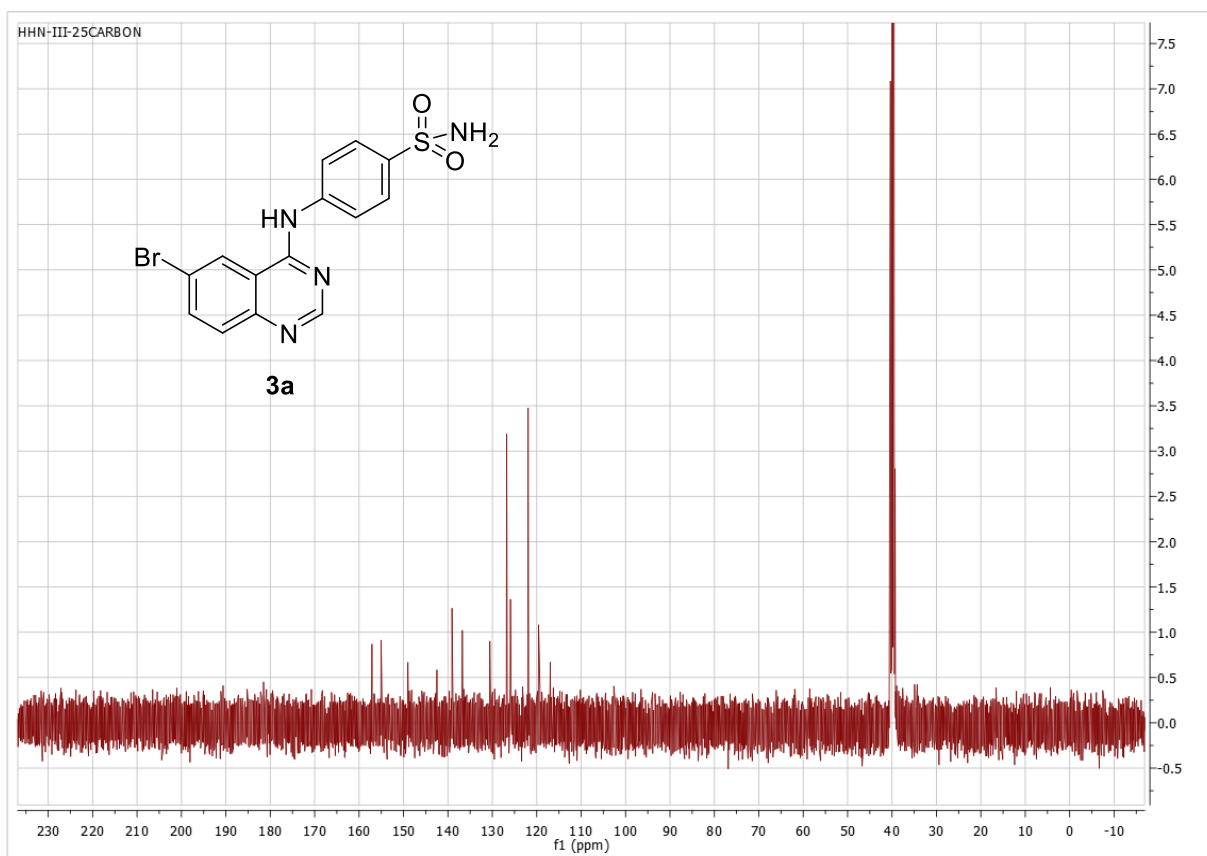
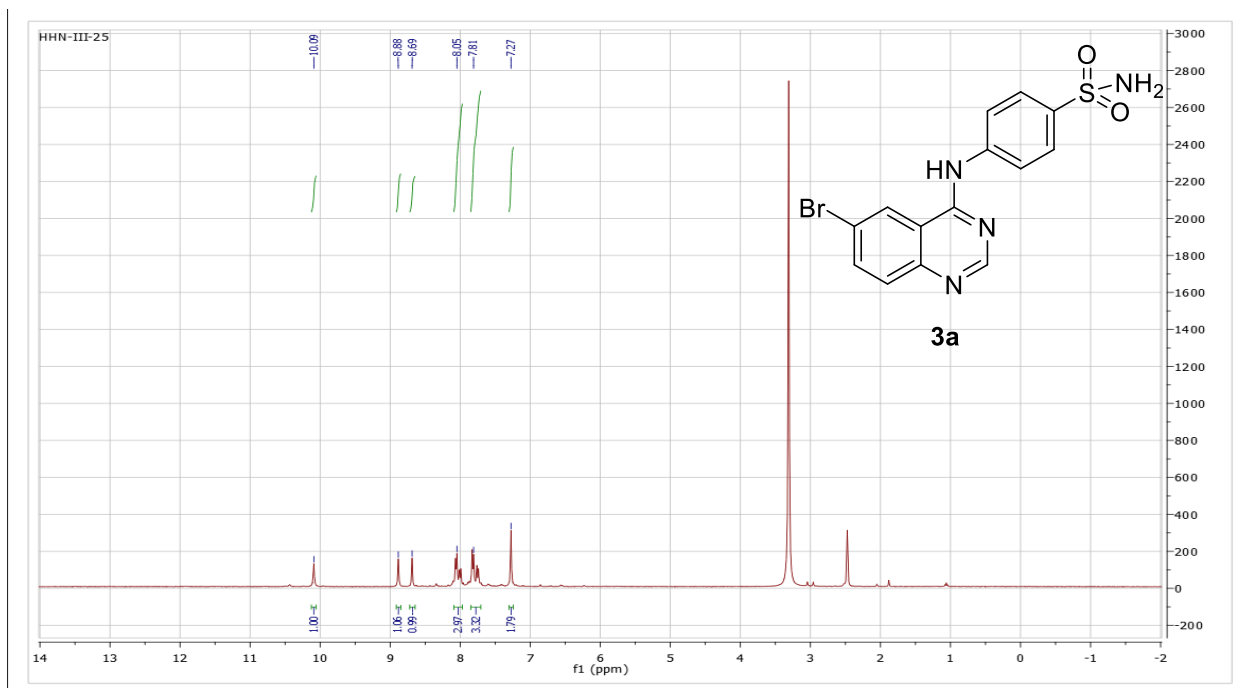


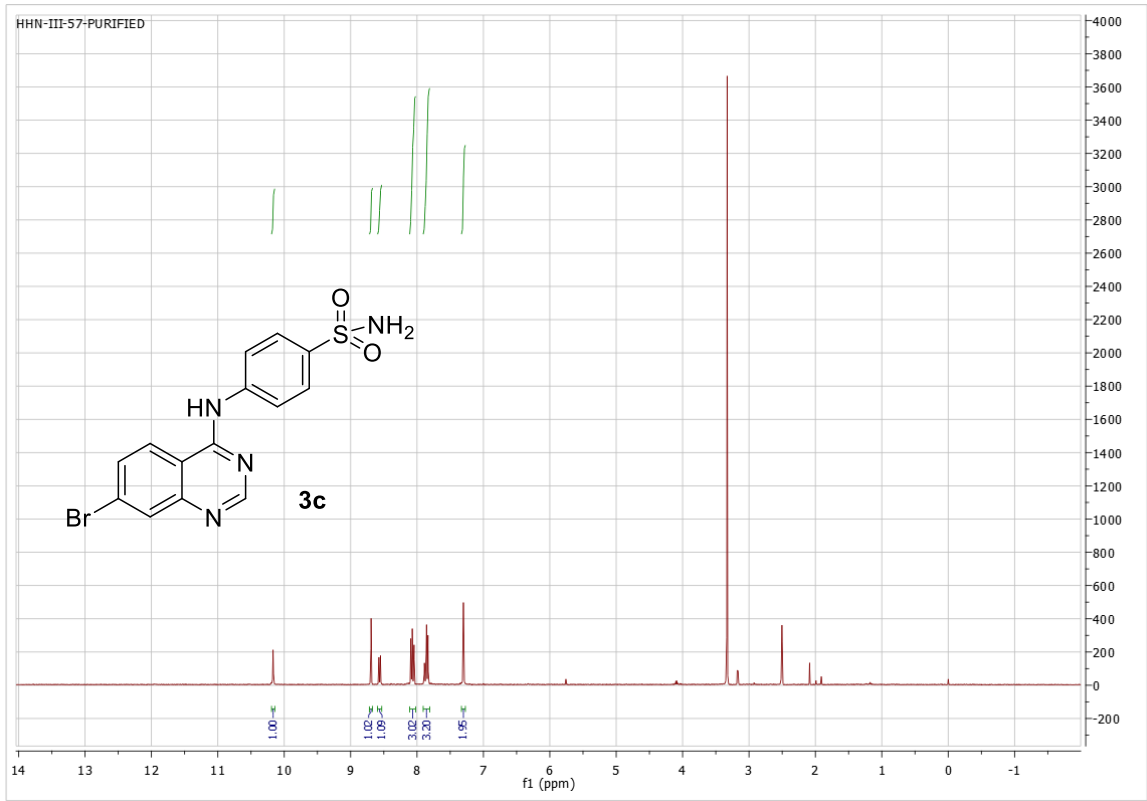
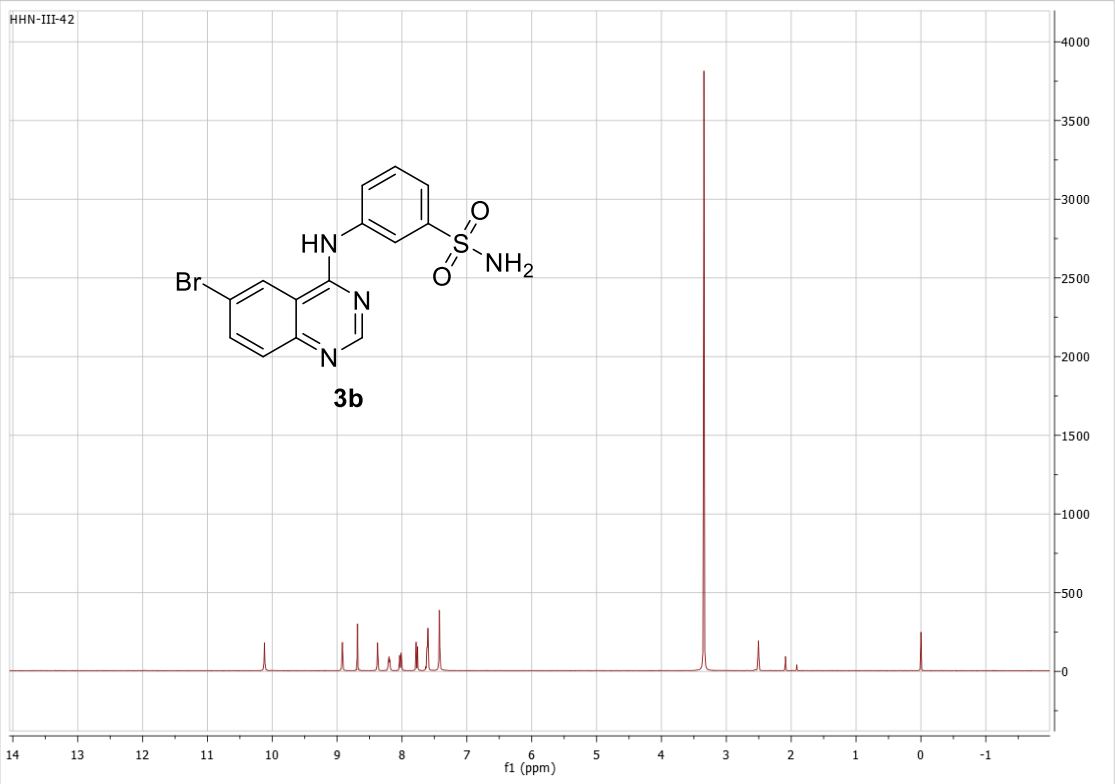
**4-Anilinoquinazoline-based Benzenesulfonamides as Nanomolar
Inhibitors of Carbonic Anhydrase Isoforms I, II, IX, and XII:
Design, Synthesis, *In-vitro*, and *In-silico* Biological Studies**

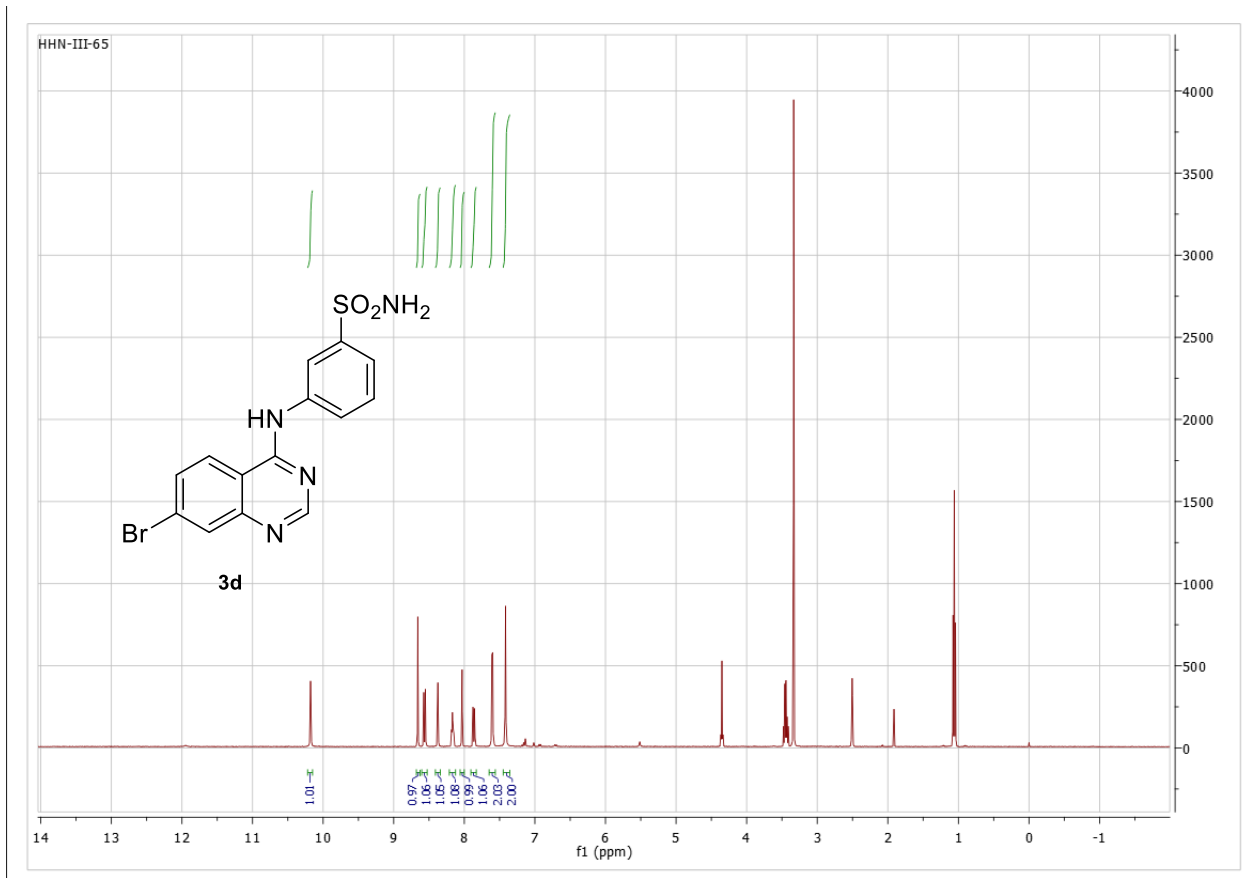
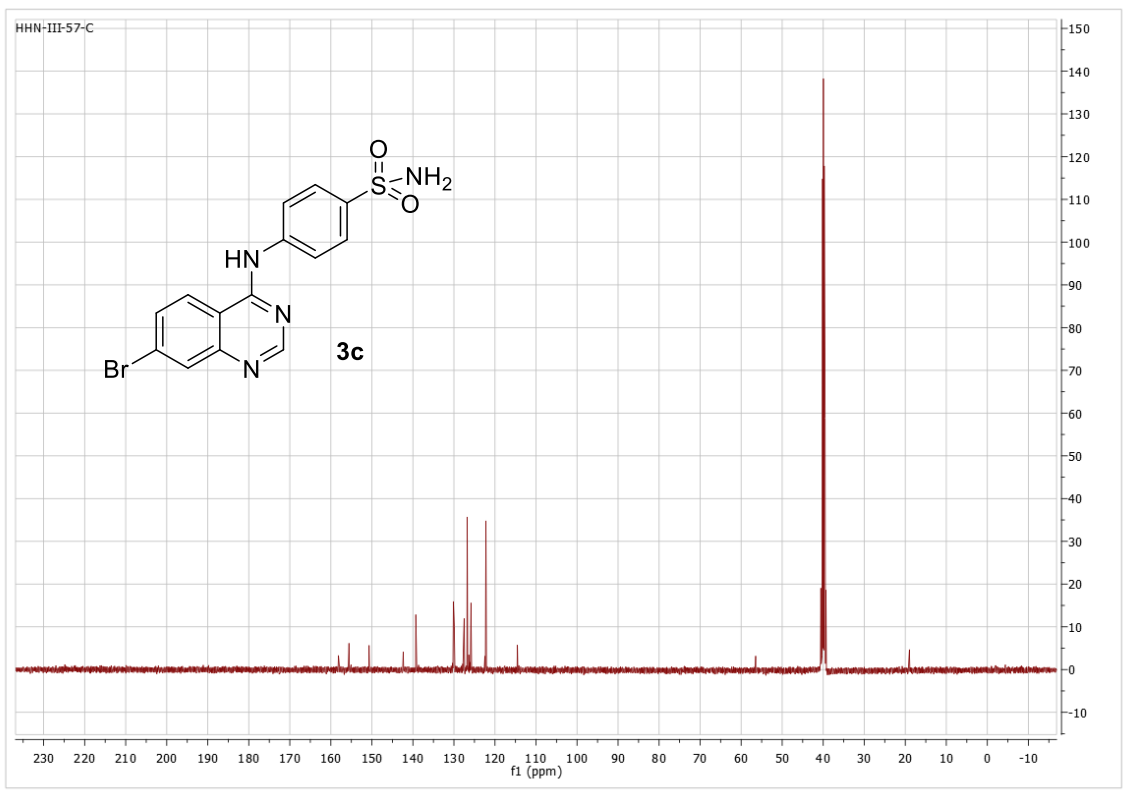
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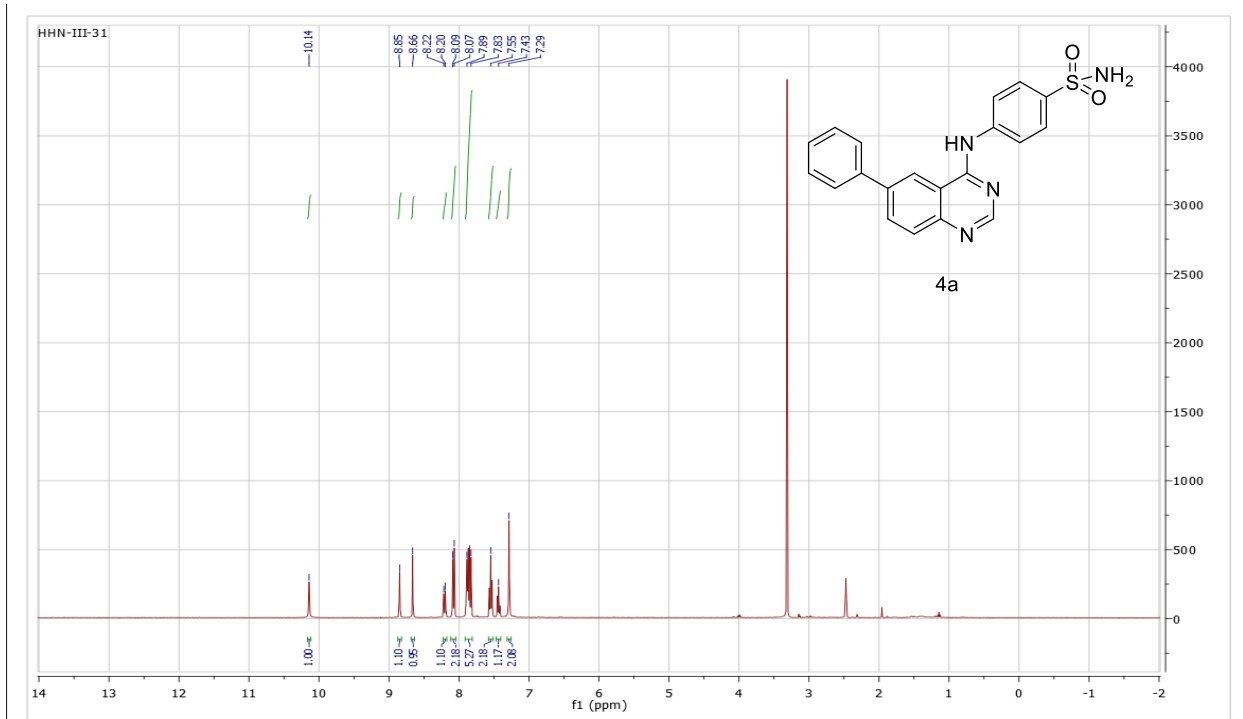
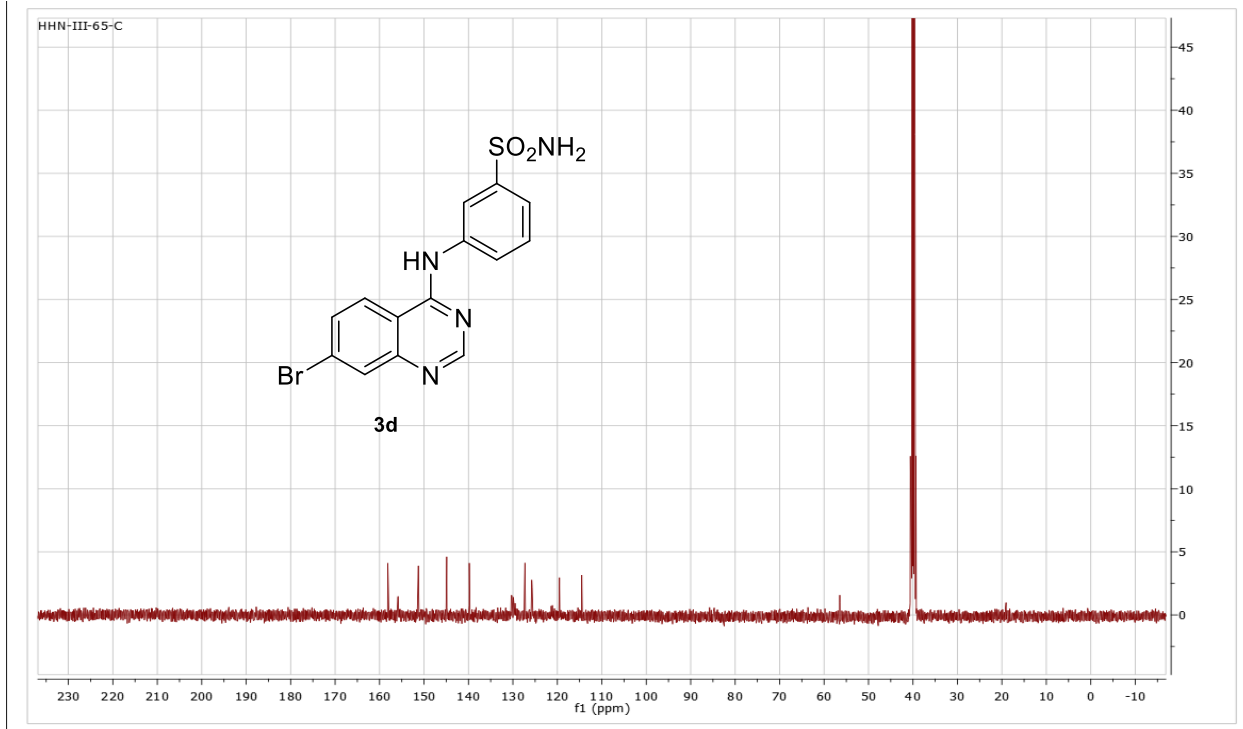
1. ^1H NMR and ^{13}C NMR data of compounds **3a-d** and **4a-l**
2. Representative HPLC purity data of the compounds **3a-d** and **4a-l**
3. Representative HRMS data of the compounds **3a-d** and **4a-l**
4. Supplementary docking figures

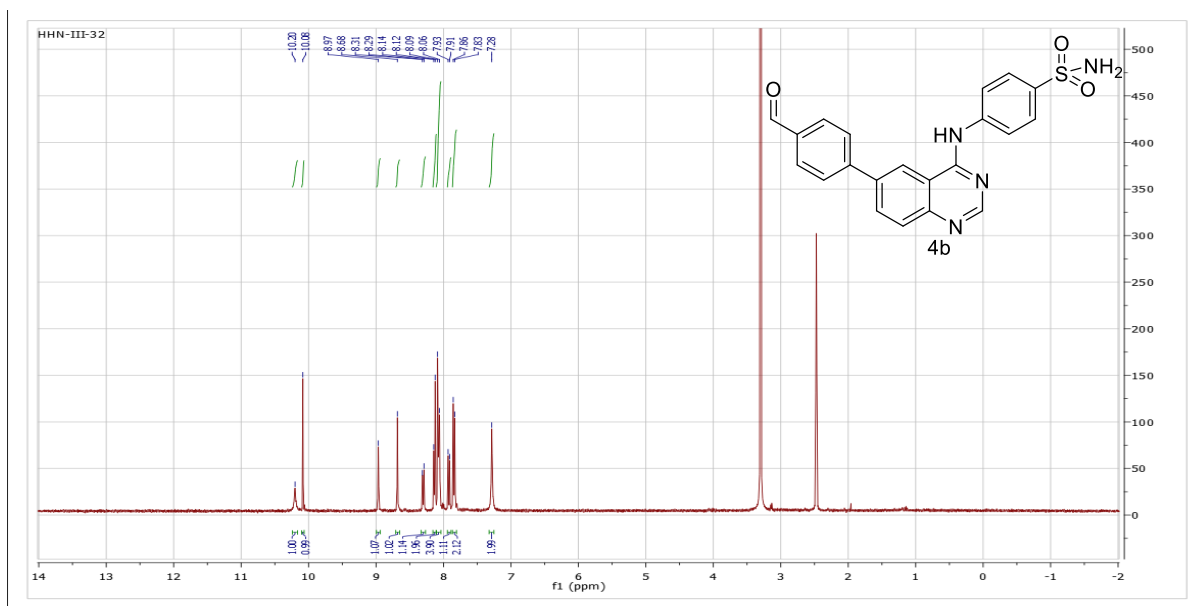
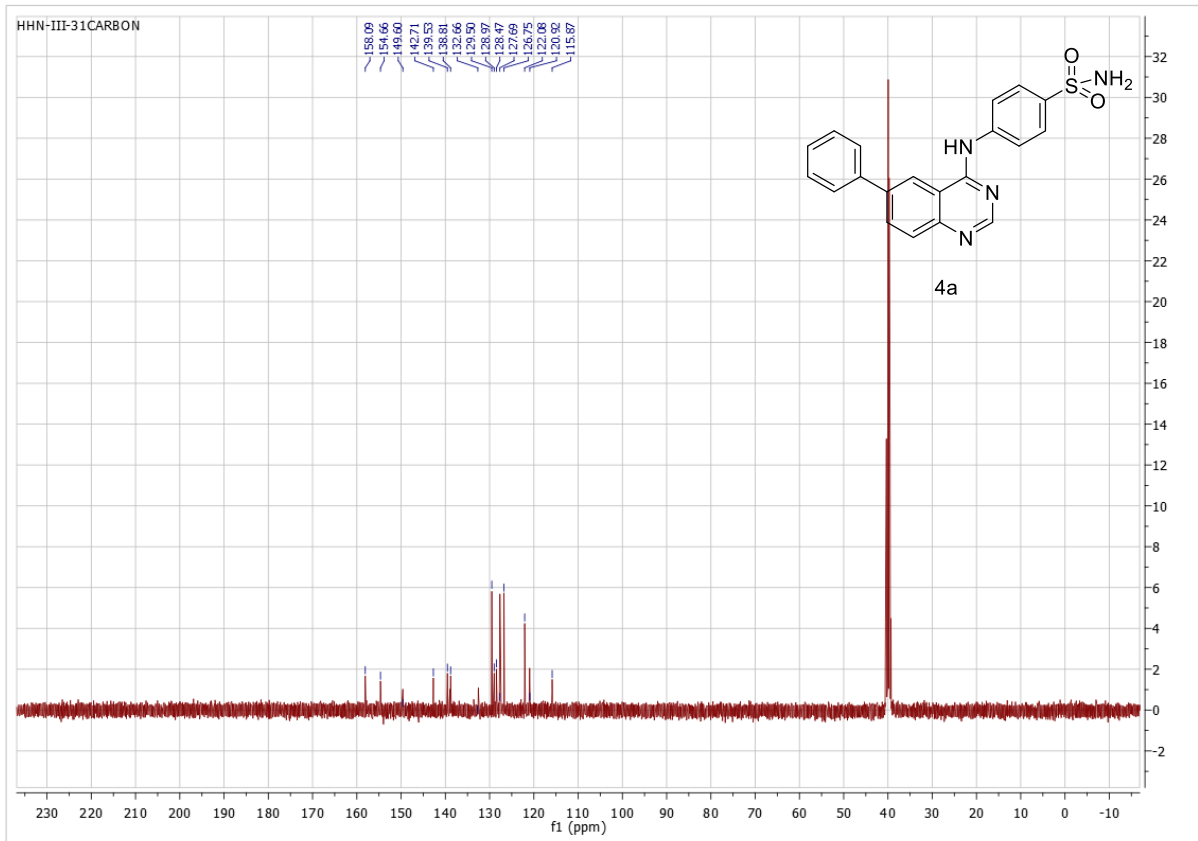
1. ¹HNMR and ¹³CNMR data of compounds 3a–d and 4a–f

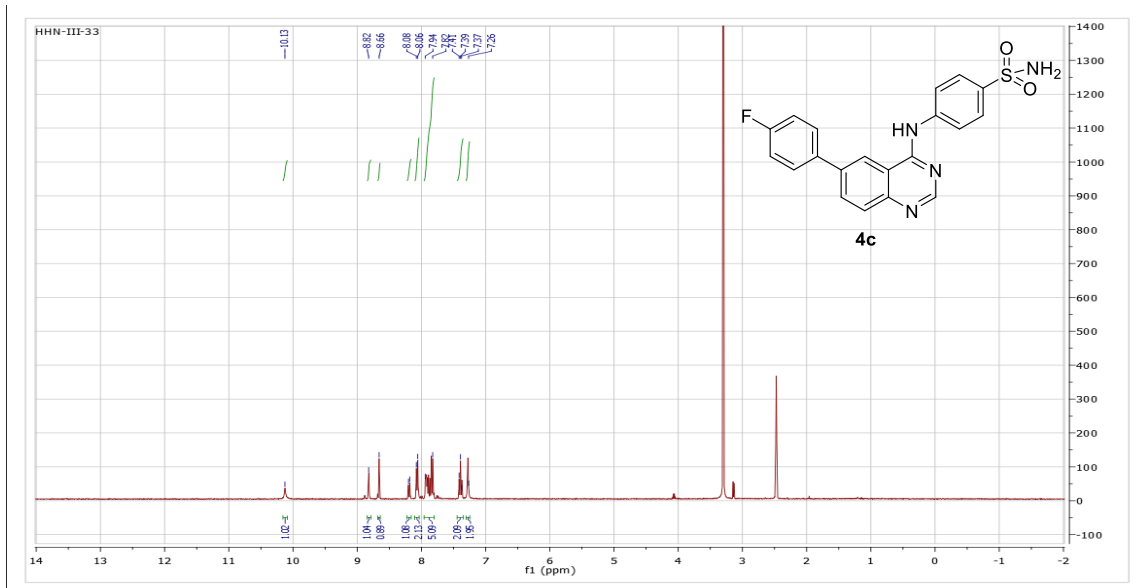
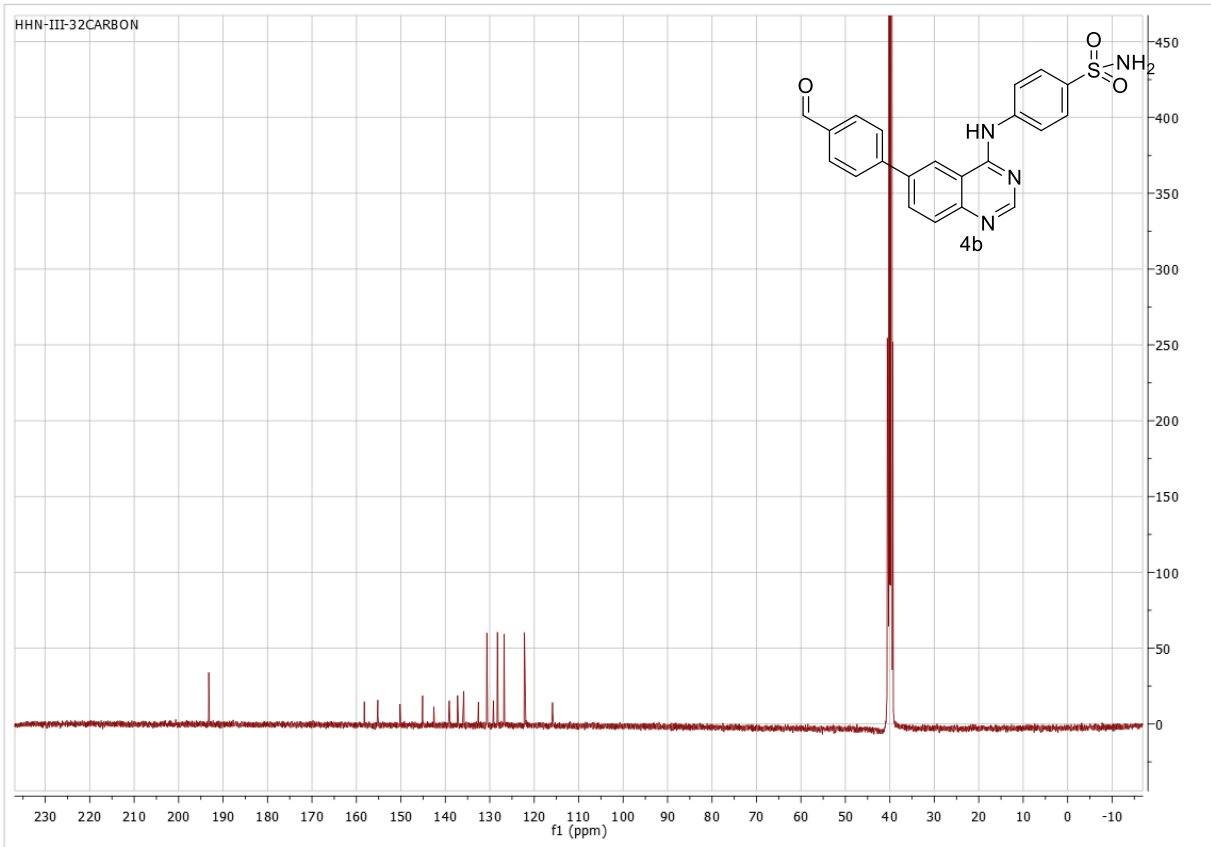




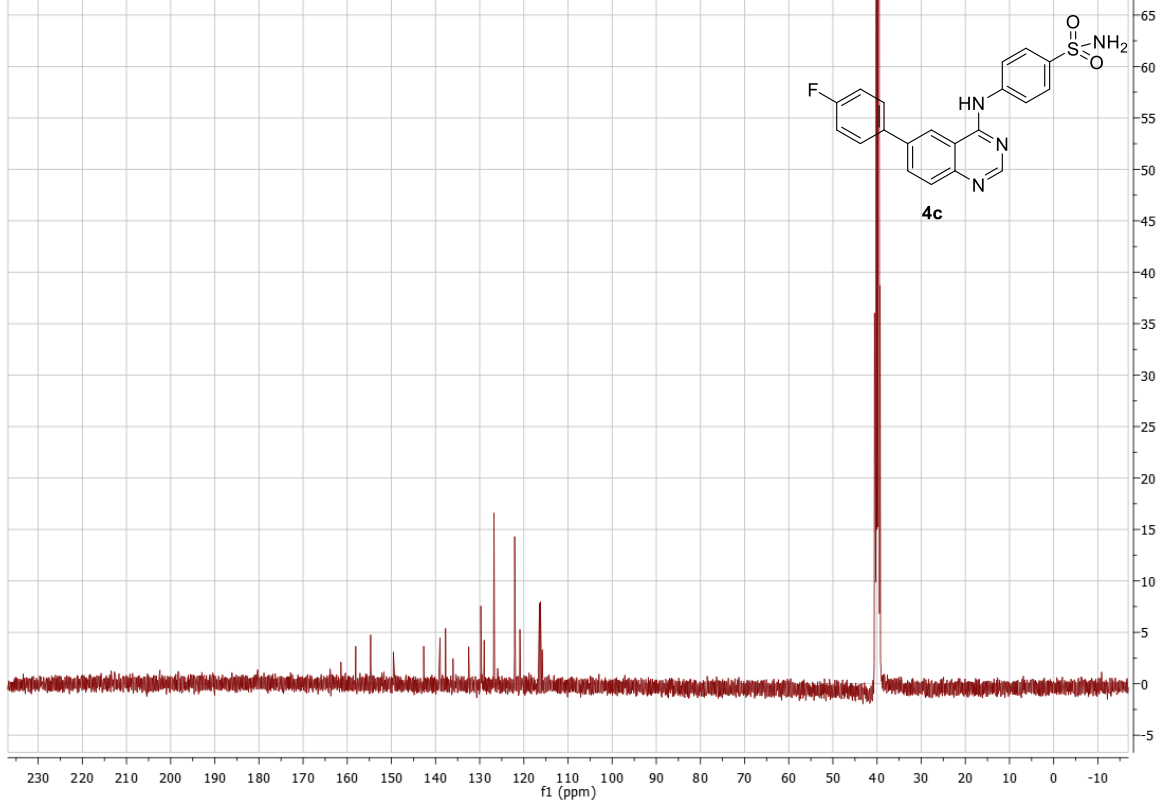




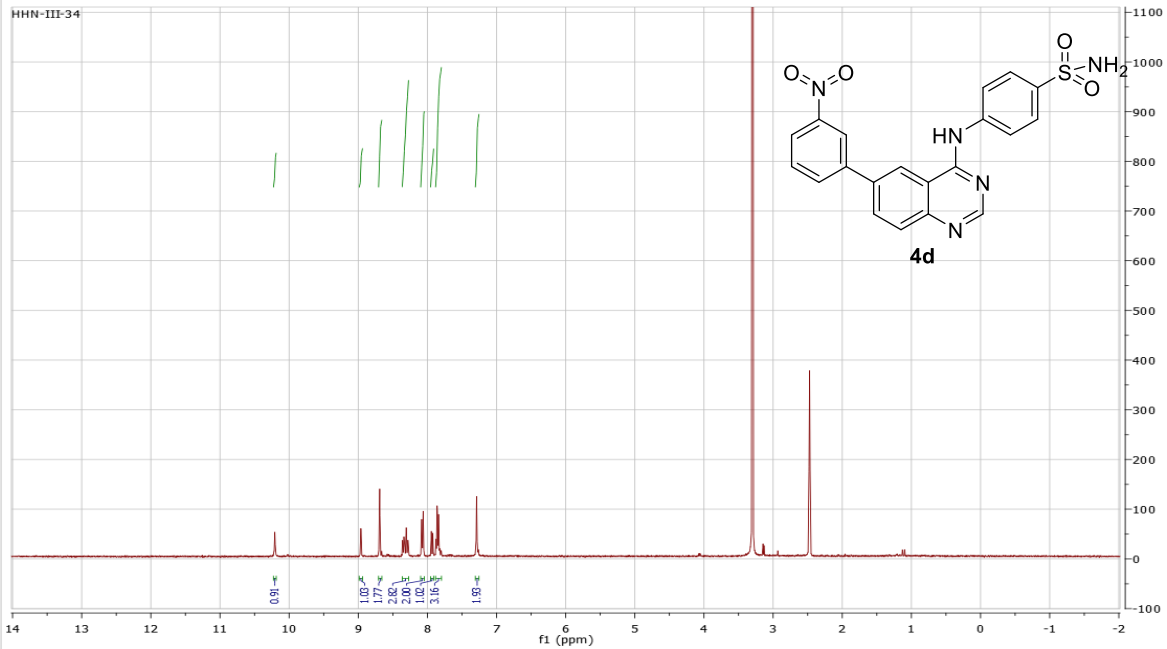


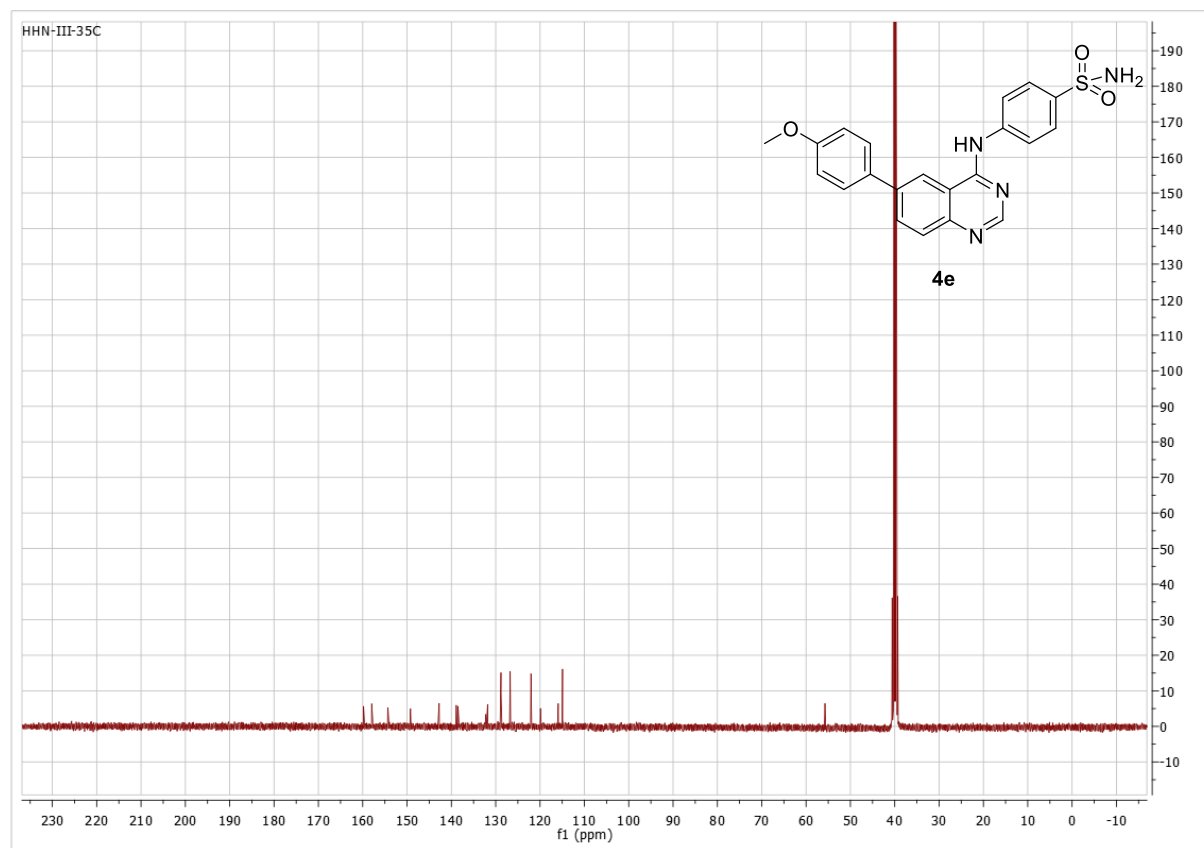
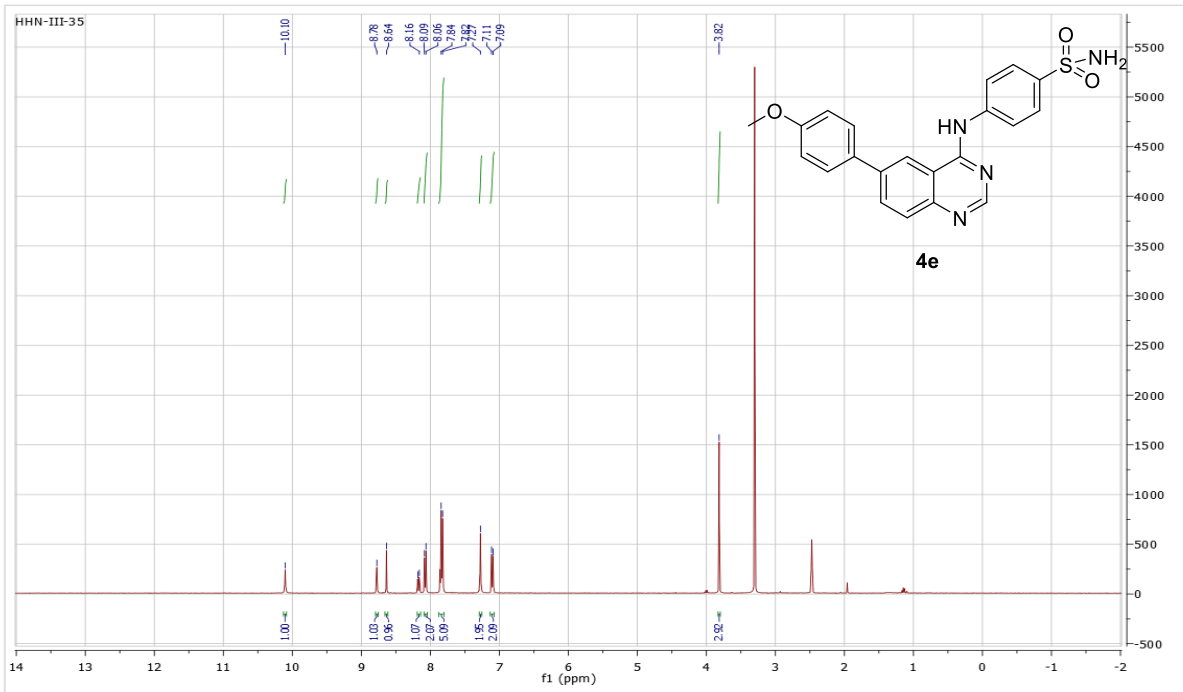


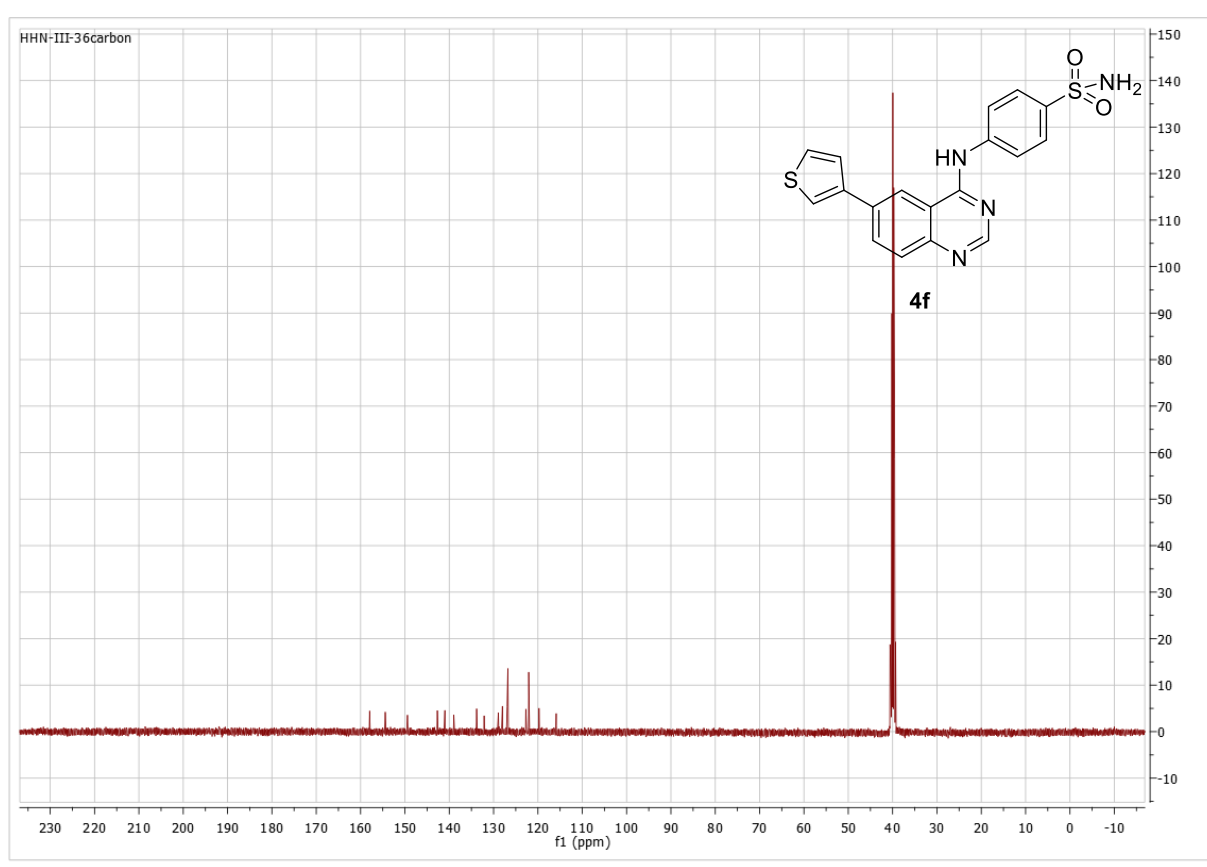
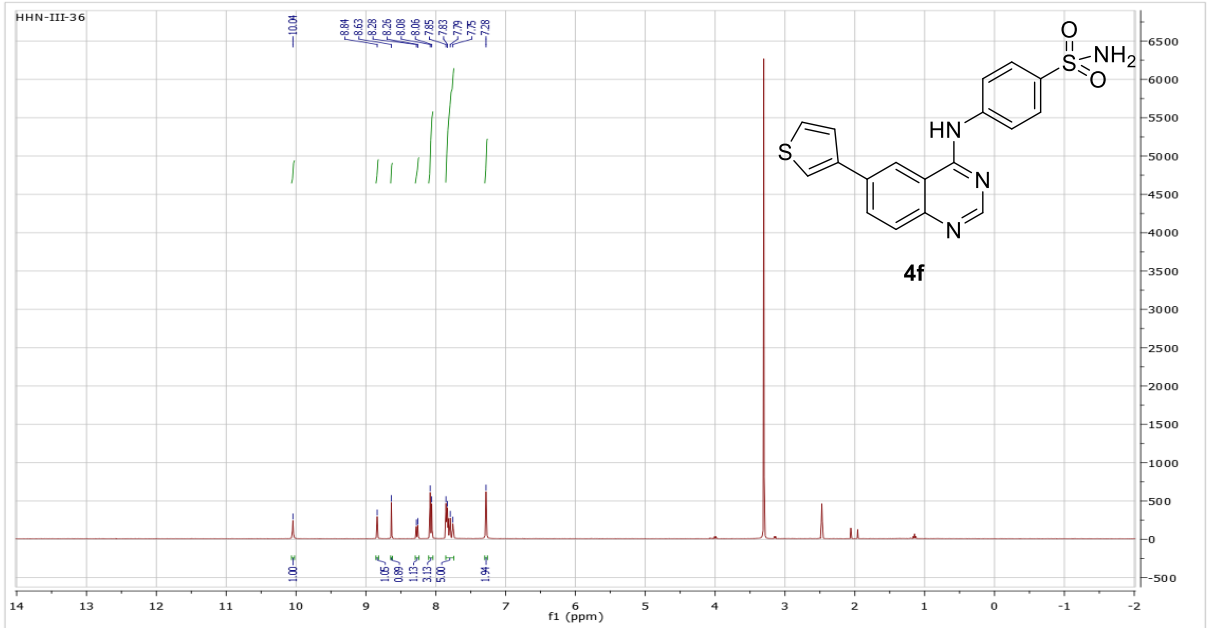
HHN-III-33carbon

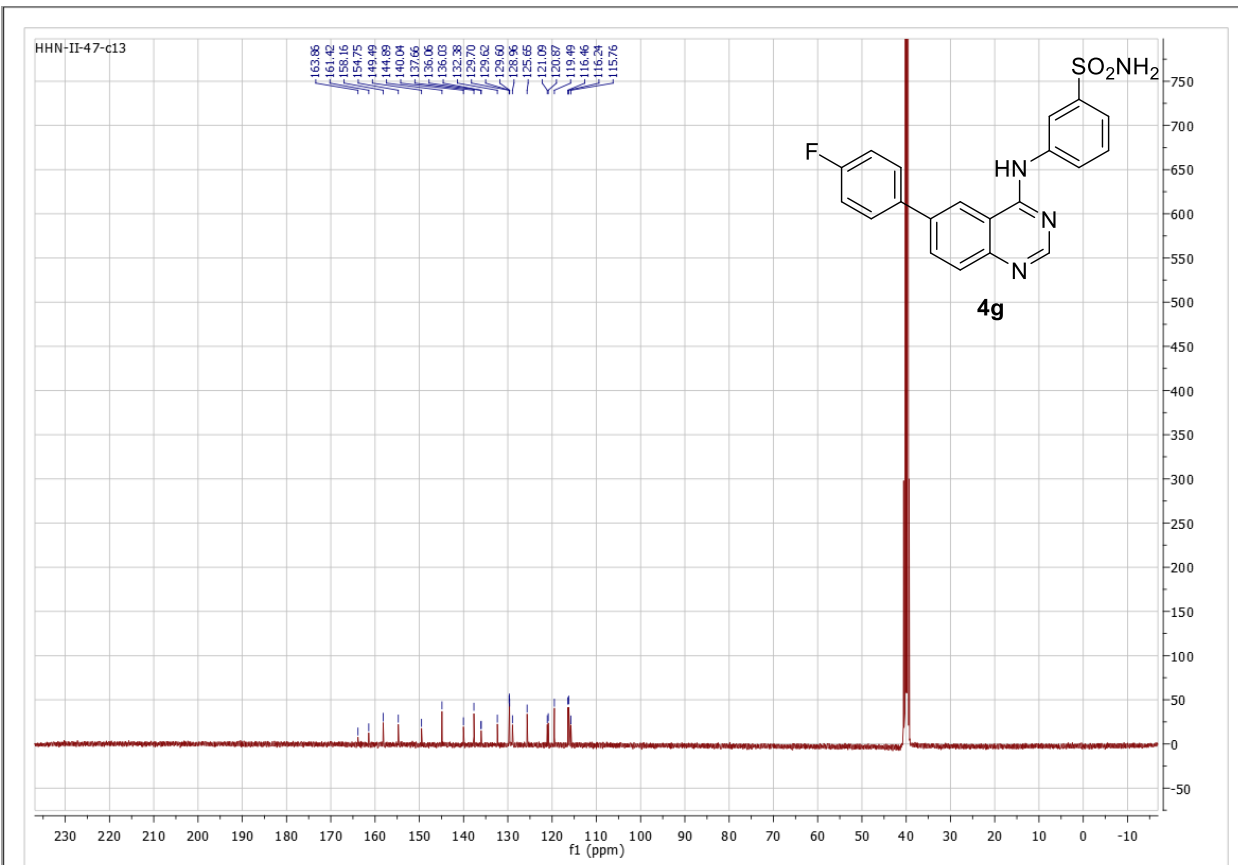
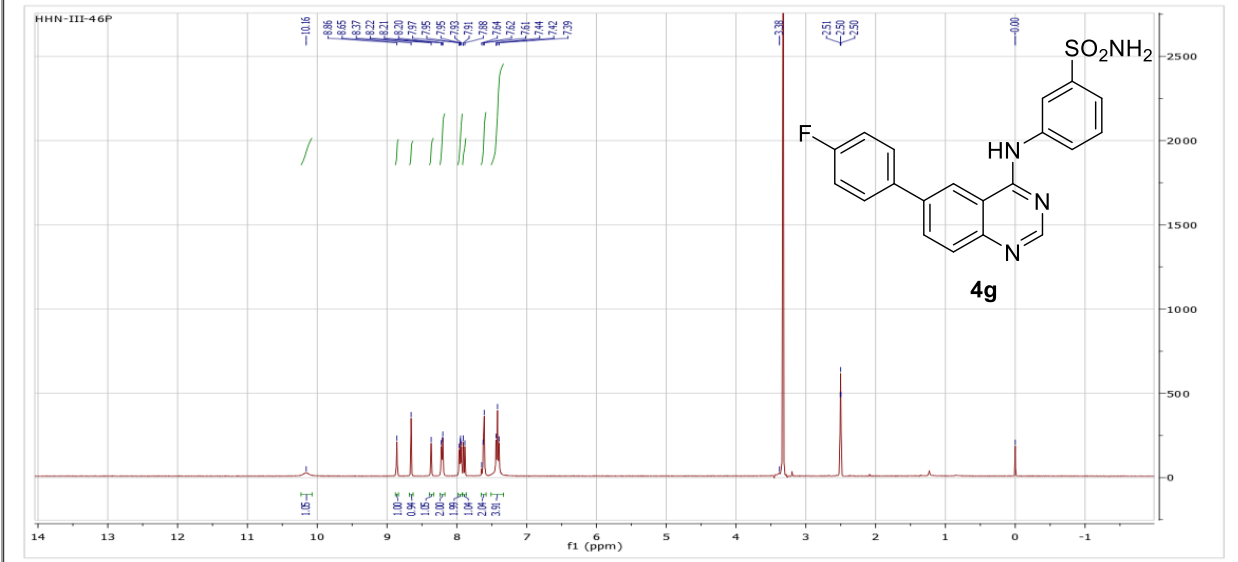


HHN-III-34

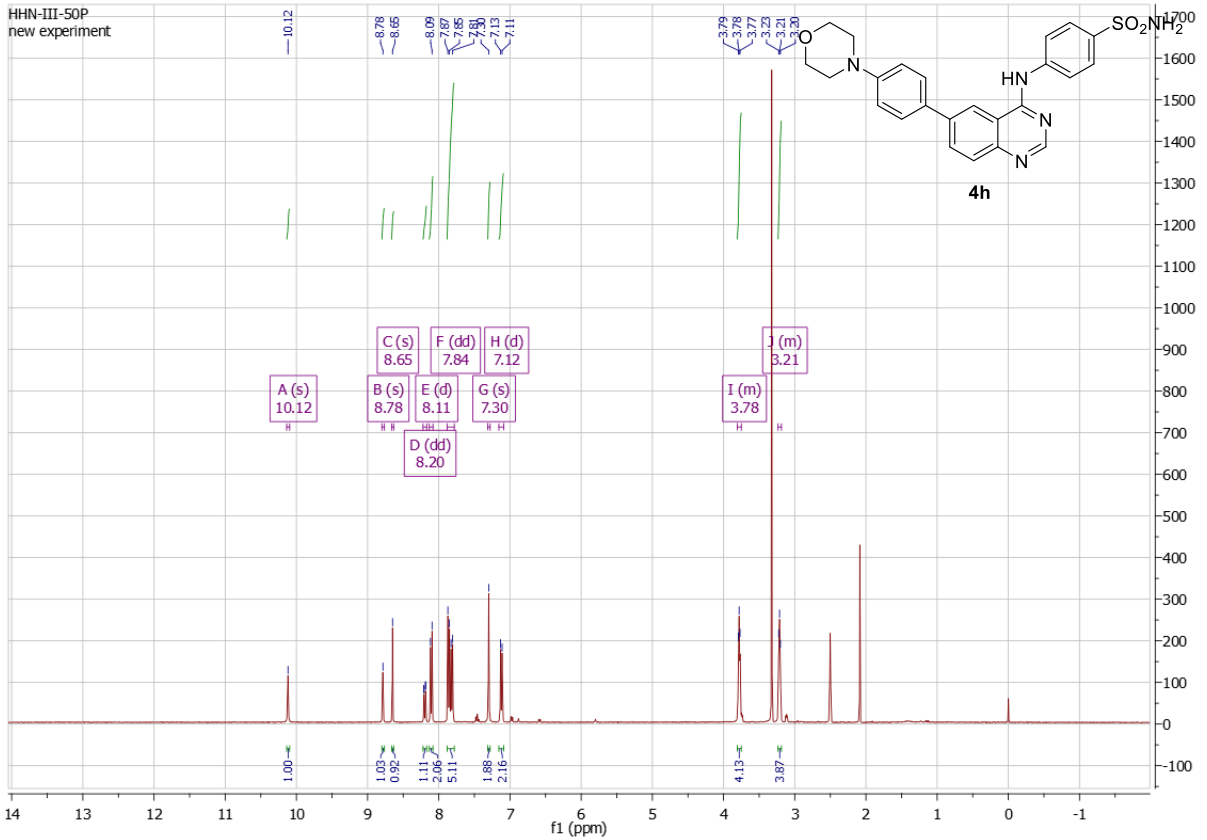




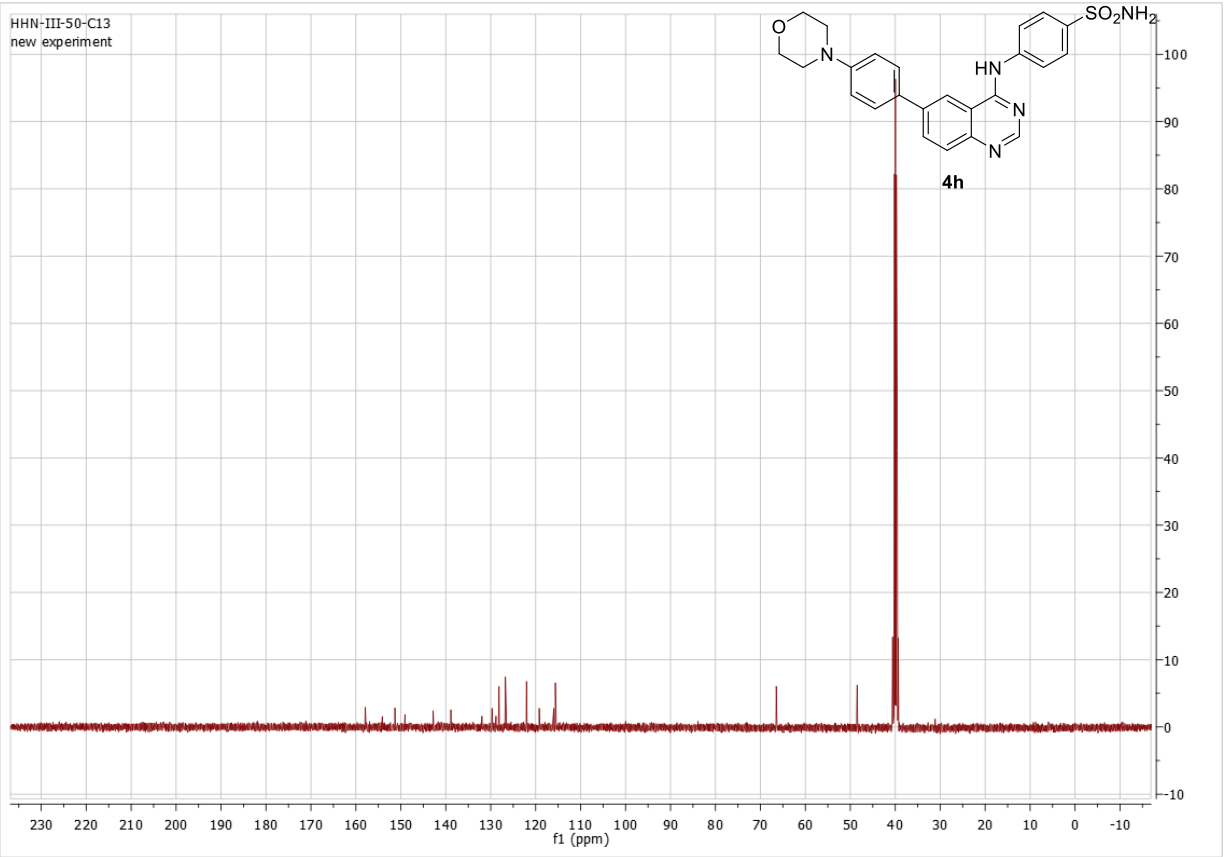


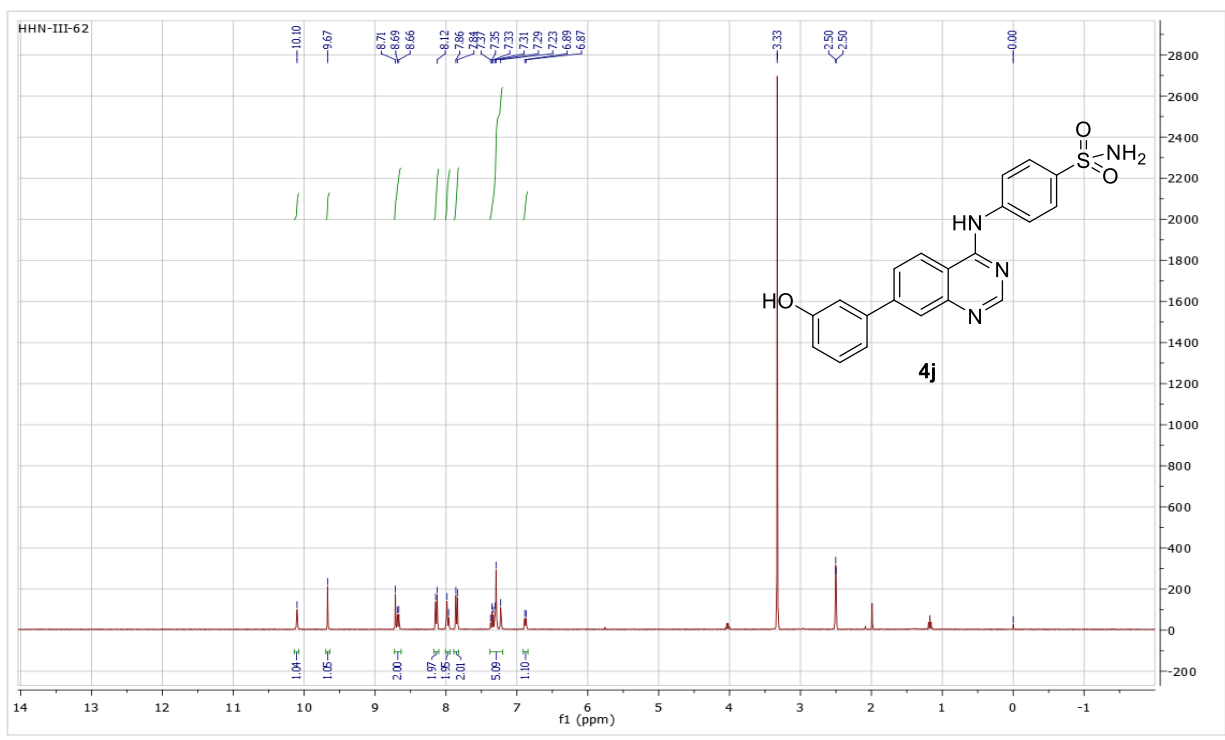
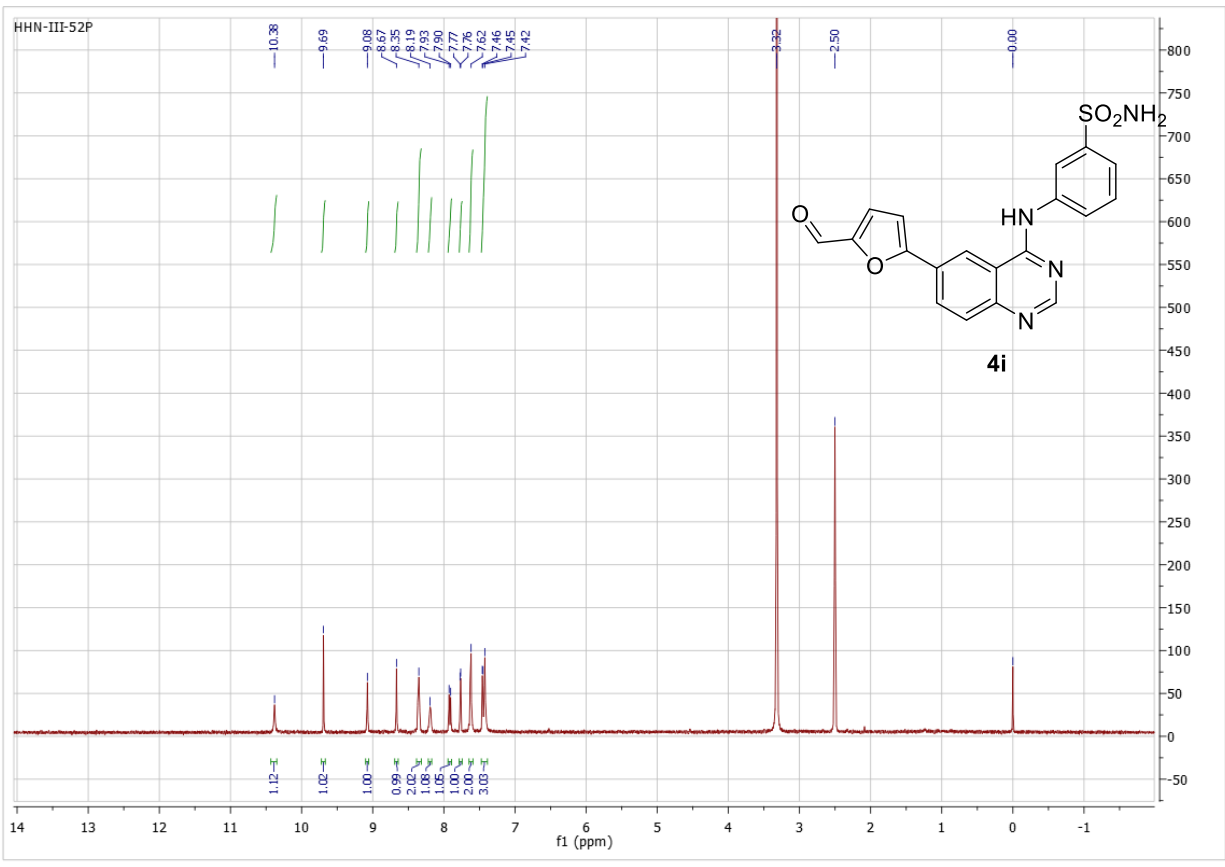


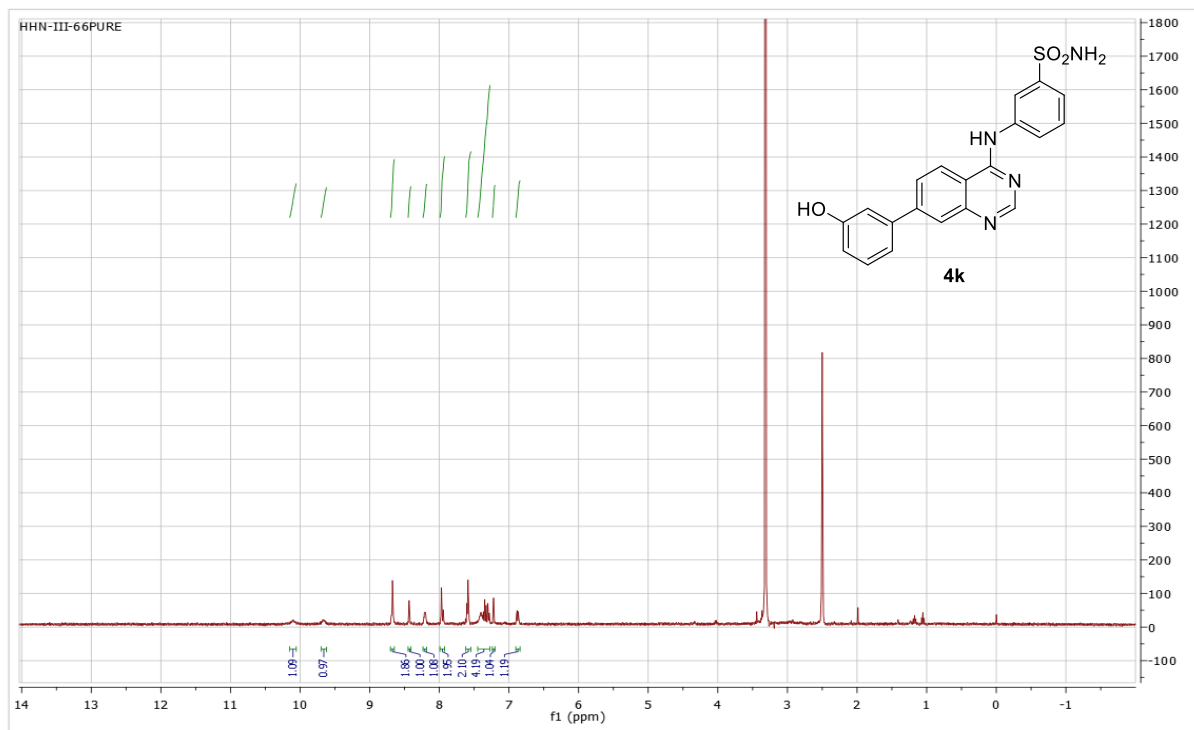
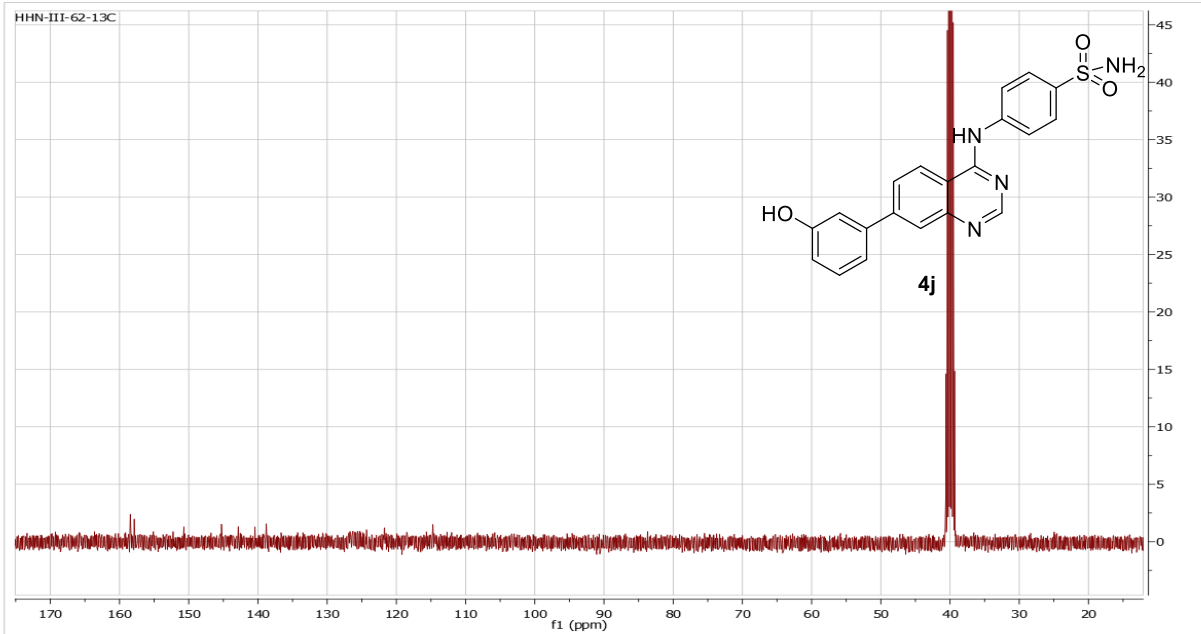
HHN-III-50P
new experiment

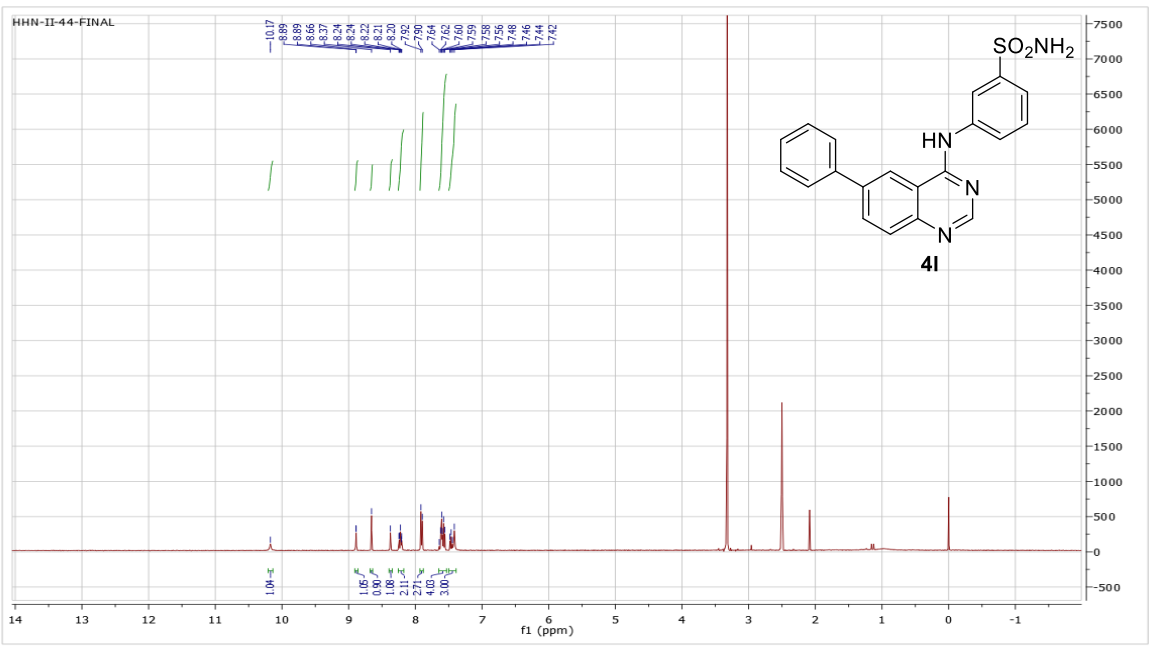


HHN-III-50-C13
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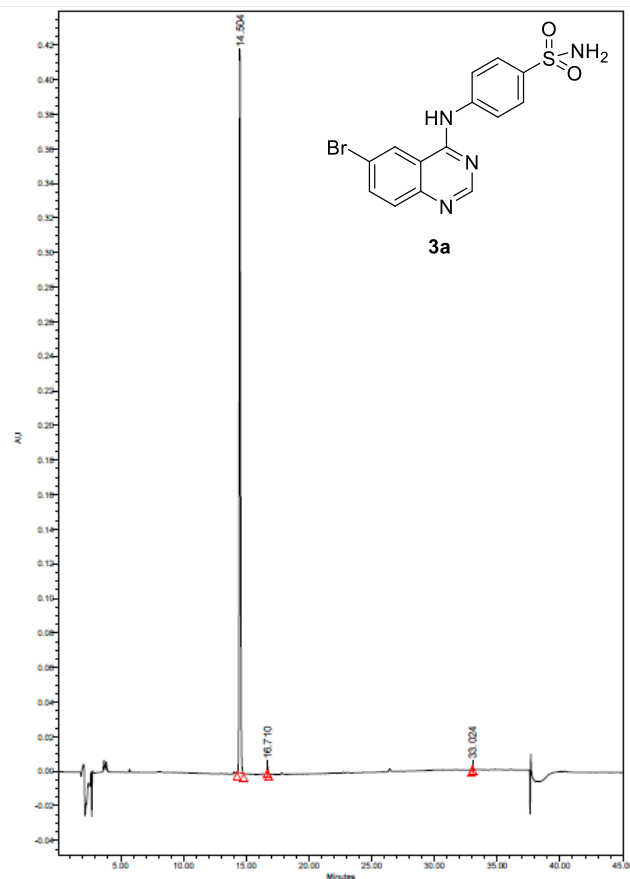






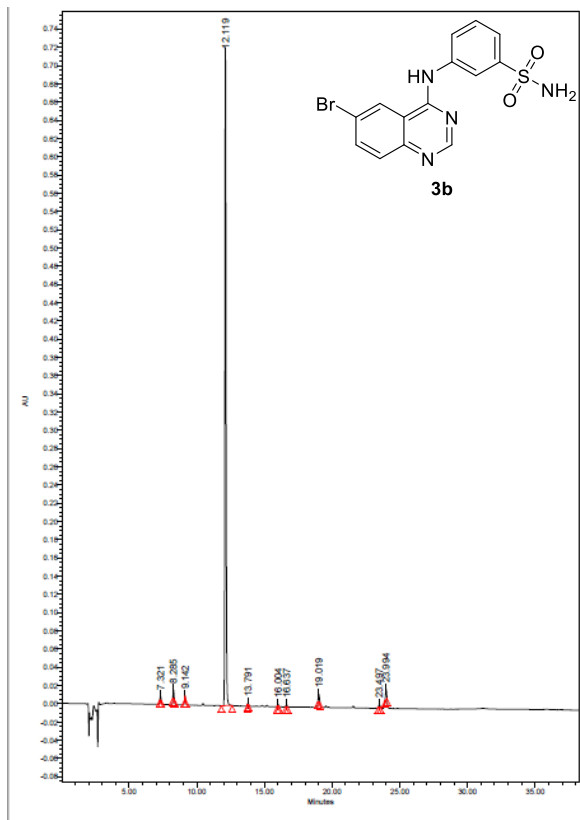


2. Representative HPLC purity data of the compounds 3a–d and 4a–f



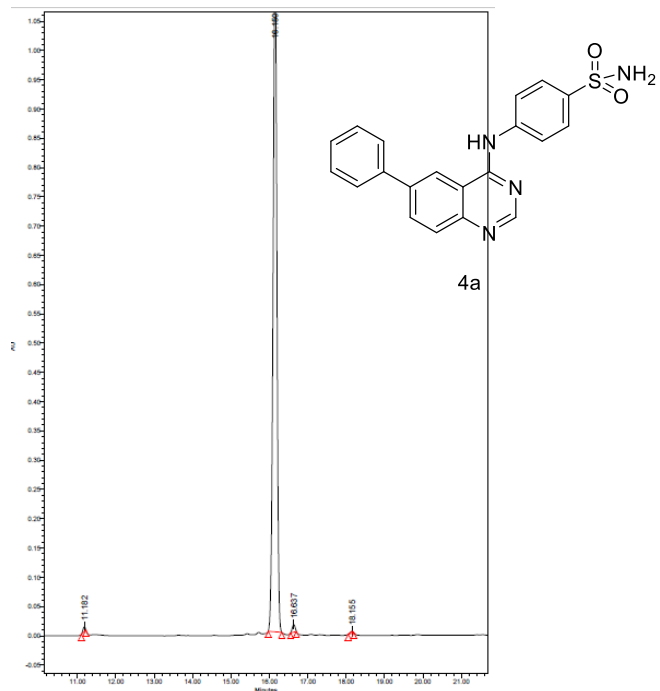
Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area ($\mu V \cdot sec$)	% Area	Height (μV)	Int Type	Amount	Units
1	14.504							2814904	99.46	418996	bb		
2	16.710							11749	0.42	2587	bb		
3	33.024							3664	0.13	851	bb		

Peak Type	Peak Codes
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2 Unknown	
3 Unknown	



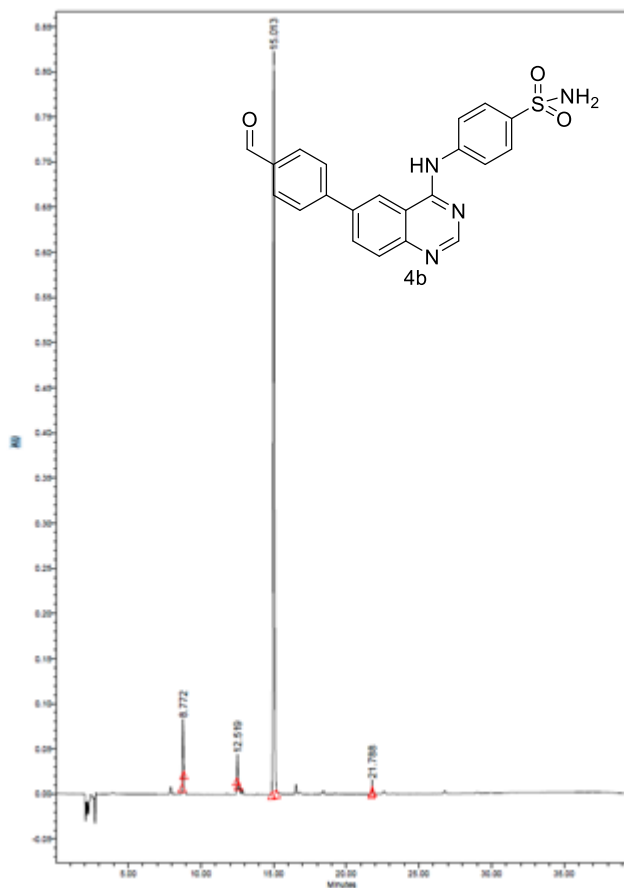
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1		7.321							19355	0.44	4478	bb		
2		8.285							40947	0.93	9778	bb		
3		9.142							12329	0.28	3927	bb		
4		12.119							4200300	95.11	719106	bb		
5		13.791							4753	0.11	1532	bb		
6		16.004							7963	0.18	1941	bb		
7		16.637							9446	0.21	1950	bb		
8		19.019							46554	1.05	8646	bb		
9		23.497							13240	0.30	2192	bb		
10		23.994							61570	1.39	11239	bb		

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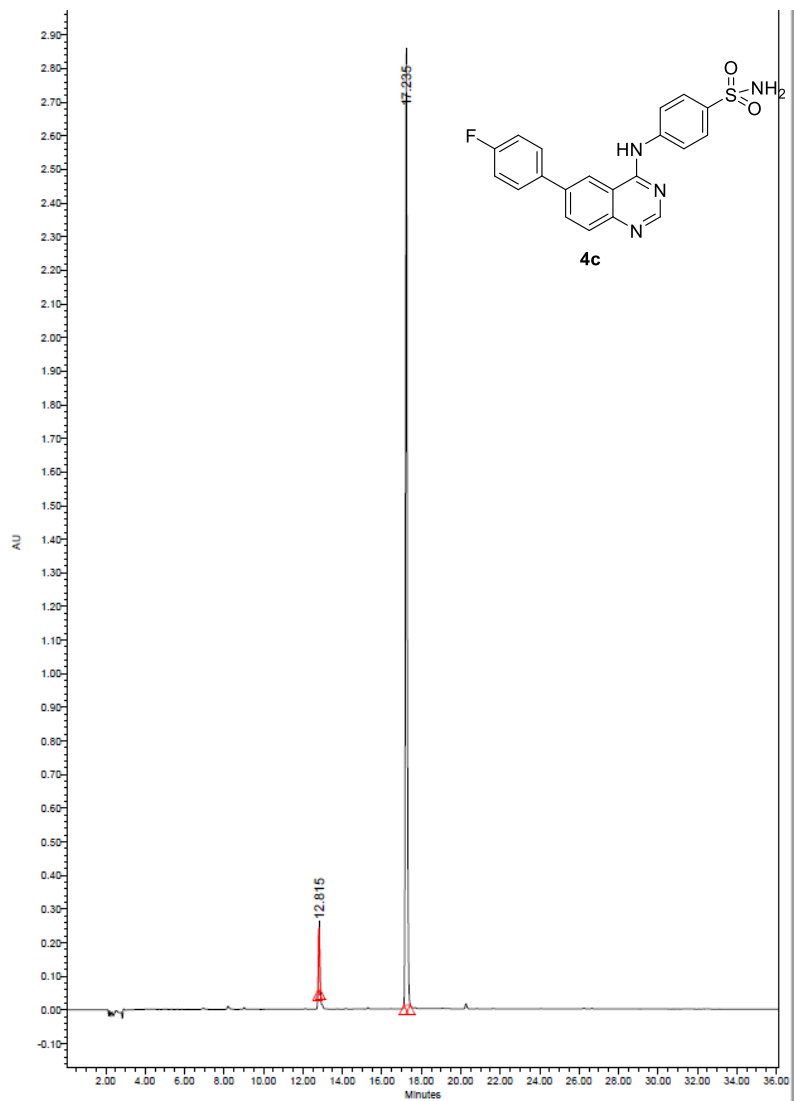
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1	11.182							32878	0.41	8074	bb		
2	16.150							7916050	98.58	1157431	bb		
3	16.637							64760	0.81	12718	bb		
4	18.155							16762	0.21	3210	bb		

Peak Type	Peak Codes
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2 Unknown	
3 Unknown	
4 Unknown	



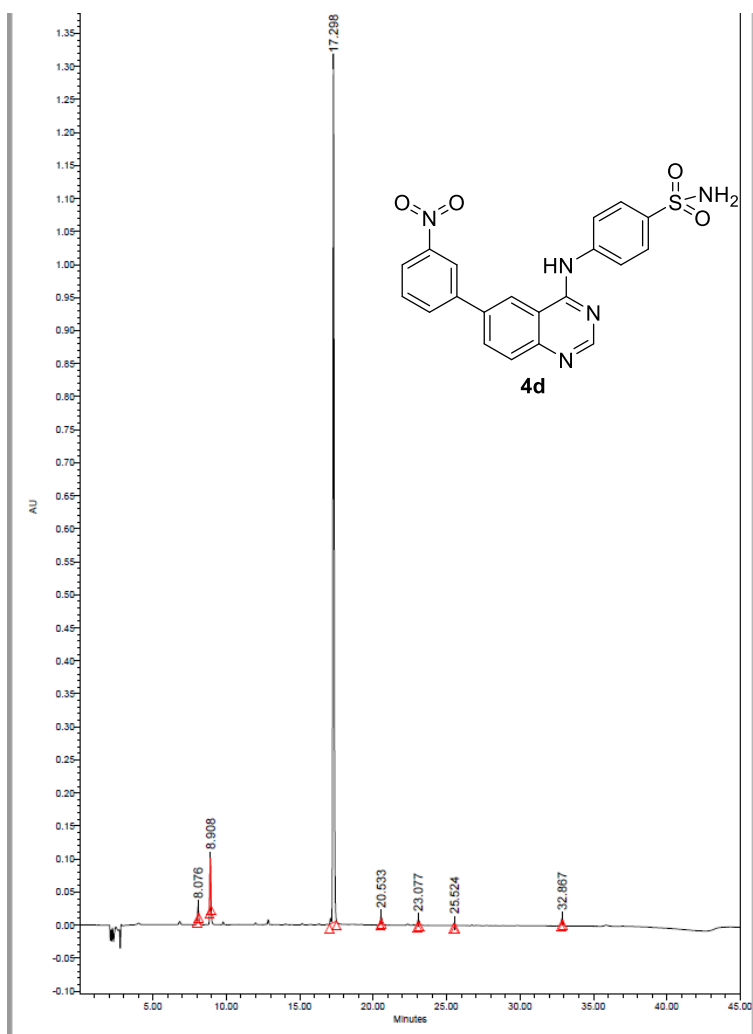
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1	8.772							227402	4.30	57247	bb		
2	12.519							76296	1.44	21075	bb		
3	15.013							4983721	94.26	818680	bb		

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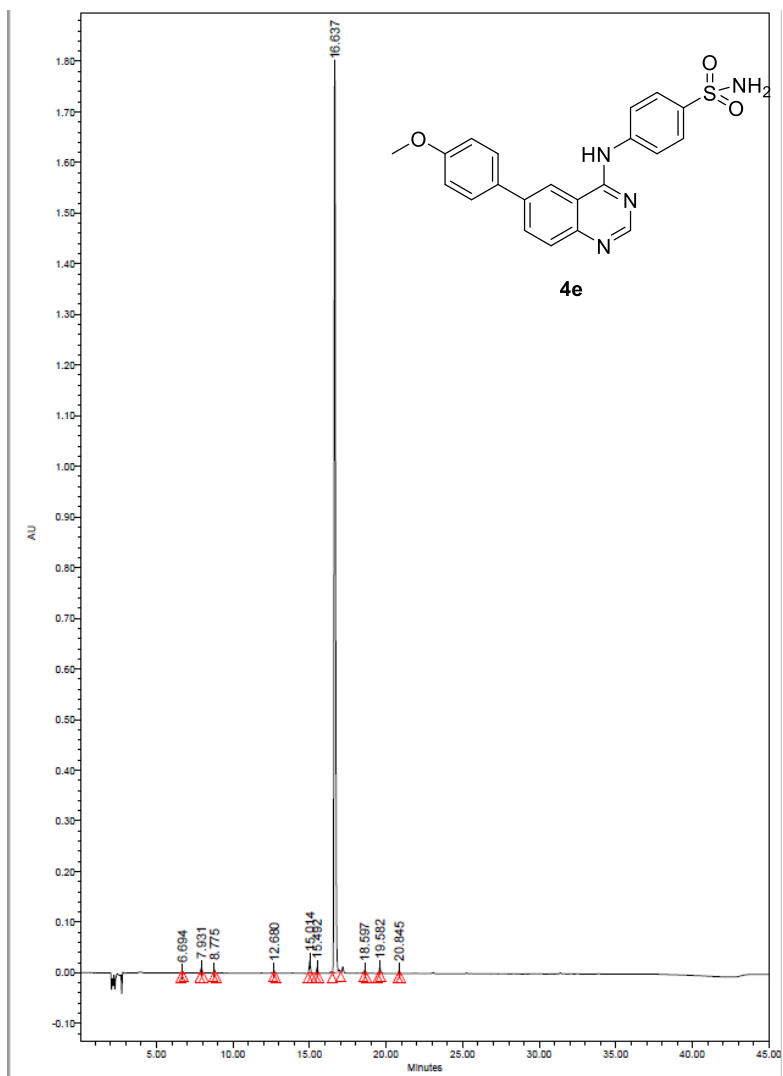
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1	12.815							830104	4.81	185459	bb		
2	17.235							16416914	95.19	2801847	bb		

Peak Type	Peak Codes
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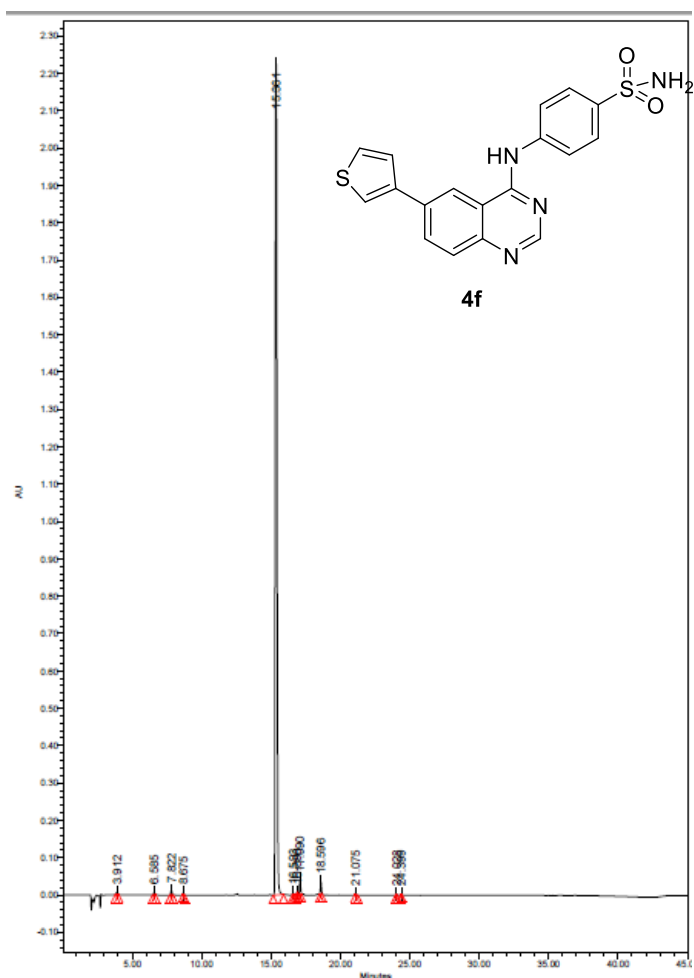
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1		8.076							47044	0.57	12618	bb		
2		8.908							302062	3.68	75700	bb		
3		17.298							7806171	95.08	1311111	bb		
4		20.533							17098	0.21	5429	bb		
5		23.077							16161	0.20	3734	bb		
6		25.524							5168	0.06	1350	bb		
7		32.867							16824	0.20	3804	bb		

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6	Unknown	
7	Unknown	



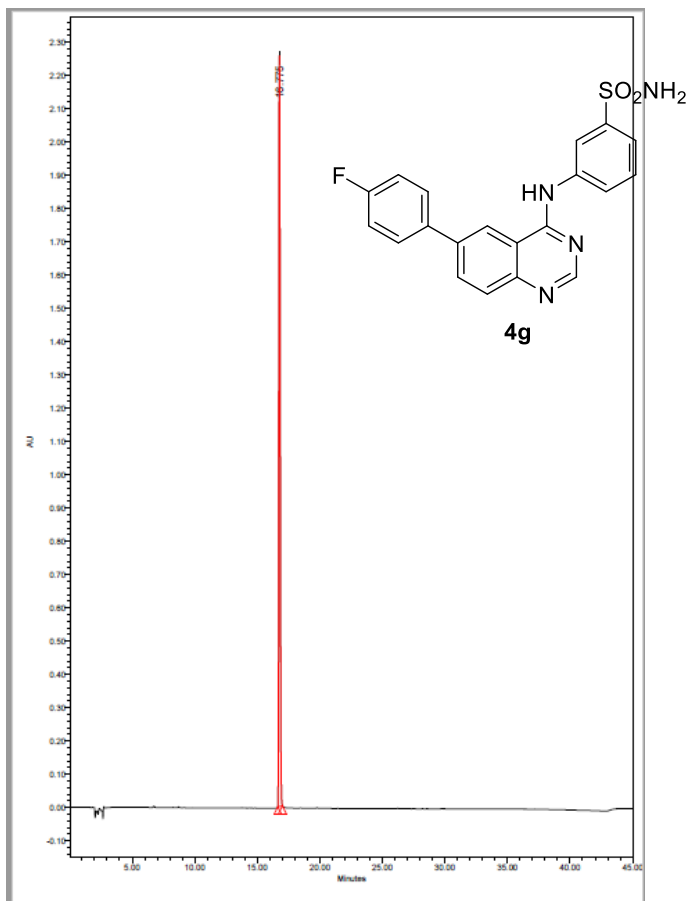
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1	6.694							14357	0.12	2244	bb		
2	7.931							58103	0.47	9352	bb		
3	8.775							26627	0.21	5630	bb		
4	12.680							20602	0.17	4220	bb		
5	15.014							144110	1.16	24188	bb		
6	15.492							61469	0.49	11138	bb		
7	16.637							12017479	96.57	1812810	bb		
8	18.597							27416	0.22	4151	bb		
9	19.582							44484	0.36	9451	bb		
10	20.845							30110	0.24	5670	bb		

Peak Type	Peak Codes
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3	Unknown
4	Unknown
5	Unknown
6	Unknown
7	Unknown



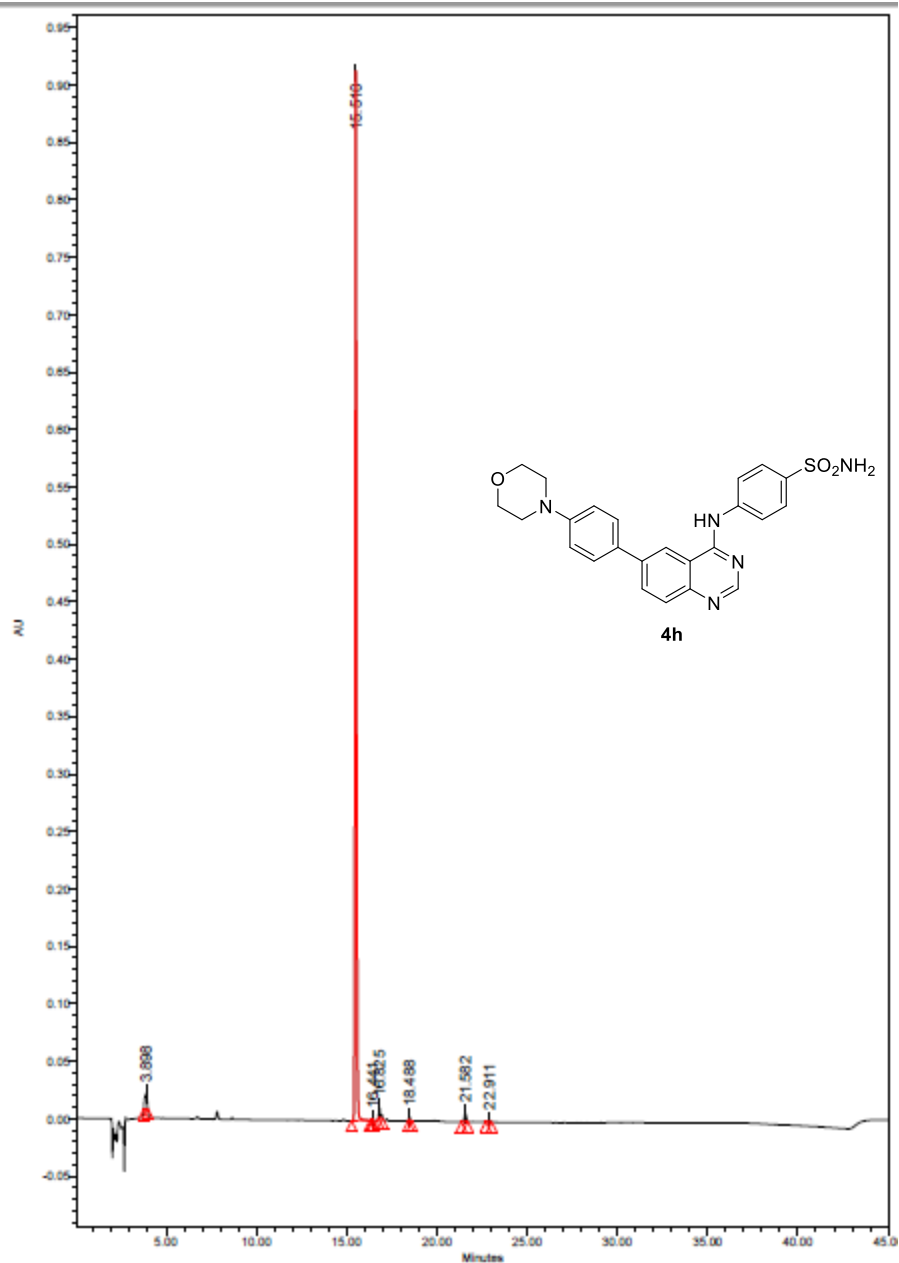
Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (μV*sec)	% Area	Height (μV)	Int Type	Amount	Units
1	3.912							38329	0.19	4362	bb		
2	6.585							39898	0.19	5960	bb		
3	7.822							74062	0.36	11982	bb		
4	8.675							9762	0.05	2722	bb		
5	15.361							19995834	97.18	2252689	bb		
6	16.593							17410	0.08	4021	bb		
7	16.890							21119	0.10	5240	bb		
8	17.090							198514	0.96	37851	bb		
9	18.596							160684	0.78	30903	bb		
10	21.075							8154	0.04	1953	bb		
11	24.028							9243	0.04	1986	bb		
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Peak Type	Peak Codes
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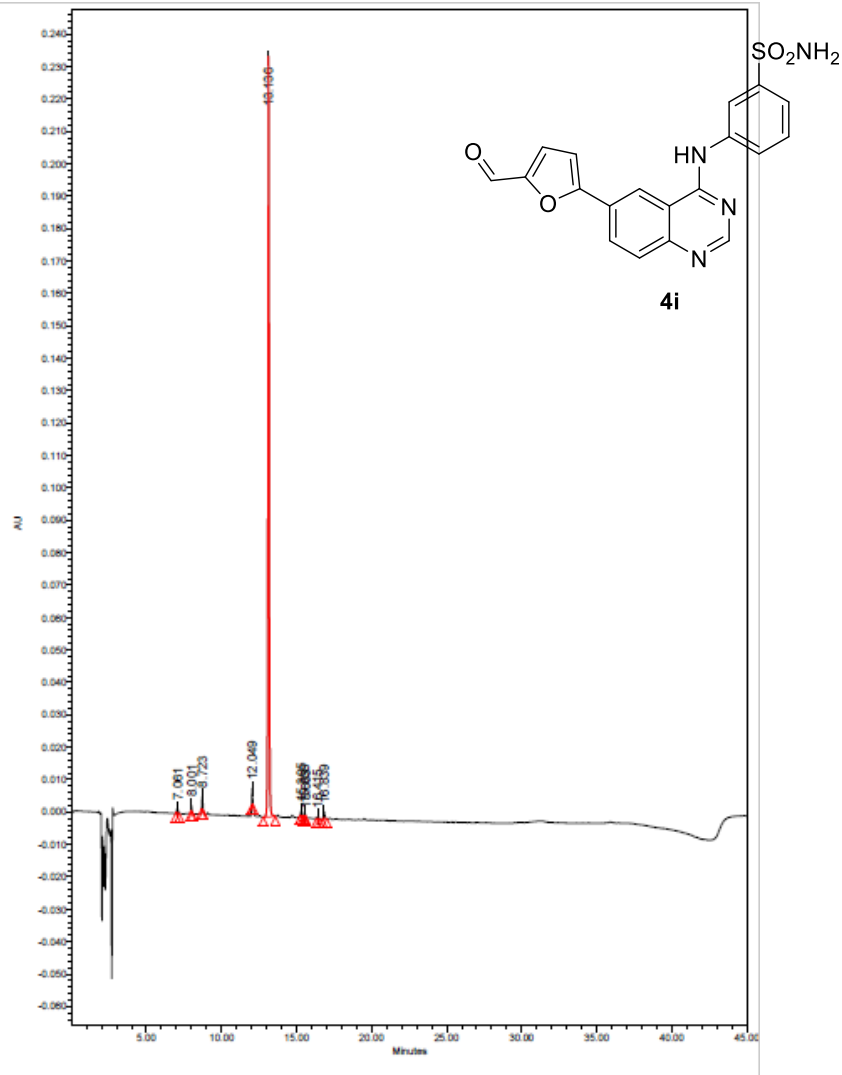


	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (μV*sec)	% Area	Height (μV)	Int Type	Amount	Units
1		16.775							16022791	100.00	2262610	bb		

	Peak Type	Peak Codes
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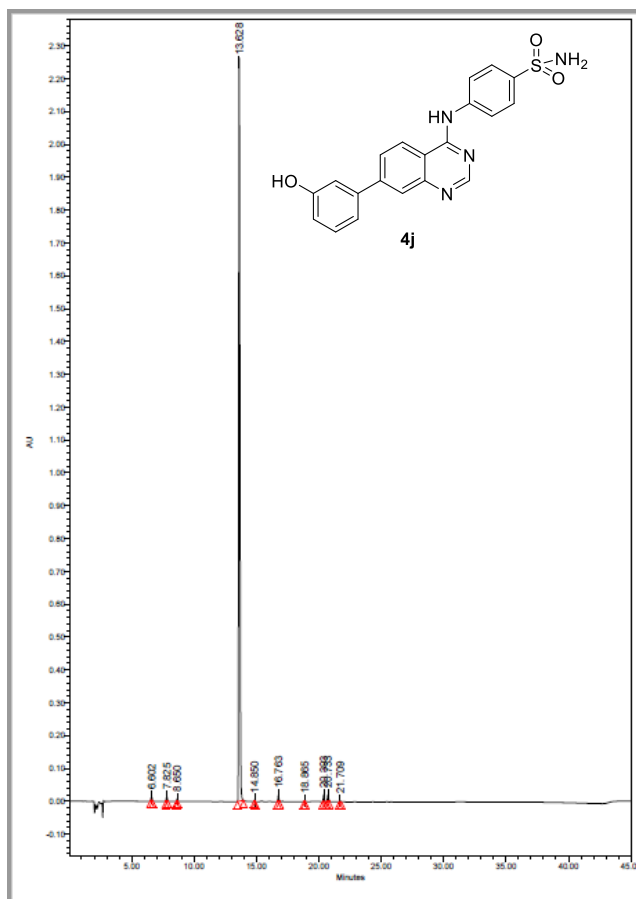


Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area ($\mu\text{V} \cdot \text{sec}$)	% Area	Height (μV)	Int Type	Amount	Units
1	3.898							122192	2.23	13150	bb		
2	15.510							5214400	95.27	905048	bb		
3	16.441							3167	0.06	867	bb		
4	16.825							54410	0.99	8926	bb		
5	18.488							14350	0.26	2914	bb		
6	21.582							52919	0.97	6797	bb		
7	22.911							11878	0.22	1330	bb		



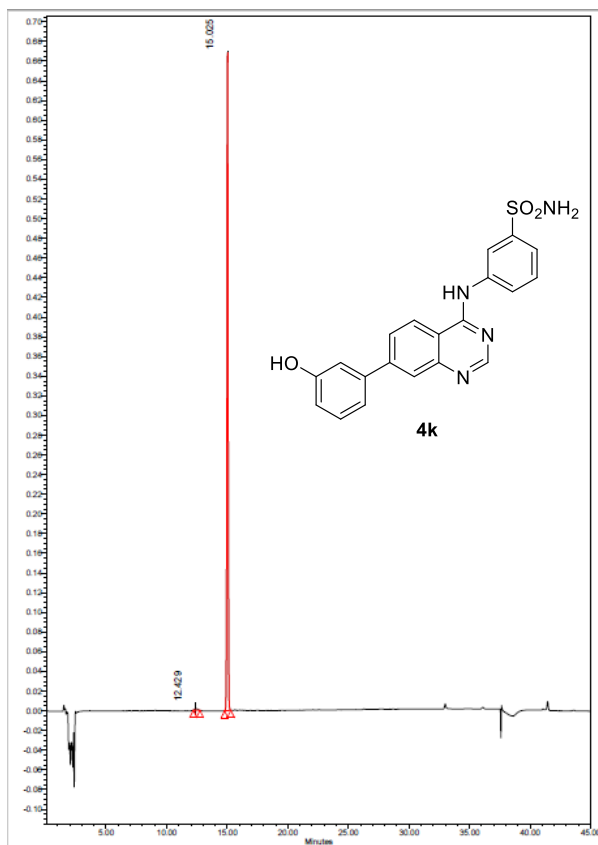
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1	7.061							10398	0.74	1388	bb		
2	8.001							6112	0.44	1742	bb		
3	8.723							16055	1.15	4045	bb		
4	12.049							17560	1.26	5014	bb		
5	13.136							1329898	95.09	232034	bb		
6	15.305							6206	0.44	1452	bb		
7	15.538							4342	0.31	1215	bb		
8	15.603							0	0.00	0	tt		
9	16.415							1704	0.12	343	bb		
10	16.839							6239	0.45	1554	bb		

Peak Type	Peak Codes
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6	Unknown
7	Unknown
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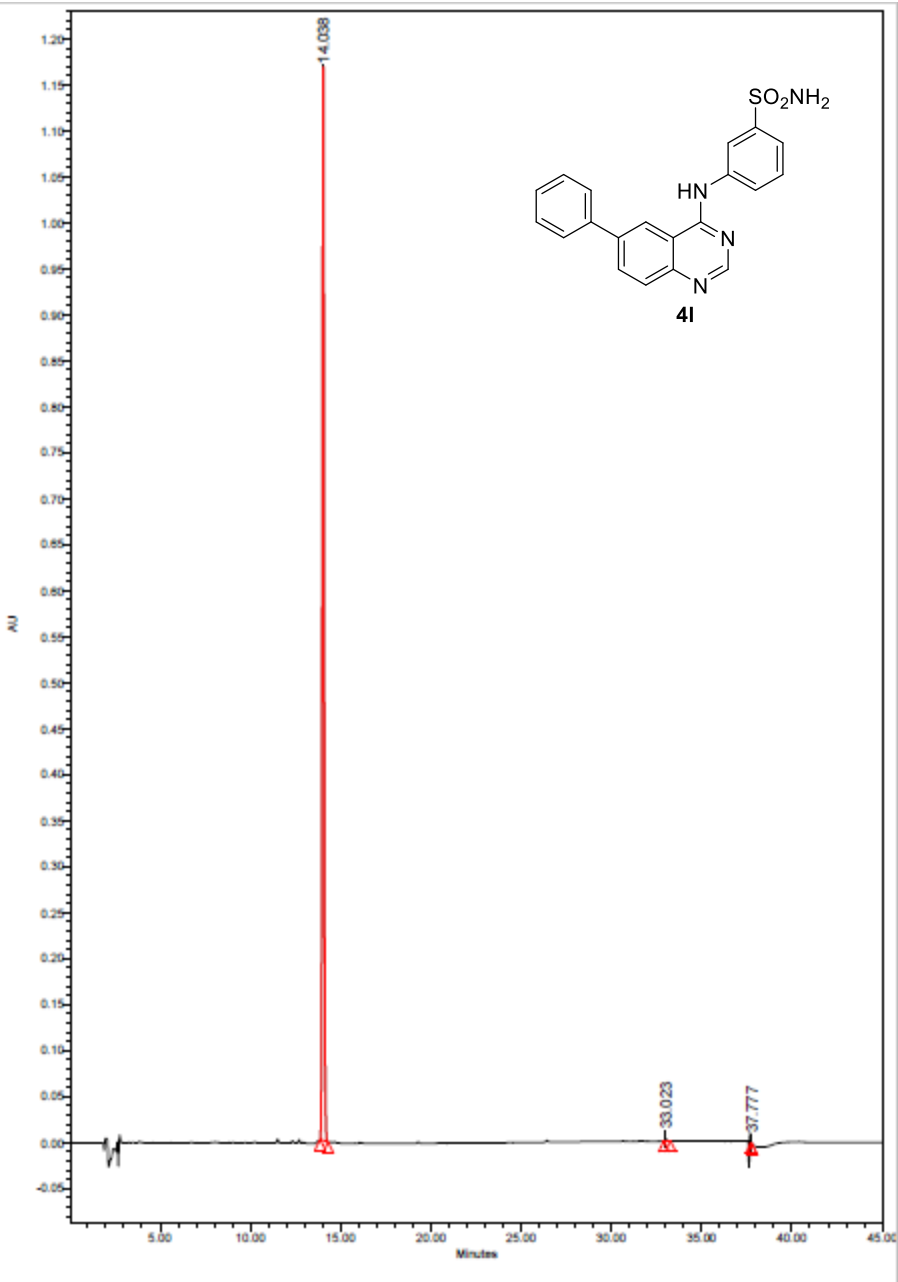
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1	6.602							61572	0.40	10046	bb		
2	7.825							61218	0.39	11418	bb		
3	8.650							24893	0.16	5862	bb		
4	13.628							15014404	96.82	2285484	bb		
5	14.850							6524	0.04	1936	bb		
6	16.763							89713	0.58	17181	bb		
7	18.865							9345	0.06	2133	bb		
8	20.393							107303	0.69	19431	bb		
9	20.733							116863	0.75	19392	bb		
10	21.709							16226	0.10	3145	bb		

Peak Type	Peak Codes
1	Unknown
2	Unknown
3	Unknown
4	Unknown
5	Unknown
6	Unknown
7	Unknown
8	Unknown
9	Unknown
10	Unknown



Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (μV*sec)	% Area	Height (μV)	Int Type	Amount	Units
1	12.429							30824	0.68	1764	bb		
2	15.025							4493452	99.32	671385	bb		

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2	Unknown	



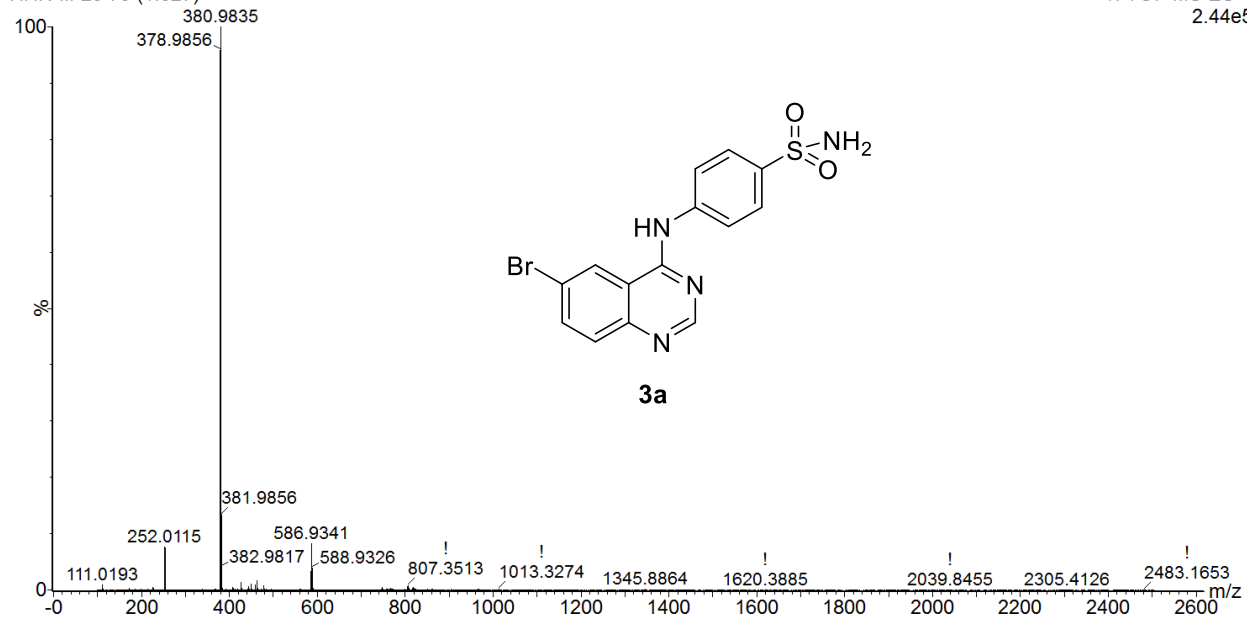
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1	14.038							7876666	99.81	1168263	bb		
2	33.023							14625	0.19	1987	bb		
3	37.777							563	0.01	-225	bb		

Peak Type	Peak Codes
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2 Unknown	
3 Unknown	I08

3. Representative HRMS data of the compounds 3a-d and 4a-f

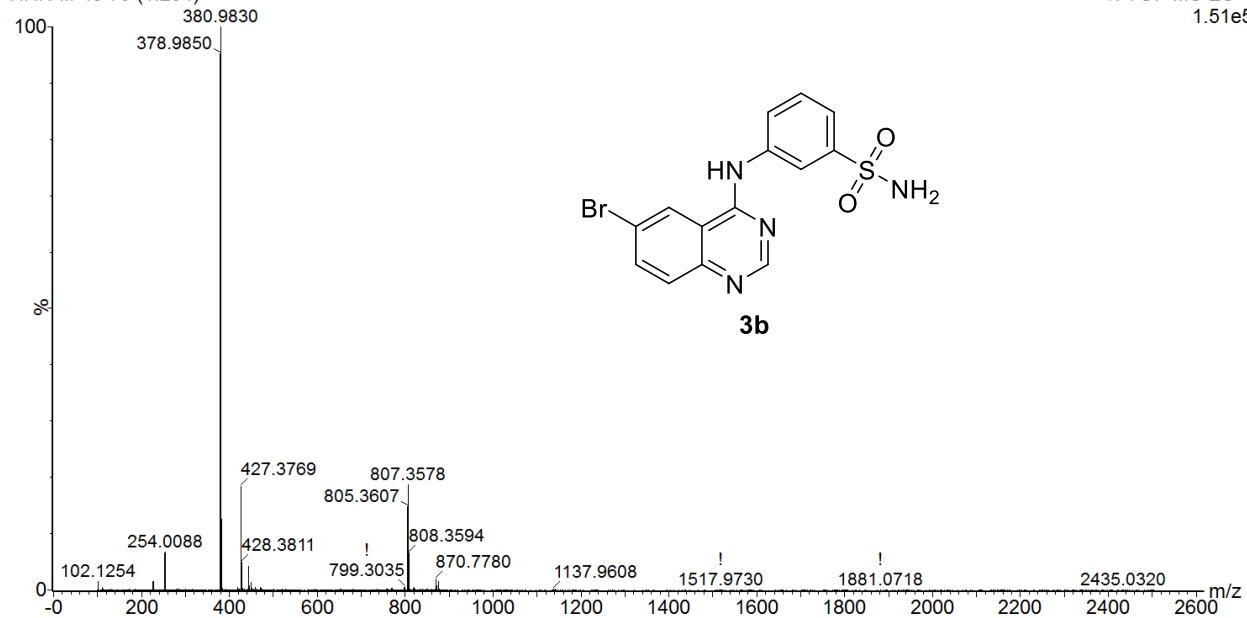
HHN-III-25 75 (1.327)

1: TOF MS ES+
2.44e5



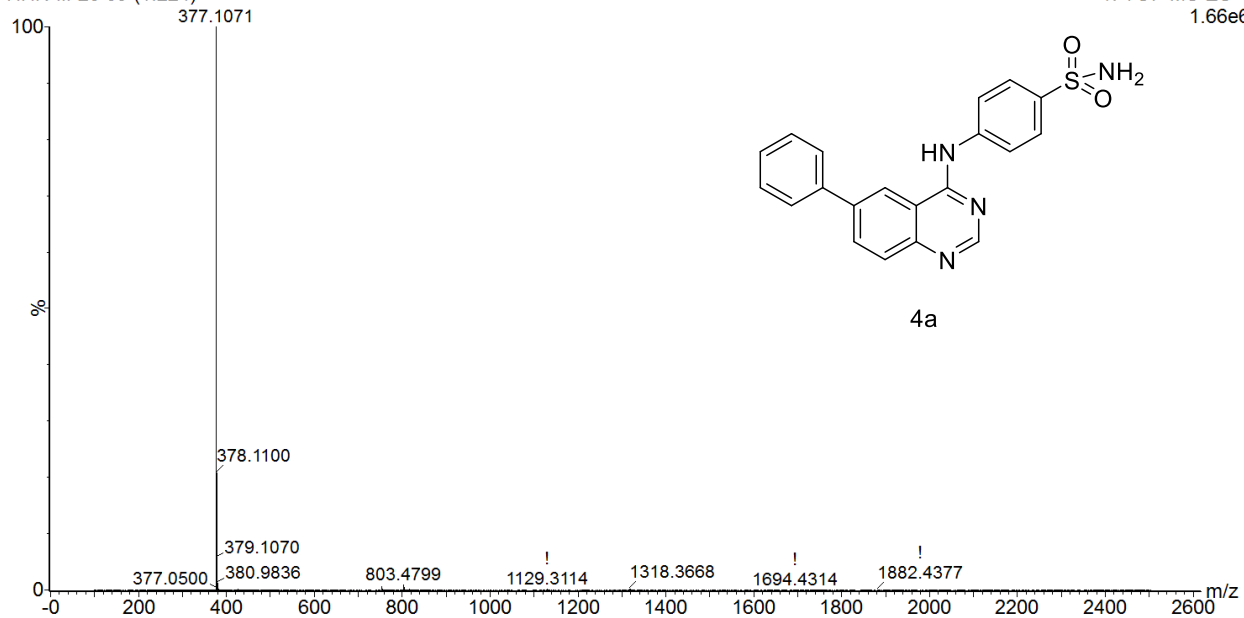
HHN-III-43 73 (1.294)

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1.51e5



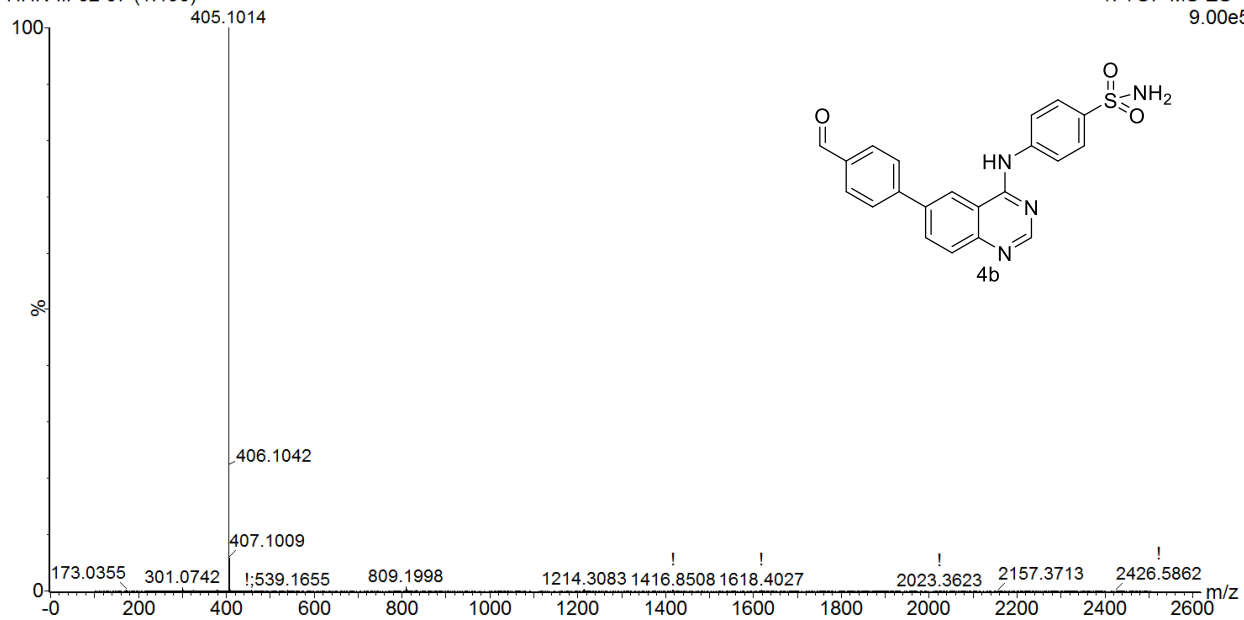
HHN-III-26 69 (1.224)

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1.66e6



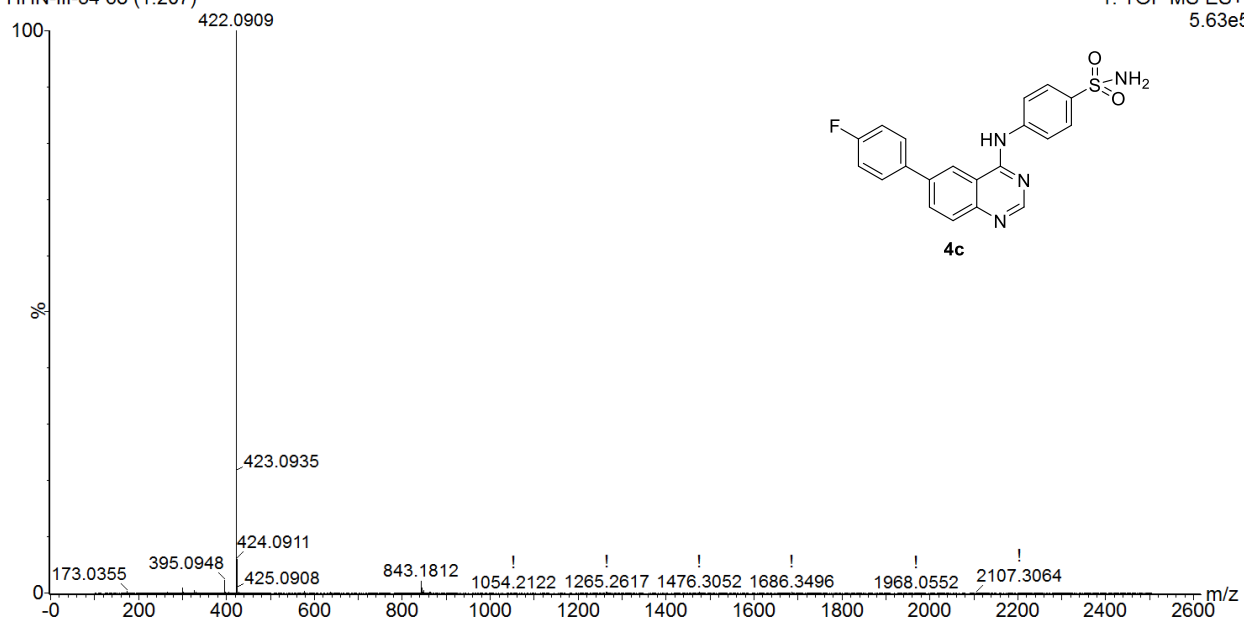
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9.00e5



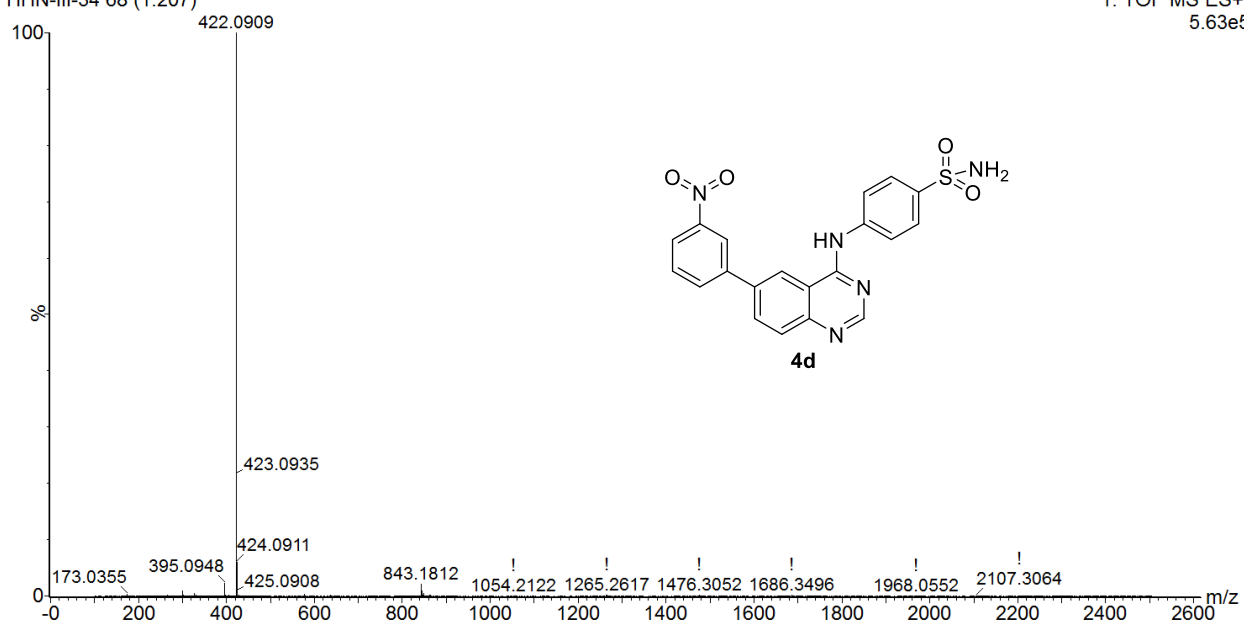
HHN-III-34 68 (1.207)

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5.63e5



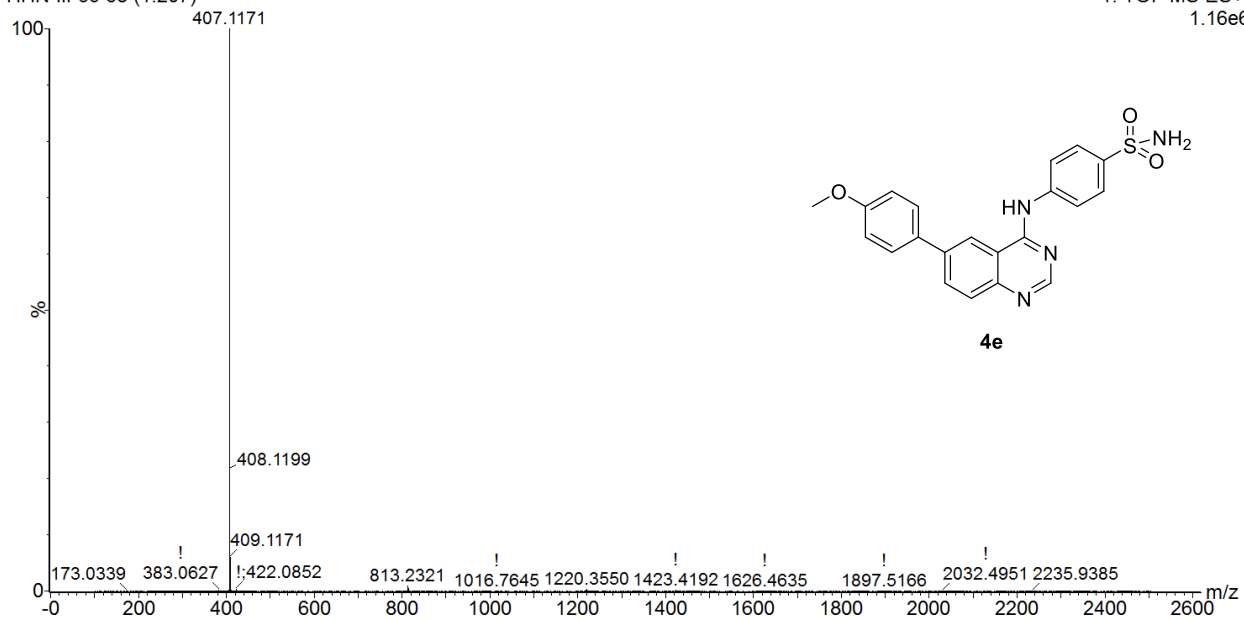
HHN-III-34 68 (1.207)

1: TOF MS ES+
5.63e5



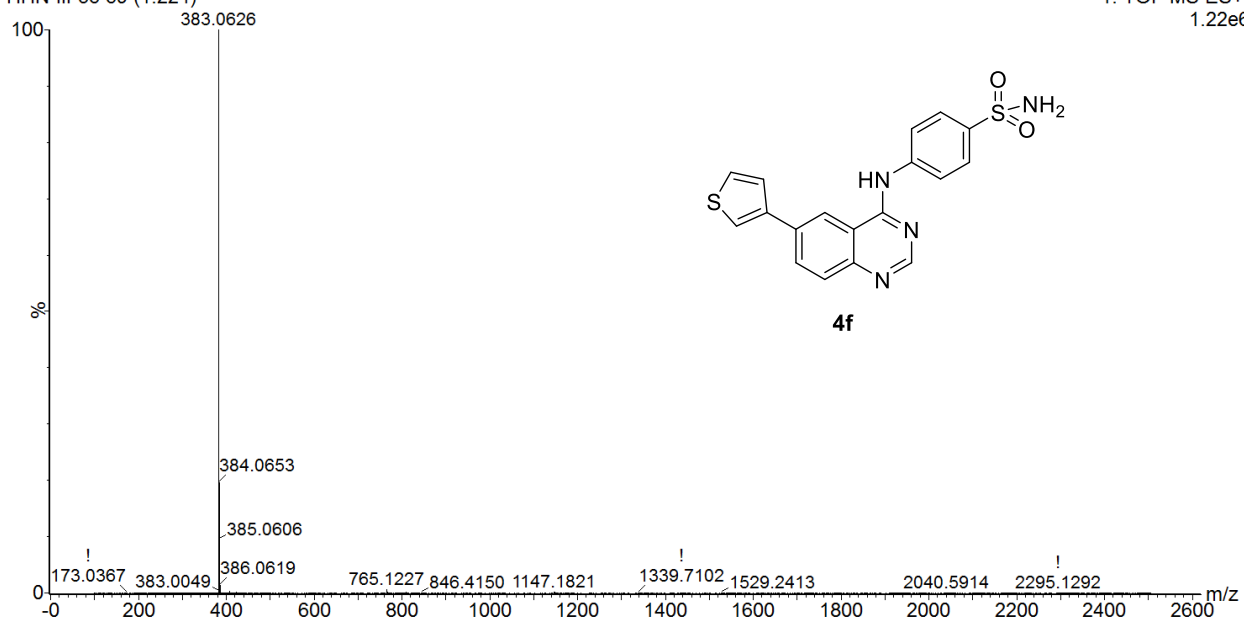
HHN-III-35 68 (1.207)

1: TOF MS ES+
1.16e6



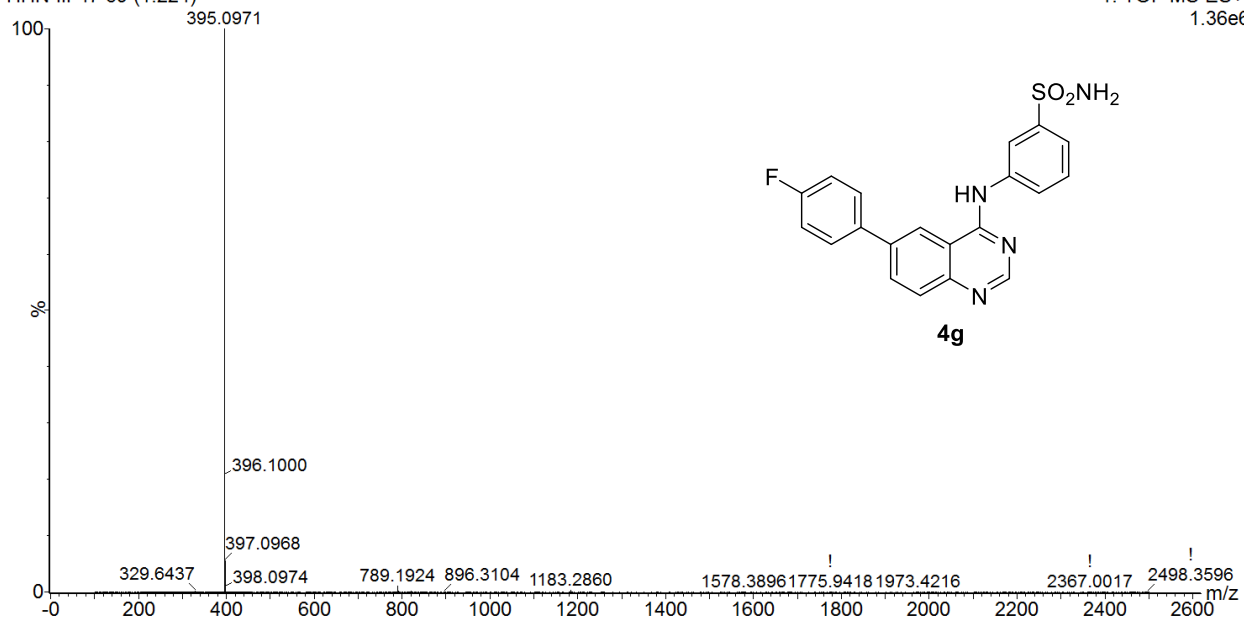
HHN-III-36 69 (1.224)

1: TOF MS ES+
1.22e6



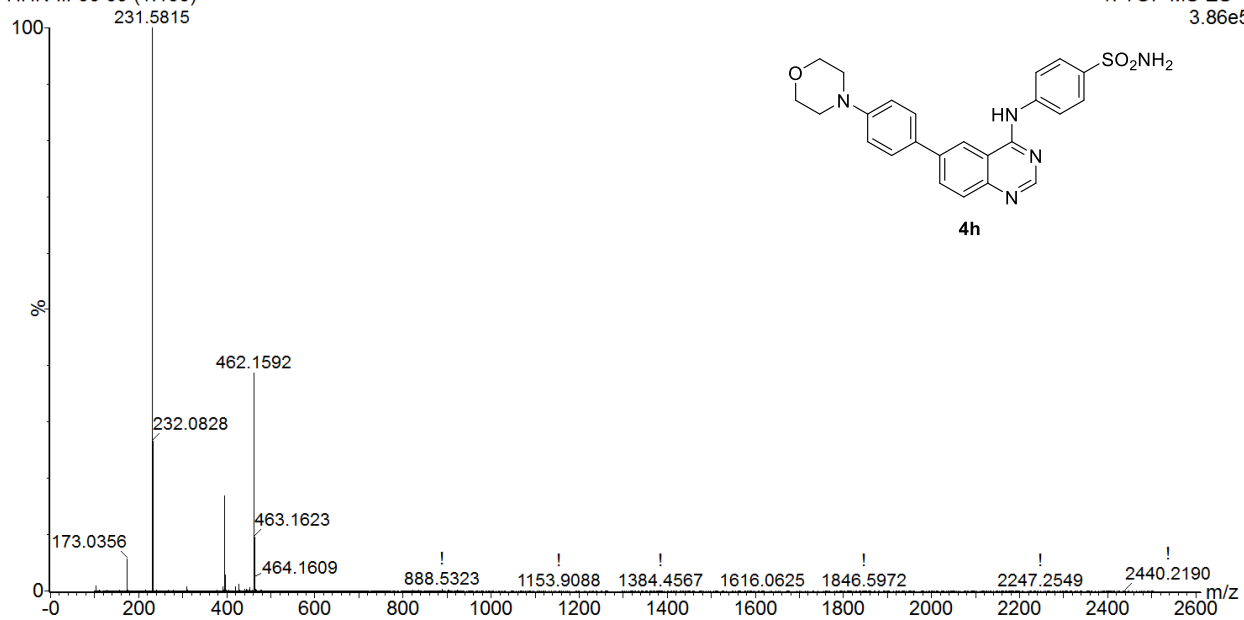
HHN-III-47 69 (1.224)

1: TOF MS ES+
1.36e6



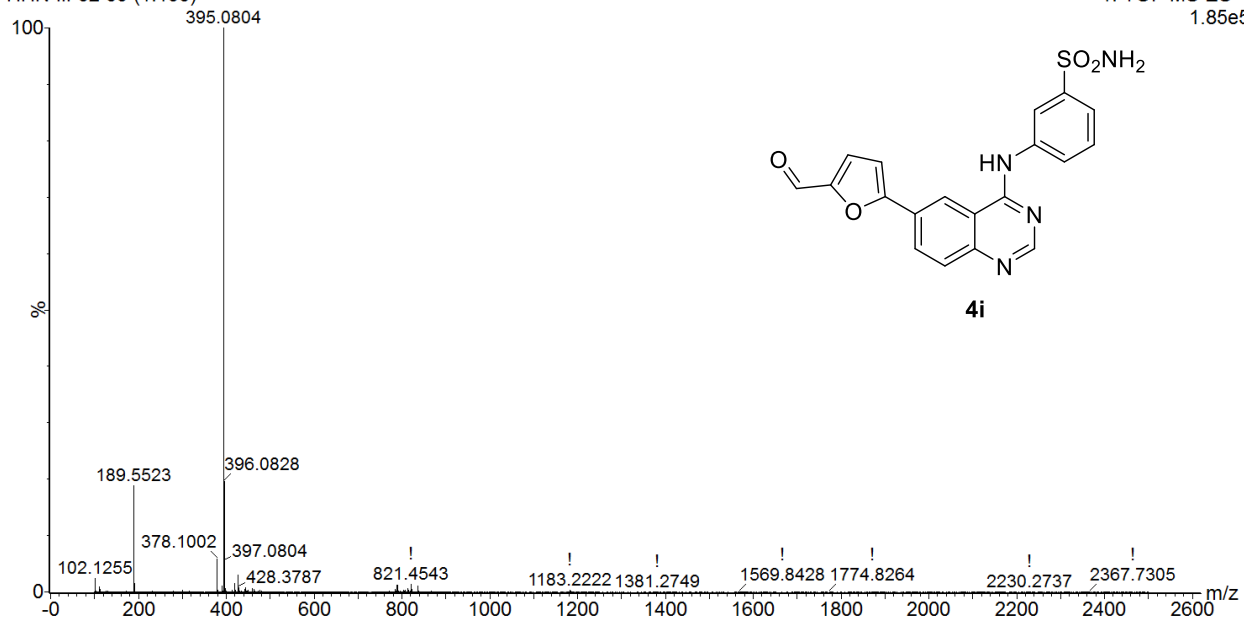
HHN-III-50 65 (1.156)

1: TOF MS ES+
3.86e5



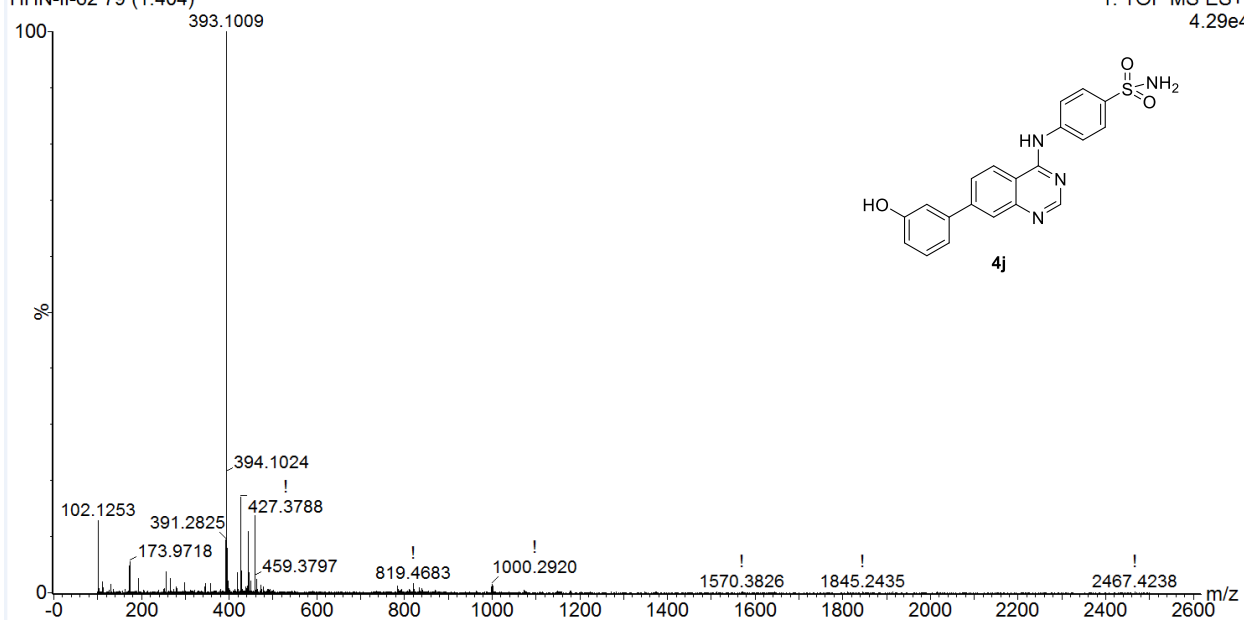
HHN-III-52 65 (1.156)

1: TOF MS ES+
1.85e5

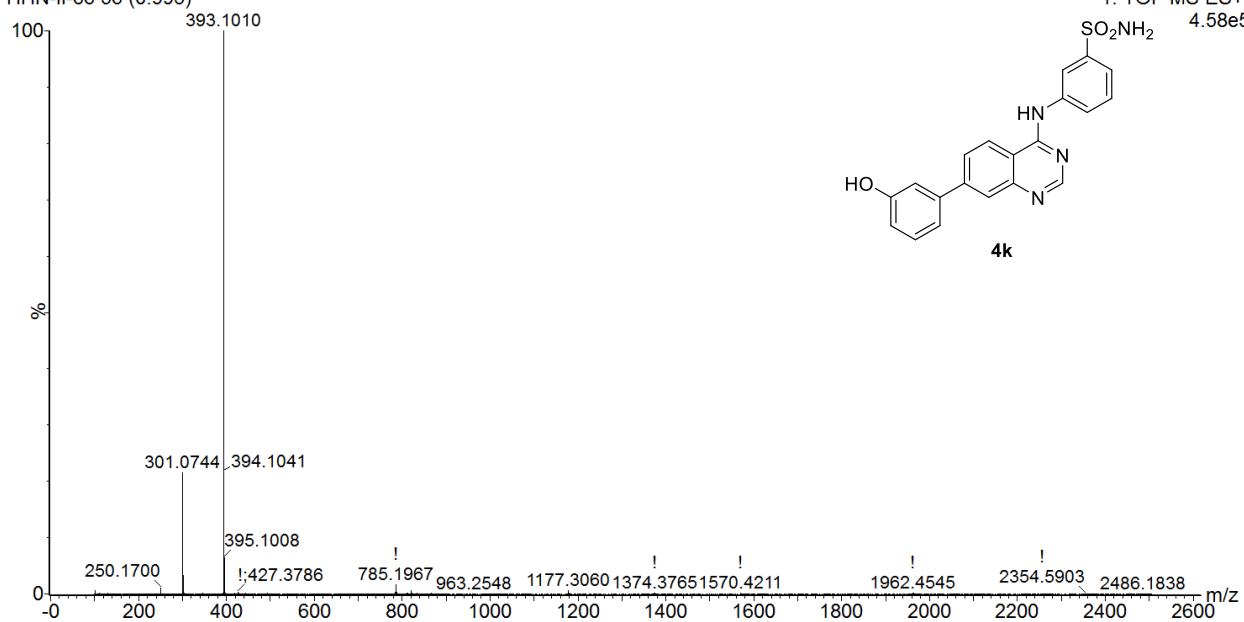


HHN-II-62 79 (1.404)

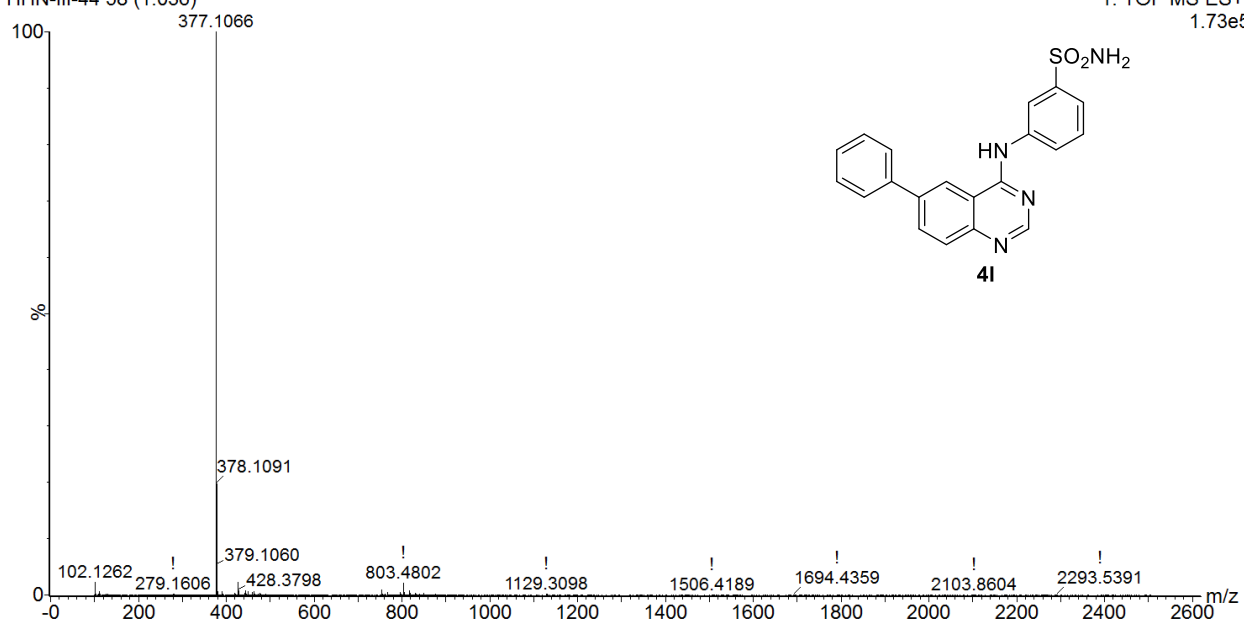
1: TOF MS ES+
4.29e4



HHN-II-66 56 (0.993)



HHN-III-44 58 (1.036)



4. Supplementary docking figures

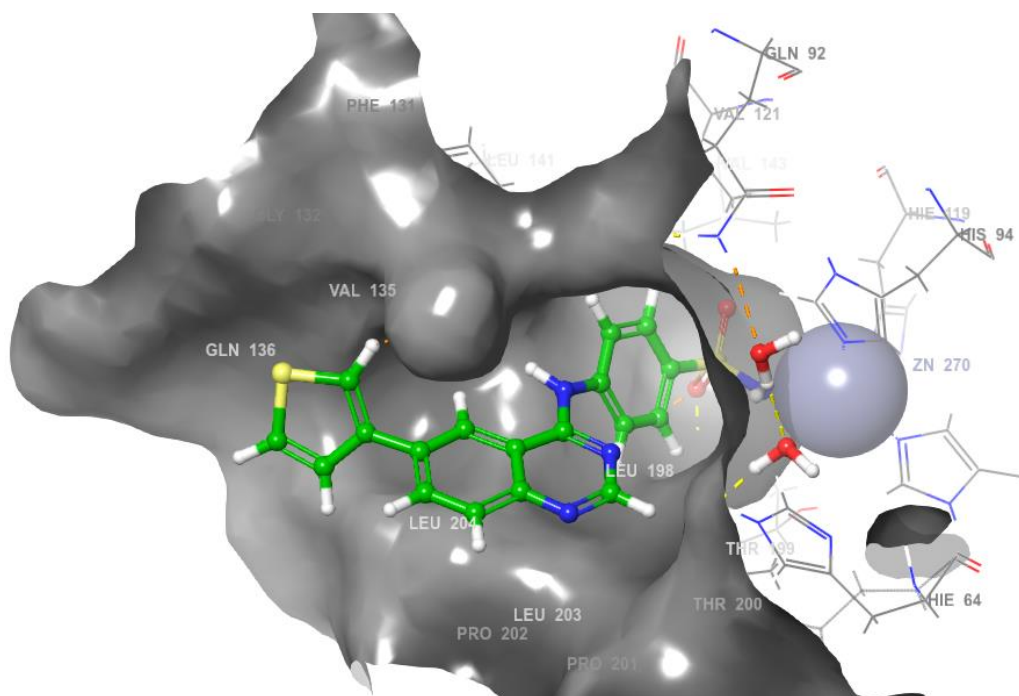


Figure S4.1. 3D model of the crystal structure of hCA II with compound 4f.

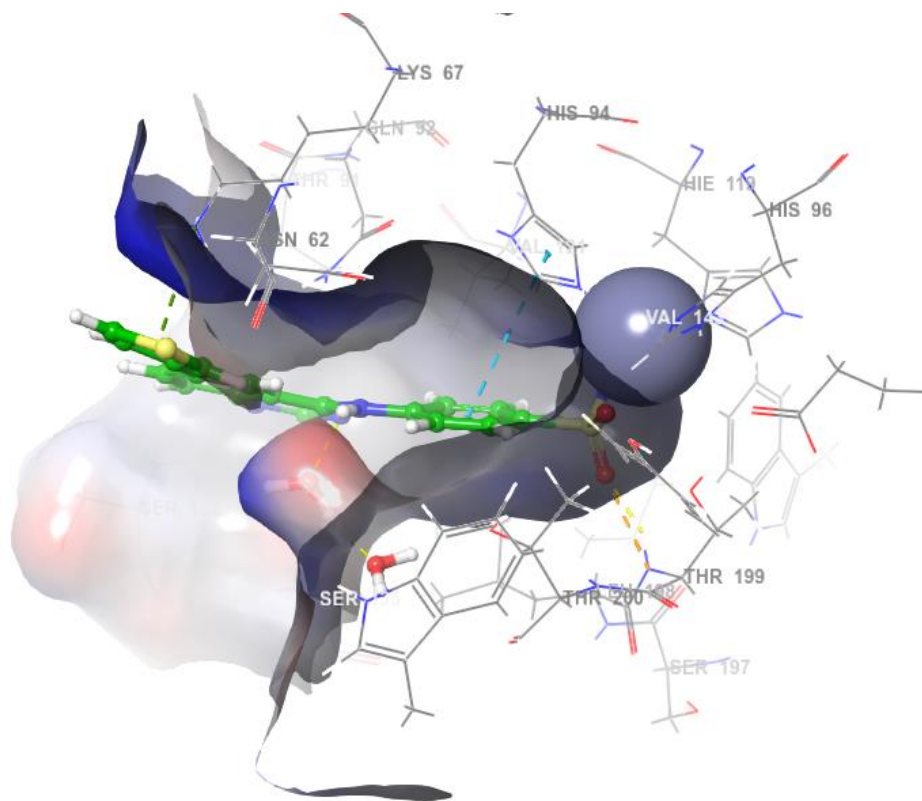
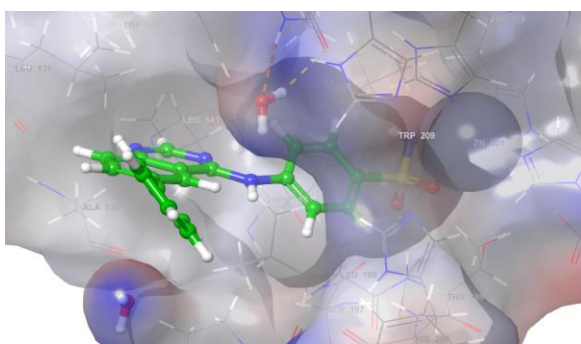
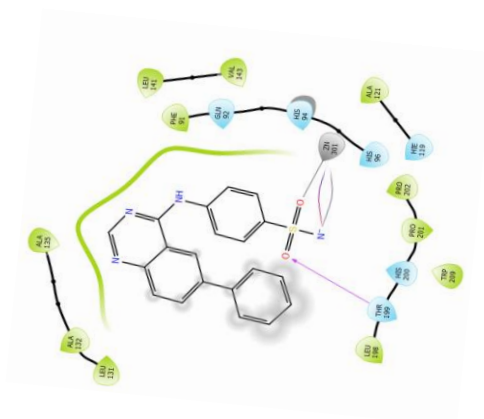


Figure S4.2. 3D model of the crystal structure of hCA XII with compound **4f**.



A



B

Figure S4.3. The interaction patterns of compound **4a** in the active sites of hCAI (A) 3D model of the crystal structure of hCA I with compound **4a**. (B) 2D interaction pattern of compound **4a** with hCA I active site.

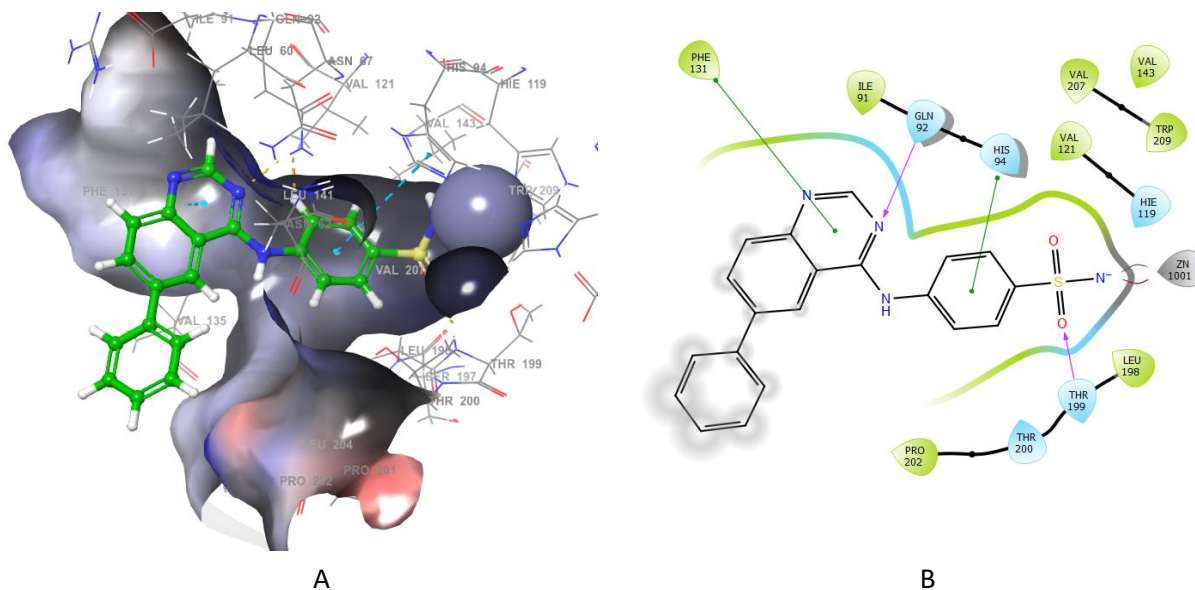


Figure S4.4. The interaction patterns of compound **4a** in the active sites of hCA IX (A) 3D model of the crystal structure of hCA IX with compound **4a**. (B) 2D interaction pattern of compound **4a** with hCA IX active site.

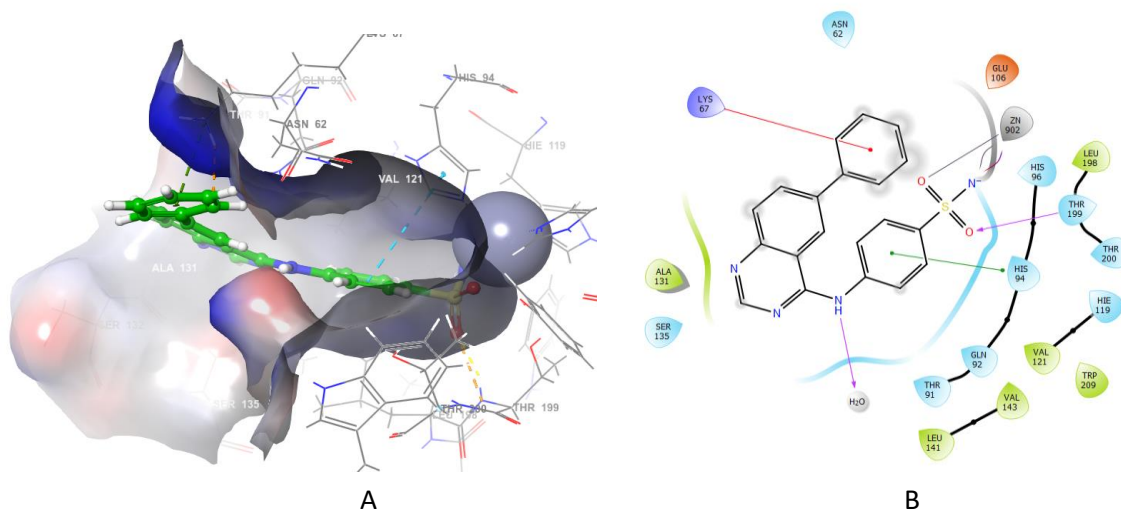


Figure S4.5. The interaction patterns of compound **4a** in the active sites of hCA XII (A) 3D model of the crystal structure of hCA XII with compound **4a**. (B) 2D interaction pattern of compound **4a** with hCA XII active site.