

Supporting Information for:

Dual Nicotinic Acetylcholine Receptors $\alpha 4\beta 2$ Antagonists/ $\alpha 7$ Agonists: Synthesis, Docking Studies and Pharmacological Evaluation of Tetrahydroisoquinolines and Tetrahydroisoquinolinium Salts

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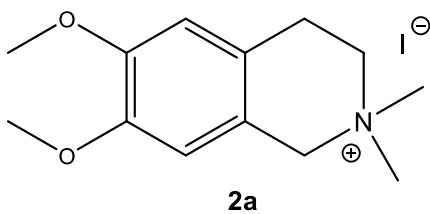
NMR spectra¹

S2

¹ Most of the NMR spectra are reprocessed in MestReNova software (version 10.0.2) from original FID's files.

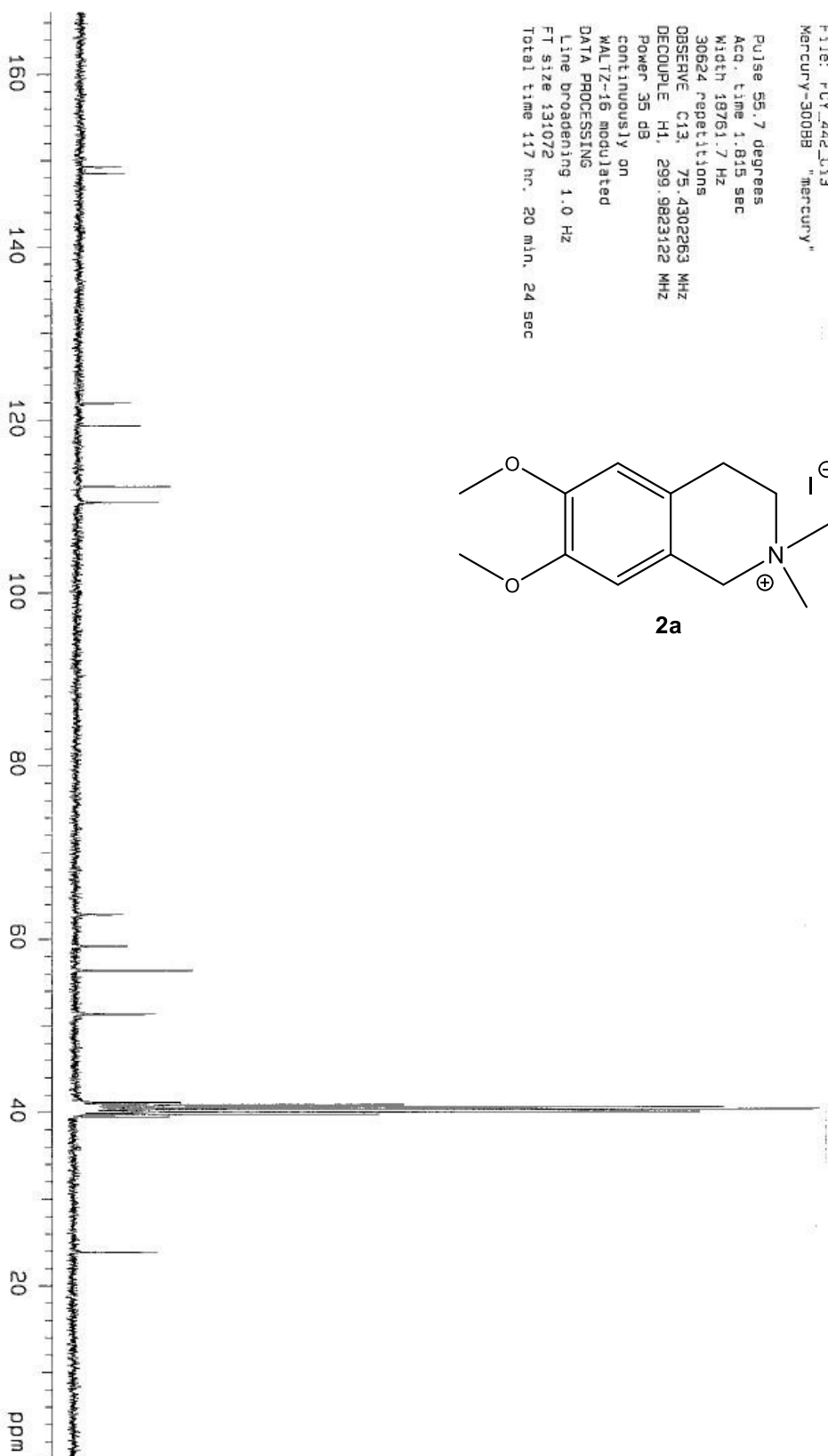
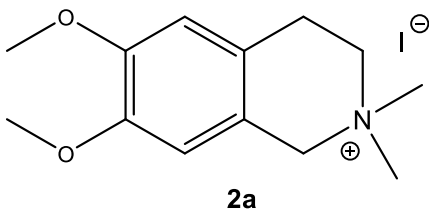
Pulse Sequence: zgpg30
Solvent: DMSO
Ambient temperature
File: FCY_442
Mercury-300BB "mercury"

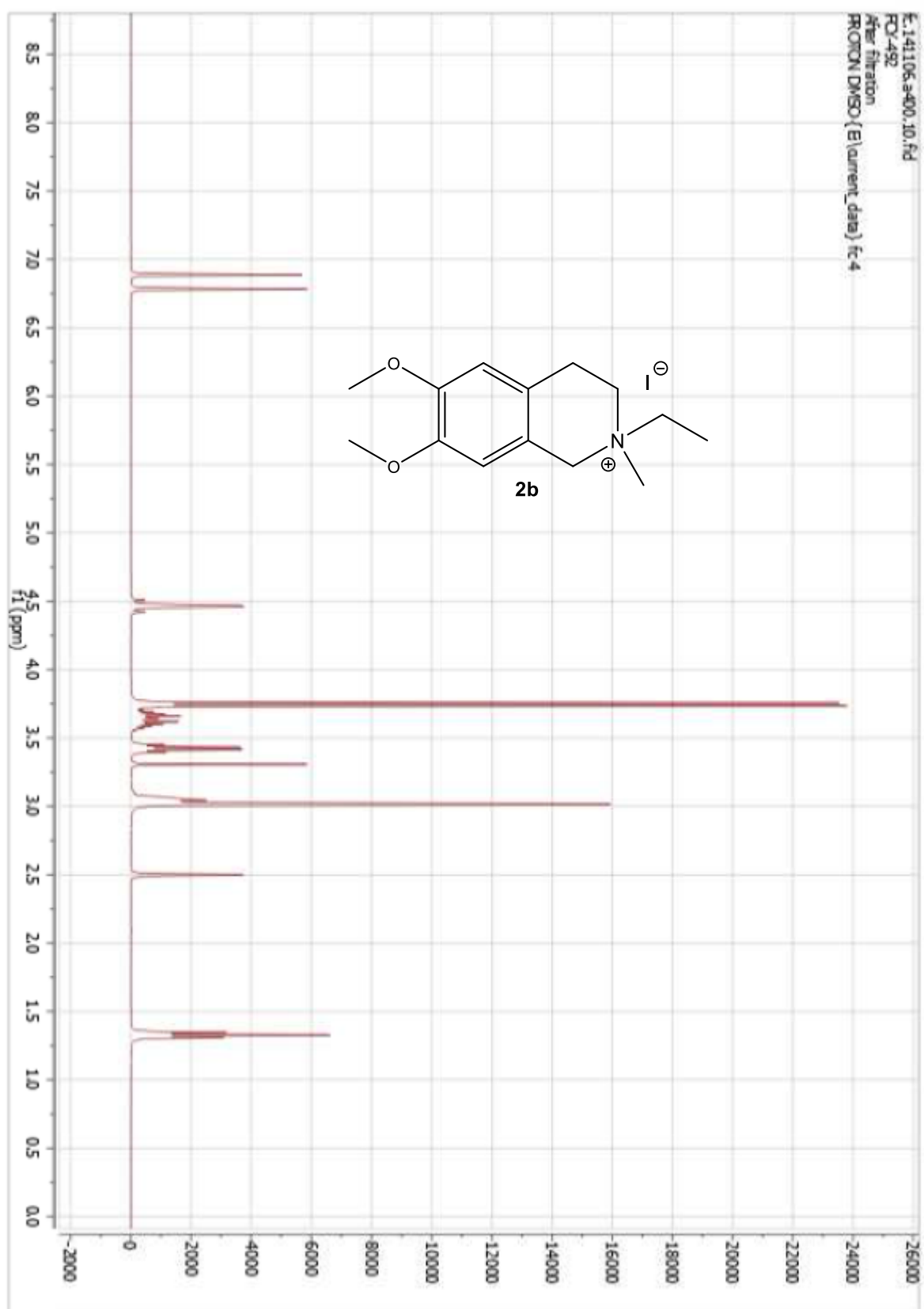
Relax. delay 1.000 sec
Pulse 71.6 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
8 repetitions
OBSERVE H1 299.9808484 MHz
DATA PROCESSING
F1 size 32768
Total time 0 min, 25 sec

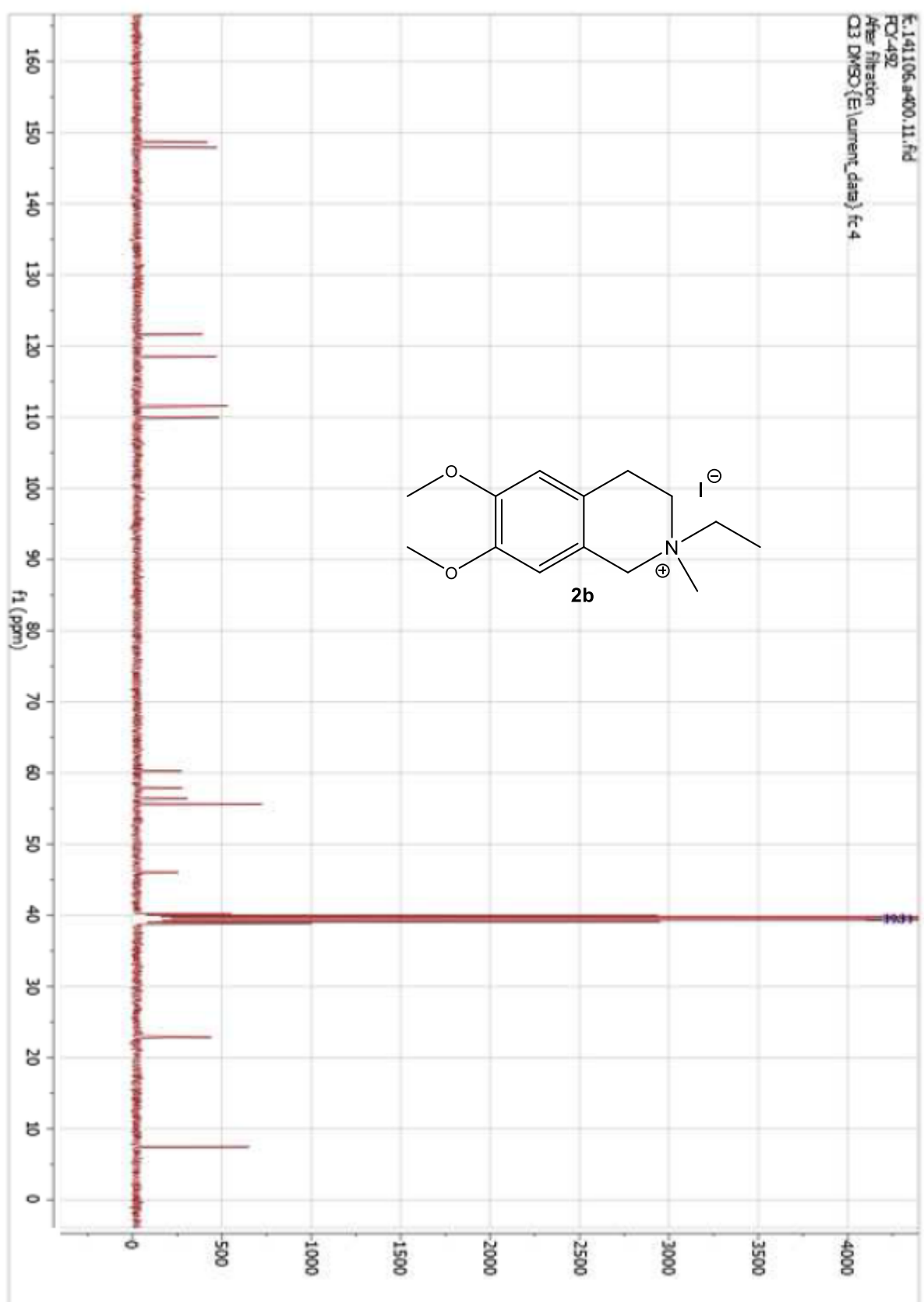


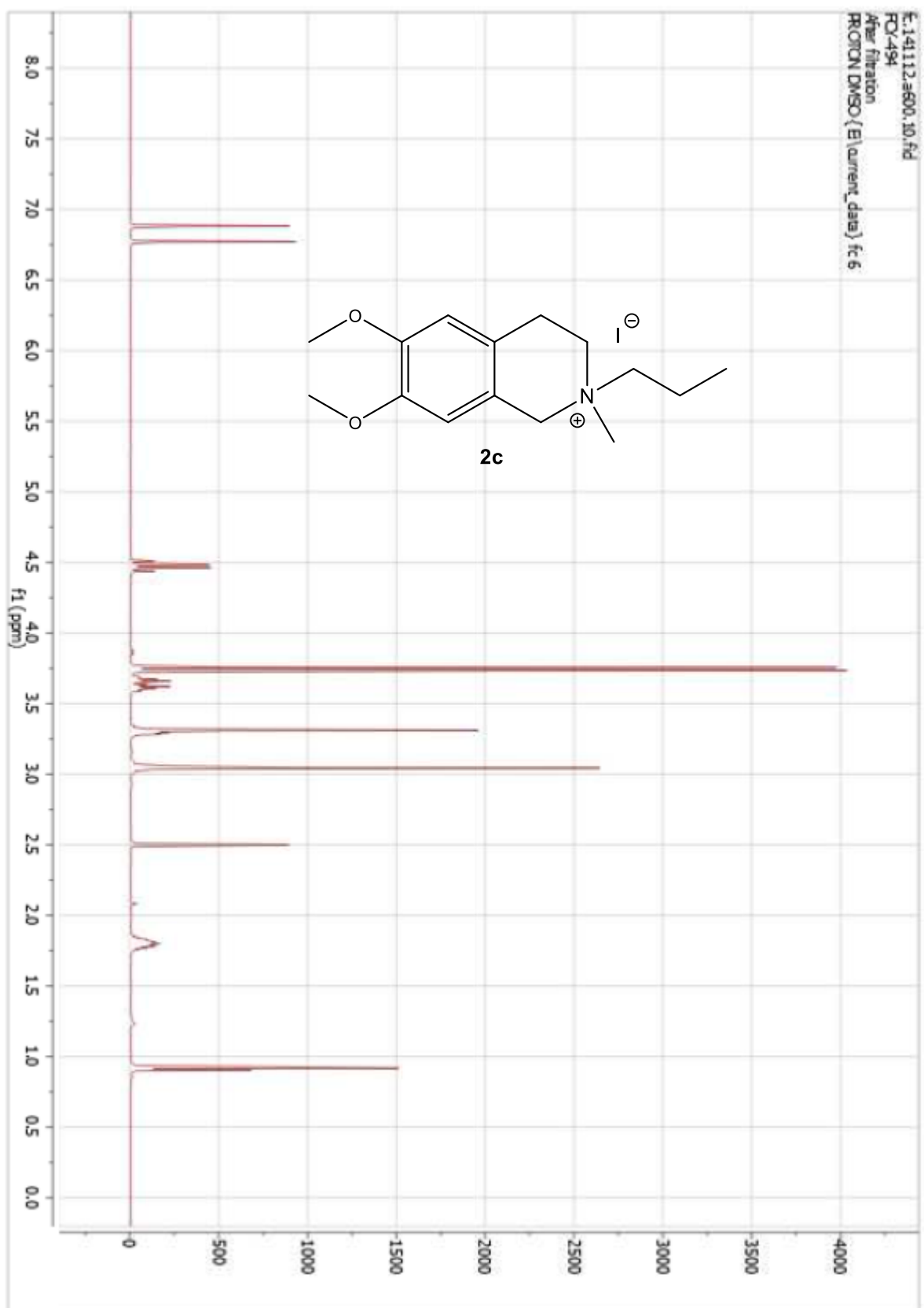
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 Solvent: DMSO
 Ambient temperature
 File: FCY_442_C13
 Mercury-300BB "Mercury"

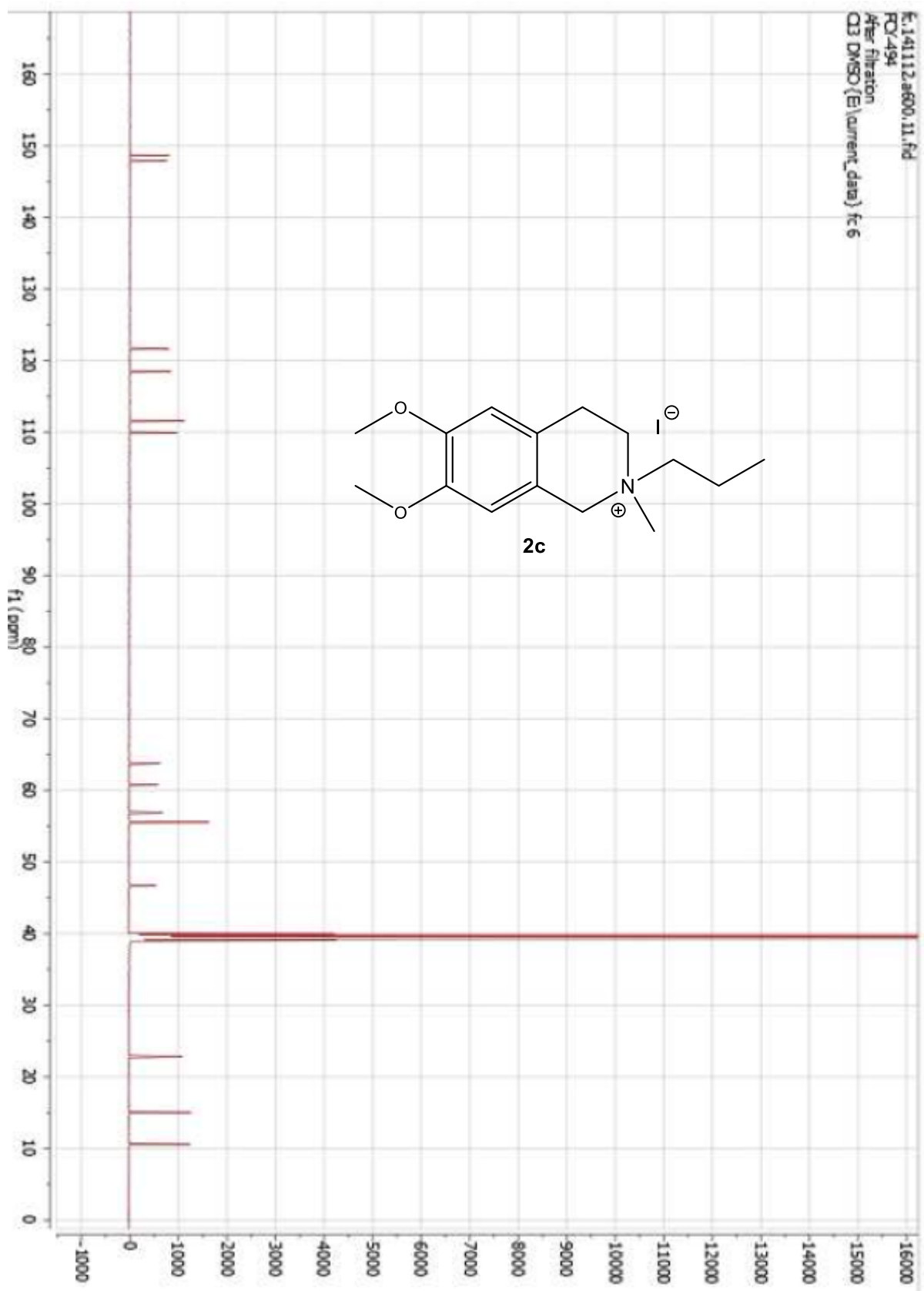
Pulse 55.7 degrees
 Acq. time 1.815 sec
 Width 18761.7 Hz
 30624 repetitions
 OBSERVE C13, 75.4302263 MHz
 DECOUPLE H1, 299.9823122 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 117 hr, 20 min, 24 sec

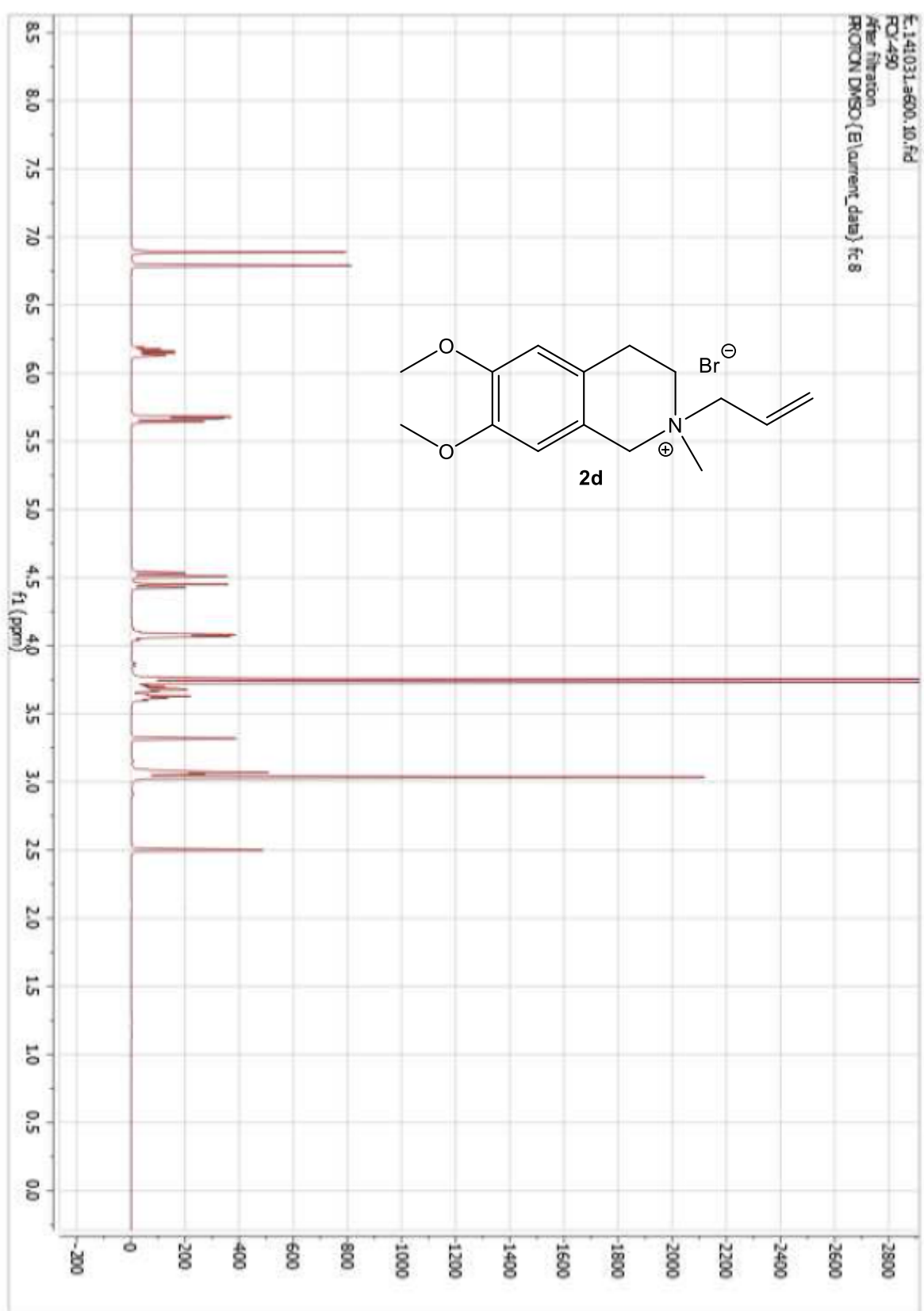


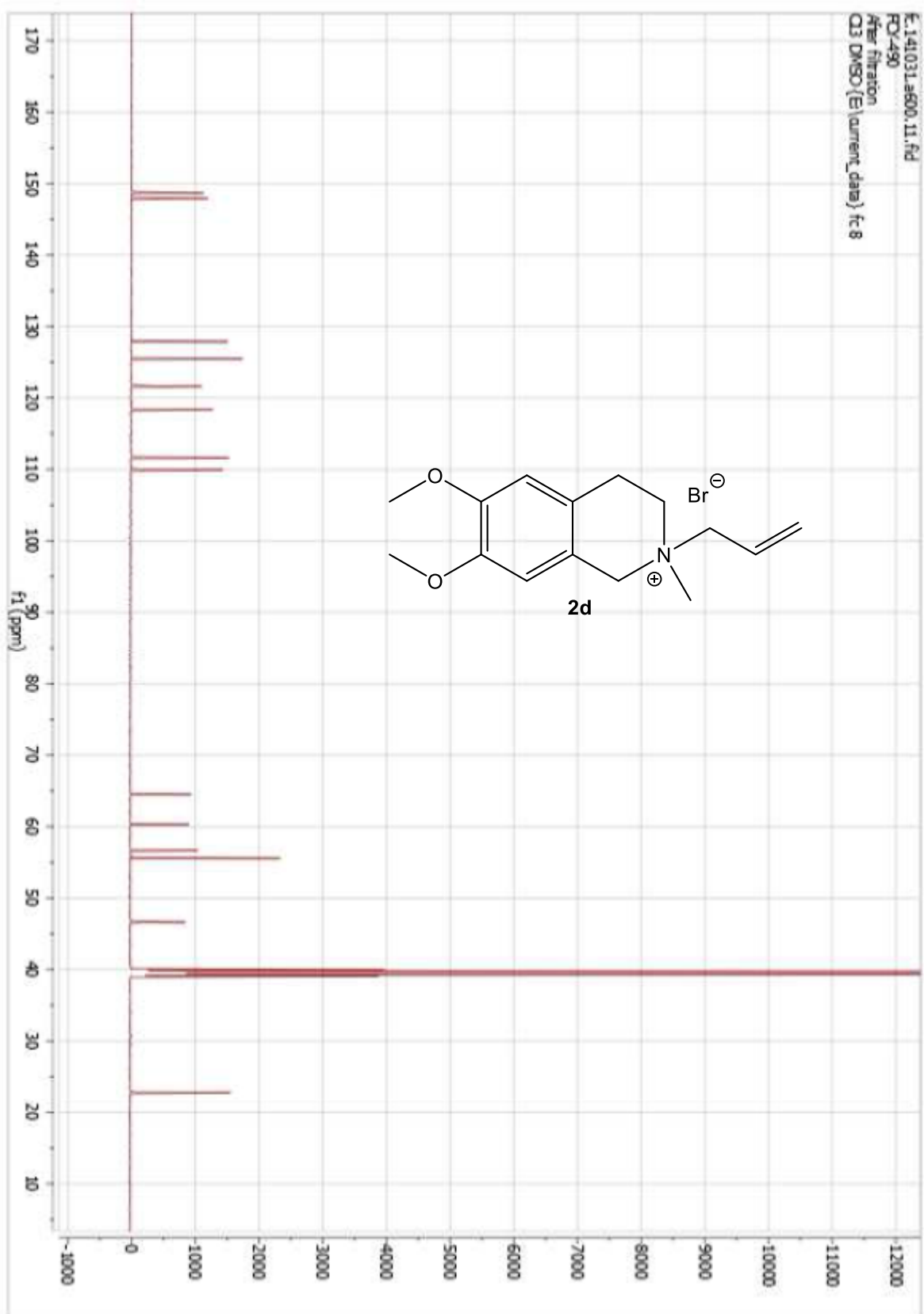


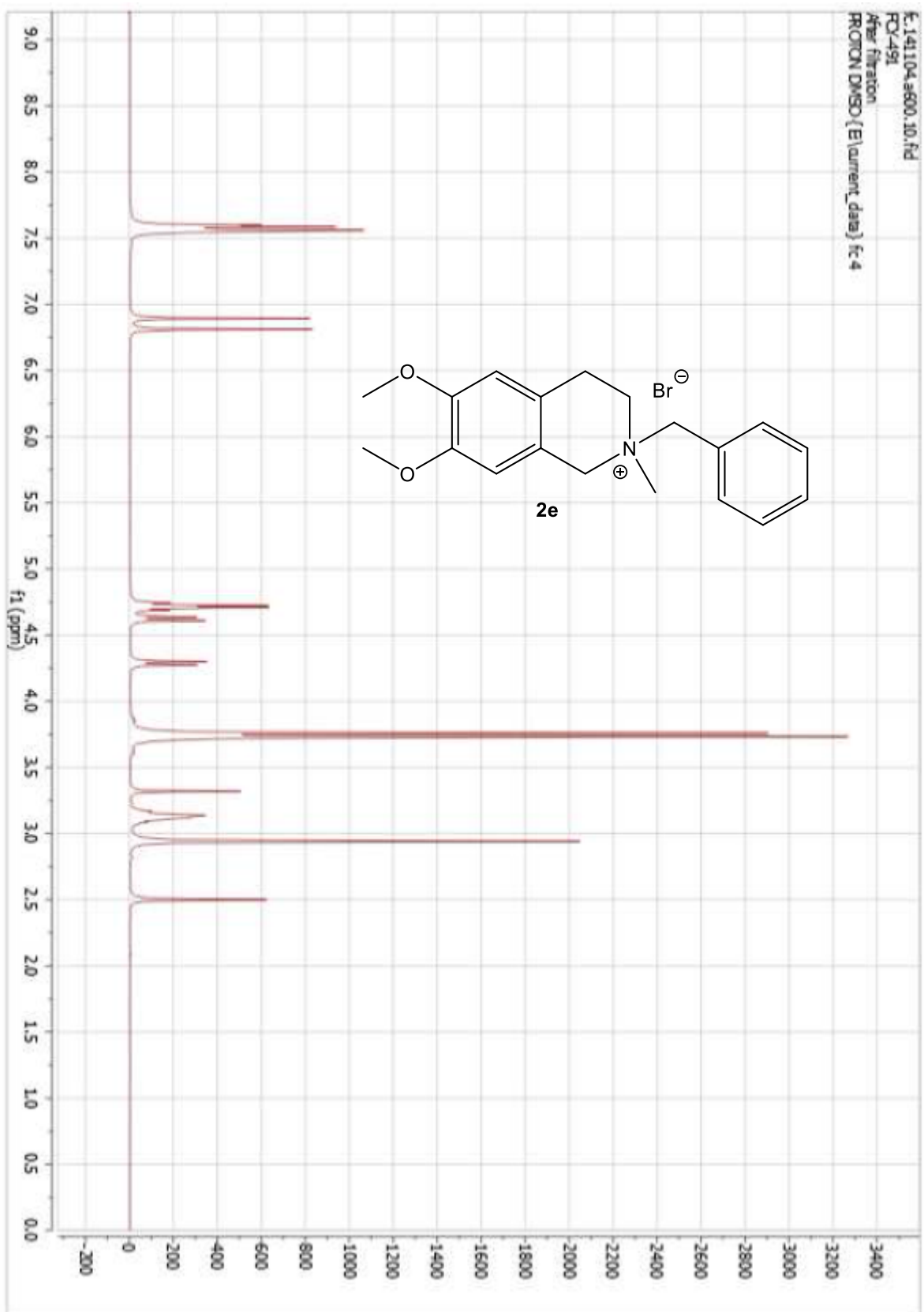


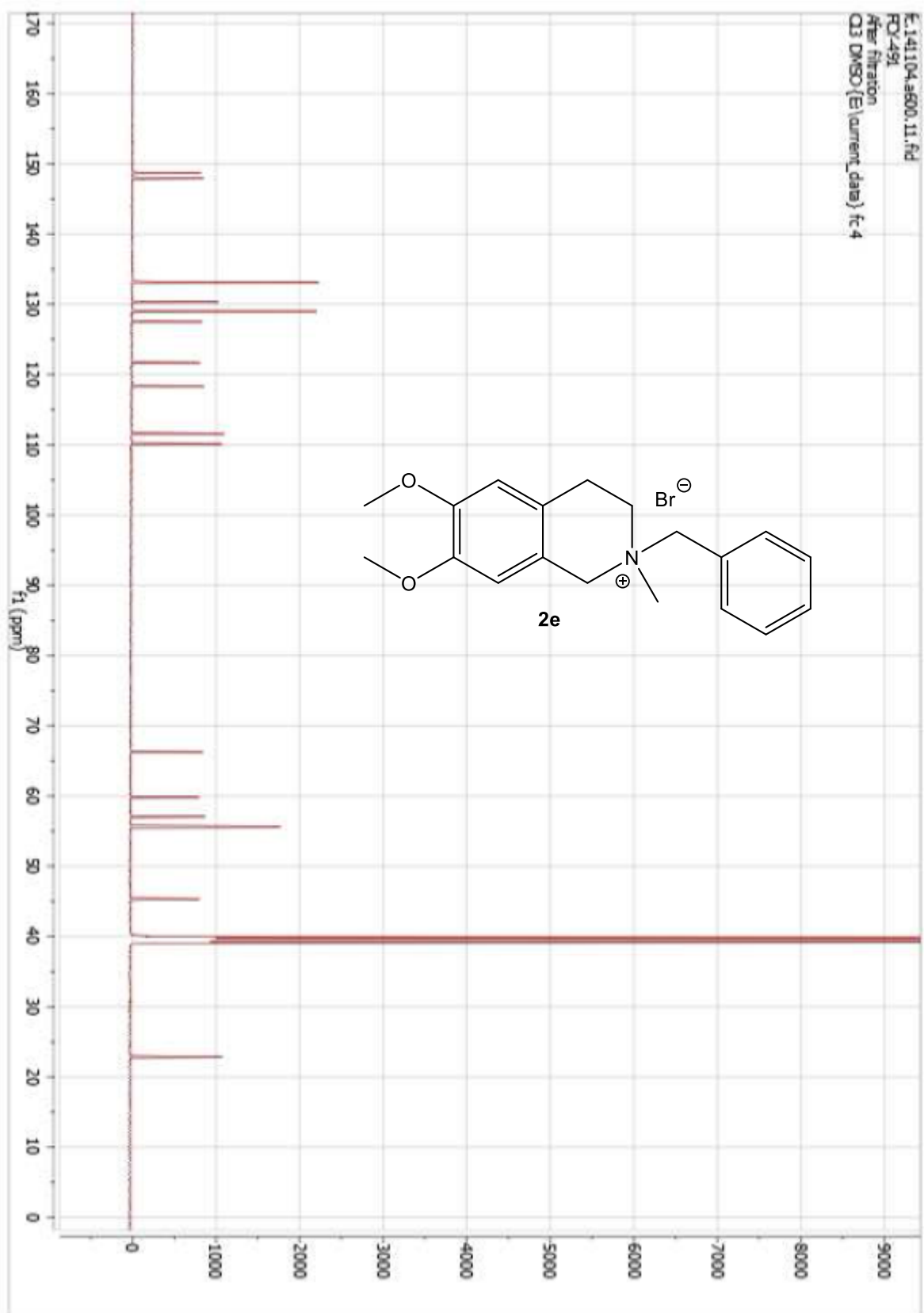






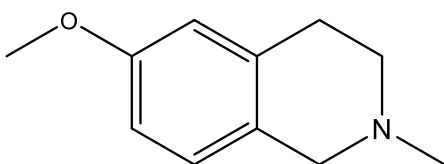




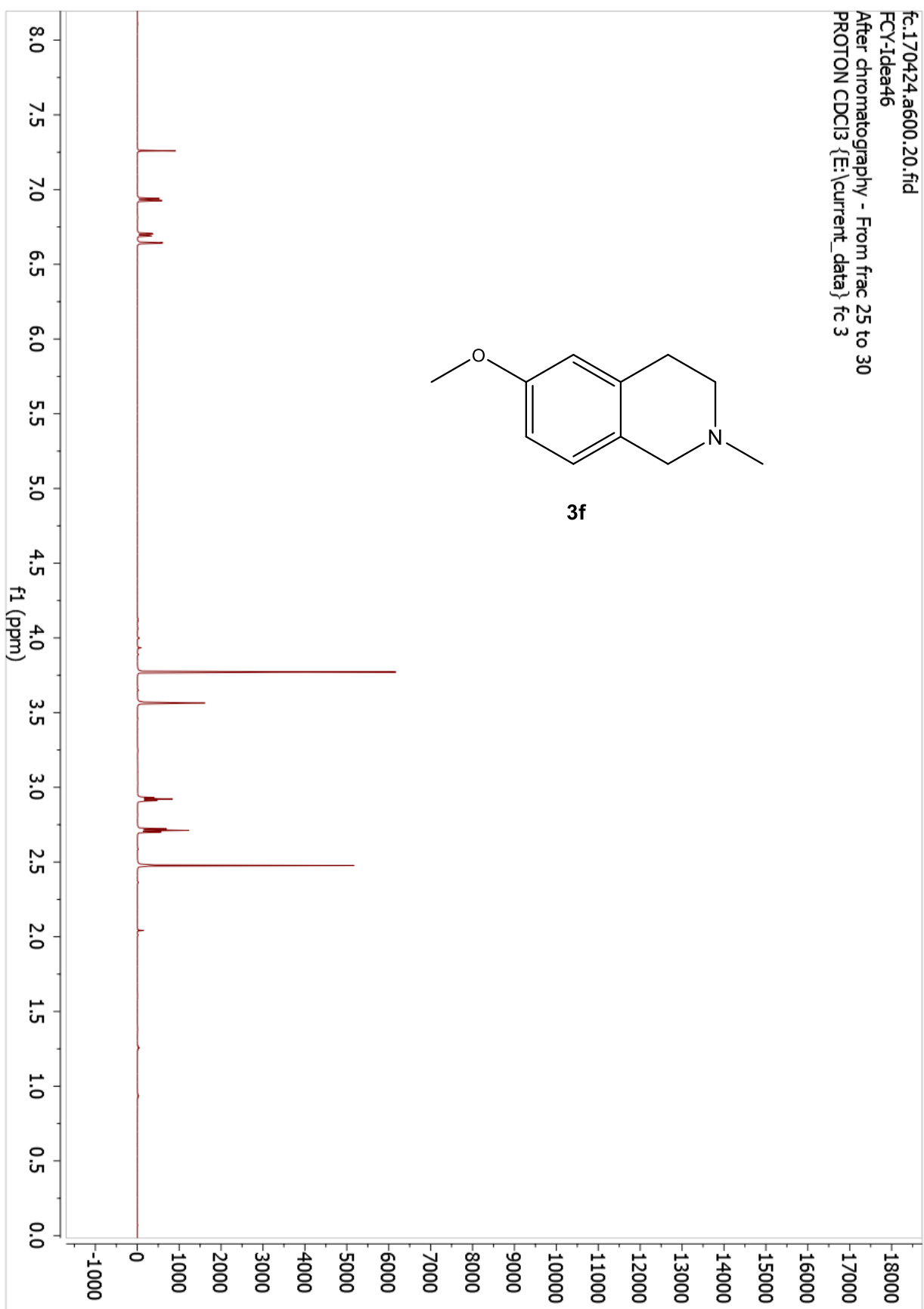


fc:170424.a600.20.fid
FCY-Idea46

After chromatography - From frac 25 to 30
PROTON CDCl3 {E:\current_data} fc 3



3f

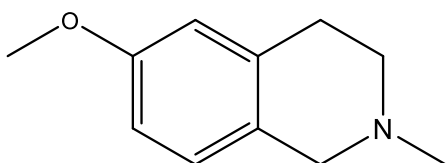


fc.170424.a600.21.fid

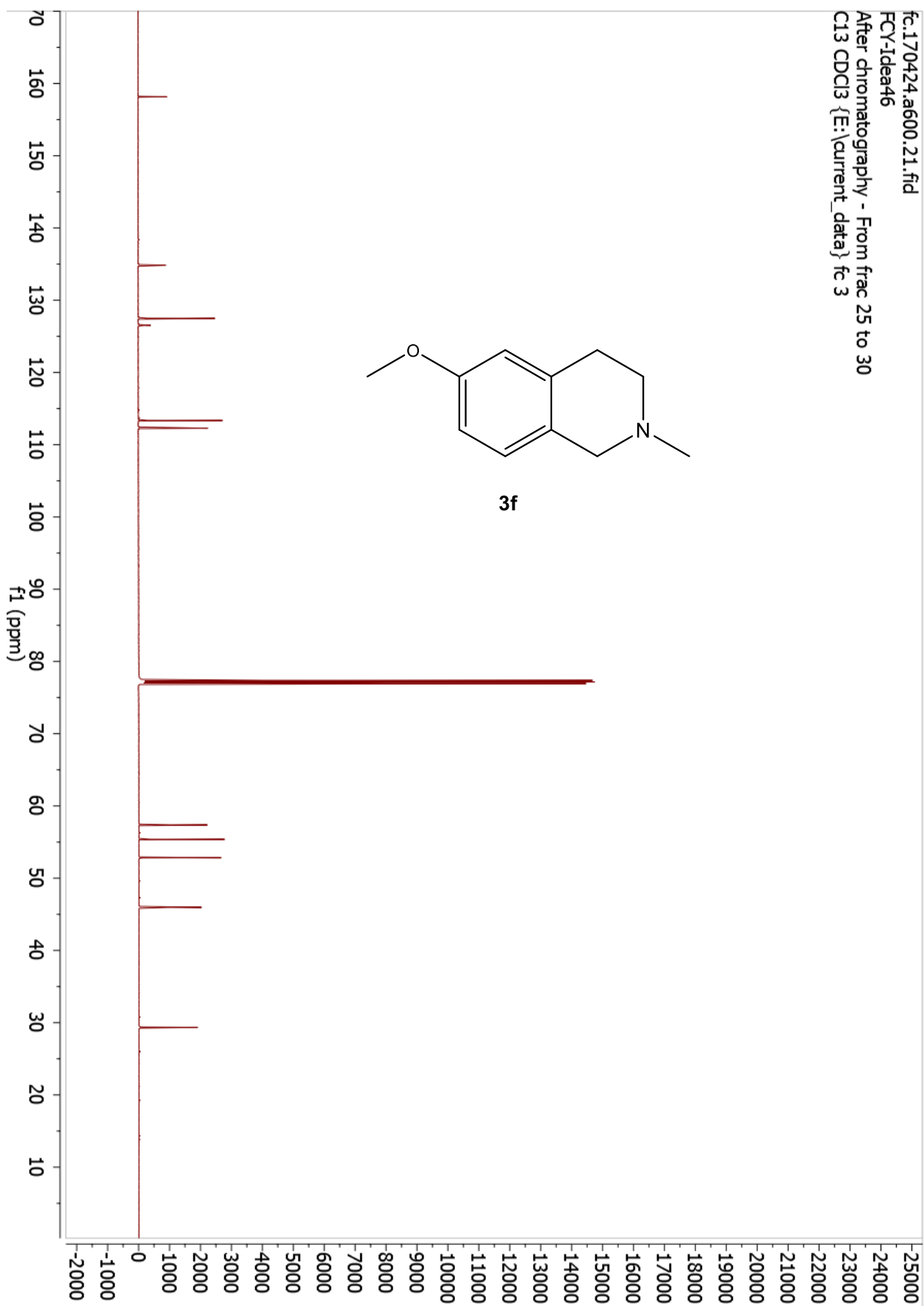
FCY-Idea46

After chromatography - From frac 25 to 30

C13 CDCl3 {E:\current_data} fc 3

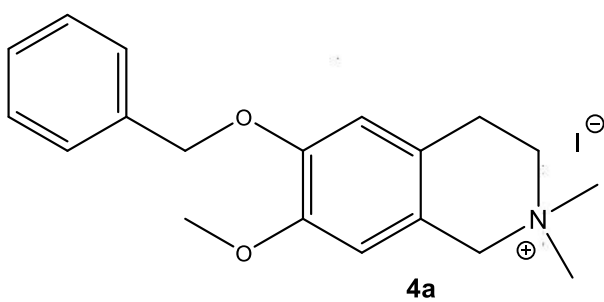


3f



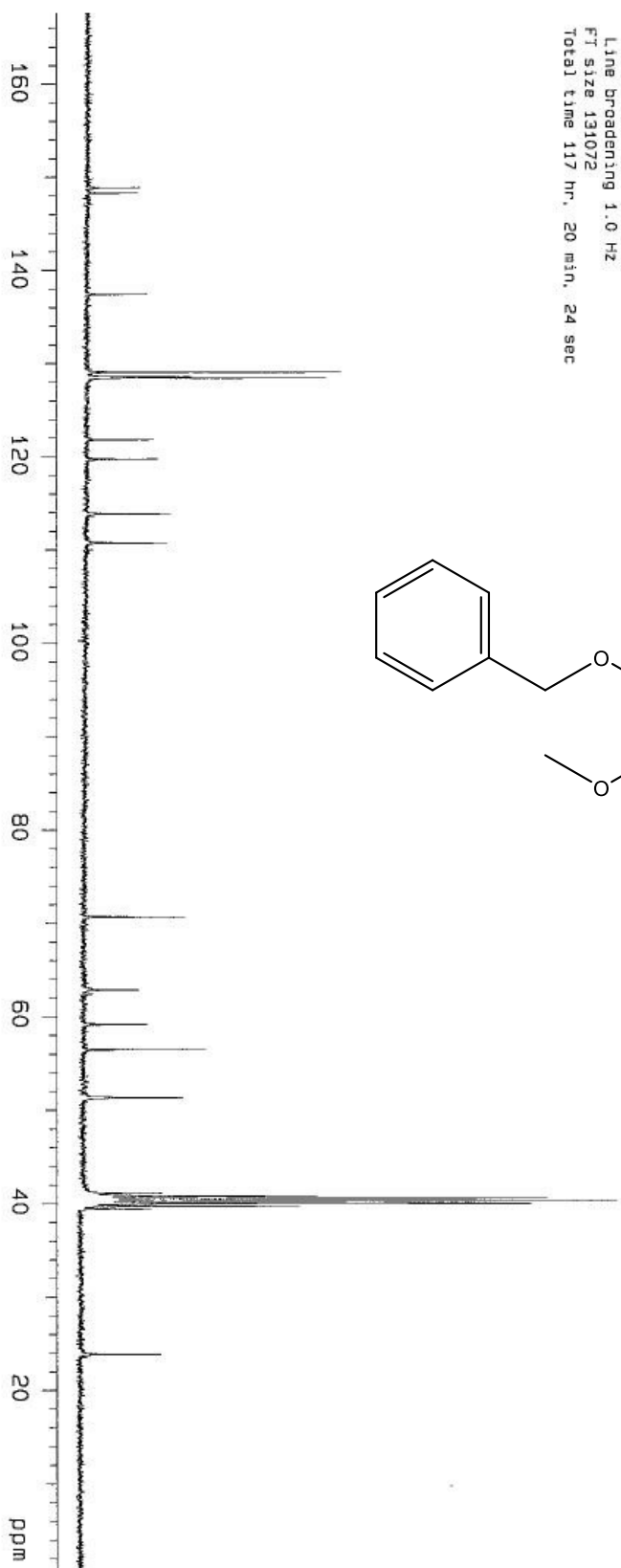
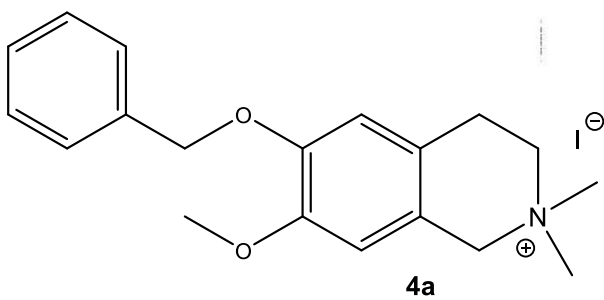
Pulse Sequence: s2pu1
 Solvent: DMSO
 Ambient temperature
 File: FCY_444
 Mercury-300BB "mercury"

Relax. delay 1.000 sec
 Pulse 71.6 degrees
 Acq. time 1.995 sec
 Width 4506.5 Hz
 6 repetitions
 OBSERVE H1 299.9808484 MHz
 DATA PROCESSING
 FT size 32768
 Total time 0 min, 19 sec



Pulse Sequence: s2pu1
 Solvent: DMSO
 Ambient temperature
 File: FCY_44a_C13
 Mercury-300BB "mercury"

Pulse 55.7 degrees
 Acq. time 1.815 sec
 Width 18761.7 Hz
 49696 repetitions
 OBSERVE C13, 75.4302263 MHz
 DECOUPLE H1, 299.9823122 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 F1 size 131072
 Total time 117 hr, 20 min, 24 sec



Pulse Sequence: zgpg30

Solvent: CDCl₃

Ambient temperature

File: F01_223_1year

Mercury-300088 "mercury"

Relax. delay 1.000 sec

Pulse 71.6 degrees

Acq. time 1.995 sec

Width 4506.5 Hz

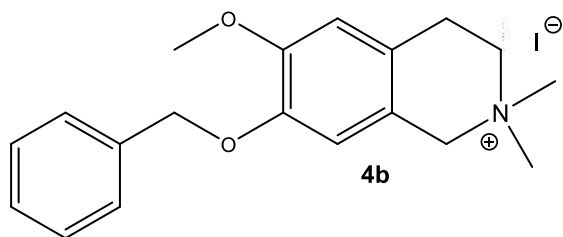
6 repetitions

OBSERVE: H1, 299.9794235 MHz

DATA PROCESSING

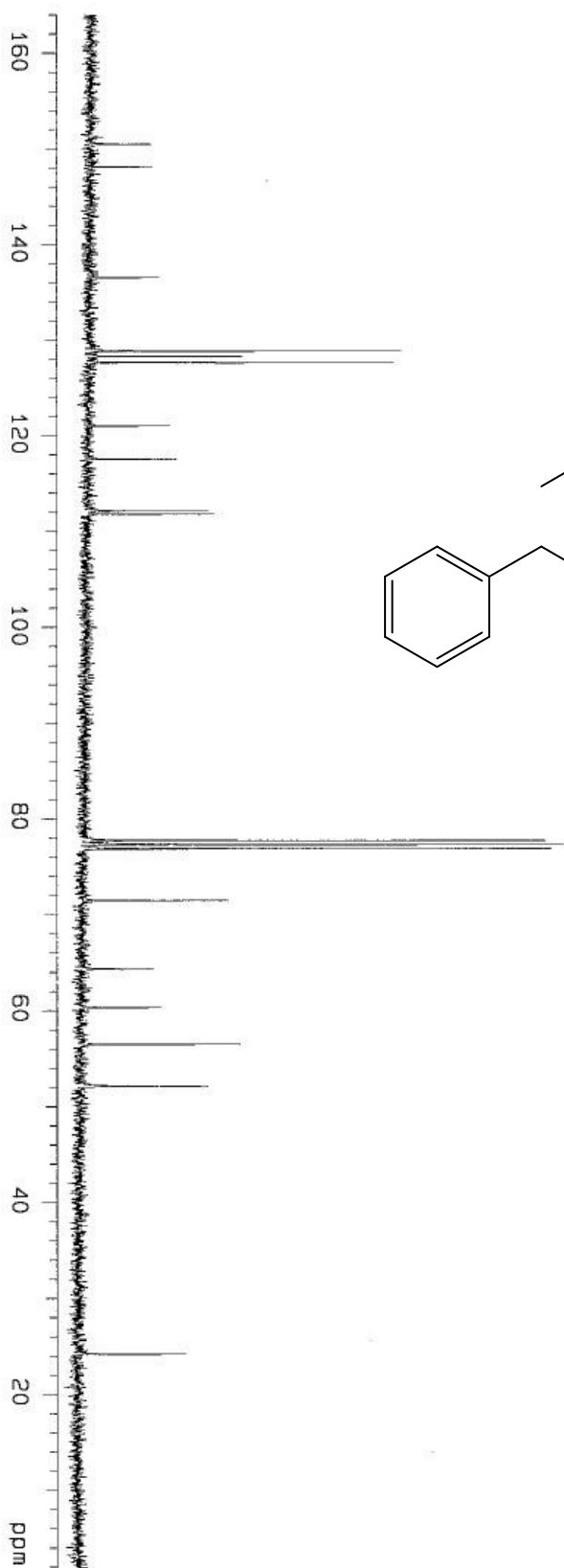
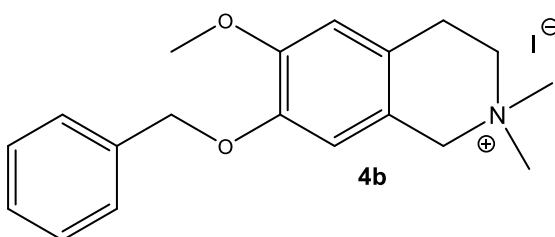
FT size 32768

Total time 0 min, 19 sec



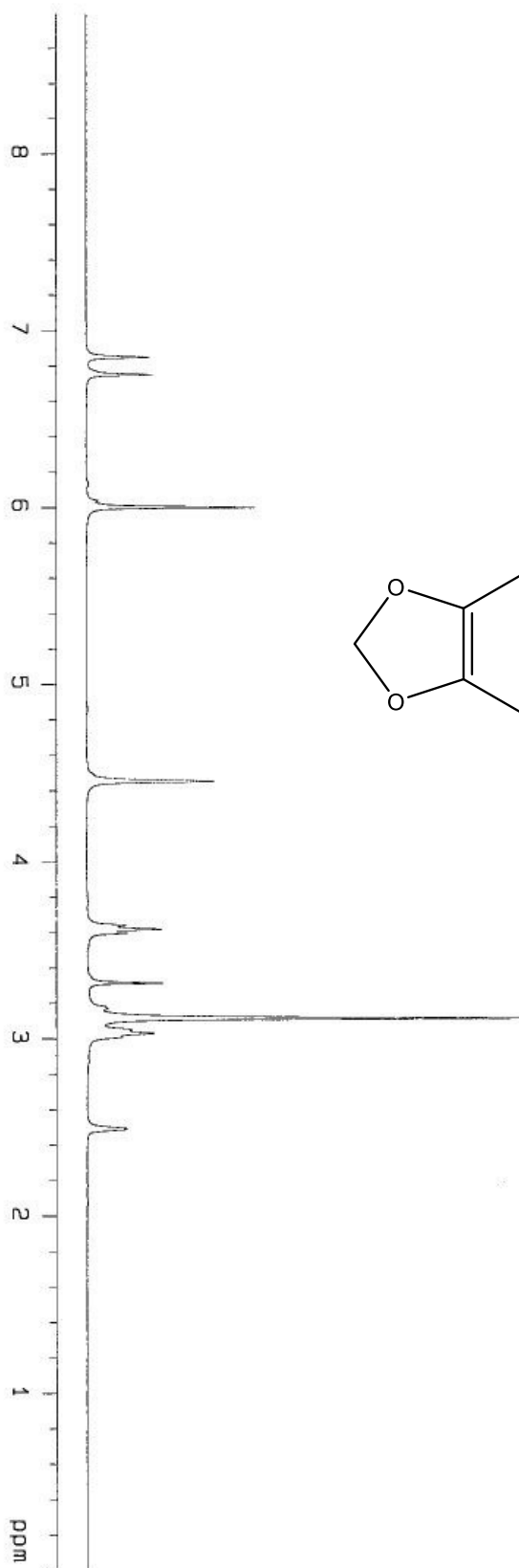
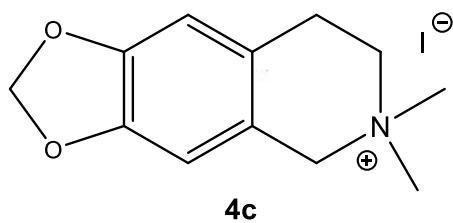
Pulse Sequence: zgpg30
 Solvent: CDCl₃
 Ambient temperature
 File: FCY_223_C13
 Mercury-30086 "mercury"

Pulse 55.7 degrees
 Acq. time 1.815 sec
 Width 18761.7 Hz
 28960 repetitions
 OBSERVE C13, 75.4296680 MHz
 DECOUPLE H1, 299.9808673 MHz
 Power 35 dB
 Continuously on
 MALTZ-15 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 117 hr, 20 min, 24 sec



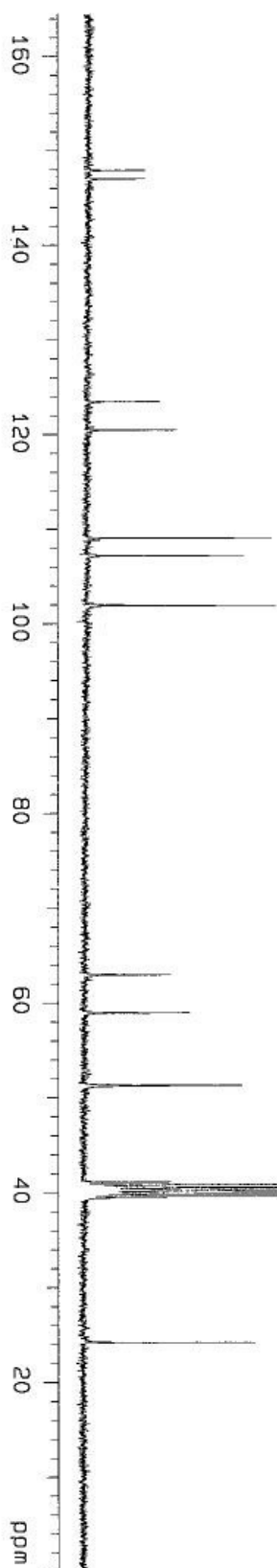
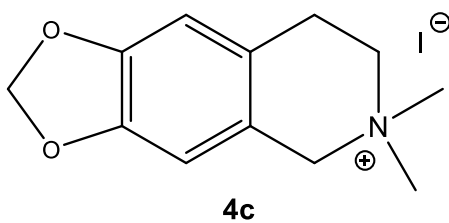
Pulse Sequence: s2pu1
 Solvent: DMSO
 Ambient temperature
 File: FCY_443
 Mercury-300BB "mercury"

Relax. delay 1.000 sec
 Pulse 71.6 degrees
 Acq. time 1.995 sec
 Width 4506.5 Hz
 6 repetitions
 OBSERVE H1 299.9808484 MHz
 DATA PROCESSING
 FI size 32768
 Total time 0 min, 19 sec



Pulse Sequence: zgpg30
 Solvent: DMSO
 Ambient temperature
 File: FCI_443_C13
 Mercury-300088 "mercury"

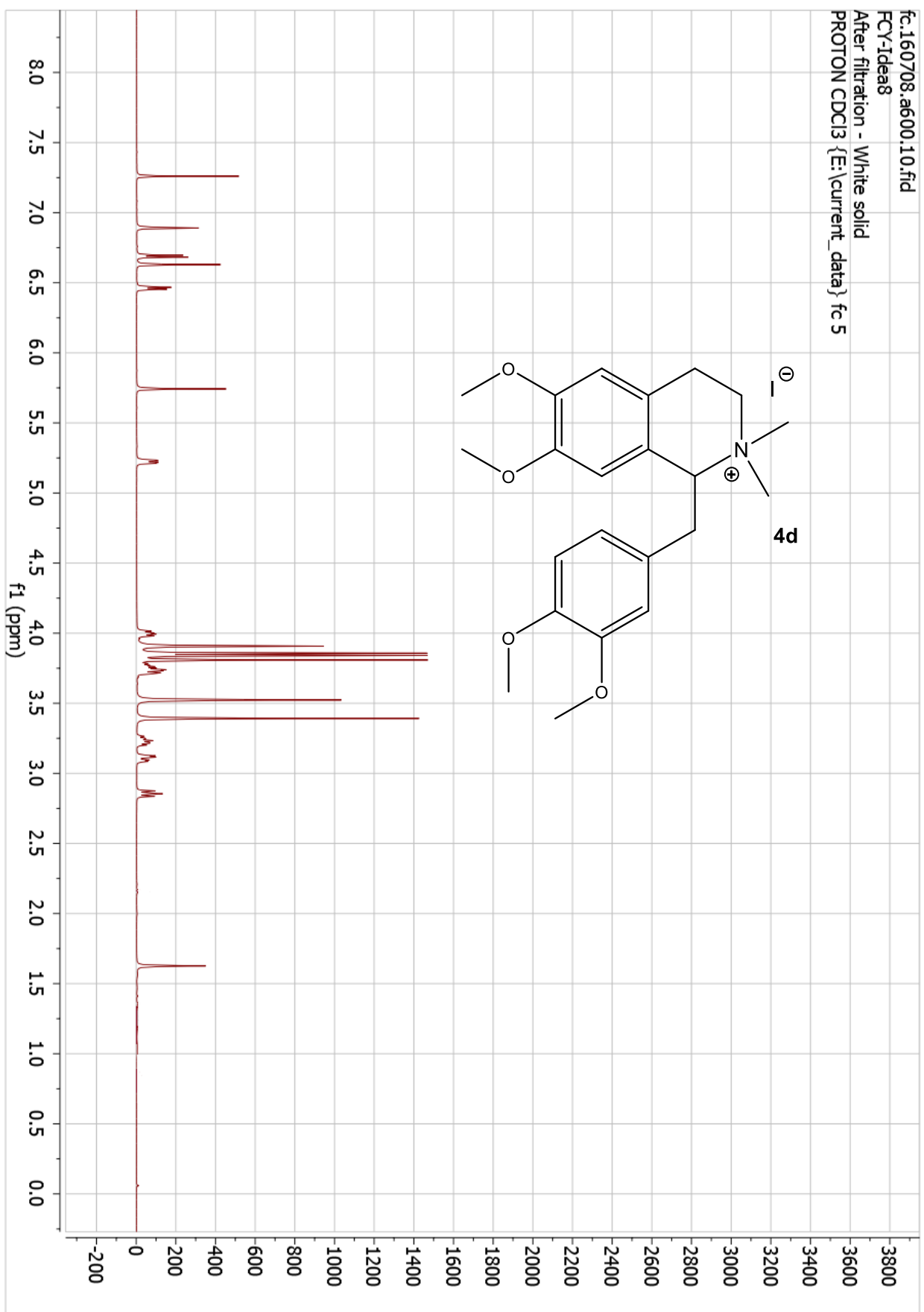
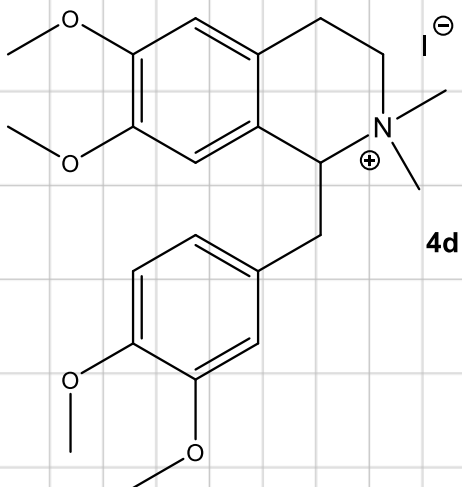
Pulse 55.7 degrees
 Acq. time 1.815 sec
 Width 18761.7 Hz
 38128 repetitions
 OBSERVE C13, 75.4302263 MHz
 DECOUPLE H1, 299.9823122 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 F1 size 131072
 Total time 117 hr, 20 min, 24 sec

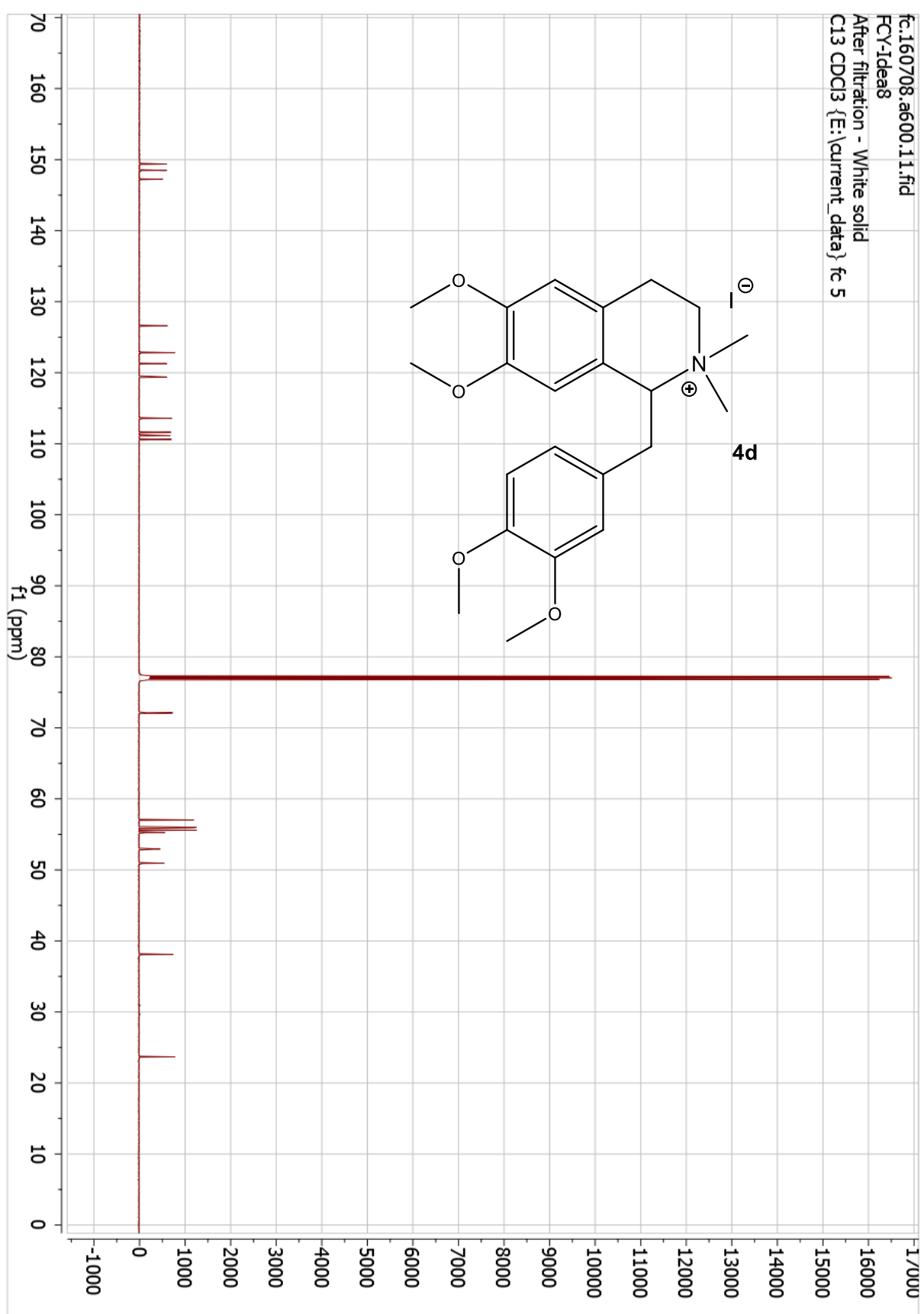


fc:160708.a600.10.fid
FCY-Idea8

After filtration - White solid

PROTON CDCl3 {E:\current_data} fc 5



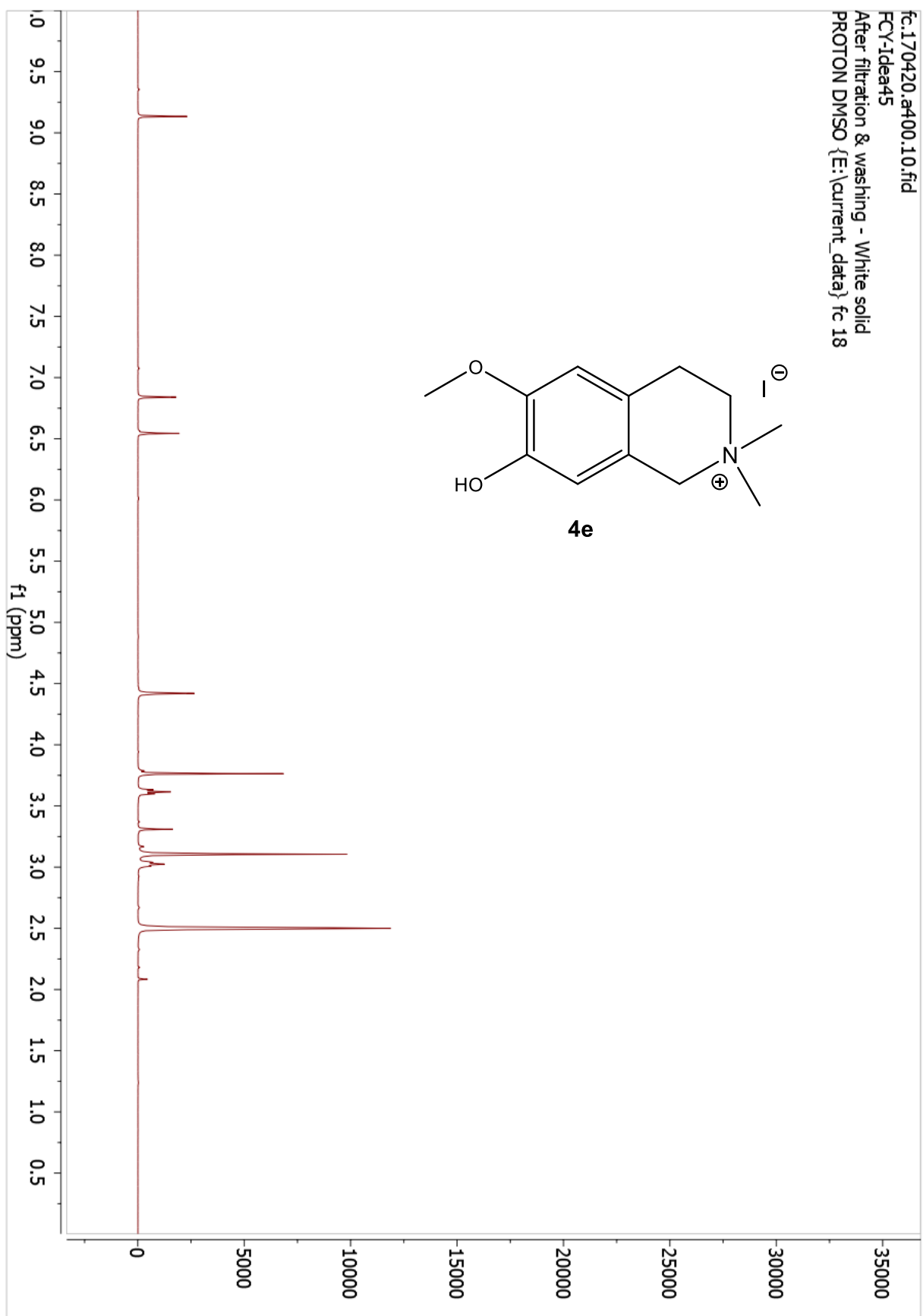
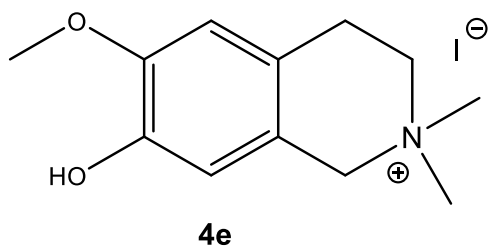


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FCY-Idea45

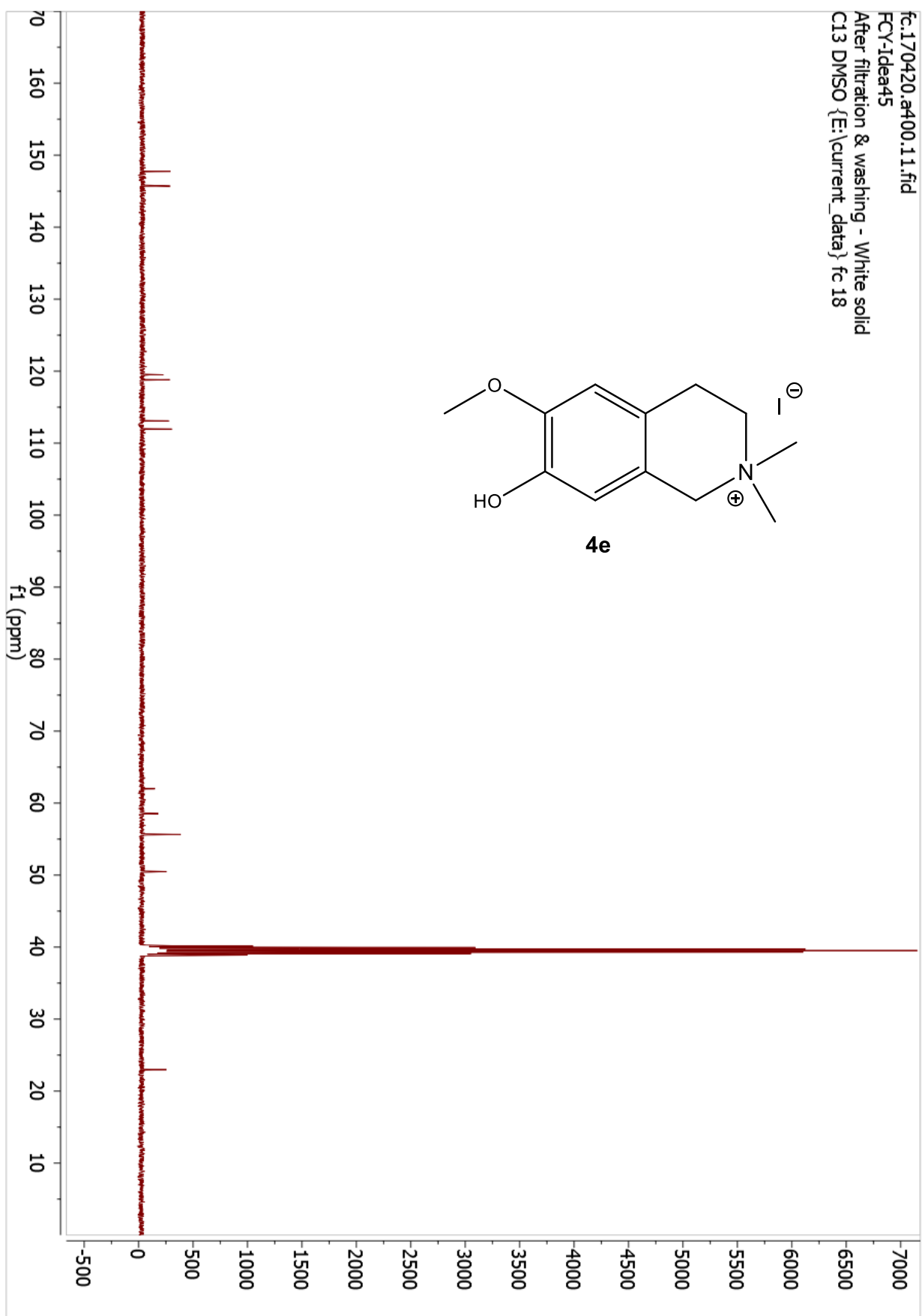
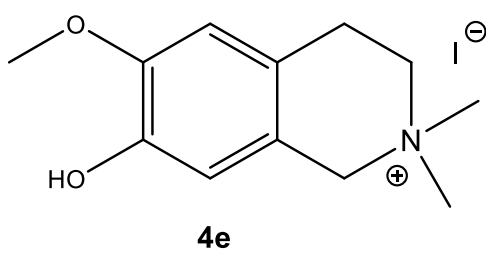
After filtration & washing - White solid

PROTON DMSO {E:\current_data} fc 18



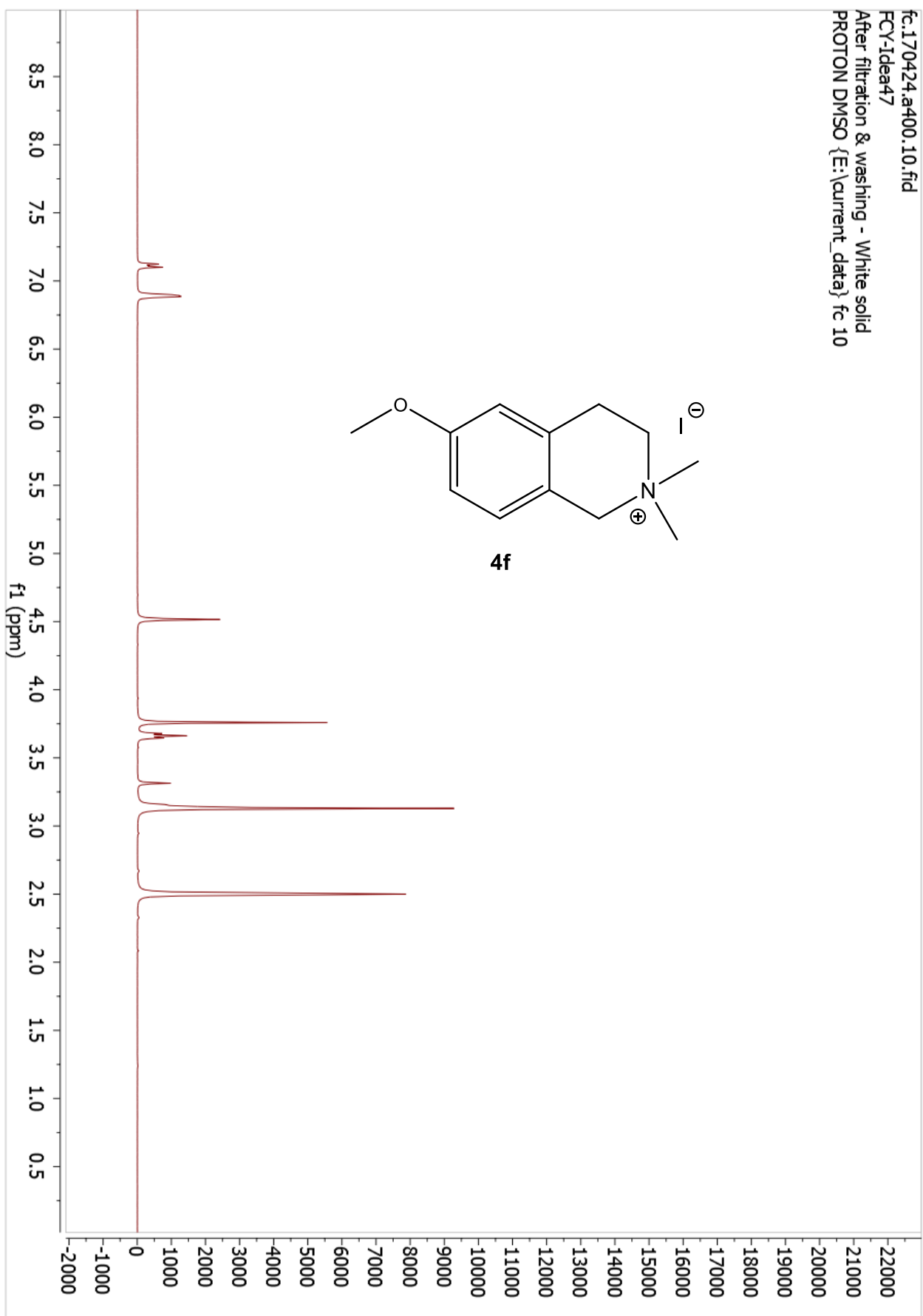
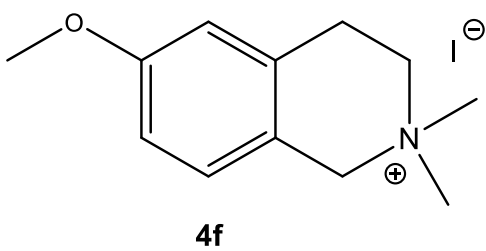
fc.170420.a400.1.fid
FCV-Idea45

After filtration & washing - White solid
C13 DMSO {E:\current_data} fc 18



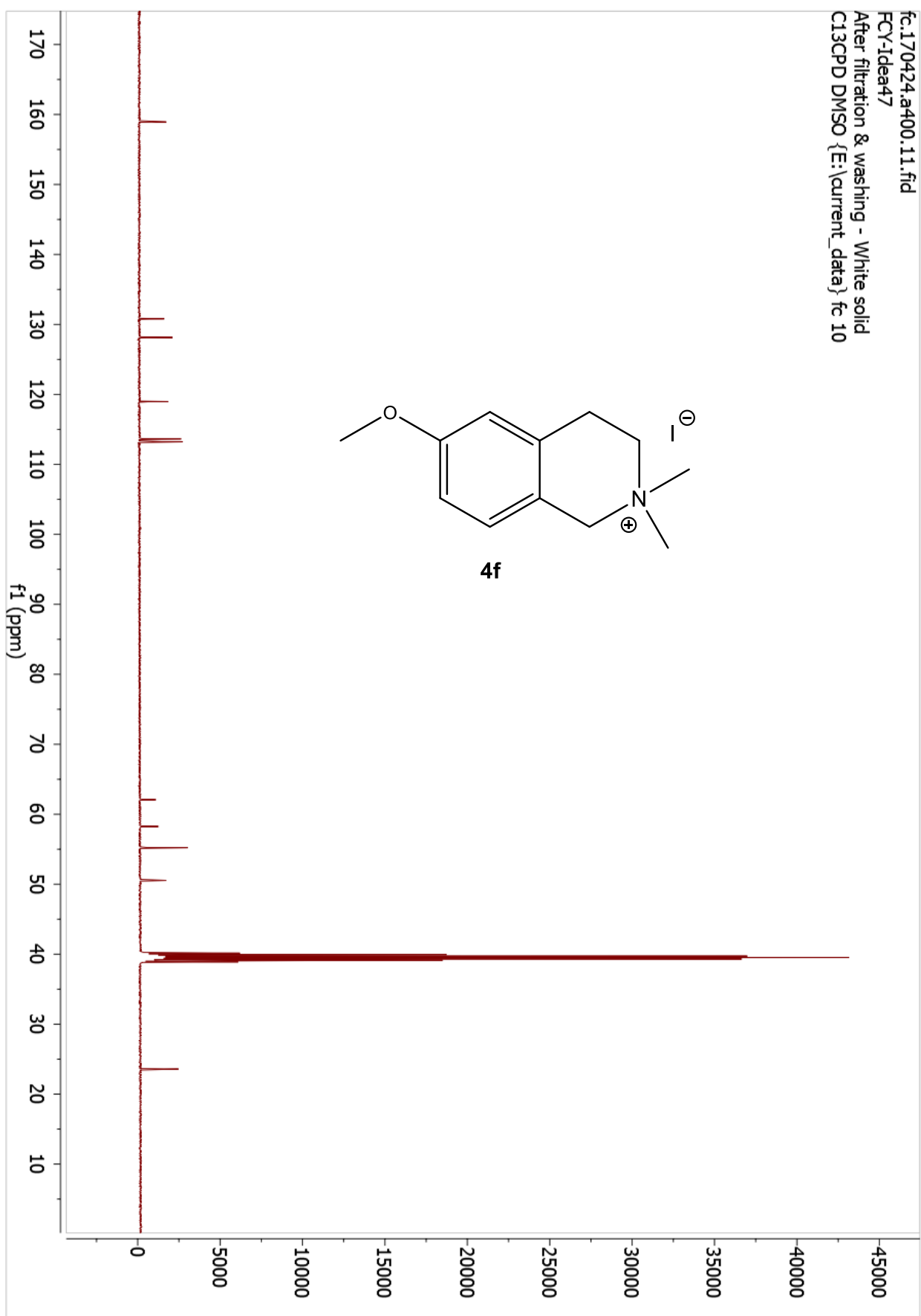
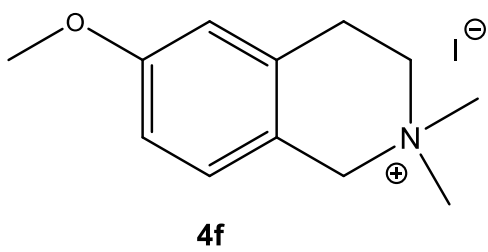
fc.170424.a400.10.fid
FCY-idea47

After filtration & washing - White solid
PROTON DMSO {E:\current_data} fc 10

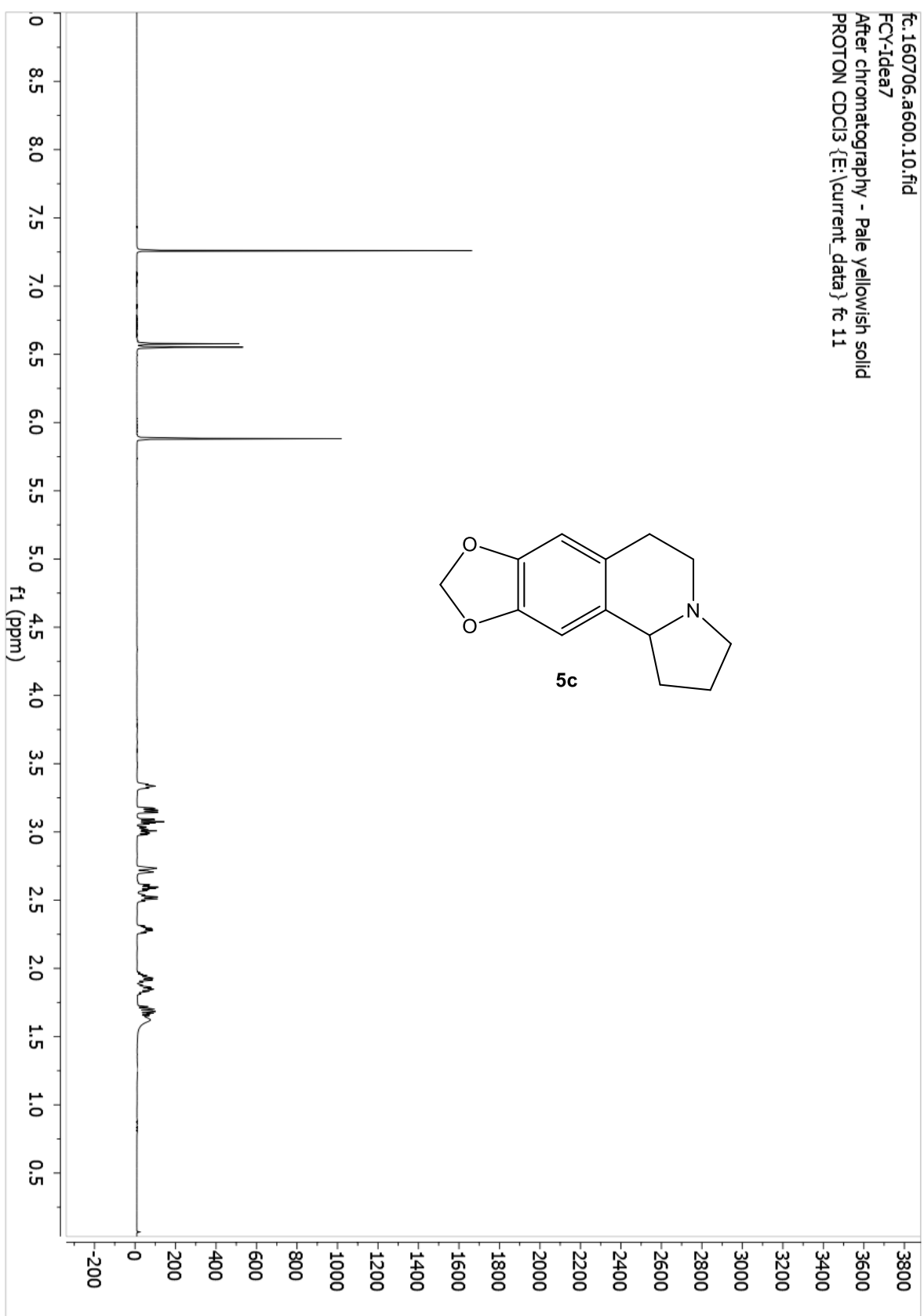
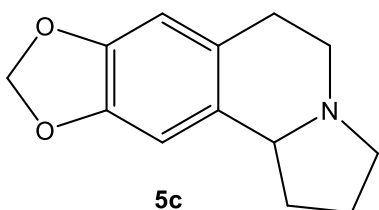


fc:170424.a400.11.fid
FCY-Idea47

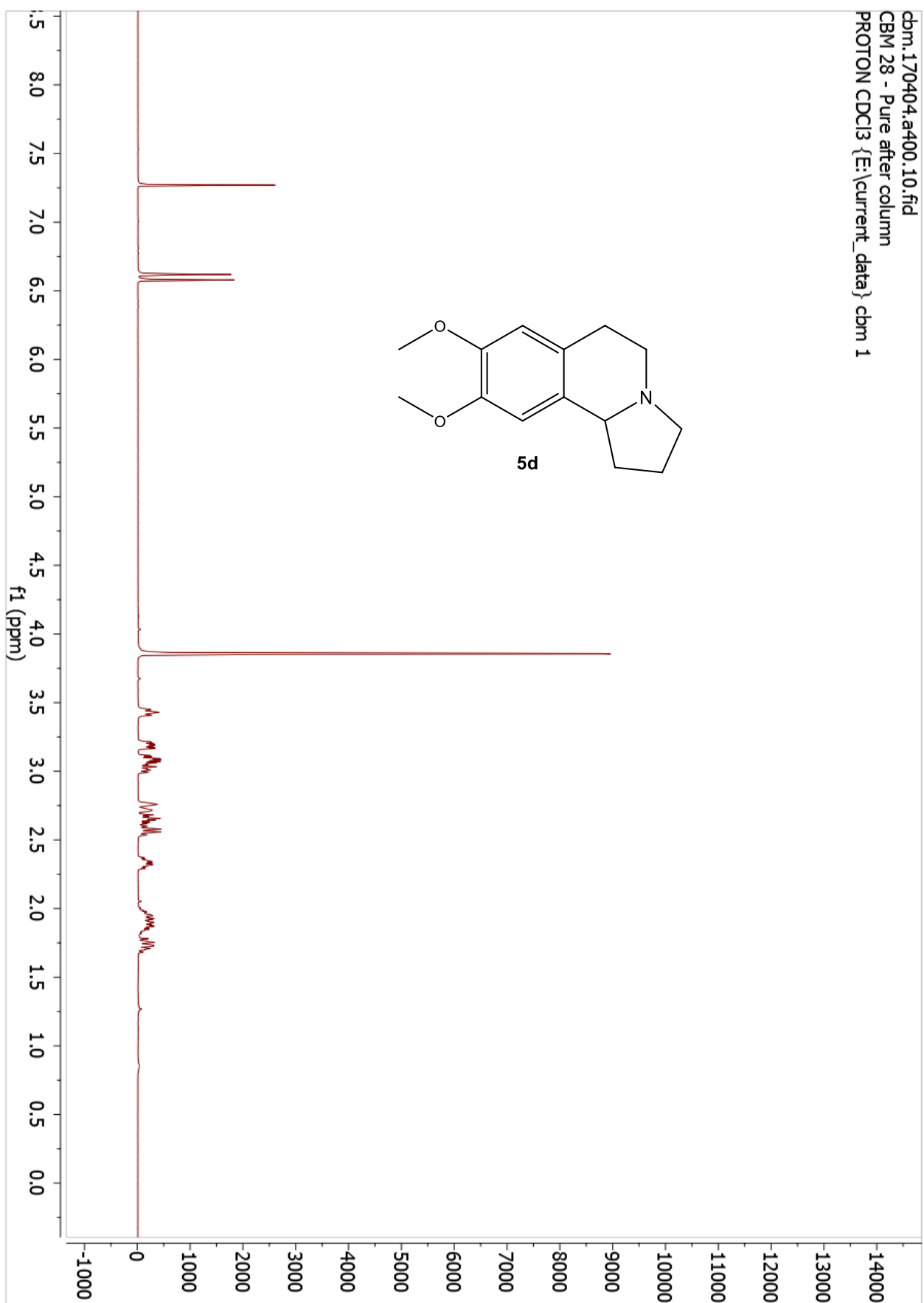
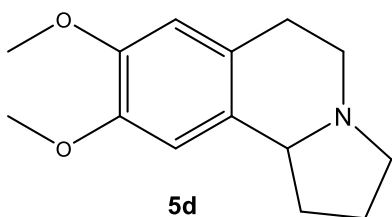
After filtration & washing - White solid
C13CPD DMSO {E:\current_data} fc 10

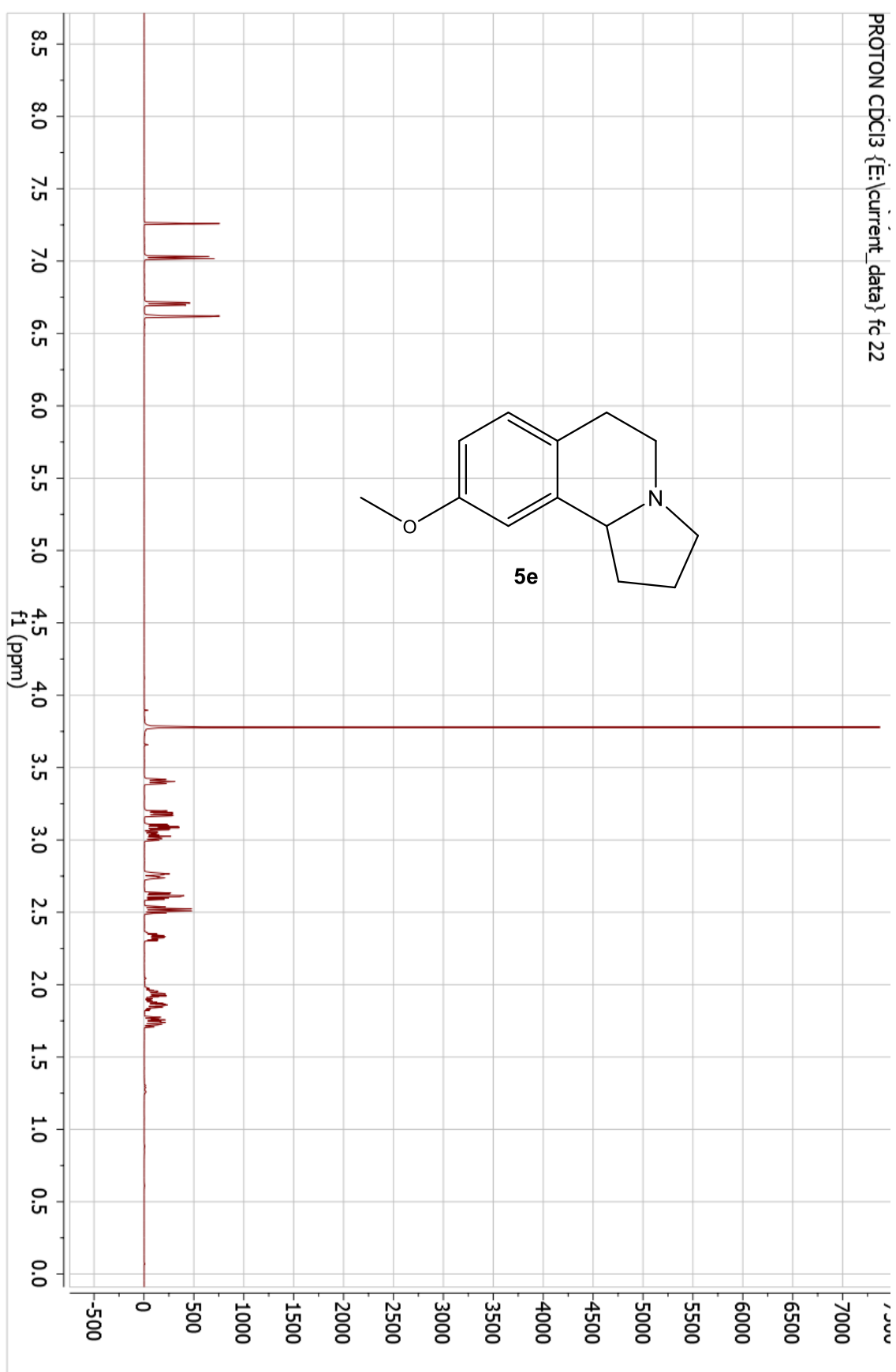


fc.160706.a600.10.fid
FCV-Idea7
After chromatography - Pale yellowish solid
PROTON CDCl3 {E:\current_data} fc 11

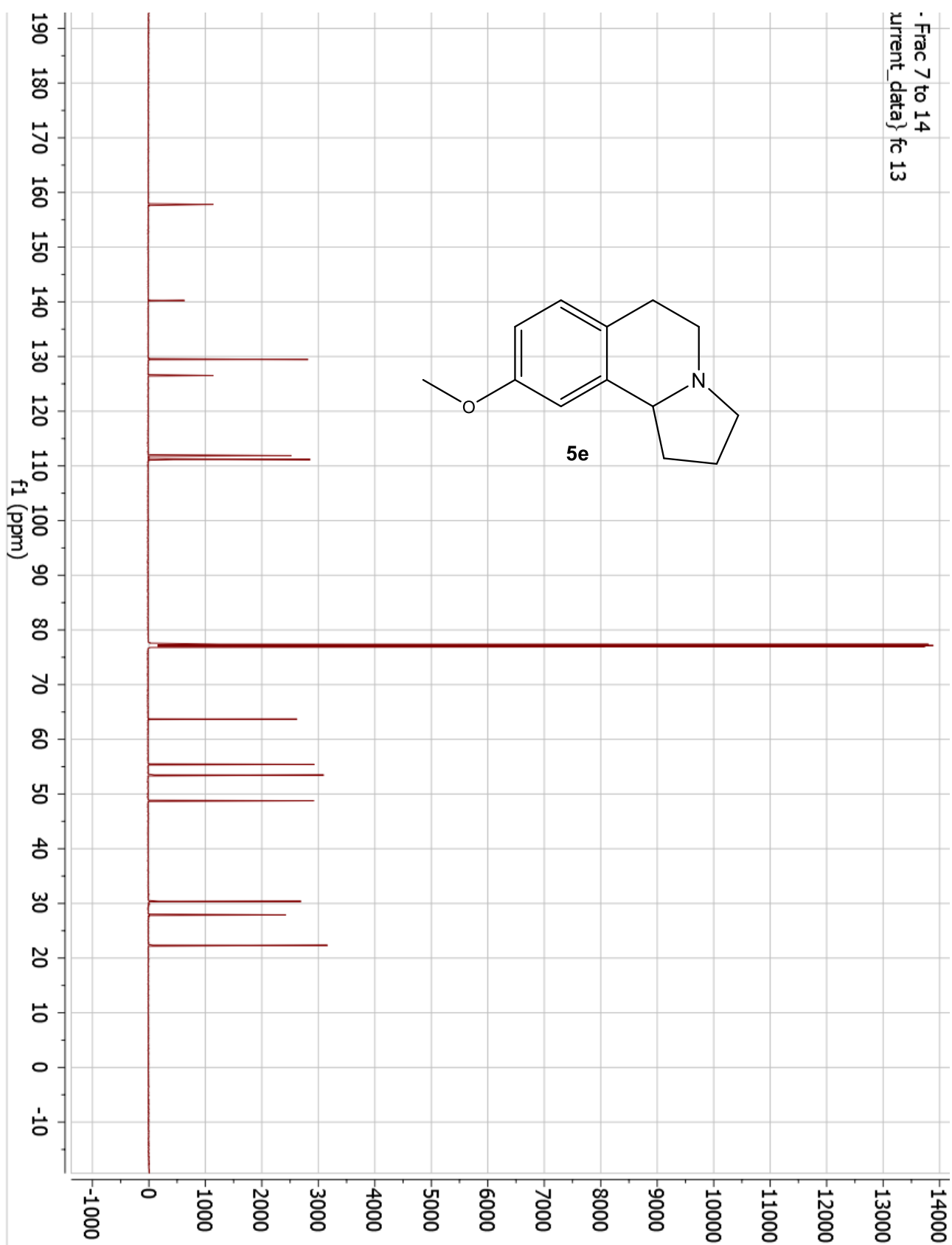


cbm.170404.a400.10.fid
CBM 28 - Pure after column
PROTON CDCl3 {E:\current_data} cbm 1





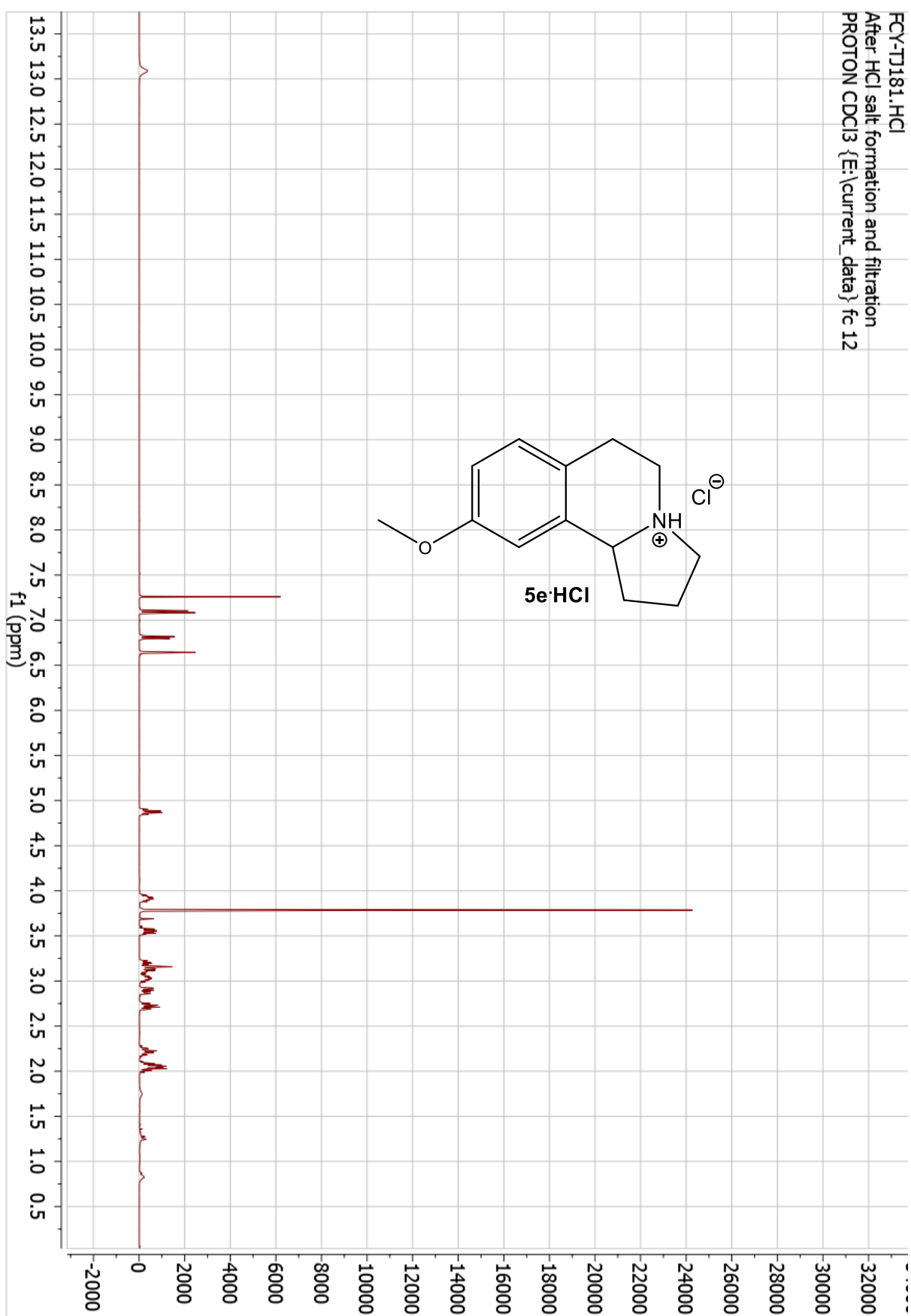
- Frac 7 to 14
current_data} fc 13



FCY-TJ181.HCl

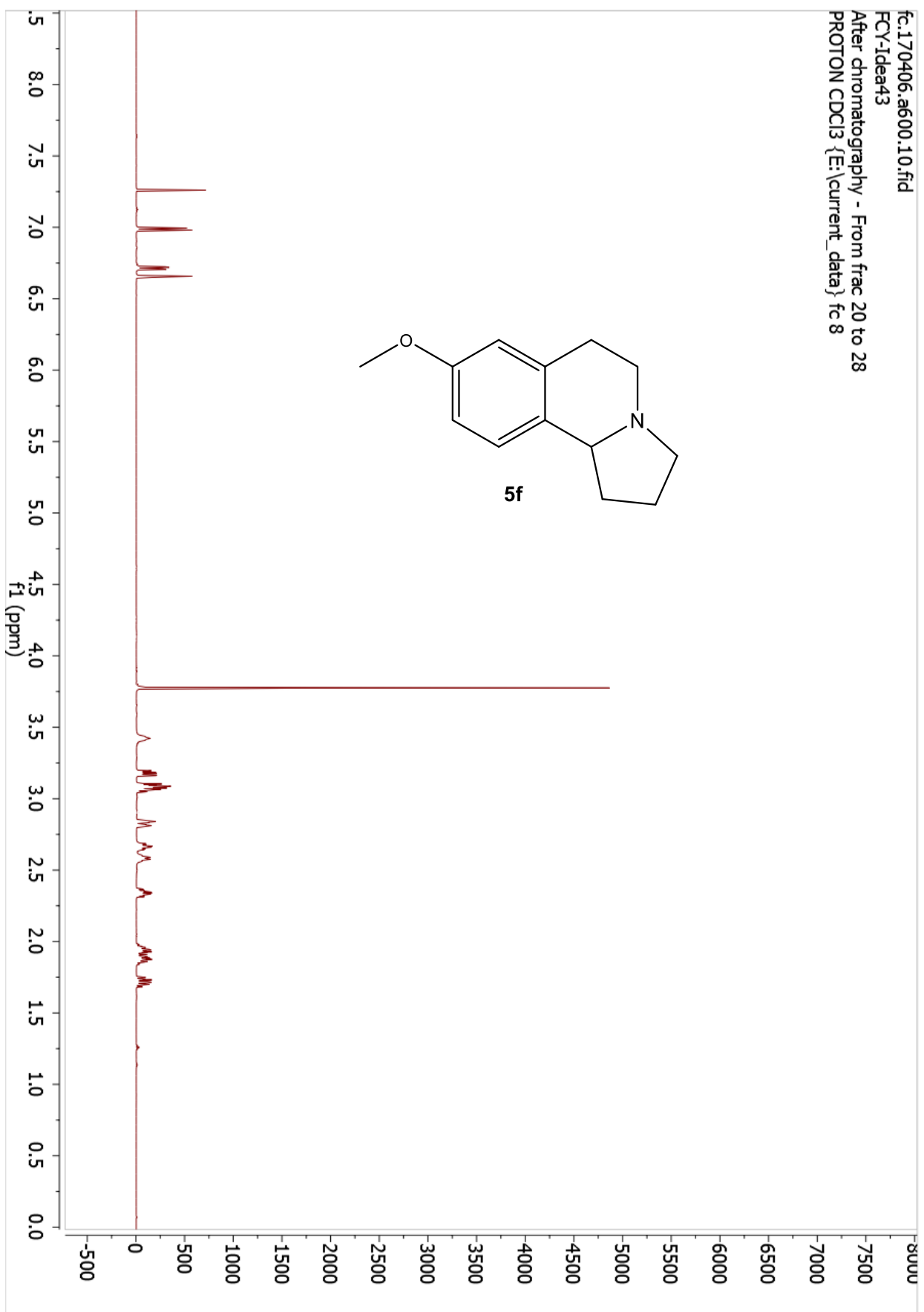
After HCl salt formation and filtration

PROTON CDCl₃ {E:\current_data} fc 12

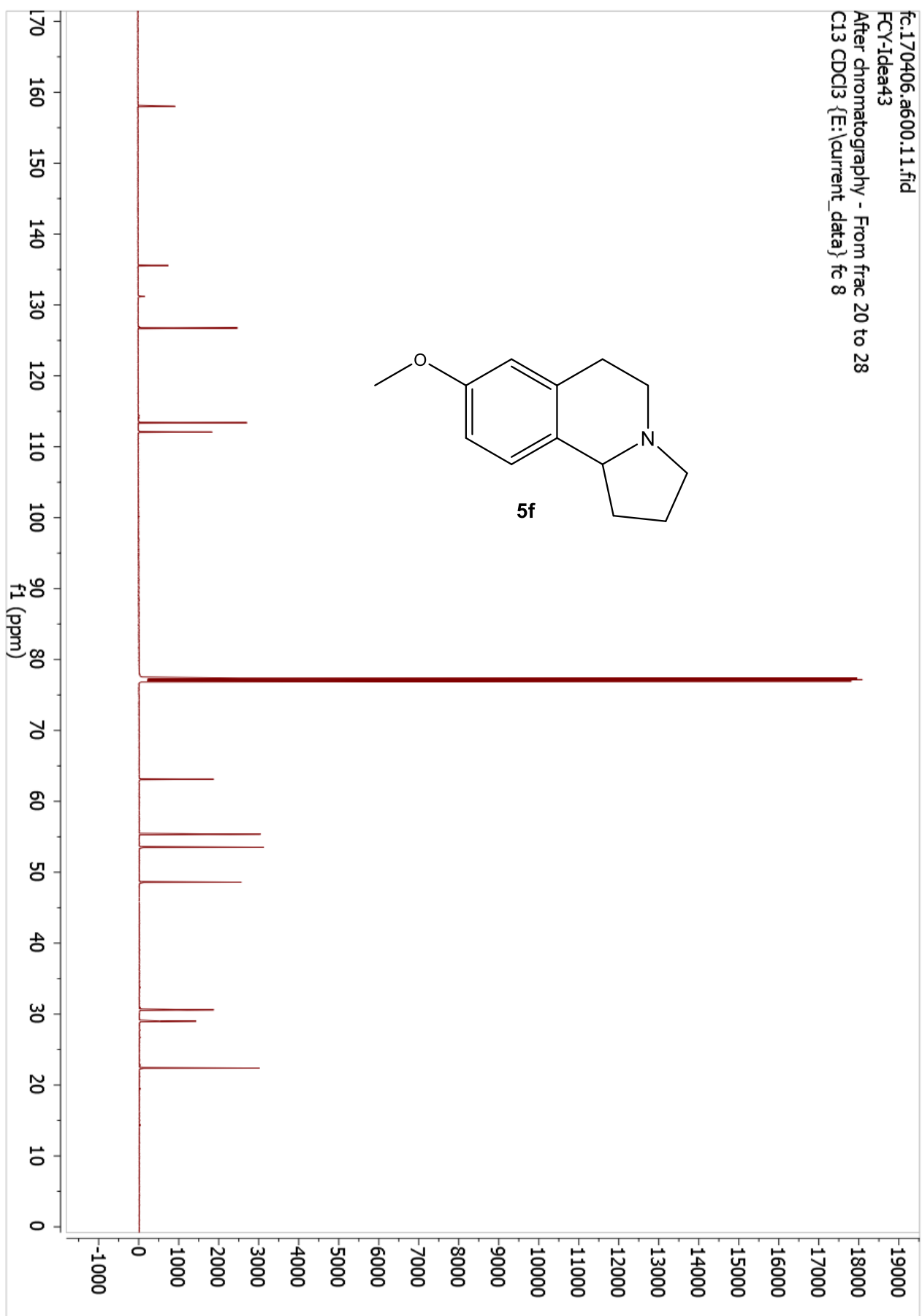


fc:170406.a600.10.fid
FCY-idea43

After chromatography - From frac 20 to 28
PROTON CDCl₃ {E:\current_data} fc 8

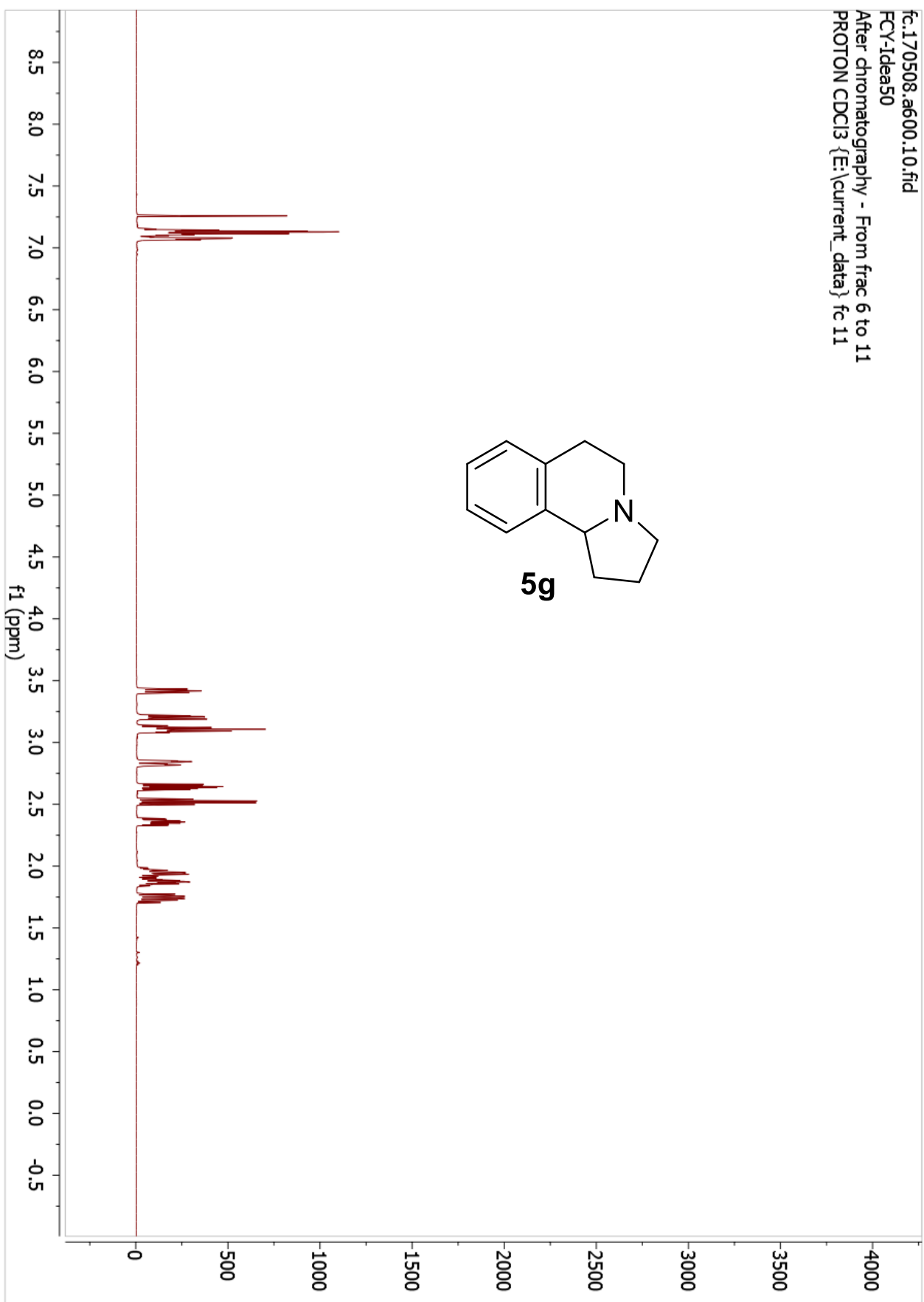
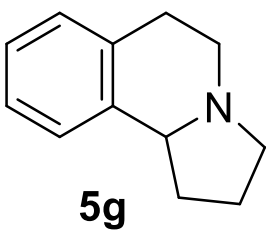


fc.170406.a600.1.fid
FCY-Idea43
After chromatography - From frac 20 to 28
C13 CDCl3 {E:\current_data} fc 8



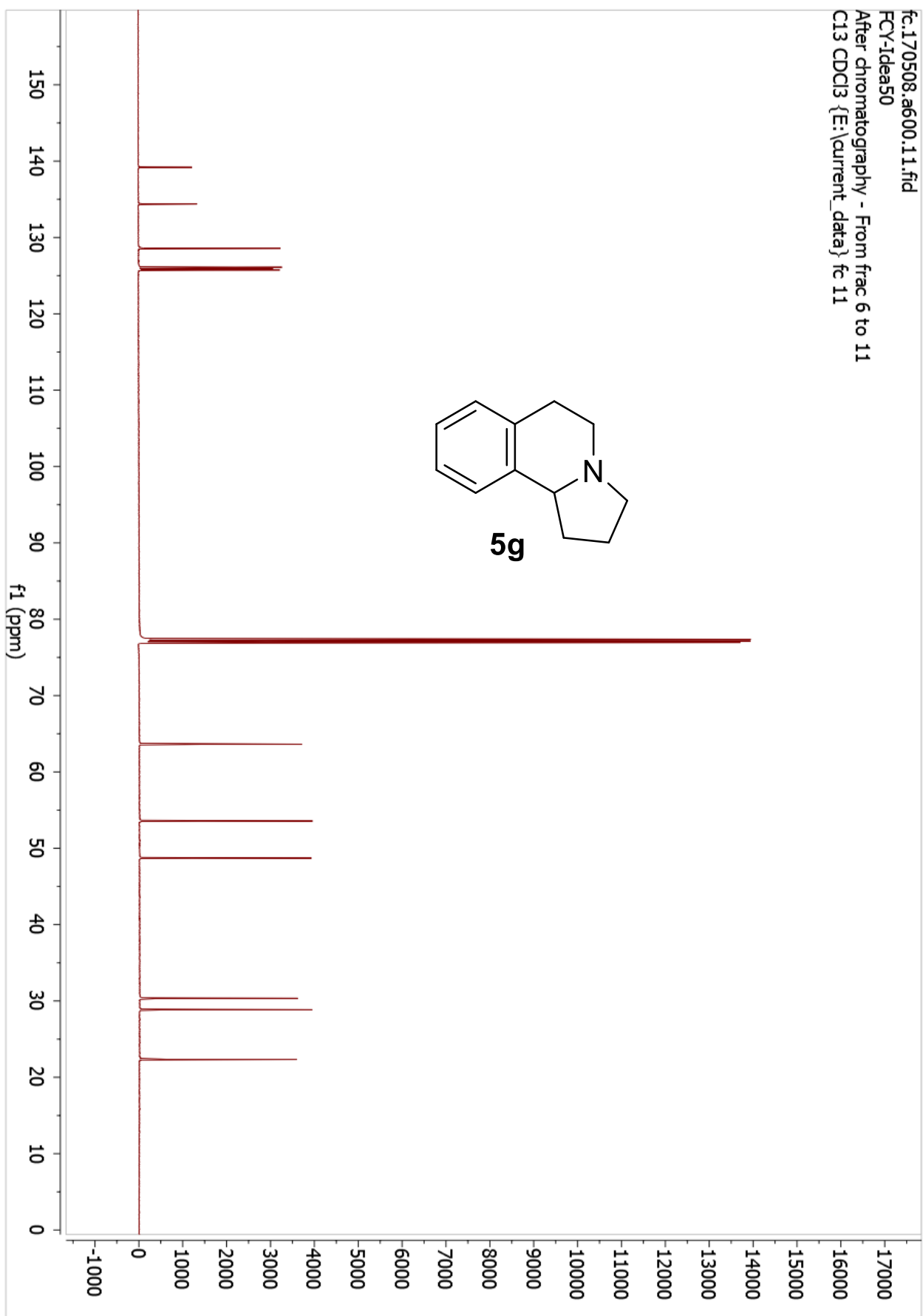
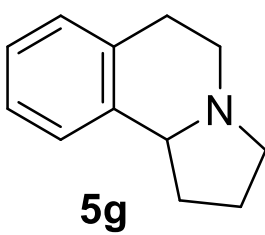
fc:170508.a600.10.fid
FCY-Idea50

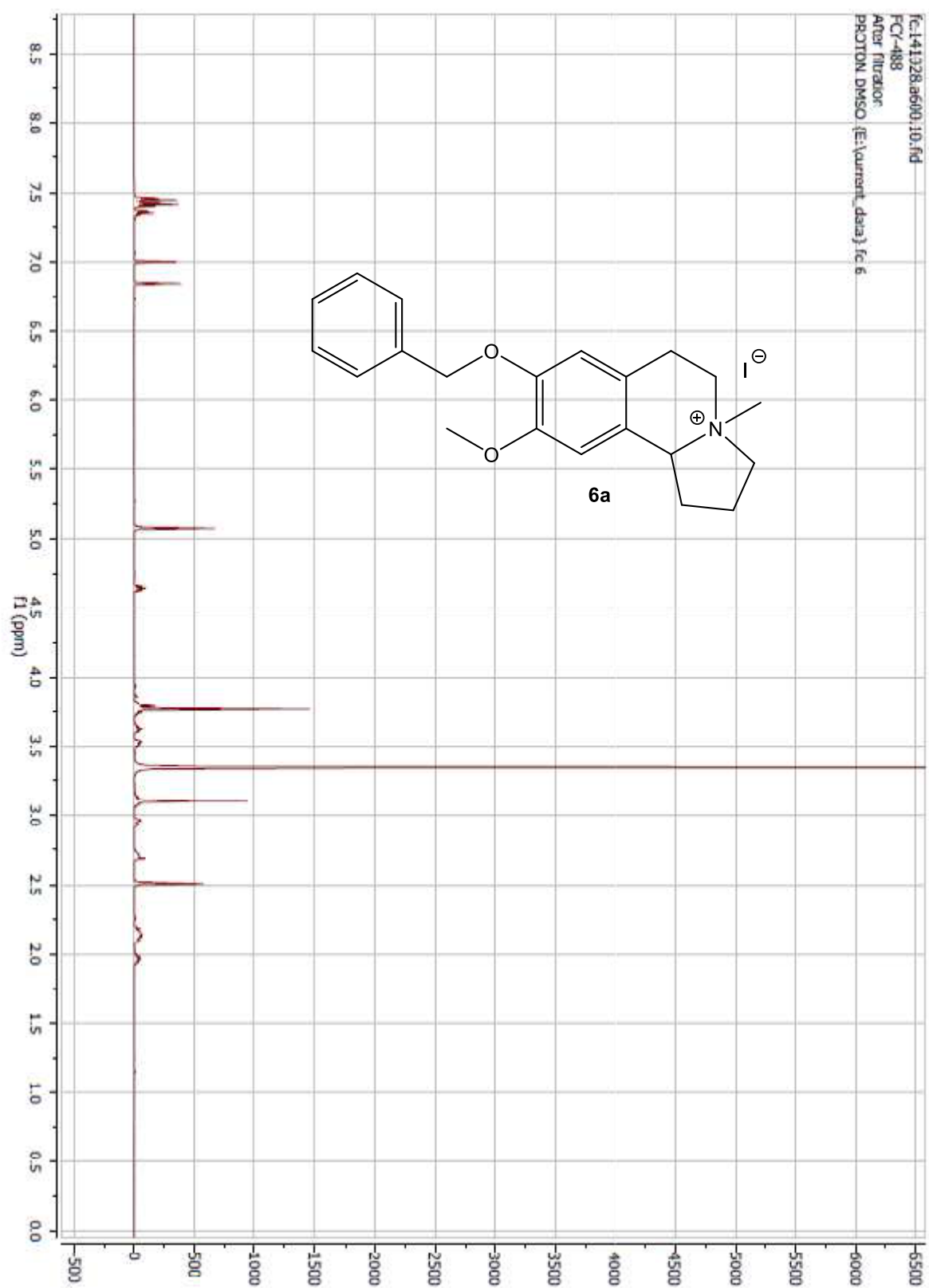
After chromatography - From frac 6 to 11
PROTON CDCl₃ {E:\current_data} fc 11

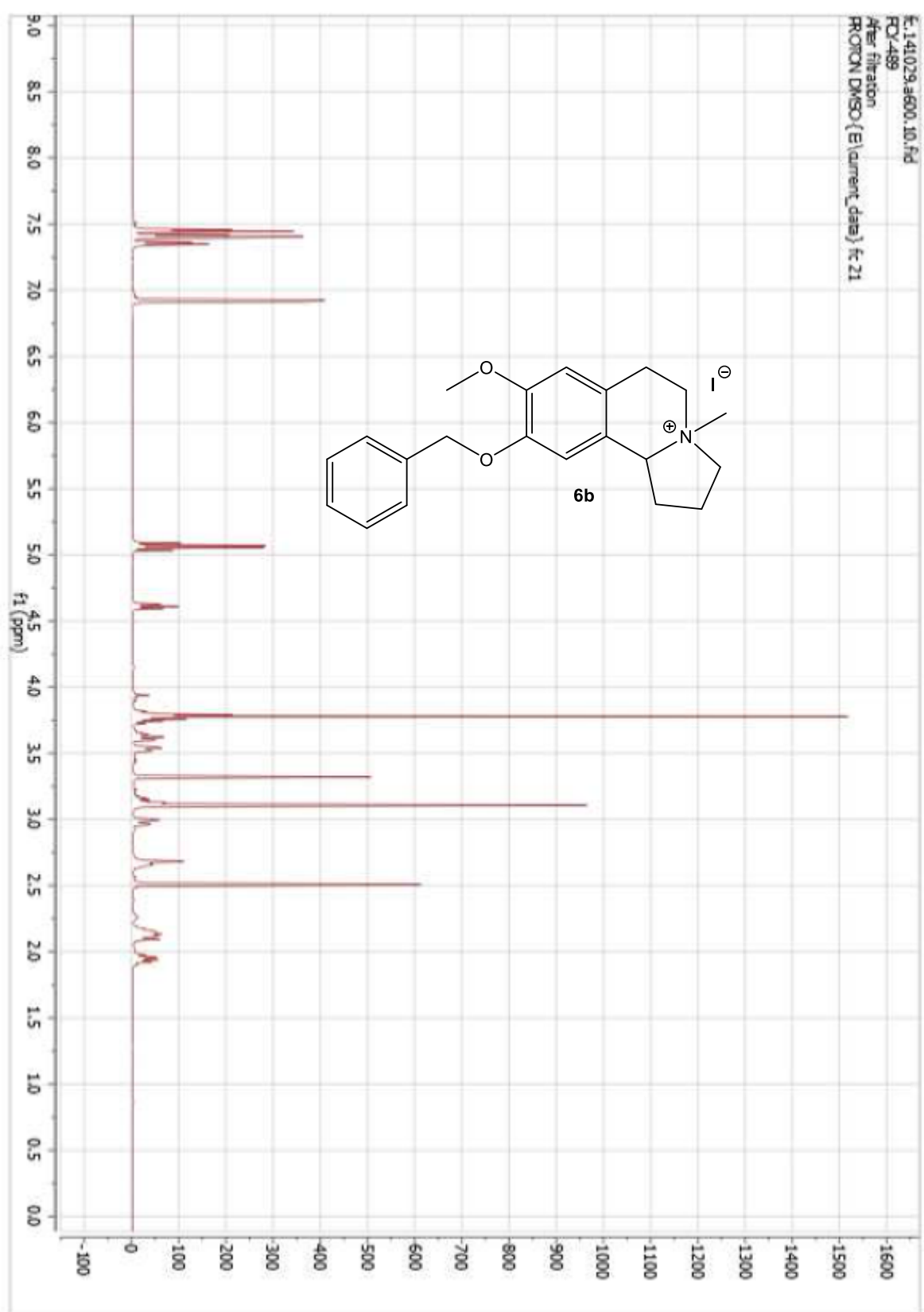


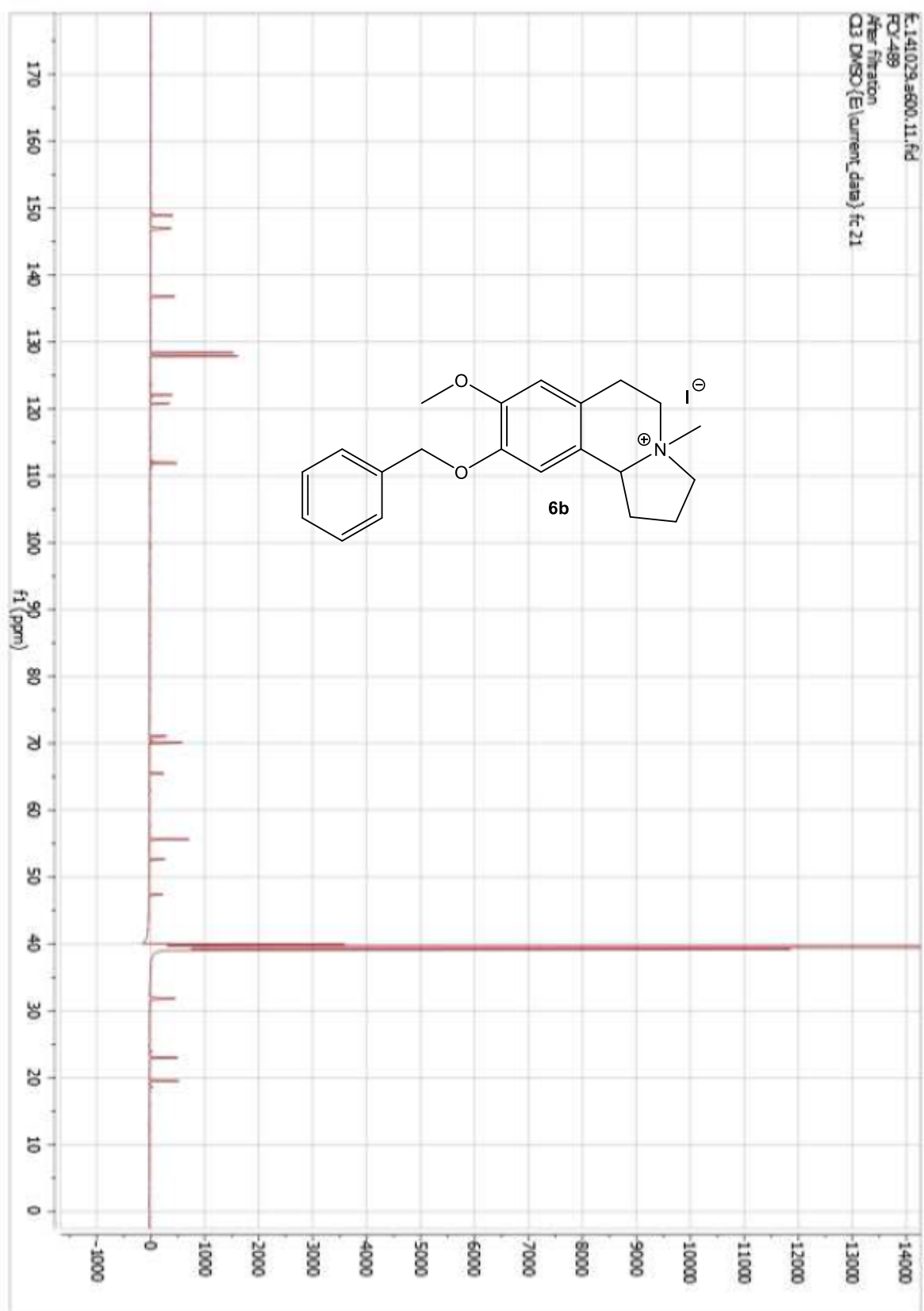
fc:170508.a600.1.1.fid
FCY-idea50

After chromatography - From frac 6 to 11
C13 CDCl3 {E:\current_data} fc 11



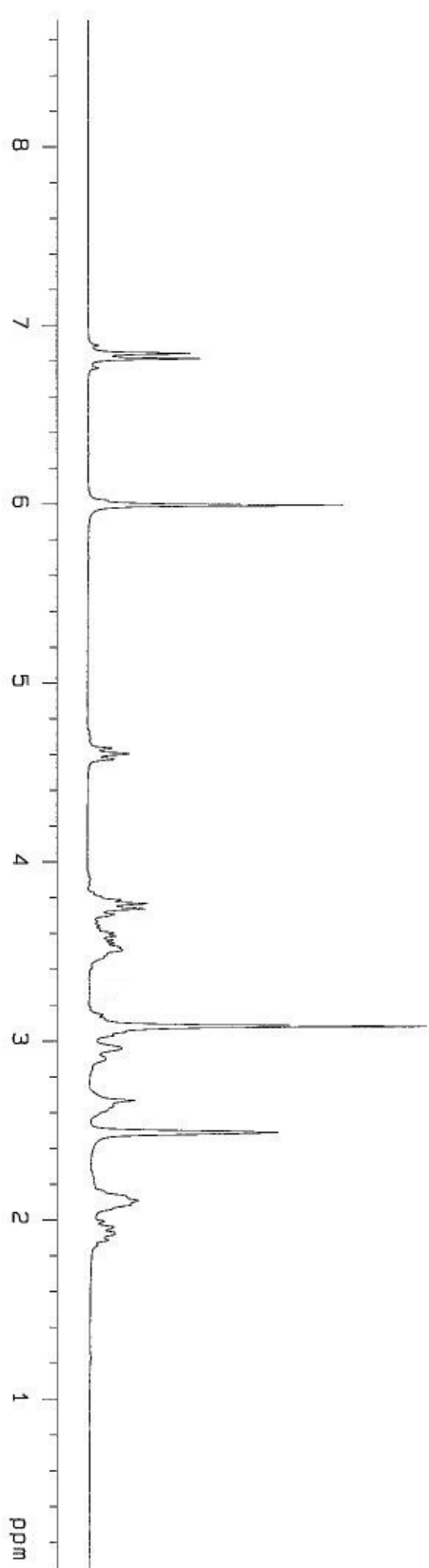
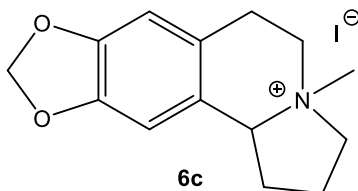






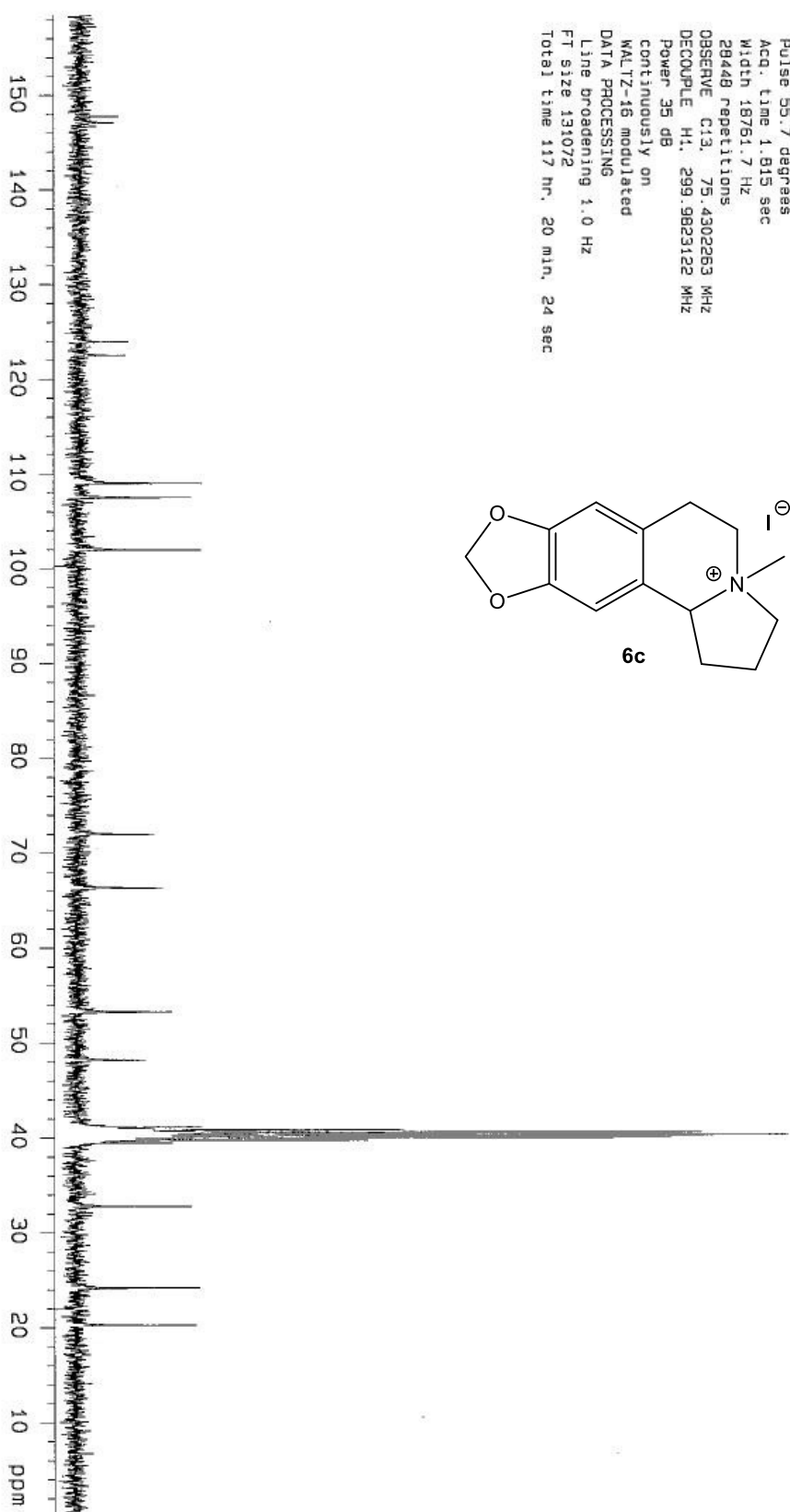
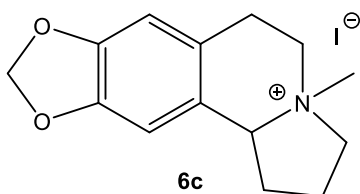
Pulse Sequence: zgpg30
Solvent: DMSO
Ambient temperature
File: FCY_460
Mercury-300BBB "mercury"

Relax. delay 1.000 sec
Pulse 71.6 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
8 repetitions
OBSERVE H1: 299.9808484 MHz
DATA PROCESSING
F1 size 32768
Total time 0 min, 25 sec



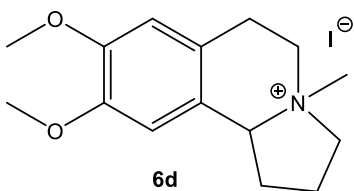
Pulse Sequence: s2pu1
Solvent: DMSO
Ambient temperature
File: FCY_460_C13
Mercury-3000B8 "mercury"

Pulse 55.7 degrees
Acq. time 1.915 sec
Width 18761.7 Hz
29448 repetitions
OBSERVE C13. 75.4302263 MHz
DECOUPLE H1. 299.9823122 MHz
Power 35 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 117 hr, 20 min, 24 sec



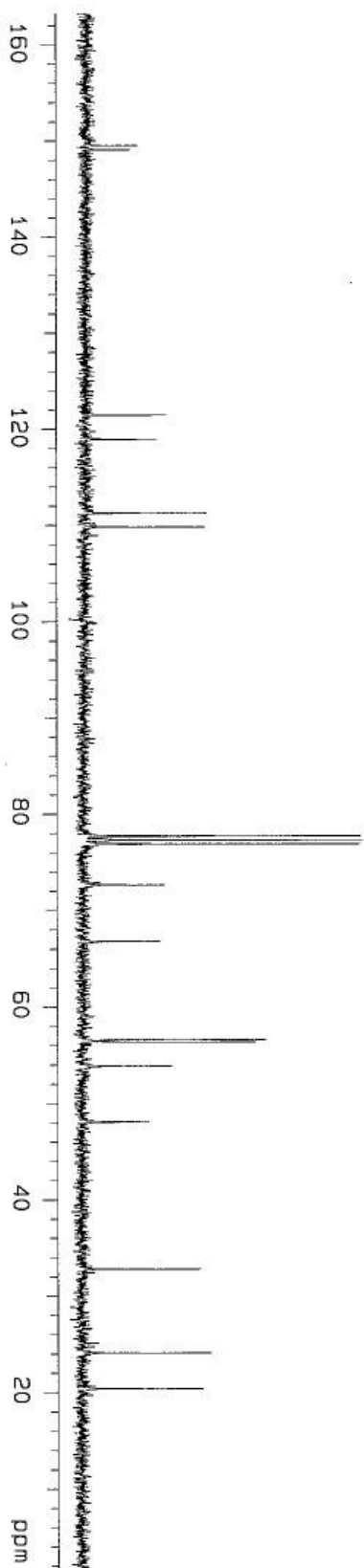
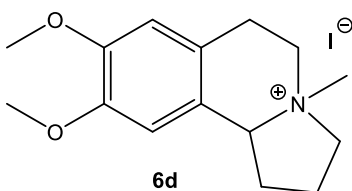
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: ECY_458
Mercury-300BB "Mercury"

Relax. delay 1.000 sec
Pulse 71.6 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
12 repetitions
OBSERVE H1 299.9794235 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 37 sec

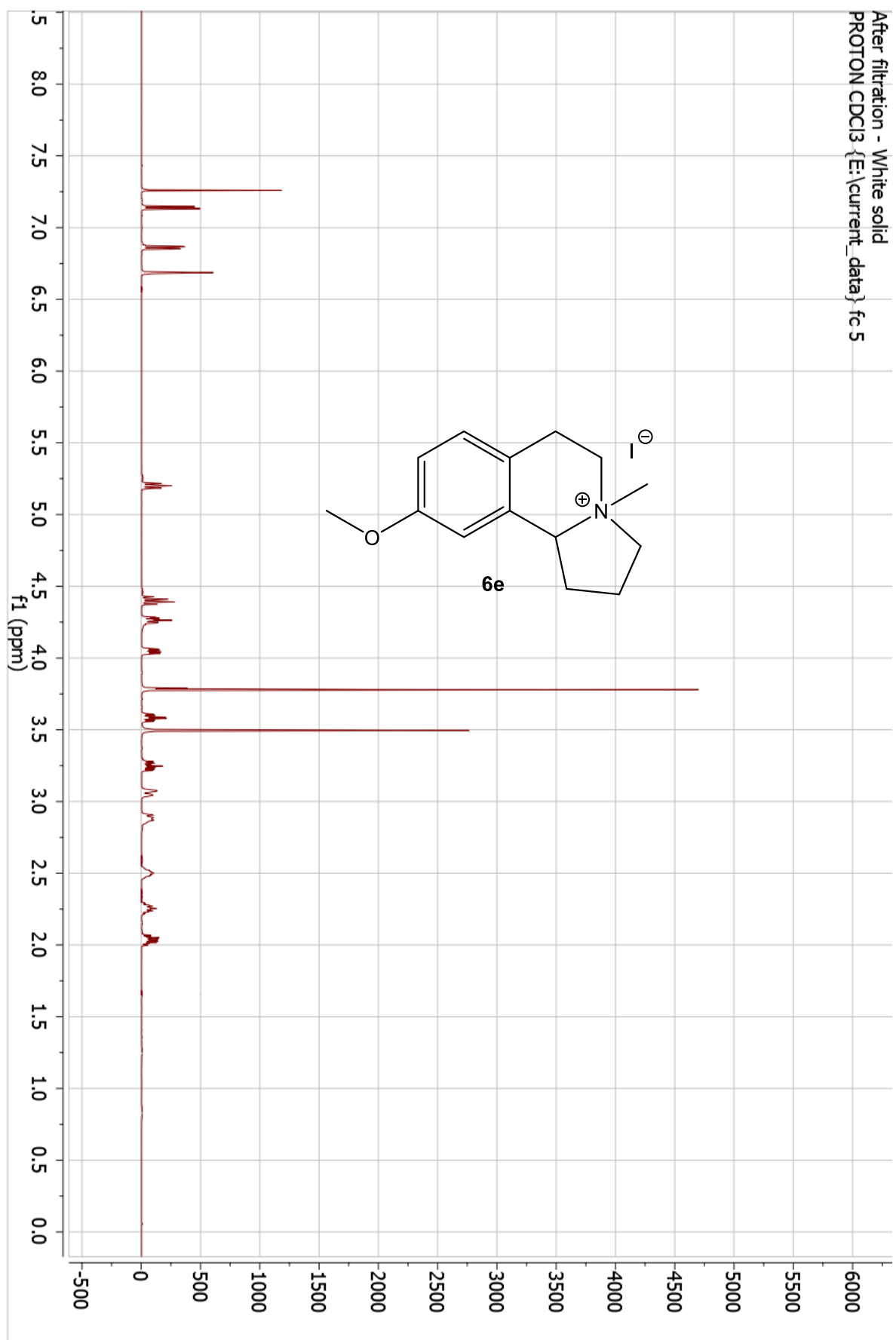


Pulse Sequence: s2pu1
 Solvent: CDCl3
 Ambient temperature
 File: FCY_458_C13
 Mercury-300BB "mercury"

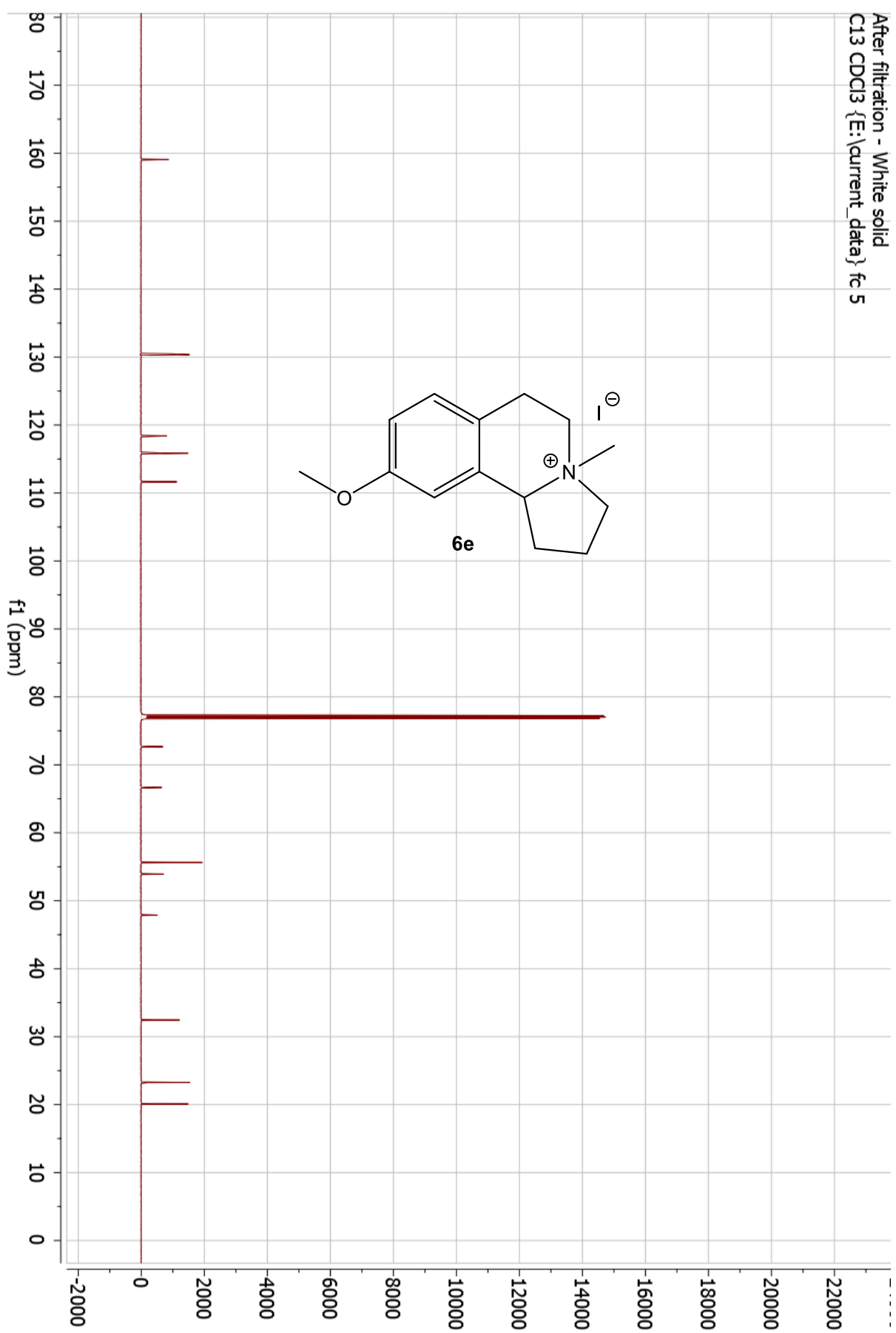
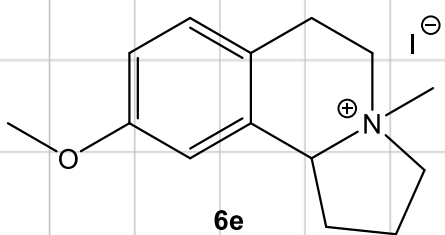
Pulse 55.7 degrees
 Acq. time 1.815 sec
 Width 18761.7 Hz
 3136 repetitions
 OBSERVE C13, 75.4298680 MHz
 DECOUPLE H1, 299.9808873 MHz
 Power 35 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 117 hr, 20 min, 24 sec



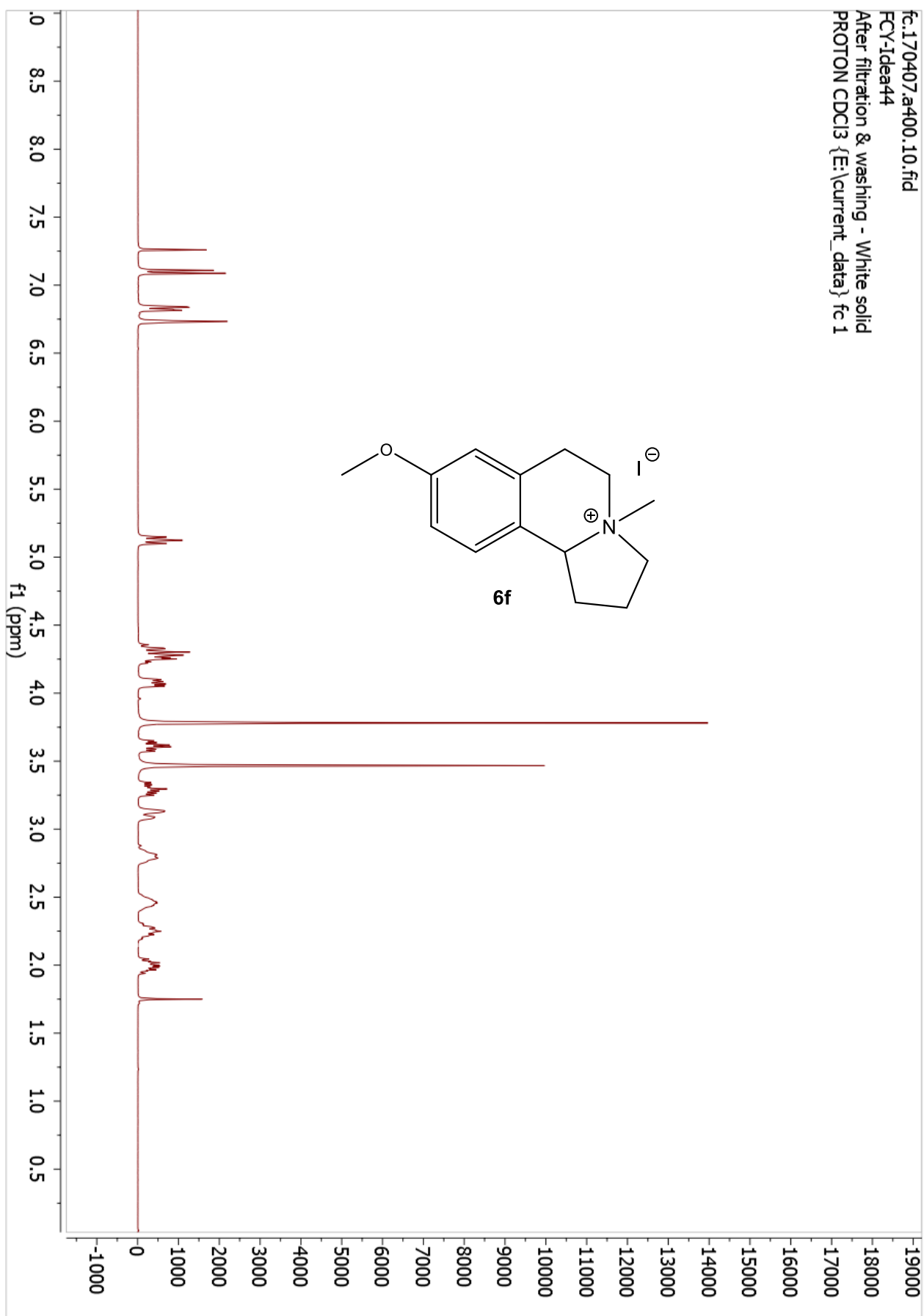
After filtration - White solid
PROTON CDCl3 {E:\current_data} fc 5



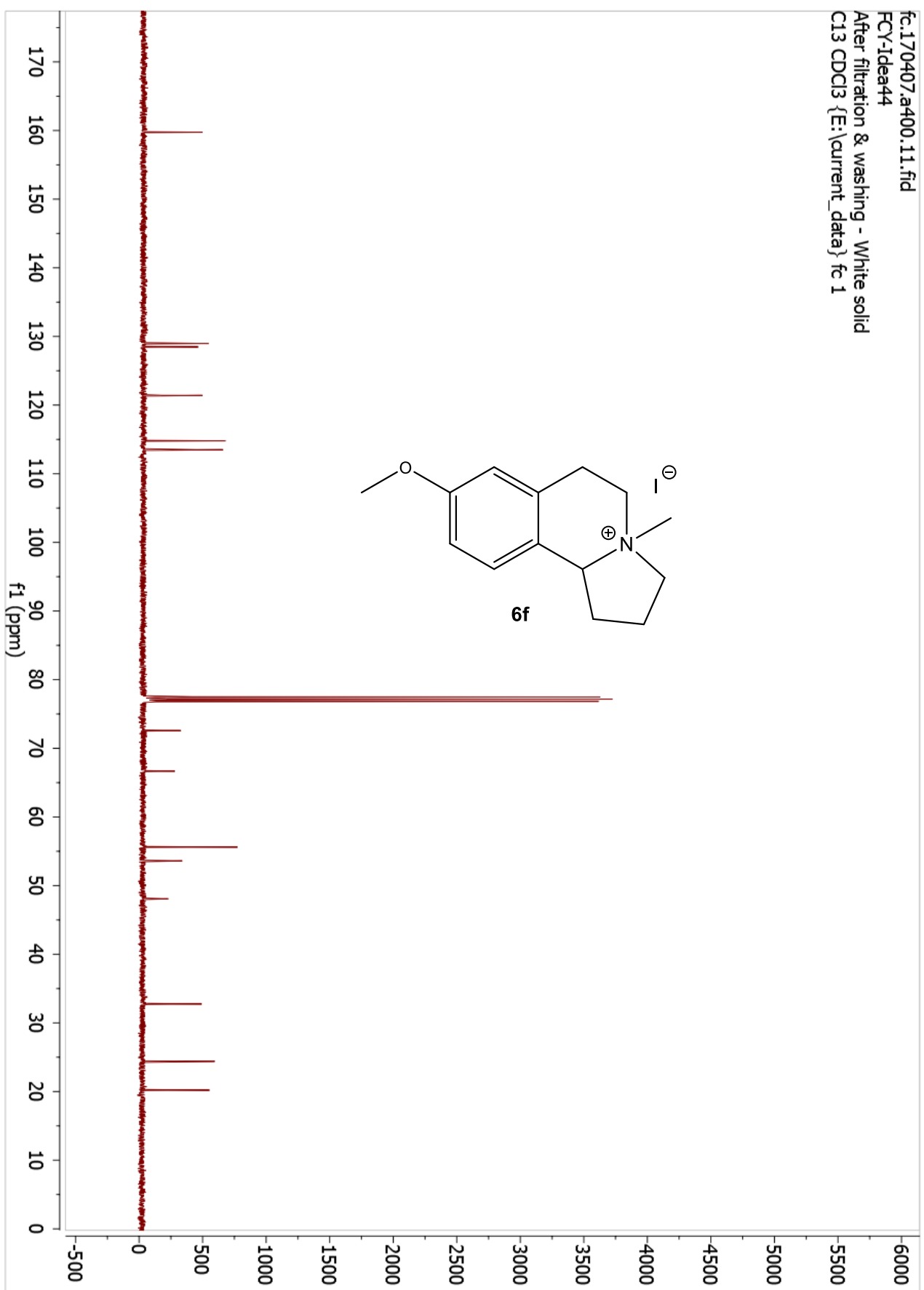
After filtration - White solid
C13 CDCl3 {E:\current_data} fc 5



fc.170407.a400.10.fid
FCY-Idea44
After filtration & washing - White solid
PROTON CDCl3 {E:\current_data} fc 1

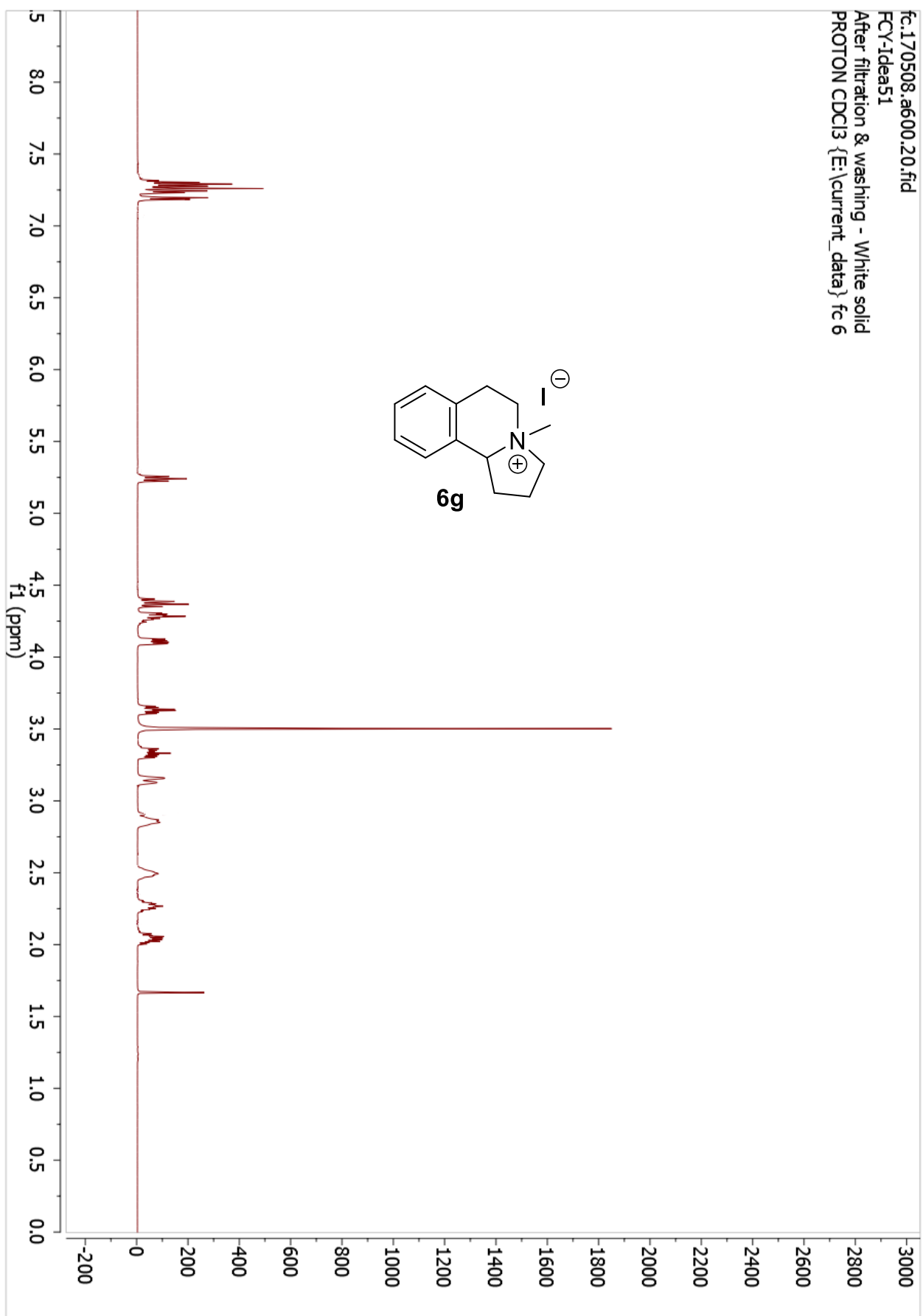


fc.170407.a400.11.fid
FCY-Idea44
After filtration & washing - White solid
C13 CDCl3 {E:\current_data} fc 1

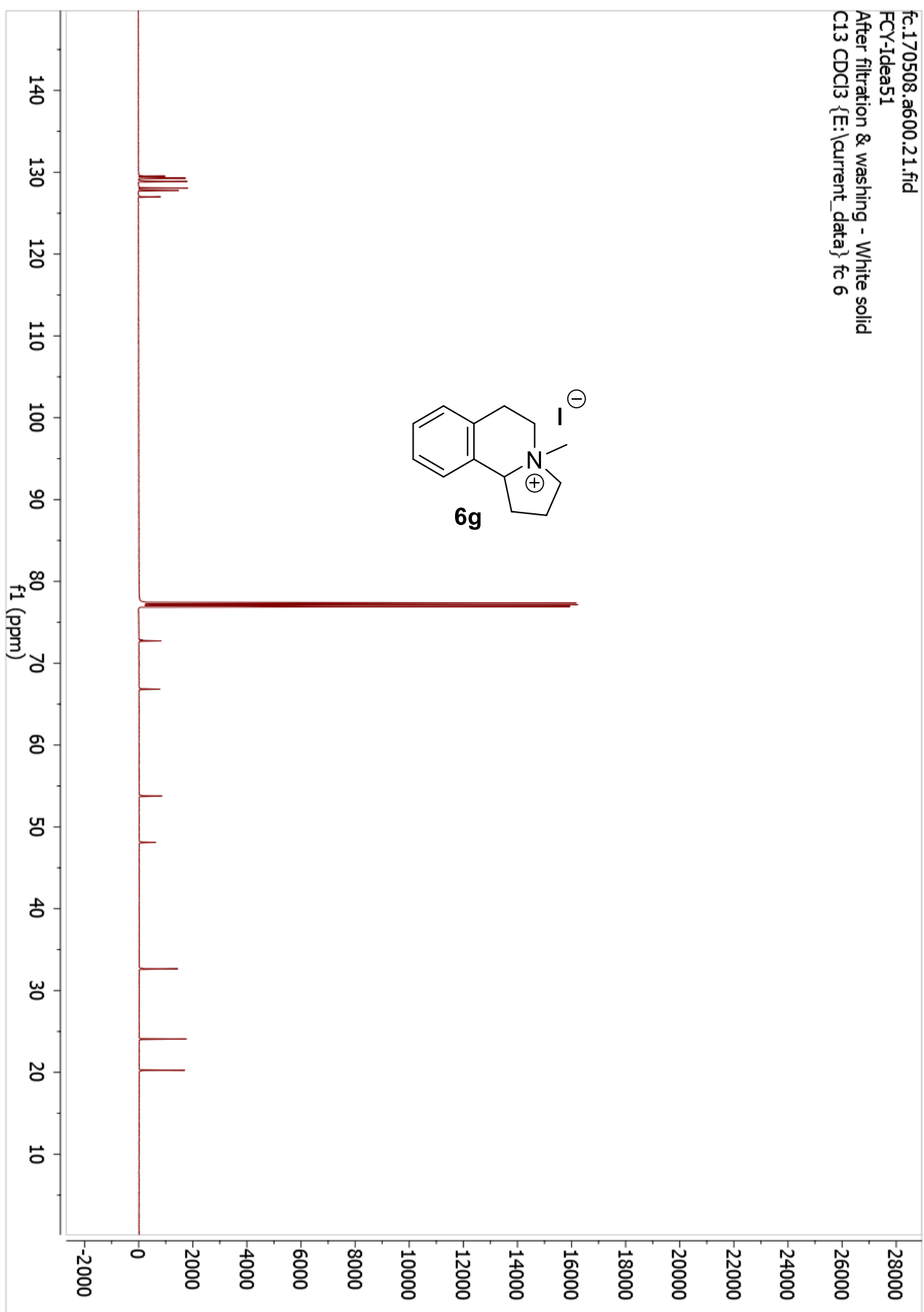
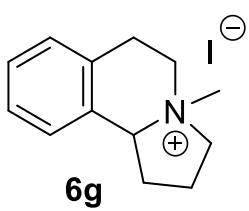


fc:170508.a600.20.fid
FCY-Idea51

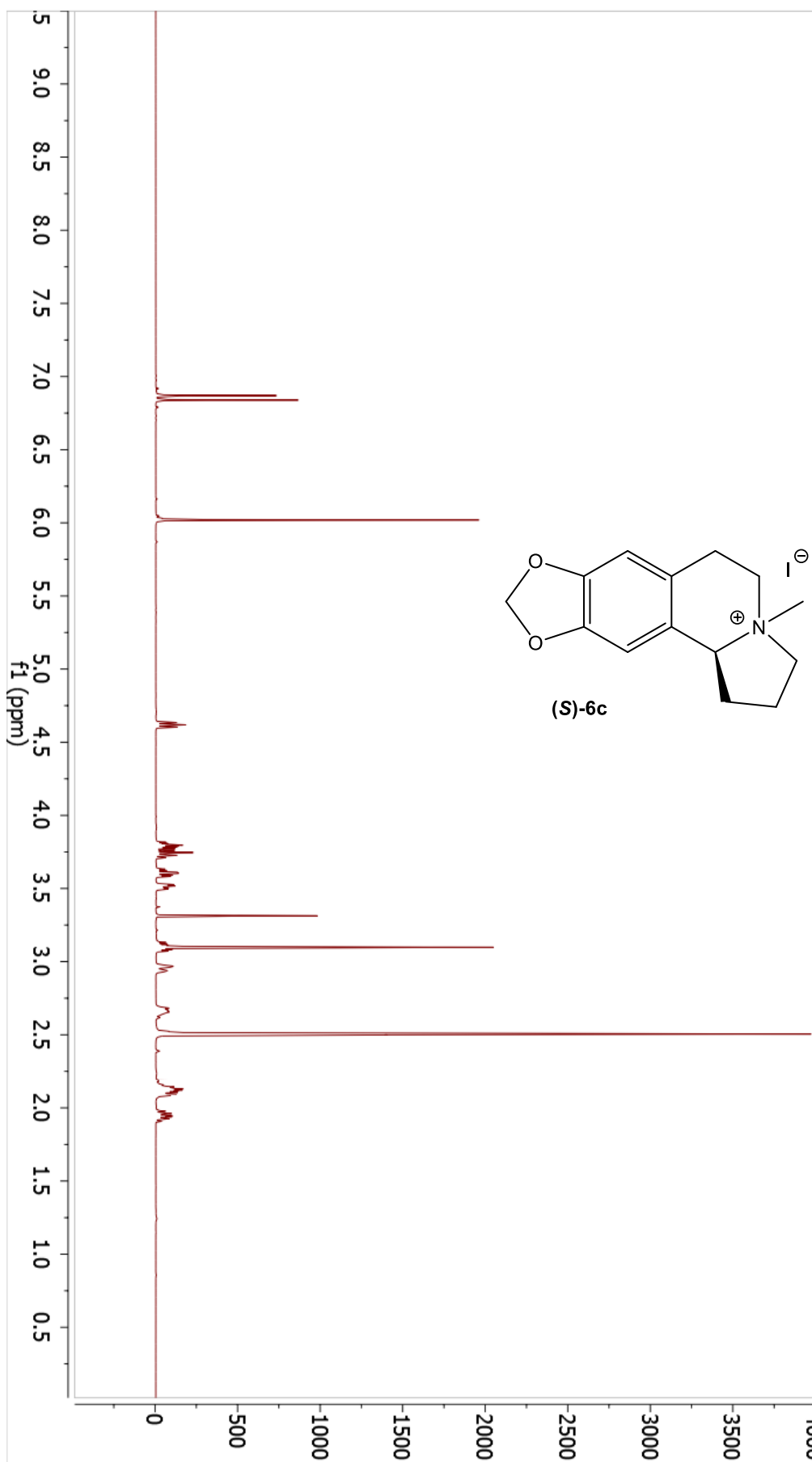
After filtration & washing - White solid
PROTON CDCl₃ {E:\current_data} fc 6



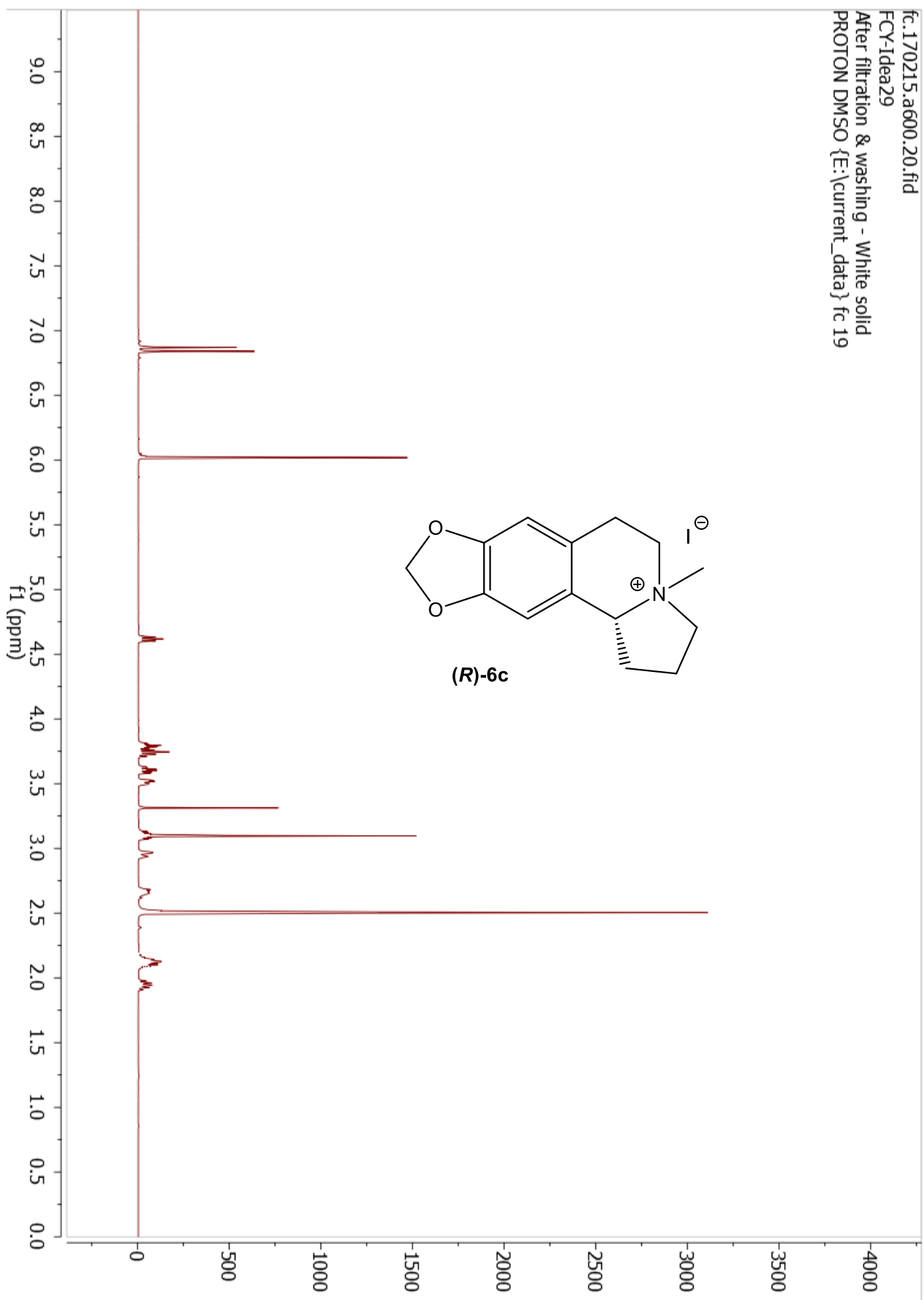
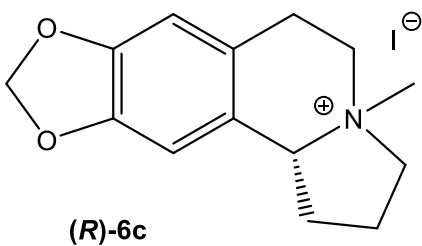
fc:170508.a600.21.fid
FCY-idea51
After filtration & washing - White solid
C13 CDCl3 {E:\current_data} fc 6



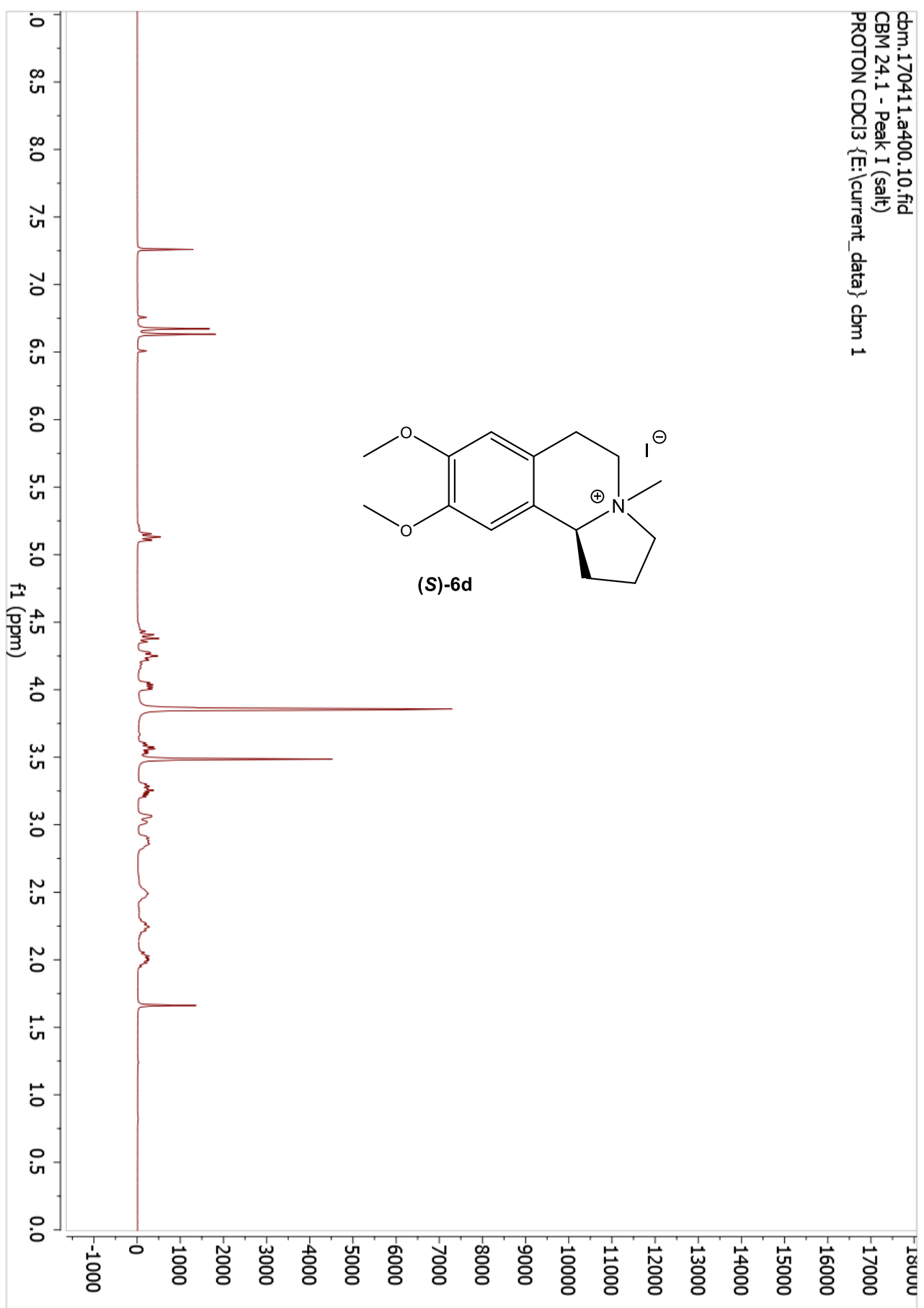
fc.170215.a600.10.fid
FCY-Idea28
After filtration & washing - White solid
PROTON DMSO {E:\current_data} fc 7



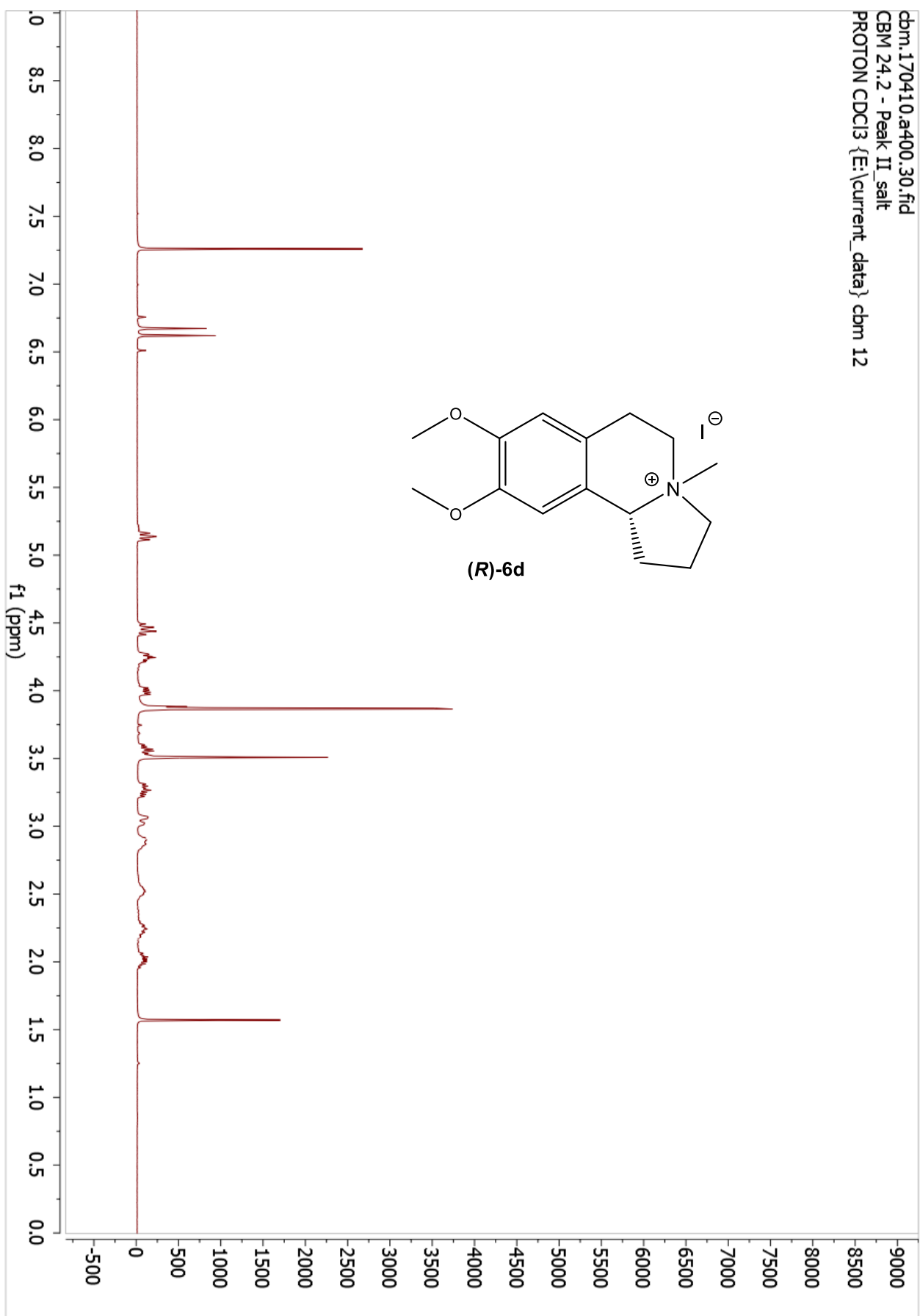
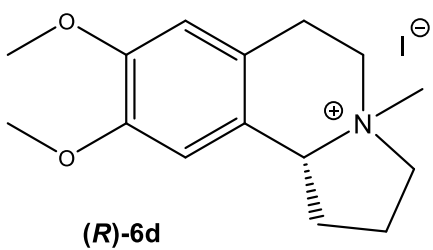
fc.170215.a600.20.fid
FCY-Idea29
After filtration & washing - White solid
PROTON DMSO {E:\current_data} fc 19



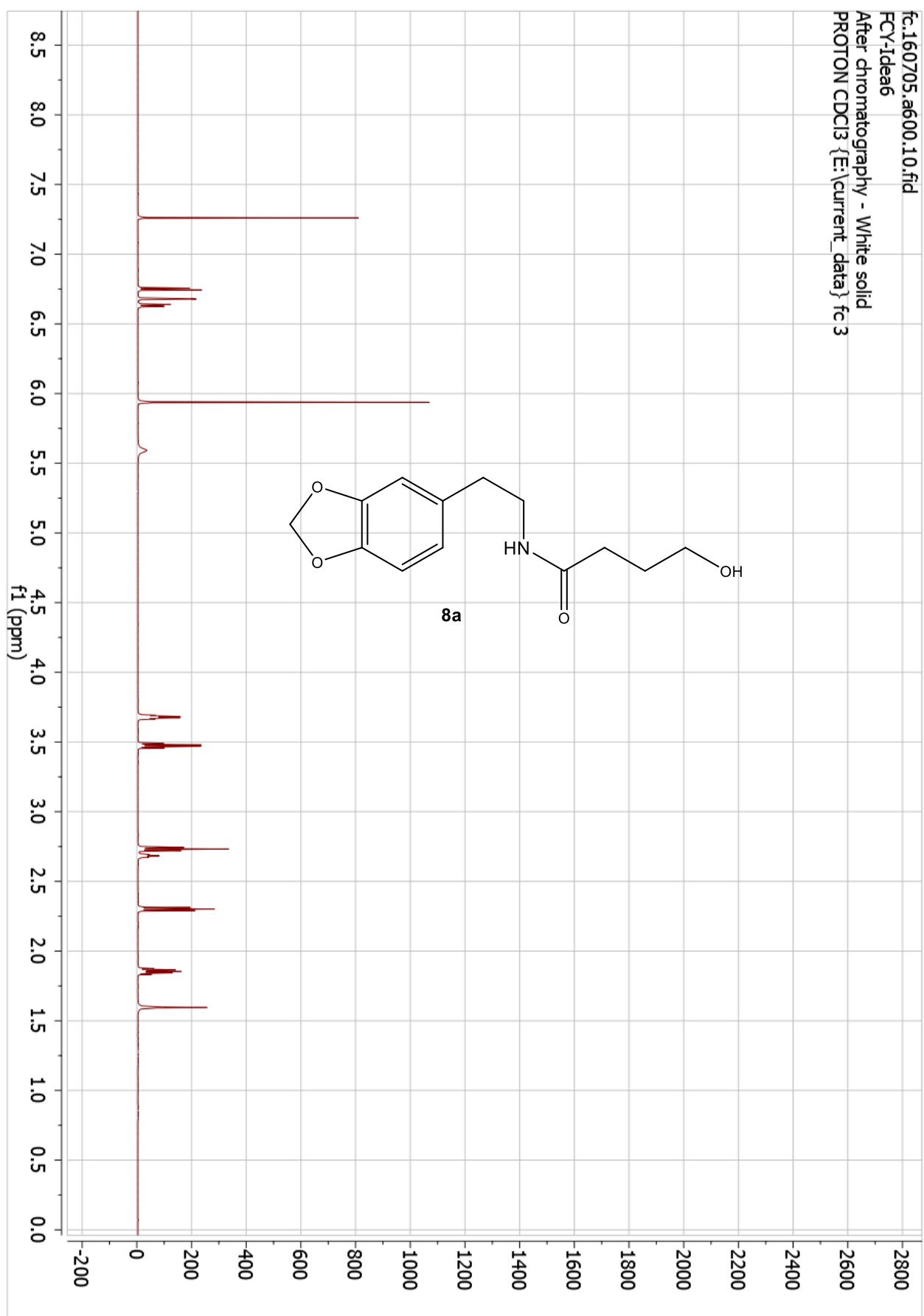
cbm.170411.a400.10.fid
CBM 24.1 - Peak 1 (salt)
PROTON CDCl3 {E:\current_data\ cbm 1



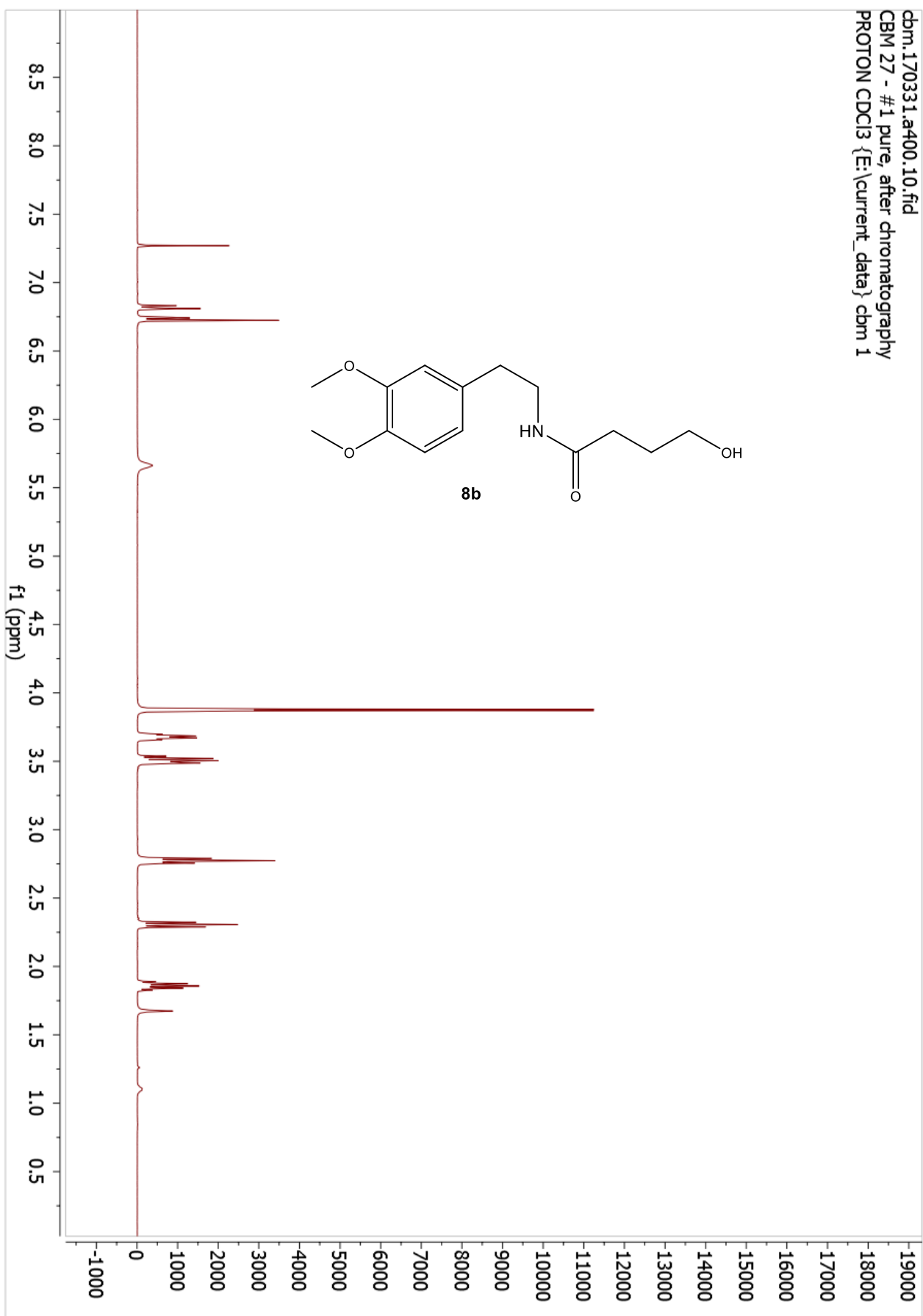
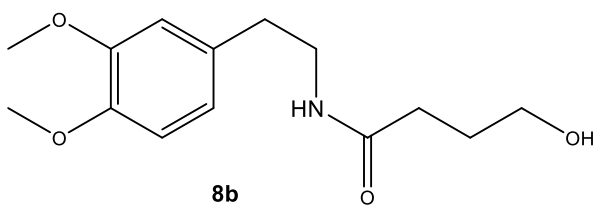
cbm.170410.a400.30.fid
CBM 24.2 - Peak II_salt
PROTON CDCl3 {E:\current_data} cbm 12



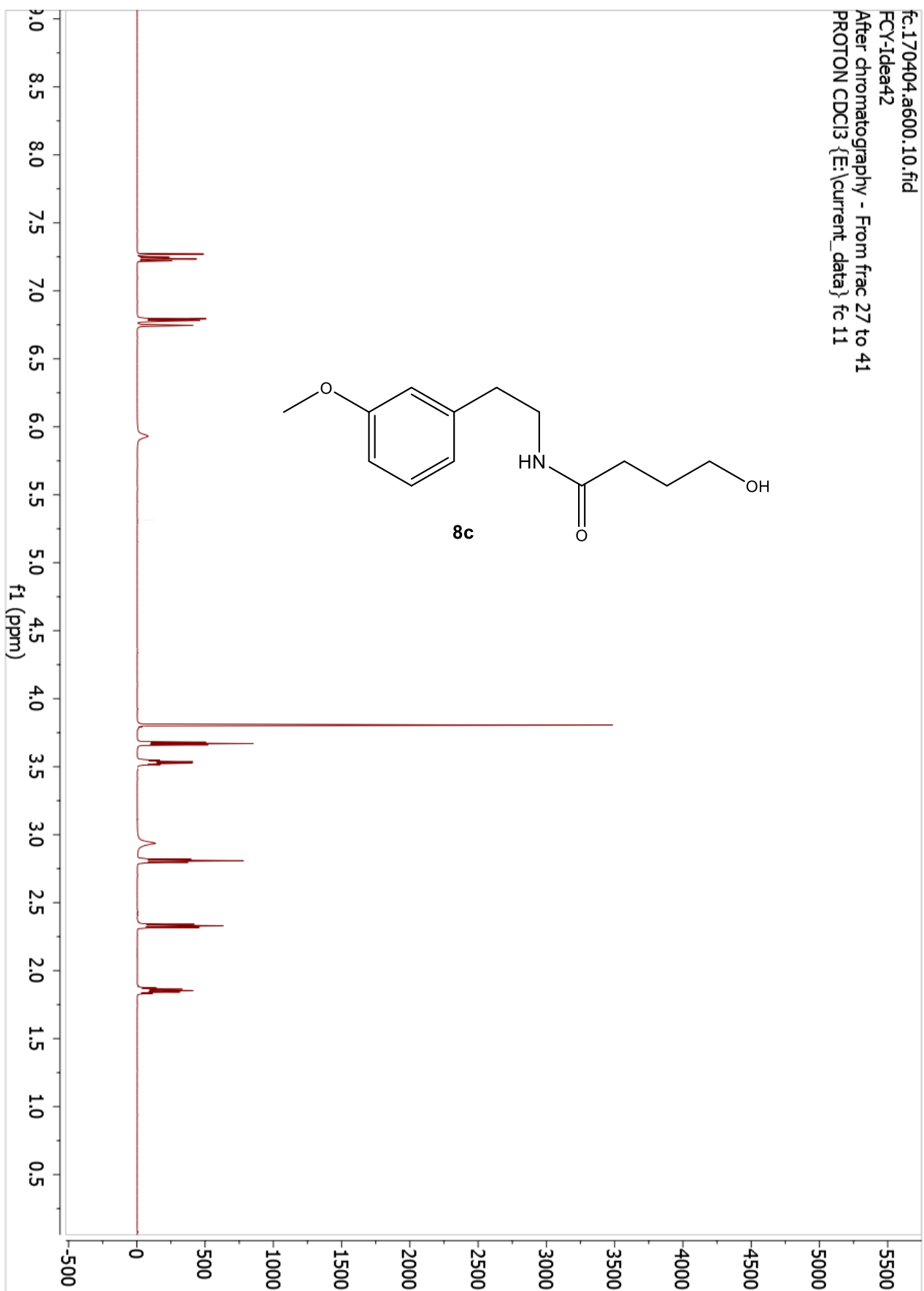
fc:160705.a600.10.fid
FCY-Idea6
After chromatography - White solid
PROTON CDCl3 {E:\current_data} fc 3



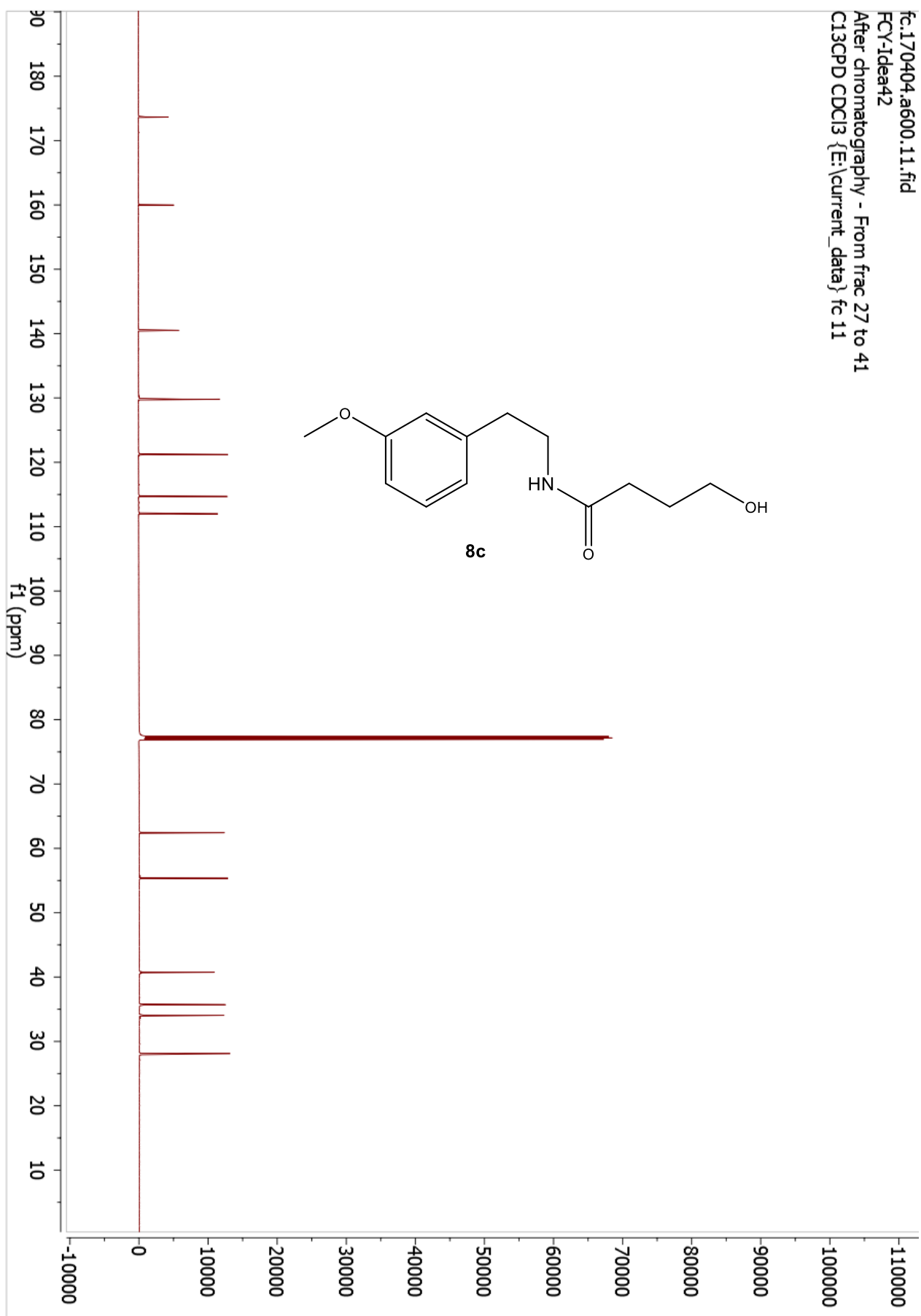
cbm.170331.a400.10.fid
CBM 27 - #1 pure, after chromatography
PROTON CDC13 {E:\current_data} cbm 1

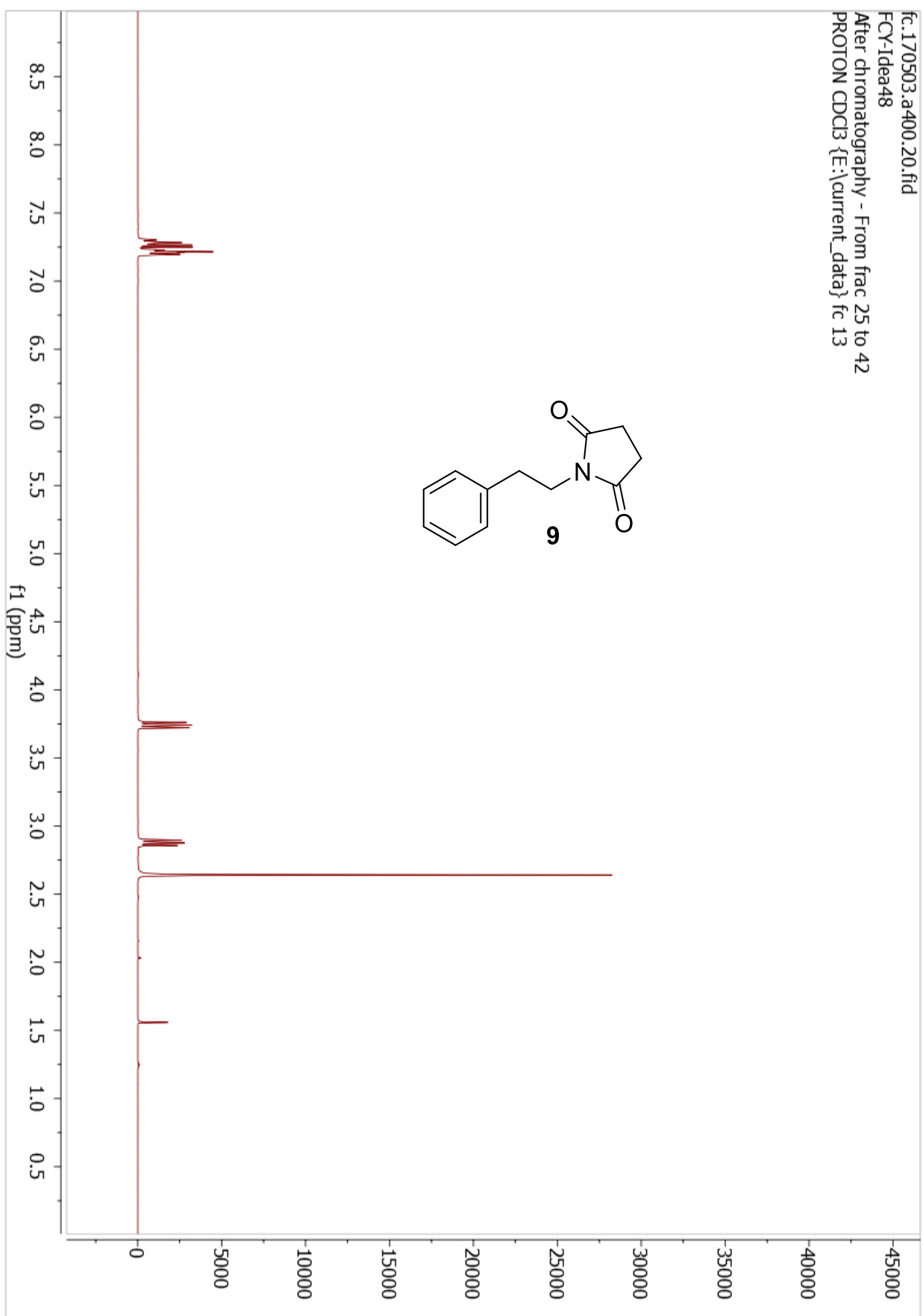


fc:170404.a600.10.fid
FCY-Idea42
After chromatography - From frac 27 to 41
PROTON CDC13 {E:\current_data} fc 11



fc:170404.a600.11.fid
FCY-Idea42
After chromatography - From frac 27 to 41
C13CPD CDC13 {E:\current_data} fc 11





fc.170503.a400.21.fid

FCY-Idea48

After chromatography - From frac 25 to 42
Cl3CPD CDCl3 {E:\current_data} fc 13

