

# Synthesis and biological evaluation of novel cinnamic acid-based antimicrobials

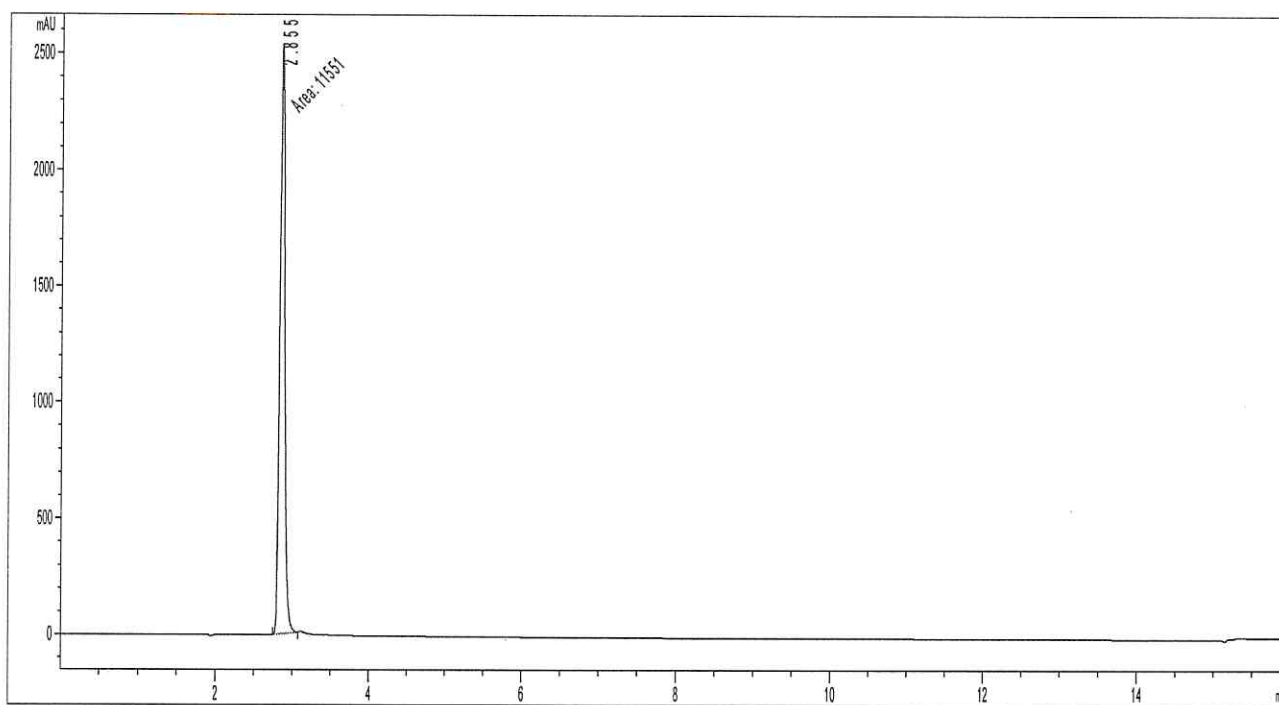
Marina Mingoia<sup>1</sup>, Carmela Conte<sup>2</sup>, Annalisa Di Rienzo<sup>3</sup>, Marilisa Pia Dimmito<sup>3</sup>, Lorella Marinucci<sup>4</sup>, Gloria Magi<sup>1</sup>, Hasan Turkez<sup>5</sup>, Maria Concetta Cufaro<sup>3,6</sup>, Piero Del Boccio<sup>3,6</sup>, Antonio Di Stefano<sup>3</sup>, and Ivana Cacciatore<sup>3,\*</sup>

- <sup>1</sup> Department of Biomedical Sciences and Public Health, Polytechnic University of Marche, Medical School, 60121 Ancona, Italy
- <sup>2</sup> Department of Pharmaceutical Sciences, University of Perugia, Via Fabretti, 48, 06123 Perugia, Italy
- <sup>3</sup> Department of Pharmacy, University "G. d'Annunzio" of Chieti-Pescara, via dei Vestini 31, 66100 Chieti Scalo, Italy
- <sup>4</sup> Department of Medicine and Surgery, University of Perugia, S. Andrea Delle Fratte, 06156 Perugia, Italy
- <sup>5</sup> Faculty of Science, Basic Medical Sciences, Medical Biology Department, Ataturk University 25240 Yakutiye, Erzurum, Turkey
- <sup>6</sup> Center for Advanced Studies and Technology (CAST), University "G. d'Annunzio" of Chieti-Pescara, via dei Vestini 31, 66100 Chieti Scalo, Italy

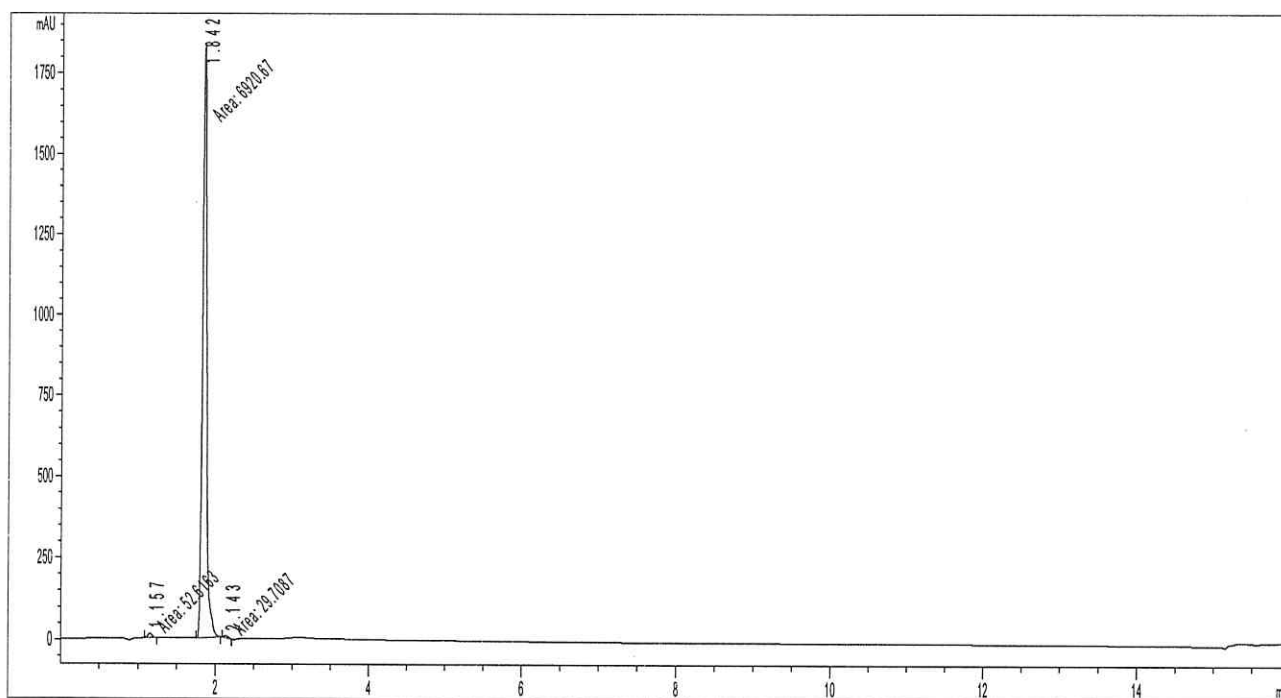
\* Correspondence: ivana.cacciatore@unich.it; Tel.: +39 871 355 44 75

## Supplementary material

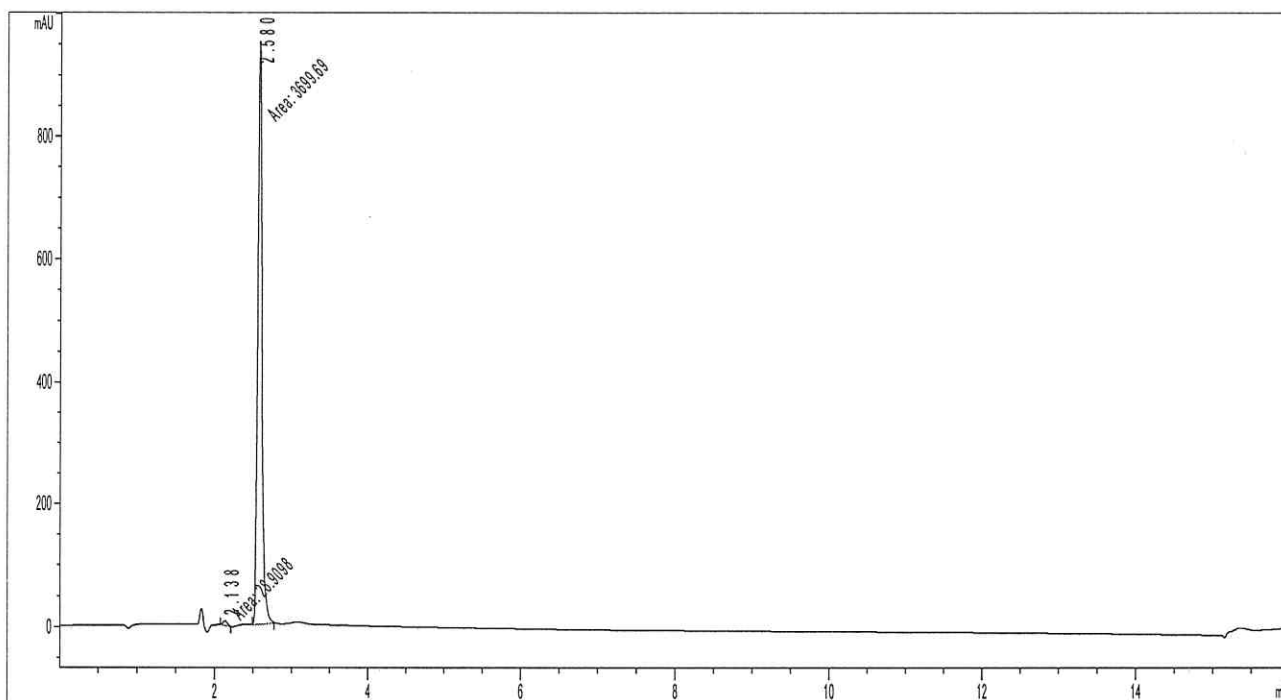
# HPLC CHROMATOGRAMS OF DM1-11



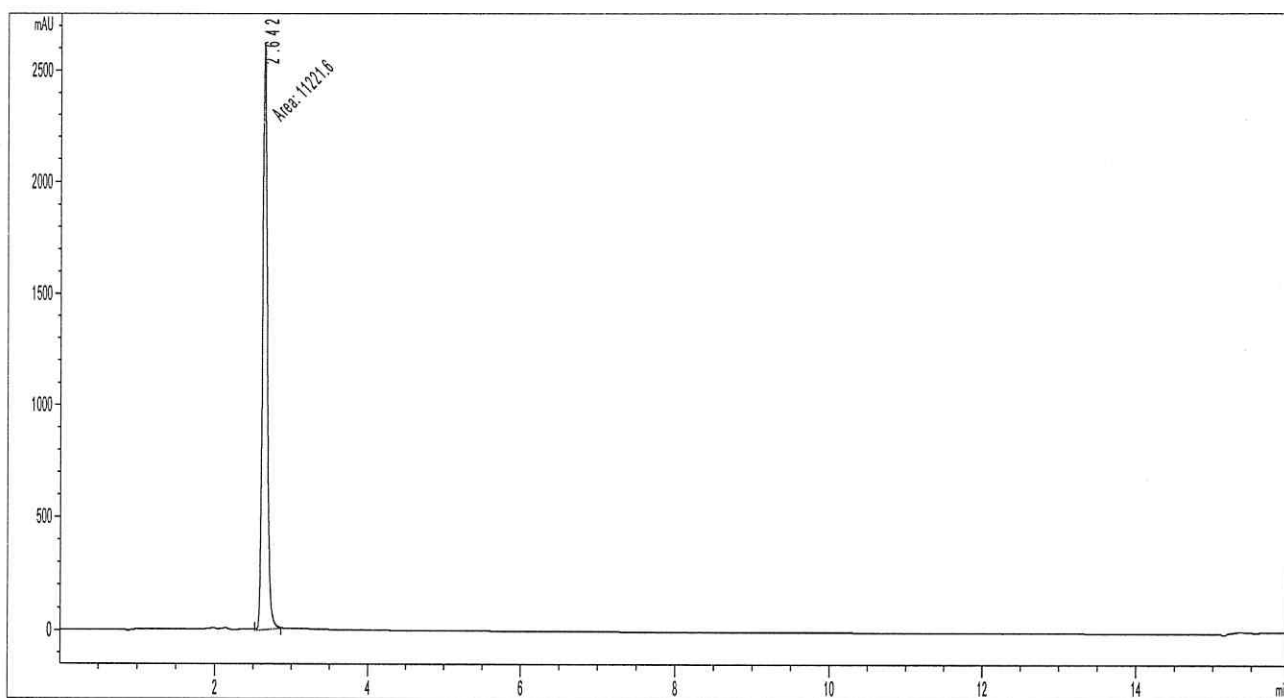
| Compound | Retention time | Area% |
|----------|----------------|-------|
| DM1      | 2.855          | 100   |



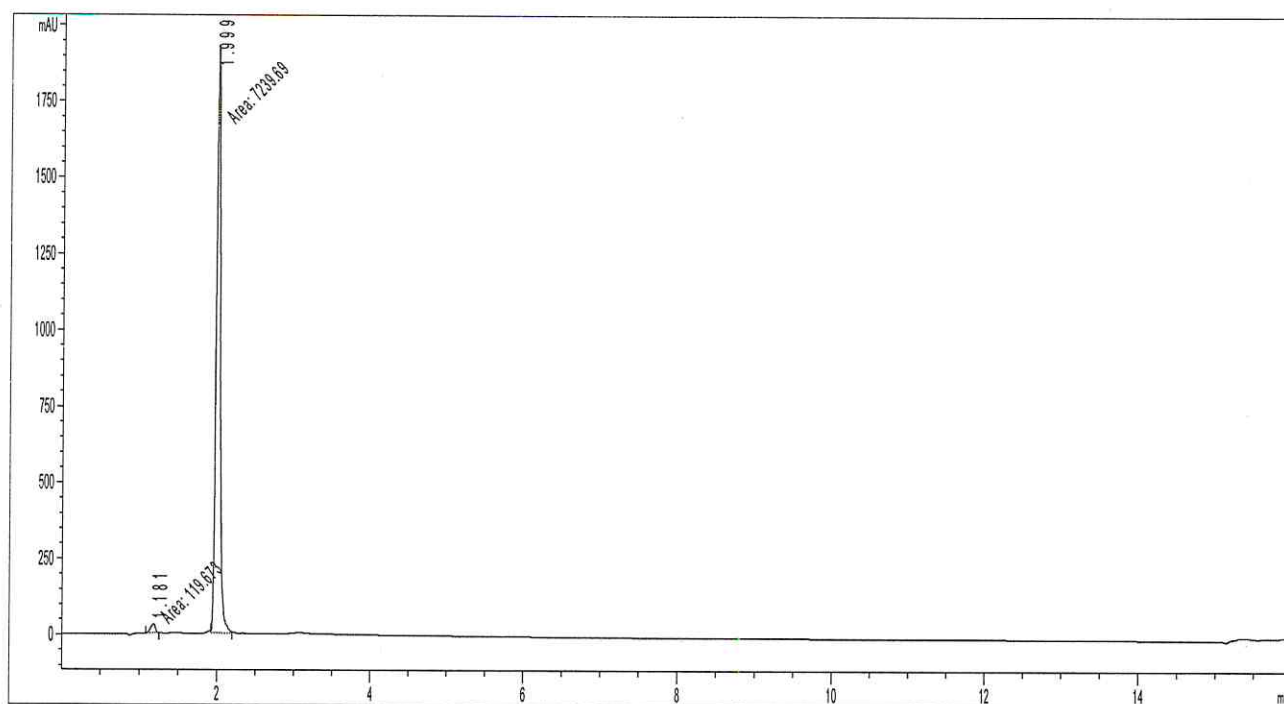
| Compound | Retention time | Area%  |
|----------|----------------|--------|
|          | 1.157          | 0.751  |
| DM2      | 1.842          | 98.824 |
|          | 2.143          | 0.424  |



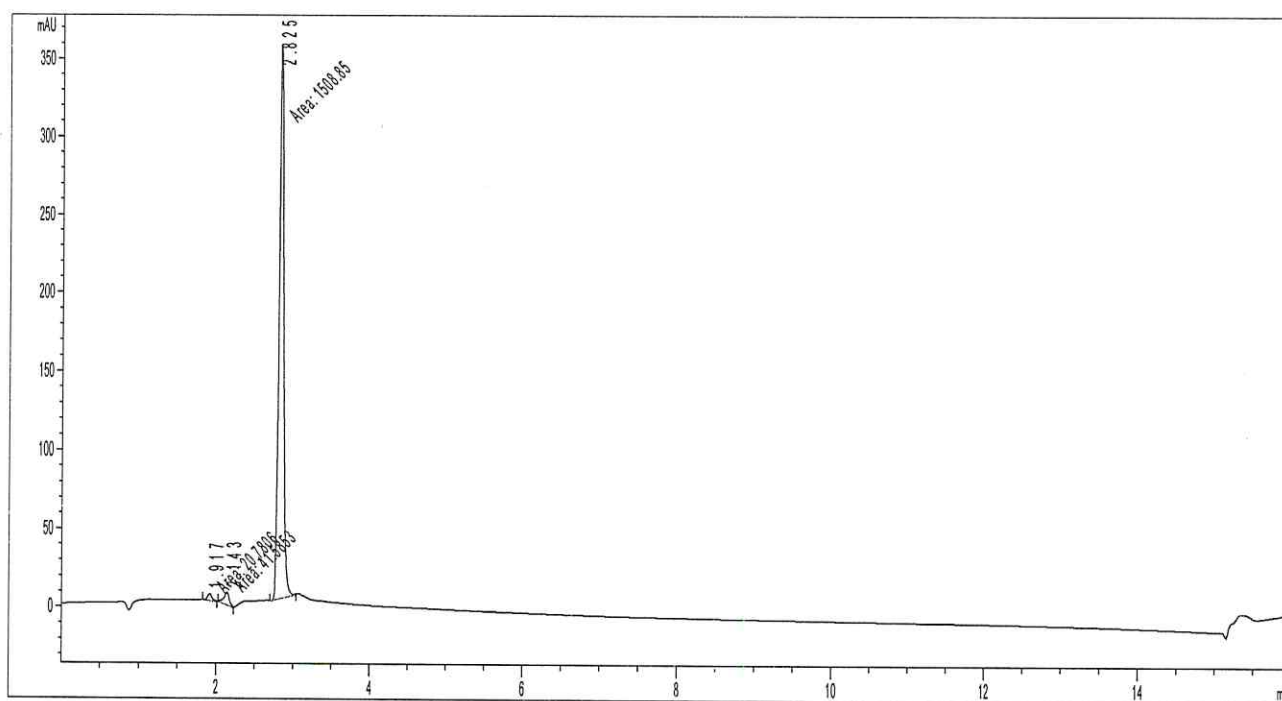
| Compound | Retention time | Area%  |
|----------|----------------|--------|
|          | 2.138          | 0.775  |
| DM3      | 2.58           | 99.225 |



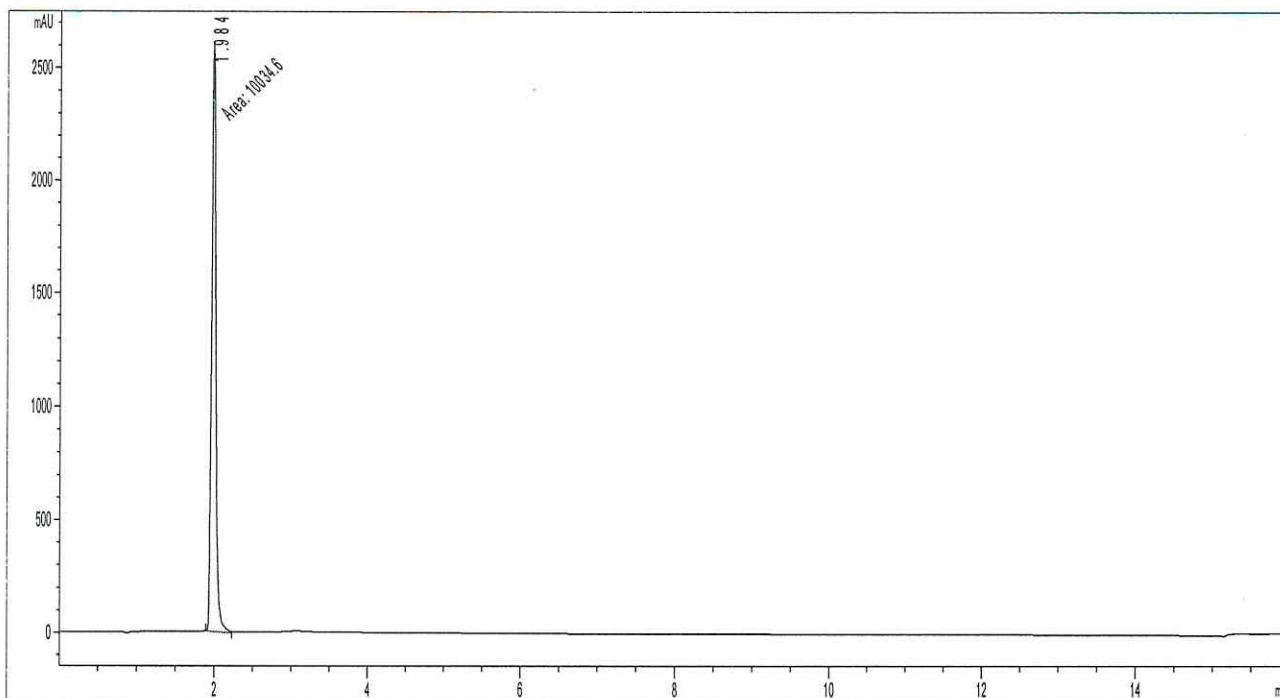
| Compound | Retention time | Area% |
|----------|----------------|-------|
| DM4      | 2.642          | 100   |



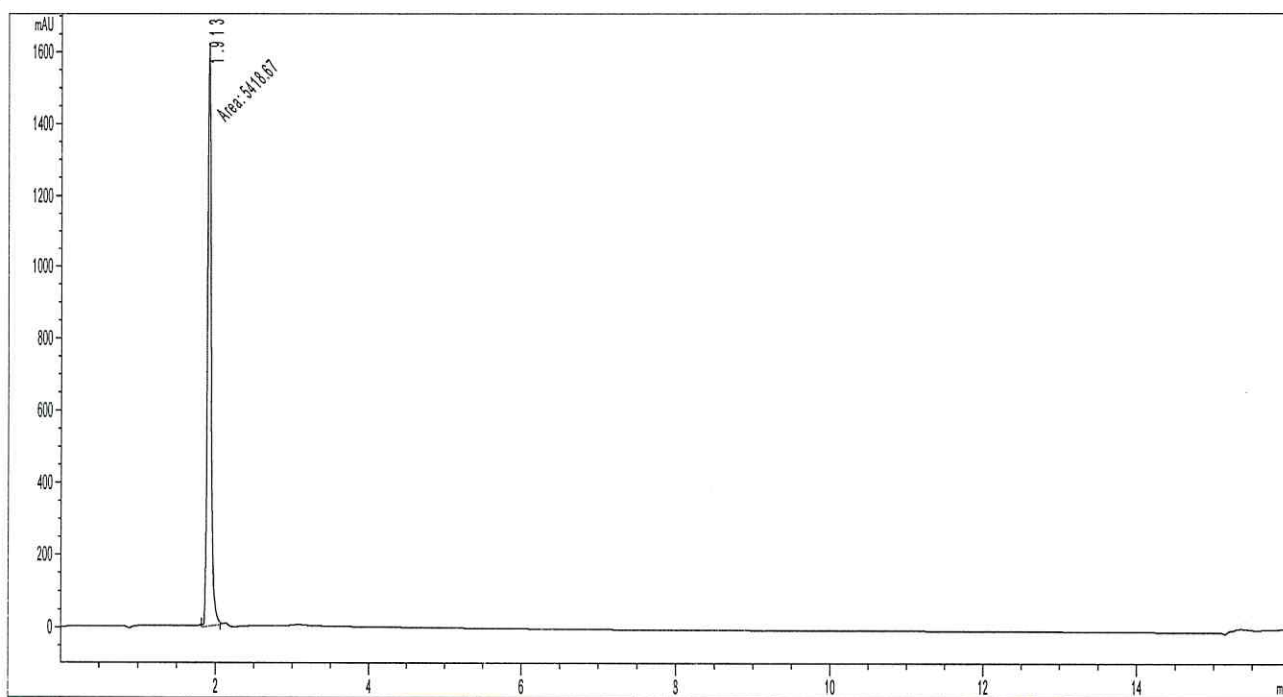
| Compound | Retention time | Area%  |
|----------|----------------|--------|
|          | 1.181          | 1.626  |
| DM5      | 1.999          | 98.374 |



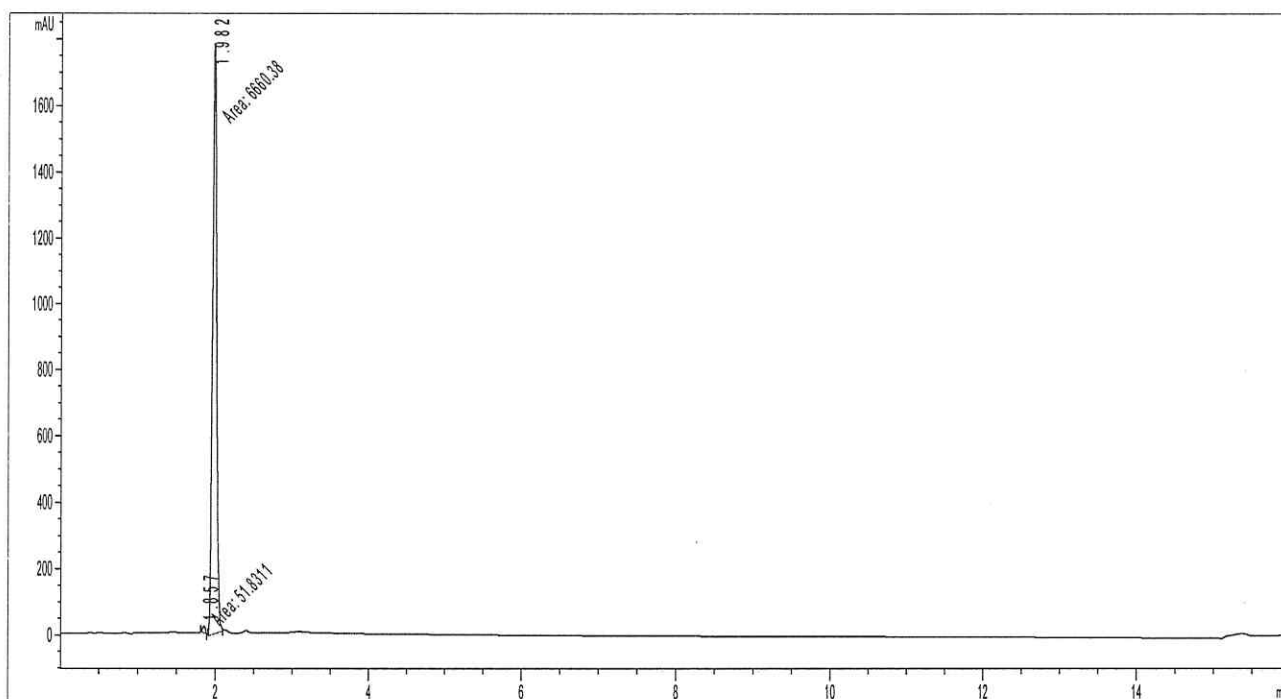
| Compound | Retention time | Area%  |
|----------|----------------|--------|
|          | 1.917          | 1.323  |
|          | 2.143          | 2.647  |
| DM6      | 2.825          | 96.031 |



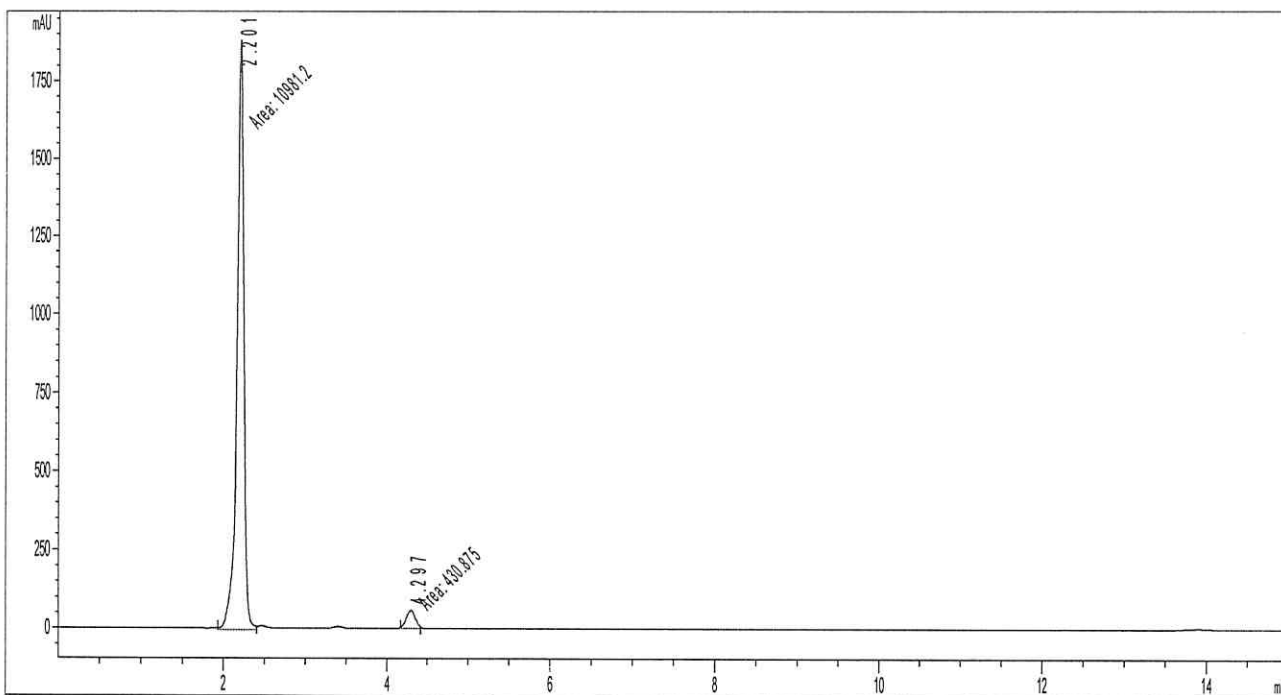
| Compound | Retention time | Area% |
|----------|----------------|-------|
| DM7      | 1.984          | 100   |



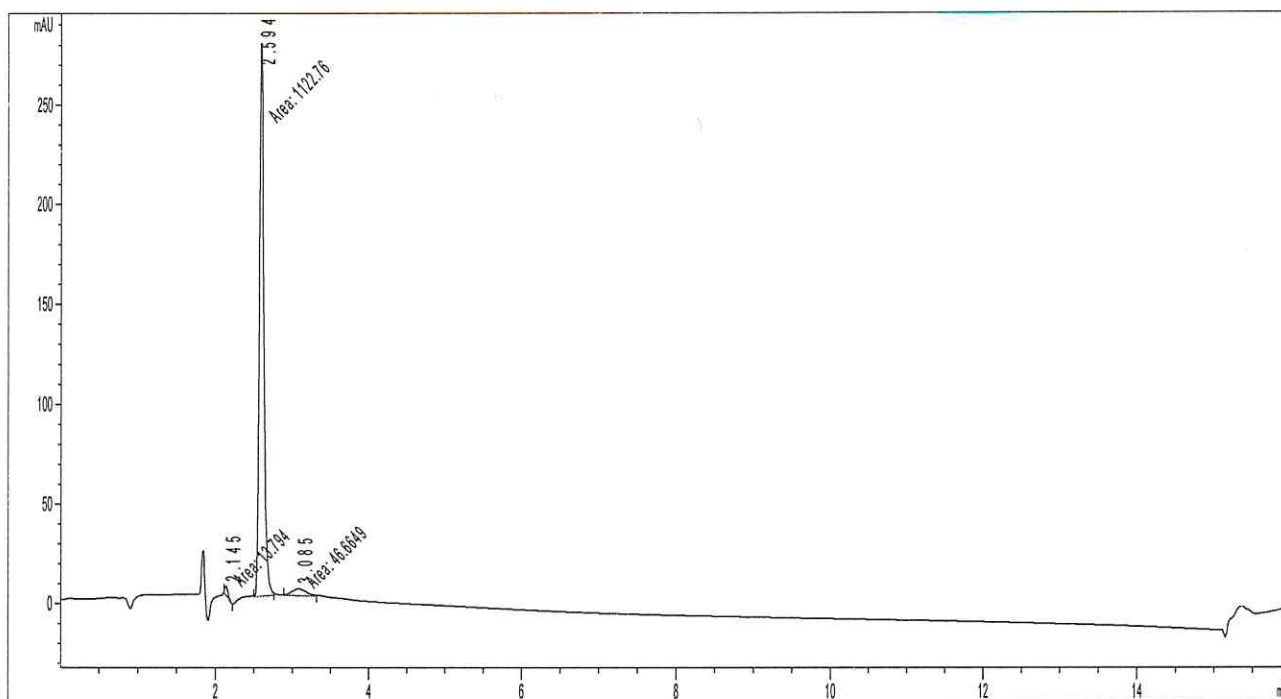
| Compound | Retention time | Area% |
|----------|----------------|-------|
| DM8      | 1.913          | 100   |



| Compound | Retention time | Area%  |
|----------|----------------|--------|
|          | 1.857          | 0.772  |
| DM9      | 1.982          | 99.228 |



| Compound | Retention time | Area%  |
|----------|----------------|--------|
| DM10     | 2.201          | 96.224 |
|          | 4.297          | 3.776  |



| Compound    | Retention time | Area%  |
|-------------|----------------|--------|
|             | 2.145          | 1.166  |
| <b>DM11</b> | 2.594          | 94.890 |
|             | 3.085          | 3.944  |

## $^1\text{H}$ - AND $^{13}\text{C}$ -NMR SPECTRA OF **DM1-11**



## Gradient Shimming

Sample Name:

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsys/data

Sample directory:

Fidfile: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: cdcl3

Data collected on: Jul 8 2019

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 3.411 sec

Width 4803.1 Hz

16 repetitions

OBSERVE H1, 300.1976543 MHz

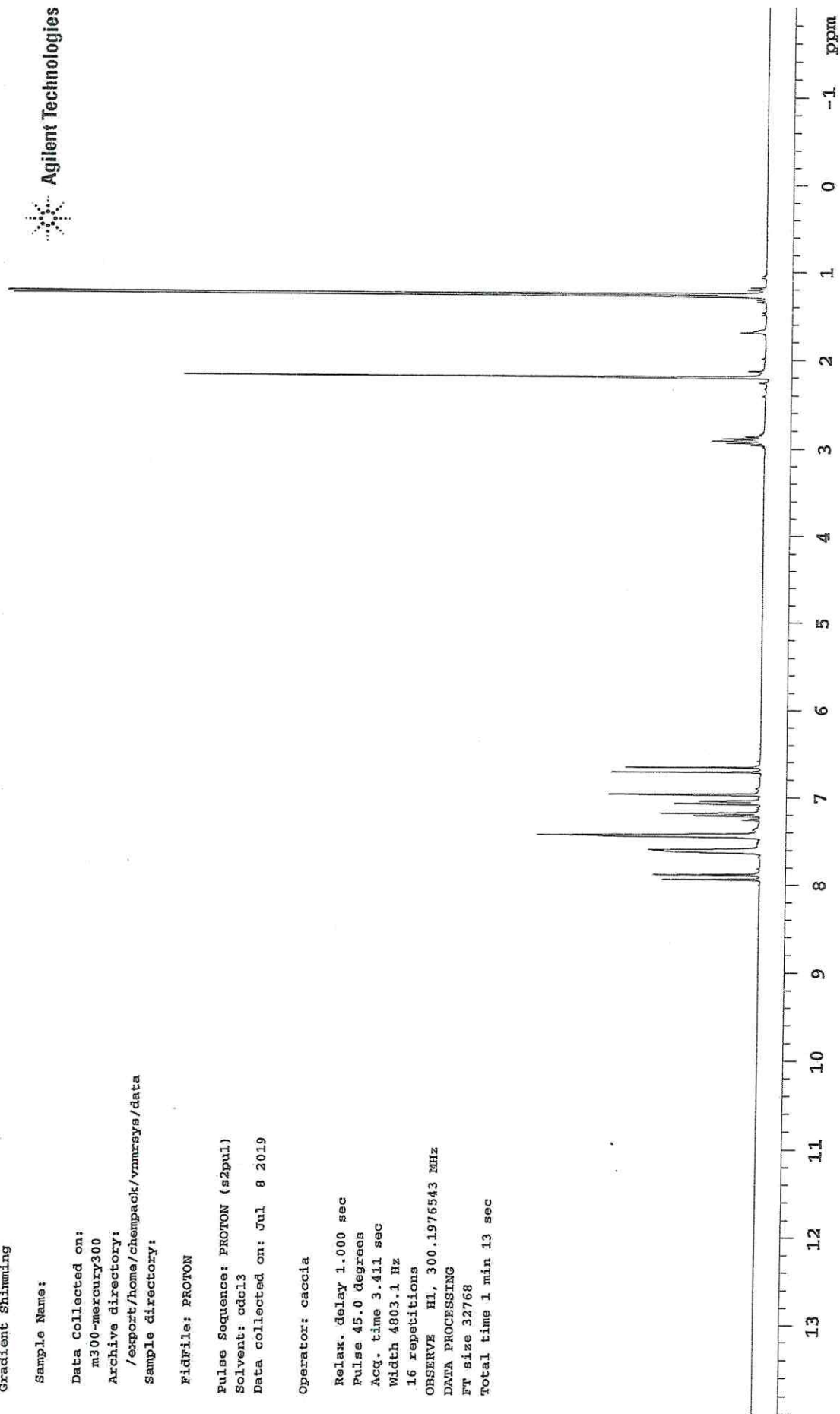
DATA PROCESSING

FT size 32768

Total time 1 min 13 sec



Agilent Technologies



## Gradient Shimming

Sample Name:

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

FidFile: CARBON

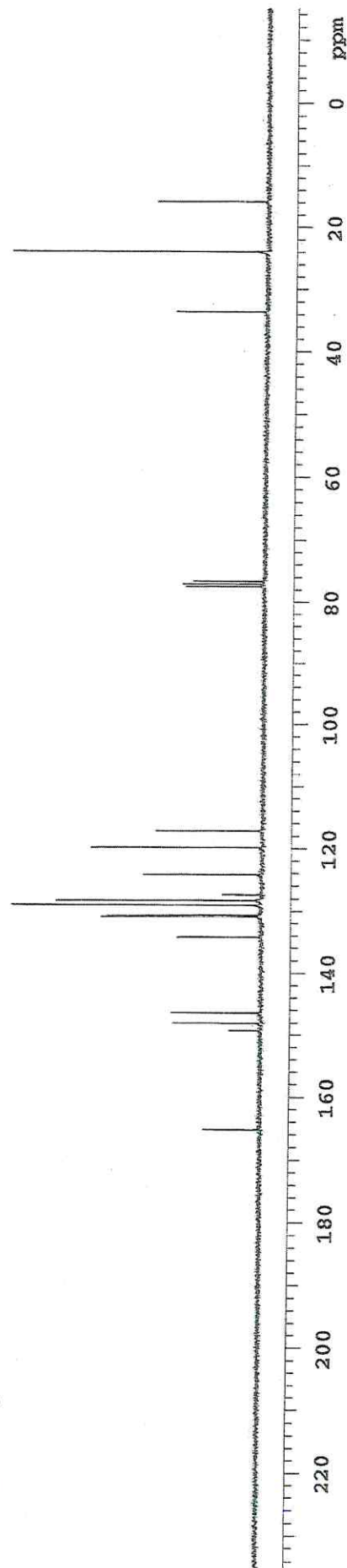
Pulse Sequence: CARBON (s2pul)  
Solvent: cdcl3  
Data collected on: Jul 22 2019

Operator: caccia

Relax. delay 1.000 sec  
Pulse 45.0 degrees  
Acq. time 0.968 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



Agilent Technologies



## Gradient Shimming

Sample Name:

DM2

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsvs/data

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: dmsd

Data collected on: Jun 11 2021

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.706 sec

Width 4803.1 Hz

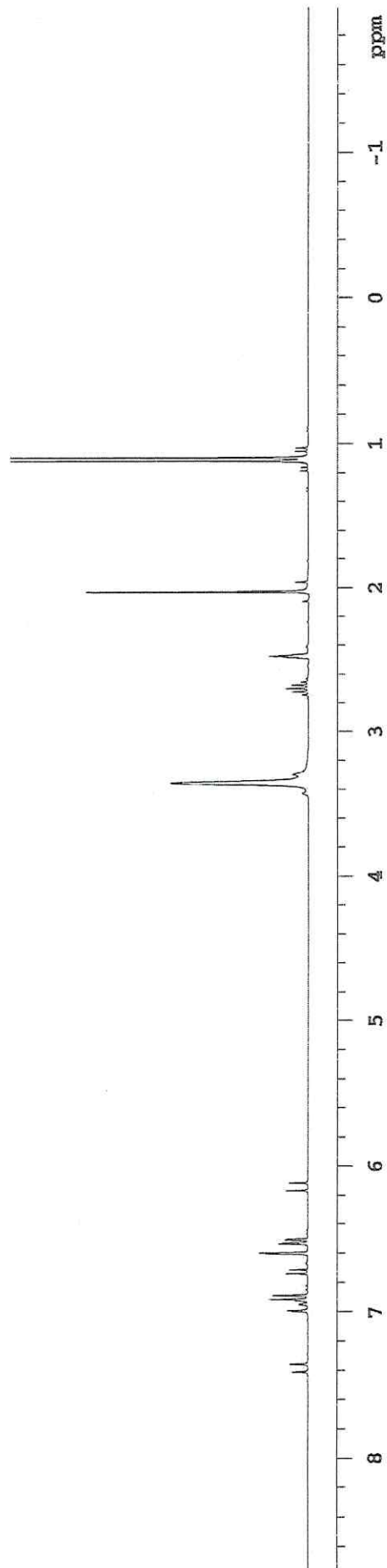
64 repetitions

OBSERVE H1, 300.1990802 MHz

DATA PROCESSING

Ft size 16384

Total time 2 min 58 sec



DM2

# Gradient Shimming

Sample Name:

DM2

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsys/data

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: dmso

Data collected on: Jun 9 2021

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

30016 repetitions

OBSERVE C13, 75.4851188 MHz

DECOUPLE H1, 300.2006240 MHz

Power 38 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

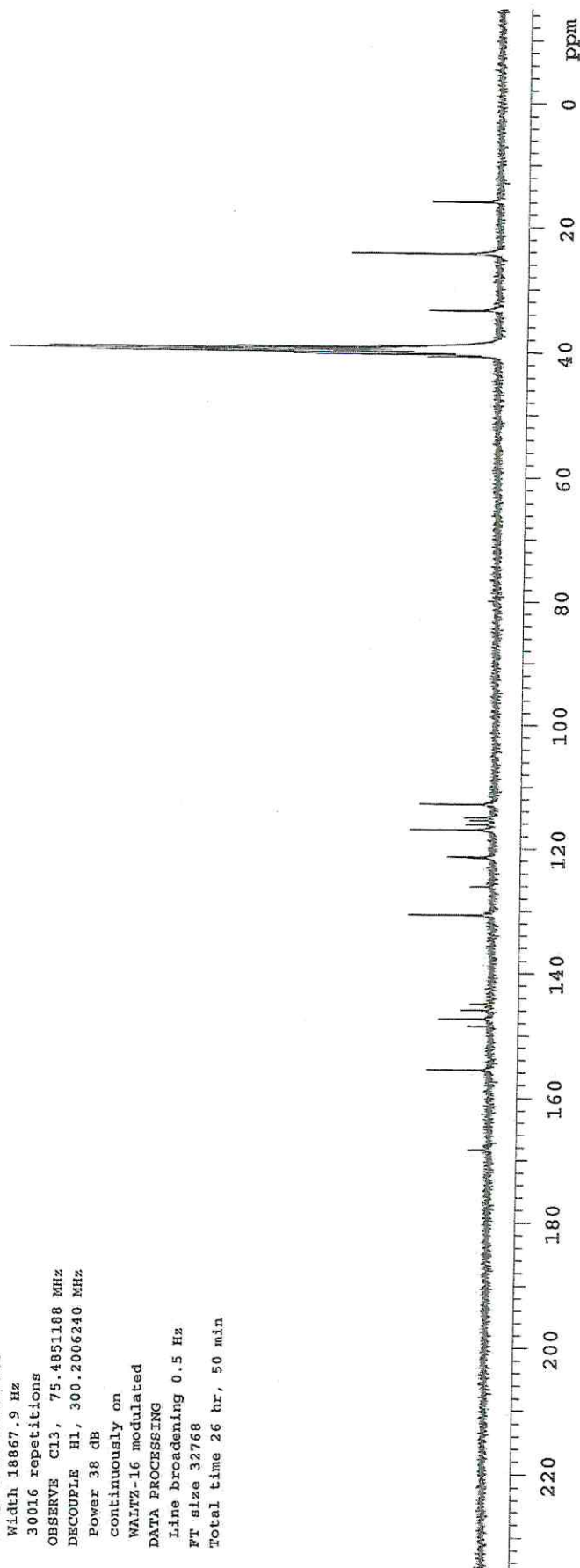
Line broadening 0.5 Hz

FT size 32768

Total time 26 hr, 50 min



512



Gradient Shimming

Sample Name:

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsvs/data

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: cdcl3

Data collected on: Nov 26 2019

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.706 sec

Width 4903.1 Hz

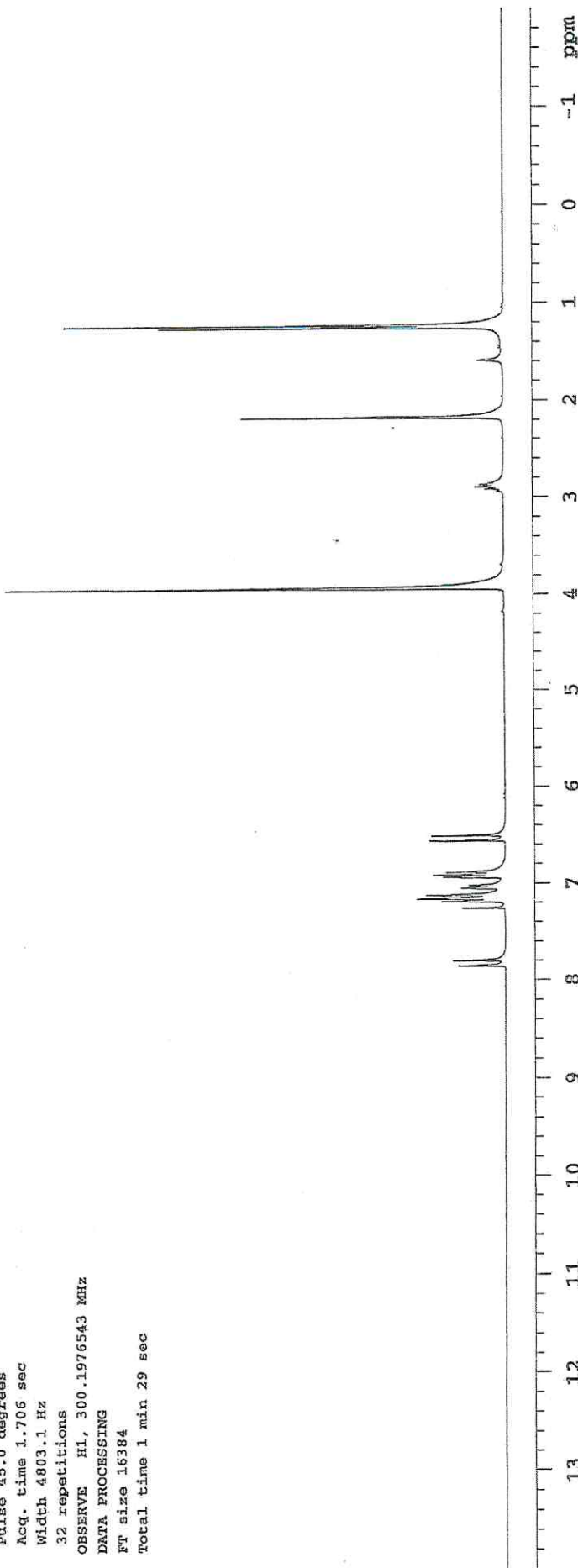
32 repetitions

OBSERVE H1, 300.1976543 MHz

DATA PROCESSING

Ft size 16384

Total time 1 min 29 sec



## Gradient Shimming

Sample Name:

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsys/data

Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)

Solvent: dmso

Data collected on: Jul 10 2019

Temp. 18.4 C / 291.6 K

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

27456 repetitions

OBSERVE C13, 75.4851188 MHz

DECOUPLE H1, 300.2006240 MHz

Power 38 dB

continuously on

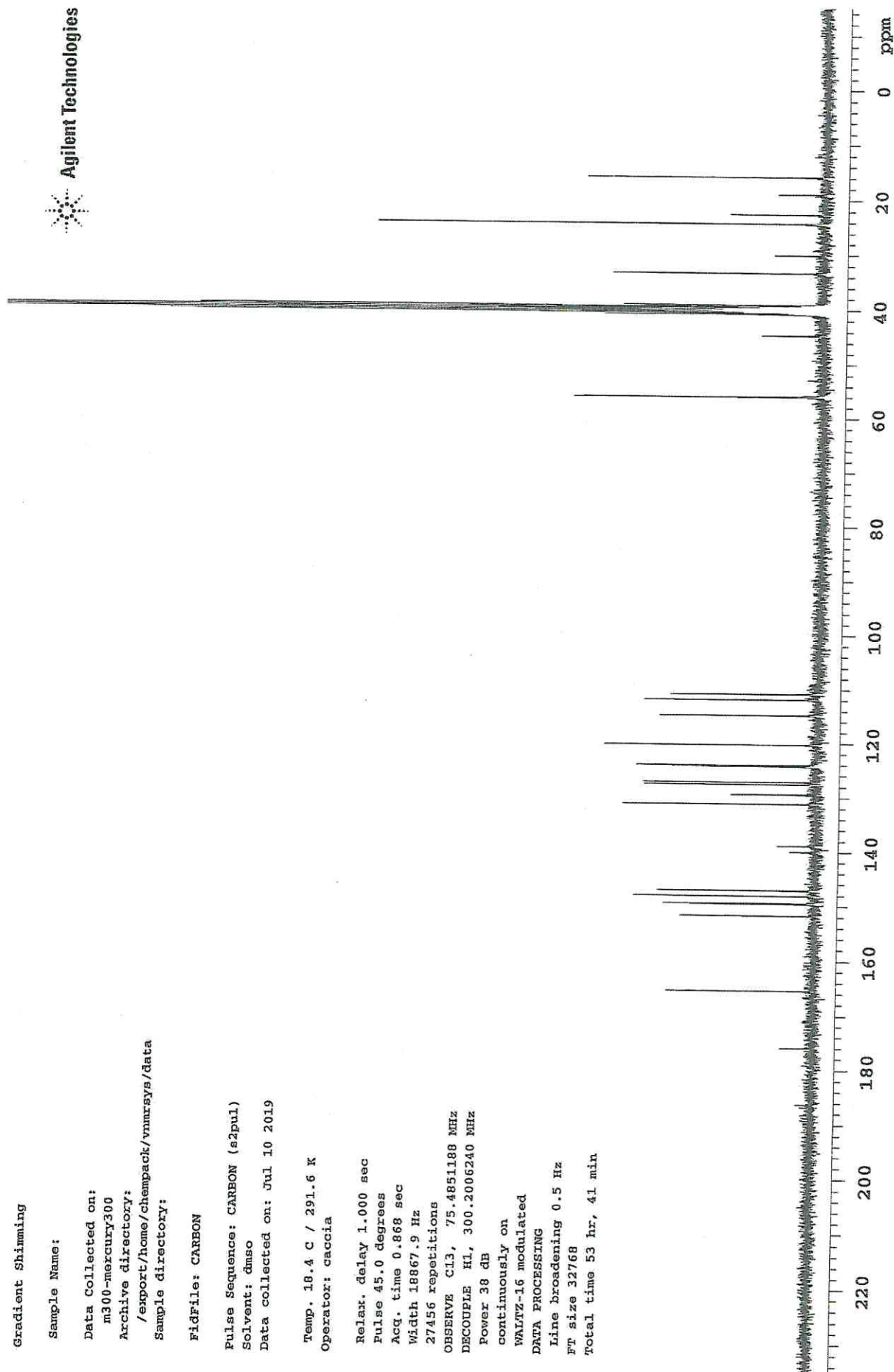
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

Ft size 32768

Total time 53 hr, 41 min



DM4

Gradient Shimming

Sample Name:

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

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)  
Solvent: cdcl3  
Data collected on: Jan 15 2020

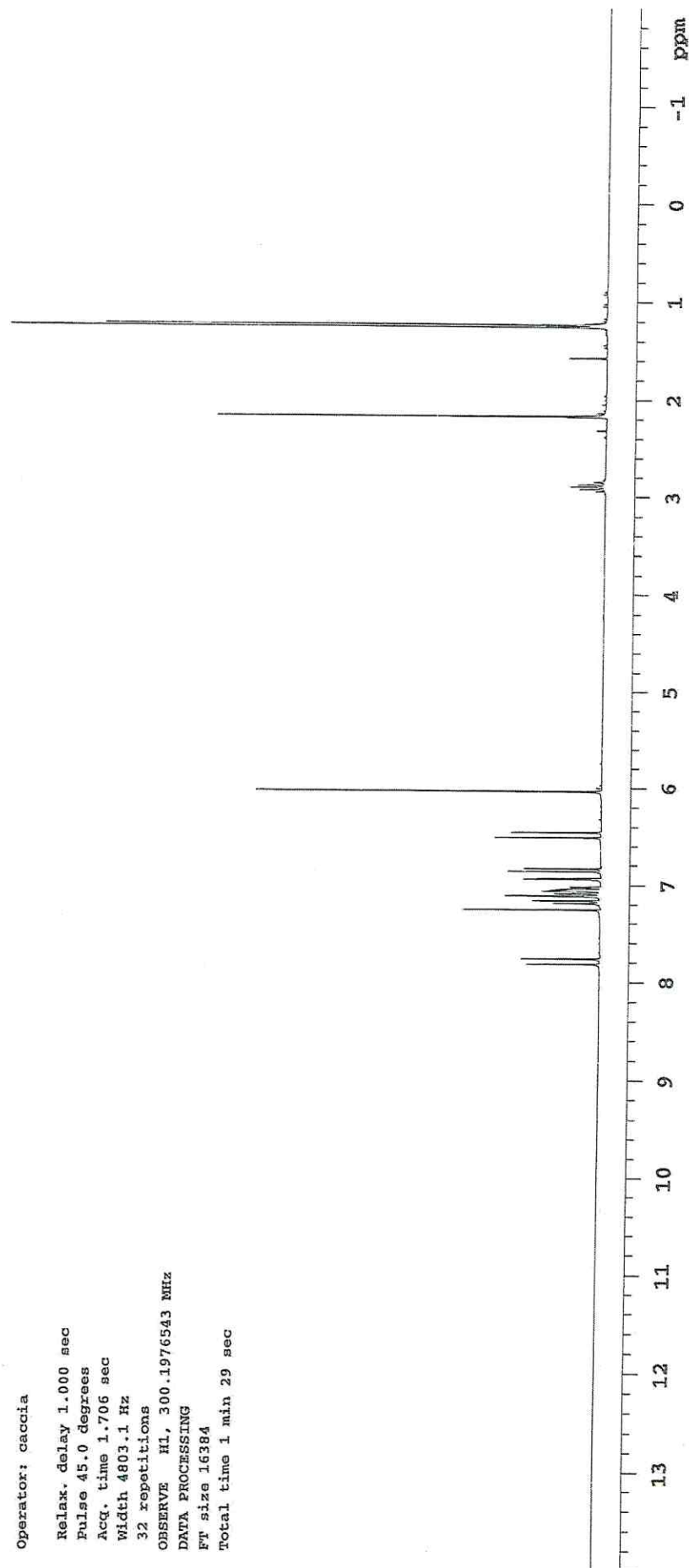
Operator: caccia

Relax. delay 1.000 sec  
Pulse 45.0 degrees  
Acq. time 1.706 sec  
Width 4803.1 Hz  
32 repetitions

OBSERVE H1, 300.1976543 MHz  
DATA PROCESSING  
FT size 16384  
Total time 1 min 29 sec



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## Gradient Shimming

Sample Name:

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: Jan 15 2020

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

10000 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

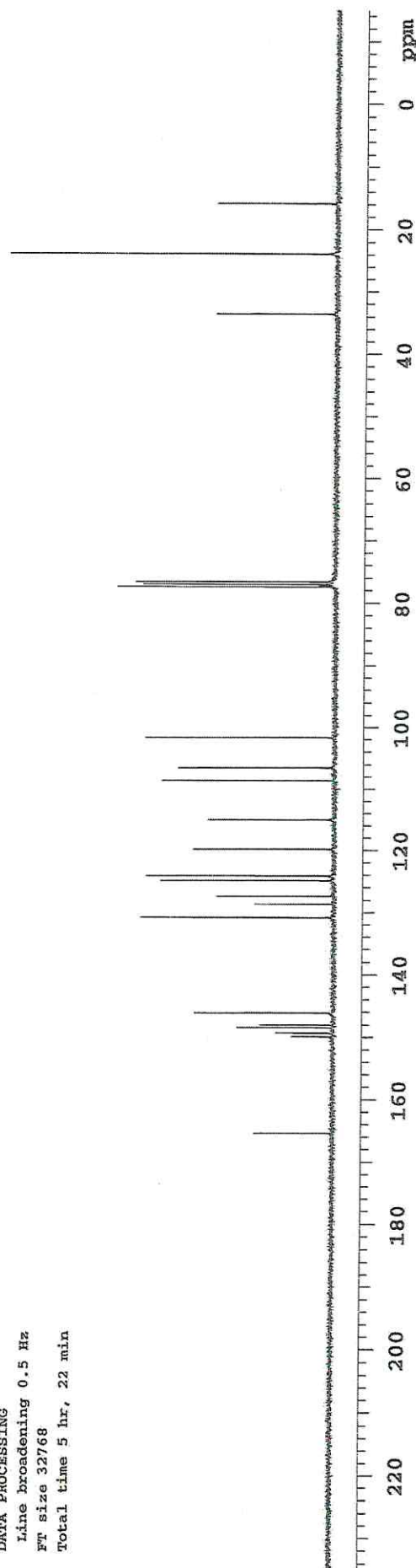
Line broadening 0.5 Hz

Ft size 32768

Total time 5 hr, 22 min



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Gradient Shimming

Sample Name:

DM5

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsys/data

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: dmso

Data collected on: Jun 10 2021

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.706 sec

Width 4803.1 Hz

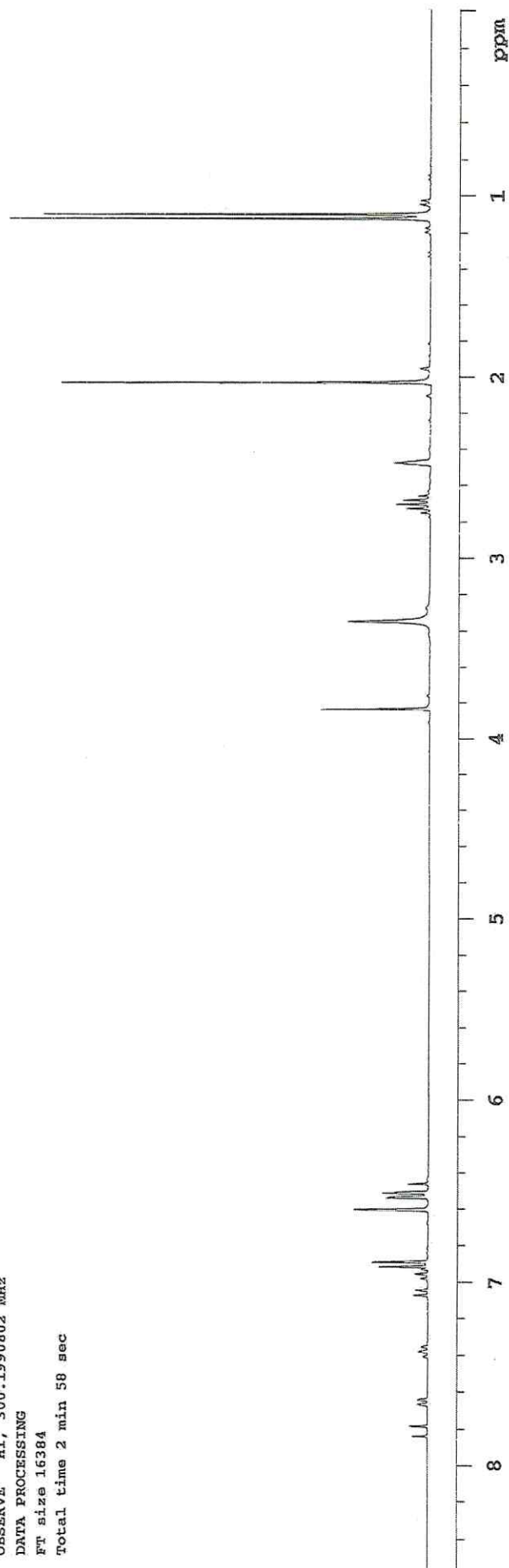
64 repetitions

OBSERVE H1, 300.1990802 MHz

DATA PROCESSING

Ft size 15384

Total time 2 min 58 sec



# Gradient Shimming

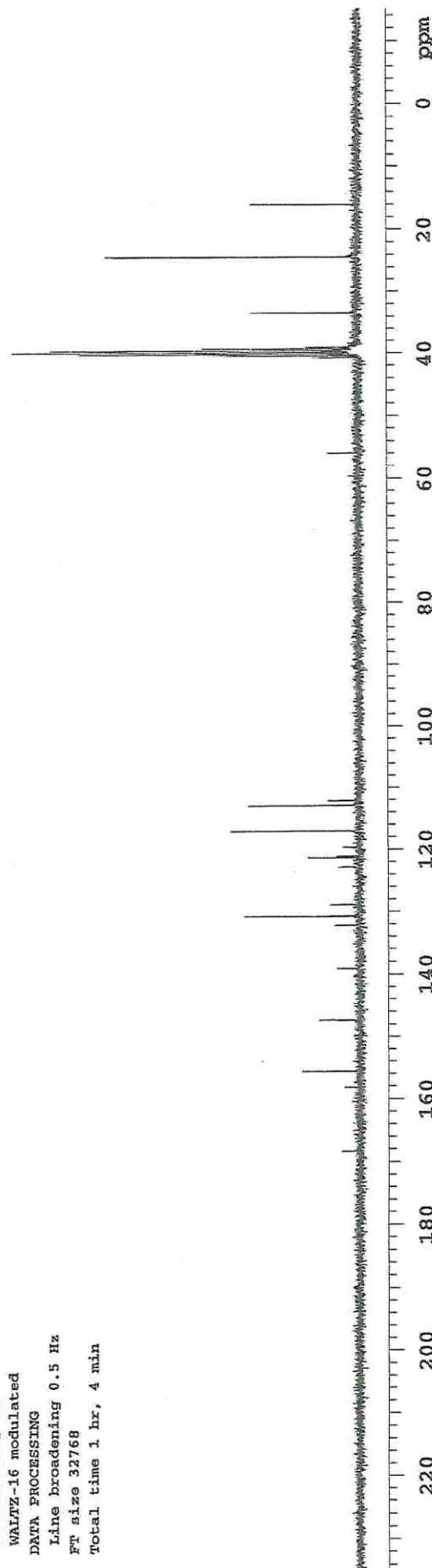
Sample Name:  
DM5  
Data Collected on:  
m300-mercury300  
Archive directory:  
/export/home/chempack/vnmrsys/data  
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)  
Solvent: dmso  
Data collected on: Jun 10 2021

Operator: caccia

Relax. delay 1.000 sec  
Pulse 45.0 degrees  
Acq. time 0.868 sec  
Width 18867.9 Hz  
1792 repetitions  
OBSERVE C13, 75.4851188 MHz  
DECOUPLE H1, 300.2006240 MHz  
Power 38 dB  
continuously on  
WAITZ-16 modulated  
DATA PROCESSING  
Line broadening 0.5 Hz  
Ft size 32768  
Total time 1 hr, 4 min



DN6



Gradient Shimming

Sample Name:

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

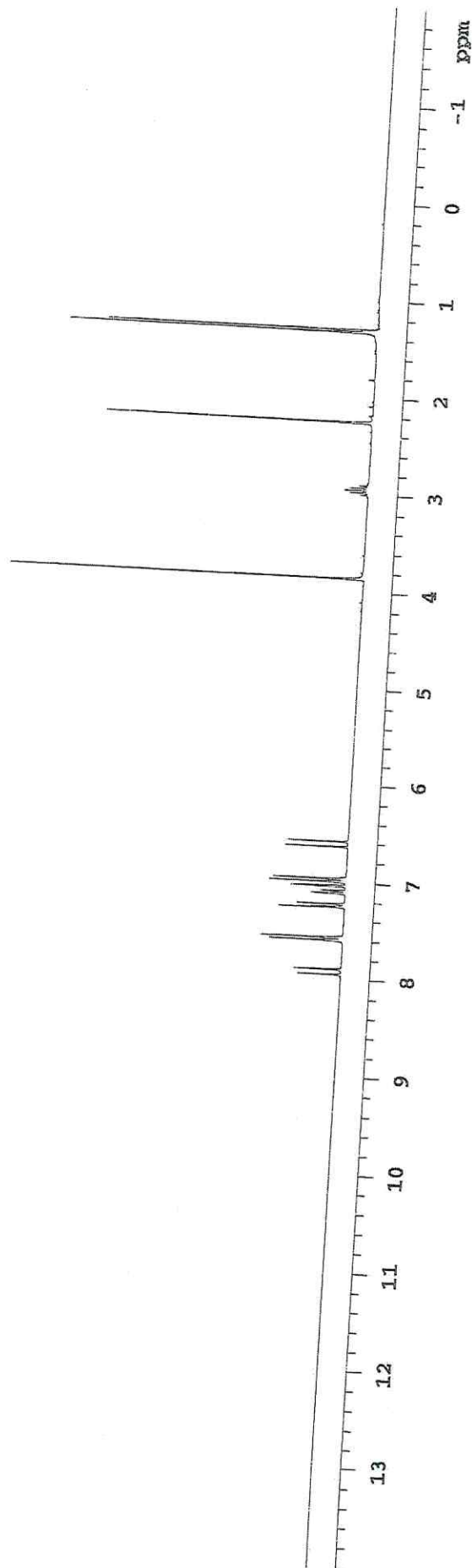
Fidfile: PROTON

Pulse Sequence: PROTON (s2pul)  
Solvent: cdcl3  
Data collected on: Dec 12 2019

Operator: caccia

Relax. delay 1.000 sec  
Pulse 45.0 degrees  
Acq. time 1.706 sec  
Width 4803.1 Hz  
32 repetitions

OBSERVE H1, 300.1976543 MHz  
DATA PROCESSING  
FT size 16384  
Total time 1 min 29 sec



## Gradient Shimming

## Sample Name:

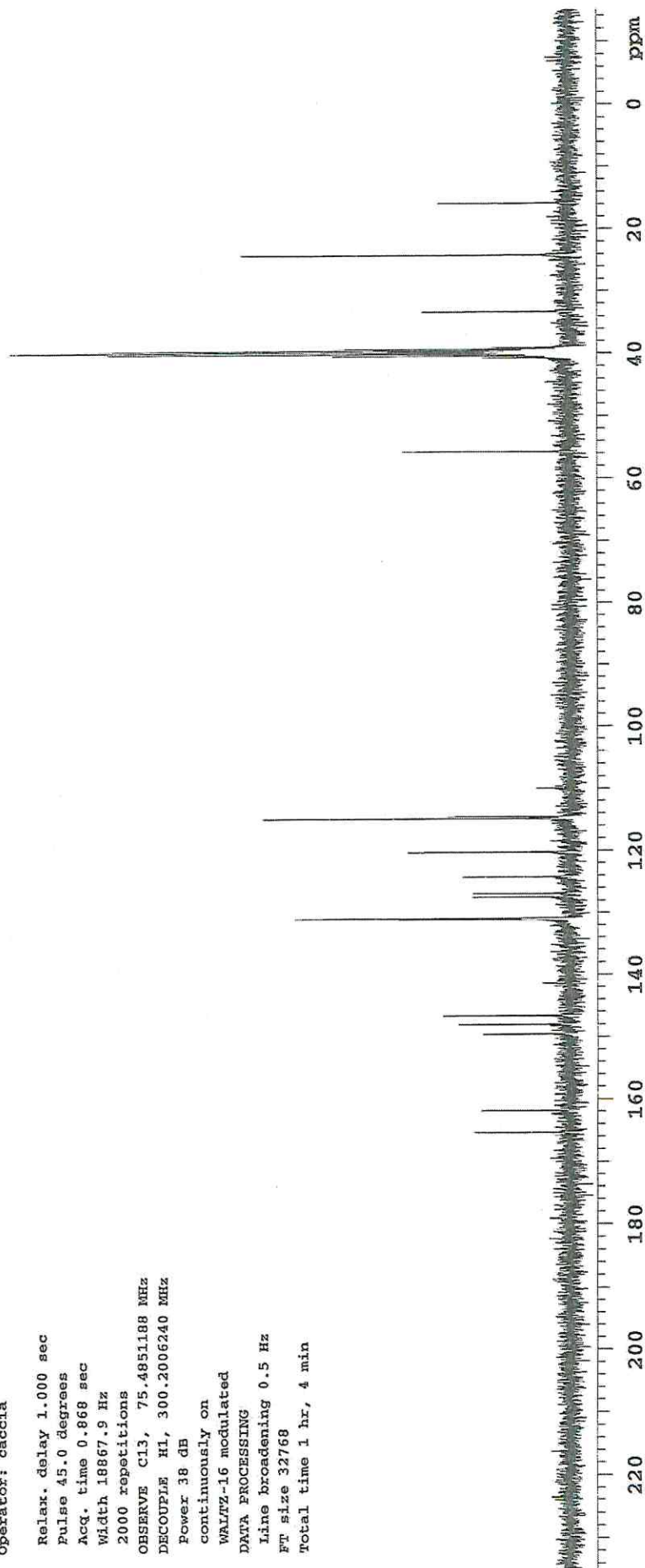
Data Collected on:  
m300-mercury300  
Archive directory:  
/export/home/chempack/vnmrsys/data  
Sample directory:

## FidFile: CARBON

Pulse Sequence: CARBON (s2pul)  
Solvent: dmsc  
Data collected on: Jul 15 2019

## Operator: caccia

Relax. delay 1.000 sec  
Pulse 45.0 degrees  
Acq. time 0.868 sec  
Width 18867.9 Hz  
2000 repetitions  
OBSERVE C13, 75.4851188 MHz  
DECOUPLE H1, 300.2006240 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 Shimming

Sample Name:

DM7

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsws/data

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: dmsc

Data collected on: Jun 10 2021

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.706 sec

Width 4803.1 Hz

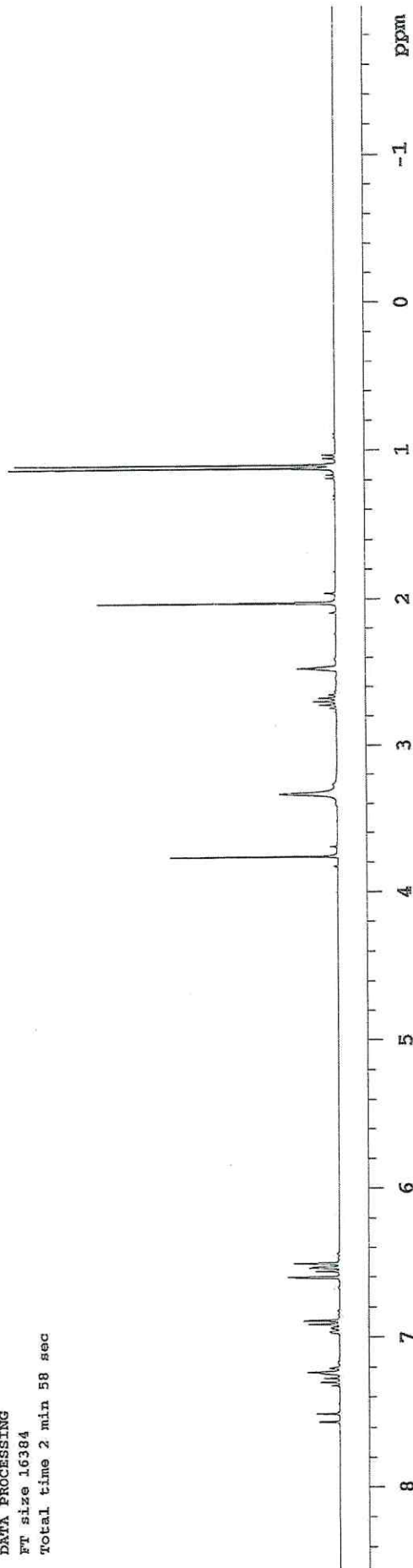
64 repetitions

OBSERVE H1, 300.1990802 MHz

DATA PROCESSING

FT size 16384

Total time 2 min 58 sec



DM7

Gradient Shimming

Sample Name:  
DM7  
Data Collected on:  
m300-mercury300  
Archive directory:  
/export/home/chempack/vnmrsws/data  
Sample directory:

Fidfile: CARBON

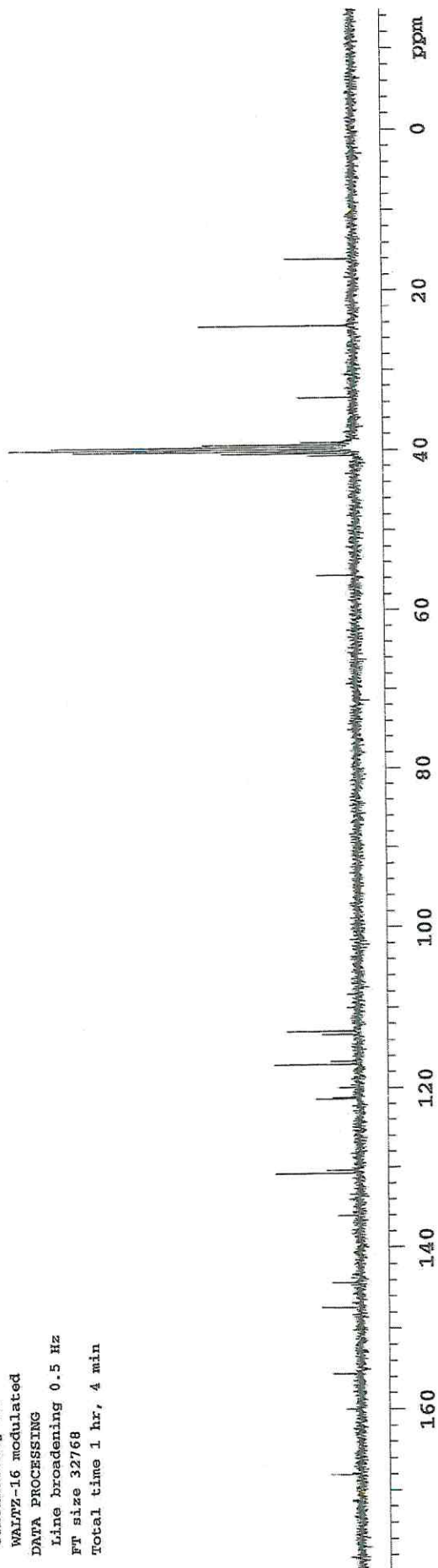
Pulse Sequence: CARBON (s2pul)  
Solvent: dmsc  
Data collected on: Jun 10 2021

Operator: caccia

Relax. delay 1.000 sec  
Pulse 45.0 degrees  
Acq. time 0.868 sec  
Width 18867.9 Hz  
1216 repetitions  
OBSERVE C13, 75.4851198 MHz  
DECOUPLE H1, 300.2006240 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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DH8

Gradient Shimming

Sample Name:

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsvs/data

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: cdcl3

Data collected on: Nov 29 2019

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.706 sec

Width 4803.1 Hz

32 repetitions

OBSERVE H1, 300.1976543 MHz

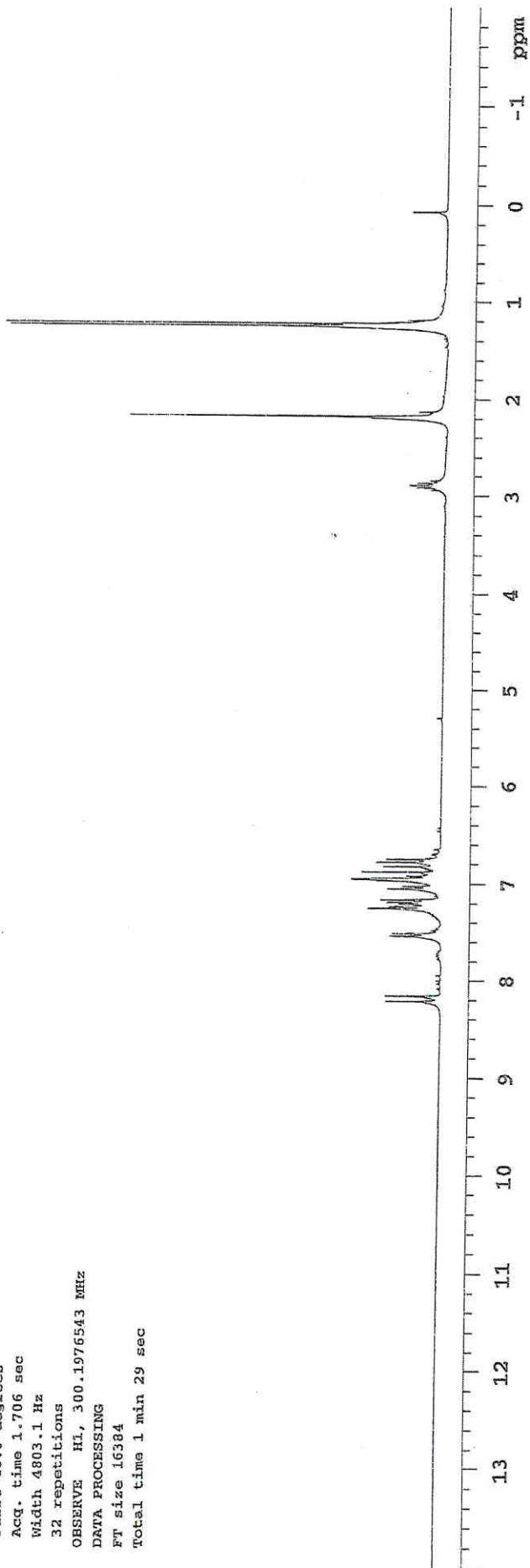
DATA PROCESSING

FT size 16384

Total time 1 min 29 sec



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Gradient Shimming

Sample Name:

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: Dec 9 2019

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 0.868 sec

Width 18867.9 Hz

24000 repetitions

OBSERVE C13, 75.4847602 MHz

DECOUPLE H1, 300.1991980 MHz

Power 38 dB

continuously on

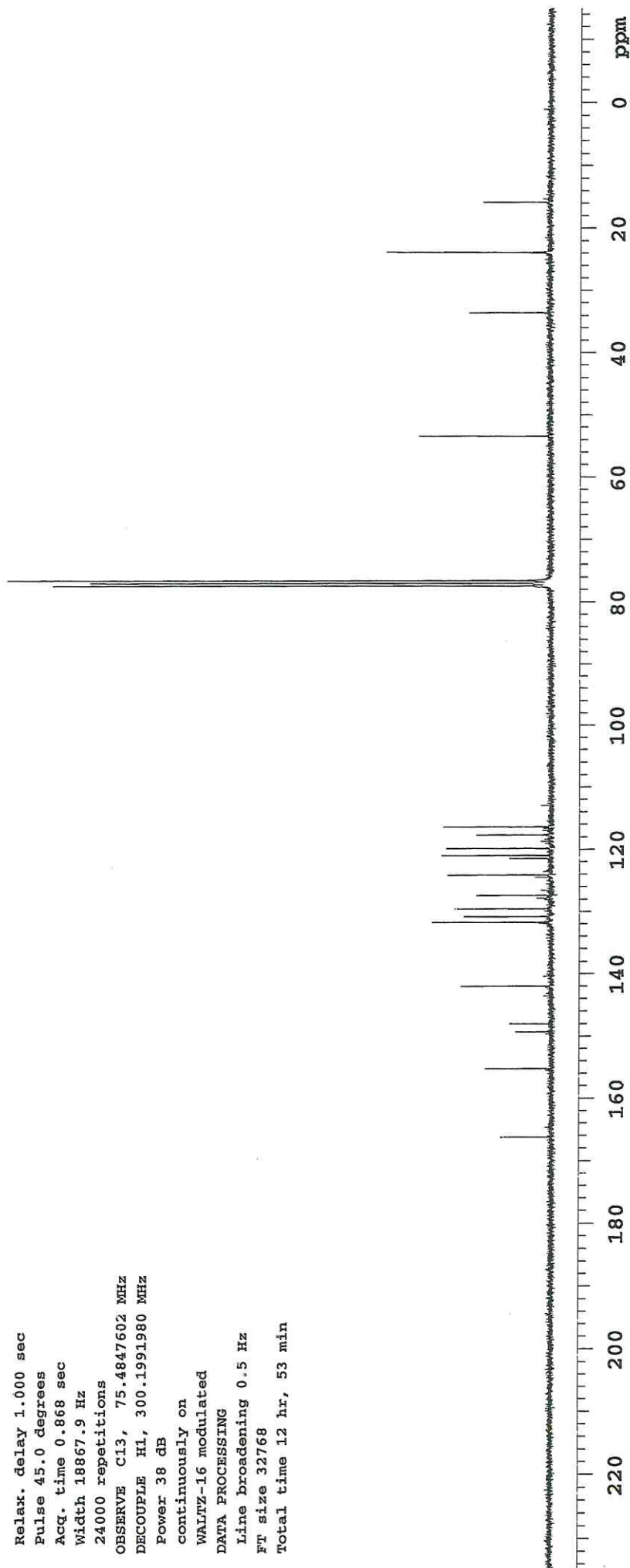
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 32768

Total time 12 hr, 53 min





Gradient Shimming

Sample Name:

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vmrsys/data

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: cdcl3

Data collected on: Jan 28 2020

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.706 sec

Width 4803.1 Hz

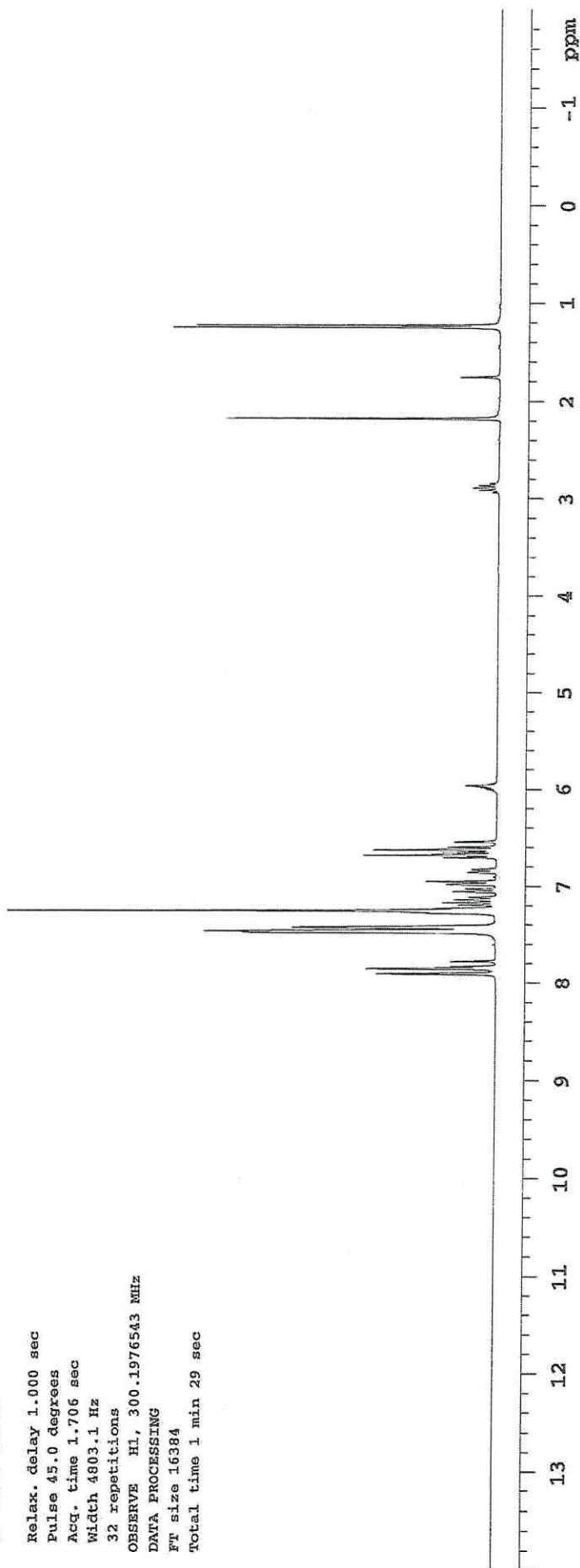
32 repetitions

OBSERVE H1, 300.1976543 MHz

DATA PROCESSING

Ft size 16384

Total time 1 min 29 sec



## Gradient Shimming

## Sample Name:

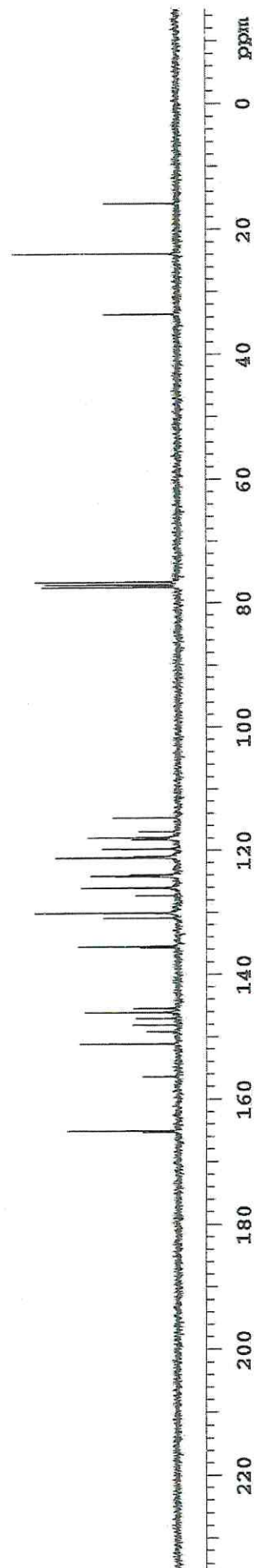
Data Collected on:  
m300-mercury300  
Archive directory:  
/export/home/chempack/vnmrsys/data  
Sample directory:

## FidFile: CARBON

Pulse Sequence: CARBON (s2pul)  
Solvent: cdcl3  
Data collected on: Jan 28 2020

## Operator: caccia

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



Gradient Shimming

Sample Name:

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

Fidfile: PROTON

Pulse Sequence: PROTON (s2pul)  
Solvent: cdcl3  
Data collected on: Jan 8 2020

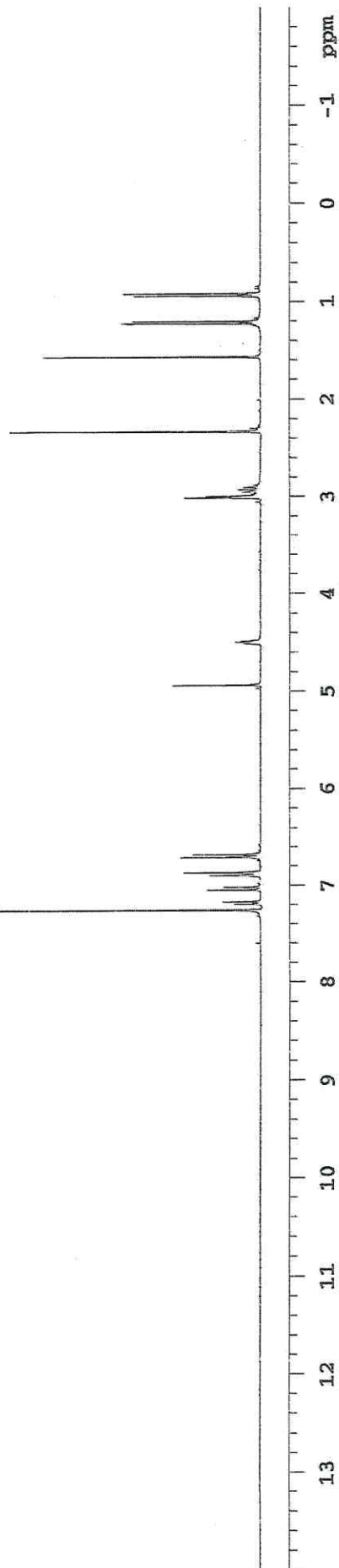
Operator: caccia

Relax. delay 1.000 sec  
Pulse 45.0 degrees  
Acq. time 1.706 sec  
Width 4803.1 Hz  
32 repetitions  
OBSERVE H1, 300.1976543 MHz  
DATA PROCESSING  
Ft size 16384  
Total time 1 min 29 sec



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DN-10



Gradient Shimming

Sample Name:

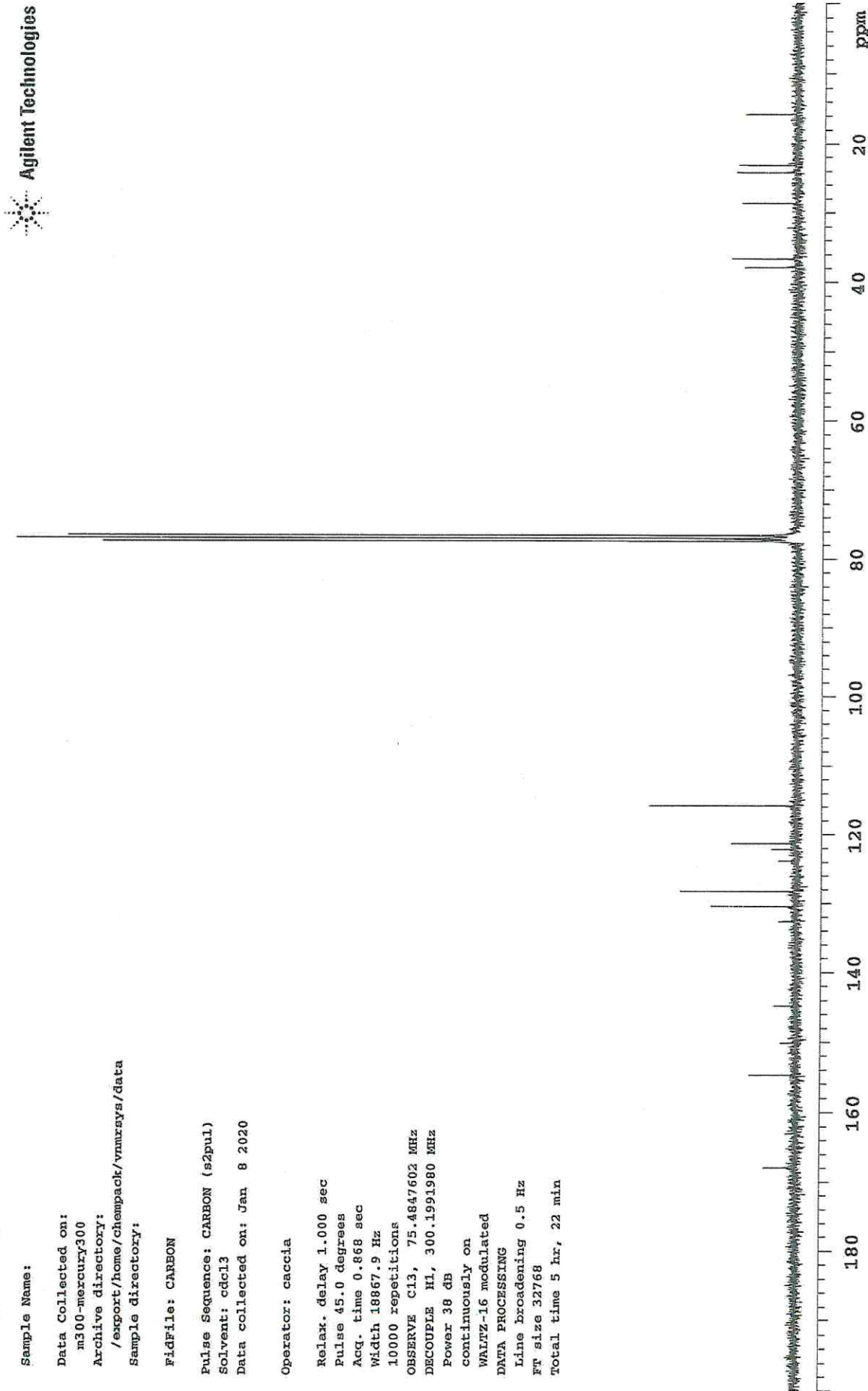
Data Collected on:  
m300-mercury300  
Archive directory:  
/export/home/chempack/vnmrsys/data  
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)  
Solvent: cdcl3  
Data collected on: Jan 8 2020

Operator: caccia

Relax. delay 1.000 sec  
Pulse 45.0 degrees  
Acq. time 0.868 sec  
Width 18867.9 Hz  
10000 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 5 hr, 22 min



DH44

Gradient Shimming

Sample Name:

Data Collected on:

m300-mercury300

Archive directory:

/export/home/chempack/vnmrsys/data

Sample directory:

FidFile: PROTON

Pulse Sequence: PROTON (s2pul)

Solvent: cdcl3

Data collected on: Jan 15 2020

Operator: caccia

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.706 sec

Width 4903.1 Hz

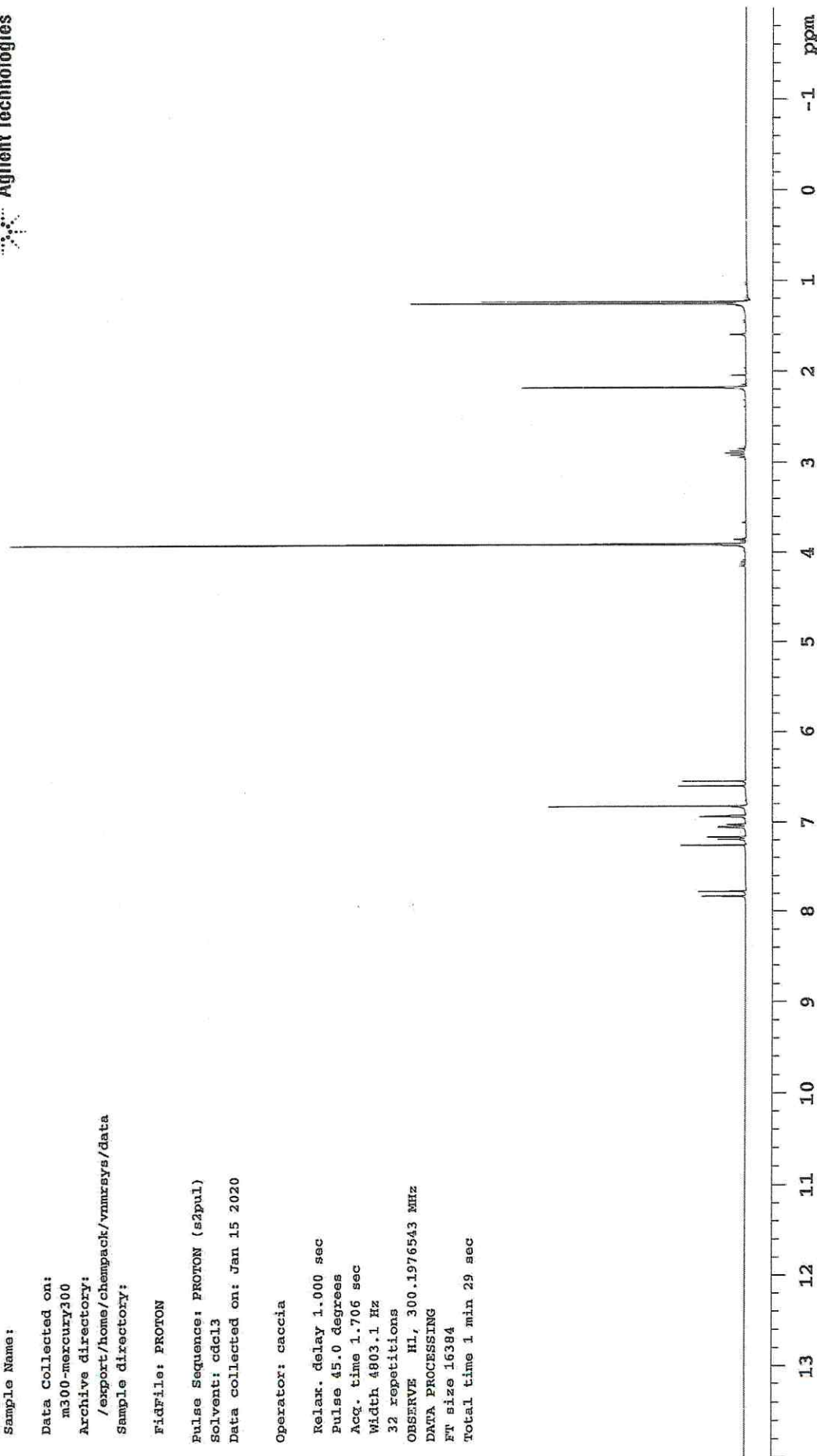
32 repetitions

OBSERVE H1, 300.1976543 MHz

DATA PROCESSING

FT size 16384

Total time 1 min 29 sec



# Gradient Shimming

Sample Name:

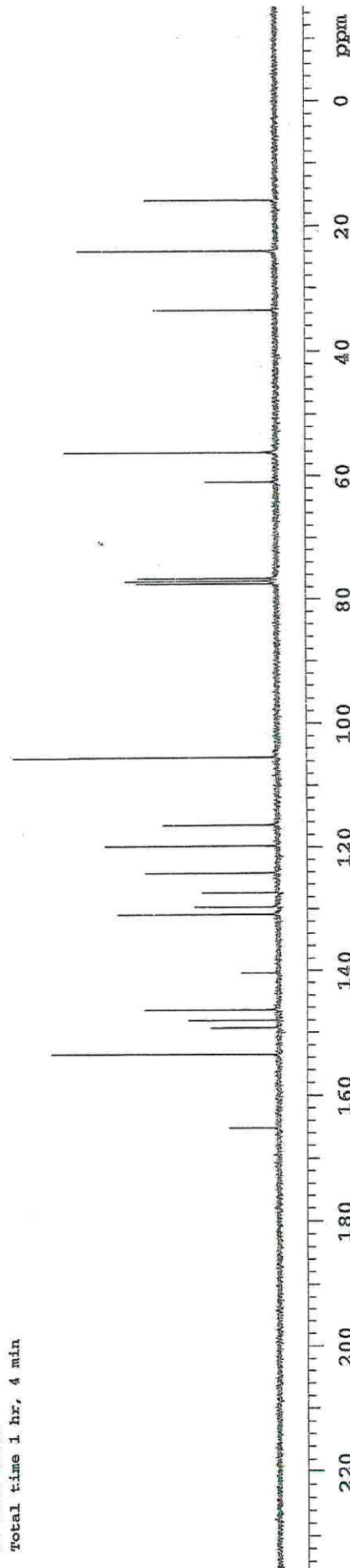
Data Collected on:  
m300-mercury300  
Archive directory:  
/export/home/chempack/vnmrsys/data  
Sample directory:

FidFile: CARBON

Pulse Sequence: CARBON (s2pul)  
Solvent: cdcl3  
Data collected on: Nov 6 2019

Operator: caccia

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



## HR-MS SPECTRA OF DM1-11

### High Resolution Mass Spectrometry Analysis

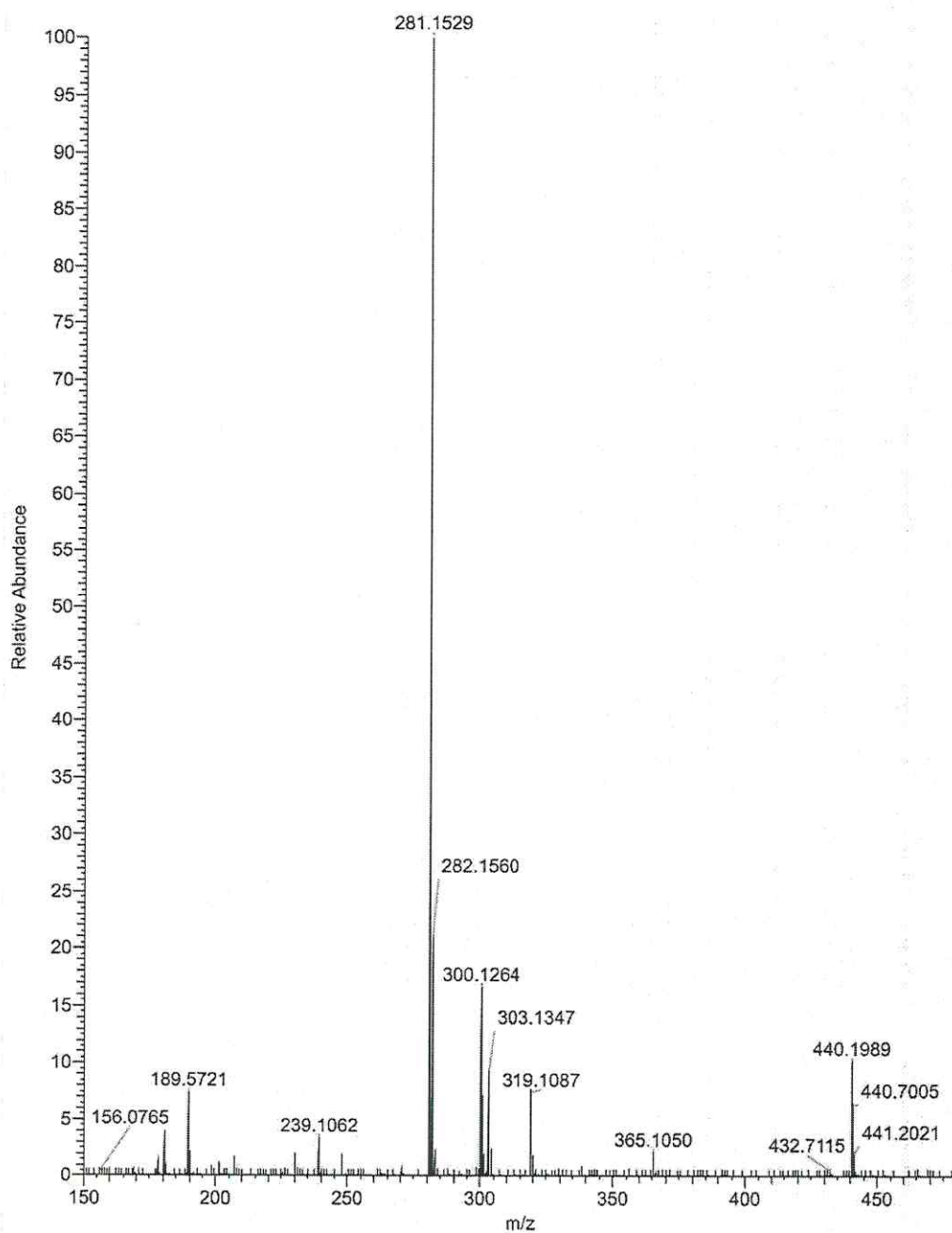
Each investigated compound was dissolved in ACN/H<sub>2</sub>O 80/20 with 0.1% of formic acid at 10 µg/mL and injected into the mass spectrometer through a syringe pump at a flow rate of 5 µL/min. The mass spectrometer used was a Thermo Fischer Orbitrap Fusion™ Tribrid™ operating in MS scan in the m/z range of 80 to 500, equipped with the Orbitrap as detector type at 240,000 of mass resolution (FWHM). Except for the **DM2** all compounds were acquired in positive ion mode.

### DM1 (280.15)

D:\data\16. February 2022 Analyses\DM-infusion\DM-1-Scan.raw 2/8/2022 10:51:33 AM

DM-1-Scan #13 RT: 0.16 AV: 1 NL: 1.95E+008

T: FTMS + p ESI Full ms [80.0000-500.0000]



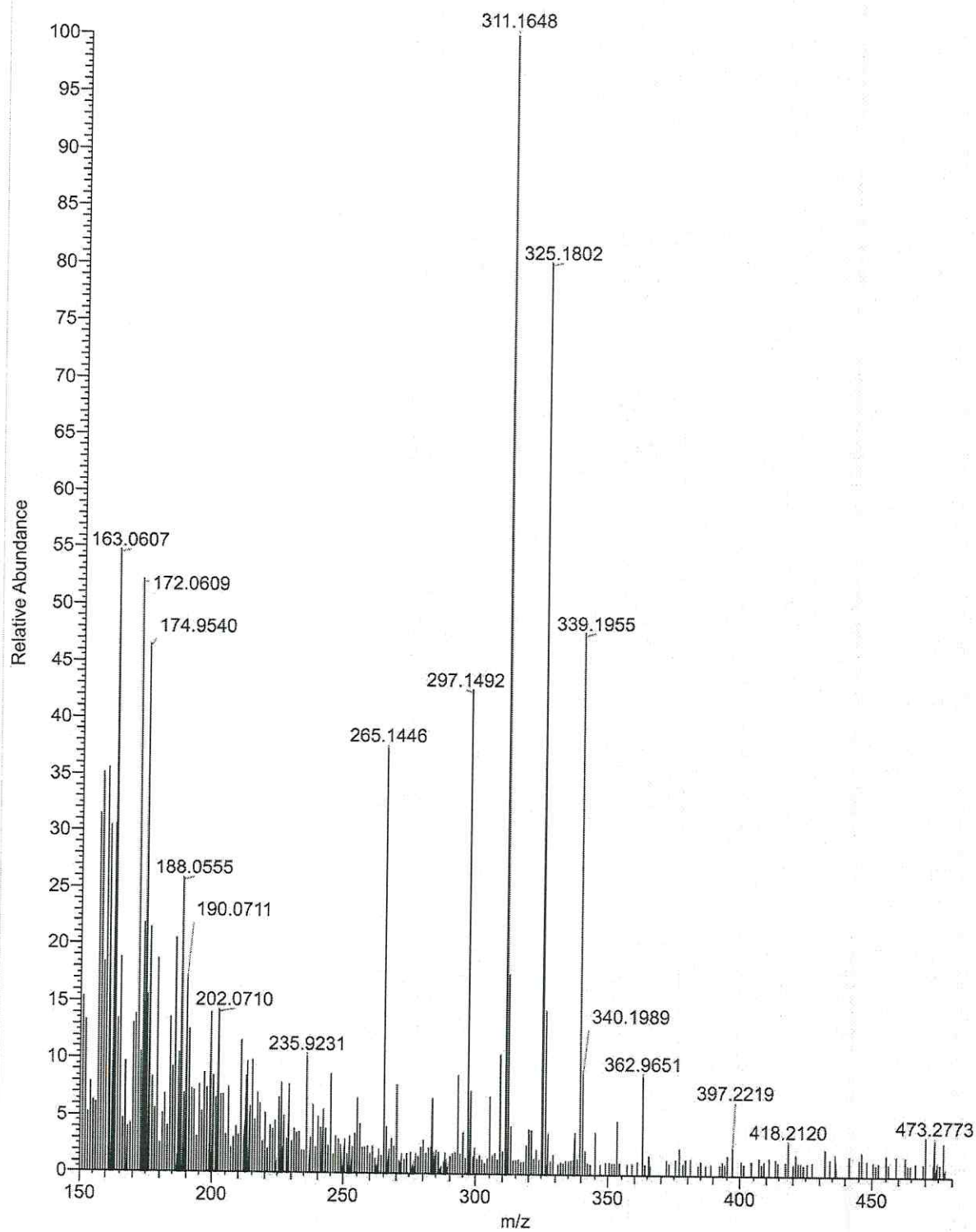


# DM2 (312.16)

D:\data\16. February 2022 Analyses\DM-infusion\DM-2bis-scan-neg...2/8/2022 10:54:51 AM

DM-2bis-scan-neg #13 RT: 0.09 AV: 1 NL: 2.04E+005

T: FTMS - p ESI Full ms [80.0000-500.0000]



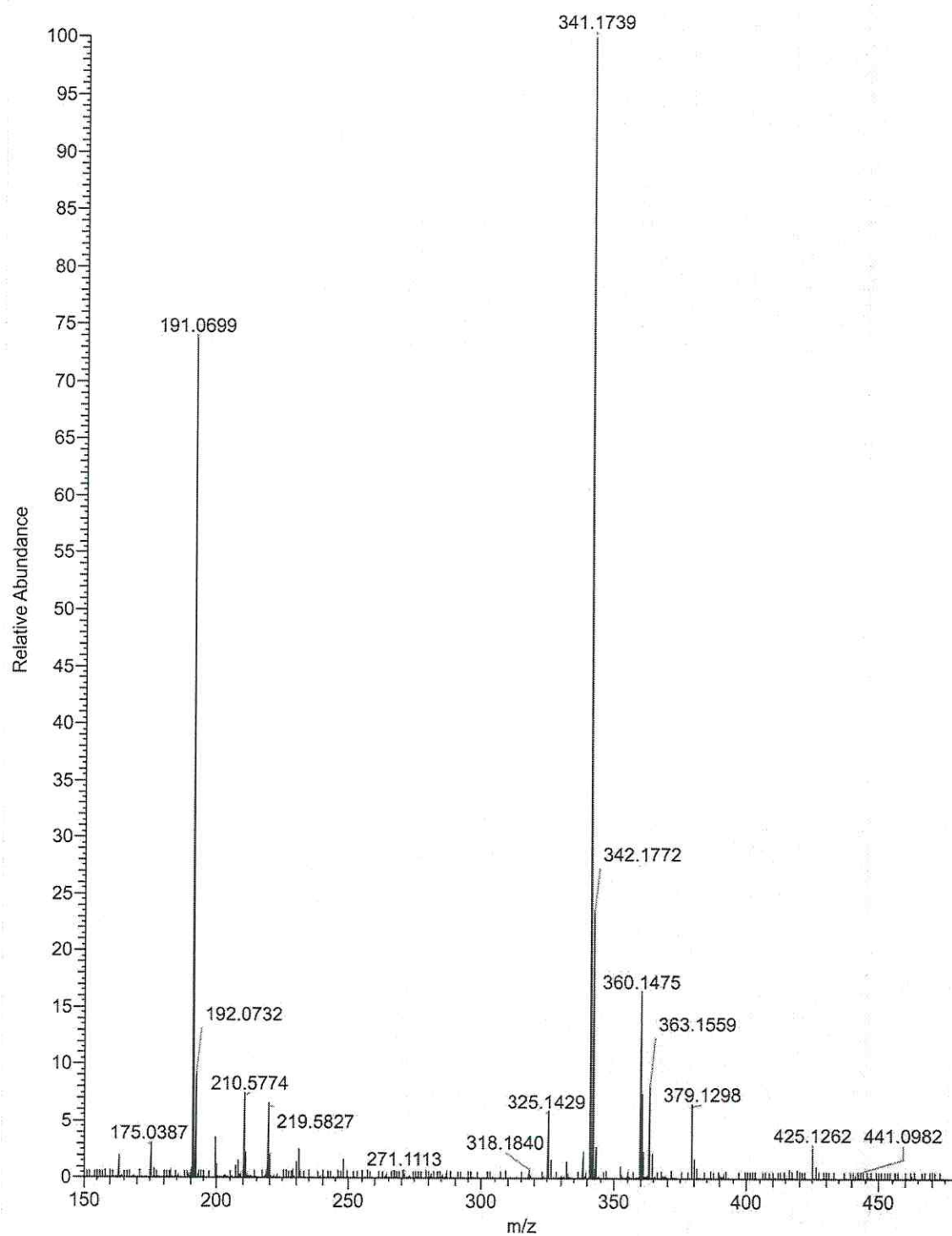


# DM3 (340.17)

D:\data\16. February 2022 Analyses\DM-infusion\DM-3-scan.raw 2/8/2022 10:55:15 AM

DM-3-scan #13 RT: 0.16 AV: 1 NL: 1.44E+008

T: FTMS + p ESI Full ms [80.0000-500.0000]

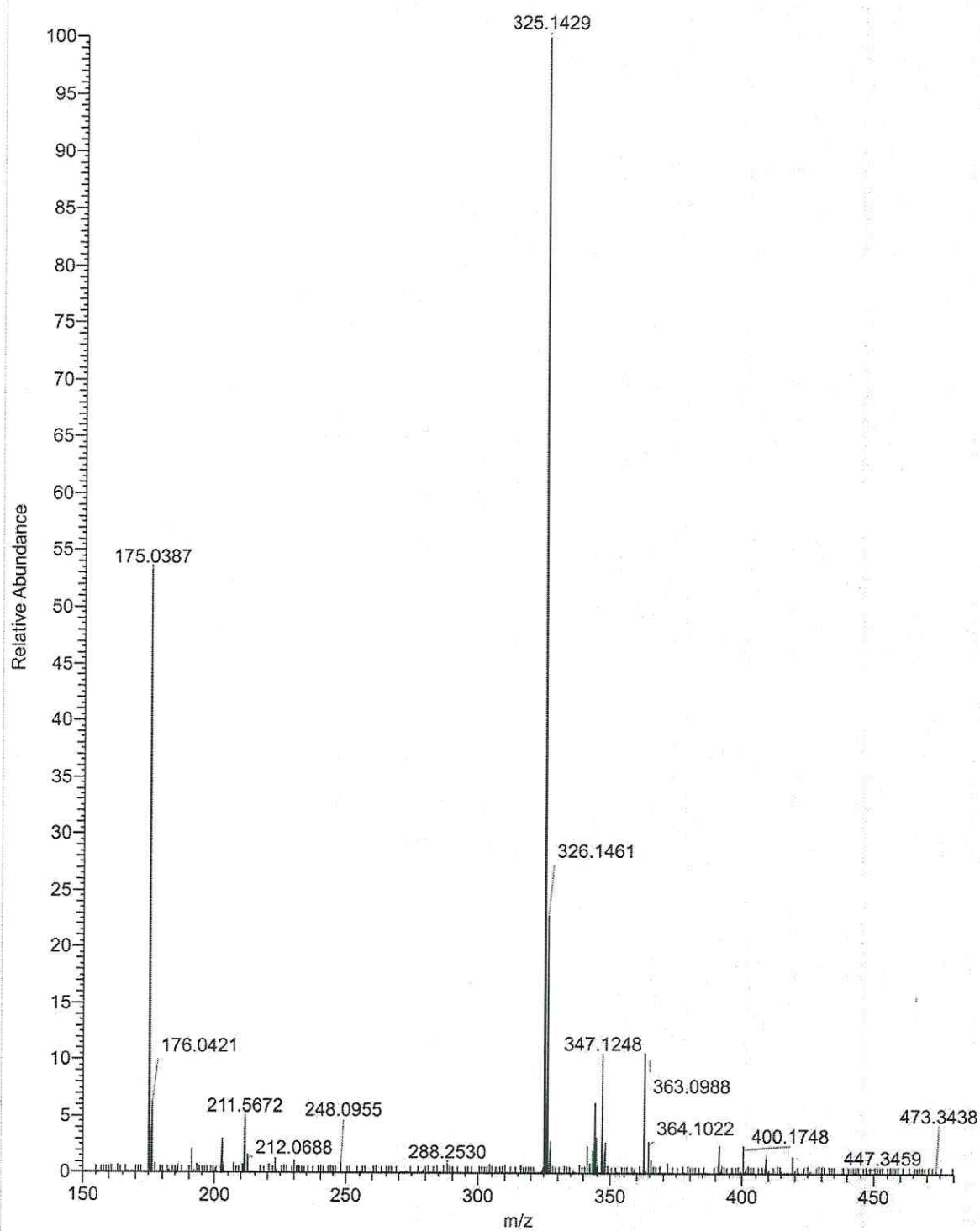


# DM4 (324.14)

D:\data\16. February 2022 Analyses\DM-infusion\DM-4-scan.raw 2/8/2022 10:55:34 AM

DM-4-scan #13 RT: 0.16 AV: 1 NL: 2.65E+008

T: FTMS + p ESI Full ms [80.0000-500.0000]

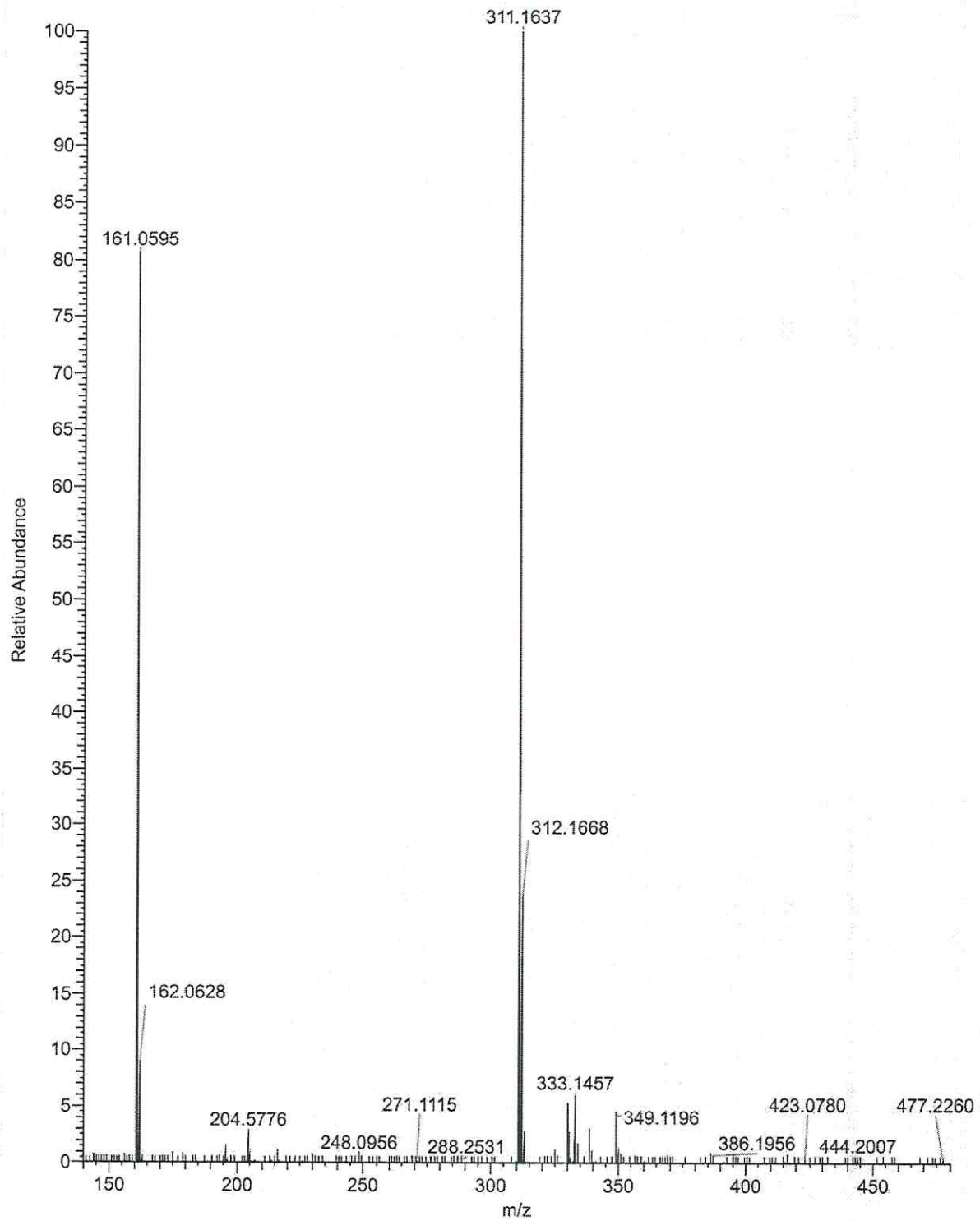


# DM5 (310.16)

D:\data\16. February 2022 Analyses\DM-infusion\DM-5-scan.raw 2/8/2022 10:56:26 AM

DM-5-scan #13 RT: 0.16 AV: 1 NL: 1.84E+008

T: FTMS + p ESI Full ms [80.0000-500.0000]

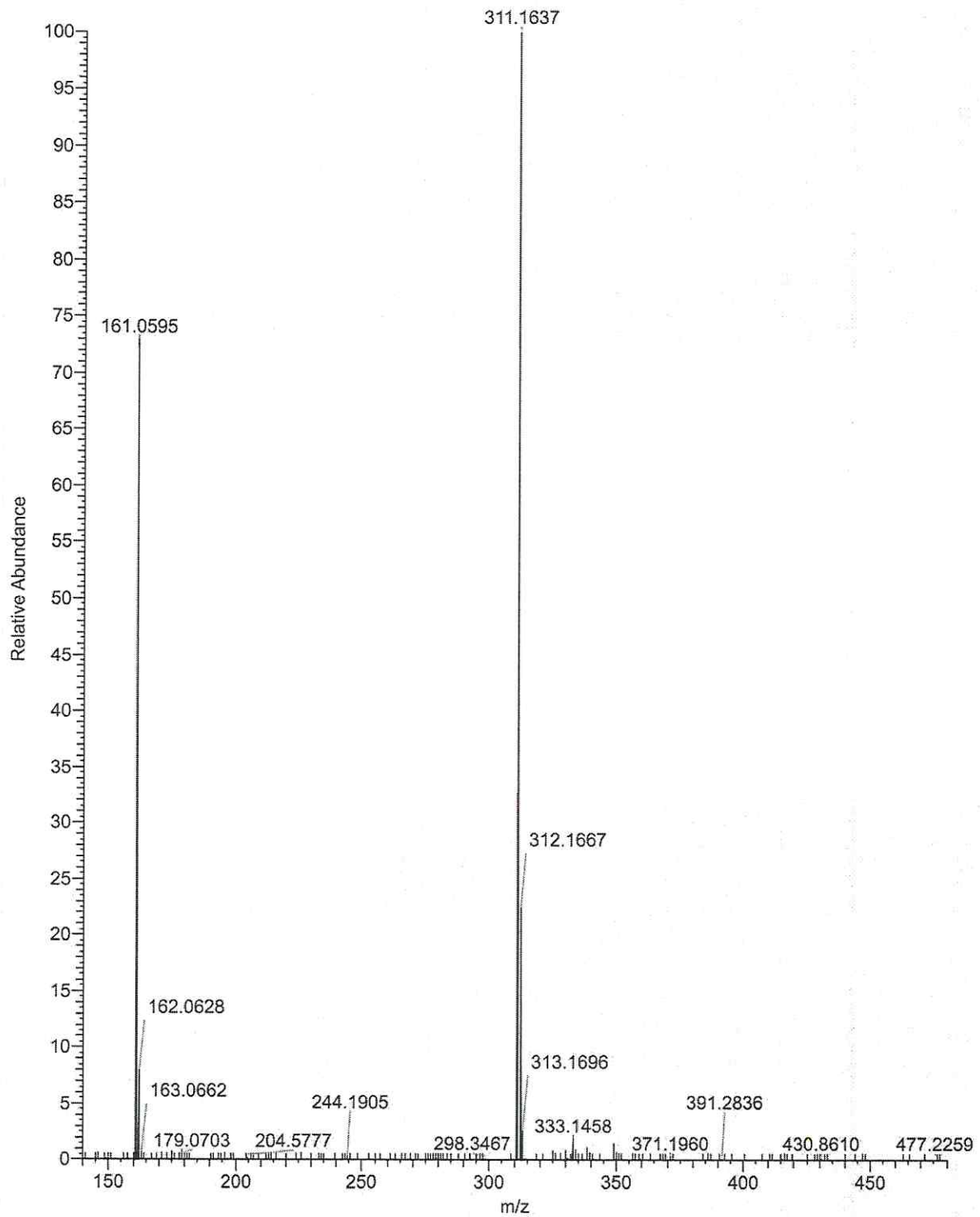


# DM6 (310.16)

D:\data\16. February 2022 Analyses\DM-infusion\DM-6-scan.raw 2/8/2022 10:57:00 AM

DM-6-scan #13 RT: 0.16 AV: 1 NL: 3.81E+008

T: FTMS + p ESI Full ms [80.0000-500.0000]

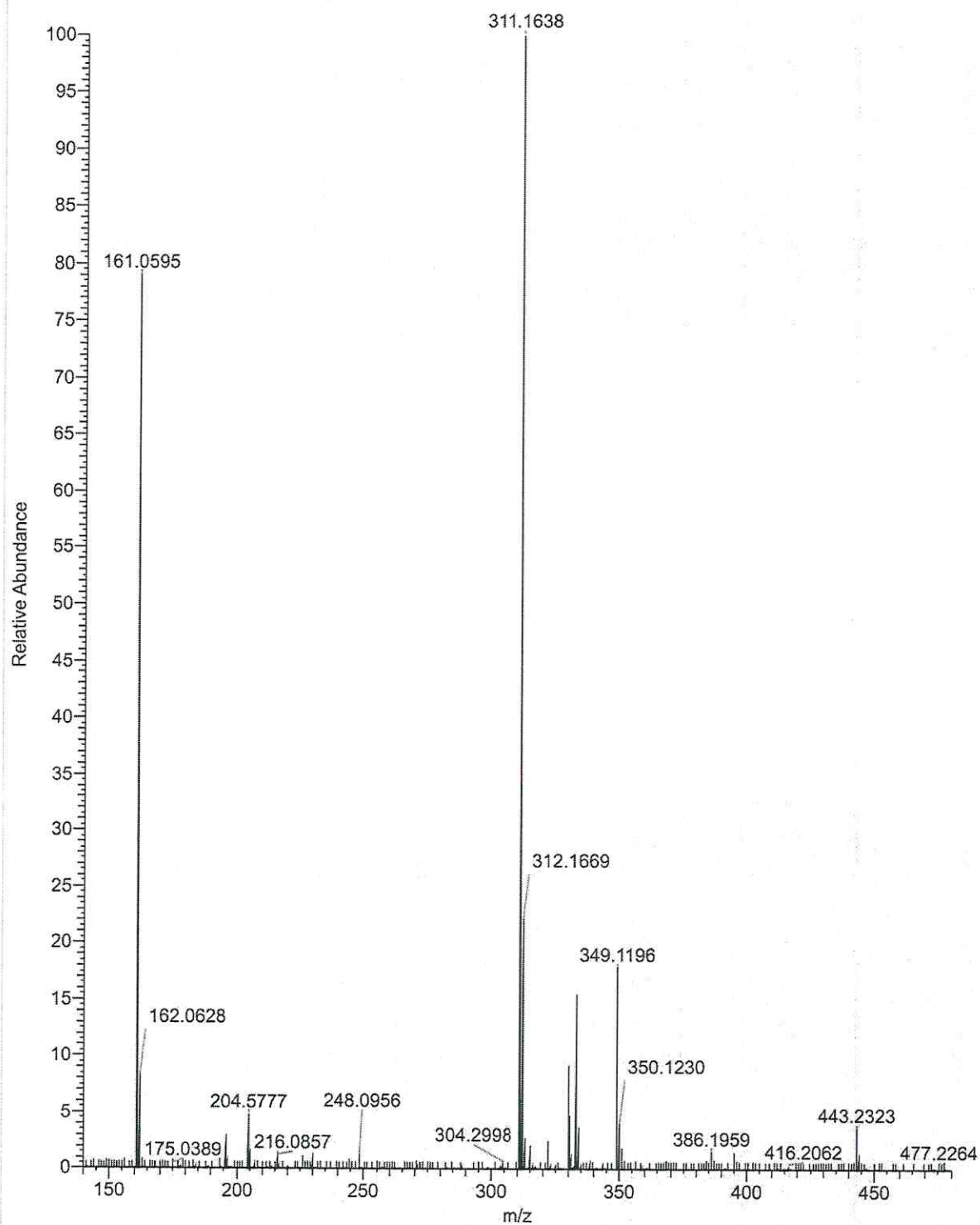


# DM7 (310.16)

D:\data\16. February 2022 Analyses\DM-infusion\DM-7-scan\_20220... 2/8/2022 10:57:22 AM

DM-7-scan\_202207042206 #13 RT: 0.16 AV: 1 NL: 2.10E+008

T: FTMS + p ESI Full ms [80.0000-500.0000]

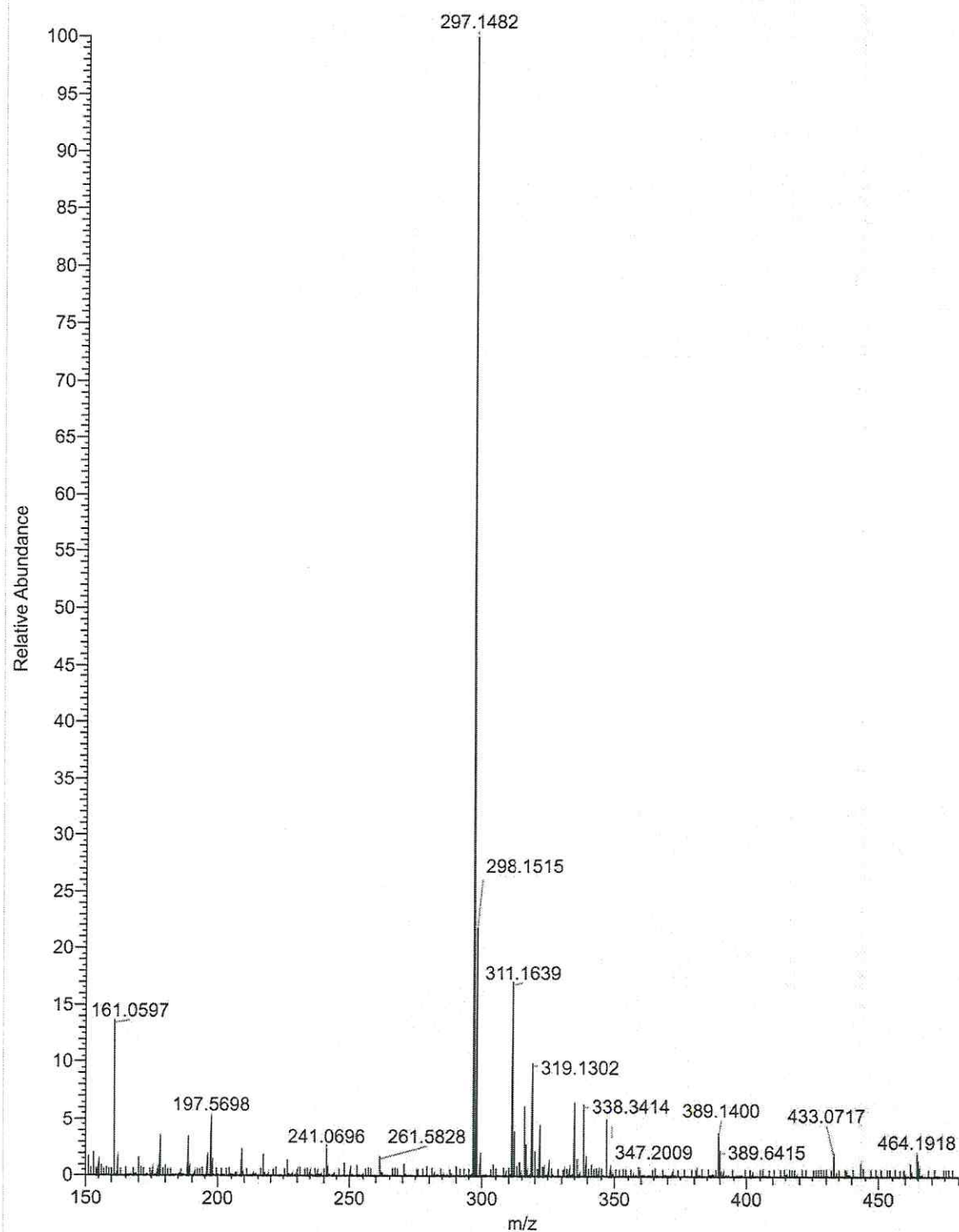


# DM8 (296.14)

D:\data\16. February 2022 Analyses\DM-infusion\DM-8-scan.raw 2/8/2022 10:58:32 AM

DM-8-scan #13 RT: 0.16 AV: 1 NL: 5.28E+007

T: FTMS + p ESI Full ms [80.0000-500.0000]

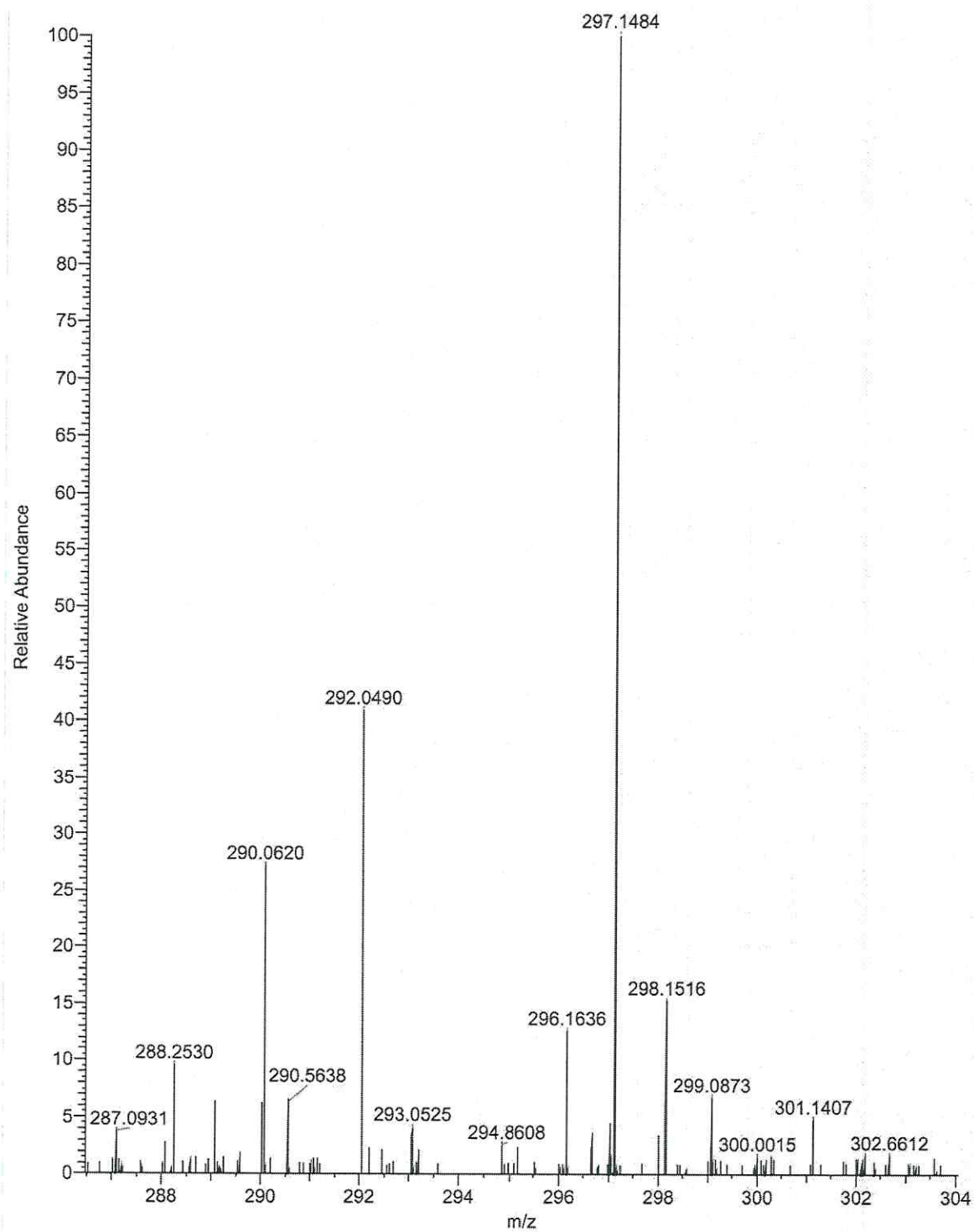


# DM9 (296.14)

D:\data\16. February 2022 Analyses\DM-infusion\DM-9-scan.raw 2/8/2022 11:02:35 AM

DM-9-scan #19-20 RT: 0.23-0.25 AV: 2 NL: 1.17E+006

T: MS

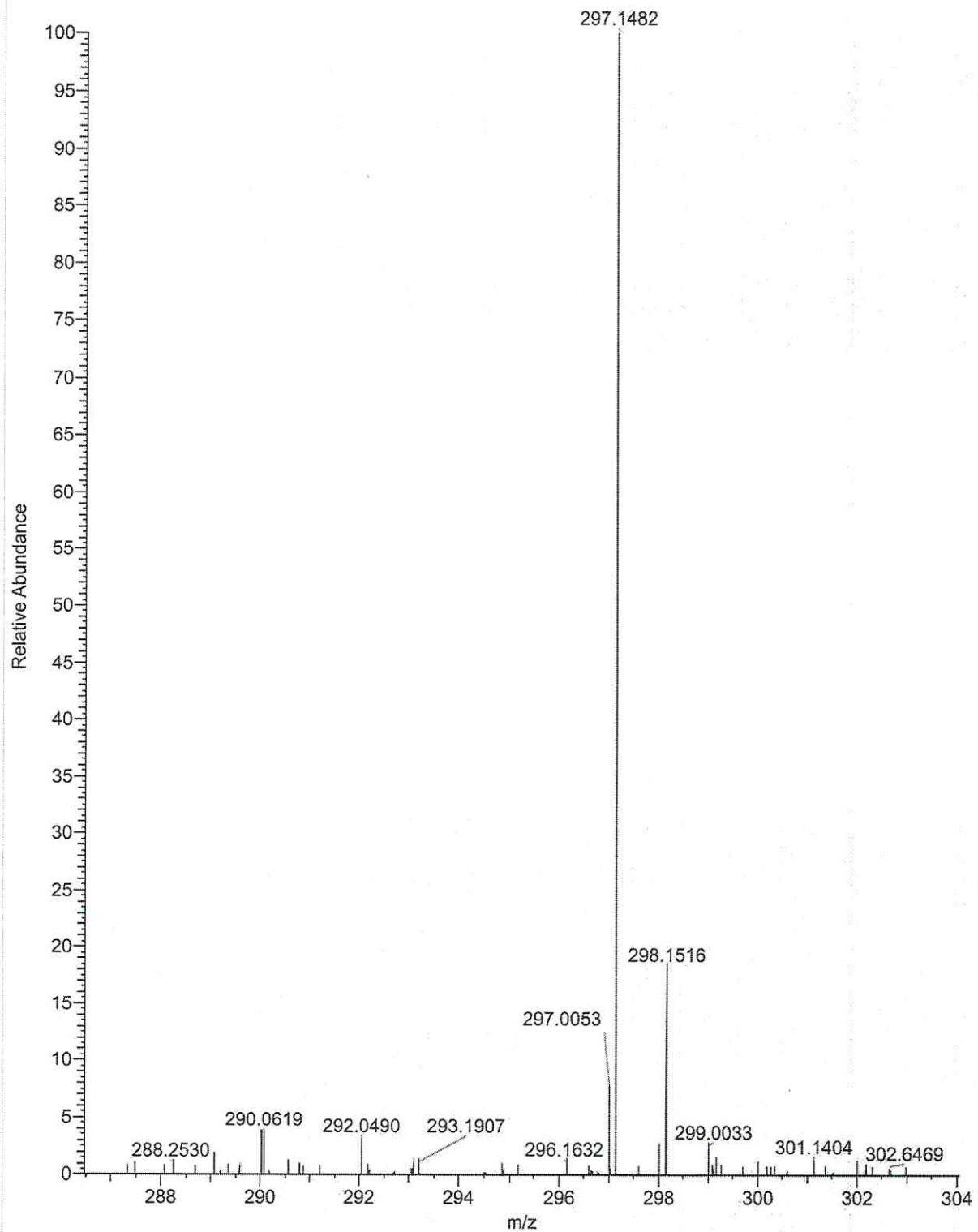


# DM10 (296.14)

D:\data\16. February 2022 Analyses\DM-infusion\DM-10-scan.raw 2/8/2022 11:03:04 AM

DM-10-scan #20 RT: 0.25 AV: 1 NL: 5.51E+006

T: FTMS + p ESI Full ms [80.0000-500.0000]





# DM11 (370.18)

D:\data\16. February 2022 Analyses\DM-infusion\DM-11-scan\_2022... 2/8/2022 11:03:55 AM

DM-11-scan\_20220207050537 #20 RT: 0.25 AV: 1 NL: 1.39E+008

T: FTMS + p ESI Full ms [80.0000-500.0000]

