

Supplementary Materials

Conformational Sampling Deciphers the Chameleonic Properties of a VHL-Based Degraders

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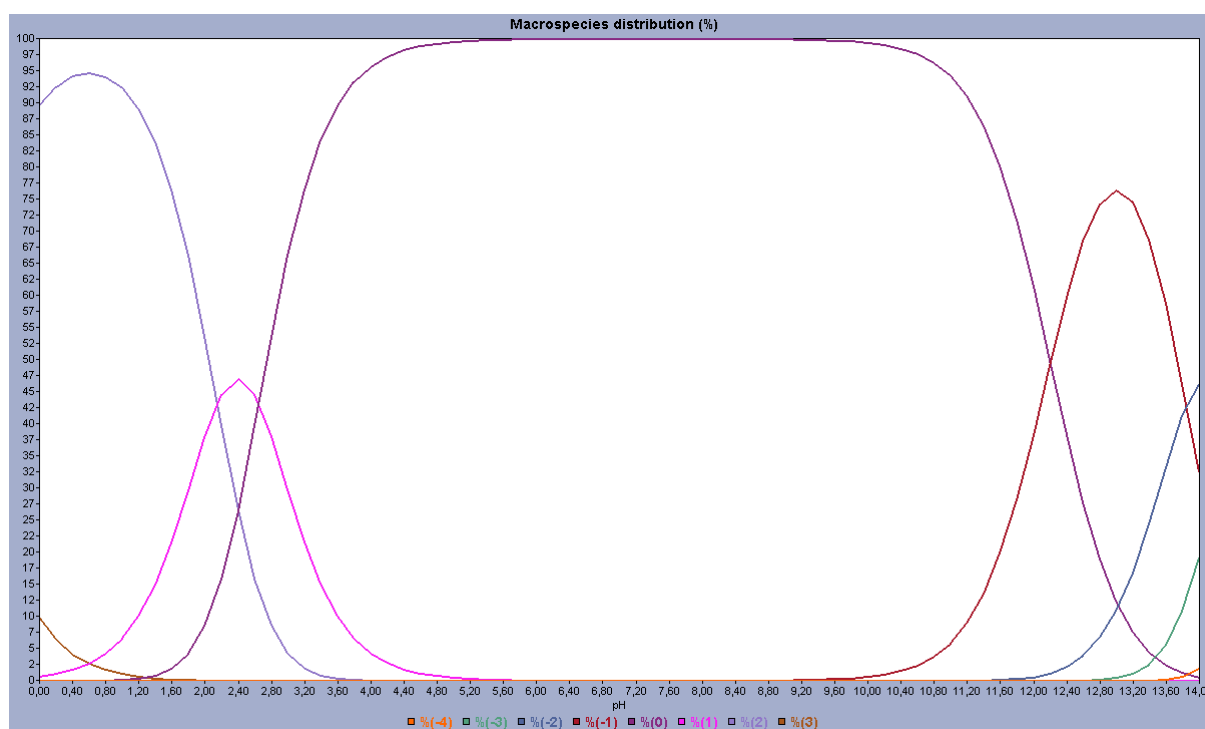
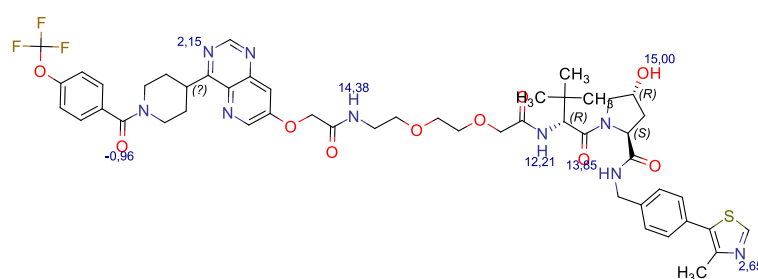


Figure S1. Predicted ionization profile and pKa values of PROTAC-1. ChemAxon tool was used.

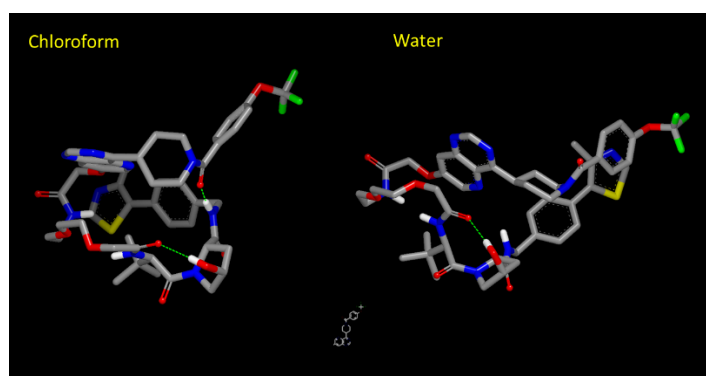


Figure S2. Comparison of the IMHBs pattern in the two solvents from Sc05.

Table S1. 2D descriptors calculated for PROTAC-1. In red Ro5 violations.

MW	RBN	PHI	nHDon	nHAcc	TPSA(Tot)
1034.12	21	19.04	4	22	264.87

Table S2. Summary of the data resulting from the conformational sampling protocols used.

	Sc01		Sc02		Sc03		Sc04		Sc05		Sc06	
	water	CHCl ₃	water	CHCl ₃	water	CHCl ₃	water	CHCl ₃	water	CHCl ₃	water	CHCl ₃
nConf	181	99	275	90	275	90	114	123	331	174	331	174
Rgyr												
Min	5.25	5.23	5.17	5.33	5.17	5.33	5.27	5.29	5.15	5.17	5.15	5.17
Max	6.69	7.01	6.84	6.3	6.84	6.3	6.44	6.99	6.83	6.35	6.83	6.35
Mean	5.78	5.79	5.79	5.96	5.79	5.96	5.73	6.13	5.76	5.6	5.76	5.6
Median	5.76	5.82	5.61	5.98	5.61	5.98	5.6	6.19	5.62	5.51	5.62	5.51
StdDev	0.23	0.26	0.46	0.16	0.46	0.16	0.36	0.36	0.4	0.27	0.4	0.27
Δ (Max water - Min CHCl ₃)	1.46		1.51		1.51		1.15		1.66		1.66	
3D PSA												
Min	238.7	224.7	238	223.2	238	223.2	241.2	233.4	235.2	230.4	235.2	230.4
Max	258.7	242.6	254.6	237	254.6	237	254.7	250.8	257	250.7	257	250.7
Mean	249.3	235.1	248.1	227.8	248.1	227.8	249.6	240.8	246.2	236.2	246.2	236.2
Median	248.9	235.1	248	227.1	248	227.06	249.82	239.74	247.14	236.03	247.14	236
StdDev	3.41	3.68	2.91	3.08	2.91	3.08	2.44	3.7	4.53	3.09	4.53	3.09
Δ (Max water - Min CHCl ₃)	34		31.4		31.4		21.3		26.6		26.6	
IMHBs												
Min	0	1	0	2	0	2	0	0	0	1	0	1
Max	3	4	3	4	3	4	2	2	2	2	2	2
Mean	0.97	2.44	1.05	3.13	1.05	3.13	0.53	1.2	1.11	1.93	1.11	1.93
Median	1	2	1	3	1	3	1	1	1	2	1	2
StDev	0.65	0.67	0.48	0.56	0.48	0.56	0.53	0.47	0.54	0.26	0.54	0.26
Δ (Max CHCl ₃ - Min water)	4		4		4		2		2		2	

Table S3. Summary of the data resulting from the post minimization performed with MOPAC.

MO01		
Starting ensemble		Sc01
Solvent		water
nConf		CHCl ₃
		100
		80
Rgyr		
Min		5.03
Max		5.9
σ		0.87
Mean		5.37
Median		5.3
StdDev		0.22
Δ (Max water - Min CHCl ₃)		0.76

3D PSA			
Min	220.8	207.9	
Max	241	232.3	
✱	20.22	24.42	
Mean	231.2	221.4	
Median	230.8	221.4	
StdDev	4.6	5.8	
Δ (Max water - Min CHCl ₃)		33.1	
IMHBs			
Min	1	1	
Max	3	3	
Mean	1.6	2.28	
Median	2	2	
StdDev	0.62	0.72	
Δ (Max CHCl ₃ - Min water)		2	