Electronic Supplementary Information for

Organocatalytic Multicomponent Reaction for the Acquisition of a Potent and Selective Inhibitor of mPTPB, a Virulence Factor of Tuberculosis

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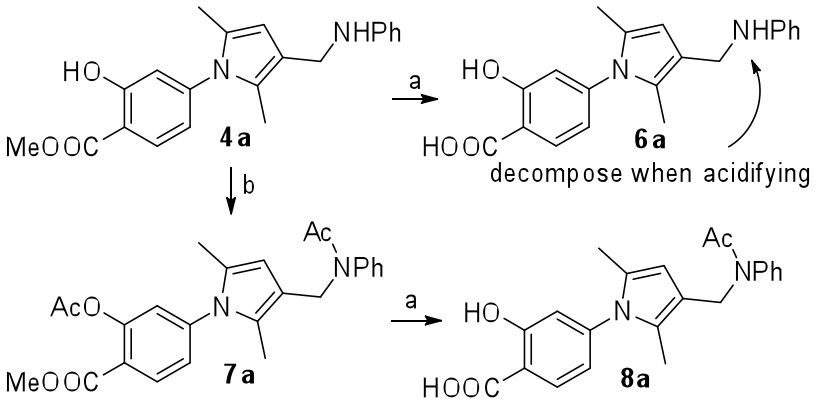
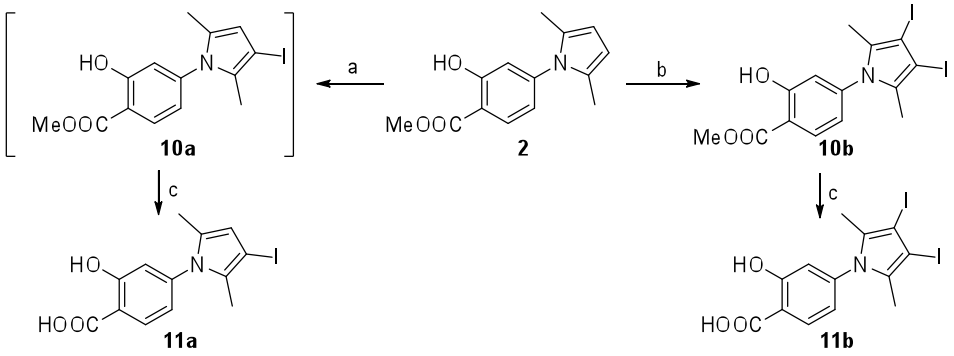
Table S1. Complete list of optimization of reaction conditions

entry	solvent	catalyst	time	ratio of **4a**/**5**/**2**, %	yield of **4a** %	yield of **5** %
1	DMSO	HOAc (20 mol%)	24 h	no reaction		
2	DMF	HOAc (20 mol%)	24 h	no reaction		
3	THF	HOAc (20 mol%)	24 h	no reaction		
4	MeCN	HOAc (20mol%)	24 h	13/8/79		
5	Et_2O	HOAc (20 mol%)	24 h	13/6/81		
6	toluene	HOAc (20 mol%)	24 h	no reaction		
7	MeOH	HOAc (20 mol%)	24 h	9/8/91		
8	CH_2Cl_2	HOAc (20 mol%)	24 h	52//22/26		
9	$CHCl_3$	HOAc (20 mol%)	24 h	48//15/37		
10	CH_2Cl_2	4-F-$PhCO_2H$(20 mol%)	24 h	47/5/48		
11	CH_2Cl_2	Proline (20 mol%)	24 h	7/0/93		
12	CH_2Cl_2	TFA (20 mol%)	24 h	decomposition		
13	CH_2Cl_2	2 M HCl (20 mol%)	24 h	26/4/70		
14	CH_2Cl_2	4-Me-$PhCO_2H$(20 mol%)	24 h	28/13/59		
15	CH_2Cl_2	3-F-5-CF_3-$PhCO_2H$(20 mol%)	24 h	50/25/25		
16	CH_2Cl_2	3,5-$(CF_3)_2$-$PhCO_2H$(20 mol%)	24 h	46/17/37		
17	CH_2Cl_2	$MeOCH_2CO_2H$ (20 mol%)	24 h	45/36/19		
18	CH_2Cl_2	$PhCH_2CO_2H$ (20 mol%)	24 h	23/10/67		
19	CH_2Cl_2	Cyc.$C_6H_{11}CO_2H$ (20 mol%)	24 h	13/10/77		
20	CH_2Cl_2	PTSA (20 mol%)	24 h	21/5/74		
21	CH_2Cl_2	$(3,5\text{-}(CF_3)_2\text{-}PhNH)_2CS$ (20 mol%)	24 h	no reaction		
22	CH_2Cl_2	diphenic acid (20 mol%)	24 h	47/23/30		
23	CH_2Cl_2	HOAc (100 mol%)	24 h	59//17/24		
24	$CHCl_3$	HOAc (100 mol%)	24 h	44/11/45		
25	CH_2Cl_2	HOAc (100 mol%)	24 h	45/9/46	85	
26	CH_2Cl_2	$MeOCH_2CO_2H$ (100 mol%)	48 h	0/100/0		75

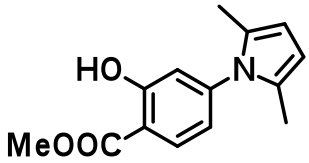


Scheme S1. Strategy to obtain stable hydrolyzed compound **8a**. a.10% LiOH, MeOH, rt, 2 h, 95% yield. b. Ac_2O (3 equiv.), DMAP (0.1 equiv.), CH_2Cl_2, rt, 2 h, 95% yield.

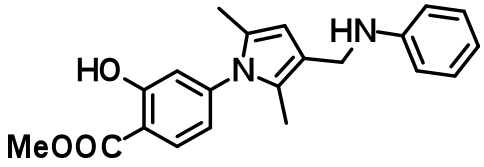


Scheme S2. Synthesis of **10a**, **10b**, **11a**, **11b.** a. I_2 (2.2 equiv.), $NaHCO_3$ (3 equiv.), ether, rt, 24 h, 60% yield. b. ICl (2.2 equiv.), $NaHCO_3$ (3 equiv.), ether, rt, 24 h, 70% yield. c. 10% LiOH, MeOH, rt, 2 h, 95% yield.

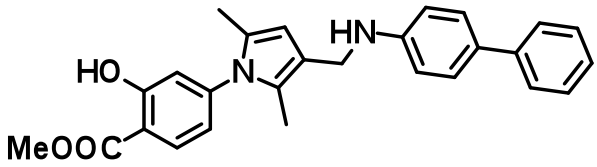
Characterizations of compounds **2**, **4a-4l**, **5**, **10a**, **10b**



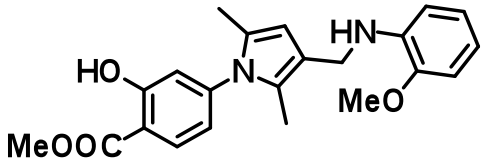
2. ^{1}H NMR (500 MHz, $CDCl_3$) 10.91 (s, 1H), 7.93 (d, *J* = 8.5 Hz, 1H), 6.86 (d, *J* = 2.0Hz, 1H), 6.76-6.74 (m, 1H), 5.91 (s, 2H), 3.99 (s, 3H), 2.08 (s, 6H). ESI-MS Cacld. for C14H16NO3 ($M+H^+$): m/z 246.1; found 246.0.



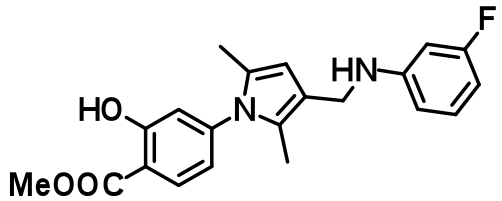
4a. ^{1}H NMR (500 MHz, $CDCl_3$) 10.93 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.22-7.19 (m, 2H), 6.85 (d, *J* = 2.0 Hz, 1H), 6.75-6.68 (m, 4H), 5.99 (s, 1H), 4.08 (s, 2H), 3.99 (s, 3H),2.07 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 162.1, 148.6, 145.3, 130.6, 129.2, 128.0, 125.8, 119.2, 117.2, 117.1, 117.1, 112.6, 111.7, 107.6, 52.5, 40.6, 12.8, 10.7. ESI-MS Cacld. for C21H21N2O3 ($M-H^+$): m/z 349.2; found 349.2.



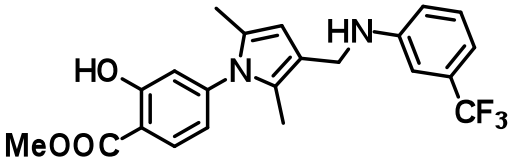
4b. ^{1}H NMR (500 MHz, $CDCl_3$) 10.92 (s, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.55 (d, *J* = 7.7 Hz, 2H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.26-7.23 (m, 1H), 6.86 (d, *J* = 1.9 Hz, 1H), 6.76-6.73 (m, 3H), 6.00 (s, 1H), 4.12 (s, 2H), 3.98 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0, 162.1, 148.0, 145.2, 141.3, 130.6, 130.0, 128.6, 128.0, 127.9, 126.2, 125.9, 125.8, 119.2, 117.1, 117.1, 112.9, 111.7, 107.6, 52.5, 40.6, 12.8, 10.7. ESI-MS Cacld. for C27H25N2O3 ($M-H^+$): m/z 425.2; found 425.0.



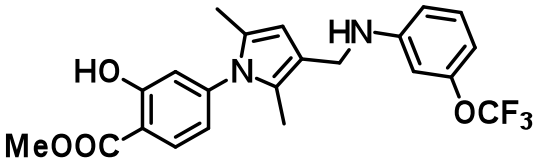
4d. ^{1}H NMR (500 MHz, $CDCl_3$) 10.92 (s, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 6.93-6.92 (m, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 6.88-6.74 (m, 3H), 6.70-6.67 (m, 1H), 6.02 (s, 1H), 4.10 (s, 2H), 4.00 (s, 3H), 3.84 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 162.1, 146.8, 145.4, 138.6, 130.6, 127.8, 125.8, 121.3, 119.3, 117.3, 117.1, 116.2, 111.6, 109.8, 109.3, 107.8, 55.3, 52.5, 40.3, 12.9, 10.8. ESI-MS Cacld. for C22H23N2O4 ($M-H^+$): m/z 379.1663; found 379.1671.



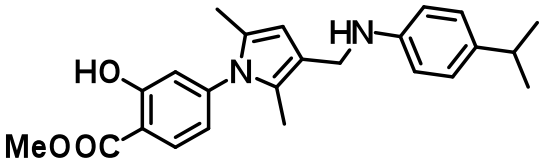
4e. ^{1}H NMR (500 MHz, $CDCl_3$) 10.93 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.11 (dd, *J* = 14.9, 8.0 Hz, 1H), 6.86 (d, *J* = 2 Hz, 1H), 6.75-6.73 (m, 1H), 6.43-6.35 (m, 3H), 5.97 (s, 1H), 4.01 (s, 2H), 4.00 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 165.1, 163.2, 162.1, 150.3, 150.3, 145.2, 130.7, 130.2, 130.1, 128.1, 125.9, 119.2, 117.1, 116.7, 111.8, 108.5, 107.5, 103.5, 103.3, 99.3, 99.0, 52.5, 40.5, 12.8, 10.7. ESI-MS Cacld.for C21H20FN2O3 ($M-H^+$): m/z 367.1463; found 367.1469.



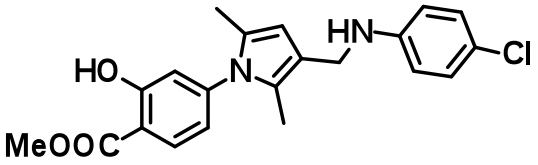
4f. ^{1}H NMR (500 MHz, $CDCl_3$) 10.93 (s, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 7.27 (d, *J* = 5.0Hz, 1H), 6.94 (d, *J* = 7.7 Hz, 1H), 6.87-6.86 (m, 2H), 6.81-6.79 (m, 1H), 6.76-6.6.74 (m, 1H), 5.98 (s, 1H), 4.10 (s, 2H), 4.00 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H). ESI-MS Cacld.for C22H20F3N2O3 ($M-H^+$): m/z 417.1432; found 417.1442.



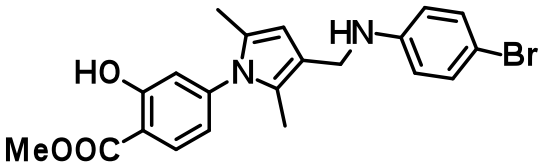
4g. ^{1}H NMR (500 MHz, $CDCl_3$) 10.93 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.06(d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 1.9 Hz, 1H), 6.76-6.73 (m, 1H), 6.63-6.62 (m, 2H), 5.98 (s, 1H), 4.06 (s, 2H), 4.00 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 162.1, 147.4, 145.2, 140.2, 130.7, 128.1, 125.9, 122.4, 119.2, 117.1, 116.8, 112.8, 111.8, 107.5, 52.5, 40.8, 12.8, 10.7. ESI-MS Cacld.for C22H20F3N2O4 ($M-H^+$): m/z 434.1465; found 434.1392.



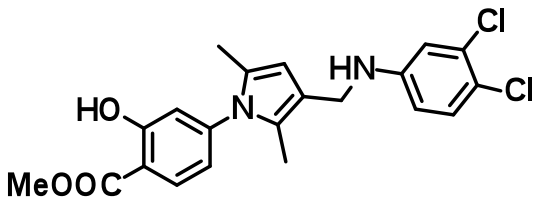
4h. ^{1}H NMR (500 MHz, $CDCl_3$) 10.92 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.09-7.08 (m, 2H), 6.86 (d, *J* = 2.0 Hz, 1H), 6.76-6.74 (m, 1H), 6.66-6.64 (m, 2H), 5.99 (s, 1H), 4.07 (s, 2H), 4.00 (s, 3H),2.83 (p, *J* = 6.9 Hz, 1H), 2.07 (s, 3H), 2.05 (s, 3H),1.24 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 162.1, 146.7, 145.3, 137.7, 130.6, 127.9, 127.0, 125.8, 119.2, 117.4, 117.1, 112.7, 111.6, 107.6, 52.5, 40.9, 33.2, 24.3, 12.8, 10.7. ESI-MS Cacld.for C24H27N2O3 ($M-H^+$): m/z 391.2109; found 391.2036.



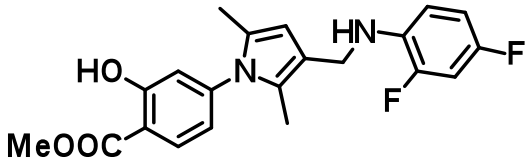
4i. ^{1}H NMR (500 MHz, $CDCl_3$) 10.93 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.14(dd, *J* = 6.8, 2.1 Hz, 2H), 6.85 (d, *J* = 1.9 Hz, 1H), 6.74(dd, *J* = 8.4, 2.0 Hz, 1H), 6.60-6.58 (m, 2H), 5.97 (s, 1H), 4.05 (s, 2H), 4.00 (s, 3H),2.07 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 162.1, 147.1, 145.2, 130.6, 129.0, 128.1, 125.8, 121.6, 119.2, 117.1, 116.8, 113.7, 111.7, 107.4, 52.5, 40.7, 12.8, 10.7. ESI-MS Cacld.for C21H21ClN2O3 ($M-H^+$): m/z 383.1168; found 383.1168.



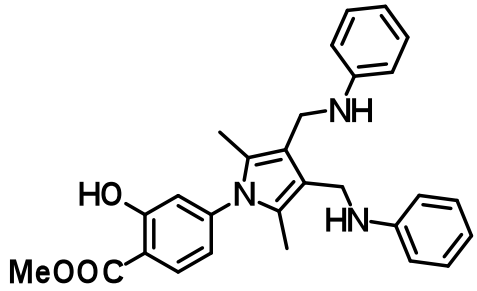
4j. ^{1}H NMR (500 MHz, $CDCl_3$) 10.92 (s, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.26(d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 2.0 Hz, 1H), 6.73(dd, *J* = 8.4, 2.0 Hz, 1H), 6.54 (d, *J* = 8.8 Hz, 2H), 5.96 (s, 1H), 4.03 (s, 2H), 3.99 (s, 3H),2.06 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0, 162.1, 147.5, 145.2, 131.8, 130.6, 128.1, 125.8, 119.2, 117.1, 116.8, 114.2, 111.7, 108.6, 107.4, 52.5, 40.6, 12.8, 10.7. ESI-MS Cacld.for C21H21BrN2O3 ($M-H^+$): m/z 427.0663; found 427.0660.



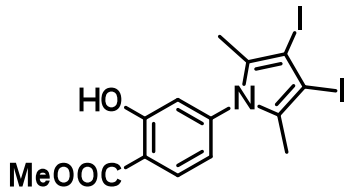
4k. ^{1}H NMR (500 MHz, $CDCl_3$) 10.93 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.19(d, *J* = 8.7Hz, 1H), 6.85 (t, *J* = 2.1 Hz, 1H), 6.75-6.73(m, 2H), 6.48 (dd, *J* = 8.8, 2.8Hz, 1H), 5.95 (s, 1H), 4.03 (s, 2H), 4.00 (s, 3H),2.06 (s, 3H), 2.05 (s, 3H). ESI-MS Cacld. for $C_{21}H_{20}Cl_2N_2O_3$ ($M-H^+$): m/z 417.0778; found 417.0783.



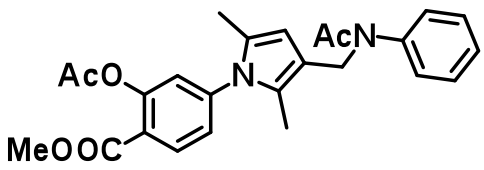
4l. ^{1}H NMR (500 MHz, $CDCl_3$) 10.92 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 6.86 (d, *J* = 2.0 Hz, 1H), 6.81-6.71(m, 4H), 5.98 (s, 1H), 4.08 (s, 2H), 4.00 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H). ESI-MS Cacld. for $C_{21}H_{20}F_2N_2O_3$ ($M-H^+$): m/z 385.1369; found 385.1368.



5. ^{1}H NMR (500 MHz, $CDCl_3$) 10.94 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.19-7.16 (m, 4H), 6.86 (d, *J* = 2.0 Hz, 1H), 6.76-6.65(m, 8H), 4.13 (s, 4H), 4.00 (s, 3H), 2.08 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 162.2, 148.5, 145.1, 130.7, 129.3, 129.2, 126.1, 119.4, 118.6, 117.6, 117.3, 116.6, 115.1, 113.2, 111.9, 52.6, 39.2, 10.7. ESI-MS Cacld.for $C_{28}H_{28}N_3O_3$ ($M-H^+$): m/z 454.2; found 454.0.

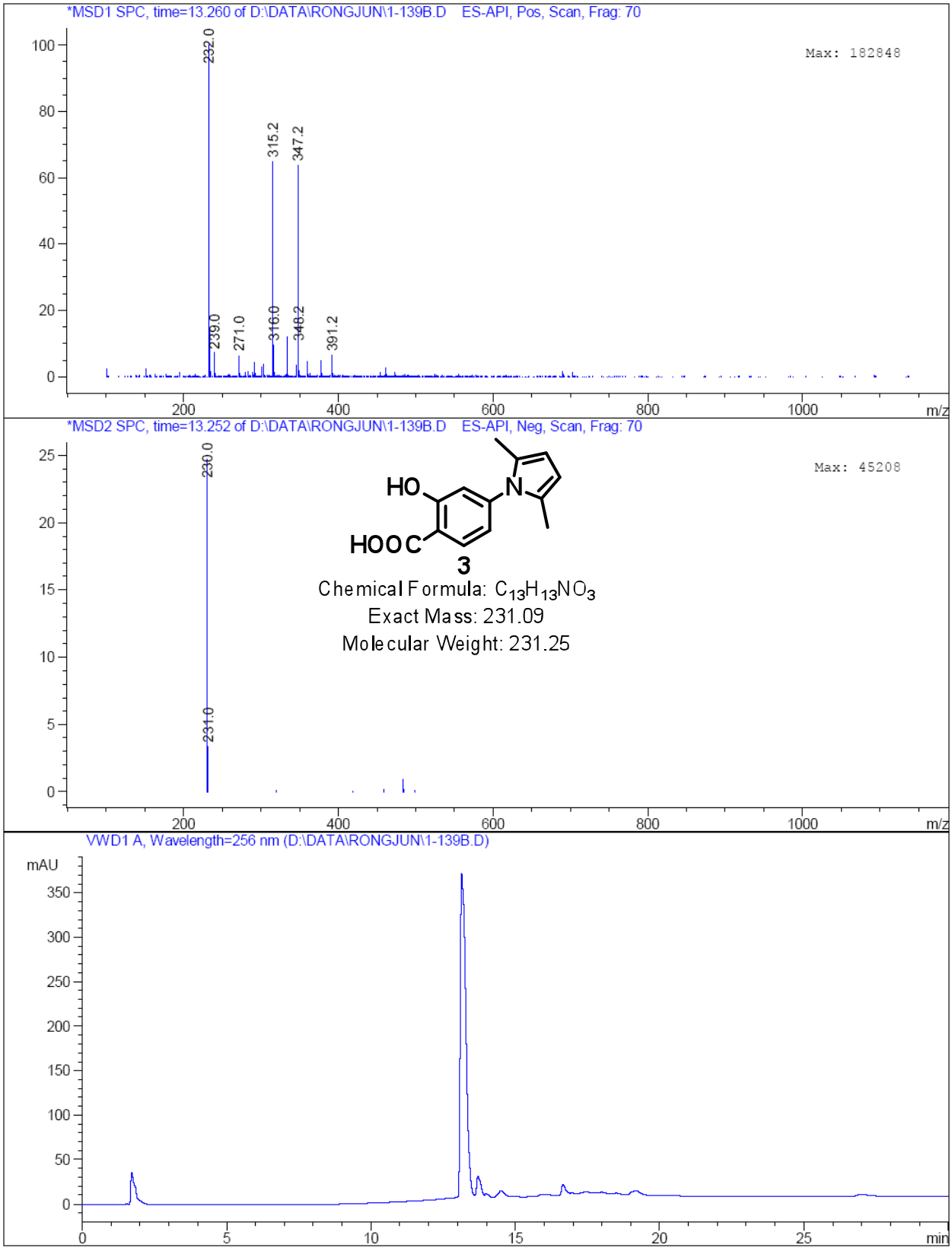


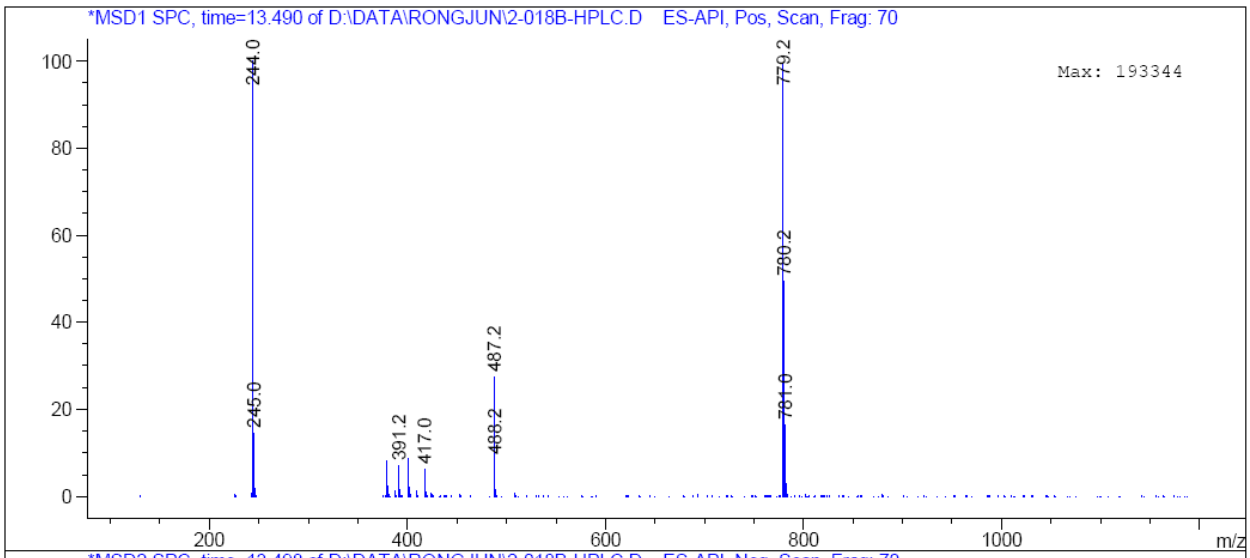
10b. ^{1}H NMR (500 MHz, $CDCl_3$) 10.95 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 2.0 Hz, 1H), 6.69-6.63 (m, 1H), 4.00 (s, 3H), 2.15 (s, 6H). ESI-MS Cacld.for $C_{14}H_{13}I_2NO_3$ ($M-H^+$): m/z 495.9; found 496.0.

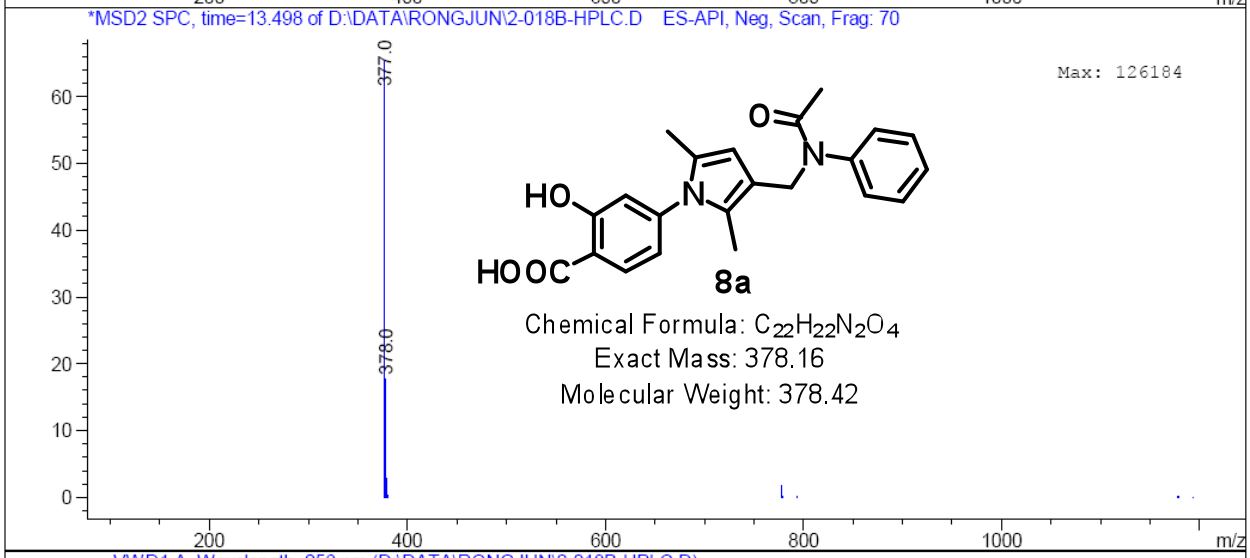


7a. ^{1}H NMR (500 MHz, $CDCl_3$) 8.06 (d, *J* = 8.3 Hz, 1H), 7.37-7.31 (m, 3H), 7.06-7.03 (m, 3H), 6.87 (d, *J* = 3.8 Hz, 1H), 5.85 (s, 1H), 4.69 (s, 2H), 3.89 (s, 3H), 2.35 (s, 3H), 2.00 (s, 3H), 1.83 (s, 3H), 1.66 (s, 3H). ESI-MS Cacld.for $C_{25}H_{27}N_2O_5$ ($M+H^+$): m/z 435.2; found 435.0.

LC-MS studies of hydrolyzed compounds **3, 8a-8l**, **9**, **11a**, **11b**

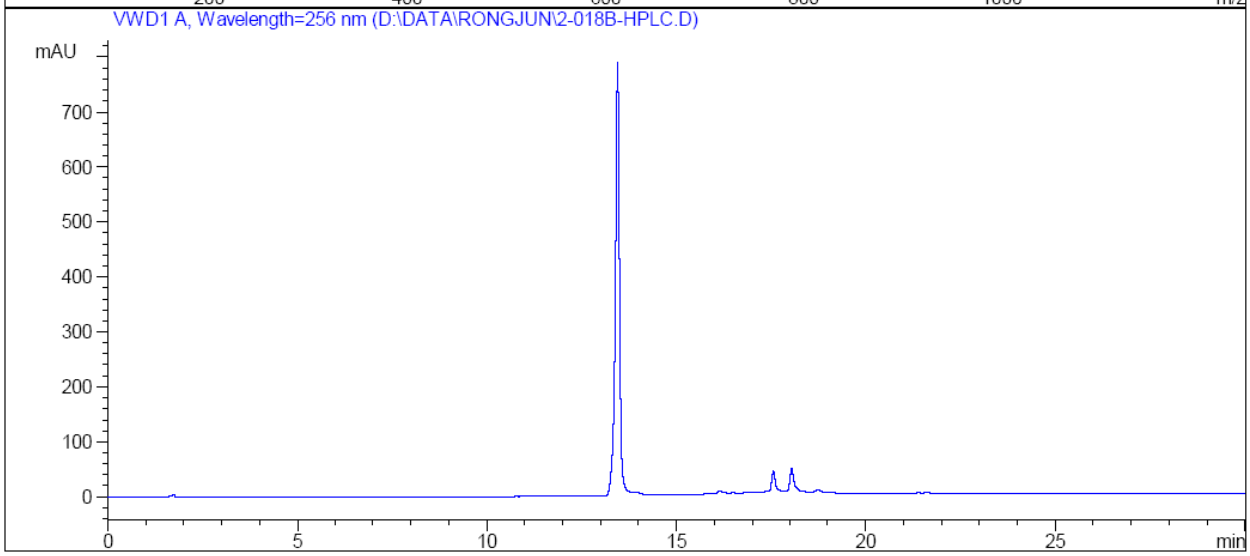


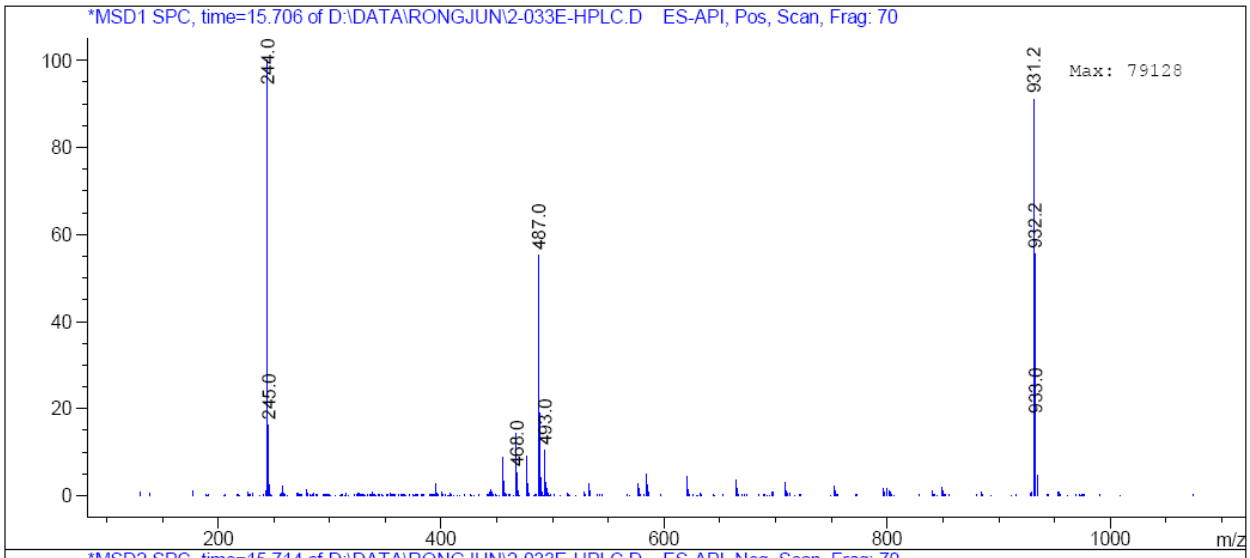


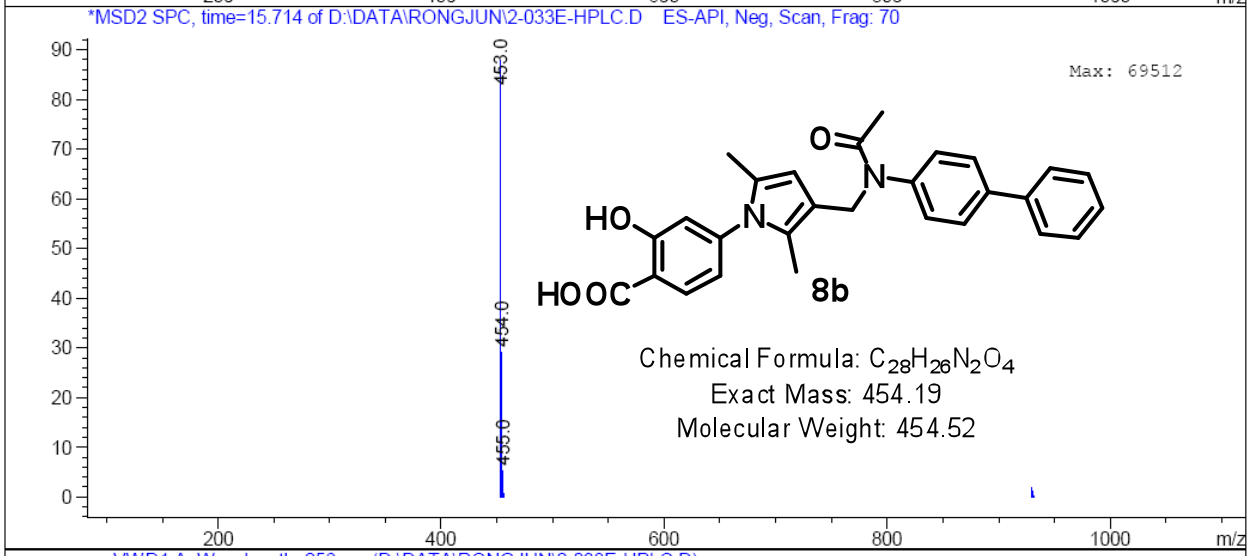


8a

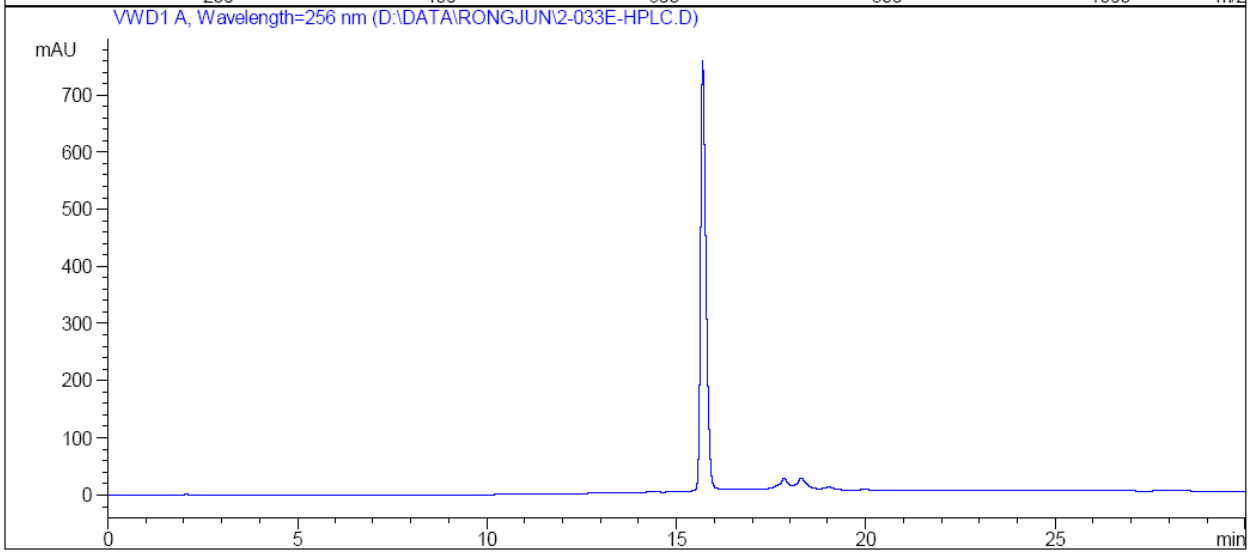
Chemical Formula: $C_{22}H_{22}N_2O_4$
Exact Mass: 378.16
Molecular Weight: 378.42

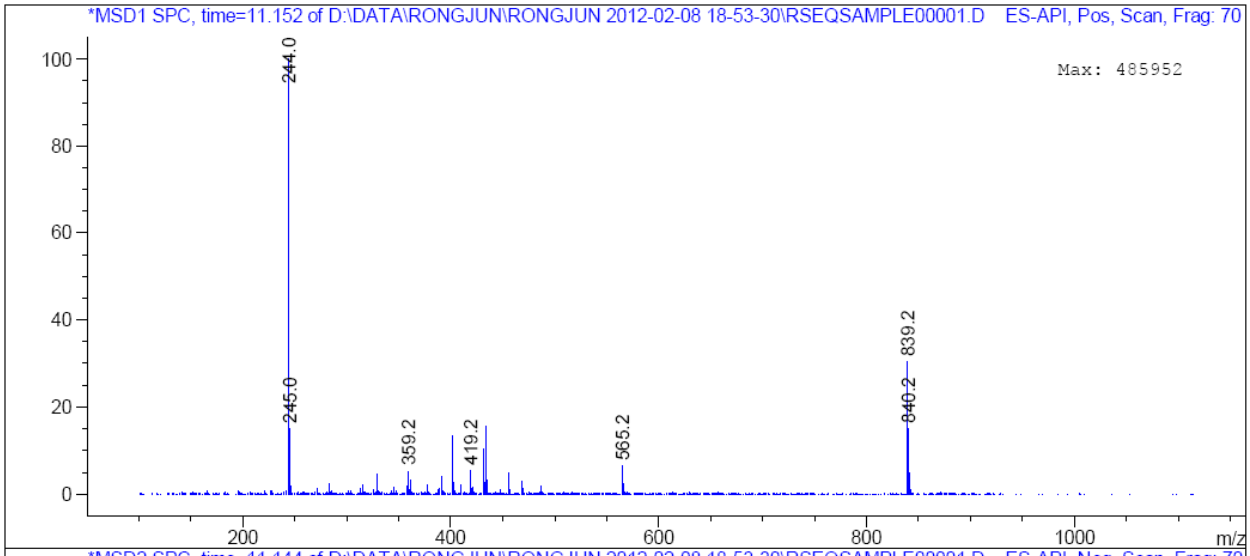


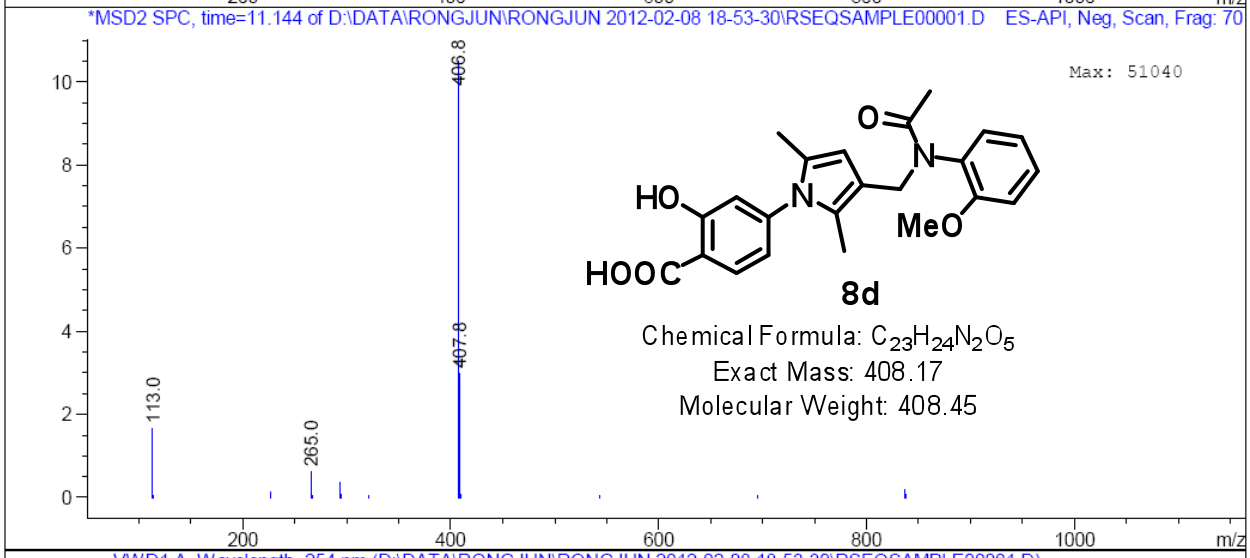




Chemical Formula: $C_{28}H_{26}N_2O_4$
Exact Mass: 454.19
Molecular Weight: 454.52

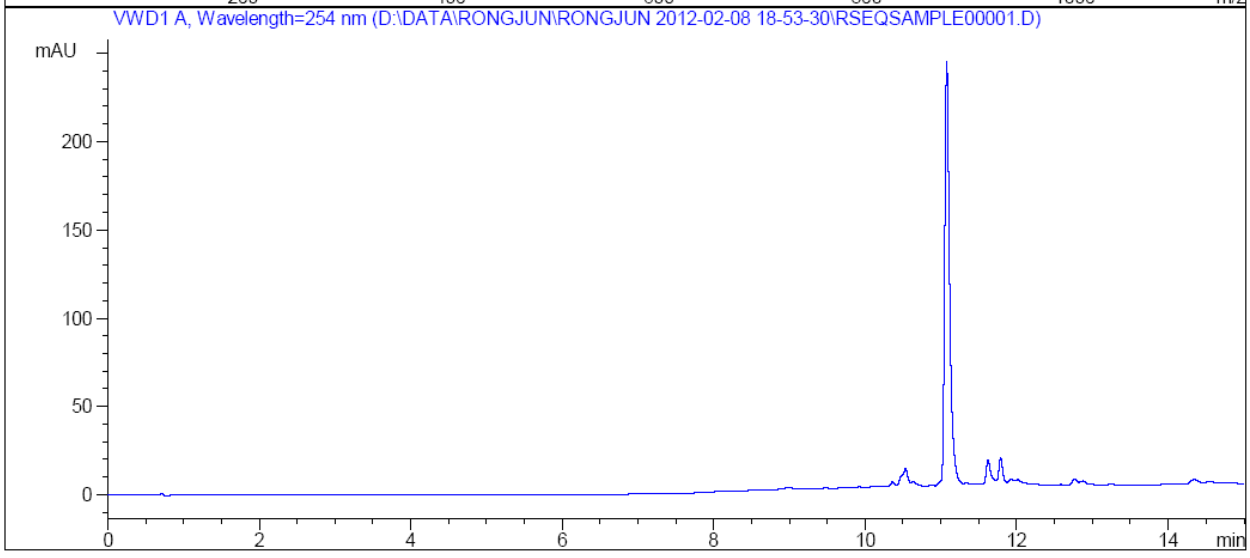


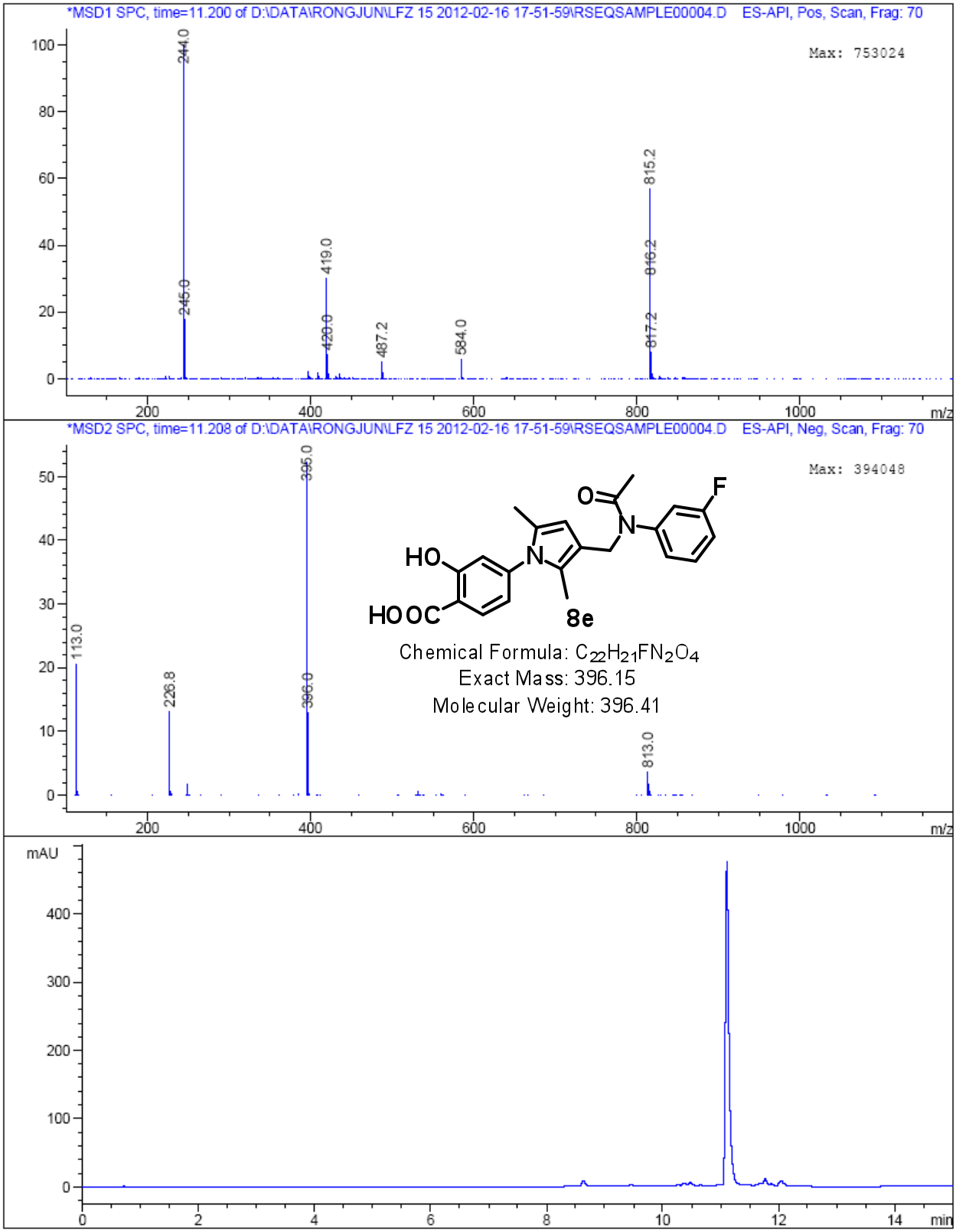




8d

Chemical Formula: $C_{23}H_{24}N_2O_5$
Exact Mass: 408.17
Molecular Weight: 408.45

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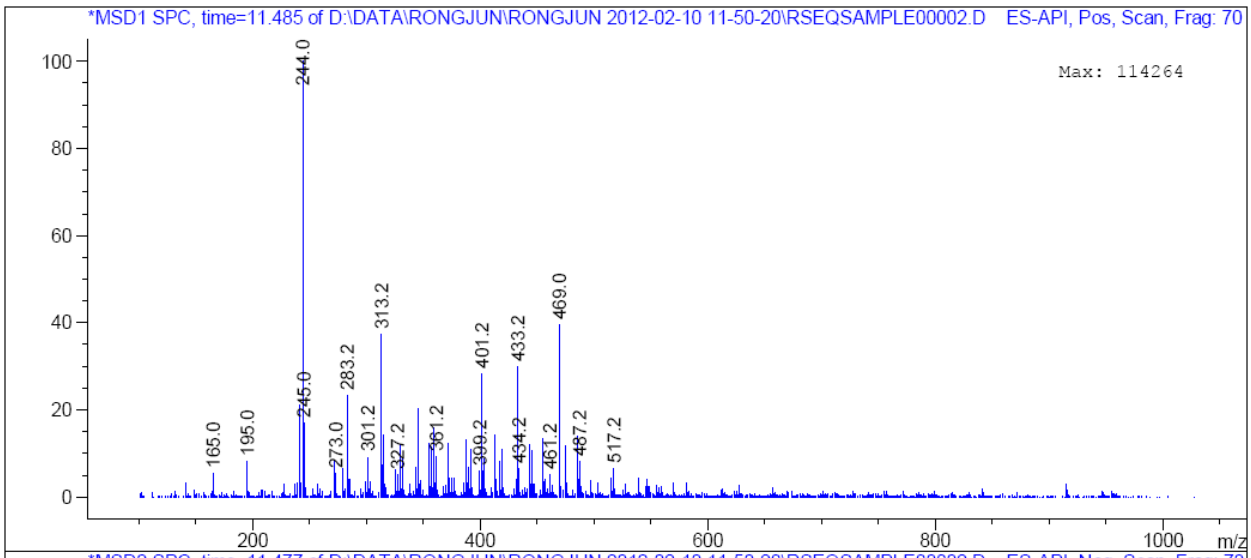
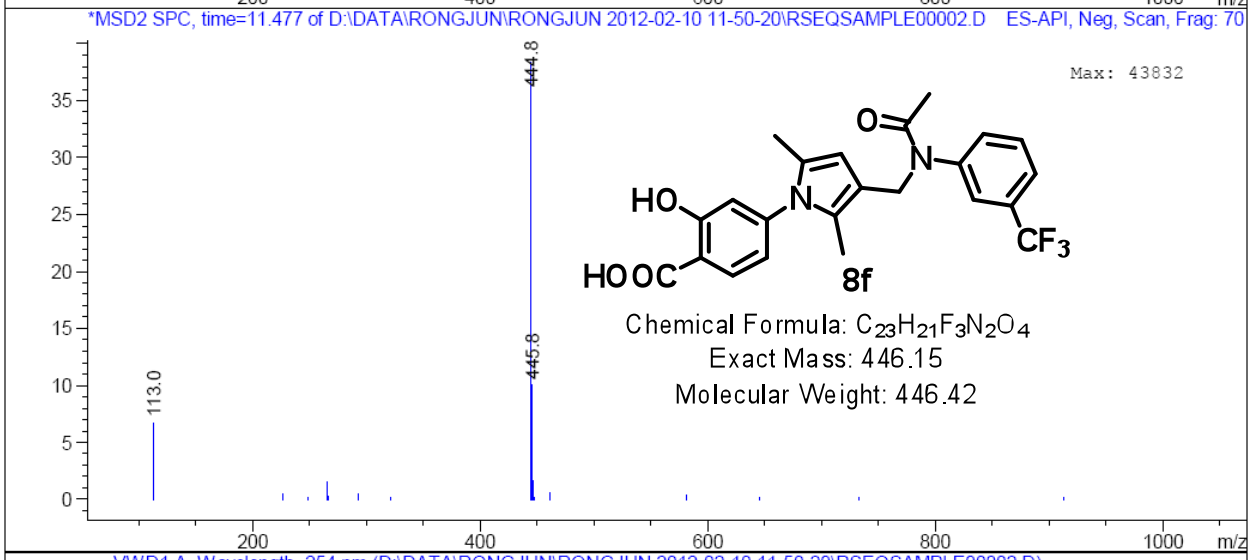
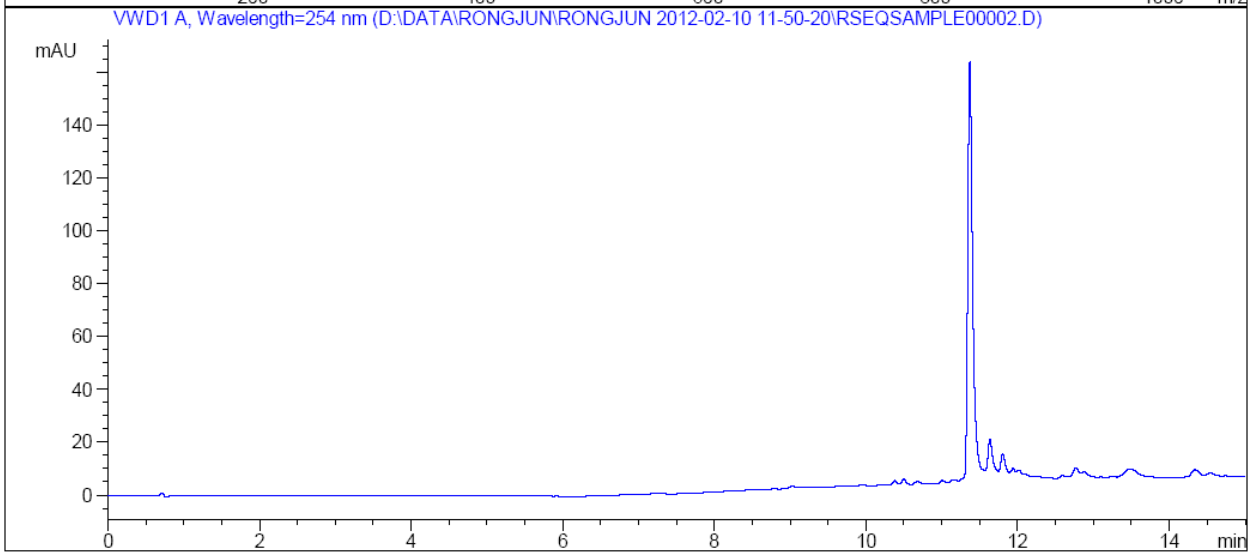
245.0
419.0
420.0
487.2
584.0
815.2
816.2
817.2
m/z
*MSD2 SPC, time=11.208 of D:\DATA\RONGJUN\LFZ 15 2012-02-16 17-51-59\RSEQSAMPLE00004.D ES-API, Neg, Scan, Frag: 70
Max: 394048
395.0
113.0
226.8
396.0
813.0
HO
HOOC
O
N
F
8e
Chemical Formula: C22H21FN2O4
Exact Mass: 396.15
Molecular Weight: 396.41
m/z
mAU
min

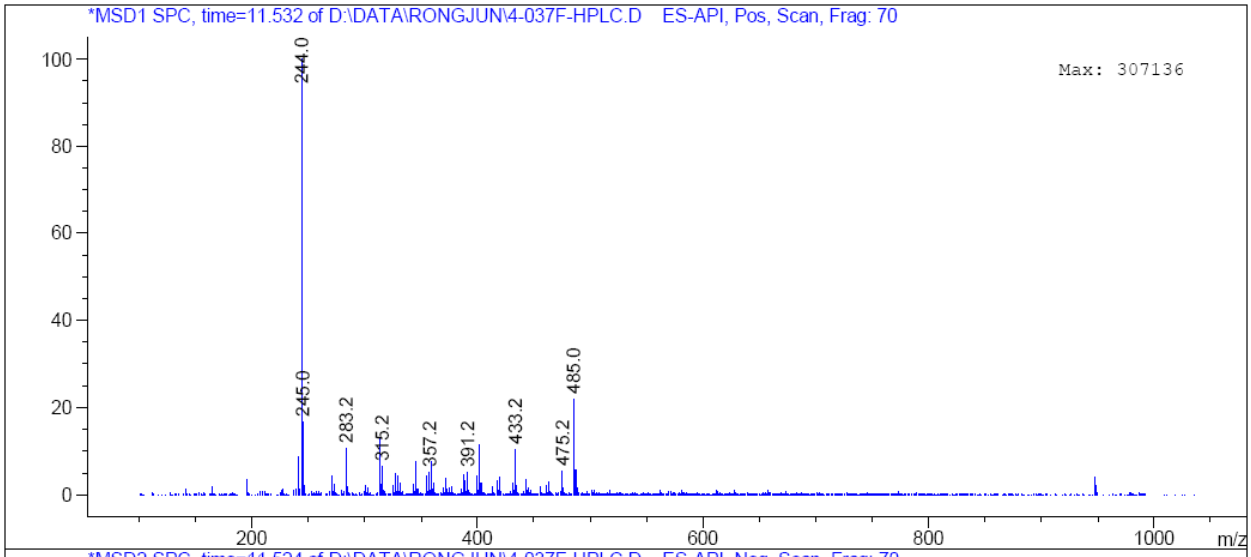


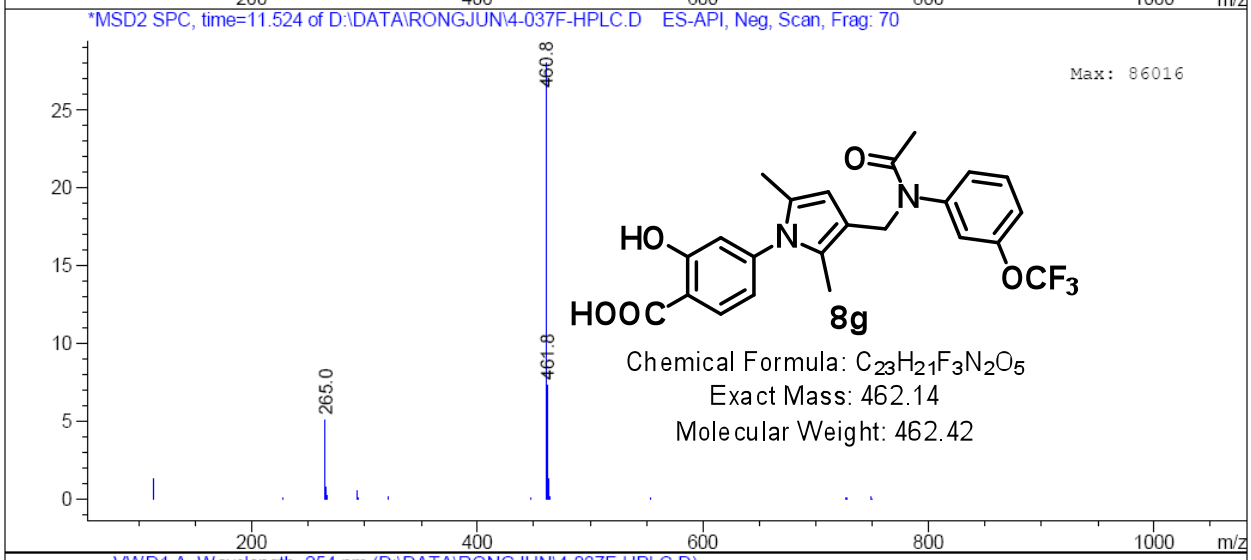


8f

Chemical Formula: $C_{23}H_{21}F_3N_2O_4$
Exact Mass: 446.15
Molecular Weight: 446.42

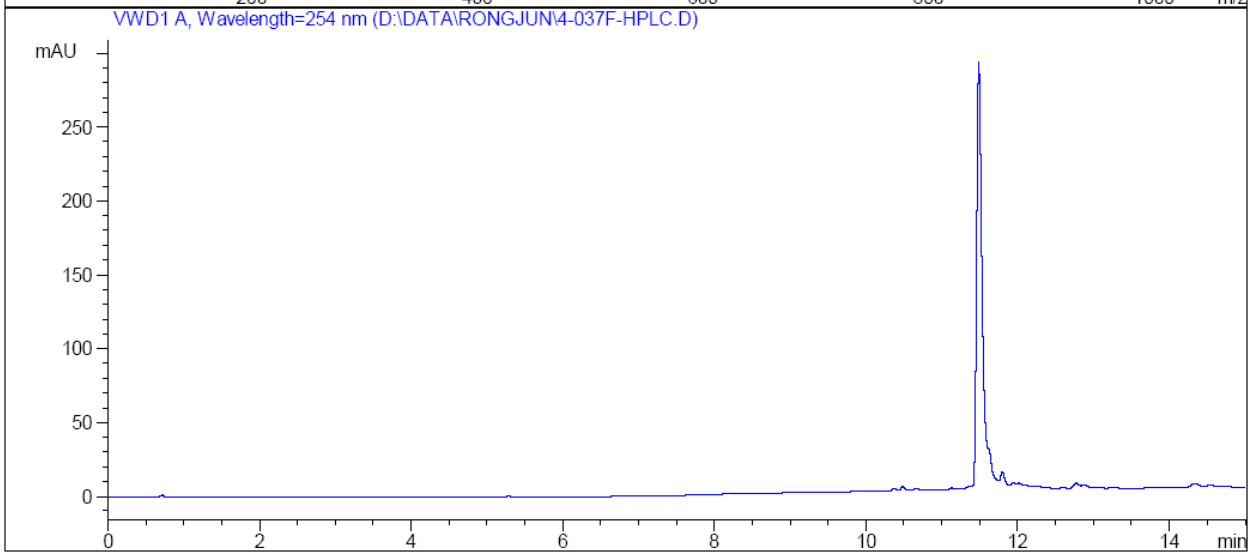


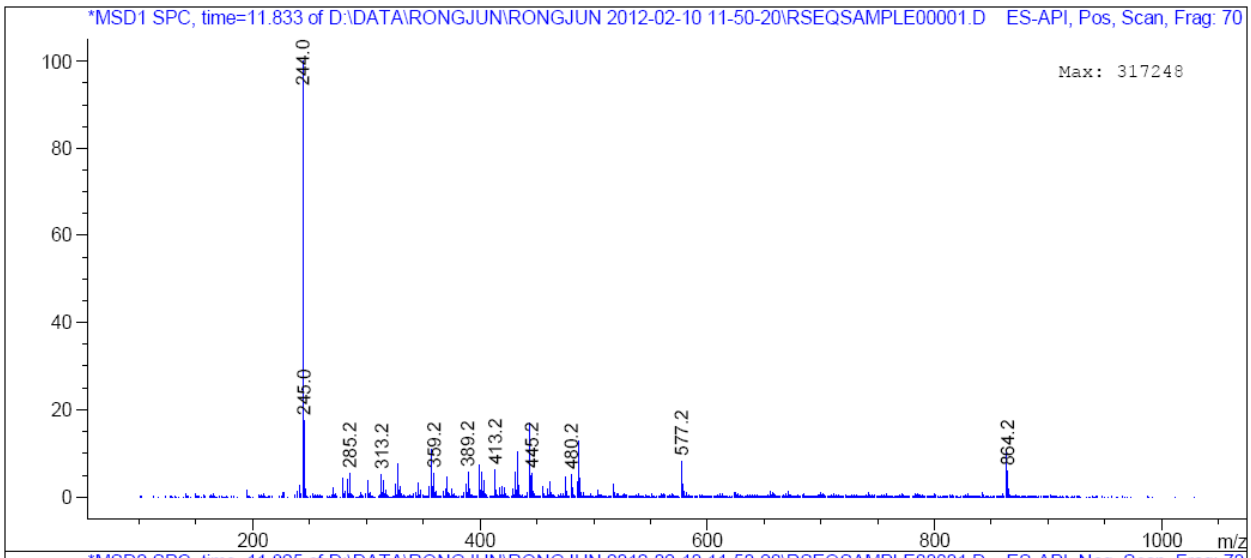


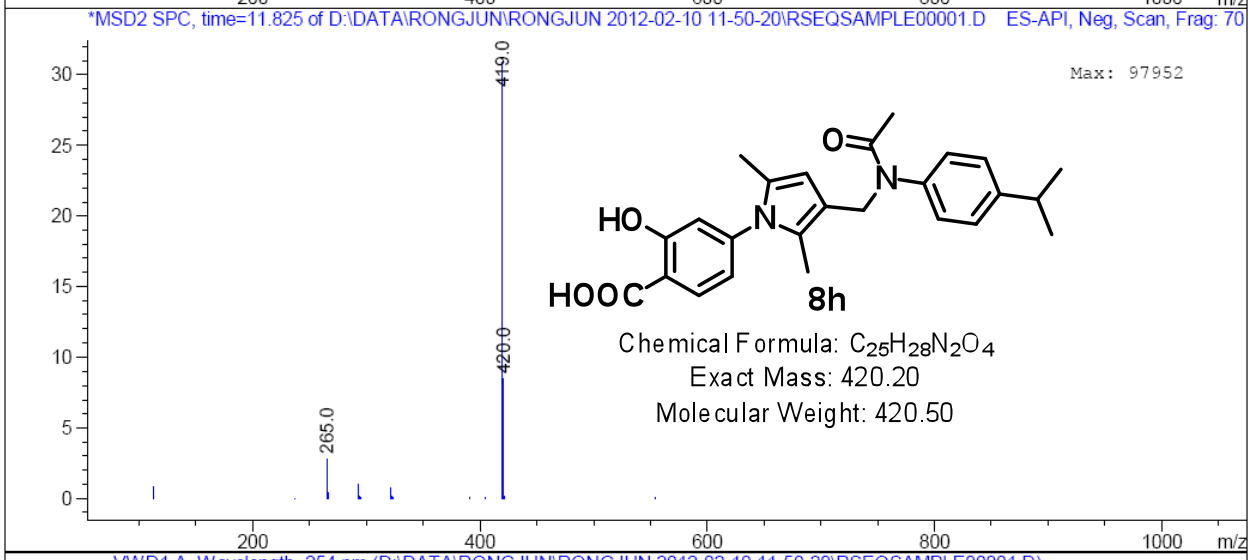


8g

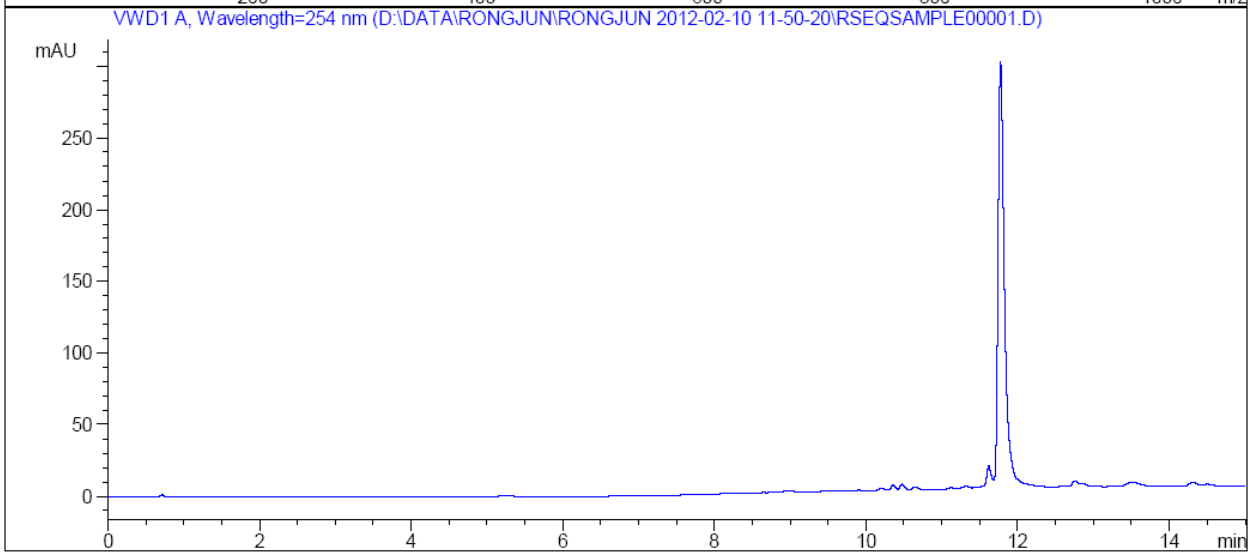
Chemical Formula: $C_{23}H_{21}F_3N_2O_5$
Exact Mass: 462.14
Molecular Weight: 462.42

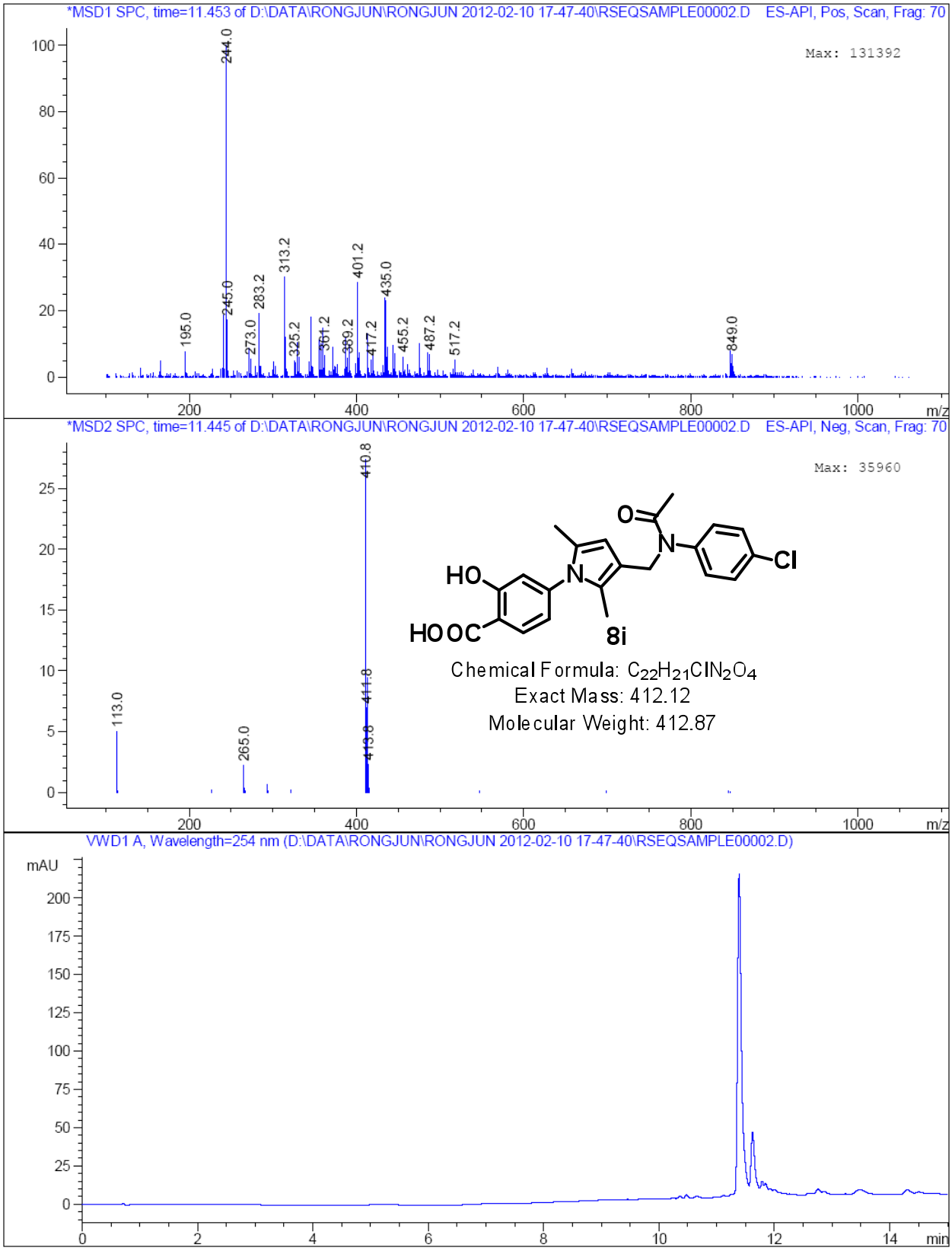






Chemical Formula: $C_{25}H_{28}N_2O_4$
Exact Mass: 420.20
Molecular Weight: 420.50

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Max: 131392
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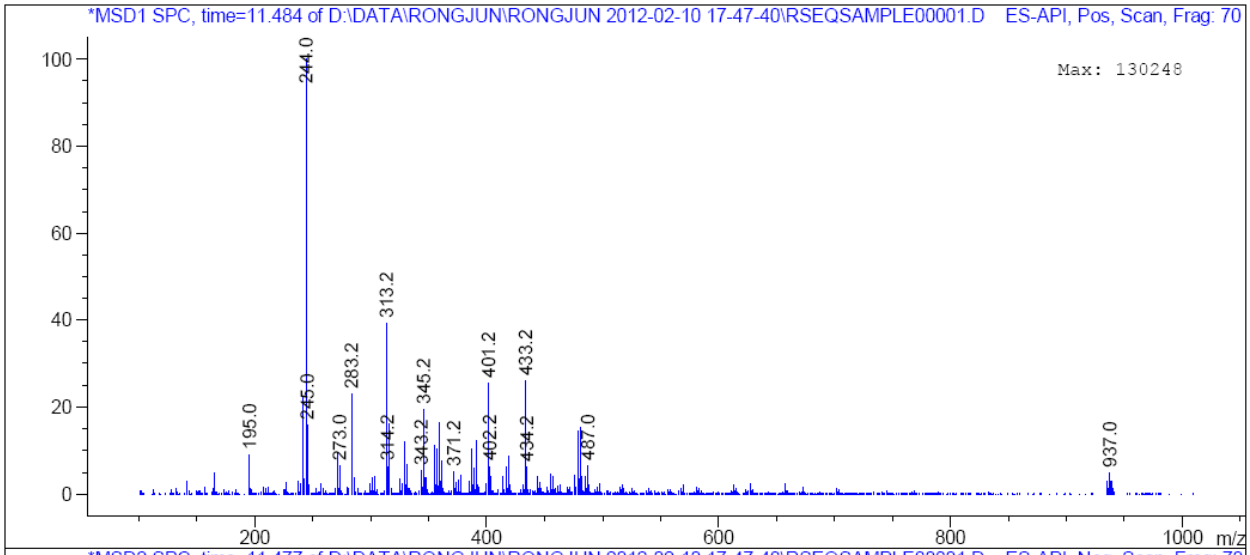
245.0
195.0
273.0
283.2
313.2
325.2
361.2
389.2
401.2
417.2
435.0
455.2
487.2
517.2
849.0
m/z
*MSD2 SPC, time=11.445 of D:\DATA\RONGJUN\RONGJUN 2012-02-10 17-47-40\RSEQSAMPLE00002.D ES-API, Neg, Scan, Frag: 70
Max: 35960
410.8
411.8
413.8
113.0
265.0
HO
HOOC
N
O
N
Cl
8i
Chemical Formula: C22H21ClN2O4
Exact Mass: 412.12
Molecular Weight: 412.87
m/z
VWD1 A, Wavelength=254 nm (D:\DATA\RONGJUN\RONGJUN 2012-02-10 17-47-40\RSEQSAMPLE00002.D)
mAU
min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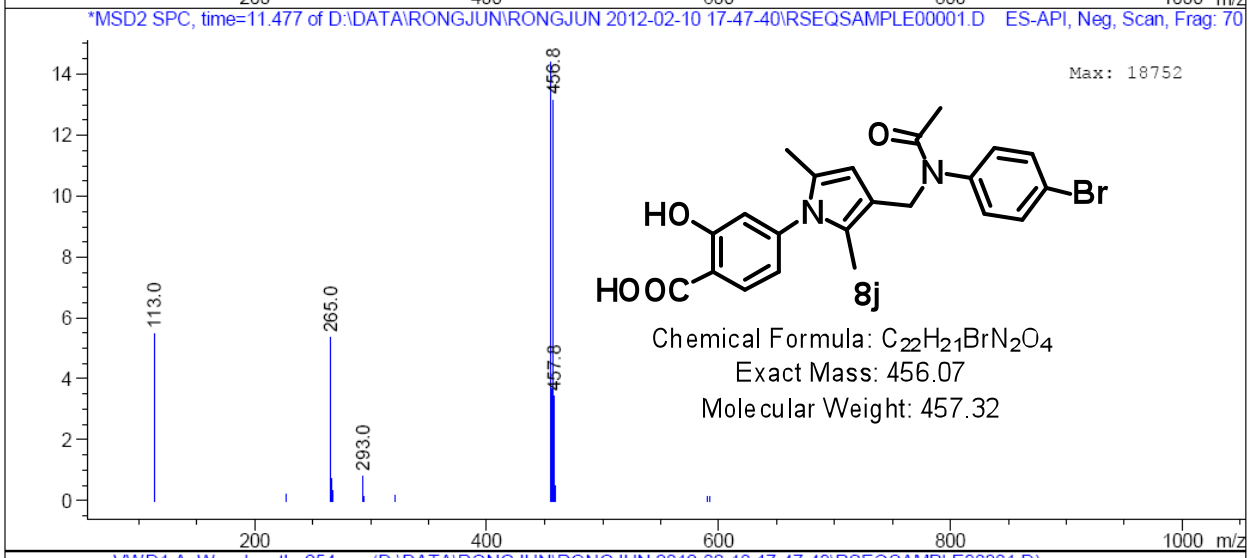
Max: 130248
244.0
313.2
283.2
345.2
401.2
433.2
195.0
245.0
273.0
314.2
343.2
371.2
402.2
434.2
487.0
937.0
m/z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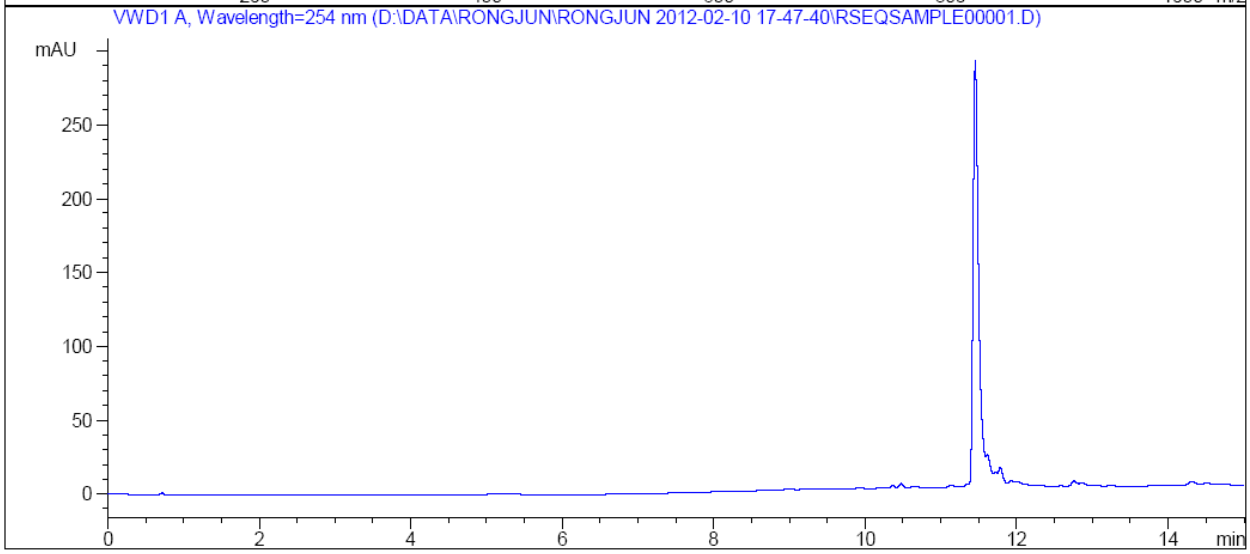
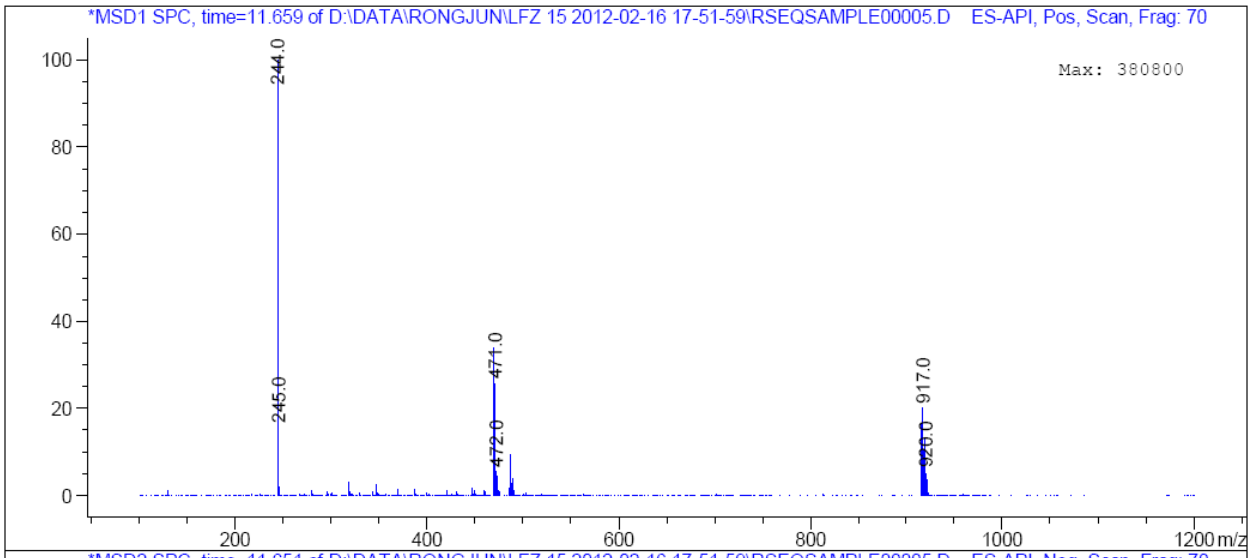
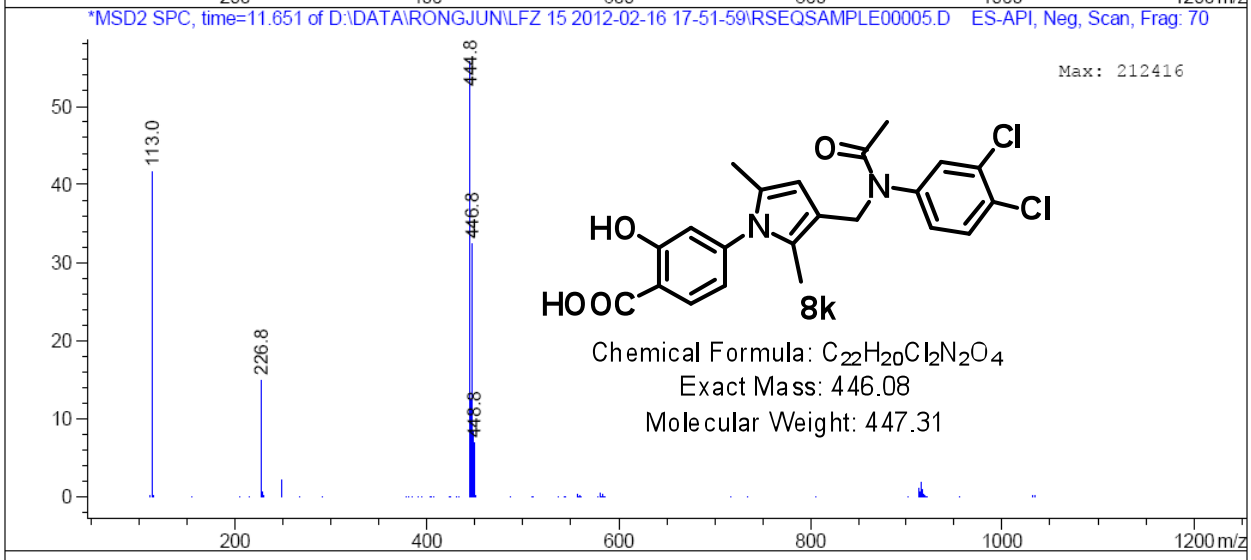
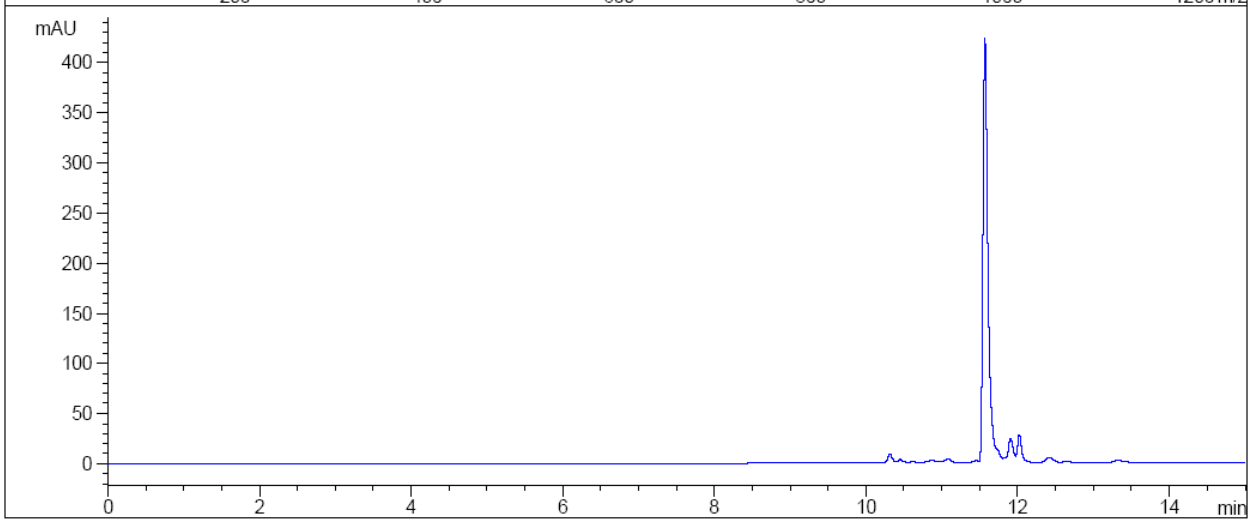
Max: 18752
456.8
457.8
113.0
265.0
293.0
m/z
HO
HOOC
O
N
Br
8j
Chemical Formula: C22H21BrN2O4
Exact Mass: 456.07
Molecular Weight: 457.32

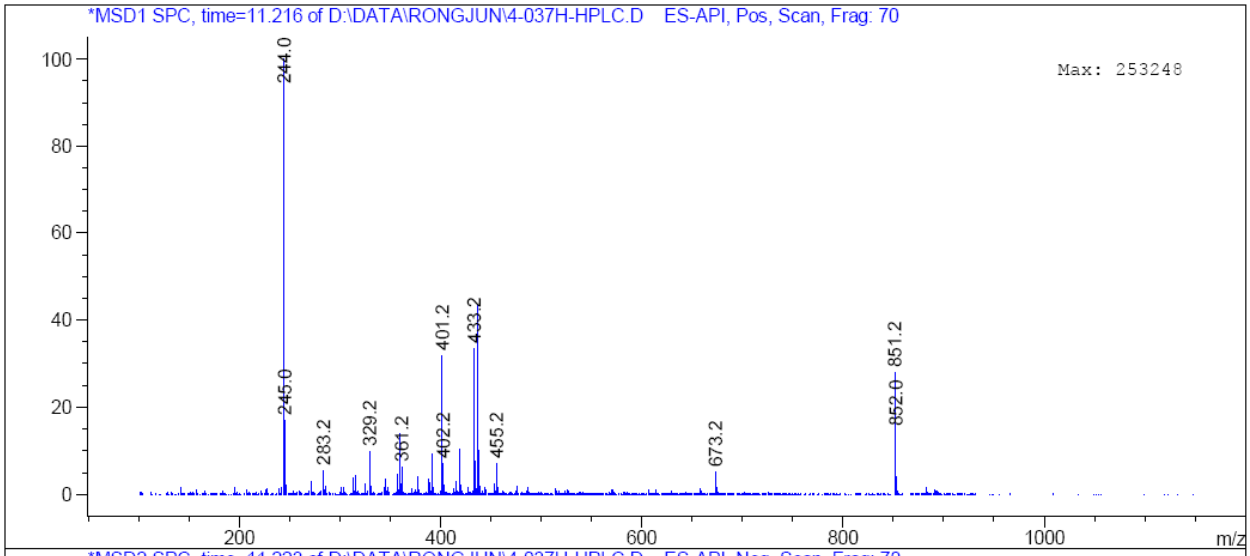

VWD1 A, Wavelength=254 nm (D:\DATA\RONGJUN\RONGJUN 2012-02-10 17-47-40\RSEQSAMPLE00001.D)
mAU
min

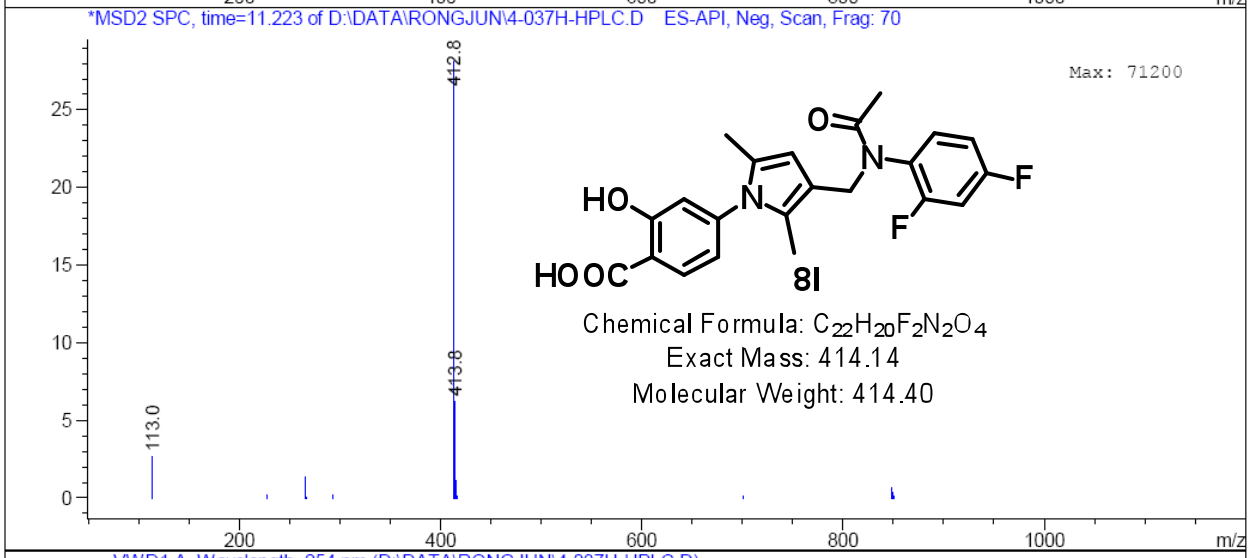




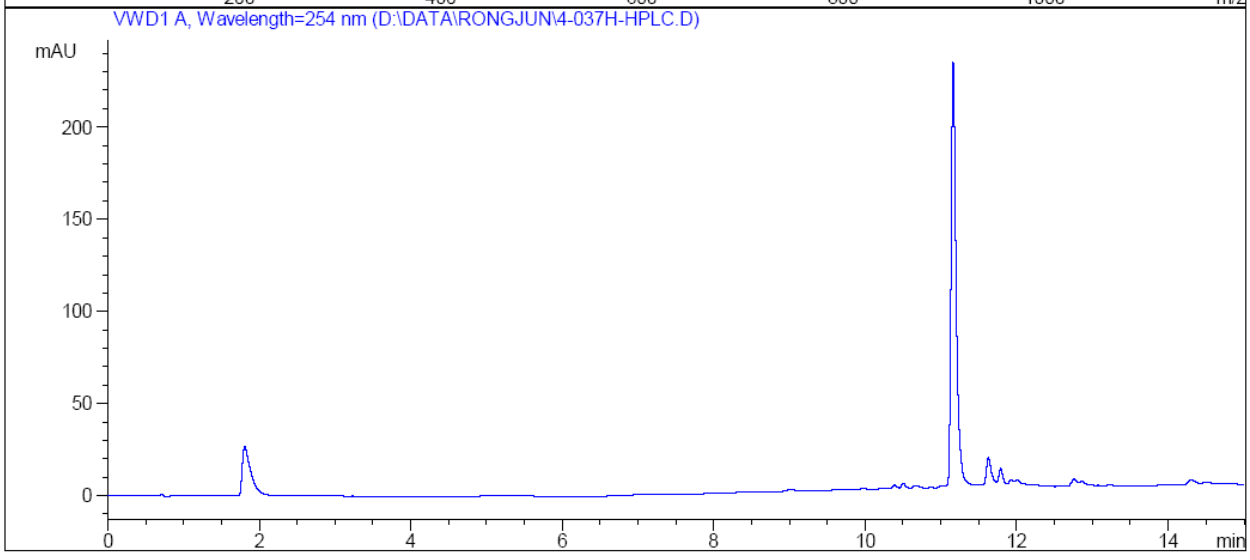
Chemical Formula: $C_{22}H_{20}Cl_2N_2O_4$
Exact Mass: 446.08
Molecular Weight: 447.31

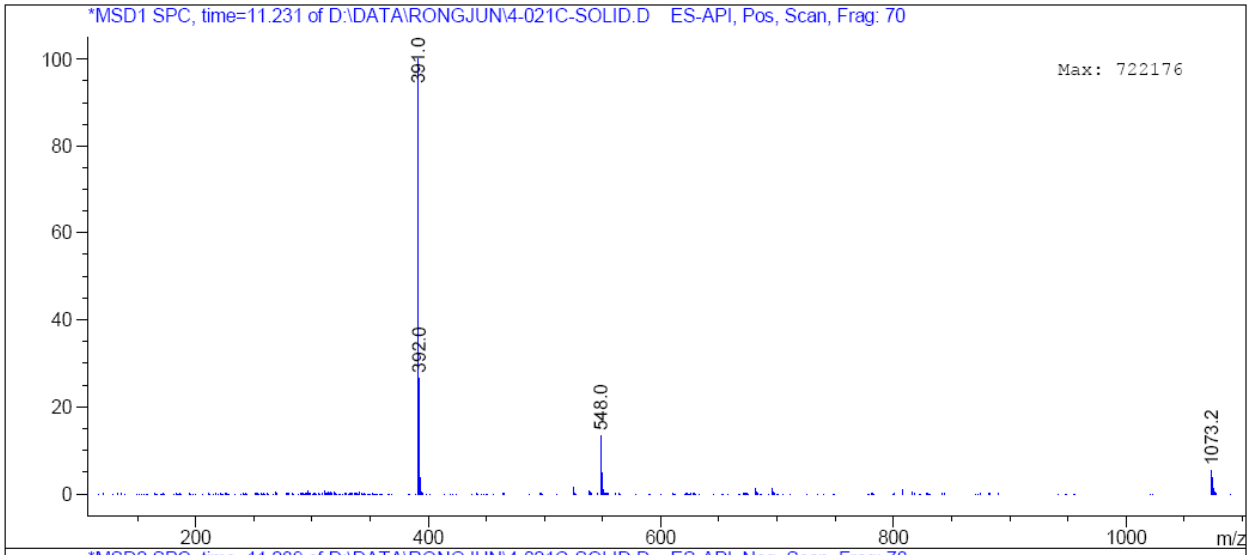


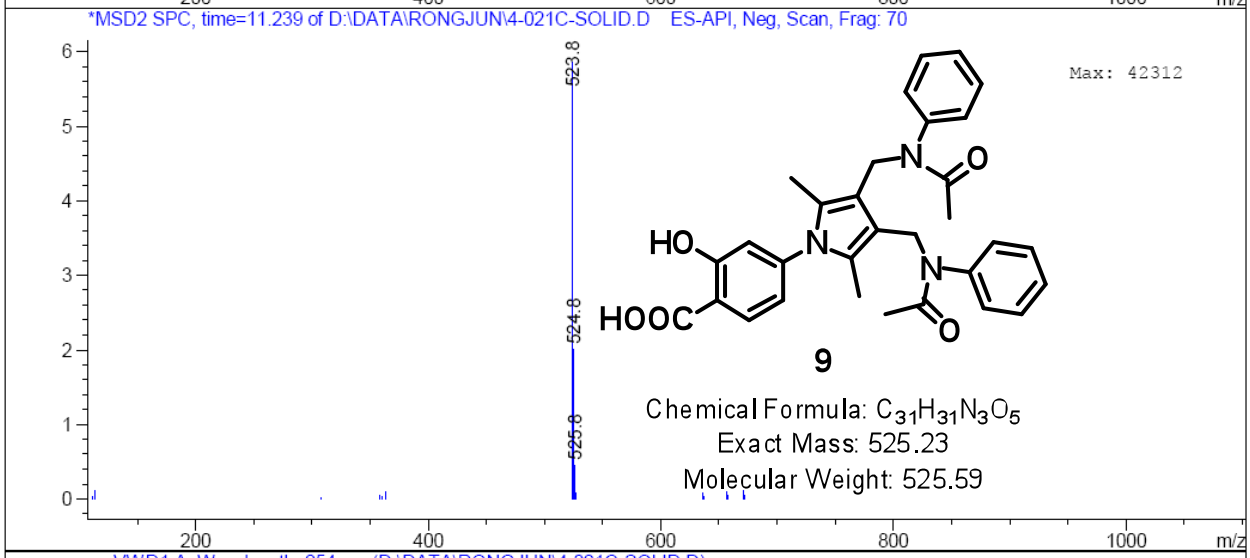




Chemical Formula: $C_{22}H_{20}F_2N_2O_4$
Exact Mass: 414.14
Molecular Weight: 414.40

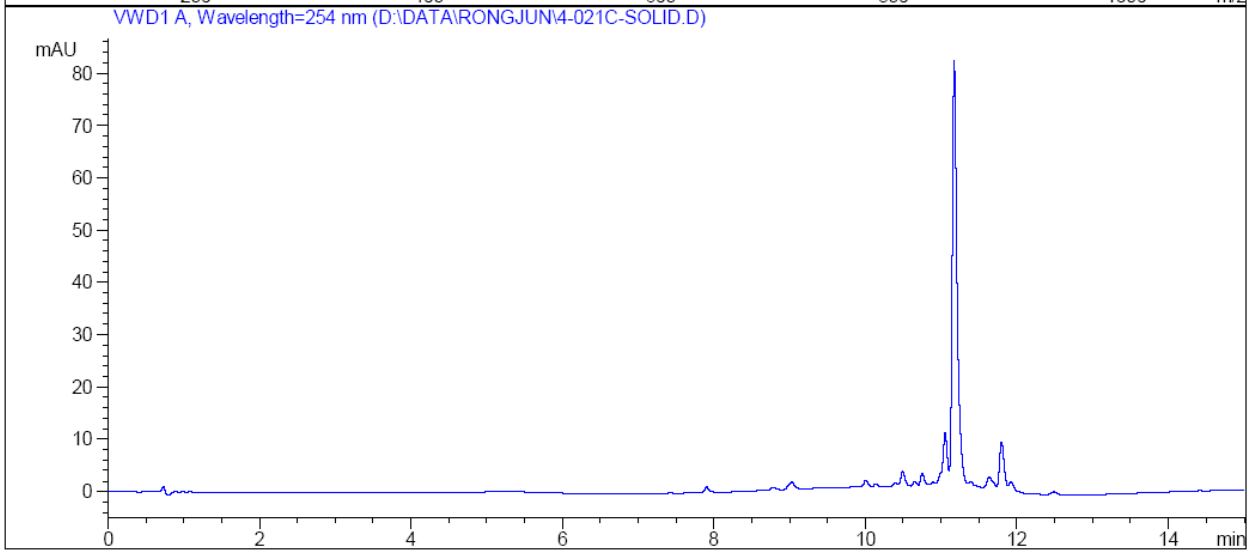


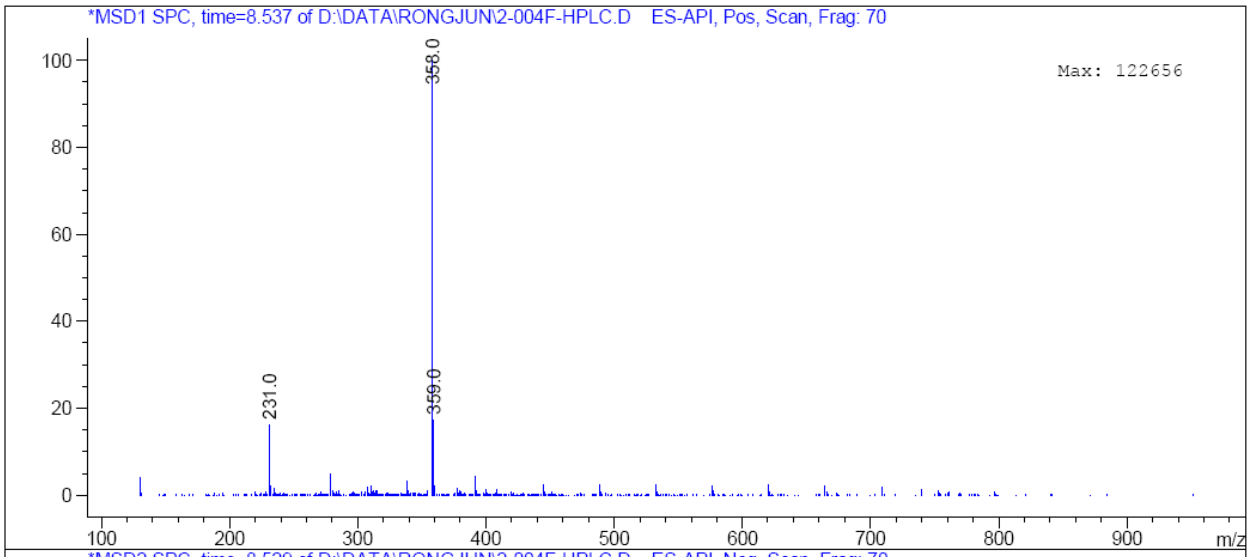




9

Chemical Formula: $C_{31}H_{31}N_3O_5$
Exact Mass: 525.23
Molecular Weight: 525.59

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Max: 122656
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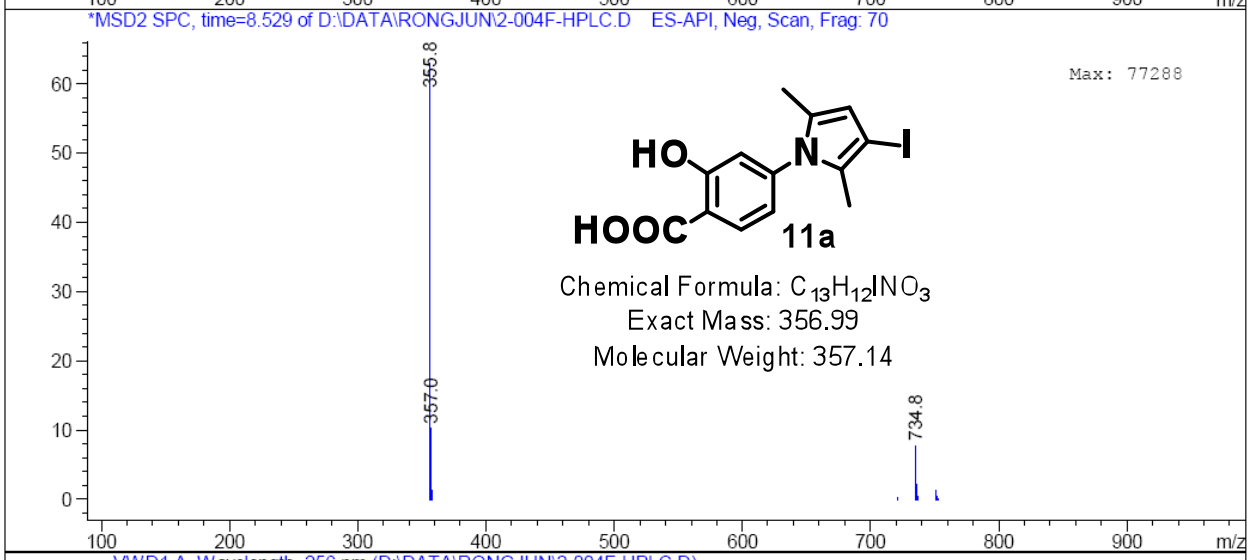
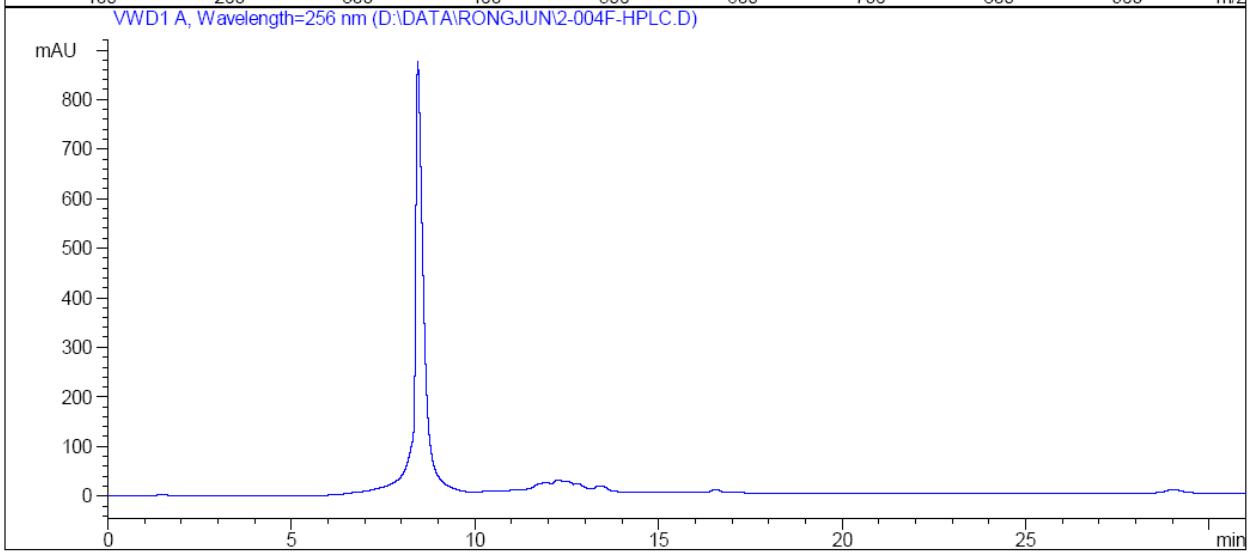
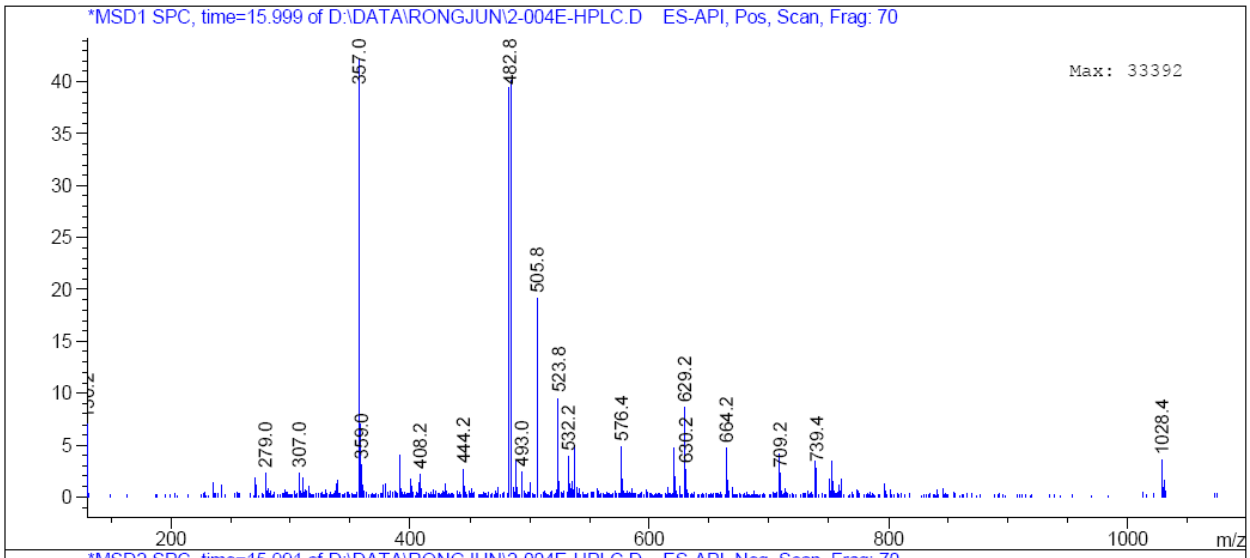
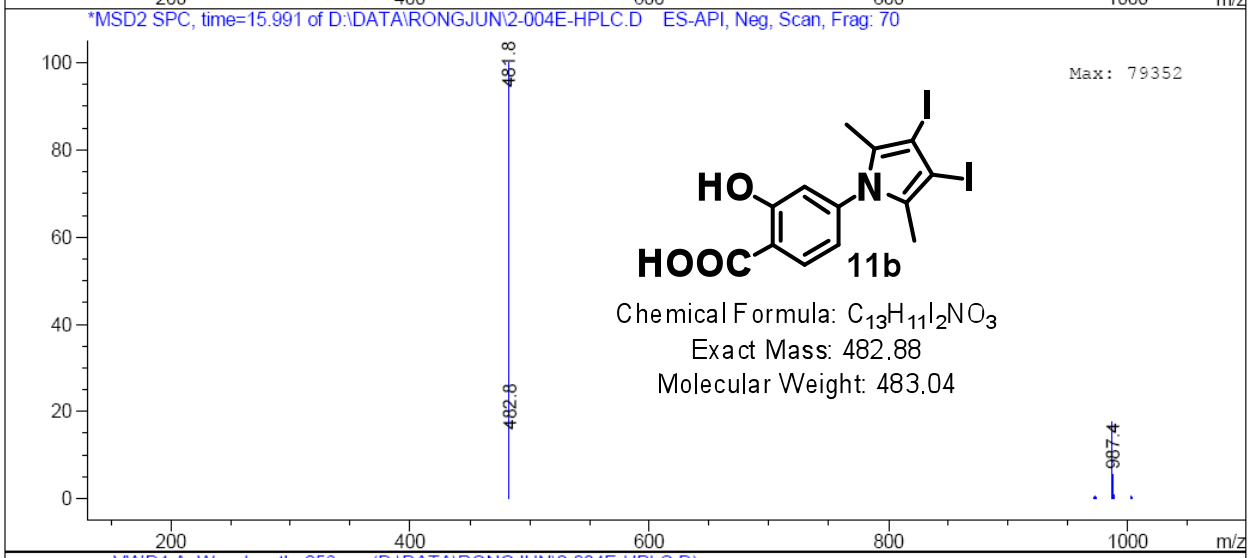
231.0
359.0
m/z

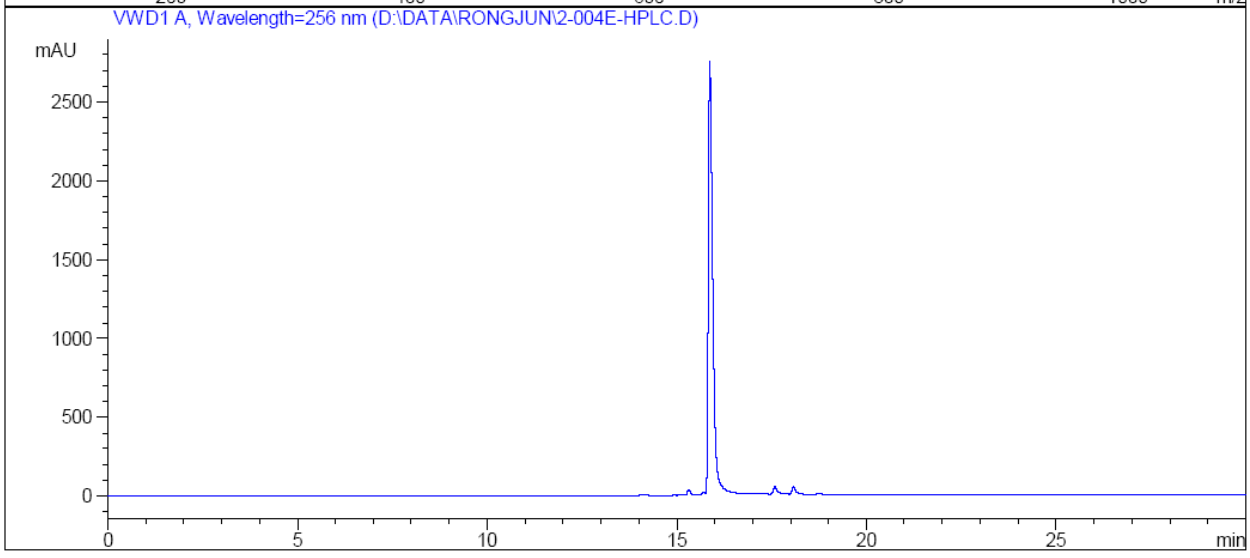

*MSD2 SPC, time=8.529 of D:\DATA\RONGJUN\2-004F-HPLC.D ES-API, Neg, Scan, Frag: 70
Max: 77288
355.8
357.0
734.8
HO
HOOC
N
I
11a
Chemical Formula: C13H12INO3
Exact Mass: 356.99
Molecular Weight: 357.14
m/z


VWD1 A, Wavelength=256 nm (D:\DATA\RONGJUN\2-004F-HPLC.D)
mAU
min

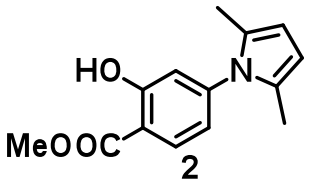




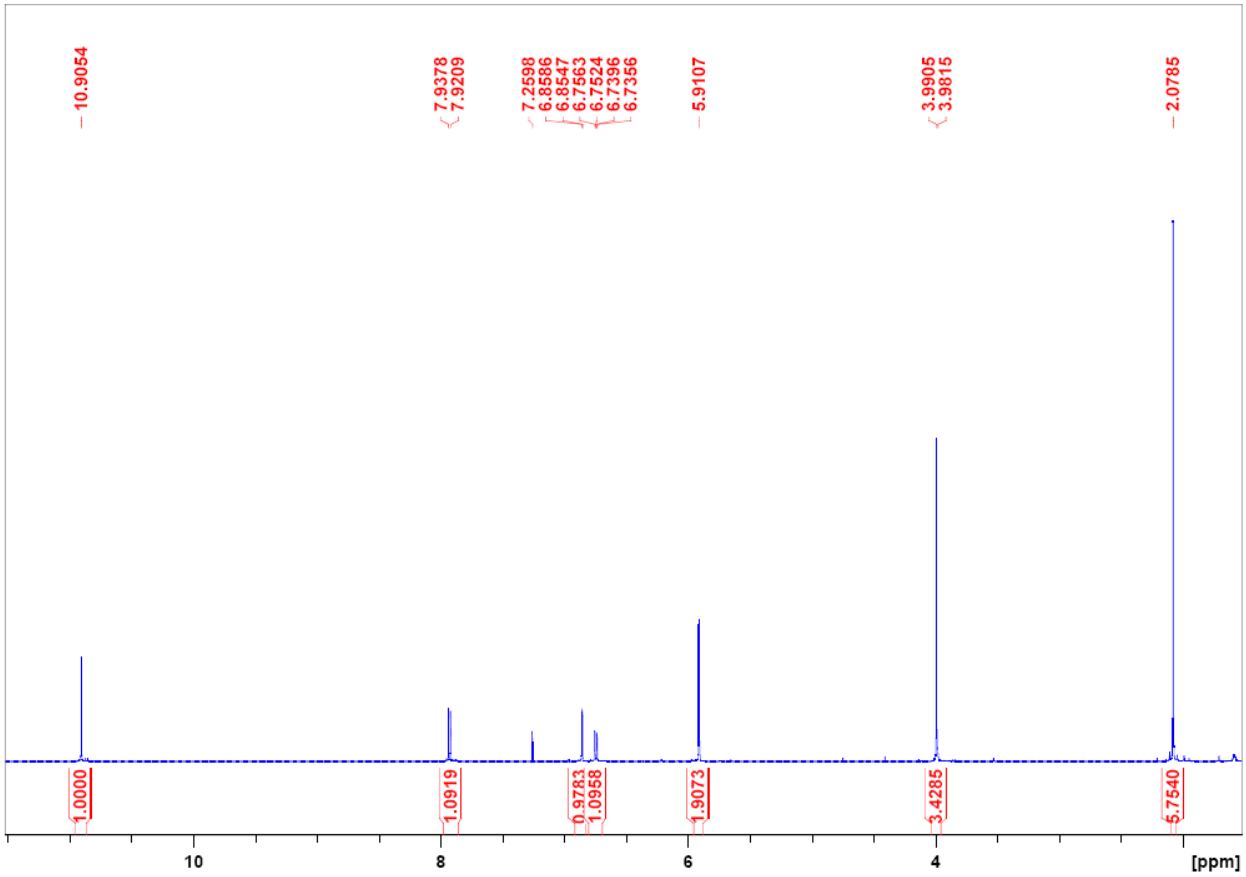
Chemical Formula: $C_{13}H_{11}I_2NO_3$
Exact Mass: 482.88
Molecular Weight: 483.04

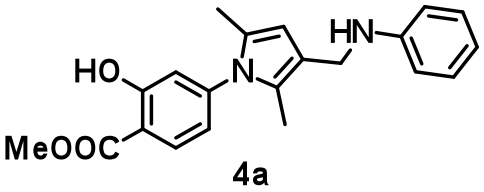


Copies of ^{1}H and ^{13}C NMR Spectra of compounds **2**, **4a-4l**, **5**, **7a**, **10b**

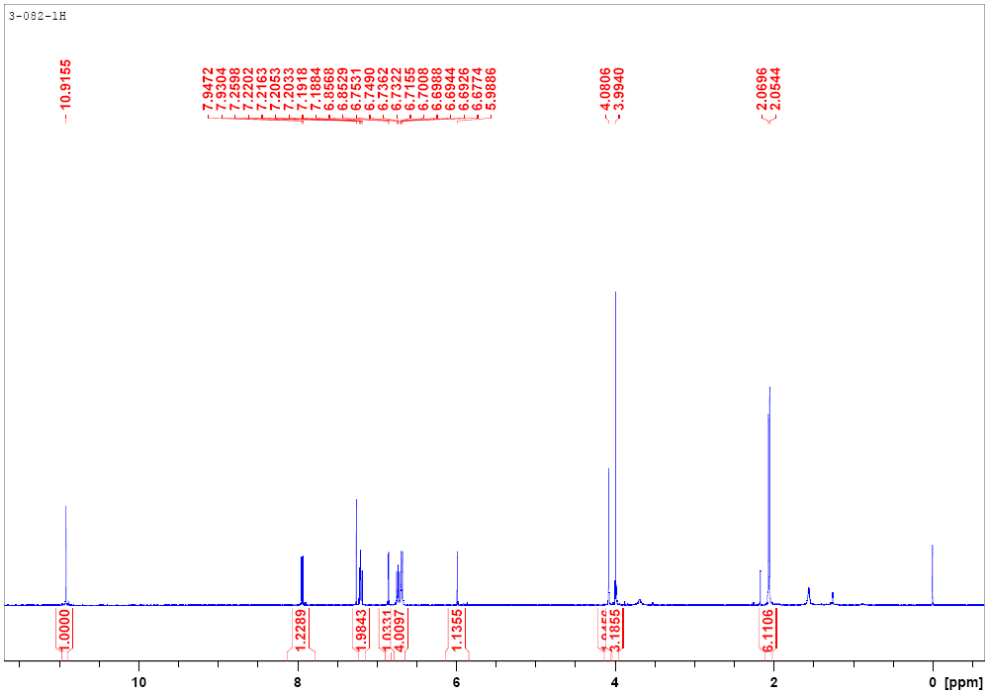


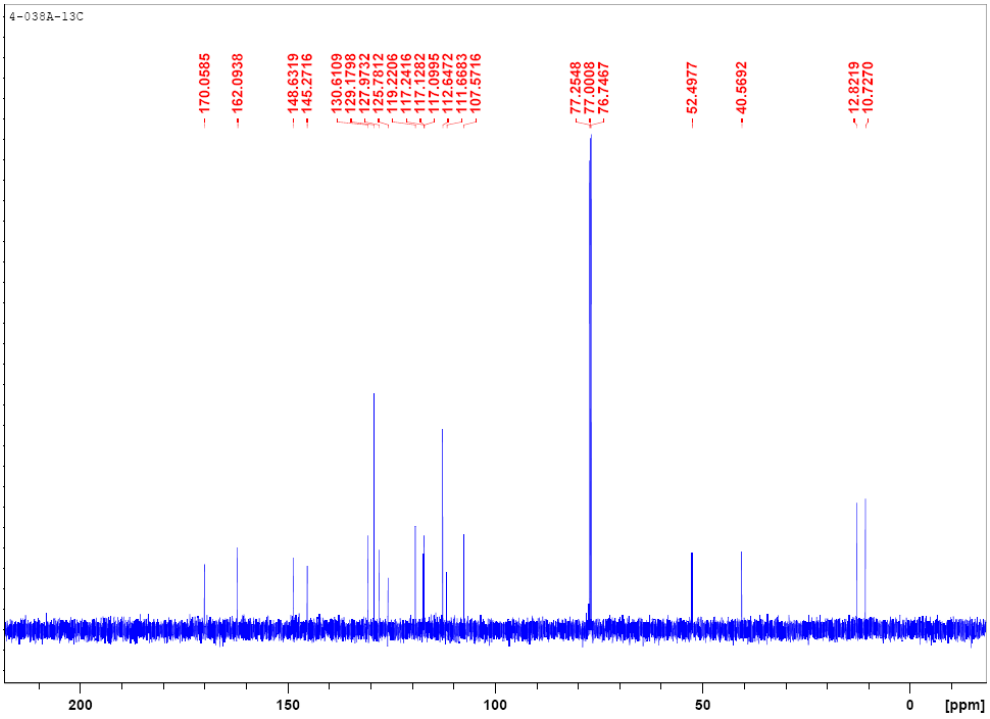
2

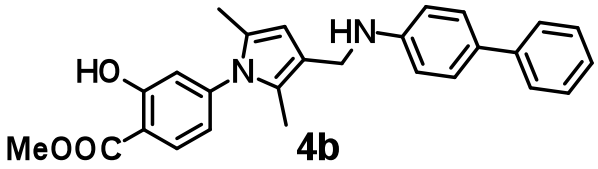



HO
N
HN
MeOOC

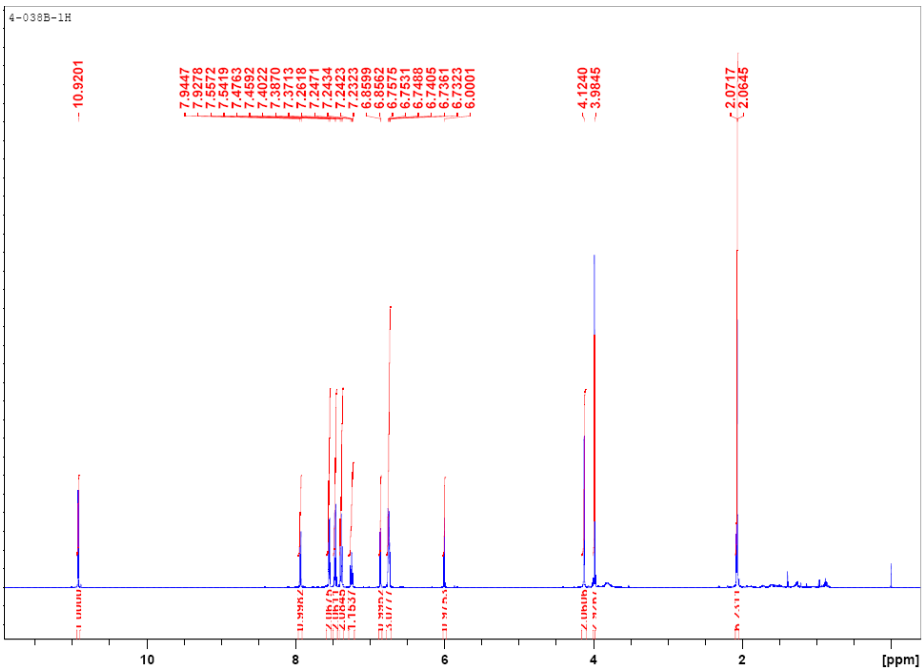
4a

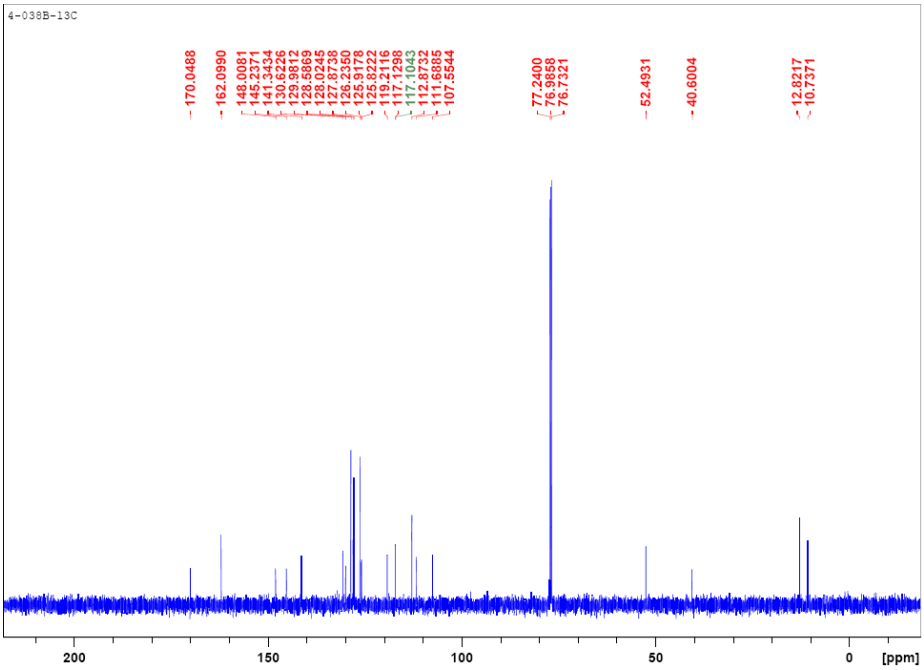

3-082-1H
10.9155
7.9472
7.9304
7.2598
7.2202
7.2163
7.2053
7.2033
7.1918
7.1884
6.8568
6.8529
6.7531
6.7490
6.7362
6.7322
6.7155
6.7008
6.6988
6.6944
6.6926
6.6774
5.9886
4.0806
3.9940
2.0696
2.0544
1.0000
1.2289
1.9843
1.0331
4.0097
1.1355
1.1455
3.1855
6.1106
10
8
6
4
2
0 [ppm]

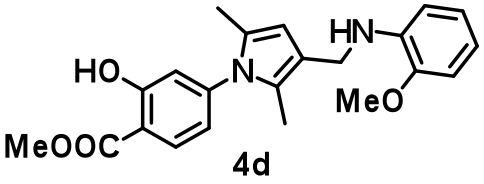

4-038A-13C
170.0585
162.0938
148.6319
145.2716
130.6109
129.1798
127.9732
126.7612
119.2206
117.2416
117.1882
117.0995
112.6572
111.6583
107.5716
77.2548
77.0008
76.7467
52.4977
40.5692
12.8219
10.7270
200
150
100
50
0 [ppm]


HO
N
HN
MeOOC

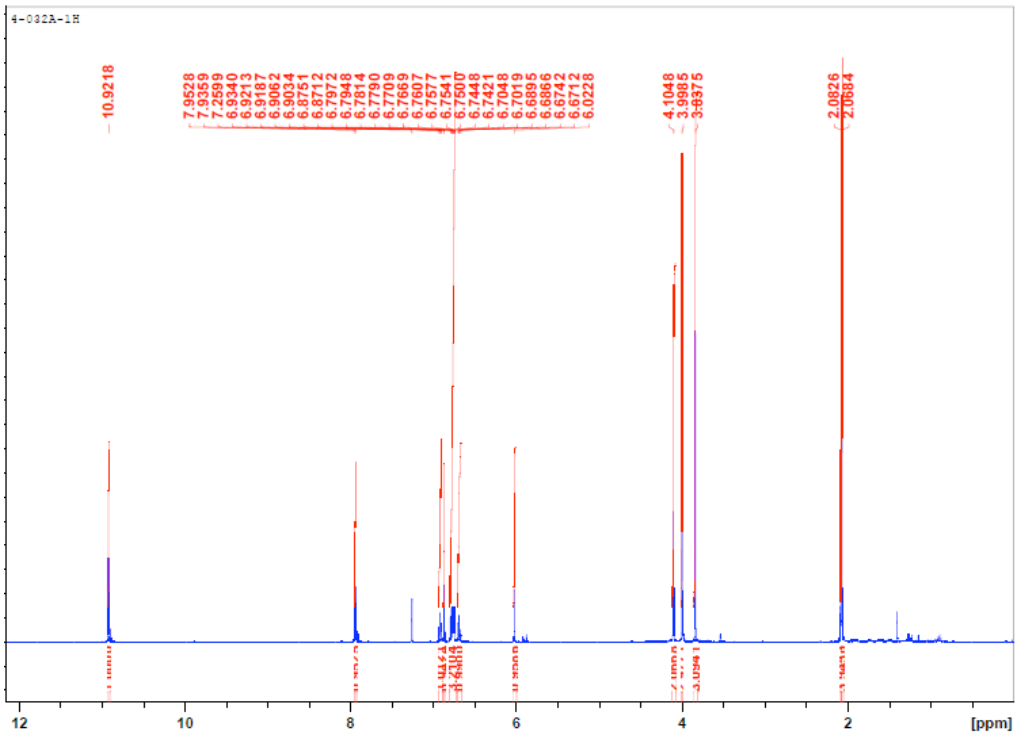
4b


4-038B-1H
10.9201
7.9447
7.9278
7.5572
7.5419
7.4763
7.4592
7.4022
7.3870
7.3713
7.2618
7.2471
7.2434
7.2423
7.2323
6.8599
6.8562
6.7575
6.7531
6.7488
6.7405
6.7361
6.7323
6.0001
4.1240
3.9845
2.0717
2.0645
10
8
6
4
2
[ppm]


4-038B-13C
170.0488
162.0990
148.0081
145.2371
141.3434
130.6226
129.9812
128.5869
128.0245
127.8738
126.2360
125.6178
125.8222
119.2116
117.1298
117.1043
112.8732
111.6885
107.5544
77.2400
76.9858
76.7321
52.4931
40.6004
12.8217
10.7371
200
150
100
50
0
[ppm]


HO
N
HN
MeO
MeOOC

4d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7.9528
7.9359
7.2599
6.9340
6.9213
6.9187
6.9062
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6.8751
6.8712
6.7972
6.7948
6.7814
6.7790
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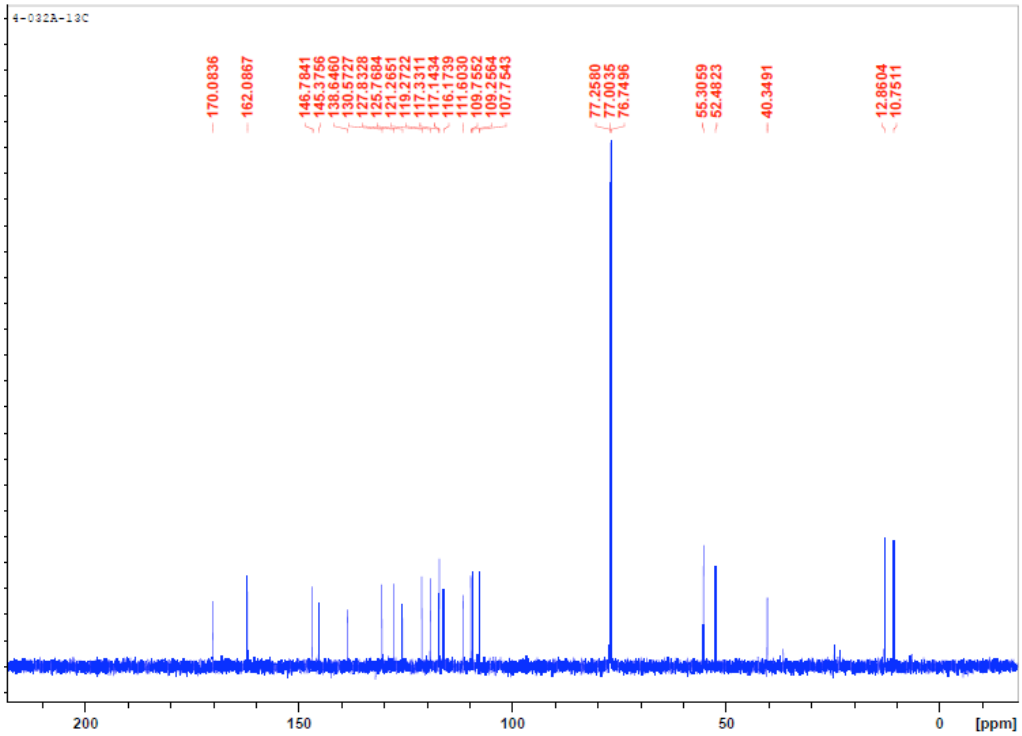
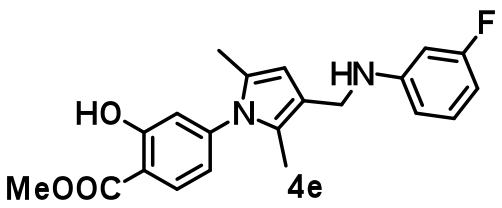
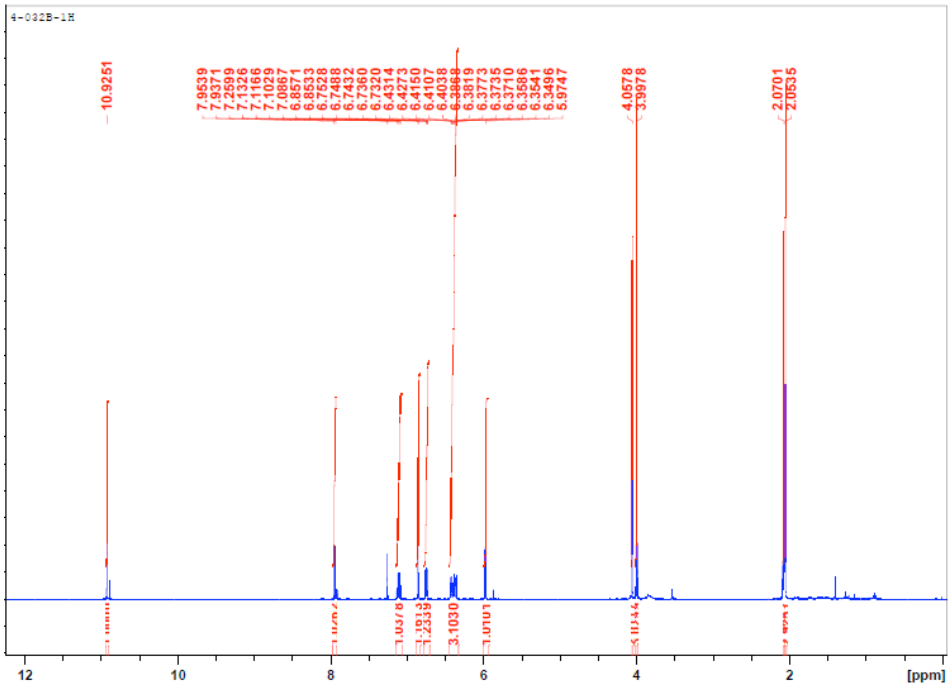
6.7669
6.7607
6.7577
6.7541
6.7500
6.7448
6.7421
6.7048
6.7019
6.6895
6.6866
6.6742
6.6712
6.0228
4.1048
3.9985
3.9375
2.0826
2.0684
12
10
8
6
4
2
[ppm]


4-032A-13C
170.0836
162.0867
146.7841
145.3756
138.6460
130.5727
127.8328
125.7684
121.2651
119.2722
117.3311
117.1434
116.1739
111.6030
109.7552
109.2564
107.7543
77.2580
77.0035
76.7496
55.3059
52.4823
40.3491
12.8604
10.7511
200
150
100
50
0
[ppm]


F
HN
HO
N
MeOOC
4e


4-032B-1H
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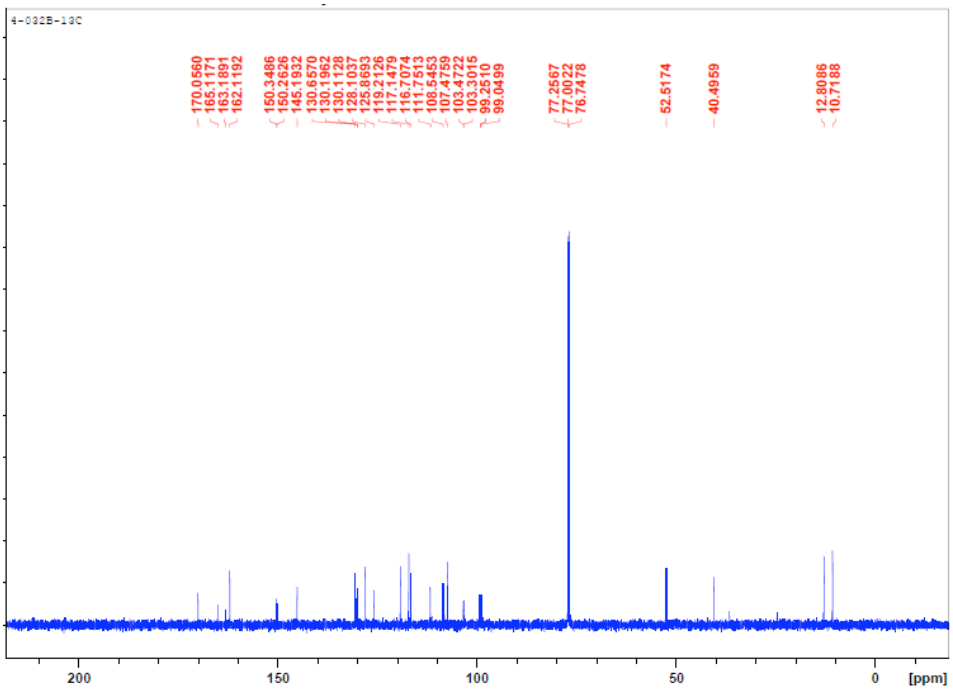
7.9371
7.2599
7.1326
7.1166
7.1029
7.0867
6.8571
6.8533
6.7528
6.7488
6.7432
6.7360
6.7320
6.4214
6.4153
6.4107
6.4038
6.3868
6.3819
6.3773
6.3735
6.3710
6.3586
6.3541
6.3496
5.9747
4.0578
3.9978
2.0701
2.0535
3.1030
12
10
8
6
4
2
[ppm]


4-032B-13C
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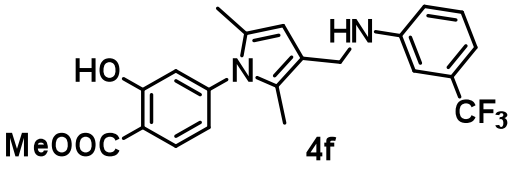
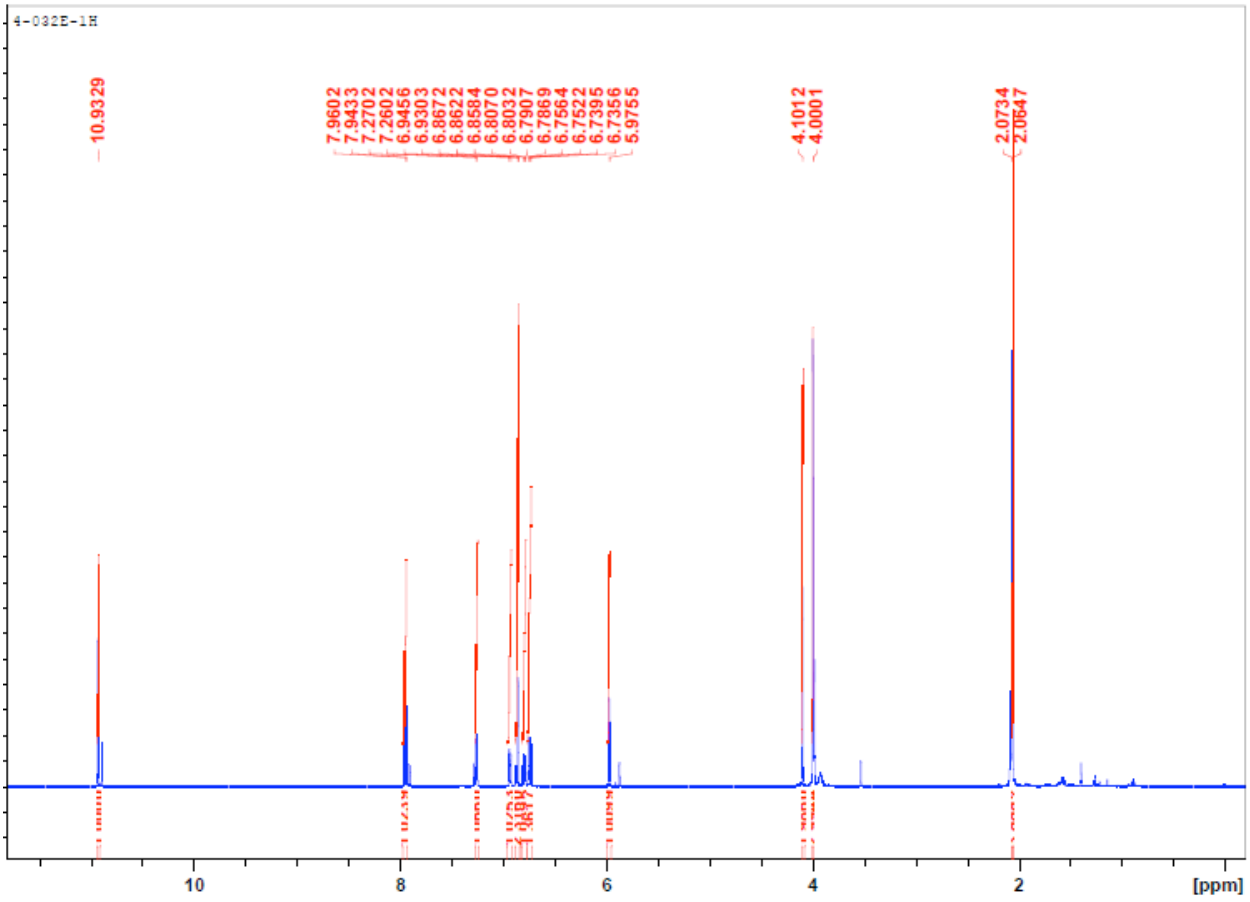
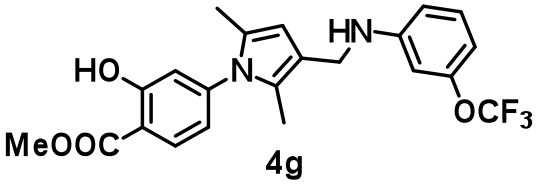
163.1891
162.1192
150.3486
150.2626
145.1932
130.6570
130.1962
130.1128
128.1037
125.8693
119.2126
117.1479
116.7074
111.7513
108.5453
107.4759
103.4722
103.3015
99.2510
99.0499
77.2567
77.0022
76.7478
52.5174
40.4959
12.8086
10.7188
200
150
100
50
0
[ppm]

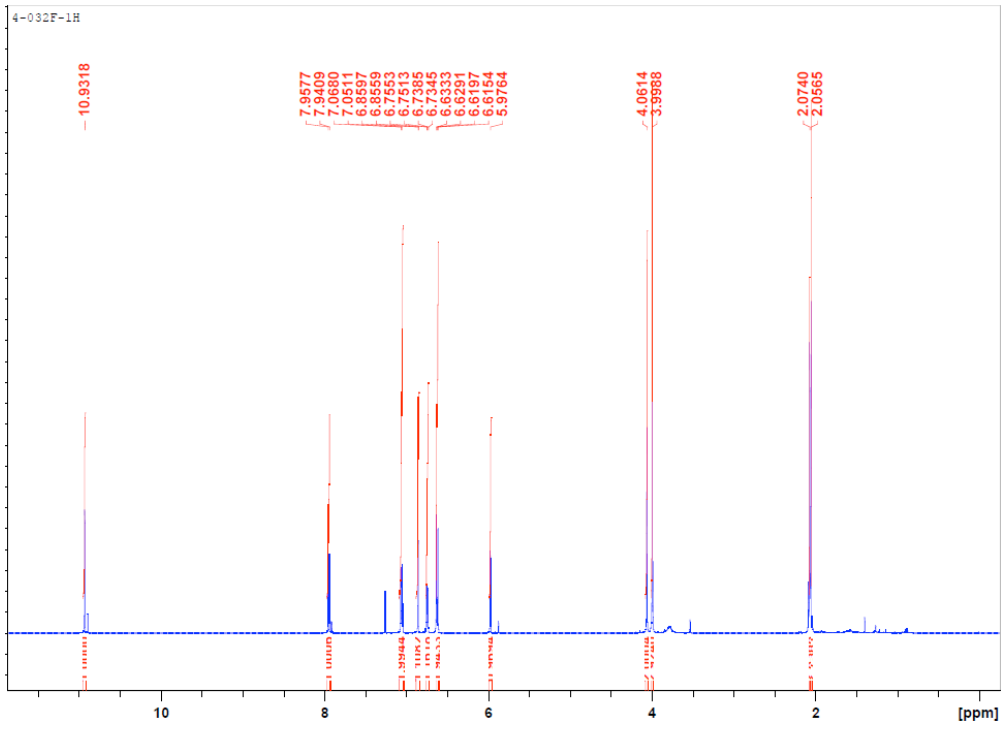

HO
N
HN
MeOOC
CF3

4f


4-032E-1H
10.9329
7.9602
7.9433
7.2702
7.2602
6.9456
6.9303
6.8672
6.8622
6.8584
6.8070
6.8032
6.7907
6.7869
6.7564
6.7522
6.7395
6.7356
5.9755
4.1012
4.0001
2.0734
2.0647
10
8
6
4
2
[ppm]


HO
N
HN
OCF3
MeOOC

4g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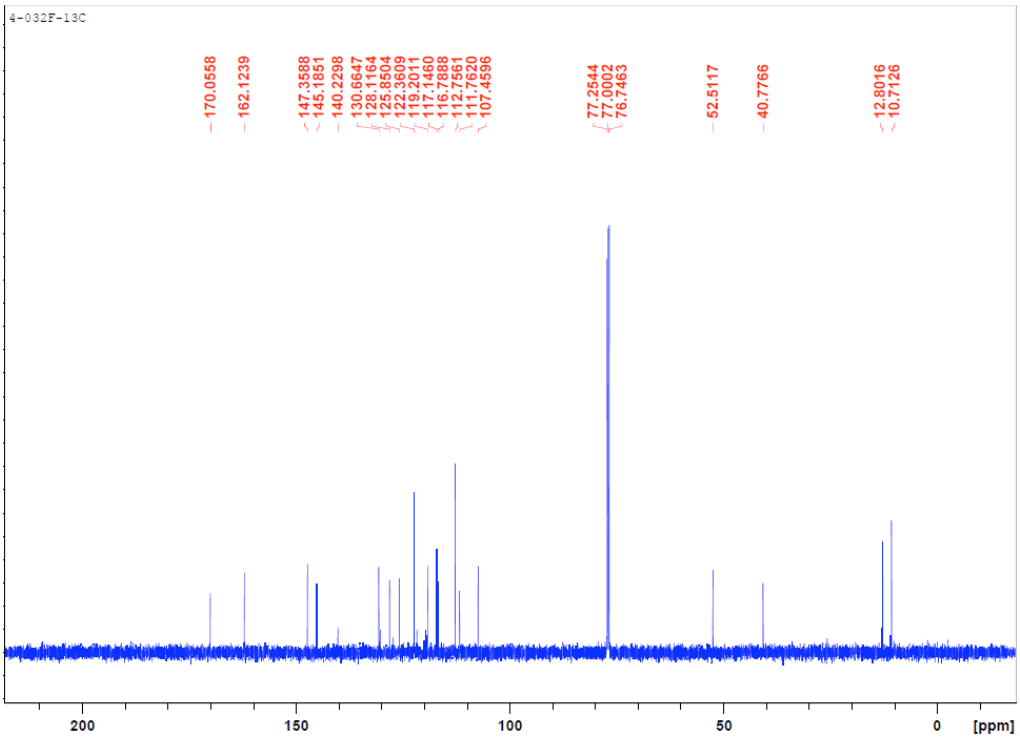
10.9318
7.9577
7.9409
7.0680
7.0511
6.8597
6.8559
6.7553
6.7513
6.7385
6.7345
6.6333
6.6291
6.6197
6.6154
5.9764
4.0614
3.9988
2.0740
2.0565
10
8
6
4
2
[ppm]


4-032F-13C
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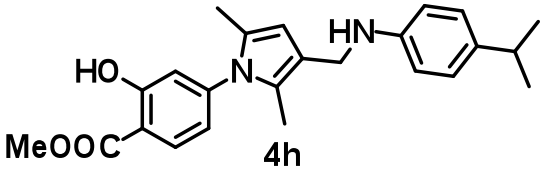
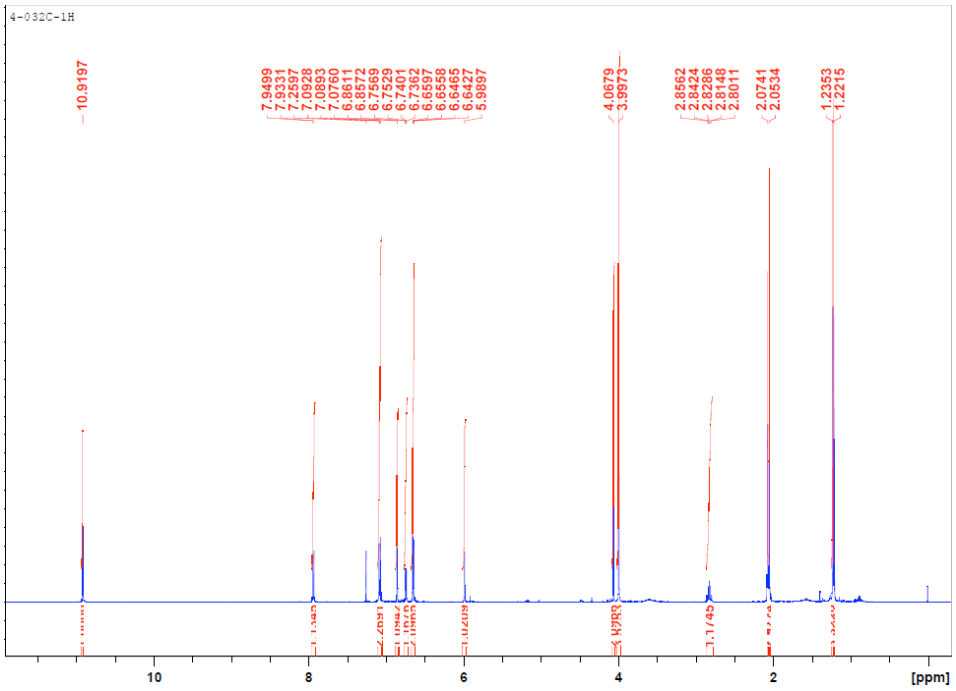
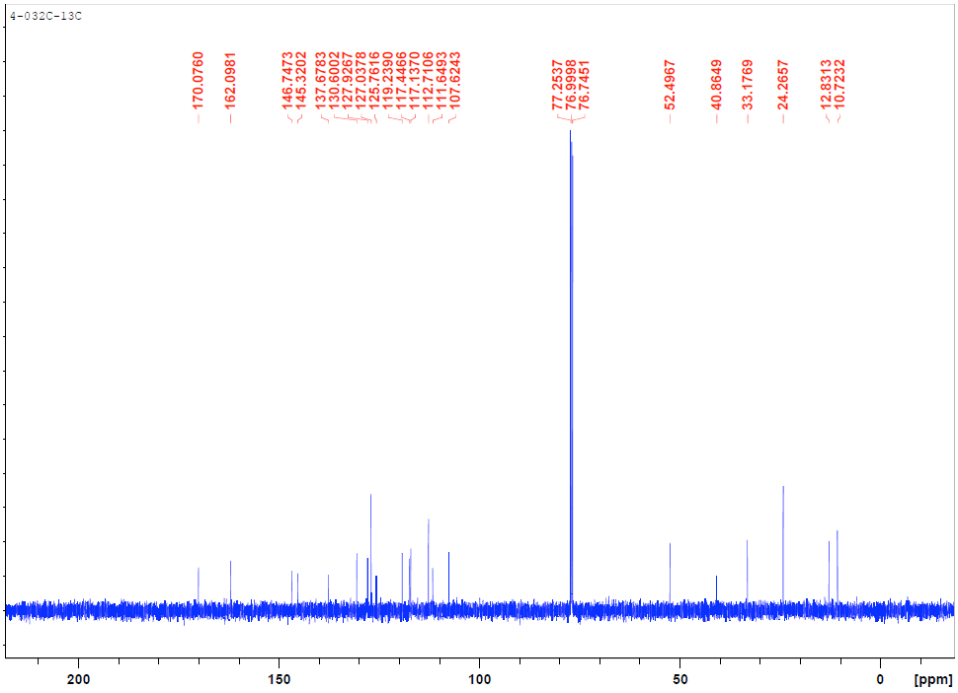
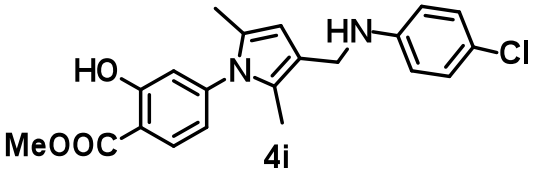
162.1239
147.3588
145.1851
140.2298
130.6647
128.1164
125.8504
122.3609
119.2011
117.1460
116.7888
112.7561
111.7620
107.4596
77.2544
77.0002
76.7463
52.5117
40.7766
12.8016
10.7126
200
150
100
50
0
[ppm]


HO
N
HN
MeOOC

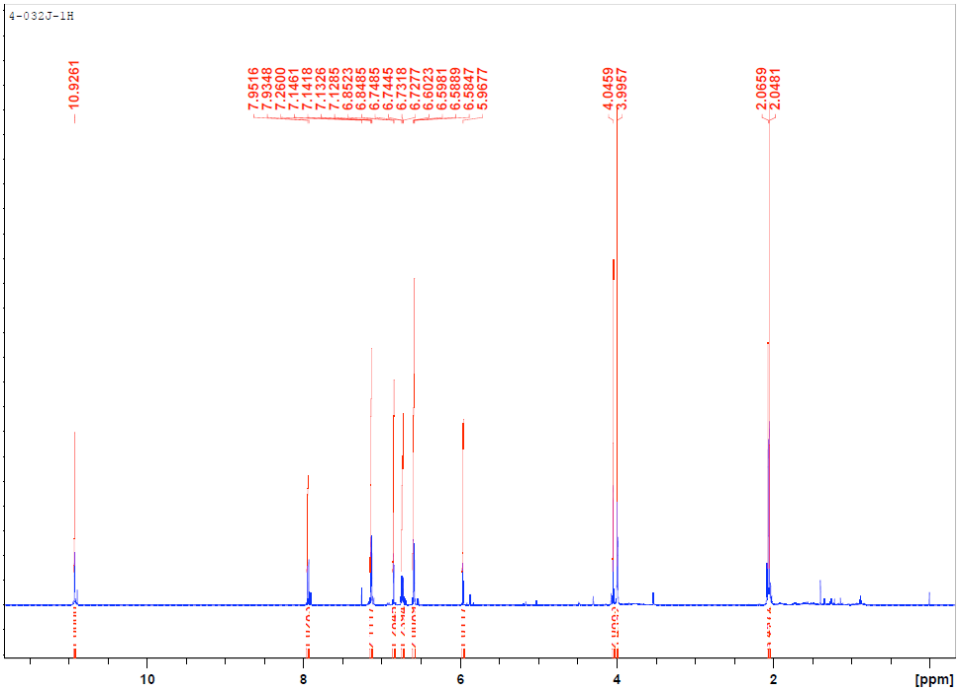
4h

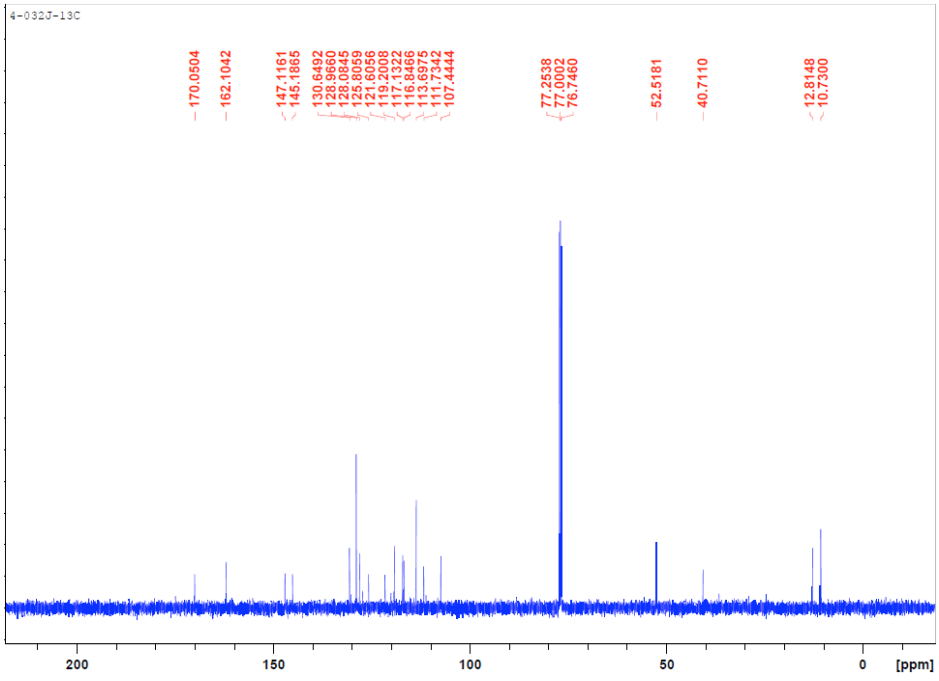

4-032C-1H
10.9197
7.9499
7.9331
7.2597
7.0893
7.0760
6.8611
6.8572
6.7569
6.7529
6.7401
6.7362
6.6597
6.6558
6.6465
6.6427
5.9897
4.0679
3.9973
2.8562
2.8424
2.8286
2.8148
2.8011
2.0741
2.0534
1.2353
1.2215
10
8
6
4
2
[ppm]

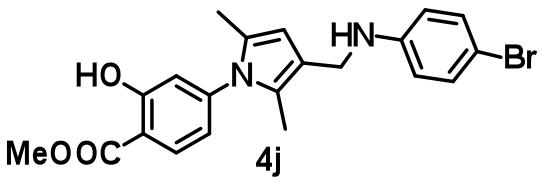

4-032C-13C
170.0760
162.0981
146.7473
145.3202
137.6783
130.6002
127.9267
127.0378
125.7616
119.2390
117.4466
117.1370
112.7106
111.6493
107.6243
77.2537
76.9998
76.7451
52.4967
40.8649
33.1769
24.2657
12.8313
10.7232
200
150
100
50
0
[ppm]


HO
N
HN
Cl
MeOOC

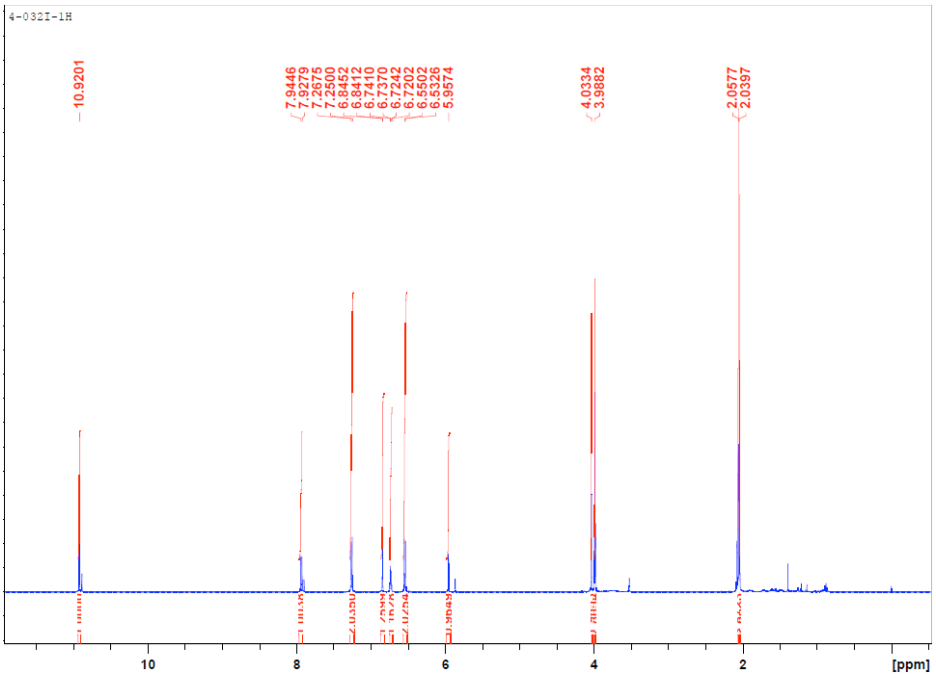
4i

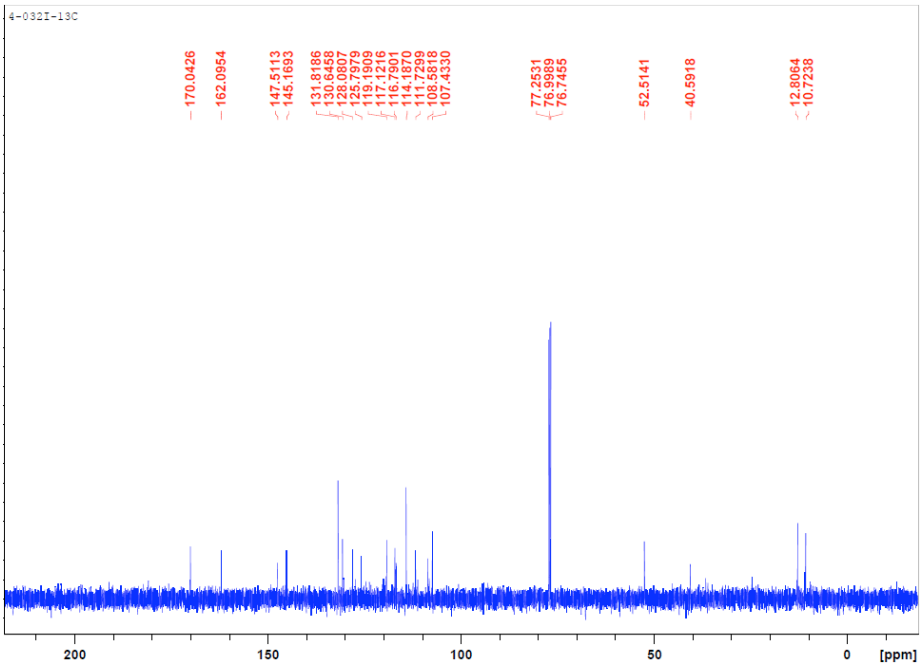

4-032J-1H
10.9261
7.9516
7.9348
7.2680
7.1461
7.1418
7.1326
7.1285
6.8523
6.8485
6.7485
6.7445
6.7318
6.7277
6.6023
6.5981
6.5889
6.5847
5.9677
4.0459
3.9957
2.0659
2.0481
10
8
6
4
2
[ppm]

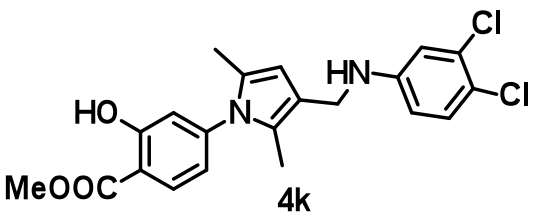

4-032J-13C
170.0504
162.1042
147.1161
145.1865
130.6492
128.9660
128.0845
125.8059
121.6056
119.2098
117.1312
116.8466
113.8975
111.7342
107.4444
77.2538
77.0002
76.7460
52.5181
40.7110
12.8148
10.7300
200
150
100
50
0
[ppm]


HO
N
HN
Br
MeOOC

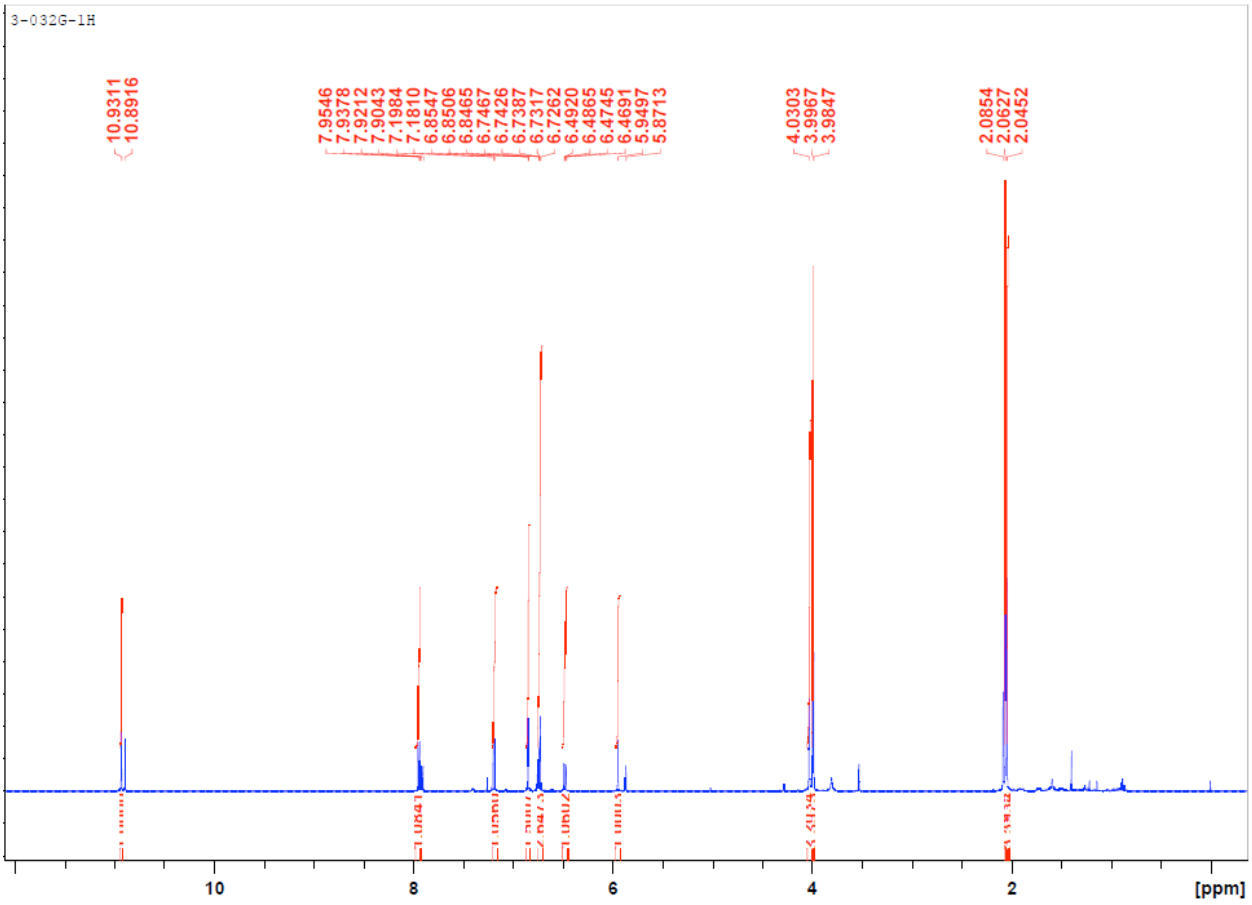
4j

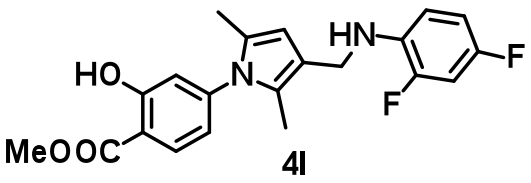

4-032I-1H
10.9201
7.9446
7.9279
7.2675
7.2500
6.8452
6.8412
6.7410
6.7370
6.7242
6.7202
6.5502
6.5326
5.9574
4.0334
3.9882
2.0577
2.0397
10
8
6
4
2
[ppm]


4-032I-13C
170.0426
162.0954
147.5113
145.1693
131.8186
130.6458
128.0807
125.7979
119.1909
117.1216
116.7901
114.1870
111.7299
108.5818
107.4330
77.2531
76.9989
76.7455
52.5141
40.5918
12.8064
10.7238
200
150
100
50
0
[ppm]

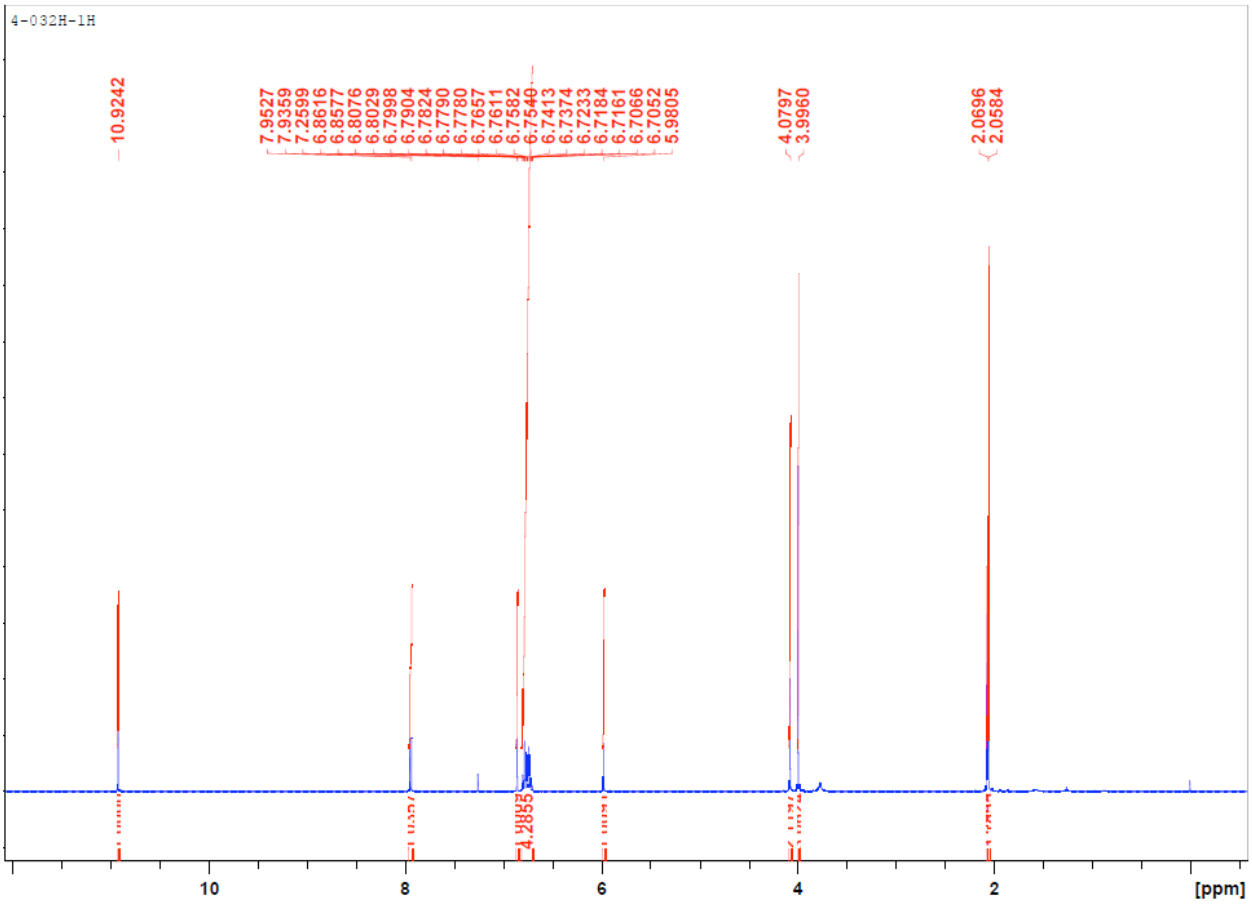

Cl
HN
Cl
HO
N
MeOOC

4k


3-032G-1H
10.9311
10.8916
7.9546
7.9378
7.9212
7.9043
7.1984
7.1810
6.8547
6.8506
6.8465
6.7467
6.7426
6.7387
6.7317
6.7262
6.4920
6.4865
6.4745
6.4691
5.9497
5.8713
4.0303
3.9967
3.9847
2.0854
2.0627
2.0452
10
8
6
4
2
[ppm]


HO
N
HN
F
F
MeOOC

4l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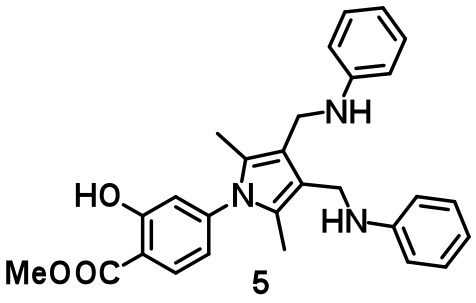
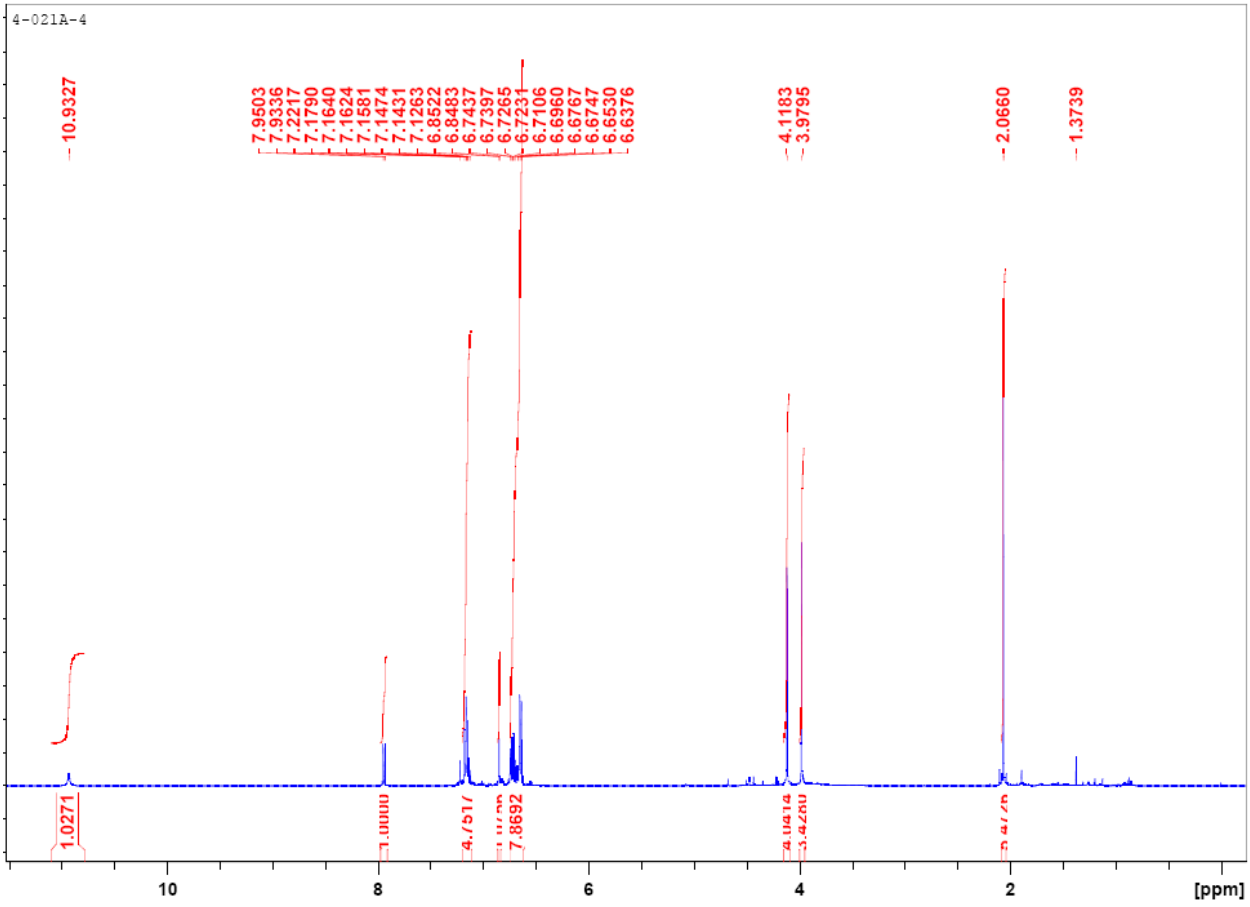
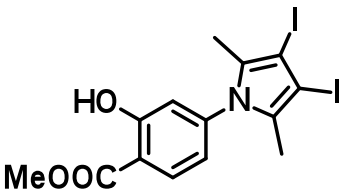
10.9242
7.9527
7.9359
7.2599
6.8616
6.8577
6.8076
6.8029
6.7998
6.7904
6.7824
6.7790
6.7780
6.7657
6.7611
6.7582
6.7540
6.7413
6.7374
6.7233
6.7184
6.7161
6.7066
6.7052
5.9805
4.0797
3.9960
2.0696
2.0584
10
8
6
4
2
[ppm]

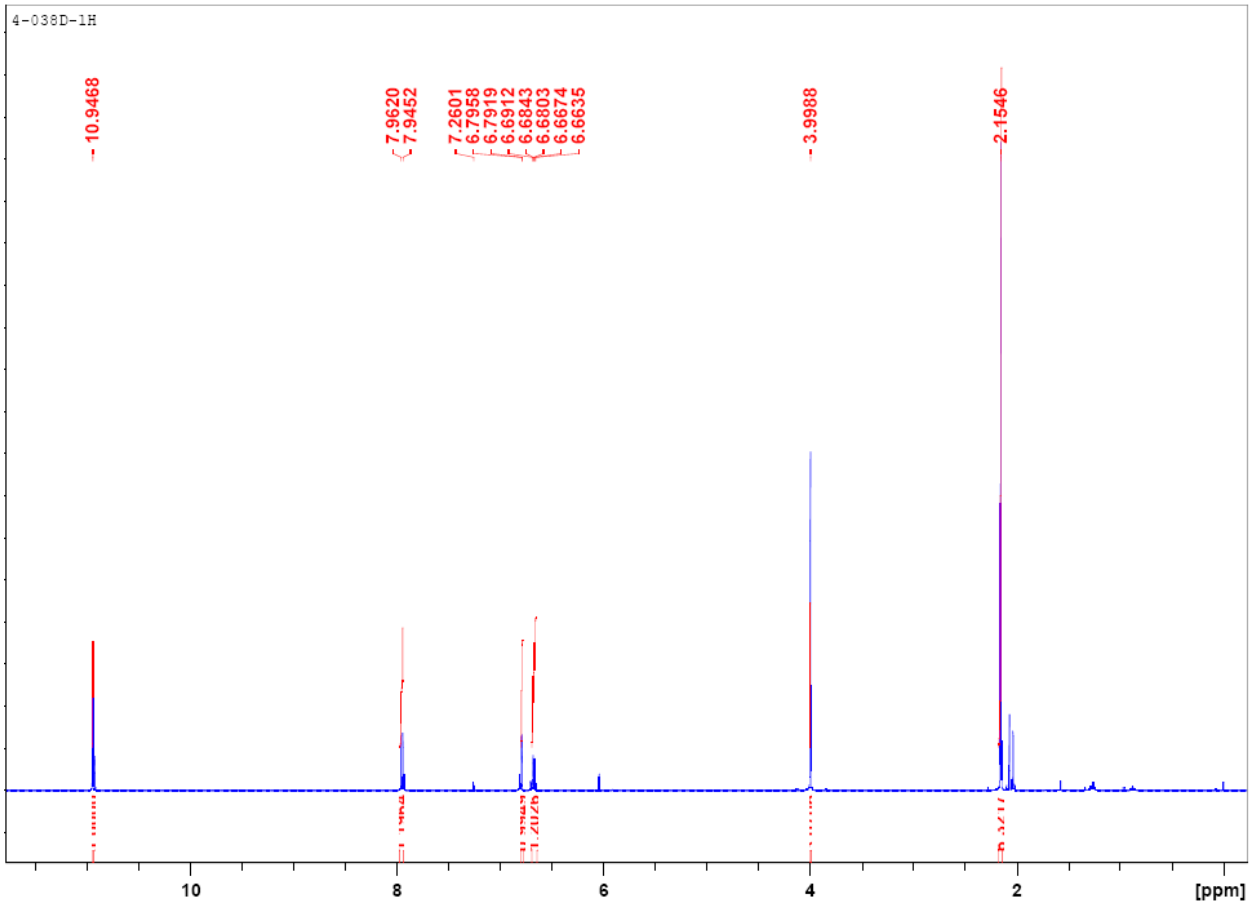

NH
HO
N
HN
MeOOC

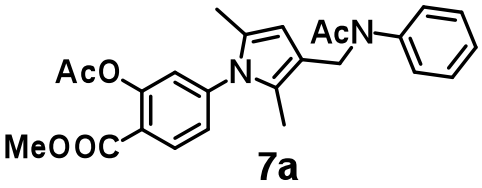
5


4-021A-4
10.9327
7.9503
7.9336
7.2217
7.1790
7.1640
7.1624
7.1581
7.1474
7.1431
7.1263
6.8522
6.8483
6.7437
6.7397
6.7265
6.7231
6.7106
6.6960
6.6767
6.6747
6.6530
6.6376
4.1183
3.9795
2.0660
1.3739
1.0271
7.8692
10
8
6
4
2
[ppm]

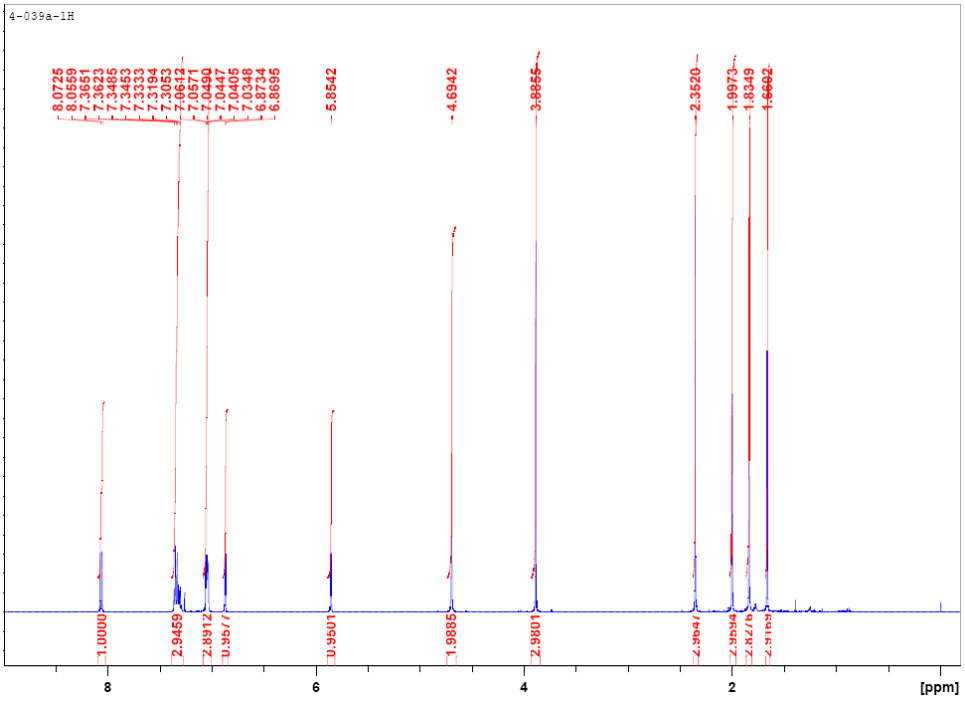

HO
MeOOC
N
I
I

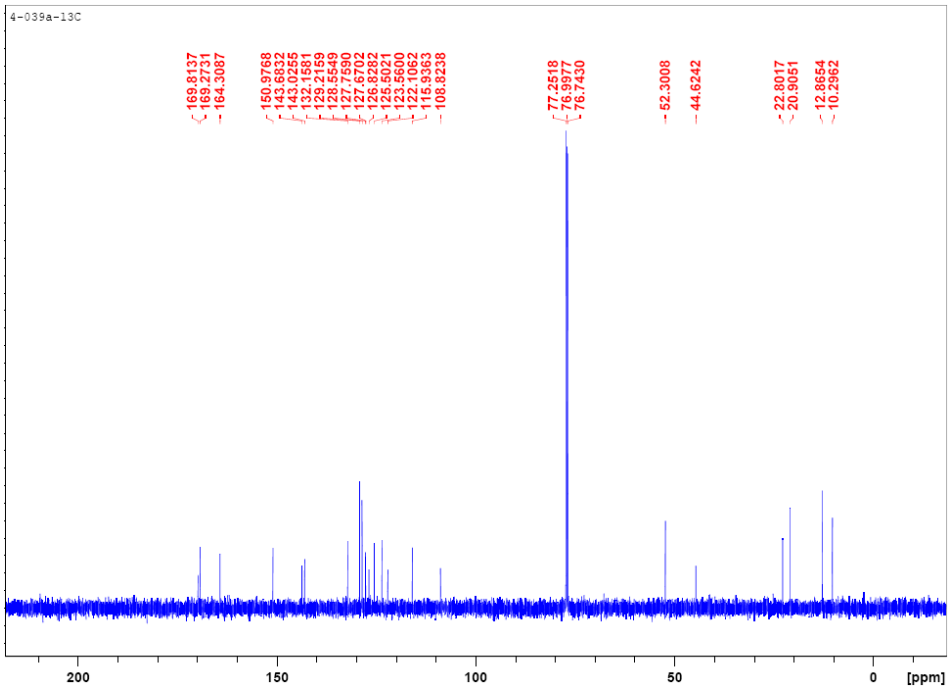
10b


4-038D-1H
10.9468
7.9620
7.9452
7.2601
6.7958
6.7919
6.6912
6.6843
6.6803
6.6674
6.6635
3.9988
2.1546
10
8
6
4
2
[ppm]


AcO
MeOOC
N
AcN

7a


4-039a-1H
8.0725
8.0569
7.3651
7.3623
7.3485
7.3453
7.3333
7.3194
7.3053
7.0612
7.0571
7.0490
7.0447
7.0405
7.0348
6.8734
6.8695
5.8542
4.6942
3.8855
2.3520
1.9973
1.8349
1.6602
1.0000
2.9459
2.8912
0.9501
1.9885
2.9801
8
6
4
2
[ppm]


4-039a-13C
169.8137
169.2731
164.3087
150.9768
143.6832
143.0255
132.1581
129.2159
128.5549
127.7590
127.6702
126.8782
126.6021
123.5600
122.1062
115.9363
108.8238
77.2518
76.9977
76.7430
52.3008
44.6242
22.8017
20.9051
12.8654
10.2962
200
150
100
50
0
[ppm]

Inhibition studies for all compounds

The inhibition assays were performed on 96-well plates at 25°C in 50 mM 3,3-dimethylglutarate buffer, pH 7.0, containing 1 mM EDTA with an ionic strength of 0.15 M adjusted by NaCl. The reaction was started by the addition of 50 μl of the enzyme to 150 μl of reaction mixture containing *p*-nitrophenyl phosphate (*p*NPP) and various concentrations of the inhibitor [final concentration of mPTPB: 20 nM, final concentration of *p*NPP: 3 mM (the K_m value)]. The reaction was quenched after 10 min by the addition of 50 μl of 5 N NaOH. The absorbance at 405 nm was detected by a Spectra MAX340 microplate spectrophotometer (Molecular Devices). IC_{50} values were calculated by fitting the absorbance at 405nm *versus* inhibitor concentration to the following equation:

$$AI/A0=IC_{50}/(IC_{50}+[I])$$

where AI is the absorbance at 405 nm of the sample in the presence of inhibitor; A0 is the absorbance at 405 nm in the absence of inhibitor; and [I] is the concentration of the inhibitor.

Expression and purification of recombinant mPTPB were described previously.[1]

[1] B. Zhou, Y. He, X. Zhang, J. Xu, Y. Luo, Y. Wang, S. G. Franzblau, Z. Yang, R. J. Chan, Y. Liu, J. Zheng, Z.-Y. Zhang, *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 4573-4578.