

Supporting Information.

Pyrazol-1-yl-Propanamides as Selective Androgen Receptor Degraders (SARD) and Pan-Antagonists for the Treatment of Enzalutamide-Resistant Prostate Cancer

Yali He,¹ Dong-Jin Hwang,¹ Suriyan Ponnusamy,² Thirumagal Thiyagarajan,² Michael

L. Mohler,¹ Ramesh Narayanan,² Duane D. Miller^{1}*

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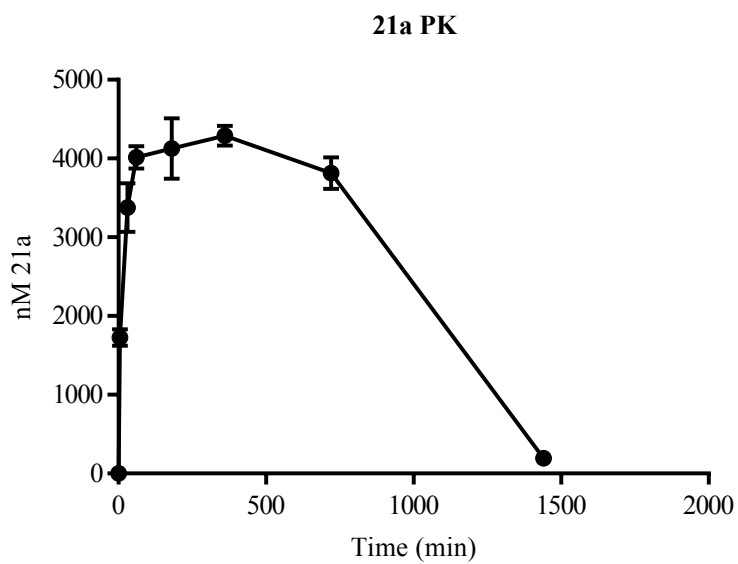
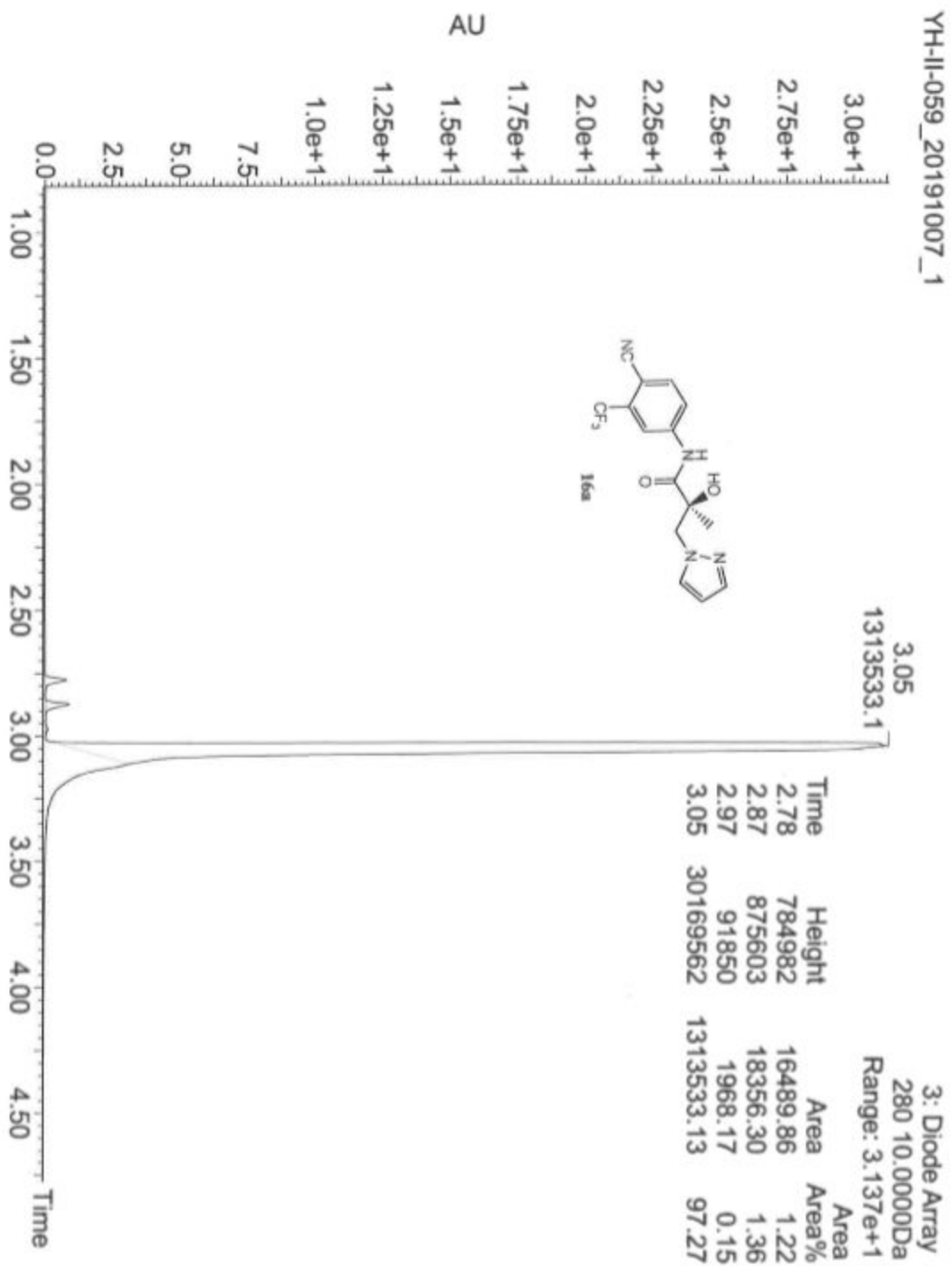


Figure S1. PK method in rats for 21a: Sprague Dawley rats were dosed with 30 mg/kg **21a** and blood was collected from jugular vein at 5 min, 30 min, 1 h, 3h, 360 h, 12 h, and 24 h post dosing. Serum was separated and analyzed using LC/MS-MS for the amount of **21a**.

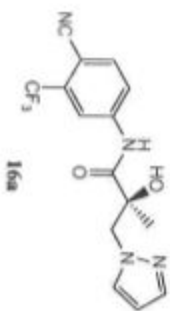
YH-II-059_20191007_1



YH-II-059_20191007_1 249 (3.084)

339.1041

1: TOF MS ES+
1.07e7

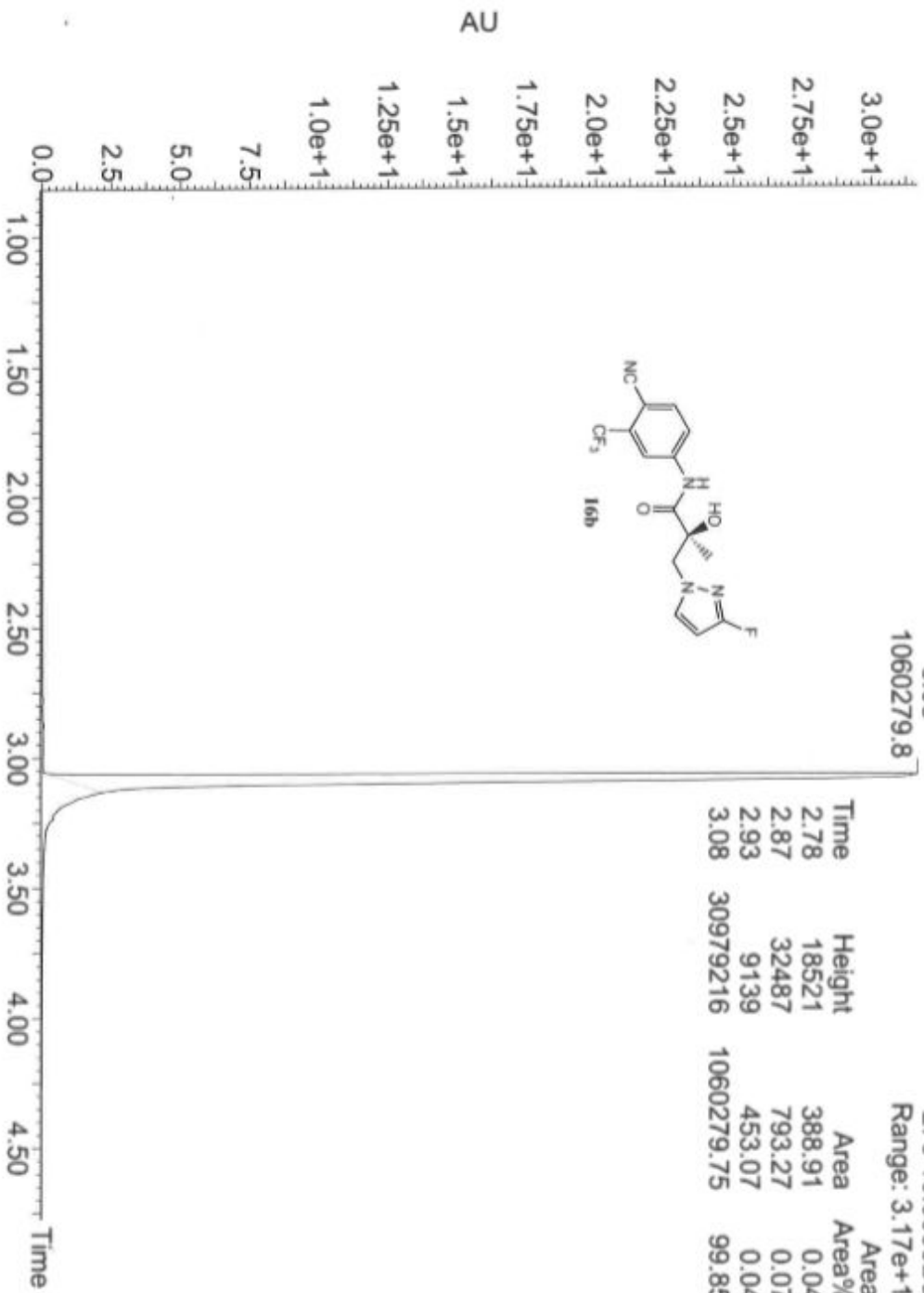


361.0862

362.0894

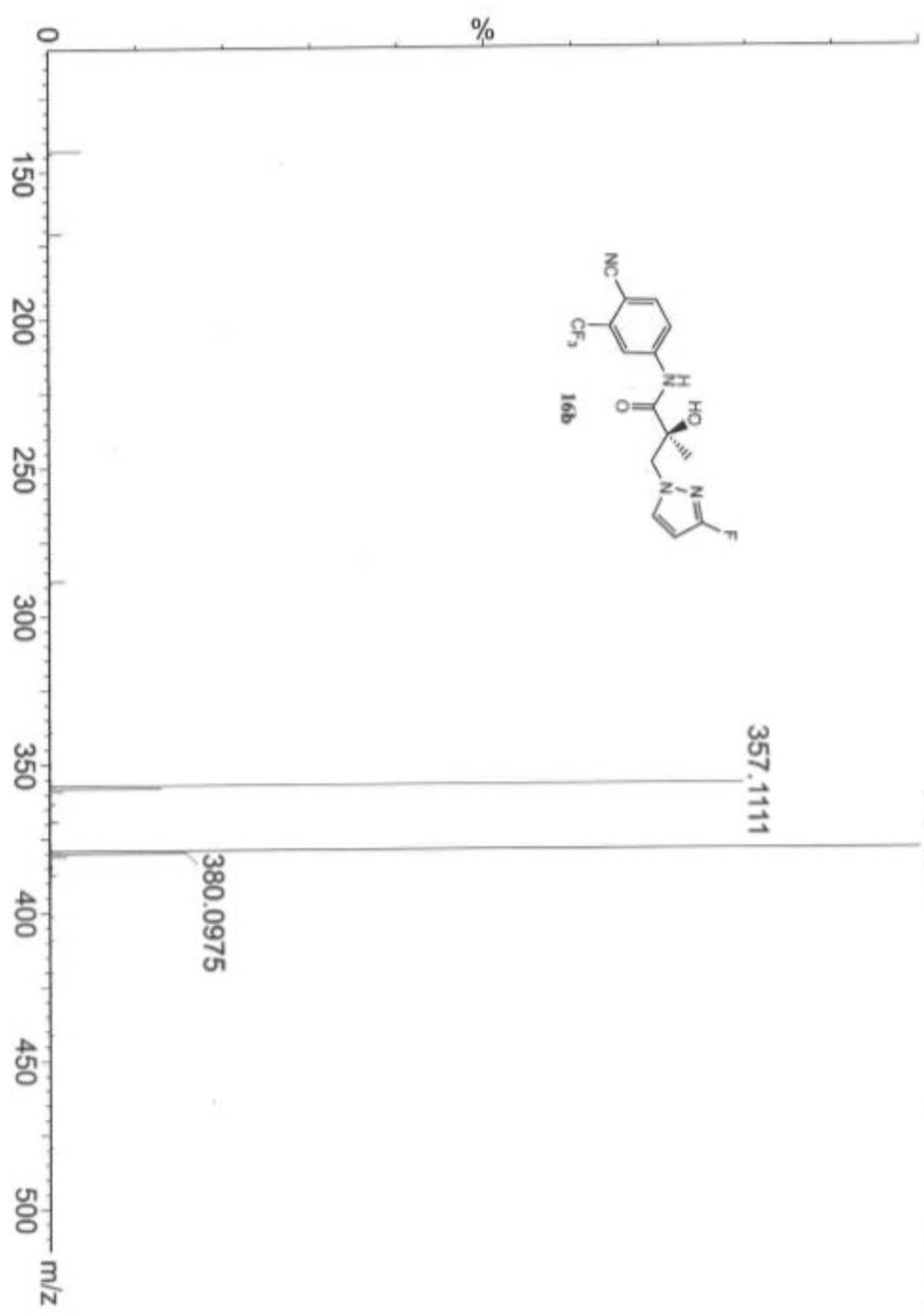


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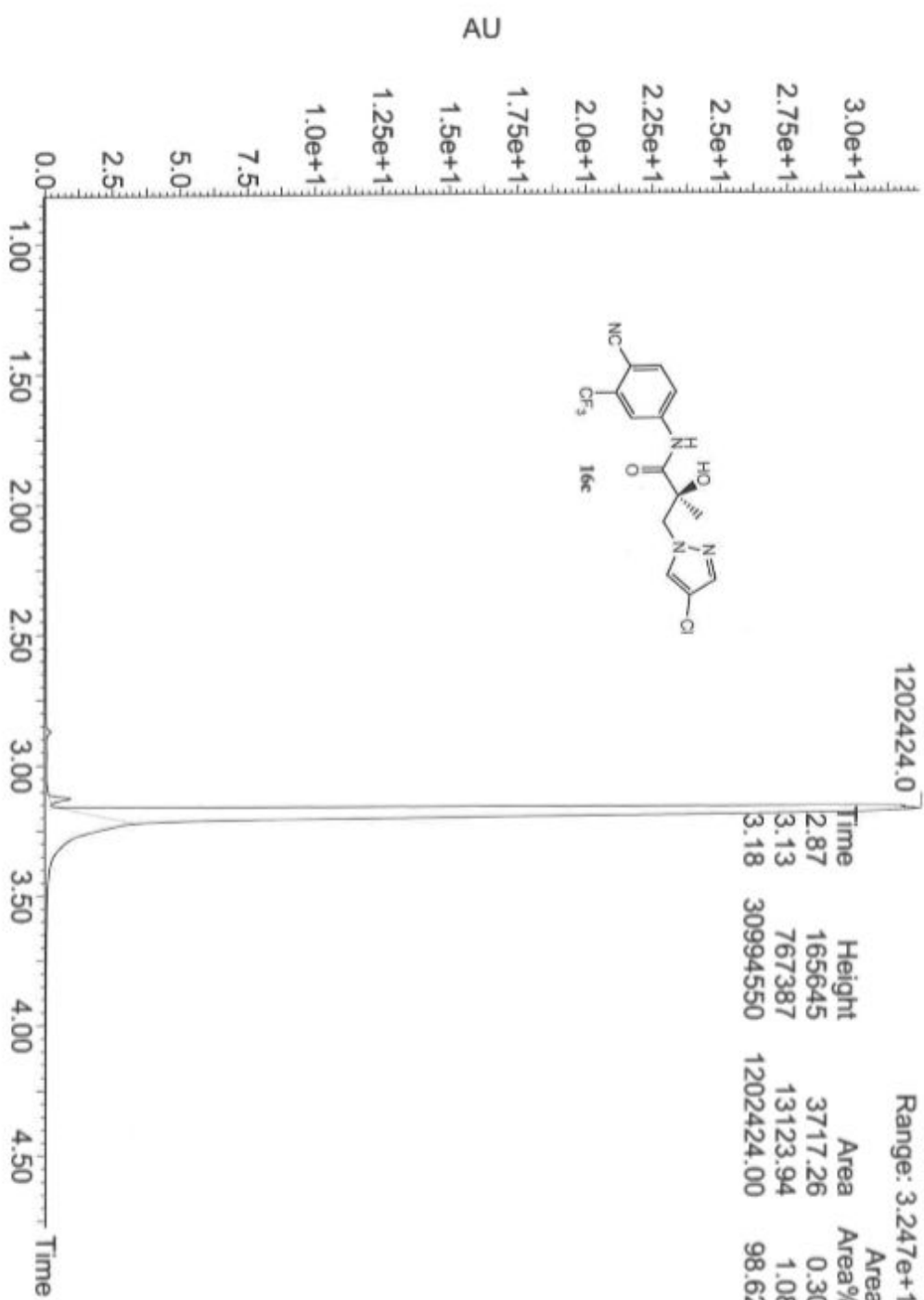


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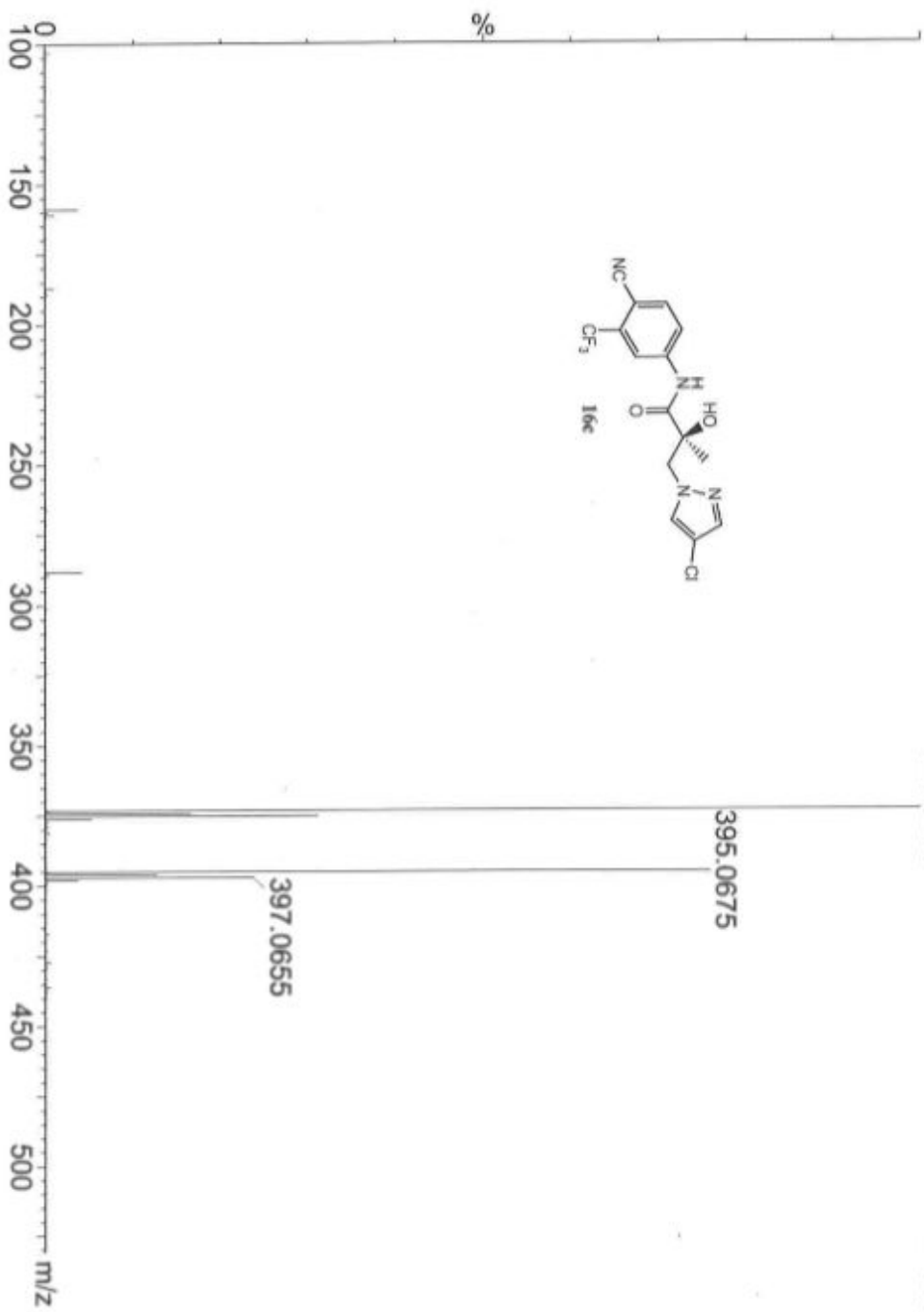


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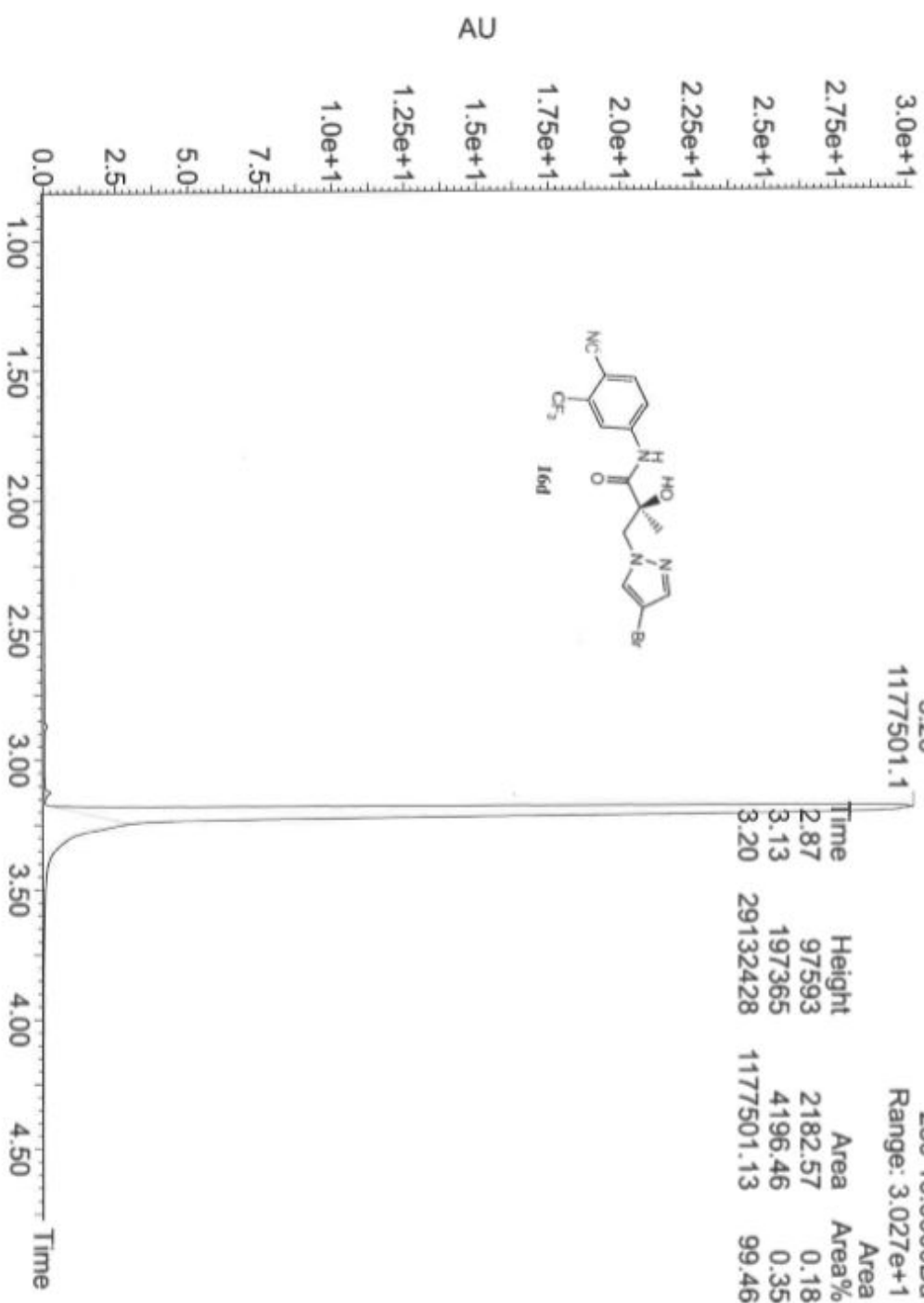


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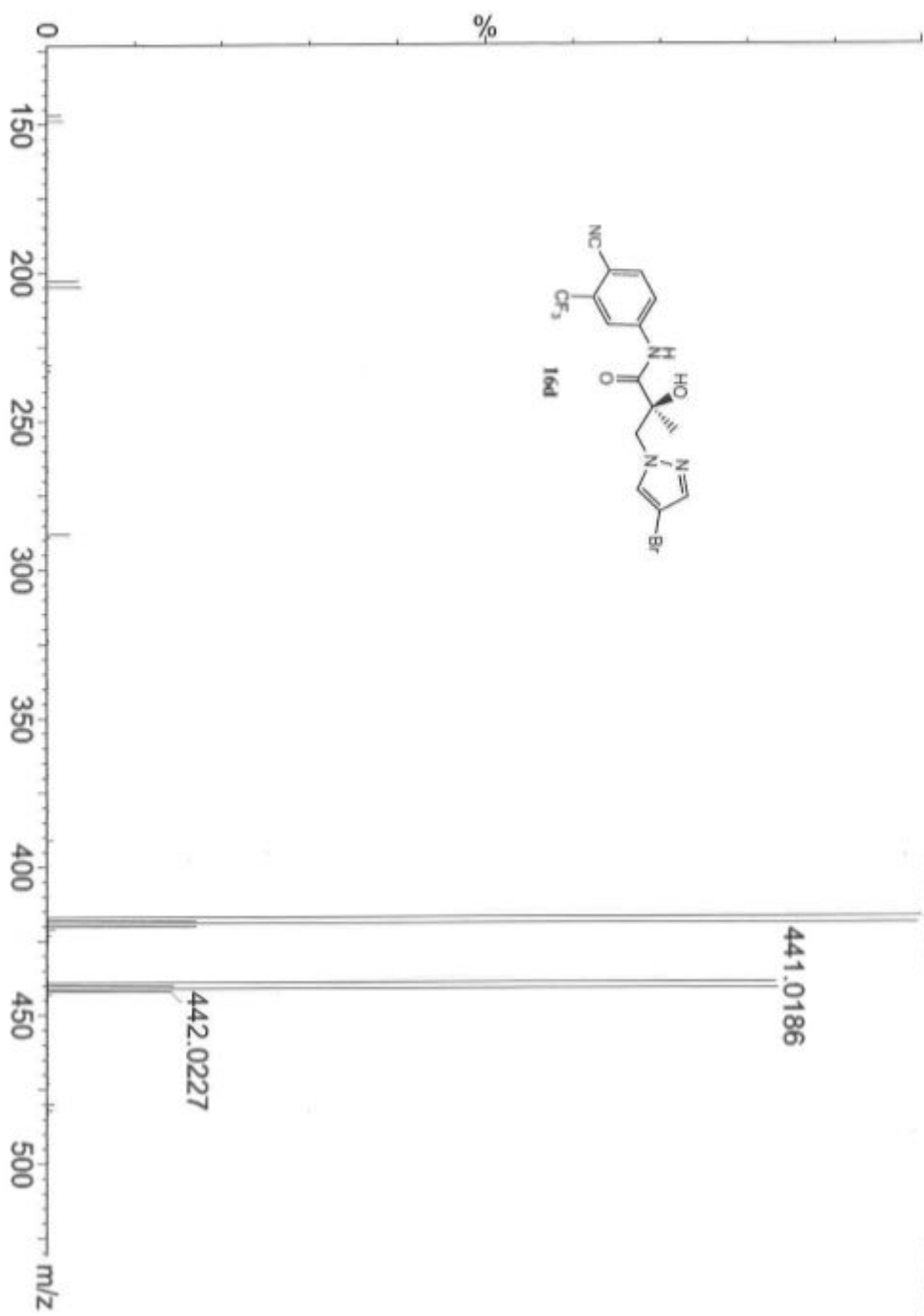


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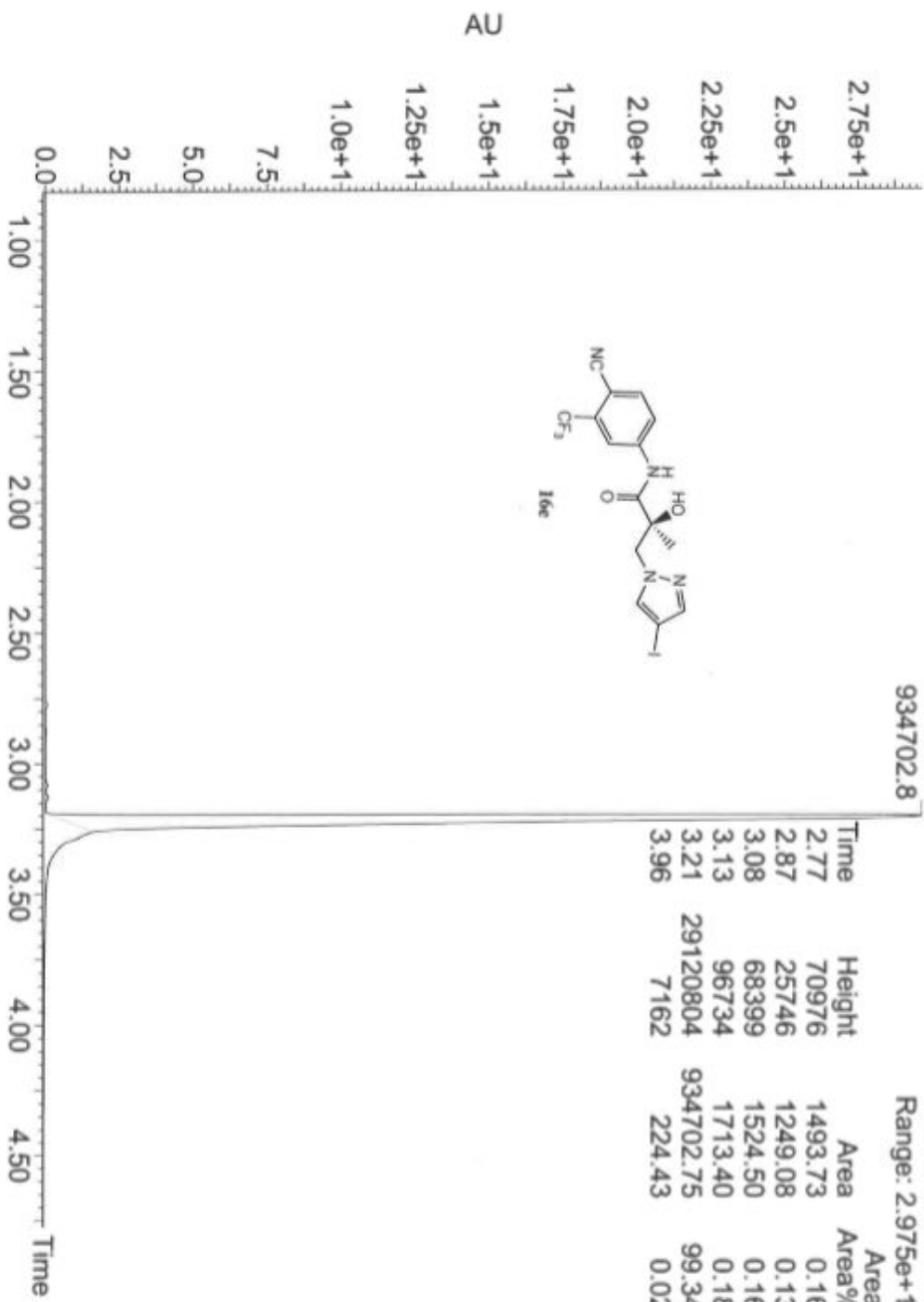


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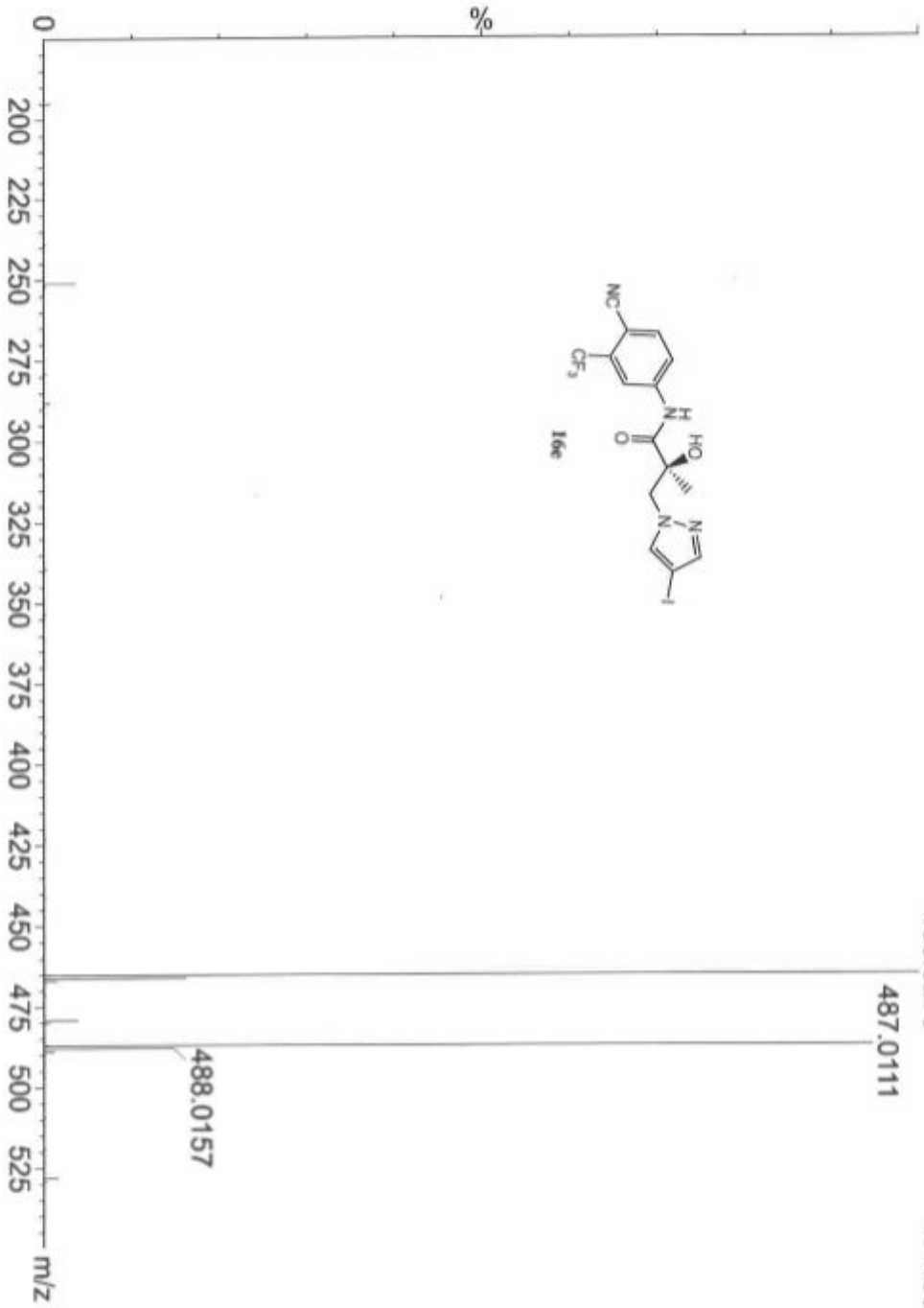
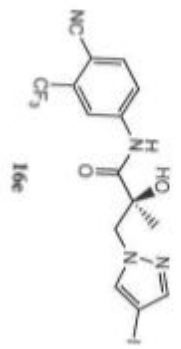


YH-II-211_20191007_6



YH-II-211_20191007_6 268 (3.258)

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465.0276
1.44e6

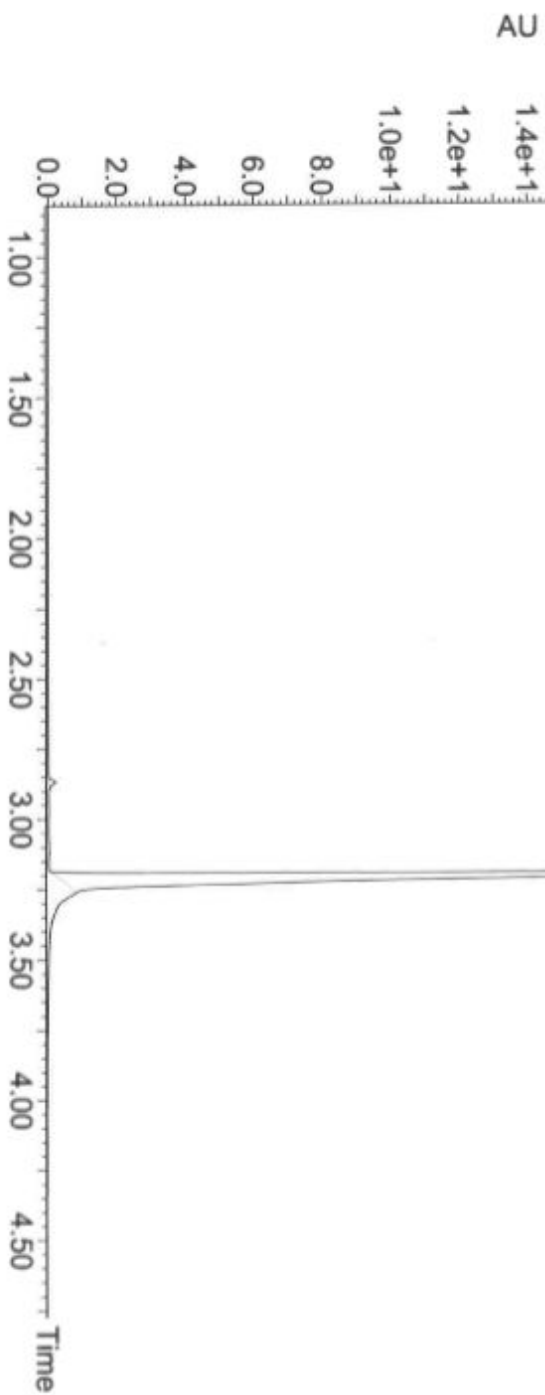
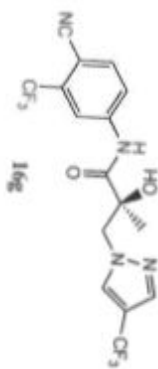


YH-II-091_20191007_8

3.21
662513.5

3: Diode Array
270 10.0000Da
Range: 2.76e+1

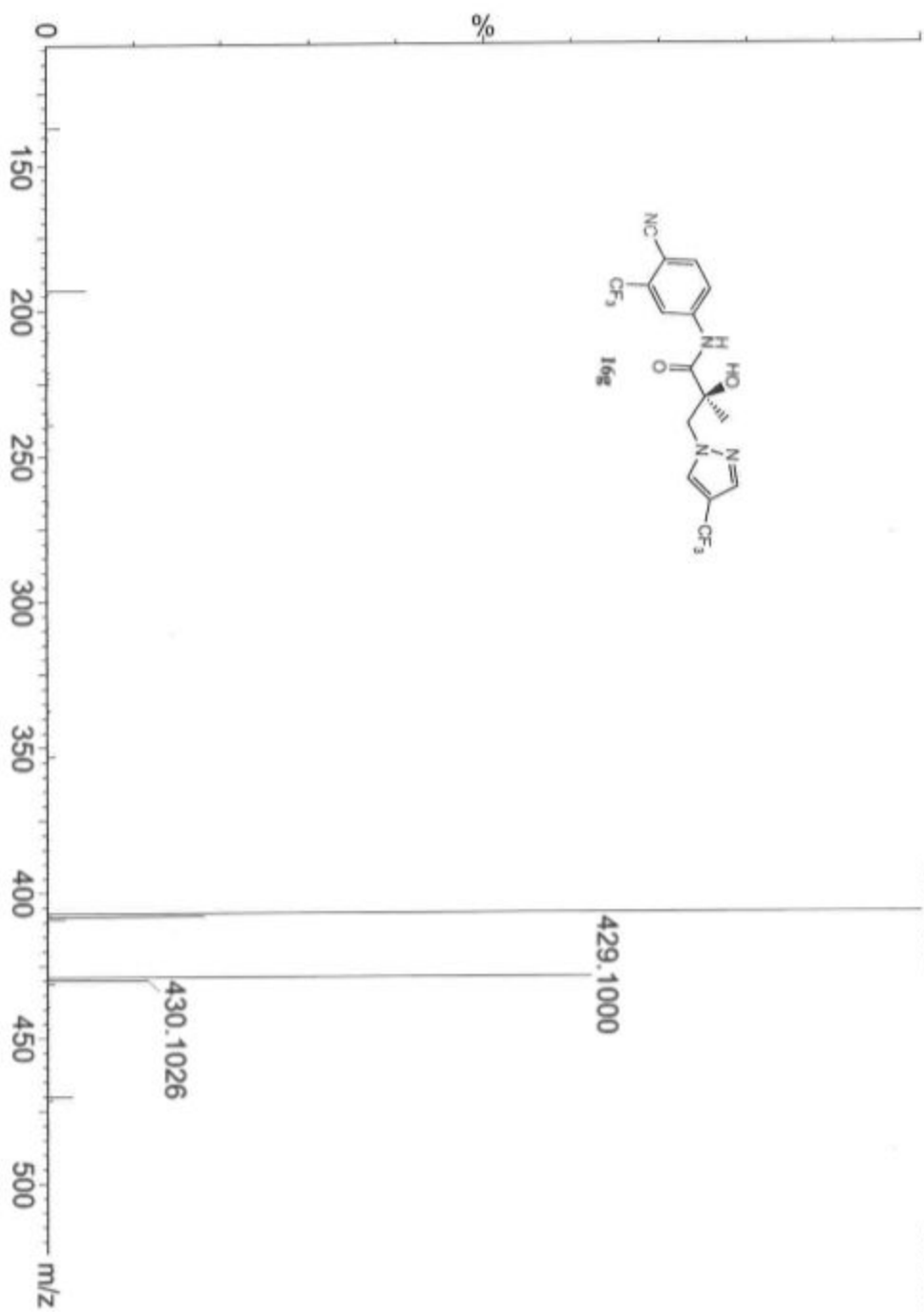
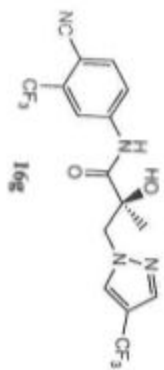
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3.12	19474	836.55	0.13
3.21	27271276	662513.50	99.15



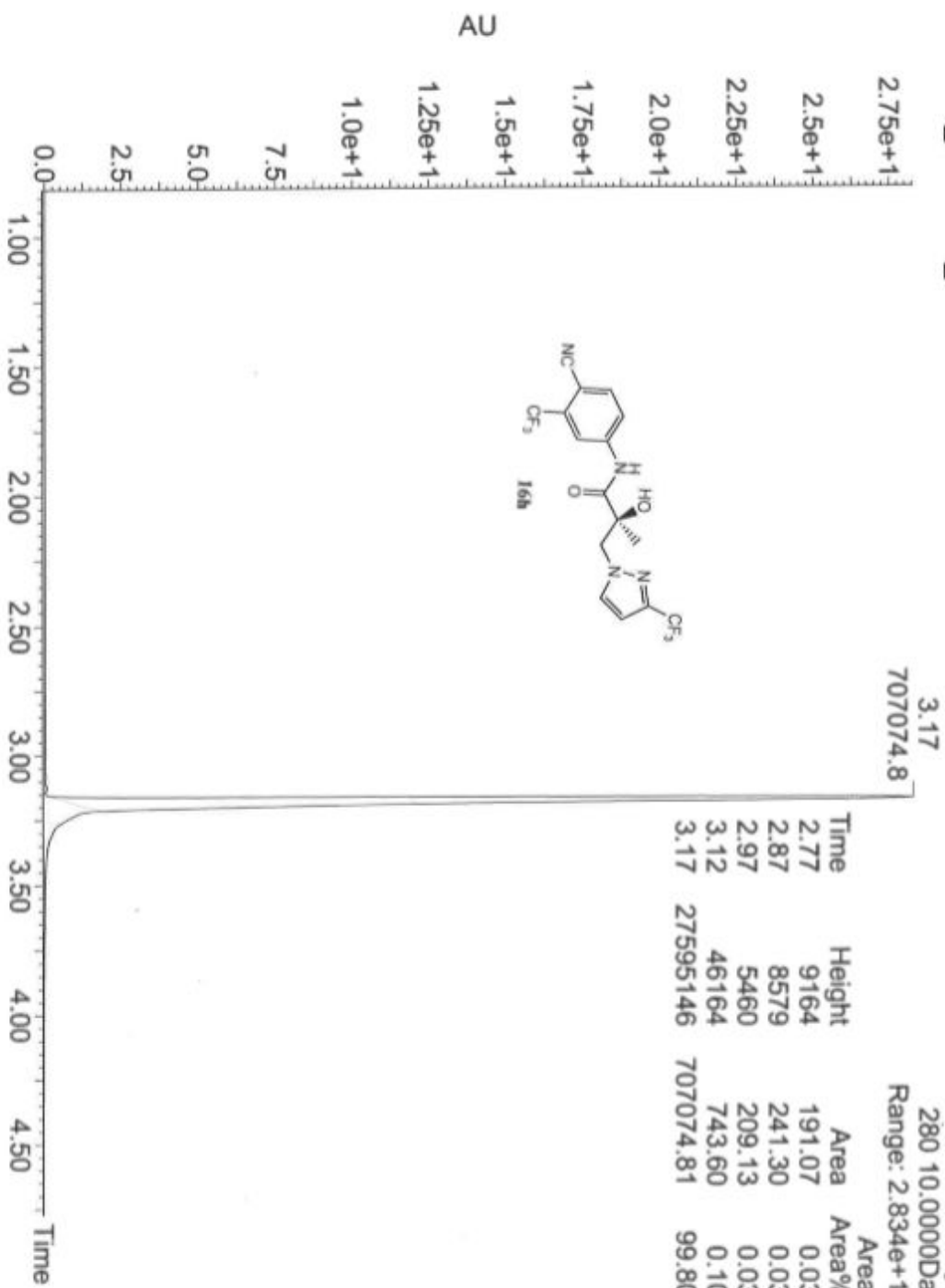
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407.1163

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9.85e5



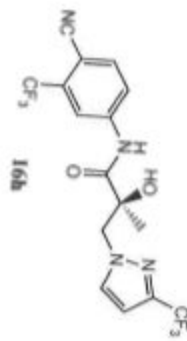
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YH-II-063_20191007_9 264 (3.224)

429.0756

1: TOF MS ES+
2.01e6



407.0931

430.0785

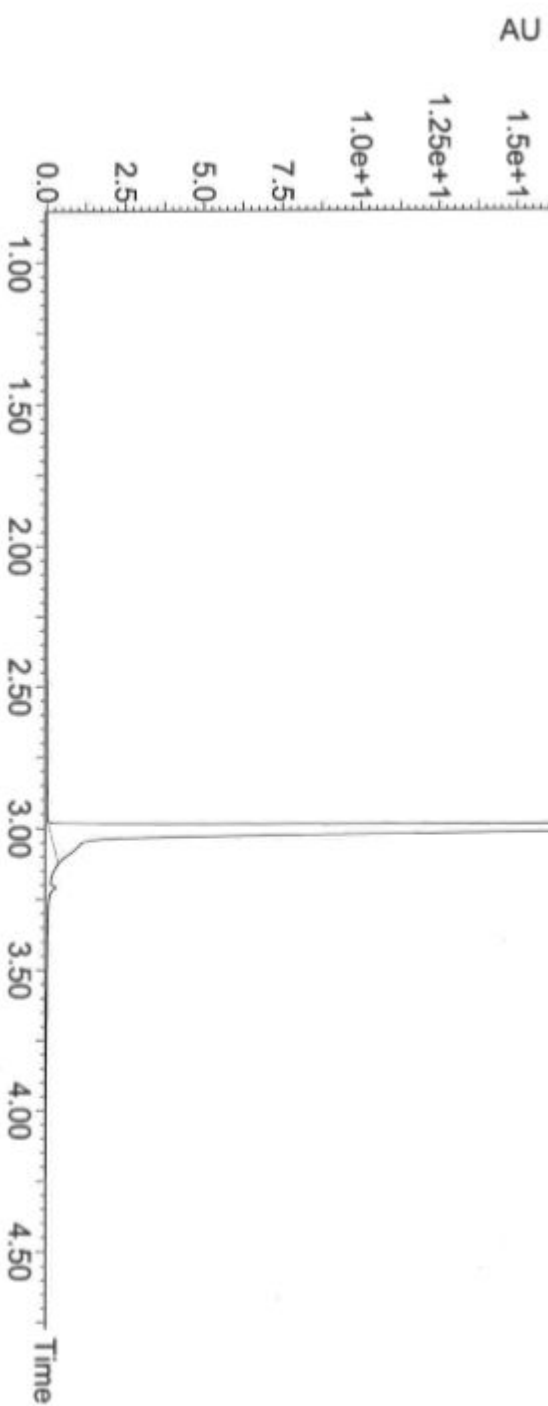
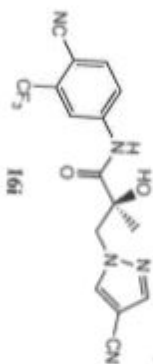


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3.00
936967.0

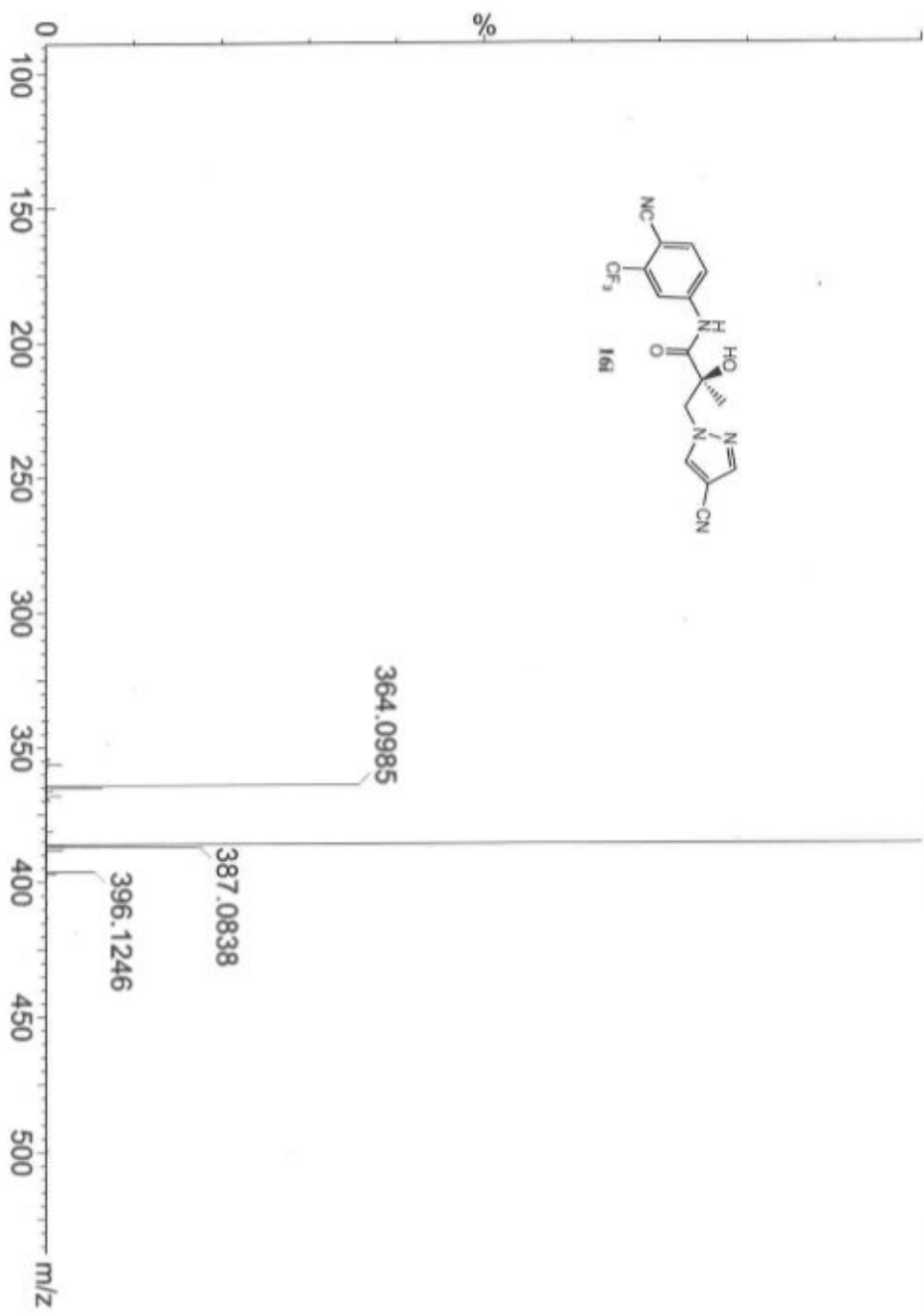
3: Diode Array
270 10.0000Da
Range: 3.028e+1

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YH-II-203_20191007_10 245 (3.049)

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2.40e6

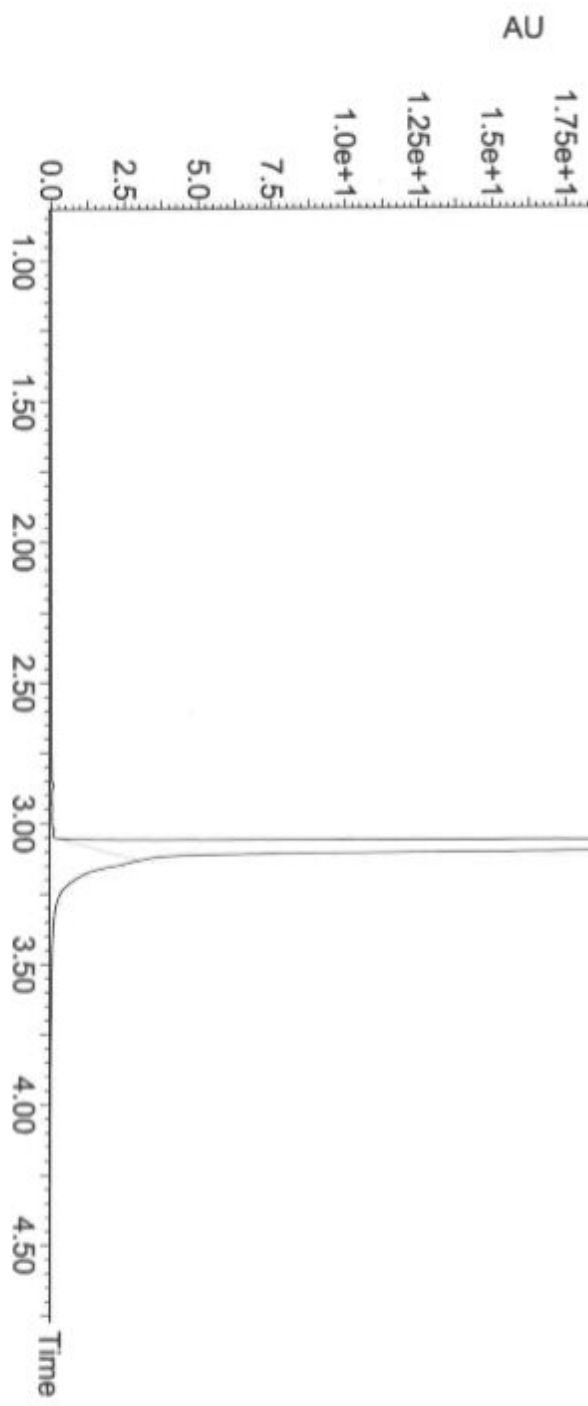
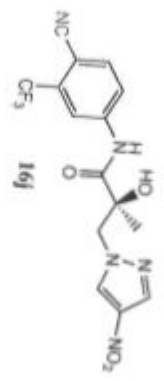


YH-III-207_20191007_11

3.08
1254775.1

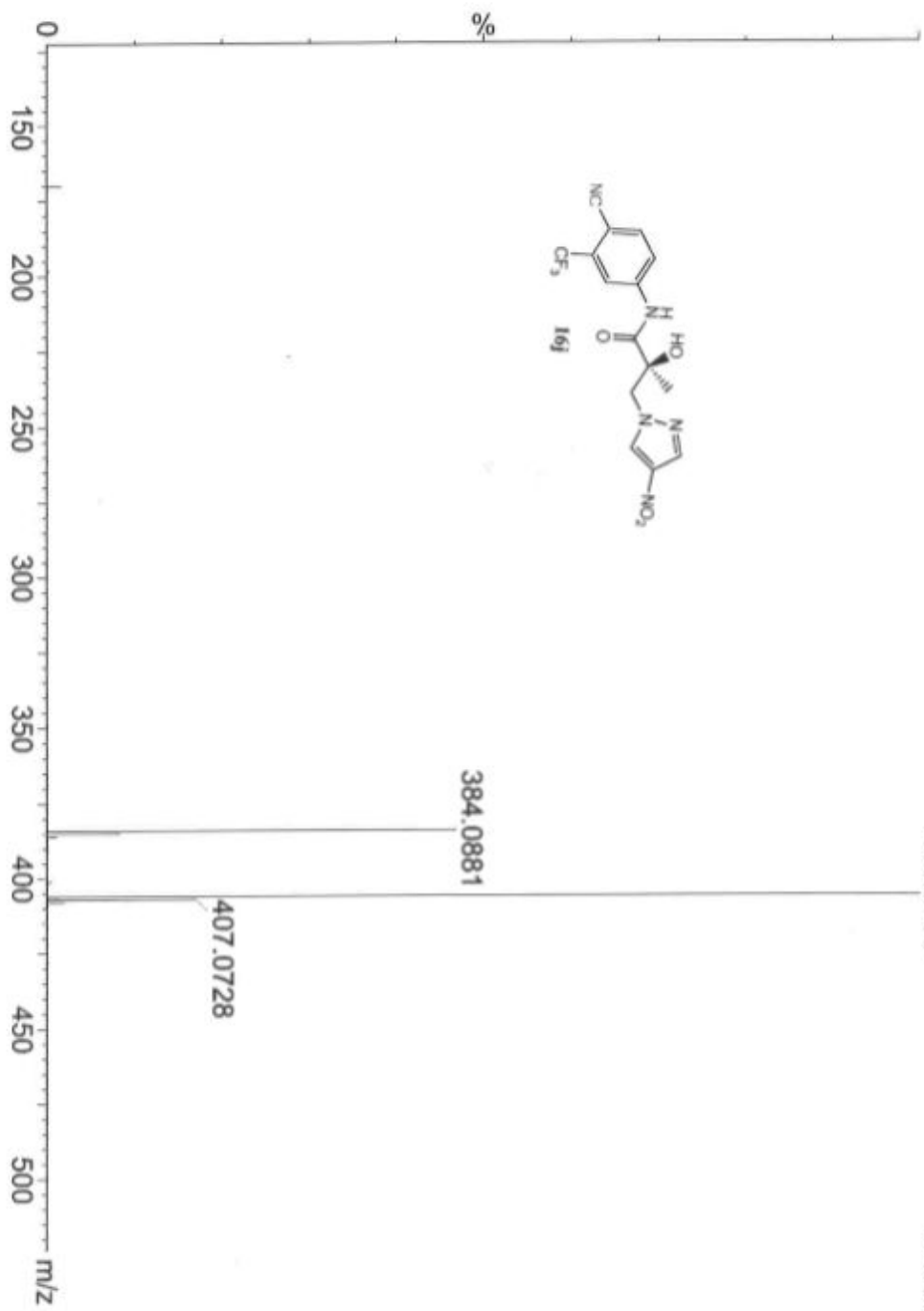
3: Diode Array
270 10.0000Da
Range: 3.226e+1

Time	Height	Area	Area%
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3.02	63967	949.33	0.08
3.08	31052224	1254775.13	99.76

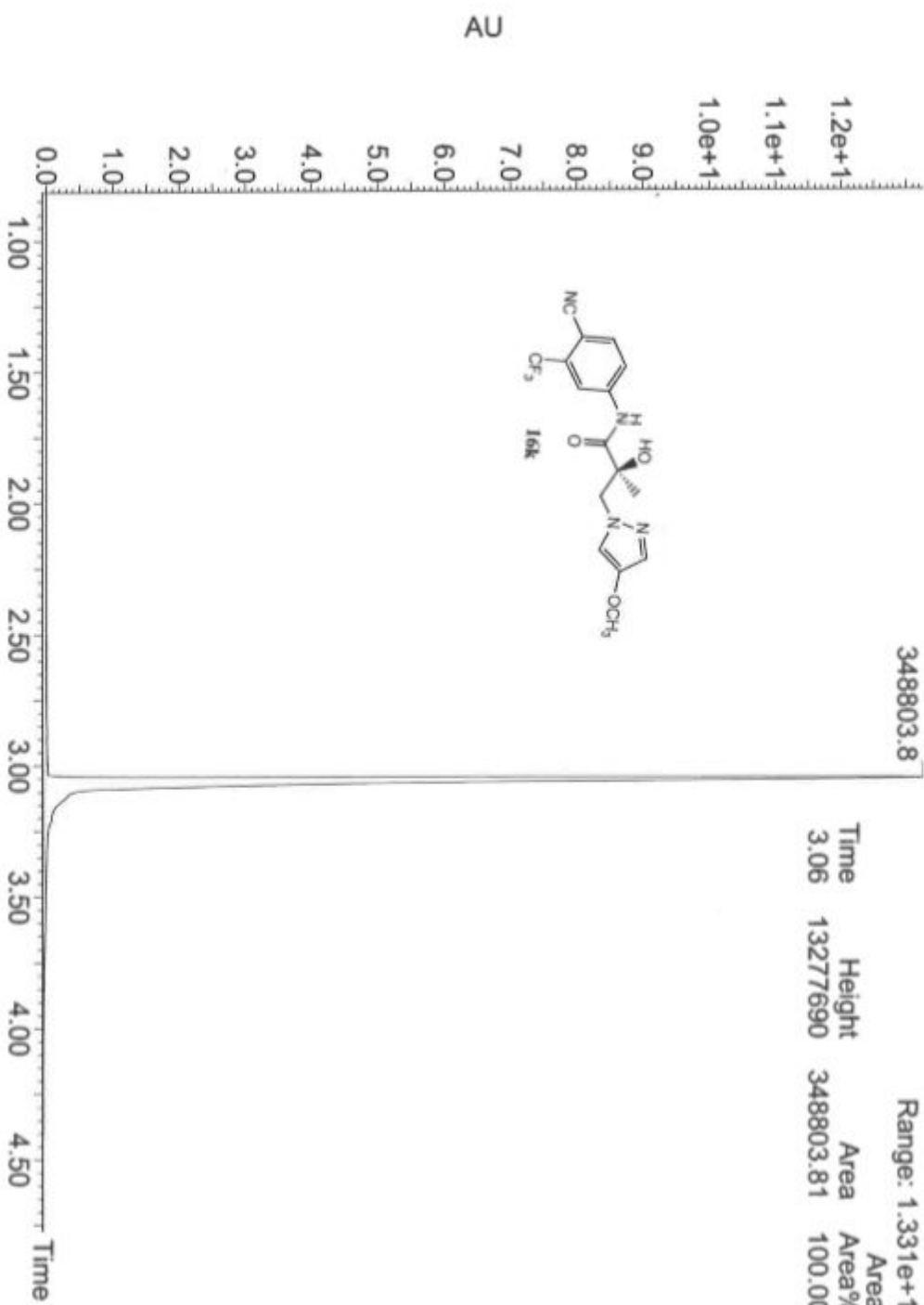


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1.69e6

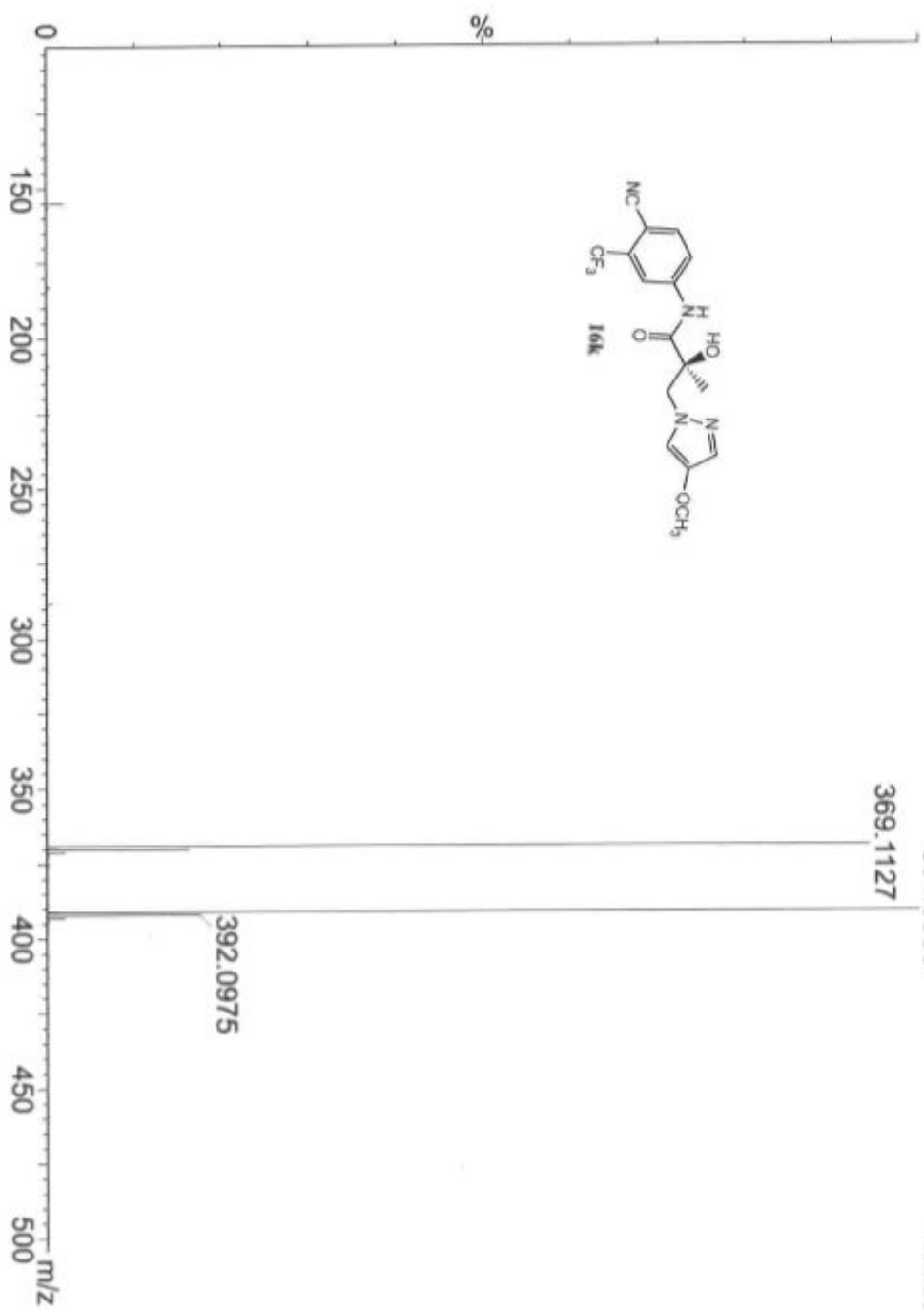
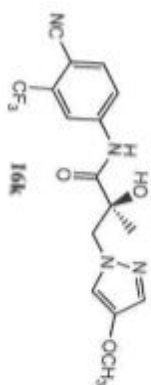


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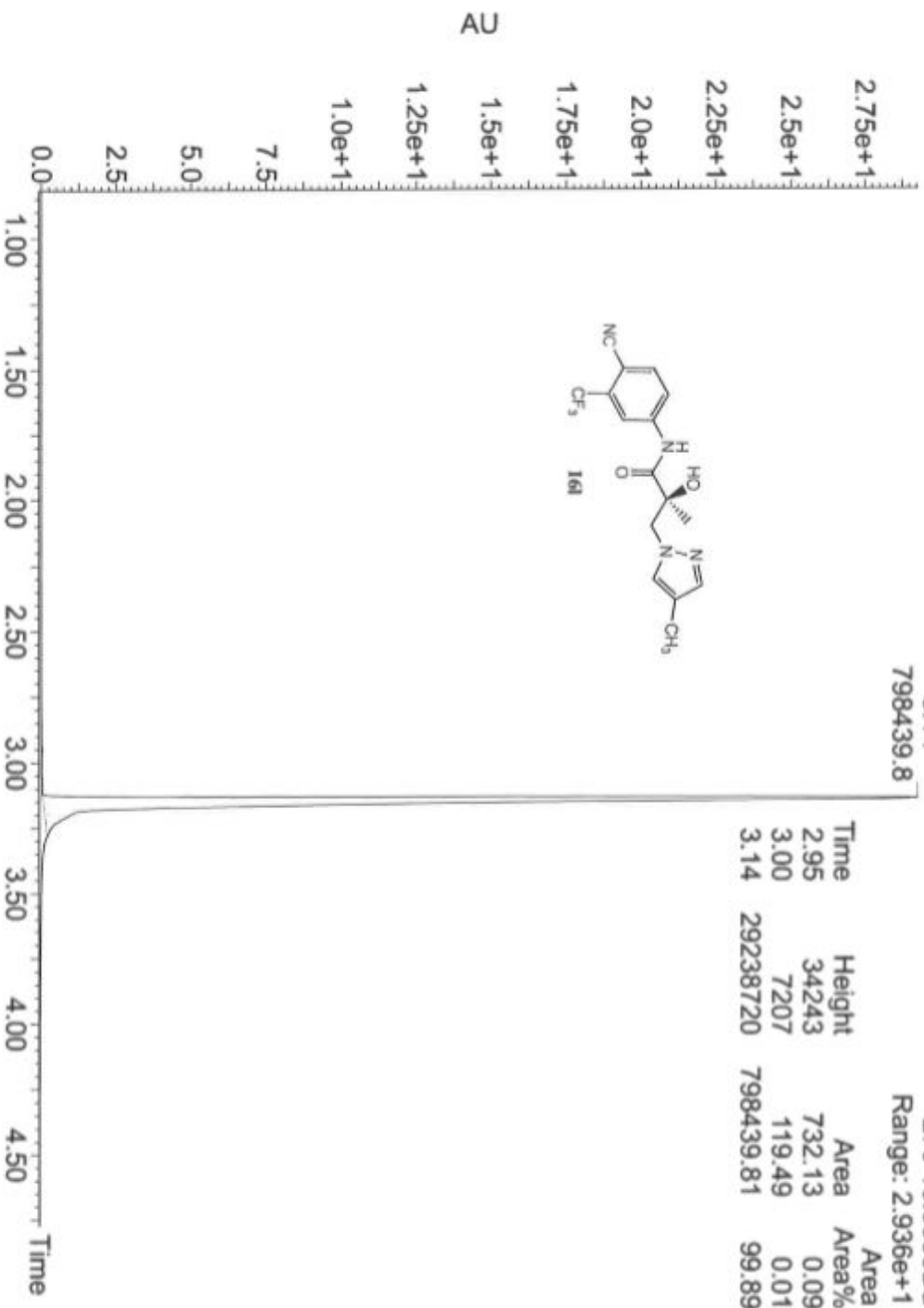


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1: TOF MS ES+
1.82e6



YH-II-281_20191007_13



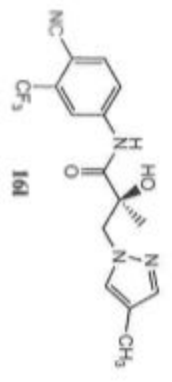
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353.1191

1: TOF MS ES+
2.32e6

375.1013

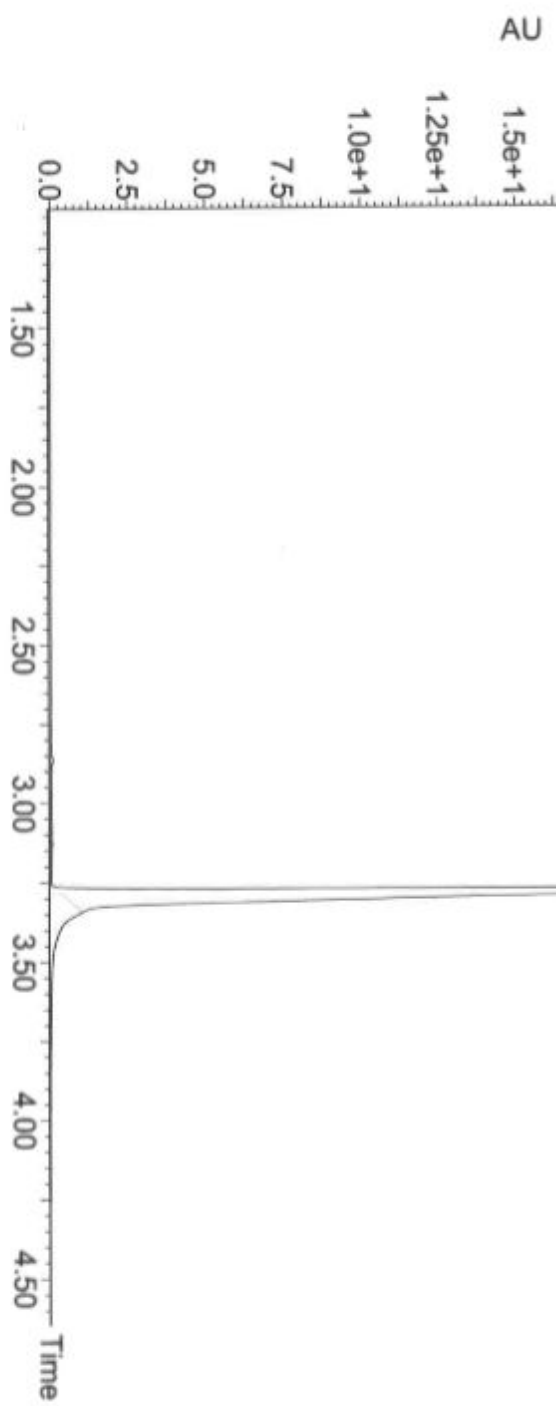
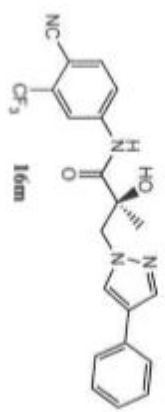
376.1040



YH-II-011_20191007_14

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Range: 3.061e+1

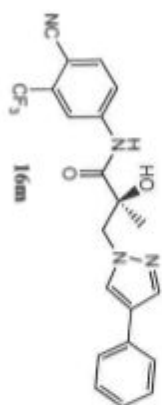
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3.13	38539	2714.62	0.33
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YH-II-011_20191007_14 275 (3.330)

437.1192

1: TOF MS ES+
2.26e6

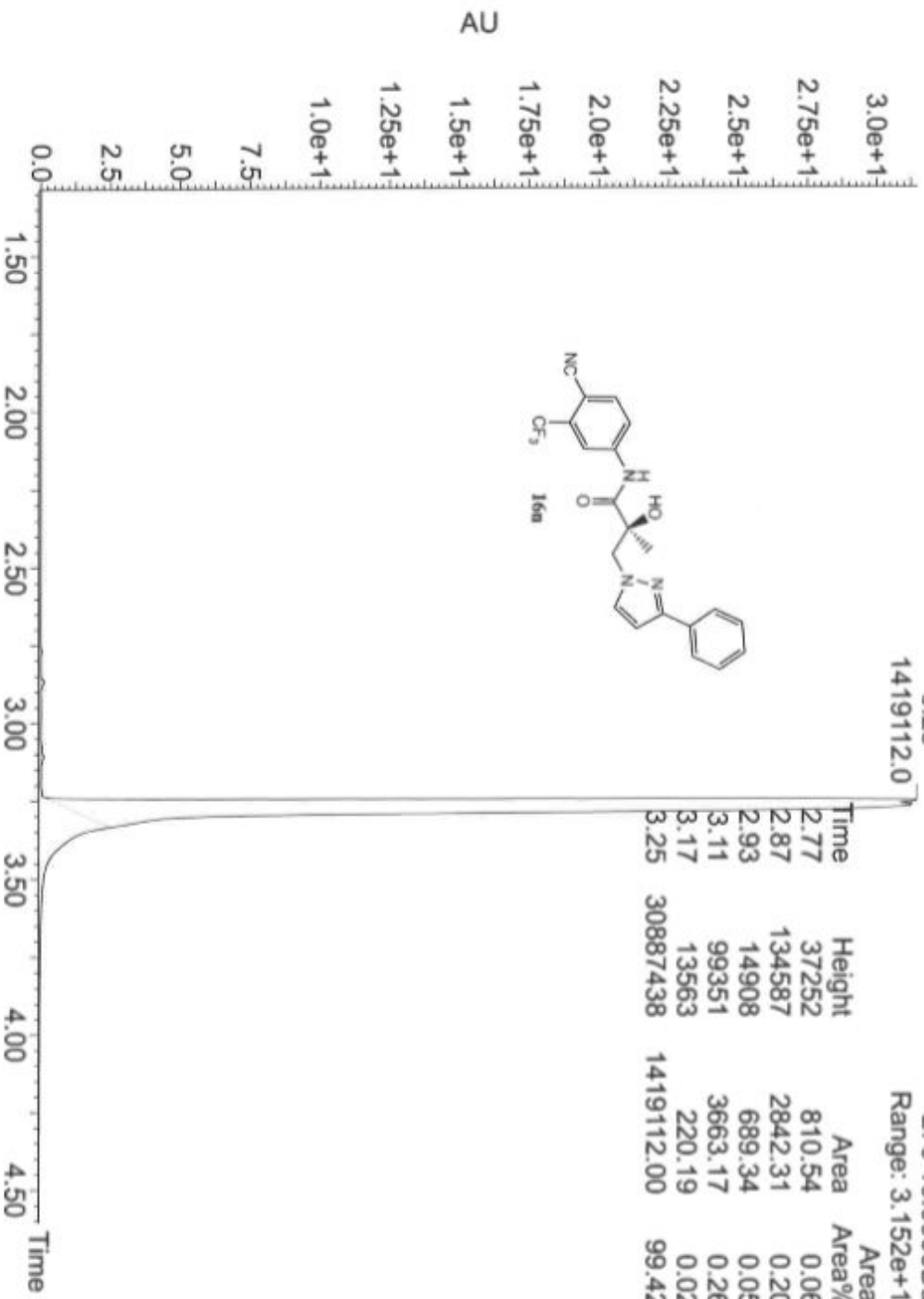


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438.1224

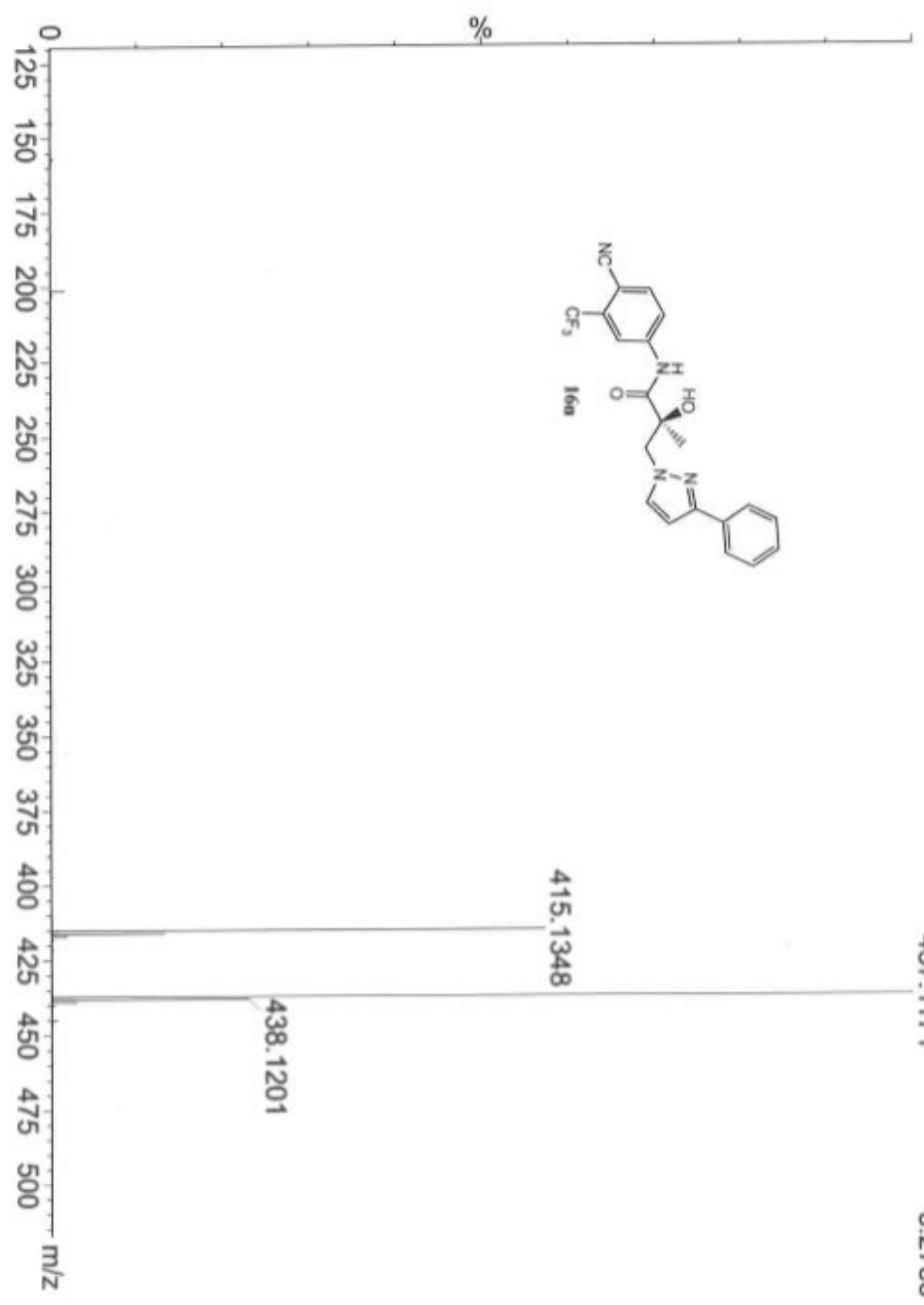
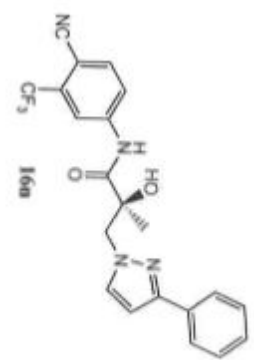


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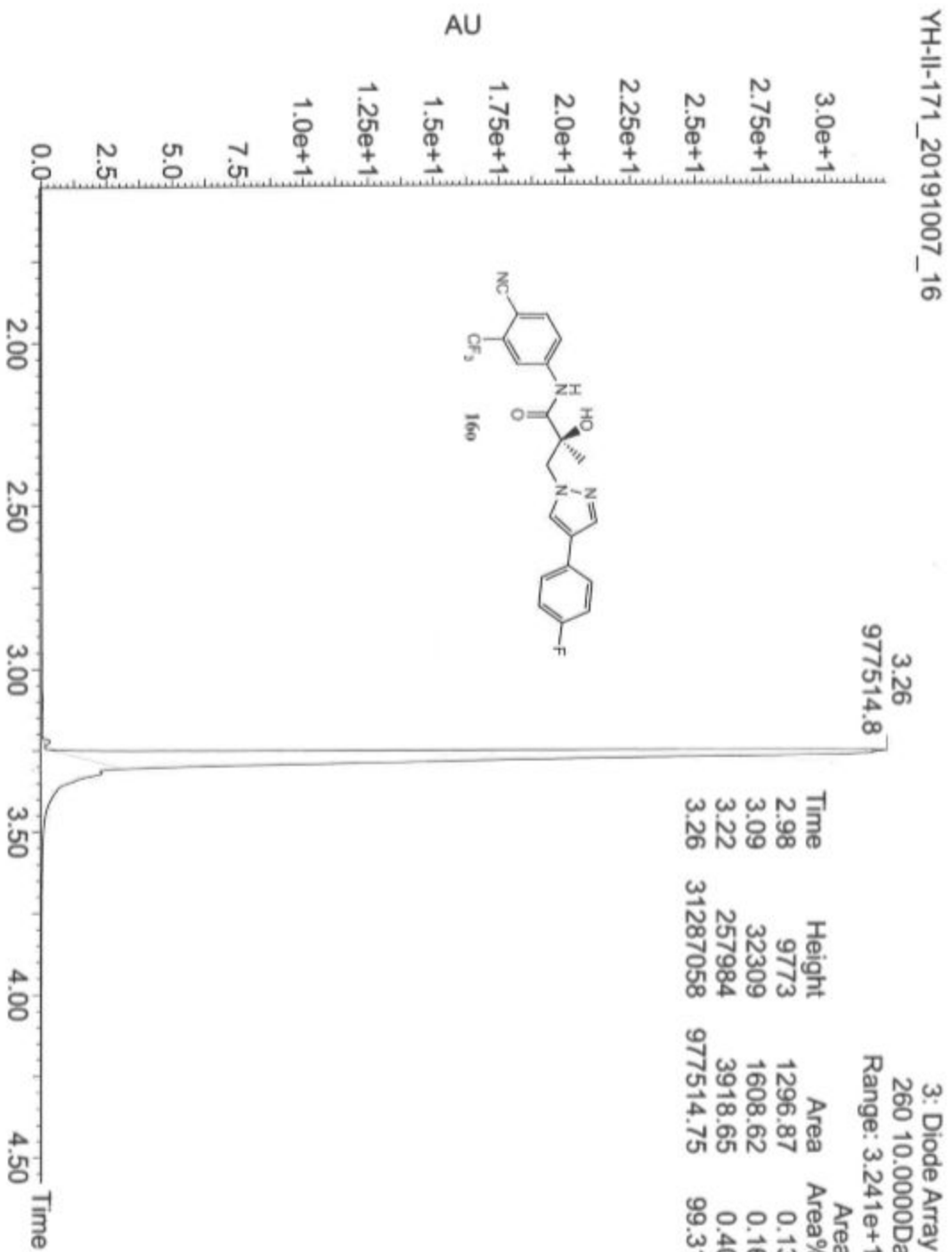


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3.27e6

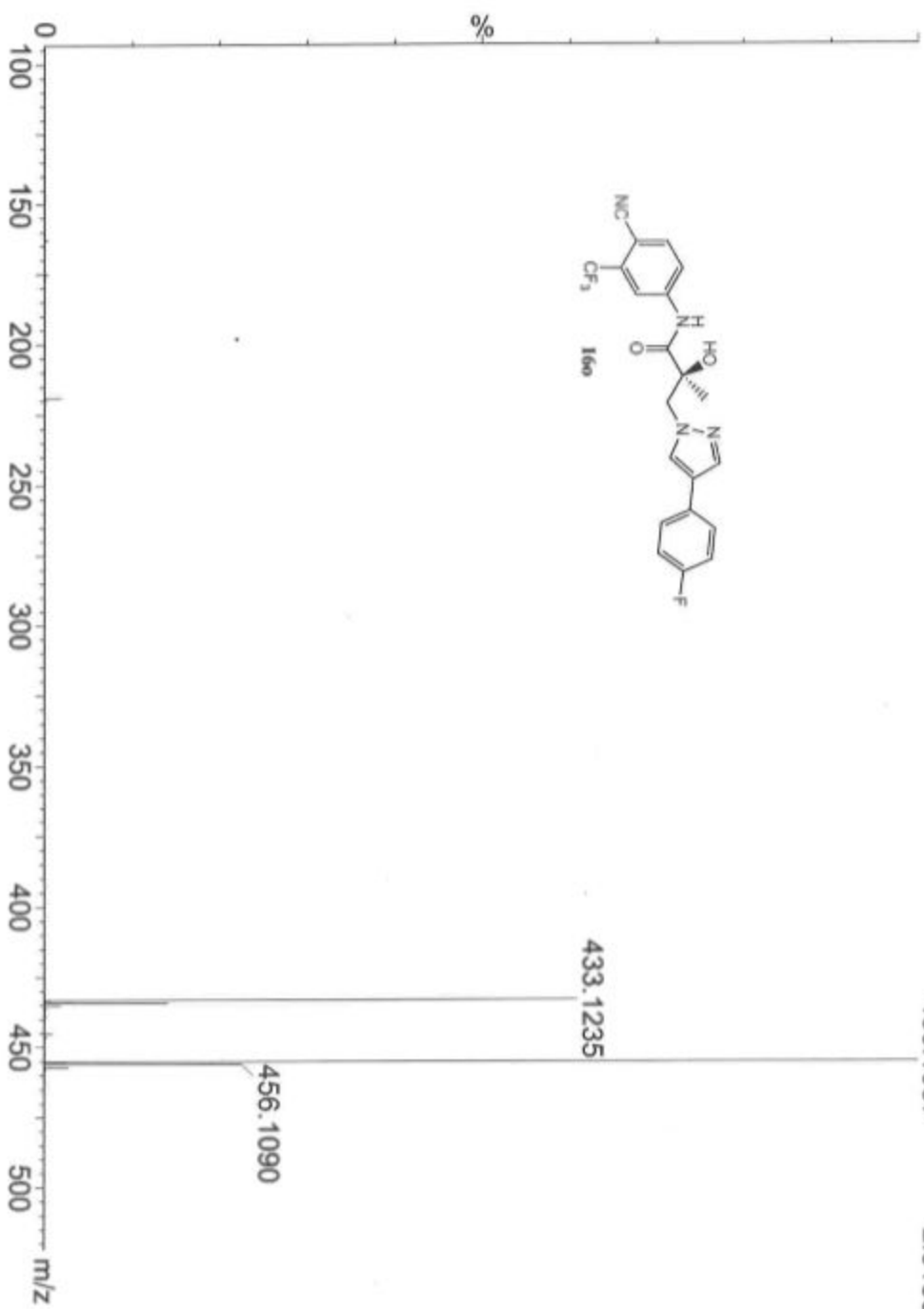
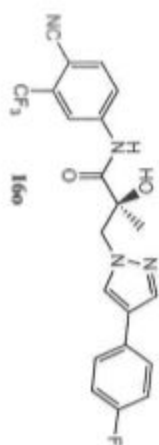


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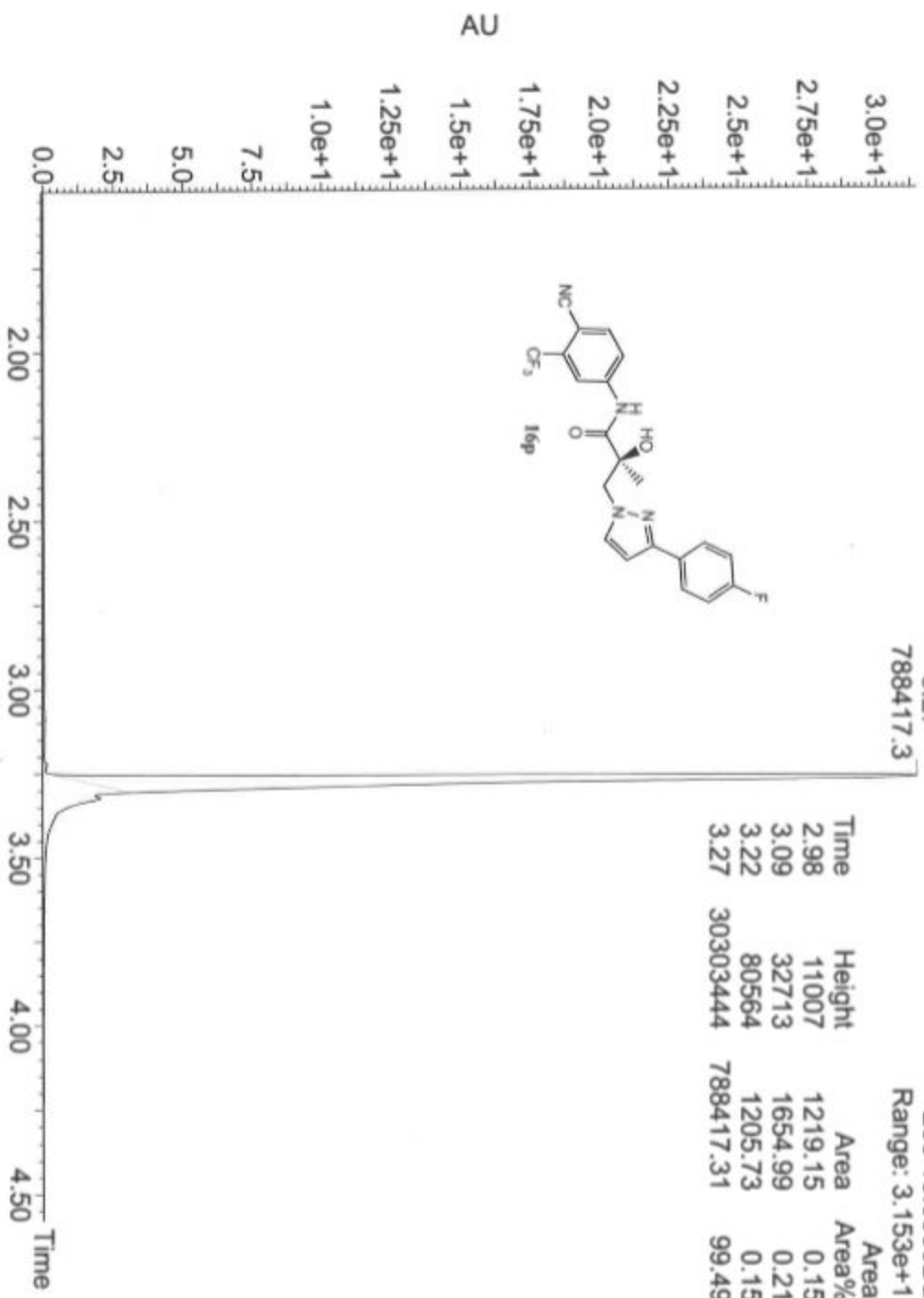


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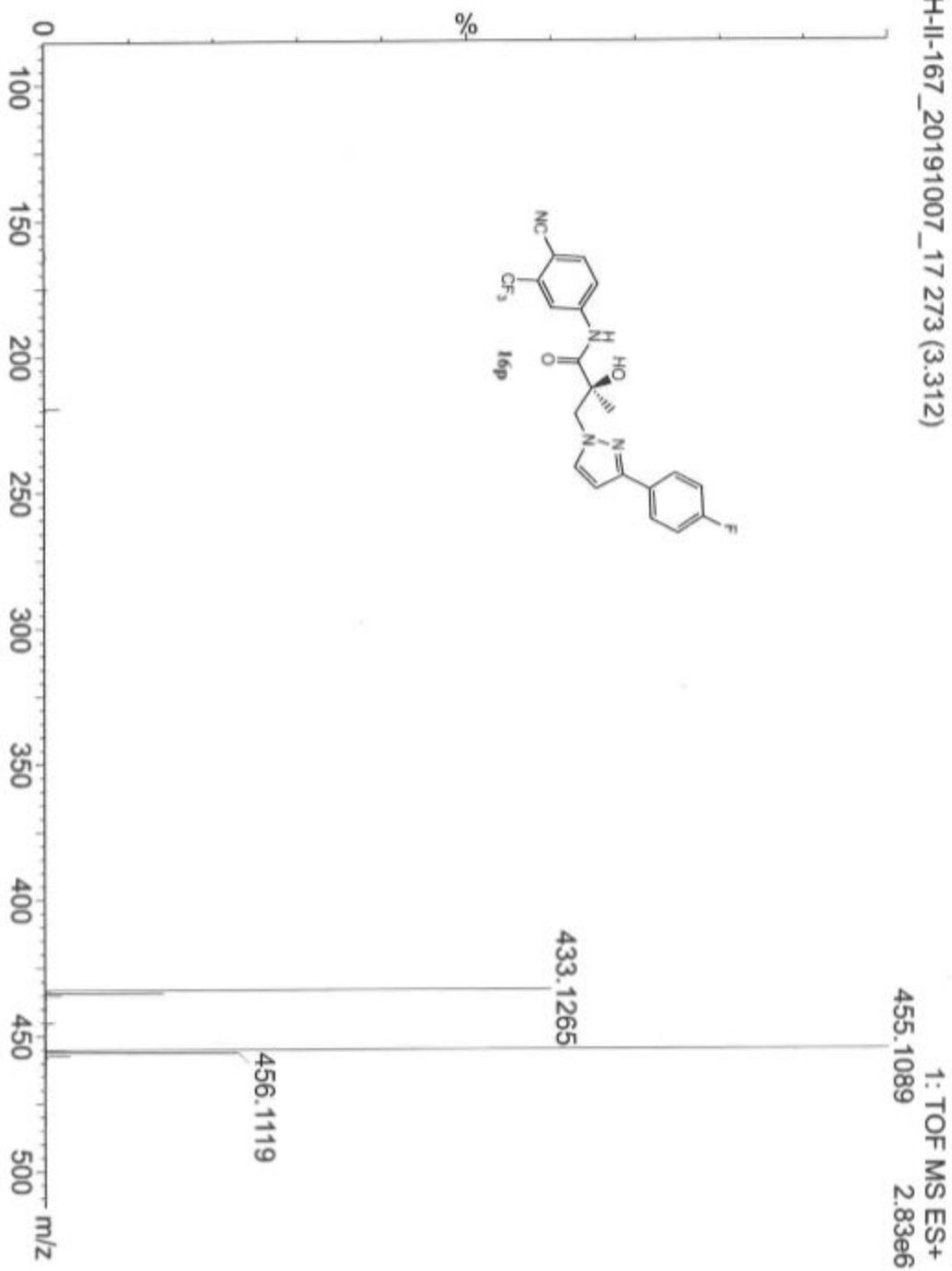
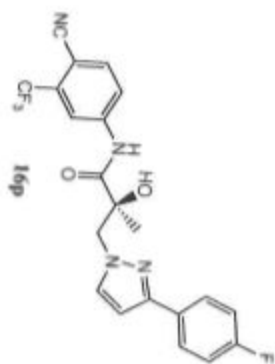
1: TOF MS ES+
455.1057 2.81e6



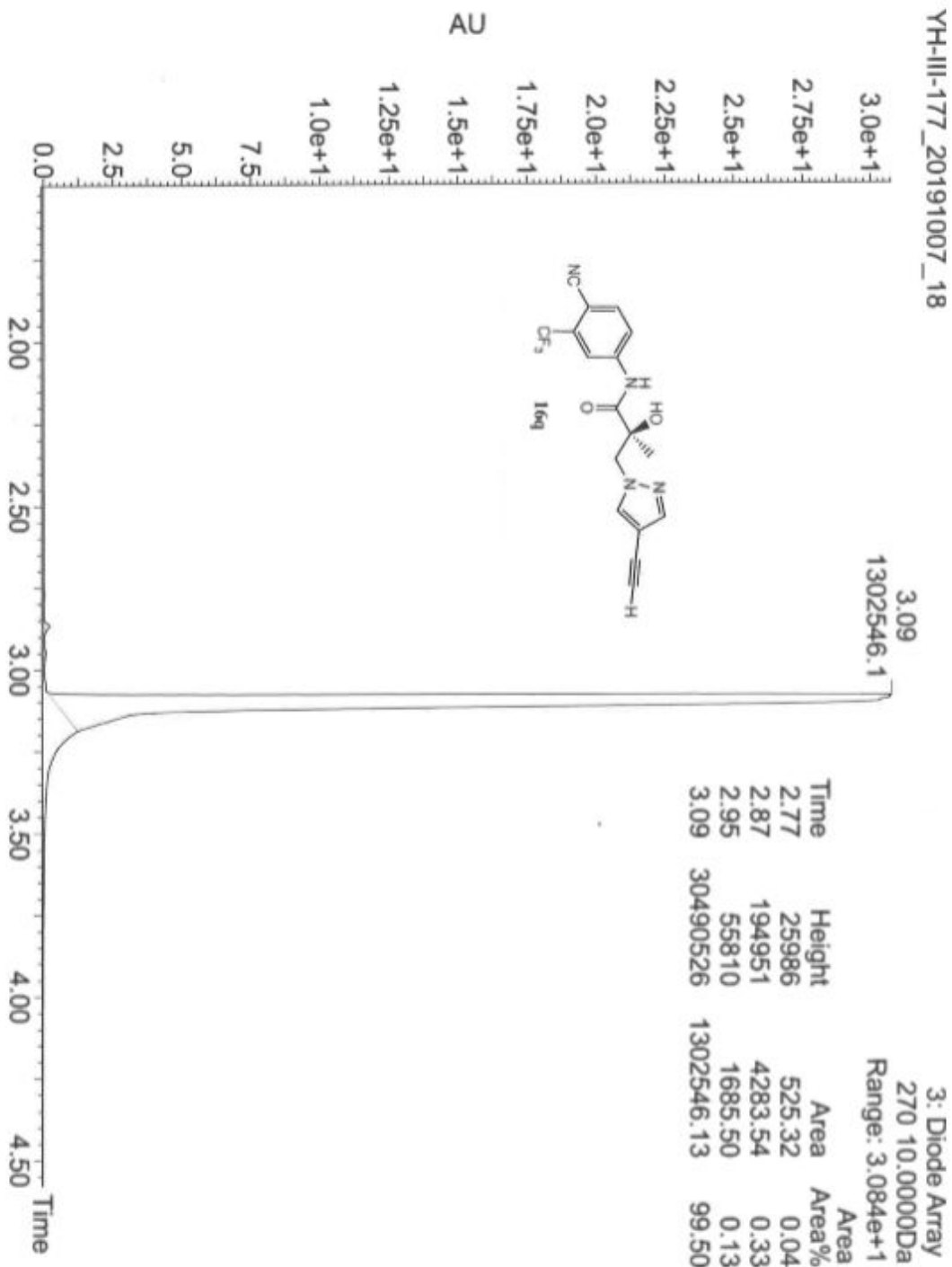
YH-II-167_20191007_17



YH-II-167_20191007_17 273 (3.312)

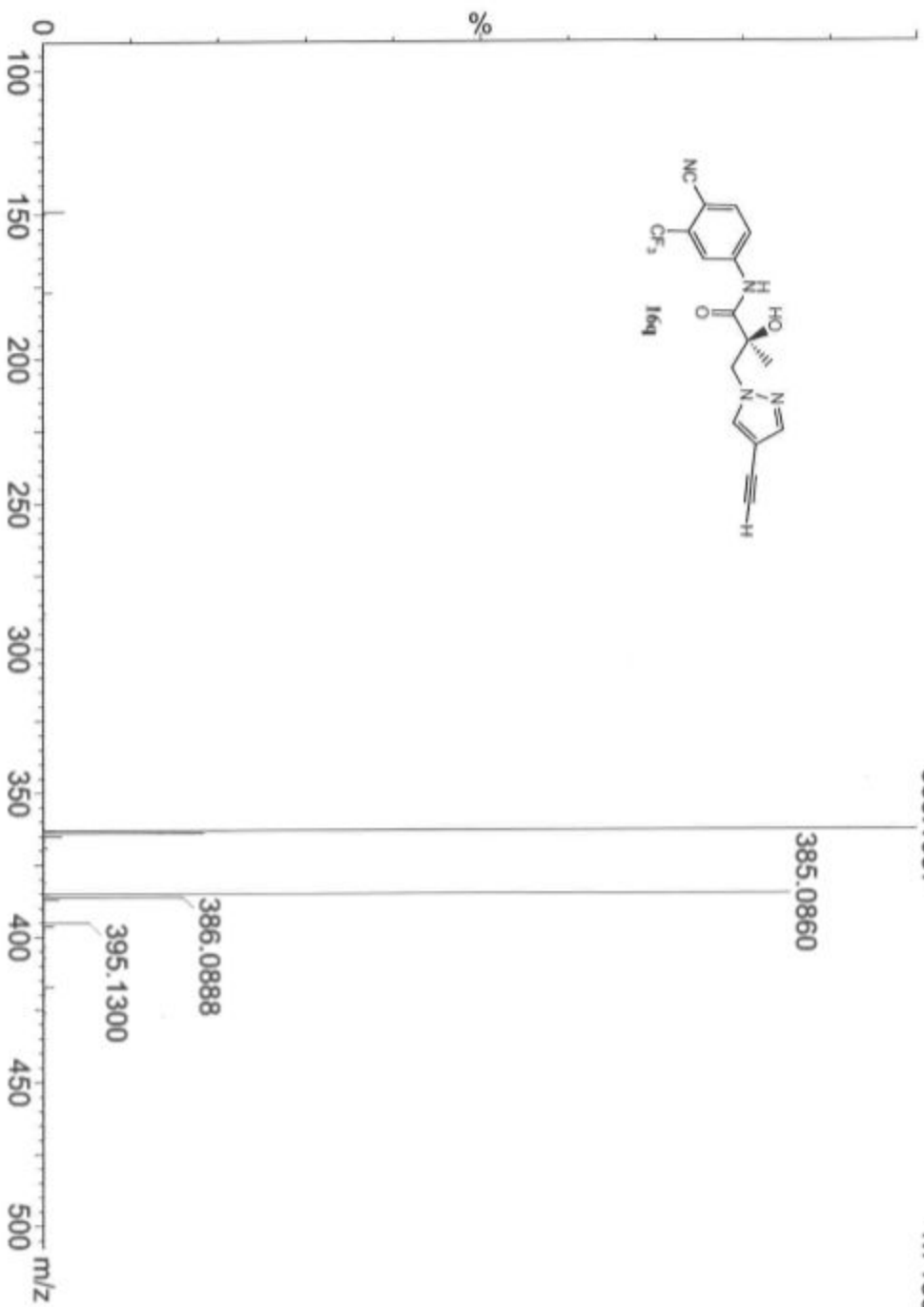
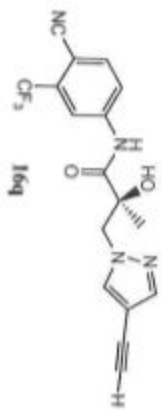


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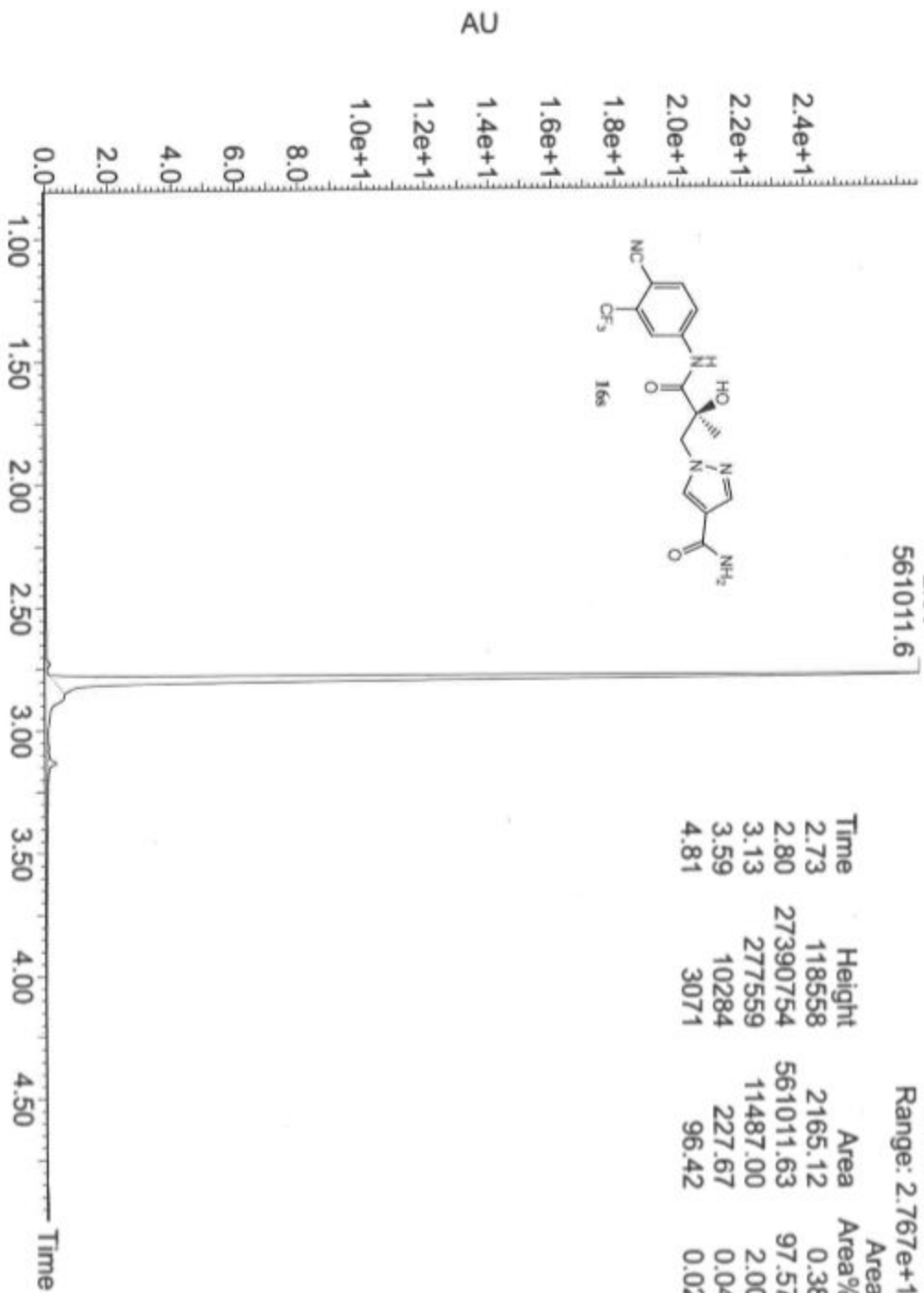


YH-III-177_20191007_18 255 (3.147)

1: TOF MS ES+
1.71e6



DJ-VII-157_16s_20191112_1



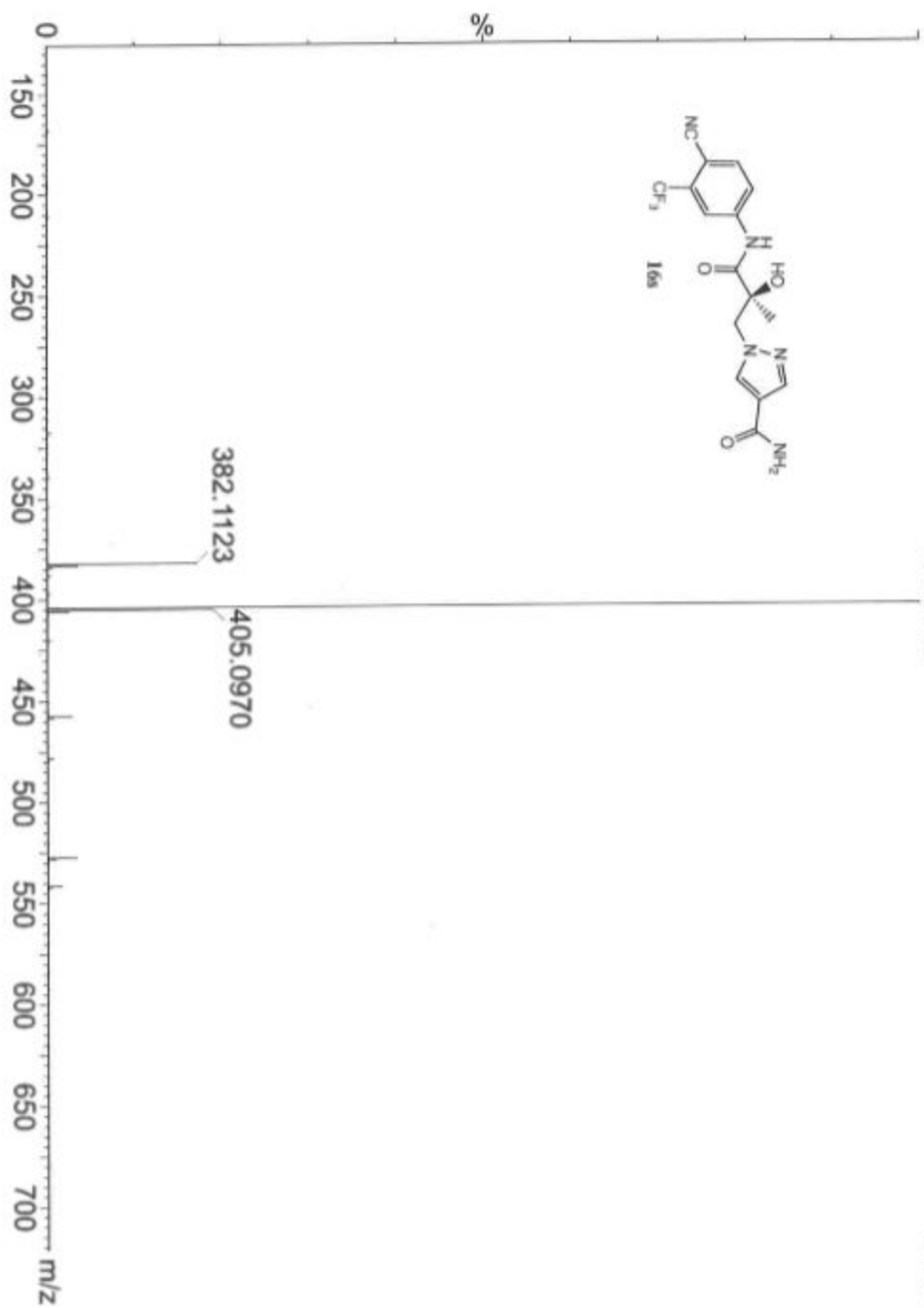
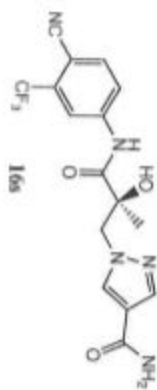
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Range: 2.767e+1

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2.80	27390754	561011.63	97.57
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3.59	10284	227.67	0.04
4.81	3071	96.42	0.02

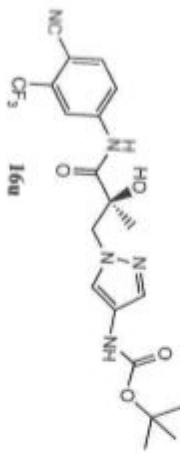
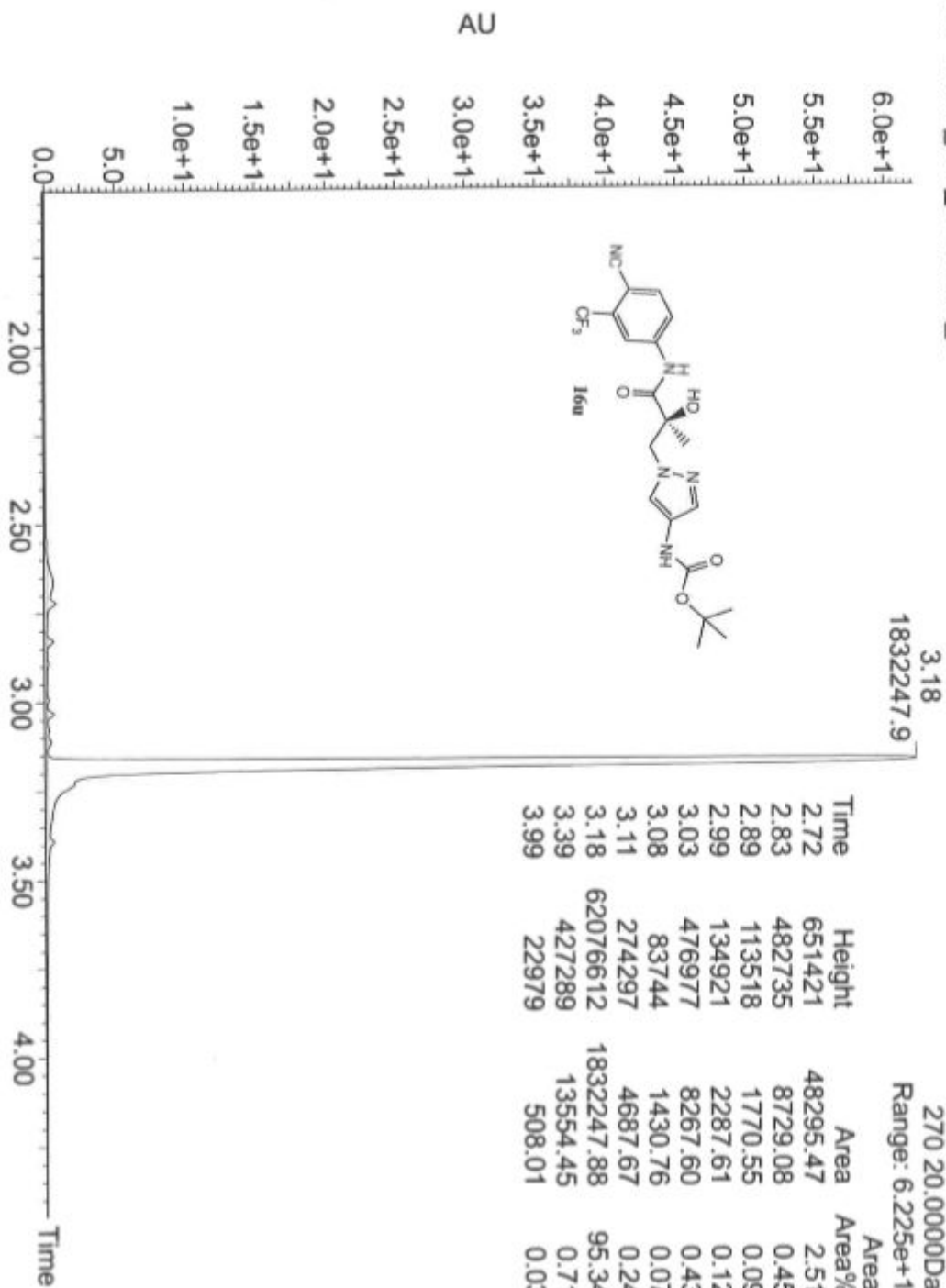
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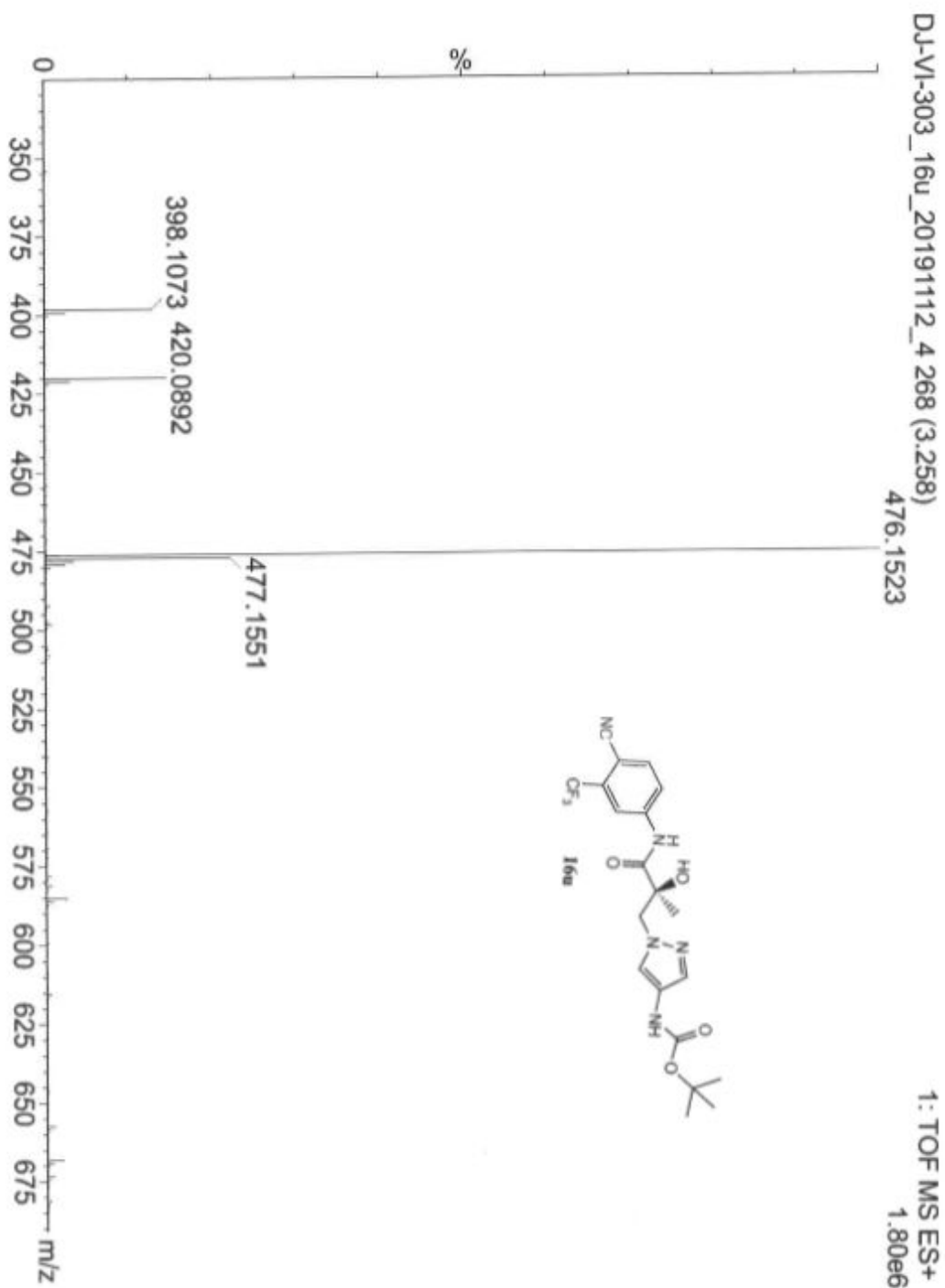
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1.42e6



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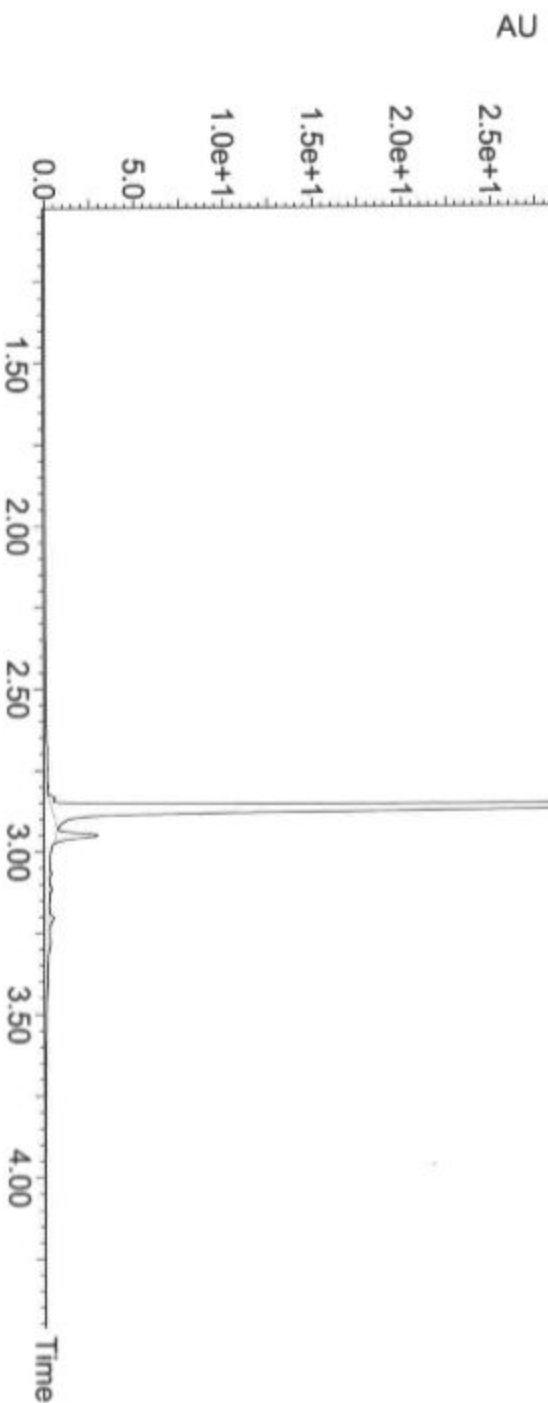
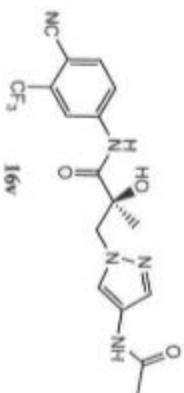


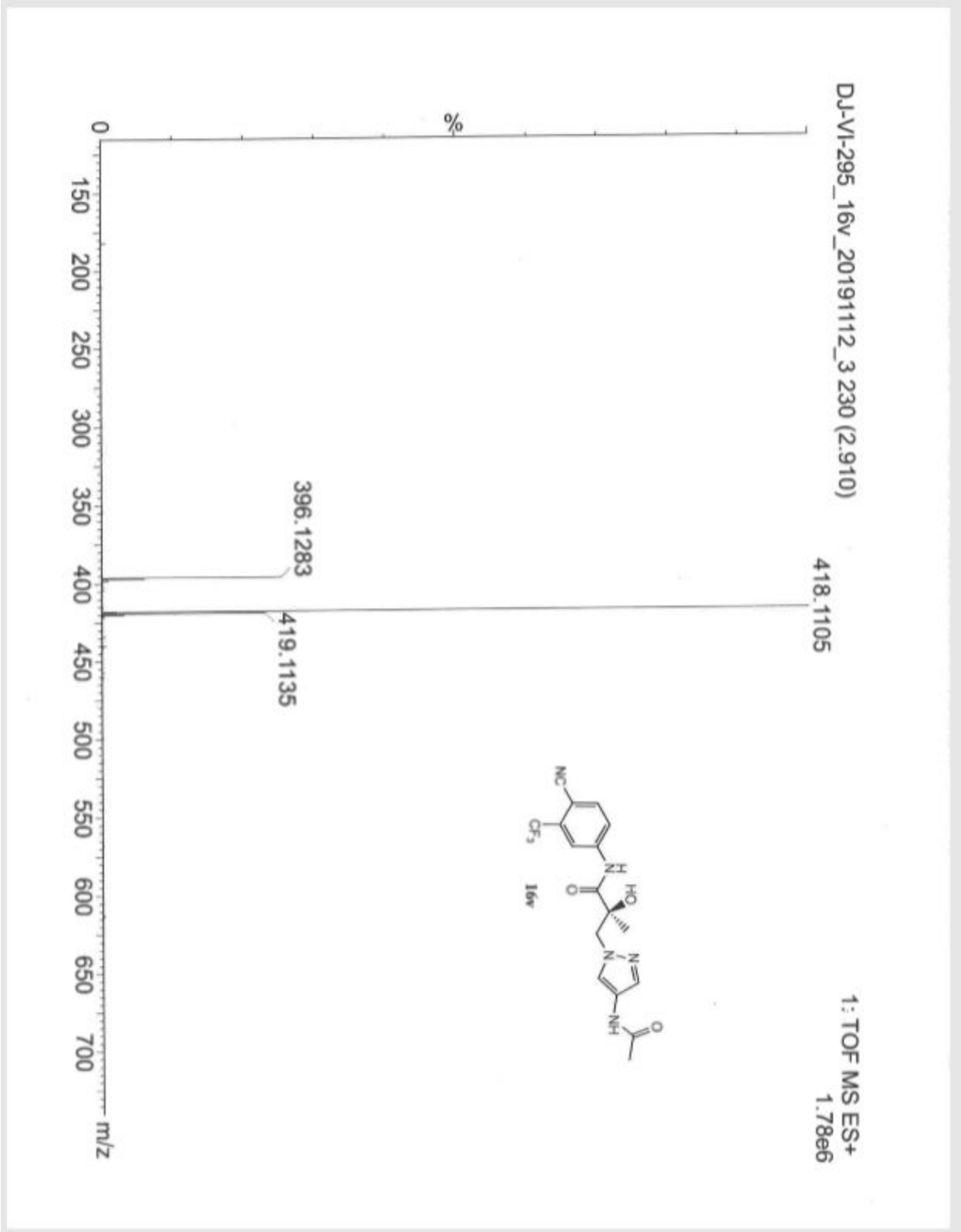
DJ-VI-295_16v_20191112_3

2.87
1072651.9

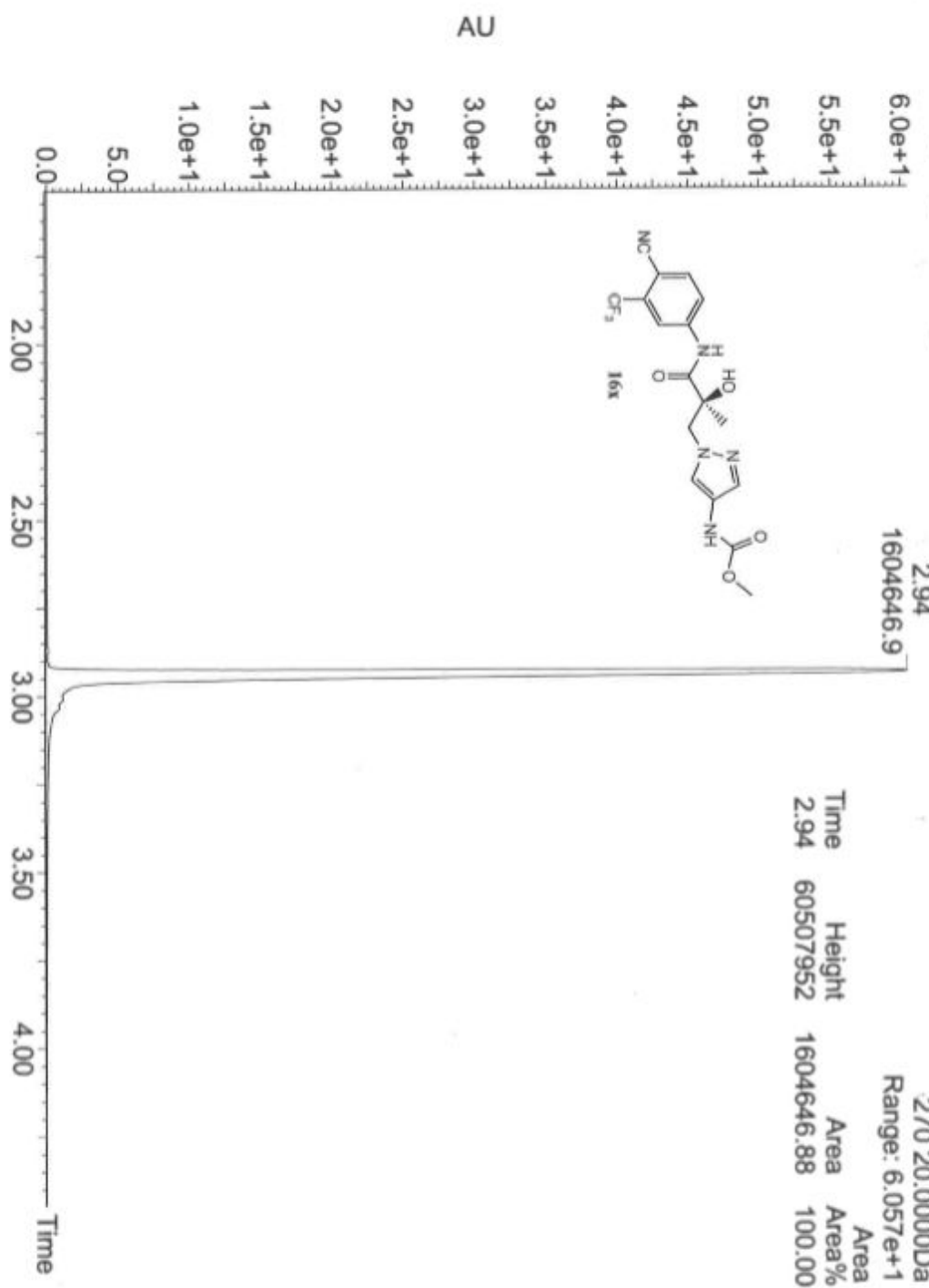
3: Diode Array
270 20.0000Da
Range: 5.335e+1

Time	Height	Area	Area%
2.80	70956	2187.71	0.19
2.87	52913068	1072651.88	94.26
2.95	2329878	42993.16	3.78
3.03	15848	197.19	0.02
3.07	103582	1900.61	0.17
3.11	149561	4361.95	0.38
3.20	287191	13453.02	1.18
3.53	10878	214.56	0.02





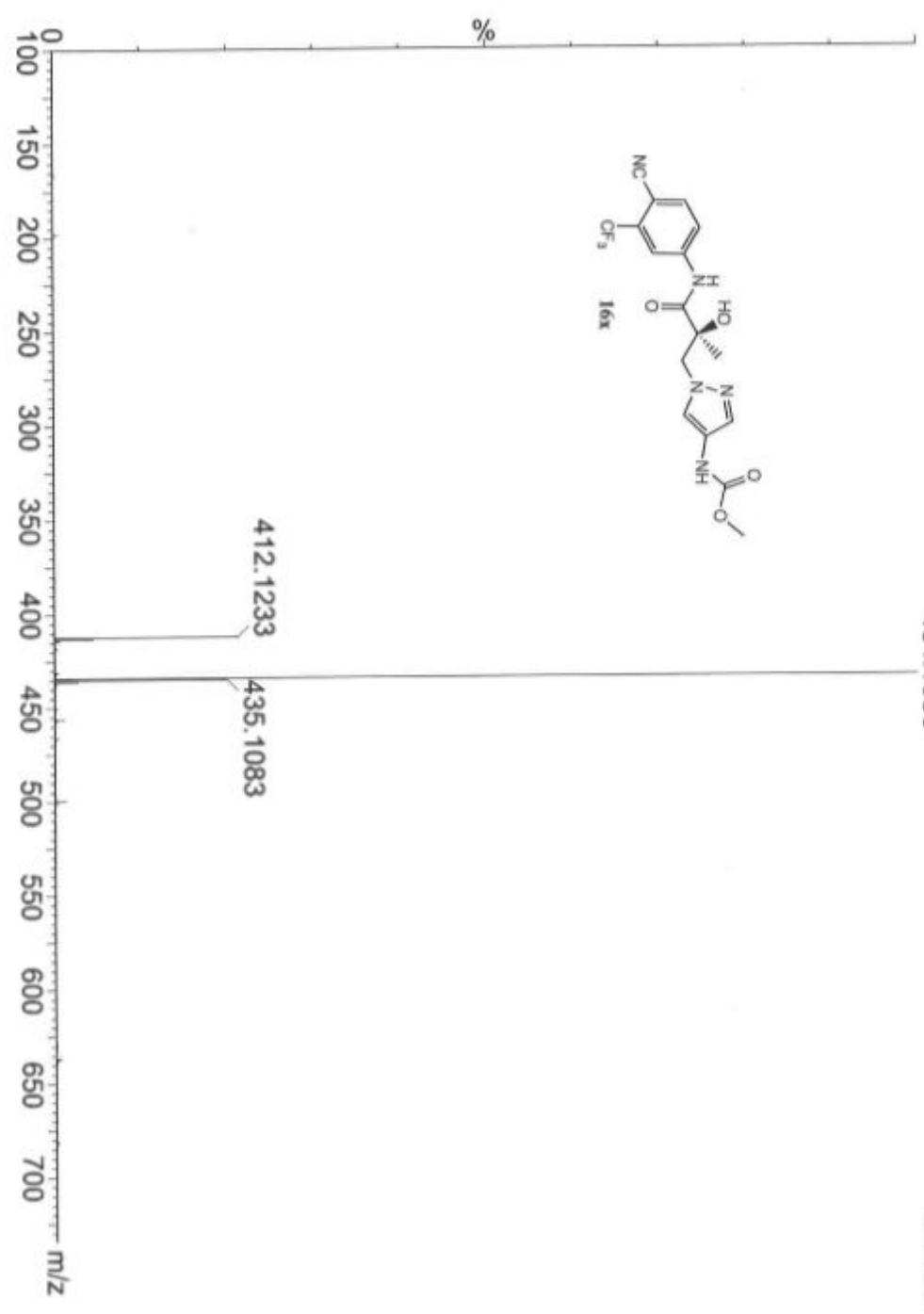
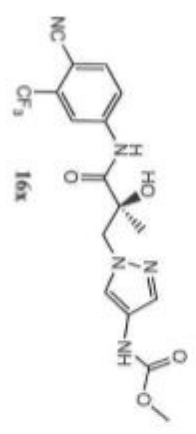
DJ-VII-003_16x_20191112_6



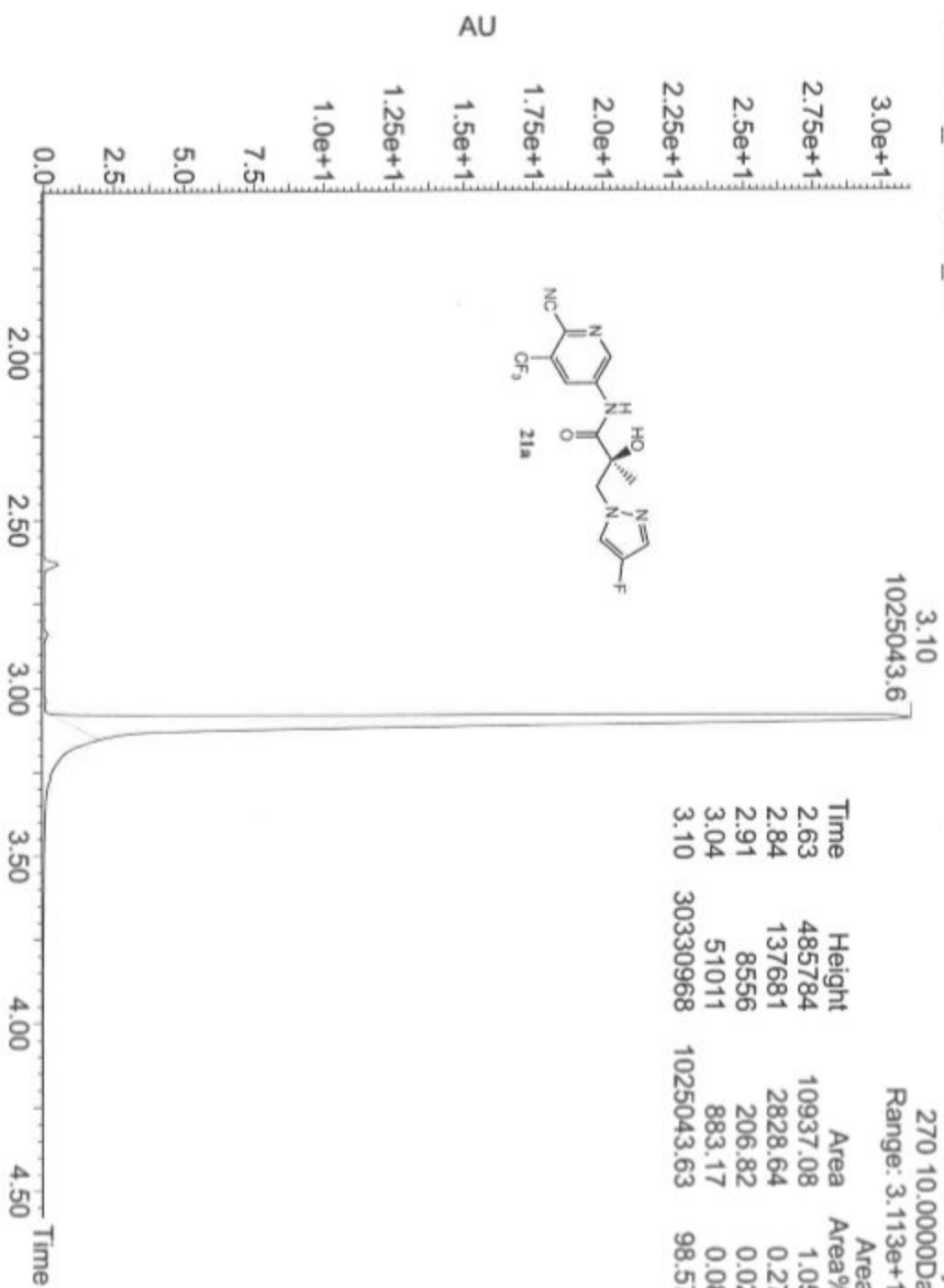
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434.1056

1: TOF MS ES+
2.01e6

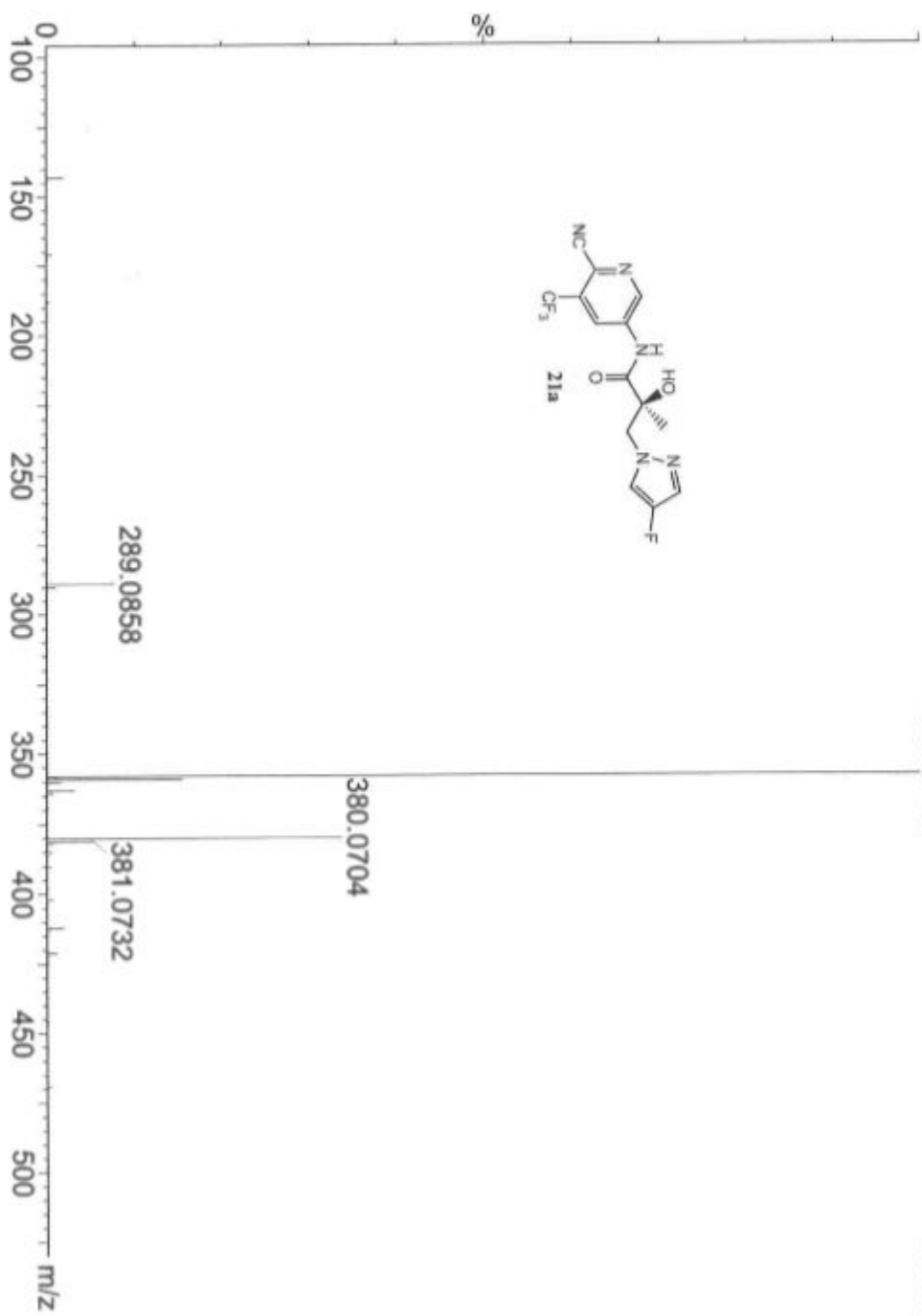


YH-II-151_20191007_20



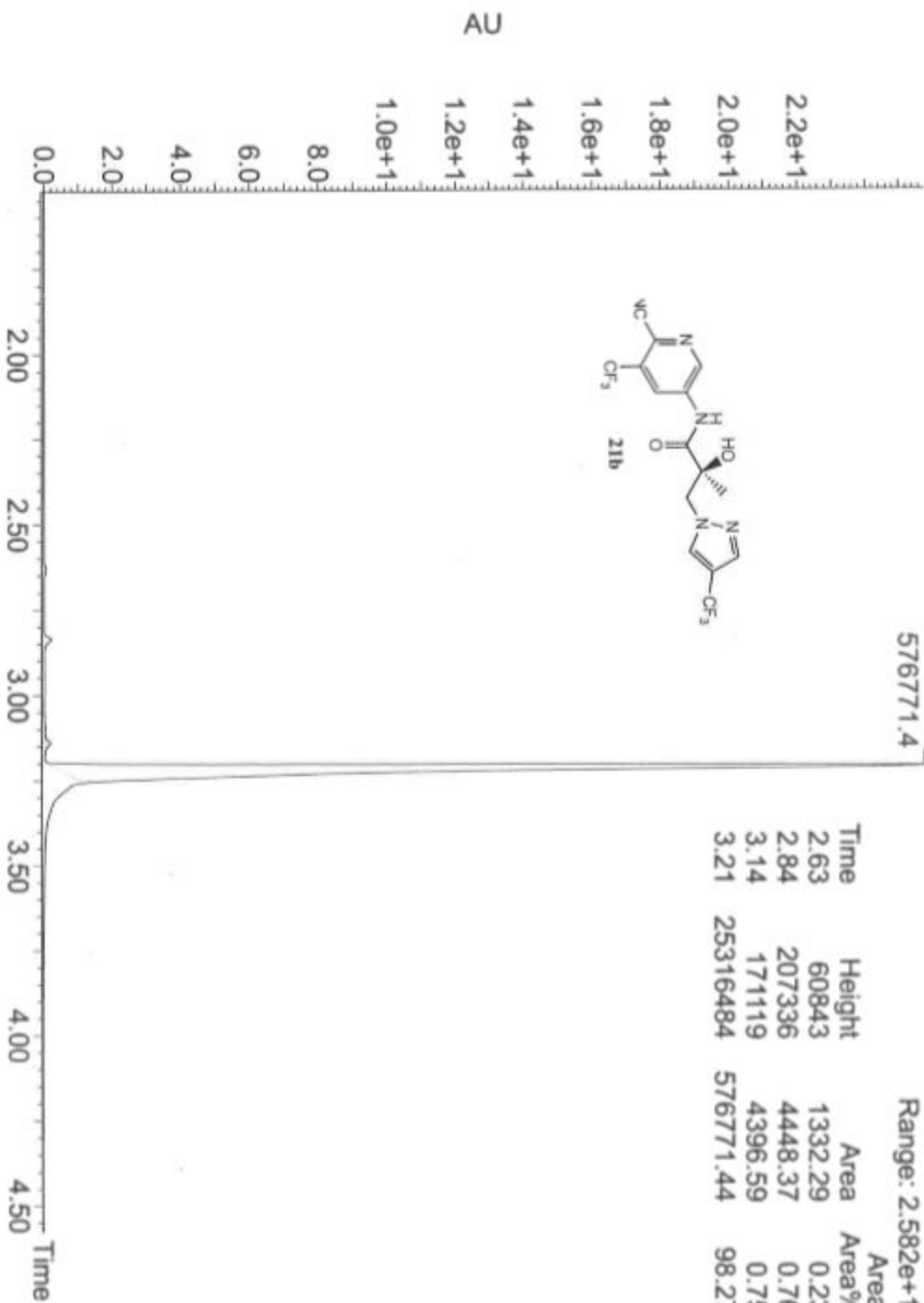
YH-II-151_20191007_20 255 (3.147)

1: TOF MS ES+
1.67e6

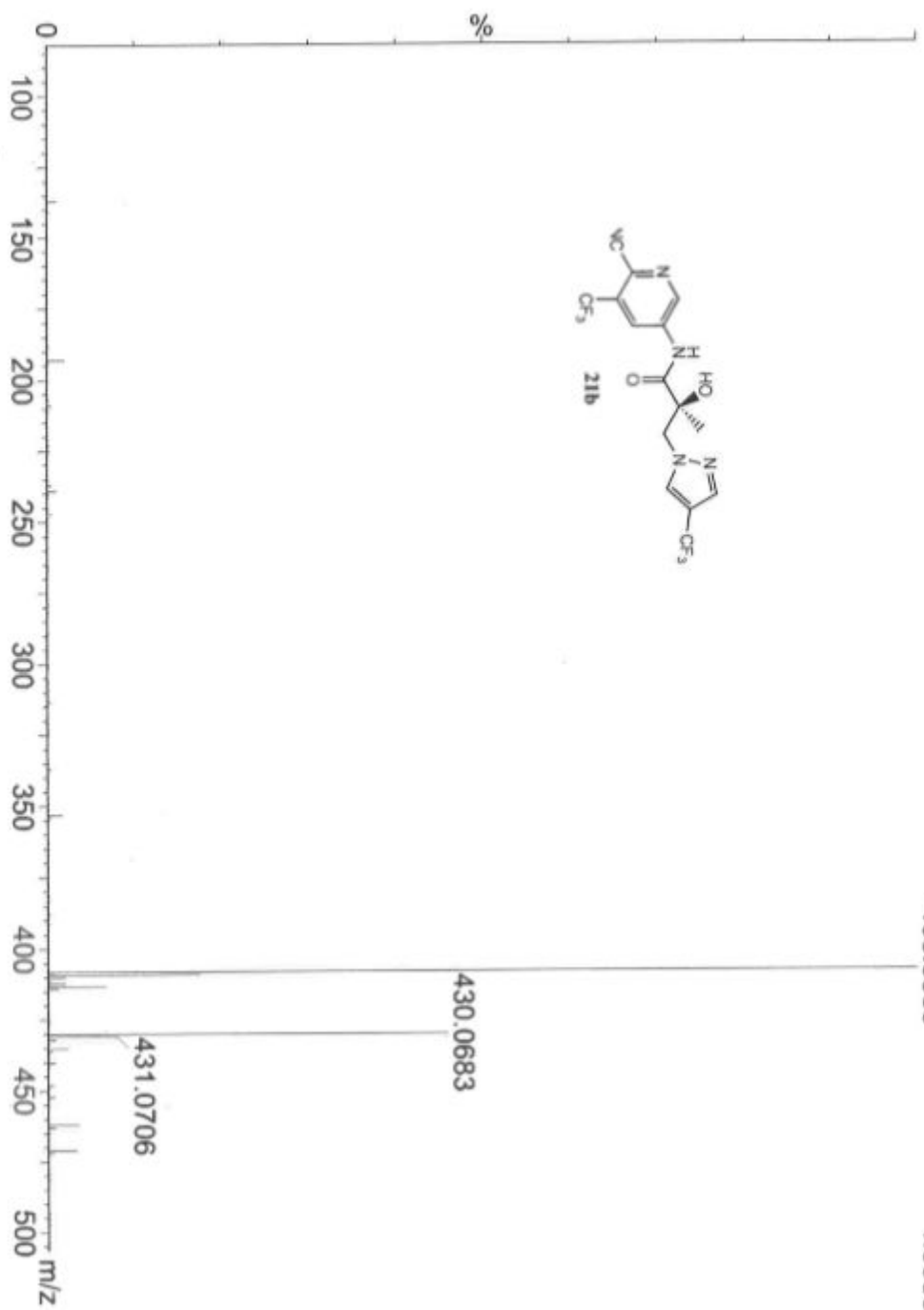
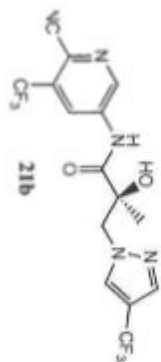


YH-II-215_20191007_21

3.21
576771.4

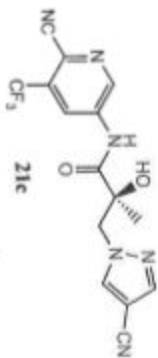


YH-II-215_20191007_21 269 (3.267)



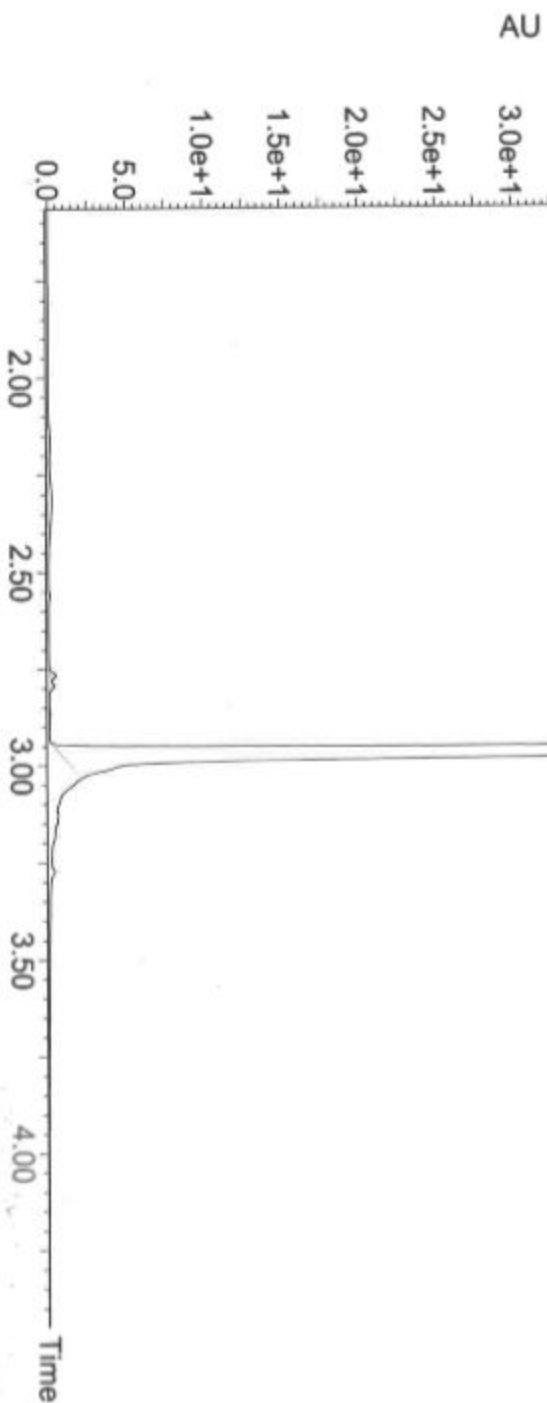
DJ-VII-105_21c_20191112_7

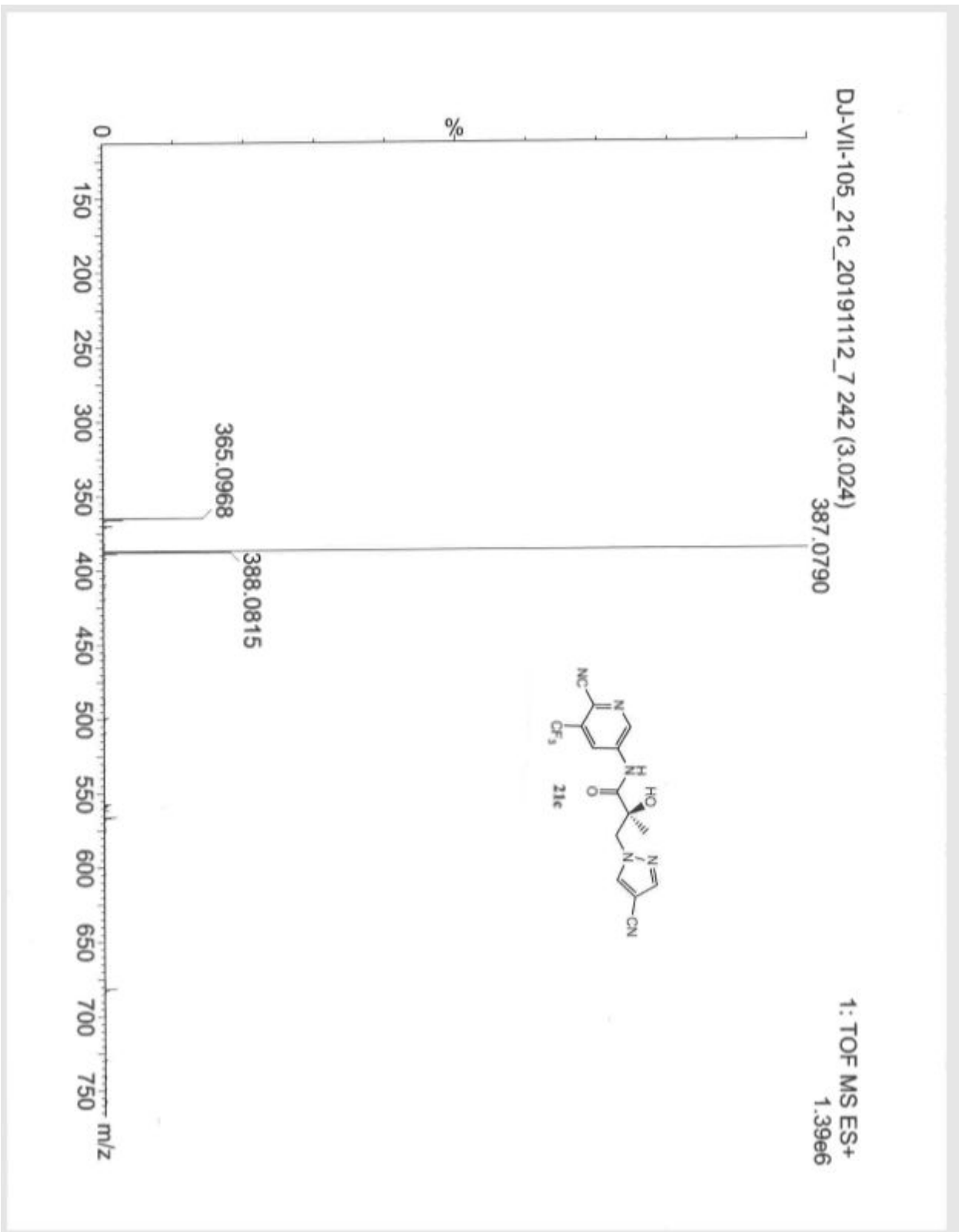
2.97
1957980.8



Time	Height	Area	Area%
2.32	230843	42442.63	2.11
2.56	80705	1832.23	0.09
2.77	358458	5488.17	0.27
2.79	237369	3509.15	0.17
2.87	57791	1432.92	0.07
2.97	60792188	1957980.75	97.28

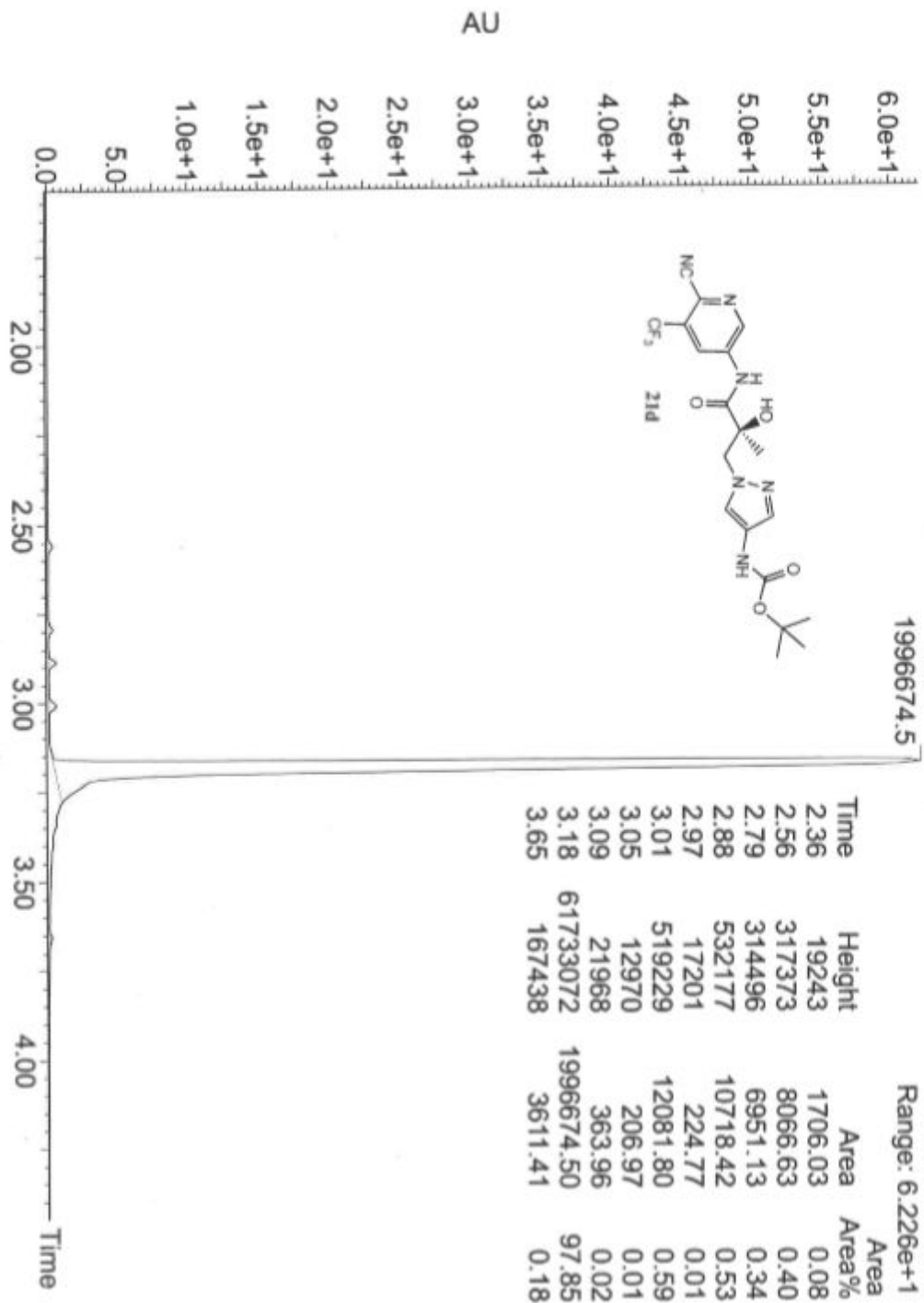
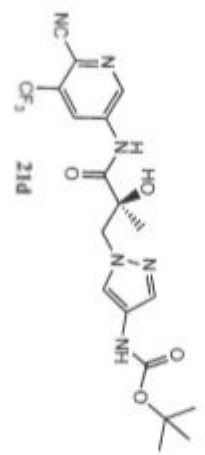
3: Diode Array
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Range: 6.162e+1





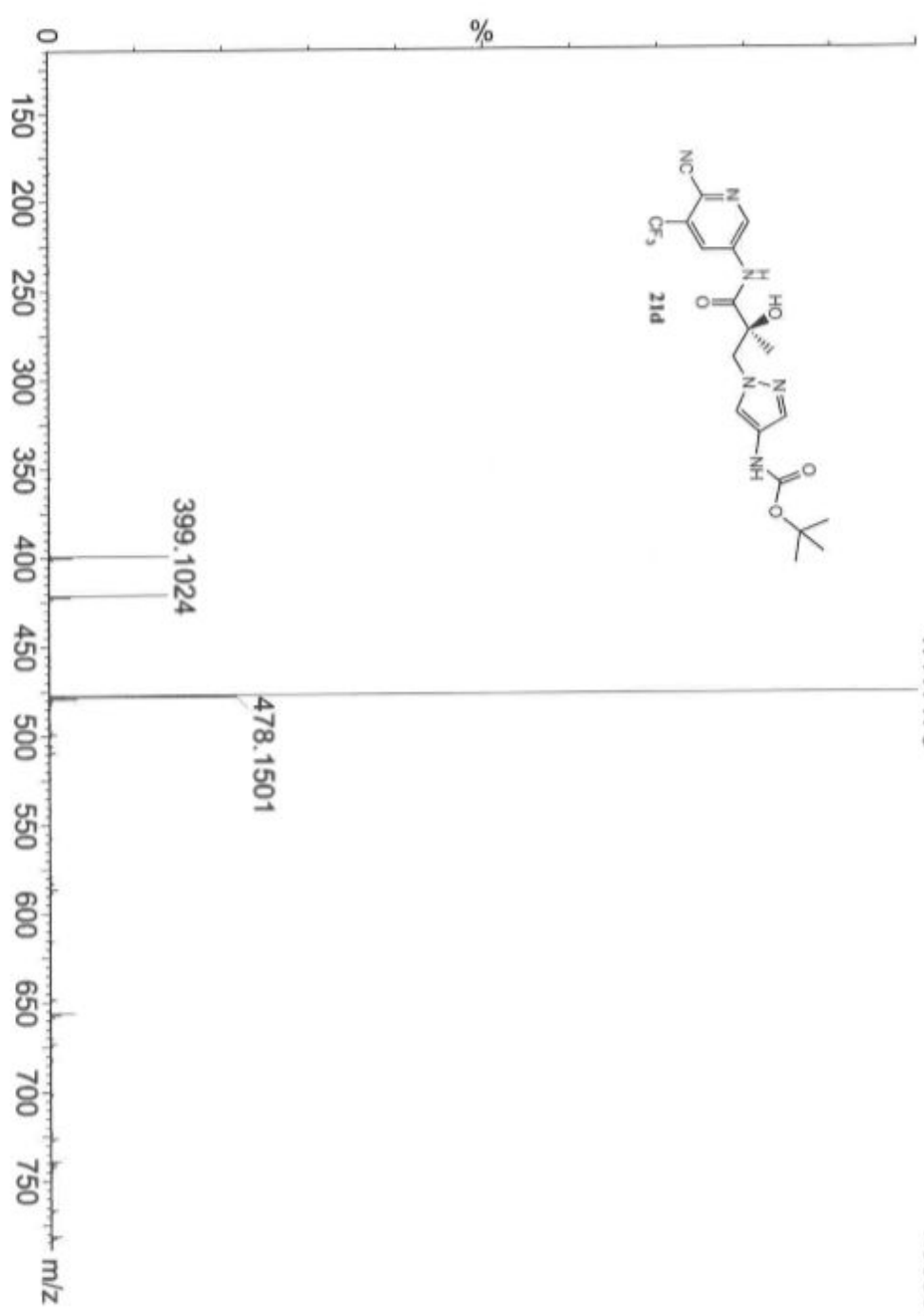
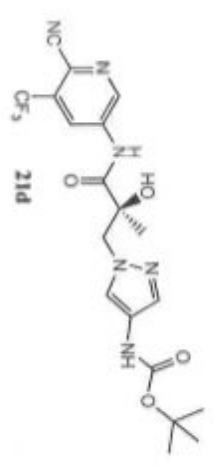
DJ-VI-297_21d_20191112_8

3.18
1996674.5



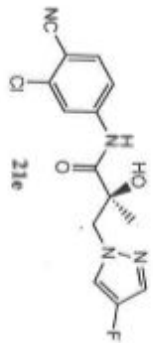
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1: TOF MS ES+
1.93e6



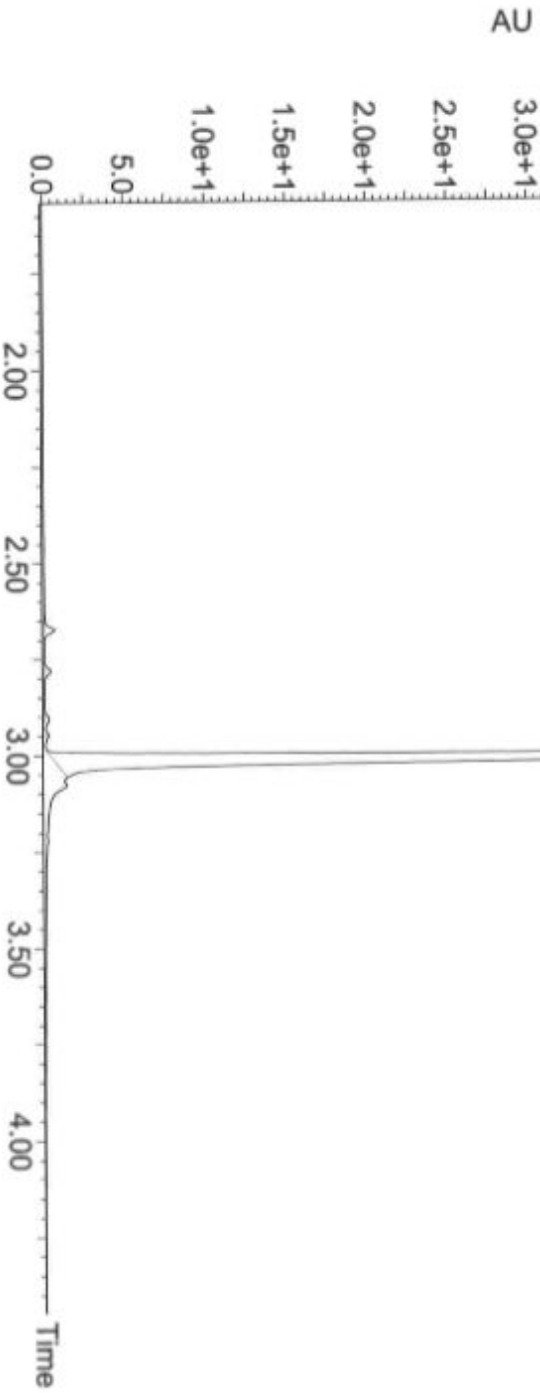
DJ-VI-167_21e_20191112_9

3.01
1386882.5



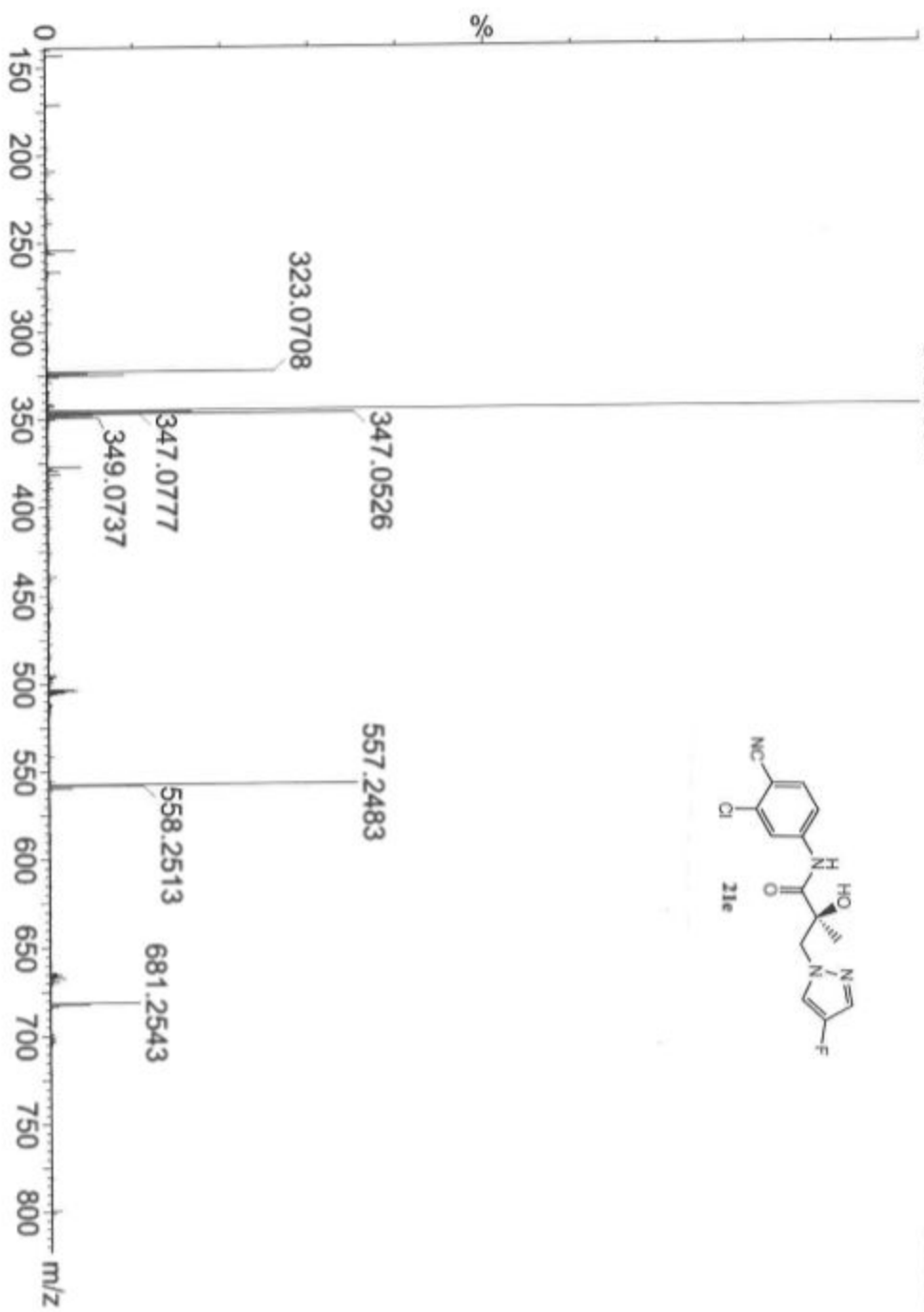
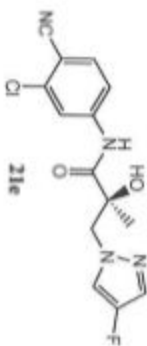
3: Diode Array
270 20.0000Da
Range: 5.866e+1

Time	Height	Area	Area%
2.45	13673	418.50	0.03
2.67	626295	13909.33	0.98
2.78	385019	7924.19	0.56
2.85	10133	182.50	0.01
2.91	236846	5660.67	0.40
2.95	182382	3262.67	0.23
3.01	57997016	1386882.50	97.79

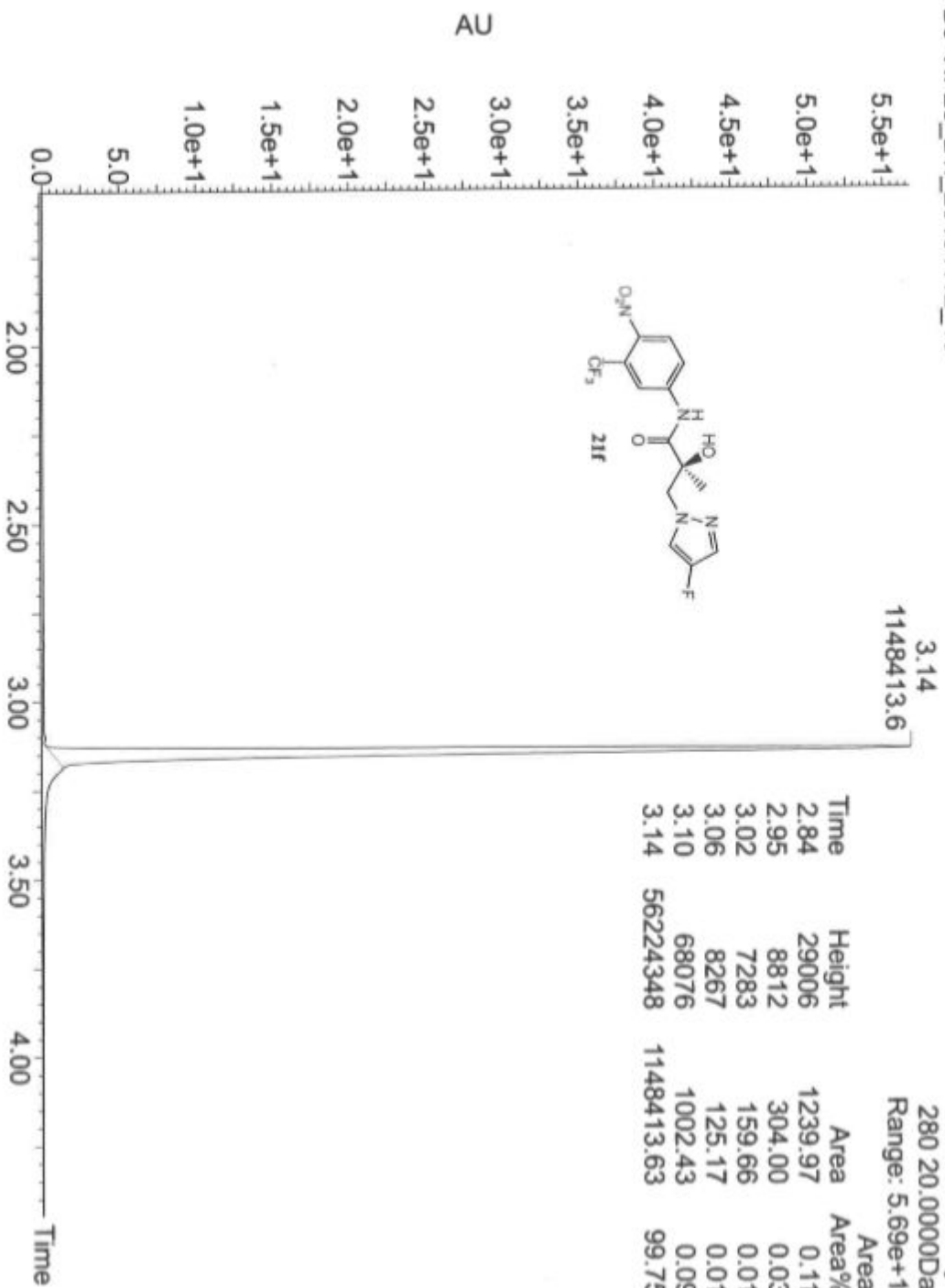


DJ-VI-167_21e_20191112_9 248 (3.075)
345.0531

1: TOF MS ES+
3.99e5



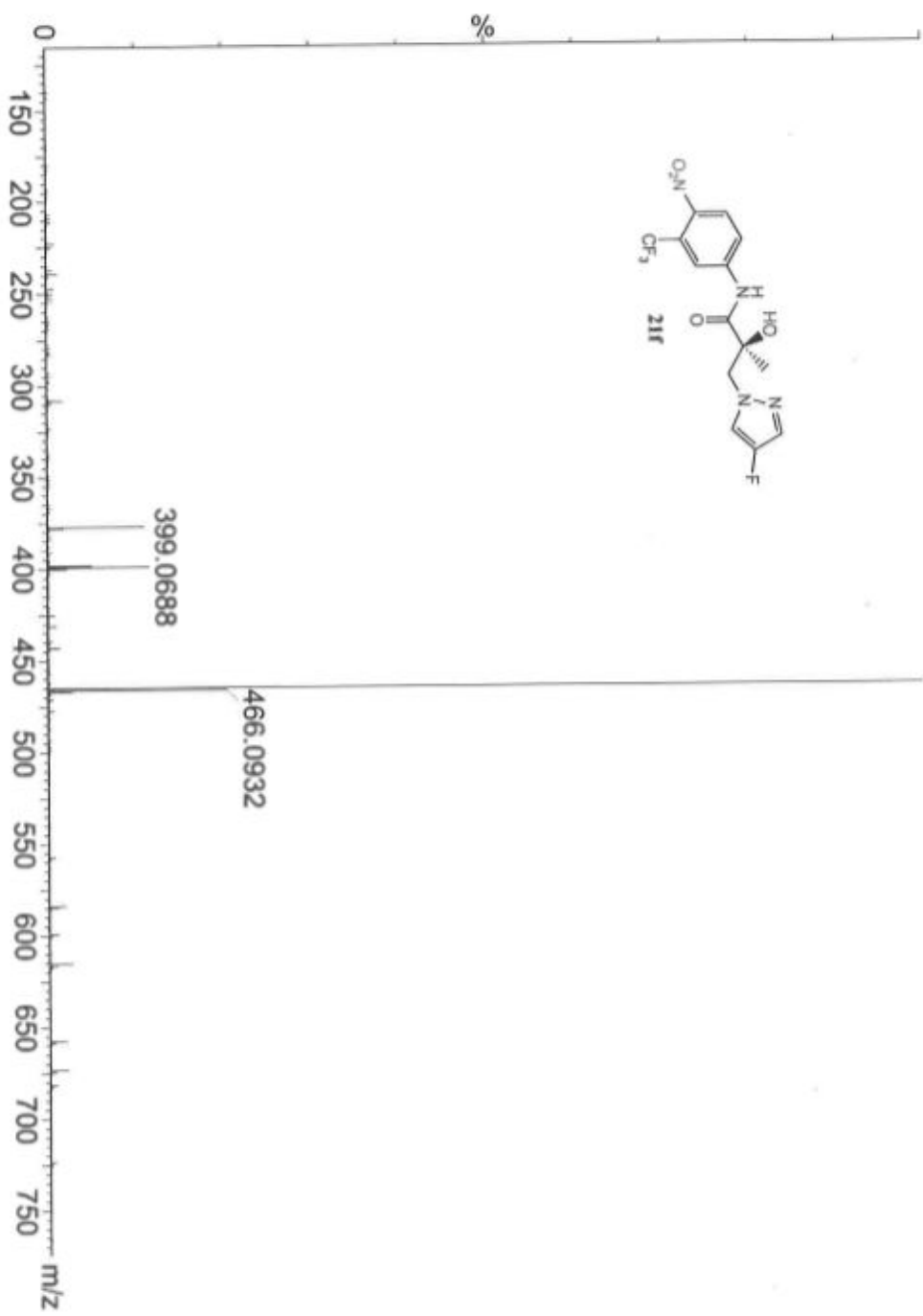
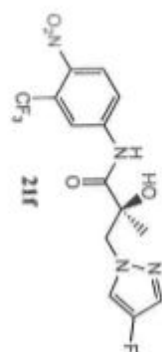
DJ-VII-23_21f_20191112_10

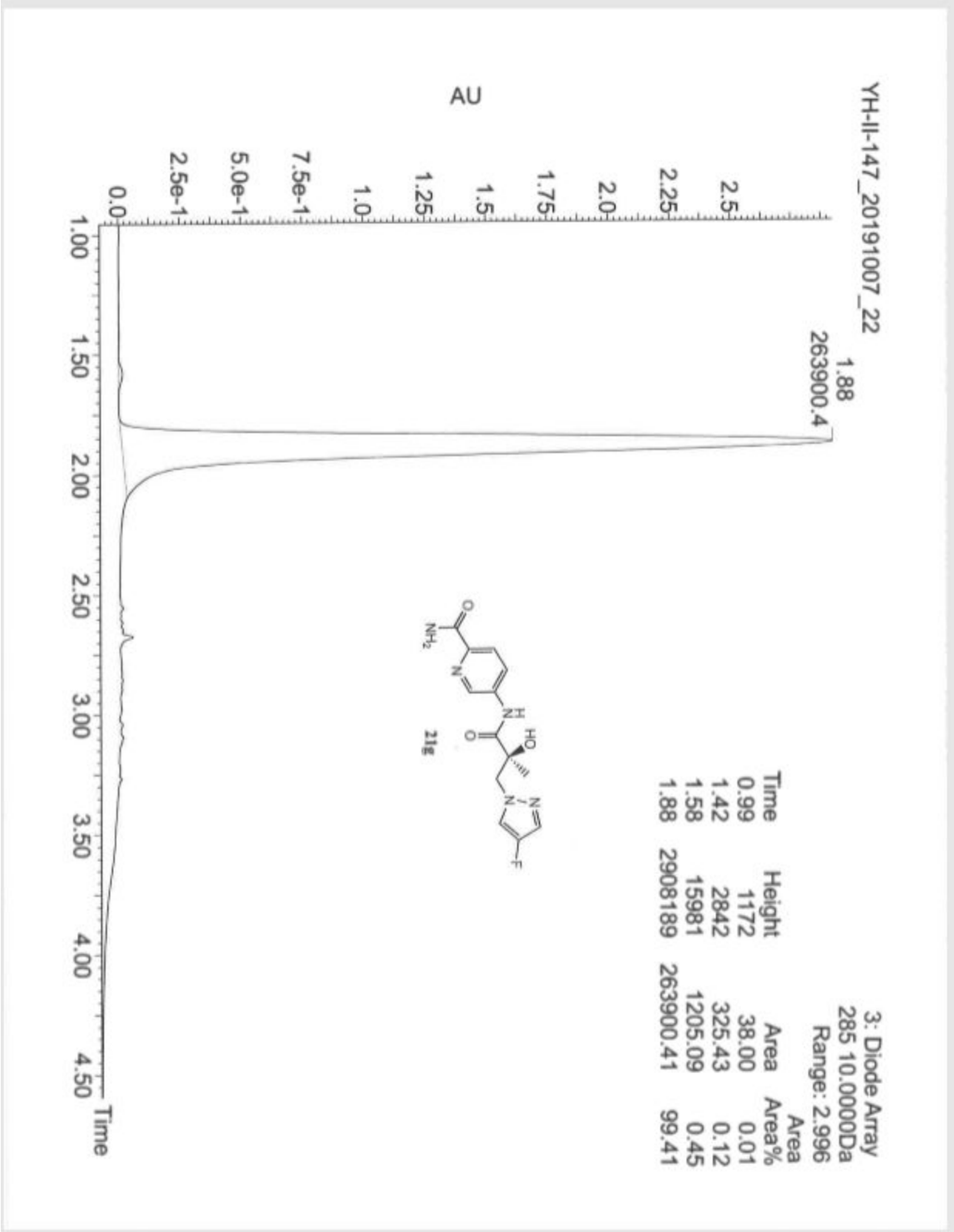


DJ-VII-23_21f_20191112_10 264 (3.224)

465.0906

1: TOF MS ES+
1.02e6

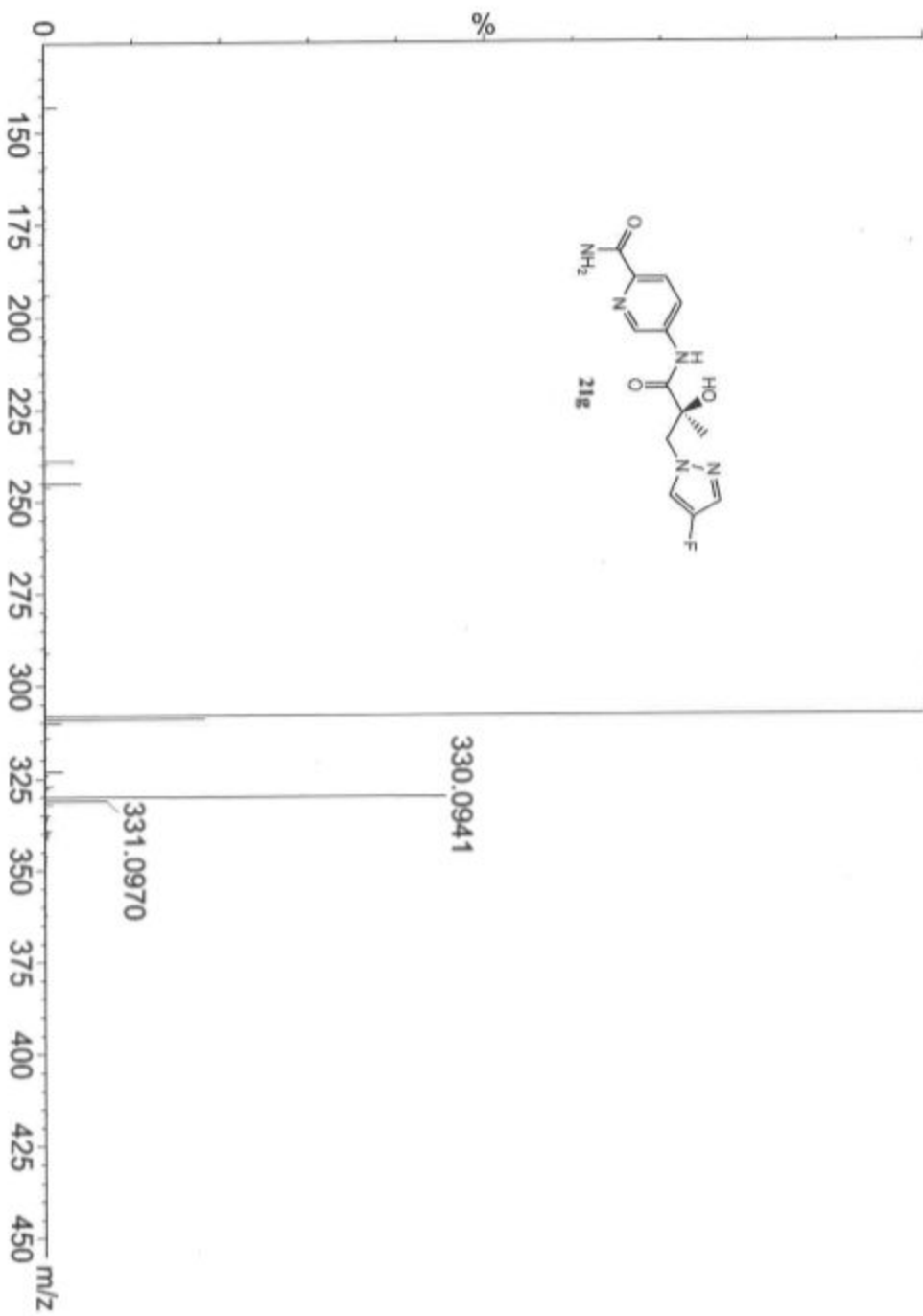
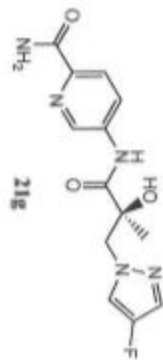




YH-II-147_20191007_22 123 (1.923)

308.1118

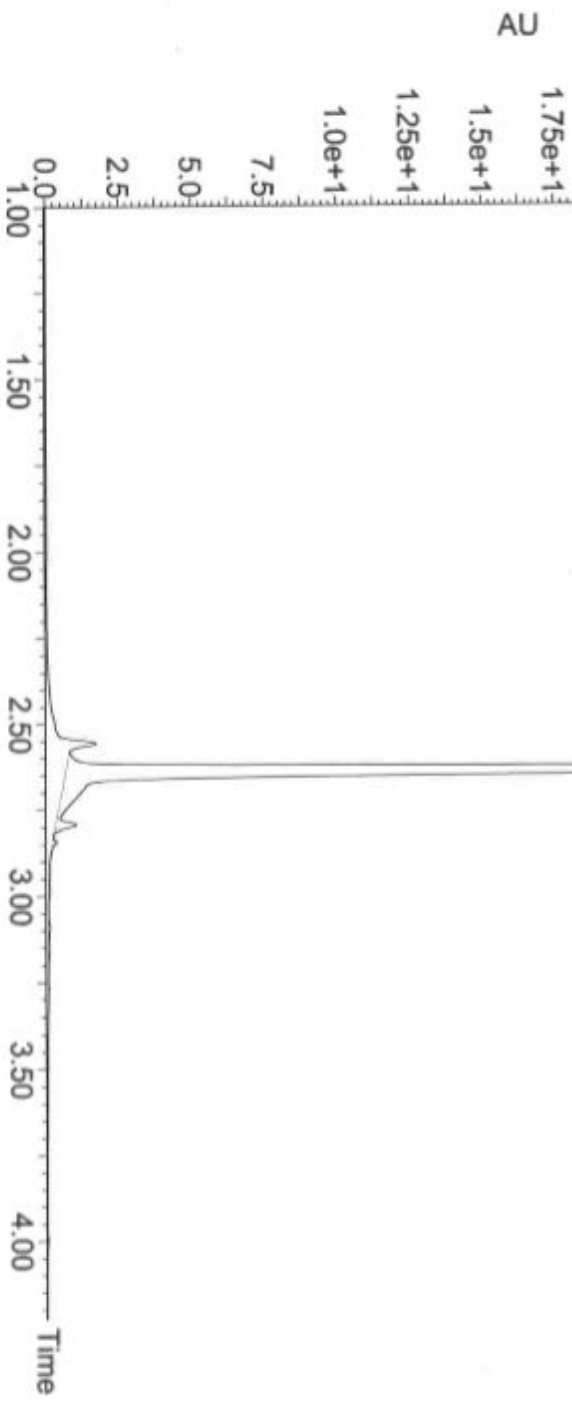
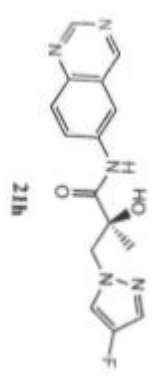
1: TOF MS ES+
1.17e6



YH-II-155B_20191007_23

2.64
944642.4

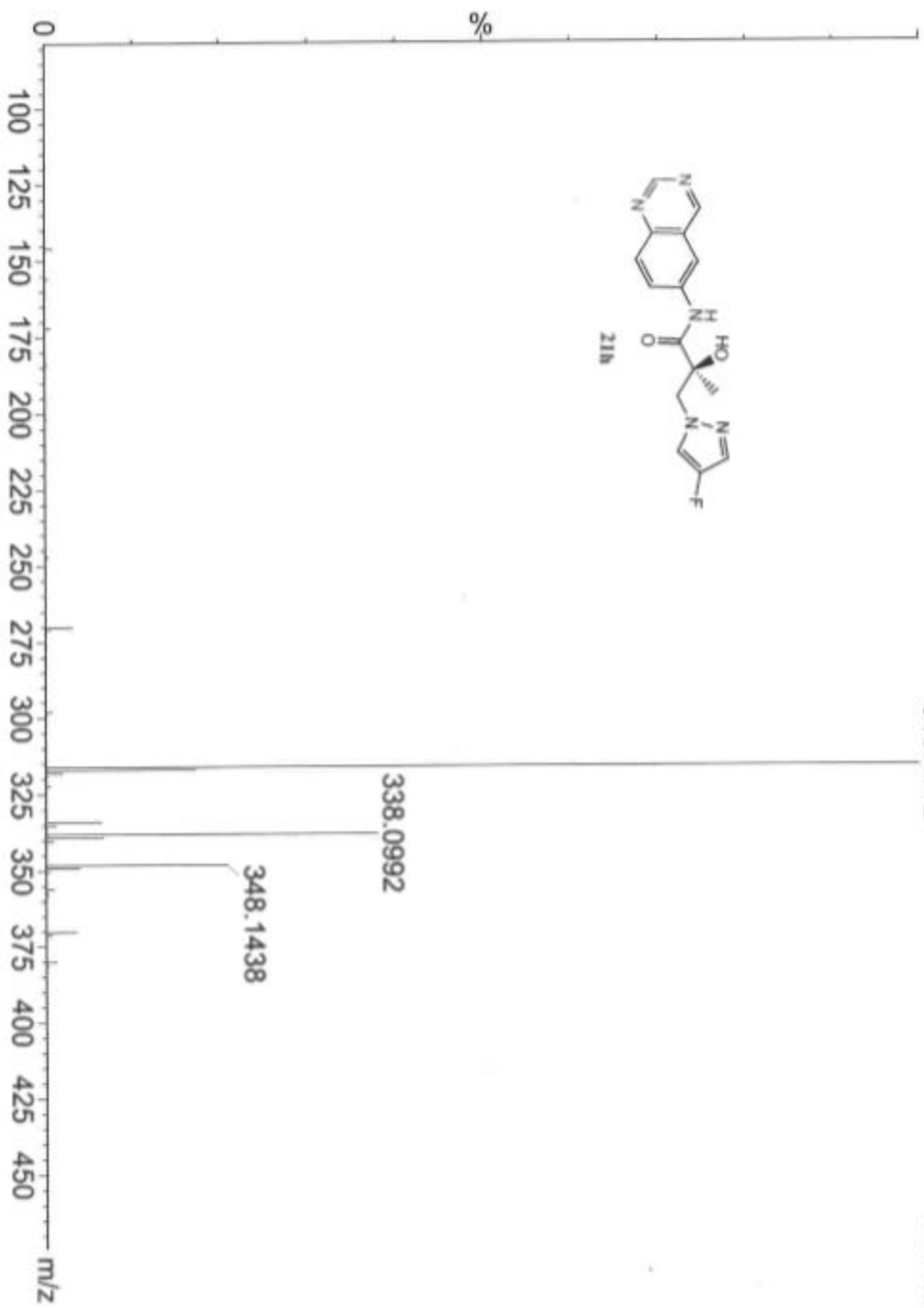
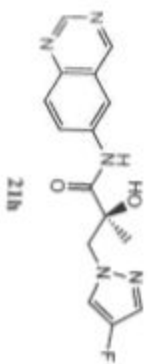
Time	Height	Area	Area%
1.97	6719	1505.61	0.15
2.56	1115472	22924.21	2.32
2.64	32037954	944642.38	95.40
2.79	703574	15173.43	1.53
2.84	129990	2182.33	0.22
2.93	8380	185.15	0.02
3.09	58335	2744.02	0.28
4.00	30184	843.22	0.09



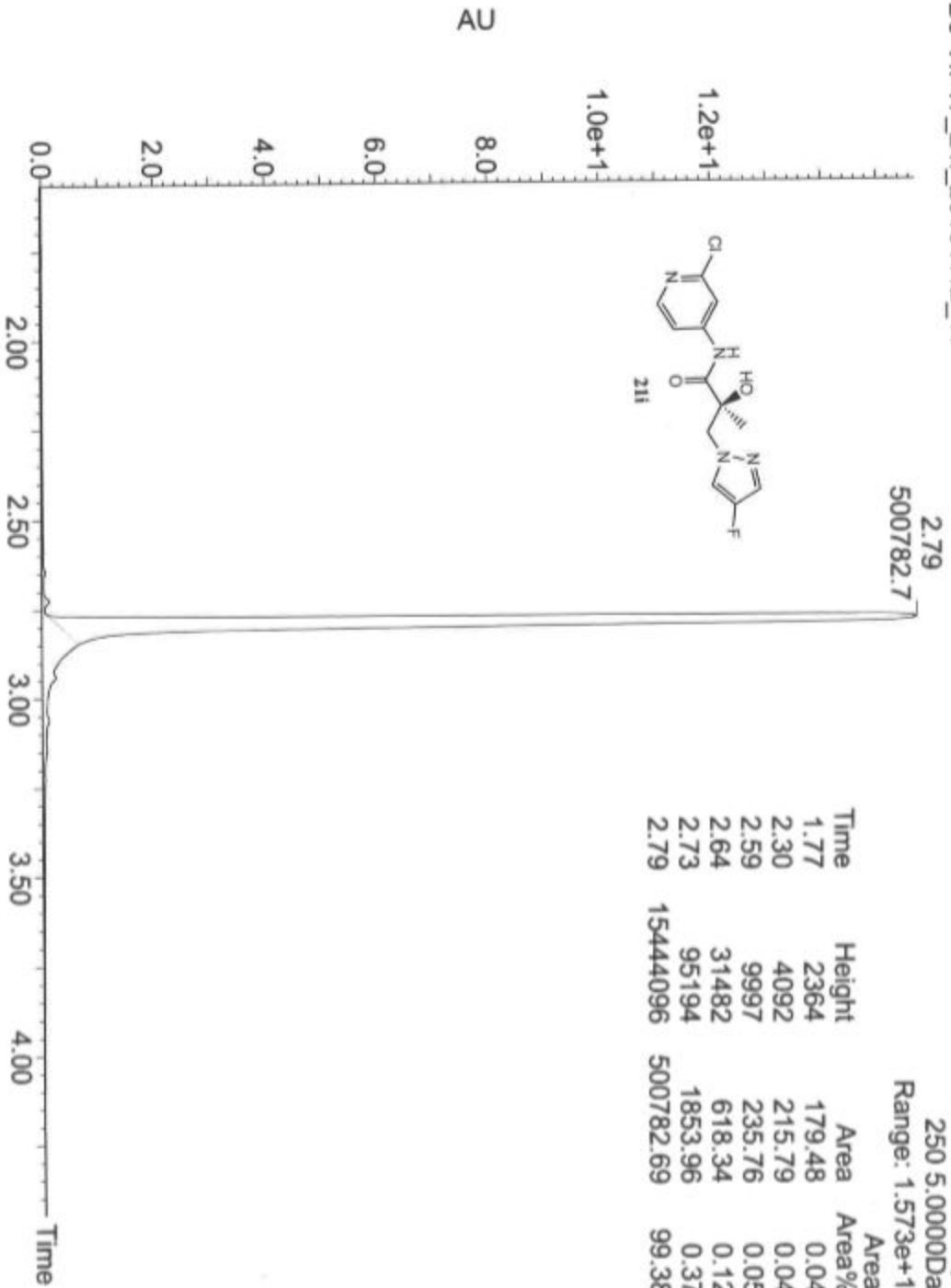
3: Diode Array
252 10.0000Da
Range: 3.272e+1

YH-II-155B_20191007_23 204 (2.675)

1: TOF MS ES+
2.81e6

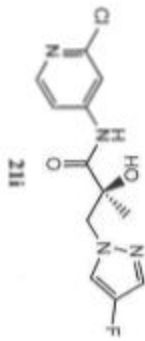
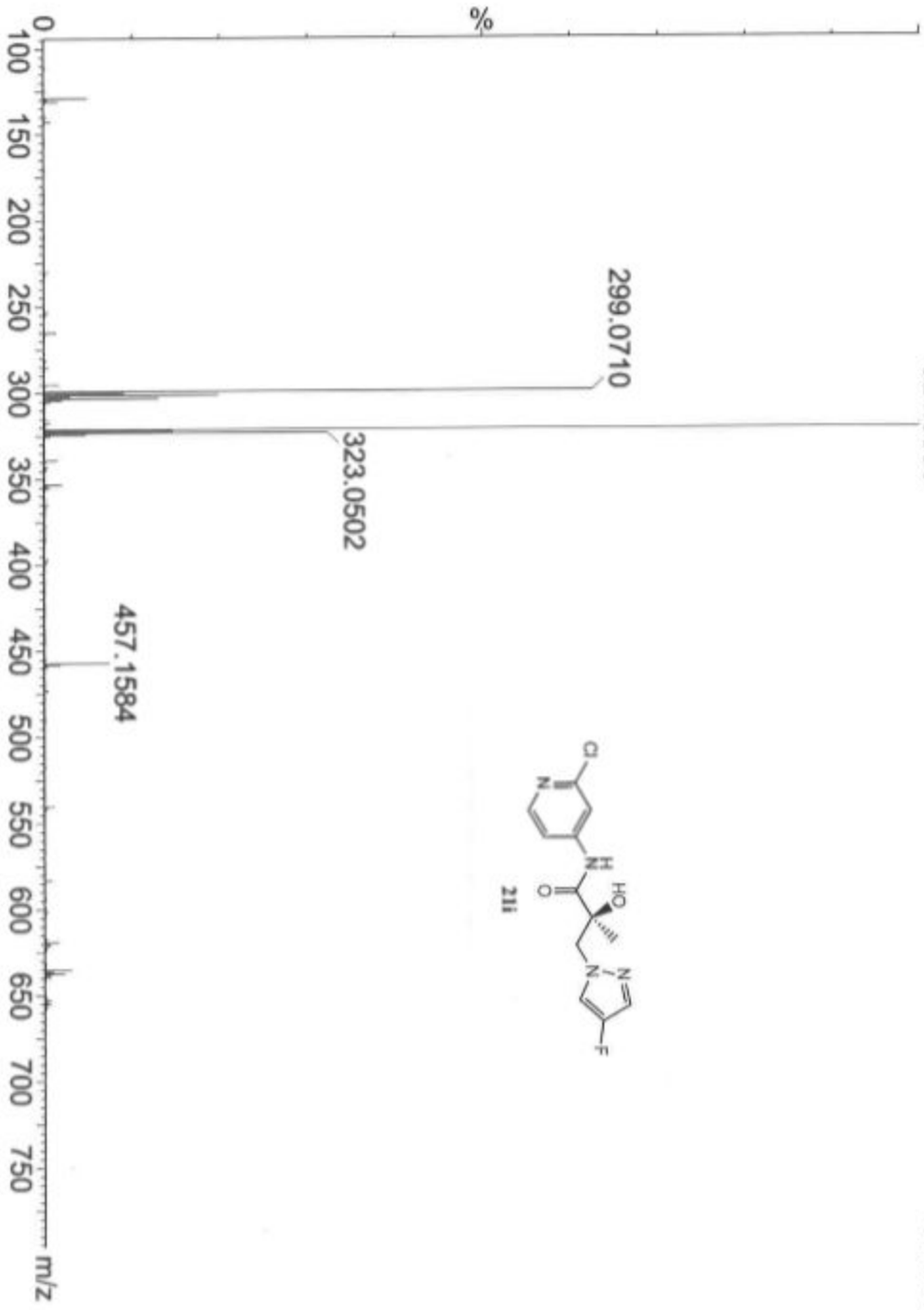


DJ-VII-17_211_20191112_11

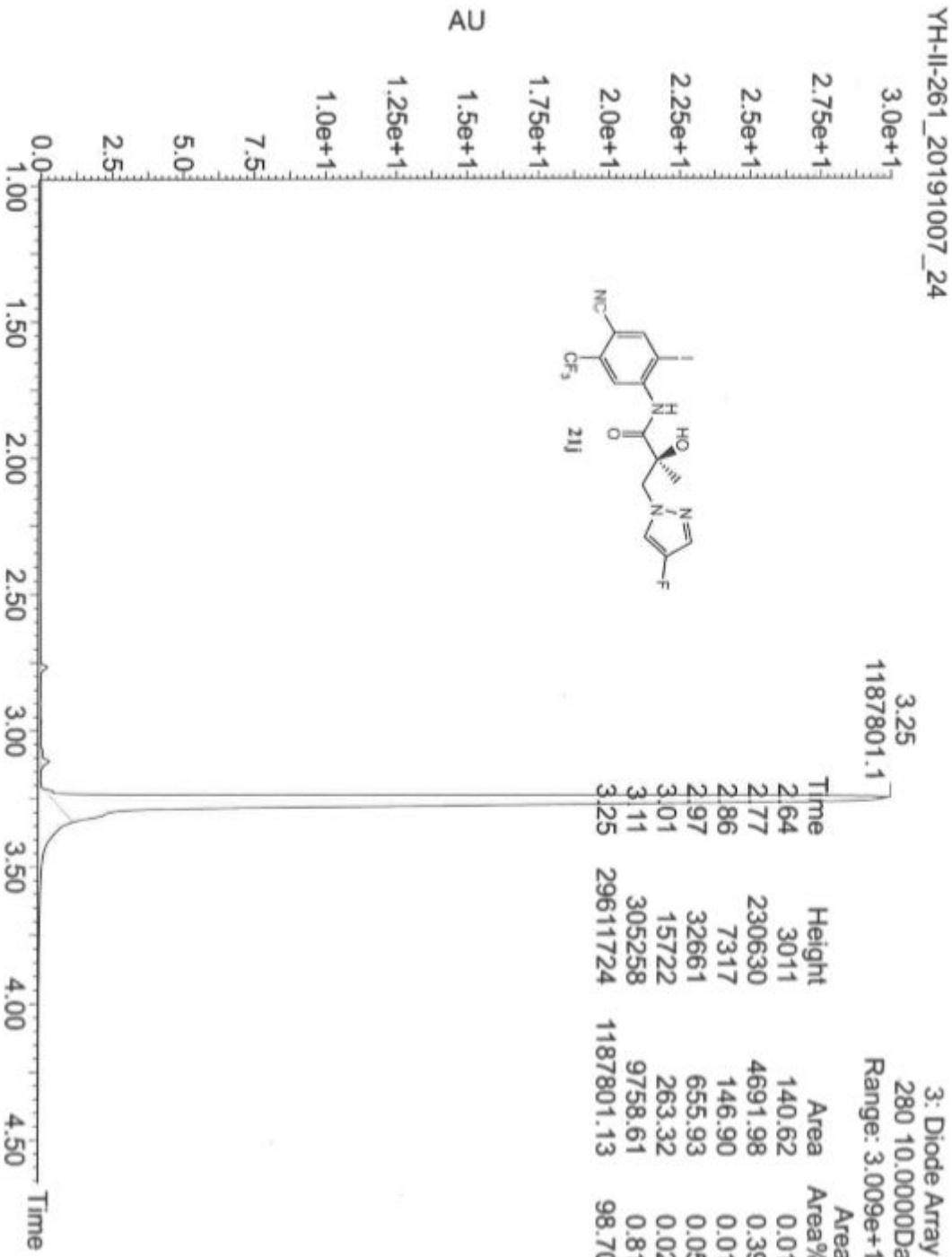


DJ-VII-17_21i_20191112_11 222 (2.841)
321.0530

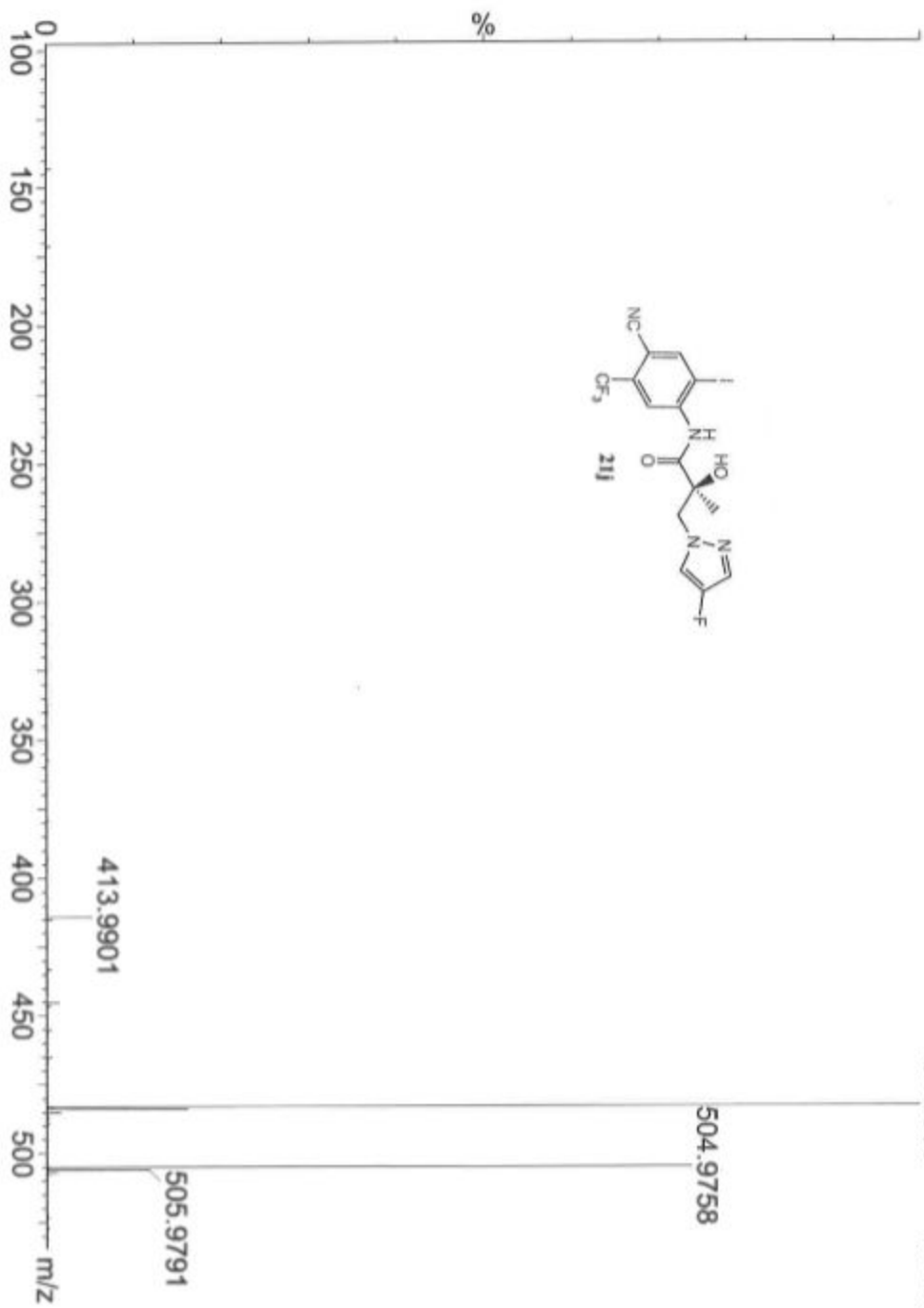
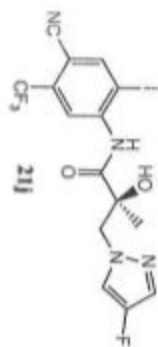
1: TOF MS ES+
6.28e5

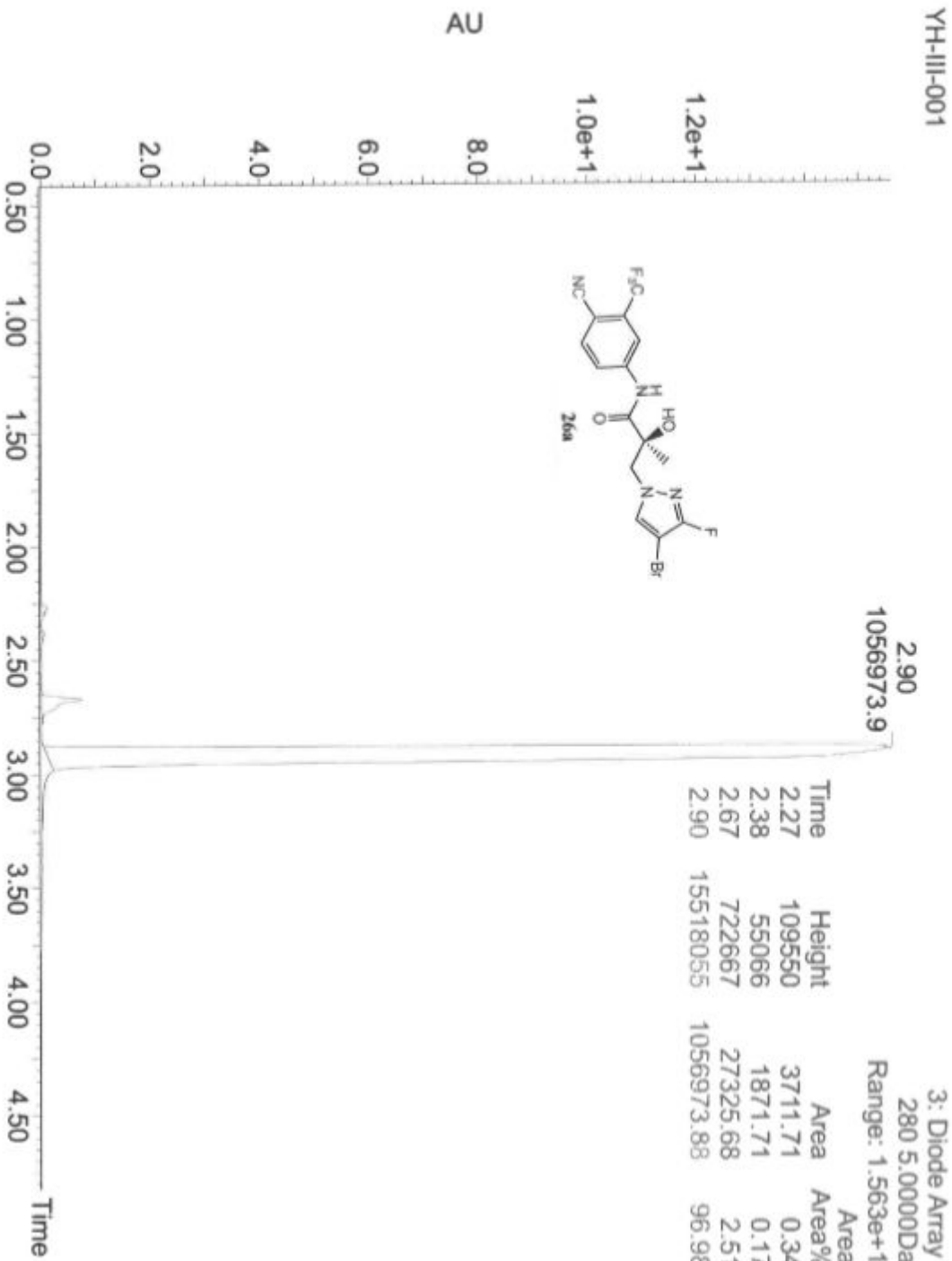


YH-II-261_20191007_24



YH-II-261_20191007_24 272 (3.304)



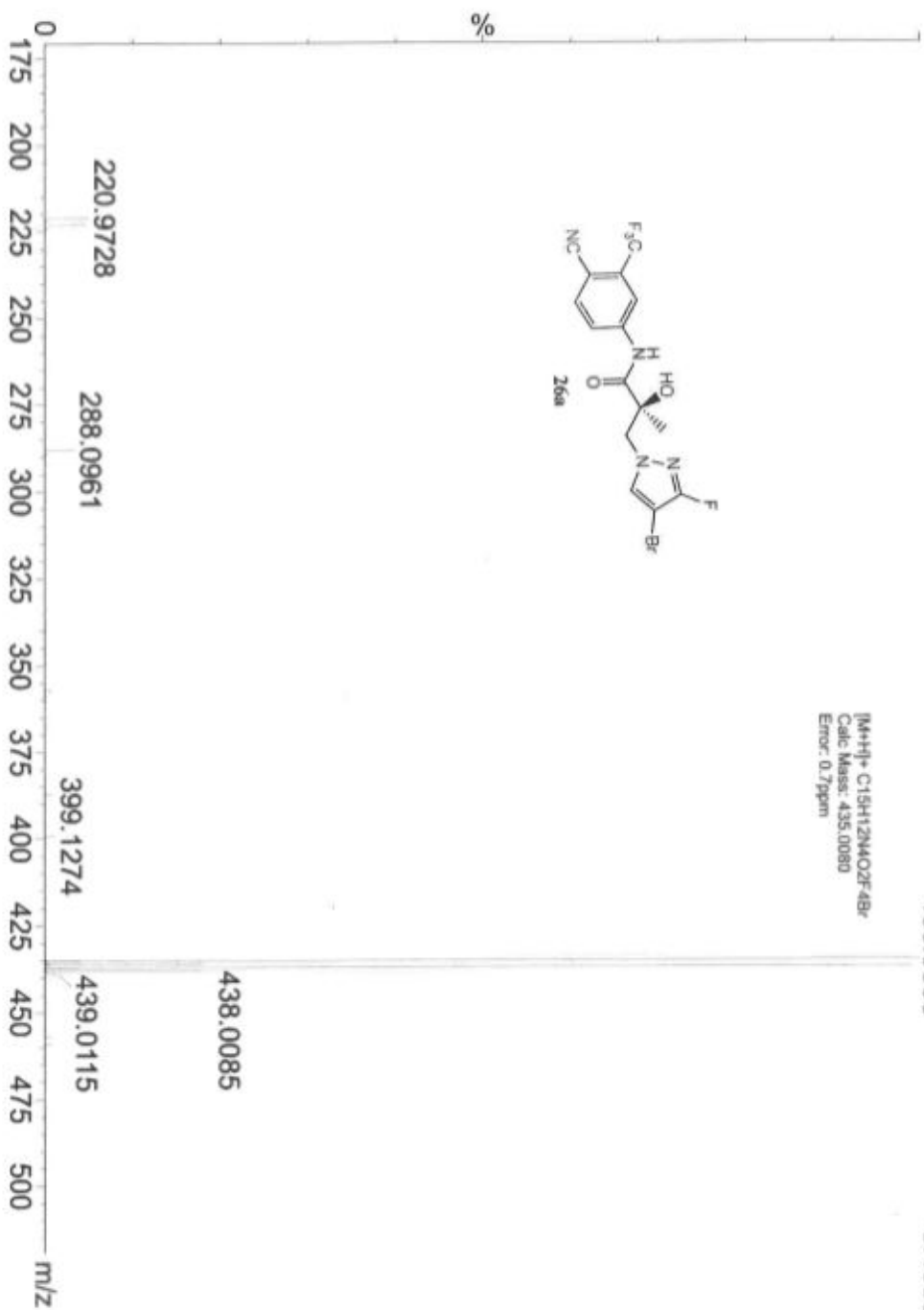
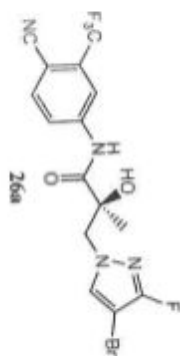


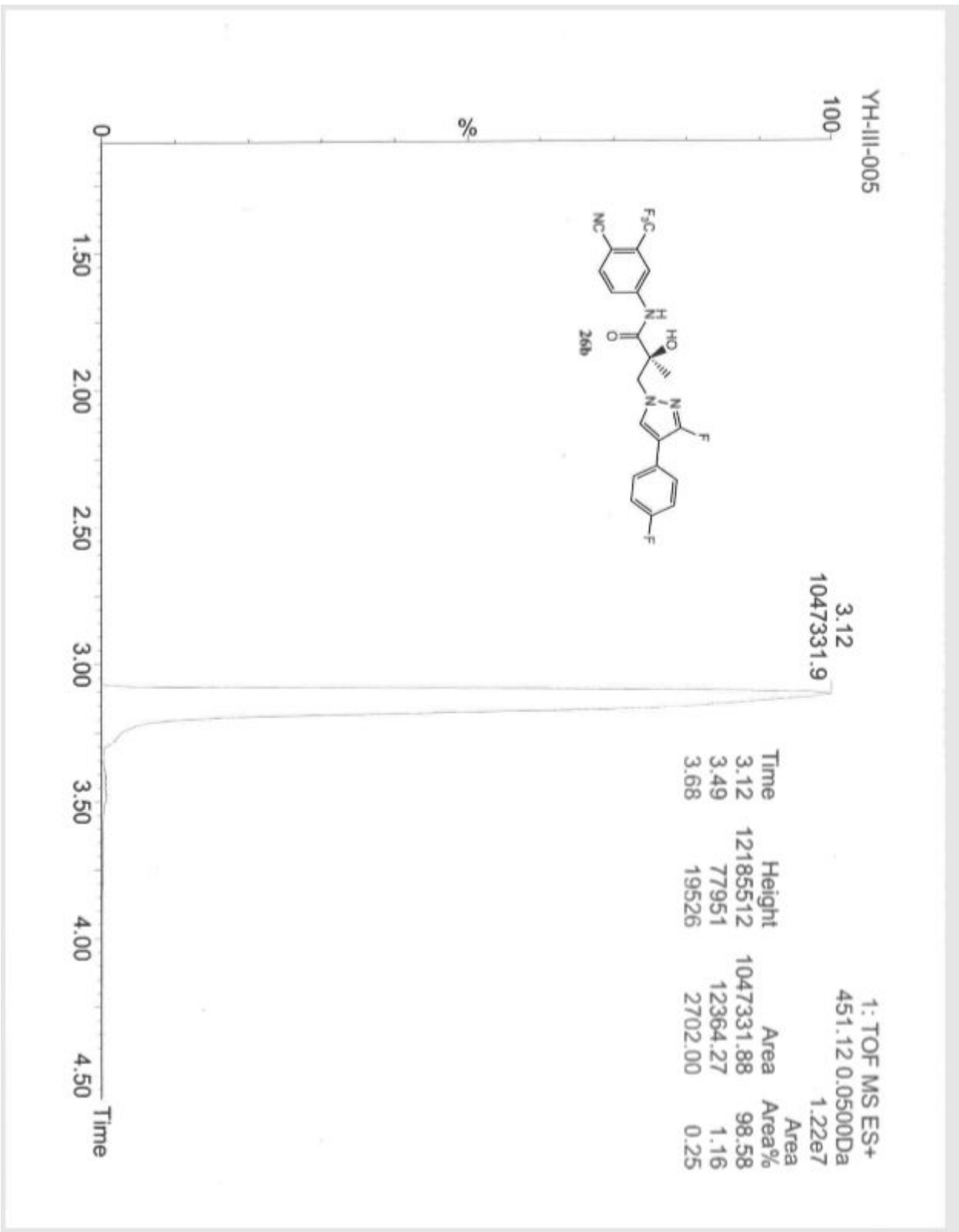
YH-III-001 269 (2.967)

435.0083

1: TOF MS ES+
8.40e6

IM+H+ C15H12NO2F4Br
Calc. Mass: 435.0080
Error: 0.7ppm

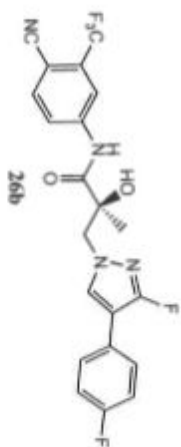




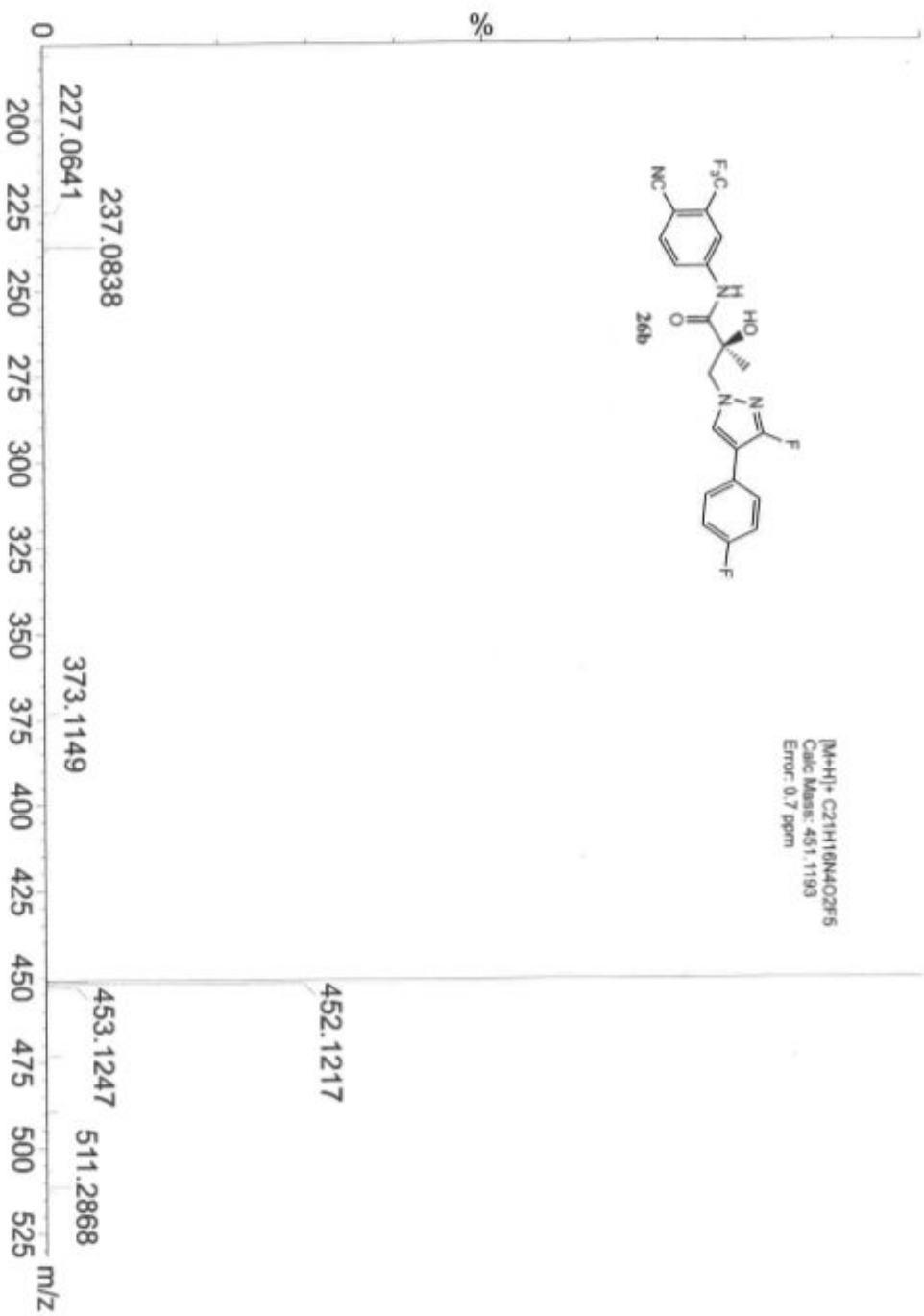
YH-III-005 288 (3.141)

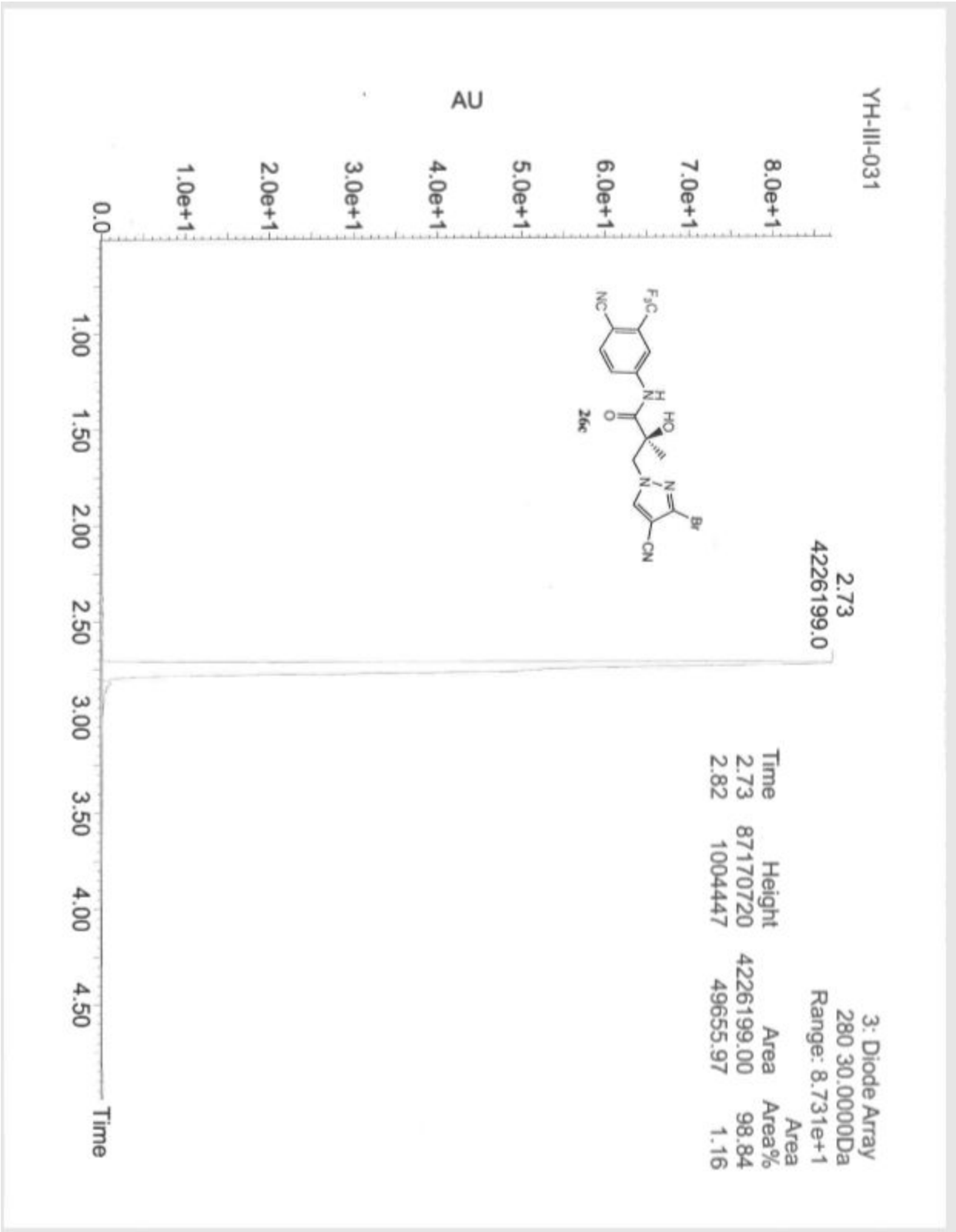
451.1196

1: TOF MS ES+
1.09e7



[M+H]⁺ C₂₁H₁₈N₂O₂F₅
Calc. Mass: 451.1193
Error: 0.7 ppm

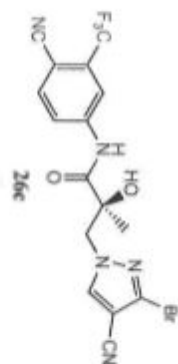




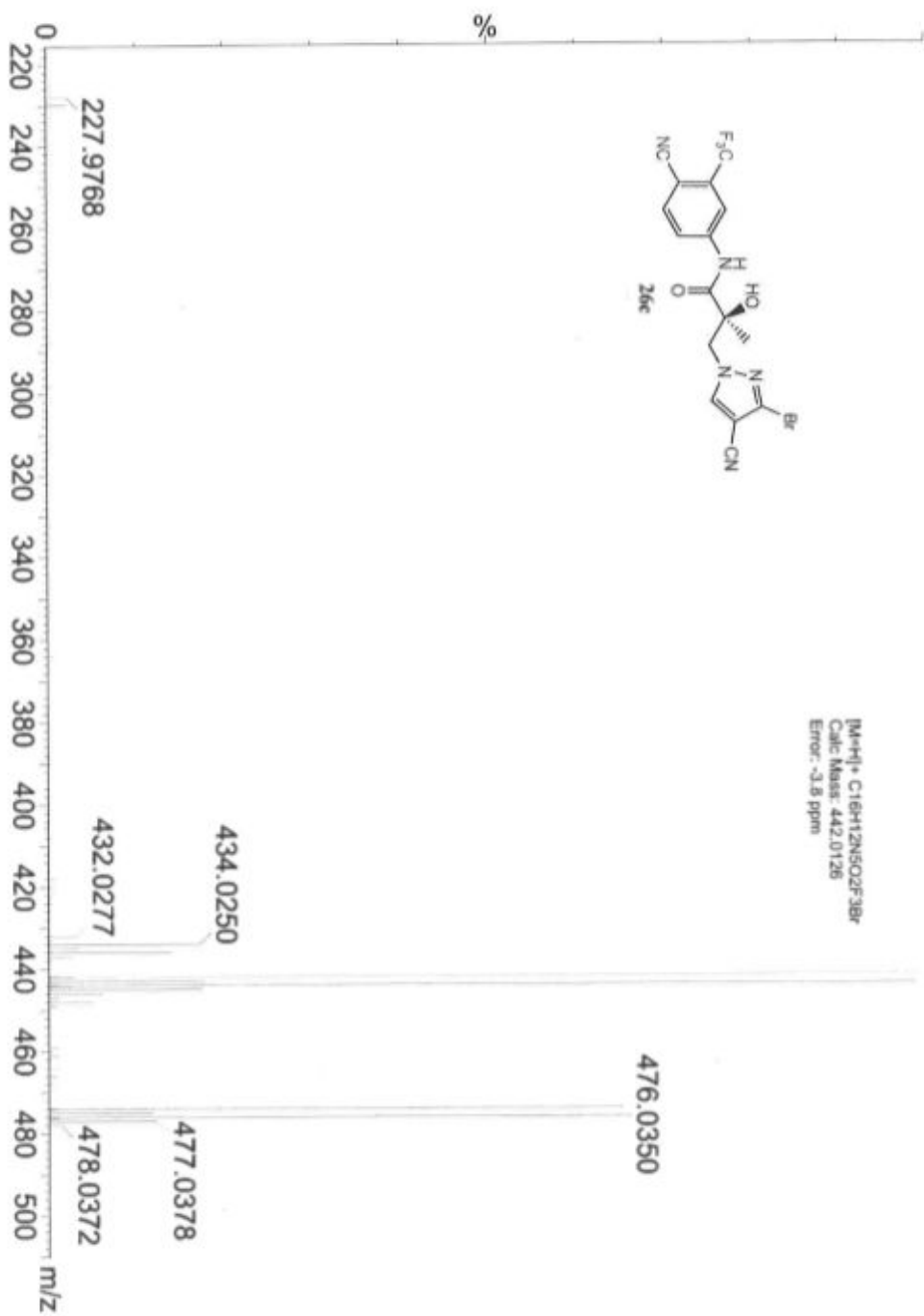
YH-III-031 248 (2.775)

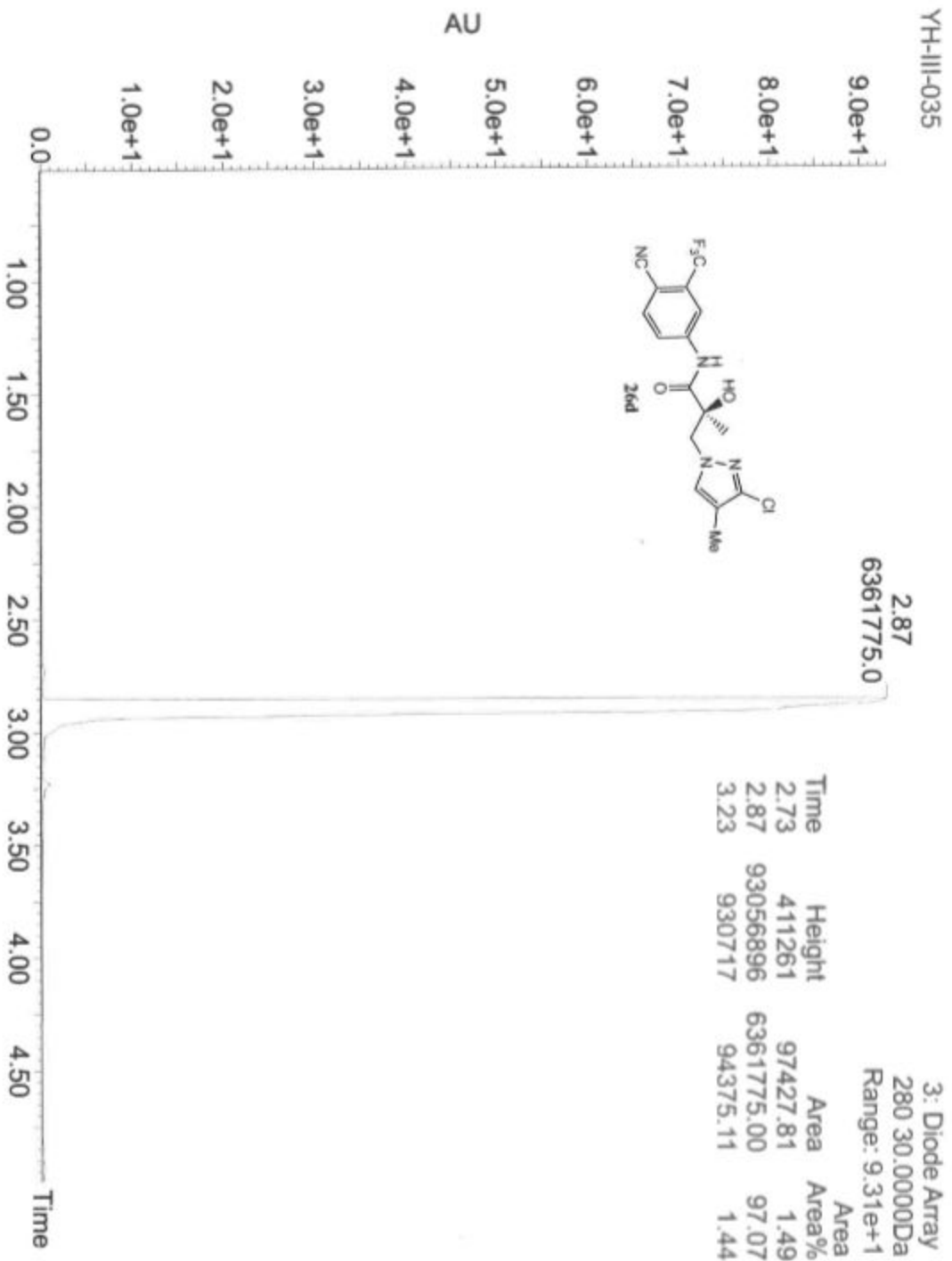
442.0109

1: TOF MS ES+
3.78e6



$M+H^+$: C₁₆H₁₂N₂O₂F₃Br
Calc Mass: 442.0126
Error: -3.8 ppm



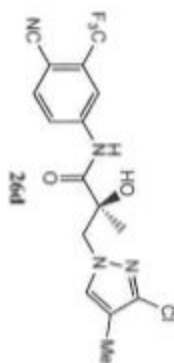


YH-III-035 260 (2.890)

387.0839

1: TOF MS ES+
1.05e7

[M+H]⁺: C₁₈H₁₅N₄O₂F₃Cl
Calc. Mass: 387.0836
Error: 0.8 ppm



%

0 150 175 200 225 250 275 300 325 350 375 400 425 450 475 m/z

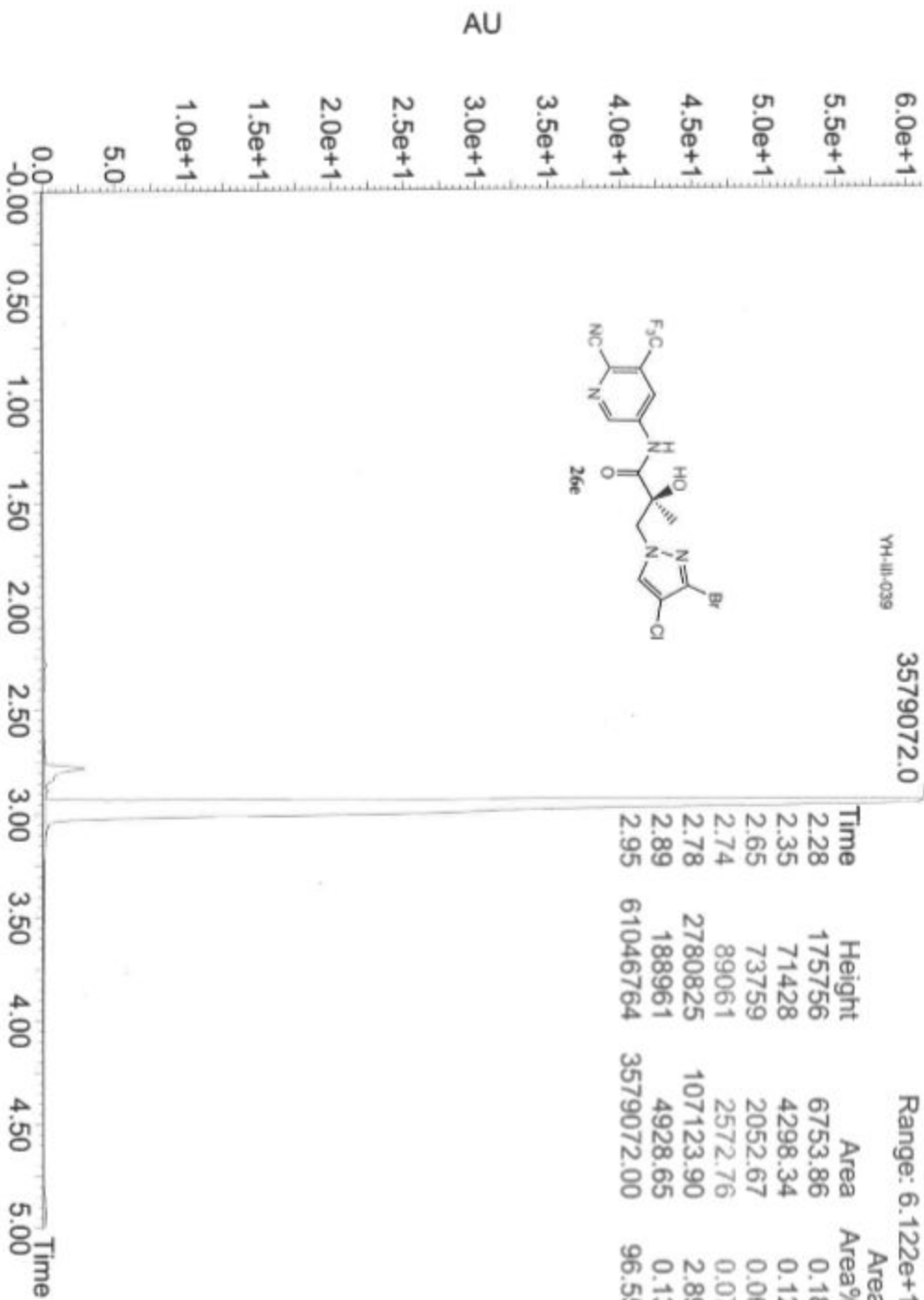
173.0480

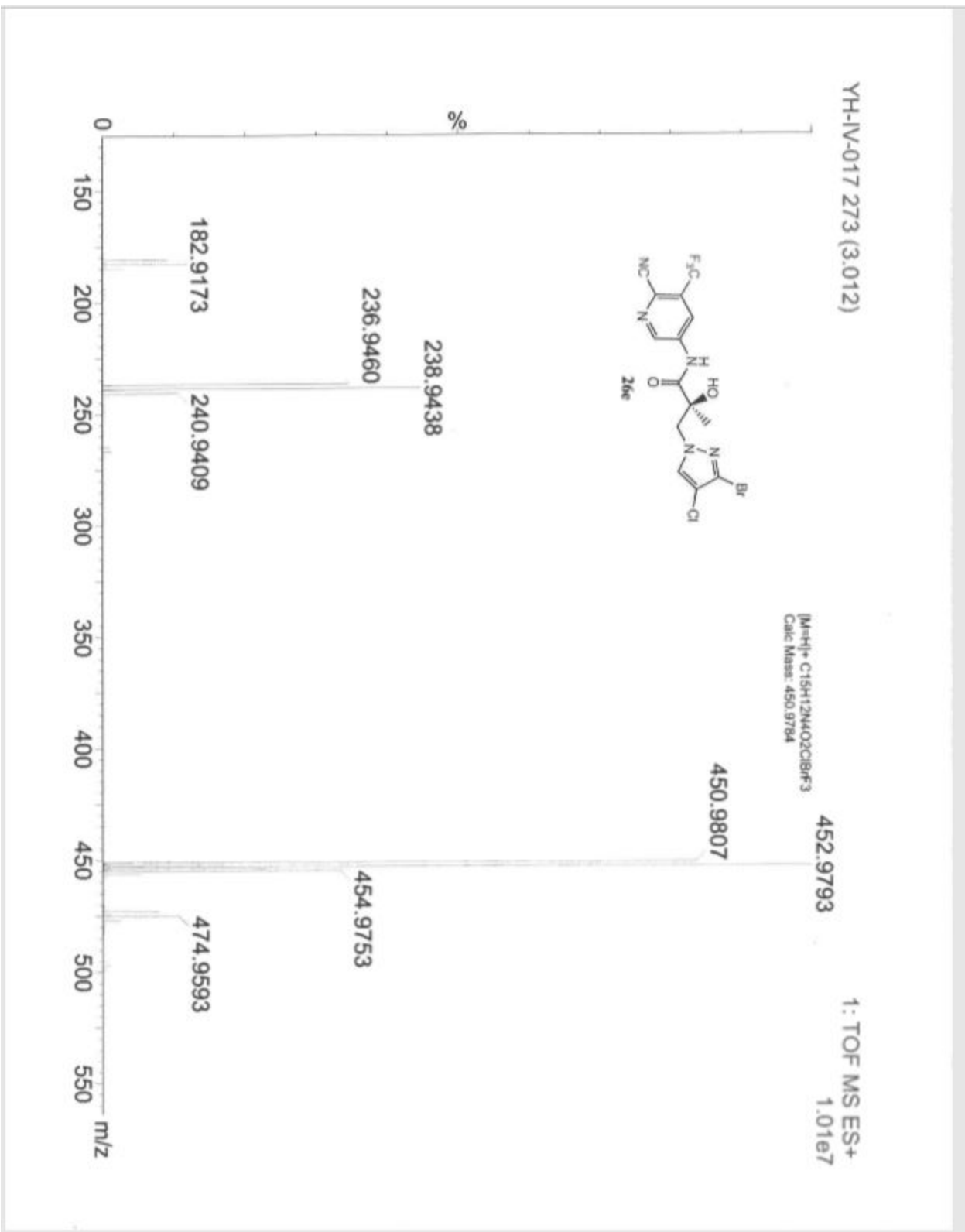
389.0803

390.0823

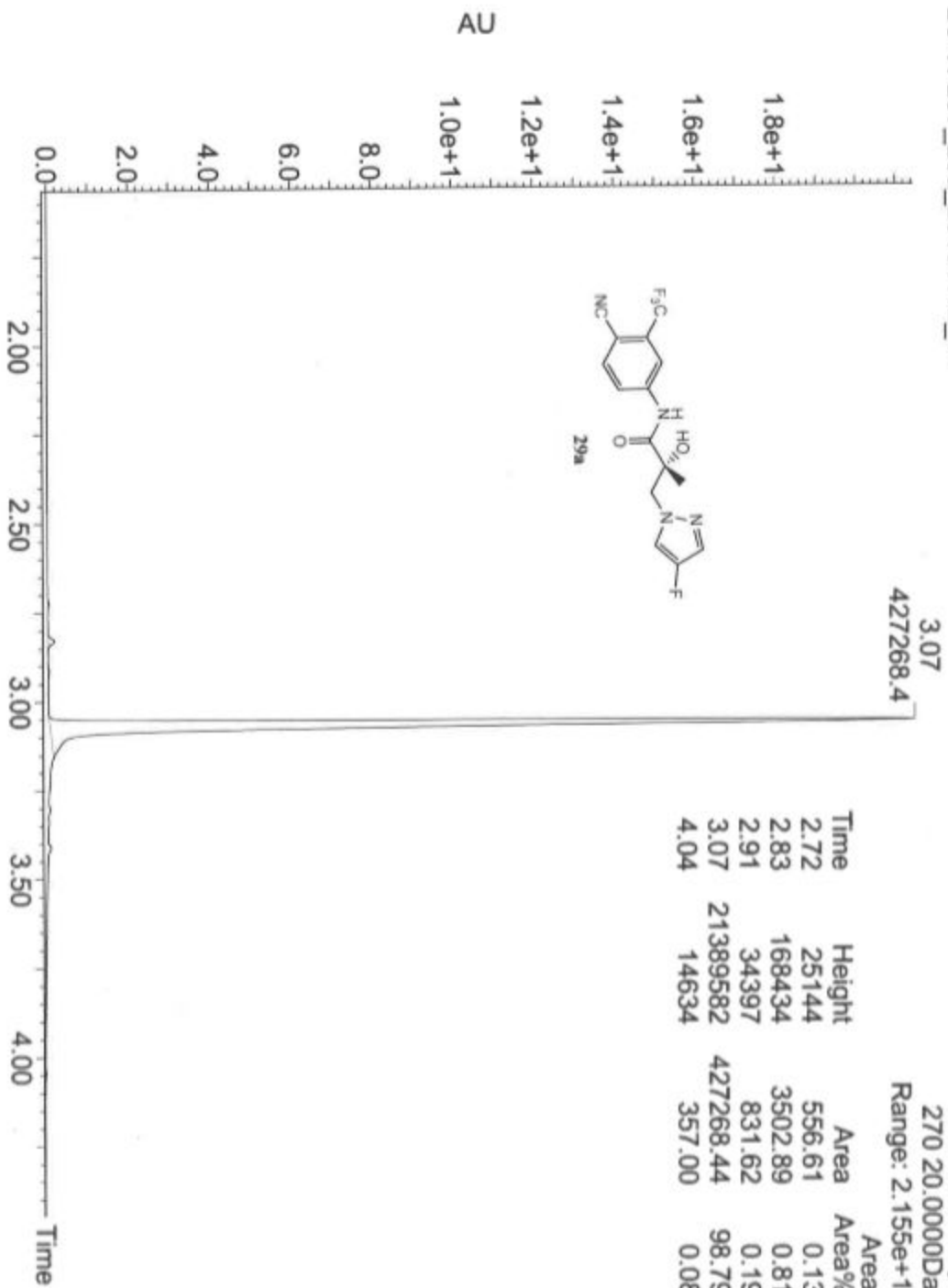
411.0614

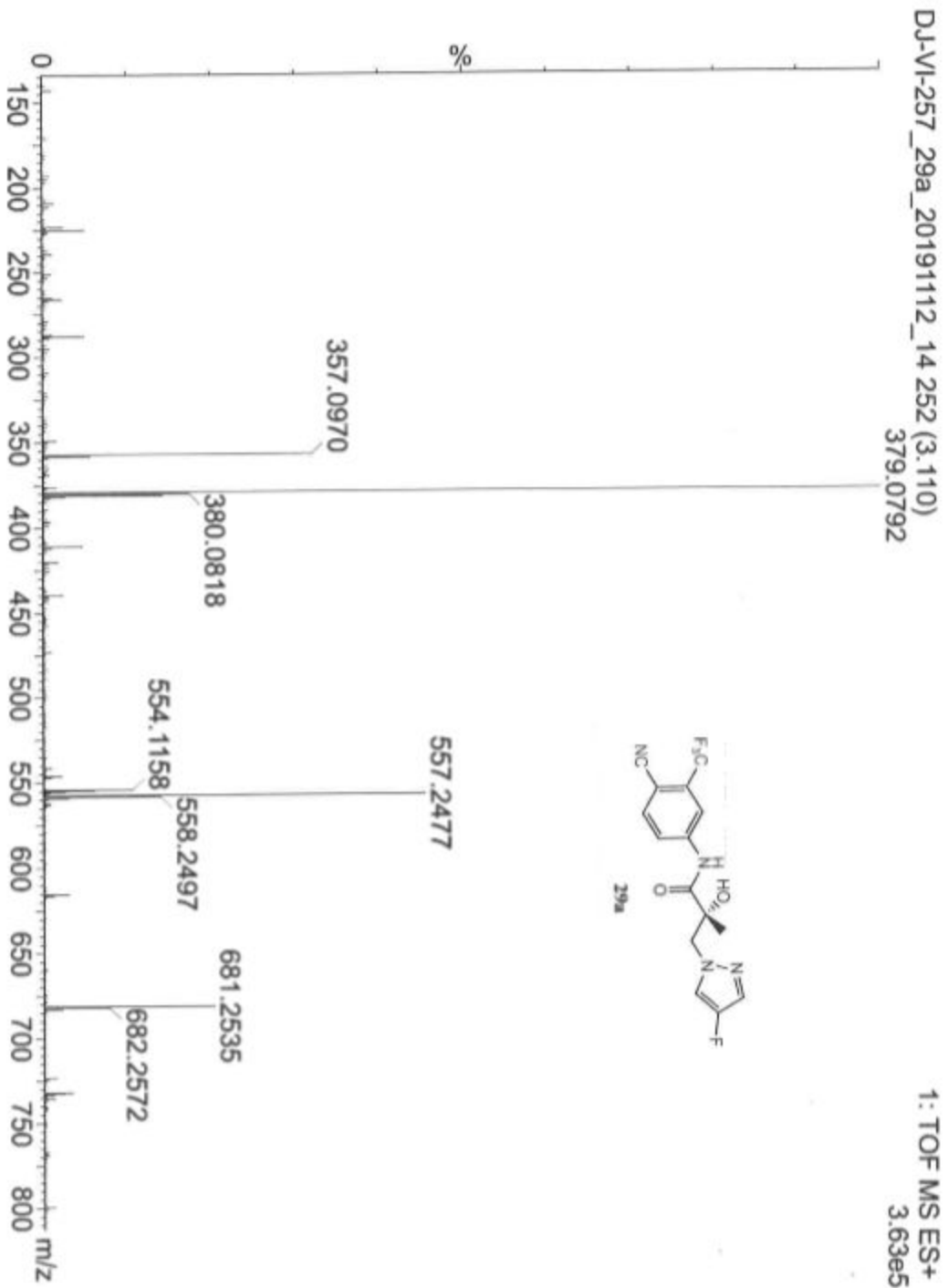
YH-IV-017





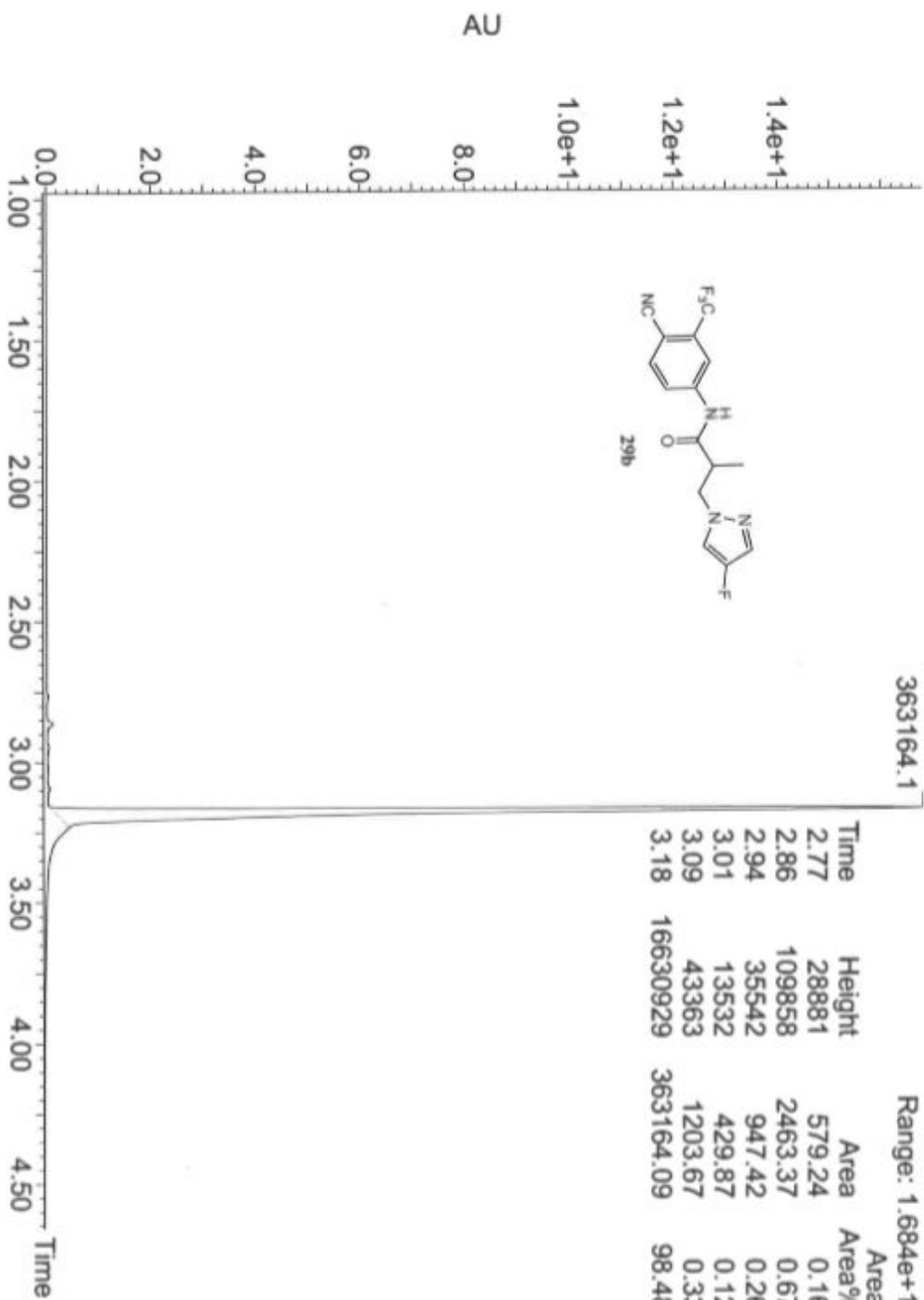
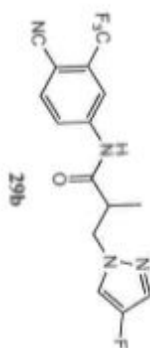
DJ-VI-257_29a_20191112_14





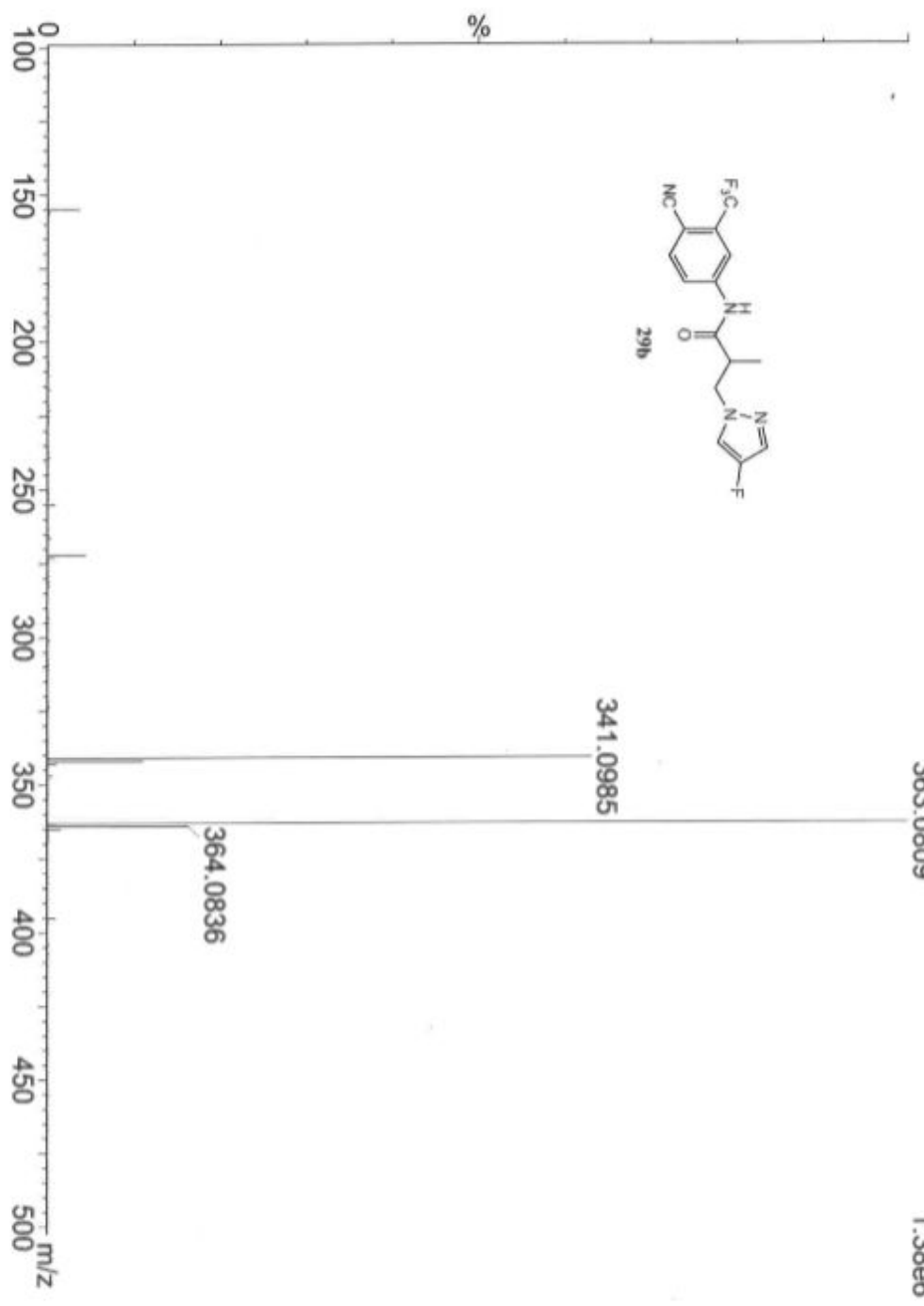
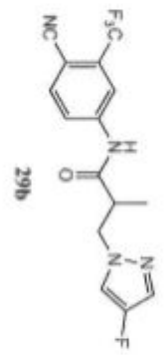
YH-II-143_20191007_25

3: Diode Array
271 10.0000Da
Range: 1.684e+1



YH-II-143_20191007_25 264 (3.224)

1: TOF MS ES+
1.38e6

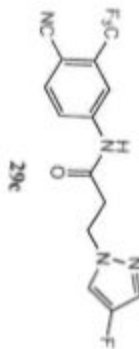


YH-II-179_20191007_26

3.13
979505.4

3: Diode Array
270 10.0000Da
Range: 3.042e+1

3.0e+1
2.75e+1
2.5e+1
2.25e+1
2.0e+1
1.75e+1
1.5e+1
1.25e+1
1.0e+1
7.5
5.0
2.5

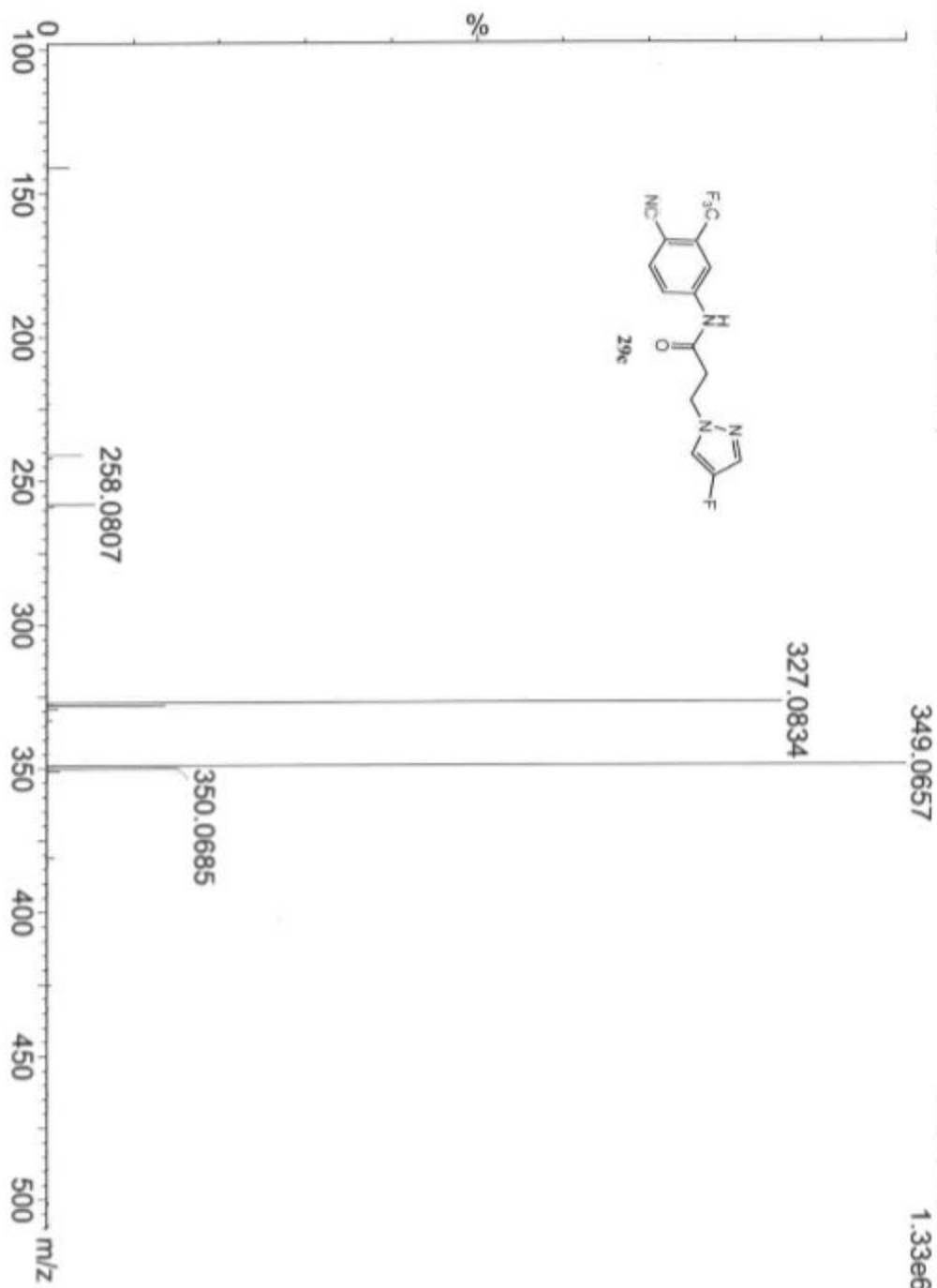


Time	Height	Area	Area%
2.77	193569	3980.40	0.40
2.86	262936	5695.06	0.57
2.95	93681	2435.11	0.25
3.02	10701	199.14	0.02
3.07	52131	1145.33	0.12
3.13	29235906	979505.44	98.64



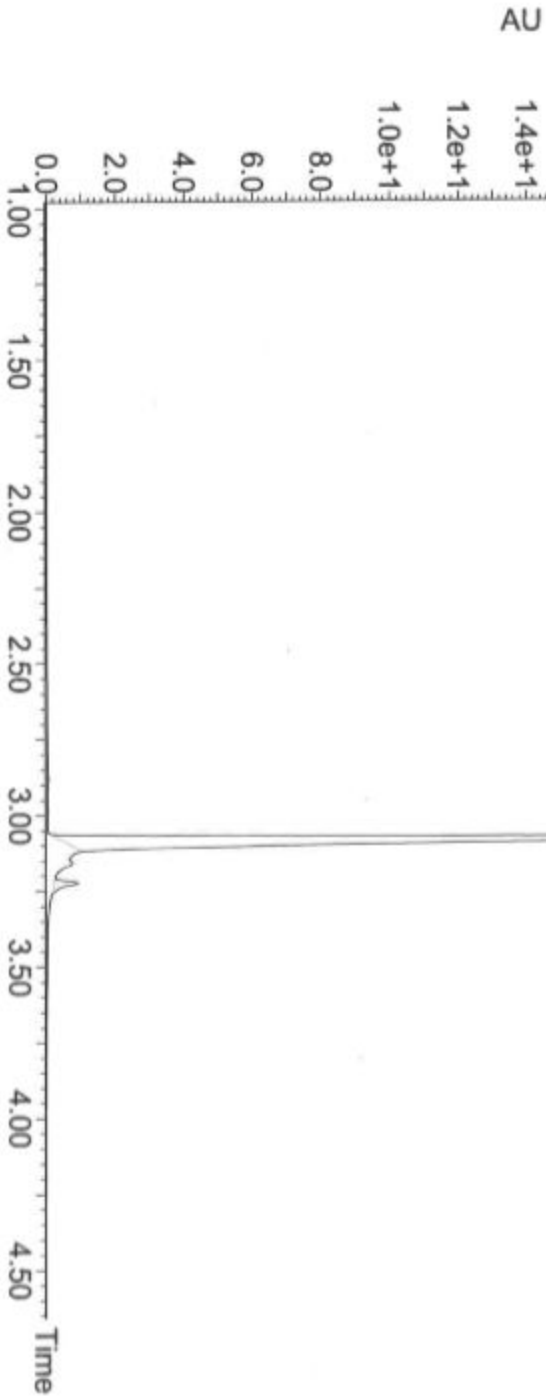
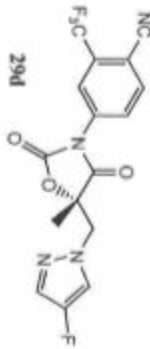
YH-II-179_20191007_26 258 (3.172)

1: TOF MS ES+
1.33e6



YH-III-173_20191007_27

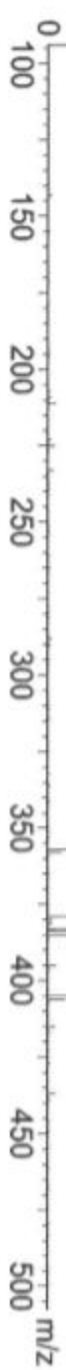
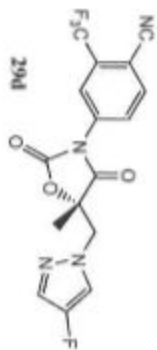
3.08
603781.0



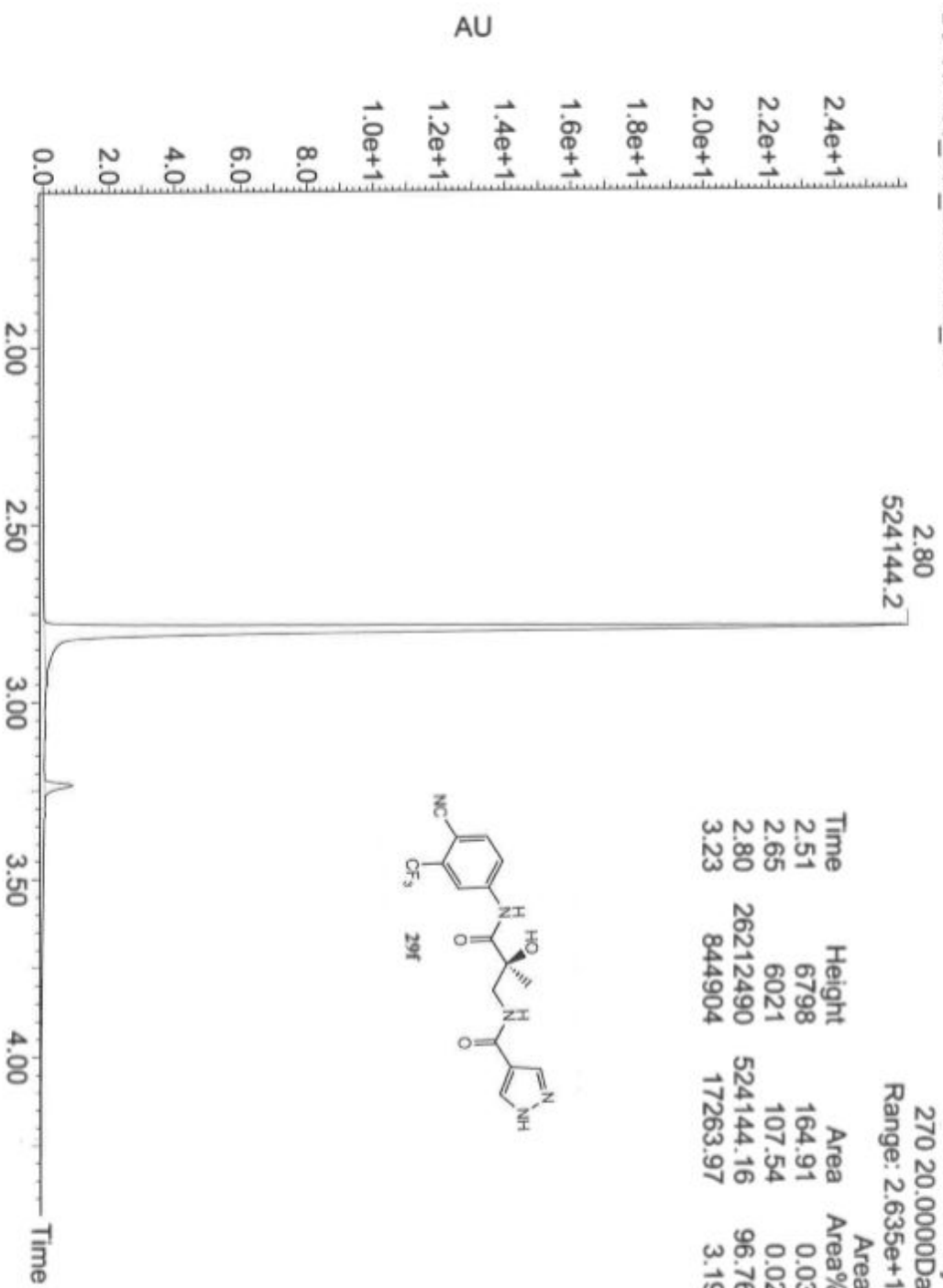
YH-III-173_20191007_27 253 (3.129)

383.0740

1: TOF MS ES+
1.09e6



DJ-VII-138_29f_20191112_16



DJ-VII-138_29f_20191112_16 221 (2.832)

404.0945

1: TOF MS ES+
1.17e6

