

Supplementary Material

Fluorinated and *N*-Acryloyl-Modified 3,5-Di[(*E*)-benzylidene]piperidin-4-one curcuminoids for the treatment of pancreatic carcinoma

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Table S1. Inhibitory concentrations (IC₅₀ in μM)¹ of EF24 and compound **2d** when applied to immortalized normal pancreatic ductal cells HPNE and monocyte cell line THP-1 after 72 h.

Cell lines	EF24	2d
HPNE	2.3 \pm 0.64	2.05 \pm 0.39
THP1	> 10 μM	>10 μM

¹ IC₅₀ values \pm SD were calculated from the dose-response curves of three independent experiments.

Table S2. Statistical analysis of dose-response curves of EF24 (**1a**), **2c**, **2d**, and **2g–i** in MiaPaCa-2 and Panc-1 pancreatic cancer cells at the indicated time points.

p values							
	Concentration (μM)	MiaPaCa-2			Panc-1		
		24 h	48 h	72 h	24 h	48 h	72 h
EF24	0						
	0.15625	0.02802	0.000758	0.068558	0.825069	0.003479	0.02982
	0.3125	0.001909	0.160187	0.033967	0.965481	0.000306	0.0442
	0.625	0.00463	0.078627	0.0003	0.879541	0.030057	0.00482
	1.25	0.008242	0.077355	0.003001	0.772516	0.048285	0.005496
	2.5	0.002328	0.000443	2.45E-05	0.22838	0.00056	0.000443
	5	0.002841	0.005327	1.07E-05	0.02047	0.000374	1.51E-05
2c	0						
	0.15625	0.001165	0.015913	0.067368	0.054244	0.063715	0.29907
	0.3125	0.010269	0.02312	0.00322	0.013919	0.023115	0.184221
	0.625	0.038427	0.013691	0.000206	0.001012	0.04302	0.040358
	1.25	0.000617	0.009385	0.00011	0.003523	0.011118	7.86E-05
	2.5	0.000689	0.007545	0.000111	0.013841	0.011989	0.001139
	5	0.000746	0.003014	7.61E-05	0.037907	0.008141	0.00069
2d	0						
	0.15625	0.070948	0.016849	0.026471	0.609201	0.009397	0.390053
	0.3125	0.022205	0.020083	0.000238	0.459126	0.052244	0.095258
	0.625	0.066718	0.015383	0.014833	0.093038	0.011609	0.004116
	1.25	0.040853	0.011428	0.00848	0.002466	8.68E-05	2.41E-09
	2.5	0.087131	0.015555	0.009426	0.000557	3.34E-05	1.62E-05
	5	0.039226	0.011247	0.011479	0.000214	2.79E-05	1.59E-05
2g	0						
	0.15625	9.21E-05	0.010536	0.722117	0.431106	0.203007	0.200738
	0.3125	0.007664	0.003592	0.033492	0.59158	0.192595	0.073197
	0.625	0.004725	0.000152	0.000186	0.477306	0.012689	0.008118
	1.25	0.001152	0.000109	0.000459	0.023684	3.61E-05	4.7E-06
	2.5	0.00304	7.17E-05	3.84E-05	0.017397	0.000892	1.76E-05
	5	0.002798	7.05E-05	6.28E-05	0.004106	0.000532	8.85E-06
2h	0						
	0.15625	2.99E-05	0.024734	0.074793	0.152711	0.246178	0.112263
	0.3125	0.00783	0.024678	0.007062	0.237733	0.164897	0.037765
	0.625	0.013537	0.004521	0.050885	0.021351	0.056353	0.005605
	1.25	0.016891	0.013405	0.019606	0.00918	0.001286	2.08E-11
	2.5	0.015843	0.016675	0.021269	0.001142	0.004546	8.57E-06
	5	0.014552	0.013094	0.02628	0.002354	0.000816	1.15E-05
2i	0						
	0.15625	0.054276	0.006122	0.067449	0.36447	0.20061	0.008287
	0.3125	0.019464	0.218863	0.00903	0.19091	0.241849	0.002689
	0.625	0.013611	0.018439	0.114977	0.012352	0.024517	0.000628
	1.25	0.000869	0.00129	0.052726	0.001207	1.56E-06	1.35E-05
	2.5	0.000674	0.001366	0.057217	0.004101	8.69E-05	1.4E-06
	5	0.000929	0.00277	0.064769	0.00103	0.000294	0.000231

Figure S1. Apoptosis induction by EF24 (**1a**) and **2d** in pancreatic cancer cell line MiaPaCa-2. Western blots of apoptotic proteins were quantified using Bio-Rad's Image lab software and expressed as compared to actin in arbitrary units.

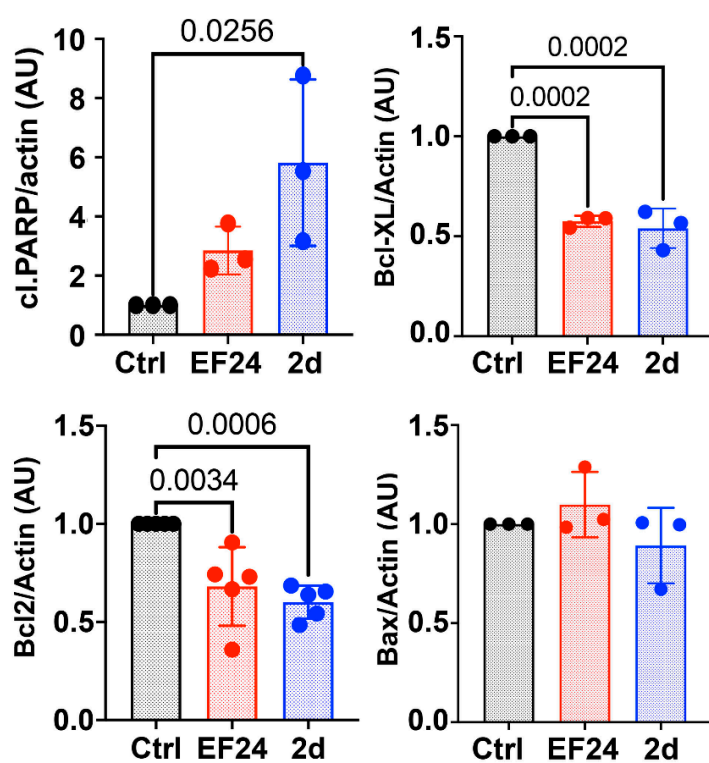
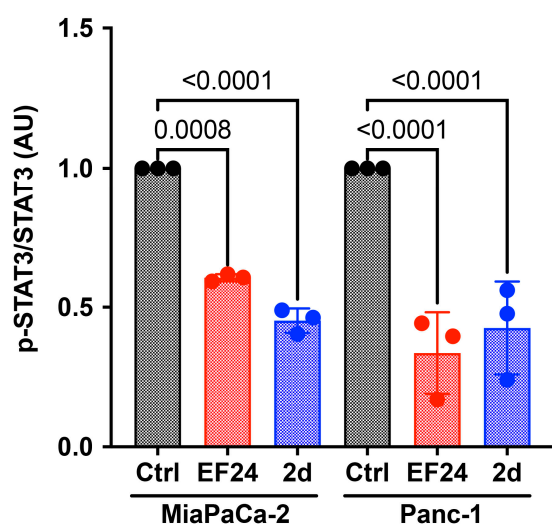
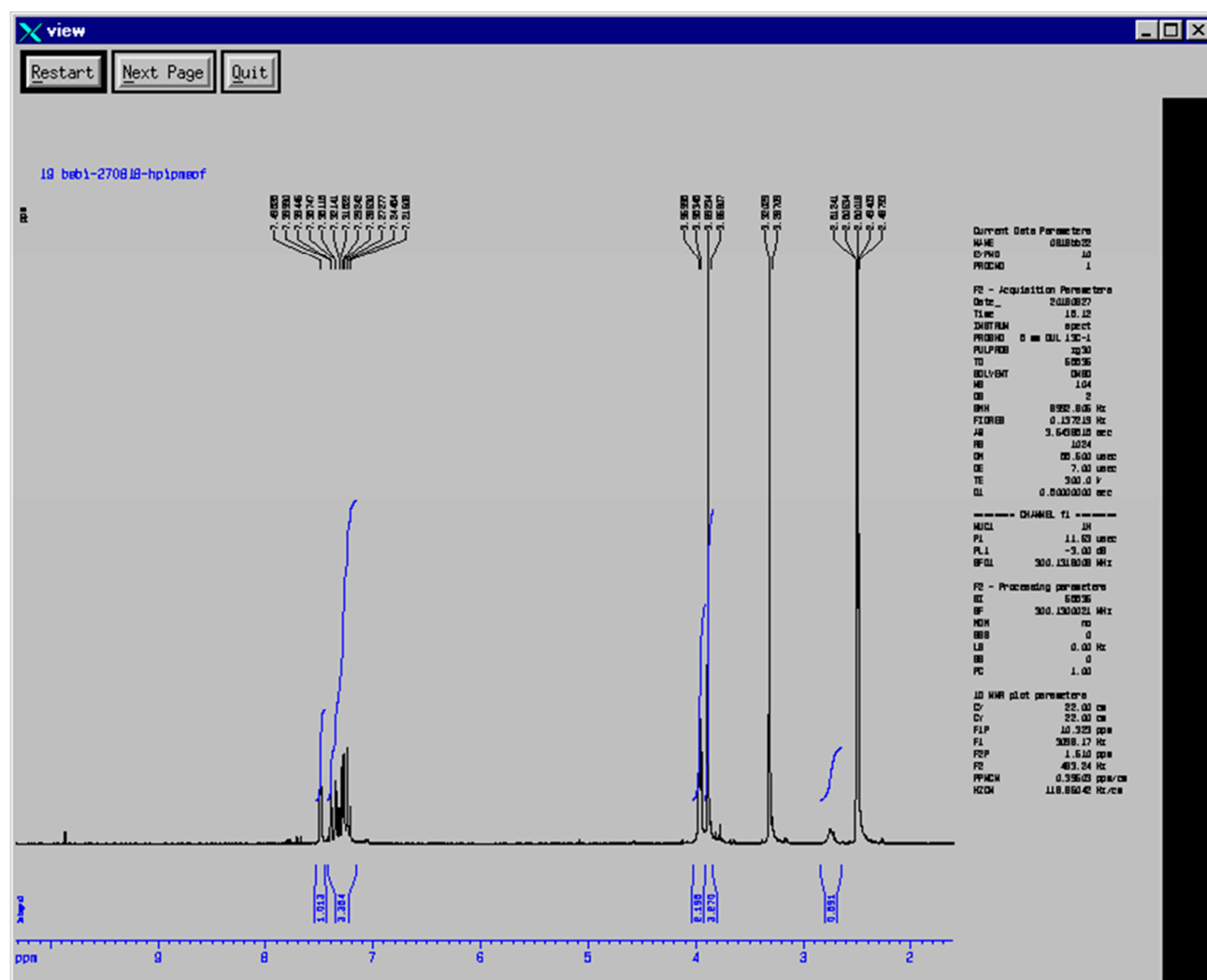


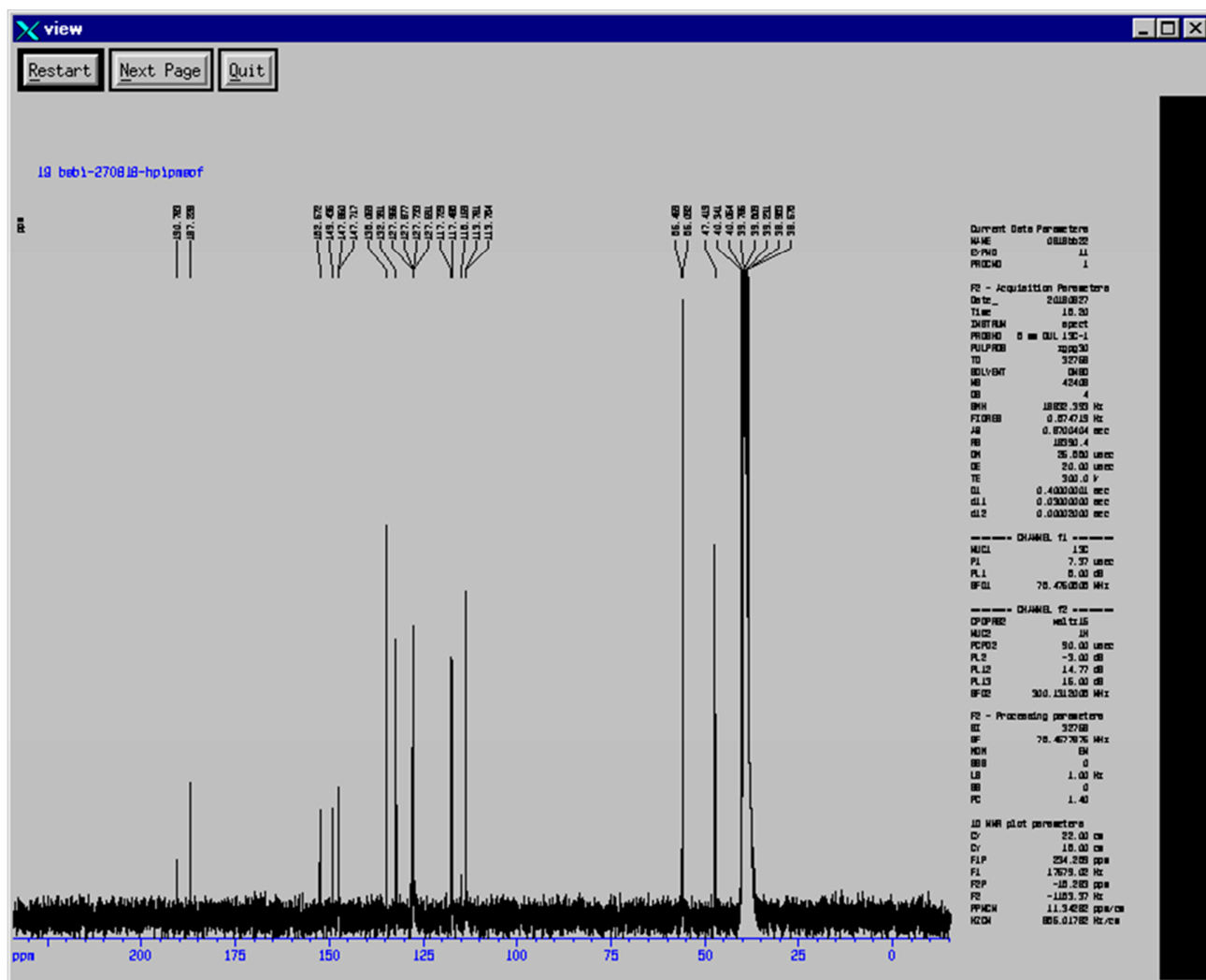
Figure S2. Protein levels of STAT3 and p-STAT3 in MiaPaCa-2 and Panc-1 pancreatic cancer cells upon treatment with EF24 and **2d**. Western blot of p-STAT3 protein was quantified using Bio-Rad's Image lab software and expressed as compared to total STAT3 in arbitrary units.



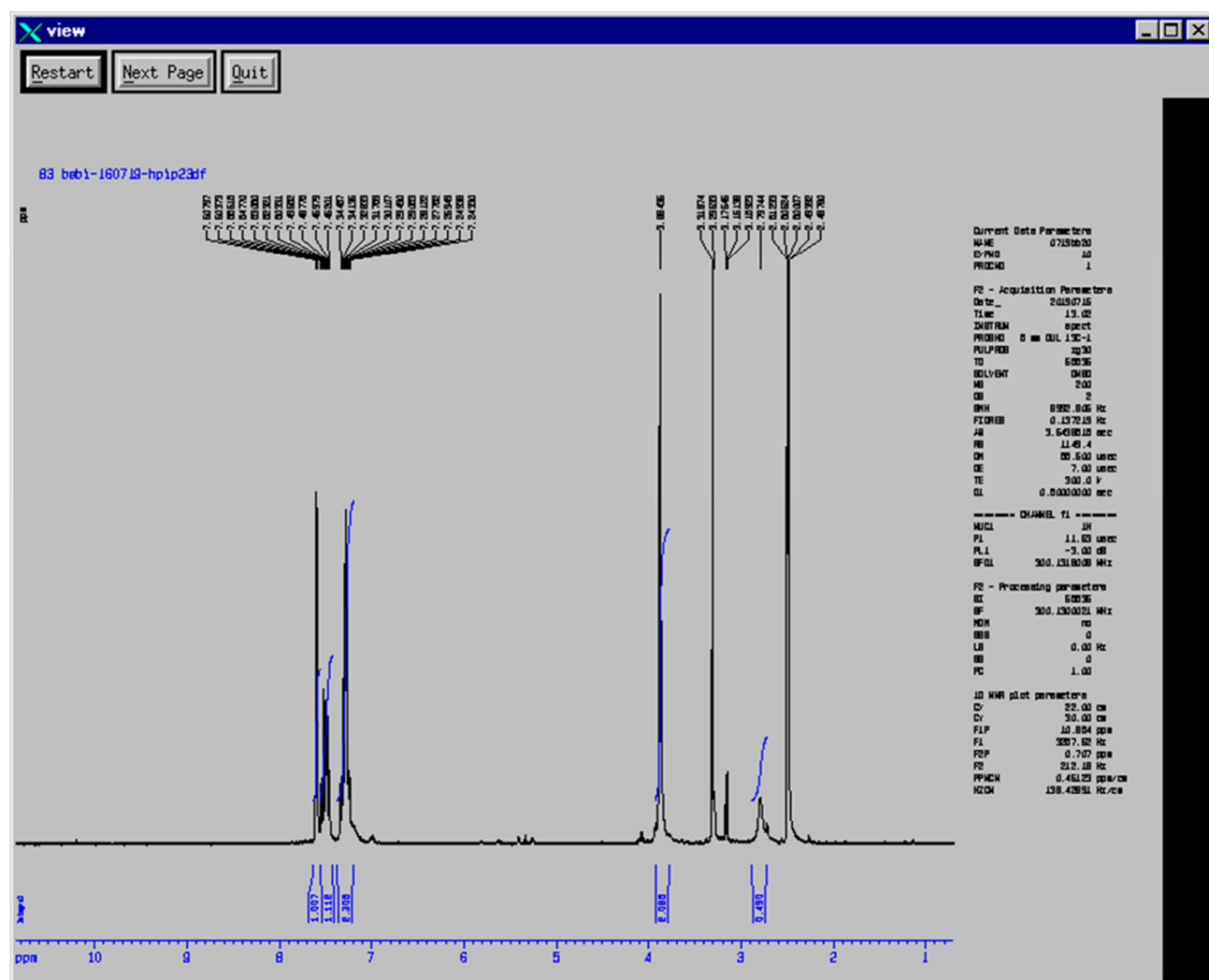
^1H NMR spectrum of **1c**



^{13}C NMR spectrum of **1c**



^1H NMR spectrum of **1e**



The screenshot displays the UXNMR software interface. At the top, there is a title bar with the 'view' logo and standard window controls. Below the title bar are three buttons: 'Restart', 'Next Page', and 'Quit'. The main window area is divided into three sections. The left section shows an NMR spectrum with a baseline and several sharp peaks. The x-axis is labeled 'ppm' and ranges from 0 to 10. The y-axis is labeled 'Intensity'. The right section displays acquisition parameters for two channels, F1 and F2. The bottom section shows the processing parameters for the F1 channel. The spectrum shows a large peak at approximately 7.5 ppm and several smaller peaks between 1 and 5 ppm. The acquisition parameters for F1 include: Date: 20090716, Time: 18.14, Instrument: spect, Probe: 5 mm QNP 1H-1, PULPROG: zgpg30, TO: 32768, DELTAT: 0.000, NS: 4096, DS: 4, BPH: 18000.000 Hz, FIDRES: 0.374718 Hz, AQ: 0.8200404 sec, RG: 65536.0, CH: 26.000 umsec, DE: 2.000 umsec, TE: 300.2 K, OL: 0.4000000 sec, dL1: 0.0300000 sec, dL2: 0.0002000 sec. The acquisition parameters for F2 include: Date: 20090716, Time: 18.14, Instrument: spect, Probe: 5 mm QNP 1H-1, PULPROG: zgpg30, TO: 32768, DELTAT: 0.000, NS: 4096, DS: 4, BPH: 18000.000 Hz, FIDRES: 0.374718 Hz, AQ: 0.8200404 sec, RG: 65536.0, CH: 26.000 umsec, DE: 2.000 umsec, TE: 300.2 K, OL: 0.4000000 sec, dL1: 0.0300000 sec, dL2: 0.0002000 sec. The processing parameters for F1 include: MUC1: 13C, PL: 7.37 umsec, PL1: 0.00 dB, RFDR: 78.476200 MHz, CPDPRG2: waltz16, MUC2: 1H, PCPD2: 90.00 umsec, PL2: -3.00 dB, PL12: 14.77 dB, PL13: 16.00 dB, RFDR: 300.131200 MHz, F2 - Processing parameters: EQ: 32768, RF: 78.467876 MHz, NCH: 0, NS: 0, LB: 1.00 Hz, BB: 0, PC: 1.40, 1D NMR plot parameters: CV: 22.00 cm, CY: 18.00 cm, F1P: 234.200 pps, F1: 1767.00 Hz, F2P: -10.200 pps, F2: -1103.37 Hz, PPMCH: 11.54000 pps/cm, KCH: 886.01700 Hz/cm.

view

Restart Next Page Quit

83 bbb1-160713-hp1p23df

ppm

Intensity

Current Data Parameters

NAME 07190030

EXPNO 11

PROCNO 1

F2 - Acquisition Parameters

Date_ 20090716

Time 18.14

INSTRUM spect

PROBHD 5 mm QNP 1H-1

PULPROG zgpg30

TO 32768

DELTA 0.000

NS 4096

DS 4

BPH 18000.000 Hz

FIDRES 0.374718 Hz

AQ 0.8200404 sec

RG 65536.0

CH 26.000 umsec

DE 2.000 umsec

TE 300.2 K

OL 0.4000000 sec

dL1 0.0300000 sec

dL2 0.0002000 sec

----- CHANNEL F1 -----

MUC1 13C

PL 7.37 umsec

PL1 0.00 dB

RFDR 78.476200 MHz

----- CHANNEL F2 -----

CPDPRG2 waltz16

MUC2 1H

PCPD2 90.00 umsec

PL2 -3.00 dB

PL12 14.77 dB

PL13 16.00 dB

RFDR 300.131200 MHz

F2 - Processing parameters

EQ 32768

RF 78.467876 MHz

NCH 0

NS 0

LB 1.00 Hz

BB 0

PC 1.40

1D NMR plot parameters

CV 22.00 cm

CY 18.00 cm

F1P 234.200 pps

F1 1767.00 Hz

F2P -10.200 pps

F2 -1103.37 Hz

PPMCH 11.54000 pps/cm

KCH 886.01700 Hz/cm

Exceed

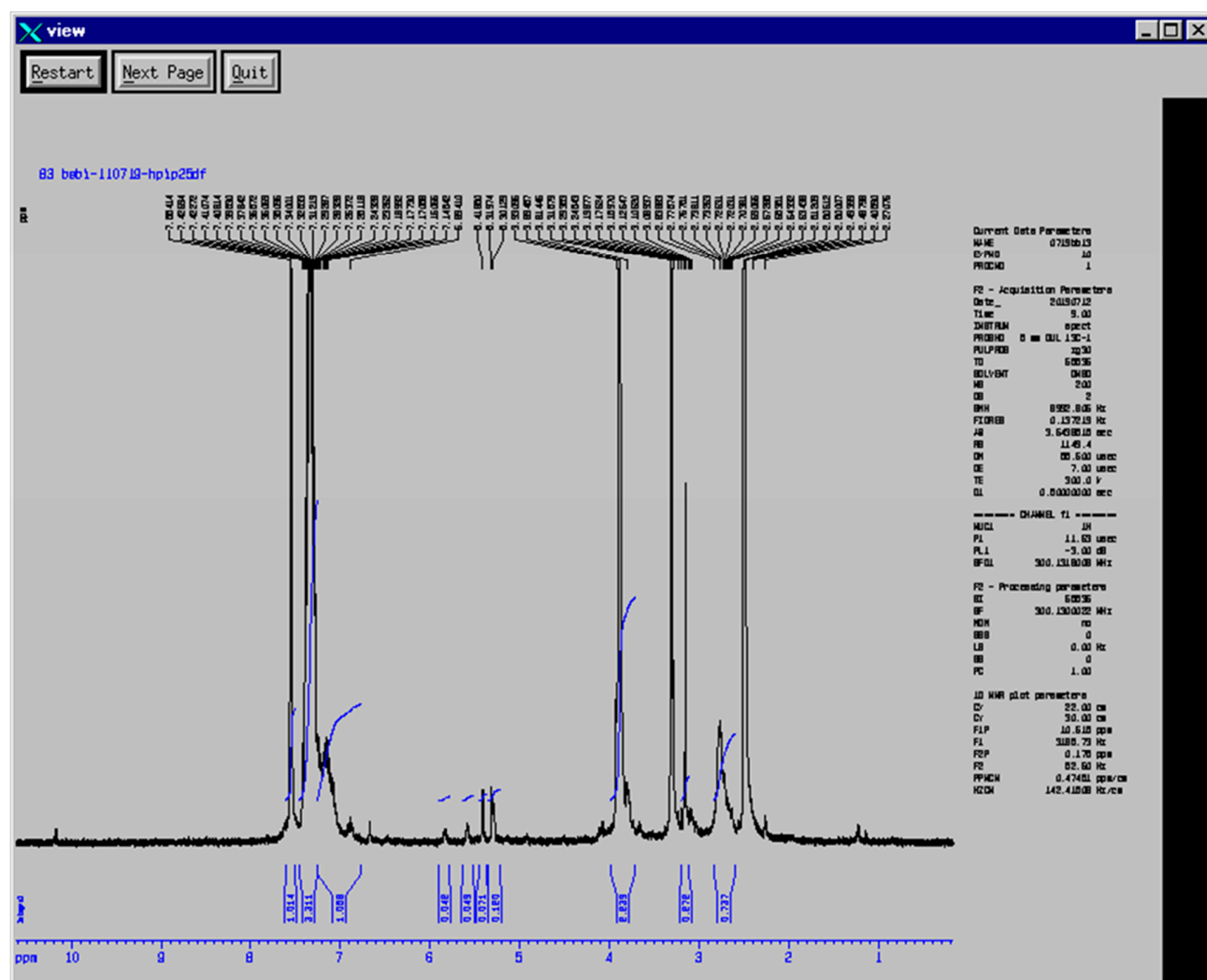
UXNMR Version 3.1 on A...

lock

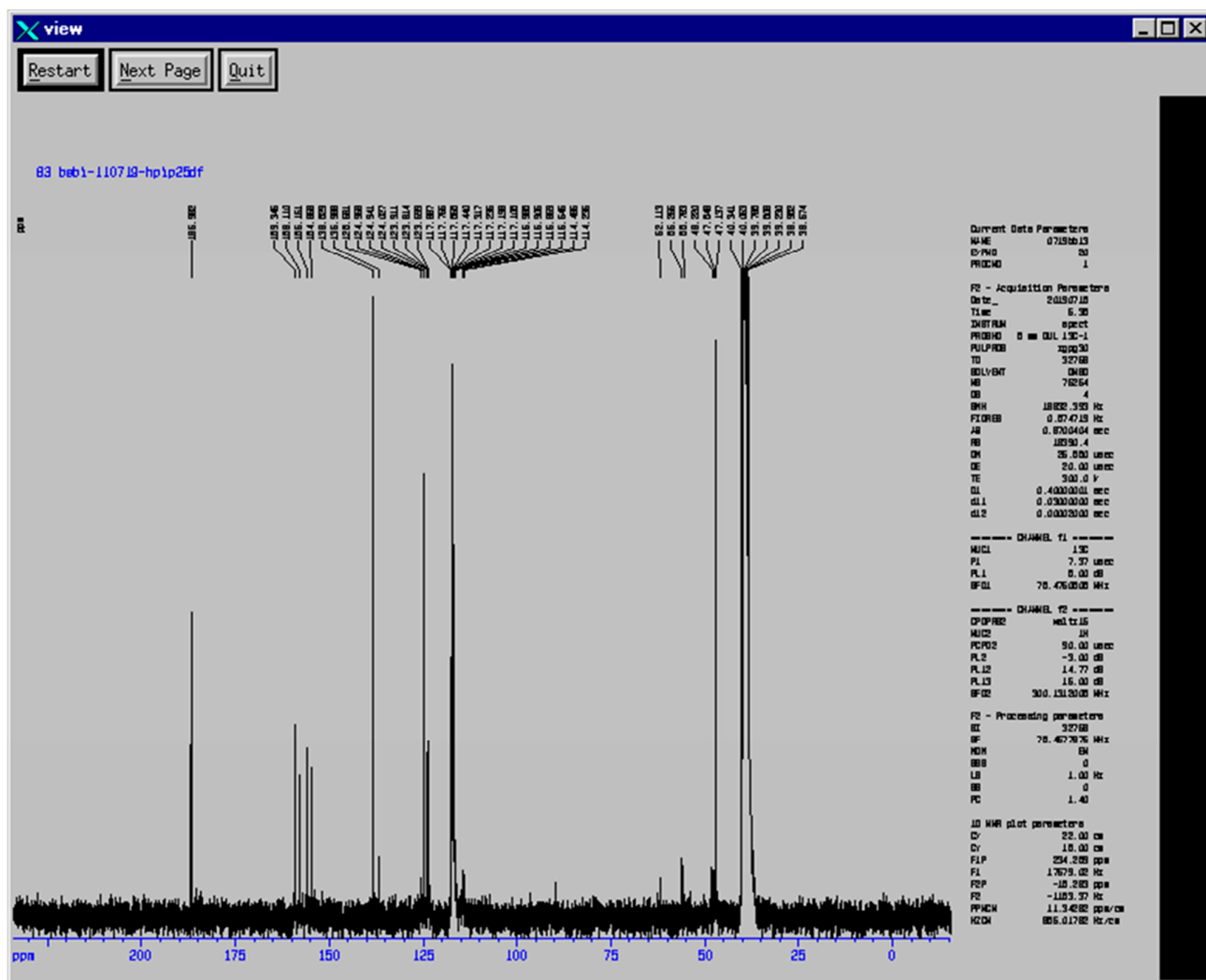
Spektrn.doc - Microsoft ...

view

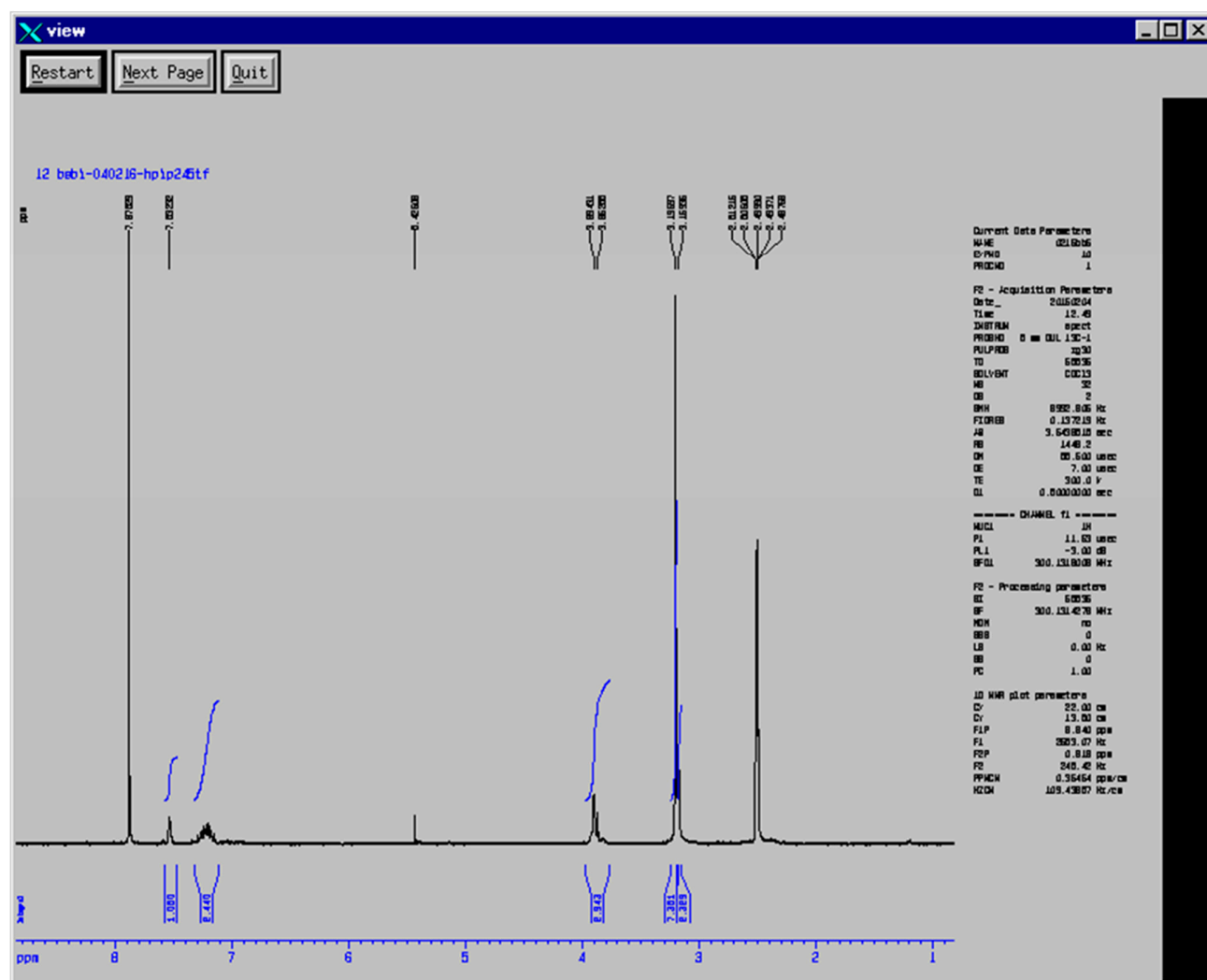
^1H NMR spectrum of **1f**



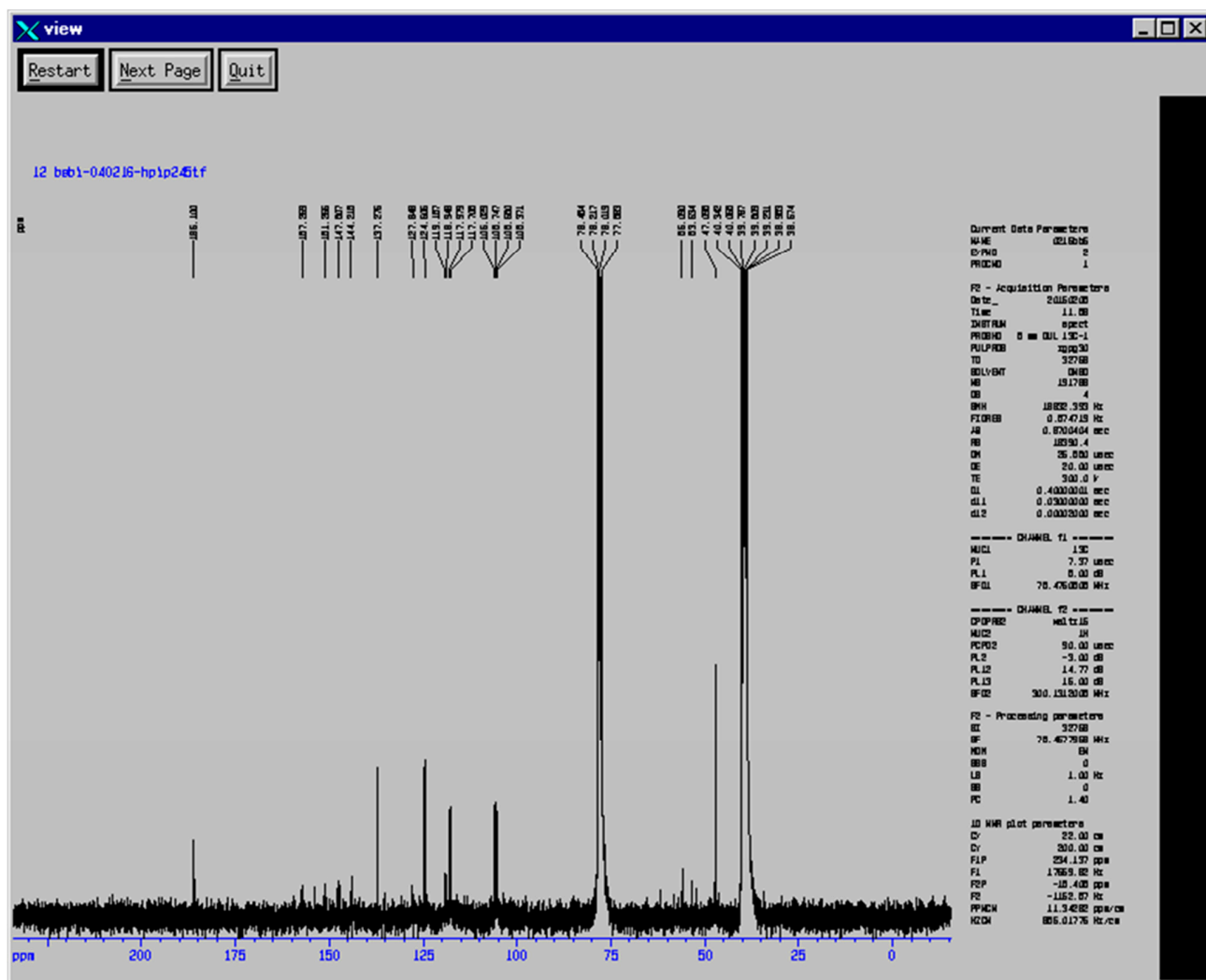
^{13}C NMR spectrum of **1f**



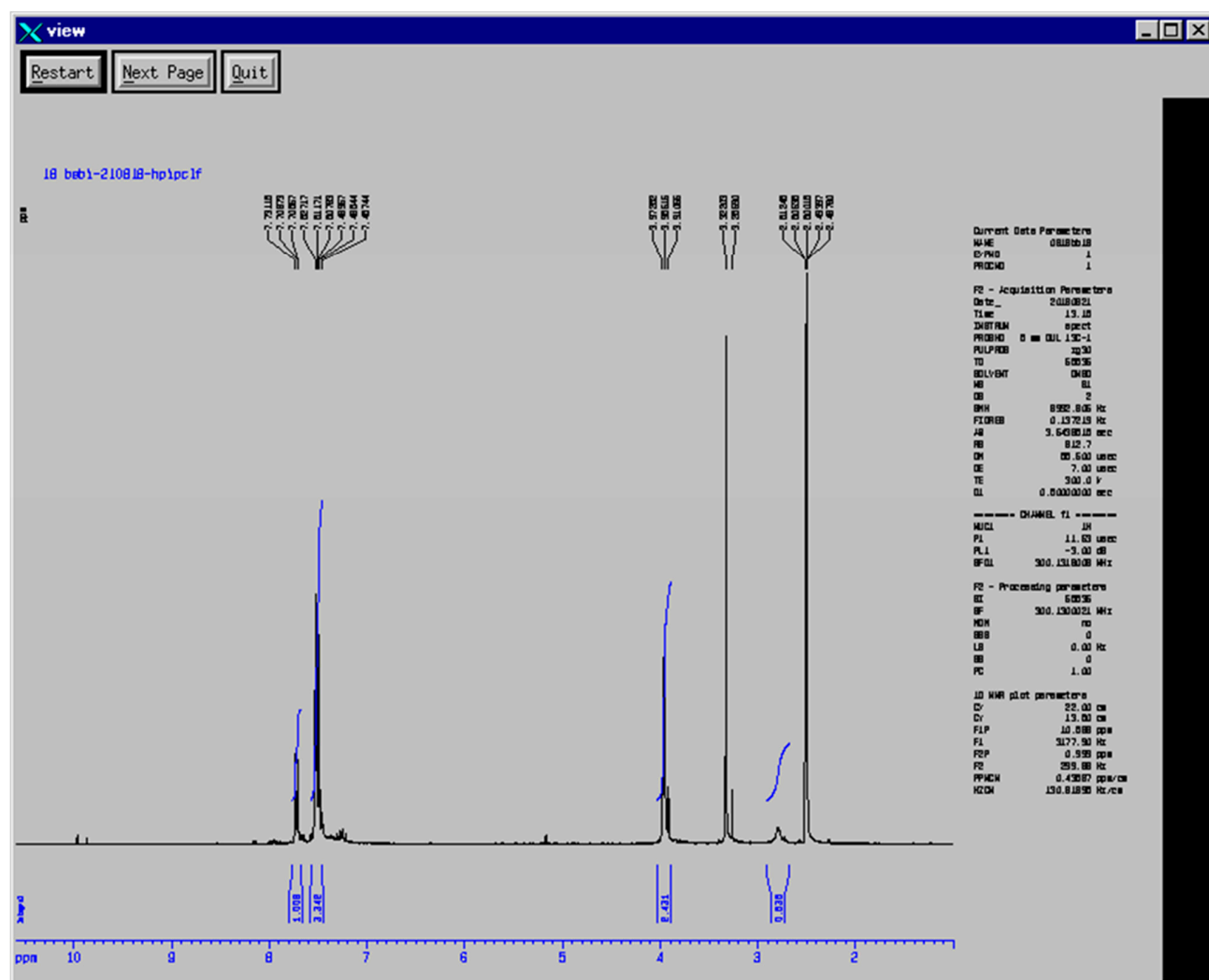
^1H NMR spectrum of **1g**



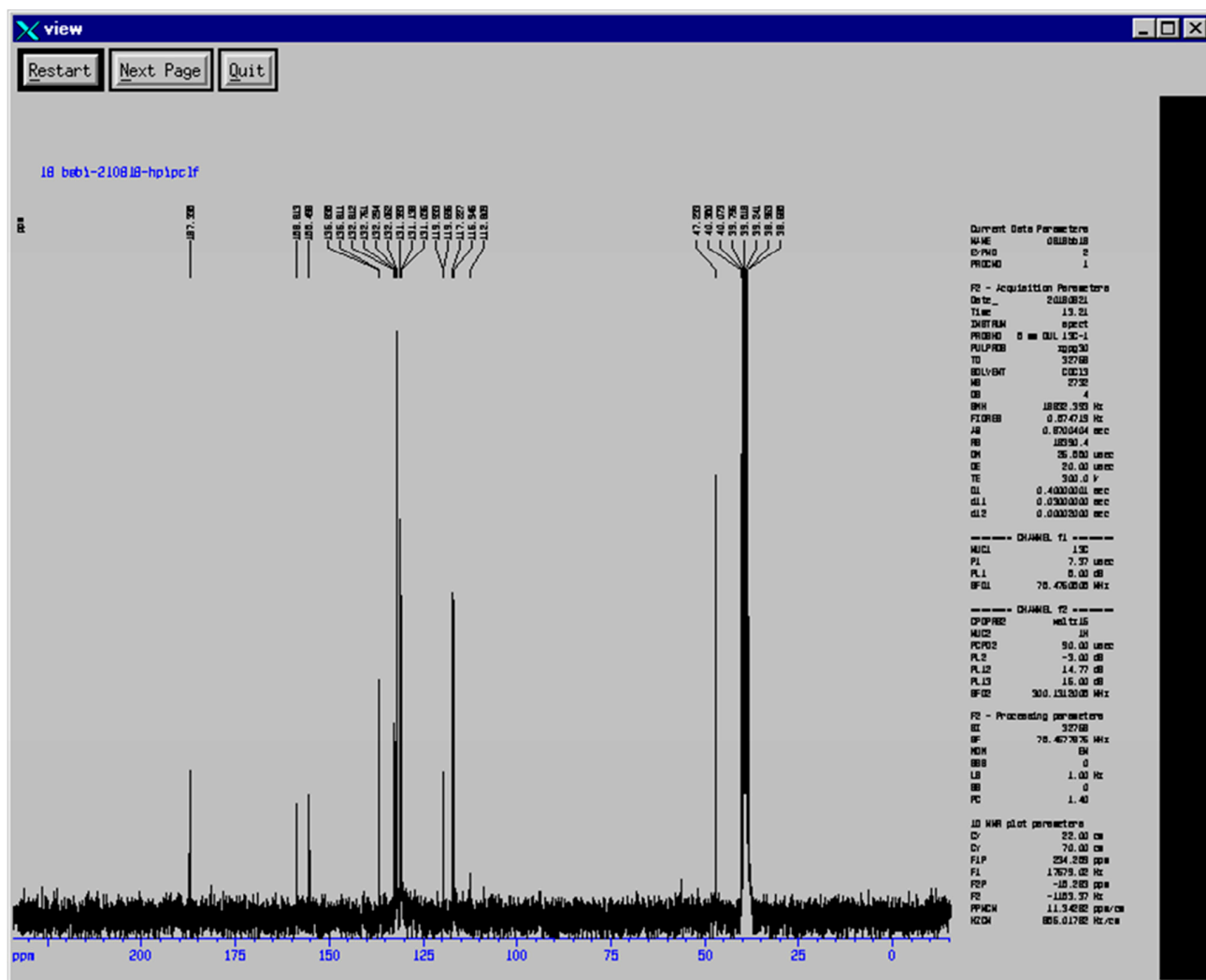
^{13}C NMR spectrum of **1g**



^1H NMR spectrum of **1h**



^{13}C NMR spectrum of **1h**



view

Restart Next Page Quit

147 bbb1-250717-acryl3f

Current Data Parameters

NAME	0717bbb17
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20170720
Time	13.20
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PROBHD	5 mm QNP 1H-1
PULPROG	zgpg30
TD	65536
SOLVENT	DMSO
NS	1.00
DS	2
SWH	8982.806 Hz
FIDRES	0.137018 Hz
AQ	5.6400000 sec
RG	11.40.4
CH	00.600 sec
DE	7.00 sec
TE	300.0 K
CL	0.5000000 sec

----- CHANNEL f1 -----

NUC1	1H
PL1	11.00 sec
PL1	-3.00 dB
RFQ1	300.1310000 MHz

F2 - Processing parameters

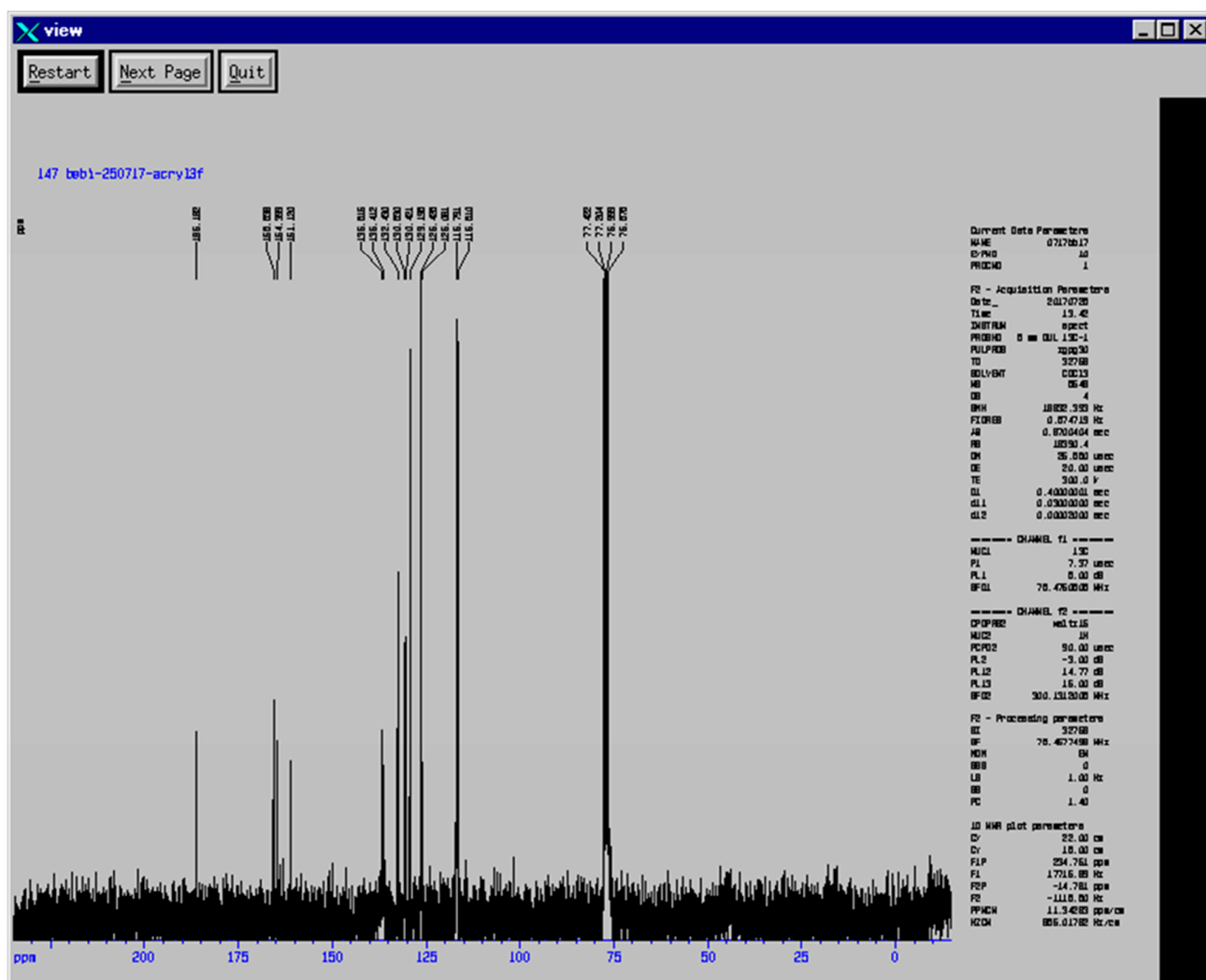
SI	65536
BF	300.1300135 MHz
NDM	no
BB	0
LB	0.00 Hz
GB	0
PC	1.00

1D NMR plot parameters

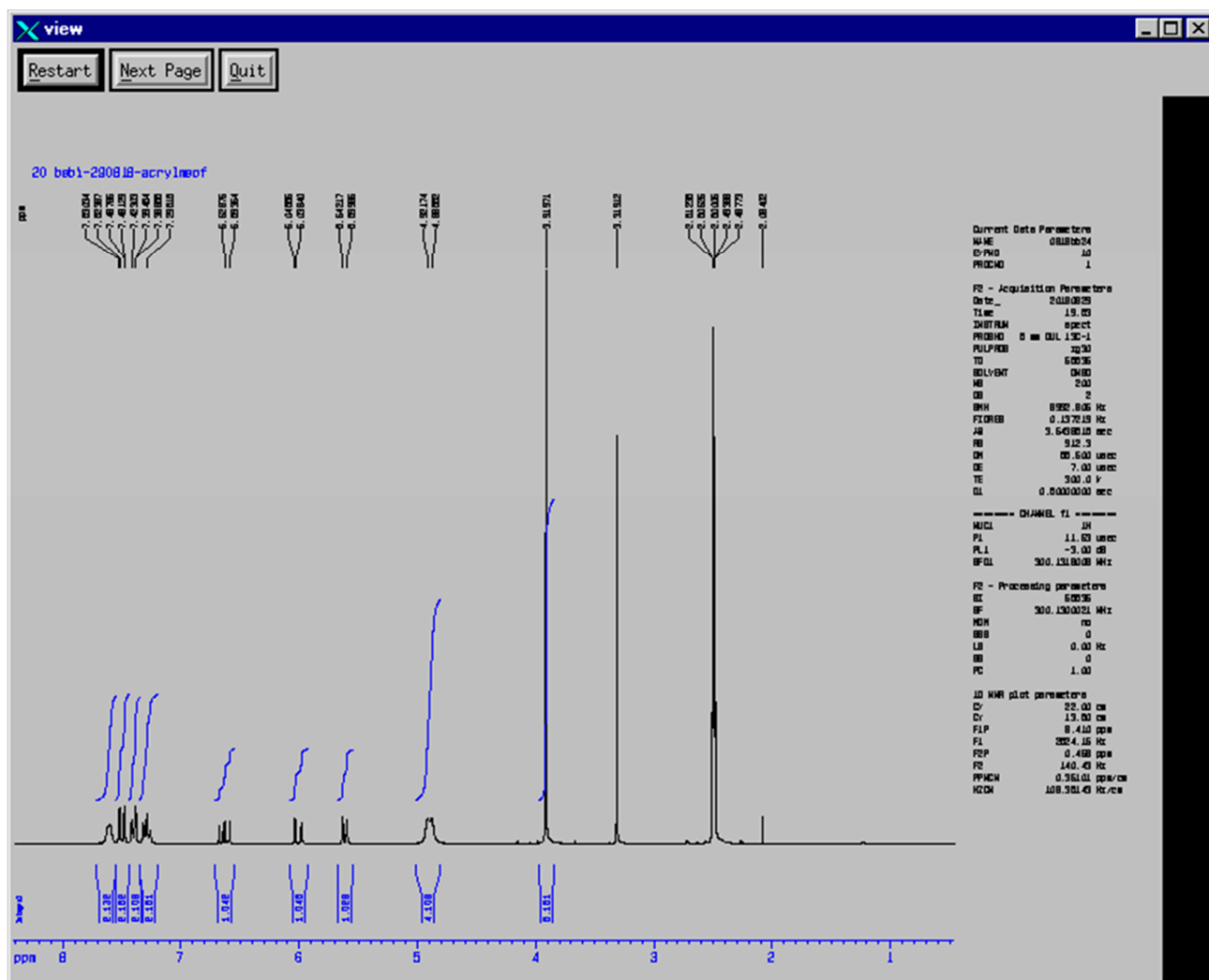
CD	22.00 cm
Cr	13.00 cm
FLP	9.225 ppm
FI	2565.75 Hz
FSP	-0.004 ppm
FE	-101.25 Hz
PPHCH	0.44040 ppm/cm
HZCM	132.77631 Hz/cm

ppm

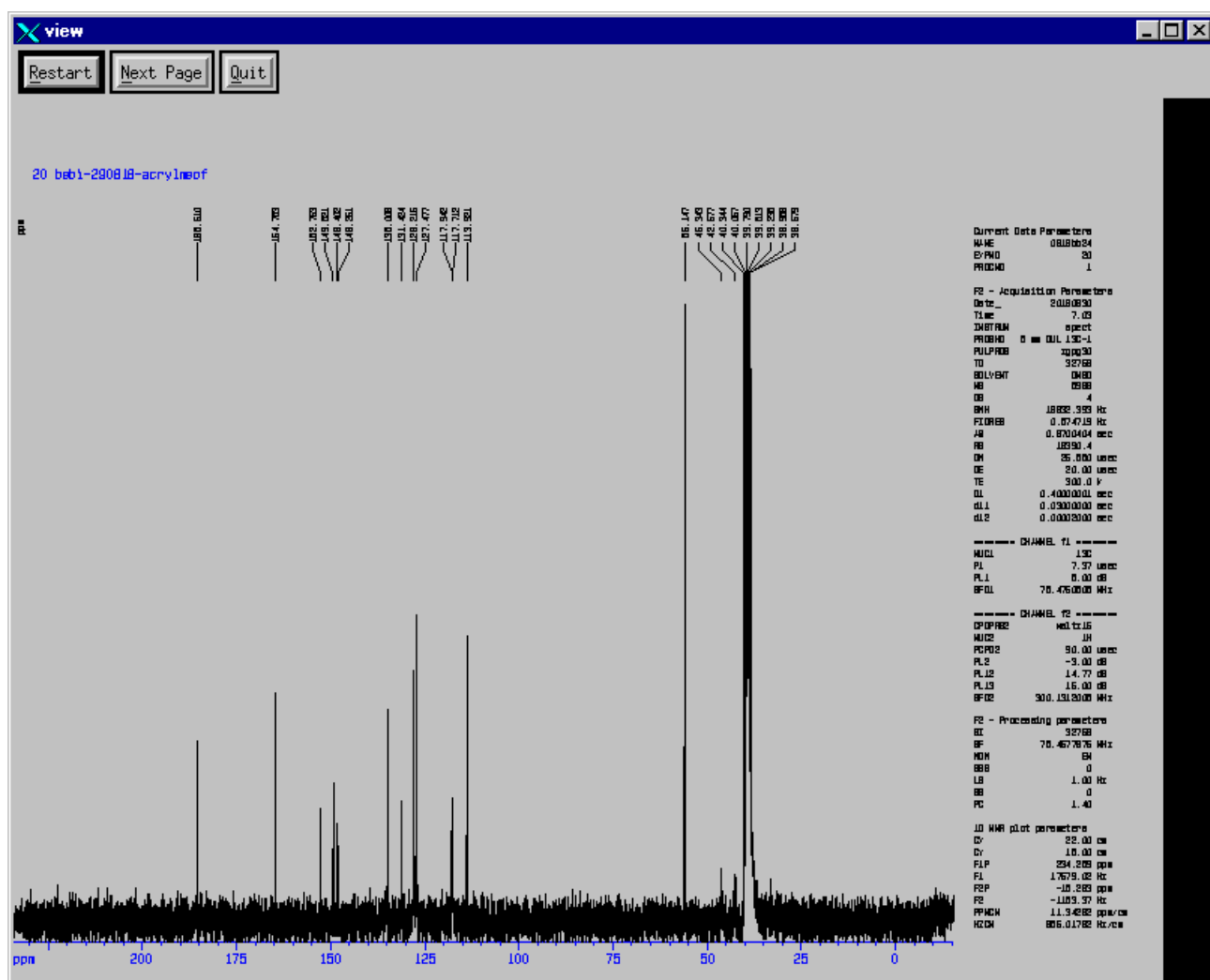
^{13}C NMR spectrum of **2b**



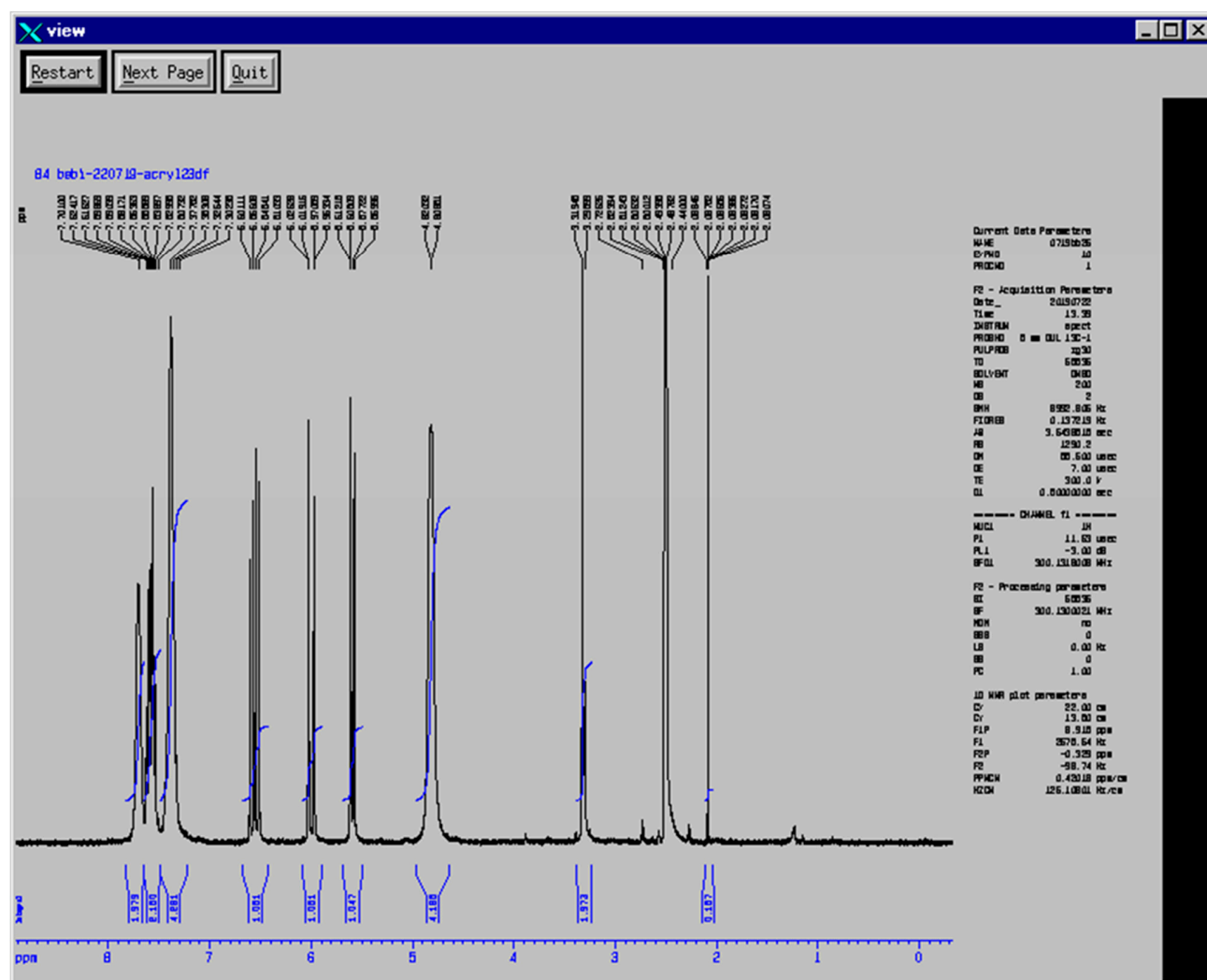
^1H NMR spectrum of **2c**



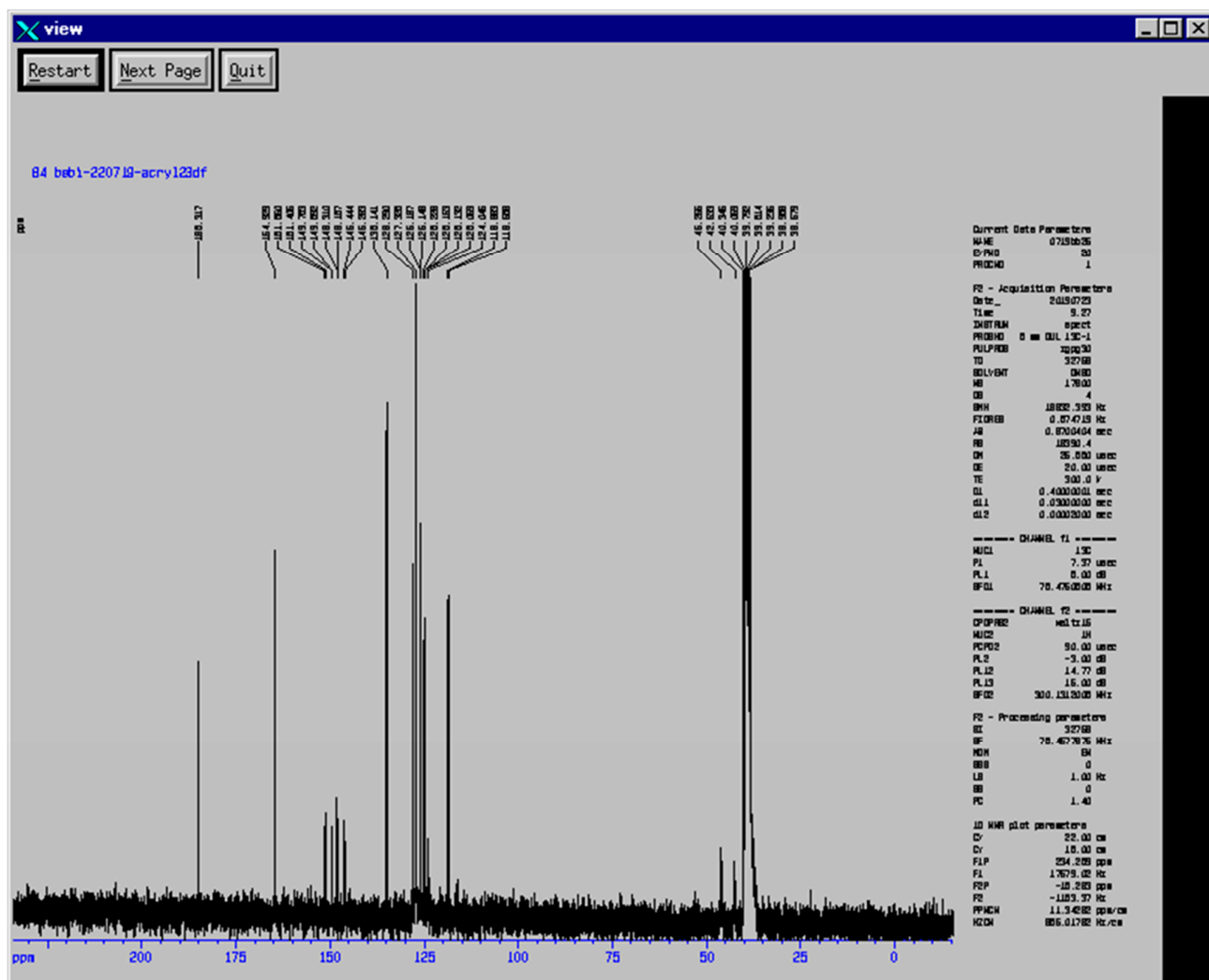
^{13}C NMR spectrum of **2c**



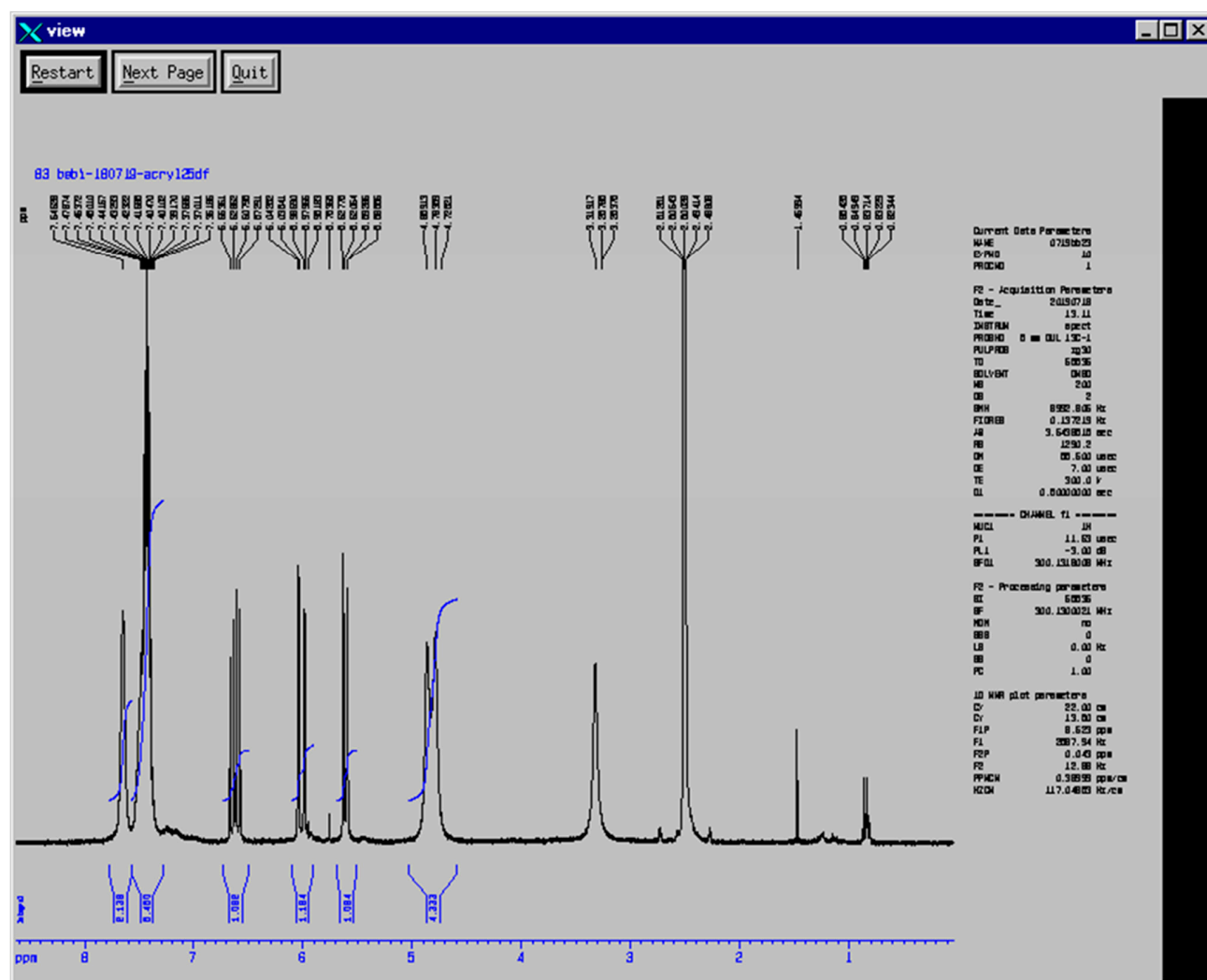
^1H NMR spectrum of **2e**



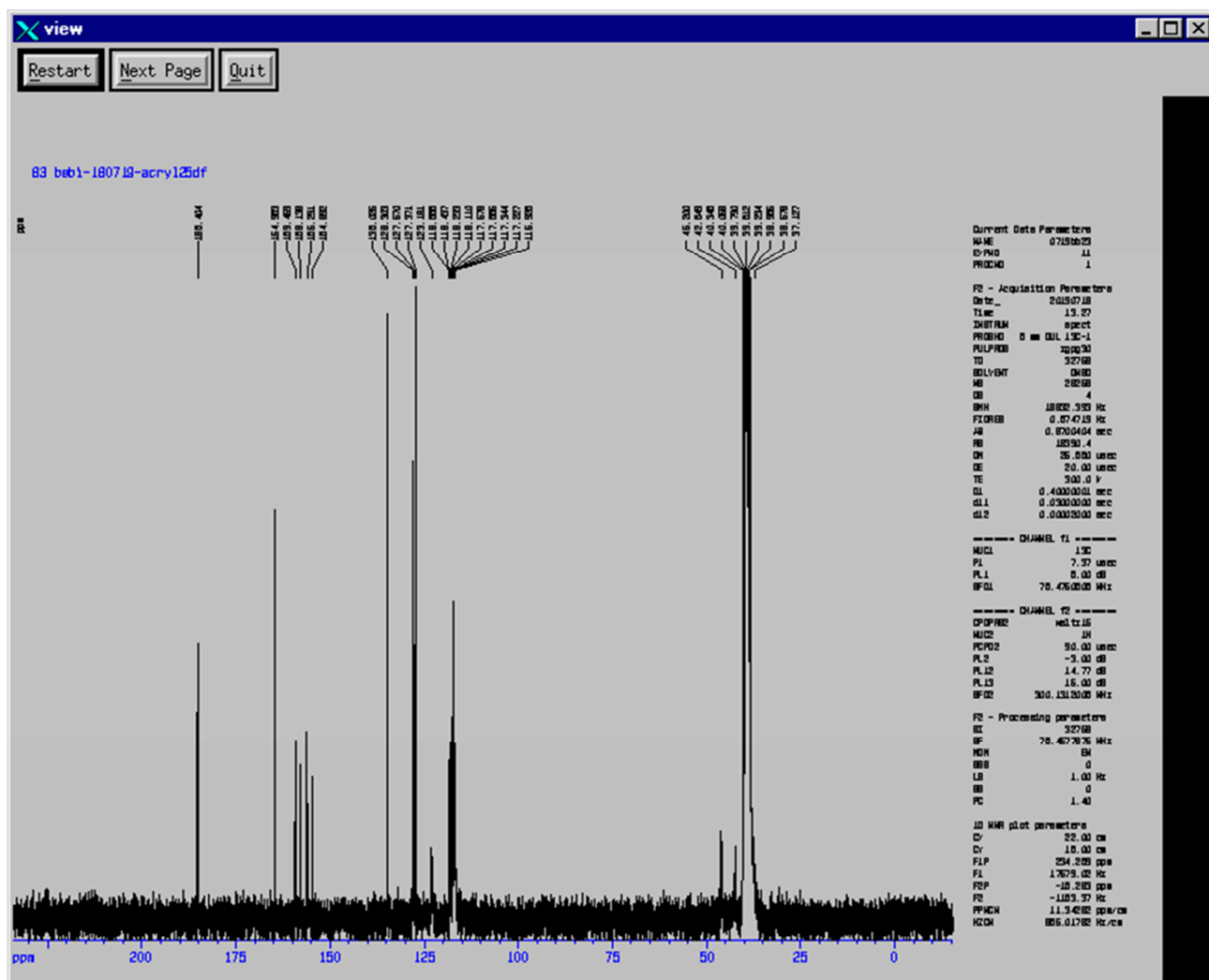
^{13}C NMR spectrum of **2e**



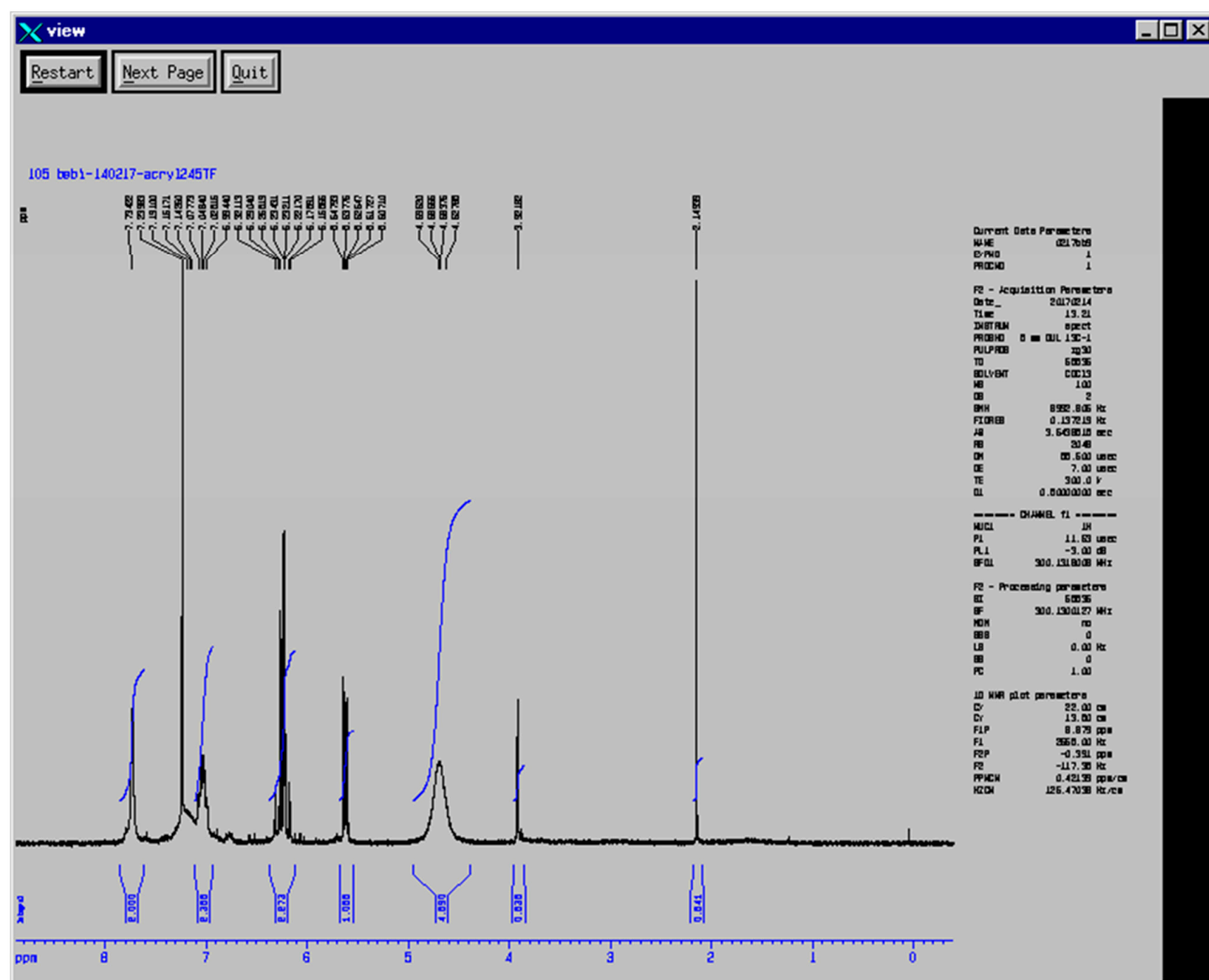
^1H NMR spectrum of **2f**



^{13}C NMR spectrum of **2f**



^1H NMR spectrum of **2g**



105 bb1-140217-acry1245TF

ppm

185.00 152.84 133.76 129.45 129.22 128.92 128.62 118.50 118.08 106.00 106.11 77.45 77.02 76.62 76.20 56.84

view

Restart Next Page Quit

Current Data Parameters
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EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
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Time 7.08
INSTRUM spect
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PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 22480
DS 4
SWH 18082.333 Hz
FIDRES 0.374718 Hz
AQ 0.870464 sec
RG 18730.4
DM 25.000 umsec
DE 2.000 umsec
TE 300.2 K
C1 0.4000000 sec
d11 0.0300000 sec
d12 0.0000000 sec

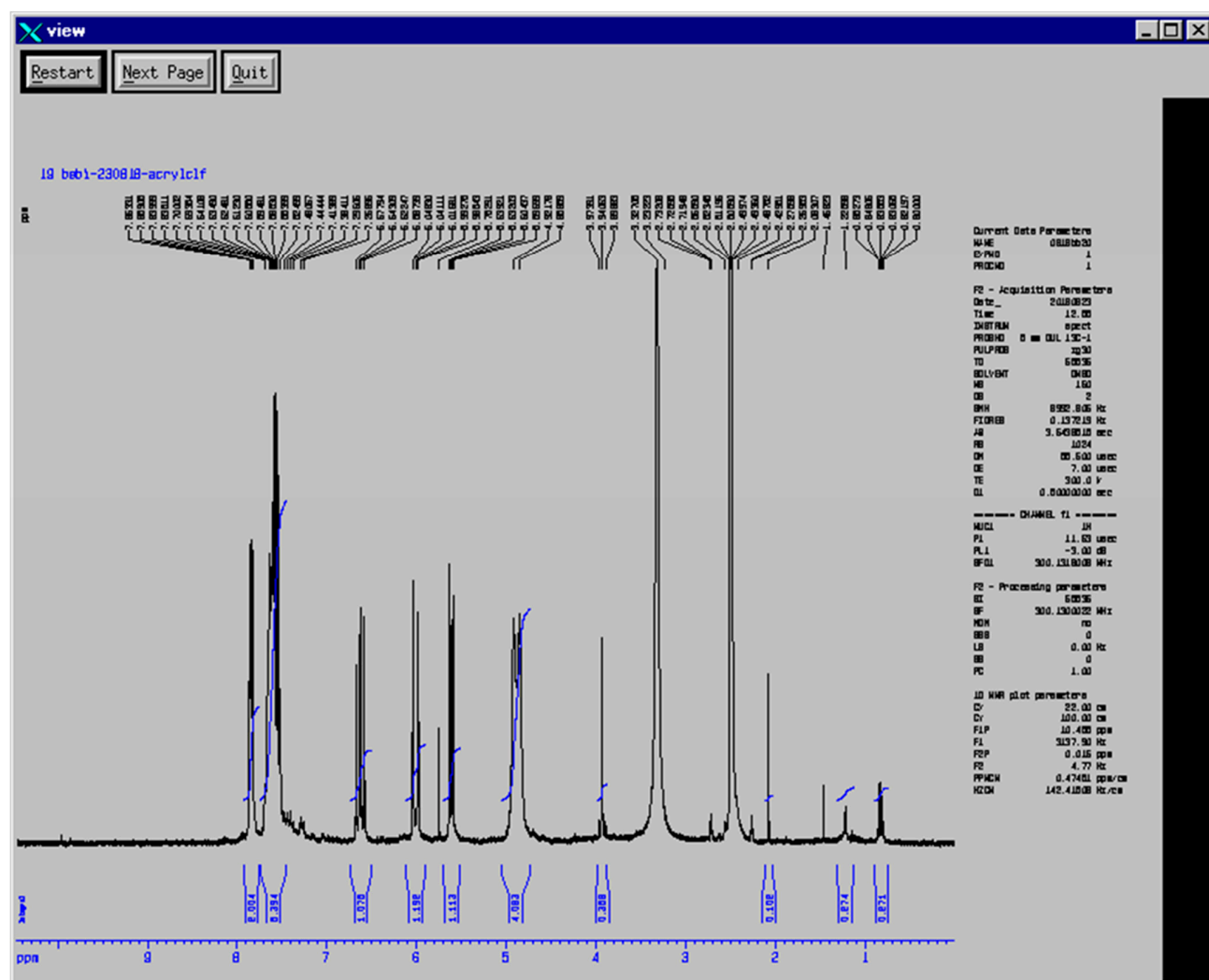
----- CHANNEL f1 -----
NUC1 13C
P1 7.37 umsec
PL1 0.00 dB
RFQ1 75.476205 MHz

----- CHANNEL f2 -----
CPDPRG2 waltz16
NUC2 1H
PCPD2 9.00 umsec
PL2 -5.00 dB
PL12 14.77 dB
PL13 16.00 dB
RFQ2 300.131200 MHz

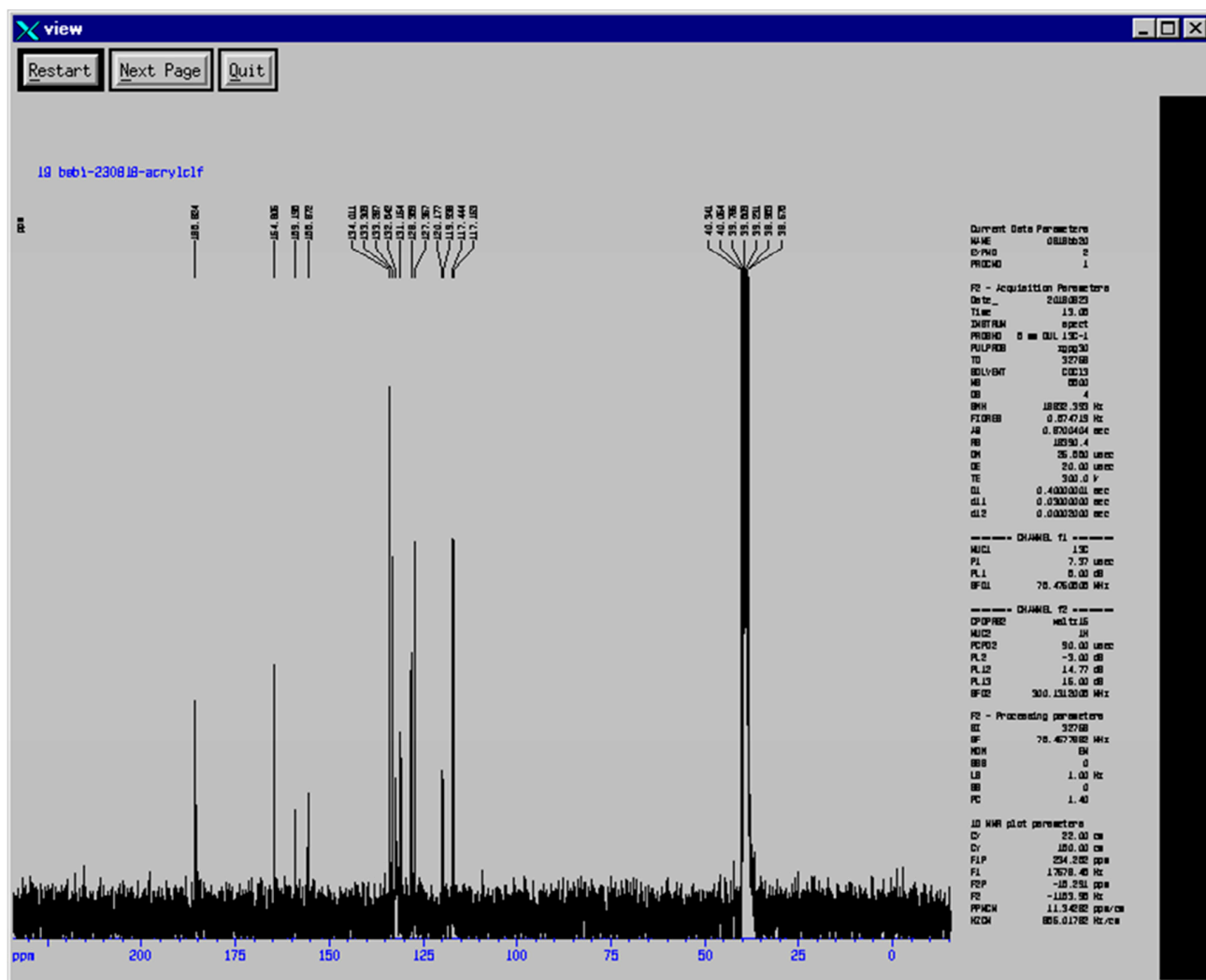
F2 - Processing parameters
SI 32768
SF 75.467486 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
Cv 22.00 cm
Cy 18.00 cm
PLP 254.776 ppm
F1 170.18.00 Hz
F2P -14.766 ppm
F2 -1114.38 Hz
PPMH 11.54023 ppm/cm
KZMH 886.01782 Hz/cm

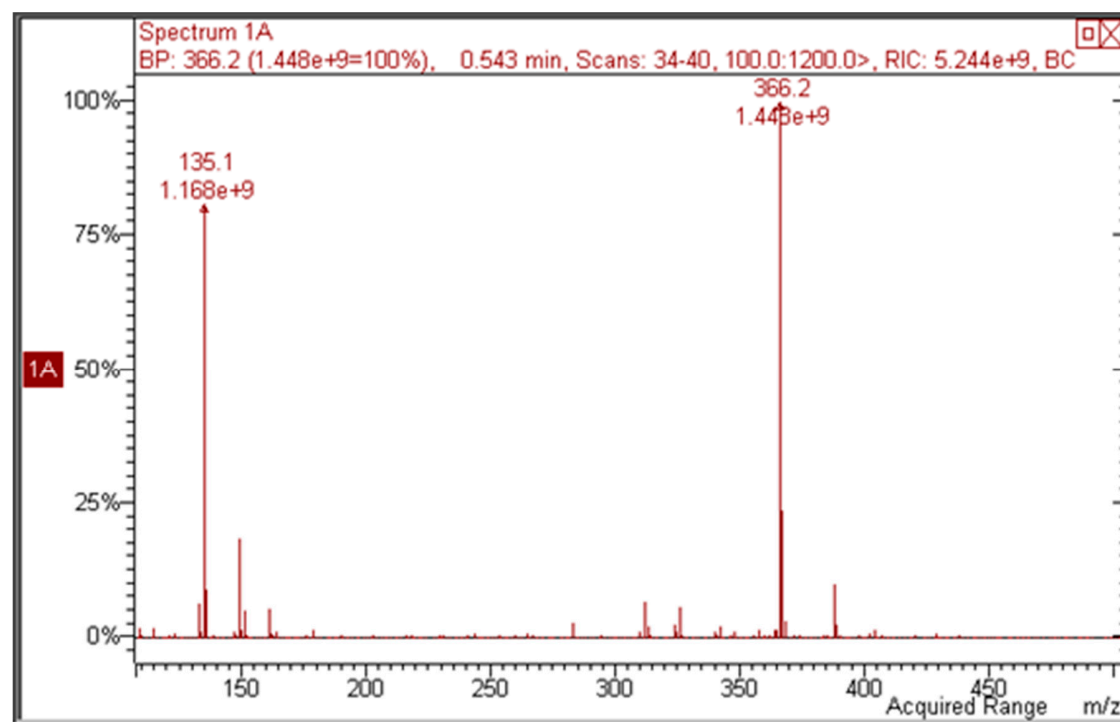
^1H NMR spectrum of **2h**



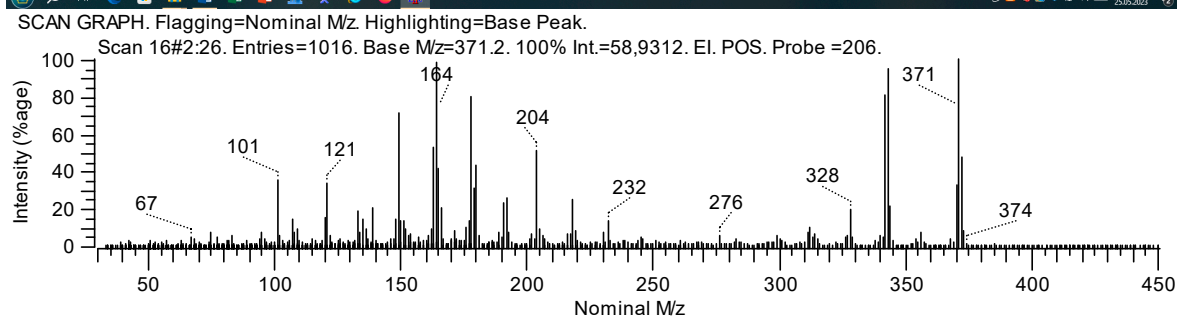
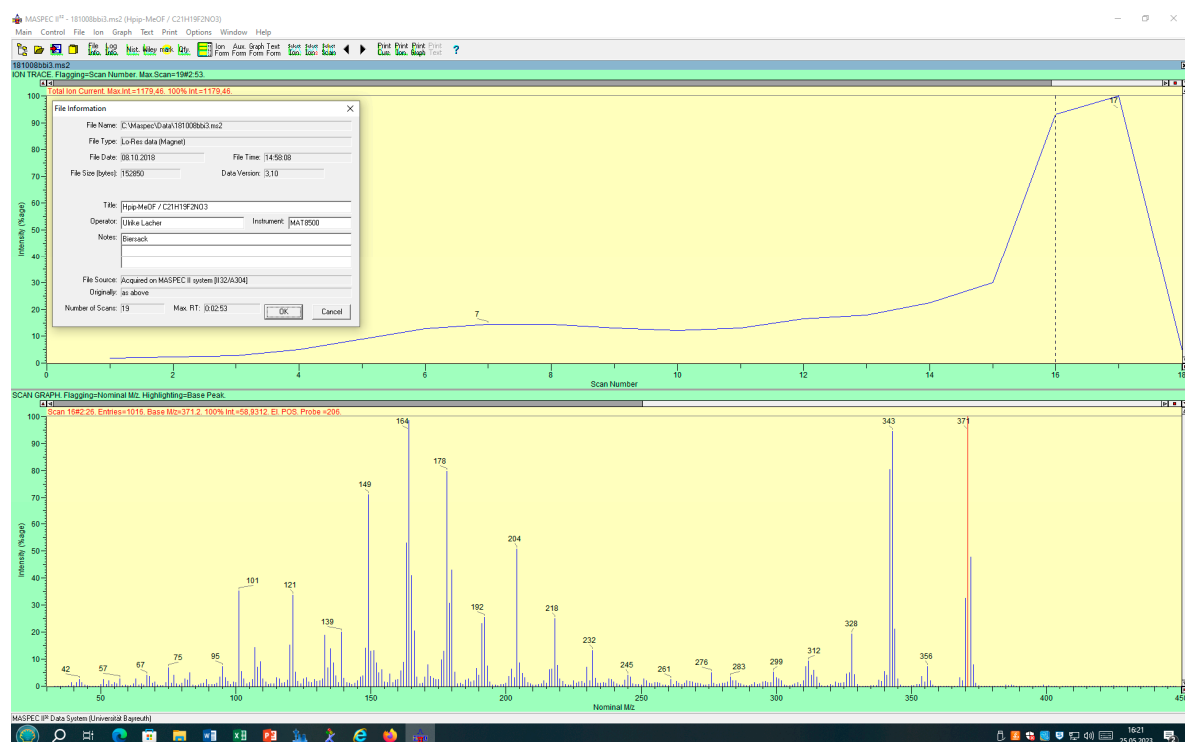
^{13}C NMR spectrum of **2h**



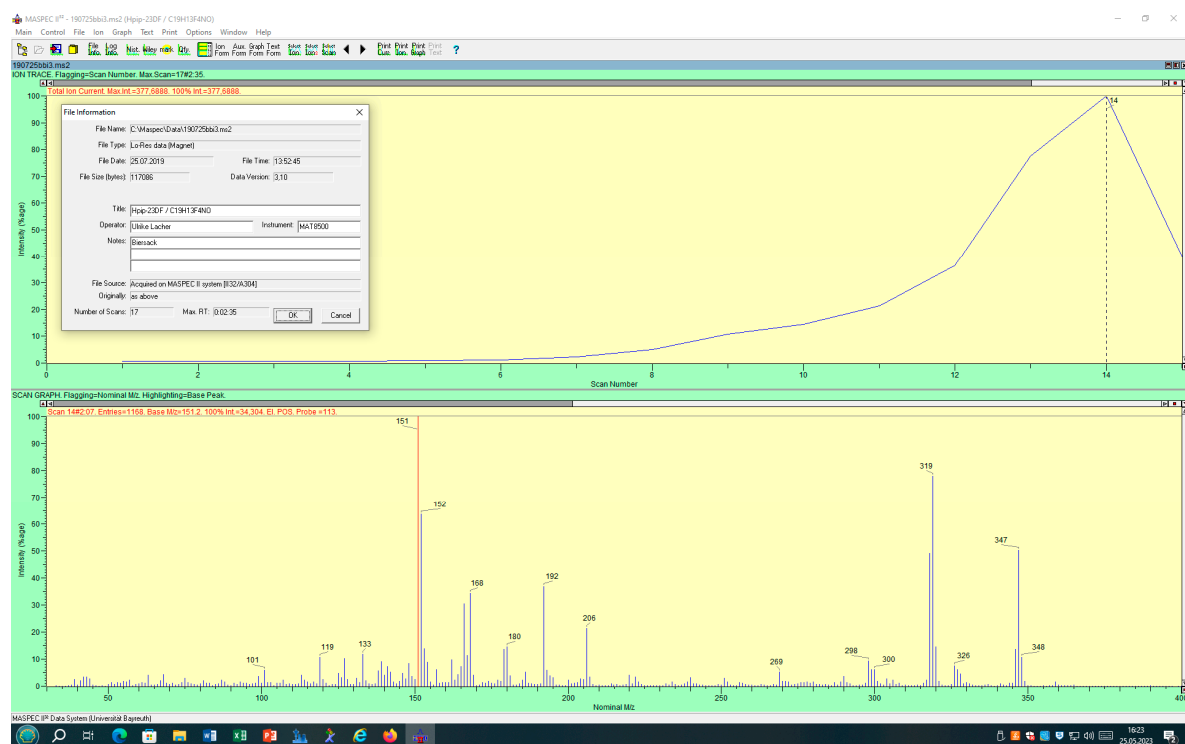
ESI-MS spectrum of **2b**



EI mass spectrum of **1c**

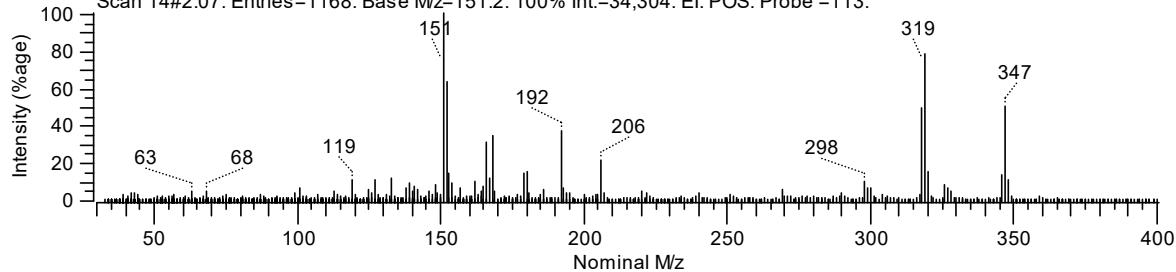


EI mass spectrum of **1e**

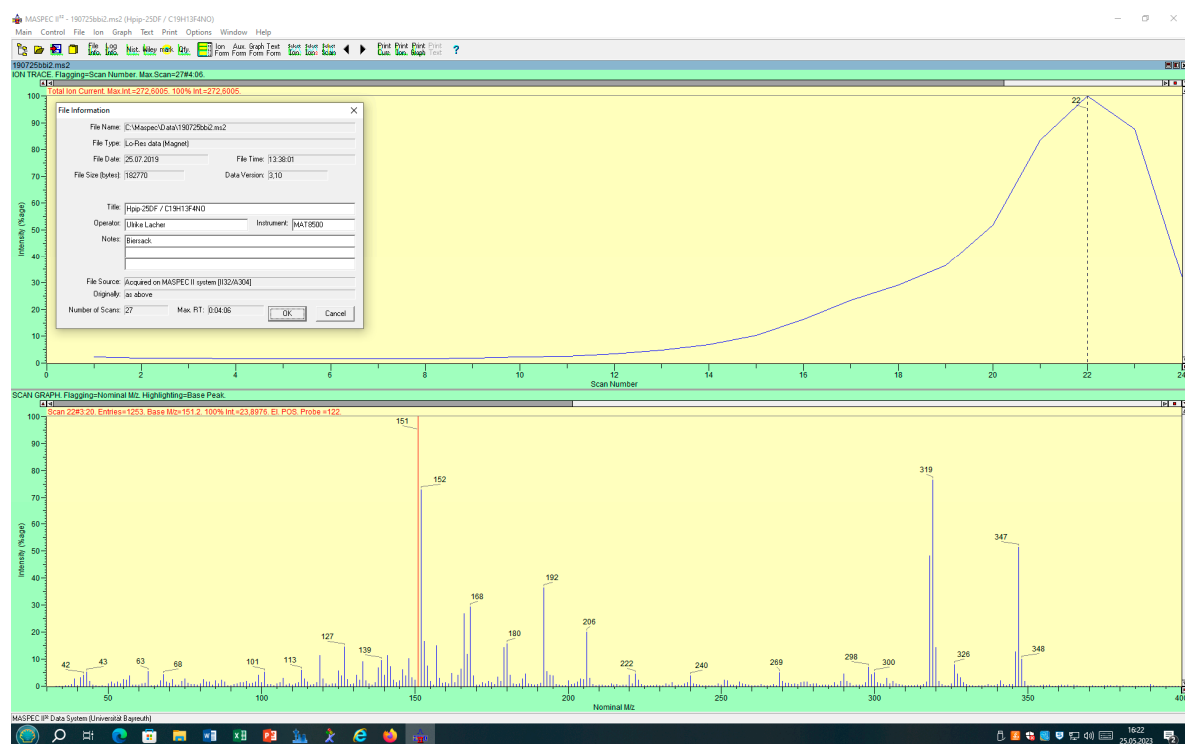


SCAN GRAPH. Flaggng=Nominal M/z. Highlighting=Base Peak.

Scan 14#2:07. Entries=1168. Base M/z=151.2. 100% Int.=34,304. EI. POS. Probe =113.

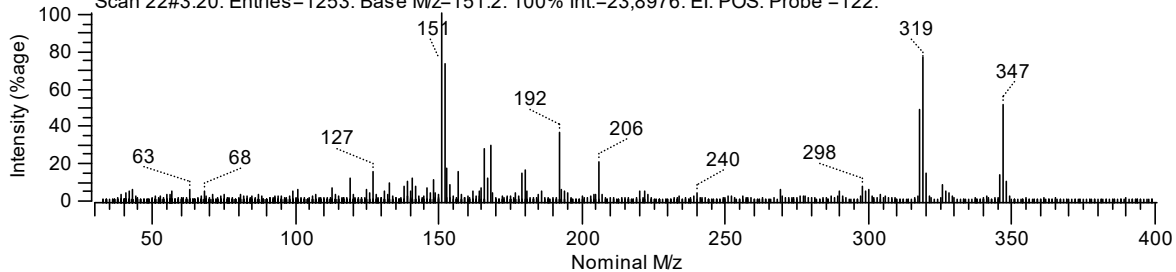


EI mass spectrum of **1f**

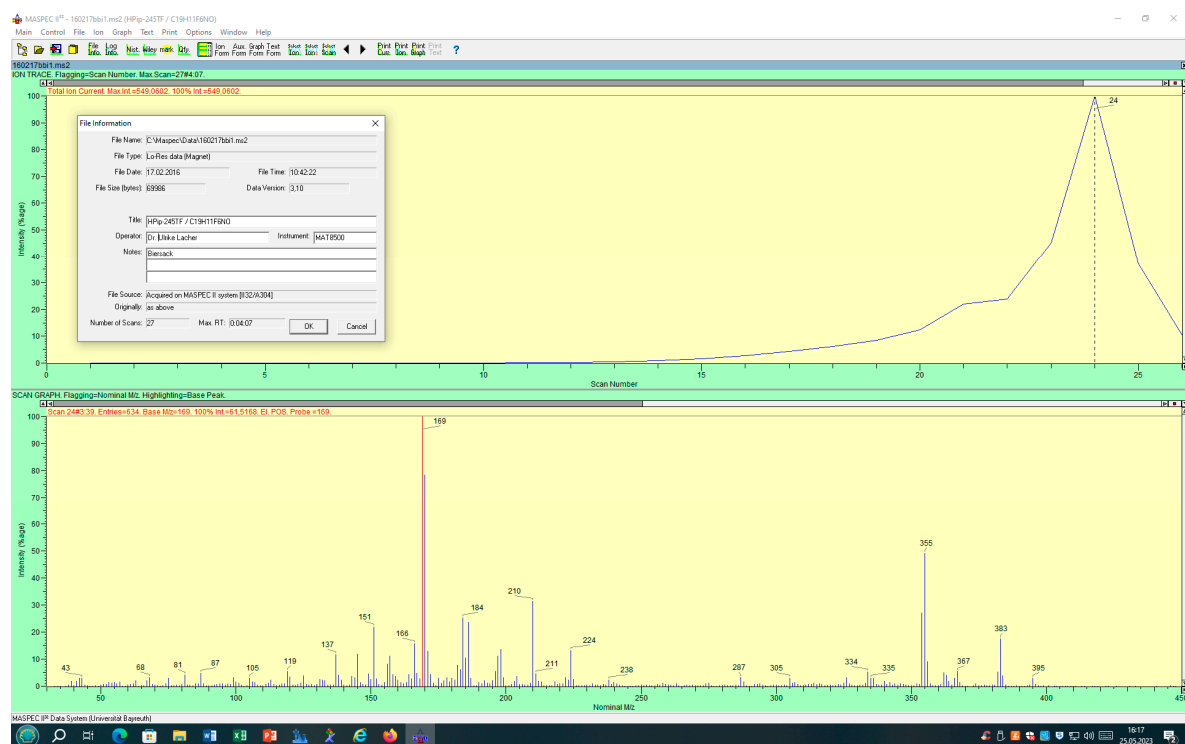


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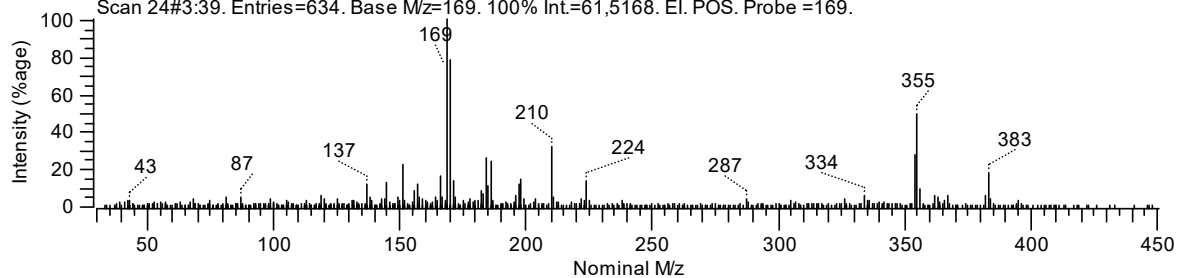
Scan 22#3:20. Entries=1253. Base M/z=151.2. 100% Int.=23,8976. EI. POS. Probe =122.



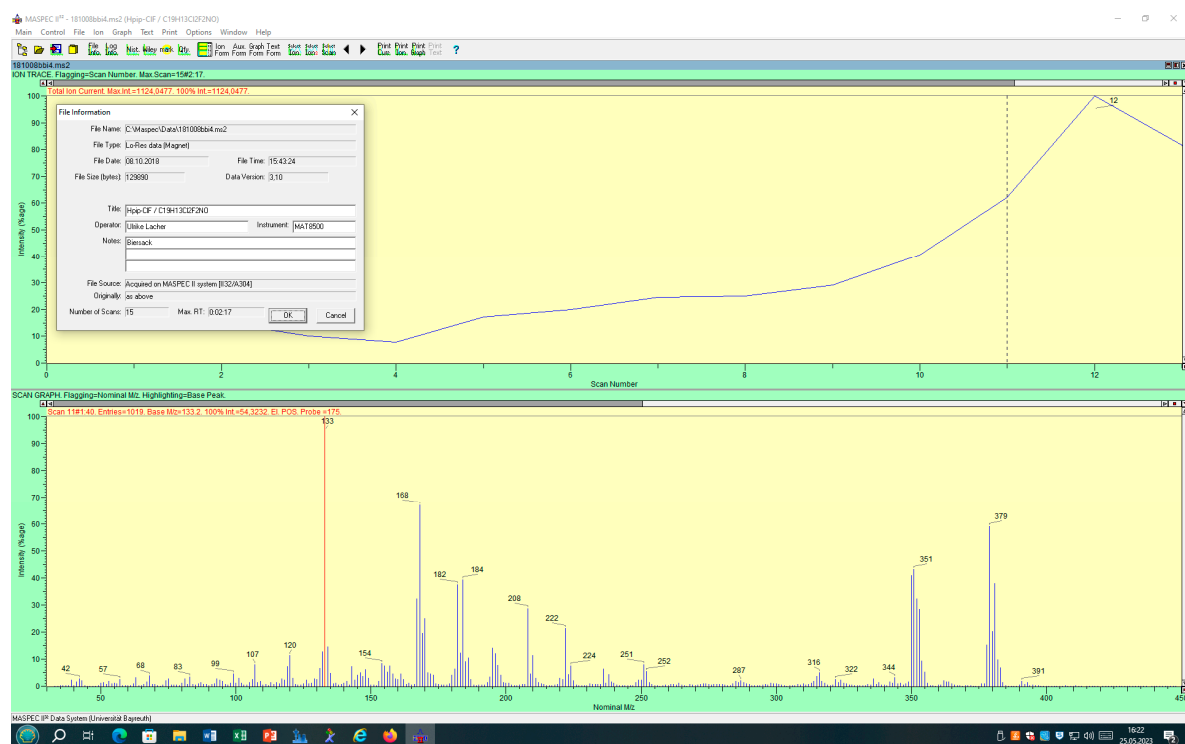
EI mass spectrum of **1g**



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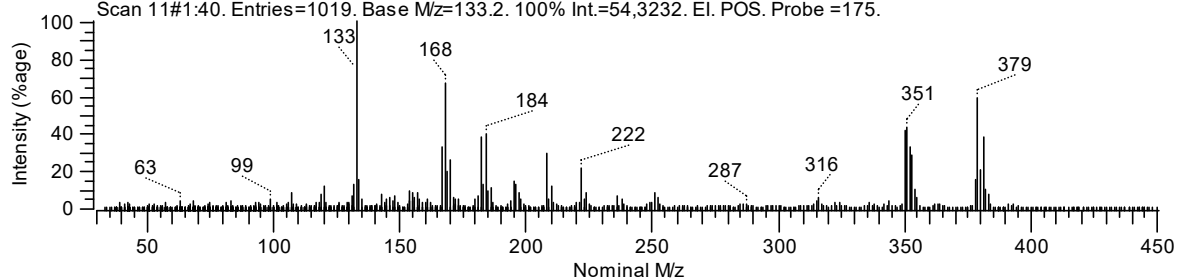


EI mass spectrum of **1h**

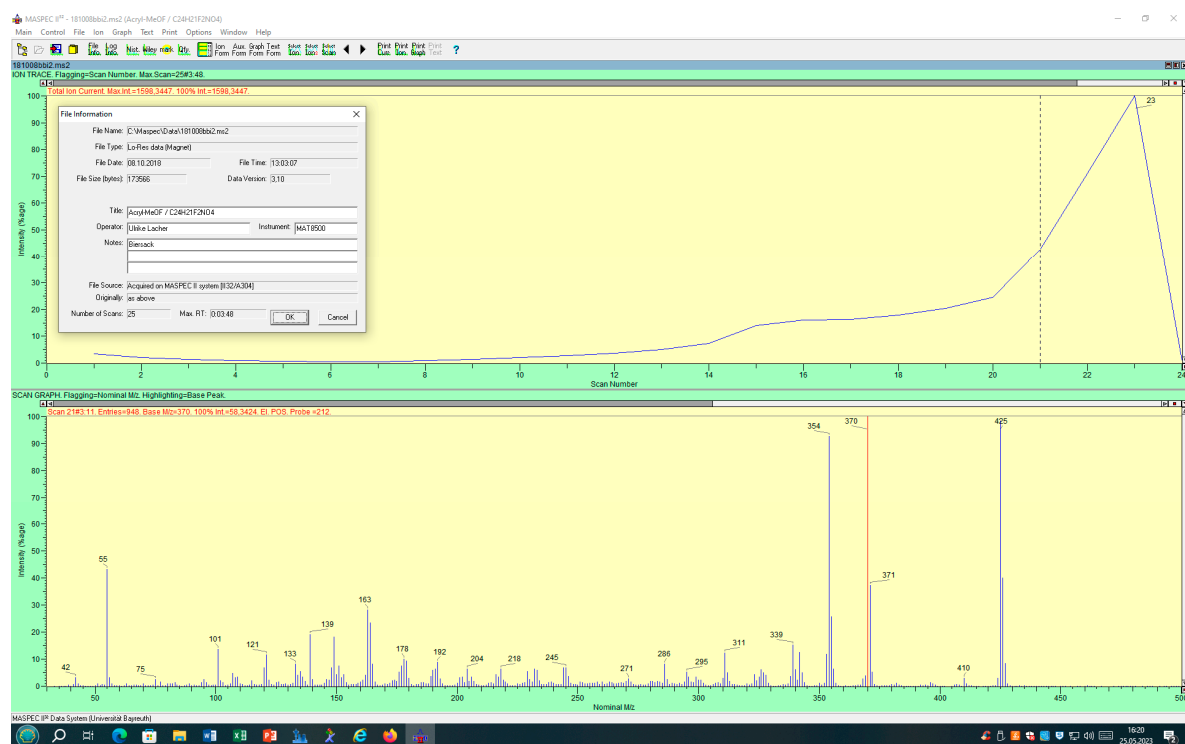


SCAN GRAPH. Flaggng=Nominal M/z. Highlighting=Base Peak.

Scan 11#1:40. Entries=1019. Base M/z=133.2. 100% Int.=54,3232. El. POS. Probe =175.

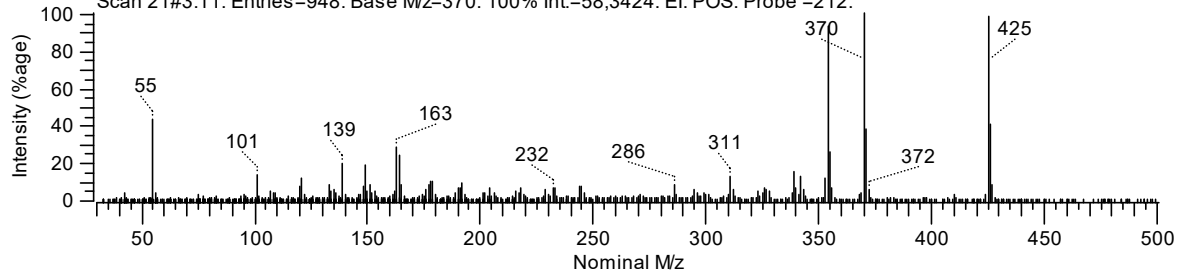


EI mass spectrum of 2c

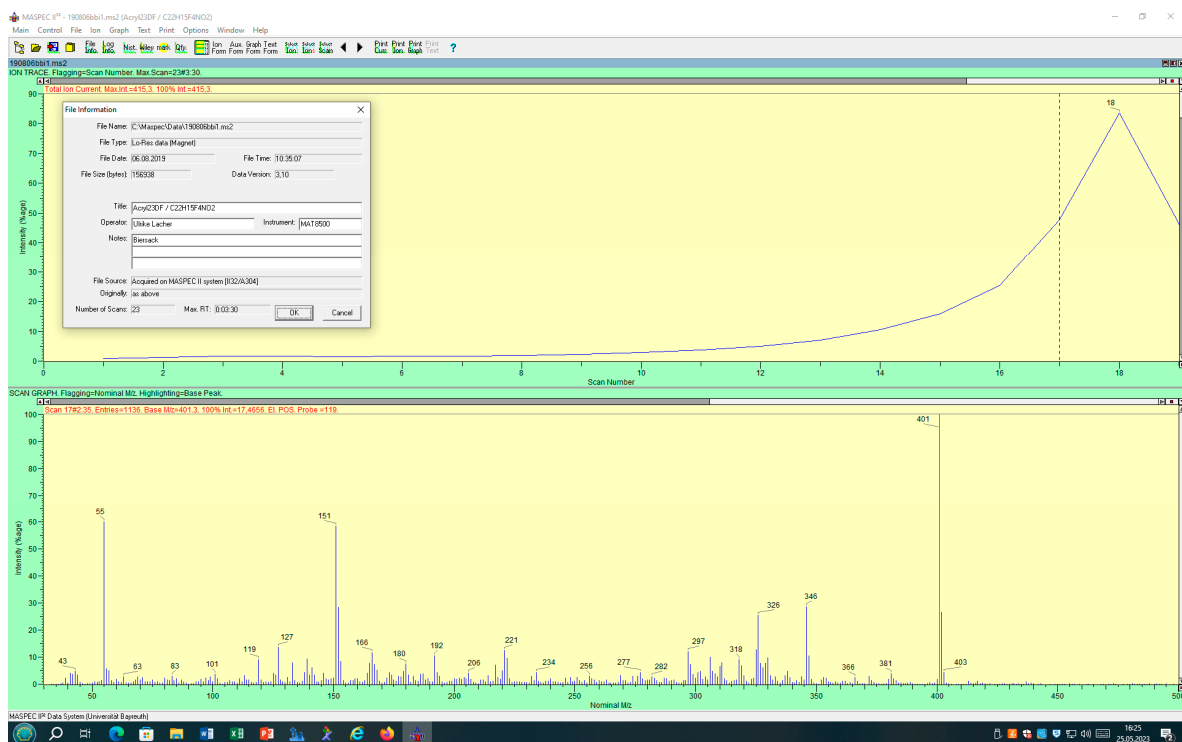


SCAN GRAPH. Flagging=Nominal M/z. Highlighting=Base Peak.

Scan 21#3:11. Entries=948. Base M/z=370. 100% Int.=58,3424. EI. POS. Probe =212.

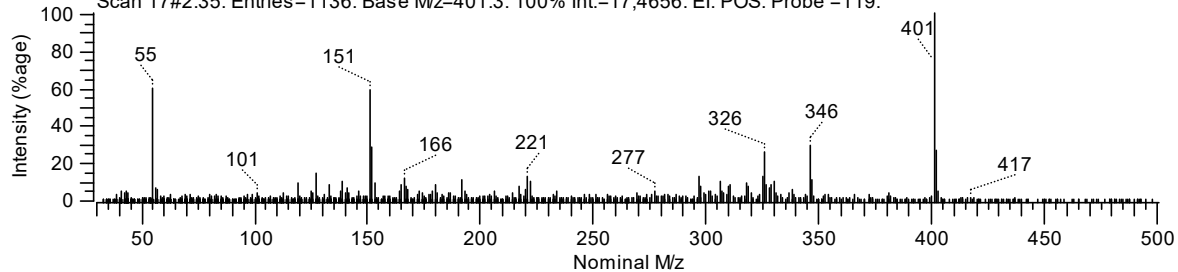


EI mass spectrum of 2e

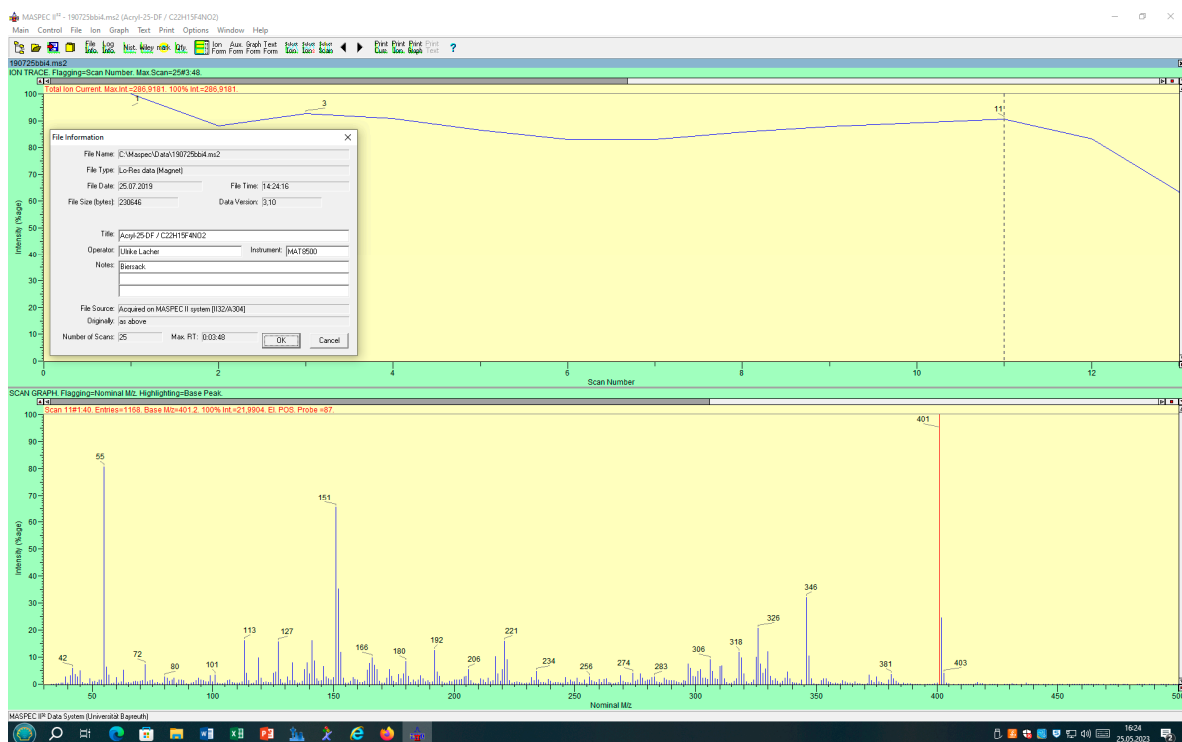


SCAN GRAPH. Flagging=Nominal M/z. Highlighting=Base Peak.

Scan 17#2:35. Entries=1136. Base M/z=401.3. 100% Int.=17,4656. EI. POS. Probe =119.

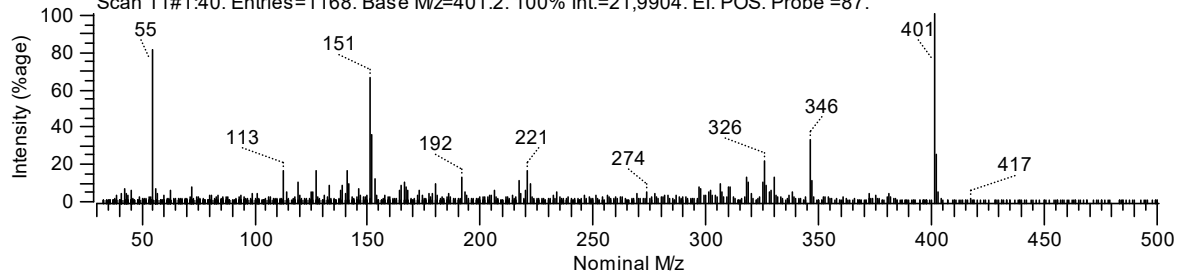


EI mass spectrum of **2f**

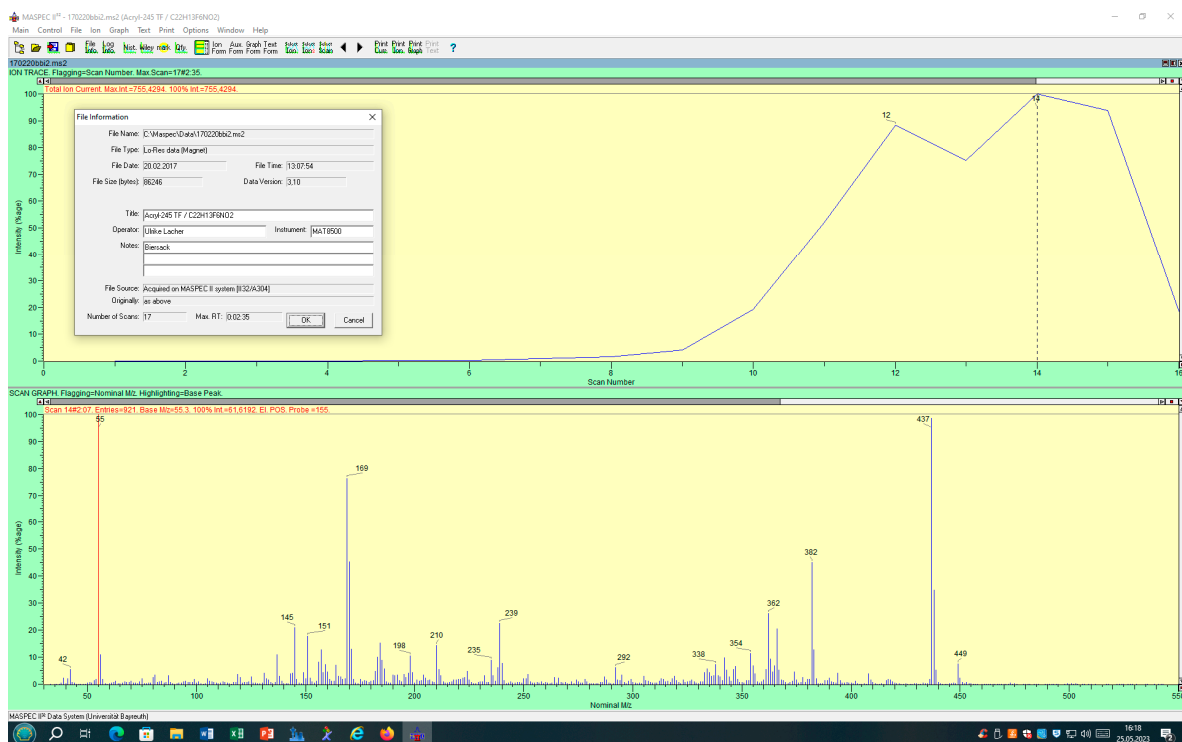


SCAN GRAPH. Flagg=Nominal M/z. Highlighting=Base Peak.

Scan 11#1:40. Entries=1168. Base M/z=401.2. 100% Int.=21,9904. El. POS. Probe =87.

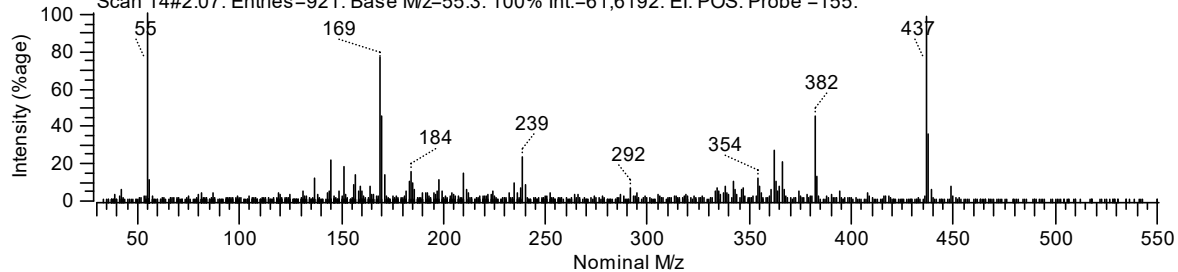


EI mass spectrum of 2g

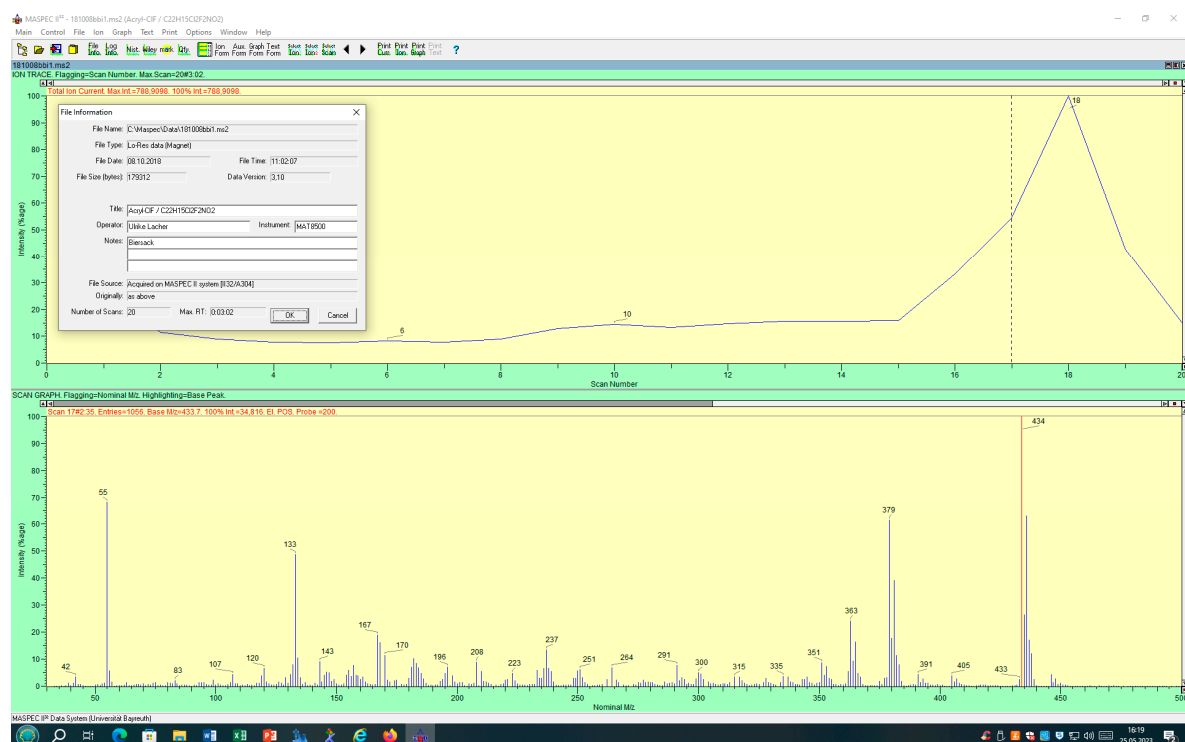


SCAN GRAPH. Flagging=Nominal M/z. Highlighting=Base Peak.

Scan 14#2:07. Entries=921. Base M/z=55.3. 100% Int.=61,6192. EI. POS. Probe =155.



EI mass spectrum of **2h**



SCAN GRAPH. Flagging=Nominal M/z. Highlighting=Base Peak.

Scan 17#2:35. Entries=1056. Base M/z=433.7. 100% Int.=34,816. EI. POS. Probe =200.

