

SUPPORTING INFORMATION

From a MMP2/CK2 multitarget approach to the identification of potent and selective MMP13 inhibitors

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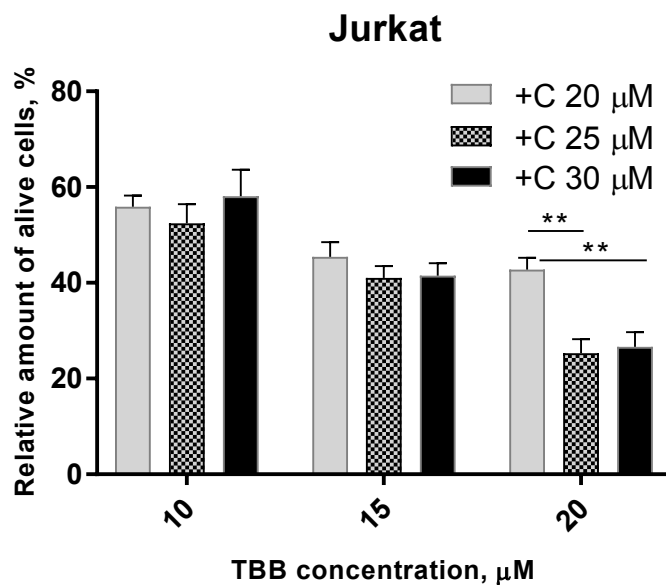
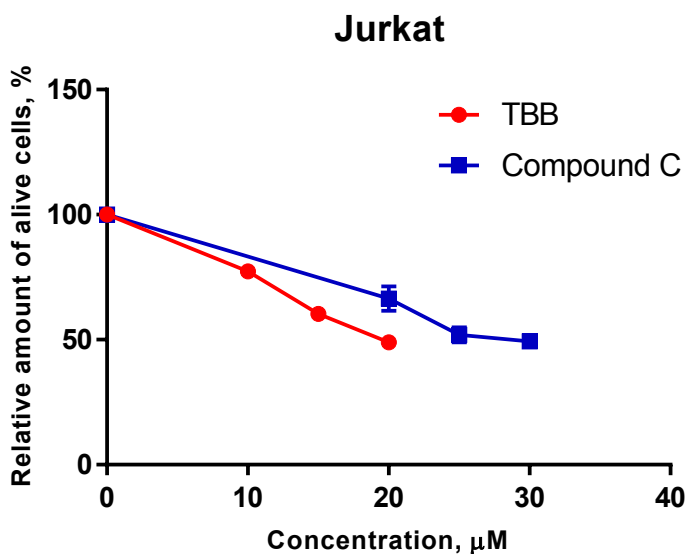
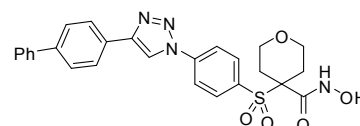
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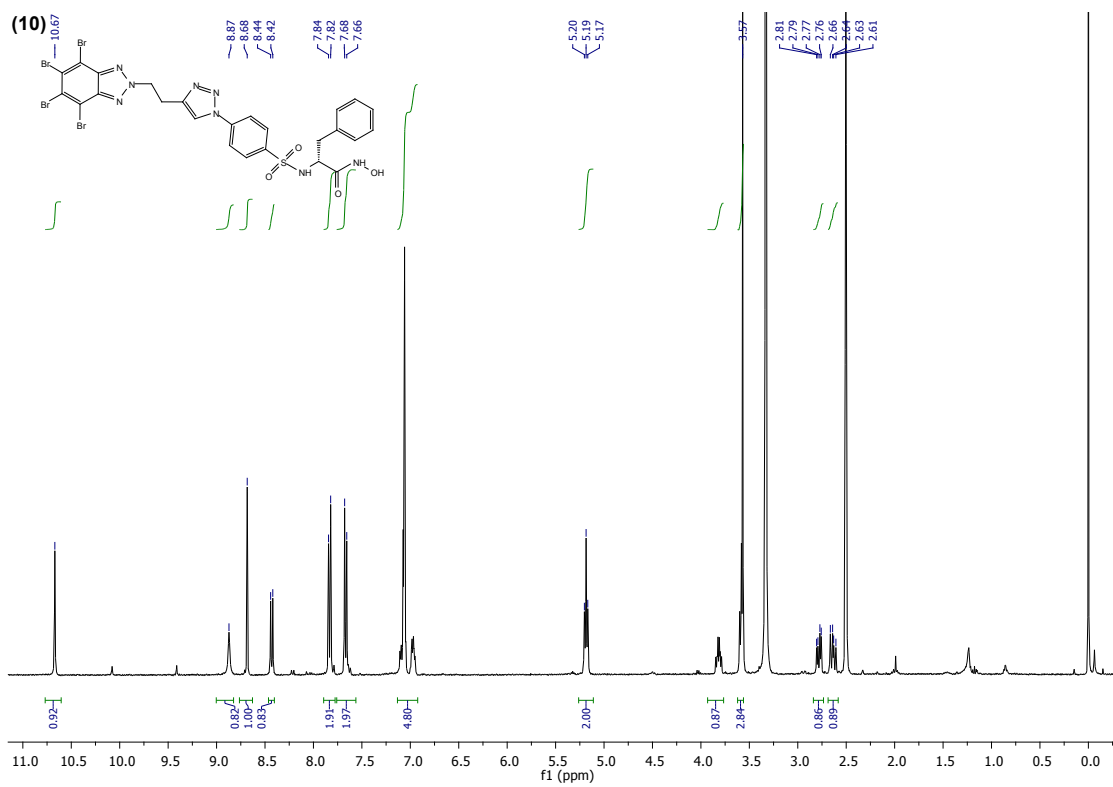
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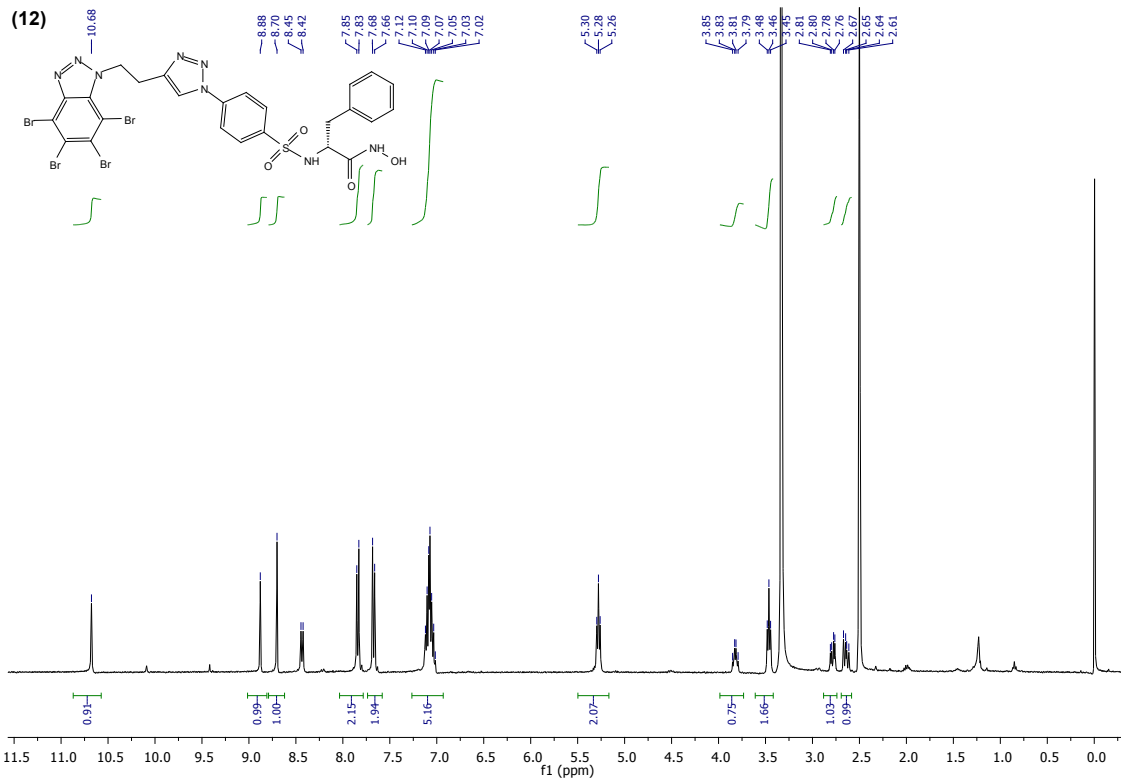
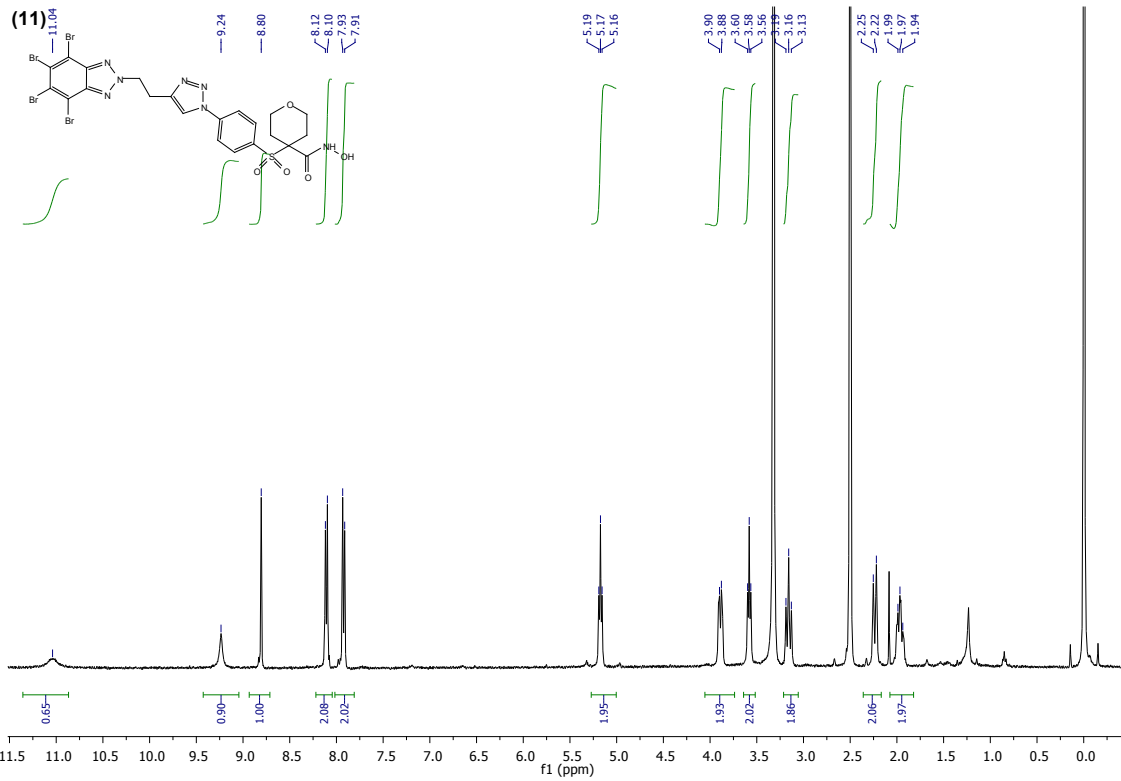
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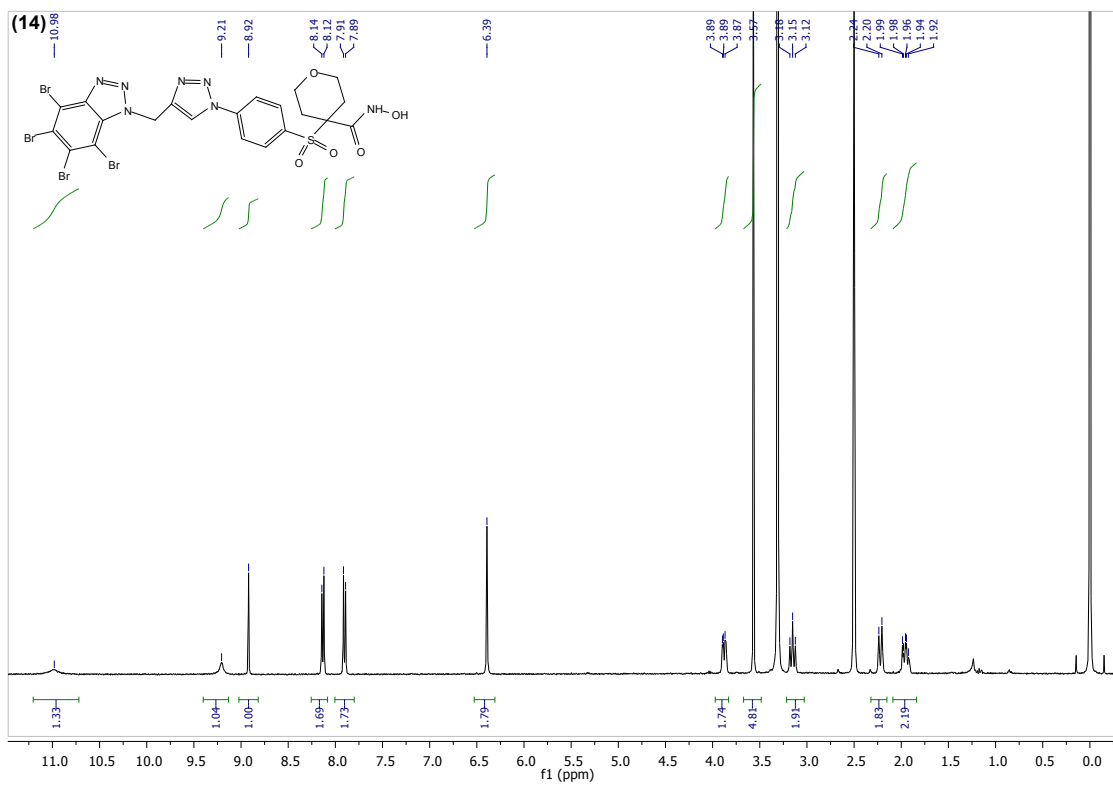
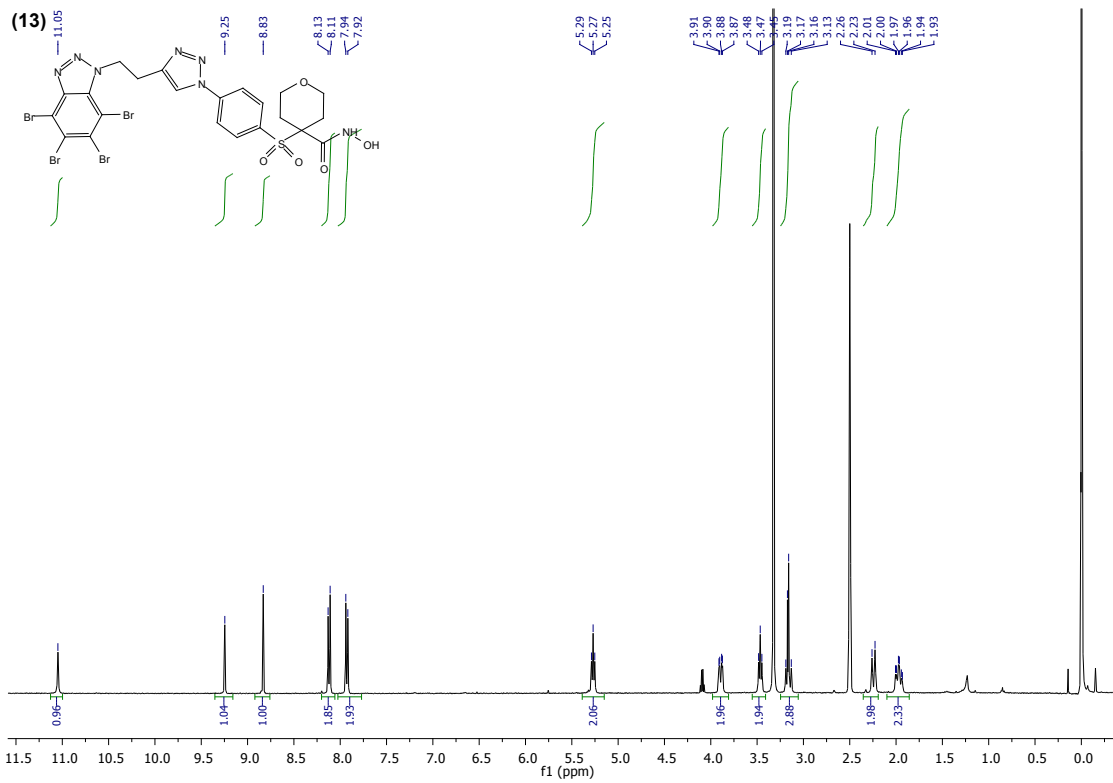
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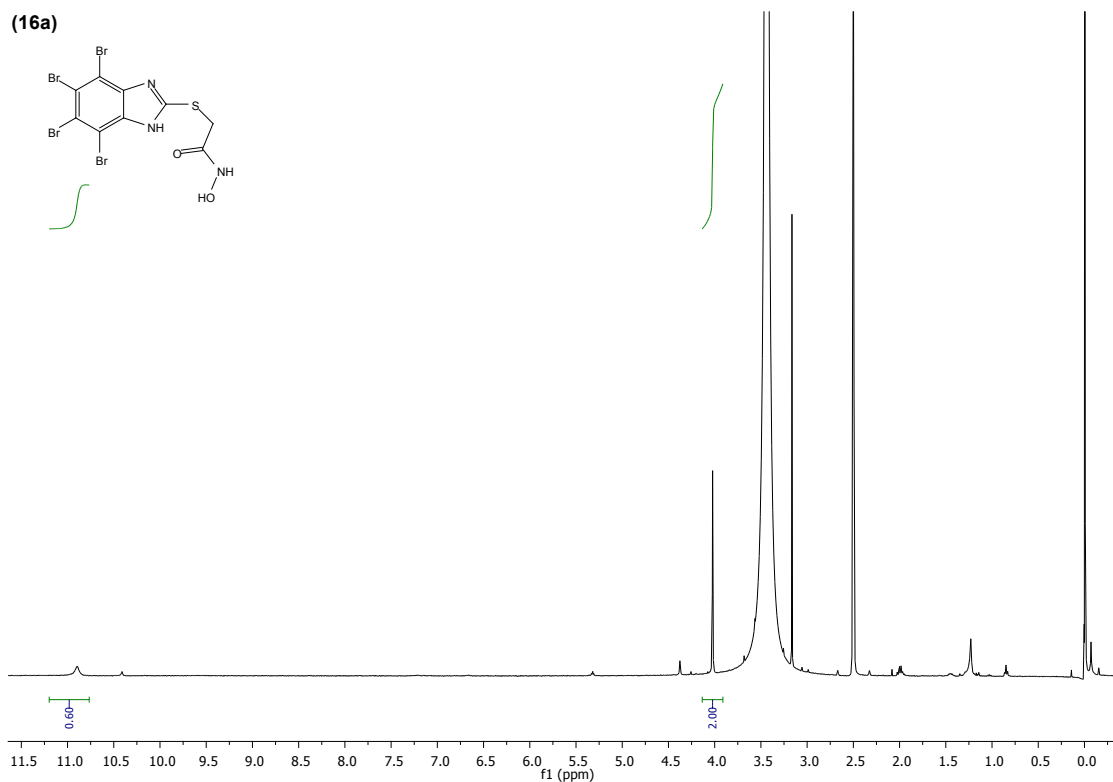
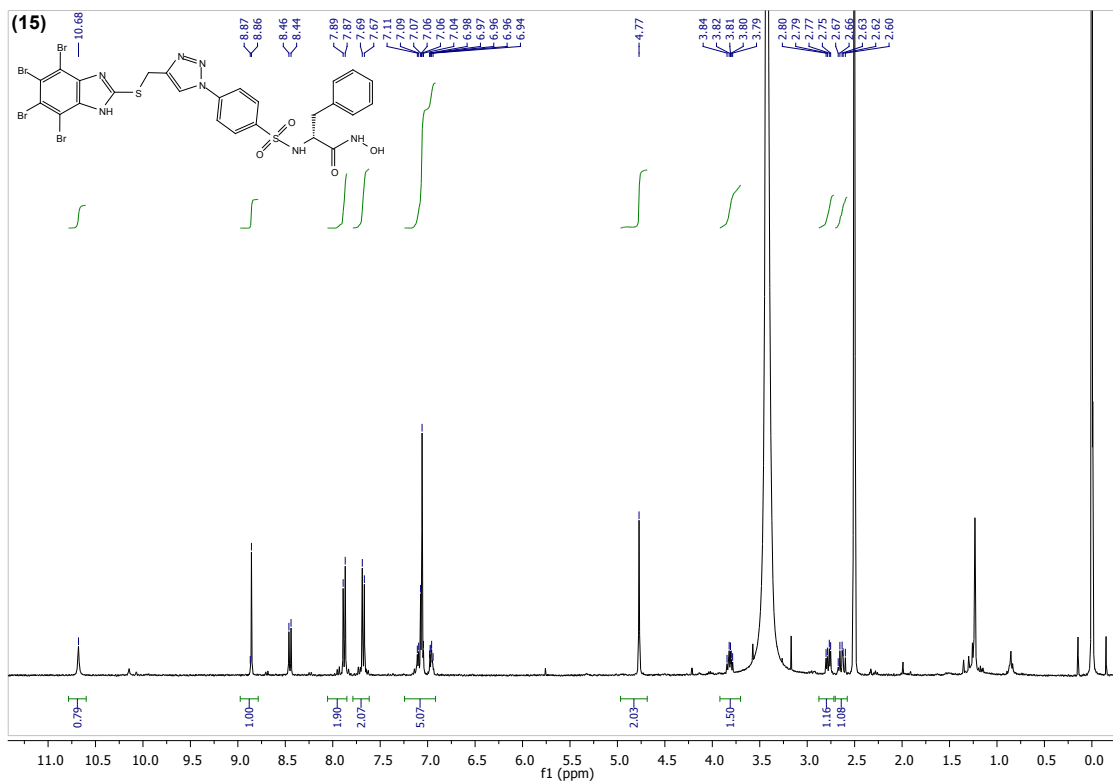
1) Figure 1. Cytotoxic effect of CK2 and MMP-2 inhibitors separately and in combination towards human T-leukemia cells of Jurkat line

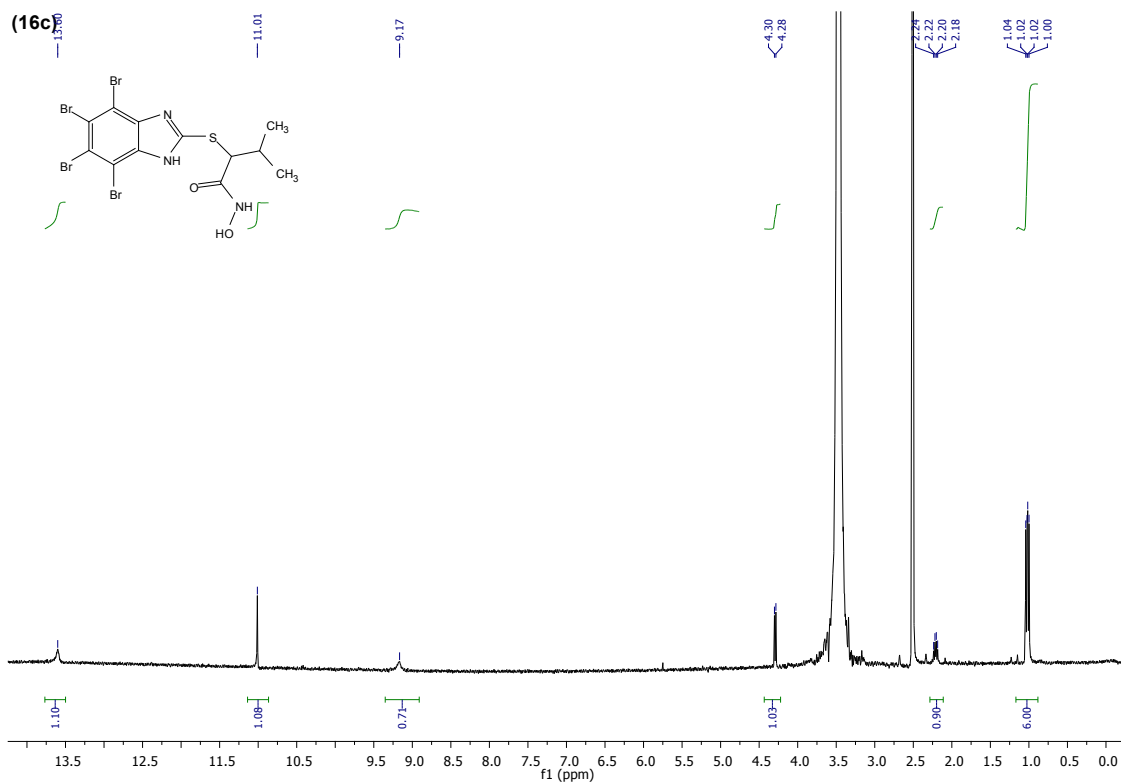
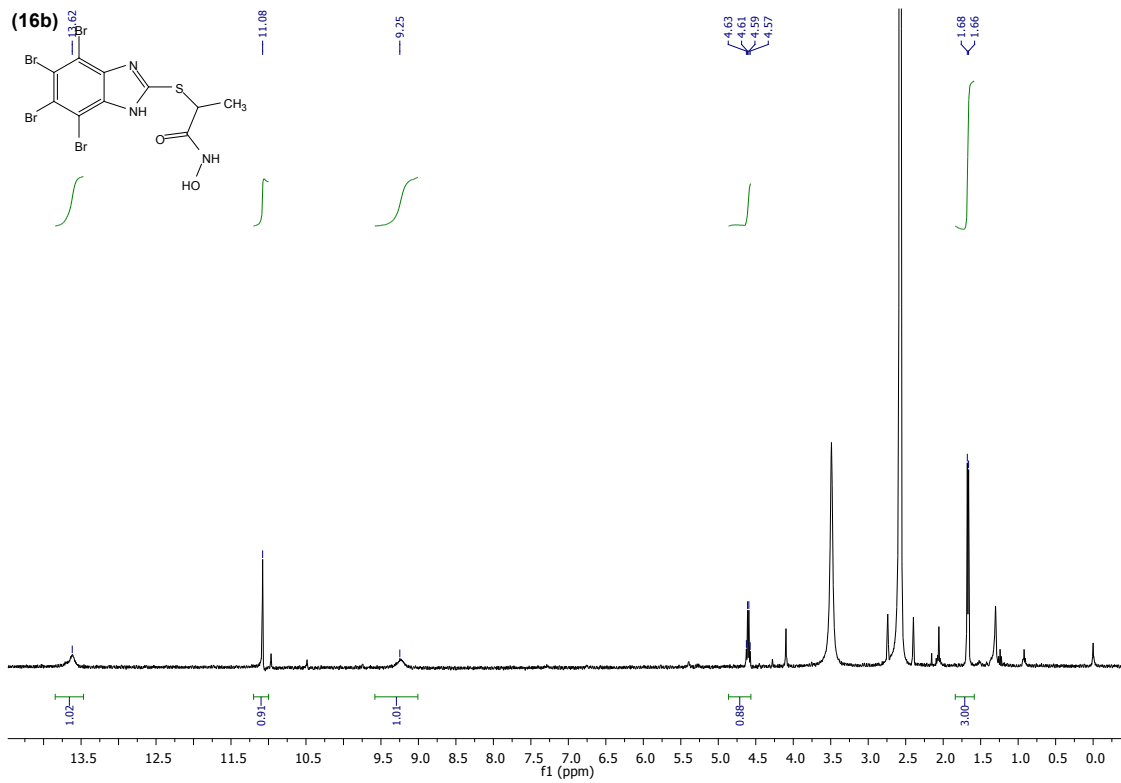


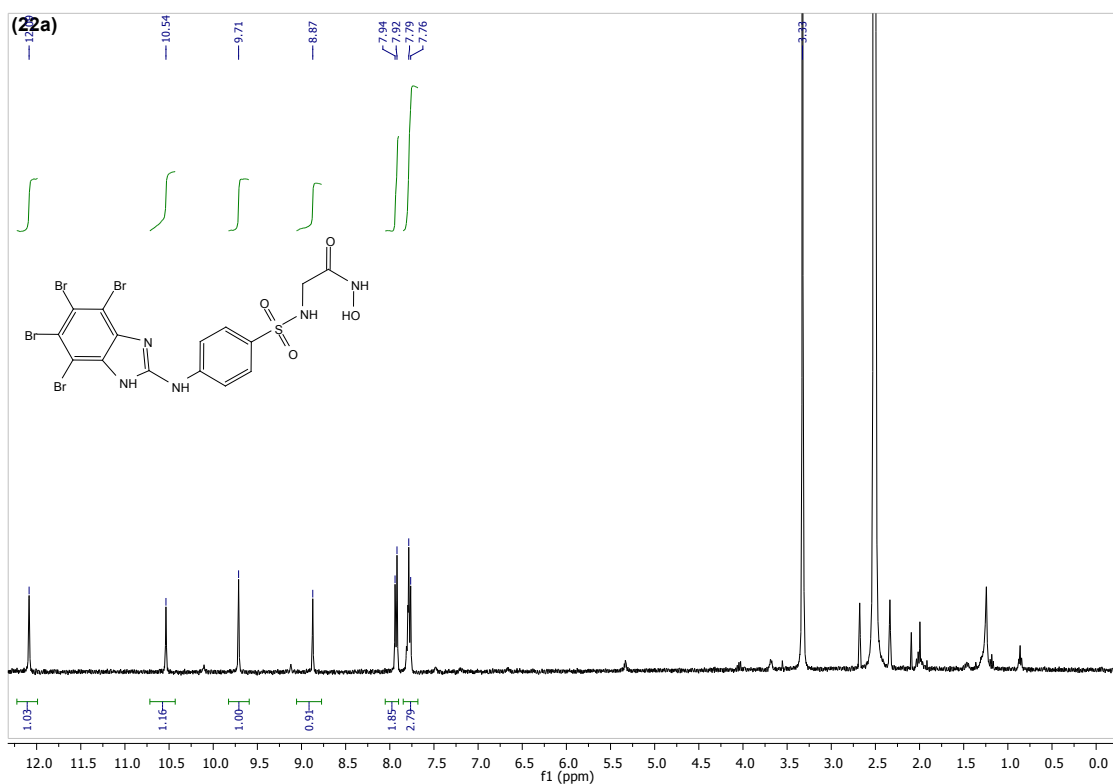
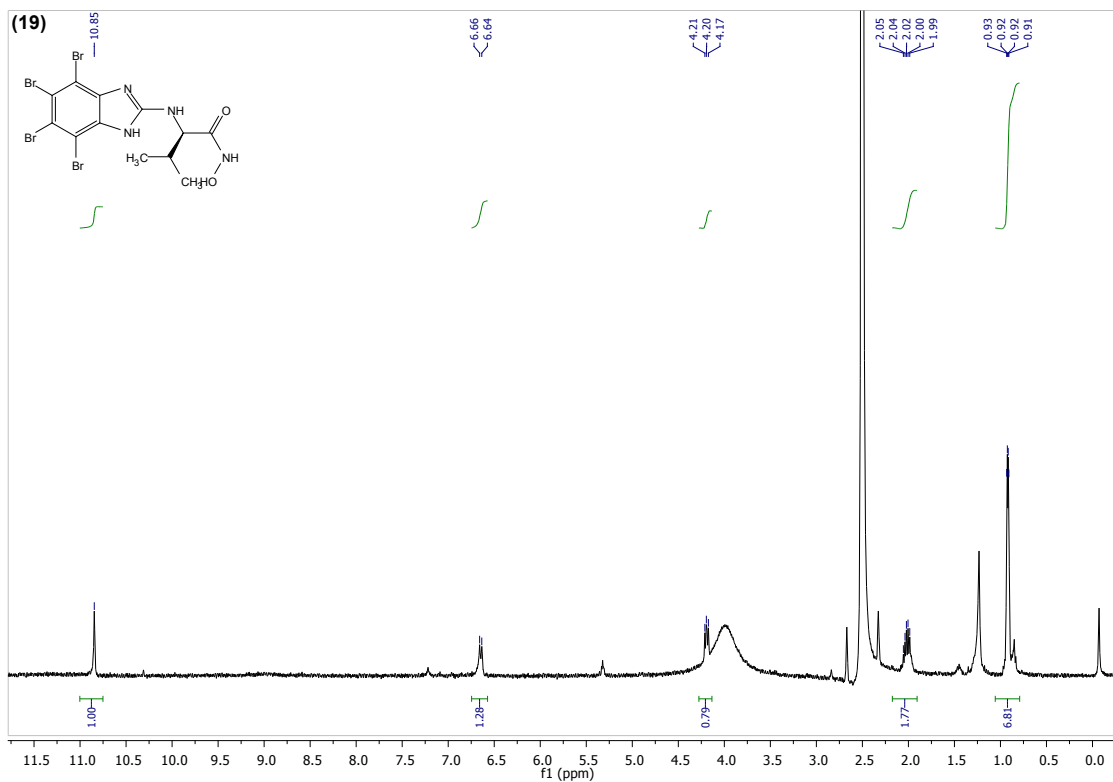


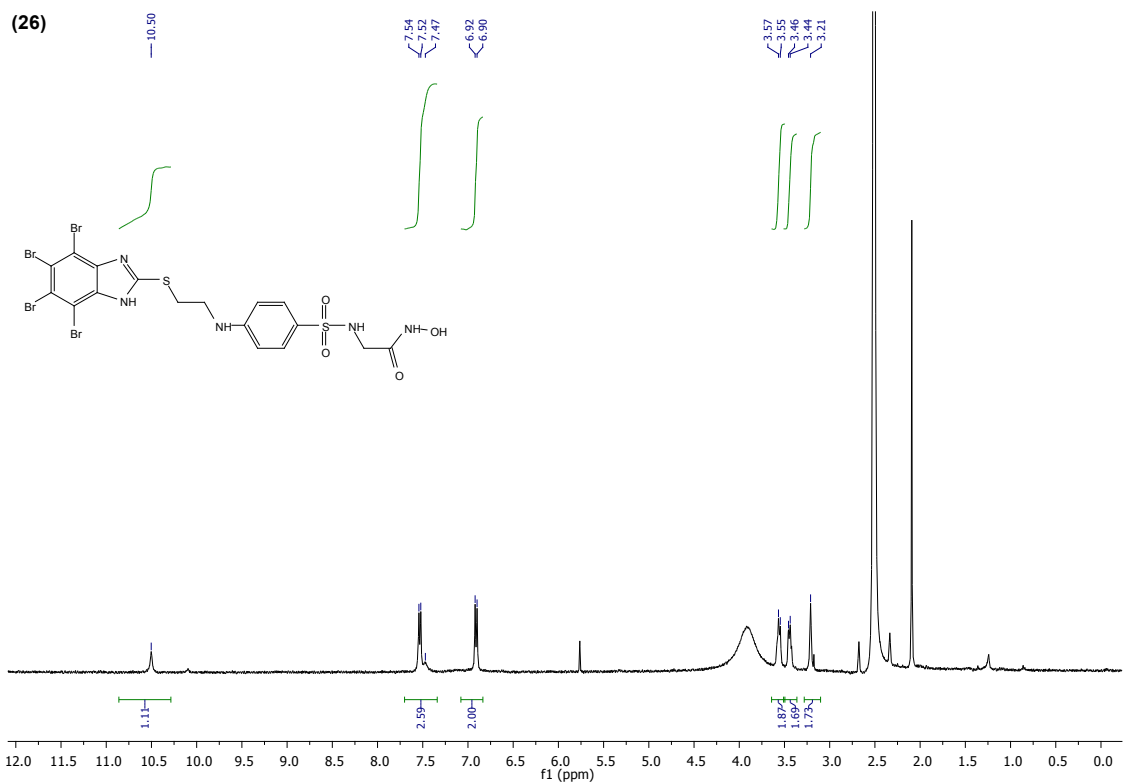
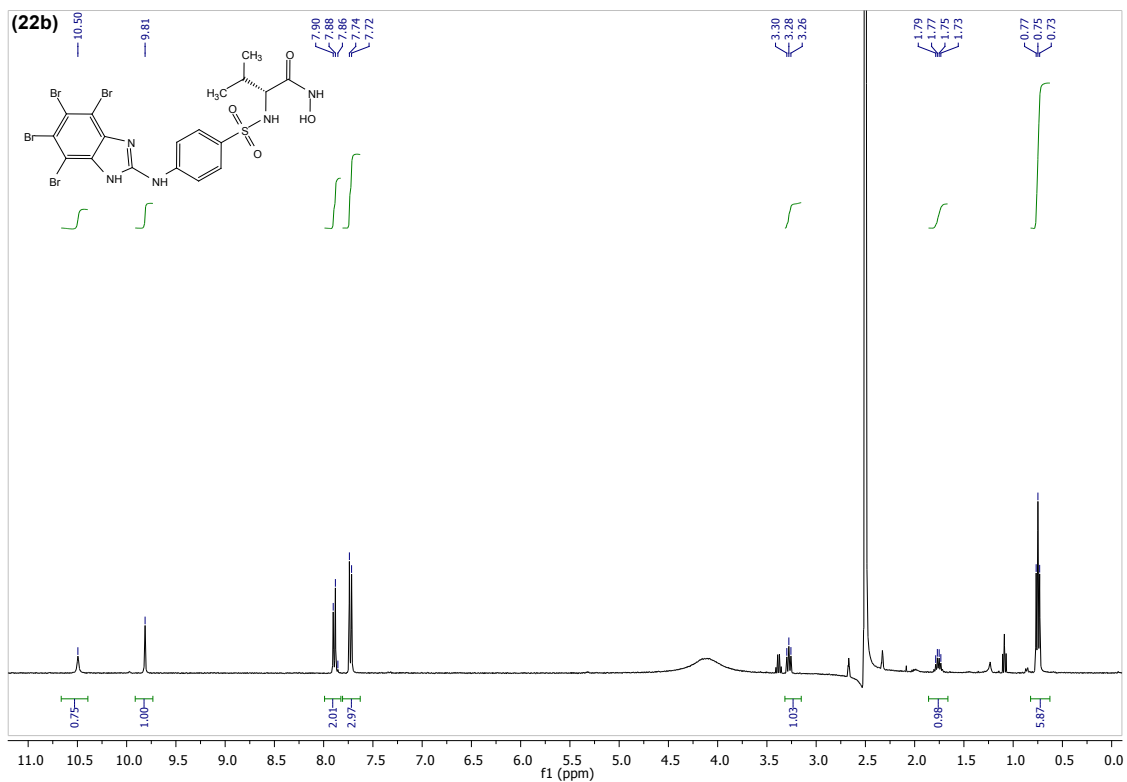






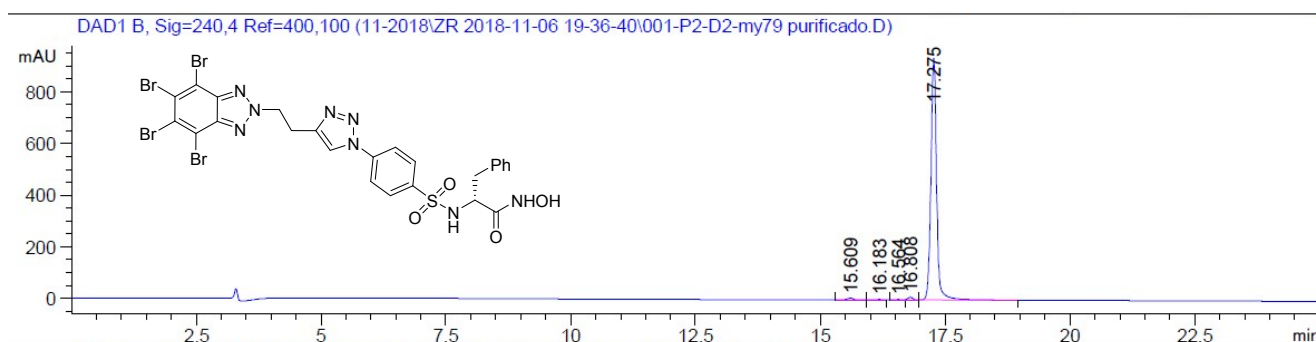






HPLC Chromatograms

Compound 10

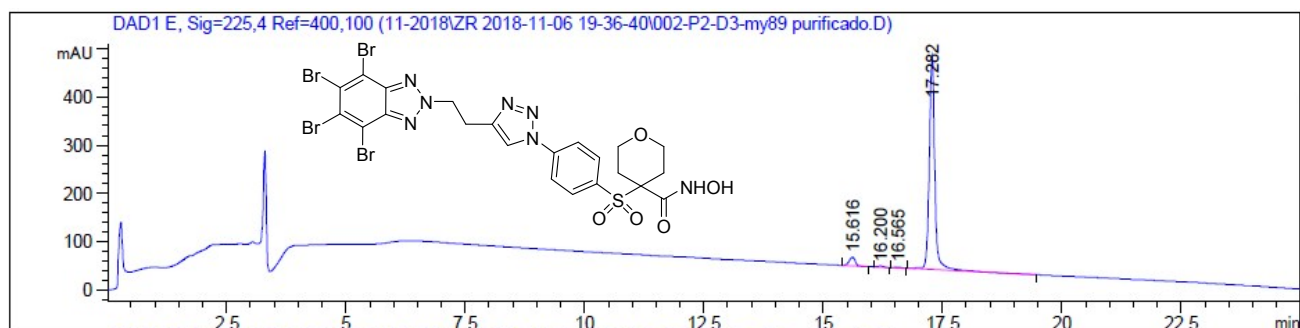


Signal 2: DAD1 B, Sig=240,4 Ref=400,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.609	BB	0.1429	61.86762	6.87823	0.8140
2	16.183	BB	0.1294	18.24036	2.18442	0.2400
3	16.564	BV E	0.1205	15.15461	1.95372	0.1994
4	16.808	VB R	0.1083	73.37231	10.39911	0.9654
5	17.275	BB	0.1205	7431.47314	937.66913	97.7812

Totals : 7600.10804 959.08461

Compound 11

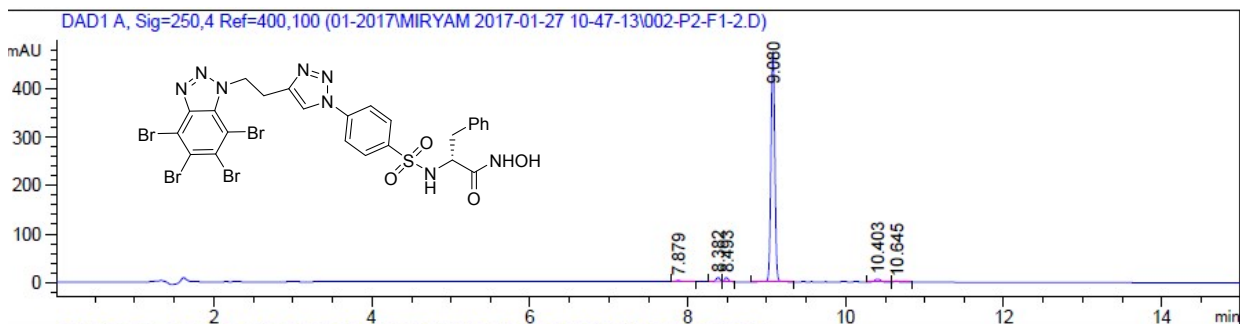


Signal 5: DAD1 E, Sig=225,4 Ref=400,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.616	VB	0.1431	162.11003	17.99987	4.2629
2	16.200	BB	0.1520	19.02493	2.01830	0.5003
3	16.565	BB	0.1189	16.12570	2.16466	0.4240
4	17.282	BB	0.1227	3605.57129	444.02097	94.8128

Totals : 3802.83195 466.20380

Compound 12



Signal 1: DAD1 A, Sig=250,4 Ref=400,100

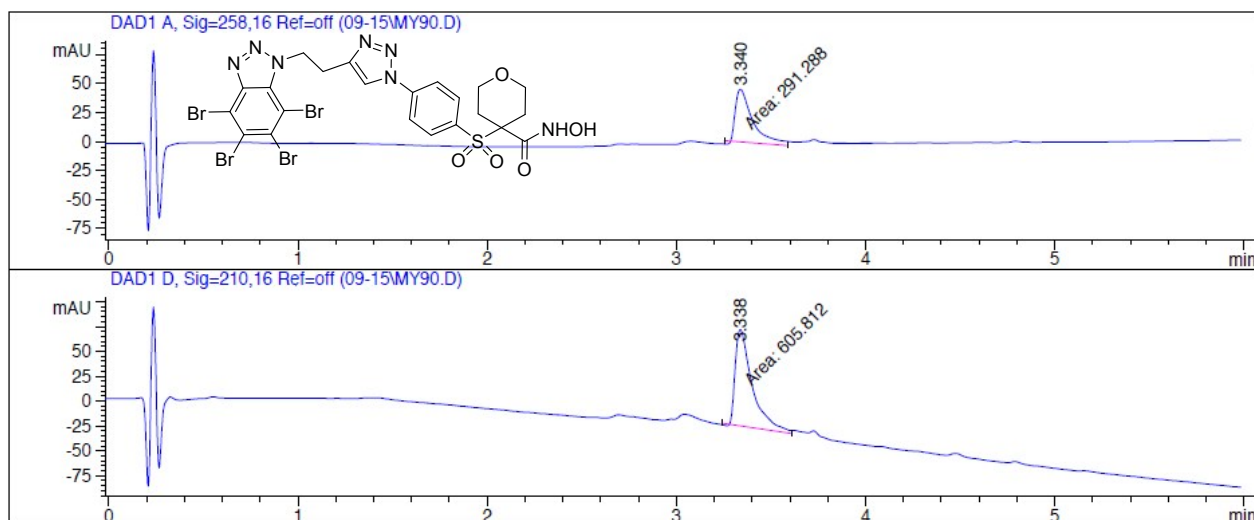
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.879	BB	0.0538	9.63612	2.82170	0.5747
2	8.382	BV	0.0530	29.17870	8.73382	1.7402
3	8.493	VB	0.0504	28.56924	8.67325	1.7038
4	9.080	BB	0.0503	1572.51172	478.78903	93.7812
5	10.403	BV	0.0823	29.12235	5.63264	1.7368
6	10.645	VB	0.0530	7.76987	2.32210	0.4634

Totals : 1676.78799 506.97254

Compound 13

Data File C:\CHEM32\1\DATA\09-15\MY90.D

Sample Name: MY90



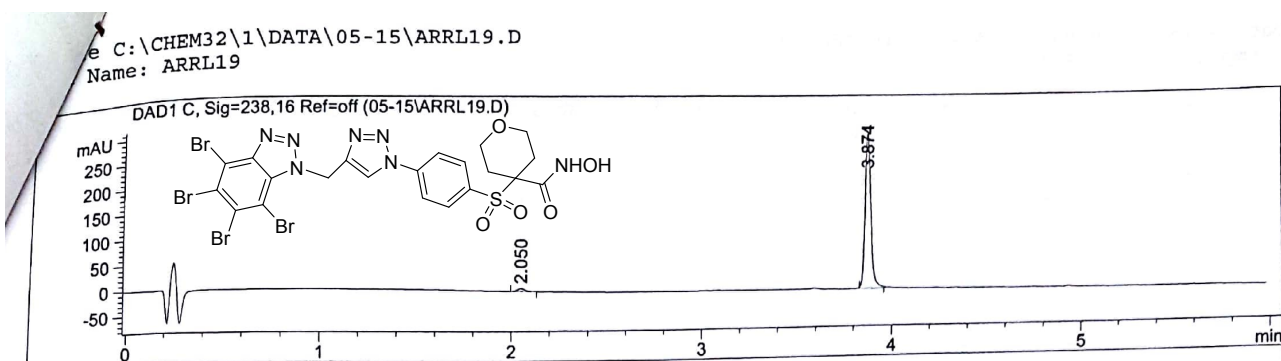
Signal 1: DAD1 A, Sig=258,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.340	MM	0.1071	291.28790	45.34159	100.0000
Totals :				291.28790	45.34159	

Signal 2: DAD1 D, Sig=210,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.338	MM	0.1043	605.81238	96.76290	100.0000

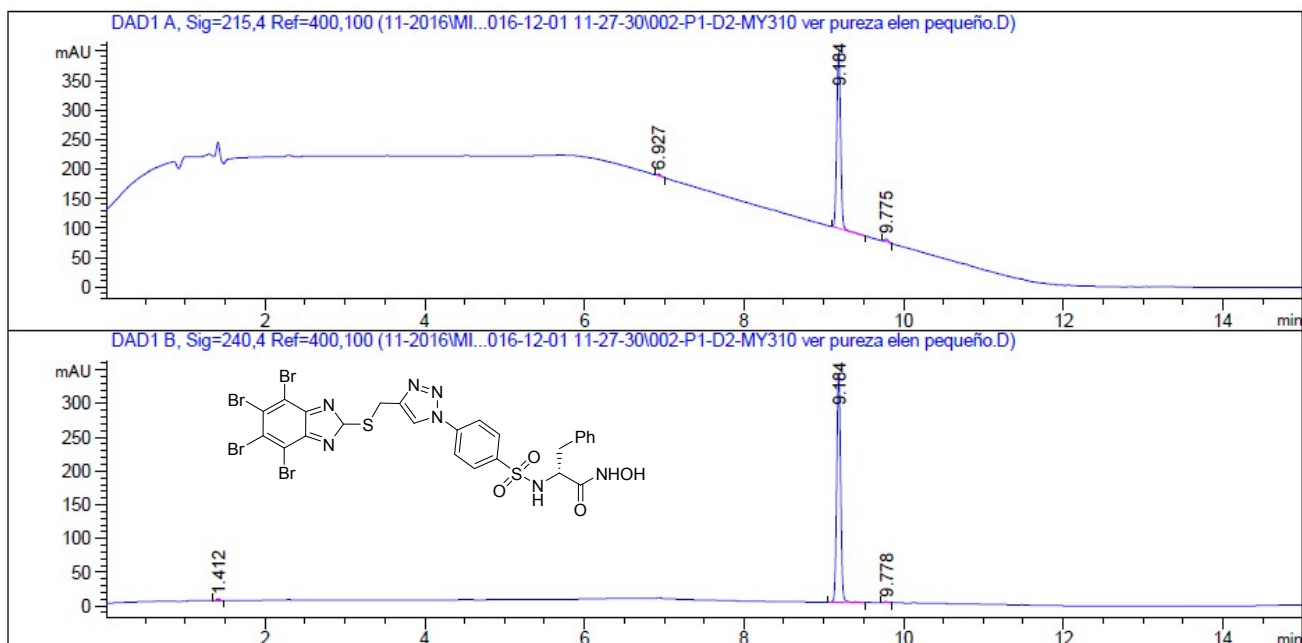
Compound 14



Signal 1: DAD1 C, Sig=238,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.050	BB	0.0463	16.15312	5.49427	2.4339
2	3.874	BB	0.0324	647.52386	309.20908	97.5661
Totals :				663.67699	314.70334	

Compound 15



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.927	BB	0.0592	10.32410	2.79042	1.0288
2	9.184	BB	0.0525	979.39569	296.72388	97.5956
3	9.775	BB	0.0500	13.80442	4.47530	1.3756

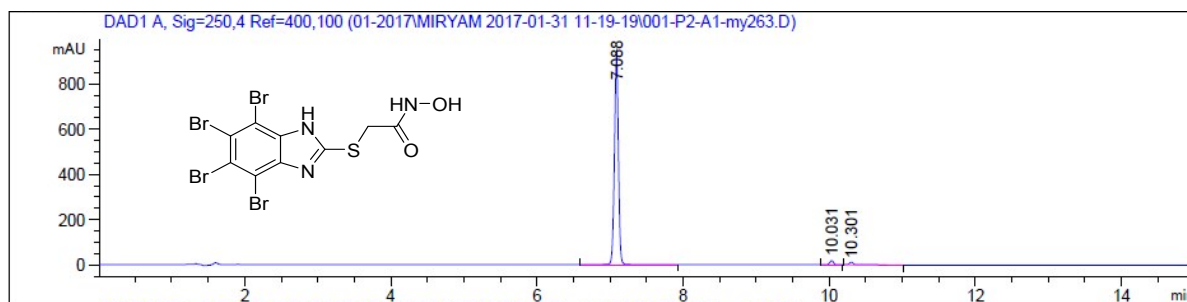
Totals : 1003.52421 303.98960

Signal 2: DAD1 B, Sig=240,4 Ref=400,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.412	BB	0.0440	6.60768	2.41005	0.5793
2	9.184	BV R	0.0526	1128.72412	341.17834	98.9501
3	9.778	BB	0.0508	5.36864	1.70418	0.4706

Totals : 1140.70044 345.29257

Compound 16a

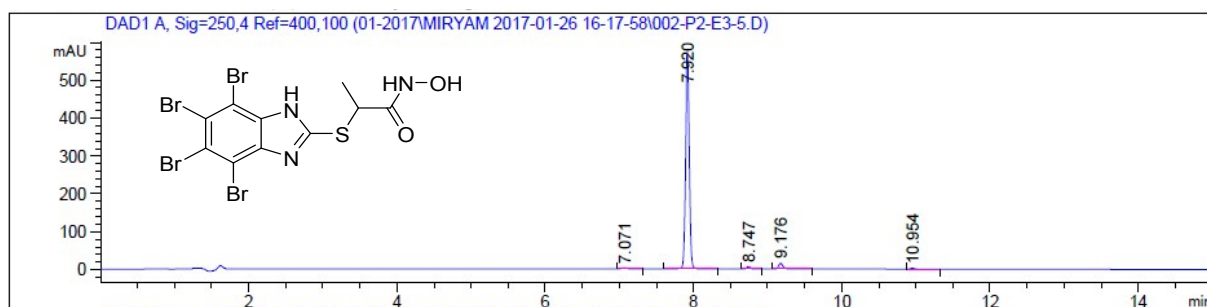


Signal 1: DAD1 A, Sig=250,4 Ref=400,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.088	BV R	0.0629	3828.67578	952.64569	97.0944
2	10.031	BB	0.0555	67.91229	19.07283	1.7222
3	10.301	BB	0.0540	46.66395	12.94800	1.1834

Totals : 3943.25203 984.66652

Compound 16b

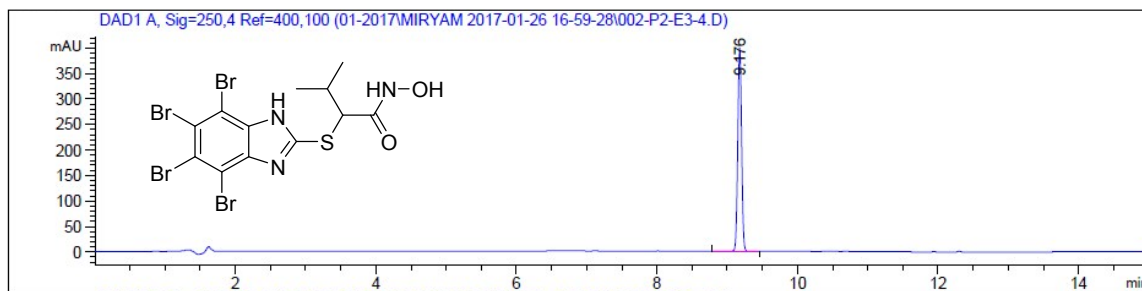


Signal 1: DAD1 A, Sig=250,4 Ref=400,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.071	BB	0.0639	9.87806	2.40503	0.4508
2	7.920	BB	0.0564	2084.50806	573.21716	95.1355
3	8.747	BB	0.0563	21.10863	5.82742	0.9634
4	9.176	BV R	0.0646	64.24592	14.82263	2.9321
5	10.954	BB	0.0593	11.35330	2.92288	0.5182

Totals : 2191.09397 599.19513

Compound 16c

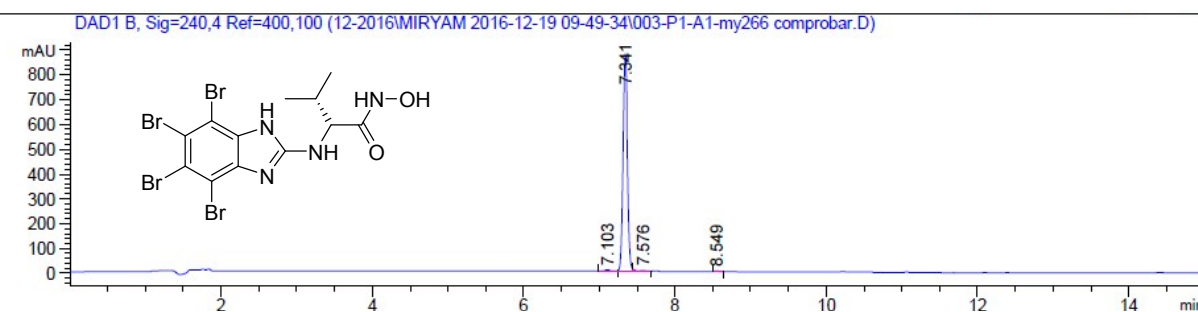


Signal 1: DAD1 A, Sig=250,4 Ref=400,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.176	BB	0.0570	1475.62732	400.65625	100.0000

Totals : 1475.62732 400.65625

Compound 19

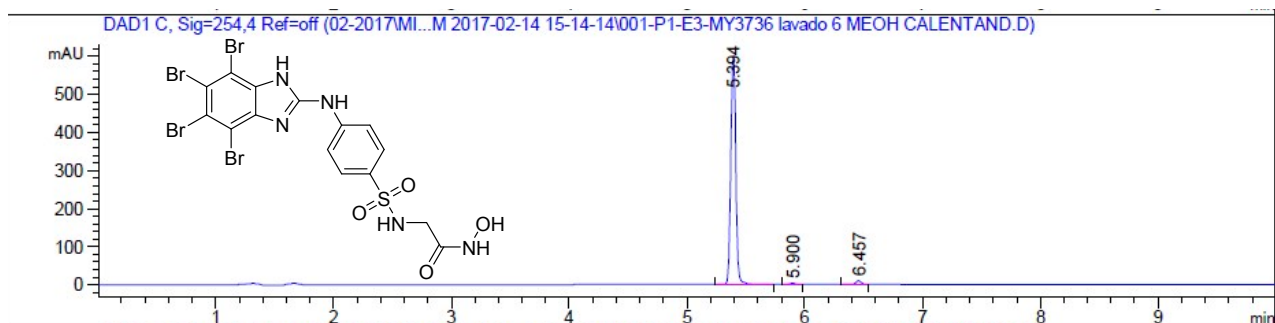


Signal 2: DAD1 B, Sig=240,4 Ref=400,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.103	BV E	0.0730	26.08159	5.33831	0.7006
2	7.341	VV R	0.0667	3666.46558	877.79877	98.4926
3	7.576	VB E	0.0808	19.16255	3.45139	0.5148
4	8.549	VB	0.0537	10.86884	3.19425	0.2920

Totals : 3722.57856 889.78270

Compound 22a

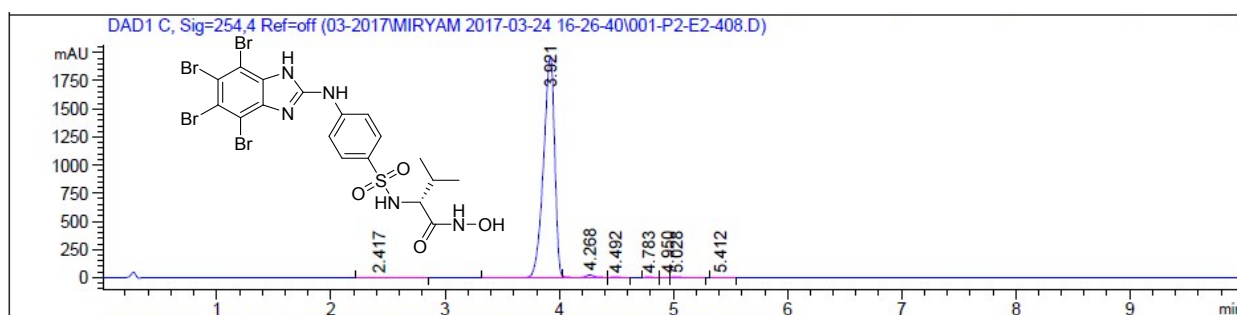


Signal 3: DAD1 C, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.394	BB	0.0465	1776.49707	600.34253	97.9191
2	5.900	BB	0.0557	9.94196	2.77997	0.5480
3	6.457	VB R	0.0467	27.81124	9.33900	1.5329

Totals : 1814.25027 612.46150

Compound 22b

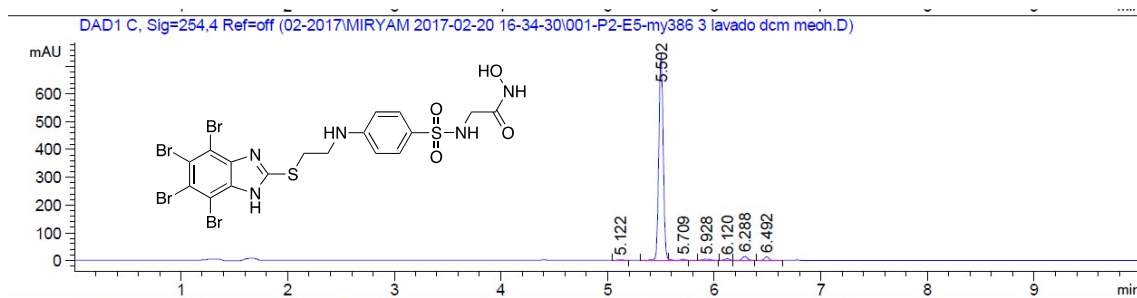


Signal 3: DAD1 C, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.417	BB	0.1622	20.04967	1.85299	0.1480
2	3.921	BV R	0.1026	1.32805e4	1971.12146	98.0400
3	4.268	VV E	0.0903	146.82066	23.68395	1.0839
4	4.492	VB E	0.0698	29.71102	6.43984	0.2193
5	4.783	VB	0.0657	19.51625	4.58278	0.1441
6	4.950	BV	0.0485	7.19500	2.30171	0.0531
7	5.028	VB	0.0707	33.33864	7.10505	0.2461
8	5.412	BB	0.0646	8.86507	2.12915	0.0654

Totals : 1.35460e4 2019.21694

Compound 26



Signal 3: DAD1 C, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.122	BB	0.0464	7.05643	2.39108	0.3065
2	5.502	BV R	0.0460	2176.44702	747.49591	94.5280
3	5.709	VV E	0.0600	10.99228	2.78540	0.4774
4	5.928	VB E	0.0687	15.79074	3.24691	0.6858
5	6.120	BB	0.0451	13.48071	4.75369	0.5855
6	6.288	VB R	0.0499	42.77067	13.17952	1.8576
7	6.492	BV R	0.0463	35.89937	12.21584	1.5592

Totals : 2302.43722 786.06835

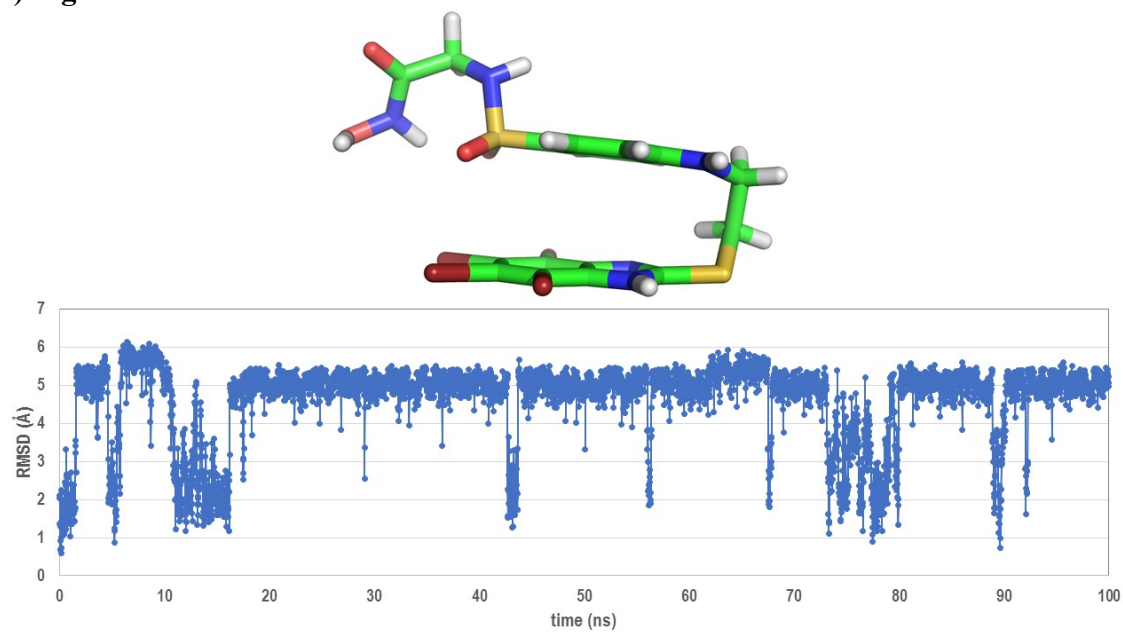


Figure 2: Top. PyMOL stick representation of the most populated conformer of **26** in water. Bottom. Graphical representation of the Root Mean Square Deviation (RMSD) of compound **26** in water.

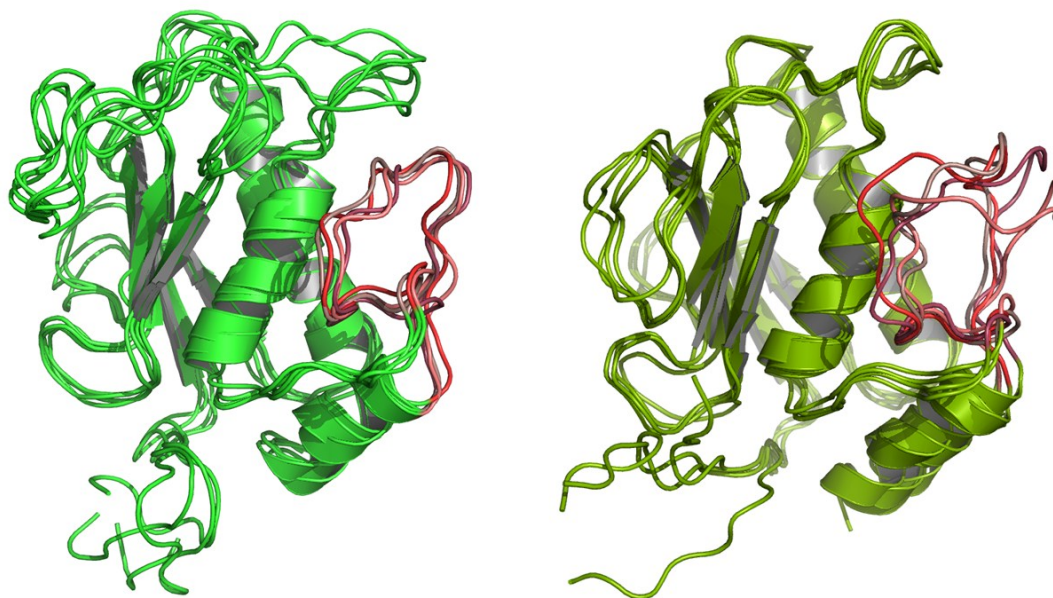


Figure 3: PyMOL stick and cartoon representation of the 4 Ω -loop conformers (represented in different shades of red) extracted from the 20ns MD simulations of MMP2 (left) and MMP13 (right). For the sake of clarity, the Ca^{2+} and Zn^{2+} ions are not represented.