

Cholic acid-based antimicrobial peptide mimics as antibacterial agents

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((4-(((3 <i>R</i> ,5 <i>R</i> ,8 <i>R</i> ,9 <i>S</i> ,10 <i>S</i> ,13 <i>R</i> ,14 <i>S</i> ,17 <i>R</i>)-17-((<i>R</i>)-5-(((<i>S</i>)-3-(1 <i>H</i> -Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1 <i>H</i> -cyclopenta[<i>a</i>]phenanthren-3-yl)oxy)-4-oxobutyl)amino)(amino)methaniminium (23).....	53

Methyl ((*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-((*L*-lysylglycyl)oxy)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoyl)-*L*-tryptophanate (25)..55

1,1',1''-((((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7,12-triyl)tris(oxy))tris(2-oxoethane-2,1-diyl))tris(azanediyl))tris(3-methyl-1-oxobutan-2-aminium) (27)57

^1H NMR and ^{13}C NMR spectra of synthesised compounds

Acquisition parameters for ^1H NMR and ^{13}C NMR spectra

^1H NMR:

Standard Bruker pulse program “zg” was used and the delay (D1) was set to 5 s.

Experiment		
PULPROG	zg	Current pulse program
AQ_mod	DQD	Acquisition mode
TD	32768	Size of fid
DS	0	Number of dummy scans
NS	8	Number of scans
TD0	1	Loop count for 'td0'
Width		
SW [ppm]	15.9778	Spectral width
SWH [Hz]	6393.862	Spectral width
AQ [sec]	2.5624576	Acquisition time
FIDRES [Hz]	0.390250	Fid resolution
FW [Hz]	4032000.000	Filter width
Nucleus 1		
NUC1	^1H	Observe nucleus
O1 [Hz]	2601.10	Transmitter frequency offset
O1P [ppm]	6.500	Transmitter frequency offset
SFO1 [MHz]	400.1726011	Transmitter frequency
BF1 [MHz]	400.1700000	Basic transmitter frequency

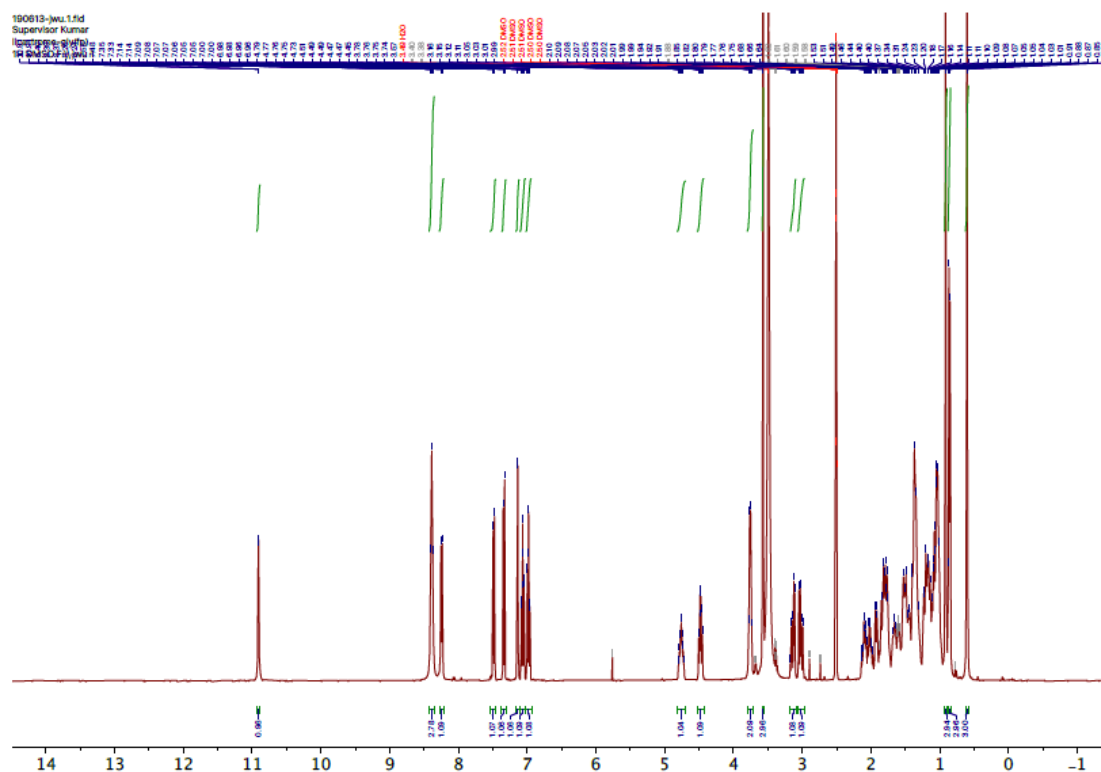
$^{13}\text{C}\{^1\text{H}\}$ NMR:

Standard Bruker pulse program “zgpg30” was used and the delay (D1) was set to 1 s.

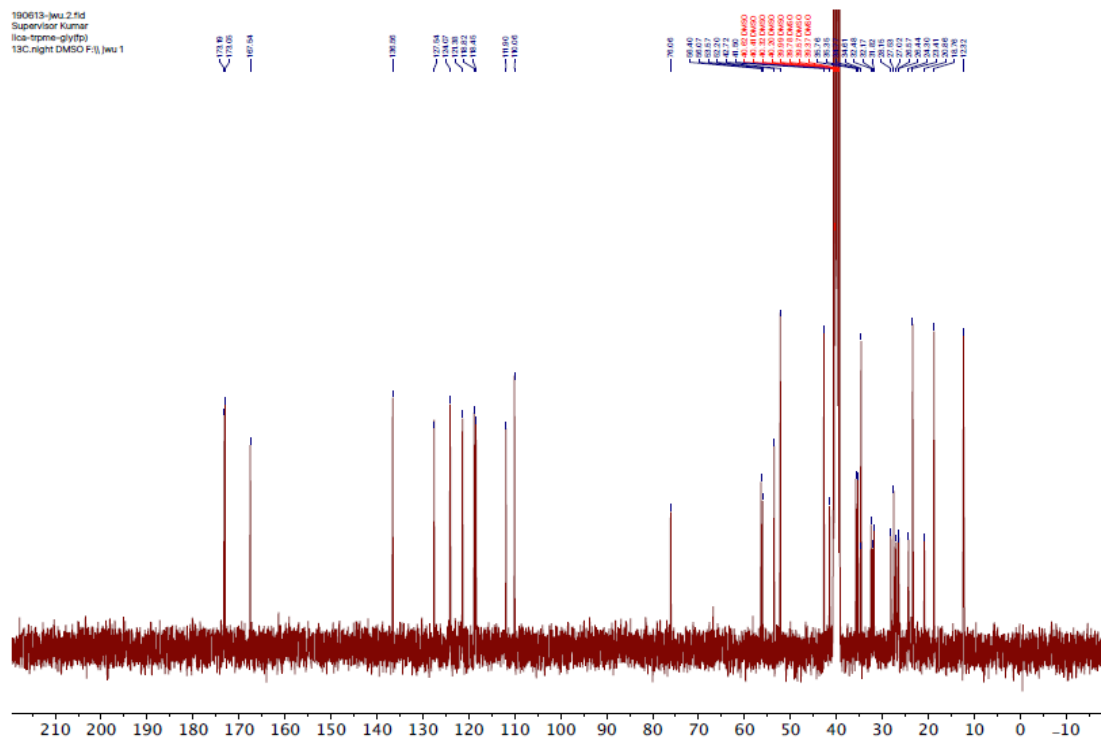
Experiment		
PULPROG	zgpg30	Current pulse program
AQ_mod	DQD	Acquisition mode
TD	65536	Size of fid
DS	2	Number of dummy scans
NS	256	Number of scans
TD0	1	Loop count for 'td0'
Width		
SW [ppm]	238.8728	Spectral width
SWH [Hz]	24038.461	Spectral width
AQ [sec]	1.3631488	Acquisition time
FIDRES [Hz]	0.733596	Fid resolution
FW [Hz]	4032000.000	Filter width
Nucleus 1		
NUC1	^{13}C	Observe nucleus
O1 [Hz]	10061.66	Transmitter frequency offset
O1P [ppm]	99.994	Transmitter frequency offset
SFO1 [MHz]	100.6328882	Transmitter frequency
BF1 [MHz]	100.6228265	Basic transmitter frequency
Nucleus 2		
NUC2	^1H	2nd nucleus
O2 [Hz]	1600.68	Frequency offset of 2nd nucleus
O2P [ppm]	4.000	Frequency offset of 2nd nucleus
SFO2 [MHz]	400.1716007	Frequency of 2nd nucleus
BF2 [MHz]	400.1700000	Basic frequency of 2nd nucleus

2-(((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)-2-oxoethan-1-aminium (**16a**)

^1H NMR (400 MHz, $\text{DMSO}-d_6$):



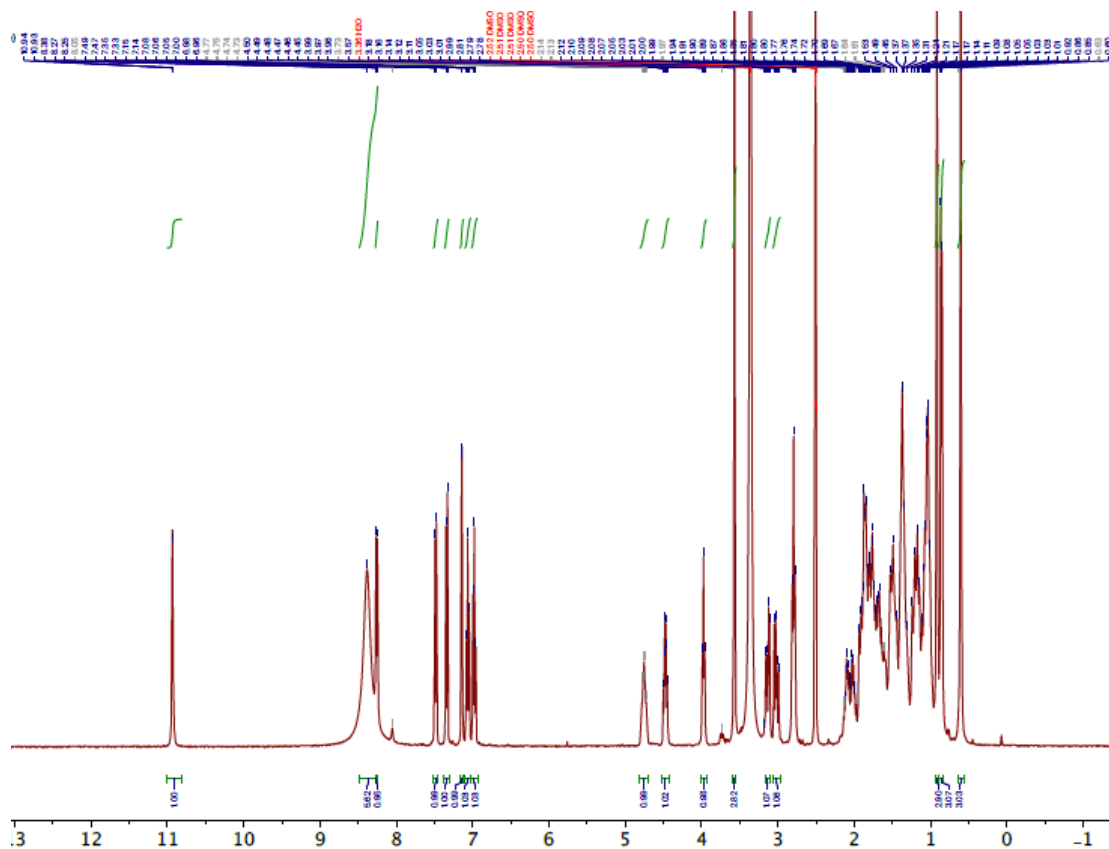
^{13}C NMR (100 MHz, $\text{DMSO}-d_6$):



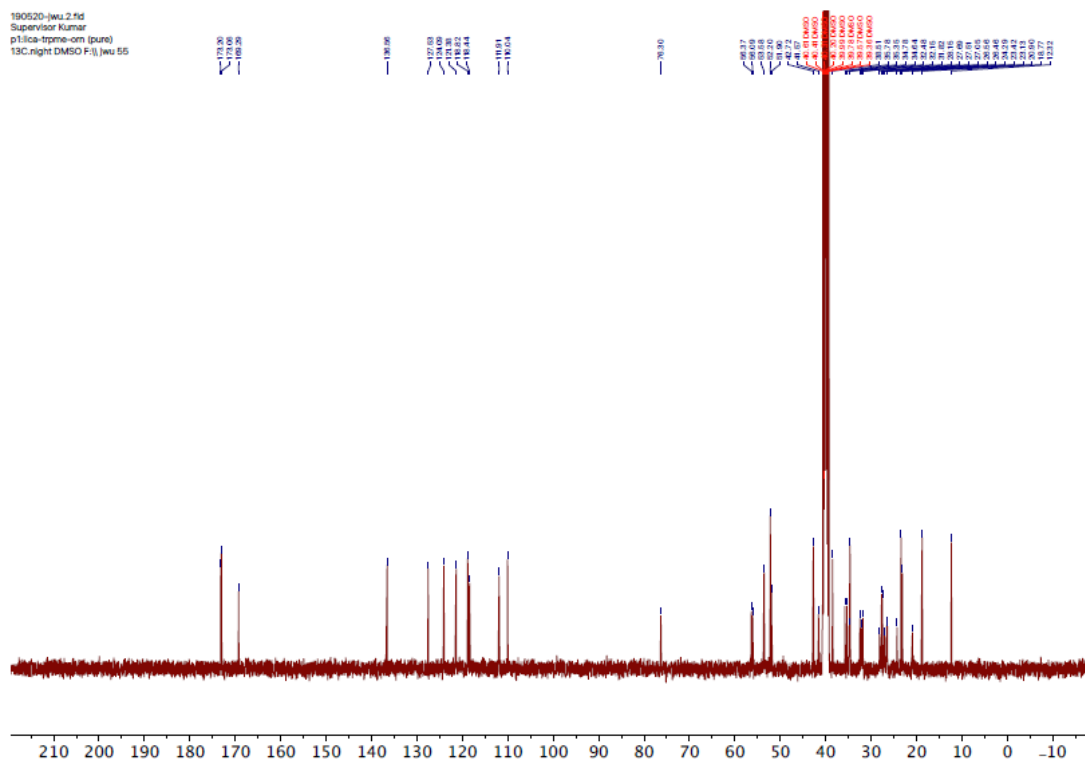
¹H NMR (400 MHz, DMSO-*d*₆):

(*S*)-5-(((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)-5-oxopentane-1,4-diaminium (**16c**)

^1H NMR (400 MHz, $\text{DMSO}-d_6$):



^{13}C NMR (100 MHz, $\text{DMSO}-d_6$):

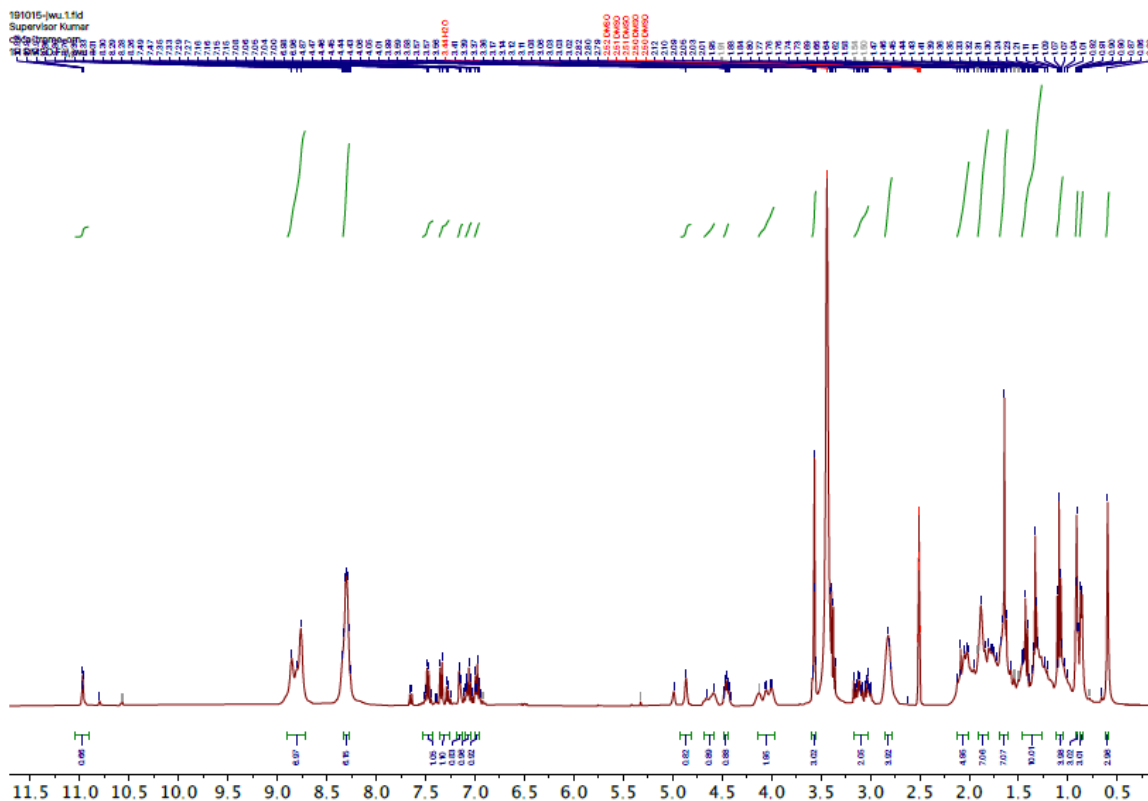


¹H NMR (400 MHz, DMSO-*d*₆):

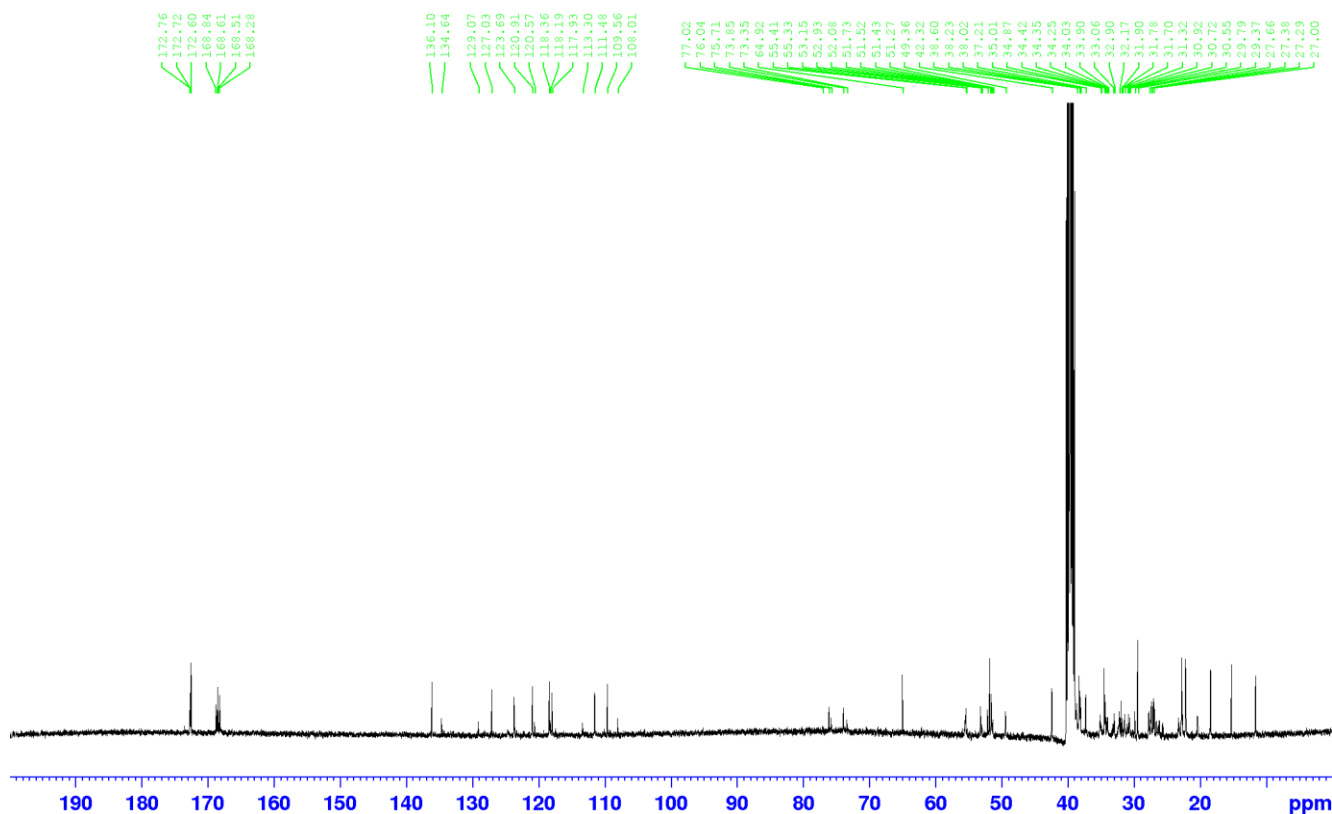
¹H NMR (400 MHz, DMSO-*d*₆):

¹H NMR (400 MHz, DMSO-*d*₆):

(4*S*,4'*S*)-5,5'-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentane-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7-diyl)bis(oxy))bis(5-oxopentane-1,4-diaminium) (**17c**)
¹H NMR (400 MHz, DMSO-*d*₆):



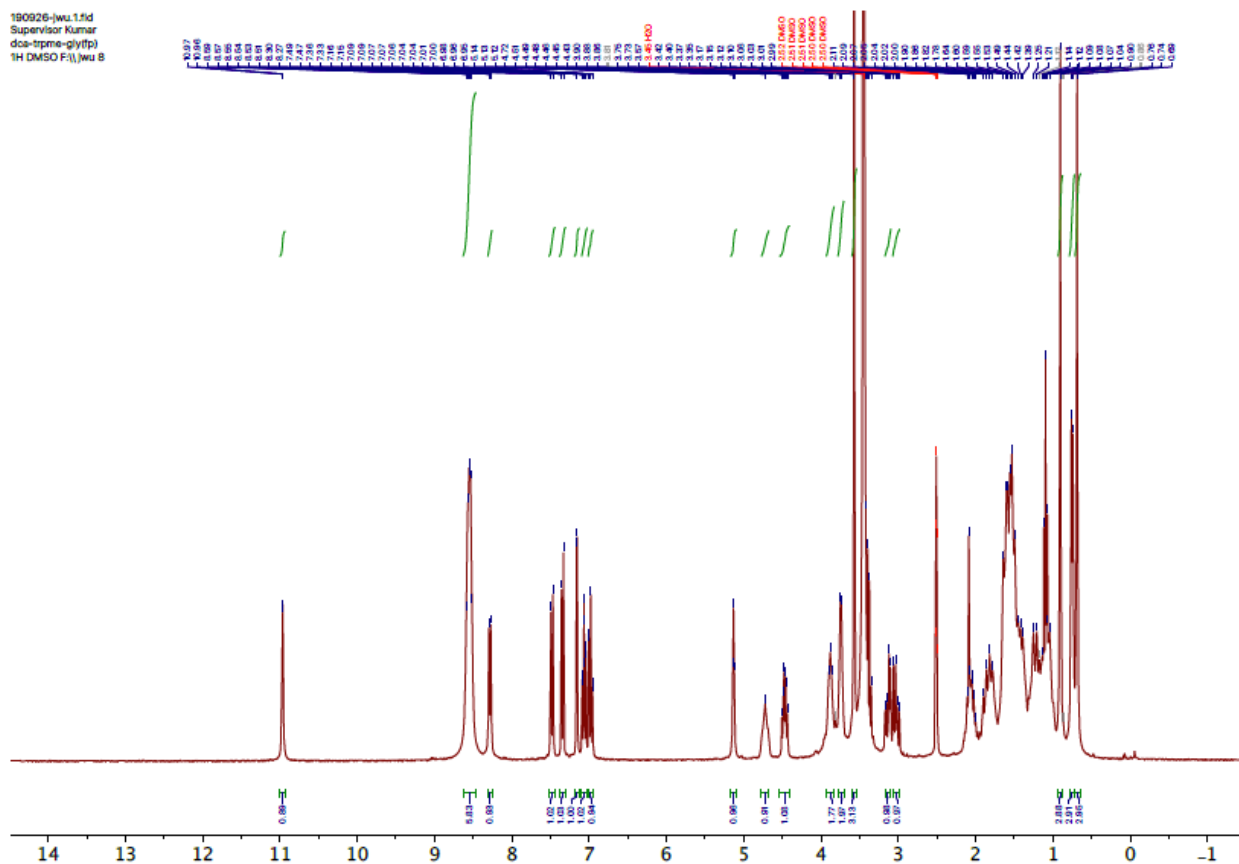
¹³C NMR (100 MHz, DMSO-*d*₆):



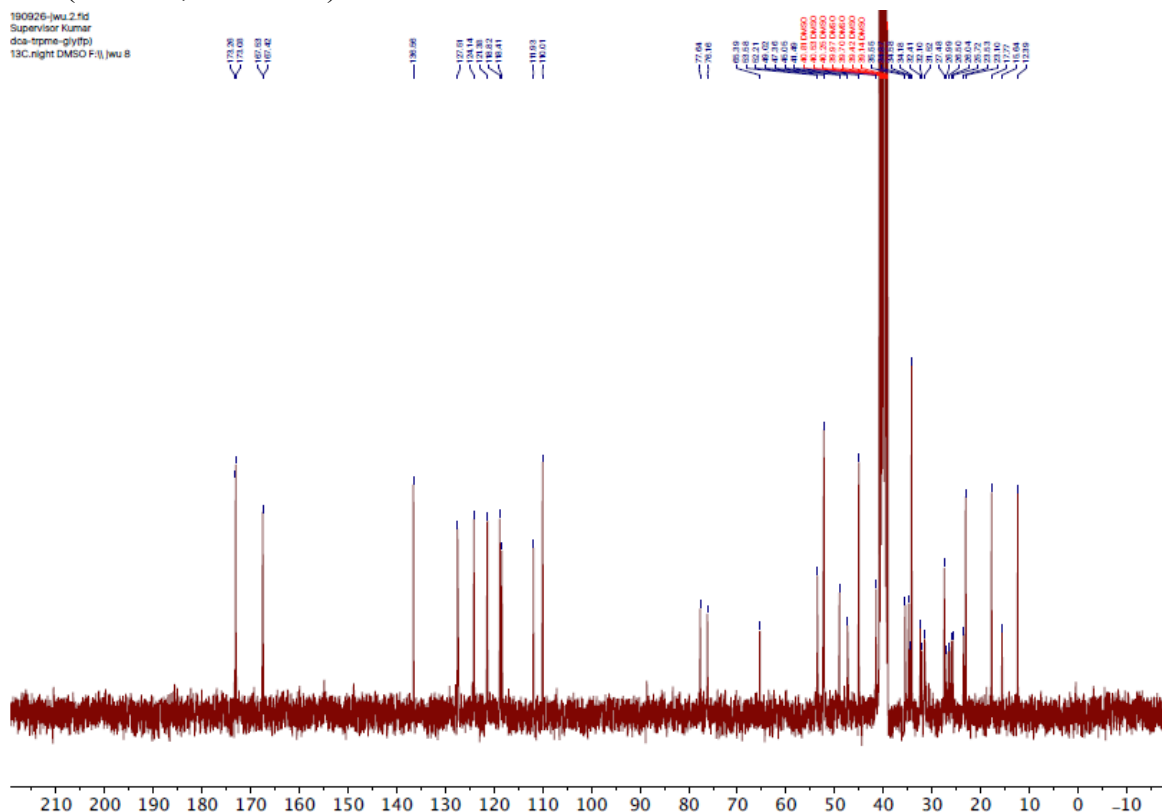
¹H NMR (600 MHz, DMSO-*d*₆):

2,2'-(((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,12-diyl)bis(oxy))bis(2-oxoethan-1-aminium) (**18a**)

¹H NMR (300 MHz, DMSO-*d*₆):

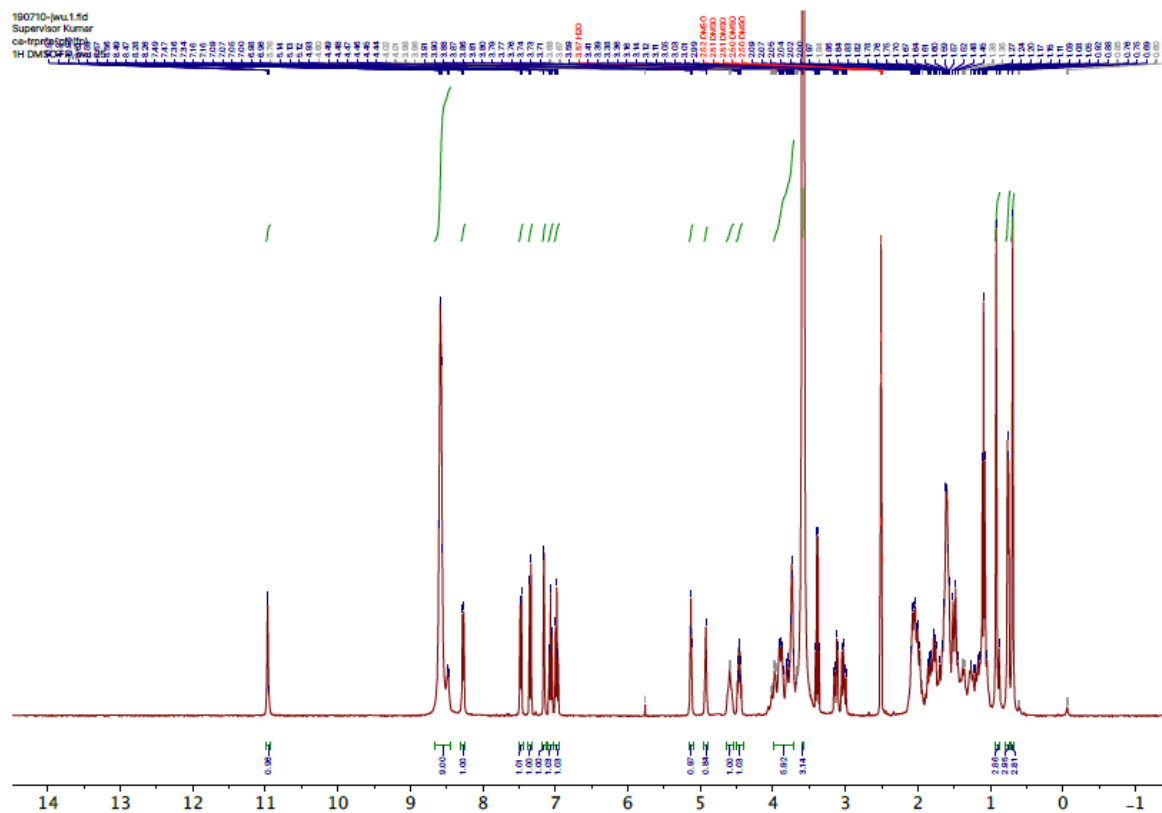


¹³C NMR (75 MHz, DMSO-*d*₆):

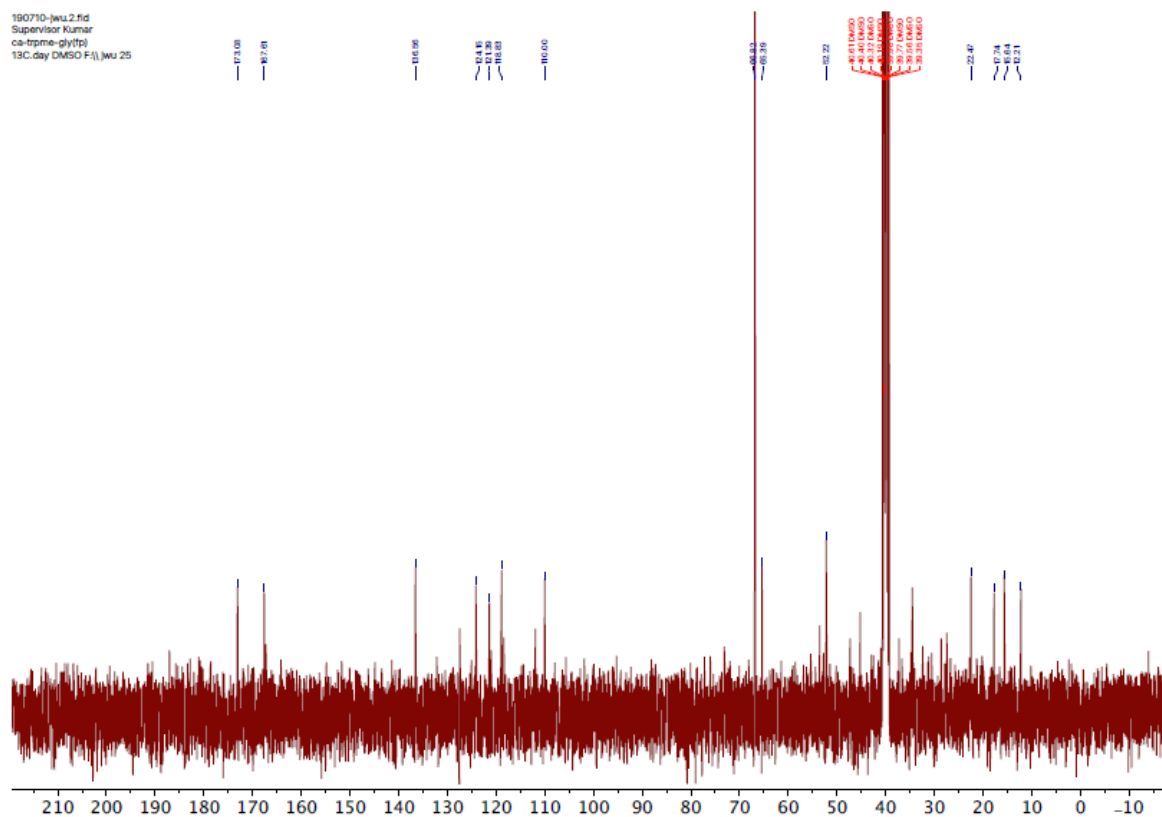


2,2'-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-3-(2-aminoacetoxy)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-7,12-diyl)bis(oxy))bis(2-oxoethan-1-aminium) (**19a**)

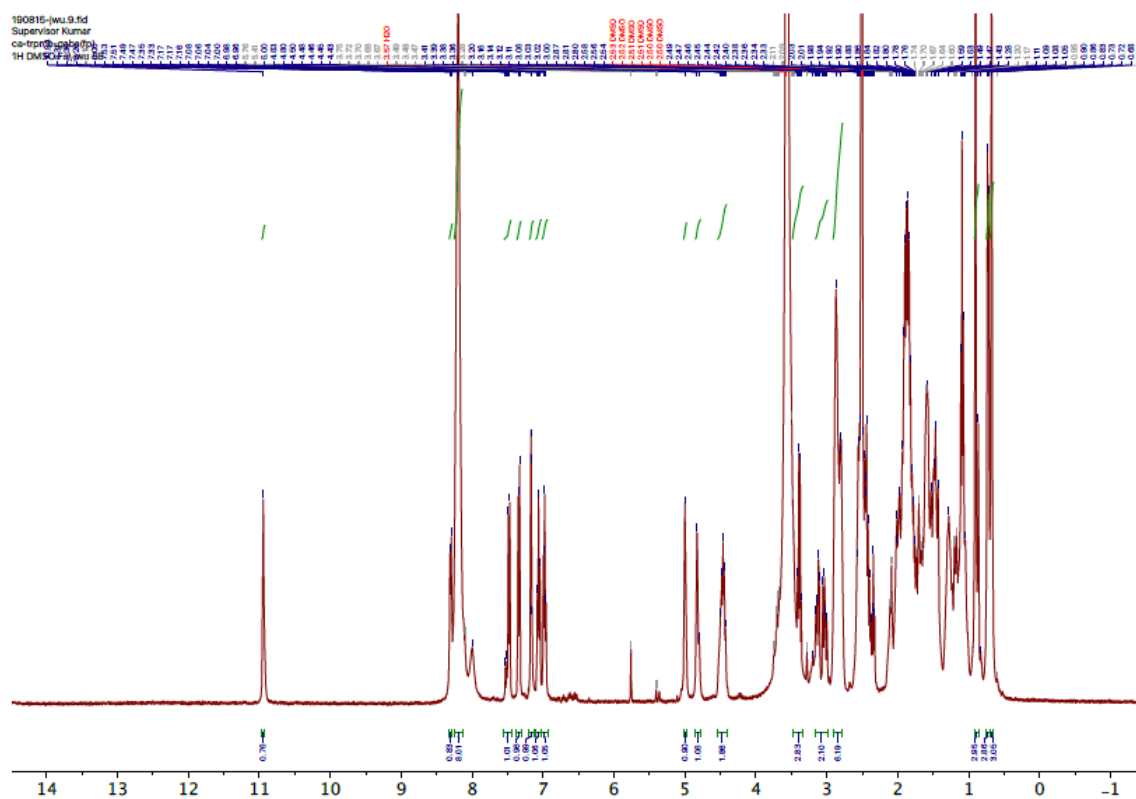
¹H NMR (400 MHz, DMSO-*d*₆):



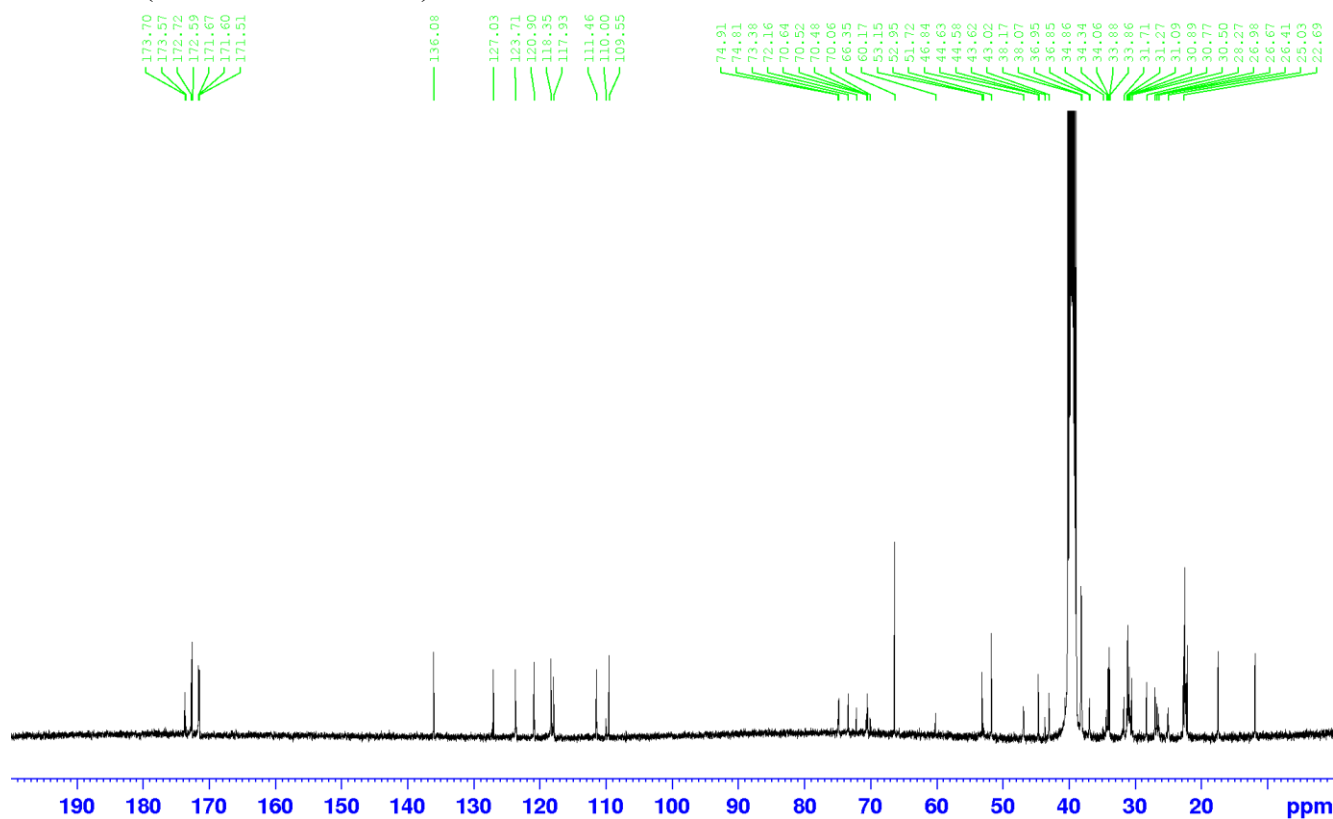
¹³C NMR (100 MHz, DMSO-*d*₆):



4,4',4''-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7,12-triyl)tris(oxy))tris(4-oxobutan-1-aminium) (**19b**)
¹H NMR (400 MHz, DMSO-*d*₆):

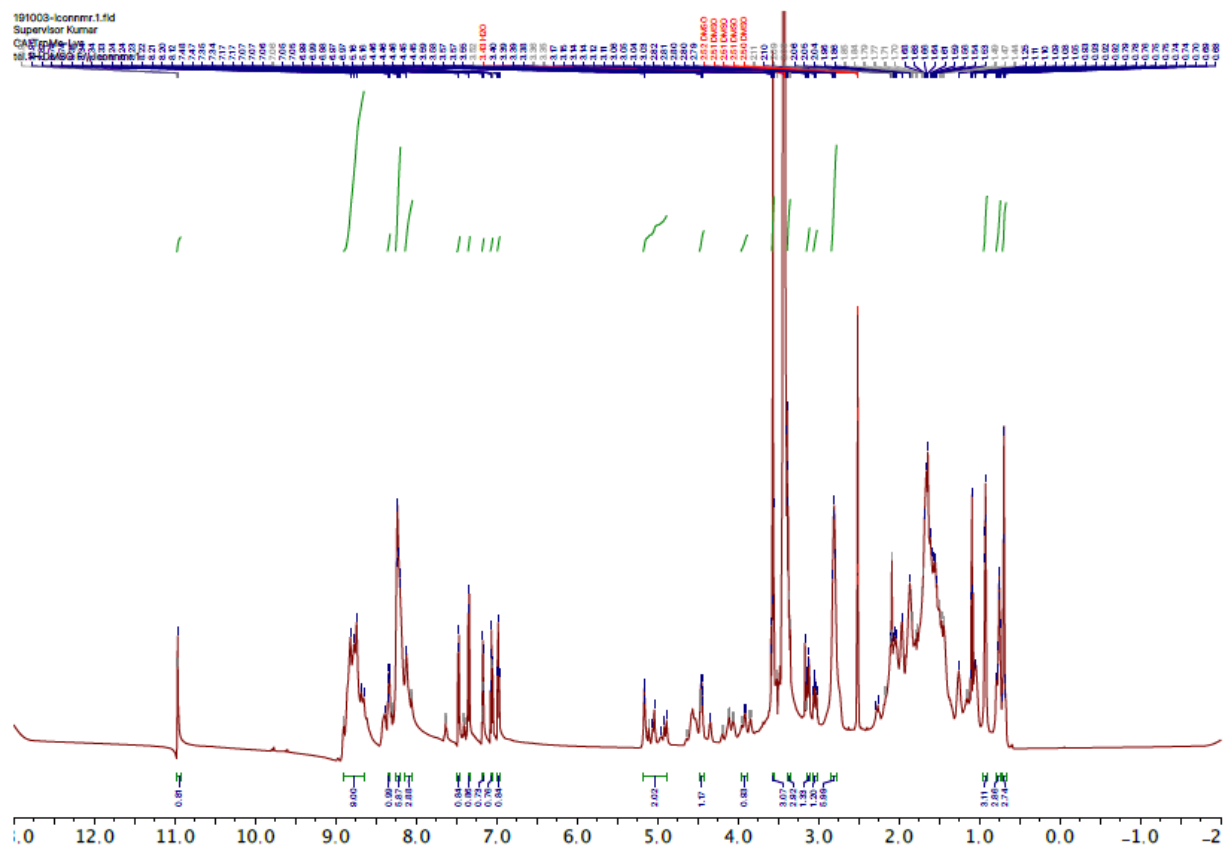


¹³C NMR (100 MHz, DMSO-*d*₆):

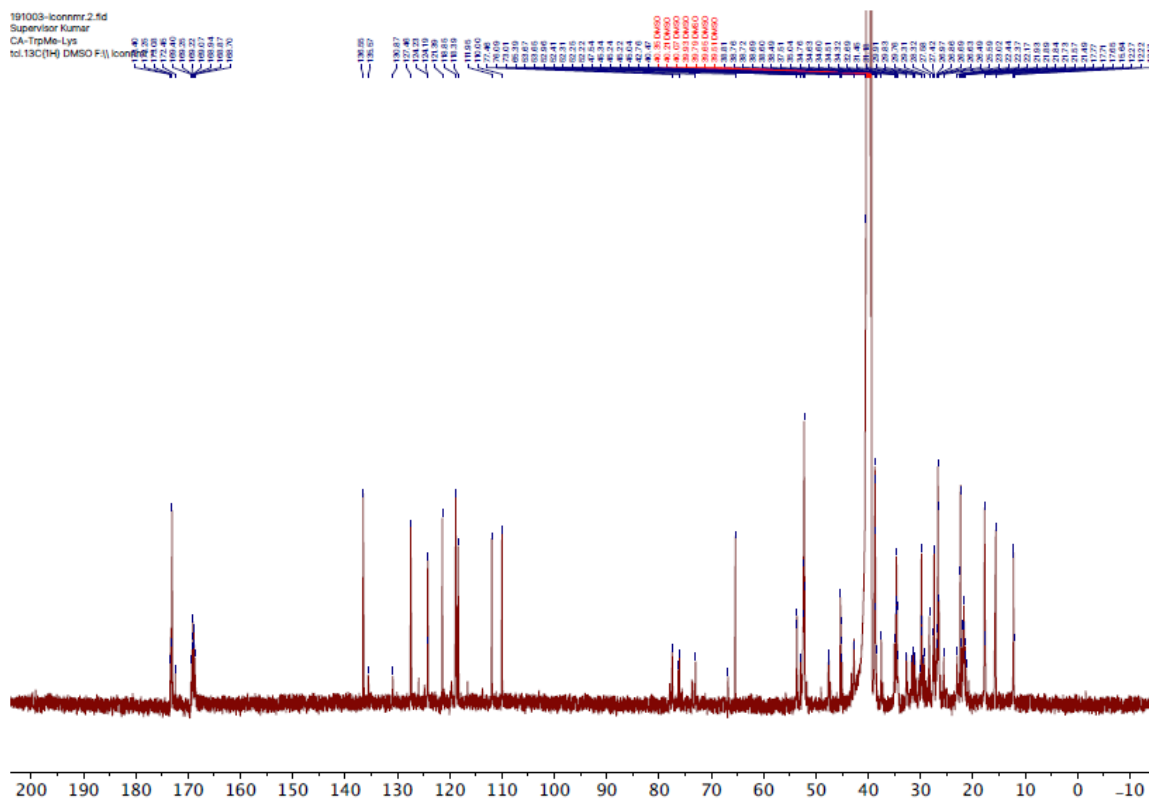


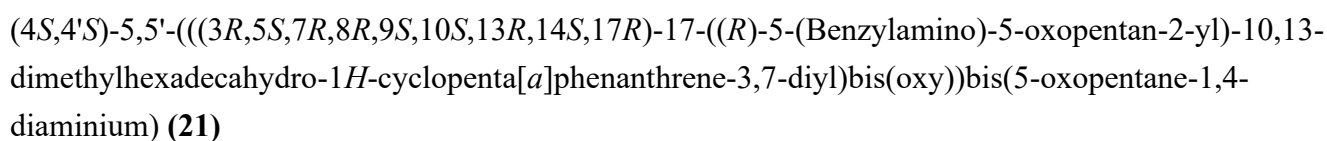
¹H NMR (600 MHz, DMSO-*d*₆):

(5*S*,5'*S*,5''*S*)-6,6',6''-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7,12-triyl)tris(oxy))tris(6-oxohexane-1,5-diaminium) (**19d**)
¹H NMR (600 MHz, DMSO-*d*₆):



¹³C NMR (150 MHz, DMSO-*d*₆):



¹H NMR (400 MHz, DMSO-*d*₆):¹H NMR (400 MHz, DMSO-*d*₆):

¹H NMR (400 MHz, DMSO-*d*₆):

¹H NMR (400 MHz, DMSO-*d*₆):

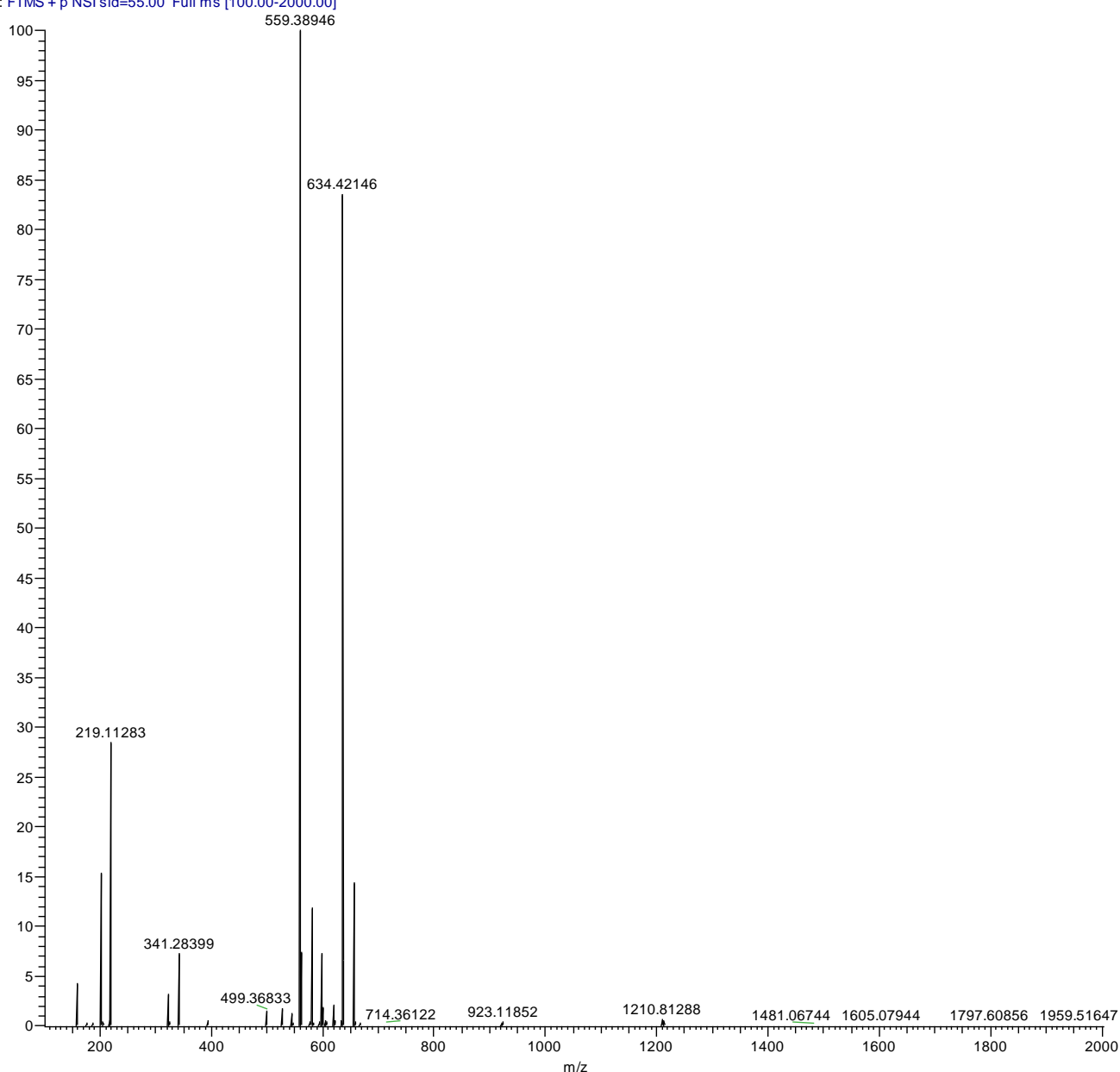
¹H NMR (600 MHz, DMSO-*d*₆):

High resolution mass spectra (HRMS) of synthesised compounds

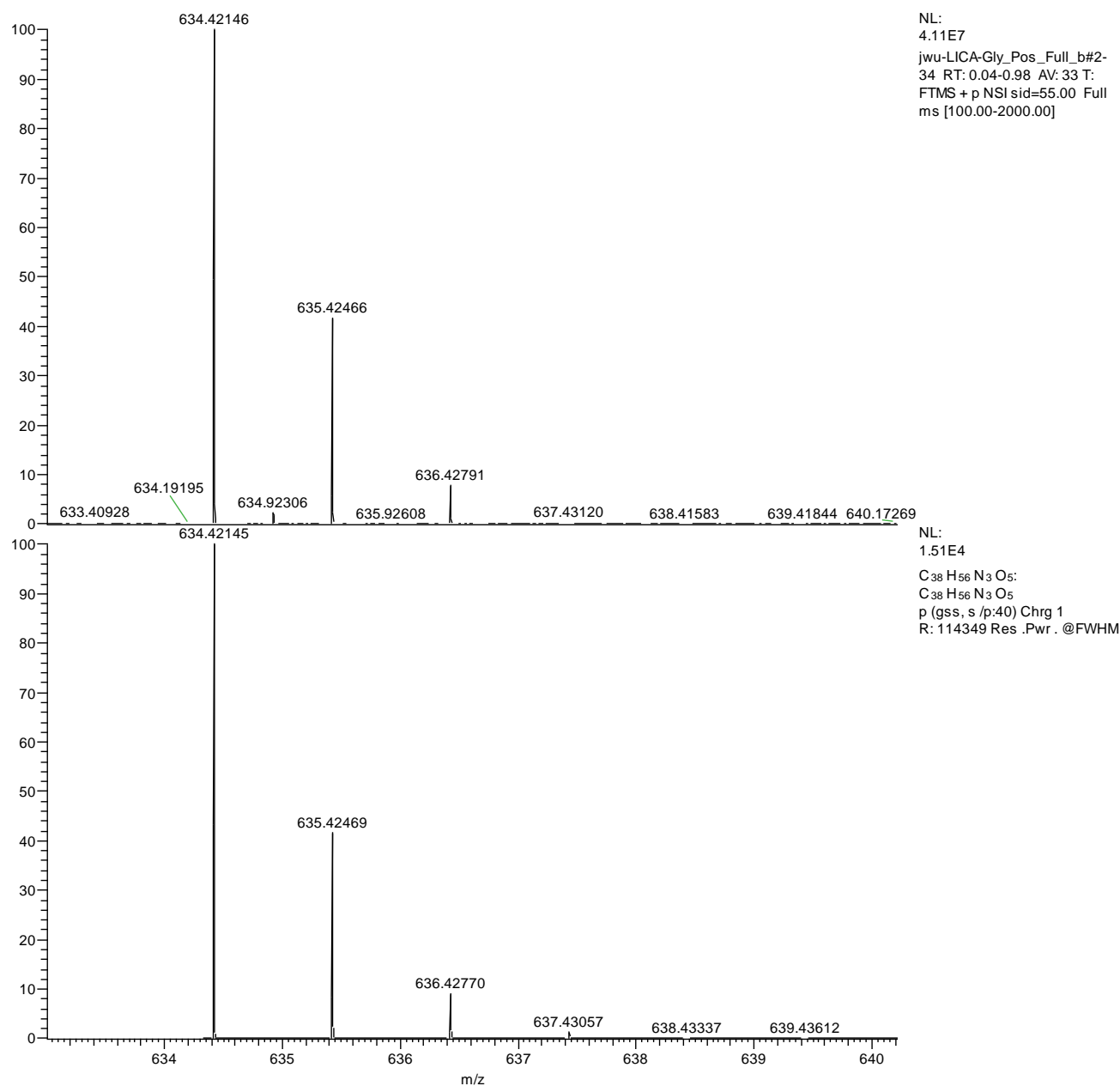
2-(((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)-2-oxoethan-1-aminium (**16a**)

Full spectrum

jwu-LICA-Gly_Pos_Full_b #2-34 RT: 0.04-0.98 AV: 33 NL: 4.92E7
T: FTMS + p NSI sid=55.00 Full ms [100.00-2000.00]



Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

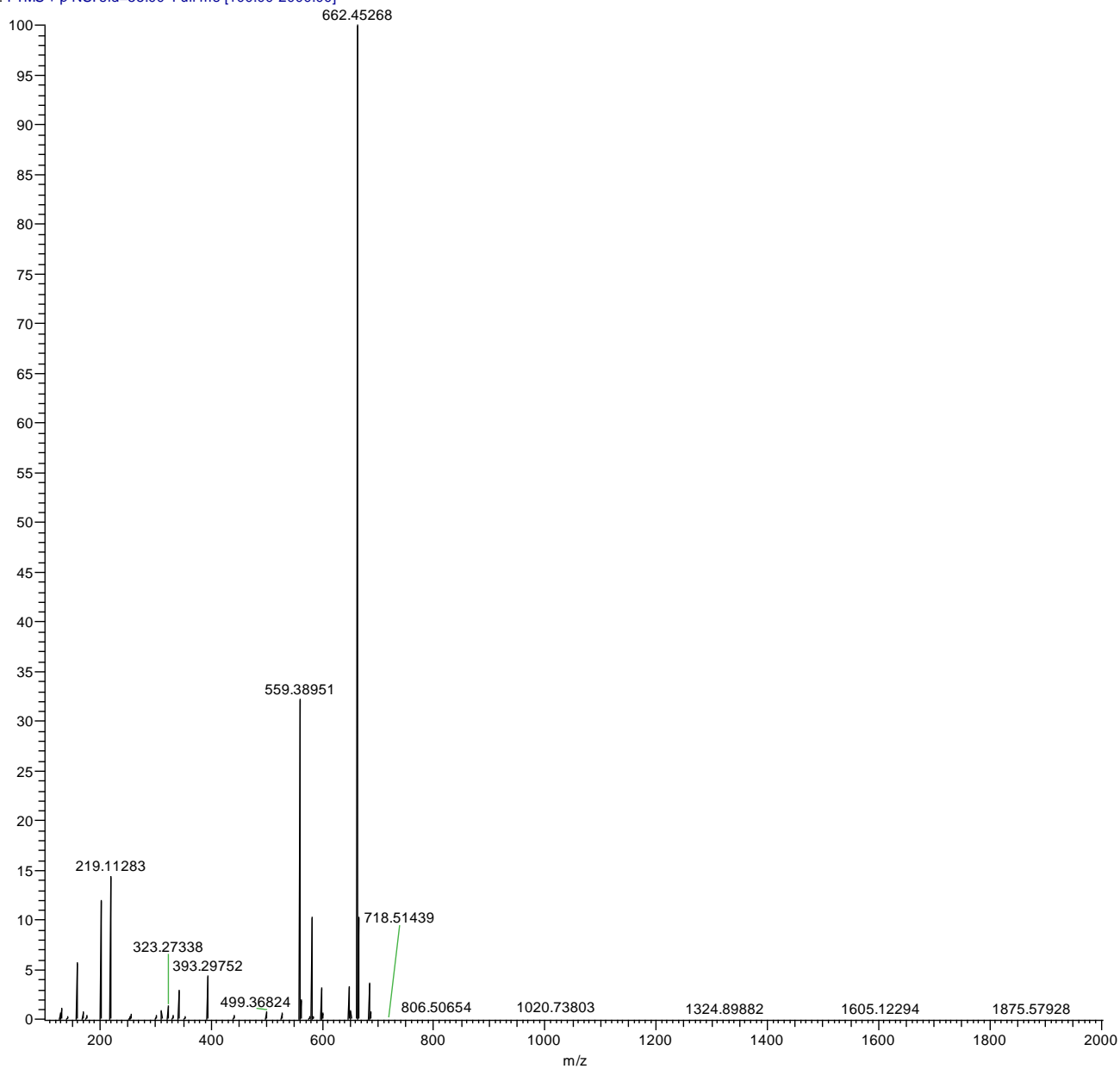


4-(((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)-4-oxobutan-1-aminium (**16b**)

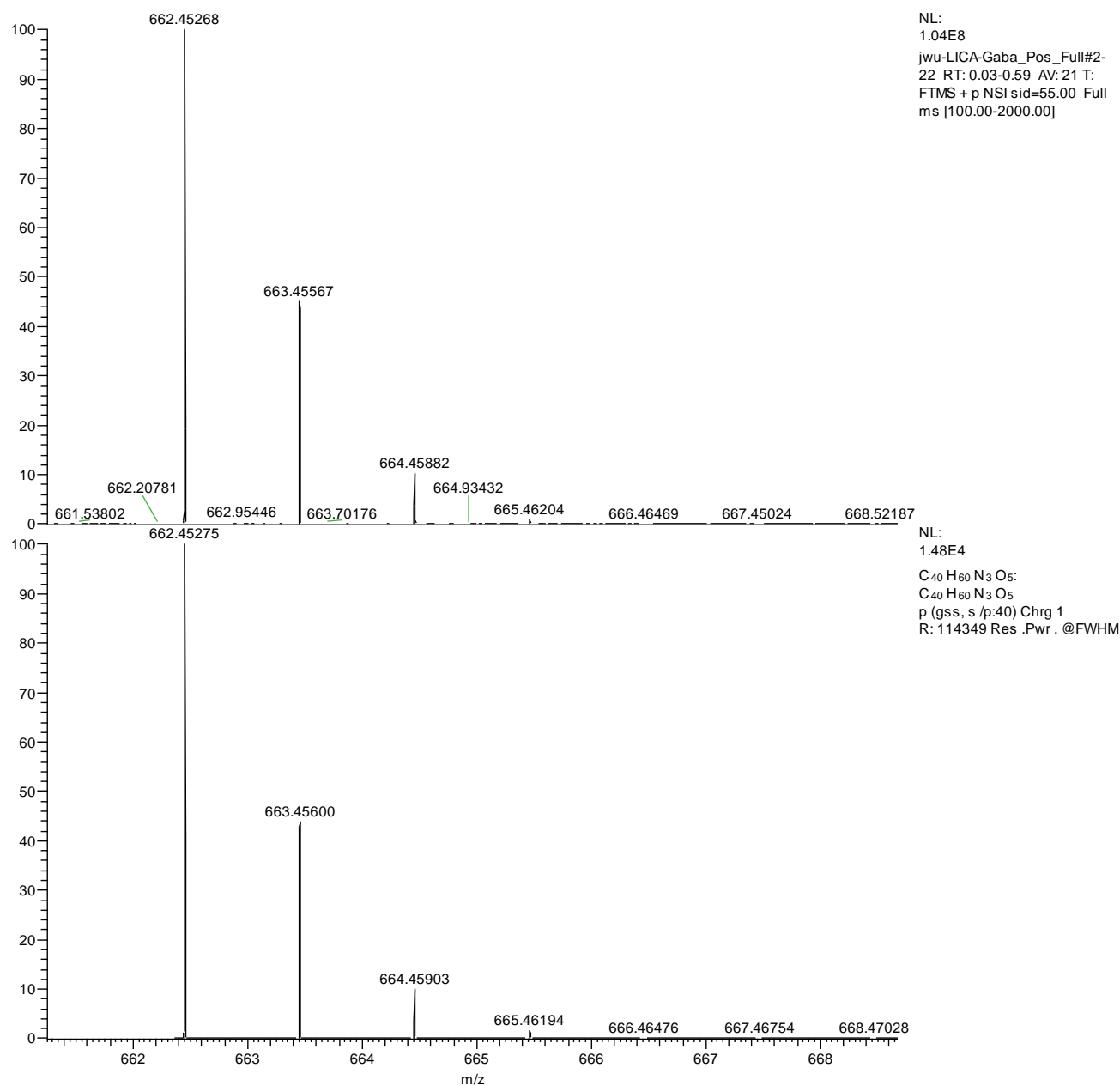
Full spectrum

jwu-LICA-Gaba_Pos_Full #2-22 RT: 0.03-0.59 AV: 21 NL: 1.04E8

T: FTMS + p NSI sid=55.00 Full ms [100.00-2000.00]



Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

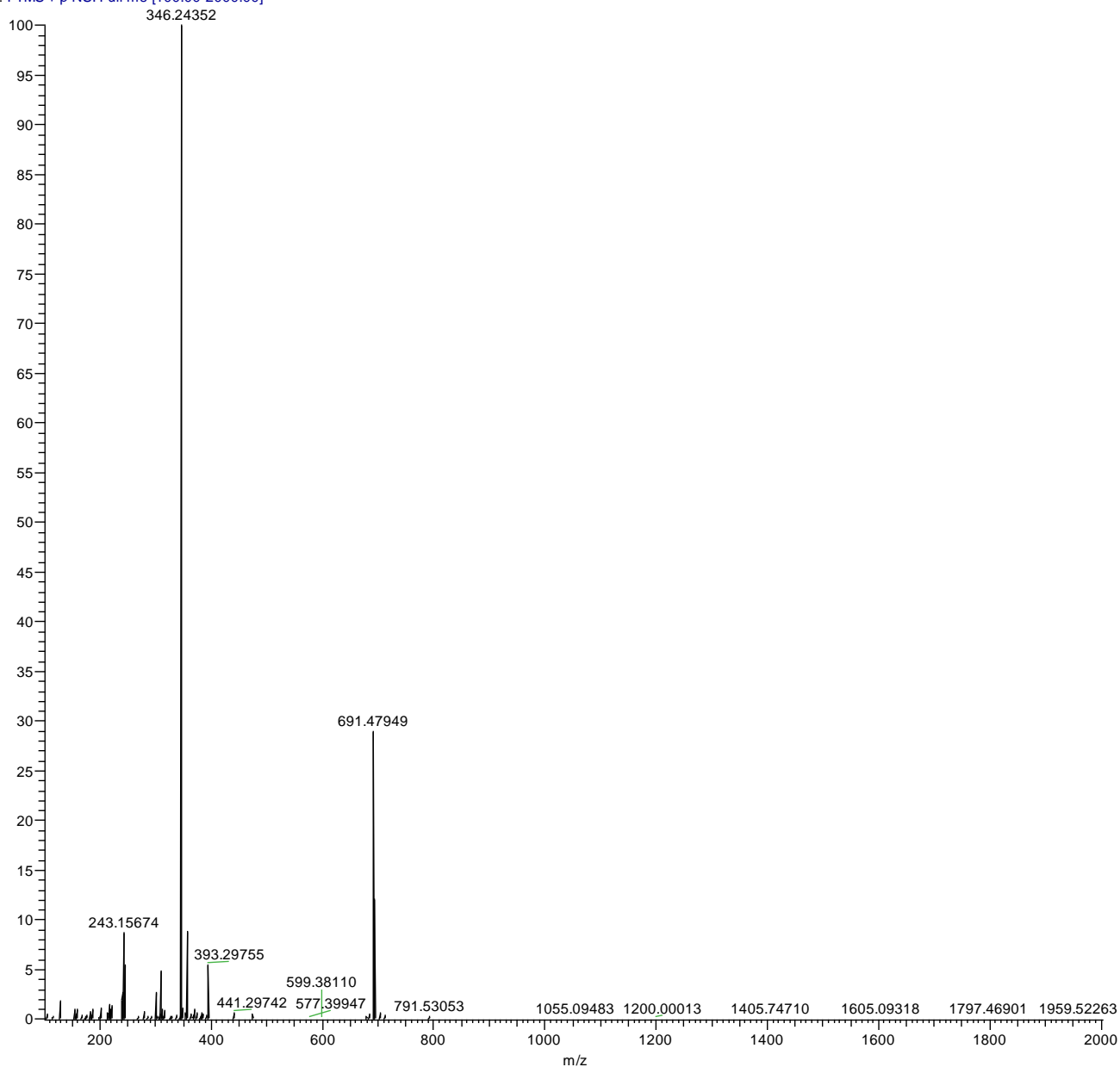


(*S*)-5-(((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)-5-oxopentane-1,4-diaminium (**16c**)

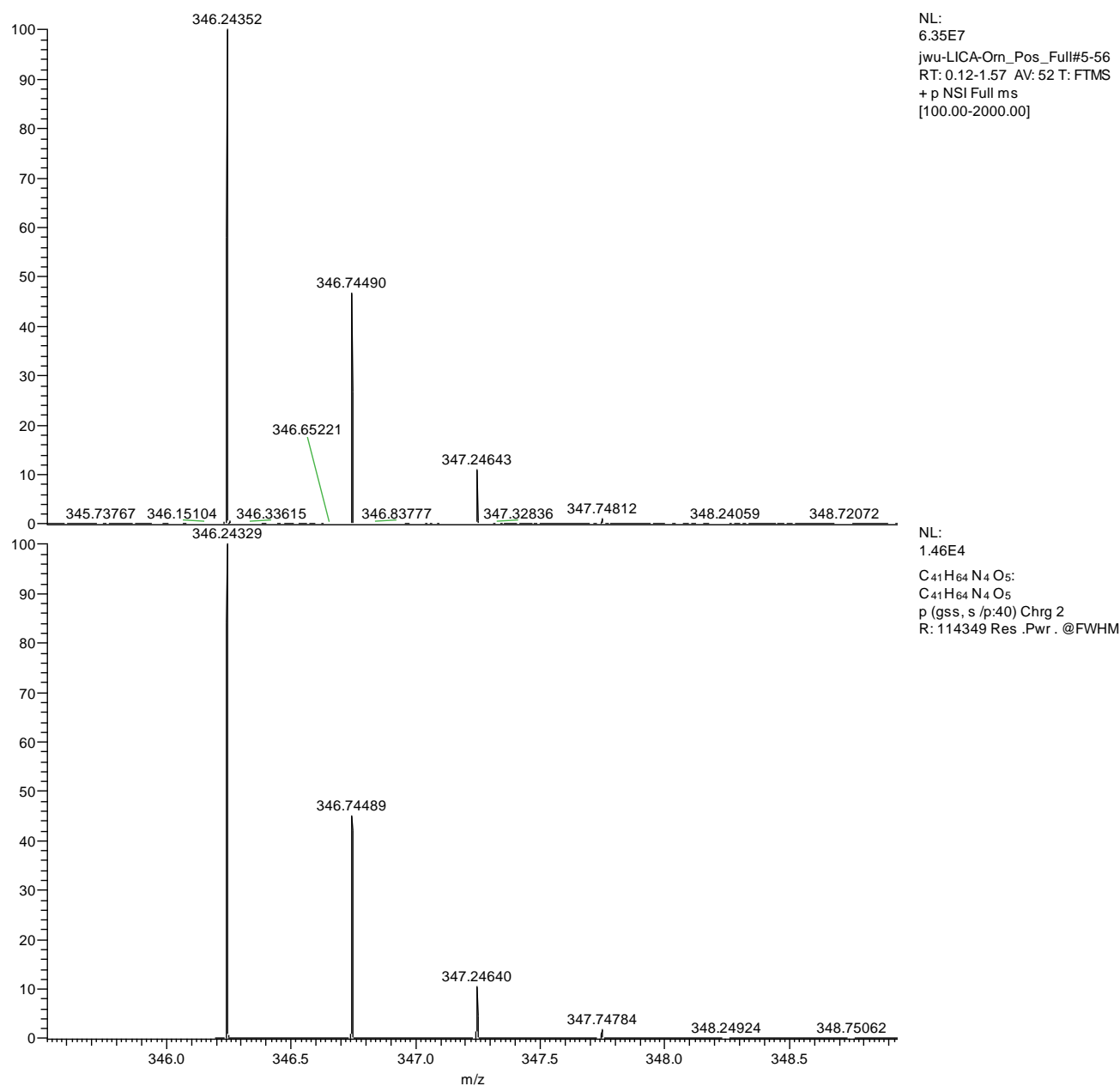
Full spectrum

jwu-LICA-Orn_Pos_Full #5-56 RT: 0.12-1.57 AV: 52 NL: 6.35E7

T: FTMS + p NSI Full ms [100.00-2000.00]



Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

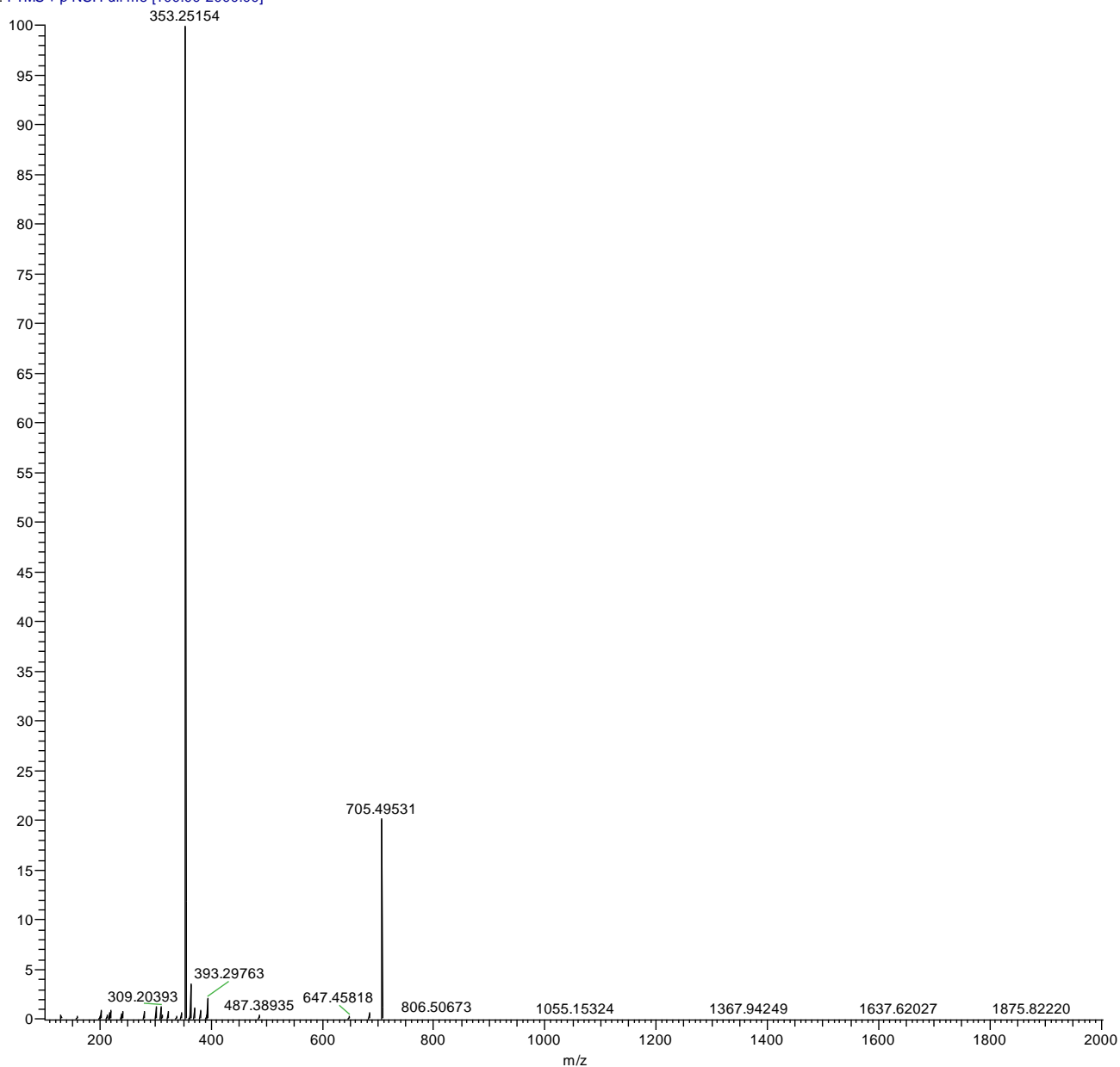


(*S*)-6-(((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)-6-oxohexane-1,5-diaminium (**16d**)

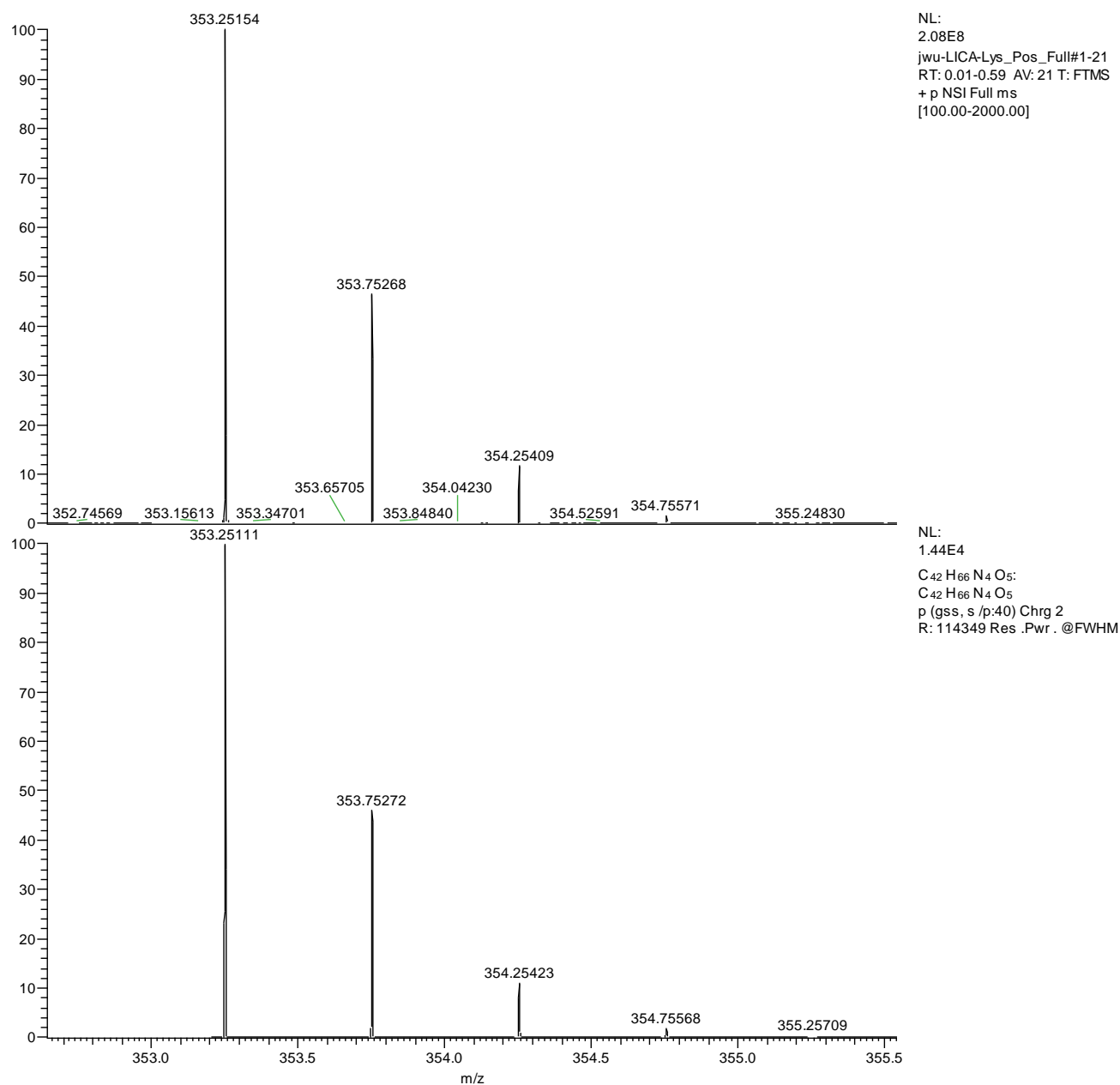
Full spectrum

jwu-LICA-Lys_Pos_Full #1-21 RT: 0.01-0.59 AV: 21 NL: 2.08E8

T: FTMS + p NSI Full ms [100.00-2000.00]

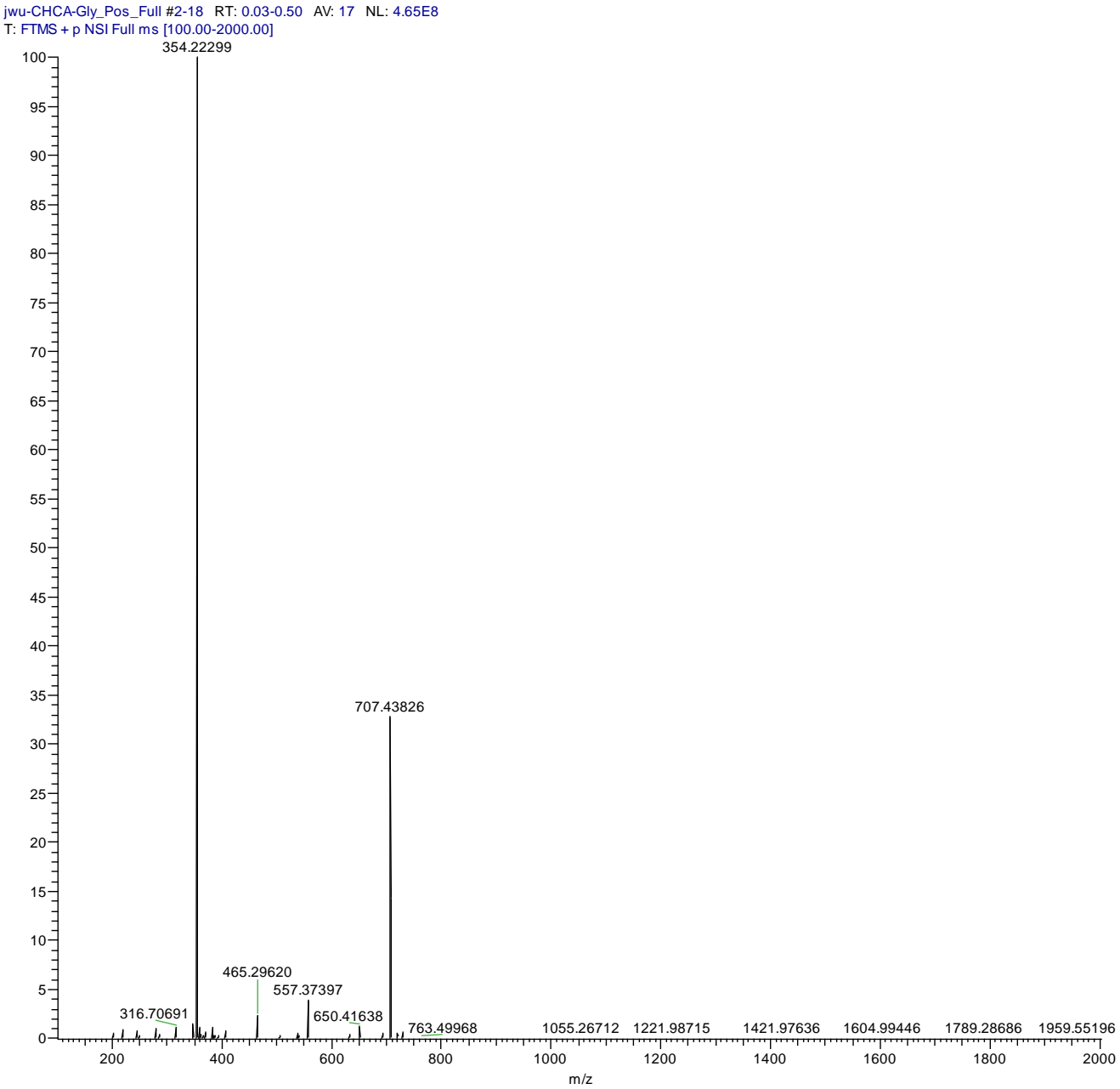


Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

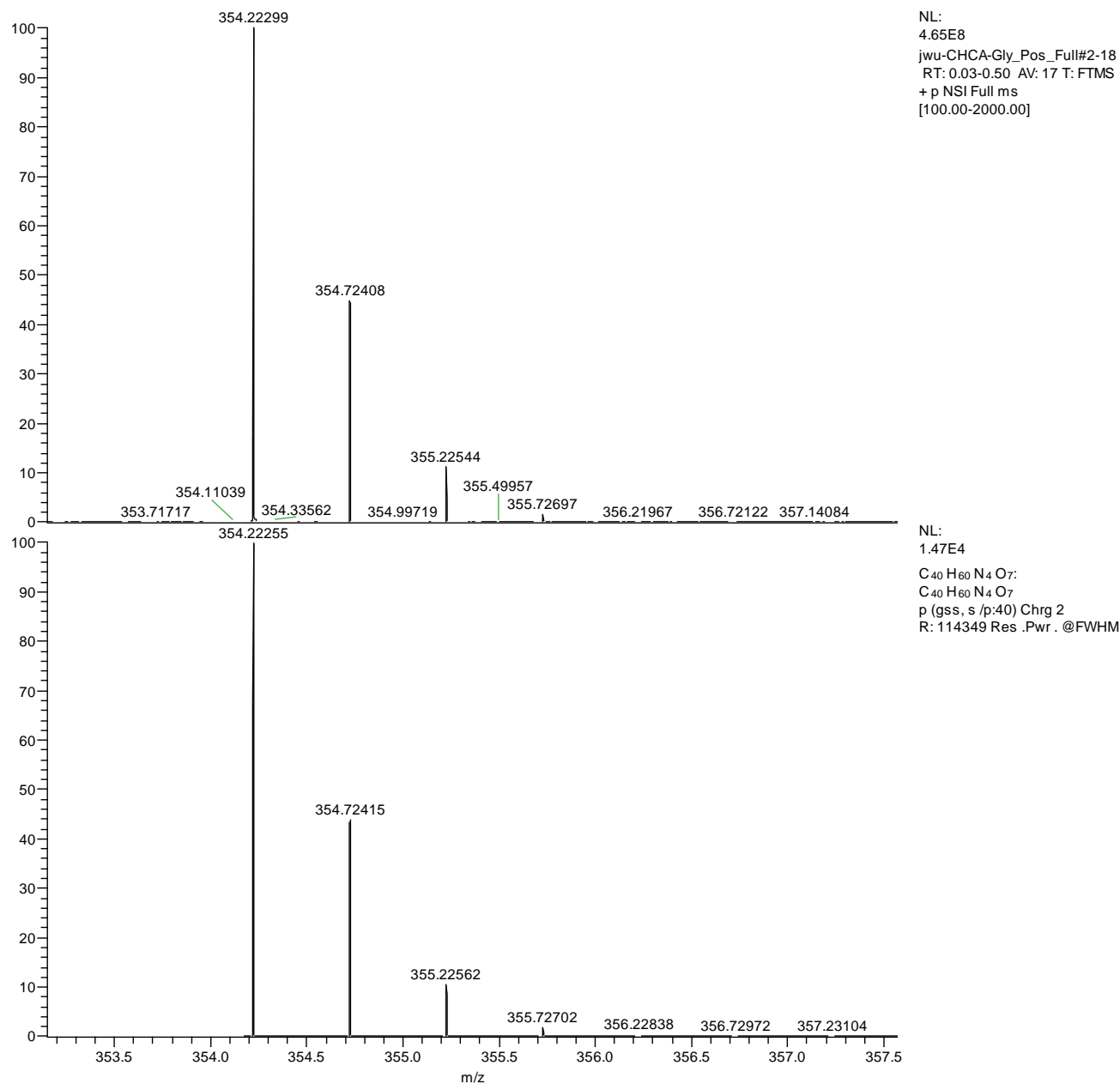


2,2'-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7-diyl)bis(oxy))bis(2-oxoethan-1-aminium) (**17a**)

Full spectrum

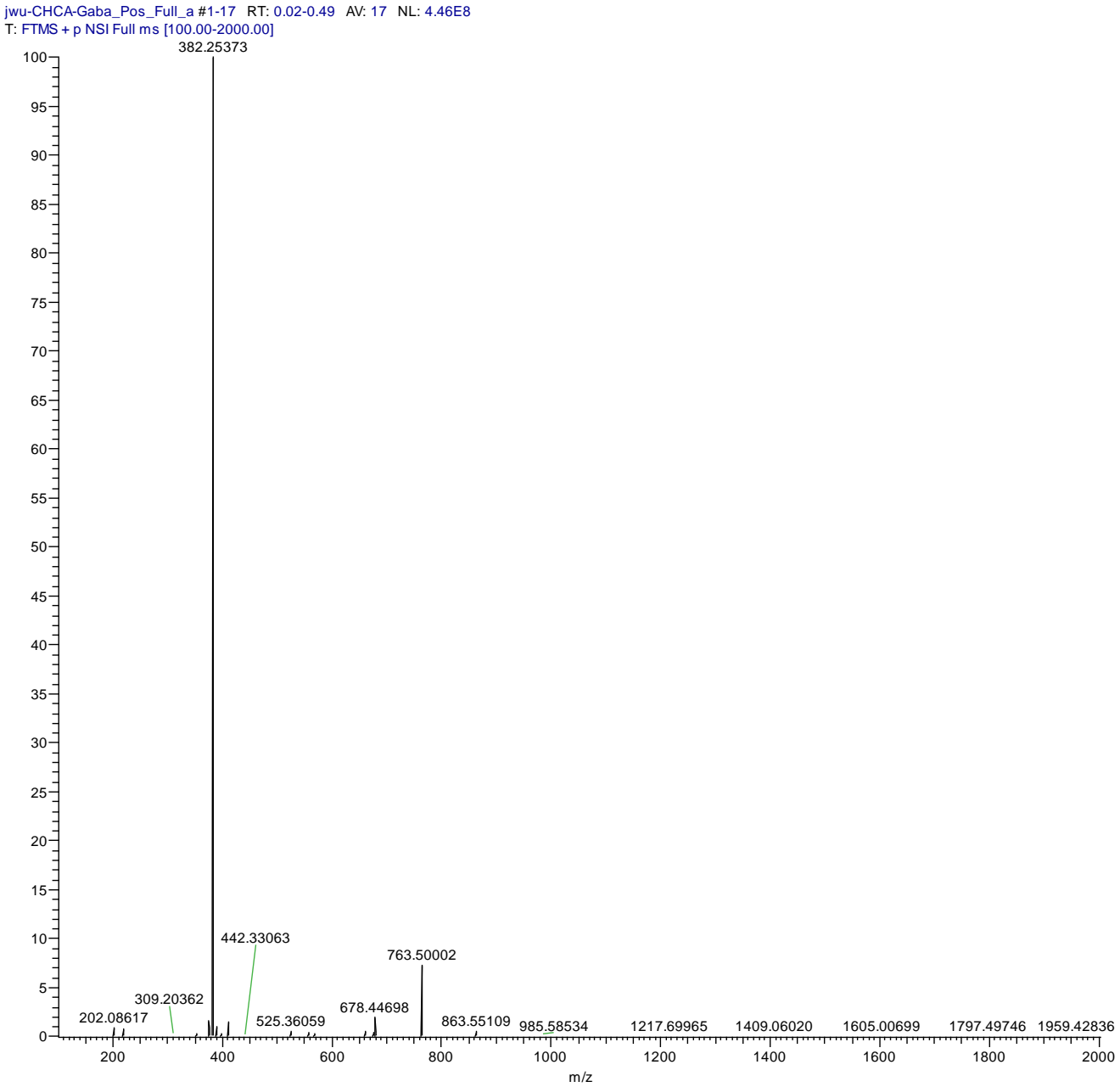


Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

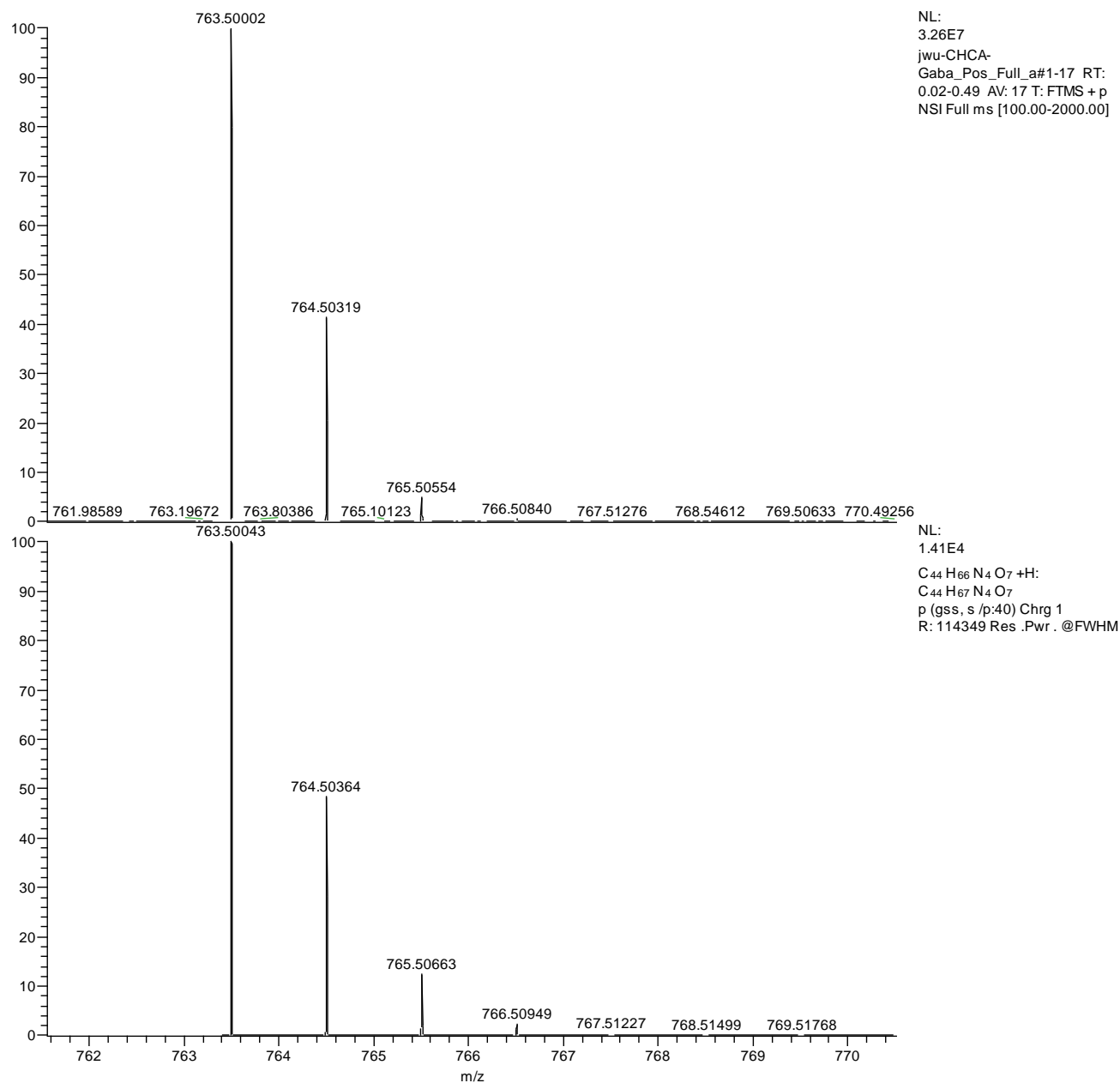


4,4'-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7-diyl)bis(oxy))bis(4-oxobutan-1-aminium) (**17b**)

Full spectrum



Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

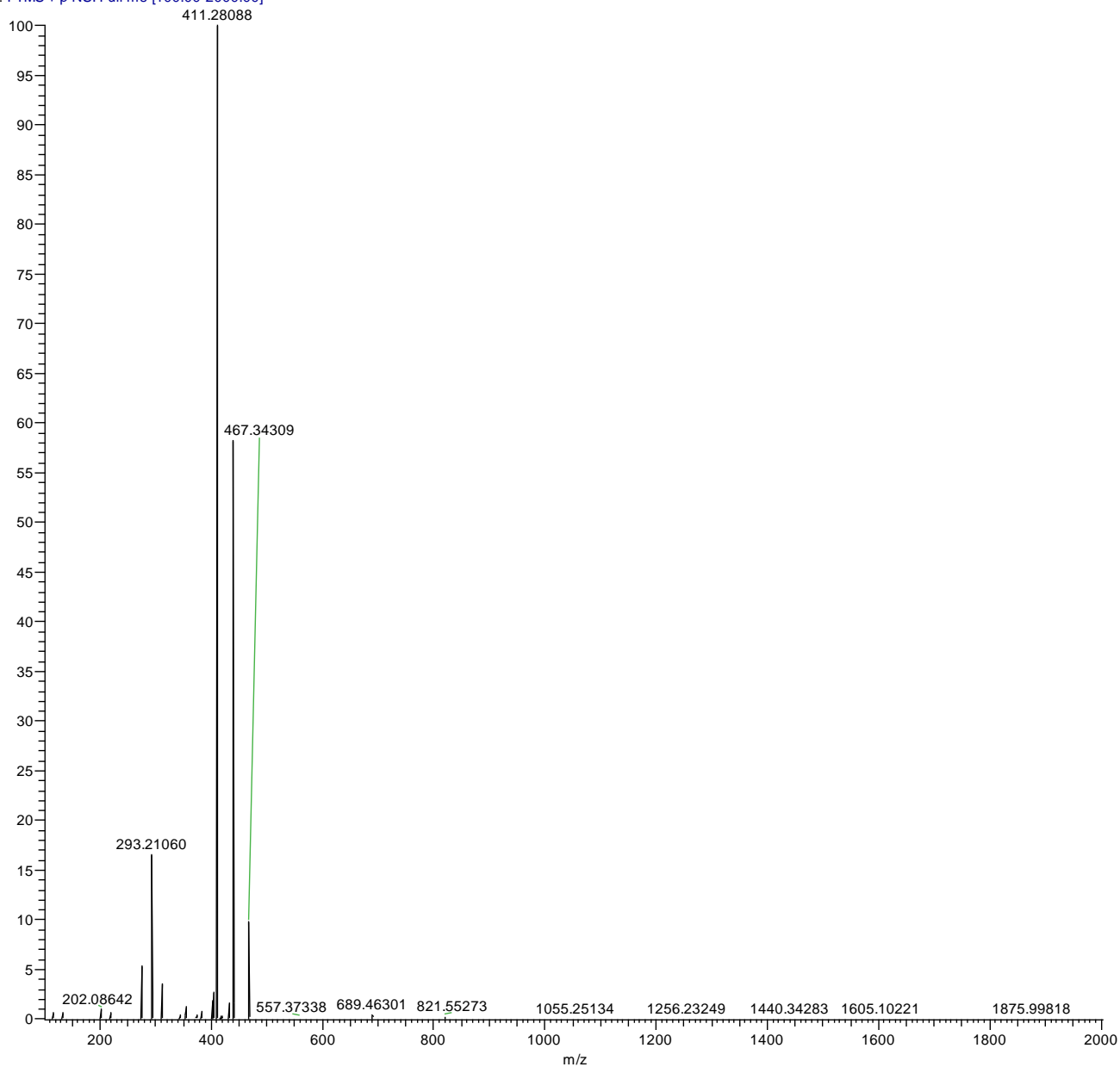


(4*S*,4'*S*)-5,5'-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7-diyl)bis(oxy))bis(5-oxopentane-1,4-diaminium) (**17c**)

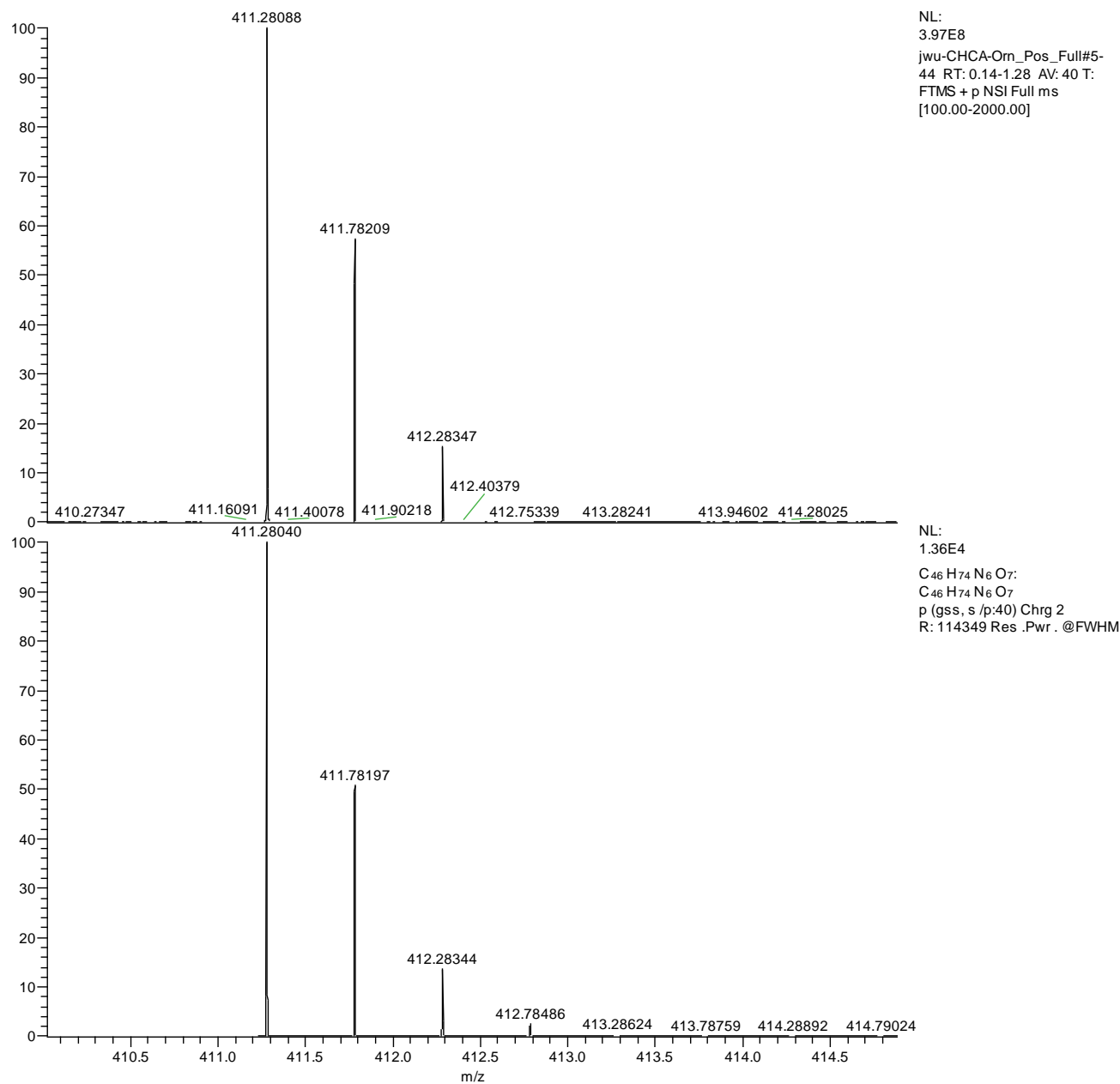
Full spectrum

jwu-CHCA-Orn_Pos_Full #5-44 RT: 0.14-1.28 AV: 40 NL: 3.97E8

T: FTMS + p NSI Full ms [100.00-2000.00]



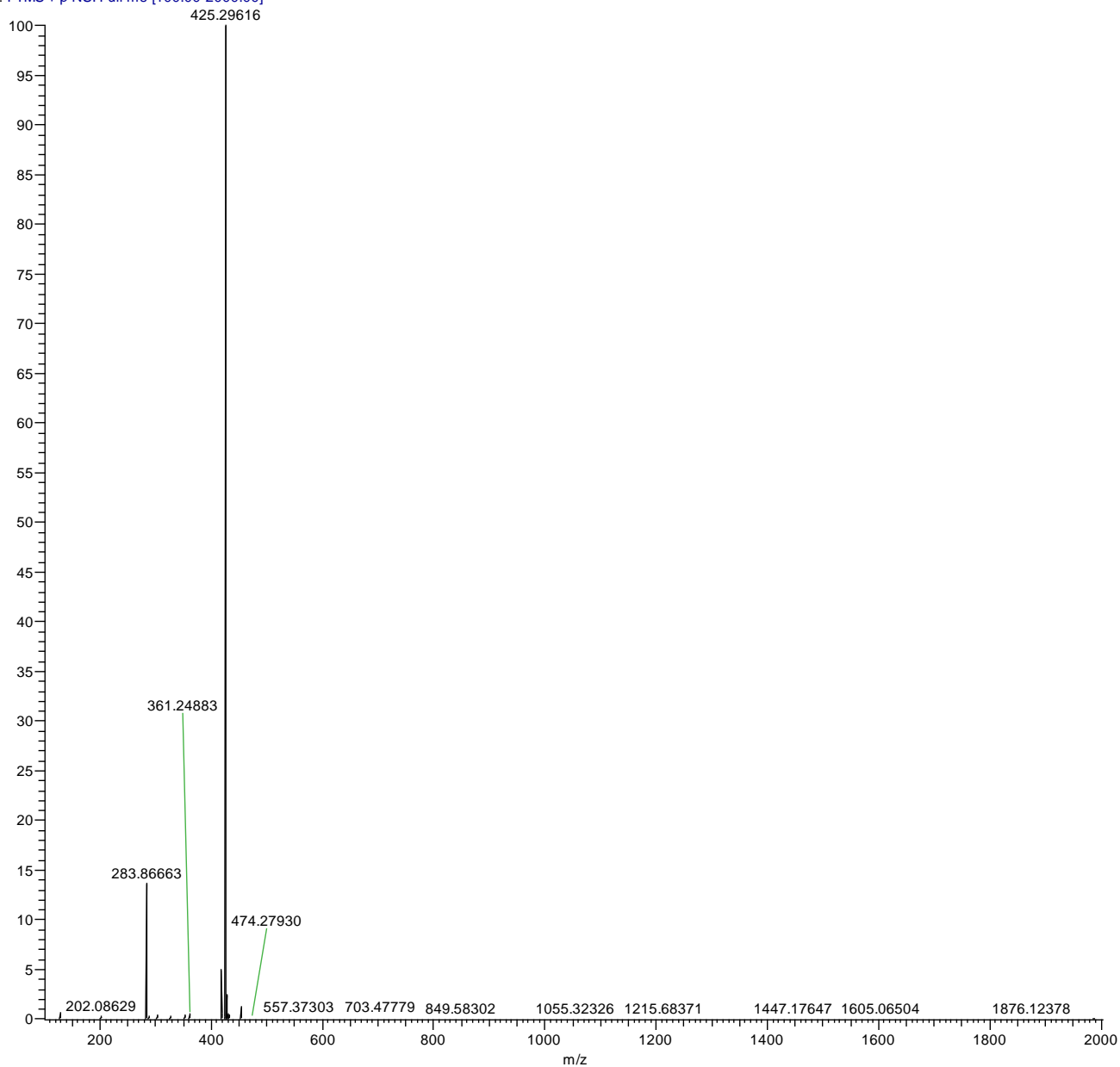
Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)



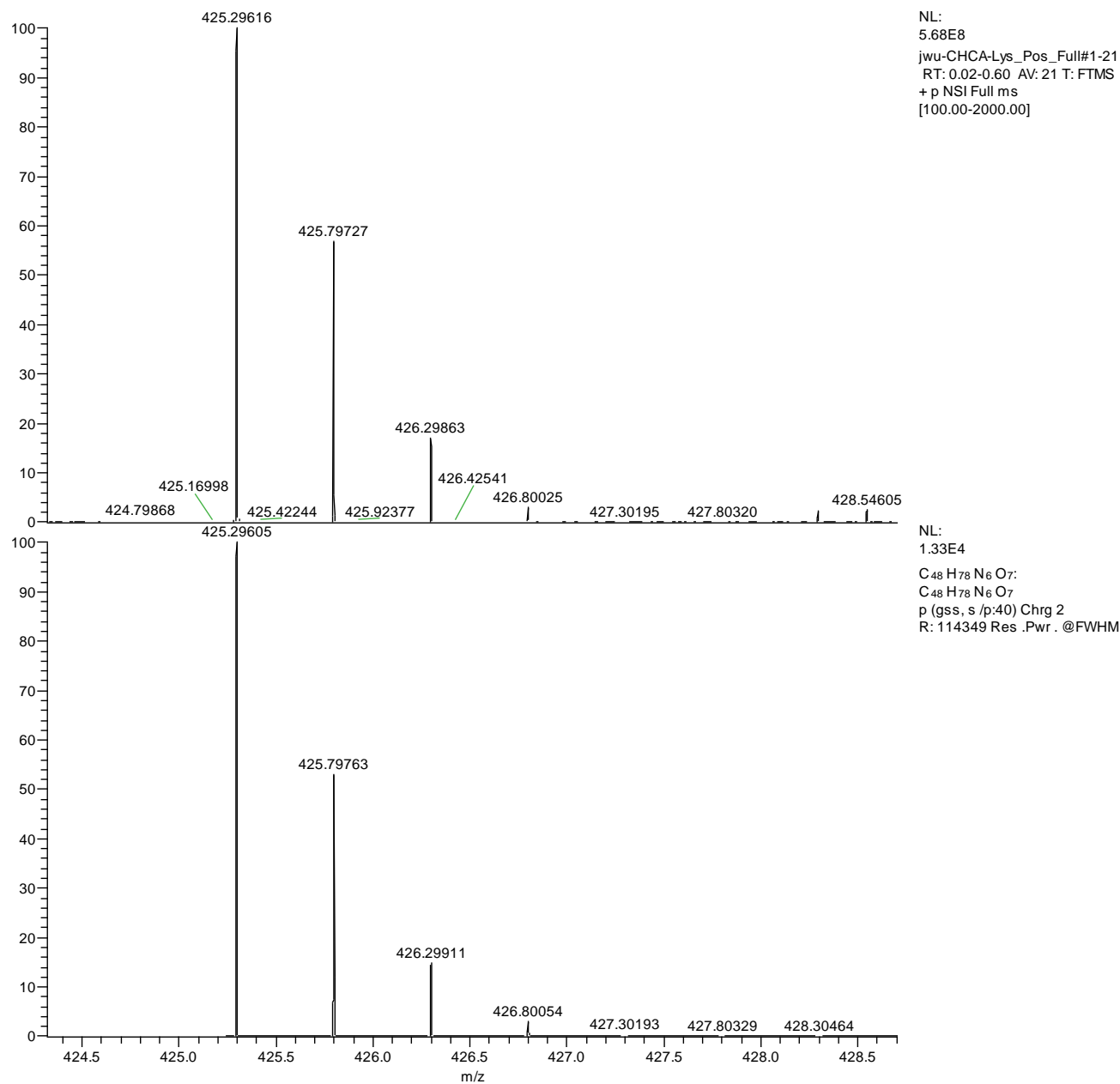
(5*S*,5'*S*)-6,6'-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7-diyl)bis(oxy))bis(6-oxohexane-1,5-diaminium) (**17d**)

Full spectrum

jwu-CHCA-Lys_Pos_Full #1-21 RT: 0.02-0.60 AV: 21 NL: 5.68E8
T: FTMS + p NSI Full ms [100.00-2000.00]



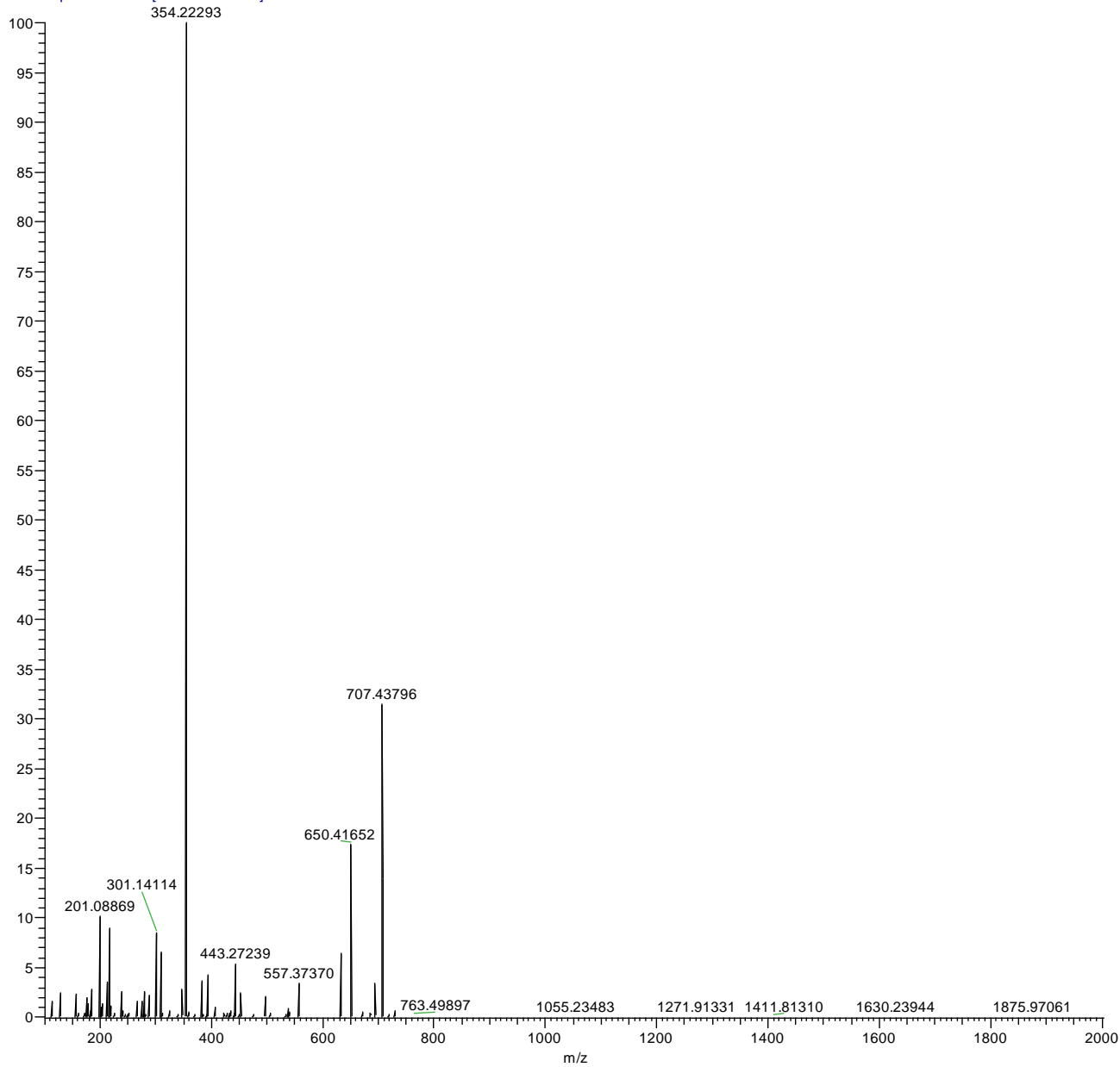
Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)



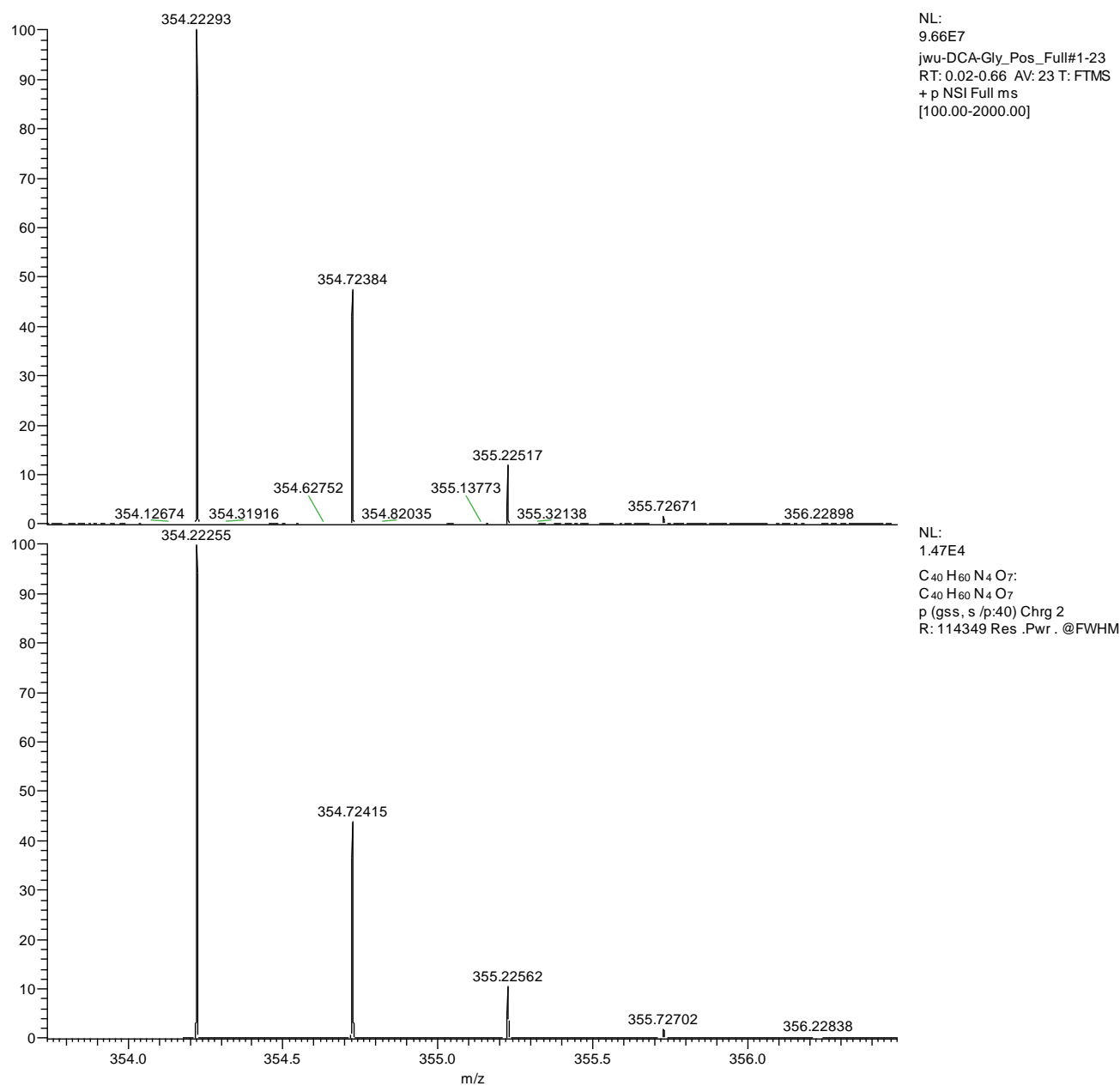
2,2'-(((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,12-diyl)bis(oxy))bis(2-oxoethan-1-aminium) (**18a**)

Full spectrum

jwu-DCA-Gly_Pos_Full #1-23 RT: 0.02-0.66 AV: 23 NL: 9.66E7
T: FTMS + p NSI Full ms [100.00-2000.00]

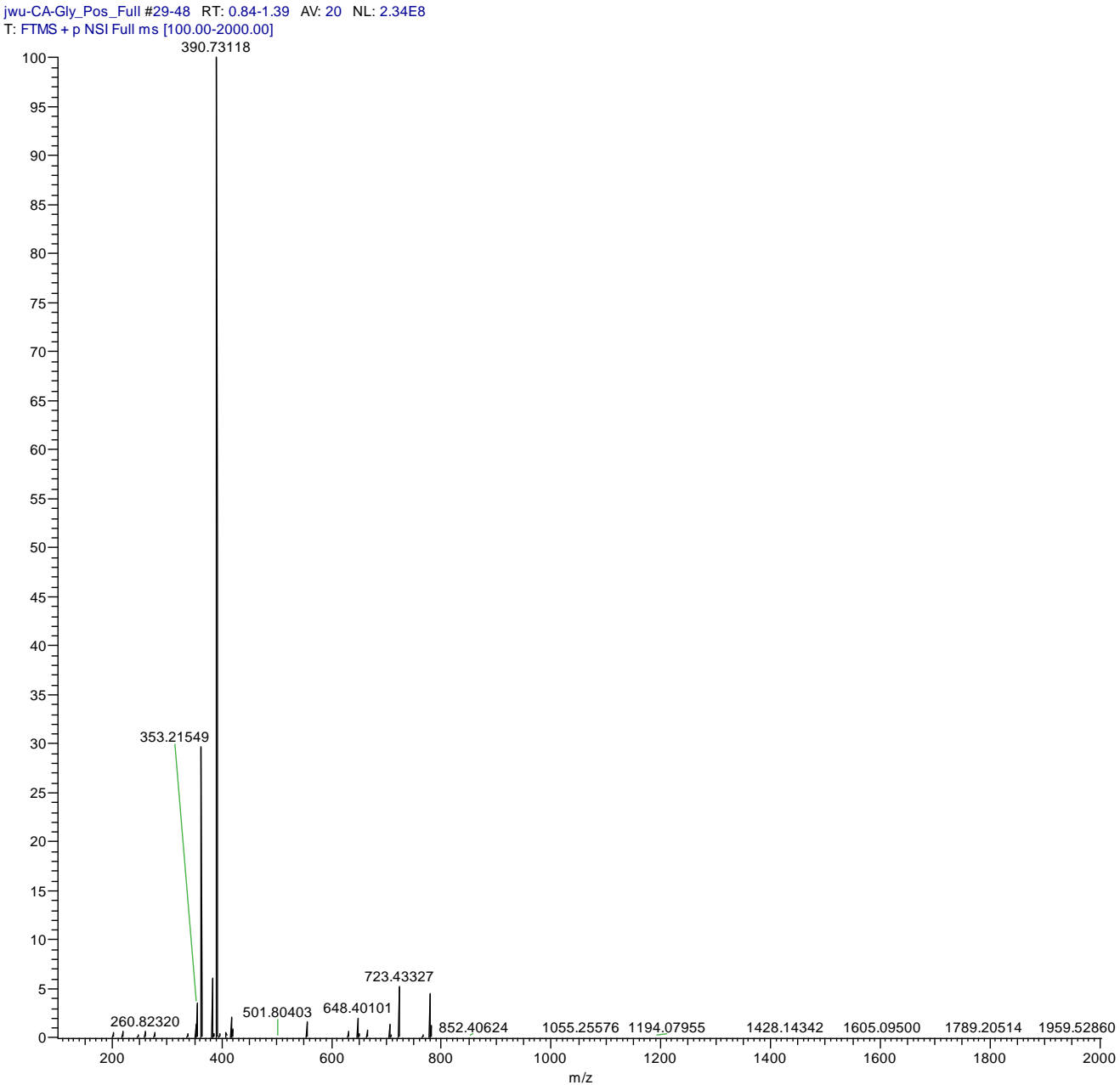


Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

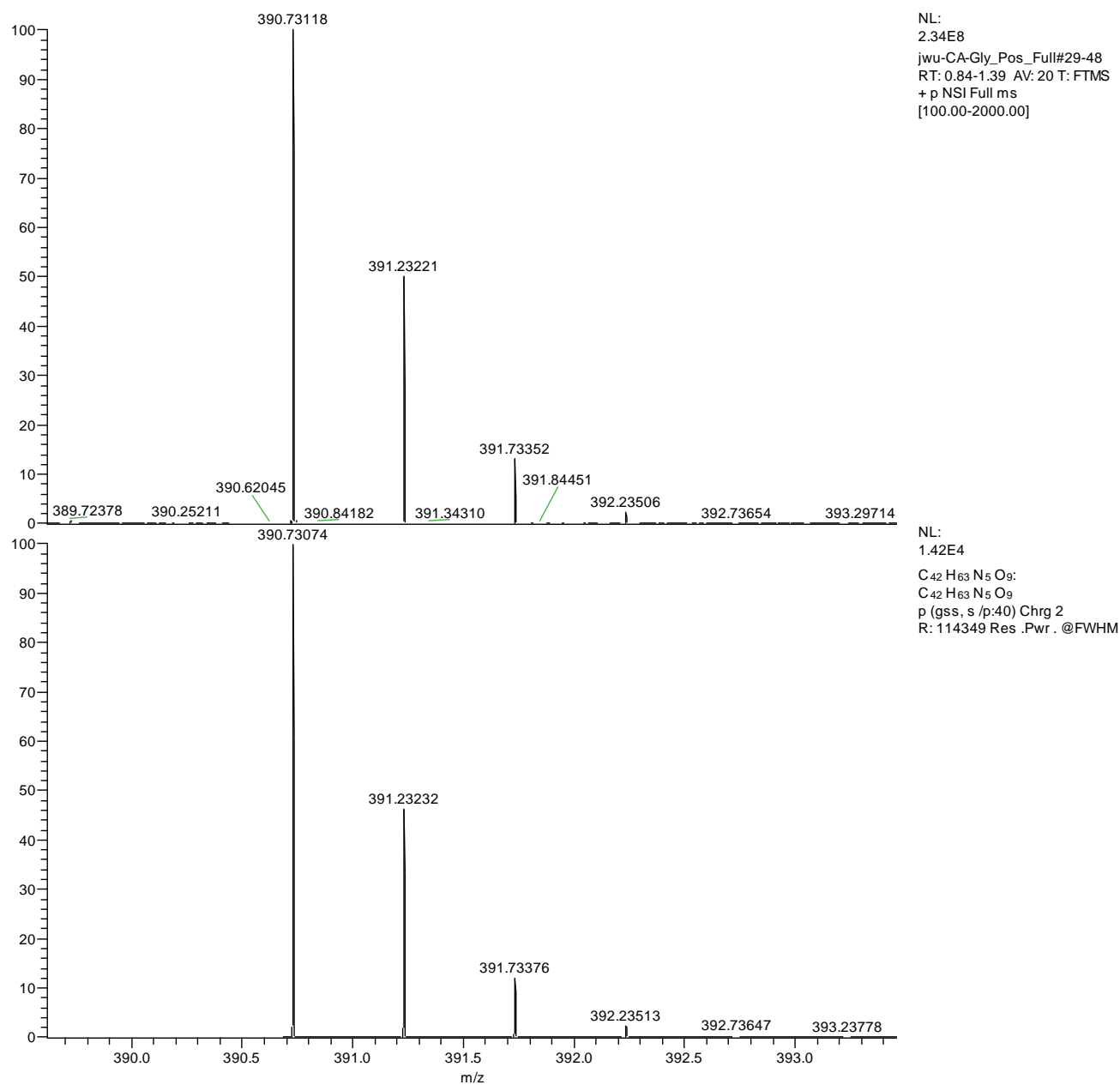


2,2'-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-3-(2-aminoacetoxy)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-7,12-diyl)bis(oxy))bis(2-oxoethan-1-aminium) (**19a**)

Full spectrum



Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

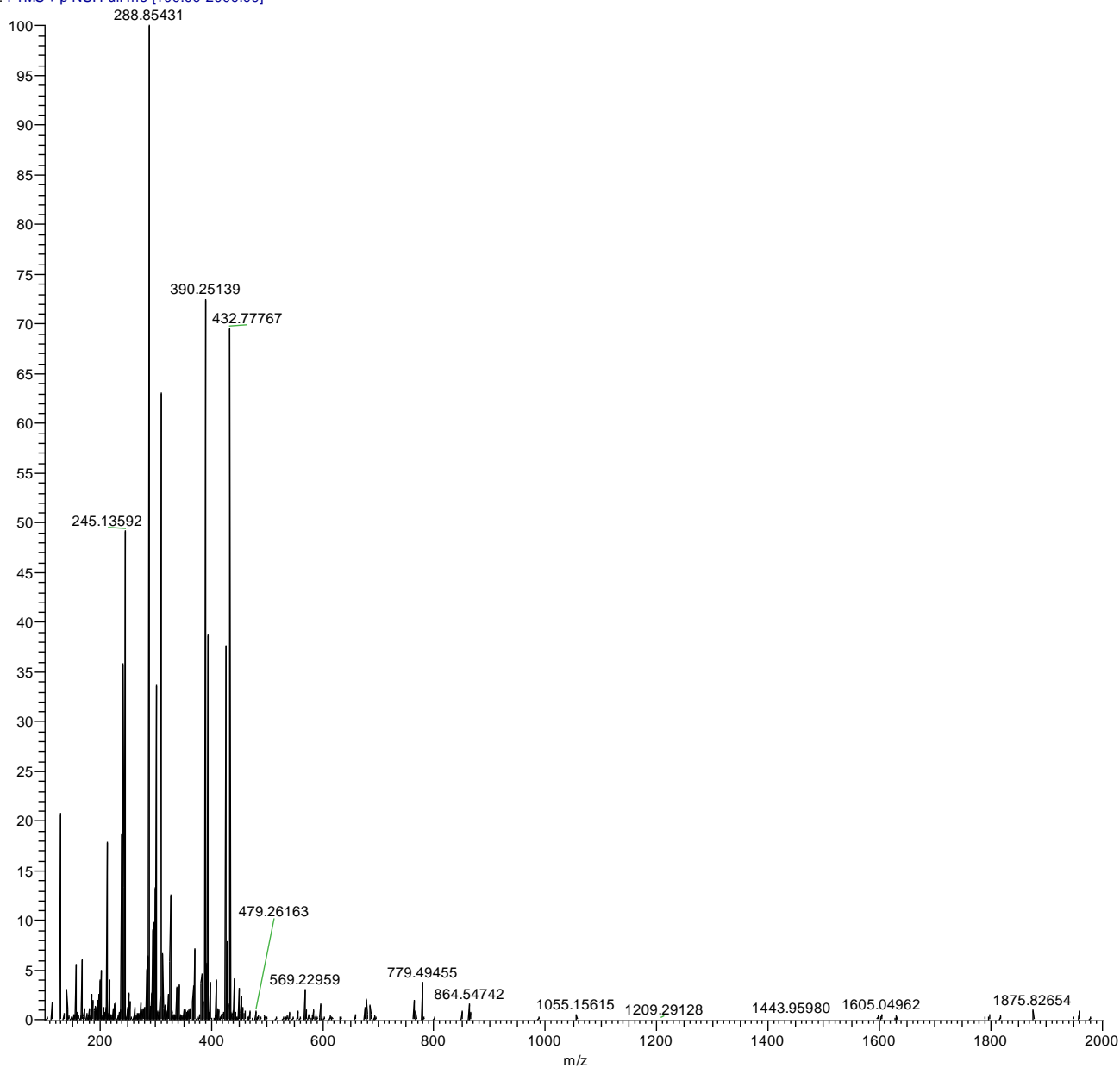


4,4',4''-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7,12-triyl)tris(oxy))tris(4-oxobutan-1-aminium) (**19b**)

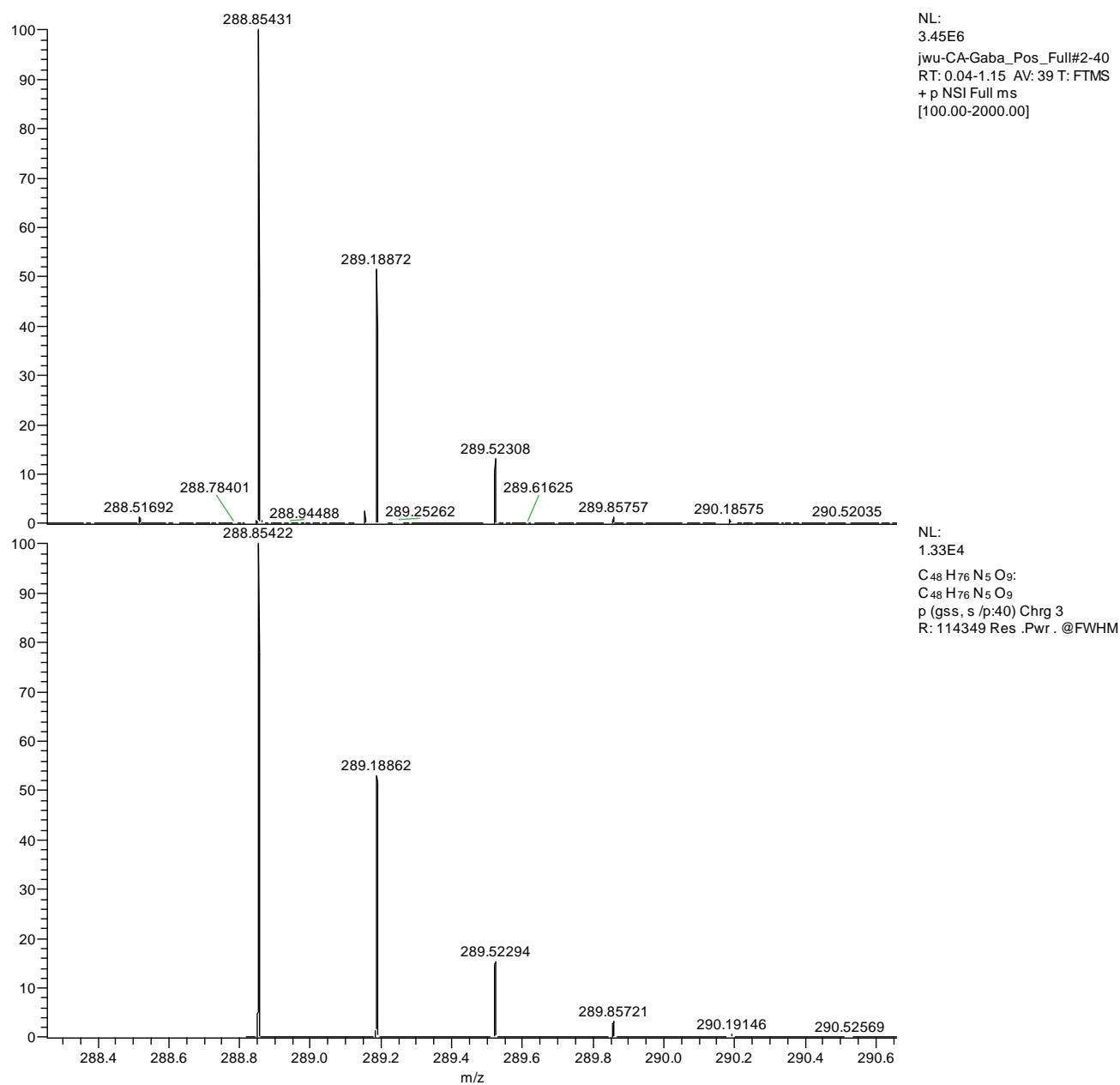
Full spectrum

jwu-CA-Gaba_Pos_Full #2-40 RT: 0.04-1.15 AV: 39 NL: 3.45E6

T: FTMS + p NSI Full ms [100.00-2000.00]



Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

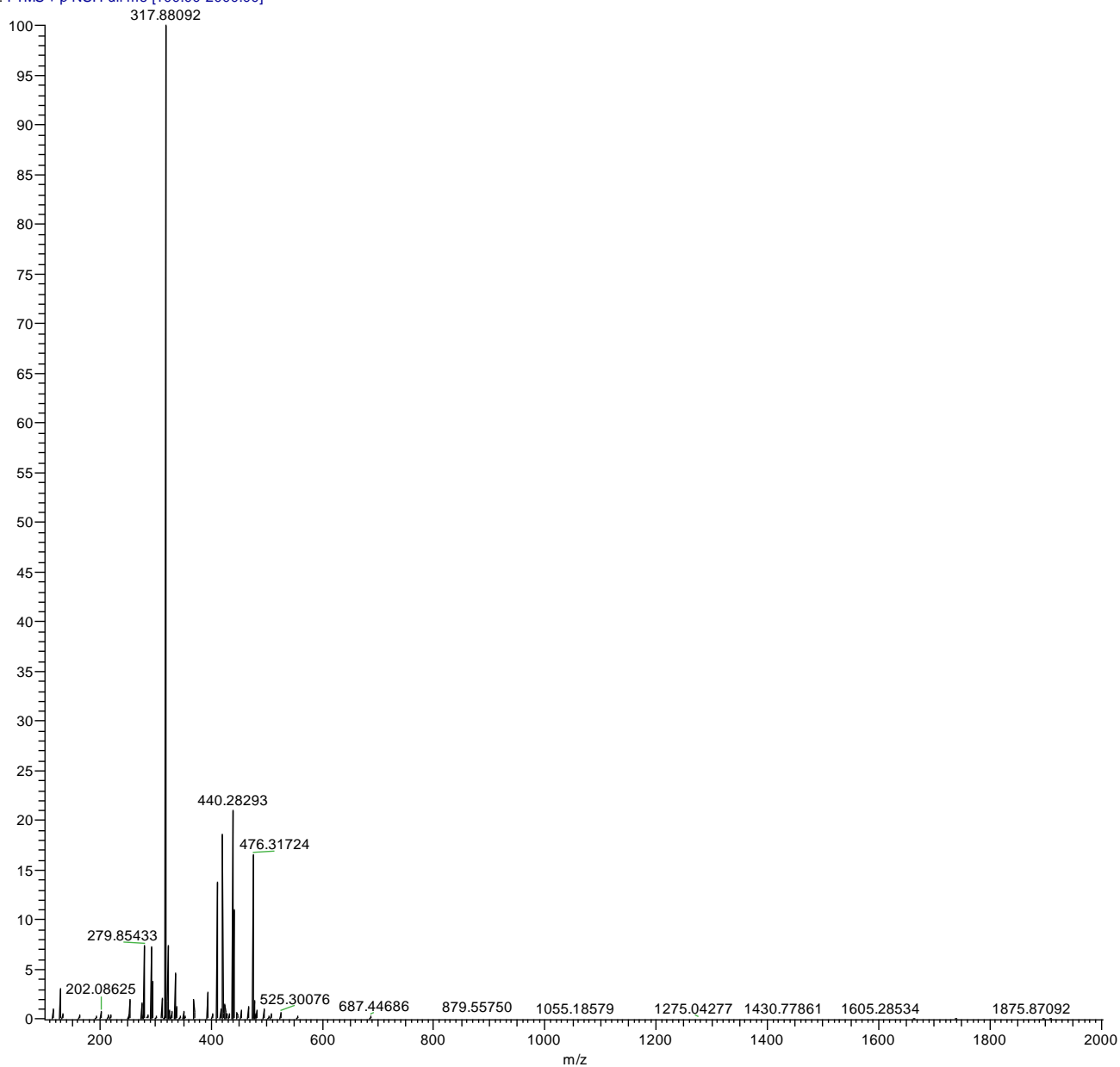


(4*S*,4'*S*,4''*S*)-5,5',5''-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7,12-triyl)tris(oxy))tris(5-oxopentane-1,4-diaminium) (**19c**)

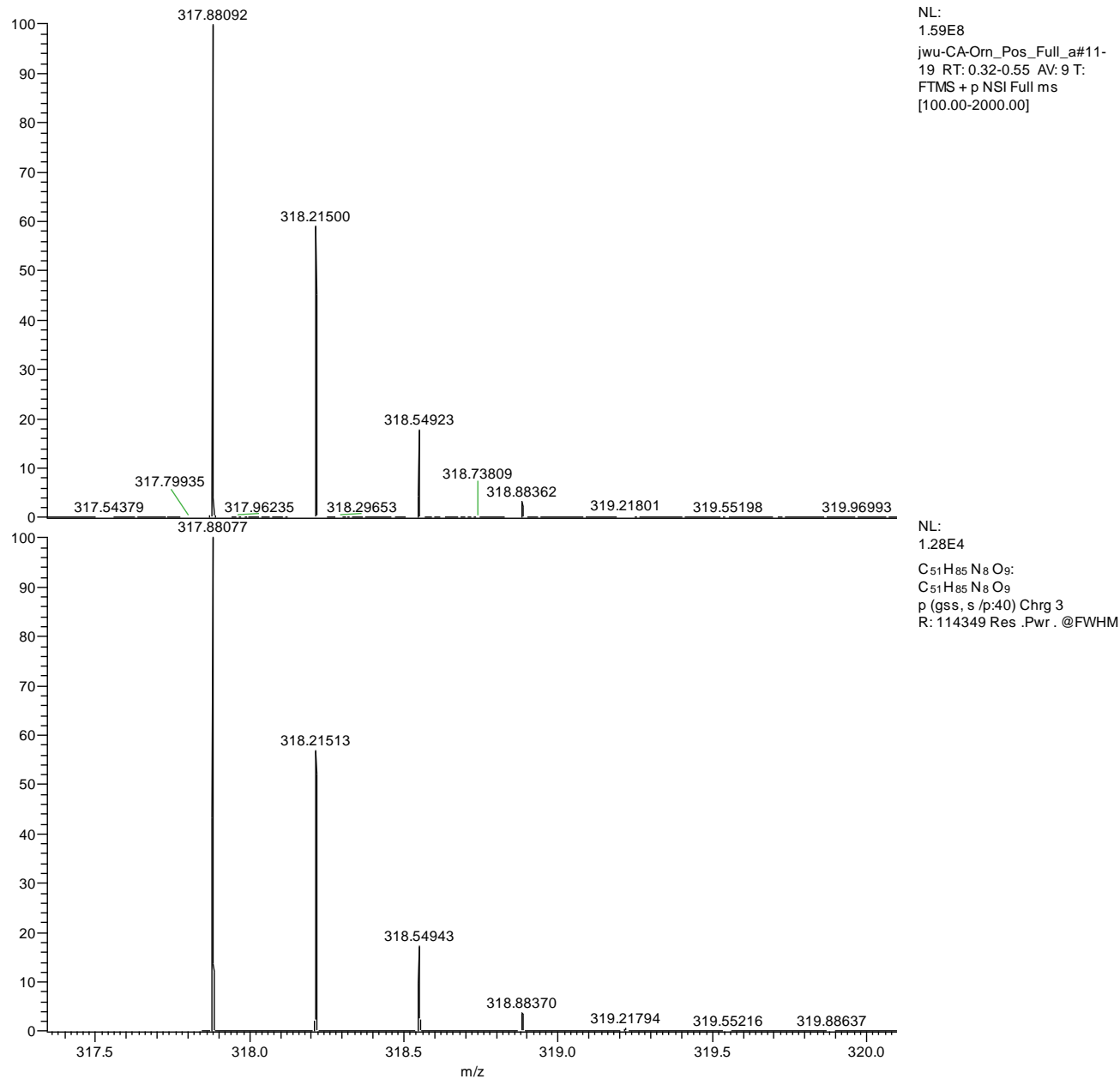
Full spectrum

jwu-CA-Orn_Pos_Full_a #11-19 RT: 0.32-0.55 AV: 9 NL: 1.59E8

T: FTMS + p NSI Full ms [100.00-2000.00]

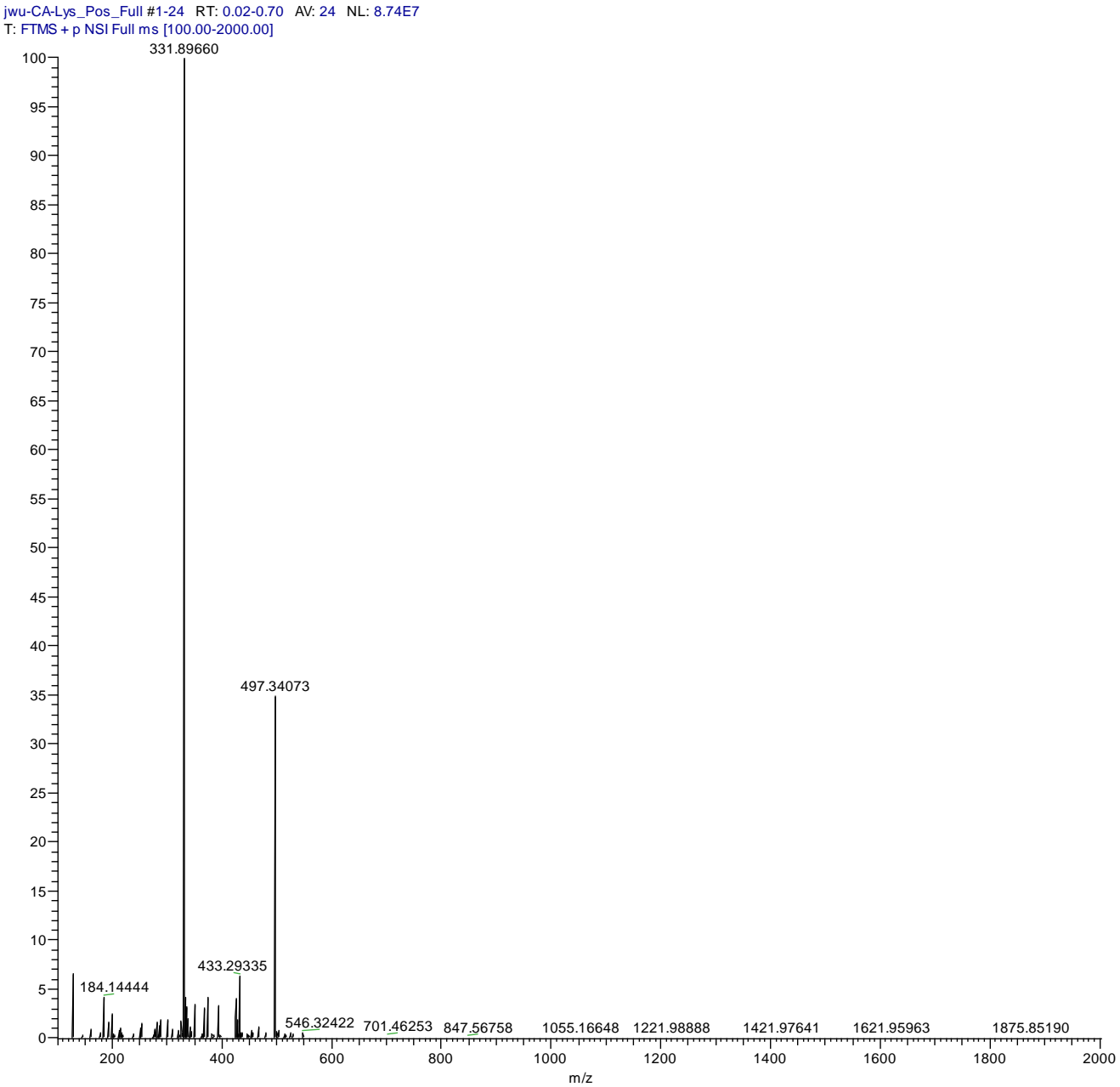


Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

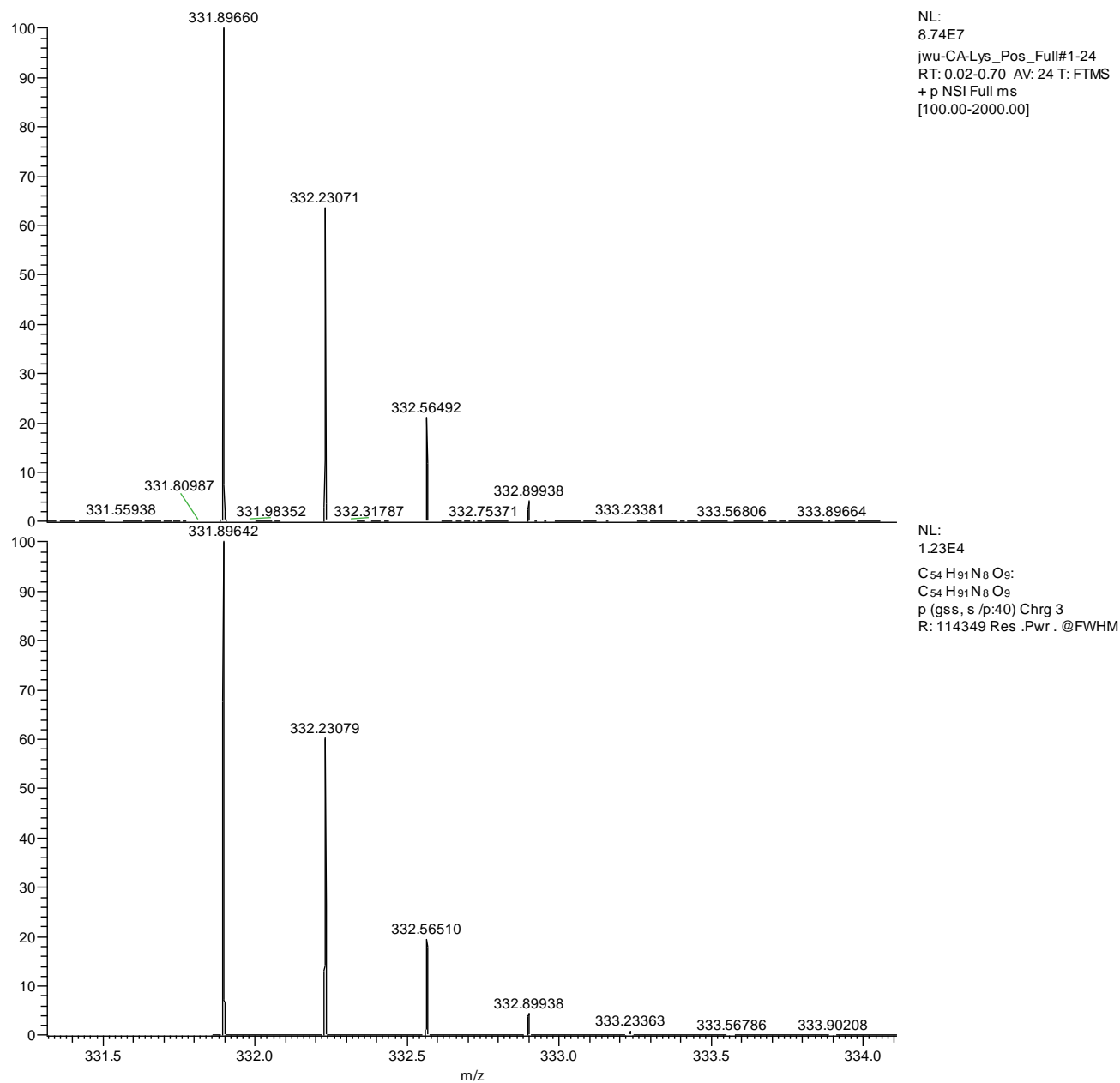


(5*S*,5'*S*,5''*S*)-6,6',6''-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7,12-triyl)tris(oxy))tris(6-oxohexane-1,5-diaminium) (**19d**)

Full spectrum



Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

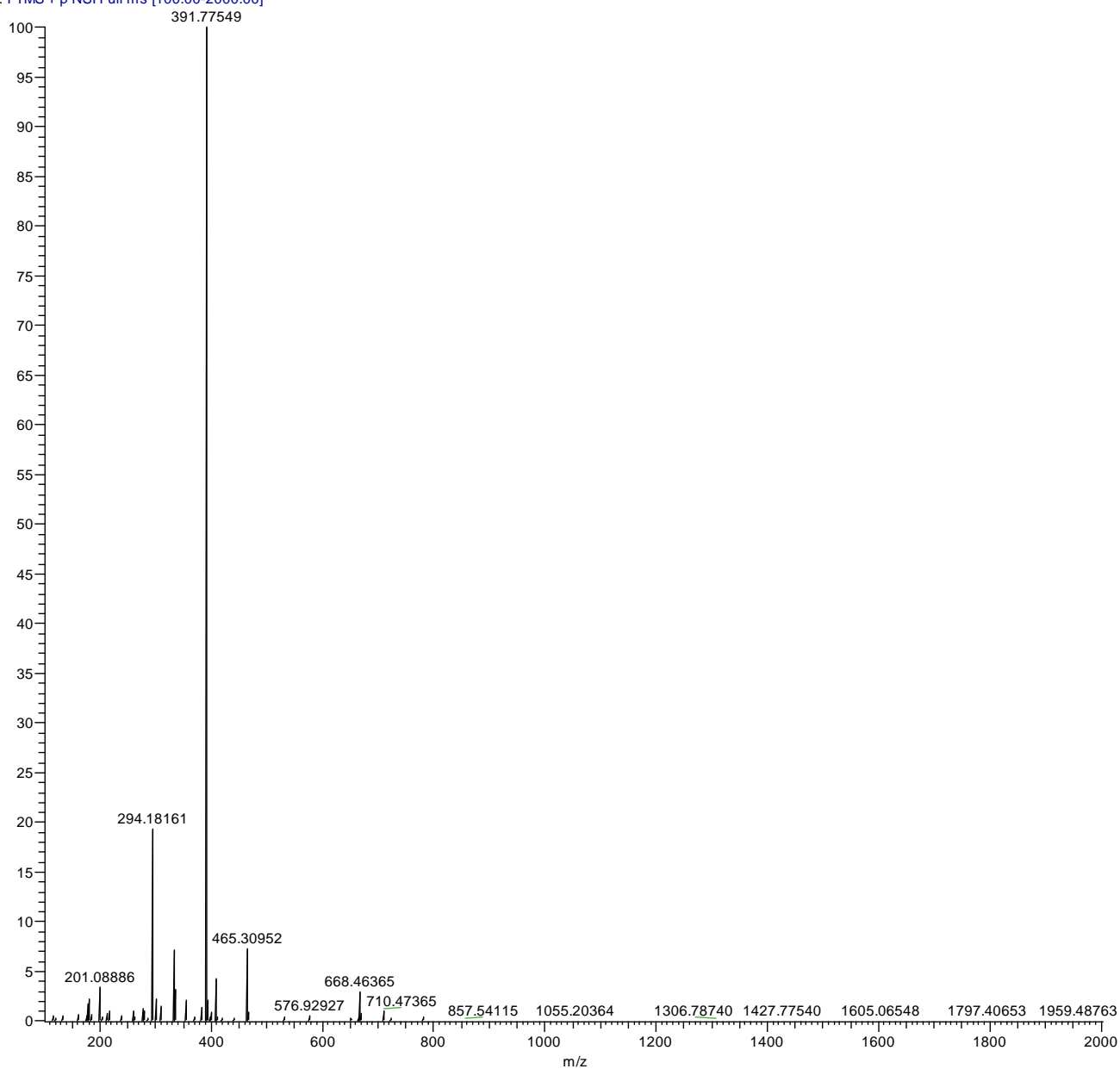


(4*S*,4'*S*)-5,5'-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-1-Methoxy-1-oxo-3-phenylpropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7-diyl)bis(oxy))bis(5-oxopentane-1,4-diaminium) (**20**)

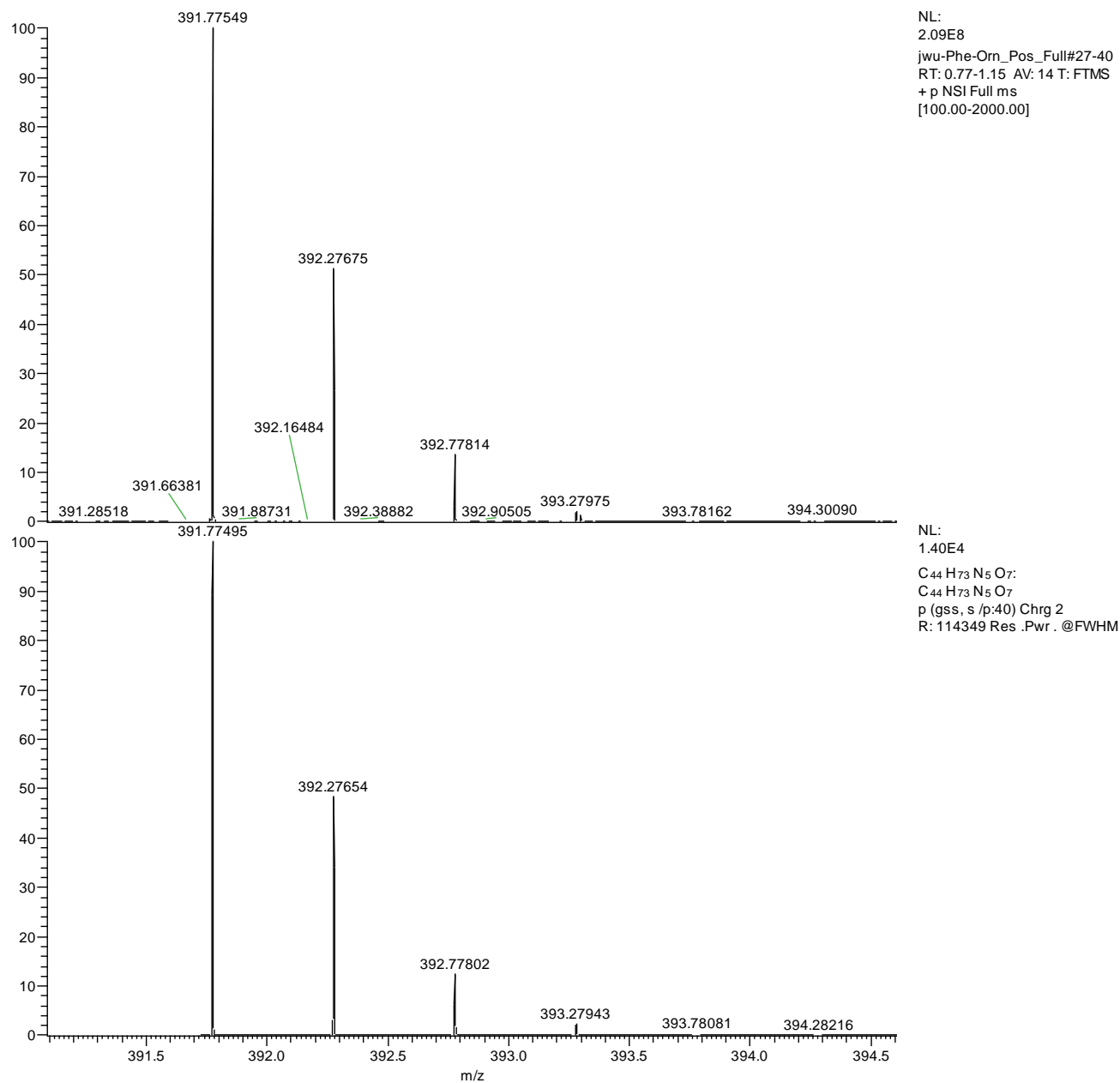
Full spectrum

jwu-Phe-Orn_Pos_Full #27-40 RT: 0.77-1.15 AV: 14 NL: 2.09E8

T: FTMS + p NSI Full ms [100.00-2000.00]



Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

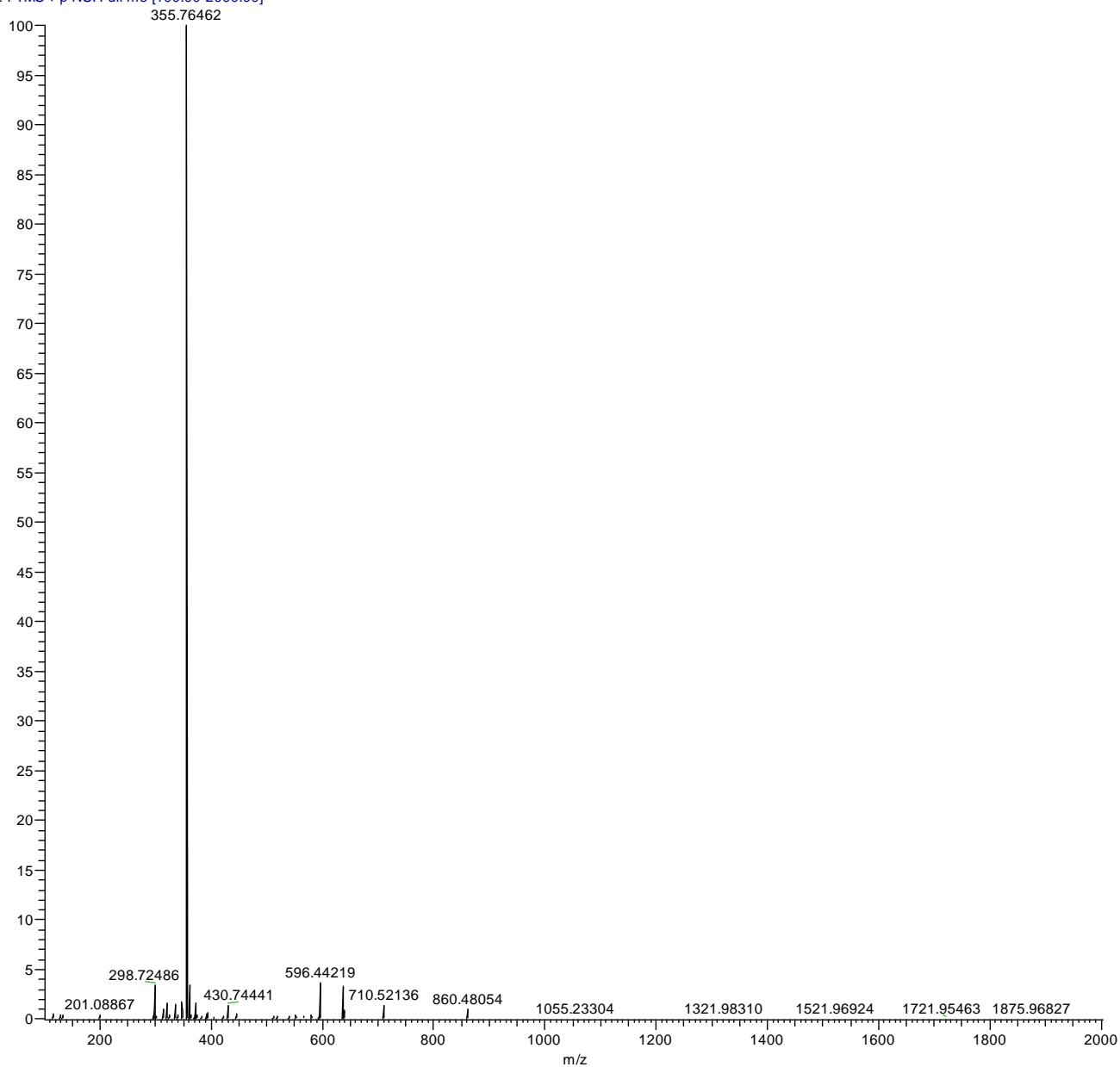


(4*S*,4'*S*)-5,5'-(((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(Benzylamino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7-diyl)bis(oxy))bis(5-oxopentane-1,4-diaminium) (**21**)

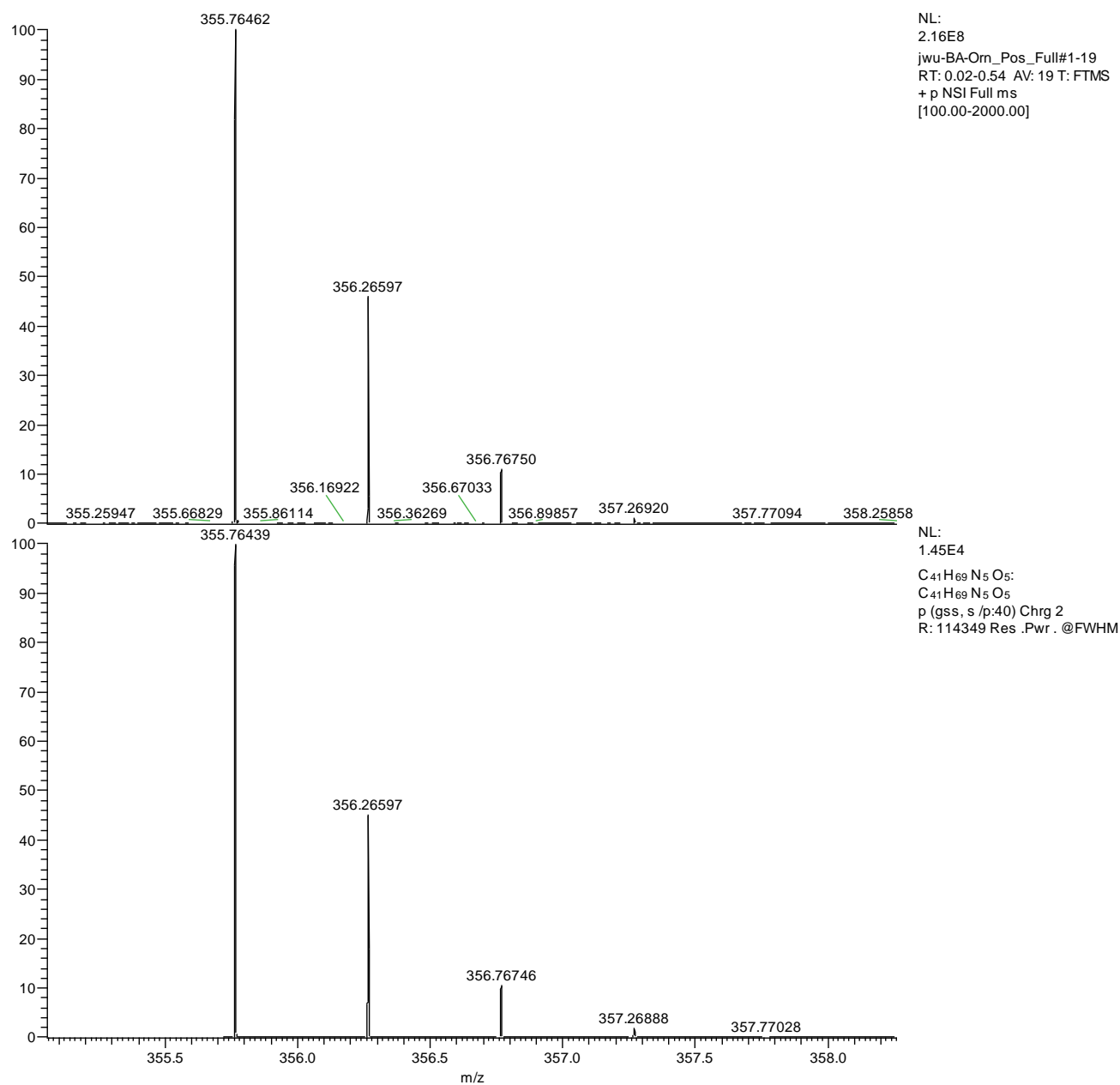
Full spectrum

jwu-BA-Orn_Pos_Full #1-19 RT: 0.02-0.54 AV: 19 NL: 2.16E8

T: FTMS + p NSI Full ms [100.00-2000.00]



Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

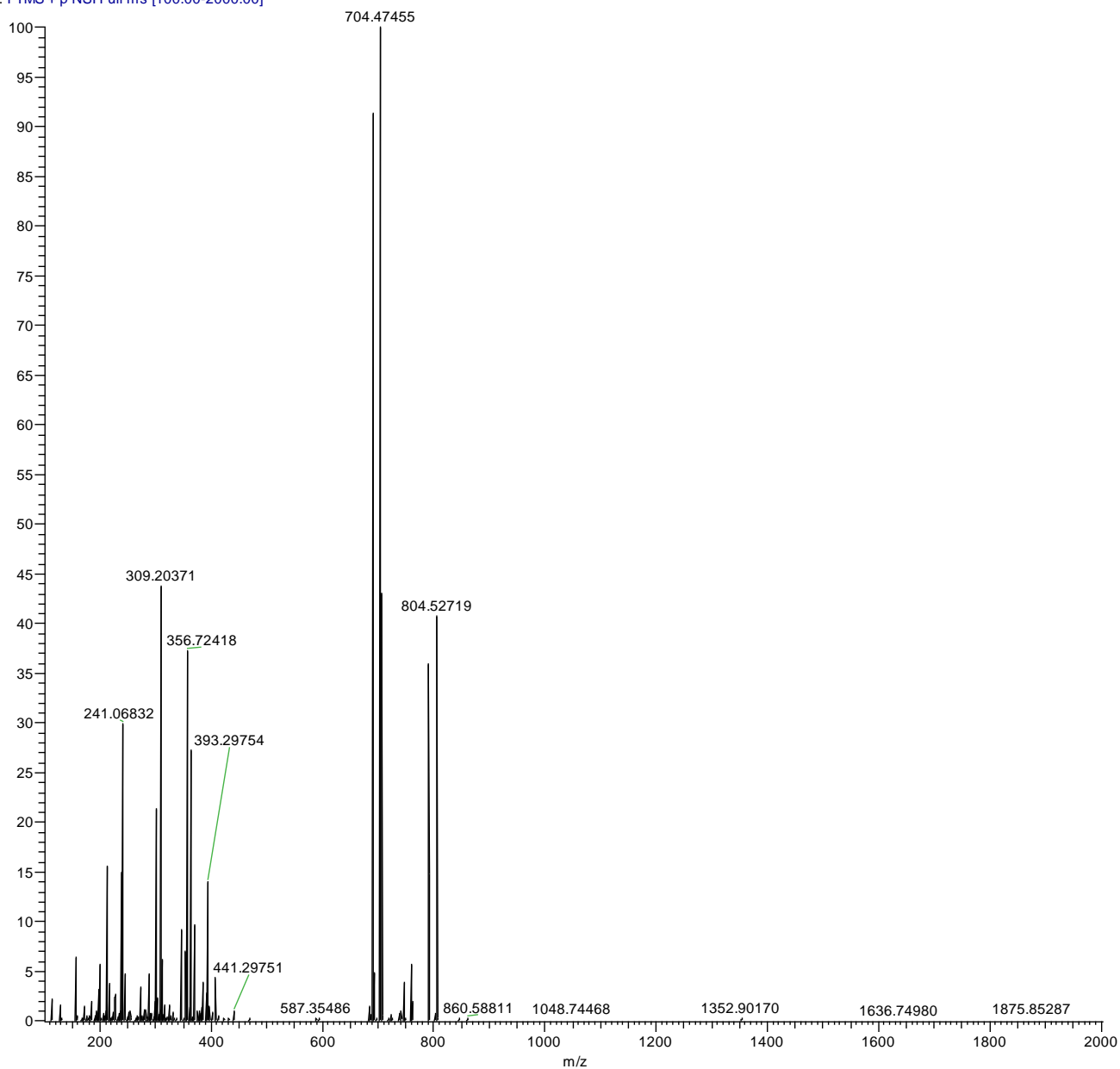


((4-(((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)-4-oxobutyl)amino)(amino)methaniminium (**23**)

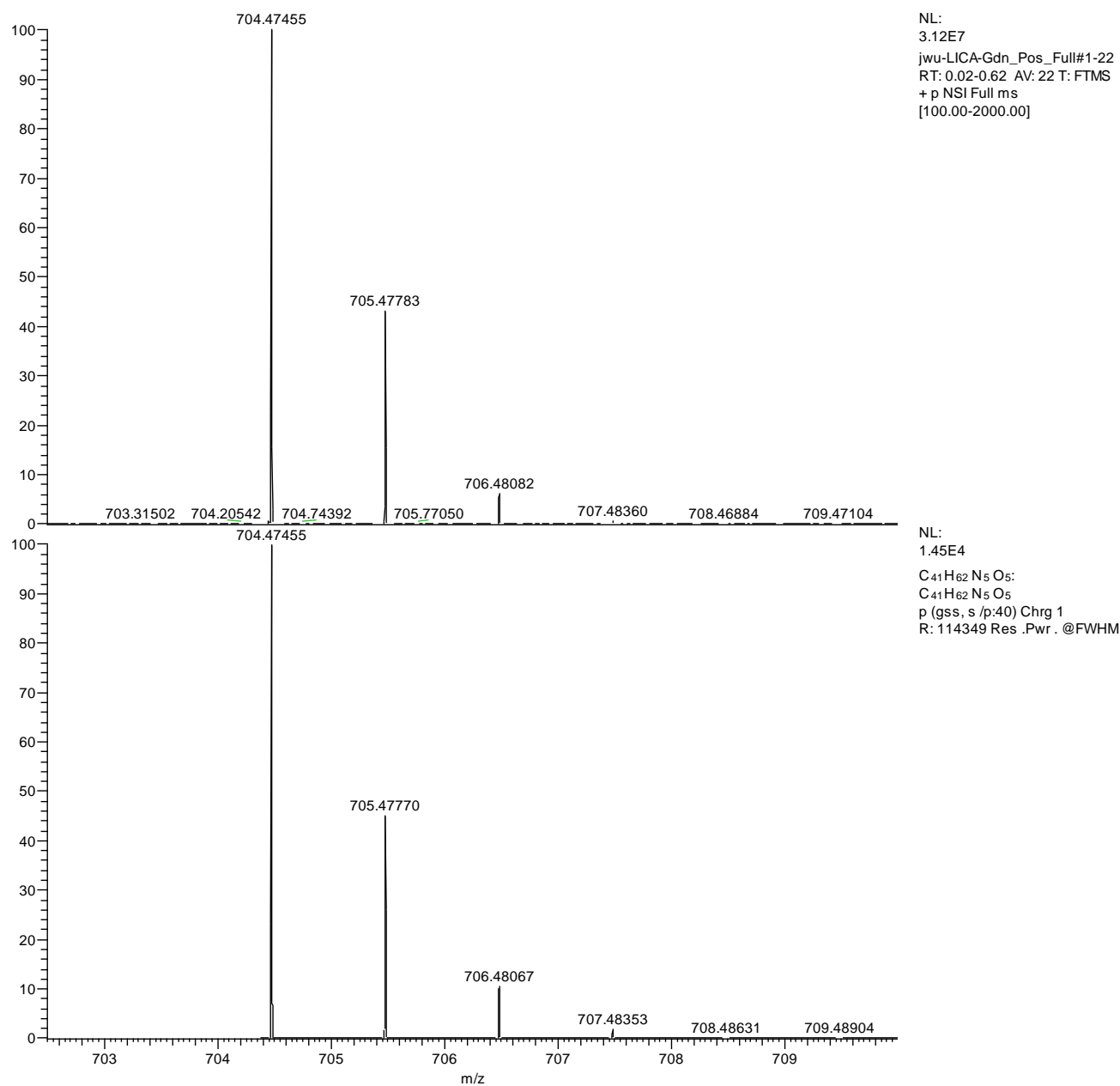
Full spectrum

jwu-LICA-Gdn_Pos_Full #1-22 RT: 0.02-0.62 AV: 22 NL: 3.12E7

T: FTMS + p NSI Full ms [100.00-2000.00]

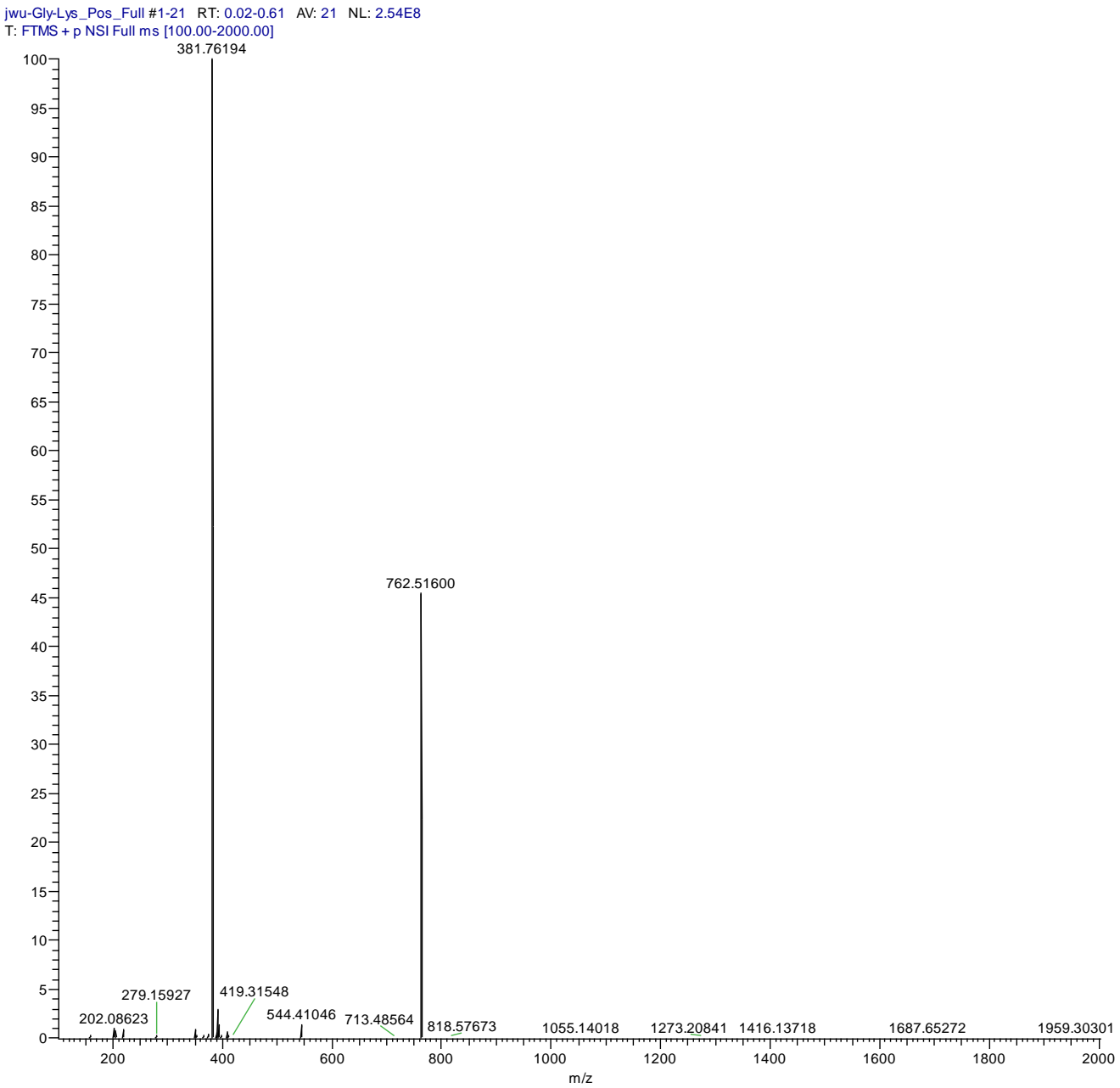


Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

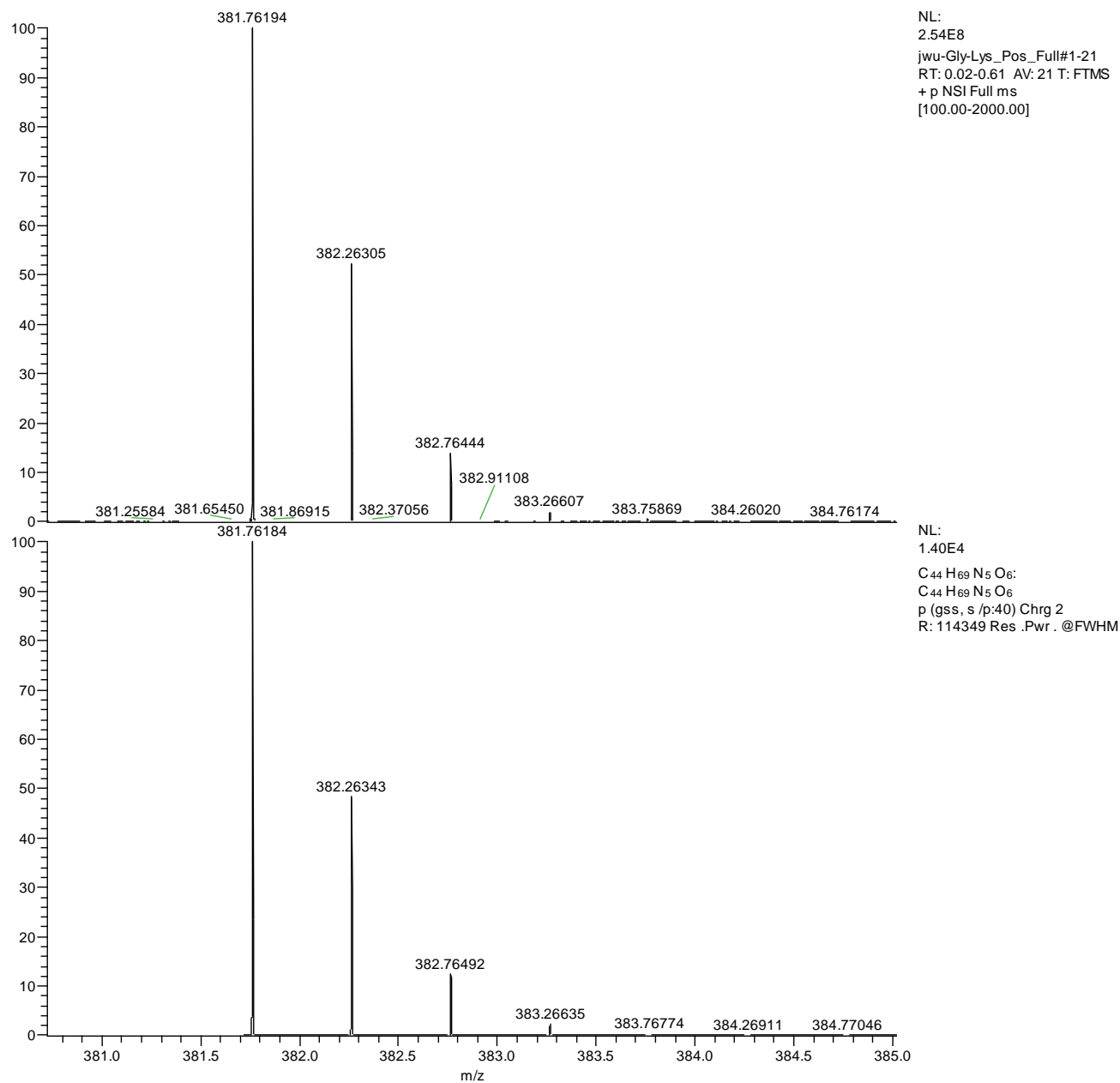


Methyl ((*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-((*L*-lysylglycyl)oxy)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoyl)-*L*-tryptophanate (**25**)

Full spectrum



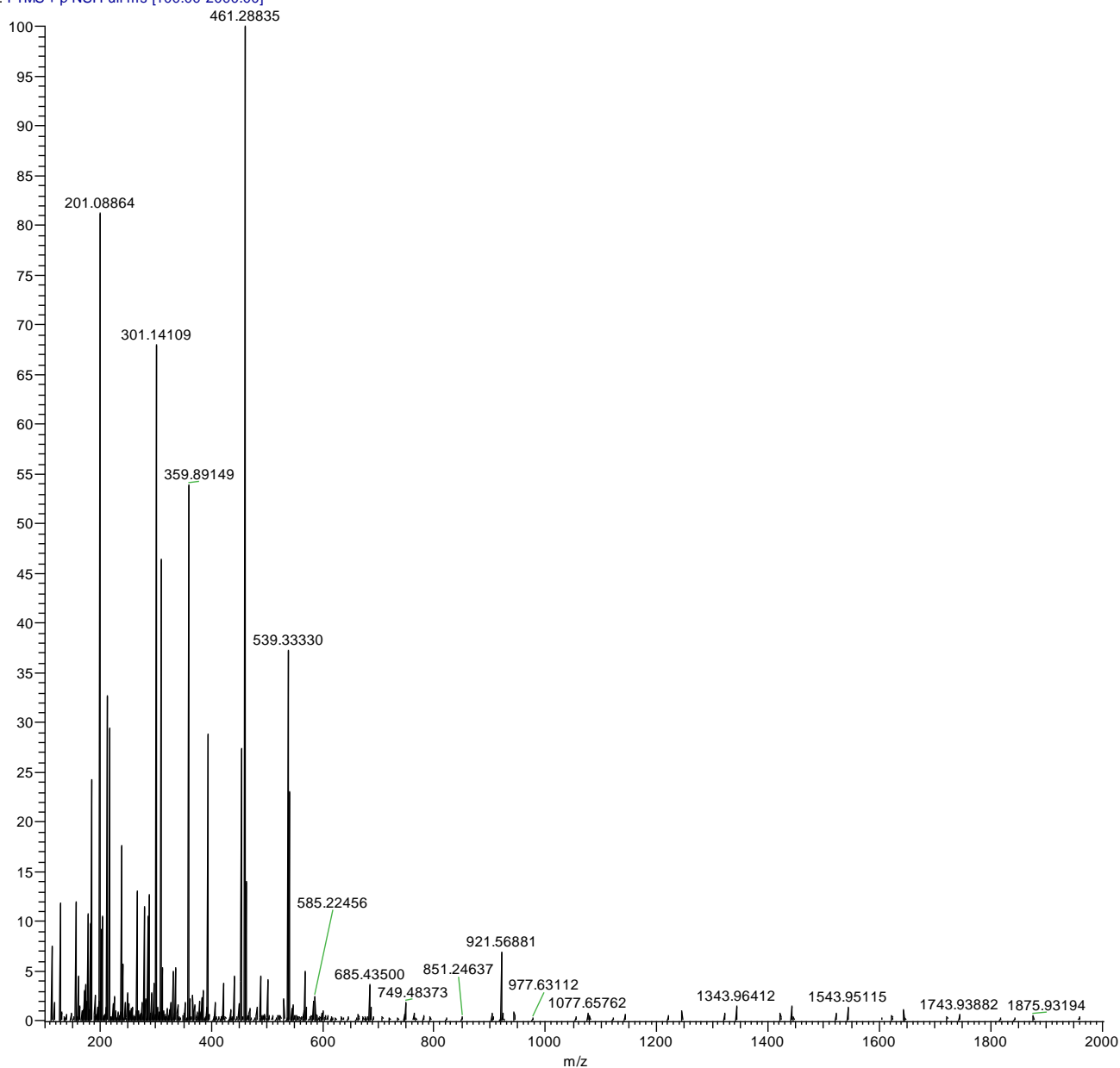
Zoomed spectrum



1,1',1''-((((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-17-((*R*)-5-(((*S*)-3-(1*H*-Indol-3-yl)-1-methoxy-1-oxopropan-2-yl)amino)-5-oxopentan-2-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-3,7,12-triyl)tris(oxy))tris(2-oxoethane-2,1-diyl))tris(azanediyl))tris(3-methyl-1-oxobutan-2-aminium) (**27**)

Full spectrum

jwu-CA-Gly-Val_Pos_Full #2-25 RT: 0.05-0.70 AV: 24 NL: 1.72E7
T: FTMS + p NSI Full ms [100.00-2000.00]



Zoomed spectrum (Top spectrum: measured mass; bottom spectrum: calculated mass)

