

Design, Synthesis and Biological Evaluation of Aromatase Inhibitors based on Sulfonates and Sulfonamides of Resveratrol

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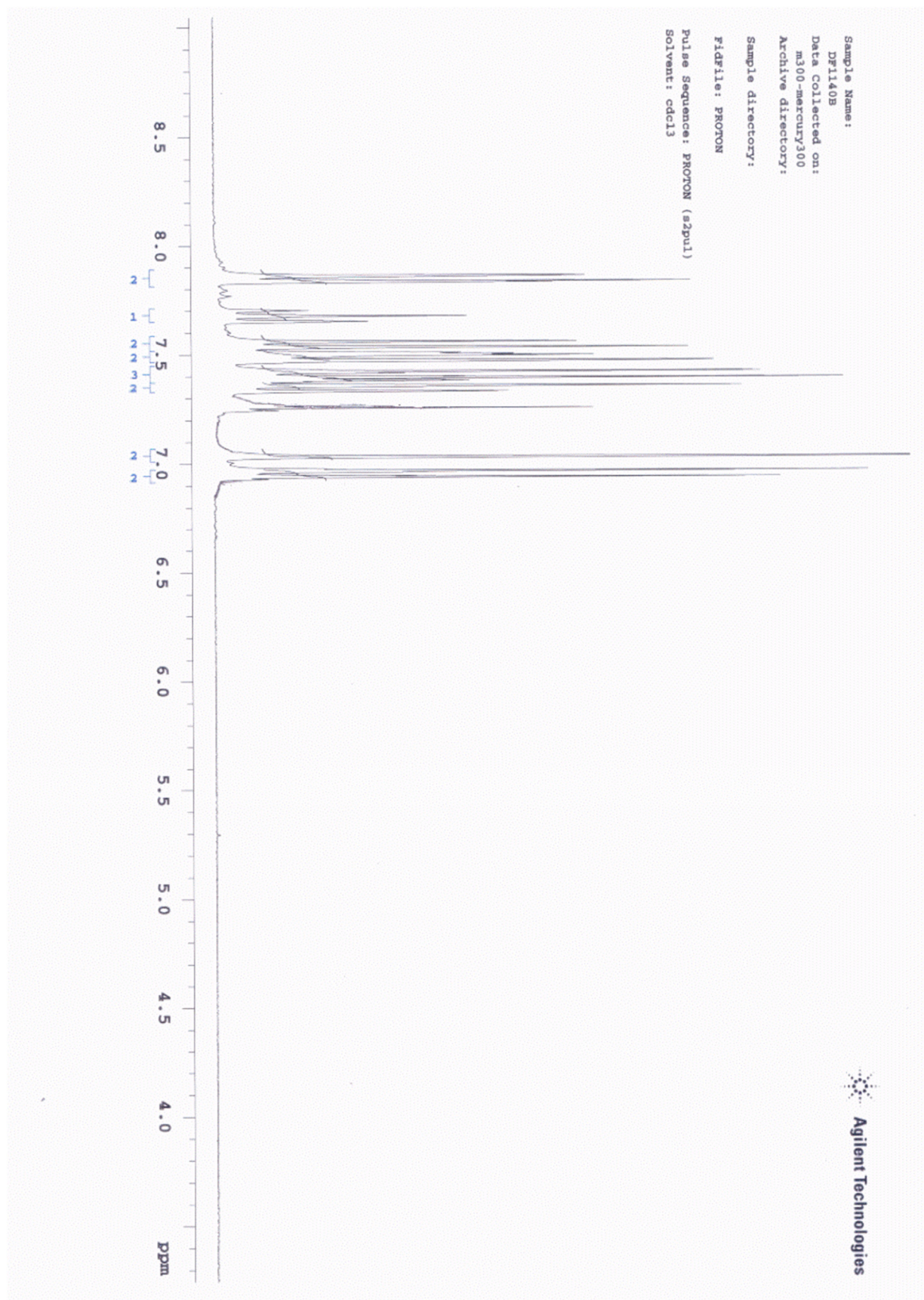
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Figure S1: ^1H and ^{13}C NMR spectrum (300 MHz, CDCl_3) of 4-[(*E*)-2-phenylvinyl]phenylbenzenesulfonate **1a**



Sample Name:

DF1140B

Data Collected on:

m300-mercury300

Archive directory:

Sample directory:

F1:File: CARBON

Pulse Sequence: CARBON (szpul)

Solvent: cdc13

Data collected on: Mar 11 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

1826 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 1 hr, 4 min

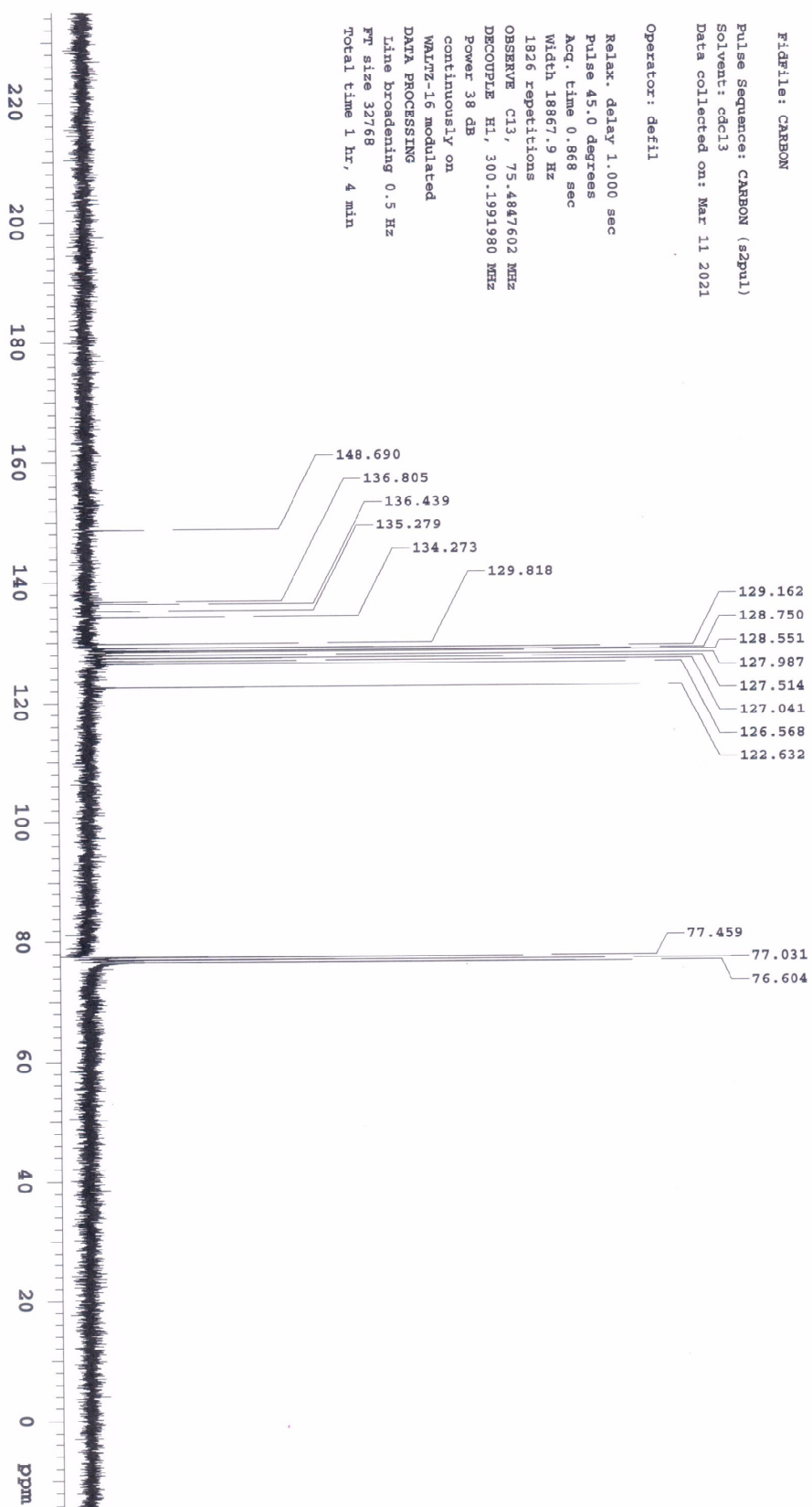
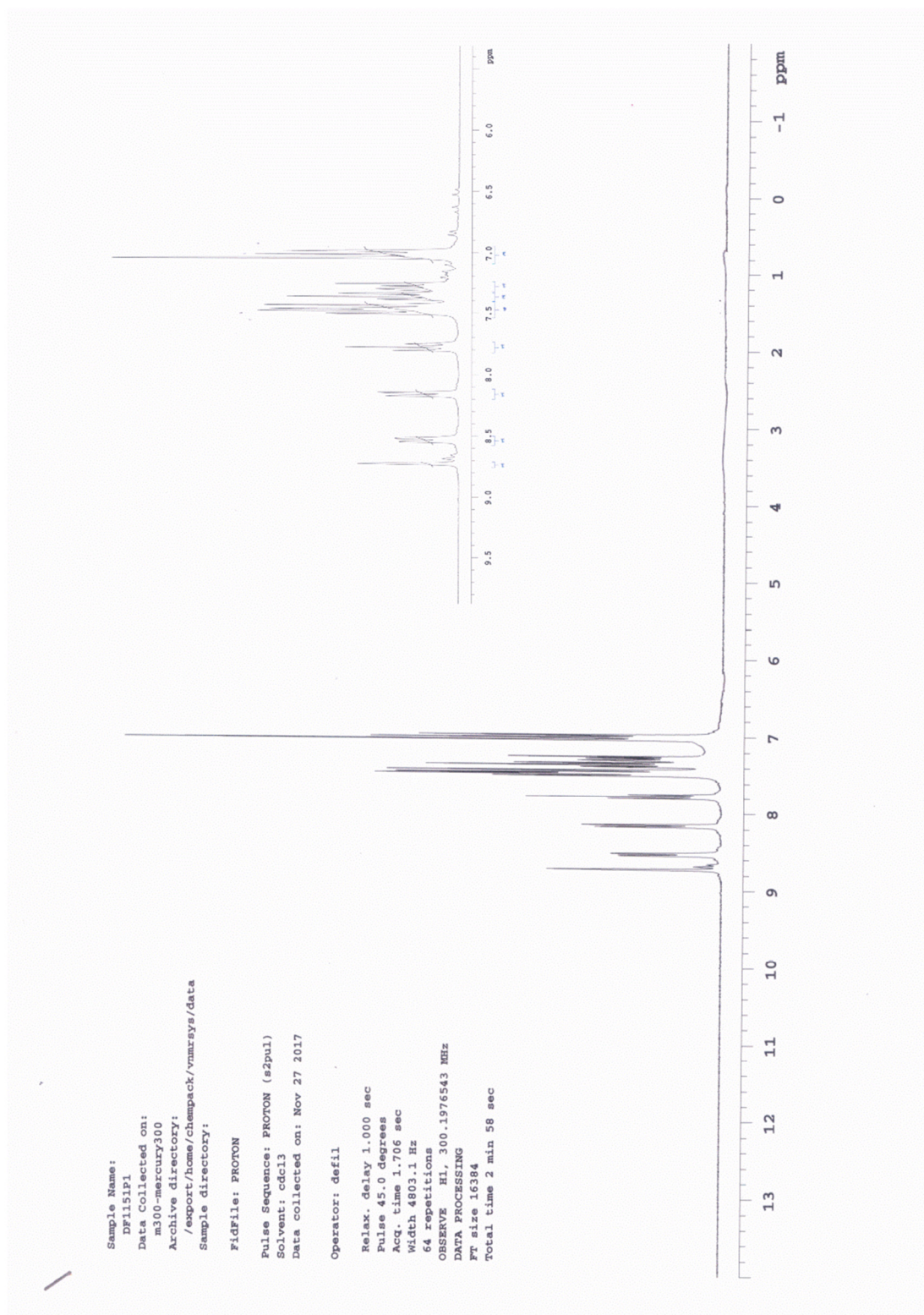


Figure S2: ^1H and ^{13}C NMR spectrum (300 MHz, CDCl_3) of 4-[(E)-2-phenylvinyl]phenyl 3-nitrobenzenesulfonate **1b**



Sample Name:
 DF151P2
 Data Collected on:
 m300-mercury300
 Archive directory:
 /export/home/chempack/vnmrSYS/data
 Sample directory:
 FIDFile: CARBON
 Pulse Sequence: CARBON (s2pul)
 Solvent: cdcl3
 Data collected on: Nov 27 2017
 Operator: defil
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 0.868 sec
 Width 18867.9 Hz
 800 repetitions
 OBSERVE C13, 75.4847602 MHz
 DECOUPLE H1, 300.1991980 MHz
 Power 38 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 32768
 Total time 25 min

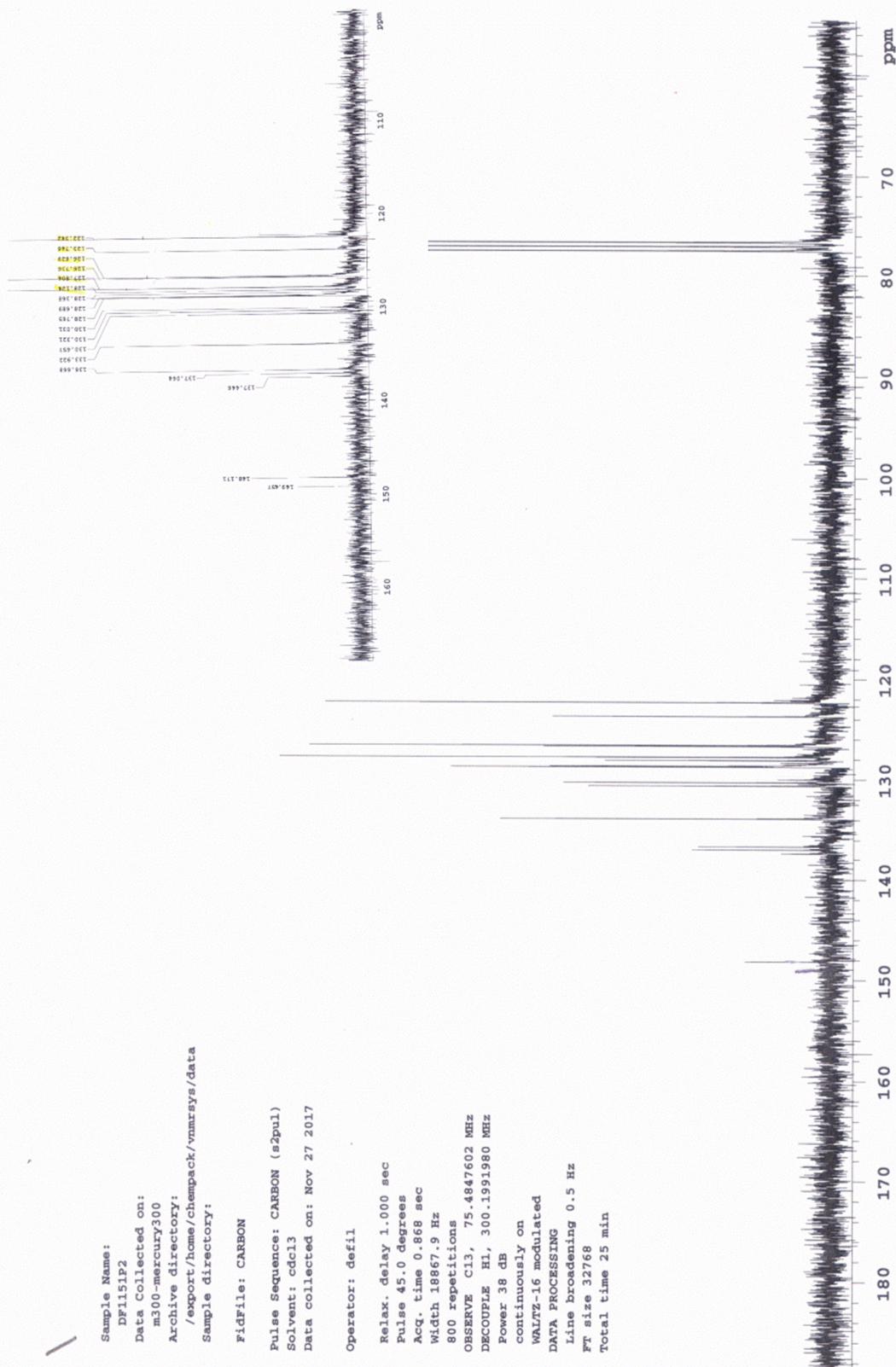
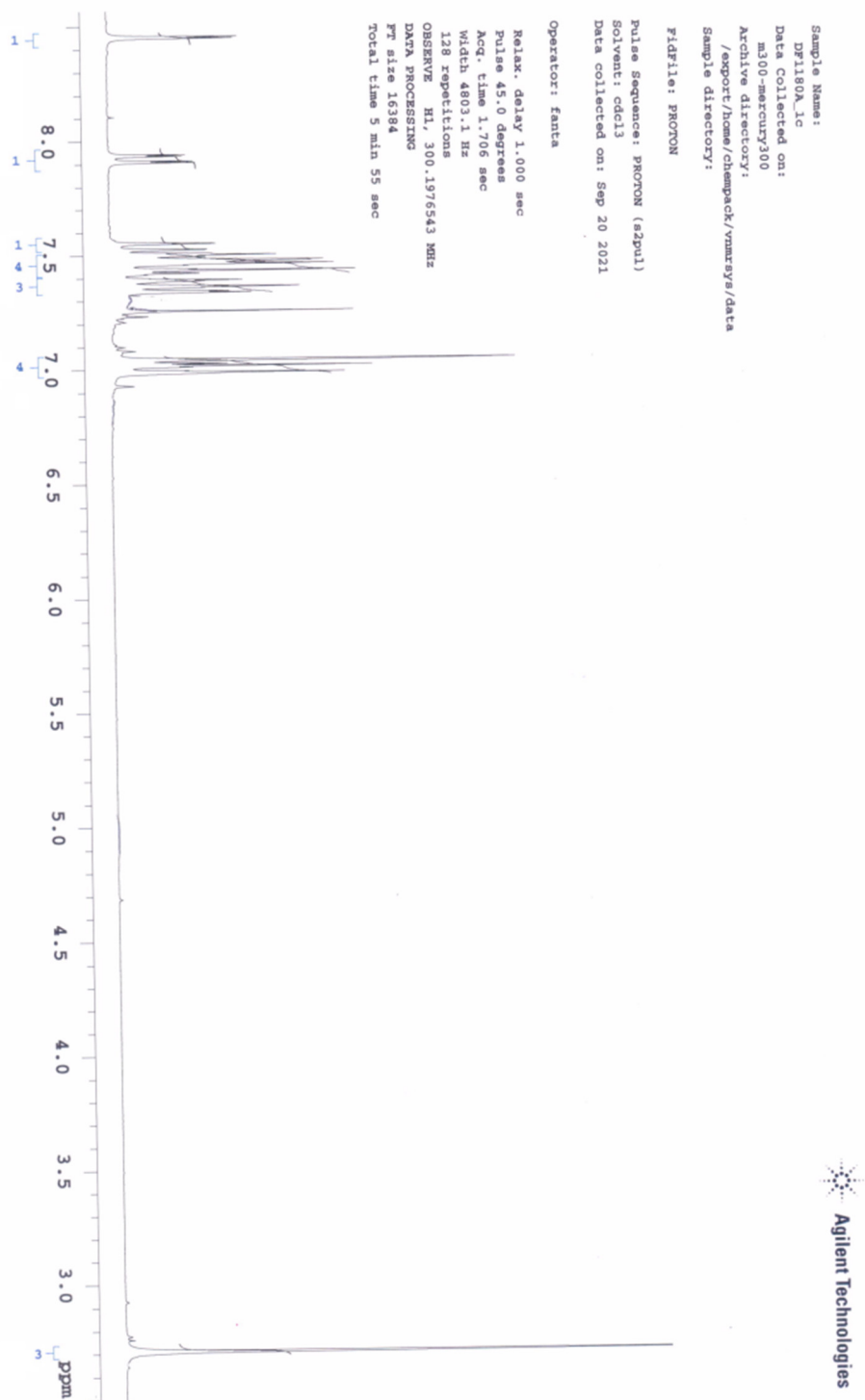


Figure S3: ^1H NMR (300 MHz, CDCl_3) and ^{13}C spectrum (300 MHz, CDCl_3) of 4-[(*E*)-2-phenylvinyl]phenyl 4-methyl-2-nitrobenzenesulfonate **1c**



Sample Name:
DF1180A
Data Collected on:
m300-mercury300
Archive directory:

Sample directory:
Fidfile: CARBON

Pulse Sequence: CARBON-13
Solvent: cdcl3
Data collected on: Mar 18 2021

Operator: defil

Relax. delay 7.000 sec
Pulse 45.0 degrees
Acq. time 0.868 sec
Width 18867.9 Hz
2000 repetitions
OBSERVE C13, 75.4847604 MHz
DECUPLE H1, 300.1991980 MHz
Power 38 dB
conting on
WALTZ-16 Modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 32768
Total time 1 hr, 4 min

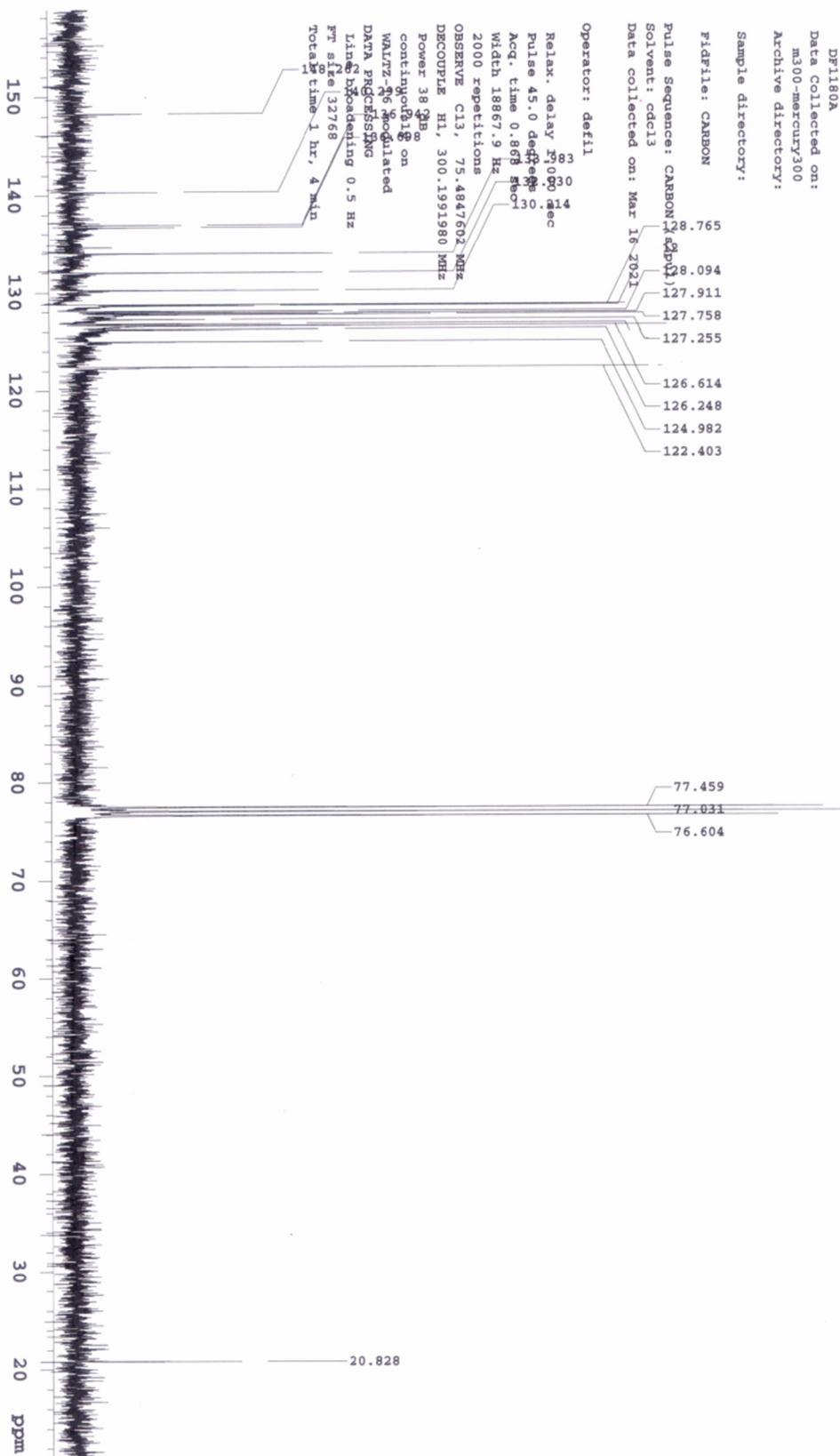
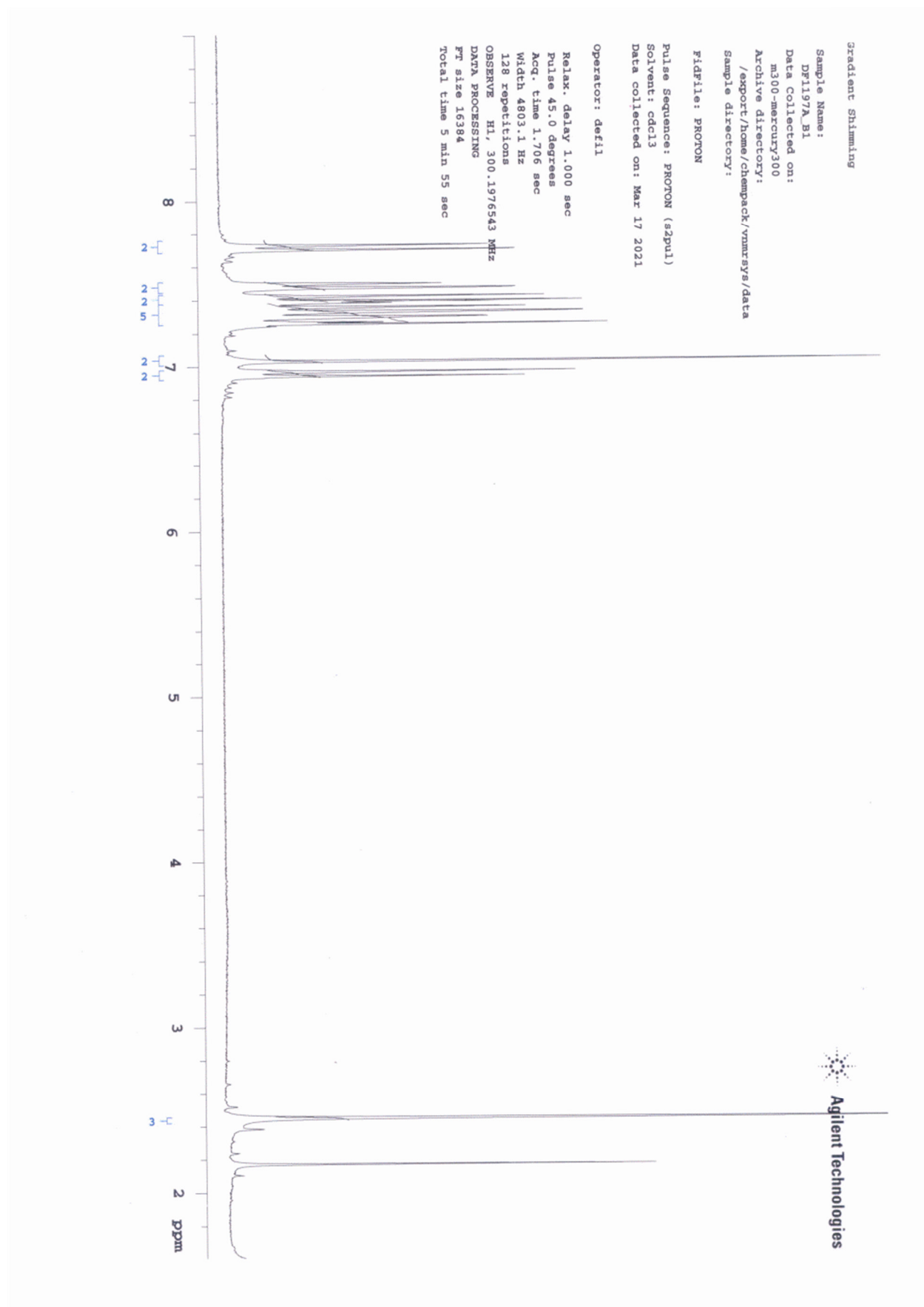


Figure S4: ^1H NMR and ^{13}C spectrum (300 MHz, CDCl_3) of 4-[(*E*)-2-phenylvinyl]phenyl 4-methylbenzenesulfonate **1d**



Gradient Shimming

Sample Name:

DF1197A_B1

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrSYS/data

Sample directory:

File: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

Data collected on: Mar 17 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

2000 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

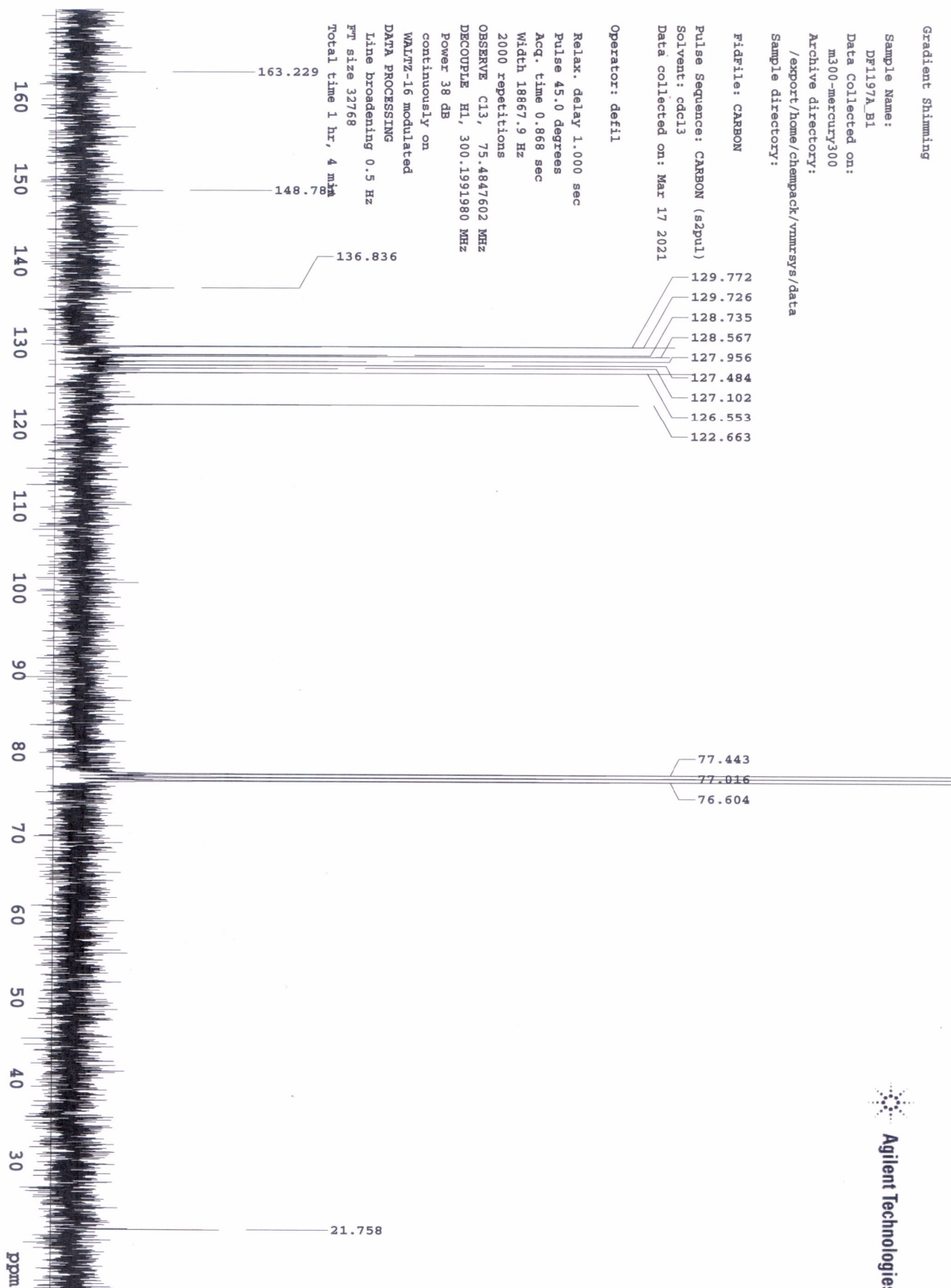
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 1 hr, 4 min





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Gradient Shimming

Sample Name:

DF1184A

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsys/data

Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

Data collected on: Mar 17 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 1867.9 Hz

2500 repetitions

OBSERVE c13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

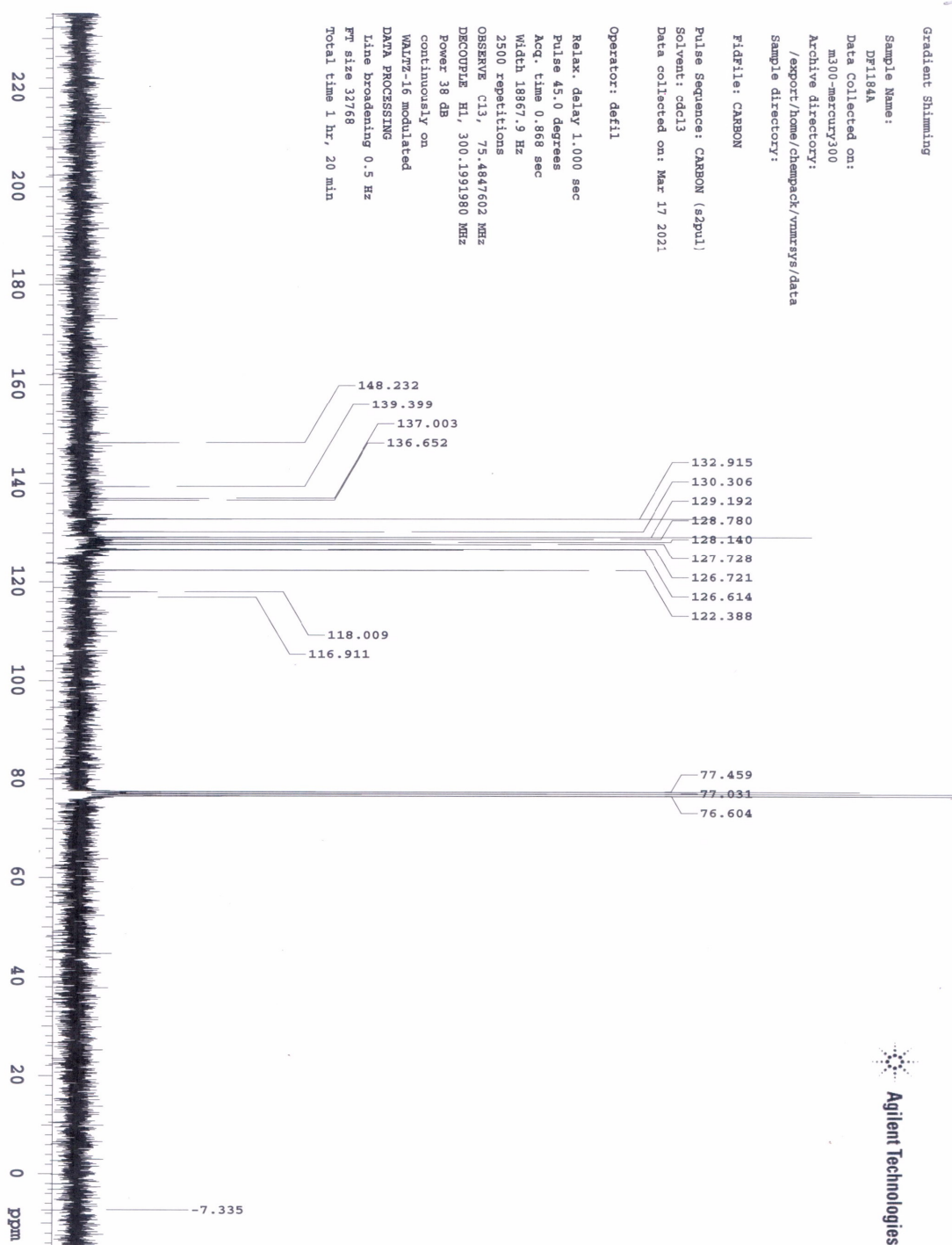
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 1 hr, 20 min



Gradient Shimming

Sample Name:

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrSYS/data

Sample directory:

File: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent:

Data collected on: Jul 11 2018

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

1200 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 38 min

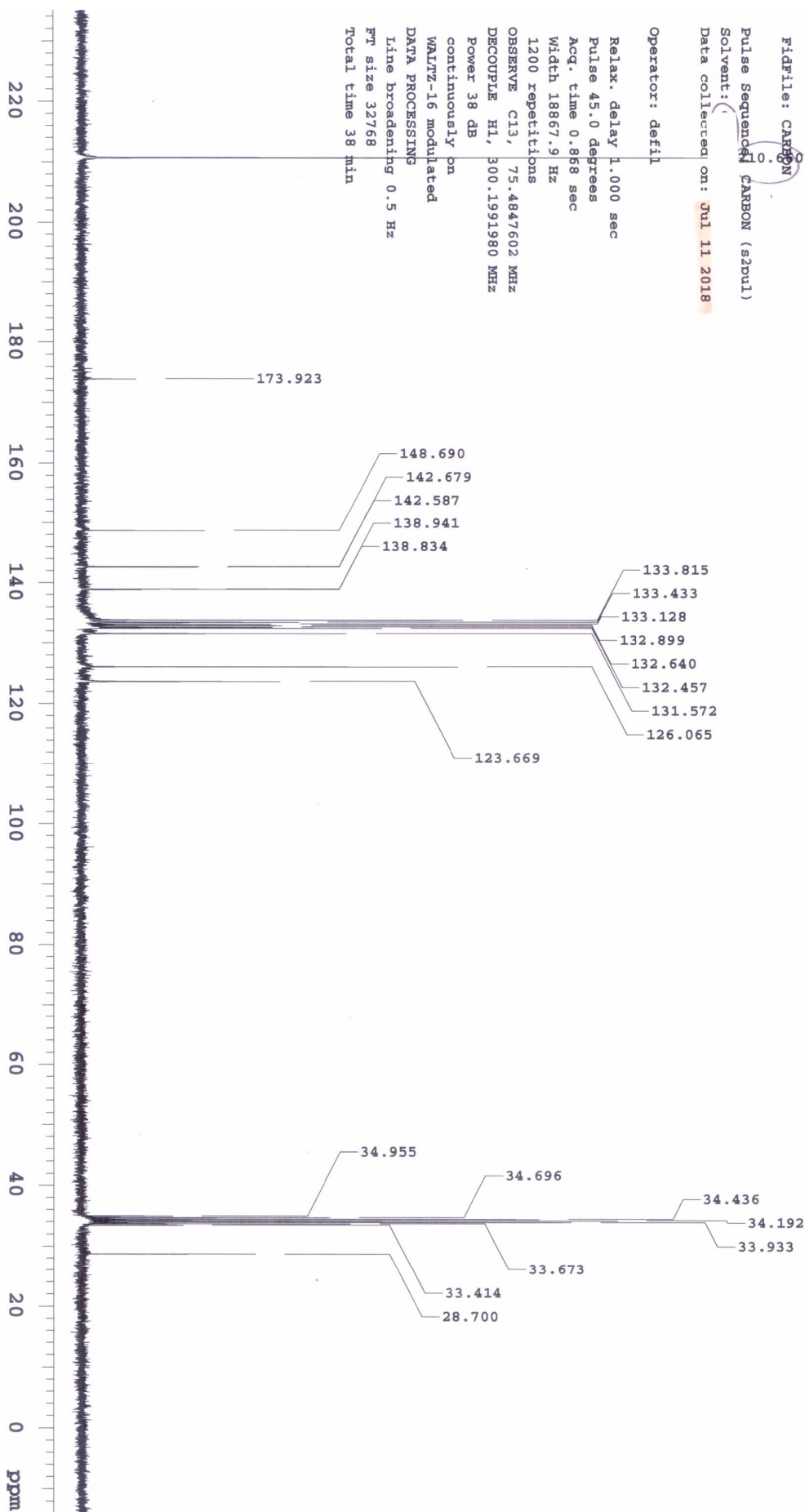
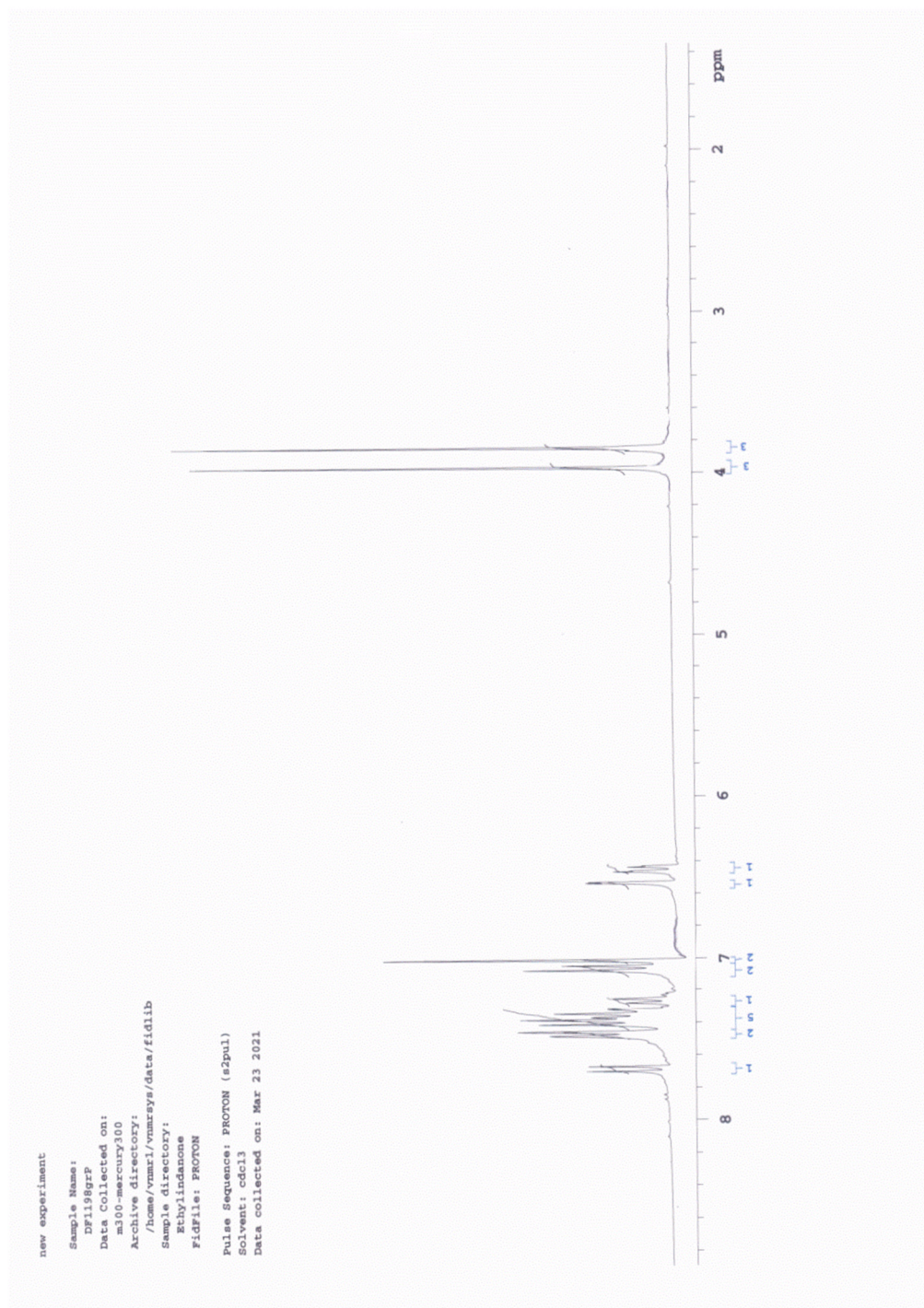


Figure S7: ^1H NMR and ^{13}C spectrum (300 MHz, CDCl_3) of 4-[(*E*)-2-phenylvinyl]phenyl 2,4-dimethoxybenzenesulfonate **1g**



Gradient Shimming

Sample Name:

DP119gerez0

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmr/sys/data

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul1)

Solvent: cdcl3

Data collected on: May 3 2018

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

797 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 25 min

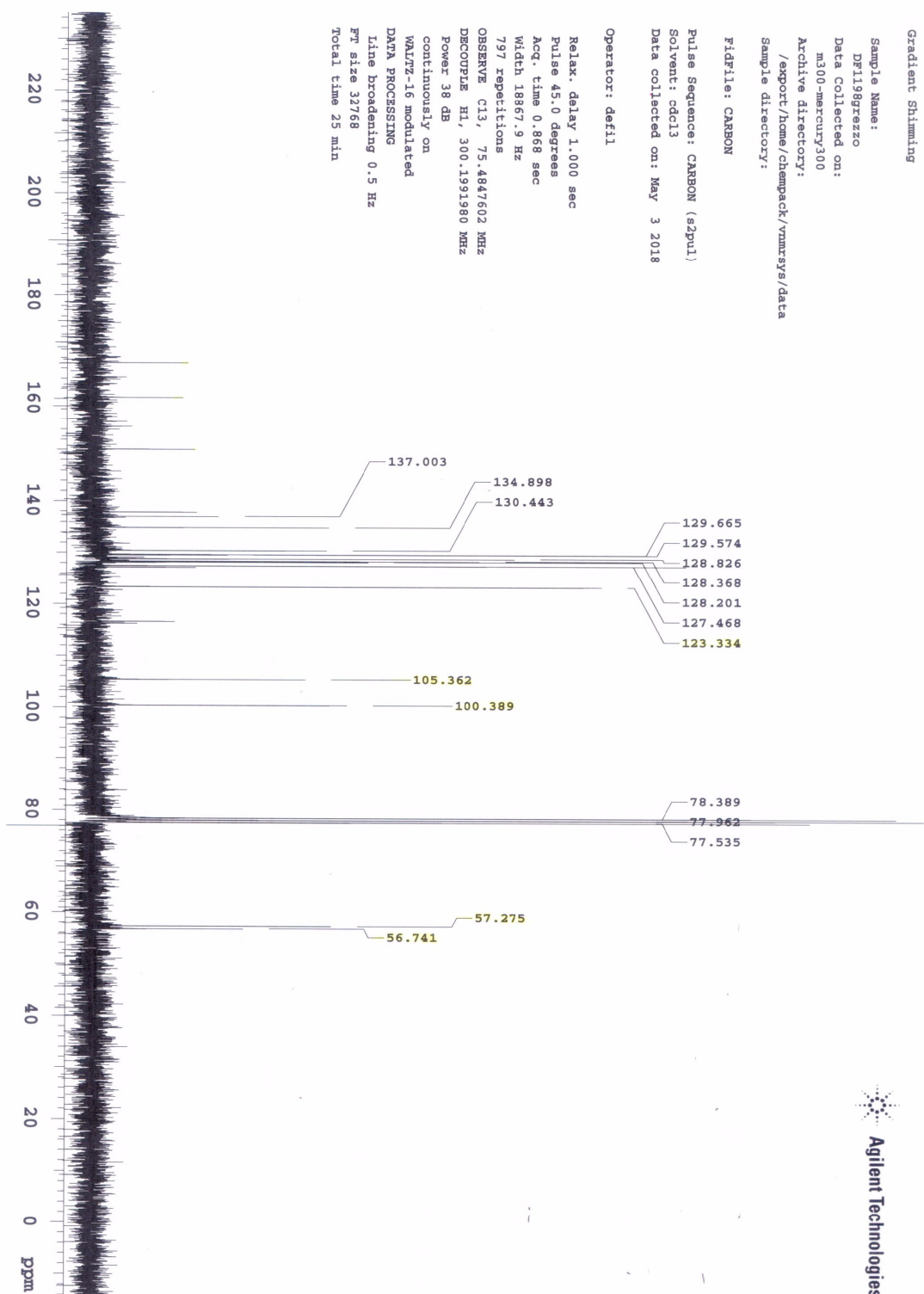
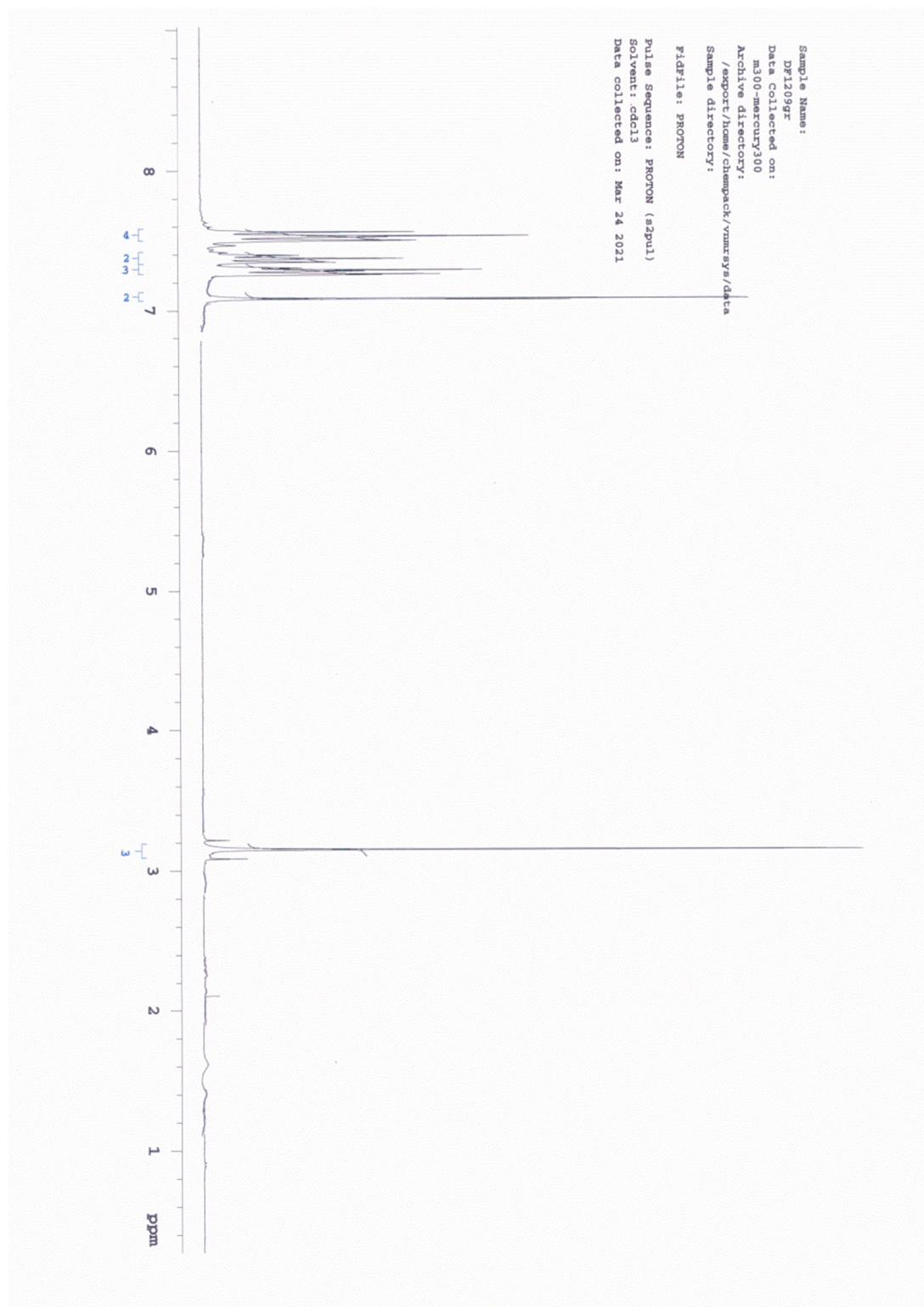


Figure S8: ^1H NMR and ^{13}C spectrum (300 MHz, CDCl_3) of 4-[(*E*)-2-phenylvinyl]phenylmethanesulfonate **1h**



Sample Name:
DF1209gr
Data Collected on:
m300-mercury300
Archive directory:
/export/home/chempack/vnmrsws/data
Sample directory:

F1df1e: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 24 2021

Operator: fanta

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.868 sec
Width 18867.9 Hz
2000 repetitions
OBSERVE C13, 75.4847602 MHz
DECOUPLE H1, 300.1991980 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
line broadening 0.5 Hz
FT size 32768
Total time 1 hr, 4 min

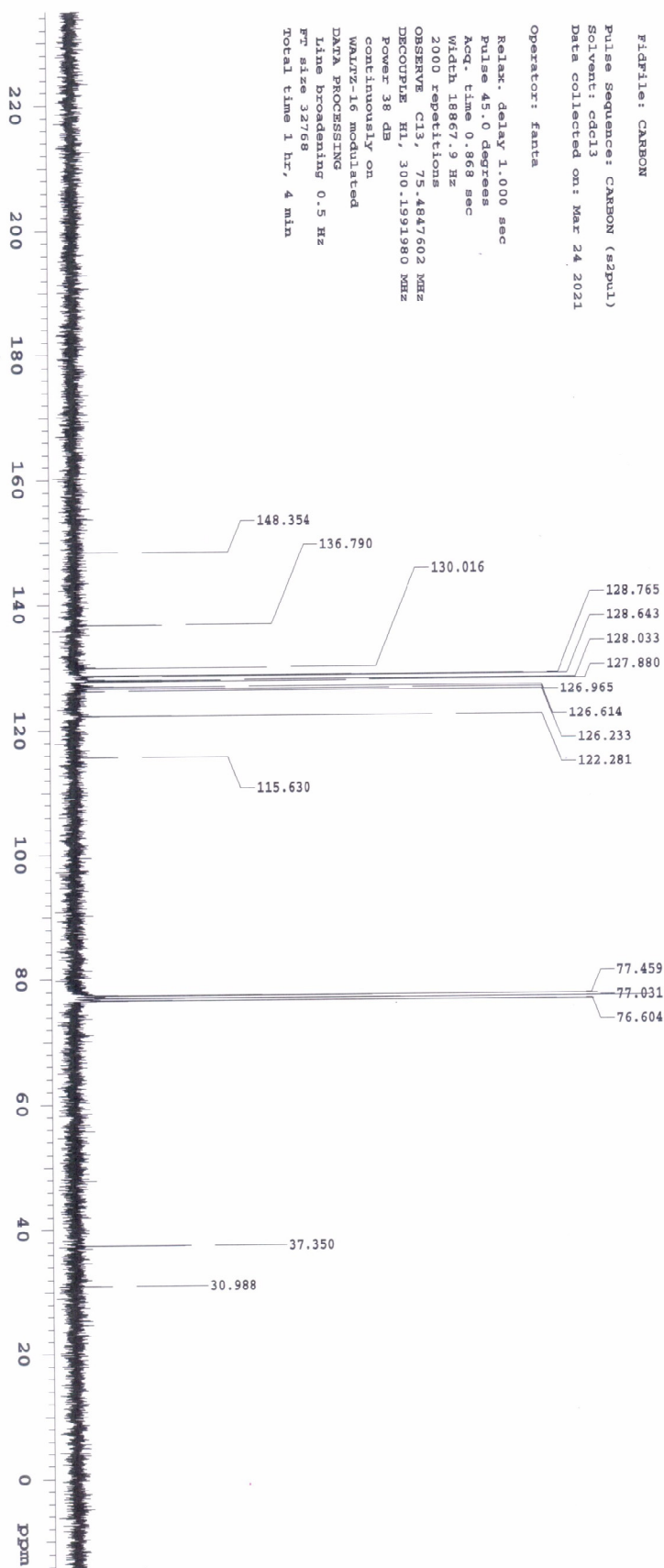
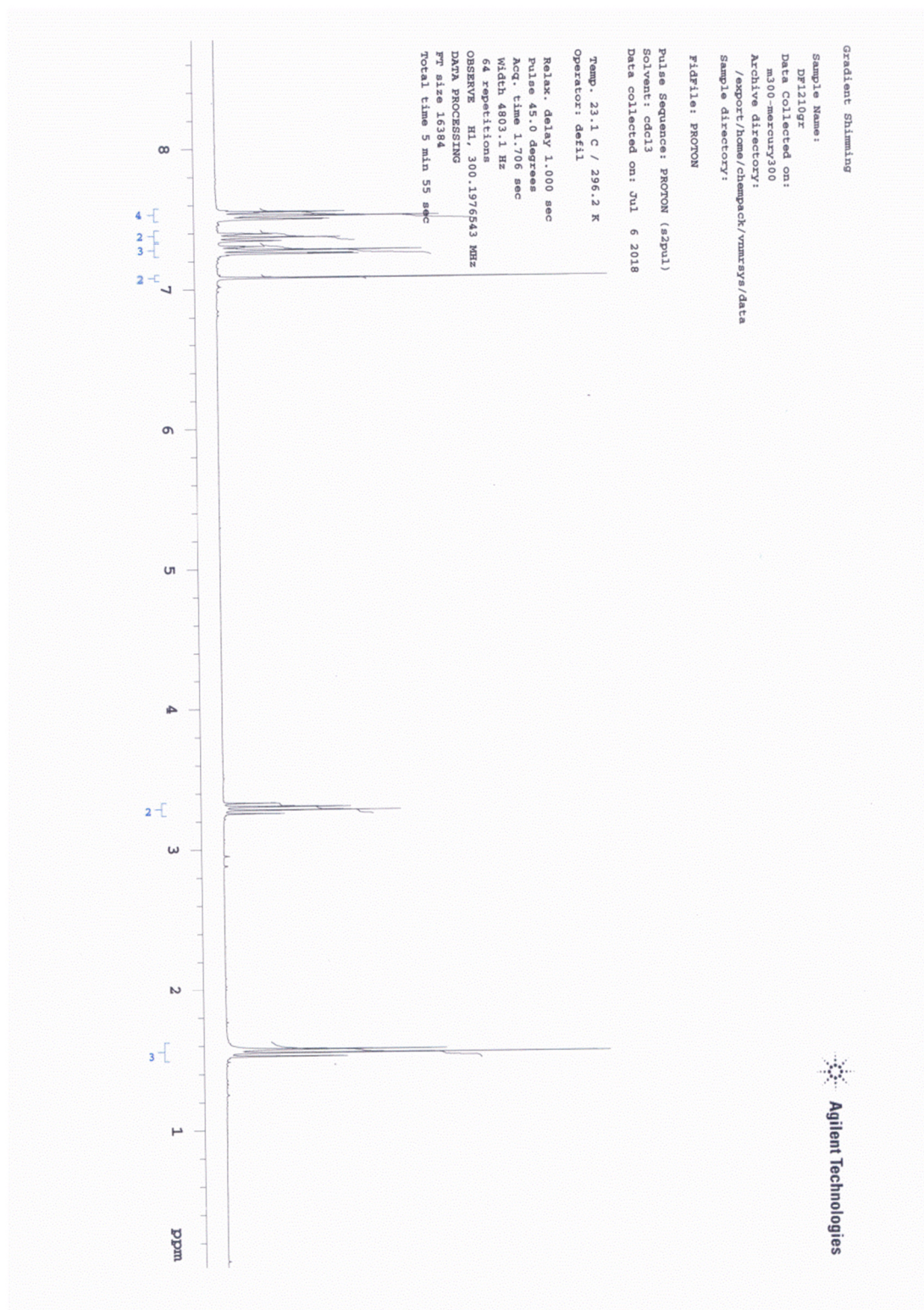


Figure S9: ^1H NMR and ^{13}C spectrum (300 MHz, CDCl_3) of 4-[(*E*)-2-phenylvinyl]phenyl ethanesulfonate **1i**



Gradient Shimming

Sample Name:
DF1210gr
Data Collected on:
m300-mercury300
Archive directory:
/export/home/chempack/vnmr/sys/data
Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 6 2018

Operator: deffil

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.868 sec
Width 18867.9 Hz
800 repetitions
OBSERVE C13, 75.4847602 MHz
DECOUPLE H1, 300.1591980 MHz
Power 38 dB
continuously ON
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 32768
Total time 25 min

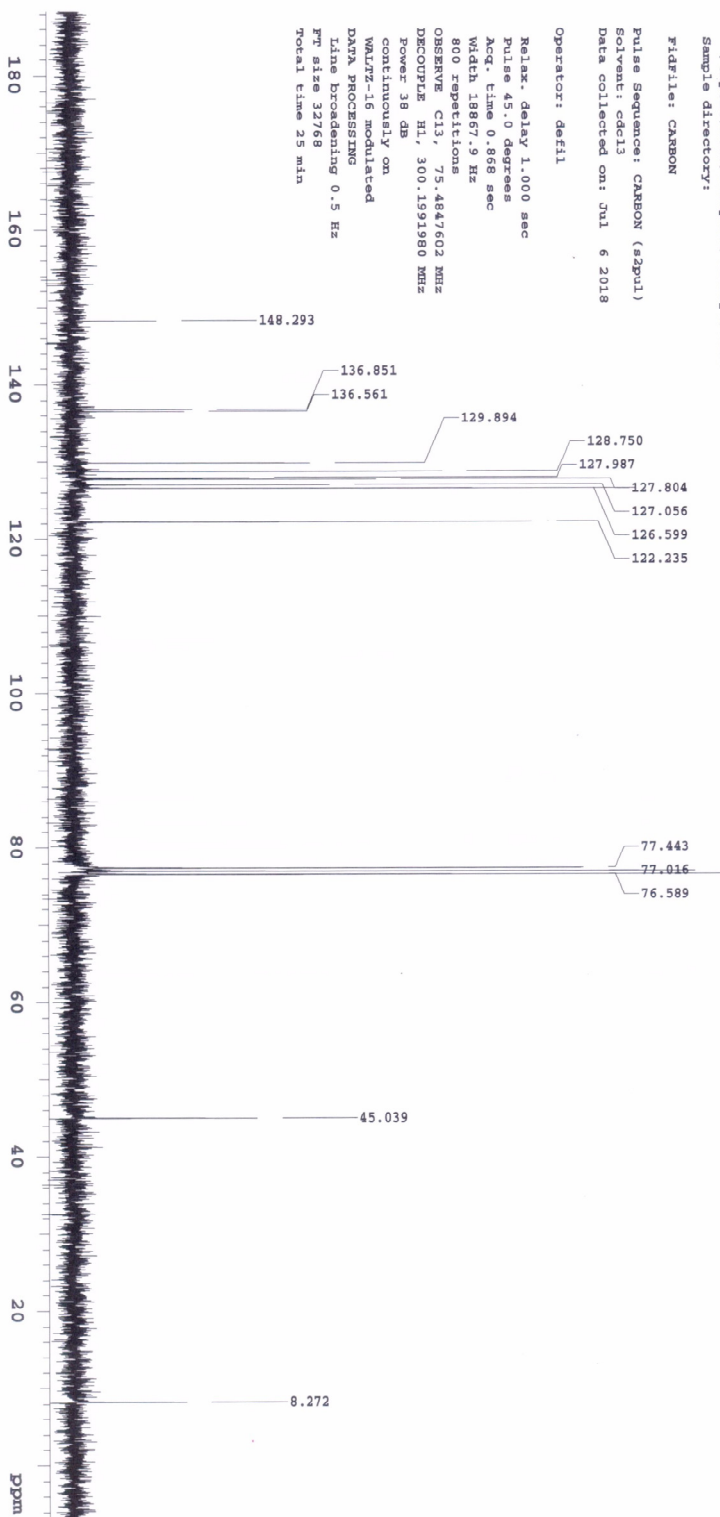
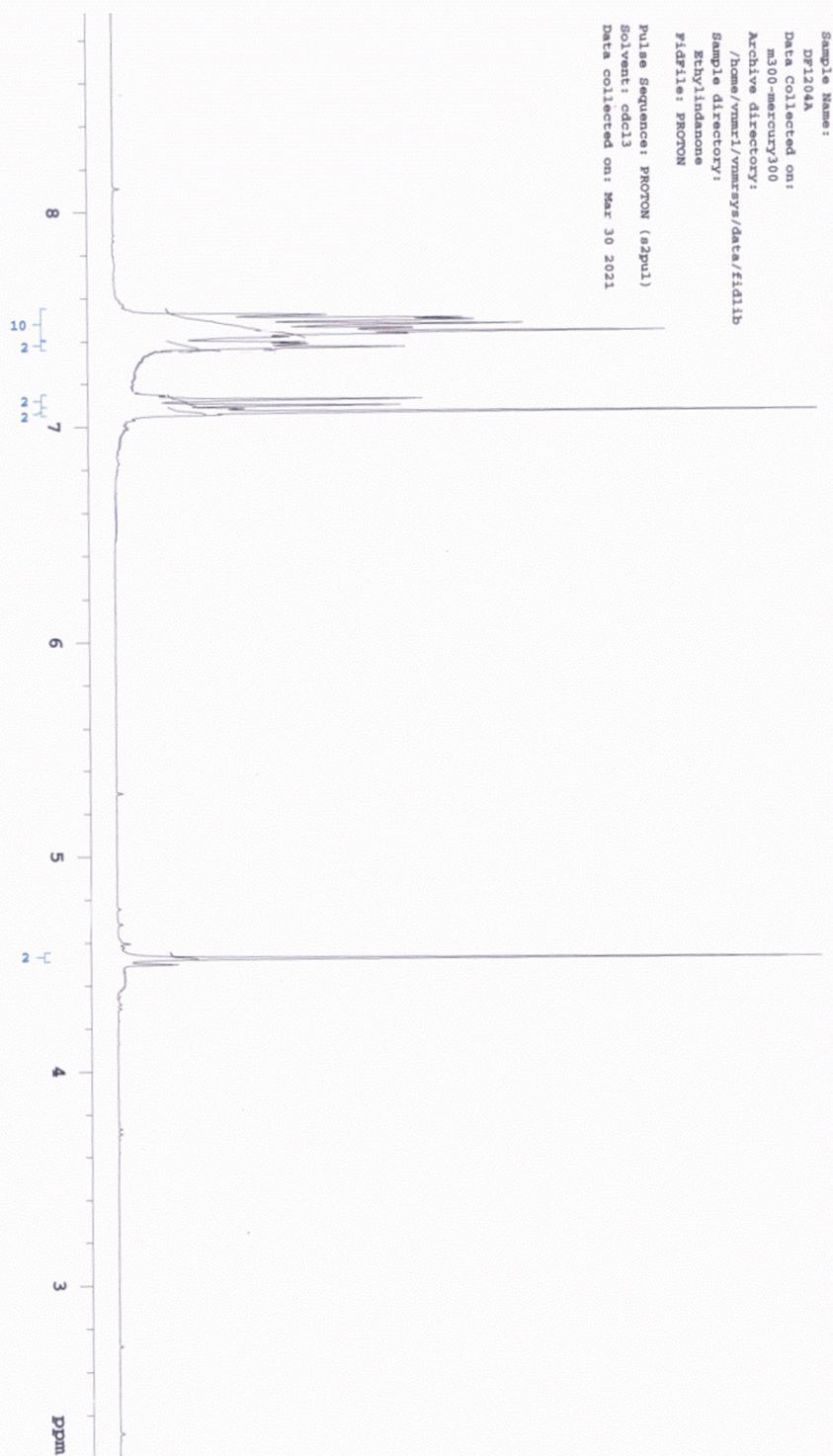


Figure S10: ^1H NMR and ^{13}C spectrum (300 MHz, CDCl_3) of 4-[(*E*)-2-phenylvinyl]phenyl phenylmethanesulfonate **1j**



new experiment

Sample Name:

DF1204A

Data Collected on:

m300-mercury300

Archive directory:

/home/vnmr1/vnmr3ys/data/df1204a

Sample directory:

ethylindanone

File: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

Data collected on: Mar 30 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

1344 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

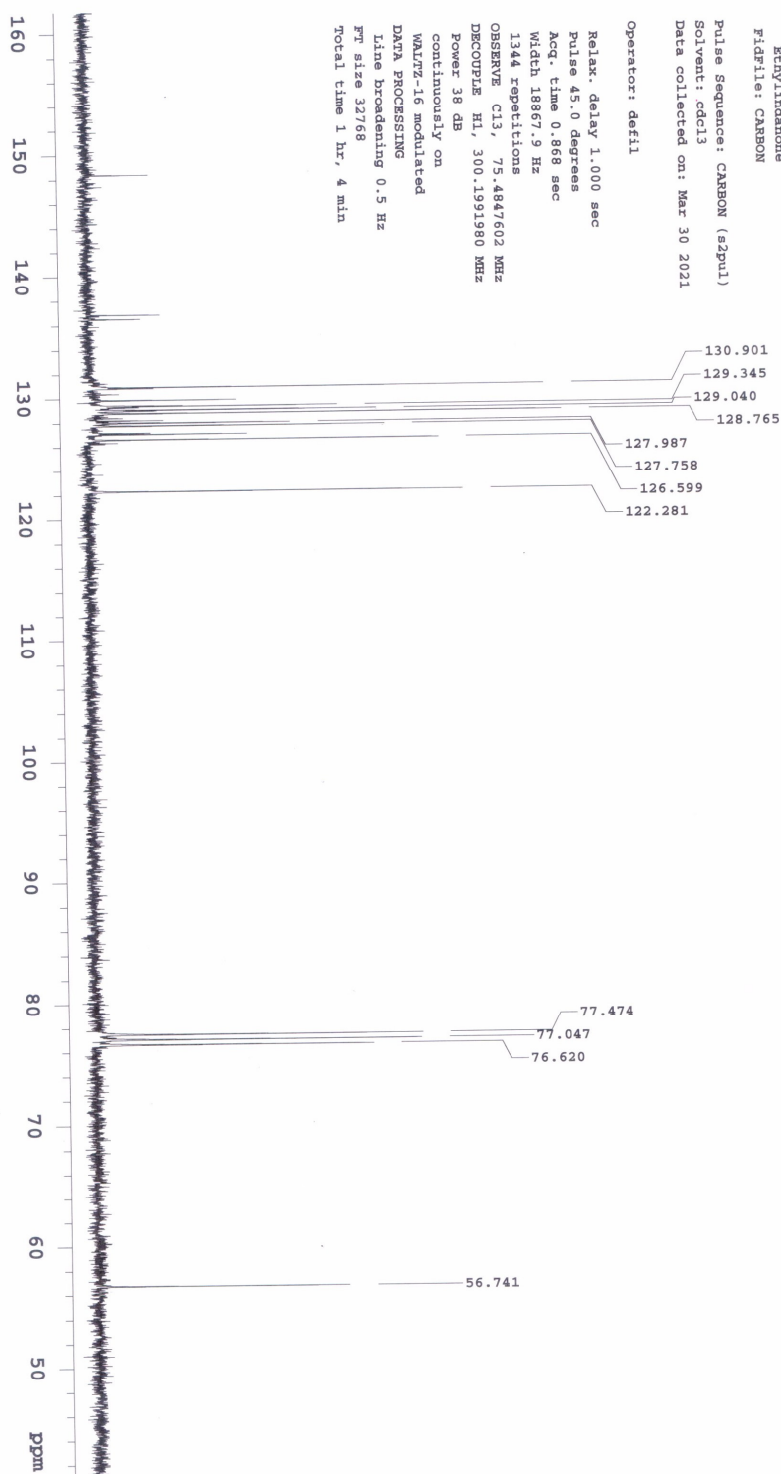
WALTZ-16 modulated

DATA PROCESSING

line broadening 0.5 Hz

FT size 32768

Total time 1 hr, 4 min



Gradient Spinning

Sample Name:

Df16A_AK-I

Data Collected on:

M300-mercury300

Archive directory:

/export/home/chempack/vmrays/data

Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (zgpg1)

Solvent: cdcl3

Data collected on: Mar 5 2018

Operator: de11

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18667.9 Hz

800 repetitions

OBSERVE C13, 75.4647602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

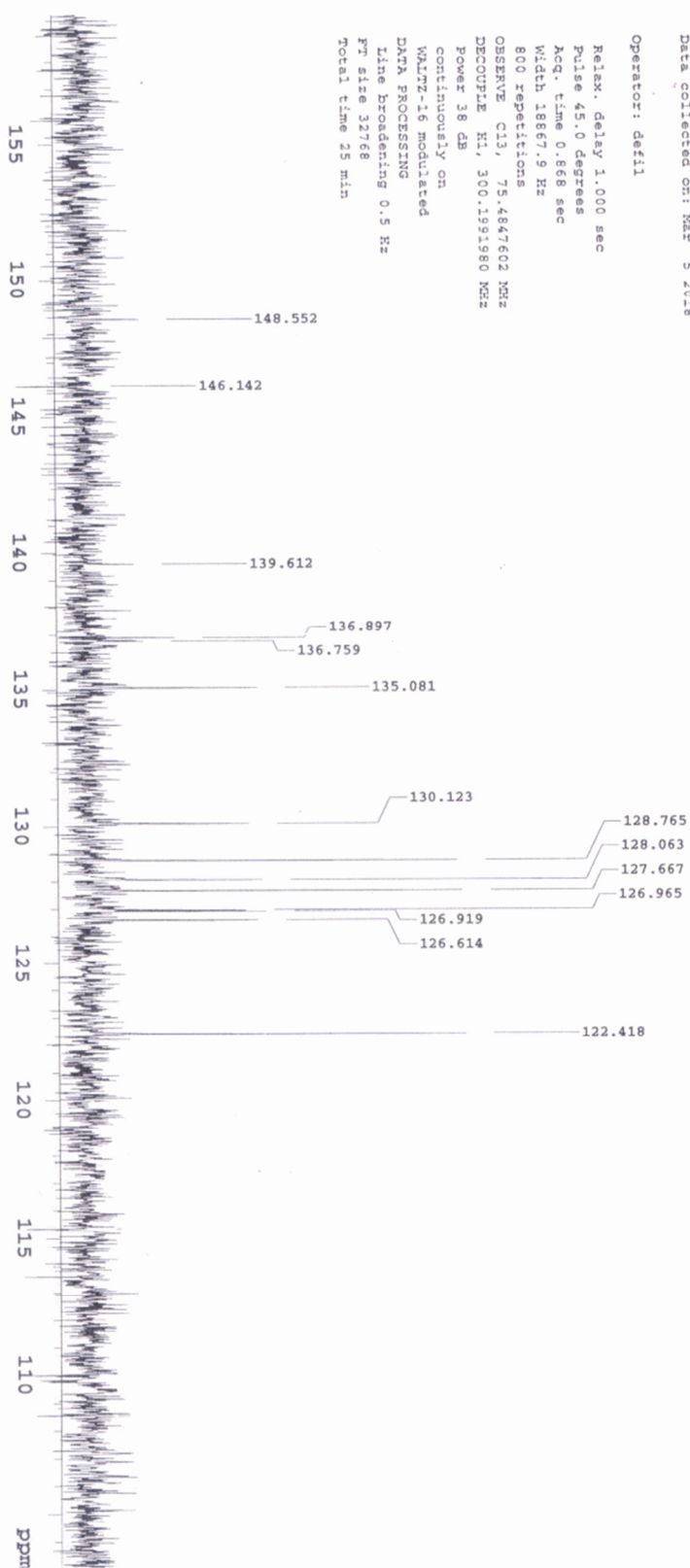
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 25 min





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Sample Name:

DF1195_6C

Data Collected on:

m300-mercury300

Archive directory:

Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

Data collected on: Mar 10 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

2341 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 1 hr, 20 min

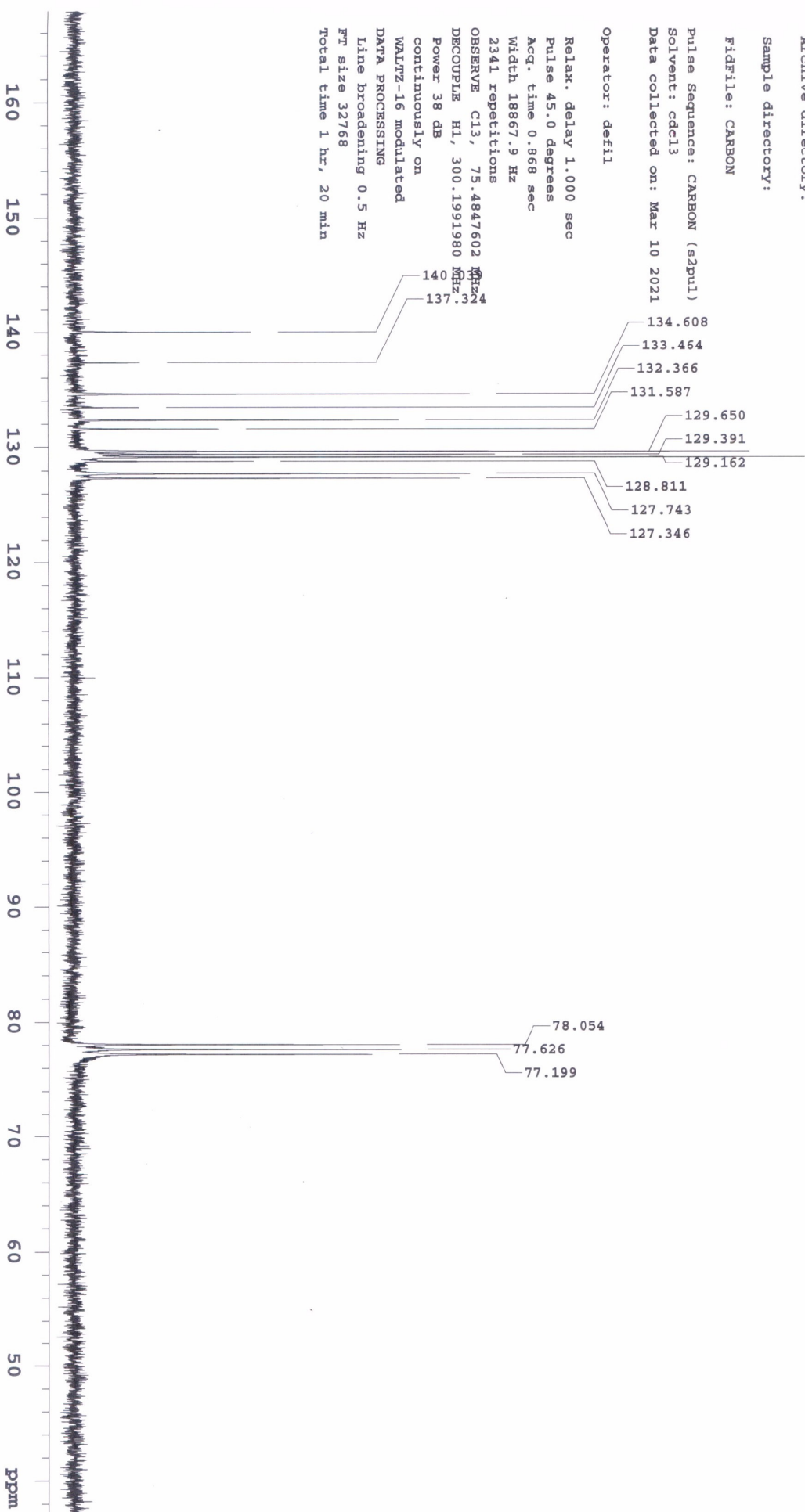
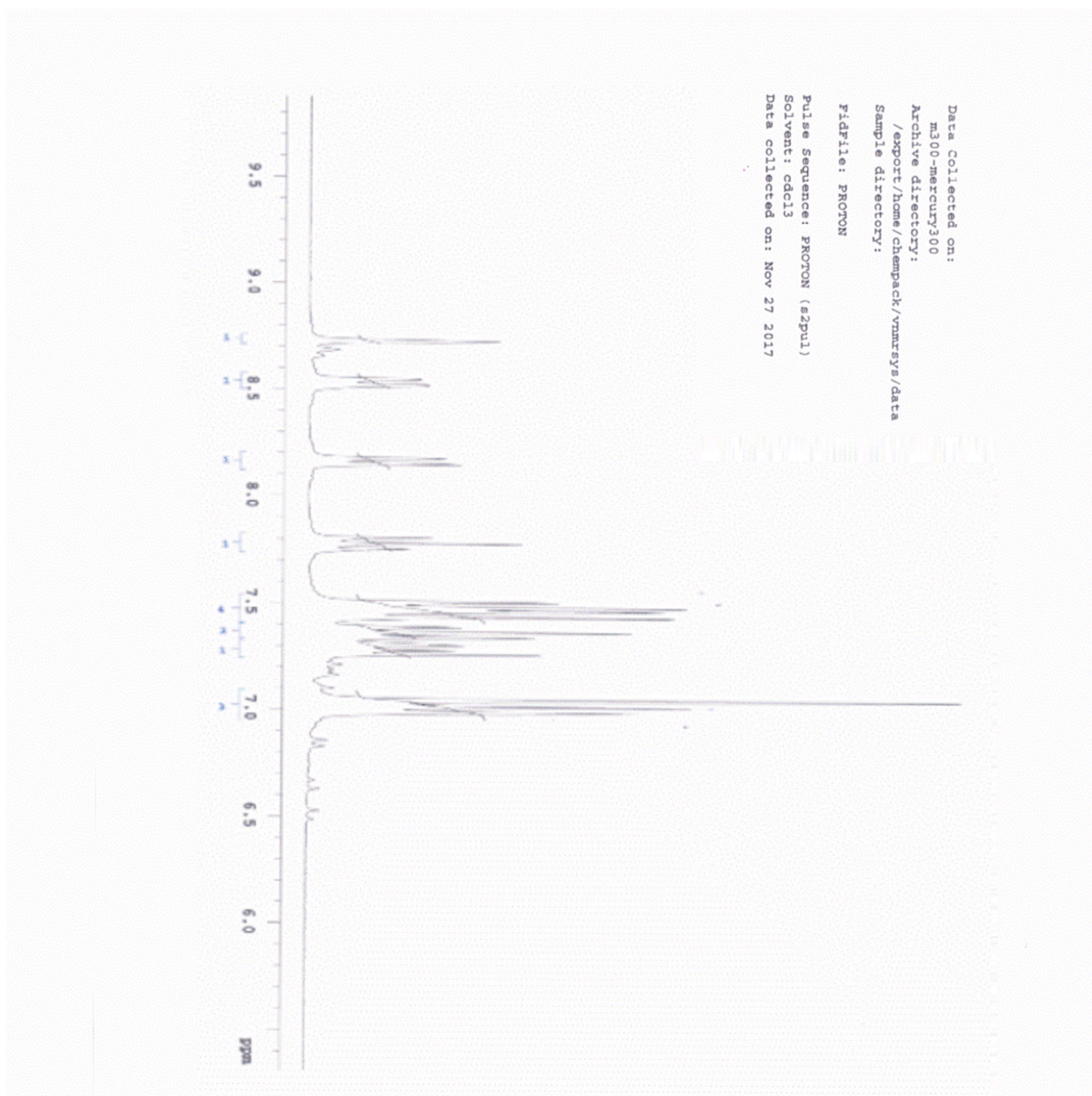


Figure S13: ^1H NMR and ^{13}C spectrum (300 MHz, CDCl_3) of
3-nitro-N-{4-[(E)-2-phenylvinyl]phenyl}benzenesulfonamide 2b



Sample Name:

Data Collected on:
m300-mercury300
Archive directory:
/export/home/chempack/vnmr/sys/data
Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Nov 27 2017

Operator: defil

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.868 sec
Width 18867.9 Hz
800 repetitions
OBSERVE C13, 75.4847602 MHz
DECOUPLE H1, 300.1991980 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
Ft size 32768
Total time 25 min

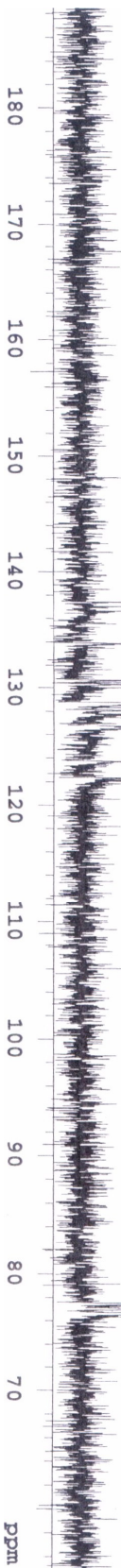
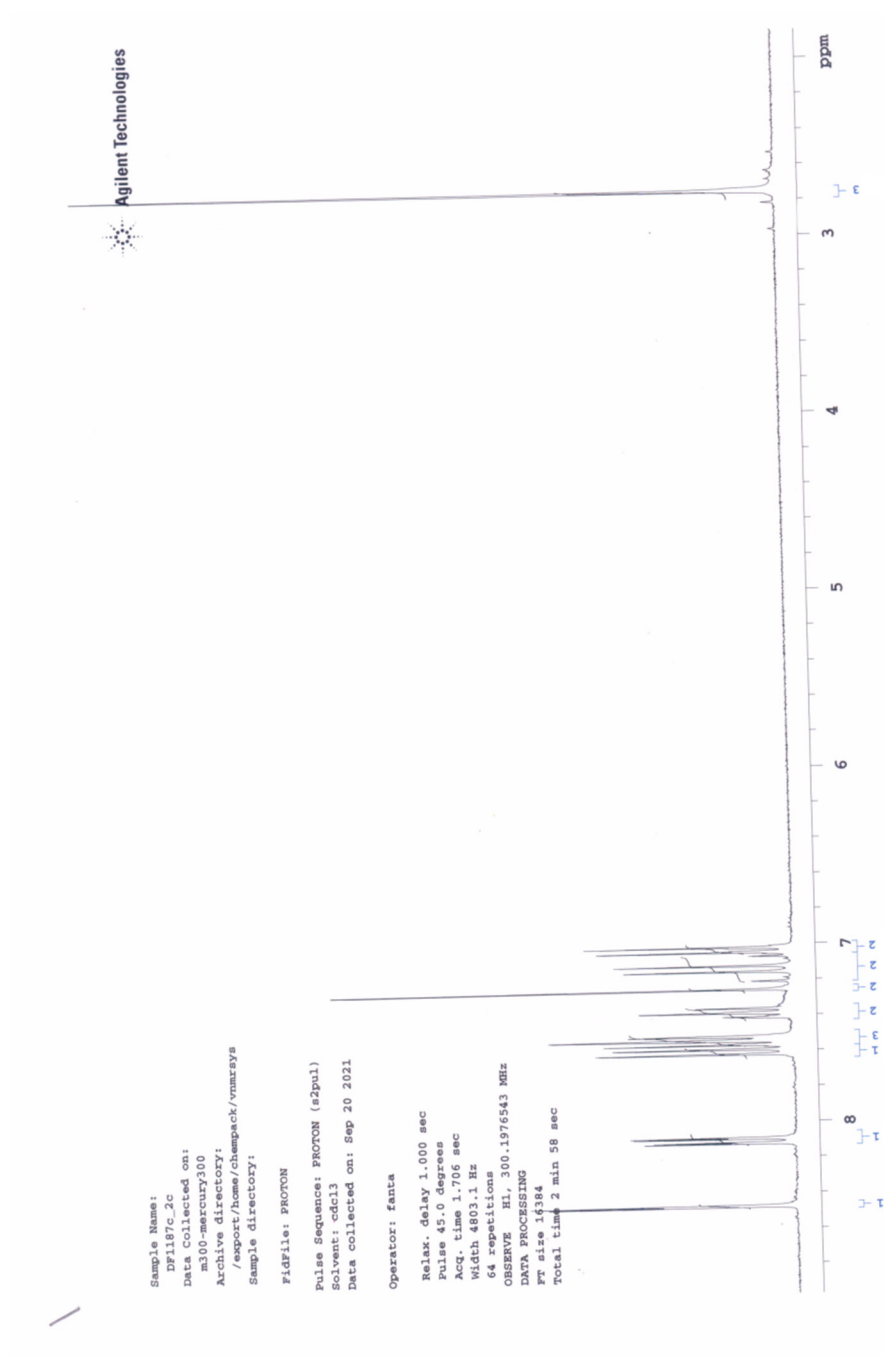


Figure S14: ^1H NMR(300 MHz, CDCl_3) and ^{13}C spectra (300 MHz, CDCl_3) of 4-methyl-3-nitro-N-{4-[(E)-2-phenylvinyl]phenyl}benzenesulfonamide **2c**



Gradient Shimming

Sample Name:

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmr/sys/data

Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (szpul)

Solvent: cdc13

Data collected on: May 15 2018

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

1297 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 48 min

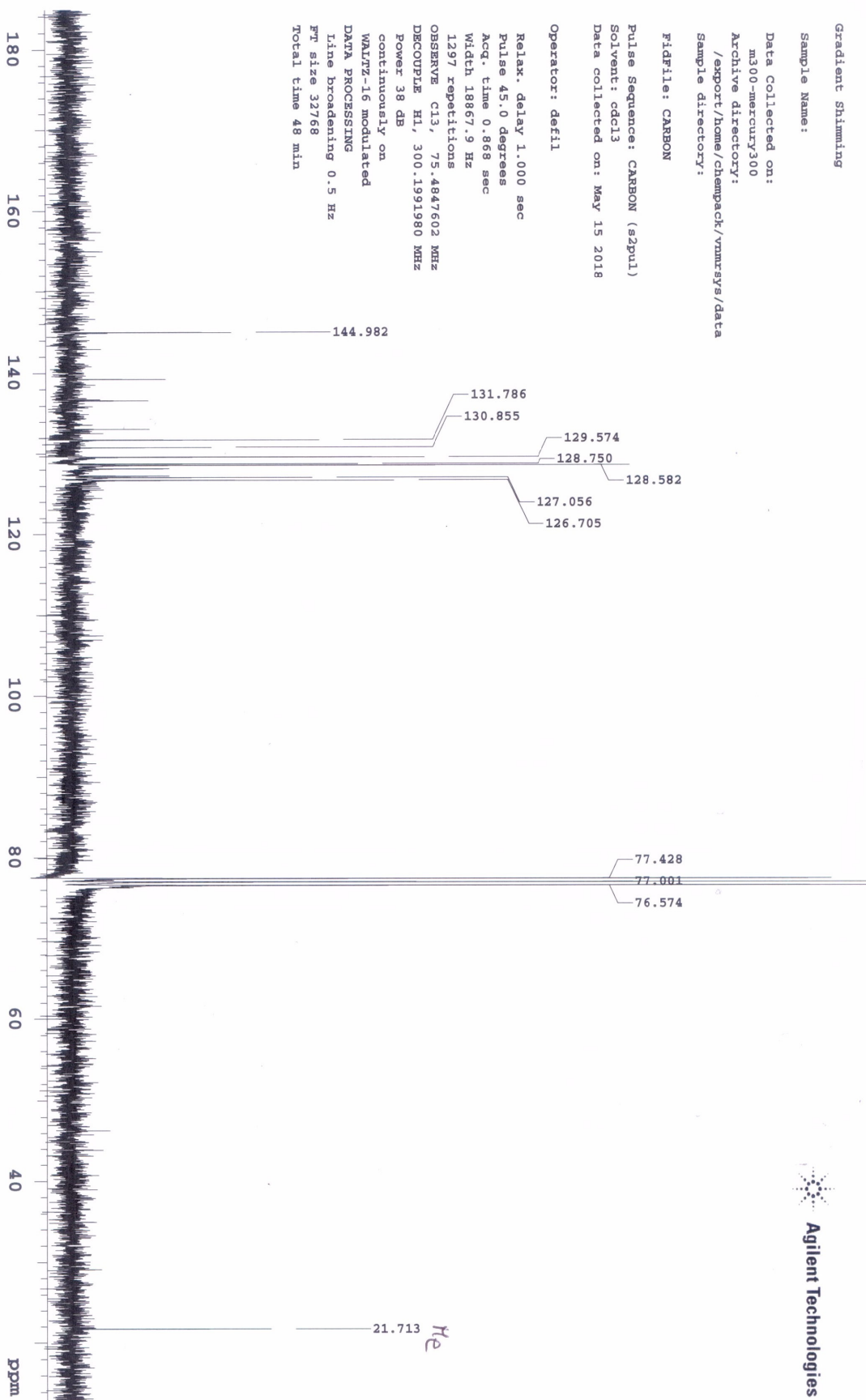
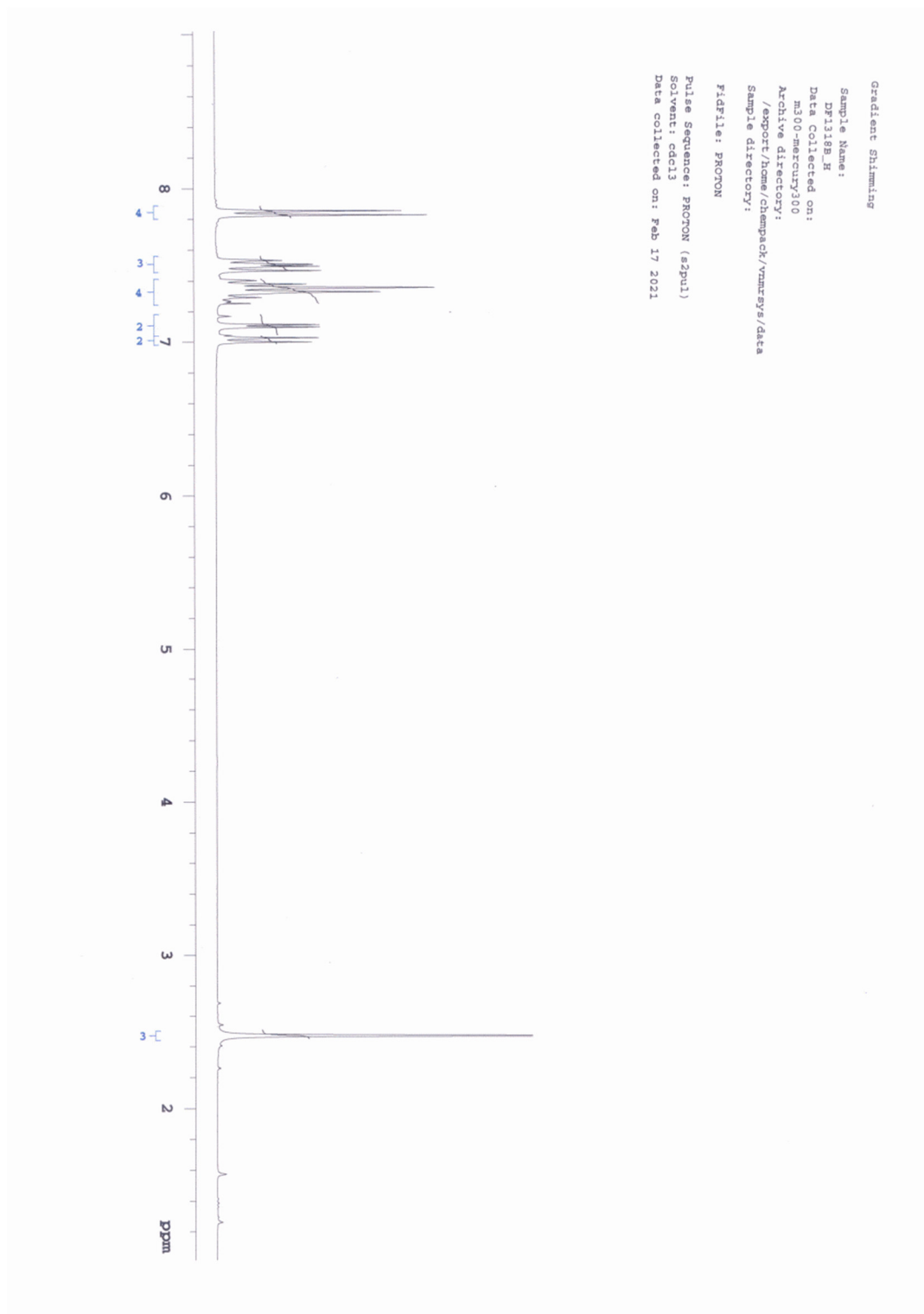


Figure S15: ^1H NMR and ^{13}C spectrum (300 MHz, CDCl_3) of 4-methyl-*N*-{4-[(*E*)-2-phenylvinyl]phenyl}benzenesulfonamide **2d**





Sample Name:

DF13185_H

Data Collected on:

m300-mercury300

Archive directory:

Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

Data collected on: Feb 18 2021

Operator: defil

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.868 sec
Width 18867.9 Hz

1500 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

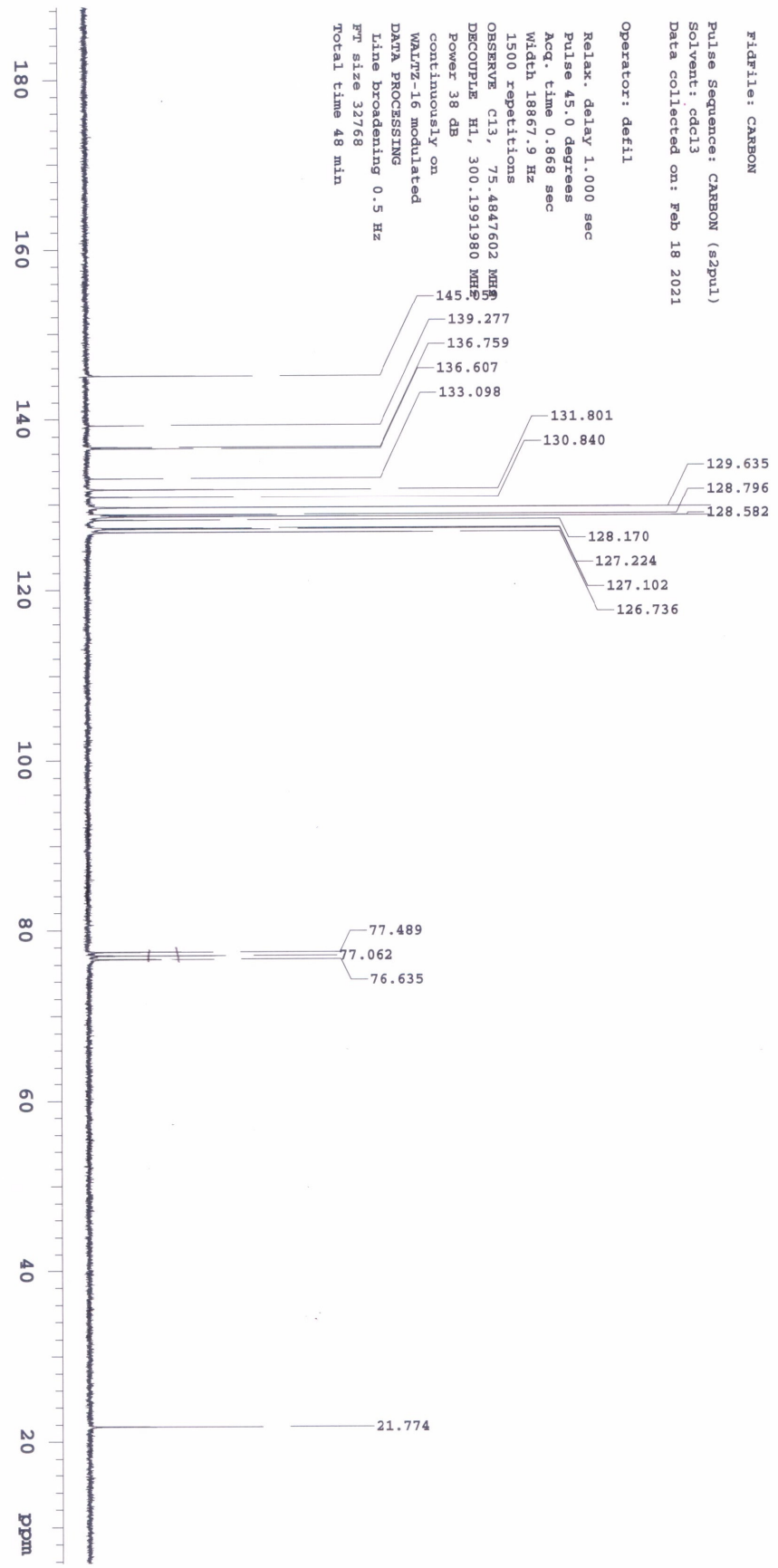
WALTZ-16 modulated

DATA PROCESSING

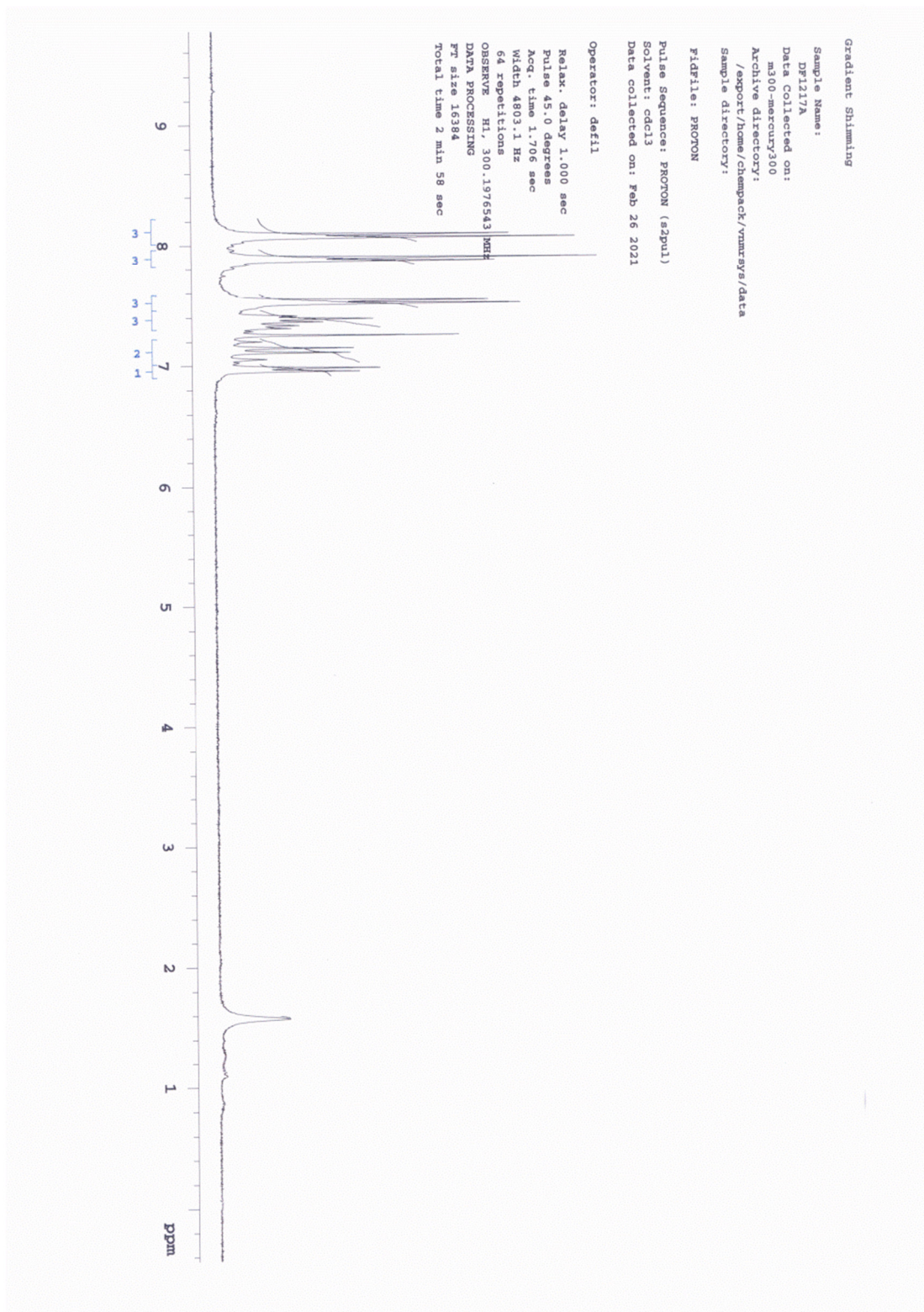
Line broadening 0.5 Hz

FT size 32768

Total time 48 min



4-cyano-N-{4-[(E)-2-phenylvinyl]phenyl}benzenesulfonamide 2e



Gradient Shimming

Sample Name:

DF1217A

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsys/data

Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (s2h13)

Solvent: cdcl3

Data collected on: Feb 26 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

1844 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 1 hr, 4 min

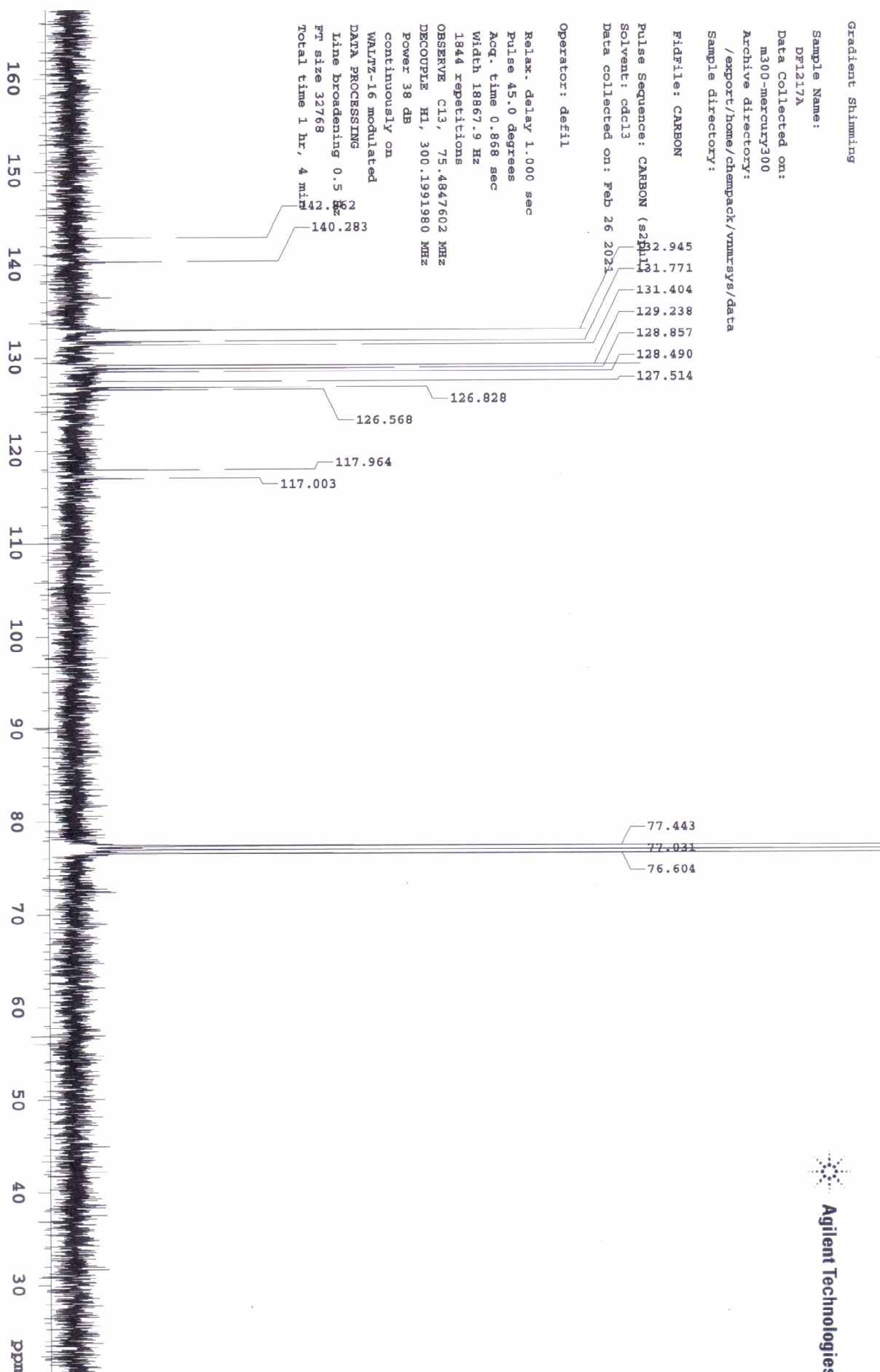
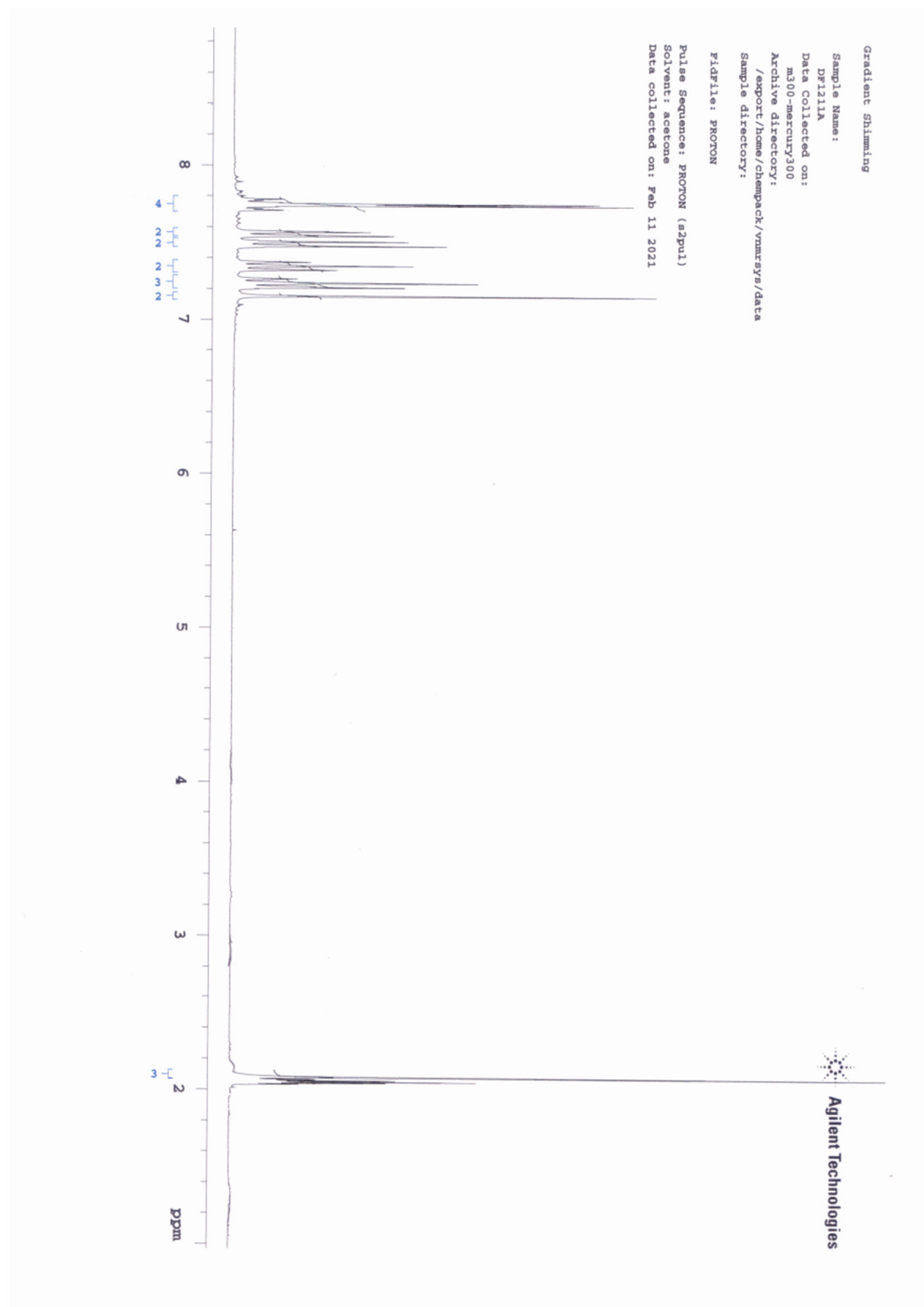


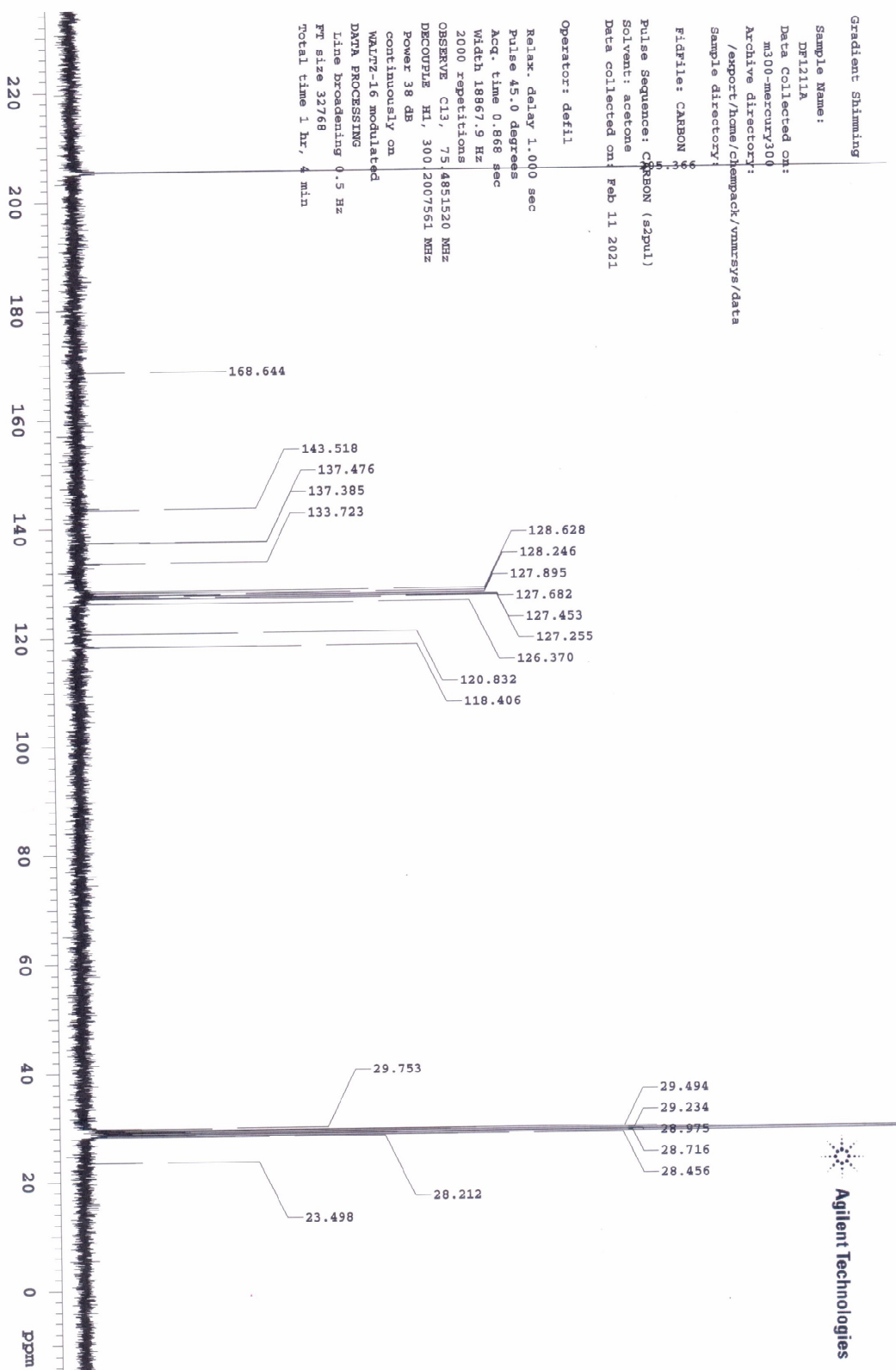
Figure S17: ^1H NMR (300 MHz, Acetone- d_6) and ^{13}C spectrum (300 MHz, CDCl_3) of *N*-{4-[(4-[(*E*)-2-phenylvinyl]phenyl)amino)sulfonyl]phenyl}acetamide **2f**



Gradient Shimming
Sample Name:
DF1211A
Data Collected on:
m300-mercury300
Archive directory:
/export/home/chempack/vnmrSYS/data
Sample directory:

F1 file: CARBON
Pulse Sequence: CARBON (szpul)
Solvent: acetone
Data collected on: Feb 11 2021

Operator: defil
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.868 sec
Width 18867.9 Hz
2000 repetitions
OBSERVE C13, 75.4851520 MHz
DECOUPLE H1, 300.2007551 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
F1 size 32768
Total time 1 hr, 4 min



Gradient Shimming

Sample Name:
DP1207C

Data Collected on:
m300-mercury300

Archive directory:
/export/home/chempack/vnmrsws/data

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: cdcl3

Data collected on: Mar 3 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.706 sec

Width 4803.1 Hz

128 repetitions

OBSERVE H1 300.197543 MHz

DATA PROCESSING

FT size 16384

Total time 5 min 35 sec

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 ppm

Gradient Shimming

Sample Name:

DF1207C

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsvs/data

Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (s2pul1)

Solvent: cdcl3

Data collected on: Mar 3 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

2000 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

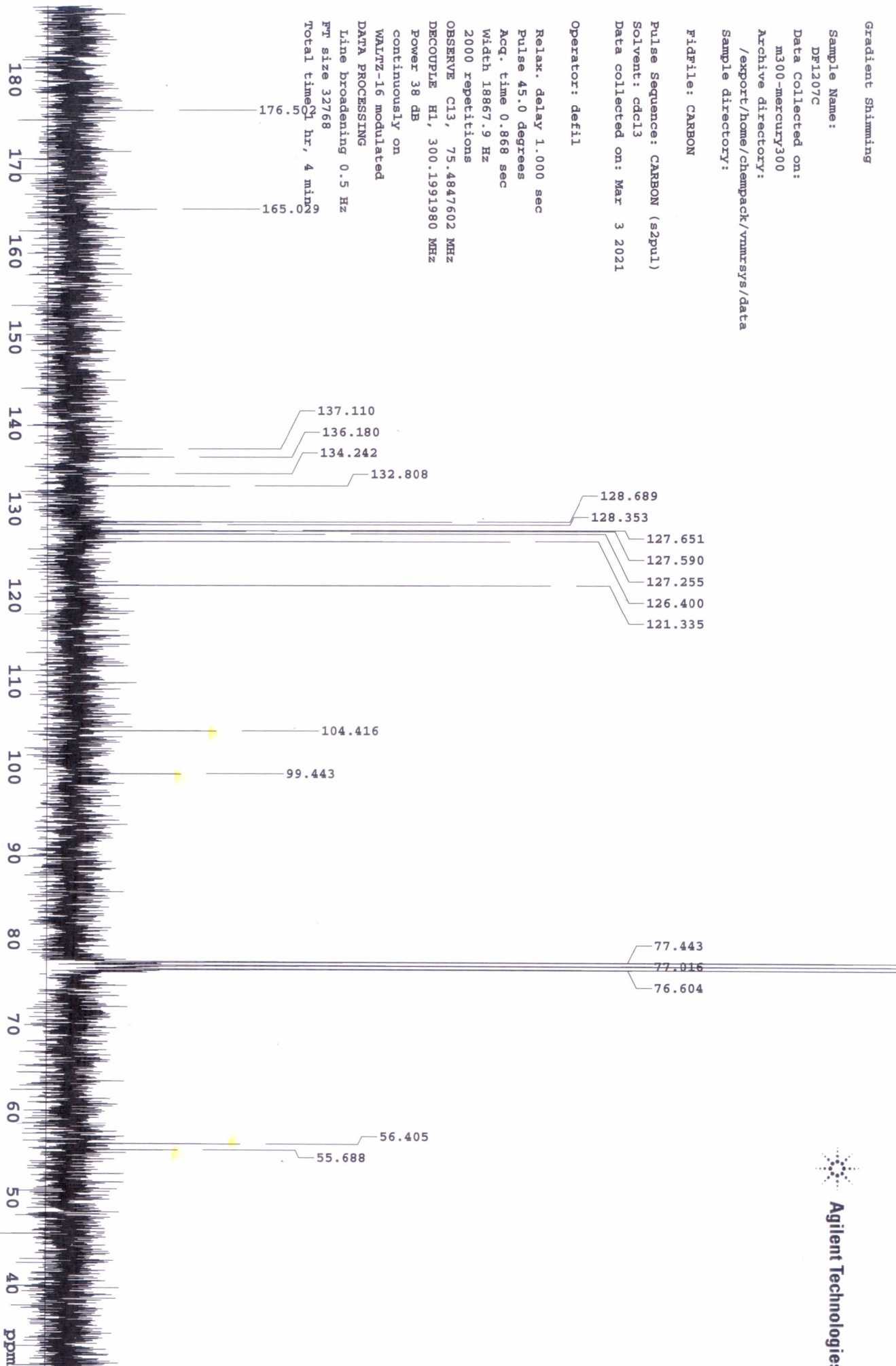
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

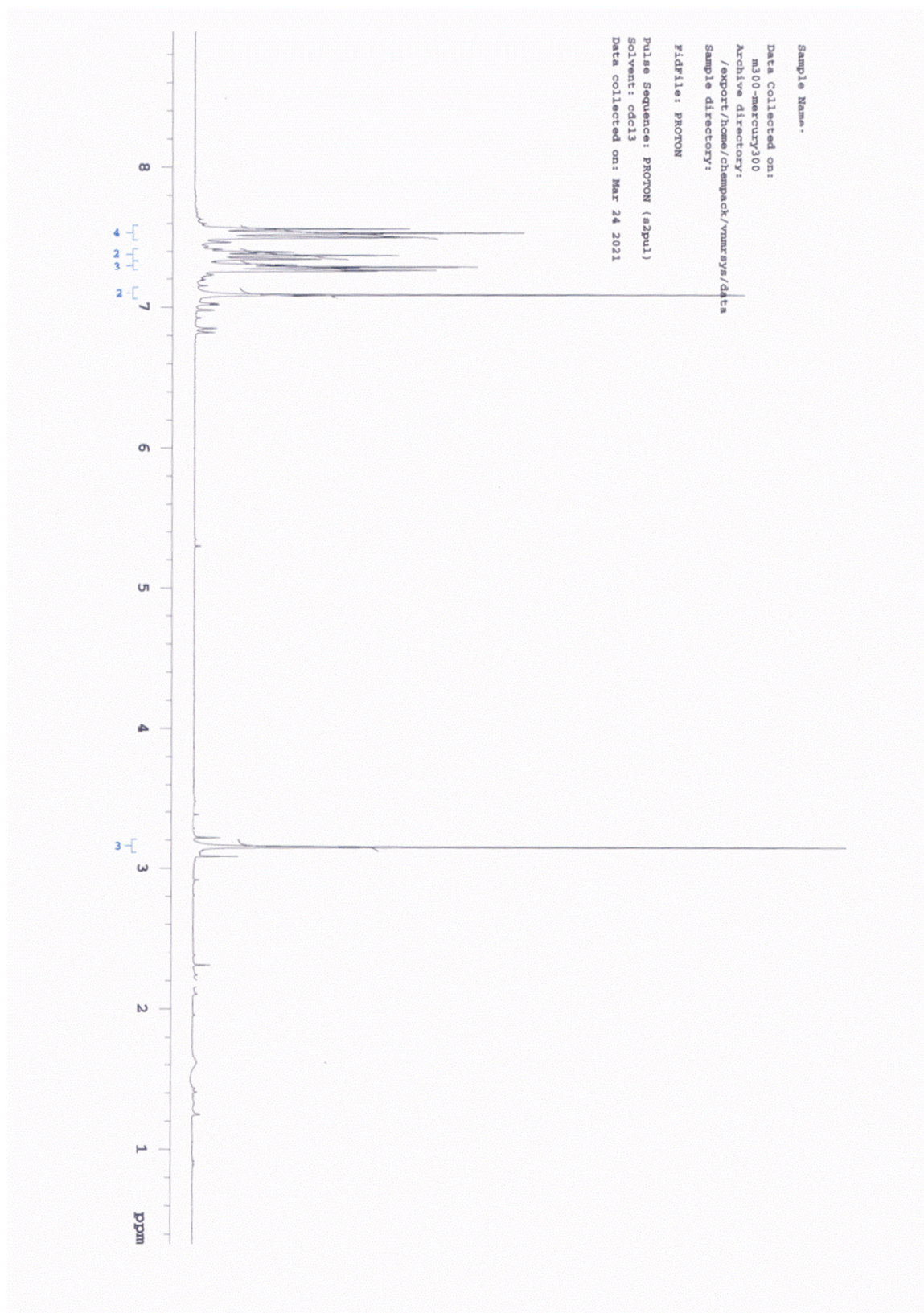
FT size 32768

Total time 4 hr, 4 min



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Figure S19: ^1H NMR and ^{13}C spectrum (300 MHz, CDCl_3) of *N*-{4-[(*E*)-2-phenylvinyl]phenyl}methanesulfonamide **2h**



Sample Name:
Df1213A
Data Collected on:
m300-mercury300
Archive directory:
/export/home/chempack/vnmr/sys/data
Sample directory:

F1dFile: CARBON

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 2 2021

Operator: fanta

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.868 sec
Width 18867.9 Hz
2000 repetitions
OBSERVE C13, 75.4847602 MHz
DECOUPLE H1, 300.1991980 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
line broadening 0.5 Hz
Fw size 32768
Total time 1 hr, 4 min

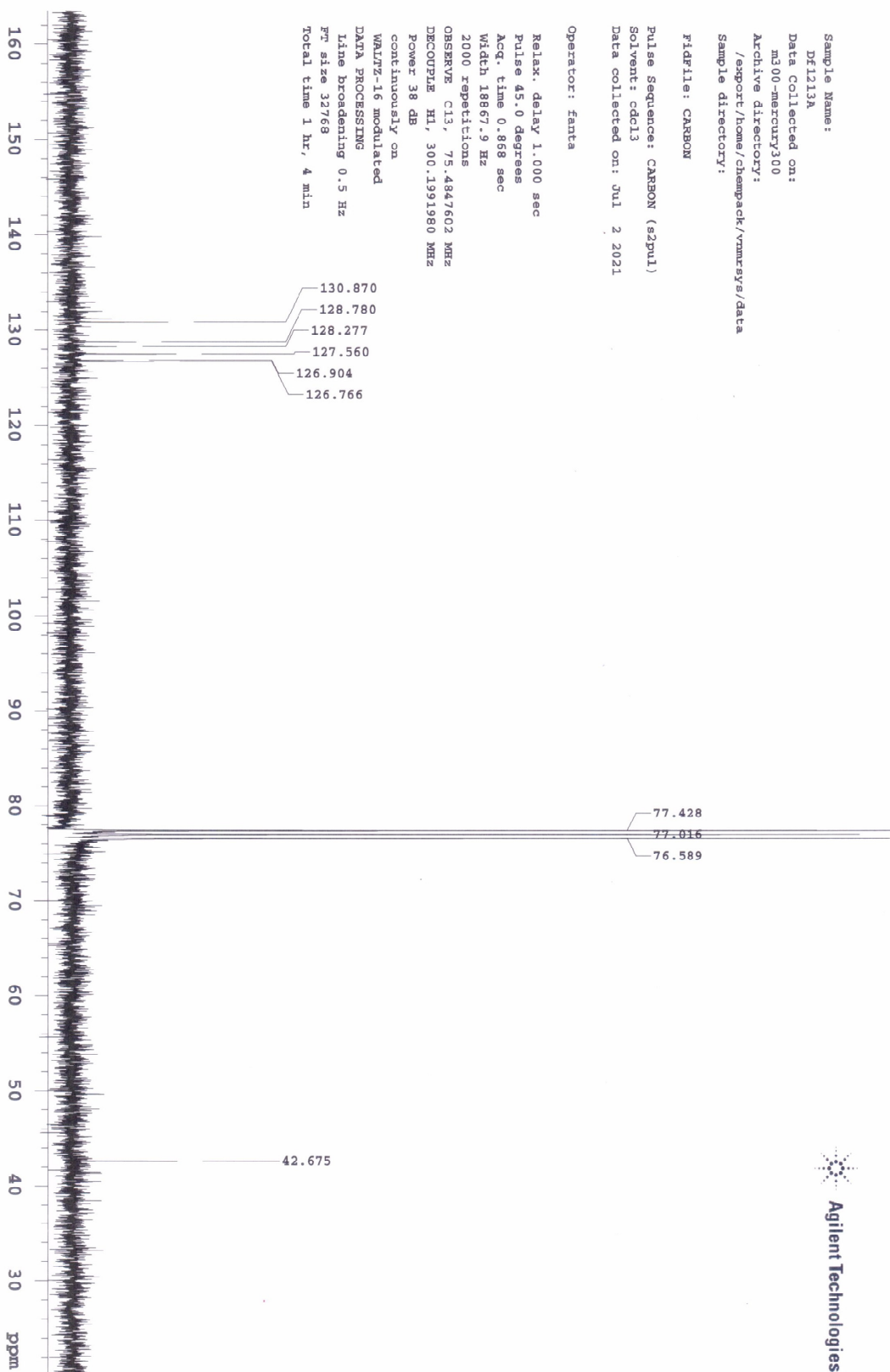
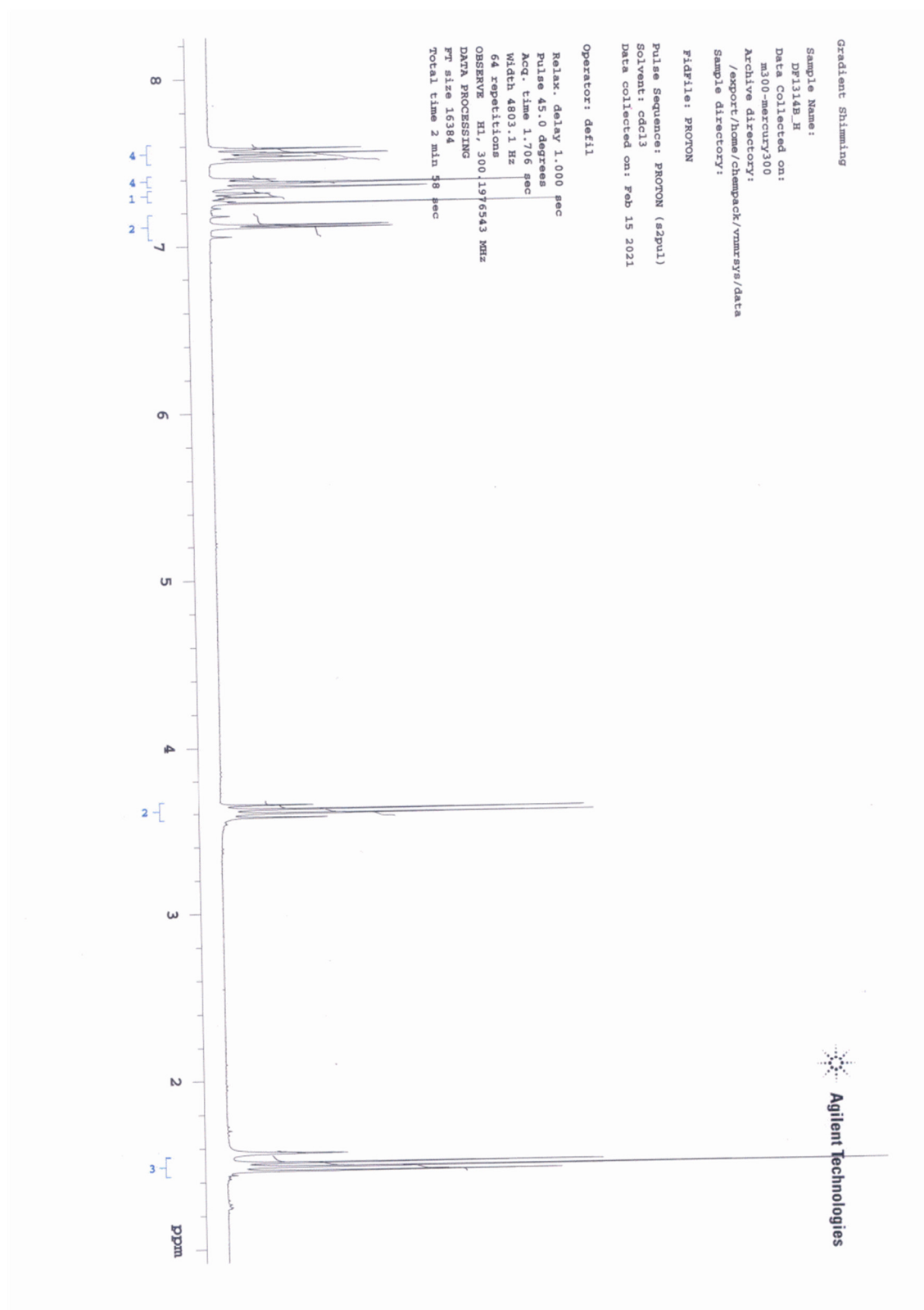


Figure S20: ^1H NMR and ^{13}C spectrum (300 MHz, CDCl_3) of *N*-{4-[(*E*)-2-phenylvinyl]phenyl}ethanesulfonamide **2i**



Gradient Shimming

Sample Name:

DF1314B_C

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmr/sys/data

Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

Data collected on: Feb 15, 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

2048 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

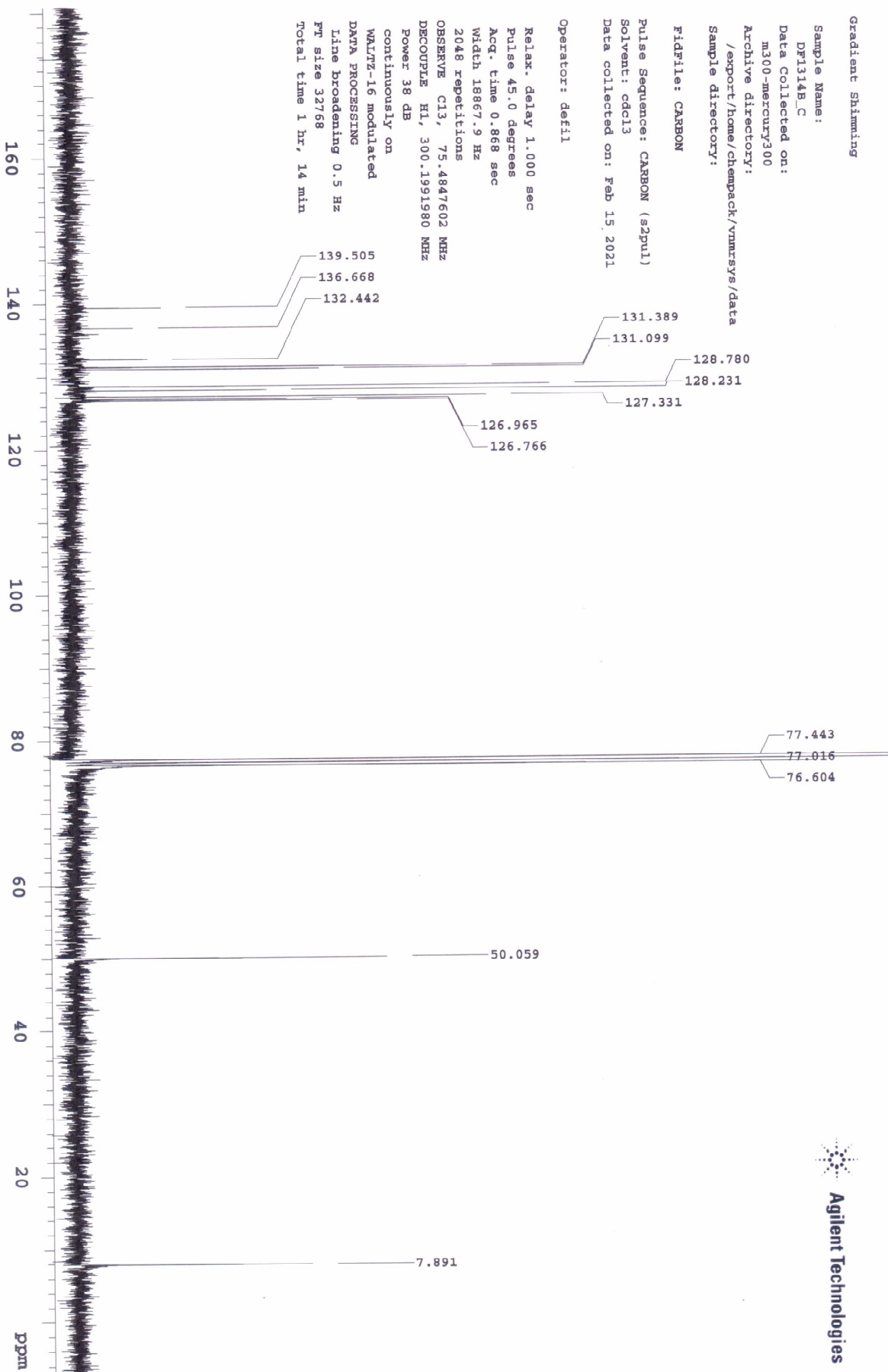
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

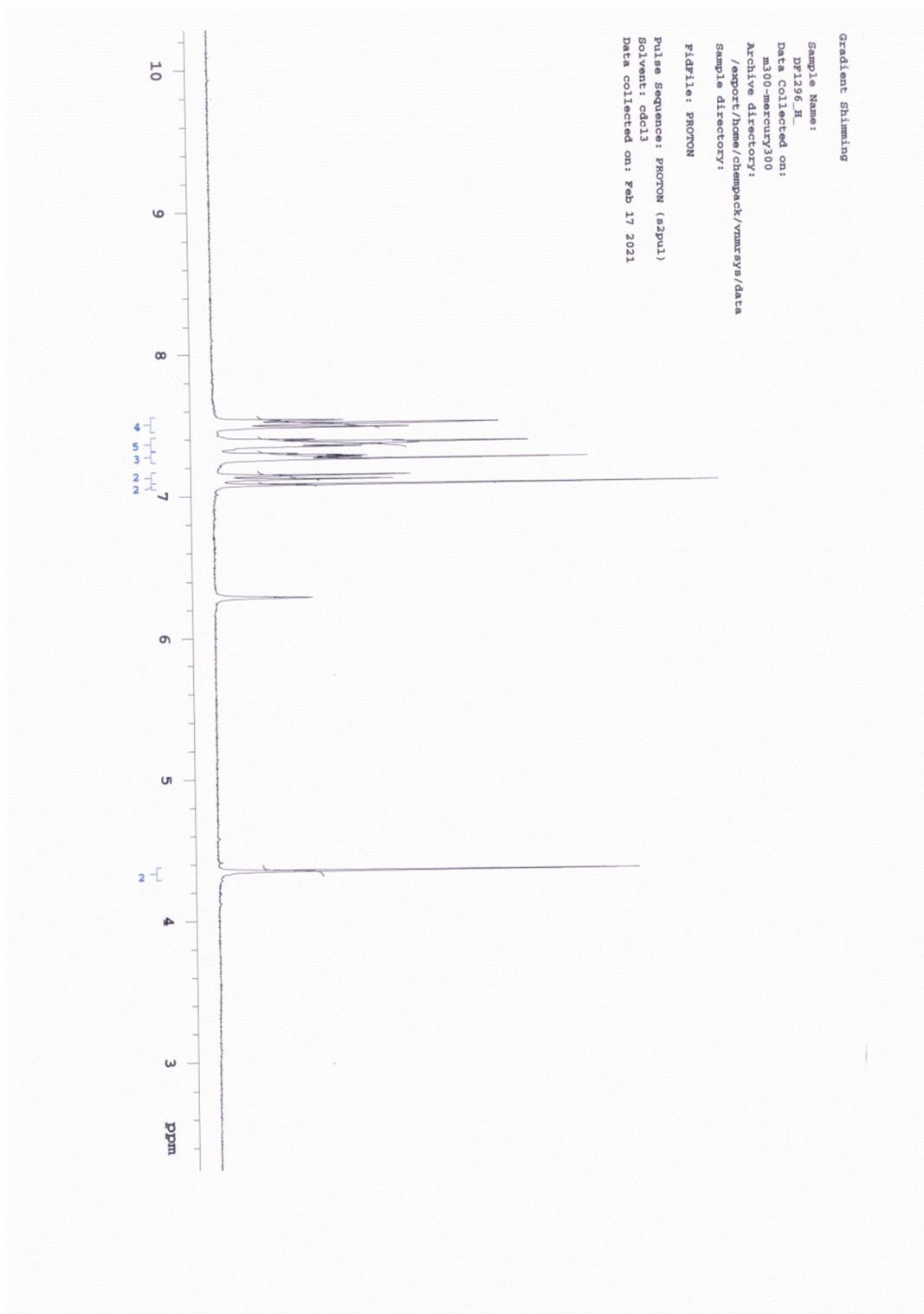
FT size 32768

Total time 1 hr, 14 min



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Figure S21: ^1H NMR and ^{13}C spectrum (300 MHz, CDCl_3) of *l*-phenyl-*N*-{4-[(*E*)-2-phenylvinyl]phenyl}methanesulfonamide-**2j**



Gradient Shimming

Sample Name:

DF1296

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmr/sys/data

Sample directory:

Fidfile: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

Data collected on: Feb 17 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.858 sec

Width 18867.9 Hz

1894 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

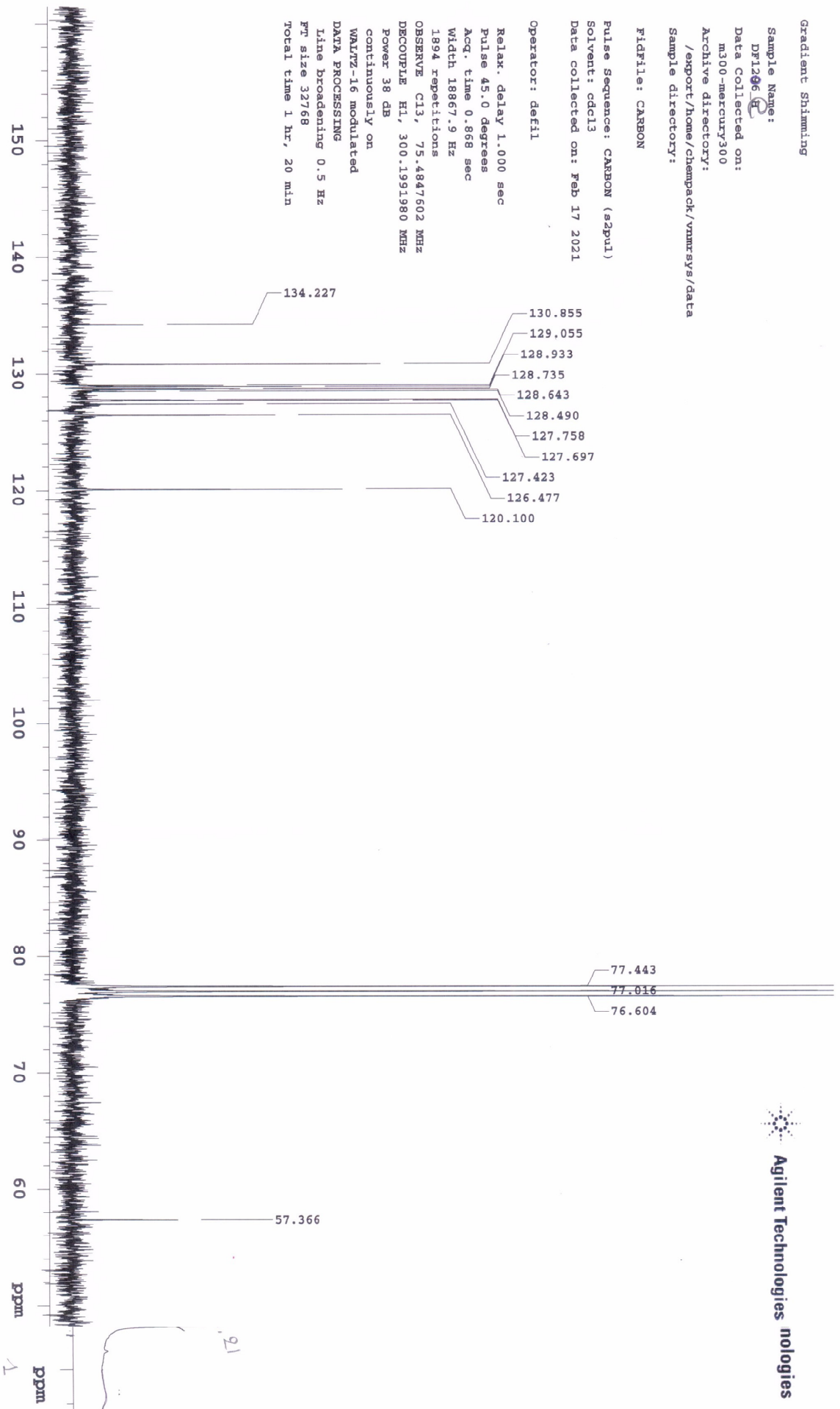
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

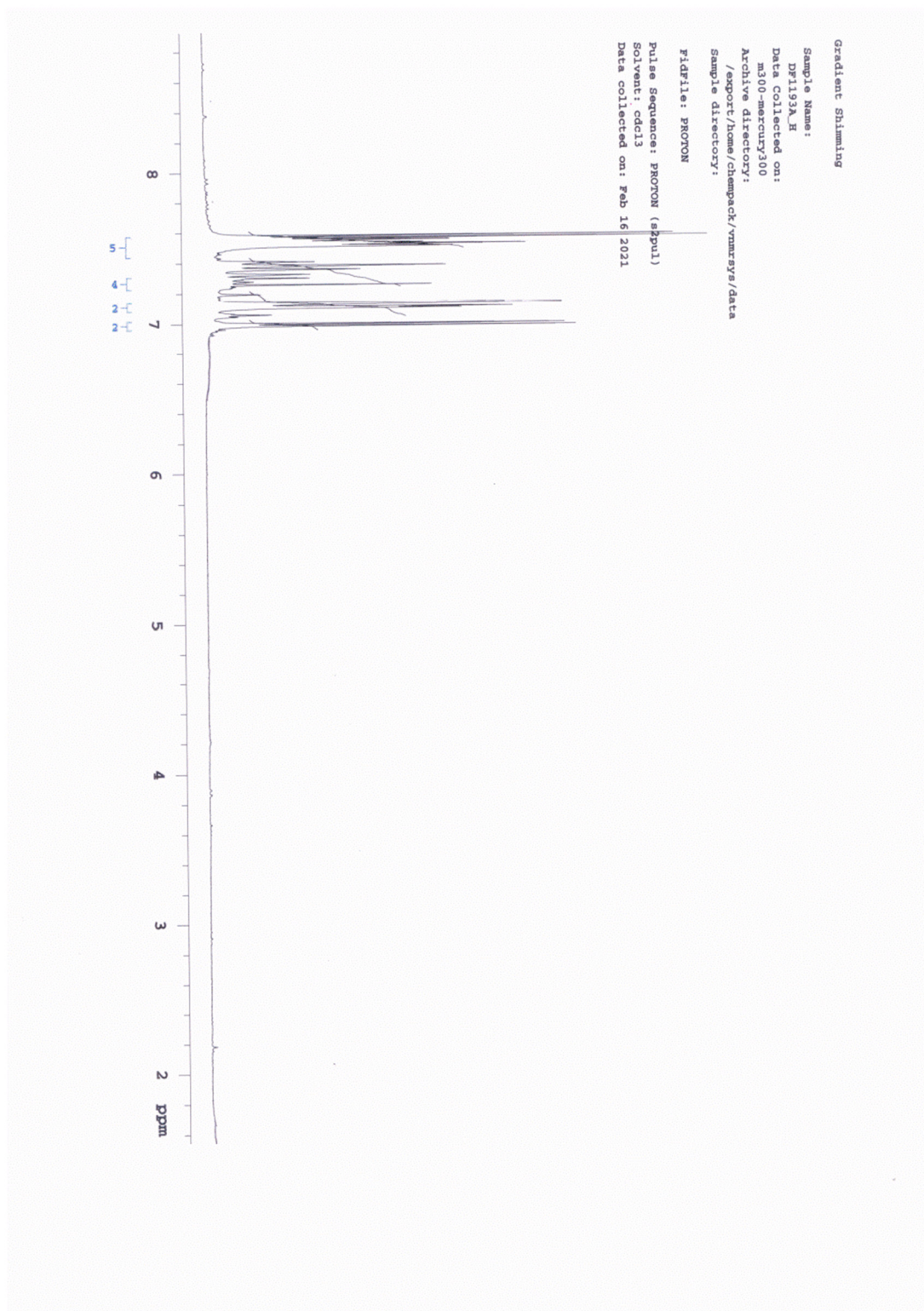
FT size 32768

Total time 1 hr, 20 min



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phenylvinyl[phenyl}thiophene-2-sulfonamide 2k



Gradient Shimming

Sample Name:

DF1193A_H

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmr/sys/data

Sample directory:

Filefile: CARBON

Pulse Sequence: CARBON (42ph1)

Solvent: cdcl3

Data collected on: Feb 16 2021

Operator: defil

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

1408 repetitions

OBSERVE C13, 75.4847603 MHz

DECOUPLE H1, 80.1191980 MHz

Power 38 dB

continuously gated

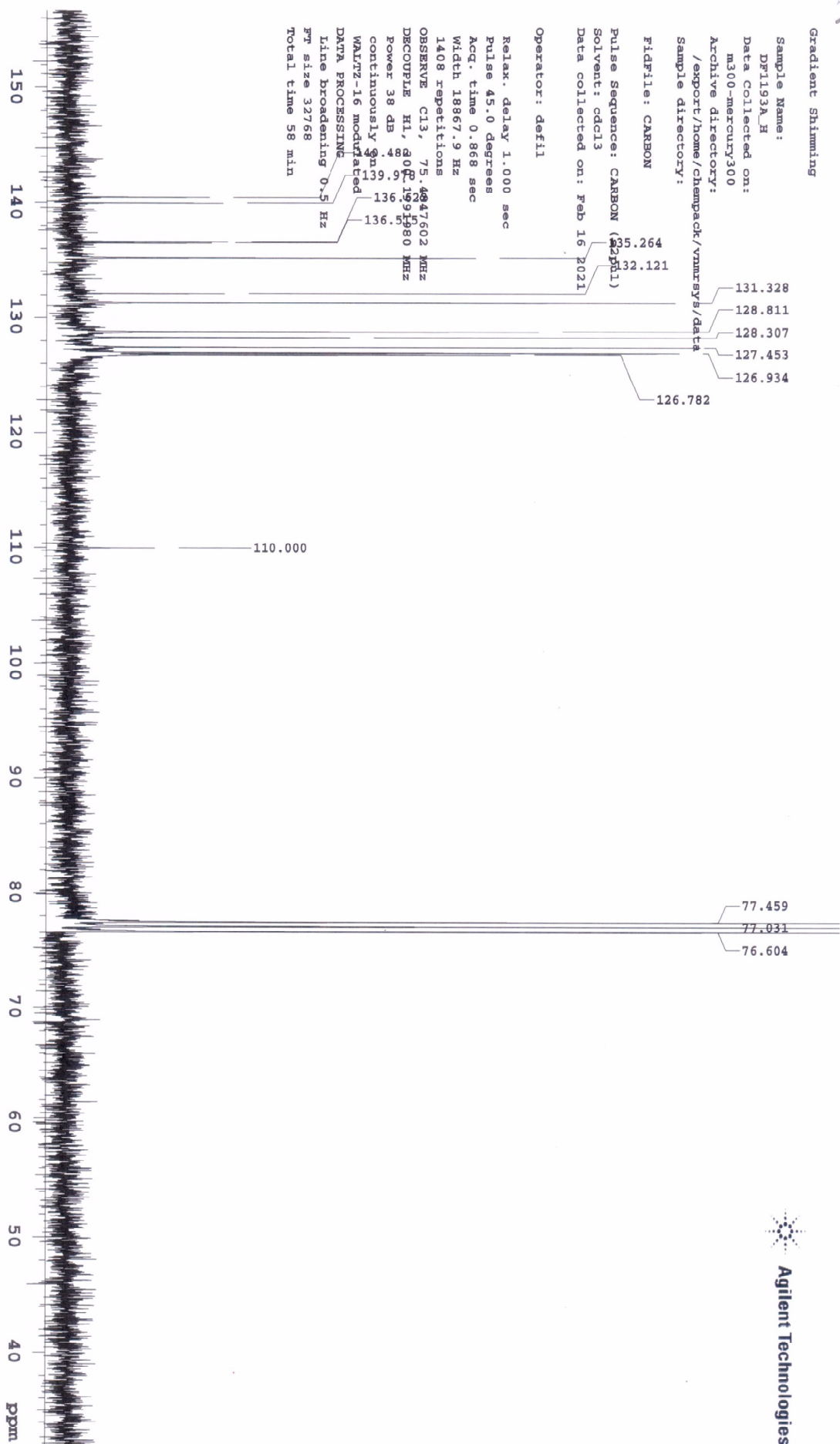
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 58 min



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Table S1. Raw data for the IC₅₀ calculation related to MCF7 cells in the presence of increasing concentrations of compounds **1b**, **1c**, **1j** and Resveratrol for 24 and 72 h.

Compound 1b (μM)	Viability (% of control) - 24 h	Viability (% of control) - 72 h
10	69.32 ± 14.99	98.33 ± 5.24
25	79.12 ± 9.66	99.99 ± 9.30
50	80.69 ± 4.08	93.39 ± 5.39
100	73.93 ± 1.87	77.31 ± 7.02
250	45.57 ± 3.42	57.01 ± 1.01
500	35.83 ± 2.22	36.11 ± 0.35

Compound 1c (μM)	Viability (% of control) - 24 h	Viability (% of control) - 72 h
10	85.23 ± 1.29	96.62 ± 6.99
25	73.08 ± 2.67	91.88 ± 5.31
50	37.39 ± 0.66	46.19 ± 1.67
100	36.17 ± 1.56	35.22 ± 2.21
250	38.64 ± 1.23	38.30 ± 4.07
500	34.30 ± 1.43	15.08 ± 0.67

Compound 1j (μM)	Viability (% of control) - 24 h	Viability (% of control) - 72 h
10	85.47 ± 6.41	96.53 ± 7.12
25	86.33 ± 14.64	95.30 ± 7.88
50	70.06 ± 3.80	87.57 ± 5.26
100	74.91 ± 9.24	72.67 ± 3.46
250	51.84 ± 3.08	69.54 ± 4.11
500	38.88 ± 5.23	46.31 ± 4.73

Resveratrol (μM)	Viability (% of control) - 24 h	Viability (% of control) - 72 h
10	80.27 ± 3.18	91.92 ± 5.44
25	84.94 ± 6.59	73.93 ± 9.52
50	87.44 ± 1.93	66.54 ± 5.77
100	78.29 ± 4.03	47.75 ± 2.67
250	60.29 ± 0.93	38.05 ± 8.70
500	34.30 ± 5.01	15.33 ± 4.88

Figure S23: Chromatograms of the active compounds **1b-c** and **1j** in neutral conditions:

Capillary column: 100 μm x 15 cm packed with Chromspher C18 dp 3 μm ; mobile phase, ACN/H₂O (75 /15 % (v/v) containing a 10 mM sodium hydrocarbonate buffer, pH 8.5; UV detection, 206 nm; the studied compounds at a final concentration of 100 $\mu\text{g/mL}$ were dissolved with a solution of 10 mM phosphate buffer (pH 7.4); injection time 15 s; flow rate, 450 nL/min.

