Supporting Information

Design and Synthesis of New 4-(3,4,5-Trimethoxyphenyl) Thiazole–Pyrimidine Derivatives as Potential Antiproliferative Agents

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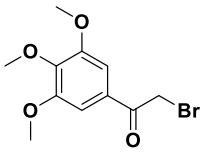
Figure S1. ^{1}H NMR and ^{13}C NMR spectra.



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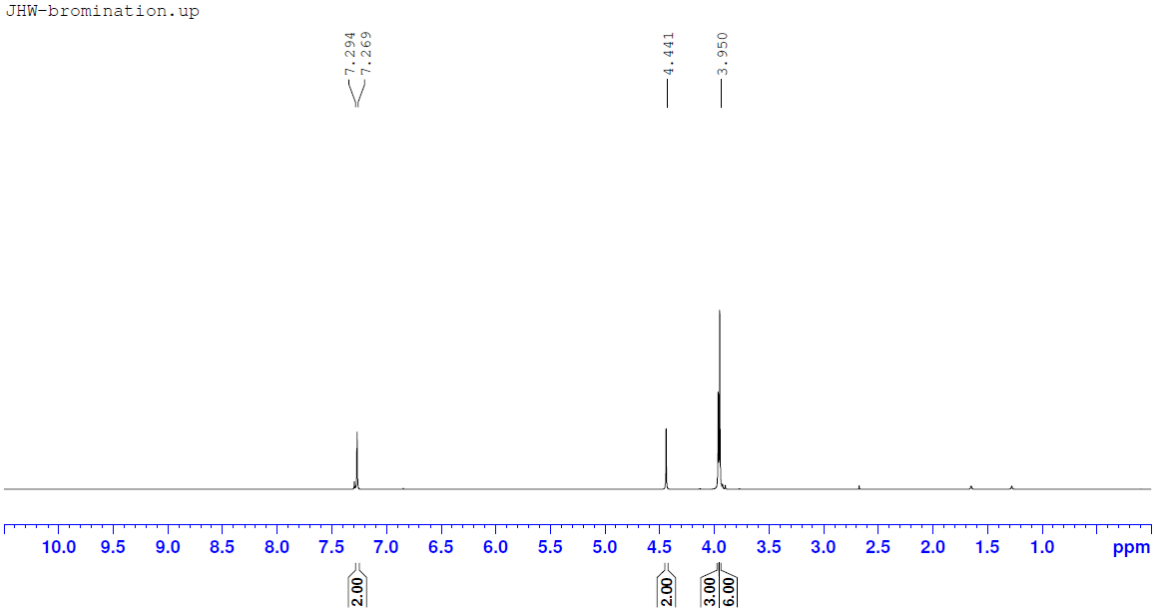

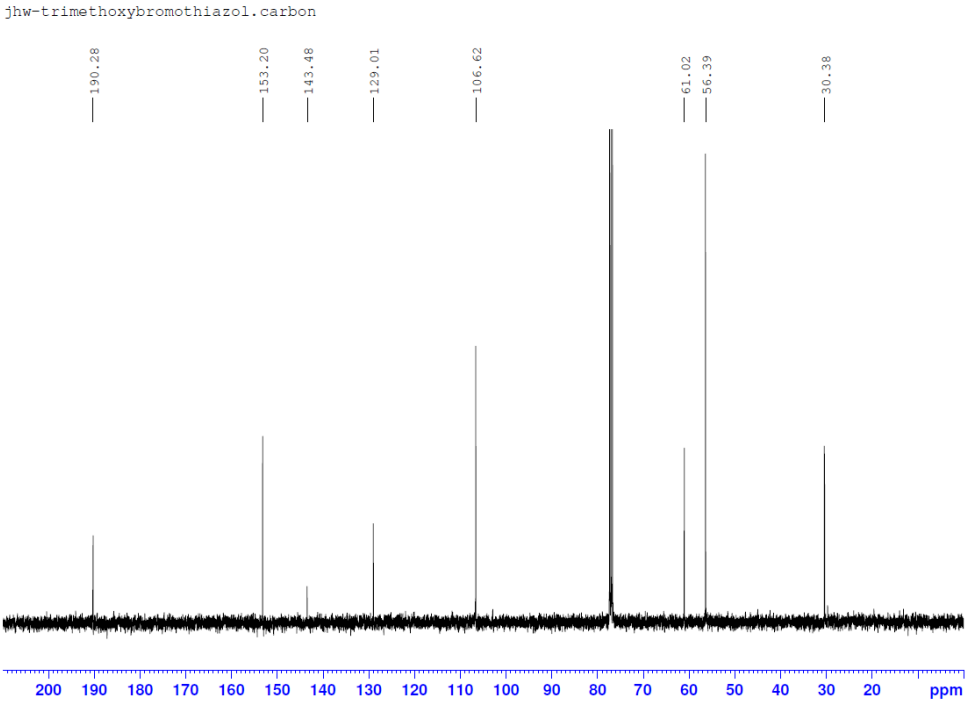

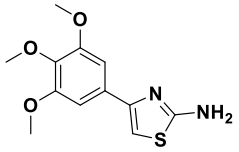

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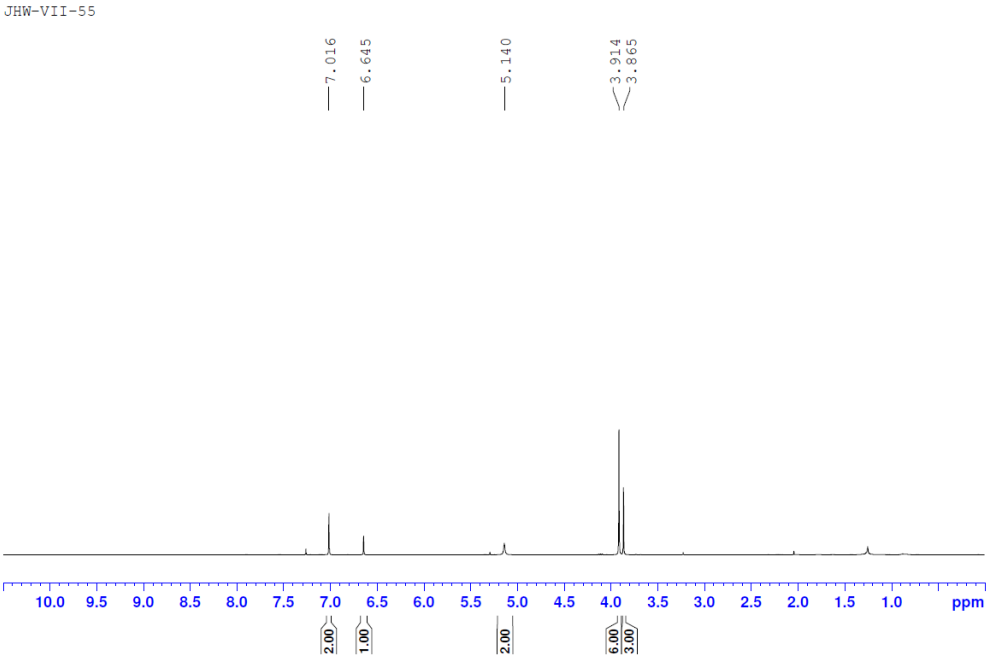
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5.140
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3.865
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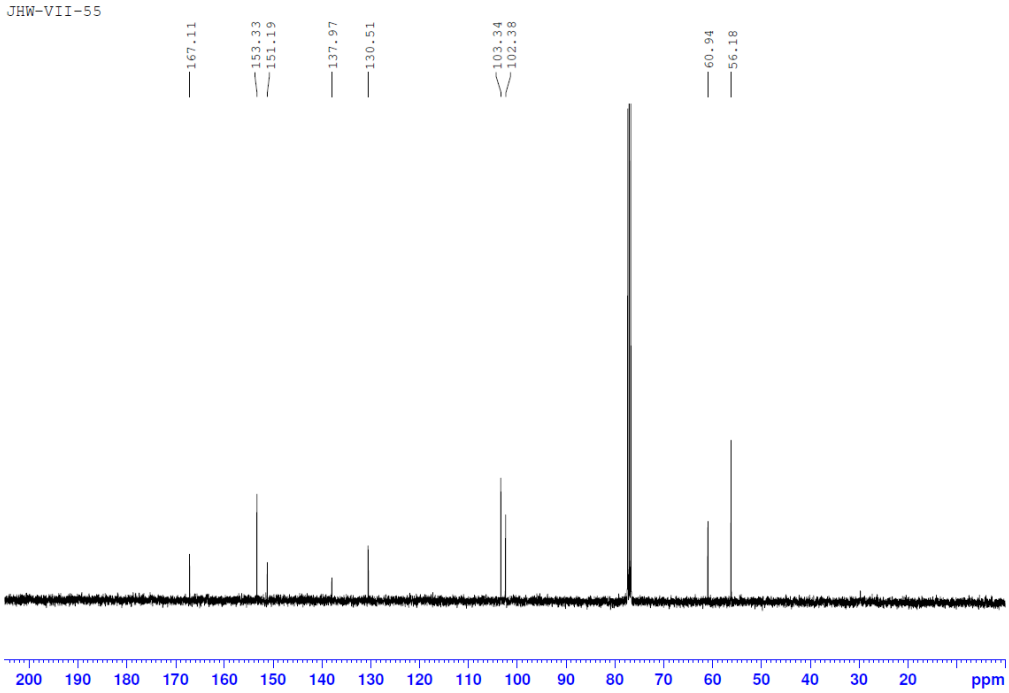
1.00
2.00
6.00
3.00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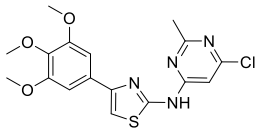

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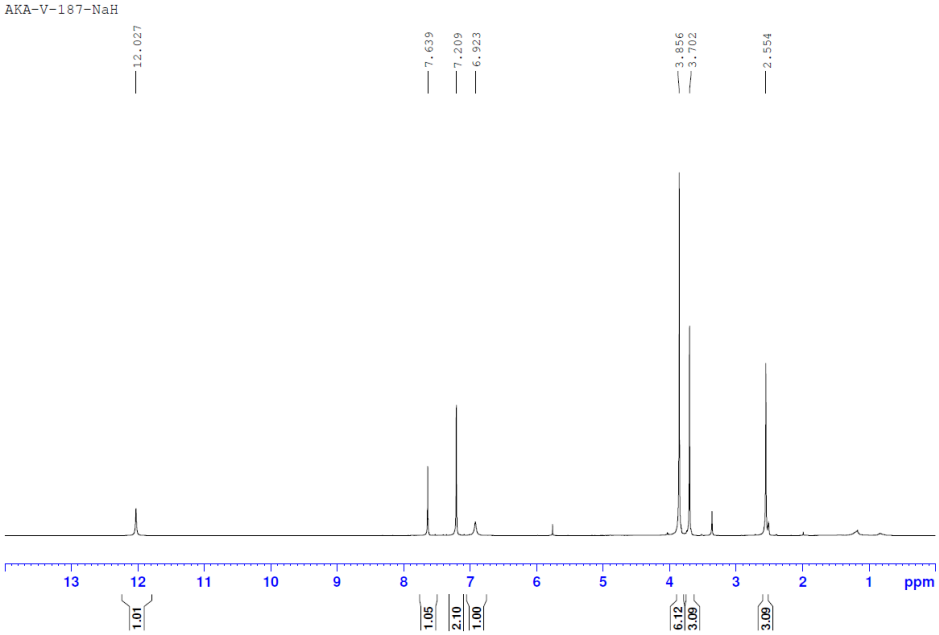
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7.209
6.923
3.856
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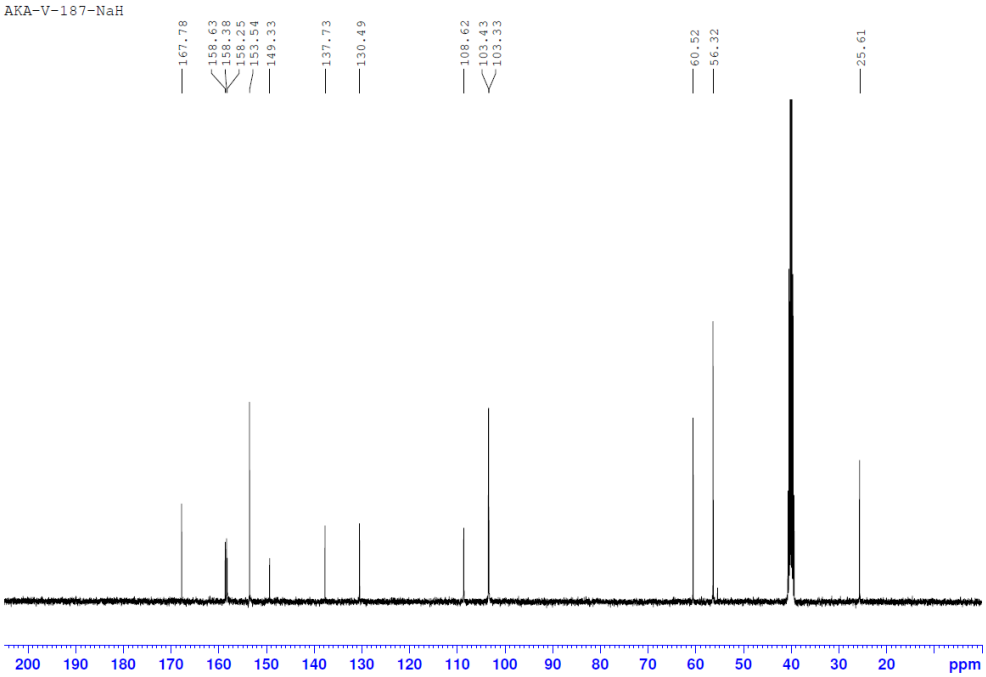
1.05
2.10
1.00
6.12
3.09
3.09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149.33
137.73
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103.33
60.52
56.32
25.61
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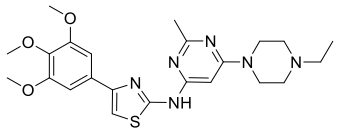

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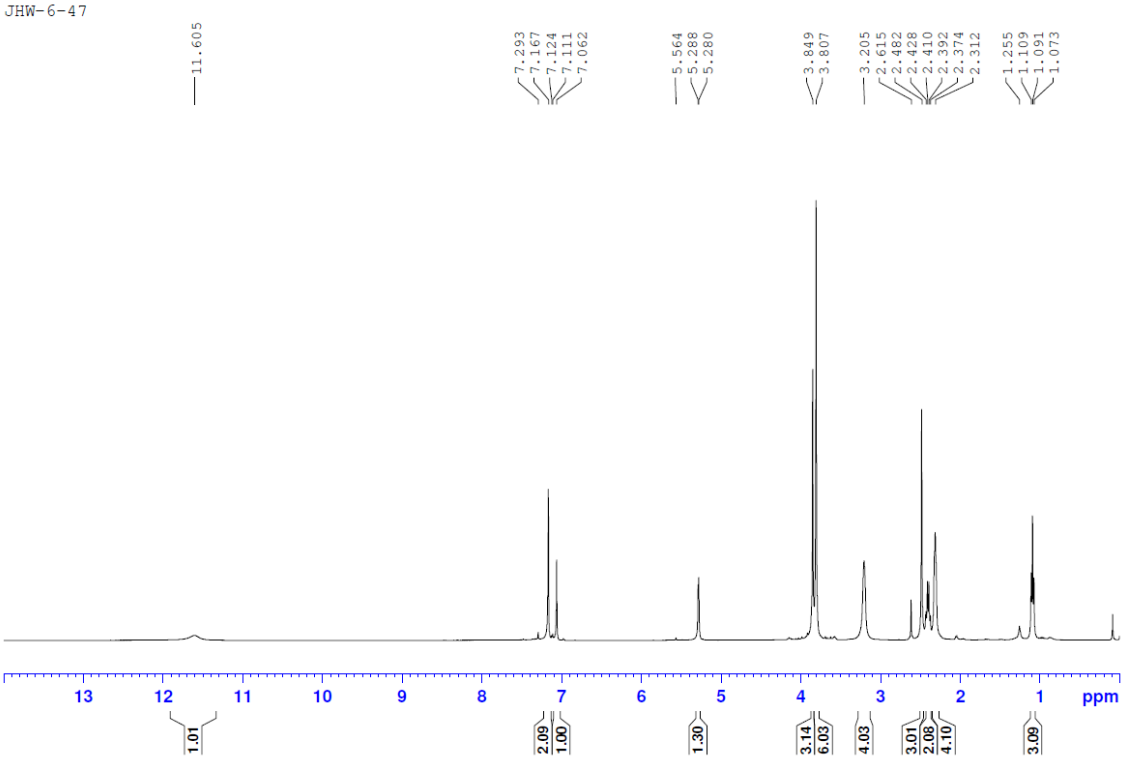
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7.167
7.124
7.111
7.062
5.564
5.288
5.280
3.849
3.807
3.205
2.615
2.482
2.428
2.410
2.392
2.374
2.312
1.255
1.109
1.091
1.073
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
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2.09
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4.03
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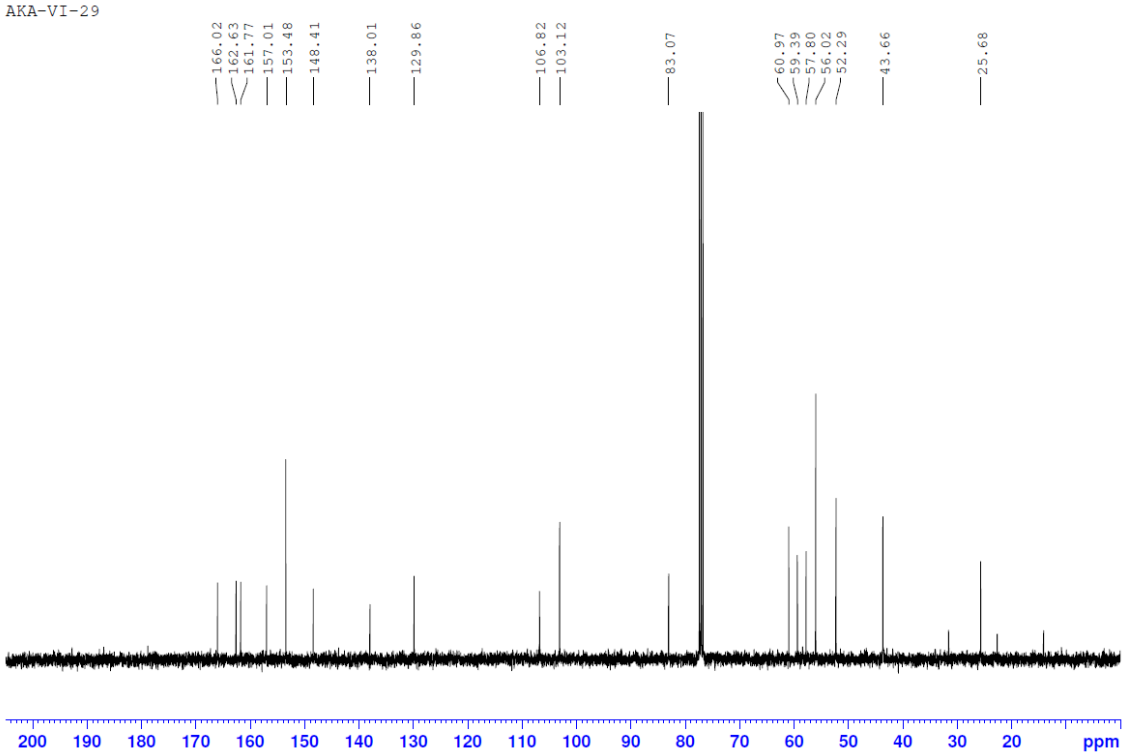
2.08
4.10
3.09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161.77
157.01
153.48
148.41
138.01
129.86
106.82
103.12
83.07
60.97
59.39
57.80
56.02
52.29
43.66
25.68
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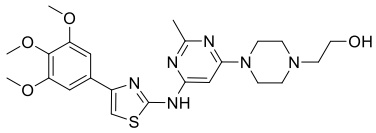

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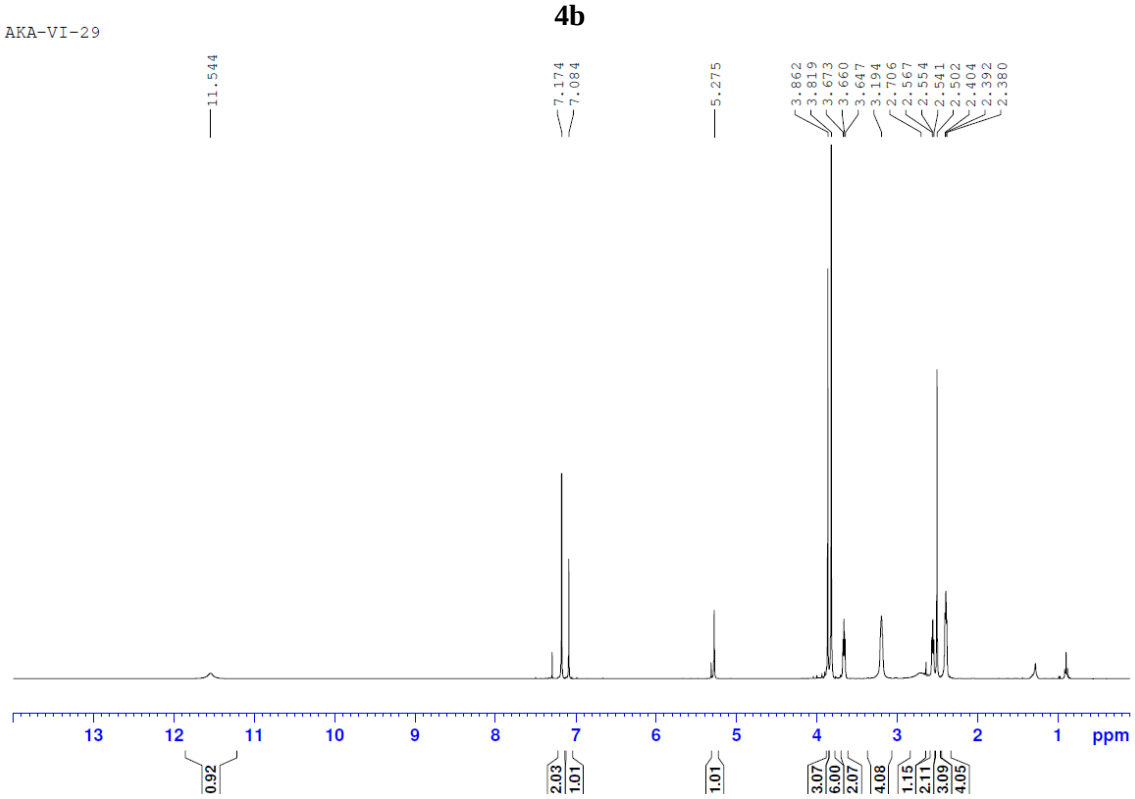
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7.084
5.275
3.862
3.819
3.673
3.660
3.647
3.194
2.706
2.567
2.554
2.541
2.502
2.404
2.392
2.380
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
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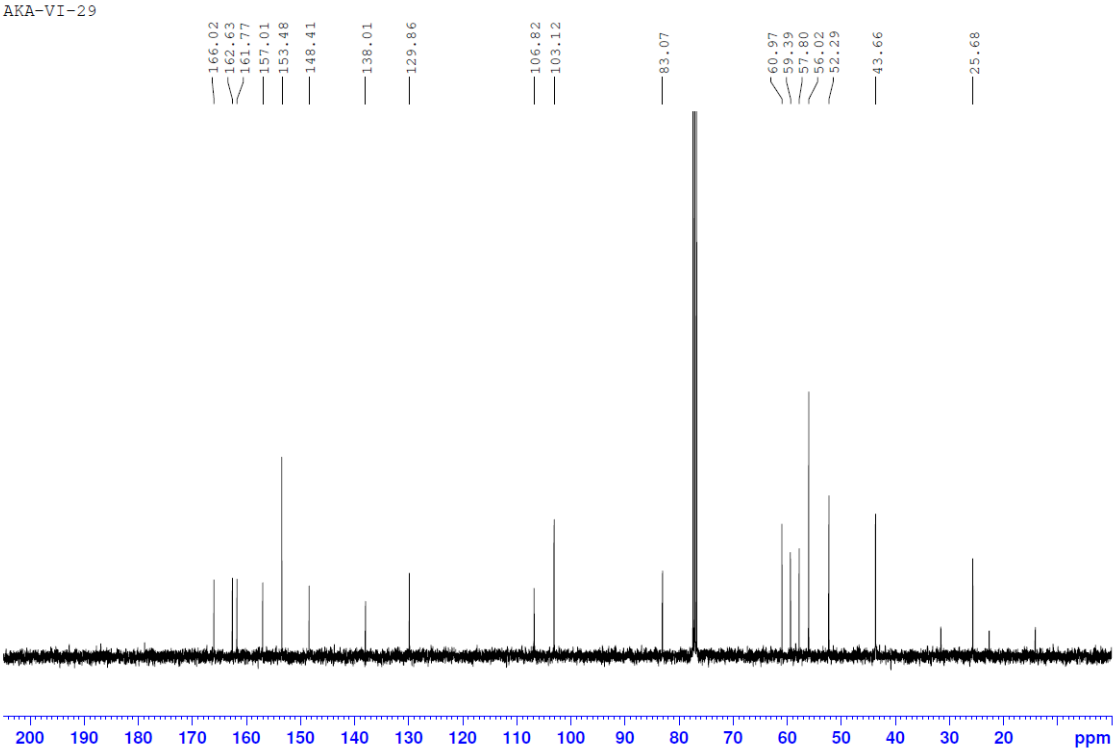
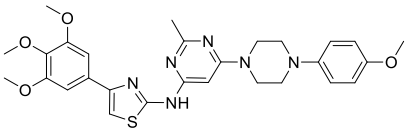
2.03
1.01
1.01
3.07
6.00
2.07
4.08
1.15
2.11
3.09
4.05


AKA-VI-29
166.02
162.63
161.77
157.01
153.48
148.41
138.01
129.86
106.82
103.12
83.07
60.97
59.39
57.80
56.02
52.29
43.66
25.68
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



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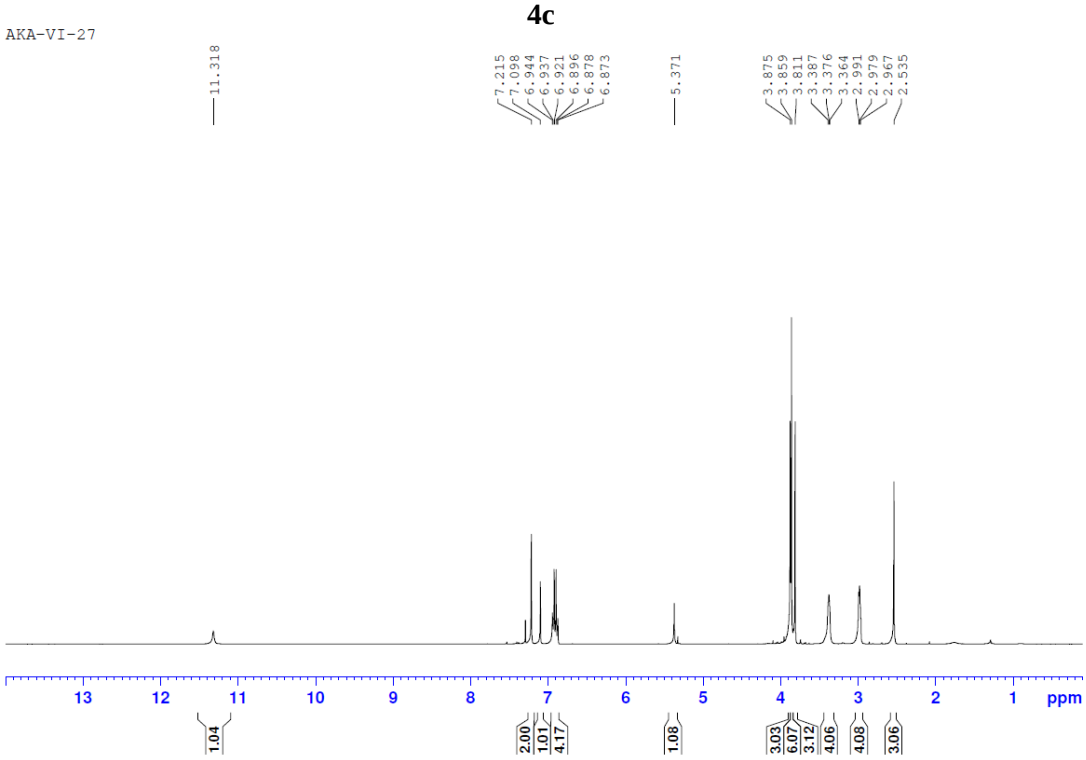
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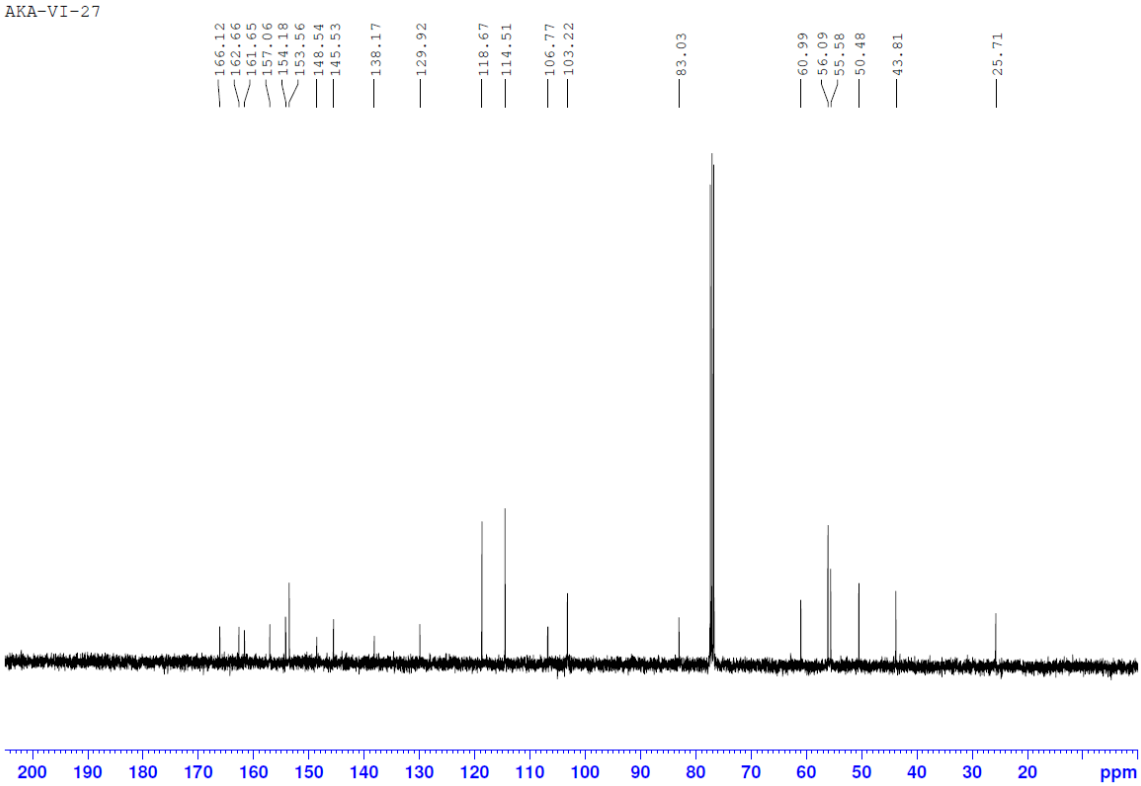
6.944
6.937
6.921
6.896
6.878
6.873
5.371
3.875
3.859
3.811
3.387
3.376
3.364
2.991
2.979
2.967
2.535
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.04
2.00
1.01
4.17
1.08
3.03
6.07
3.12
4.06
4.08
3.06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166.12
162.66
161.65
157.06
154.18
153.56
148.54
145.53
138.17
129.92
118.67
114.51
106.77
103.22
83.03
60.99
56.09
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43.81
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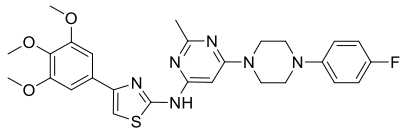

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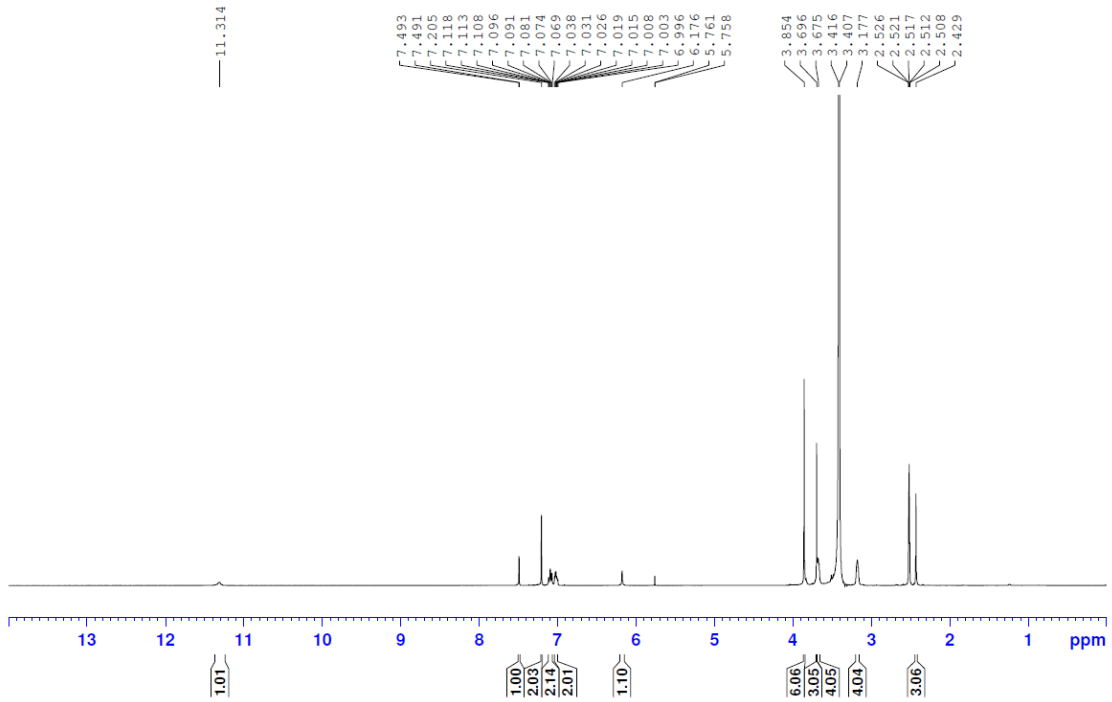
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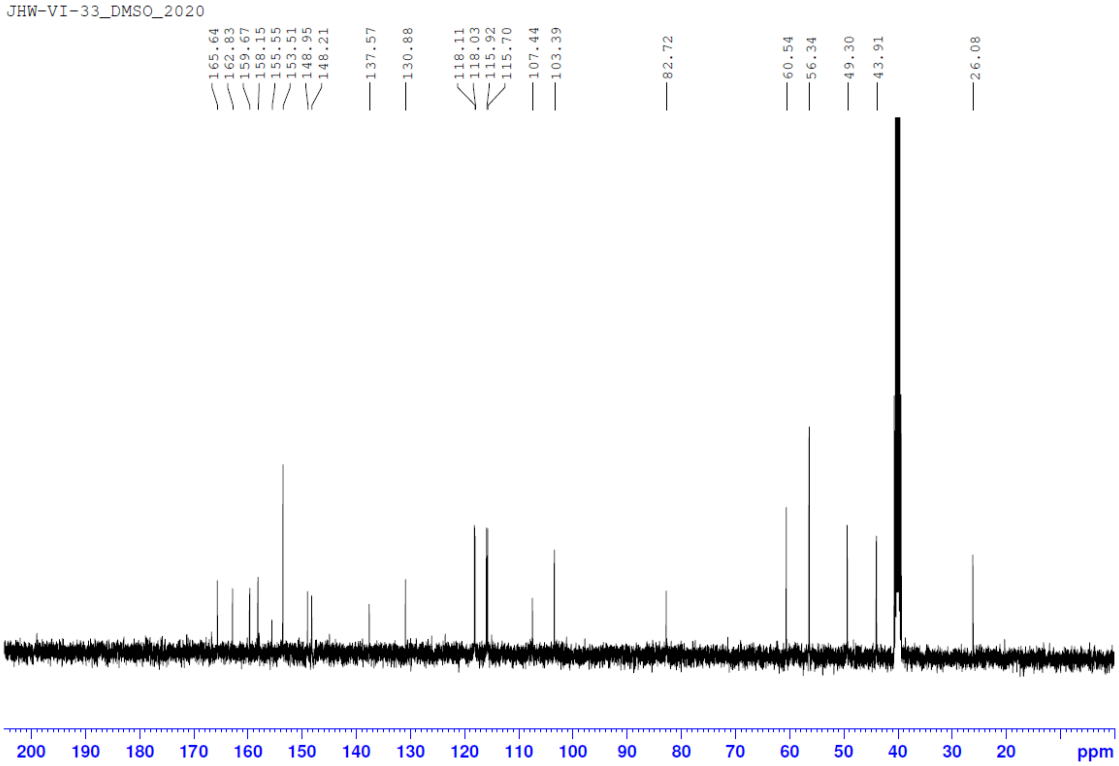
11.314
7.493
7.491
7.205
7.118
7.113
7.108
7.096
7.091
7.081
7.074
7.069
7.038
7.031
7.026
7.019
7.015
7.008
7.003
6.996
6.176
5.761
5.758
3.854
3.696
3.675
3.416
3.407
3.177
2.526
2.521
2.517
2.512
2.508
2.429
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.01
1.00
2.03
2.14
2.01
1.10
6.06
3.05
4.05
4.04
3.06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159.67
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153.51
148.95
148.21
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130.88
118.11
118.03
115.92
115.70
107.44
103.39
82.72
60.54
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49.30
43.91
26.08
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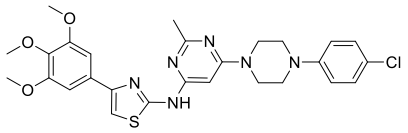

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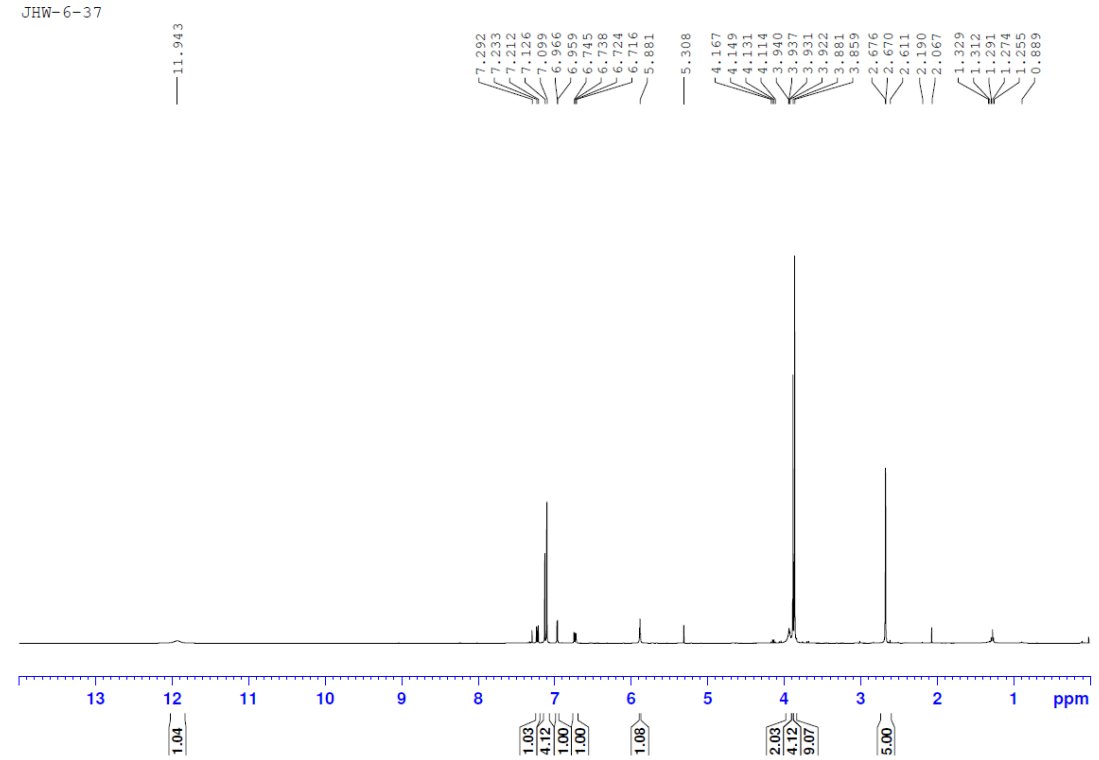
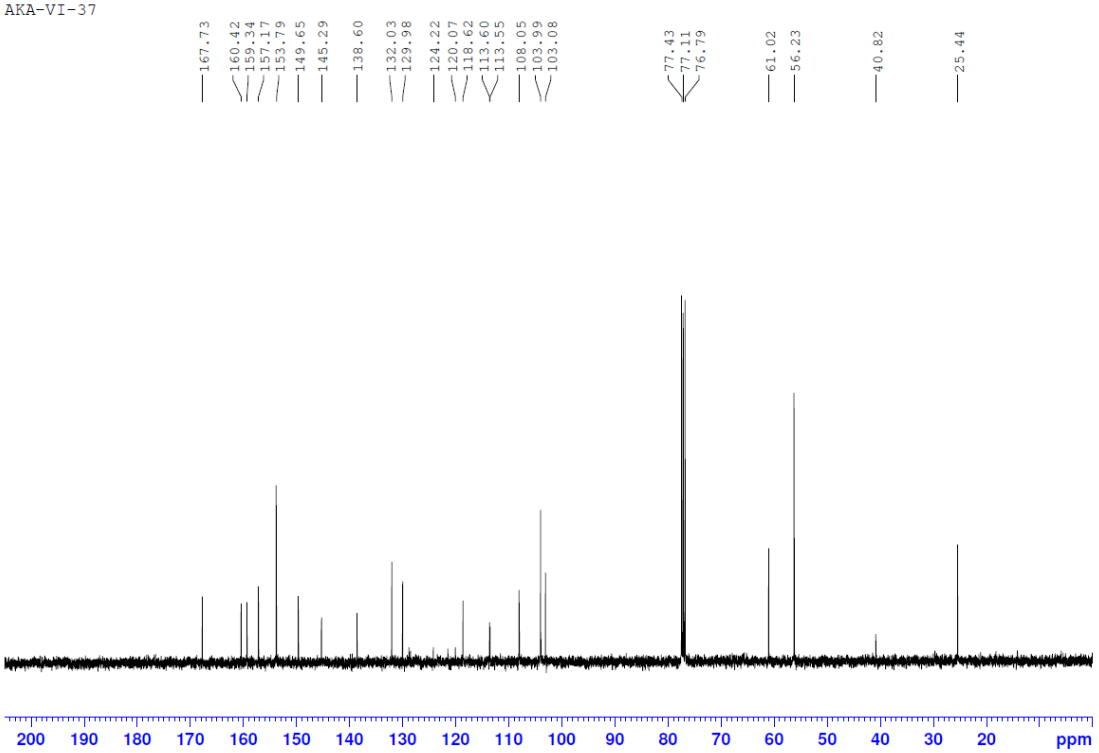

JHW-6-37
11.943
7.292
7.233
7.212
7.126
7.099
6.966
6.959
6.745
6.738
6.724
6.716
5.881
5.308
4.167
4.149
4.131
4.114
3.940
3.937
3.931
3.922
3.881
3.859
2.676
2.670
2.611
2.190
2.067
1.329
1.312
1.291
1.274
1.255
0.889
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.04
1.03
4.12
1.00
1.00
1.08
2.03
4.12
9.07
5.00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167.73
160.42
159.34
157.17
153.79
149.65
145.29
138.60
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129.98
124.22
120.07
118.62
113.60
113.55
108.05
103.99
103.08
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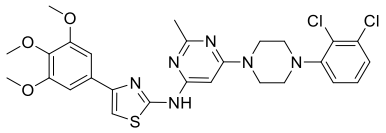

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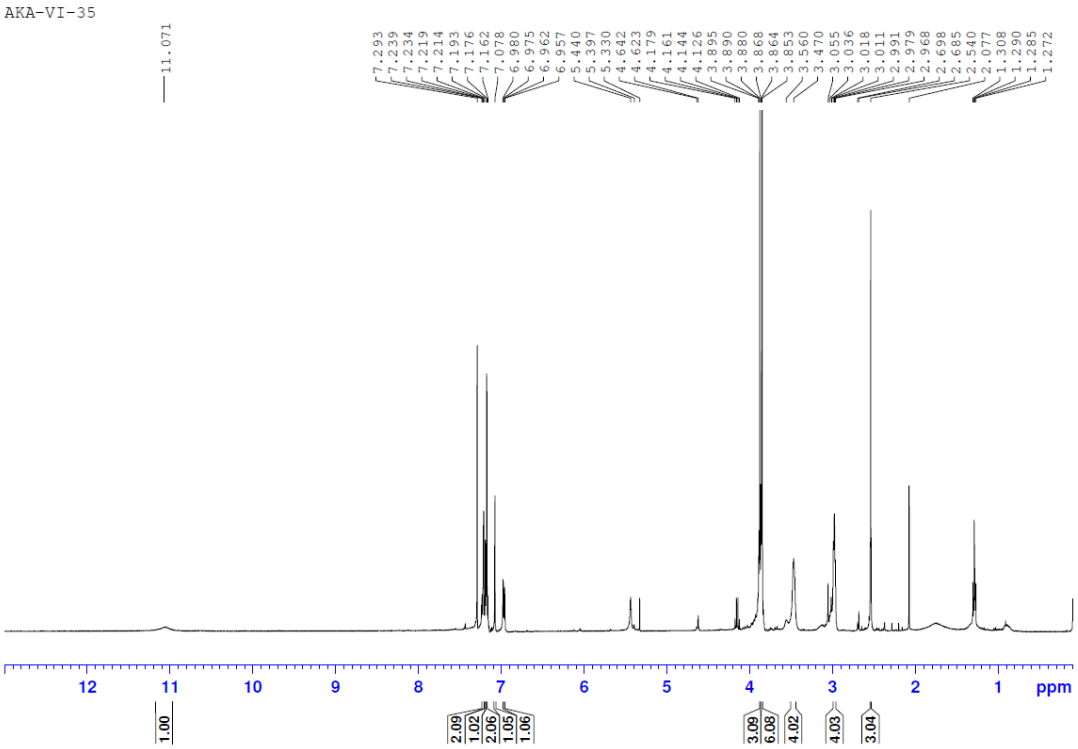
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11.071
7.293 7.259 7.234 7.219 7.214 7.193 7.176 7.162 7.078 6.980 6.975 6.962 6.957 5.440 5.397 5.330 4.642 4.623 4.179 4.161 4.144 4.126 3.895 3.890 3.880 3.868 3.864 3.853 3.560 3.470 3.055 3.036 3.018 3.011 2.991 2.979 2.968 2.698 2.685 2.540 2.077 1.308 1.290 1.285 1.272
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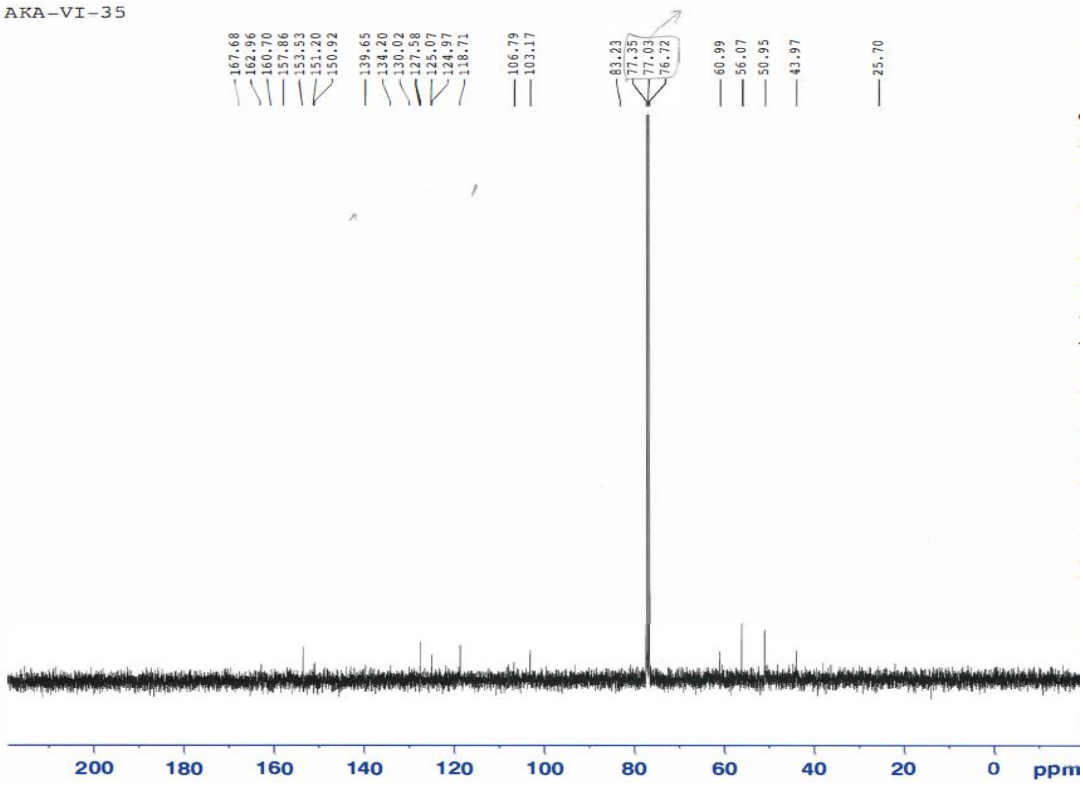
1.00 2.09 1.02 2.06 1.05 1.06 3.09 6.08 4.02 4.03 3.04


AKA-VI-35
167.68 162.96 160.70 157.86 153.53 151.20 150.92 139.65 134.20 130.02 127.58 125.07 124.97 118.71 106.79 103.17 83.23 77.35 77.03 76.72 60.99 56.07 50.95 43.97 25.70
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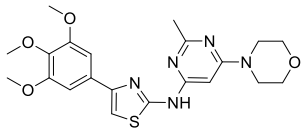

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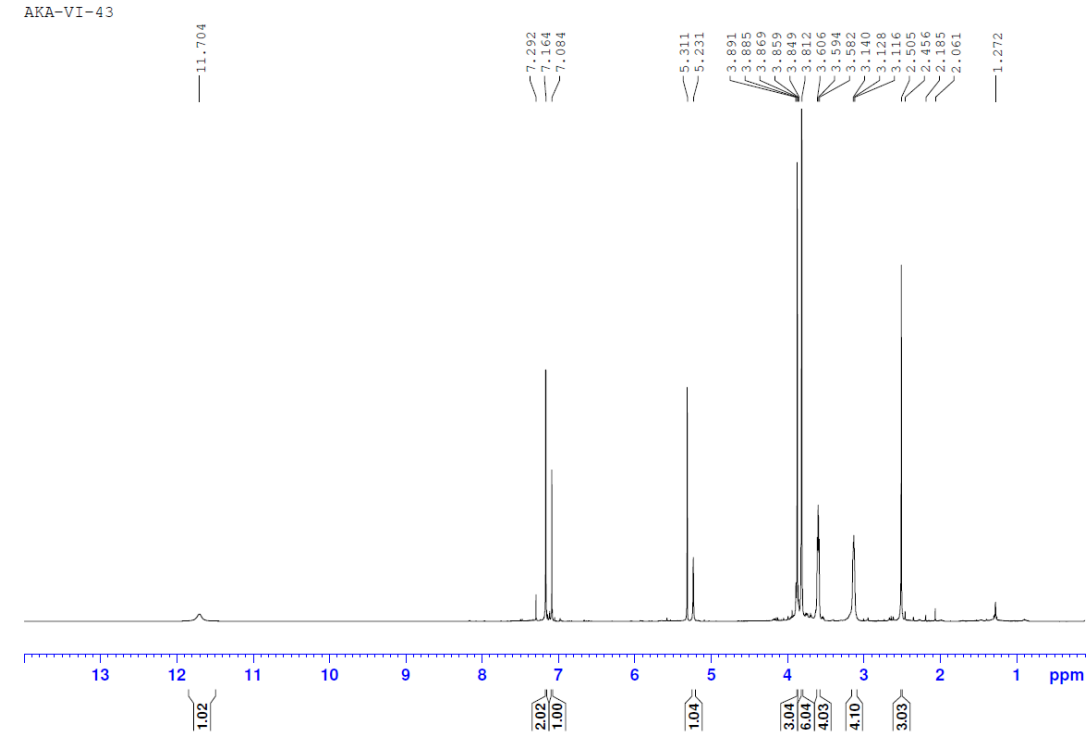
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11.704
7.292
7.164
7.084
5.311
5.231
3.891
3.885
3.869
3.859
3.849
3.812
3.606
3.594
3.582
3.140
3.128
3.116
2.505
2.456
2.185
2.061
1.272
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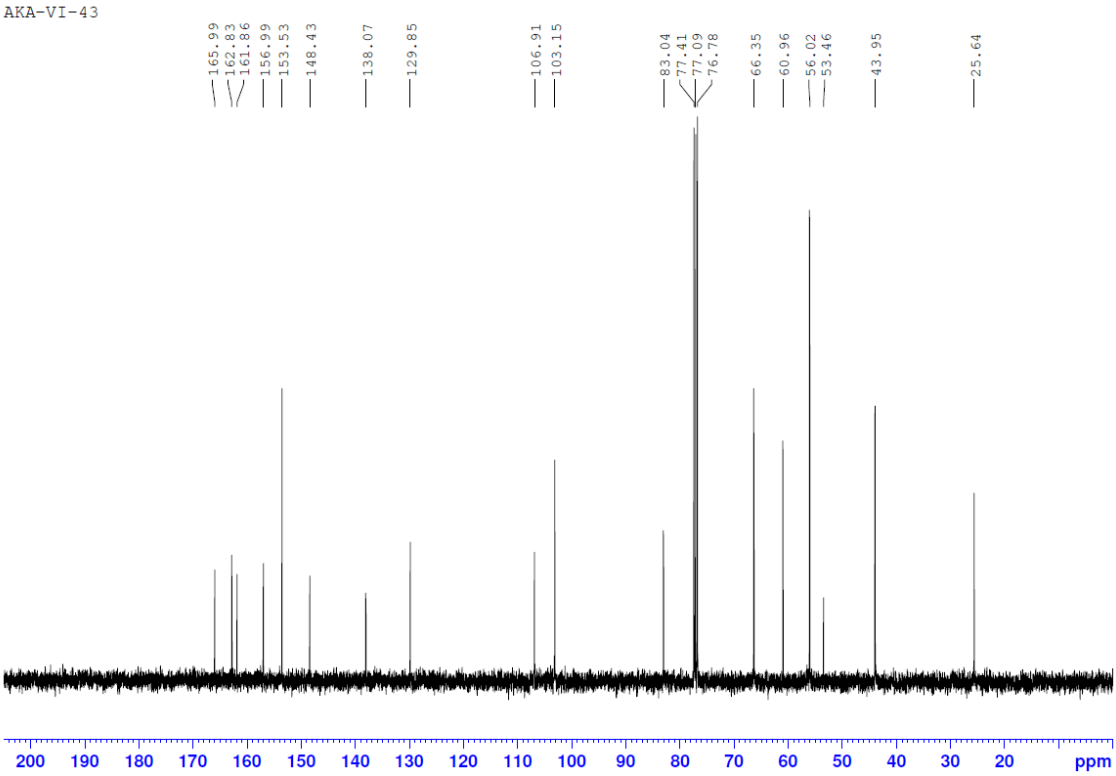
1.02
2.02
1.00
1.04
3.04
6.04
4.03
4.10
3.03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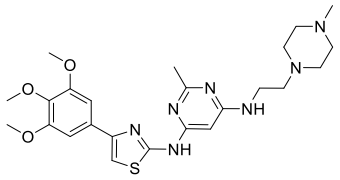
165.99
162.83
161.86
156.99
153.53
148.43
138.07
129.85
106.91
103.15
83.04
77.41
77.09
76.78
66.35
60.96
56.02
53.46
43.95
25.64
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



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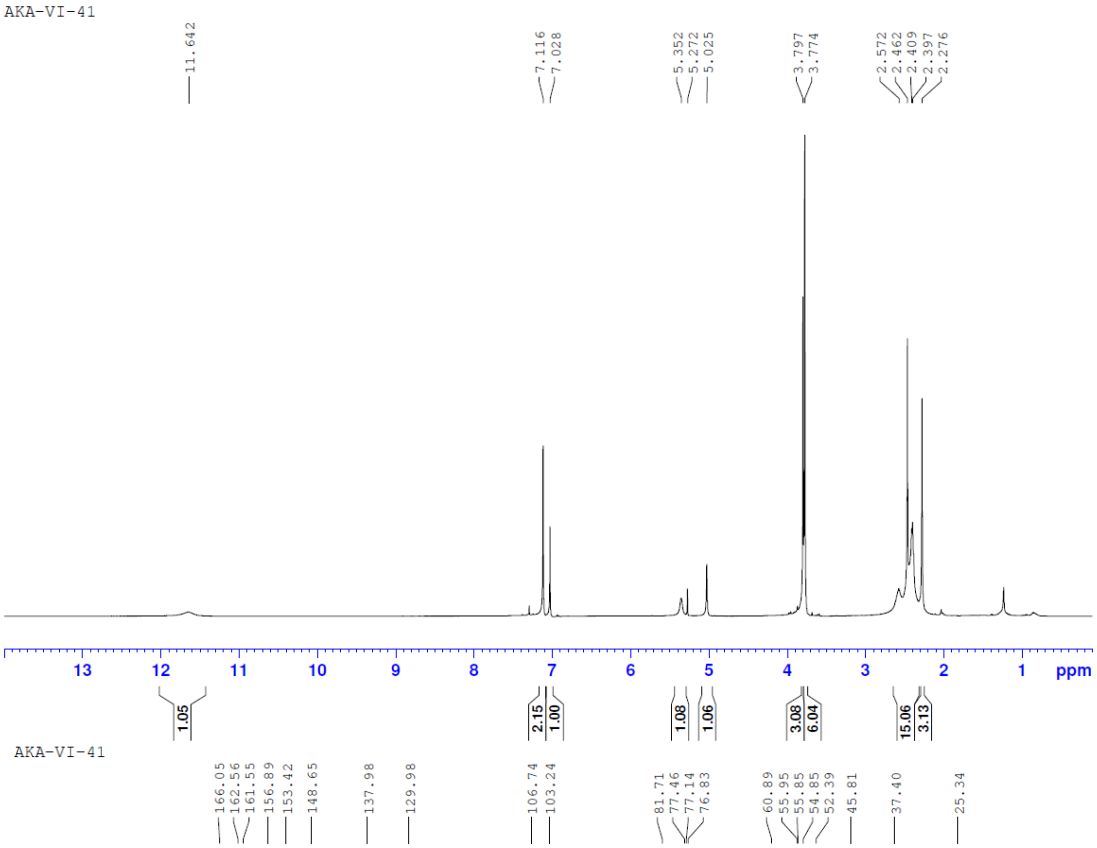
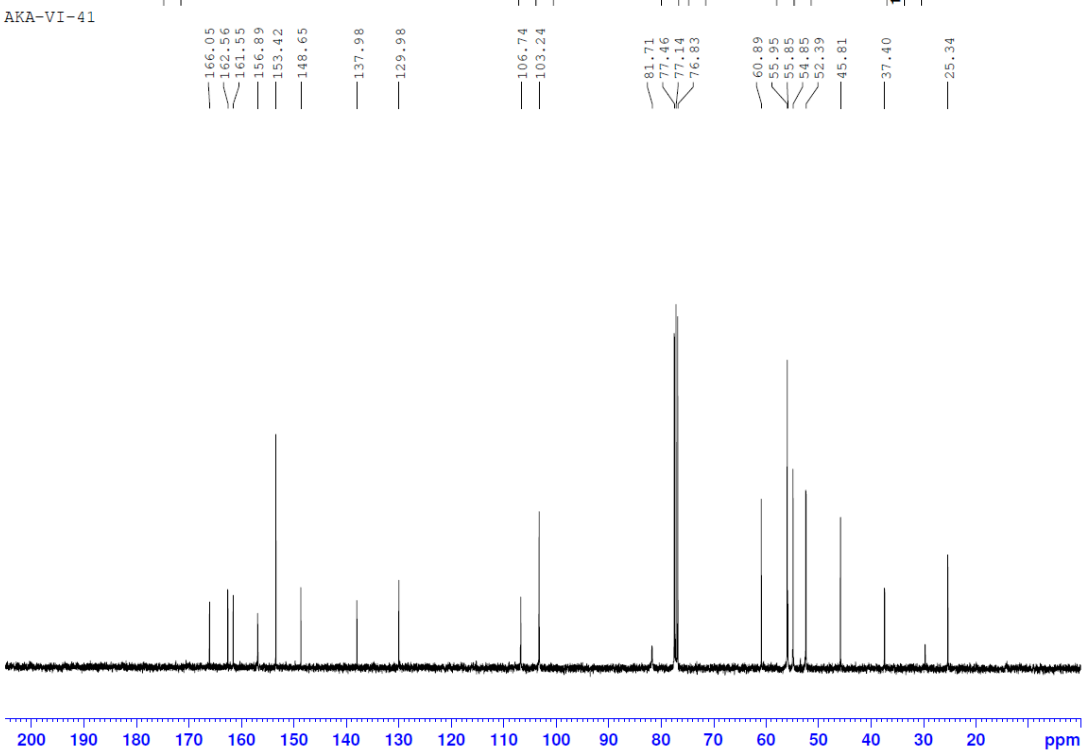
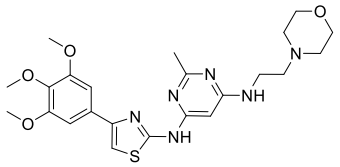

AKA-VI-41
11.642
7.116
7.028
5.352
5.272
5.025
3.797
3.774
2.572
2.462
2.409
2.397
2.276
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.05
2.15
1.00
1.08
1.06
3.08
6.04
15.06
3.13


AKA-VI-41
166.05
162.56
161.55
156.89
153.42
148.65
137.98
129.98
106.74
103.24
81.71
77.46
77.14
76.83
60.89
55.95
55.85
54.85
52.39
45.81
37.40
25.34
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



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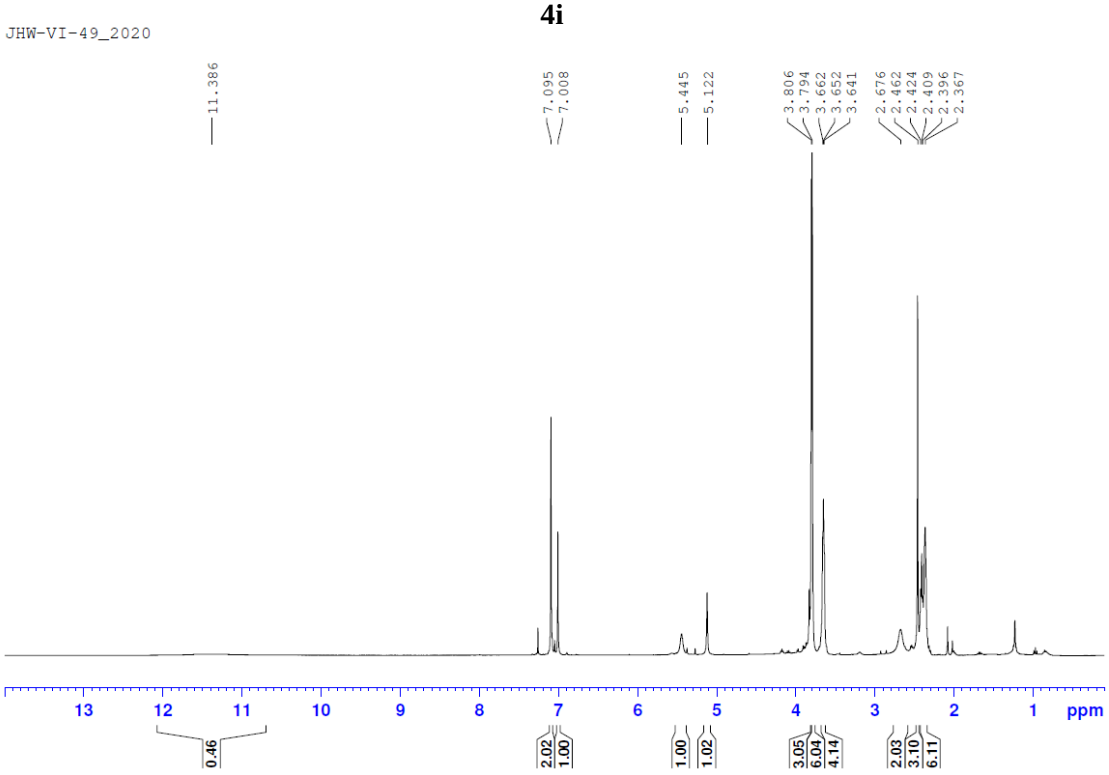
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5.445
5.122
3.806
3.794
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3.652
3.641
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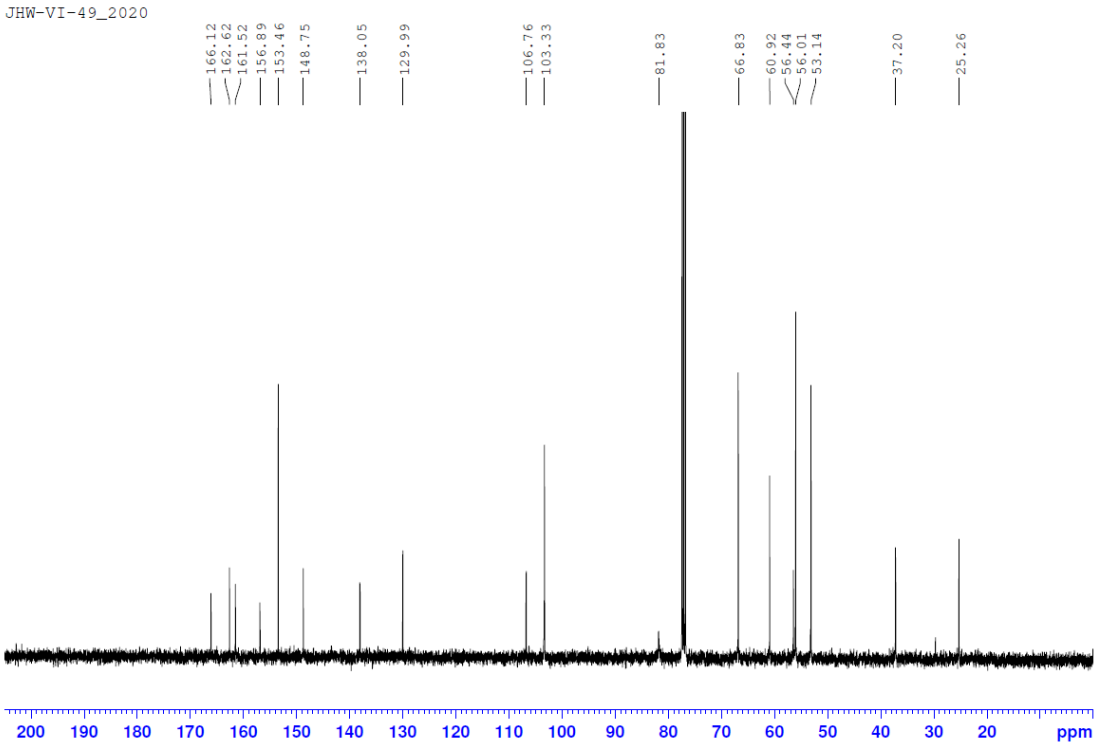
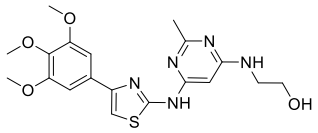
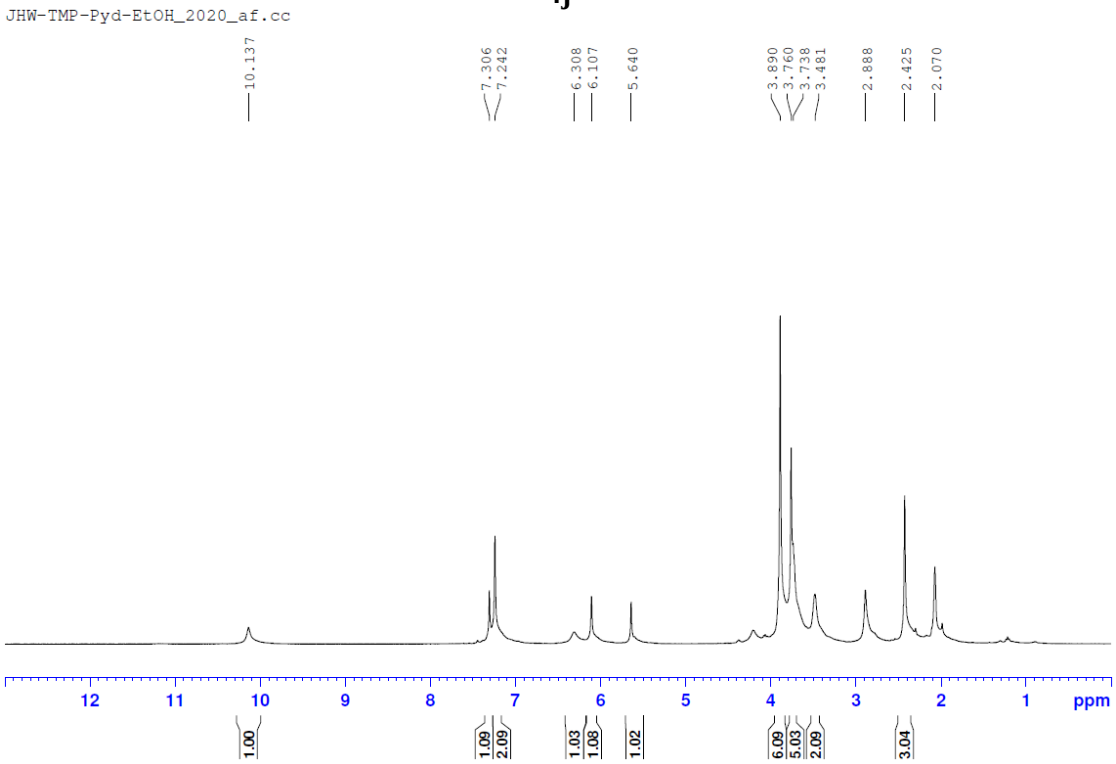
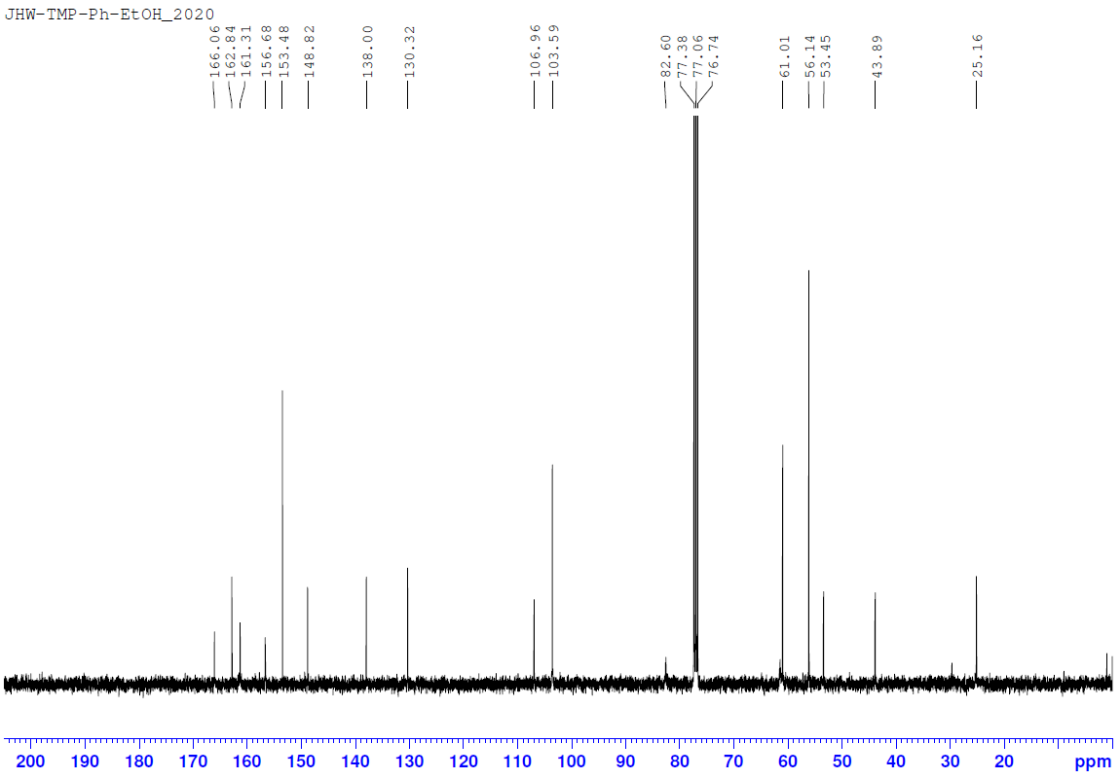
2.462
2.424
2.409
2.396
2.367
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.46
2.02
1.00
1.00
1.02
3.05
6.04
4.14
2.03
3.10
6.11

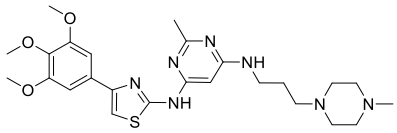

JHW-VI-49_2020
166.12
162.62
161.52
156.89
153.46
148.75
138.05
129.99
106.76
103.33
81.83
66.83
60.92
56.44
56.01
53.14
37.20
25.26
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



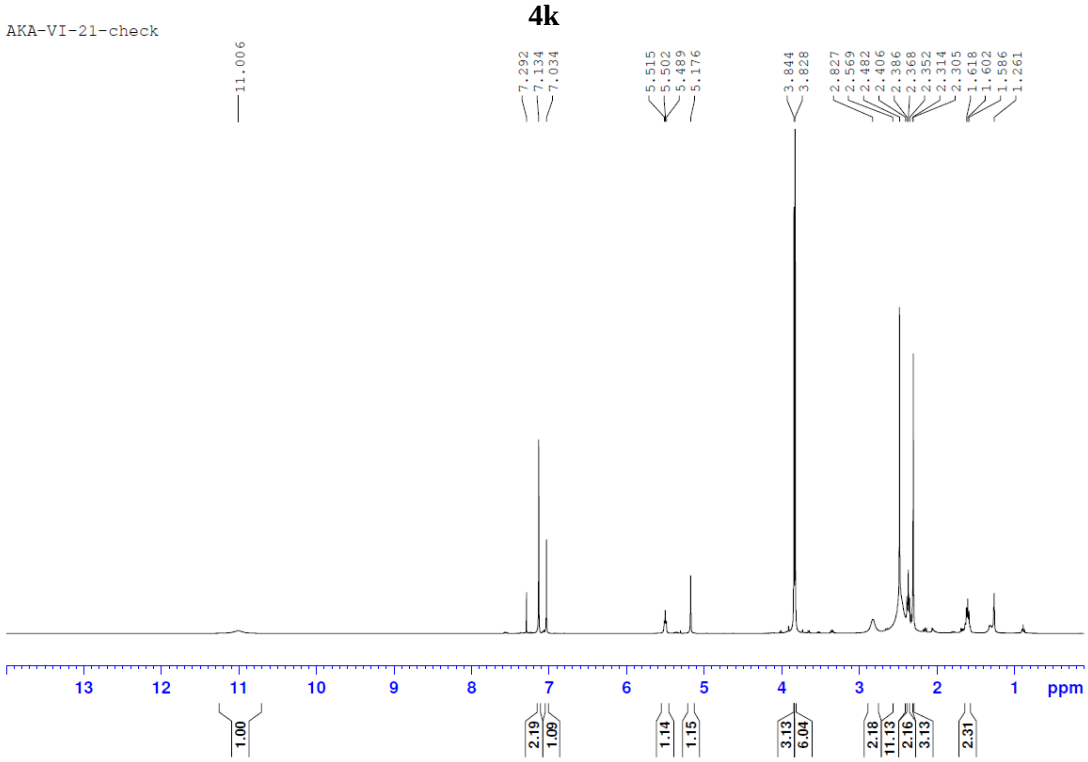
4j

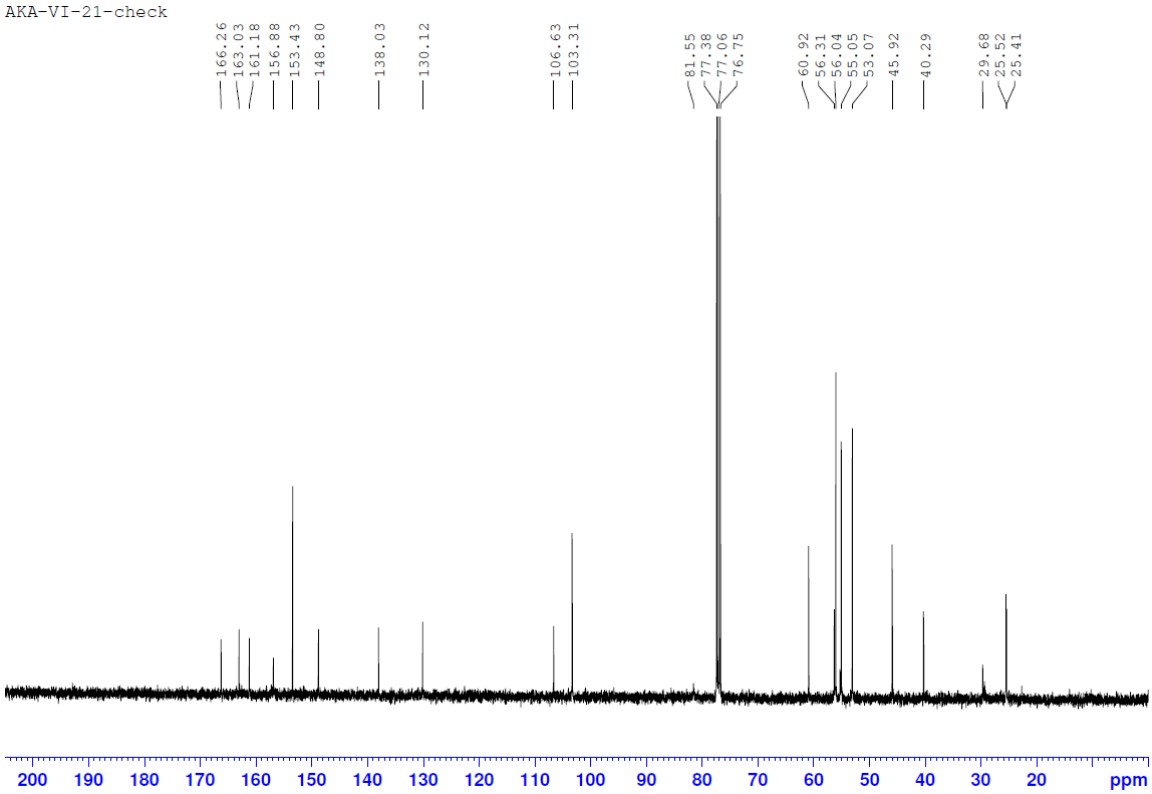

JHW-TMP-Pyd-EtOH_2020_af.cc
10.137
7.306
7.242
6.308
6.107
5.640
3.890
3.760
3.738
3.481
2.888
2.425
2.070
12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.00
1.09
2.09
1.03
1.08
1.02
6.09
5.03
2.09
3.04

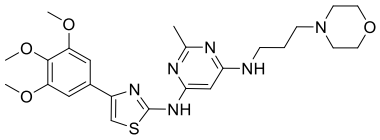

JHW-TMP-Ph-EtOH_2020
166.06
162.84
161.31
156.68
153.48
148.82
138.00
130.32
106.96
103.59
82.60
77.38
77.06
76.74
61.01
56.14
53.45
43.89
25.16
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



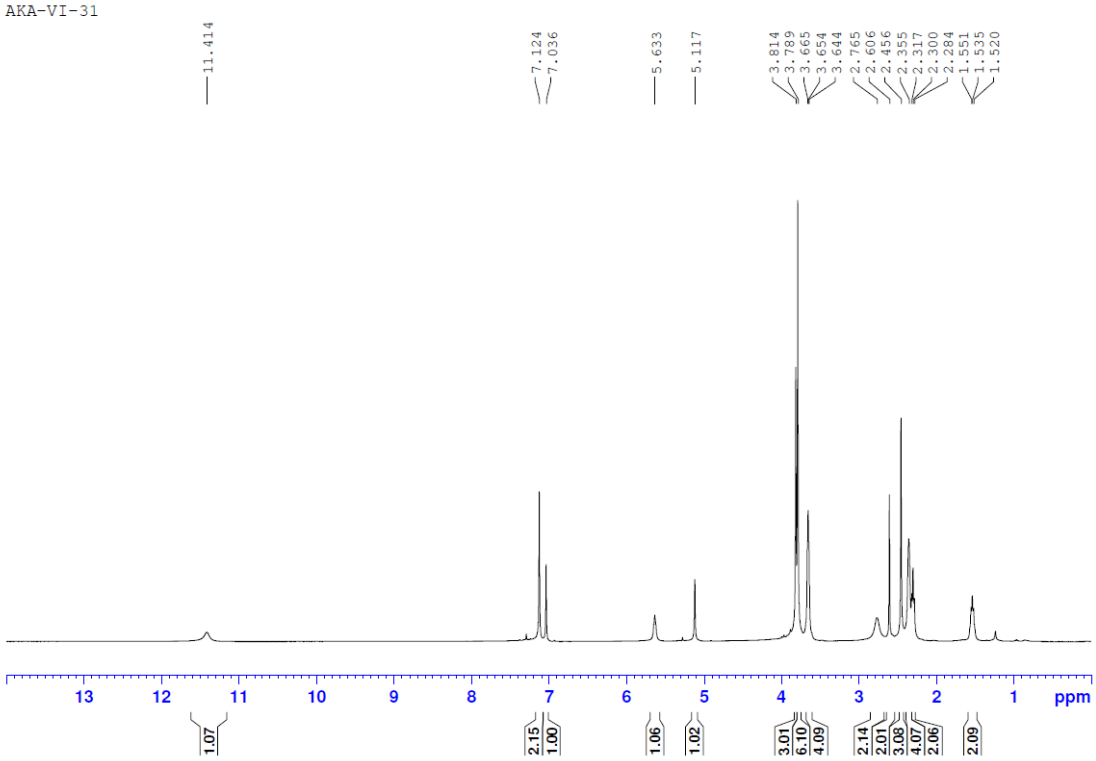
4k

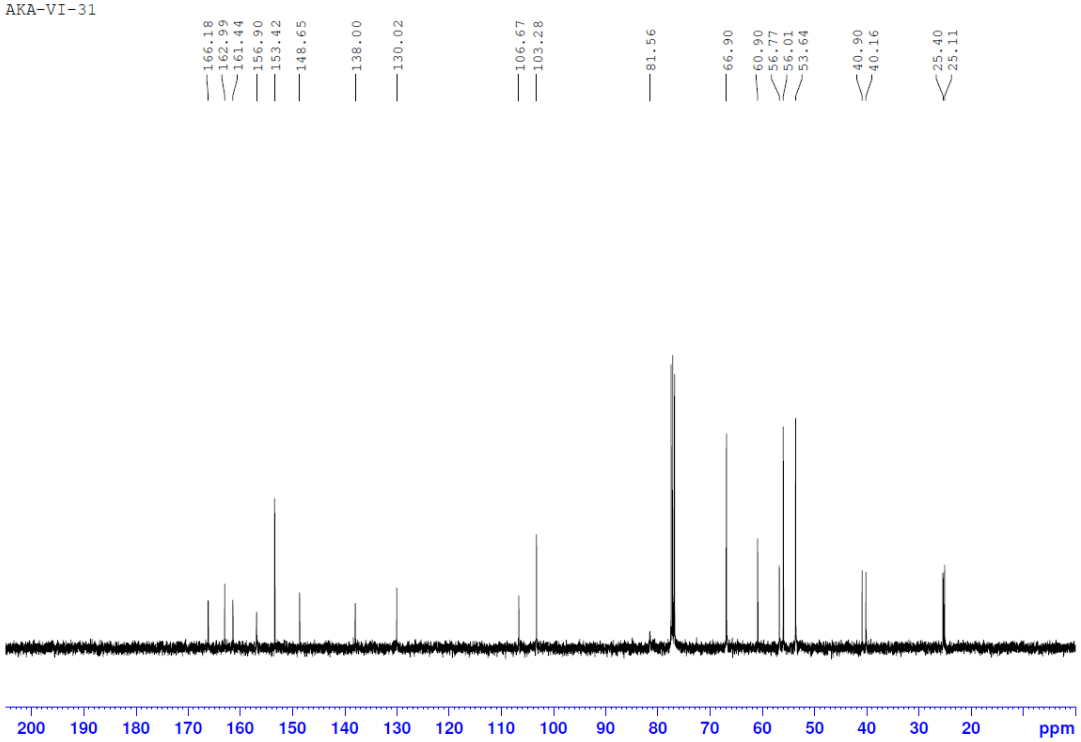

AKA-VI-21-check
11.006
7.292
7.134
7.034
5.515
5.502
5.489
5.176
3.844
3.828
2.827
2.569
2.482
2.406
2.386
2.368
2.352
2.314
2.305
1.618
1.602
1.586
1.261
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.00
2.19
1.09
1.14
1.15
3.13
6.04
2.18
11.13
2.16
3.13
2.31

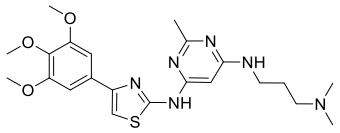

AKA-VI-21-check
166.26
163.03
161.18
156.88
153.43
148.80
138.03
130.12
106.63
103.31
81.55
77.38
77.06
76.75
60.92
56.31
56.04
55.05
53.07
45.92
40.29
29.68
25.52
25.41
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



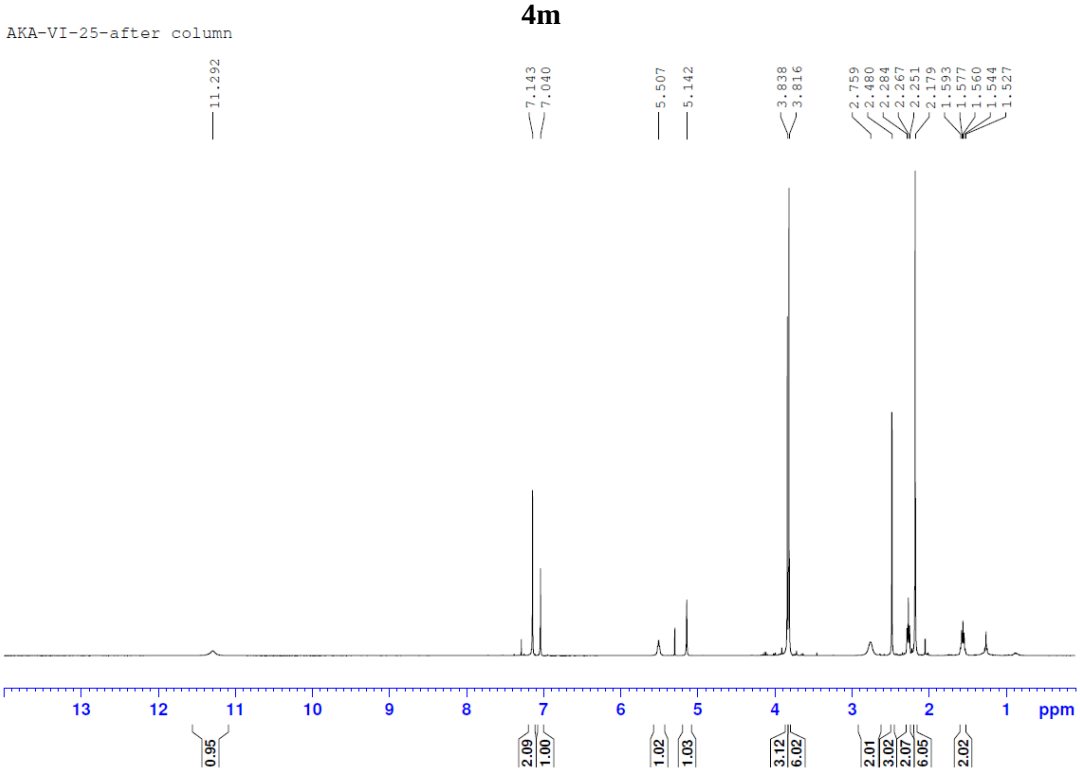
4l

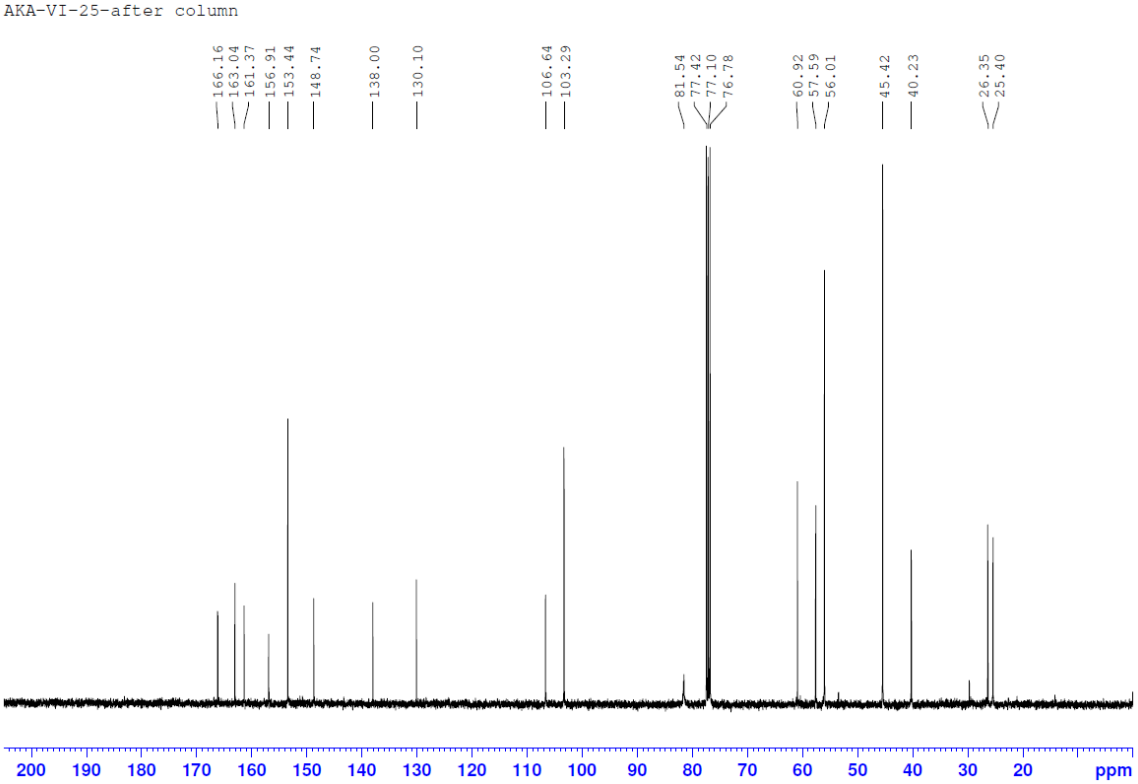

AKA-VI-31
11.414
7.124
7.036
5.633
5.117
3.814
3.789
3.665
3.654
3.644
2.765
2.606
2.456
2.355
2.317
2.300
2.284
1.551
1.535
1.520
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
1.07
2.15
1.00
1.06
1.02
3.01
6.10
4.09
2.14
2.01
3.08
4.07
2.06
2.09

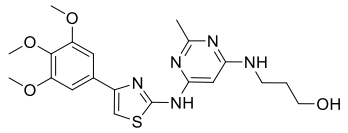

AKA-VI-31
166.18
162.99
161.44
156.90
153.42
148.65
138.00
130.02
106.67
103.28
81.56
66.90
60.90
56.77
56.01
53.64
40.90
40.16
25.40
25.11
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



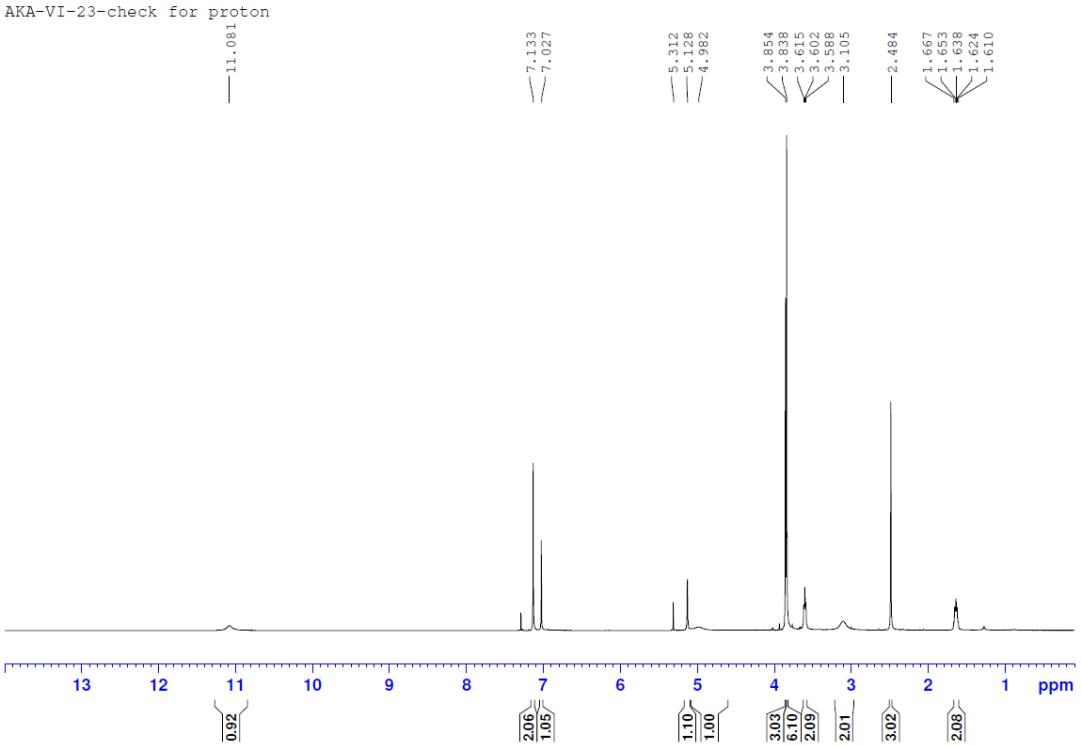
4m


AKA-VI-25-after column
11.292
7.143
7.040
5.507
5.142
3.838
3.816
2.759
2.480
2.284
2.267
2.251
2.179
1.593
1.577
1.560
1.544
1.527
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.95
2.09
1.00
1.02
1.03
3.12
6.02
2.01
3.02
2.07
6.05
2.02


AKA-VI-25-after column
166.16
163.04
161.37
156.91
153.44
148.74
138.00
130.10
106.64
103.29
81.54
77.42
77.10
76.78
60.92
57.59
56.01
45.42
40.23
26.35
25.40
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



4n


AKA-VI-23-check for proton
11.081
7.133
7.027
5.312
5.128
4.982
3.854
3.838
3.615
3.602
3.588
3.105
2.484
1.667
1.653
1.638
1.624
1.610
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.92
2.06
1.05
1.10
1.00
3.03
6.10
2.09
2.01
3.02
2.08

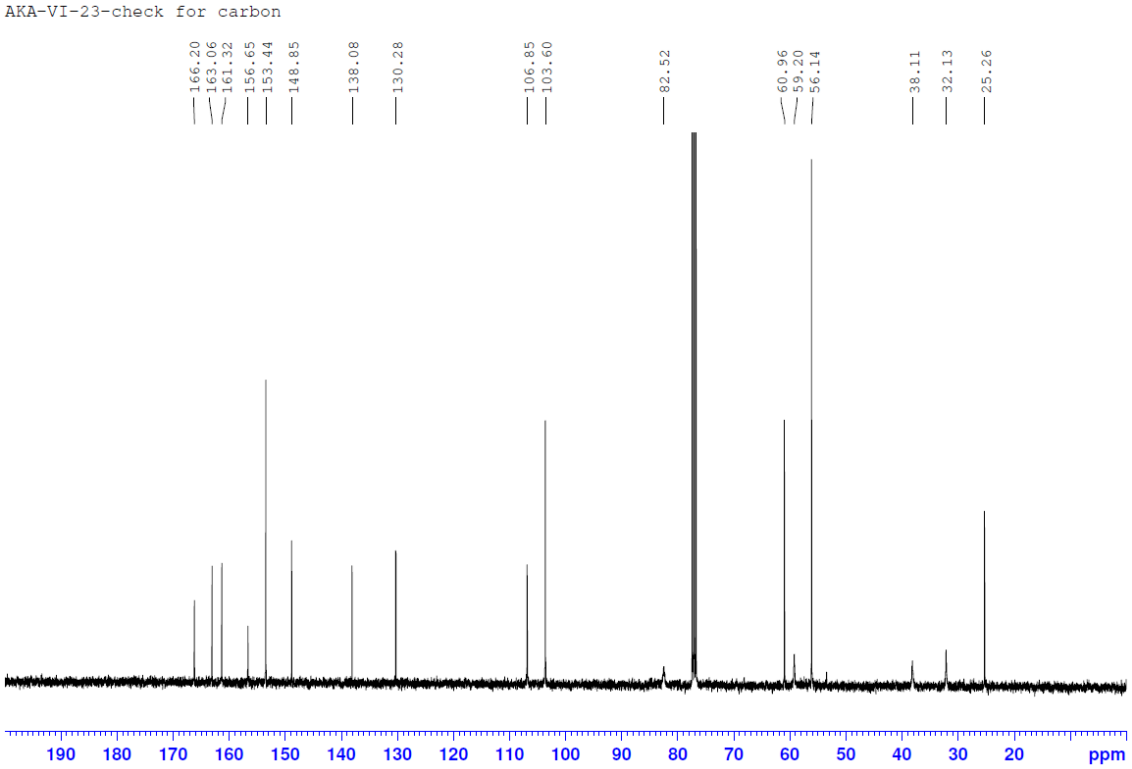
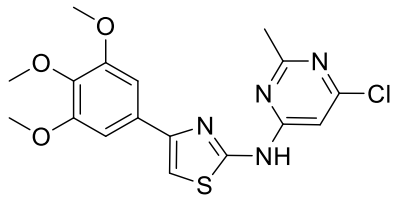
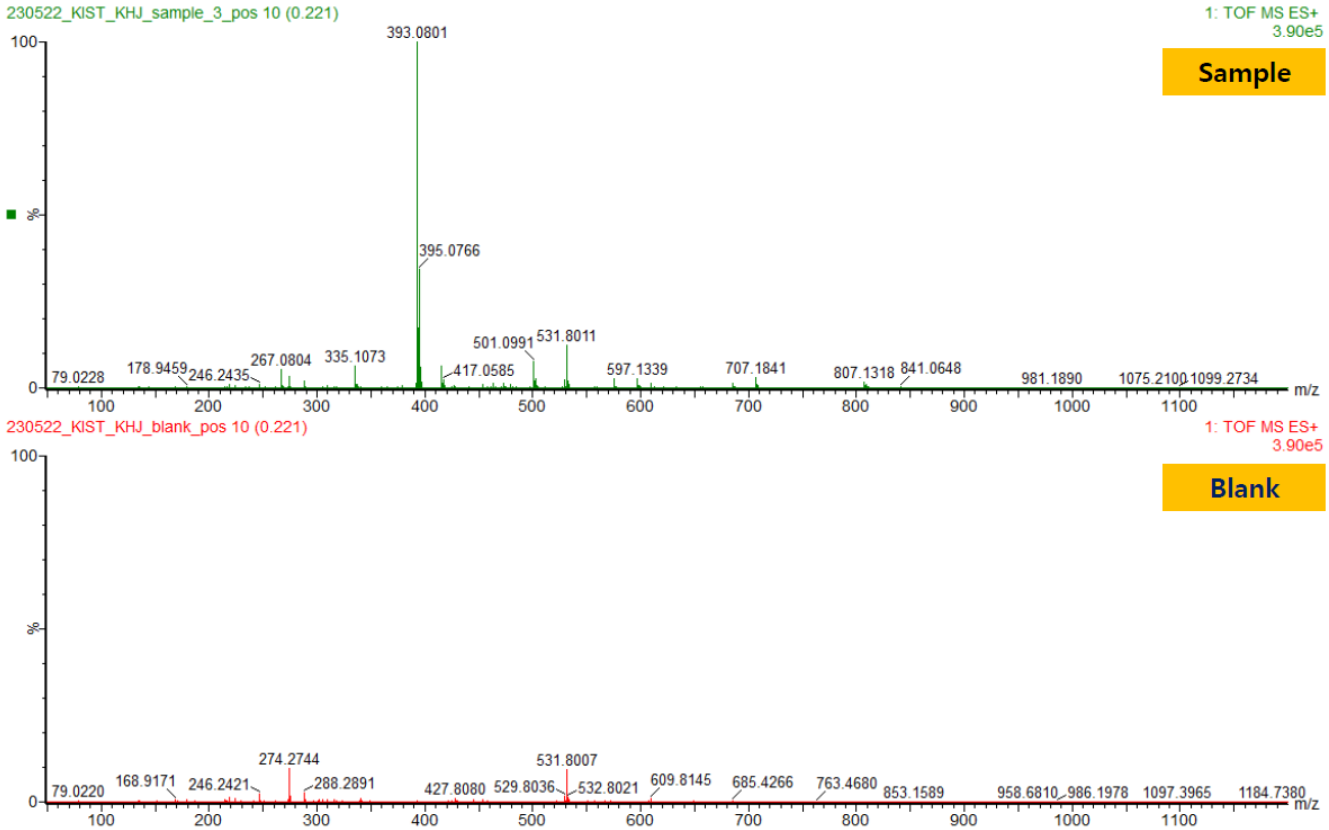
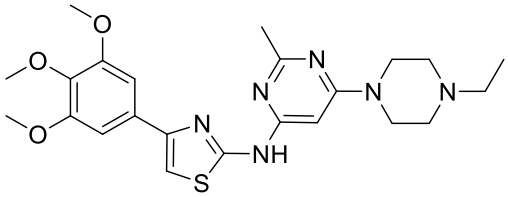

AKA-VI-23-check for carbon
166.20
163.06
161.32
156.65
153.44
148.85
138.08
130.28
106.85
103.60
82.52
60.96
59.20
56.14
38.11
32.13
25.26
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

Figure S2. HRMS charts.



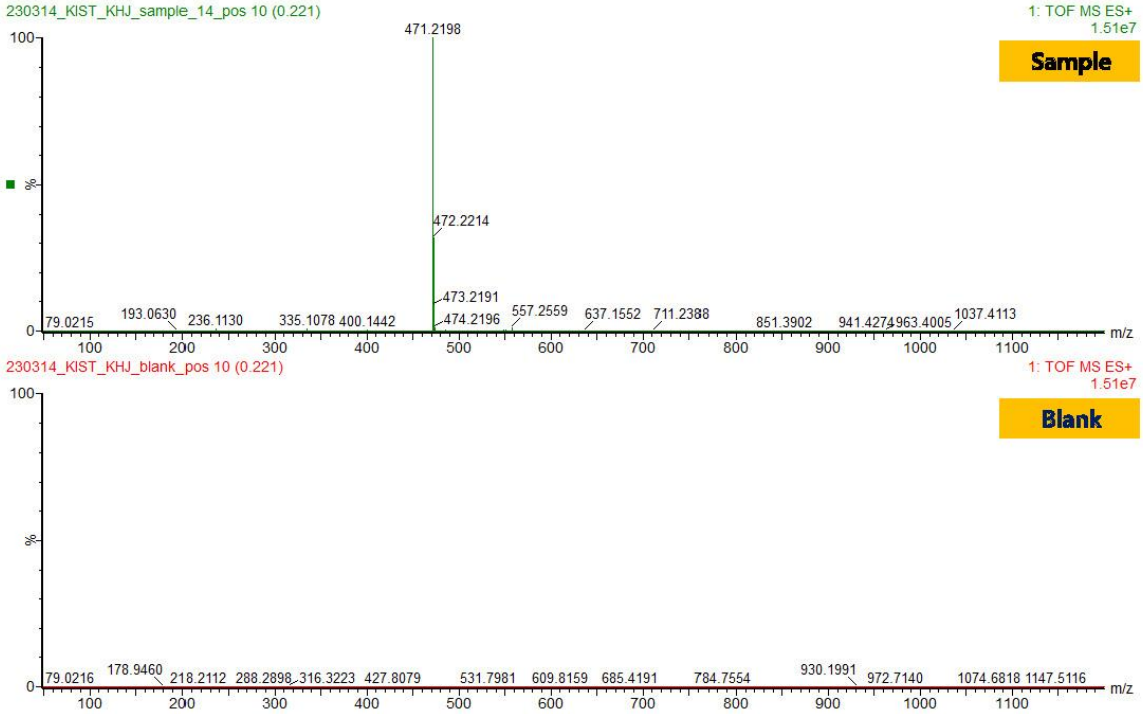
3

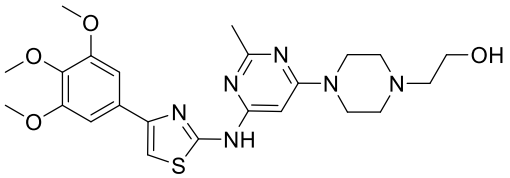




4a

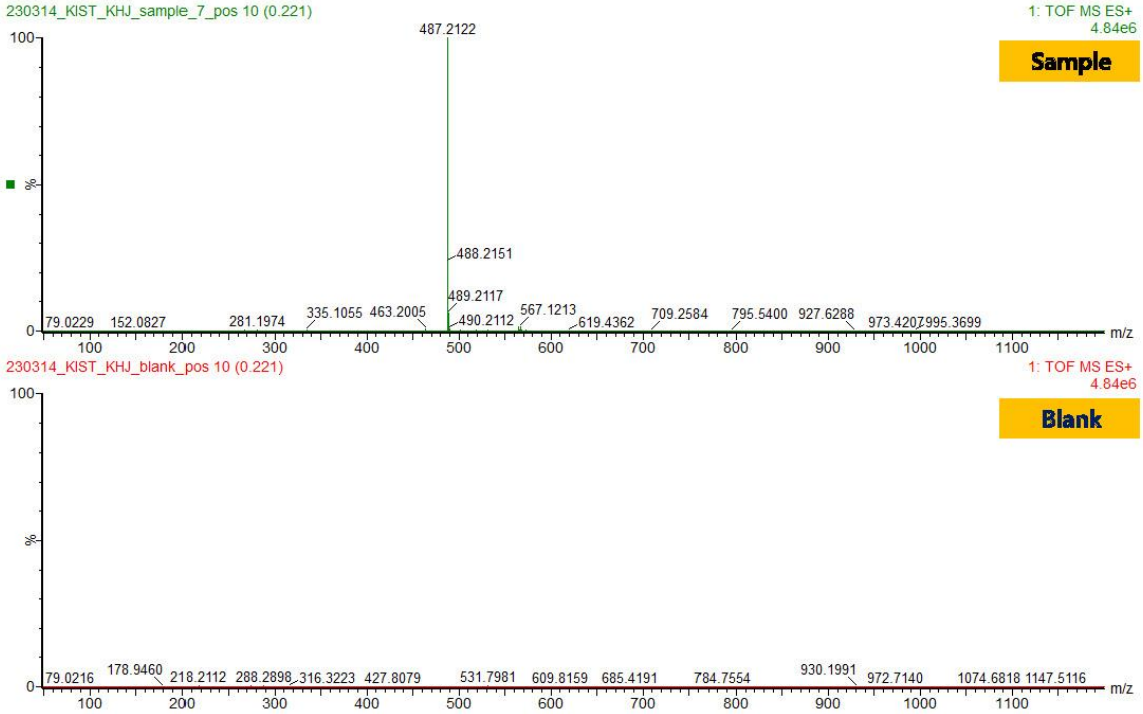
Mass Spectrum: JHW-I-20 (Positive mode)

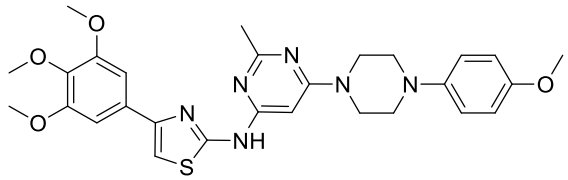




4b

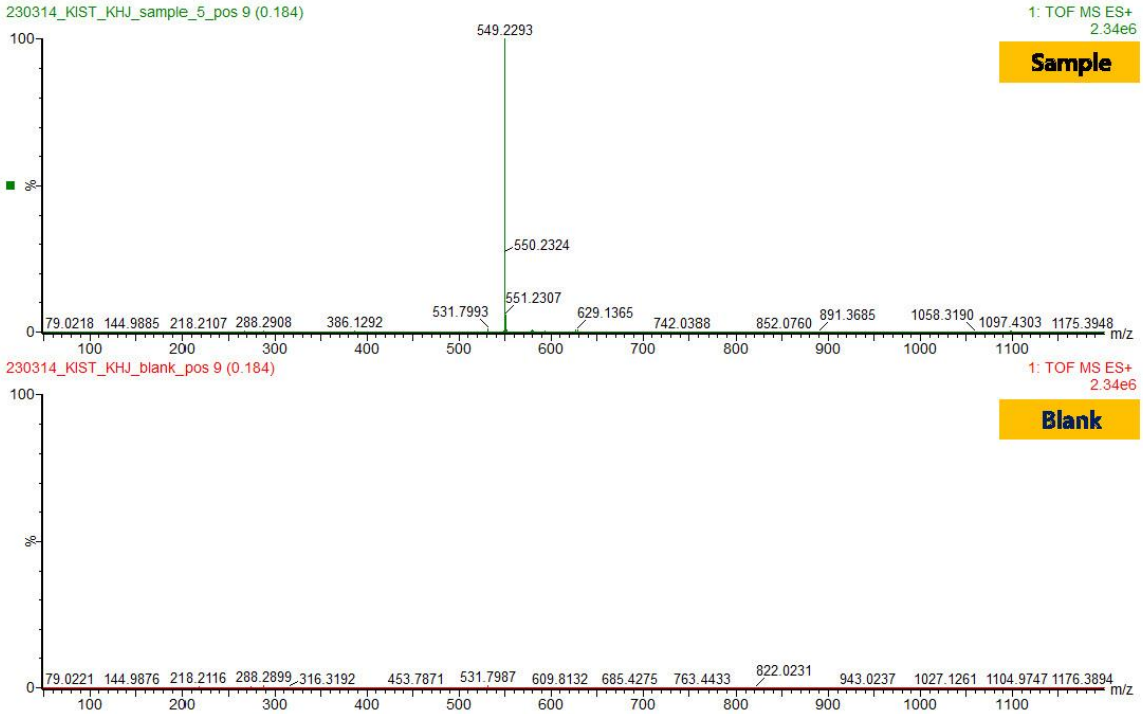
Mass Spectrum: JHW-I-7 (Positive mode)

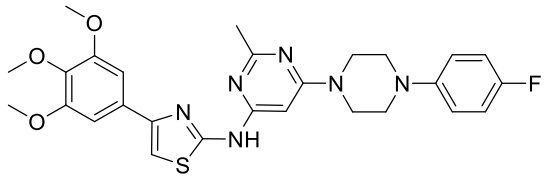




4c

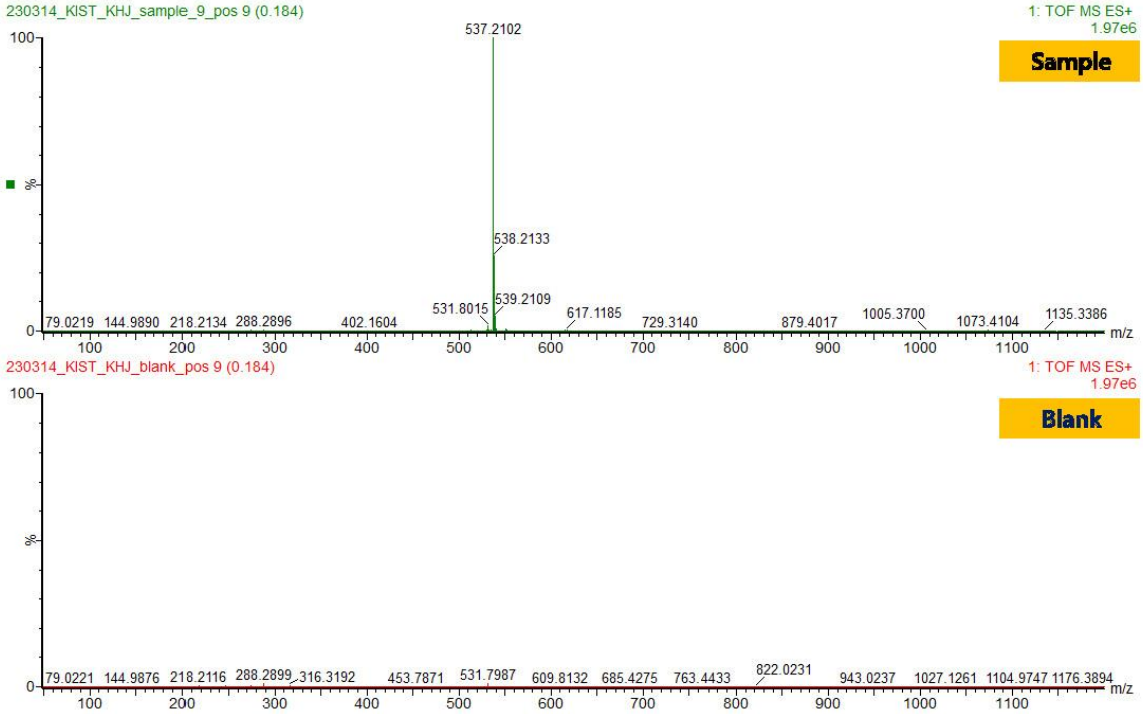
Mass Spectrum: JHW-I-2 (Positive mode)

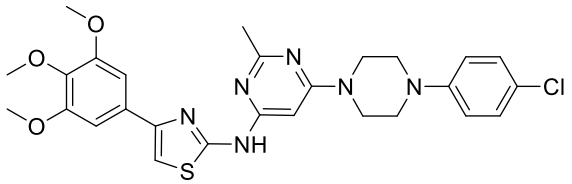




4d

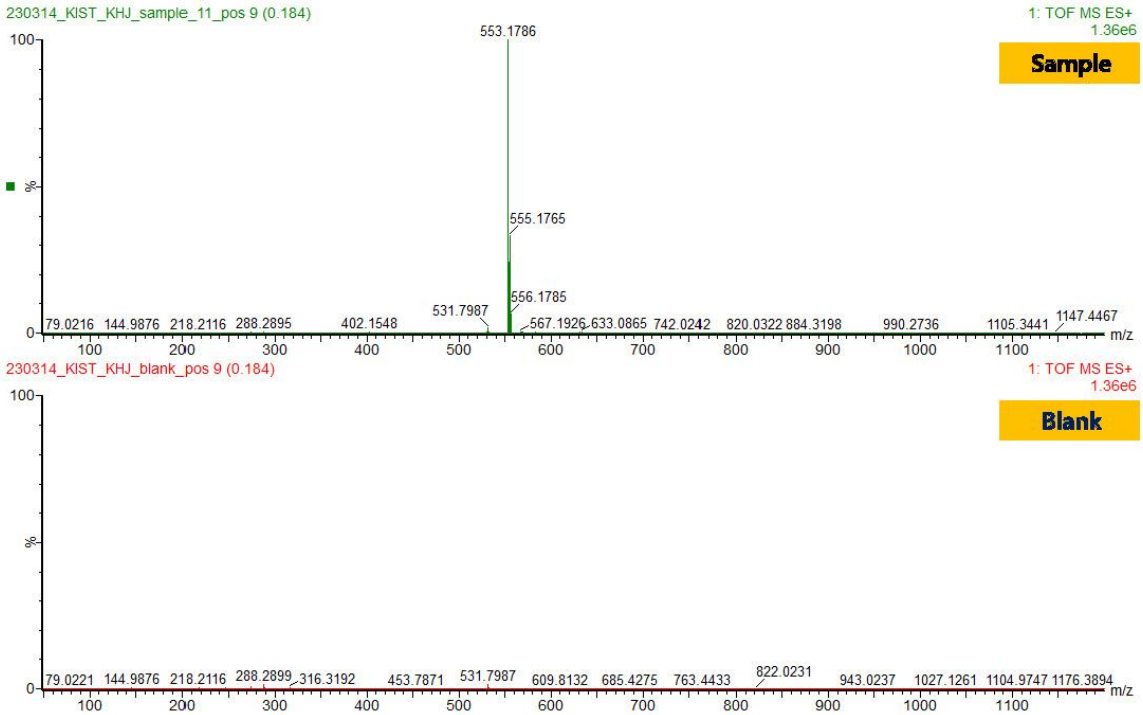
Mass Spectrum: JHW-I-10 (Positive mode)

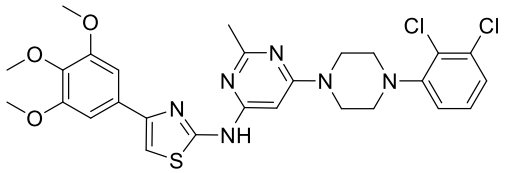




4e

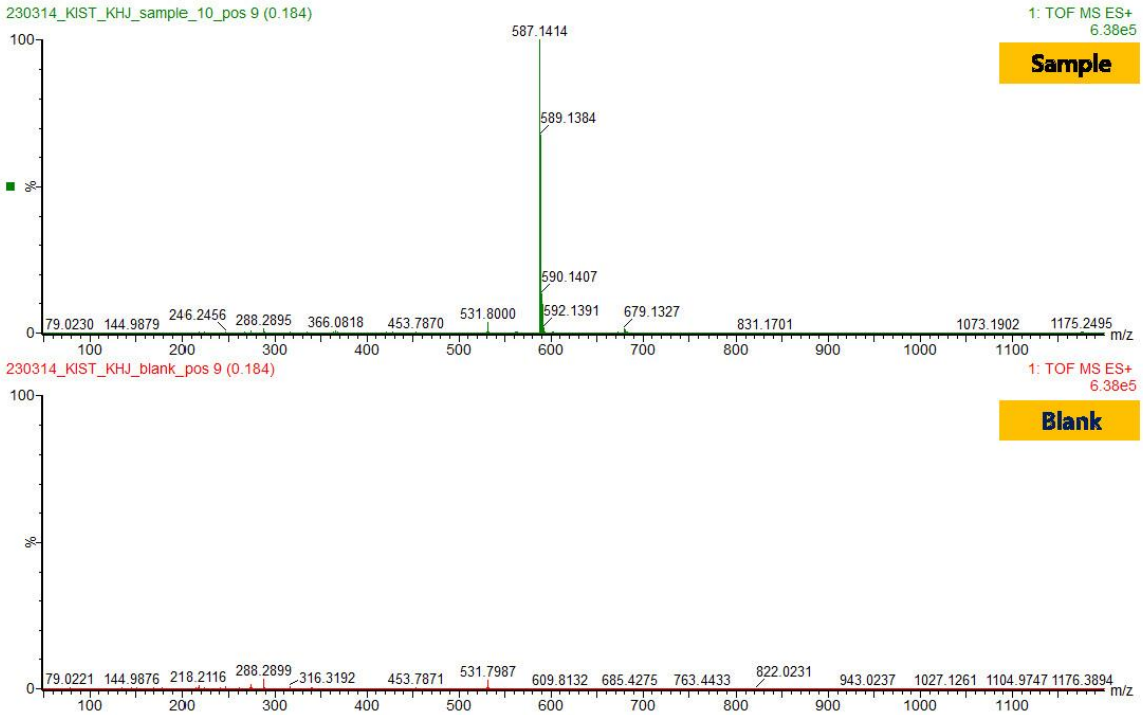
Mass Spectrum: JHW-I-12 (Positive mode)

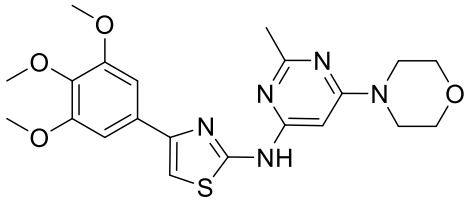




4f

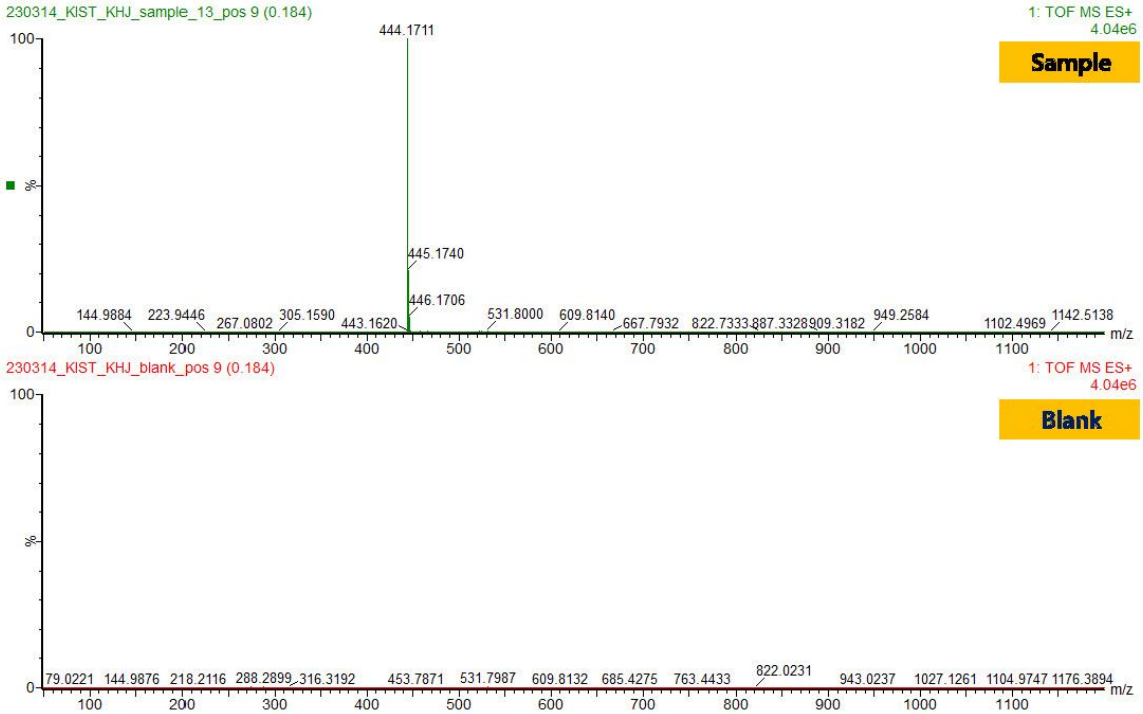
Mass Spectrum: JHW-I-11 (Positive mode)

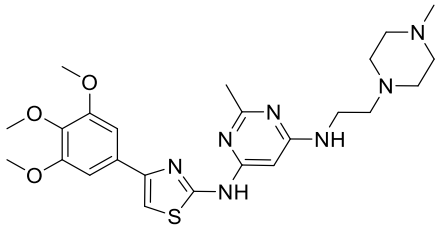




4g

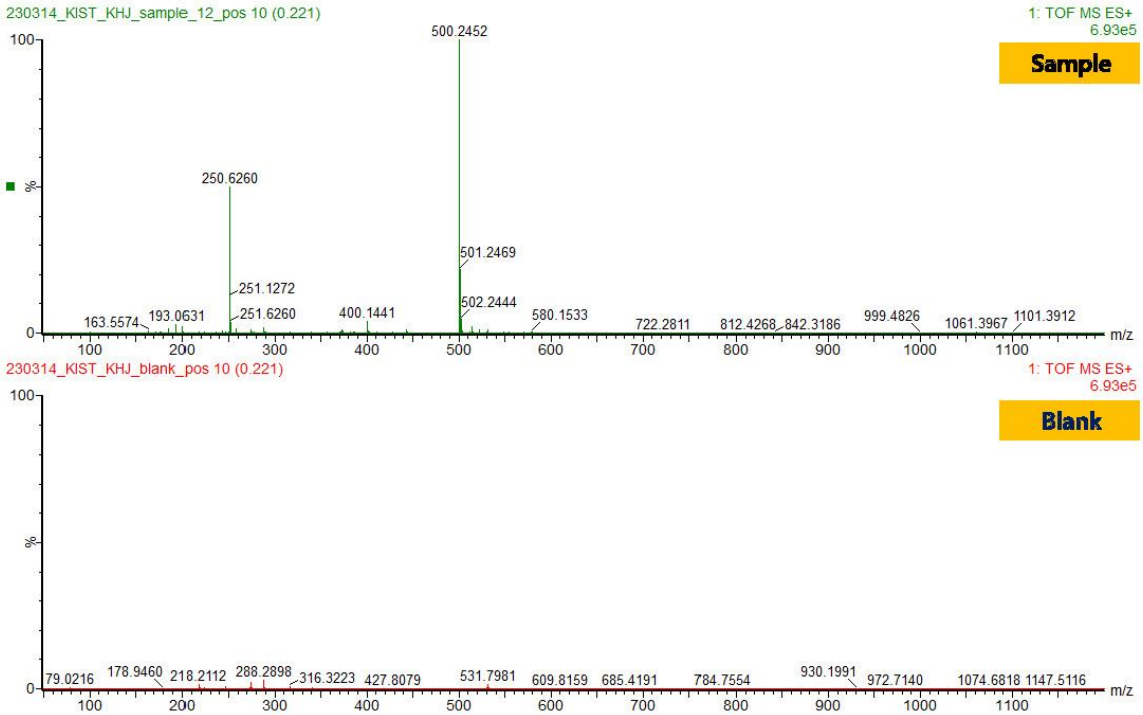
Mass Spectrum: JHW-I-18 (Positive mode)

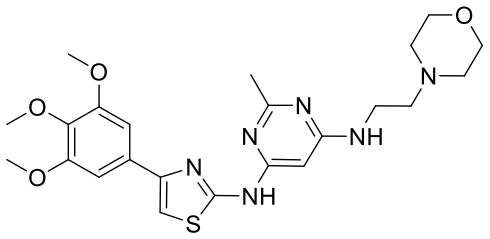




4h

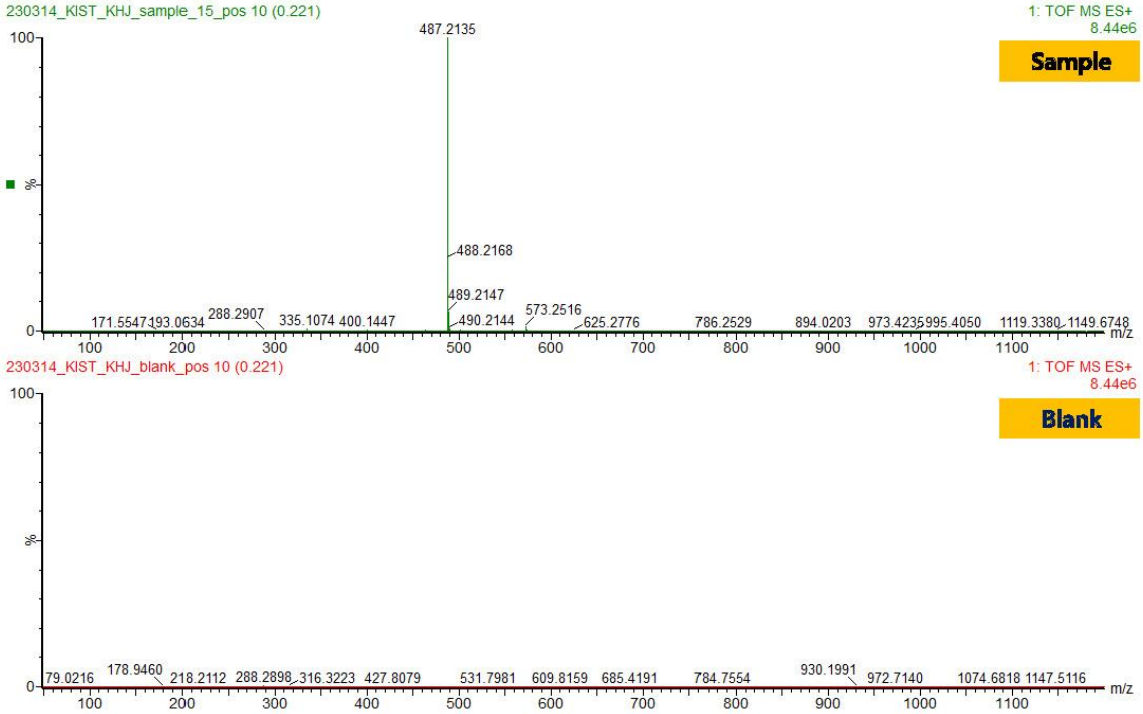
Mass Spectrum: JHW-I-8 (Positive mode)

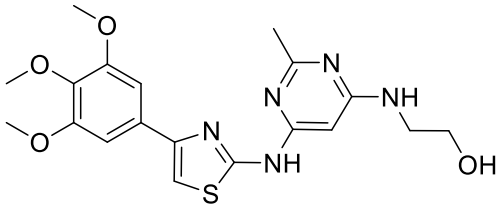




4i

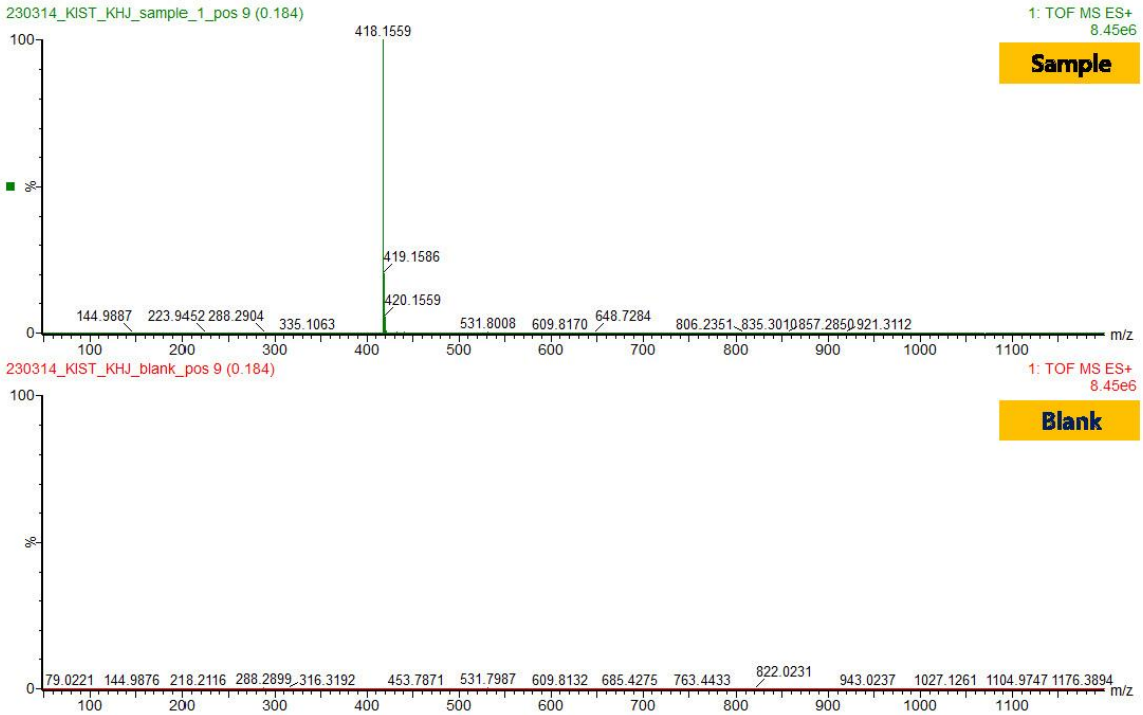
Mass Spectrum: JHW-I-22 (Positive mode)

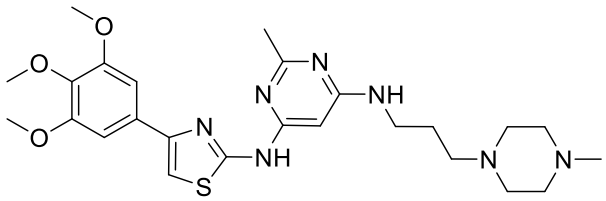




4j

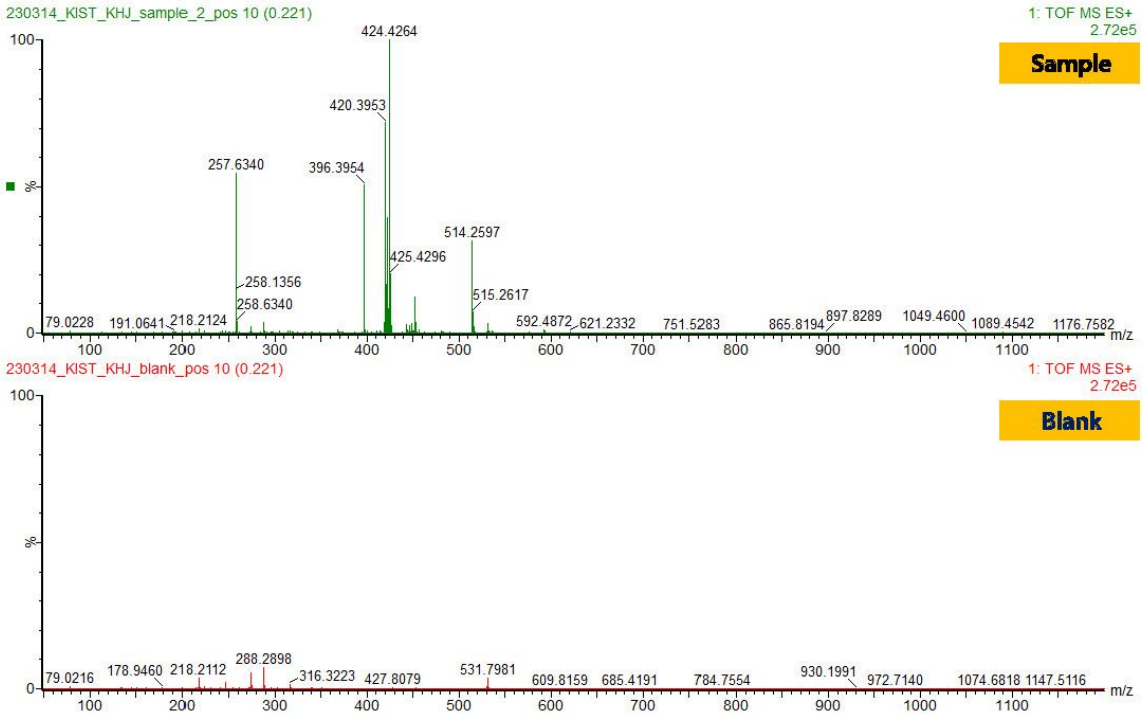
Mass Spectrum: JHW-I-19 (Positive mode)

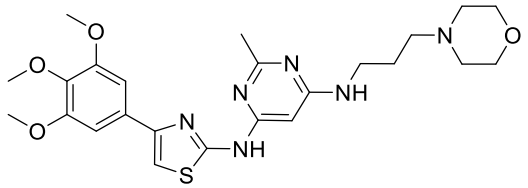




4k

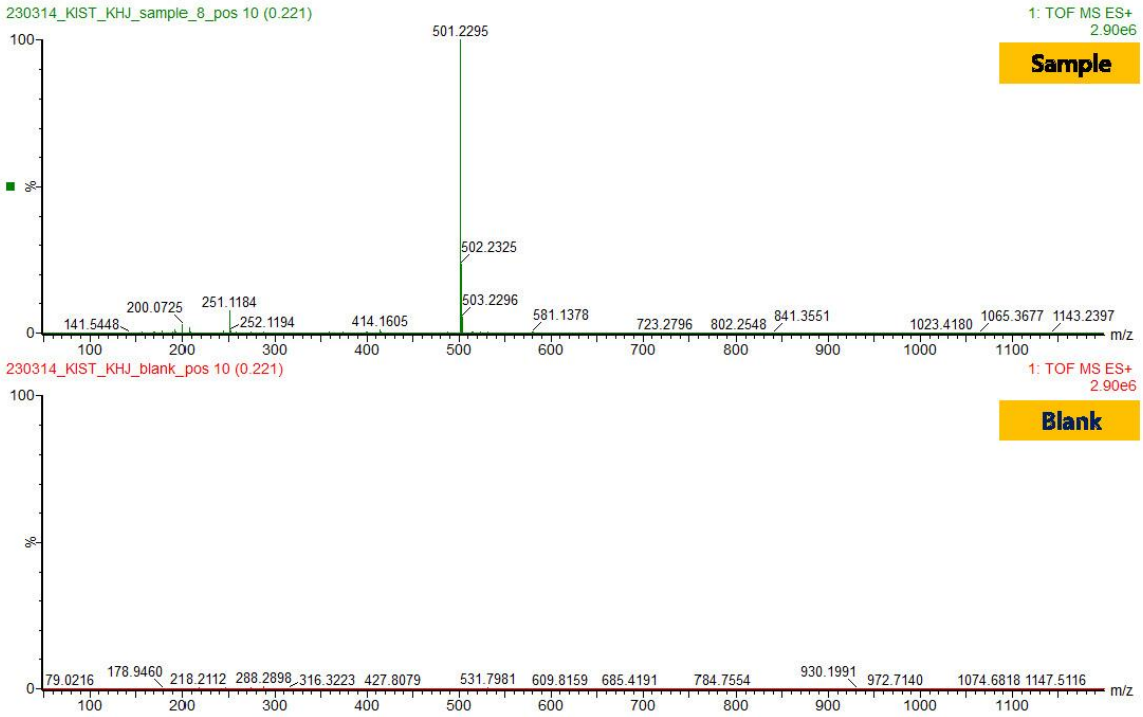
Mass Spectrum: JHW-I-101 (Positive mode)

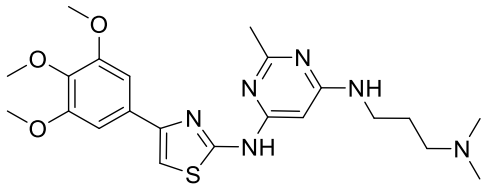




4l

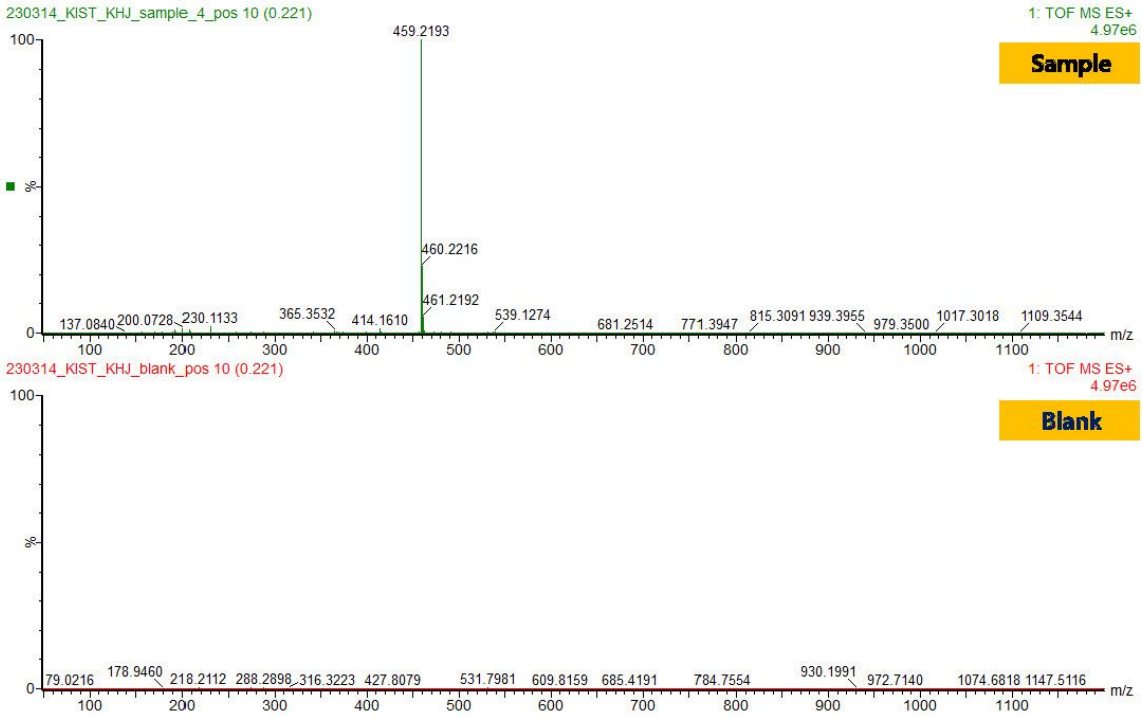
Mass Spectrum: JHW-I-6 (Positive mode)

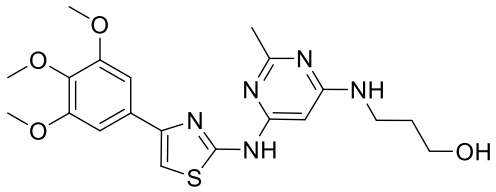




4m

Mass Spectrum: JHW-I-0 (Positive mode)





4n

Mass Spectrum: JHW-I-102 (Positive mode)

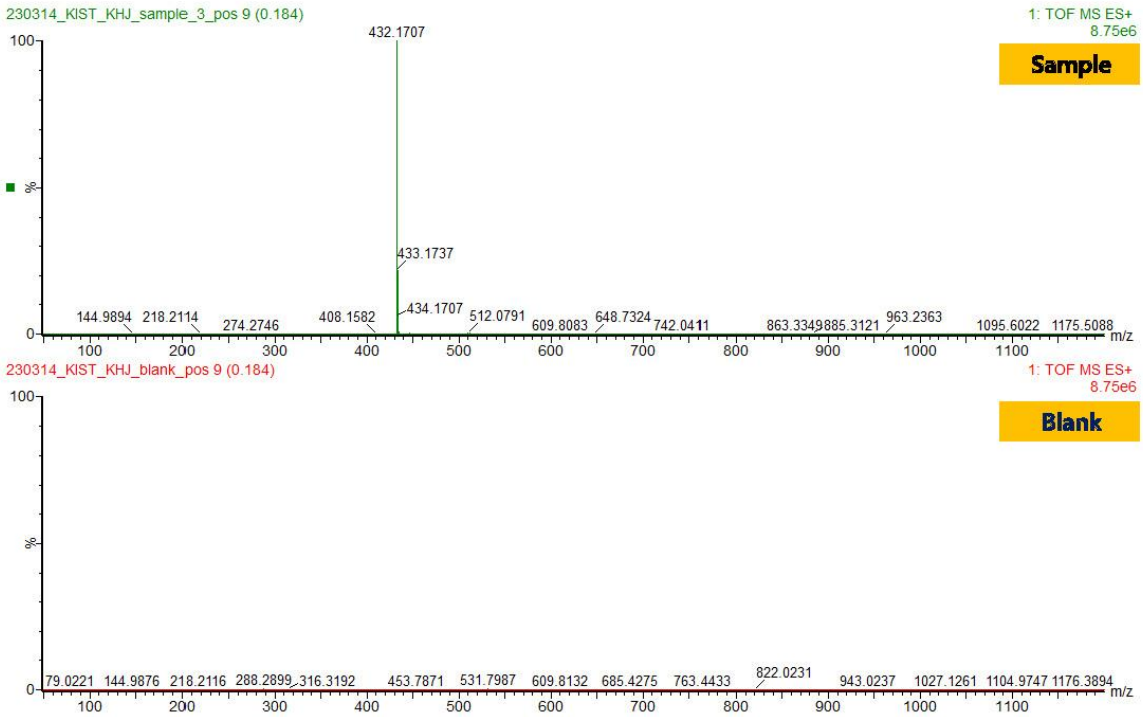
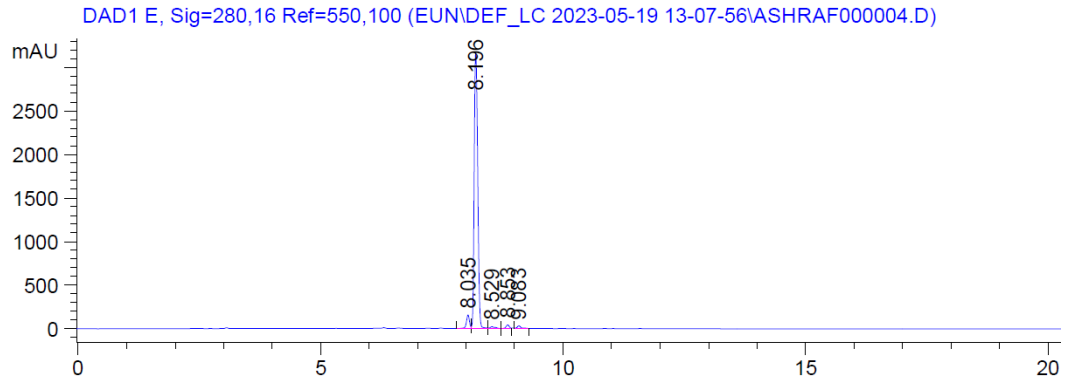


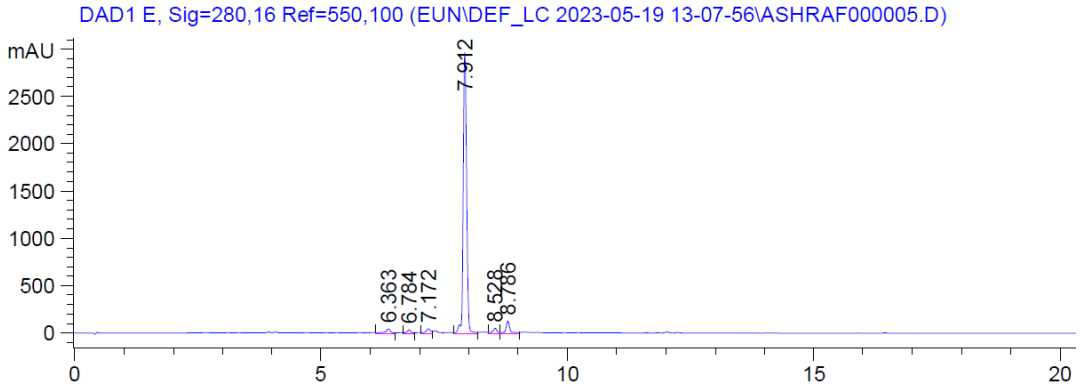
Figure S3. HPLC chromatograms.

4a



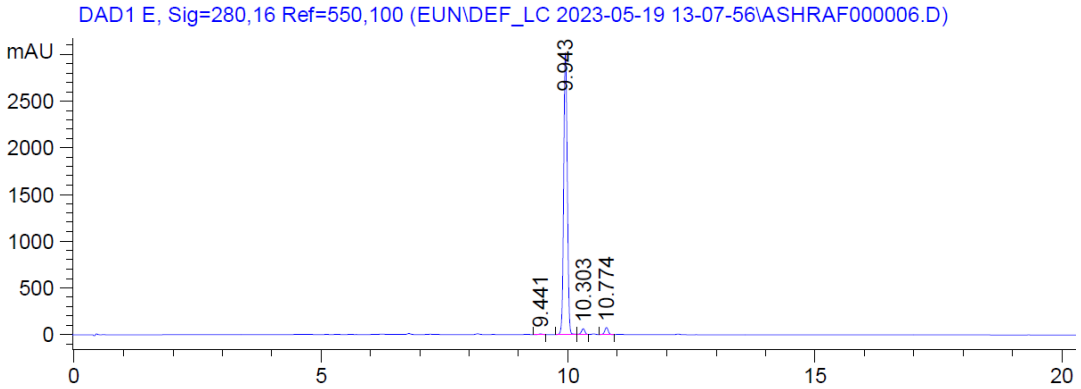
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.035	MM	0.0577	457.36737	132.04756	2.7660
2	8.196	MM	0.0832	1.57902e4	3164.52417	95.4942
3	8.529	MM	0.0661	63.35807	15.98133	0.3832
4	8.853	MM	0.0624	130.91321	34.96431	0.7917
5	9.083	MM	0.0629	93.40739	24.75652	0.5649

4b



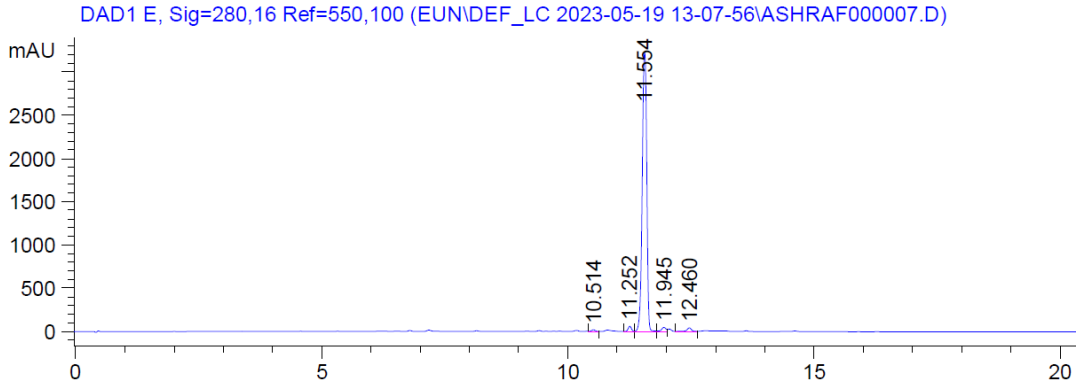
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.363	MM	0.0579	104.45980	30.07361	0.6206
2	6.784	MM	0.0617	105.35685	28.43876	0.6260
3	7.172	MM	0.1036	201.37787	32.40592	1.1964
4	7.912	MM	0.0880	1.59298e4	3017.06812	94.6430
5	8.528	MM	0.0591	133.52155	37.67151	0.7933
6	8.786	MM	0.0581	356.94733	102.36401	2.1207

4c



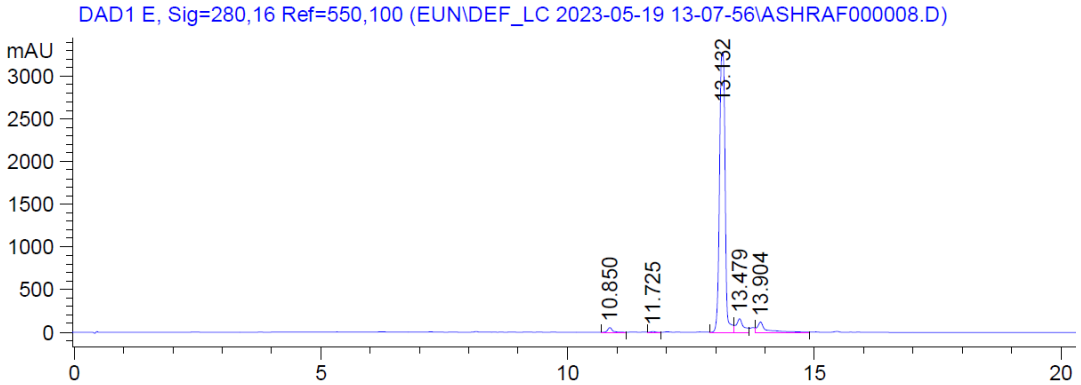
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.441	MM	0.0531	16.21639	5.09241	0.1000
2	9.943	MM	0.0861	1.56719e4	3035.16284	96.6872
3	10.303	MM	0.0711	240.45490	56.35232	1.4835
4	10.774	MM	0.0697	280.30371	67.05331	1.7293

4d



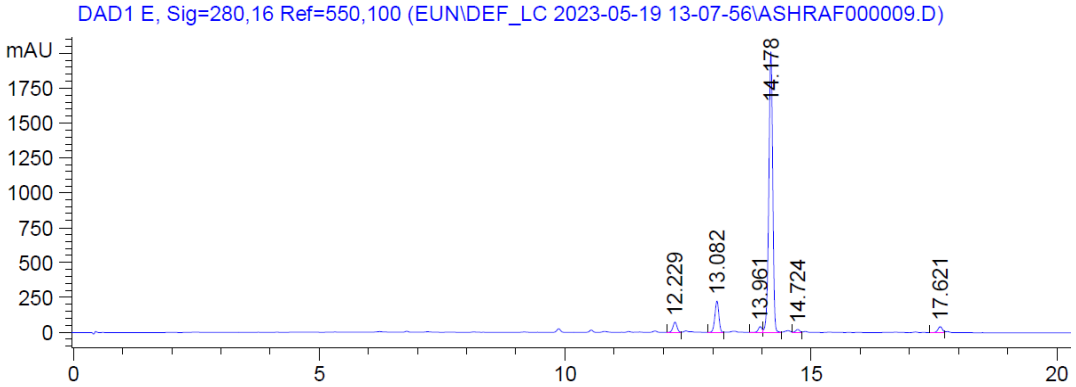
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.514	MM	0.0753	77.76376	17.22113	0.3557
2	11.252	MM	0.0665	216.86659	54.37672	0.9920
3	11.554	MM	0.1083	2.11809e4	3259.49268	96.8853
4	11.945	MM	0.1191	256.63257	35.92110	1.1739
5	12.460	MM	0.0647	129.67278	33.39864	0.5931

4e



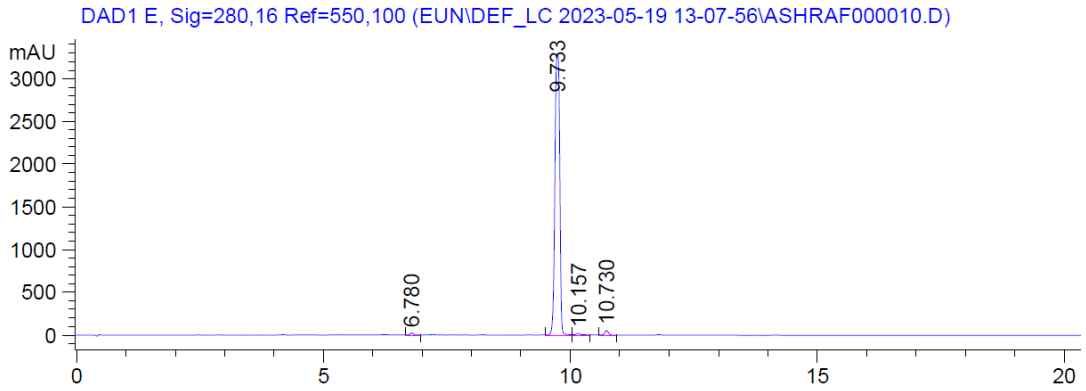
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.850	MM	0.1166	499.76828	71.45486	1.7694
2	11.725	MM	0.0707	96.67144	22.77393	0.3423
3	13.132	MM	0.1342	2.66627e4	3310.72241	94.3956
4	13.479	MM	0.0859	480.88800	93.28278	1.7025
5	13.904	MM	0.0964	505.66022	87.38710	1.7902

4f



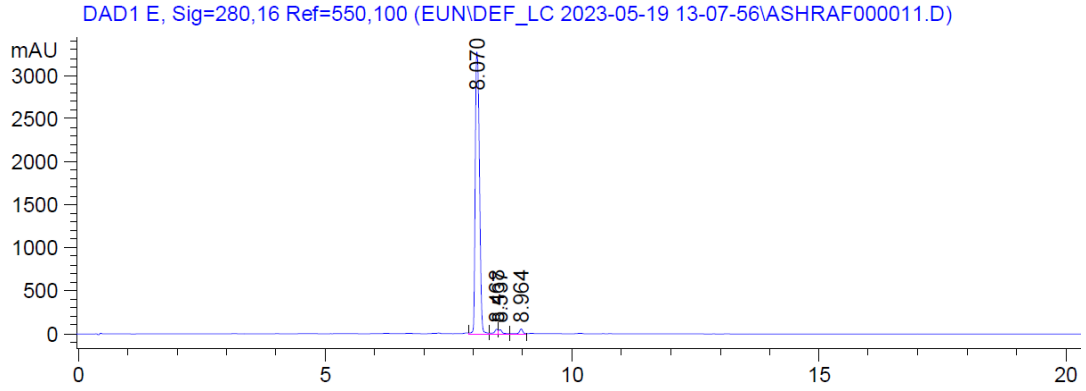
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.229	MM	0.0822	322.45212	65.40206	2.3795
2	13.082	MM	0.0871	1124.90076	215.34500	8.3011
3	13.961	MM	0.0571	78.17709	22.80712	0.5769
4	14.178	MM	0.0961	1.17756e4	2041.36389	86.8967
5	14.724	MM	0.0714	70.45380	16.43960	0.5199
6	17.621	MM	0.0884	179.66888	33.85971	1.3259

4g



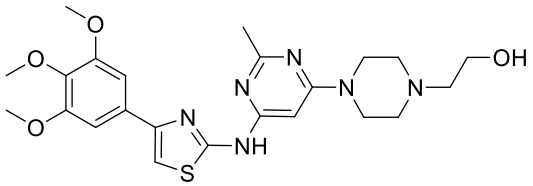
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.780	MM	0.0608	79.60249	21.80945	0.3454
2	9.733	MM	0.1142	2.26509e4	3305.02319	98.2748
3	10.157	MM	0.0773	76.37163	16.46140	0.3314
4	10.730	MM	0.0786	241.64787	51.23416	1.0484

4h

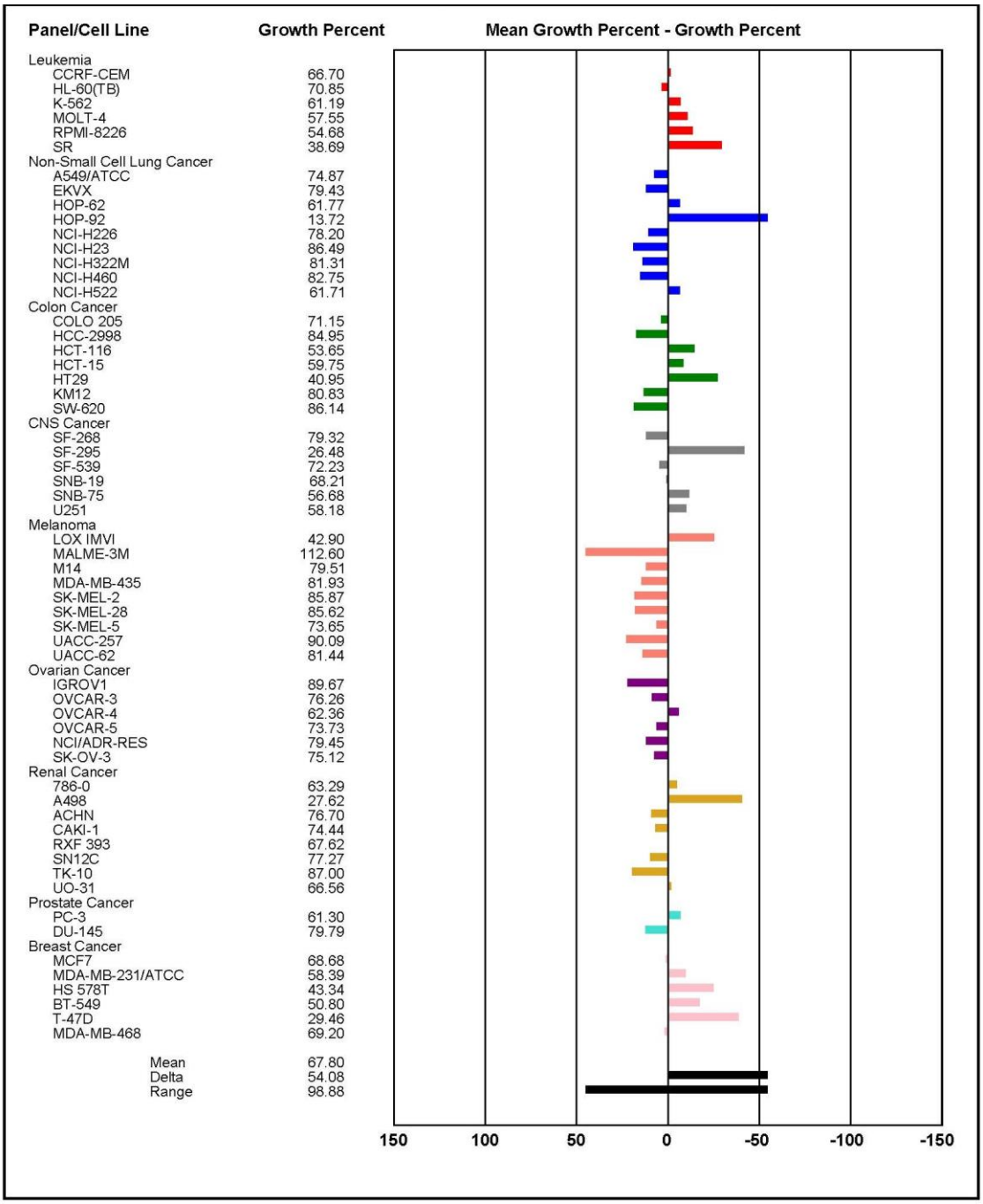


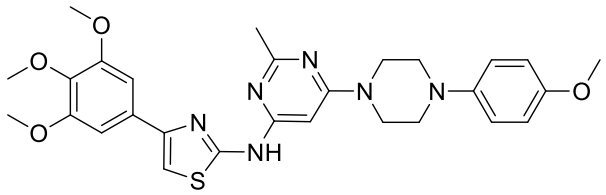
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.070	MM	0.1006	1.99534e4	3306.17407	97.5942
2	8.468	MM	0.0707	192.10826	45.29160	0.9396
3	8.537	MM	0.0603	148.93129	41.17998	0.7284
4	8.964	MM	0.0566	150.83940	44.44966	0.7378

Figure S4. NCI-60 cell line screening results.



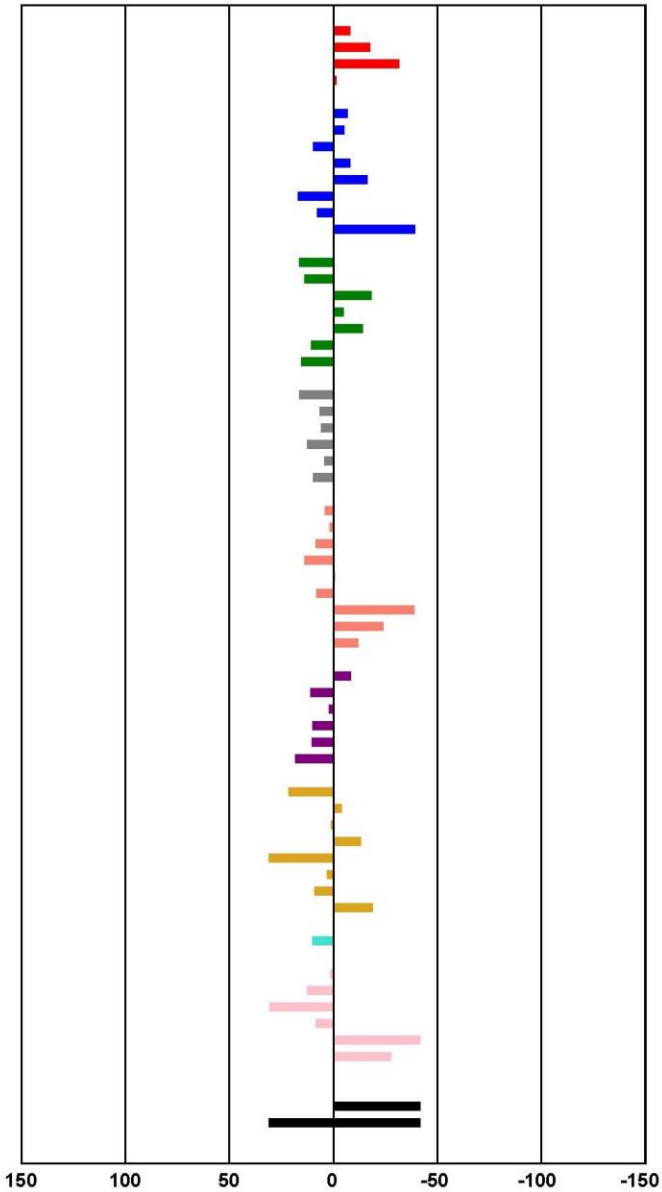
4b

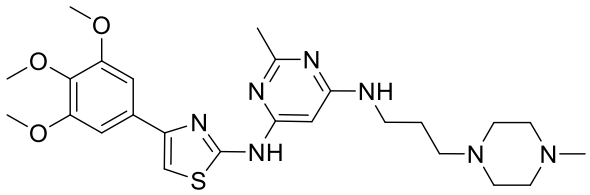




4c

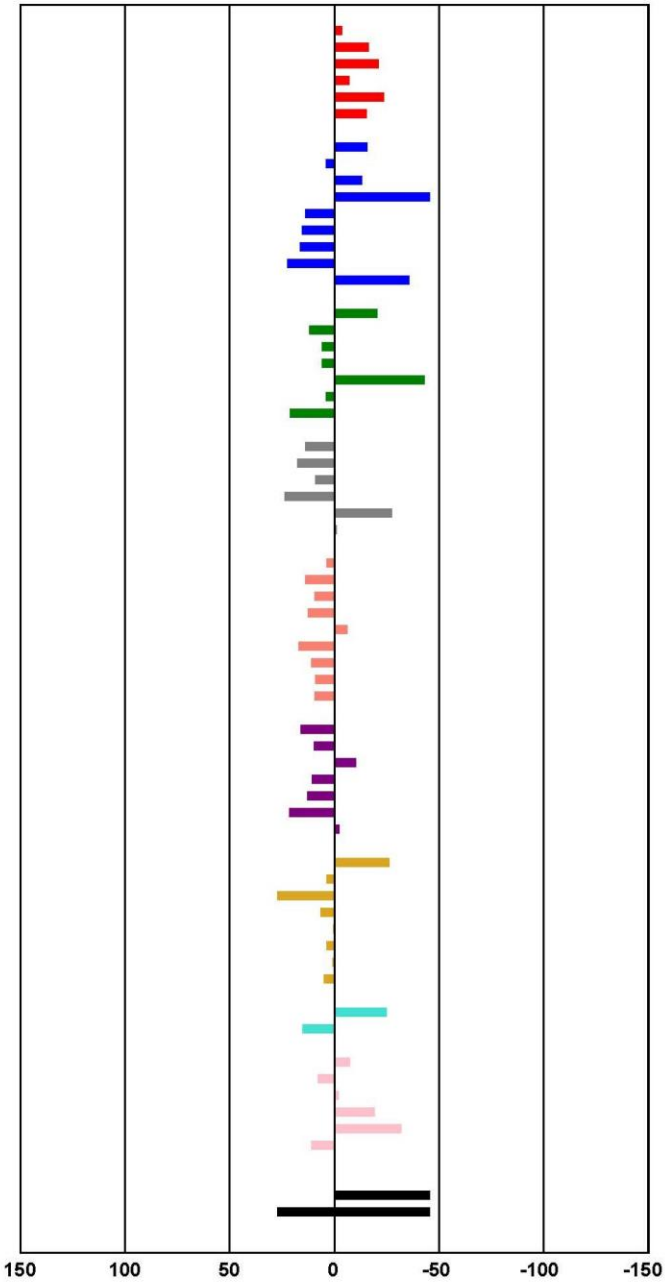
Panel/Cell Line	Growth Percent
Leukemia	
HL-60(TB)	70.79
K-562	61.40
MOLT-4	47.42
SR	77.35
Non-Small Cell Lung Cancer	
A549/ATCC	72.14
EKVX	73.61
HOP-62	88.05
NCI-H226	70.69
NCI-H23	62.60
NCI-H322M	95.28
NCI-H460	86.14
NCI-H522	39.58
Colon Cancer	
COLO 205	94.73
HCC-2998	92.16
HCT-116	60.65
HCT-15	74.06
HT29	64.66
KM12	88.89
SW-620	93.67
CNS Cancer	
SF-268	94.76
SF-295	84.65
SF-539	84.05
SNB-19	90.98
SNB-75	82.52
U251	87.86
Melanoma	
LOX IMVI	82.25
MALME-3M	80.16
M14	86.57
MDA-MB-435	92.14
SK-MEL-2	78.28
SK-MEL-28	86.35
SK-MEL-5	39.99
UACC-257	54.93
UACC-62	67.01
Ovarian Cancer	
IGROV1	70.53
OVCAR-3	89.23
OVCAR-4	80.31
OVCAR-5	88.20
NCI/ADR-RES	88.54
SK-OV-3	96.62
Renal Cancer	
786-0	99.64
A498	75.06
ACHN	79.43
CAKI-1	65.75
RXF 393	109.35
SN12C	81.29
TK-10	87.47
UO-31	60.07
Prostate Cancer	
DU-145	88.42
Breast Cancer	
MCF7	79.77
MDA-MB-231/ATCC	90.80
HS 578T	108.98
BT-549	86.61
T-47D	37.02
MDA-MB-468	51.26
Mean	78.56
Delta	41.54
Range	72.33

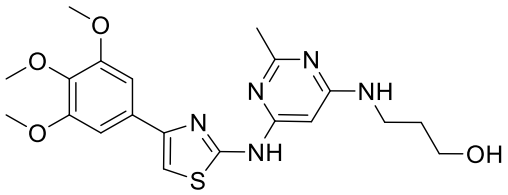


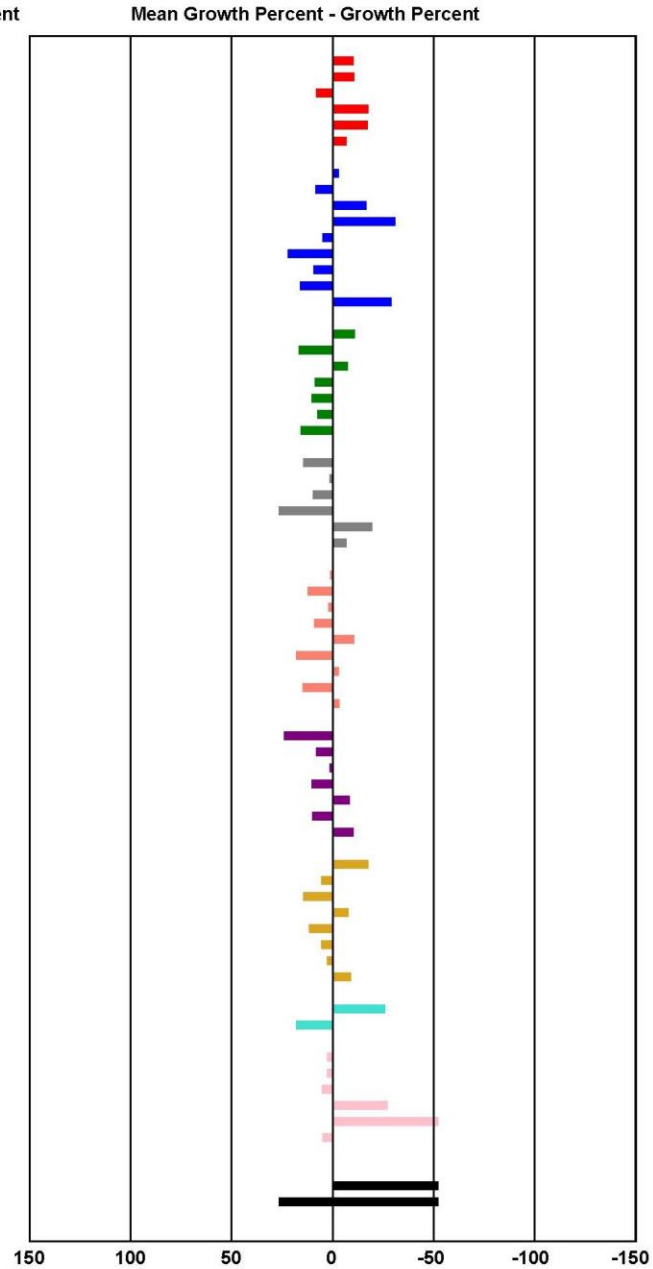


4k

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	77.17
HL-60(TB)	64.74
K-562	59.78
MOLT-4	73.93
RPMI-8226	57.15
SR	65.58
Non-Small Cell Lung Cancer	
A549/ATCC	65.23
EKVX	84.35
HOP-62	67.82
HOP-92	35.36
NCI-H226	94.17
NCI-H23	95.81
NCI-H322M	96.83
NCI-H460	102.75
NCI-H522	45.37
Colon Cancer	
COLO 205	60.45
HCC-2998	92.15
HCT-116	86.30
HCT-15	86.16
HT29	37.80
KM12	84.13
SW-620	101.57
CNS Cancer	
SF-268	94.15
SF-295	97.91
SF-539	89.49
SNB-19	104.07
SNB-75	53.42
U251	79.86
Melanoma	
LOX IMVI	83.94
MALME-3M	94.12
M14	89.69
MDA-MB-435	92.83
SK-MEL-2	74.80
SK-MEL-28	97.37
SK-MEL-5	91.18
UACC-257	89.22
UACC-62	89.61
Ovarian Cancer	
IGROV1	96.41
OVCAR-3	90.06
OVCAR-4	70.65
OVCAR-5	90.86
OVCAR-8	93.26
NCI/ADR-RES	101.90
SK-OV-3	78.54
Renal Cancer	
786-0	54.72
A498	84.09
ACHN	107.54
CAKI-1	86.78
RXF 393	80.89
SN12C	83.97
TK-10	81.02
UO-31	85.13
Prostate Cancer	
PC-3	56.18
DU-145	95.48
Breast Cancer	
MCF7	73.38
MDA-MB-231/ATCC	87.98
HS 578T	78.91
BT-549	61.76
T-47D	48.97
MDA-MB-468	91.31
Mean	80.60
Delta	45.24
Range	72.18





4n

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	73.52
HL-60(TB)	73.14
K-562	91.26
MOLT-4	66.35
RPMI-8226	66.47
SR	76.98
Non-Small Cell Lung Cancer	
A549/ATCC	80.92
EKVX	91.58
HOP-62	67.13
HOP-92	52.86
NCI-H226	88.30
NCI-H23	105.31
NCI-H322M	92.80
NCI-H460	99.41
NCI-H522	54.77
Colon Cancer	
COLO 205	73.10
HCC-2998	99.89
HCT-116	76.60
HCT-15	91.96
HT29	93.68
KM12	90.89
SW-620	98.95
CNS Cancer	
SF-268	97.72
SF-295	84.81
SF-539	92.95
SNB-19	109.91
SNB-75	64.36
U251	77.07
Melanoma	
LOX IMVI	84.40
MALME-3M	95.59
M14	85.44
MDA-MB-435	92.38
SK-MEL-2	73.31
SK-MEL-28	101.27
SK-MEL-5	80.97
UACC-257	98.14
UACC-62	80.73
Ovarian Cancer	
IGROV1	107.29
OVCAR-3	91.47
OVCAR-4	84.58
OVCAR-5	93.69
OVCAR-8	75.40
NCI/ADR-RES	93.19
SK-OV-3	73.48
Renal Cancer	
786-0	66.33
A498	88.82
ACHN	97.74
CAKI-1	76.29
RXF 393	94.72
SN12C	88.91
TK-10	85.85
UO-31	74.87
Prostate Cancer	
PC-3	57.95
DU-145	101.19
Breast Cancer	
MCF7	86.10
MDA-MB-231/ATCC	85.91
HS 578T	88.50
BT-549	56.70
T-47D	31.61
MDA-MB-468	88.26
Mean	83.56
Delta	51.95
Range	78.30