

SUPPLEMENTARY MATERIAL

Synthesis of Ethyl Pyrimidine-Quinolincarboxylates Selected from Virtual Screening as Enhanced Lactate Dehydrogenase (LDH) Inhibitors

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1. In-silico studies

Table S1. Affinity and energy values (kcal/mol) involved in the interaction of esters (**15-18**)(a-d) with the main aminoacid residues when docked in the **W31** site of *h*LDHA. Pose selection was done according to the best affinity value.

Hybrid	Affinity	Arg ¹⁶⁸	His ¹⁹²	Asn ¹³⁷	Asp ¹⁹⁴
15a	-9.060	-2.8	0.0	0.0	0.0
15b	-10.403	0.0	-3.0	-3.3	0.0
15c	-9.661	-6.0	0.0	0.0	0.0
15d	-10.063	-6.1	0.0	0.0	0.0
16a	-9.180	-6.2	0.0	0.0	0.0
16b	-10.396	-5.9	0.0	0.0	0.0
16c	-9.068	-6.8	0.0	0.0	0.0
16d	-9.961	-6.5	0.0	0.0	0.0
17a	-9.564	-5.8	0.0	0.0	0.0
17b	-9.611	-5.8	0.0	0.0	0.0
17c	-9.329	-6.3	0.0	0.0	0.0
17d	-10.490	-6.1	0.0	0.0	0.0
18a	-9.571	-2.1	0.0	0.0	0.0
18b	-9.740	-5.5	0.0	0.0	0.0
18c	-9.303	0.0	-7.1	-1.1	0.0
18d	-10.470	-6.4	0.0	0.0	0.0

Table S2. Affinity and energy values (kcal/mol) involved in the interaction of esters (**15-18**)(a-d) with the main aminoacid residues when docked in the **NADH** site of *h*LDHA. Pose selection was done according to the best affinity value.

Hybrid	Affinity	Asp ⁵¹	Val ¹³⁵	Arg ⁹⁸	Val ³⁰
NADH	-13.280	-7.7	-3.7	-16.9	-5.6
15a	-9.092	0.0	0.0	0.0	-0.7
15b	-9.728	0.0	0.0	-3.8	0.0
15c	-9.570	0.0	0.0	0.0	-0.7
15d	-9.027	0.0	0.0	0.0	0.0
16a	-9.403	0.0	0.0	0.0	-4.7
16b	-9.396	0.0	0.0	0.0	-0.9
16c	-9.706	0.0	0.0	0.0	-0.7
16d	-9.524	0.0	0.0	-5.1	0.0
17a	-9.276	0.0	0.0	0.0	0.0
17b	-8.334	0.0	0.0	-4.0	0.0
17c	-9.624	0.0	0.0	0.0	0.0
17d	-10.180	-1.5	0.0	0.0	-3.2
18a	-8.718	0.0	0.0	0.0	0.0
18b	-9.742	0.0	0.0	0.0	0.0
18c	-9.759	0.0	0.0	-4.5	0.0
18d	-10.140	-5.2	0.0	0.0	-2.4

Table S3. Affinity and energy values (kcal/mol) involved in the interaction of esters (**15-18**)(a-d) with the main aminoacid residues when docked in the **extended** site of *h*LDHA. Pose selection was done according to the best affinity value.

Hybrid	Affinity	Arg ¹⁶⁸	His ¹⁹²	Asn ¹³⁷	Asp ¹⁹⁴	Asp ⁵¹	Val ¹³⁵	Arg ⁹⁸	Val ³⁰
15a	-8.467	0.0	0.0	-2.8	0.0	0.0	0.0	0.0	0.0
15b	-8.167	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
15c	-8.230	-0.8	0.0	-4.3	0.0	0.0	0.0	0.0	0.0
15d	-8.074	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
16a	-8.244	0.0	0.0	-0.8	-3.9	0.0	0.0	0.0	0.0
16b	-8.183	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
16c	-8.279	-0.9	0.0	-4.3	0.0	0.0	0.0	0.0	0.0
16d	-8.546	0.0	-2.1	-2.1	0.0	0.0	0.0	0.0	0.0
17a	-8.219	0.0	0.0	-2.0	-4.2	0.0	0.0	0.0	0.0
17b	-8.434	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
17c	-8.436	-0.7	0.0	-4.3	0.0	0.0	0.0	0.0	0.0
17d	-8.248	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
18a	-8.482	0.0	0.0	-2.7	0.0	0.0	0.0	0.0	0.0
18b	-9.198	0.0	-0.9	-3.6	0.0	0.0	0.0	0.0	0.0
18c	-8.636	-0.9	0.0	-4.3	0.0	0.0	0.0	0.0	0.0
18d	-8.077	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table S4. Affinity and energy values (kcal/mol) involved in the interaction of selected pose (according to the reported filtering criteria) for esters (**15-18**)(a-d) with the main aminoacid residues when docked in the **W31** site of *h*LDHA.

R ₁	Aryl	Hybrid	Affinity	Arg ¹⁶⁸	His ¹⁹²	Asn ¹³⁷	Asp ¹⁹⁴
H	4-ClC ₆ H ₄	15a	-9.885	-5.5	0.0	0.0	0.0
	Naphth-2-yl	15b	-9.441	-8.7	0.0	0.0	0.0
	C ₆ H ₅	15c	-9.477	-5.2	-0.5	0.0	-3.3
	Styryl	15d	-10.001	-6.4	0.0	0.0	0.0
F	4-ClC ₆ H ₄	16a	-9.767	-6.5	0.0	0.0	0.0
	Naphth-2-yl	16b	-10.375	-6.0	0.0	0.0	0.0
	C ₆ H ₅	16c	-9.084	-6.8	-1.0	0.0	0.0
	Styryl	16d	-10.106	-6.3	0.0	0.0	0.0
Cl	4-ClC ₆ H ₄	17a	-10.052	-6.2	0.0	0.0	0.0
	Naphth-2-yl	17b	-10.440	-6.4	0.0	0.0	0.0
	C ₆ H ₅	17c	-9.568	-7.6	0.0	0.0	-0.6
	Styryl	17d	-10.194	-6.4	0.0	0.0	0.0
Br	4-ClC ₆ H ₄	18a	-9.919	-4.8	-0.6	0.0	0.0
	Naphth-2-yl	18b	-10.214	-5.7	0.0	0.0	-0.5
	C ₆ H ₅	18c	-9.836	-6.4	0.0	0.0	0.0
	Styryl	18d	-10.150	-6.4	0.0	0.0	0.0

Table S5. Affinity and energy values (kcal/mol) involved in the interaction of selected pose for esters (15-18)(a-d) with the main aminoacid residues when docked in the **extended** site of *h*LDHB.

Hybrid	Affinity	Asp ⁵³	Val ⁹⁹	Val ¹³⁷	Ser ¹⁶²	Gln ³¹	Gly ⁹⁸	Arg ¹⁰⁰	Val ³²	Asn ¹³⁹
NADH	-13.805	-8.7	-2.0	-4.5	-0.9	-5.8	0.0	-14.8	-6.2	-4.9
15a	-8.709	-0.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
15b	-8.790	0.0	0.0	0.0	0.0	0.0	0.0	-0.6	0.0	0.0
15c	-7.533	0.0	-0.6	0.0	0.0	0.0	-4.0	0.0	0.0	0.0
15d	-7.501	0.0	0.0	0.0	0.0	0.0	-6.4	0.0	0.0	0.0
16a	-8.219	0.0	0.0	0.0	0.0	0.0	-2.9	0.0	0.0	0.0
16b	-8.347	0.0	0.0	0.0	0.0	0.0	-2.1	0.0	0.0	0.0
16c	-8.130	0.0	0.0	0.0	0.0	0.0	-4.4	0.0	0.0	0.0
16d	-7.533	-0.6	0.0	0.0	0.0	-3.4	0.0	0.0	0.0	0.0
17a	-8.095	0.0	0.0	0.0	0.0	0.0	-5.4	0.0	0.0	0.0
17b	-8.241	0.0	0.0	0.0	0.0	0.0	-3.7	0.0	0.0	0.0
17c	-7.770	0.0	0.0	0.0	0.0	0.0	-7.0	0.0	0.0	0.0
17d	-7.727	0.0	0.0	0.0	0.0	0.0	-6.7	0.0	0.0	0.0
18a	-8.849	-0.7	0.0	0.0	0.0	0.0	0.0	-2.9	0.0	0.0
18b	-9.286	-0.5	0.0	0.0	0.0	0.0	-2.5	0.0	-4.4	0.0
18c	-7.302	0.0	0.0	0.0	0.0	0.0	-3.9	0.0	0.0	0.0
18d	-7.791	0.0	0.0	0.0	0.0	-3.3	0.0	-2.8	0.0	0.0

Table S6. Affinity and energy values (kcal/mol) involved in the interaction of selected pose for esters (15-18)(a-d) with the main aminoacid residues when docked in the **H1U** site of *h*LDHB.

Hybrid	Affinity	Glu214	Ser203	Ser211	Lys310
15a	-6.883	-7.2	0.0	0.0	-0.5
15b	-7.560	-6.8	0.0	0.0	-6.4
15c	-7.117	-5.0	0.0	-3.8	0.0
15d	-7.126	-7.1	0.0	0.0	0.0
16a	-7.840	-9.8	0.0	0.0	-11.1
16b	-7.742	-7.1	0.0	0.0	-0.5
16c	-6.707	-7.6	0.0	-0.5	-6.2
16d	-7.260	-6.4	0.0	0.0	0.0
17a	-7.994	-9.7	0.0	0.0	-8.4
17b	-6.921	-8.2	0.0	0.0	-6.9
17c	-6.884	-6.8	0.0	0.0	-7.3
17d	-7.348	-6.2	0.0	0.0	-1.4
18a	-8.057	-9.6	0.0	0.0	-10.6
18b	-7.036	-8.1	0.0	0.0	-7.7
18c	-7.049	-6.8	0.0	0.0	-7.3
18d	-6.772	-8.1	0.0	0.0	-7.1

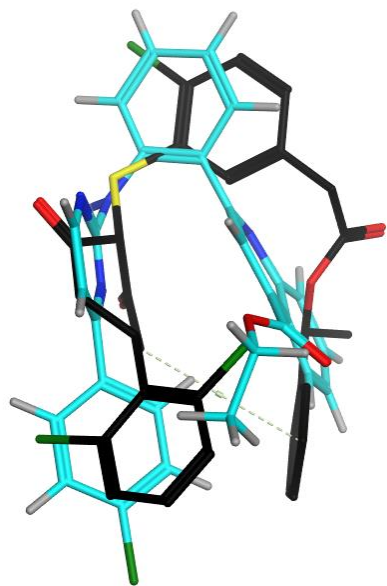


Figure S1. Pose comparison of **15a** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

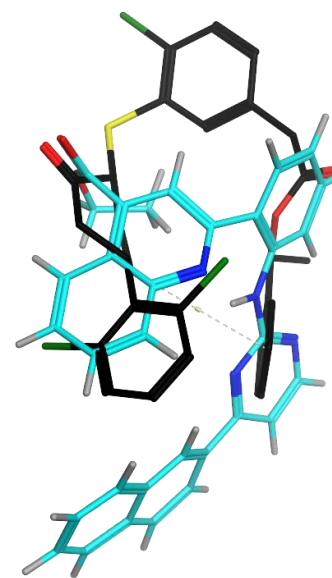


Figure S2. Pose comparison of **15b** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

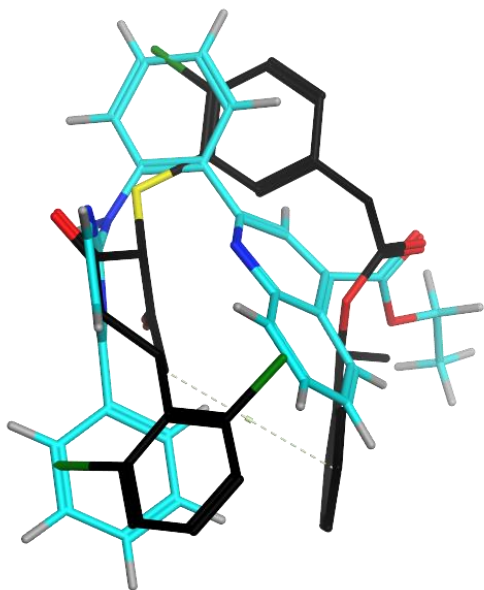


Figure S3. Pose comparison of **15c** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

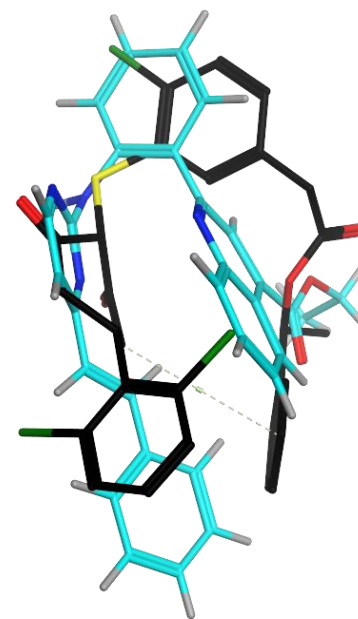


Figure S4. Pose comparison of **15d** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

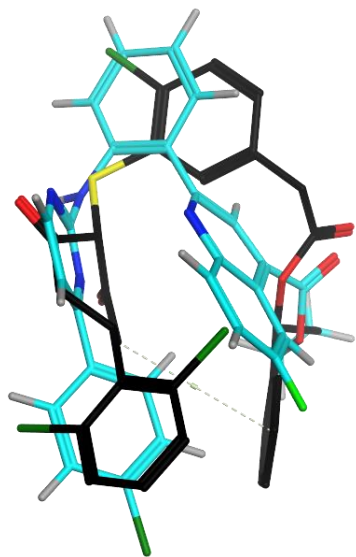


Figure S5. Pose comparison of **16a** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

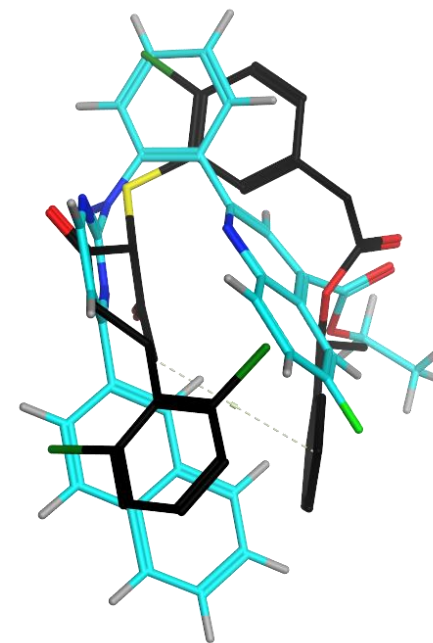


Figure S6. Pose comparison of **16b** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

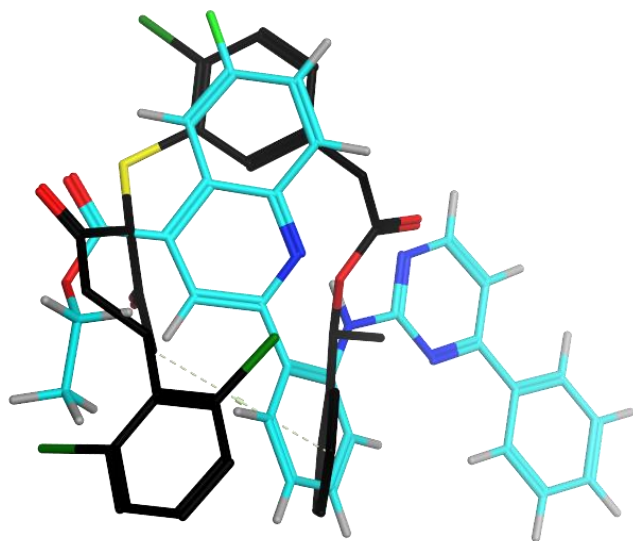


Figure S7. Pose comparison of **16c** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

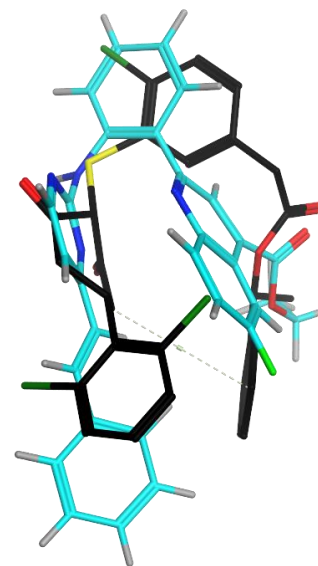


Figure S8. Pose comparison of **16d** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

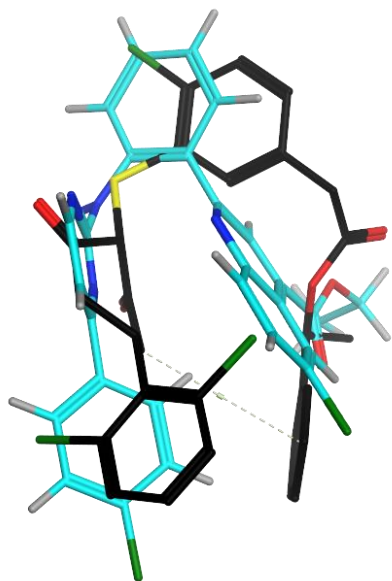


Figure S9. Pose comparison of **17a** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

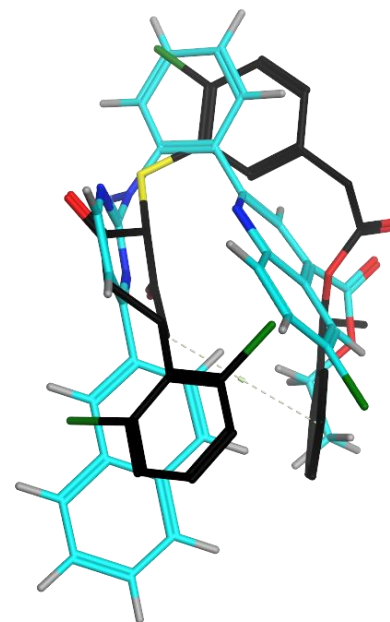


Figure S10. Pose comparison of **17b** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

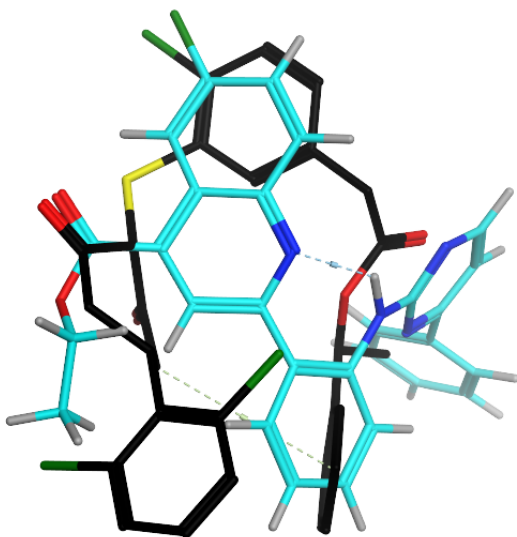


Figure S11. Pose comparison of **17c** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

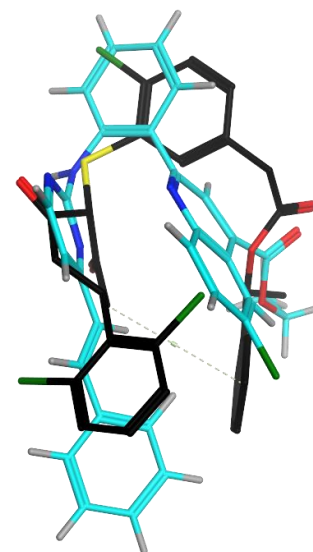


Figure S12. Pose comparison of **17d** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

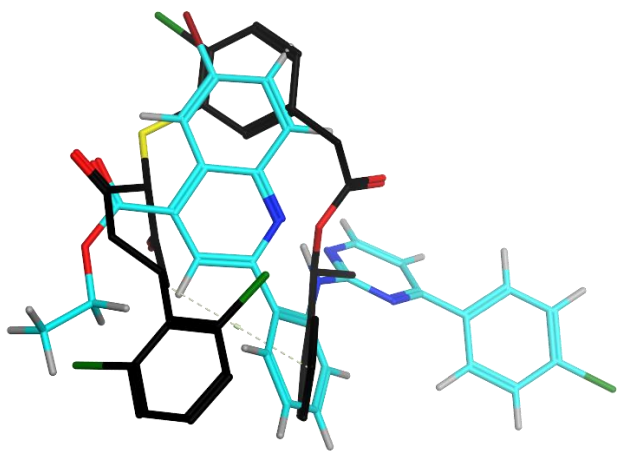


Figure S13. Pose comparison of **18a** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

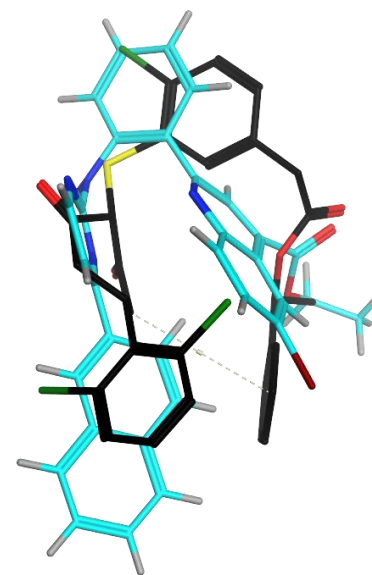


Figure S14. Pose comparison of **18b** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

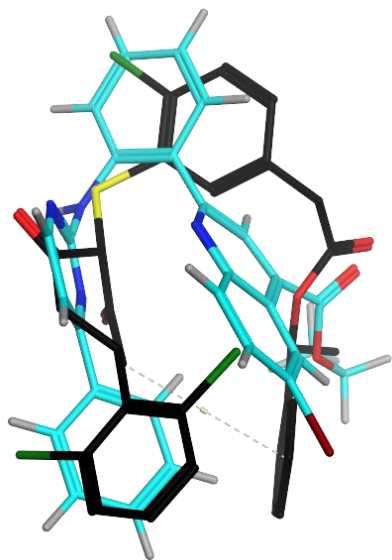


Figure S15. Pose comparison of **18c** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

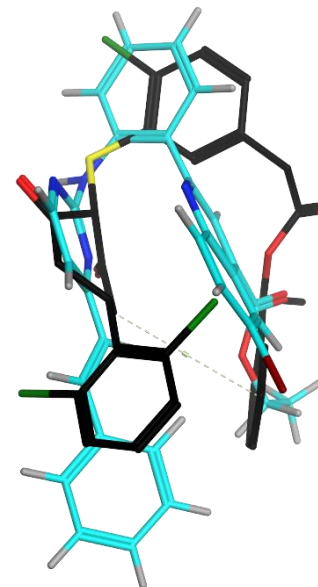


Figure S16. Pose comparison of **18d** (turquoise) and reference **W31** (black) in the *h*LDHA active site.

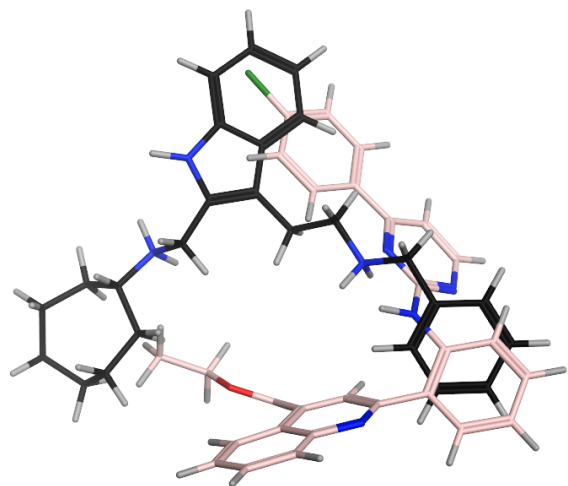


Figure S17. Pose comparison of **15a** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

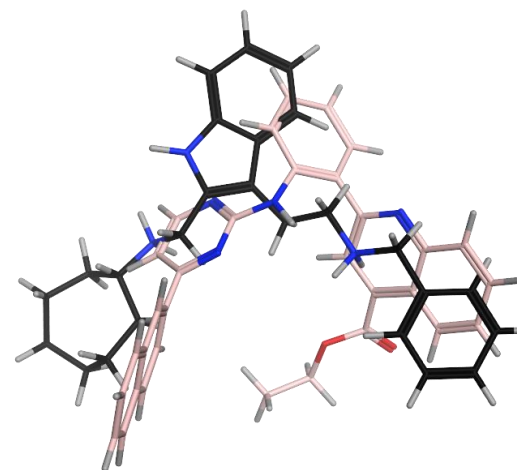


Figure S18. Pose comparison of **15b** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

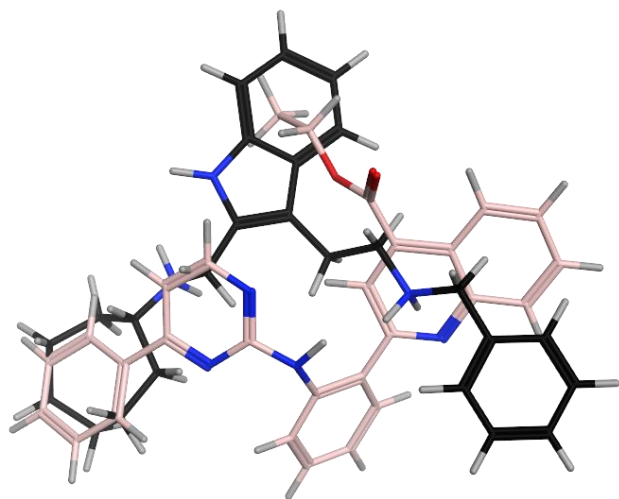


Figure S19. Pose comparison of **15c** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

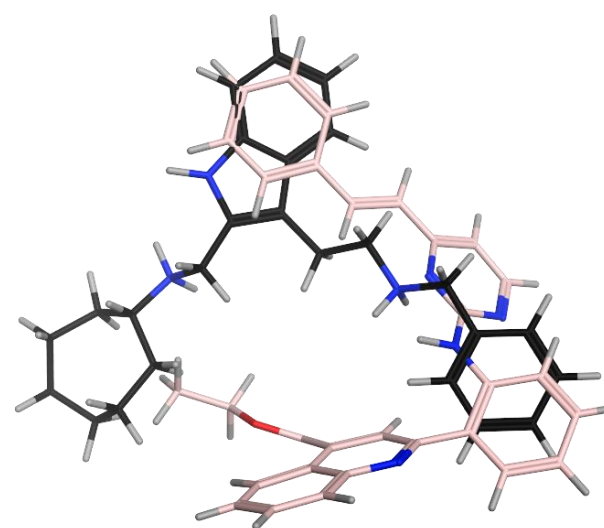


Figure S20. Pose comparison of **15d** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

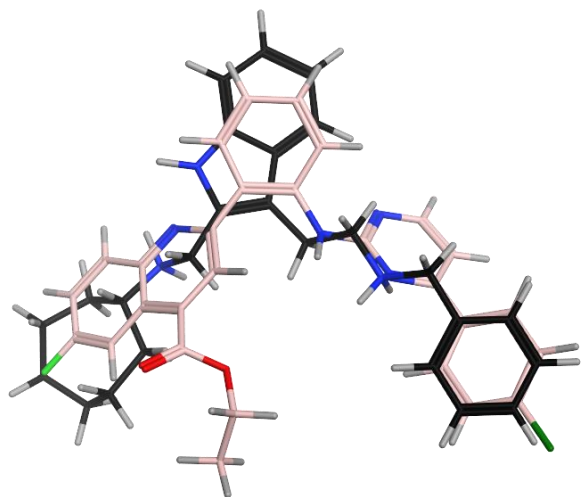


Figure S21. Pose comparison of **16a** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

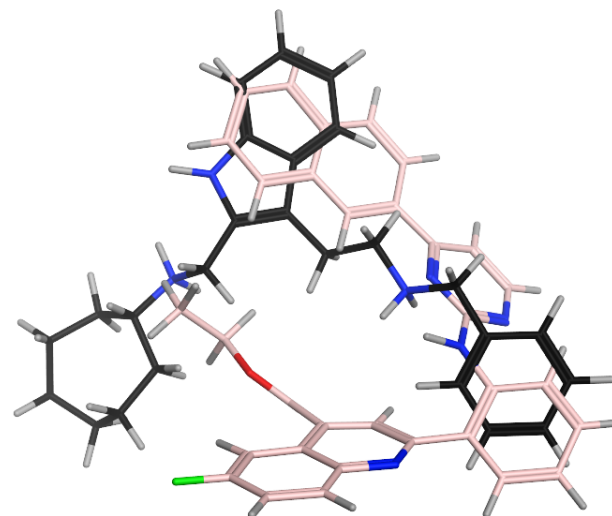


Figure S22. Pose comparison of **16b** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

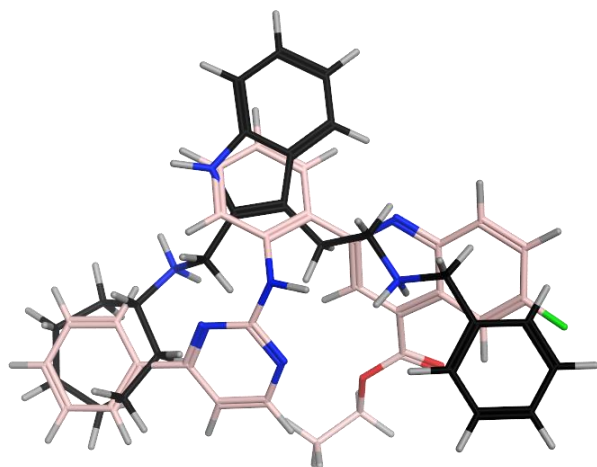


Figure S23. Pose comparison of **16c** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

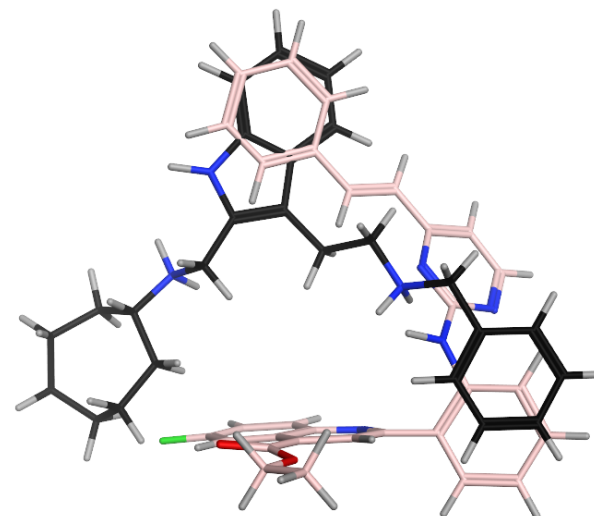


Figure S24. Pose comparison of **16d** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

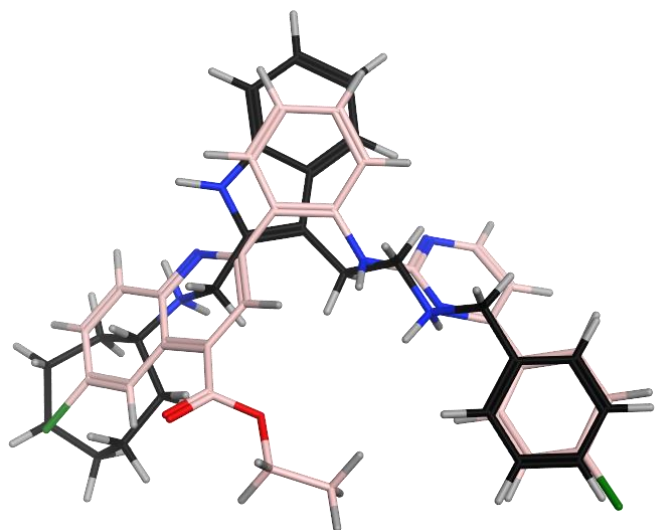


Figure S25. Pose comparison of **17a** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

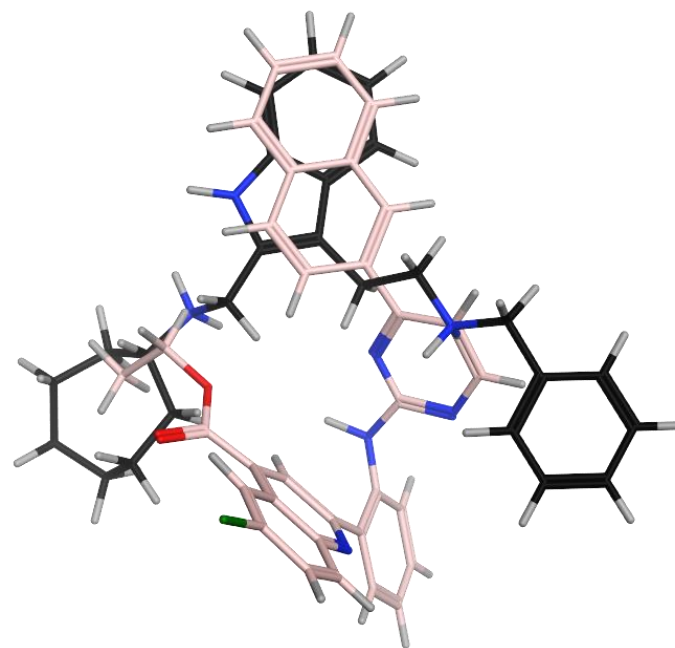


Figure S26. Pose comparison of **17b** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

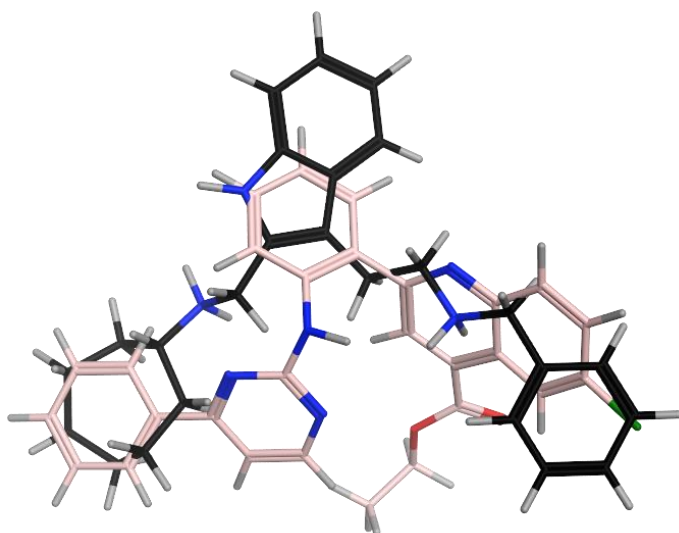


Figure S27. Pose comparison of **17c** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

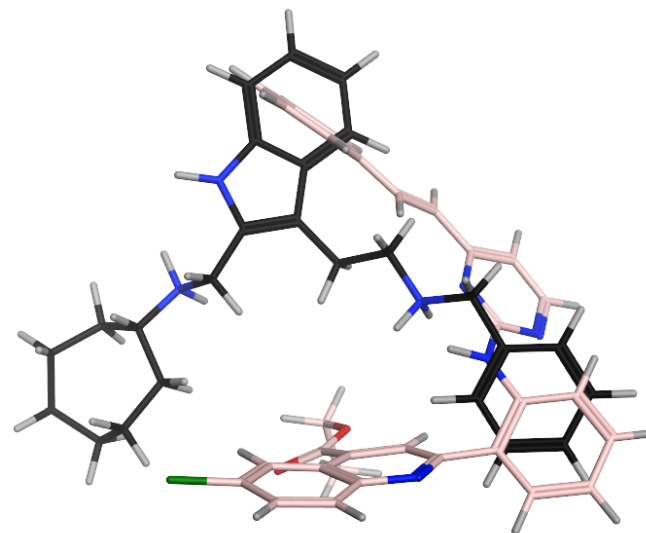


Figure S28. Pose comparison of **17d** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

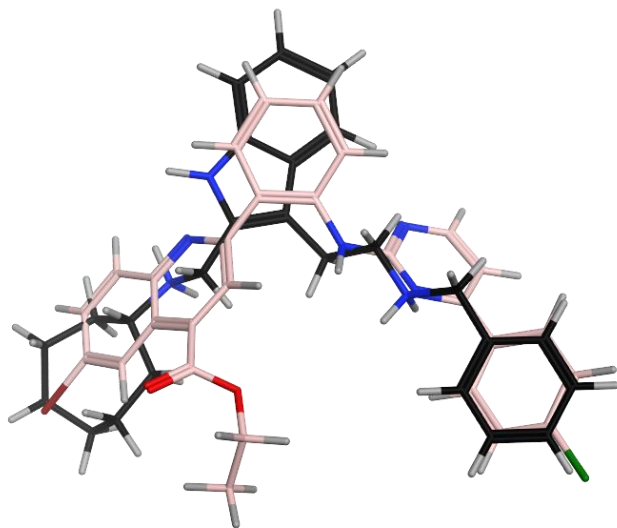


Figure S29. Pose comparison of **18a** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

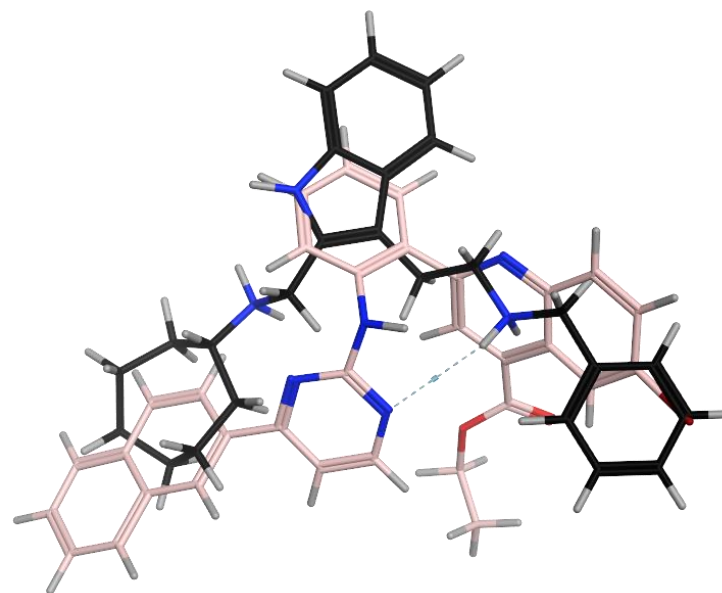


Figure S30. Pose comparison of **18b** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

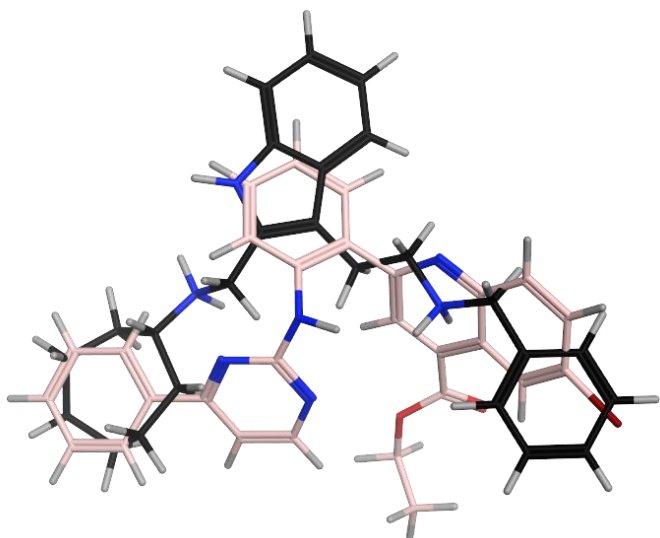


Figure S31. Pose comparison of **18c** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

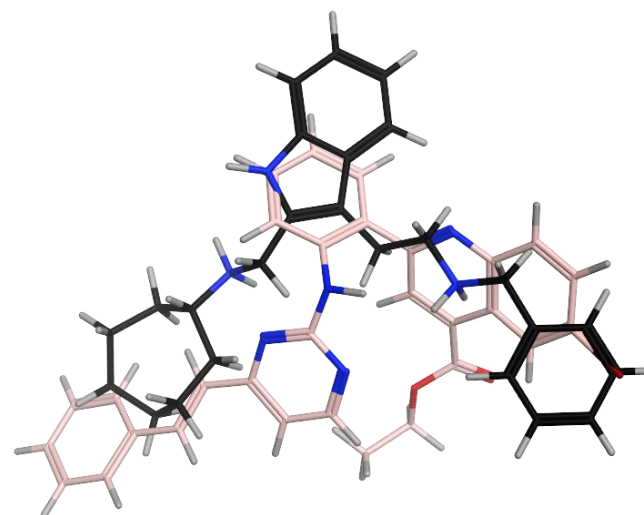
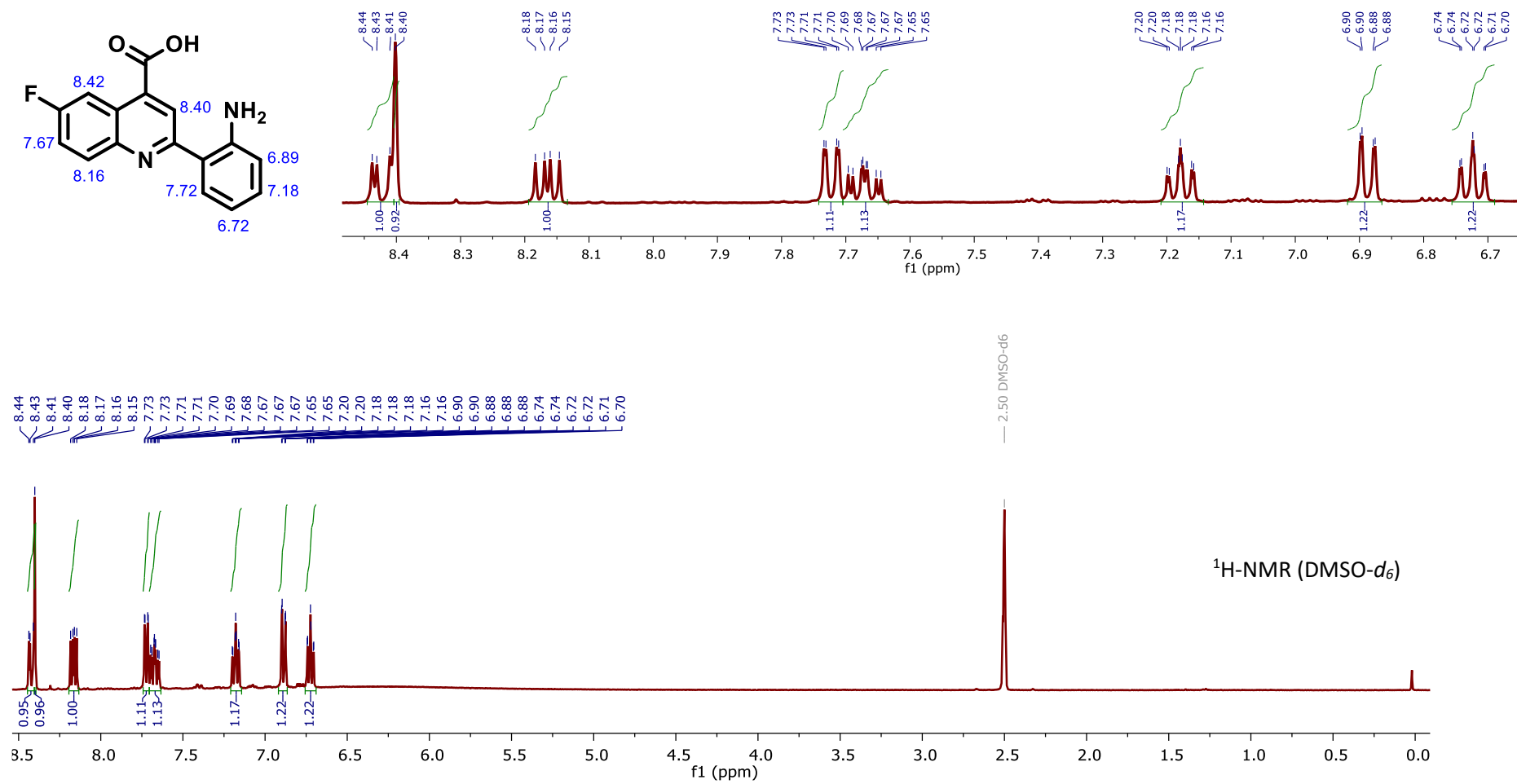
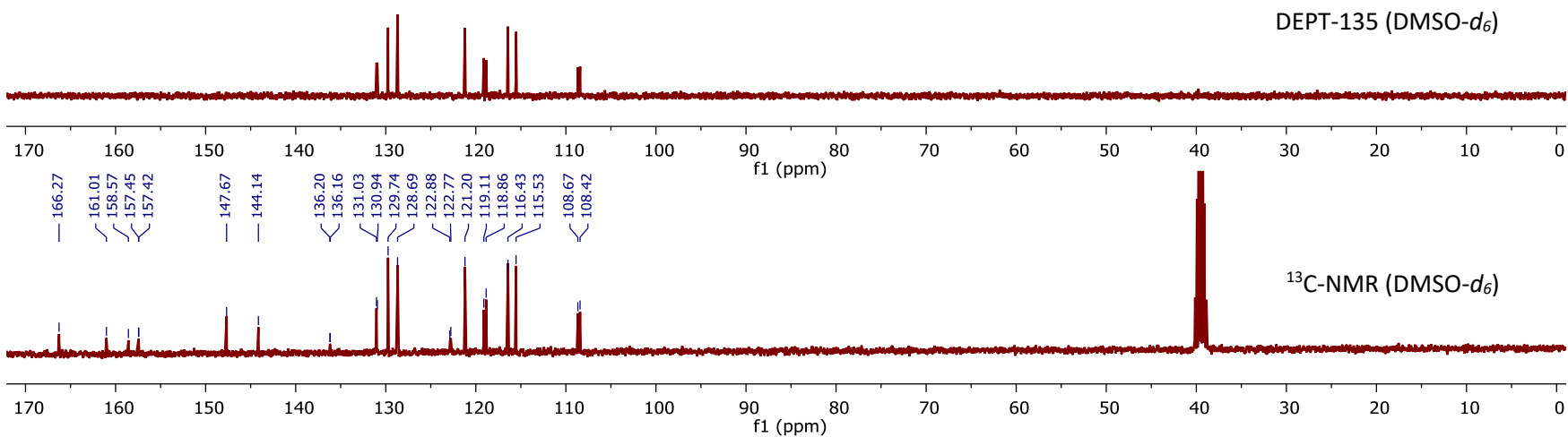


Figure S32. Pose comparison of **18d** (pink) and reference **H1U** (black) in the *h*LDHB allosteric site.

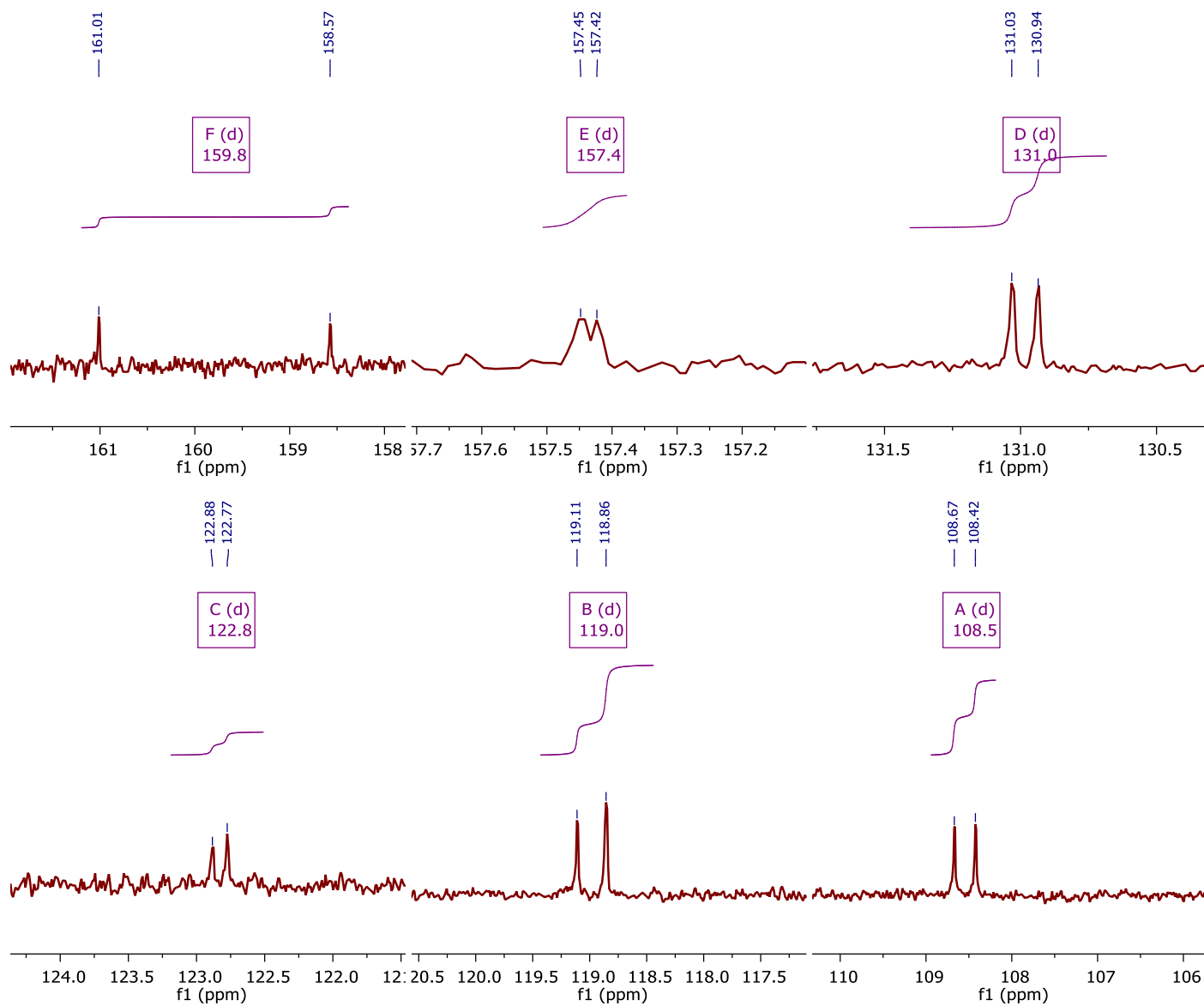
2. Structure characterization

Compound 4

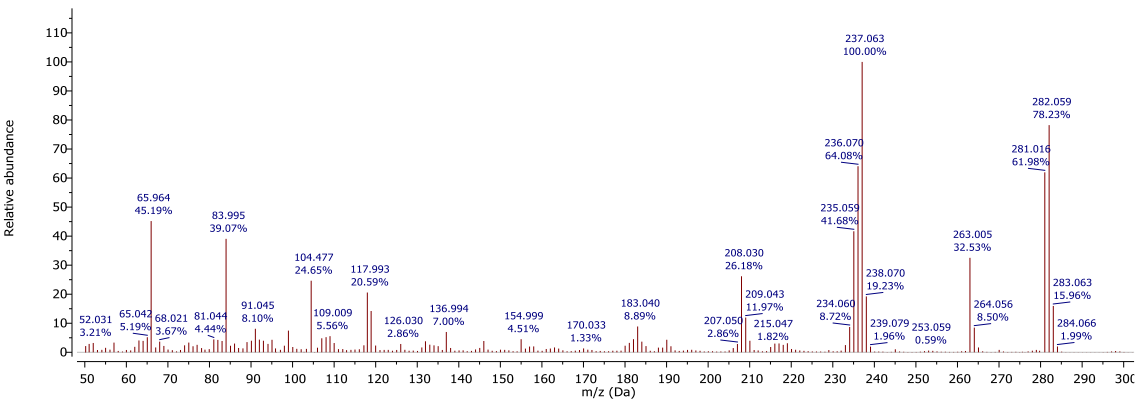




^{13}C - ^{19}F couplings in ^{13}C -NMR. Only coupled peaks have been represented to make it easier to understand.

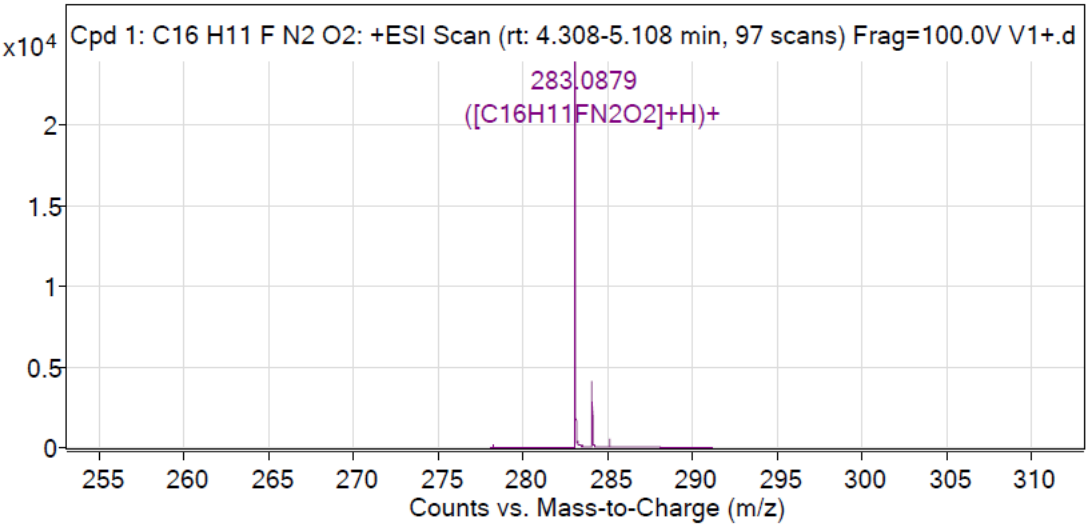


EI MS (70eV)



ESI-QTOF (positive ionization)

MS Zoomed Spectrum

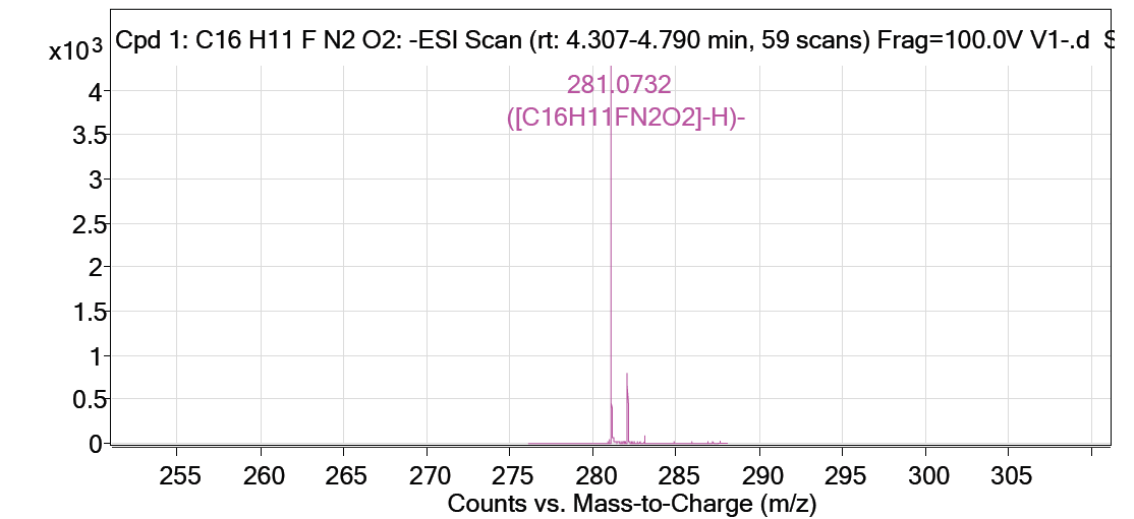


MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
283.0879	283.0877	-0.65	1	23979.17	C16H11FN2O2	(M+H)+
284.0912	284.0909	-1.16	1	4124.12	C16H11FN2O2	(M+H)+
285.0938	285.0936	-0.82	1	465.64	C16H11FN2O2	(M+H)+
286.097	286.0961	-2.9	1	46.11	C16H11FN2O2	(M+H)+

ESI-QTOF (negative ionization)

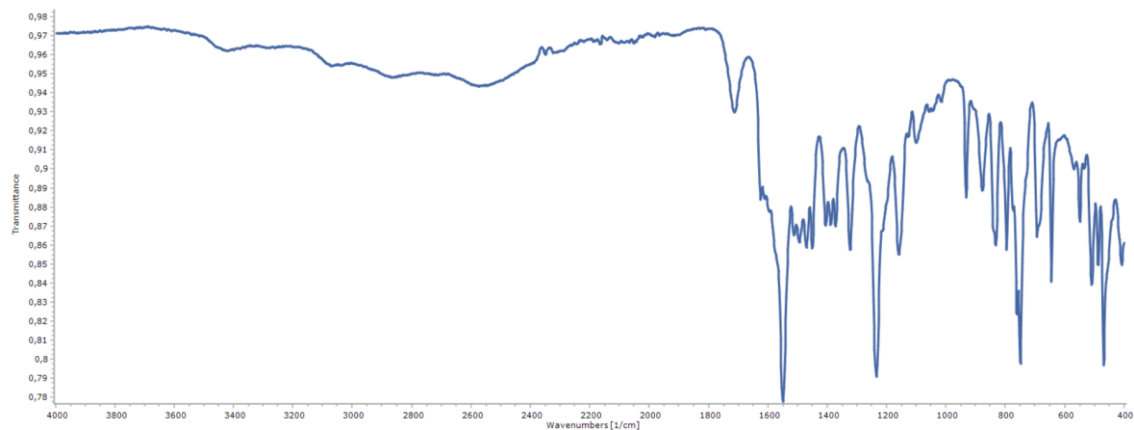
MS Zoomed Spectrum



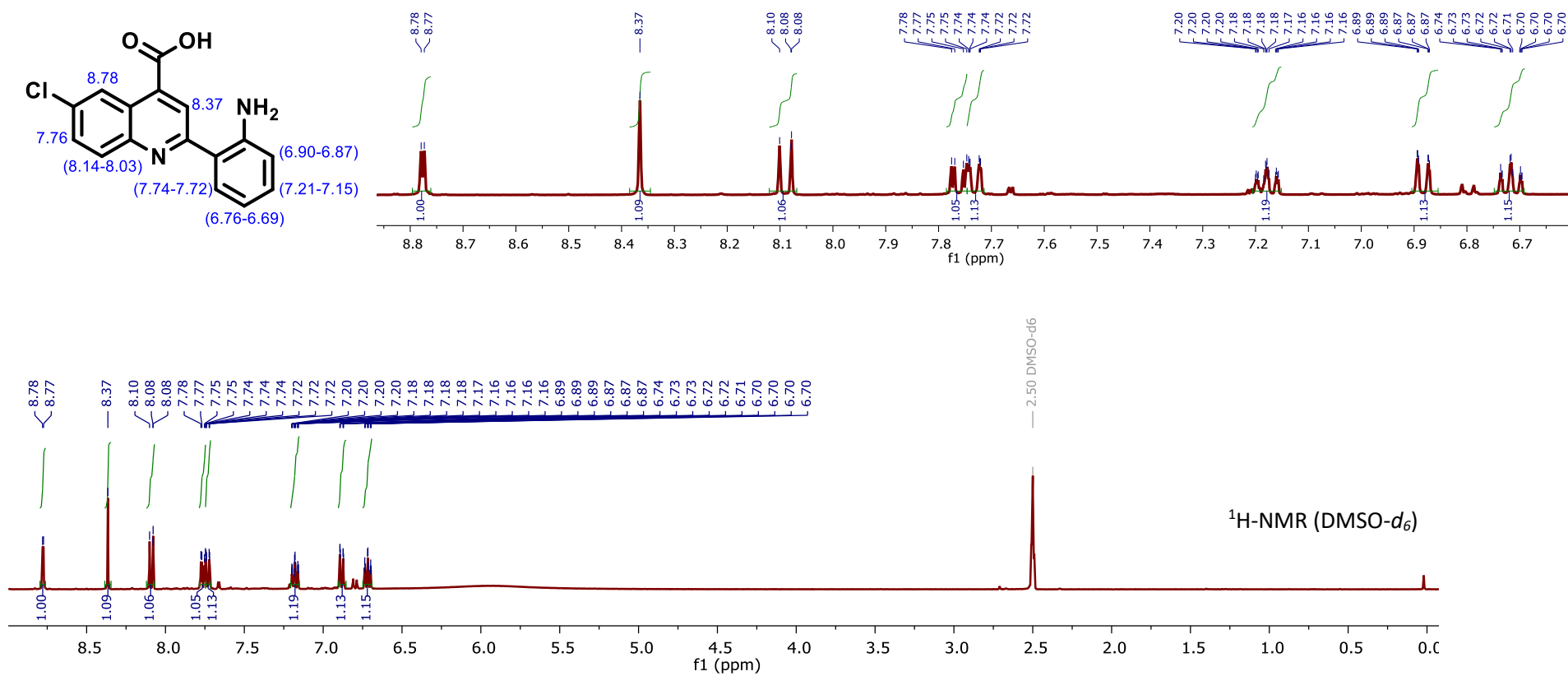
MS Spectrum Peak List

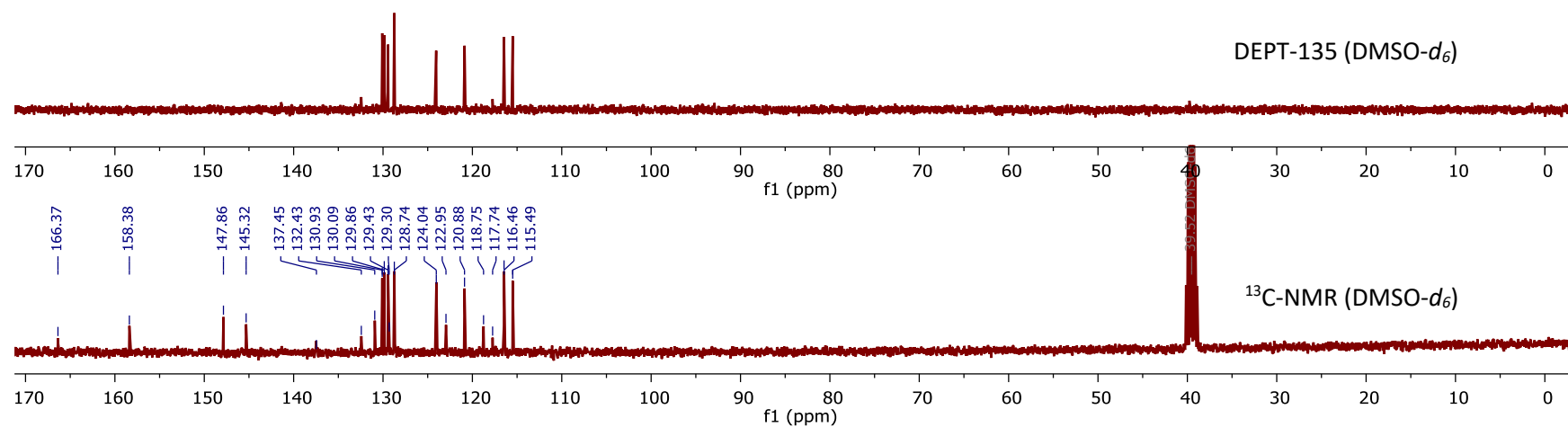
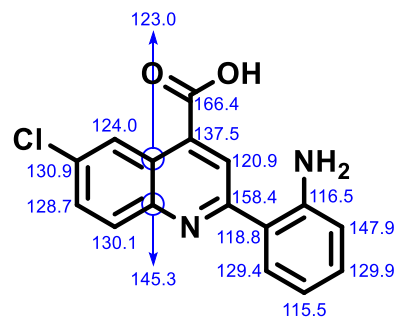
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
281.0732	281.0732	0.1	1	4354.5	C16H11FN2O2	(M-H)-
282.0763	282.0763	-0.05	1	808.67	C16H11FN2O2	(M-H)-
283.0795	283.079	-1.84	1	89.17	C16H11FN2O2	(M-H)-

IR

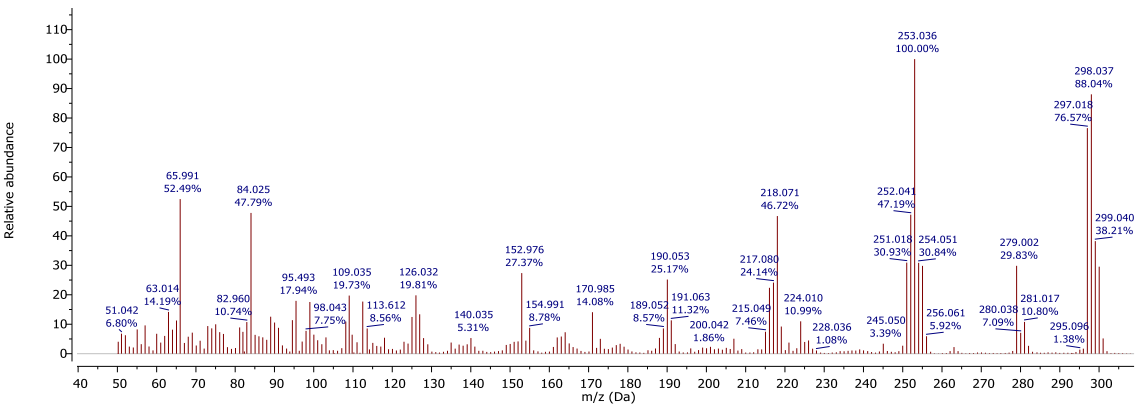


Compound 5



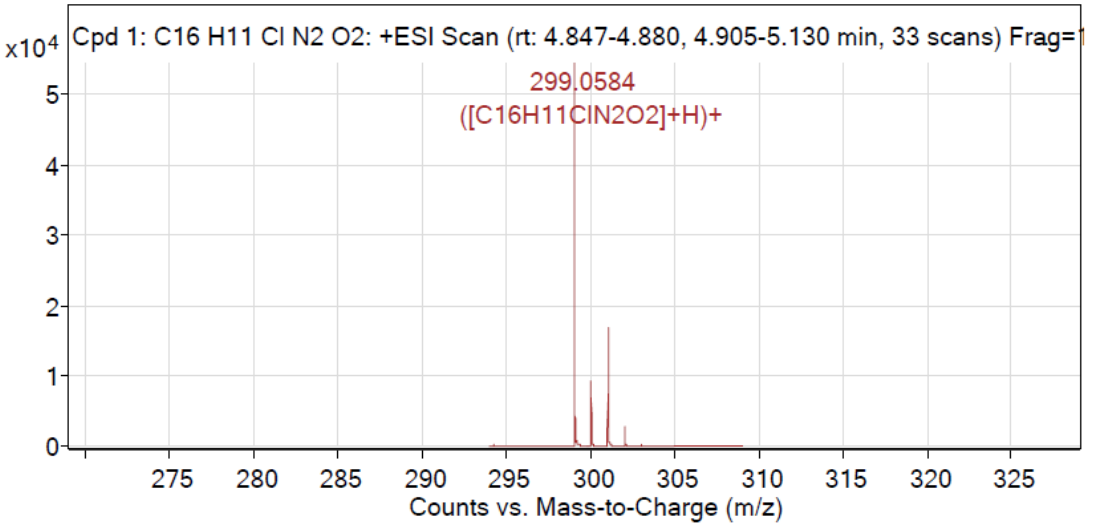


EI MS (70eV)



ESI-QTOF (positive ionization)

MS Zoomed Spectrum

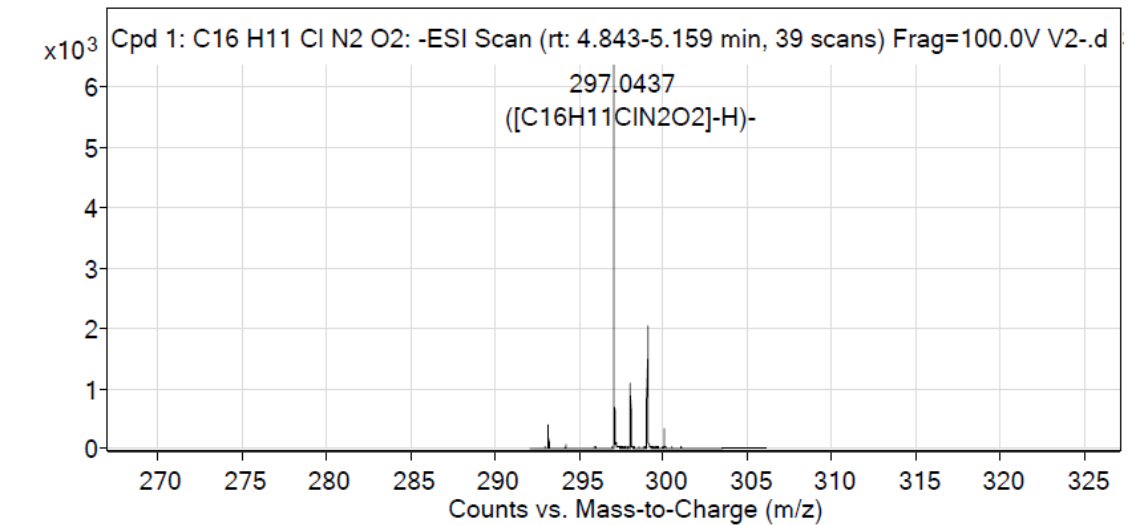


MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
299.0584	299.0582	-0.58	1	54928.41	C16H11ClN2O2	(M+H)+
300.0614	300.0613	-0.18	1	9197.05	C16H11ClN2O2	(M+H)+
301.0557	301.0557	-0.02	1	17015.27	C16H11ClN2O2	(M+H)+
302.0587	302.0586	-0.52	1	2882.98	C16H11ClN2O2	(M+H)+
303.0614	303.0612	-0.71	1	338.4	C16H11ClN2O2	(M+H)+
304.0634	304.0637	1.23	1	36.11	C16H11ClN2O2	(M+H)+

ESI-QTOF (negative ionization)

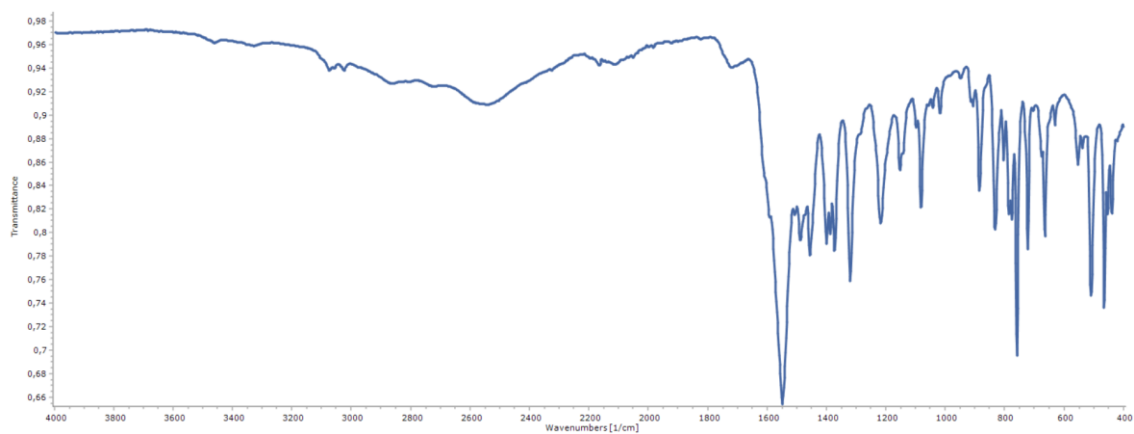
MS Zoomed Spectrum



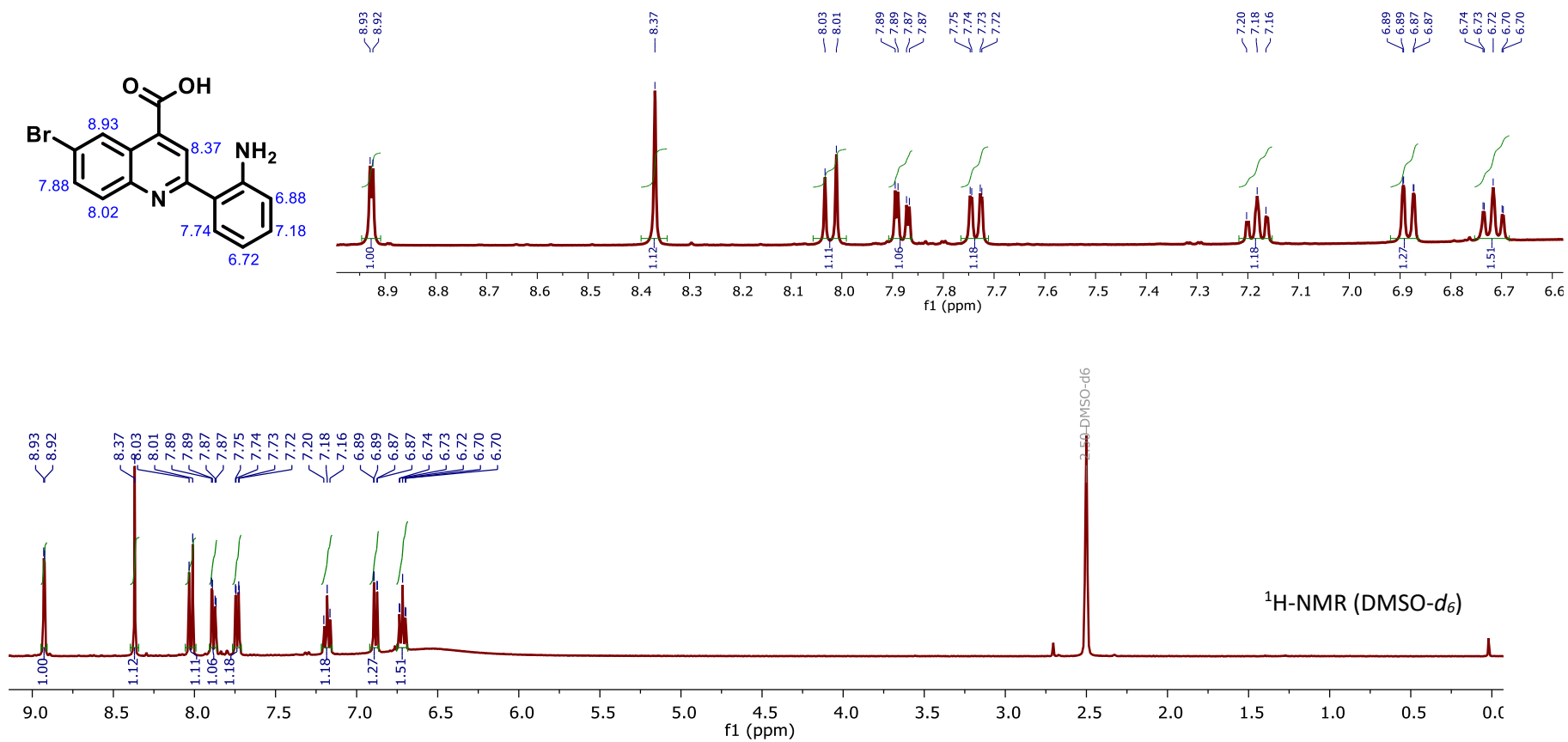
MS Spectrum Peak List

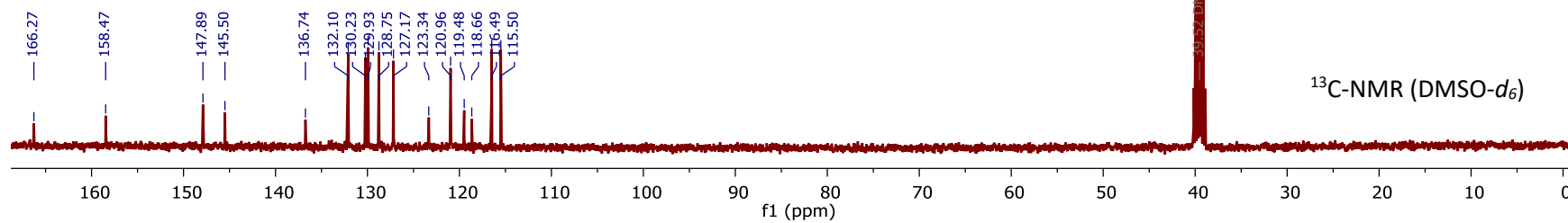
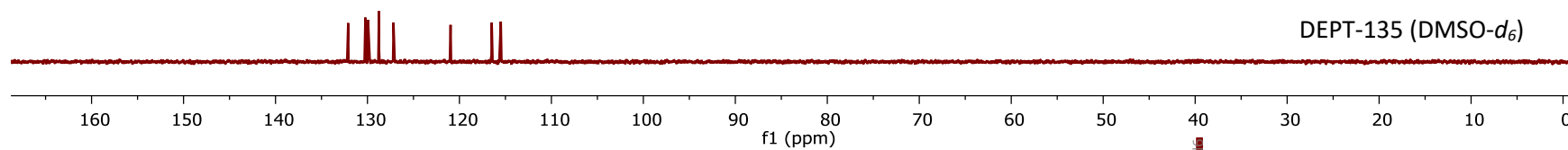
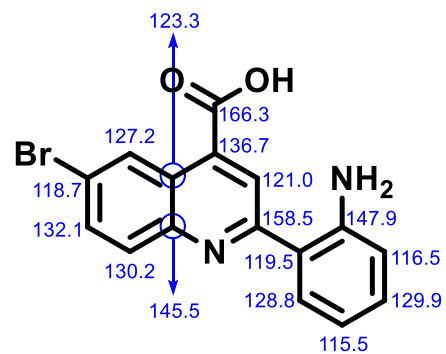
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
297.0437	297.0436	-0.15	1	6371.53	C16H11ClN2O2	(M-H)-
298.0471	298.0468	-1.04	1	1097.88	C16H11ClN2O2	(M-H)-
299.0413	299.0412	-0.51	1	2092.87	C16H11ClN2O2	(M-H)-
300.0437	300.044	0.94	1	342.55	C16H11ClN2O2	(M-H)-
301.0487	301.0466	-6.76	1	31.24	C16H11ClN2O2	(M-H)-

IR

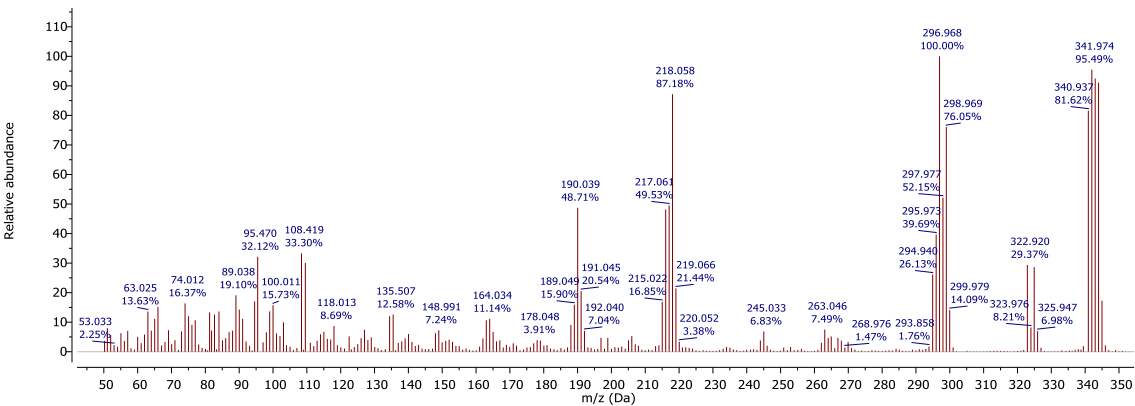


Compound 6



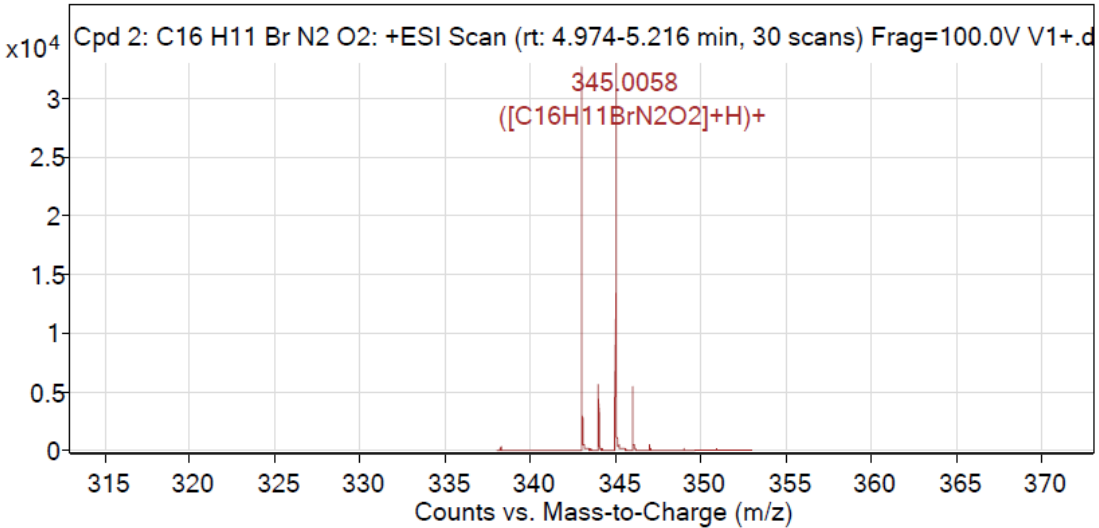


EI MS (70eV)



ESI-QTOF (positive ionization)

MS Zoomed Spectrum

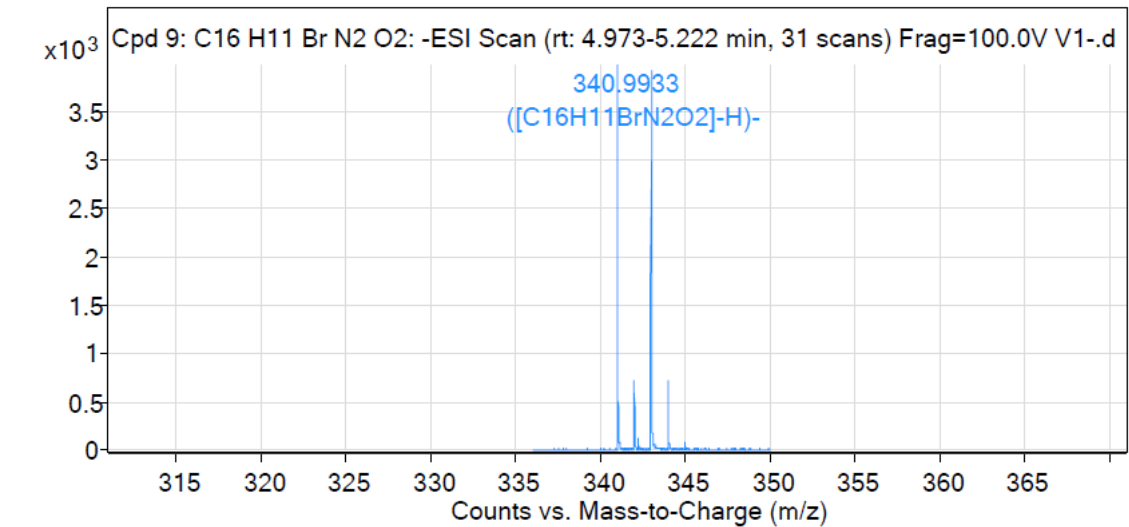


MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
343.0076	343.0077	0.19	1	32719.25	C16H11BrN2O2	(M+H)+
344.0108	344.0108	-0.06	1	5710.41	C16H11BrN2O2	(M+H)+
345.0058	345.0058	-0.02	1	33001.97	C16H11BrN2O2	(M+H)+
346.0088	346.0088	0.11	1	5543.34	C16H11BrN2O2	(M+H)+
347.0118	347.0115	-0.83	1	545.28	C16H11BrN2O2	(M+H)+
348.0167	348.0141	-7.46	1	63.63	C16H11BrN2O2	(M+H)+

ESI-QTOF (negative ionization)

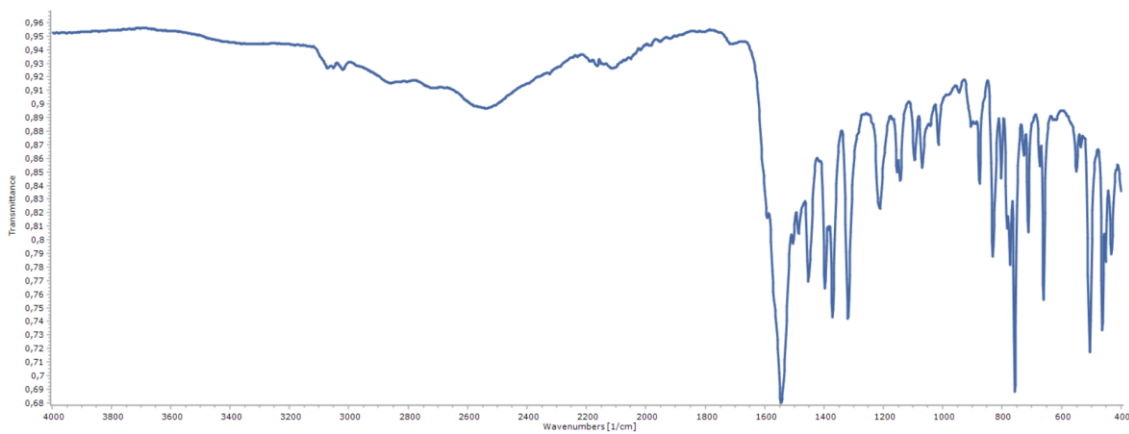
MS Zoomed Spectrum



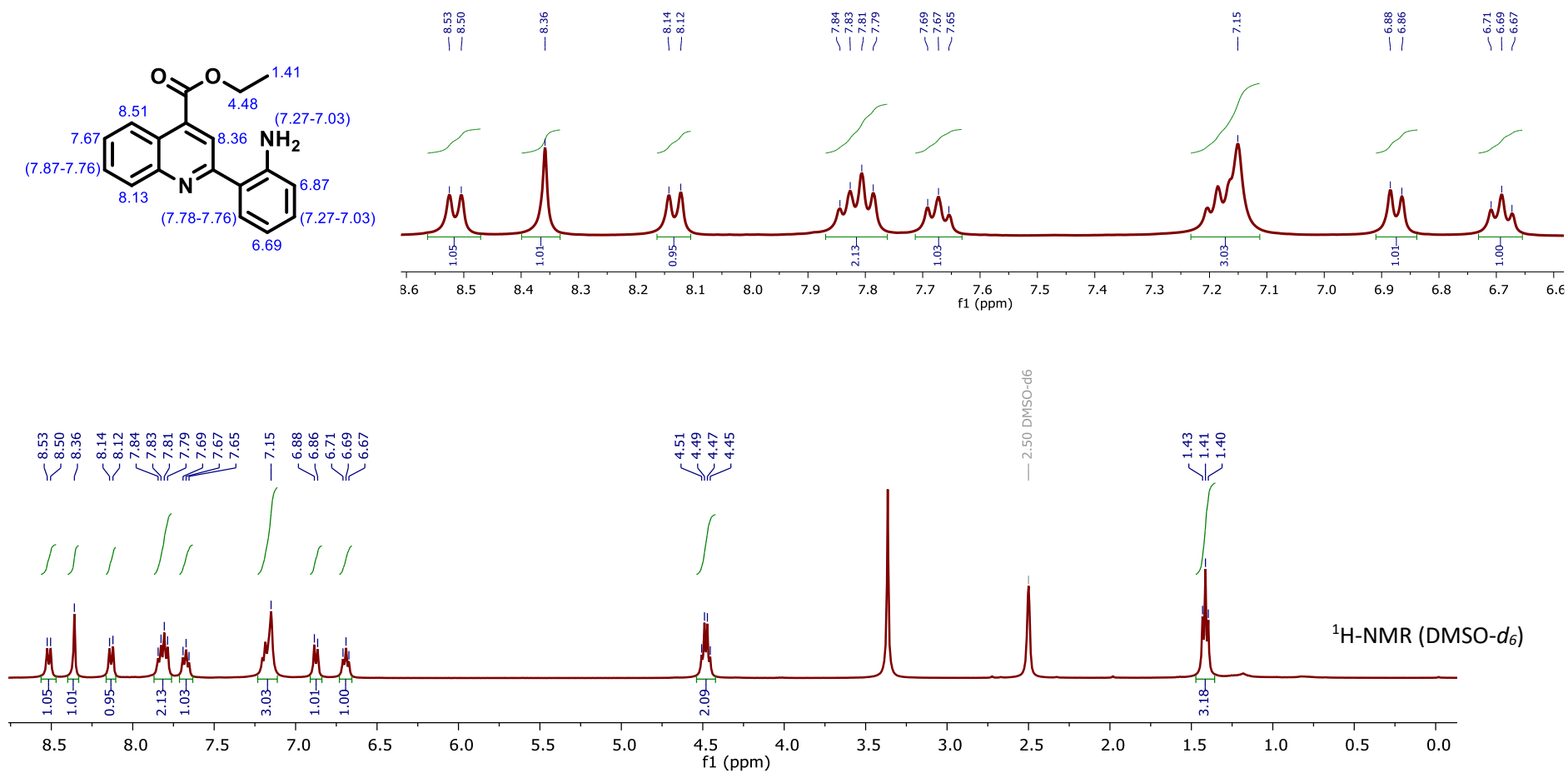
MS Spectrum Peak List

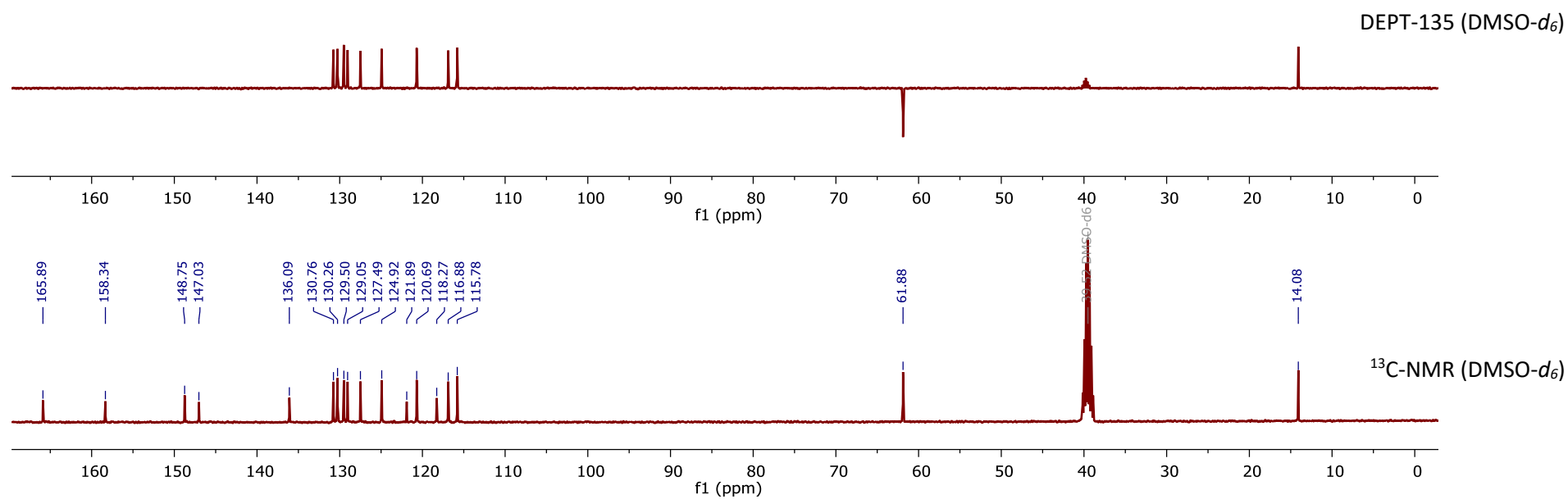
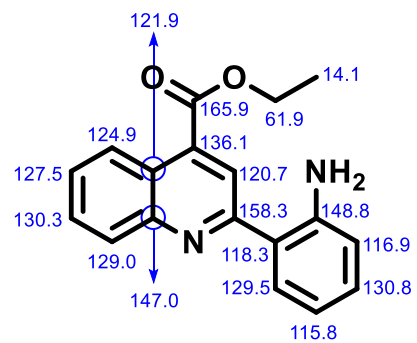
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
340.9933	340.9931	-0.49	1	4083.53	C ₁₆ H ₁₁ BrN ₂ O ₂	(M-H)-
341.9964	341.9962	-0.38	1	733.42	C ₁₆ H ₁₁ BrN ₂ O ₂	(M-H)-
342.9915	342.9912	-0.85	1	3978.05	C ₁₆ H ₁₁ BrN ₂ O ₂	(M-H)-
343.9944	343.9943	-0.29	1	722.68	C ₁₆ H ₁₁ BrN ₂ O ₂	(M-H)-
344.9979	344.9969	-2.91	1	84.04	C ₁₆ H ₁₁ BrN ₂ O ₂	(M-H)-

IR

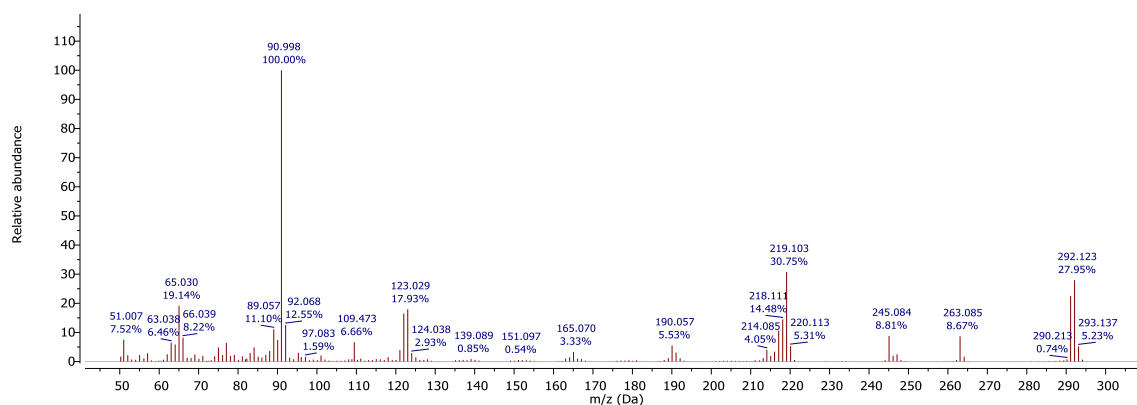


Compound 9



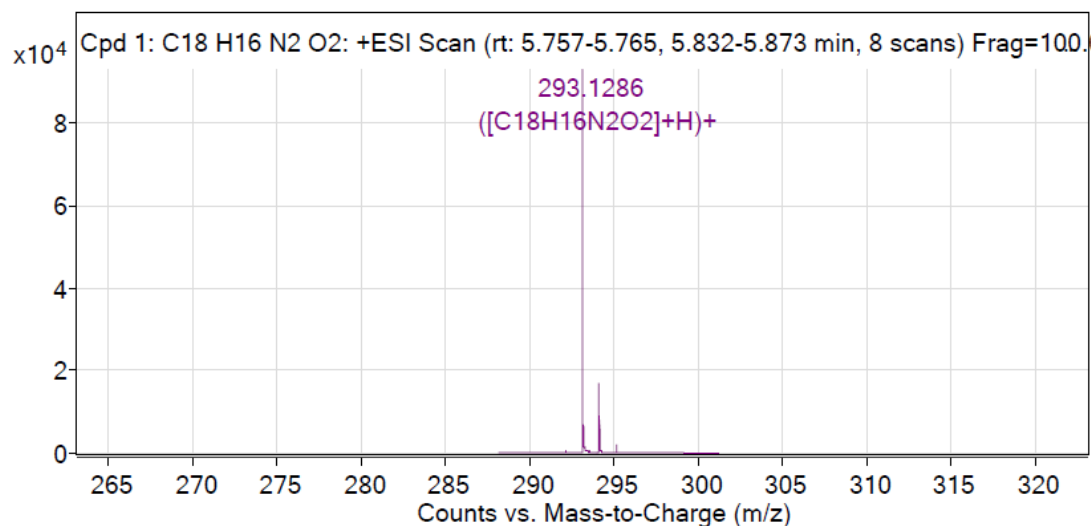


EI MS (70eV)



ESI-QTOF (positive ionization)

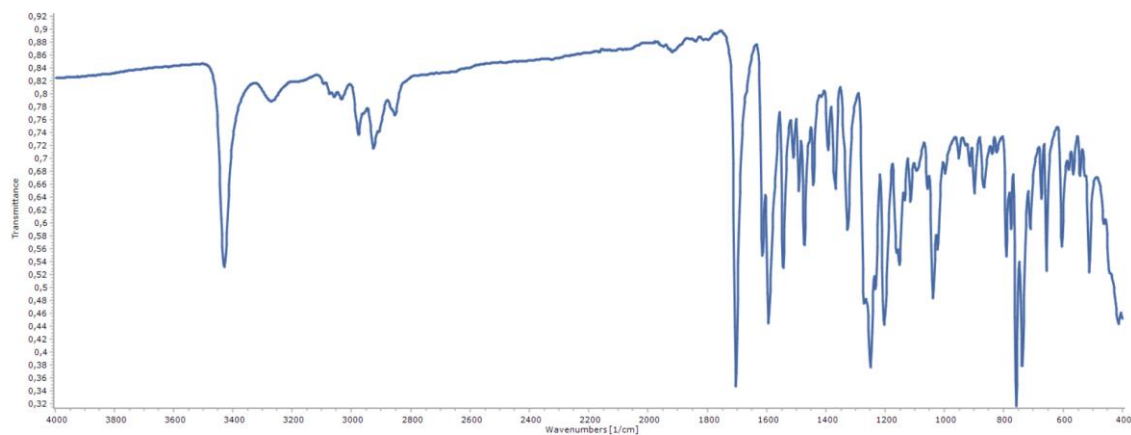
MS Zoomed Spectrum



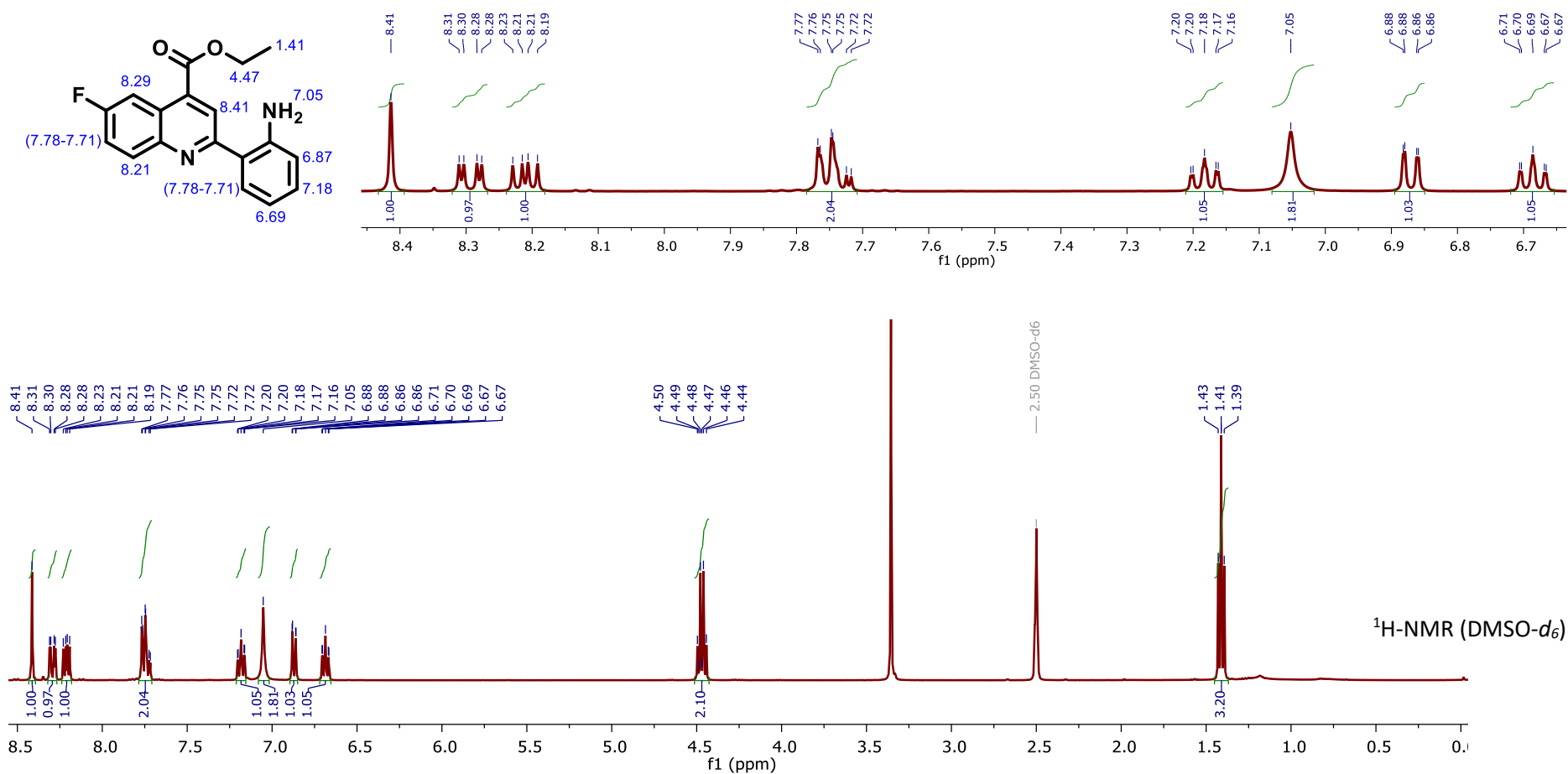
MS Spectrum Peak List

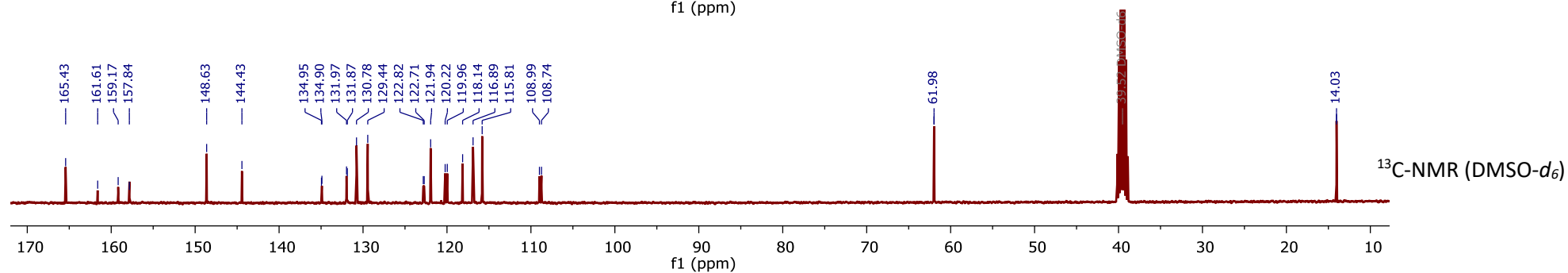
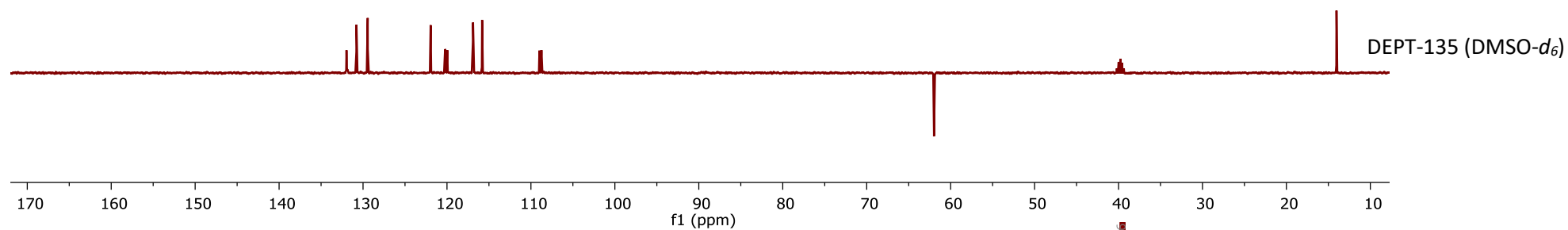
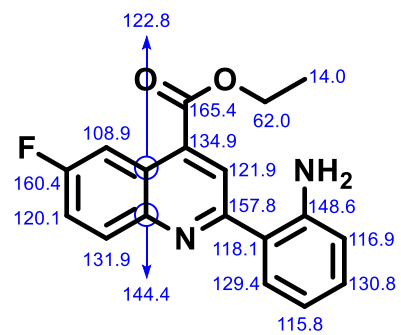
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
293.1286	293.1285	-0.56	1	93212.11	C18H16N2O2	(M+H)+
294.1319	294.1316	-1.12	1	17093.06	C18H16N2O2	(M+H)+
295.1344	295.1344	0.09	1	2107.36	C18H16N2O2	(M+H)+
296.1386	296.1371	-5.08	1	196.75	C18H16N2O2	(M+H)+

IR

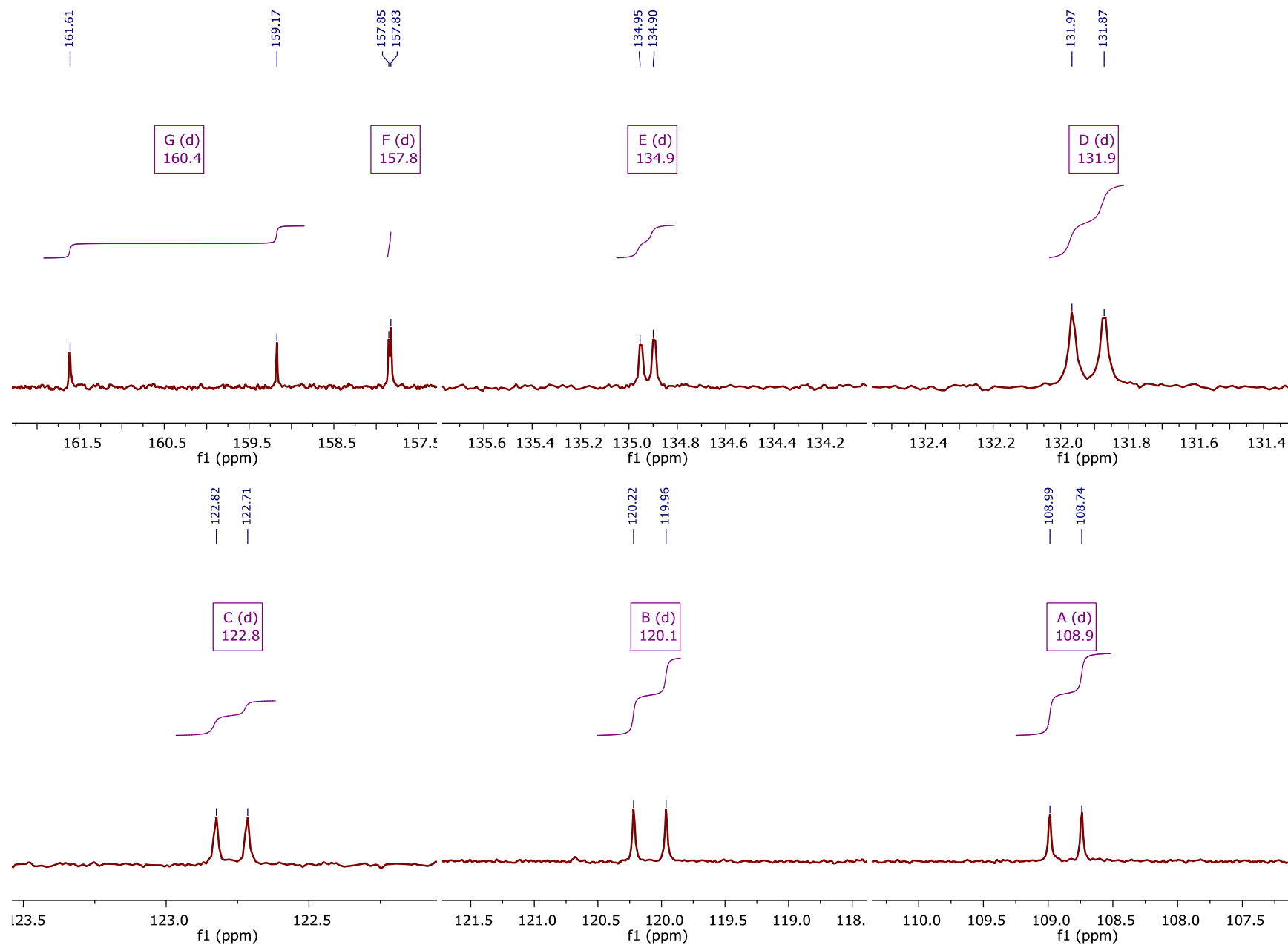


Compound 10

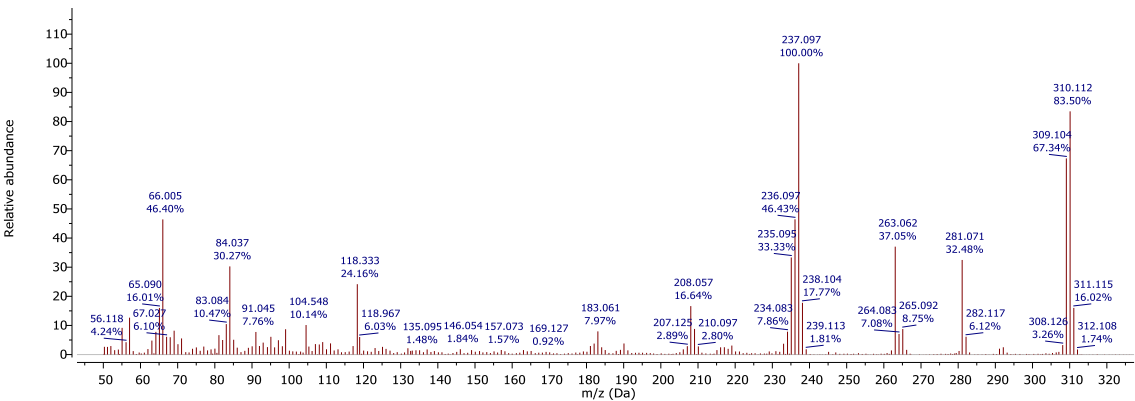




^{13}C - ^{19}F couplings in ^{13}C -NMR. Only coupled peaks have been represented to make it easier to understand.

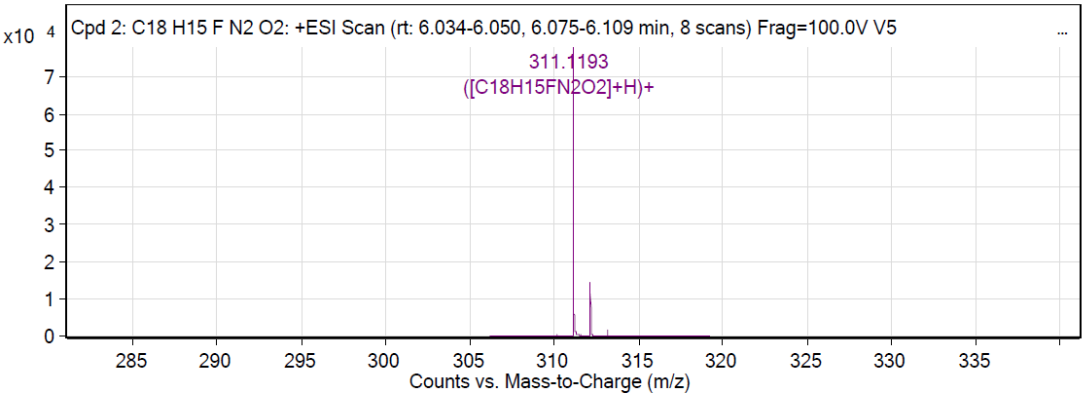


EI MS (70eV)



ESI-QTOF (positive ionization)

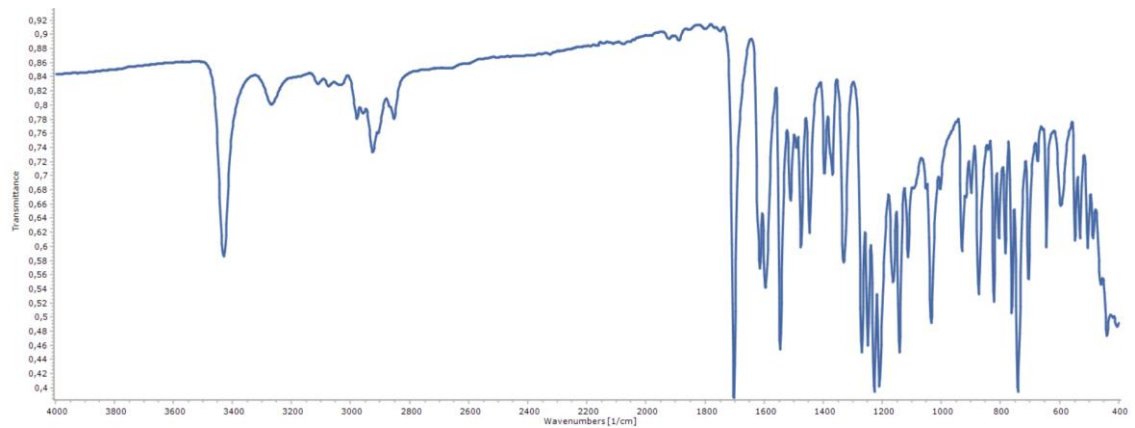
MS Zoomed Spectrum



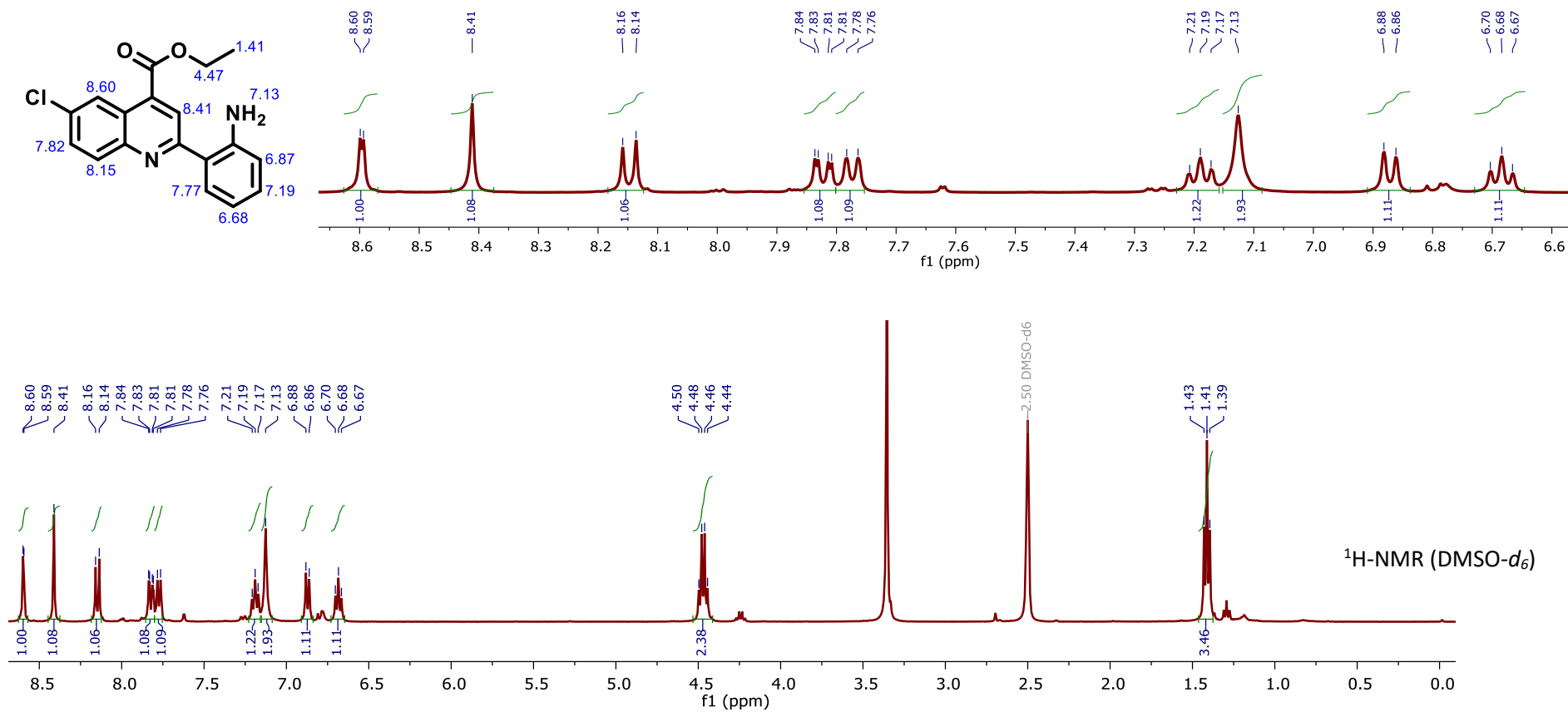
MS Spectrum Peak List

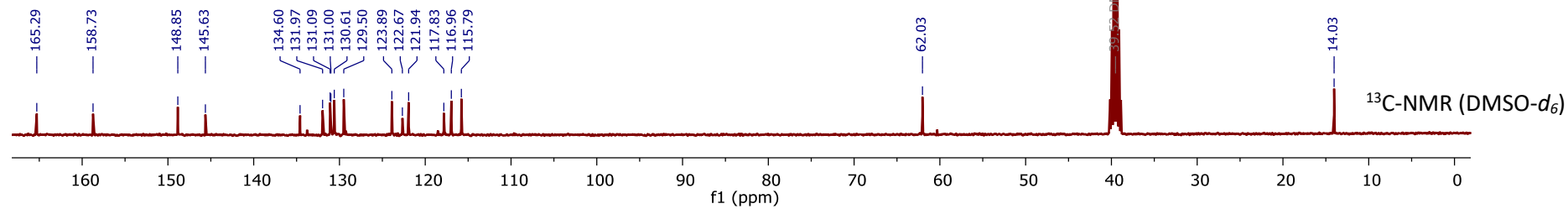
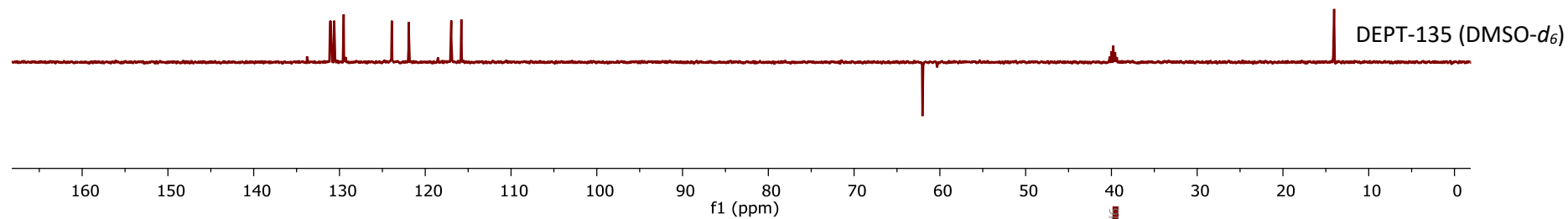
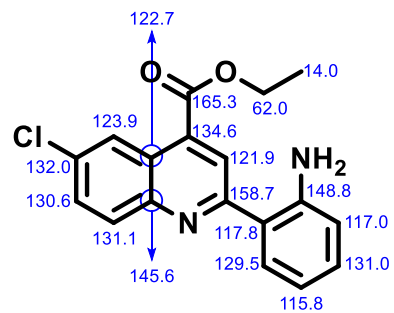
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
311.1193	311.119	-0.76	1	78483.28	C18H15FN2O2	(M+H)+
312.1226	312.1222	-1.42	1	14394.33	C18H15FN2O2	(M+H)+
313.1259	313.125	-2.92	1	1625.32	C18H15FN2O2	(M+H)+
314.1284	314.1276	-2.51	1	147.62	C18H15FN2O2	(M+H)+

IR

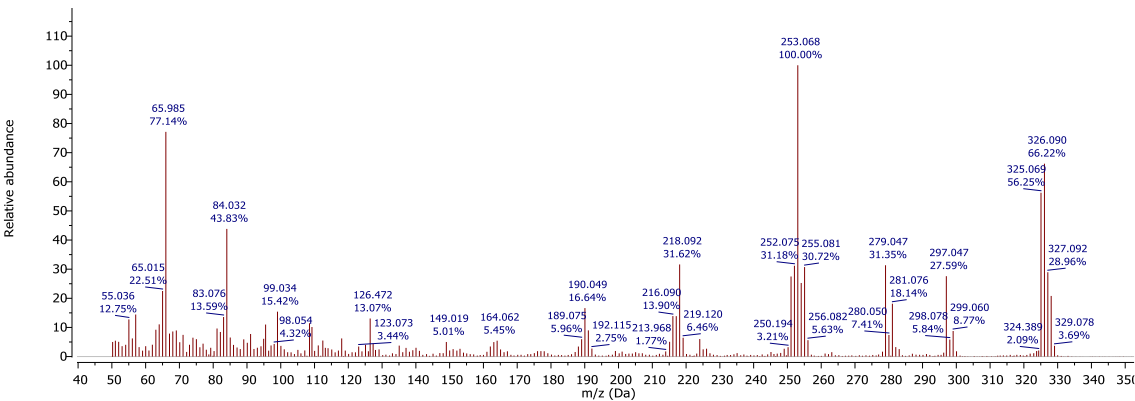


Compound 11



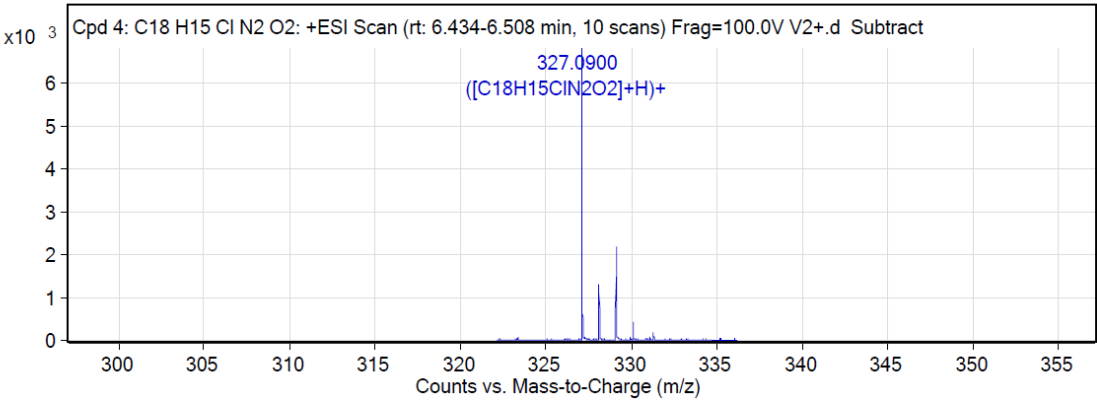


EI MS (70eV)



ESI-QTOF (positive ionization)

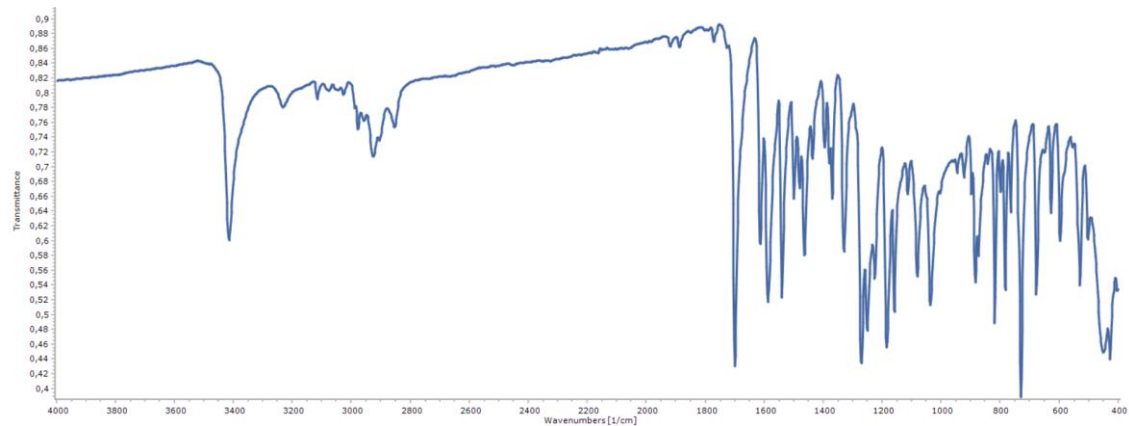
MS Zoomed Spectrum



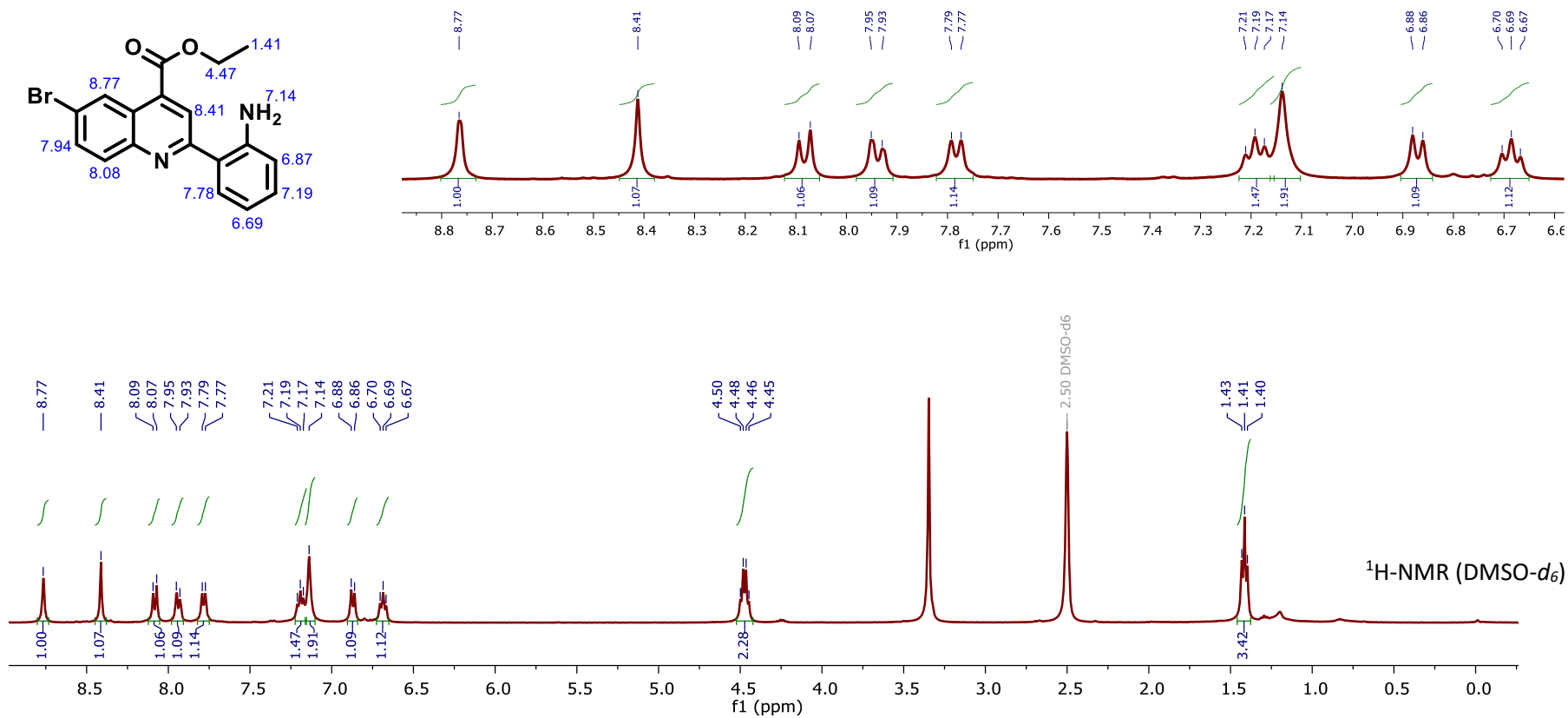
MS Spectrum Peak List

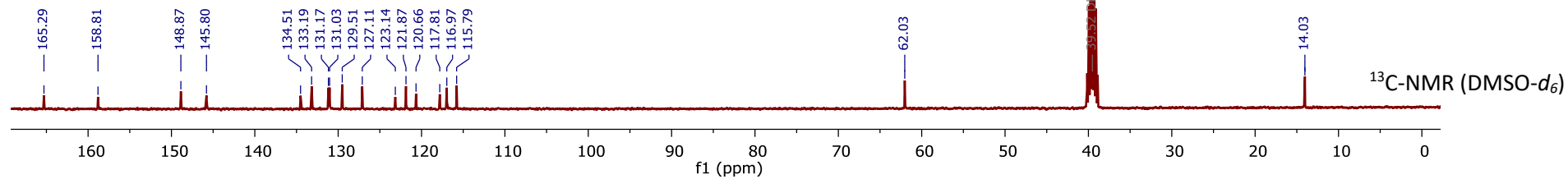
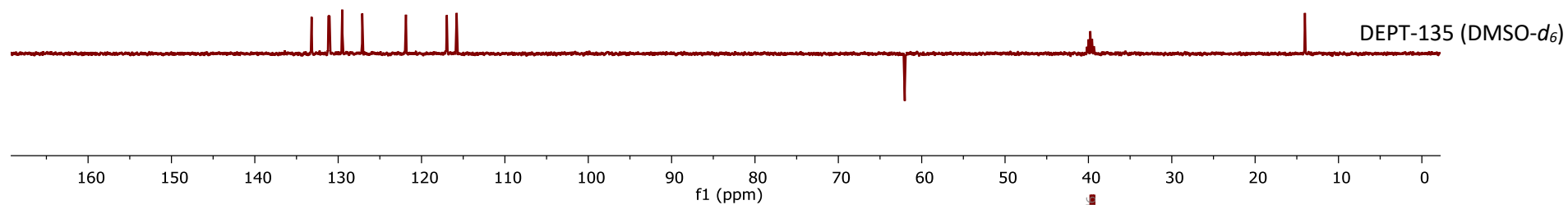
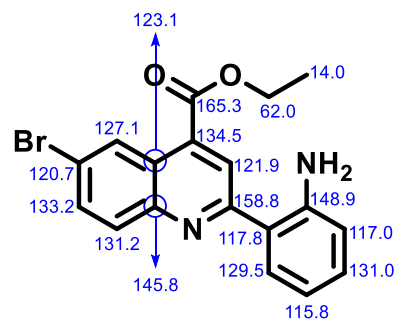
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
327.09	327.0895	-1.5	1	6856.84	C18H15ClN2O2	(M+H)+
328.0932	328.0926	-1.61	1	1321.54	C18H15ClN2O2	(M+H)+
329.0875	329.0872	-1.2	1	2242.85	C18H15ClN2O2	(M+H)+
330.0897	330.0899	0.77	1	429.65	C18H15ClN2O2	(M+H)+
331.0925	331.0926	0.39	1	72.54	C18H15ClN2O2	(M+H)+

IR

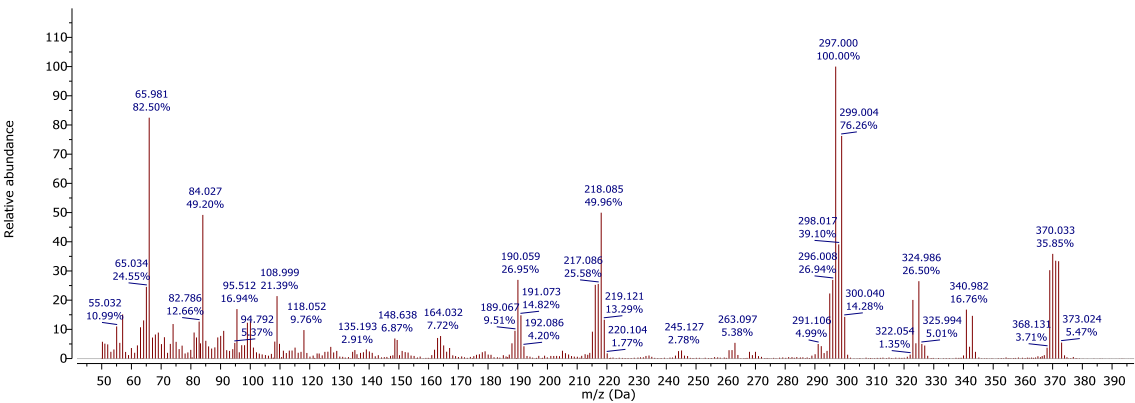


Compound 12



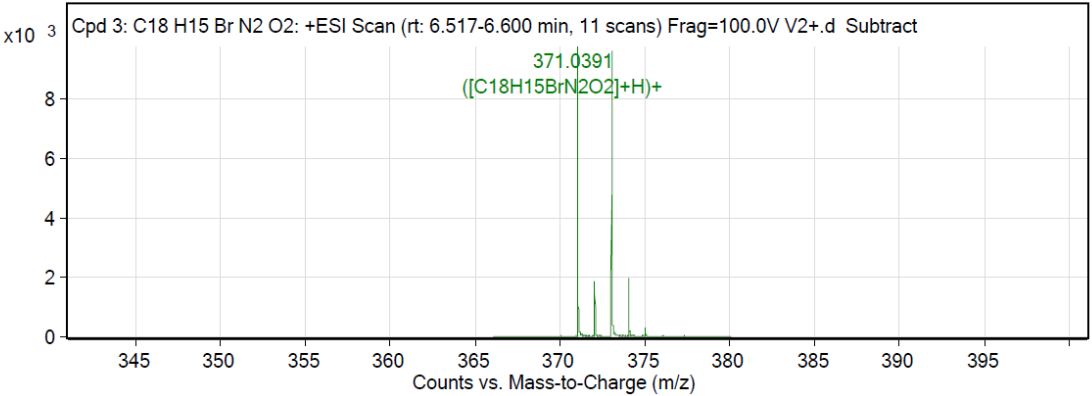


EI MS (70eV)



ESI-QTOF (positive ionization)

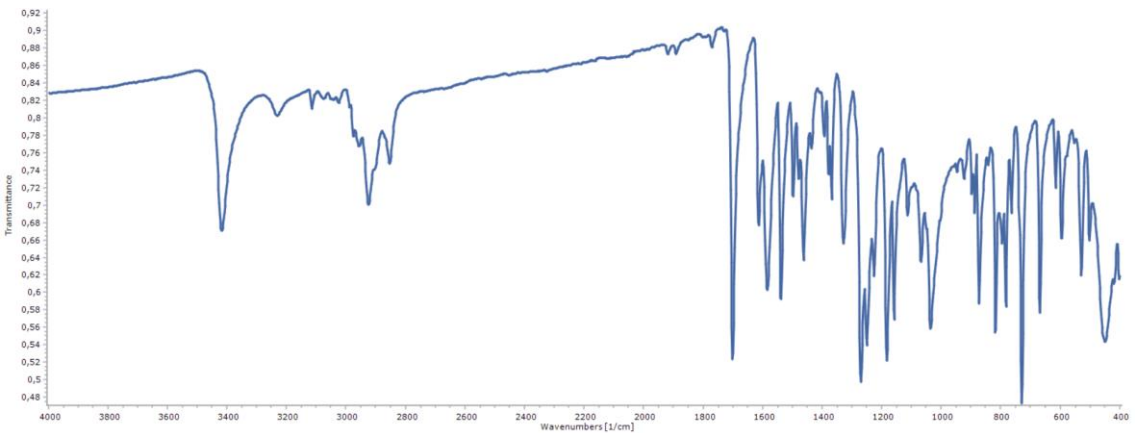
MS Zoomed Spectrum



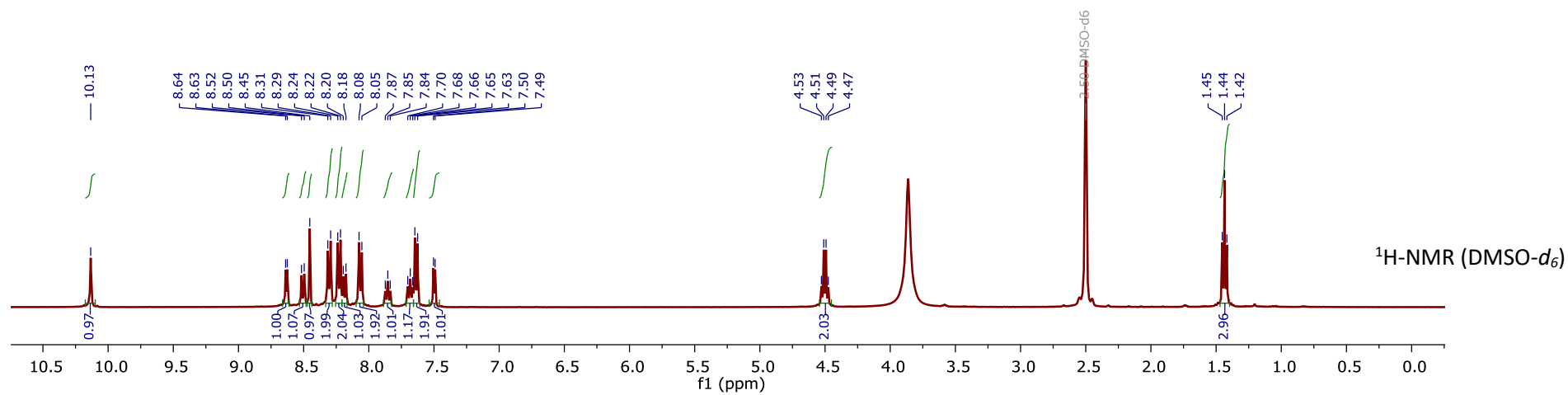
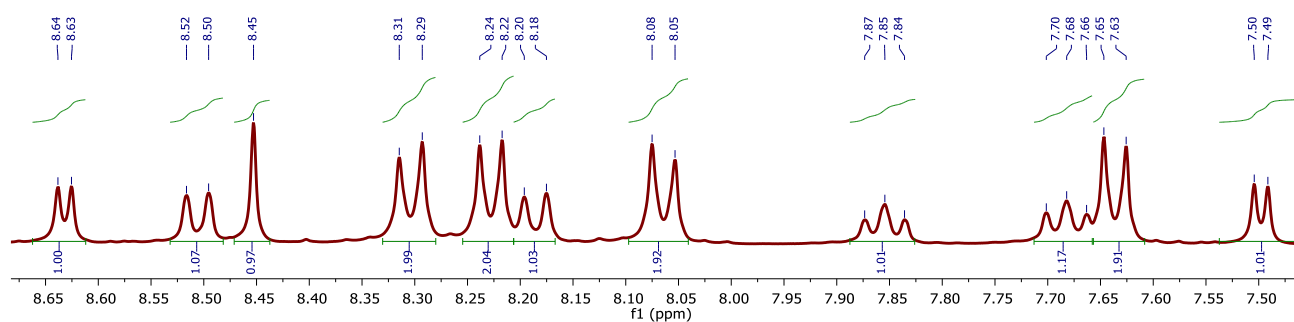
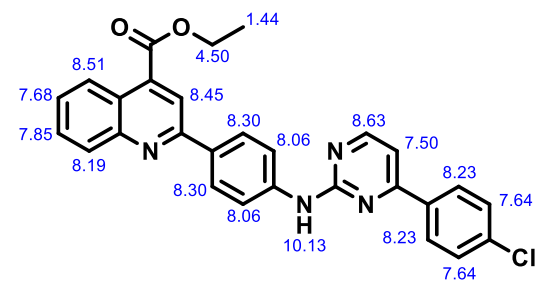
MS Spectrum Peak List

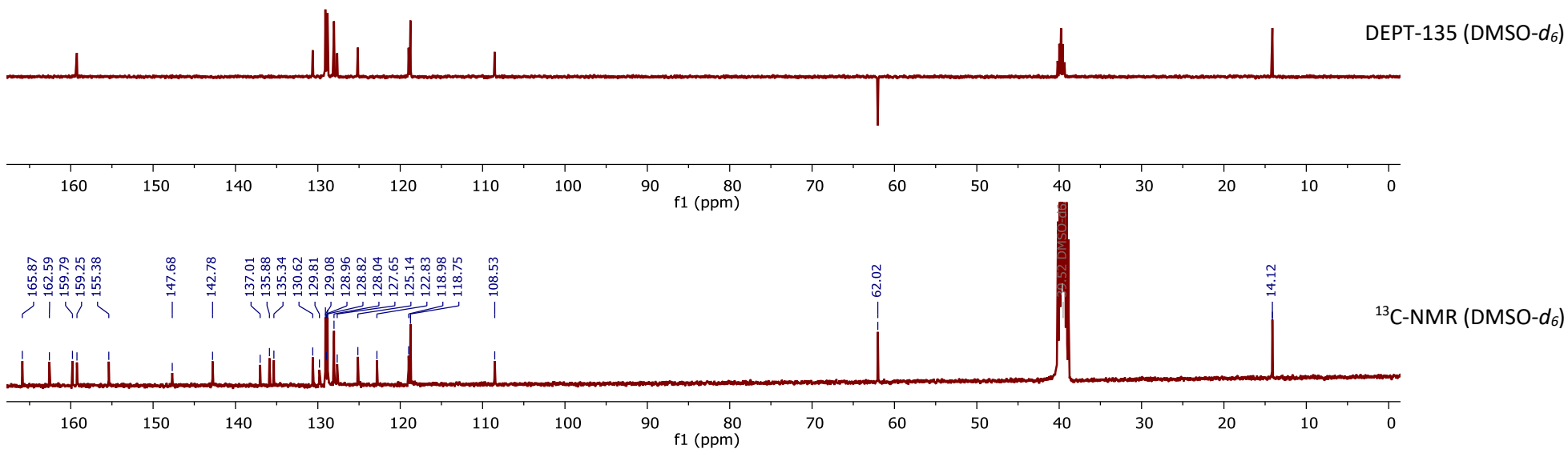
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
371.0391	371.039	-0.44	1	9931.9	C ₁₈ H ₁₅ BrN ₂ O ₂	(M+H)+
372.0419	372.0421	0.5	1	1882.26	C ₁₈ H ₁₅ BrN ₂ O ₂	(M+H)+
373.0372	373.0371	-0.19	1	9657.04	C ₁₈ H ₁₅ BrN ₂ O ₂	(M+H)+
374.0401	374.0402	0.14	1	1987.29	C ₁₈ H ₁₅ BrN ₂ O ₂	(M+H)+
375.0419	375.0429	2.63	1	289.29	C ₁₈ H ₁₅ BrN ₂ O ₂	(M+H)+

IR

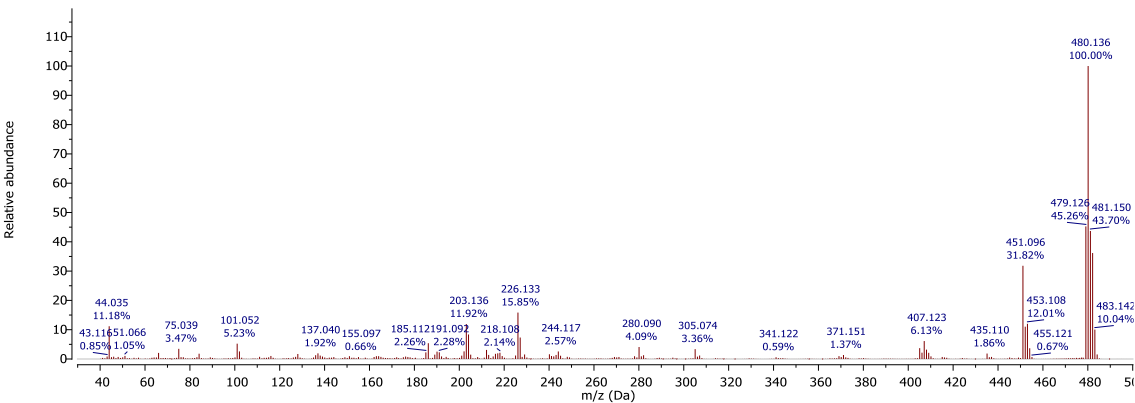


Compound 13a



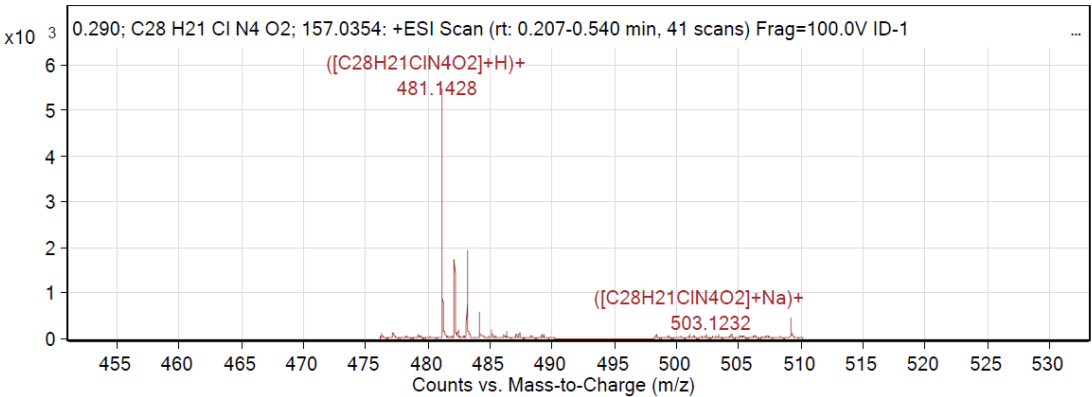


EI MS (70eV)



ESI-QTOF (positive ionization)

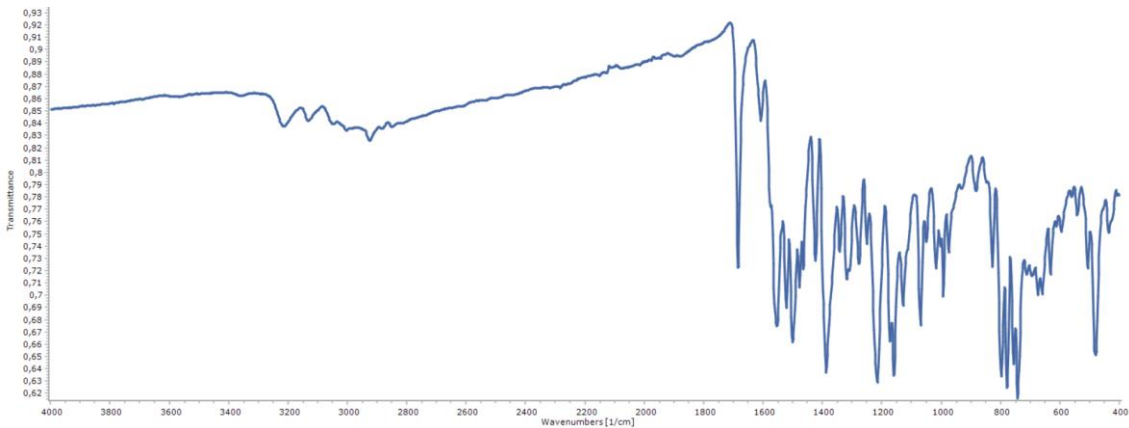
MS Zoomed Spectrum



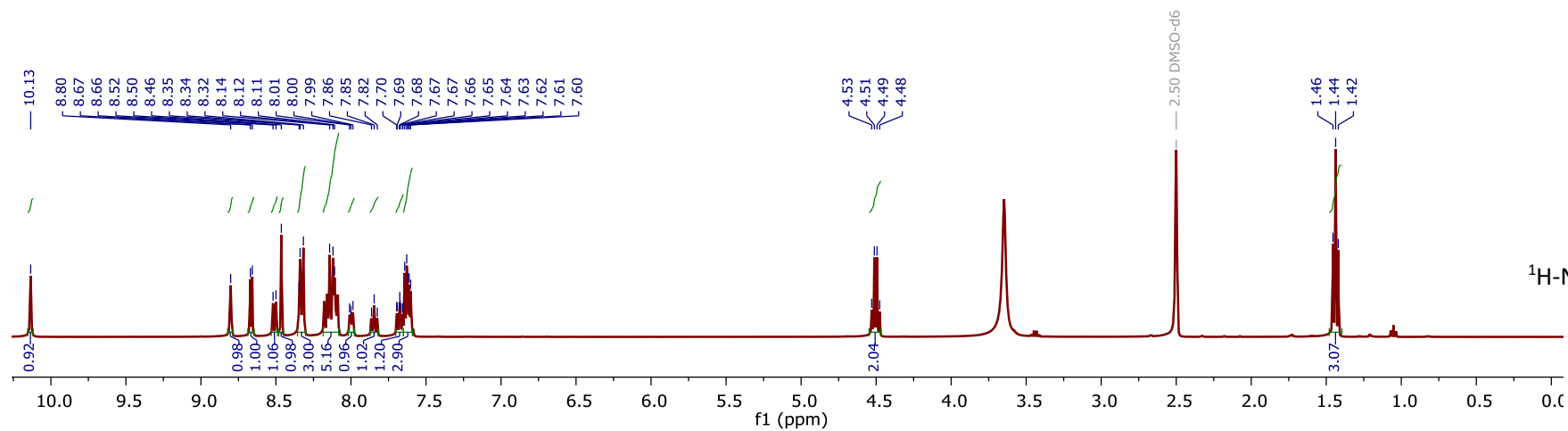
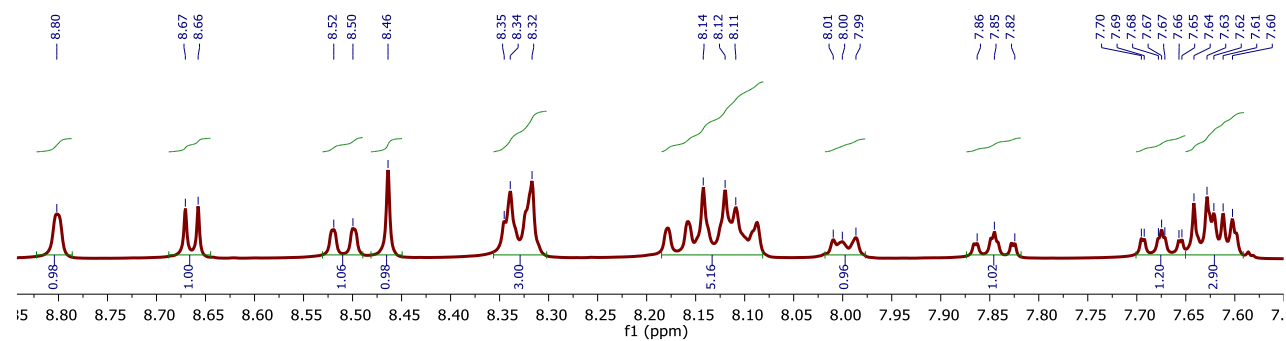
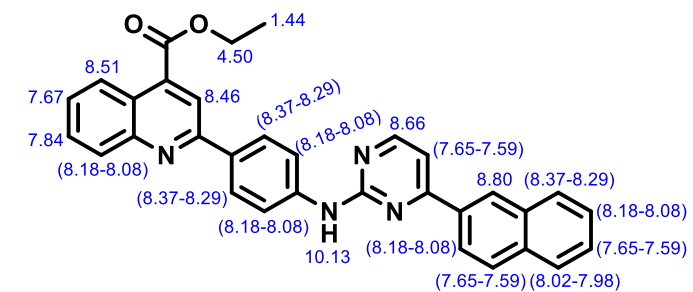
MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
481.1428	481.1426	-0.45	1	5473.86	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H) ⁺
482.1467	482.1457	-2.2	1	1771.85	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H) ⁺
483.1418	483.1409	-1.88	1	1951.64	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H) ⁺
484.1443	484.1432	-2.15	1	578.14	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H) ⁺
485.1449	485.1459	2.2	1	147.64	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H) ⁺
503.1232	503.1245	2.7	1	73.82	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+Na) ⁺
504.1162	504.1276	22.55	1	43.03	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+Na) ⁺
505.1281	505.1229	-10.27	1	58.35	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+Na) ⁺

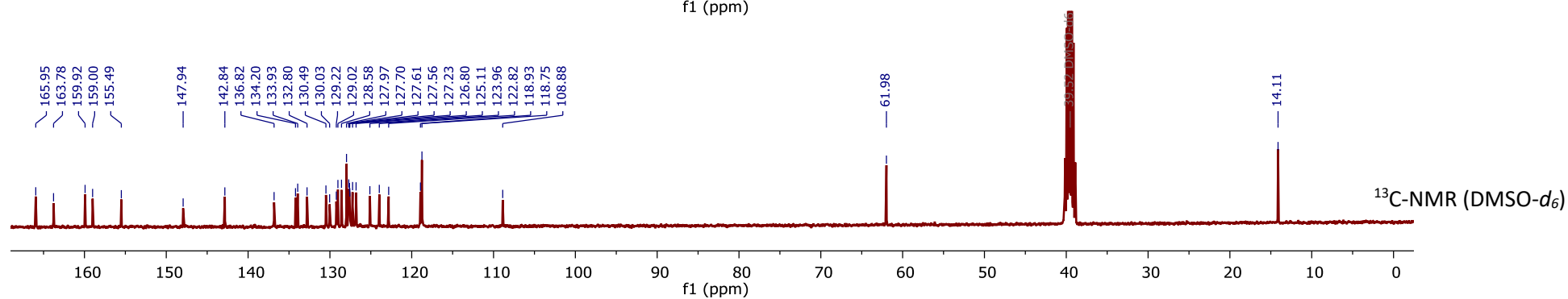
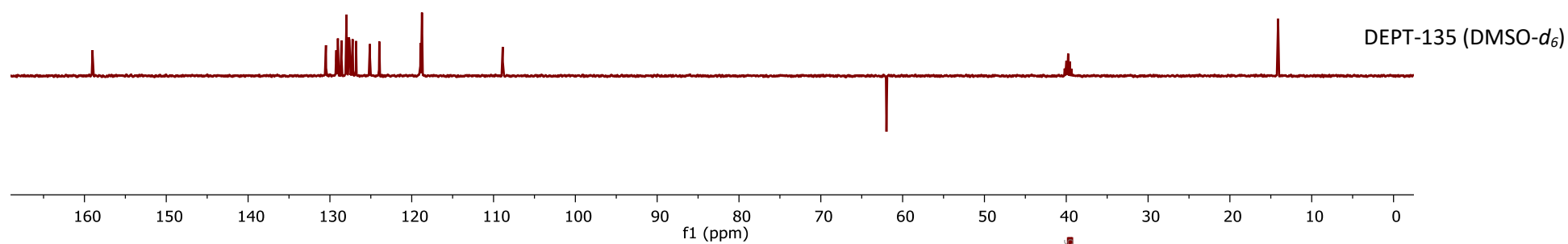
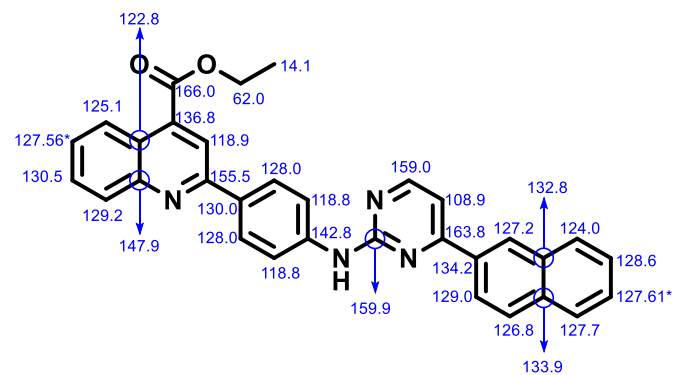
IR



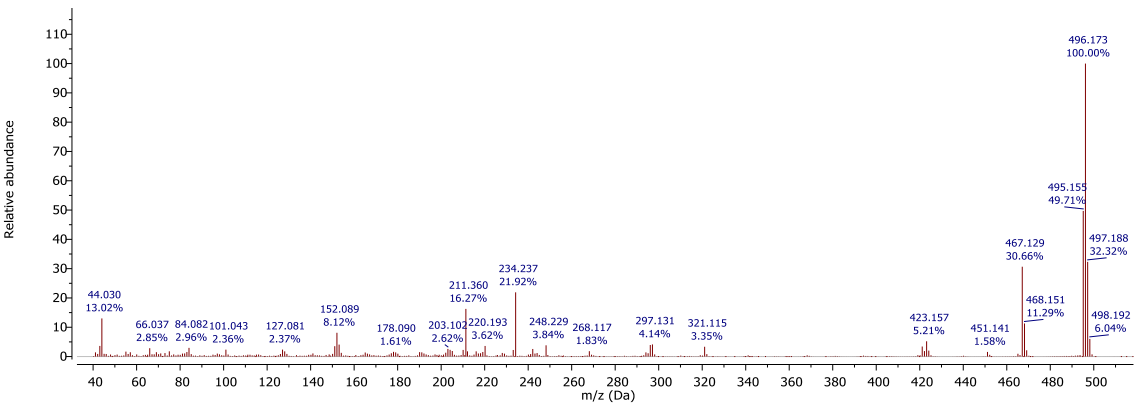
Compound **13b**



¹H-NMR (DMSO-*d*₆)

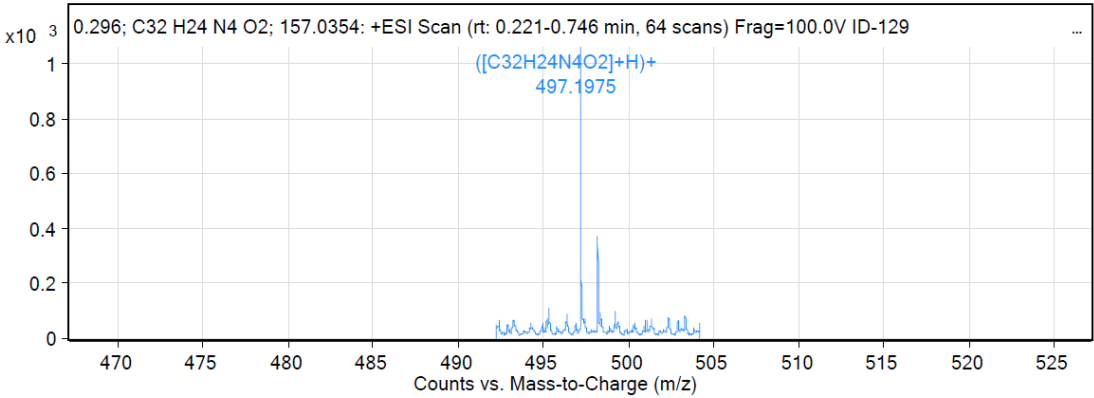


EI MS (70eV)



ESI-QTOF (positive ionization)

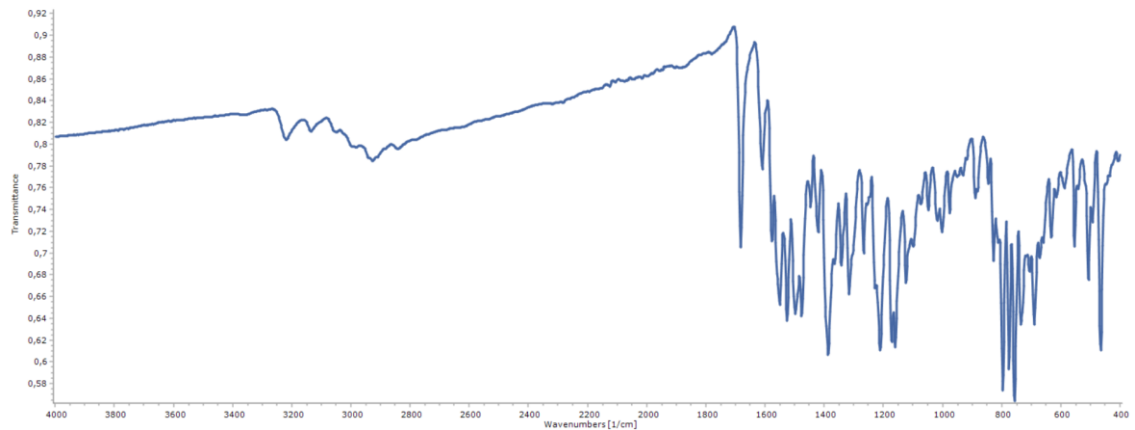
MS Zoomed Spectrum



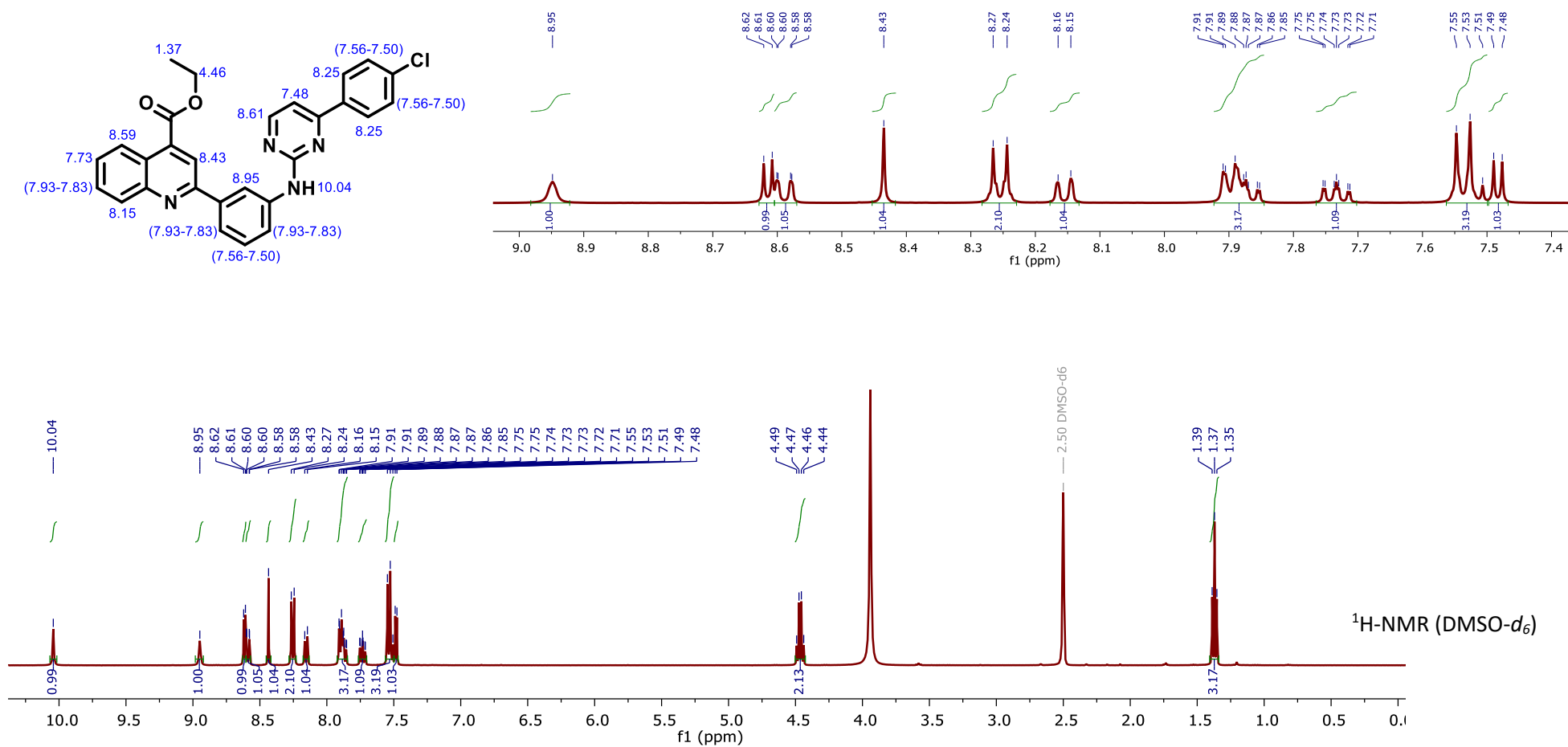
MS Spectrum Peak List

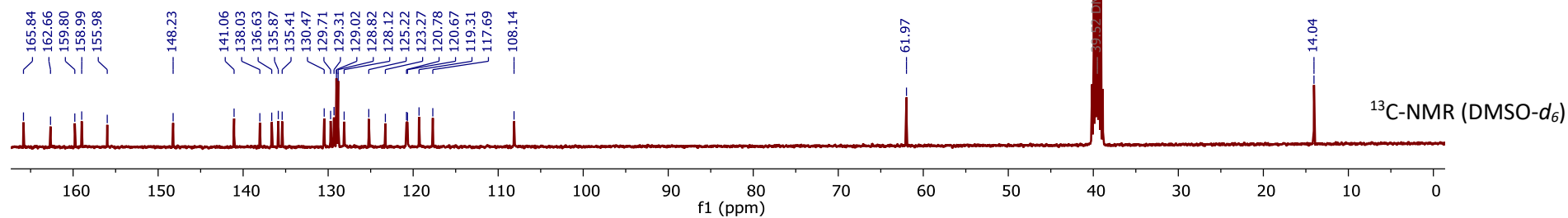
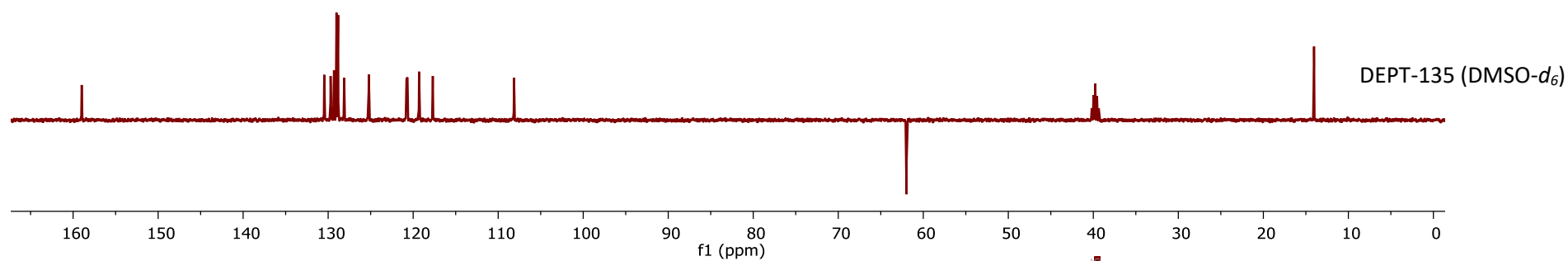
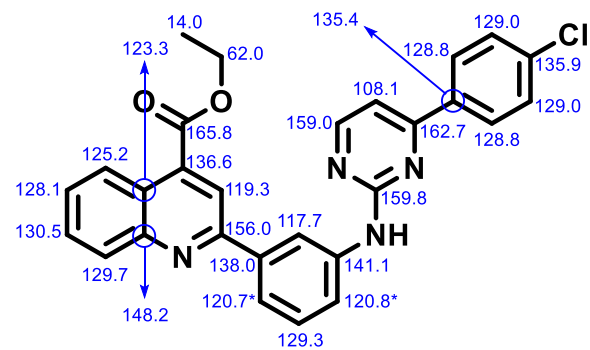
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
497.1975	497.1972	-0.5	1	1060.32	C32H24N4O2	(M+H)+
498.2009	498.2003	-1.09	1	374.05	C32H24N4O2	(M+H)+
499.2054	499.2033	-4.16	1	96.6	C32H24N4O2	(M+H)+

IR

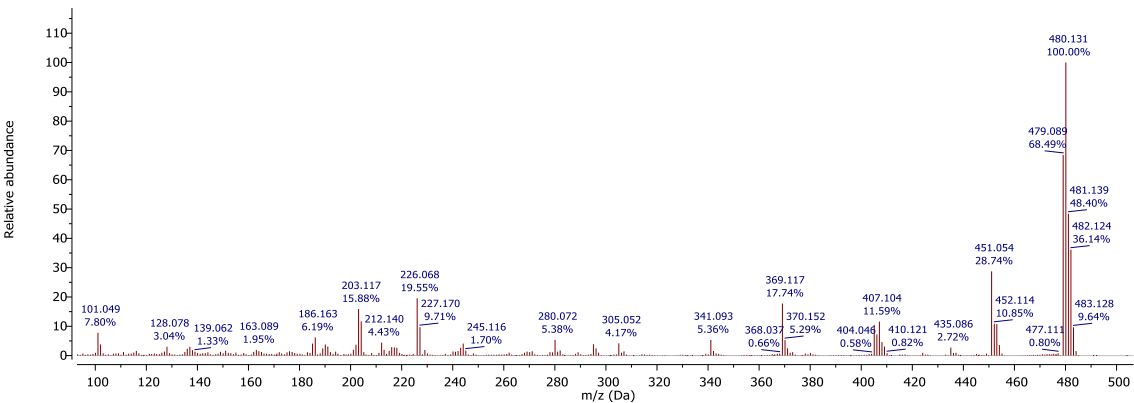


Compound **14a**



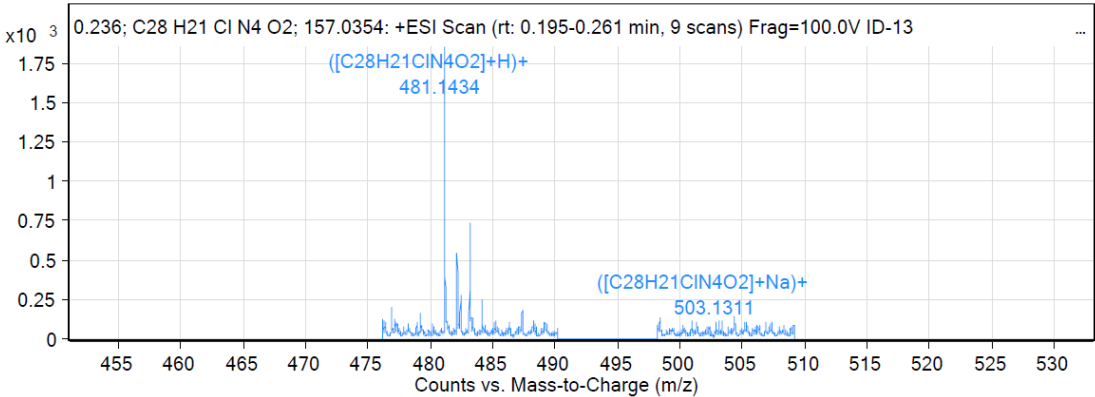


EI MS (70eV)



ESI-QTOF (positive ionization)

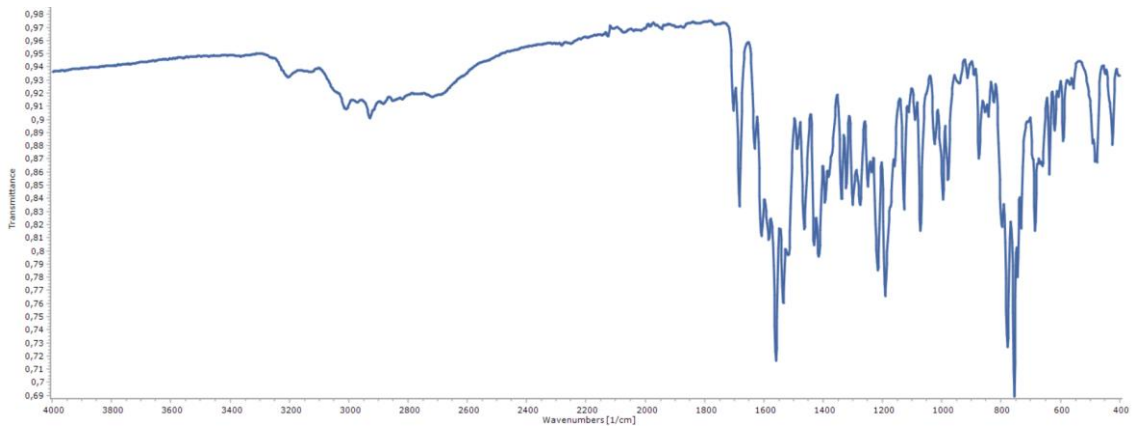
MS Zoomed Spectrum



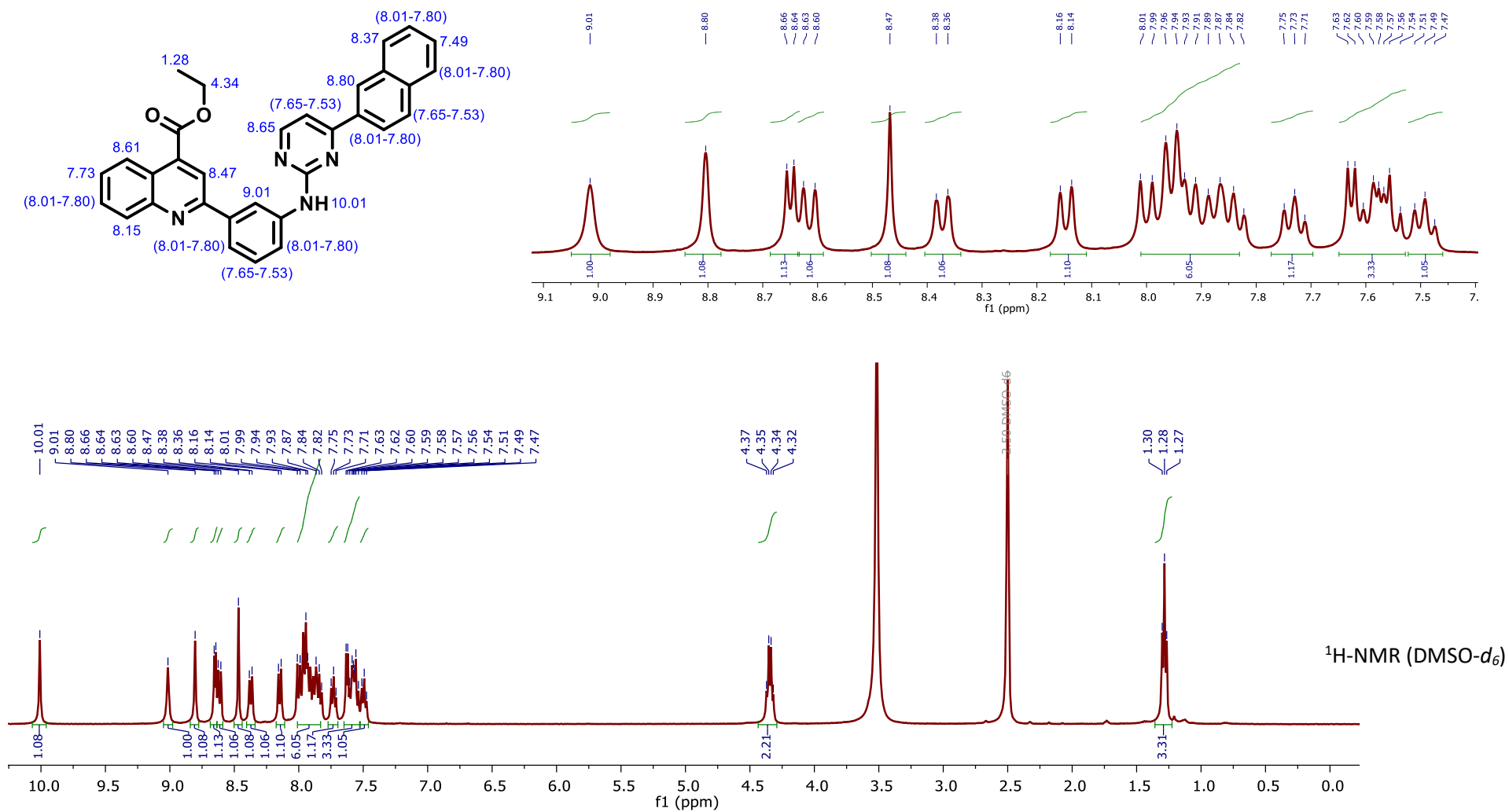
MS Spectrum Peak List

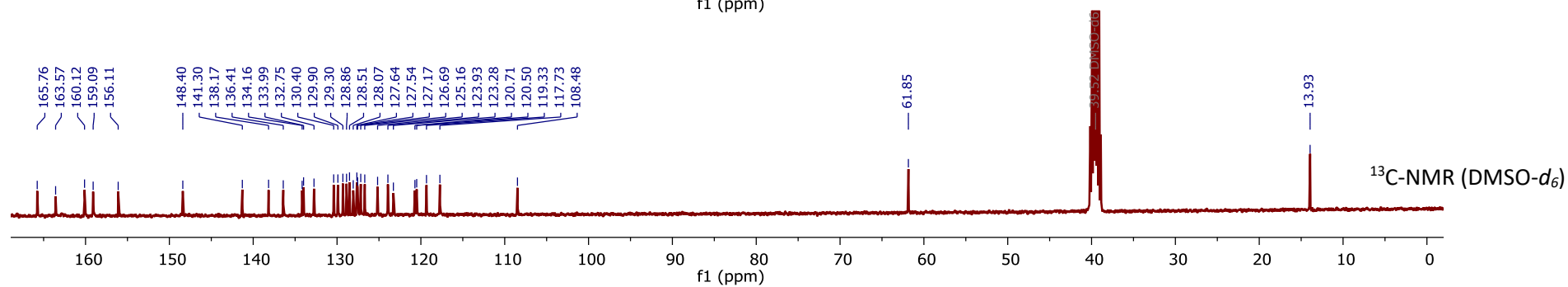
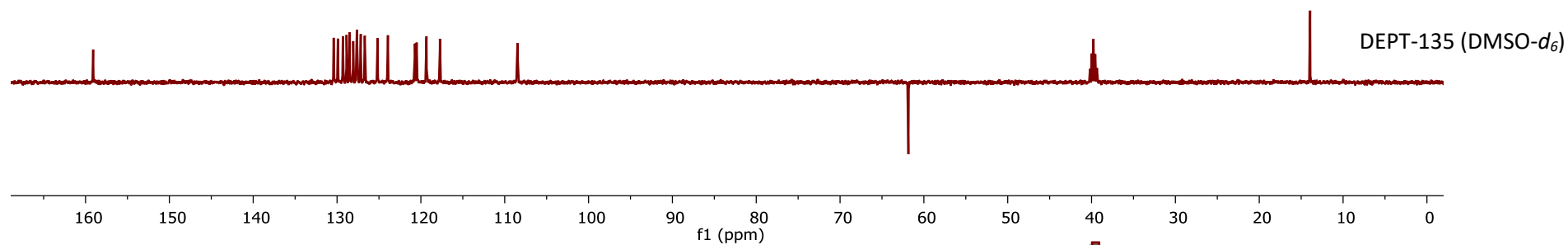
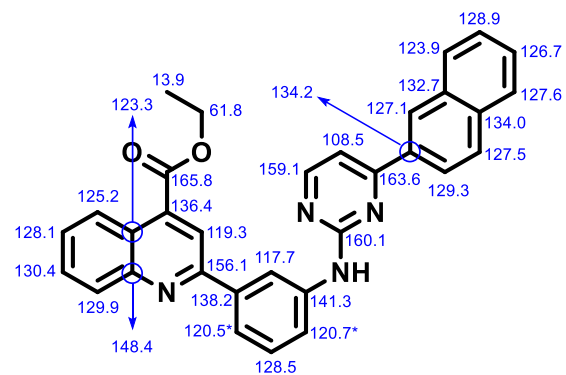
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
481.1434	481.1426	-1.65	1	1858.02	C28H21ClN4O2	(M+H)+
482.1468	482.1457	-2.28	1	550.61	C28H21ClN4O2	(M+H)+
483.1417	483.1409	-1.51	1	743.43	C28H21ClN4O2	(M+H)+
484.1446	484.1432	-2.87	1	248.57	C28H21ClN4O2	(M+H)+
485.1464	485.1459	-0.93	1	79.29	C28H21ClN4O2	(M+H)+
503.1311	503.1245	-13.12	1	117.9	C28H21ClN4O2	(M+Na)+
504.1385	504.1276	-21.55	1	65.09	C28H21ClN4O2	(M+Na)+

IR

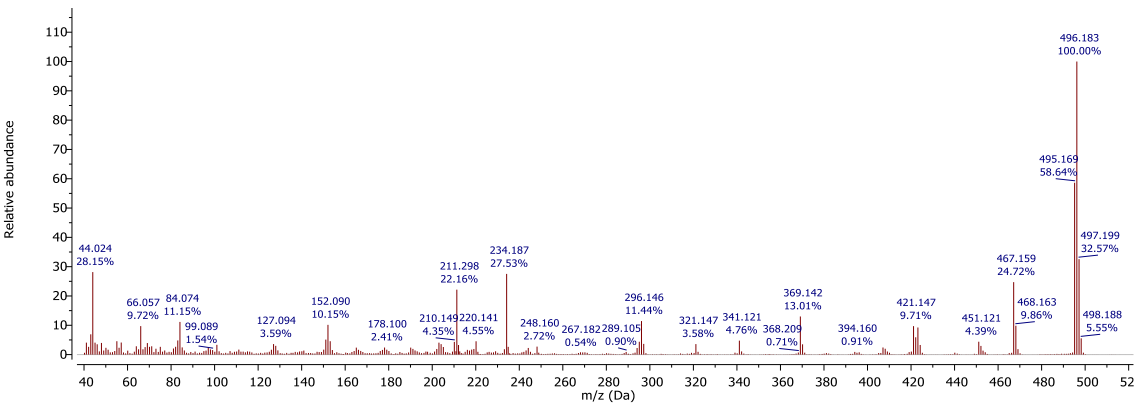


Compound **14b**



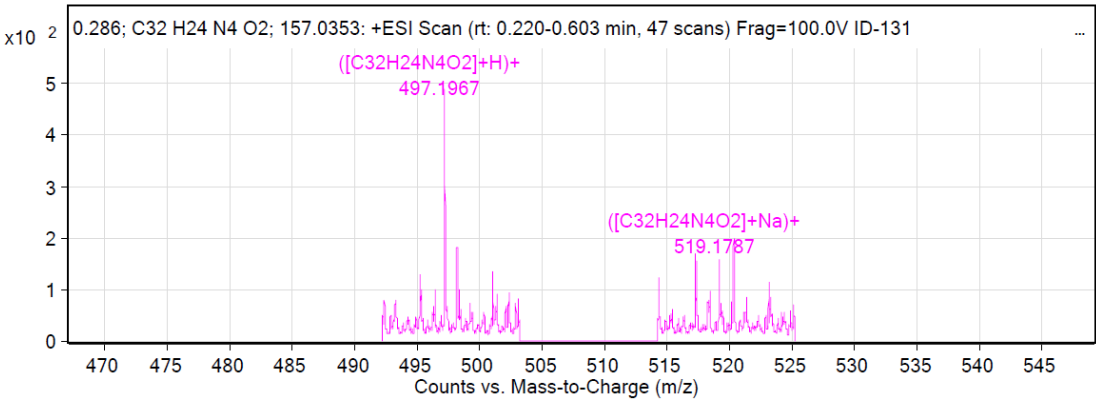


EI MS (70eV)



ESI-QTOF (positive ionization)

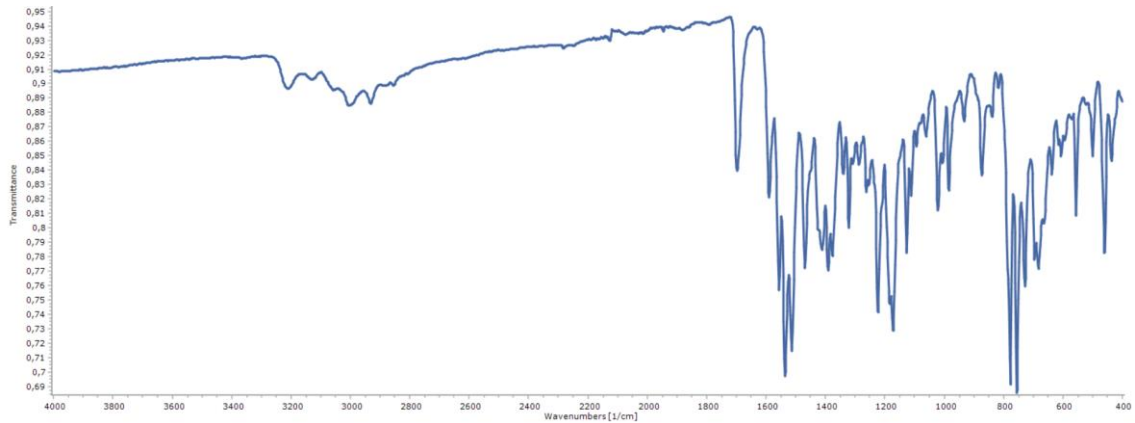
MS Zoomed Spectrum



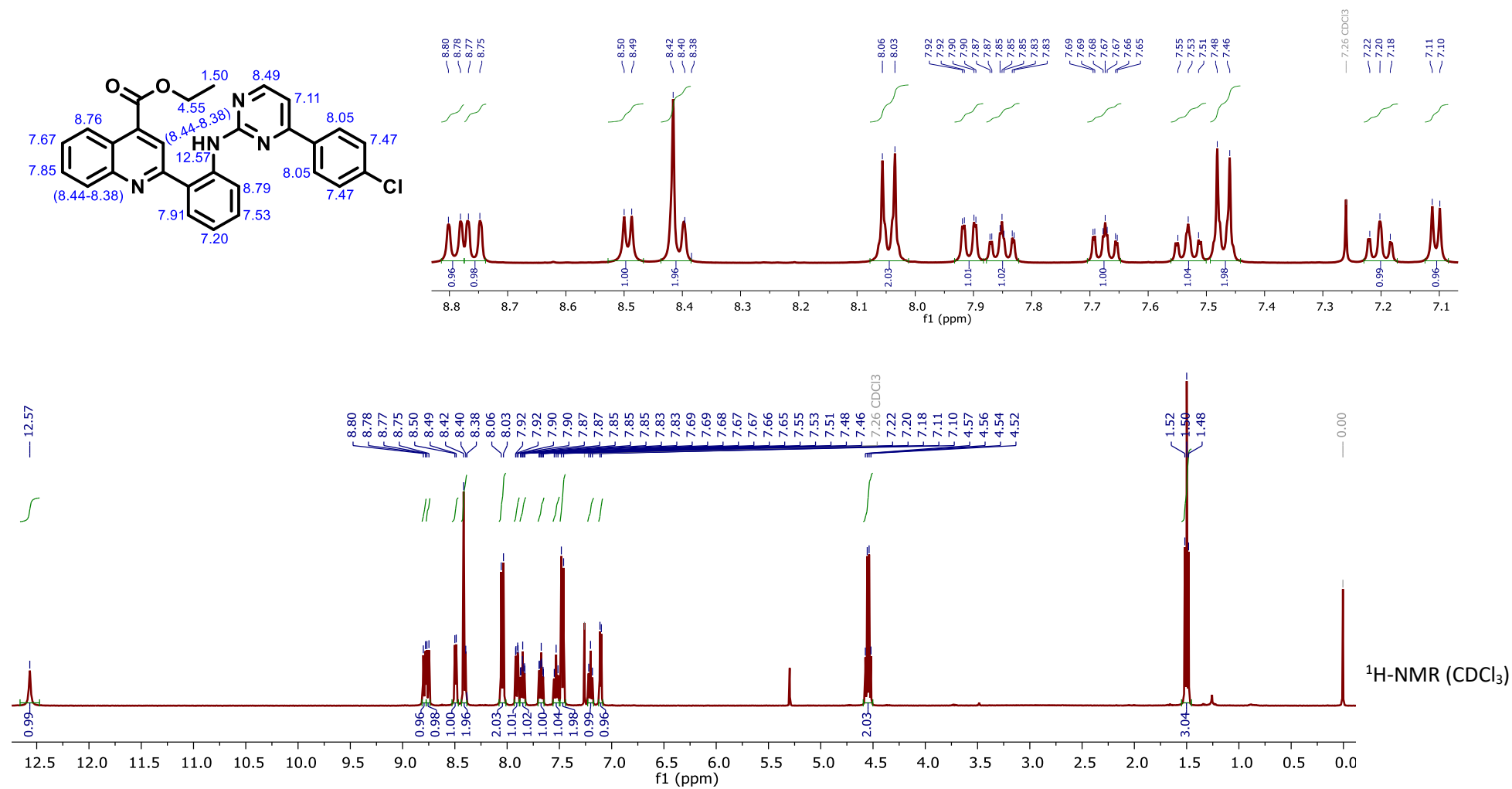
MS Spectrum Peak List

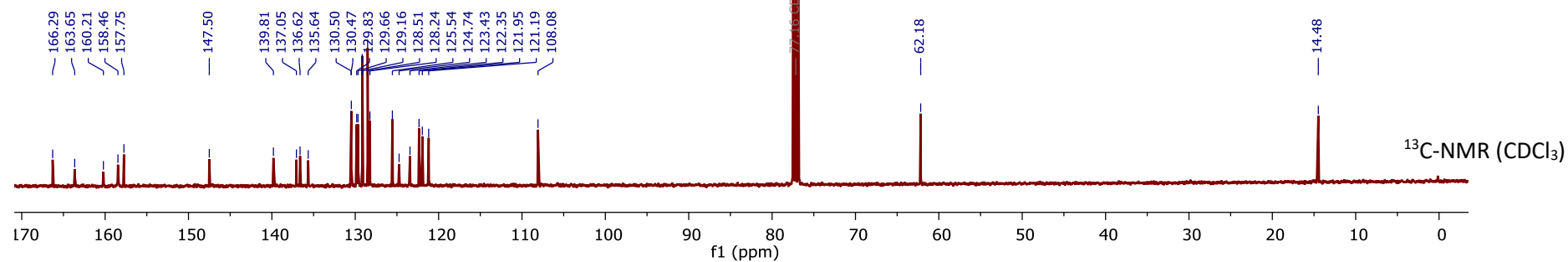
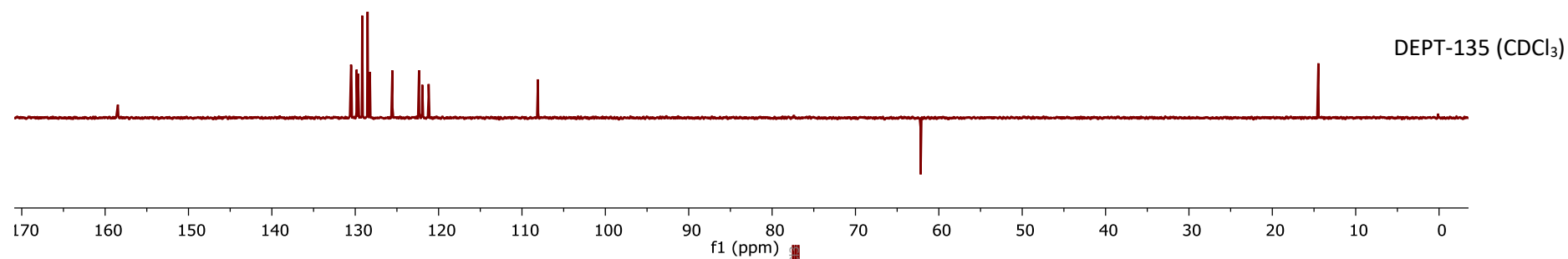
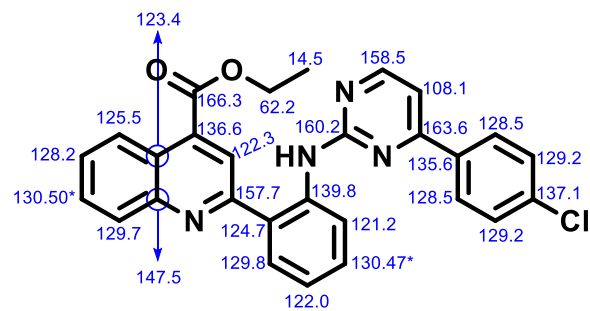
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
497.1967	497.1972	0.96	1	490.44	C32H24N4O2	(M+H)+
498.202	498.2003	-3.42	1	184.71	C32H24N4O2	(M+H)+
519.1787	519.1791	0.77	1	157.58	C32H24N4O2	(M+Na)+
520.1797	520.1823	4.9	1	75.74	C32H24N4O2	(M+Na)+

IR

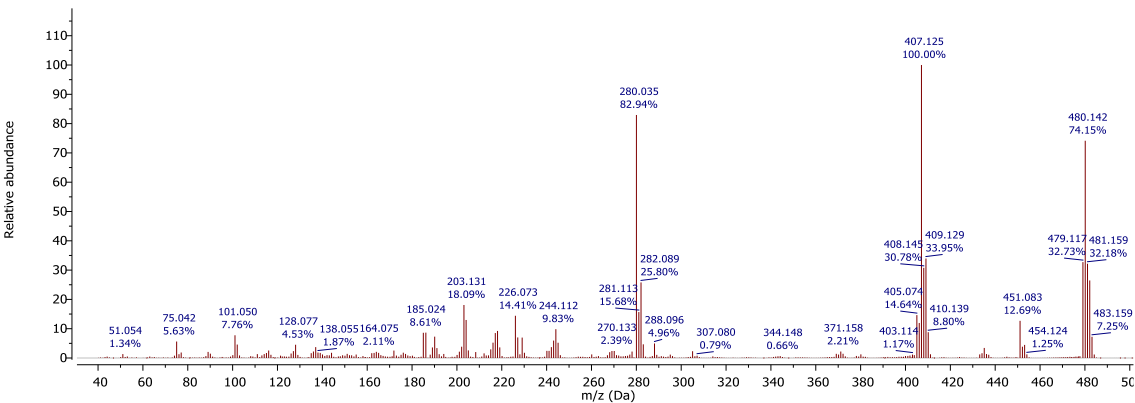


Compound 15a



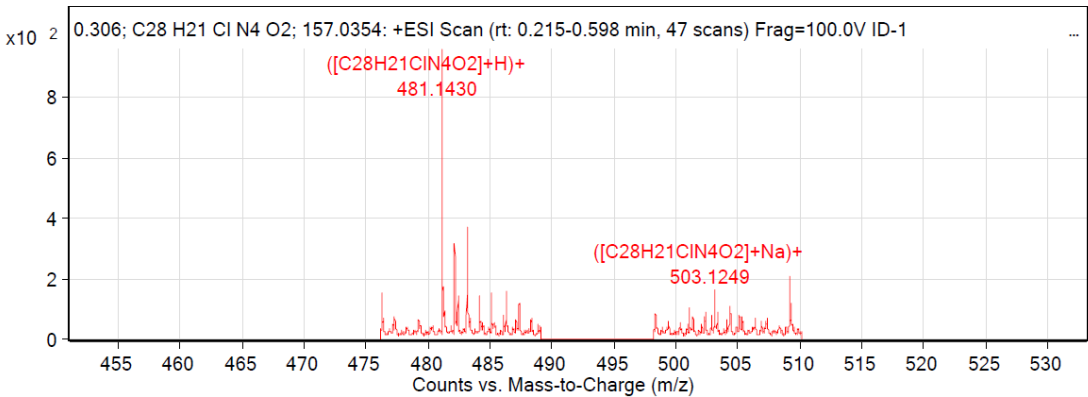


EI MS (70eV)



ESI-QTOF (positive ionization)

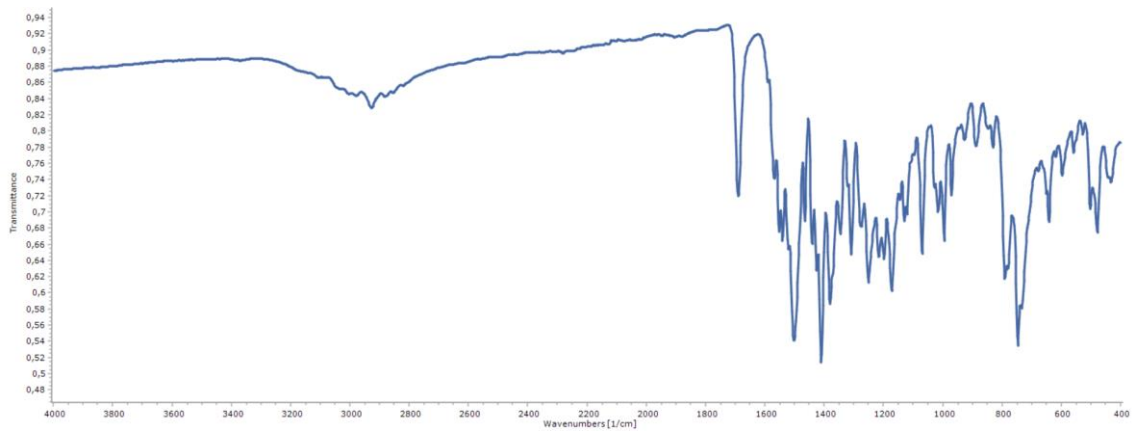
MS Zoomed Spectrum



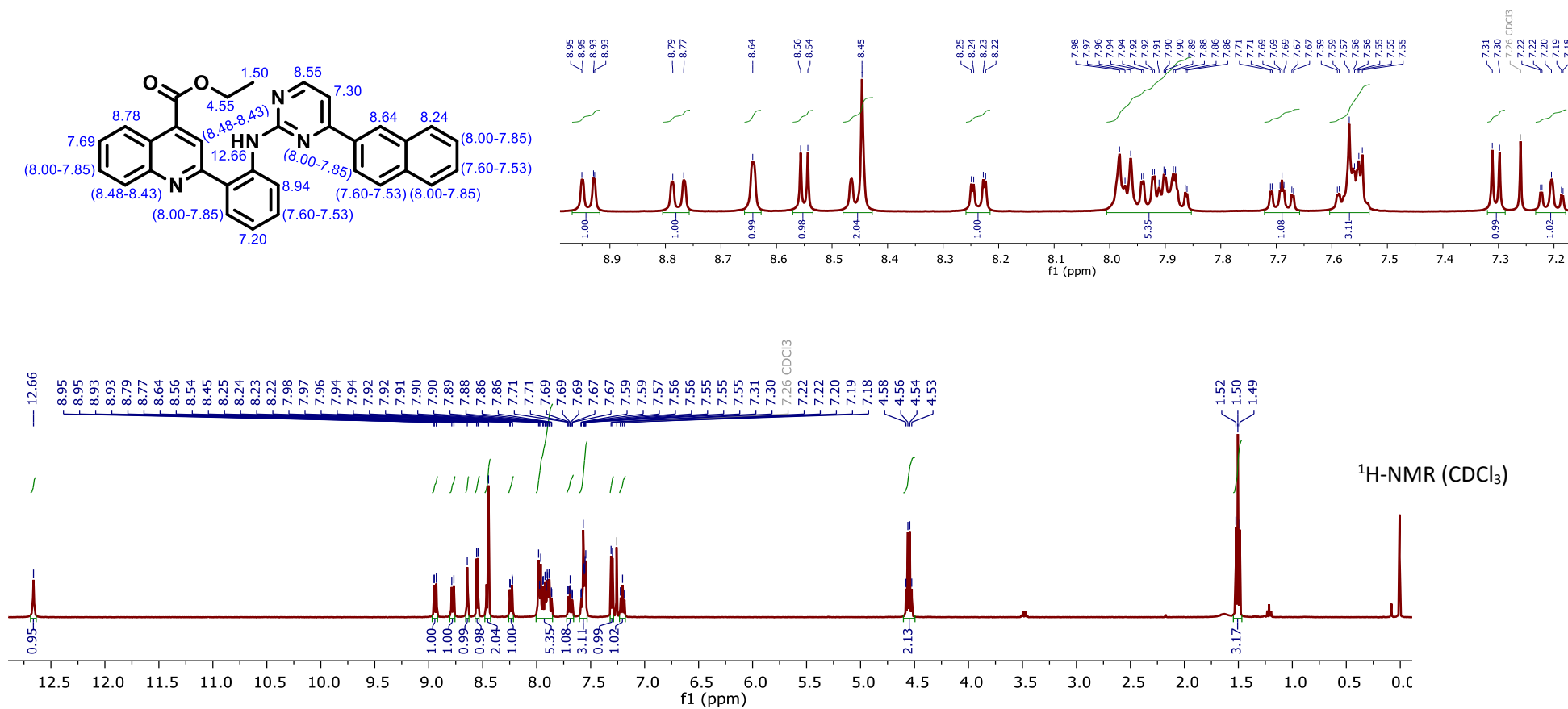
MS Spectrum Peak List

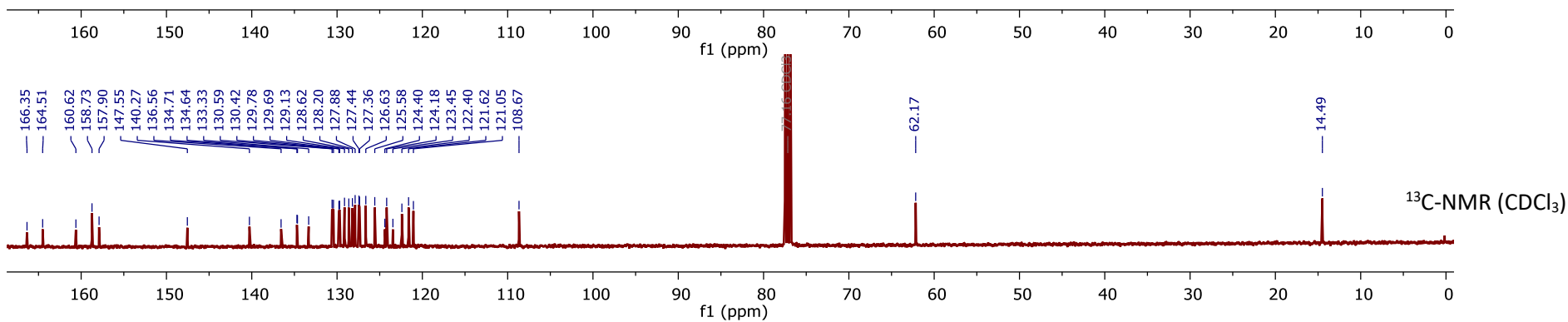
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
481.143	481.1426	-0.86	1	958.46	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H) ⁺
482.1492	482.1457	-7.24	1	319.89	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H) ⁺
483.1421	483.1409	-2.53	1	372.52	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H) ⁺
484.1443	484.1432	-2.3	1	144.92	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H) ⁺
503.1249	503.1245	-0.83	1	162.5	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+Na) ⁺
504.1304	504.1276	-5.45	1	65.44	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+Na) ⁺
505.1271	505.1229	-8.34	1	78.57	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+Na) ⁺

IR

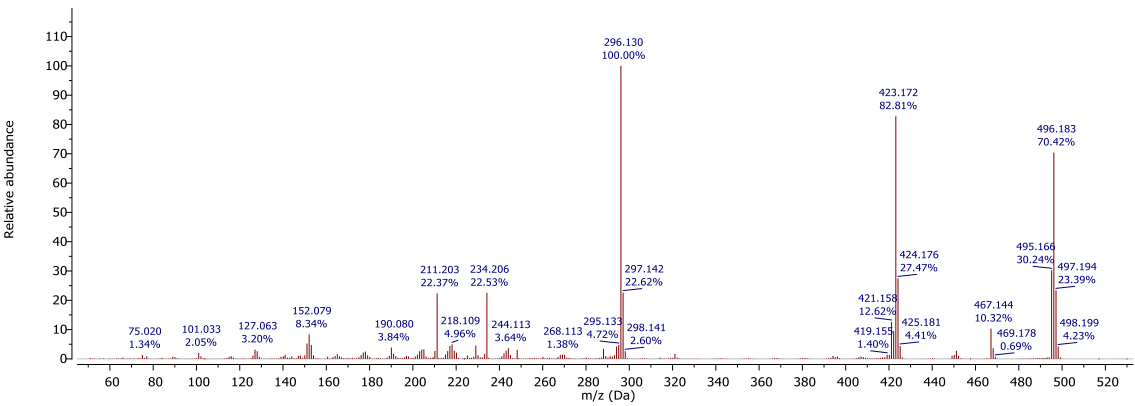


Compound 15b



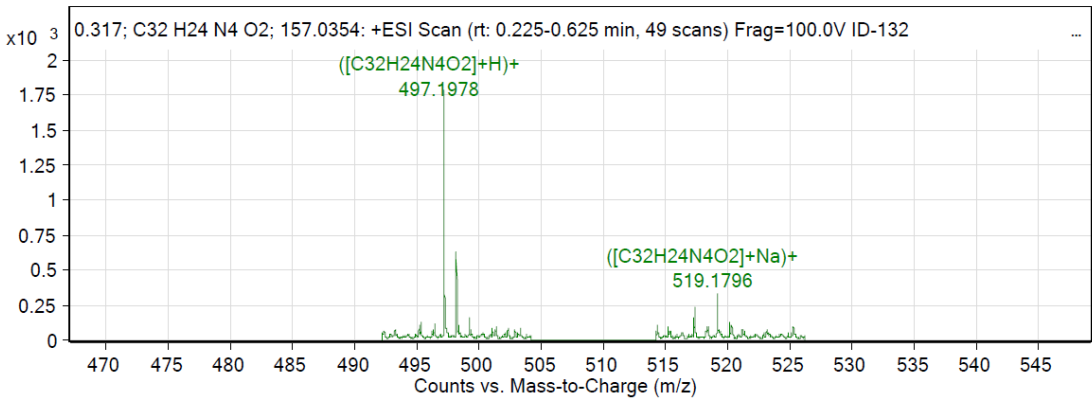


EI MS (70eV)



ESI-QTOF (positive ionization)

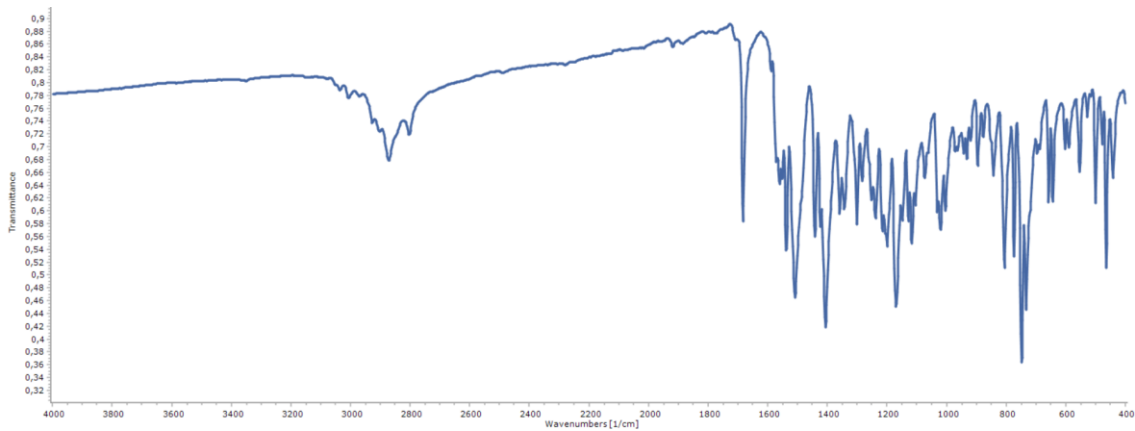
MS Zoomed Spectrum



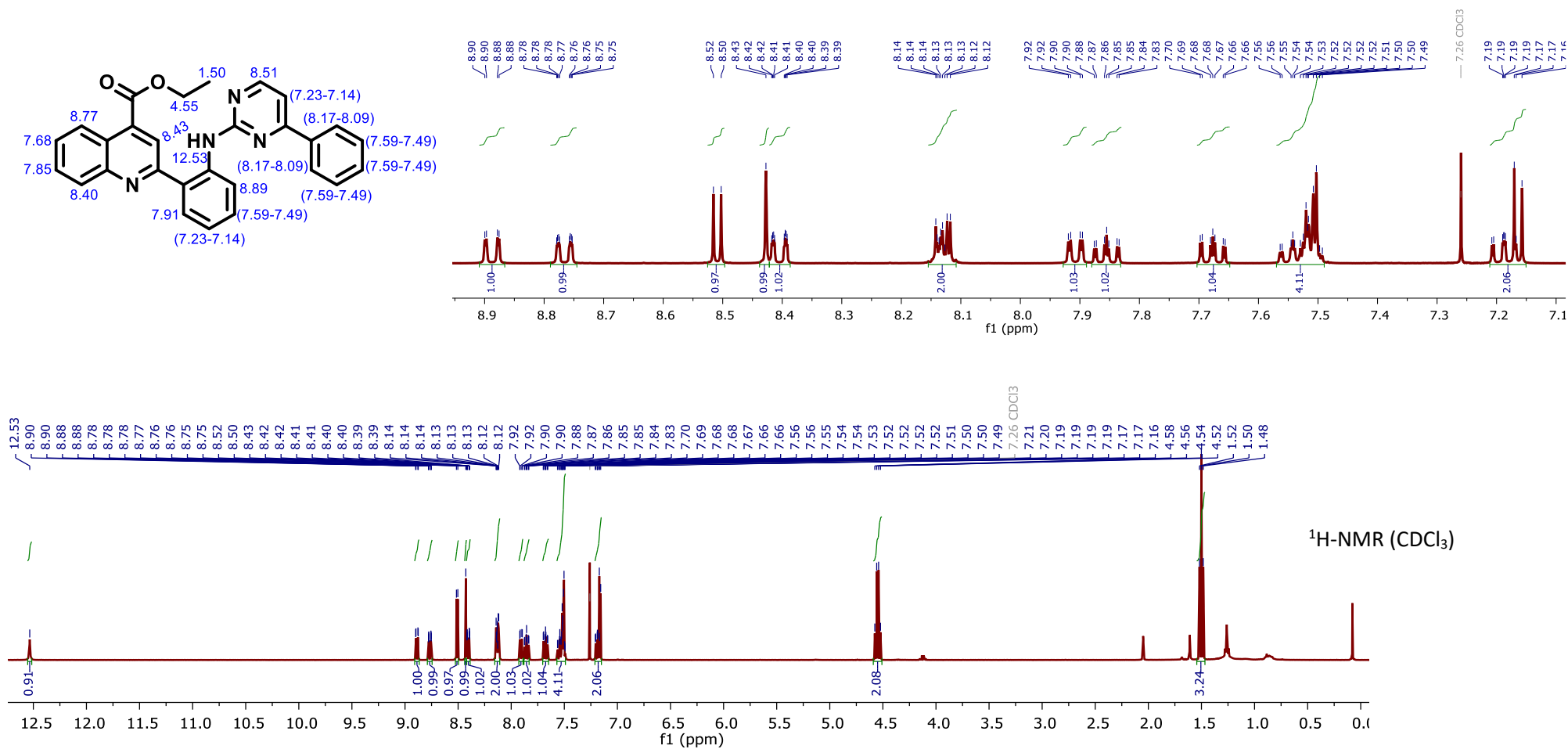
MS Spectrum Peak List

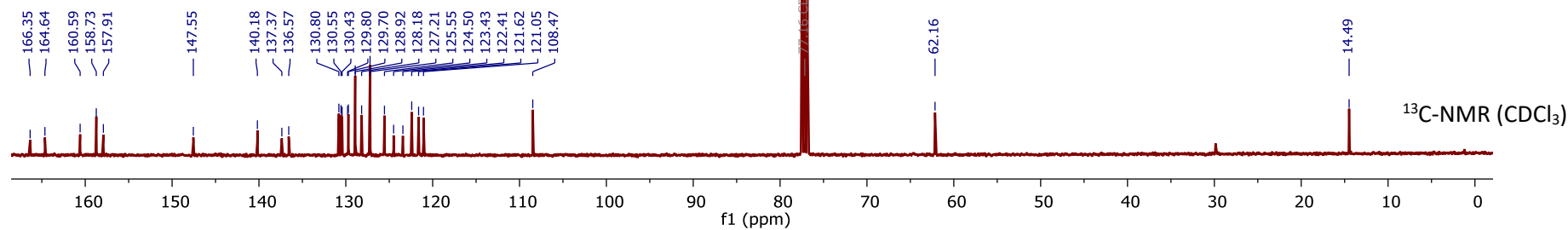
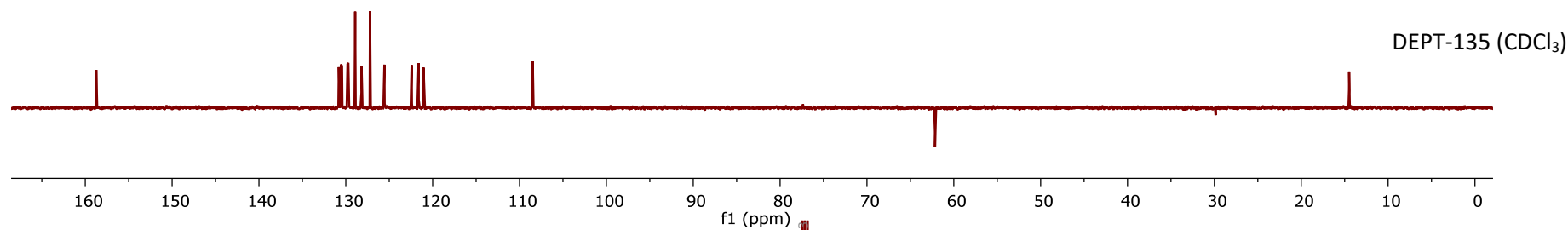
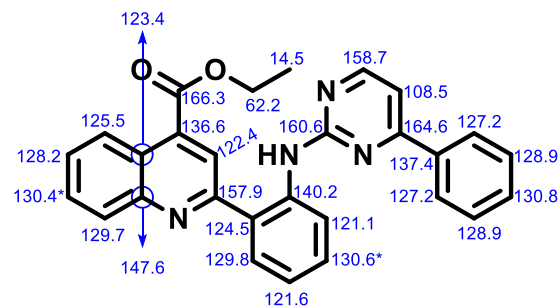
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
497.1978	497.1972	-1.27	1	1785.93	C32H24N4O2	(M+H)+
498.201	498.2003	-1.35	1	630.23	C32H24N4O2	(M+H)+
499.205	499.2033	-3.42	1	158.46	C32H24N4O2	(M+H)+
519.1796	519.1791	-0.93	1	333.82	C32H24N4O2	(M+Na)+
520.1818	520.1823	0.96	1	127.21	C32H24N4O2	(M+Na)+
521.1743	521.1853	21.01	1	73.03	C32H24N4O2	(M+Na)+

IR

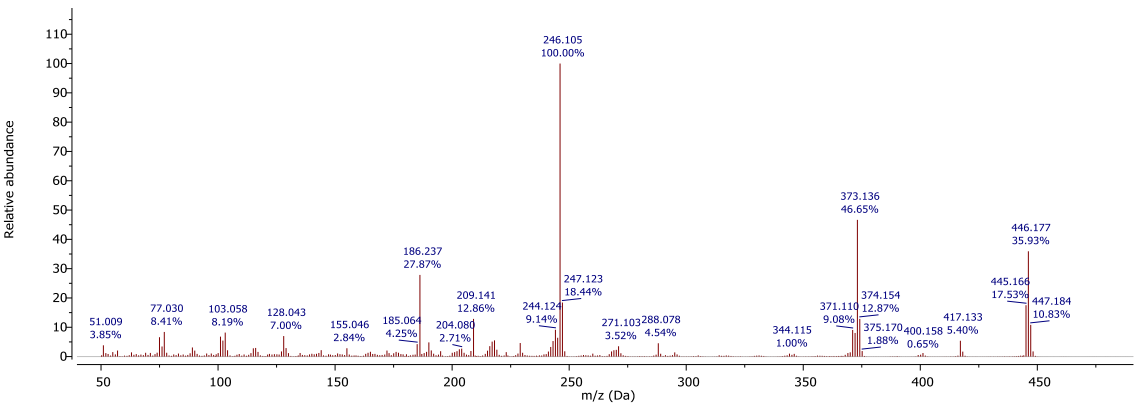


Compound 15c



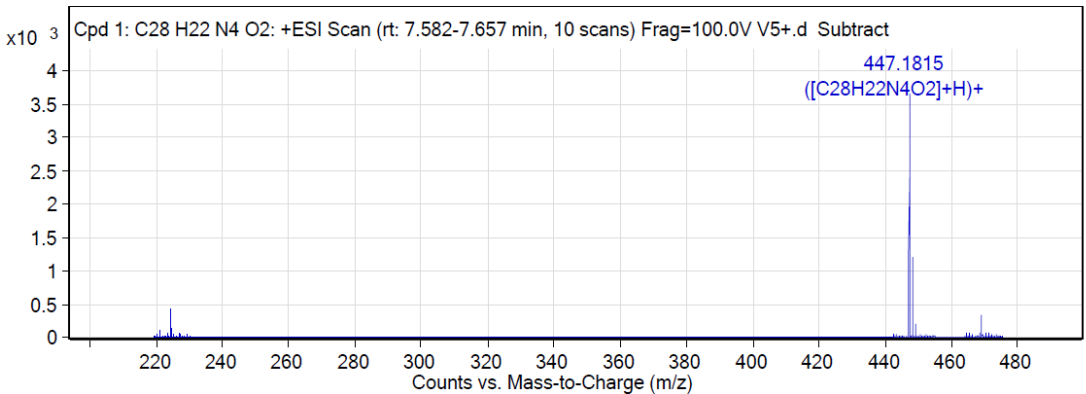


EI MS (70eV)



ESI-QTOF (positive ionization)

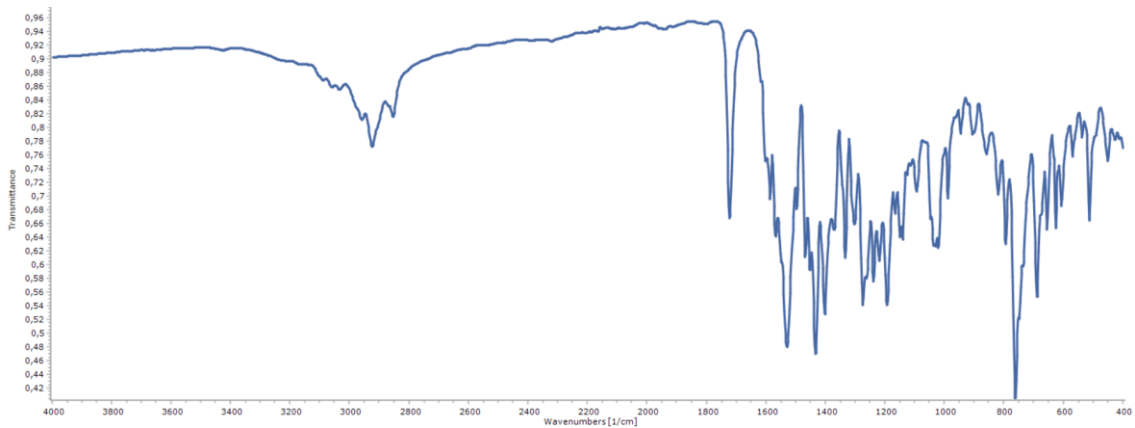
MS Zoomed Spectrum



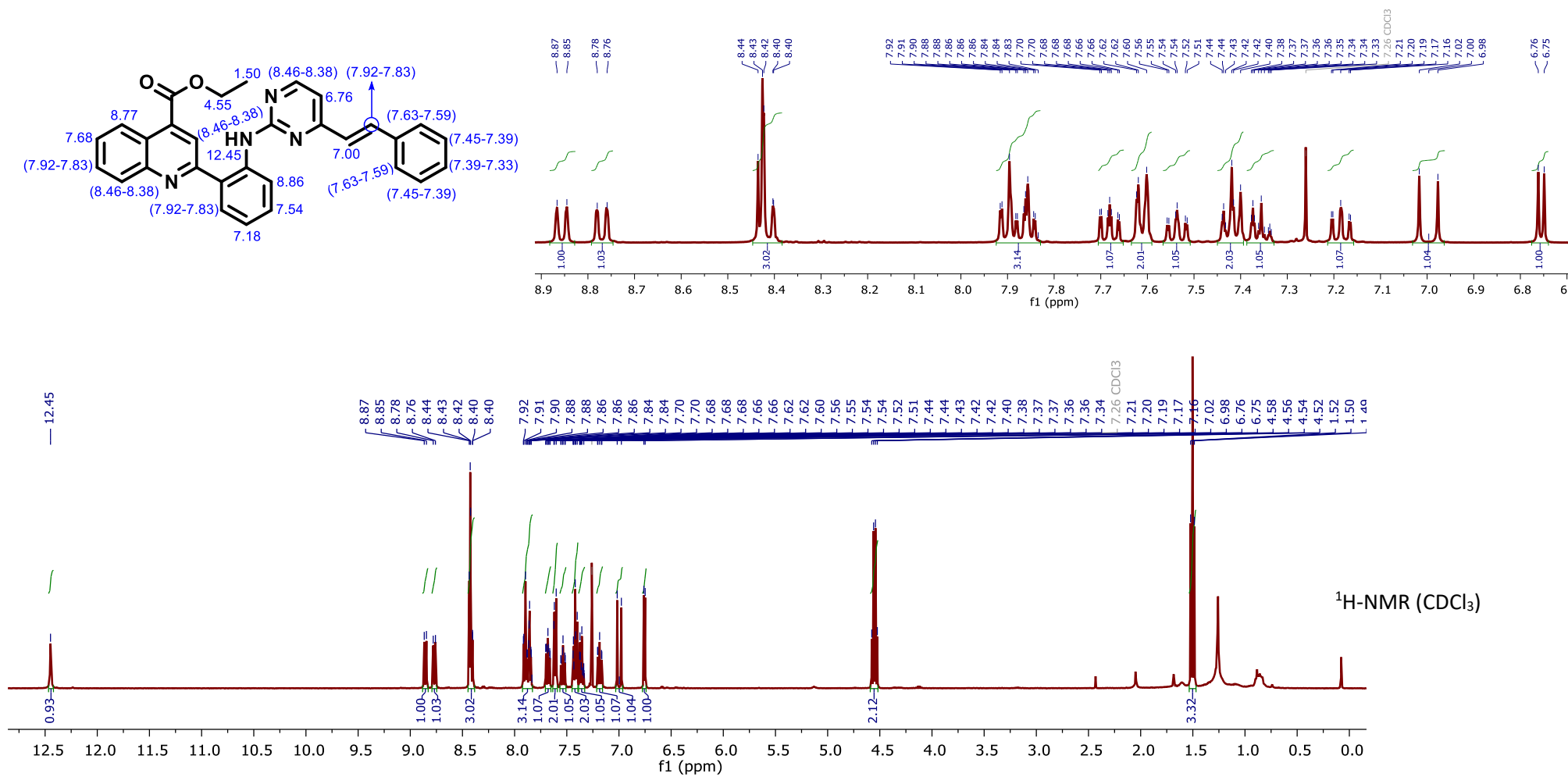
MS Spectrum Peak List

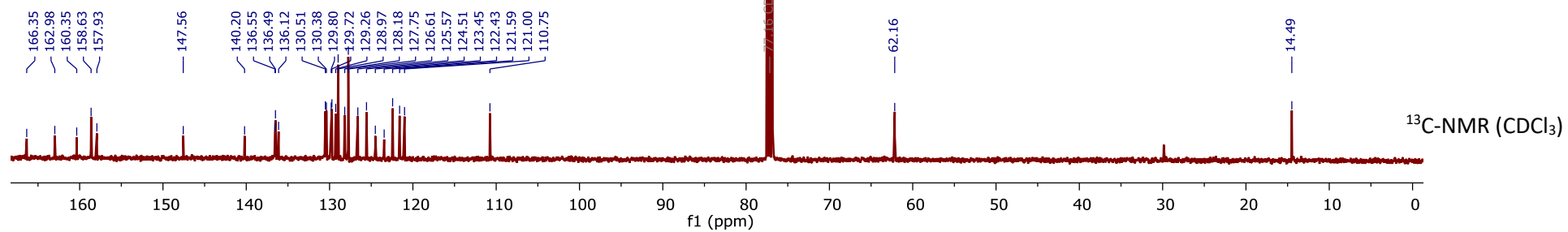
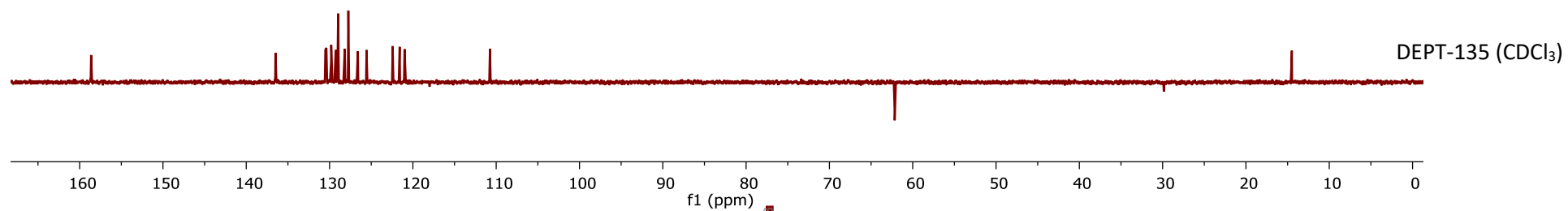
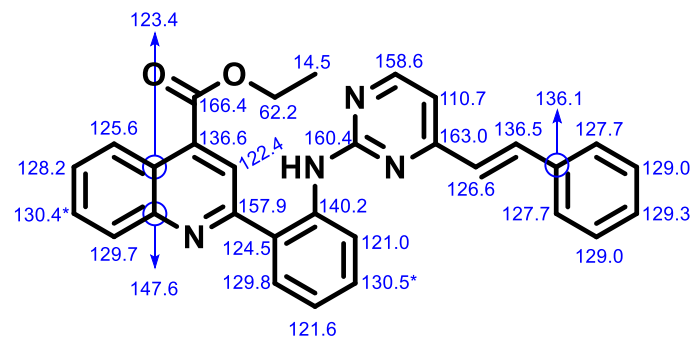
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
224.0945	224.0944	-0.17	2	424.48	C ₂₈ H ₂₂ N ₄ O ₂	(M+2H)+2
224.5961	224.596	-0.65	2	142.09	C ₂₈ H ₂₂ N ₄ O ₂	(M+2H)+2
225.1031	225.0974	-25.18	2	29.09	C ₂₈ H ₂₂ N ₄ O ₂	(M+2H)+2
447.1815	447.1816	0.12	1	3716.82	C ₂₈ H ₂₂ N ₄ O ₂	(M+H)+
448.185	448.1846	-0.73	1	1213.93	C ₂₈ H ₂₂ N ₄ O ₂	(M+H)+
449.1875	449.1876	0.19	1	205.03	C ₂₈ H ₂₂ N ₄ O ₂	(M+H)+
450.1954	450.1904	-11.02	1	28.23	C ₂₈ H ₂₂ N ₄ O ₂	(M+H)+
469.1622	469.1635	2.8	1	338.05	C ₂₈ H ₂₂ N ₄ O ₂	(M+Na)+
470.1666	470.1666	-0.12	1	77.08	C ₂₈ H ₂₂ N ₄ O ₂	(M+Na)+

IR

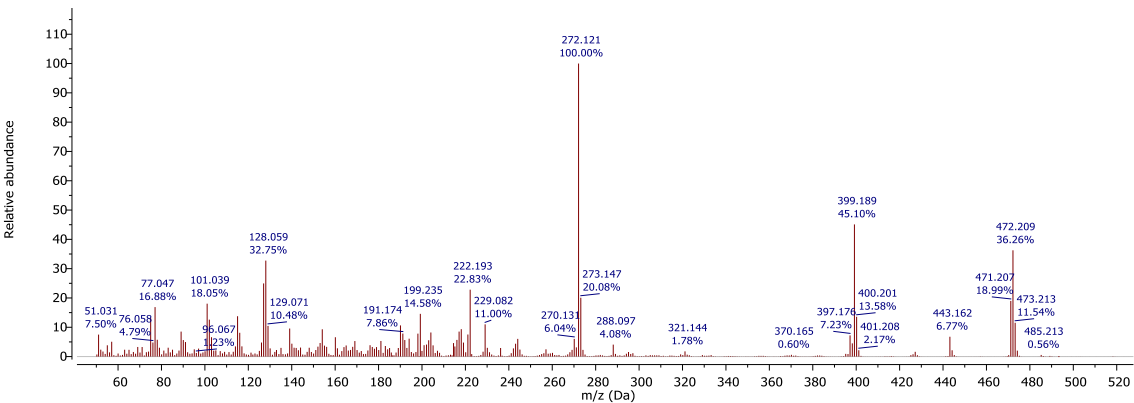


Compound 15d



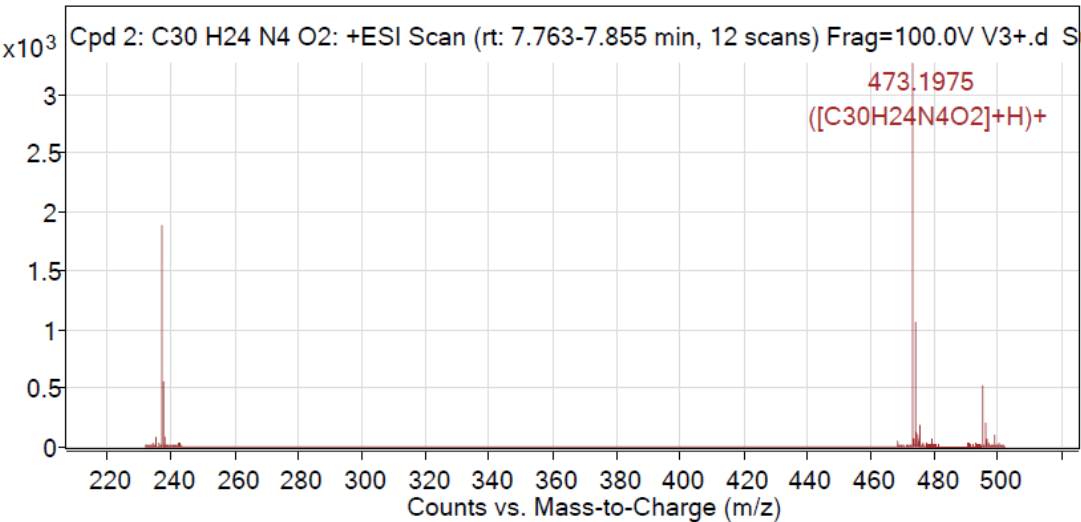


EI MS (70eV)



ESI-QTOF (positive ionization)

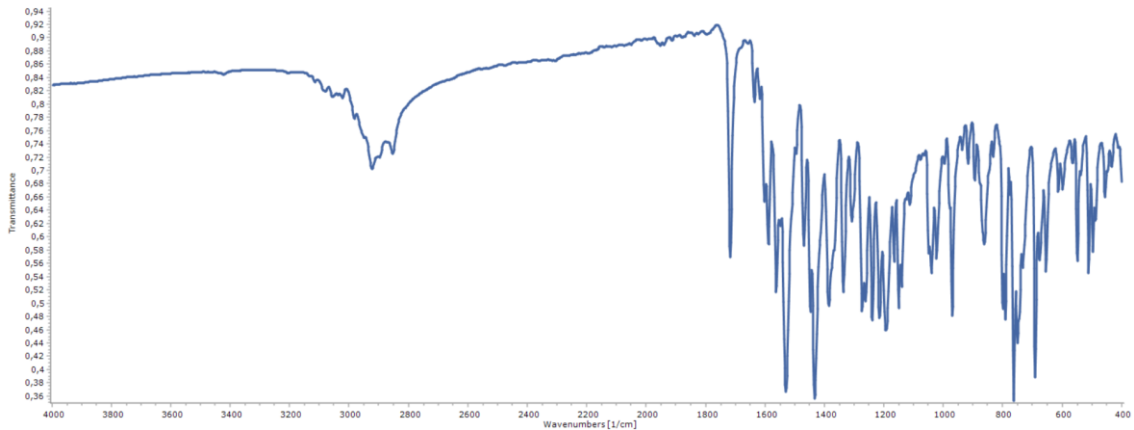
MS Zoomed Spectrum



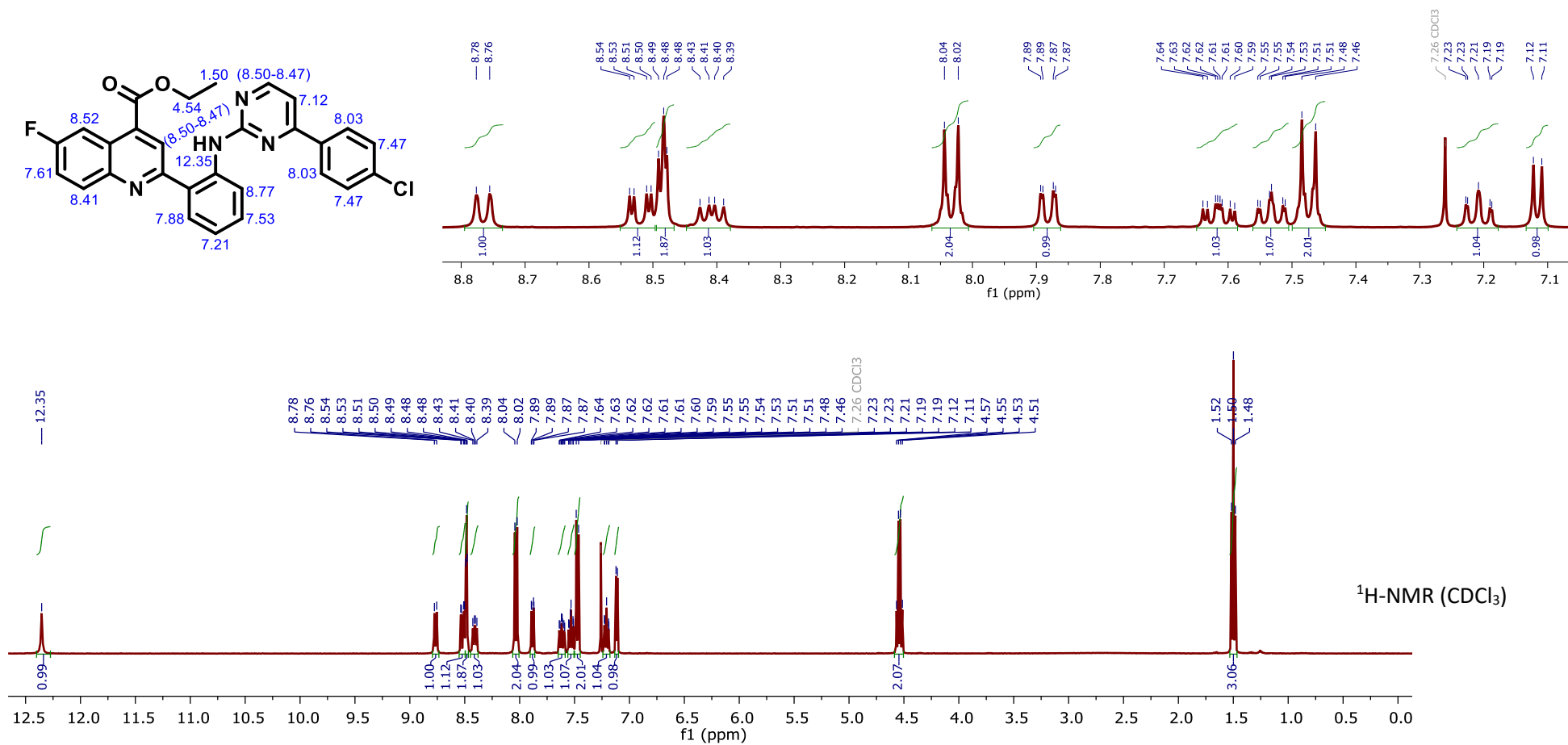
MS Spectrum Peak List

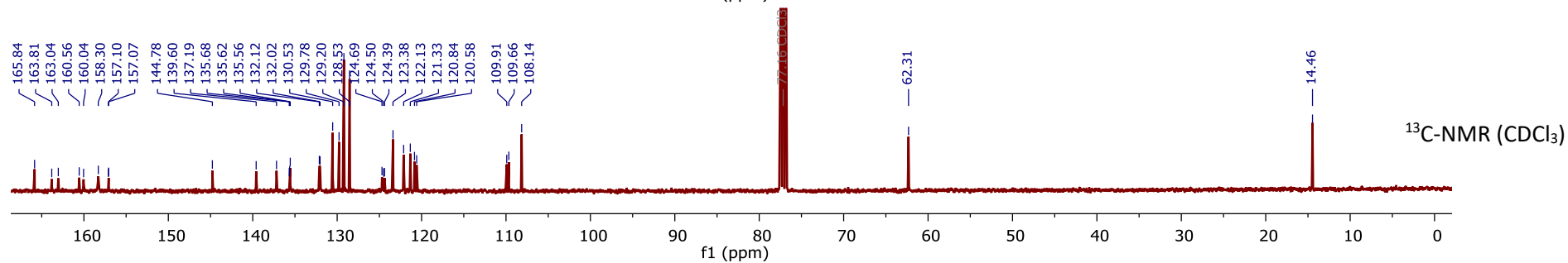
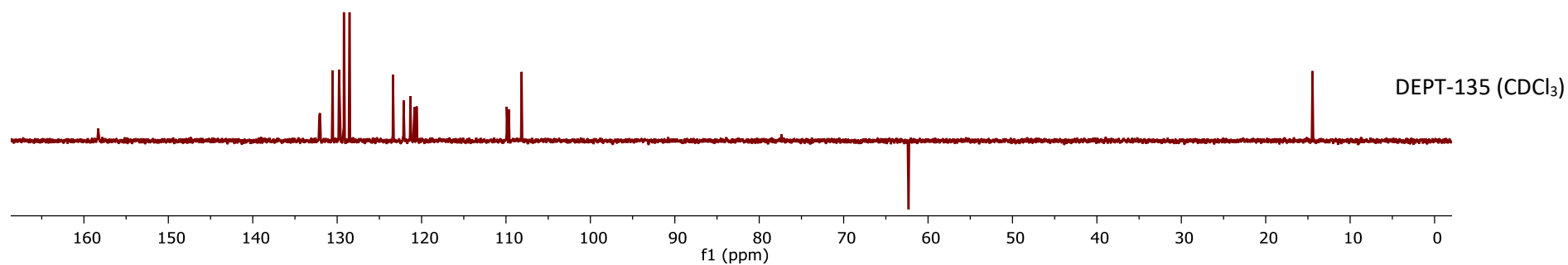
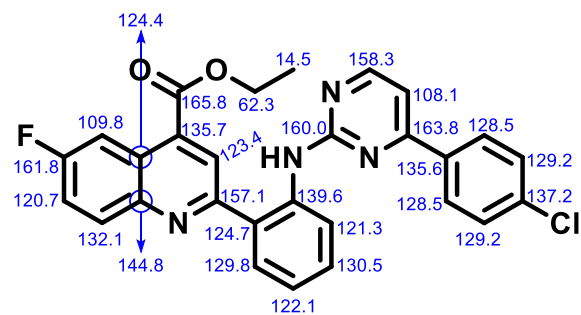
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
237.102	237.1022	0.88	2	1889.49	C ₃₀ H ₂₄ N ₄ O ₂	(M+2H)+2
237.6038	237.6038	0.14	2	556.44	C ₃₀ H ₂₄ N ₄ O ₂	(M+2H)+2
238.1072	238.1053	-8.09	2	83.07	C ₃₀ H ₂₄ N ₄ O ₂	(M+2H)+2
473.1975	473.1972	-0.69	1	3276.68	C ₃₀ H ₂₄ N ₄ O ₂	(M+H)+
474.1992	474.2003	2.26	1	1068.28	C ₃₀ H ₂₄ N ₄ O ₂	(M+H)+
475.2035	475.2033	-0.36	1	180.66	C ₃₀ H ₂₄ N ₄ O ₂	(M+H)+
476.2018	476.2061	9.07	1	27.33	C ₃₀ H ₂₄ N ₄ O ₂	(M+H)+
495.1783	495.1791	1.73	1	518.96	C ₃₀ H ₂₄ N ₄ O ₂	(M+Na)+
496.1815	496.1823	1.52	1	205.6	C ₃₀ H ₂₄ N ₄ O ₂	(M+Na)+
497.1807	497.1852	9.06	1	35.19	C ₃₀ H ₂₄ N ₄ O ₂	(M+Na)+

IR

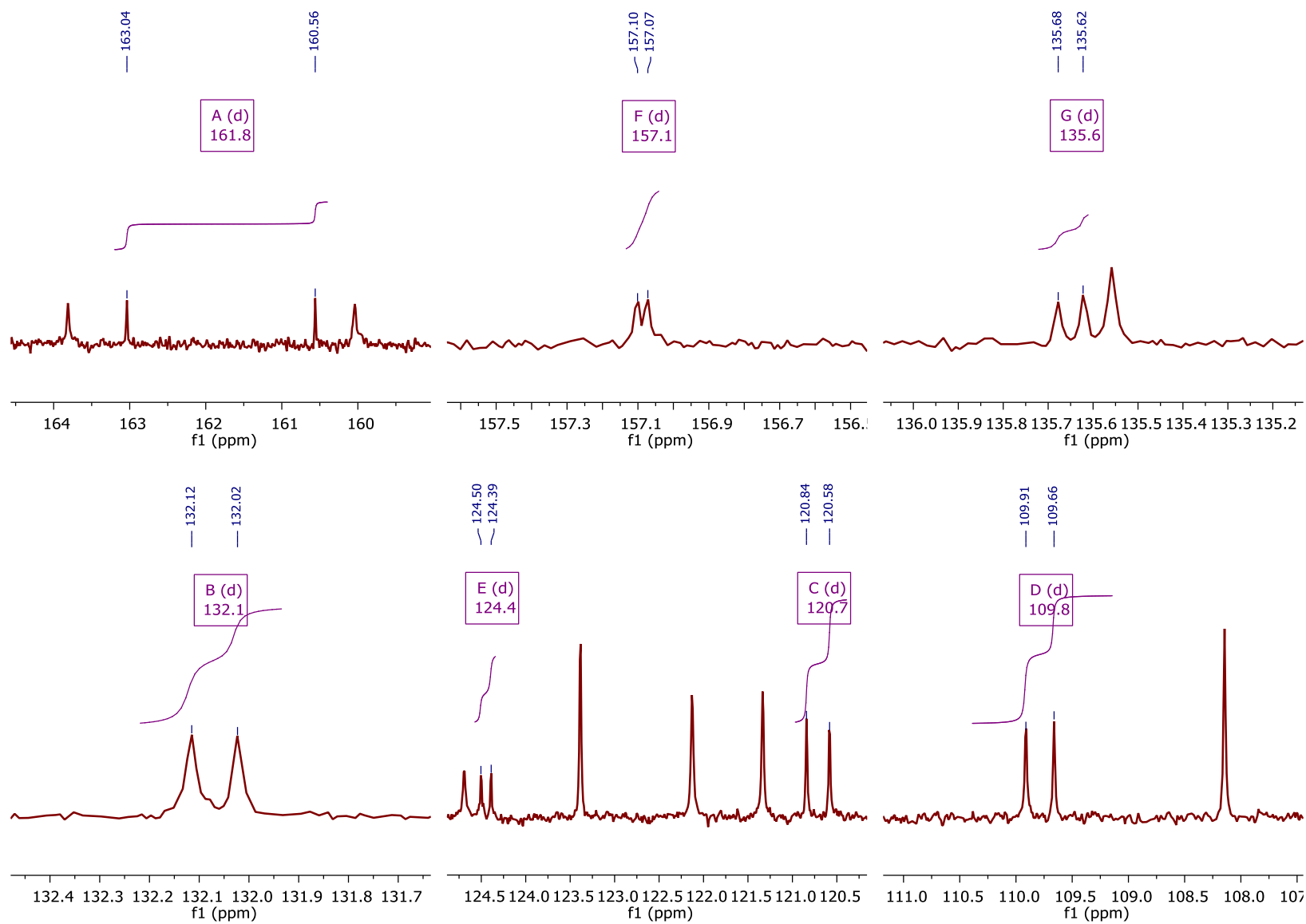


Compound 16a

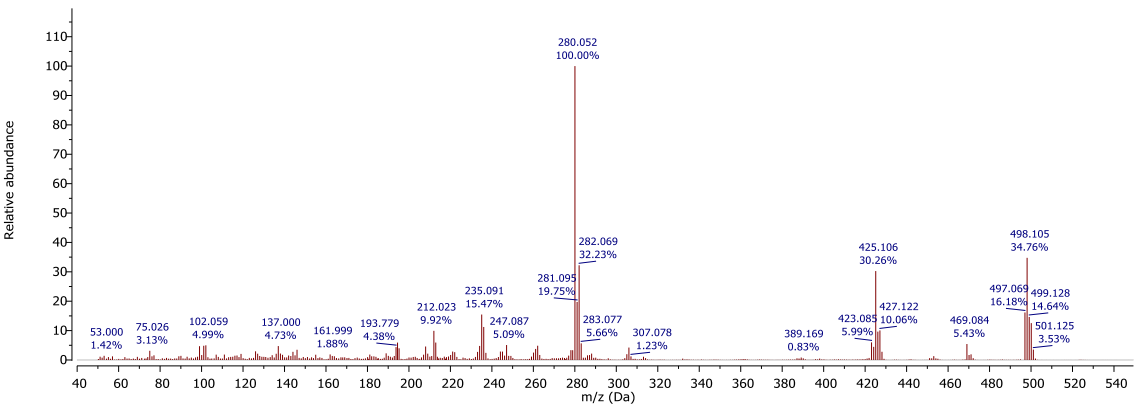




^{13}C - ^{19}F couplings in ^{13}C -NMR. Only coupled peaks have been represented to make it easier to understand.

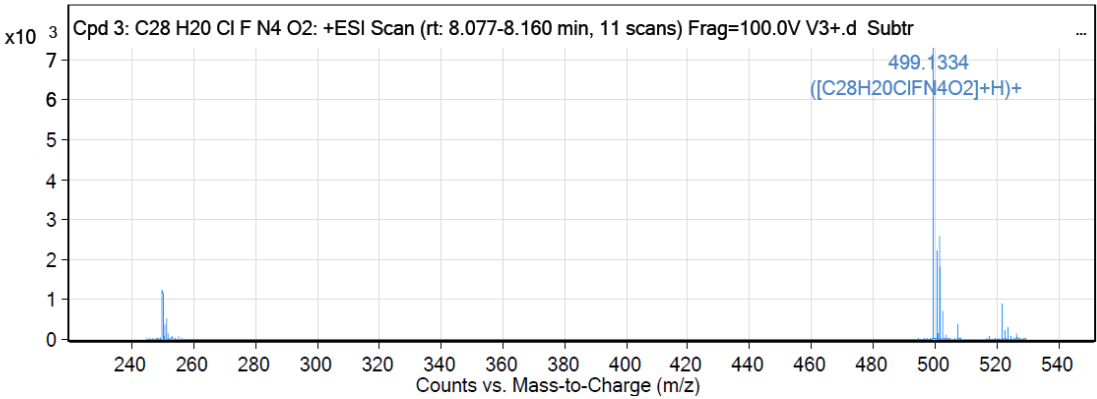


EI MS (70eV)



ESI-QTOF (positive ionization)

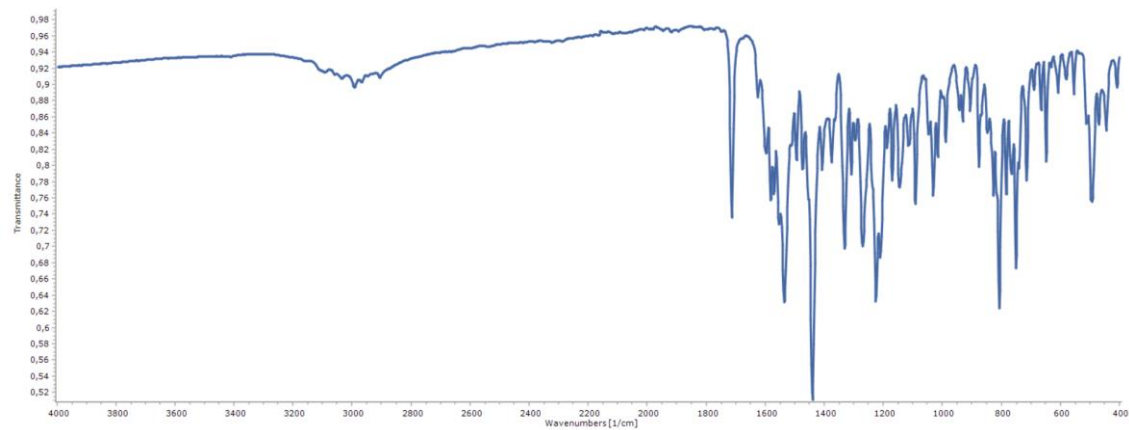
MS Zoomed Spectrum



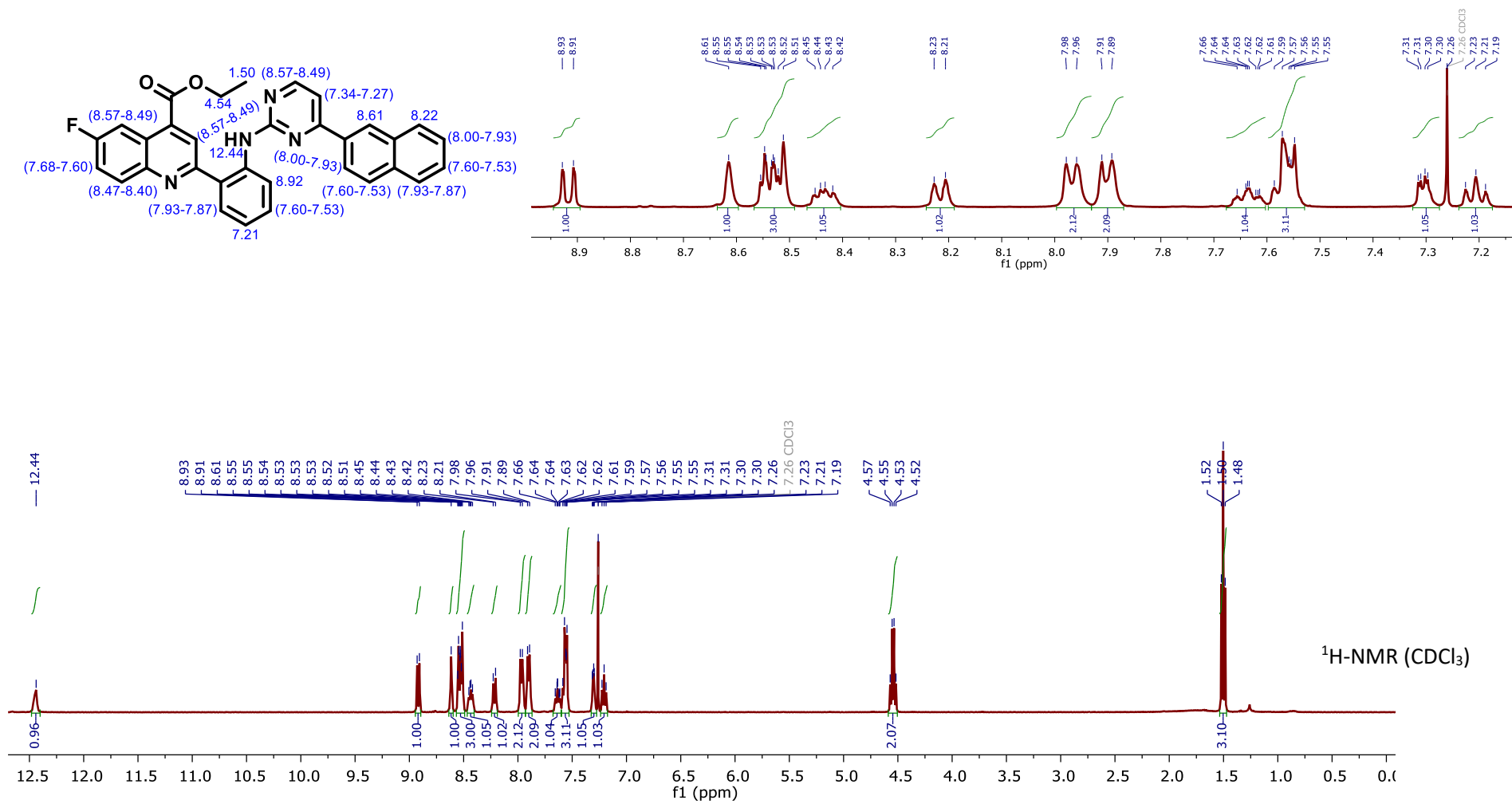
MS Spectrum Peak List

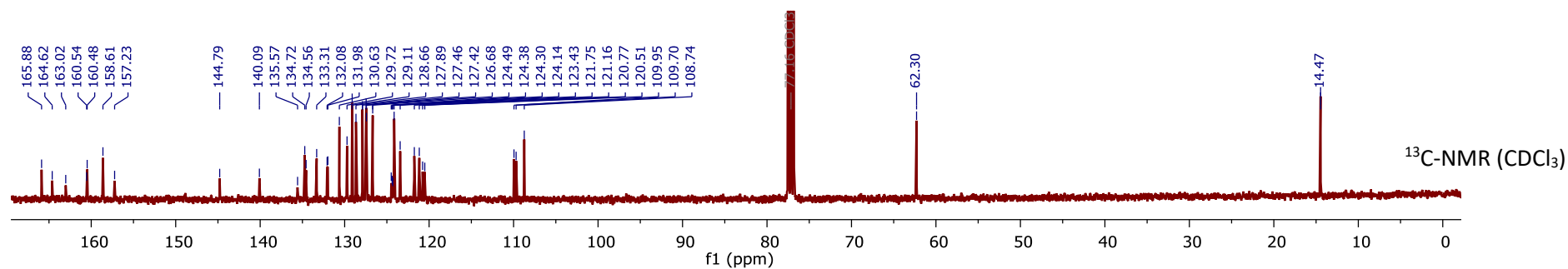
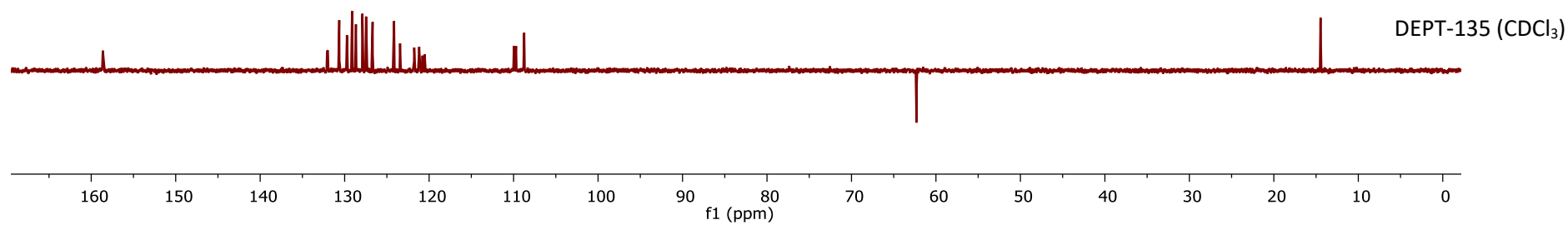
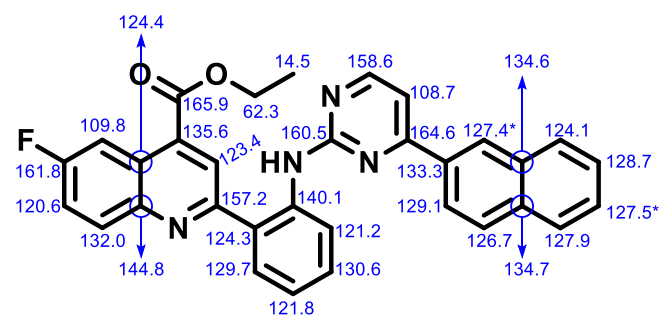
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
250.0705	250.0702	-1.26	2	1256.05	C ₂₈ H ₂₀ ClFN ₄ O ₂	(M+2H)+2
250.5715	250.5718	0.99	2	369.37	C ₂₈ H ₂₀ ClFN ₄ O ₂	(M+2H)+2
251.0693	251.0694	0.55	2	517.77	C ₂₈ H ₂₀ ClFN ₄ O ₂	(M+2H)+2
499.1334	499.1332	-0.45	1	7497.92	C ₂₈ H ₂₀ ClFN ₄ O ₂	(M+H)+
500.136	500.1362	0.44	1	2226.17	C ₂₈ H ₂₀ ClFN ₄ O ₂	(M+H)+
501.1321	501.1315	-1.25	1	2621.84	C ₂₈ H ₂₀ ClFN ₄ O ₂	(M+H)+
502.1341	502.1338	-0.67	1	708.56	C ₂₈ H ₂₀ ClFN ₄ O ₂	(M+H)+
521.1152	521.1151	-0.1	1	907.89	C ₂₈ H ₂₀ ClFN ₄ O ₂	(M+Na)+
522.1182	522.1182	-0.05	1	228.96	C ₂₈ H ₂₀ ClFN ₄ O ₂	(M+Na)+
523.1112	523.1134	4.25	1	300.4	C ₂₈ H ₂₀ ClFN ₄ O ₂	(M+Na)+

IR

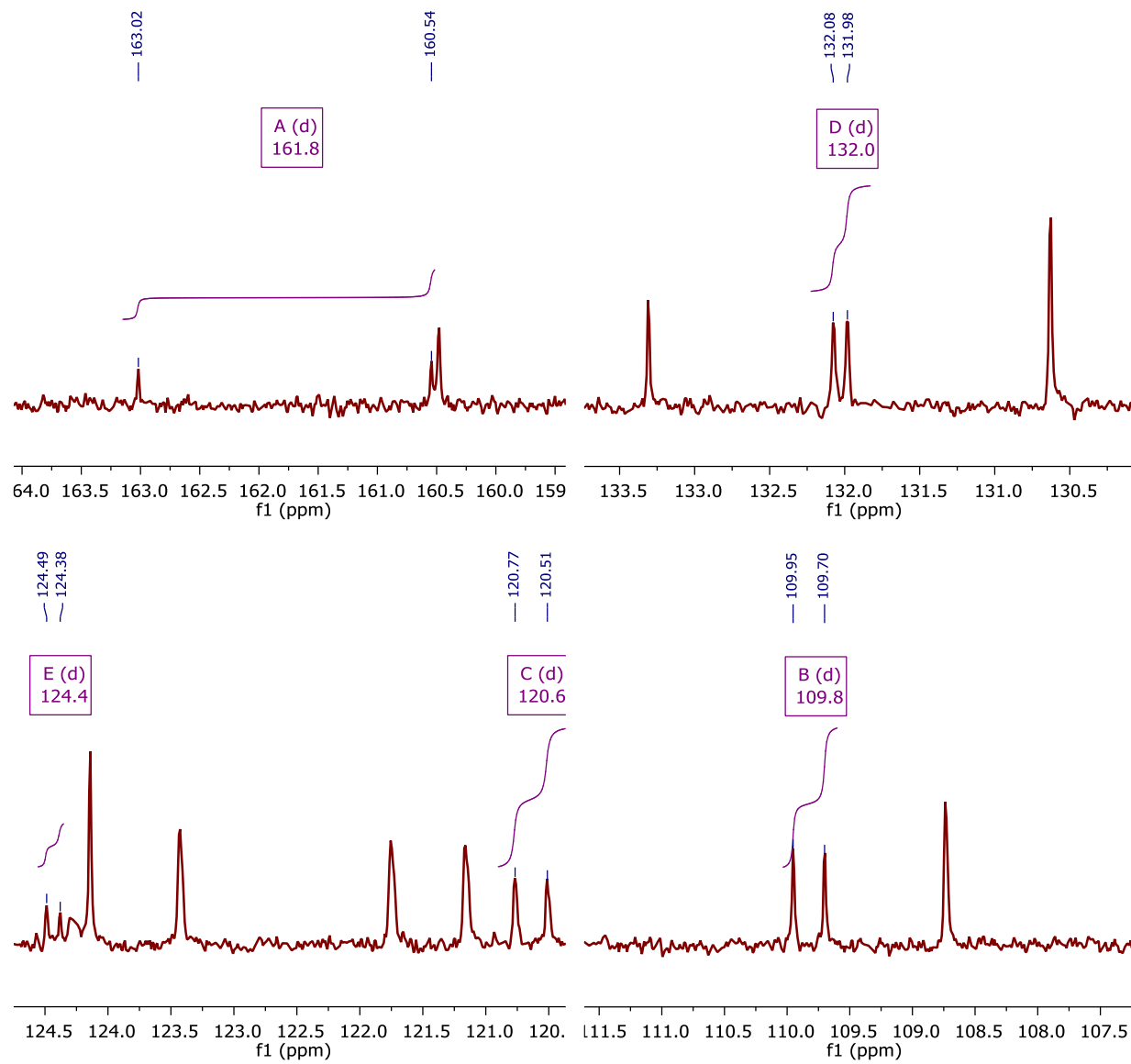


Compound **16b**

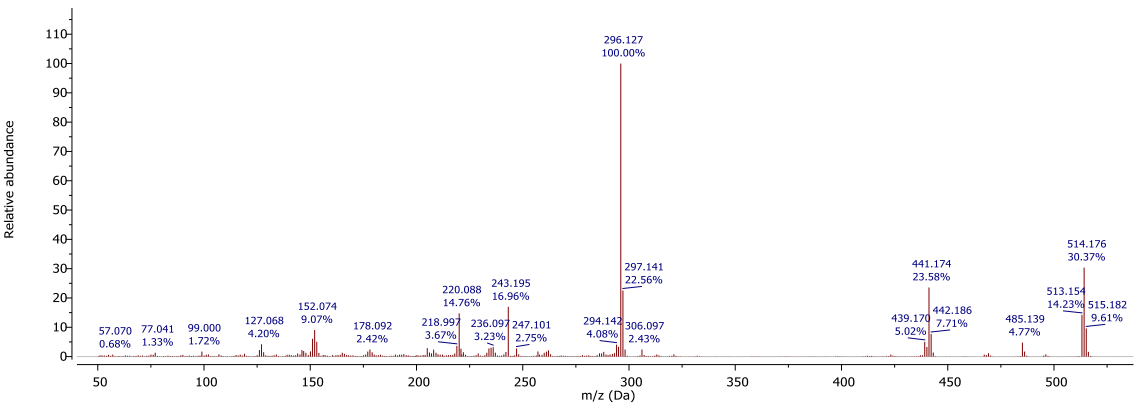




^{13}C - ^{19}F couplings in ^{13}C -NMR. Only coupled peaks have been represented to make it easier to understand.

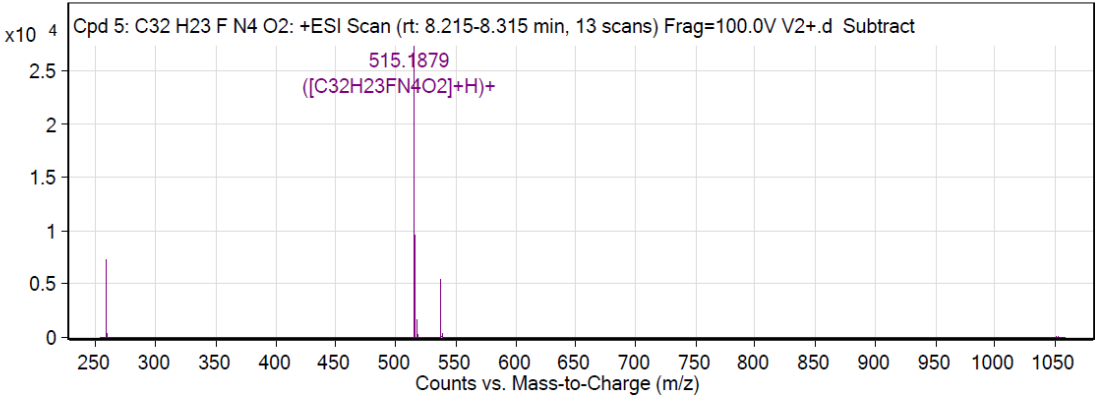


EI MS (70eV)



ESI-QTOF (positive ionization)

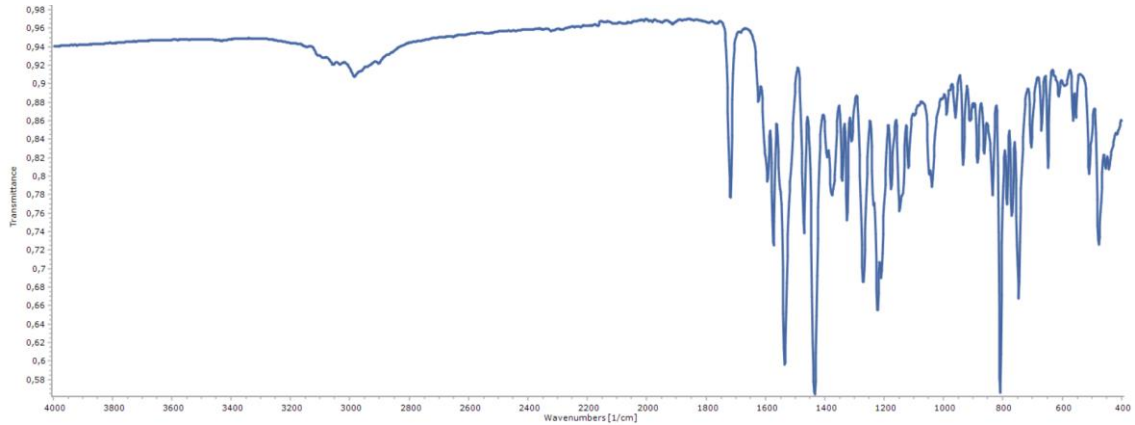
MS Zoomed Spectrum



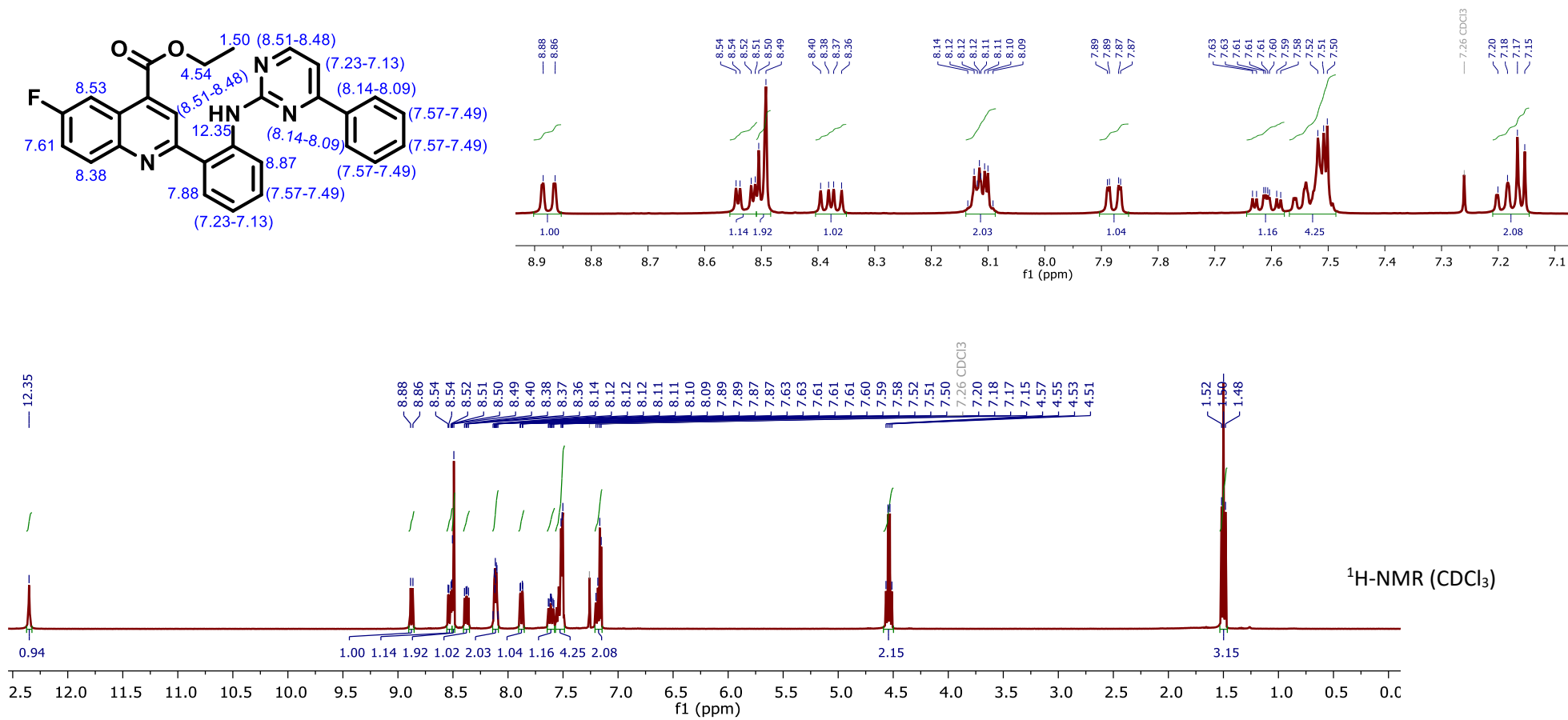
MS Spectrum Peak List

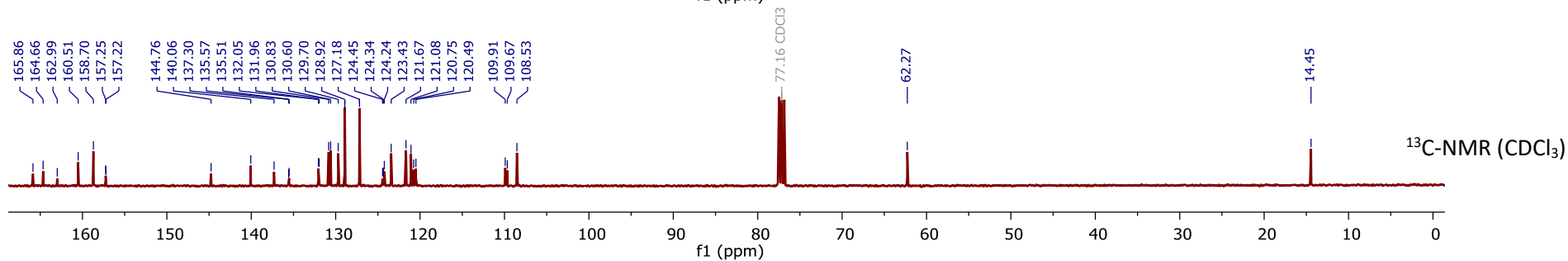
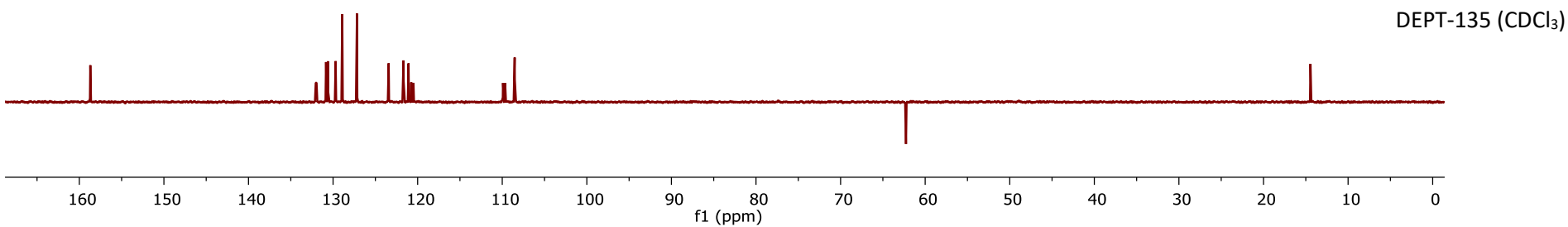
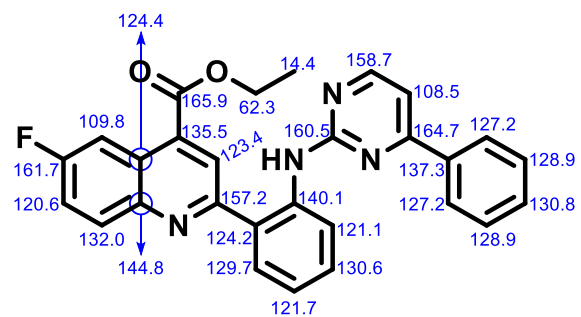
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
258.0976	258.0975	-0.47	2	7289.61	C32H23FN4O2	(M+2H)+2
258.5991	258.5991	0.05	2	2508.09	C32H23FN4O2	(M+2H)+2
259.1002	259.1006	1.61	2	459.76	C32H23FN4O2	(M+2H)+2
515.1879	515.1878	-0.32	1	27761.03	C32H23FN4O2	(M+H)+
516.1914	516.1909	-1.02	1	9549.47	C32H23FN4O2	(M+H)+
517.1939	517.1939	0.07	1	1710.24	C32H23FN4O2	(M+H)+
537.1699	537.1697	-0.34	1	5640.11	C32H23FN4O2	(M+Na)+
538.1734	538.1728	-1.07	1	1936.79	C32H23FN4O2	(M+Na)+
539.1759	539.1758	-0.14	1	461.44	C32H23FN4O2	(M+Na)+
1051.3494	1051.3502	0.76	1	218.16	C32H23FN4O2	(2M+Na)+

IR

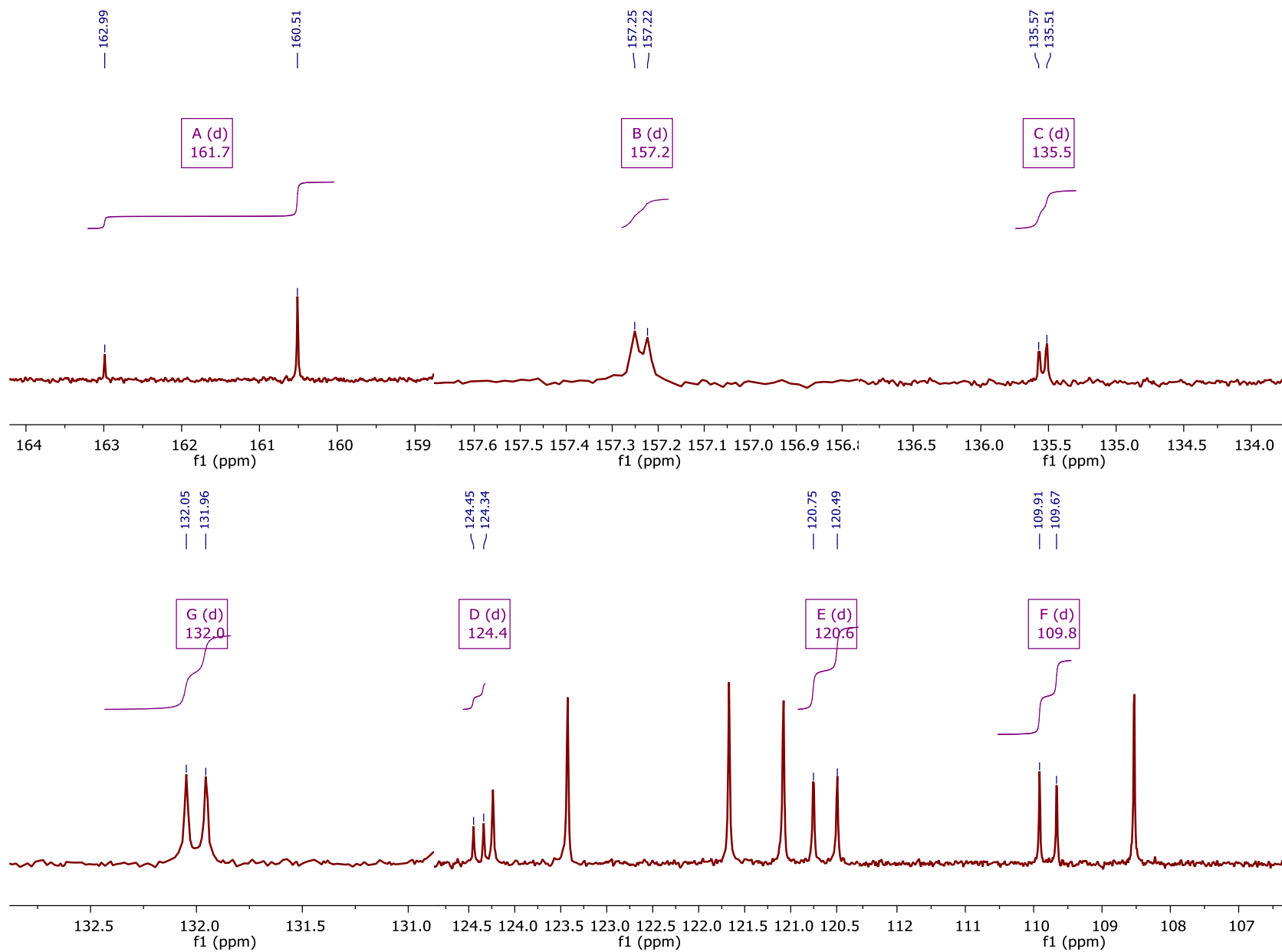


Compound **16c**

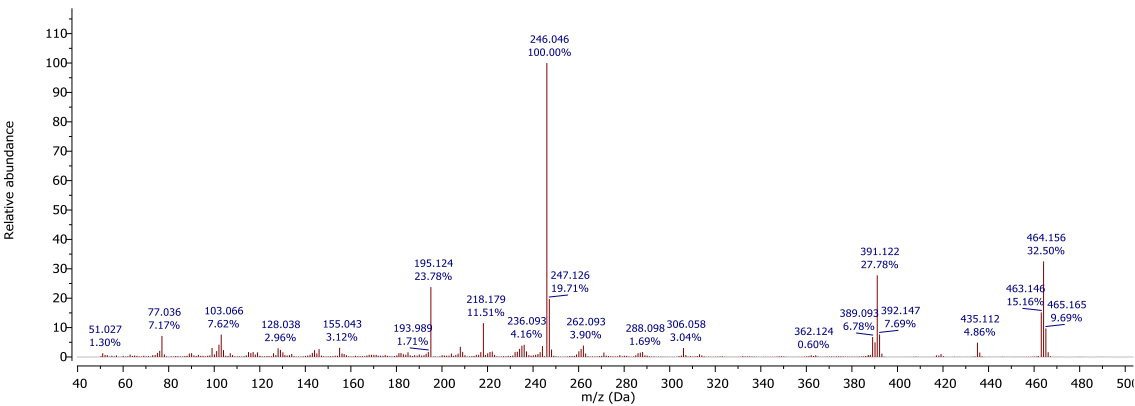




^{13}C - ^{19}F couplings in ^{13}C -NMR. Only coupled peaks have been represented to make it easier to understand.

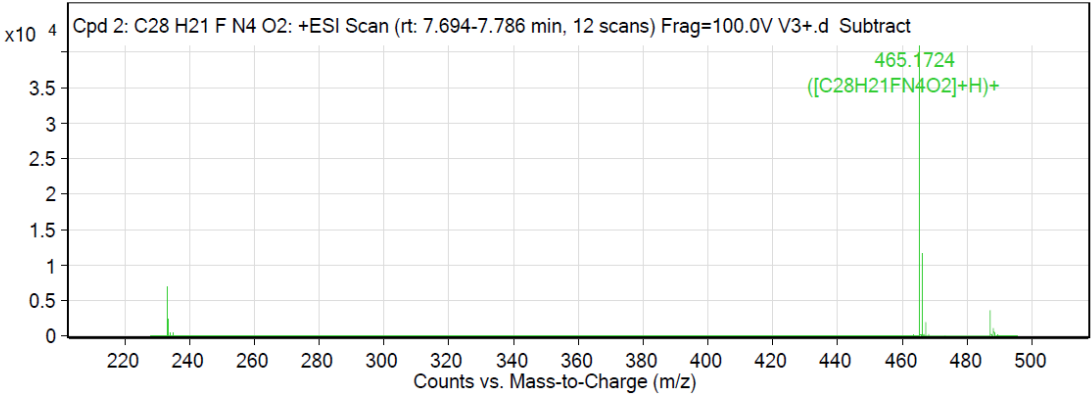


EI MS (70eV)



ESI-QTOF (positive ionization)

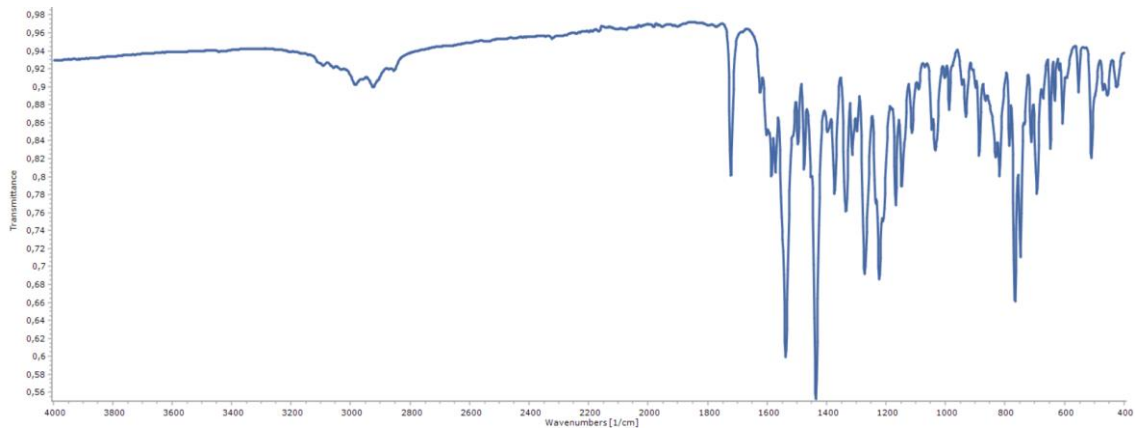
MS Zoomed Spectrum



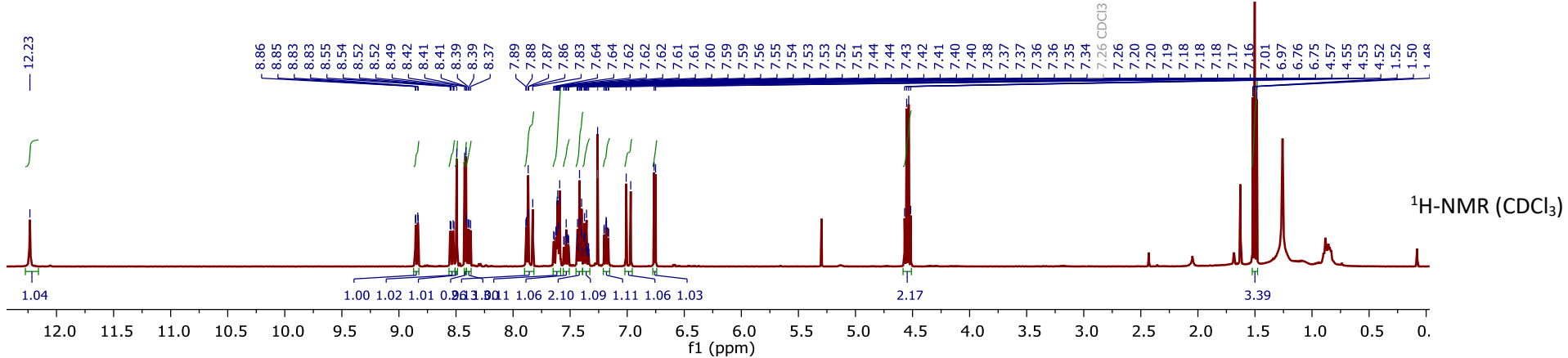
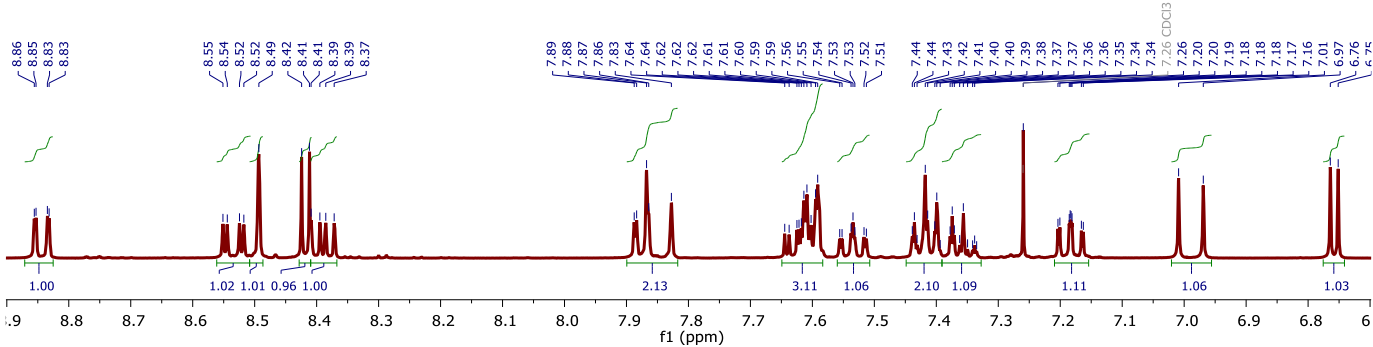
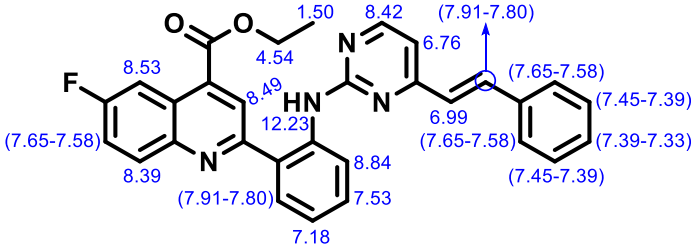
MS Spectrum Peak List

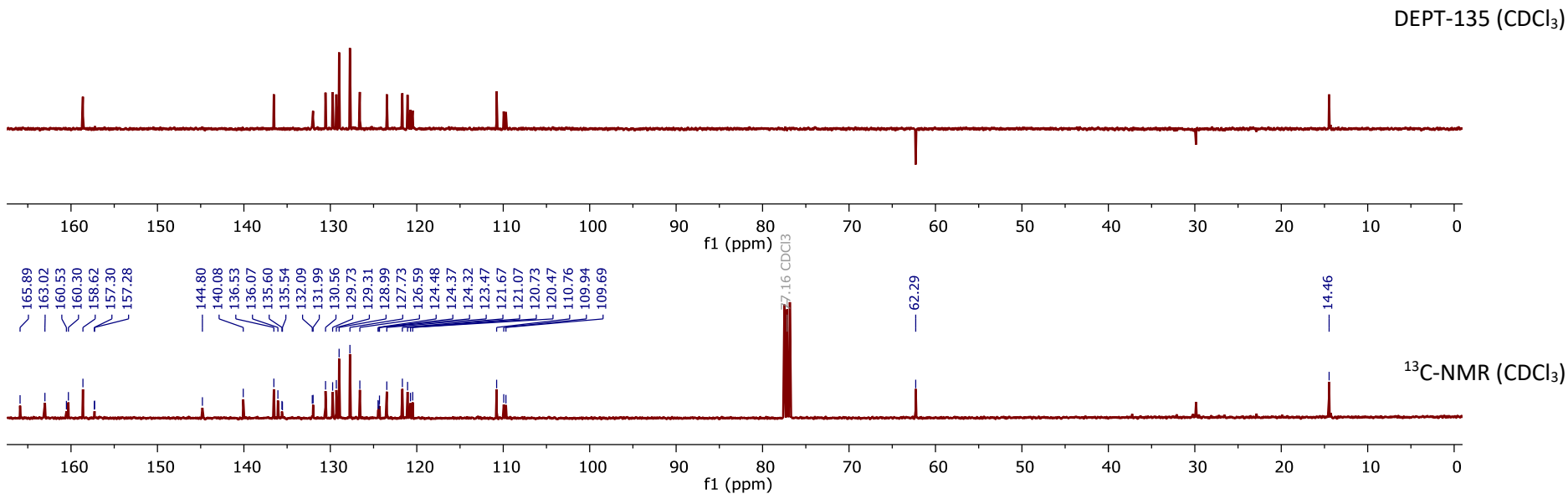
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
233.0897	233.0897	-0.02	2	6990.25	C28H21FN4O2	(M+2H)+2
233.5913	233.5913	-0.41	2	2270.24	C28H21FN4O2	(M+2H)+2
234.093	234.0927	-1.37	2	455.6	C28H21FN4O2	(M+2H)+2
465.1724	465.1721	-0.51	1	41167.47	C28H21FN4O2	(M+H)+
466.1756	466.1752	-0.75	1	11882.28	C28H21FN4O2	(M+H)+
467.1786	467.1782	-0.87	1	1978.88	C28H21FN4O2	(M+H)+
468.1807	468.181	0.5	1	270.14	C28H21FN4O2	(M+H)+
487.1541	487.1541	-0.01	1	3637.43	C28H21FN4O2	(M+Na)+
488.1566	488.1572	1.2	1	1146.81	C28H21FN4O2	(M+Na)+
489.1589	489.1601	2.51	1	183.59	C28H21FN4O2	(M+Na)+

IR

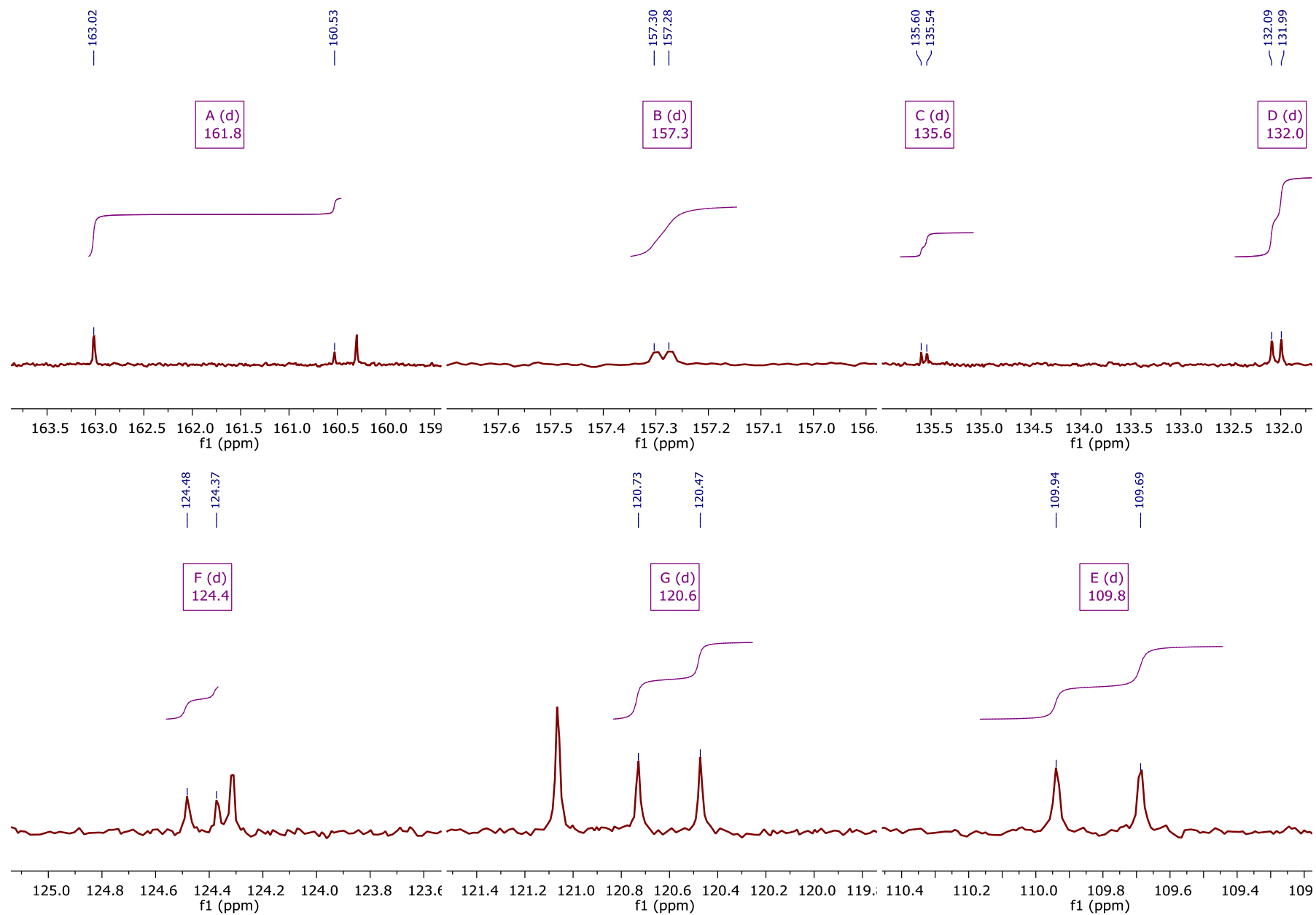


Compound 16d

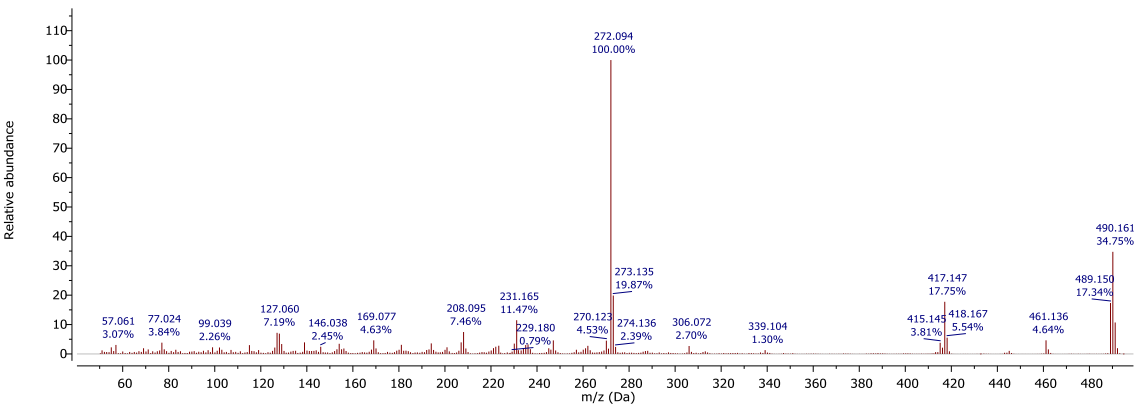




^{13}C - ^{19}F couplings in ^{13}C -NMR. Only coupled peaks have been represented to make it easier to understand.

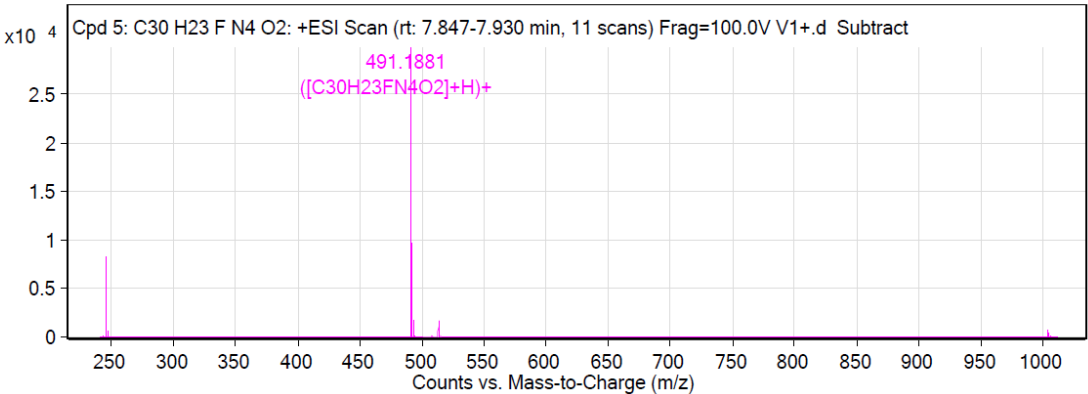


EI MS (70eV)



ESI-QTOF (positive ionization)

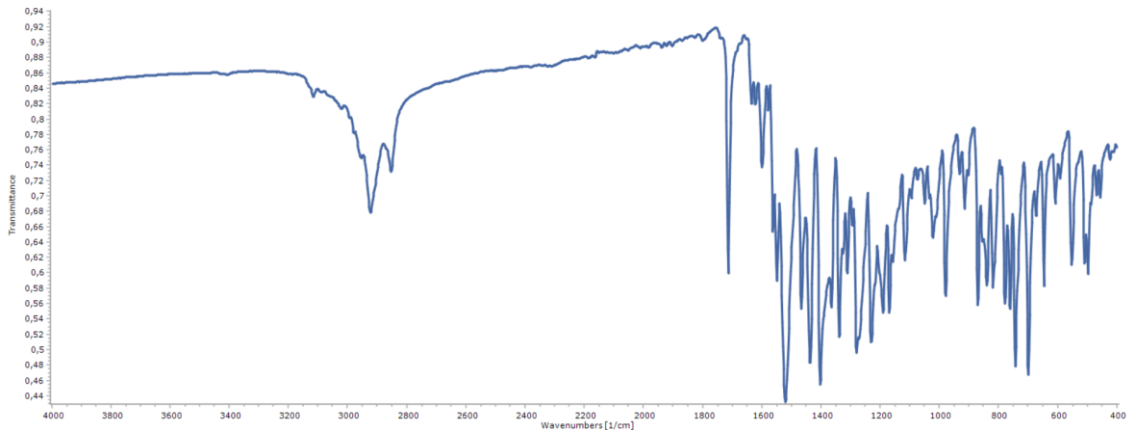
MS Zoomed Spectrum



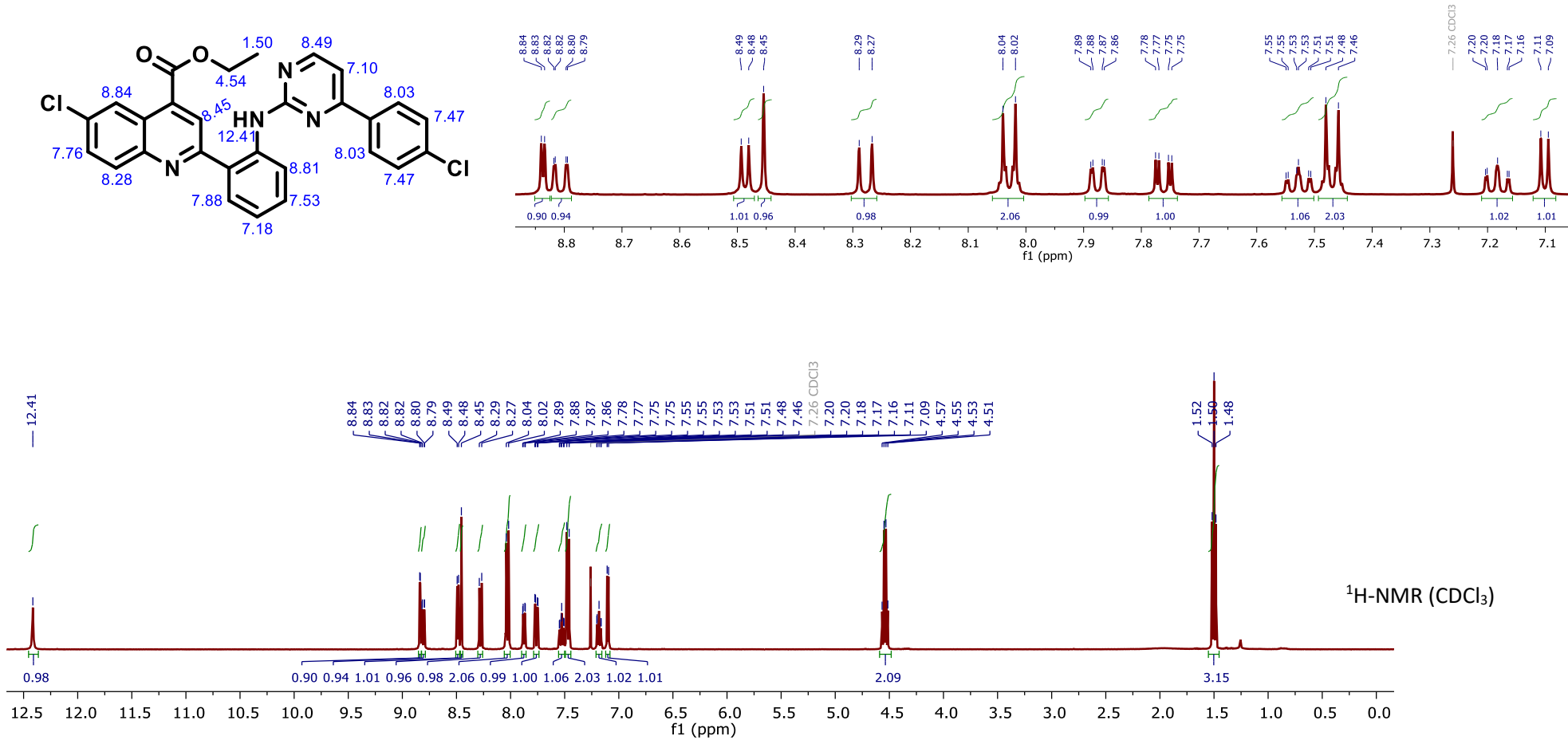
MS Spectrum Peak List

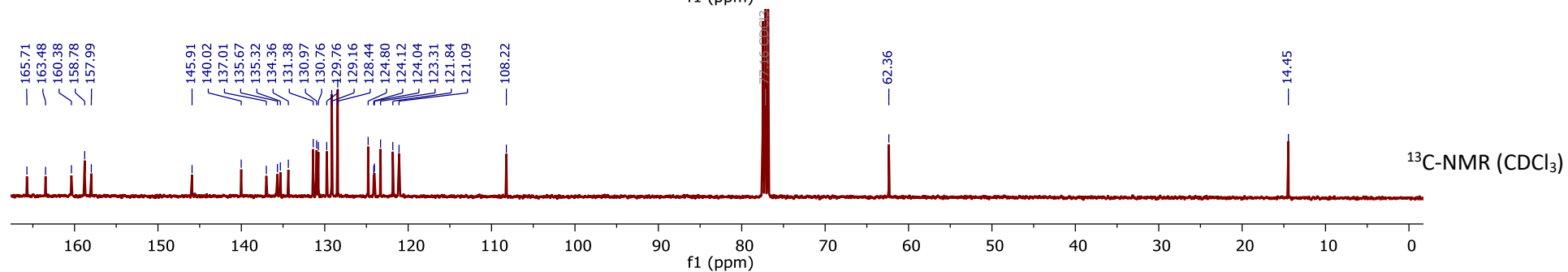
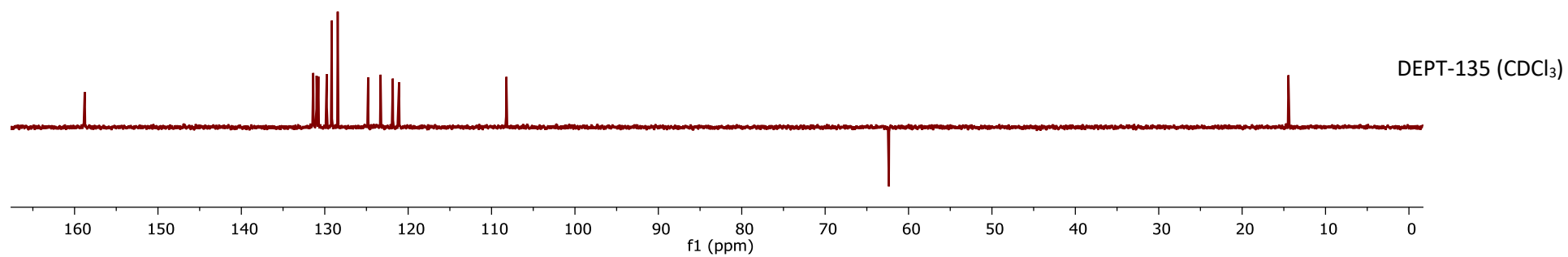
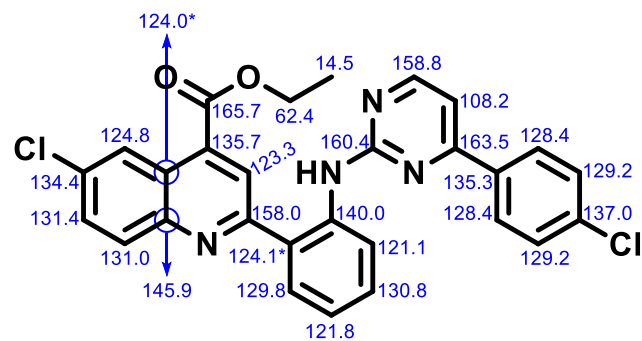
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
246.0977	246.0975	-0.76	2	8294.67	C30H23FN4O2	(M+2H)+2
246.5989	246.5991	0.83	2	2792.43	C30H23FN4O2	(M+2H)+2
247.1008	247.1006	-1.07	2	568.16	C30H23FN4O2	(M+2H)+2
491.1881	491.1878	-0.67	1	30014.32	C30H23FN4O2	(M+H)+
492.1913	492.1909	-0.8	1	9804.74	C30H23FN4O2	(M+H)+
493.1942	493.1939	-0.6	1	1775.04	C30H23FN4O2	(M+H)+
513.1707	513.1697	-1.83	1	1687.41	C30H23FN4O2	(M+Na)+
514.1715	514.1728	2.51	1	632.44	C30H23FN4O2	(M+Na)+
1003.3504	1003.3502	-0.14	1	802.72	C30H23FN4O2	(2M+Na)+
1004.3531	1004.3533	0.27	1	522.24	C30H23FN4O2	(2M+Na)+

IR

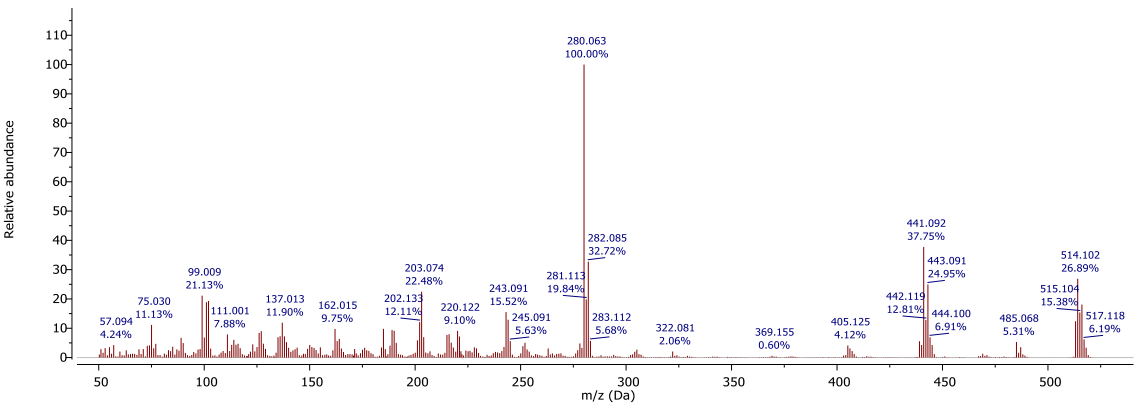


Compound 17a



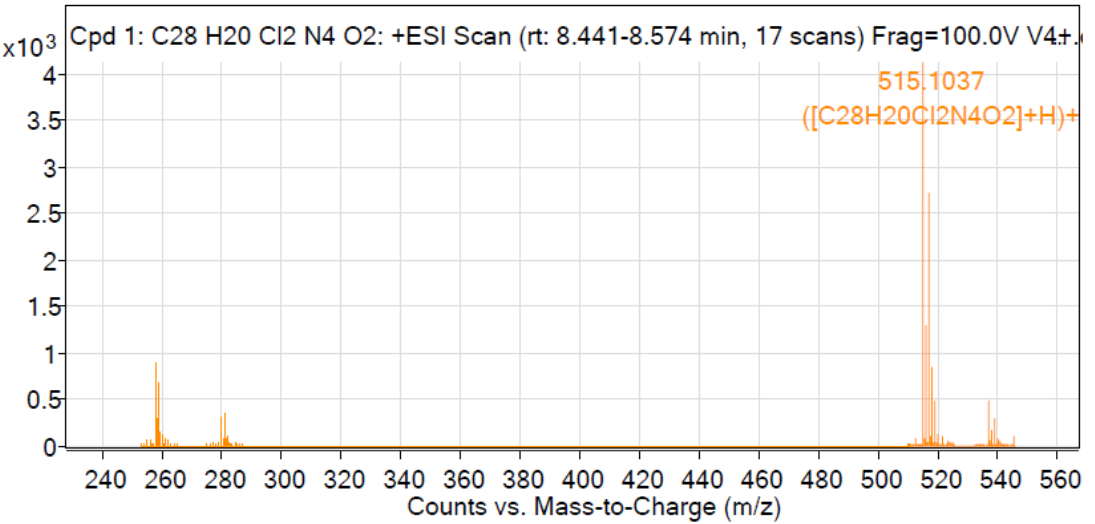


EI MS (70eV)



ESI-QTOF (positive ionization)

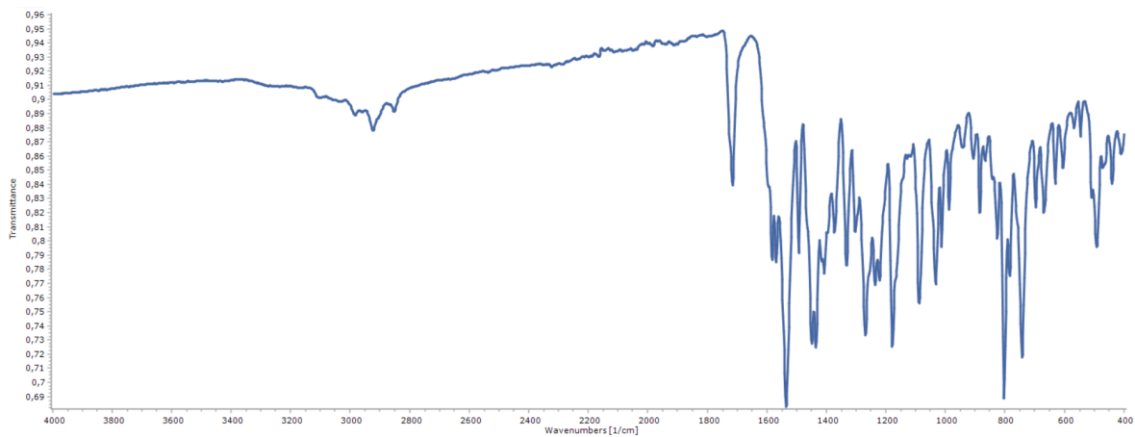
MS Zoomed Spectrum



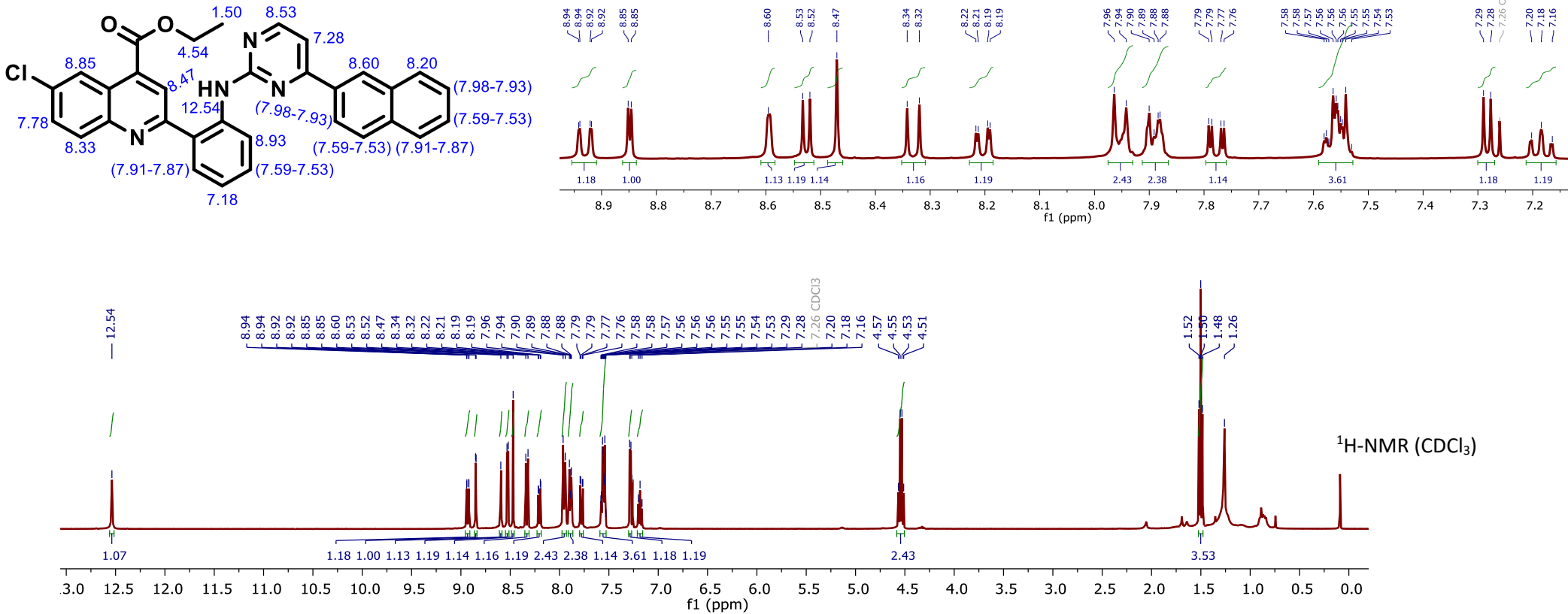
MS Spectrum Peak List

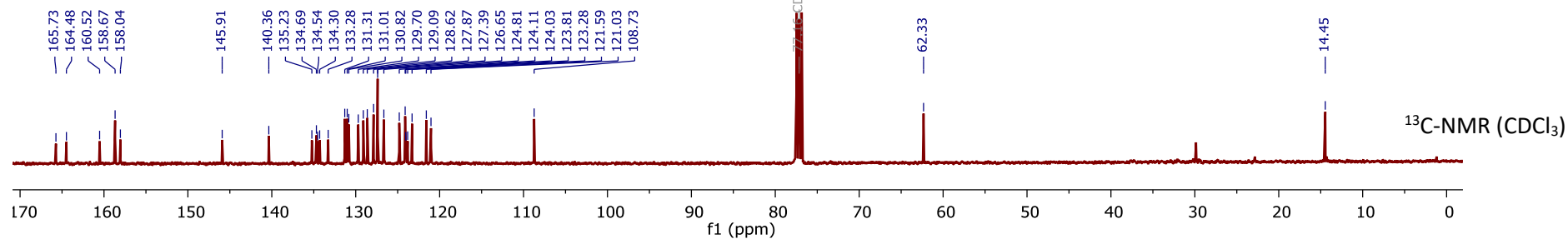
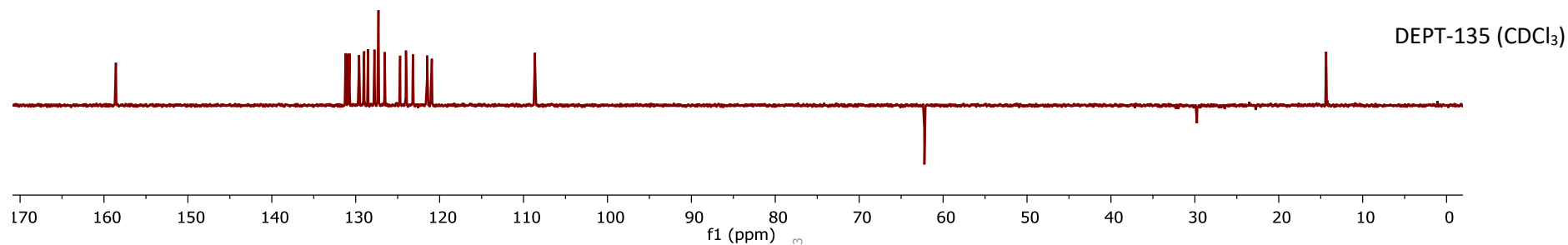
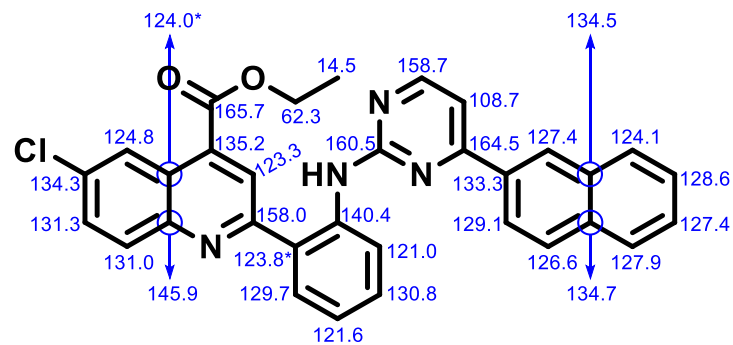
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
258.0563	258.0554	-3.31	2	911.94	C ₂₈ H ₂₀ Cl ₂ N ₄ O ₂	(M+2H)+2
259.0539	259.0543	1.65	2	676.93	C ₂₈ H ₂₀ Cl ₂ N ₄ O ₂	(M+2H)+2
280.0298	280.0374	26.99	2	313.4	C ₂₈ H ₂₀ Cl ₂ N ₄ O ₂	(M+2Na)+2
281.0292	281.0363	24.98	2	366.71	C ₂₈ H ₂₀ Cl ₂ N ₄ O ₂	(M+2Na)+2
515.1037	515.1036	-0.08	1	4132.52	C ₂₈ H ₂₀ Cl ₂ N ₄ O ₂	(M+H)+
516.1071	516.1067	-0.86	1	1302.22	C ₂₈ H ₂₀ Cl ₂ N ₄ O ₂	(M+H)+
517.101	517.1014	0.72	1	2715.84	C ₂₈ H ₂₀ Cl ₂ N ₄ O ₂	(M+H)+
518.1046	518.104	-1.05	1	856.73	C ₂₈ H ₂₀ Cl ₂ N ₄ O ₂	(M+H)+
519.1002	519.1	-0.27	1	482.72	C ₂₈ H ₂₀ Cl ₂ N ₄ O ₂	(M+H)+
537.0854	537.0856	0.35	1	493.46	C ₂₈ H ₂₀ Cl ₂ N ₄ O ₂	(M+Na)+

IR

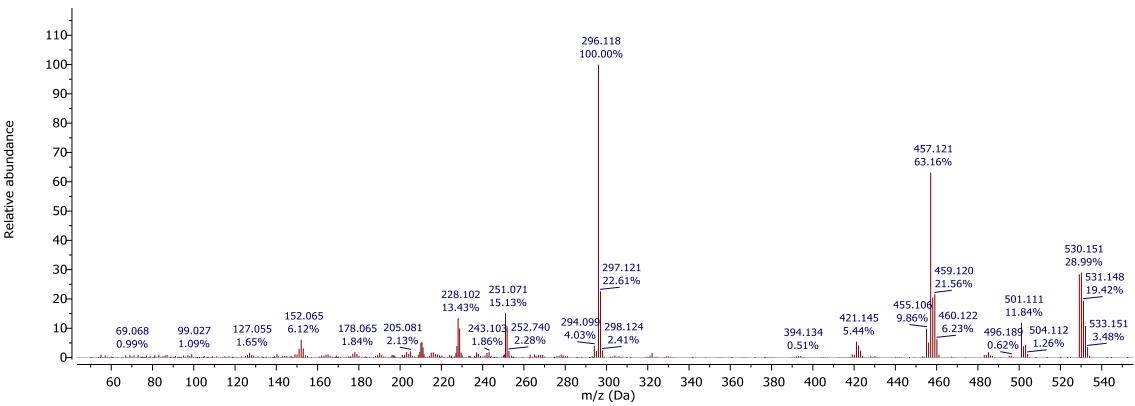


Compound 17b



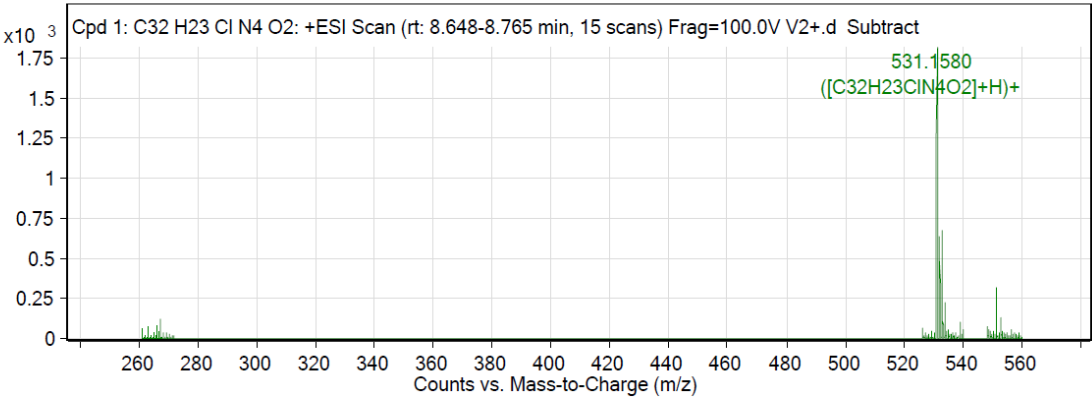


EI MS (70eV)



ESI-QTOF (positive ionization)

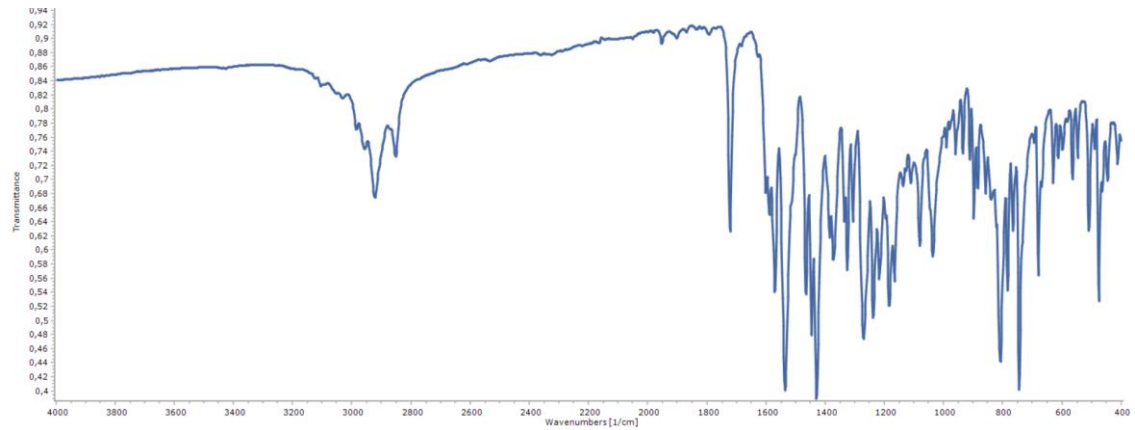
MS Zoomed Spectrum



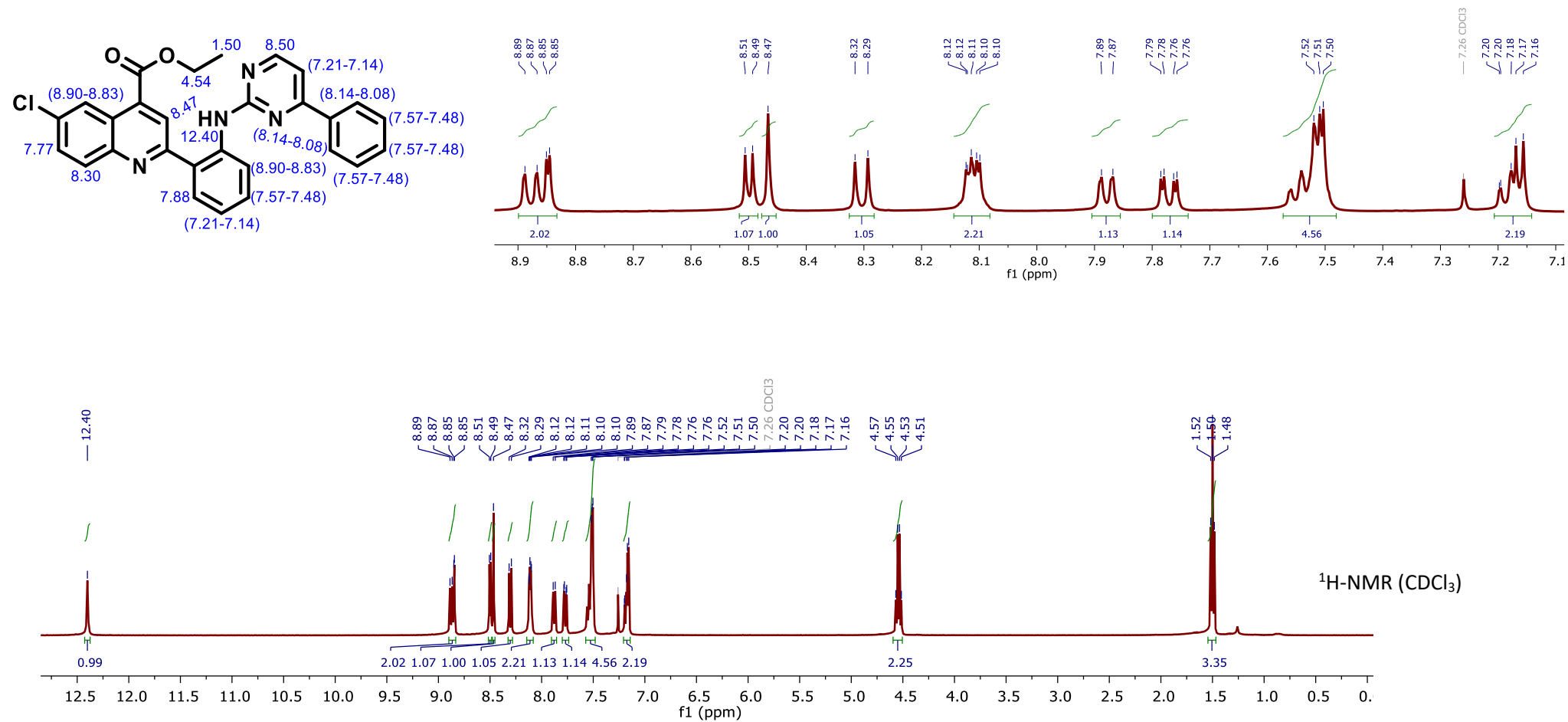
MS Spectrum Peak List

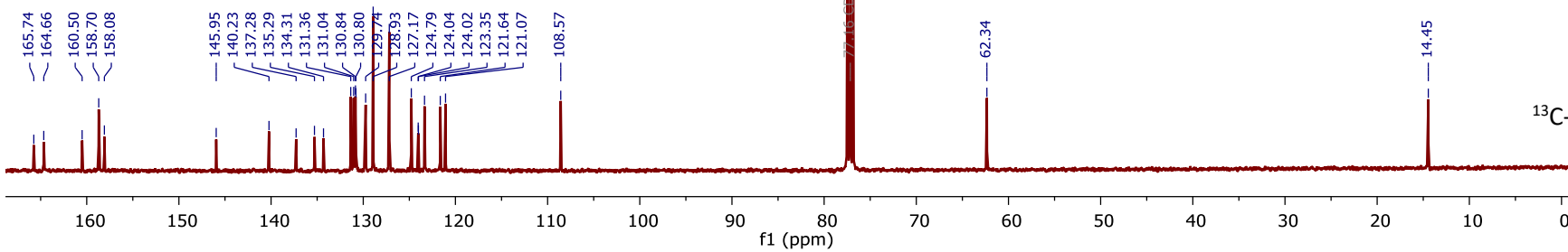
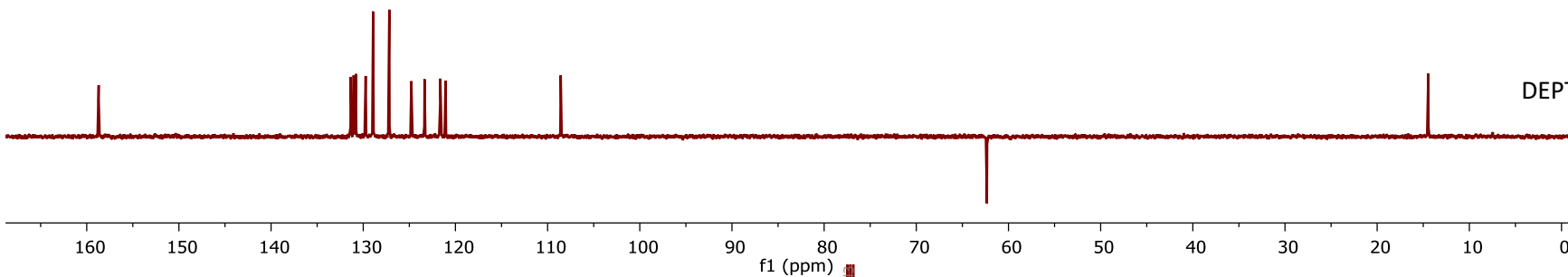
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
266.0844	266.0828	-6.08	2	83.09	C32H23ClN4O2	(M+2H)+2
266.5848	266.5843	-1.63	2	49.47	C32H23ClN4O2	(M+2H)+2
531.158	531.1582	0.49	1	1876.26	C32H23ClN4O2	(M+H)+
532.1624	532.1614	-1.92	1	648.25	C32H23ClN4O2	(M+H)+
533.1573	533.1569	-0.83	1	675.78	C32H23ClN4O2	(M+H)+
534.158	534.159	2.02	1	228.35	C32H23ClN4O2	(M+H)+
535.1643	535.1617	-4.83	1	53.32	C32H23ClN4O2	(M+H)+
553.1393	553.1402	1.65	1	133.97	C32H23ClN4O2	(M+Na)+
554.1487	554.1433	-9.71	1	35.44	C32H23ClN4O2	(M+Na)+
555.1365	555.1388	4.12	1	41.97	C32H23ClN4O2	(M+Na)+

IR

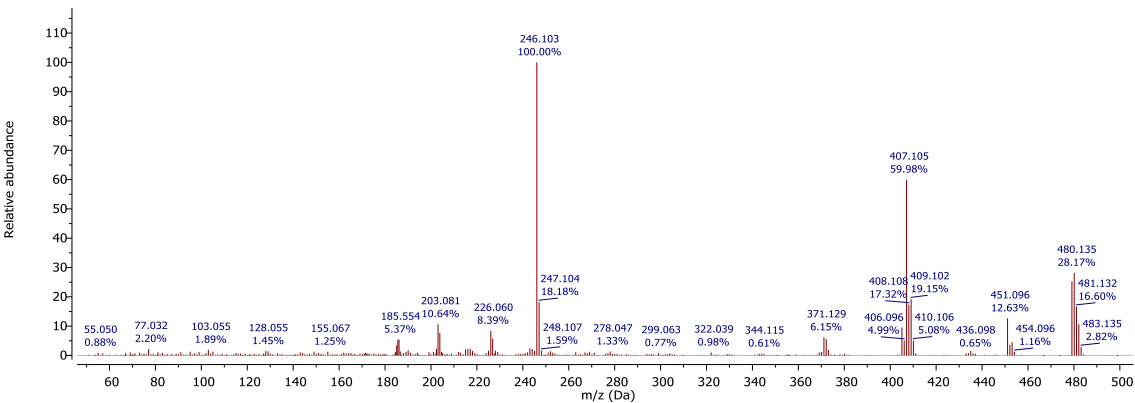


Compound 17c



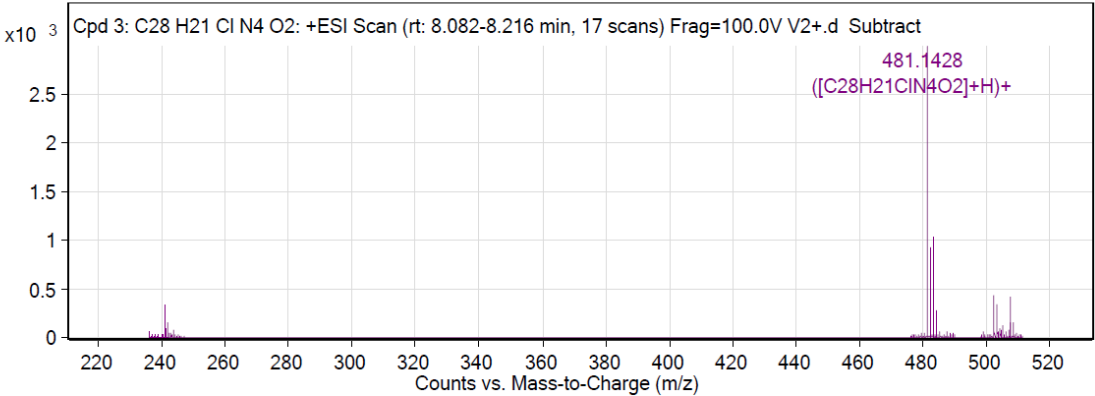


EI MS (70eV)



ESI-QTOF (positive ionization)

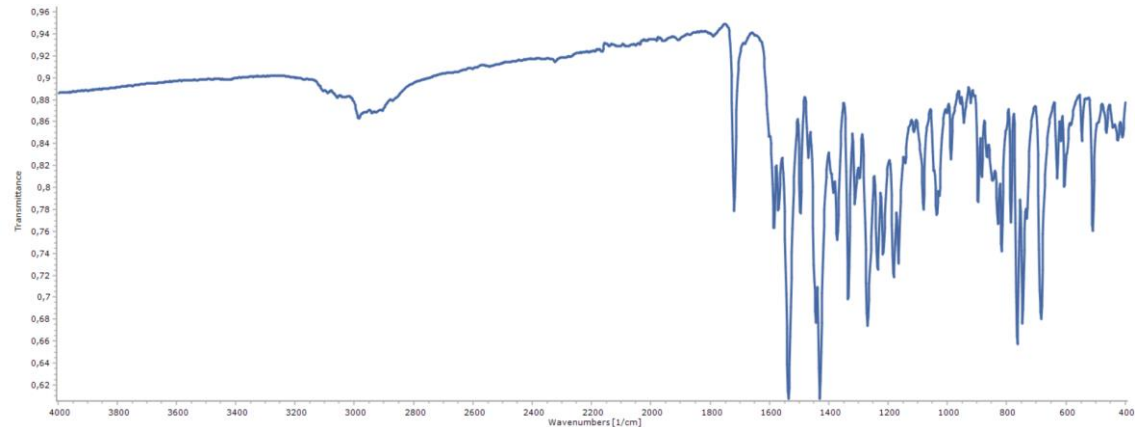
MS Zoomed Spectrum



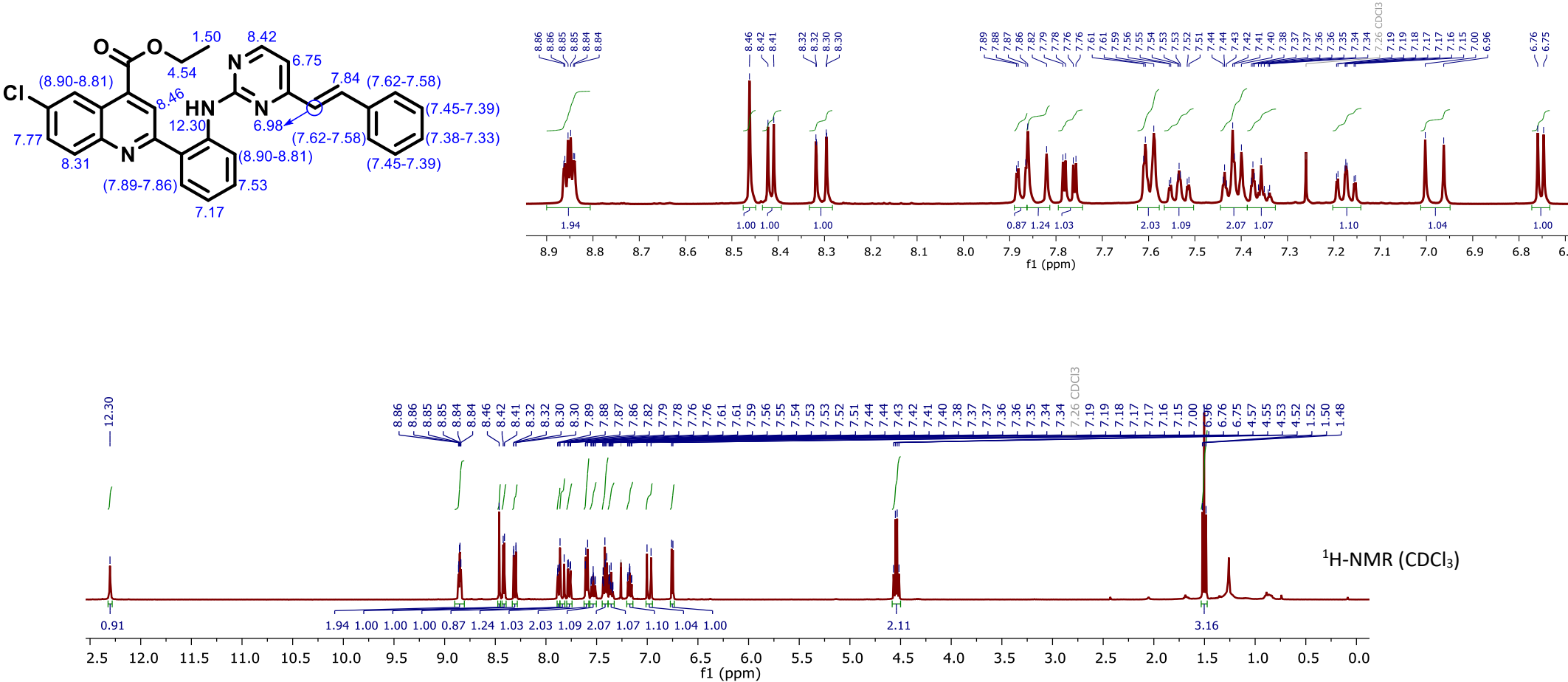
MS Spectrum Peak List

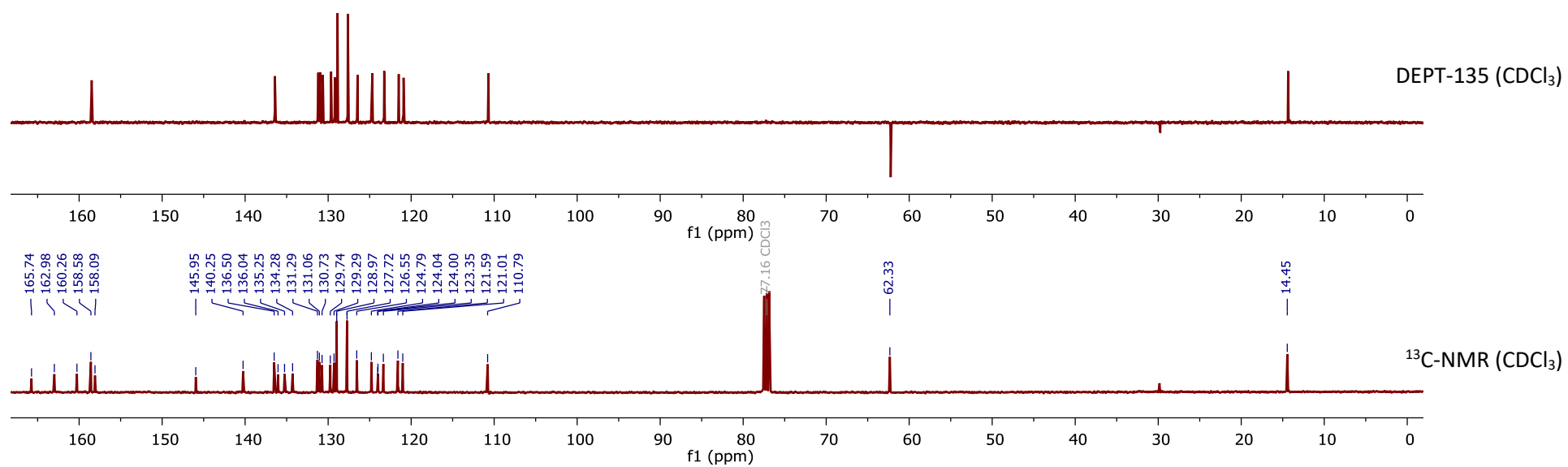
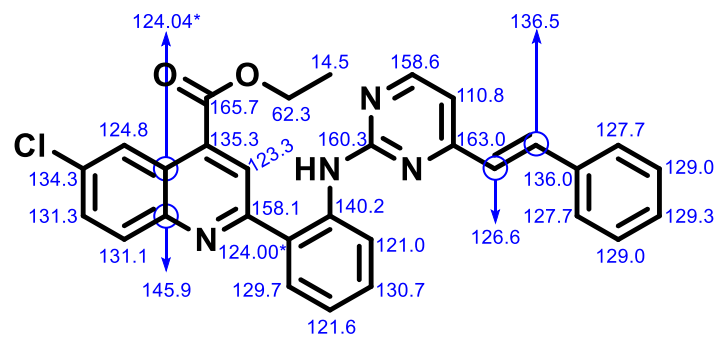
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
241.0747	241.0749	0.79	2	351.13	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+2H)+2
241.5762	241.5765	1.3	2	98.06	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+2H)+2
242.073	242.0741	4.54	2	167.99	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+2H)+2
481.1428	481.1426	-0.49	1	3019.39	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H)+
482.1458	482.1457	-0.29	1	921.27	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H)+
483.1411	483.1409	-0.29	1	1029.44	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H)+
484.1433	484.1432	-0.07	1	278.04	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+H)+
503.1234	503.1245	2.3	1	340.26	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+Na)+
504.125	504.1276	5.1	1	87.89	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+Na)+
505.1216	505.1229	2.44	1	118.29	C ₂₈ H ₂₁ ClN ₄ O ₂	(M+Na)+

IR

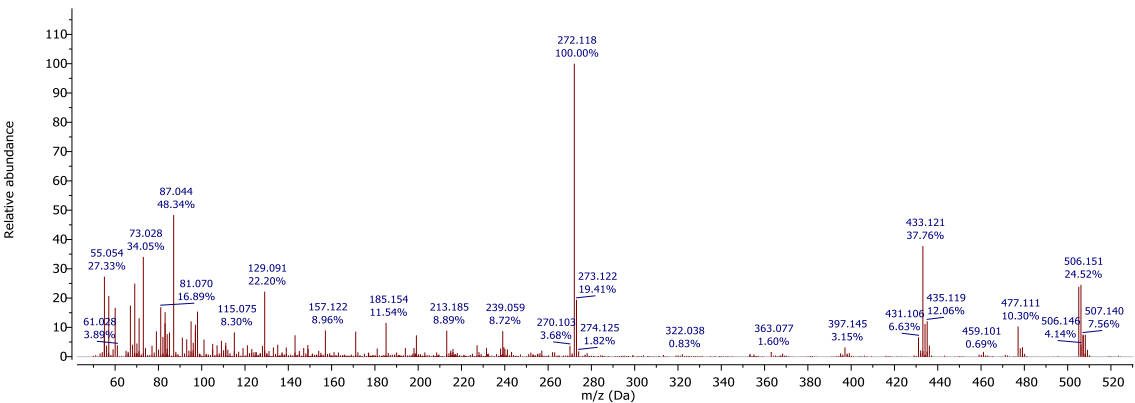


Compound 17d



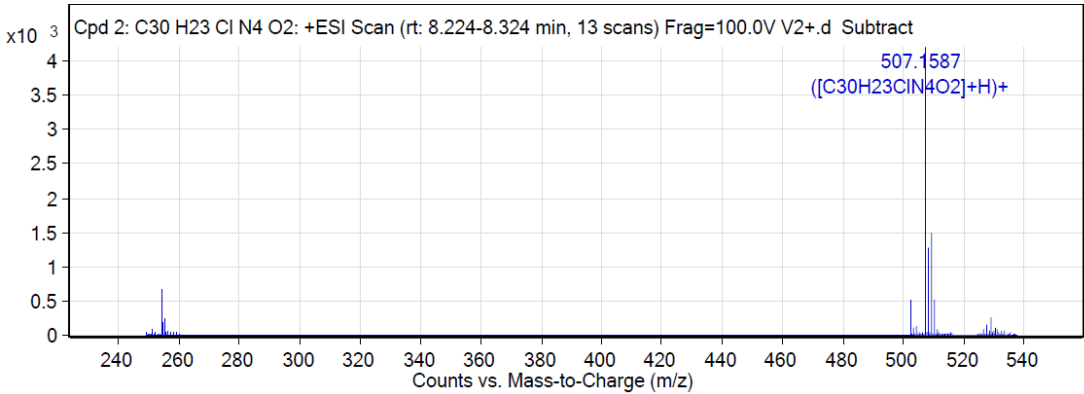


EI MS (70eV)



ESI-QTOF (positive ionization)

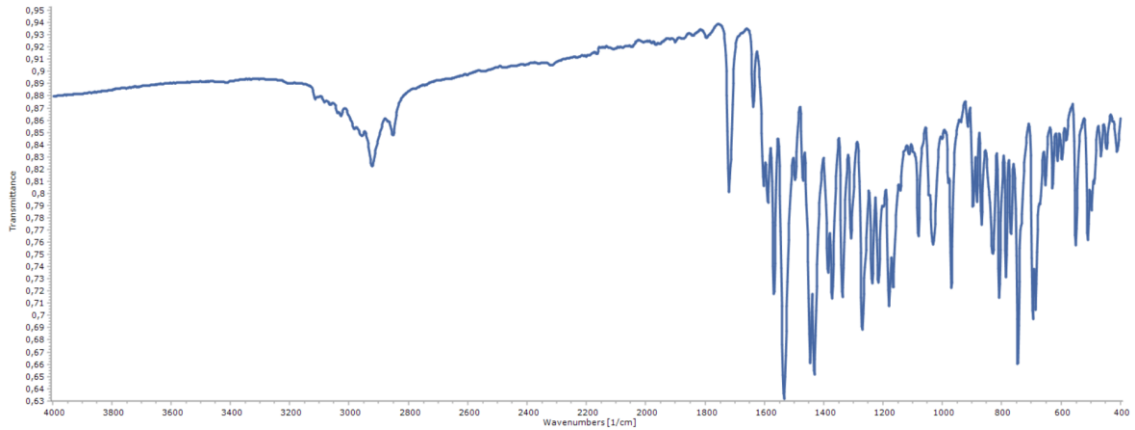
MS Zoomed Spectrum



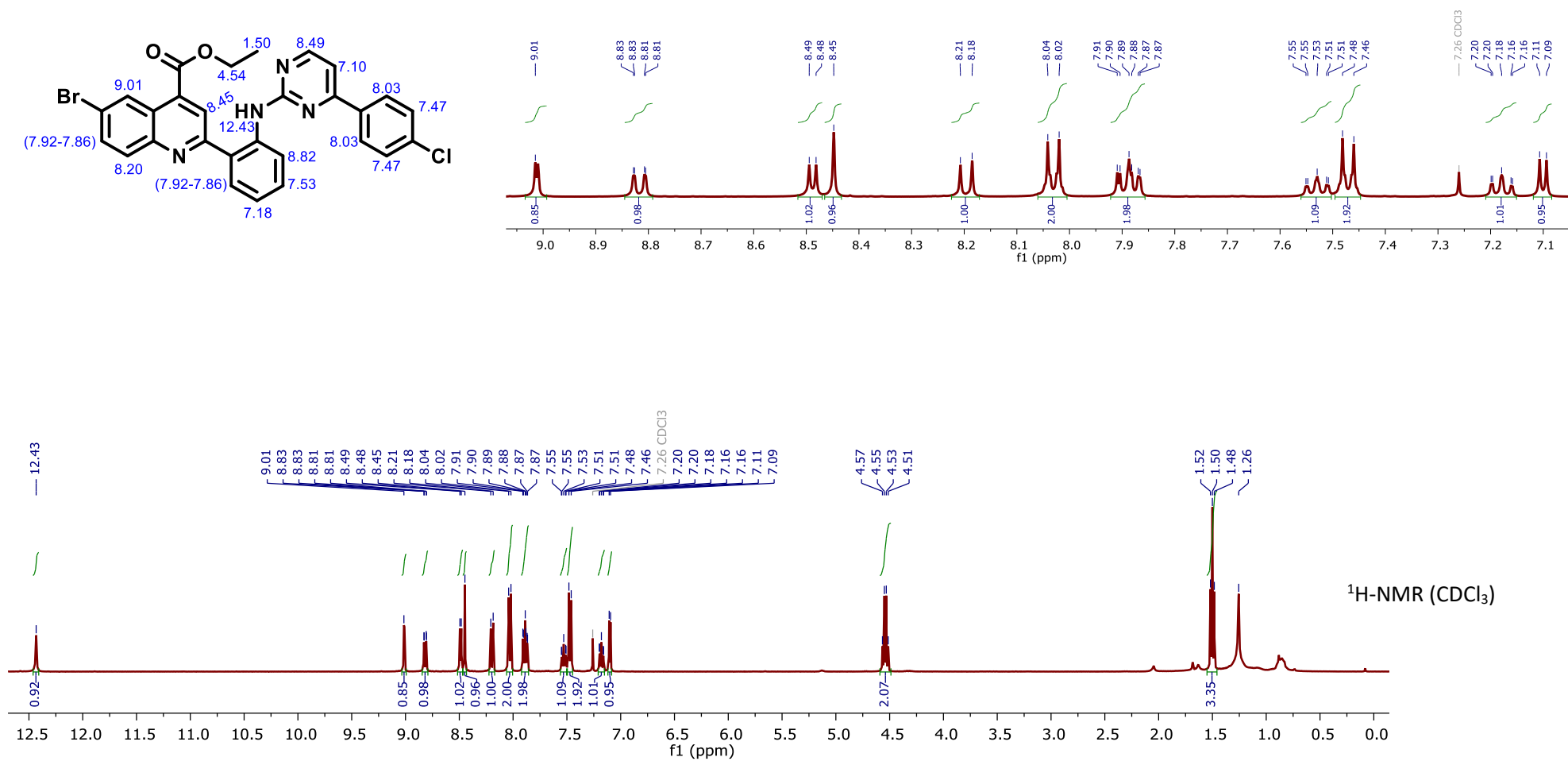
MS Spectrum Peak List

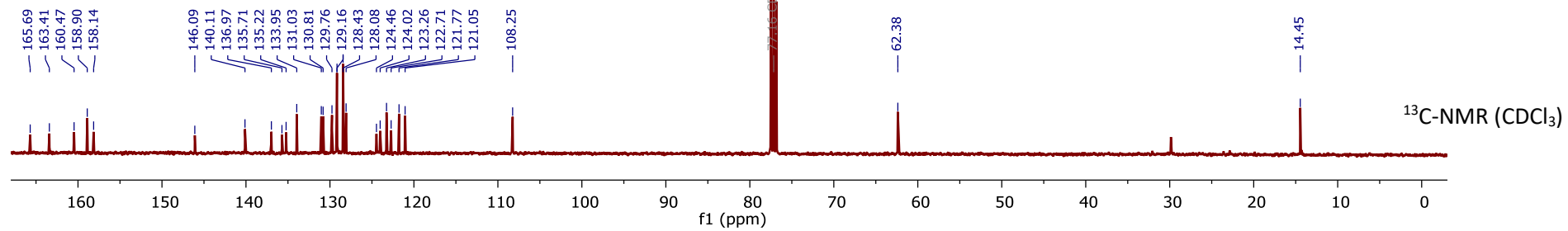
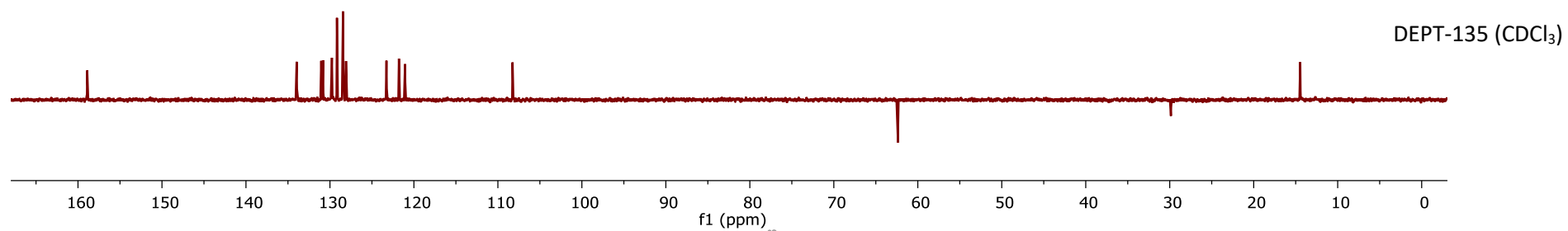
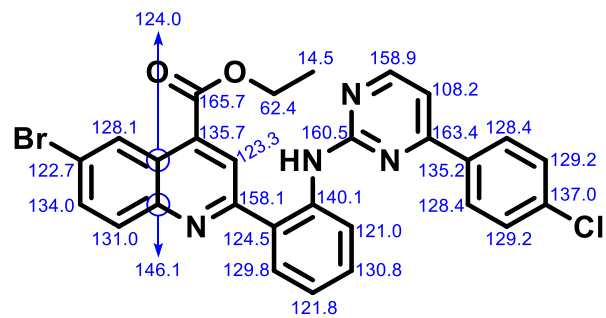
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
254.0823	254.0828	1.97	2	698	C ₃₀ H ₂₃ ClN ₄ O ₂	(M+2H)+2
254.585	254.5843	-2.84	2	197.81	C ₃₀ H ₂₃ ClN ₄ O ₂	(M+2H)+2
255.0822	255.082	-0.67	2	215.16	C ₃₀ H ₂₃ ClN ₄ O ₂	(M+2H)+2
507.1587	507.1582	-0.96	1	4194.85	C ₃₀ H ₂₃ ClN ₄ O ₂	(M+H)+
508.1616	508.1613	-0.52	1	1314.03	C ₃₀ H ₂₃ ClN ₄ O ₂	(M+H)+
509.157	509.1567	-0.58	1	1522	C ₃₀ H ₂₃ ClN ₄ O ₂	(M+H)+
510.1582	510.159	1.56	1	525.51	C ₃₀ H ₂₃ ClN ₄ O ₂	(M+H)+
511.1611	511.1617	1.2	1	90.95	C ₃₀ H ₂₃ ClN ₄ O ₂	(M+H)+
529.1405	529.1402	-0.61	1	264.16	C ₃₀ H ₂₃ ClN ₄ O ₂	(M+Na)+
531.141	531.1387	-4.47	1	97.29	C ₃₀ H ₂₃ ClN ₄ O ₂	(M+Na)+

IR

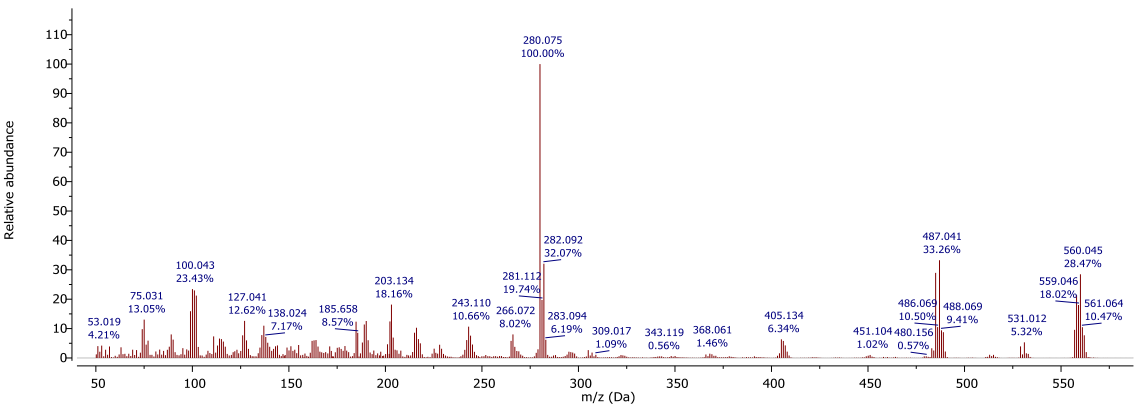


Compound **18a**



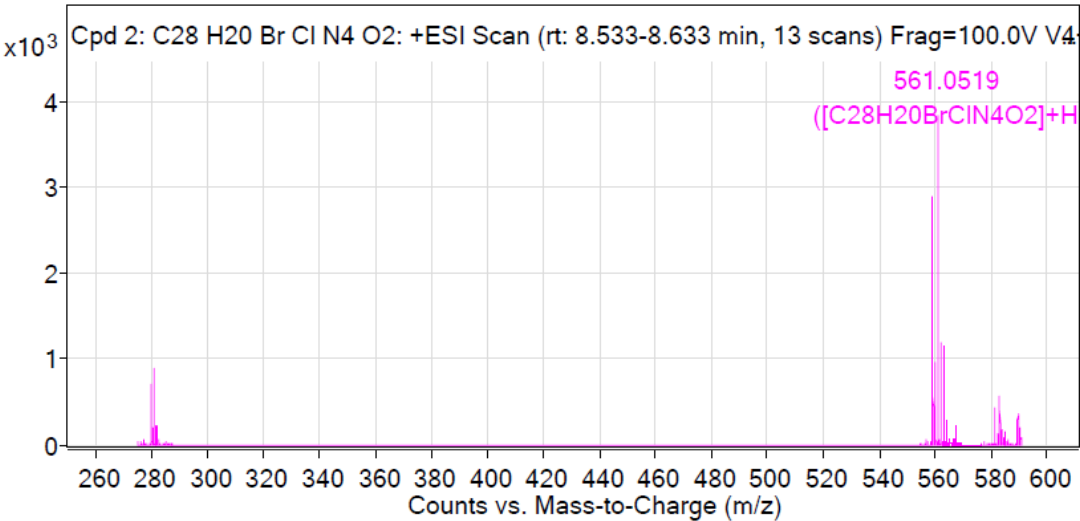


EI MS (70eV)



ESI-QTOF (positive ionization)

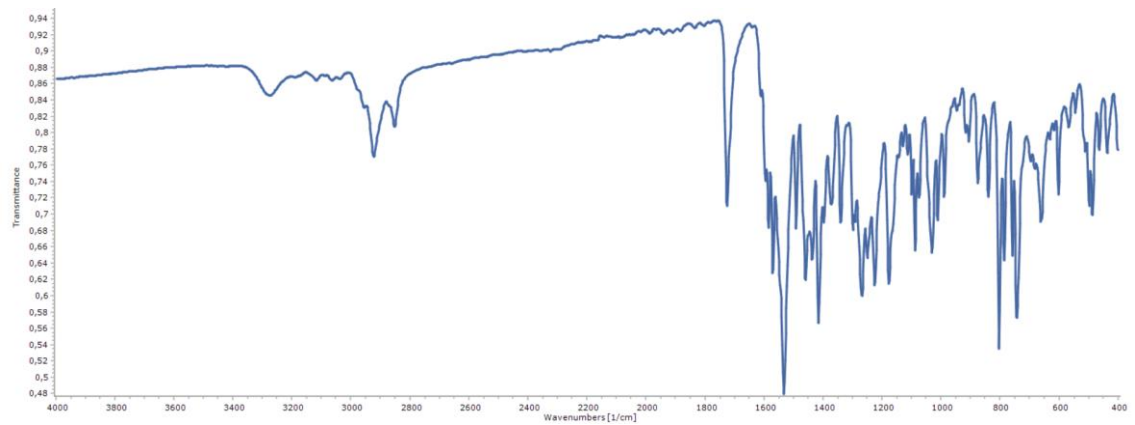
MS Zoomed Spectrum



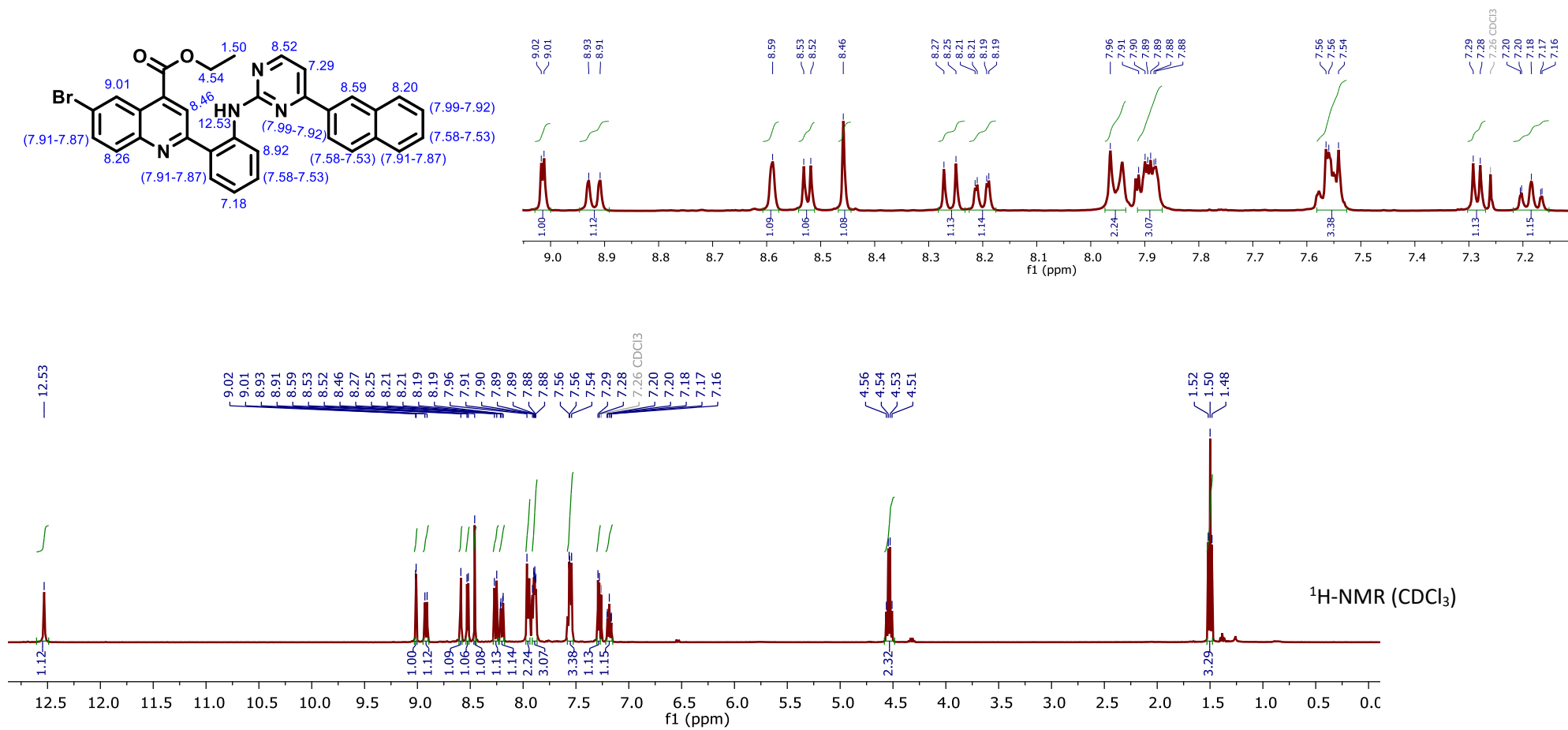
MS Spectrum Peak List

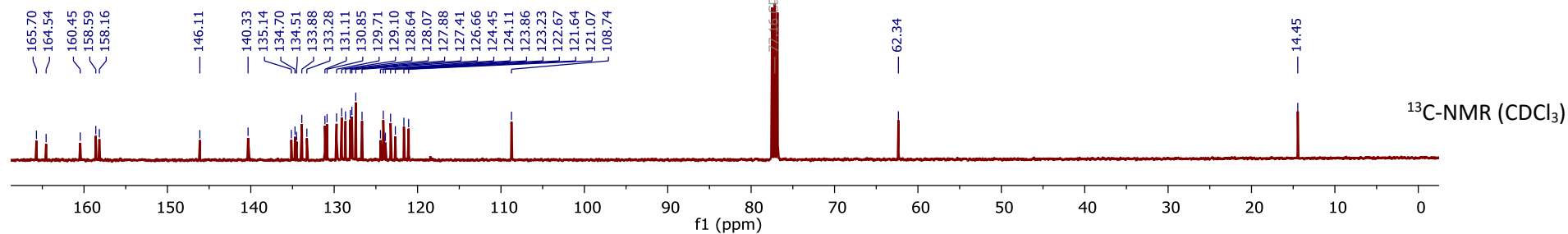
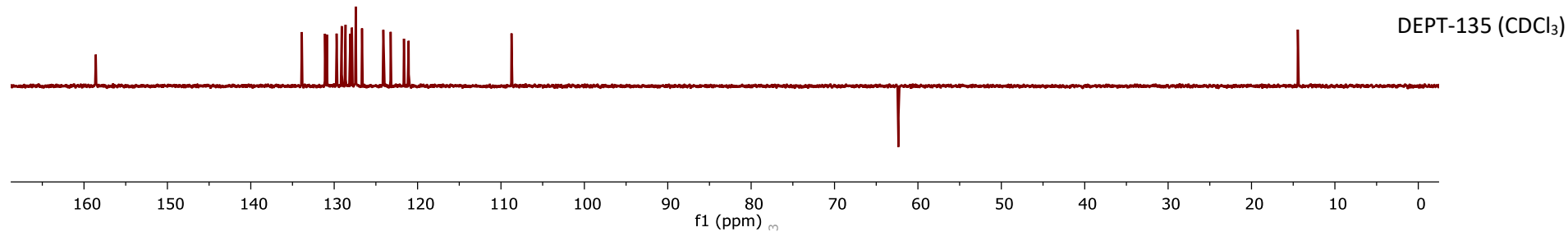
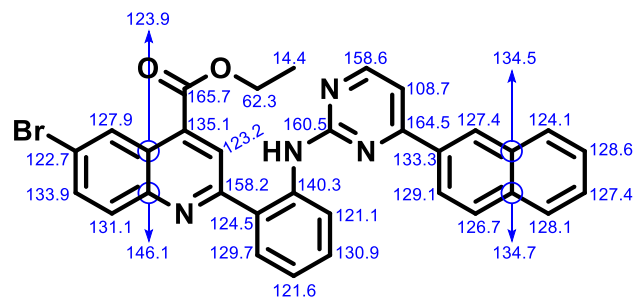
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
280.0303	280.0302	-0.41	2	710.43	C ₂₈ H ₂₀ BrClN ₄ O ₂	(M+2H)+2
281.0294	281.0292	-0.5	2	905.43	C ₂₈ H ₂₀ BrClN ₄ O ₂	(M+2H)+2
559.053	559.0531	0.1	1	2964.42	C ₂₈ H ₂₀ BrClN ₄ O ₂	(M+H)+
560.0554	560.0562	1.33	1	986.36	C ₂₈ H ₂₀ BrClN ₄ O ₂	(M+H)+
561.0519	561.0512	-1.37	1	3902.9	C ₂₈ H ₂₀ BrClN ₄ O ₂	(M+H)+
562.0535	562.054	0.92	1	1190.65	C ₂₈ H ₂₀ BrClN ₄ O ₂	(M+H)+
563.0493	563.0497	0.66	1	1154.18	C ₂₈ H ₂₀ BrClN ₄ O ₂	(M+H)+
564.0516	564.0518	0.34	1	313.9	C ₂₈ H ₂₀ BrClN ₄ O ₂	(M+H)+
581.0343	581.035	1.31	1	436.42	C ₂₈ H ₂₀ BrClN ₄ O ₂	(M+Na)+
583.0332	583.0331	-0.16	1	578.74	C ₂₈ H ₂₀ BrClN ₄ O ₂	(M+Na)+

IR

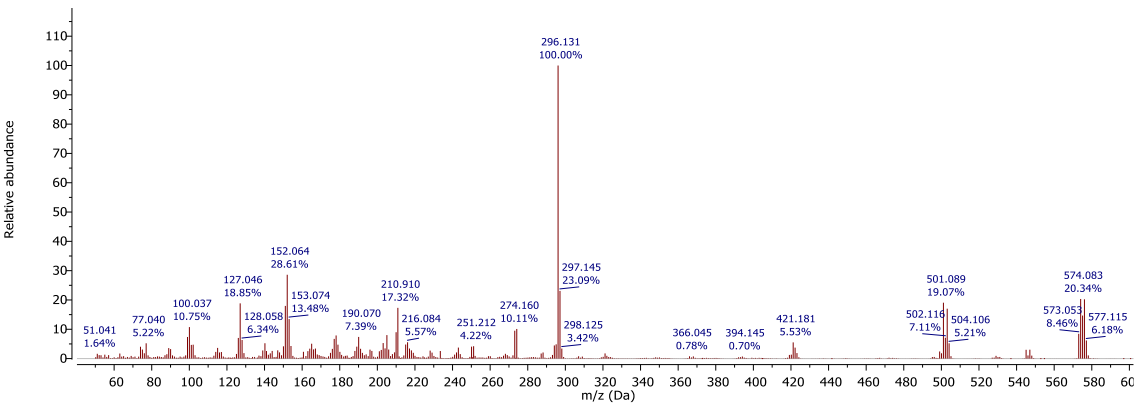


Compound **18b**



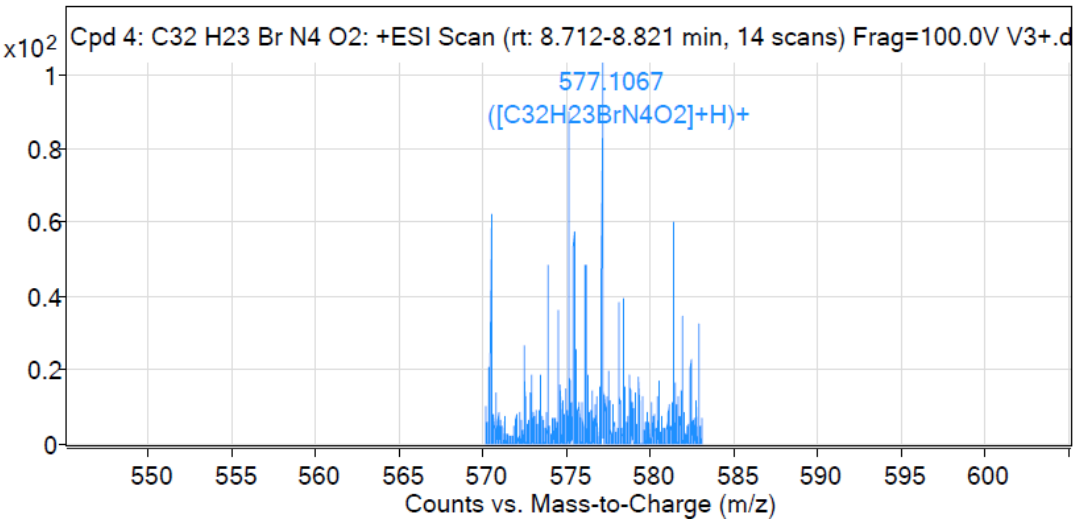


EI MS (70eV)



ESI-QTOF (positive ionization)

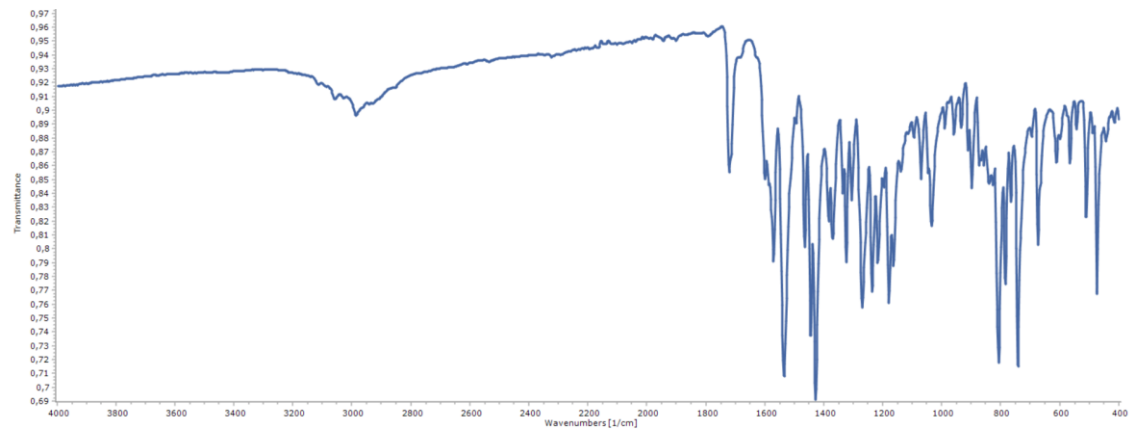
MS Zoomed Spectrum



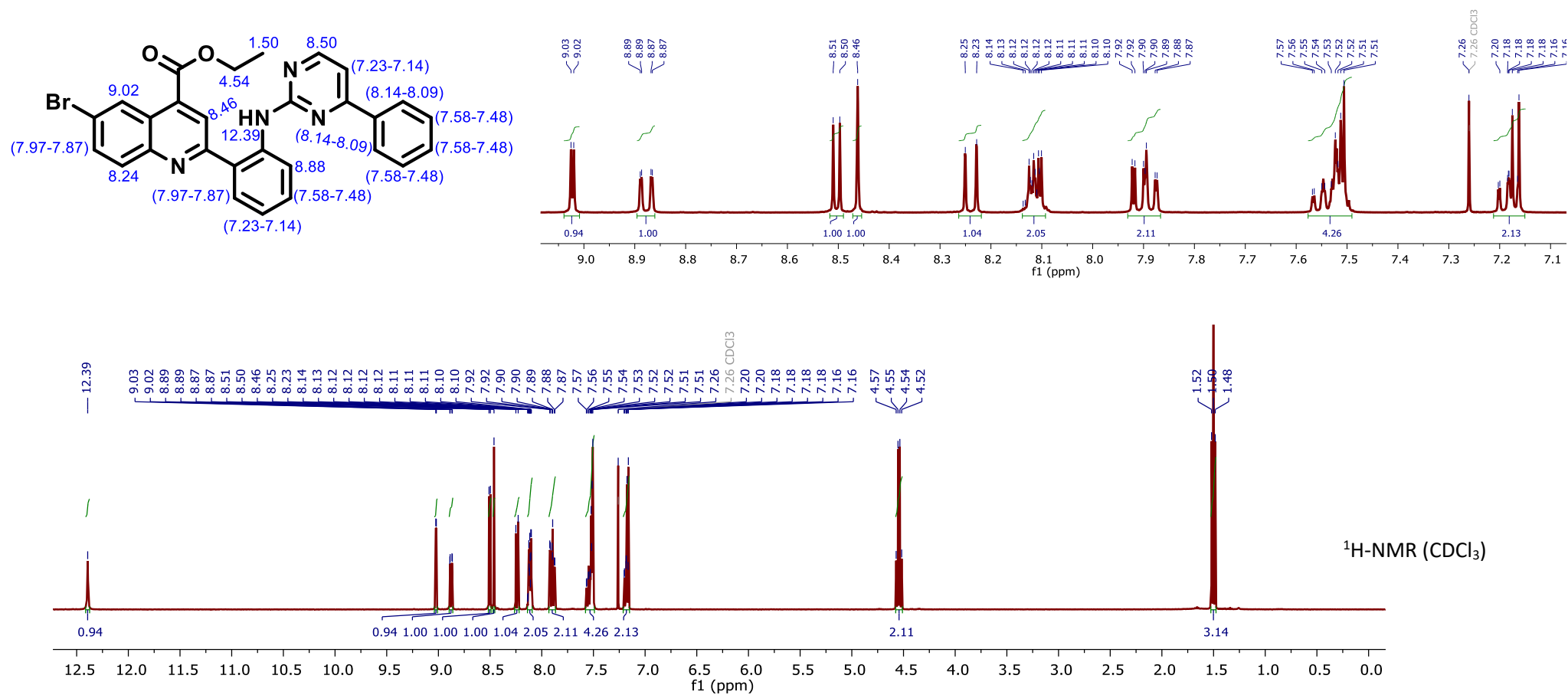
MS Spectrum Peak List

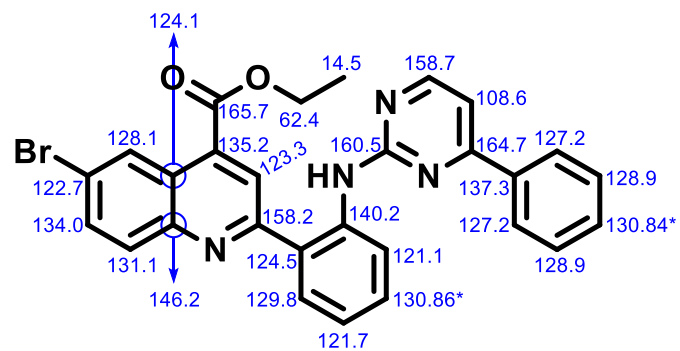
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
575.1075	575.1077	0.45	1	90.95	C ₃₂ H ₂₃ BrN ₄ O ₂	(M+H)+
576.1155	576.1108	-8.1	1	49.22	C ₃₂ H ₂₃ BrN ₄ O ₂	(M+H)+
577.1067	577.1062	-0.87	1	106.68	C ₃₂ H ₂₃ BrN ₄ O ₂	(M+H)+
578.104	578.109	8.57	1	39.53	C ₃₂ H ₂₃ BrN ₄ O ₂	(M+H)+

IR

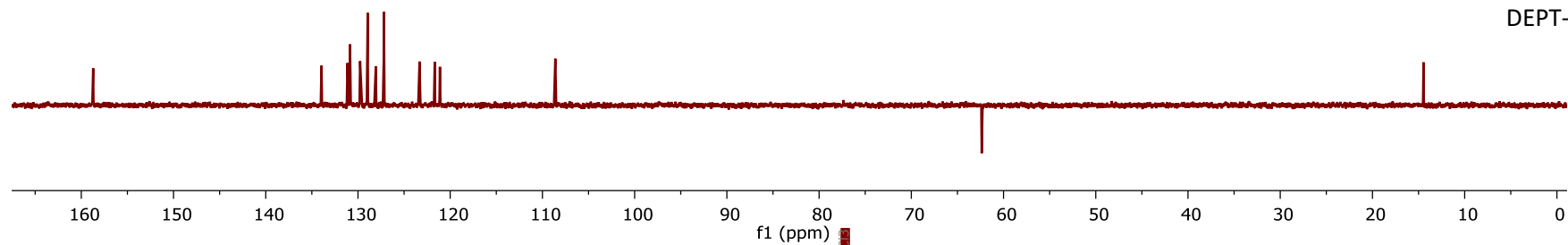


Compound 18c

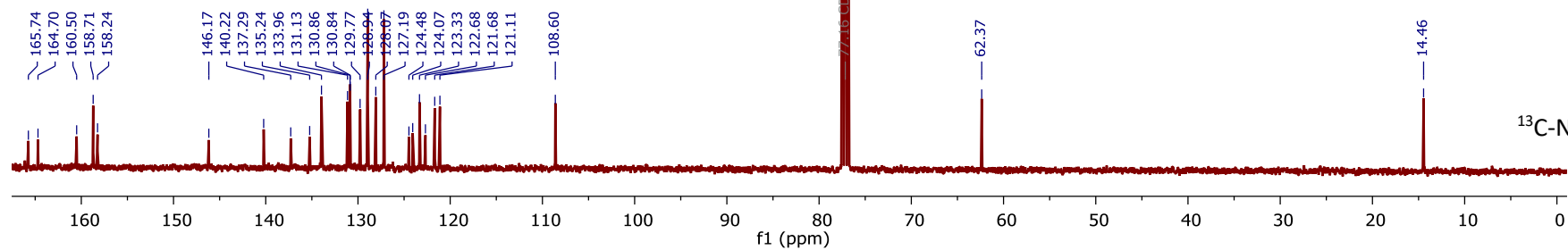




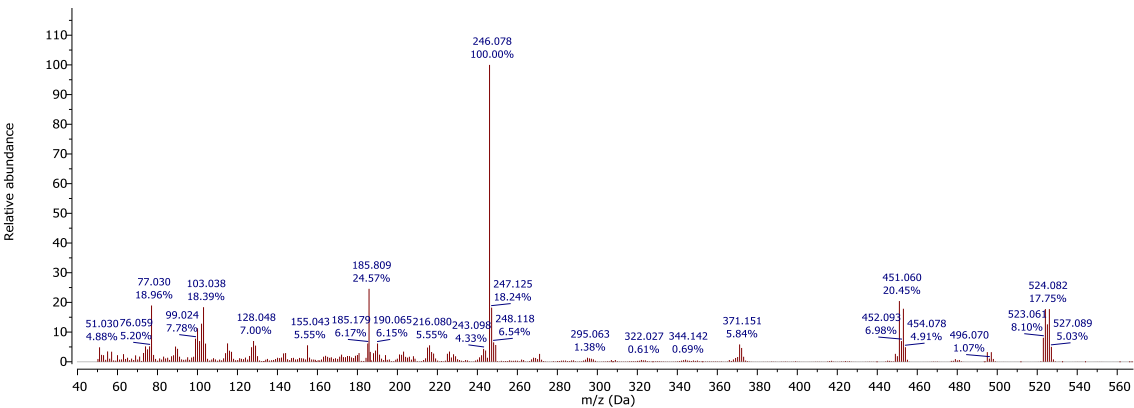
DEPT-135 (CDCl_3)



^{13}C -NMR (CDCl_3)

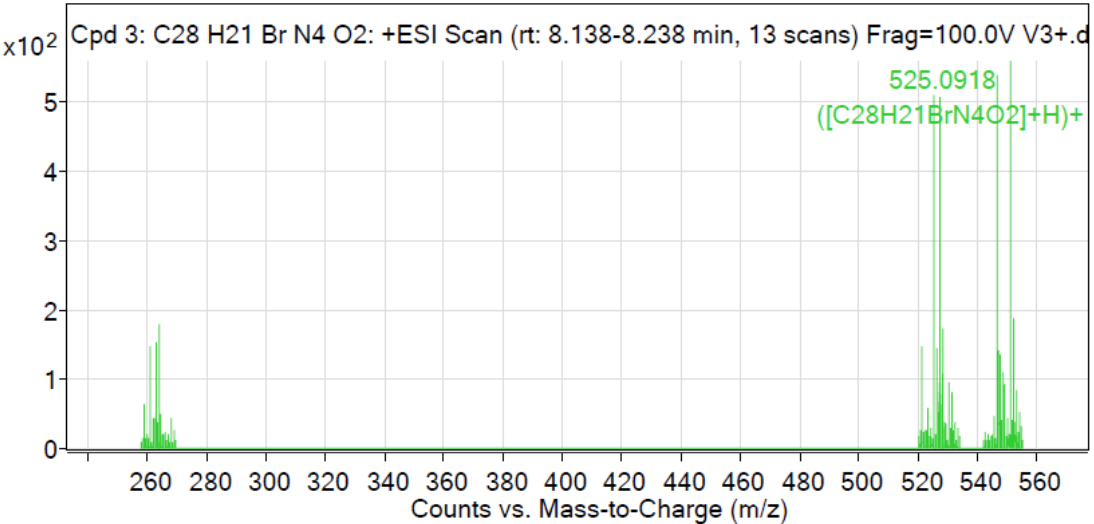


EI MS (70eV)



ESI-QTOF (positive ionization)

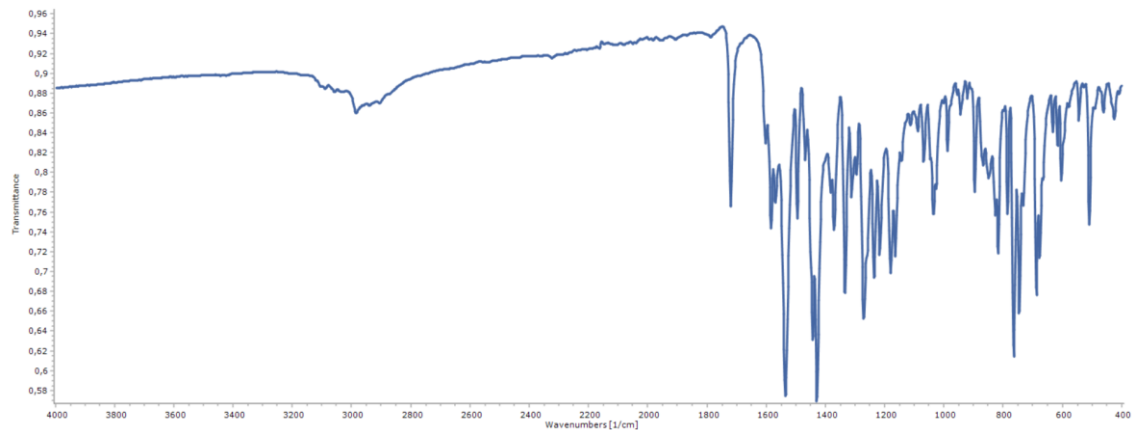
MS Zoomed Spectrum



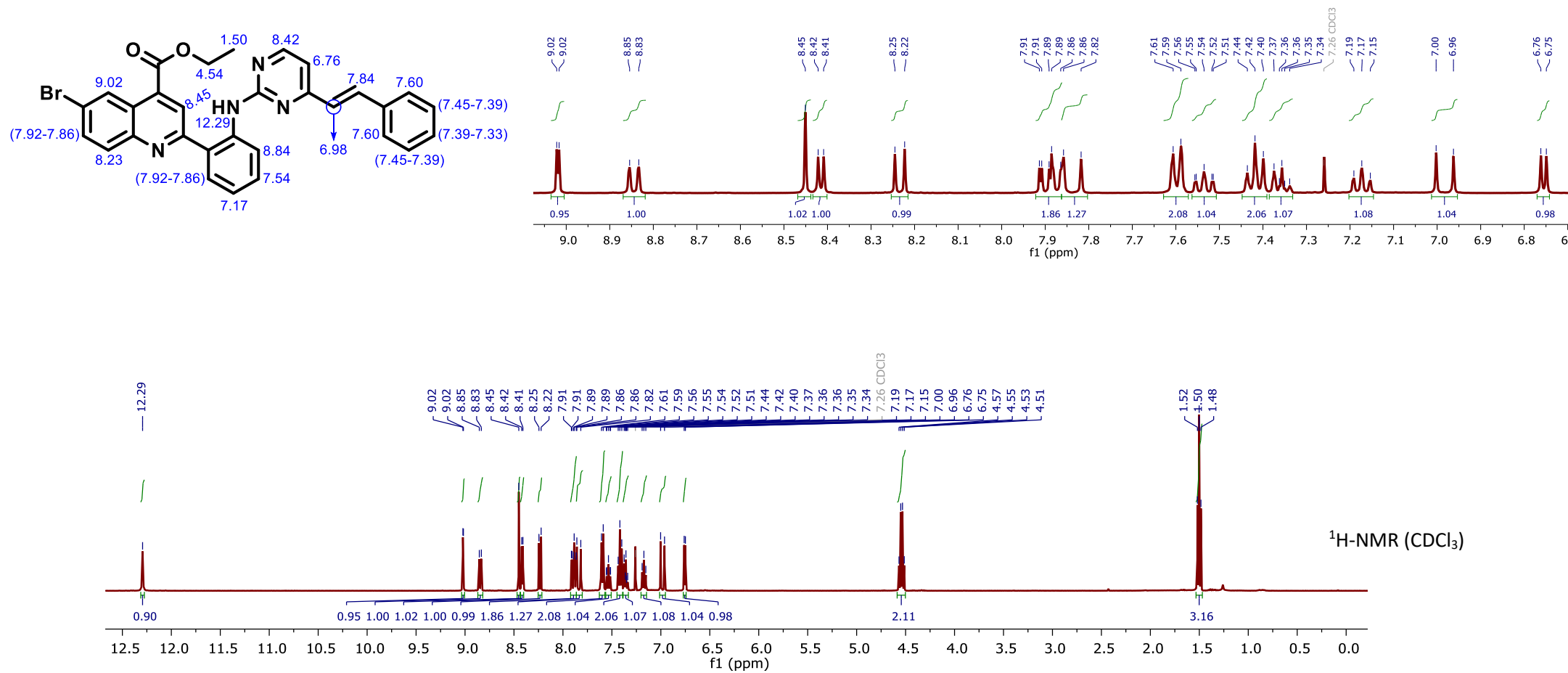
MS Spectrum Peak List

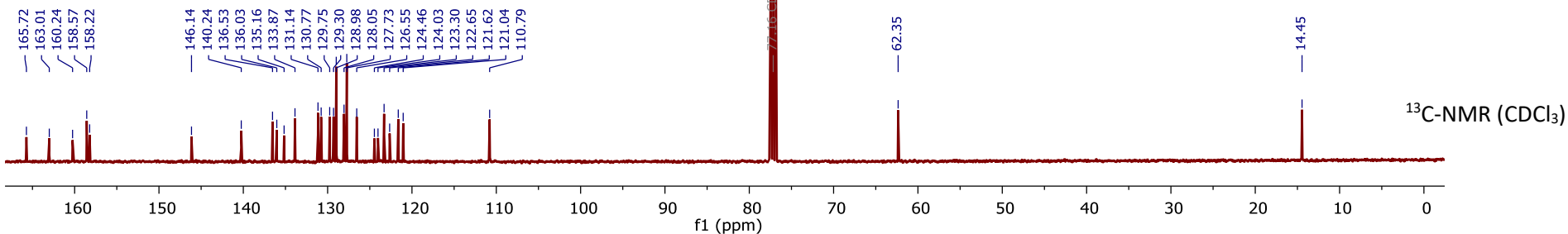
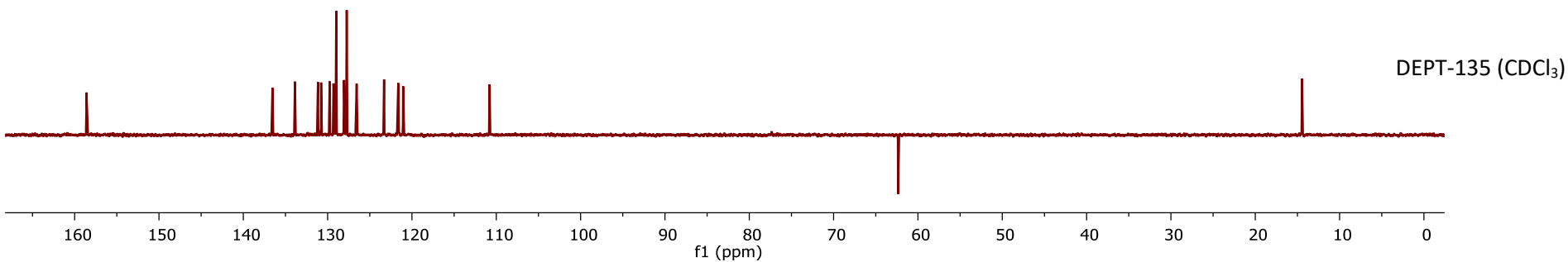
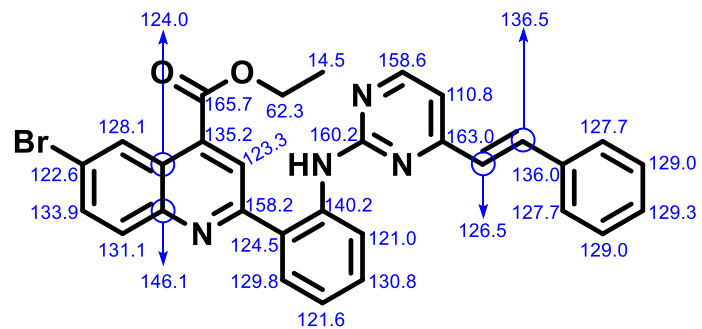
m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
263.0489	263.0497	2.95	2	152.08	C ₂₈ H ₂₁ BrN ₄ O ₂	(M+2H)+2
264.0483	264.0489	2.25	2	180.29	C ₂₈ H ₂₁ BrN ₄ O ₂	(M+2H)+2
264.5542	264.5503	-14.99	2	48.69	C ₂₈ H ₂₁ BrN ₄ O ₂	(M+2H)+2
525.0918	525.0921	0.57	1	515.22	C ₂₈ H ₂₁ BrN ₄ O ₂	(M+H)+
526.0949	526.0952	0.46	1	145.53	C ₂₈ H ₂₁ BrN ₄ O ₂	(M+H)+
527.0899	527.0904	0.99	1	508.34	C ₂₈ H ₂₁ BrN ₄ O ₂	(M+H)+
528.0919	528.0933	2.68	1	178.83	C ₂₈ H ₂₁ BrN ₄ O ₂	(M+H)+
547.0758	547.074	-3.31	1	141.71	C ₂₈ H ₂₁ BrN ₄ O ₂	(M+Na)+
549.0754	549.0724	-5.44	1	92.4	C ₂₈ H ₂₁ BrN ₄ O ₂	(M+Na)+
550.0731	550.0752	3.83	1	44.81	C ₂₈ H ₂₁ BrN ₄ O ₂	(M+Na)+

IR

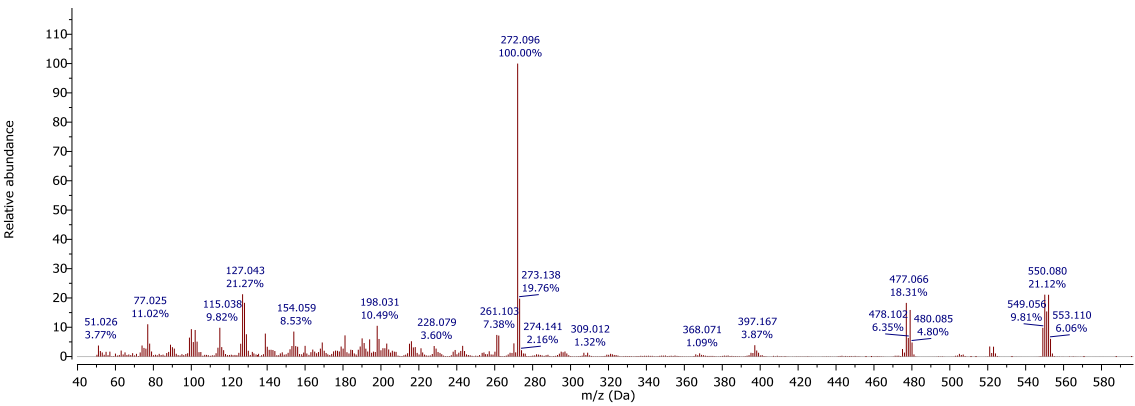


Compound **18d**



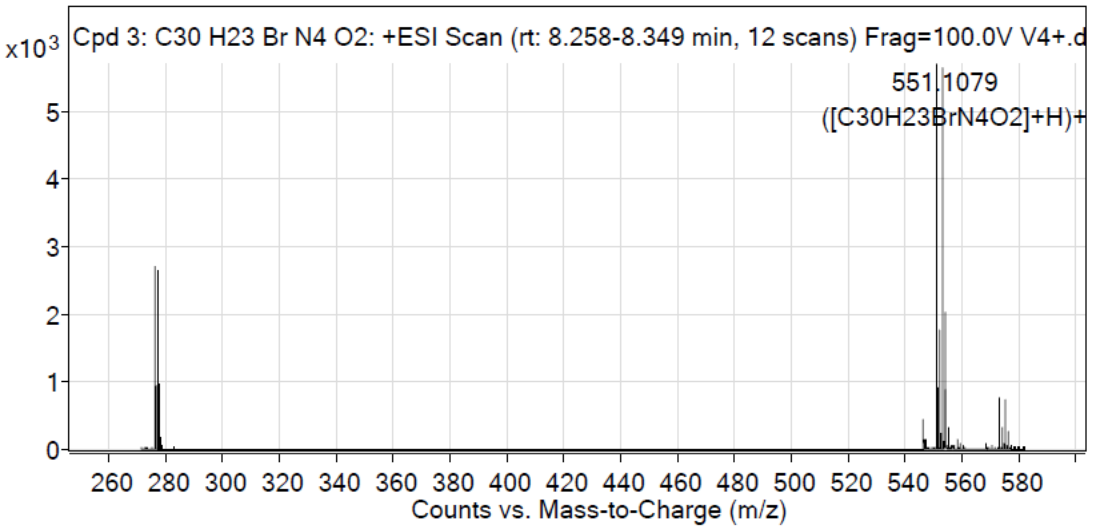


EI MS (70eV)



ESI-QTOF (positive ionization)

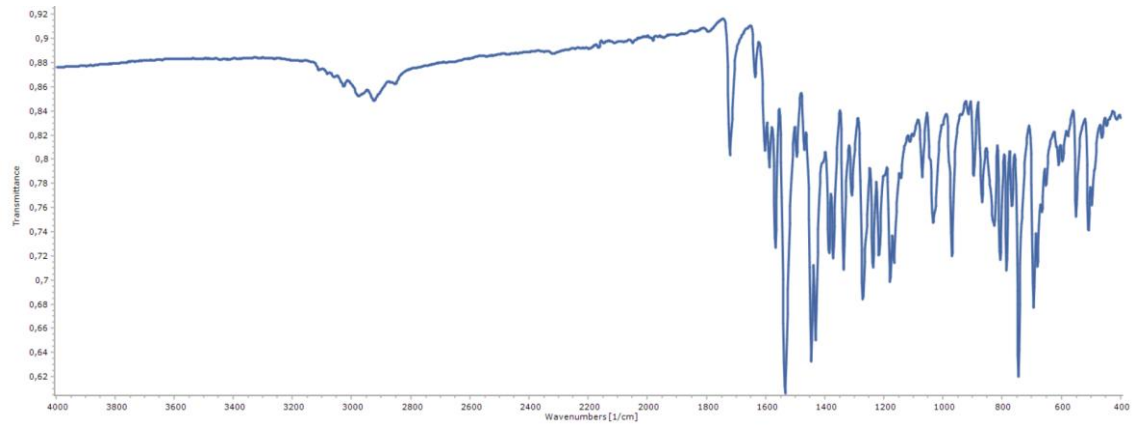
MS Zoomed Spectrum



MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
276.0575	276.0575	-0.04	2	2698.16	C ₃₀ H ₂₃ BrN ₄ O ₂	(M+2H)+2
276.5592	276.5591	-0.6	2	953.46	C ₃₀ H ₂₃ BrN ₄ O ₂	(M+2H)+2
277.0567	277.0567	0.1	2	2748.94	C ₃₀ H ₂₃ BrN ₄ O ₂	(M+2H)+2
277.5581	277.5581	-0.1	2	984.77	C ₃₀ H ₂₃ BrN ₄ O ₂	(M+2H)+2
551.1079	551.1077	-0.3	1	5713.22	C ₃₀ H ₂₃ BrN ₄ O ₂	(M+H)+
552.1117	552.1108	-1.56	1	1802.24	C ₃₀ H ₂₃ BrN ₄ O ₂	(M+H)+
553.1063	553.1061	-0.22	1	5708.04	C ₃₀ H ₂₃ BrN ₄ O ₂	(M+H)+
554.1096	554.109	-1.16	1	2043.45	C ₃₀ H ₂₃ BrN ₄ O ₂	(M+H)+
573.0888	573.0897	1.56	1	764.8	C ₃₀ H ₂₃ BrN ₄ O ₂	(M+Na)+
575.0882	575.0881	-0.13	1	753.29	C ₃₀ H ₂₃ BrN ₄ O ₂	(M+Na)+

IR



3. Biological assays

3.1. LDHA dose-response inhibition curves

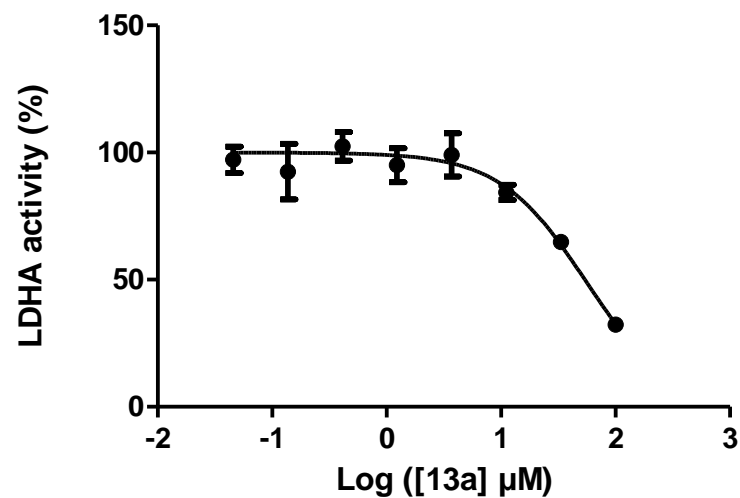


Figure S33. LDHA inhibition curve of compound **13a** (mean \pm SD of $n = 3$ replicates)

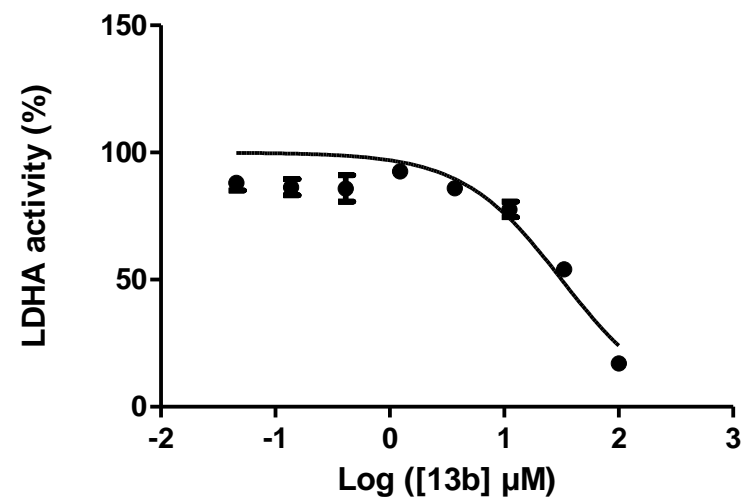


Figure S34. LDHA inhibition curve of compound **13b** (mean \pm SD of $n = 3$ replicates)

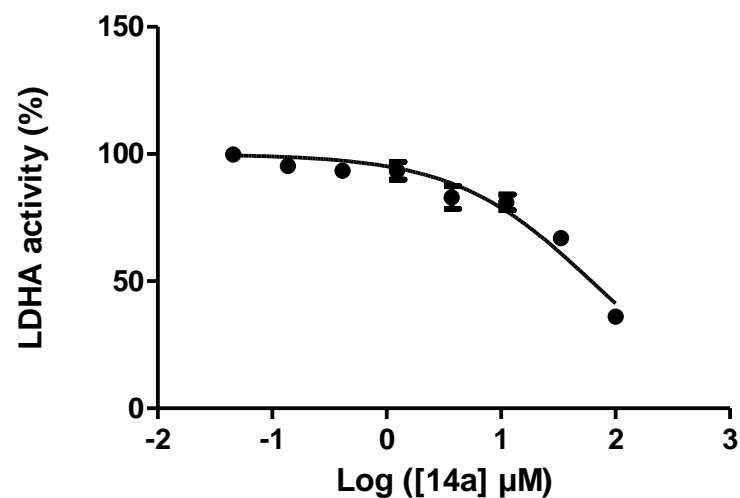


Figure S35. LDHA inhibition curve of compound **14a** (mean \pm SD of $n = 3$ replicates)

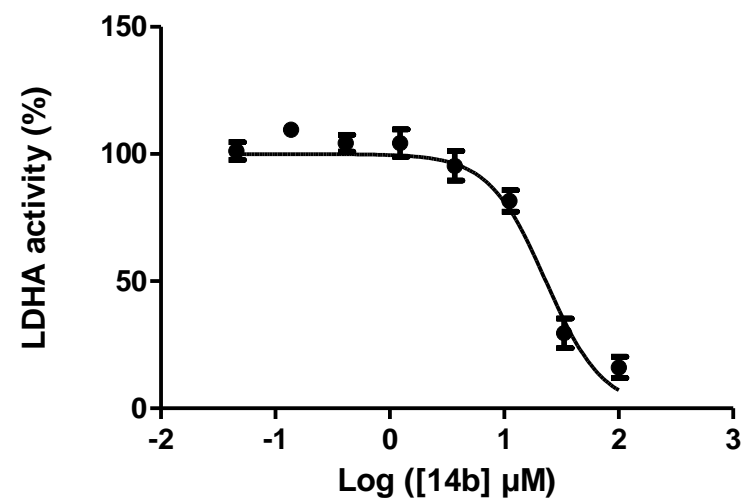


Figure S36. LDHA inhibition curve of compound **14b** (mean \pm SD of $n = 3$ replicates)

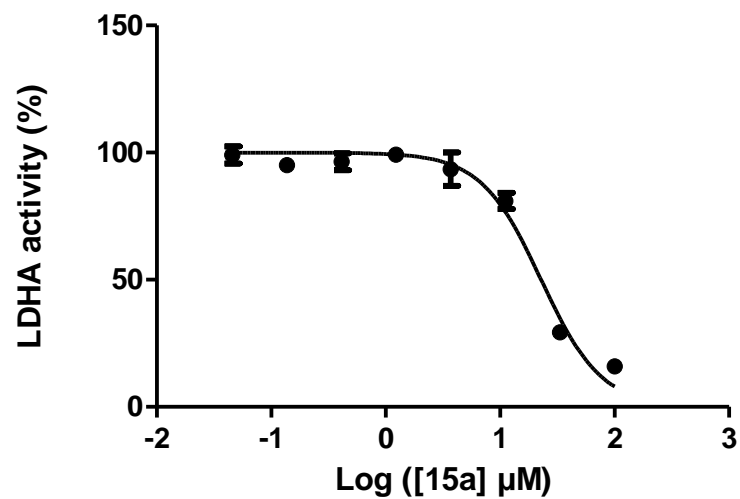


Figure S37. LDHA inhibition curve of compound **15a** (mean \pm SD of $n = 3$ replicates)

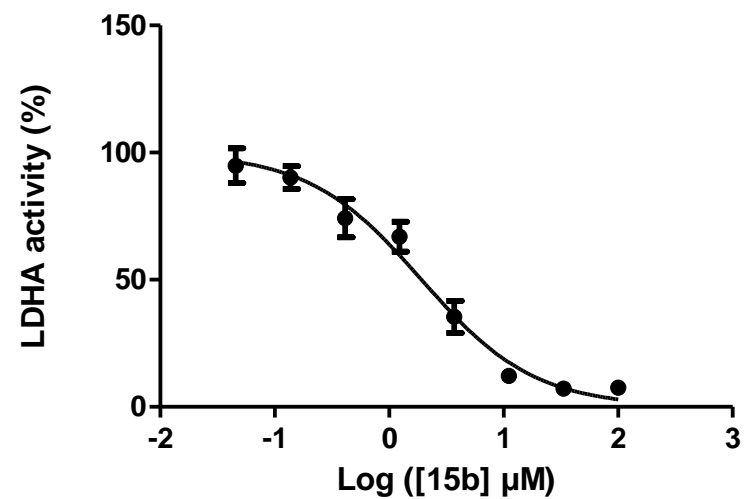


Figure S38. LDHA inhibition curve of compound **15b** (mean \pm SD of $n = 3$ replicates)

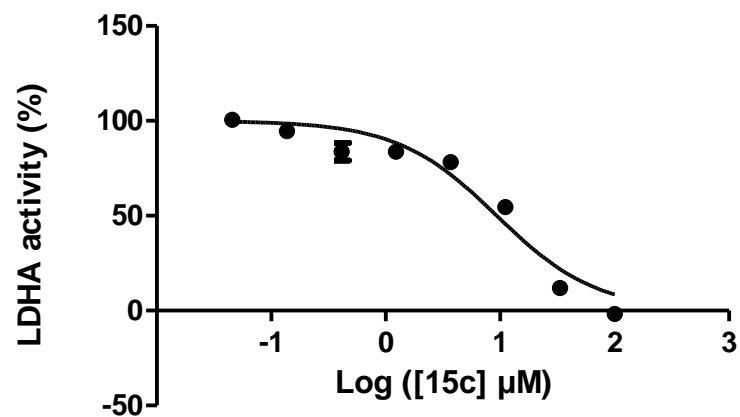


Figure S39. LDHA inhibition curve of compound **15c** (mean \pm SD of $n = 3$ replicates)

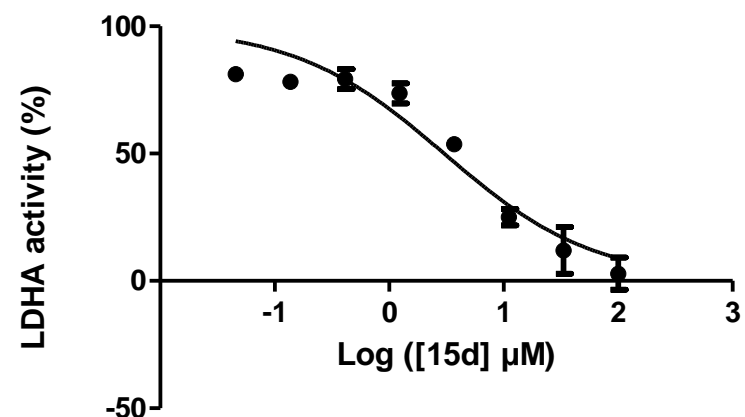


Figure S40. LDHA inhibition curve of compound **15d** (mean \pm SD of $n = 3$ replicates)

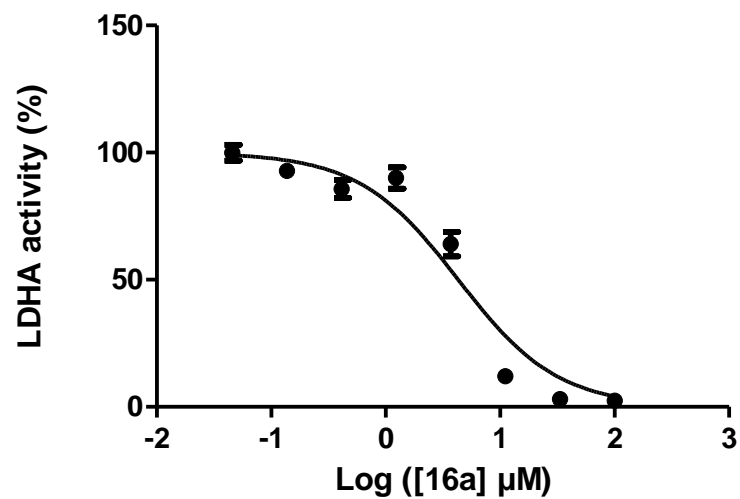


Figure S41. LDHA inhibition curve of compound **16a** (mean \pm SD of $n = 3$ replicates)

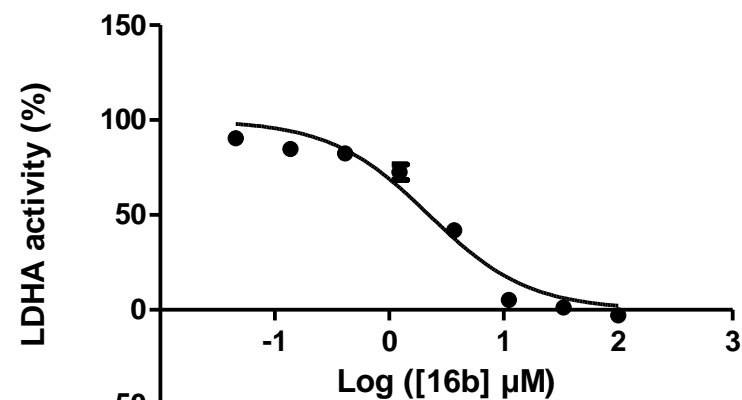


Figure S42. LDHA inhibition curve of compound **16b** (mean \pm SD of $n = 3$ replicates)

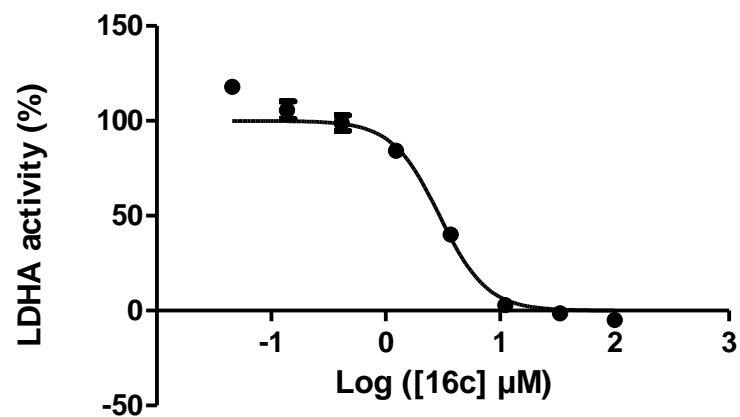


Figure S43. LDHA inhibition curve of compound **16c** (mean \pm SD of $n = 3$ replicates)

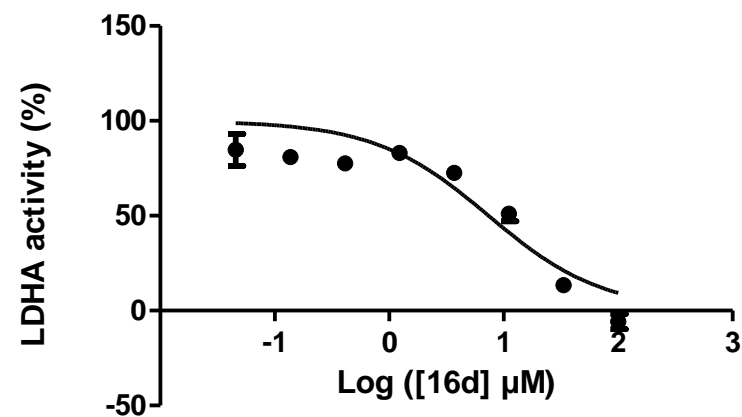


Figure S44. LDHA inhibition curve of compound **16d** (mean \pm SD of $n = 3$ replicates)

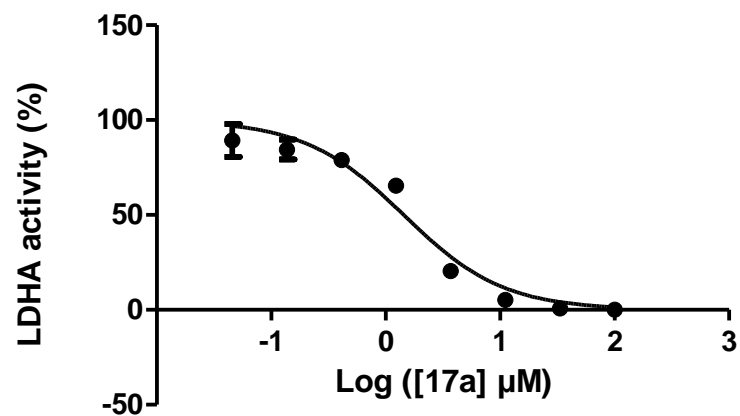


Figure S45. LDHA inhibition curve of compound **17a** (mean \pm SD of $n = 3$ replicates)

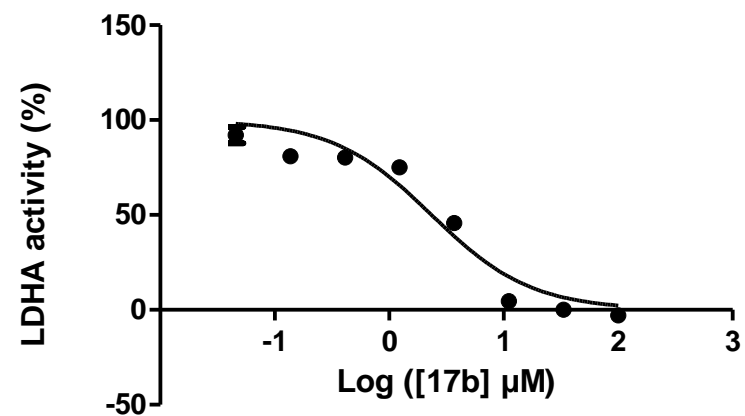


Figure S46. LDHA inhibition curve of compound **17b** (mean \pm SD of $n = 3$ replicates)

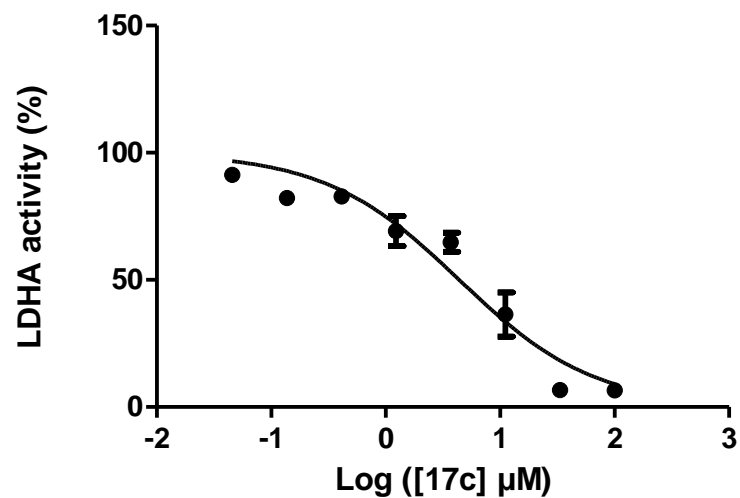


Figure S47. LDHA inhibition curve of compound **17c** (mean \pm SD of $n = 3$ replicates)

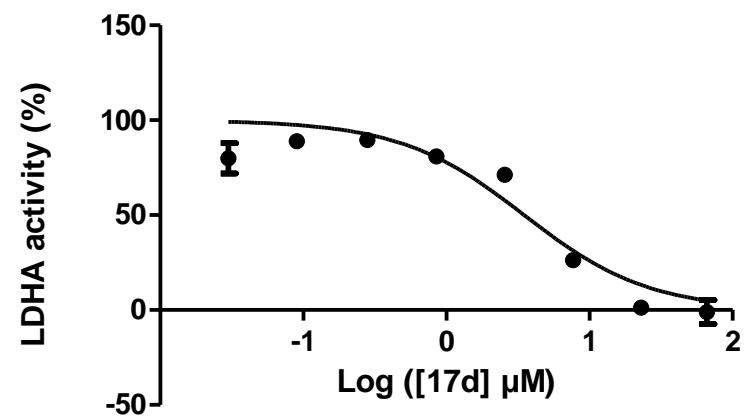


Figure S48. LDHA inhibition curve of compound **17d** (mean \pm SD of $n = 3$ replicates)

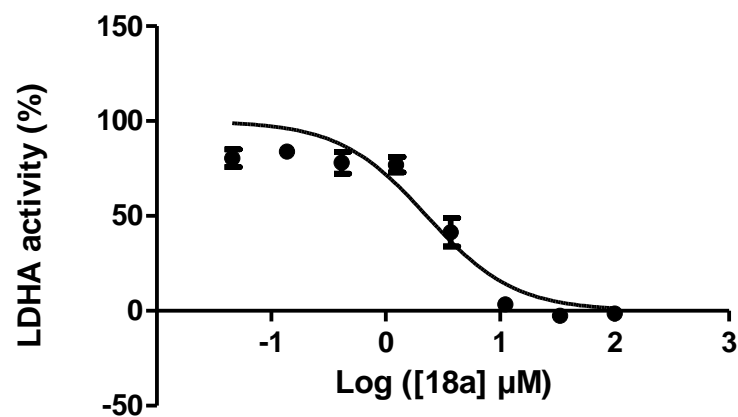


Figure S49. LDHA inhibition curve of compound **18a** (mean \pm SD of $n = 3$ replicates)

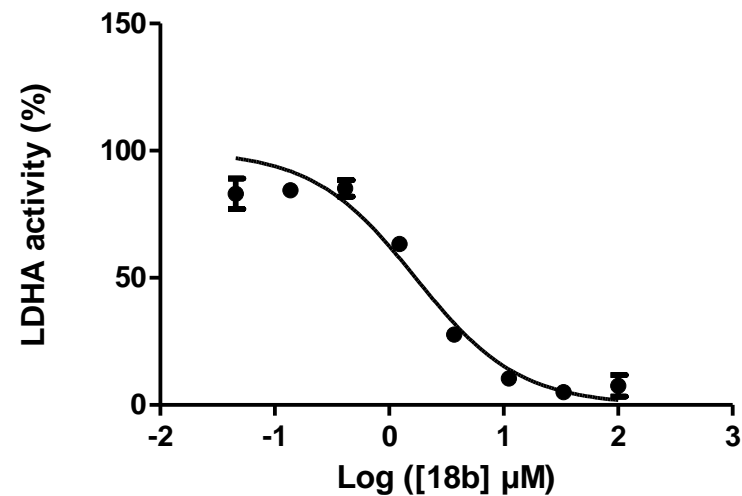


Figure S50. LDHA inhibition curve of compound **18b** (mean \pm SD of $n = 3$ replicates)

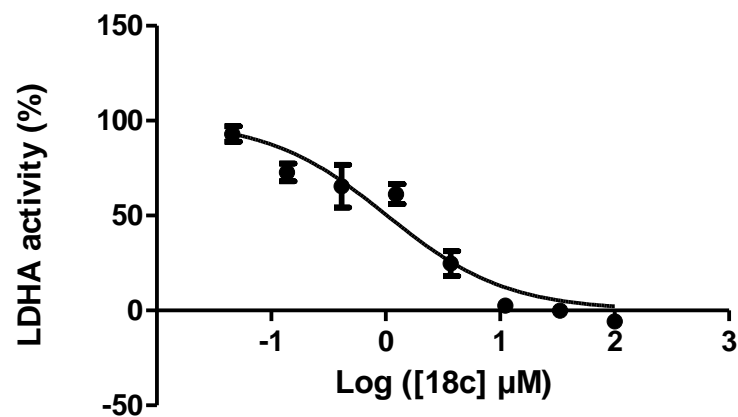


Figure S51. LDHA inhibition curve of compound **18c** (mean \pm SD of $n = 3$ replicates)

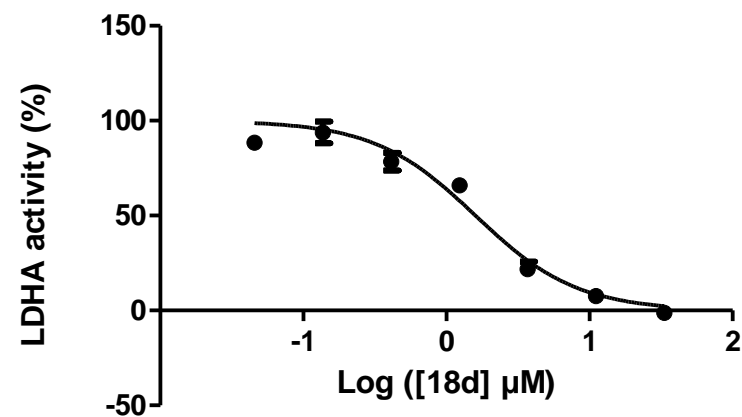


Figure S52. LDHA inhibition curve of compound **18d** (mean \pm SD of $n = 3$ replicates)

3.2. LDHB dose-response inhibition curves

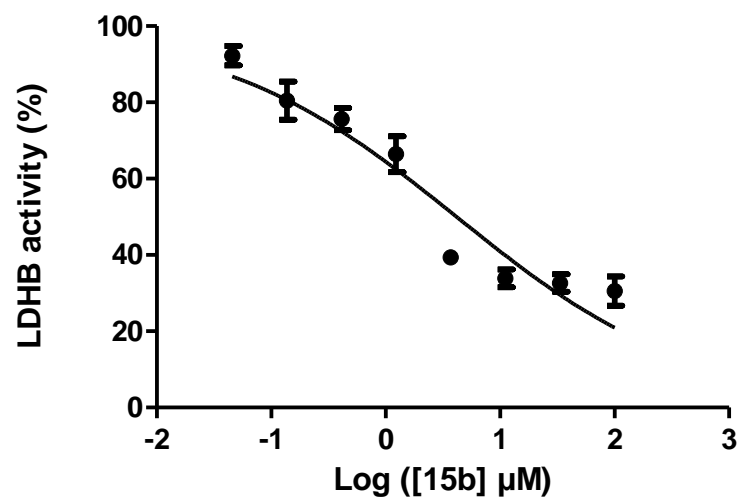


Figure S53. LDHB inhibition curve of compound **15b** (mean \pm SD of $n = 3$ replicates)

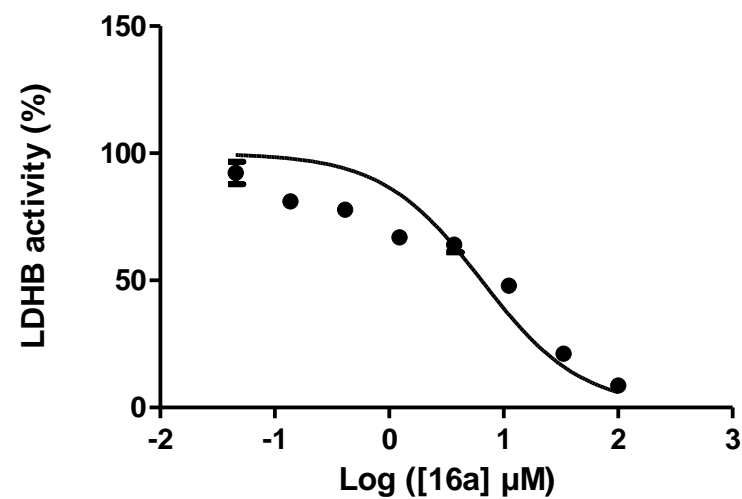


Figure S54. LDHB inhibition curve of compound **16a** (mean \pm SD of $n = 3$ replicates)

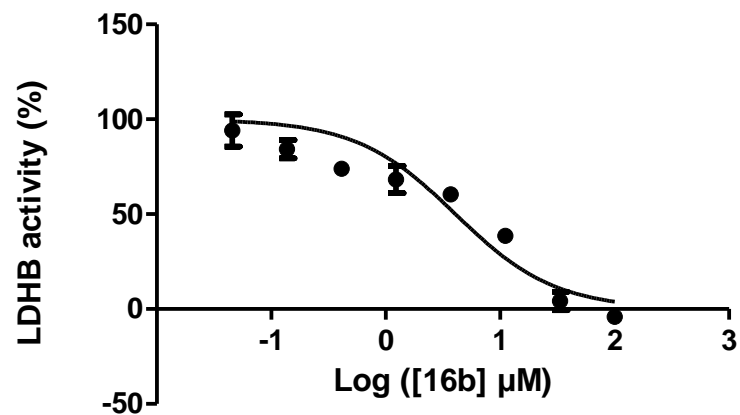


Figure S55. LDHB inhibition curve of compound **16b** (mean \pm SD of $n = 3$ replicates)

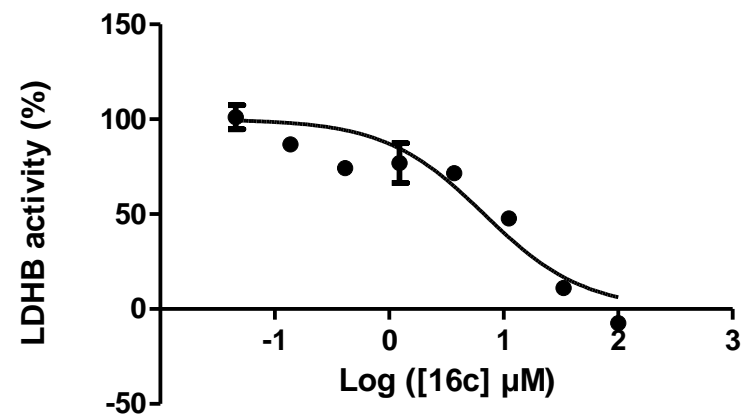


Figure S56. LDHB inhibition curve of compound **16c** (mean \pm SD of $n = 3$ replicates)

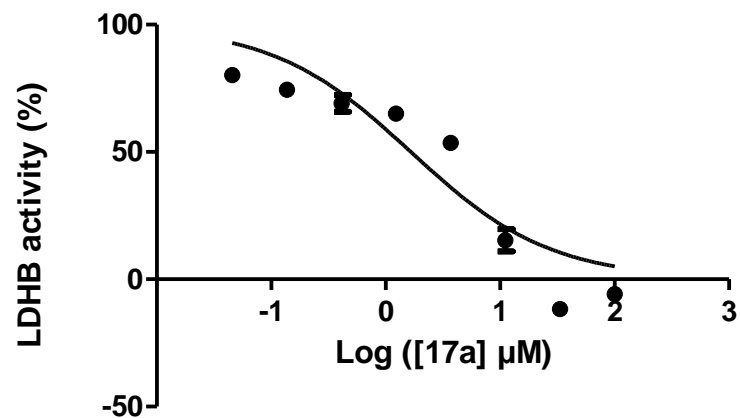


Figure S57. LDHB inhibition curve of compound **17a** (mean \pm SD of $n = 3$ replicates)

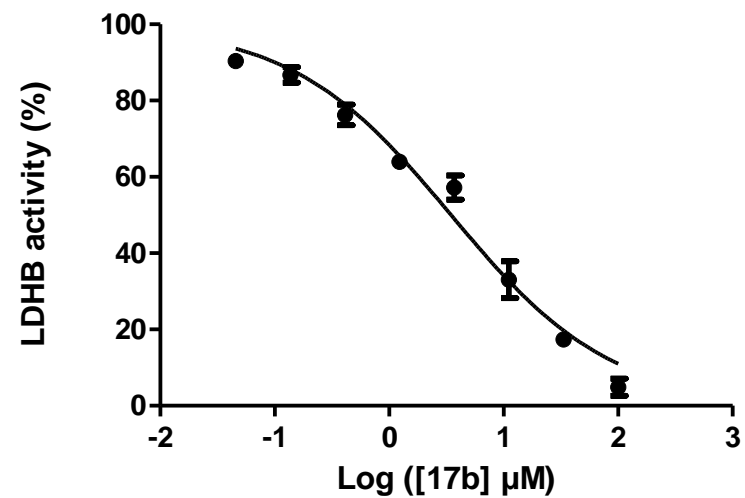


Figure S58. LDHB inhibition curve of compound **17b** (mean \pm SD of $n = 3$ replicates)

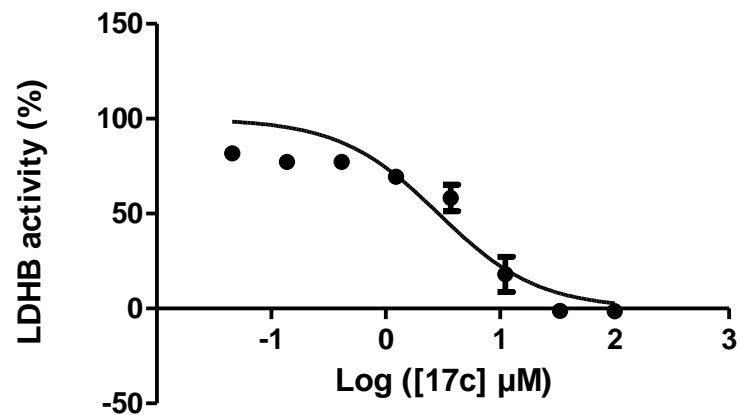


Figure S59. LDHB inhibition curve of compound **17c** (mean \pm SD of $n = 3$ replicates)

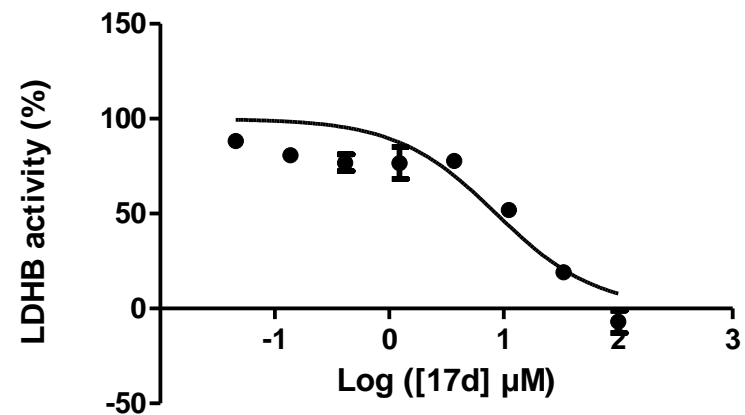


Figure S60. LDHB inhibition curve of compound **17d** (mean \pm SD of $n = 3$ replicates)

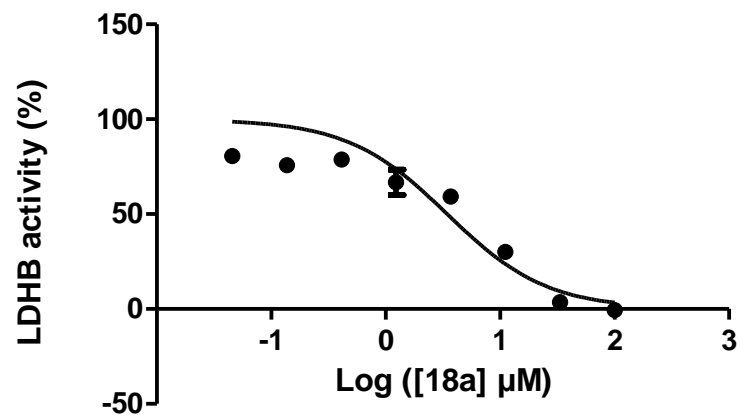


Figure S61. LDHB inhibition curve of compound **18a** (mean \pm SD of $n = 3$ replicates)

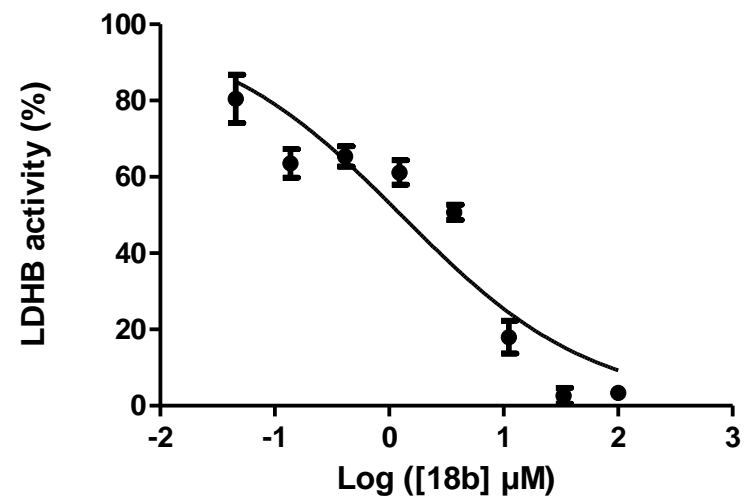


Figure S62. LDHB inhibition curve of compound **18b** (mean \pm SD of $n = 3$ replicates)

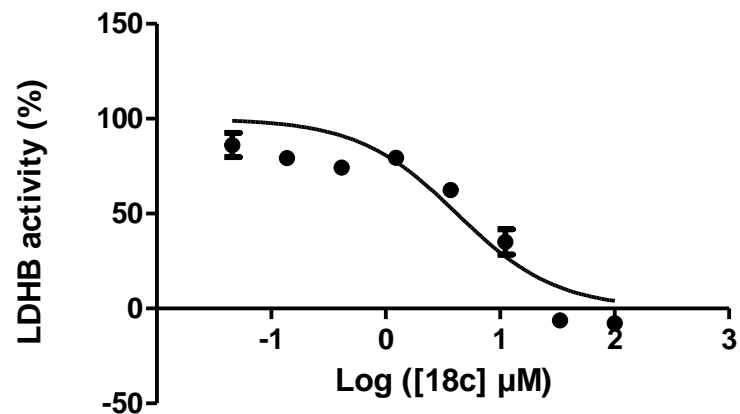


Figure S63. LDHB inhibition curve of compound **18c** (mean \pm SD of $n = 3$ replicates)

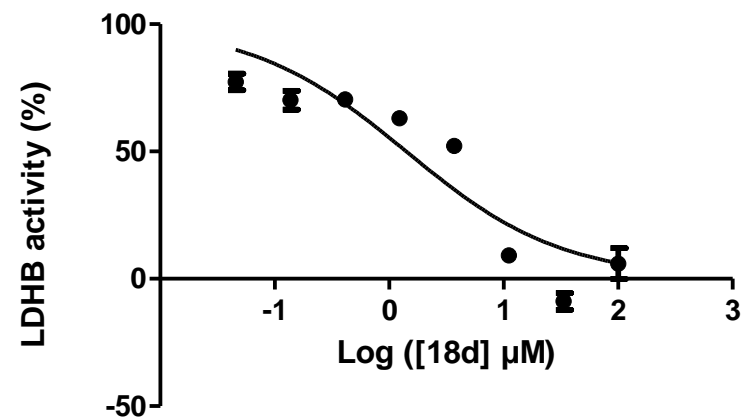


Figure S64. LDHB inhibition curve of compound **18d** (mean \pm SD of $n = 3$ replicates)

