

Supporting Information

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Identification of Selective Inhibitors of the Potassium Channel Kv1.1–1.2₍₃₎ by High-Throughput Virtual Screening and Automated Patch Clamp

Sören J. Wacker,^[a] Wiktor Jurkowski,^[b] Katie J. Simmons,^[c] Colin W. G. Fishwick,^[c]
A. Peter Johnson,^[c] David Madge,^[d] Erik Lindahl,^[b, e] Jean-Francois Rolland,^{*,[d]} and
Bert L. de Groot^{*,[a]}

cmdc_201100600_sm_miscellaneous_information.pdf

Table S1: Original ranks of the 14 hits according to the implementations A and B and the three used consensus scoring methods, rank2max, rank2number and rank2rank.

ID	Implementation A			Implementation B			IC50
	rank2max	rank2number	rank2rank	rank2max	rank2number	rank2rank	
1	94	216	55	n.e.	n.e.	n.e.	0.71
2	121	373	225	n.e.	n.e.	n.e.	0.79
3	86	575	181	n.e.	n.e.	n.e.	1.41
4	170	228	208	n.e.	n.e.	n.e.	1.62
5	72	455	132	n.e.	n.e.	n.e.	2.98
6	91	410	91	n.e.	n.e.	n.e.	4.07
7	80	583	152	8	35	10	1.53
8	2399	2084	1137	68	184	115	0.58
9	418	1086	333	9	70	23	0.93
10	323	471	315	7	23	8	1.66
11	1204	782	352	133	88	73	2.71
12	3563	1805	1401	137	112	53	3.7
13	267	740	444	13	51	30	3.77
14	303	754	354	112	78	100	5.94

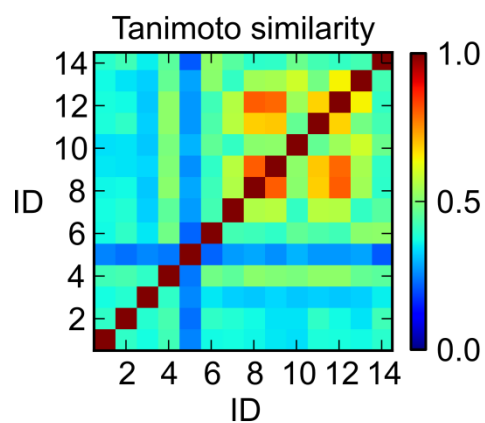


Figure S1. Tanimoto-similarity of the 14 active compounds.

Table S2: BEDROC and AROC values according to scores and subscores of Vina, Glide, eHiTS and FlexX.

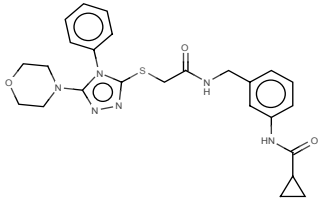
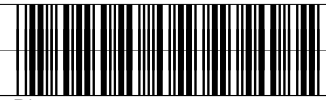
Score/Sub-Score	BEDROC	AROC
Autodock-Vina	0.5191	0.706
FlexX_Ambig-Score	0.2356	0.5589
FlexX_AnzMatch	0.1066	0.4086
FlexX_AvgVolume	0.1325	0.5001
FlexX_Clash-Score	0.0422	0.392
FlexX_Lipo-Score	0.5898	0.7029
FlexX_Match-Score	0.0232	0.3718
FlexX_MaxVolume	0.0904	0.4485
FlexX_Rot-Score	0.1874	0.4307
FlexX_Total-Score	0.1094	0.4387
ChemScore_Clash-Score	0.1049	0.4641
ChemScore_FragNo	0.239	0.3545
ChemScore_Lipo-Score	0.5485	0.7312
ChemScore_Match-Score	0.0106	0.327
ChemScore_MaxVolume	0.1068	0.4917
ChemScore_Rot-Score	0.2193	0.4657
ChemScore_Total-Score	0.3361	0.6317
Glide_XP-Electro	0.0256	0.3793
Glide_XP-HBond	0.0215	0.3804
Glide_XP-LipophilicEvdW	0.6058	0.7254
Glide_XP-Penalties	0.1741	0.4052
Glide_XP-PhobicPenal	0.2063	0.5101
Glide_XP-RotPenal	0.0696	0.5022
Glide_XP-Sitemap	0.3578	0.6
Glide_ecoul	0.0259	0.3851
Glide_einternal	0.1101	0.392
Glide_emodel	0.5611	0.7073
Glide_energy	0.5393	0.6945
Glide_evdw	0.67	0.7406
Glide_gscore	0.3146	0.5475
eHiTS_Energy	0.3355	0.6136
eHiTS_Score	0.1648	0.5041
eHiTS_Term-Coulomb	0.1632	0.5416
eHiTS_Term-H_bond	0.0894	0.4321
eHiTS_Term-Lcover	0.1312	0.4798
eHiTS_Term-Lipophil	0.124	0.4542
eHiTS_Term-LlogD	0.0861	0.3868
eHiTS_Term-Rcharge	0.0529	0.3715
eHiTS_Term-Rcover	0.2297	0.4745
eHiTS_Term-RlogD	0.2451	0.5364
eHiTS_Term-Rshape	0.298	0.5632
eHiTS_Term-depth	0.4401	0.6932
eHiTS_Term-entropy	0.0513	0.3396
eHiTS_Term-family	0.4456	0.7025
eHiTS_Term-other	0.2119	0.5413
eHiTS_Term-pi_stack	0.2414	0.533
eHiTS_Term-solvent	0.2521	0.6055
eHiTS_Term-steric	0.3027	0.5495
eHiTS_Term-strain	0.5824	0.7351

Table S3: Inhibitors of Kv1.1 and Kv1.2. Sources: Drug Bank, Tocris Bioscience. NA stands for Data Not Available and "-" no indication of particular target					
Name/INN	CAS	Pubmed ID	Kv1.1 IC50 (μM)	Kv1.2 IC50 (μM)	Other targets/ IC50 (μM)
Nifedipine	21829-25-4	7517498	NA	NA	NA
Amitriptyline	50-48-6	17456683	22	-	Kv7.2/7.3 10
4-Aminopyridine Fampridine	504-24-5	19413590	170	230	Kv1.4, Kv4.2
Nerispidine	119229-65-1	19413590	3.6	3.7	NavX 11.9
AM 92016 hydrochloride	178894-81-0	15967421	NA	NA	NA
KN-93	139298-40-1	16368898	-	1	Kv1.4, Kv1.5, Kv2.1, Kv3.2, Kv4.2 hERG

Spectral Data

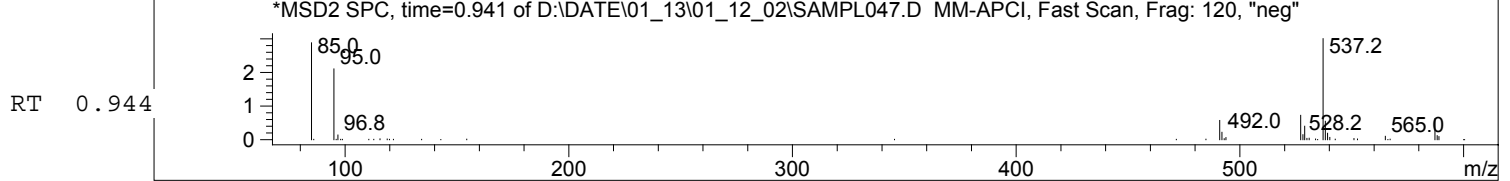
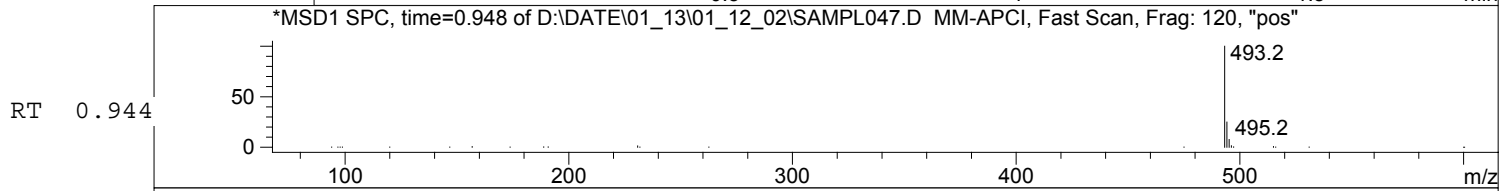
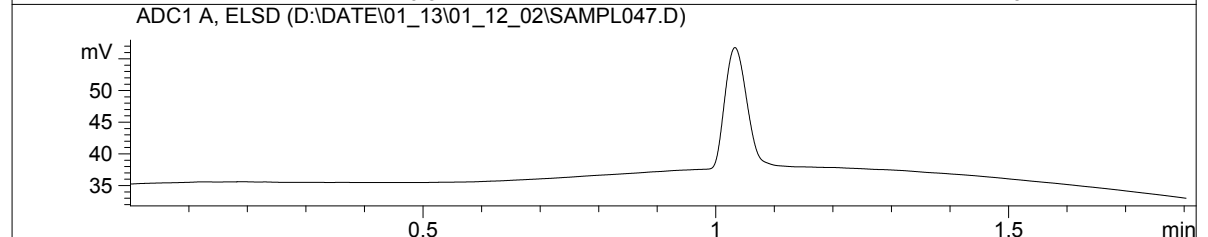
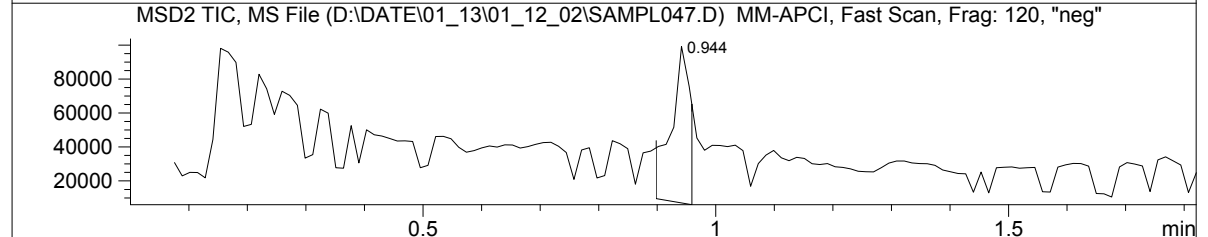
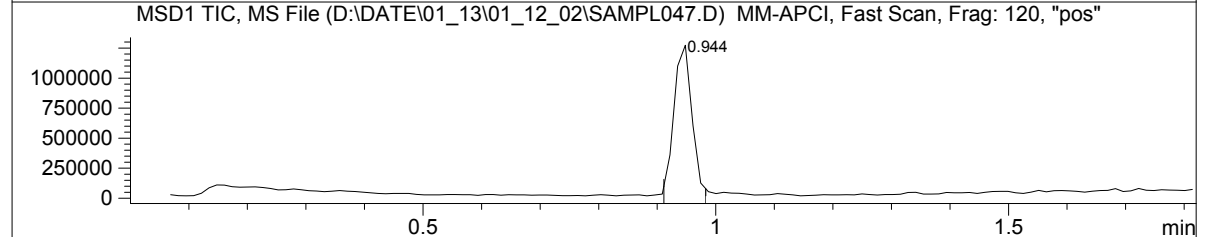
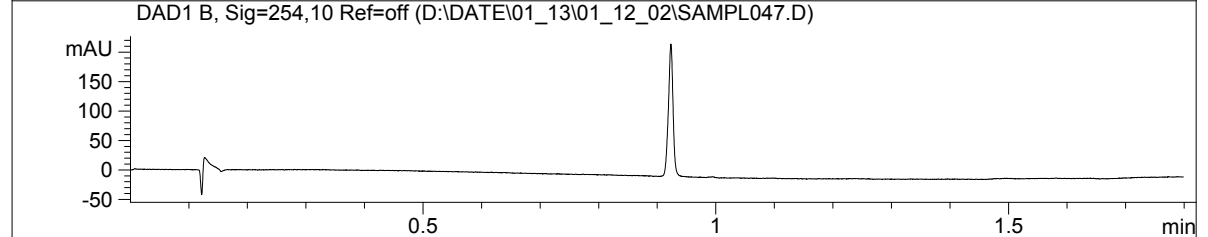
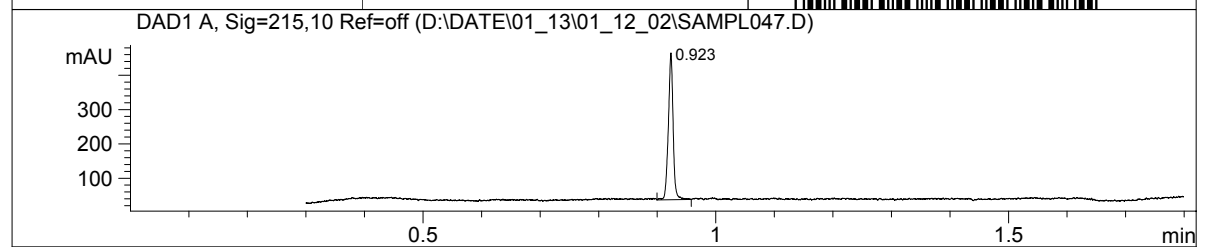
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4532116



Mol Wt 492.593
Exact Mass 492.22

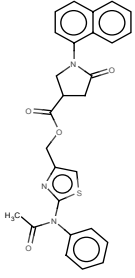
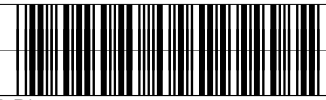
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Compound ID: 1

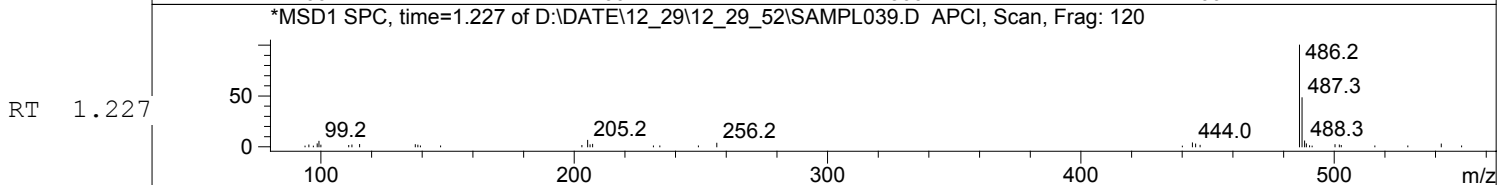
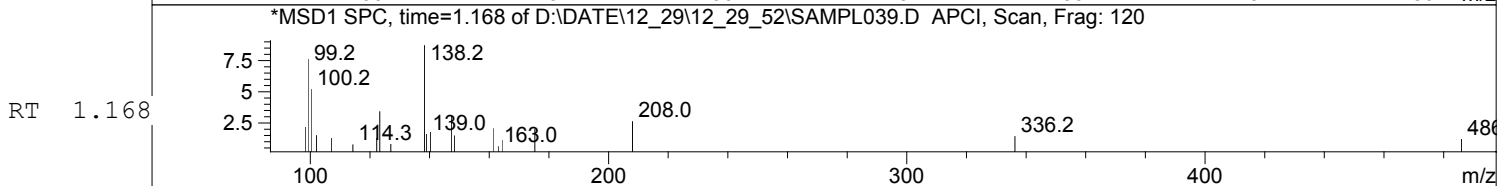
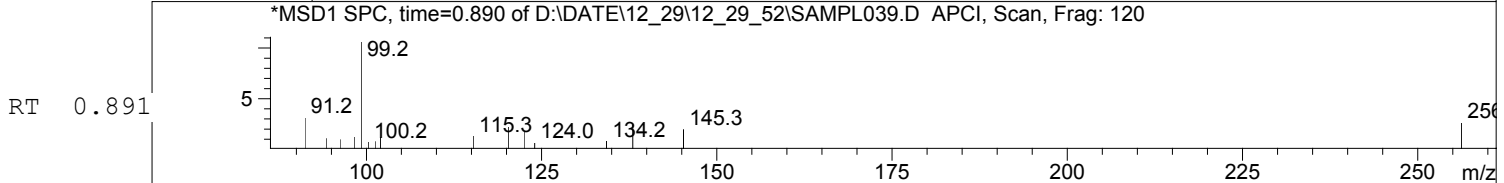
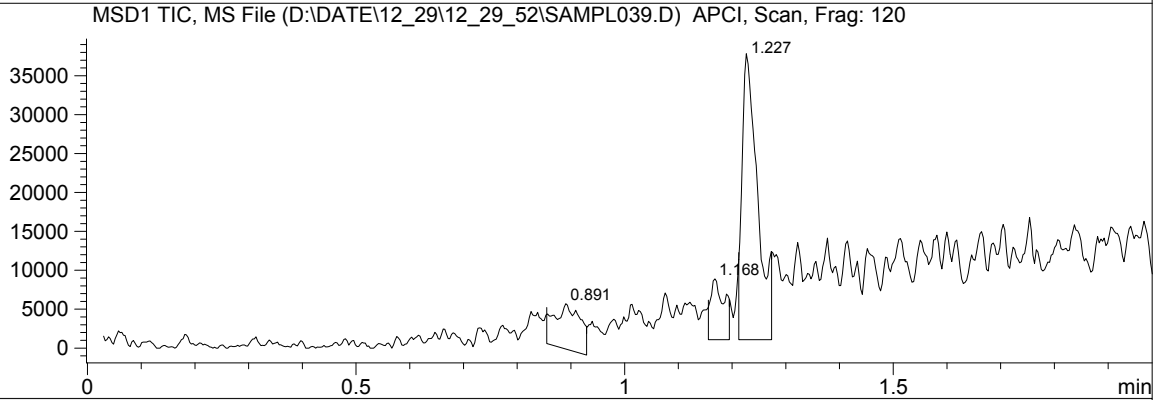
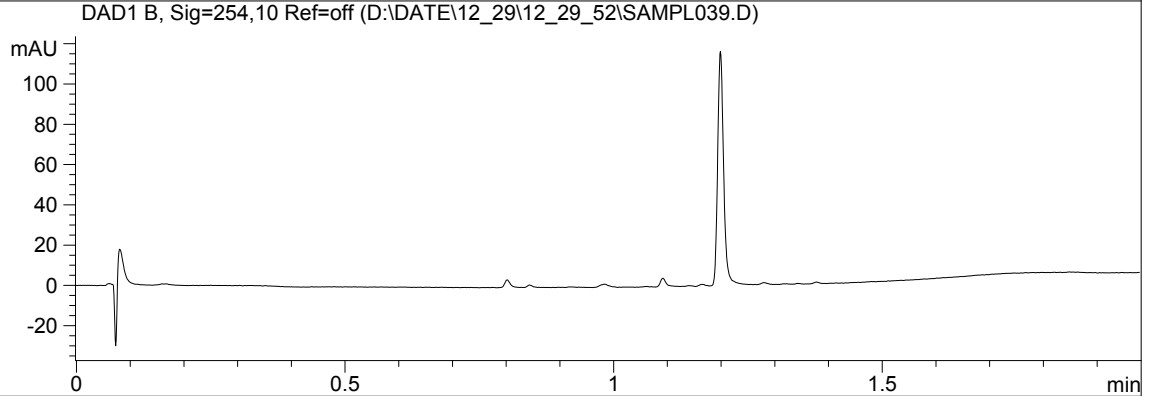
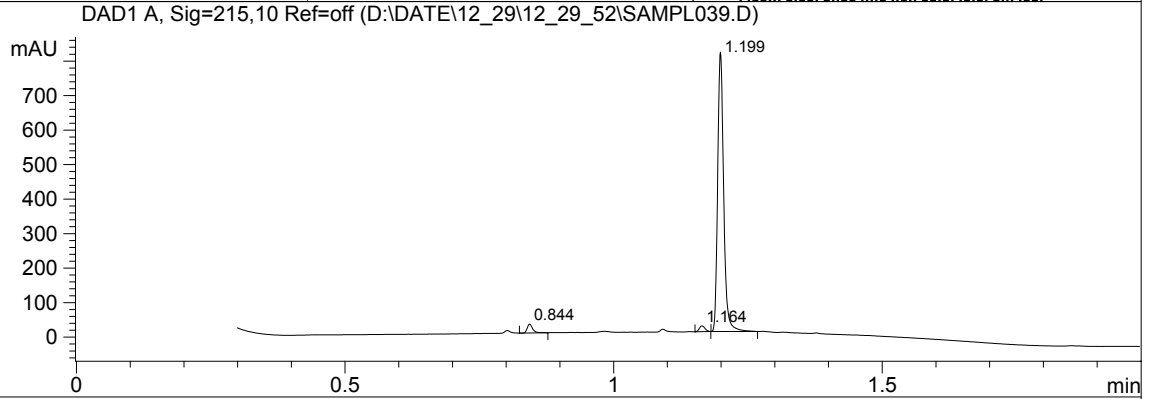
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4532085



Mol Wt 485.554
Exact Mass 485.16

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2	1.164	1.88
3	1.199	95.39

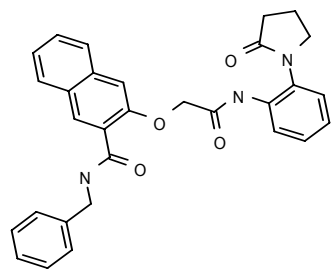
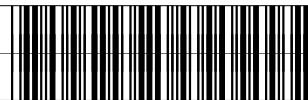


Compound ID: 2

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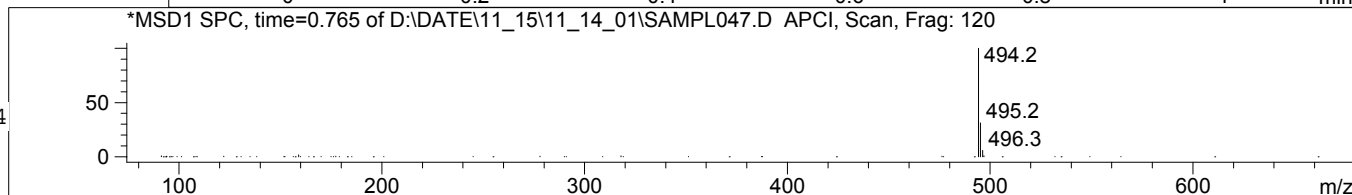
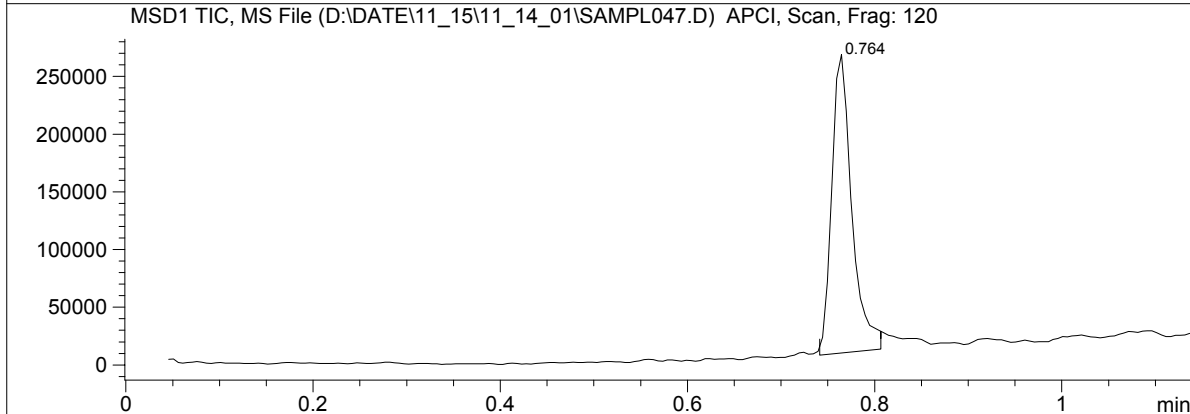
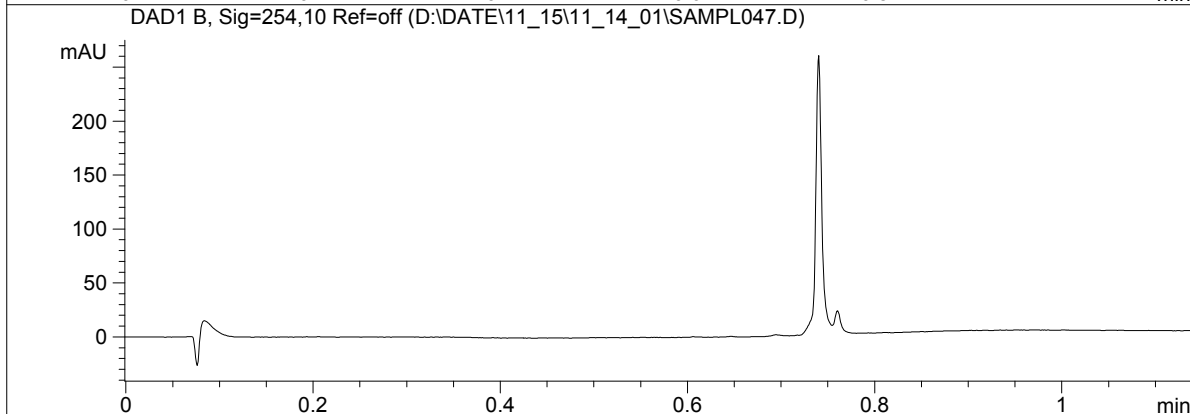
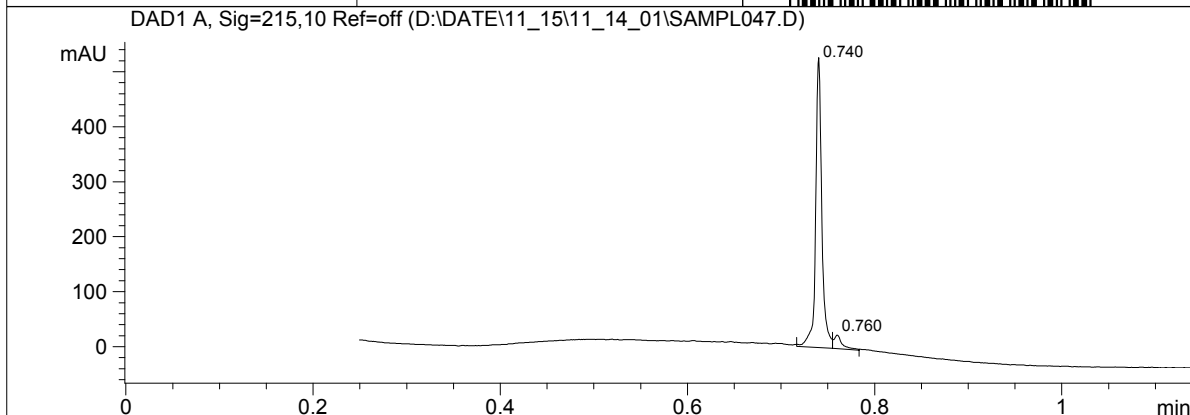
2013129

OK



mw = 493.57

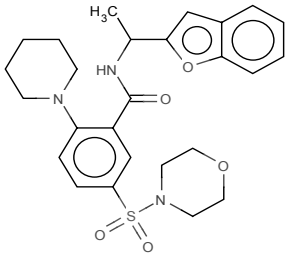
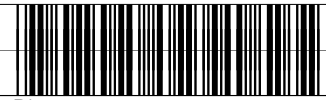
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2	0.760	5.91



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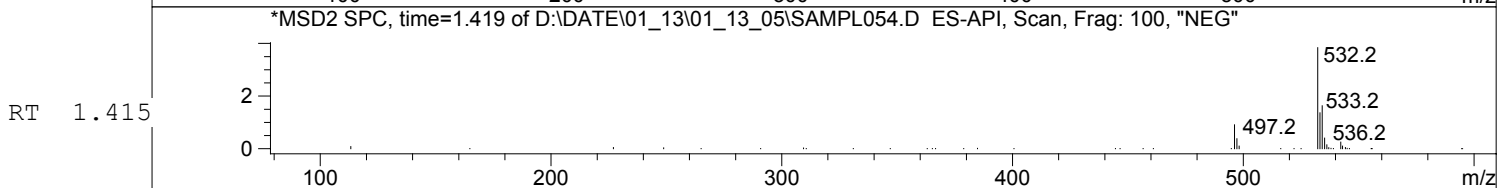
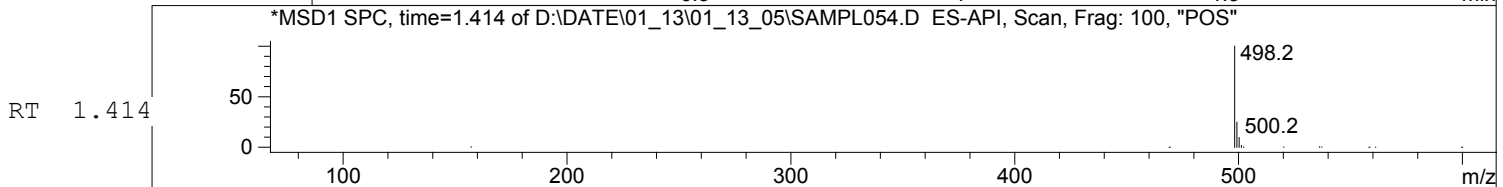
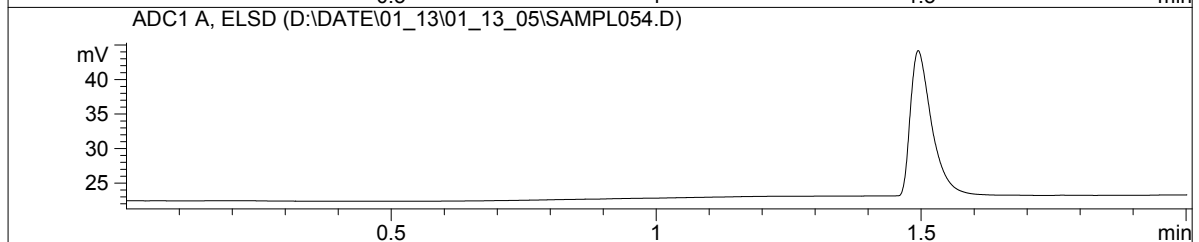
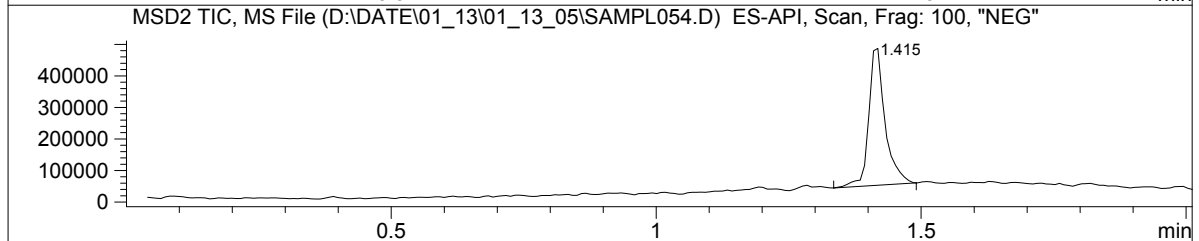
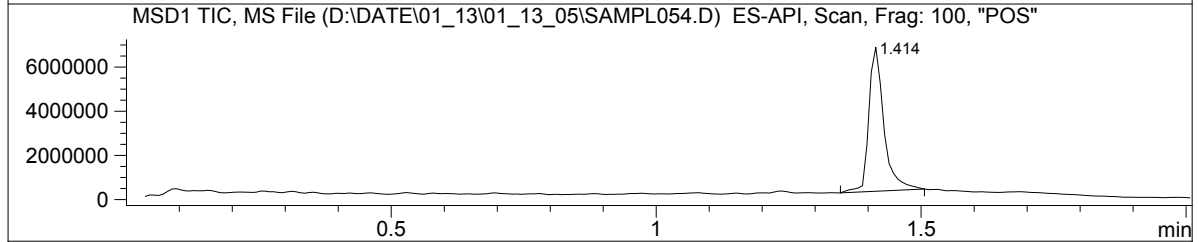
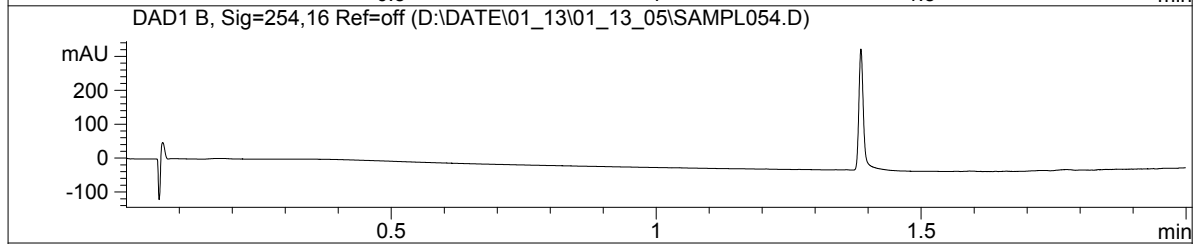
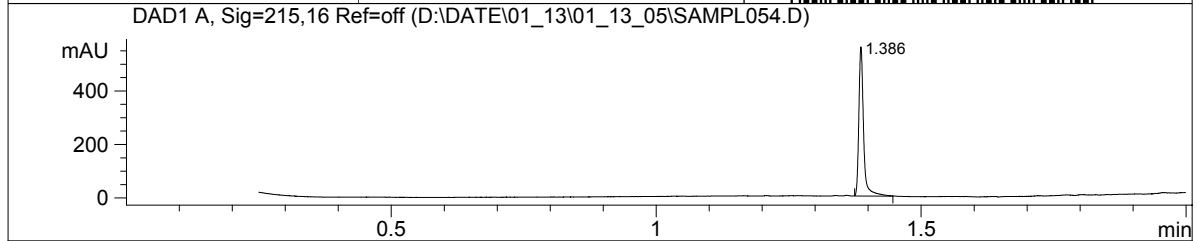
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Ret_Time: 1.386 min

4532160



Mol Wt 497.606
Exact Mass 497.23

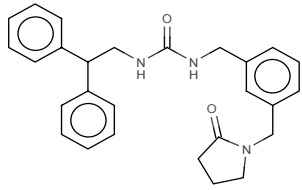
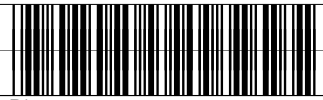
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Compound ID: 4

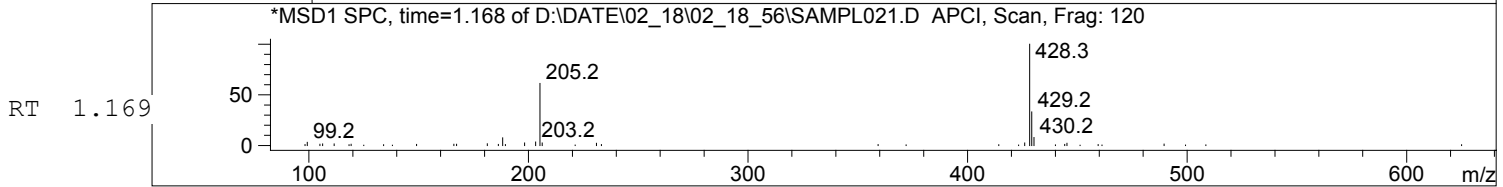
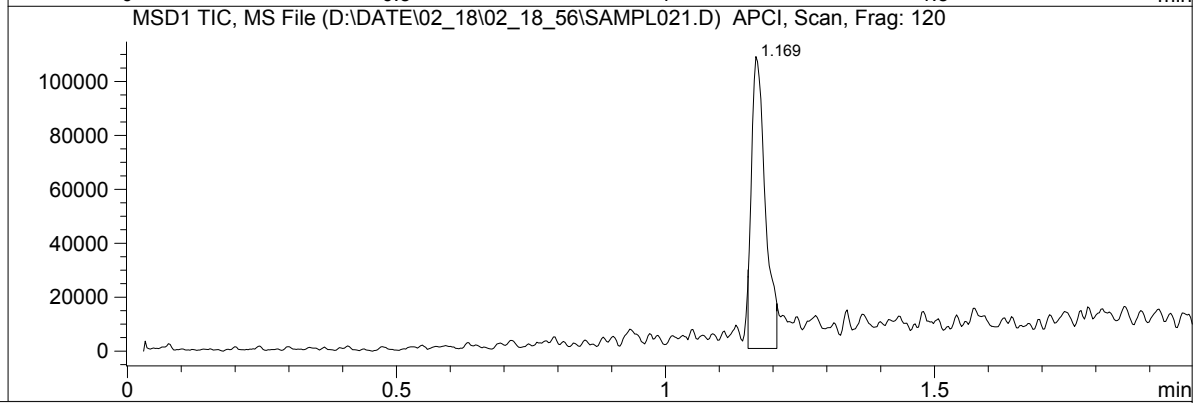
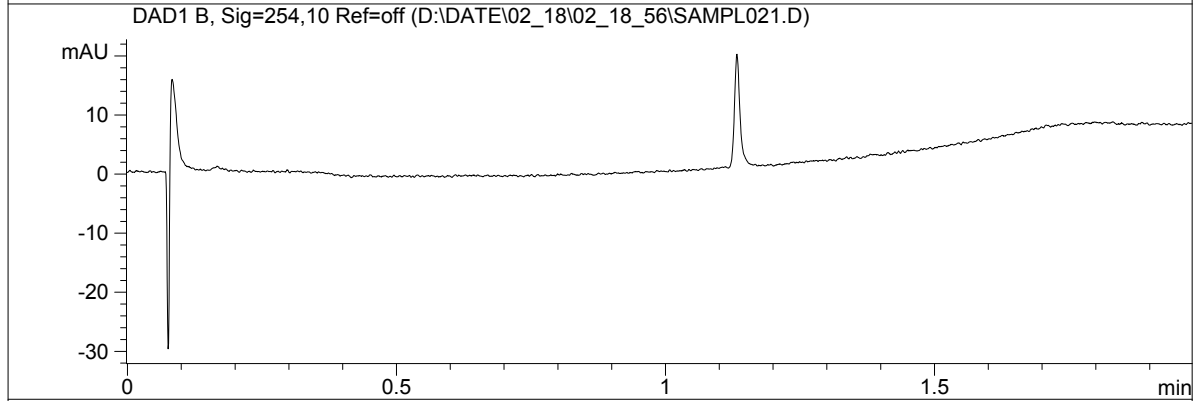
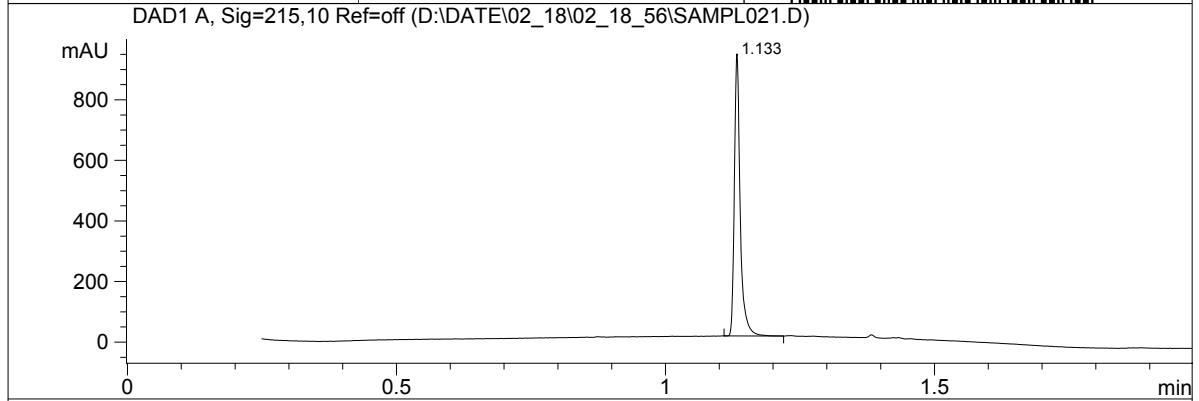
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4531970



Mol Wt 427.538
Exact Mass 427.27

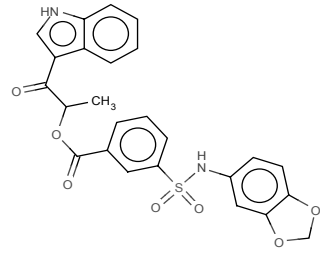
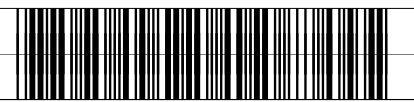
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Compound ID: 5

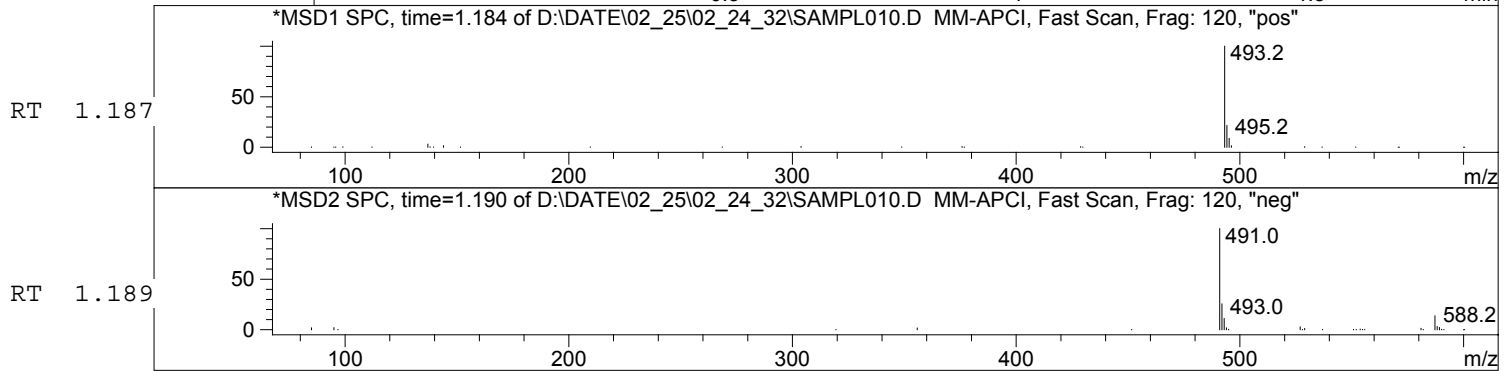
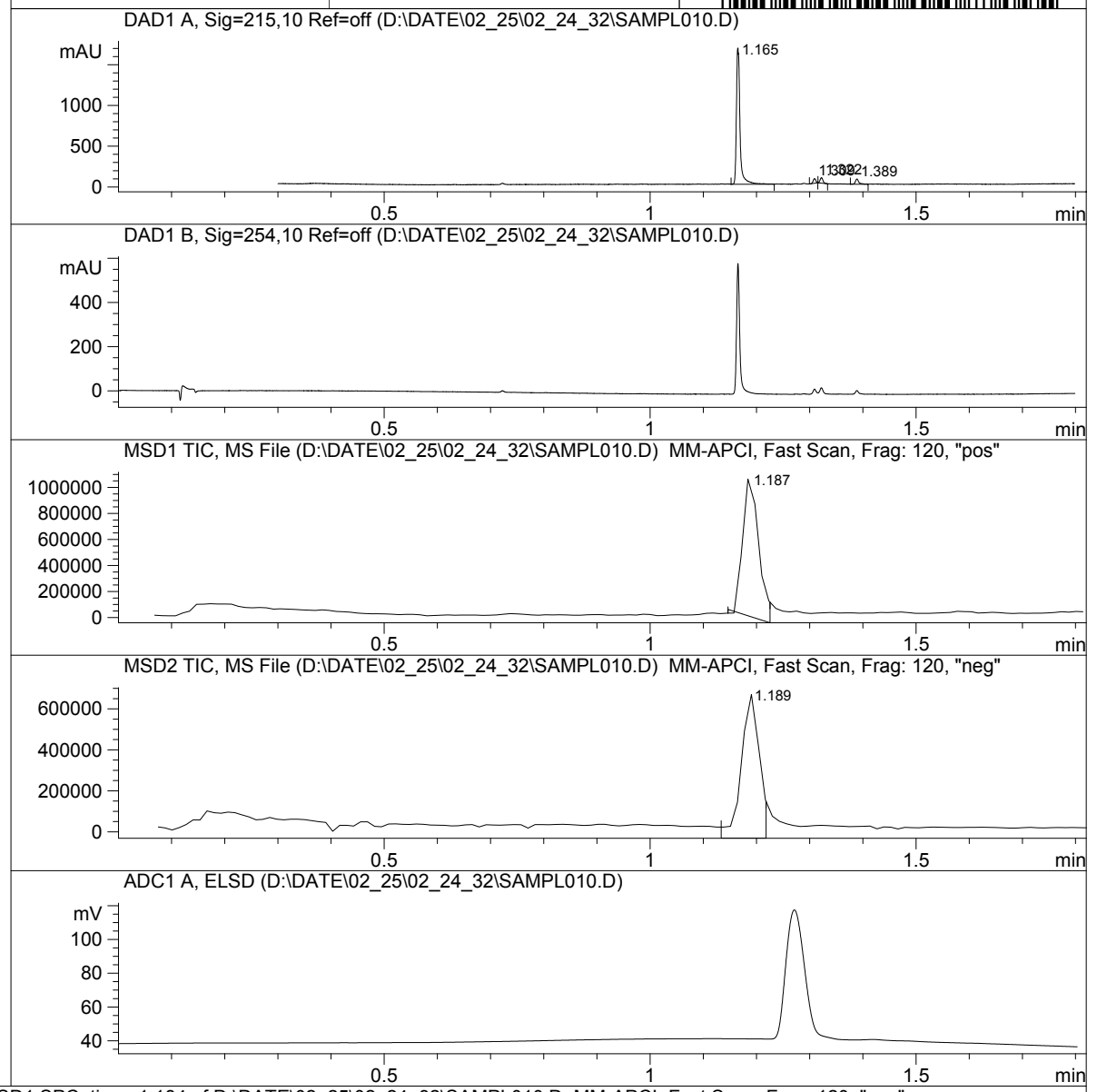
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3390363\$2



Mol Wt 492.5
Exact Mass 492.1

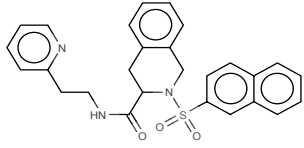
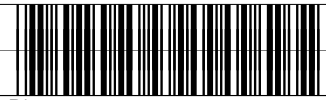
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3	1.322	2.91
4	1.389	3.48



Compound ID: 6

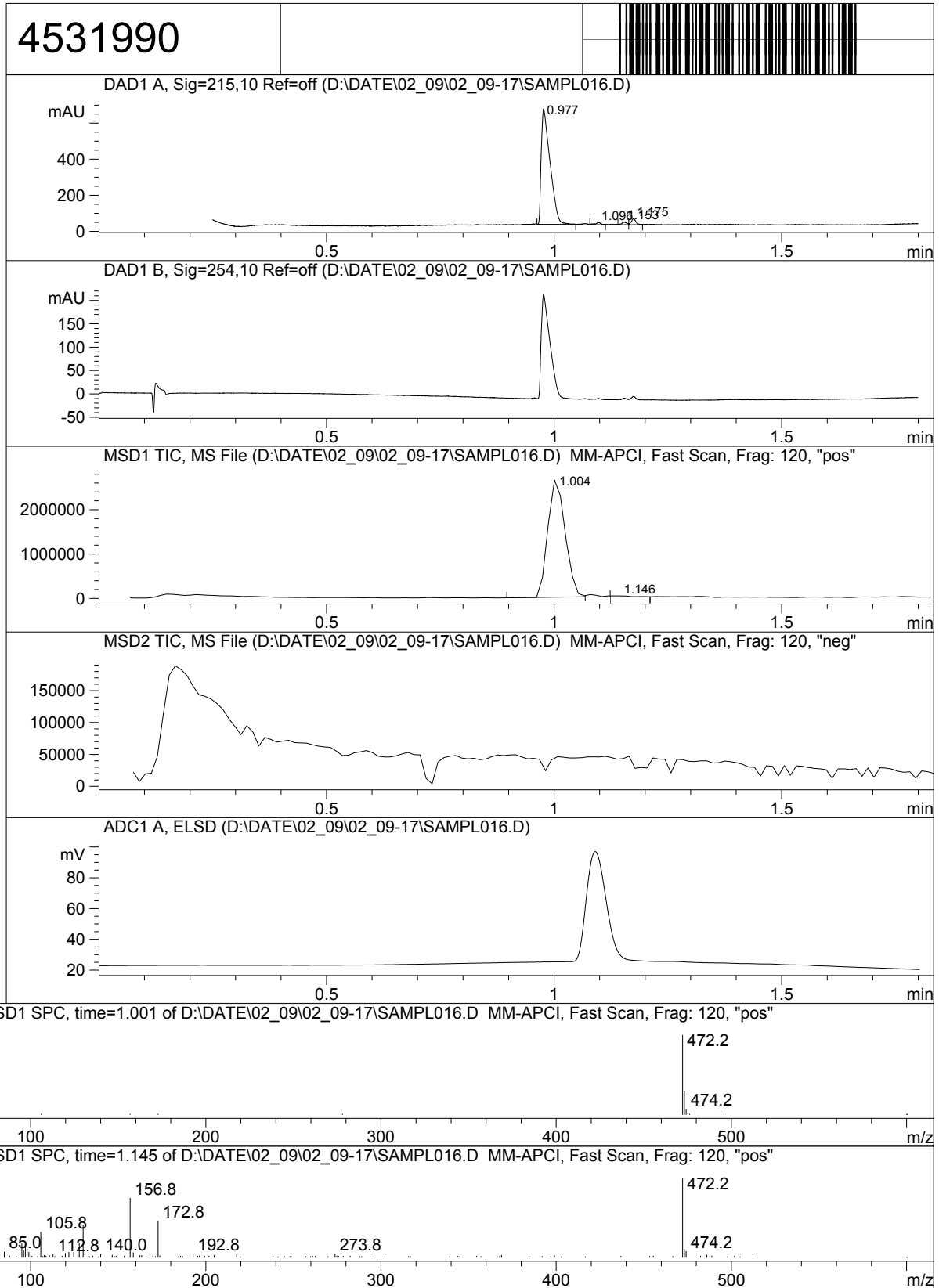
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4531990



Mol Wt 471.571
Exact Mass 471.19

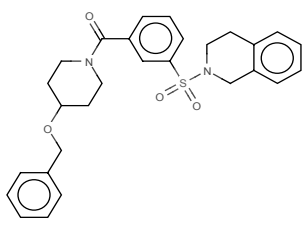
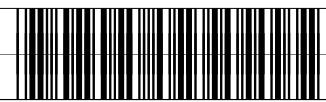
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4	1.175	2.56



Compound ID: 7

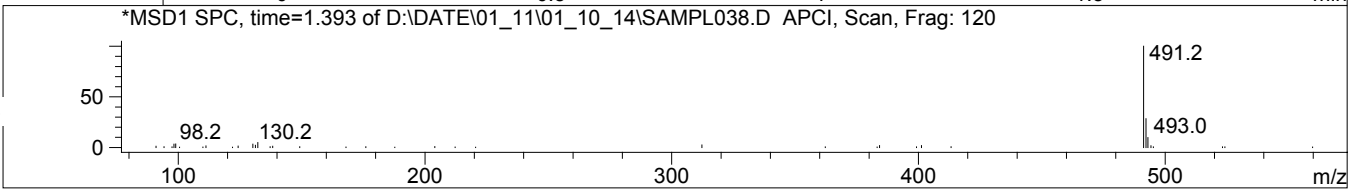
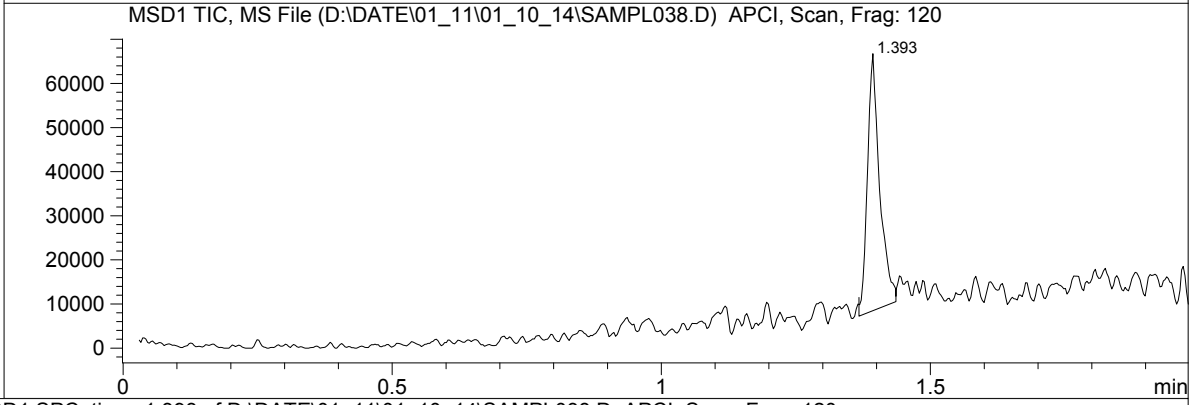
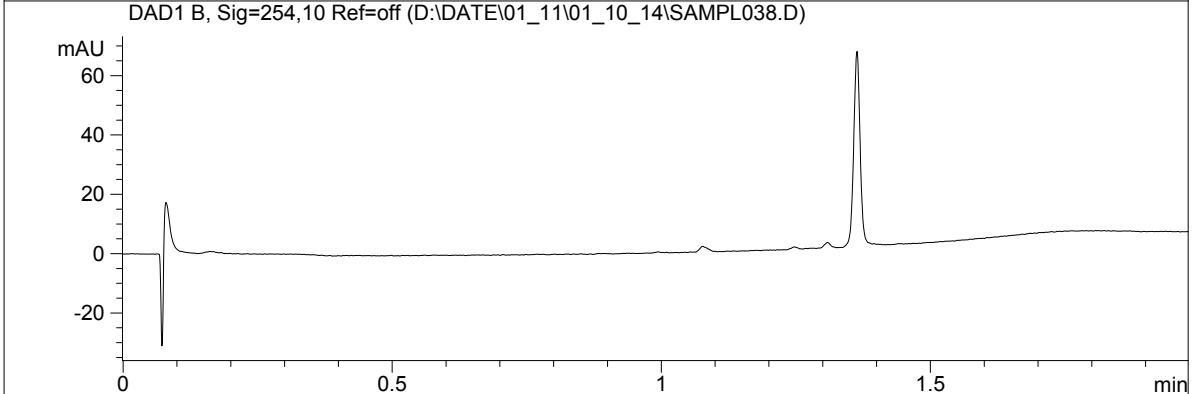
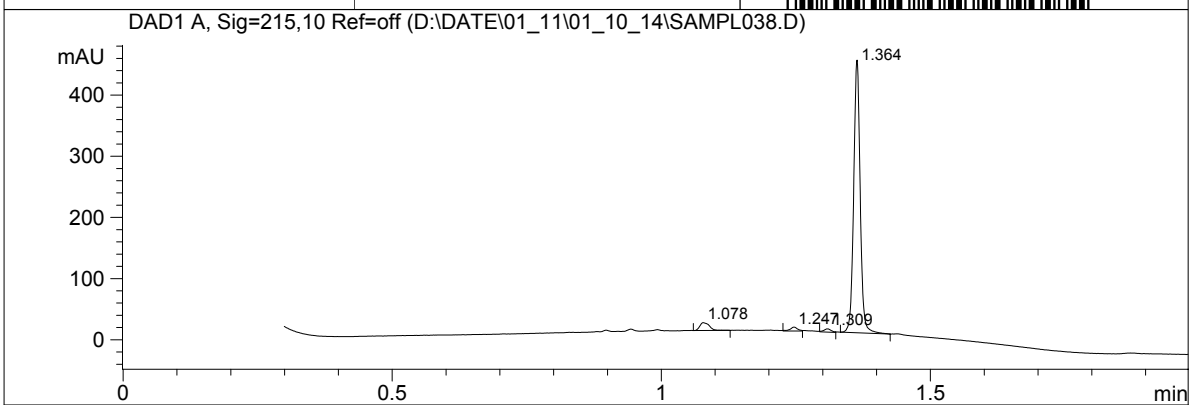
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4532129



Mol Wt 490.614
Exact Mass 490.23

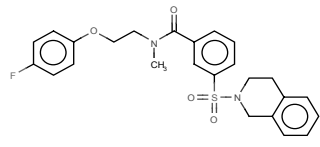
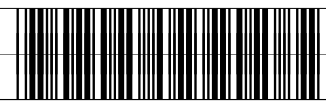
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Compound ID: 8

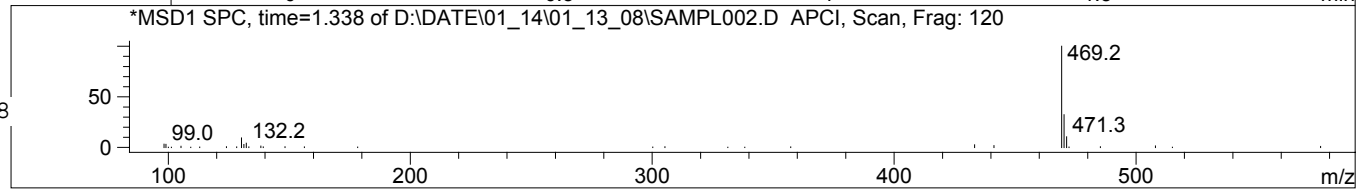
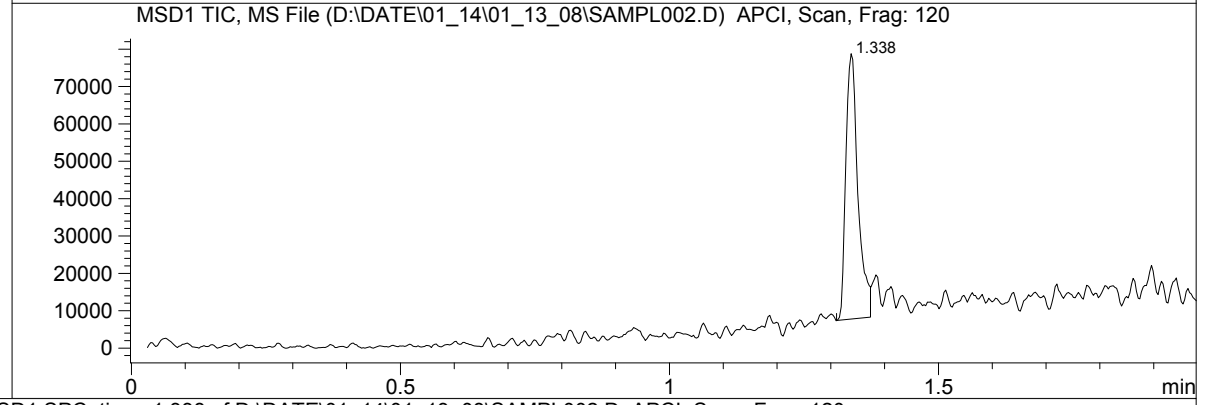
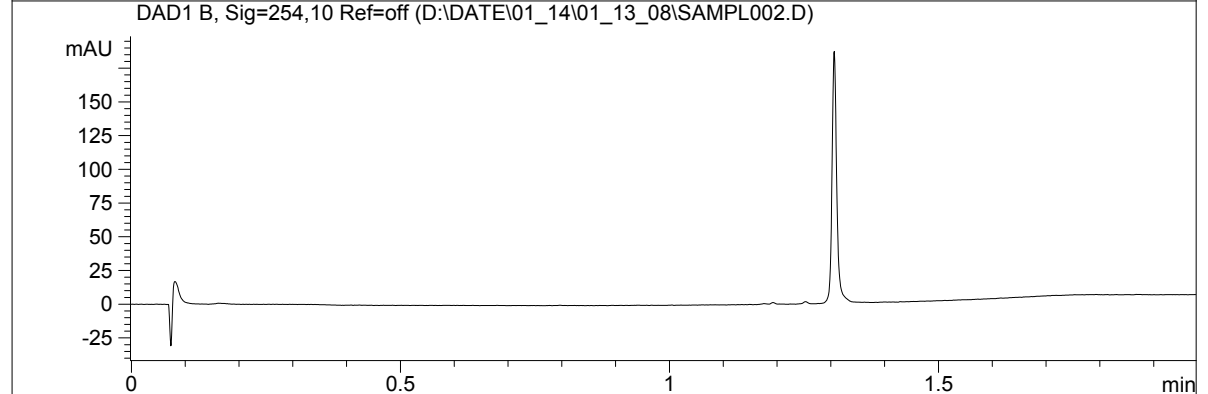
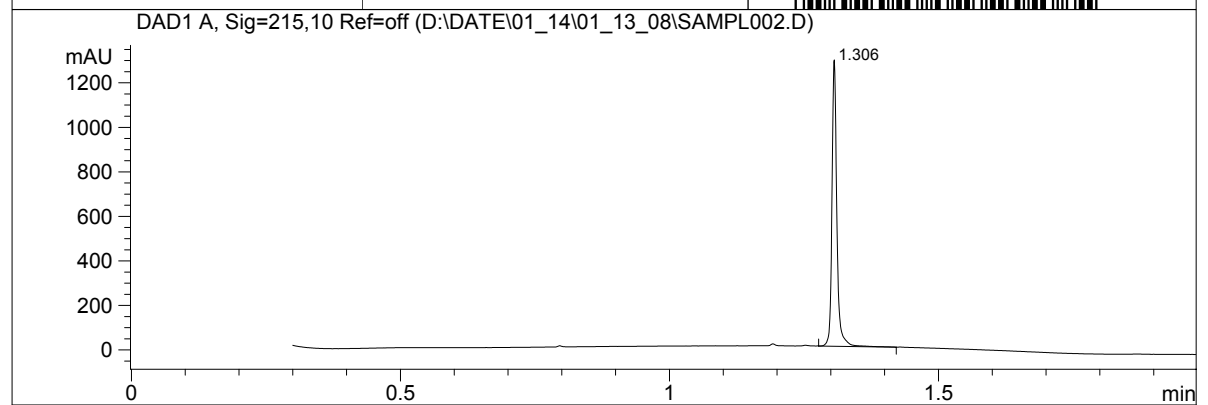
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4532153



Mol Wt 468.54
Exact Mass 468.18

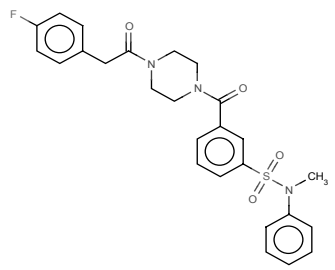
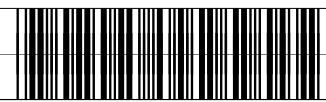
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Compound ID: 9

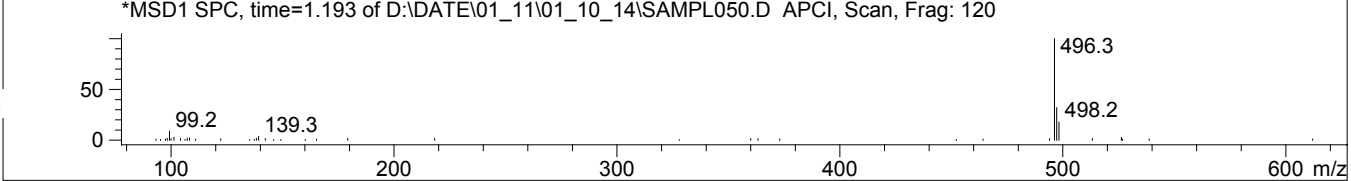
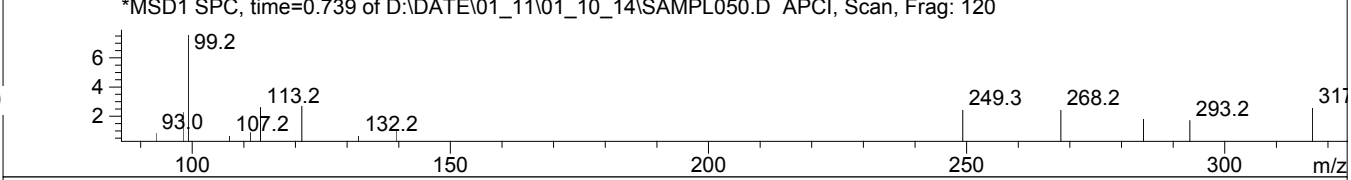
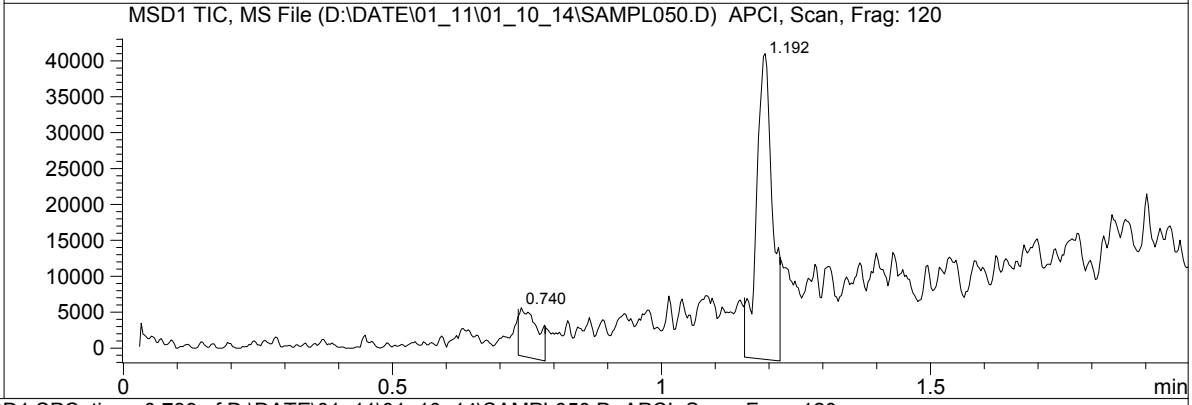
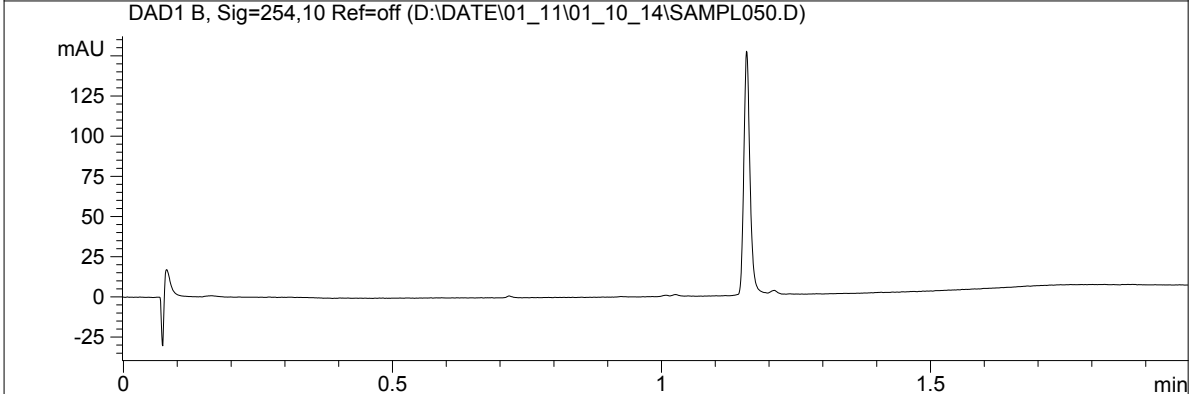
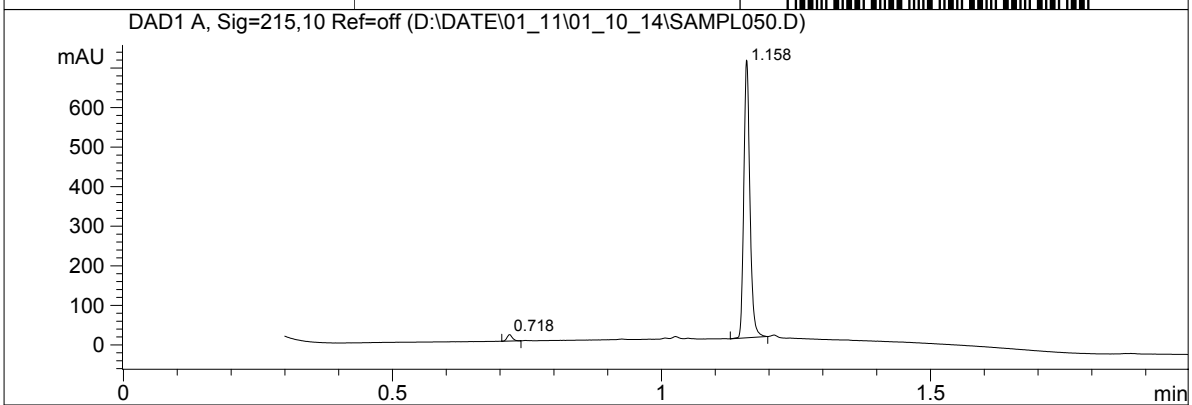
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4532004

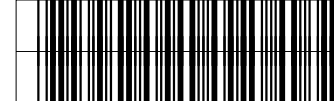


Mol Wt 495.566
Exact Mass 495.19

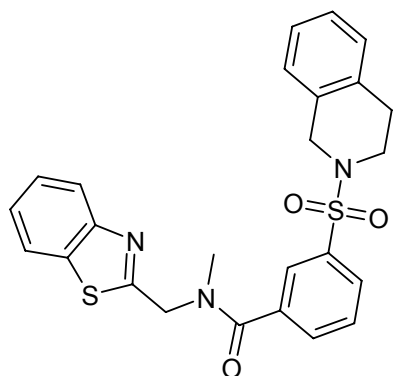
#	Time	Area%
1	0.718	2.03
2	1.158	97.97



Compound ID: 10

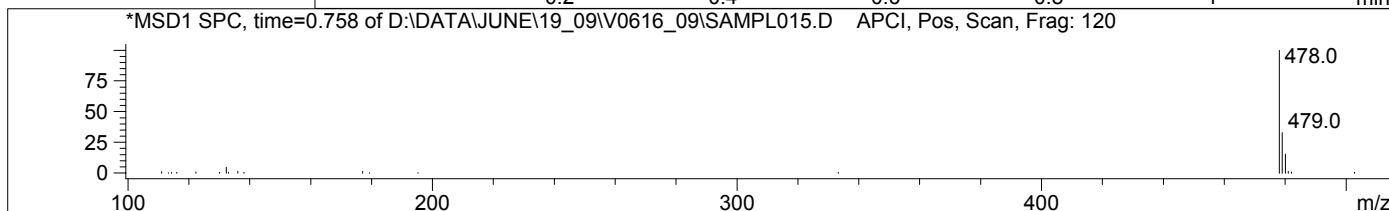
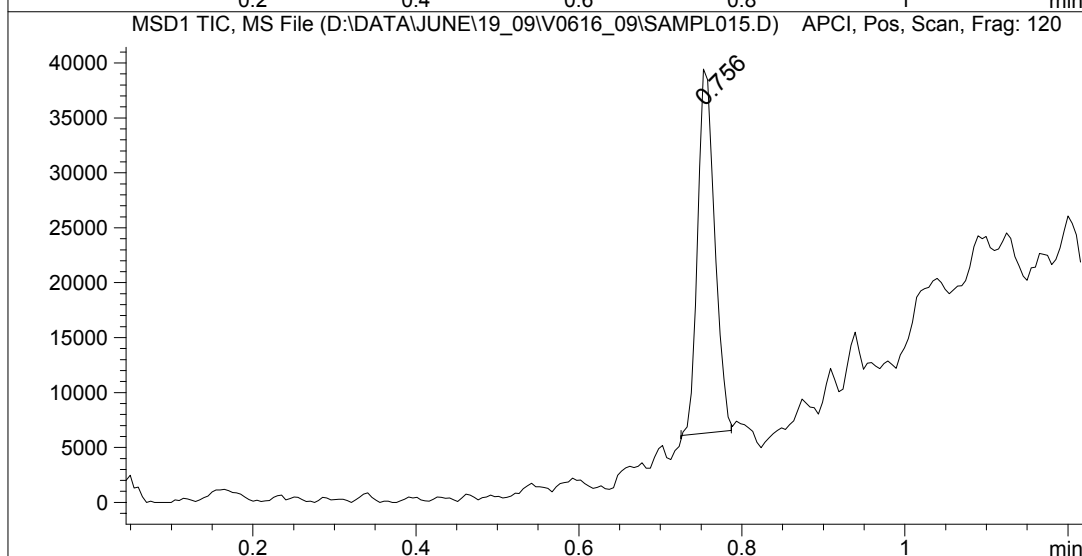
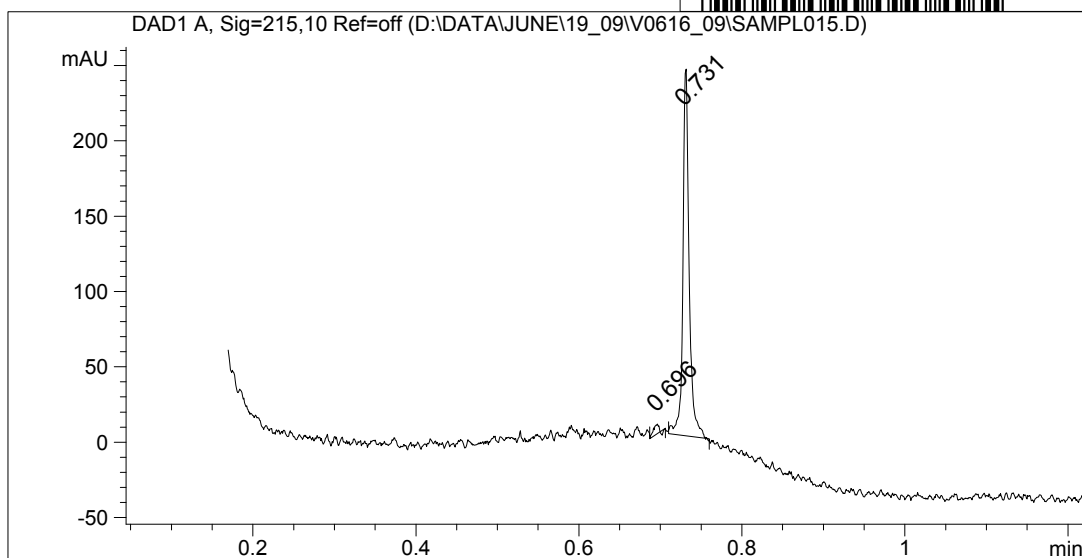


MaxPeak: 97.65%
Ret_Time: 0.731 min



mw = 477,61

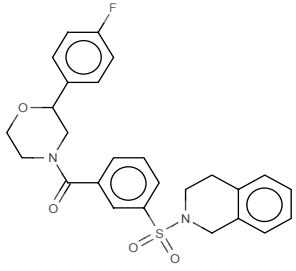
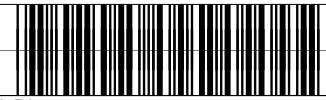
#	Time	Area%
1	0.696	2.35
2	0.731	97.65



Compound ID: 11

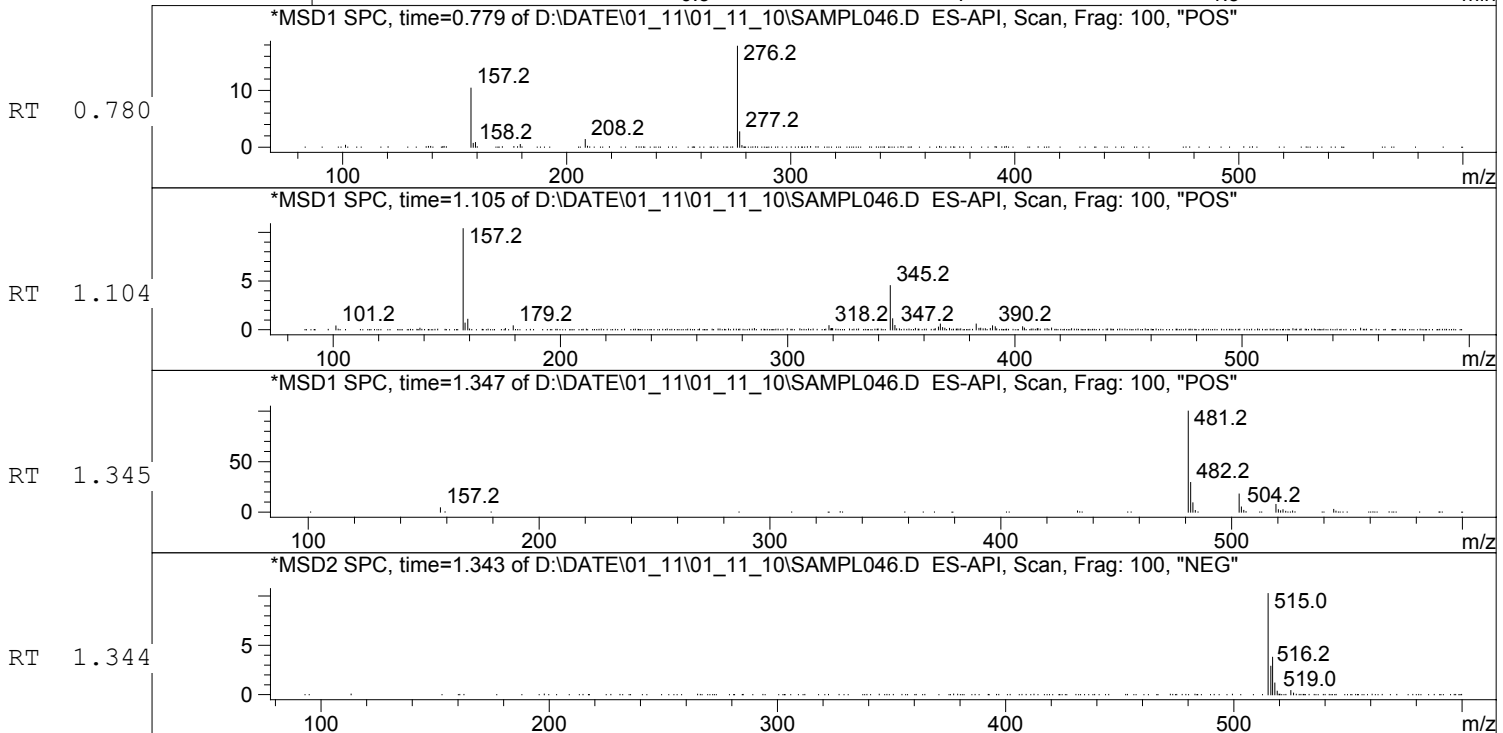
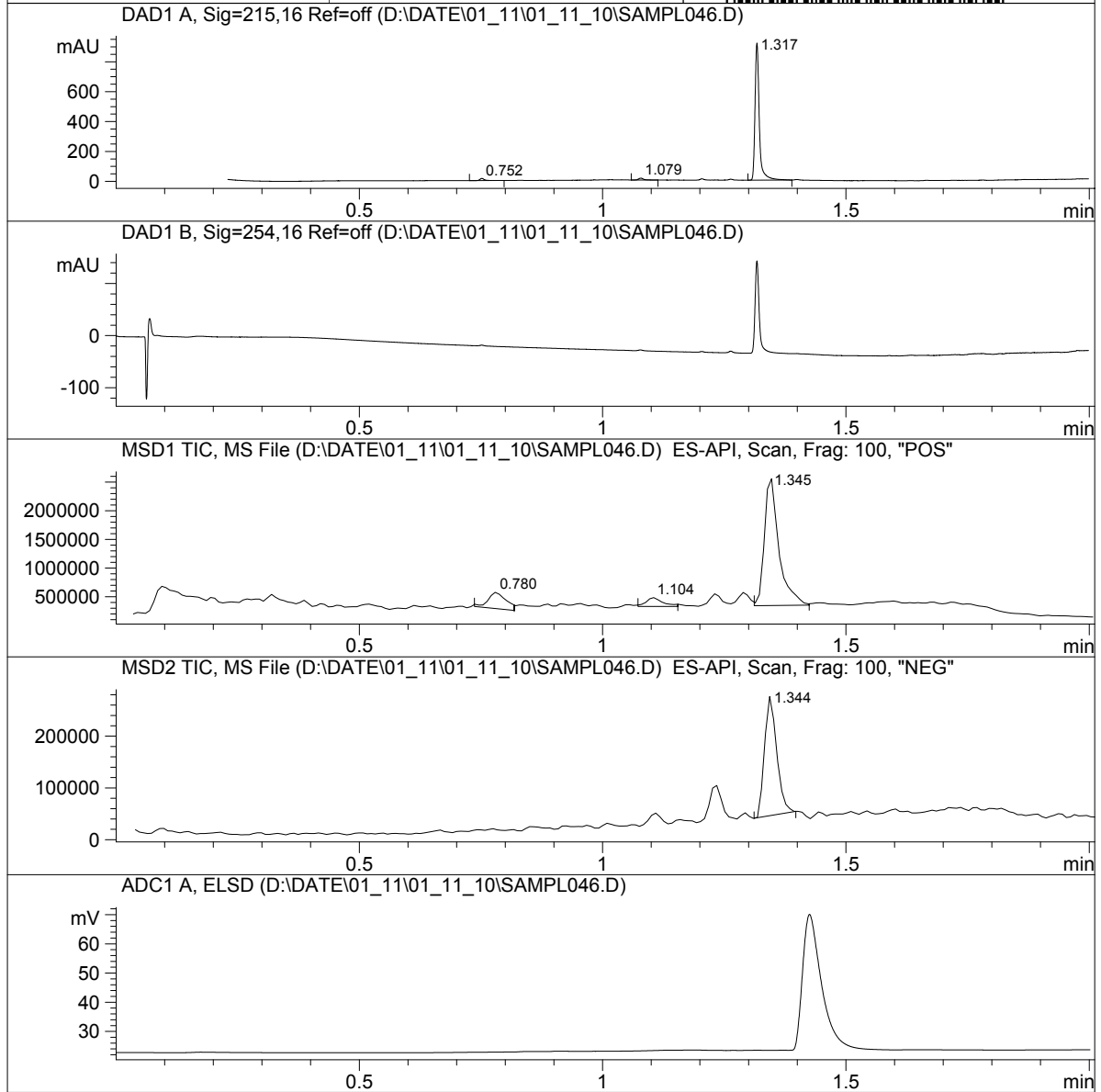
MaxPeak: 96.68%
Ret_Time: 1.317 min

4532022



Mol Wt 480.551
Exact Mass 480.18

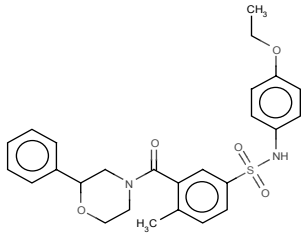
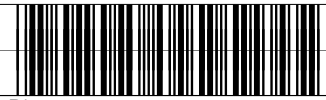
#	Time	Area%
1	0.752	1.71
2	1.079	1.61
3	1.317	96.68



Compound ID: 12

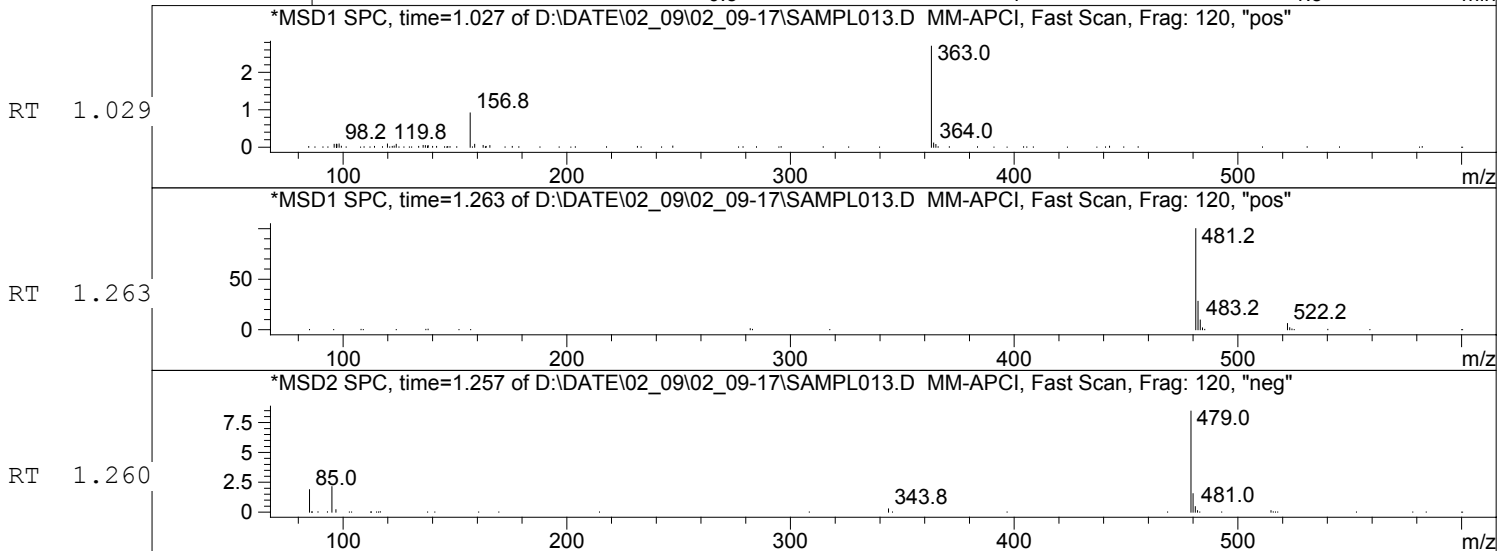
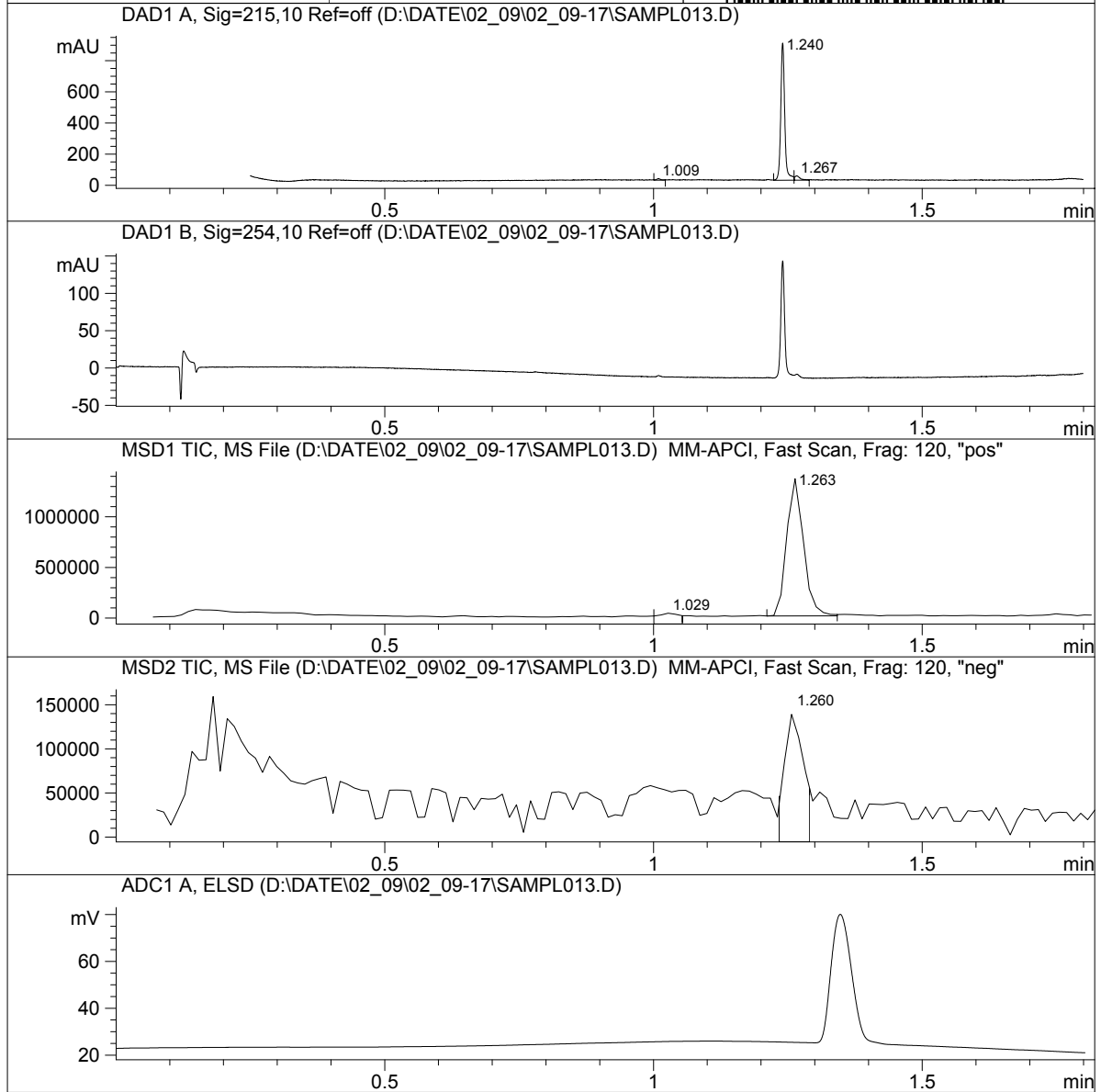
MaxPeak: 94.66%
Ret_Time: 1.240 min

4532001



Mol Wt 480.576
Exact Mass 480.2

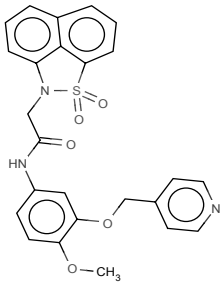
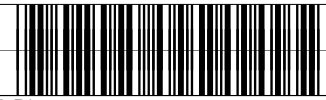
#	Time	Area%
1	1.009	1.14
2	1.240	94.66
3	1.267	4.19



Compound ID: 13

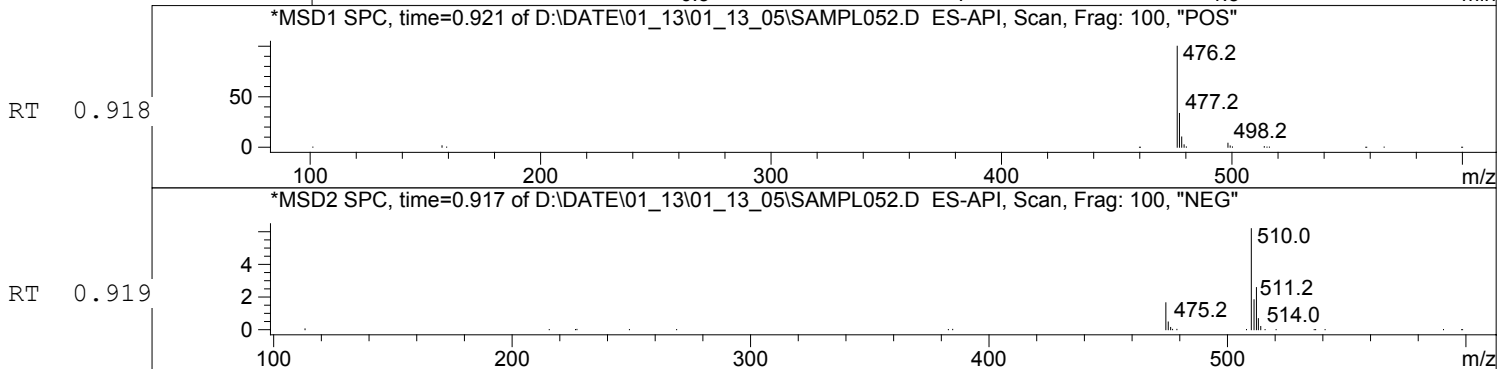
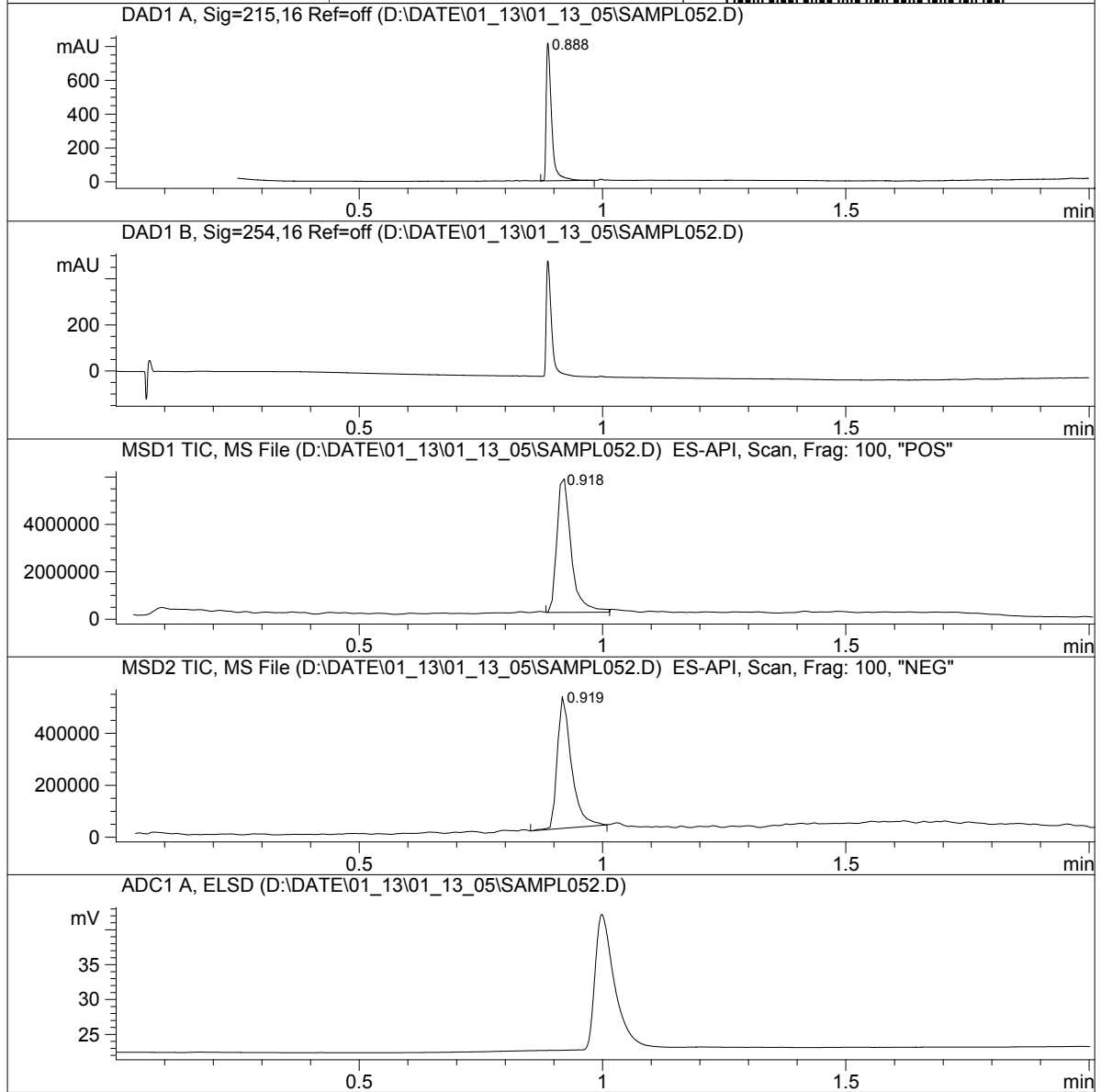
MaxPeak: 100.00%
Ret_Time: 0.888 min

4532099



Mol Wt 475.516
Exact Mass 475.13

#	Time	Area%
1	0.888	100.00



Compound ID: 14