Supporting Information

For

Ligand growing experiments suggested 4-amino and 4-ureido pyridazin-3(2*H*)-one as novel scaffold for FABP4 inhibition

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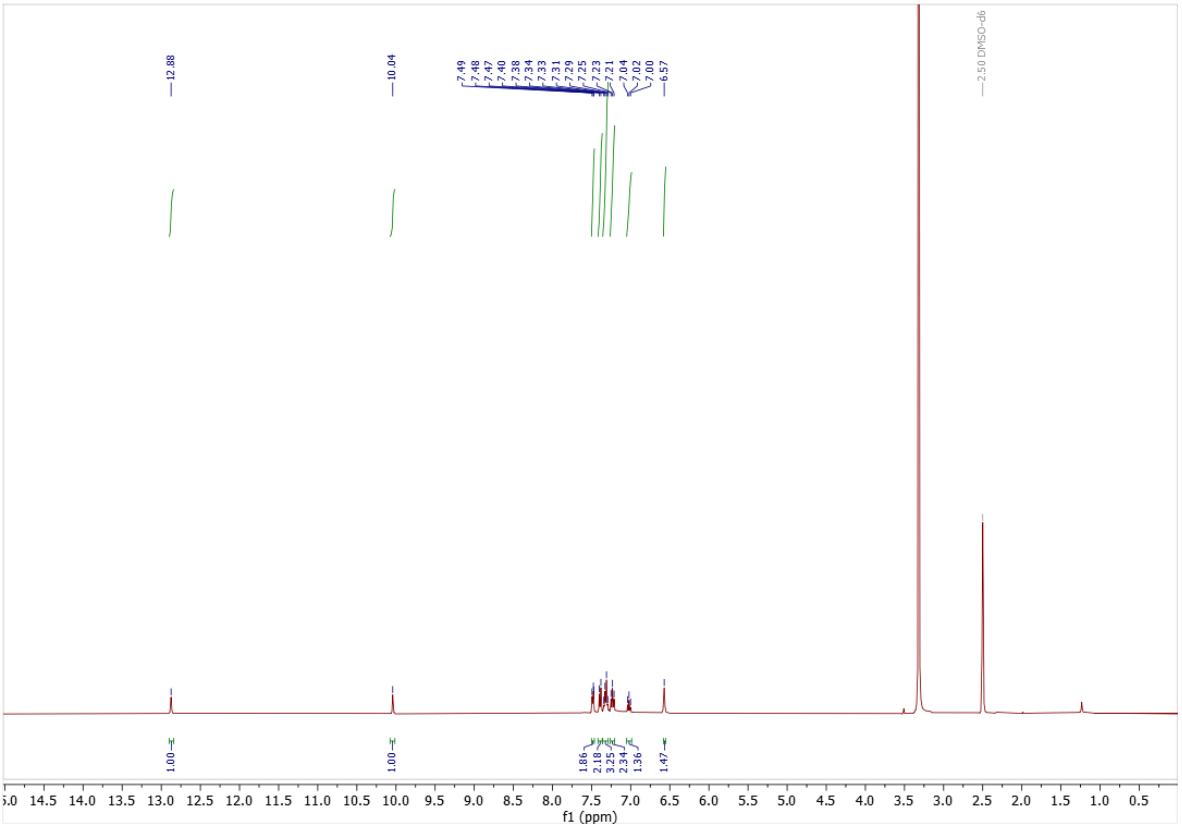
^{1}H- NMR

4a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7.00
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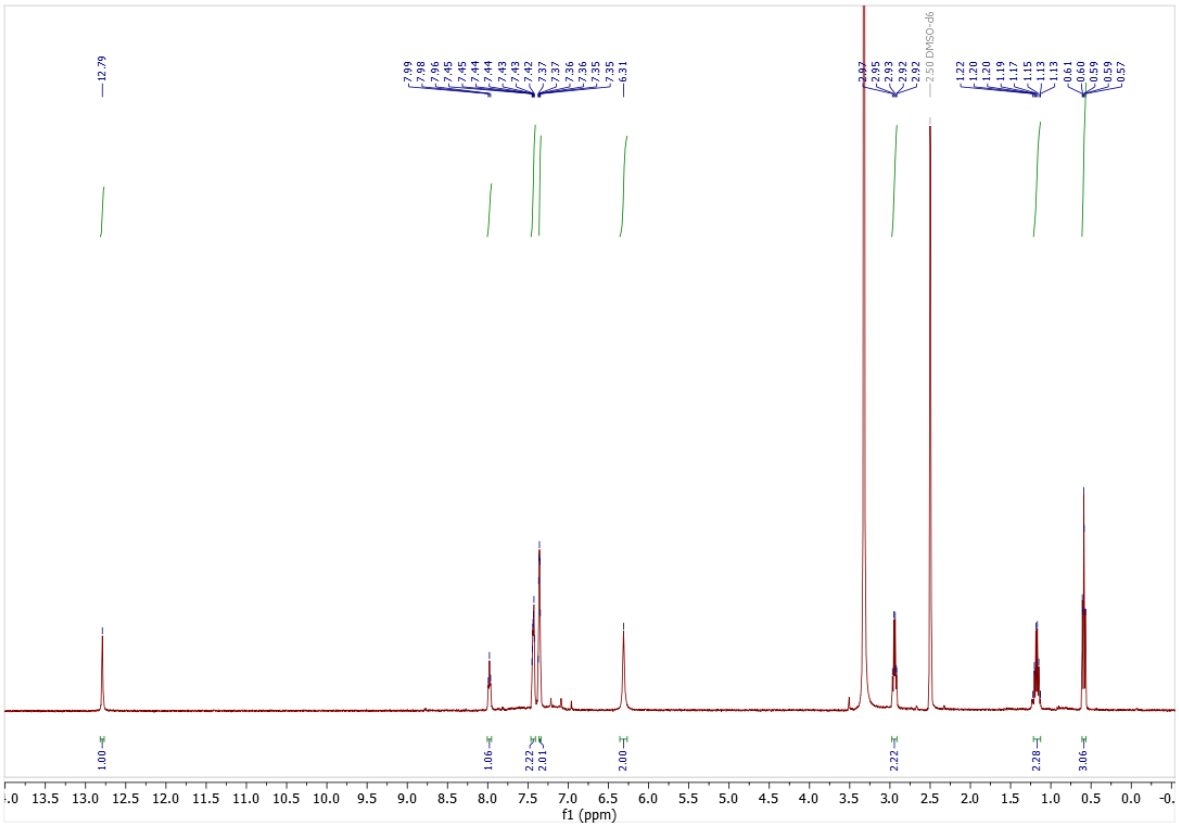
f1 (ppm)

4b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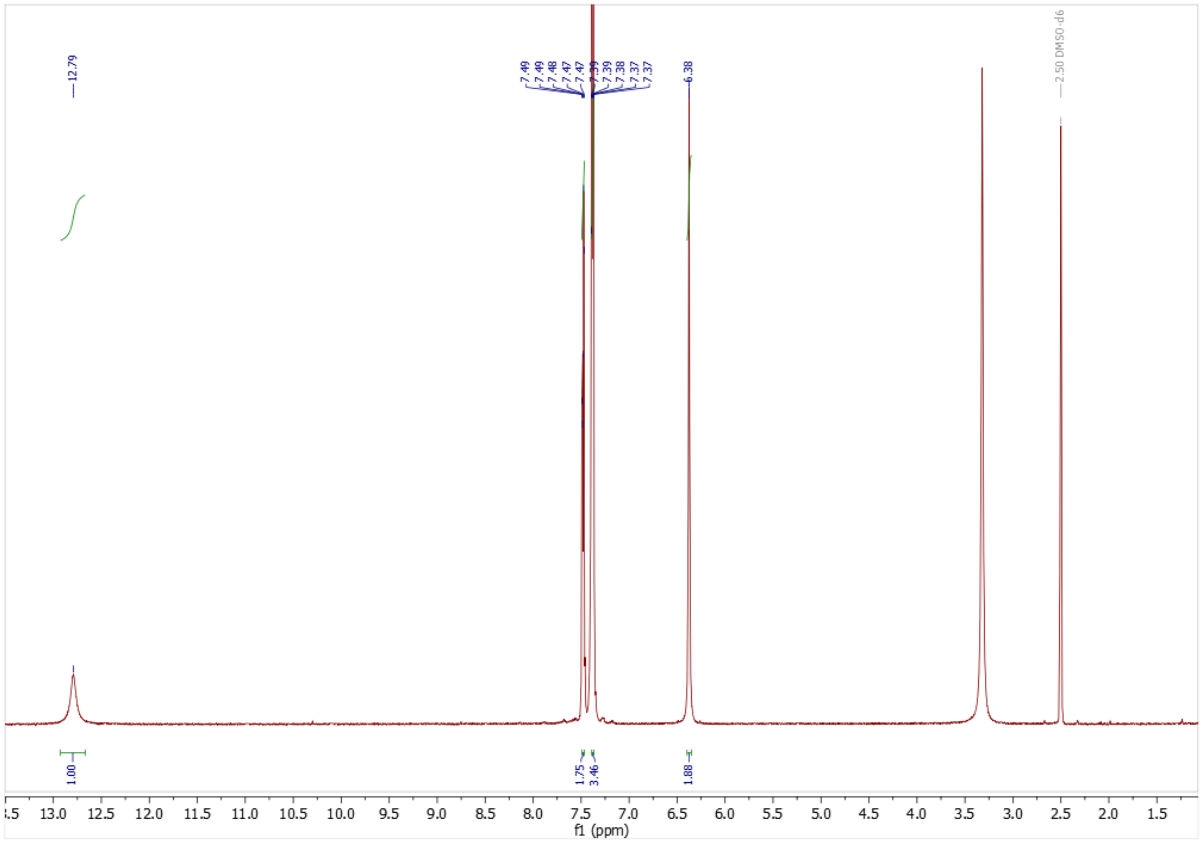
f1 (ppm)

6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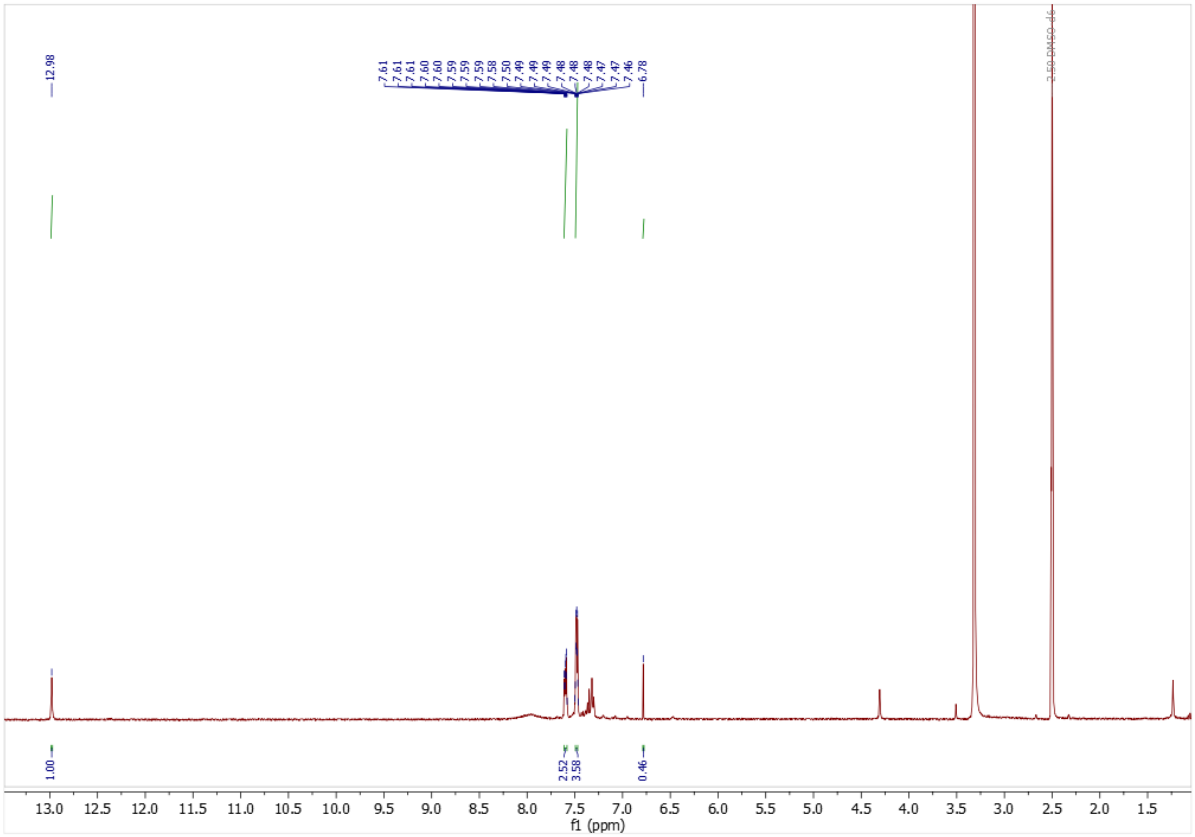
f1 (ppm)

7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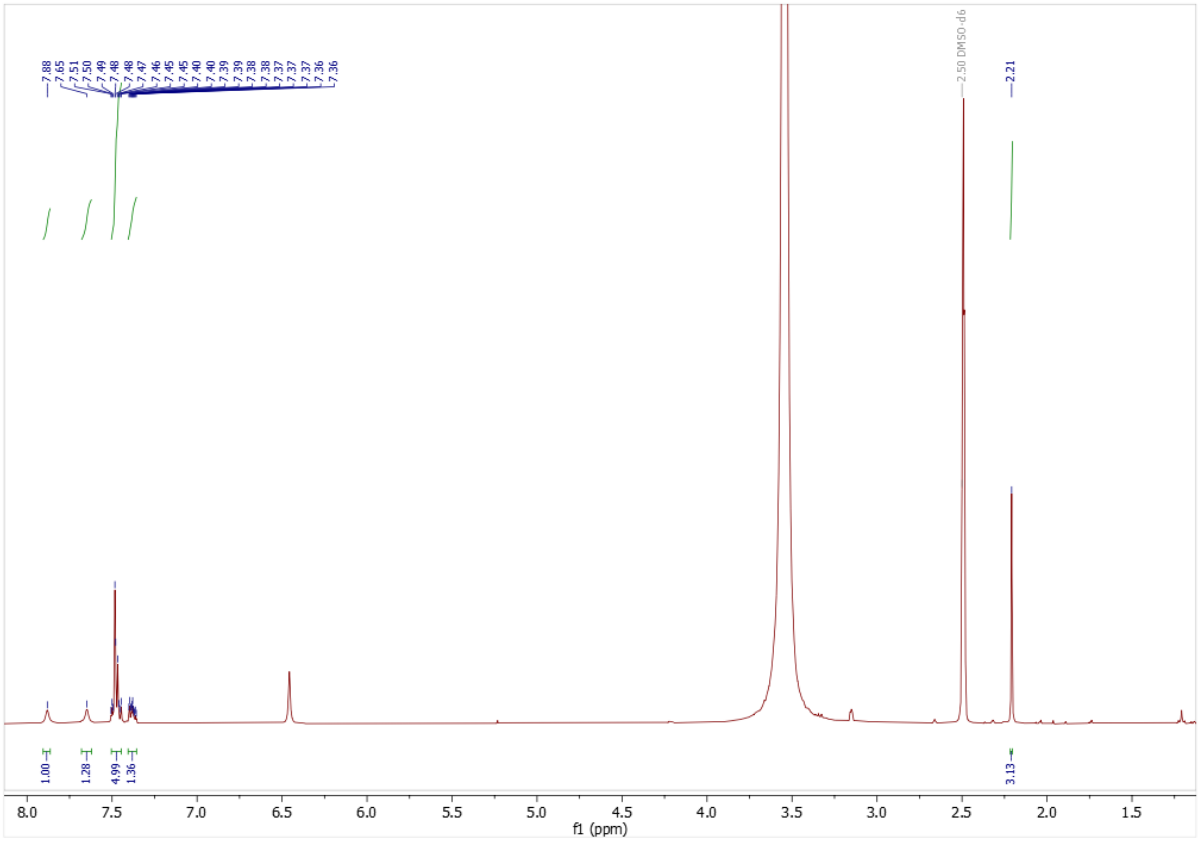
f1 (ppm)

16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7.39
7.39
7.38
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7.37
7.37
7.36
7.36
2.50 DMSO-d6
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1.36
3.13
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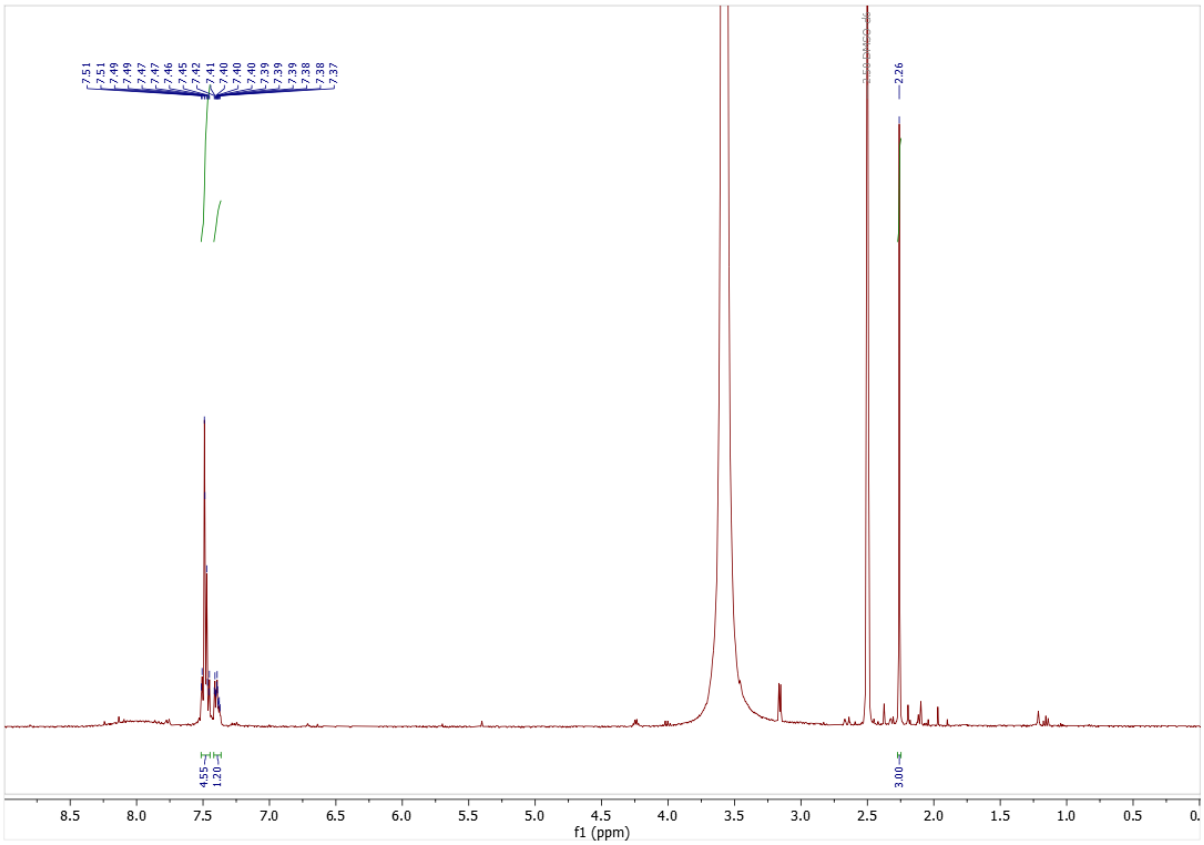
f1 (ppm)

17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7.39
7.38
7.38
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f1 (ppm)

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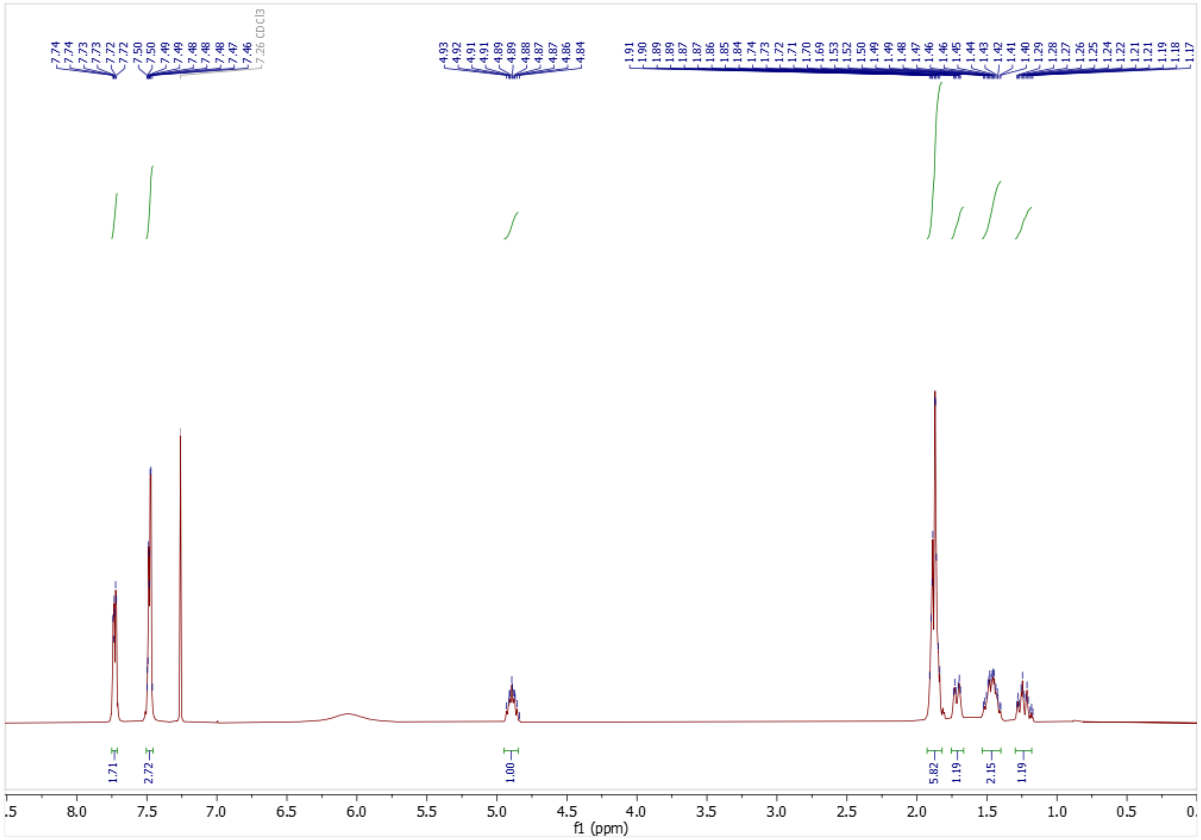

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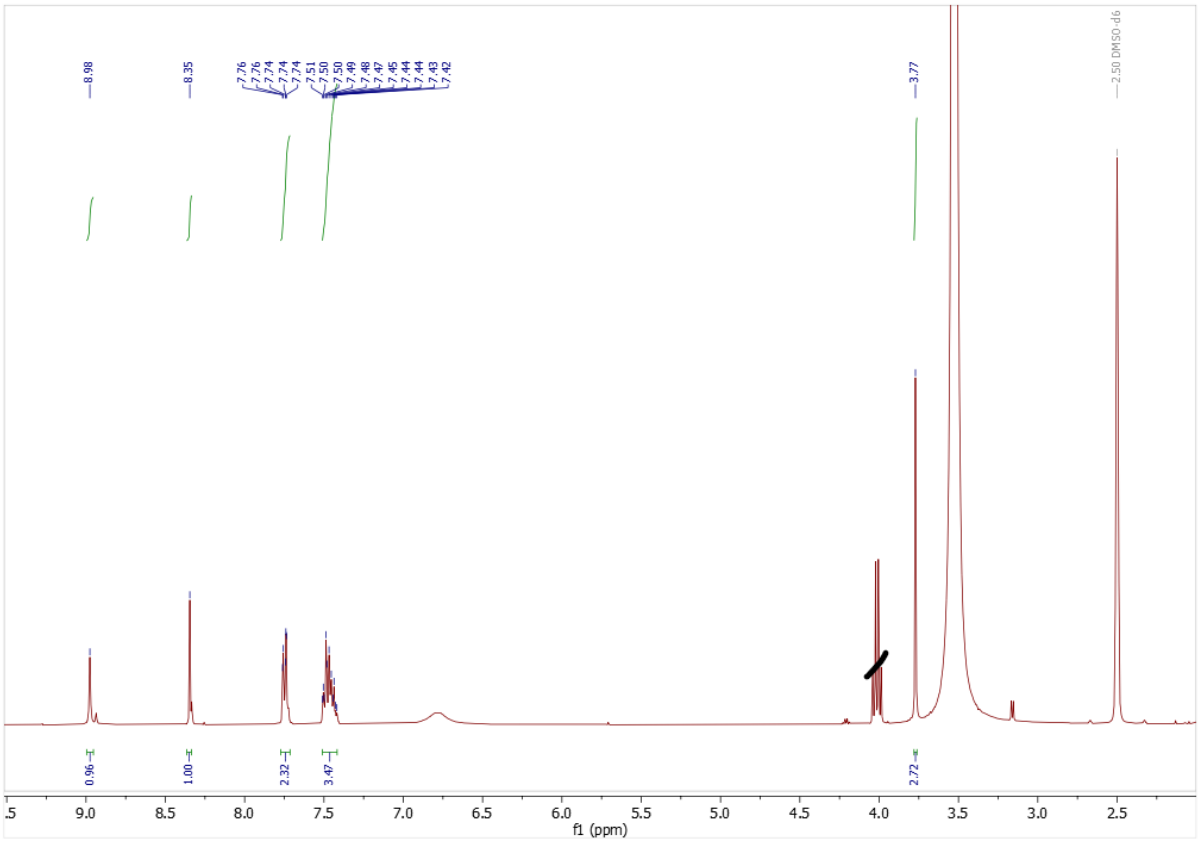

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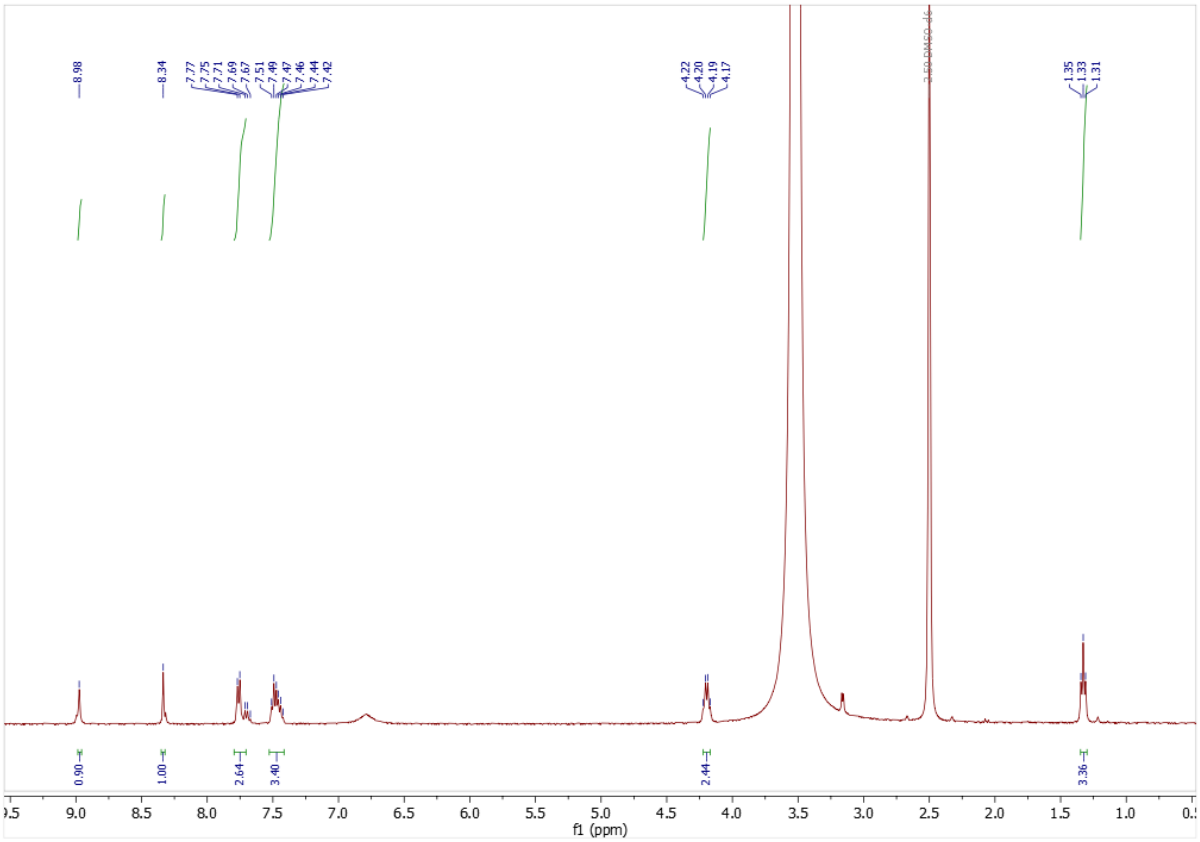
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7.42
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4.20
4.19
4.17
3.50 DMSO-d6
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f1 (ppm)

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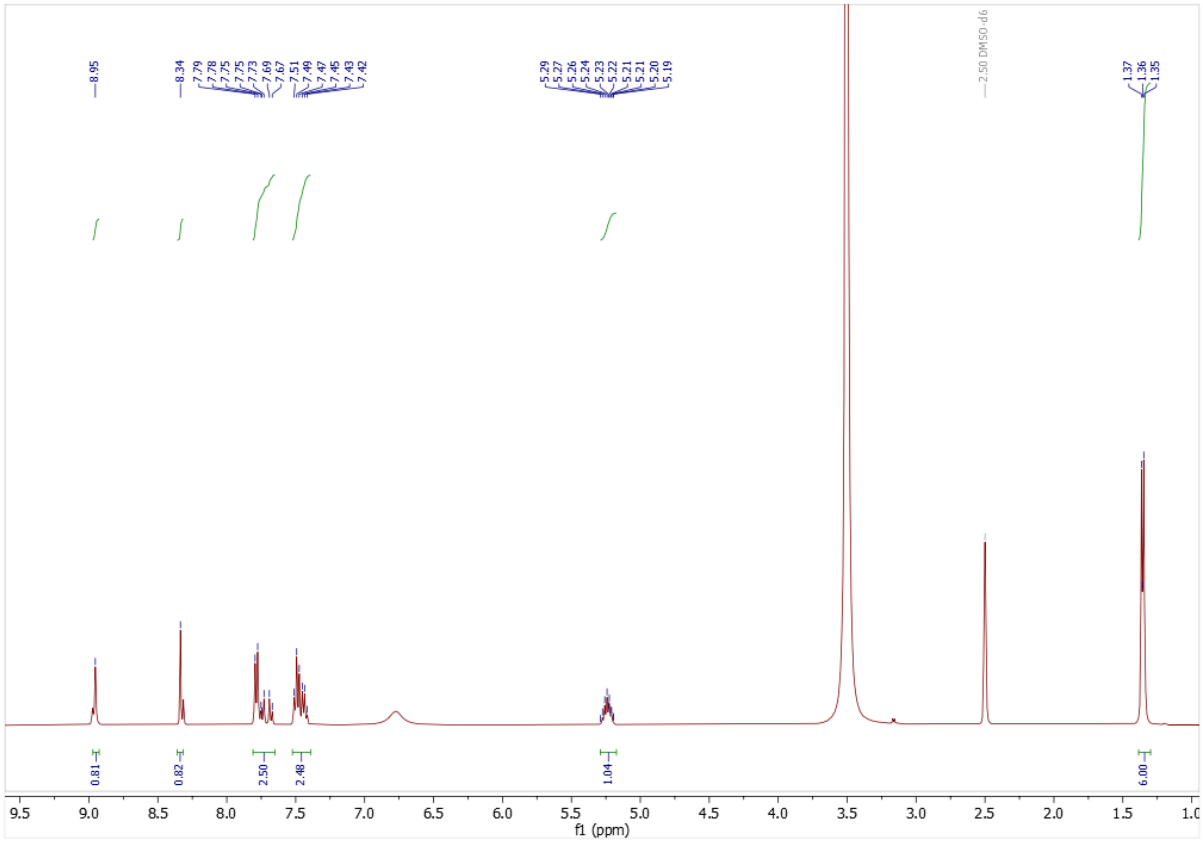
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5.24
5.23
5.22
5.21
5.21
5.20
5.19
2.50 DMSO-d6
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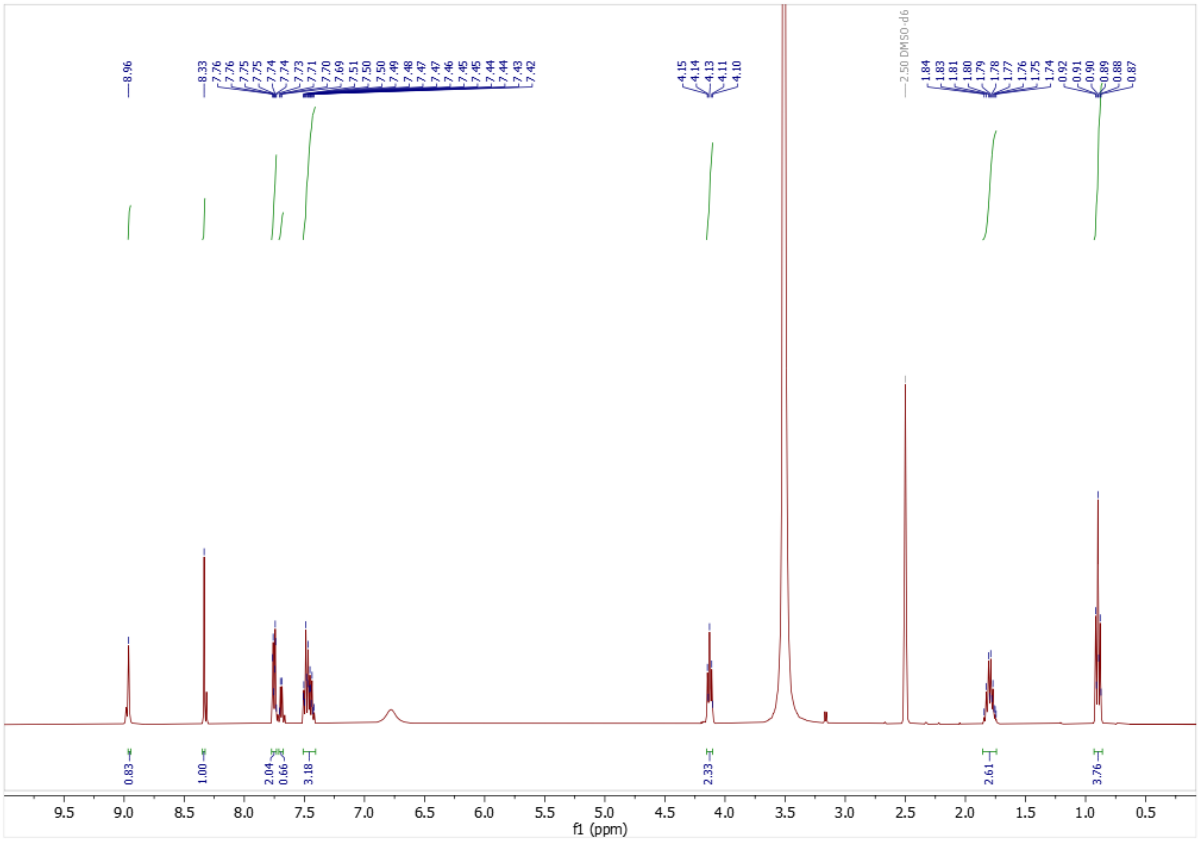
f1 (ppm)

25e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7.48
7.47
7.46
7.45
7.44
7.43
7.42
4.15
4.14
4.13
4.11
4.10
2.50 DMSO-d6
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1.81
1.80
1.79
1.78
1.77
1.76
1.75
1.74
0.92
0.91
0.90
0.89
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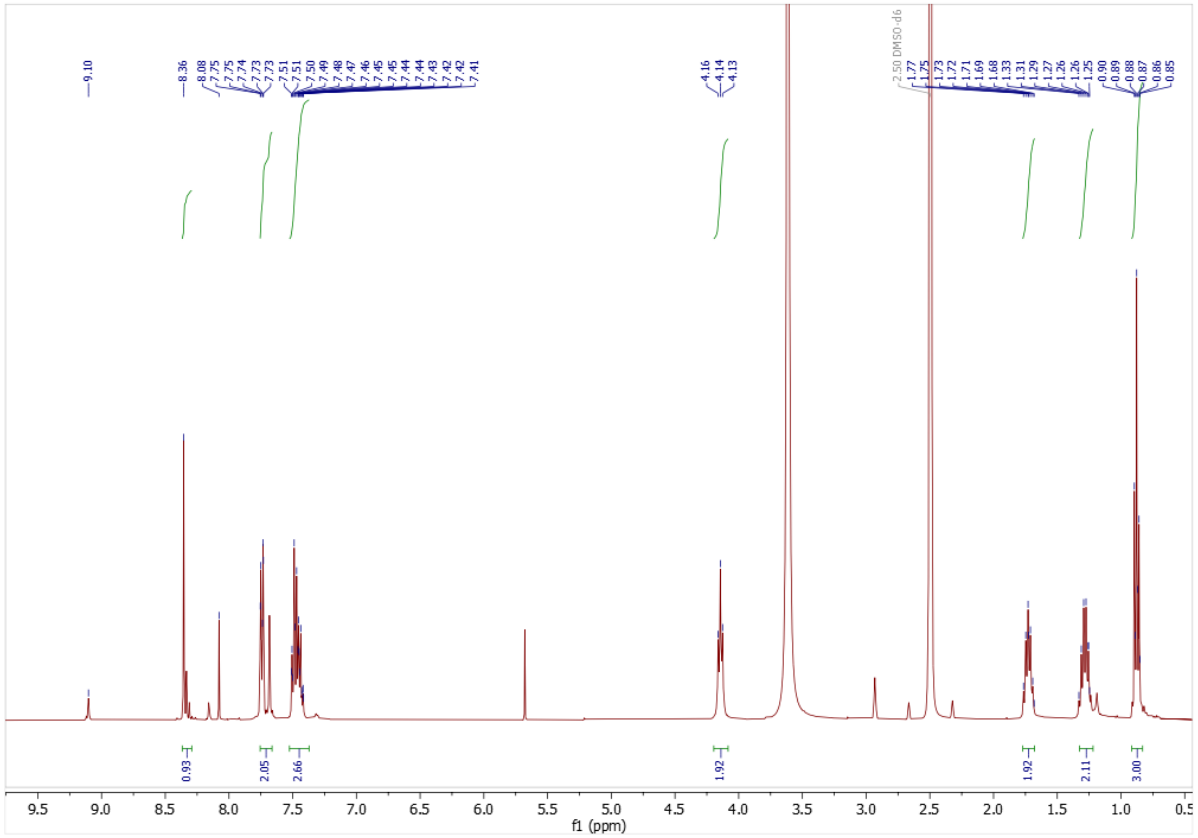
f1 (ppm)

25f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7.44
7.43
7.42
7.41
4.16
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1.71
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1.27
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0.89
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1.92
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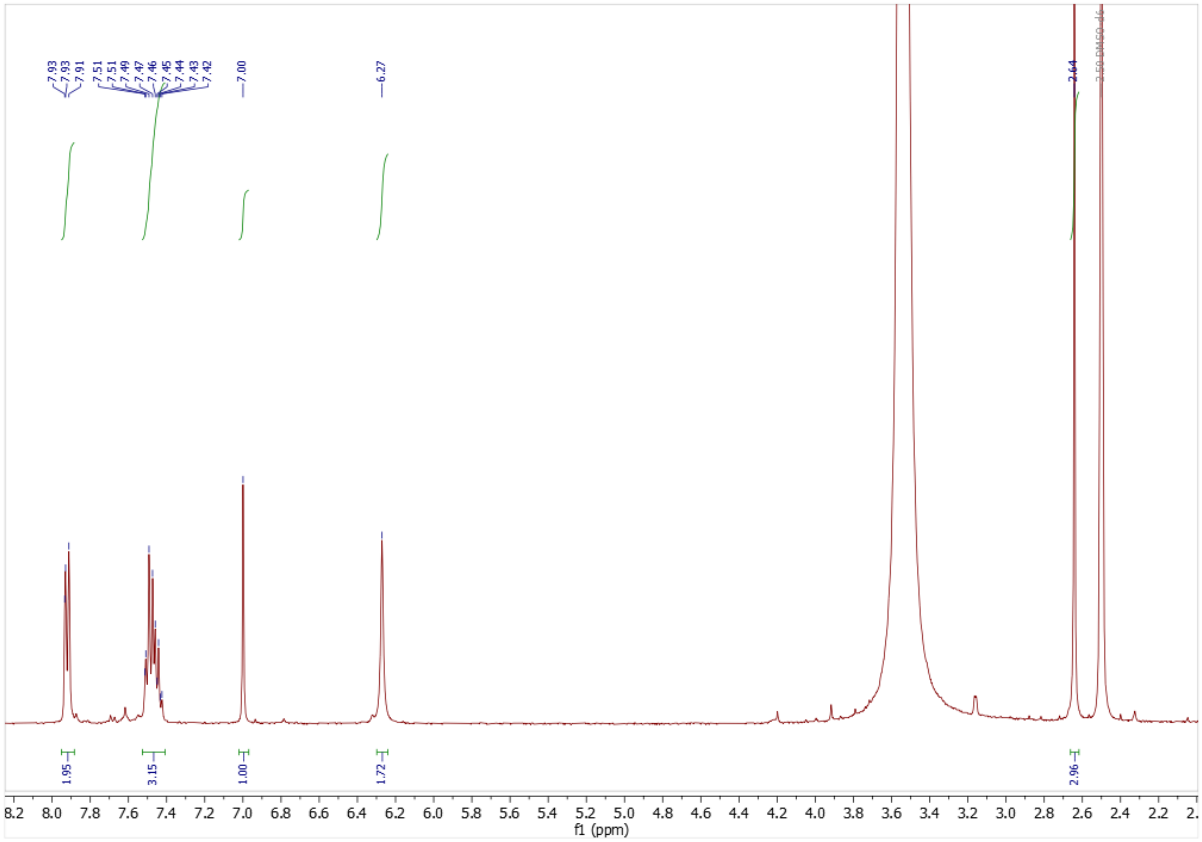
f1 (ppm)

27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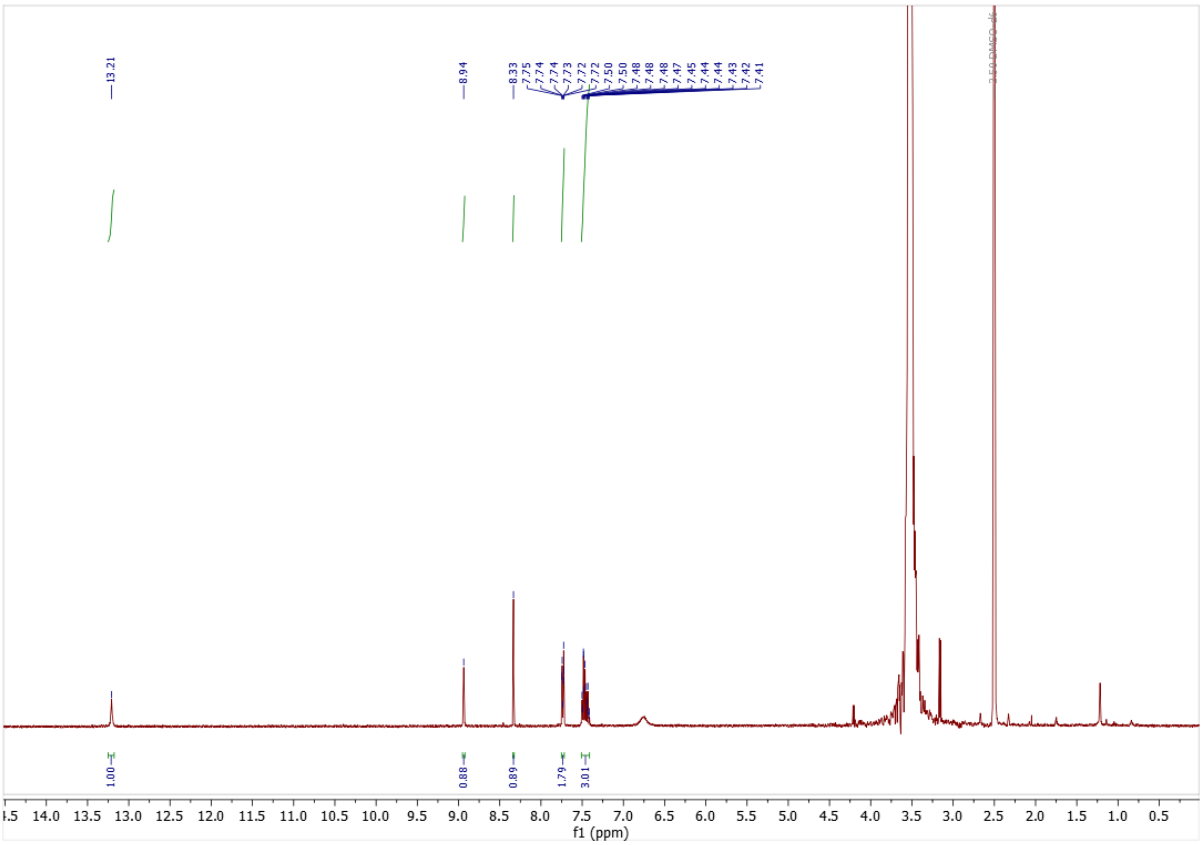
f1 (ppm)

28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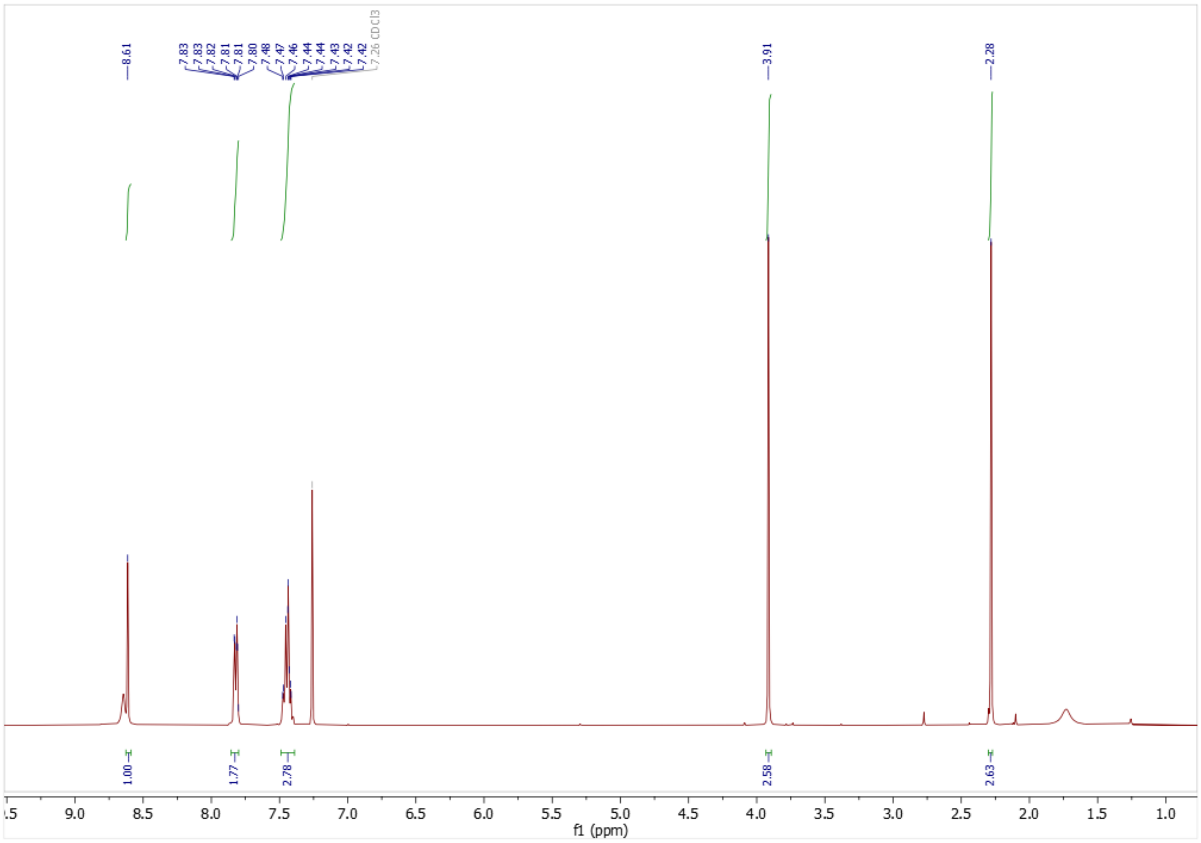
f1 (ppm)

29a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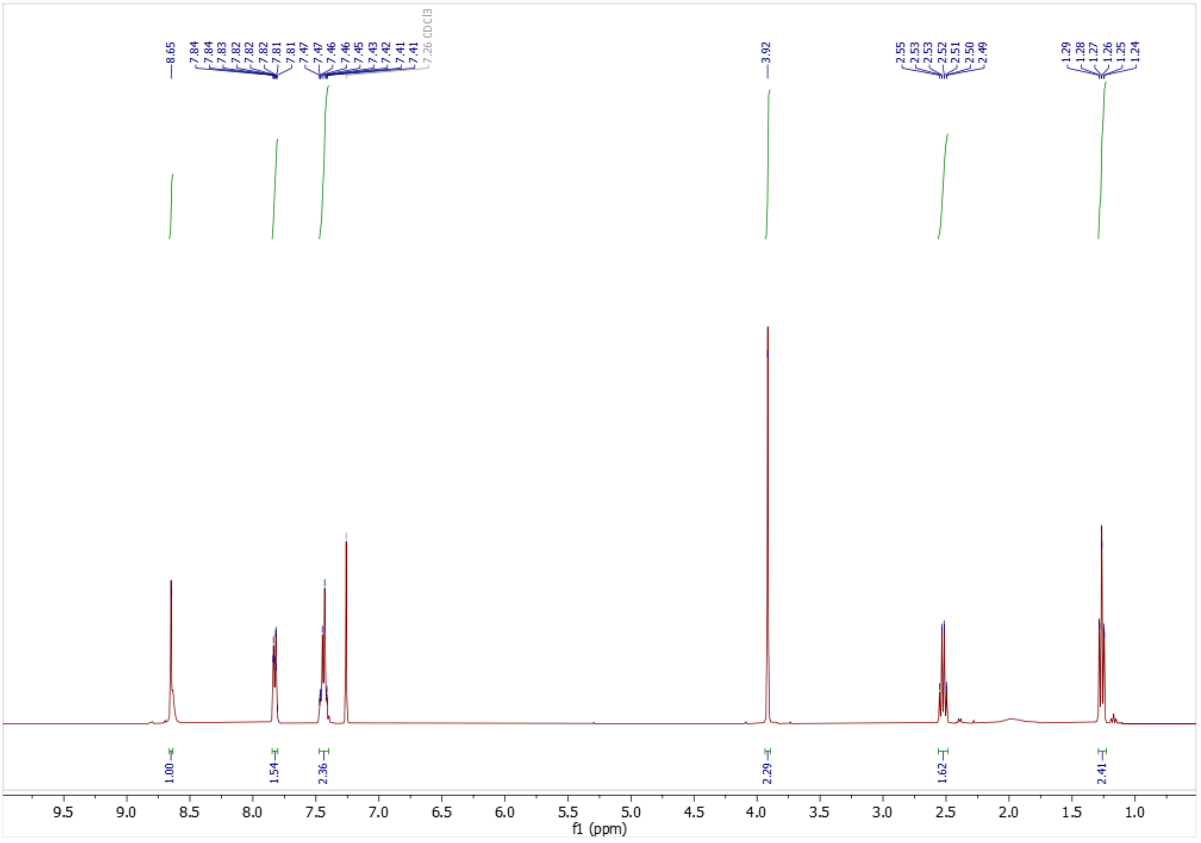
2.63
f1 (ppm)

29b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2.52
2.51
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2.49
1.29
1.28
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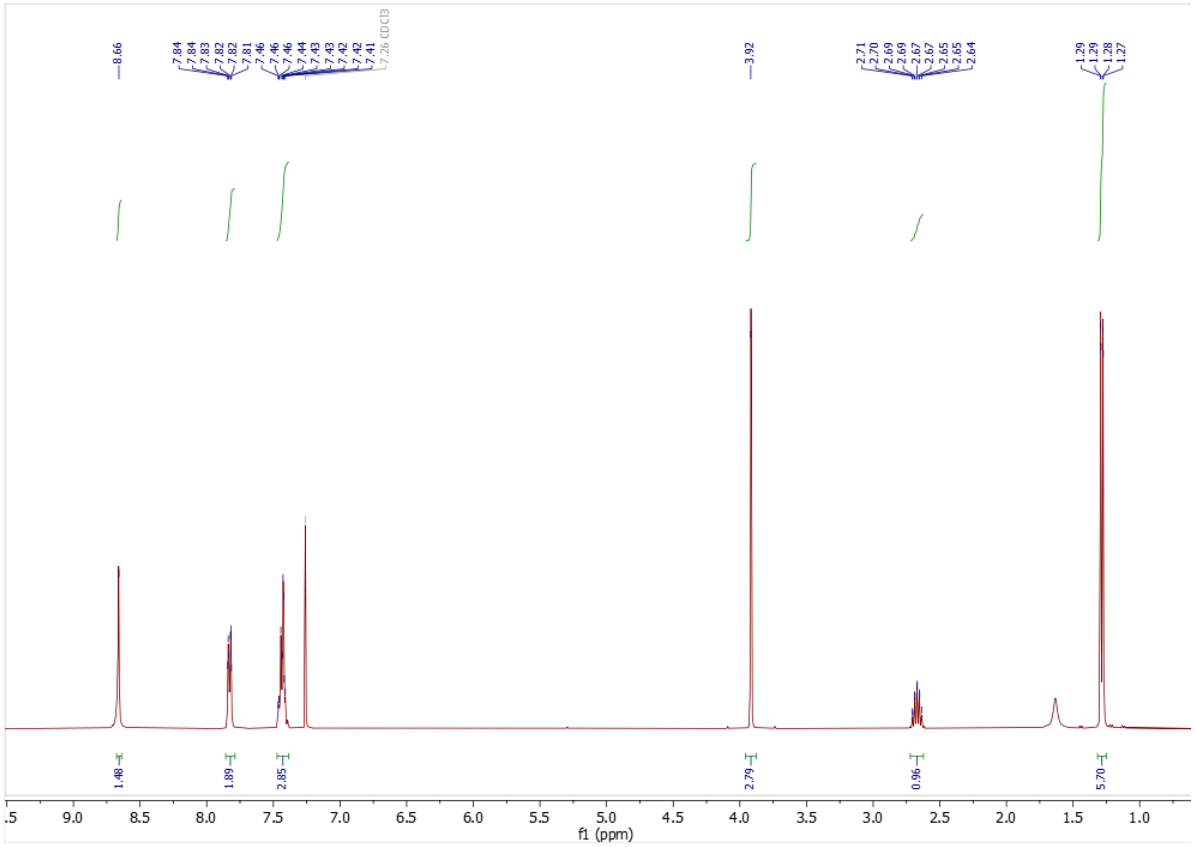
f1 (ppm)

29c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7.42
7.42
7.41
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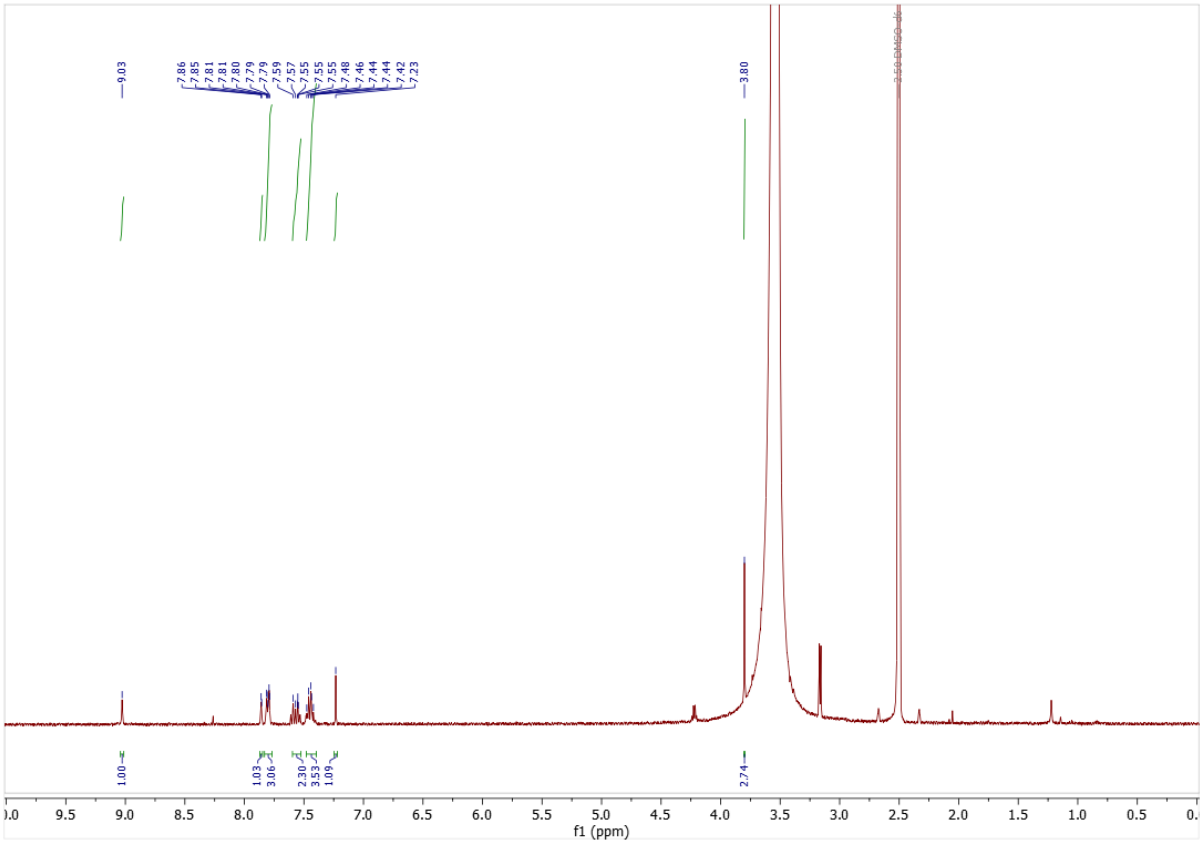
30a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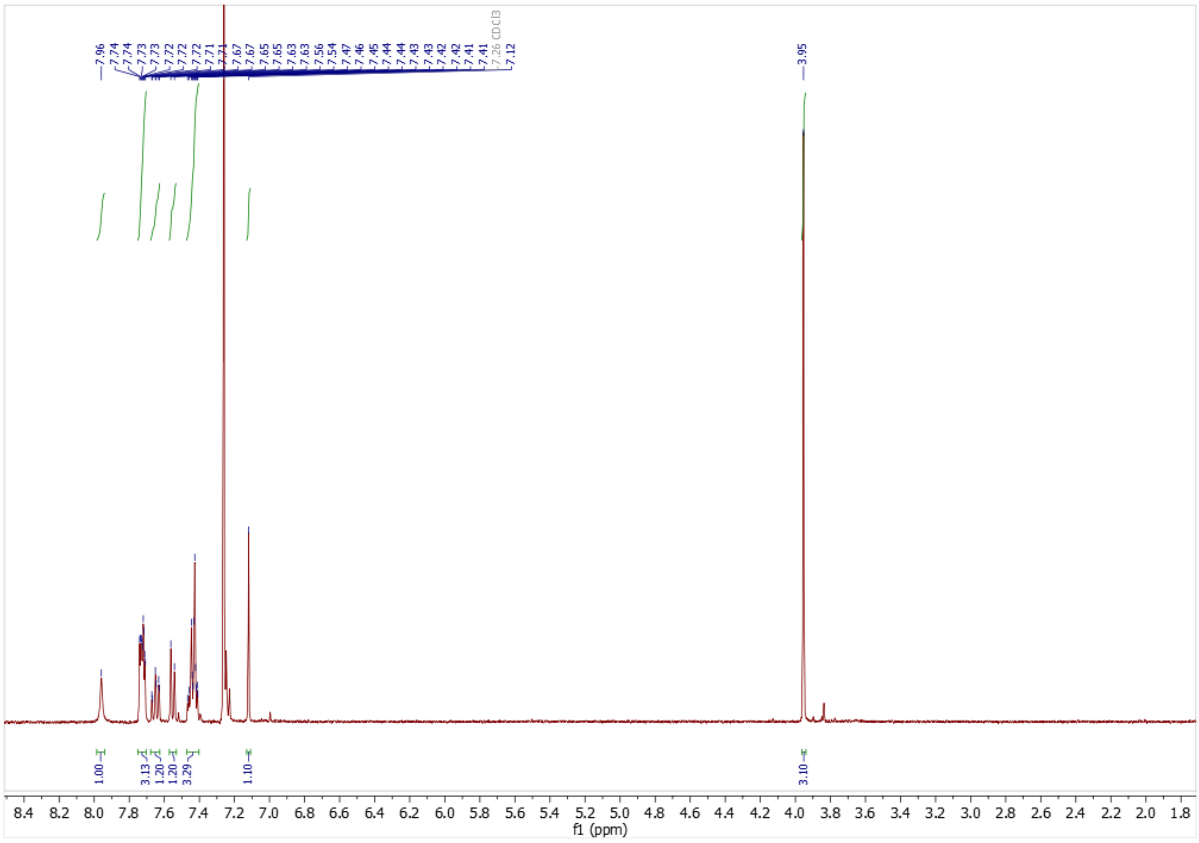
f1 (ppm)

30b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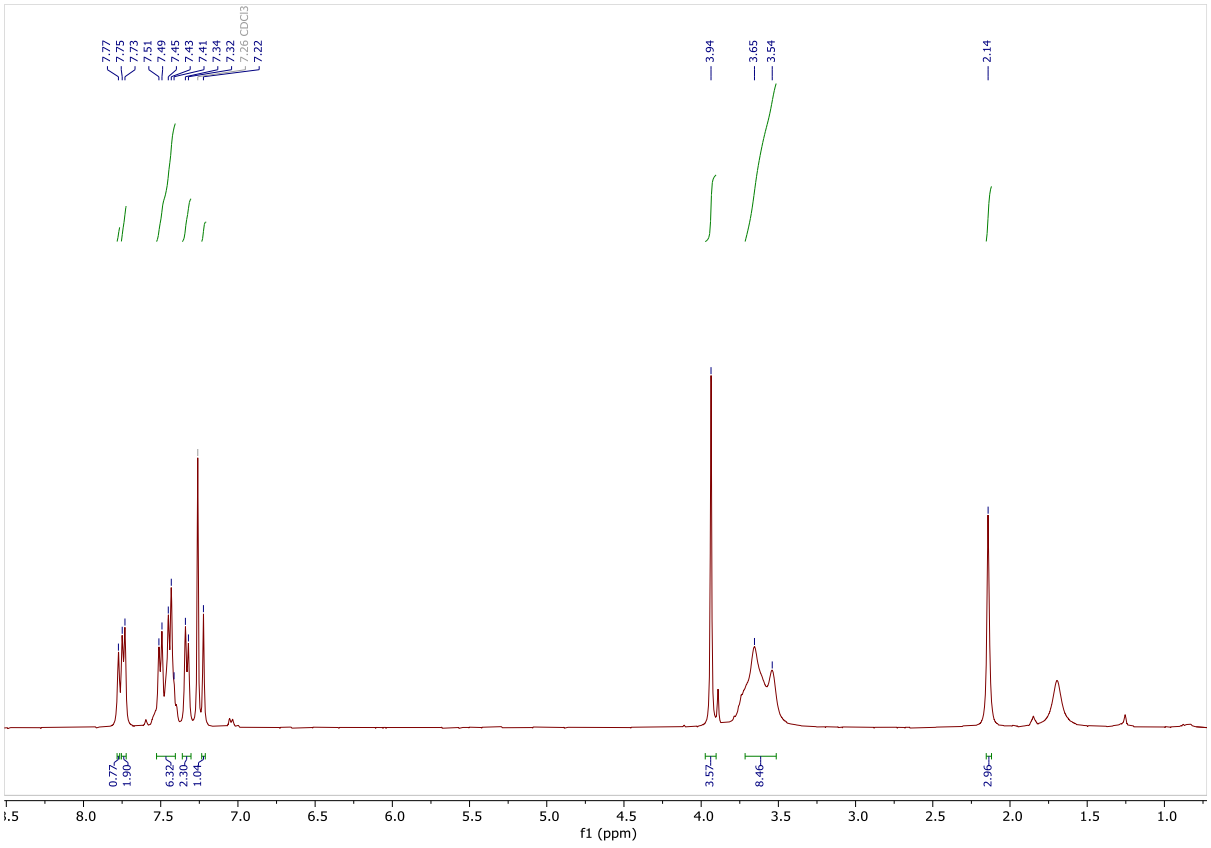
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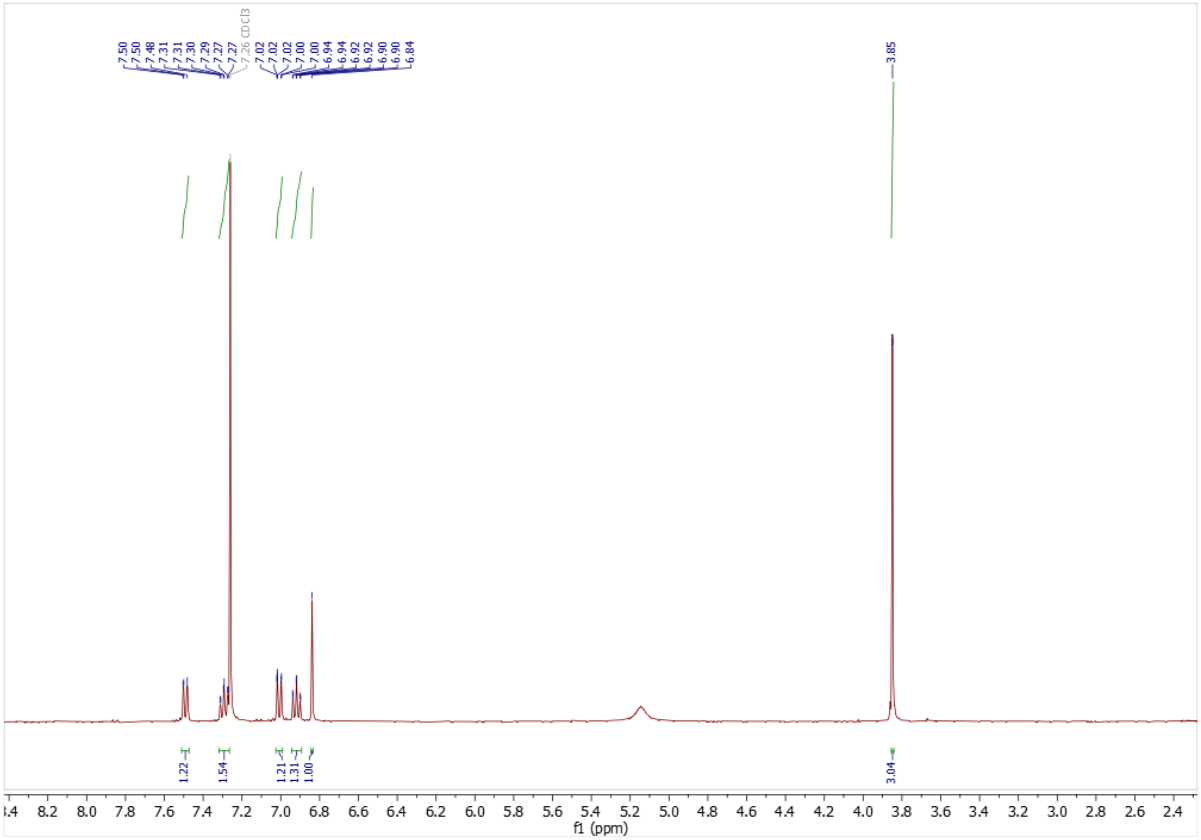
f1 (ppm)

42a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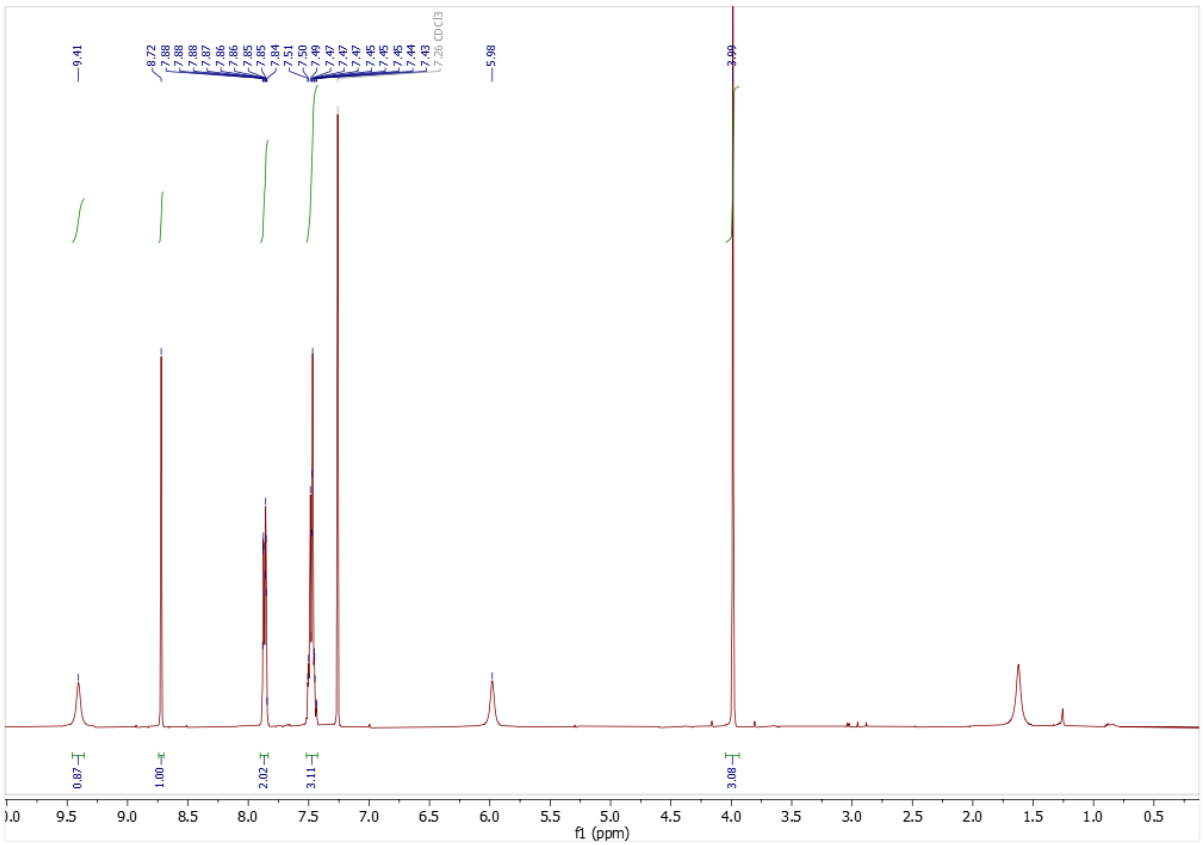
3.04
f1 (ppm)

51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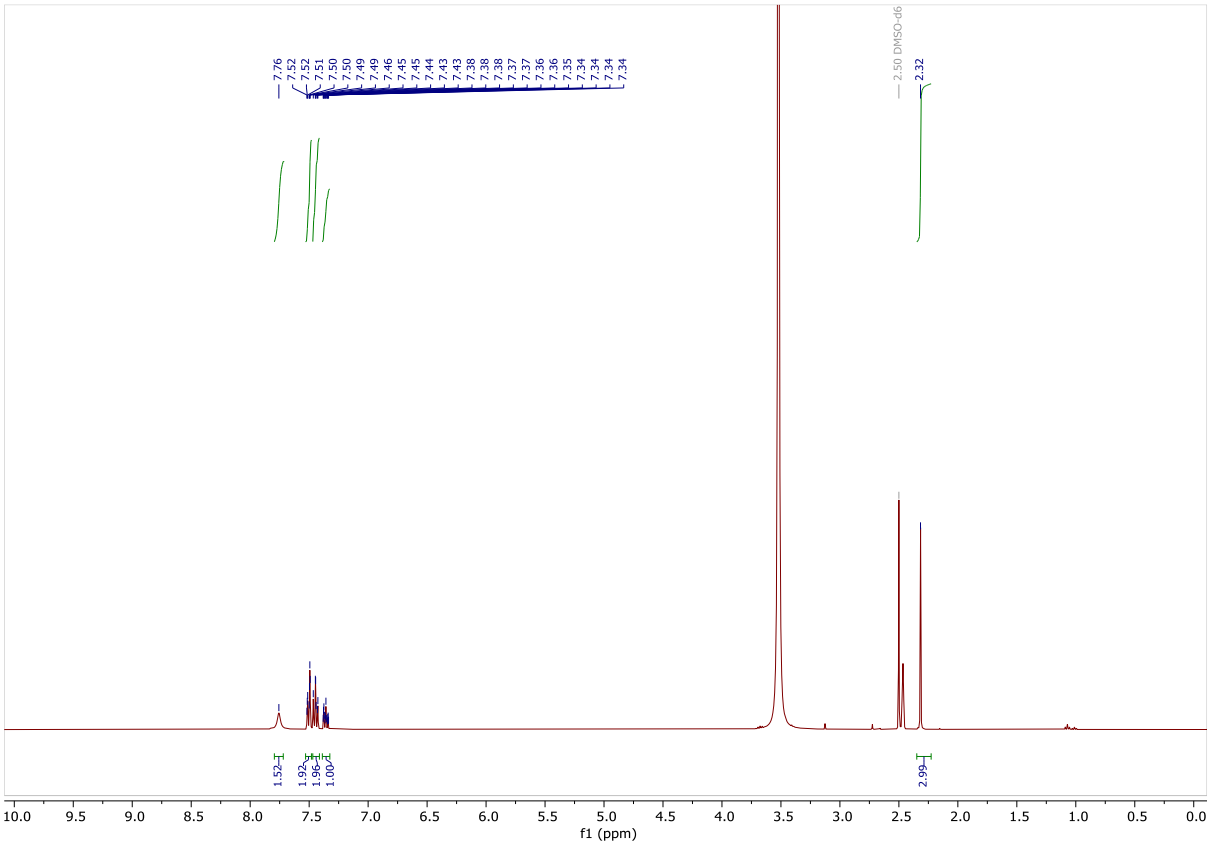
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7.43
7.38
7.38
7.38
7.37
7.37
7.36
7.36
7.35
7.34
7.34
7.34
7.34
2.50 DMSO-d6
2.32
1.52
1.92
1.96
1.00
2.99
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

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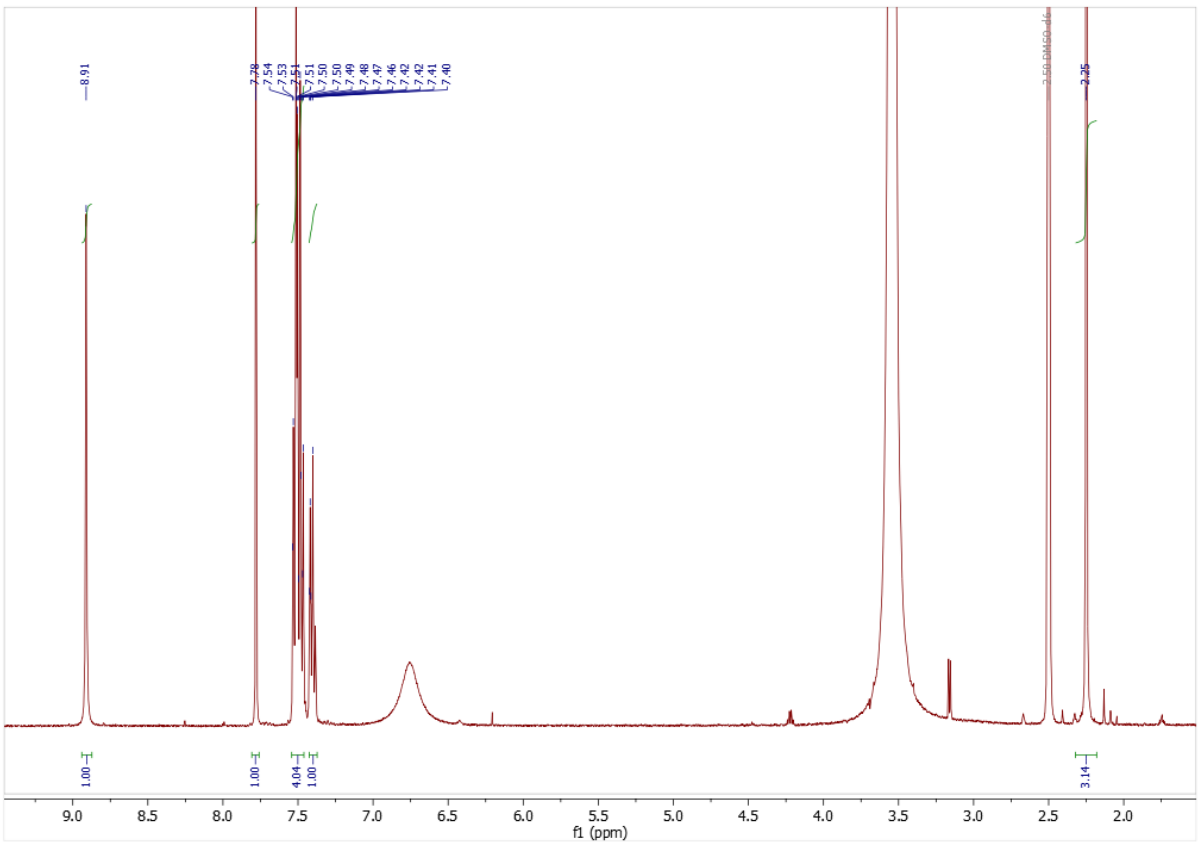
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7.42
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2.50 DMSO-d6
2.25
1.00
1.00
4.04
1.00
3.14
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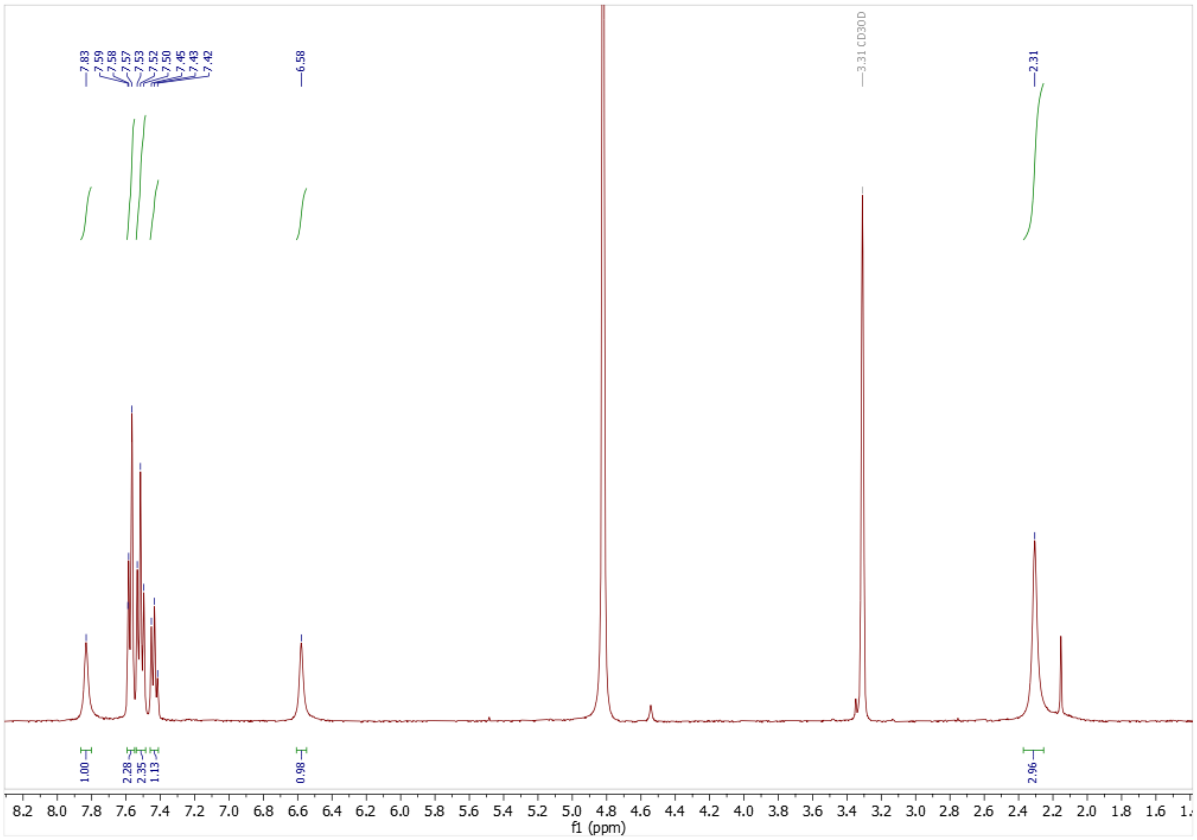
f1 (ppm)

57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7.57
7.53
7.52
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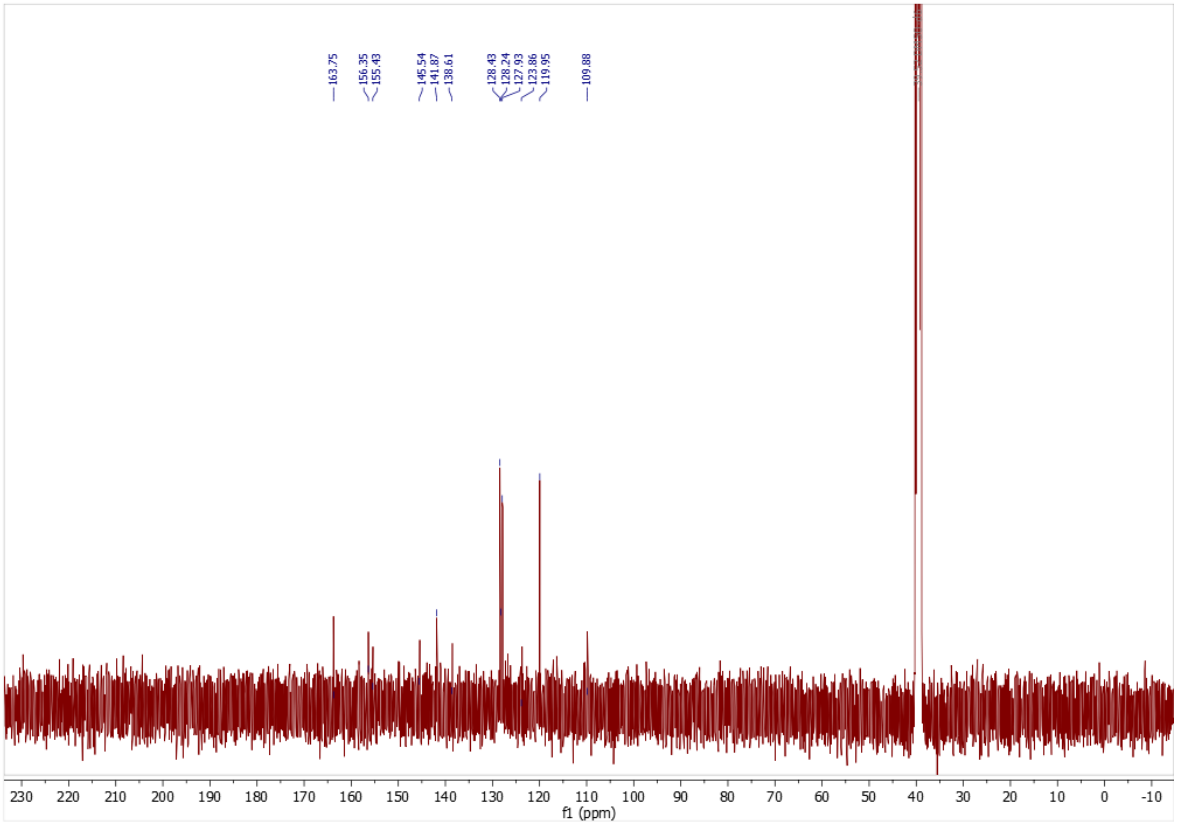
7.46
7.43
7.42
6.58
3.31 CD3OD
2.31
1.00
2.28
2.35
1.13
0.98
2.96
8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6
f1 (ppm)

^{13}C-NMRs

4a



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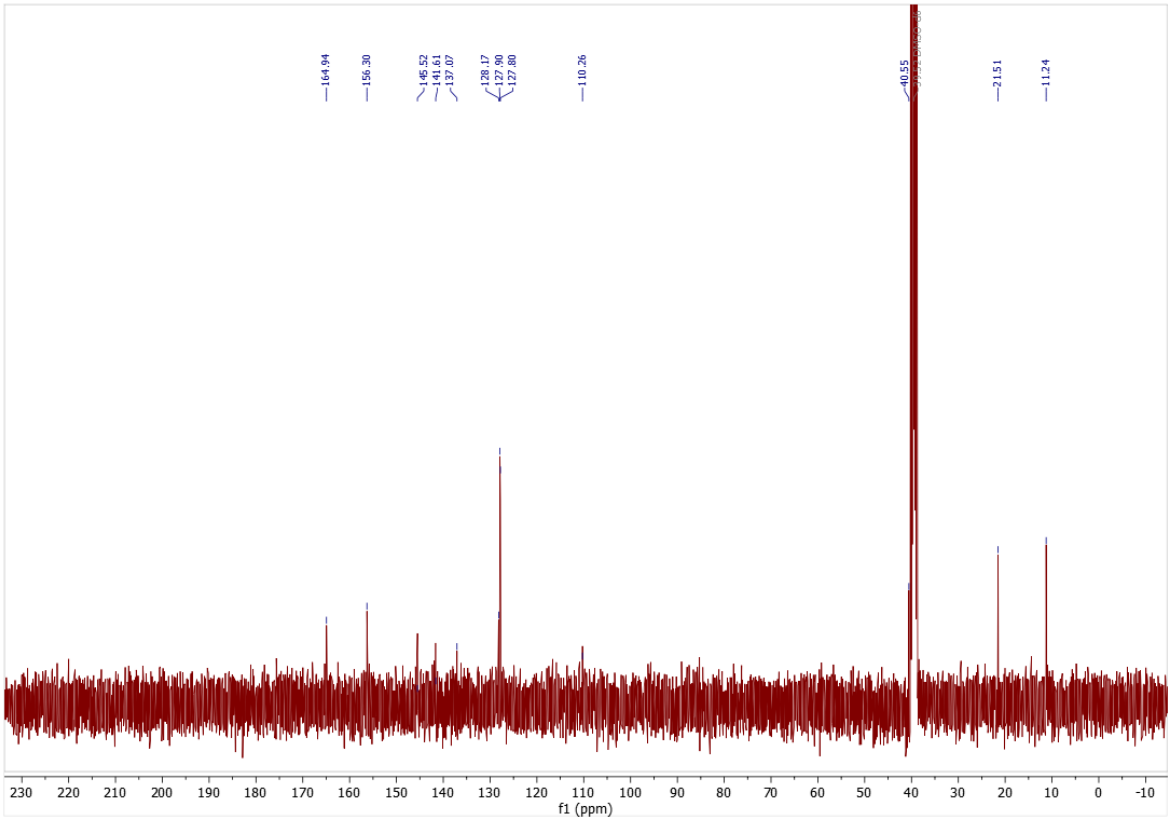

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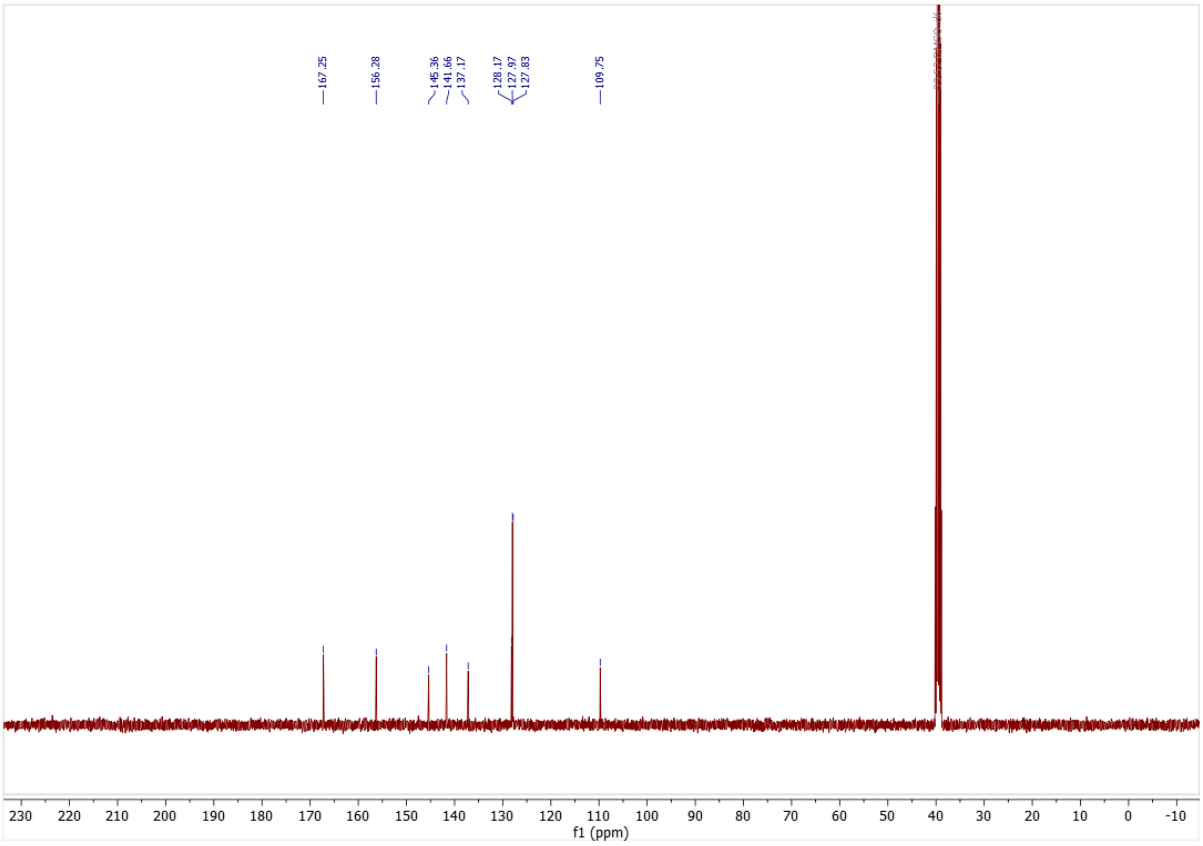
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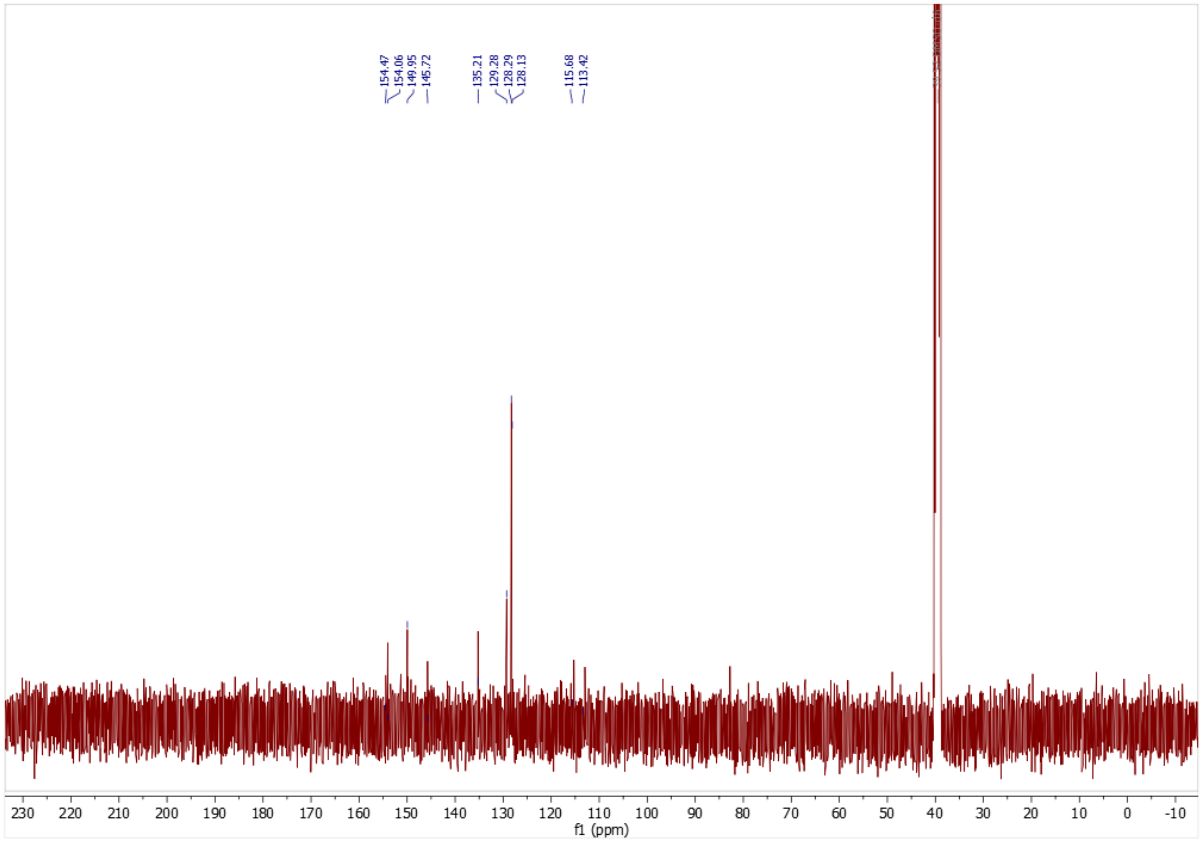
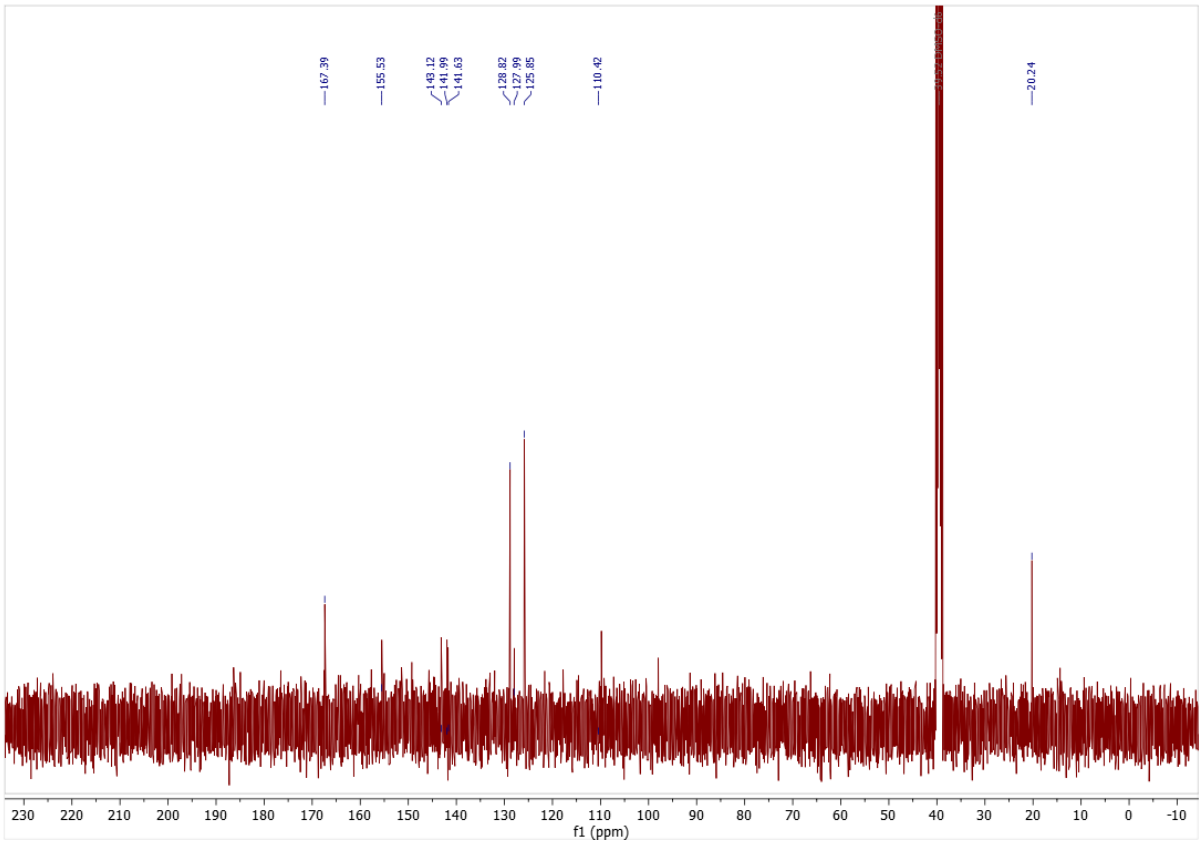
141.66
137.17
128.17
127.97
127.83
109.75
f1 (ppm)

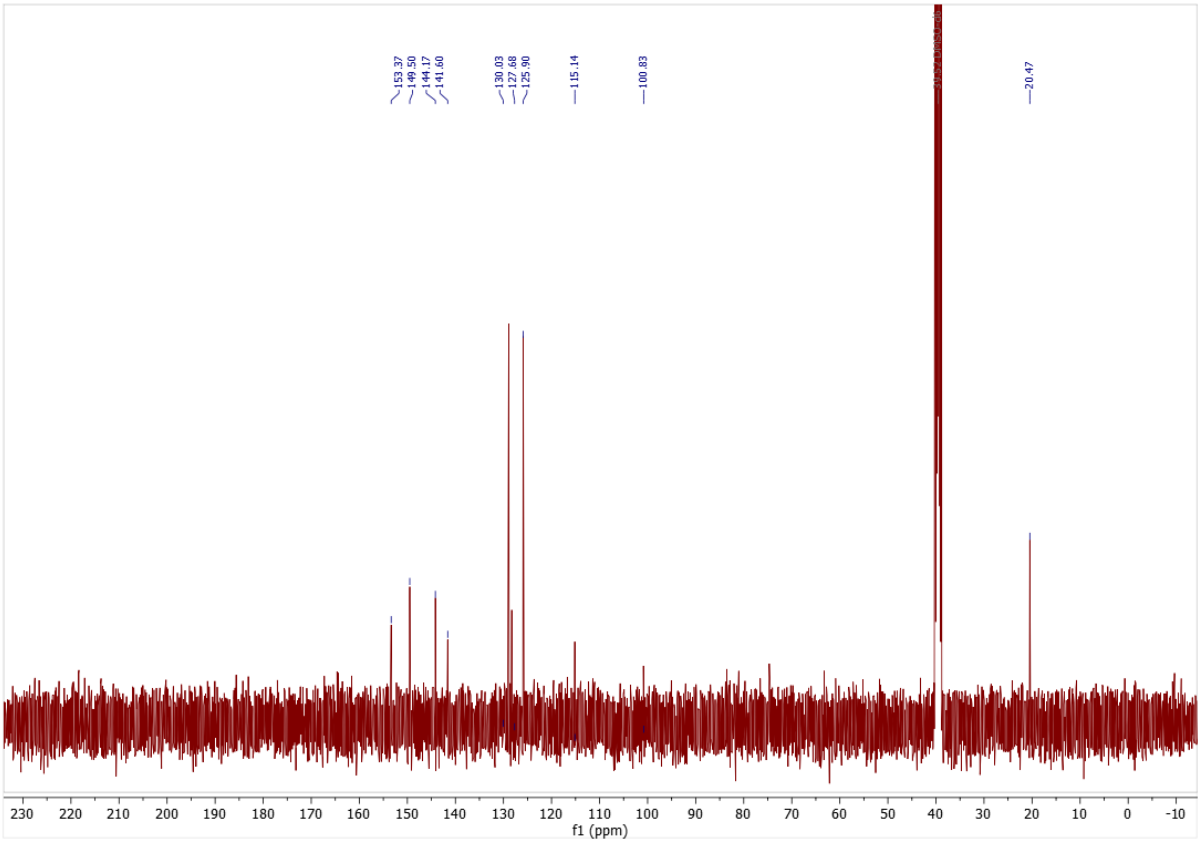
7


154.47
154.06
149.95
146.72
135.21
129.28
128.29
128.13
115.68
113.42
f1 (ppm)

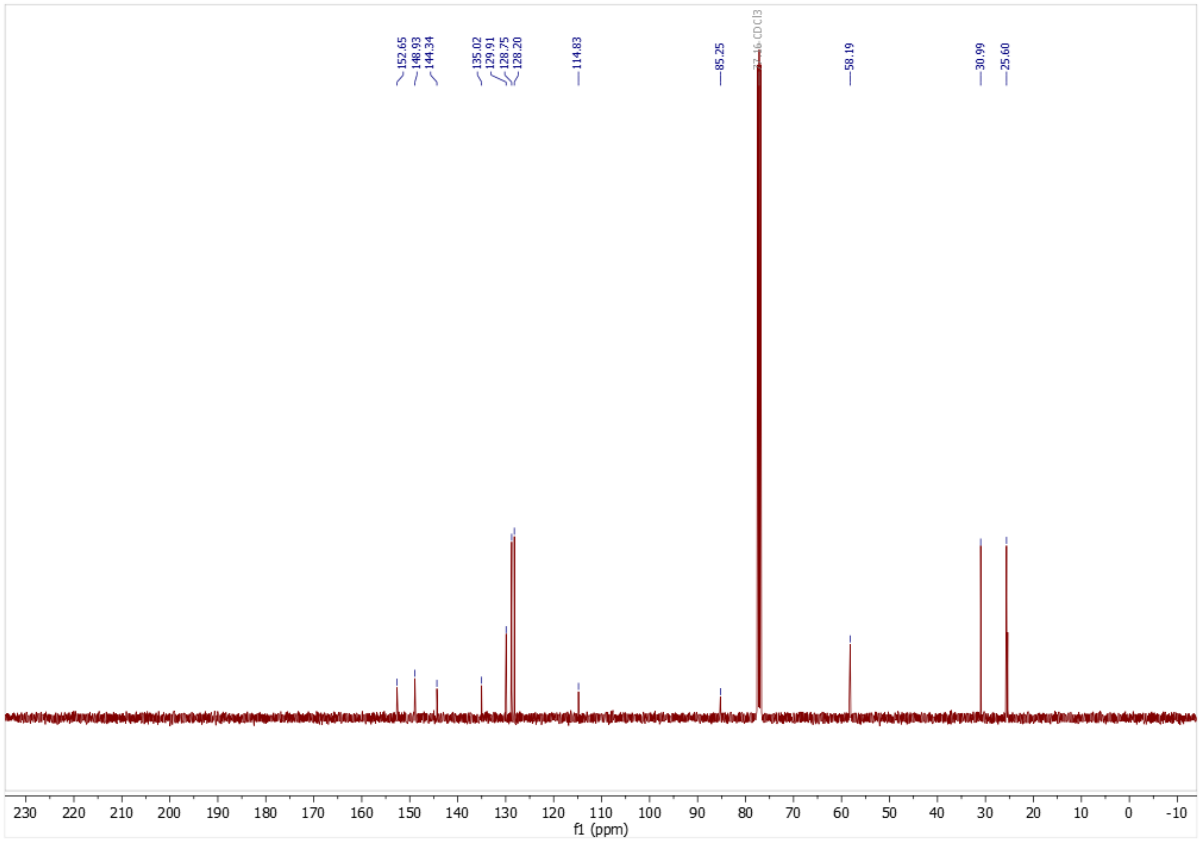
16


167.39
155.53
143.12
141.99
141.63
128.82
127.99
125.85
110.42
20.24
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

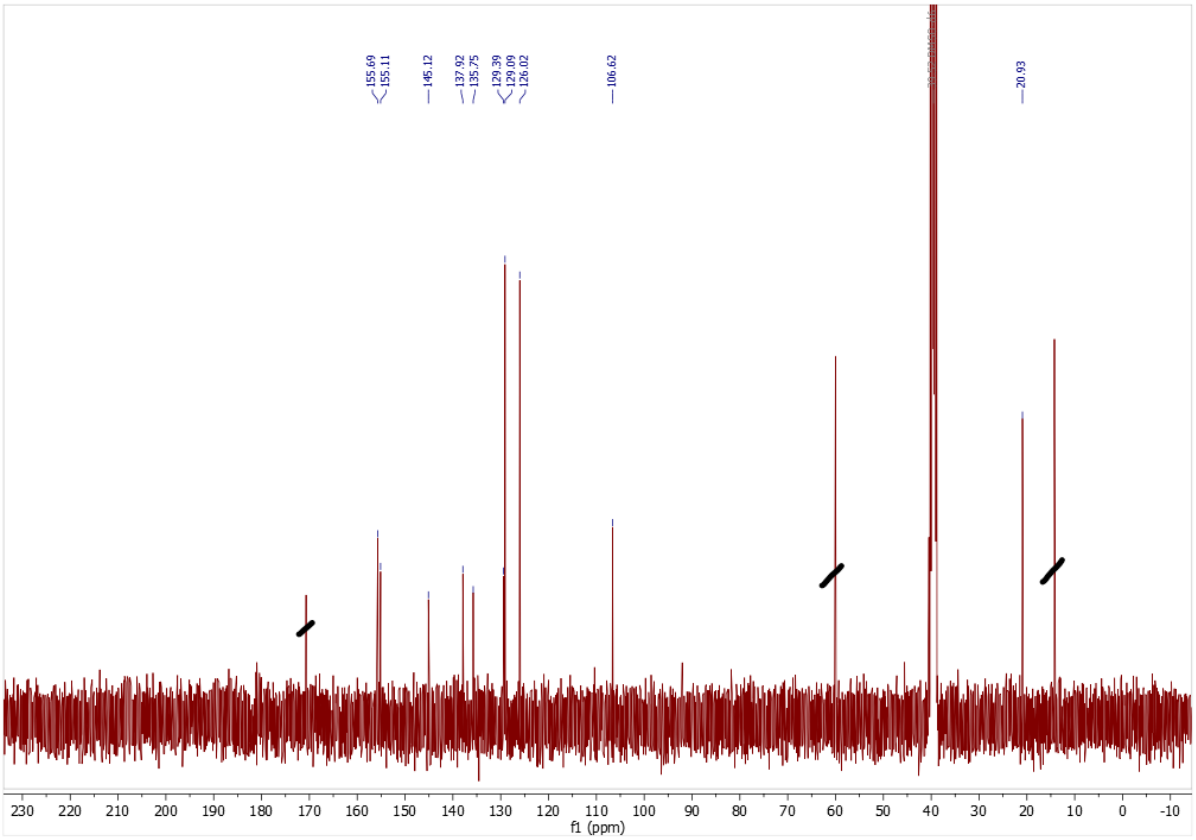
17


153.37
149.50
144.17
141.60
130.03
127.68
125.90
115.14
100.83
20.47
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

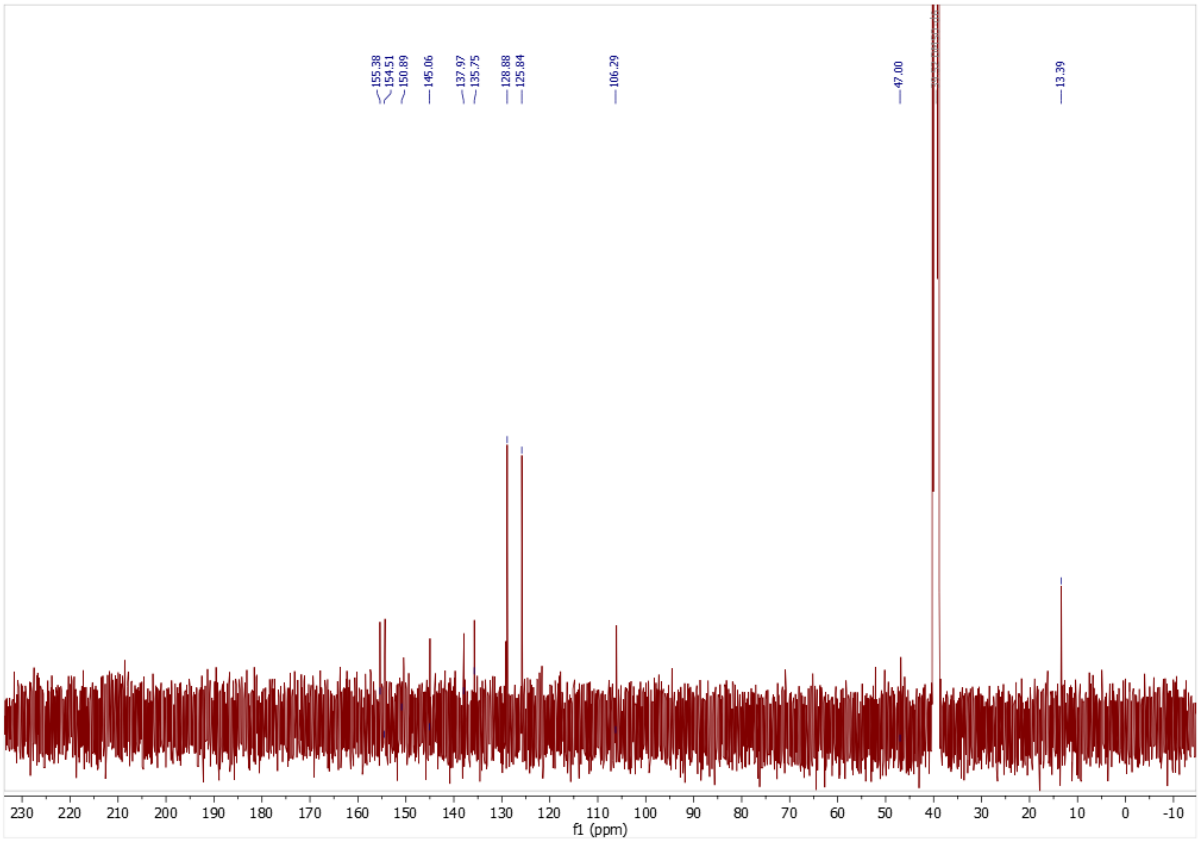
22



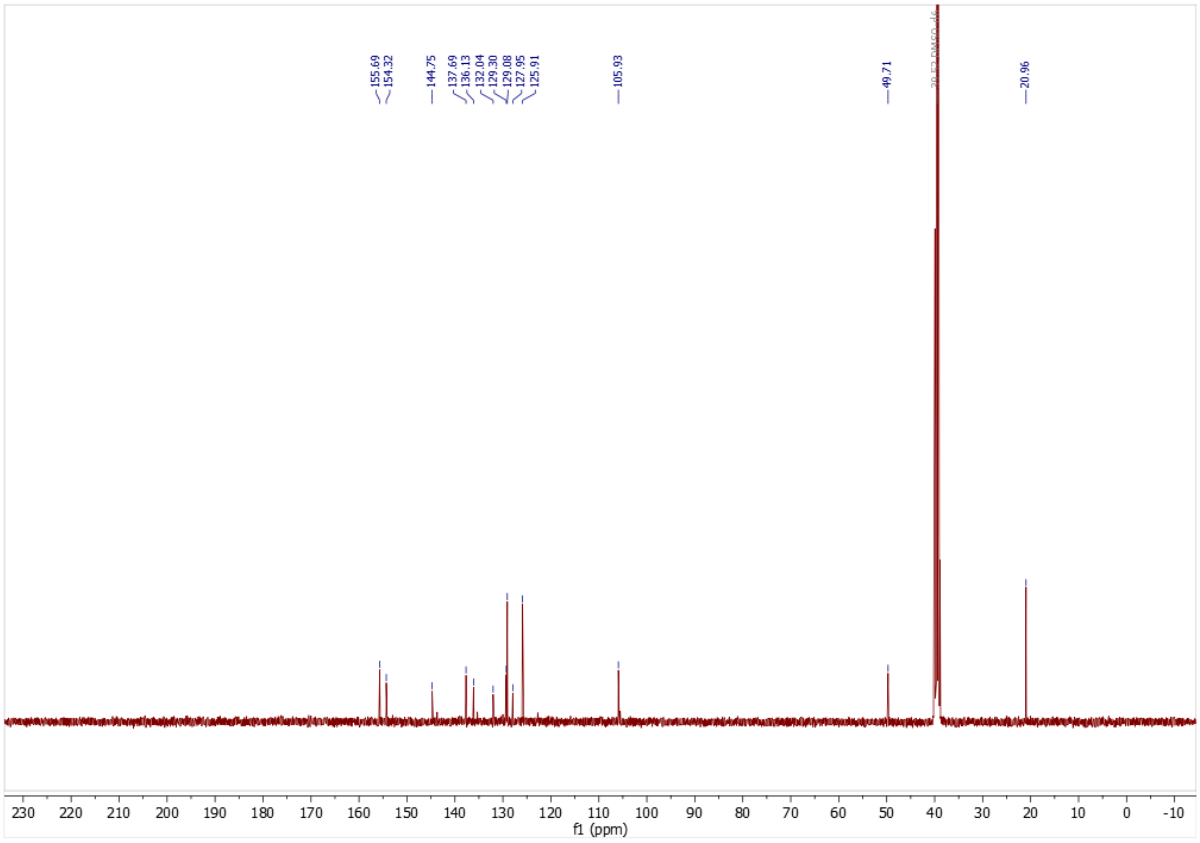
25a (EtOAc crossed)



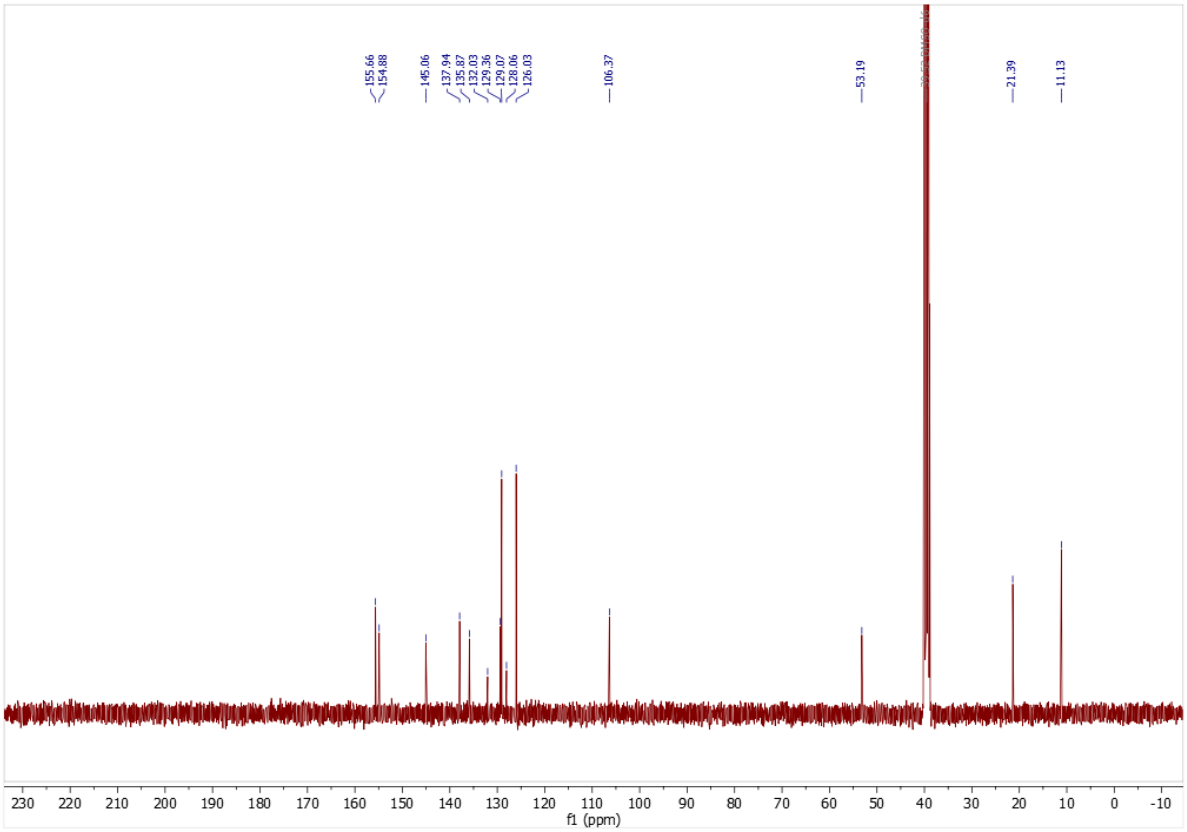
25c


155.38
154.51
150.89
145.06
137.97
135.75
128.88
125.84
106.29
47.00
13.39
f1 (ppm)

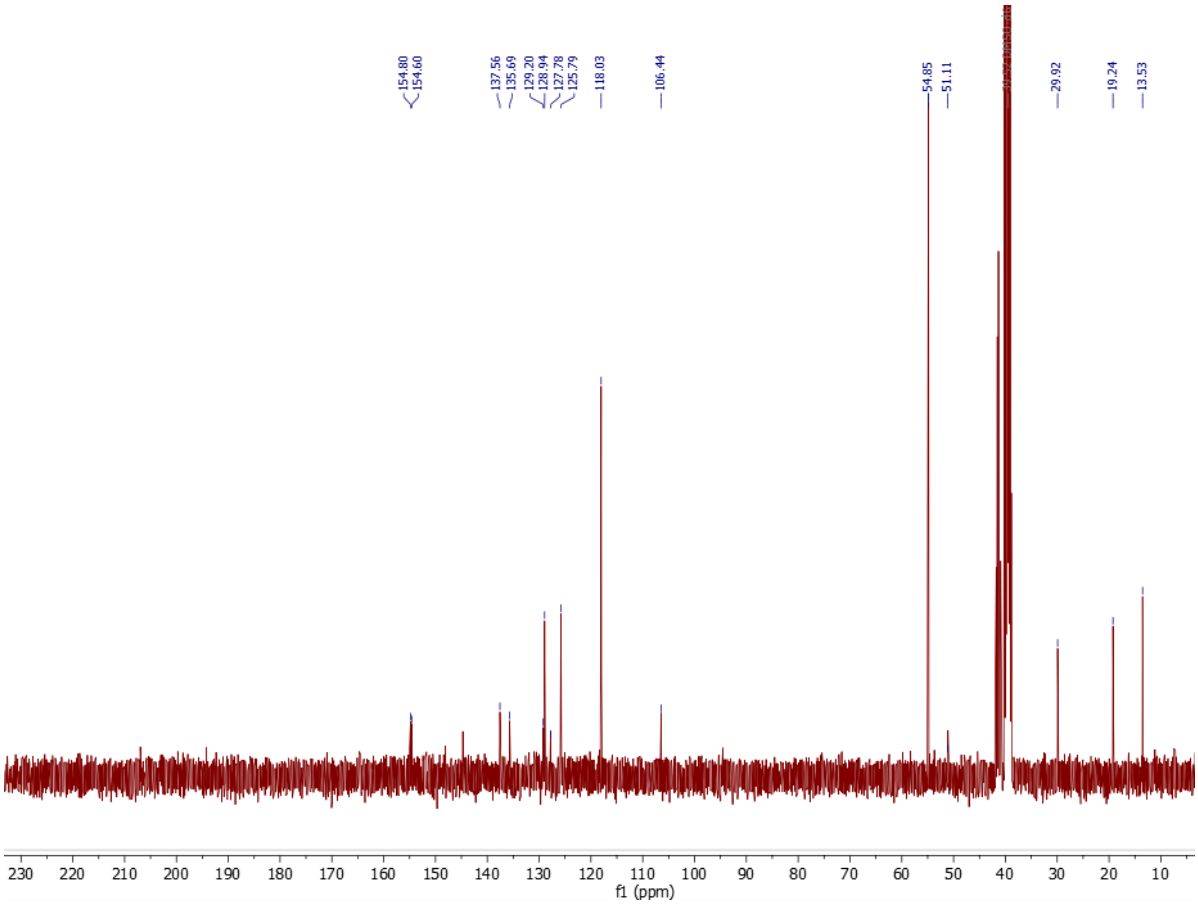
25d


155.69
154.32
144.75
137.69
136.13
132.04
129.30
129.08
127.95
125.91
105.93
49.71
20.96
f1 (ppm)

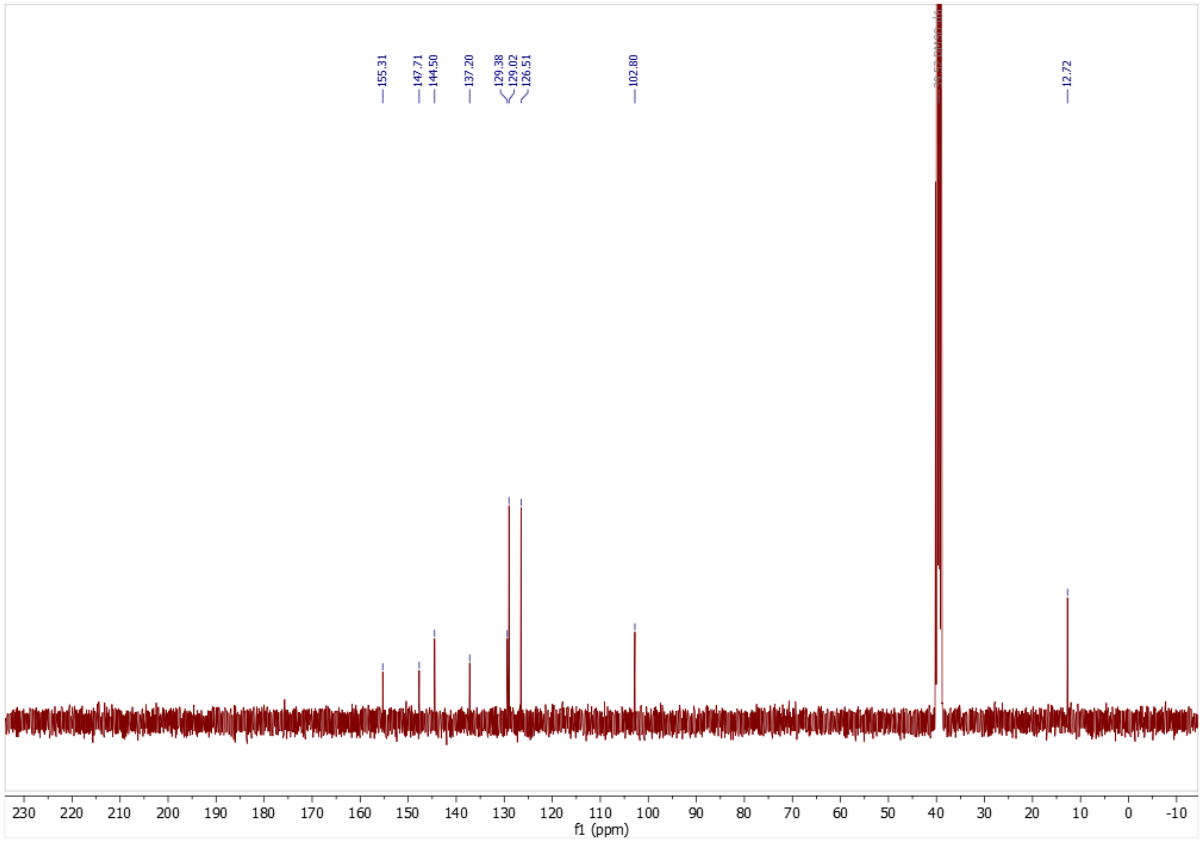
25e


155.66
154.88
145.06
137.94
135.87
132.03
129.36
129.07
128.06
126.03
106.37
53.19
21.39
11.13
f1 (ppm)

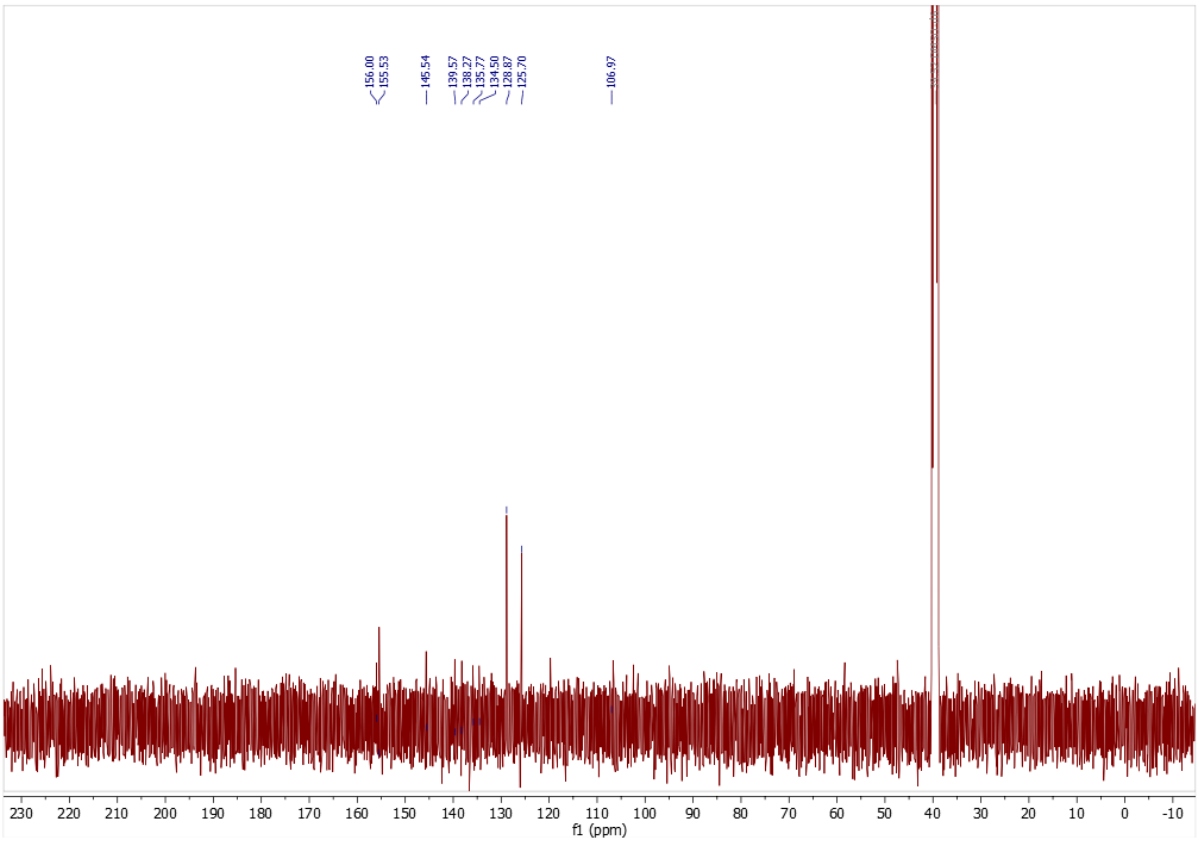
25f


154.80
154.60
137.56
135.69
129.20
128.94
127.78
125.79
118.03
106.44
54.85
51.11
29.92
19.24
13.53
f1 (ppm)

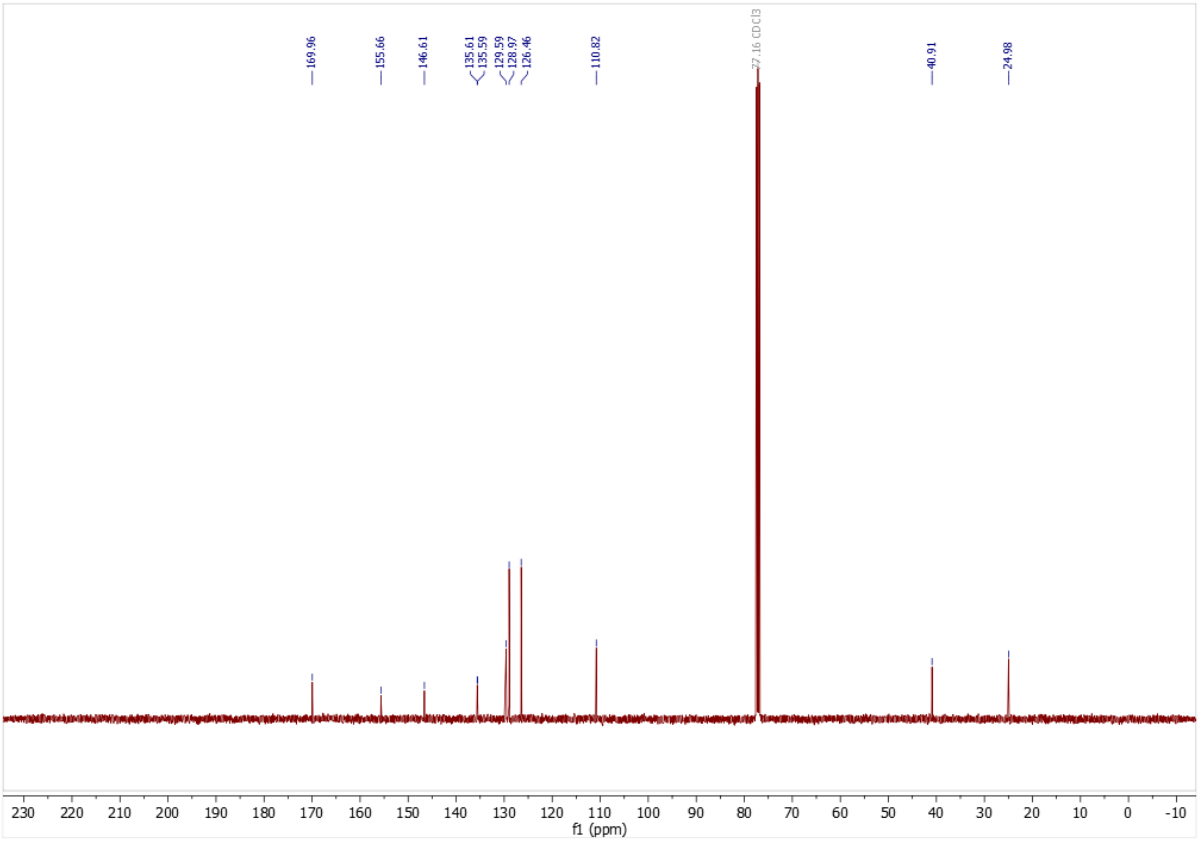
27


155.31
147.71
144.50
137.20
129.38
129.02
126.51
102.80
12.72
f1 (ppm)

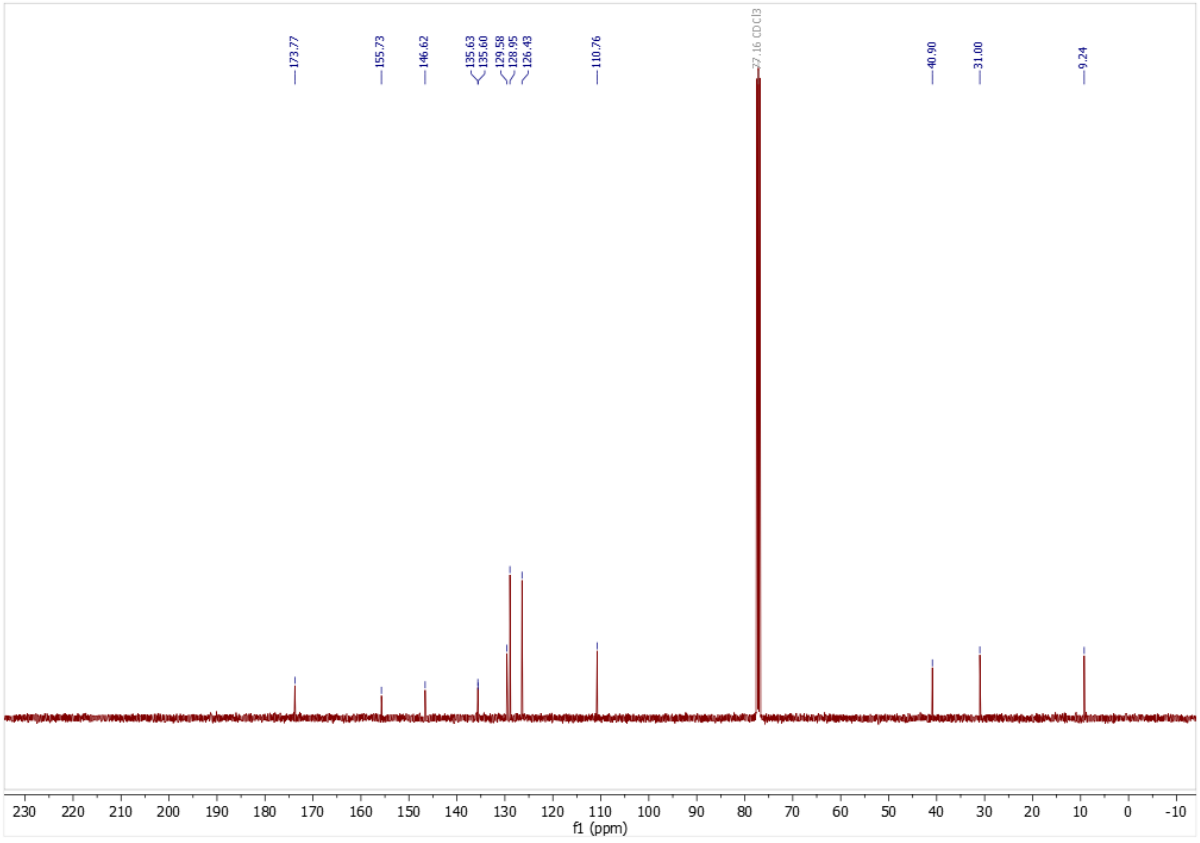
28


156.00
155.53
145.54
139.57
138.27
135.77
134.50
128.87
125.70
106.97
f1 (ppm)

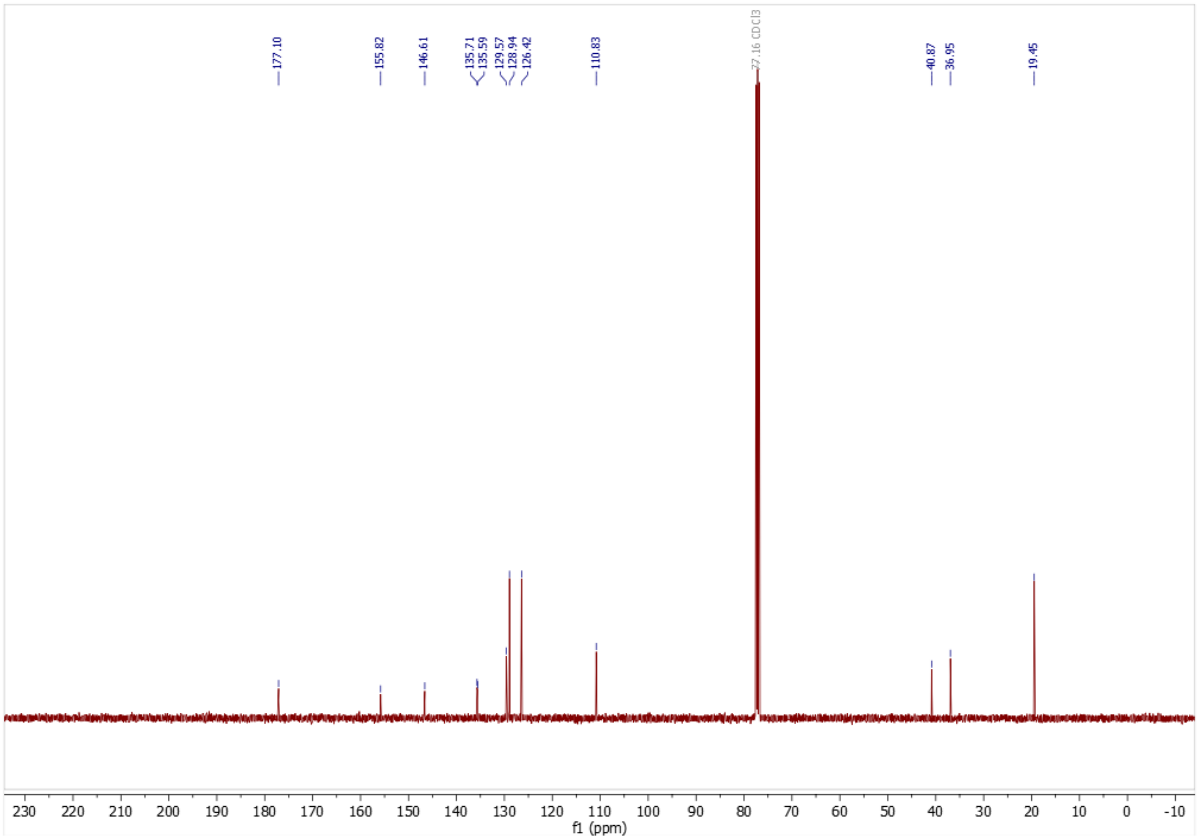
29a


169.96
155.66
146.61
135.61
135.59
129.59
128.97
126.46
110.82
77.16 CDCl3
40.91
24.98
f1 (ppm)

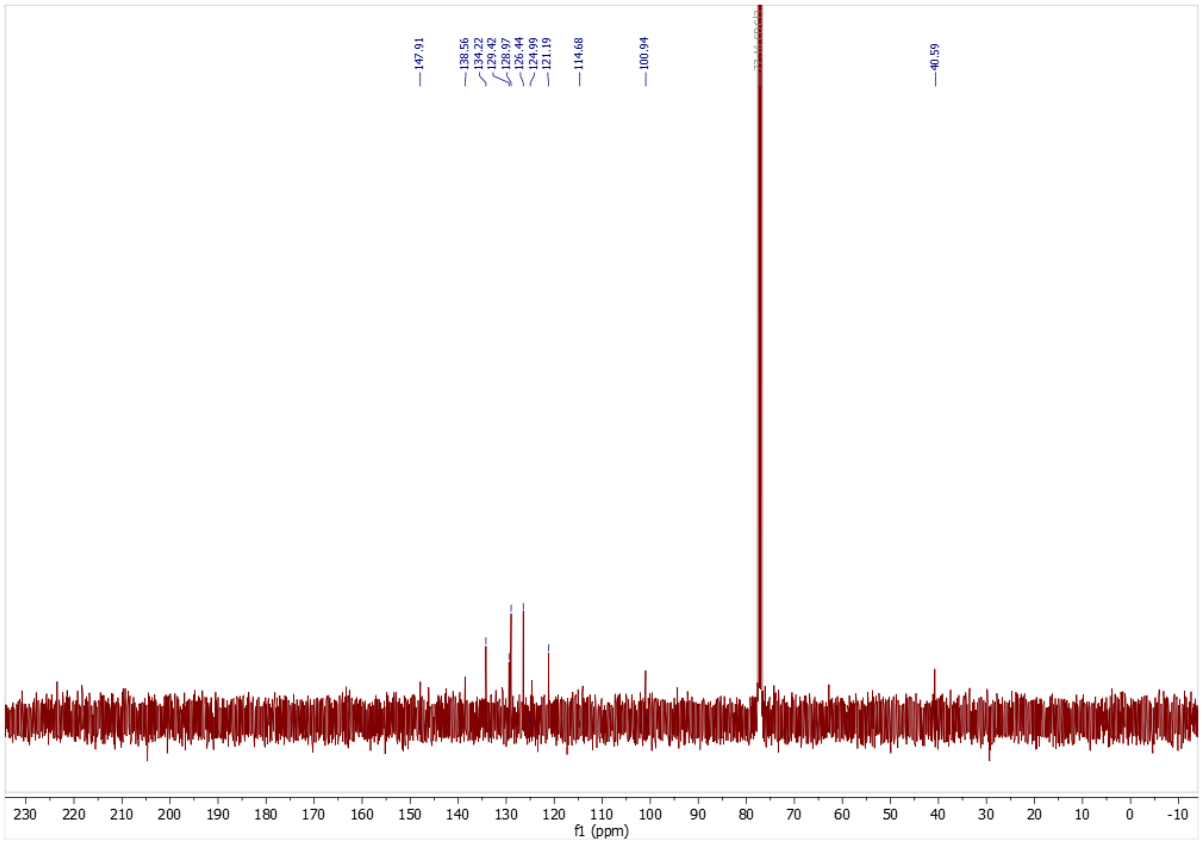
29b


173.77
155.73
146.62
135.63
135.60
129.58
128.95
126.43
110.76
77.16 CDCl3
40.90
31.00
9.24
f1 (ppm)

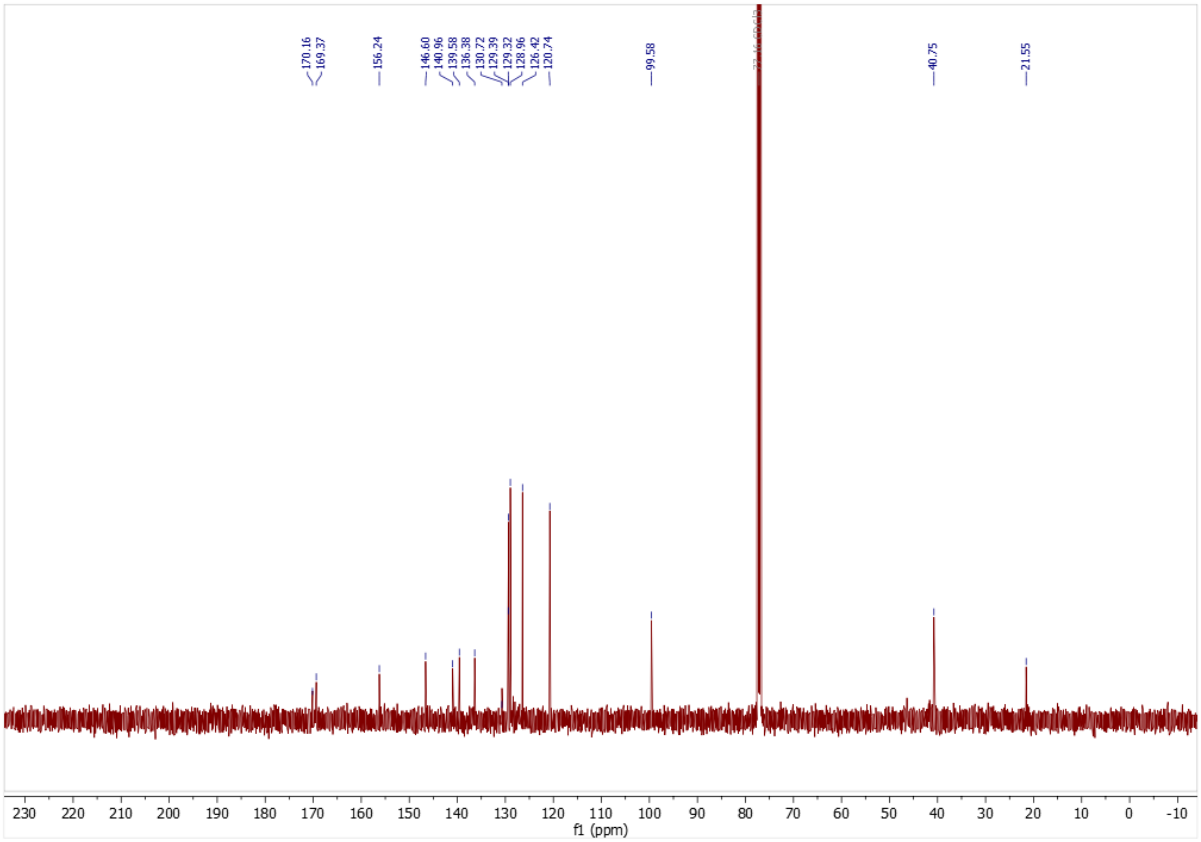
29c


177.10
155.82
146.61
135.71
135.59
129.57
128.94
126.42
110.83
77.16 CDCl3
40.87
36.95
19.45
f1 (ppm)

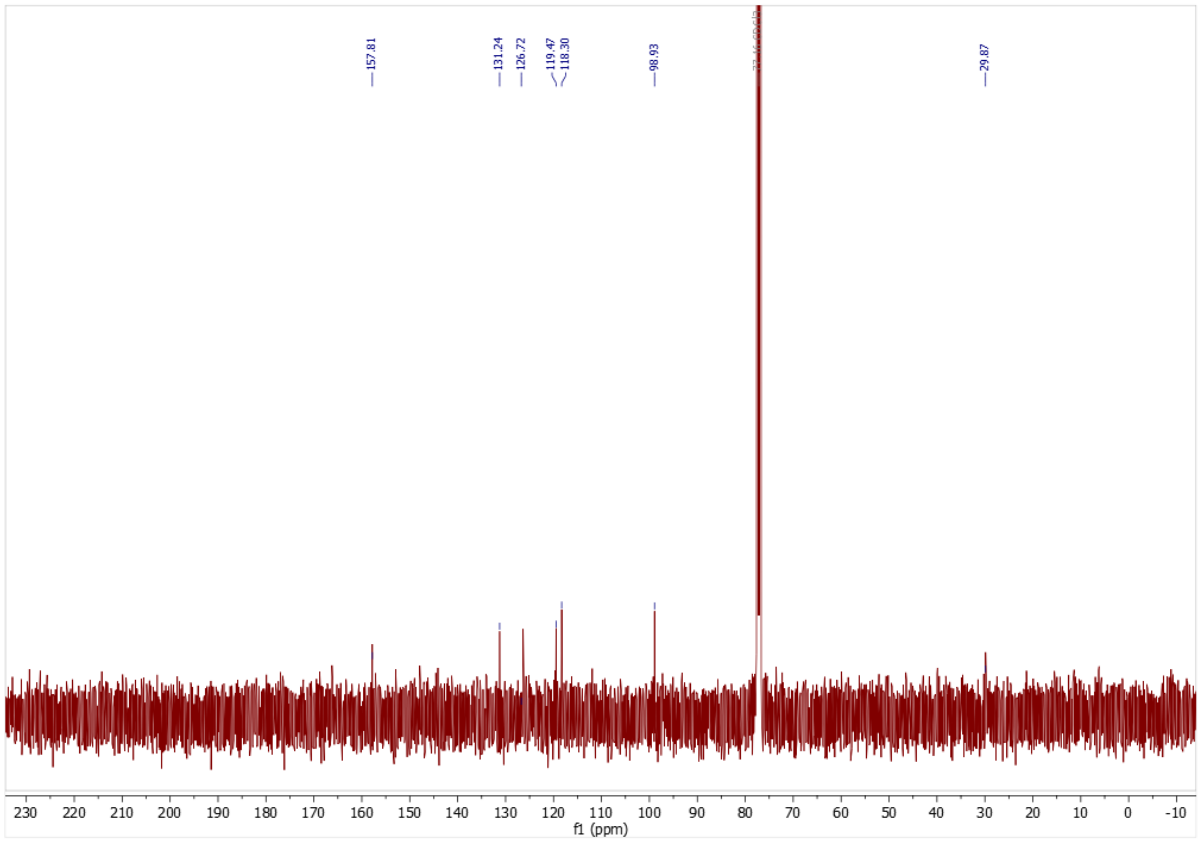
30b


147.91
138.56
134.22
129.42
128.97
126.44
124.99
121.19
114.68
100.94
40.59
f1 (ppm)

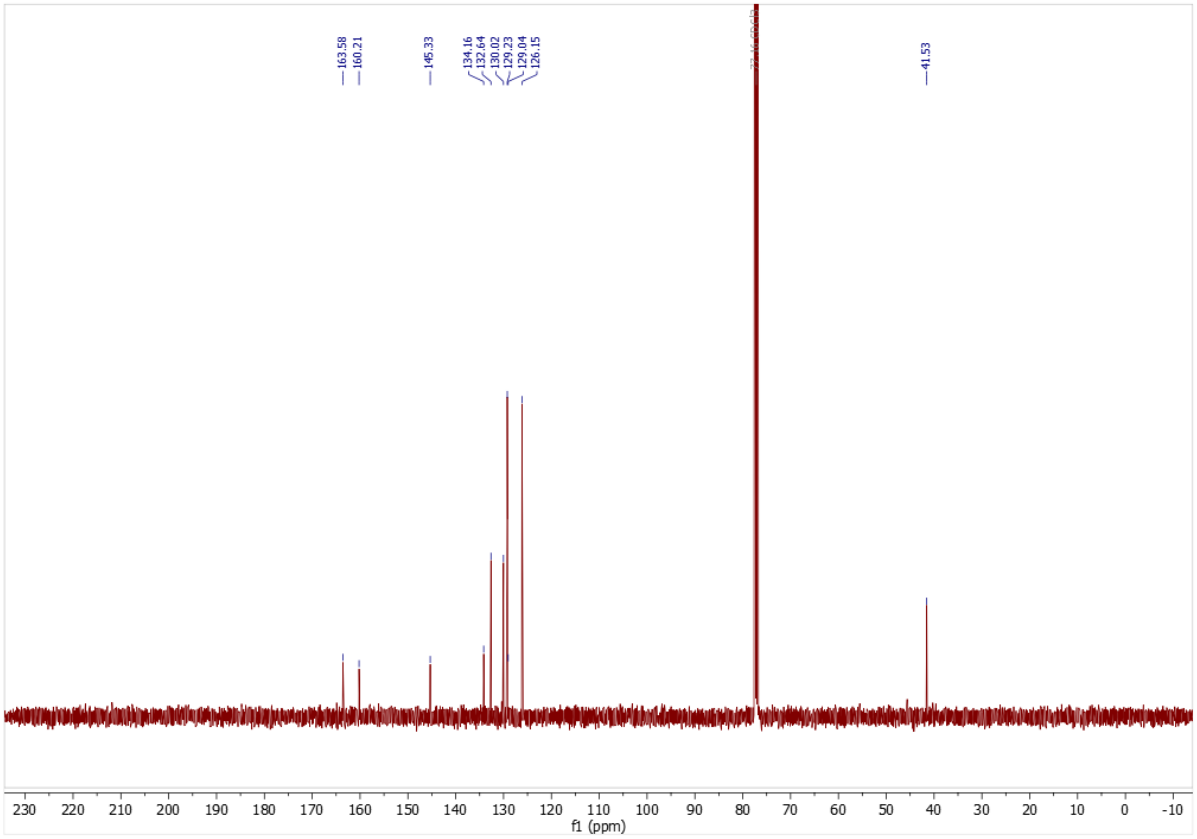
35


170.16
169.37
156.24
146.60
140.96
139.58
136.38
130.72
129.39
129.32
128.96
126.42
120.74
99.58
40.75
21.55
f1 (ppm)

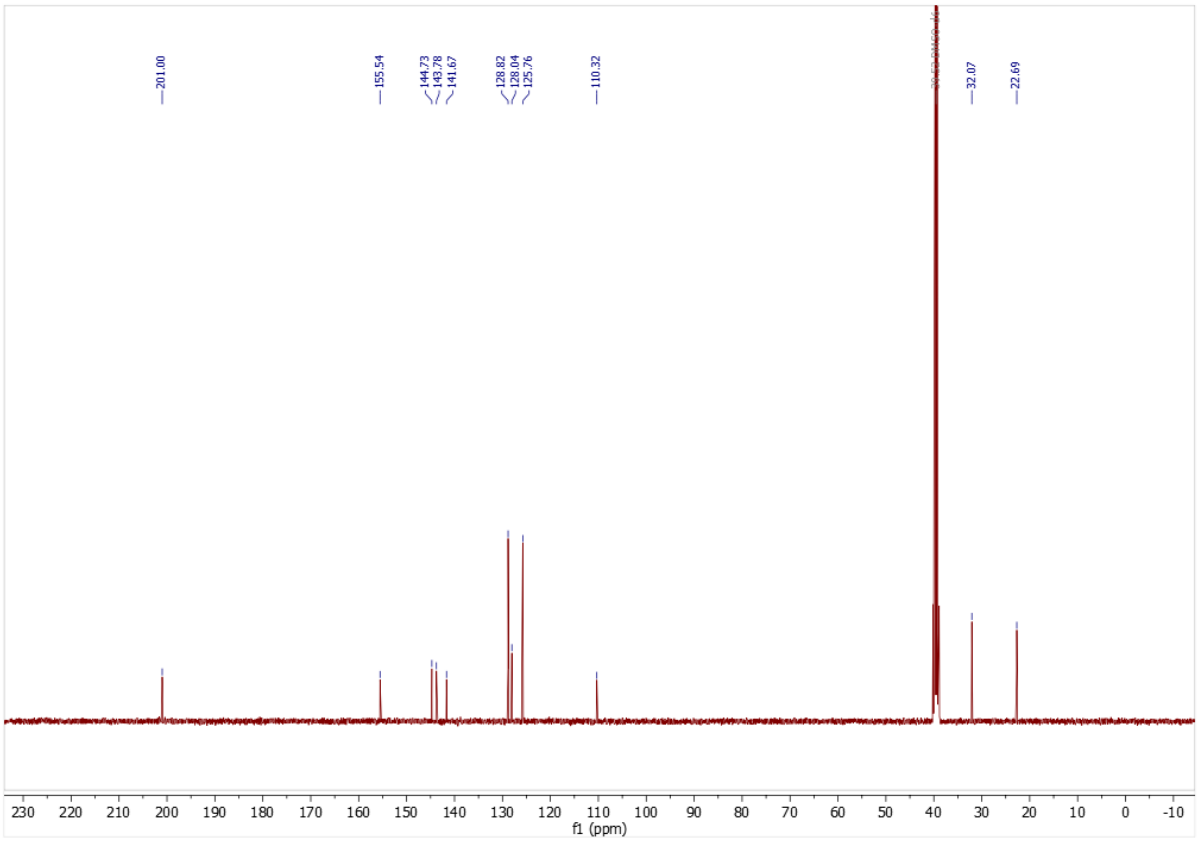
42a


157.81
131.24
126.72
119.47
118.30
98.93
29.87
f1 (ppm)

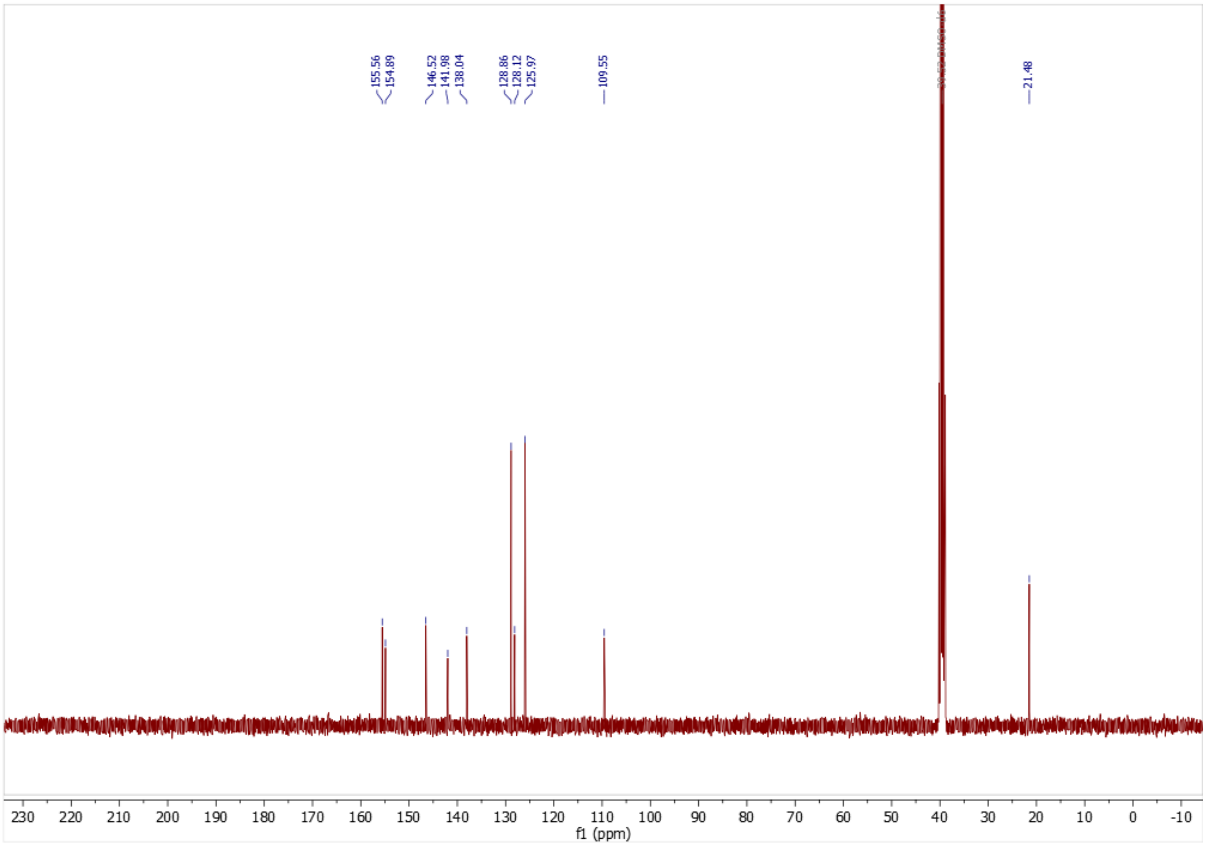
51


163.58
160.21
145.33
134.16
132.64
130.02
129.23
129.04
126.15
41.53
f1 (ppm)

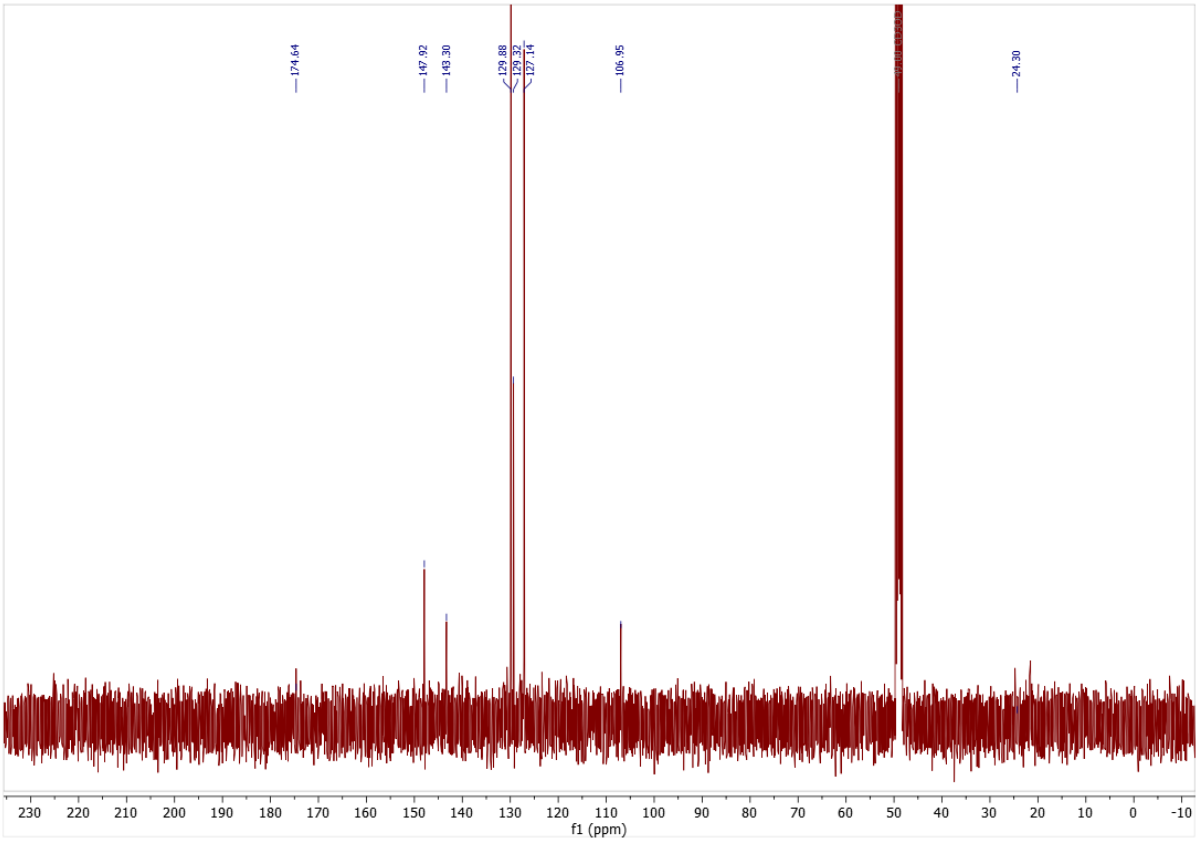
54


201.00
155.54
144.73
143.78
141.67
128.82
128.04
125.76
110.32
32.07
22.69
f1 (ppm)

55

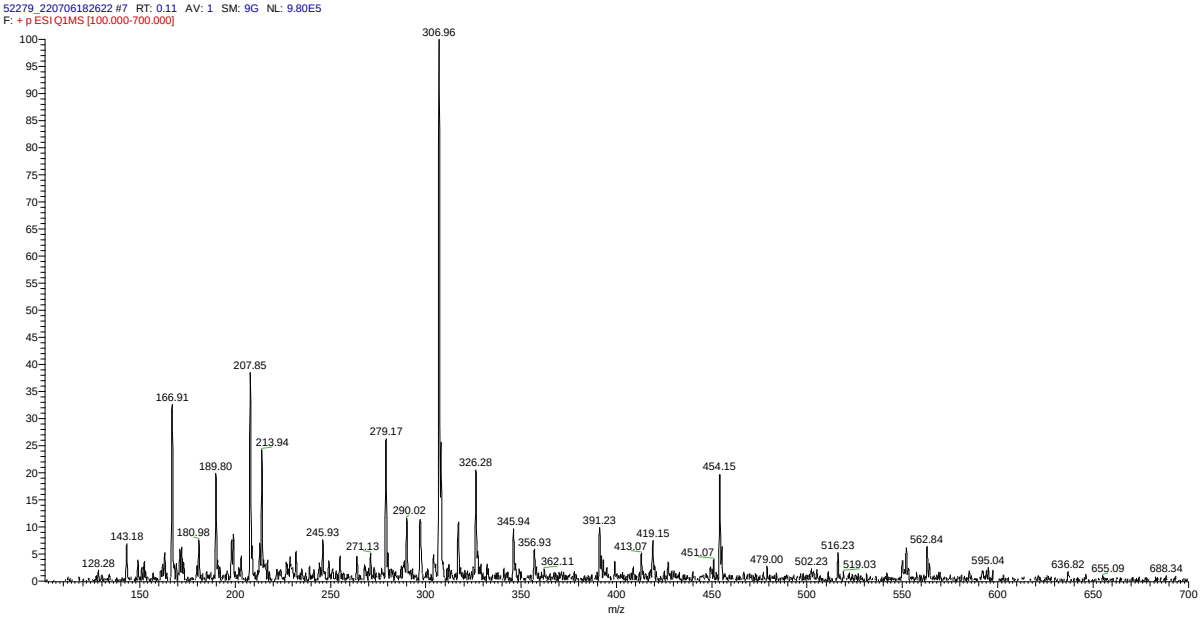

155.56
154.89
146.52
141.98
138.04
128.86
128.12
125.97
109.55
21.48
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

57

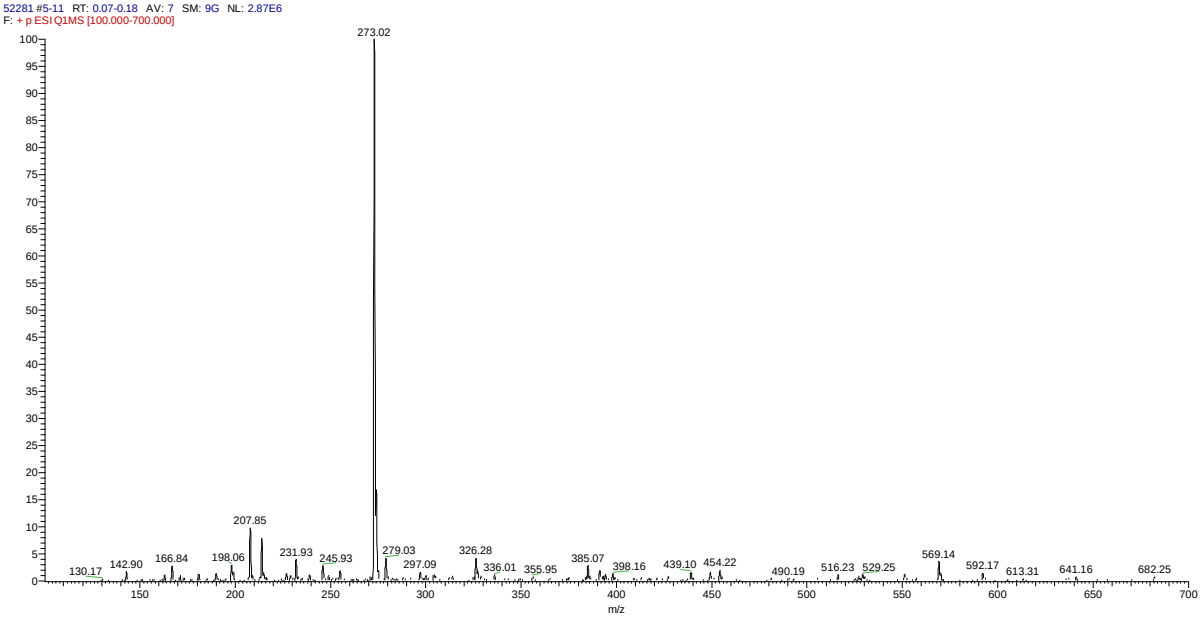

174.64
147.92
143.30
129.88
129.32
127.14
106.95
24.30
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

Mass spectra

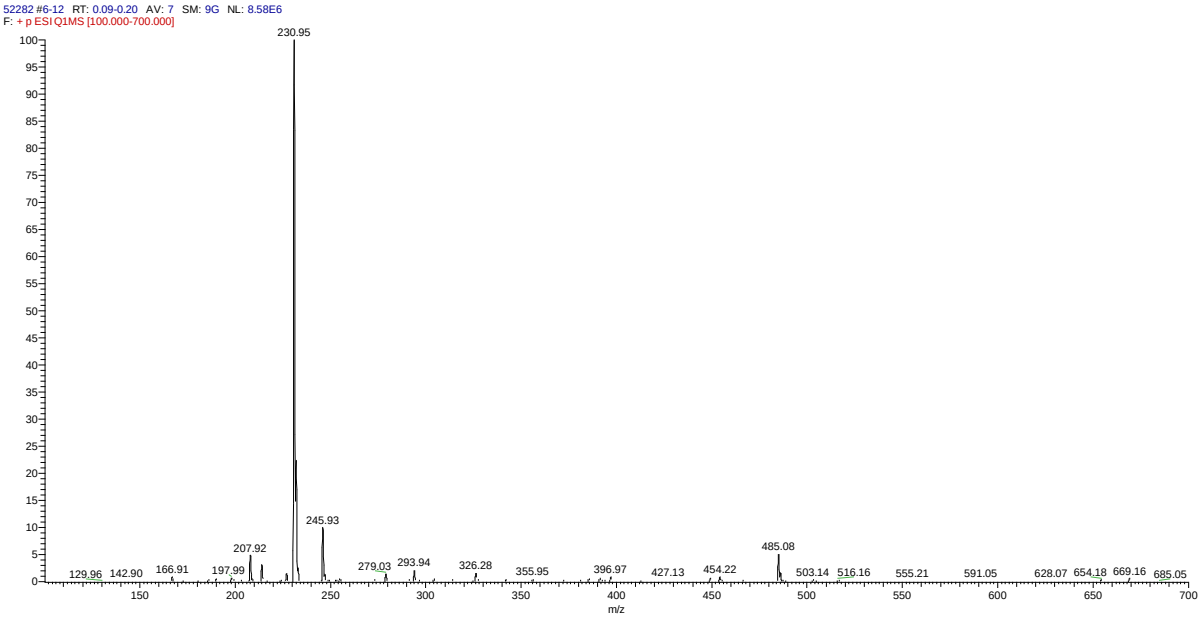
4a



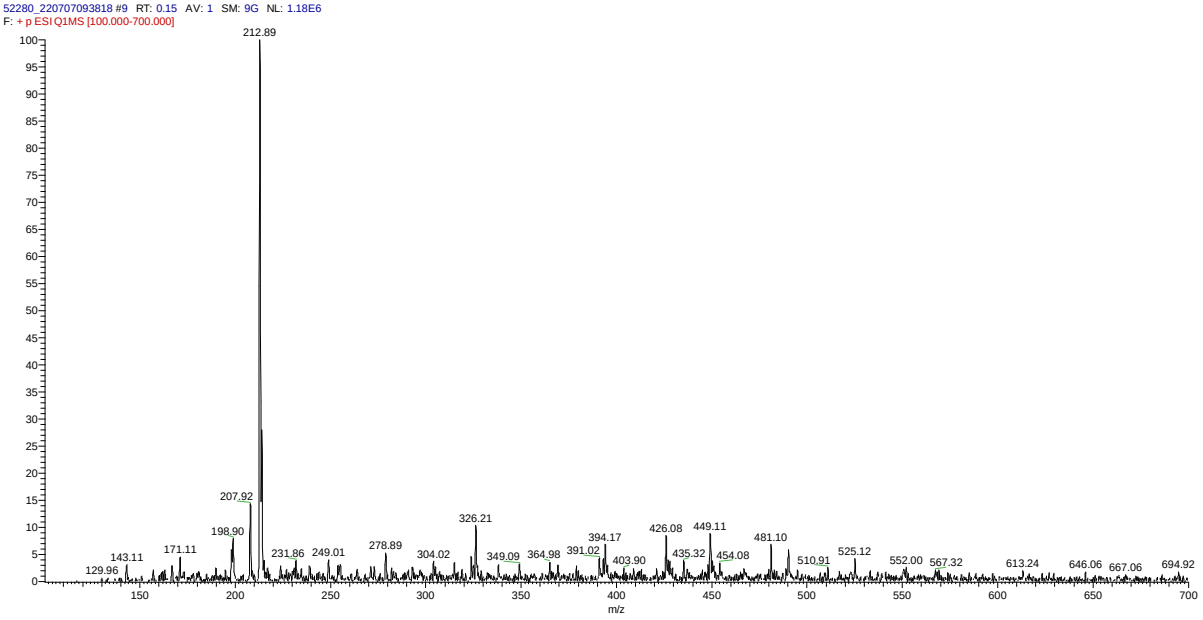
4b



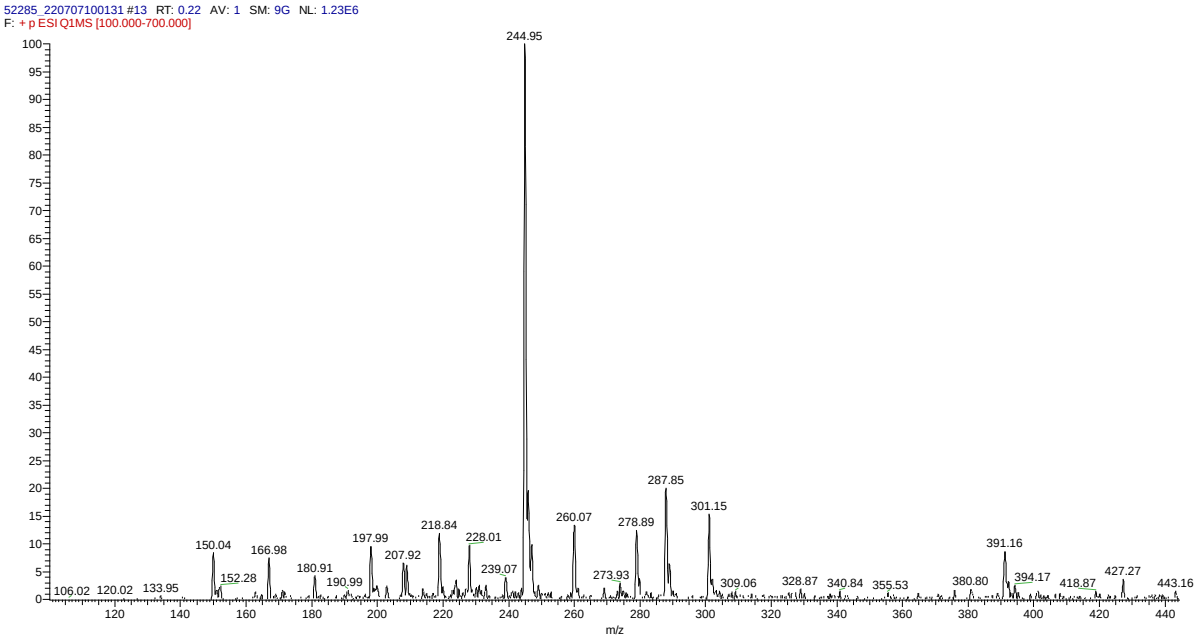
6


52282 #6-12 RT: 0.09-0.20 AV: 7 SM: 9G NL: 8.58E6
F: + p ESI Q1MS [100.000-700.000]
230.95
245.93
207.92
485.08
129.96
142.90
166.91
197.99
279.03
293.94
326.28
355.95
396.97
427.13
454.22
503.14
516.16
555.21
591.05
628.07
654.18
669.16
685.05
m/z

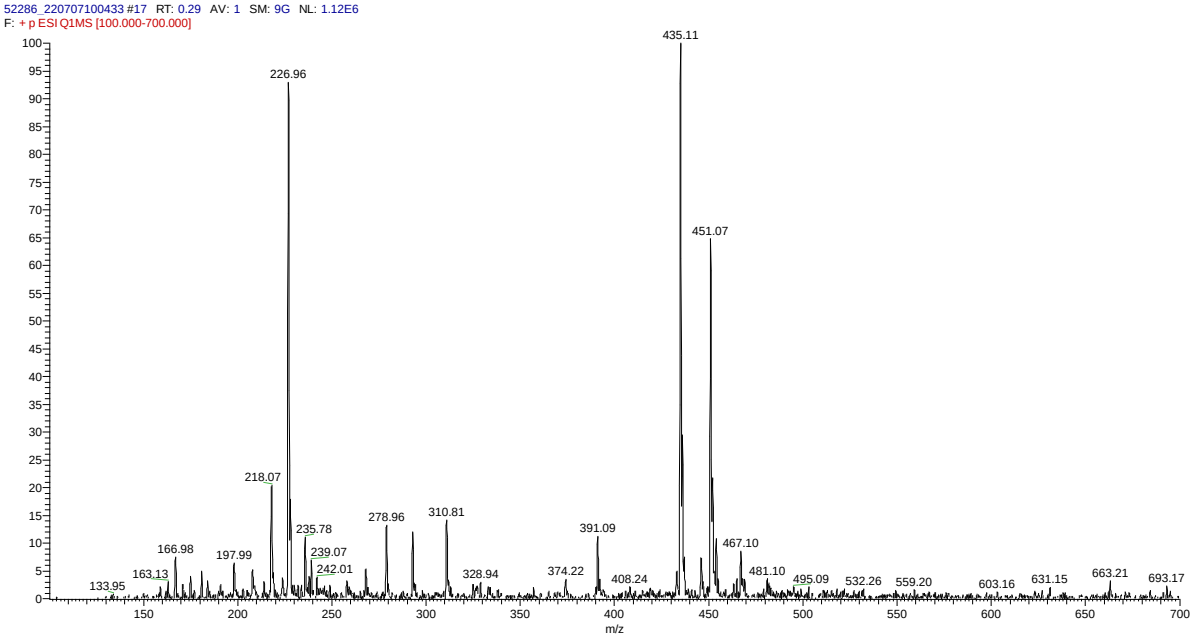
7


52280_220707093818 #9 RT: 0.15 AV: 1 SM: 9G NL: 1.18E6
F: + p ESI Q1MS [100.000-700.000]
212.89
207.92
326.21
198.90
394.17
426.08
449.11
481.10
171.11
143.11
129.96
231.86
249.01
278.89
304.02
349.09
364.98
391.02
403.90
435.32
454.08
510.91
525.12
552.00
567.32
613.24
646.06
667.06
694.92
m/z

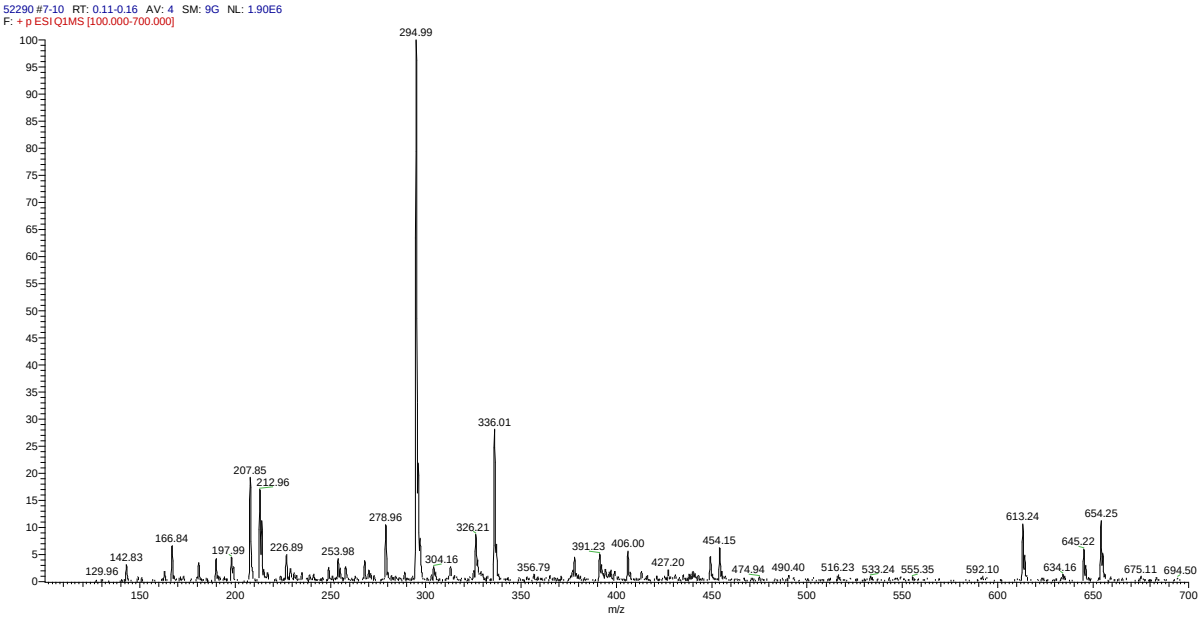
16


52285_220707100131 #13 RT: 0.22 AV: 1 SM: 9G NL: 1.23E6
F: + p ESI Q1MS [100.000-700.000]
244.95
287.85
301.15
260.07
278.89
218.84
228.01
197.99
207.92
150.04
166.98
239.07
180.91
152.28
190.99
273.93
391.16
394.17
427.27
106.02
120.02
133.95
309.06
328.87
340.84
355.53
380.80
418.87
443.16
m/z

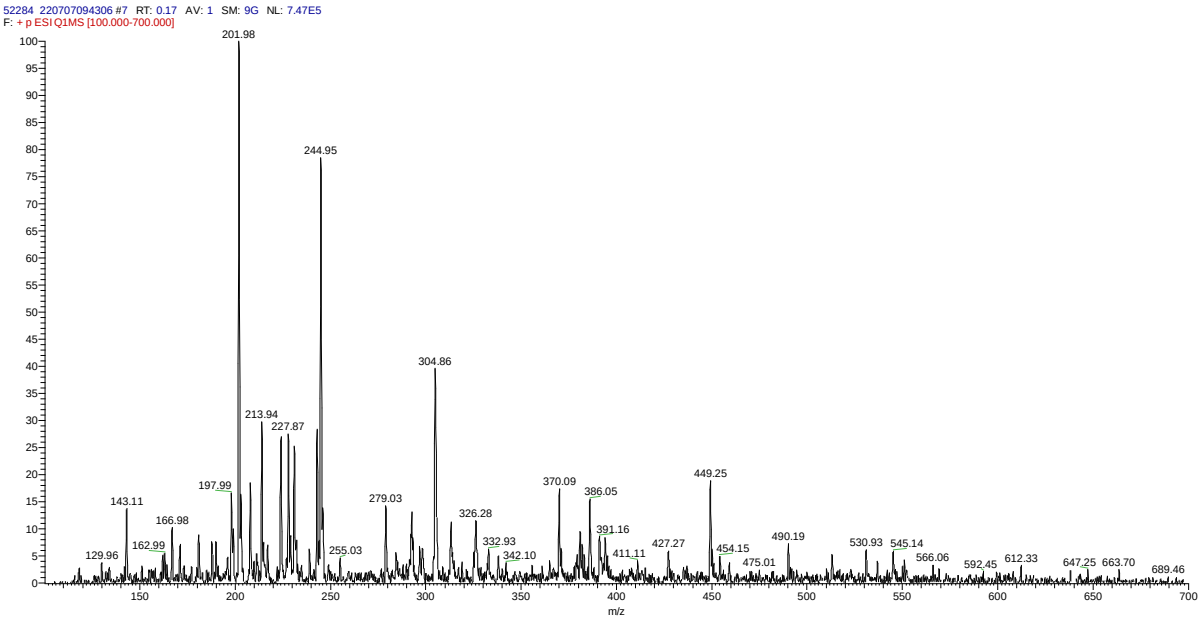
17


52286_220707100433 #17 RT: 0.29 AV: 1 SM: 9G NL: 1.12E6
F: + p ESI Q1MS [100.000-700.000]
435.11
226.96
451.07
218.07
278.96
310.81
235.78
391.09
166.98
239.07
197.99
467.10
242.01
163.13
481.10
133.95
328.94
374.22
408.24
495.09
532.26
559.20
603.16
631.15
663.21
693.17
m/z

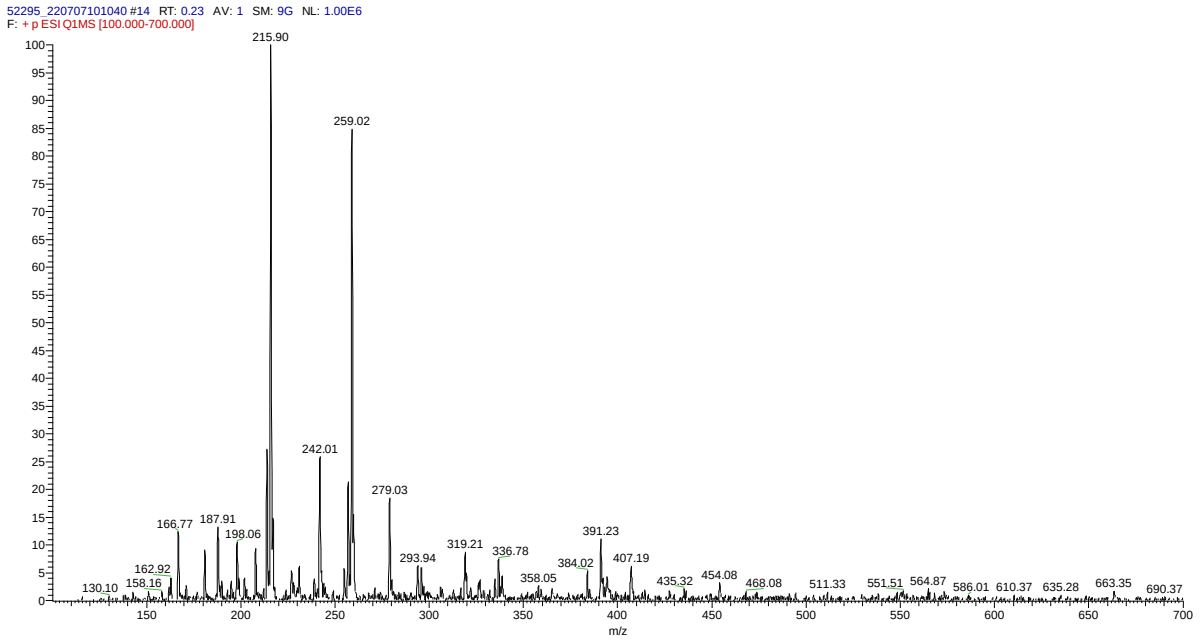
22


52290 #7-10 RT: 0.11-0.16 AV: 4 SM: 9G NL: 1.90E6
F: + p ESI Q1MS [100.000-700.000]
294.99
336.01
207.85
212.96
278.96
326.21
166.84
197.99
226.89
253.98
304.16
142.83
129.96
356.79
391.23
406.00
427.20
454.15
474.94
490.40
516.23
533.24
555.35
592.10
613.24
634.16
645.22
654.25
675.11
694.50
m/z

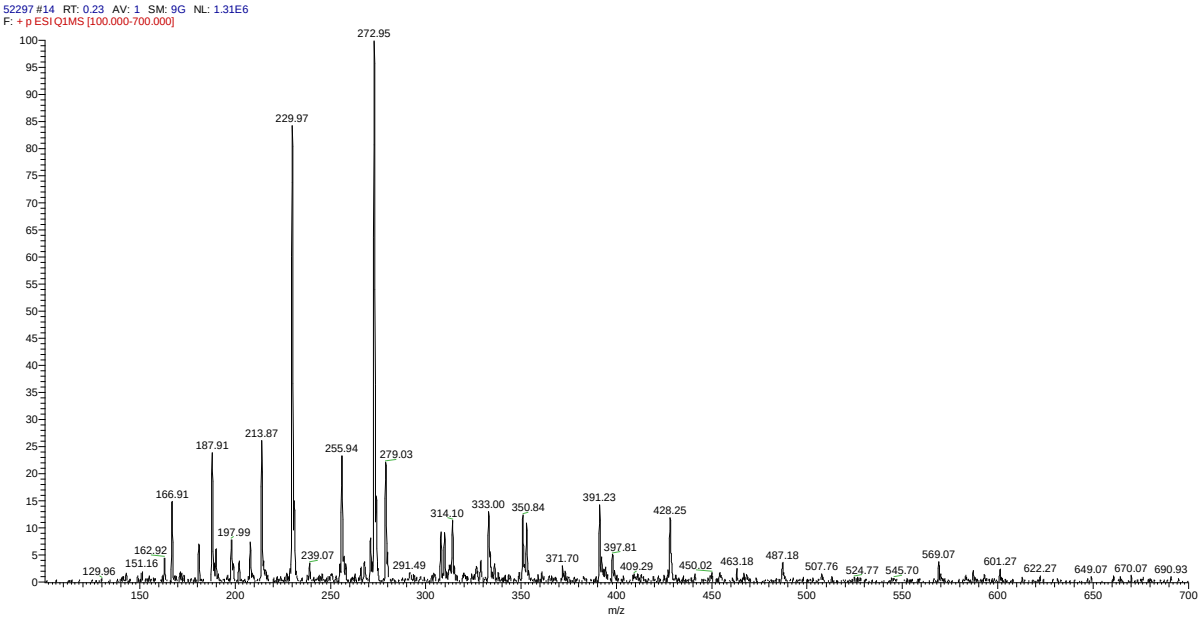
25a


52284 220707094306 #7 RT: 0.17 AV: 1 SM: 9G NL: 7.47E5
F: + p ESI Q1MS [100.000-700.000]
201.98
244.95
304.86
213.94
227.87
197.99
143.11
166.98
162.99
129.96
279.03
326.28
332.93
342.10
255.03
370.09
386.05
391.16
411.11
427.27
449.25
454.15
475.01
490.19
530.93
545.14
566.06
592.45
612.33
647.25
663.70
689.46
m/z

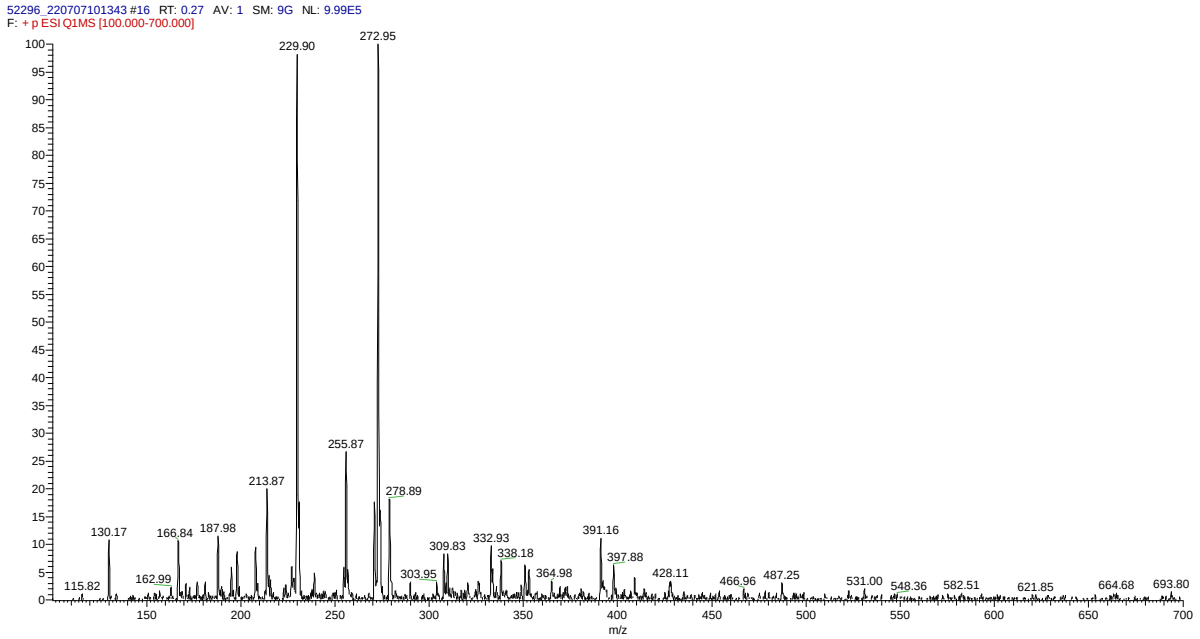
25c


52295_220707101040 #14 RT: 0.23 AV: 1 SM: 9G NL: 1.00E6
F: + p ESI Q1MS [100.000-700.000]
215.90
259.02
242.01
279.03
166.77
187.91
198.06
391.23
319.21
336.78
293.94
384.02
407.19
162.92
158.16
358.05
130.10
435.32
454.08
468.08
511.33
551.51
564.87
586.01
610.37
635.28
663.35
690.37
m/z

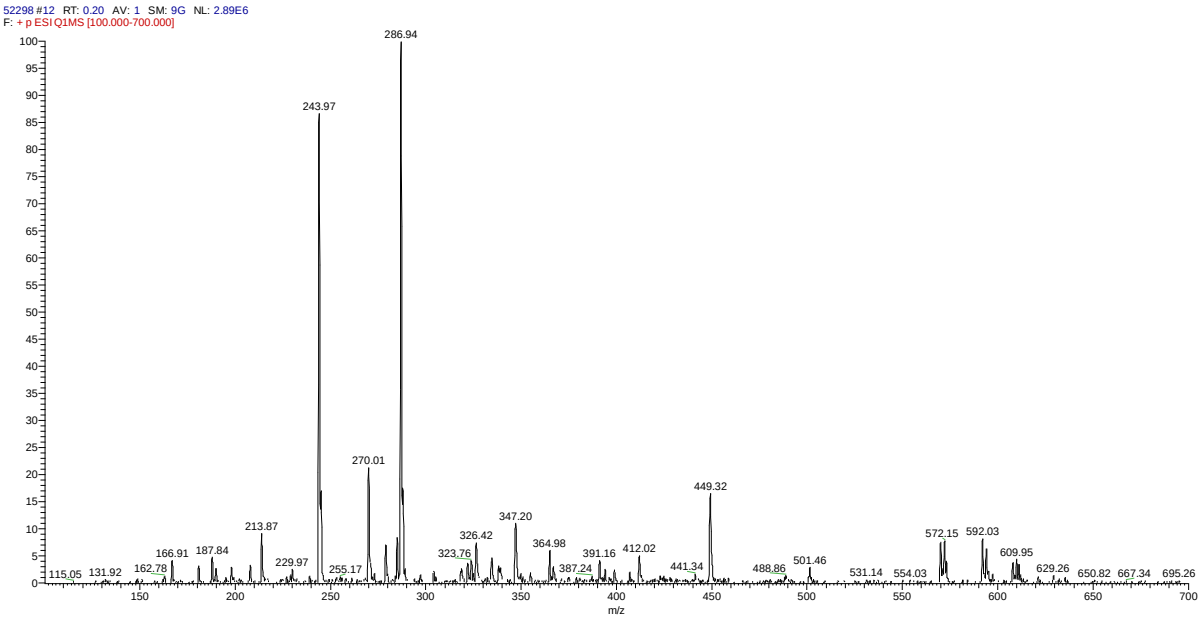
25d


52297 #14 RT: 0.23 AV: 1 SM: 9G NL: 1.31E6
F: + p ESI Q1MS [100.000-700.000]
272.95
229.97
213.87
187.91
255.94
279.03
166.91
314.10
333.00
350.84
391.23
428.25
197.99
162.92
151.16
239.07
371.70
397.81
129.96
291.49
409.29
450.02
463.18
487.18
507.76
524.77
545.70
569.07
601.27
622.27
649.07
670.07
690.93
m/z

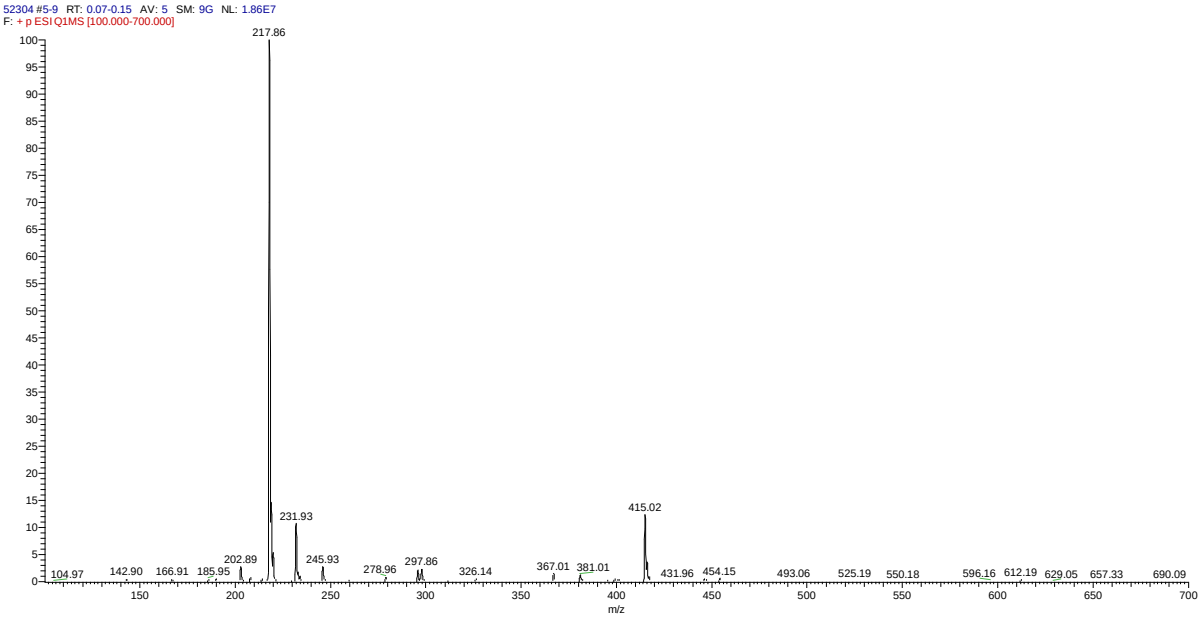
25e


52296_220707101343 #16 RT: 0.27 AV: 1 SM: 9G NL: 9.99E5
F: + p ESI Q1MS [100.000-700.000]
229.90
272.95
255.87
213.87
278.89
130.17
166.84
187.98
309.83
332.93
338.18
391.16
397.88
115.82
162.99
303.95
364.98
428.11
466.96
487.25
531.00
548.36
582.51
621.85
664.68
693.80
m/z

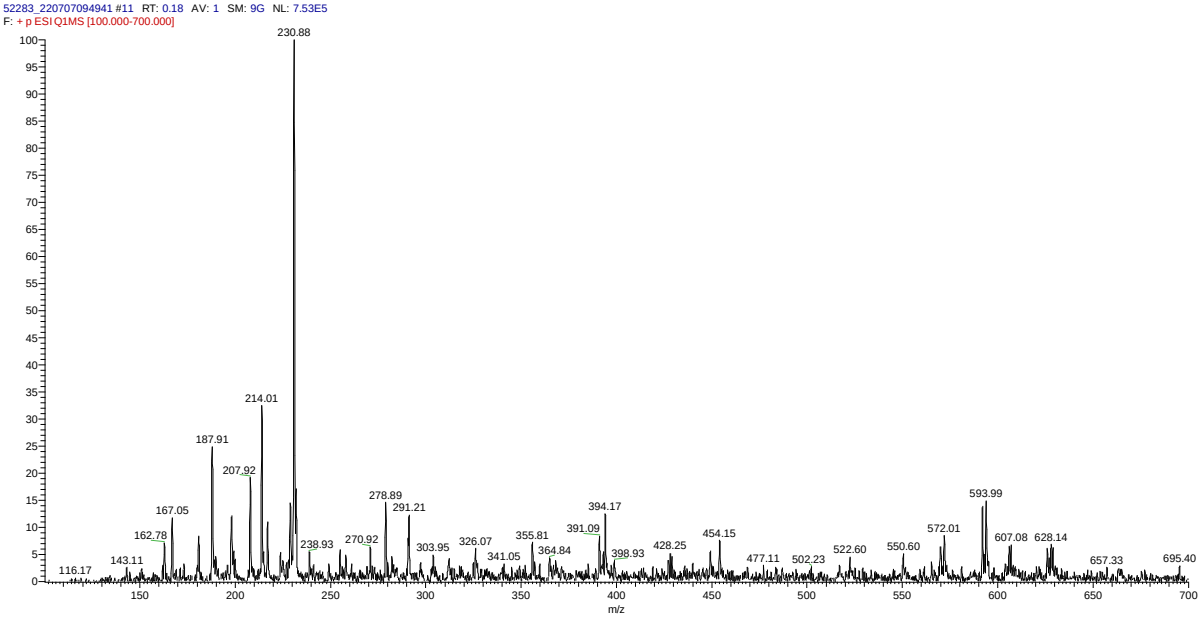
25f


52298 #12 RT: 0.20 AV: 1 SM: 9G NL: 2.89E6
F: + p ESI Q1MS [100.000-700.000]
286.94
243.97
270.01
449.32
213.87
347.20
326.42
364.98
166.91
187.84
323.76
391.16
412.02
572.15
592.03
609.95
115.05
131.92
162.78
229.97
255.17
387.24
441.34
488.86
501.46
531.14
554.03
629.26
650.82
667.34
695.26
m/z

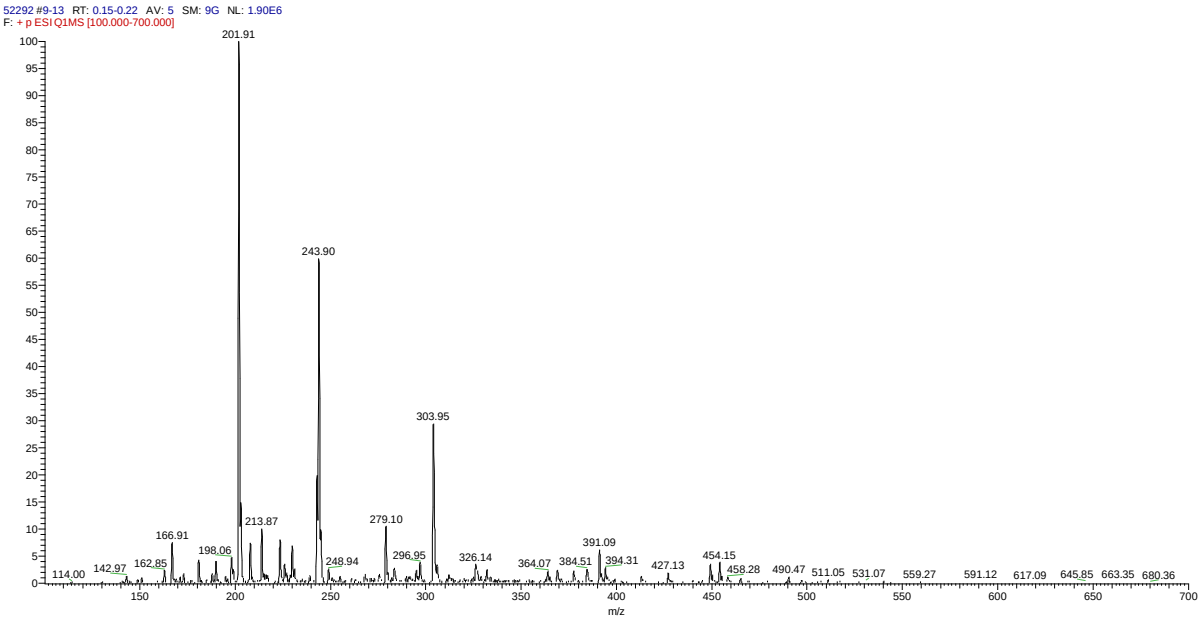
27


52304 #5-9 RT: 0.07-0.15 AV: 5 SM: 9G NL: 1.86E7
F: + p ESI Q1MS [100.000-700.000]
217.86
231.93
415.02
202.89
245.93
278.96
297.86
326.14
367.01
381.01
431.96
454.15
493.06
525.19
550.18
596.16
612.19
629.05
657.33
690.09
104.97
142.90
166.91
185.95
m/z

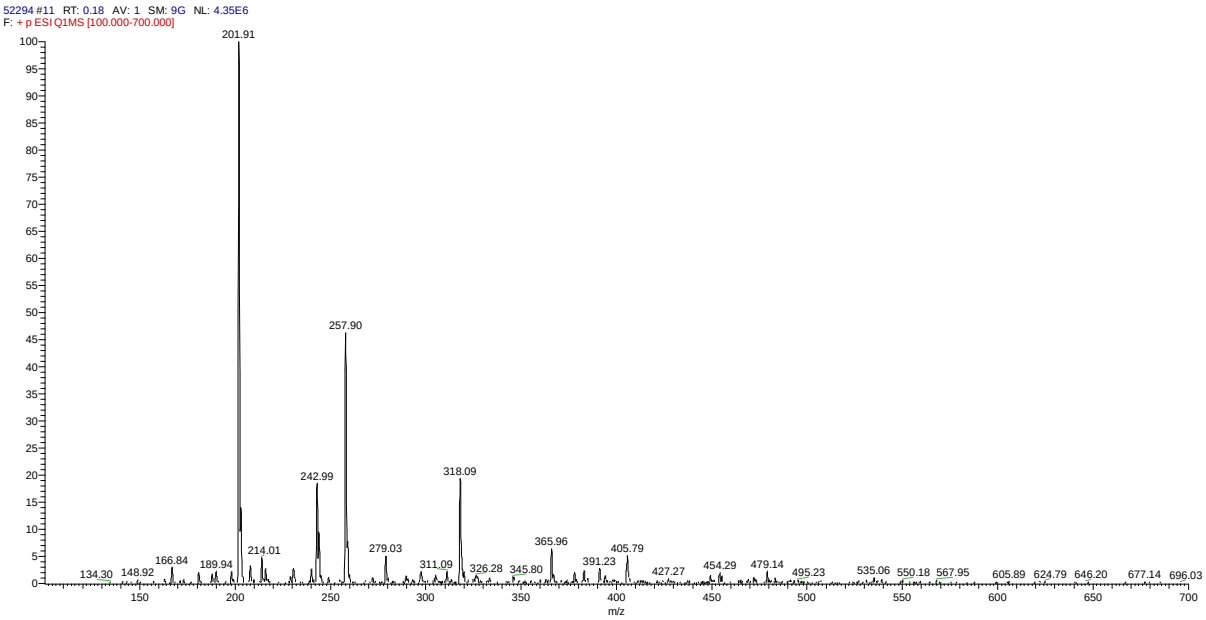
28


52283_220707094941 #11 RT: 0.18 AV: 1 SM: 9G NL: 7.53E5
F: + p ESI Q1MS [100.000-700.000]
230.88
214.01
187.91
207.92
278.89
291.21
167.05
162.78
394.17
391.09
593.99
572.01
607.08
628.14
454.15
428.25
550.60
522.60
502.23
477.11
657.33
695.40
116.17
143.11
238.93
270.92
303.95
326.07
341.05
355.81
364.84
398.93
m/z

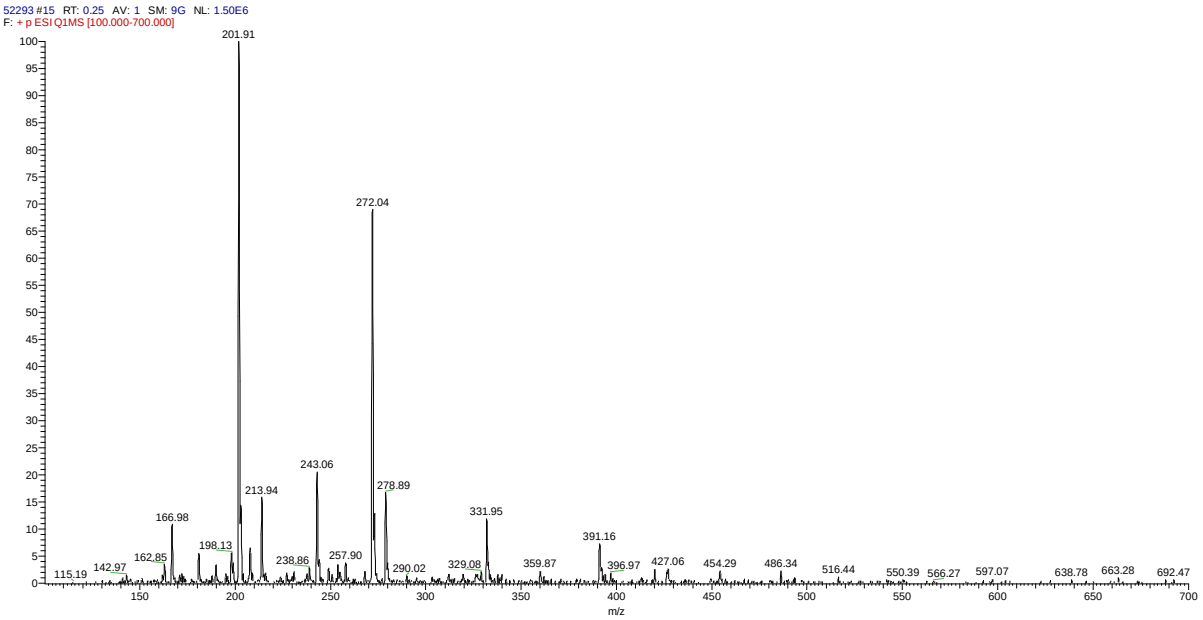
29a


52292 #9-13 RT: 0.15-0.22 AV: 5 SM: 9G NL: 1.90E6
F: + p ESI Q1MS [100.000-700.000]
201.91
243.90
303.95
166.91
213.87
279.10
198.06
391.09
296.95
326.14
248.94
454.15
114.00
142.97
162.85
364.07
384.51
394.31
427.13
458.28
490.47
511.05
531.07
559.27
591.12
617.09
645.85
663.35
680.36
m/z

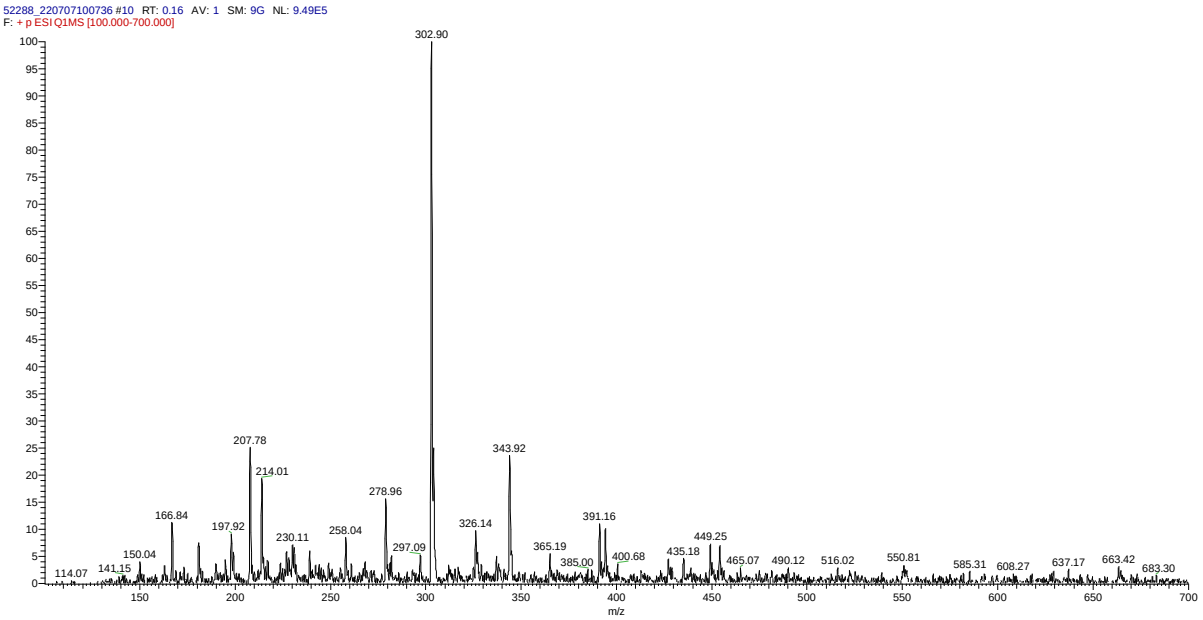
29b


52294 #11 RT: 0.18 AV: 1 SM: 9G NL: 4.35E6
F: + p ESI Q1MS [100.000-700.000]
201.91
257.90
242.99
318.09
214.01
279.03
365.96
166.84
405.79
134.30
148.92
189.94
311.09
326.28
345.80
391.23
427.27
454.29
479.14
495.23
535.06
550.18
567.95
605.89
624.79
646.20
677.14
696.03
m/z

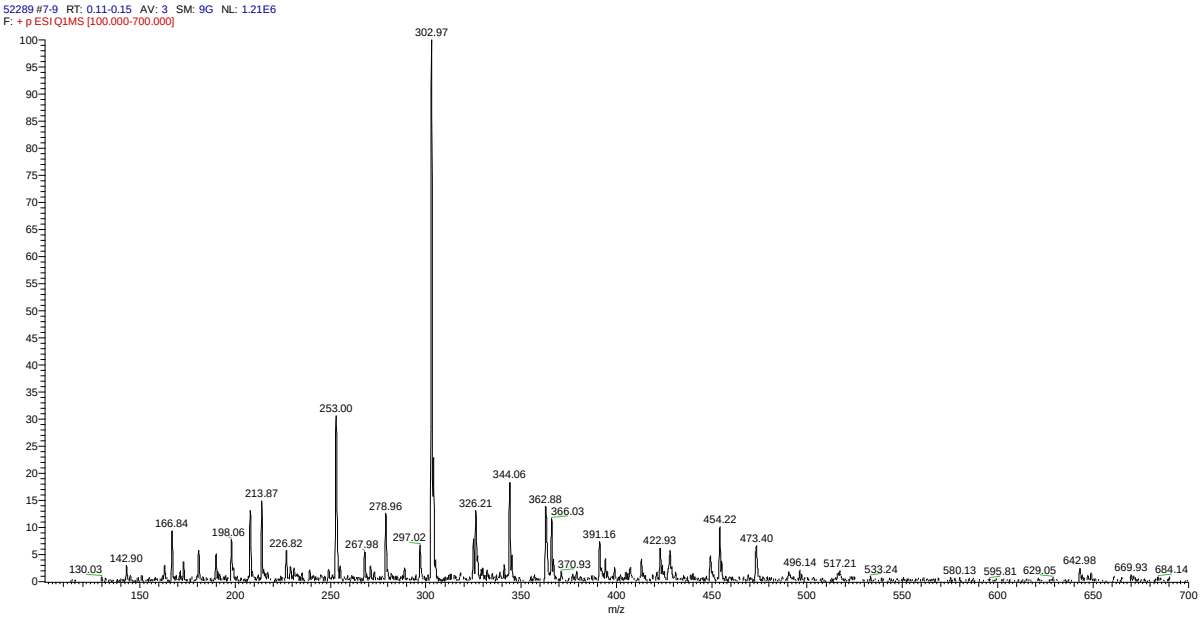
29c


52293 #15 RT: 0.25 AV: 1 SM: 9G NL: 1.50E6
F: + p ESI Q1MS [100.000-700.000]
201.91
272.04
243.06
213.94
278.89
166.98
331.95
391.16
198.13
162.85
257.90
238.86
115.19
142.97
290.02
329.08
359.87
396.97
427.06
454.29
486.34
516.44
550.39
566.27
597.07
638.78
663.28
692.47
m/z

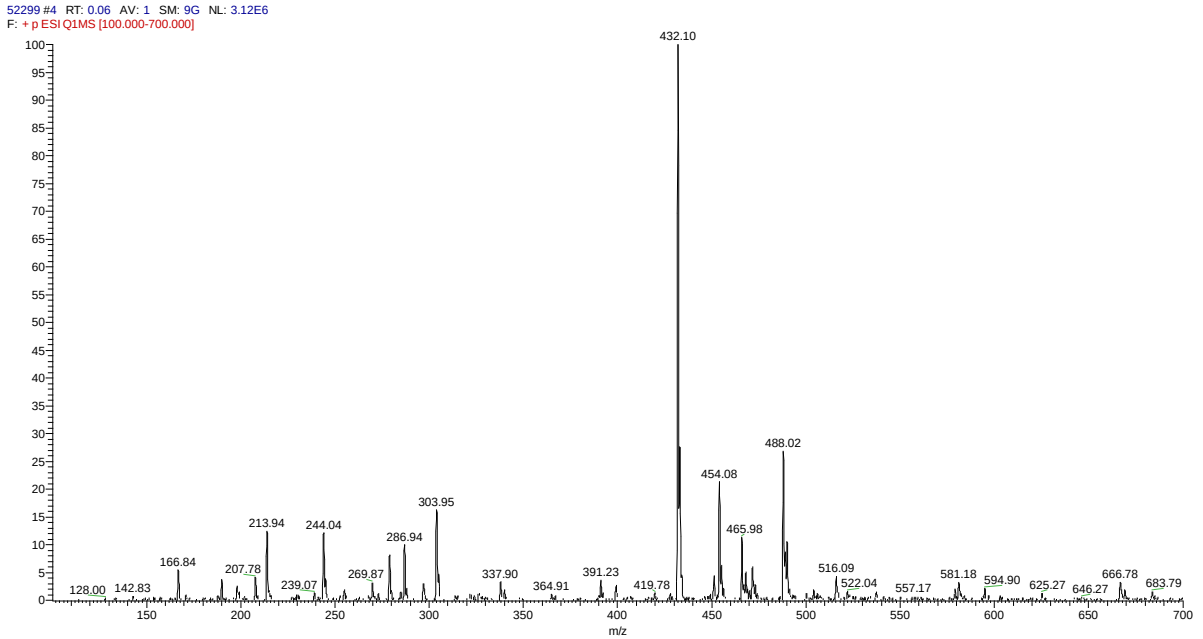
30a


52288_220707100736 #10 RT: 0.16 AV: 1 SM: 9G NL: 9.49E5
F: + p ESI Q1MS [100.000-700.000]
302.90
207.78
343.92
214.01
278.96
166.84
326.14
391.16
197.92
230.11
258.04
365.19
449.25
150.04
297.09
385.00
400.68
435.18
465.07
490.12
516.02
550.81
585.31
608.27
637.17
663.42
683.30
114.07
141.15
m/z

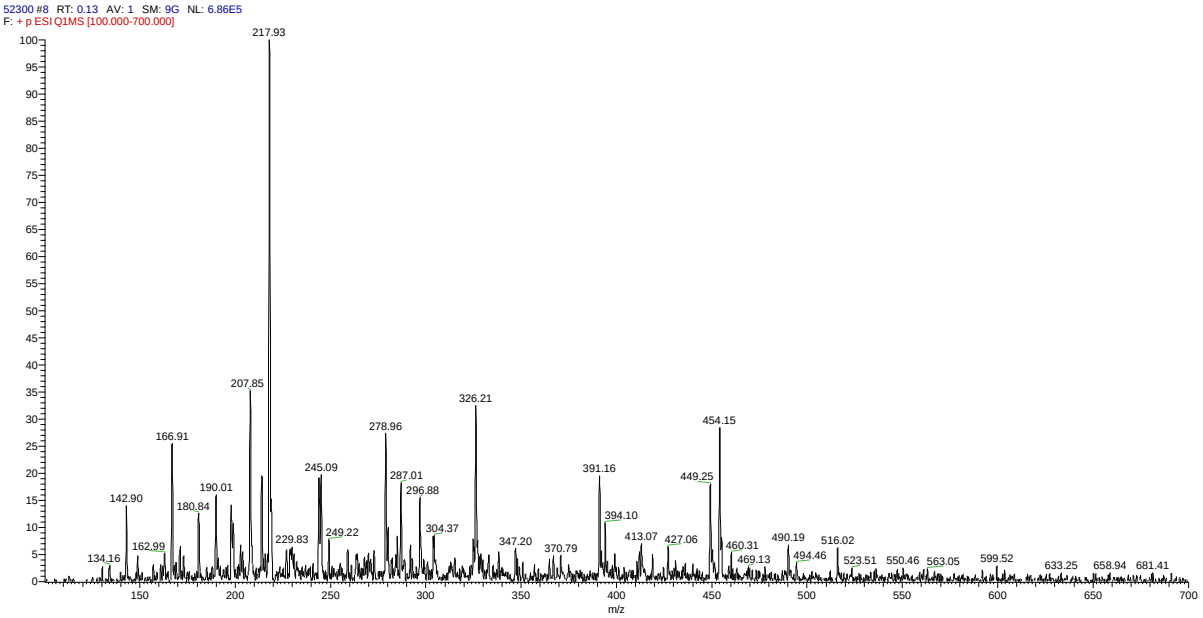
30b


52289 #7-9 RT: 0.11-0.15 AV: 3 SM: 9G NL: 1.21E6
F: + p ESI Q1MS [100.000-700.000]
302.97
253.00
344.06
213.87
278.96
326.21
362.88
366.03
166.84
198.06
226.82
267.98
297.02
391.16
422.93
454.22
473.40
130.03
142.90
370.93
496.14
517.21
533.24
580.13
595.81
629.05
642.98
669.93
684.14
m/z

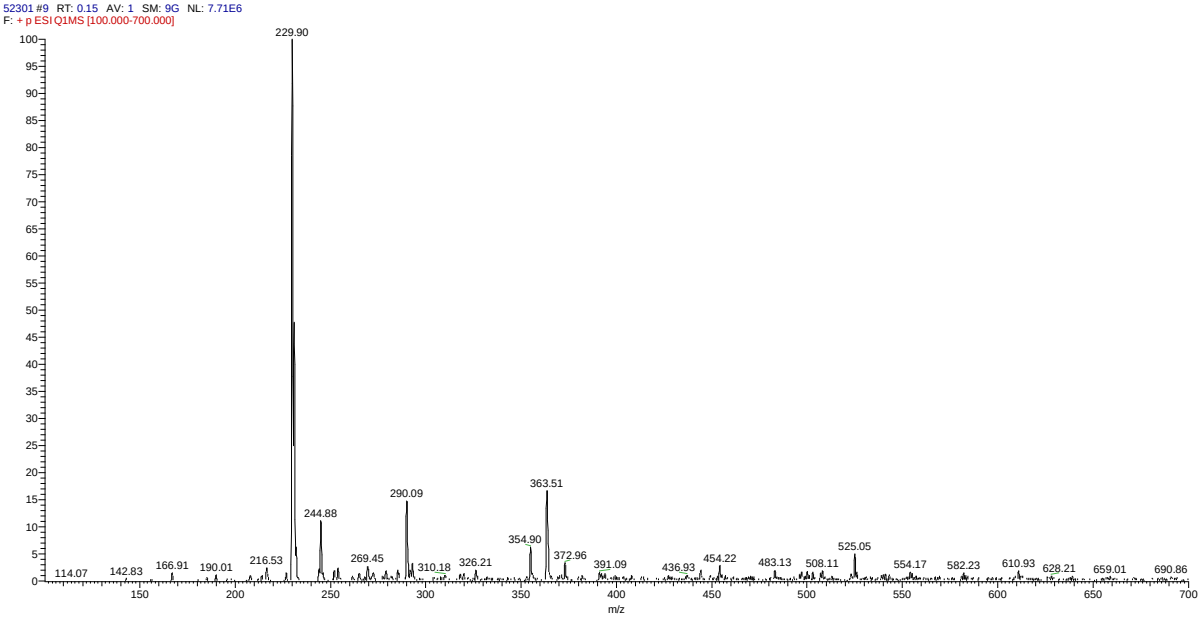
35


52299 #4 RT: 0.06 AV: 1 SM: 9G NL: 3.12E6
F: + p ESI Q1MS [100.000-700.000]
432.10
488.02
454.08
303.95
213.94
244.04
286.94
465.98
166.84
207.78
239.07
269.87
337.90
364.91
391.23
419.78
516.09
522.04
557.17
581.18
594.90
625.27
646.27
666.78
683.79
128.00
142.83
m/z

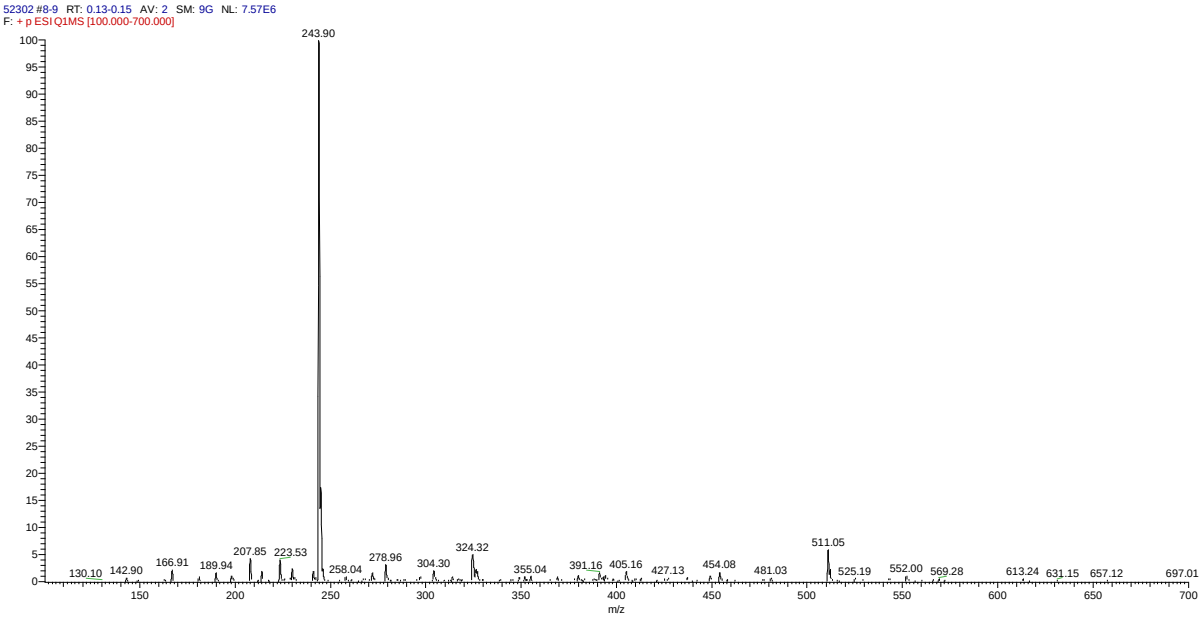
42a


52300 #8 RT: 0.13 AV: 1 SM: 9G NL: 6.86E5
F: + p ESI Q1MS [100.000-700.000]
217.93
207.85
326.21
278.96
454.15
166.91
245.09
391.16
287.01
449.25
190.01
296.88
142.90
180.84
394.10
304.37
229.83
249.22
347.20
370.79
413.07
427.06
460.31
490.19
516.02
134.16
162.99
469.13
494.46
523.51
550.46
563.05
599.52
633.25
658.94
681.41
m/z

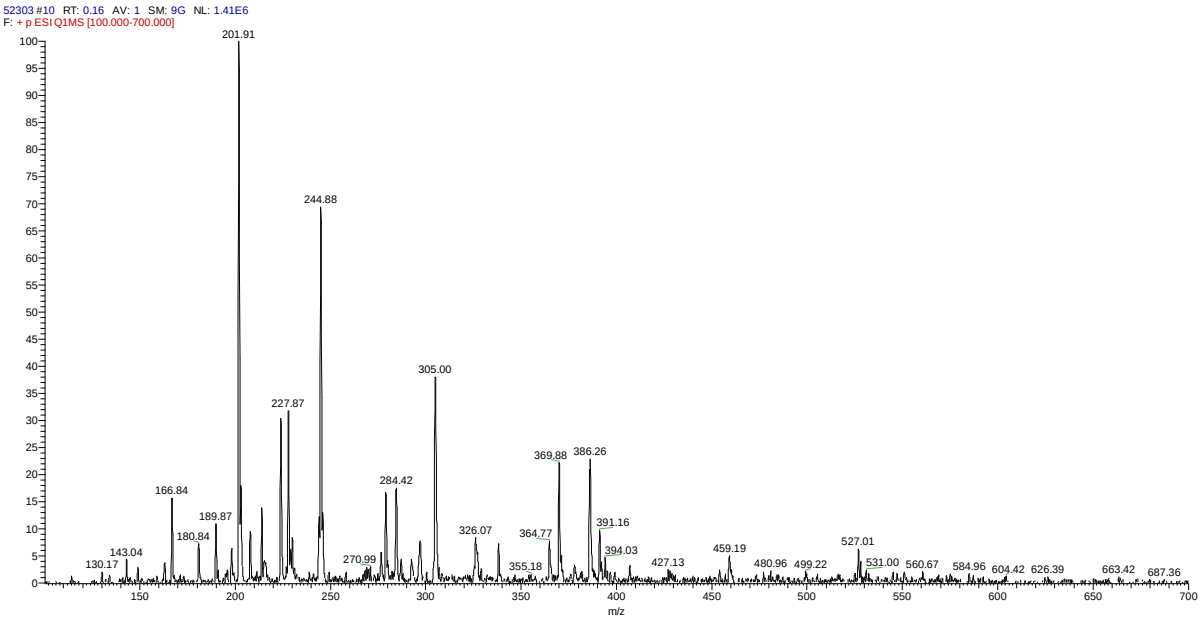
51


52301 #9 RT: 0.15 AV: 1 SM: 9G NL: 7.71E6
F: + p ESI Q1MS [100.000-700.000]
229.90
363.51
290.09
244.88
354.90
525.05
372.96
114.07
142.83
166.91
190.01
216.53
269.45
310.18
326.21
391.09
436.93
454.22
483.13
508.11
554.17
582.23
610.93
628.21
659.01
690.86
m/z

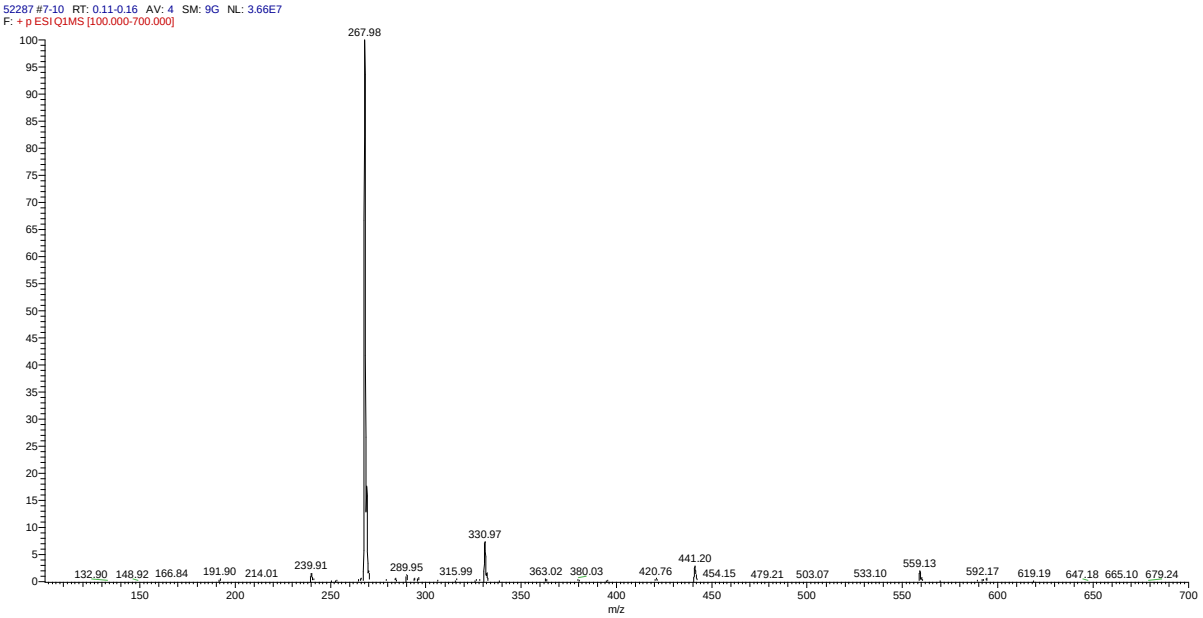
54


52302 #8-9 RT: 0.13-0.15 AV: 2 SM: 9G NL: 7.57E6
F: + p ESI Q1MS [100.000-700.000]
243.90
511.05
207.85
223.53
324.32
166.91
189.94
278.96
304.30
130.10
142.90
258.04
355.04
391.16
405.16
427.13
454.08
481.03
525.19
552.00
569.28
613.24
631.15
657.12
697.01
m/z

55

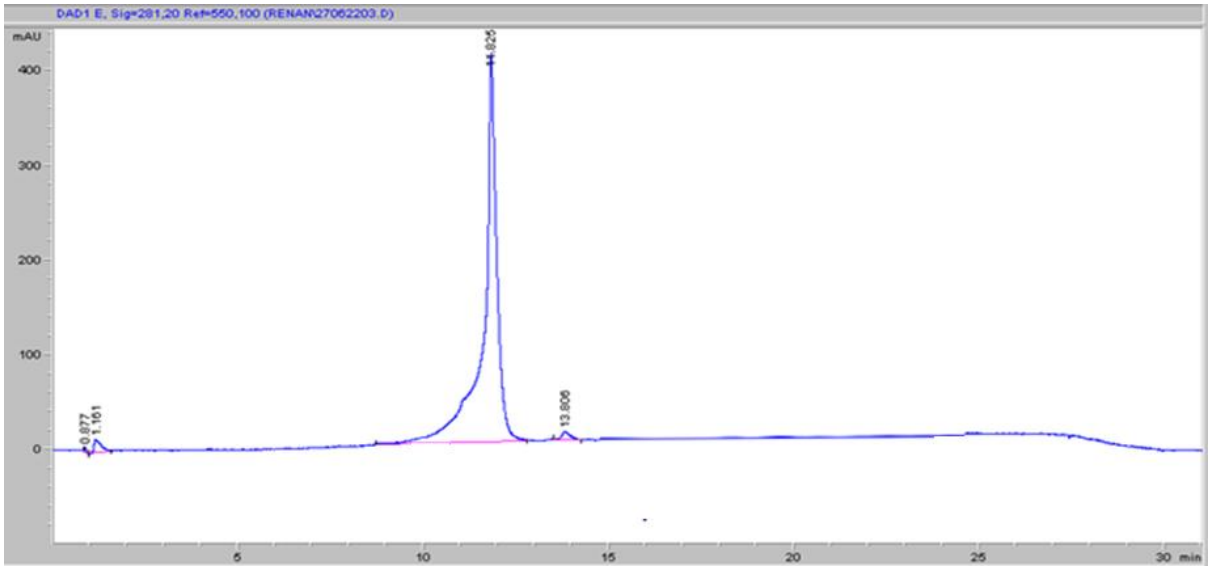

52303 #10 RT: 0.16 AV: 1 SM: 9G NL: 1.41E6
F: + p ESI Q1MS [100.000-700.000]
201.91
244.88
305.00
227.87
369.88
386.26
284.42
166.84
189.87
391.16
326.07
364.77
180.84
394.03
143.04
130.17
270.99
355.18
427.13
459.19
527.01
480.96
499.22
531.00
560.67
584.96
604.42
626.39
663.42
687.36
m/z

57

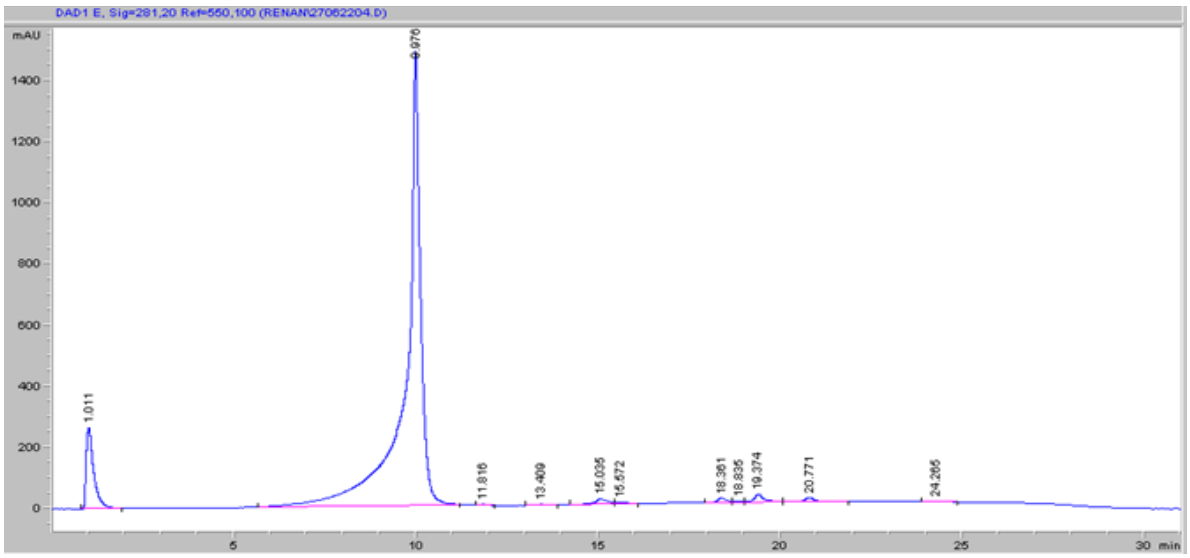

52287 #7-10 RT: 0.11-0.16 AV: 4 SM: 9G NL: 3.66E7
F: + p ESI Q1MS [100.000-700.000]
267.98
330.97
441.20
559.13
239.91
289.95
315.99
132.90
148.92
166.84
191.90
214.01
363.02
380.03
420.76
454.15
479.21
503.07
533.10
592.17
619.19
647.18
665.10
679.24
m/z

HPLC chromatograms

4a

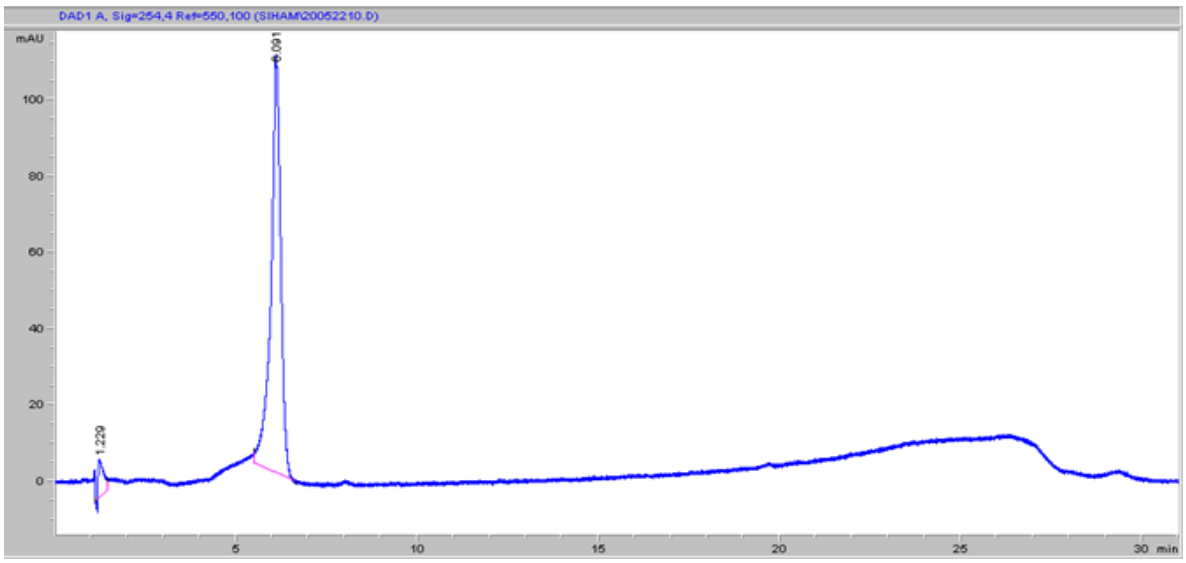


4b

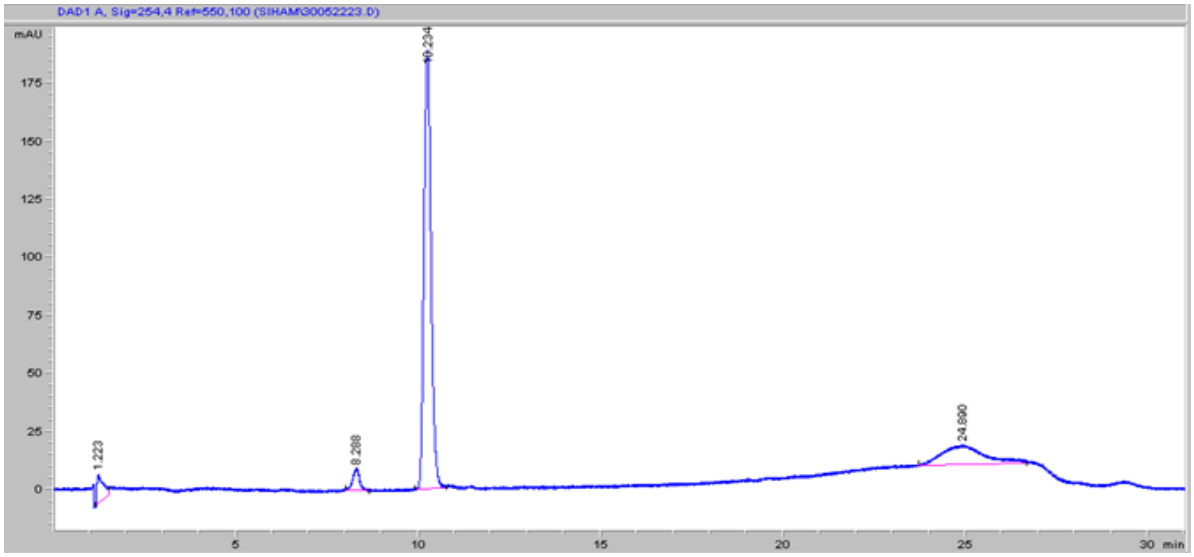


1.011 DMSO peak

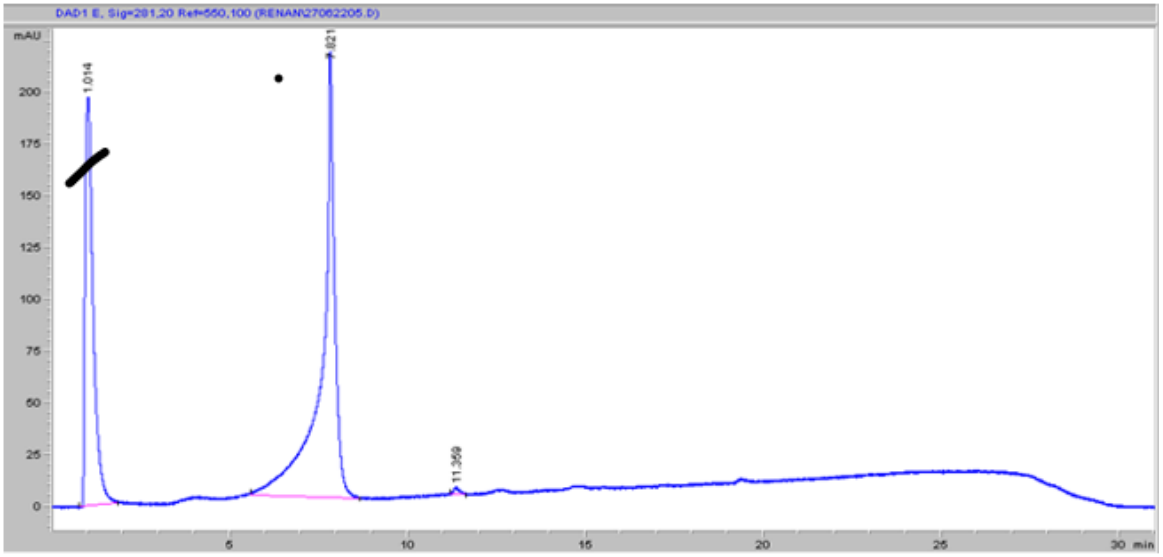
6


DAD1 A, Sig=254,4 Ref=550,100 (SIHAM\20052210.D)
mAU
100
80
60
40
20
0
6.091
1.229
5
10
15
20
25
30 min

7

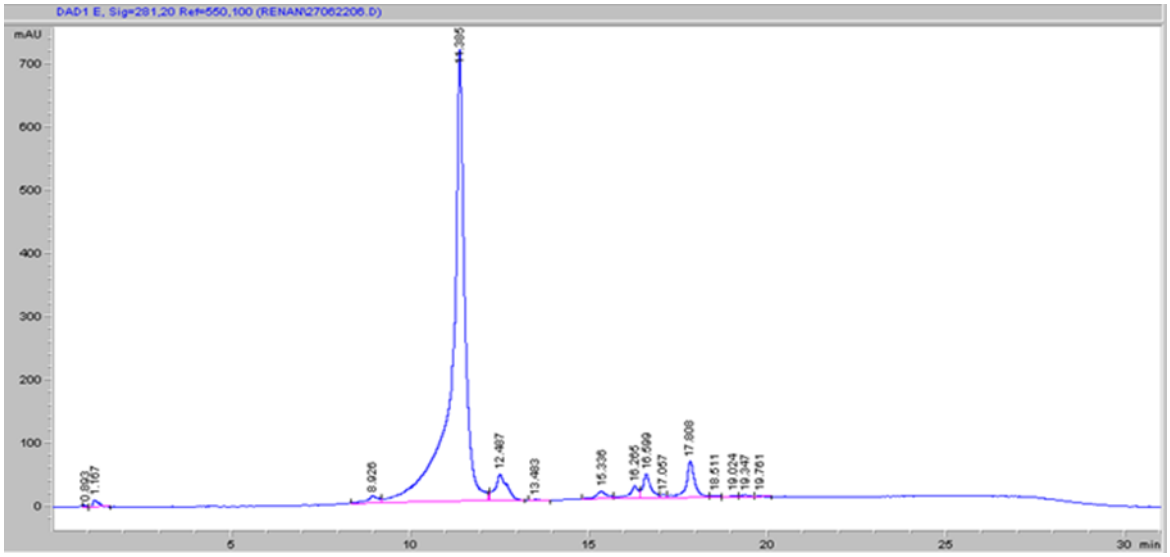

DAD1 A, Sig=254,4 Ref=550,100 (SIHAM\30052223.D)
mAU
175
150
125
100
75
50
25
0
10.234
24.890
1.223
8.288
5
10
15
20
25
30 min

16

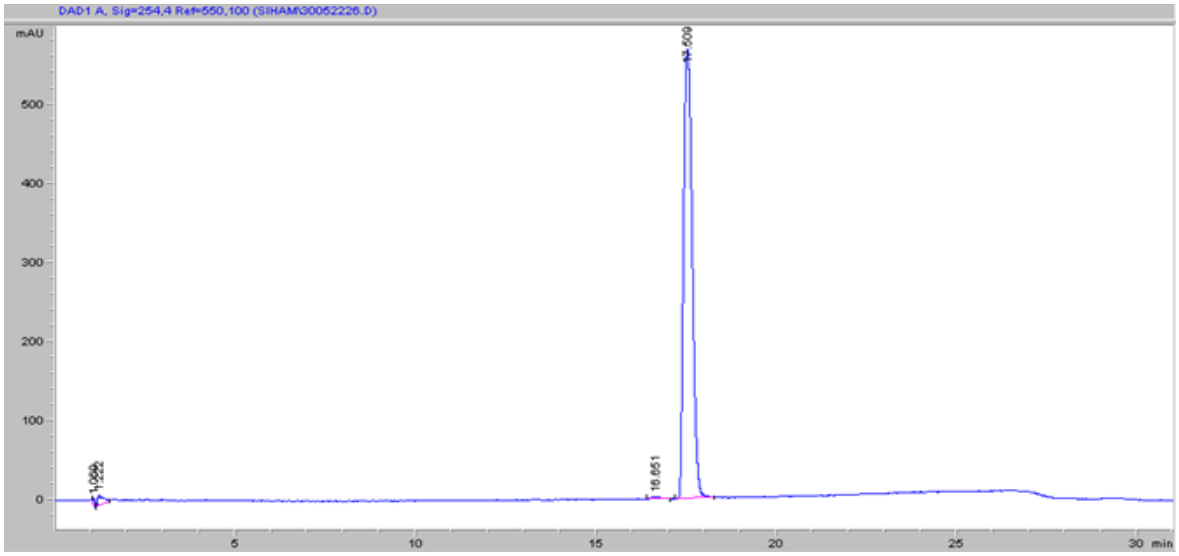


1.014 DMSO peak

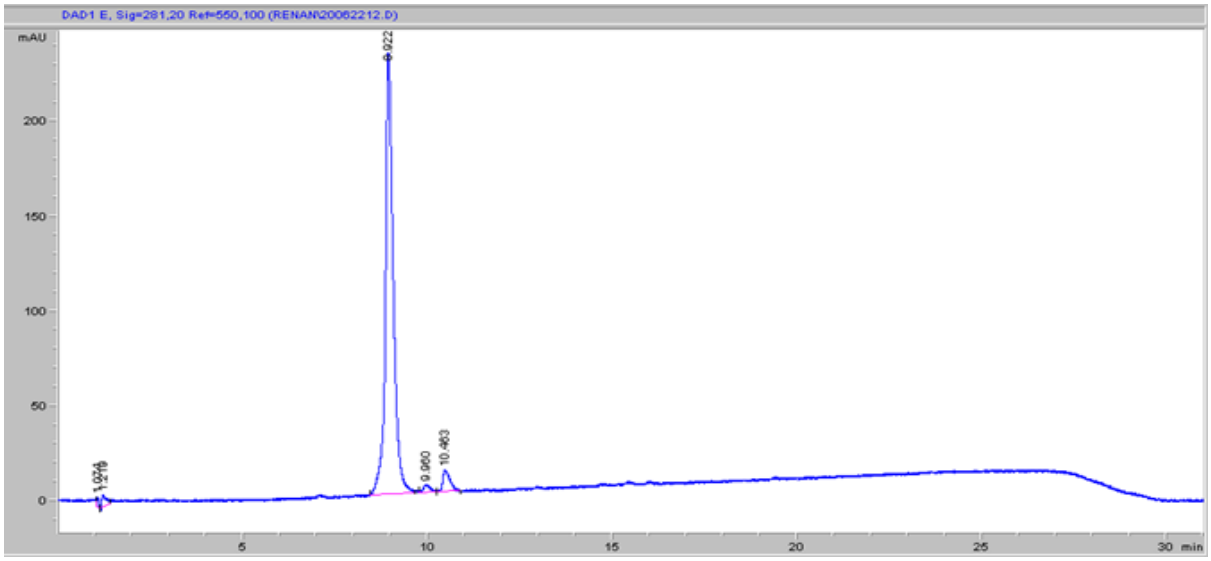
17



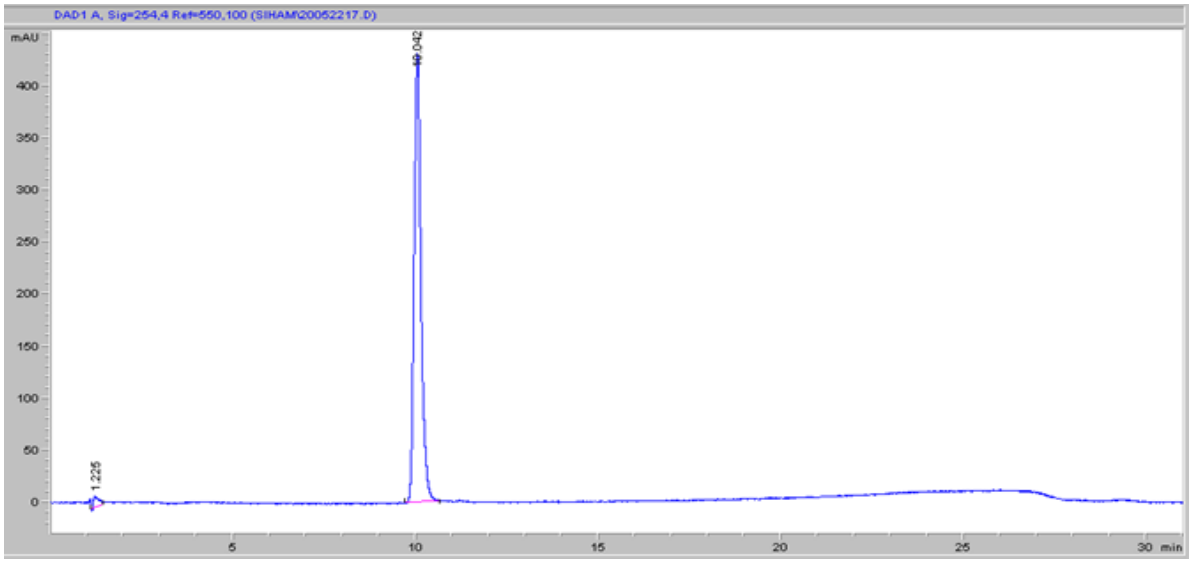
22


DAD1 A, Sig=254,4 Ref=550,100 (SIHAM\30052226.D)
mAU
500
400
300
200
100
0
16.651
5
10
15
20
25
30 min

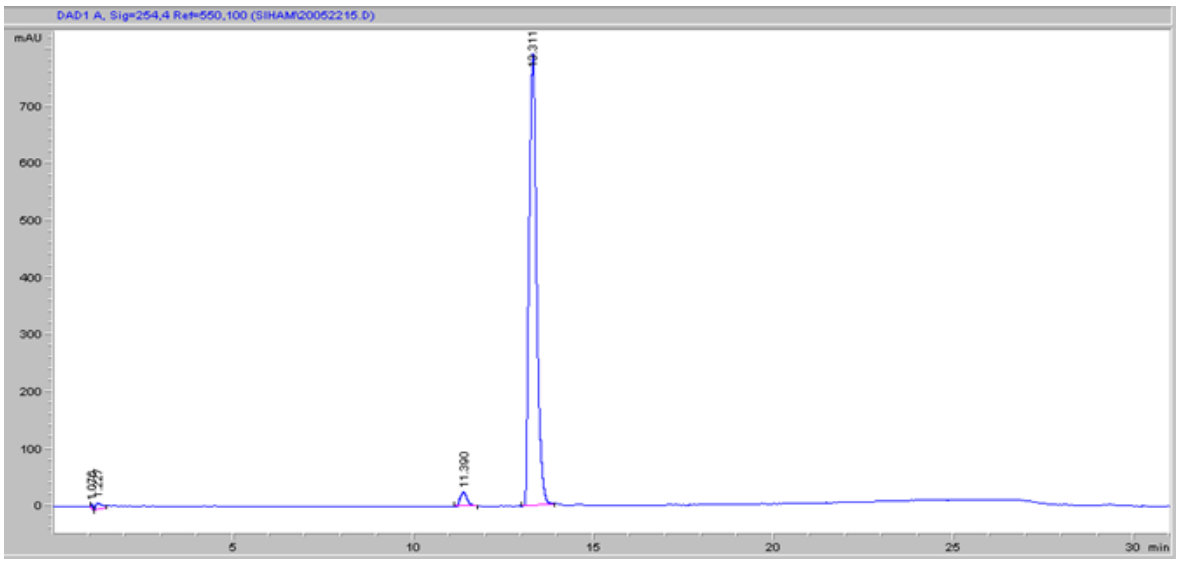
27


DAD1 E, Sig=281,20 Ref=550,100 (RENAN\20062212.D)
mAU
200
150
100
50
0
9.922
9.960
10.493
5
10
15
20
25
30 min

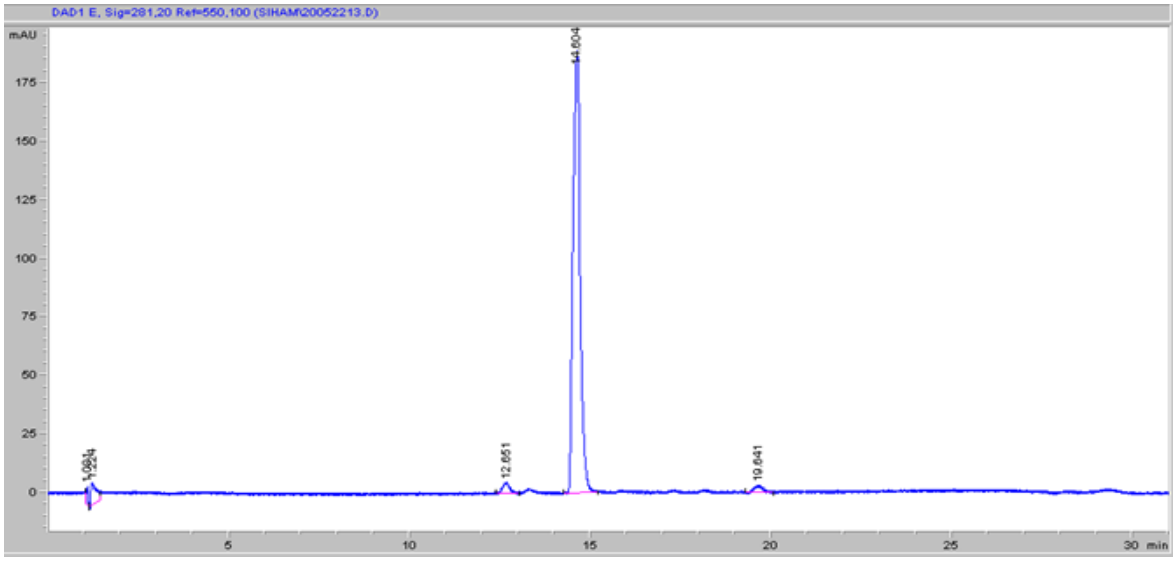
28


DAD1 A, Sig=254,4 Ref=550,100 (SIHAM\20052217.D)
mAU
400
350
300
250
200
150
100
50
0
1.225
10.042
5
10
15
20
25
30 min

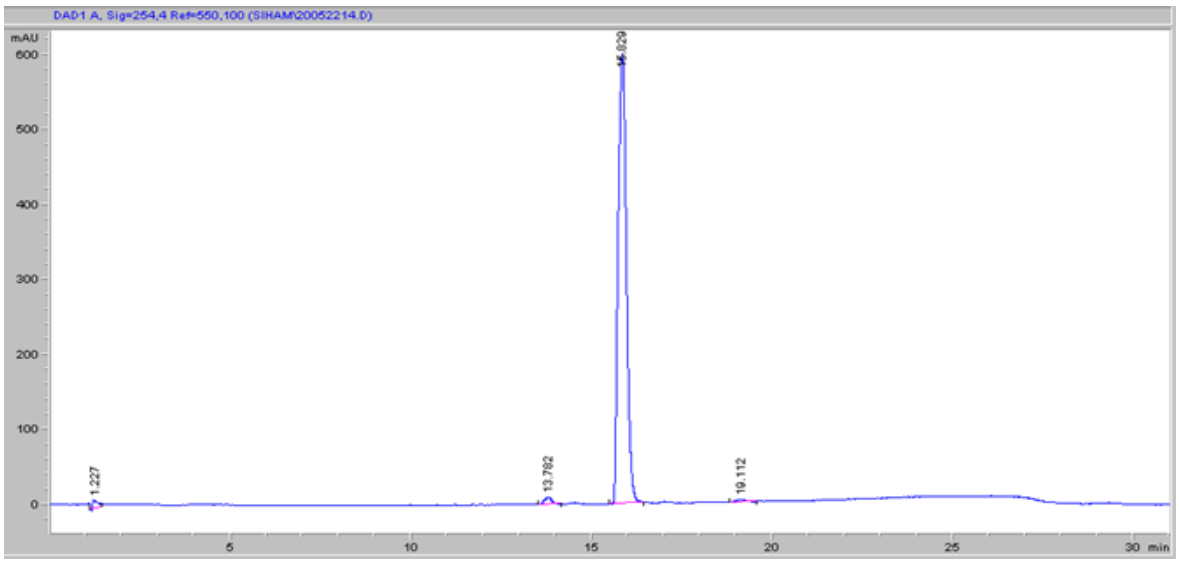
29a


DAD1 A, Sig=254,4 Ref=550,100 (SIHAM\20052215.D)
mAU
700
600
500
400
300
200
100
0
1.026
1.225
11.300
13.311
5
10
15
20
25
30 min

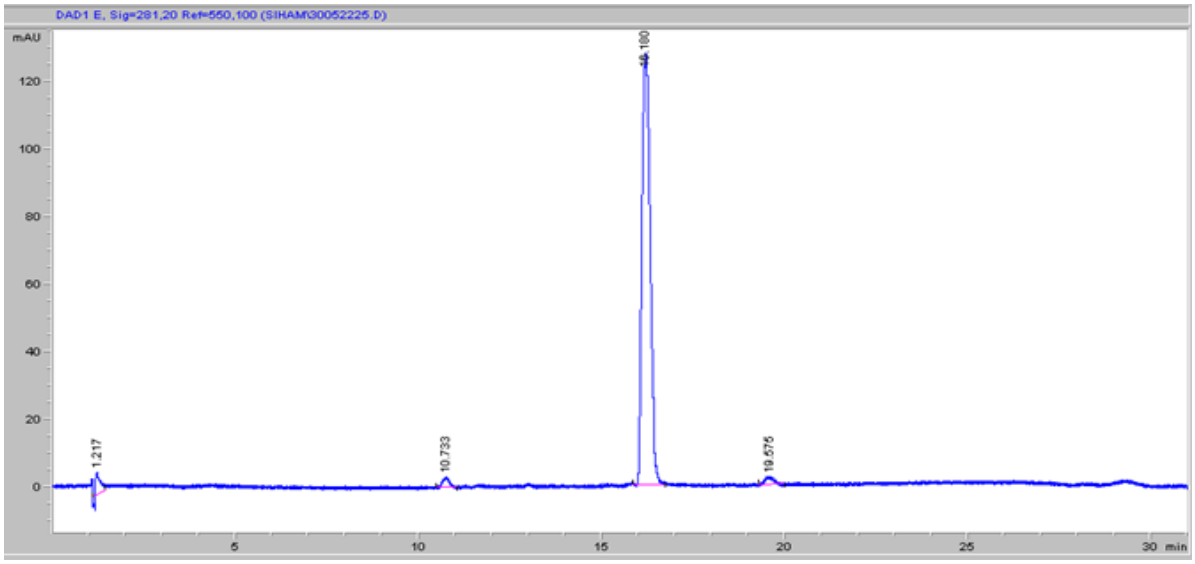
29b


DAD1 E, Sig=281,20 Ref=550,100 (SIHAM\20052213.D)
mAU
175
150
125
100
75
50
25
0
1.224
12.651
14.604
19.641
5
10
15
20
25
30 min

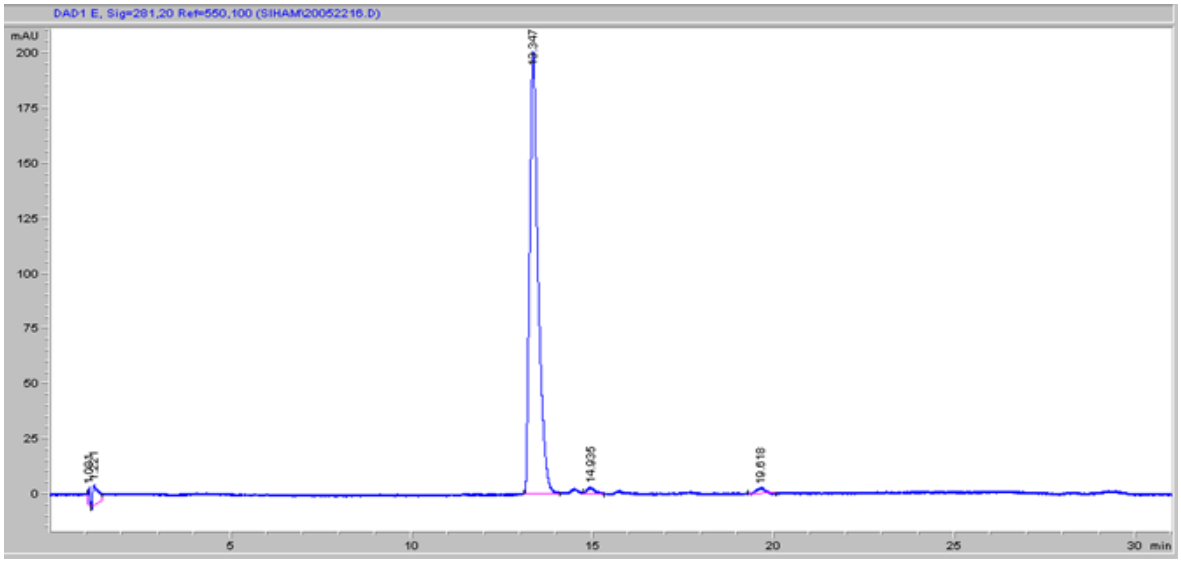
29c


DAD1 A, Sig=254,4 Ref=550,100 (SIHAM\20052214.D)
mAU
600
500
400
300
200
100
0
1.227
13.782
14.829
19.112
5
10
15
20
25
30 min

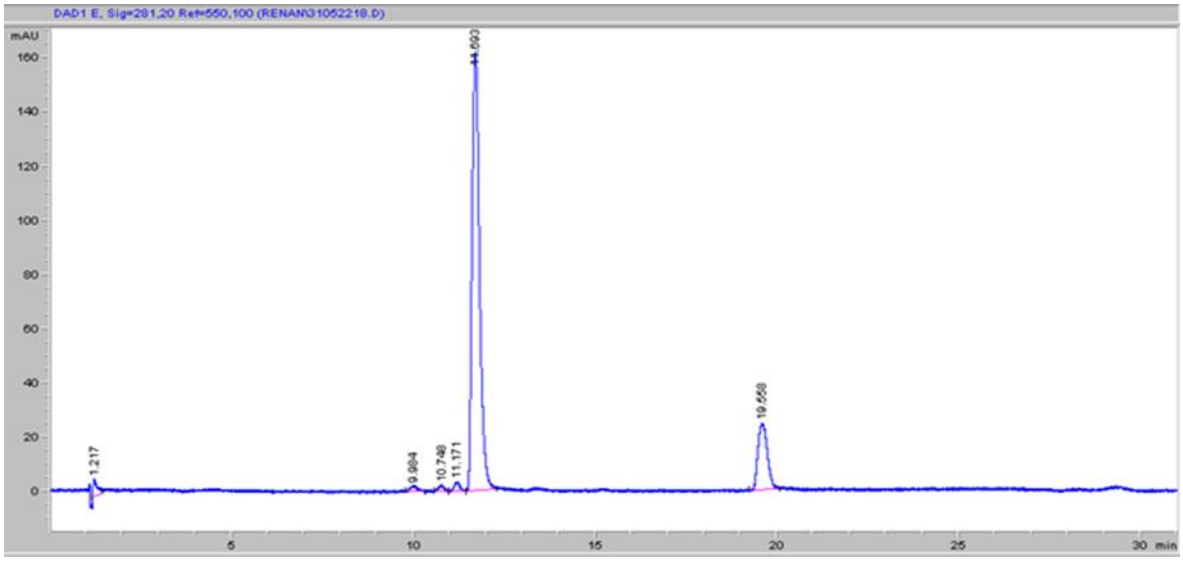
30b


DAD1 E, Sig=281,20 Ref=550,100 (SIHAM\30052225.D)
mAU
120
100
80
60
40
20
0
1.217
10.733
16.180
19.575
5
10
15
20
25
30 min

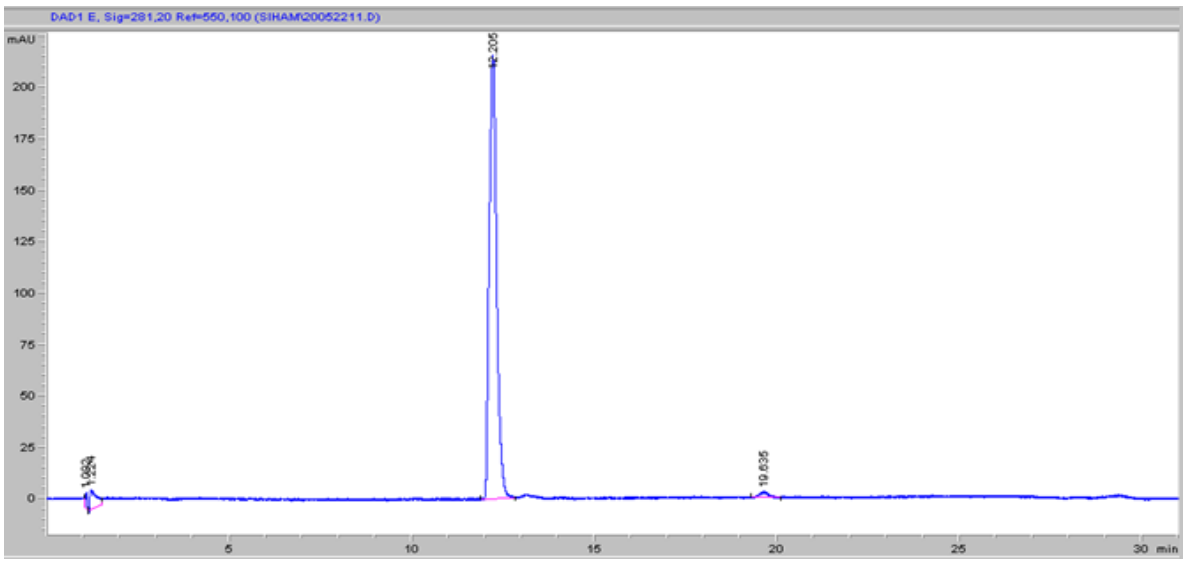
35


DAD1 E, Sig=281,20 Ref=550,100 (SIHAM\20052216.D)
mAU
200
175
150
125
100
75
50
25
0
1.221
12.347
14.935
19.618
5
10
15
20
25
30 min

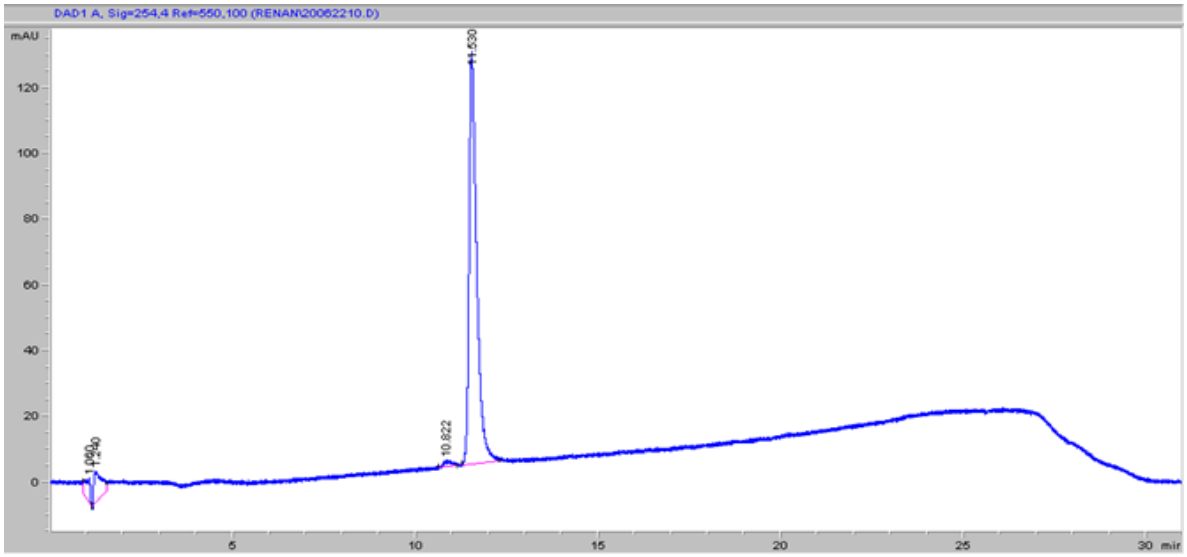
42a


DAD1 E, Sig=281,20 Ref=550,100 (RENAN\31052218.D)
mAU
160
140
120
100
80
60
40
20
0
1.217
9.904
10.748
11.171
14.693
19.558
5
10
15
20
25
30 min

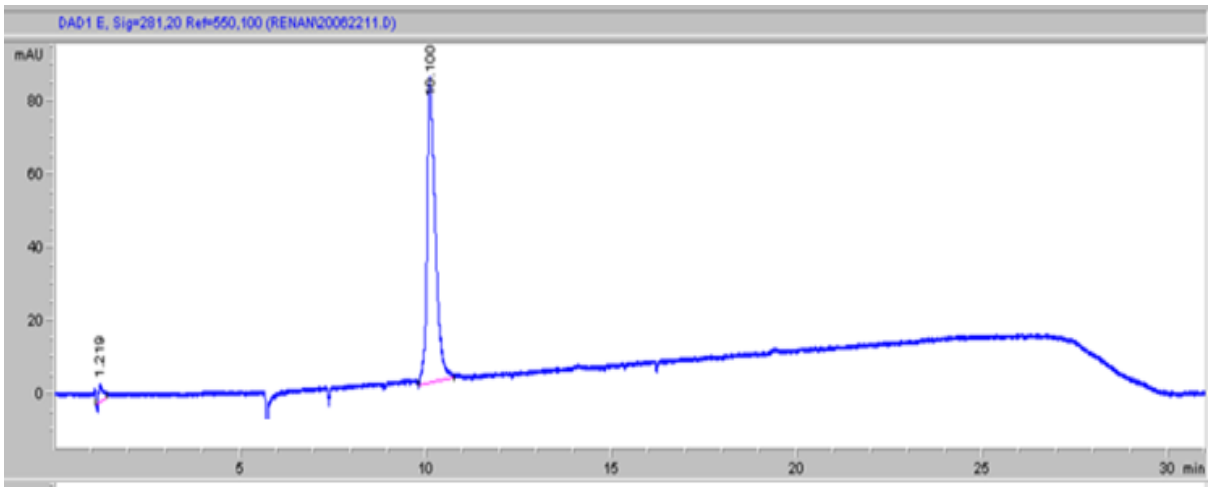
51


DAD1 E, Sig=281,20 Ref=550,100 (SIHAM\20052211.D)
mAU
200
175
150
125
100
75
50
25
0
1.224
12.205
19.635
5
10
15
20
25
30 min

54


DAD1 A, Sig=254,4 Ref=550,100 (RENAN\20062210.D)
mAU
120
100
80
60
40
20
0
11.530
10.822
1.050
1.240
5
10
15
20
25
30 min

55


DAD1 E, Sig=281,20 Ref=550,100 (RENAN\20062211.D)
mAU
80
60
40
20
0
10.100
1.219
5
10
15
20
25
30 min

57

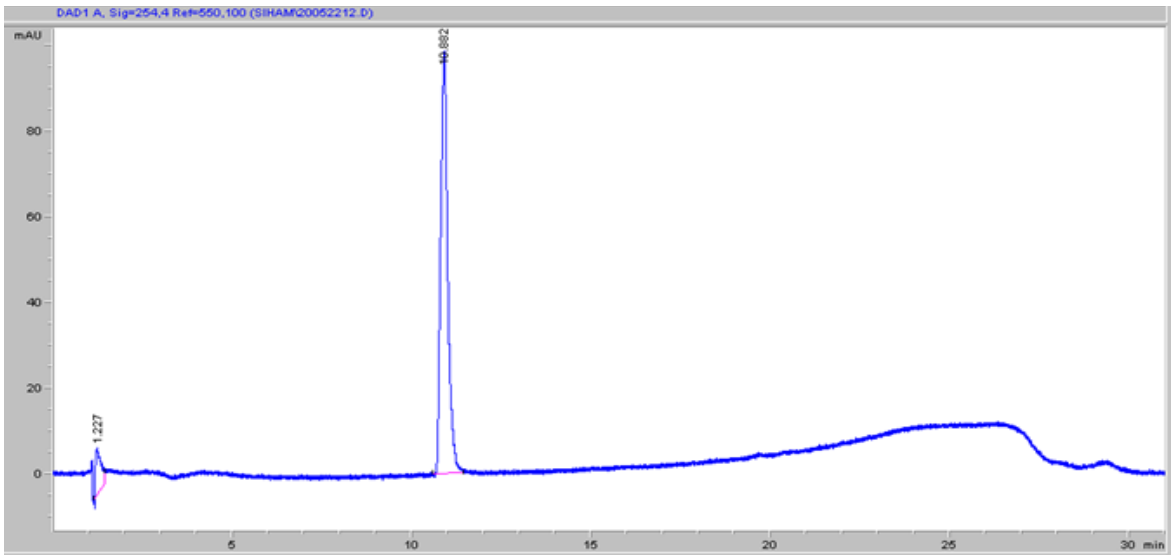

DAD1 A, Sig=254,4 Ref=550,100 (SIHAM\20052212.D)
mAU
80
60
40
20
0
1.227
5
10
15
20
25
30 min

Table S1. 50 best compounds generated with scaffold hopping replacement.

Rank	Structure	Score	Field Score	Shape Score
1	CN1N=C(C)C(SCC(N2CCCCC2)=O)CC1=O	0.881	0.837	0.925
2	FC(F)(F)c1cccc(SCC(=O)N2CCCCC2)c1	0.869	0.807	0.93
3	Clc1cccc(SCC(=O)N2CCCCC2)c1	0.861	0.792	0.931
4	Clc1ccc(S(=O)(=O)CC(=O)N2CCCCC2)cc1C(F)(F)F	0.853	0.813	0.893
5	Fc1ccc(N)c(SCC(=O)N2CCCCC2)c1	0.85	0.81	0.889
6	Fc1cccc(SCC(=O)N2CCCCC2)c1	0.849	0.787	0.912
7	Fc1cc(N)cc(SCC(=O)N2CCCCC2)c1	0.848	0.775	0.922
8	FC(F)(F)c1ccnc(SCC(=O)N2CCCCC2)n1	0.847	0.82	0.875
9	FC(F)(F)c1ccnc(S(=O)(=O)CC(=O)N2CCCCC2)c1	0.846	0.782	0.909
11	O=C(N1CCCCC1)CC/C=C/CCCC	0.844	0.811	0.877
10	Brc1ccc(N)c(S(=O)(=O)CC(=O)N2CCCCC2)c1	0.844	0.806	0.882
12	O=S(=O)(CC(=O)N1CCCCC1)c2cccc3c2ncs3	0.836	0.773	0.899
13	FC(F)(F)c1ccc(c(S(=O)(=O)CC(=O)N2CCCCC2)c1)C	0.832	0.785	0.879
14	Clc1ccc(N)c(S(=O)(=O)CC(=O)N2CCCCC2)c1	0.83	0.779	0.88
15	O=S(=O)(CC(=O)N1CCCCC1)c2cccc(N(C)C)c2	0.829	0.766	0.892
17	O=S(=O)(c1cc(C(C)(C)C)ccc1C)CC(=O)N2CCCCC2	0.826	0.783	0.869
18	Fc1ccc(SCC(=O)N2CCCCC2)cc1F	0.826	0.761	0.89
16	O=C(N1CCCCC1)COc2cccc(N(C)C)c2	0.826	0.758	0.894
19	O=C(N1CCCCC1)CSc2cccc(N)c2	0.826	0.755	0.896
20	FC(F)(F)c1ccc(N)c(C(=O)CC(=O)N2CCCCC2)c1	0.825	0.74	0.911
21	OCc1cccc(SCC(=O)N2CCCCC2)c1	0.825	0.71	0.94
23	O=C(N1CCCCC1)CC(c2nccc(n2)C)C	0.823	0.763	0.883
22	FC(F)(F)c1cccc(C(O)CC(=O)N2CCCCC2)c1	0.823	0.76	0.886
25	O=C(N1CCCCC1)CC(=O)c2cc(N)cc(OC)c2	0.821	0.724	0.918
24	Fc1cc(cc(CCC(=O)N2CCCCC2)c1)C(F)(F)F	0.821	0.721	0.921
26	O=C(N1CCCCC1)CSc2cccc(c2N)C	0.82	0.764	0.875
27	Clc1cc(nc(SCC(=O)N2CCCCC2)n1)N	0.818	0.789	0.847
28	FC(F)(F)c1cc(nc(SCC(=O)N2CCCCC2)n1)C	0.817	0.726	0.907
29	FC(F)(F)c1cc(C(=O)CC(=O)N2CCCCC2)ccc1C	0.816	0.749	0.884
30	O=S(=O)(N1CCCC1)NCCC(=O)N2CCCCC2	0.815	0.748	0.883
33	O=S(=O)(CC(=O)N1CCCCC1)c2cccc(OC)c2	0.815	0.742	0.888
31	O=C(N1CCCCC1)CC(=O)c2cccc(OC)n2	0.815	0.736	0.895
32	FC(F)(F)c1ccc(F)c(C(=O)CC(=O)N2CCCCC2)c1	0.815	0.733	0.898
34	O=C(N1CCCCC1)CCCc2c(oc(n2)C)C	0.814	0.74	0.888
36	Clc1cccc(S(=O)(=O)CC(=O)N2CCCCC2)c1	0.813	0.771	0.855
35	O=C(N1CCCCC1)CC[NH2+]CCCSC	0.813	0.761	0.866
37	O=C(N1CCCCC1)CCCNc2cccc[nH+]2	0.813	0.747	0.878
38	Fc1cc(N)cc(CCC(=O)N2CCCCC2)c1	0.812	0.727	0.897
39	O=C(N1CCCCC1)CC(=O)c2cncc(OC)n2	0.812	0.721	0.902
43	O=C(N1CCCCC1)CSc2nc(OC)cc(OC)n2	0.811	0.745	0.876
42	O=C(N1CCCCC1)CSc2ccc3CCCc3c2	0.811	0.74	0.882
40	O=C(N1CCCCC1)CCSc2nccc(n2)C	0.811	0.733	0.889
41	O=C(N1CCCCC1)CCCc2cccc(n2)C	0.811	0.732	0.889
44	O=C(N1CCCCC1)CCCc2nc(cc(n2)C)C	0.809	0.737	0.88

45	O=C(N1CCCCC1)COc2cccc(c2)C=O	0.809	0.728	0.889
46	FC(F)(F)c1cc(S(=O)(=O)CC(=O)N2CCCCC2)ccc1C	0.808	0.749	0.866
48	I/C=C/CCC(=O)N1CCCCC1	0.807	0.775	0.839
47	O=C(N1CCCCC1)CSc2nsc(n2)N	0.807	0.766	0.848
50	O=C(N1CCCCC1)CSc2cnccc2	0.807	0.736	0.877