Supporting Info

Synthesis, Structural Modification and Bioactivity Evaluation of Substituted Acridones as Potent Microtubule Affinity-Regulating Kinase 4 Inhibitors

Maria Voura,[a] Saleha Anwar,[b] Ioanna Sigala,[c] Eleftheria Parasidou,[a] Souzanna Fragoulidou,[a] Md. Imtaiyaz Hassan[b]* and Vasiliki Sarli[a]*

[a] Laboratory of Organic Chemistry, Department of Chemistry, Aristotle University of Thessaloniki, University Campus, 54124, Thessaloniki, Greece, sarli@chem.auth.gr

[b] Centre for interdisciplinary research in Basic Sciences, Jamia Millia Islamia, Jamia Nagar, New Delhi, 110025, India.

[c] Laboratory of Biochemistry, Department of Chemistry, Aristotle University of Thessaloniki, University Campus, 54124, Thessaloniki, Greece.

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Table S1. Docking scores and interactions between MARK4 and synthesized acridones.

Compound	Binding score (Kcal/mol)	Hydrogen bonds	Other interacting residues
9a	-9.4	Ala135 (2.90 Å)	Ala83, Val70, Glu133, Val116, Met132, Ala195, Asn183, Glu182, Asp196, Gly63, Ile62, Gly138, Tyr134, Leu185
9b	-9.5	-	Ala135, Ala195, Ala83, Val116, Met132, Val70, Asp196, Lys85, Ala68, Lys69, Gly65, Gly63, Leu185, Glu139, Gly138, Ile62, Tyr134
9c	-10.0	Gly65 (3.09 Å)	Ala135, Ala195, Ala83, Glu133, Val116, Met132, Lys64, Gly63, Lys69, Lys85, Ala68, Val70, Asp196, Leu185, Glu139, Gly138, Ile62, Tyr134
9d	-9.5	Gly65 (3.08 Å)	Ala135, Ala195, Val116, Lys85, Ala83, Val70, Met132, Asp196, Ala68, Lys69, Lys64, Gly63, Leu185, Glu139, Gly138, Ile62, Tyr134
9e	-9.7	Gly65 (3.00 Å) Lys85 (3.07 Å)	Ala135, Ile62, Tyr134, Ala195, Ala83, Val116, Met132, Gly63, Val70, Ala68, Lys64, Lys69, Asp196, Lys85, Leu185, Glu139, Gly138
9f	-8.6	Ala135 (3.14 Å)	Ala135, Leu185, Gly138, Glu139, Glu182, Asn183, Asp196, Ala195, Val70, Val116, Ala83, Met132, Glu133, Lys85, Tyr134
9g	-9.5	-	Ala135, Leu185, Ala83, Glu133, Ala195, Val116, Met132, Gly63, Asp196, Lys64, Lys69, Gly65, Ala68, Lys85, Val70, Glu139, Gly138, Ile62, Tyr134
9h	-9.6	Gly65 (2.99 Å)	Ala135, Leu185, Ala83, Glu133, Ala195, Val116, Met132, Val70, Asp196, Lys69, Lys64, Ala68, Gly63, Glu139, Gly138, Ile62, Tyr134
9i	-9.9	Gly65 (3.08 Å)	Ala135, Ala195, Glu133, Ala83, Gly63, Met132, Val116, Lys85, Lys64, Asp196, Lys69, Ala68, Val70, Leu185, Glu139, Gly138, Ile62, Tyr134
10	-9.6	Ala135 (2.80 Å) Glu182 (2.01 Å) Asn183 (1.85 Å) Asp196 (2.75 Å)	Val70, Ala83, Glu133, Ala195, Met132, Val116, Gly63, Ile62, Gly138, Tyr134, Leu185
15a	-10.0	Ala135 (2.80 Å)	Val70, Ala83, Glu133, Val116, Ala195, Met132, Asn183, Glu182, Asp196, Gly65, Phe67, Ala68, Lys85, Gly63, Leu185, Ile62, Gly138, Tyr134
15b	-10.6	Ala135 (2.87 Å)	Ala83, Glu133, Val116, Val70, Ala195, Met132, Asn183, Glu182, Lys85, Ala68, Asn66, Gly65, Phe67, Ile87, Glu103, Gly198, Asp196, Gly63, Ile62, Leu185, Gly138, Tyr134
15c	-10.5	Ala135 (2.79 Å)	Ala83, Glu133, Val116, Val70, Ala195, Met132, Asn183, Glu182, Asp196, Lys85, Gly65, Ala68, Gly198, Glu103, Phe67, Gly63, Leu185, Ile62, Gly138, Tyr134
15d	-10.4	Ala135 (2.80 Å)	Ala83, Glu133, Val116, Val70, Ala195, Met132, Asn183, Glu182, Asp196, Lys85, Ala68, Gly65, Phe67, Gly198, Gly63, Leu185, Ile62, Gly138, Tyr134
15e	-10.3	Ala135 (2.80 Å)	Ala83, Glu133, Val116, Val70, Ala195, Met132, Asn183, Glu182, Asp196, Lys85, Gly65, Ala68, Phe67, Gly198, Gly63, Leu185, Ile62, Gly138, Tyr134
16a	-10.3	Ala135 (2.83 Å)	Val70, Glu133, Ala83, Leu185, Met132, Val116, Ala195, Gly63, Gly65, Lys64, Gly198, Asp178, Lys85, Glu182, Asp196, Tyr134, Gly138, Ile62
16c	-10.7	Ala135 (3.02 Å) Ala68 (3.66 Å)	Ala83, Val70, Glu133, Val116, Ala195, Gly63, Glu182, Asp196, Lys85, Phe67, Asn66, Ala68, Gly65, Ile62, Gly138, Tyr134, Leu185, Ala135
16b	-10.8	Ala135 (3.02 Å) Lys85 (3.24 Å)	Ala83, Glu133, Val116, Val70, Ala195, Gly63, Glu182, Gly198, Phe67, Gly65, Asn66, Asp196, Ala68, Ile62, Tyr134, Gly138, Leu185, Ala135
16d	-10.1	Ala135 (2.88 Å)	Val70, Ala83, Glu133, Val116, Ala195, Met132, Gly63, Gly65, Ala68, Glu182, Lys64, Asp196, Leu185, Gly138, Tyr134, Ile62
16e	-10.3	Ala135 (2.85 Å) Lys85 (3.36 Å) Asn66 (3.11 Å)	Ala83, Glu133, Ala195, Val116, Val70, Gly63, Met132, Ala68, Lys64, Gly65, Phe199, Asp178, Glu182, Asp196, Tyr134, Ile62, Gly138, Leu185
16f	-10.3	Ala135 (2.82 Å) Phe199 (3.38 Å)	Val70, Ala83, Glu133, Val116, Met132, Ala195, Gly63, Gly65, Lys64, Asp178, Gly198, Glu182, Asp196, Leu185, Tyr134, Gly138, Ile62
16g	-10.1	Ala135 (3.01 Å)	Ala83, Glu133, Val116, Ala195, Val70, Gly63, Glu182, Ala68, Gly65, Asn66, Phe67, Ser96, Leu92, Leu100, Ile87, Lys85, Asp196, Ile62, Gly138, Tyr134, Leu185, Ala135

Table S1 (*Continued*). Docking scores and interactions between MARK4 and synthesized acridones.

Compound	Binding score (Kcal/mol)	Hydrogen bonds	Other interacting residues
16h	-10.0	Ala135 (2.86 Å)	Val70, Ala83, Glu133, Val116, Ala195, Met132, Gly65, Ala68, Glu182, Asn183, Gly63, Asp196, Leu185, Gly138, Ile62, Tyr134
20	-9.9	Ala135 (3.80 Å) Asp196 (1.98 Å) Glu139 (2.62 Å)	Ala83, Glu133, Ala195, Val116, Glu182, Val70, Ala68, Lys85, Lys69, Gly65, Lys64, Glu139, Ile62, Gly63, Gly138, Tyr134, Leu185
23a	-10.5	Ala135 (2.85 Å) Asp196 (1.87 Å)	Ala83, Glu133, Val116, Met132, Ala195, Gly63, Glu139, Asp142, Lys64, Glu182, Gly138, Ala68, Lys85, Gly65, Lys69, Tyr134, Leu185, Ile62, Val70
23b	-10.6	Ala135 (2.80 Å) Asp196 (1.85 Å)	Leu185, Glu133, Ala83, Ala195, Met132, Val116, Glu182, Val70, Gly63, Lys85, Ala68, Lys69, Gly65, Lys64, Glu139, Asp142, Gly138, Tyr134, Ile62
23c	-10.3	Ala135 (2.87 Å) Asp196 (1.87 Å)	Ala83, Glu133, Val116, Met132, Ala195, Gly63, Glu139, Asp142, Lys64, Glu182, Gly138, Ala68, Lys85, Gly65, Lys69, Tyr134, Leu185, Ile62, Val70
23d	-10.4	Ala135 (2.85 Å) Asp196 (1.95 Å)	Ala83, Glu133, Val116, Met132, Ala195, Gly63, Glu139, Asp142, Ser136, Glu182, Lys64, Gly138, Ala68, Lys85, Gly65, Lys69, Leu185, Tyr134, Val70, Ile62, Ala135

Table S2. Druglikeness of synthesized acridones. (MW: Molecular Weight, MLogP: Lipophilicity, HBD: Hydrogen Bond Donor, HBA: Hydrogen Bond Acceptor, r.b.: rotatable bonds, TPSA: Topological Polar Surface Area)

Compound	MW (g/mol)	MLogP	HBD	HBA	r.b.	TPSA (Å²)	Druglikeness	
							Lipinski	Veber
9a	299.37	3.78	0	1	2	22.00	Yes (0 violations)	Yes (0 violations)
9b	313.39	3.99	0	1	2	22.00	Yes (0 violations)	Yes (0 violations)
9c	367.36	4.58	0	4	3	22.00	Yes (1 violation)	Yes (0 violations)
9d	317.36	4.15	0	2	2	22.00	Yes (1 violation)	Yes (0 violations)
9e	335.35	4.53	0	3	2	22.00	Yes (1 violation)	Yes (0 violations)
9f	263.33	3.31	0	1	2	22.00	Yes (0 violations)	Yes (0 violations)
9g	355.47	4.63	0	1	3	22.00	Yes (1 violation)	Yes (0 violations)
9h	324.38	3.04	0	2	2	45.79	Yes (0 violations)	Yes (0 violations)
9i	344.36	2.63	0	3	3	67.82	Yes (0 violations)	Yes (0 violations)
10	314.38	3.16	1	1	2	48.02	Yes (0 violations)	Yes (0 violations)
15a	425.52	2.81	0	3	5	45.55	Yes (0 violations)	Yes (0 violations)
15b	481.63	3.59	0	3	6	45.55	Yes (0 violations)	Yes (0 violations)
15c	470.52	1.83	0	5	6	91.37	Yes (0 violations)	Yes (0 violations)
15d	450.53	2.13	0	4	5	69.34	Yes (0 violations)	Yes (0 violations)
15e	443.51	3.18	0	4	5	45.55	Yes (0 violations)	Yes (0 violations)
16a	473.95	3.07	0	3	5	62.62	Yes (0 violations)	Yes (0 violations)
16c	457.50	2.97	0	4	5	62.62	Yes (0 violations)	Yes (0 violations)
16b	457.50	2.97	0	4	5	62.62	Yes (0 violations)	Yes (0 violations)
16d	484.50	1.65	0	5	6	108.44	Yes (0 violations)	Yes (0 violations)
16e	510.54	1.71	0	5	7	108.44	Yes (1 violation)	Yes (0 violations)
16f	508.40	3.53	0	3	5	62.62	Yes (1 violation)	Yes (0 violations)
16g	575.50	4.10	0	9	7	62.62	Yes (1 violation)	Yes (0 violations)
16h	429.47	1.43	0	4	5	75.76	Yes (0 violations)	Yes (0 violations)
20	453.49	2.07	3	4	7	104.19	Yes (0 violations)	Yes (0 violations)
23a	542.63	3.07	3	3	9	95.99	Yes (1 violation)	Yes (0 violations)
23b	546.59	3.25	3	4	9	95.99	Yes (1 violation)	Yes (0 violations)
23c	563.05	3.34	3	3	9	95.99	Yes (1 violation)	Yes (0 violations)
23d	600.66	2.88	3	5	12	122.29	Yes (1 violation)	No (1 violation)

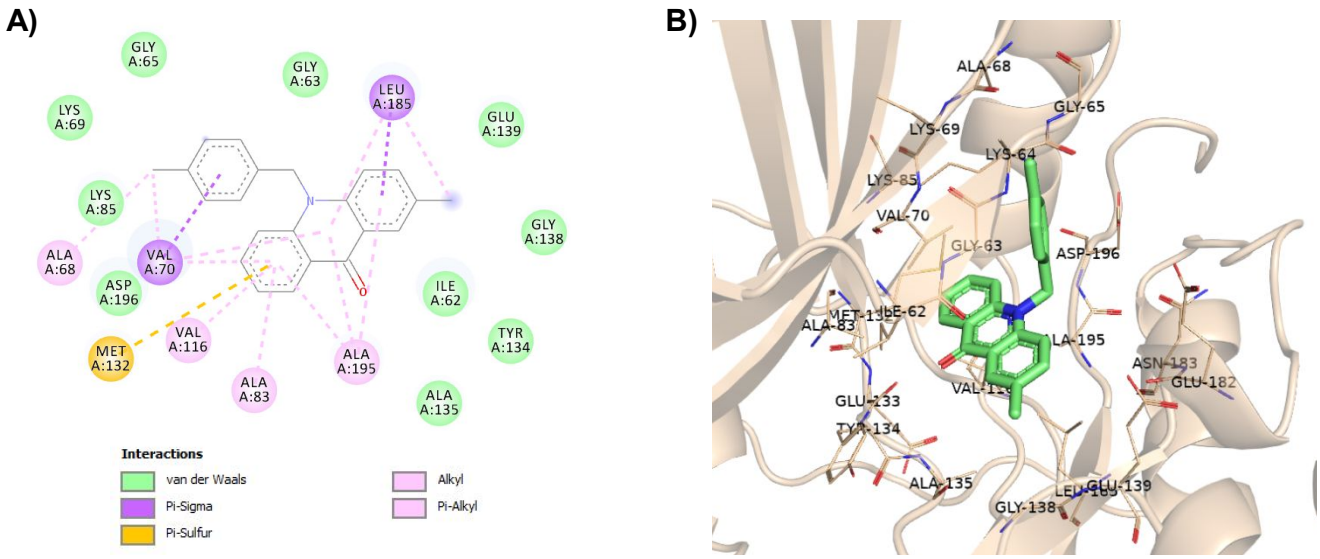


Figure S1. (A) 2D molecular docking model of compound **9b** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **9b** in the active site of MARK4 (BIOVIA Discovery Studio).

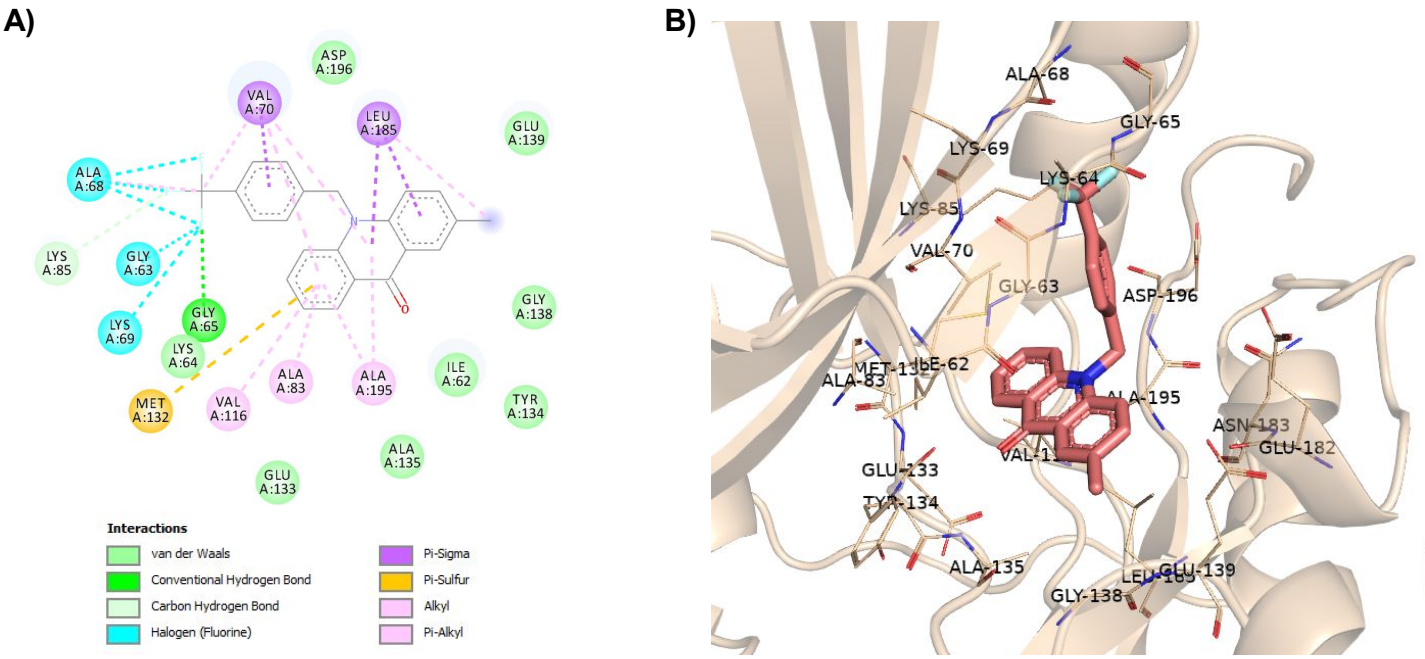


Figure S2. (A) 2D molecular docking model of compound **9c** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **9c** in the active site of MARK4 (BIOVIA Discovery Studio).

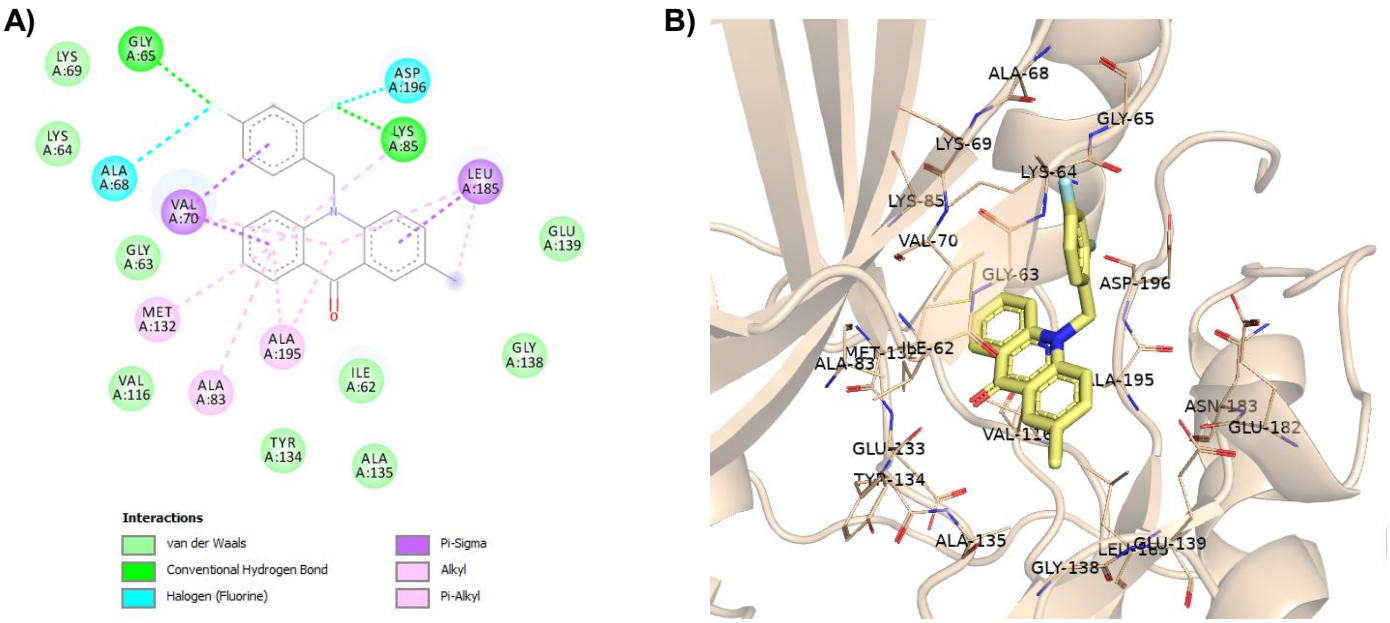


Figure S3. (A) 2D molecular docking model of compound **9e** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **9e** in the active site of MARK4 (BIOVIA Discovery Studio).

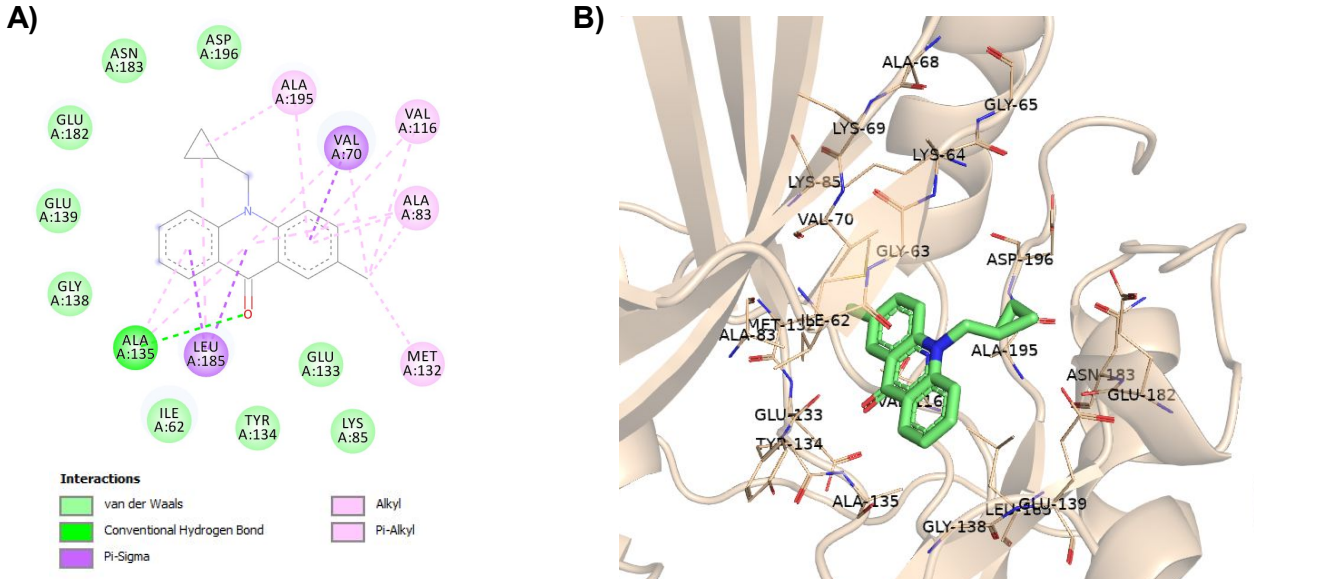


Figure S4. (A) 2D molecular docking model of compound **9f** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **9f** in the active site of MARK4 (BIOVIA Discovery Studio).

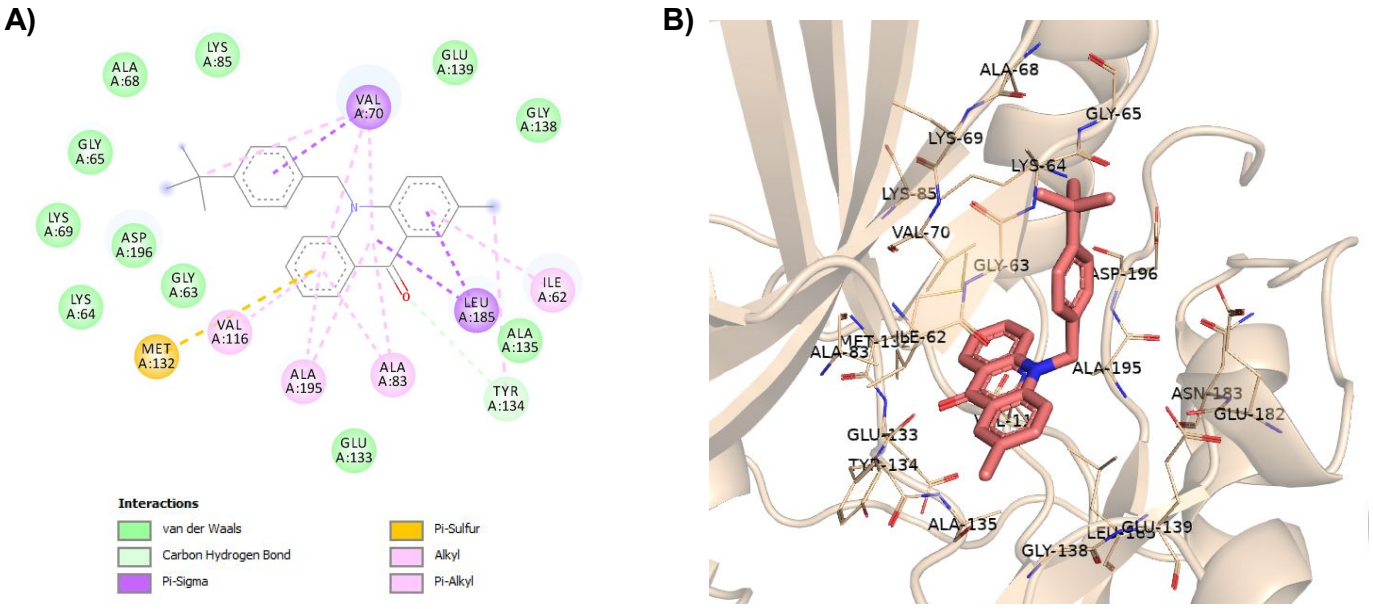


Figure S5. (A) 2D molecular docking model of compound **9g** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **9g** in the active site of MARK4 (BIOVIA Discovery Studio).

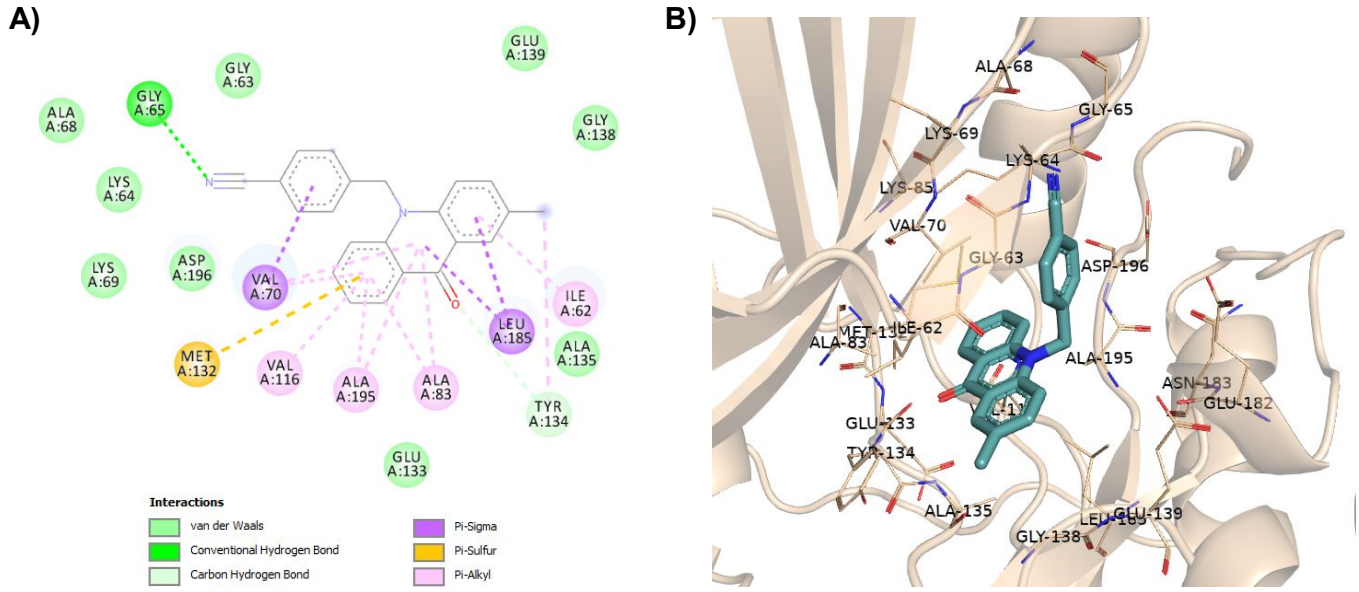


Figure S6. (A) 2D molecular docking model of compound **9h** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **9h** in the active site of MARK4 (BIOVIA Discovery Studio).

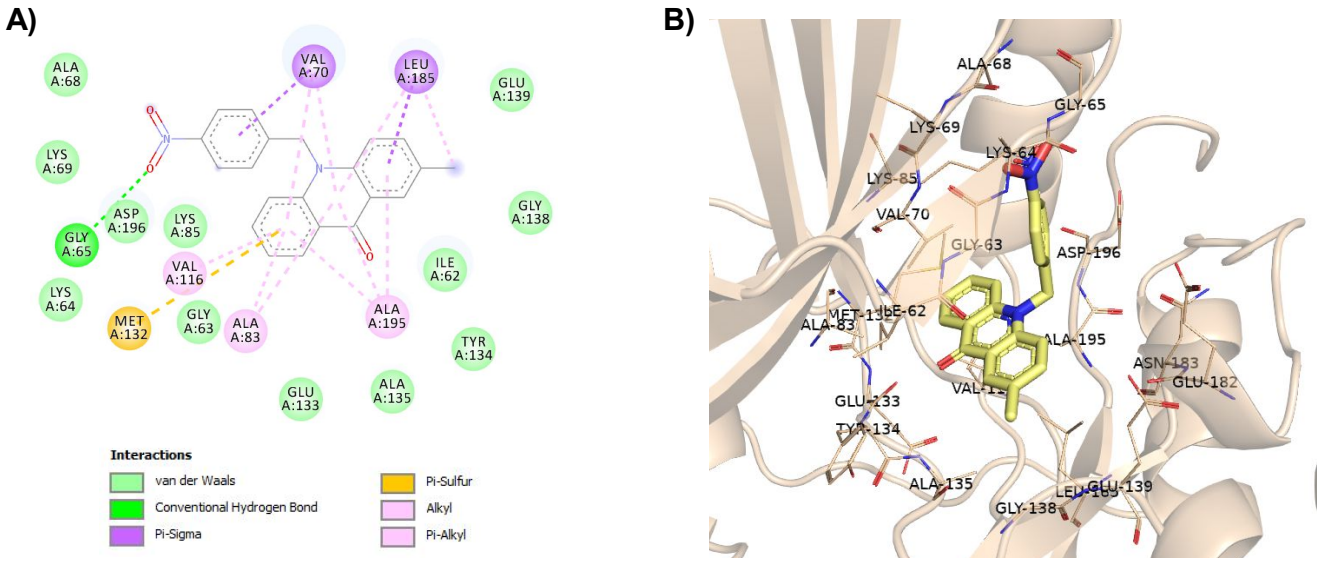


Figure S7. (A) 2D molecular docking model of compound **9i** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **9i** in the active site of MARK4 (BIOVIA Discovery Studio).

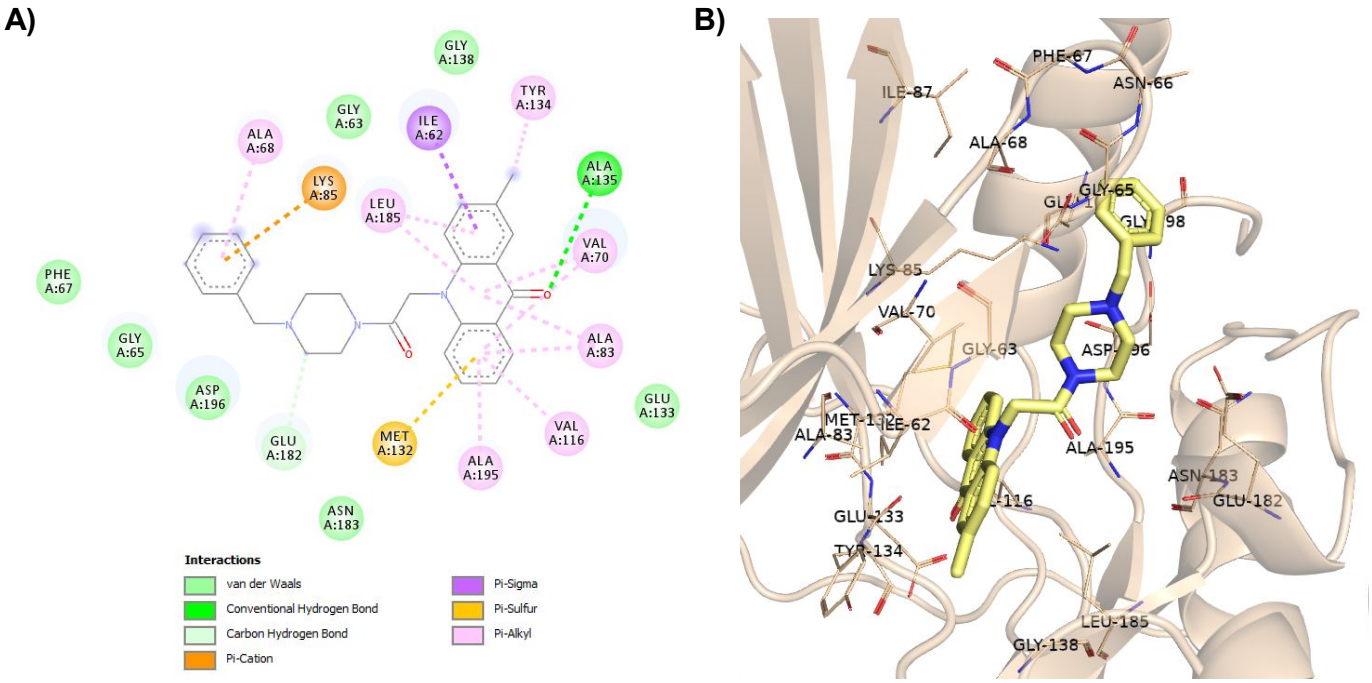


Figure S8. (A) 2D molecular docking model of compound **15a** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **15a** in the active site of MARK4 (BIOVIA Discovery Studio).

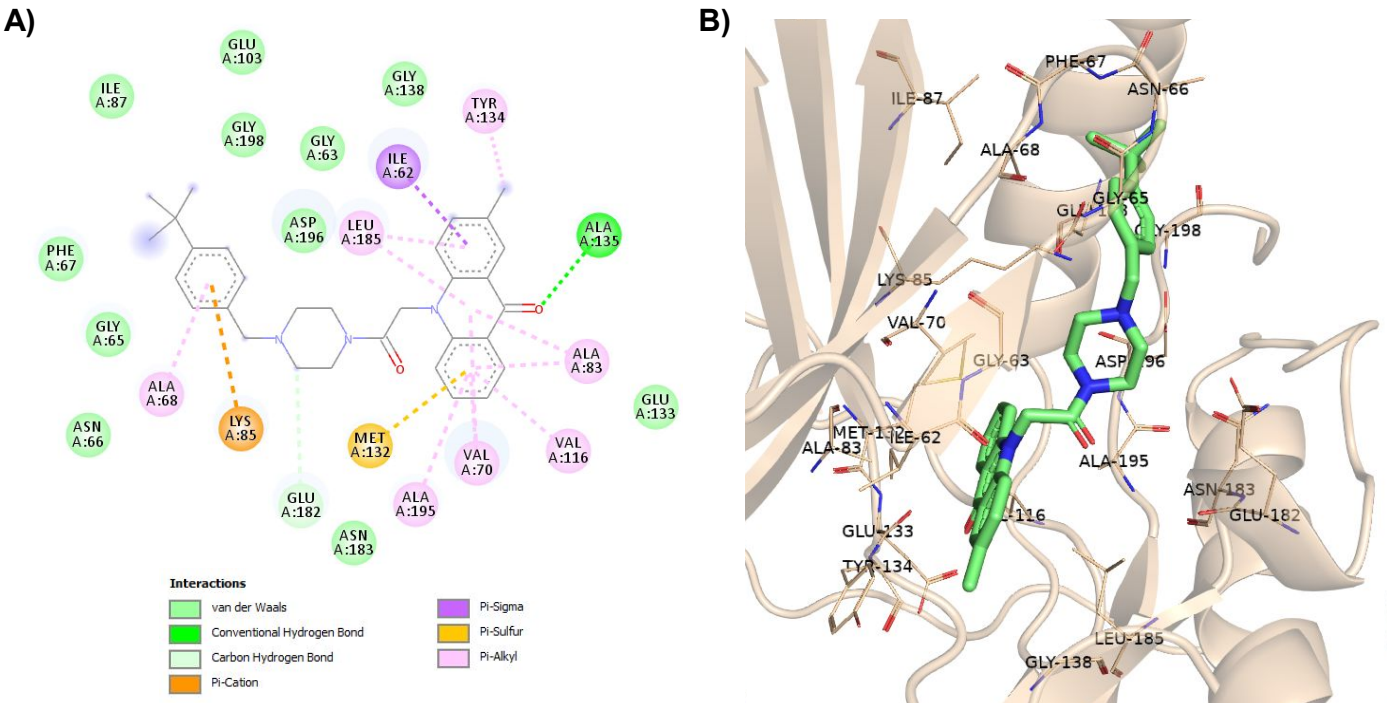


Figure S9. (A) 2D molecular docking model of compound **15b** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **15b** in the active site of MARK4 (BIOVIA Discovery Studio).

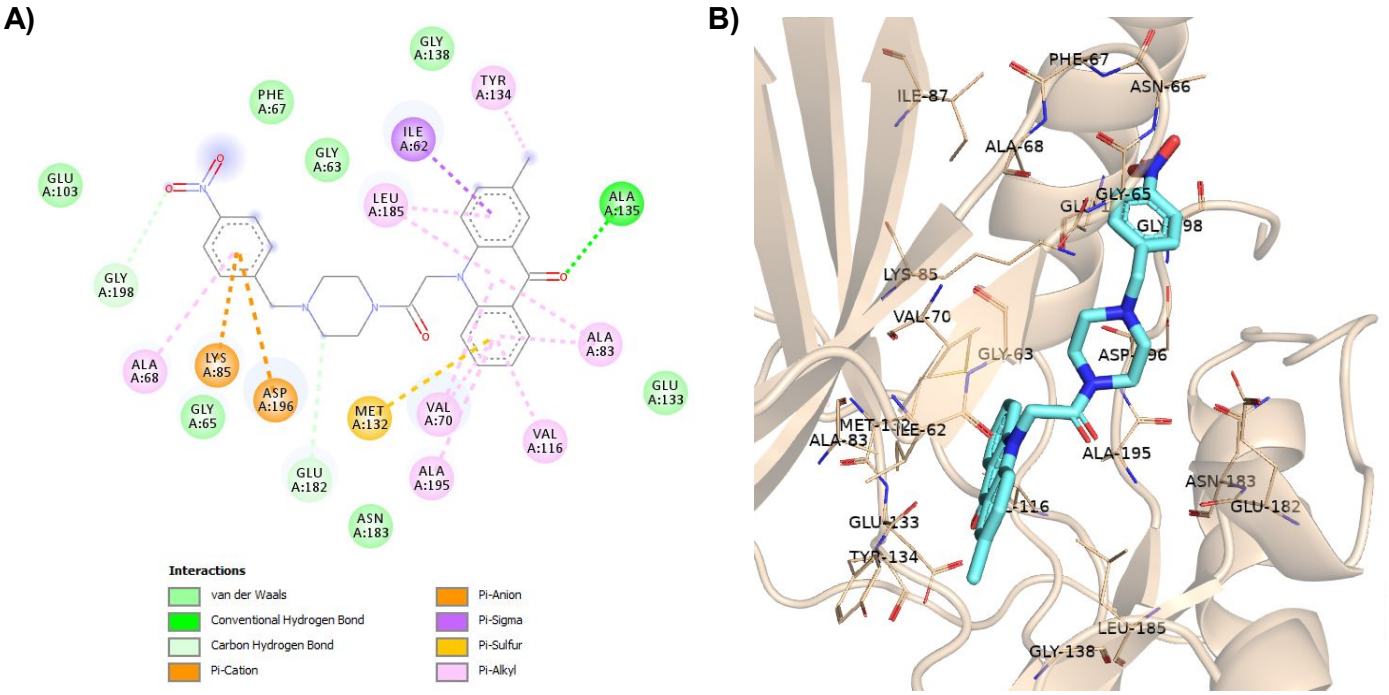


Figure S10. (A) 2D molecular docking model of compound **15c** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **15c** in the active site of MARK4 (BIOVIA Discovery Studio).

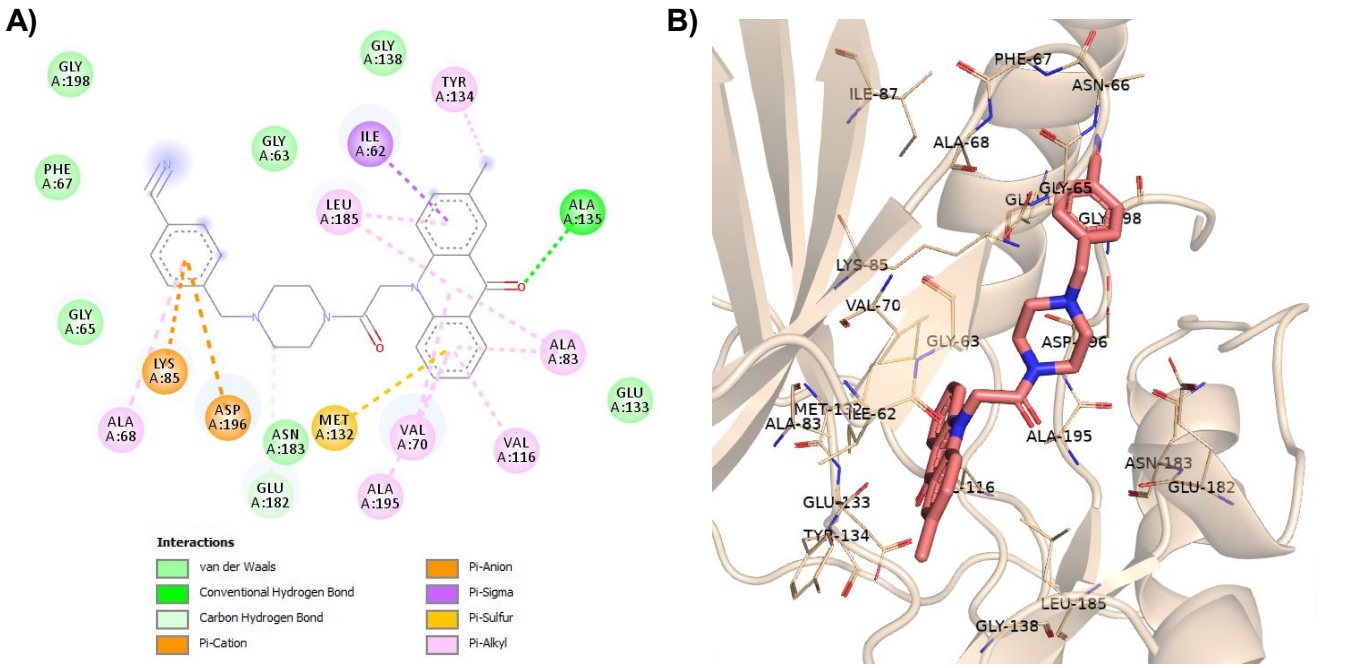


Figure S11. (A) 2D molecular docking model of compound **15d** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **15d** in the active site of MARK4 (BIOVIA Discovery Studio).

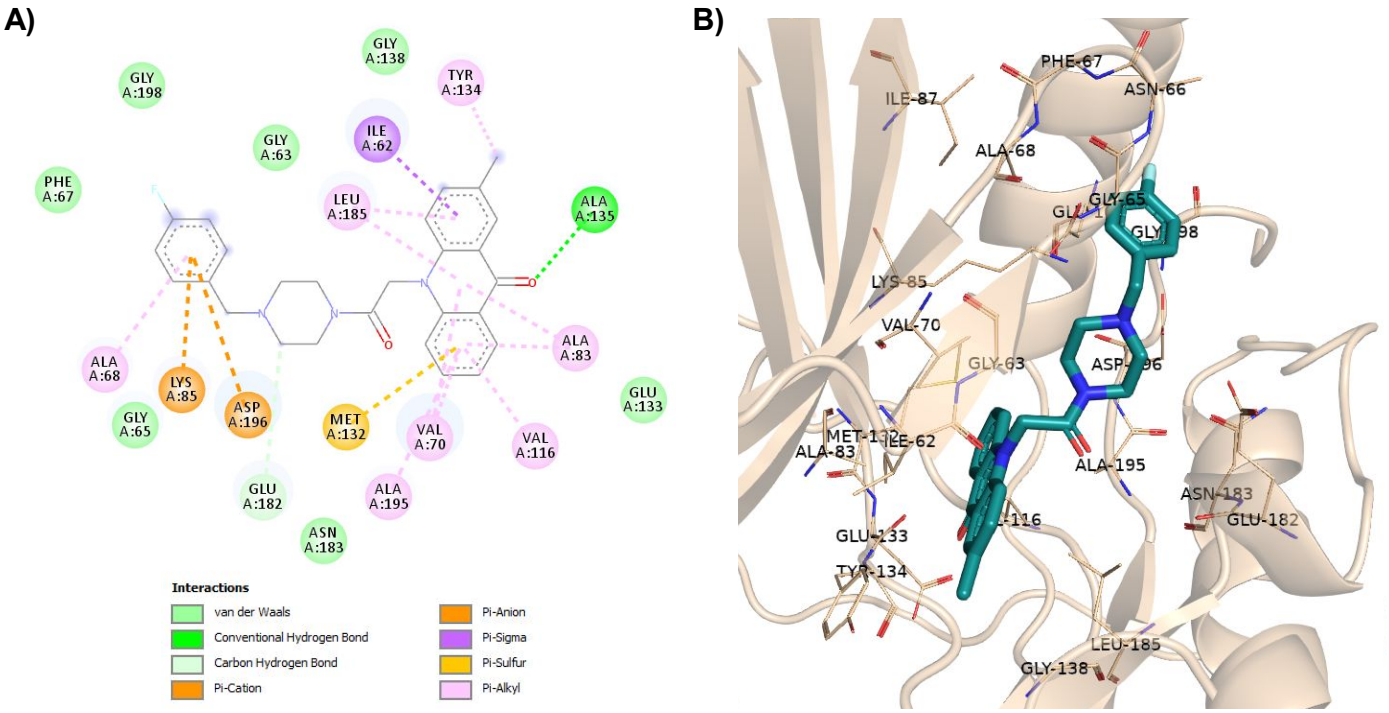


Figure S12. (A) 2D molecular docking model of compound **15e** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **15e** in the active site of MARK4 (BIOVIA Discovery Studio).

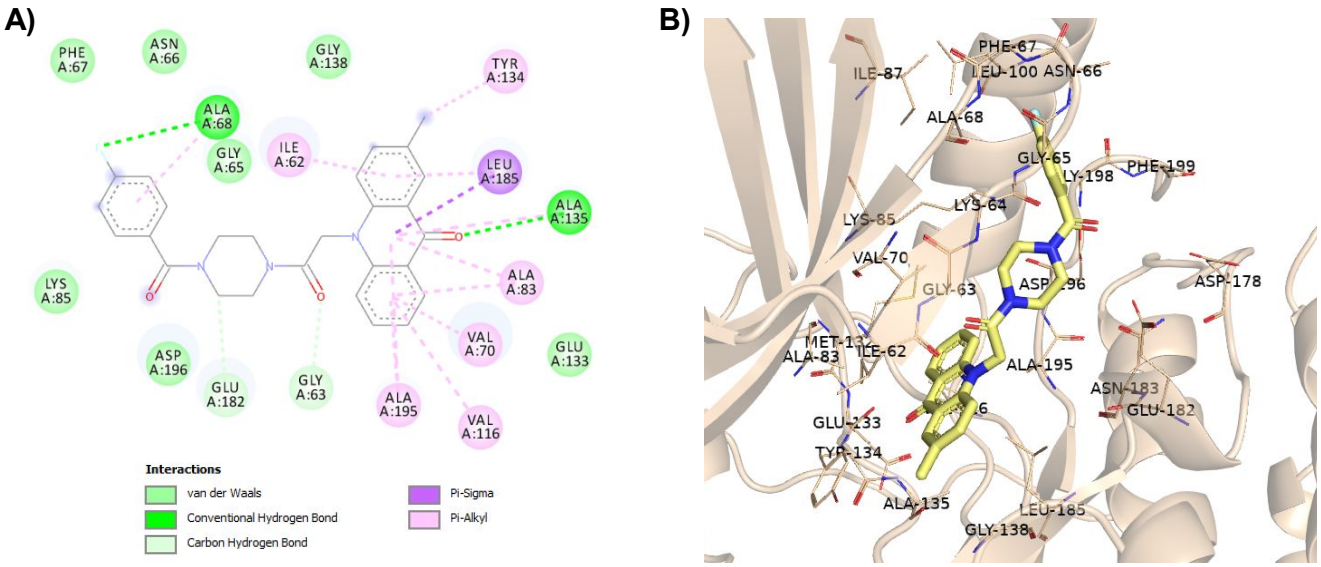


Figure S13. (A) 2D molecular docking model of compound **16c** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **16c** in the active site of MARK4 (BIOVIA Discovery Studio).

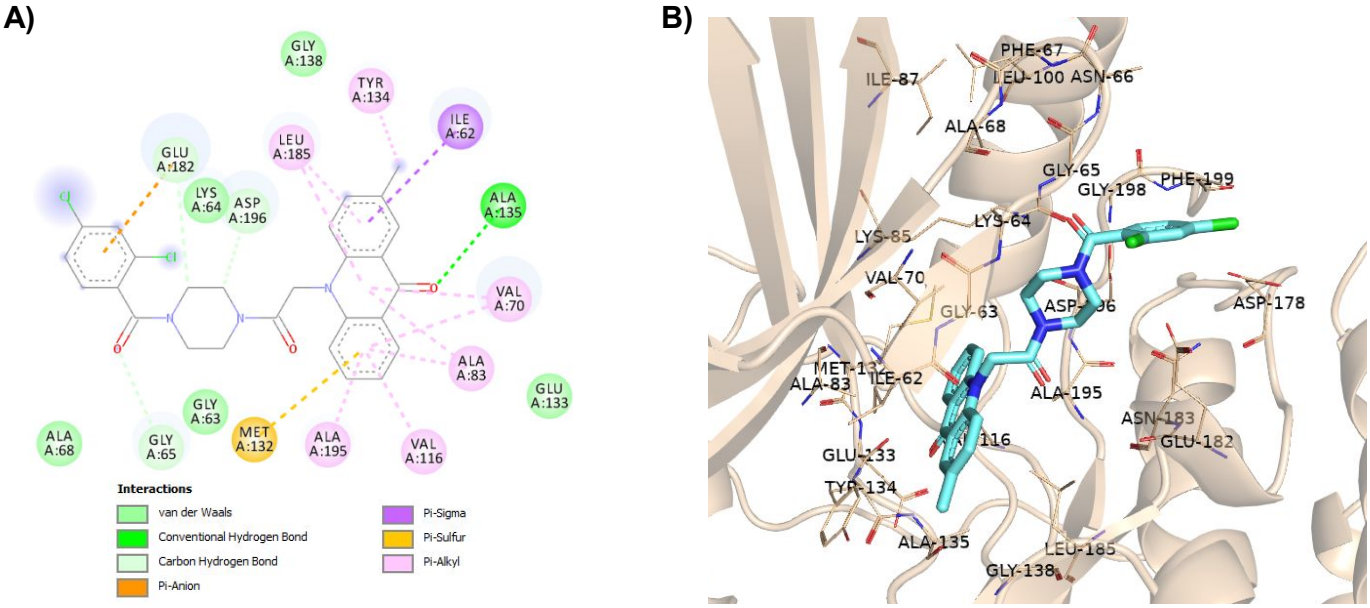


Figure S14. (A) 2D molecular docking model of compound **16d** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **16d** in the active site of MARK4 (BIOVIA Discovery Studio).

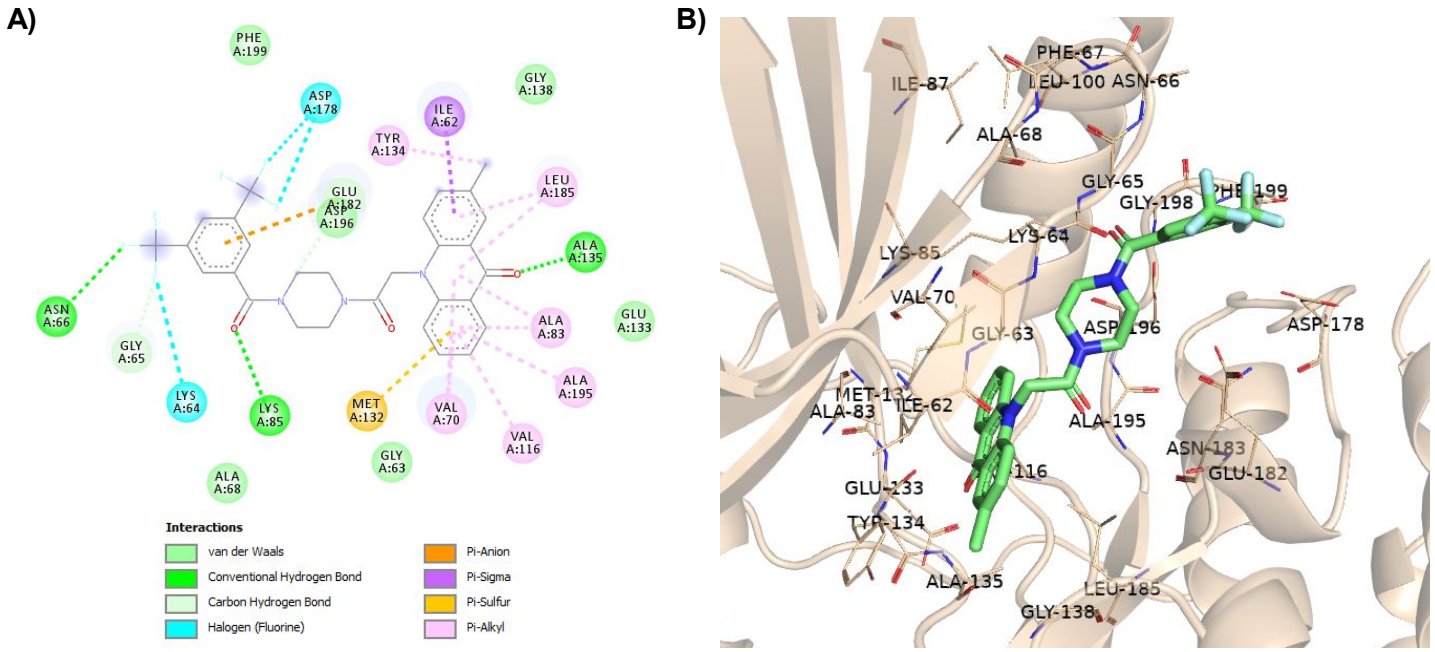


Figure S15. (A) 2D molecular docking model of compound **16e** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **16e** in the active site of MARK4 (BIOVIA Discovery Studio).

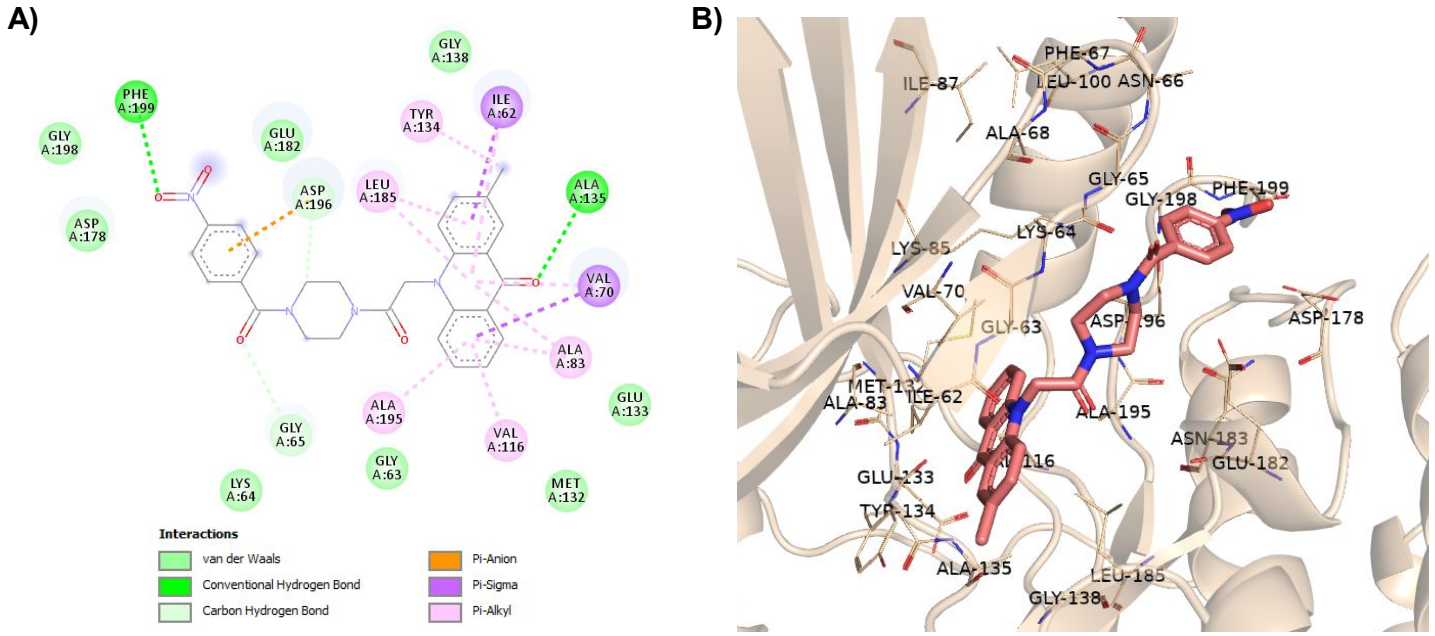


Figure S16. (A) 2D molecular docking model of compound **16f** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **16f** in the active site of MARK4 (BIOVIA Discovery Studio).

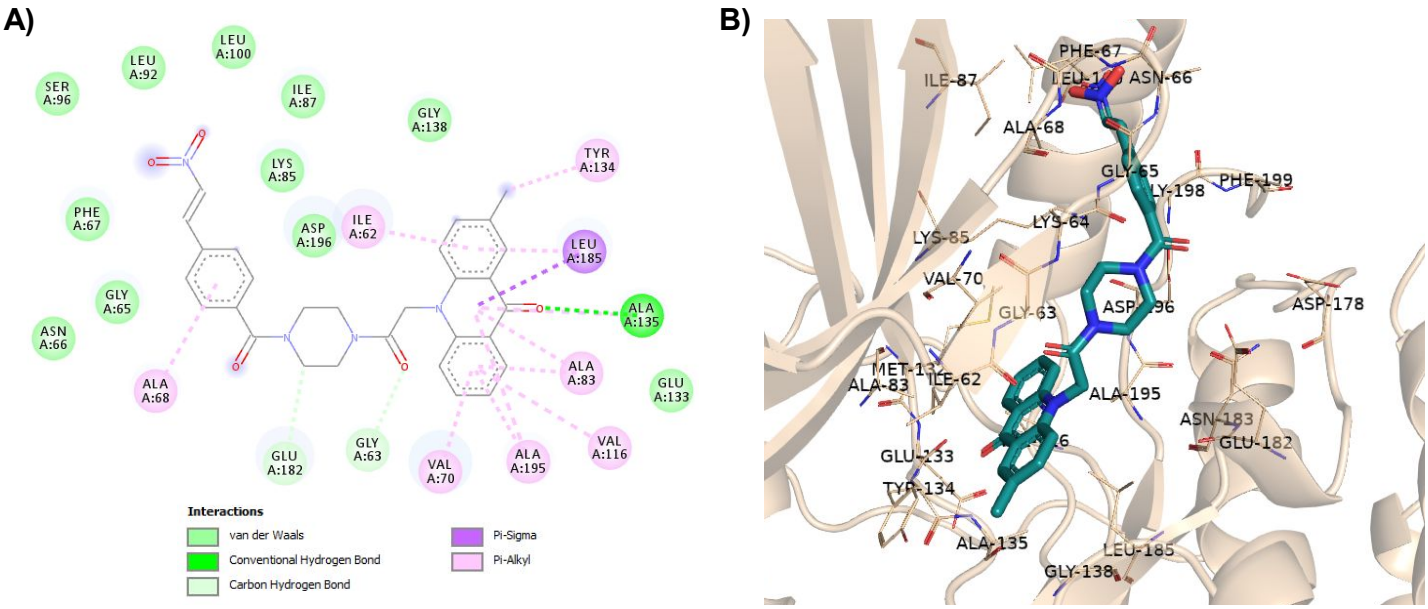


Figure S17. (A) 2D molecular docking model of compound **16g** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **16g** in the active site of MARK4 (BIOVIA Discovery Studio).

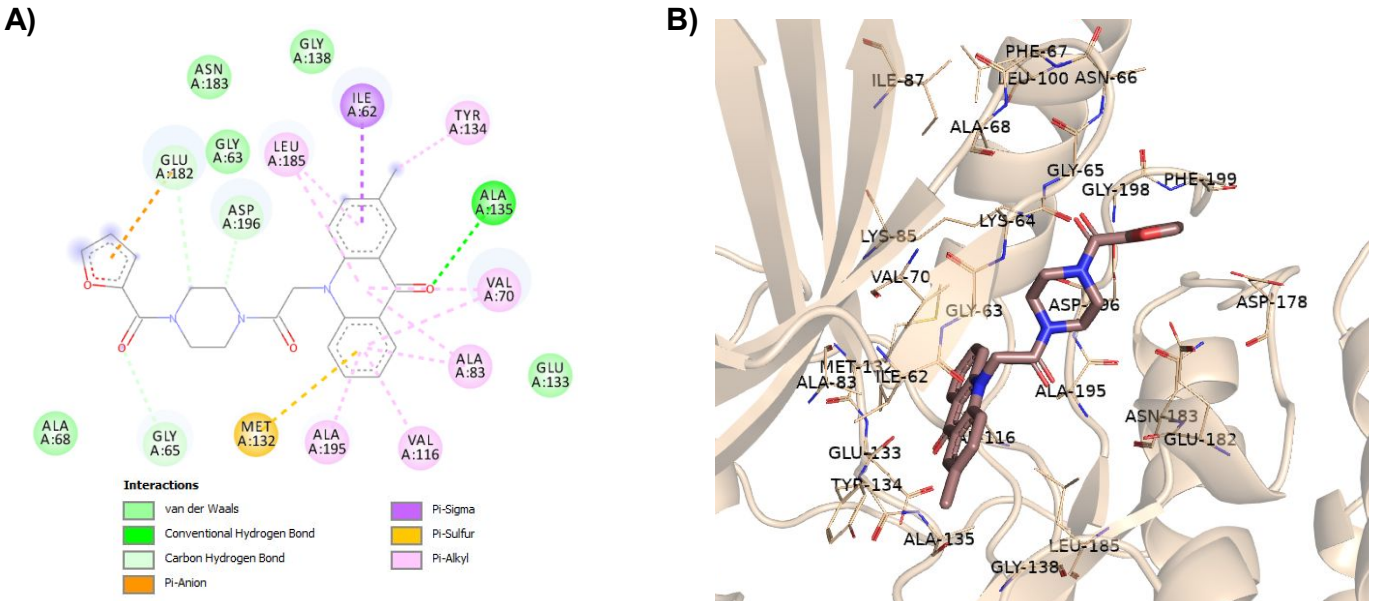


Figure S18. (A) 2D molecular docking model of compound **16h** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **16h** in the active site of MARK4 (BIOVIA Discovery Studio).

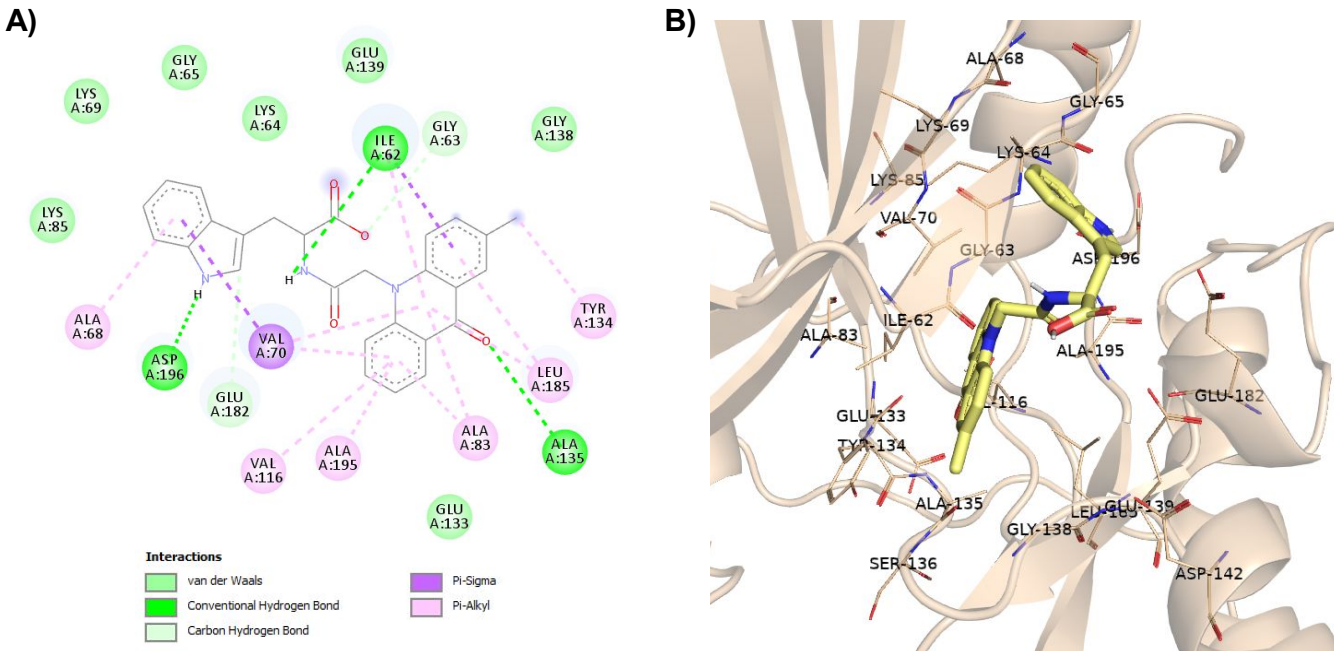


Figure S19. (A) 2D molecular docking model of compound **20** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **20** in the active site of MARK4 (BIOVIA Discovery Studio).

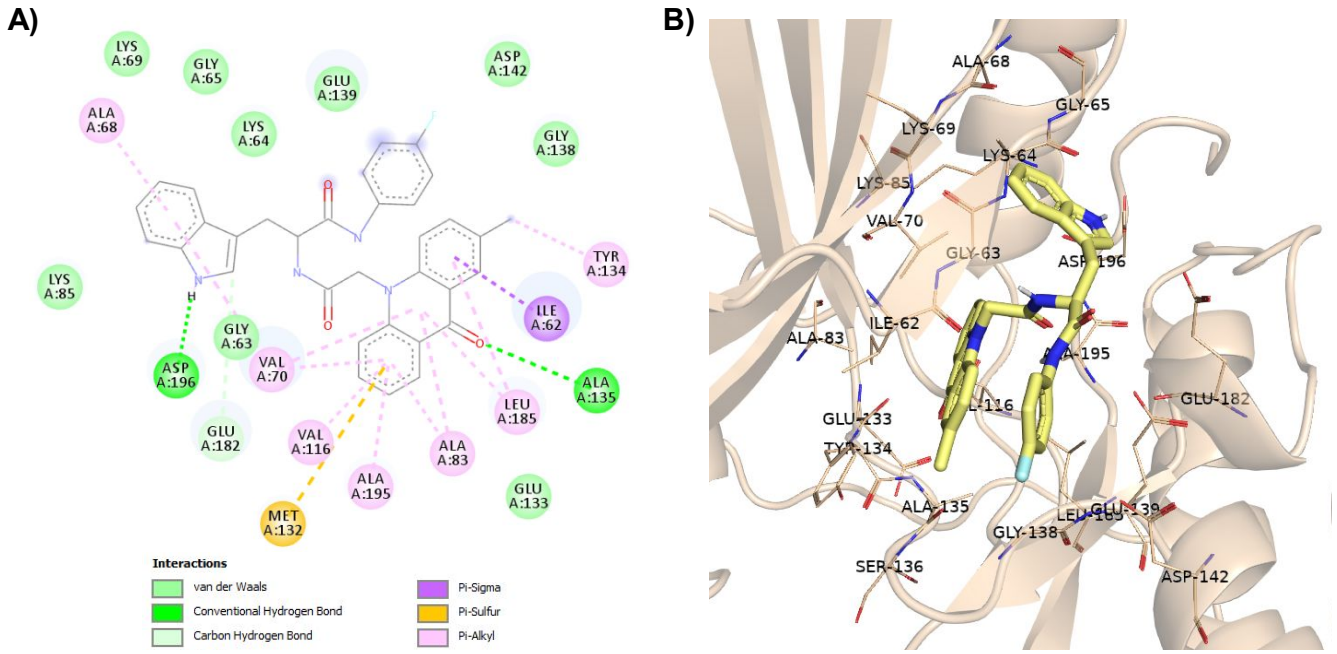


Figure S20. (A) 2D molecular docking model of compound **23b** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **23b** in the active site of MARK4 (BIOVIA Discovery Studio).

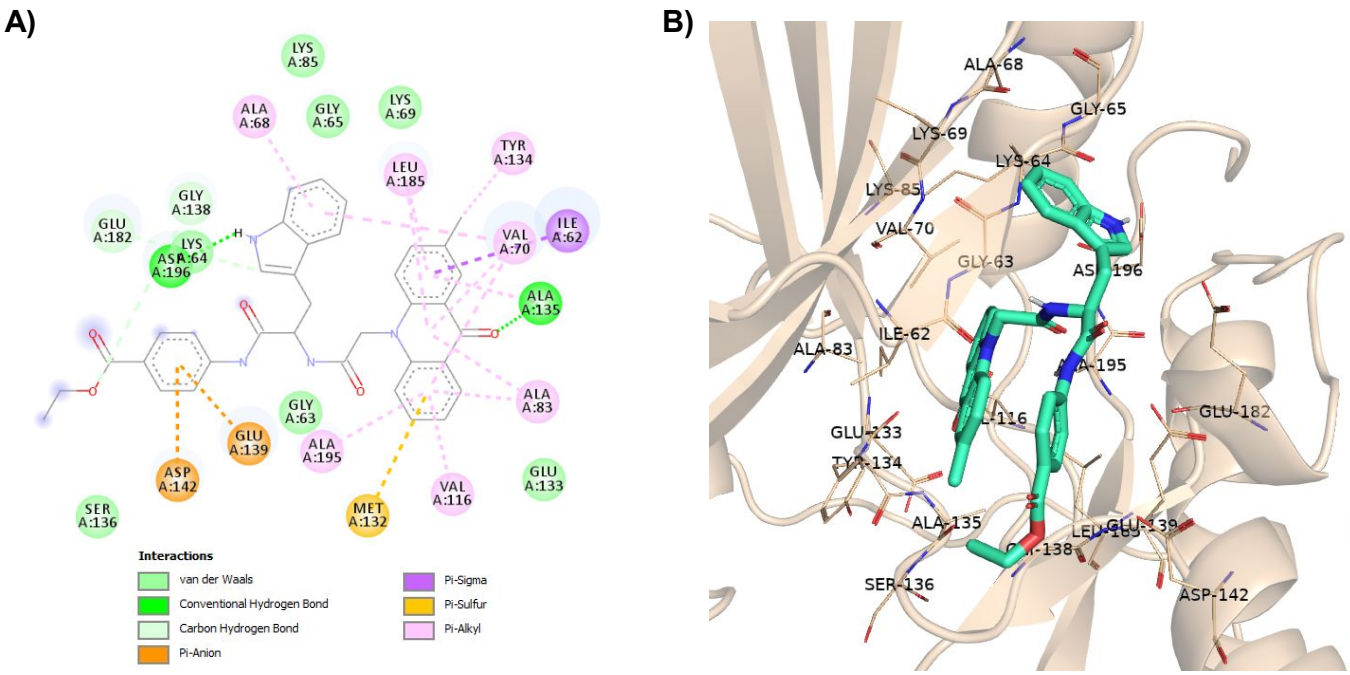
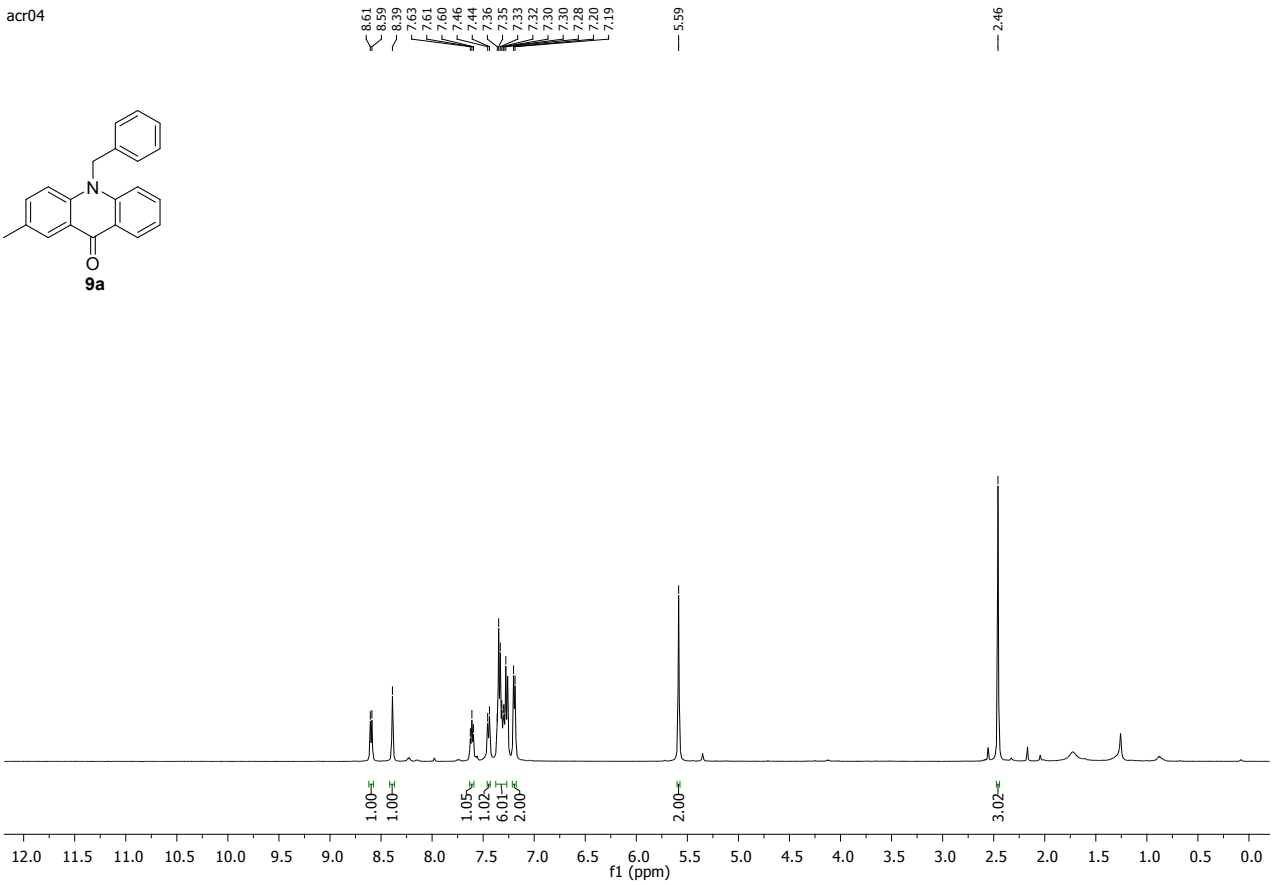


Figure S21. (A) 2D molecular docking model of compound **23d** in the active site of MARK4 (PDB code: 5ES1). **(B)** 3D model of the interaction between compound **23d** in the active site of MARK4 (BIOVIA Discovery Studio).


acr04
8.61
8.59
8.39
7.63
7.61
7.60
7.46
7.44
7.36
7.35
7.33
7.32
7.30
7.30
7.28
7.20
7.19
5.59
2.46
N
O
9a
1.00
1.00
1.05
1.02
6.01
2.00
2.00
3.02
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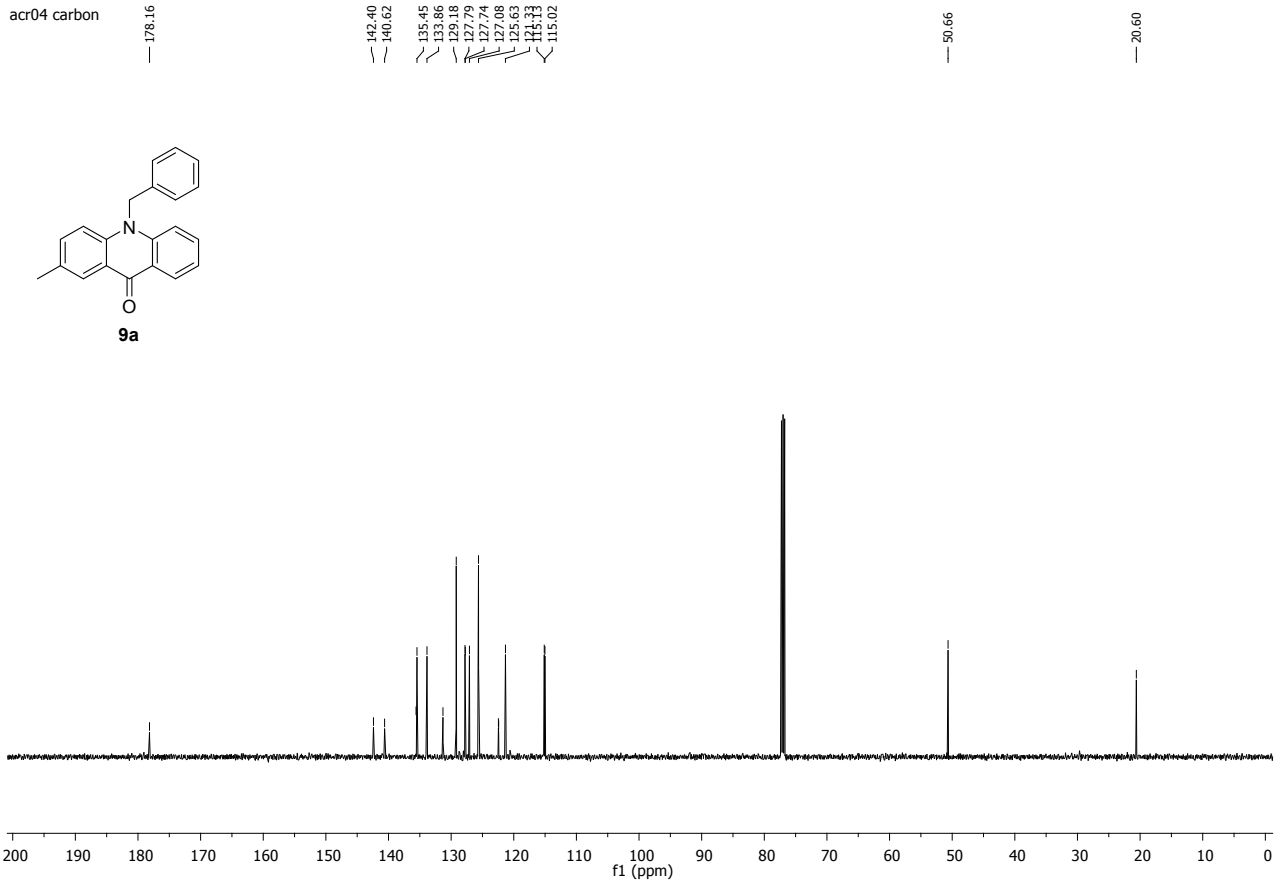
f1 (ppm)


acr04 carbon
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127.08
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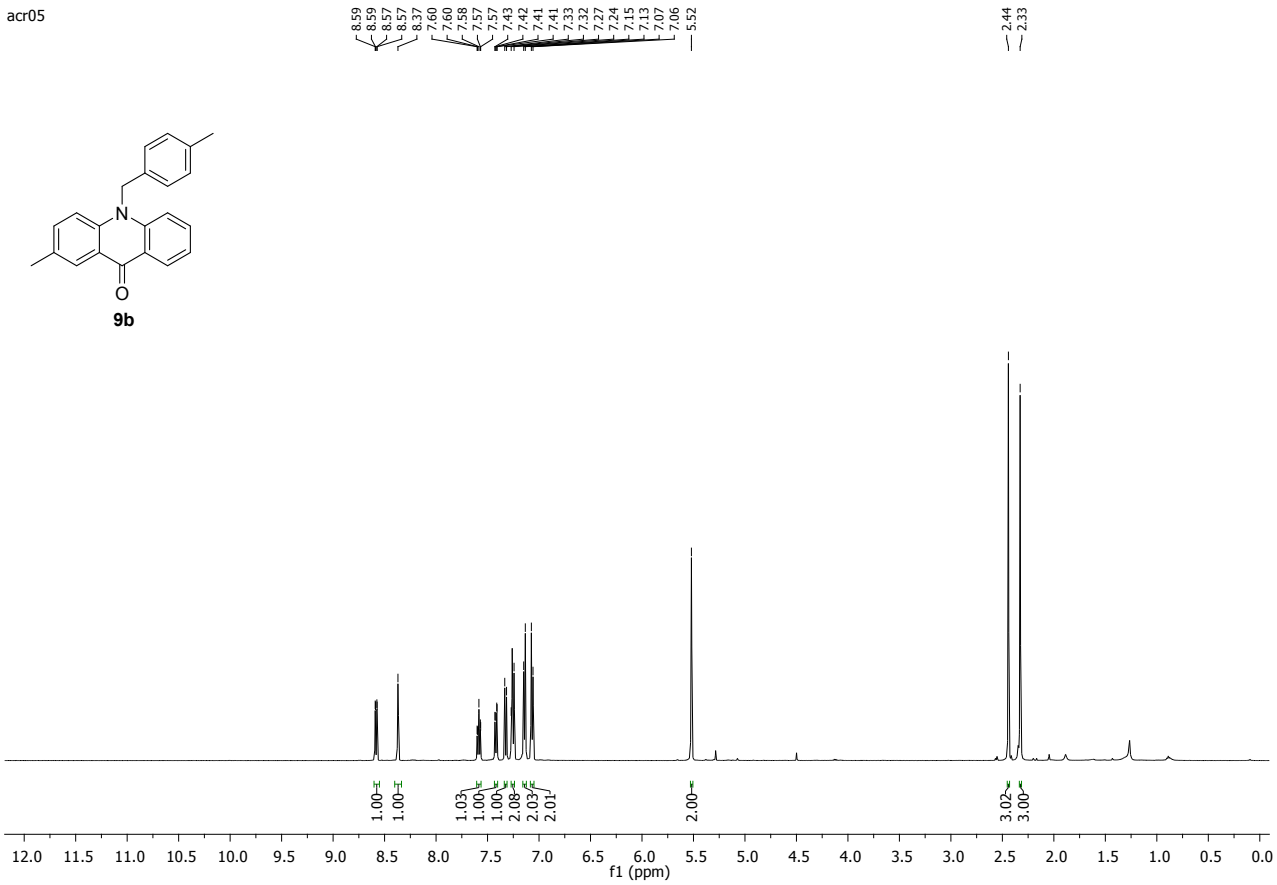
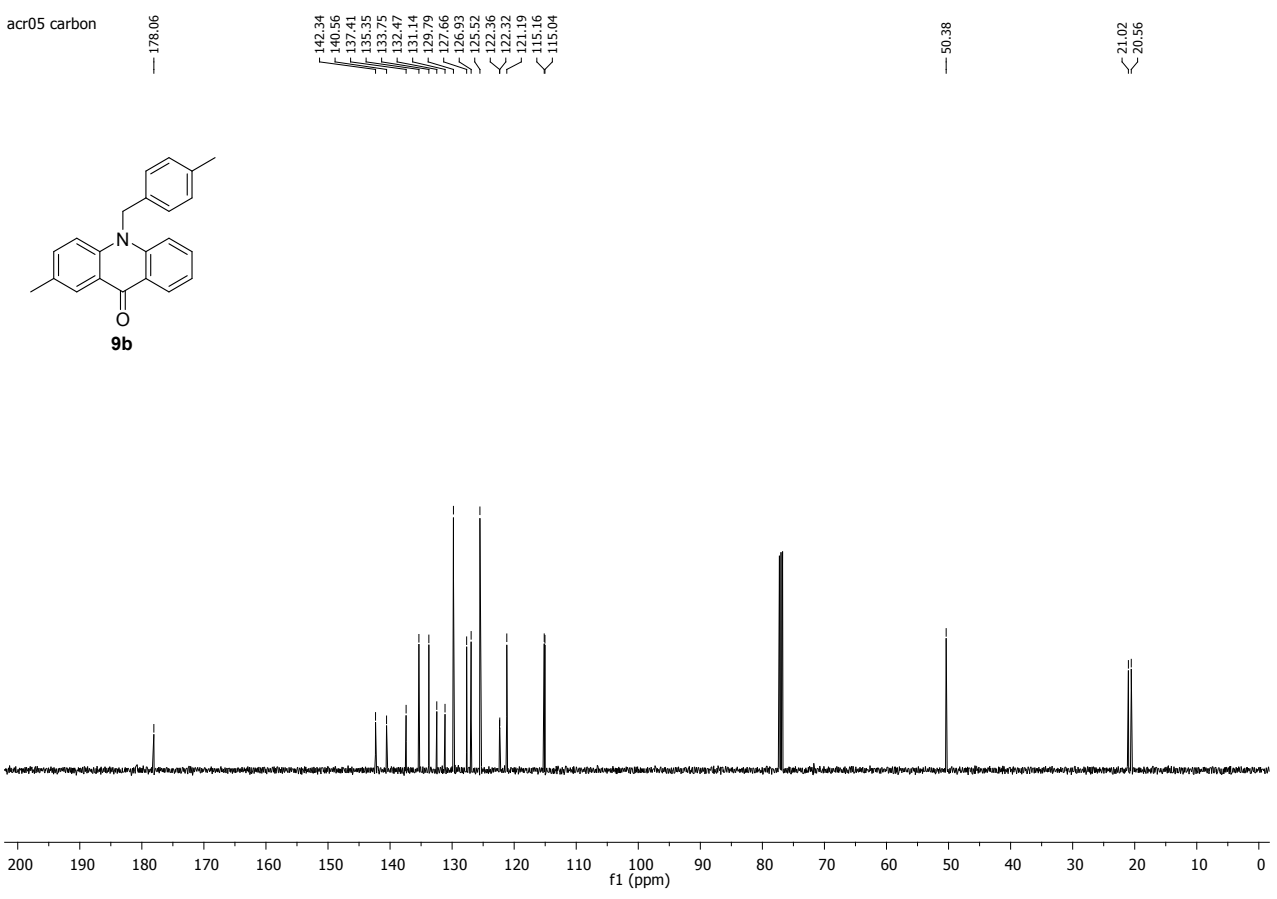
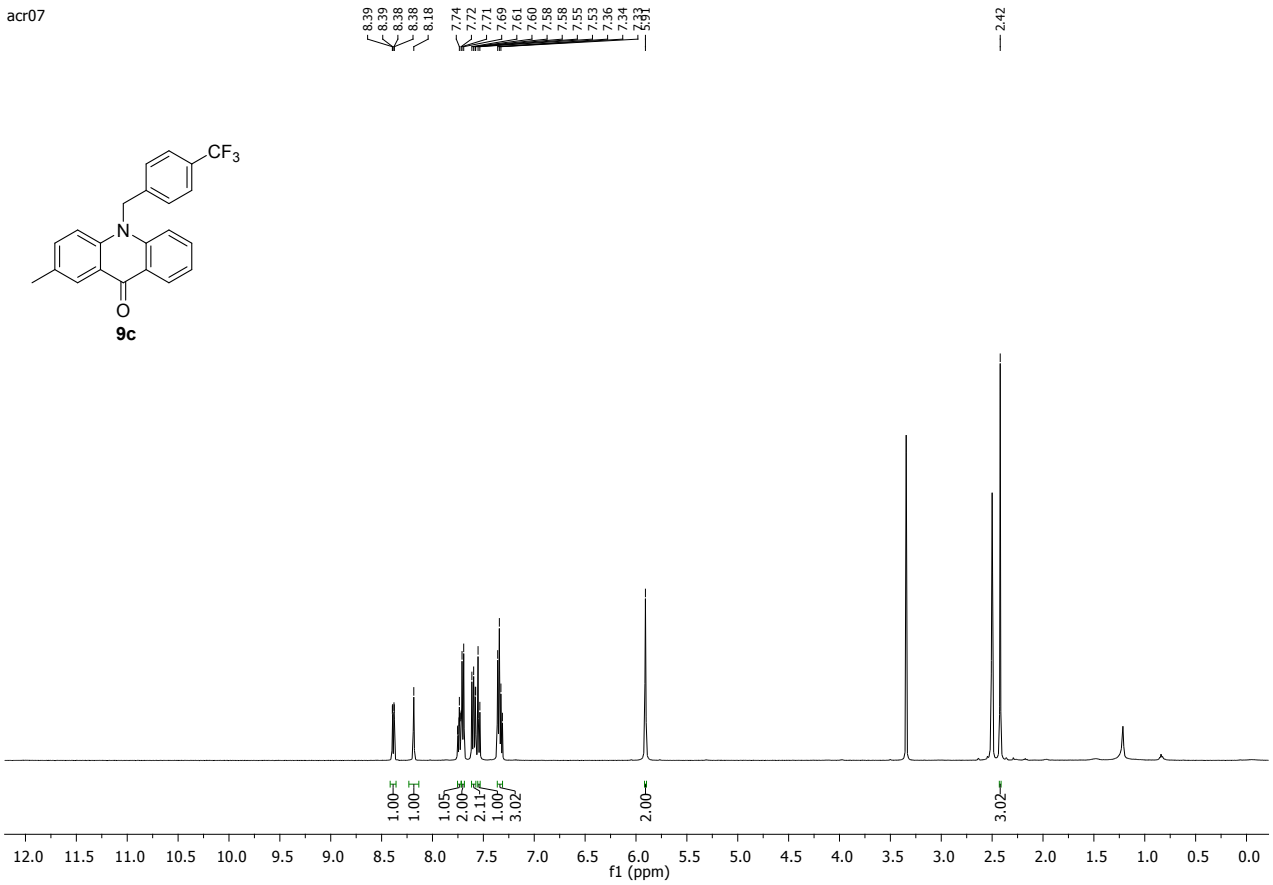
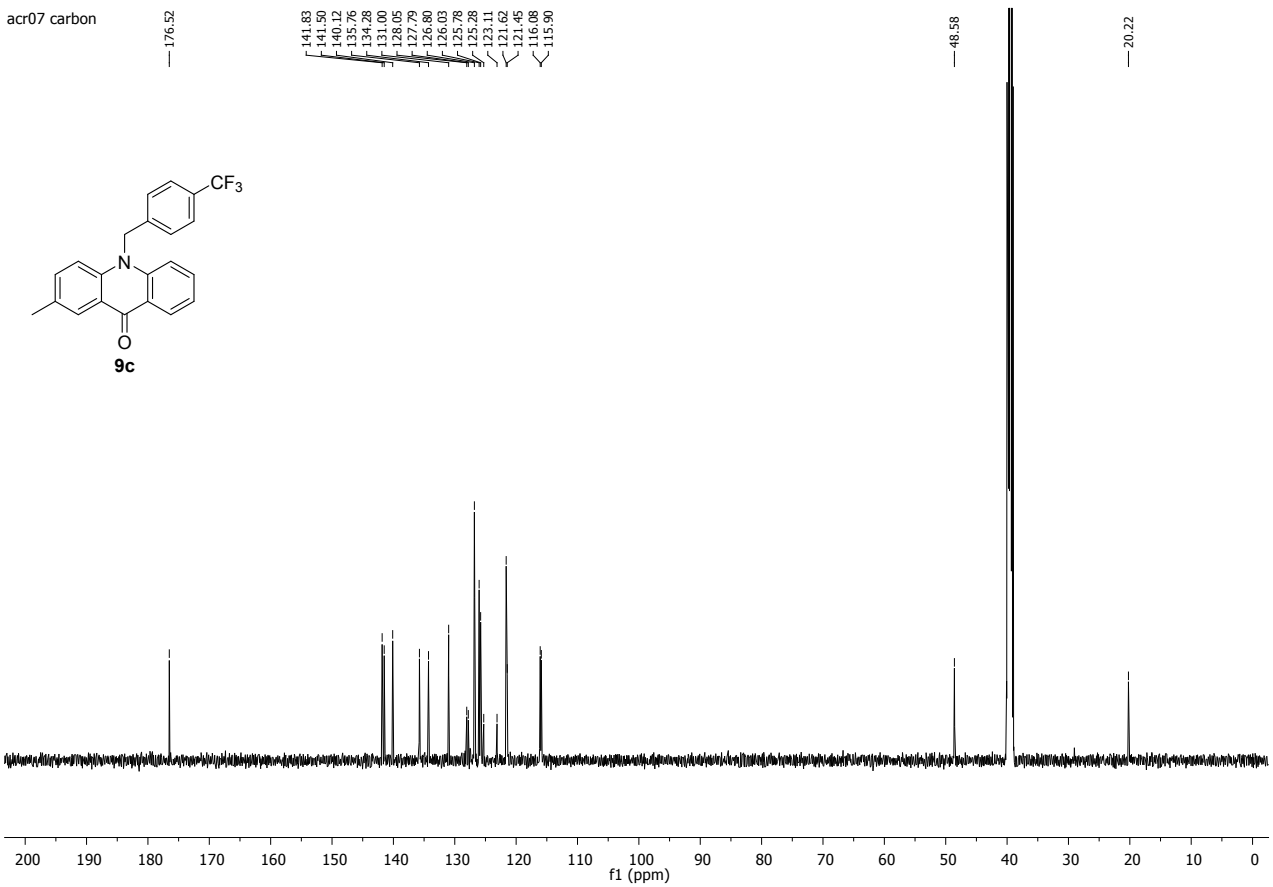
121.33
115.02
50.66
20.60
N
O
9a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

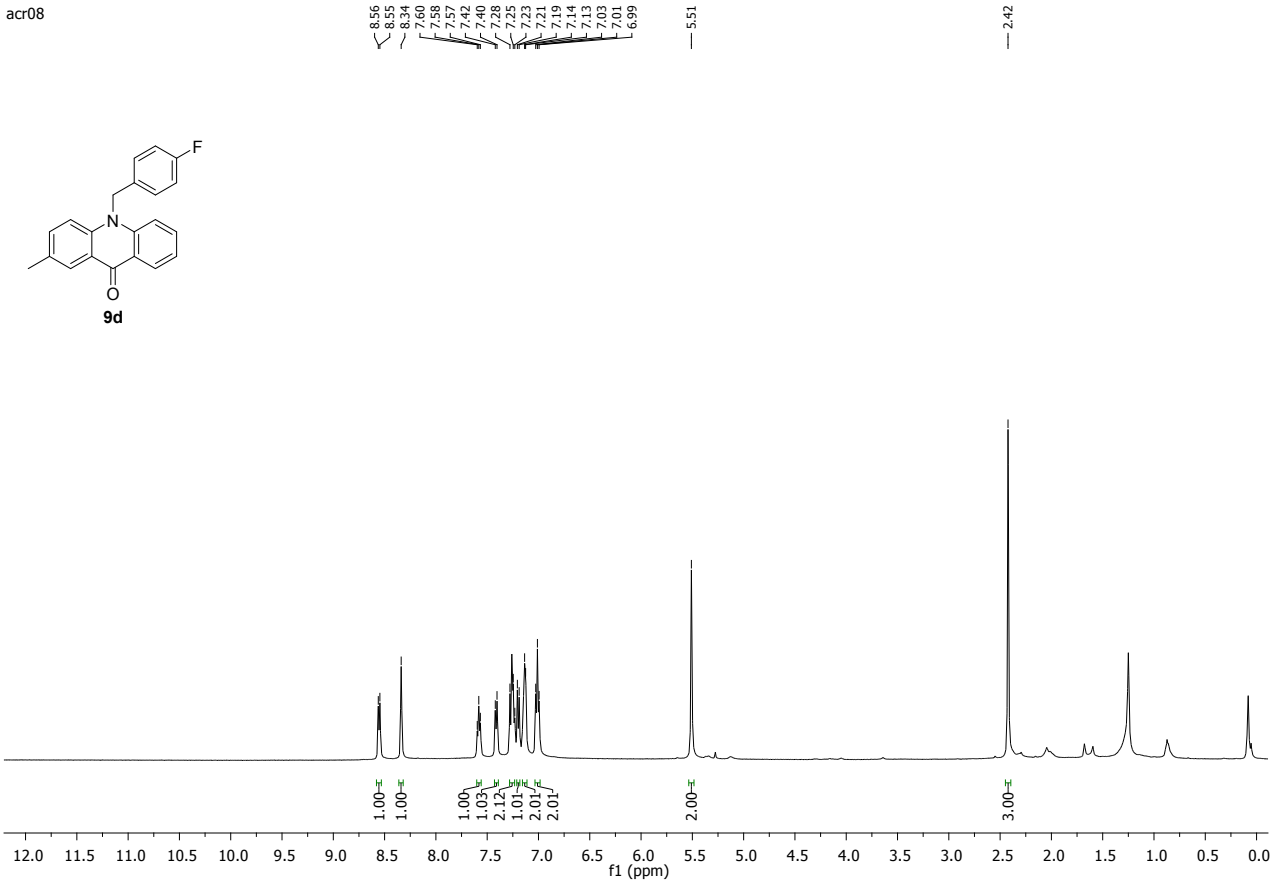

acr05
8.59
8.59
8.57
8.57
8.37
7.60
7.60
7.58
7.57
7.57
7.43
7.42
7.41
7.41
7.33
7.32
7.27
7.24
7.15
7.13
7.07
7.06
5.52
2.44
2.33
9b
1.00
1.00
1.03
1.00
1.00
2.08
2.03
2.01
2.00
3.02
3.00
f1 (ppm)


acr05 carbon
178.06
142.34
140.56
137.41
135.35
133.75
132.47
131.14
129.79
127.66
126.93
125.52
122.36
122.32
121.19
115.16
115.04
50.38
21.02
20.56
9b
f1 (ppm)


acr07
8.39
8.39
8.38
8.38
8.18
7.74
7.72
7.71
7.69
7.61
7.60
7.58
7.58
7.55
7.53
7.36
7.34
7.33
7.31
2.42
CF3
N
O
9c
1.00
1.00
1.05
2.00
2.11
1.00
3.02
2.00
3.02
12.0 11.5 11.0 10.5 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)

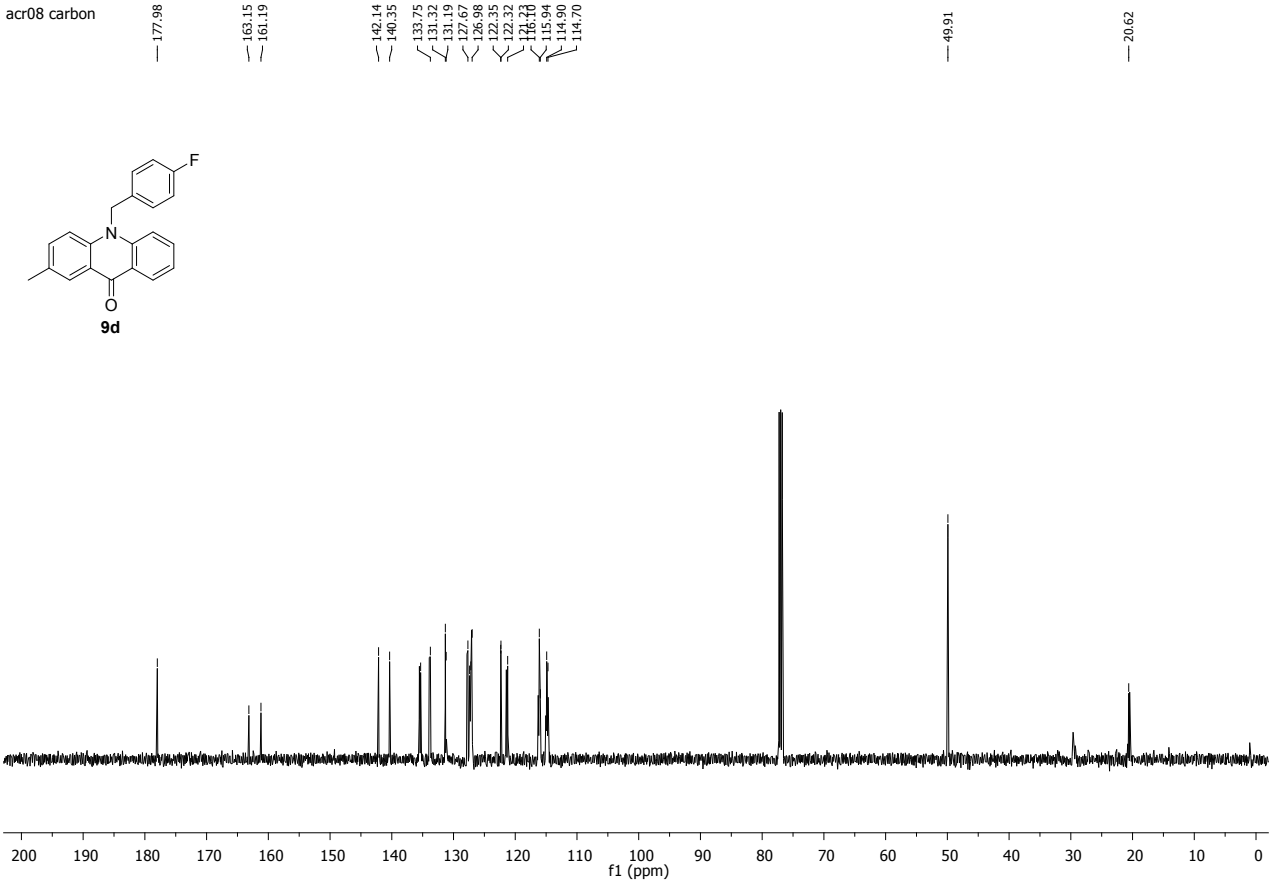

acr07 carbon
176.52
141.83
141.50
140.12
135.76
134.28
131.00
128.05
127.79
126.80
126.03
125.78
125.28
123.11
121.62
121.45
116.08
115.90
48.58
20.22
CF3
N
O
9c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

acr08

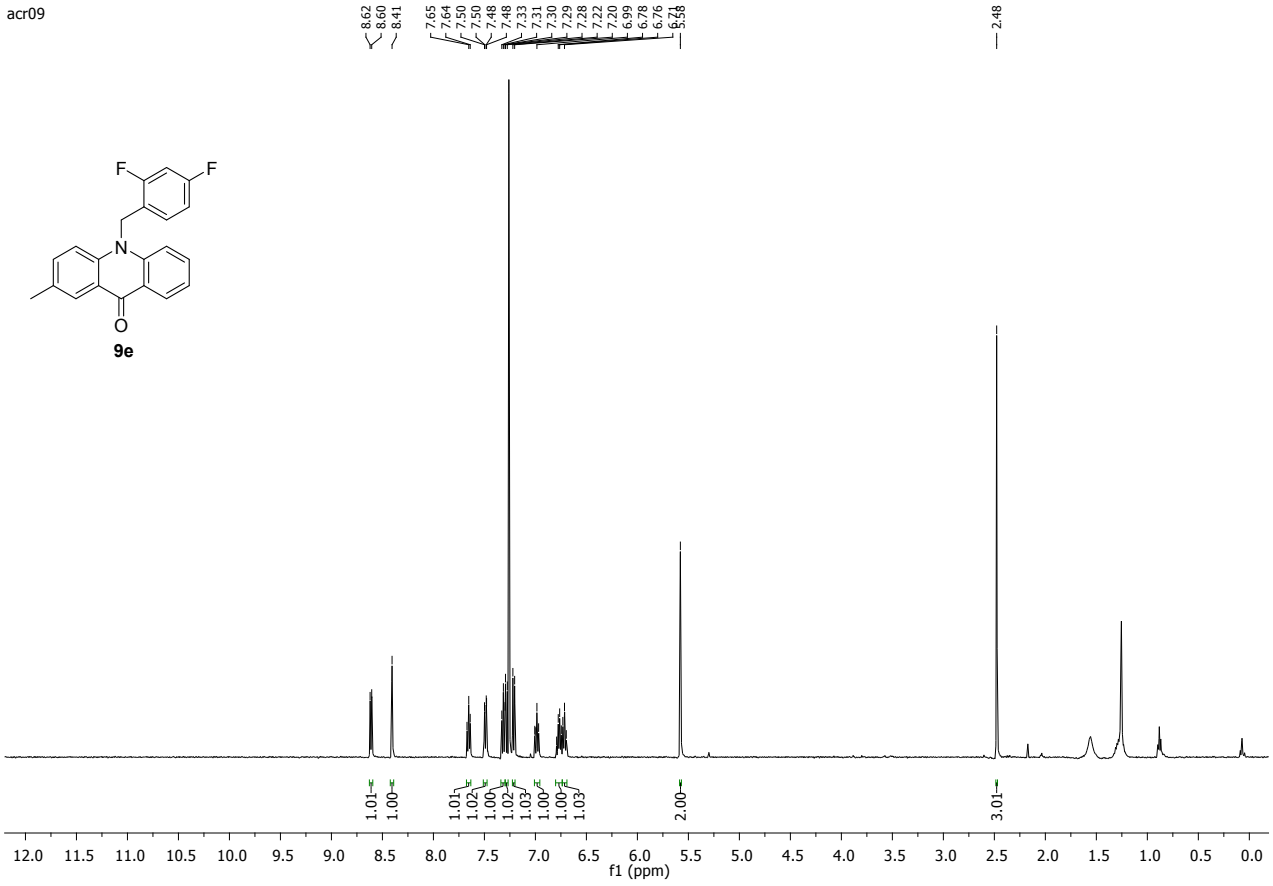


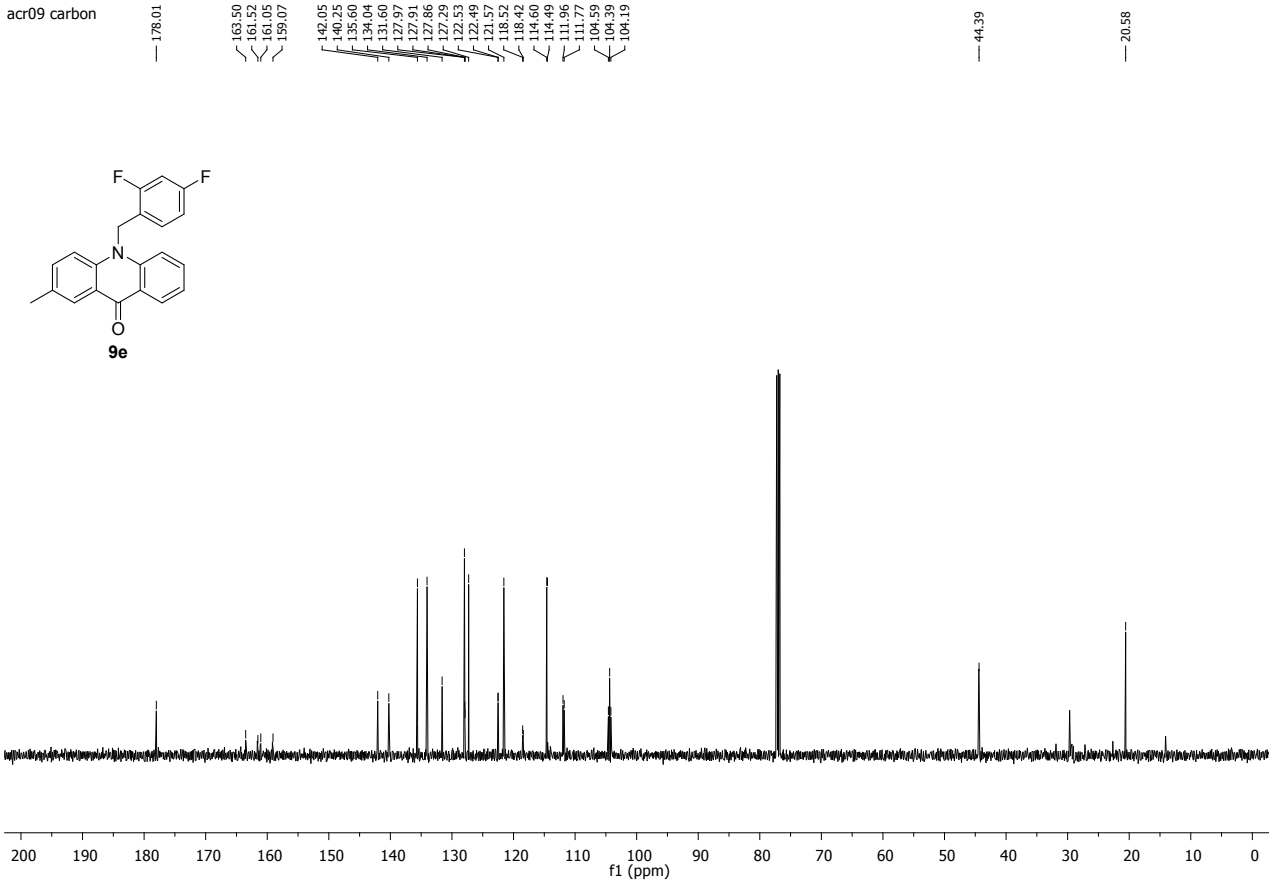
9d

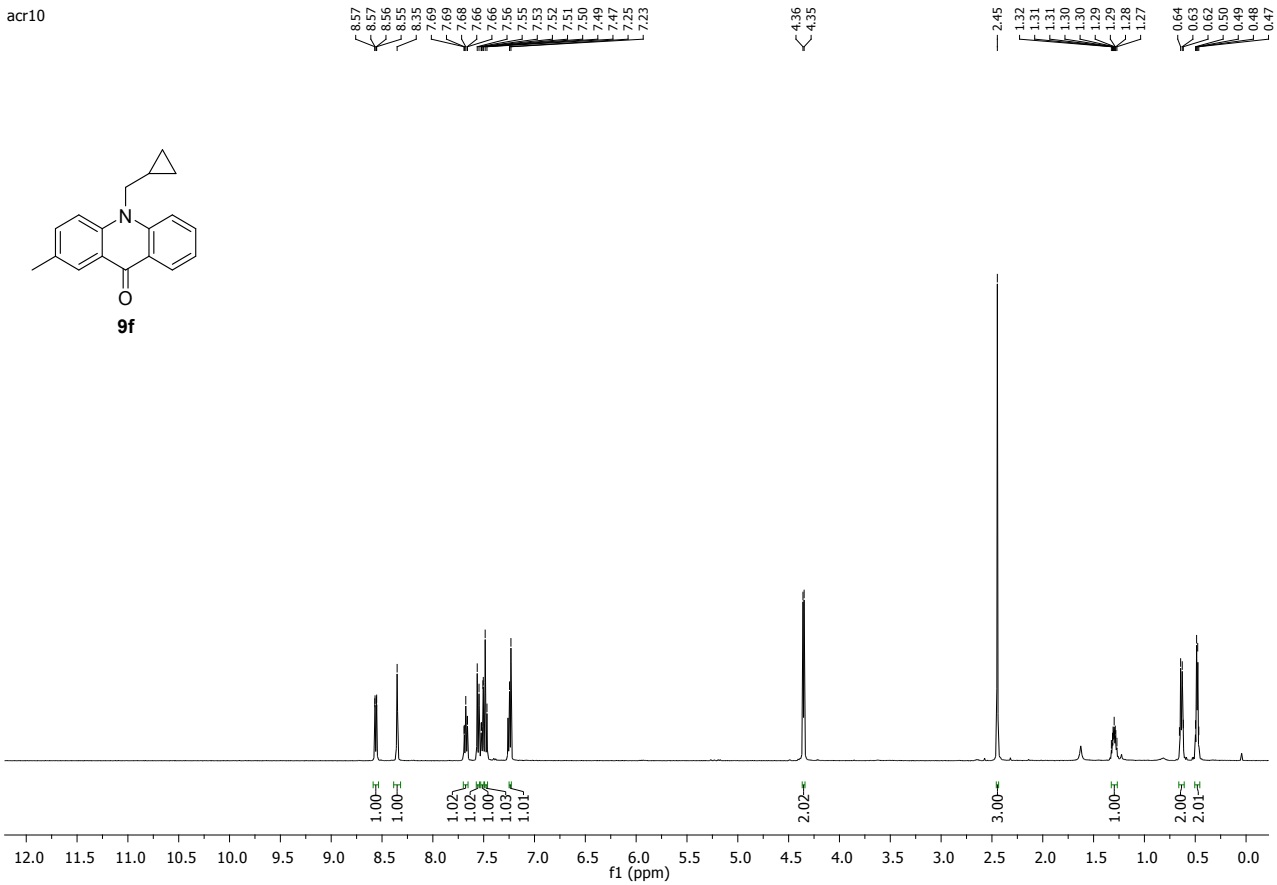
acr08 carbon

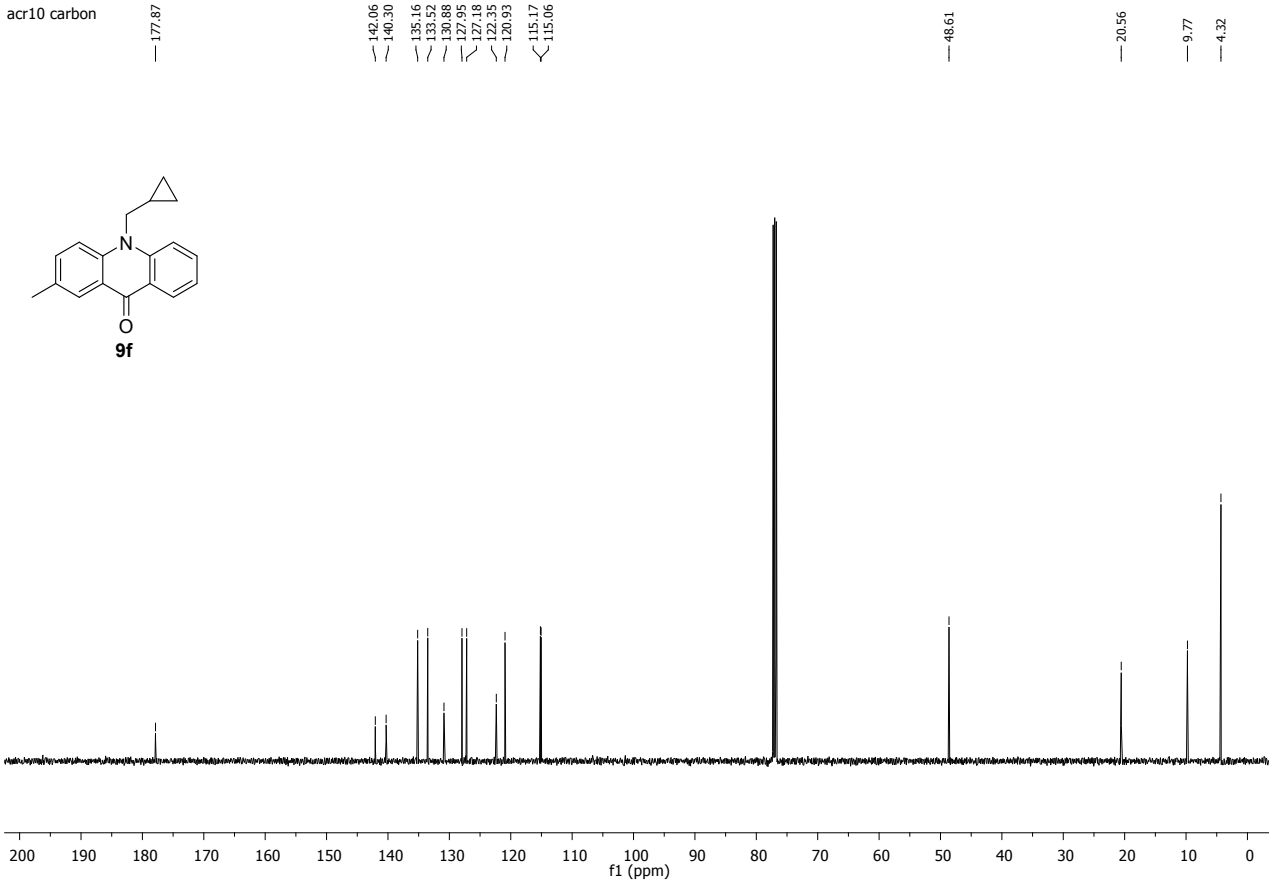


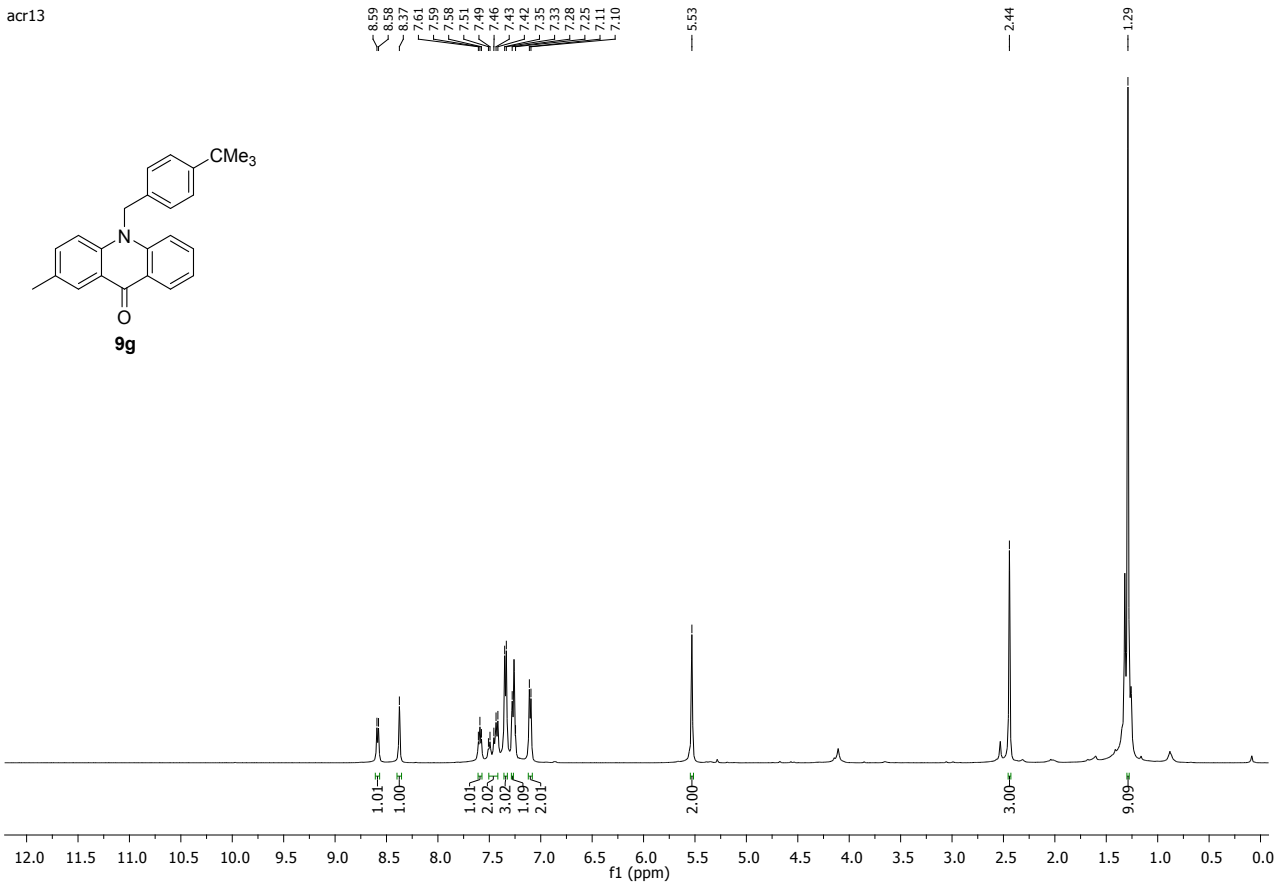
9d

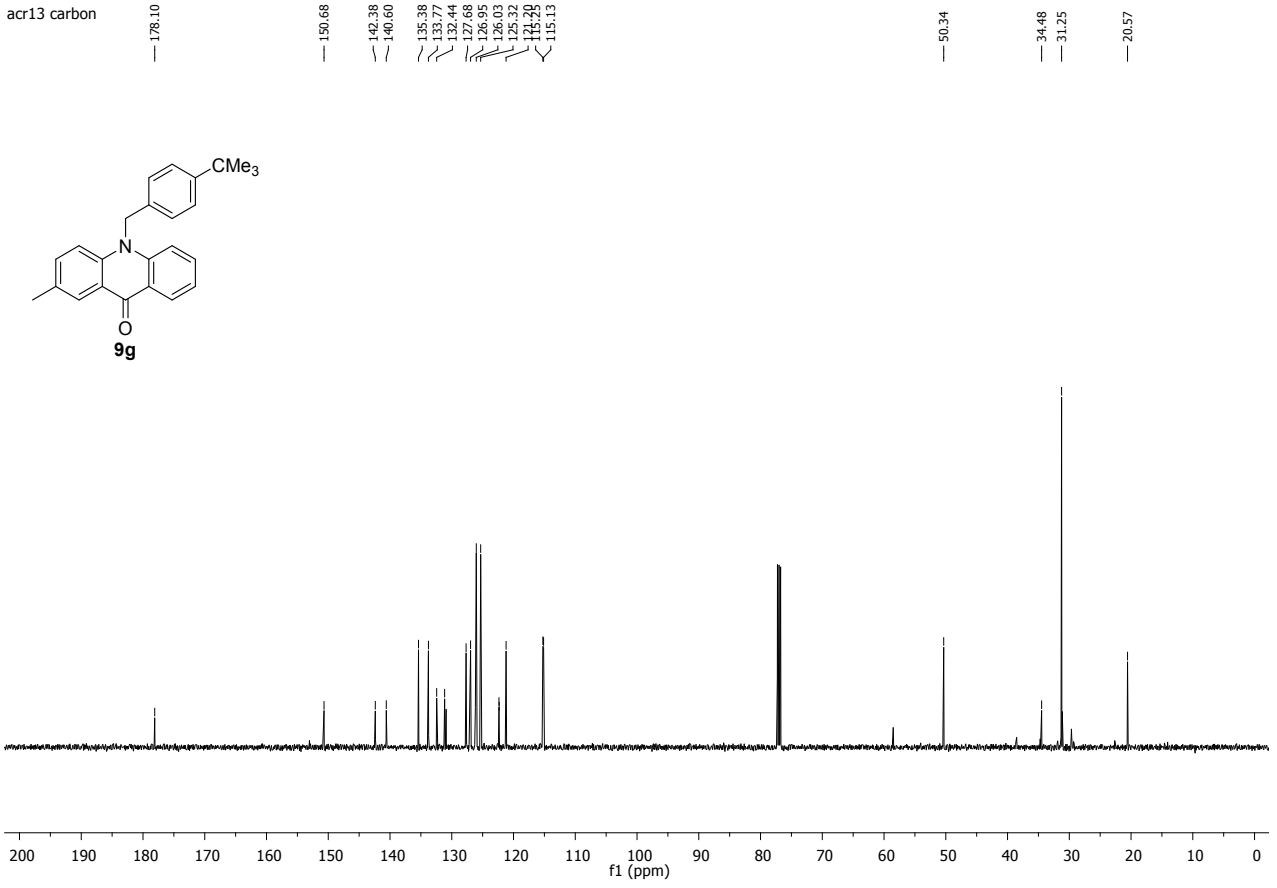

acr09
8.62
8.60
8.41
7.65
7.64
7.50
7.50
7.48
7.48
7.33
7.31
7.30
7.29
7.28
7.22
7.20
6.99
6.78
6.76
6.71
6.58
2.48
F
F
N
O
9e
1.01
1.00
1.01
1.02
1.00
1.02
1.03
1.00
1.00
1.03
2.00
3.01
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

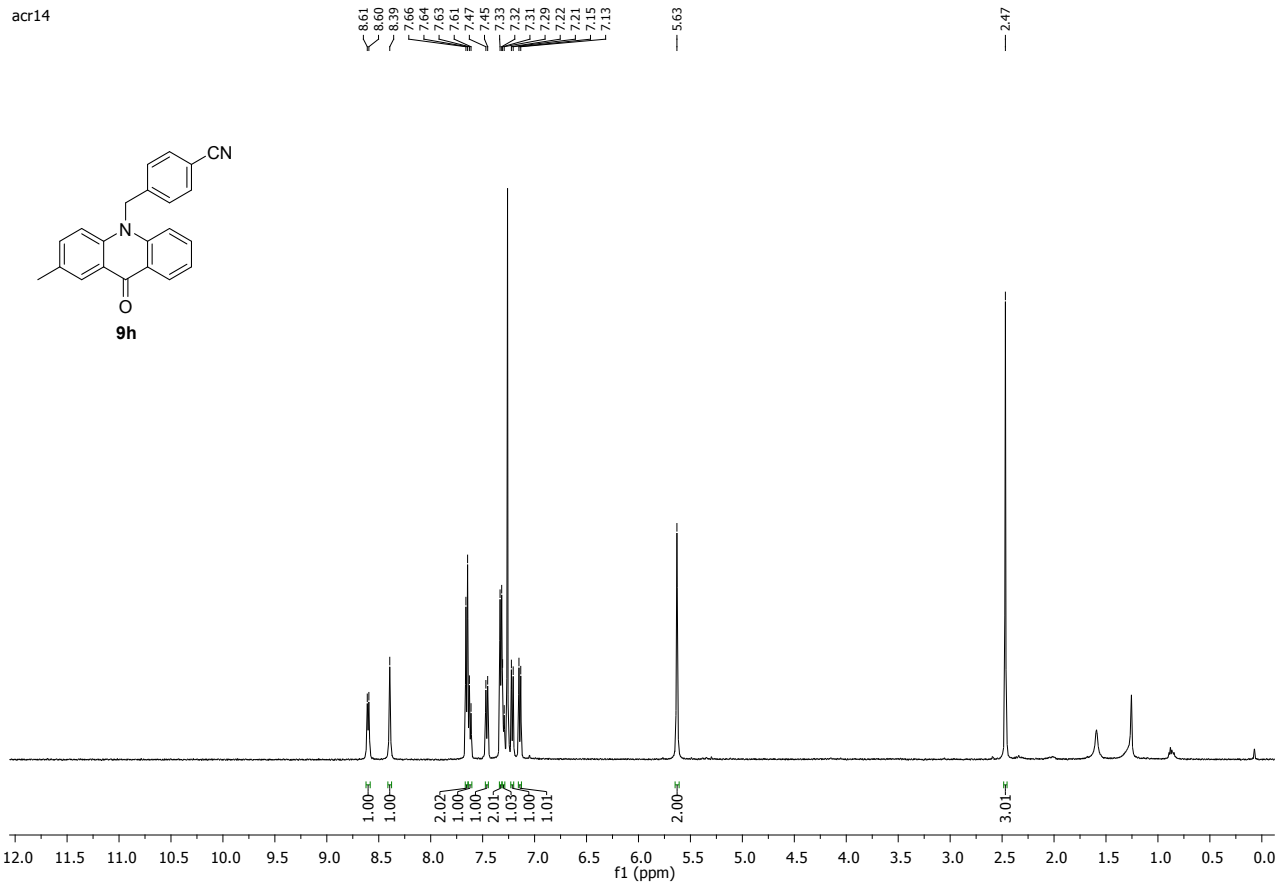

acr09 carbon
178.01
163.50
161.52
161.05
159.07
142.05
140.25
135.60
134.04
131.60
127.97
127.91
127.86
127.29
122.53
122.49
121.57
118.52
118.42
114.60
114.49
111.96
111.77
104.59
104.39
104.19
44.39
20.58
F
F
N
O
9e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

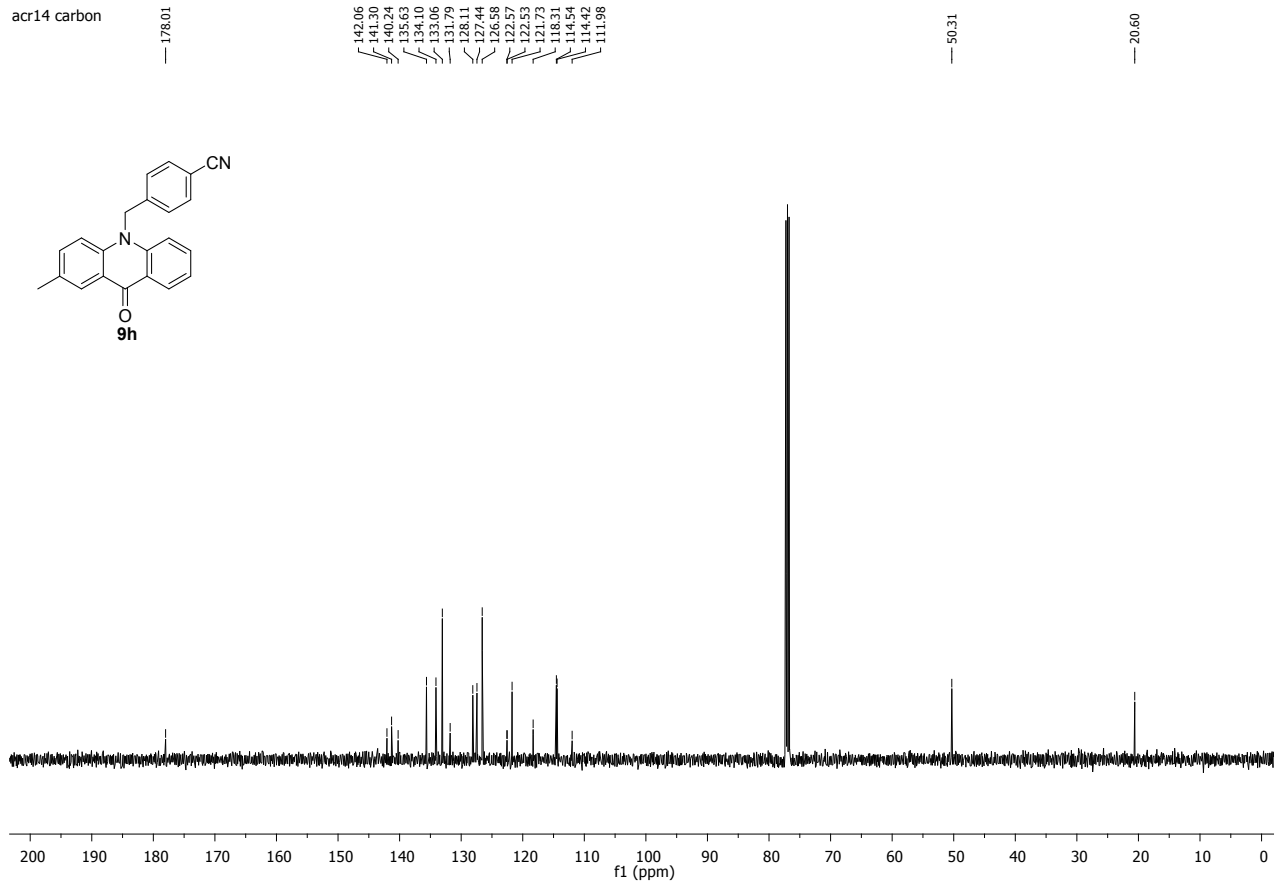

acr10
8.57
8.57
8.56
8.55
8.35
7.69
7.69
7.68
7.66
7.66
7.56
7.55
7.53
7.52
7.51
7.50
7.49
7.47
7.25
7.23
4.36
4.35
2.45
1.32
1.31
1.31
1.30
1.30
1.29
1.29
1.28
1.27
0.64
0.63
0.62
0.50
0.49
0.48
0.47
N
O
9f
1.00
1.00
1.02
1.02
1.00
1.03
1.01
2.02
3.00
1.00
2.00
2.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 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)

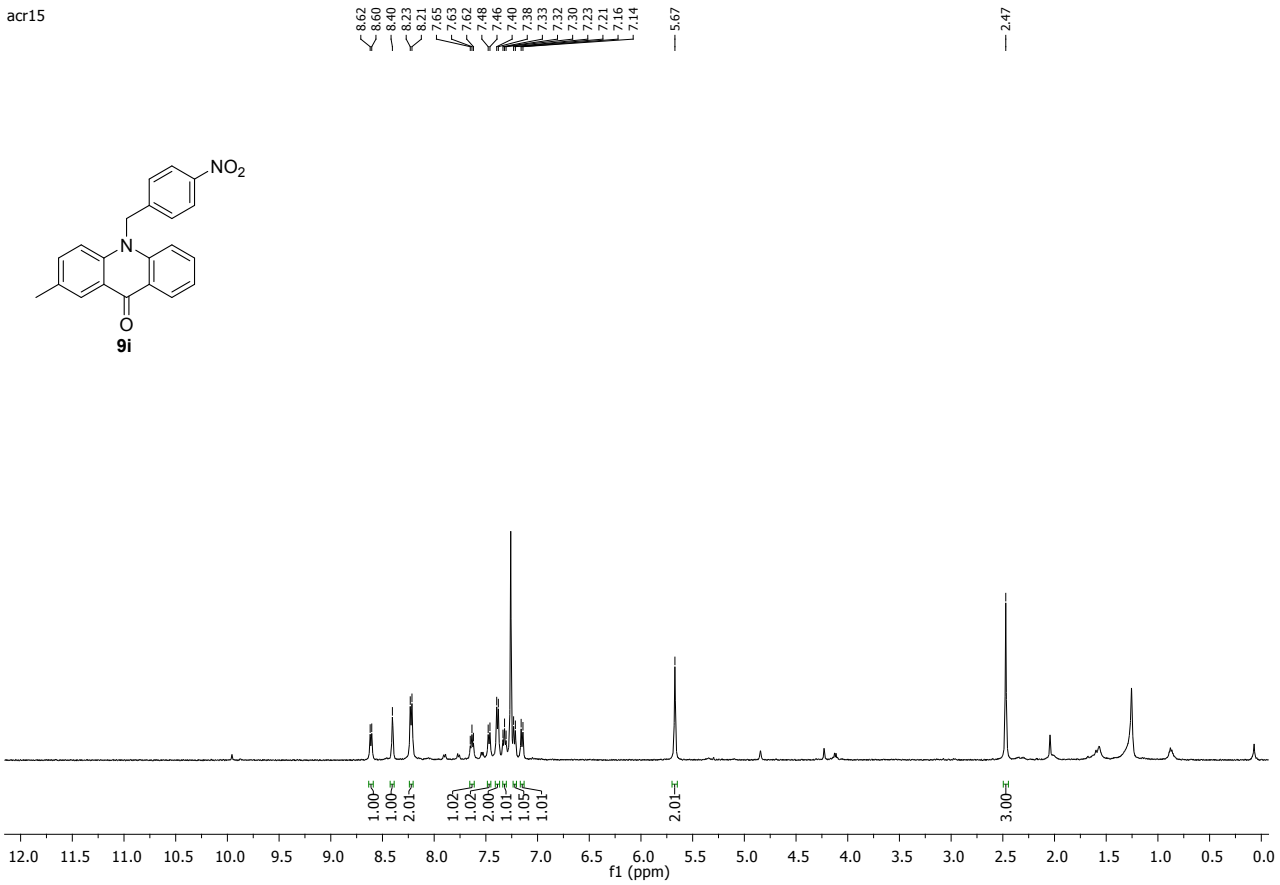

acr10 carbon
177.87
142.06
140.30
135.16
133.52
130.88
127.95
127.18
122.35
120.93
115.17
115.06
48.61
20.56
9.77
4.32
N
O
9f
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

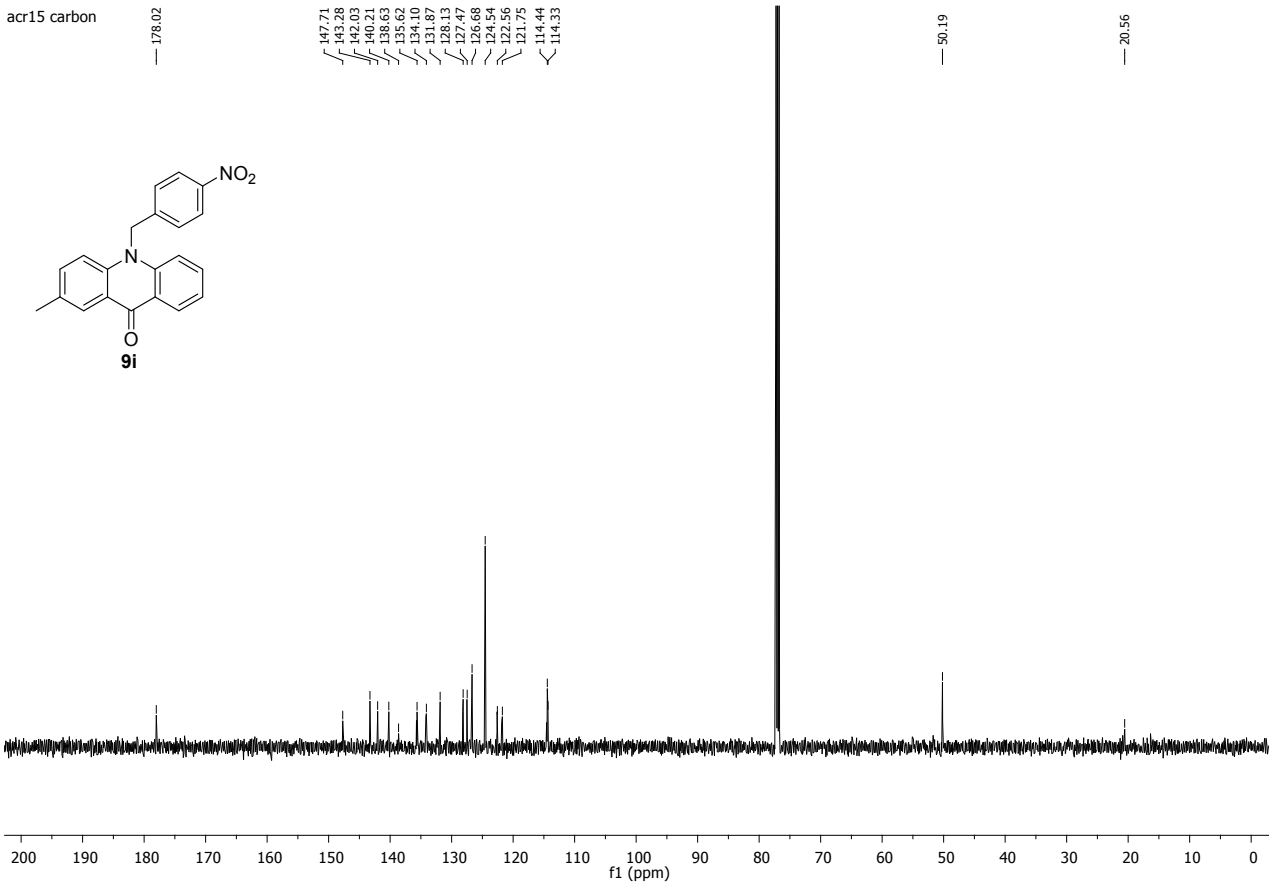

acr13
8.59
8.58
8.37
7.61
7.59
7.58
7.51
7.49
7.46
7.43
7.42
7.35
7.33
7.28
7.25
7.11
7.10
5.53
2.44
1.29
CMe3
N
O
9g
1.01
1.00
1.01
2.02
3.02
1.09
2.01
2.00
3.00
9.09
f1 (ppm)


acr13 carbon
178.10
150.68
142.38
140.60
135.38
133.77
132.44
127.68
126.95
126.03
125.32
121.20
115.25
115.13
50.34
34.48
31.25
20.57
CMe3
N
O
9g
f1 (ppm)

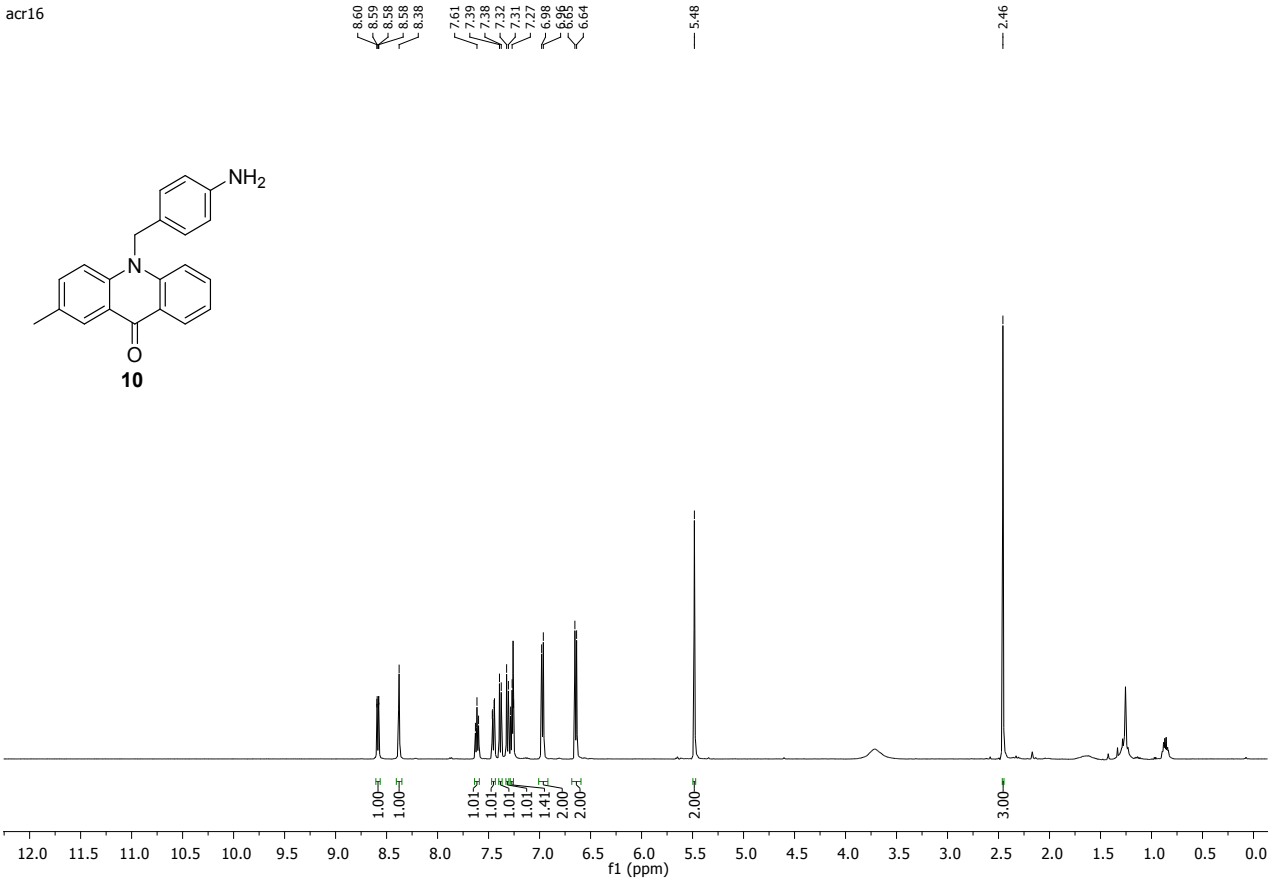

acr14
8.61
8.60
8.39
7.66
7.64
7.63
7.61
7.47
7.45
7.33
7.32
7.31
7.29
7.22
7.21
7.15
7.13
5.63
2.47
CN
N
O
9h
1.00
1.00
2.02
1.00
1.00
2.01
1.03
1.00
1.01
2.00
3.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


acr14 carbon
178.01
142.06
141.30
140.24
135.63
134.10
133.06
131.79
128.11
127.44
126.58
122.57
122.53
121.73
118.31
114.54
114.42
111.98
50.31
20.60
CN
N
O
9h
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

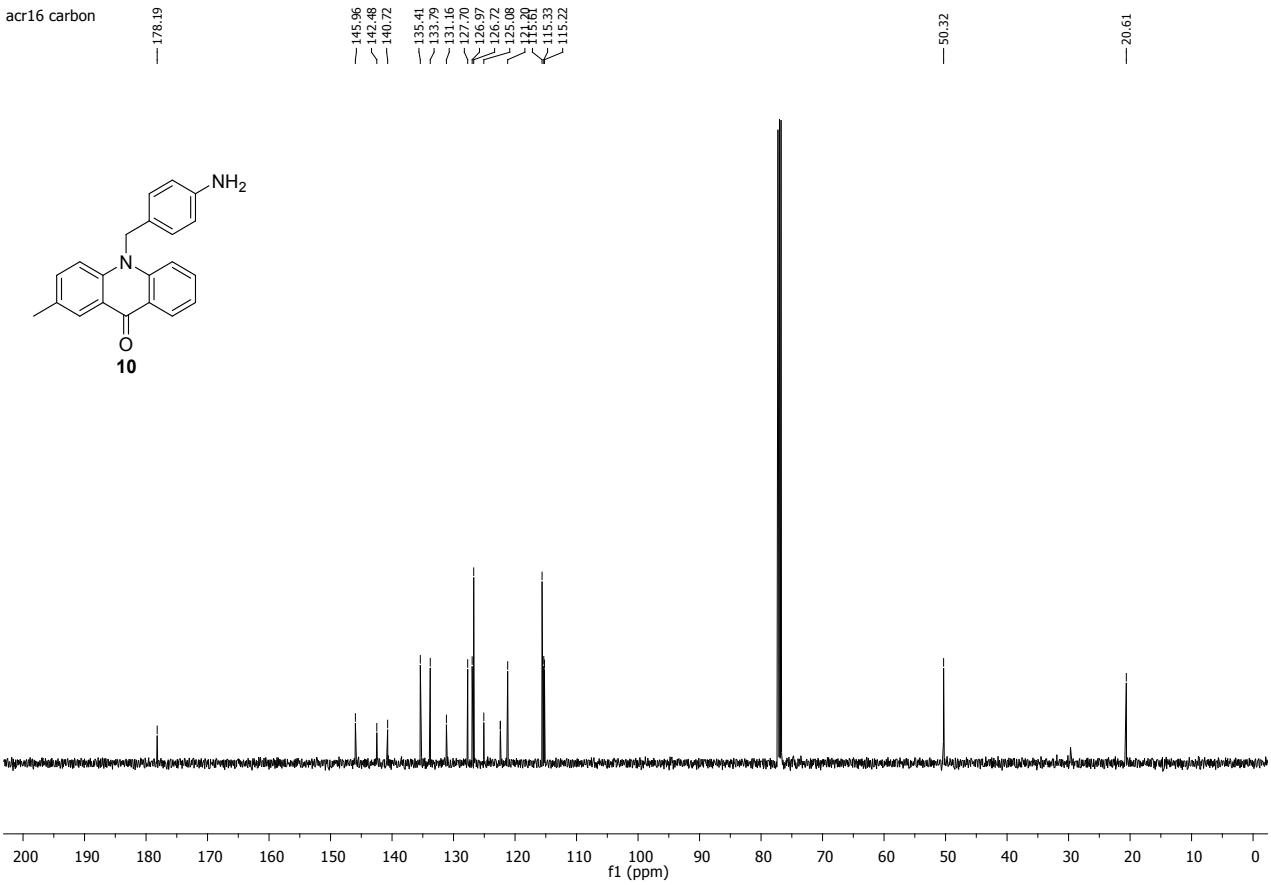

acr15
8.62
8.60
8.40
8.23
8.21
7.65
7.63
7.62
7.48
7.46
7.40
7.38
7.33
7.32
7.30
7.23
7.21
7.16
7.14
5.67
2.47
NO2
N
O
9i
1.00
1.00
2.01
1.02
1.02
2.00
1.01
1.05
1.01
2.01
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


acr15 carbon
178.02
147.71
145.28
142.03
140.21
138.63
135.62
134.10
131.87
128.13
127.47
126.68
124.54
122.56
121.75
114.44
114.33
50.19
20.56
NO2
N
O
9i
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

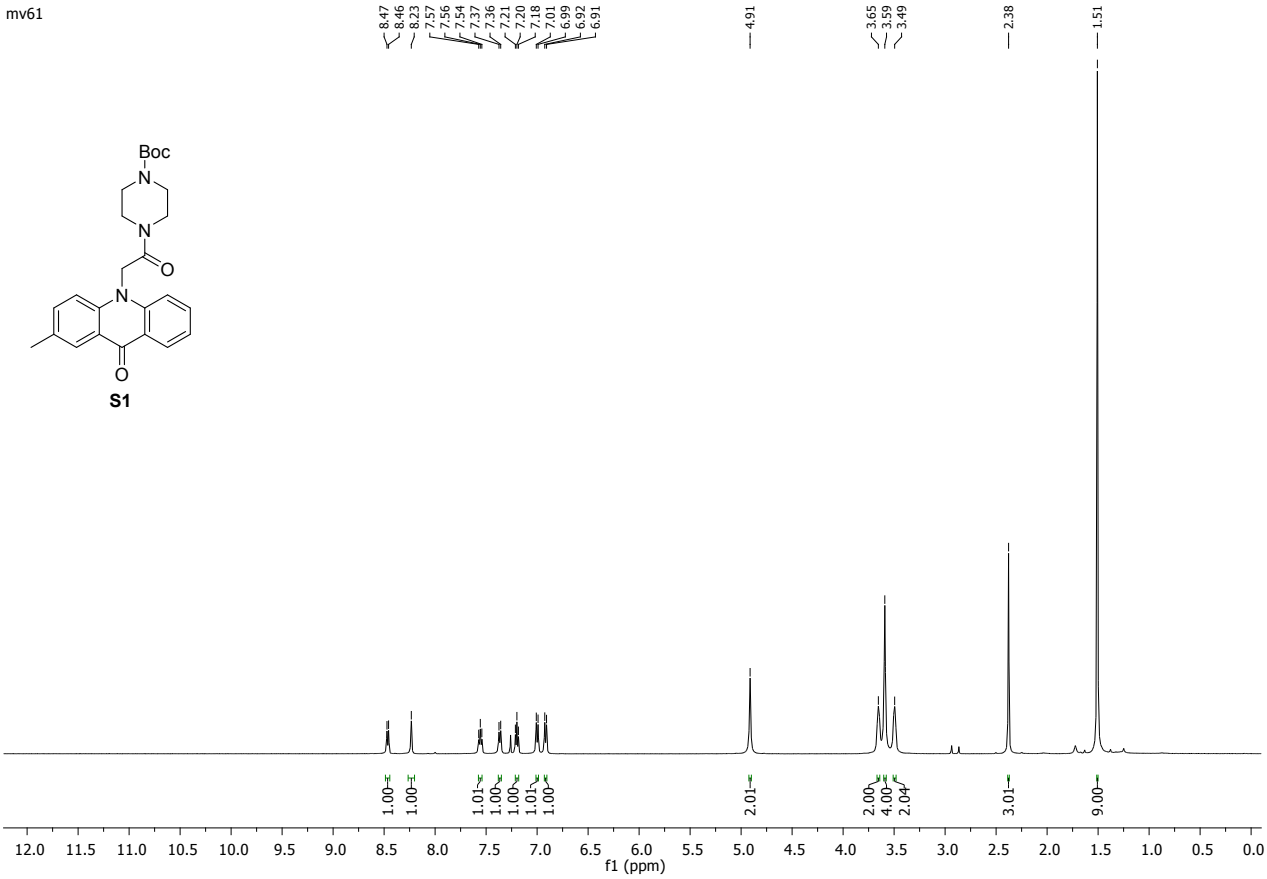
acr16



acr16 carbon

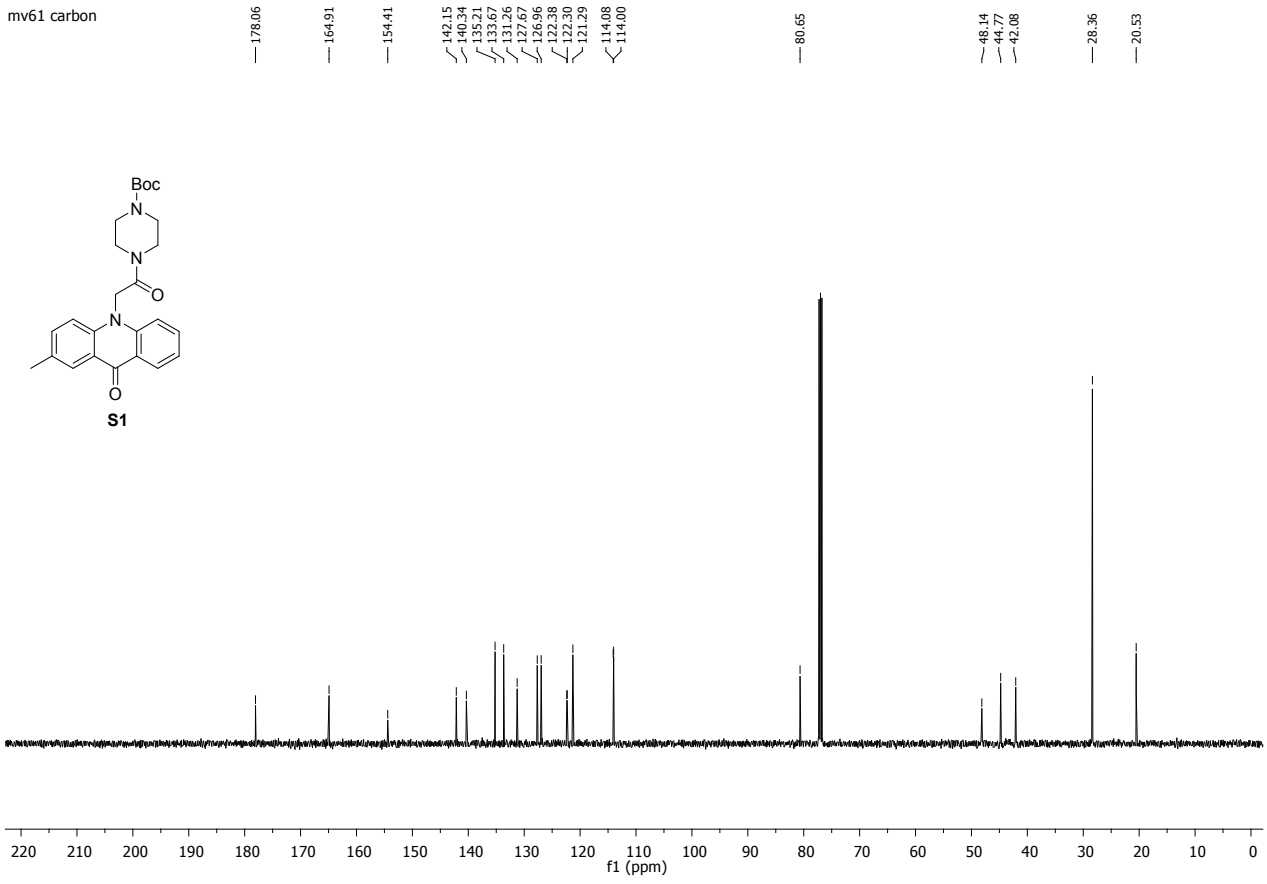


mv61

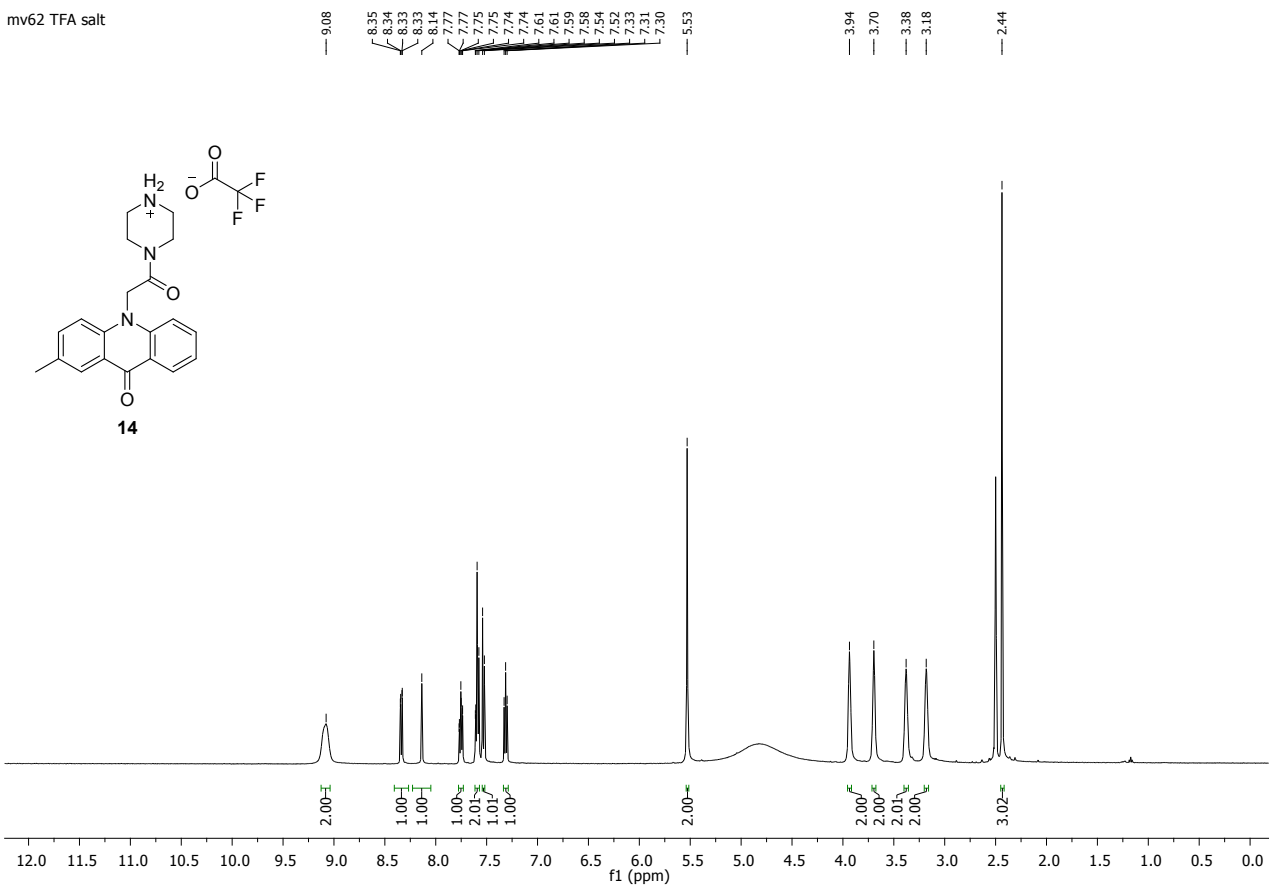


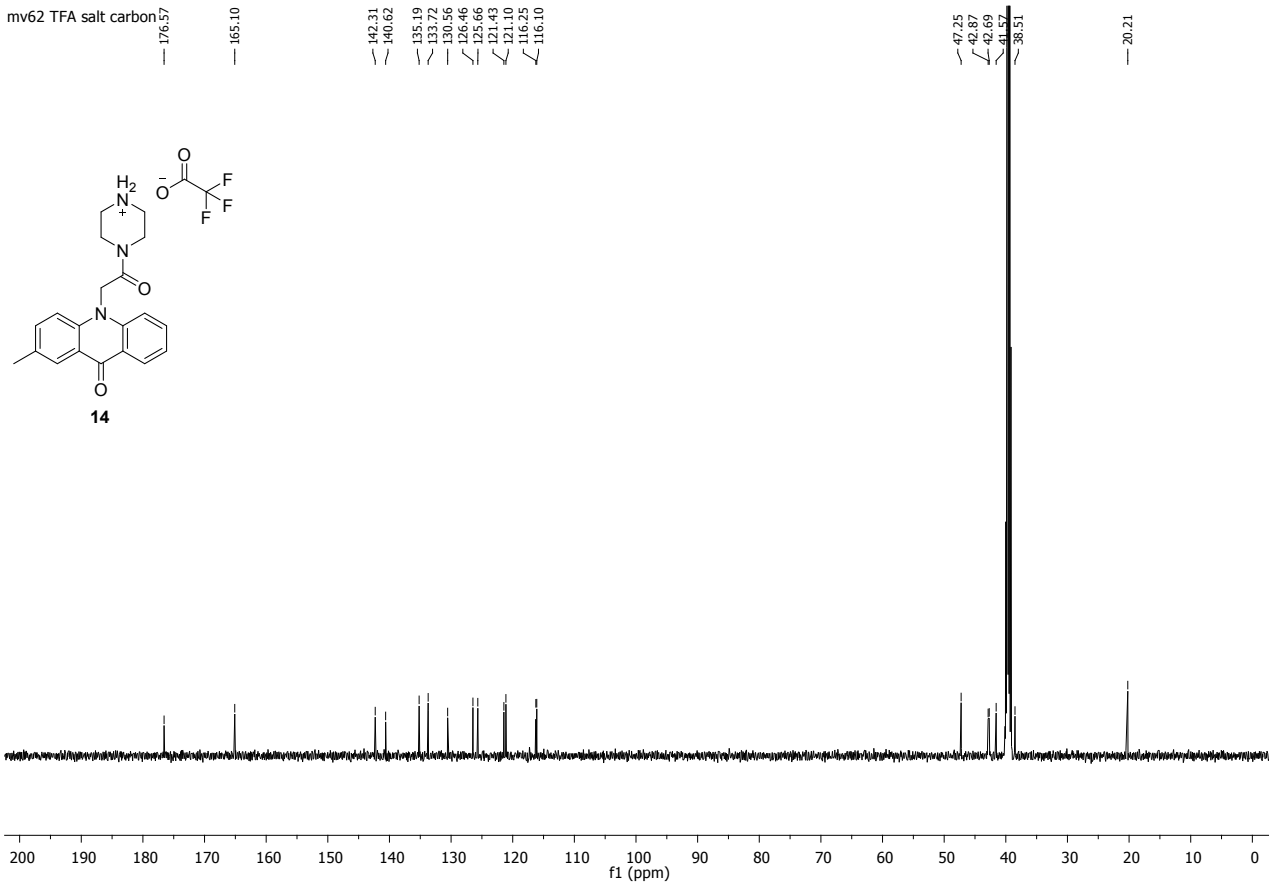
S1

mv61 carbon

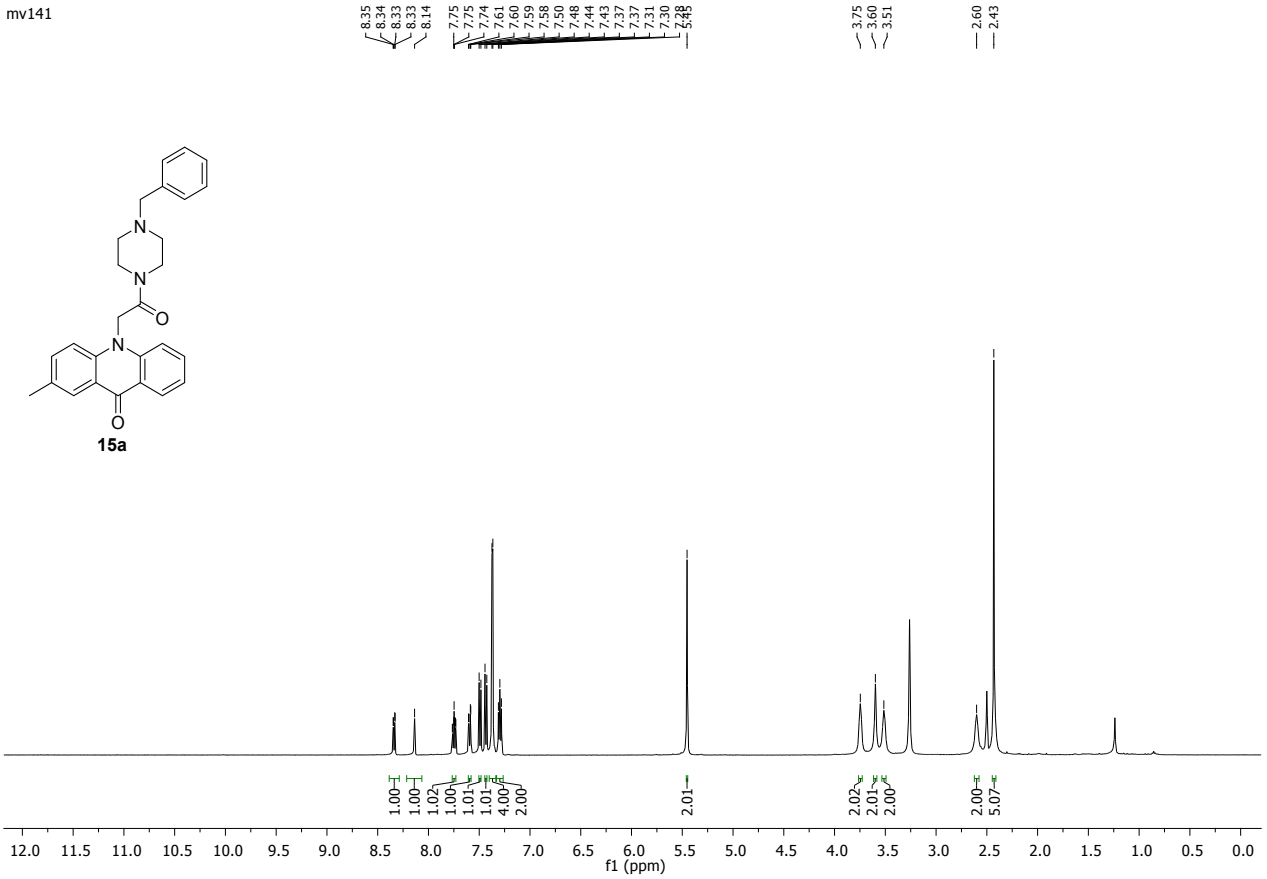


S1


mv62 TFA salt
9.08
8.35
8.34
8.33
8.33
8.14
7.77
7.77
7.75
7.75
7.74
7.74
7.61
7.61
7.59
7.58
7.54
7.52
7.33
7.31
7.30
5.53
3.94
3.70
3.38
3.18
2.44
14
2.00
1.00
1.00
1.00
2.01
1.01
1.00
2.00
2.00
2.00
2.01
2.00
3.02
f1 (ppm)

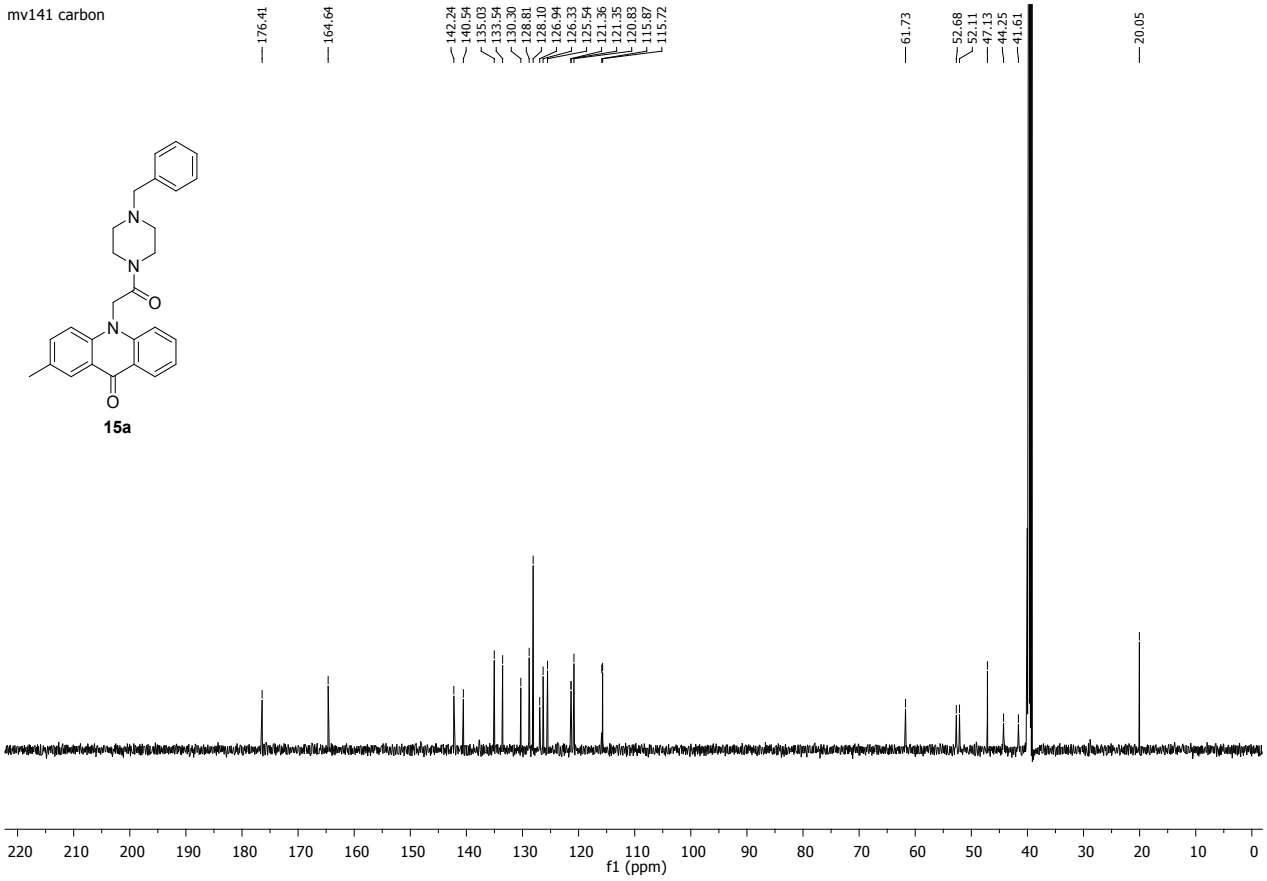

mv62 TFA salt carbon
176.57
165.10
142.31
140.62
135.19
133.72
130.56
126.46
125.66
121.43
121.10
116.25
116.10
47.25
42.87
42.69
41.57
38.51
20.21
14
f1 (ppm)

mv141

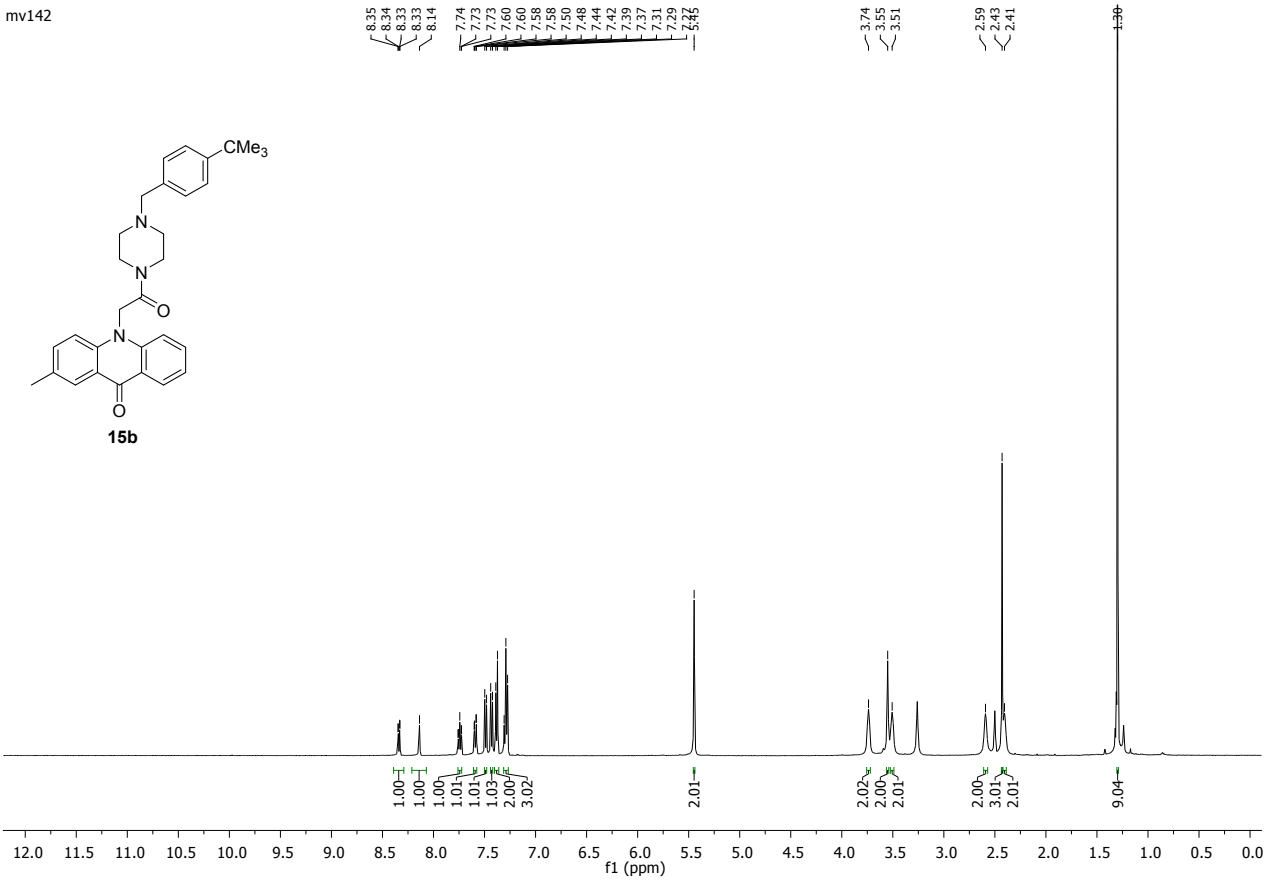


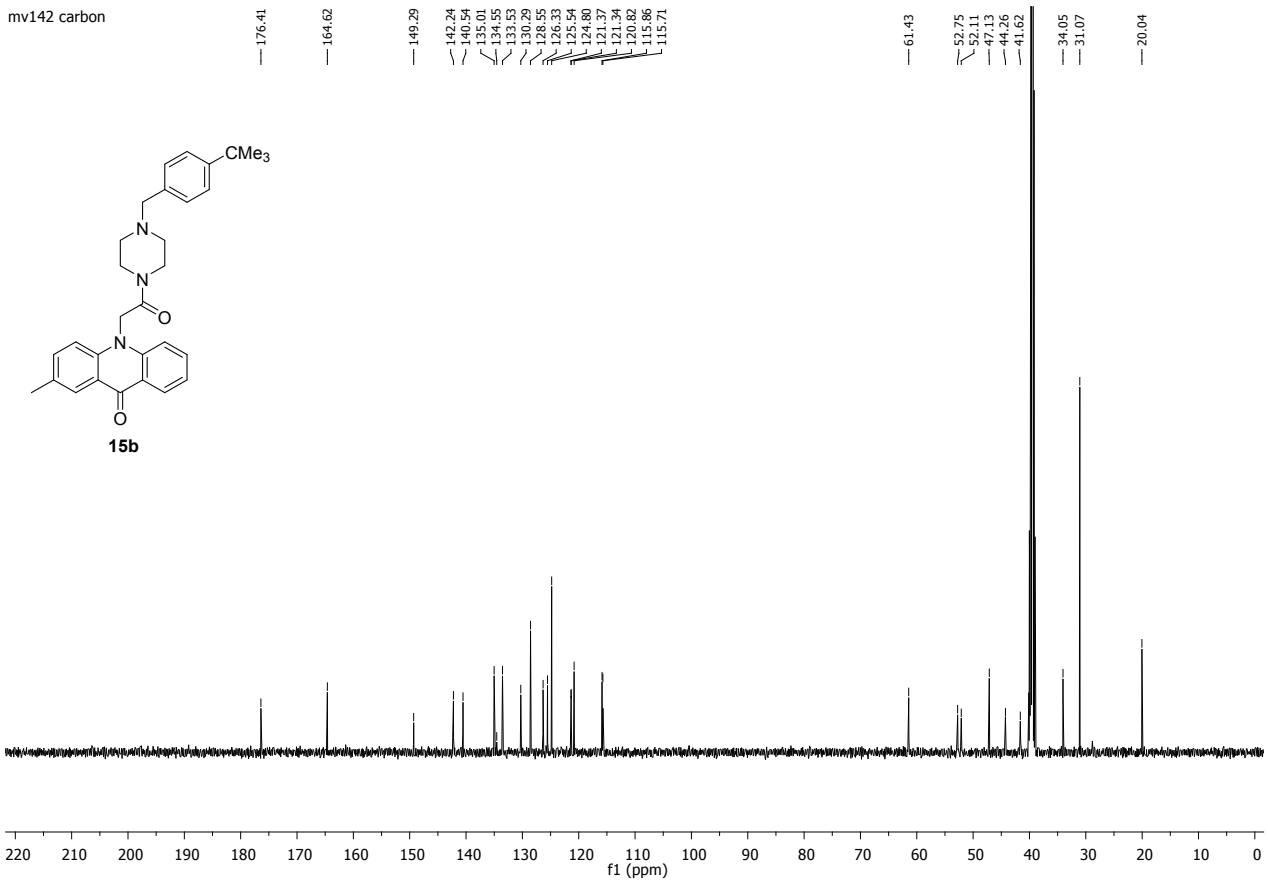
15a

mv141 carbon

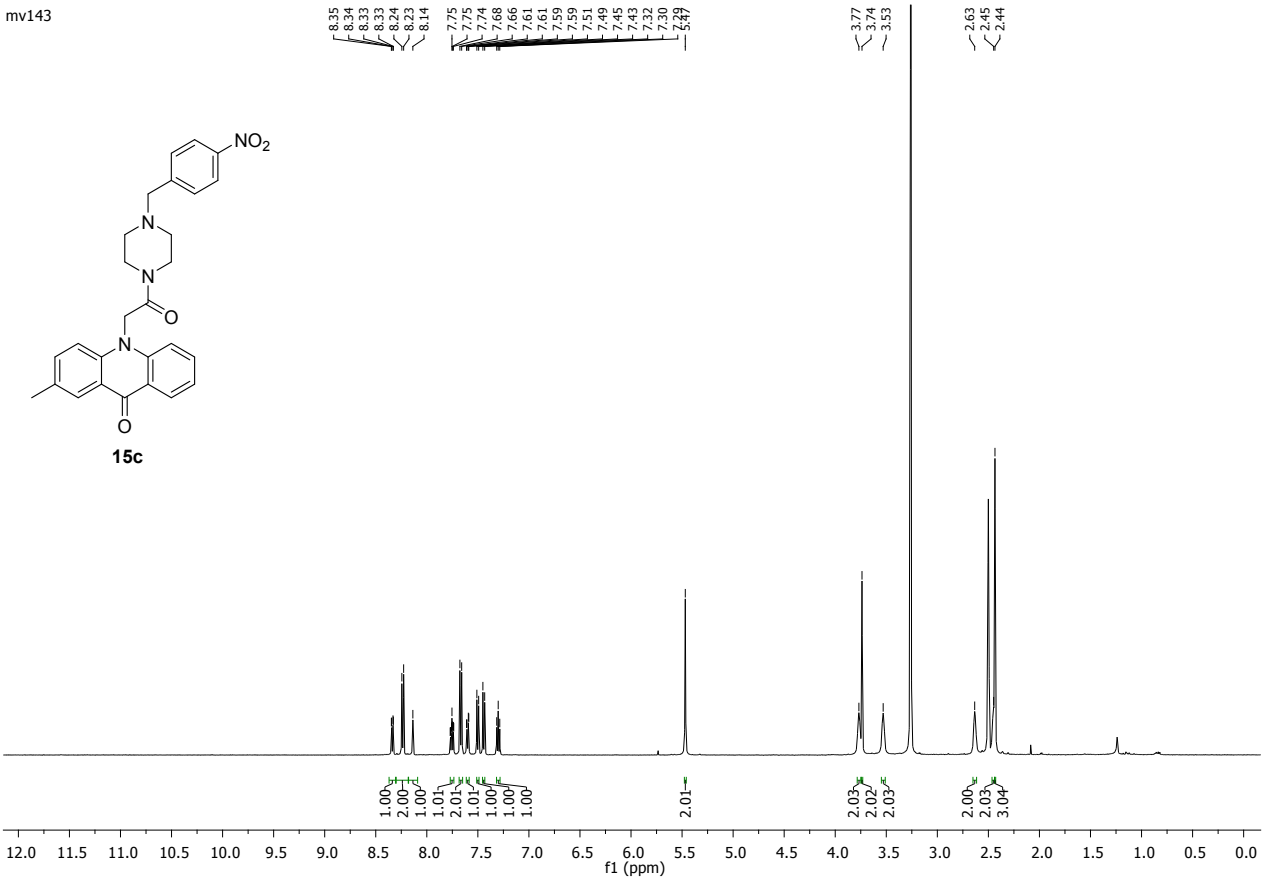


15a


mv142
8.35
8.34
8.33
8.33
8.14
7.74
7.73
7.73
7.60
7.60
7.58
7.58
7.50
7.48
7.44
7.42
7.39
7.37
7.31
7.29
7.27
5.45
3.74
3.55
3.51
2.59
2.43
2.41
1.30
CMe3
N
N
O
N
O
15b
1.00
1.00
1.00
1.01
1.01
1.03
2.00
3.02
2.01
2.02
2.00
2.01
2.00
3.01
2.01
9.04
12.0
11.5
11.0
10.5
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)

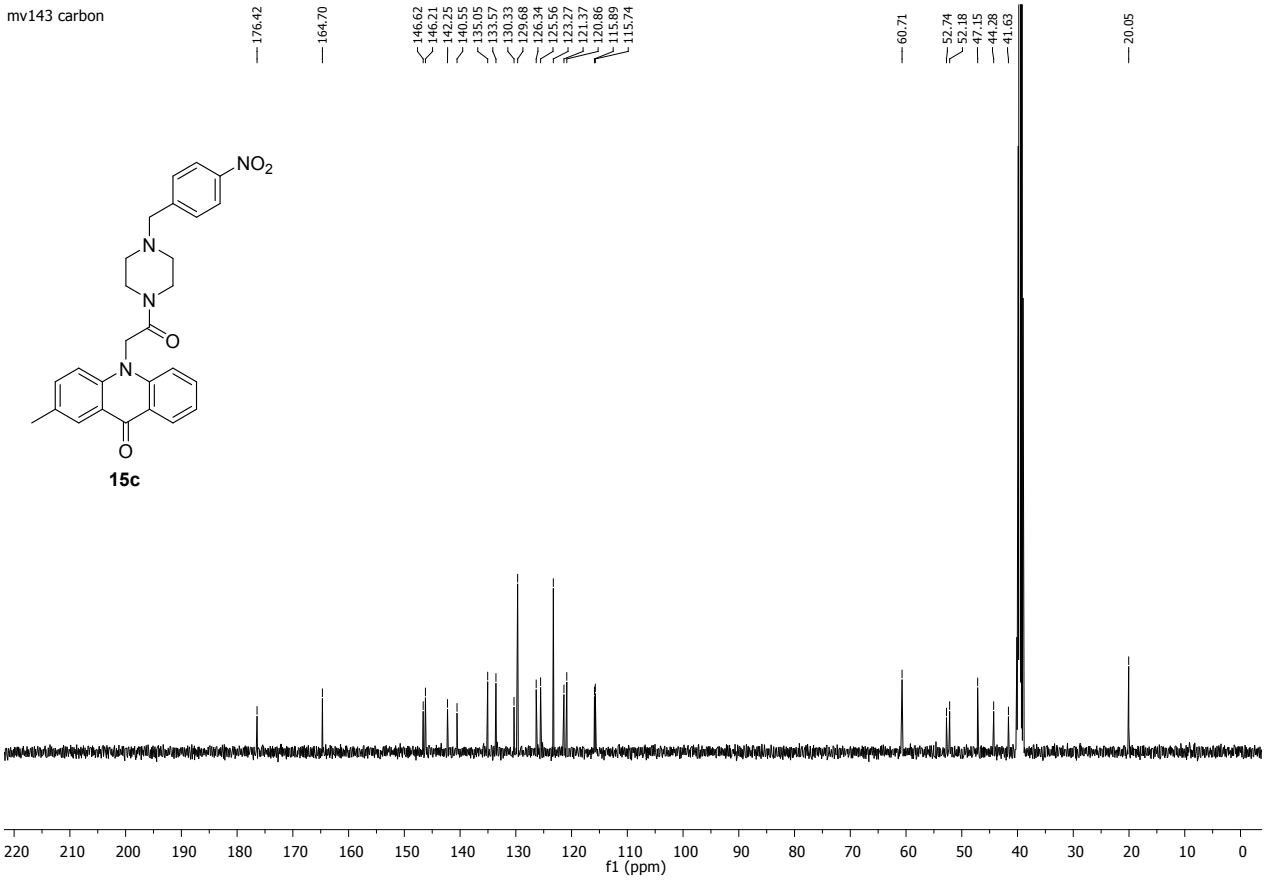

mv142 carbon
176.41
164.62
149.29
142.24
140.54
135.01
134.55
133.53
130.29
128.55
126.33
125.54
124.80
121.37
121.34
120.82
115.86
115.71
61.43
52.75
52.11
47.13
44.26
41.62
34.05
31.07
20.04
CMe3
N
N
O
N
O
15b
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

mv143



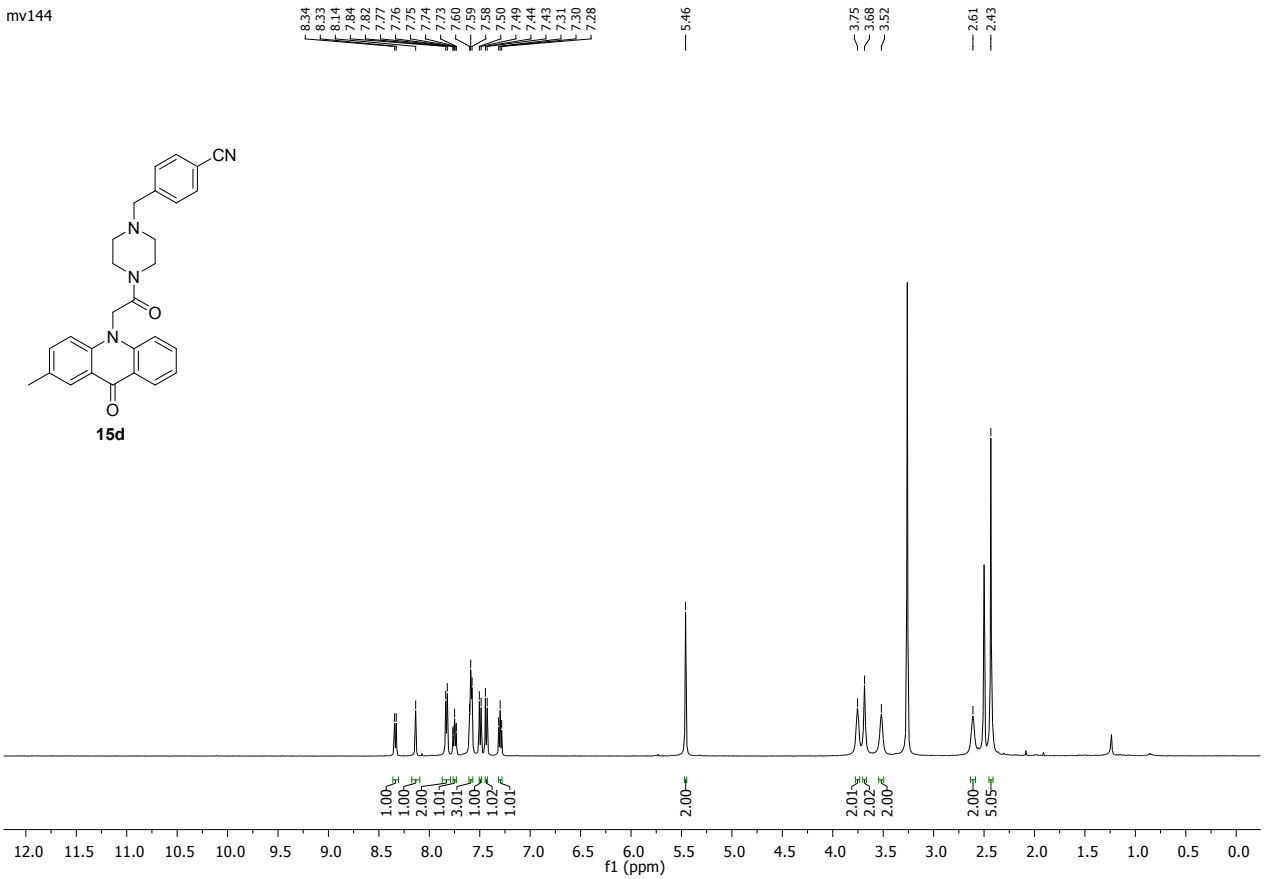
15c

mv143 carbon



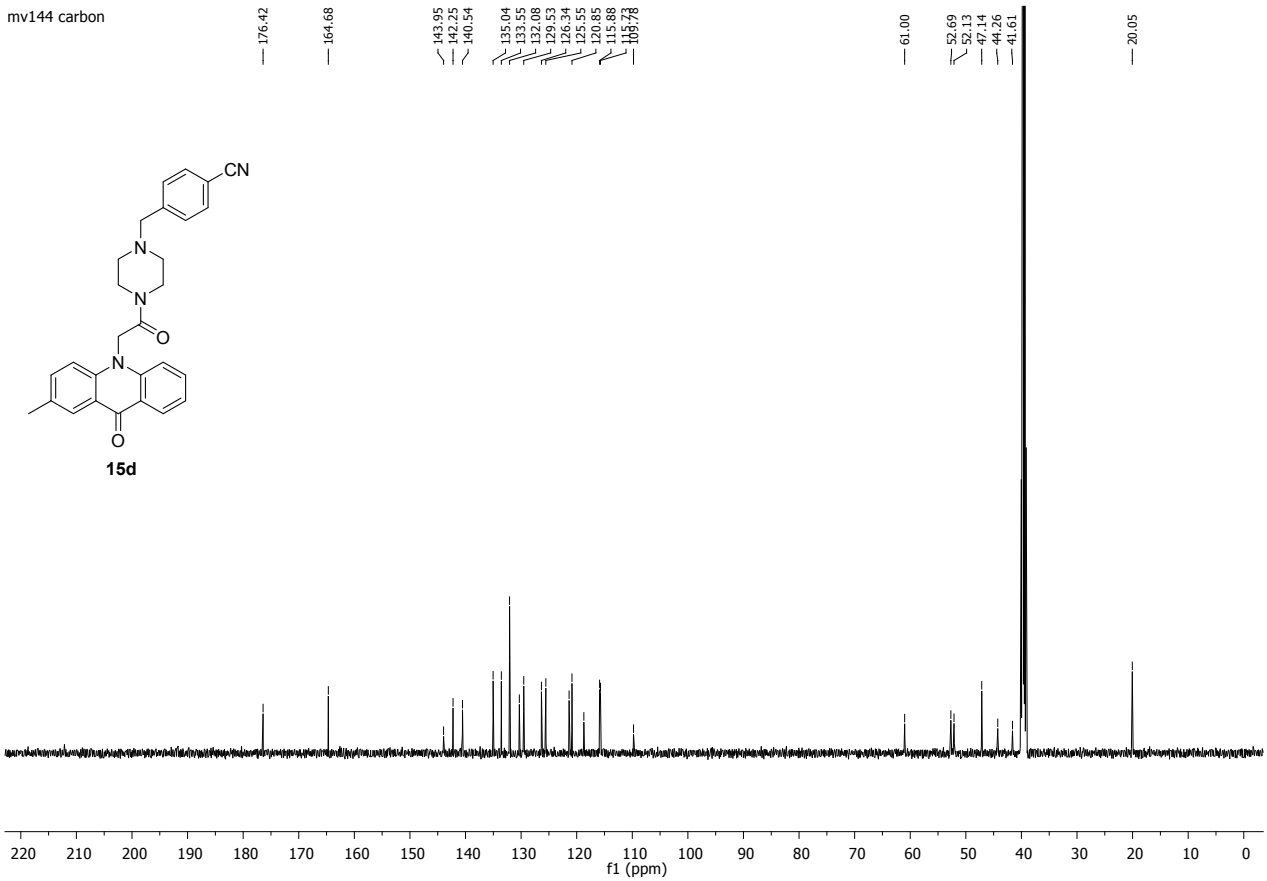
15c

mv144



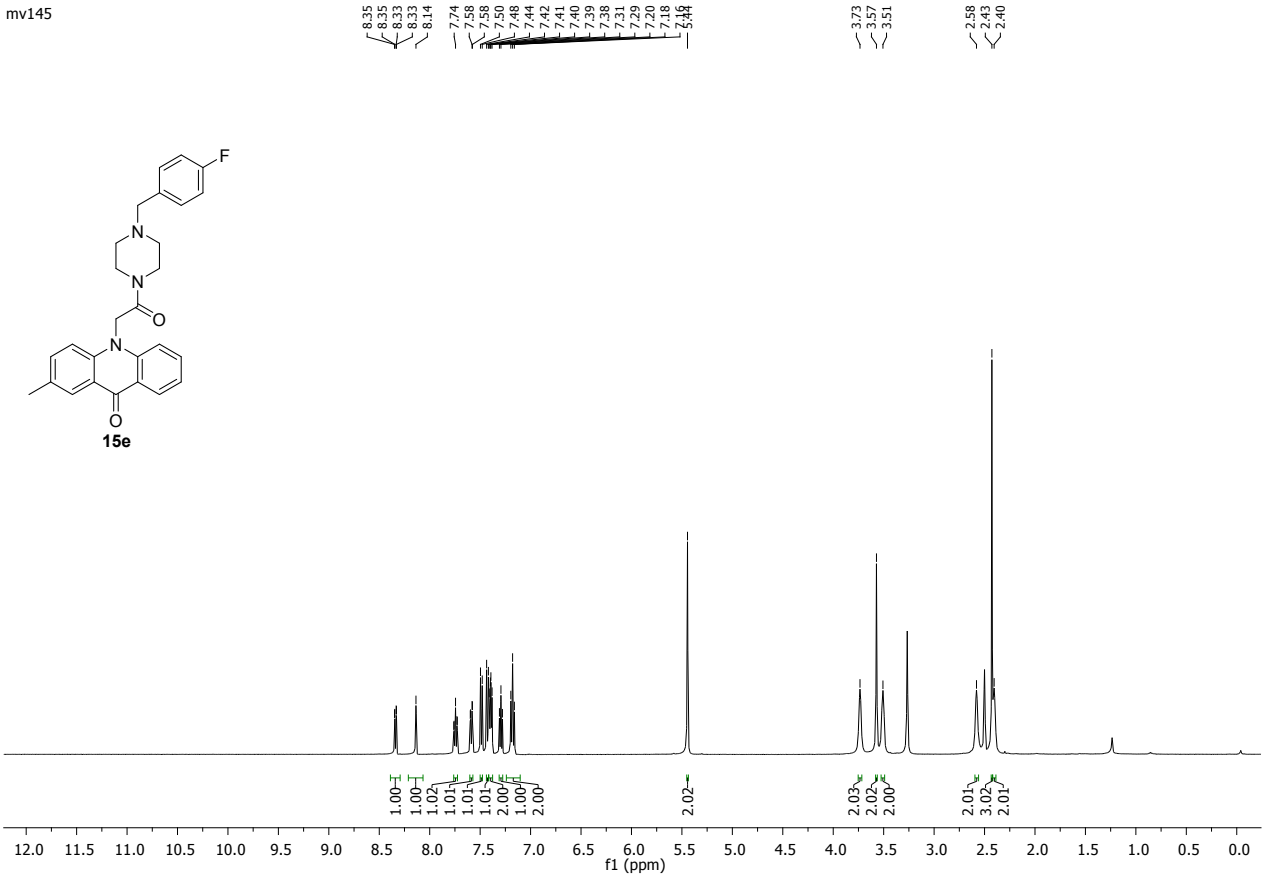
15d

mv144 carbon

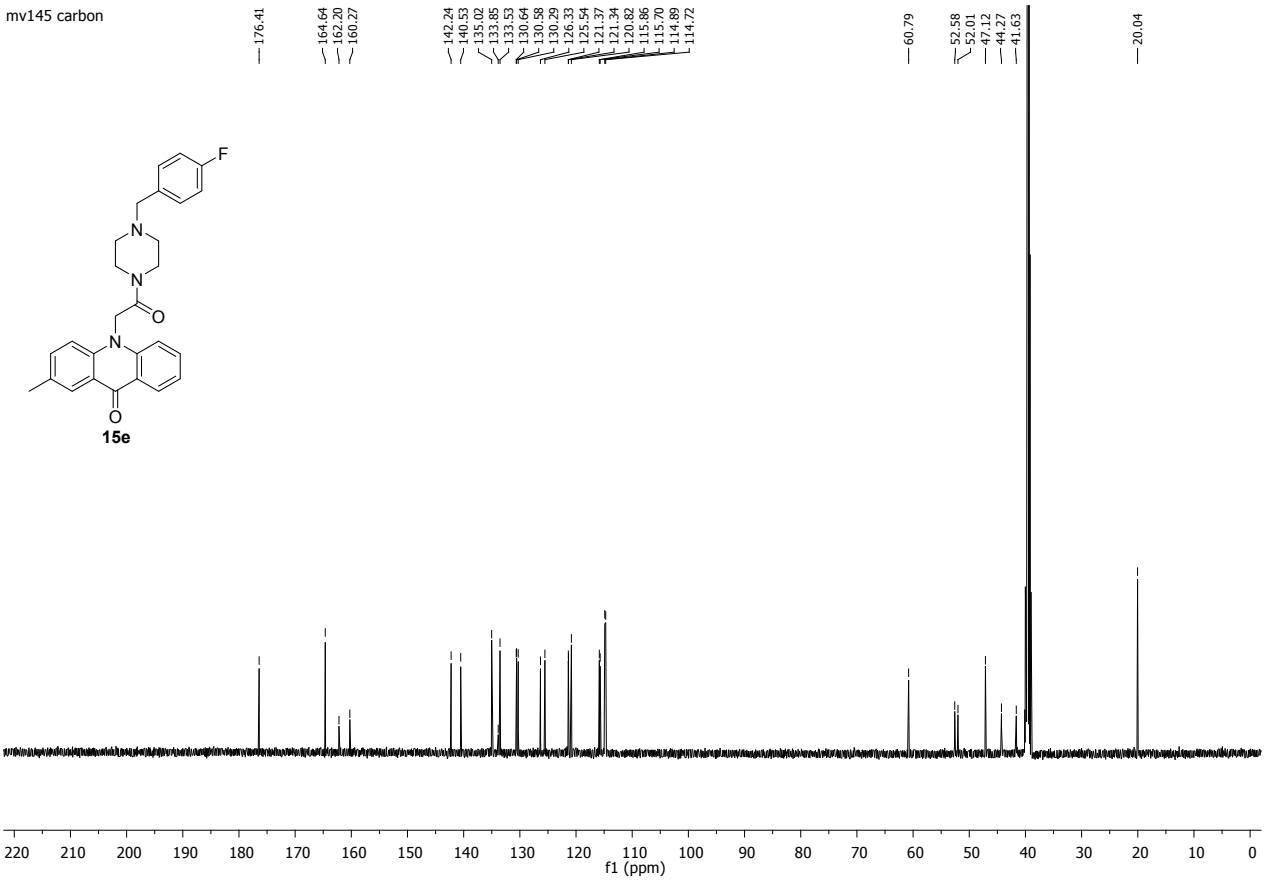


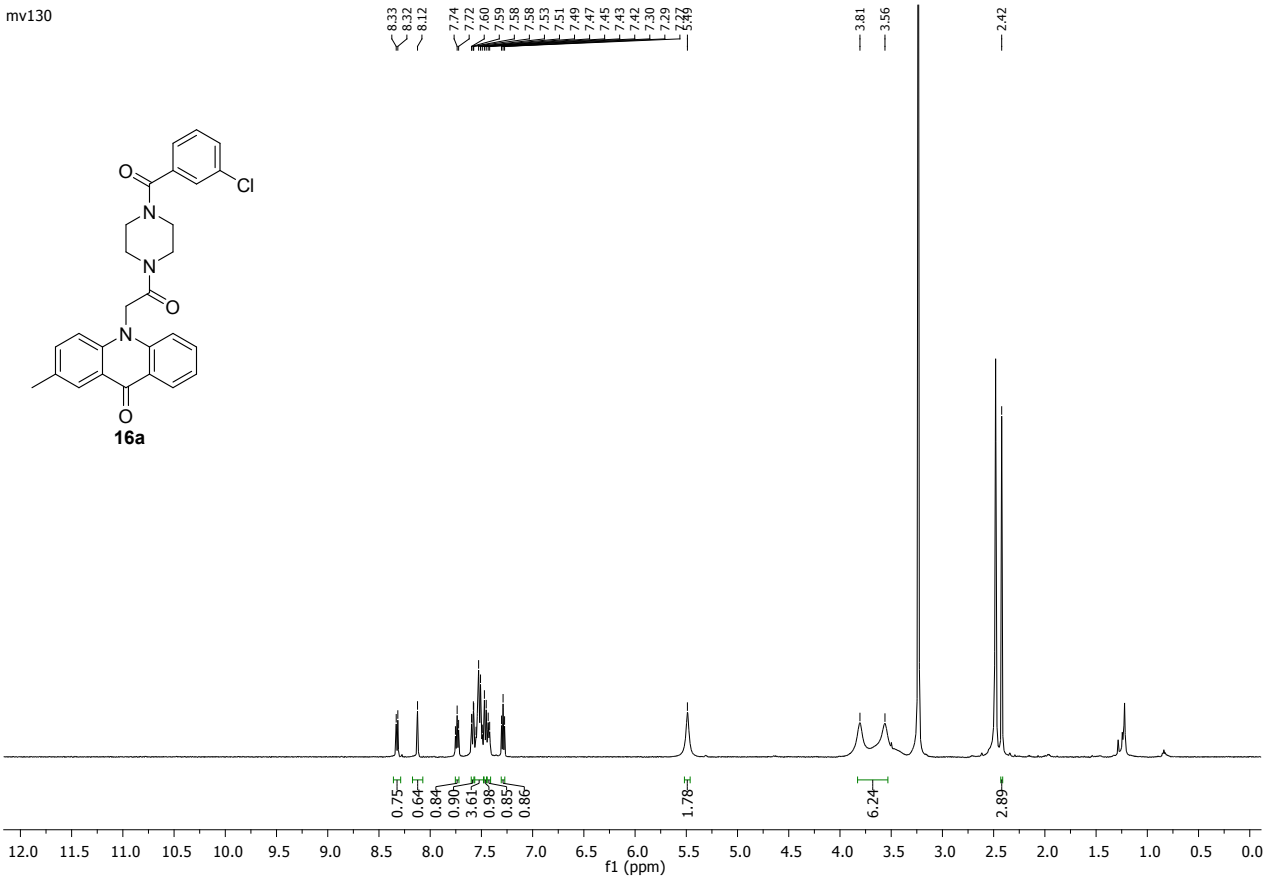
15d

mv145

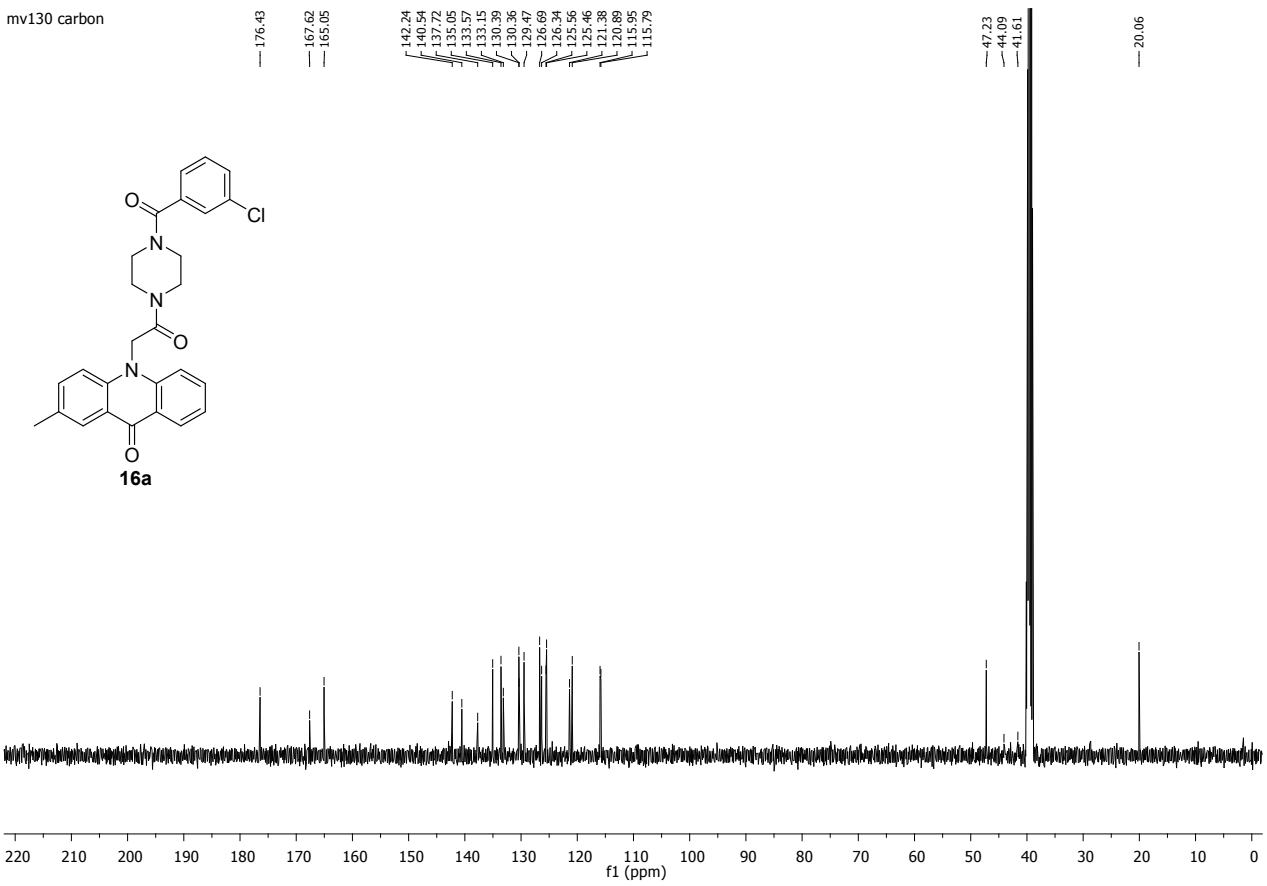


mv145 carbon



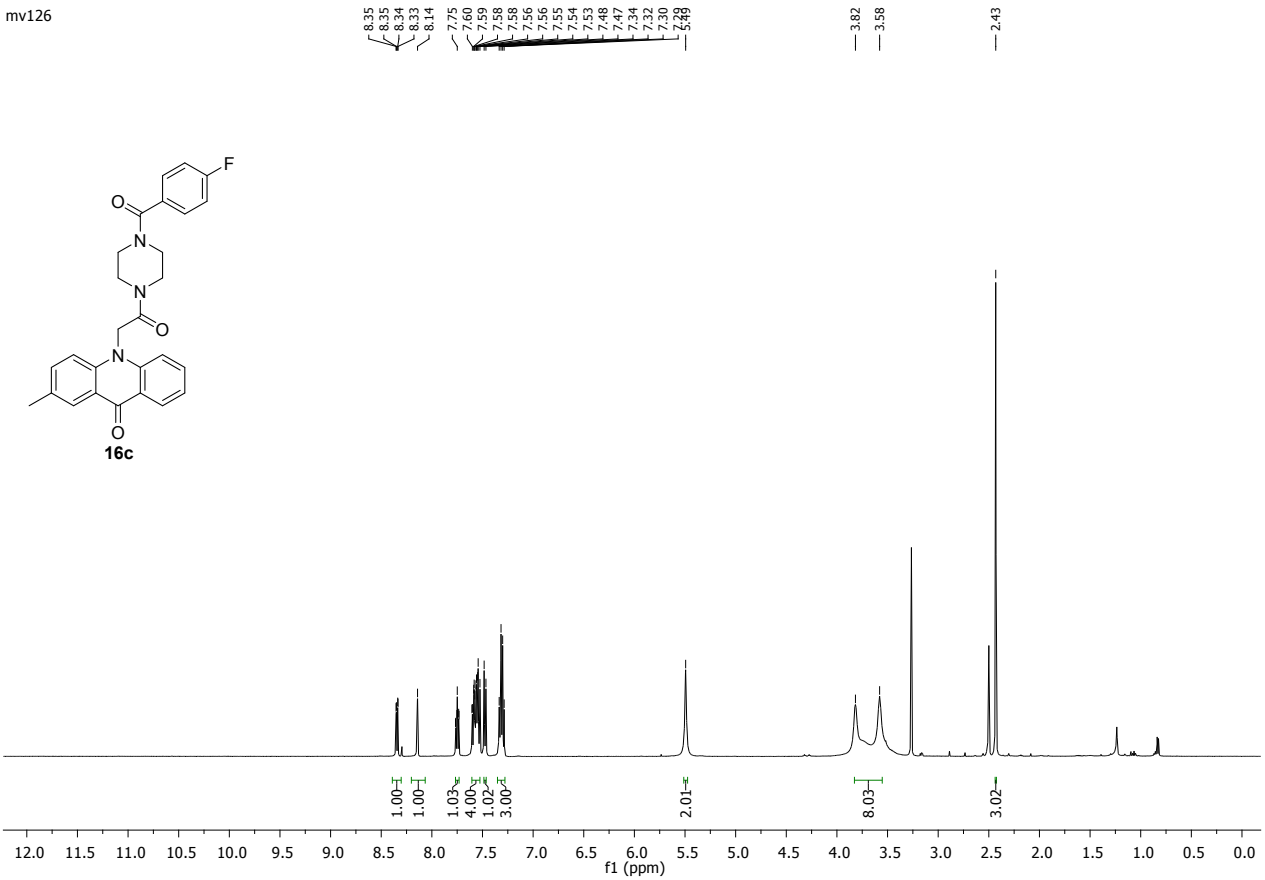

mv130
8.33
8.32
8.12
7.74
7.72
7.60
7.59
7.58
7.58
7.53
7.51
7.49
7.47
7.45
7.43
7.42
7.30
7.29
3.81
3.56
2.42
0.75
0.64
0.84
0.90
3.61
0.98
0.85
0.86
1.78
6.24
2.89
f1 (ppm)

16a

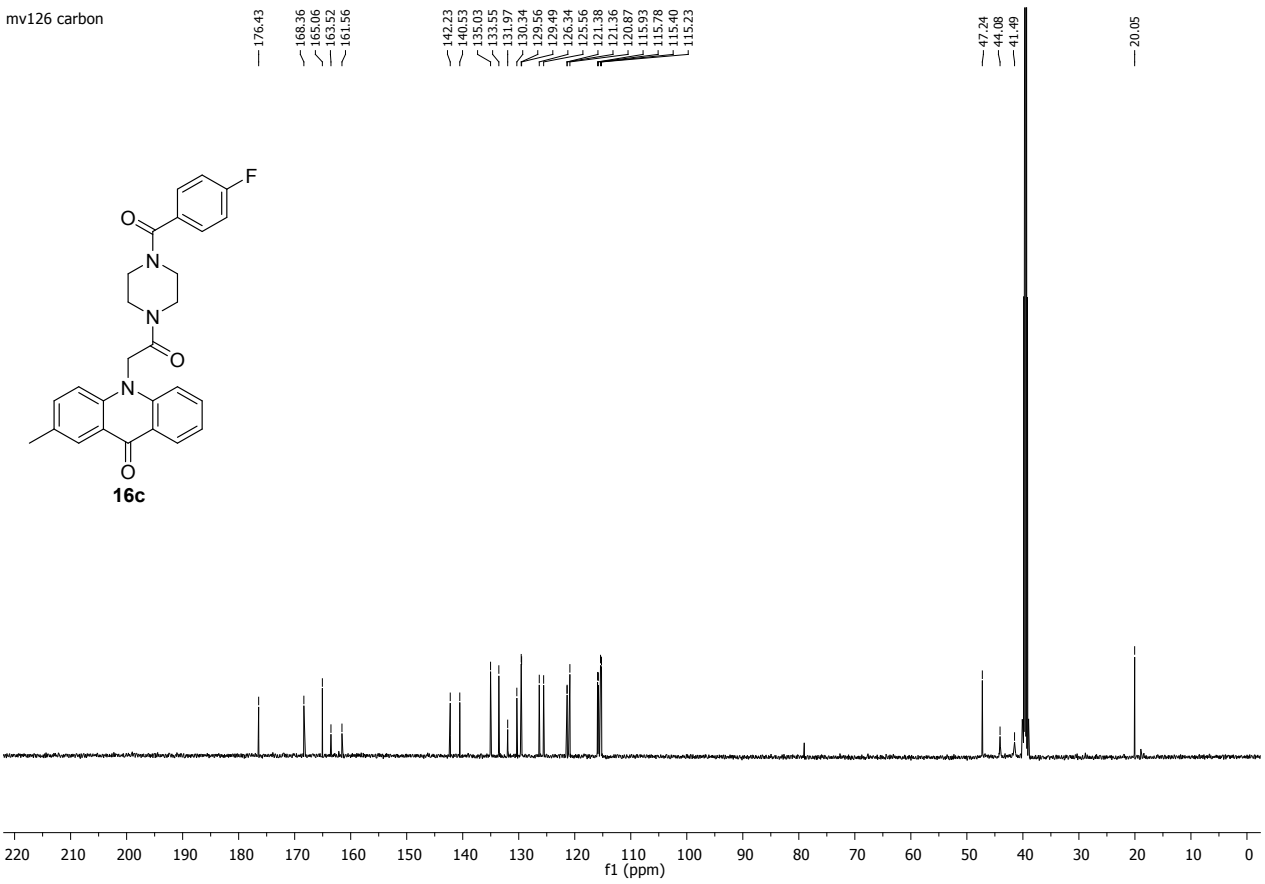

mv130 carbon
176.43
167.62
165.05
142.24
140.54
137.72
135.05
133.57
133.15
130.39
130.36
129.47
126.69
126.34
125.56
125.46
121.38
120.89
115.95
115.79
47.23
44.09
41.61
20.06
f1 (ppm)

16a

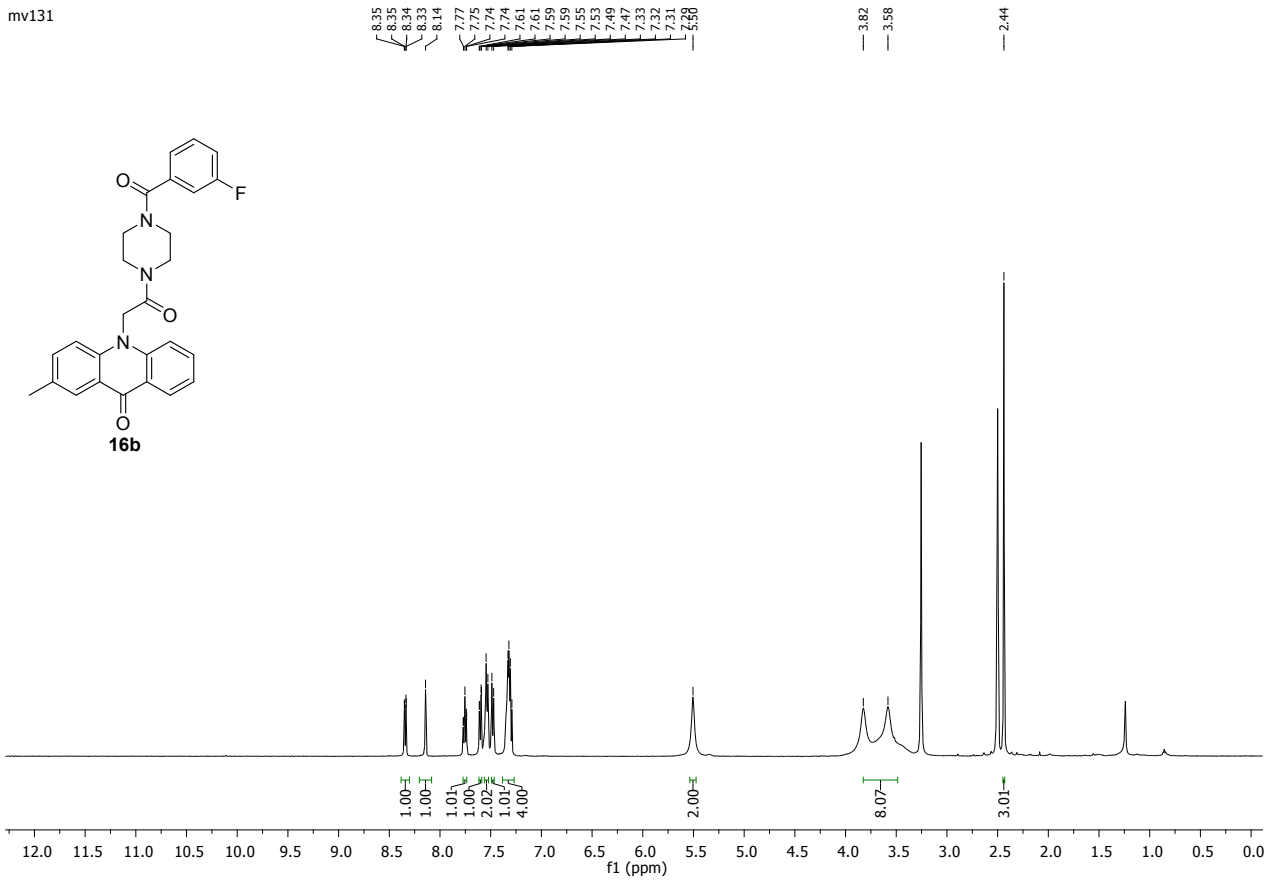
mv126



mv126 carbon

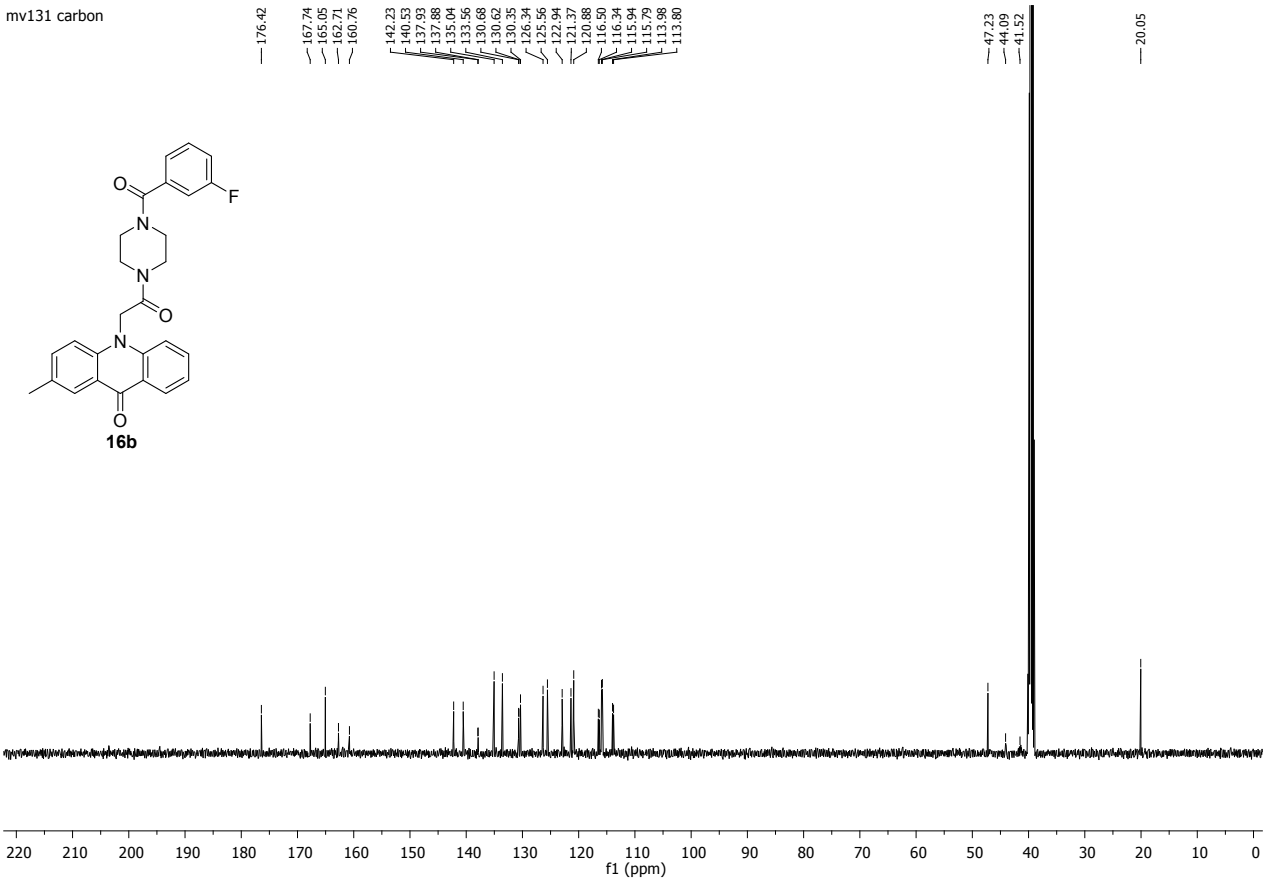


mv131

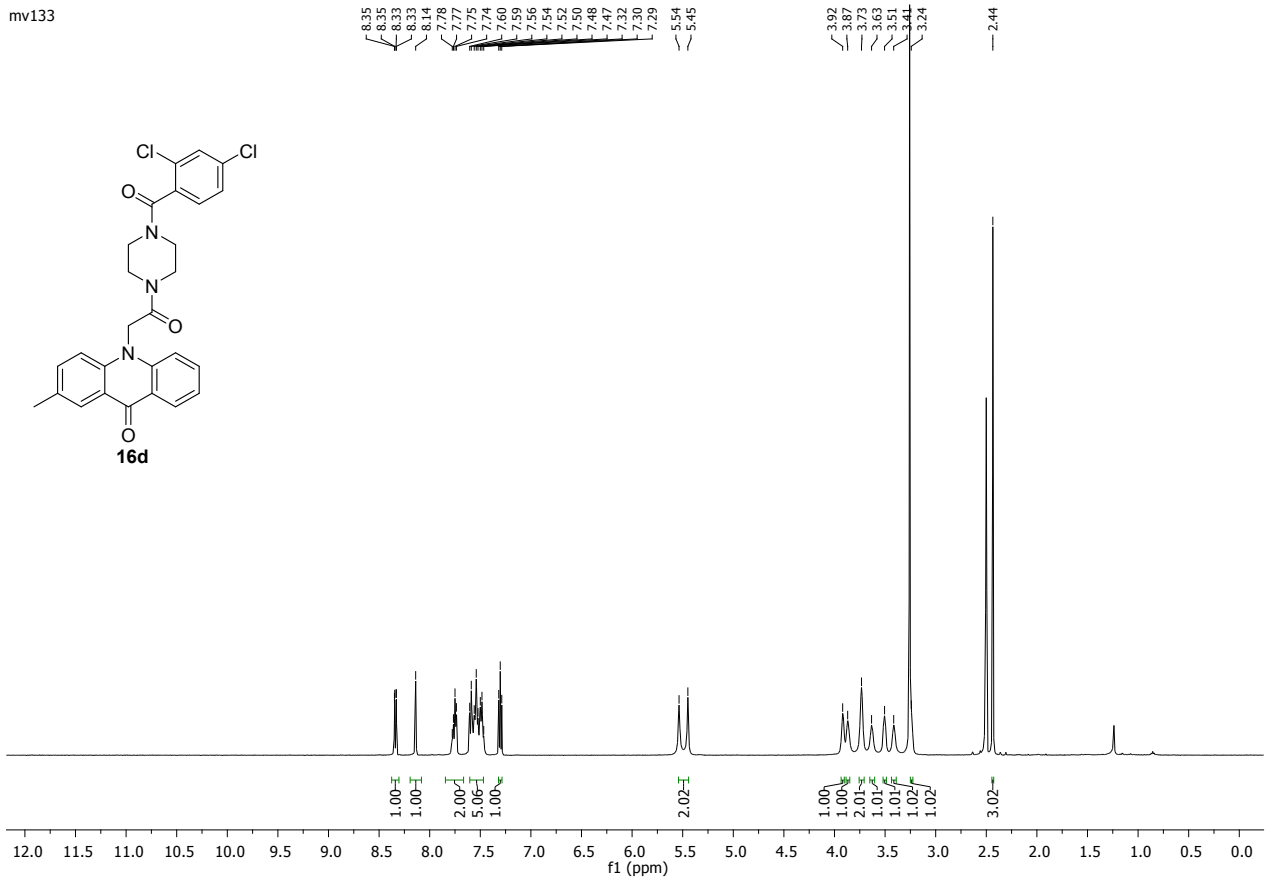


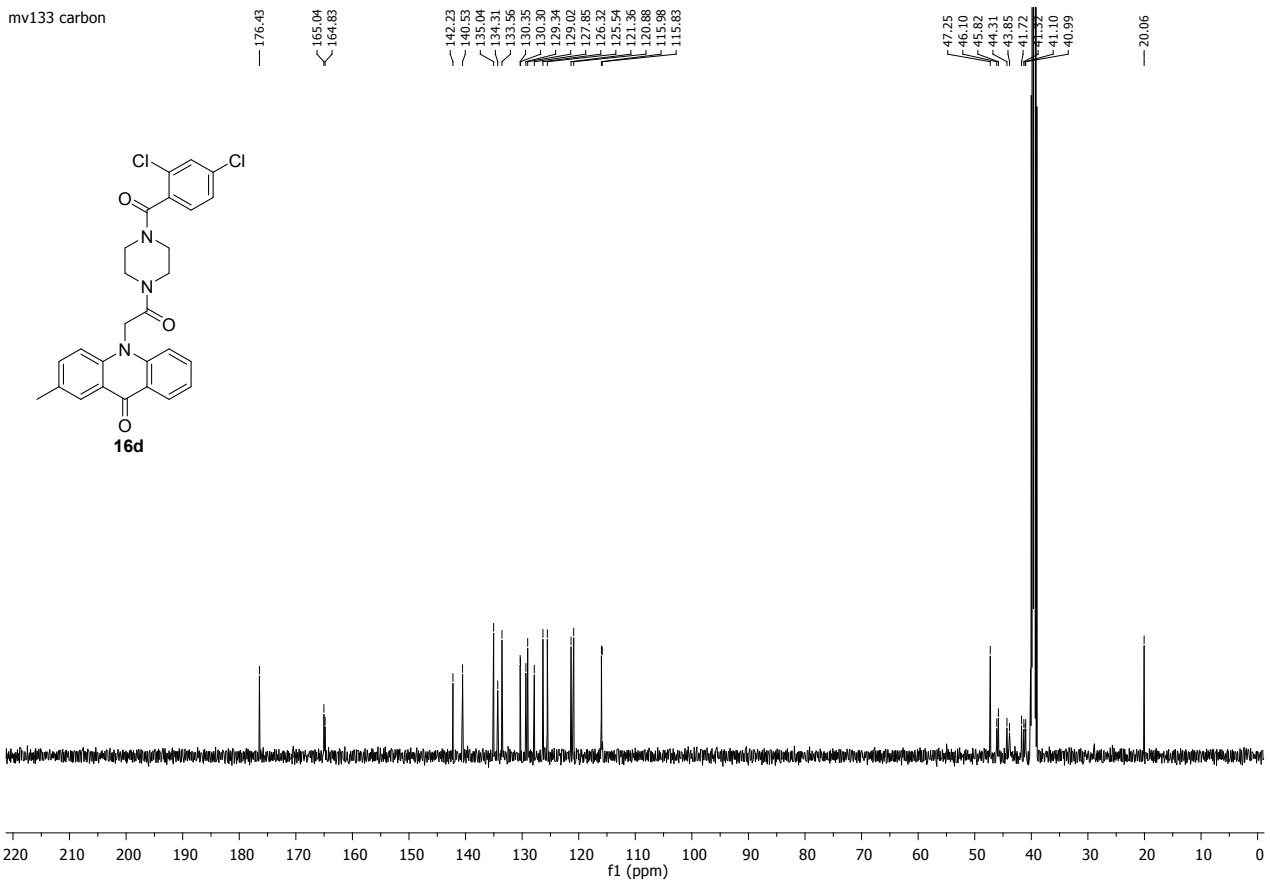
16b

mv131 carbon

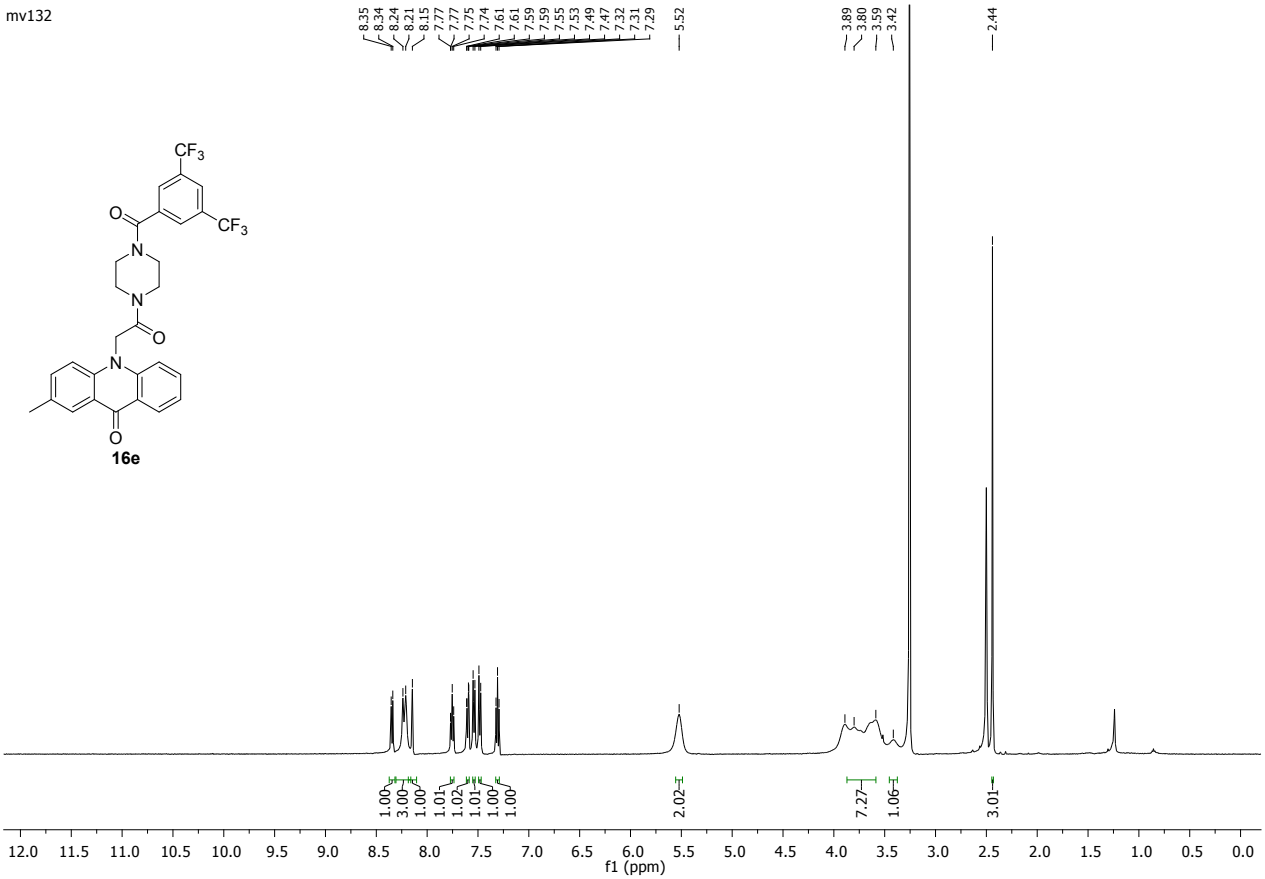


16b


mv133
8.35
8.35
8.33
8.33
8.14
7.78
7.77
7.75
7.74
7.60
7.59
7.56
7.54
7.52
7.50
7.48
7.47
7.32
7.30
7.29
5.54
5.45
3.92
3.87
3.73
3.63
3.51
3.41
3.24
2.44
Cl
Cl
O
N
N
O
N
O
O
16d
1.00
1.00
2.00
5.06
1.00
2.02
1.00
1.00
2.01
1.01
1.02
1.02
3.02
12.0 11.5 11.0 10.5 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)

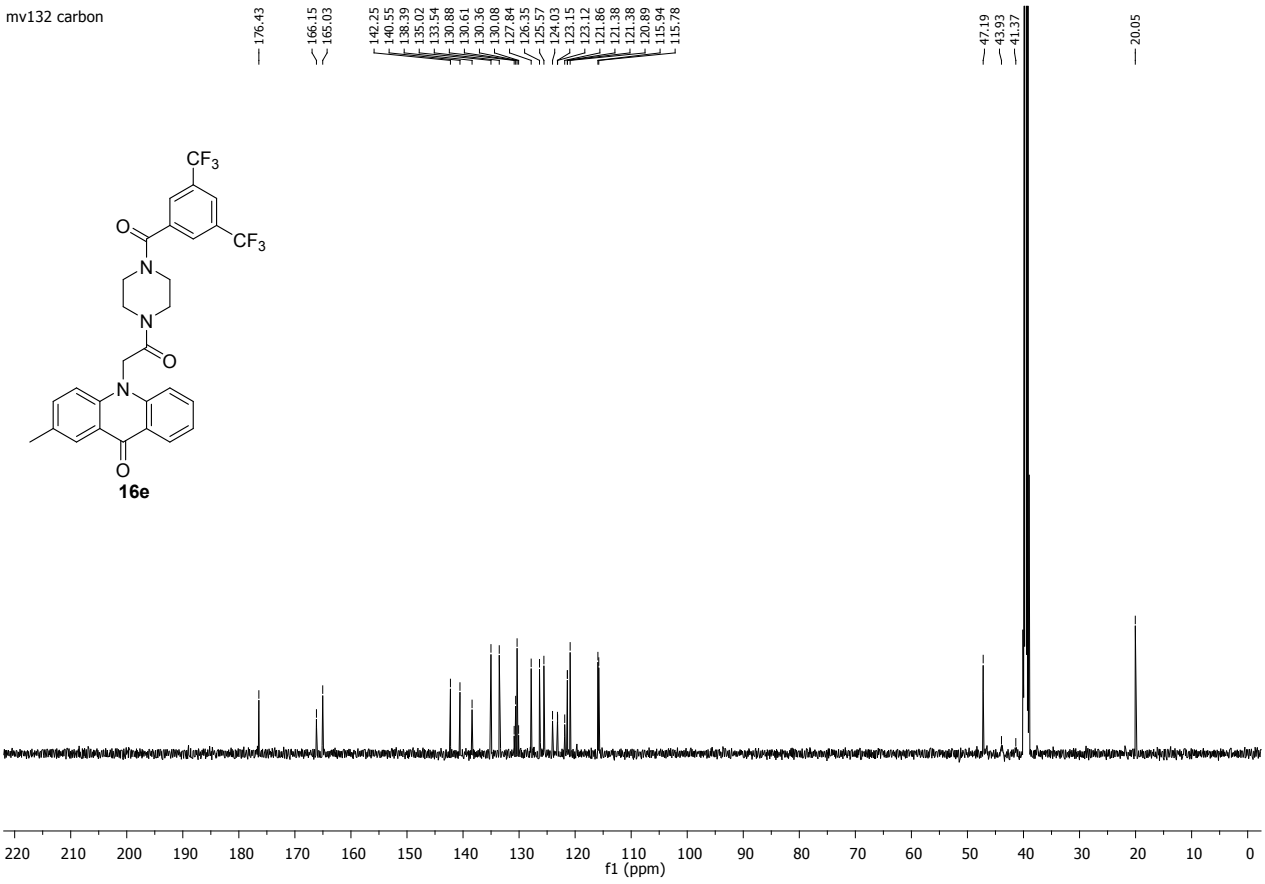

mv133 carbon
176.43
165.04
164.83
142.23
140.53
135.04
134.31
133.56
130.35
130.30
129.34
129.02
127.85
126.32
125.54
121.36
120.88
115.98
115.83
47.25
46.10
45.82
44.31
43.85
41.72
41.32
41.10
40.99
20.06
Cl
Cl
O
N
N
O
N
O
O
16d
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

mv132



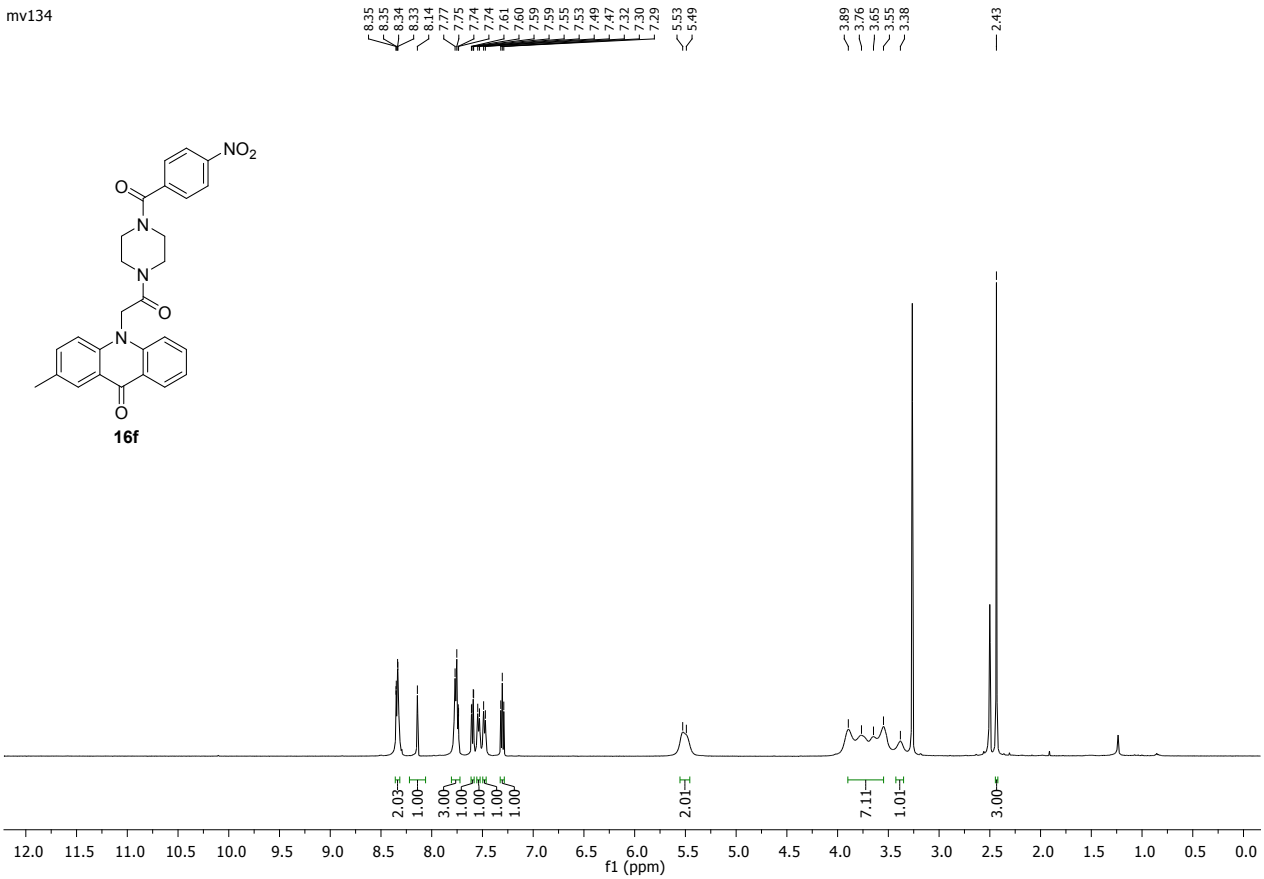
16e

mv132 carbon

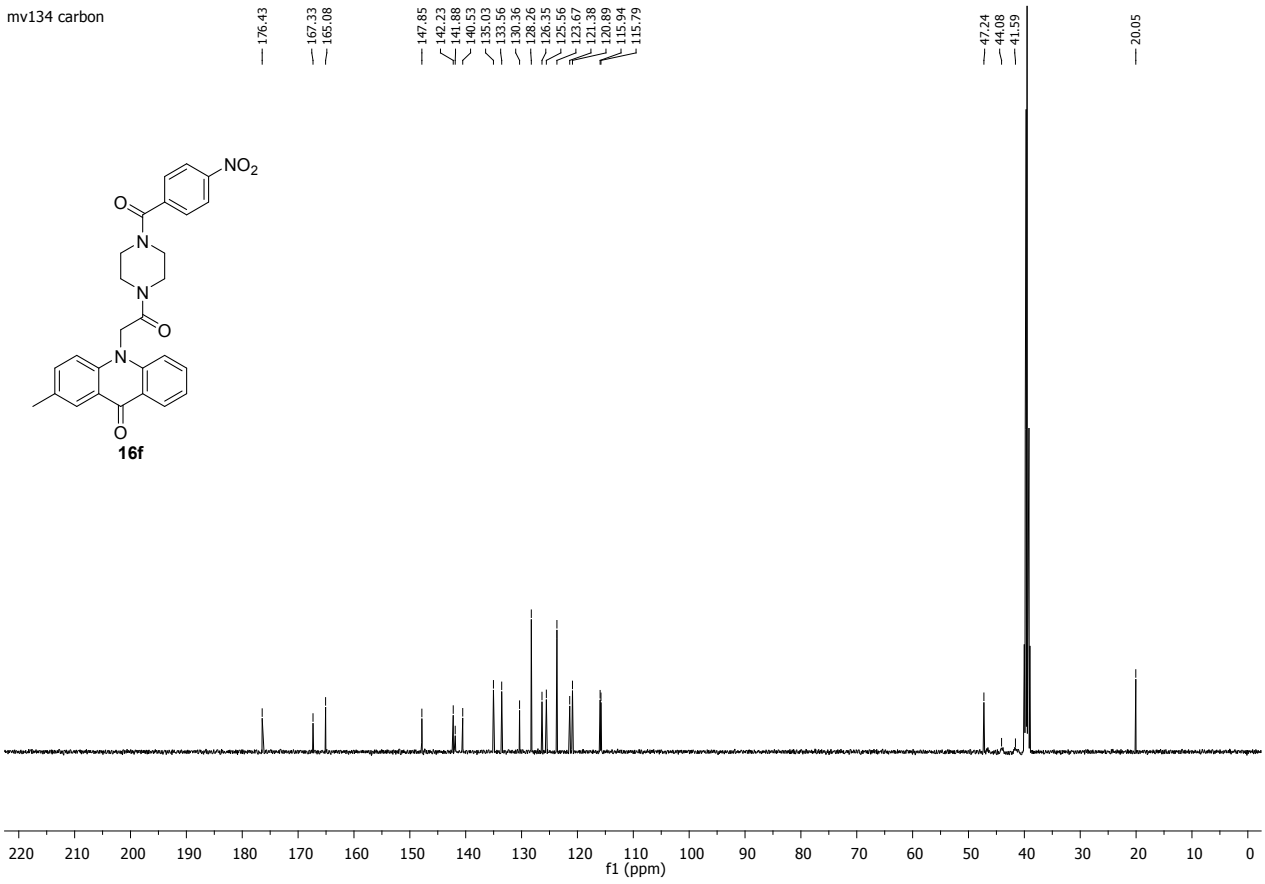


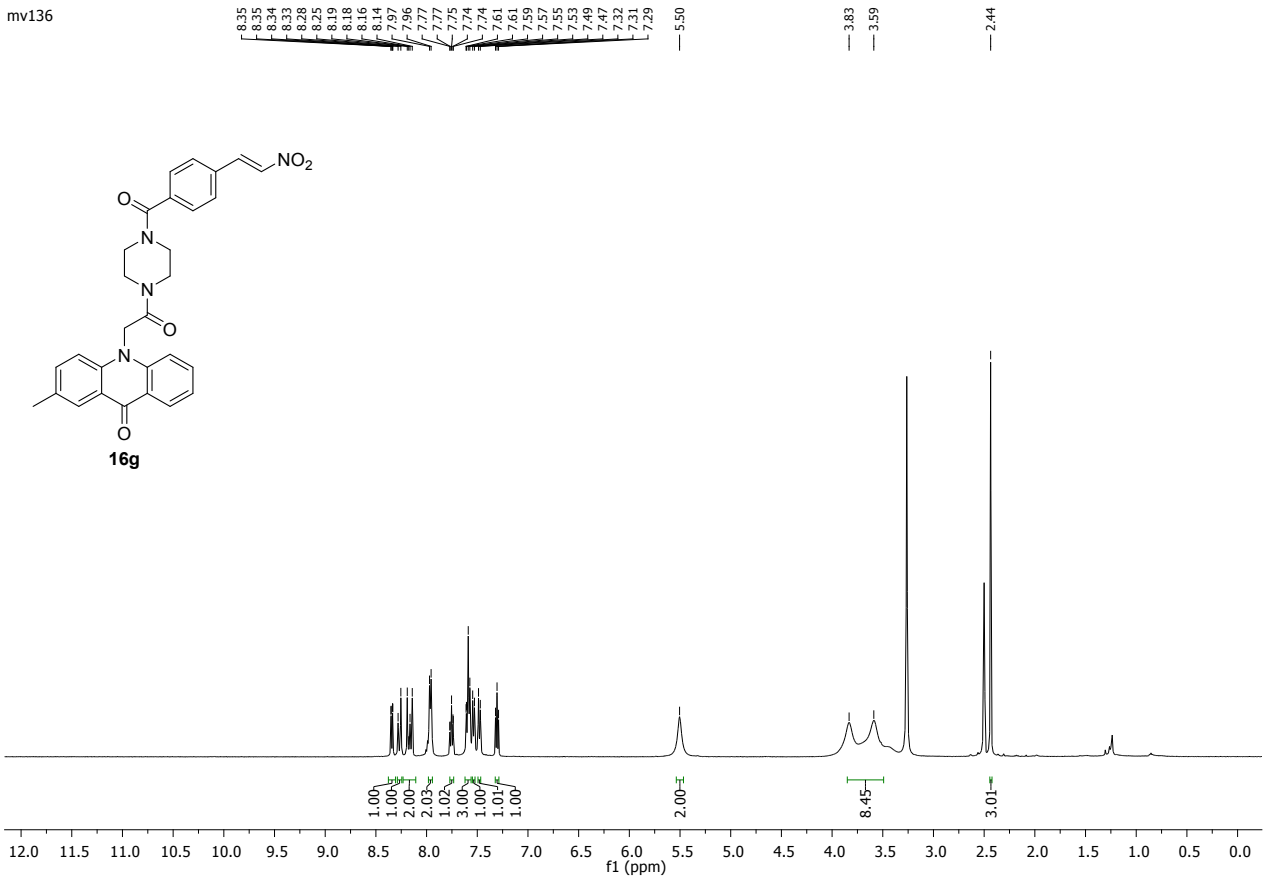
16e

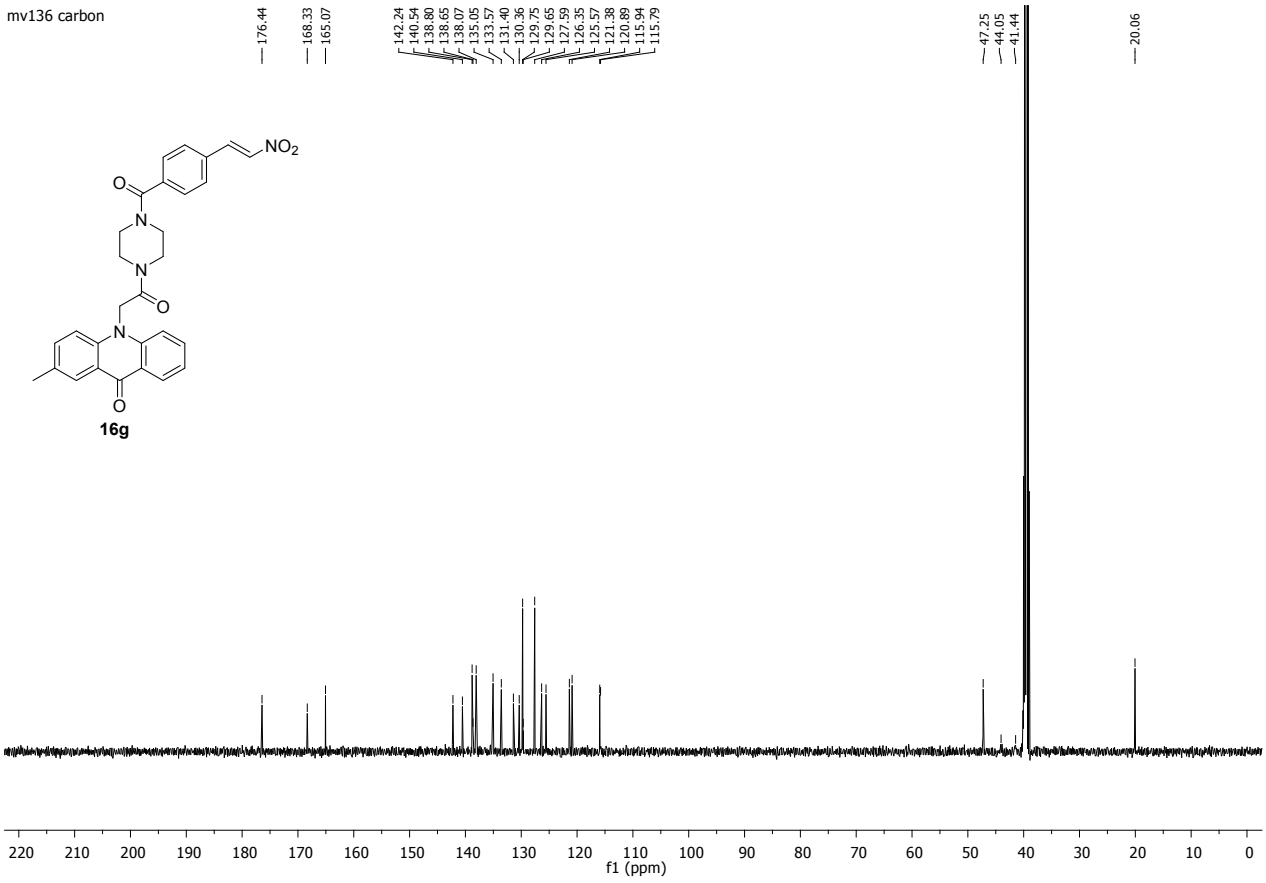
mv134

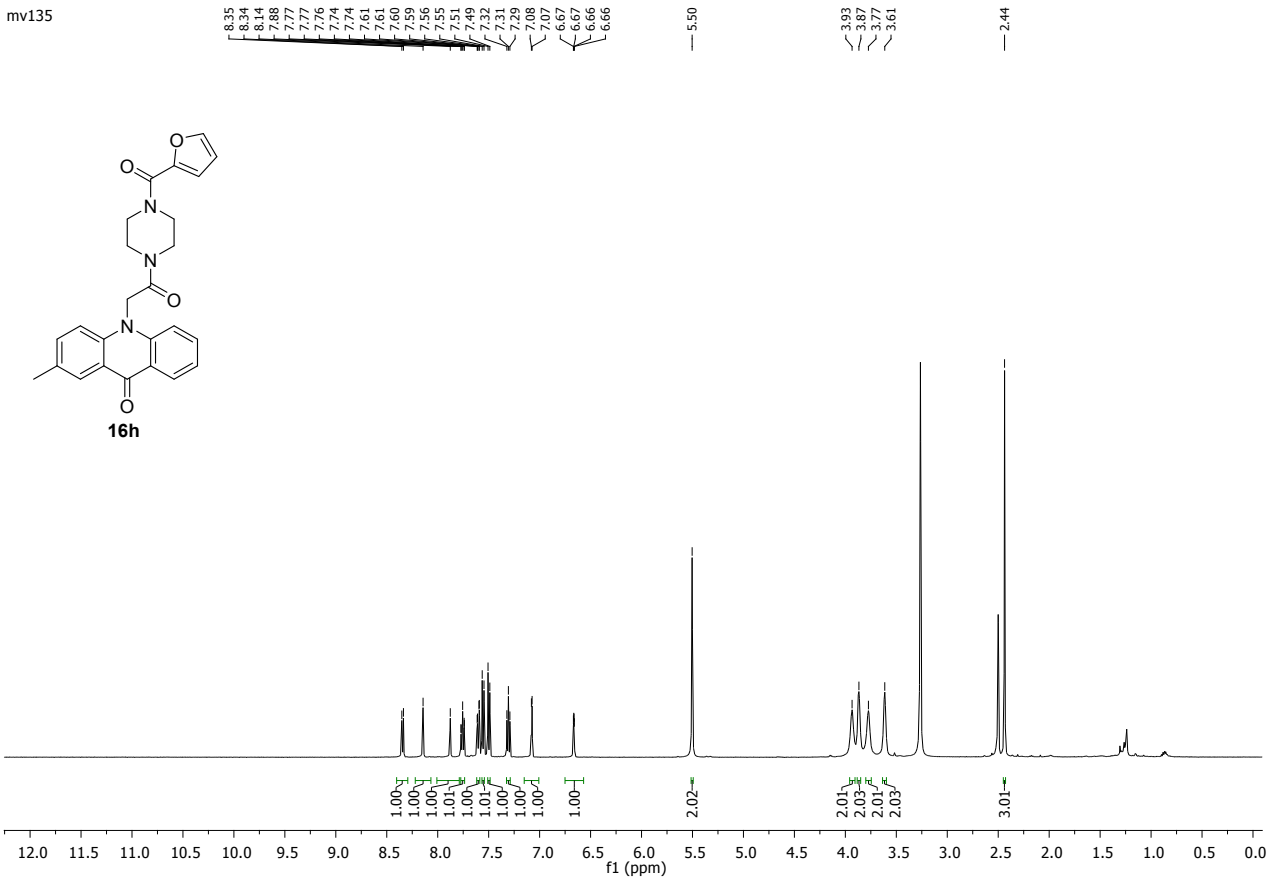


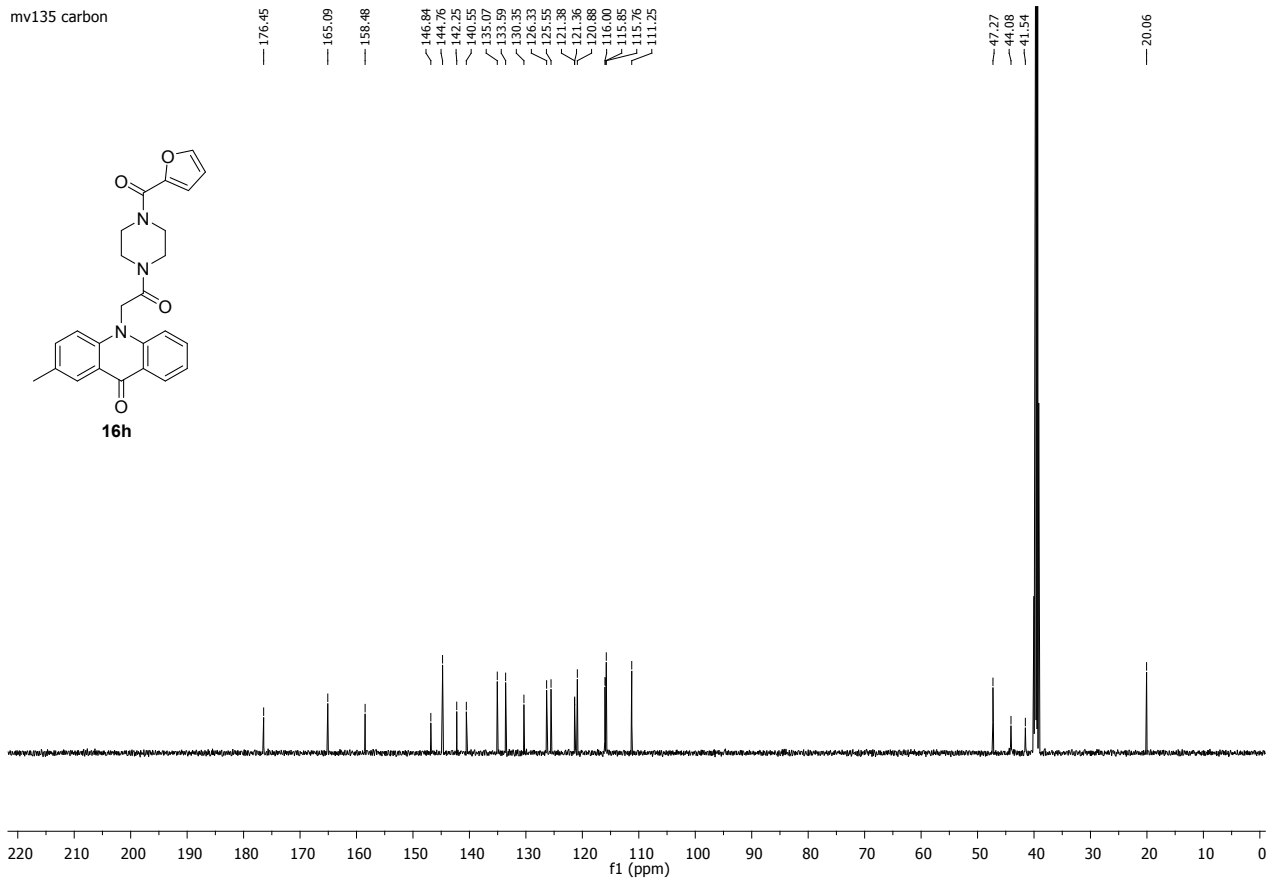
mv134 carbon

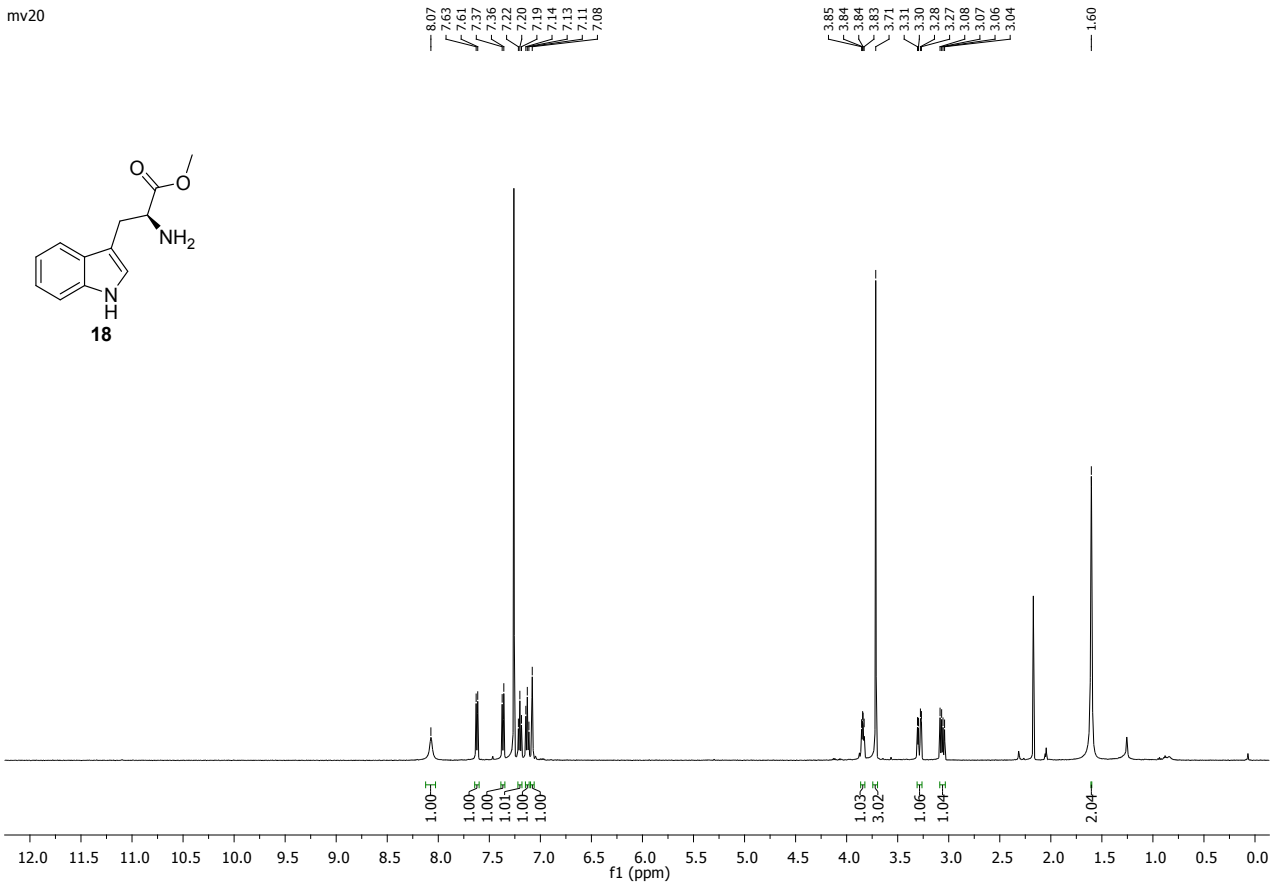


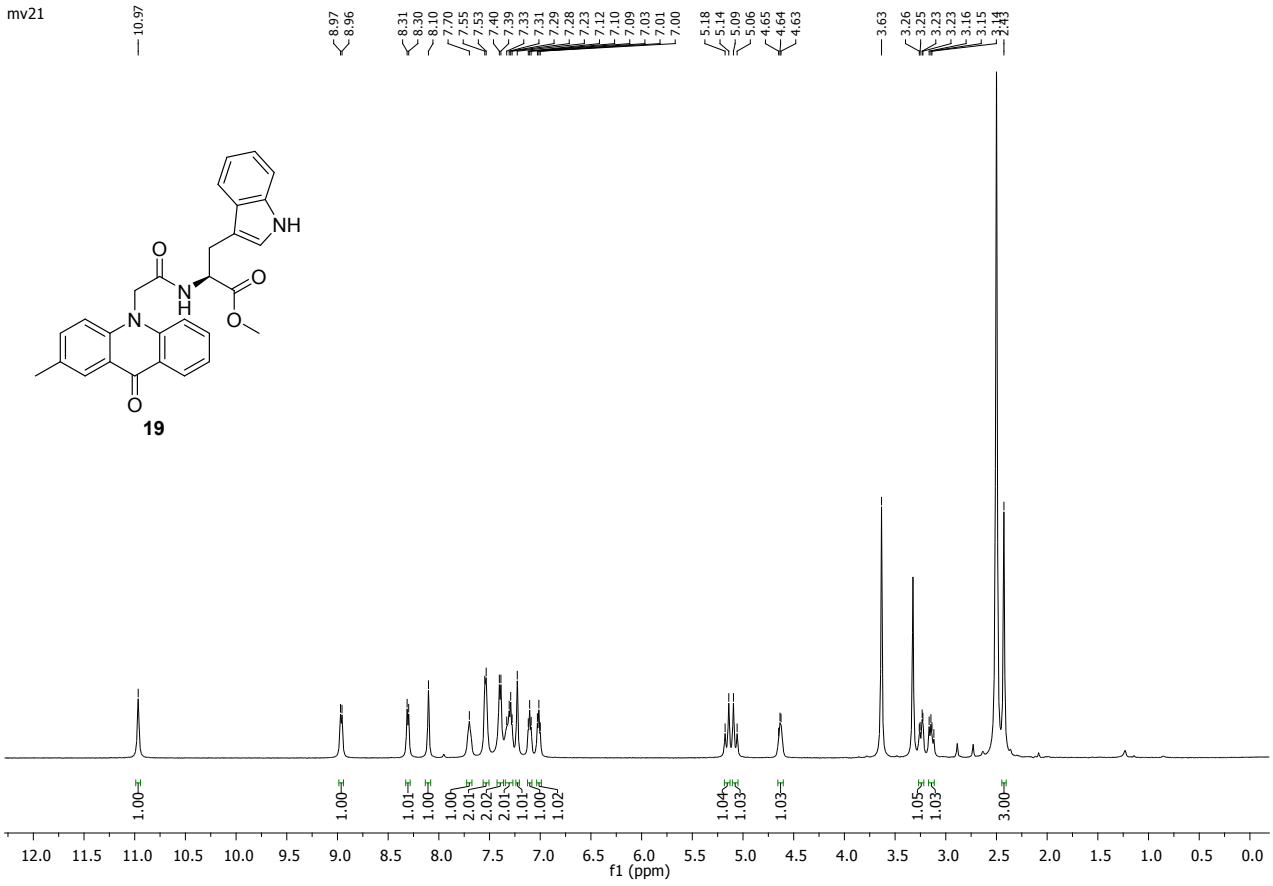

mv136
8.35
8.35
8.34
8.33
8.28
8.25
8.19
8.18
8.16
8.14
7.97
7.96
7.77
7.77
7.75
7.74
7.74
7.61
7.61
7.59
7.57
7.55
7.53
7.49
7.47
7.32
7.31
7.29
5.50
3.83
3.59
2.44
NO2
O
N
N
O
N
O
O
16g
1.00
1.00
2.00
2.03
1.02
3.00
1.00
1.01
1.00
2.00
8.45
3.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 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)

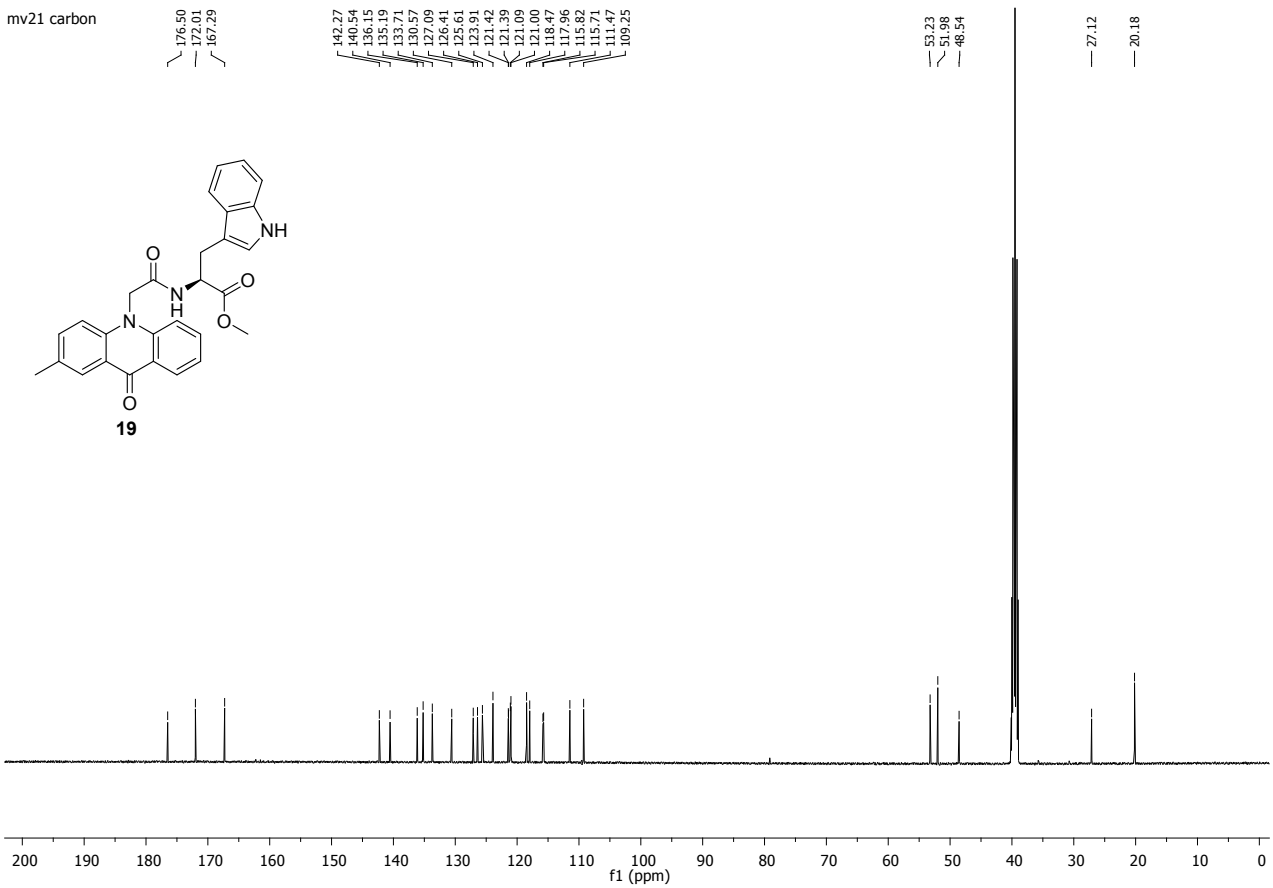

mv136 carbon
176.44
168.33
165.07
142.24
140.54
138.80
138.65
138.07
135.05
133.57
131.40
130.36
129.75
129.65
127.59
126.35
125.57
121.38
120.89
115.94
115.79
47.25
44.05
41.44
20.06
NO2
O
N
N
O
N
O
O
16g
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

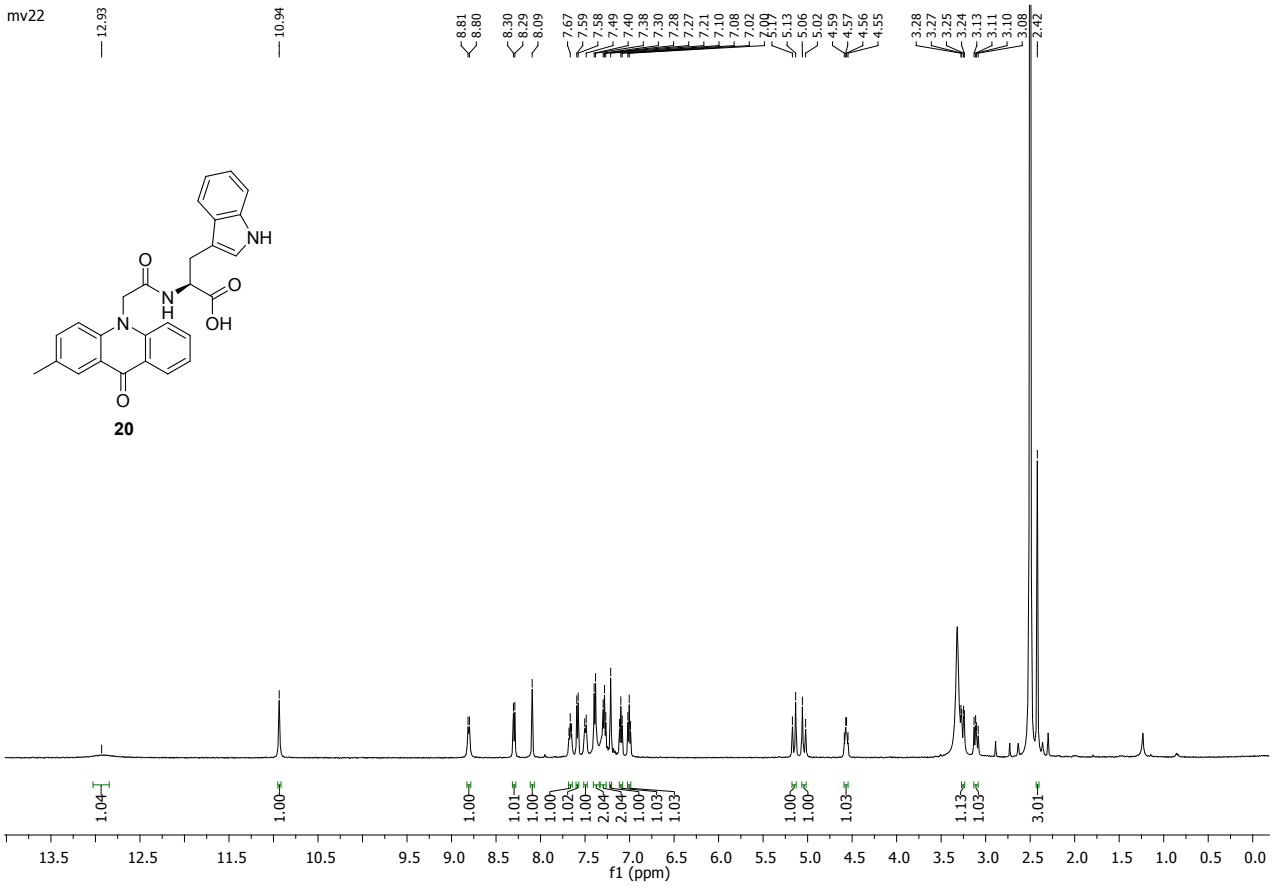

mv135
8.35
8.34
8.14
7.88
7.77
7.77
7.76
7.74
7.74
7.61
7.61
7.60
7.59
7.56
7.55
7.51
7.49
7.32
7.31
7.29
7.08
7.07
6.67
6.67
6.66
6.66
5.50
3.93
3.87
3.77
3.61
2.44
16h
1.00
1.00
1.00
1.01
1.00
1.01
1.00
1.00
1.00
1.00
2.02
2.01
2.03
2.01
2.03
3.01
f1 (ppm)

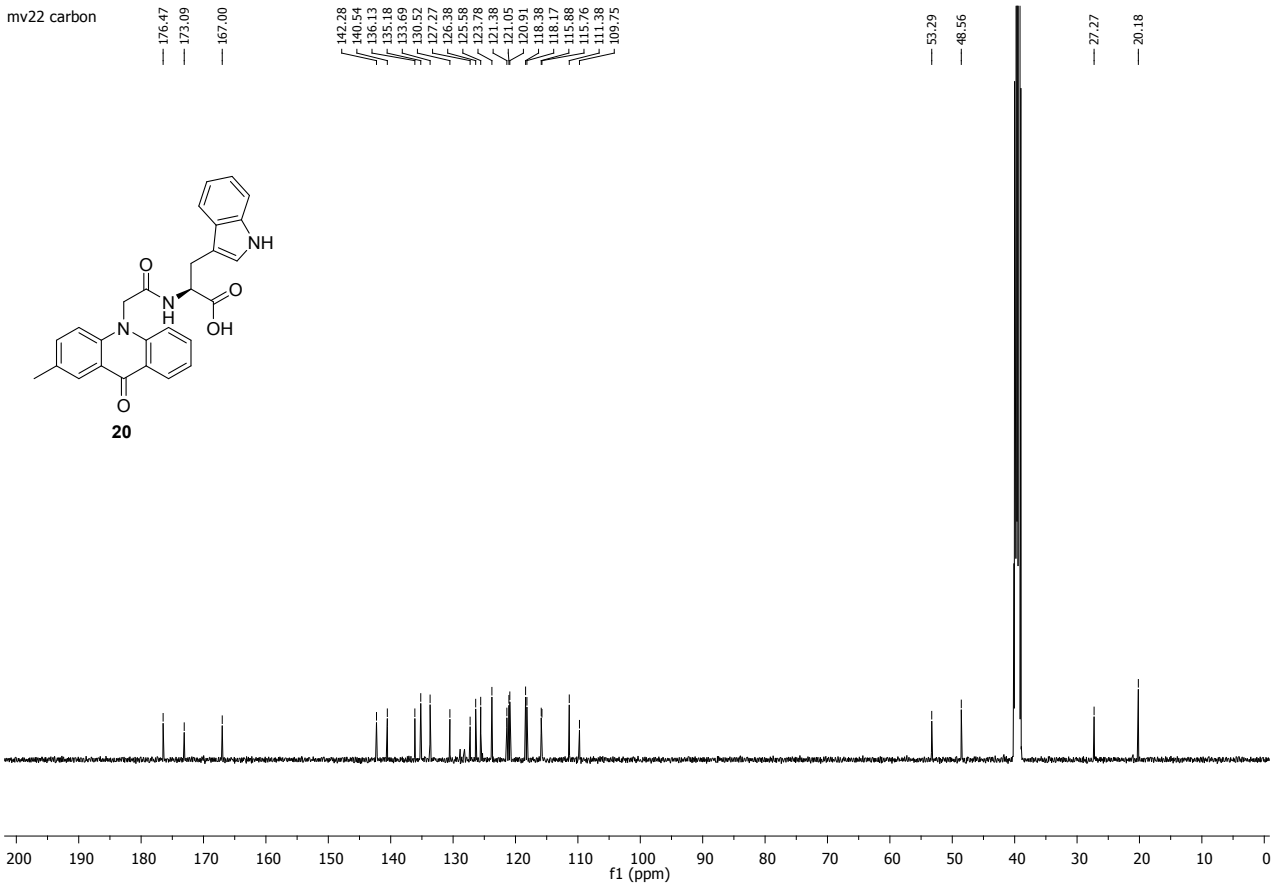

mv135 carbon
176.45
165.09
158.48
146.84
144.76
142.25
140.55
135.07
133.59
130.35
126.33
125.55
121.38
121.36
120.88
116.00
115.85
115.76
111.25
47.27
44.08
41.54
20.06
16h
f1 (ppm)

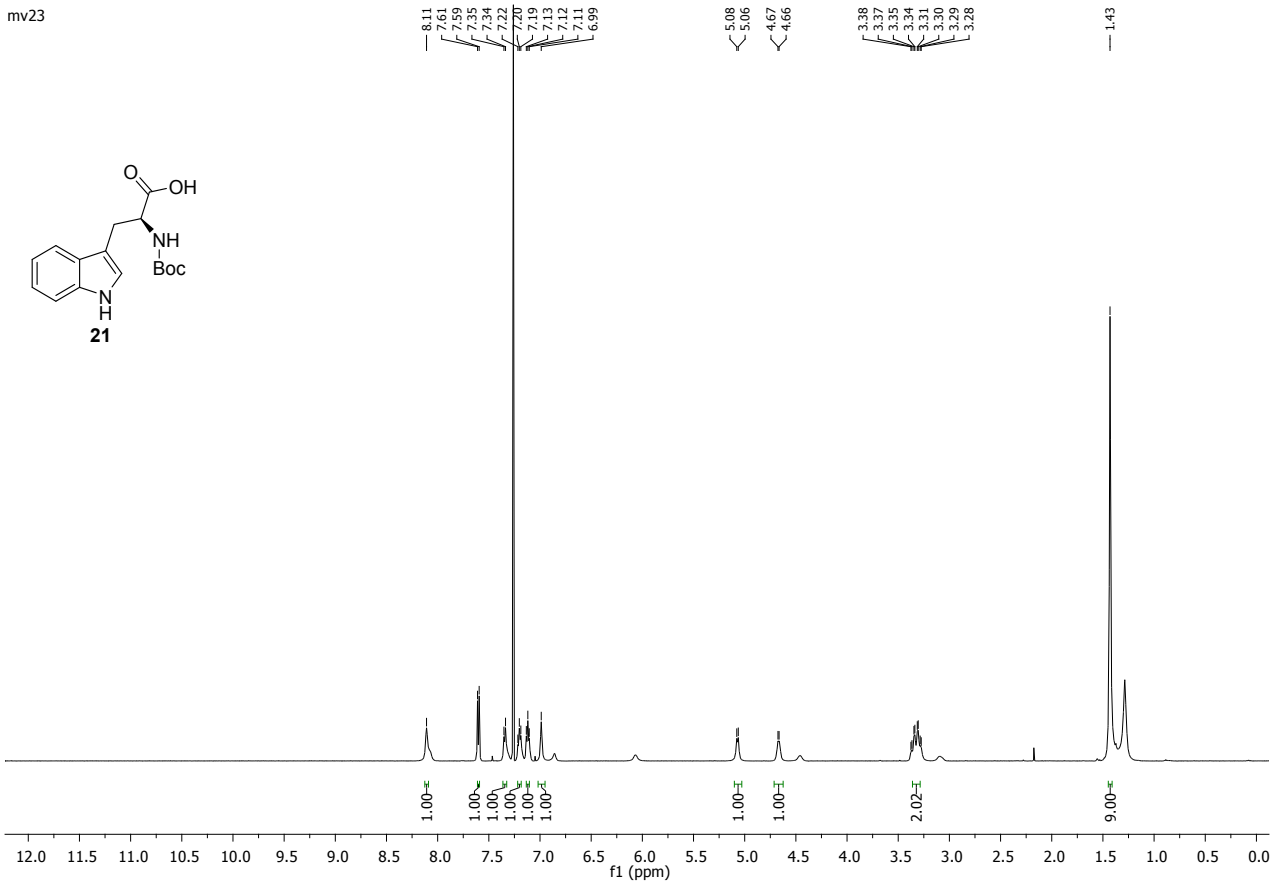

mv20
8.07
7.63
7.61
7.37
7.36
7.22
7.20
7.19
7.14
7.13
7.11
7.08
3.85
3.84
3.84
3.83
3.71
3.31
3.30
3.28
3.27
3.08
3.07
3.06
3.04
1.60
O
O
NH2
N
H
18
1.00
1.00
1.00
1.01
1.00
1.00
1.03
3.02
1.06
1.04
2.04
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

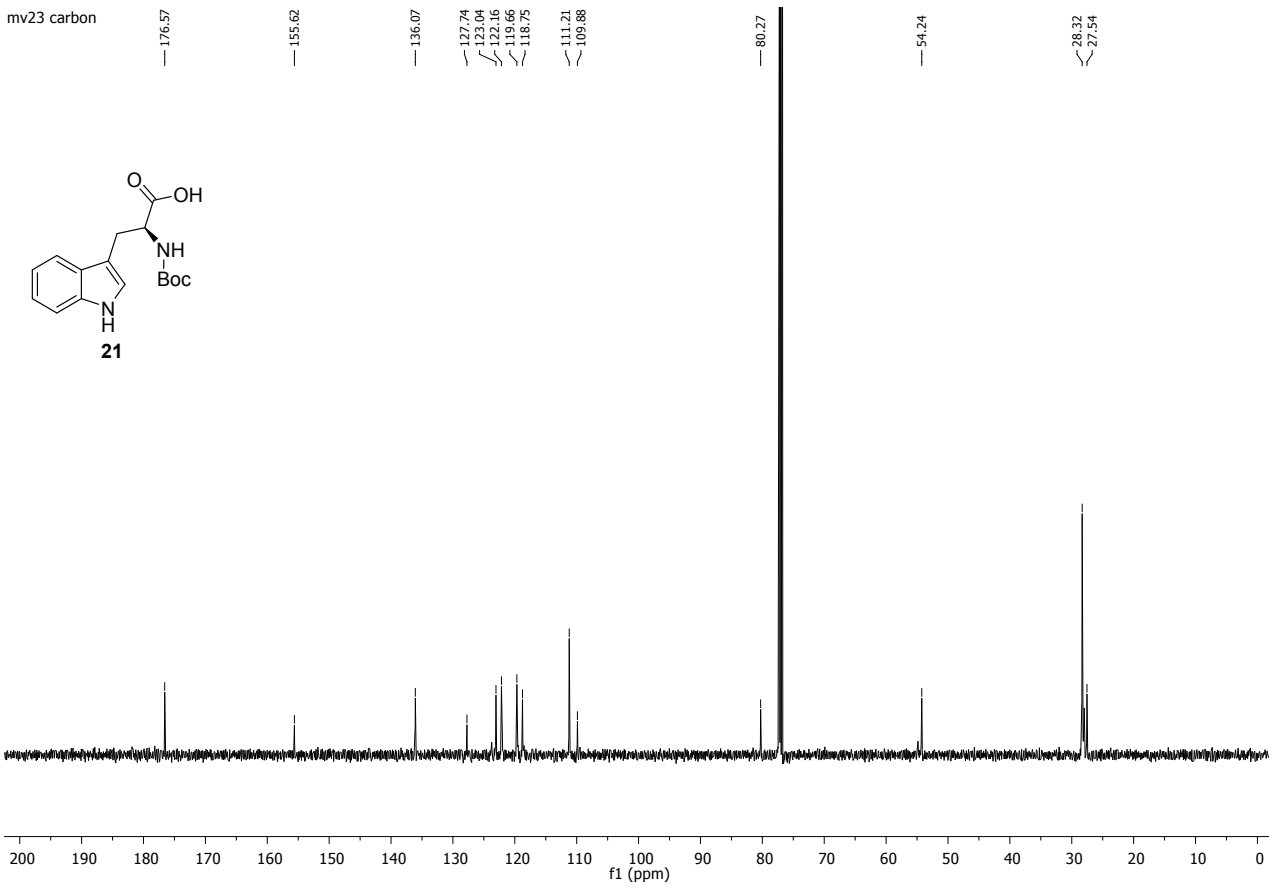

mv21
10.97
8.97
8.96
8.31
8.30
8.10
7.70
7.55
7.53
7.40
7.39
7.33
7.31
7.29
7.28
7.23
7.12
7.10
7.09
7.03
7.01
7.00
5.18
5.14
5.09
5.06
4.65
4.64
4.63
3.63
3.26
3.25
3.23
3.23
3.16
3.15
3.14
3.13
NH
O
N
H
O
O
N
O
19
1.00
1.00
1.01
1.00
1.00
2.01
2.02
2.01
1.01
1.00
1.02
1.04
1.03
1.03
1.05
1.03
3.00
12.0 11.5 11.0 10.5 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)

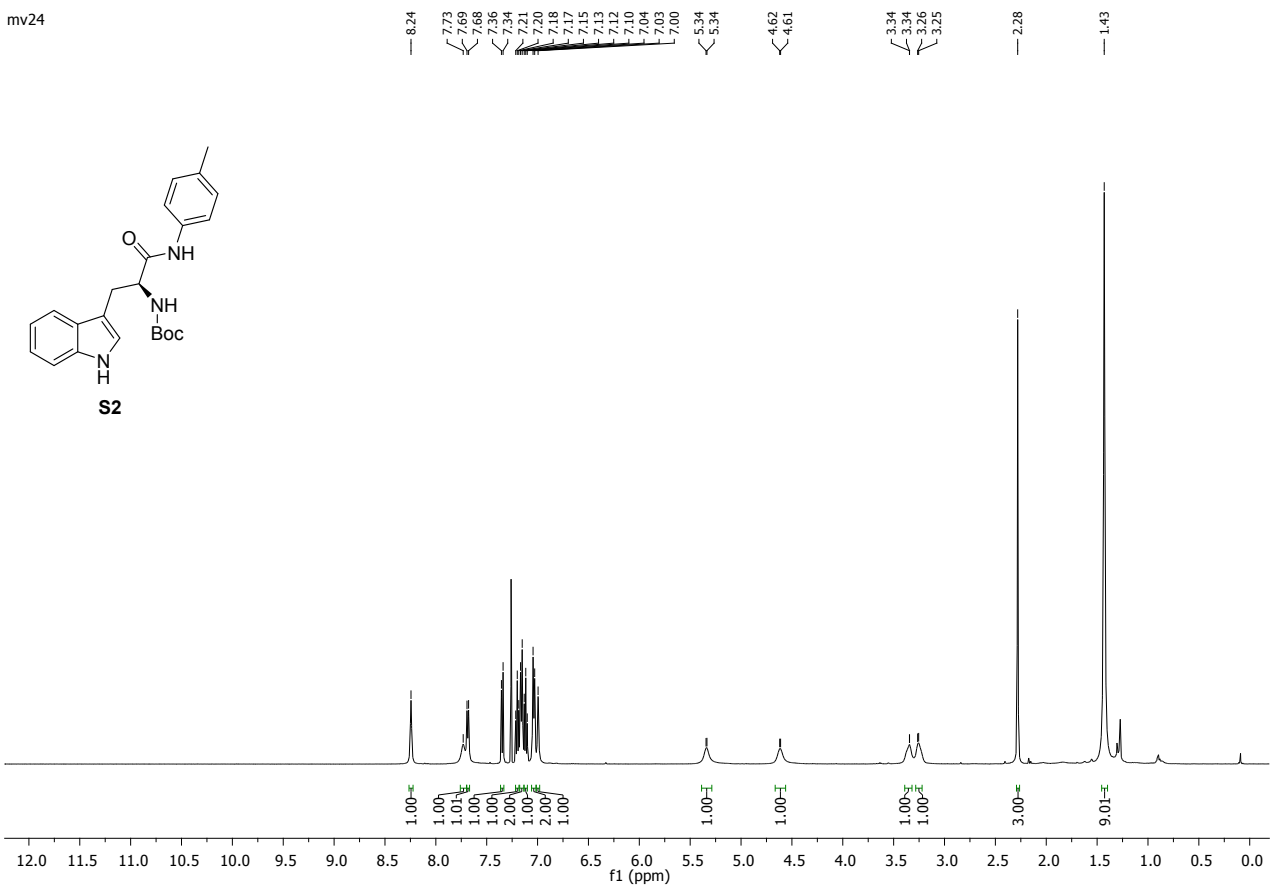

mv21 carbon
176.50
172.01
167.29
142.27
140.54
136.15
135.19
133.71
130.57
127.09
126.41
125.61
123.91
121.42
121.39
121.09
121.00
118.47
117.96
115.82
115.71
111.47
109.25
53.23
51.98
48.54
27.12
20.18
NH
O
N
H
O
O
N
O
19
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

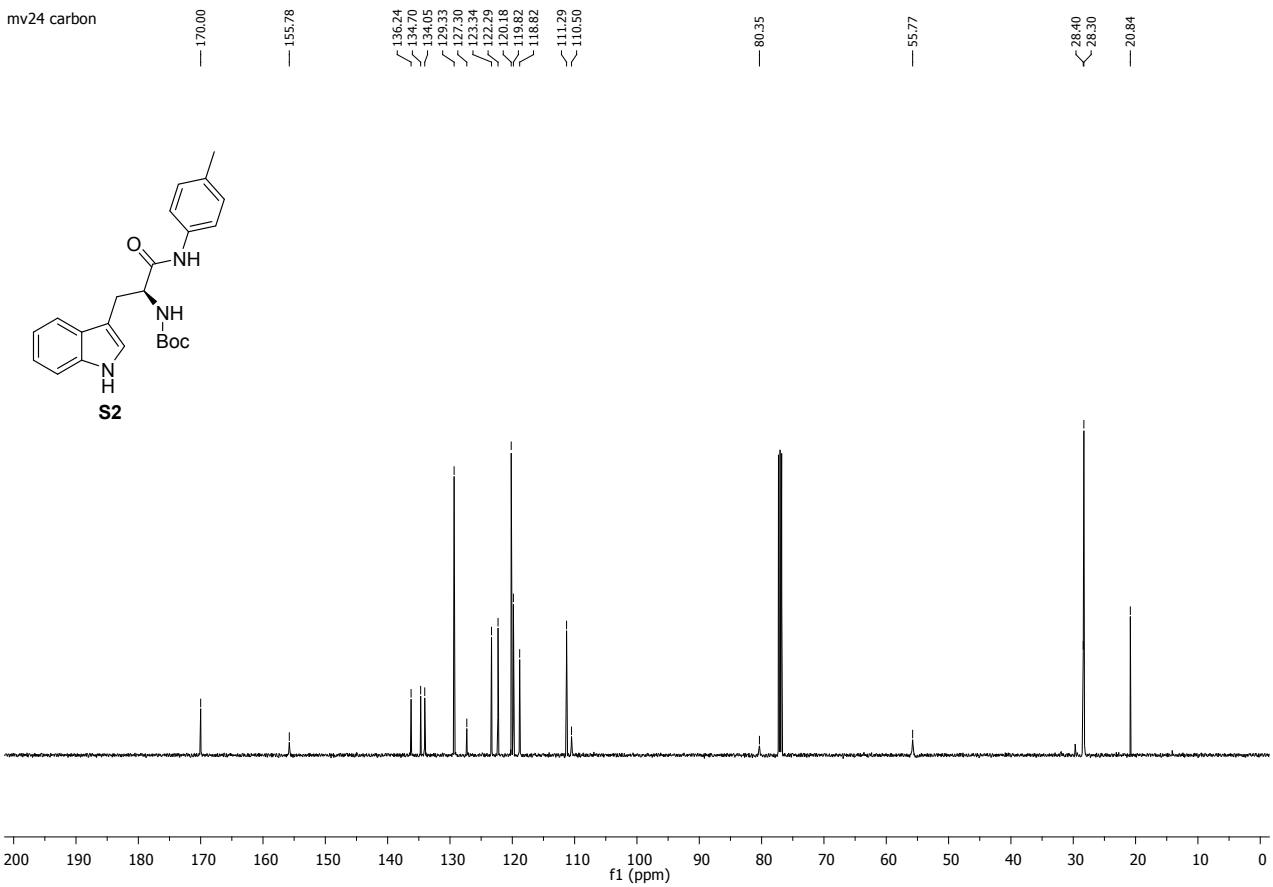

mv22
12.93
10.94
8.81
8.80
8.30
8.29
8.09
7.67
7.59
7.58
7.49
7.40
7.38
7.30
7.28
7.27
7.21
7.10
7.08
7.02
5.17
5.13
5.06
5.02
4.59
4.57
4.56
4.55
3.28
3.27
3.25
3.24
3.13
3.11
3.10
3.08
2.42
NH
O
N
H
O
OH
N
O
20
1.04
1.00
1.00
1.01
1.00
1.00
1.02
1.00
2.04
2.04
1.00
1.03
1.03
1.00
1.00
1.03
1.13
1.03
3.01
13.5
12.5
11.5
10.5
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)


mv22 carbon
176.47
173.09
167.00
142.28
140.54
136.13
135.18
133.69
130.52
127.27
126.38
125.58
123.78
121.38
121.05
120.91
118.38
118.17
115.88
115.76
111.38
109.75
53.29
48.56
27.27
20.18
NH
O
N
H
O
OH
N
O
20
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

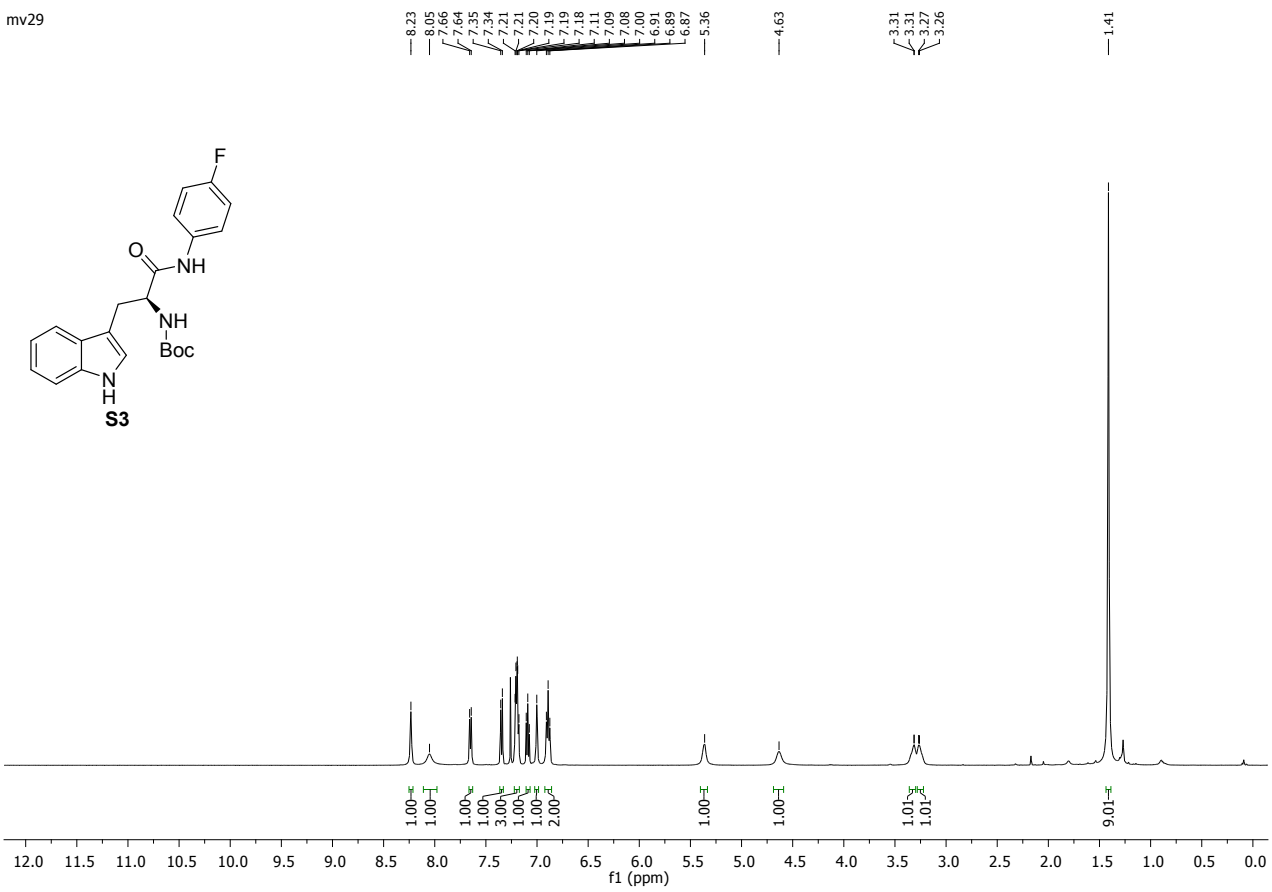

mv23
8.11
7.61
7.59
7.35
7.34
7.22
7.20
7.19
7.13
7.12
7.11
6.99
5.08
5.06
4.67
4.66
3.38
3.37
3.35
3.34
3.31
3.30
3.29
3.28
1.43
O
OH
NH
Boc
N
H
21
1.00
1.00
1.00
1.00
1.00
1.00
1.00
2.02
9.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


mv23 carbon
176.57
155.62
136.07
127.74
123.04
122.16
119.66
118.75
111.21
109.88
80.27
54.24
28.32
27.54
O
OH
NH
Boc
N
H
21
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


mv24
8.24
7.73
7.69
7.68
7.36
7.34
7.21
7.20
7.18
7.17
7.15
7.13
7.12
7.10
7.04
7.03
7.00
5.34
5.34
4.62
4.61
3.34
3.34
3.26
3.25
2.28
1.43
O
NH
NH
Boc
N
H
S2
1.00
1.00
1.01
1.00
1.00
2.00
1.00
2.00
1.00
1.00
1.00
1.00
3.00
9.01
12.0 11.5 11.0 10.5 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)

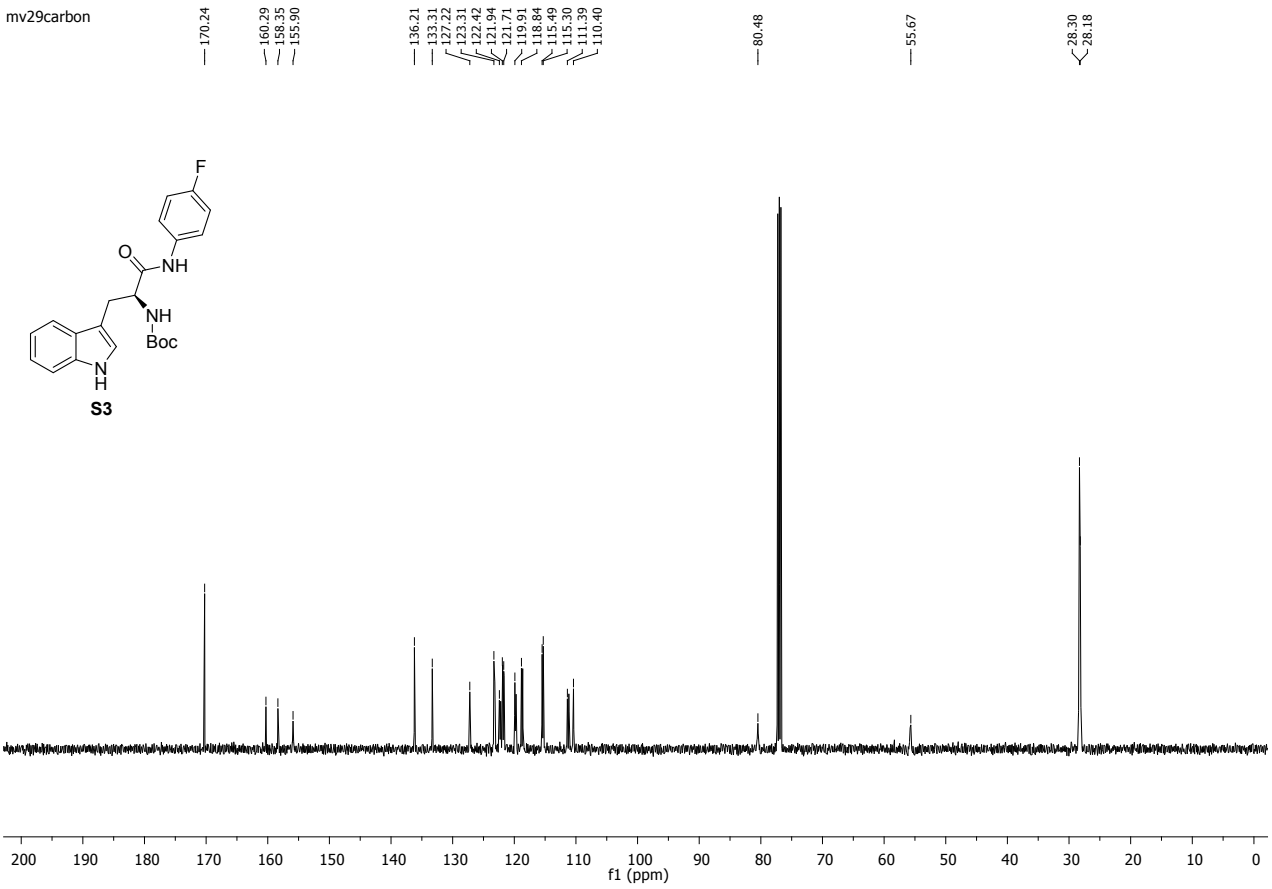

mv24 carbon
170.00
155.78
136.24
134.70
134.05
129.33
127.30
123.34
122.29
120.18
119.82
118.82
111.29
110.50
80.35
55.77
28.40
28.30
20.84
O
NH
NH
Boc
N
H
S2
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

mv29

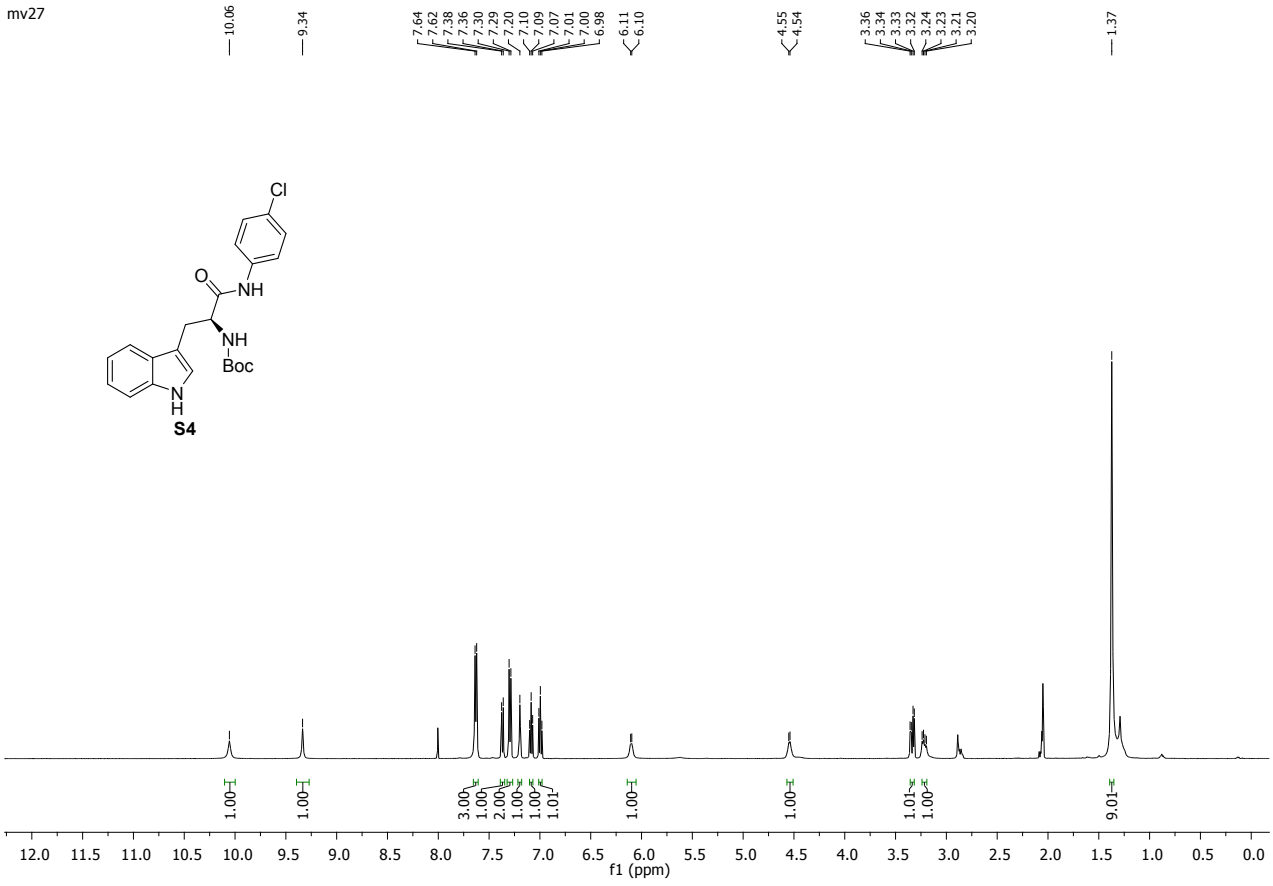


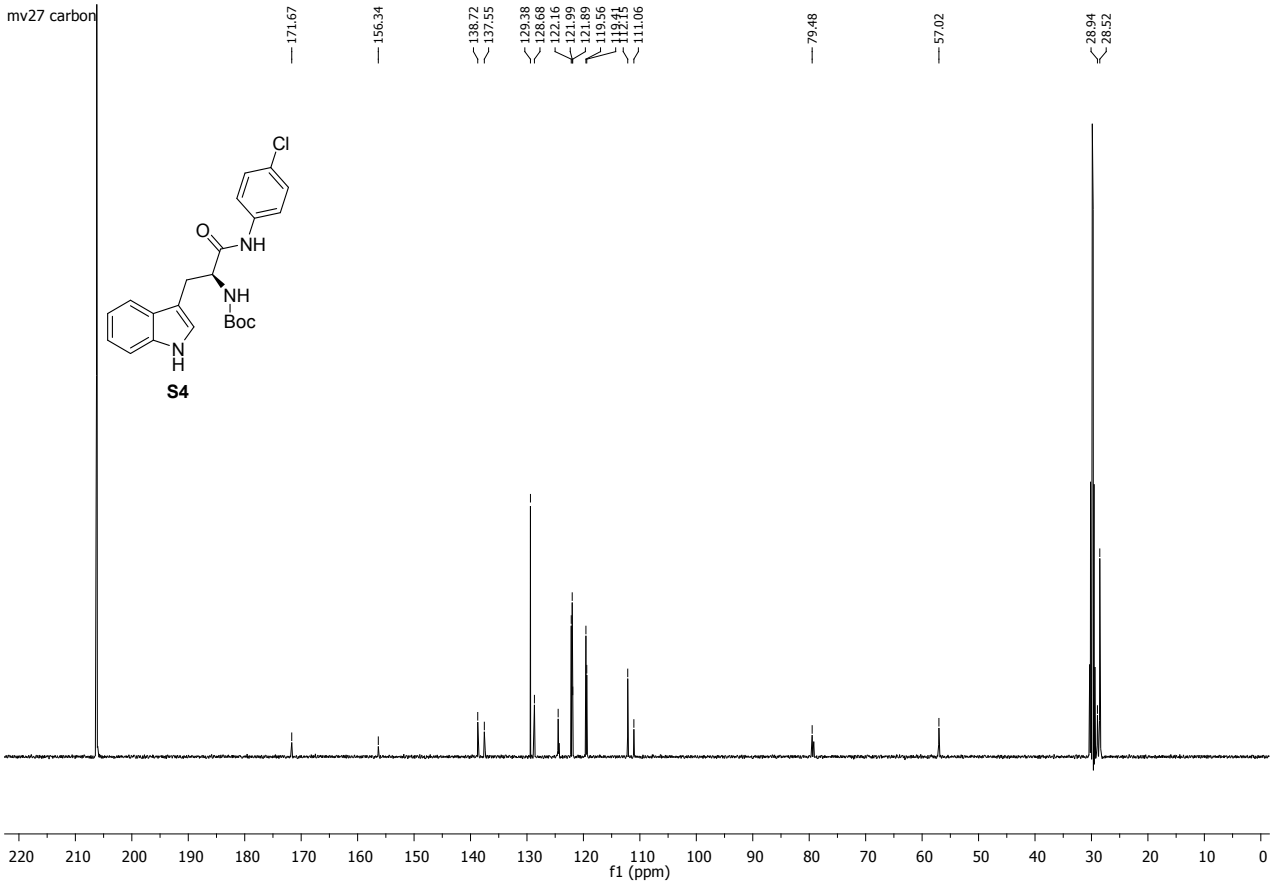
S3

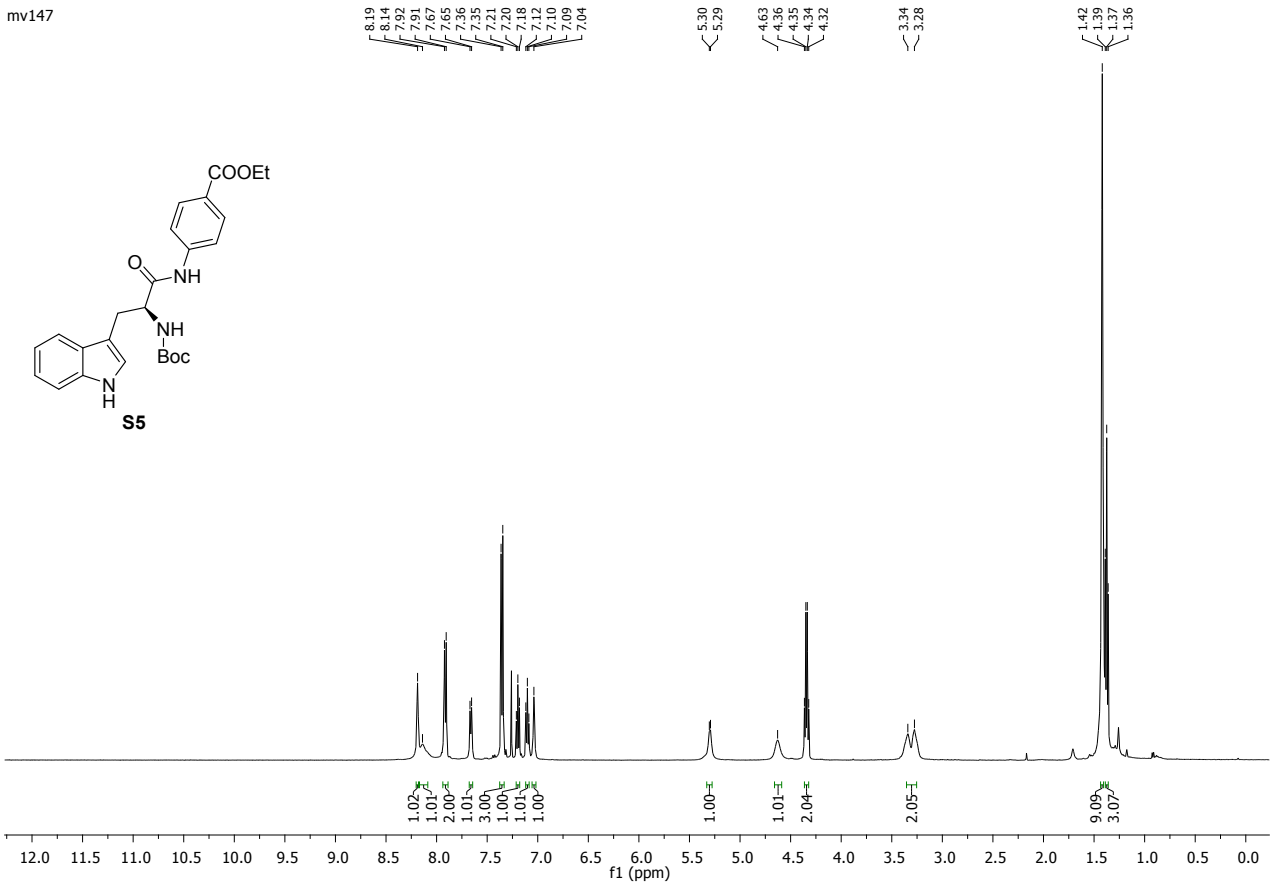
mv29carbon

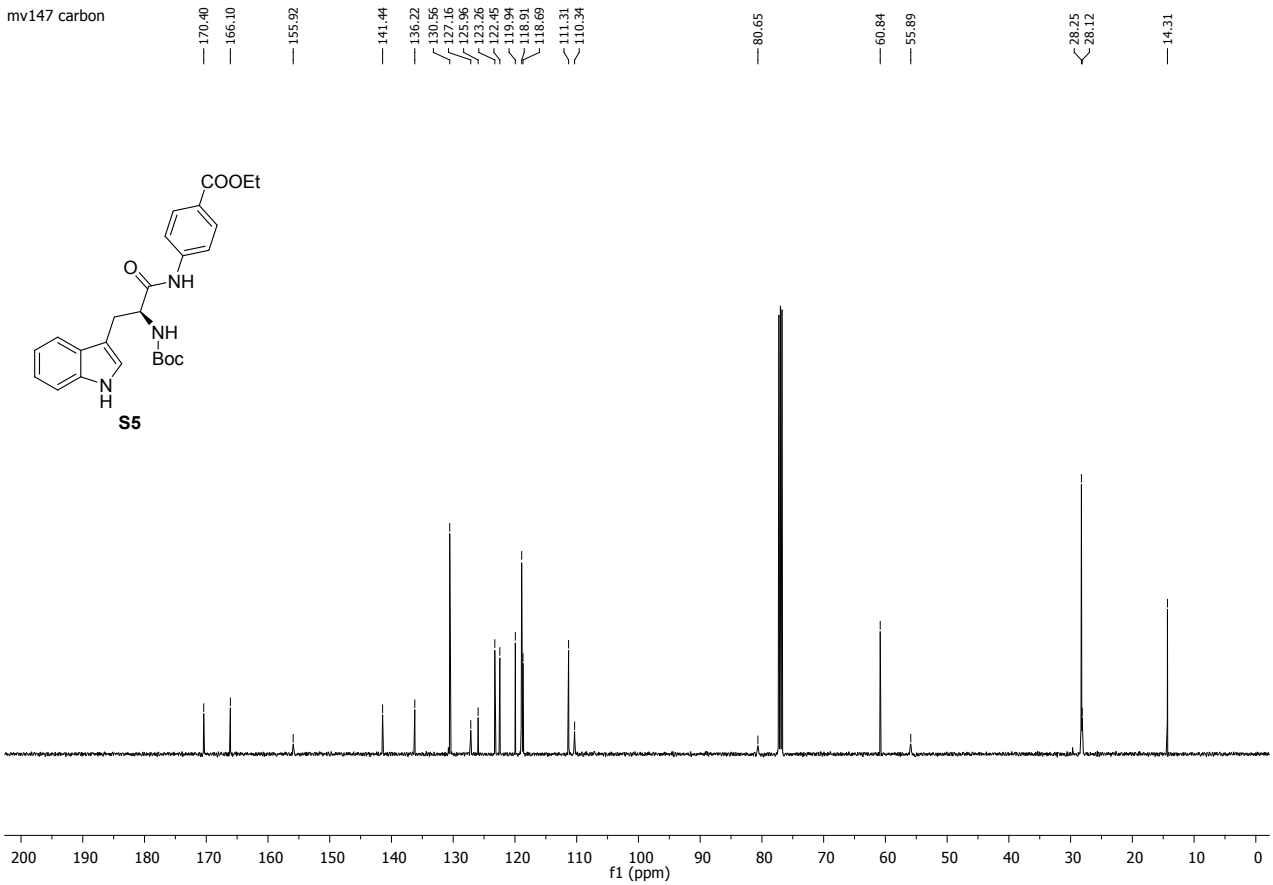


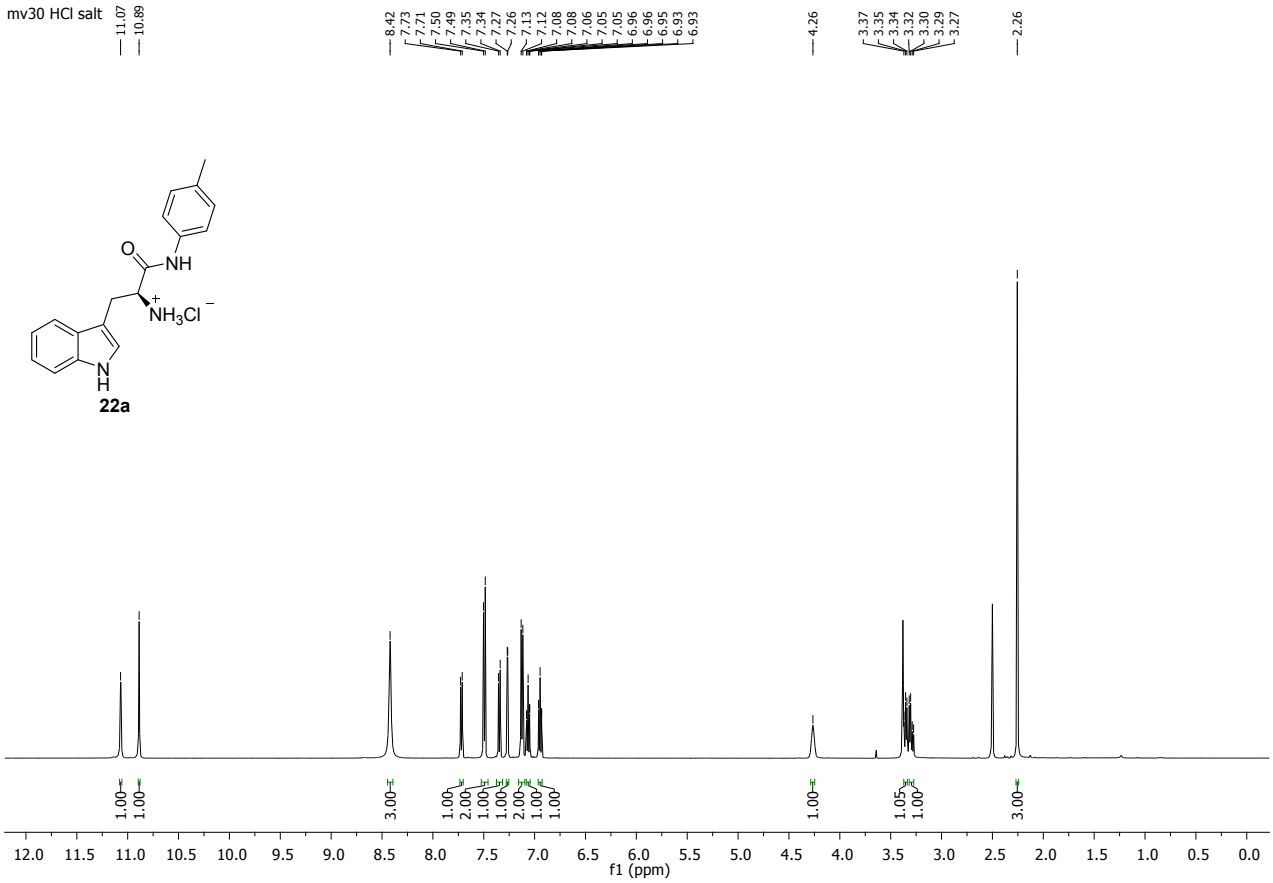
S3

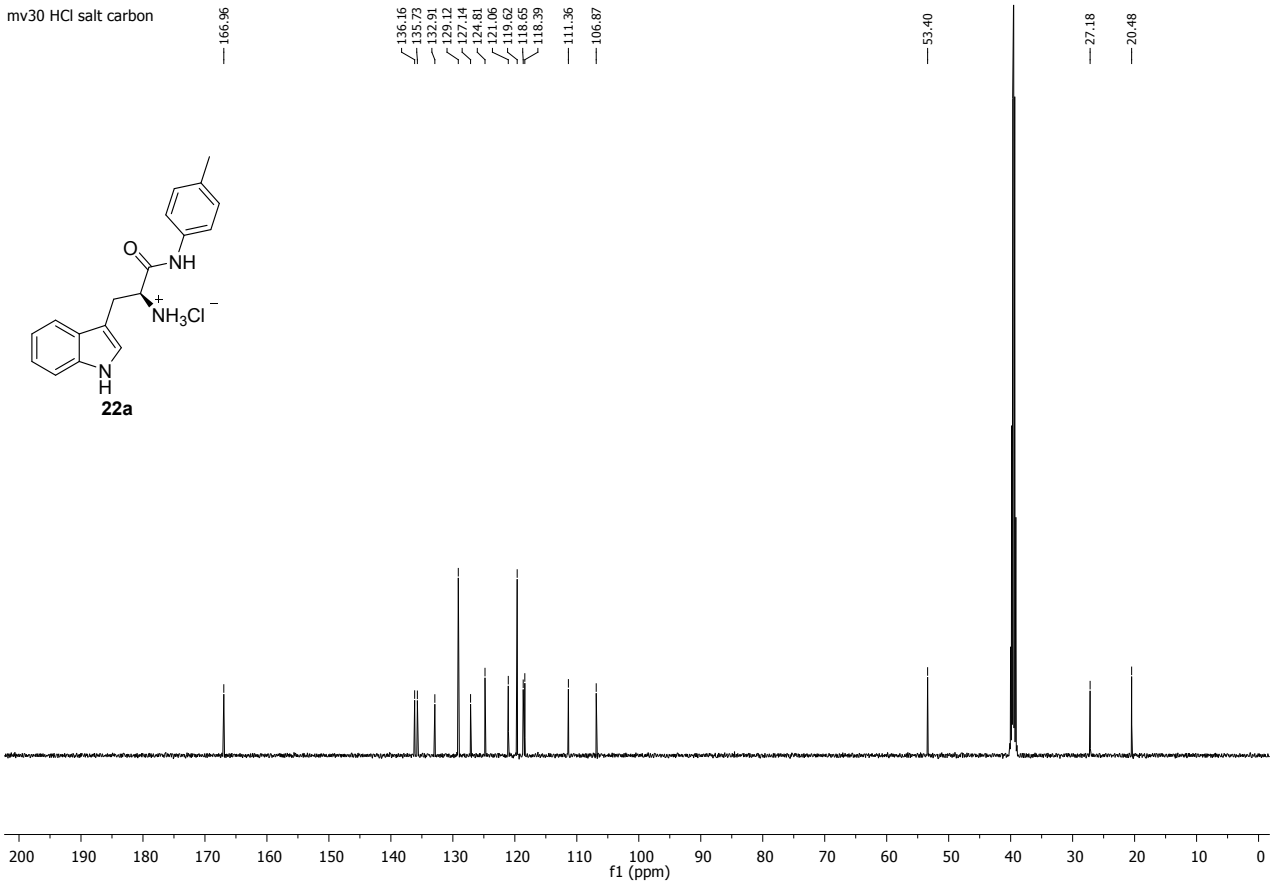

mv27
10.06
9.34
7.64
7.62
7.38
7.36
7.30
7.29
7.20
7.10
7.09
7.07
7.01
7.00
6.98
6.11
6.10
4.55
4.54
3.36
3.34
3.33
3.32
3.24
3.23
3.21
3.20
1.37
Cl
O
NH
NH
Boc
N
H
S4
1.00
1.00
3.00
1.00
2.00
1.00
1.00
1.01
1.00
1.00
1.01
1.00
9.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

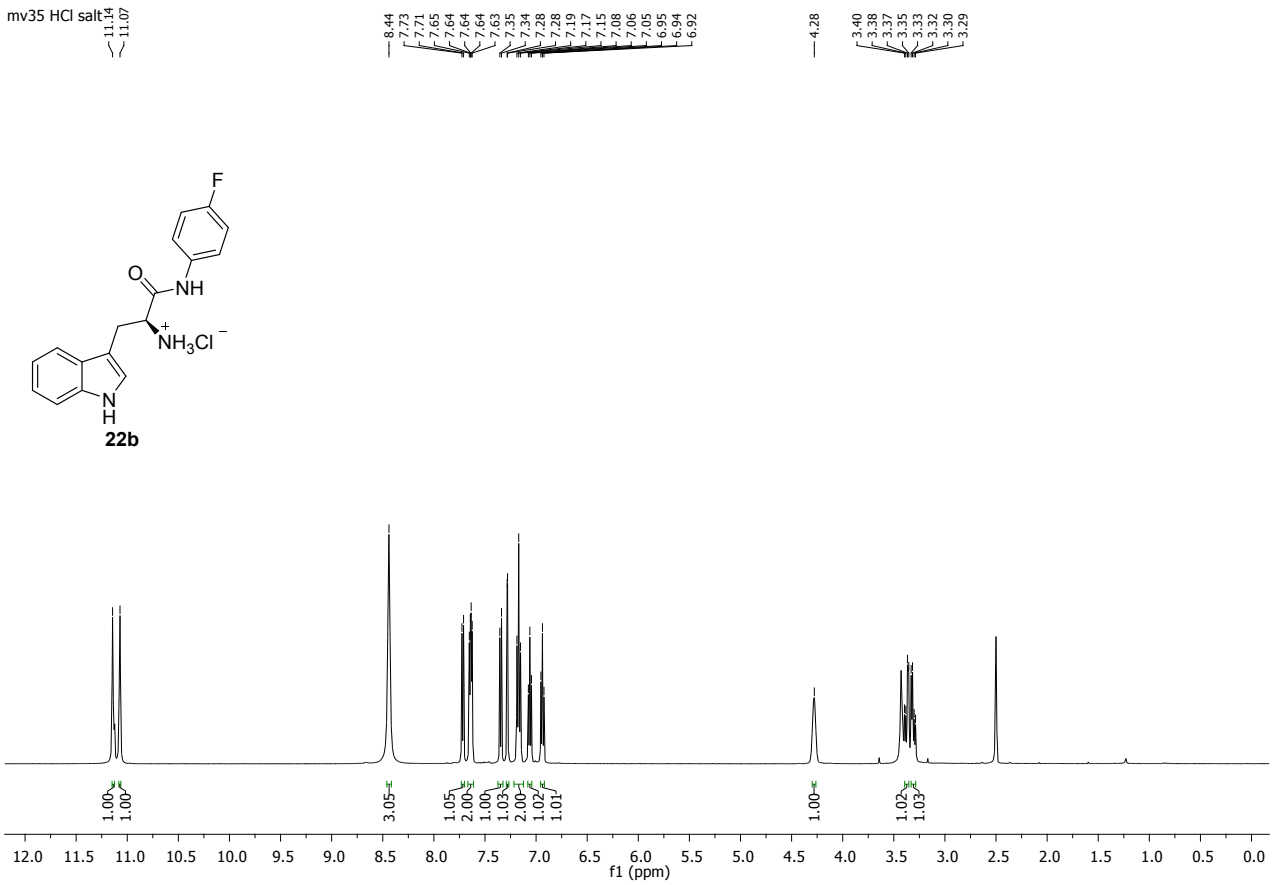

mv27 carbon
171.67
156.34
138.72
137.55
129.38
128.68
122.16
121.99
121.89
119.56
119.41
112.15
111.06
79.48
57.02
28.94
28.52
Cl
O
NH
NH
Boc
N
H
S4
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

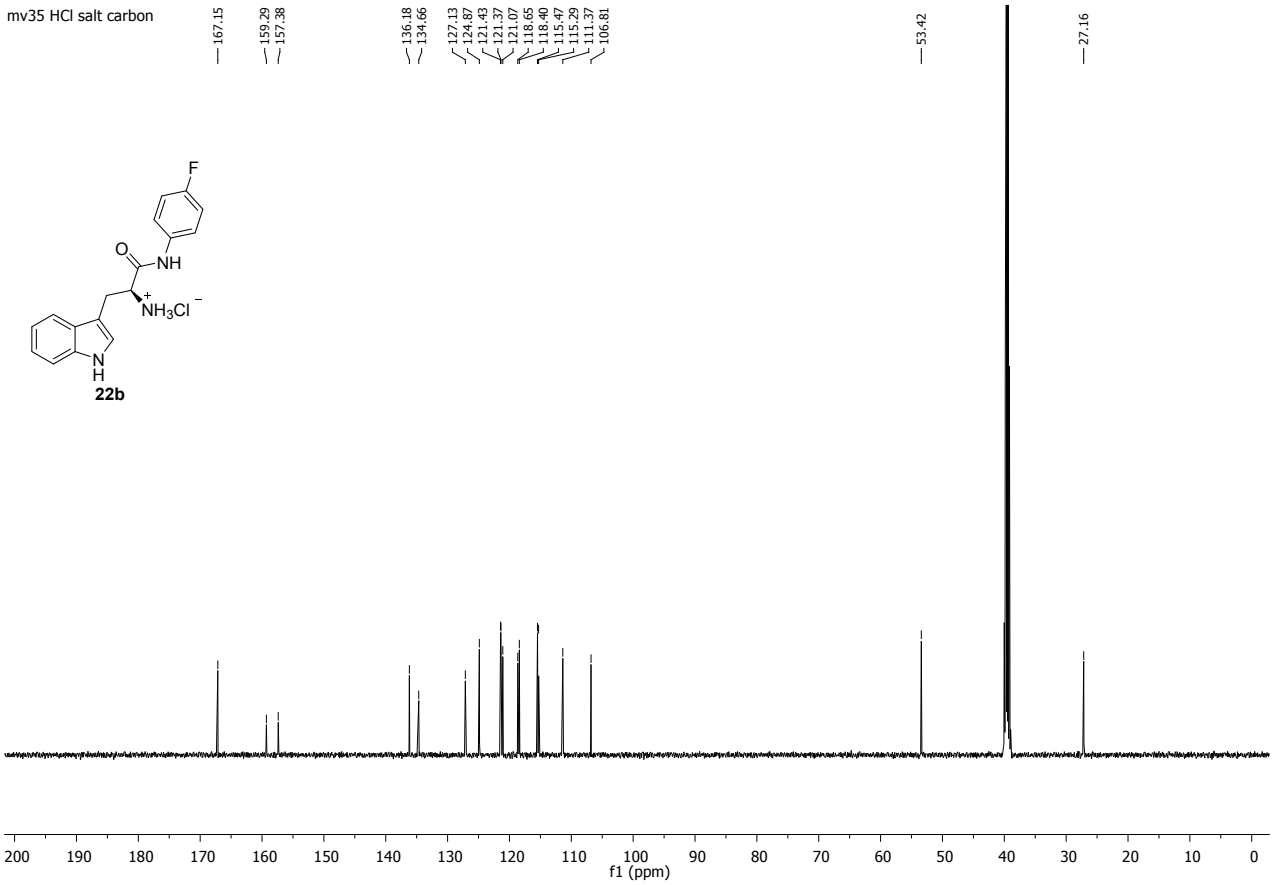

mv147
8.19
8.14
7.92
7.91
7.67
7.65
7.36
7.35
7.21
7.20
7.18
7.12
7.10
7.09
7.04
5.30
5.29
4.63
4.36
4.35
4.34
4.32
3.34
3.28
1.42
1.39
1.37
1.36
COOEt
O
NH
NH
Boc
N
H
S5
1.02
1.01
2.00
1.01
3.00
1.00
1.01
1.00
1.00
1.01
2.04
2.05
9.09
3.07
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

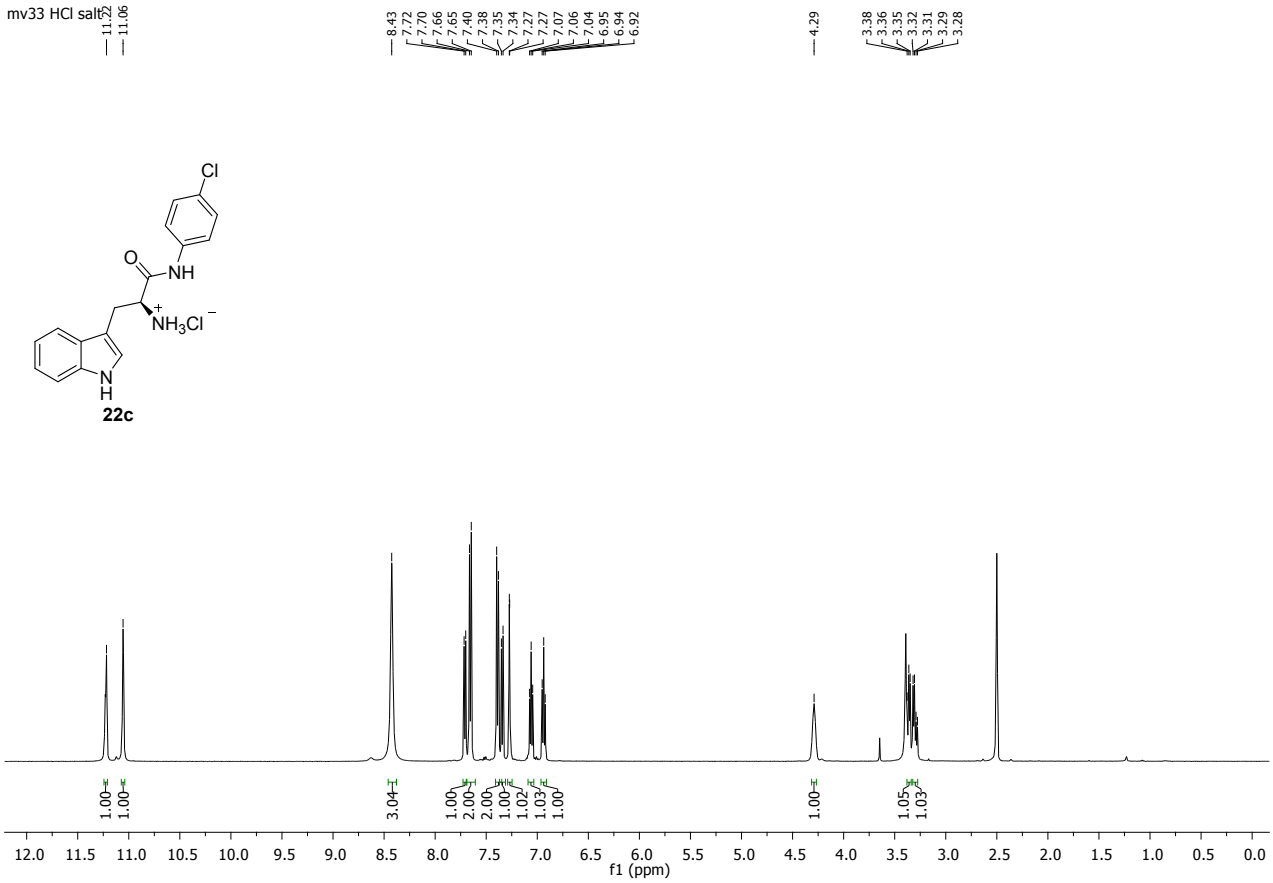

mv147 carbon
170.40
166.10
155.92
141.44
136.22
130.56
127.16
125.96
123.26
122.45
119.94
118.91
118.69
111.31
110.34
80.65
60.84
55.89
28.25
28.12
14.31
COOEt
O
NH
NH
Boc
N
H
S5
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

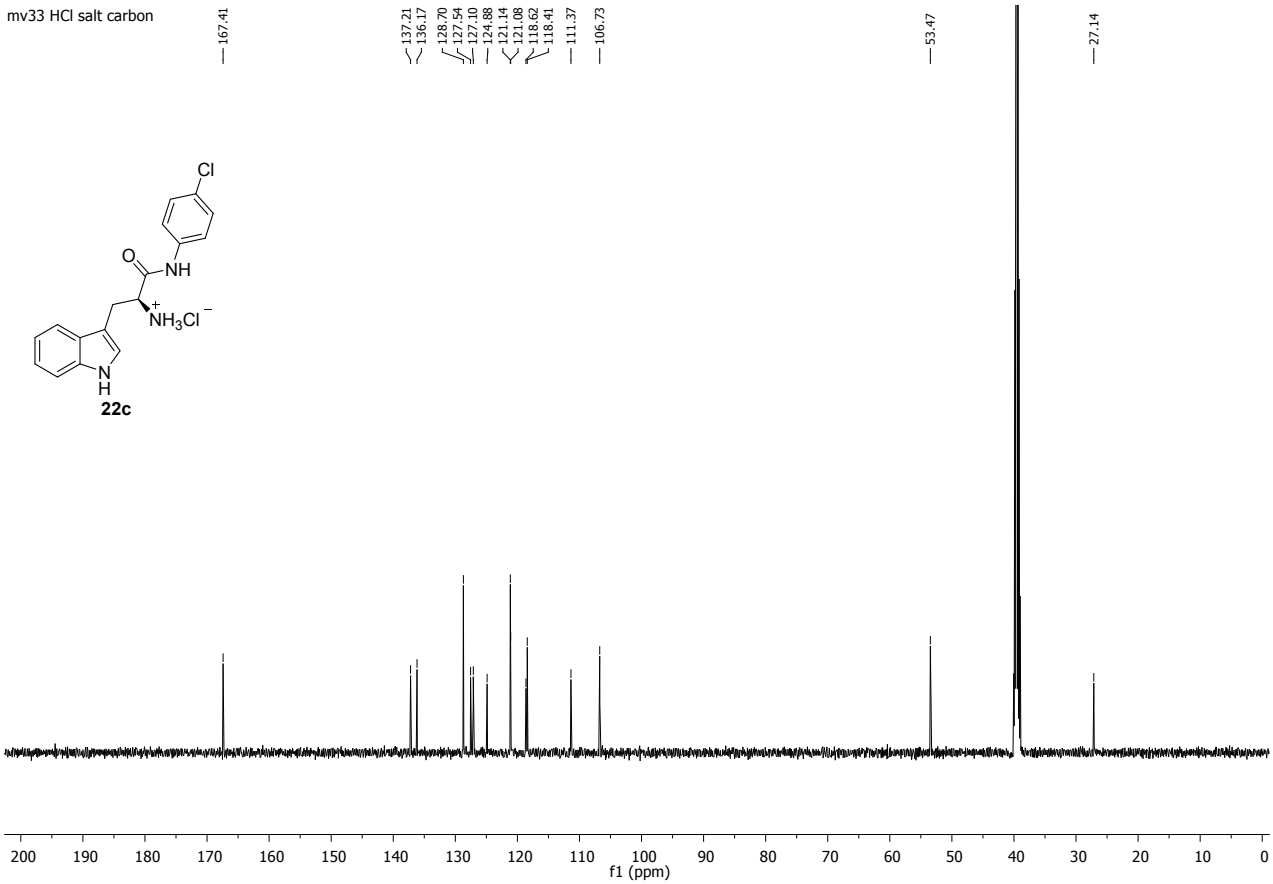

mv30 HCl salt
11.07
10.89
8.42
7.73
7.71
7.50
7.49
7.35
7.34
7.27
7.26
7.13
7.12
7.08
7.08
7.06
7.05
7.05
6.96
6.96
6.95
6.93
6.93
4.26
3.37
3.35
3.34
3.32
3.30
3.29
3.27
2.26
O
NH
NH3Cl
N
H
22a
1.00
1.00
3.00
1.00
2.00
1.00
1.00
2.00
1.00
1.00
1.00
1.05
1.00
3.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 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)

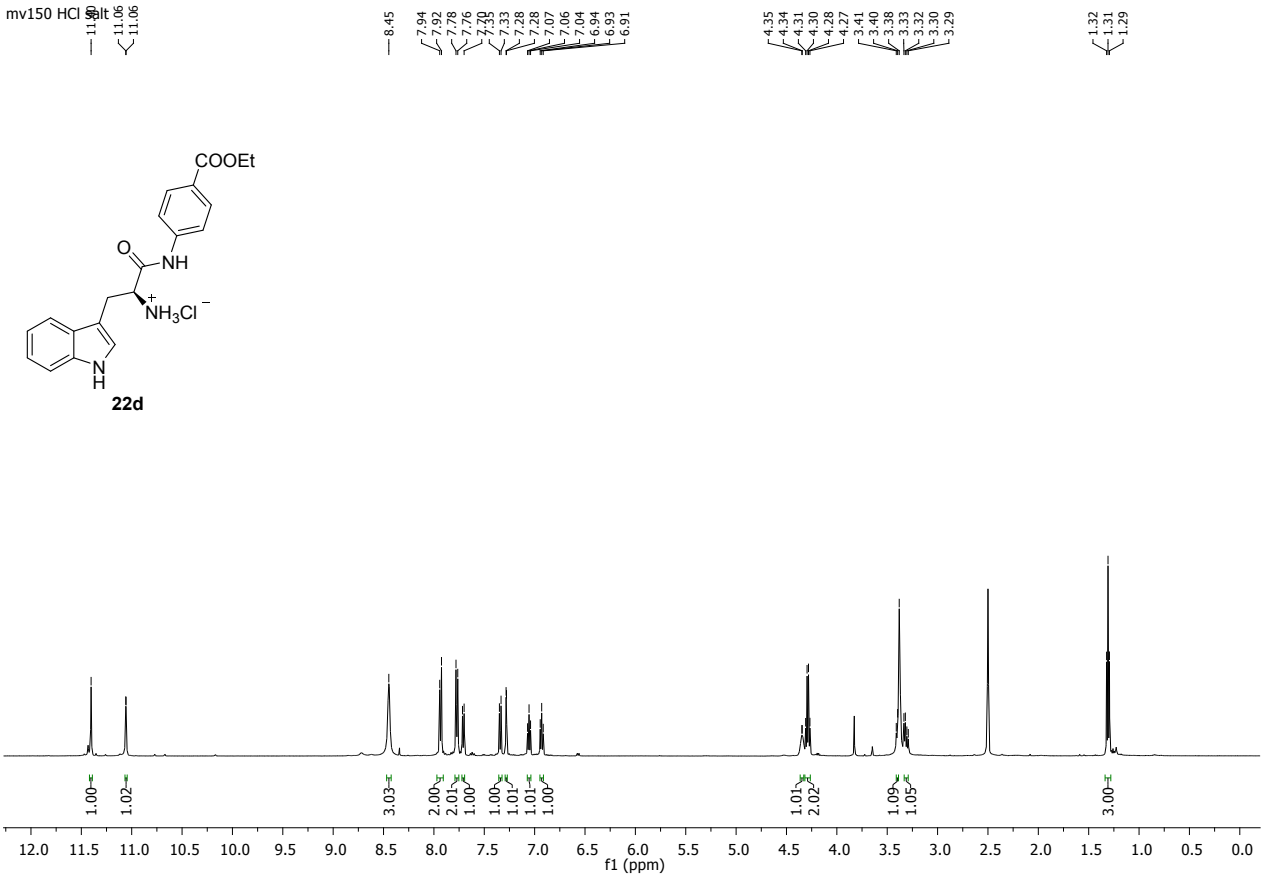

mv30 HCl salt carbon
166.96
136.16
135.73
132.91
129.12
127.14
124.81
121.06
119.62
118.65
118.39
111.36
106.87
53.40
27.18
20.48
O
NH
NH3Cl
N
H
22a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

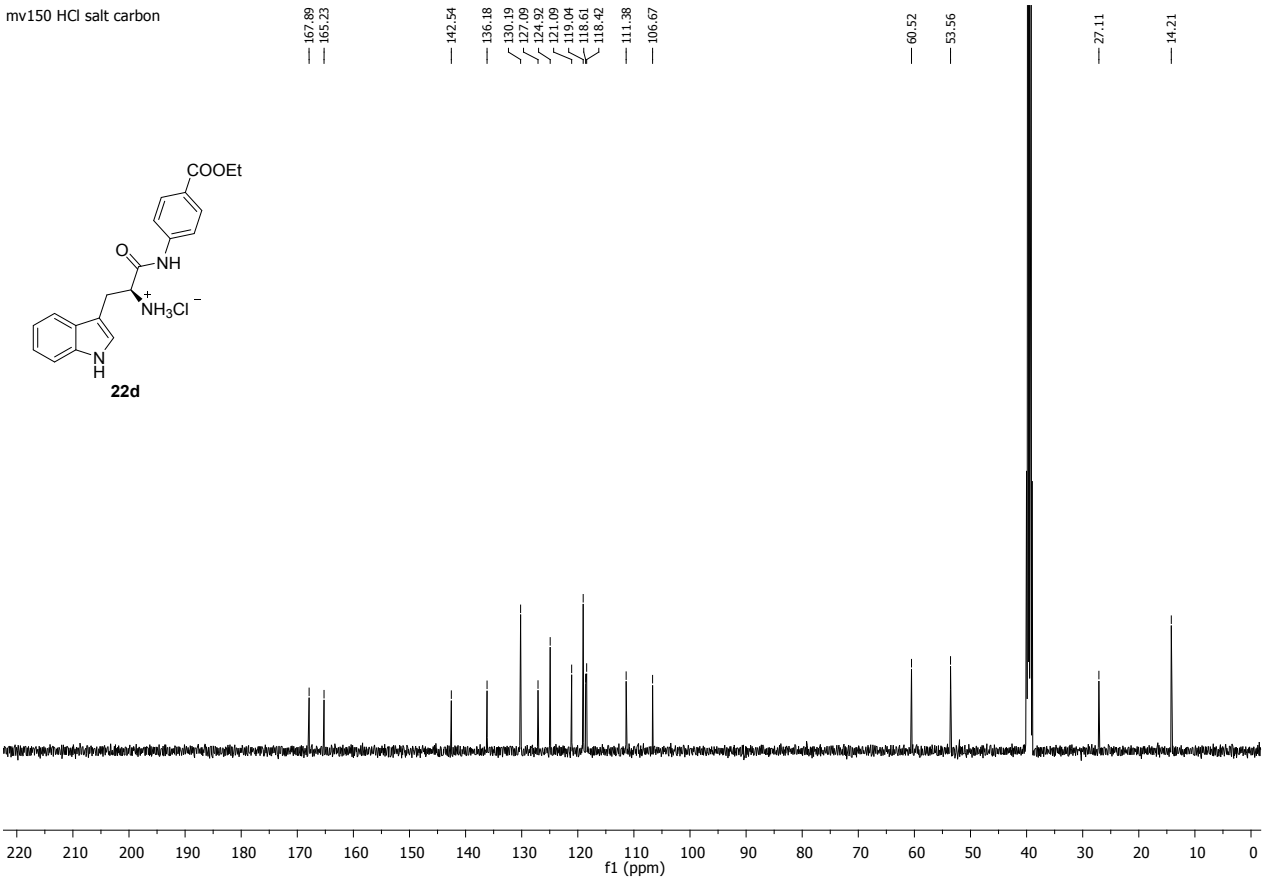

mv35 HCl salt
11.14
11.07
8.44
7.73
7.71
7.65
7.64
7.64
7.64
7.63
7.35
7.34
7.28
7.28
7.19
7.17
7.15
7.08
7.06
7.05
6.95
6.94
6.92
4.28
3.40
3.38
3.37
3.35
3.33
3.32
3.30
3.29
F
O
NH
NH3Cl
N
H
22b
1.00
1.00
3.05
1.05
2.00
1.00
1.03
2.00
1.02
1.01
1.00
1.02
1.03
f1 (ppm)

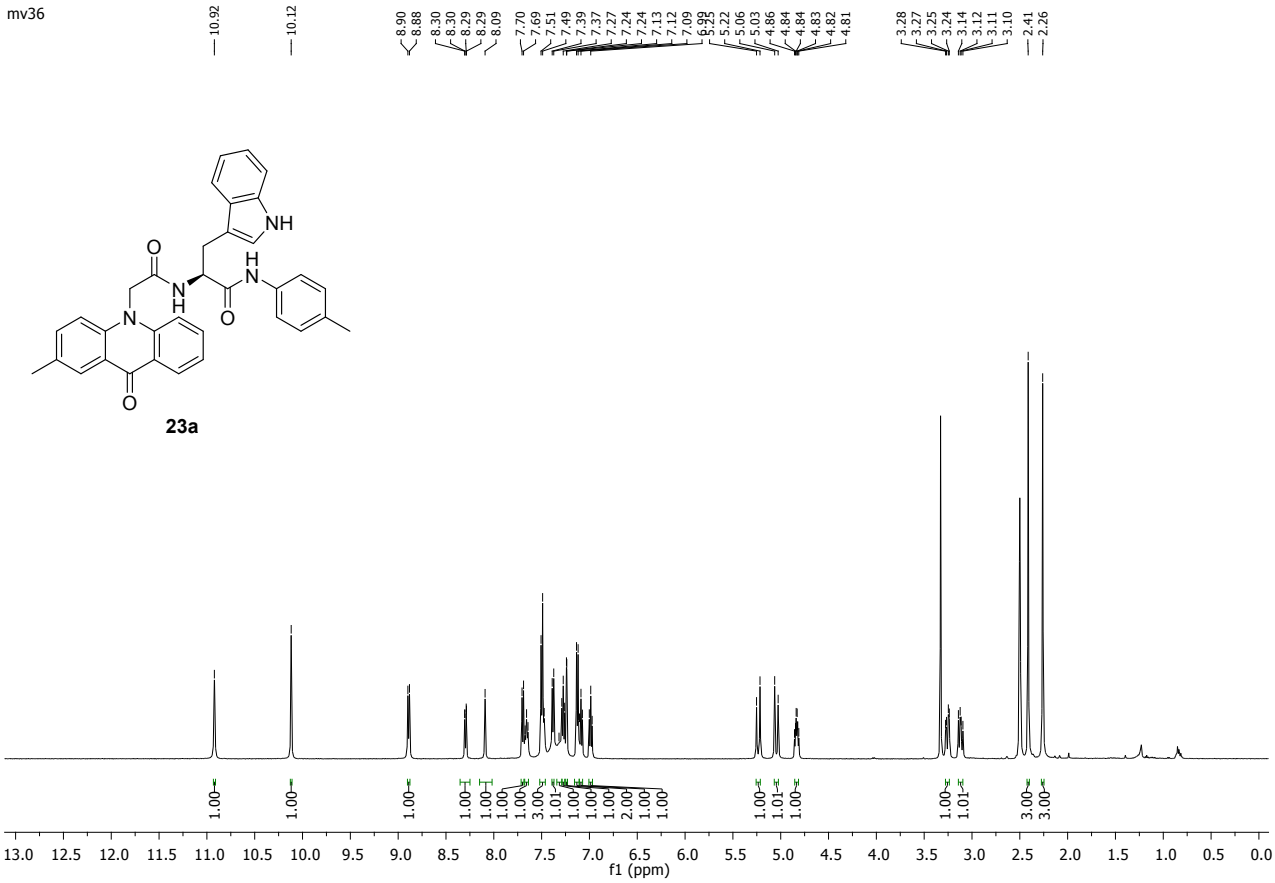

mv35 HCl salt carbon
167.15
159.29
157.38
136.18
134.66
127.13
124.87
121.43
121.37
121.07
118.65
118.40
115.47
115.29
111.37
106.81
53.42
27.16
F
O
NH
NH3Cl
N
H
22b
f1 (ppm)

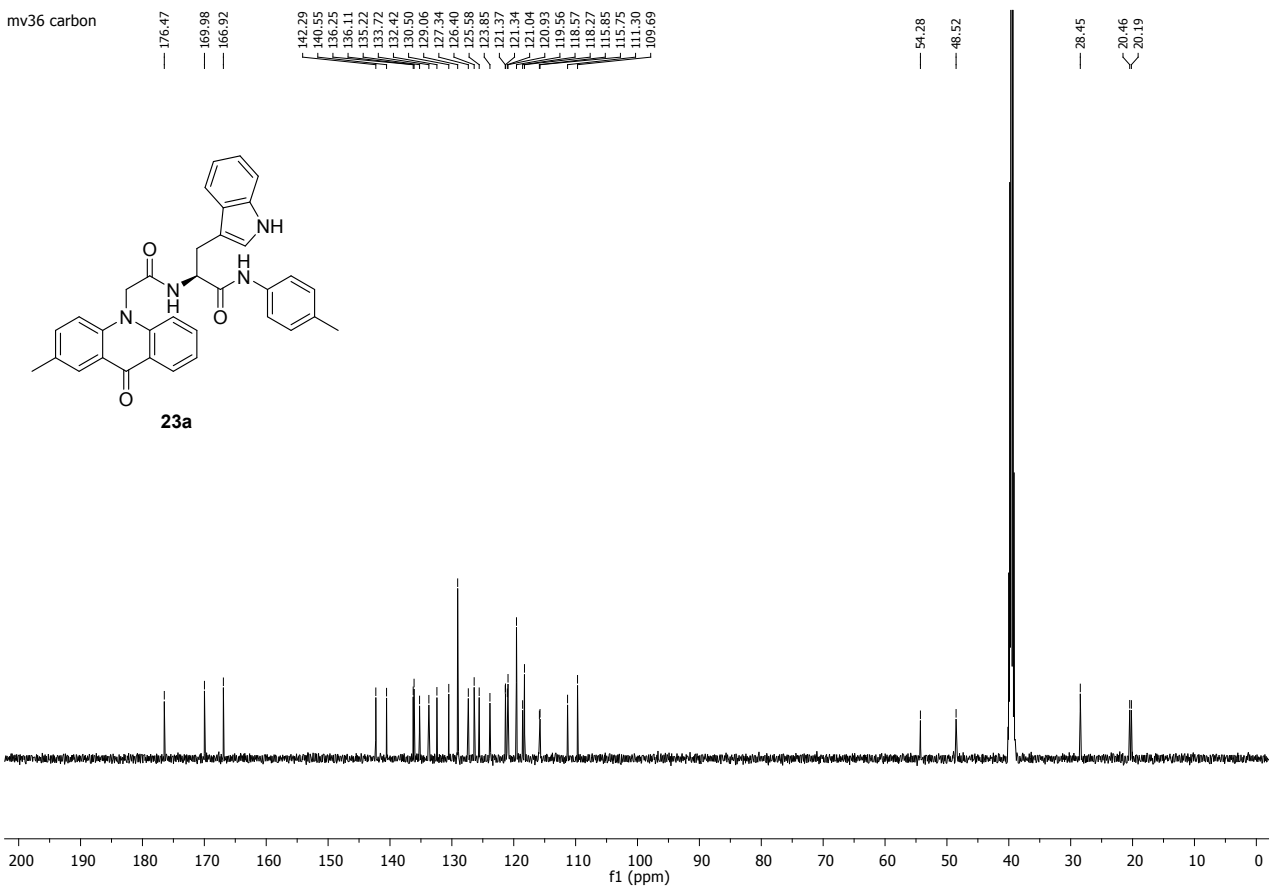

mv33 HCl salt2
11.22
11.06
8.43
7.72
7.70
7.66
7.65
7.40
7.38
7.35
7.34
7.27
7.27
7.07
7.06
7.04
6.95
6.94
6.92
4.29
3.38
3.36
3.35
3.32
3.31
3.29
3.28
Cl
O
NH
NH3Cl
N
H
22c
1.00
1.00
3.04
1.00
2.00
2.00
1.00
1.02
1.03
1.00
1.00
1.05
1.03
f1 (ppm)

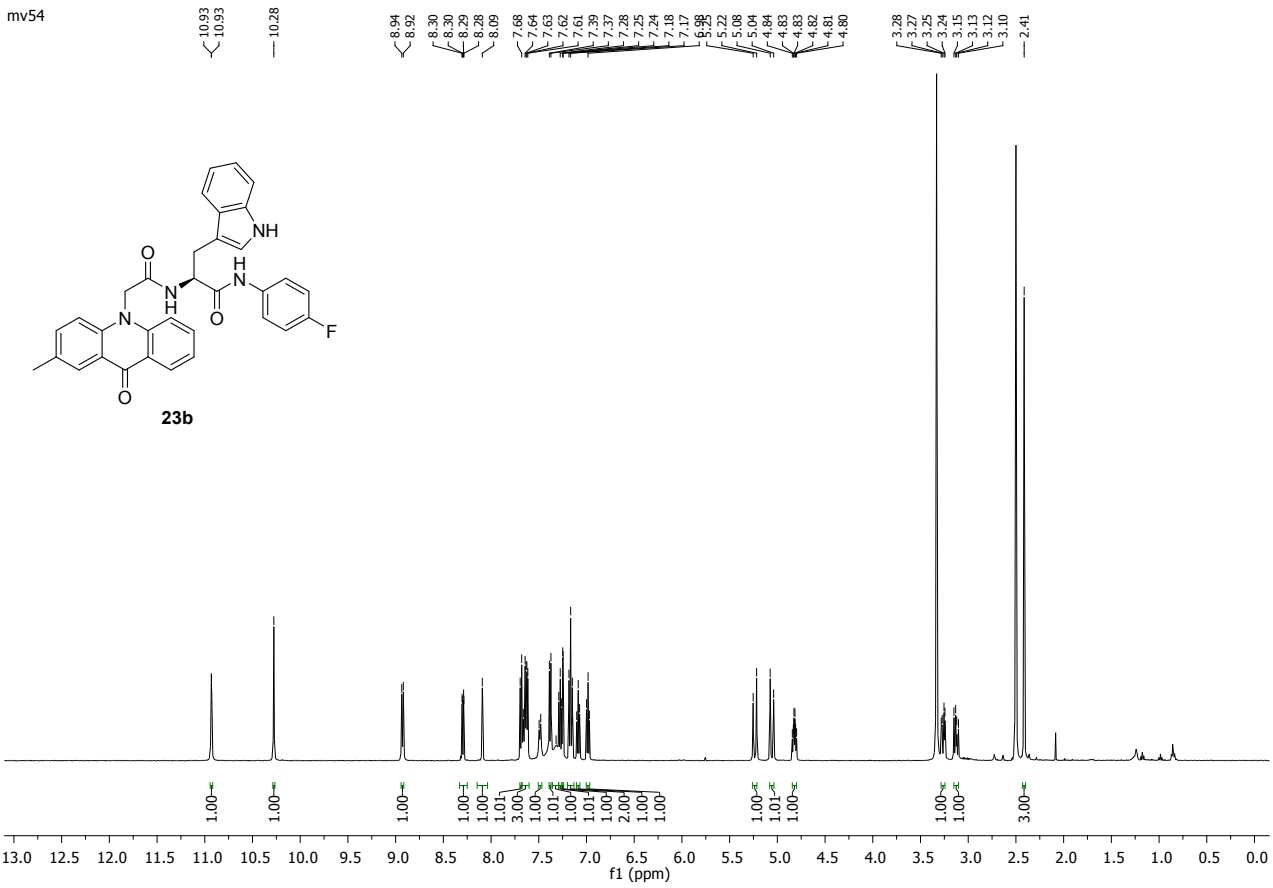

mv33 HCl salt carbon
167.41
137.21
136.17
128.70
127.54
127.10
124.88
121.14
121.08
118.62
118.41
111.37
106.73
53.47
27.14
Cl
O
NH
NH3Cl
N
H
22c
f1 (ppm)

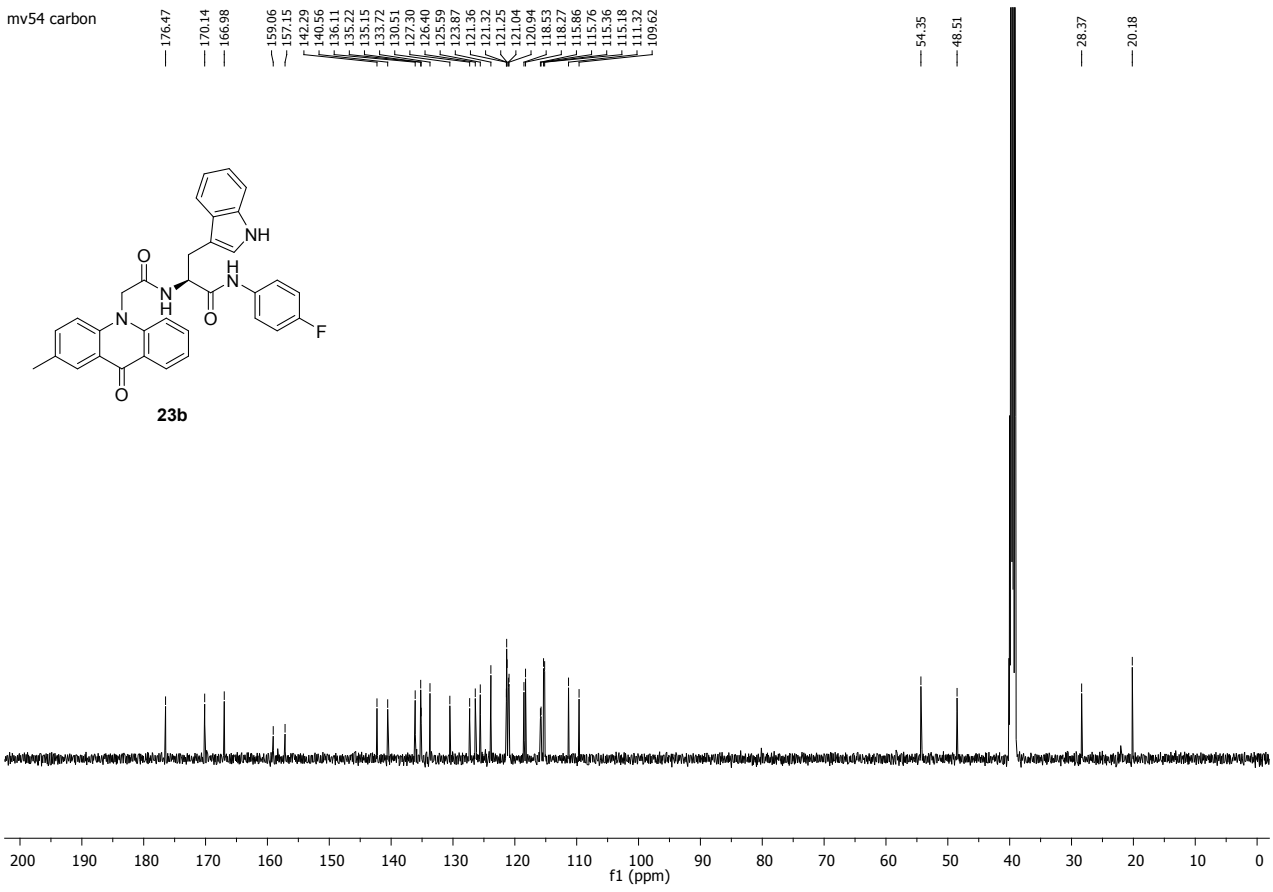

mv150 HCl salt
11.06
11.06
8.45
7.94
7.92
7.78
7.76
7.35
7.33
7.28
7.28
7.07
7.06
7.04
6.94
6.93
6.91
4.35
4.34
4.31
4.30
4.28
4.27
3.41
3.40
3.38
3.33
3.32
3.30
3.29
1.32
1.31
1.29
COOEt
O
NH
NH3Cl
N
H
22d
1.00
1.02
3.03
2.00
2.01
1.00
1.00
1.01
1.01
1.00
1.01
2.02
1.09
1.05
3.00
12.0 11.5 11.0 10.5 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)

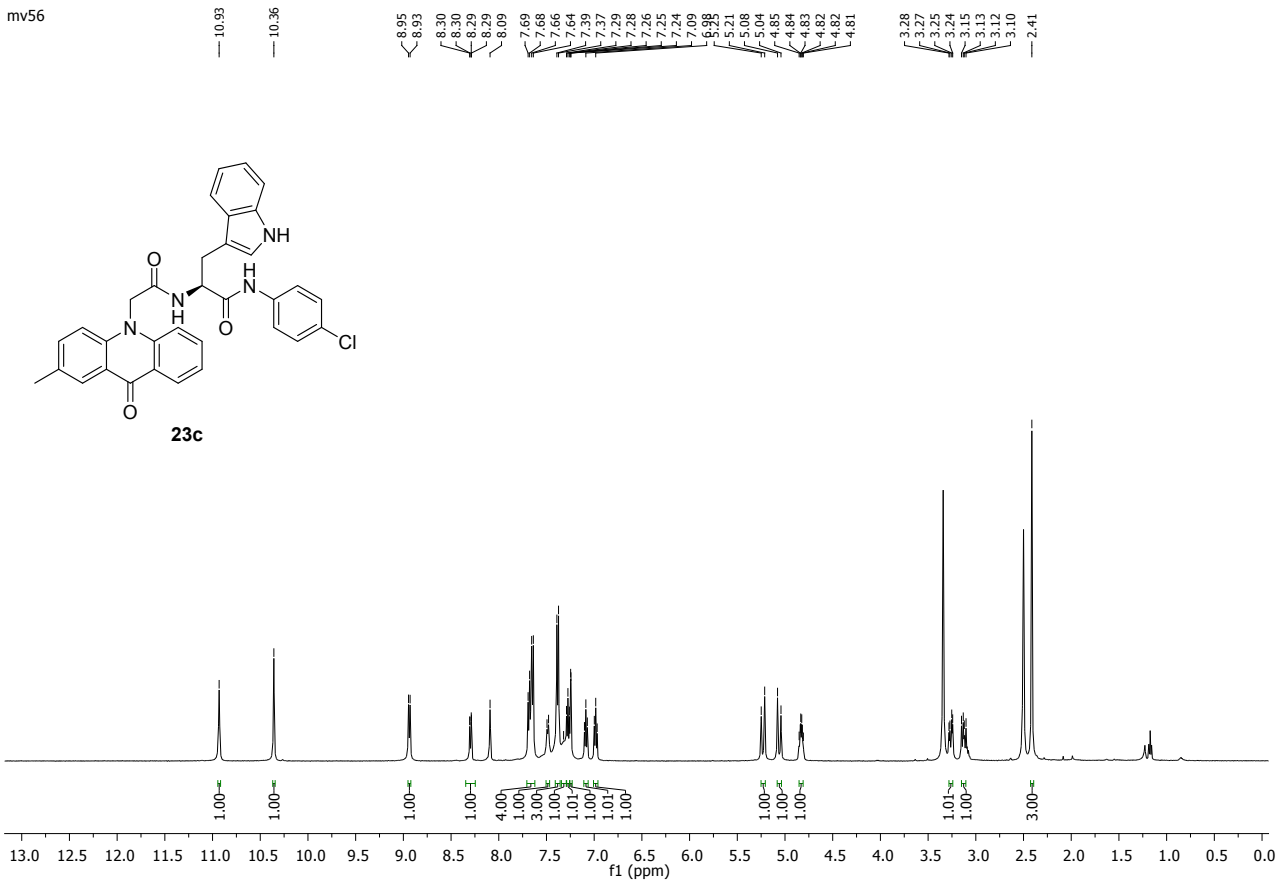

mv150 HCl salt carbon
167.89
165.23
142.54
136.18
130.19
127.09
124.92
121.09
119.04
118.61
118.42
111.38
106.67
60.52
53.56
27.11
14.21
COOEt
O
NH
NH3Cl
N
H
22d
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

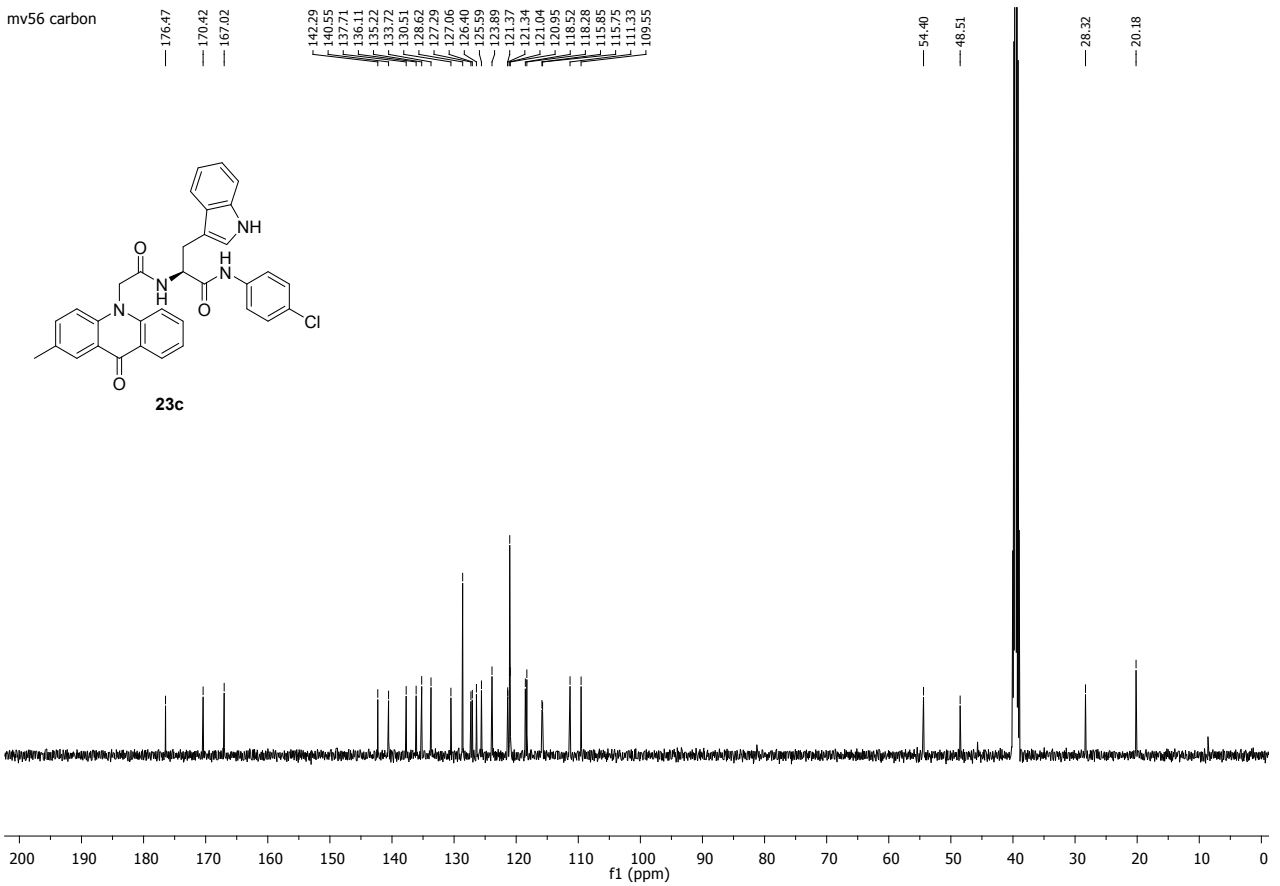

mv36
10.92
10.12
8.90
8.88
8.30
8.30
8.29
8.29
8.09
7.70
7.69
7.51
7.49
7.39
7.37
7.27
7.24
7.24
7.13
7.12
7.09
6.99
6.98
5.22
5.06
5.03
4.86
4.84
4.84
4.83
4.82
4.81
3.28
3.27
3.25
3.24
3.14
3.12
3.11
3.10
2.41
2.26
NH
O
N
H
N
O
N
O
23a
1.00
1.00
1.00
1.00
1.00
1.00
3.00
1.01
1.00
1.00
1.00
2.00
1.00
1.00
1.01
1.00
1.00
1.01
3.00
3.00
13.0 12.5 12.0 11.5 11.0 10.5 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)

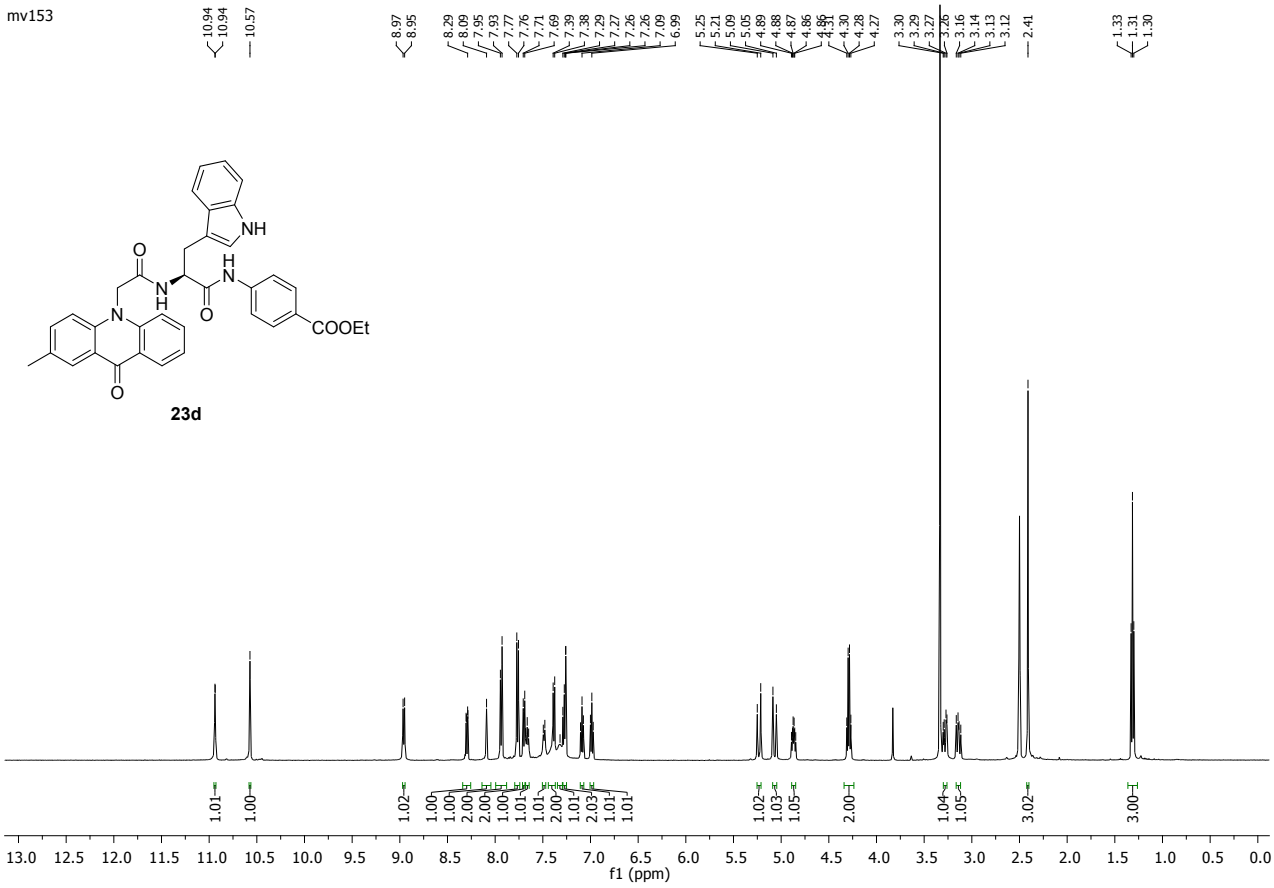

mv36 carbon
176.47
169.98
166.92
142.29
140.55
136.25
136.11
135.22
133.72
132.42
130.50
129.06
127.34
126.40
125.58
123.85
121.37
121.34
121.04
120.93
119.56
118.57
118.27
115.85
115.75
111.30
109.69
54.28
48.52
28.45
20.46
20.19
NH
O
N
H
N
O
N
O
23a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

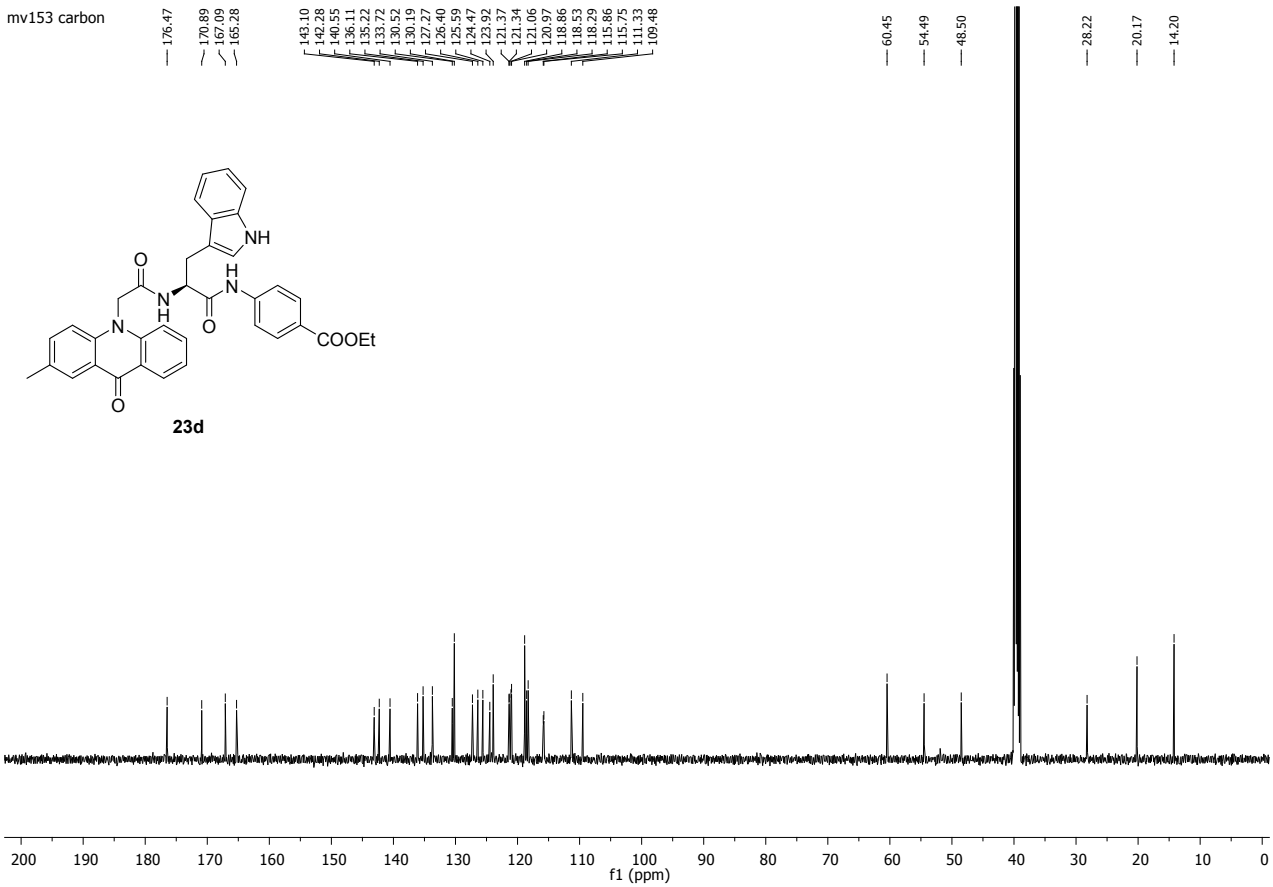

mv54
10.93
10.93
10.28
8.94
8.92
8.30
8.30
8.29
8.28
8.09
7.68
7.64
7.63
7.62
7.61
7.39
7.37
7.28
7.25
7.24
7.18
7.17
6.98
6.95
5.22
5.08
5.04
4.84
4.83
4.83
4.82
4.81
4.80
3.28
3.27
3.25
3.24
3.15
3.13
3.12
3.10
2.41
NH
O
N
H
H
N
O
F
N
O
23b
1.00
1.00
1.00
1.00
1.00
1.01
3.00
1.00
1.01
1.00
1.01
1.00
2.00
1.00
1.00
1.01
1.01
1.00
1.00
1.00
3.00
13.0 12.5 12.0 11.5 11.0 10.5 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)


mv54 carbon
176.47
170.14
166.98
159.06
157.15
142.29
140.56
136.11
135.22
135.15
133.72
130.51
127.30
126.40
125.59
123.87
121.36
121.32
121.25
121.04
120.94
118.53
118.27
115.86
115.76
115.36
115.18
111.32
109.62
54.35
48.51
28.37
20.18
NH
O
N
H
H
N
O
F
N
O
23b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


mv56
10.93
10.36
8.95
8.93
8.30
8.30
8.29
8.29
8.09
7.69
7.68
7.66
7.64
7.39
7.37
7.29
7.28
7.26
7.25
7.24
7.09
6.38
6.35
5.21
5.08
5.04
4.85
4.84
4.83
4.82
4.82
4.81
3.28
3.27
3.25
3.24
3.15
3.13
3.12
3.10
2.41
NH
O
N
H
N
H
O
Cl
N
O
23c
1.00
1.00
1.00
1.00
4.00
1.00
3.00
1.00
1.01
1.00
1.01
1.00
1.00
1.00
1.00
1.01
1.00
3.00
13.0 12.5 12.0 11.5 11.0 10.5 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)


mv56 carbon
176.47
170.42
167.02
142.29
140.55
137.71
136.11
135.22
133.72
130.51
128.62
127.29
127.06
126.40
125.59
123.89
121.37
121.34
121.04
120.95
118.52
118.28
115.85
115.75
111.33
109.55
54.40
48.51
28.32
20.18
NH
O
N
H
N
H
O
Cl
N
O
23c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


mv153
10.94
10.94
10.57
8.97
8.95
8.29
8.09
7.95
7.93
7.77
7.76
7.71
7.69
7.39
7.38
7.29
7.27
7.26
7.26
7.09
6.99
5.25
5.21
5.09
5.05
4.89
4.88
4.87
4.86
4.31
4.30
4.28
4.27
3.30
3.29
3.27
3.26
3.16
3.14
3.13
3.12
2.41
1.33
1.31
1.30
NH
O
N
H
N
H
O
N
O
COOEt
23d
1.01
1.00
1.02
1.00
1.00
2.00
2.00
1.00
1.01
1.01
2.00
1.01
2.03
1.01
1.02
1.03
1.05
2.00
1.04
1.05
3.02
3.00
13.0 12.5 12.0 11.5 11.0 10.5 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)


mv153 carbon
176.47
170.89
167.09
165.28
143.10
142.28
140.55
136.11
135.22
133.72
130.52
130.19
127.27
126.40
125.59
124.47
123.92
121.37
121.34
121.06
120.97
118.86
118.53
118.29
115.86
115.75
111.33
109.48
60.45
54.49
48.50
28.22
20.17
14.20
NH
O
N
H
N
H
O
N
O
COOEt
23d
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Analytical method for compounds **9a-i** and **10**:

LC-MS/HPLC: LC-20AD Shimadzu connected to Shimadzu LCMS-2010EV

Mobile Phase A: 0.1% FA in water

Mobile Phase B: methanol

HPLC column: Poroshell 120 EC-C18, 4.6 x 100 mm, 2.7 µm

Flow rate: 0.4 mL/min

Run time: 20 min

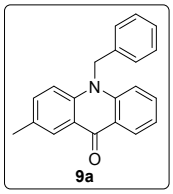
Column temperature: 26°C

UV detector: 254 nm

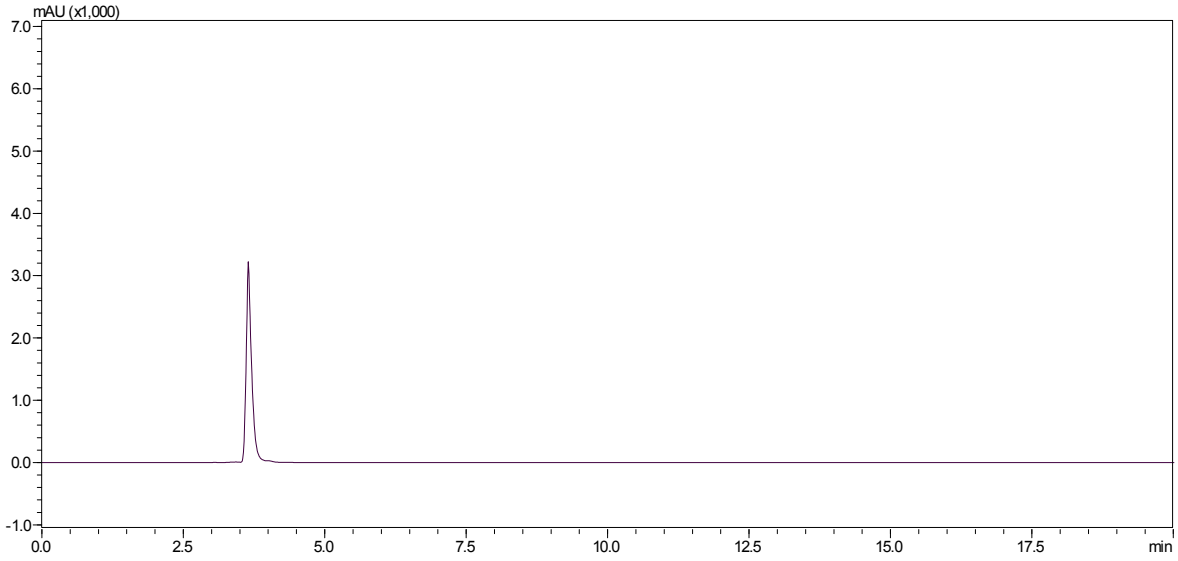
MS detector: 1.65 kV

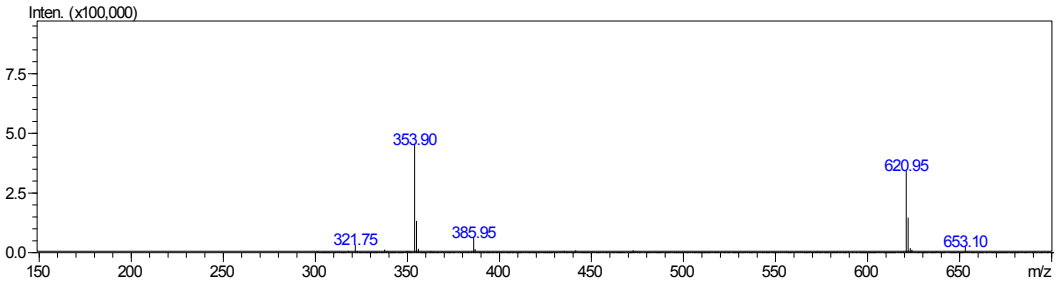
LC isocratic:

Time (min)	Mobile Phase A (%)	Mobile Phase B (%)
0	0	100
20	0	100

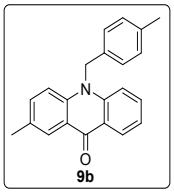


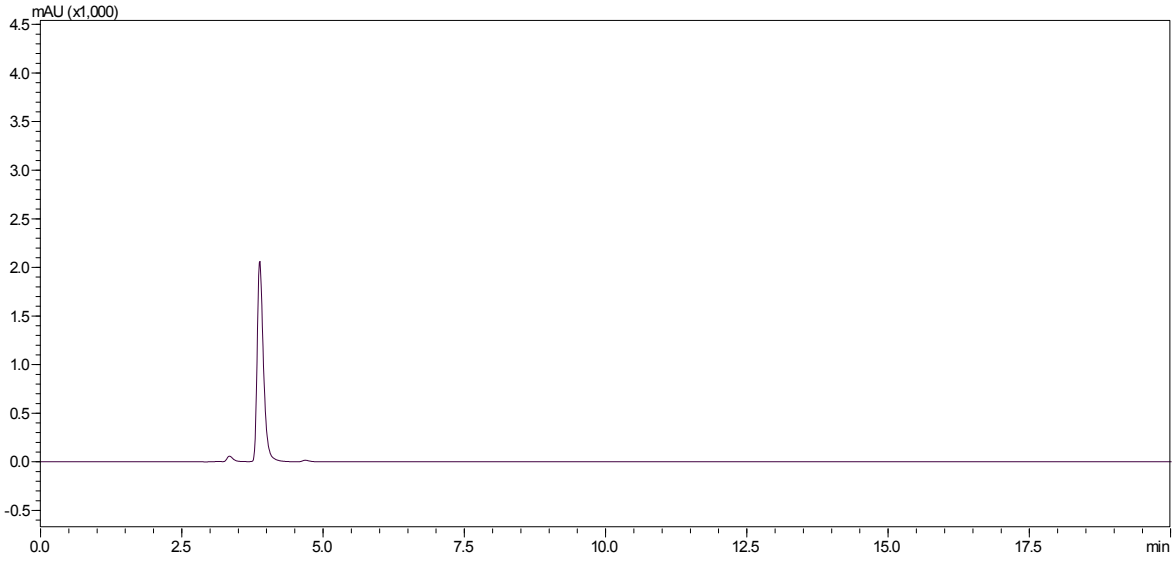
9a

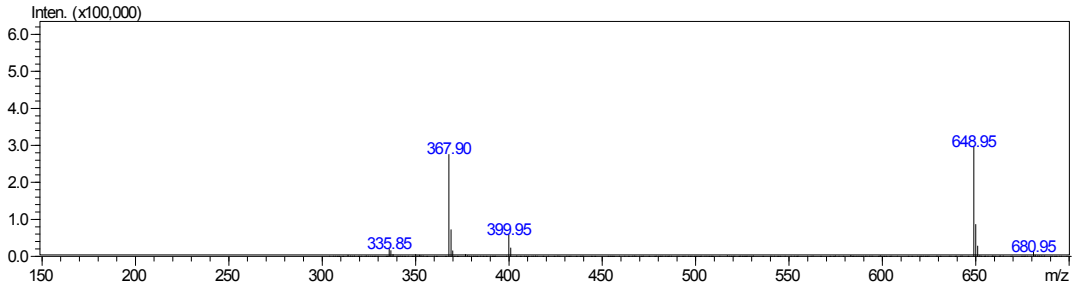




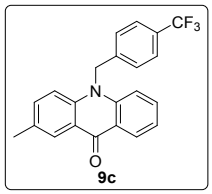
ESI-MS, positive mode: m/z calcd mass for $C_{22}H_{21}NO_2Na$ $[M + MeOH + Na]^+$ = 454.15; found 353.90.







ESI-MS, positive mode: m/z calcd mass for $C_{23}H_{23}NO_2Na$ $[M + MeOH + Na]^+$ = 368.16; found 367.90.



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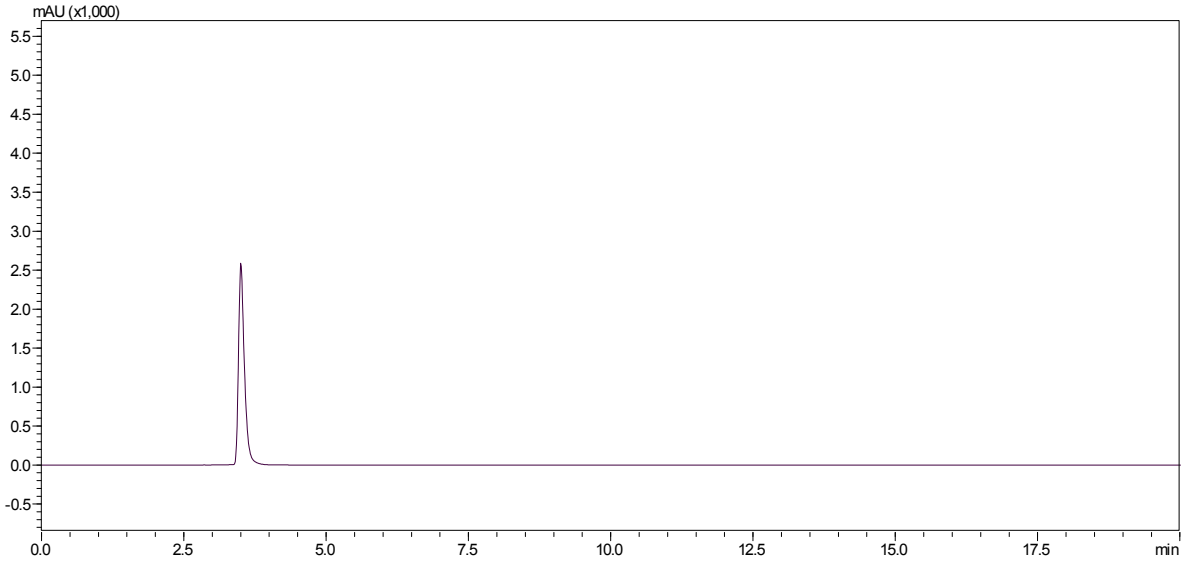
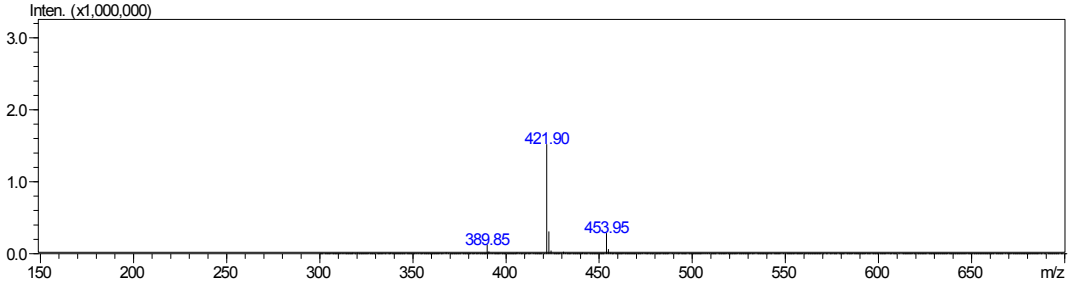
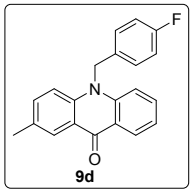
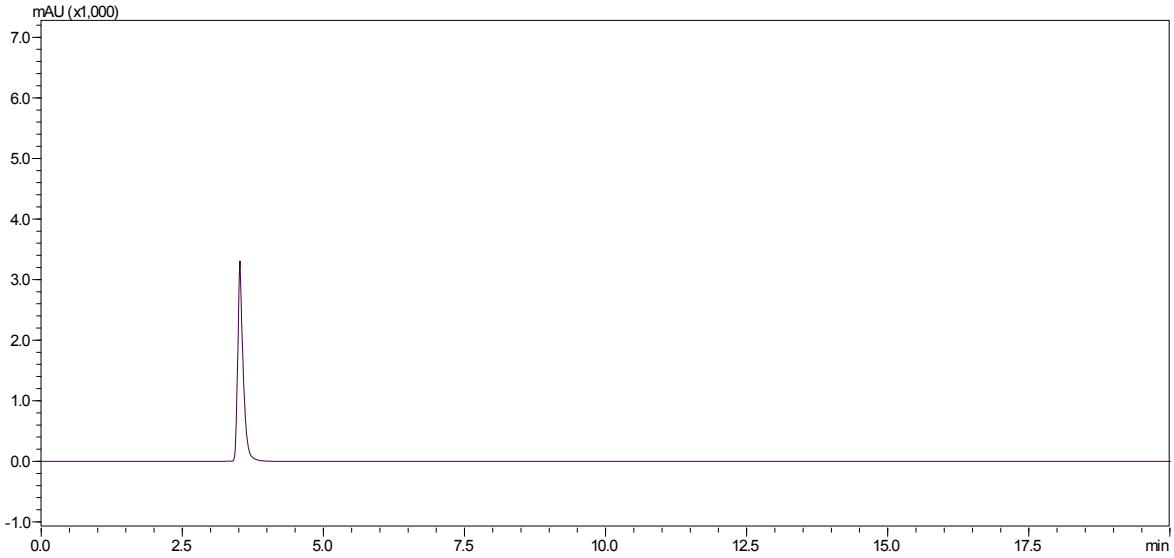
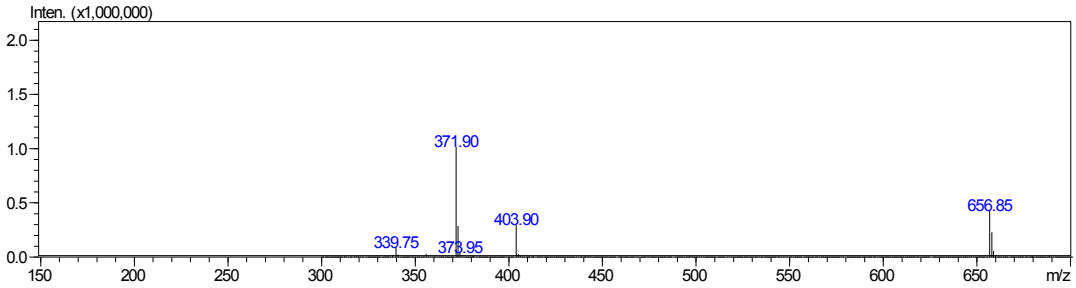




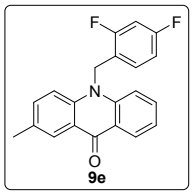
ESI-MS, positive mode: m/z calcd mass for $C_{23}H_{20}F_3NO_2Na$ $[M + MeOH + Na]^+$ = 422.13; found 421.90.

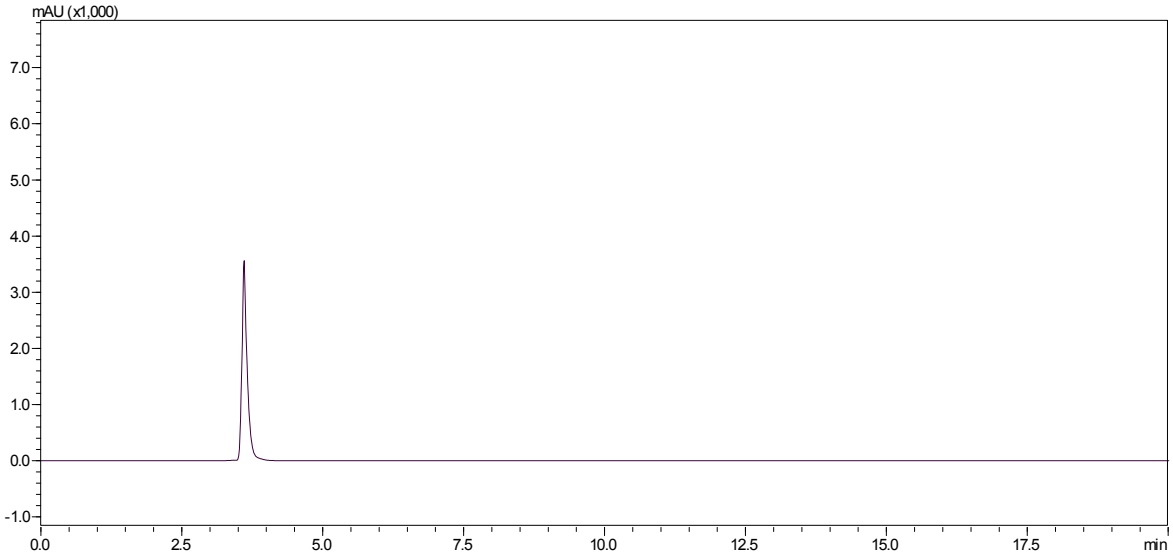


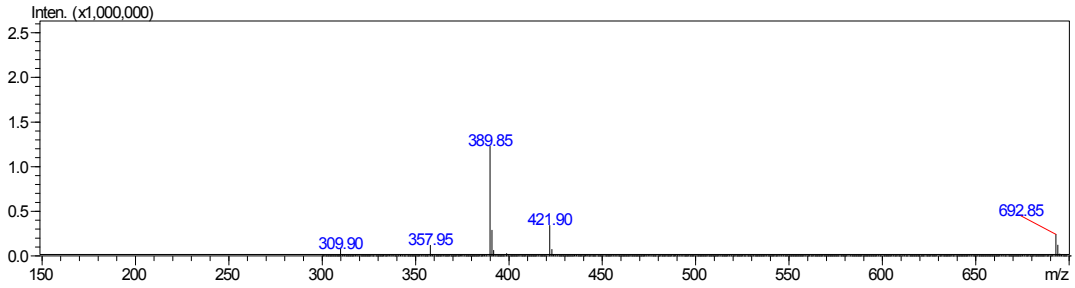




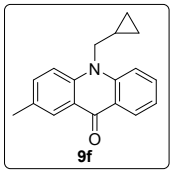
ESI-MS, positive mode: m/z calcd mass for $C_{22}H_{20}FNO_2Na$ $[M + MeOH + Na]^+$ = 372.14; found 371.90.

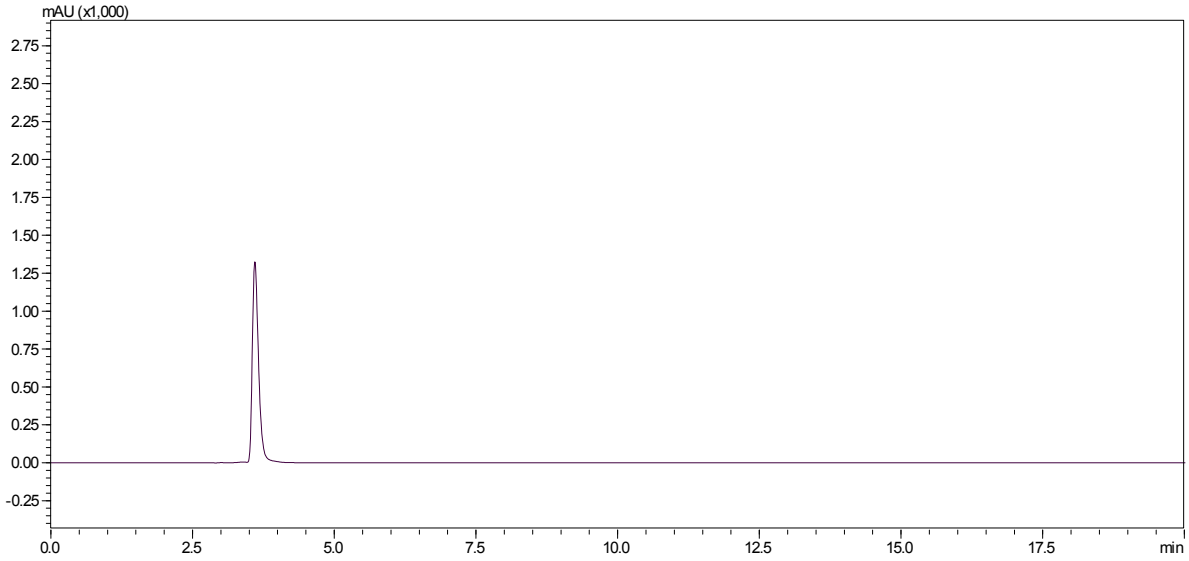


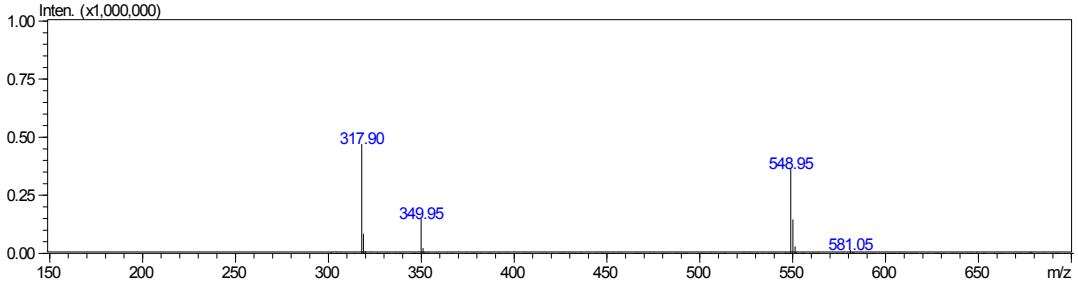




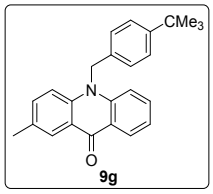
ESI-MS, positive mode: m/z calcd mass for $C_{22}H_{19}F_2NO_2Na$ $[M + MeOH + Na]^+$ = 390.13; found 389.85.







ESI-MS, positive mode: m/z calcd mass for $C_{19}H_{21}NO_2Na$ $[M + MeOH + Na]^+$ = 318.15; found 317.90.



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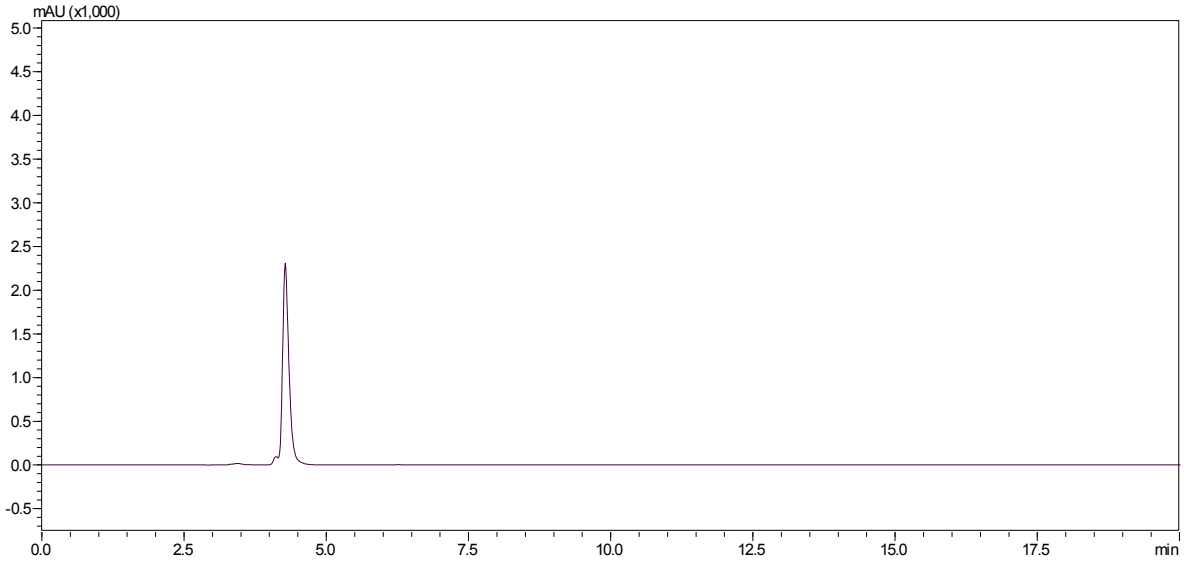
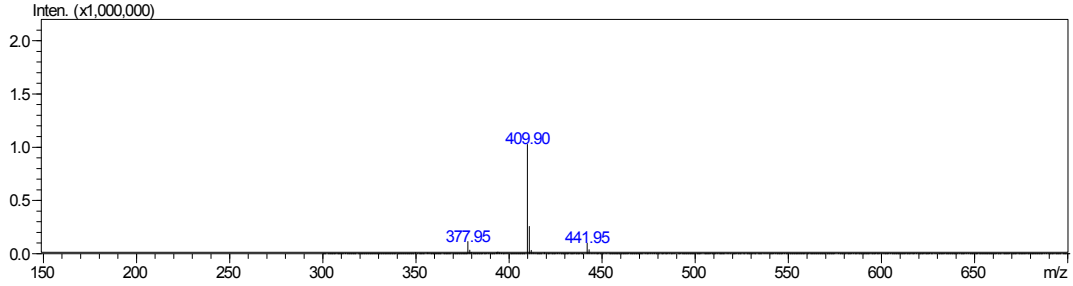
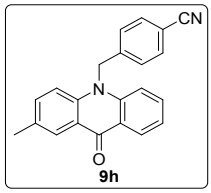




ESI-MS, positive mode: m/z calcd mass for $C_{26}H_{29}NO_2Na$ $[M + MeOH + Na]^+$ = 410.21; found 409.90.



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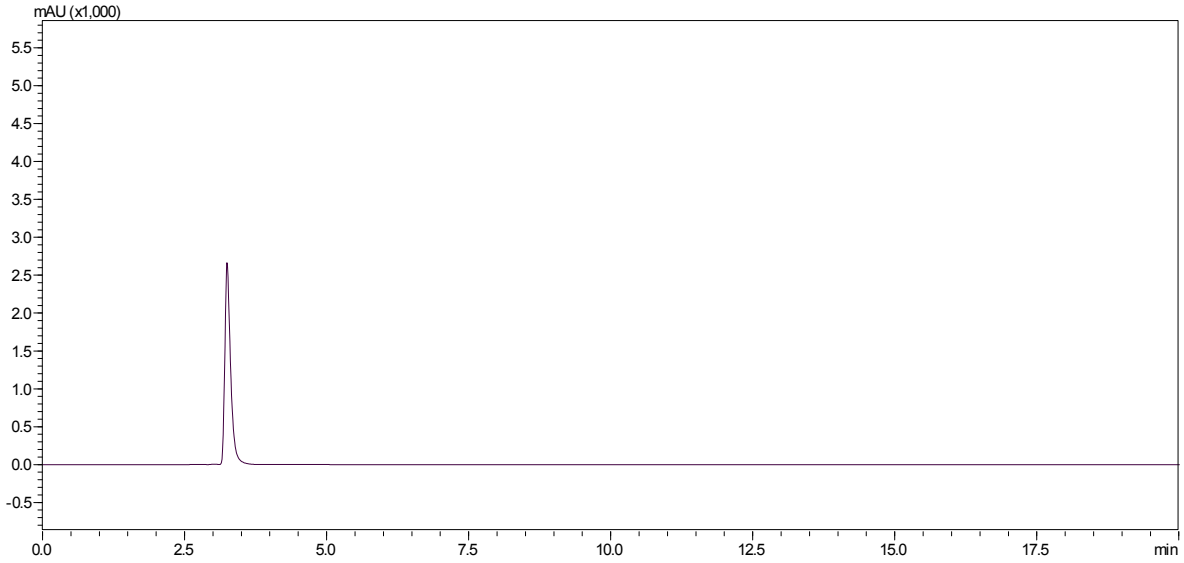
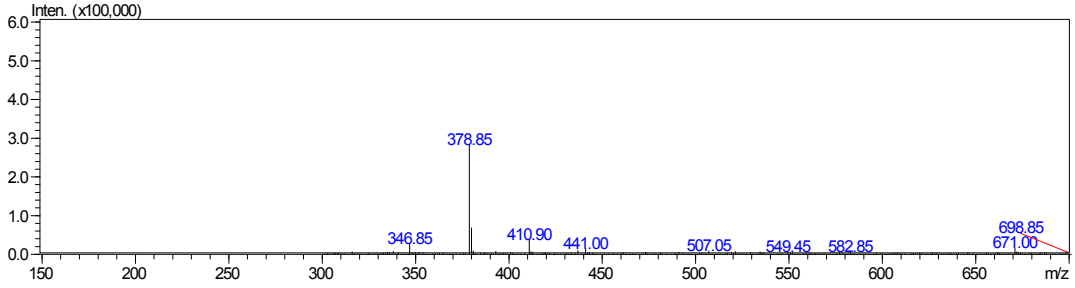
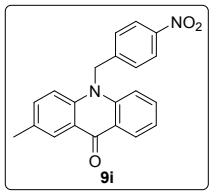




ESI-MS, positive mode: m/z calcd mass for $C_{23}H_{20}N_2O_2Na$ $[M + MeOH + Na]^+$ = 379.14; found 378.85.



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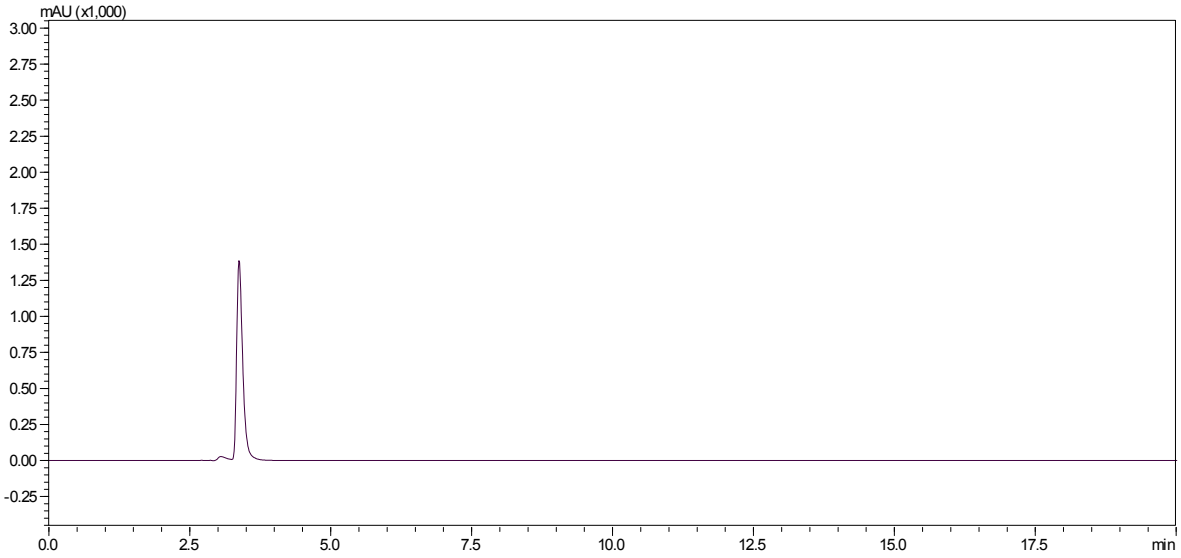
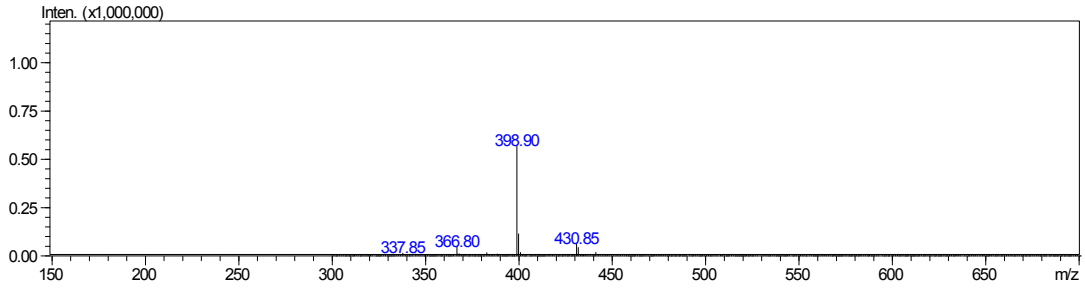
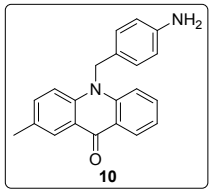
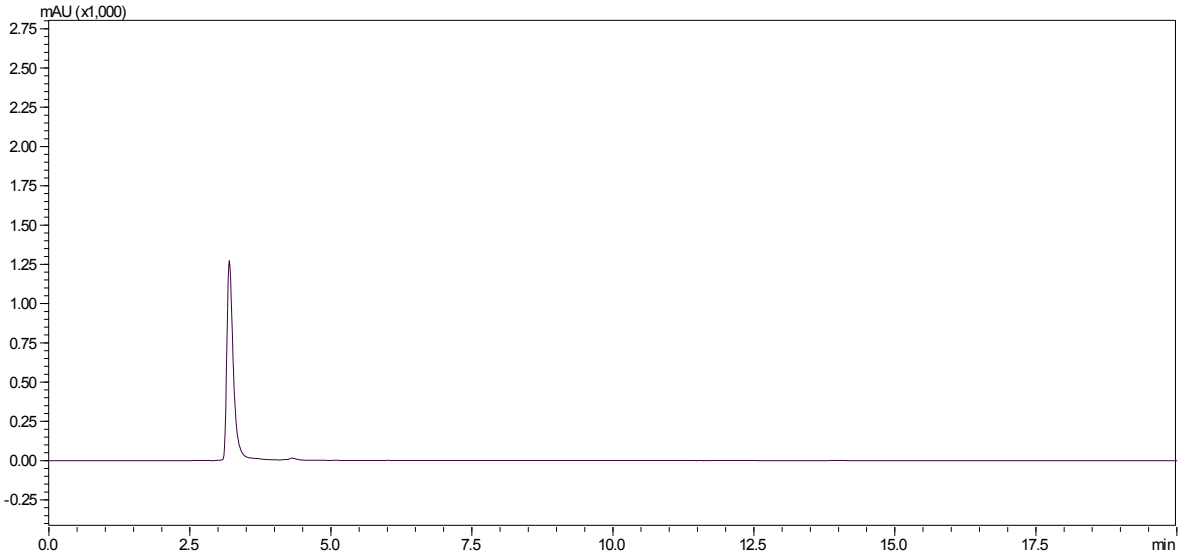
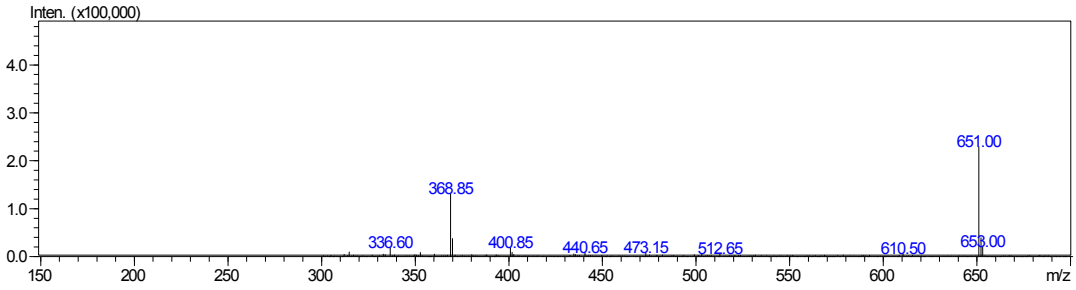




ESI-MS, positive mode: m/z calcd mass for $C_{22}H_{20}N_2O_4Na$ $[M + MeOH + Na]^+$ = 399.13; found 398.90.







ESI-MS, positive mode: m/z calcd mass for $C_{22}H_{22}N_2O_2Na$ $[M + MeOH + Na]^+$ = 369.16; found 368.85.

Analytical method for compounds **S1**, **15a-d** and **16a-h**:

LC-MS/HPLC: LC-20AD Shimadzu connected to Shimadzu LCMS-2010EV

Mobile Phase A: 0.1% FA in water

Mobile Phase B: methanol

HPLC column: SUPELCO Discovery C18 25 cm x 4.6 mm, 5 µm

Flow rate: 0.4 mL/min

Run time: 20 min

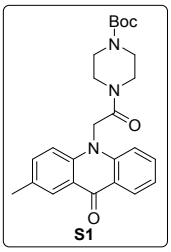
Column temperature: 26°C

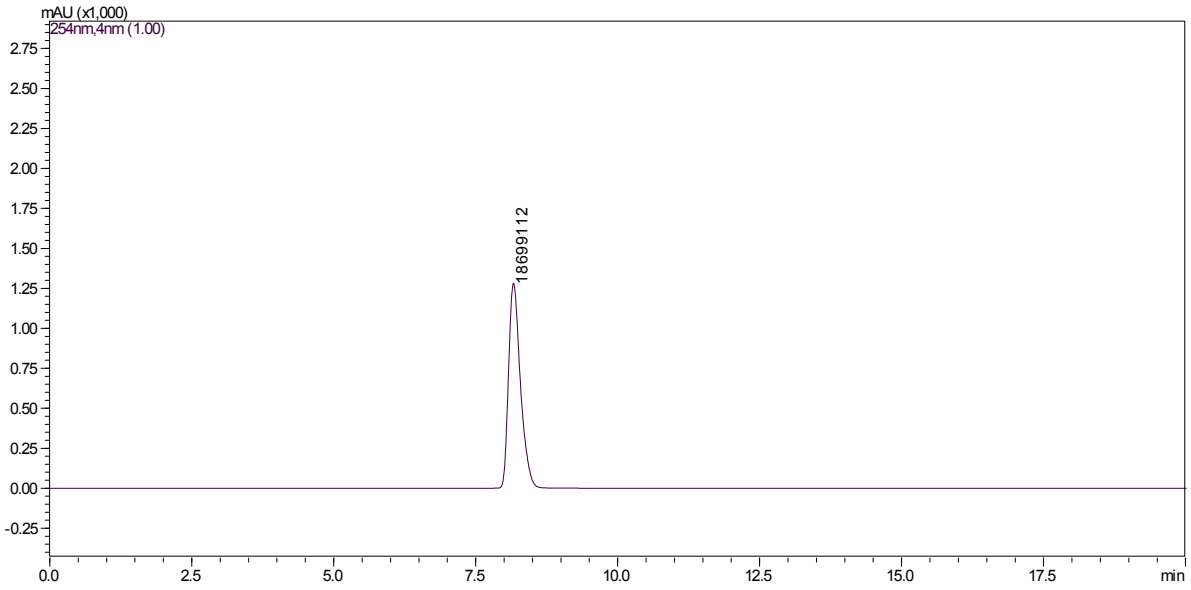
UV detector: 254 nm

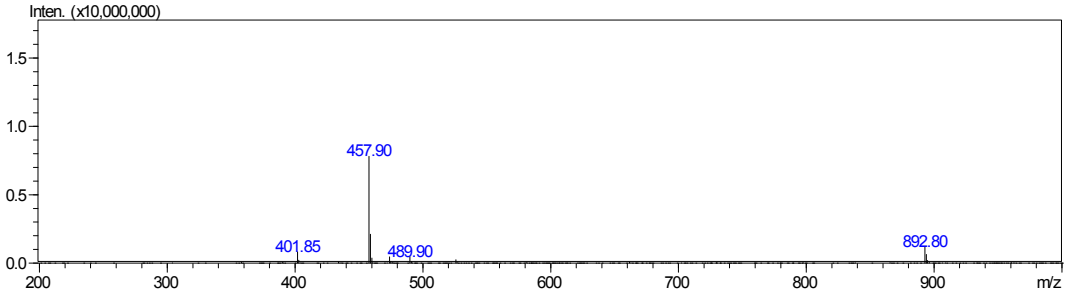
MS detector: 1.65 kV

LC isocratic:

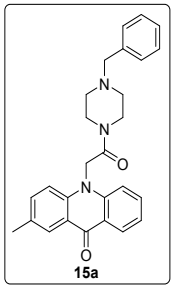
Time (min)	Mobile Phase A (%)	Mobile Phase B (%)
0	0	100
20	0	100

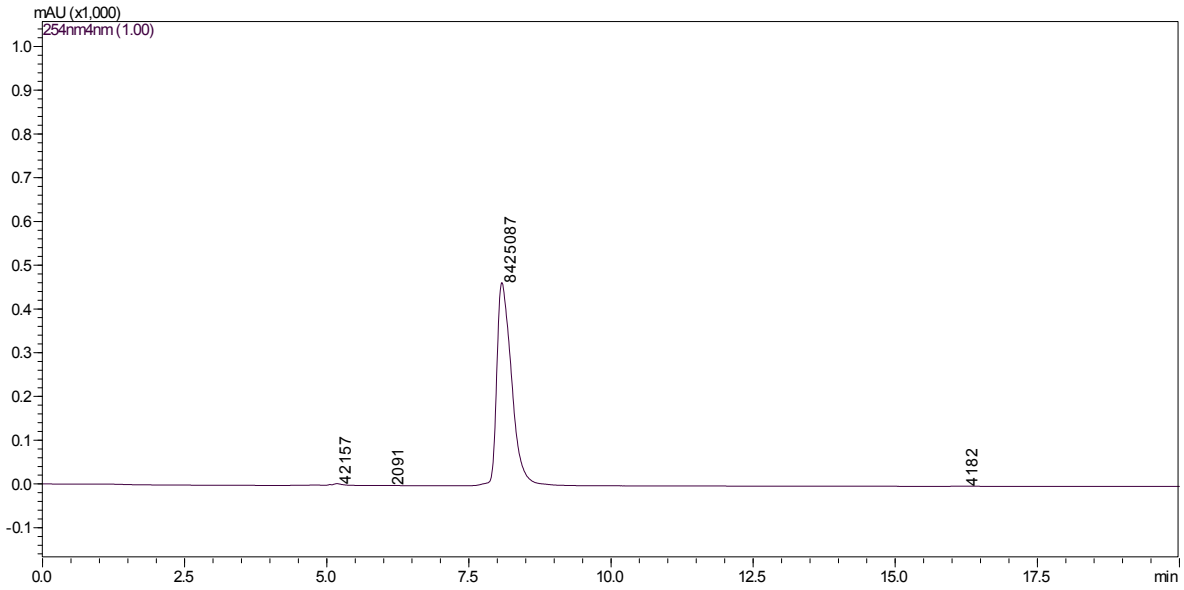


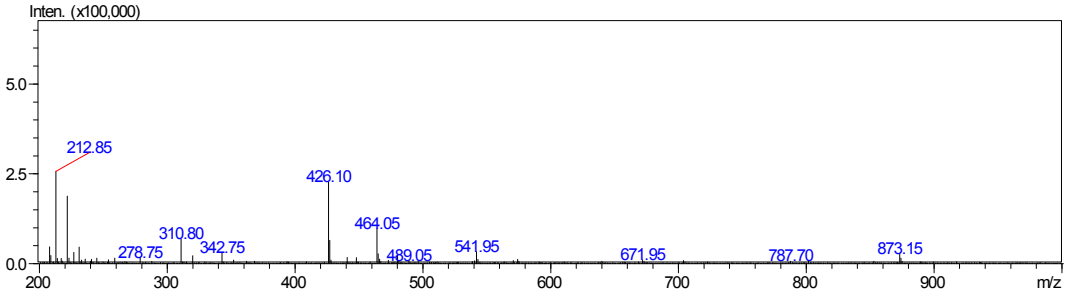




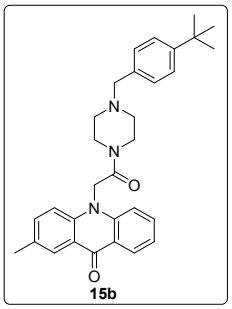
ESI-MS, positive mode: m/z calcd mass for $C_{25}H_{29}N_3O_4Na$ $[M + Na]^+$ = 458.20; found 457.90.

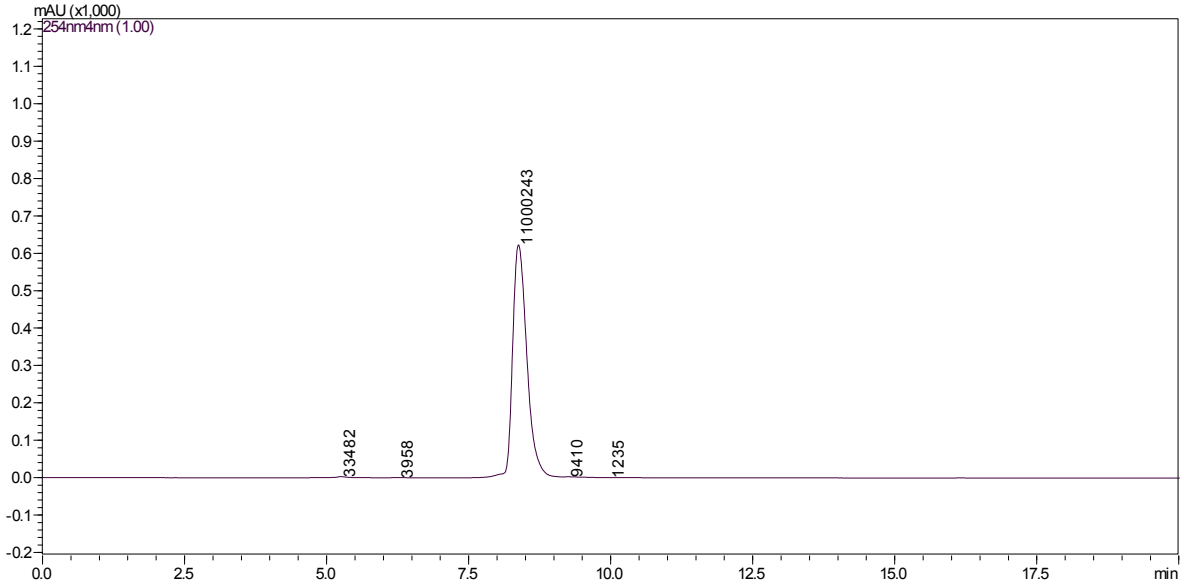


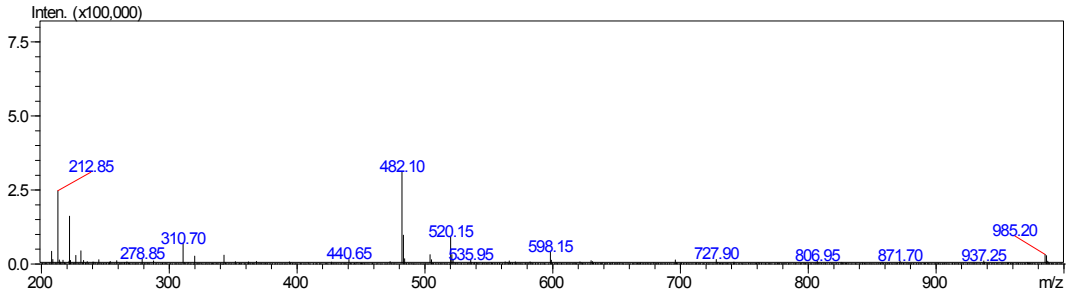




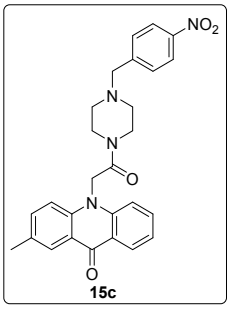
ESI-MS, positive mode: m/z calcd mass for $C_{27}H_{28}N_3O_2$ $[M + H]^+$ = 426.22; found 426.10.



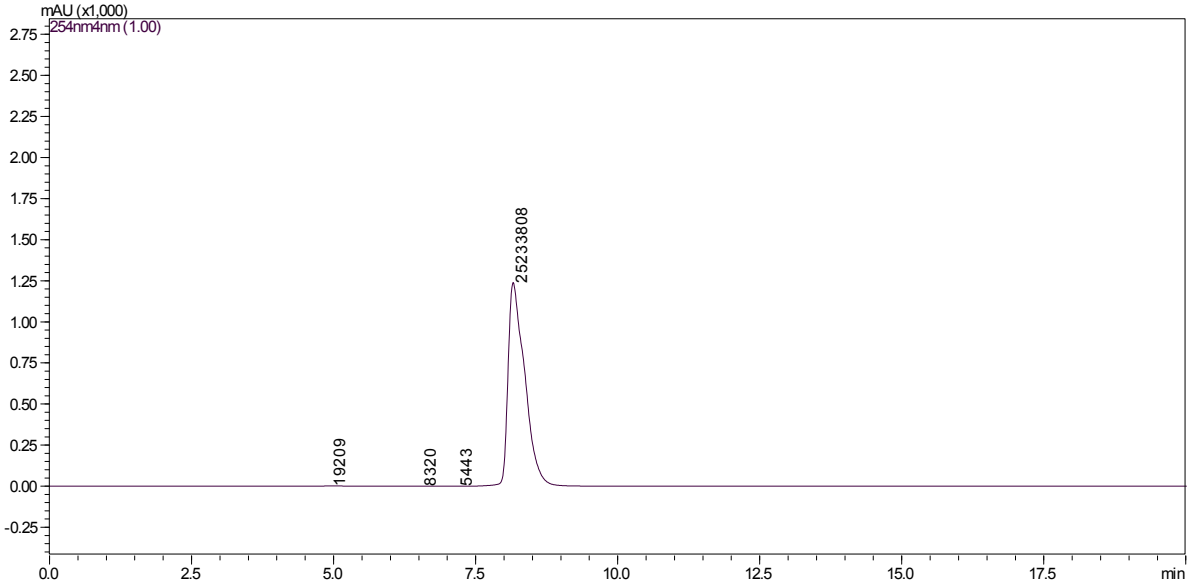


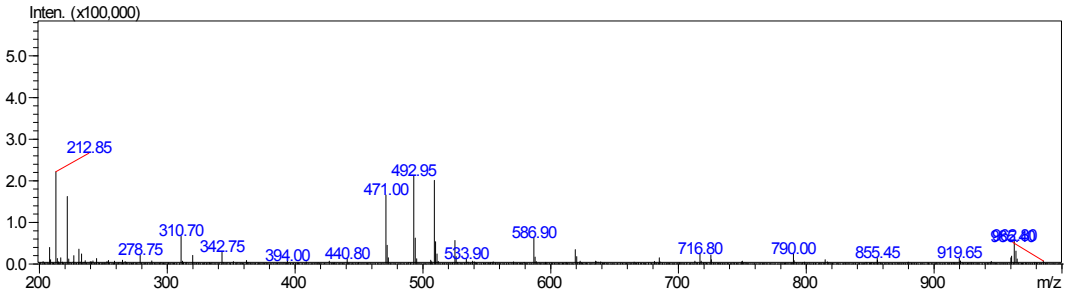


ESI-MS, positive mode: m/z calcd mass for $C_{31}H_{36}N_3O_2$ $[M + H]^+$ = 482.28; found 482.10.

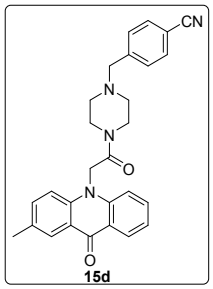


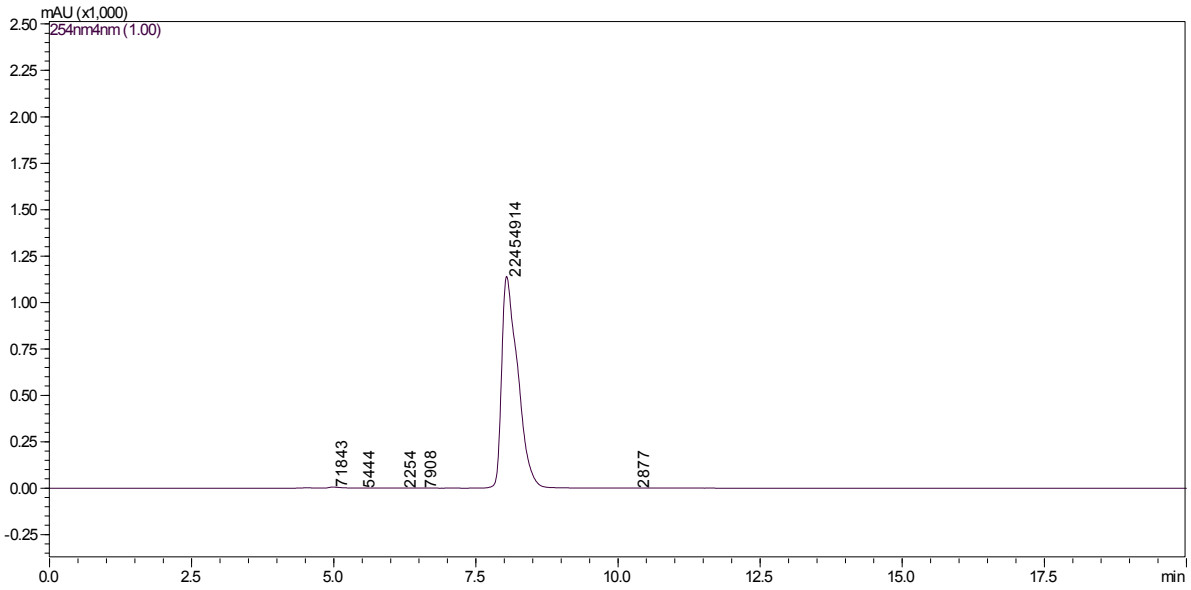
15c

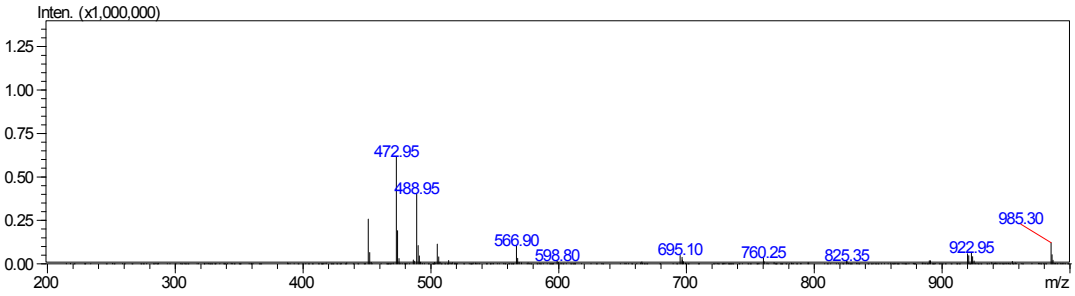




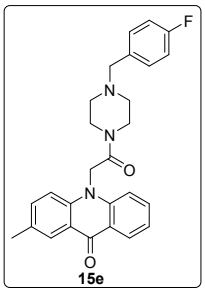
ESI-MS, positive mode: m/z calcd mass for $C_{27}H_{27}N_4O_4$ $[M + H]^+$ = 471.20; found 471.00.

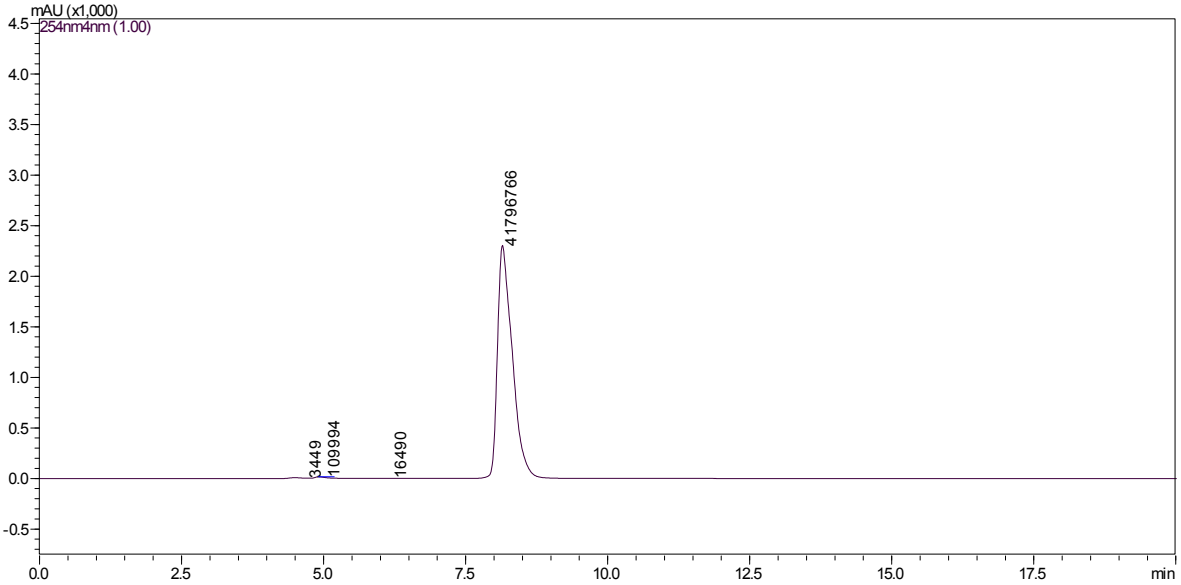


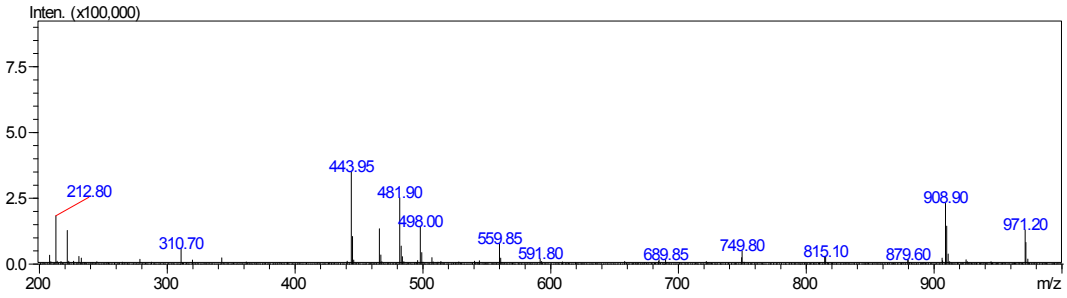




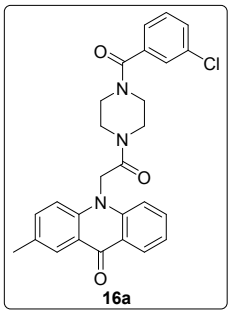
ESI-MS, positive mode: m/z calcd mass for $C_{28}H_{26}N_4O_2Na$ $[M + Na]^+$ = 473.19; found 472.95.

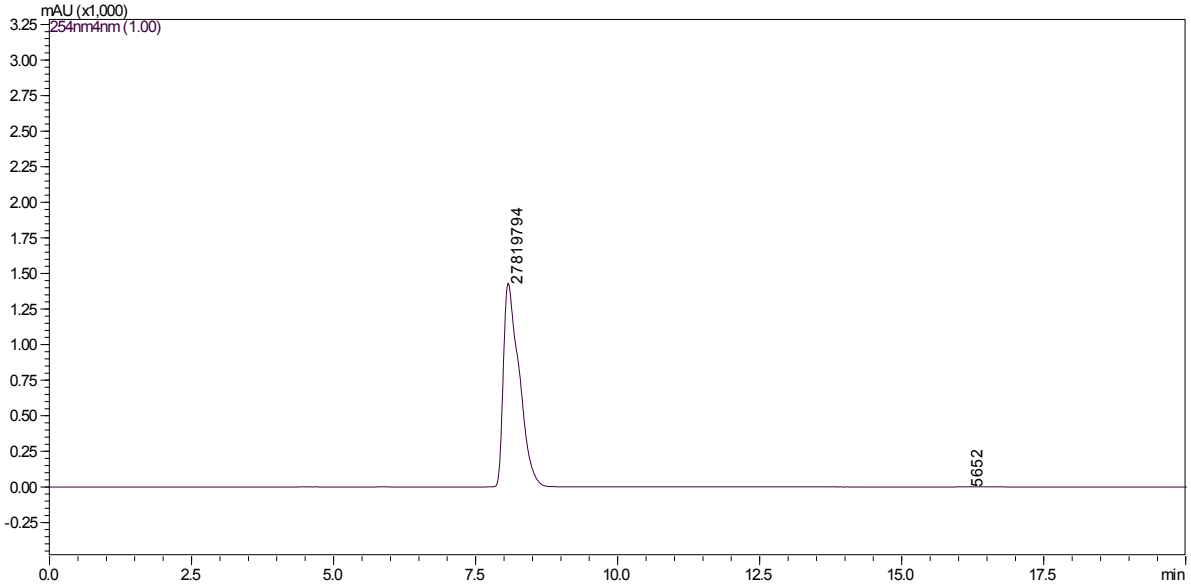


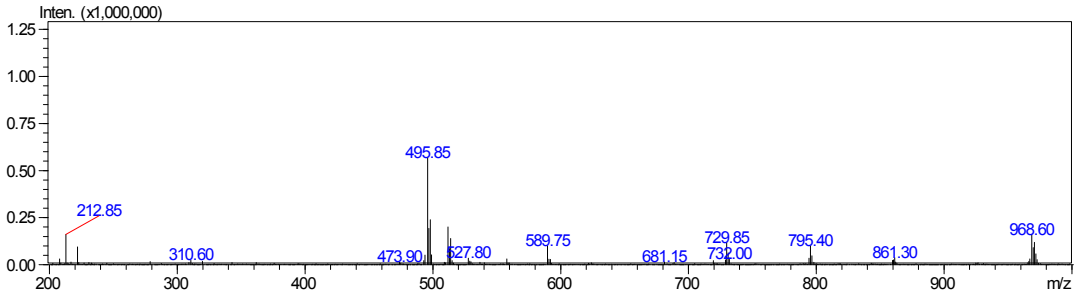




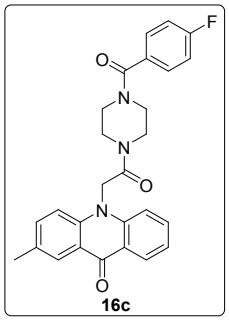
ESI-MS, positive mode: m/z calcd mass for $C_{27}H_{27}FN_3O_2$ $[M + H]^+$ = 444.21; found 441.95.

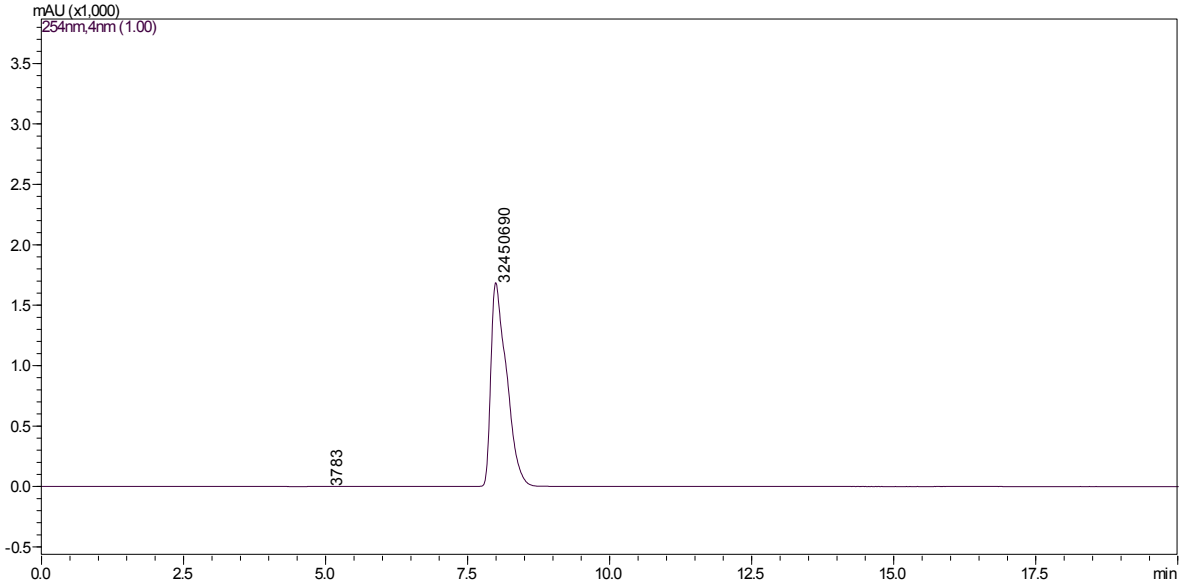


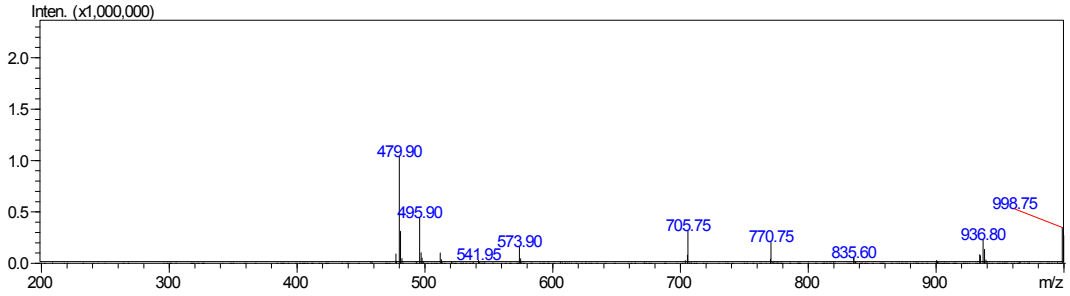




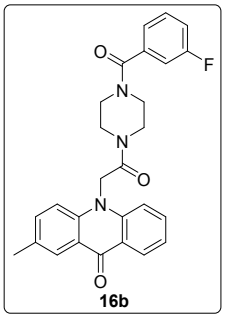
ESI-MS, positive mode: m/z calcd mass for $C_{27}H_{24}ClN_3O_3Na$ $[M + Na]^+$ = 496.14; found 495.85.

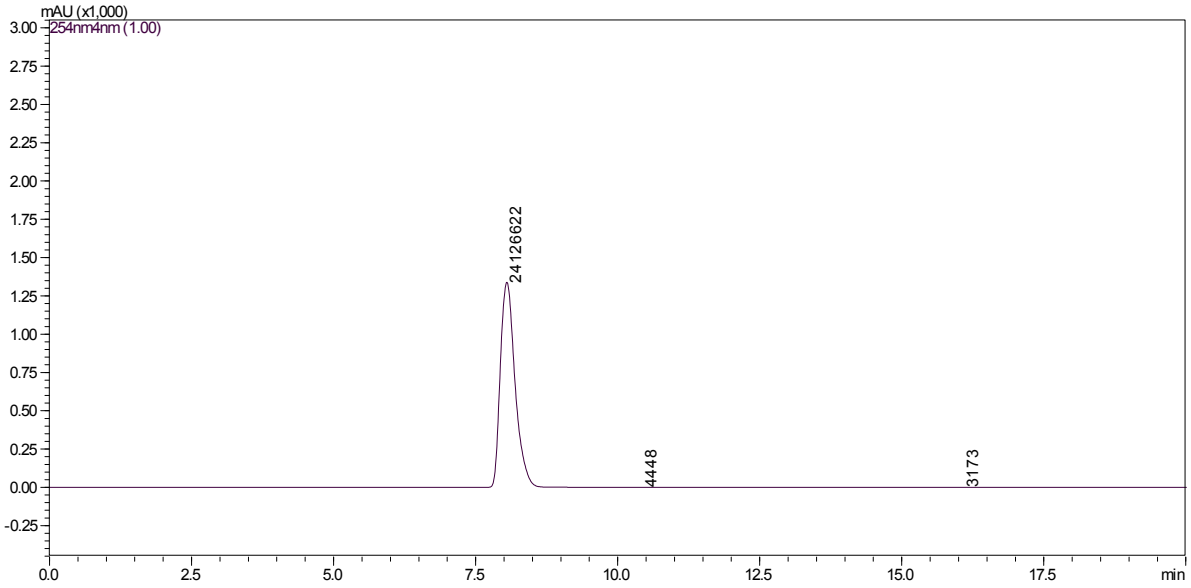


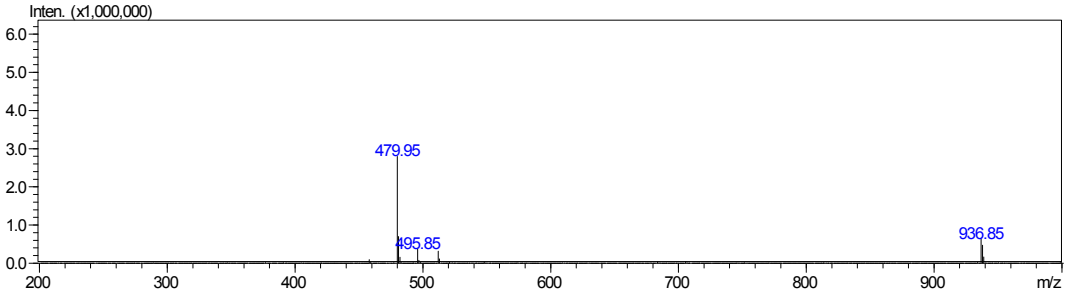




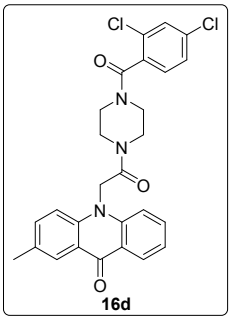
ESI-MS, positive mode: m/z calcd mass for $C_{27}H_{24}FN_3O_3Na$ $[M + Na]^+$ = 480.17; found 479.90.

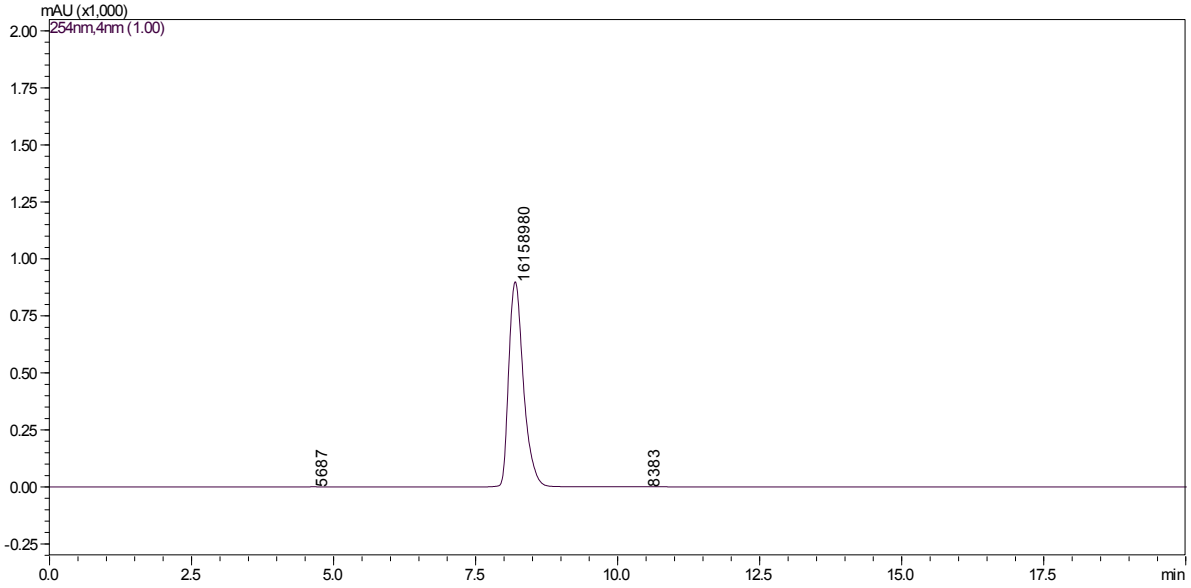


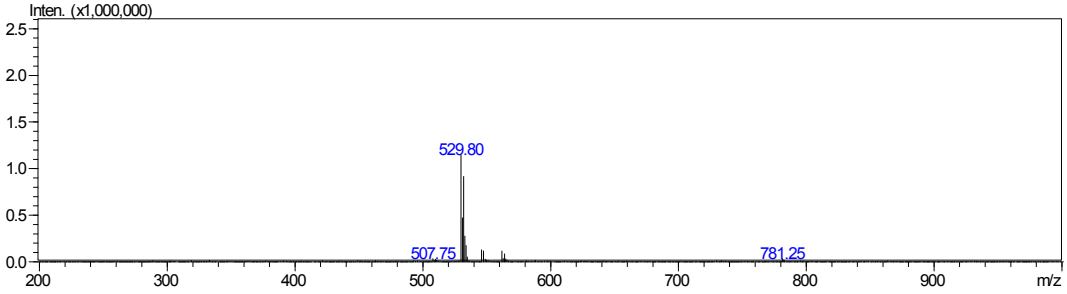




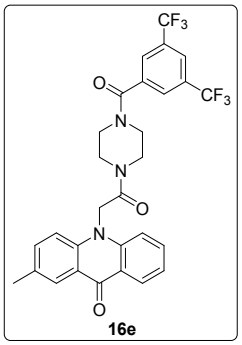
ESI-MS, positive mode: m/z calcd mass for $C_{27}H_{24}FN_3O_3Na$ $[M + Na]^+$ = 480.17; found 479.95.







ESI-MS, positive mode: m/z calcd mass for $C_{27}H_{23}Cl_2N_3O_3Na$ $[M + Na]^+$ = 530.10; found 529.80.



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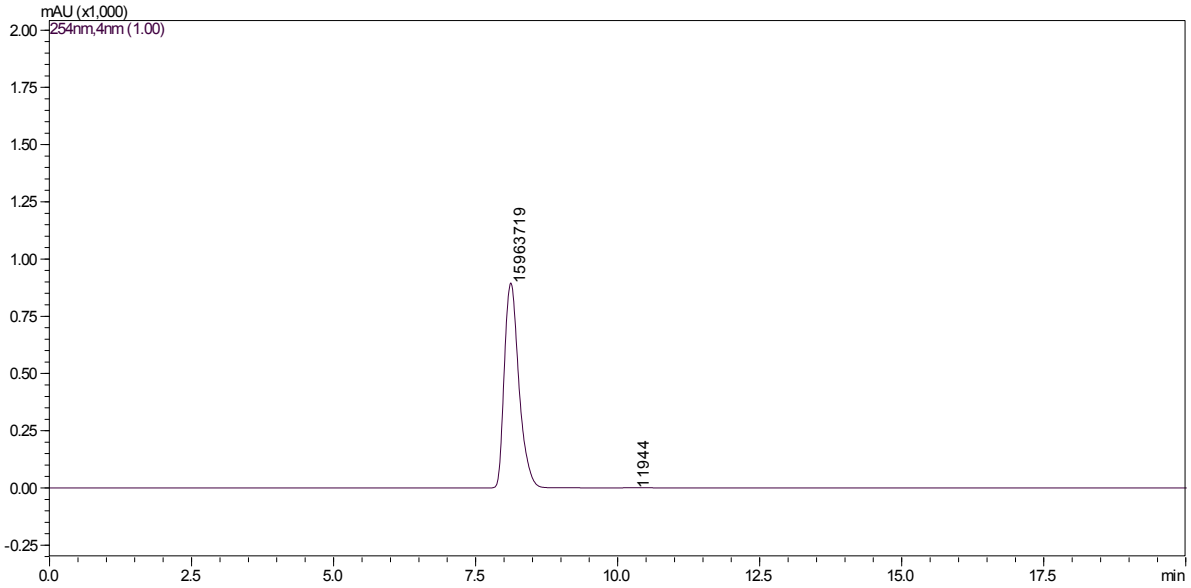
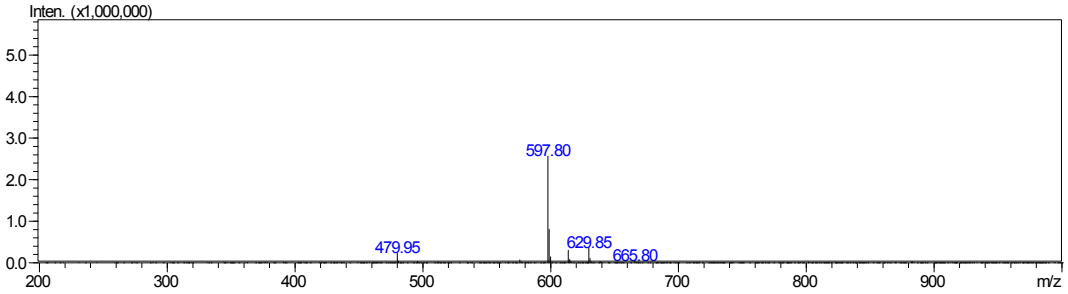
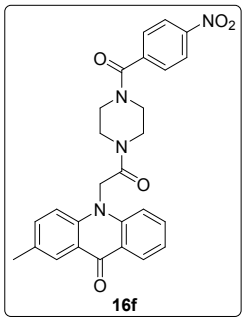
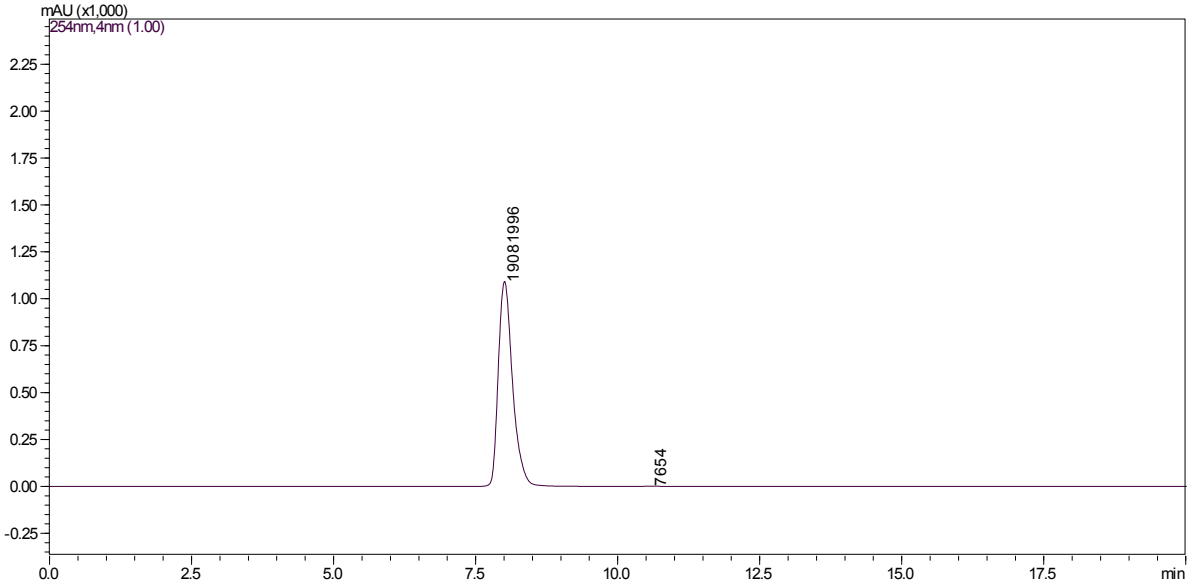
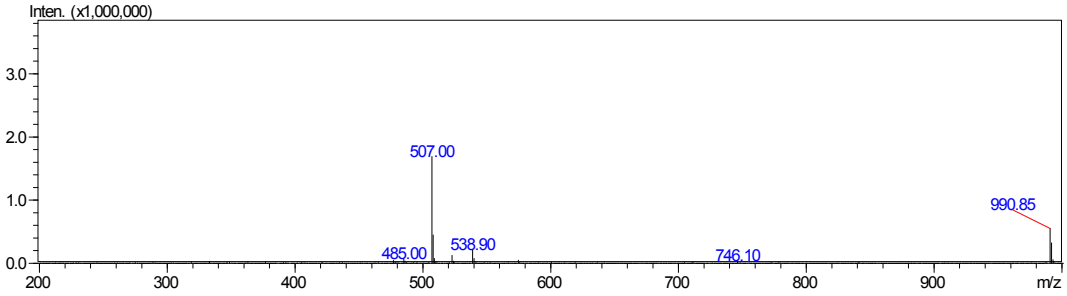




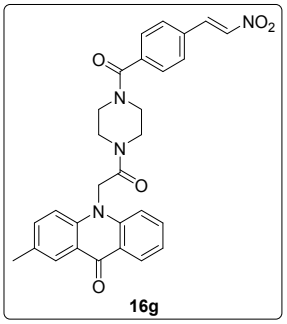
ESI-MS, positive mode: m/z calcd mass for $C_{29}H_{23}F_6N_3O_3Na$ $[M + Na]^+$ = 598.15; found 597.80.

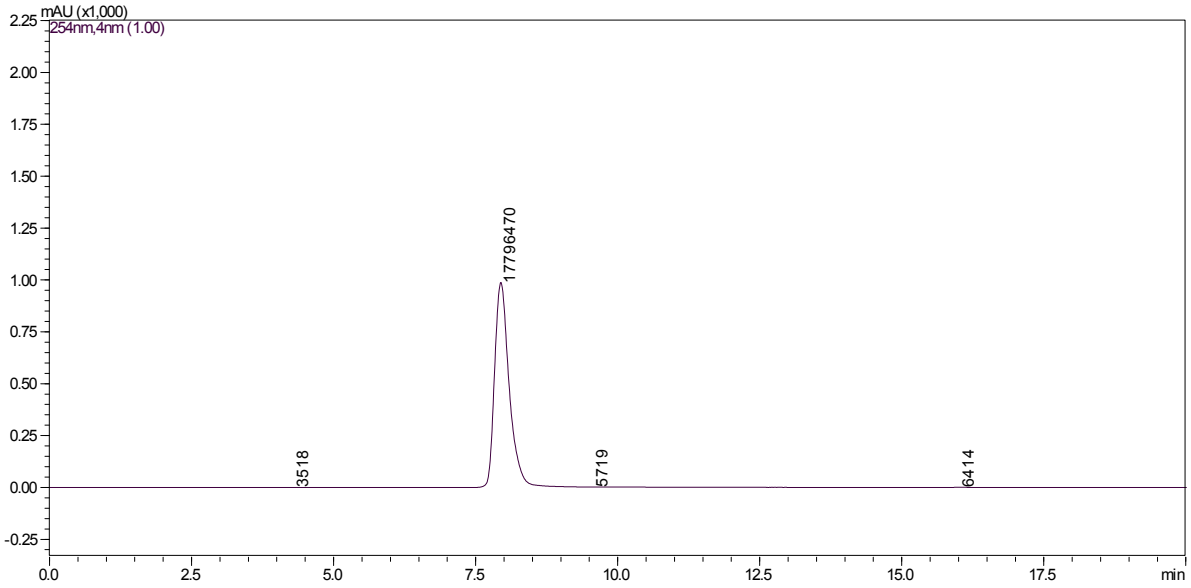


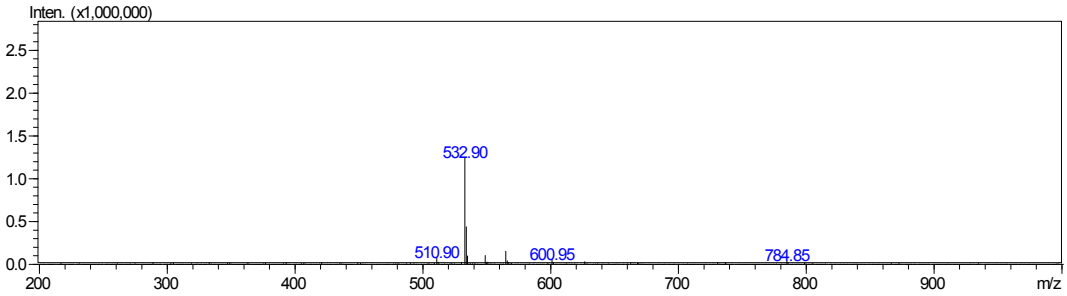




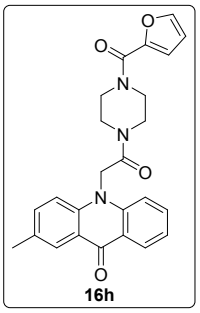
ESI-MS, positive mode: m/z calcd mass for $C_{27}H_{24}N_4O_5Na$ $[M + Na]^+$ = 507.16; found 507.00.

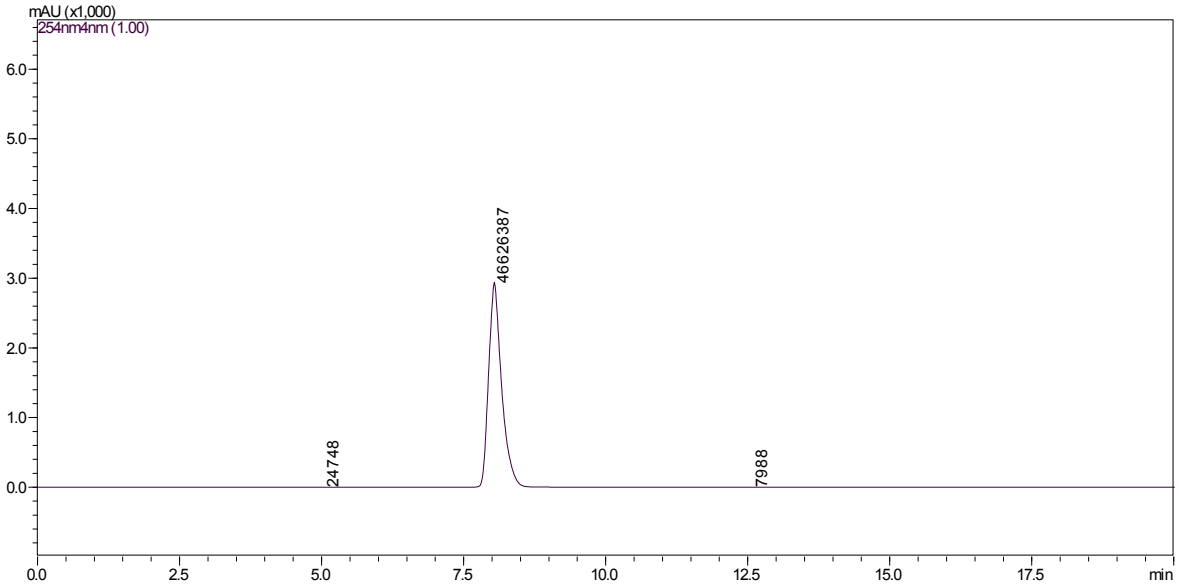


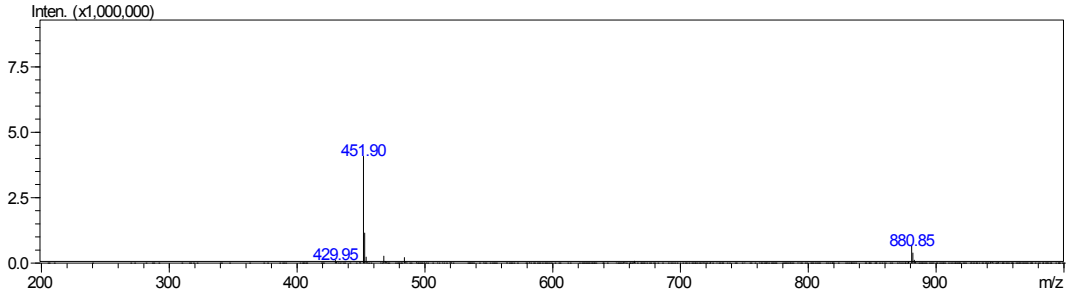




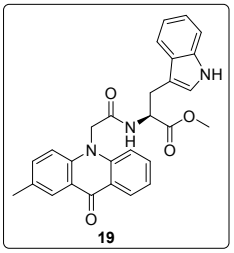
ESI-MS, positive mode: m/z calcd mass for $C_{29}H_{26}N_4O_5Na$ $[M + Na]^+$ = 533.18; found 532.90.

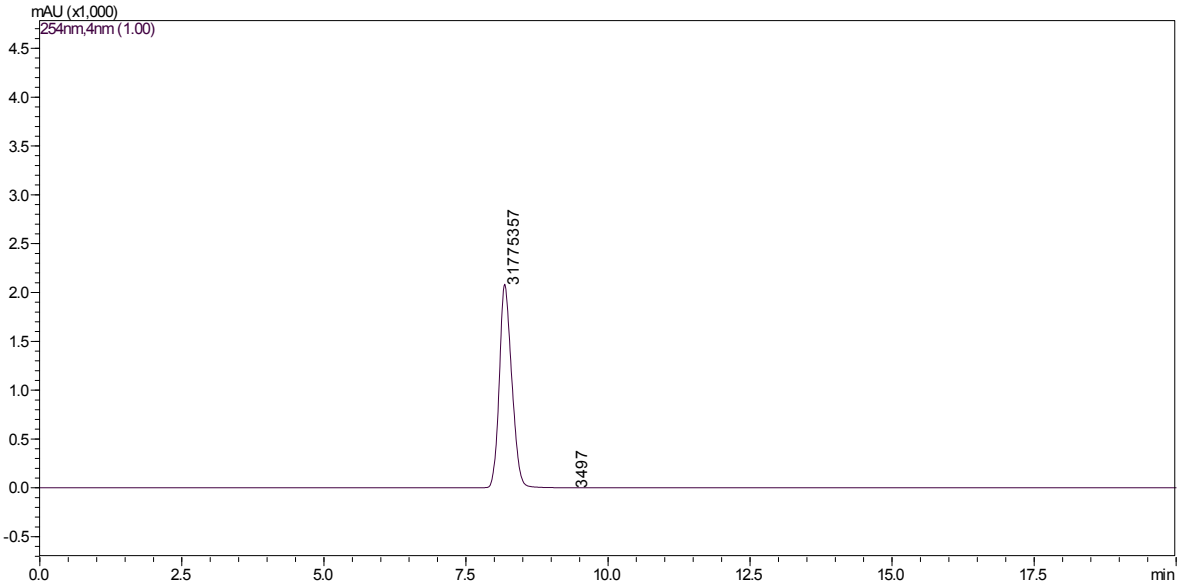


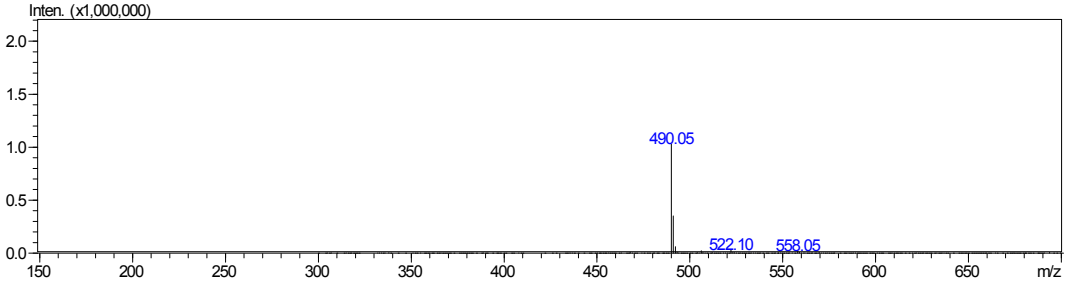




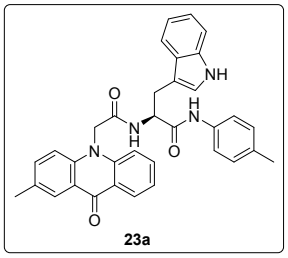
ESI-MS, positive mode: m/z calcd mass for $C_{25}H_{23}N_3O_4Na$ $[M + Na]^+$ = 452.16; found 451.90.

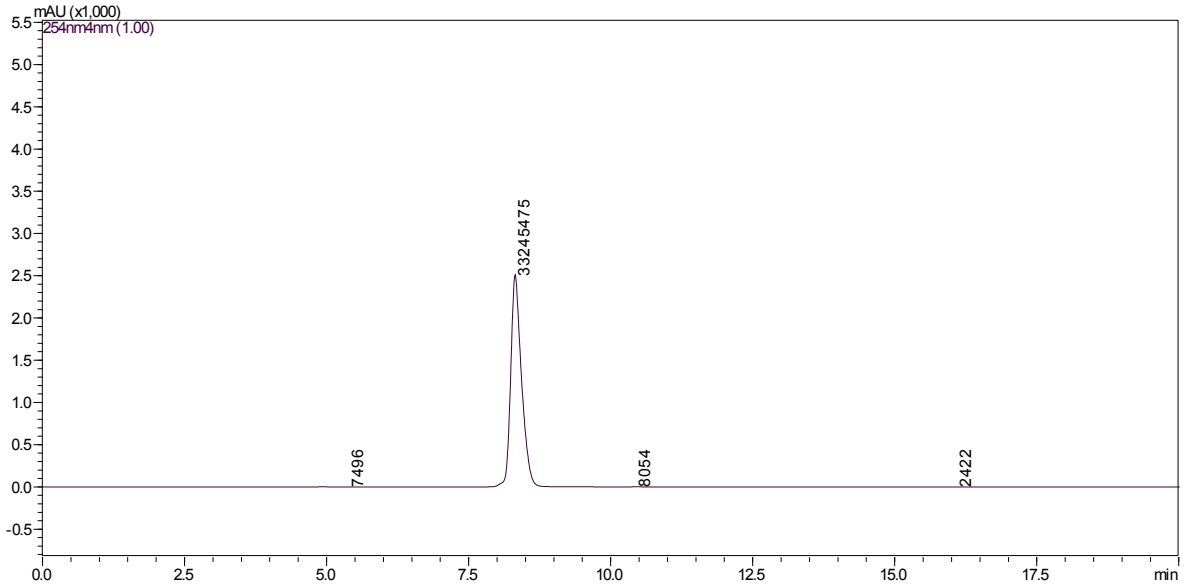


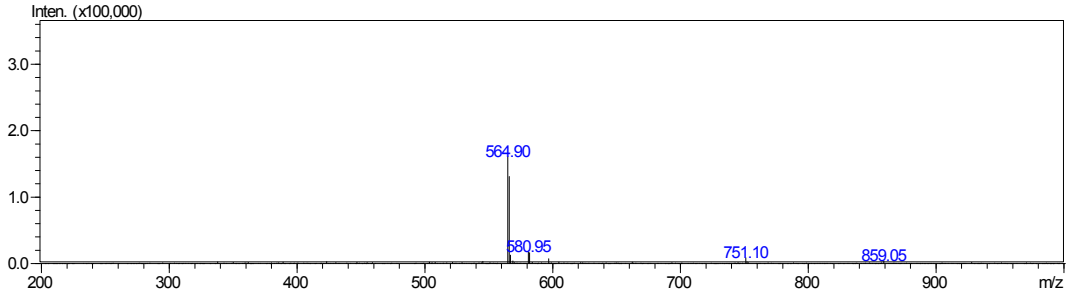




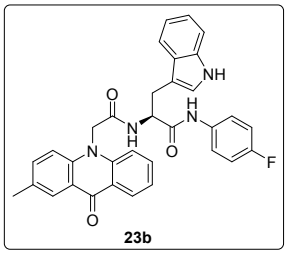
ESI-MS, positive mode: m/z calcd mass for $C_{28}H_{25}N_3O_4Na$ $[M + Na]^+$ = 490.17; found 490.05.



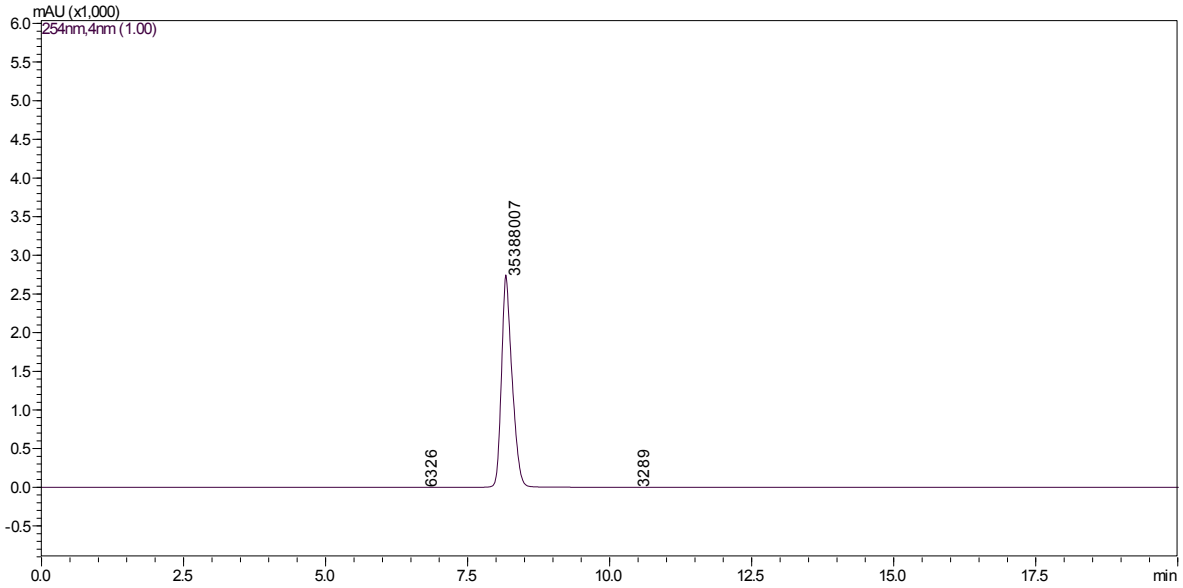


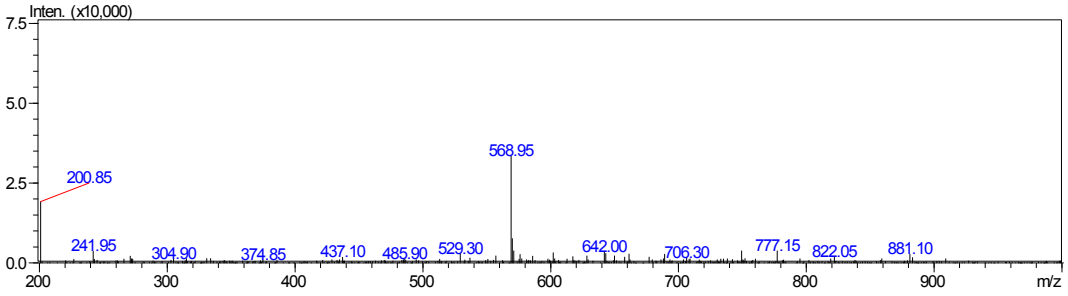


ESI-MS, positive mode: m/z calcd mass for $C_{34}H_{30}N_4O_3Na$ $[M + Na]^+$ = 565.22; found 564.90.

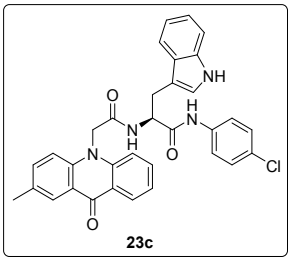


23b





ESI-MS, positive mode: m/z calcd mass for $C_{33}H_{27}FN_4O_3Na$ $[M + Na]^+$ = 569.20; found 568.95.



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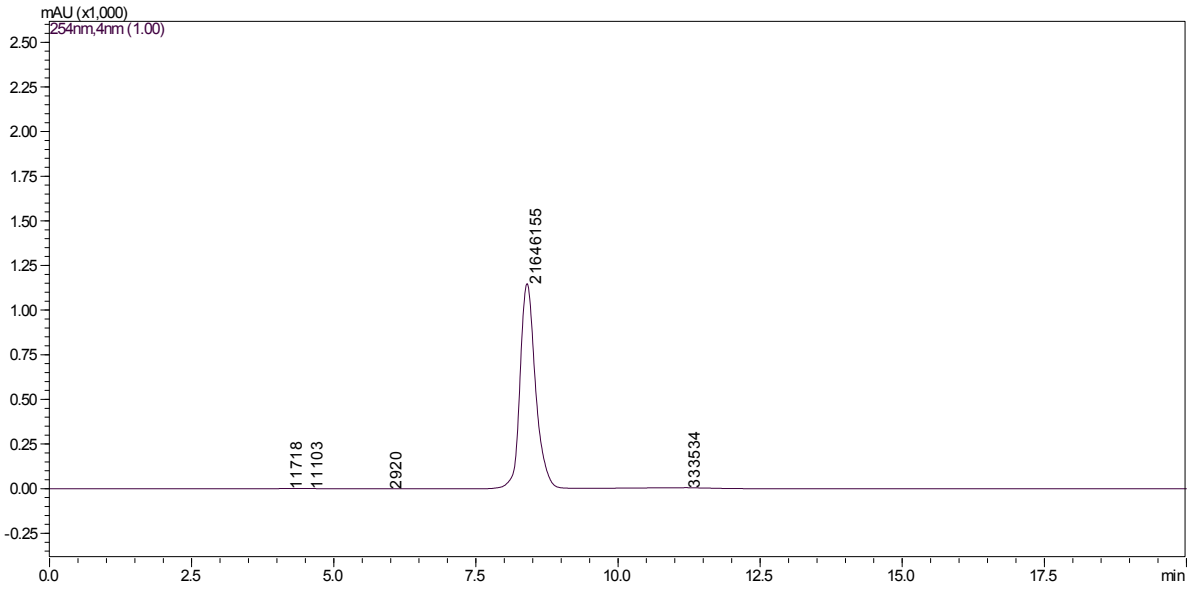
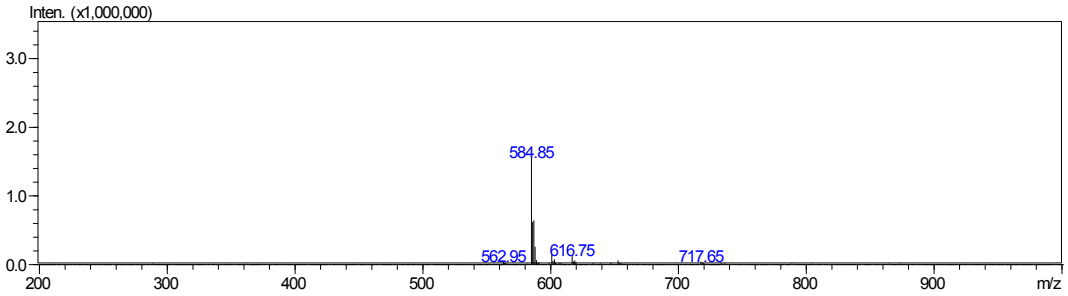
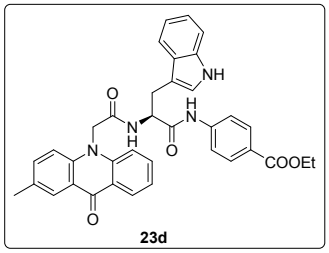
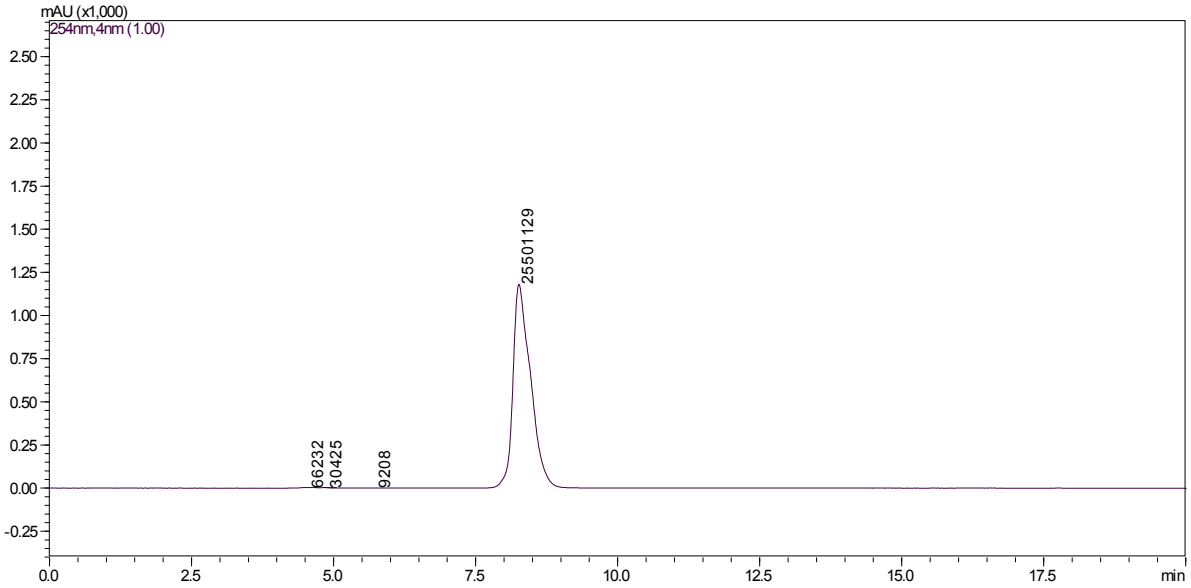


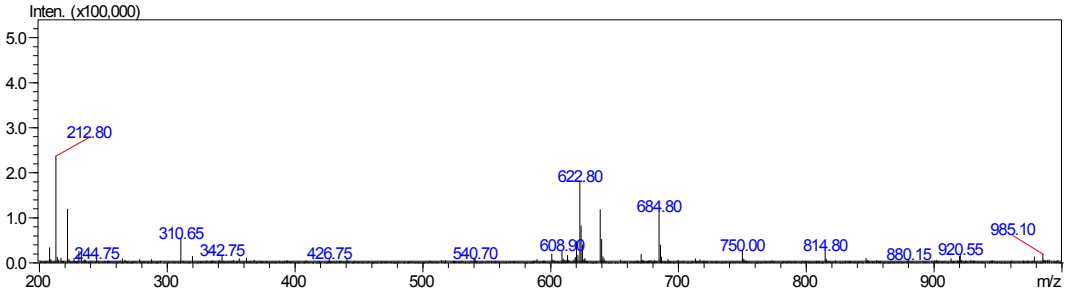


ESI-MS, positive mode: m/z calcd mass for $C_{33}H_{27}ClN_4O_3Na$ $[M + Na]^+$ = 585.17; found 584.85.



23d





ESI-MS, positive mode: m/z calcd mass for $C_{36}H_{32}N_4O_5Na$ $[M + Na]^+$ = 623.22; found 622.80.

Analytical method for compounds **14** and **20**:

LC-MS/HPLC: LC-20AD Shimadzu connected to Shimadzu LCMS-2010EV

Mobile Phase A: 0.1% FA in water

Mobile Phase B: 0.1% FA in acetonitrile

HPLC column: Poroshell 120 EC-C18, 4.6 x 100 mm, 2.7 µm

Flow rate: 0.4 mL/min

Run time: 40 min

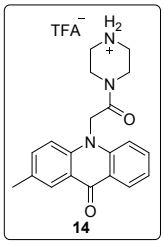
Column temperature: 26°C

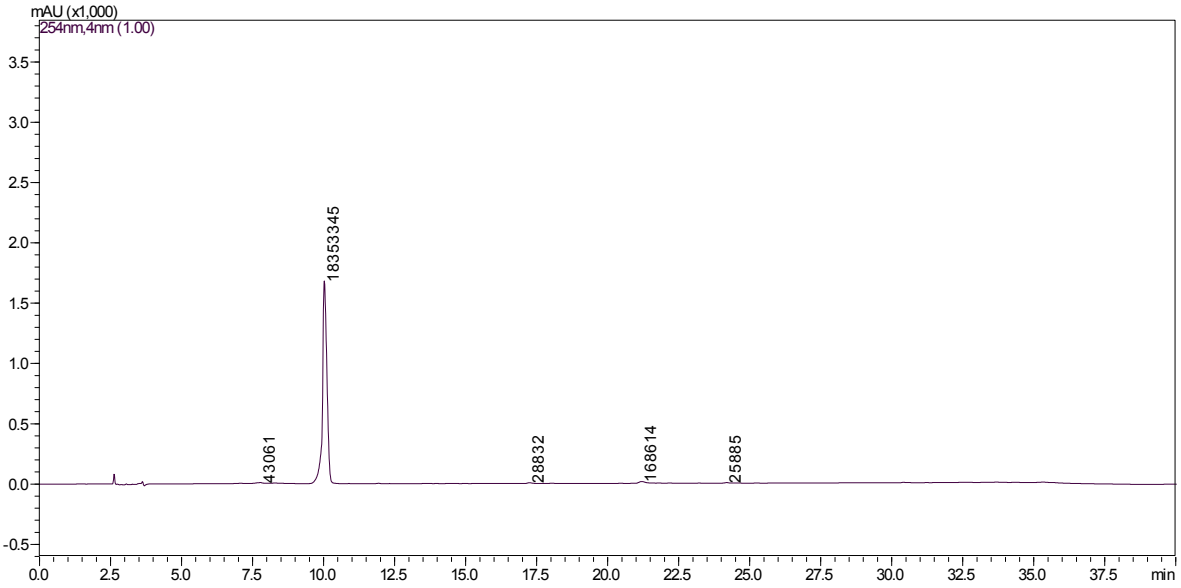
UV detector: 254 nm

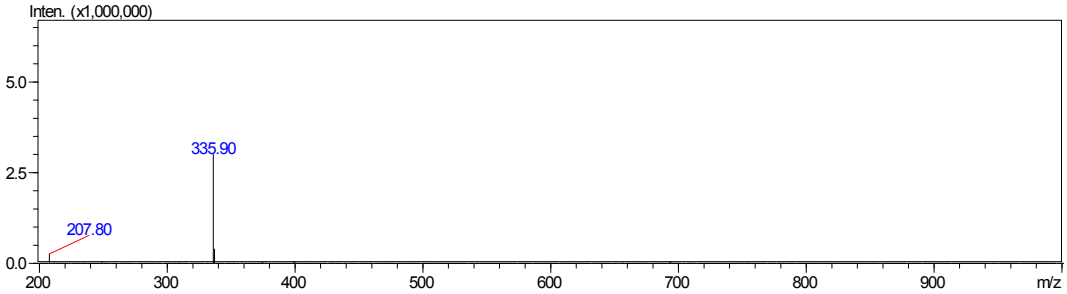
MS detector: 1.65 kV

LC isocratic:

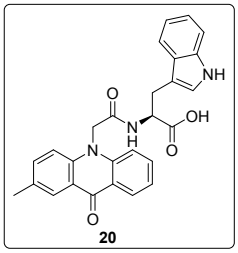
Time (min)	Mobile Phase A (%)	Mobile Phase B (%)
0	90	10
30	10	90
32	10	90
35	10	90
40	90	10

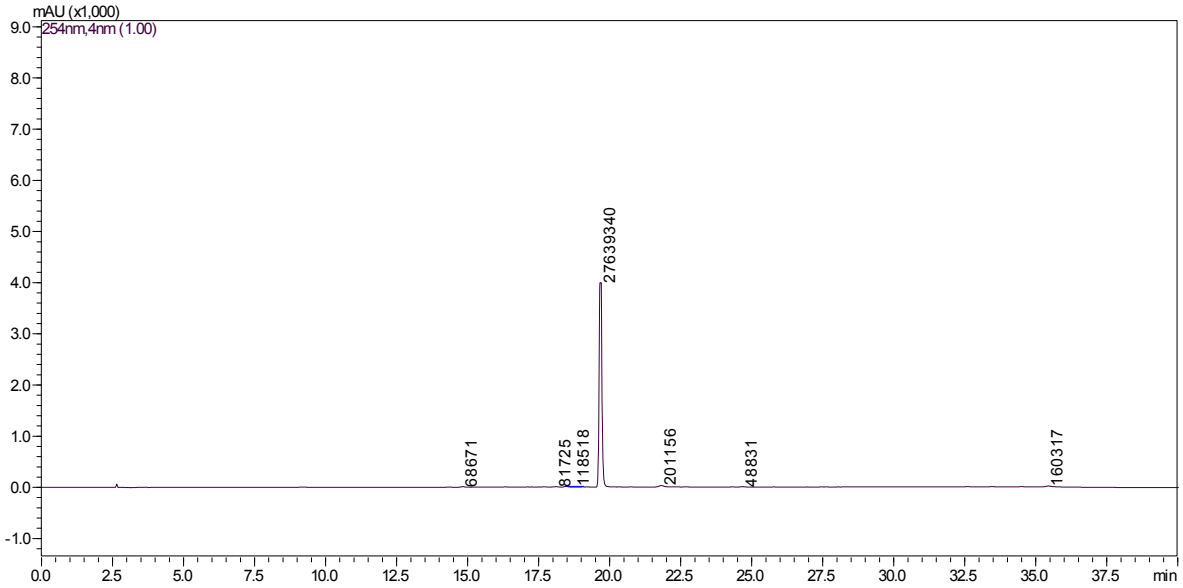


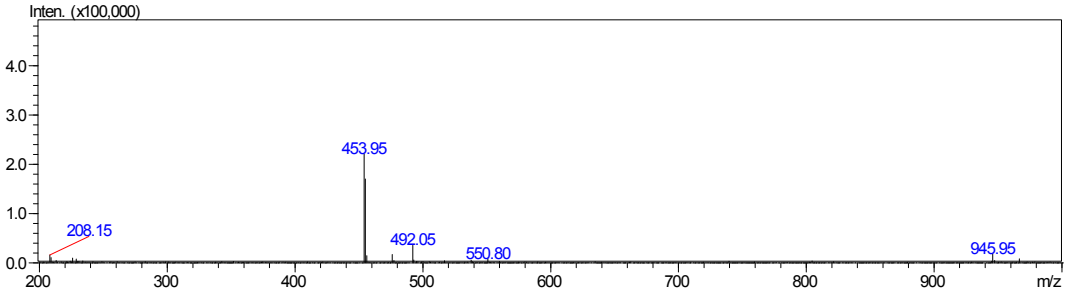




ESI-MS, positive mode: m/z calcd mass for $C_{20}H_{22}N_3O_2$ $[M + H]^+$ = 336.17; found 335.90.







ESI-MS, positive mode: m/z calcd mass for $C_{27}H_{24}N_3O_4$ $[M + H]^+$ = 454.17; found 453.95.