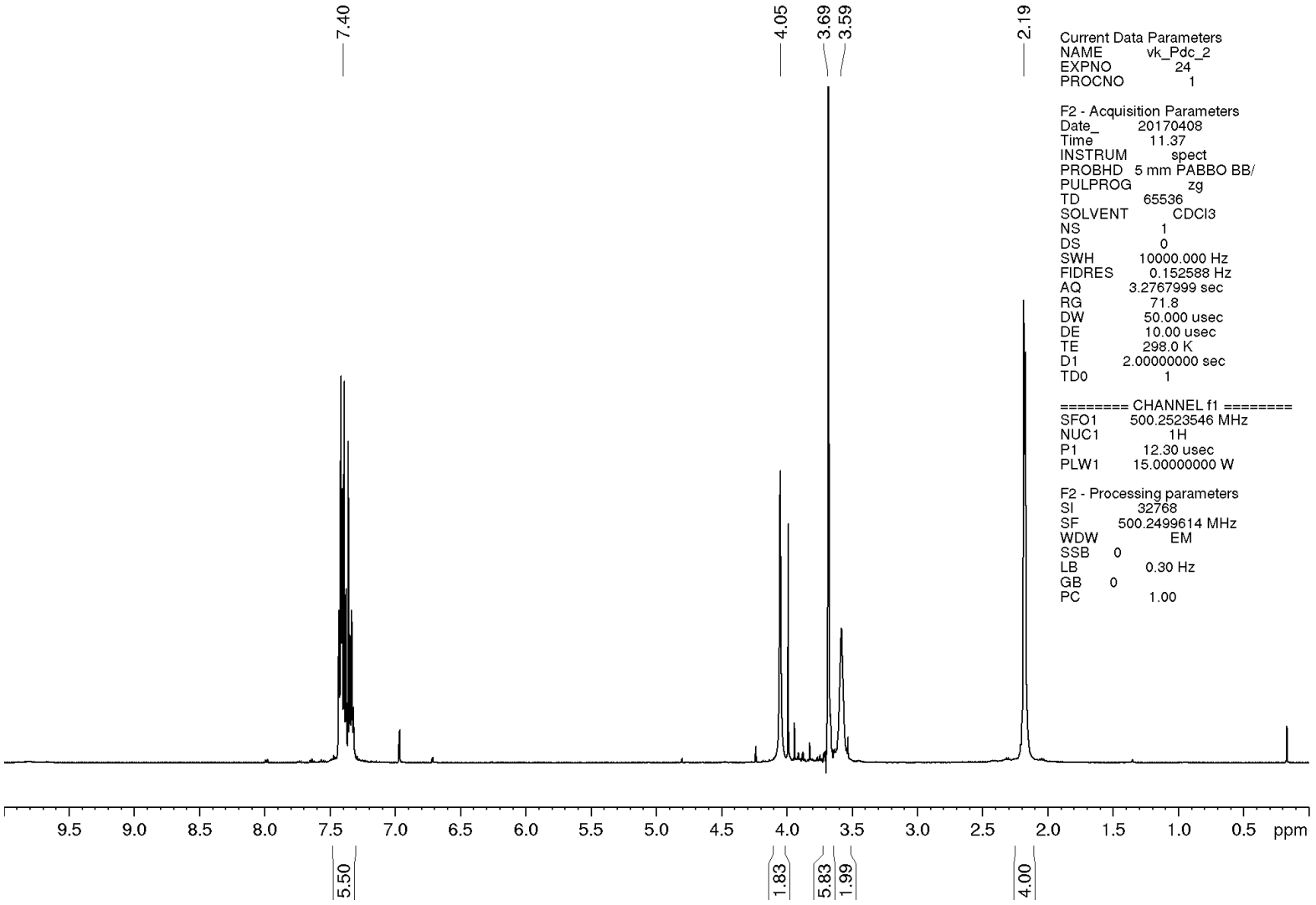
Compound **3c** in buffered deuterium oxide



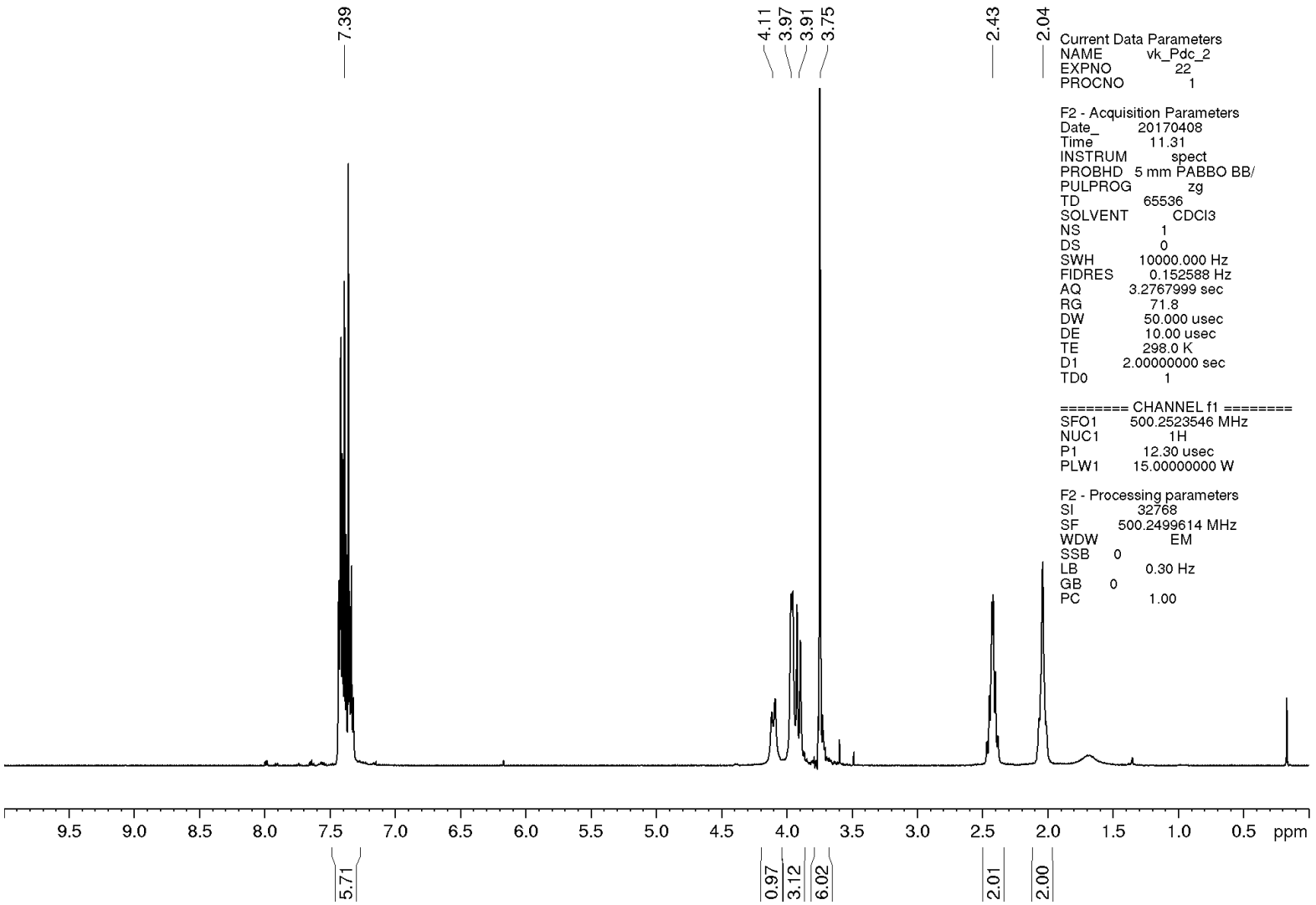

174.49
174.00
173.48
170.37
59.97
59.74
53.47
53.05
41.51
29.34
26.41
21.54
Current Data Parameters
NAME vk_Pdc_2
EXPNO 571
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170514
Time 17.13
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zgig30
TD 32768
SOLVENT D2O
NS 2048
DS 8
SWH 40760.871 Hz
FIDRES 1.243923 Hz
AQ 0.4019541 sec
RG 2050
DW 12.267 usec
DE 10.00 usec
TE 299.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 256
======== CHANNEL f1 ========
SFO1 176.0763711 MHz
NUC1 13C
P1 11.50 usec
PLW1 250.00000000 W
======== CHANNEL f2 ========
SFO2 700.1721005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 75.00 usec
PLW2 15.00000000 W
PLW12 0.37300000 W
F2 - Processing parameters
SI 32768
SF 176.0578870 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.50
176 174 172 170 ppm
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Copies of the NMR spectra for rest of compounds

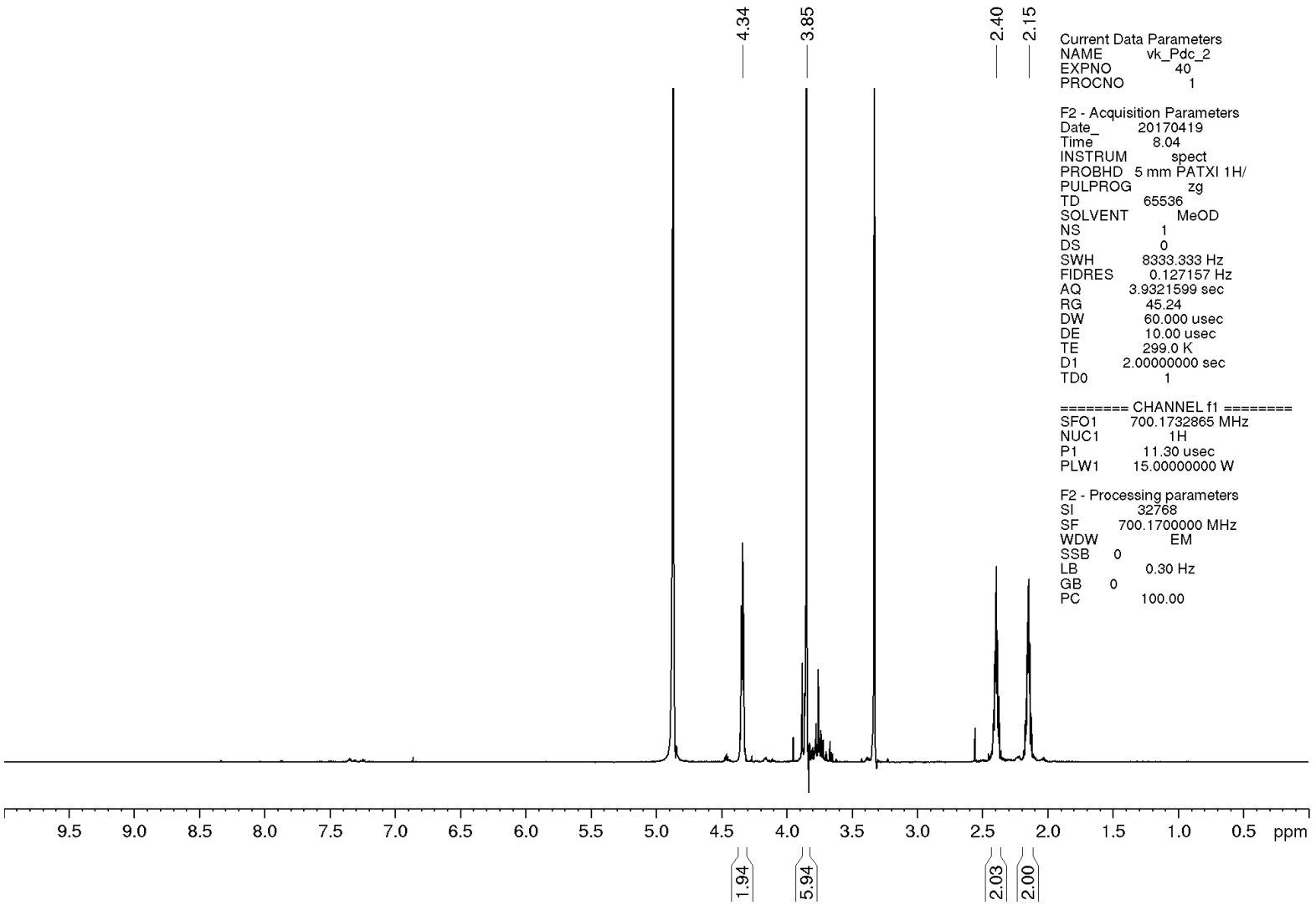
Bn-(MeO)mPdc-OMe in chloroform-d



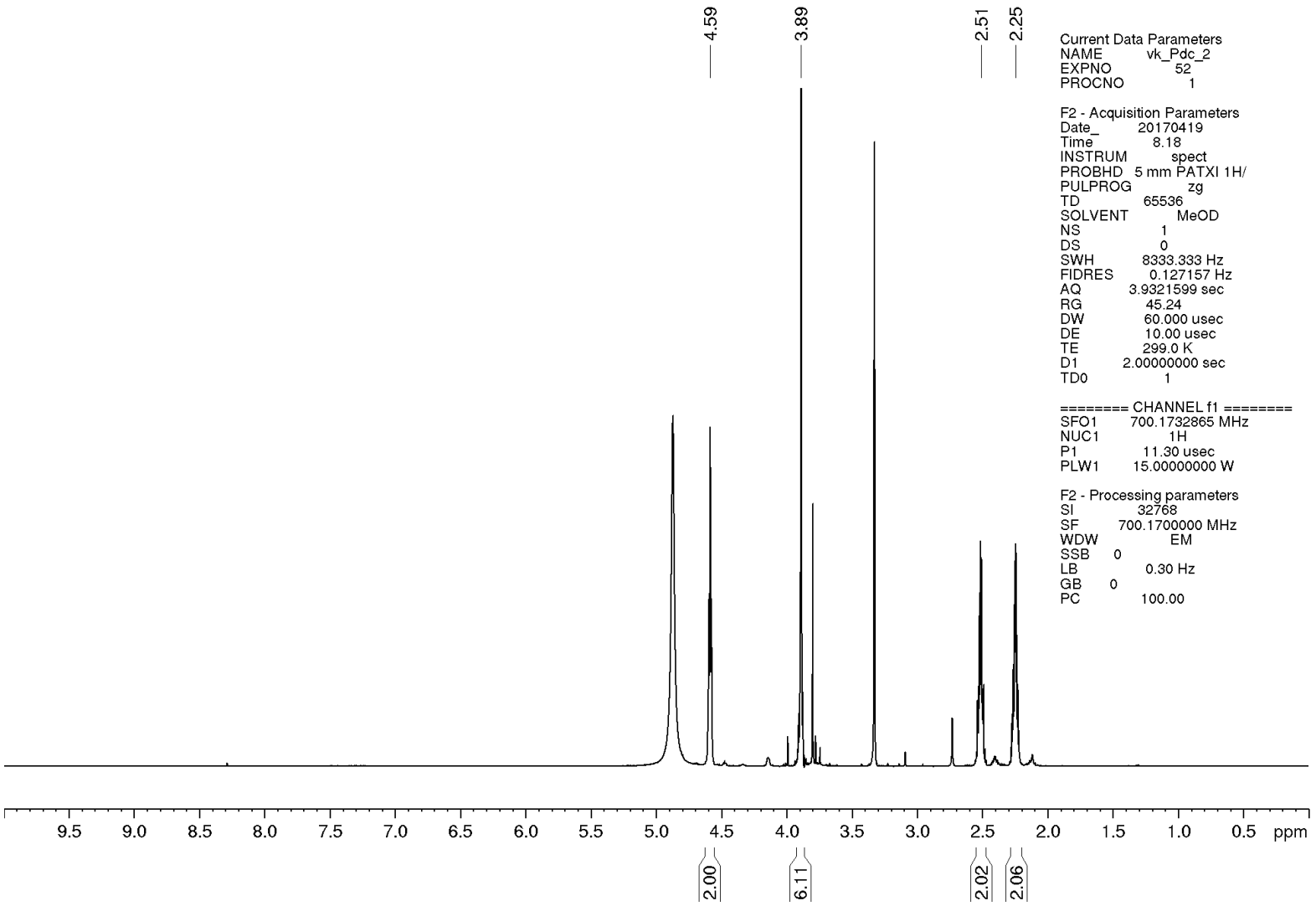
Bn-(MeO)rPdc-OMe in chloroform-d



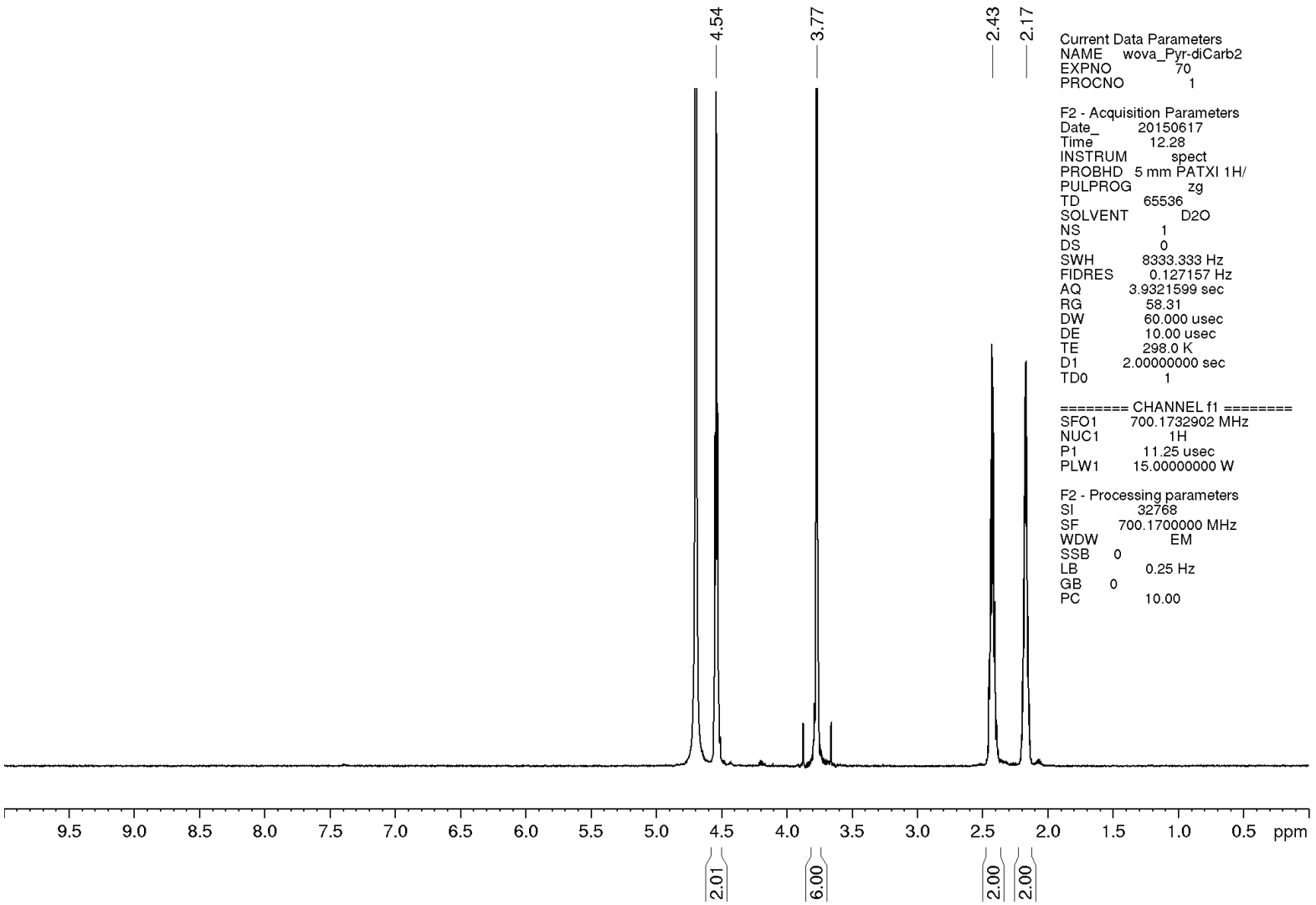
HCl·H-(MeO)mPdc-OMe in methanol-d_4



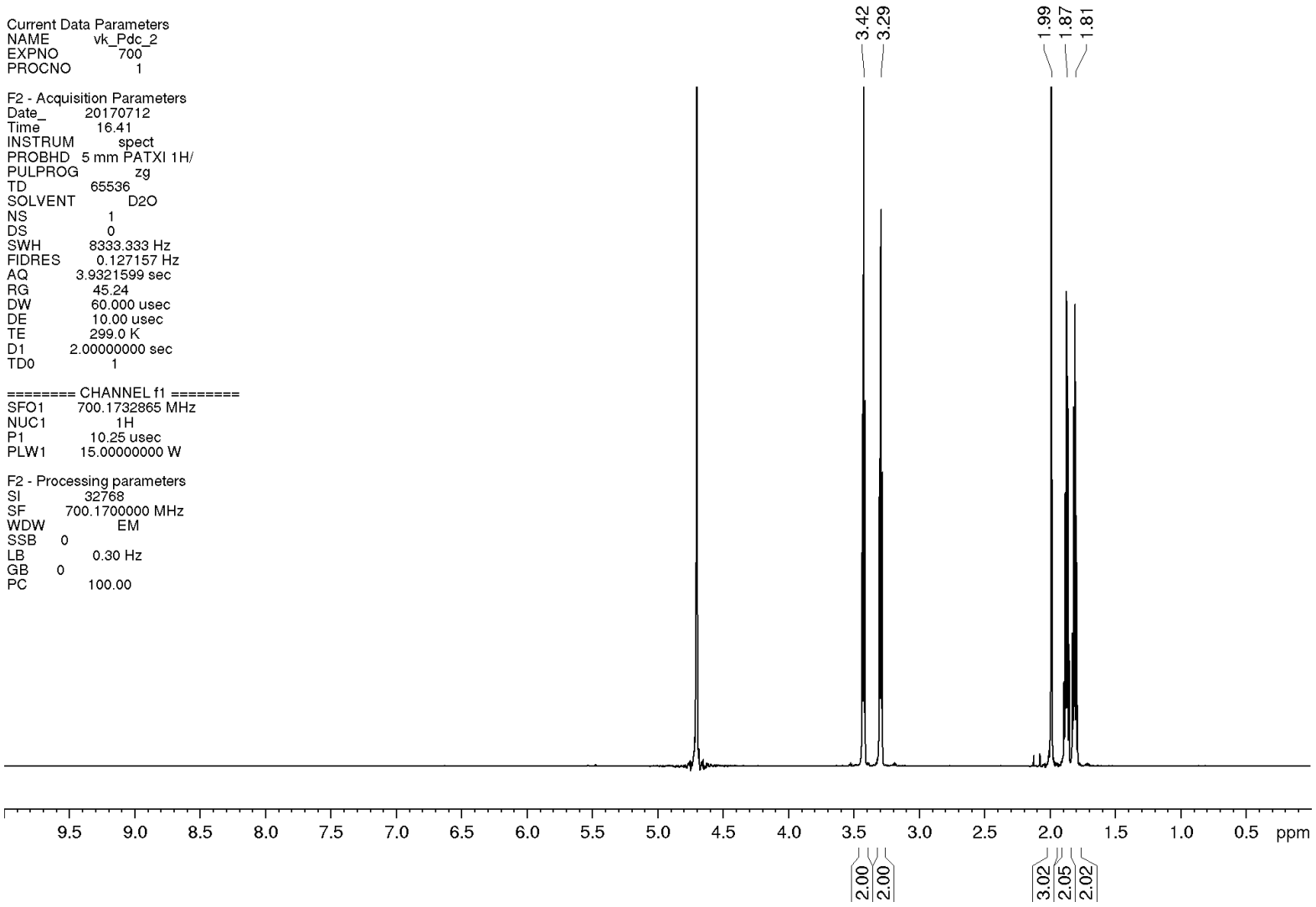
HCl·H-(MeO)rPdc-OMe in methanol-d_4



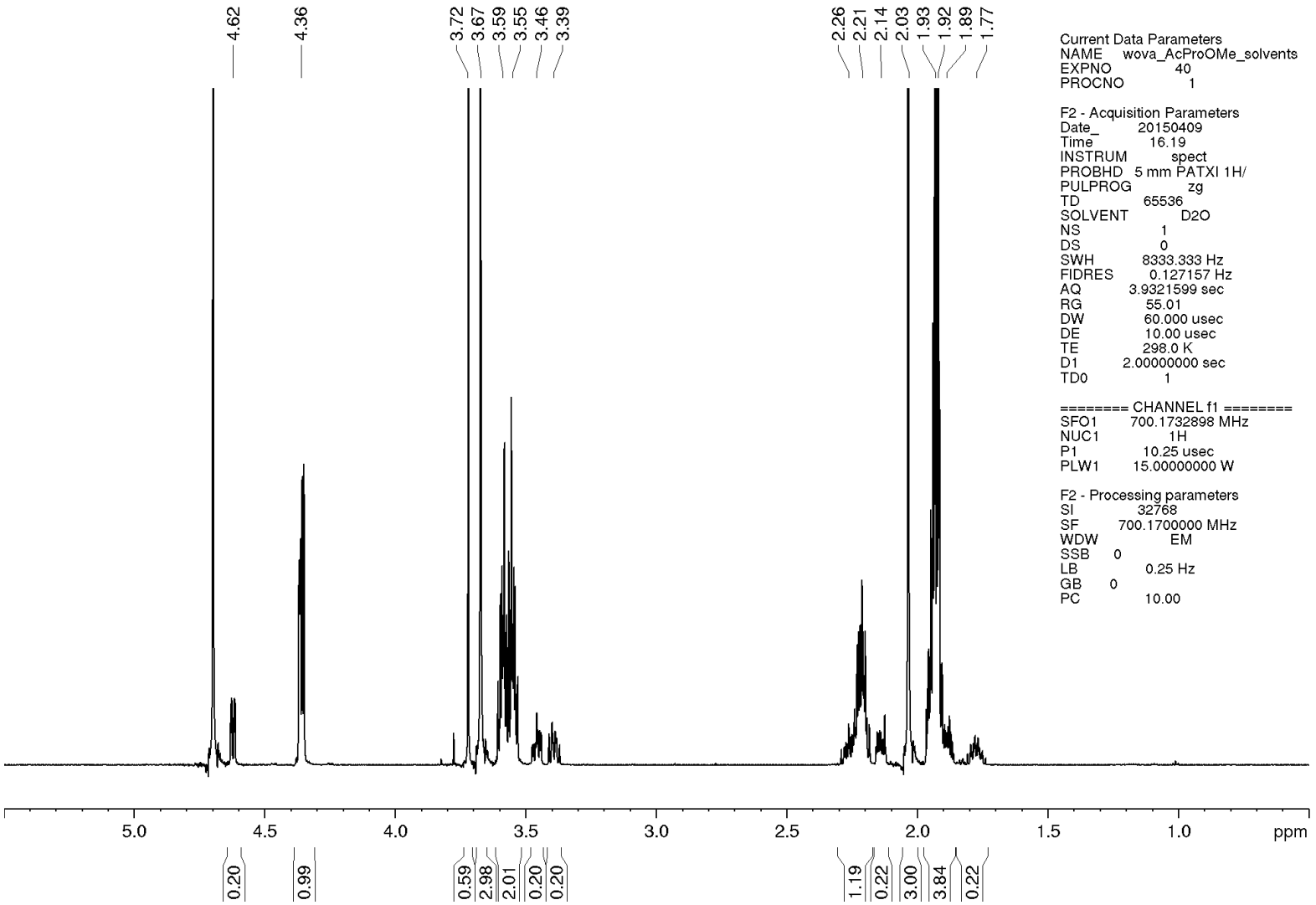
in deuterium oxide:



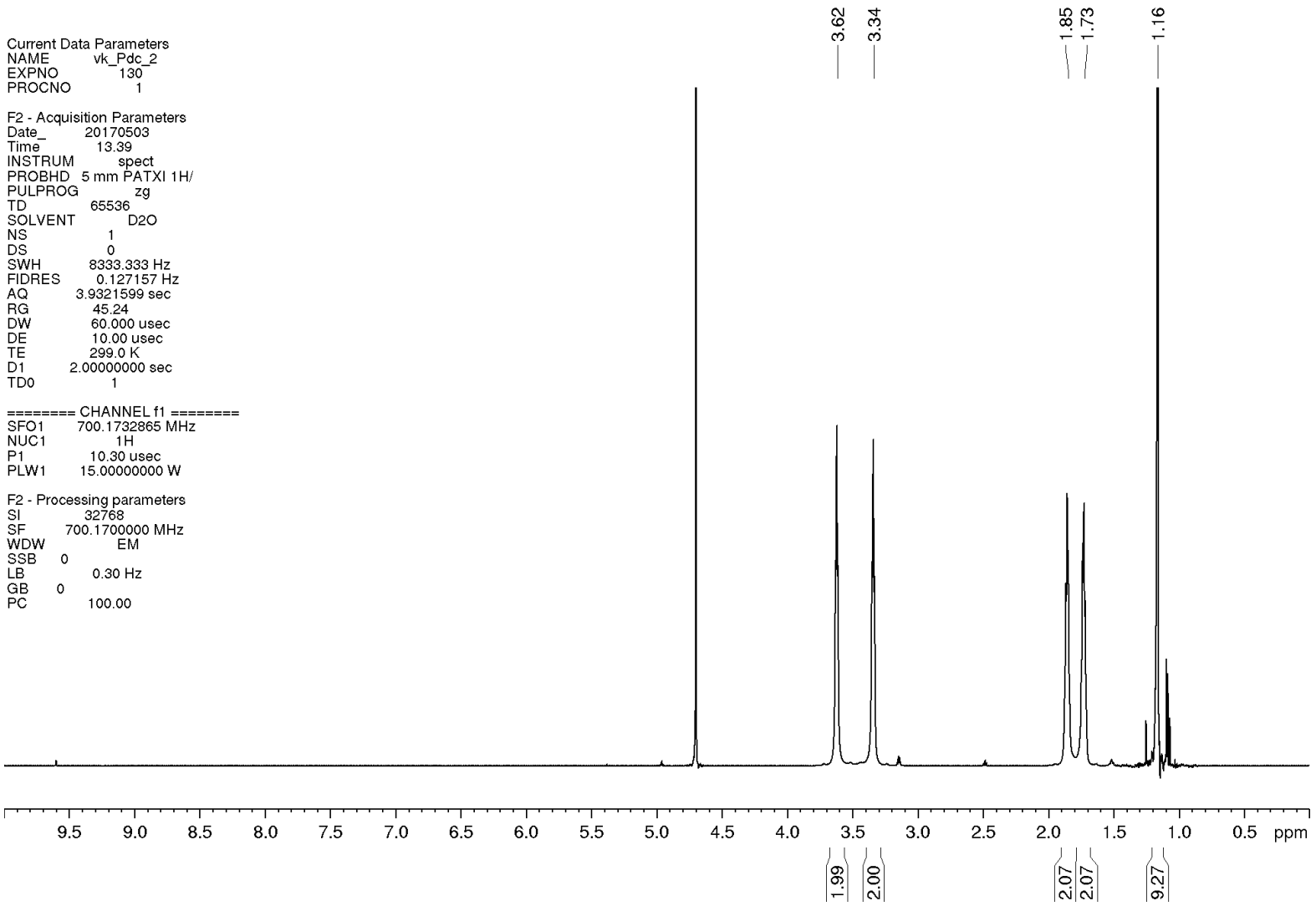
Compound **4a** in deuterium oxide:



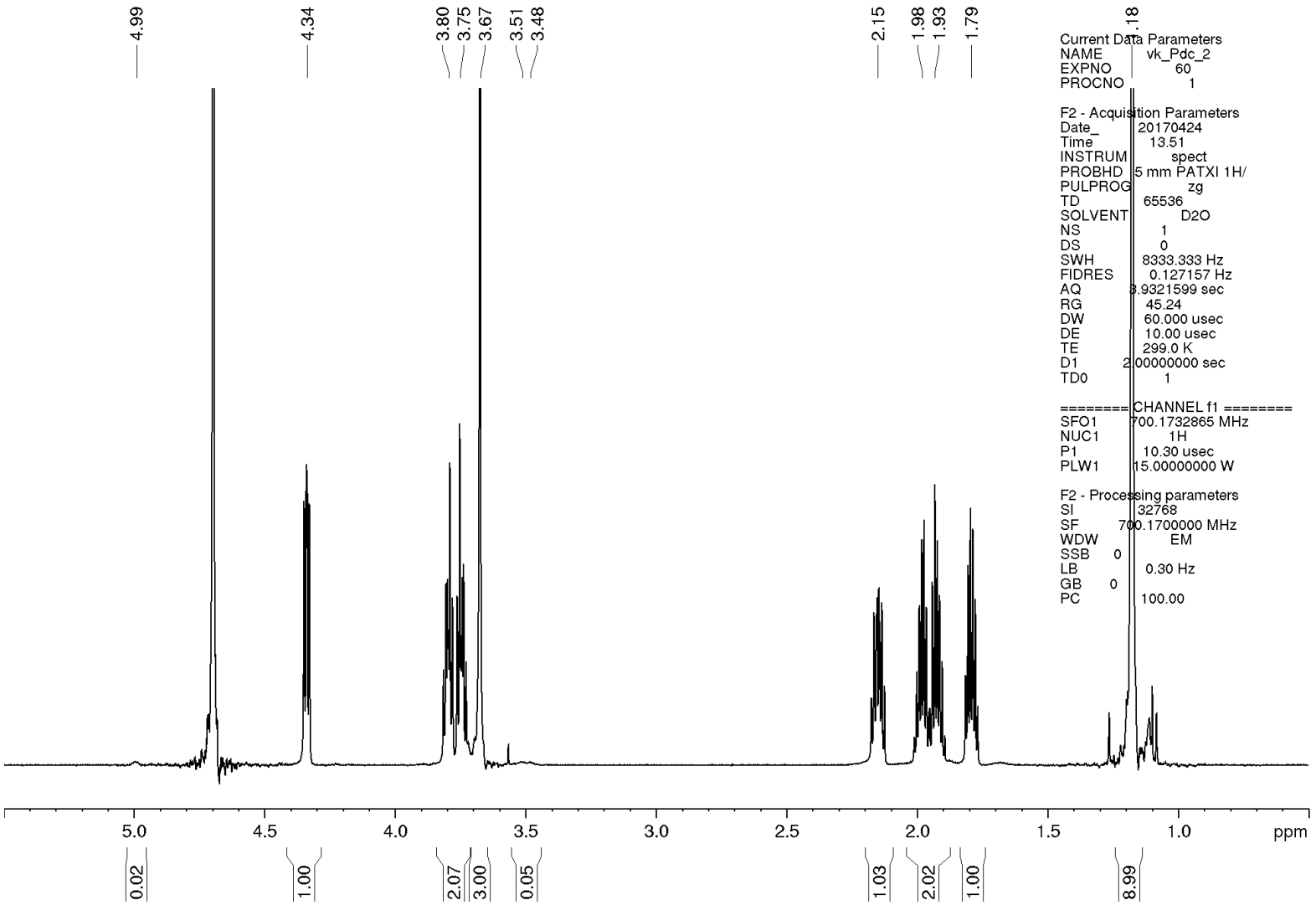
Compound **5a** in deuterium oxide:



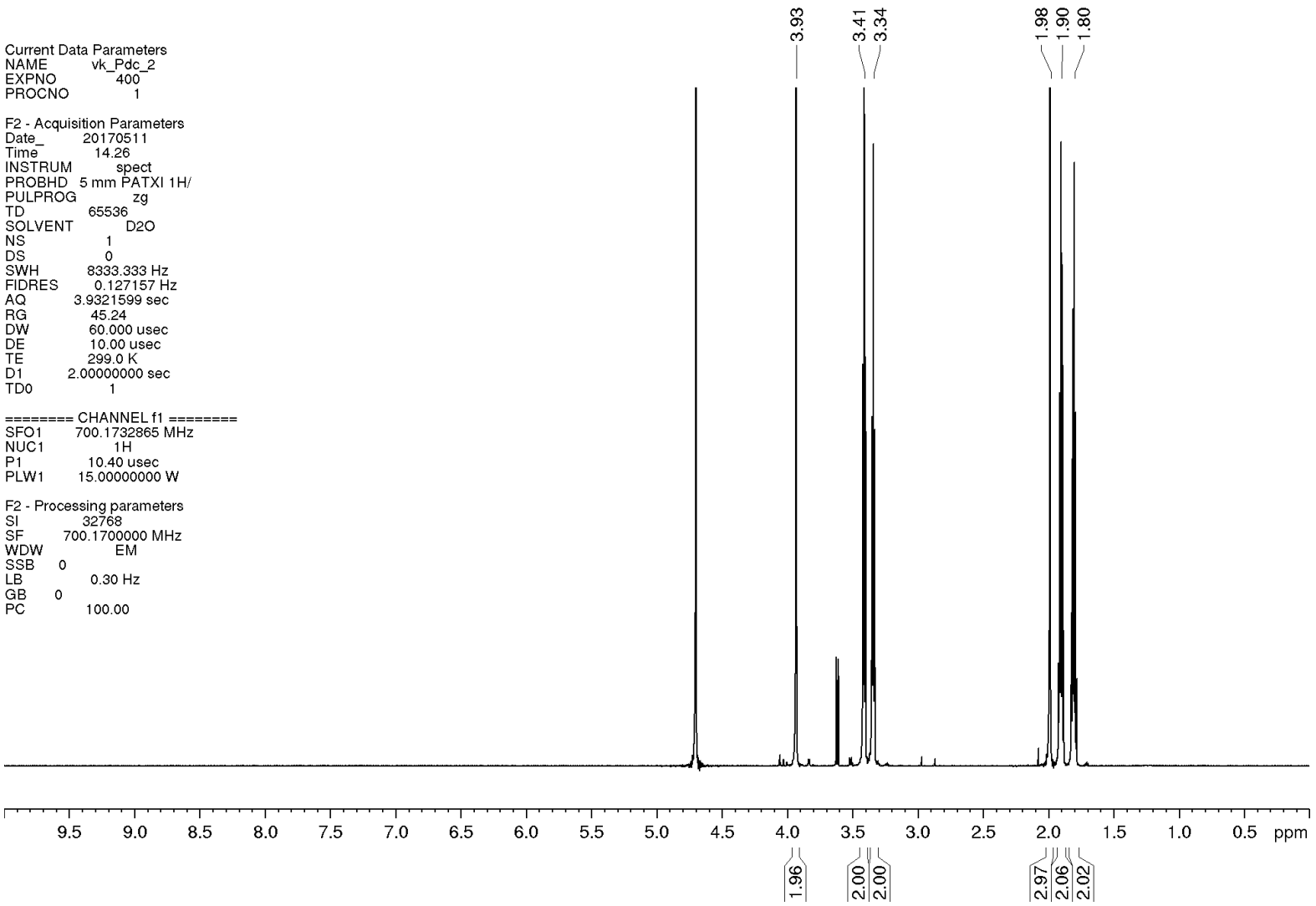
Compound **4b** in deuterium oxide:



Compound **5b** in deuterium oxide:



Compound **4c** in buffered deuterium oxide



Compound **5c** in deuterium oxide: