Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

An Alternative and Efficient Synthesis of MLN4924, A Selective NEDD8 Inhibitor

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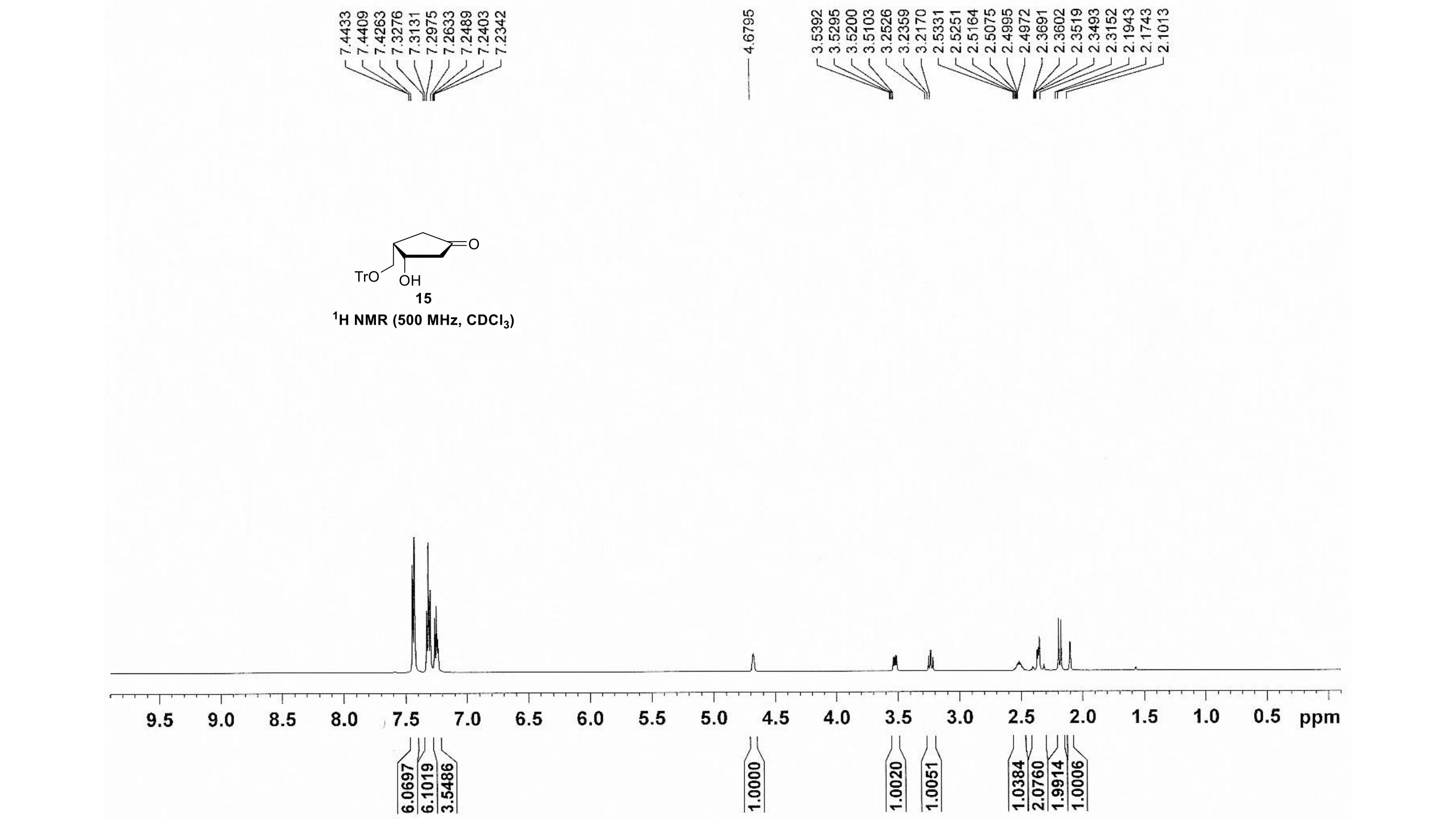
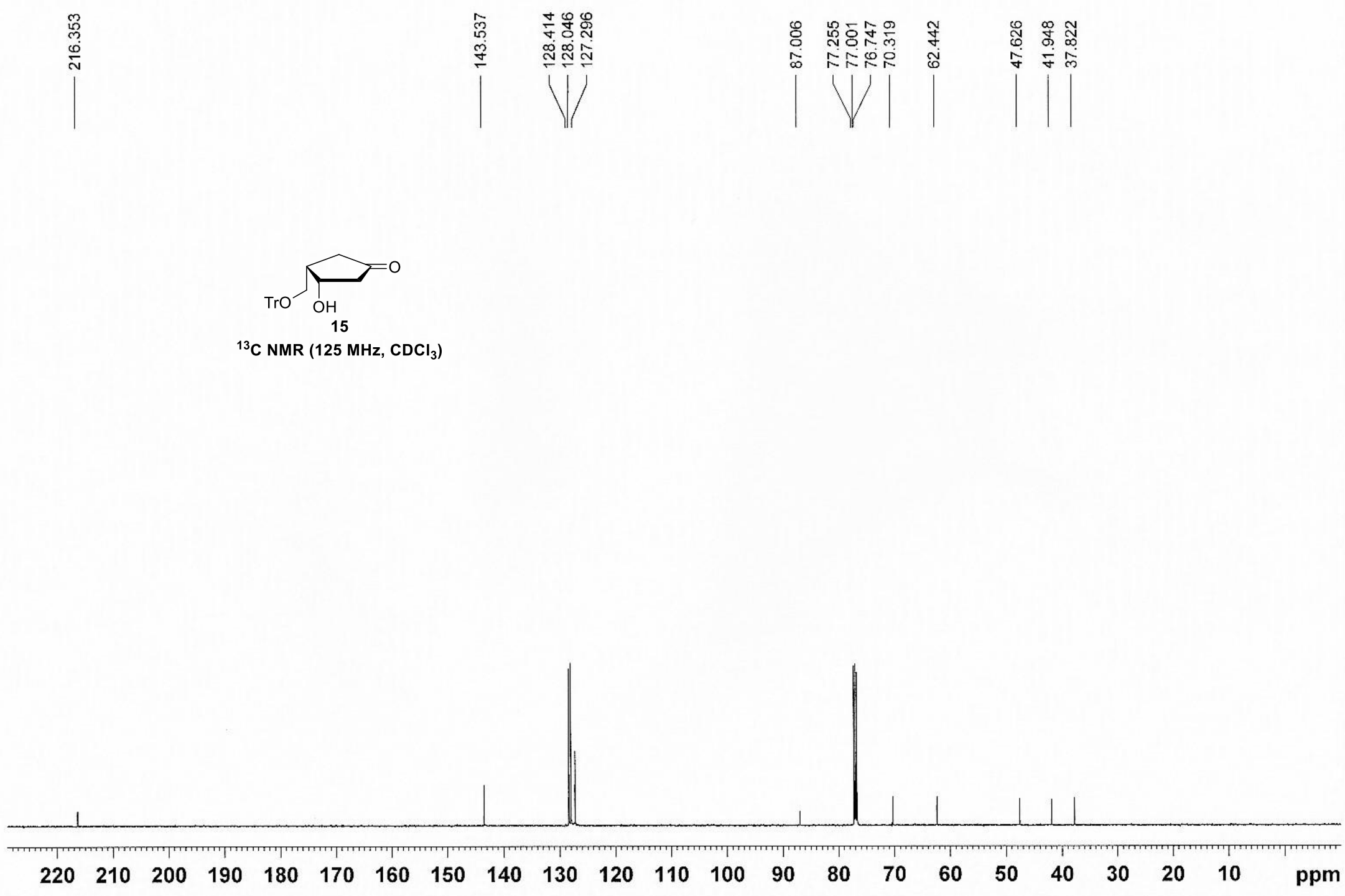


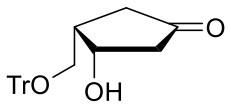
15

^{1}H NMR (500 MHz, $CDCl_3$)



15

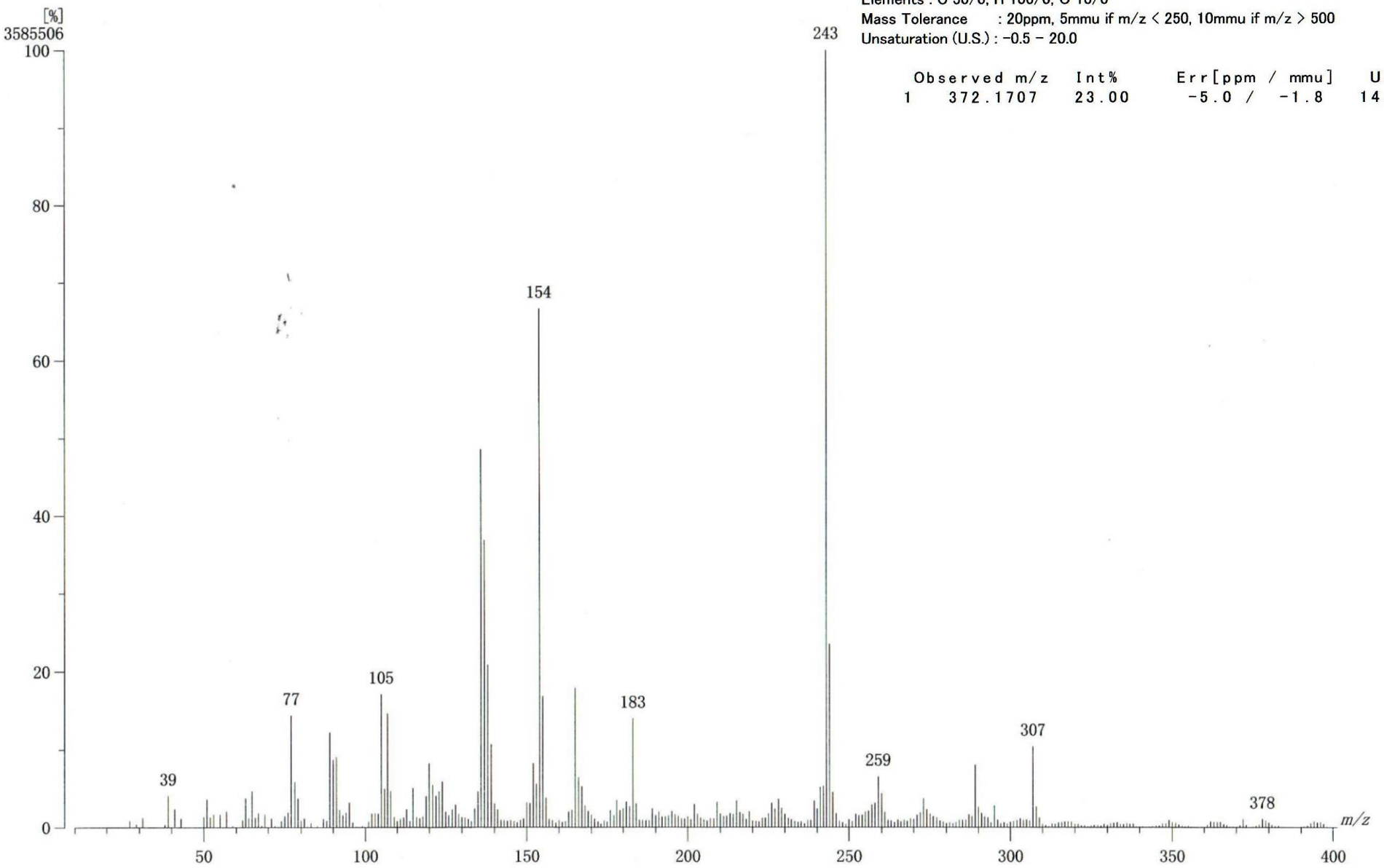
^{13}C NMR (125 MHz, $CDCl_3$)

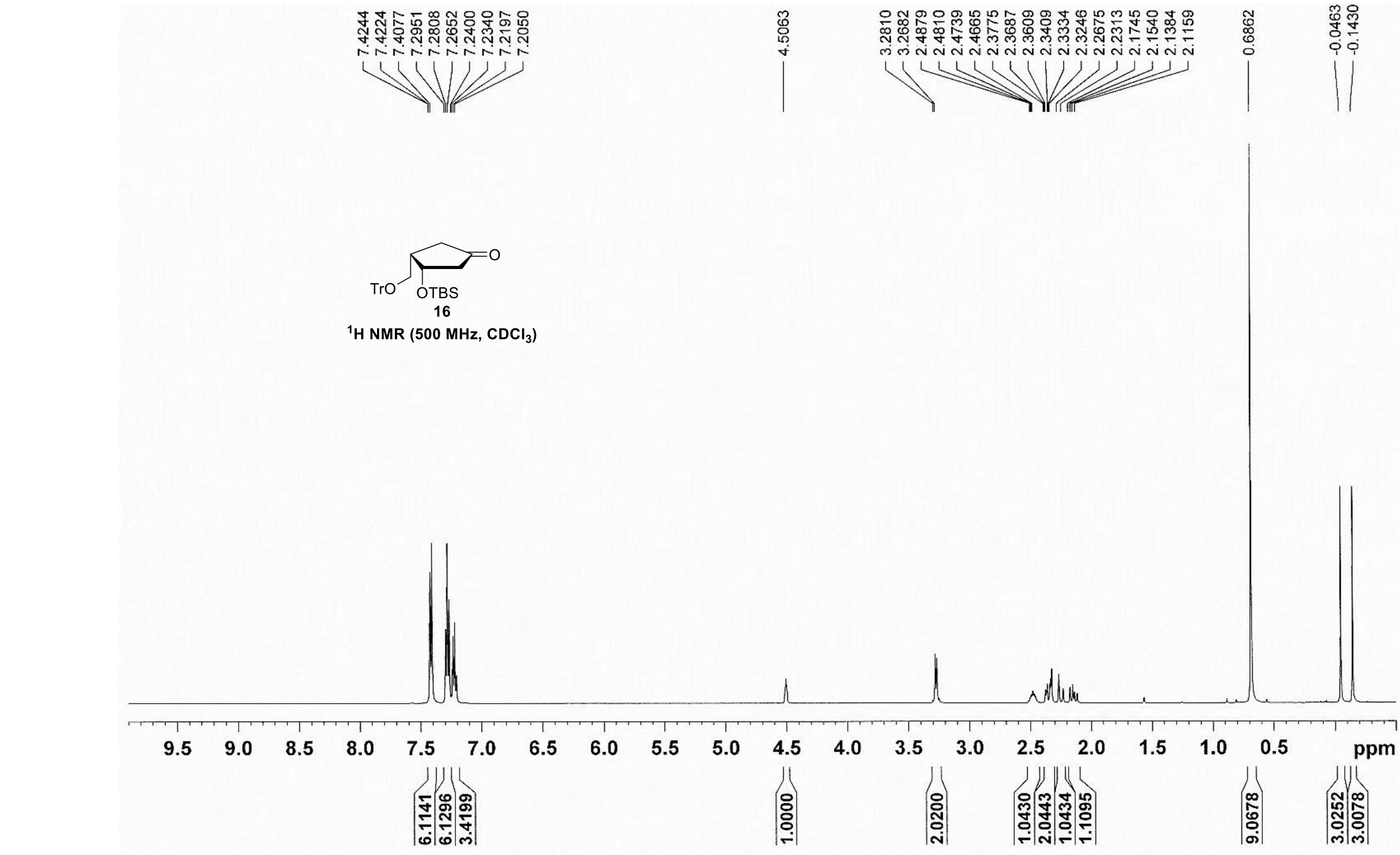


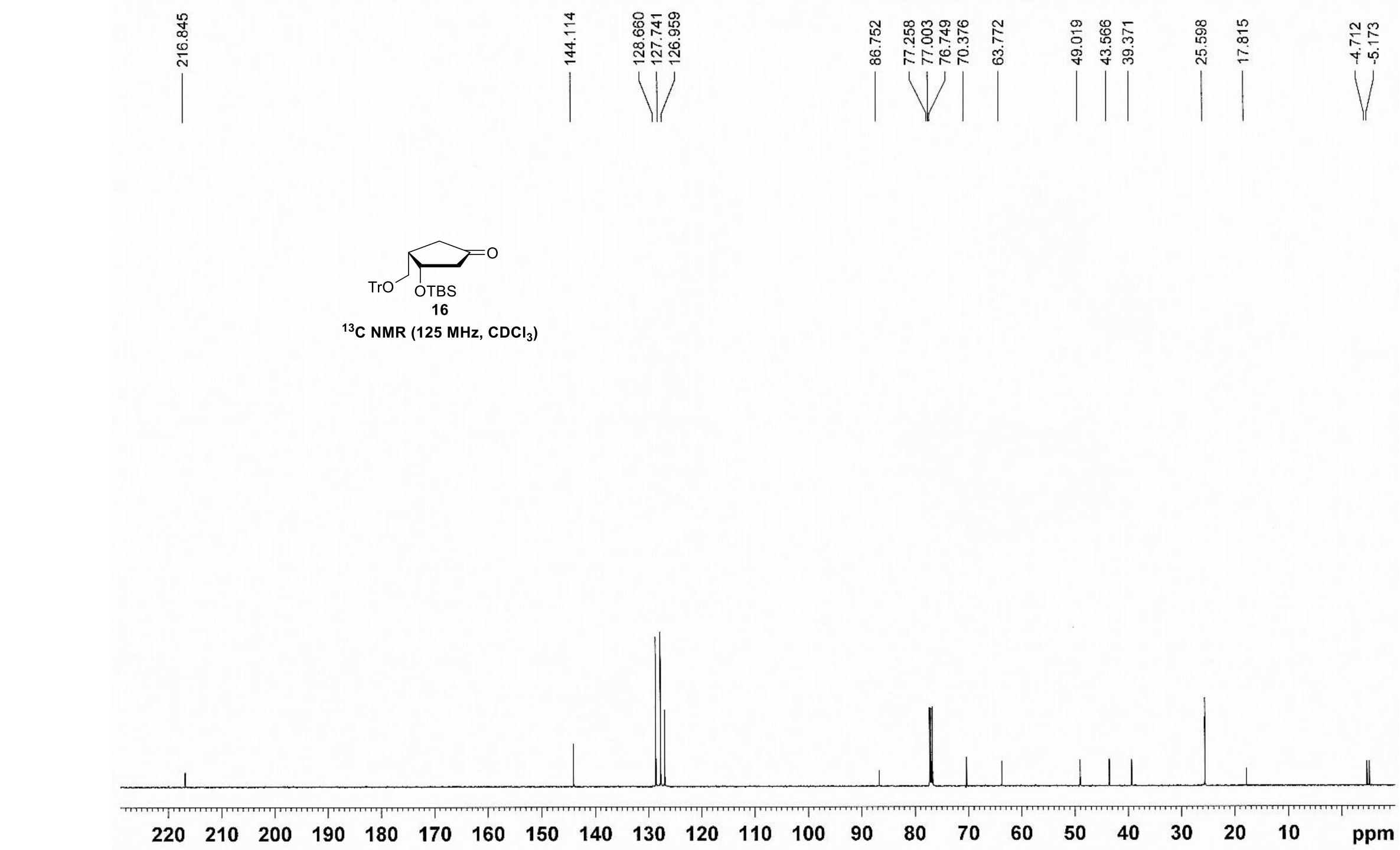
15
HRMS

Data : T0404003 Date : 04-Apr-2019 08:42
Instrument : MStation
Sample : A
Note : m-NBA
Inlet : Direct Ion Mode : FAB+
RT : 3.44 min Scan# : (60,66)+(16,21)
Elements : C 50/0, H 100/0, O 10/0
Mass Tolerance : 20ppm, 5mmu if m/z < 250, 10mmu if m/z > 500
Unsaturation (U.S.) : -0.5 - 20.0

	Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
1	372.1707	23.00	-5.0 / -1.8	14.0	C25 H24 O3

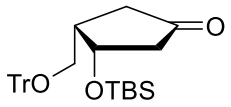



7.4244
7.4224
7.4077
7.2951
7.2808
7.2652
7.2400
7.2340
7.2197
7.2050
4.5063
3.2810
3.2682
2.4879
2.4810
2.4739
2.4665
2.3775
2.3687
2.3609
2.3409
2.3334
2.3246
2.2675
2.2313
2.1745
2.1540
2.1384
2.1159
0.6862
-0.0463
-0.1430
O
TrO
OTBS
16
^{1}H NMR (500 MHz, $CDCl_3$)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
6.1141
6.1296
3.4199
1.0000
2.0200
1.0430
2.0443
1.0434
1.1095
9.0678
3.0252
3.0078



16

^{13}C NMR (125 MHz, $CDCl_3$)

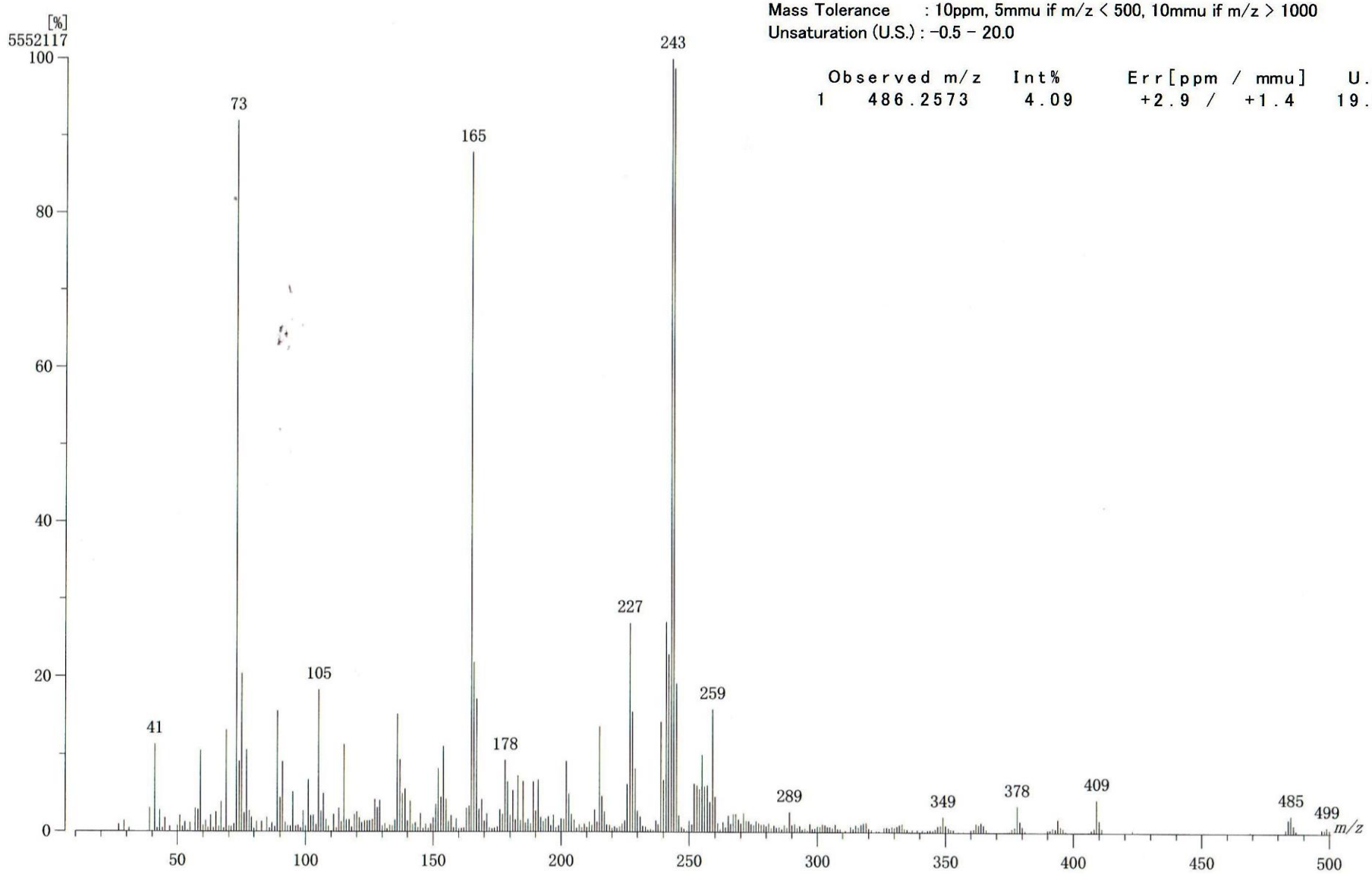


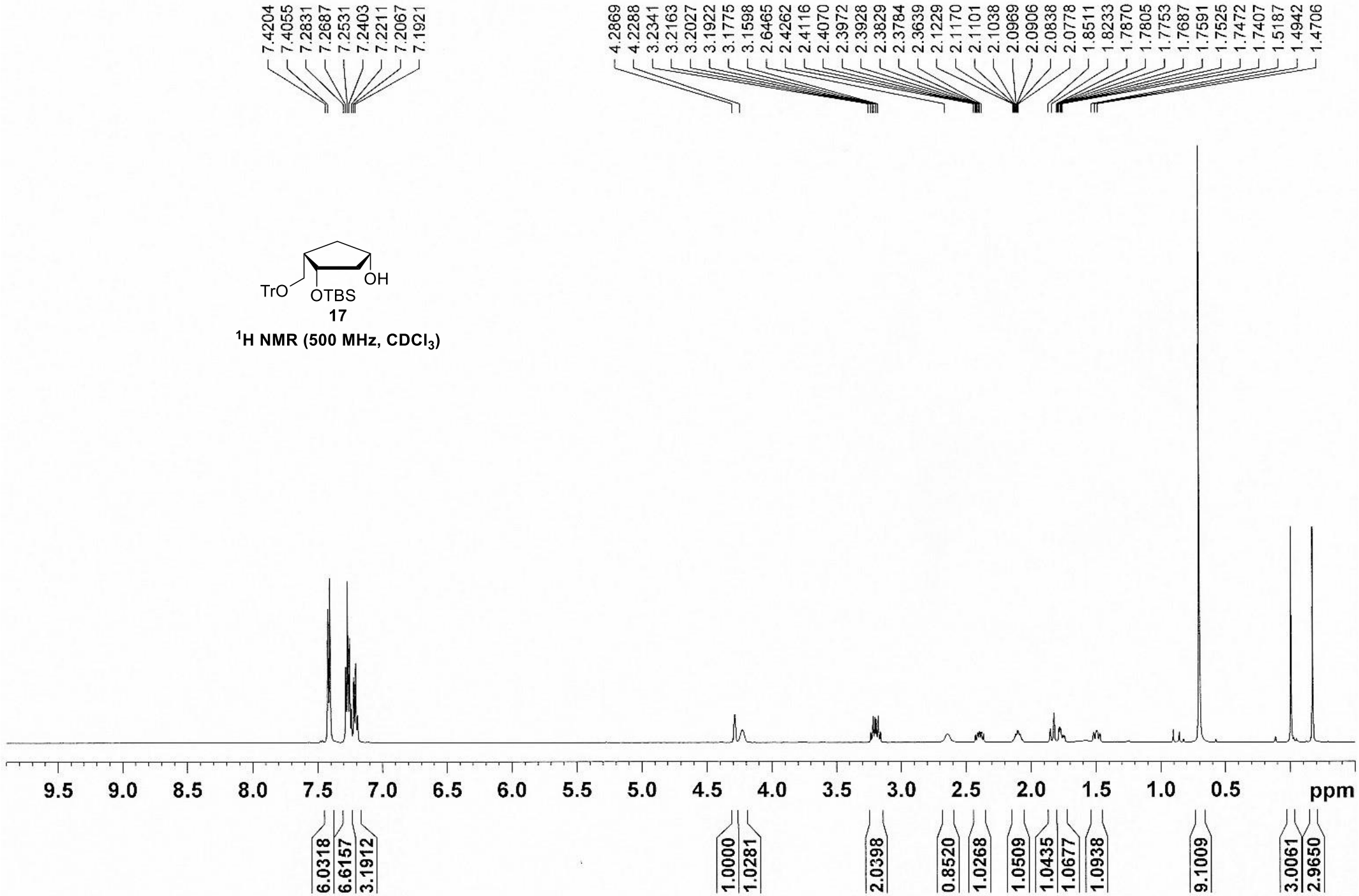
16

HRMS (FAB+)

Data : T0404005 Date : 04-Apr-2019 18:57
Instrument : MStation
Sample : B
Note : m-NBA
Inlet : Direct Ion Mode : FAB+
RT : 2.63 min Scan# : (46,52)
Elements : C 50/0, H 100/0, O 10/0, 28Si 1/0, 29Si 1/0, 30Si 1/0
Mass Tolerance : 10ppm, 5mmu if m/z < 500, 10mmu if m/z > 1000
Unsaturation (U.S.) : -0.5 - 20.0

	Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
1	486.2573	4.09	+2.9 / +1.4	19.0	C35 H34 O2

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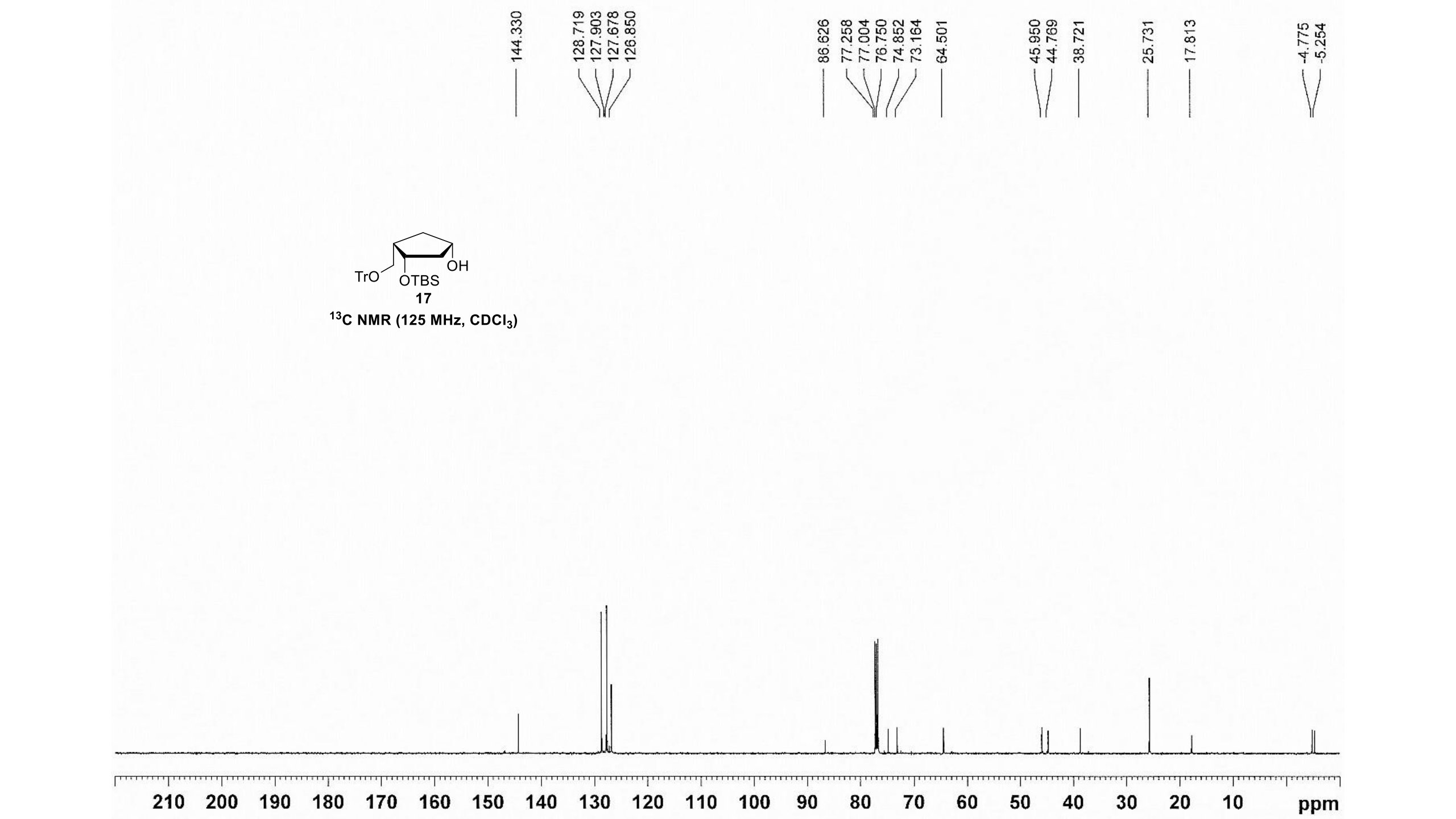
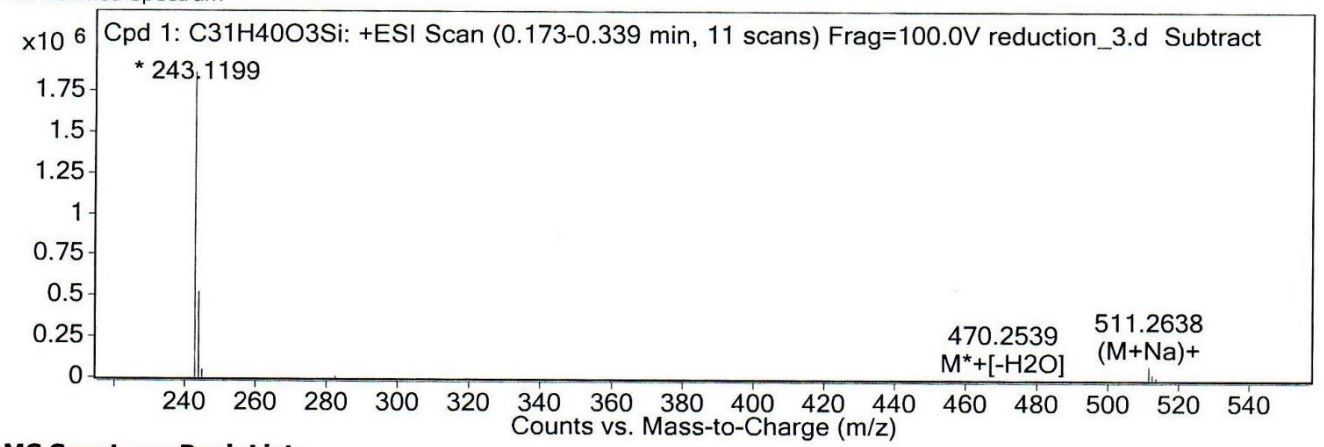
7.4055
7.2831
7.2687
7.2531
7.2403
7.2211
7.2067
7.1921
4.2869
4.2288
3.2341
3.2163
3.2027
3.1922
3.1775
3.1598
2.6465
2.4262
2.4116
2.4070
2.3972
2.3928
2.3829
2.3784
2.3639
2.1229
2.1170
2.1101
2.1038
2.0969
2.0906
2.0838
2.0778
1.8511
1.8233
1.7870
1.7805
1.7753
1.7687
1.7591
1.7525
1.7472
1.7407
1.5187
1.4942
1.4706
TrO
OTBS
OH
17
^{1}H NMR (500 MHz, $CDCl_3$)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
6.0318
6.6157
3.1912
1.0000
1.0281
2.0398
0.8520
1.0268
1.0509
1.0435
1.0677
1.0938
9.1009
3.0061
2.9650



^{13}C NMR (125 MHz, $CDCl_3$)

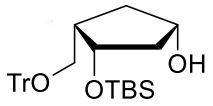
Qualitative Compound Report

MS Zoomed Spectrum



MS Spectrum Peak List

m/z	*Calc m/z*	Diff(ppm)	z	Abund	Formula	Ion
243.1199				1857543		
243.2565				116908		
243.2995				37826		
244.1195				526558		
244.1565				10165		
245.1241	245.1446	-83.86		45627	C31 H42 O3 Si	(M+2H)+2
470.2539	470.2636	-20.46	1	149	C31 H38 O2 Si	M*+[-H2O]
511.2638	511.2639	-0.16	1	85309	C31 H40 Na O3 Si	(M+Na)+
512.2669	512.2668	0.12	1	32683	C31 H40 Na O3 Si	(M+Na)+
527.2372	527.2378	-1.28	1	1390	C31 H40 K O3 Si	(M+K)+



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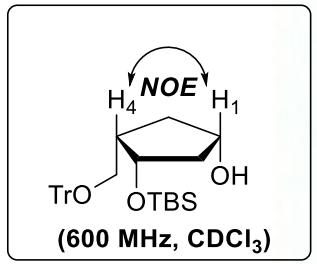
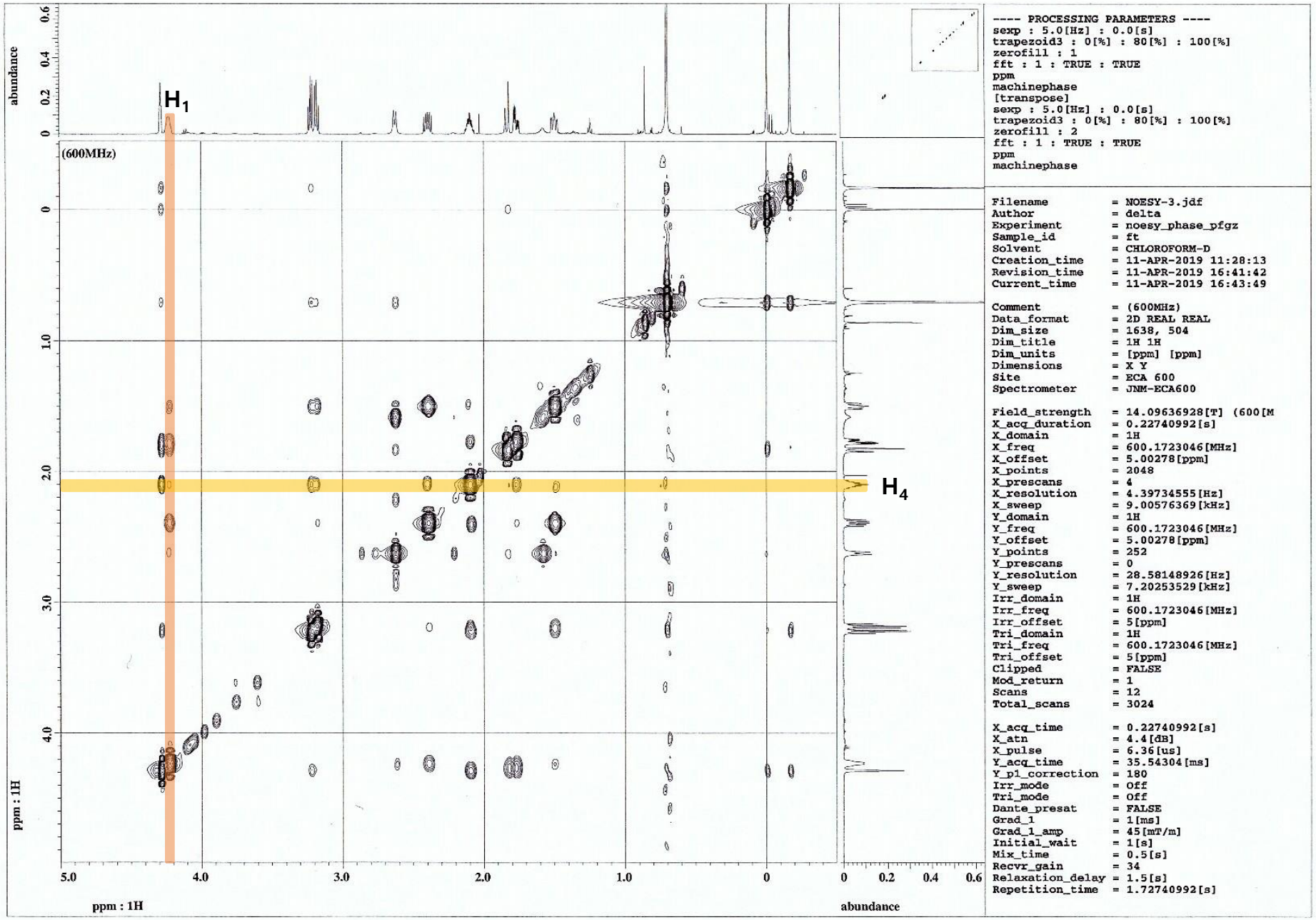
HRMS (ESI)

--- End Of Report ---



(600 MHz, $CDCl_3$)




```
---- PROCESSING PARAMETERS ----
sexp : 5.0[Hz] : 0.0[s]
trapezoid3 : 0[%] : 80[%] : 100[%]
zerofill : 1
fft : 1 : TRUE : TRUE
ppm
machinephase
[transpose]
sexp : 5.0[Hz] : 0.0[s]
trapezoid3 : 0[%] : 80[%] : 100[%]
zerofill : 2
fft : 1 : TRUE : TRUE
ppm
machinephase
```

```
Filename          = NOESY-3.jdf
Author            = delta
Experiment        = noesy_phase_pfgz
Sample_id         = ft
Solvent           = CHLOROFORM-D
Creation_time     = 11-APR-2019 11:28:13
Revision_time     = 11-APR-2019 16:41:42
Current_time      = 11-APR-2019 16:43:49

Comment           = (600MHz)
Data_format       = 2D REAL REAL
Dim_size          = 1638, 504
Dim_title         = 1H 1H
Dim_units         = [ppm] [ppm]
Dimensions        = X Y
Site              = ECA 600
Spectrometer      = JNM-ECA600

Field_strength    = 14.09636928[T] (600[M
X_acq_duration    = 0.22740992[s]
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X_resolution      = 4.39734555[Hz]
X_sweep           = 9.00576369[kHz]
Y_domain          = 1H
Y_freq            = 600.1723046[MHz]
Y_offset          = 5.00278[ppm]
Y_points          = 252
Y_prescans        = 0
Y_resolution      = 28.58148926[Hz]
Y_sweep           = 7.20253529[kHz]
Irr_domain        = 1H
Irr_freq          = 600.1723046[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 600.1723046[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 12
Total_scans       = 3024

X_acq_time        = 0.22740992[s]
X_atn             = 4.4[dB]
X_pulse           = 6.36[us]
Y_acq_time        = 35.54304[ms]
Y_pi_correction   = 180
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Grad_1            = 1[ms]
Grad_1_amp        = 45[mT/m]
Initial_wait      = 1[s]
Mix_time          = 0.5[s]
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Relaxation_delay  = 1.5[s]
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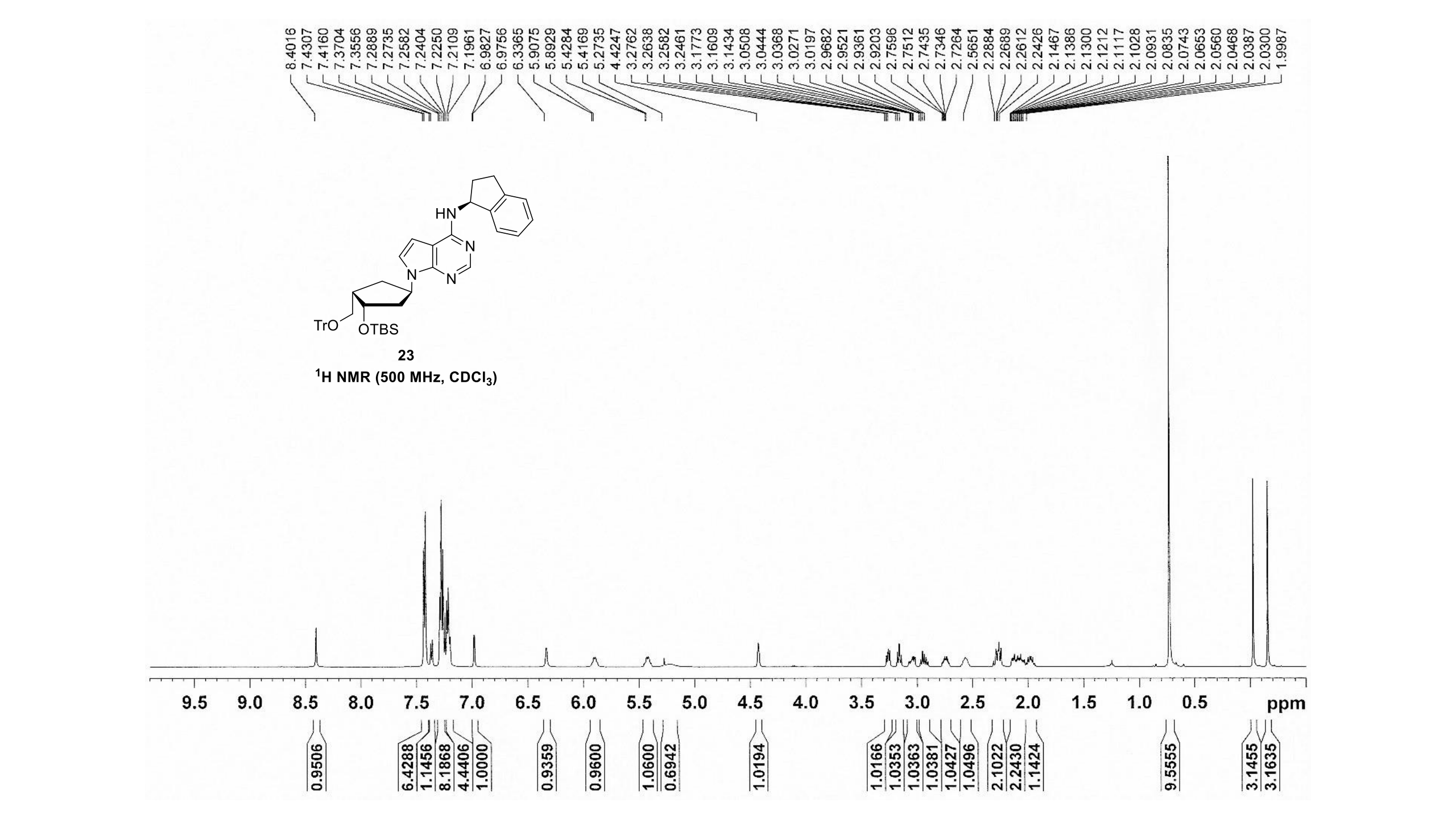
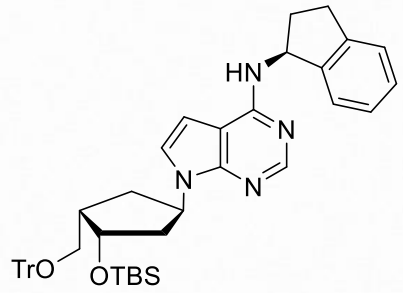


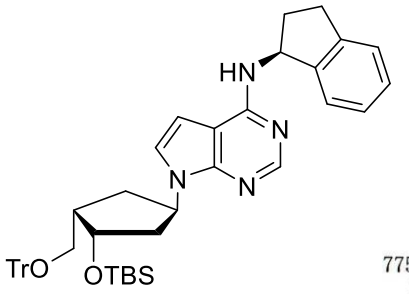
23

^{1}H NMR (500 MHz, $CDCl_3$)



23

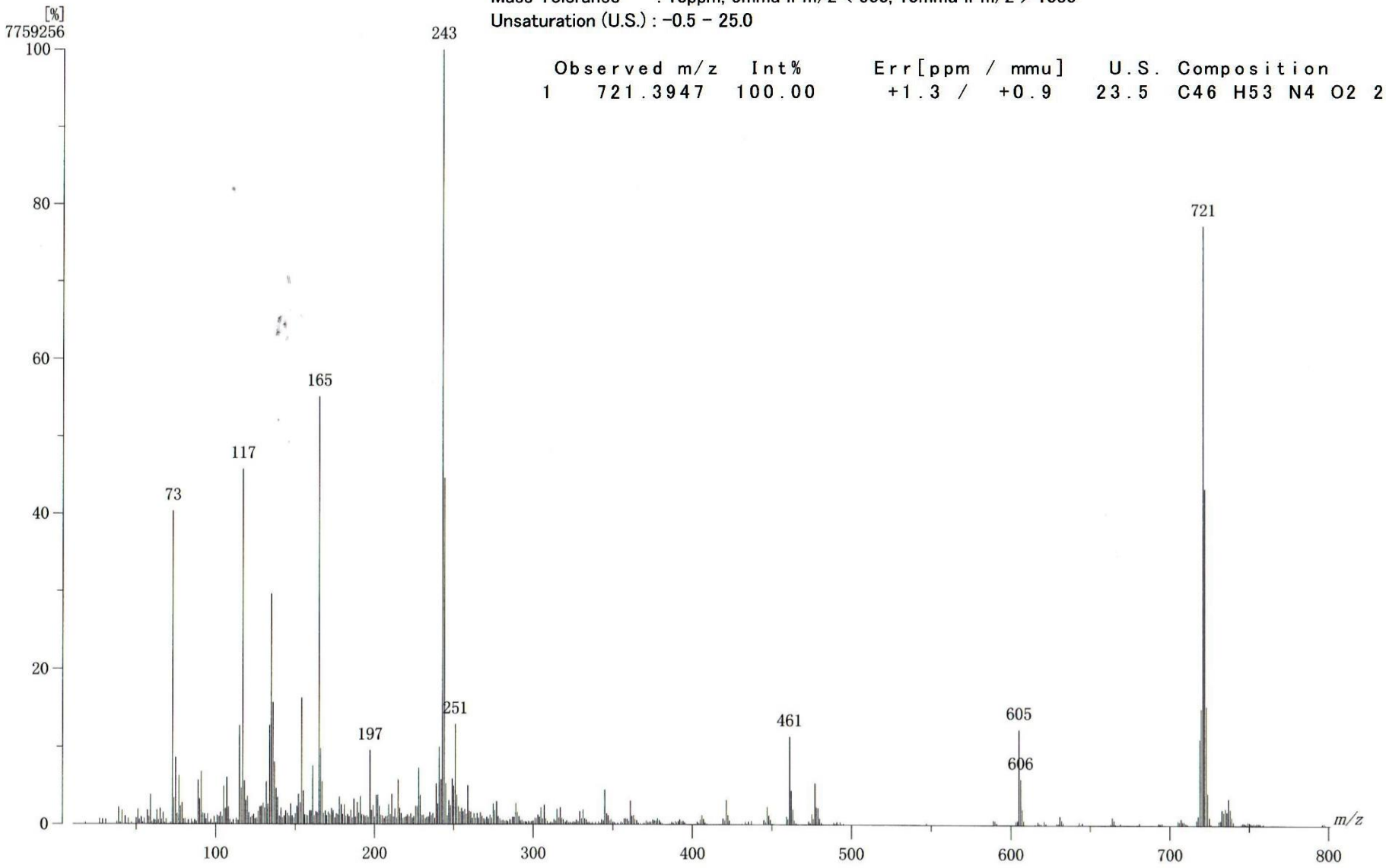
^{13}C NMR (125 MHz, $CDCl_3$)

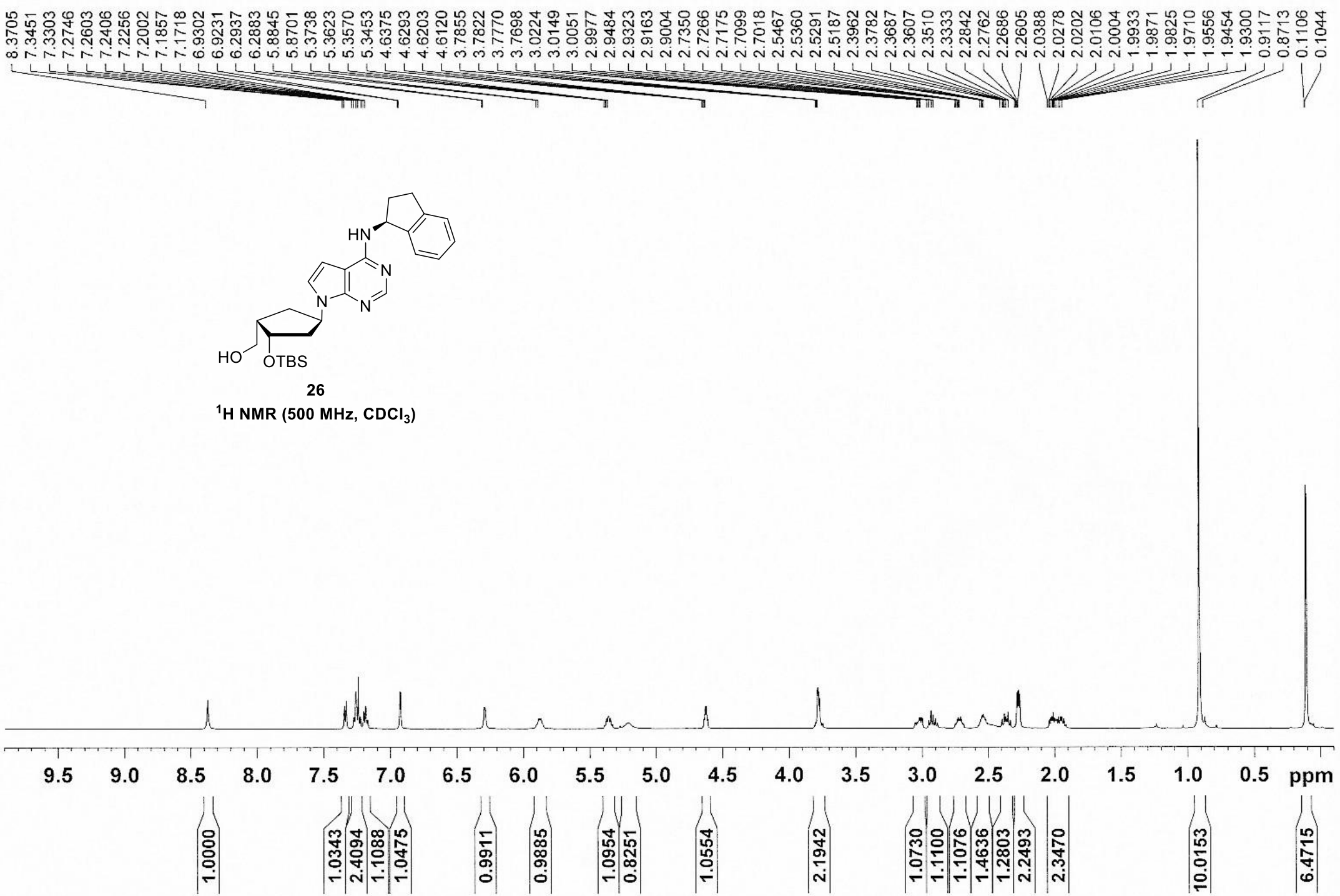


23
HRMS (FAB+)

Data : T0404008 Date : 05-Apr-2019 09:42
Instrument : MStation
Sample : D
Note : m-NBA
Inlet : Direct Ion Mode : FAB+
RT : 0.00 min Scan# : (1,59)
Elements : C 50/0, H 100/0, N 4/0, O 3/0, 28Si 1/0, 29Si 1/0, 30Si 1/0
Mass Tolerance : 10ppm, 5mmu if m/z < 500, 10mmu if m/z > 1000
Unsaturation (U.S.) : -0.5 - 25.0

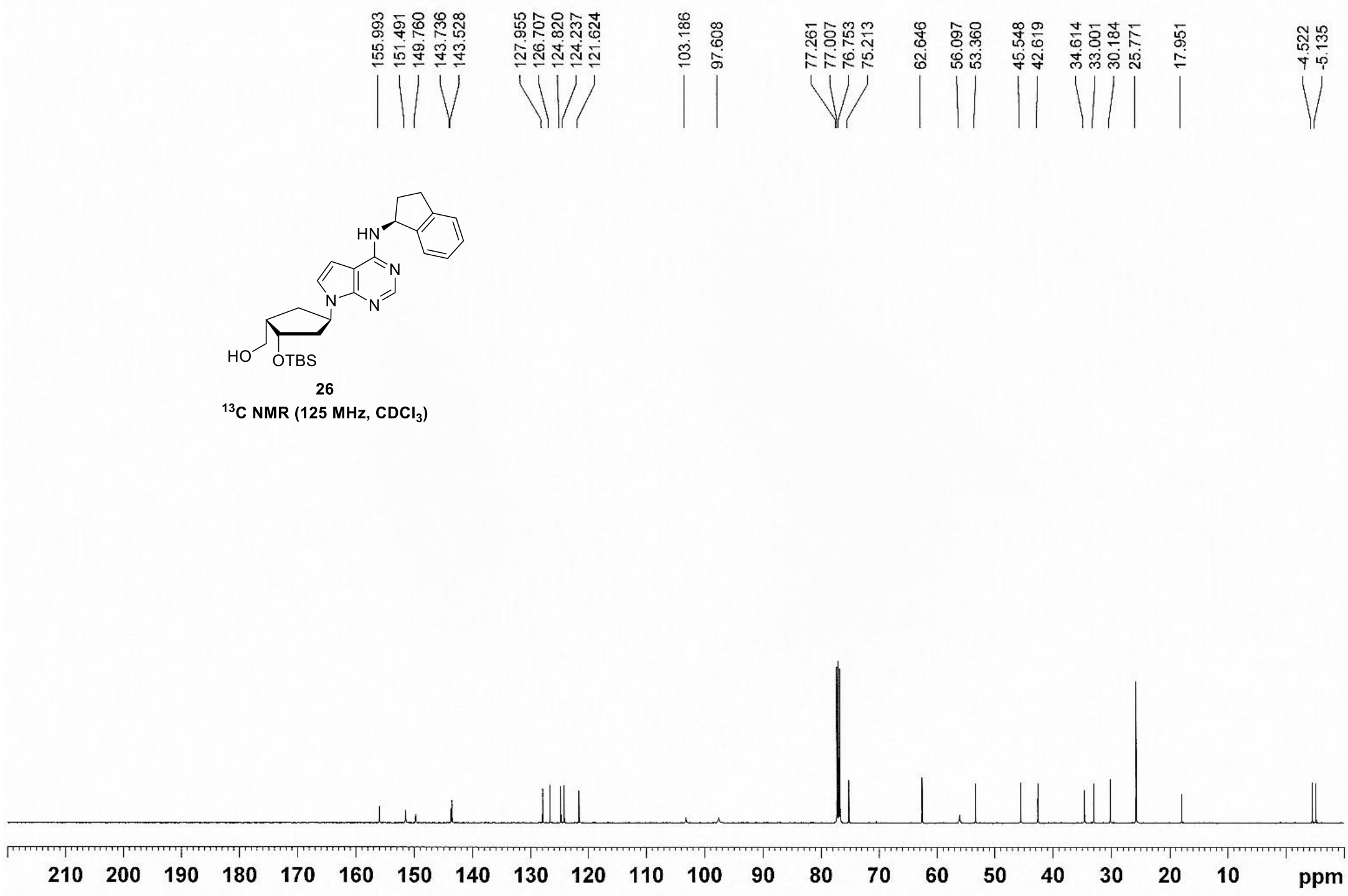
	Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
1	721.3947	100.00	+1.3 / +0.9	23.5	C46 H53 N4 O2 28Si





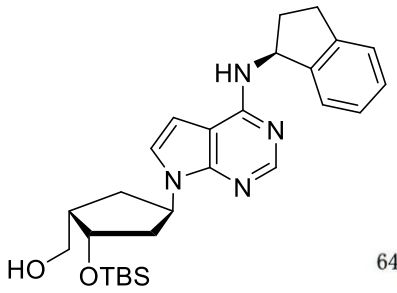
26

^{1}H NMR (500 MHz, $CDCl_3$)



26

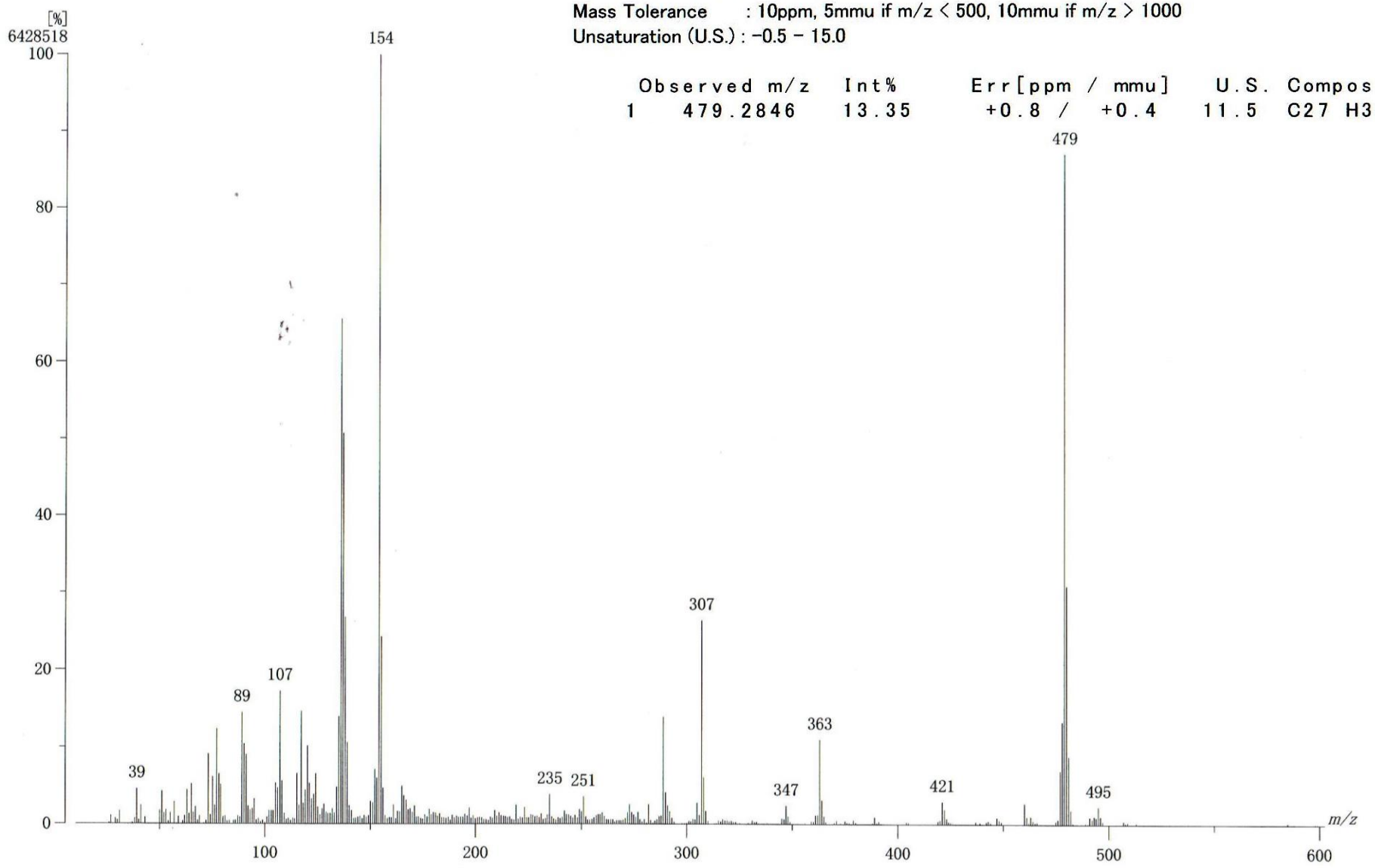
^{13}C NMR (125 MHz, $CDCl_3$)

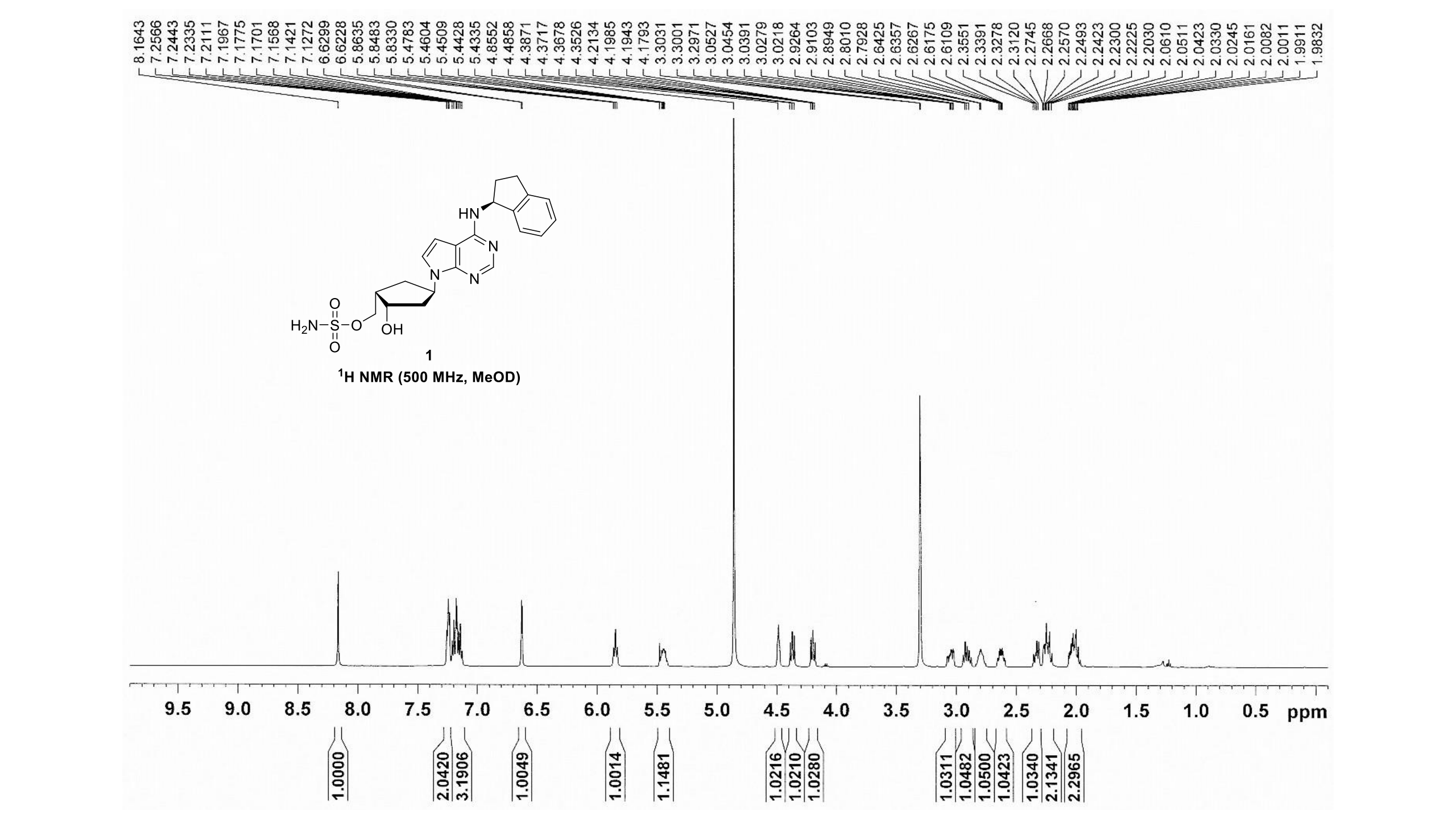


26
HRMS (FAB+)

Data : T0404010 Date : 05-Apr-2019 11:33
Instrument : MStation
Sample : E
Note : m-NBA
Inlet : Direct Ion Mode : FAB+
RT : 1.87 min Scan# : (33,57)
Elements : C 50/0, H 100/0, N 4/0, O 3/0, 28Si 1/0, 29Si 1/0, 30Si 1/0
Mass Tolerance : 10ppm, 5mmu if m/z < 500, 10mmu if m/z > 1000
Unsaturation (U.S.) : -0.5 - 15.0

	Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
1	479.2846	13.35	+0.8 / +0.4	11.5	C27 H39 N4 O2 28Si




8.1643
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7.2443
7.2335
7.2111
7.1967
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7.1568
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7.1272
6.6299
6.6228
5.8635
5.8483
5.8330
5.4783
5.4604
5.4509
5.4428
5.4335
4.8552
4.4858
4.3871
4.3717
4.3678
4.3526
4.2134
4.1985
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4.1793
3.3031
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3.2971
3.0527
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3.0279
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2.9264
2.9103
2.8949
2.8010
2.7928
2.6425
2.6357
2.6267
2.6175
2.6109
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2.3278
2.3120
2.2745
2.2668
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2.2225
2.2030
2.0610
2.0511
2.0423
2.0330
2.0245
2.0161
2.0082
2.0011
1.9911
1.9832
HN
N
N
N
H2N–S–O
O
O
OH
1
1H NMR (500 MHz, MeOD)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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2.0420
3.1906
1.0049
1.0014
1.1481
1.0216
1.0210
1.0280
1.0311
1.0482
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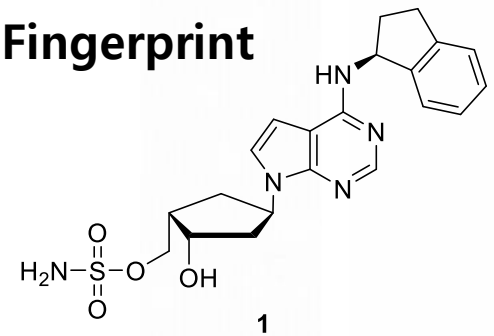
1.0423
1.0340
2.1341
2.2965

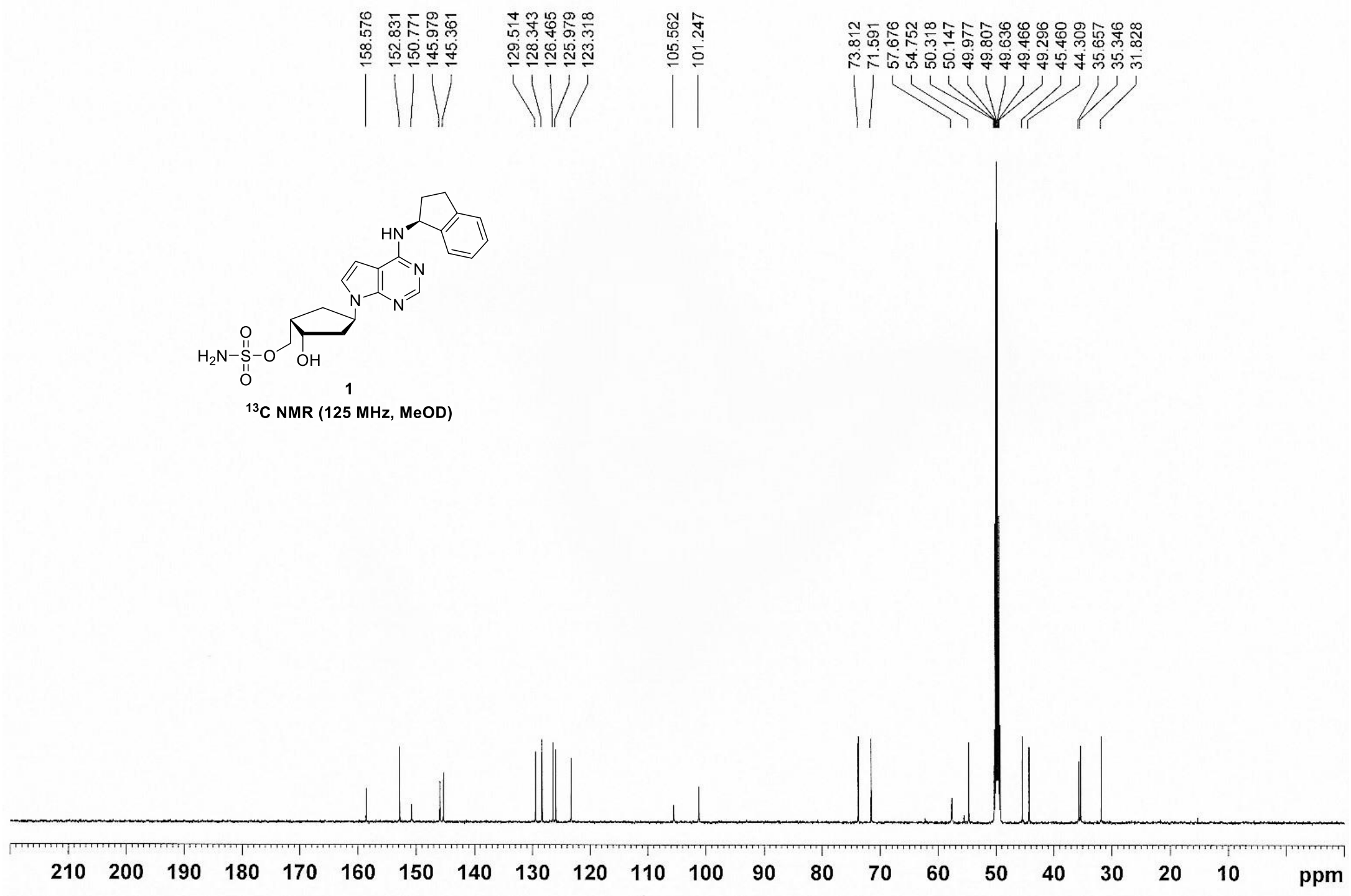
Fingerprint



1

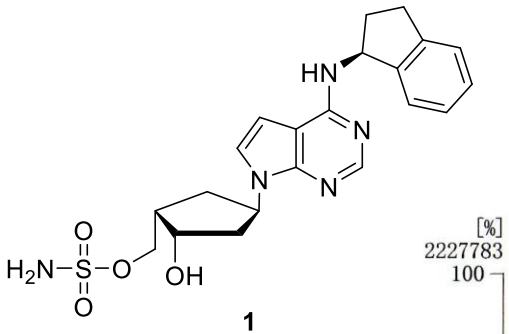
^{1}H NMR (500 MHz, MeOD)

T. A. Soucy, *et al. Nature*, 2009, **458**, 732,



1

^{13}C NMR (125 MHz, MeOD)

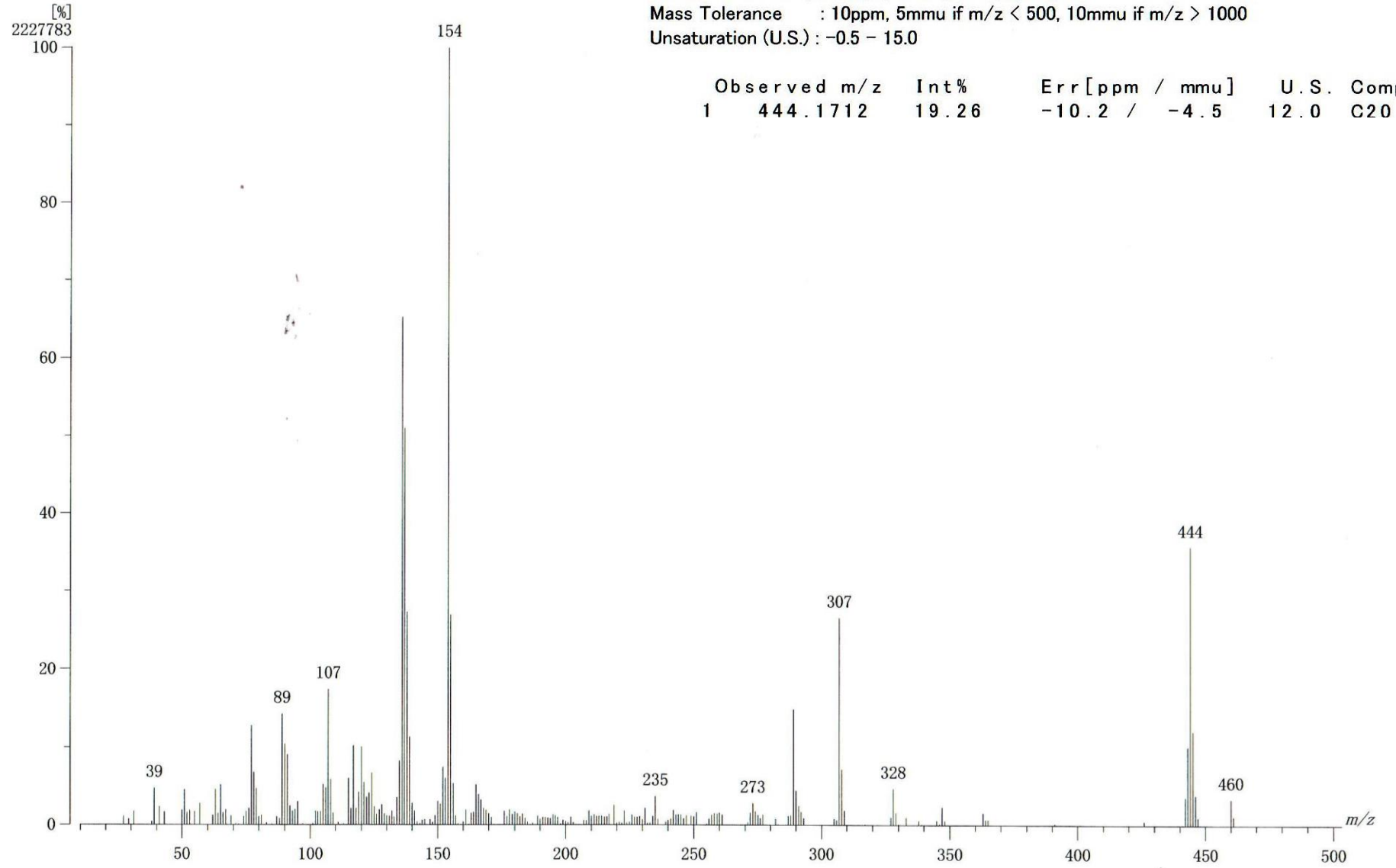


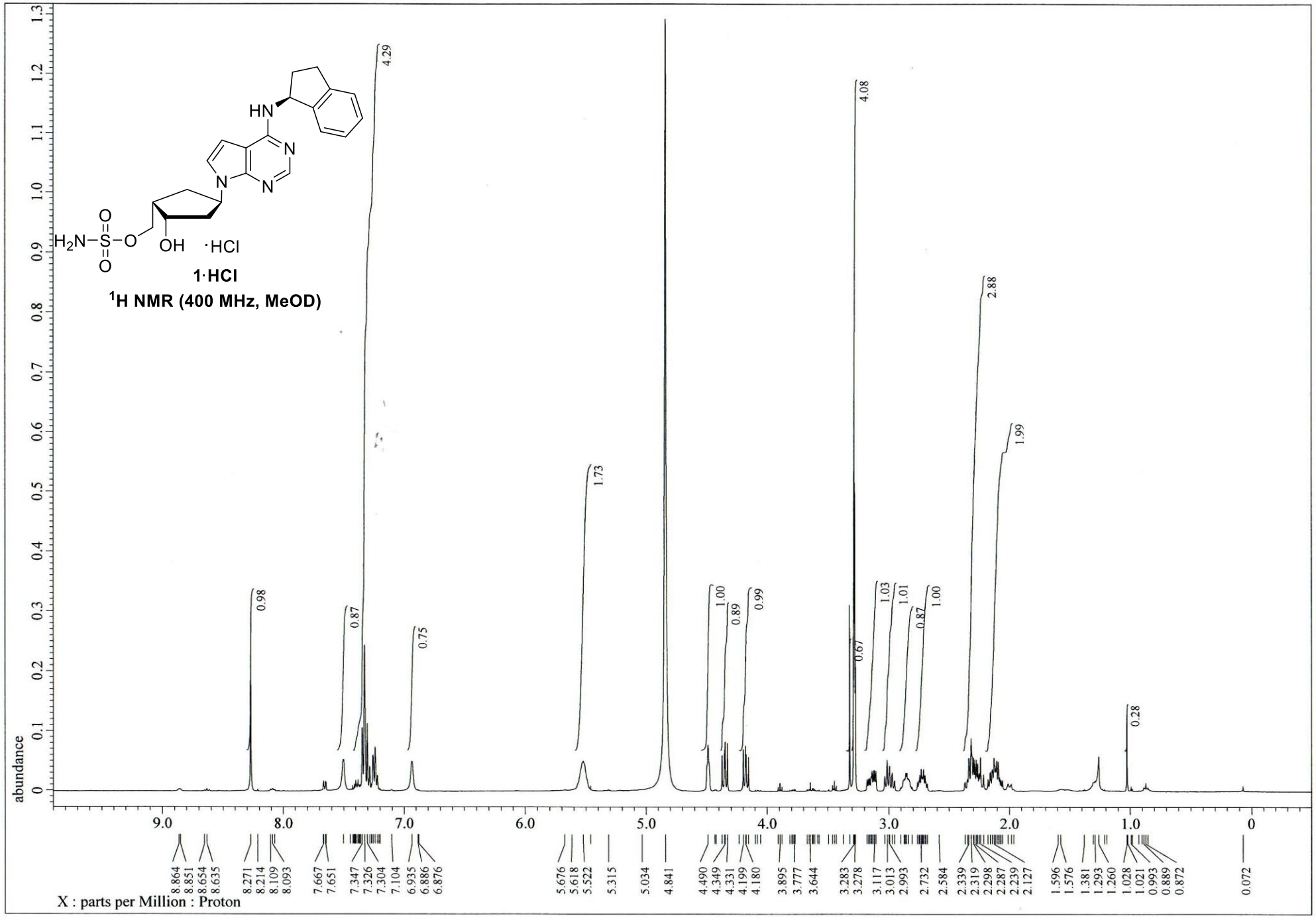
1

HRMS (FAB+)

Data : T0404012 Date : 05-Apr-2019 14:13
Instrument : MStation
Sample : F
Note : m-NBA
Inlet : Direct Ion Mode : FAB+
RT : 0.00 min Scan# : (1,42)
Elements : C 50/0, H 100/0, N 6/0, O 10/0, S 1/0
Mass Tolerance : 10ppm, 5mmu if m/z < 500, 10mmu if m/z > 1000
Unsaturation (U.S.) : -0.5 - 15.0

	Observed m/z	Int%	Err[ppm / mmu]	U.S.	Composition
1	444.1712	19.26	-10.2 / -4.5	12.0	C20 H24 N6 O6




1·HCl
1H NMR (400 MHz, MeOD)
abundance
X : parts per Million : Proton

T. A. Soucy, *et al. Nature*, 2009, **458**, 732,