

ChemMedChem

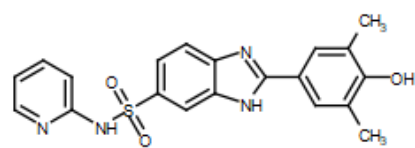
Supporting Information

Discovery of Benzo[*d*]imidazole-6-sulfonamides as Bromodomain and Extra-Terminal Domain (BET) Inhibitors with Selectivity for the First Bromodomain

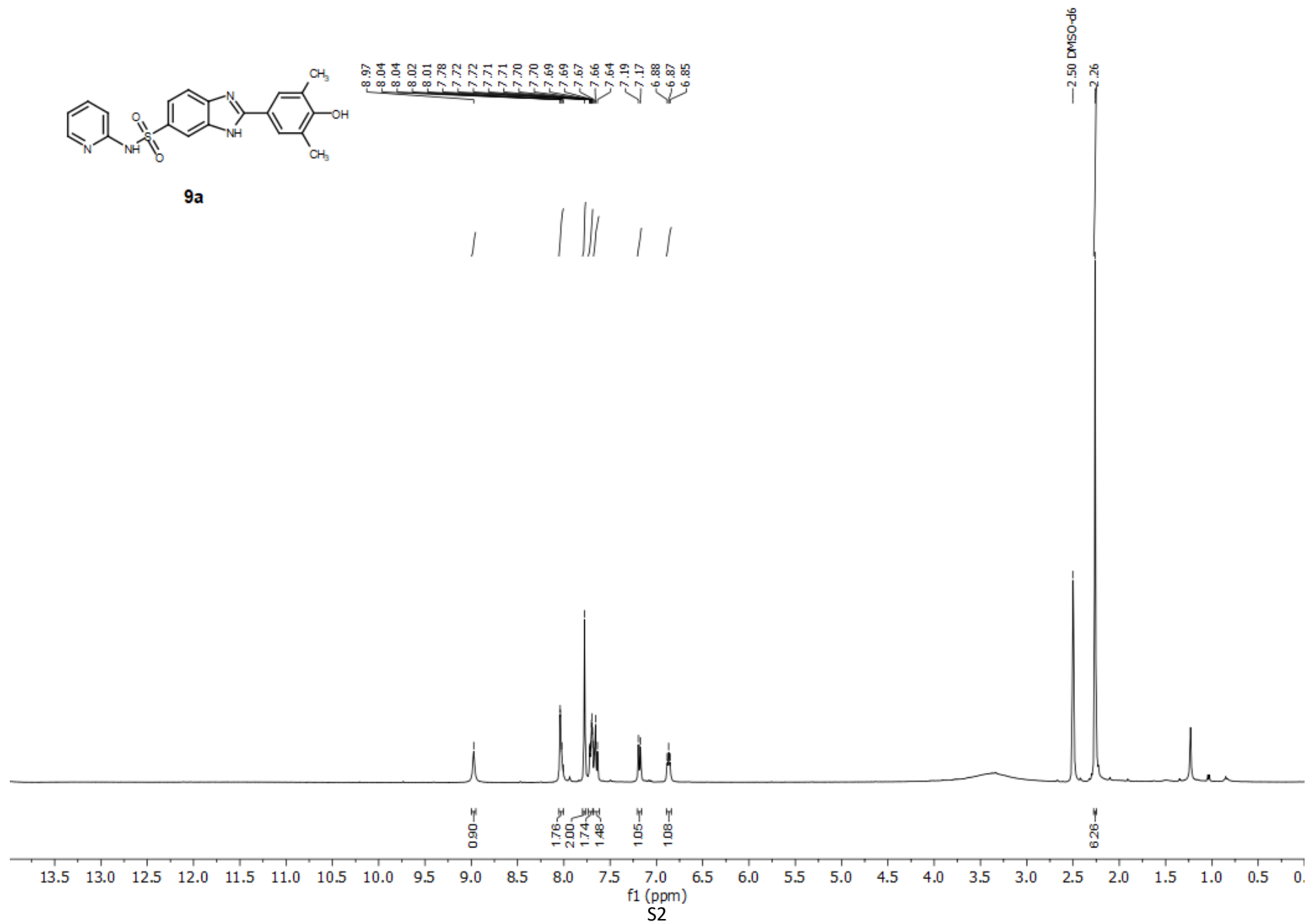
Alessandra Cipriano⁺, Ciro Milite⁺, Alessandra Feoli, Monica Viviano, Giacomo Pepe, Pietro Campiglia, Giuliana Sarno, Sarah Picaud, Satomi Imaide, Nikolai Makukhin, Panagis Filippakopoulos, Alessio Ciulli, Sabrina Castellano,^{*} and Gianluca Sbardella

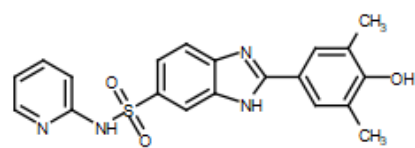
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¹ H-NMR and ¹³ C-NMR spectra of compounds 9a–p	S2–S33
HRMS spectra of compounds 9a–p	S34–S49
HPLC traces of compounds 9a–p	S50–S65



9a





9a

156.11
154.44

139.92

127.30

124.82

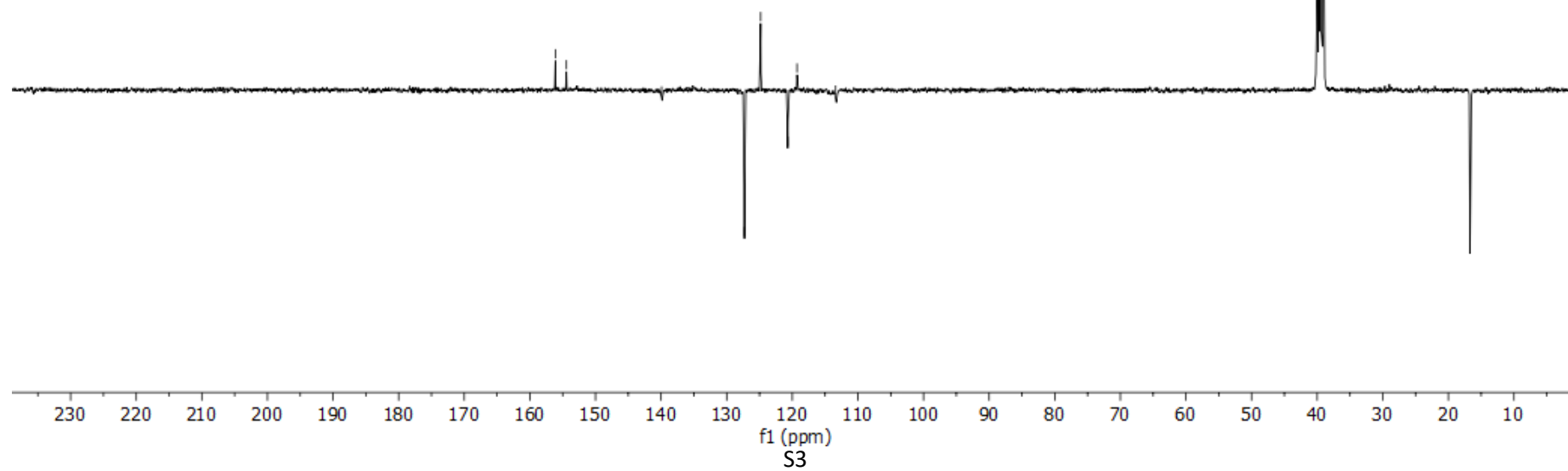
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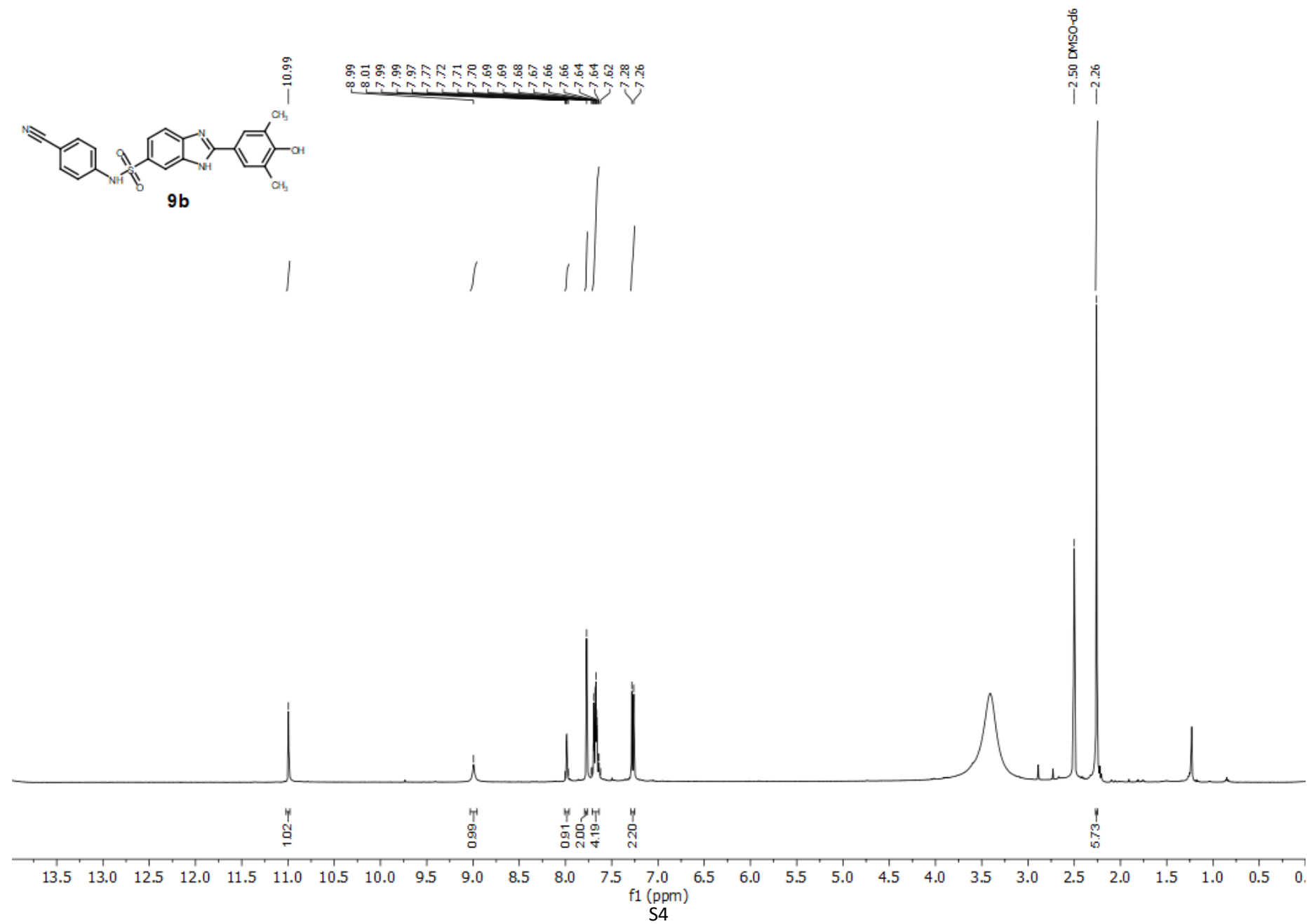
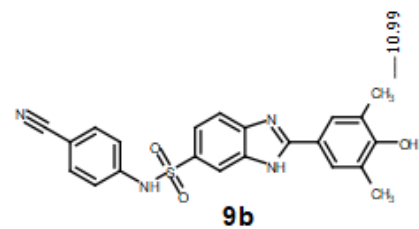
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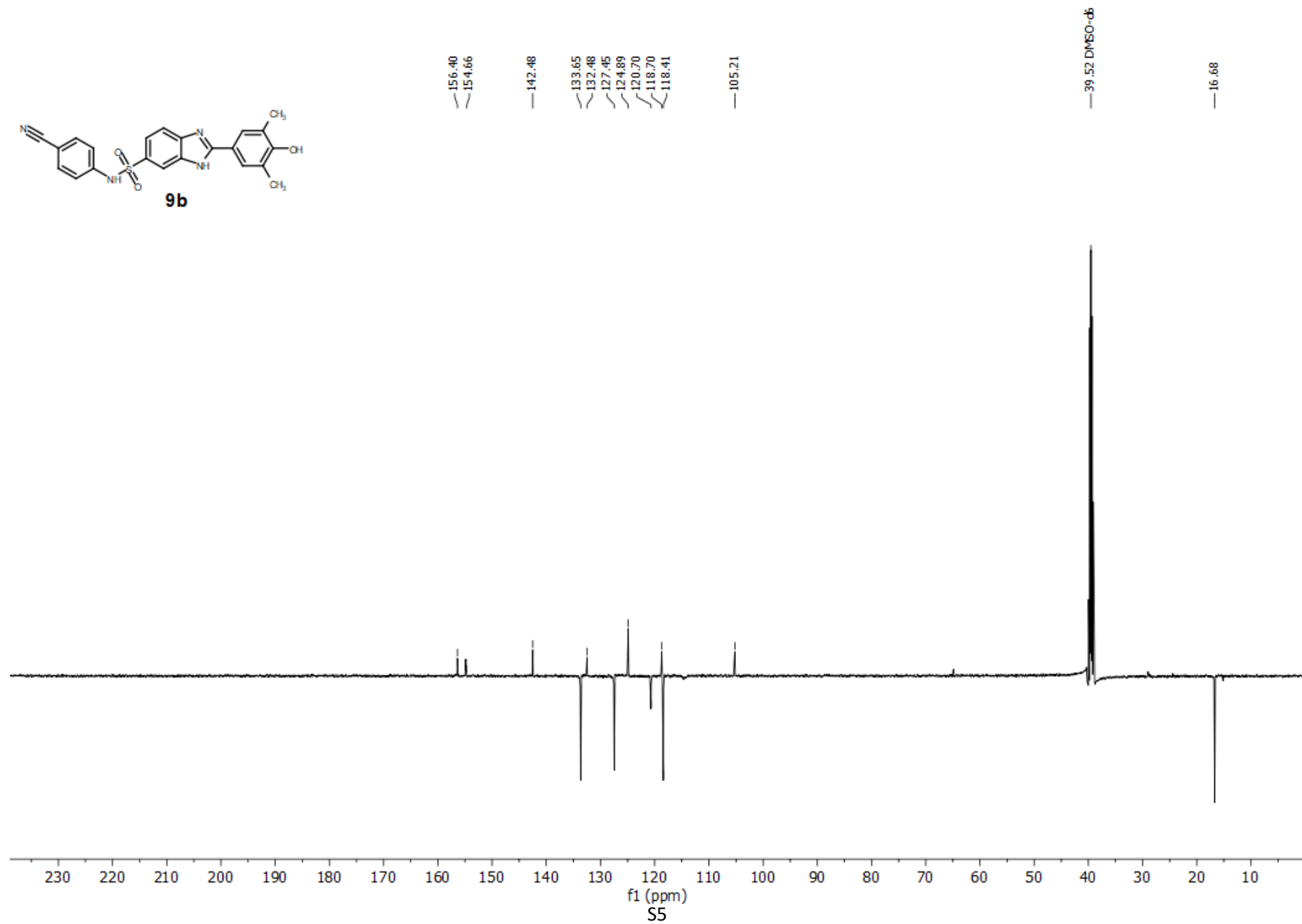
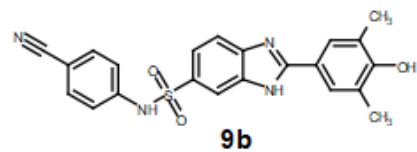
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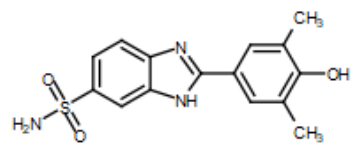
39.52 DMSO-d₆

16.69

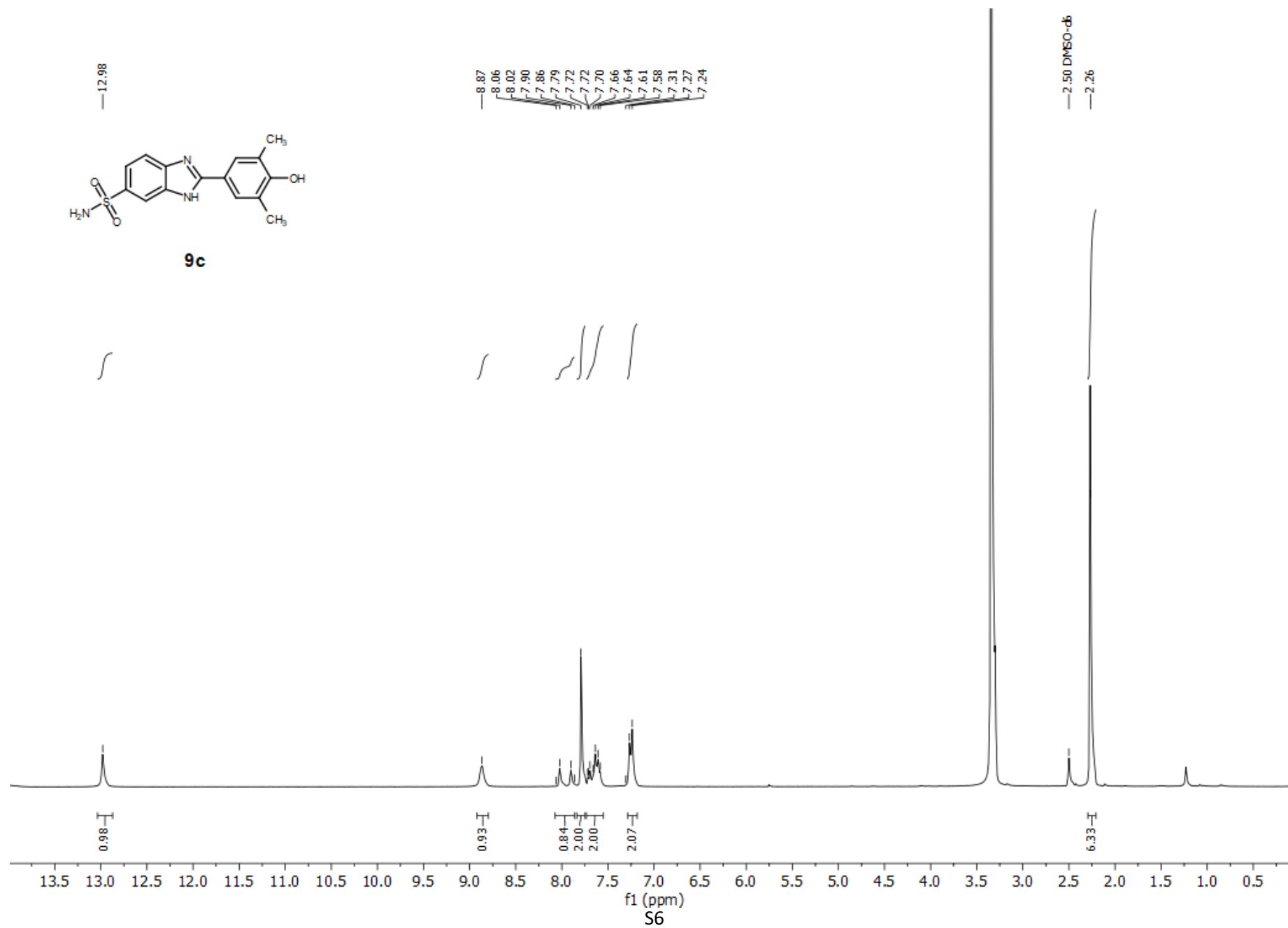


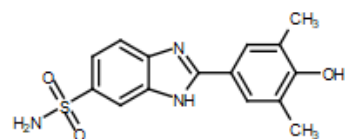




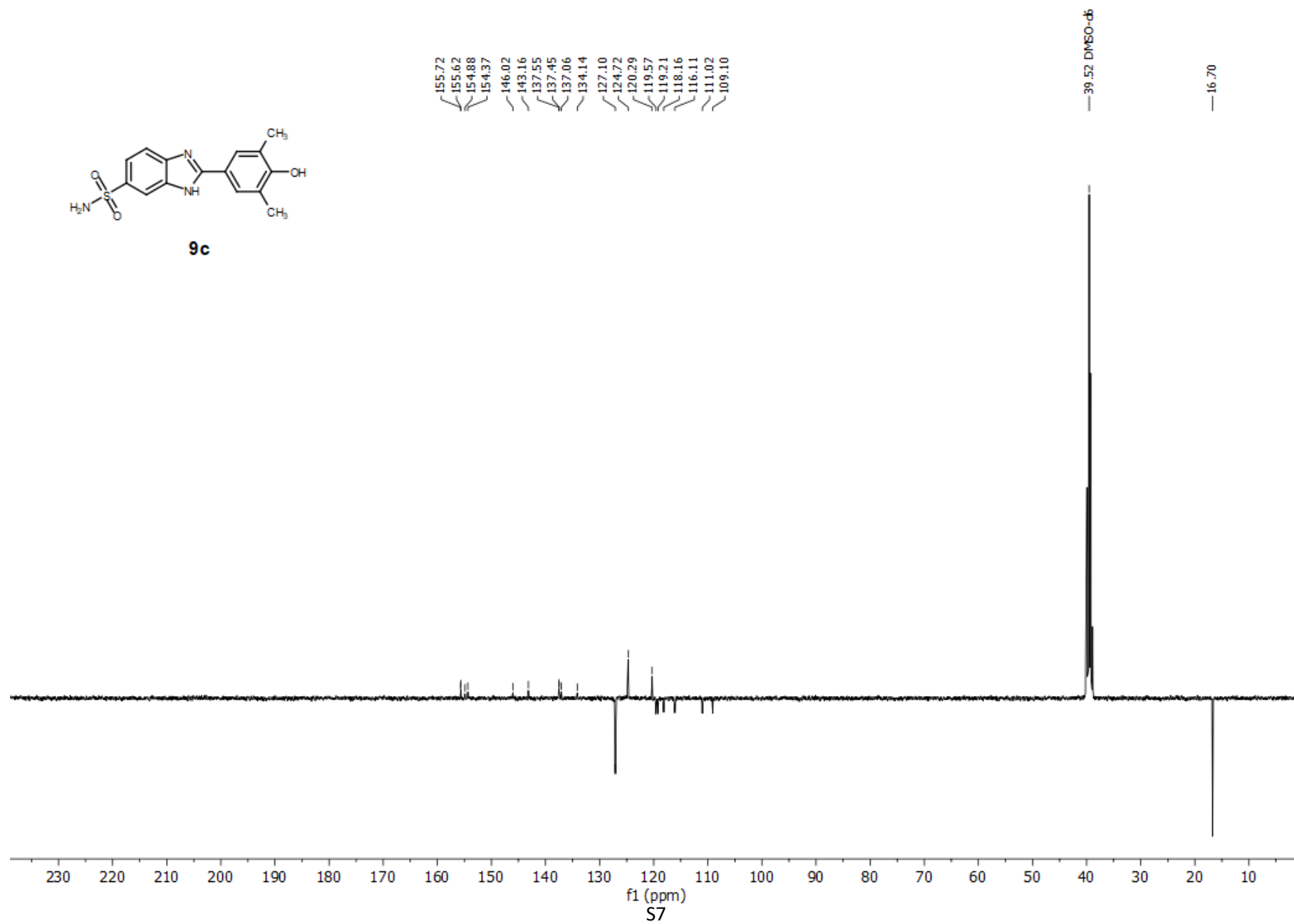


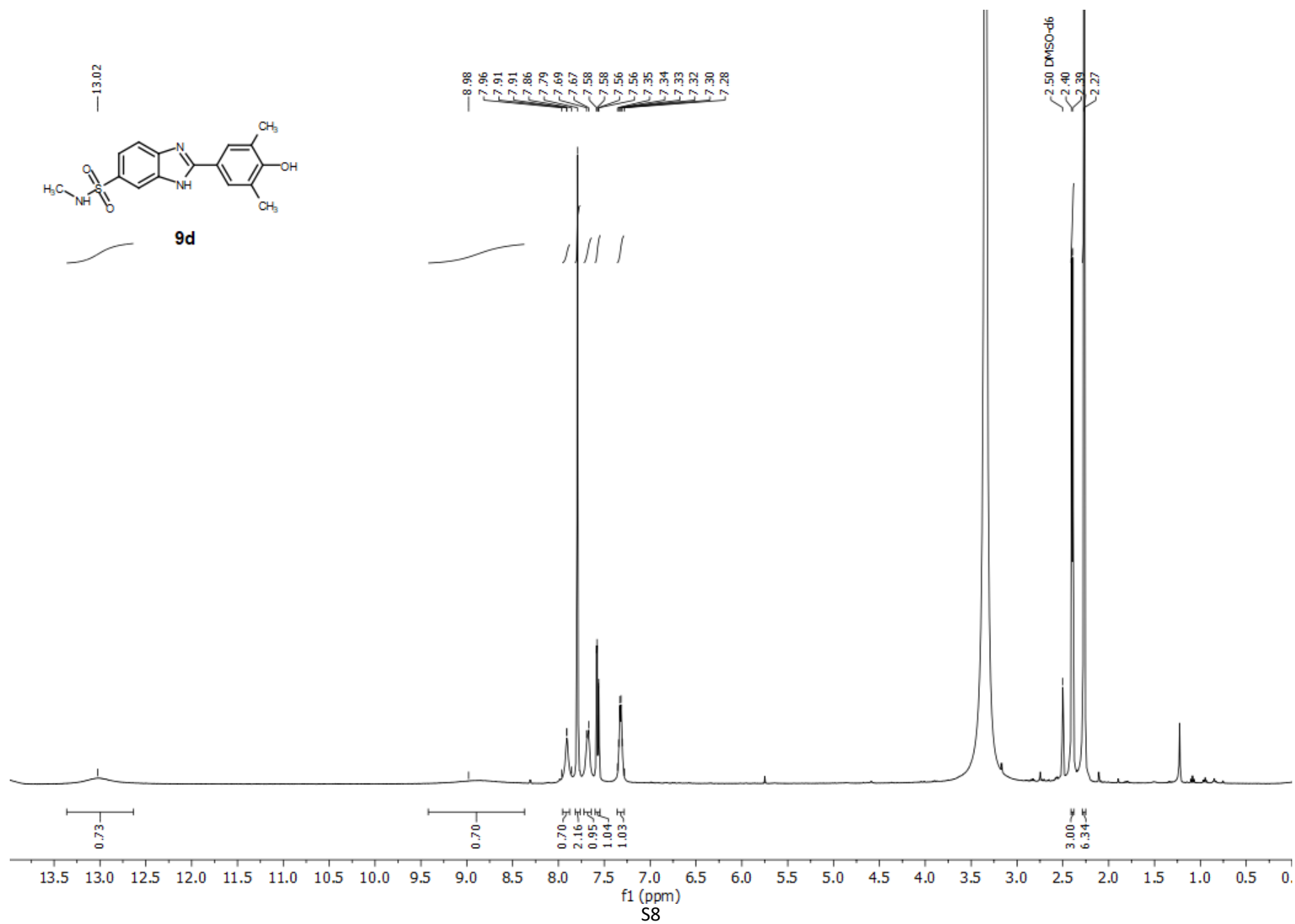
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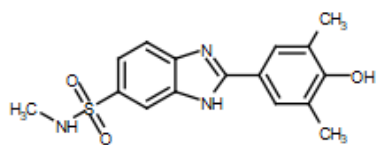




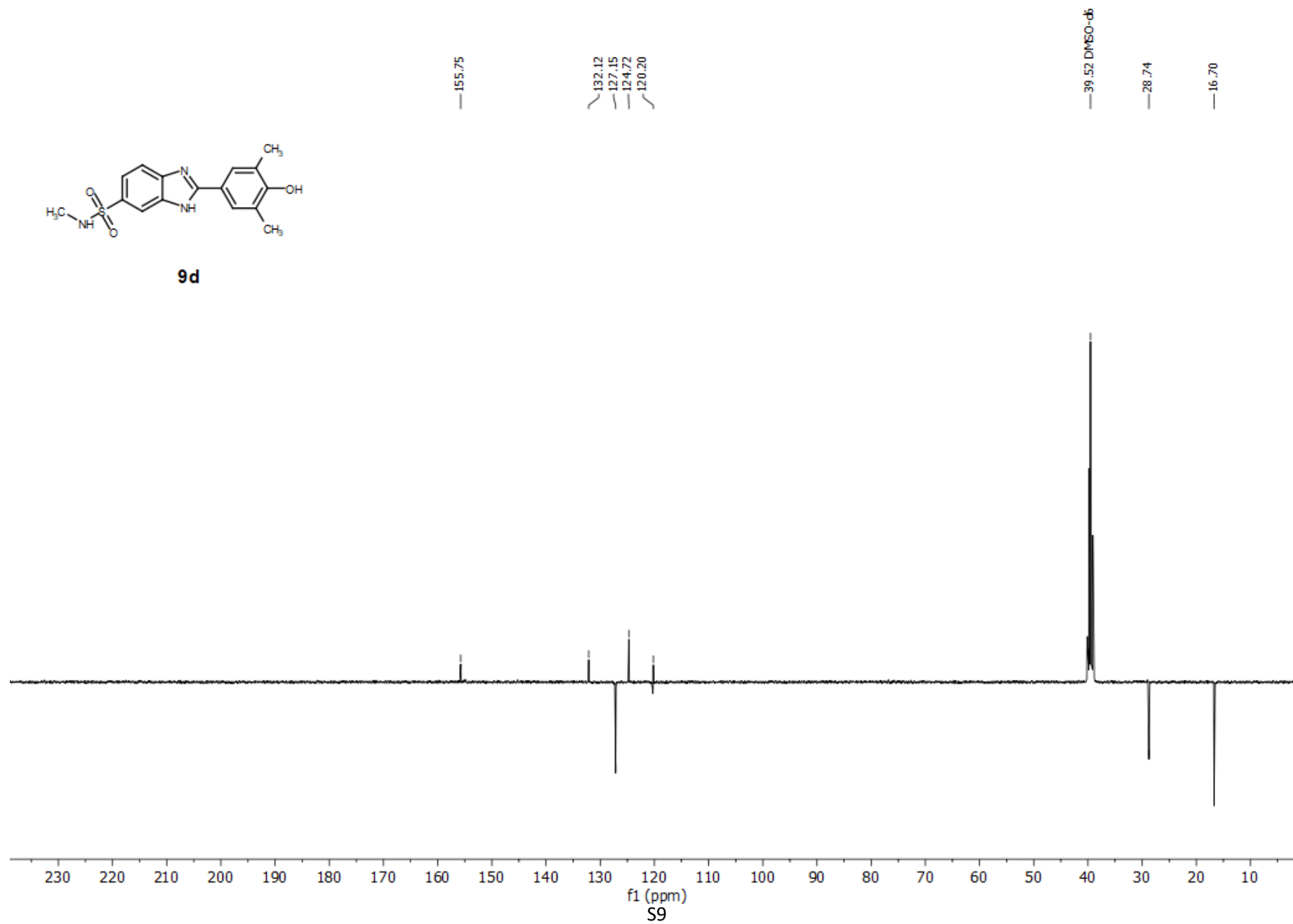
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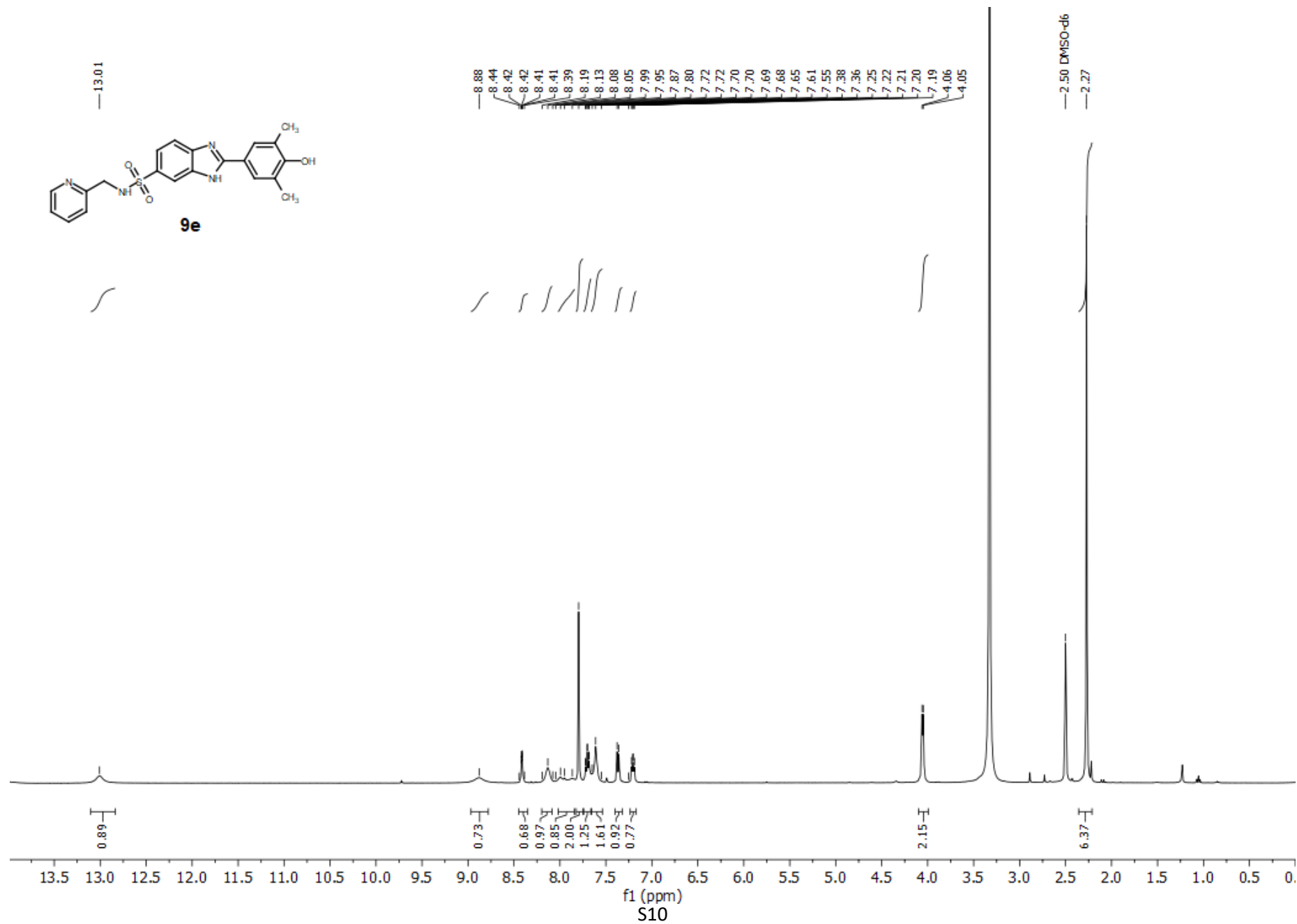
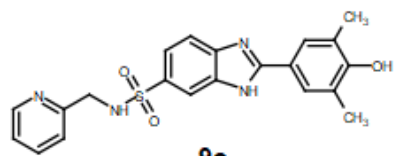


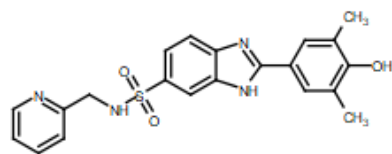




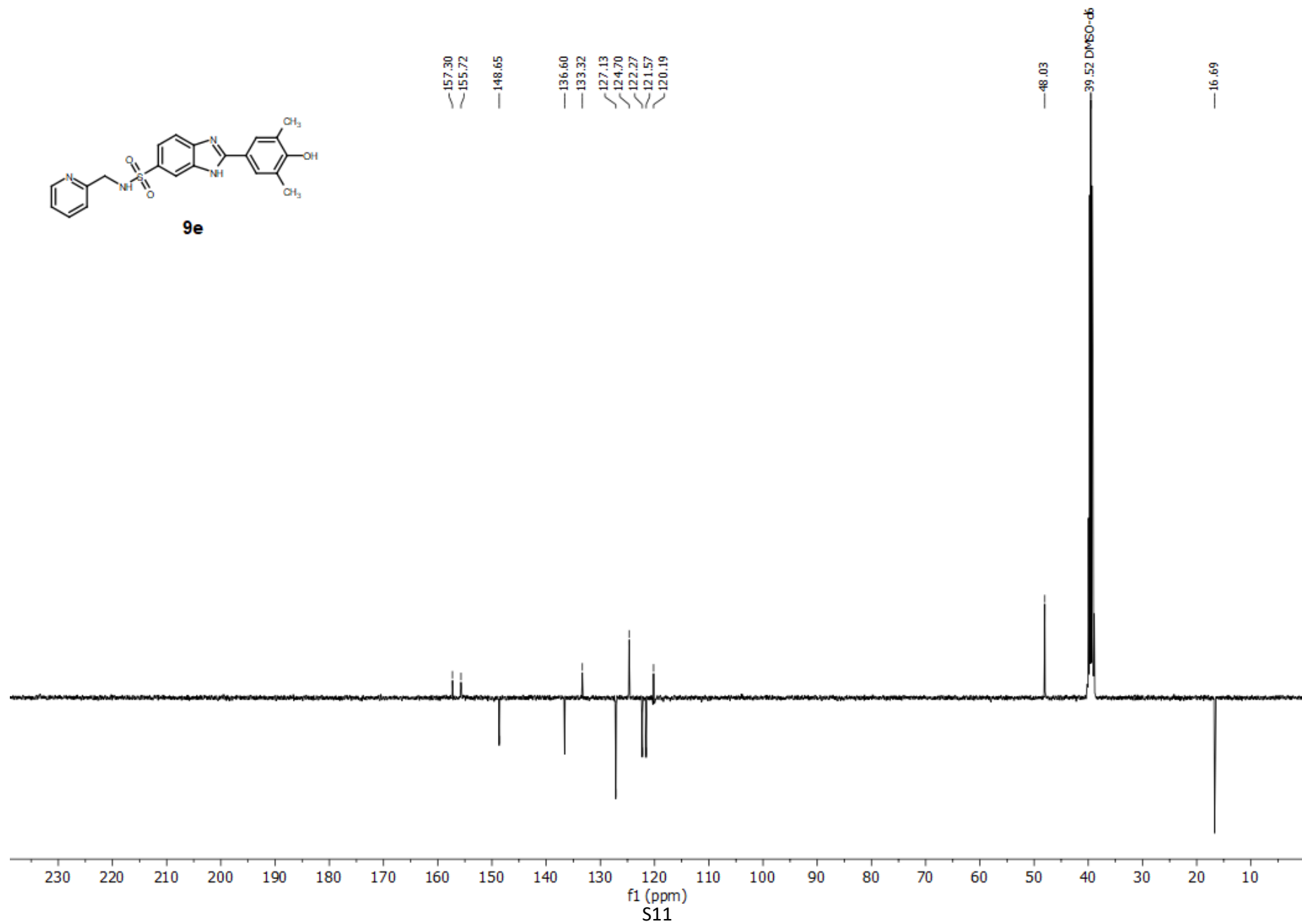
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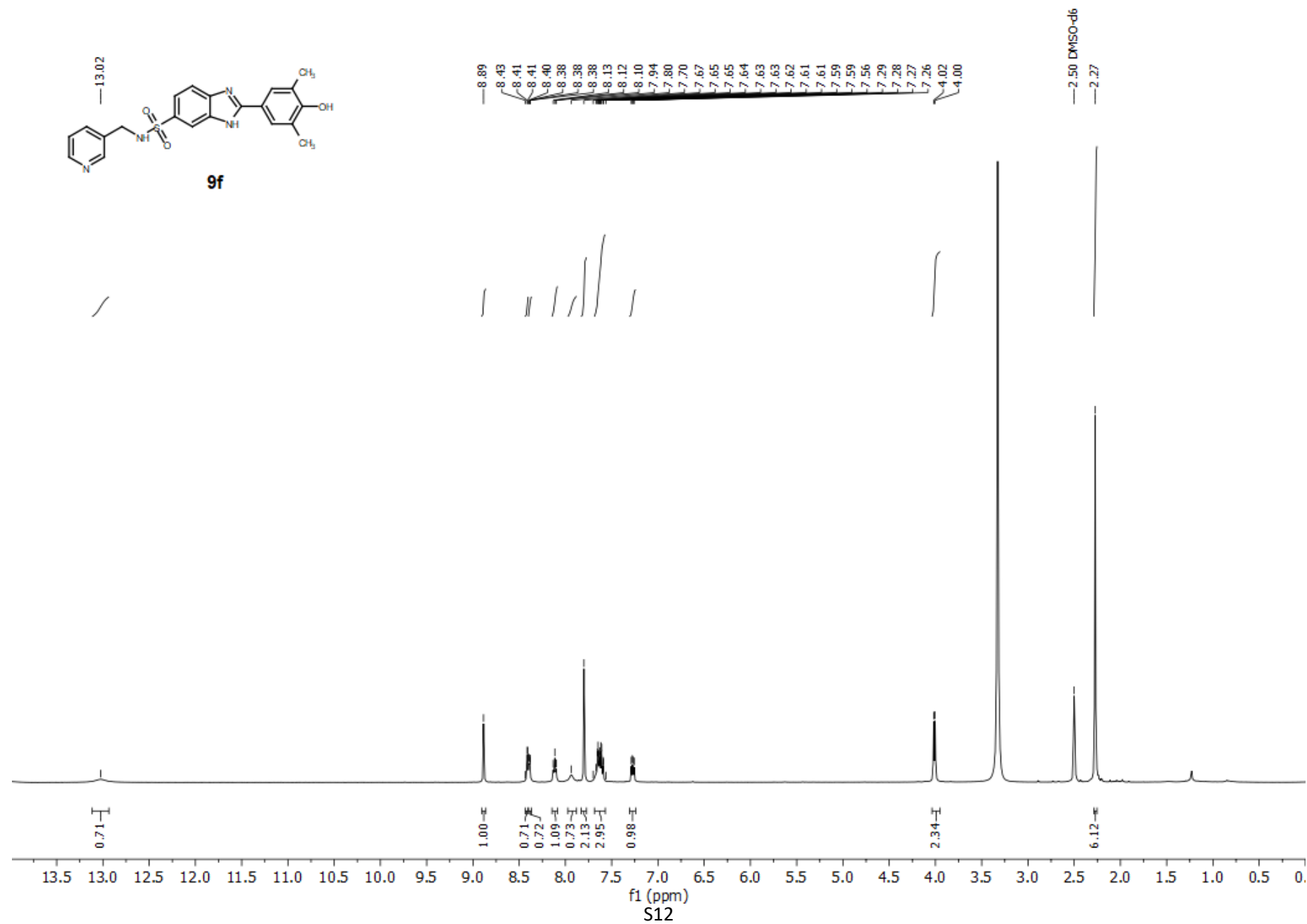
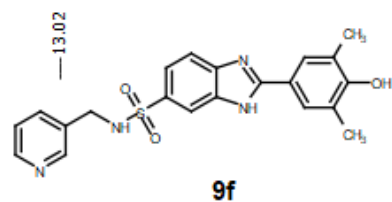


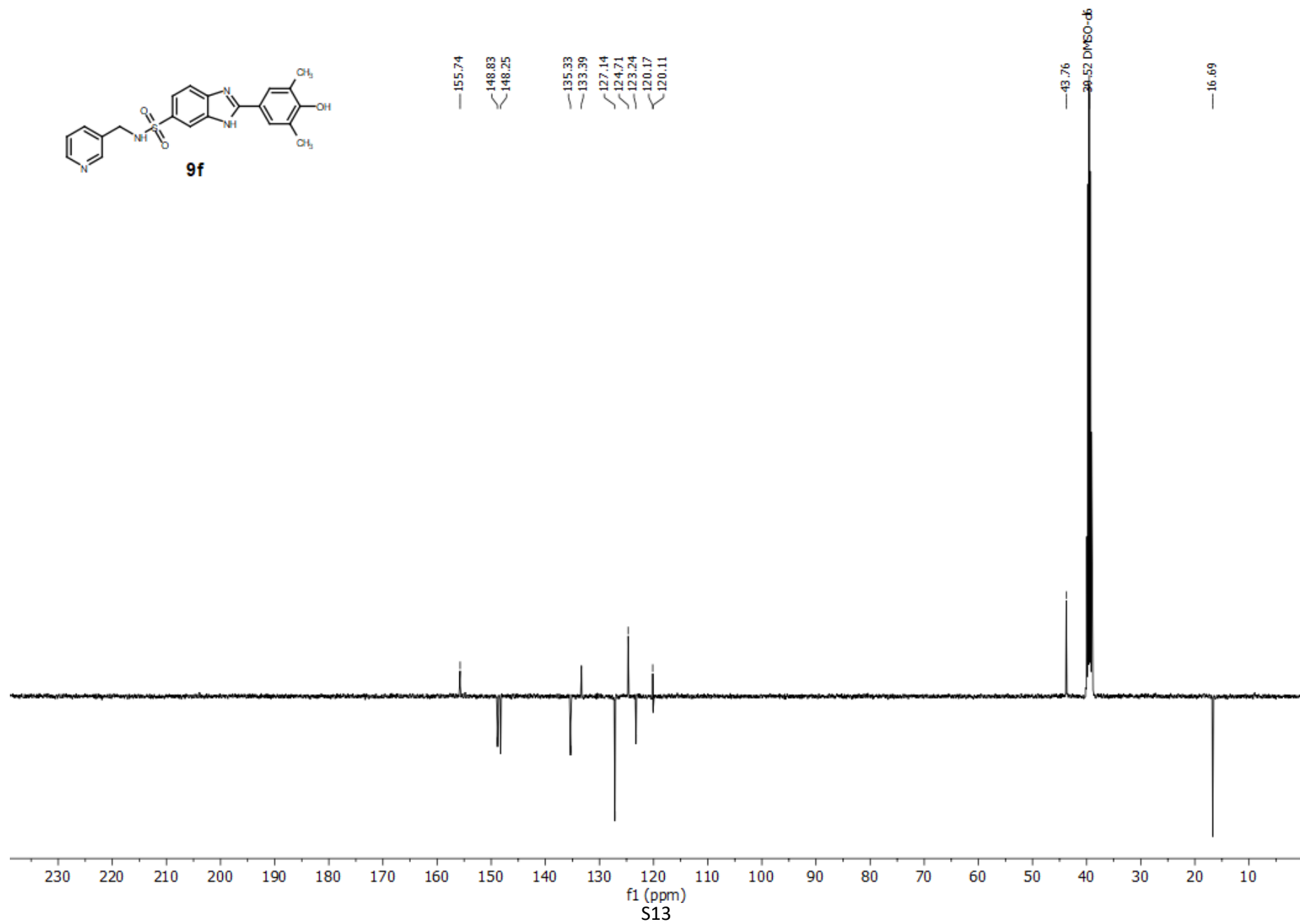
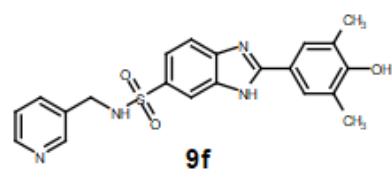


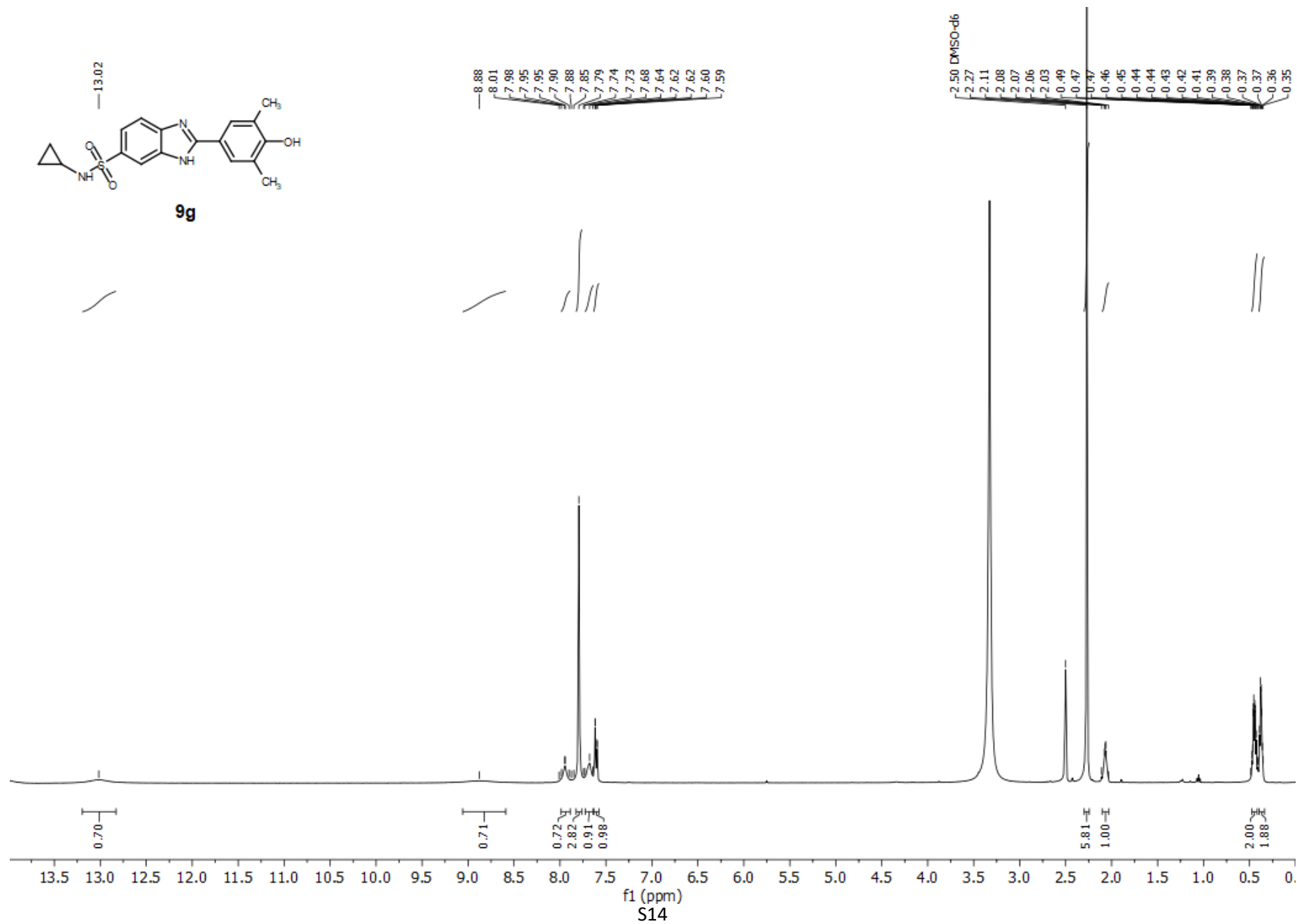
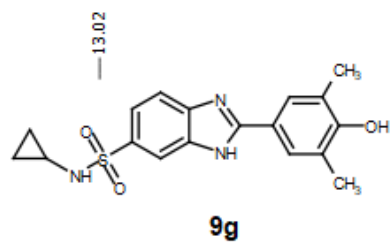


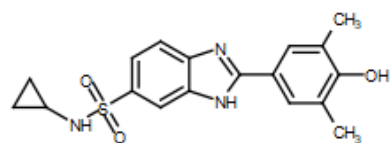
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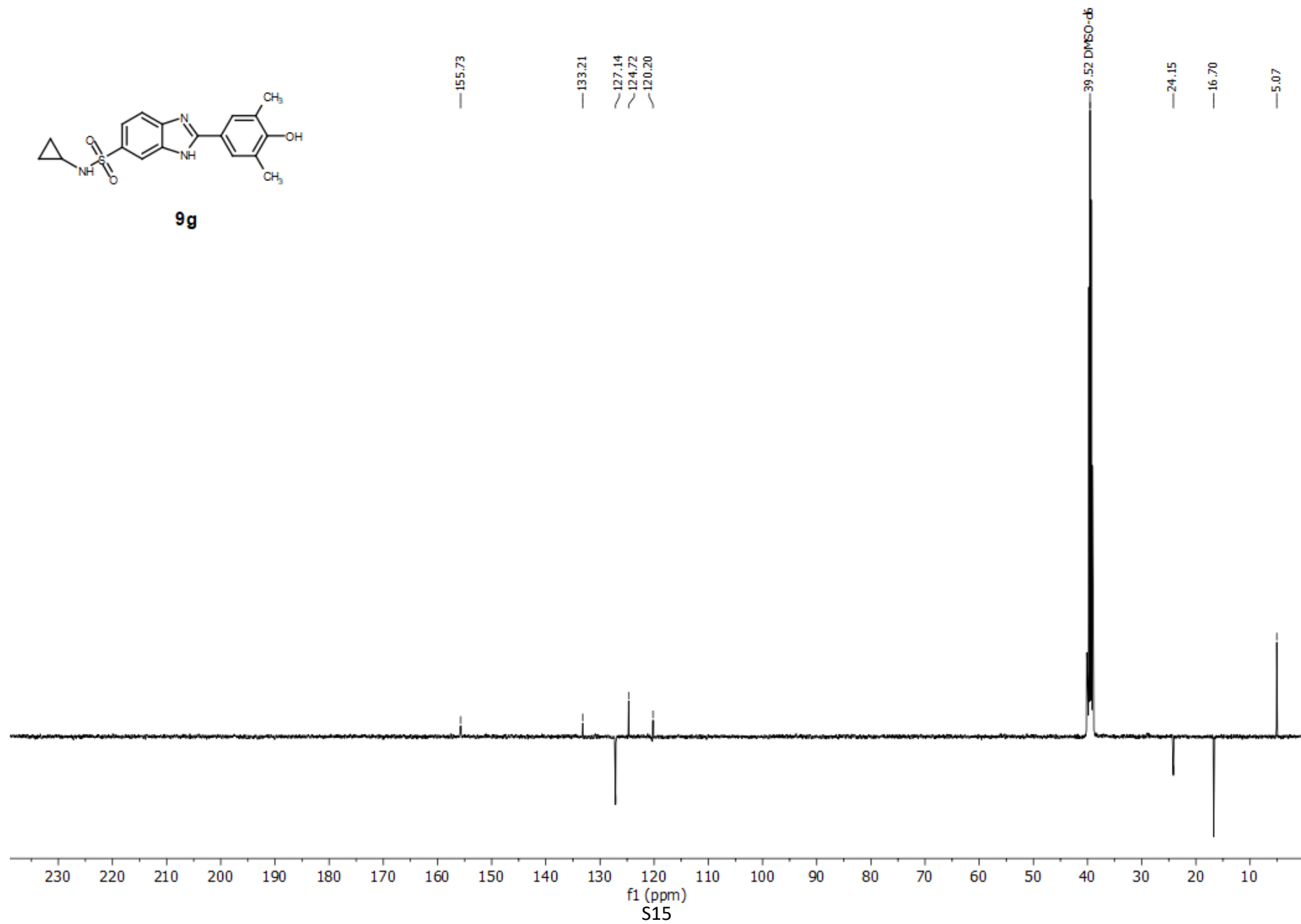


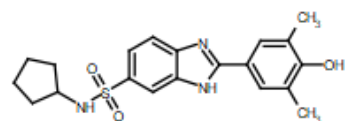




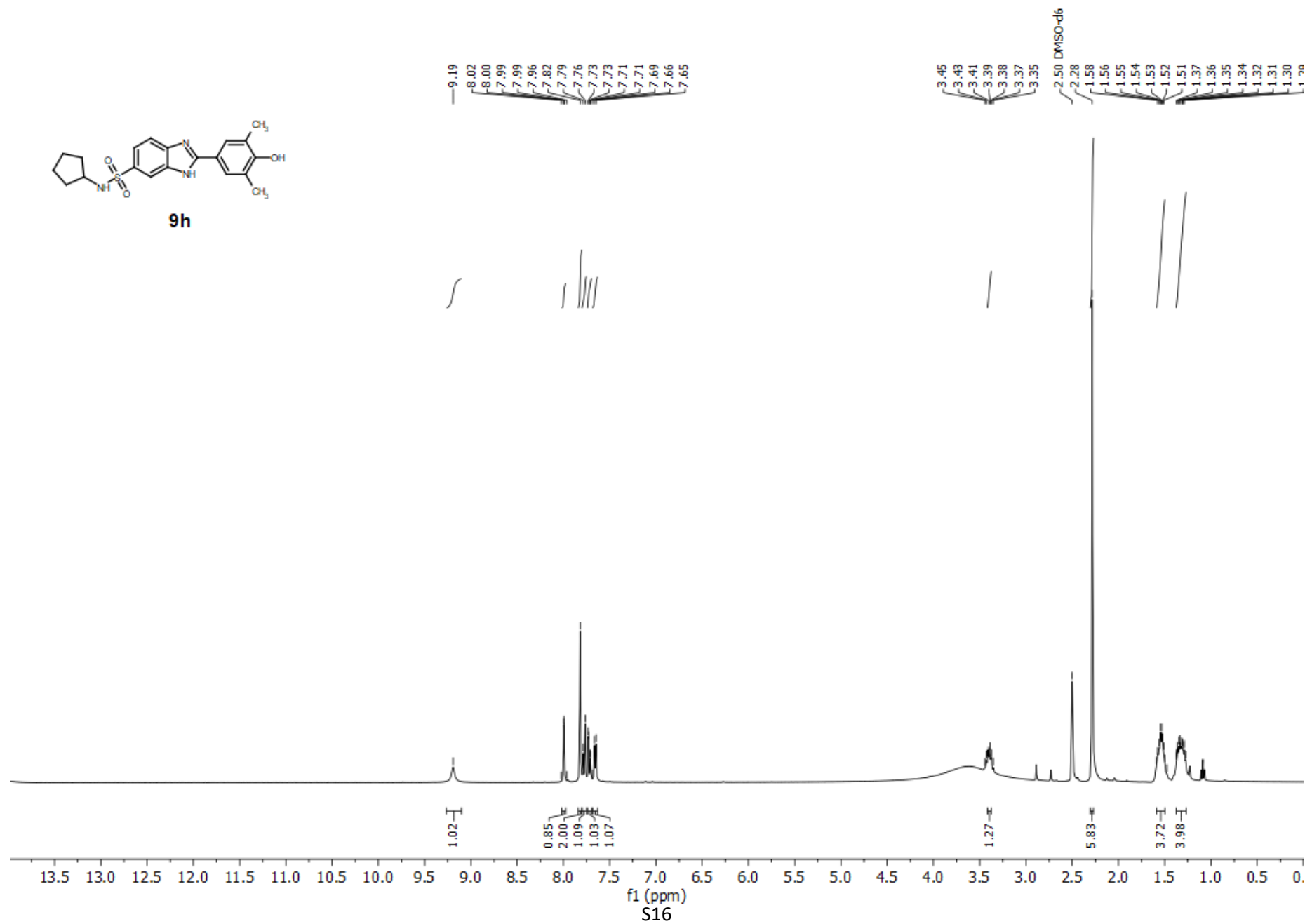


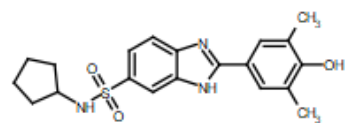
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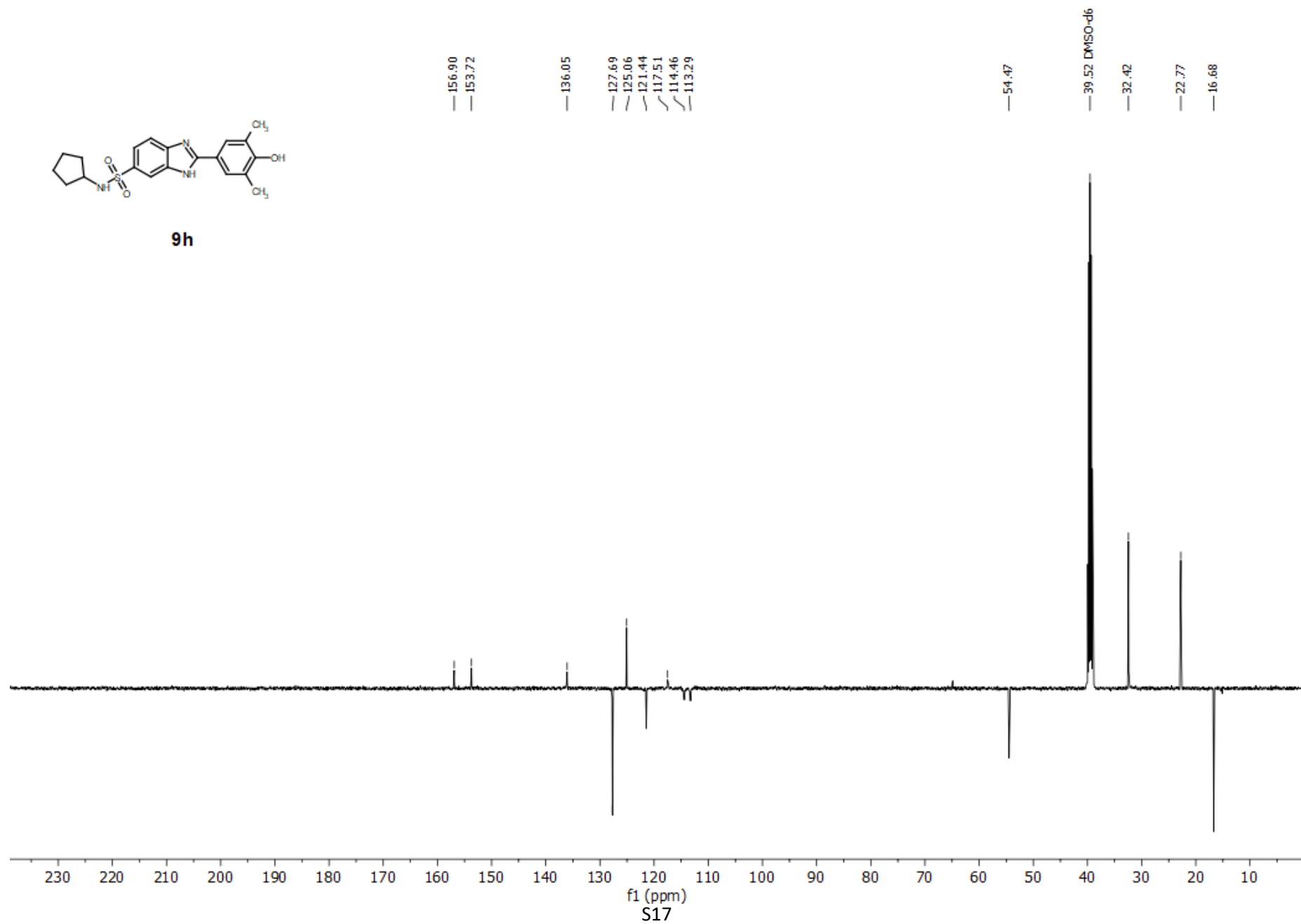


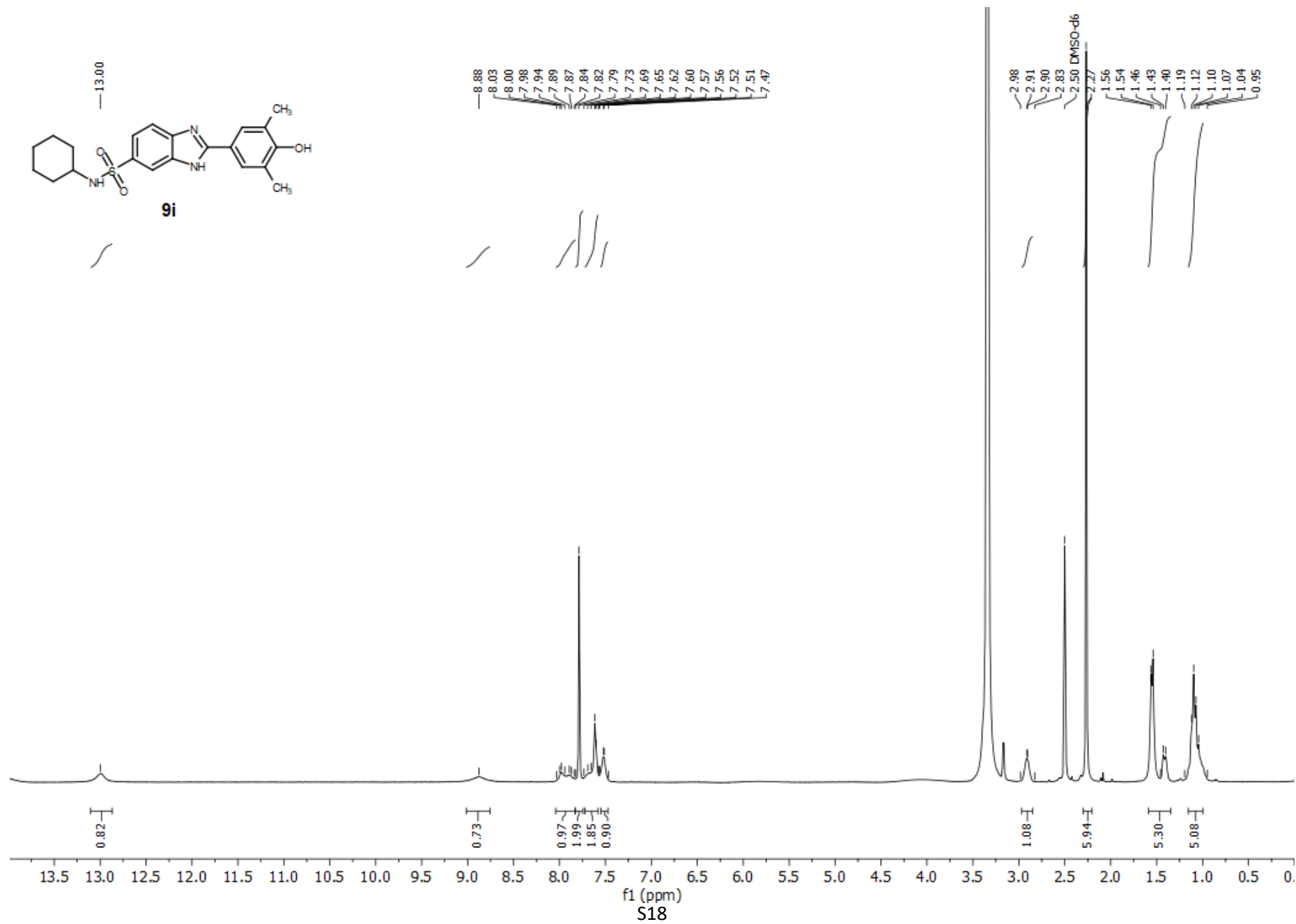
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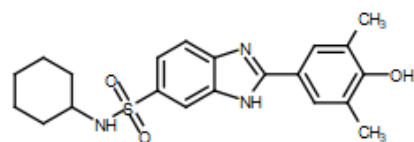




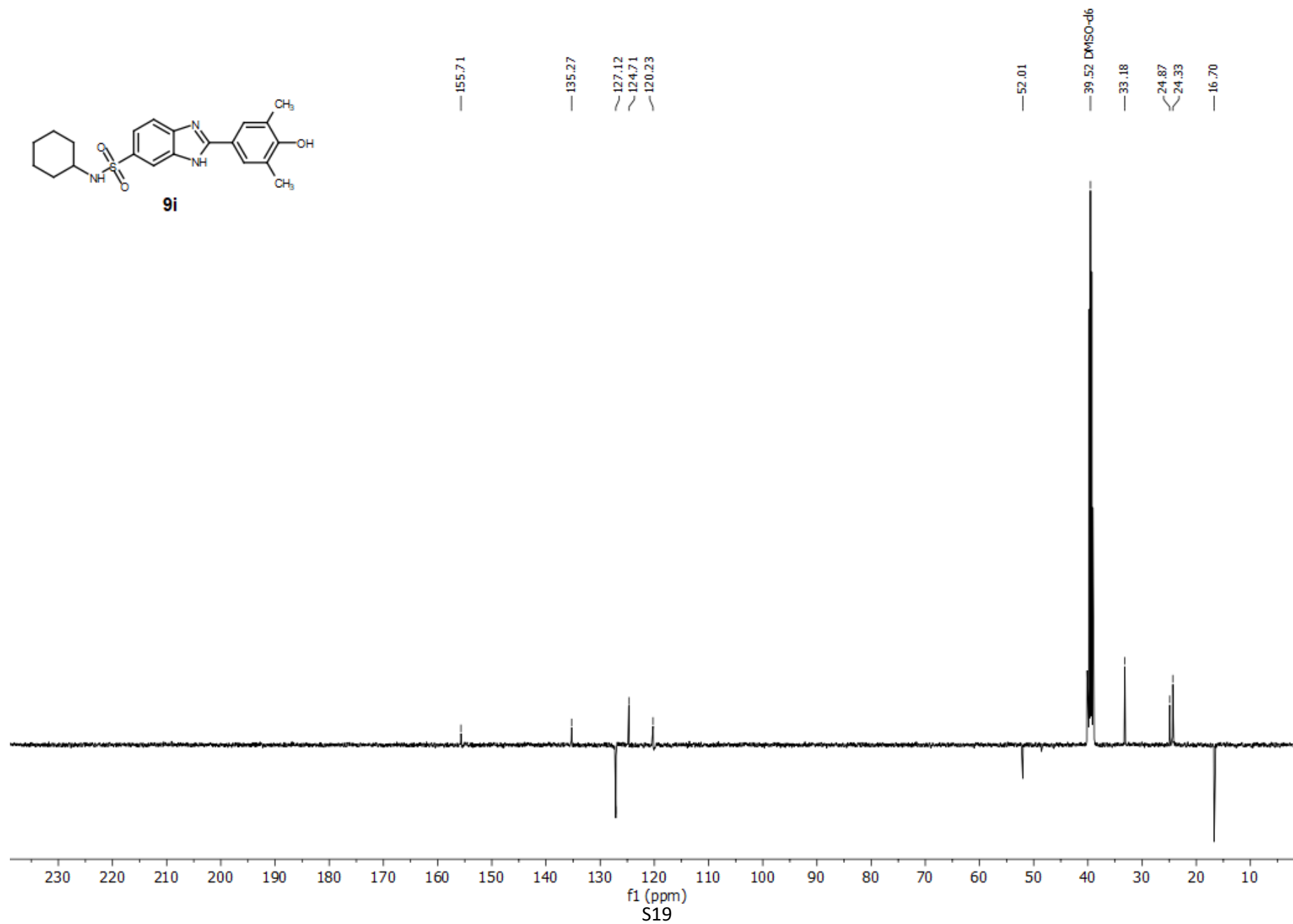
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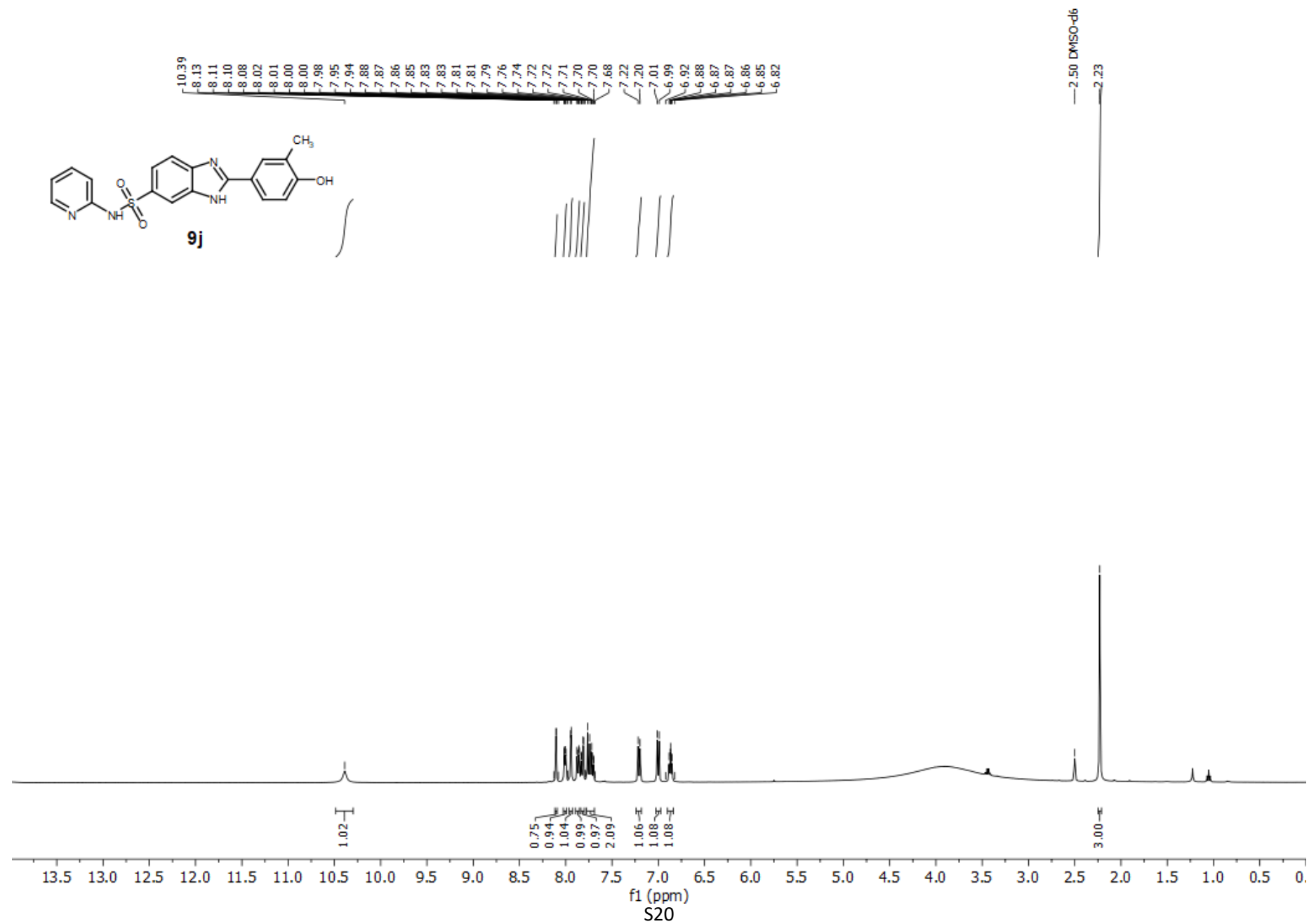


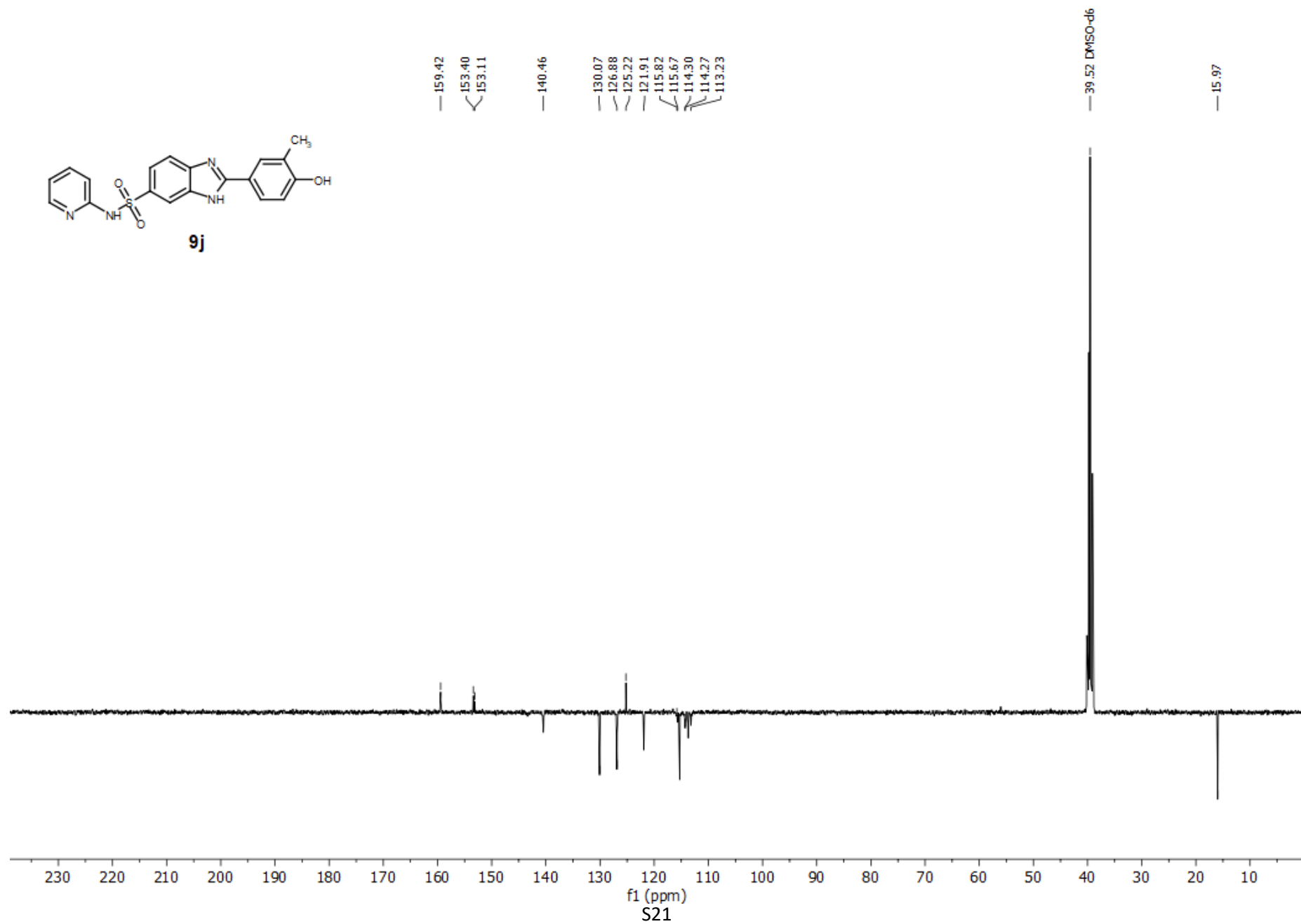
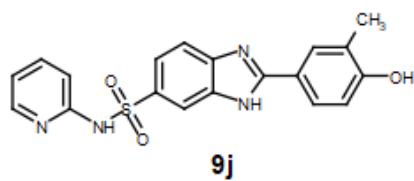


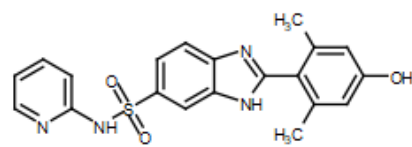


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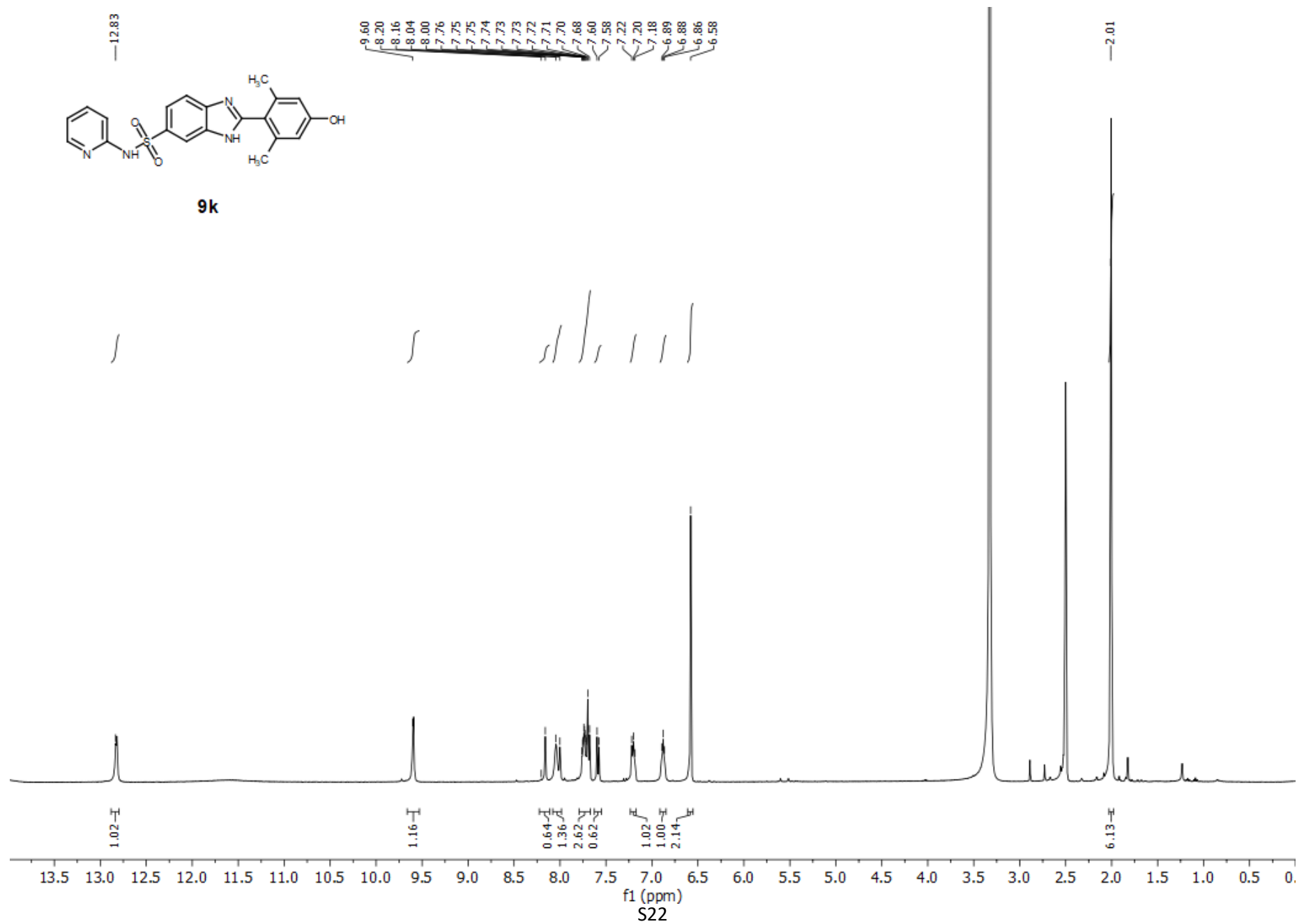


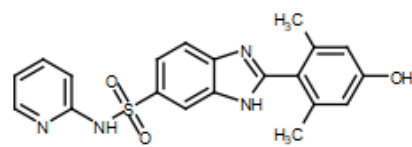




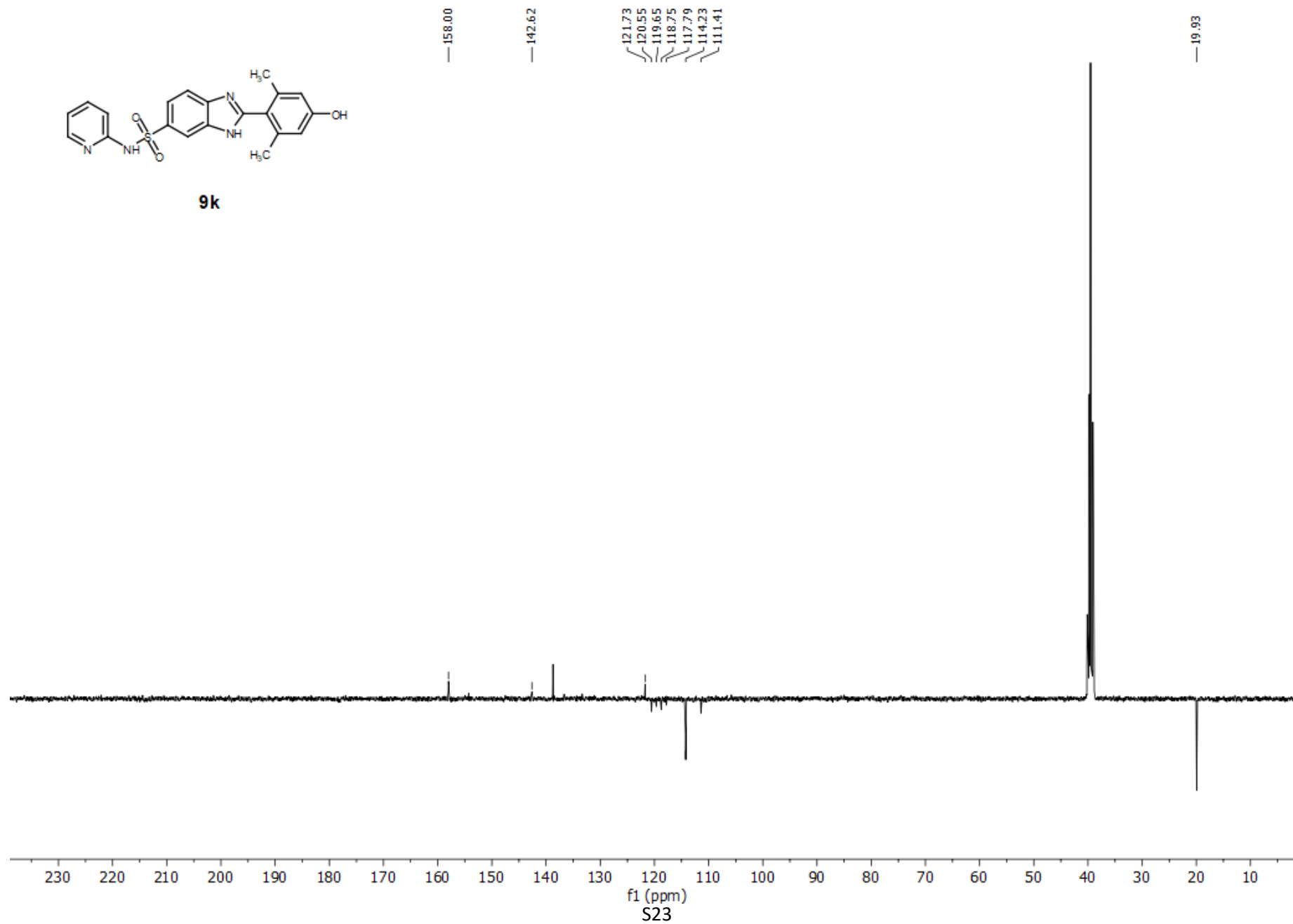


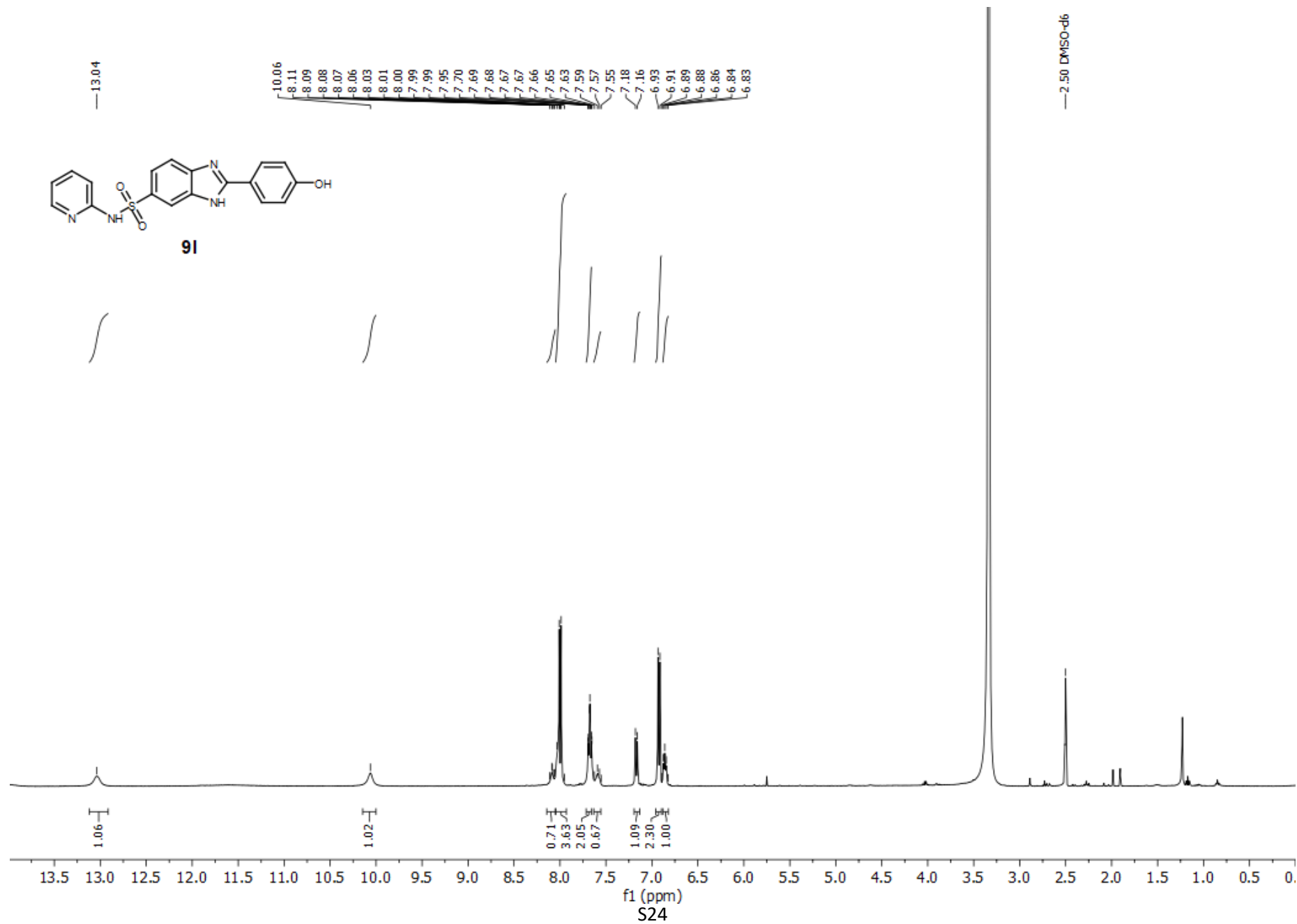
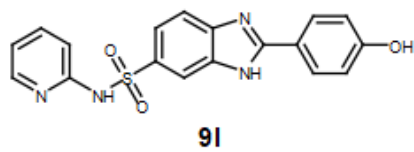
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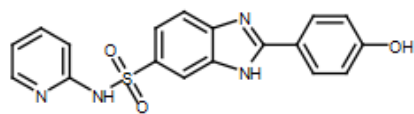




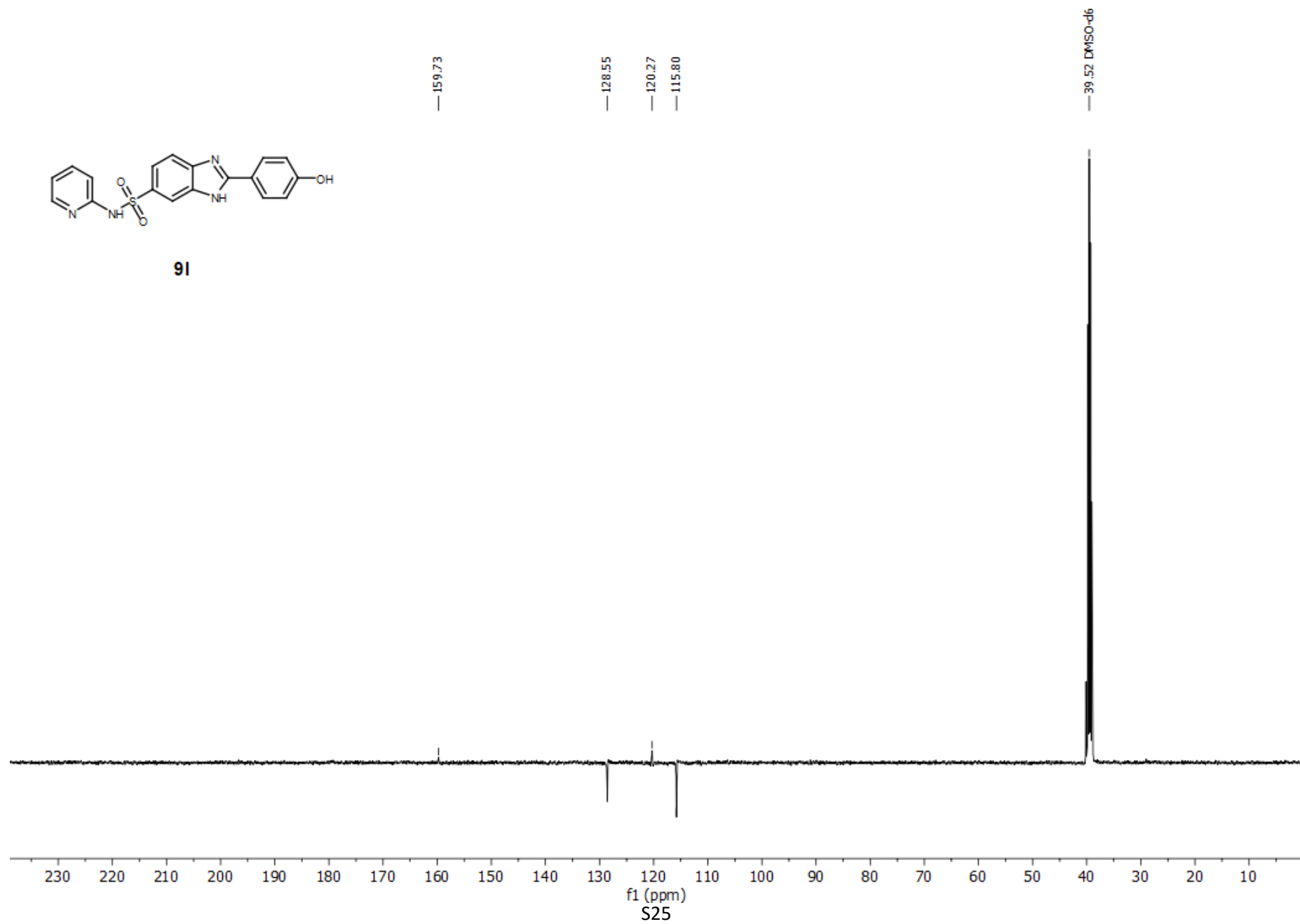
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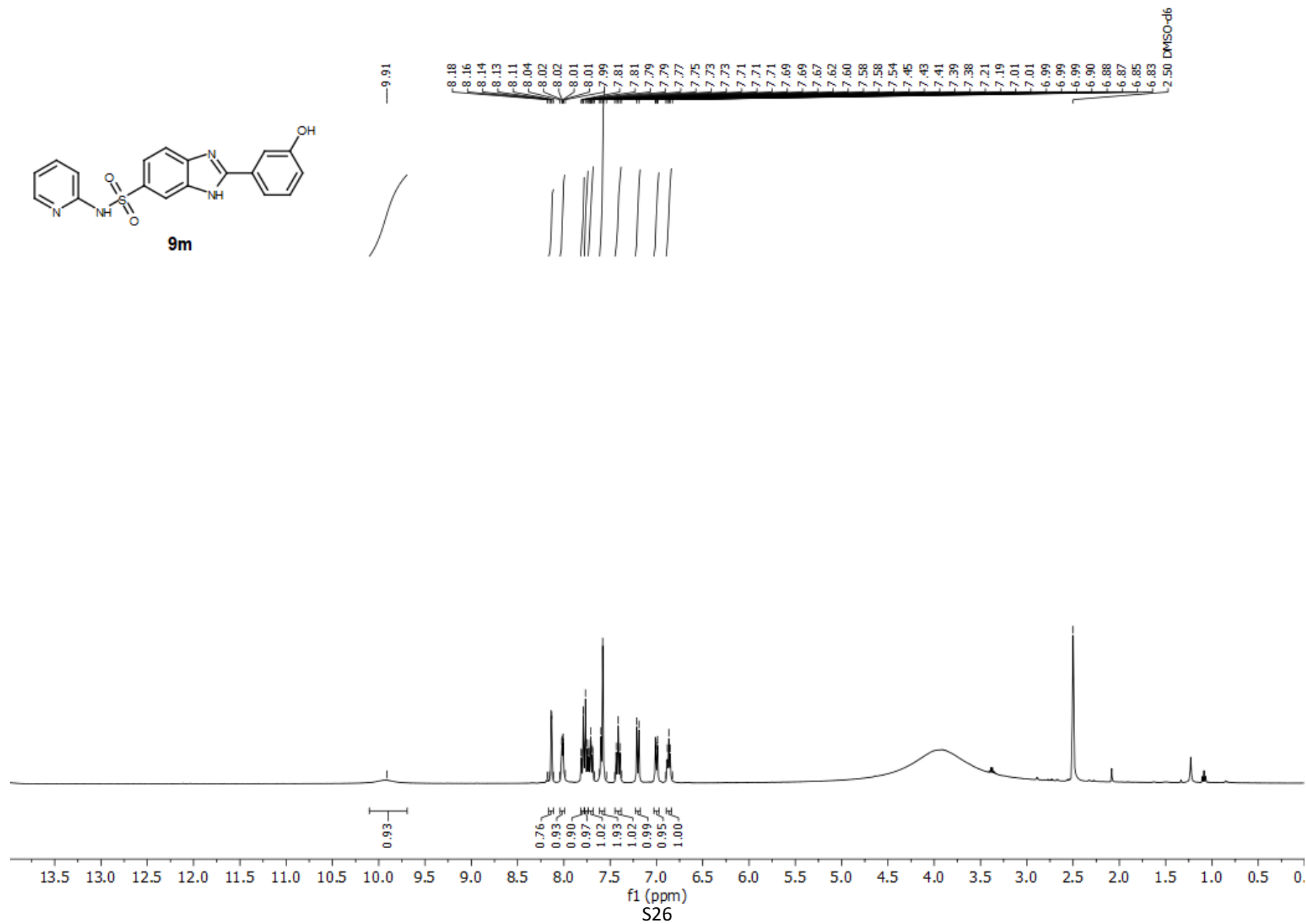
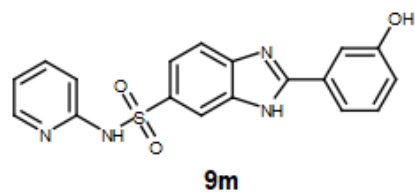


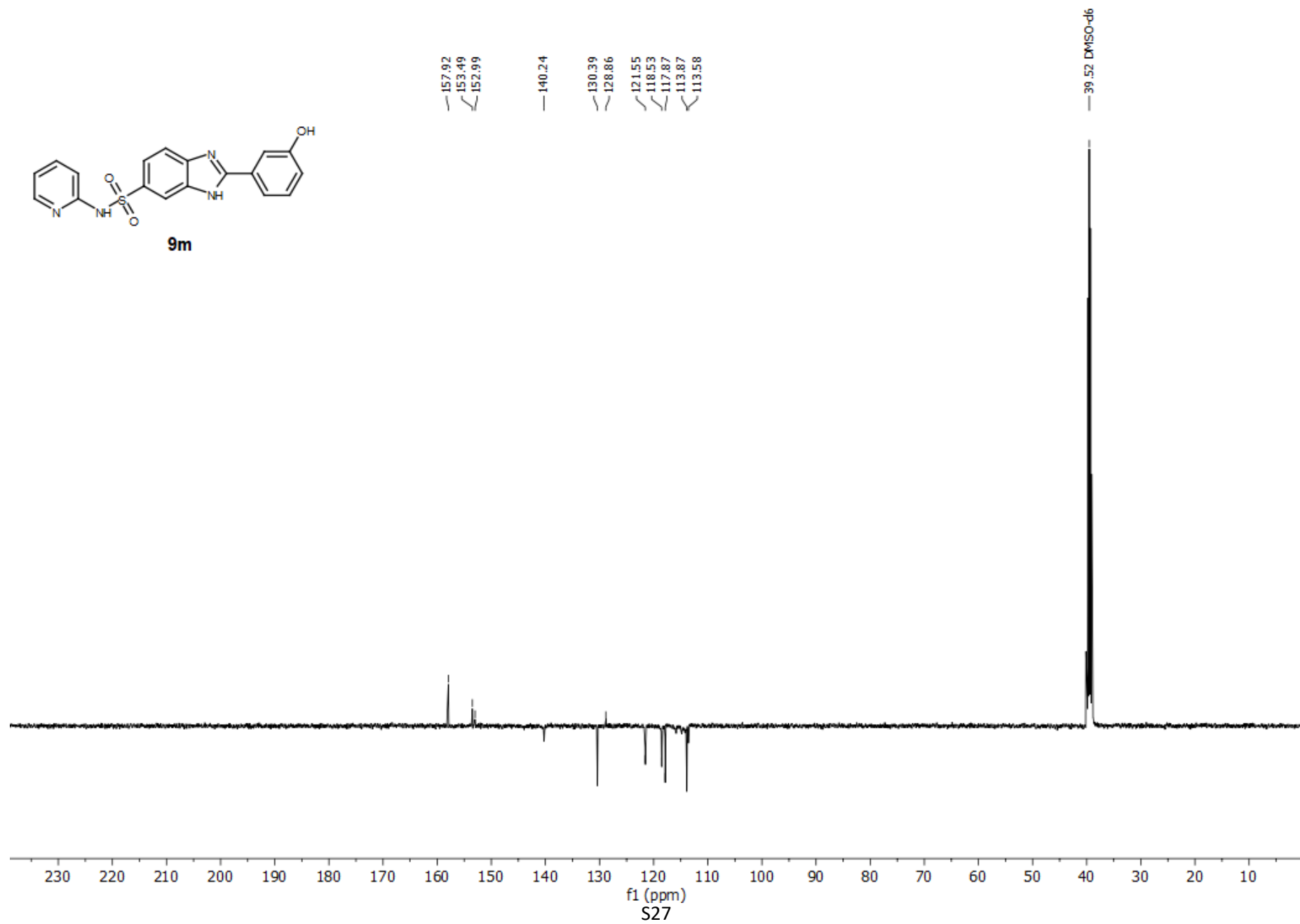
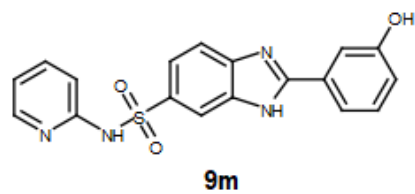


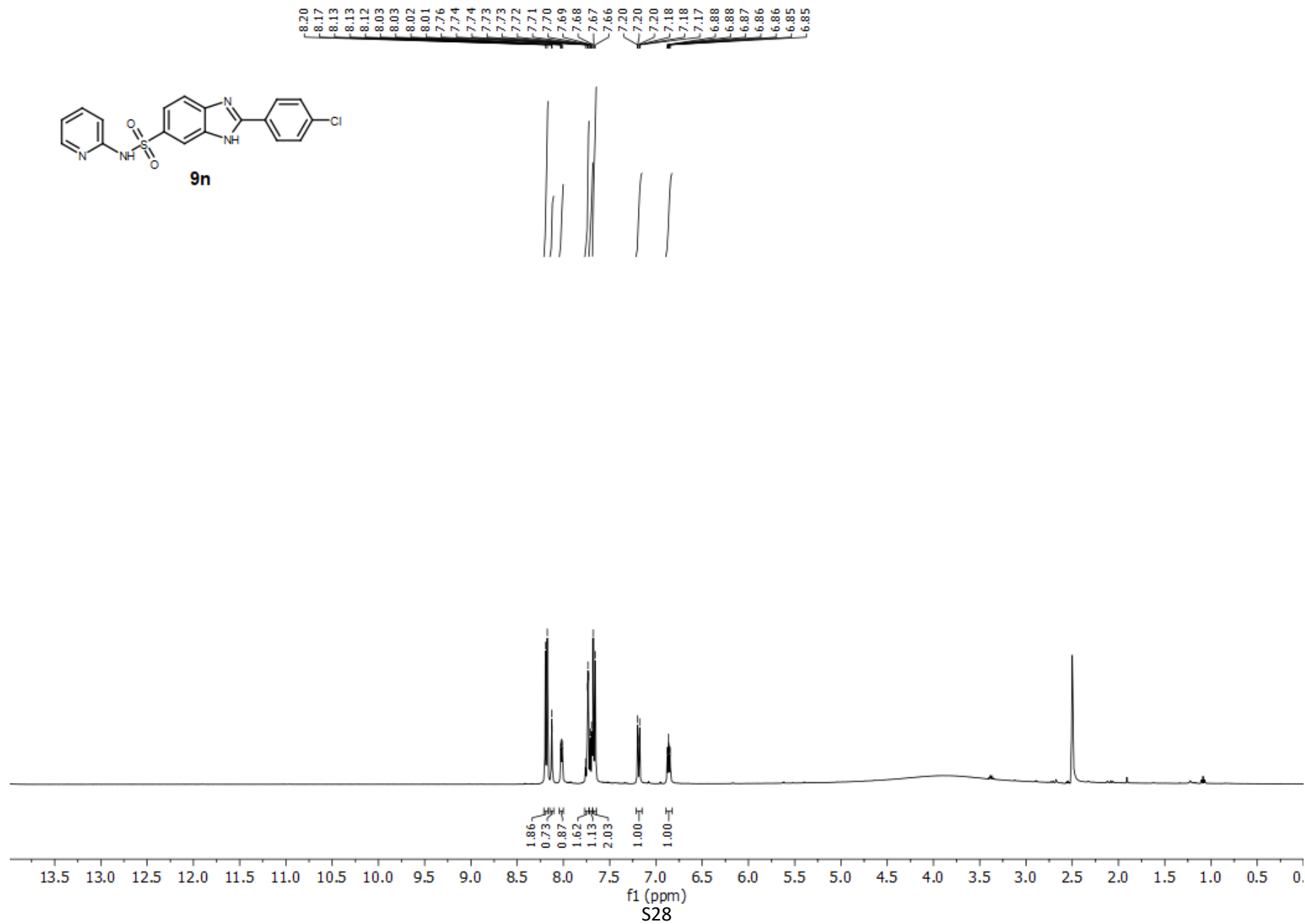
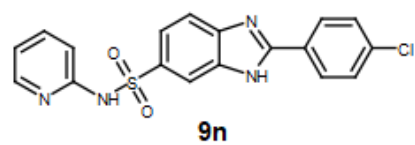


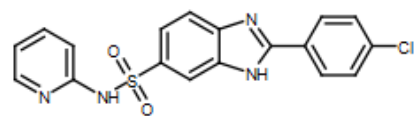
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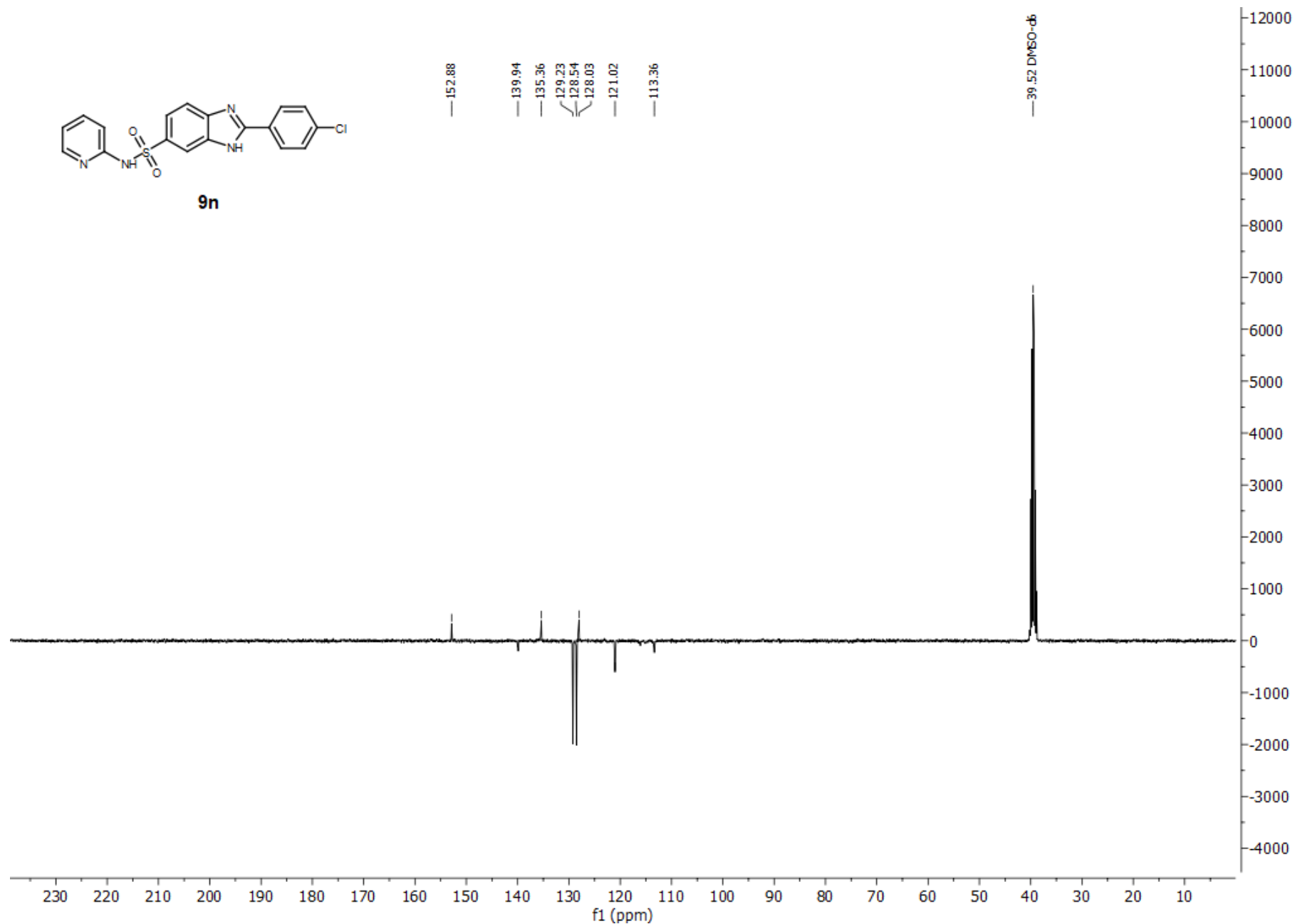


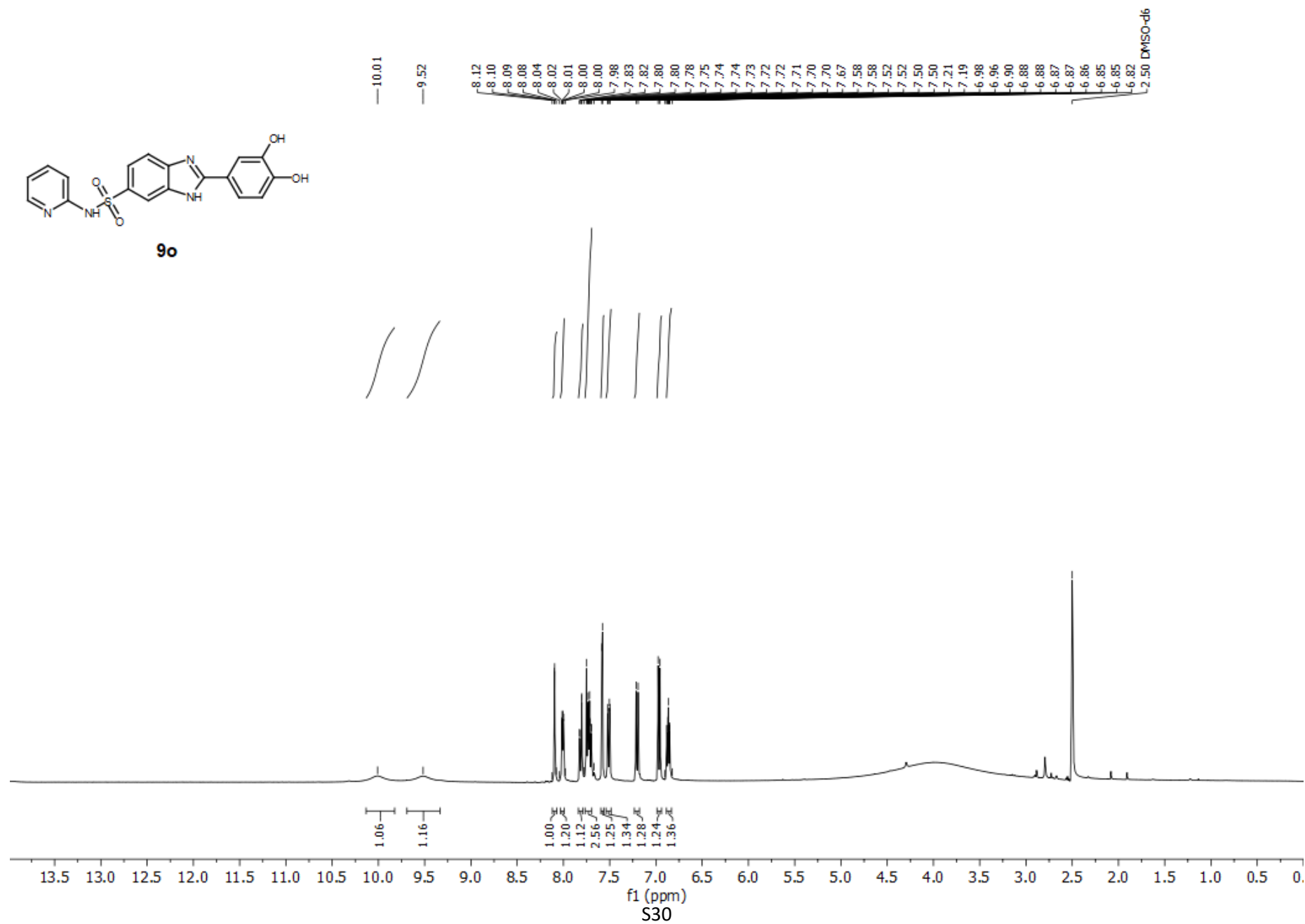
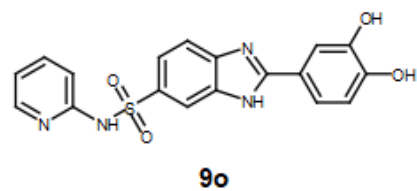


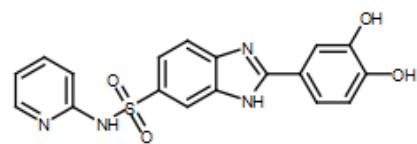




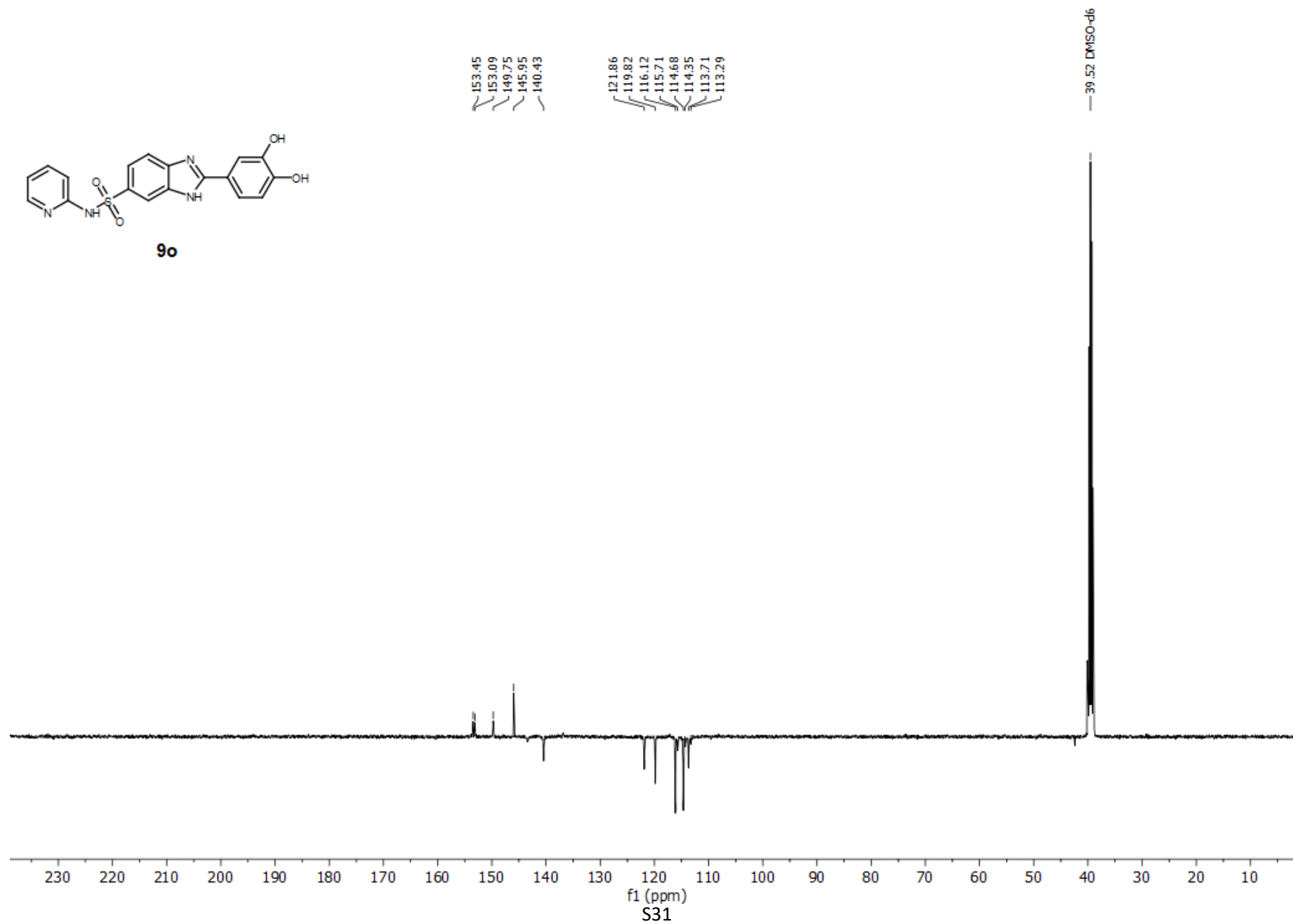
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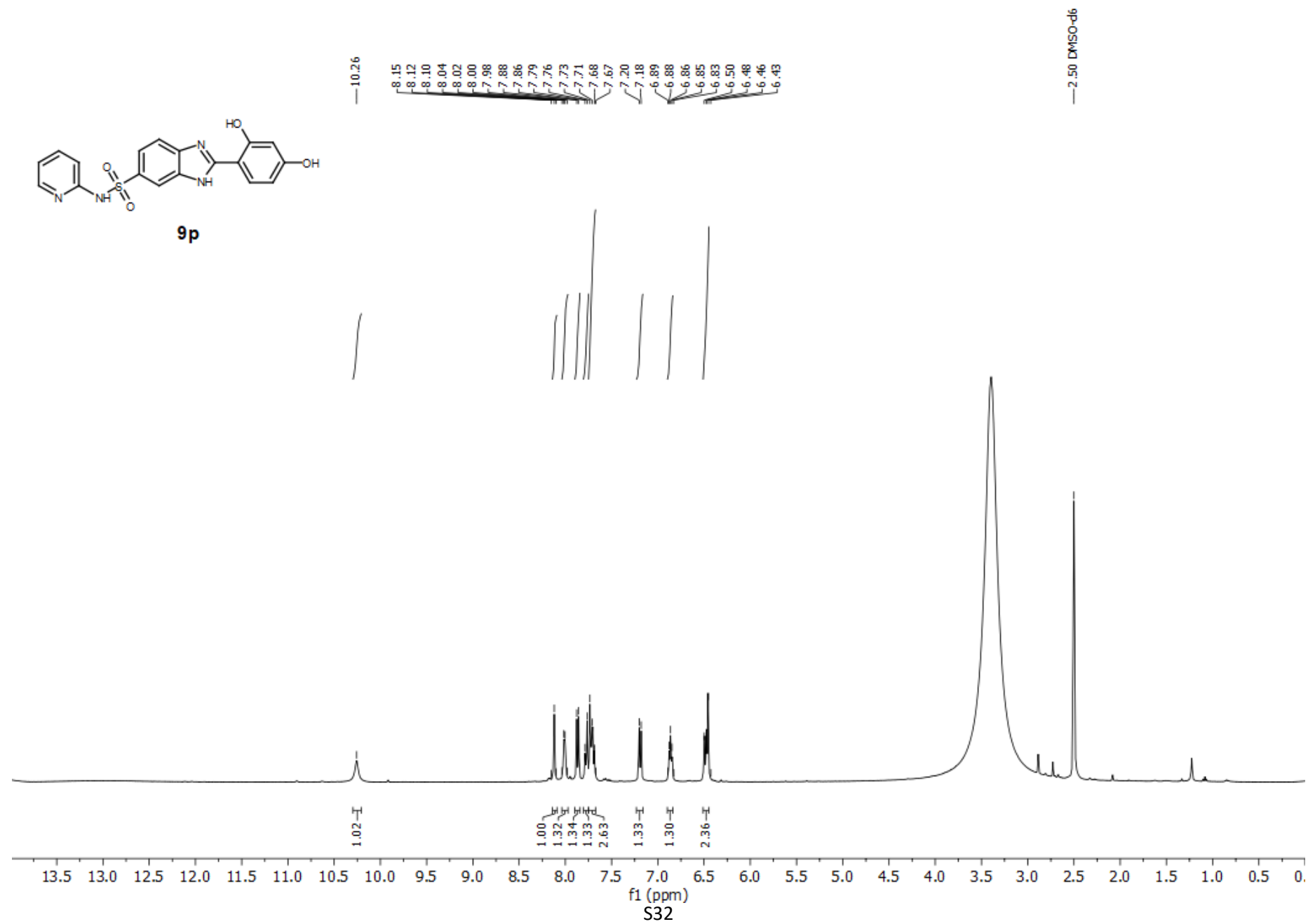


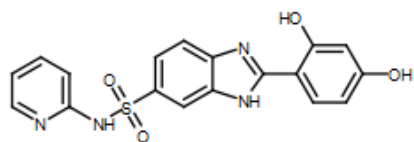




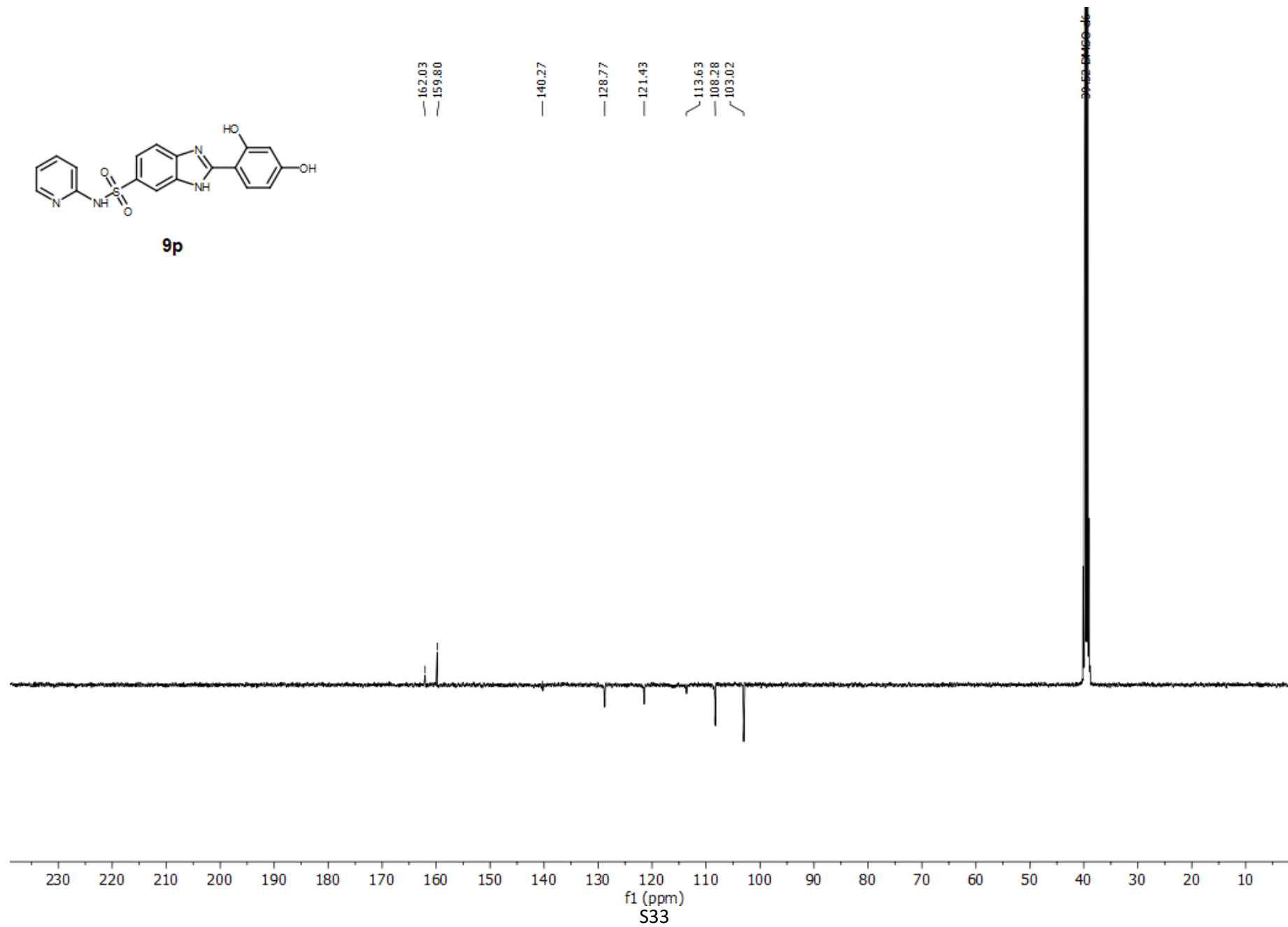
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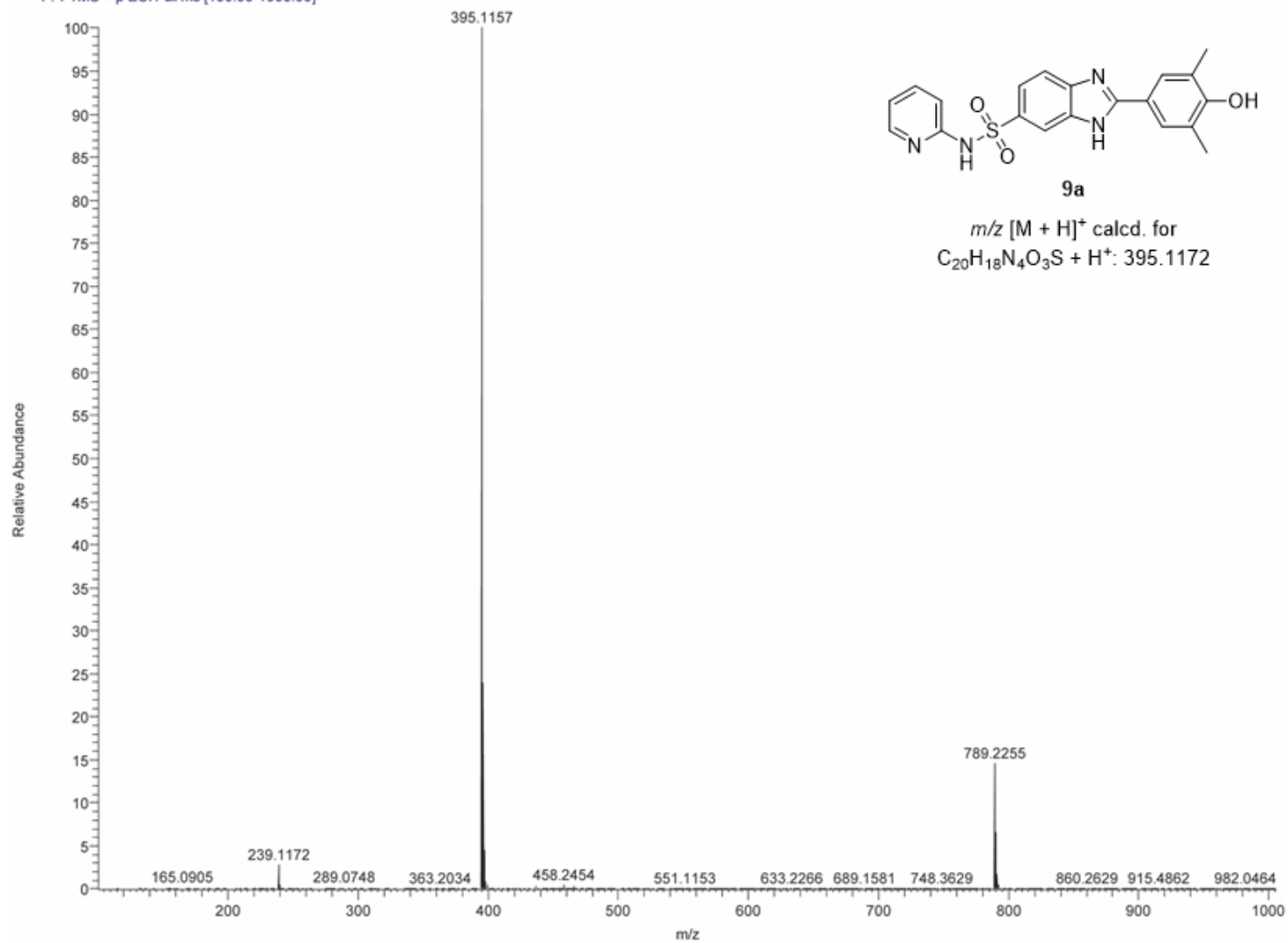




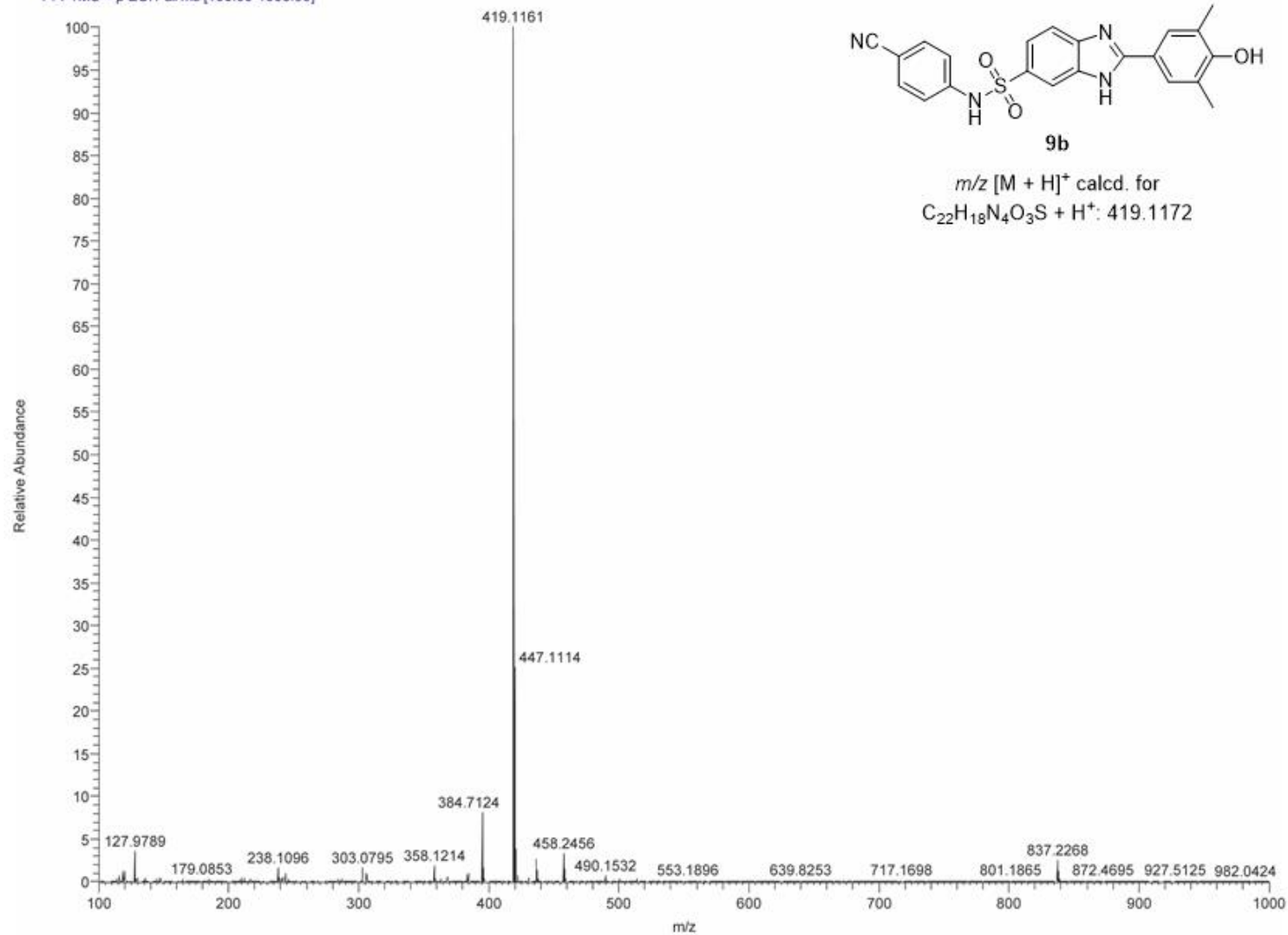
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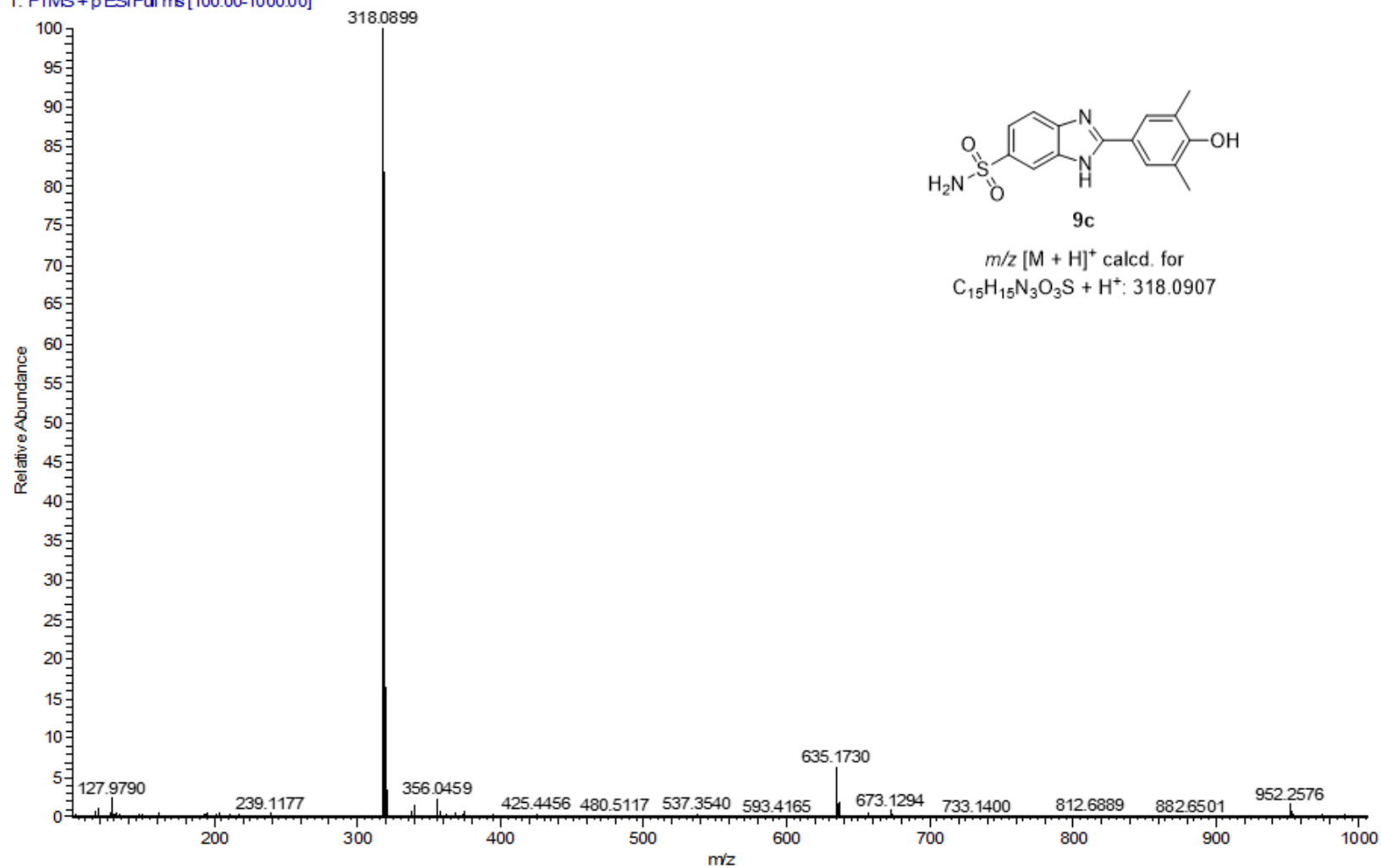
8A_EML765 #113-119 RT: 0.89-0.94 AV: 7 NL: 1.39E9
F: FTMS + p ESI Full ms [100.00-1000.00]



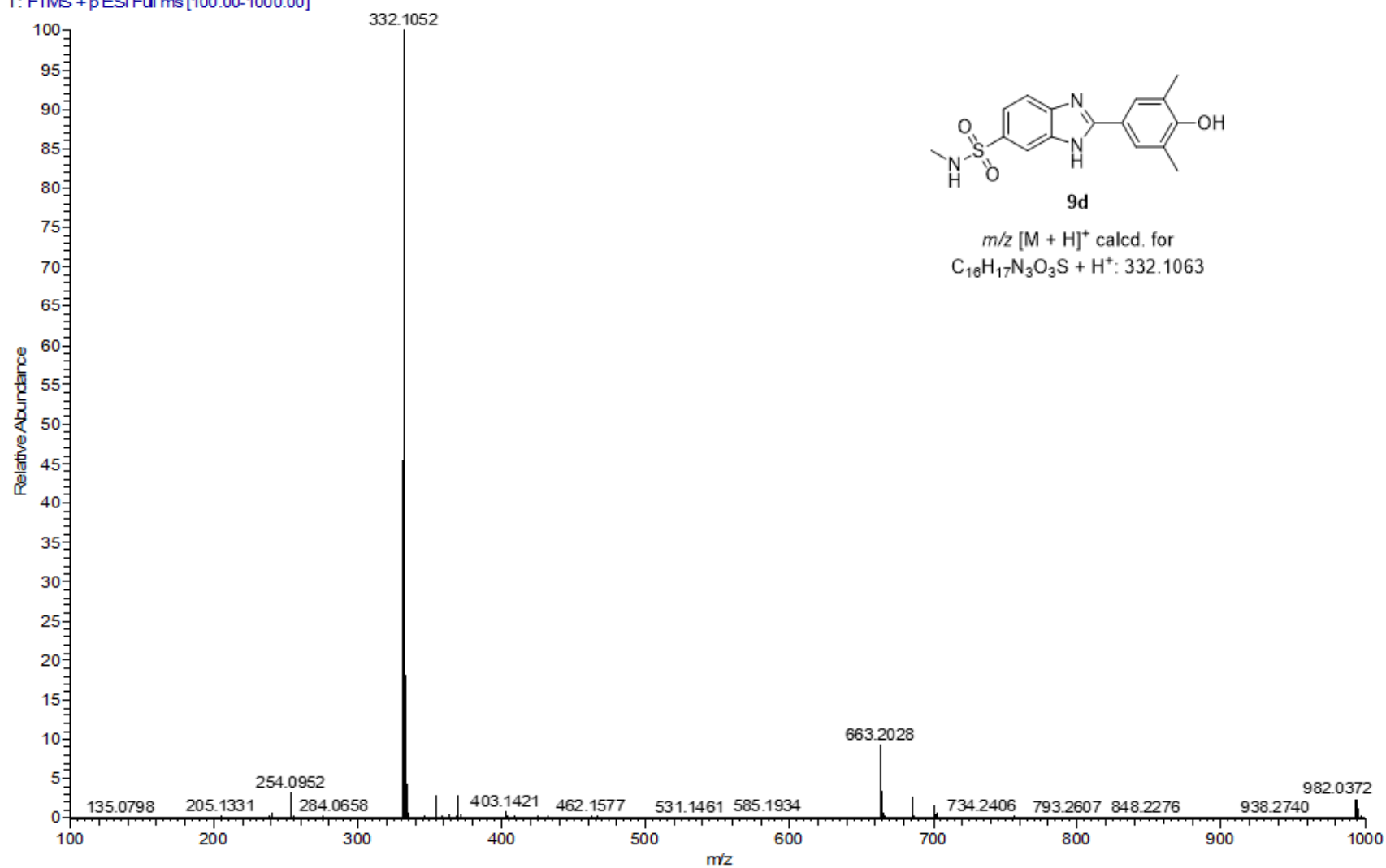
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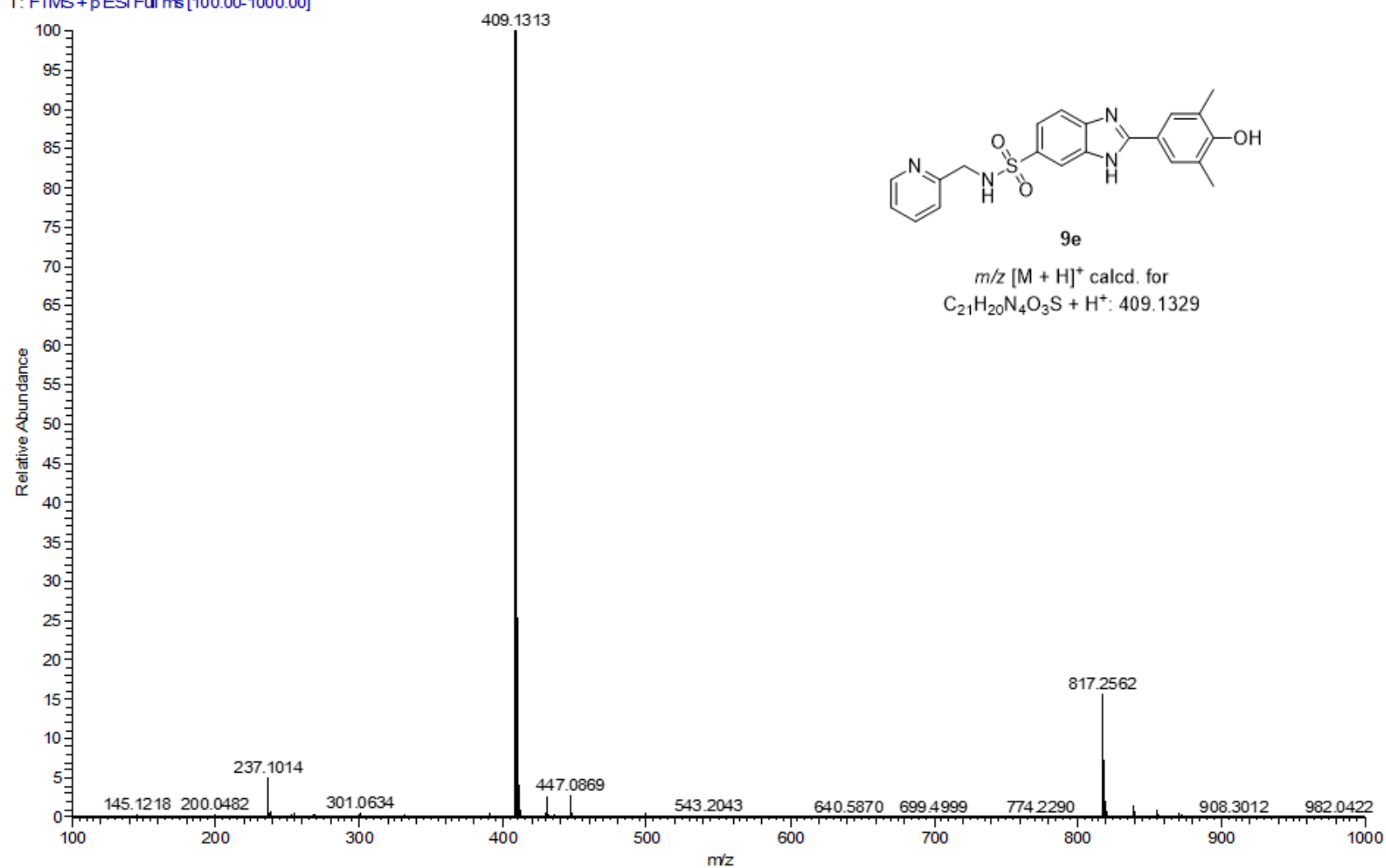
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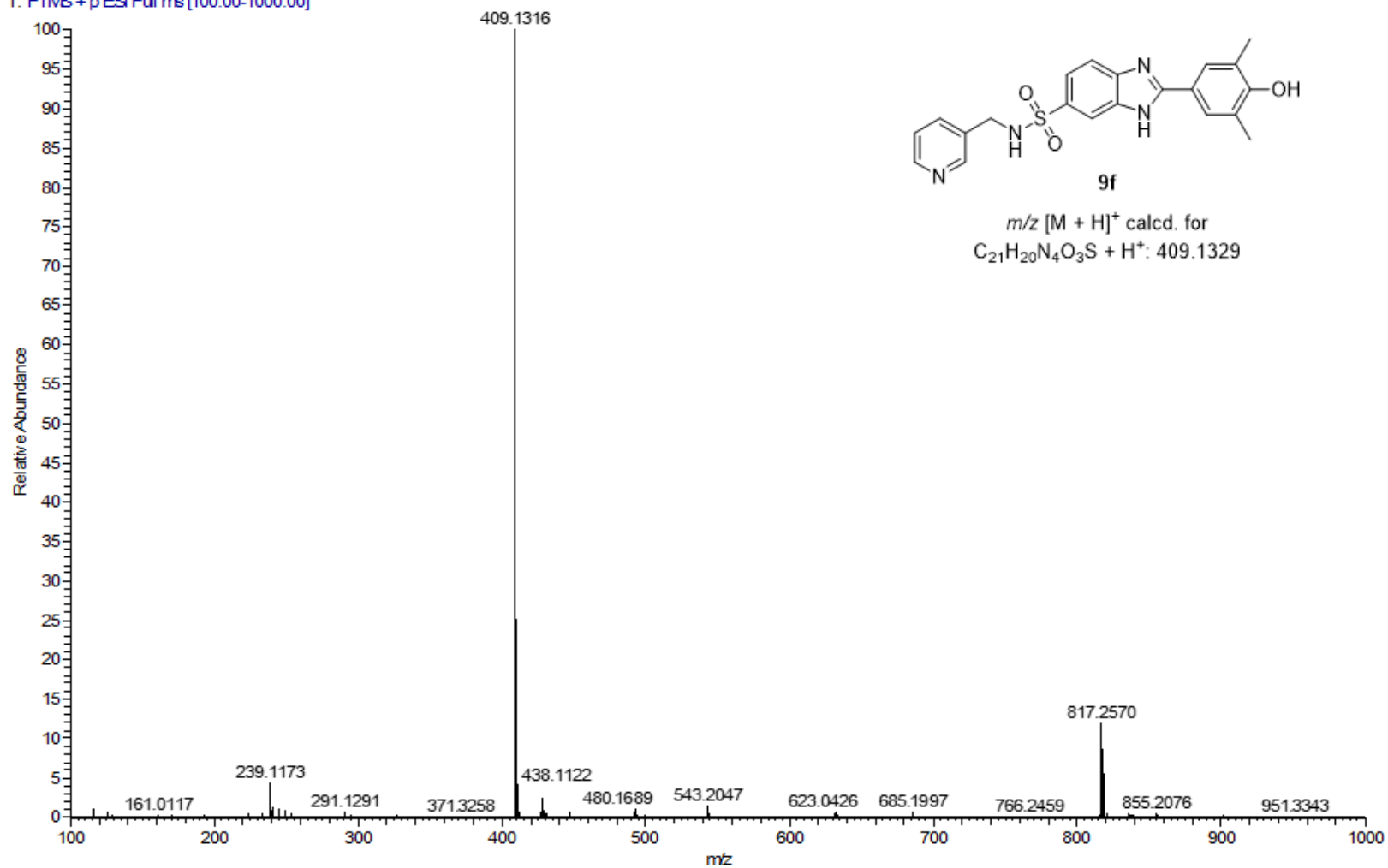
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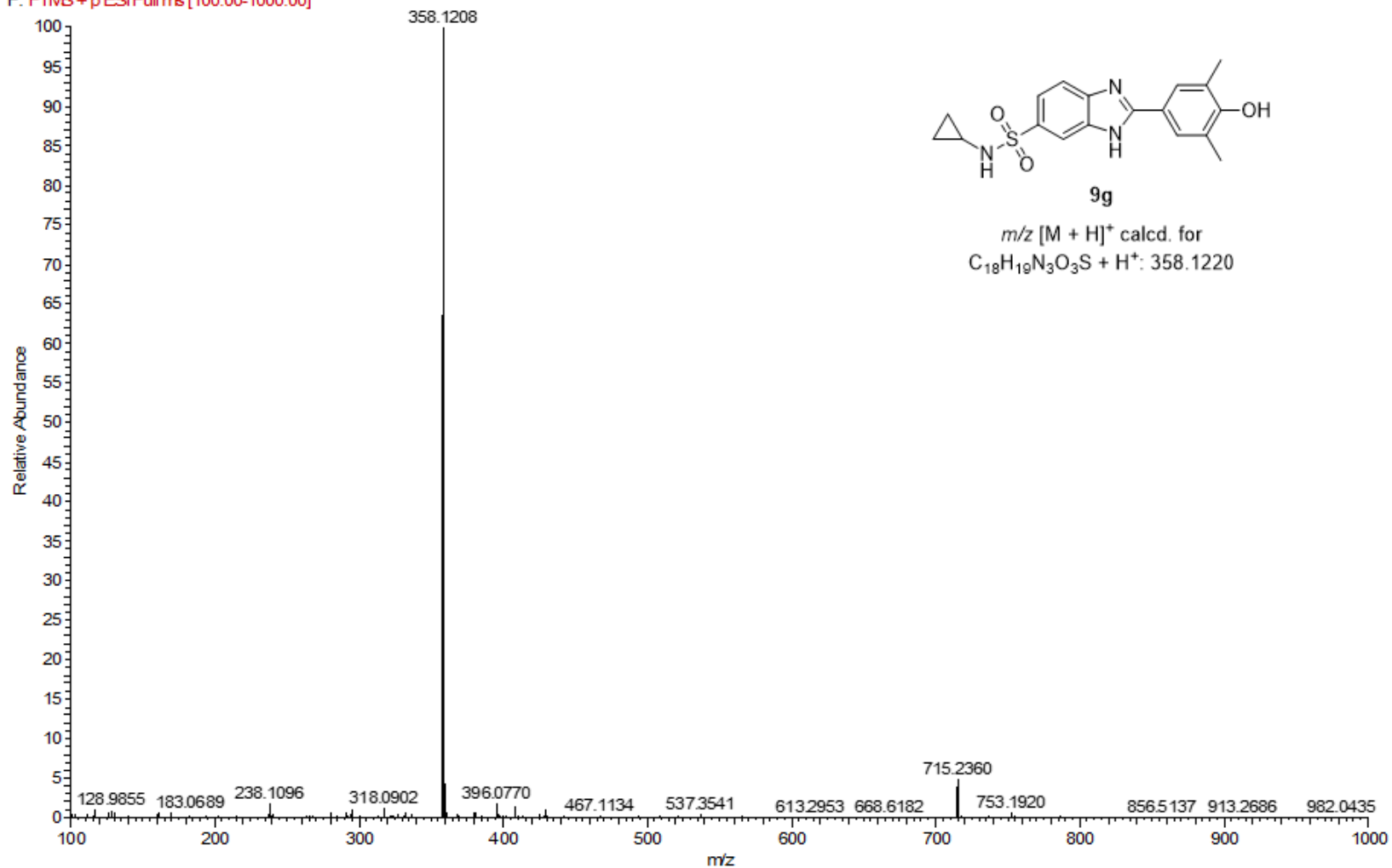
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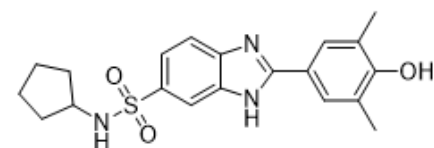
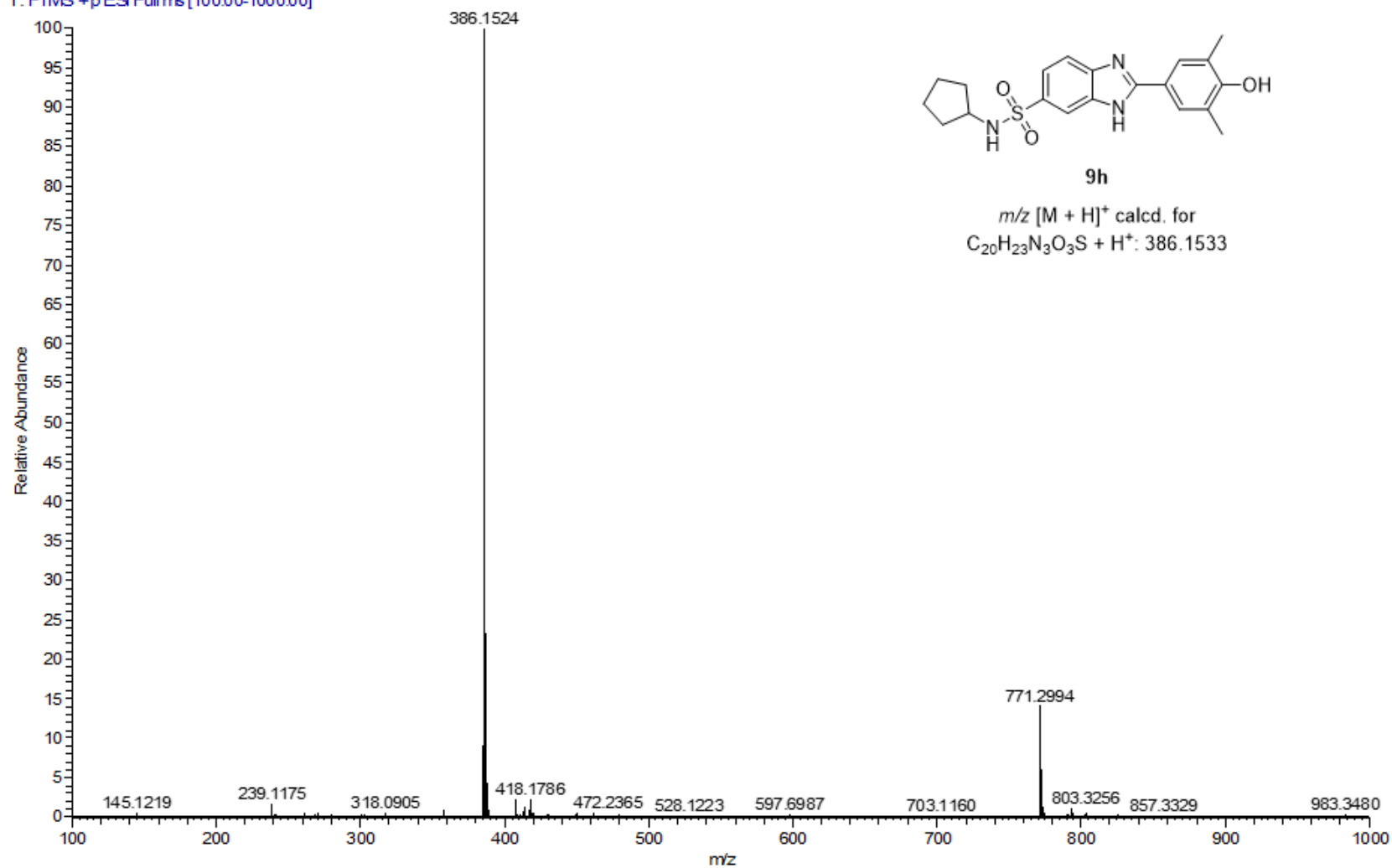
8F EML796 #239 RT: 1.88 AV: 1 NL: 2.38E8
T: FTMS + p ESI Full ms [100.00-1000.00]



8G_EVL801#321 RT: 2.53 AV: 1 NL: 1.23E8
 F: FTMS + p ESI Full ms [100.00-1000.00]



8H_EML797 #124 RT: 0.98 AV: 1 NL: 1.06E8
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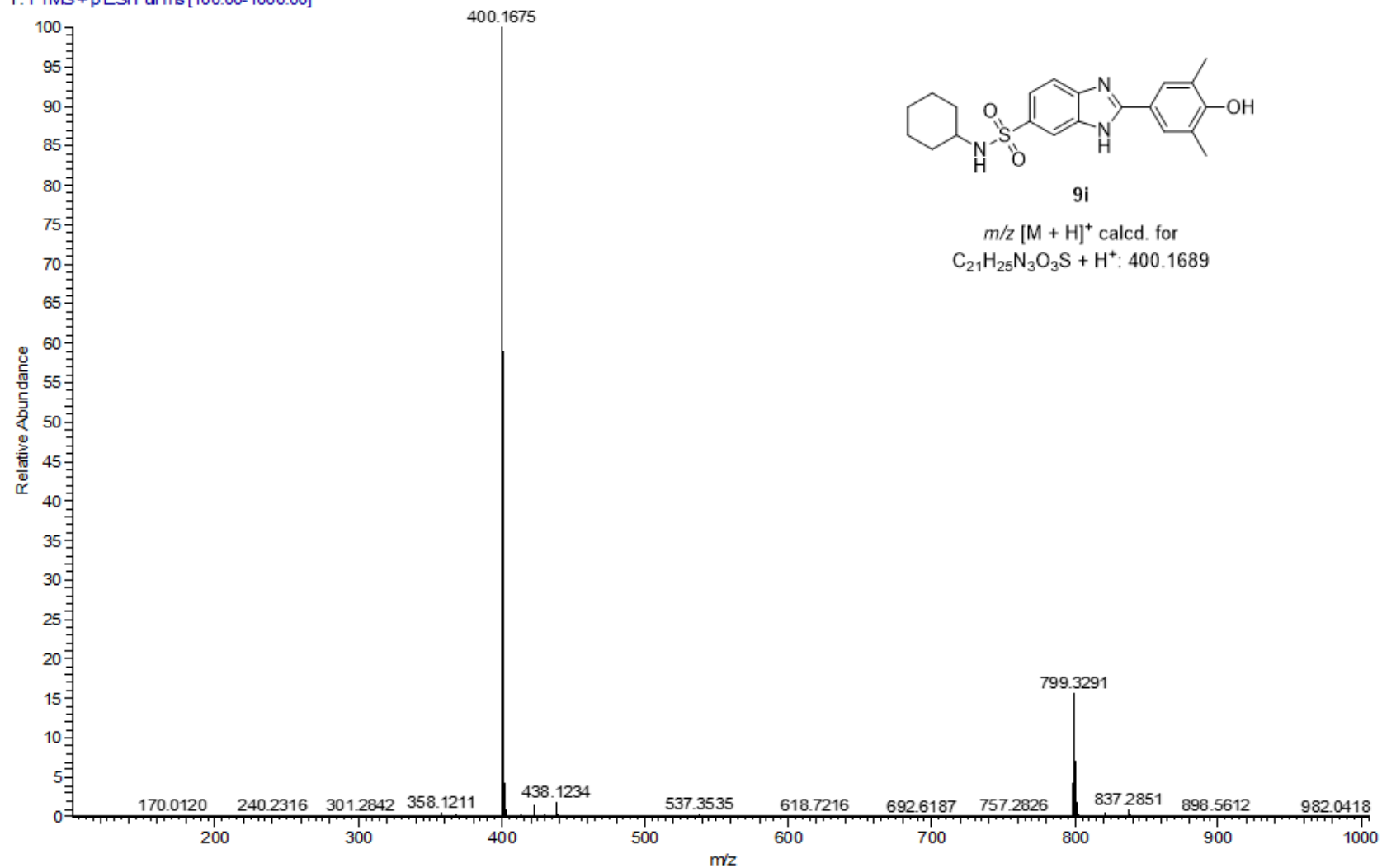


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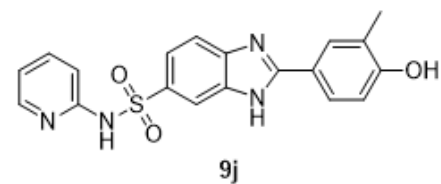
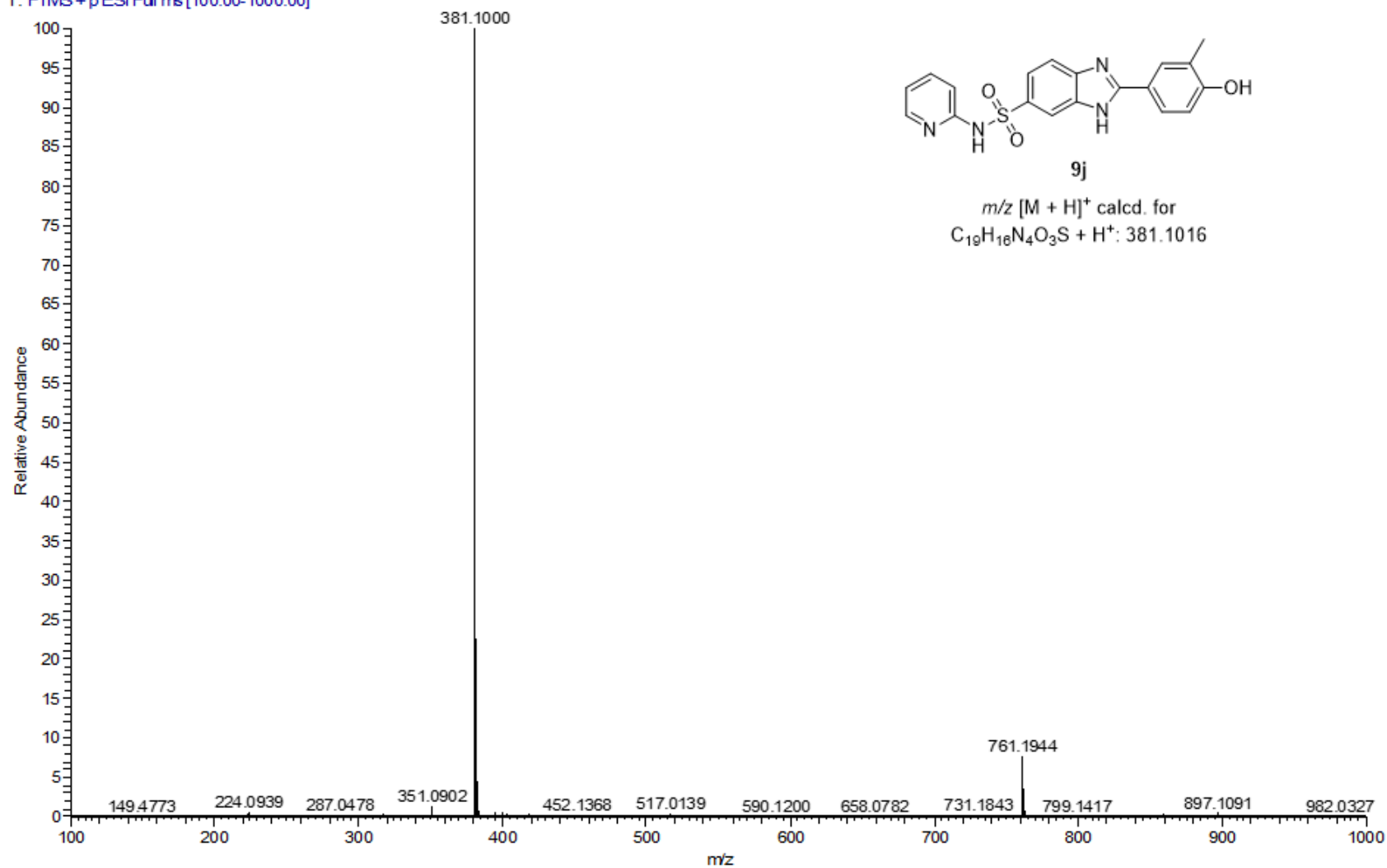
m/z [M + H]⁺ calcd. for
C₂₀H₂₃N₃O₃S + H⁺: 386.1533

8I_EML802 #157-158 RT: 1.24-1.25 AV: 2 NL: 1.32E8

T: FTMS+pESI Full ms [100.00-1000.00]

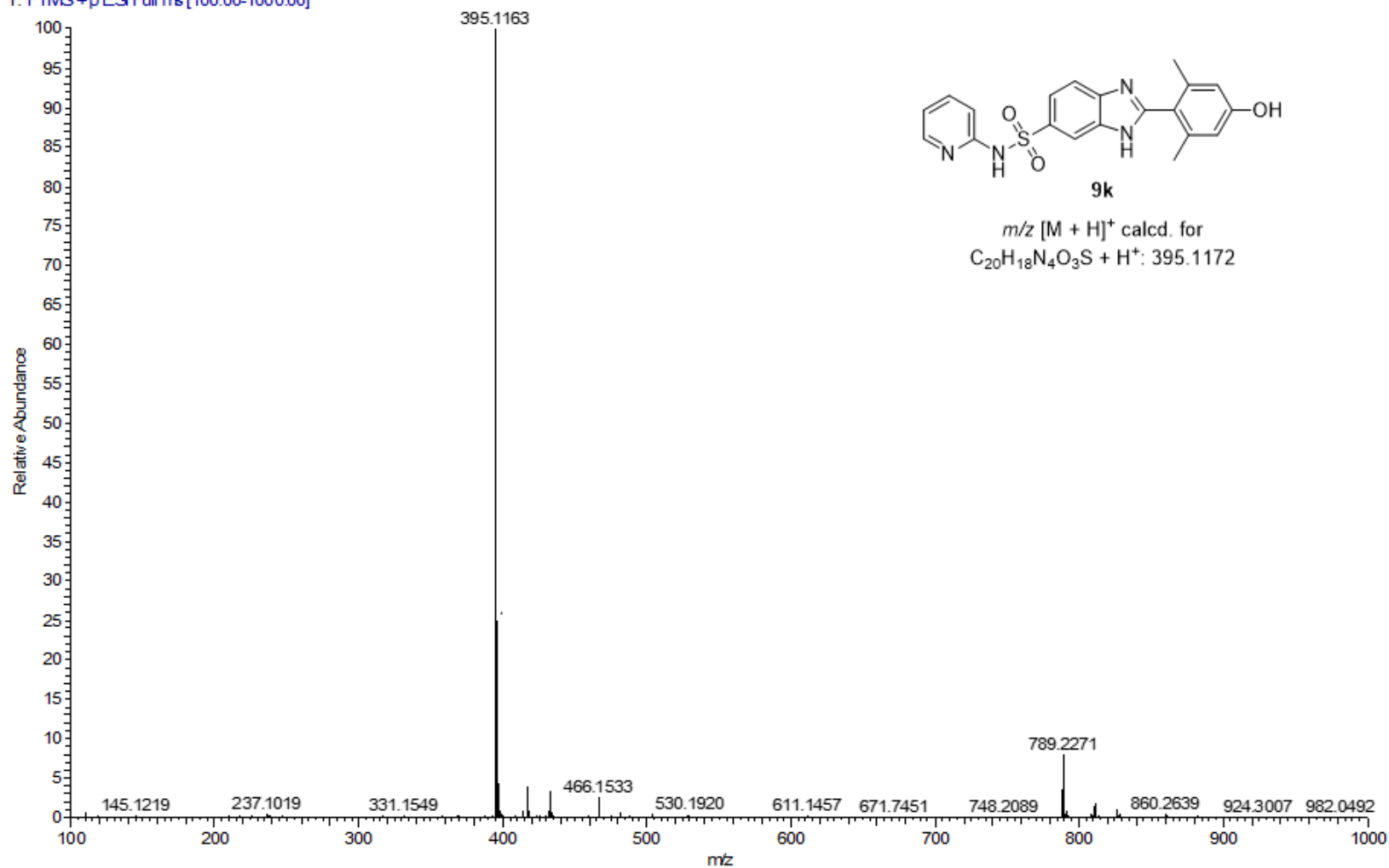


8J_EML806 #92 RT: 0.72 AV: 1 NL: 4.73E8
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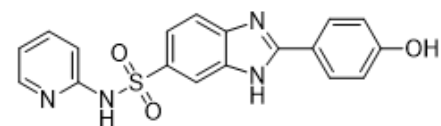
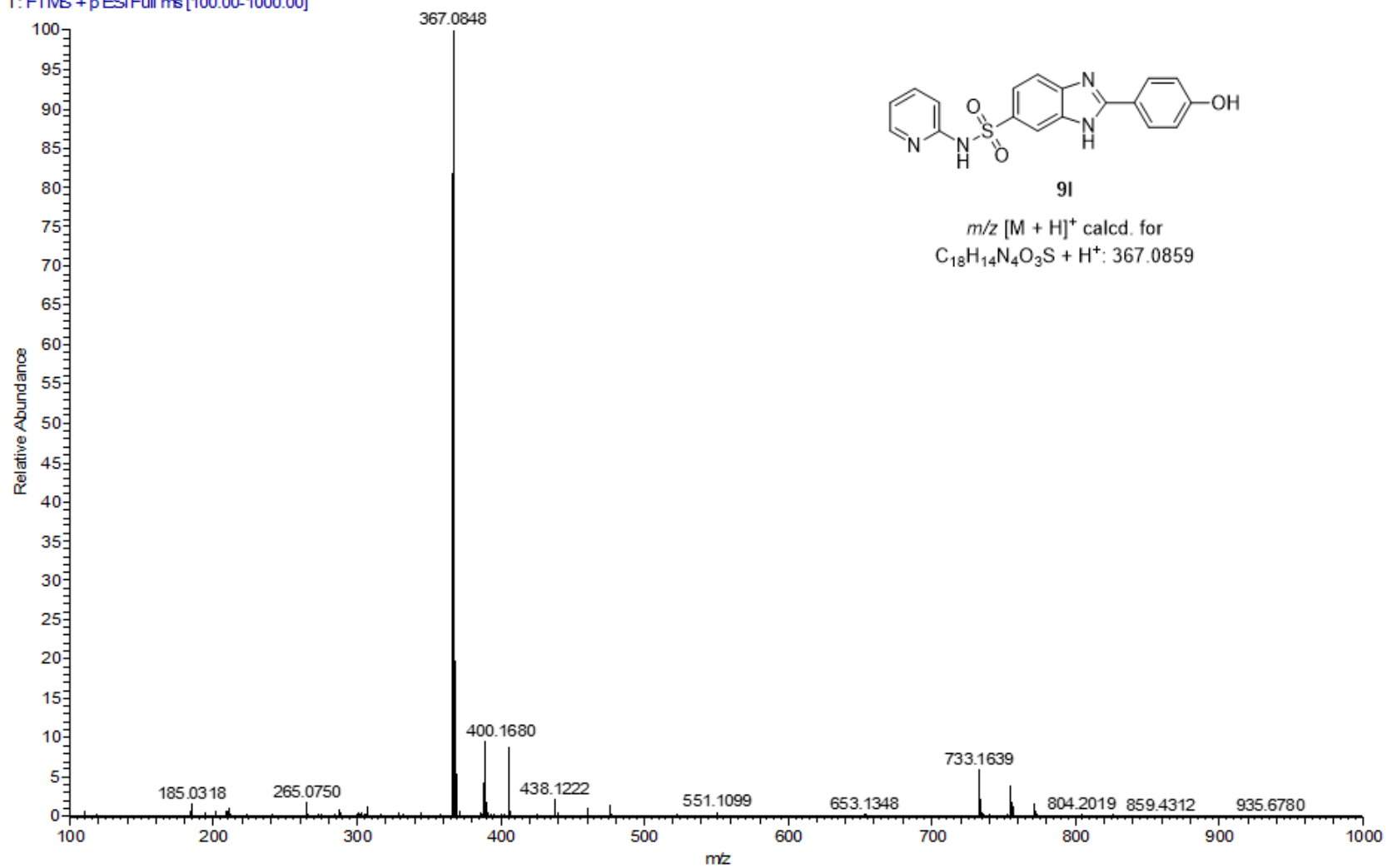


m/z $[M + H]^+$ calcd. for
 $C_{19}H_{16}N_4O_3S + H^+$: 381.1016

8K EML766 #126 RT: 1.00 AV: 1 NL: 1.04E8
T: FTMS+p ESI Full ms [100.00-1000.00]



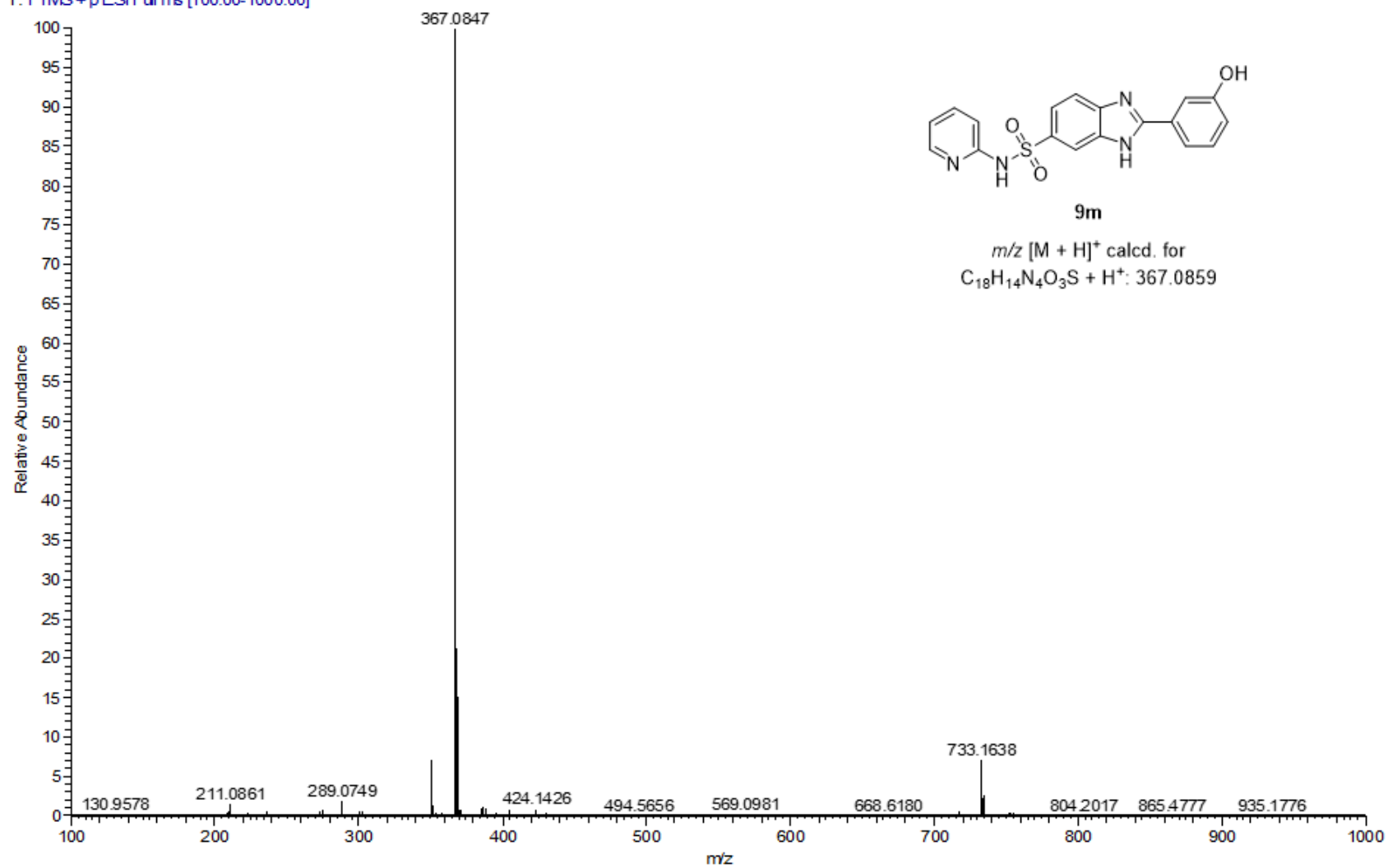
8L_EML760 #97 RT: 0.77 AV: 1 NL: 9.92E7
T: FTMS + p ESI Full ms [100.00-1000.00]



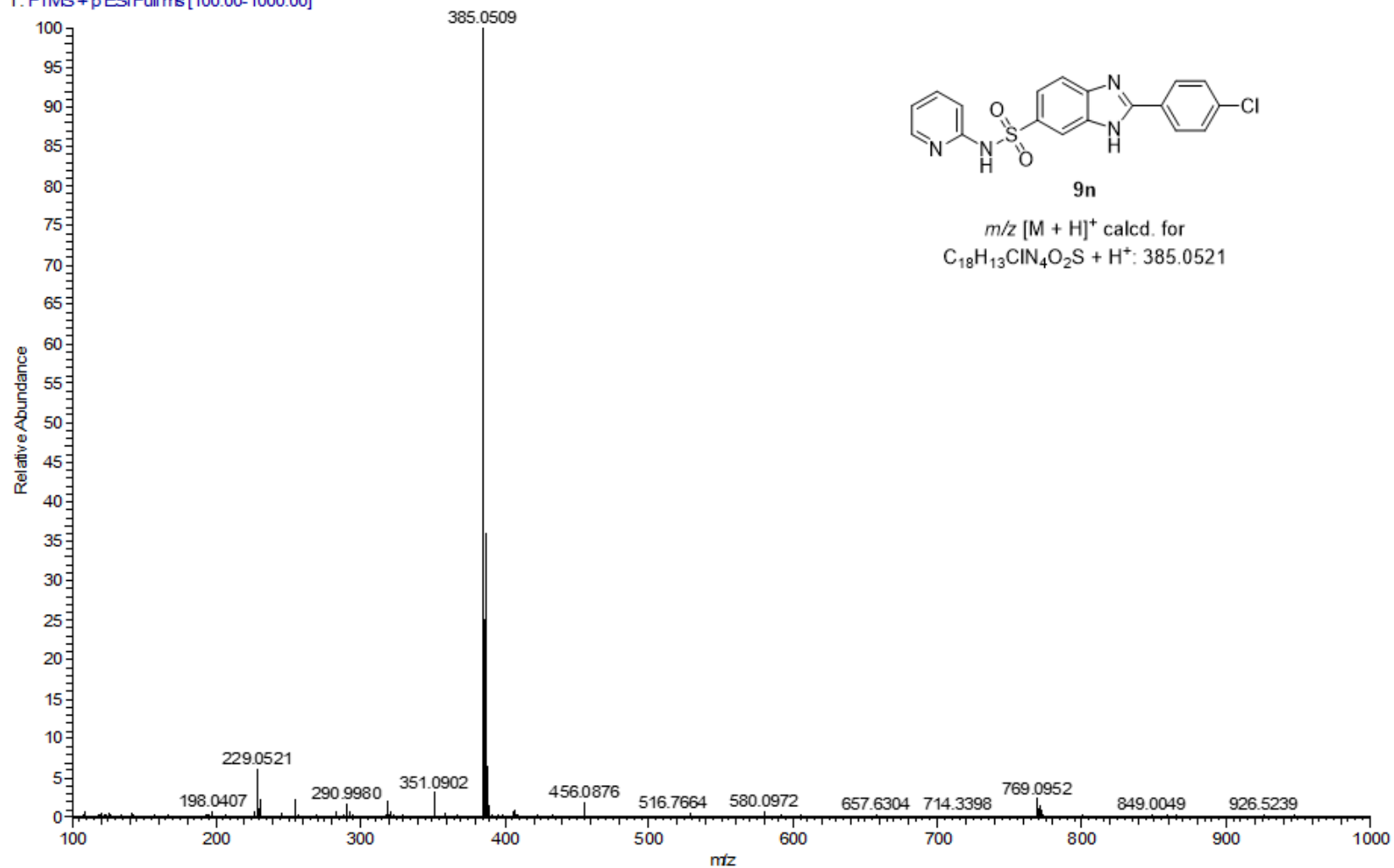
9I

m/z $[M + H]^+$ calcd. for
 $C_{18}H_{14}N_4O_3S + H^+$: 367.0859

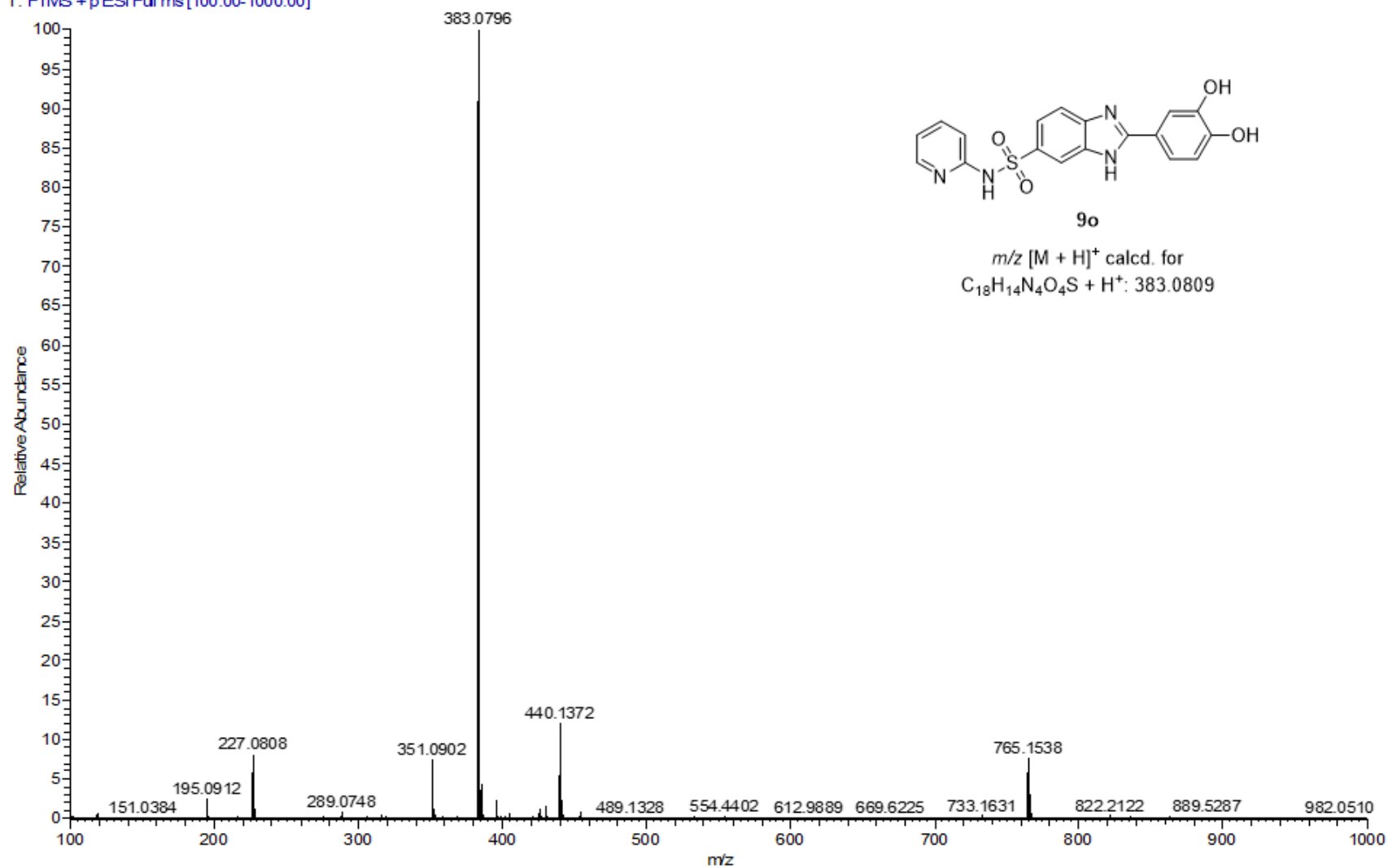
8M_EML761 #120 RT: 0.94 AV: 1 NL: 3.95E8
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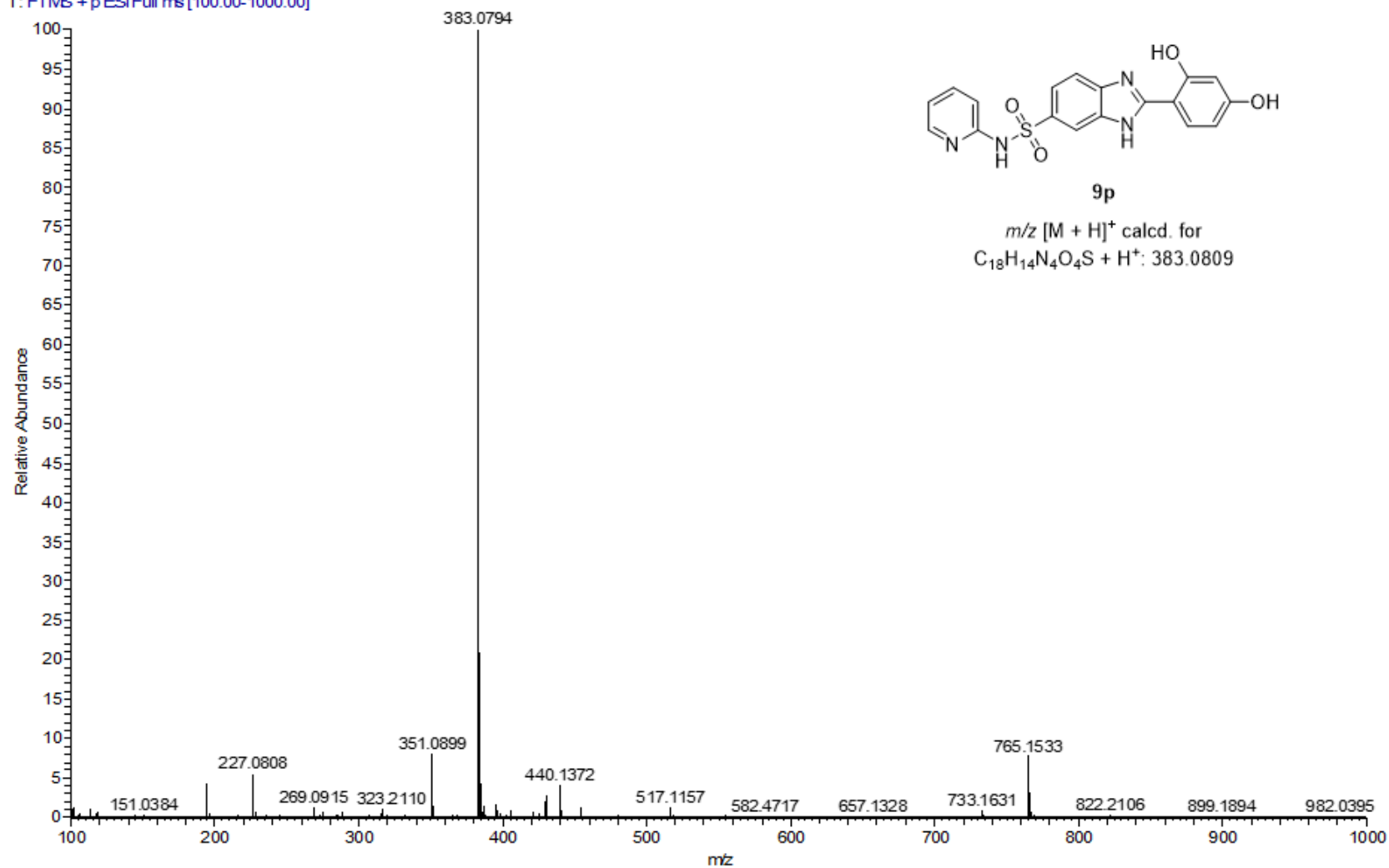
8N_EML762 #205 RT: 1.63 AV: 1 NL: 8.82E6
T: FTMS + p ESI Full ms [100.00-1000.00]



8O_EML764 #95 RT: 0.75 AV: 1 NL: 3.58E8
T: FTMS + p ESI Full ms [100.00-1000.00]



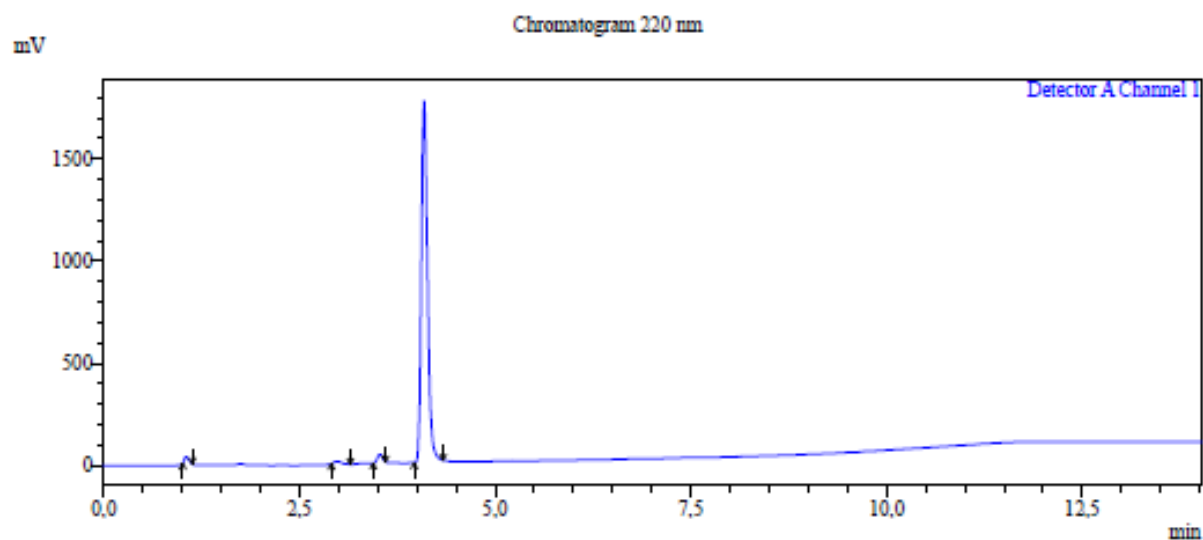
8P_EML763 #40 RT: 0.32 AV: 1 NL: 1.63E8
T: FTMS +p ESI Full ms [100.00-1000.00]



HPLC traces of **9a**

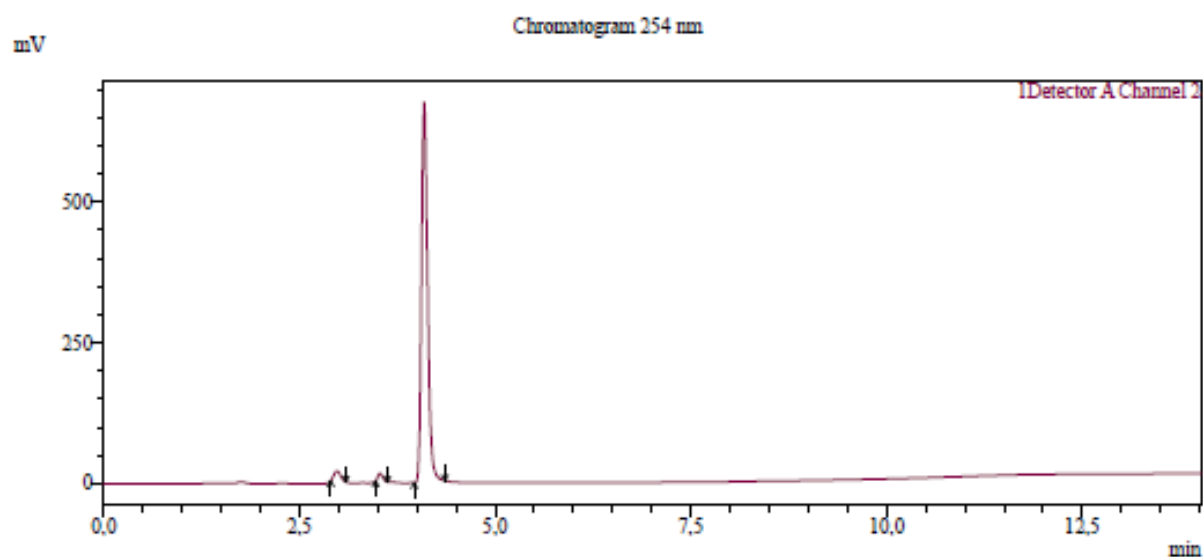
SHIMADTZU HPLC ANALYSIS REPORT

Data File Name : 9a.lcd



Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	1,051	33117	131564	1,311
2	2,976	12986	77010	0,767
3	3,524	39416	178698	1,780
4	4,089	1769378	9650849	96,142
Total		1854896	10038120	100,000



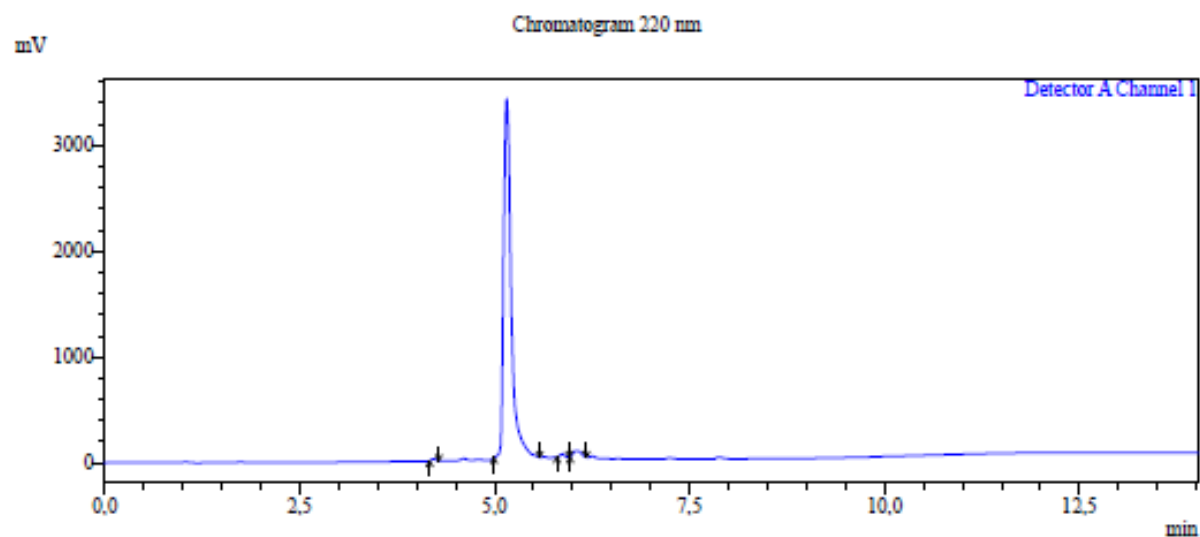
Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	2,975	17866	106834	2,801
2	3,526	13552	59309	1,555
3	4,090	675095	3647669	95,644
Total		706513	3813812	100,000

HPLC traces of **9b**

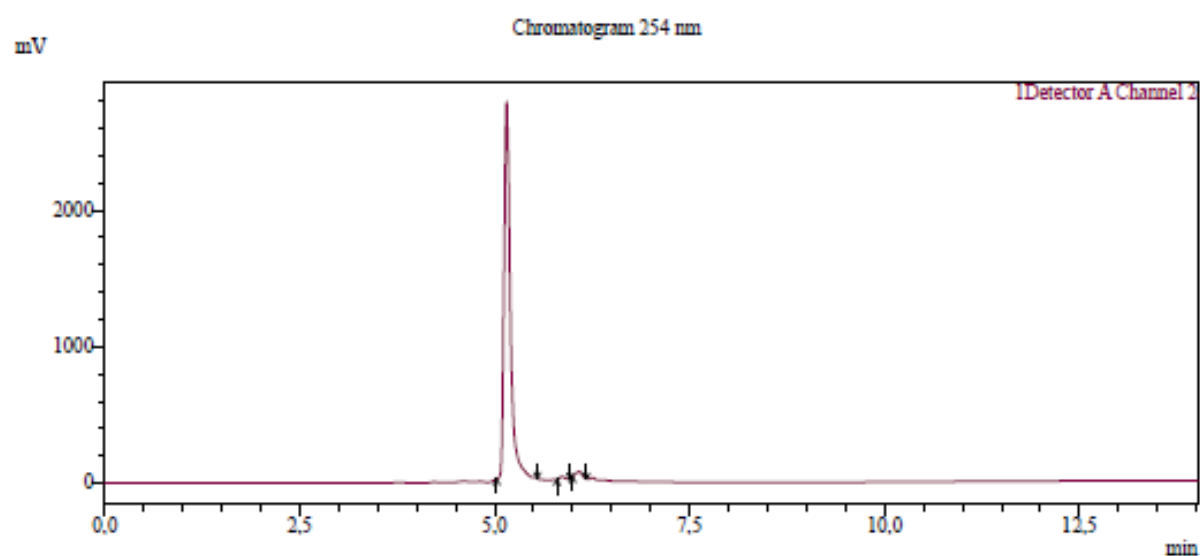
SHIMADTZU HPLC ANALYSIS REPORT

Data File Name : 9b.lcd



Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	4.216	17997	70489	0.299
2	5.151	3386268	23006903	97.485
3	5.860	26800	111581	0.473
4	6.042	58079	411416	1.743
Total		3489144	23600389	100.000



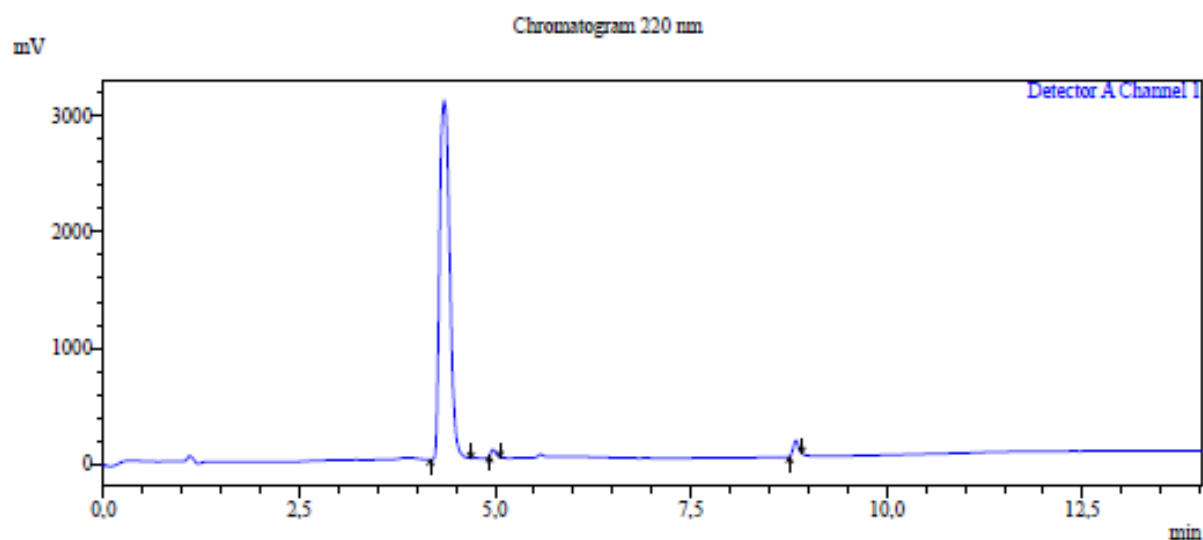
Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	5.150	2758959	15629586	97.885
2	5.860	20312	83199	0.521
3	6.081	45023	254523	1.594
Total		2824294	15967308	100.000

HPLC traces of **9c**

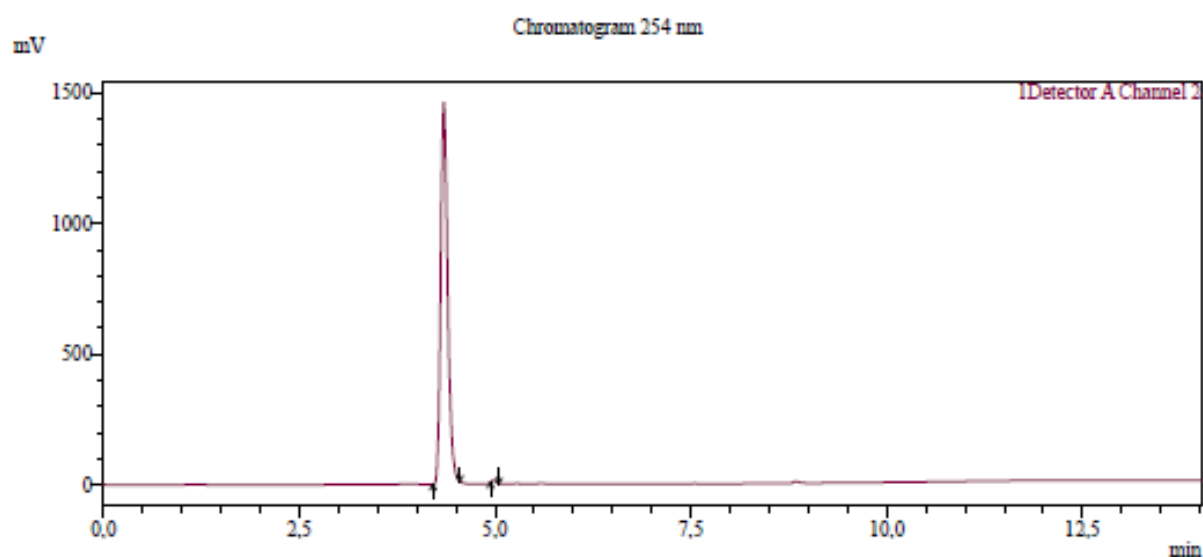
SHIMADTZU HPLC ANALYSIS REPORT

Data File Name : 9c.lcd



Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	4.347	3079413	27546681	97.145
2	4.972	59588	250804	0.884
3	8.835	124158	558682	1.970
Total		3263159	28356167	100.000



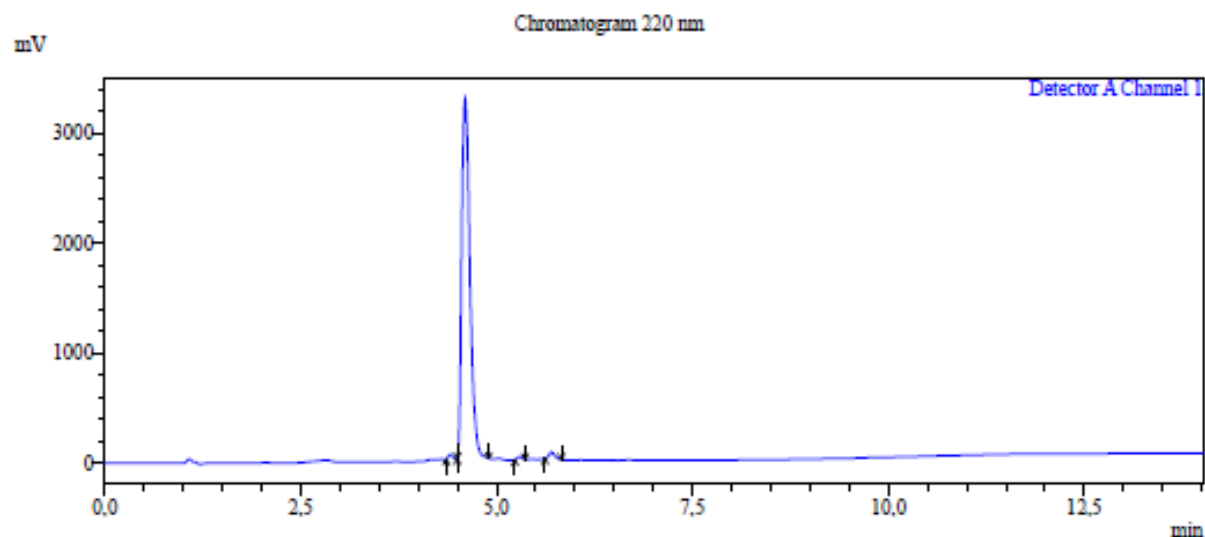
Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	4.342	1454730	9031112	99.691
2	4.973	8058	28037	0.309
Total		1462788	9059149	100.000

HPLC traces of **9d**

SHIMADTZU HPLC ANALYSIS REPORT

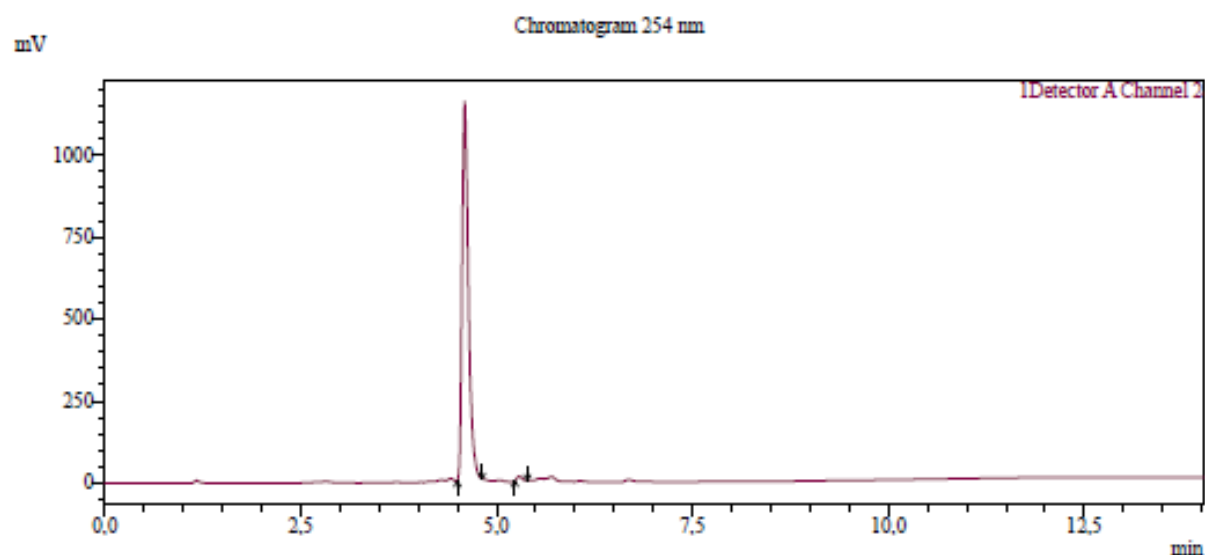
Data File Name : 9d.lcd



Peak Table

Detector A Channel 1 220nm

Peak#	Ret. Time	Height	Area	Area%
1	4,408	41405	143761	0,591
2	4,595	3268500	23753726	97,662
3	5,289	24918	104063	0,428
4	5,696	63523	320720	1,319
Total		3398347	24322270	100,000



Peak Table

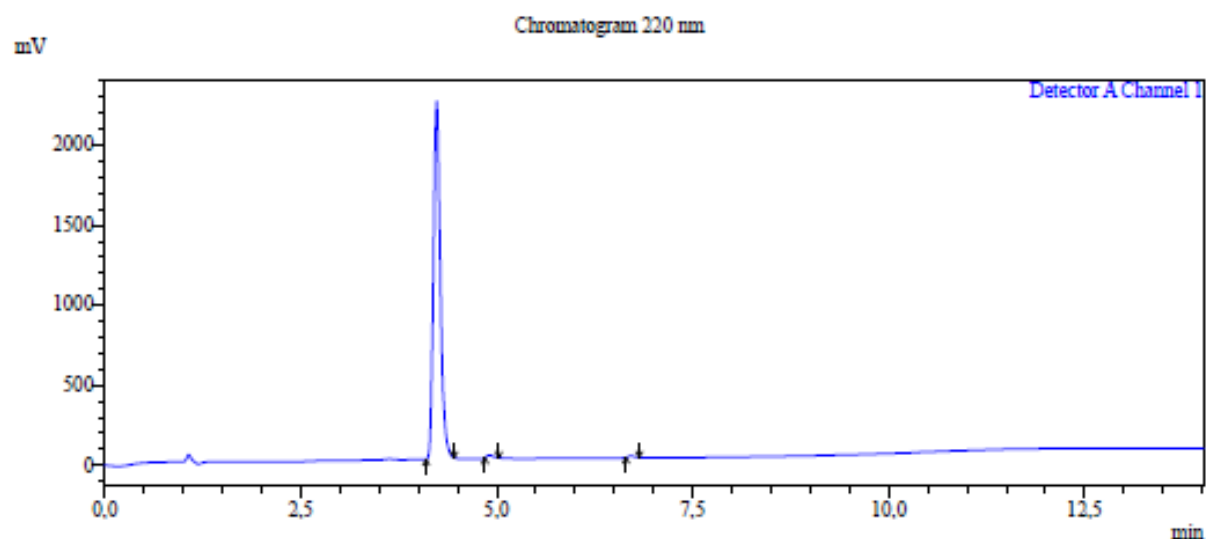
Detector A Channel 2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	4,589	1154286	6490078	99,125
2	5,287	13246	57271	0,875
Total		1167532	6547349	100,000

HPLC traces of 9e

SHIMADTZU HPLC ANALYSIS REPORT

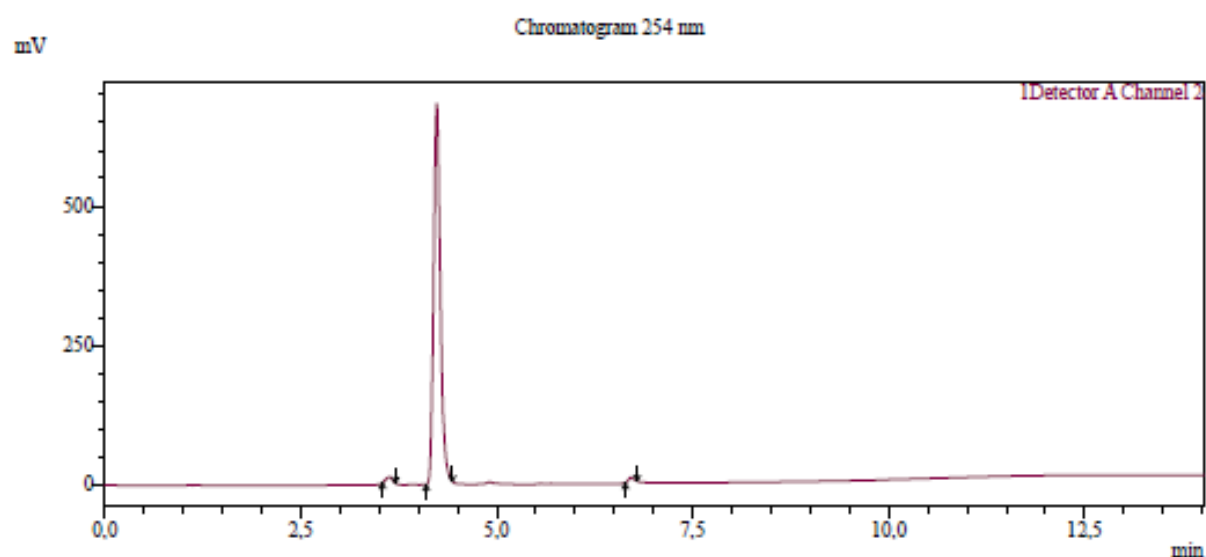
Data File Name : 9e.lcd



Peak Table

Detector A Channel 1 220nm

Peak#	Ret. Time	Height	Area	Area%
1	4,229	2236517	13639886	98,960
2	4,901	17641	89022	0,646
3	6,708	10795	54294	0,394
Total		2264954	13783202	100,000



Peak Table

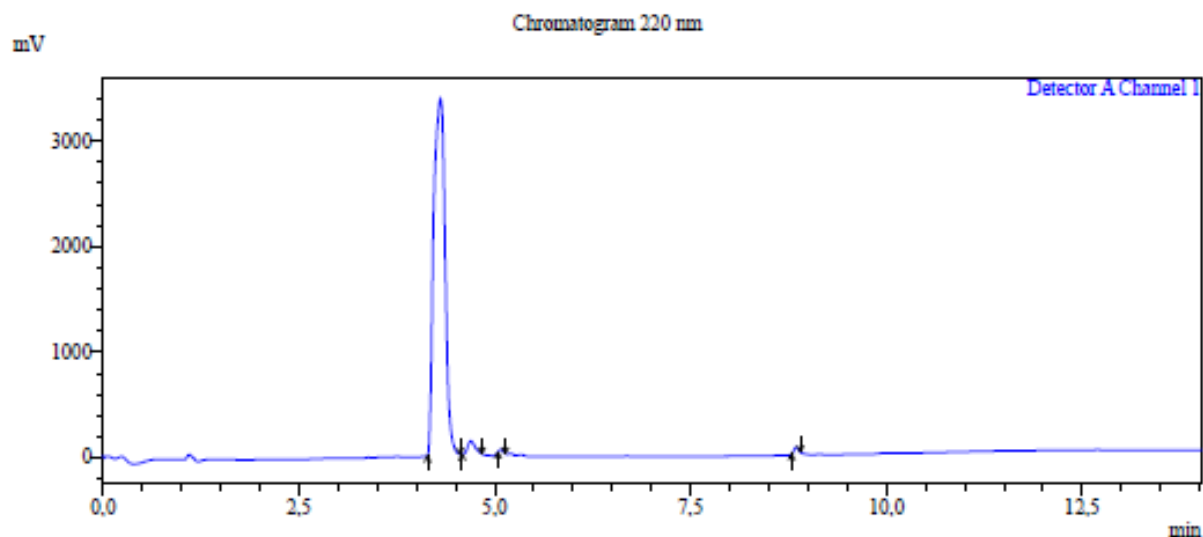
Detector A Channel 2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	3,628	10954	61410	1,482
2	4,231	681238	4043733	97,573
3	6,710	8253	39186	0,946
Total		700445	4144329	100,000

HPLC traces of 9f

SHIMADTZU HPLC ANALYSIS REPORT

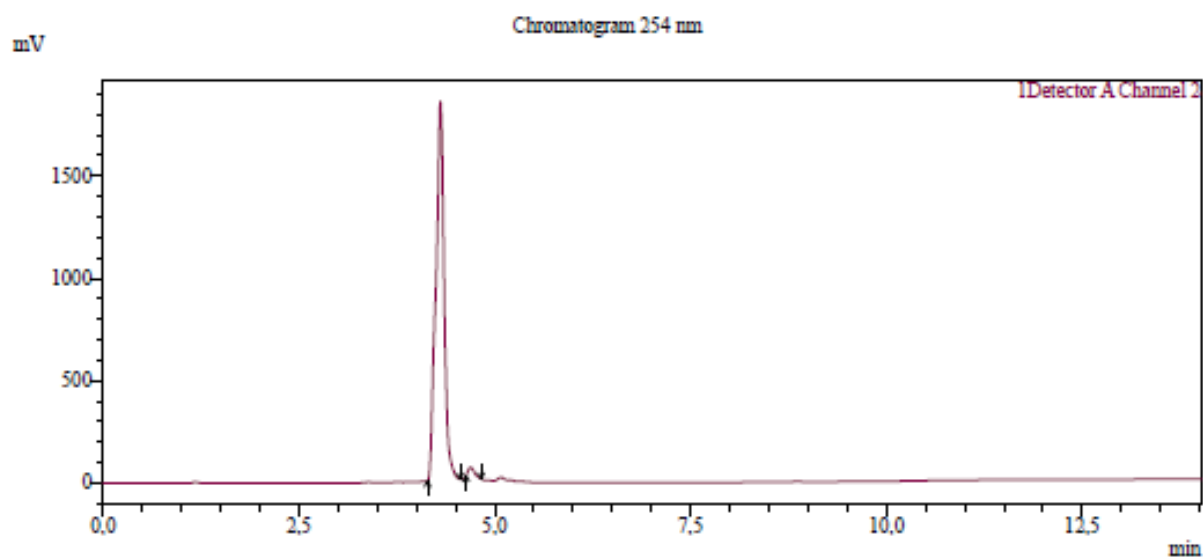
Data File Name : 9f.lcd



Peak Table

Detector A Channel 1 220nm

Peak#	Ret. Time	Height	Area	Area%
1	4.303	3377695	33989208	96.843
2	4.691	125023	802847	2.287
3	5.076	30748	100188	0.285
4	8.846	55045	204997	0.584
Total		3588510	35097240	100.000



Peak Table

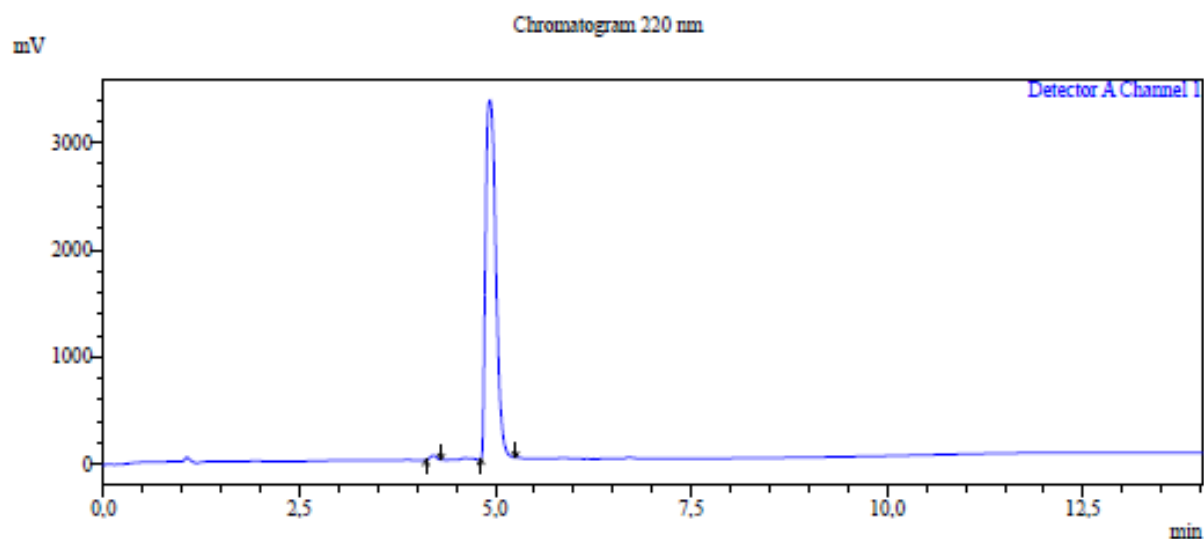
Detector A Channel 2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	4.303	1852582	13573715	98.211
2	4.688	45974	247320	1.789
Total		1898556	13821035	100.000

HPLC traces of 9g

SHIMADTZU HPLC ANALYSIS REPORT

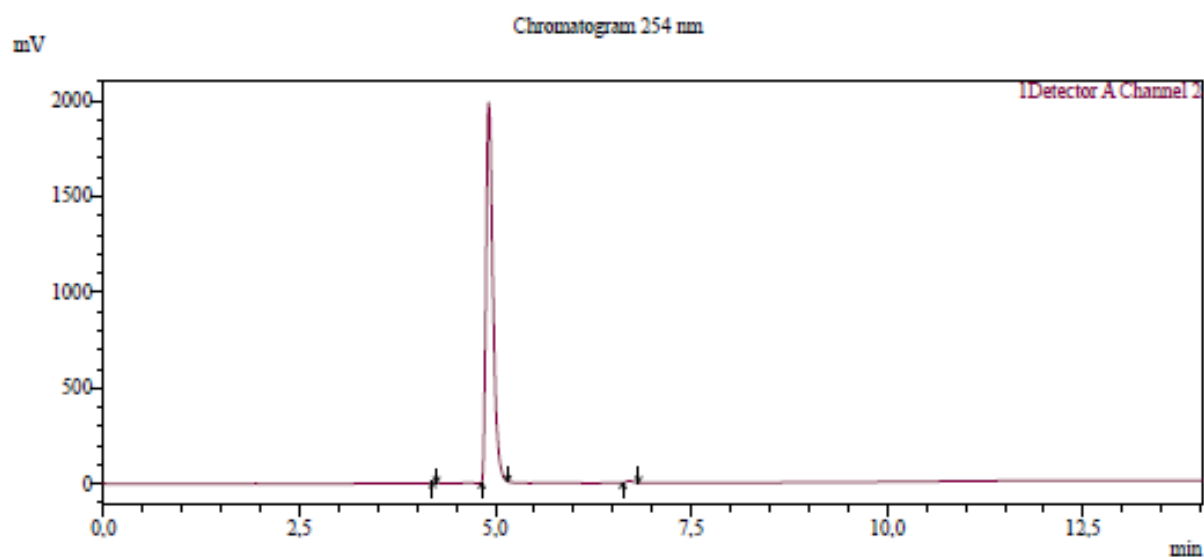
Data File Name : 9g.lcd



Peak Table

Detector A Channel 1 220nm

Peak#	Ret. Time	Height	Area	Area%
1	4.203	40446	213417	0.699
2	4.926	3342802	30306116	99.301
Total		3383248	30519533	100.000



Peak Table

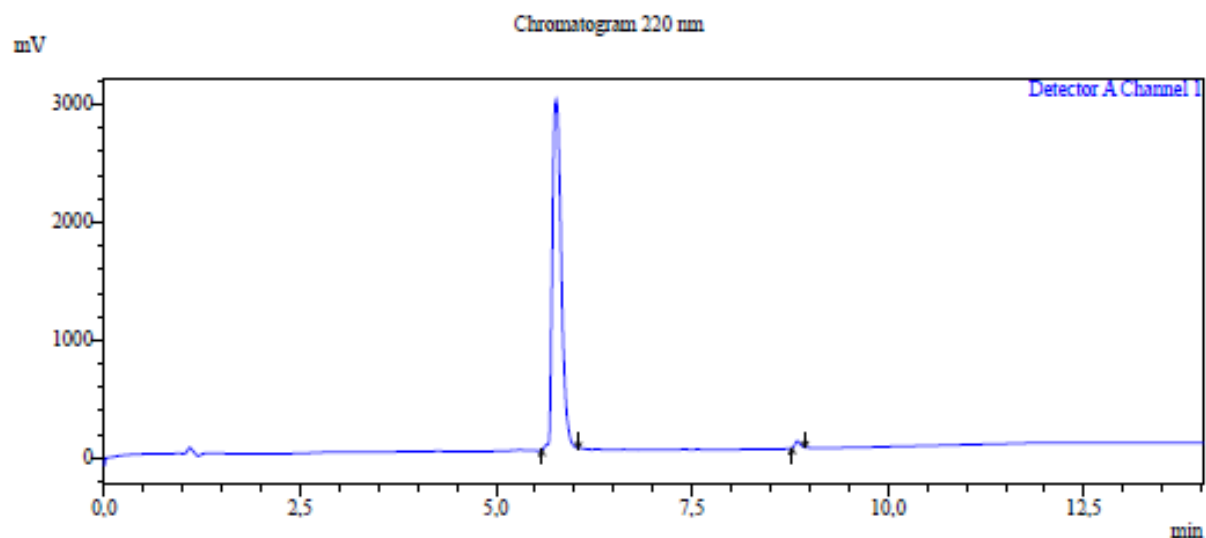
Detector A Channel 2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	4.207	655	1433	0.012
2	4.912	1987165	12197337	99.538
3	6.702	10161	55124	0.450
Total		1997981	12253894	100.000

HPLC traces of 9h

SHIMADTZU HPLC ANALYSIS REPORT

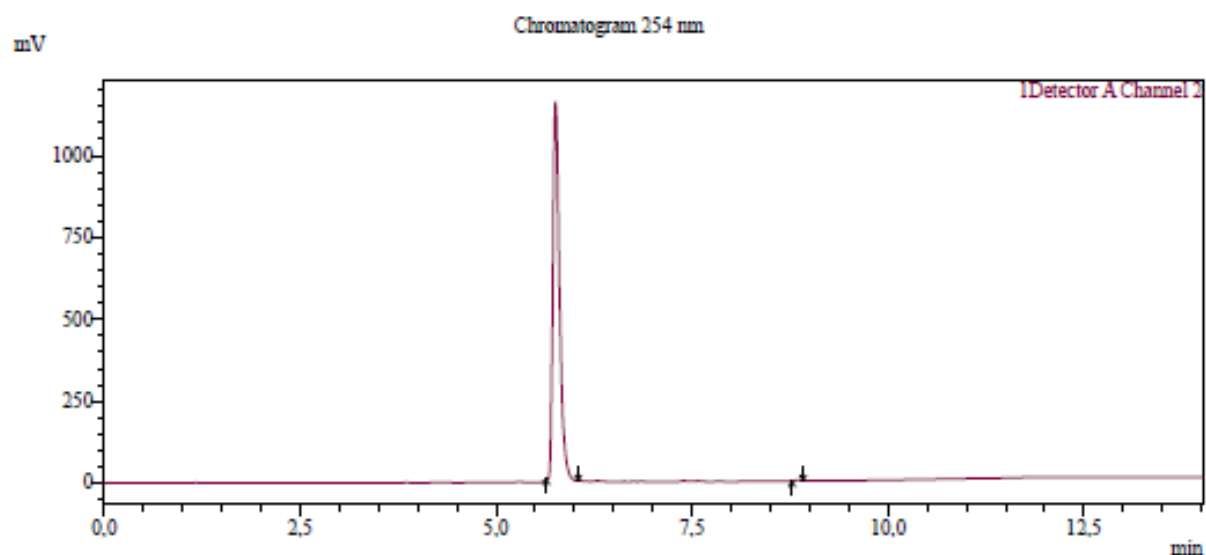
Data File Name : 9h.lcd



Peak Table

Detector A Channel 1 220nm

Peak#	Ret. Time	Height	Area	Area%
1	5.763	2968519	23225231	98.855
2	8.841	56209	268997	1.145
Total		3024727	23494229	100.000



Peak Table

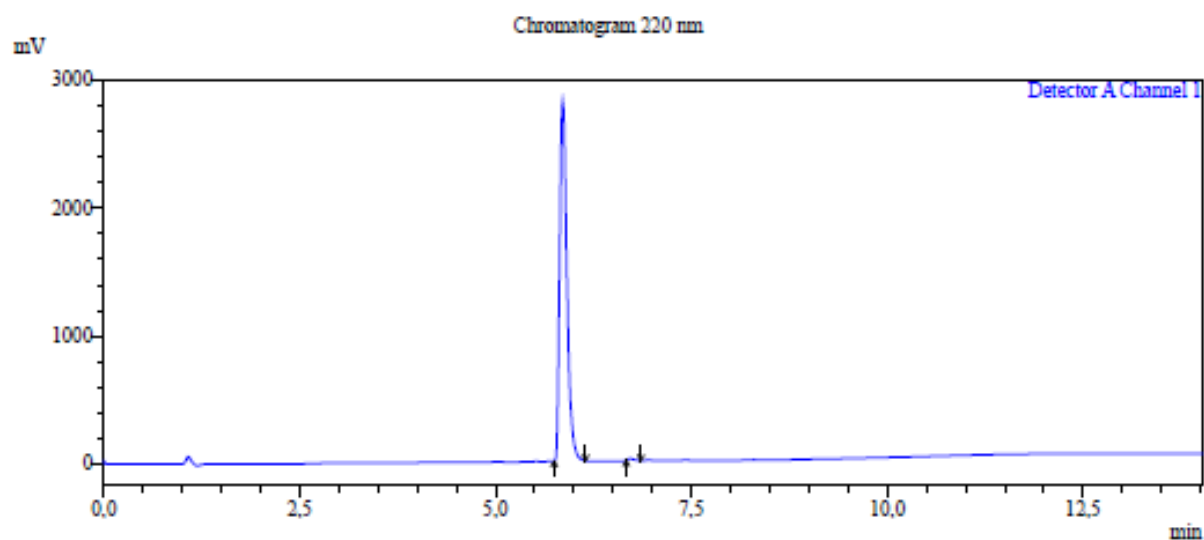
Detector A Channel 2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	5.755	1154112	6753407	99.841
2	8.843	2442	10740	0.159
Total		1156554	6764148	100.000

HPLC traces of 9i

SHIMADTZU HPLC ANALYSIS REPORT

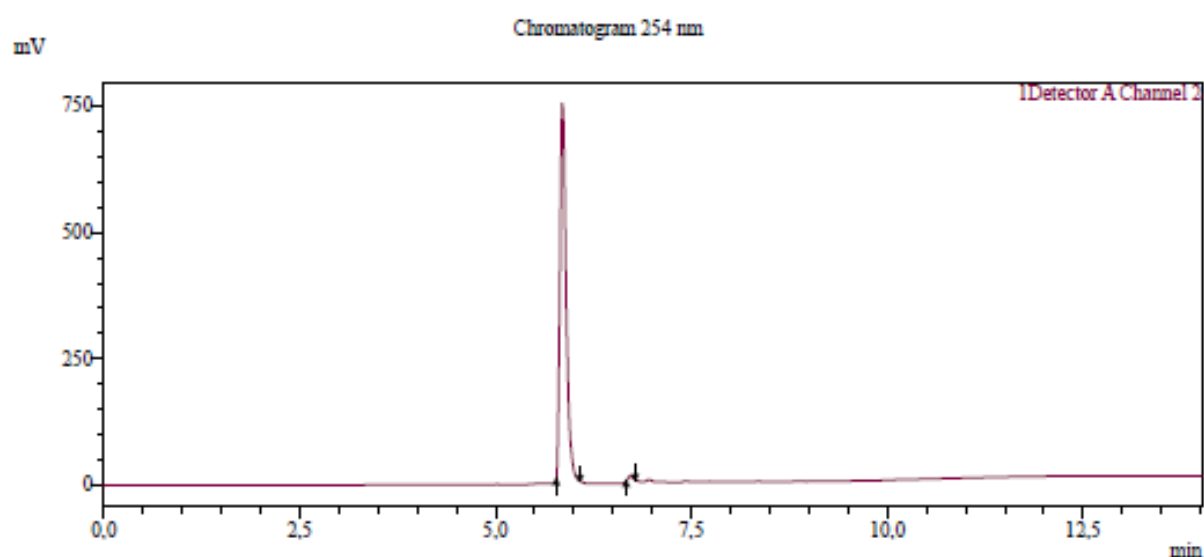
Data File Name : 9i.lcd



Peak Table

Detector A Channel 1 220nm

Peak#	Ret. Time	Height	Area	Area%
1	5.853	2815285	18166805	99.620
2	6.714	13421	69363	0.380
Total		2828707	18236168	100.000



Peak Table

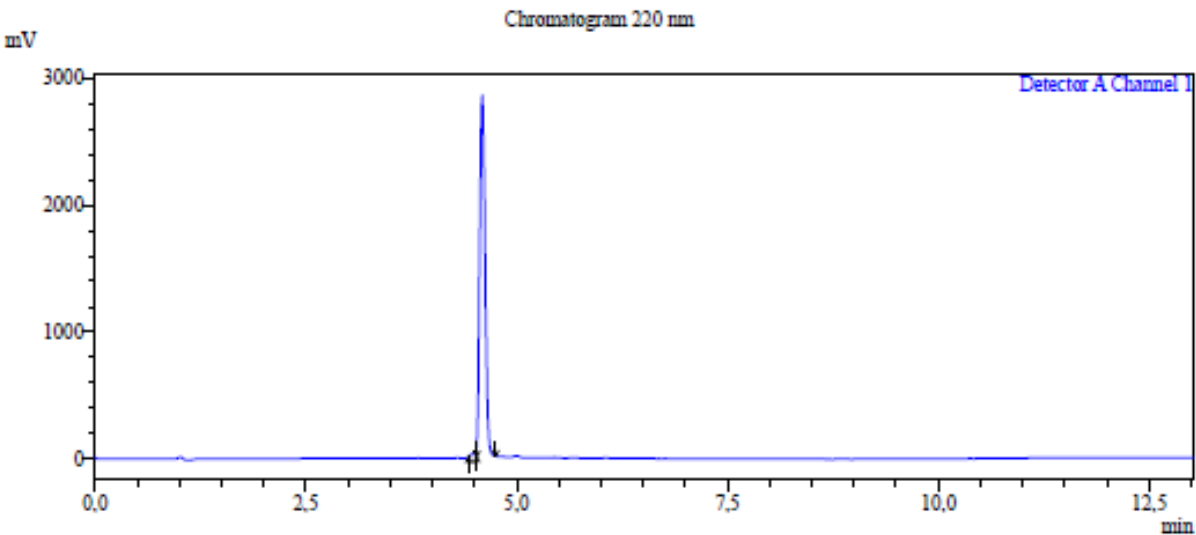
Detector A Channel 2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	5.850	742645	4081445	99.126
2	6.716	8989	35991	0.874
Total		751634	4117436	100.000

HPLC traces of **9j**

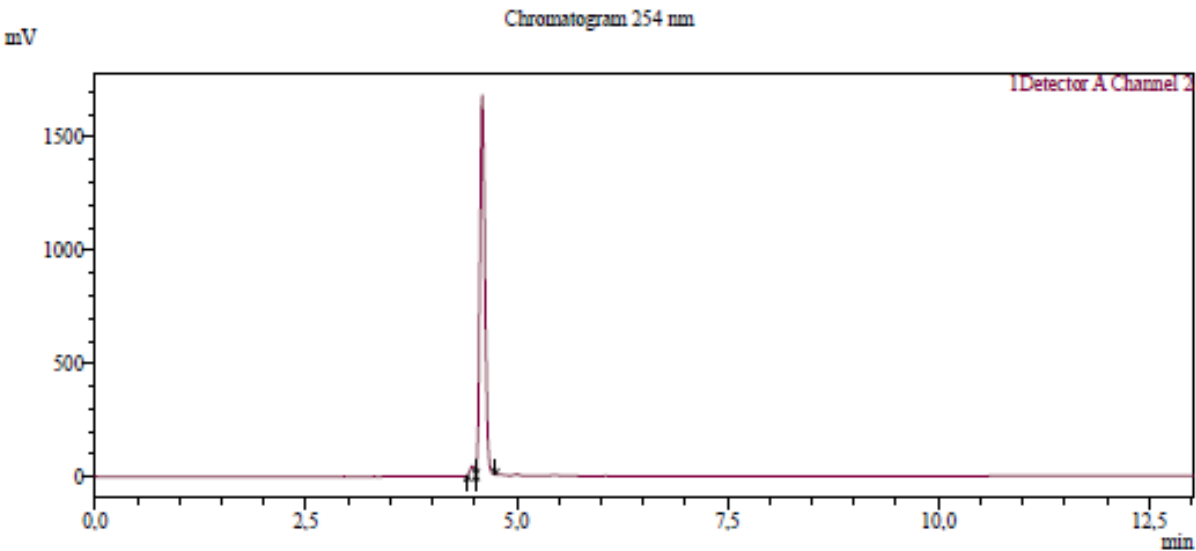
SHIMADTZU HPLC ANALYSIS REPORT

Data File Name : 9j.lcd



Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	4.517	39112	143161	1.116
2	4.587	2850292	12680531	98.884
Total		2889404	12823691	100.000



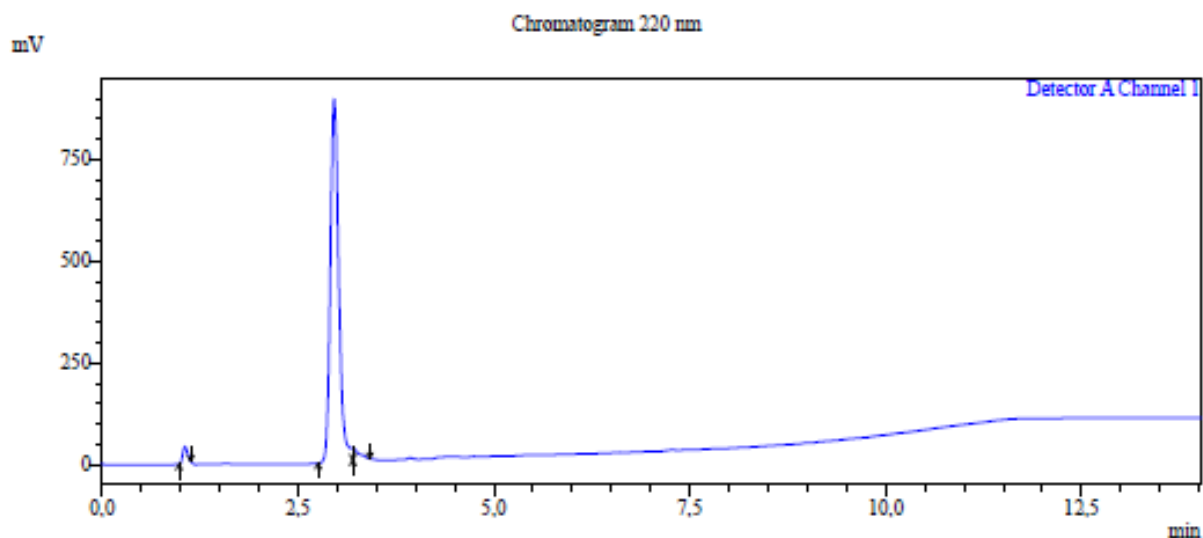
Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	4.471	39358	154526	2.160
2	4.586	1679278	6999723	97.840
Total		1718635	7154249	100.000

HPLC traces of 9k

SHIMADTZU HPLC ANALYSIS REPORT

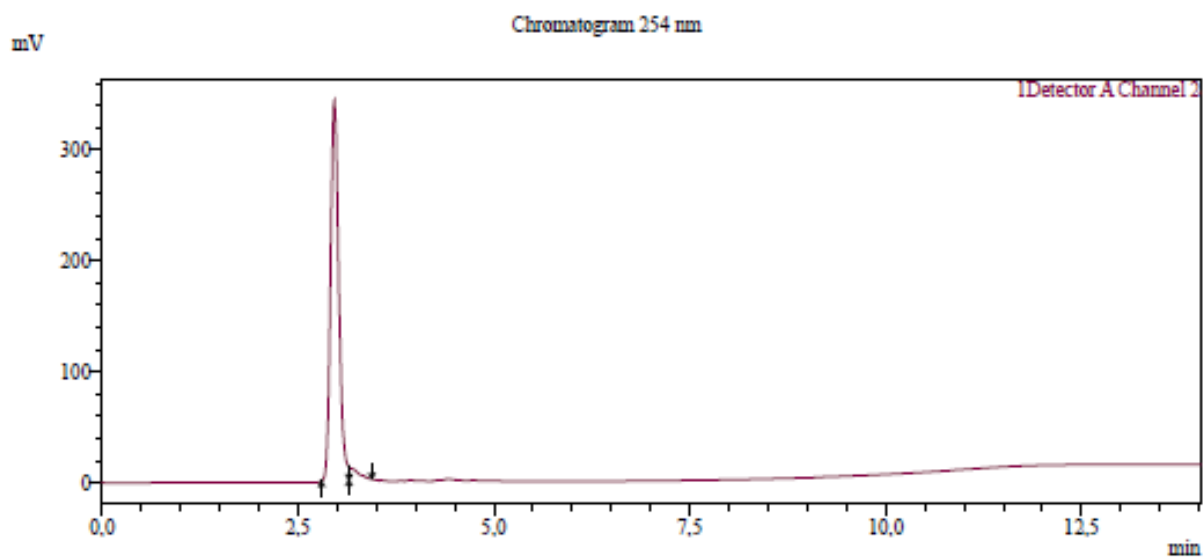
Data File Name : 9k.lcd



Peak Table

Detector A Channel 1 220nm

Peak#	Ret. Time	Height	Area	Area%
1	1.054	39241	163321	2,331
2	2.958	890402	6687870	95,465
3	3.200	28665	154416	2,204
Total		958309	7005607	100,000



Peak Table

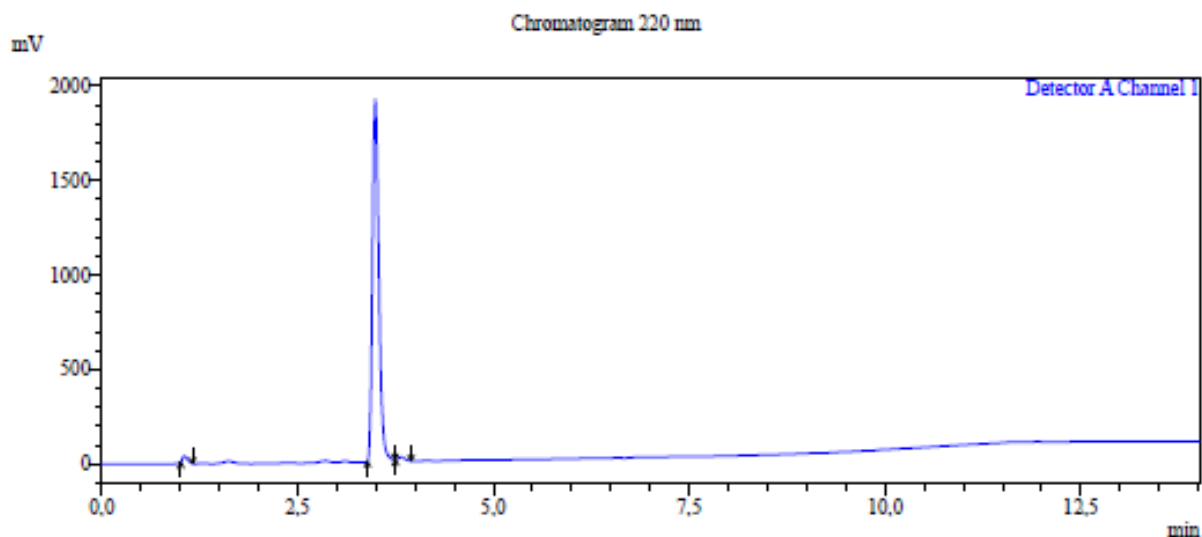
Detector A Channel 2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	2.959	342127	2511994	96,750
2	3.158	10970	84373	3,250
Total		353097	2596367	100,000

HPLC traces of 9I

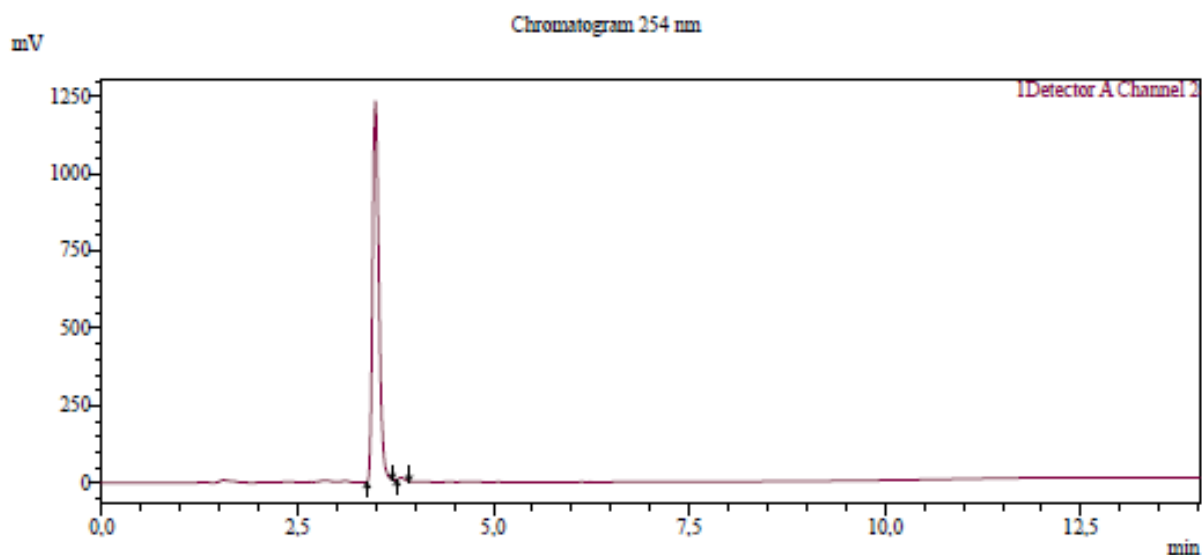
SHIMADTZU HPLC ANALYSIS REPORT

Data File Name : 9I.lcd



Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	1,051	35684	154824	1,403
2	3,488	1917483	10795214	97,818
3	3,818	15955	85990	0,779
Total		1969122	11036028	100,000



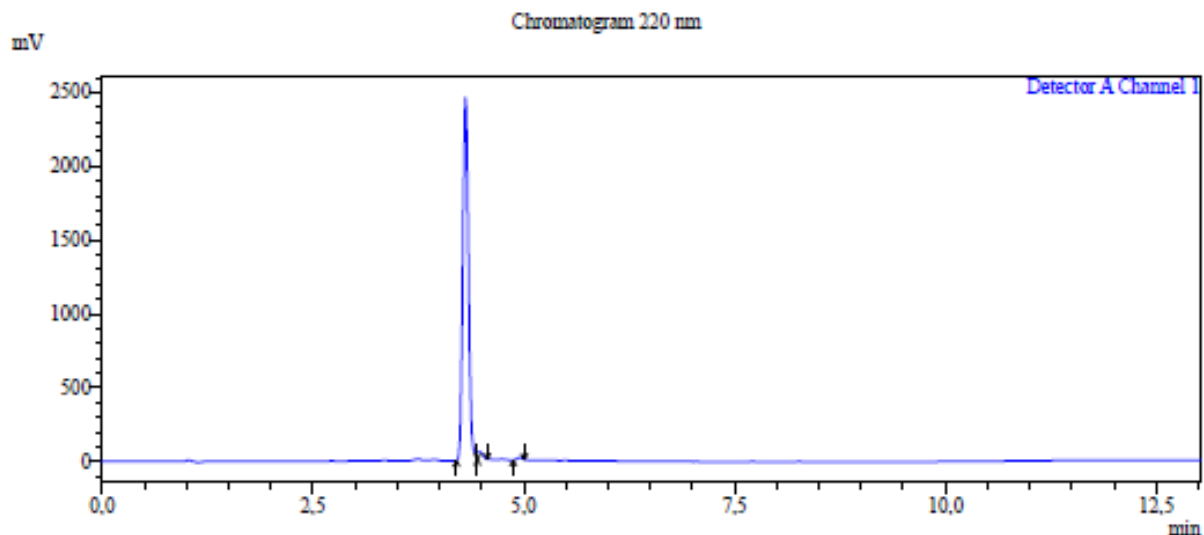
Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	3,489	1231130	6905990	99,386
2	3,817	8712	42664	0,614
Total		1239842	6948654	100,000

HPLC traces of 9m

SHIMADTZU HPLC ANALYSIS REPORT

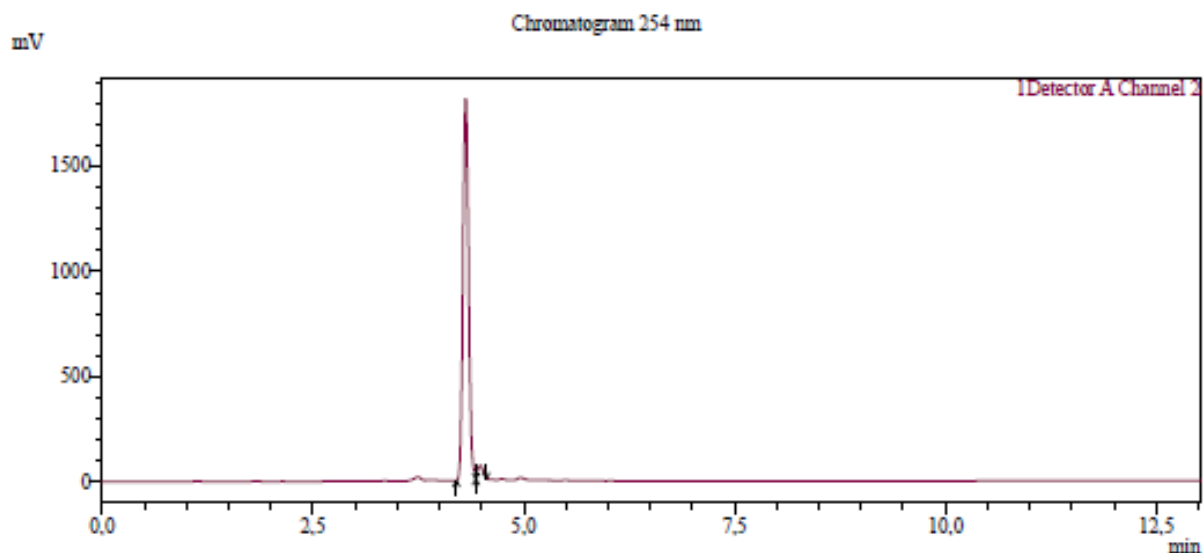
Data File Name : 9m.lcd



Peak Table

Detector A Channel 1 220nm

Peak#	Ret. Time	Height	Area	Area%
1	4.305	2459205	11508429	97.744
2	4.474	50796	204173	1.734
3	4.948	15401	61470	0.522
Total		2525402	11774072	100.000



Peak Table

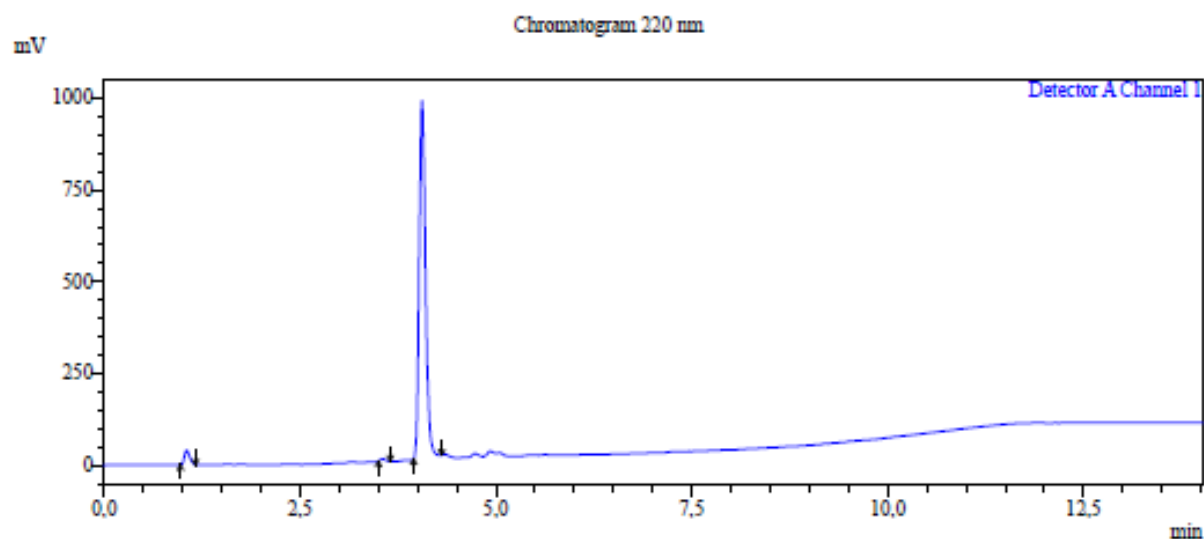
Detector A Channel 2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	4.308	1811651	8491301	96.750
2	4.481	63556	285223	3.250
Total		1875207	8776524	100.000

HPLC traces of 9n

SHIMADTZU HPLC ANALYSIS REPORT

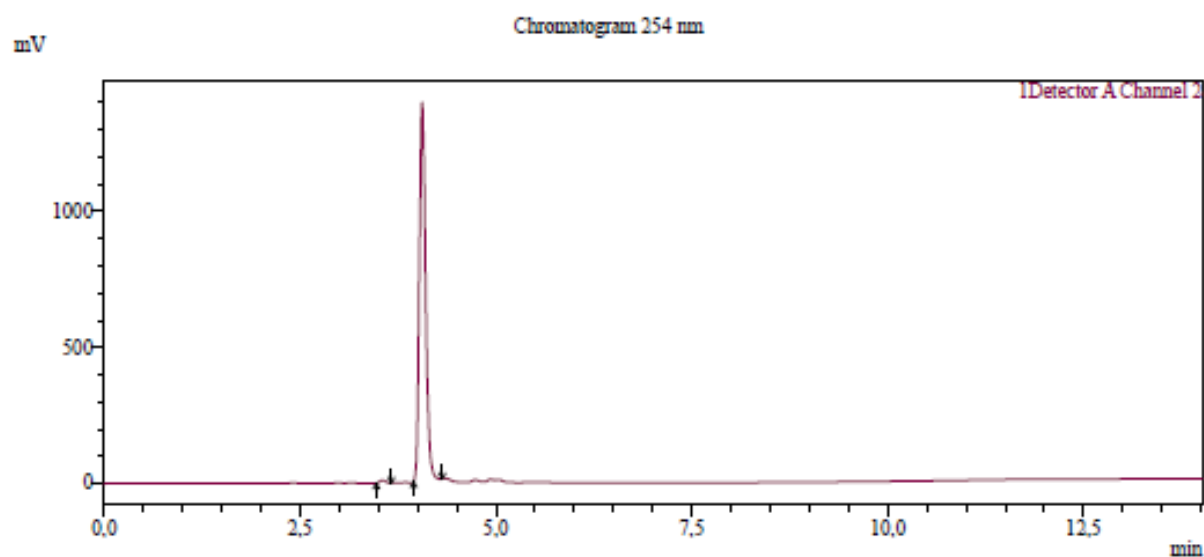
Data File Name : 9n.lcd



Peak Table

Detector A Channel 1 220nm

Peak#	Ret. Time	Height	Area	Area%
1	1,050	39573	191193	3,381
2	3,549	6090	26712	0,472
3	4,054	974828	5437845	96,147
Total		1020492	5655750	100,000



Peak Table

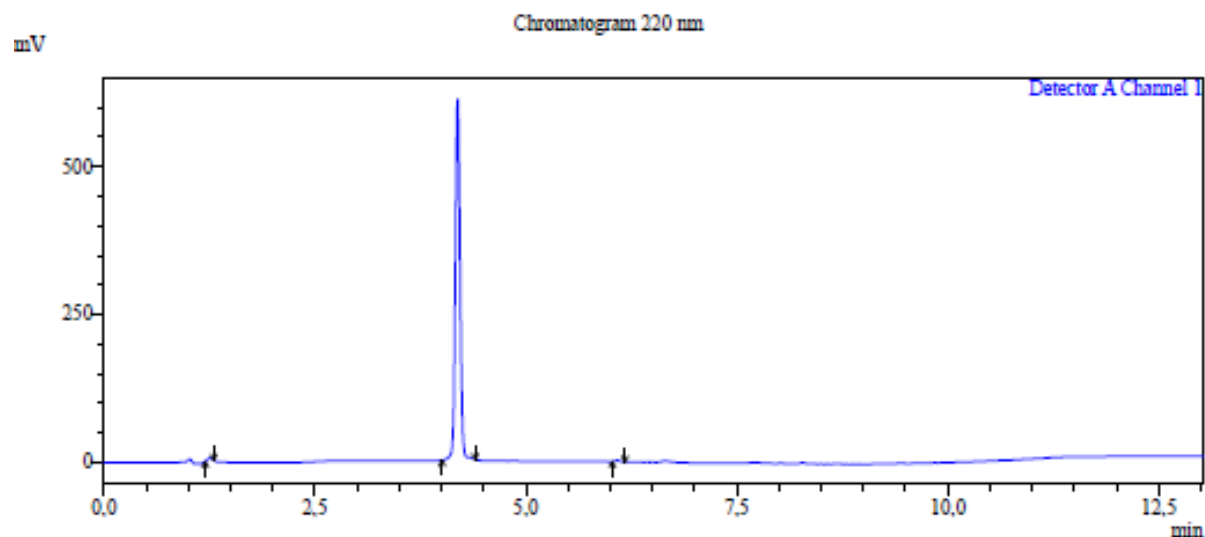
Detector A Channel 2 254nm

Peak#	Ret. Time	Height	Area	Area%
1	3,550	10673	54610	0,702
2	4,056	1391841	7725783	99,298
Total		1402514	7780393	100,000

HPLC traces of 9o

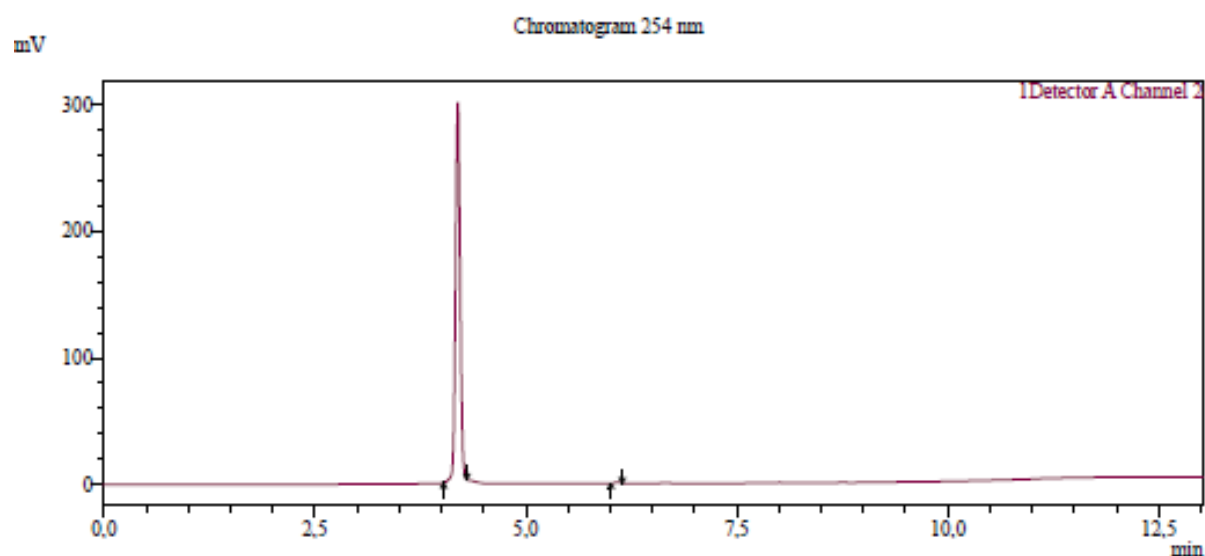
SHIMADTZU HPLC ANALYSIS REPORT

Data File Name : 9o.lcd



Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	1,256	4674	17074	0,708
2	4,186	610468	2386253	98,938
3	6,079	2317	8550	0,354
Total		617459	2411877	100,000



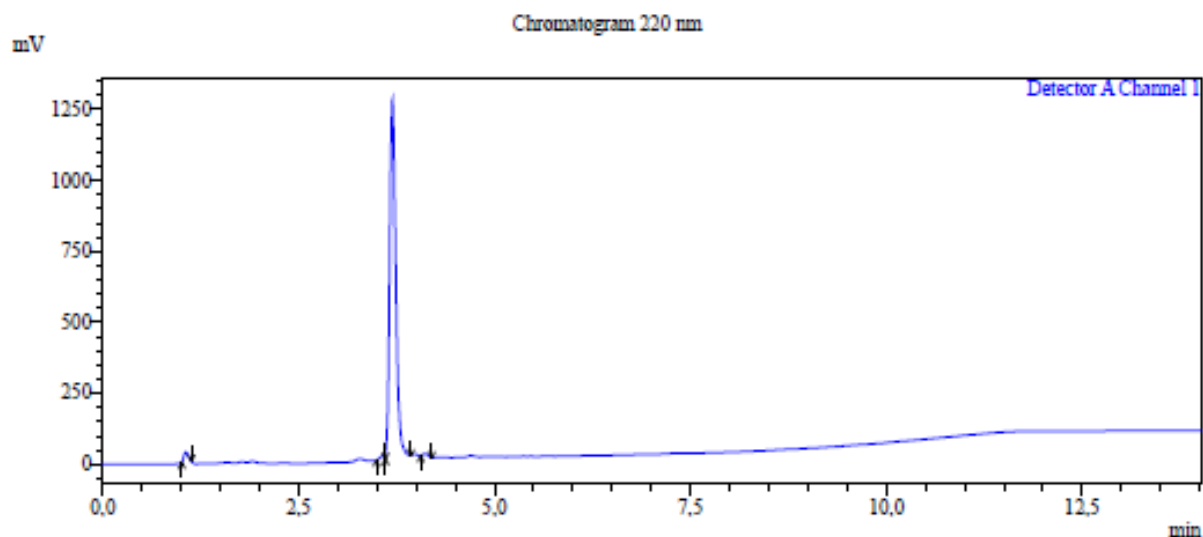
Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	4,190	298864	1142505	99,653
2	6,079	1035	3984	0,347
Total		299899	1146489	100,000

HPLC traces of 9p

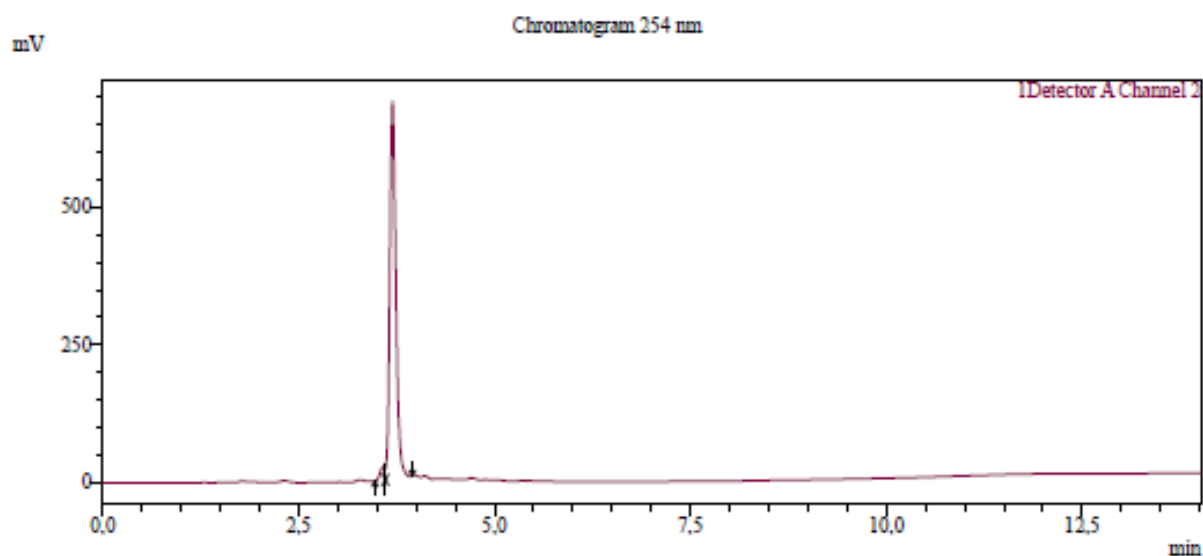
SHIMADTZU HPLC ANALYSIS REPORT

Data File Name : 9p.lcd



Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	1.058	35002	139106	1.961
2	3.600	13243	64279	0.906
3	3.693	1265966	6847955	96.533
4	4.108	10220	42553	0.600
Total		1324430	7093892	100.000



Peak Table

Peak#	Ret. Time	Height	Area	Area%
1	3.569	23055	104858	2.769
2	3.694	684383	3681838	97.231
Total		707437	3786695	100.000