

Supplementary Information for

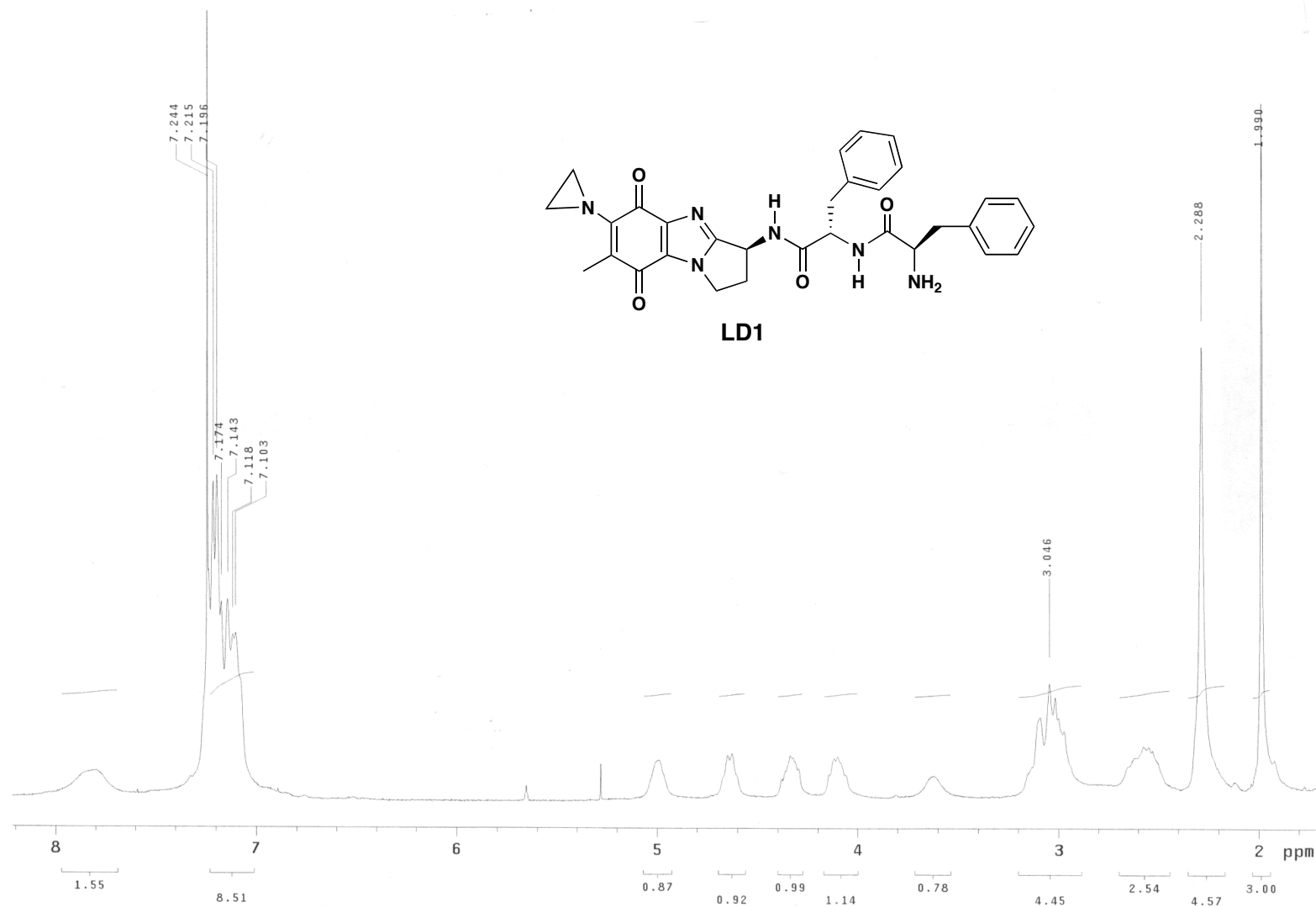
Triple Molecular Target Approach to Selective Melanoma Cytotoxicity

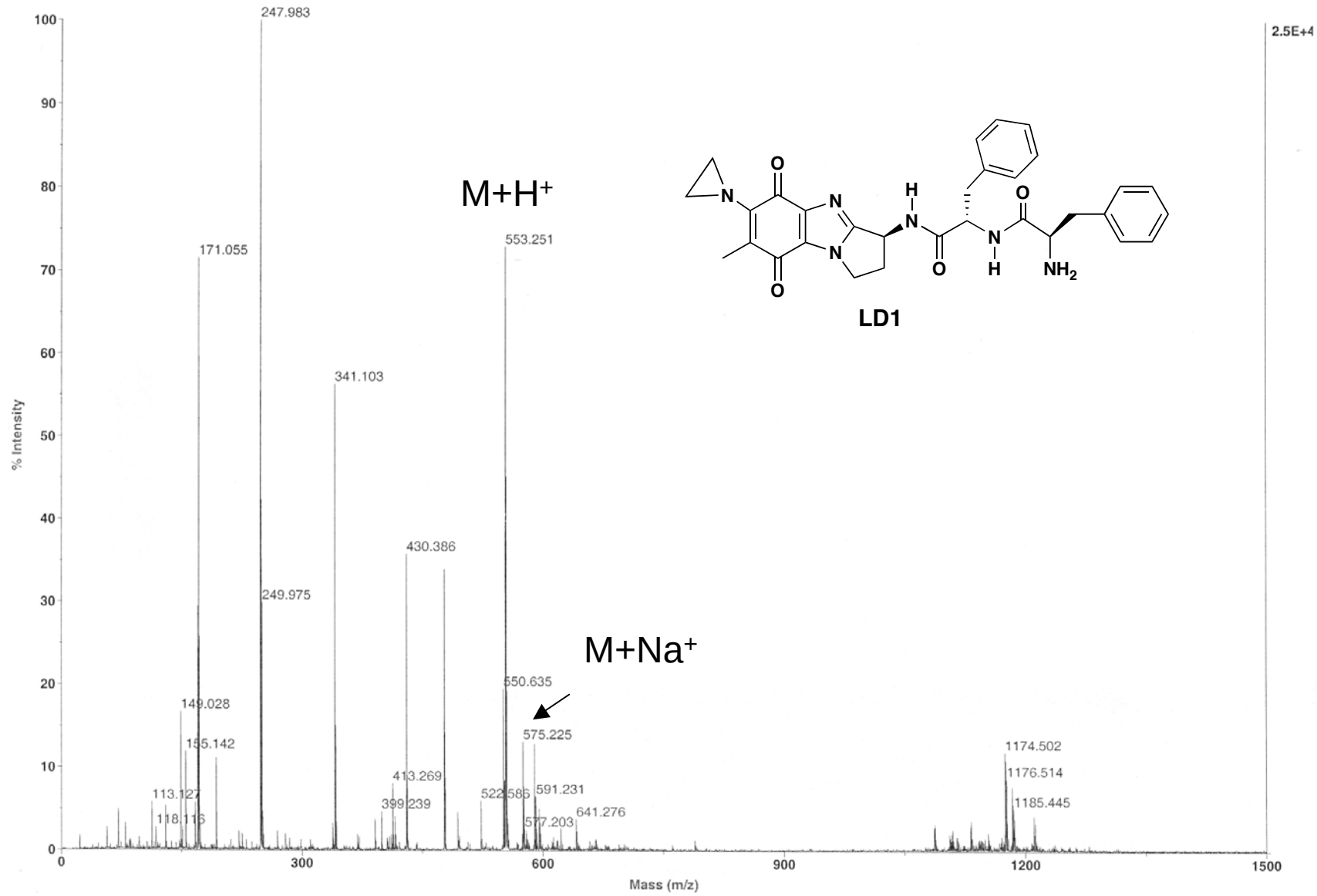
Edward B. Skibo, Akmal Jamil, Douglas Hansen, and Brittany Austin

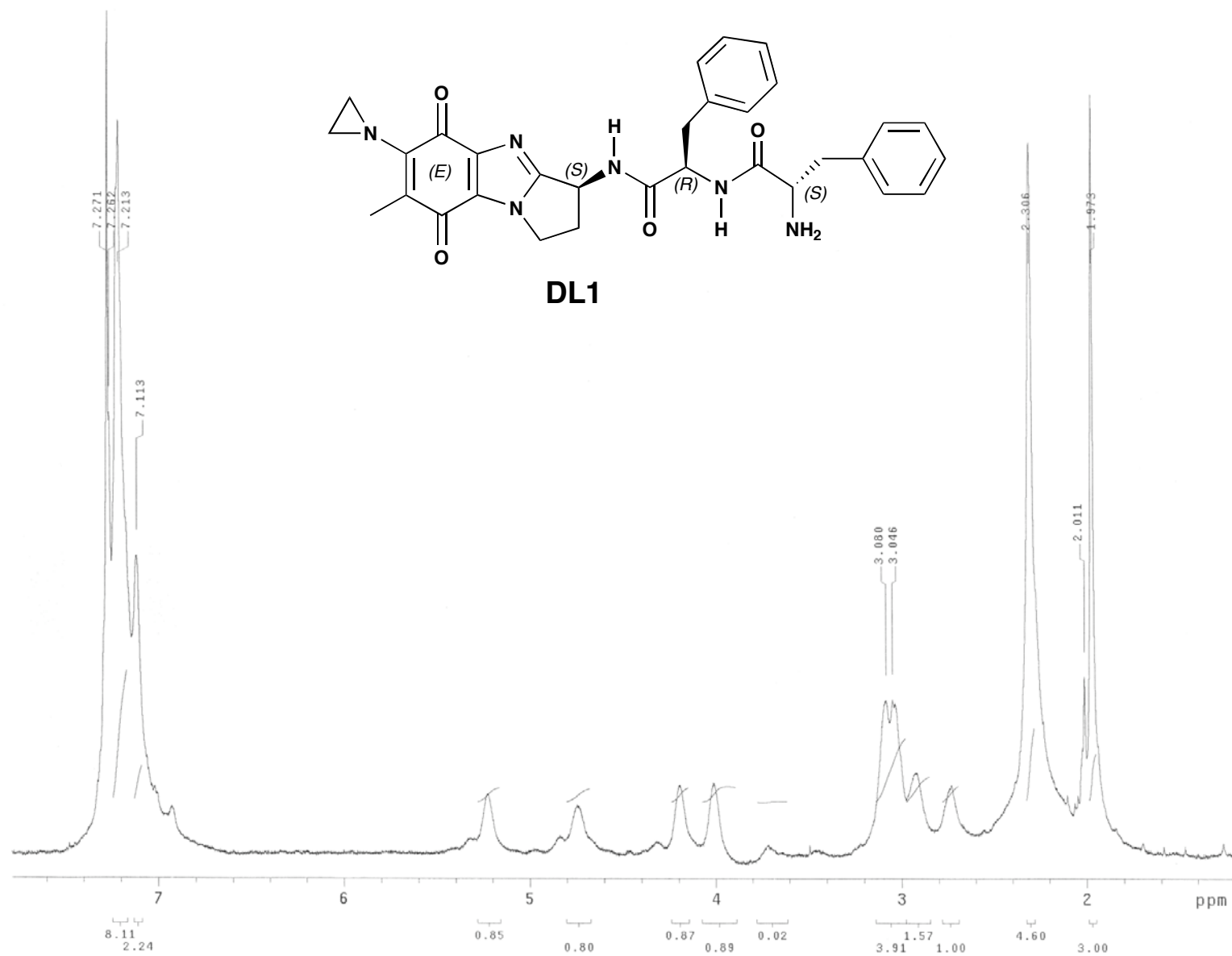
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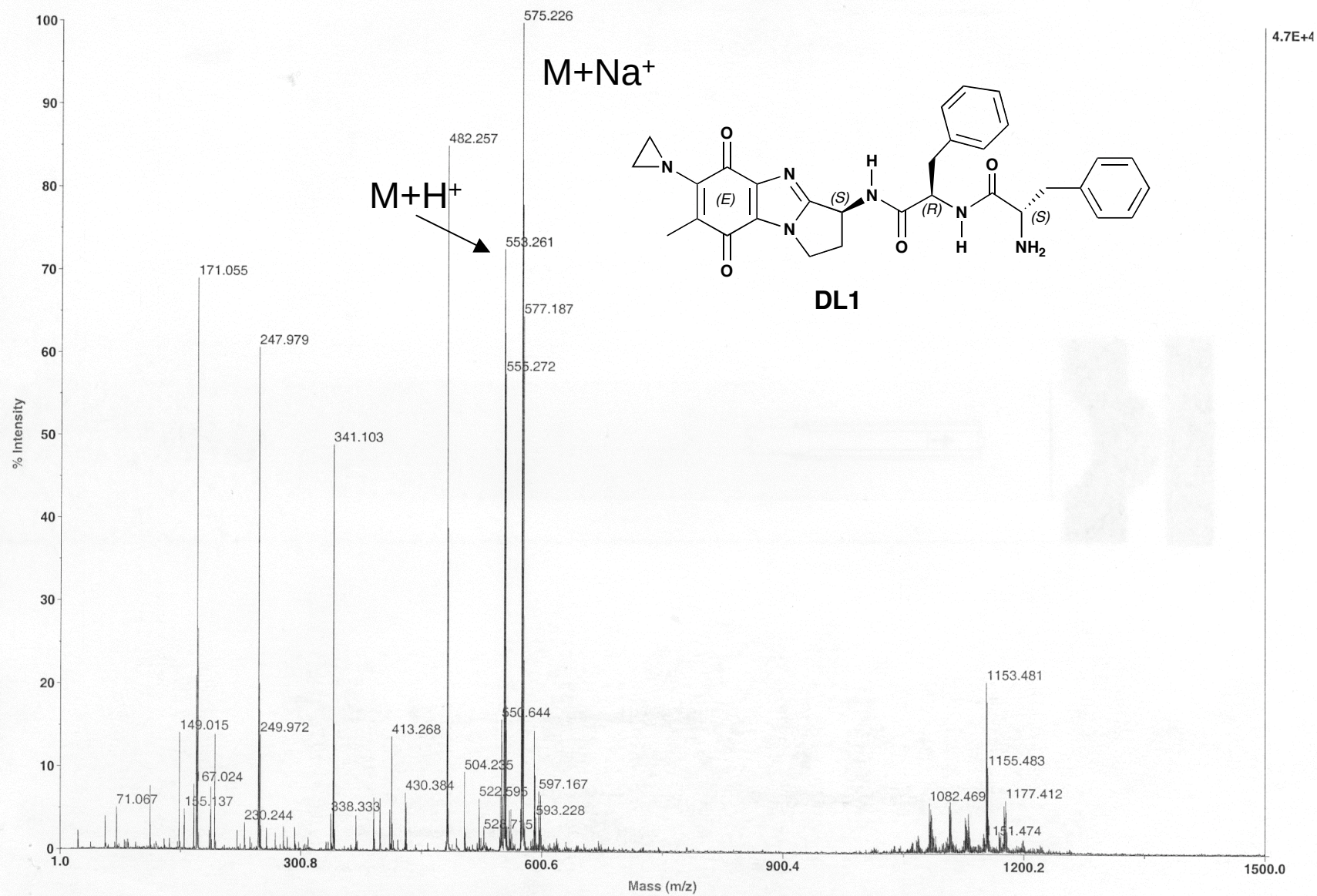
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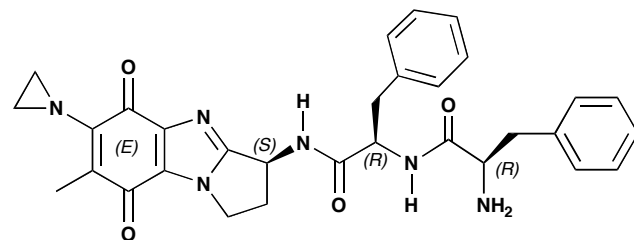




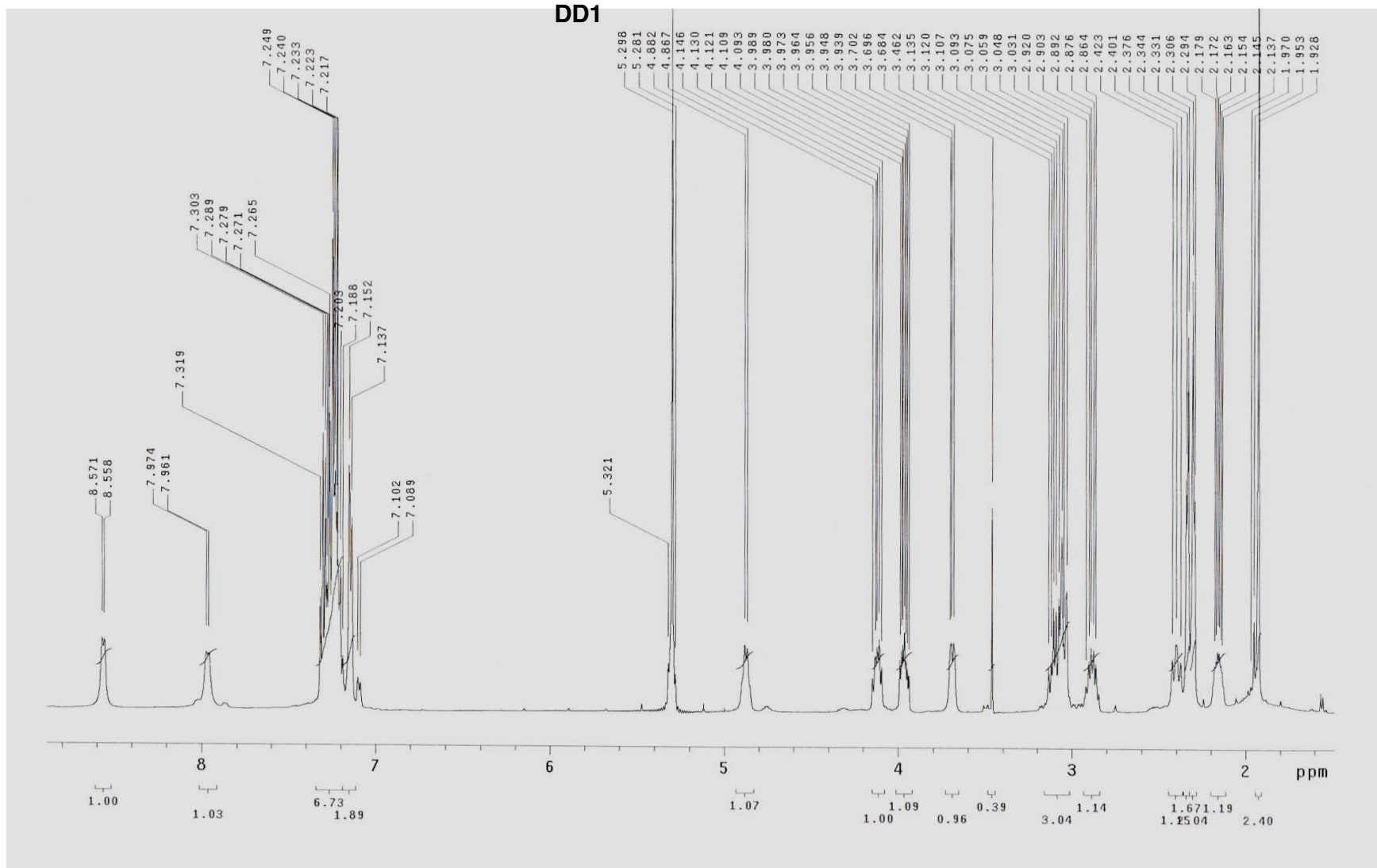


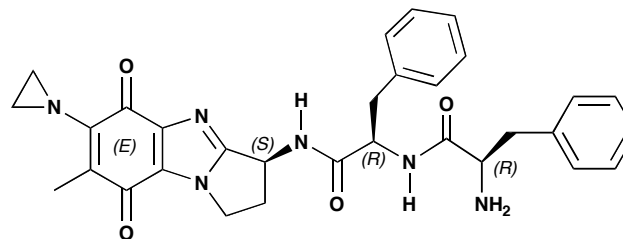


sample #A LR4-157 for A - levil 4 OH BMN motif



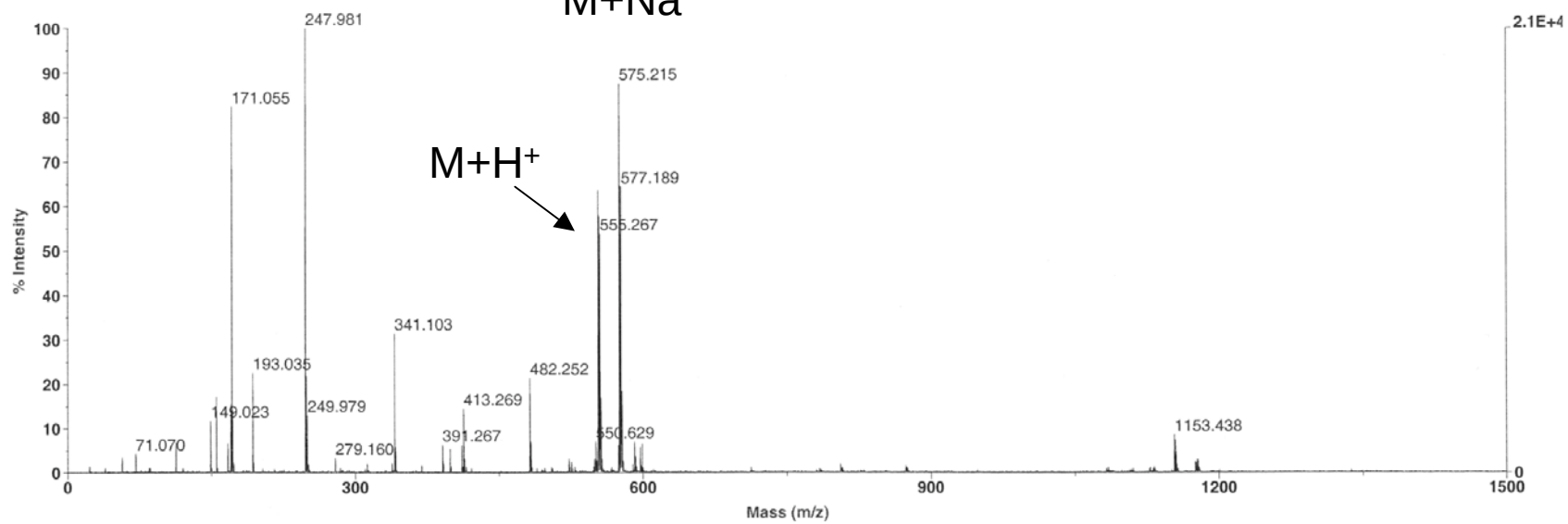
DD1

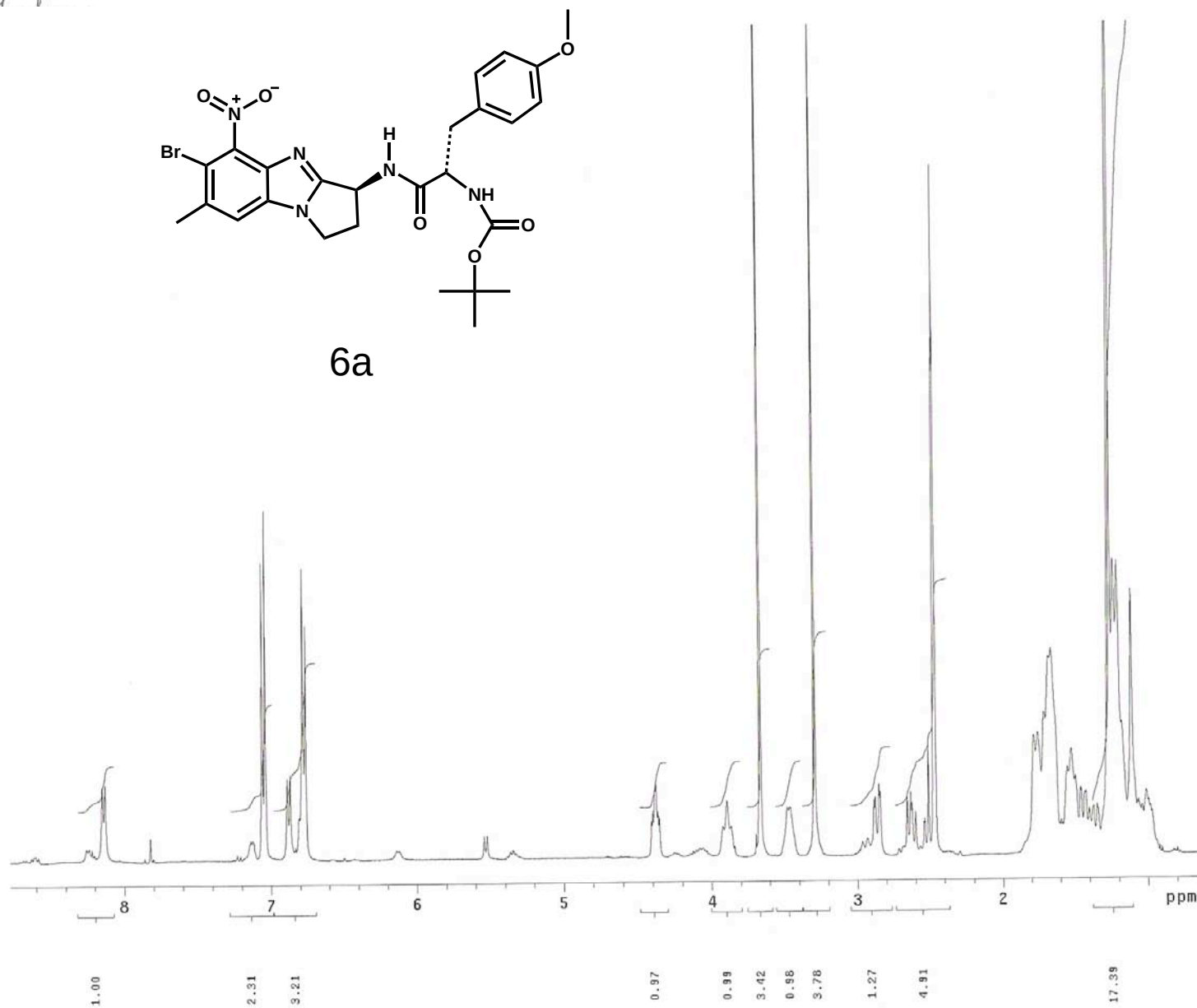


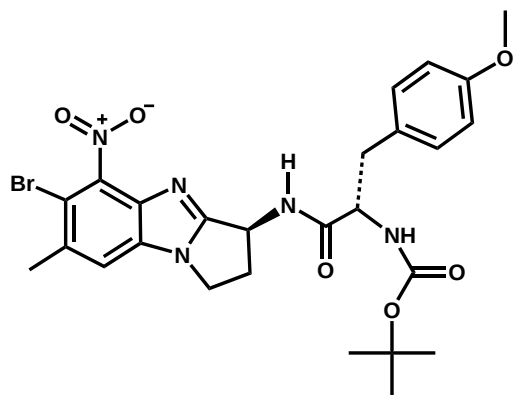


$M+Na^+$

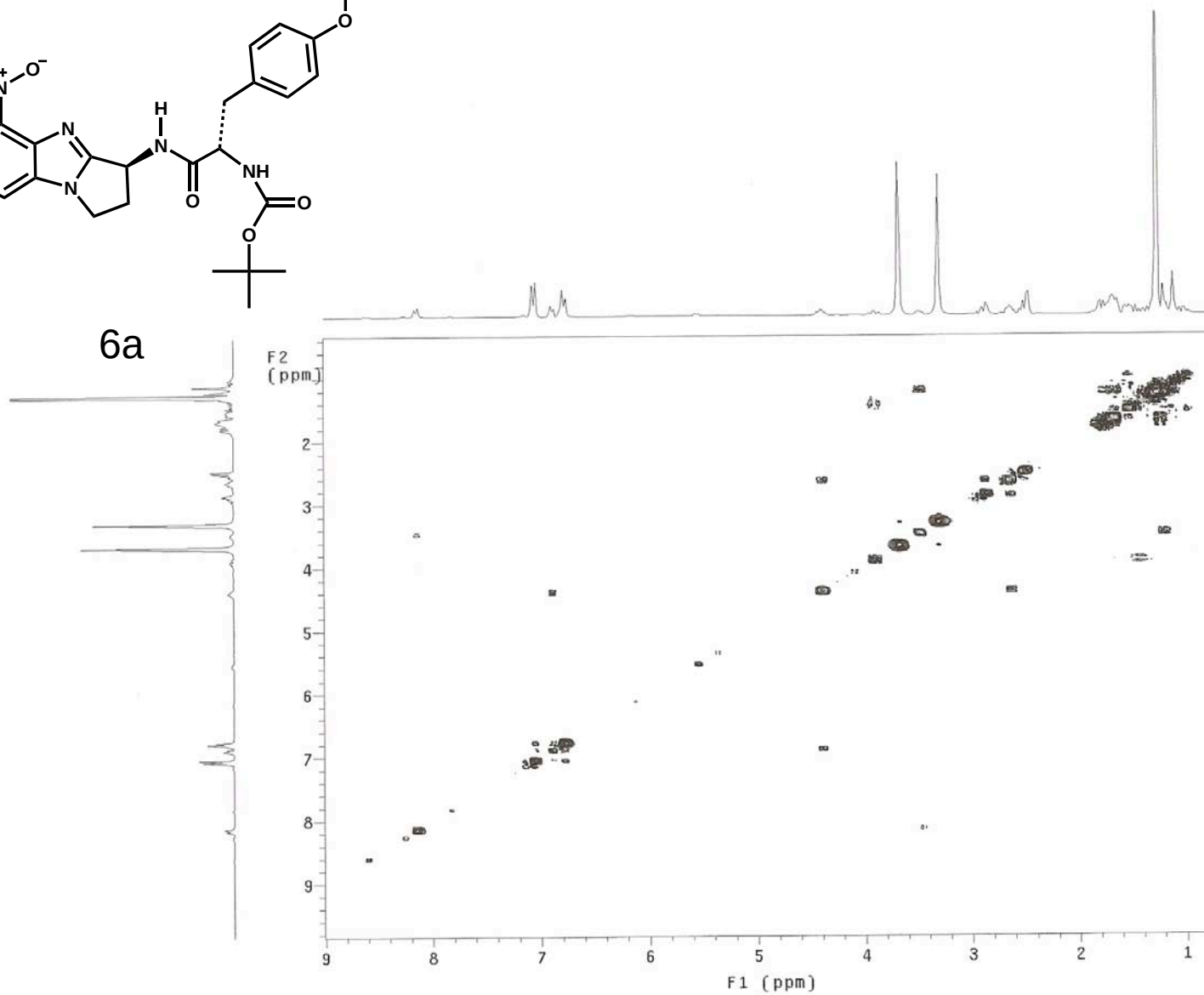
DD1

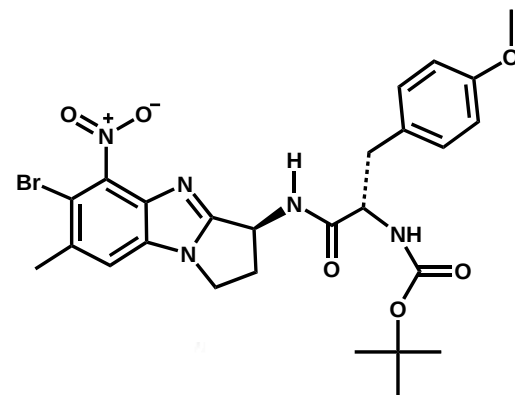






6a





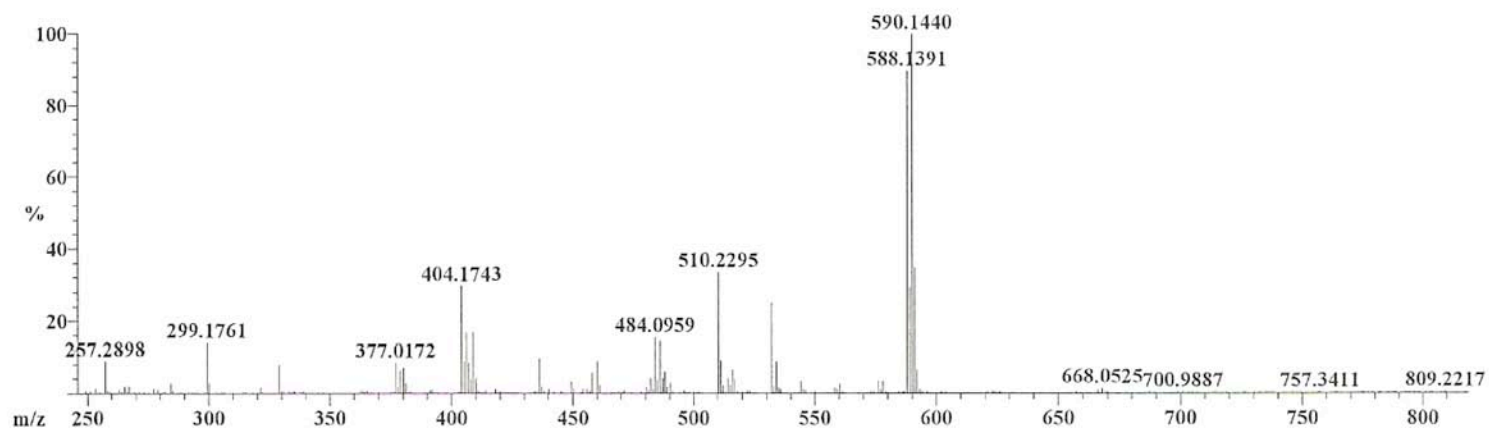
6a

#Ions: 760

Scan: 50 (35-39)

R.T.: 1.97

Base: m/z 590; 66.2%FS TIC: 5203698

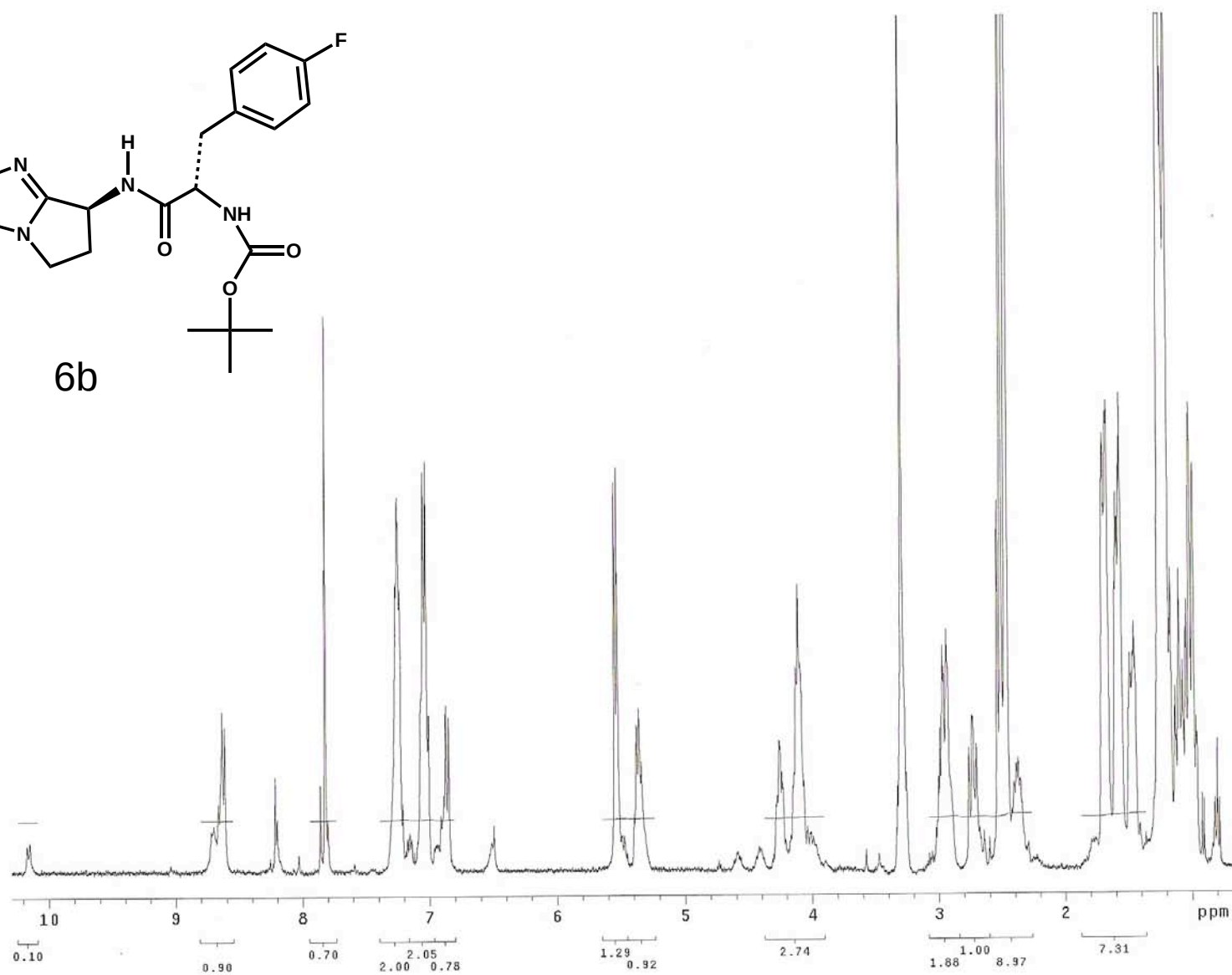
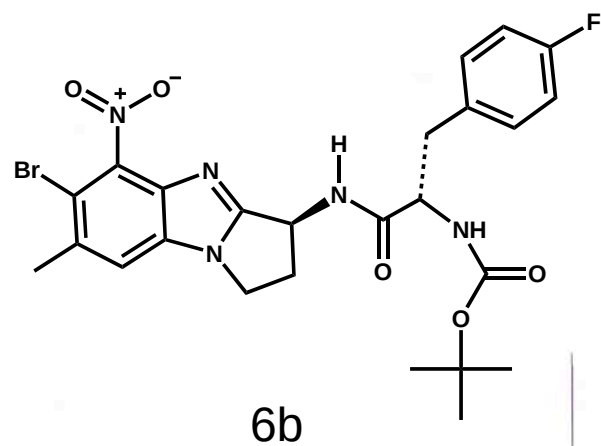


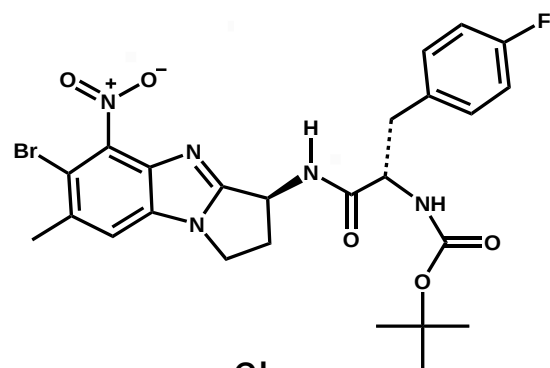
Selected Isotopes : $\text{C}_{26}\text{H}_{31}\text{N}_5\text{O}_6\text{Br}_{0-1}^{81}\text{Br}_{0-1}$

Error Limit : 100 ppm

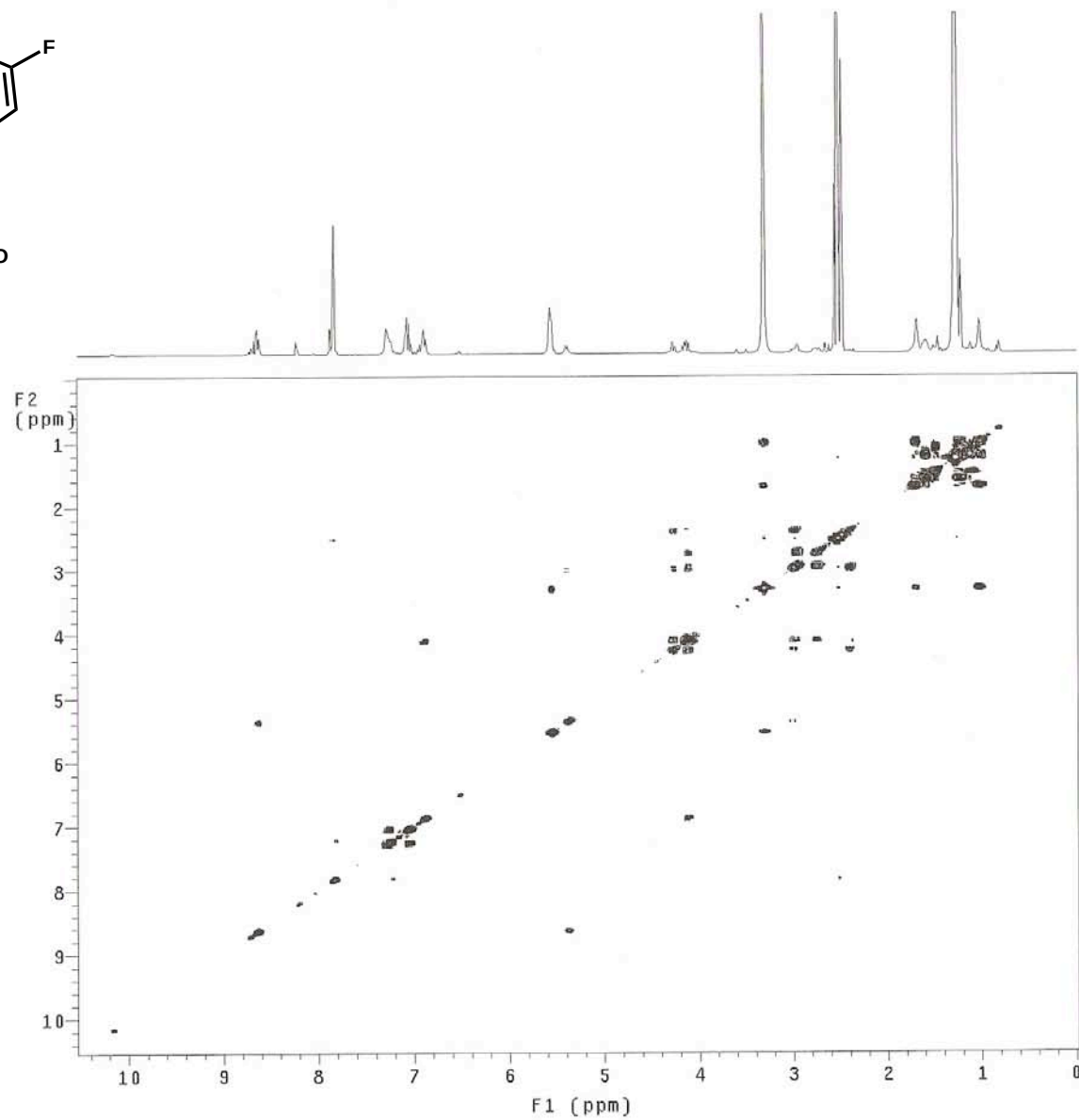
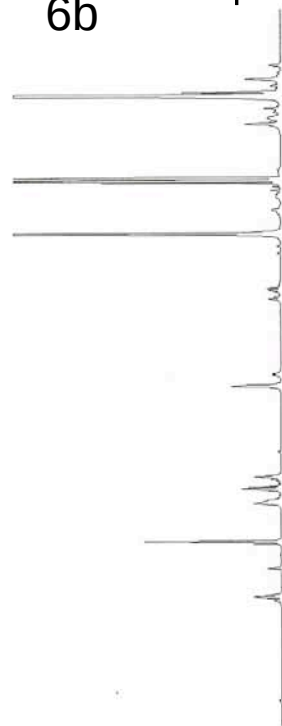
Unsaturation Limits : 12 to 30

<u>Measured Mass</u>	<u>% Base</u>	<u>Formula</u>	<u>Calculated Mass</u>	<u>Error</u>	<u>Unsaturation</u>
588.1391	89.8%	$\text{C}_{26}\text{H}_{31}\text{N}_5\text{O}_6\text{Br}$	588.1458	-11.0	13.5
590.1440	100.0%	$\text{C}_{26}\text{H}_{31}\text{N}_5\text{O}_6^{81}\text{Br}$	590.1437	0.5	13.5





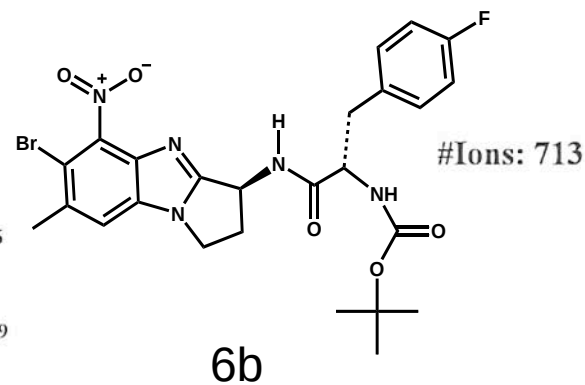
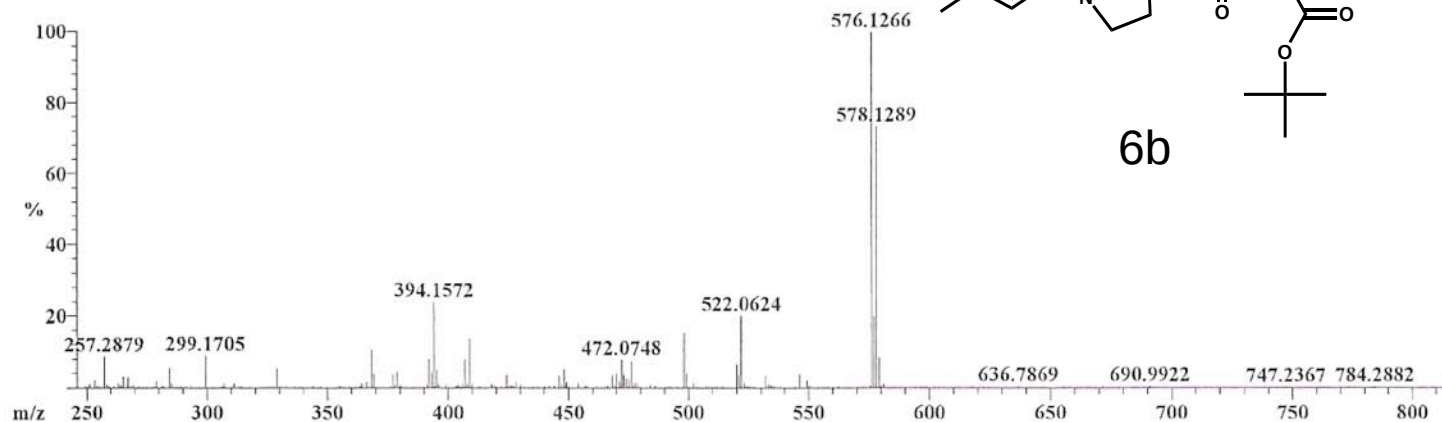
6b



Scan: 50 (24)

Base: m/z 576; 51.9%FS TIC: 2979808

R.T.: 1.97



Selected Isotopes : $C H N_5 O_5 F_{0-1} Br_{0-1} {}^{81}Br_{0-1}$

Error Limit : 100 ppm

Unsaturation Limits : 12 to 30

<u>Measured Mass</u>	<u>% Base</u>	<u>Formula</u>	<u>Calculated Mass</u>	<u>Error</u>	<u>Unsaturation</u>
576.1266	100.0%	$C_{25}H_{28}N_5O_5FBr$	576.1258	1.4	13.5
578.1289	73.4%	$C_{25}H_{28}N_5O_5F{}^{81}Br$	578.1237	8.9	13.5

File: exp

Pulse Sequence: s2pu1

Solvent: dms

Temp. 23.0 C / 296.1 K

Operator: walkup

VNMRS-400 "400MR"

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 2.049 sec

Width 4807.7 Hz

8 repetitions

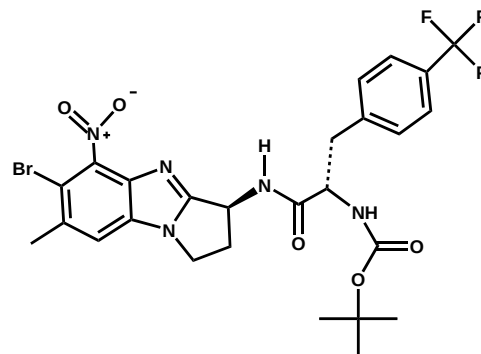
OBSERVE H1, 399.6498738 MHz

DATA PROCESSING

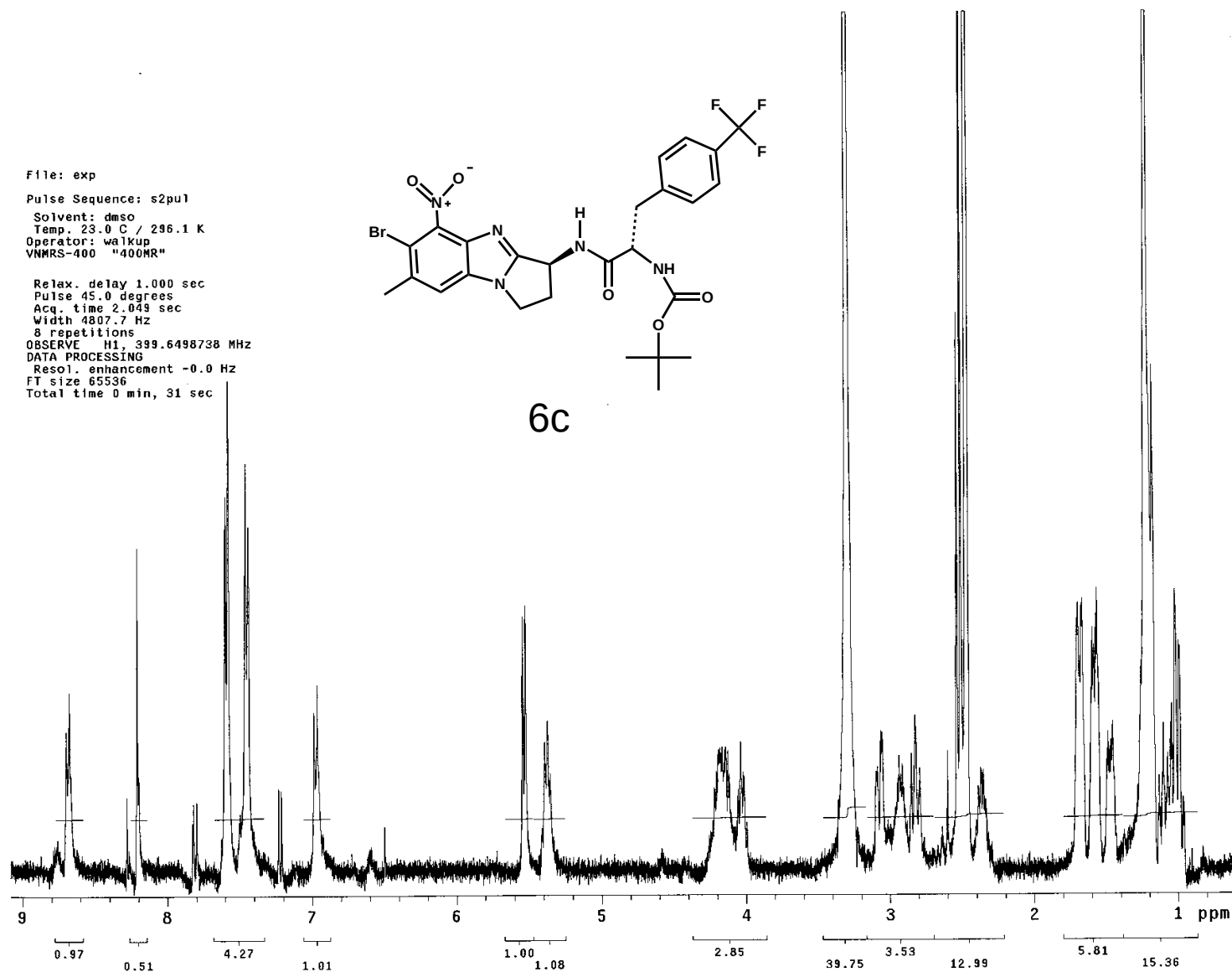
Resol. enhancement -0.0 Hz

FT size 65536

Total time 0 min, 31 sec



6c



File: exp

Pulse Sequence: gCDSY

Solvent: dmsd

Temp. 23.0 C / 296.1 K

Operator: walkup

VNMR-400 "400MR"

Relax. delay 1.000 sec

Acq. time 0.213 sec

Width 4006.4 Hz

ZD Width 4006.4 Hz

4 repetitions

128 increments

OBSERVE H1, 399.6498738 MHz

DATA PROCESSING

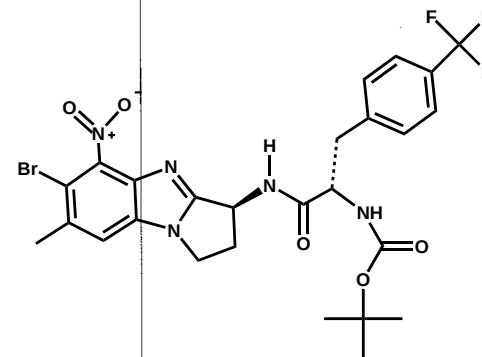
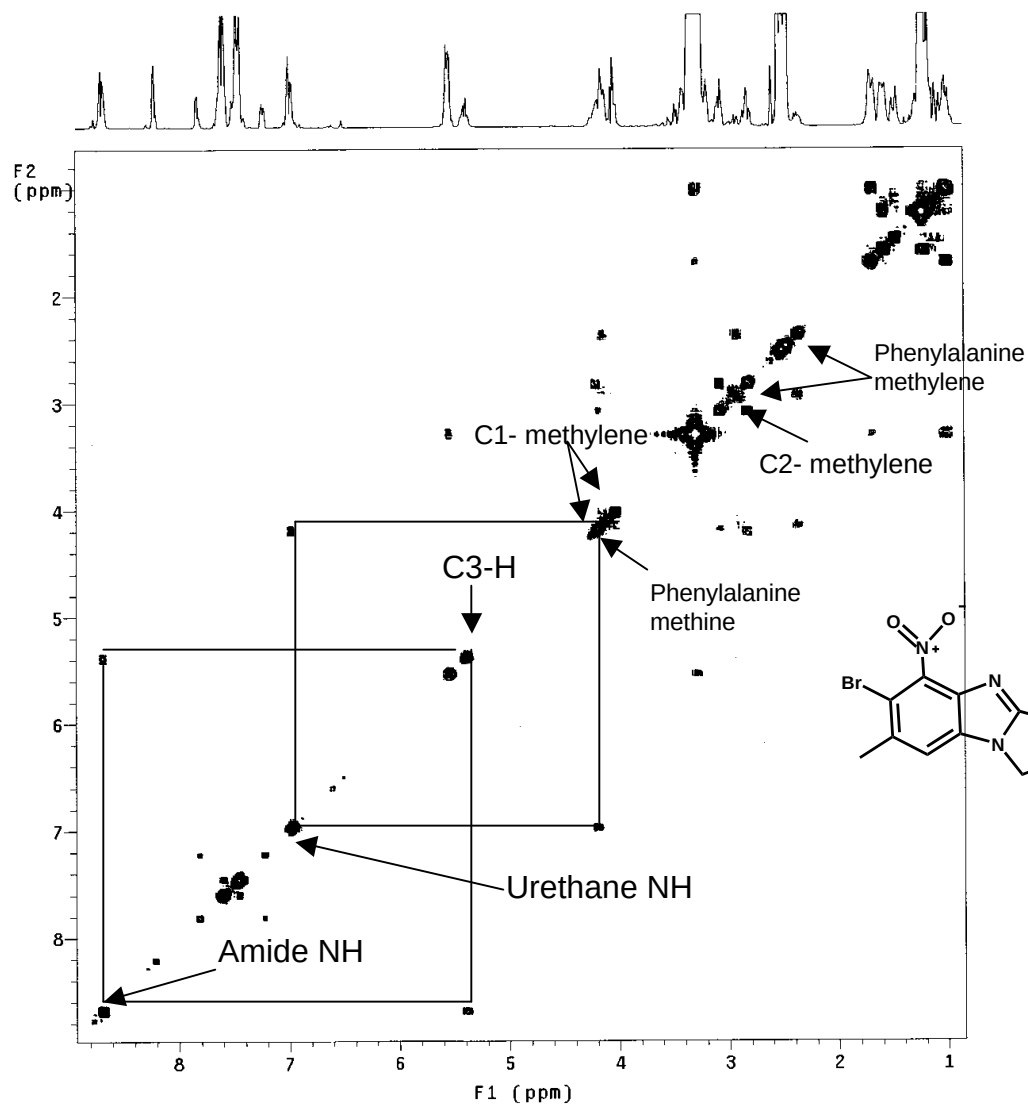
Sine bell 0.100 sec

F1 DATA PROCESSING

Sine bell 0.036 sec

FT size 2048 x 2048

Total time 10 min, 58 sec

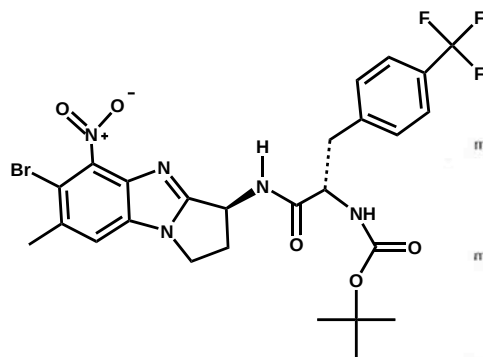


6c

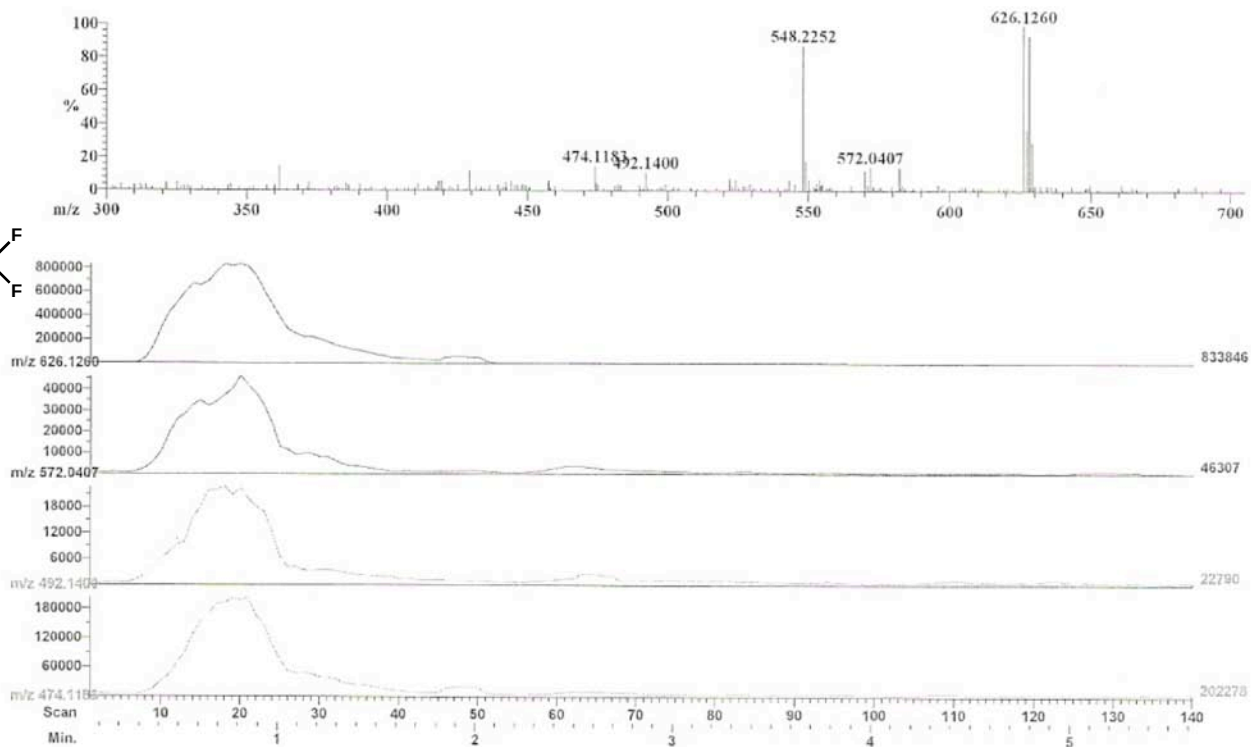
Scan: 9 (3-5)
Base: m/z 626; 2.7%FS TIC: 284964

R.T.: .37

#Ions: 299



6c



Scan: 9 (3-5)
Base: m/z 626; 2.7%FS TIC: 284964

R.T.: .37

#Ions: 299

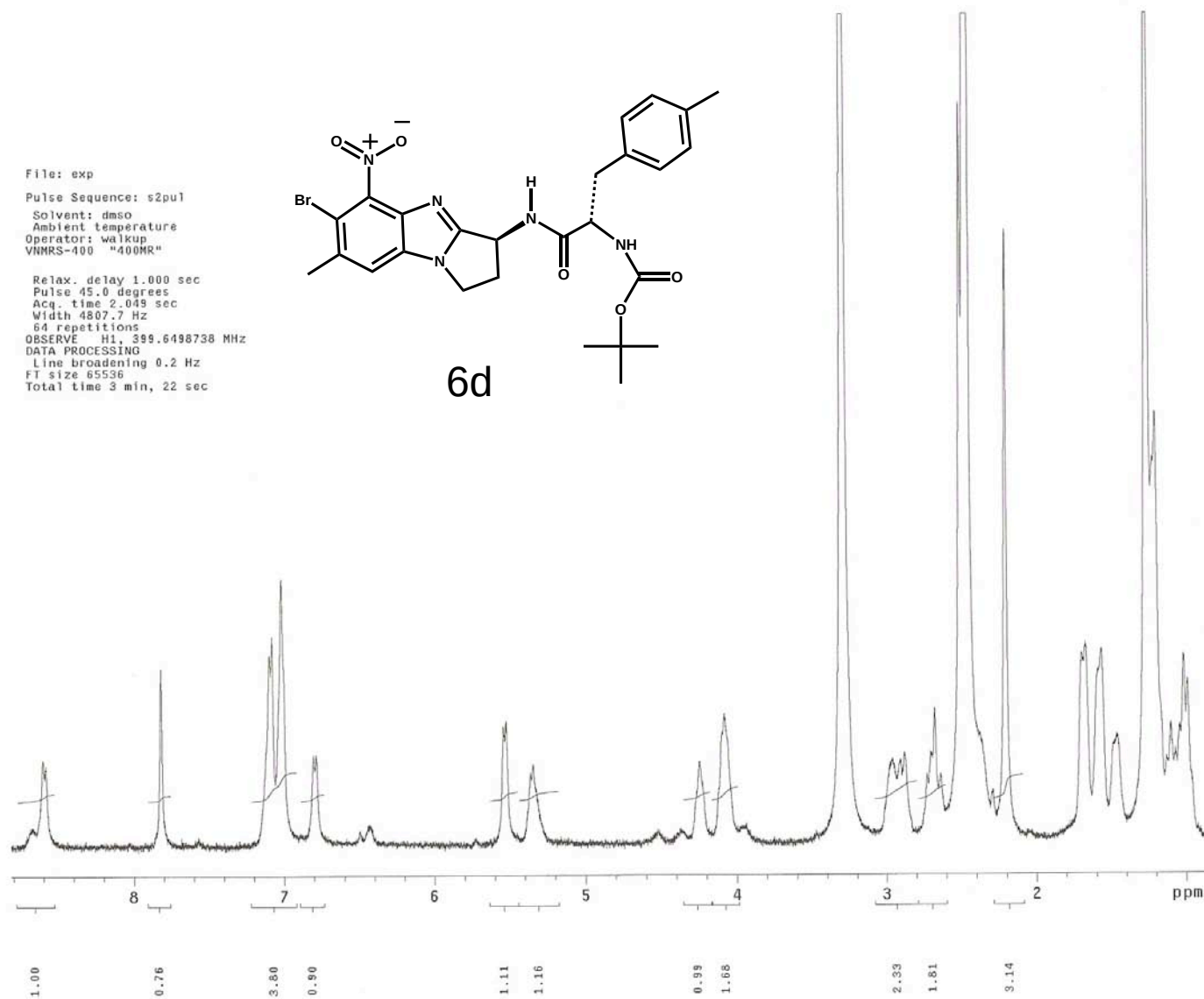
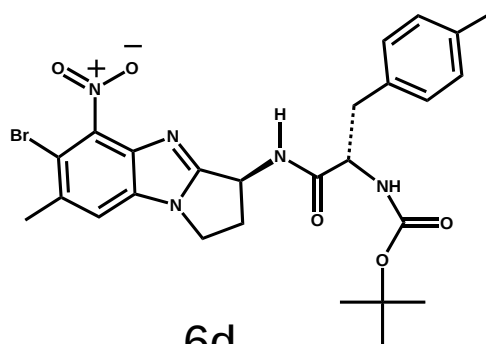
Selected Isotopes : $C_5H_{0.3}O_5F_{0.3}Br_{0.1}N_5$

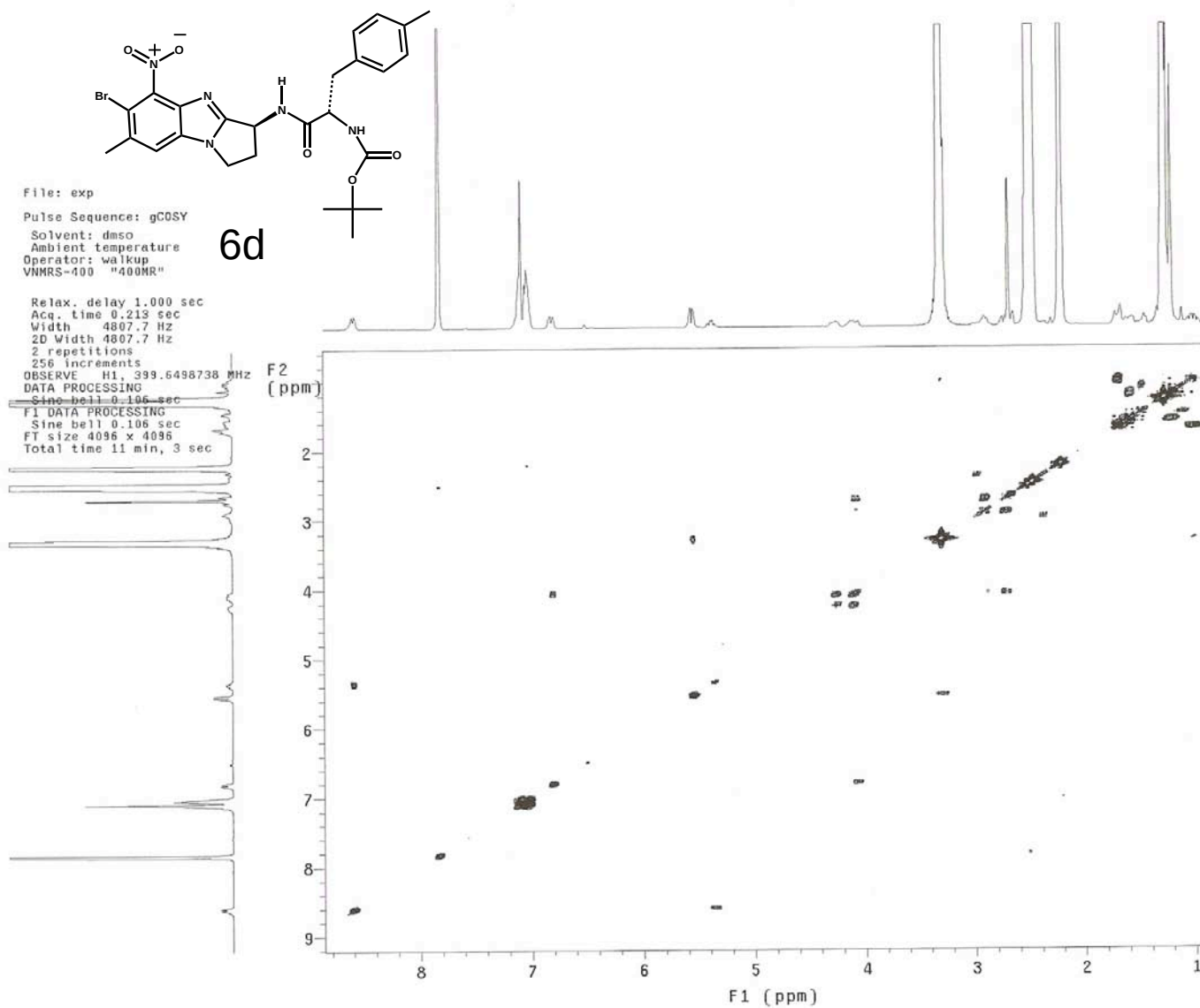
Error Limit : 10 ppm

Unsaturation Limits : 0 to 50

<u>Measured Mass</u>	<u>% Base</u>	<u>Formula</u>	<u>Calculated Mass</u>	<u>Error</u>	<u>Unsaturation</u>
626.1260	100.0%	$C_{26}H_{28}O_5F_3BrN_5$	626.1226	5.5	13.5

File: exp
Pulse Sequence: s2pu1
Solvent: dmsO
Ambient temperature
Operator: walkup
VNMRS-400 "400MR"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 4807.7 Hz
64 repetitions
OBSERVE H1, 399.6498738 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 22 sec

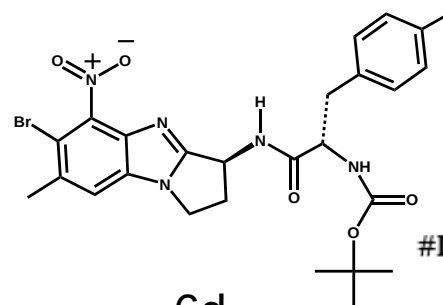




Scan: 36-40 (23)

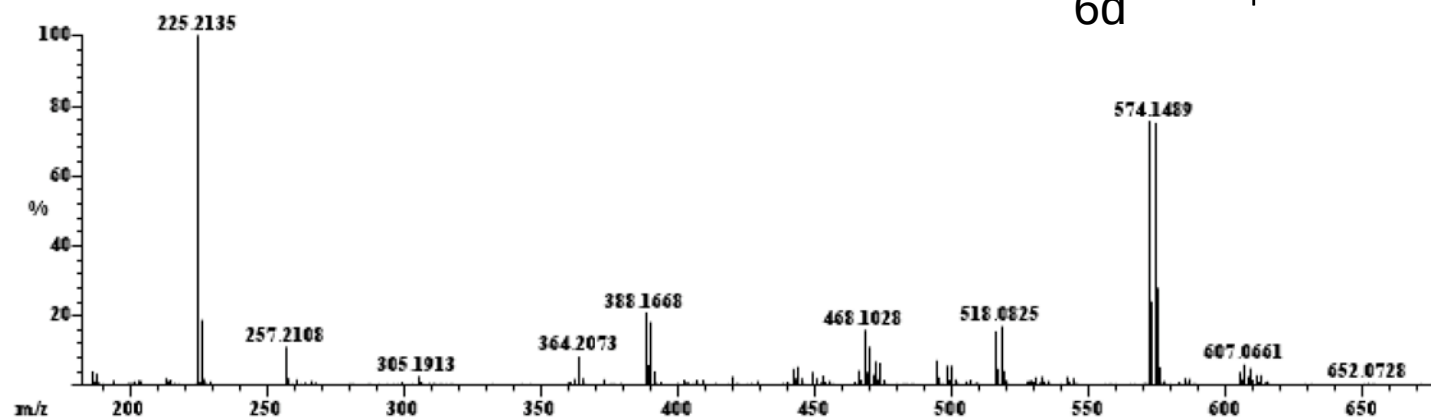
R.T.: 2.15

Base: m/z 225; 83.4%FS TIC: 6519490 (Max Inten : 874803)



6d

#Ions: 2218

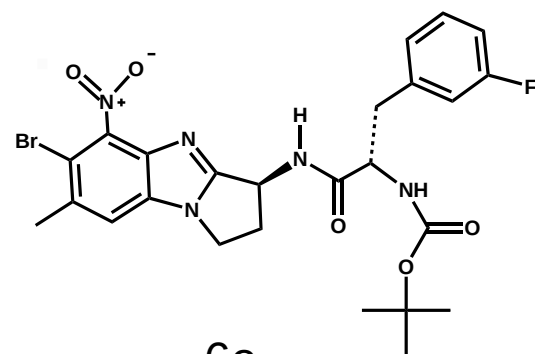


Selected Isotopes : C H N₅ O₅ Br_{0.1} ⁸¹Br_{0.1}

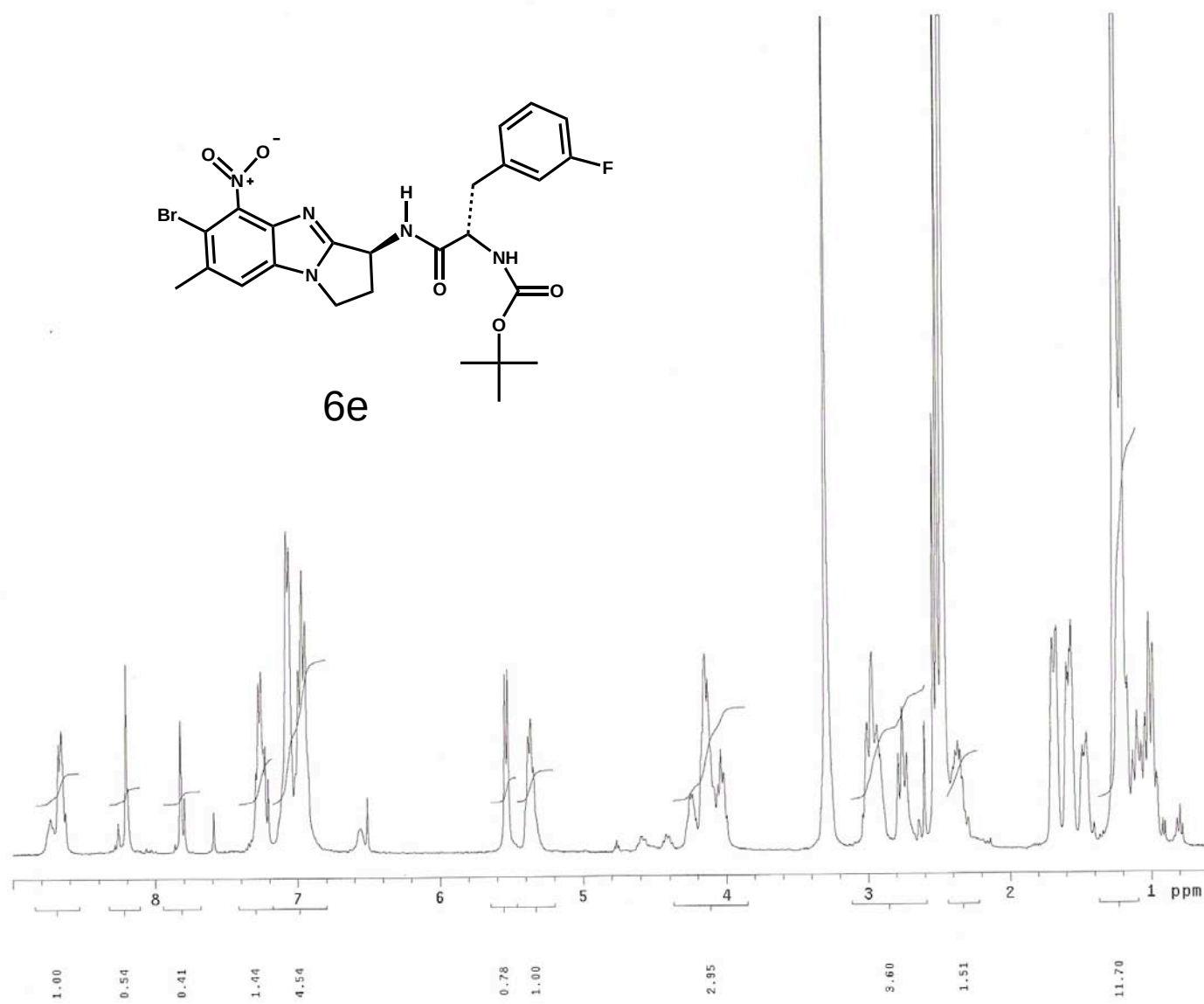
Error Limit : 20 ppm

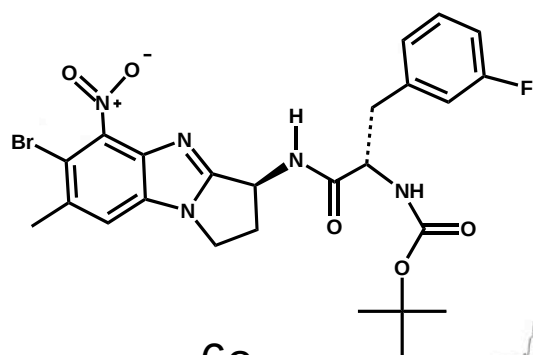
Unsaturation Limits : 0 to 50

<u>Measured Mass</u>	<u>% Base</u>	<u>Formula</u>	<u>Calculated Mass</u>	<u>Error</u>	<u>Unsaturation</u>
516.0851	15.2%	C ₂₂ H ₂₃ N ₅ O ₅ Br	516.0882	-6.1	13.5
518.0825	16.7%	C ₂₂ H ₂₃ N ₅ O ₅ ⁸¹ Br	518.0862	-7.2	13.5
572.1535	75.3%	C ₂₆ H ₃₁ N ₅ O ₅ Br	572.1508	4.6	13.5
574.1489	74.9%	C ₂₆ H ₃₁ N ₅ O ₅ ⁸¹ Br	574.1488	0.2	13.5

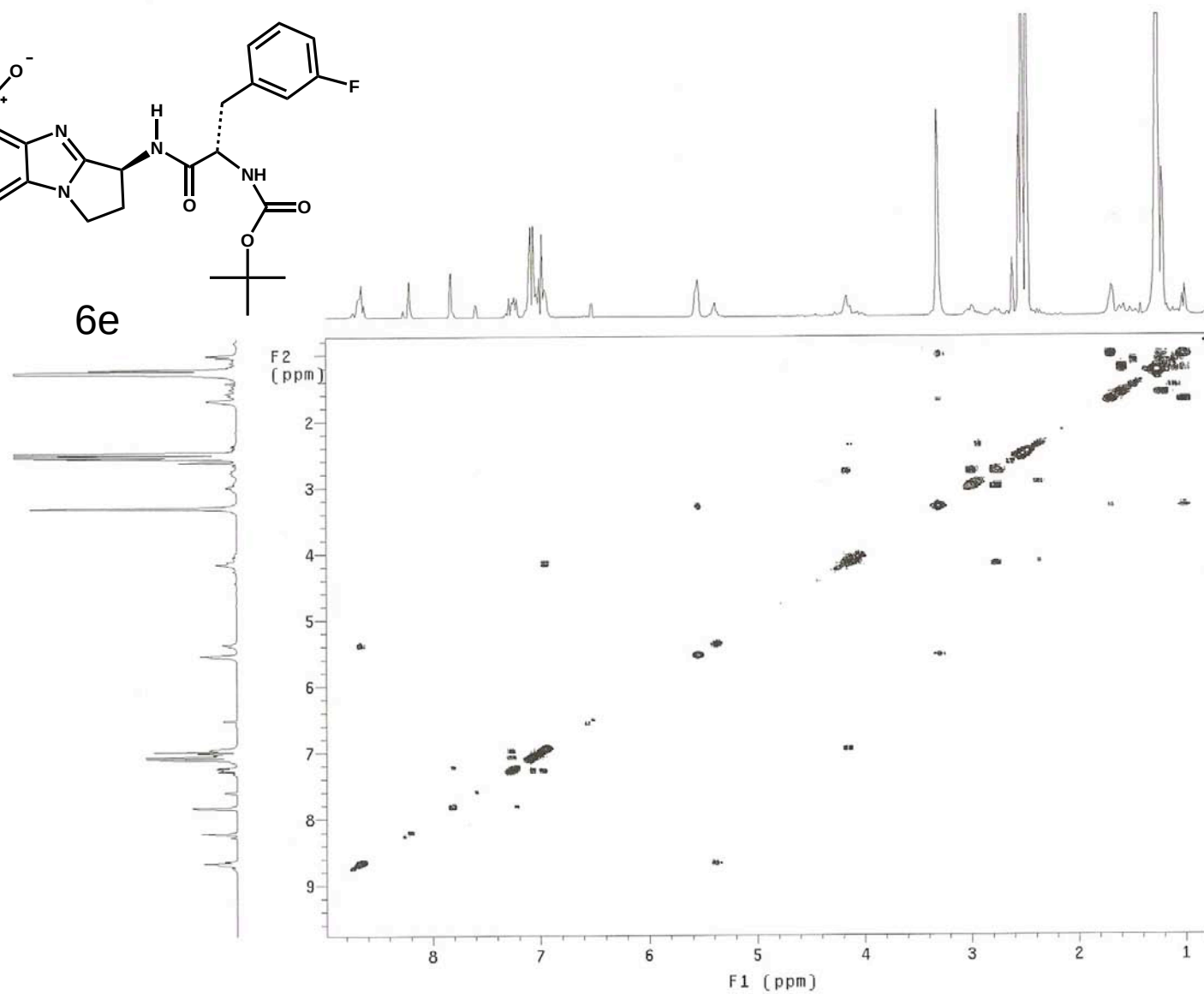


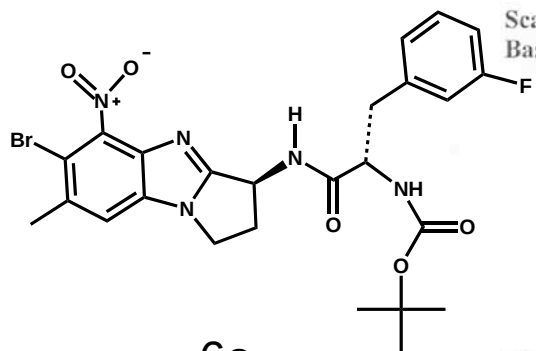
6e





6e



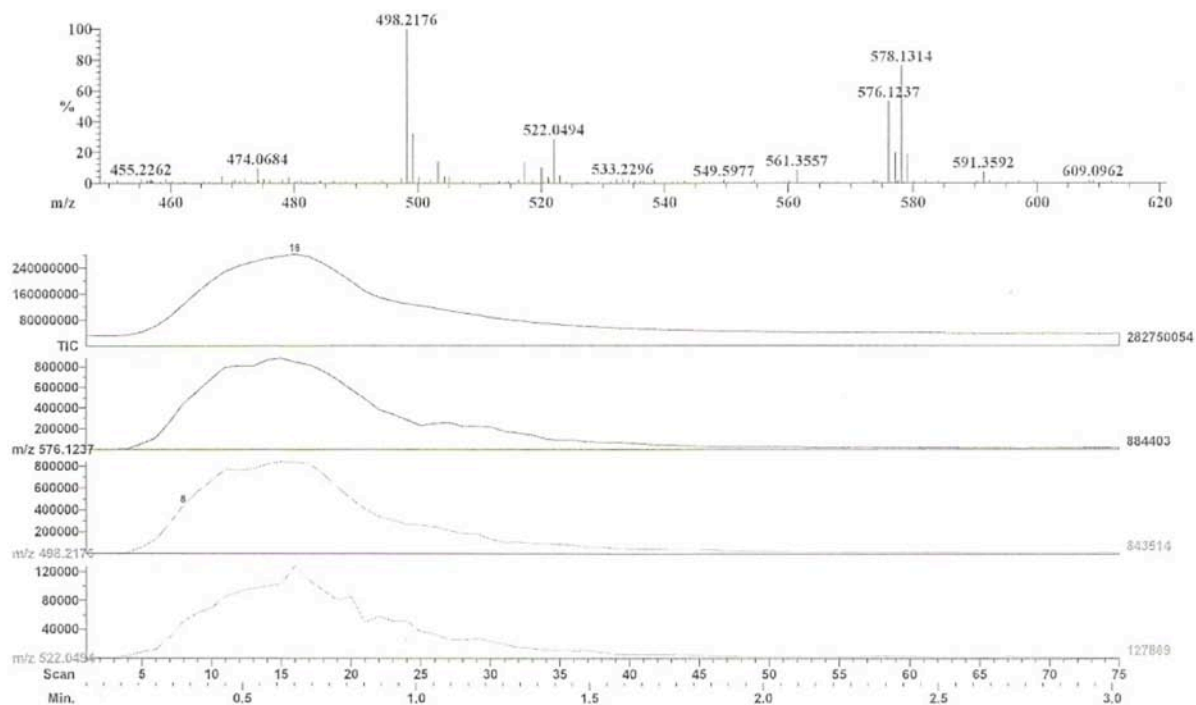


6e

Scan: 6 (3-5)
Base: m/z 498; 4.1%FS TIC: 427374

R.T.: .25

#Ions: 346



Scan: 6 (3-5)
Base: m/z 498; 4.1%FS TIC: 427374

R.T.: .25

#Ions: 346

Selected Isotopes : $\text{C}_{25}\text{H}_{28}\text{N}_5\text{O}_5\text{F}_{0-1}\text{Br}_{0-1}$

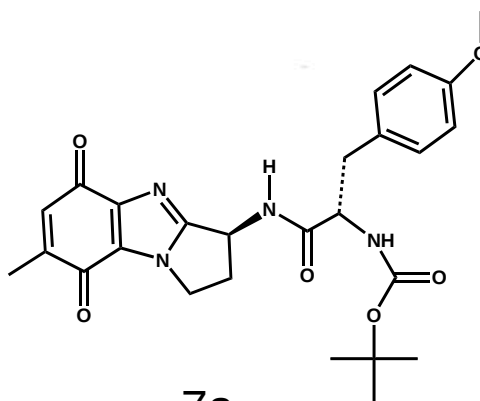
Error Limit : 5 ppm

Unsaturation Limits : 0 to 50

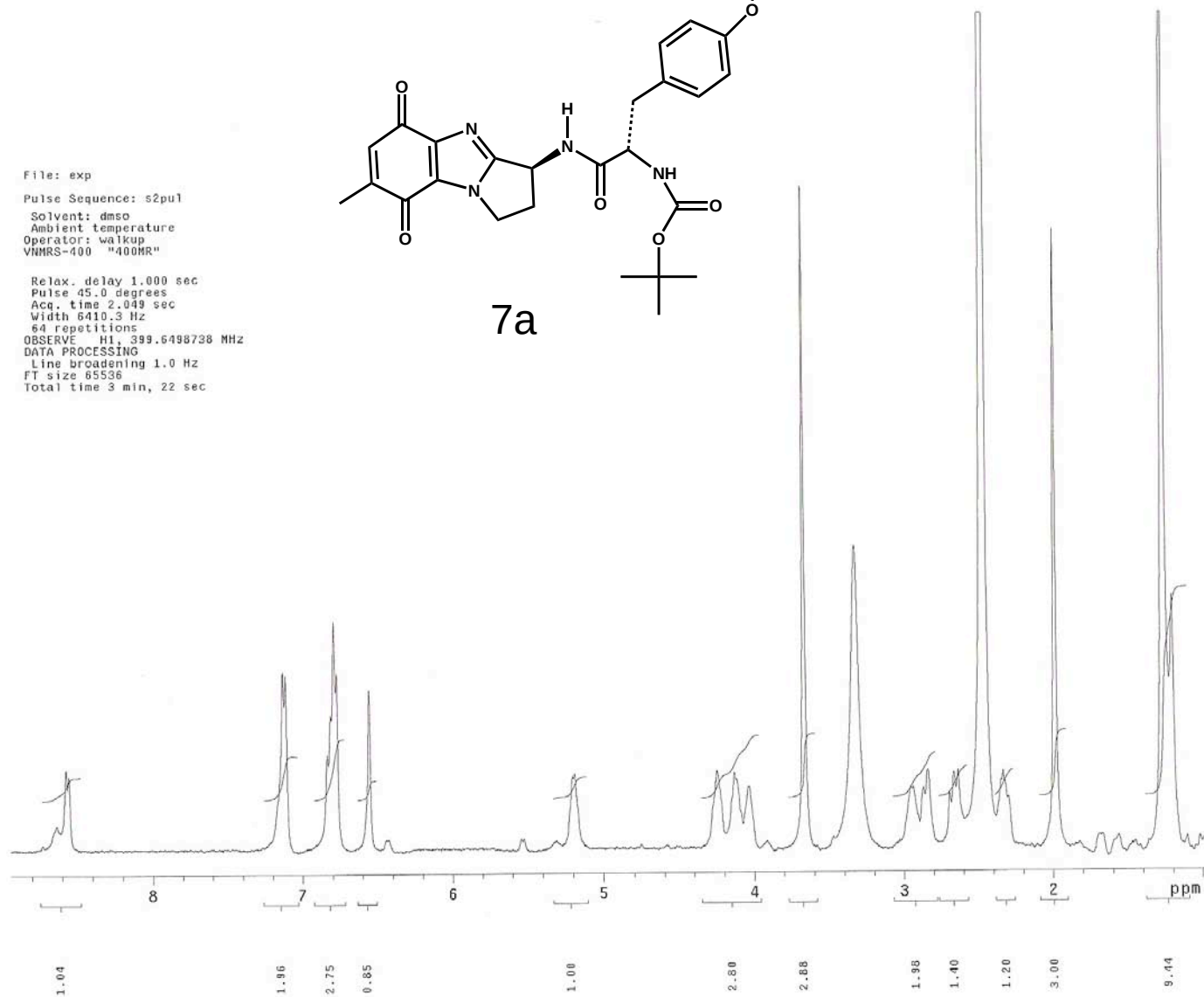
<u>Measured Mass</u>	<u>% Base</u>	<u>Formula</u>	<u>Calculated Mass</u>	<u>Error</u>	<u>Unsaturation</u>
576.1237	53.3%	$\text{C}_{25}\text{H}_{28}\text{N}_5\text{O}_5\text{F Br}$	576.1258	-3.6	13.5

File: exp
Pulse Sequence: s2pu1
Solvent: dmsd
Ambient temperature
Operator: walkup
VNMRS-400 "400MR"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 6410.3 Hz
64 repetitions
OBSERVE H1, 399.6498738 MHz
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 3 min, 22 sec



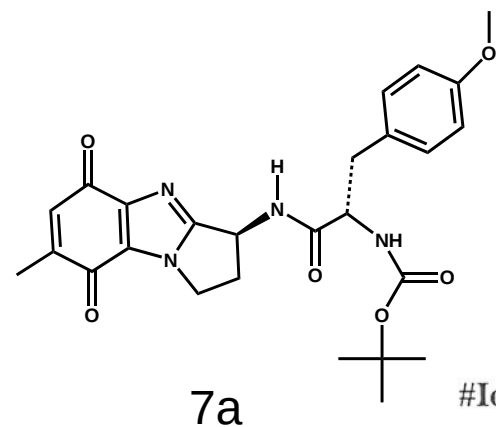
7a



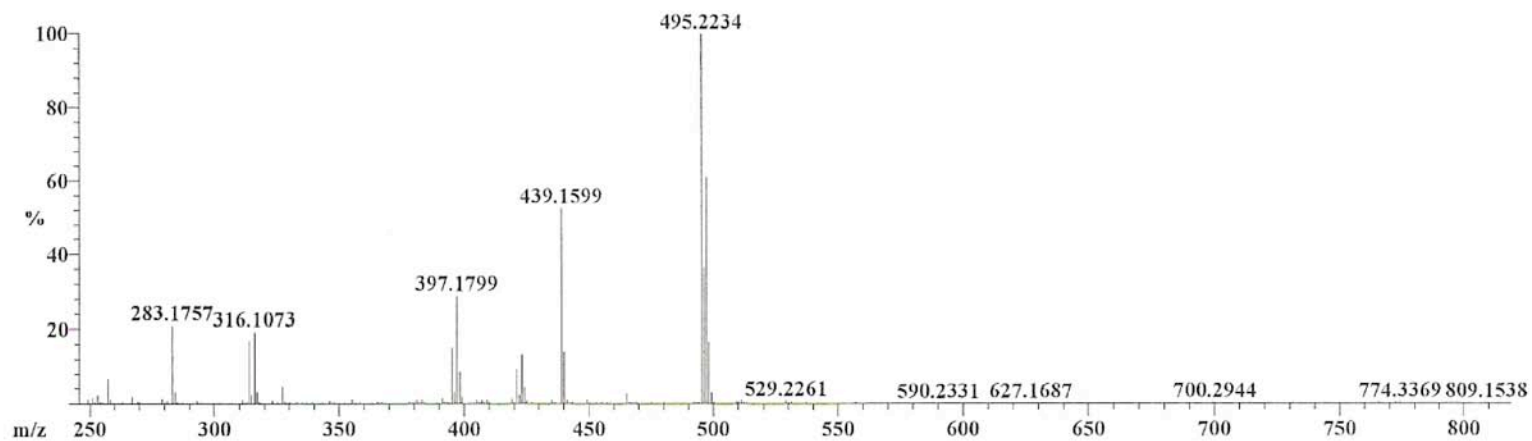
Scan: 40-50 (14-17)

Base: m/z 495; 60.2%FS TIC: 3413858

R.T.: 1.83



#Ions: 2070

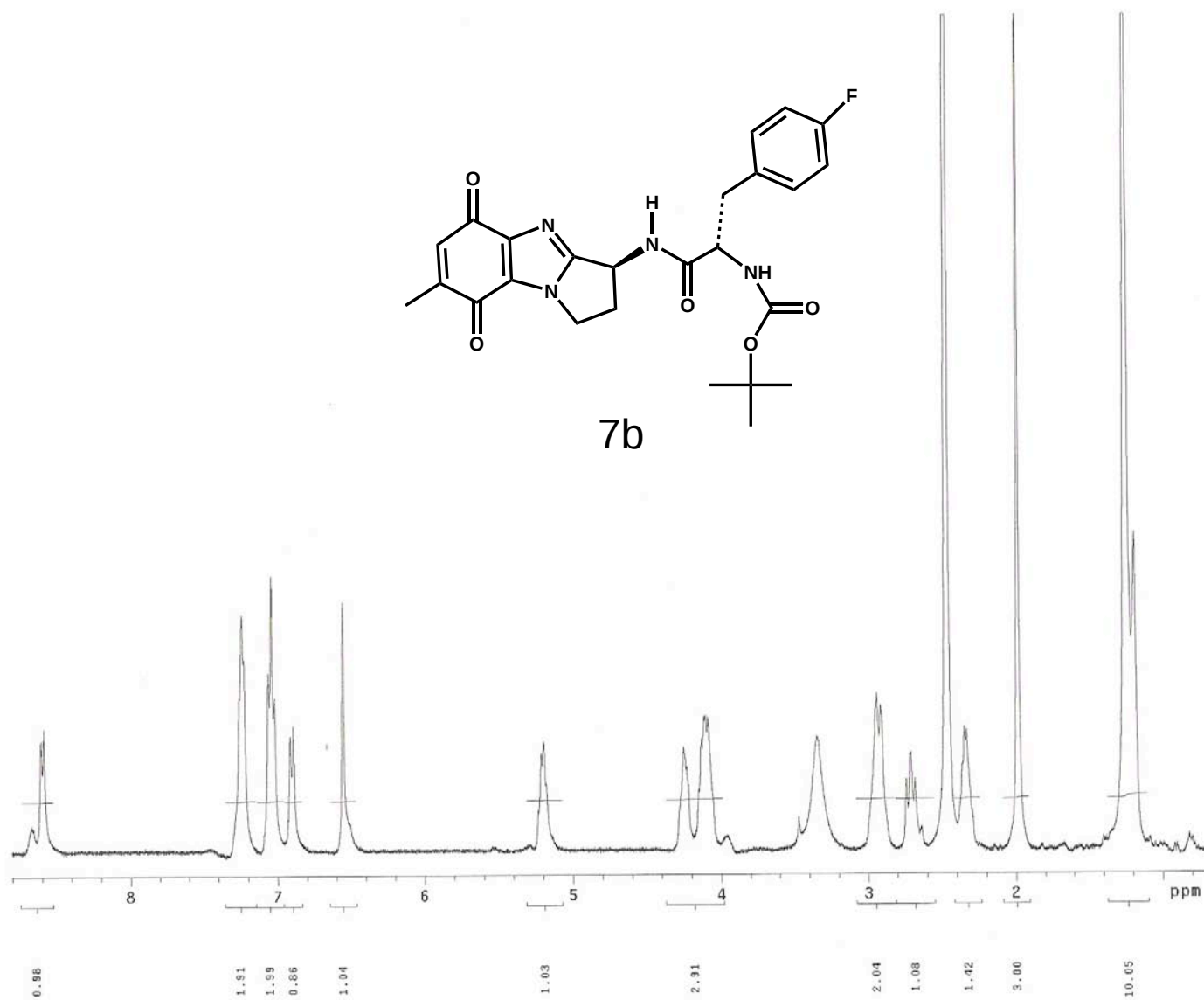
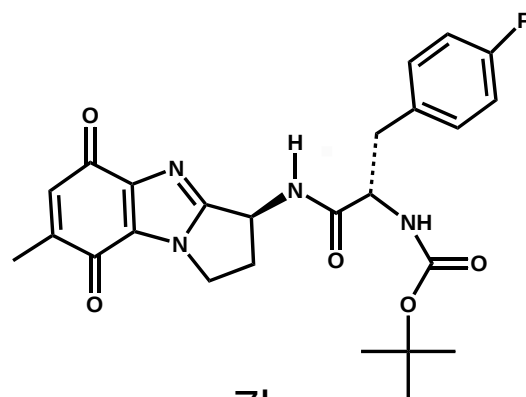


Selected Isotopes : C H N₄O₆

Error Limit : 100 ppm

Unsaturation Limits : 12 to 30

<u>Measured Mass</u>	<u>% Base</u>	<u>Formula</u>	<u>Calculated Mass</u>	<u>Error</u>	<u>Unsaturation</u>
495.2234	100.0%	C ₂₆ H ₃₁ N ₄ O ₆	495.2244	-1.9	13.5



File: exp

Pulse Sequence: gCOSY

Solvent: dmsd

Ambient temperature

Operator: walkup

VNMRS-400 "400MR"

Relax. delay 1.000 sec

Acq. time 0.213 sec

Width 4807.7 Hz

2D Width 4807.7 Hz

4 repetitions

128 increments

OBSERVE H1 399.6498738 MHz

DATA PROCESSING

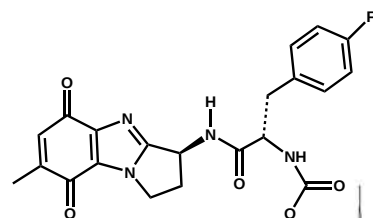
Sine bell 0.106 sec

F1 DATA PROCESSING

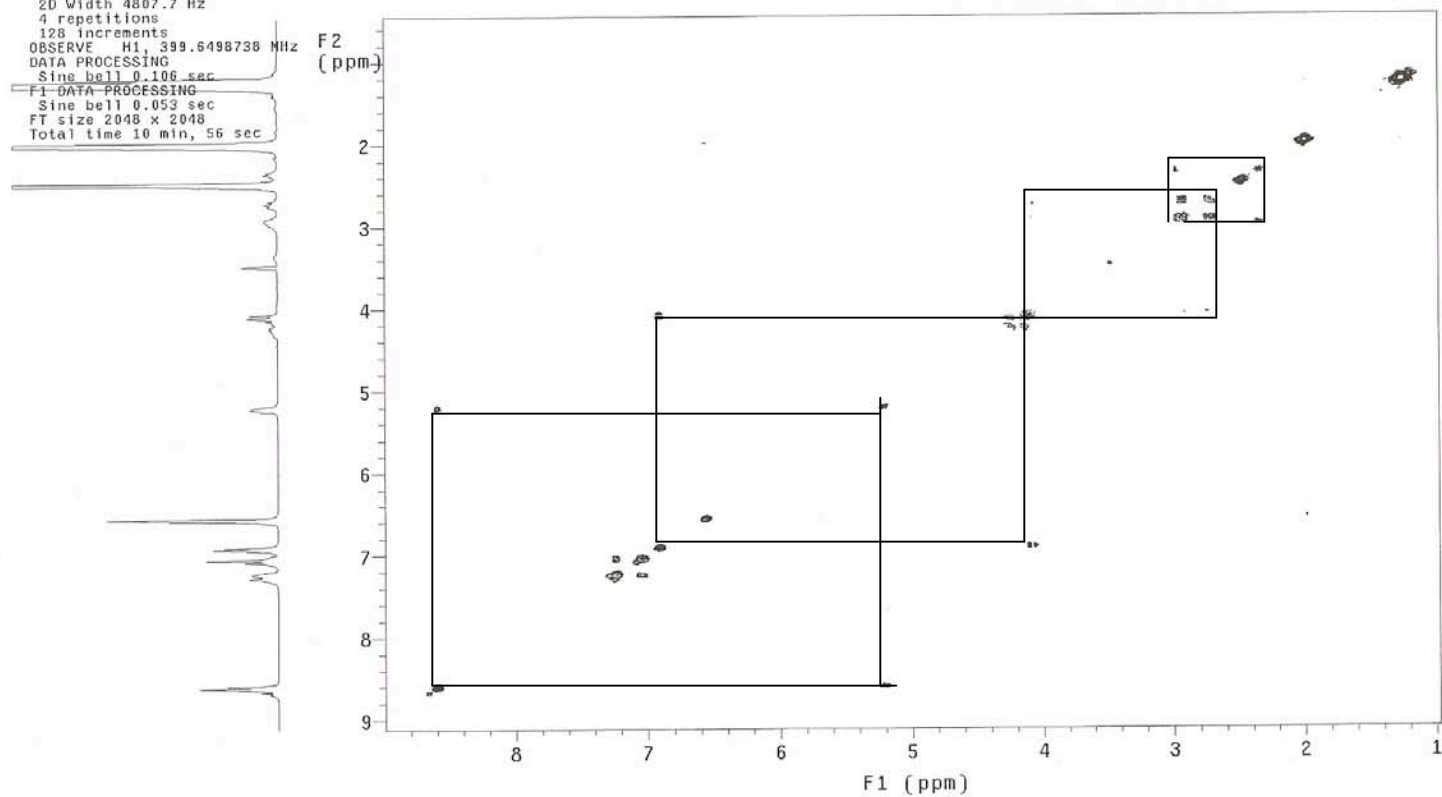
Sine bell 0.053 sec

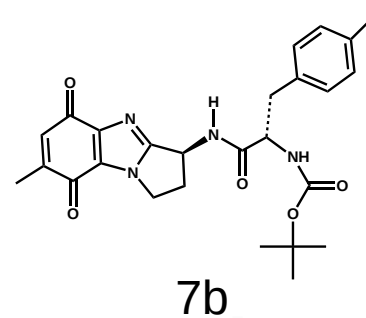
FT size 2048 x 2048

Total time 10 min, 56 sec



7b



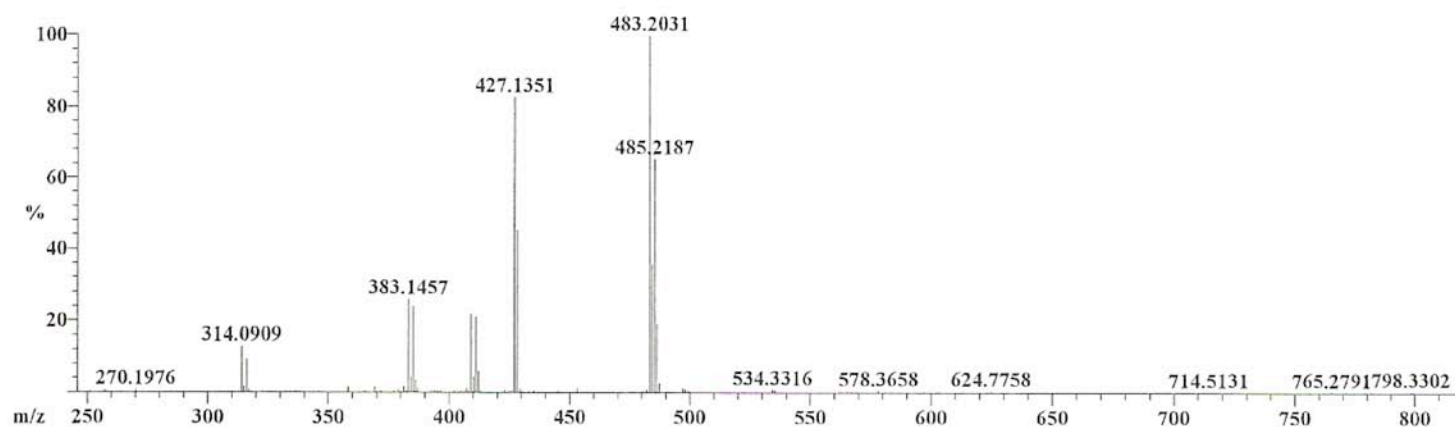


Scan: 47 (28-32)

R.T.: 1.9

Base: m/z 483; 77.1%FS TIC: 4472804

#Ions: 734

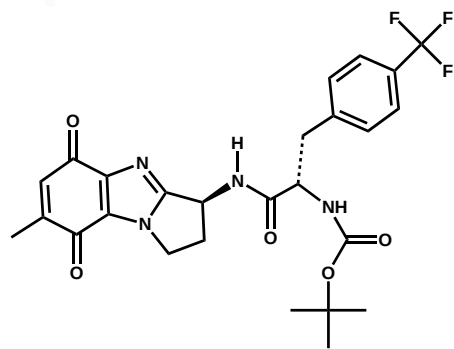


Selected Isotopes : C H N₄ O₅ F₀₋₁

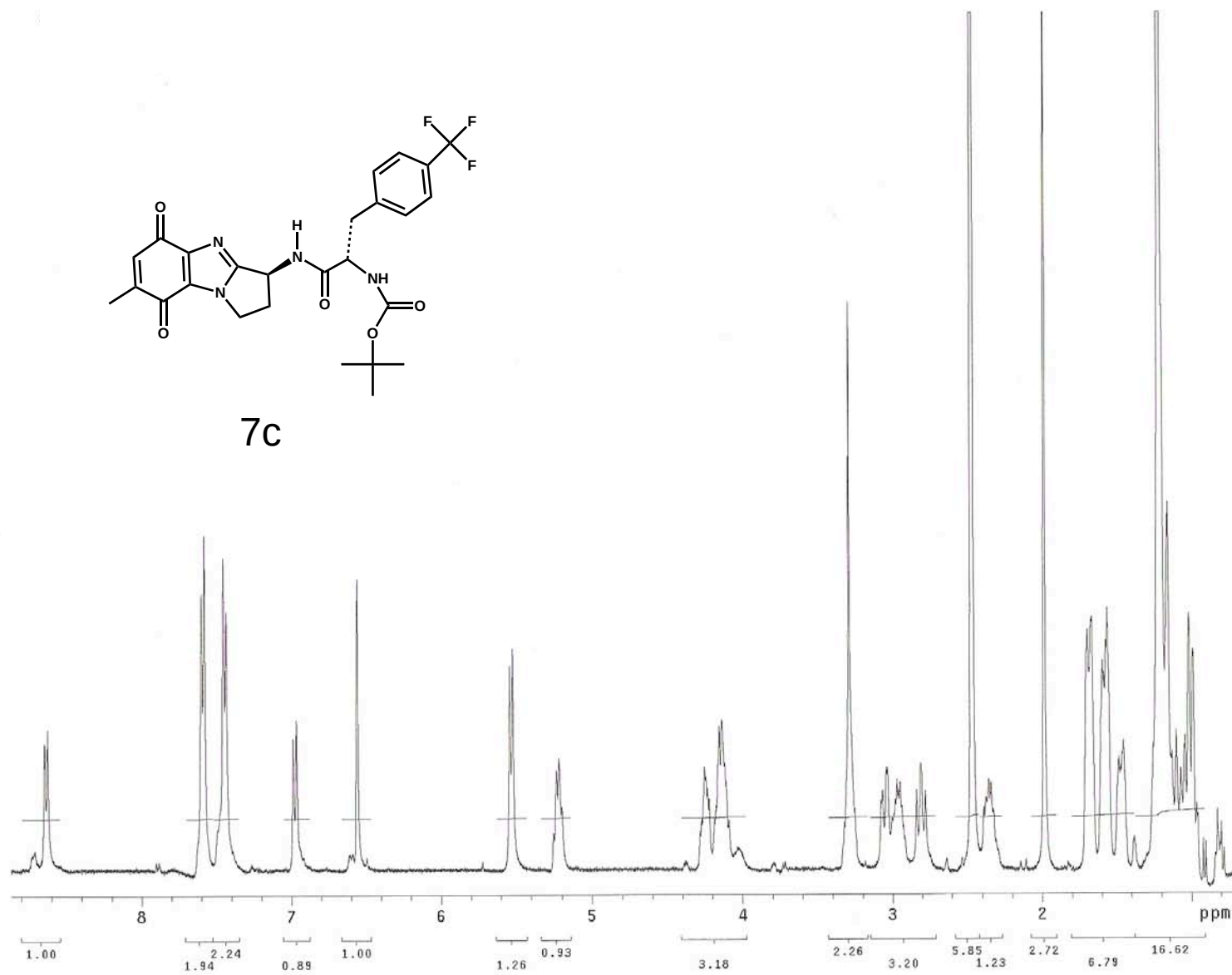
Error Limit : 100 ppm

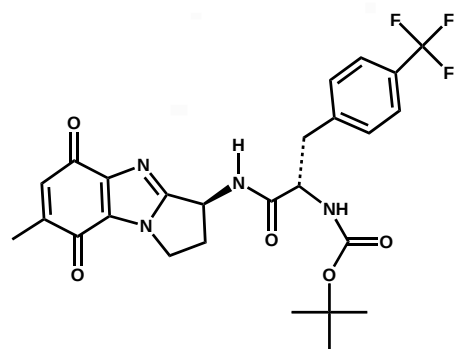
Unsaturation Limits : 12 to 30

<u>Measured Mass</u>	<u>% Base</u>	<u>Formula</u>	<u>Calculated Mass</u>	<u>Error</u>	<u>Unsaturation</u>
483.2031	100.0%	C ₂₅ H ₂₈ N ₄ O ₅ F	483.2044	-2.6	13.5

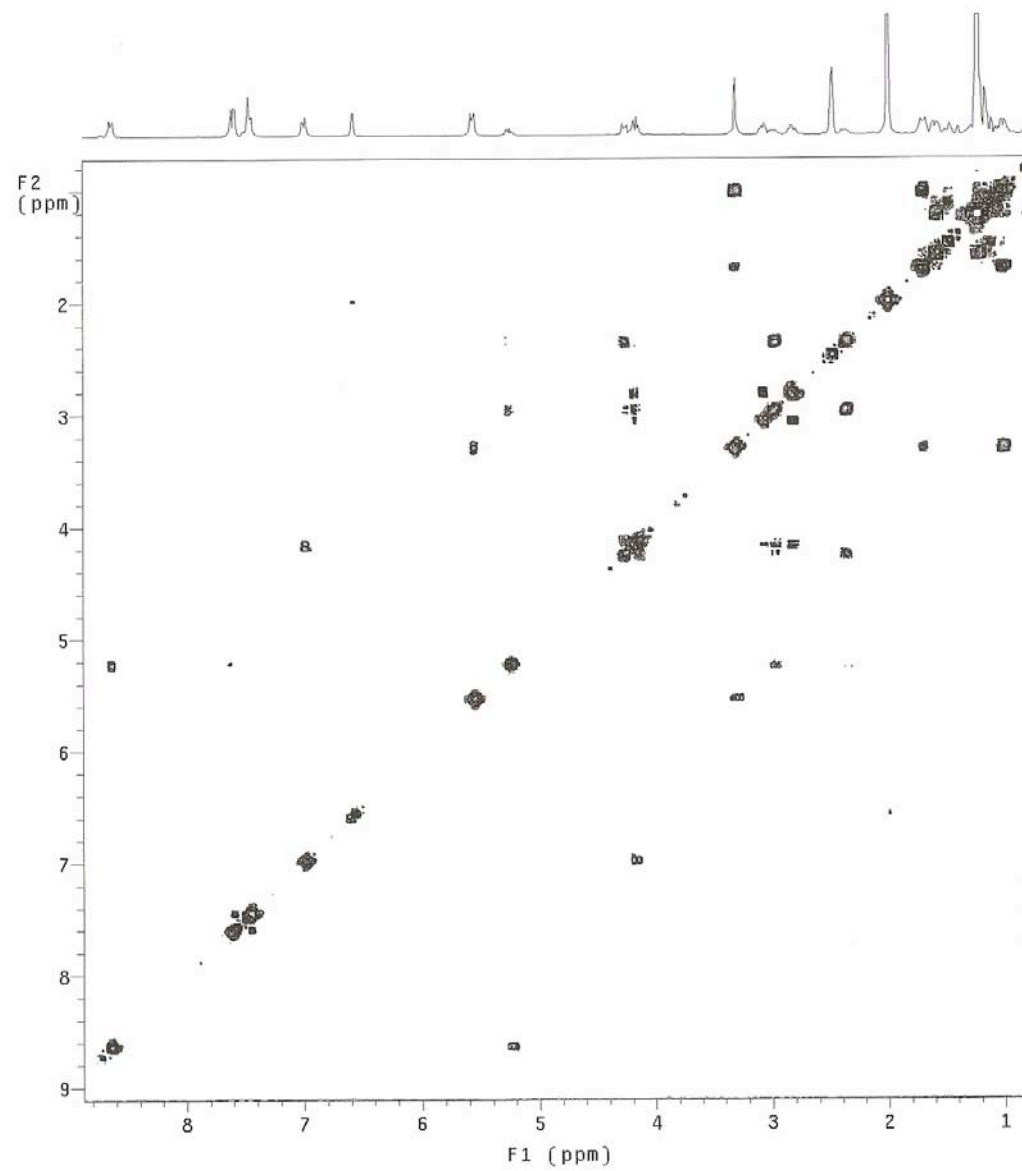


7c





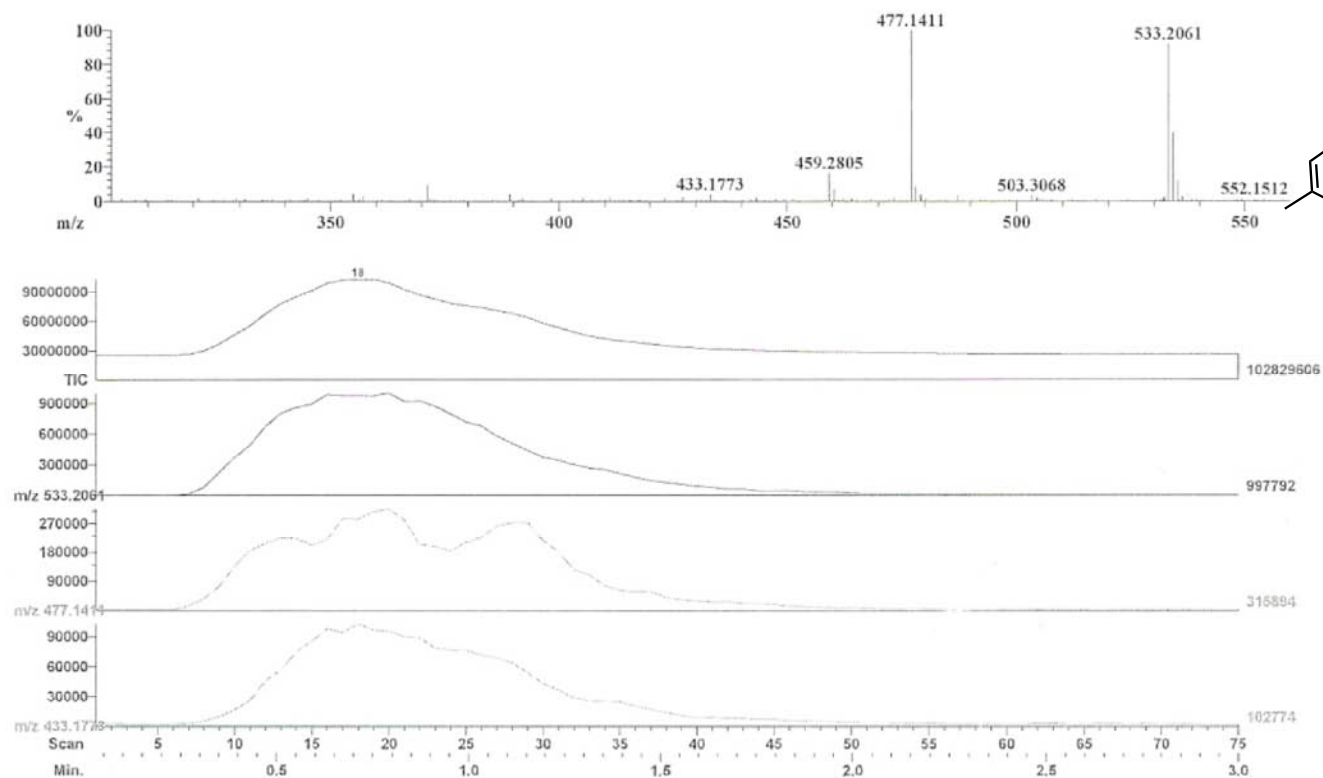
7c



Scan: 9 (3-5)
Base: m/z 477; 6.5%FS TIC: 336731

R.T.: .35

#Ions: 268



7c

Scan: 9 (3-5)
Base: m/z 477; 6.5%FS TIC: 336731

R.T.: .35

#Ions: 268

Selected Isotopes : $\text{CHN}_{3-4}\text{O}_{4-6}\text{F}_{0-3}$

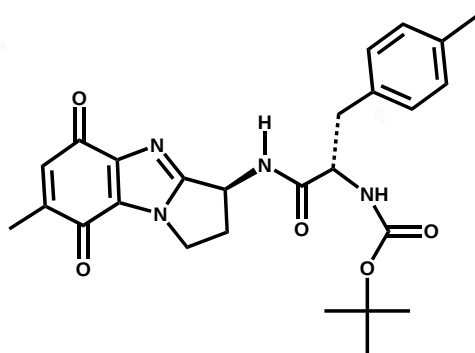
Error Limit : 10 ppm

Unsaturation Limits : 0 to 50

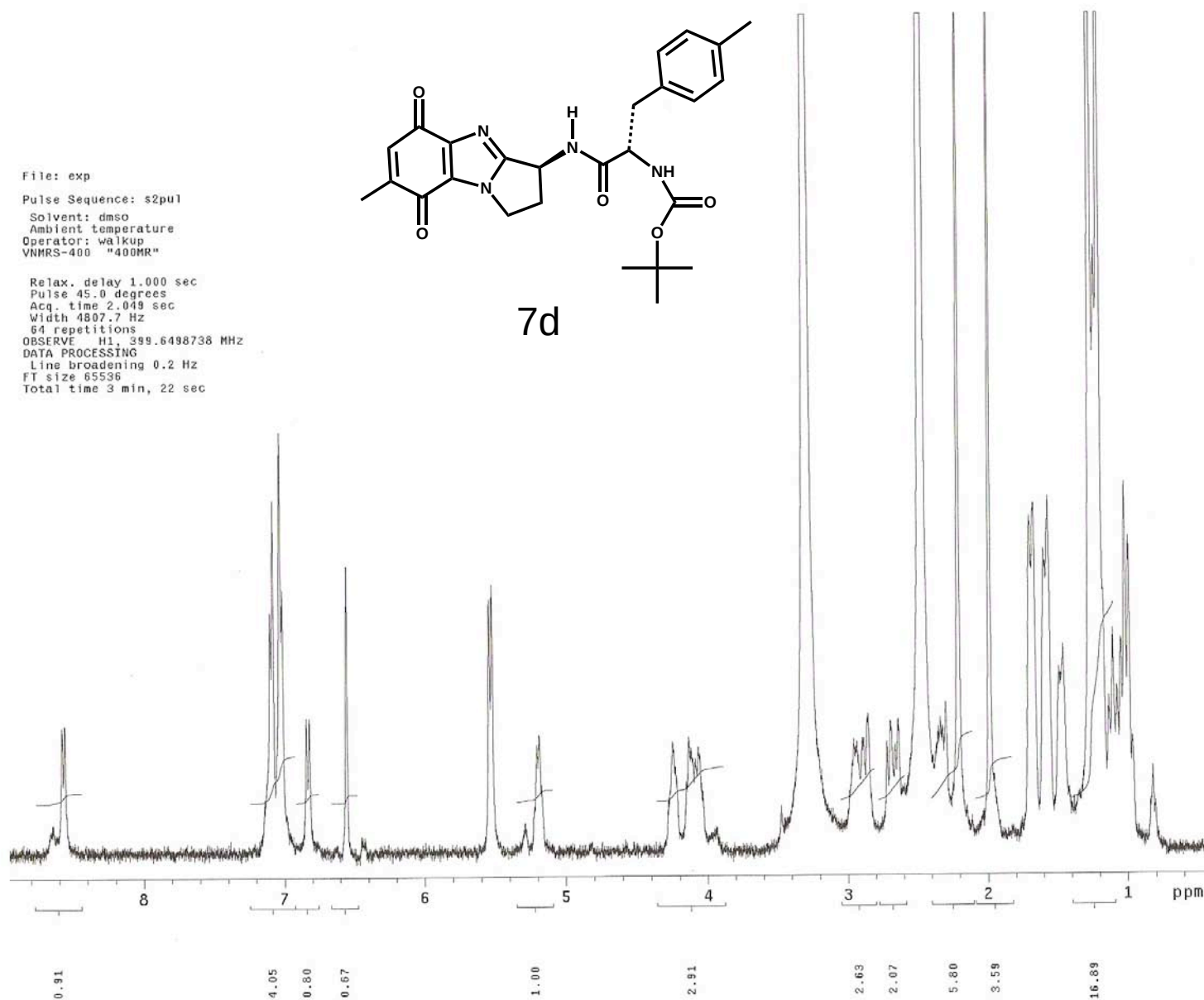
<u>Measured Mass</u>	<u>% Base</u>	<u>Formula</u>	<u>Calculated Mass</u>	<u>Error</u>	<u>Unsaturation</u>
533.2061	92.4%	$\text{C}_{26}\text{H}_{28}\text{N}_4\text{O}_5\text{F}_3$	533.2012	9.2	13.5

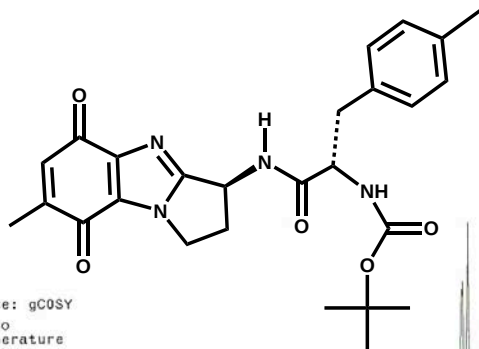
File: exp
Pulse Sequence: s2pu1
Solvent: dms0
Ambient temperature
Operator: walkup
VNMRS-400 "400MR"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 4807.7 Hz
64 repetitions
OBSERVE H1, 399.6498738 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min, 22 sec



7d

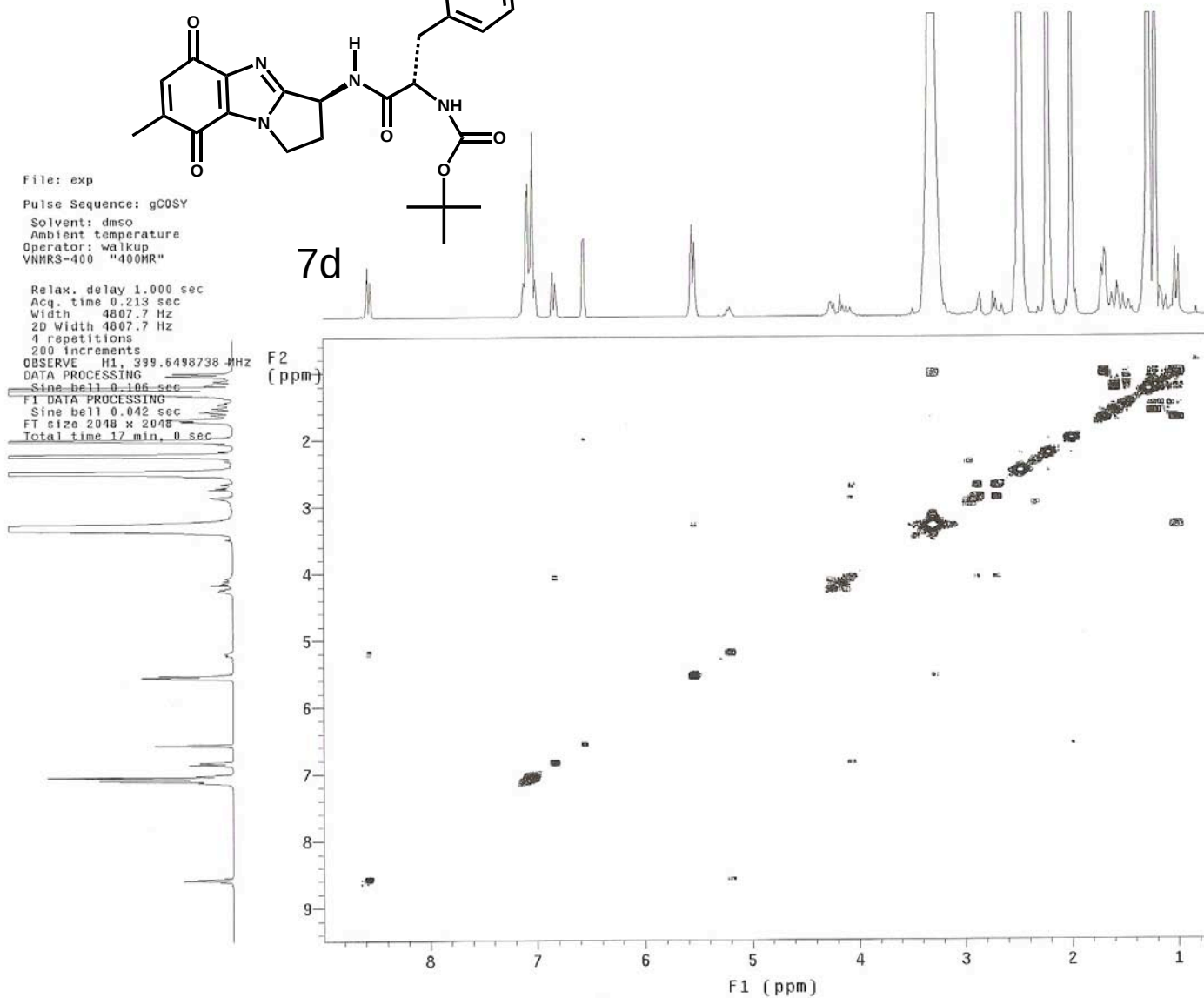


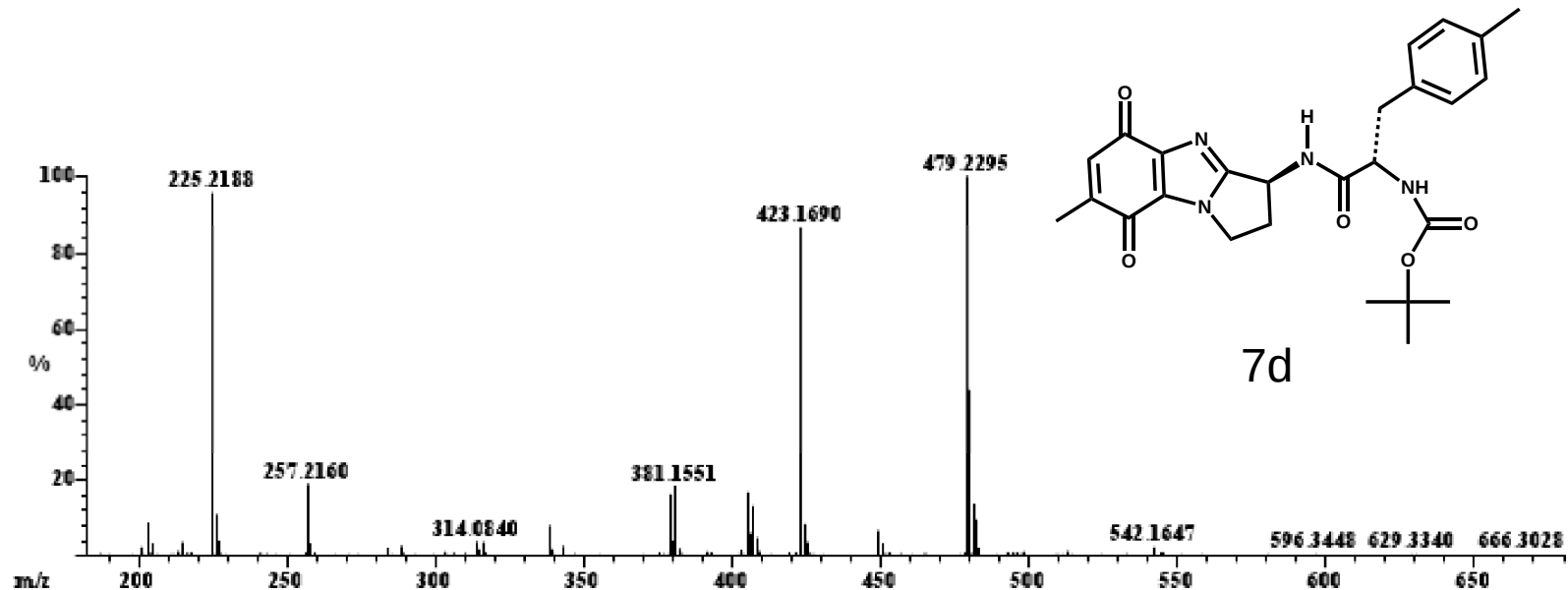


File: exp
Pulse Sequence: gC0SY
Solvent: dmsc
Ambient temperature
Operator: walkup
VNMR5-400 "400MR"

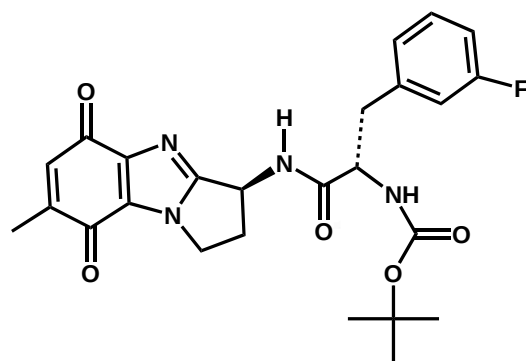
Relax. delay 1.000 sec
Acq. time 0.213 sec
Width 4807.7 Hz
2D Width 4807.7 Hz
4 repetitions
200 increments
OBSERVE H1, 399.6498738 MHz
DATA PROCESSING
Sine bell 0.106 sec
F1 DATA PROCESSING
Sine bell 0.042 sec
FT size 2048 x 2048
Total time 17 min, 0 sec

7d

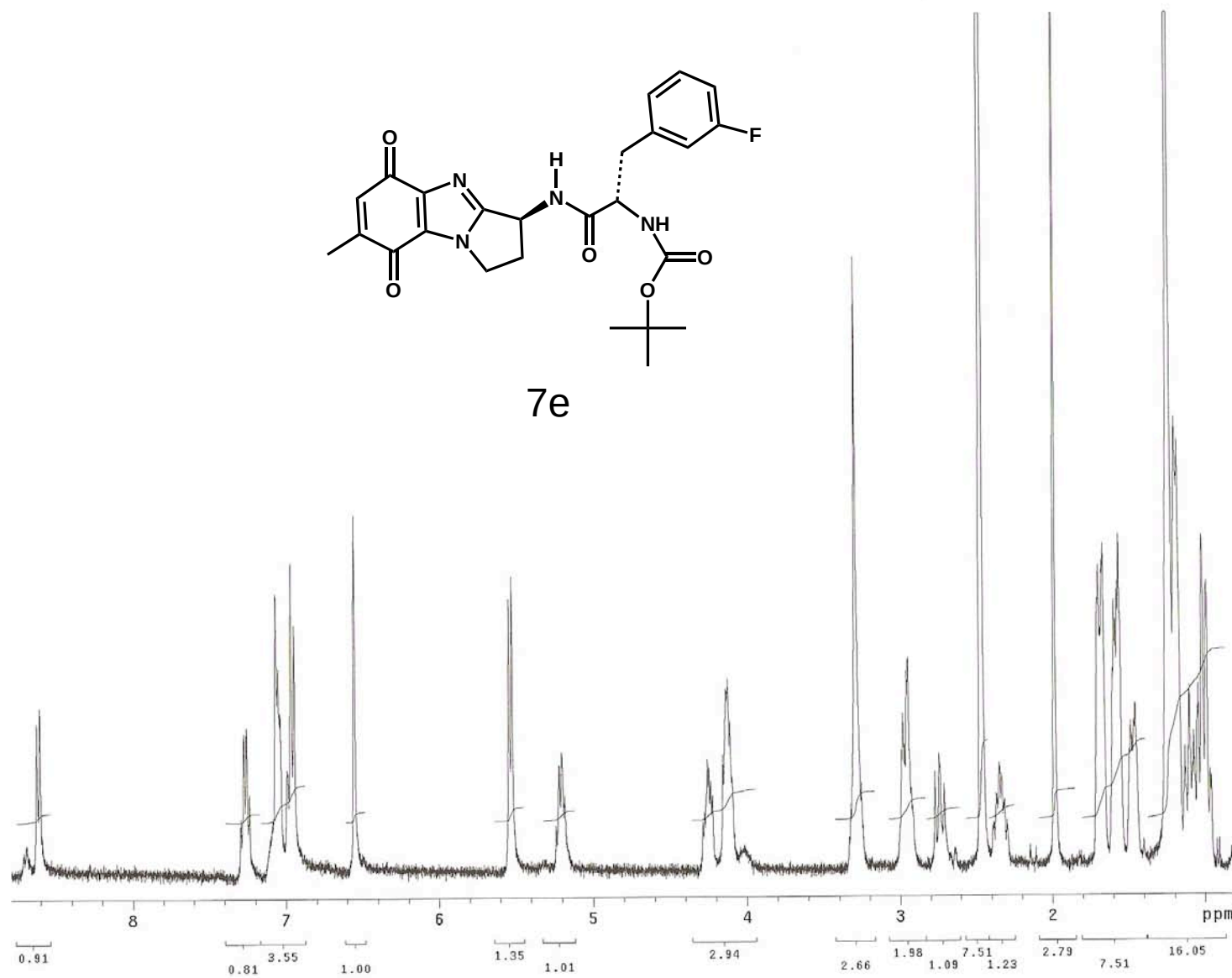


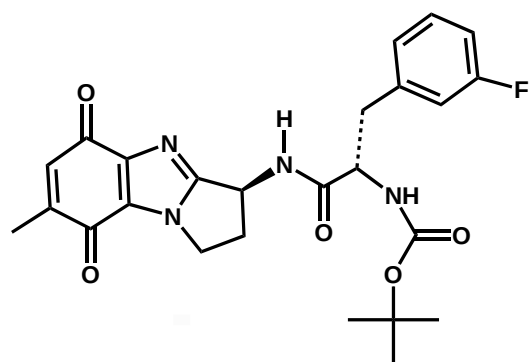


Selected Isotopes : C H N ₄ O ₅		Error Limit : 20 ppm		Unsaturation Limits : 0 to 50	
<u>Measured Mass</u>	<u>% Base</u>	<u>Formula</u>	<u>Calculated Mass</u>	<u>Error</u>	<u>Unsaturation</u>
423.1690	86.3%	C ₂₂ H ₂₃ N ₄ O ₅	423.1668	5.1	13.5
479.2295	100.0%	C ₂₆ H ₃₁ N ₄ O ₅	479.2294	0.1	13.5

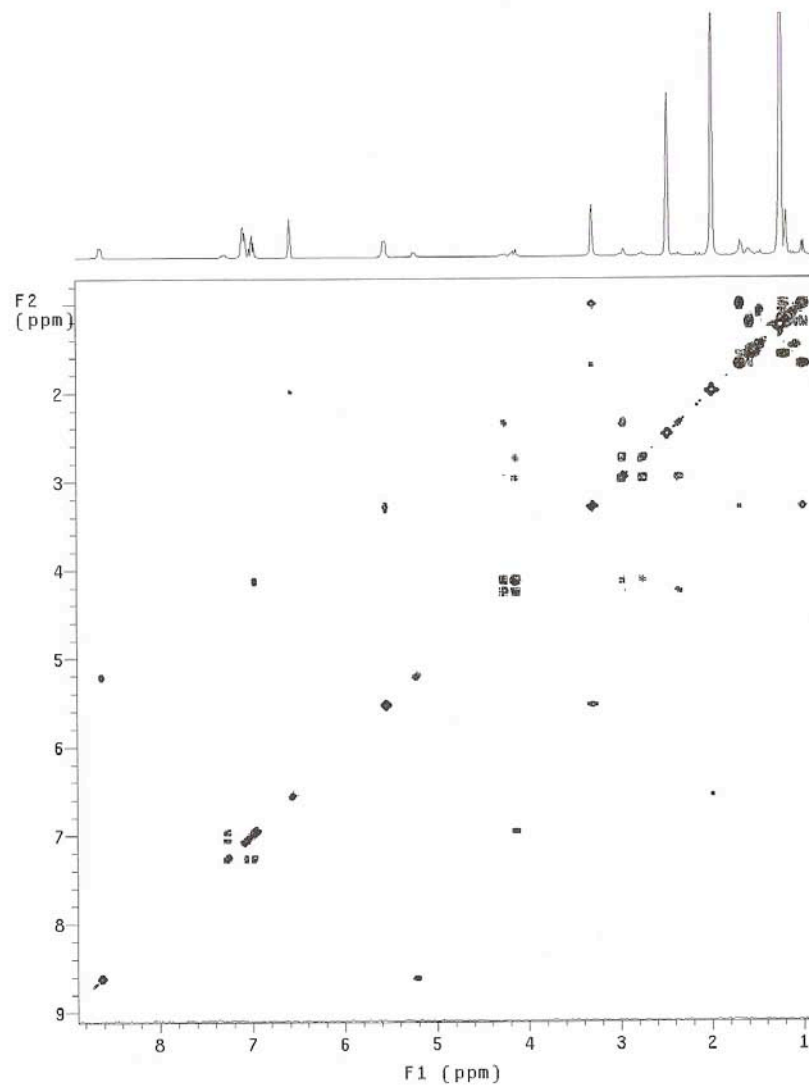


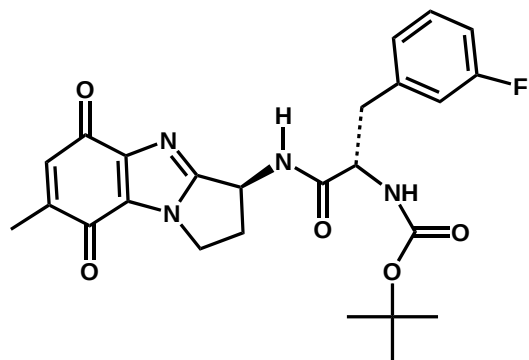
7e





7e



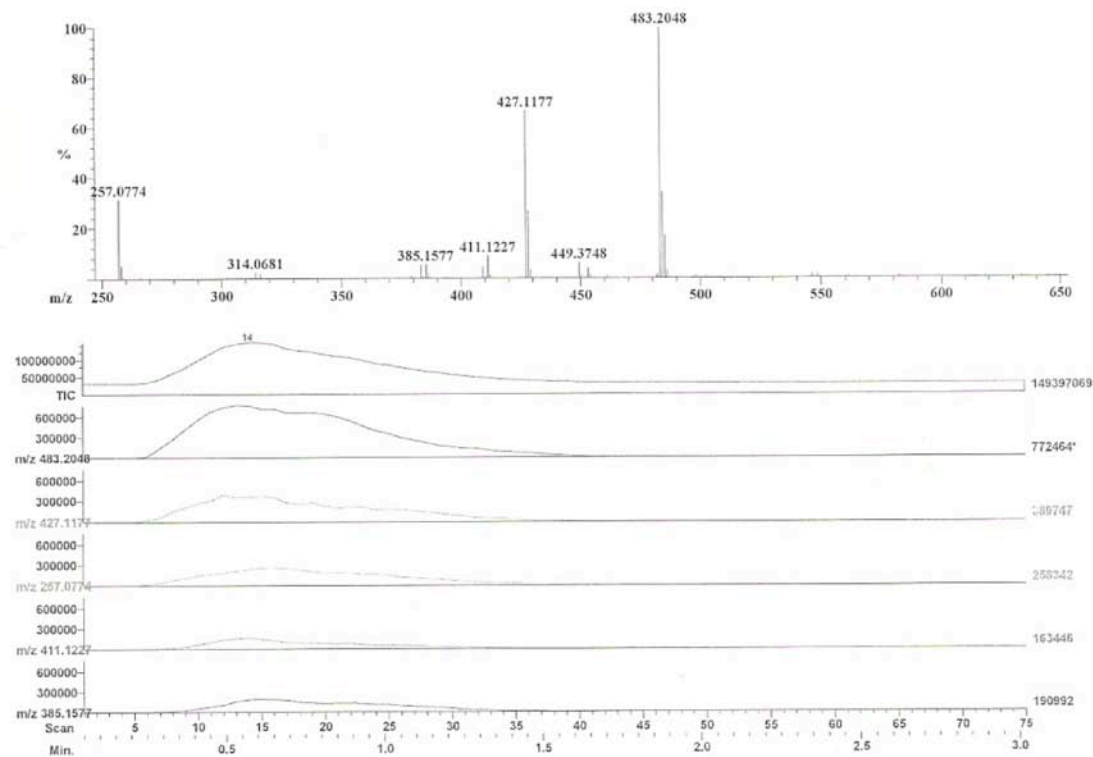


7e

Scan: 10 (3-5)
Base: m/z 483; 60.4%FS TIC: 2547142

R.T.: .42

#Ions: 441



Scan: 10 (3-5)
Base: m/z 483; 60.4%FS TIC: 2547142

R.T.: .42

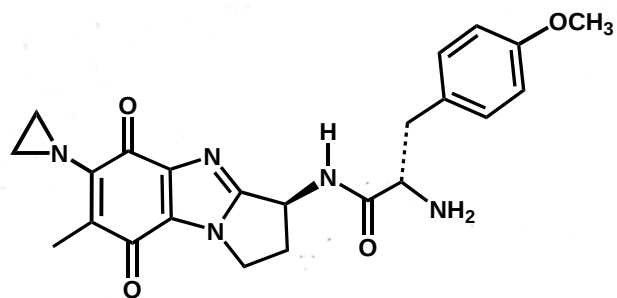
#Ions: 441

Selected Isotopes : C₂₅H₂₈N₄O₅F

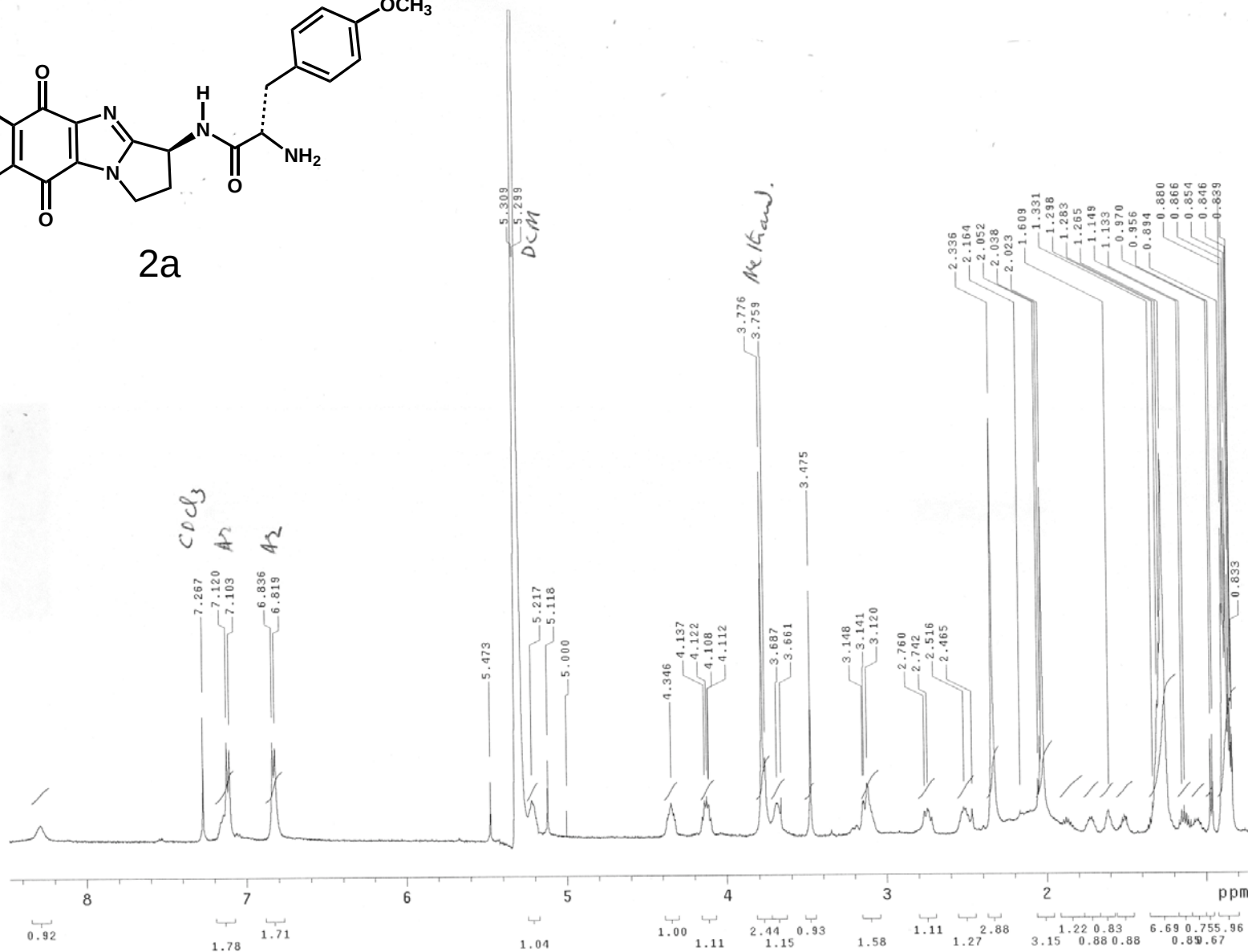
Error Limit : 10 ppm

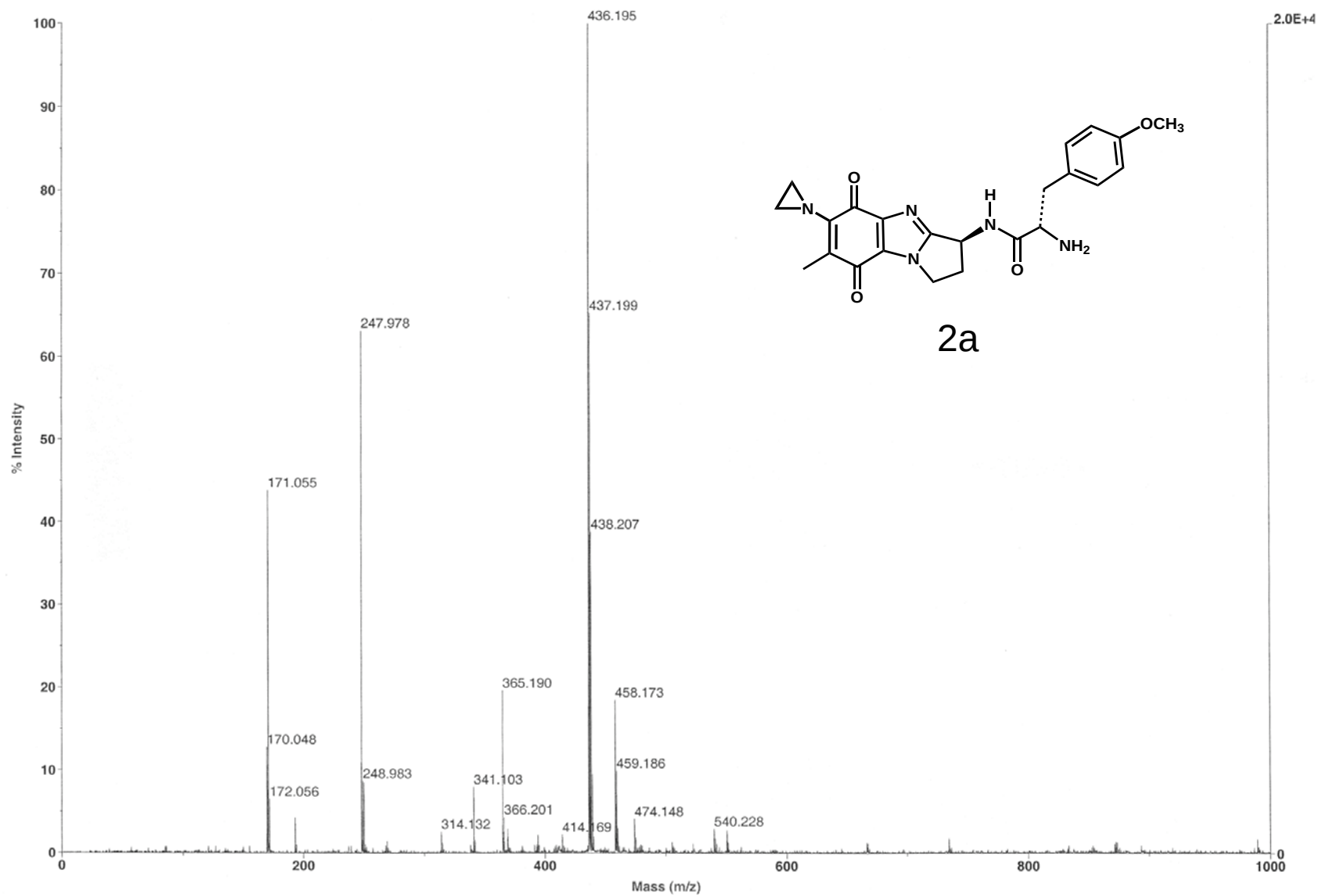
Unsaturation Limits : 0 to 50

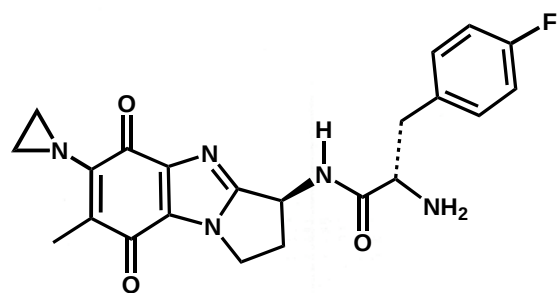
<u>Measured Mass</u>	<u>% Base</u>	<u>Formula</u>	<u>Calculated Mass</u>	<u>Error</u>	<u>Unsaturation</u>
483.2048	100.0%	C ₂₅ H ₂₈ N ₄ O ₅ F	483.2044	0.9	13.5



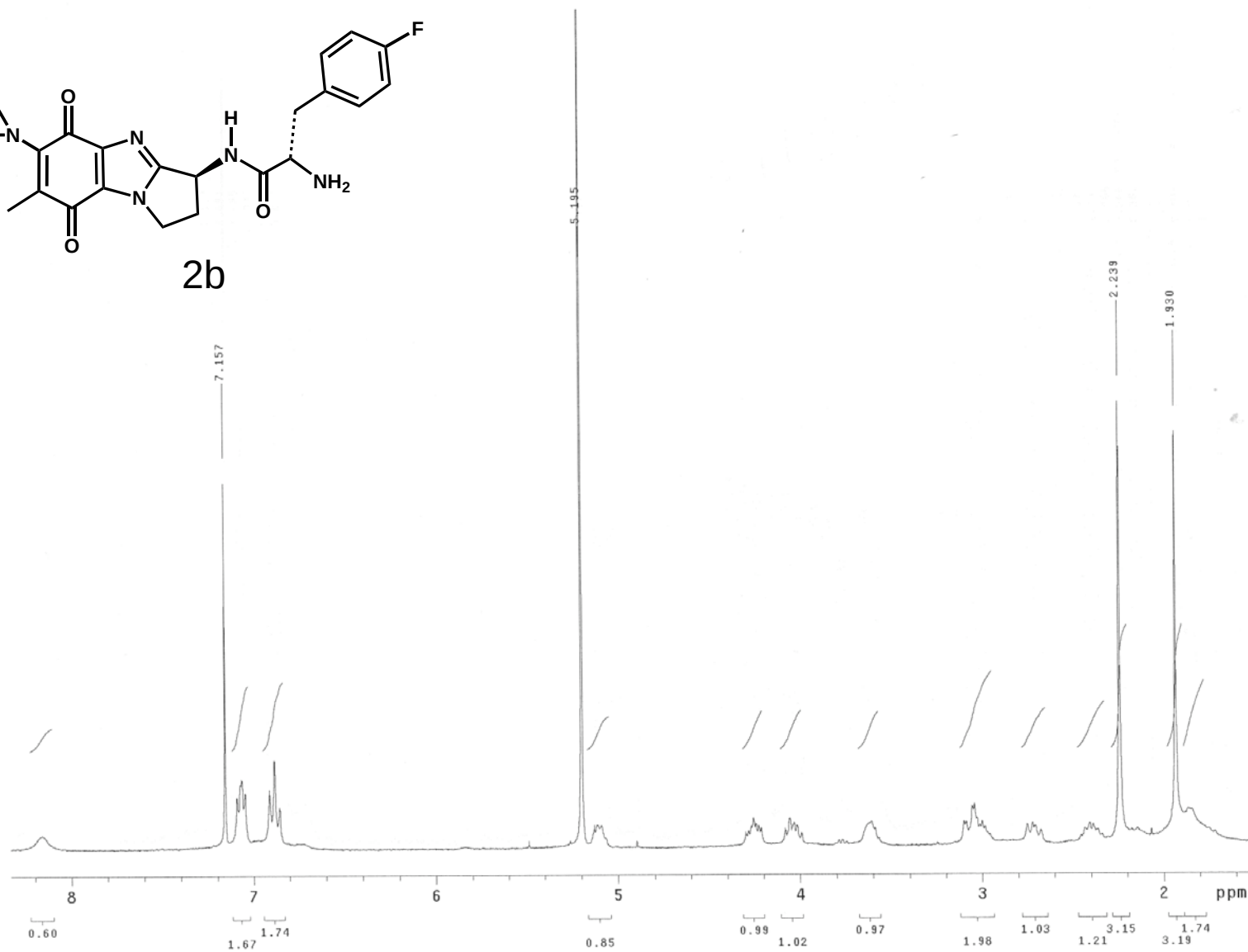
2a

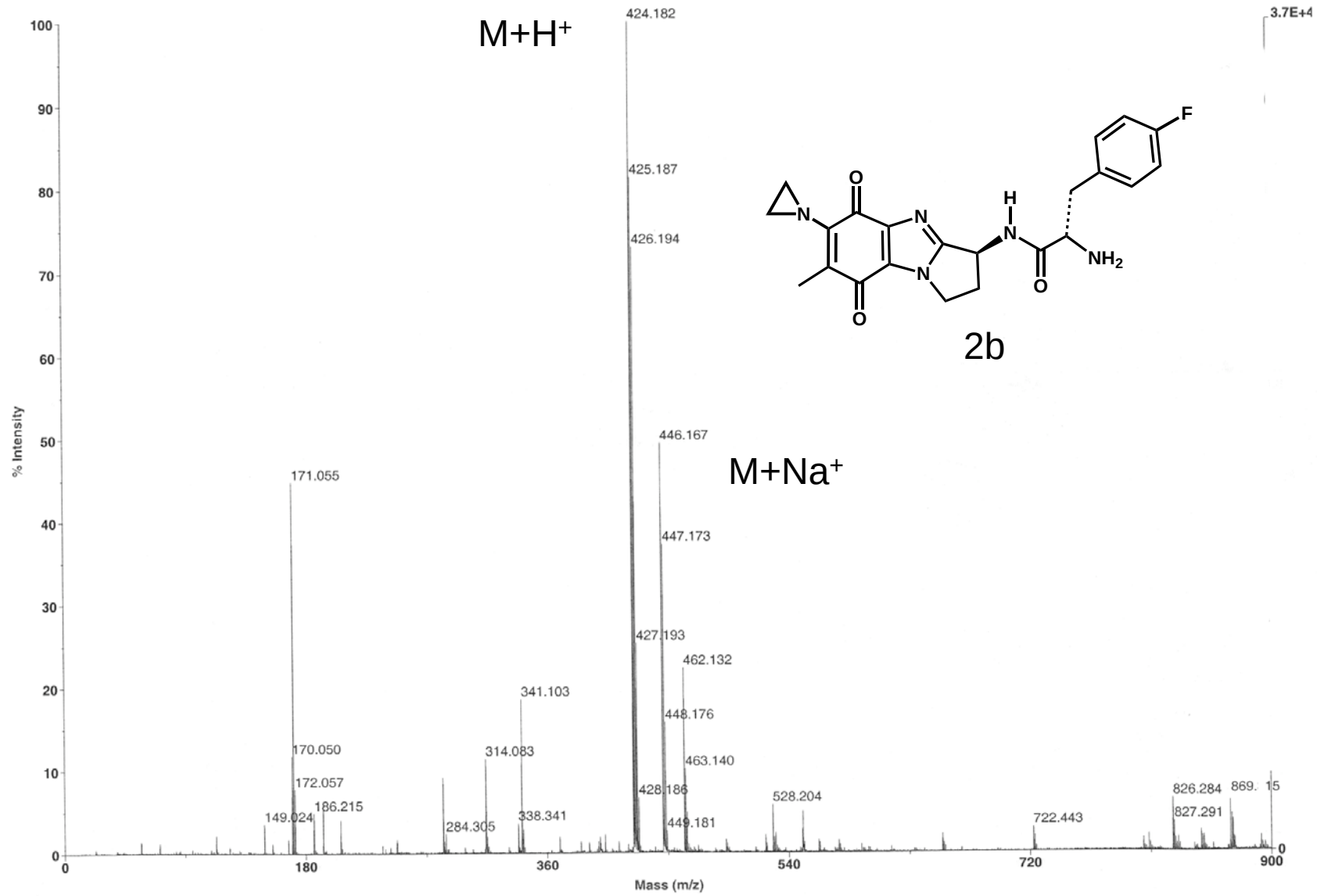






2b





H1_trifluoromethylPBI, 3mm natorac, 500 MHz

File : home/wakeup/skibo_data/Inova500/jamil/H1_trifluoromethylPBI.fid

Pulse Sequence: s2pu1

Solvent: CDC13

Temp. 24.0 C / 297.1 K

File: H1_trifluoromethylPBI

VNMR5-500 "asnmr99.la.asu.edu"

Pulse 64.9 degrees

Acq. time 2.048 sec

Width 8000.0 Hz

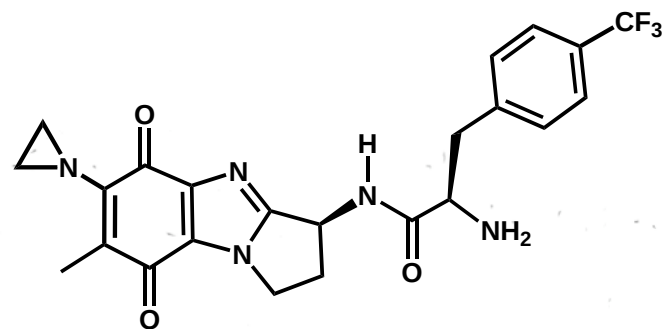
256 repetitions

OBSERVE H1, 499.8788477 MHz

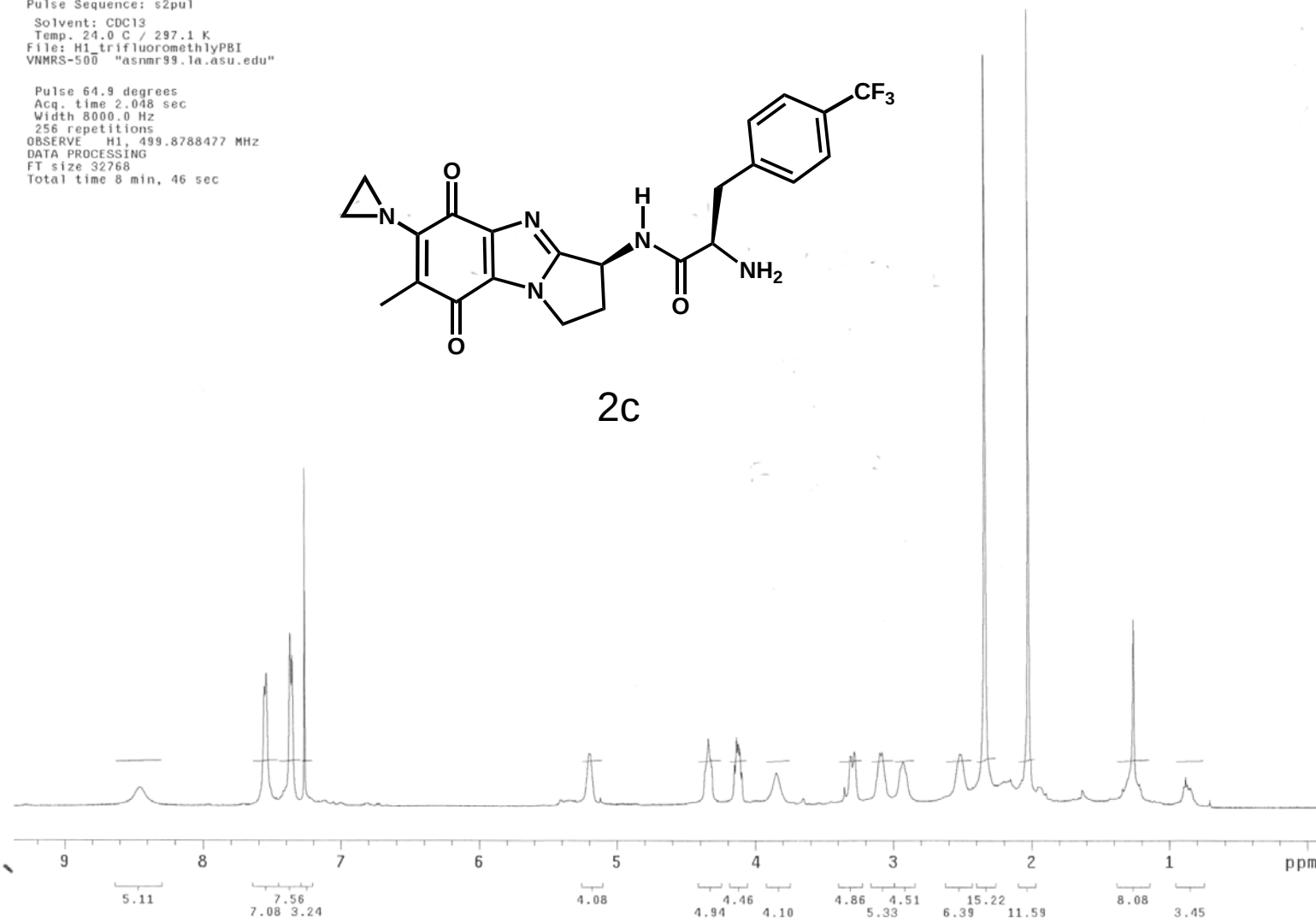
DATA PROCESSING

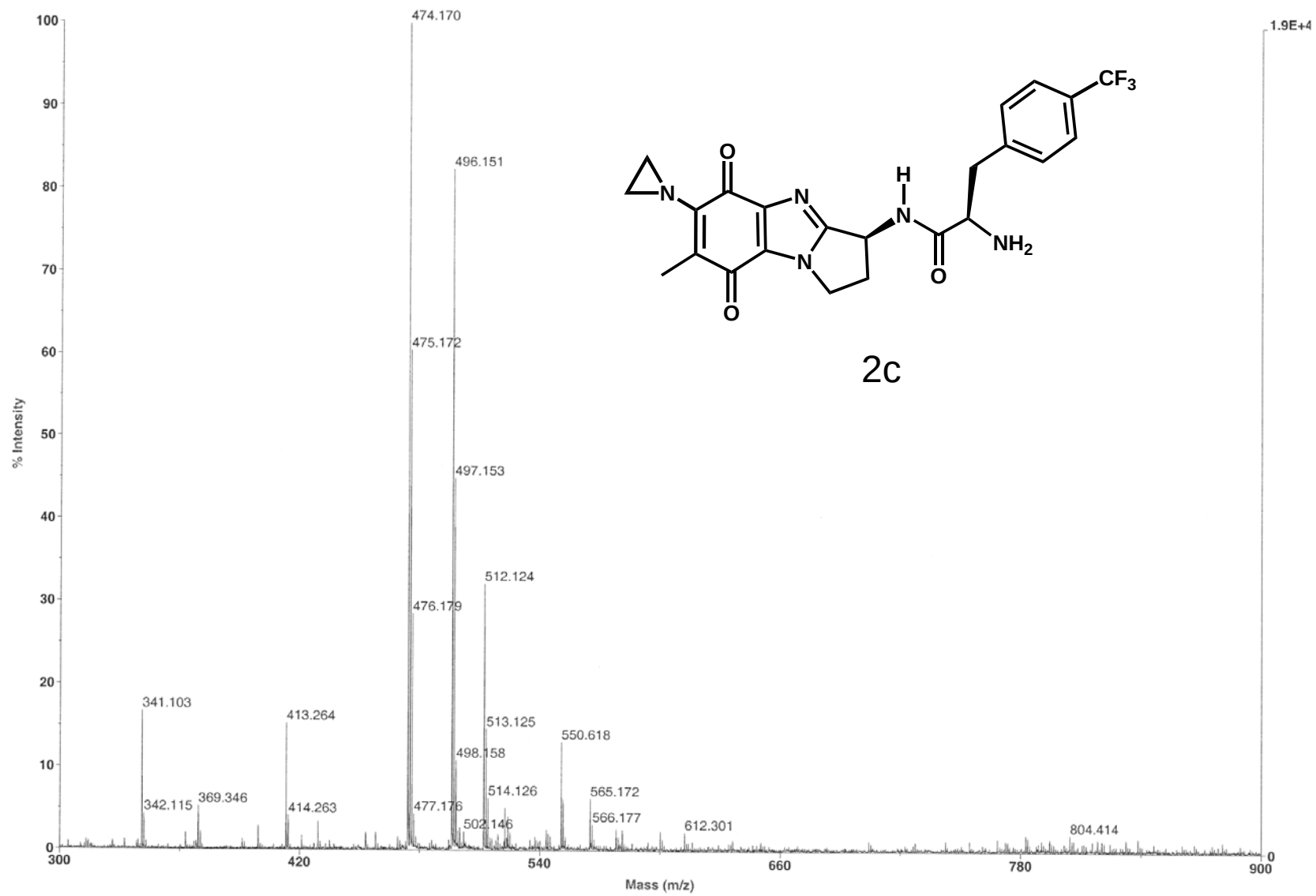
FT size 32768

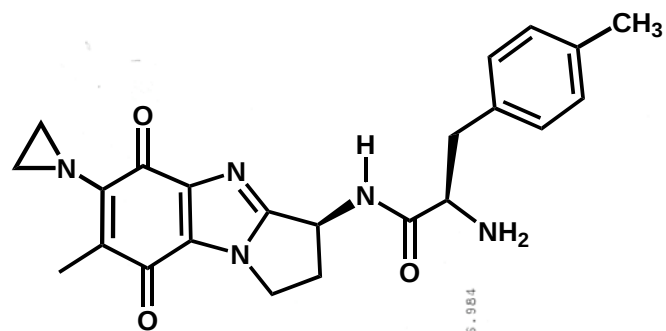
Total time 8 min, 46 sec



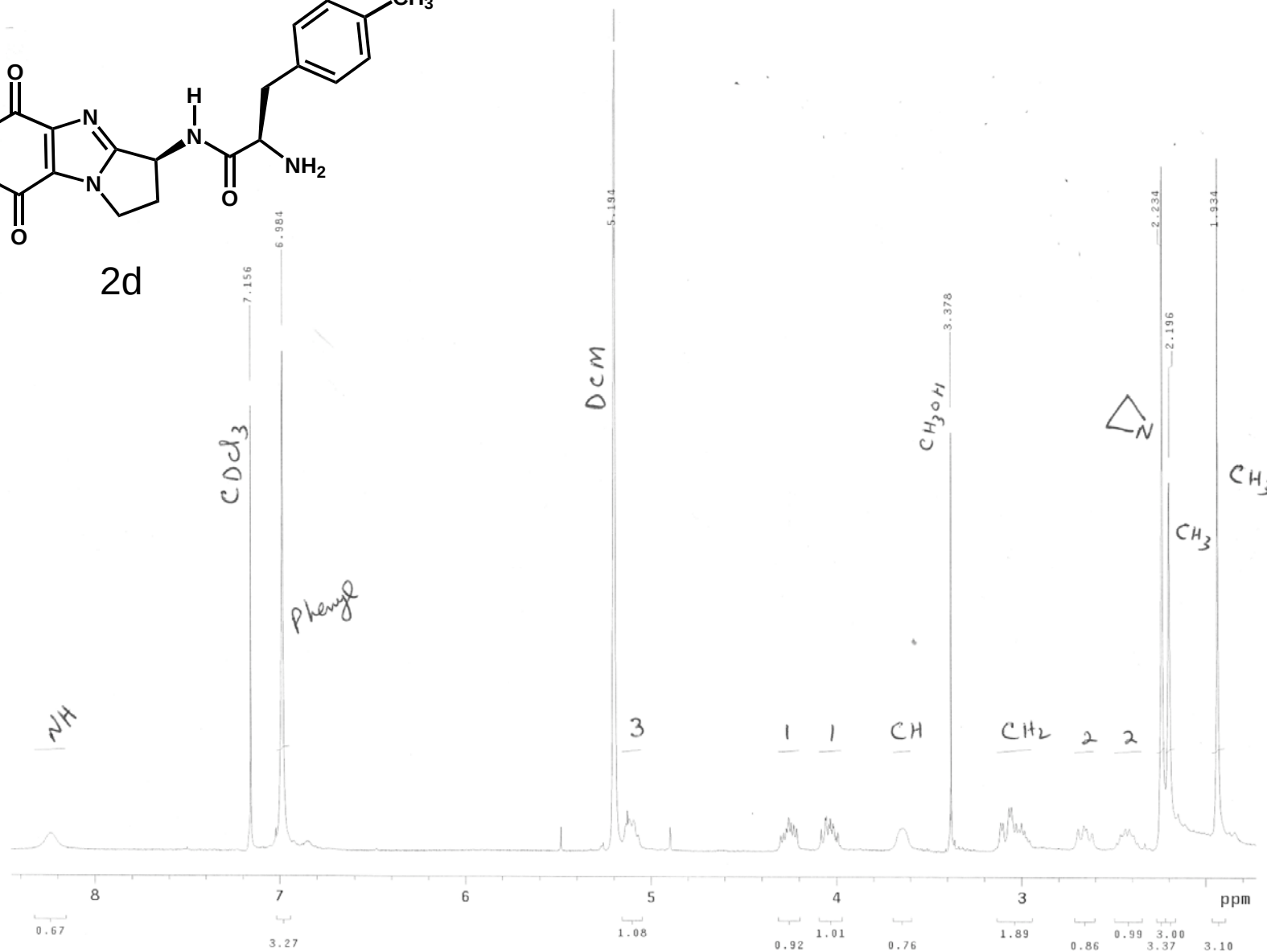
2c

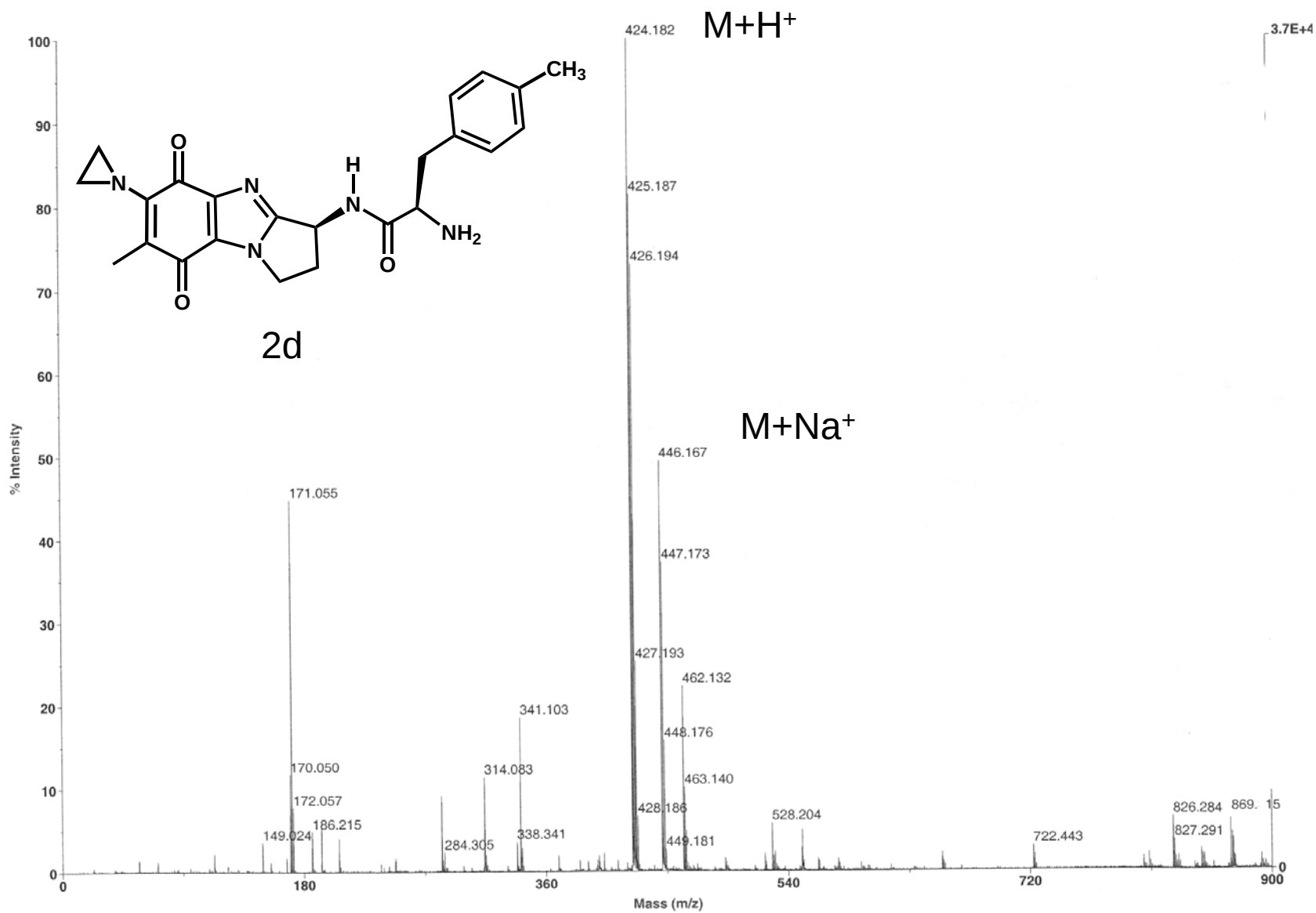


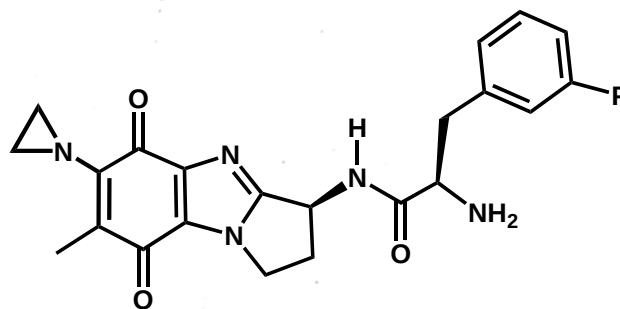




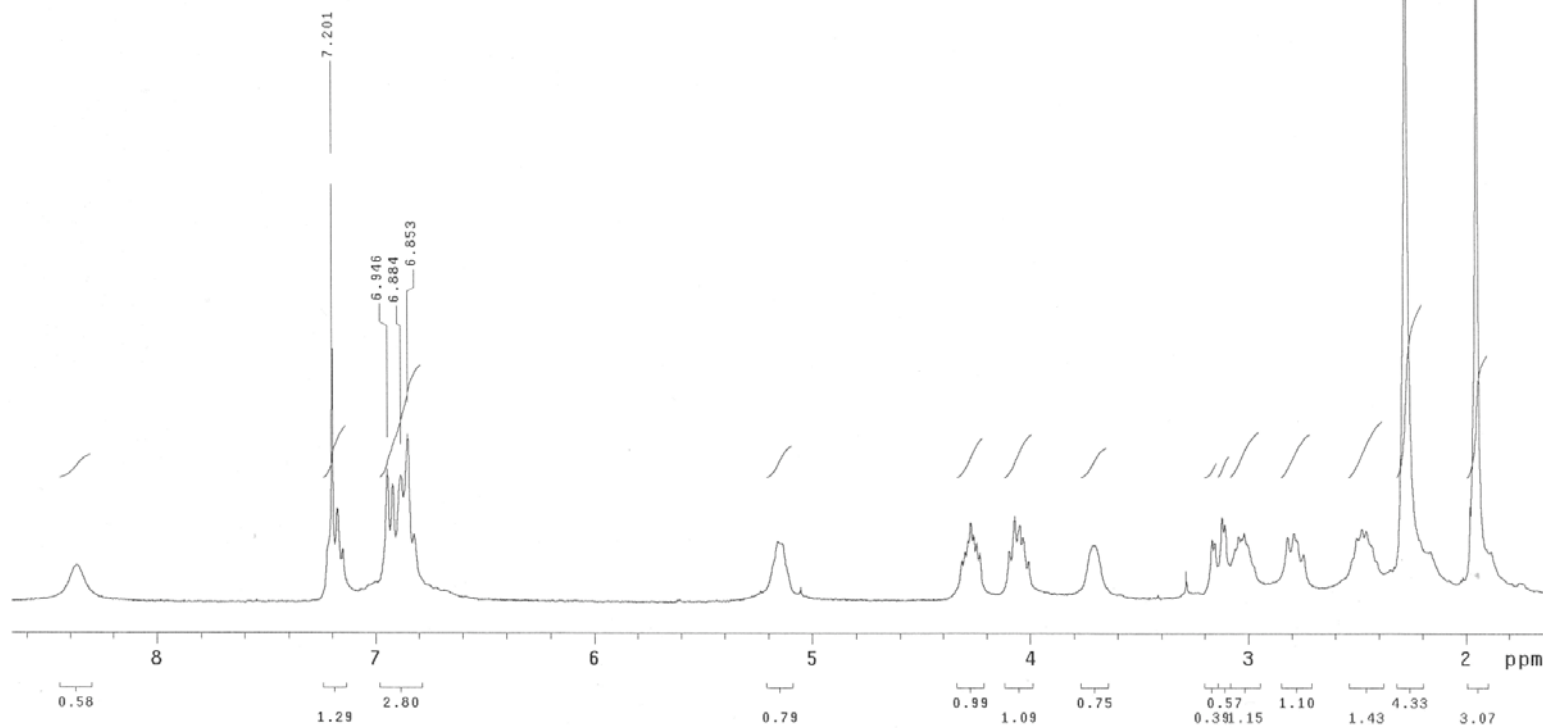
2d

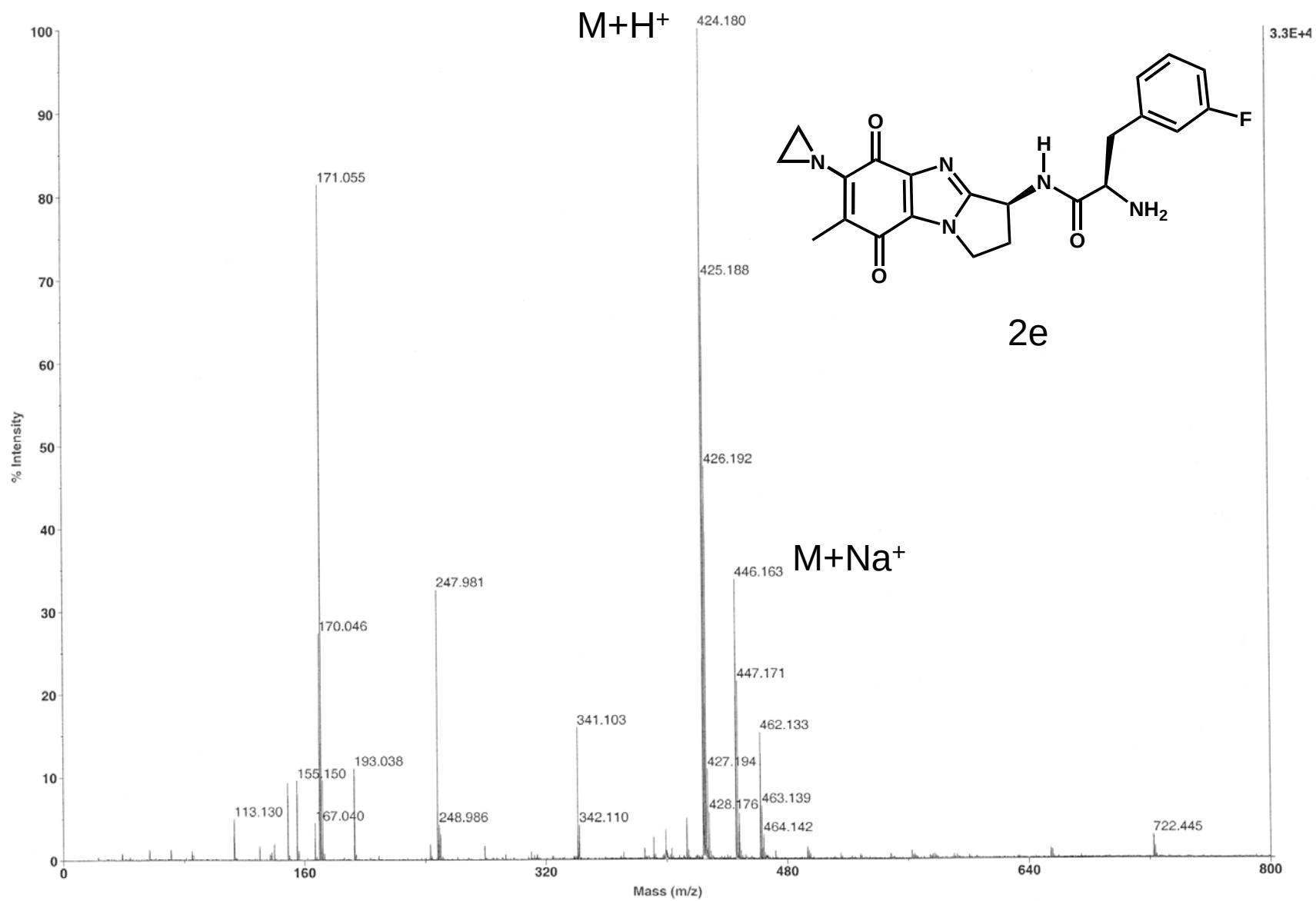






2e





Mean Graph for LL-1

Leukemia

NSC Lung

Colon

CNS

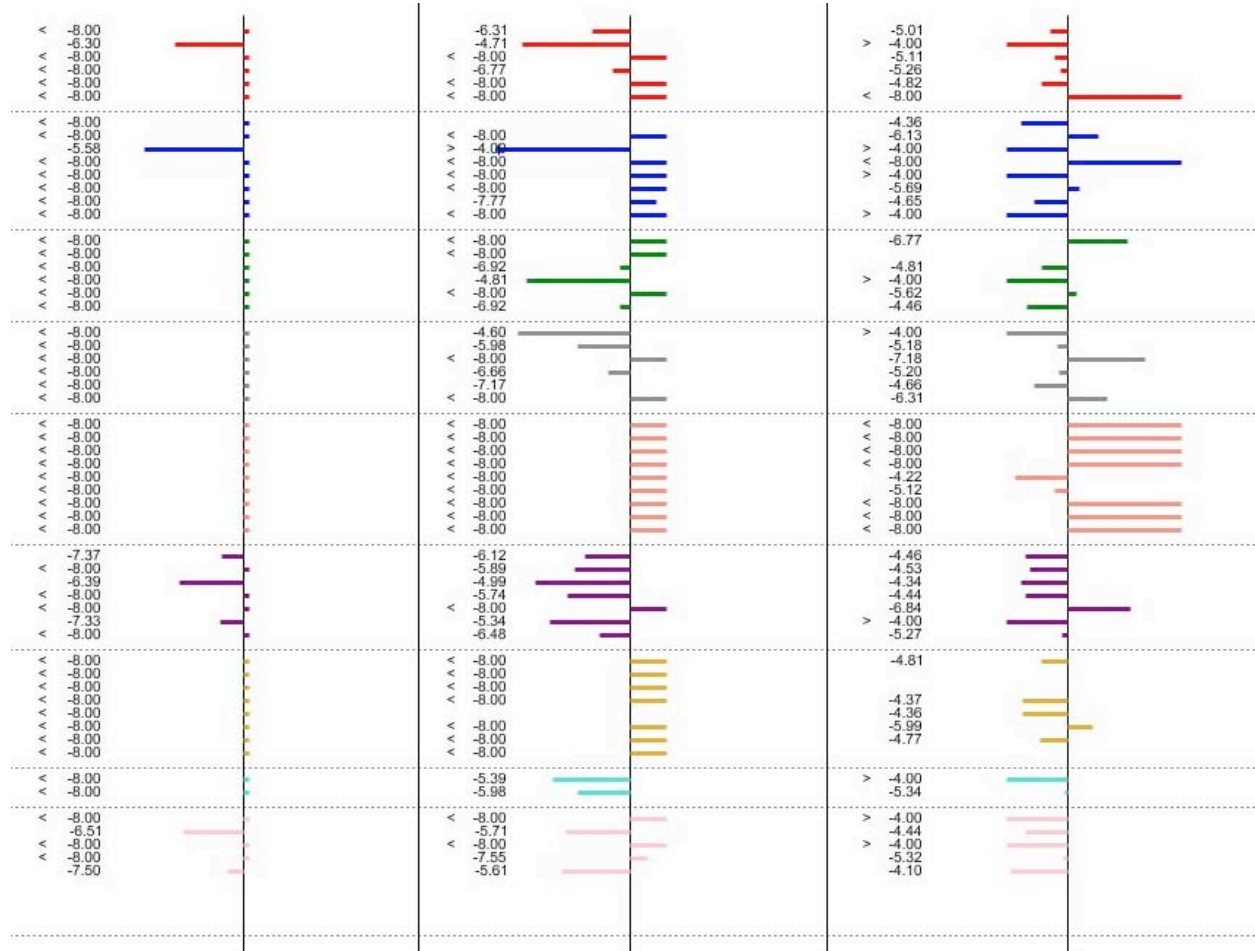
Melanoma

Ovarian

Renal

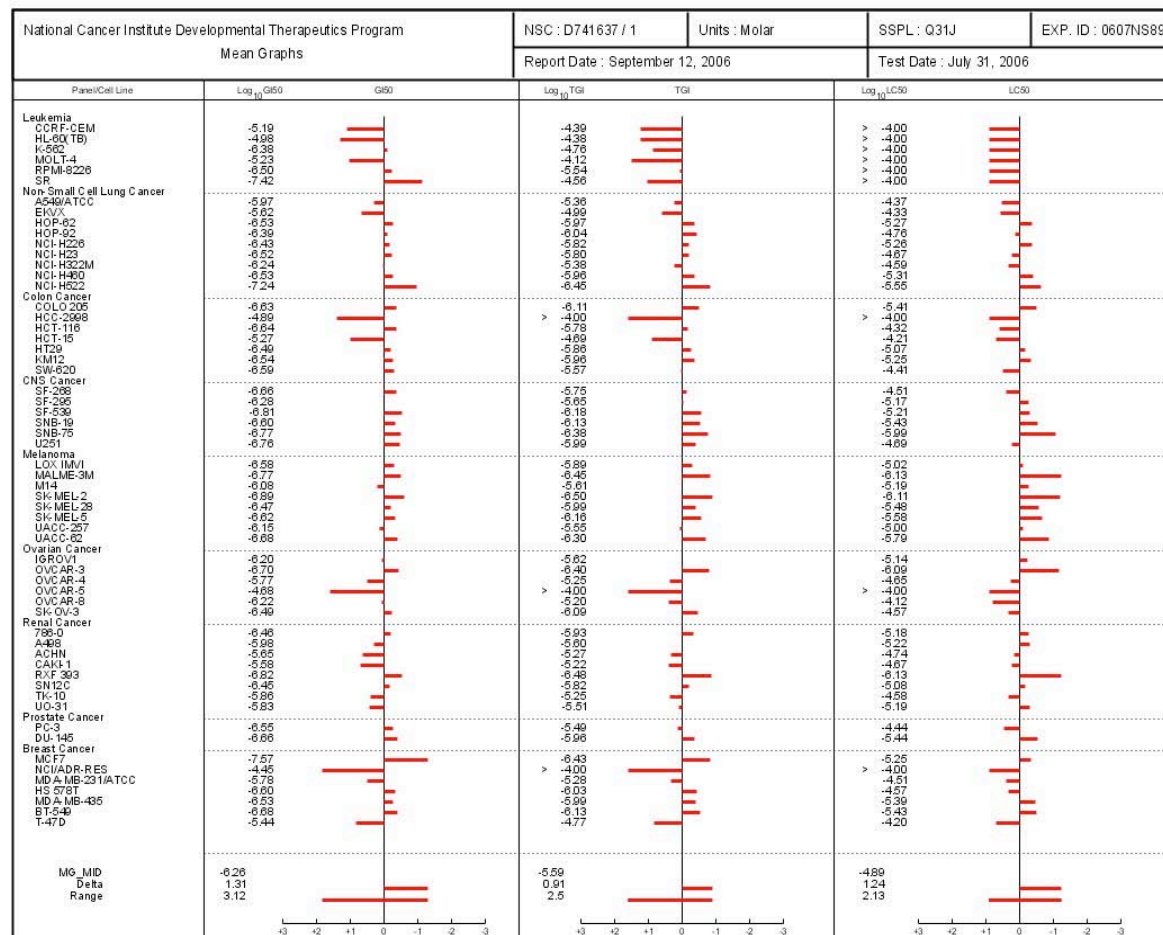
Prostate

Breast



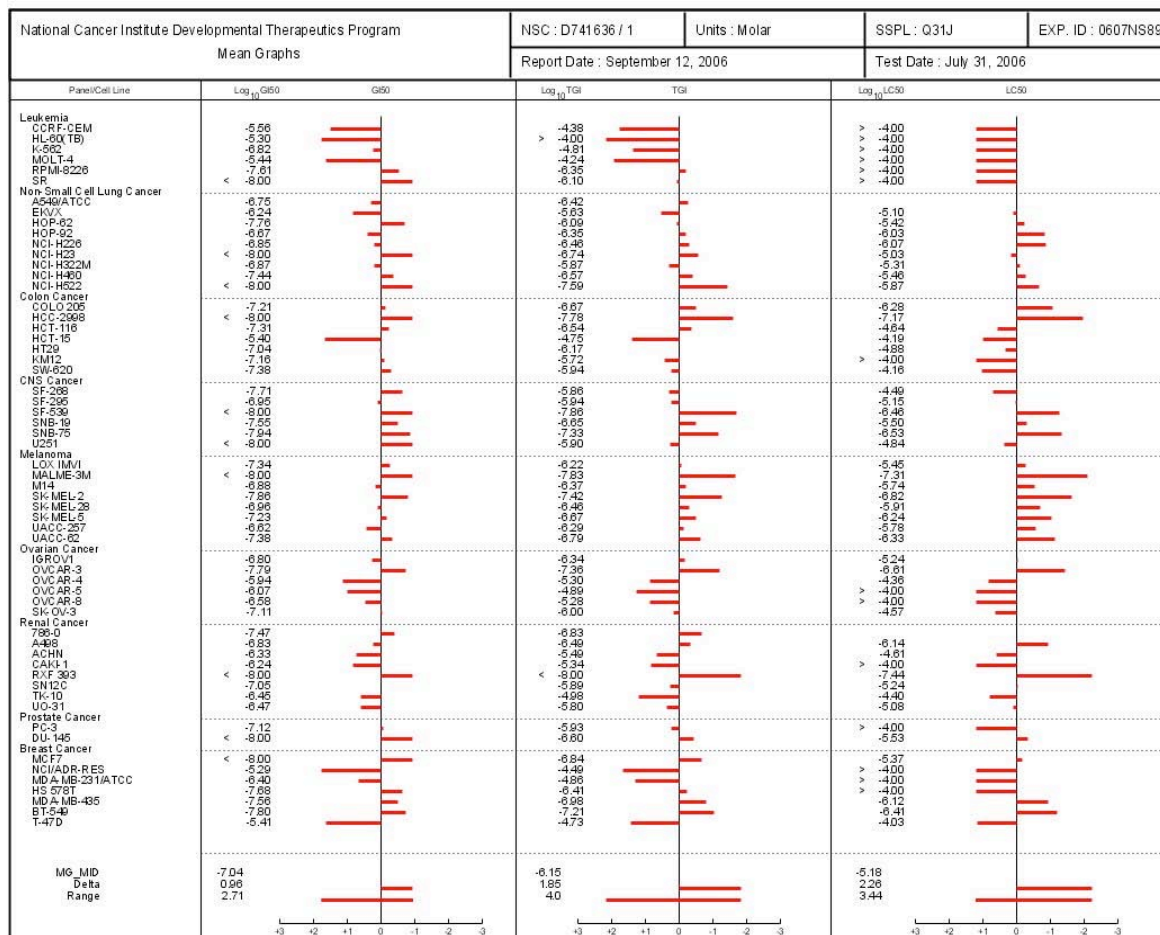
Mean Graph for DL-1

Leukemia
NSC Lung
Colon
CNS
Melanoma
Ovarian
Renal
Prostate
Breast



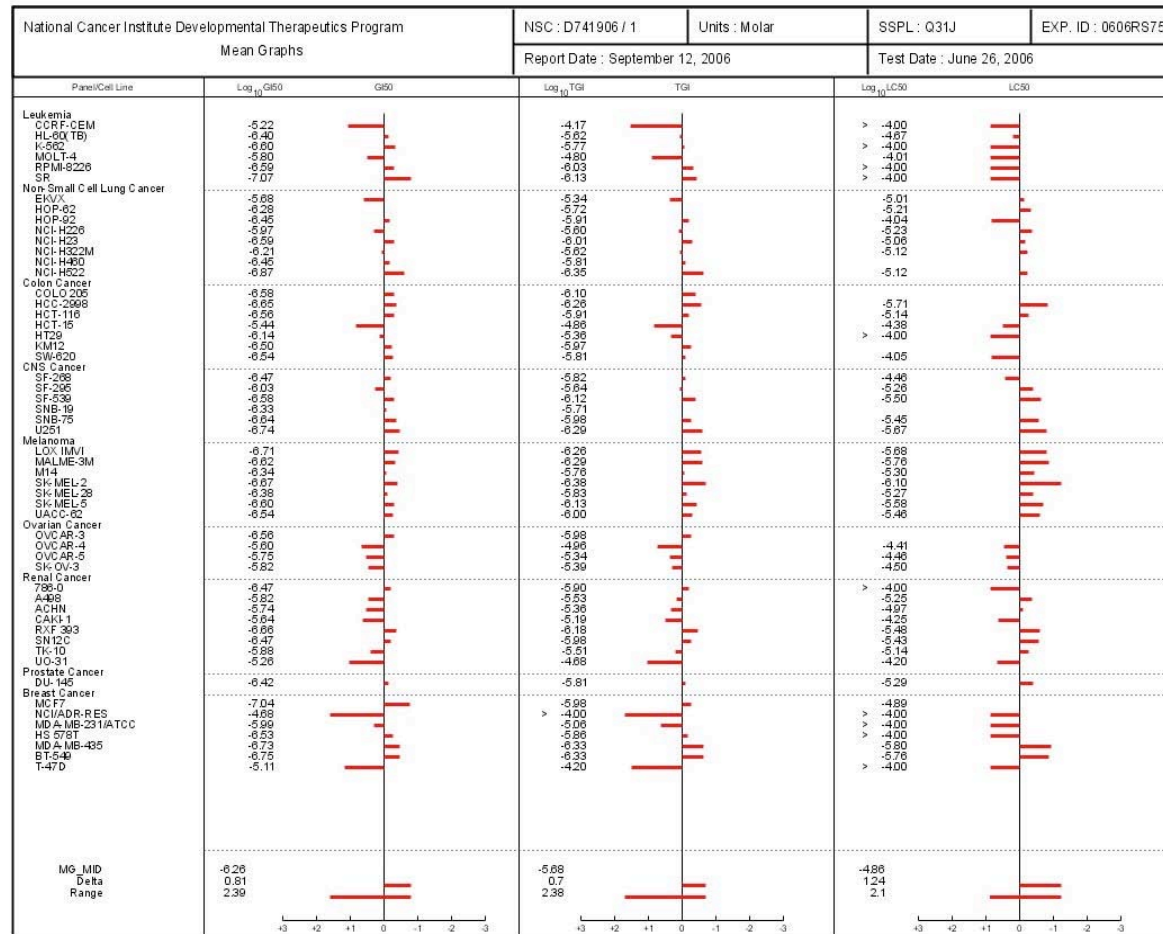
Mean Graph for LD-1

Leukemia
NSC Lung
Colon
CNS
Melanoma
Ovarian
Renal
Prostate
Breast

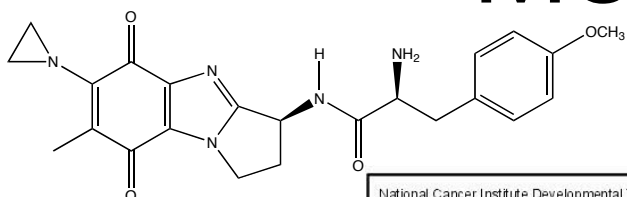


Mean Graph for DD-1

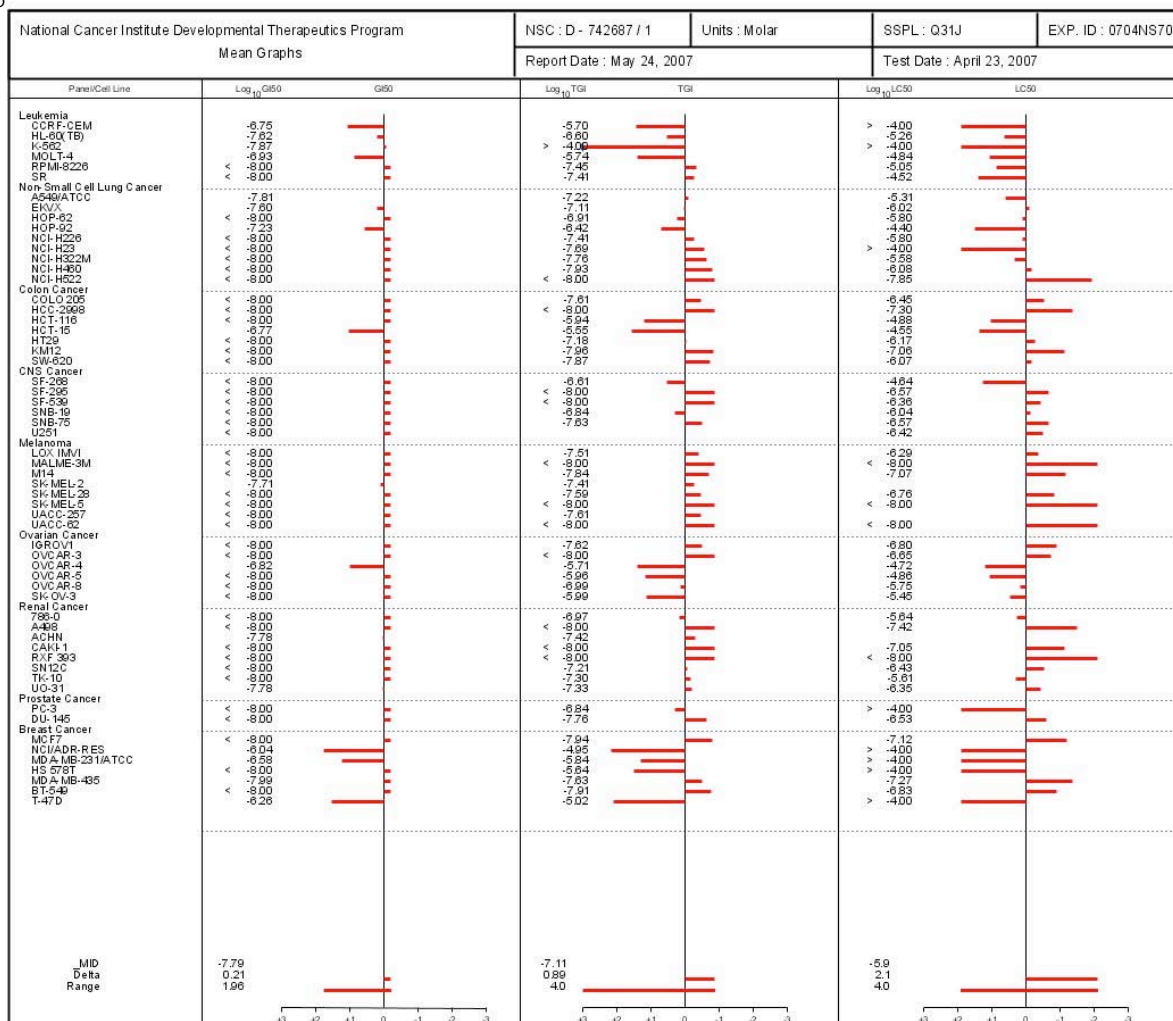
Leukemia
NSC Lung
Colon
CNS
Melanoma
Ovarian
Renal
Prostate
Breast



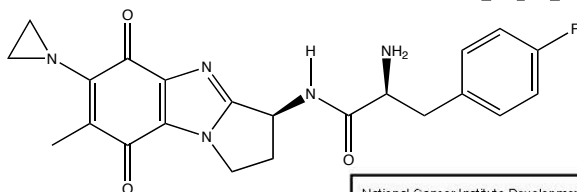
Mean Graph for 2a



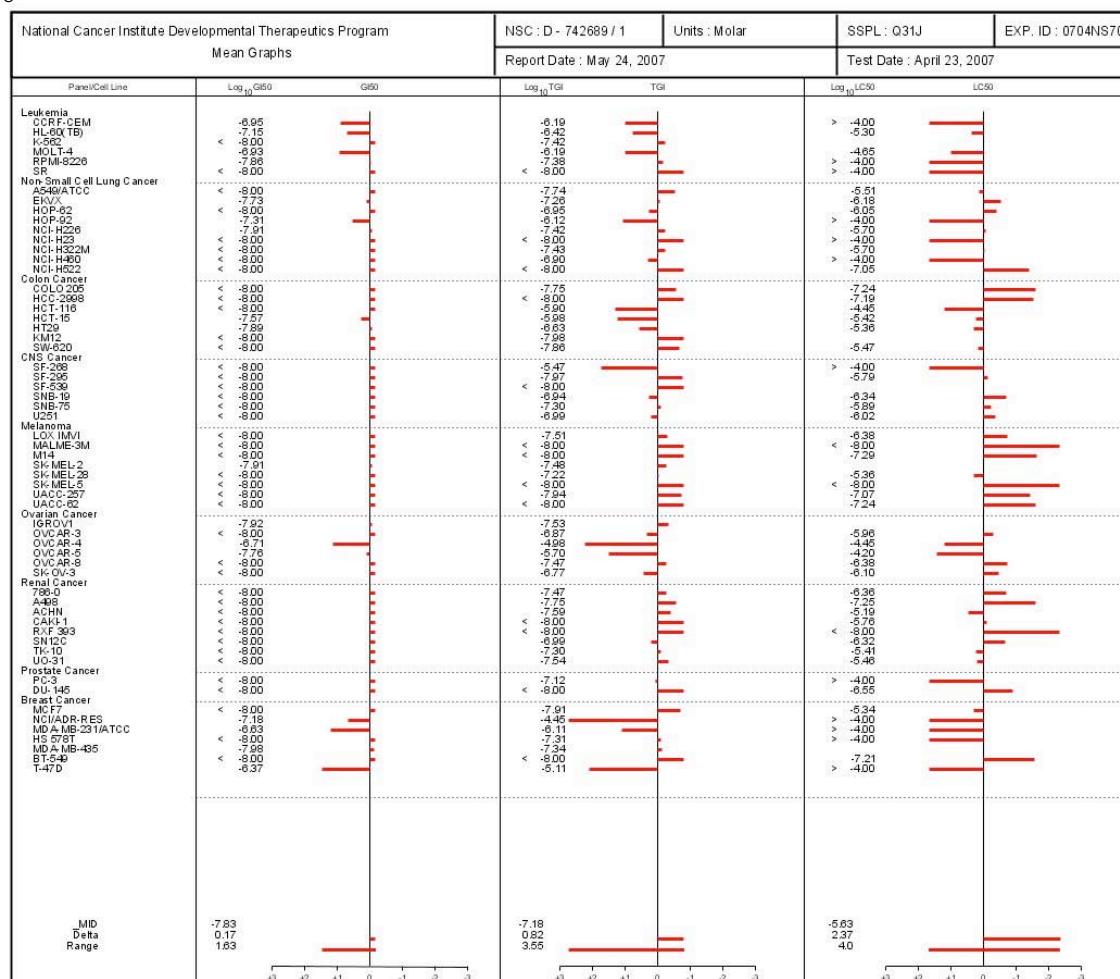
Leukemia
NSC Lung
Colon
CNS
Melanoma
Ovarian
Renal
Prostate
Breast



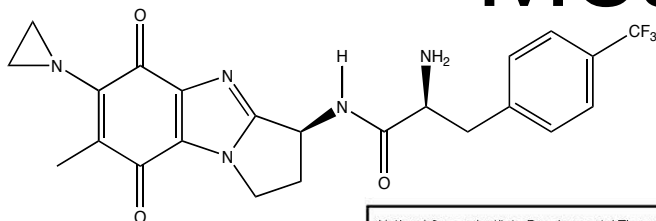
Mean Graph for 2b



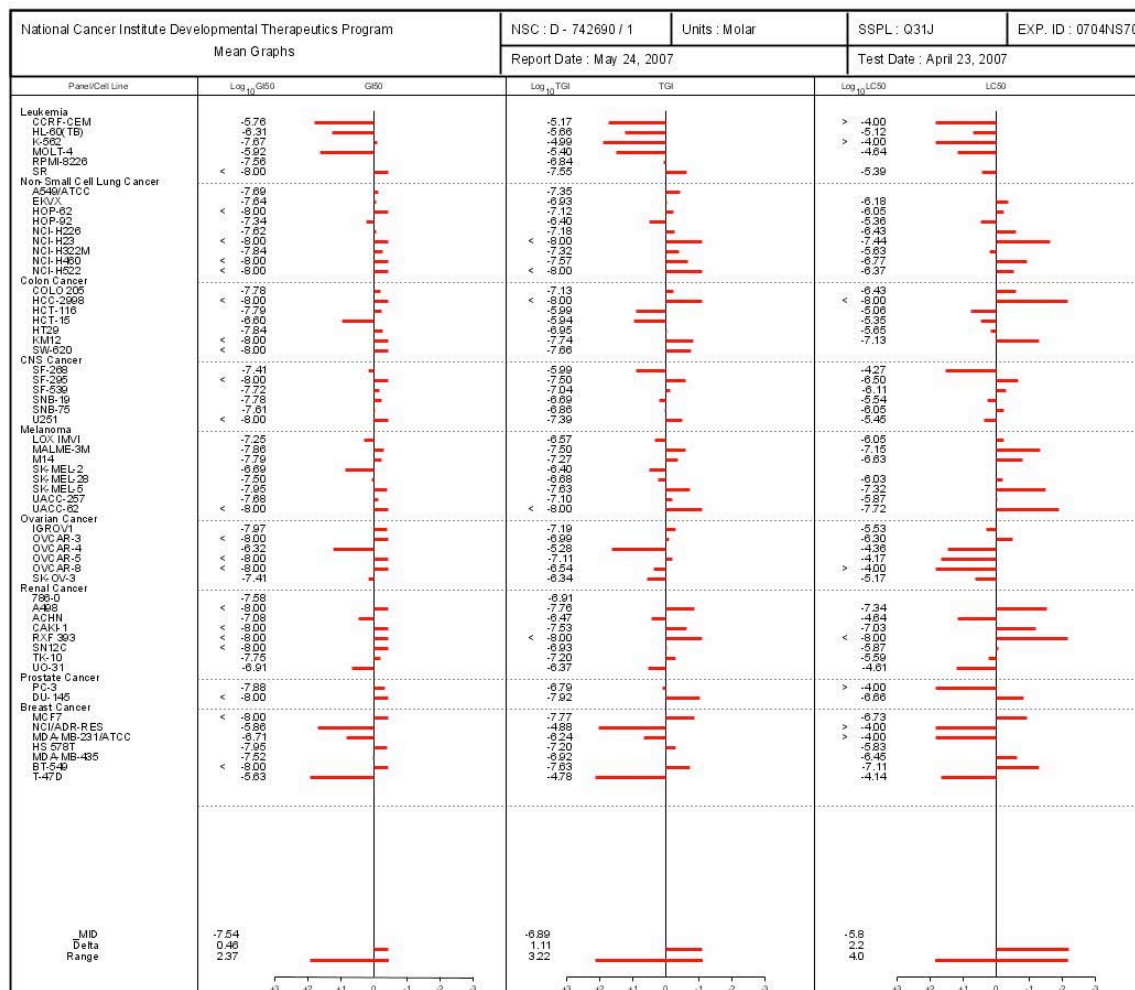
Leukemia
NSC Lung
Colon
CNS
Melanoma
Ovarian
Renal
Prostate
Breast



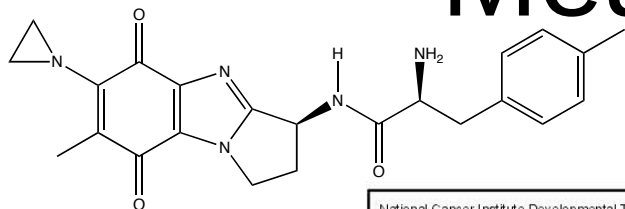
Mean Graph for 2c



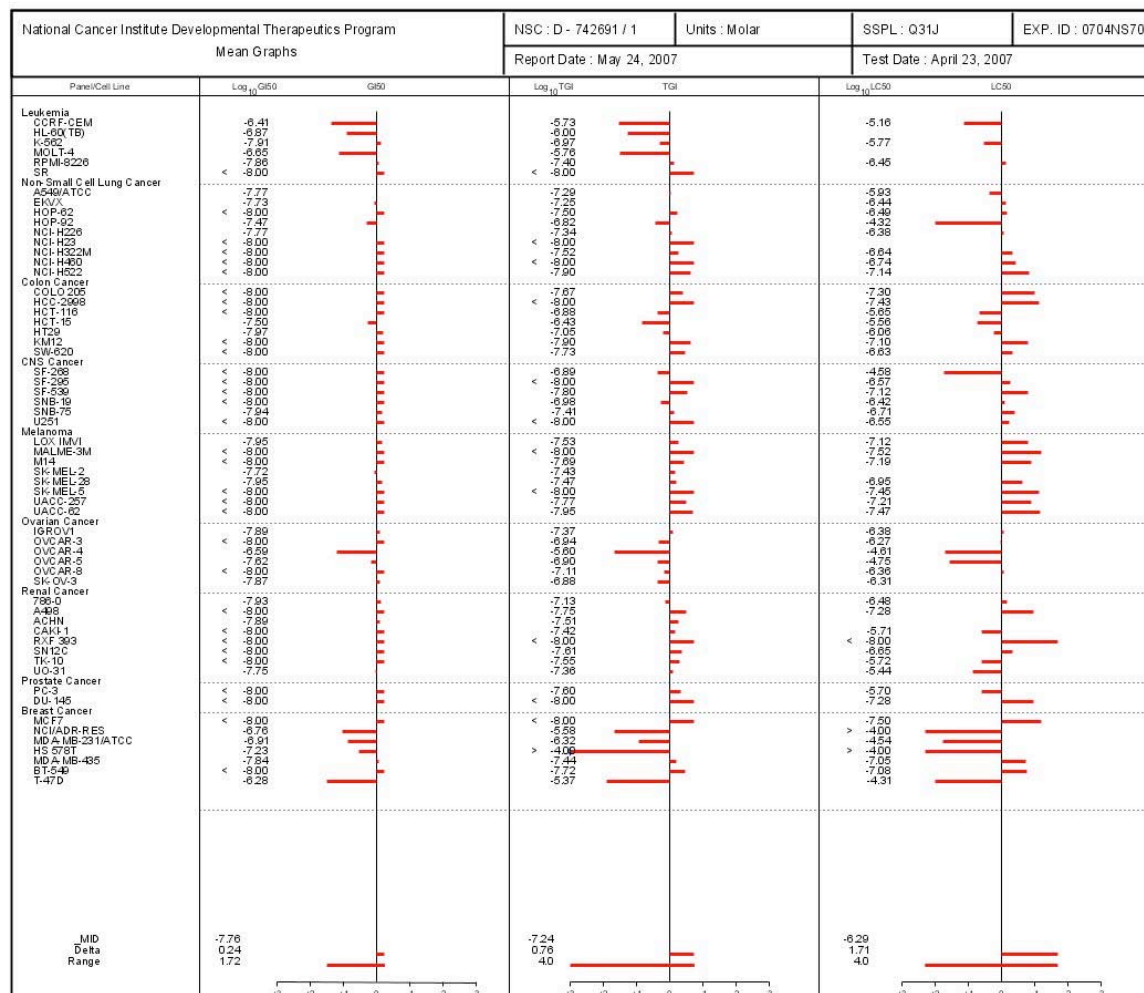
Leukemia
NSC Lung
Colon
CNS
Melanoma
Ovarian
Renal
Prostate
Breast



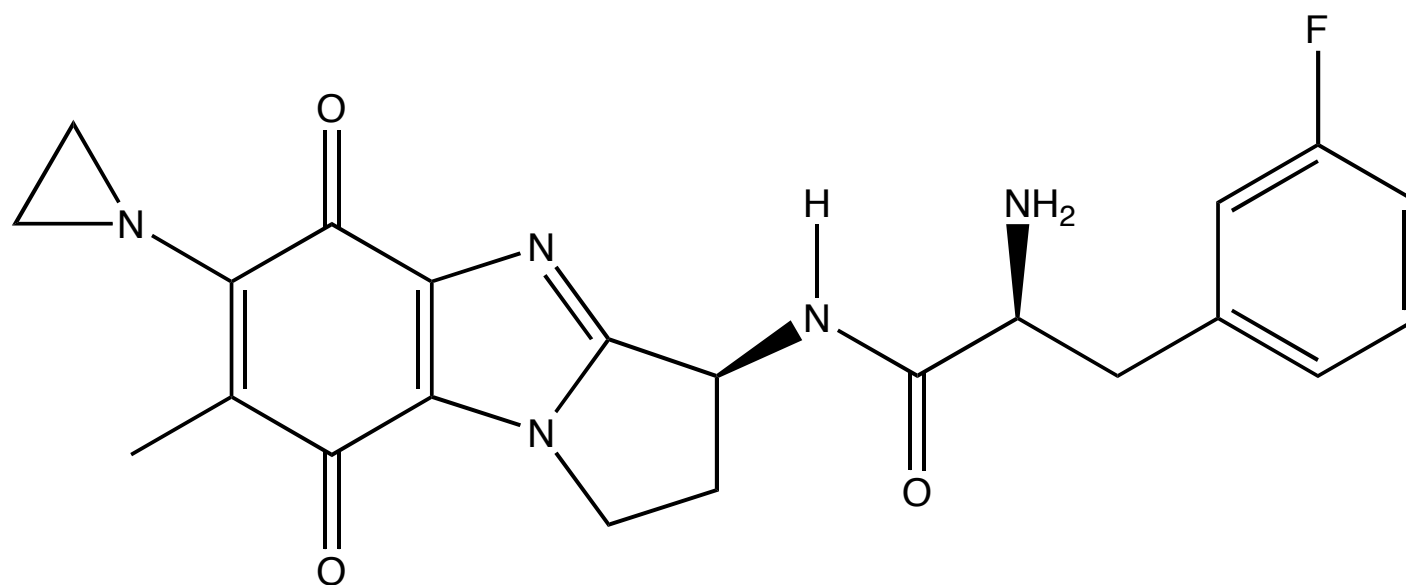
Mean Graph for 2d



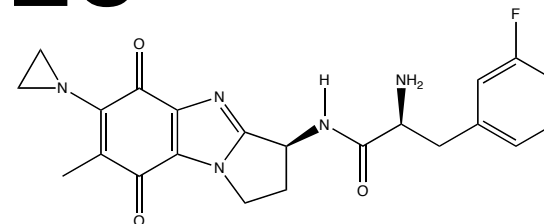
Leukemia
NSC Lung
Colon
CNS
Melanoma
Ovarian
Renal
Prostate
Breast



AJ-84-147, 742692



Mean Graph for 2e



Leukemia
NSC Lung
Colon
CNS
Melanoma
Ovarian
Renal
Prostate
Breast

