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Supporting information for article:

**Structures of endothiapsin-fragment complexes by
crystallographic fragment-screening using a novel, diverse and
affordable 96-compound-fragment library**

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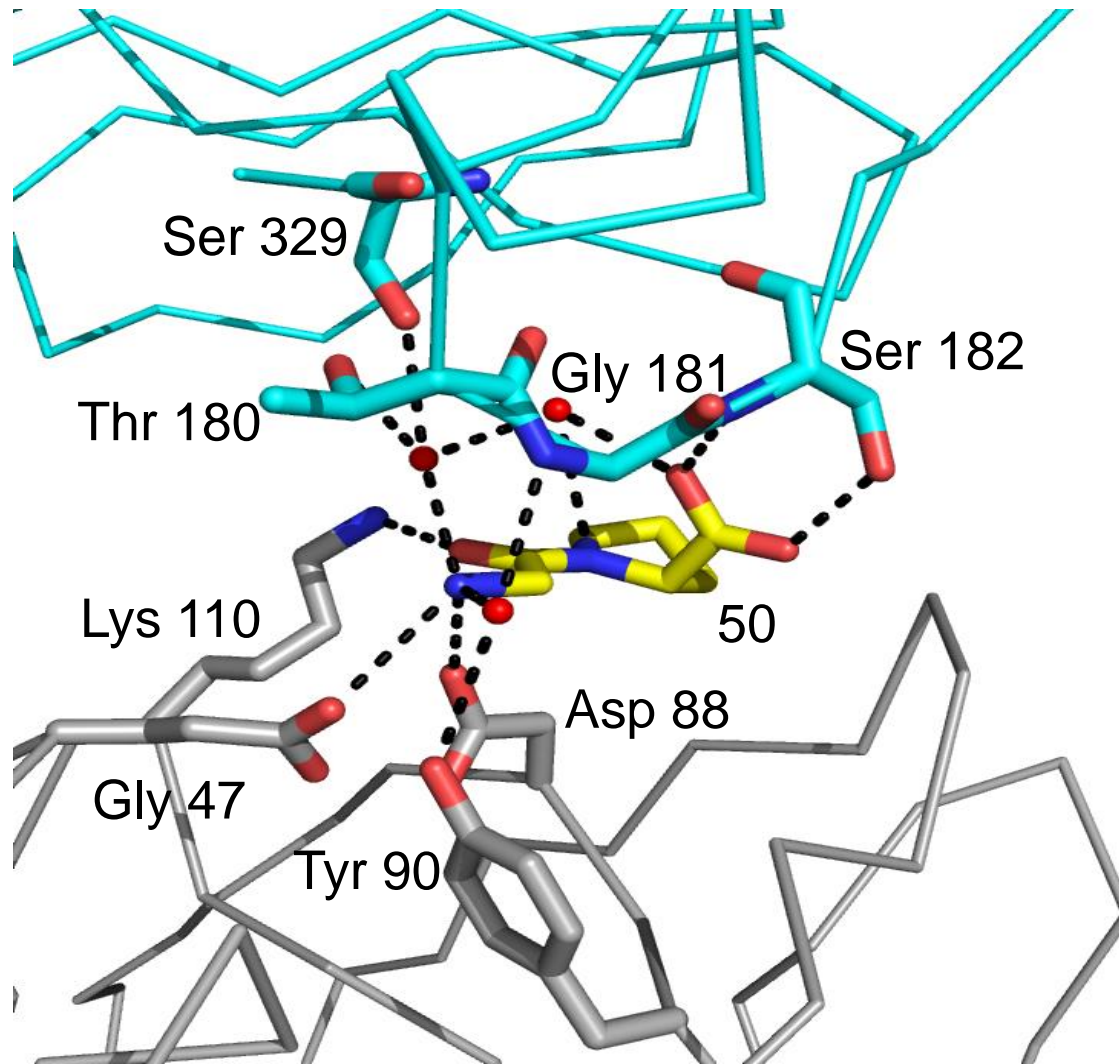
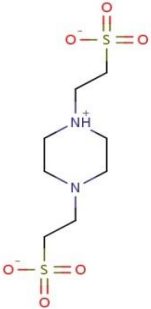
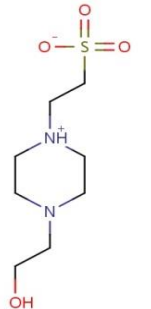
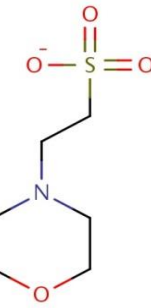
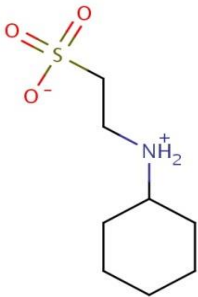
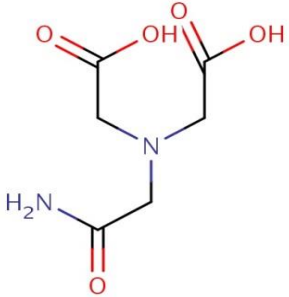
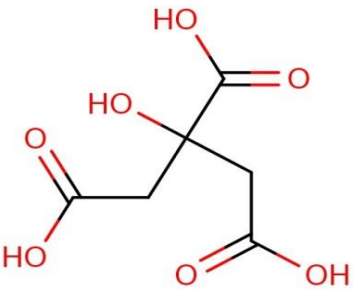
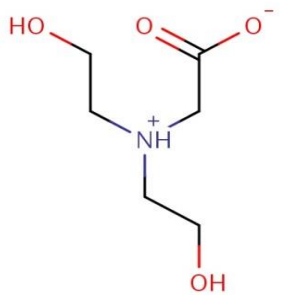
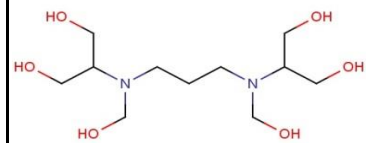
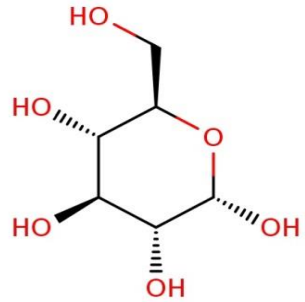


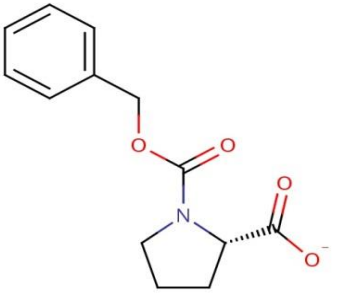
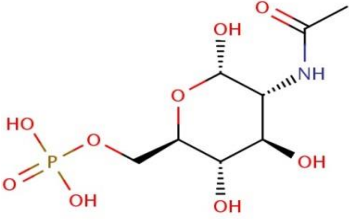
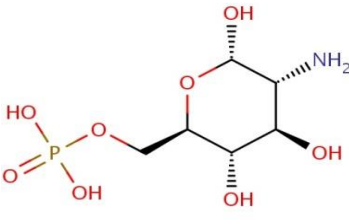
Figure S1: A more detailed representation of the binding of compound 50 (GlyPro) to the interface between two symmetry-related EP molecules. Shown are the C α -traces of the 2 EP molecules (in grey and cyan), as well as all main chain or side chain atoms of the amino acid residues participating in a contact to GlyPro. Water molecules, which take part in a contact are also shown (red spheres).

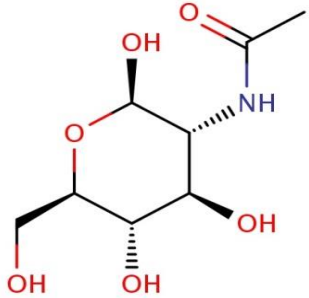
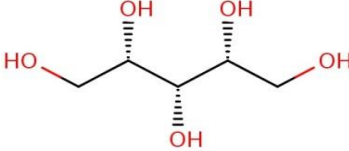
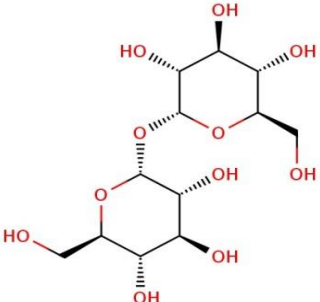
Table S1: 96-compound fragment library - detailed information.

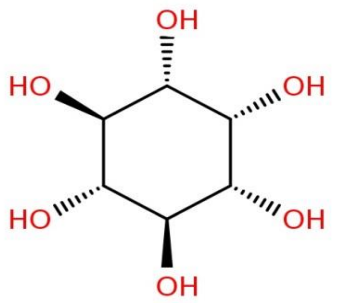
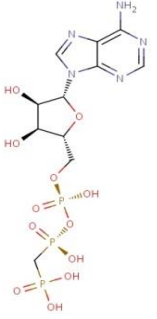
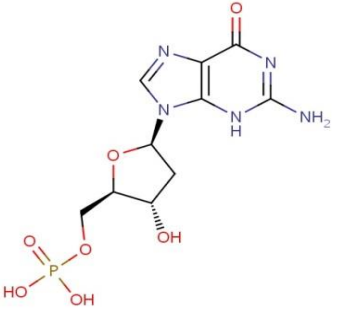
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
1		5625-37-6	PIPES / piperazine-N,N'-bis(ethanesulfonic acid)	301,36	110,10	-2,69	3.3 mM at 100°C	
2		75277-39-3	HEPES / sodium-N-(2-hydroxyethyl) piperazin-N'-(2-ethanesulfonate)	238,31	79,12	-2,19	1.9 M	
3		4432-31-9	MES / 2-(N-morpholino) ethanesulfonic acid	194,23	63,68	-1,46	1.3 M	

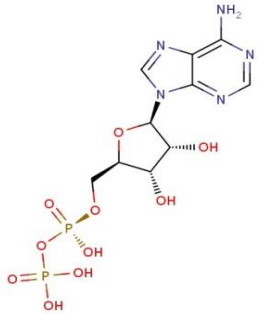
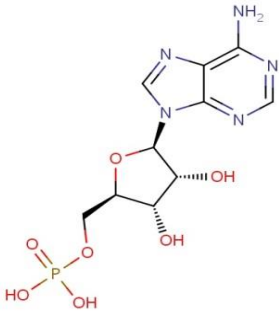
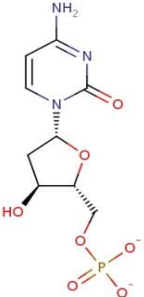
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
4		103-47-9	CHES / N-Cyclohexyl-2-aminoethanesulfonic acid	207,29	67,82	0,69	851.3 mM	
5		26239-55-4	ADA / N-(2-acetamido)iminodiacetic acid	190,15	120,93	-2,05	841.2 mM in 1MNaOH	
6		68-04-2	Citric acid trisodium salt dihydrate	192,12	132.13	-1,53	2.6 M	

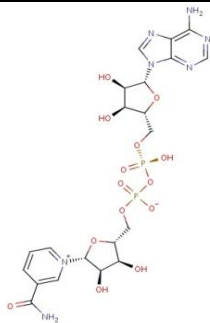
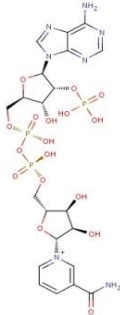
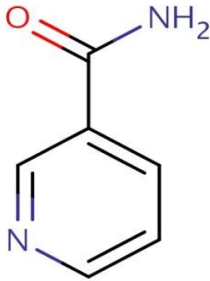
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) _a [[]	Solubility ^[b]	LD50 [mg/kg]
7		150-25-4	Bicine / N,N-bis(2-hydroxyethyl)glycine	163,17	85.03	-1,60	2.0 M	
8		64431-96-5	Bis-Tris Propane / 1,3-bis[tris(hydroxymethyl) methylamino]propane	282,34	127,86	-3,22	1.5 M	
9		50-99-7	D-(+)-Glucose	180,16	110,38	-2,93	5.1 M	

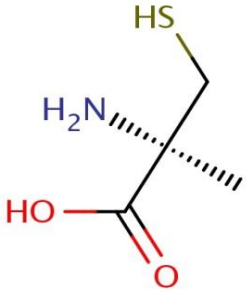
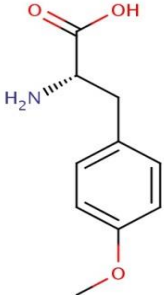
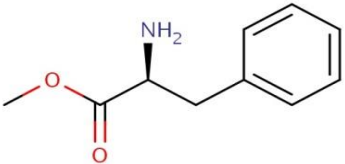
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
10		1148-11-4	Z-Pro-OH / 1-[(Benzyloxy)carbonyl]-L-proline	248,26	69,67	2,09	very soluble	
11		102029-88-9	N-Acetyl-D-glucosamine 6-phosphate sodium salt	301,19	166	-3,9	144.8 mM	
12		3616-42-0	D-Glucosamine 6-phosphate	259,15	162,70	-4,04	192.9 mM	

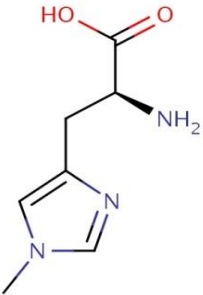
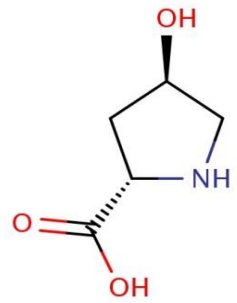
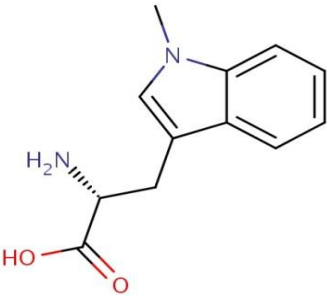
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
13		7512-17-6	<i>N</i> -Acetyl-D-glucosamine	221,21	119,25	-2,99	226.0 mM	
14		87-99-0	D-Xylitol	152,15	101.15	-2,82	328.5 mM	
15		6138-23-4	D-(+)-Trehalose dihydrate	342,30	189,53	-4,85	132.2 mM	

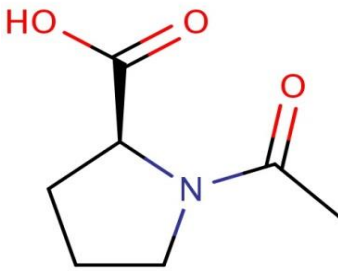
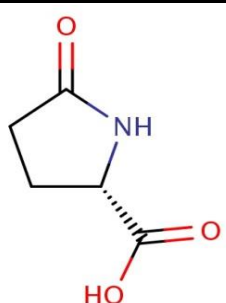
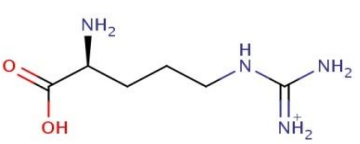
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
16		87-89-8	myo-Inositol / 1,2,3,4,5,6-Hexahydroxycyclohexane	180,16	121,38	-3,50	277.47 mM	
17		7414-56-4	AMP-PCP disodium salt / β,γ-Methyleneadenosine 5'- triphosphate disodium salt	505,21	269,90	-5,40	182.1 mM	
18		52558-16-4	2'-Deoxyguanosine 5'-monophosphate sodium salt hydrate (dGMP)	347,22	181,52	-2,09	144.0 mM	

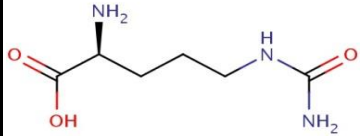
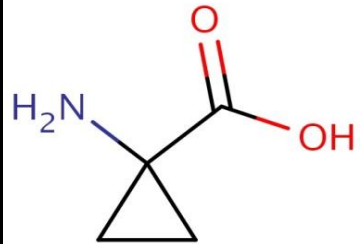
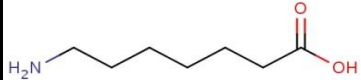
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
19		20398-34-9	Adenosine 5'-diphosphate sodium salt (ADP)	427,20	232,60	-4,09	117.0 mM	
20		4578-31-8	Adenosine 5'-monophosphate disodium salt (AMP)	347,22	186,07	-3,21	no Info	
21		1032-65-1	2'-Deoxycytidine 5'-monophosphate (dCMP)	305,18	148,59	-2,50	162.8 in 1 M NH ₄ OH	

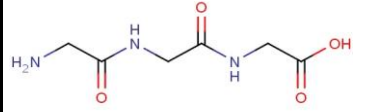
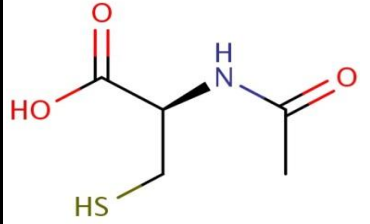
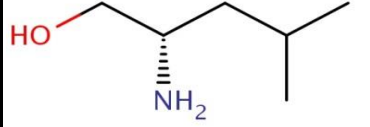
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
22		53-84-9	β-Nicotinamide adenine dinucleotide hydrate (β-NAD)	665,45	317,62	-6,01	75.4 mM	
24		53-59-8	β-Nicotinamide adenine dinucleotide phosphate hydrate (β-NADP)	746,43	365,35	-6,71	67.3 mM	
25		98-92-0	Nicotinamide / Pyridine-3-carboxylic acid amide	122,13	55,98	-0,38	819.0 mM	3500 (rat oral)

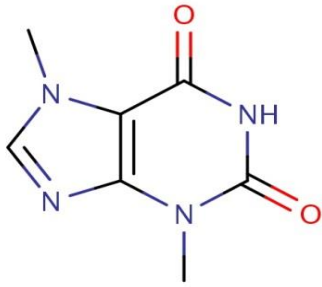
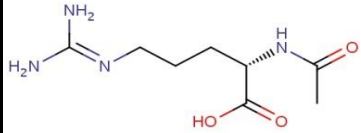
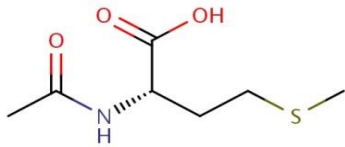
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) _a [[]	Solubility ^[b]	LD50 [mg/kg]
26		1187-84-4	2-methyl-L-cysteine / (R)-2-Amino-3-(methylmercapto)propionic acid	135,19	102,12	-2,54	369 mM	
28		6230-11-1	O-methyl-L-tyrosine	195,22	72,55	-1,57	NA	
29		7524-50-7	L-Phenylalanine methyl ester hydrochloride	179,22	52,32	1,14	NA	

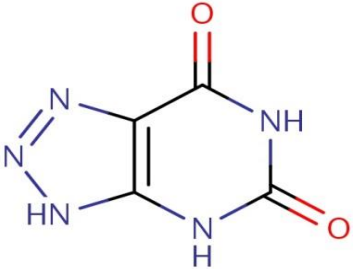
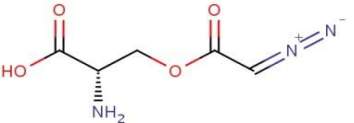
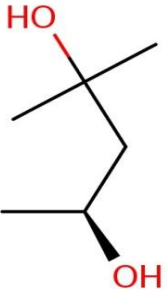
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30		332-80-9	1-Methyl-L-histidine	169,18	81,14	-3,44	NA	
31		51-35-4	trans-4-Hydroxy-L-proline	131,13	69,56	-0,96	381.4 mM	
32		110117-83-4	1-Methyl-D-tryptophan	218,26	68,25	-0,77	soluble in water (slightly), and acitic acid	

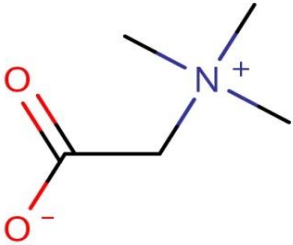
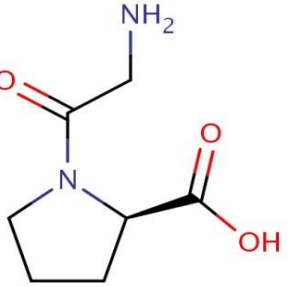
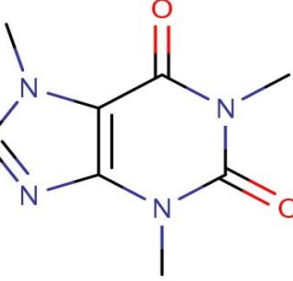
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33		68-95-1	N-Acetyl-L-proline	157,17	57,61	-0,10	NA	
34		98-79-3	L-Pyroglutamic acid	129,11	66,40	-0,78	774.6 mM – 1.2 M	
35		74-79-3	D-Arginine	175,21	126,96	-3,41	287.0 mM	

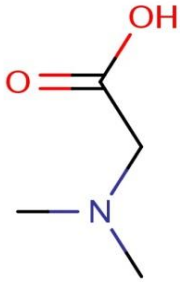
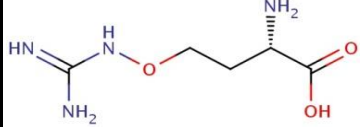
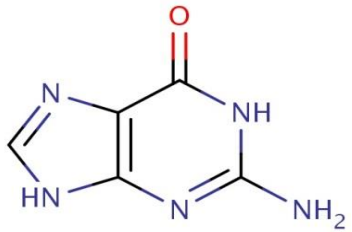
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
36		372-75-8	L-Citrulline / (S)-2-Amino-5-ureidopentanoic acid	175,19	118,44	-3,97	1.1 M	
37		22059-21-8	1-Aminocyclopropane-carboxylic acid	101,10	63,32	-2,80	484.7 – 504.5 mM	
39		929-17-9	7-Aminoptanoic acid	145,20	63,32	0,74	NA	

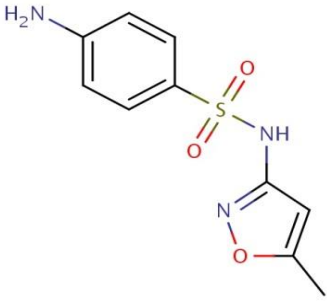
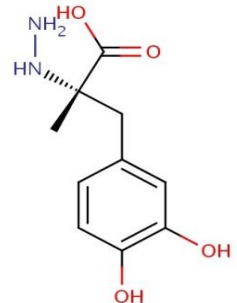
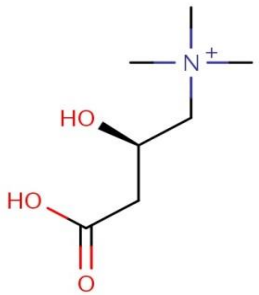
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
40		556-33-2	Glycyl-glycyl-glycine	143,19	49,33	0,94	0.5 M	
41		616-91-1	N-acetyl-L-cysteine	163,20	105,20	-0,38	612.8 mM	
42		7533-40-6	(S)-(+)-Leucinol / (S)-2-Amino-4-methyl-1-pentanol	117,19	46,25	0,56	NA	

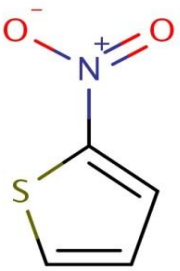
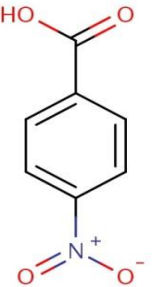
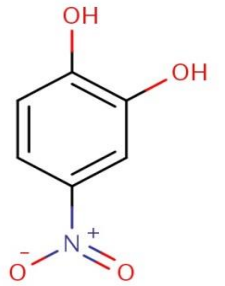
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
43		83-67-0	Theobromine / 2,6-Dihydroxy-3,7-dimethylpurine	180,17	67,23	-0,80	< 5.6 mM	1265 (rat oral)
44		210545-23-6	N-alpha-Acetyl-L-arginine dihydrate	216,24	130,80	-0,97	NA	
45		65-82-7	N-Acetyl-L-methionine	191,25	66,40	0,17	NA	

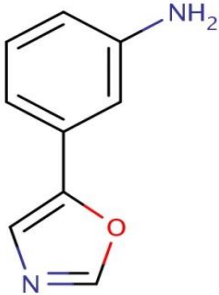
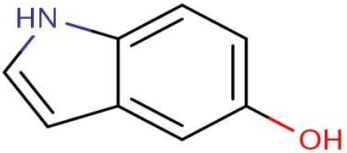
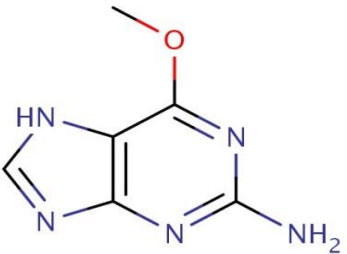
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
46		1468-26-4	8-Azaxanthine monohydrate	153,10	99,77	-1,18	NA	
47		115-02-6	Azaserine / O-Diazoacetyl-L-serine	173,13	101,98	-4,18	288.9 mM	
48		107-41-5	Hexylene glycol / (±)-2-Methyl-2,4-pentandiol	118,18	40,46	0,68	1 M	

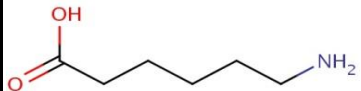
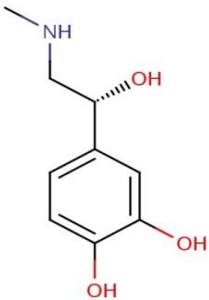
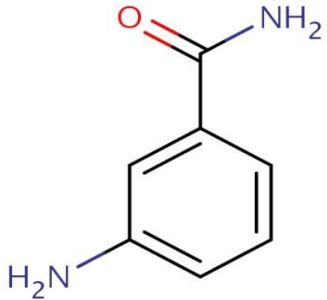
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
49		107-43-7	Betaine	117,15	40,13	-0,53	13.7 M	11179 (rat oral), 830 (mouse i.v.)
50		704-15-4	Gly-Pro / Glycylproline	172,18	83,63	-1,14	290.4 mM	
51		58-08-2	Caffeine / 1,3,7-Trimethylxanthine	194,19	58,44	-0,60	82.4 mM	367.7 (rat oral)

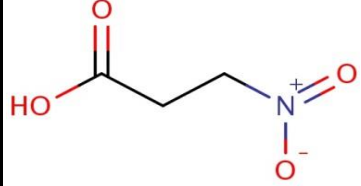
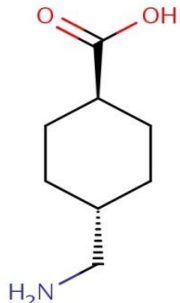
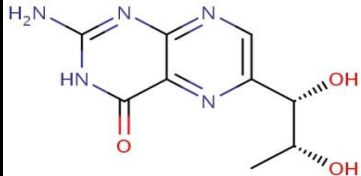
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
52		1118-68-9	N,N-Dimethylglycine	103,12	40,54	-0,33	485.0 mM	
53		543-38-4	L-Canavanine / L-α-Amino-γ-(guanidinoxy)-n-butyric acid	176,18	134,45	-3,61	567.5 mM	
55		73-40-5	Guanine / 2-Amino-1,7-dihydro-6H-purin-6-one	151,13	96,16	-1,32	165.5 mM in 5 M HCl	

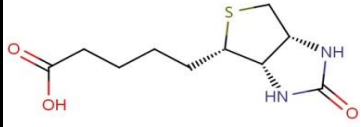
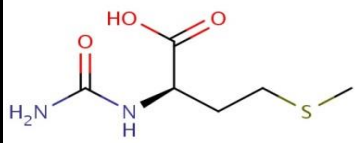
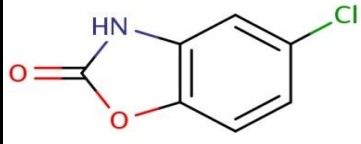
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
56		723-46-6	Sulfamethoxazole / 4-Amino-N-(5-methyl-3-isoxazolyl) benzenesulfonamide	253,28	98,22	0,93	< 4.0 mM	
57		28860-95-9	S-(-)-Carbidopa / (S)-3-(3,4-Dihydroxy-phenyl)-2- hydrazino-2-methylpropanoic acid	226,23	115,81	0,35	21.7 – 22.6 mM in methanol + 1 drop HCl	
58		541-15-1	L-Carnitine / Vitamin BT; (-)-(R)-3-Hydroxy-4- (trimethylammonio) butyrate	162,21	57,53	-1,13	310.2 mM	6890 (rat oral)

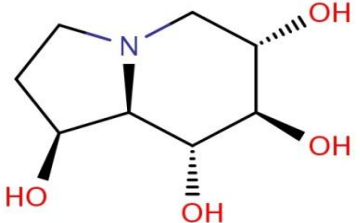
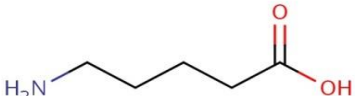
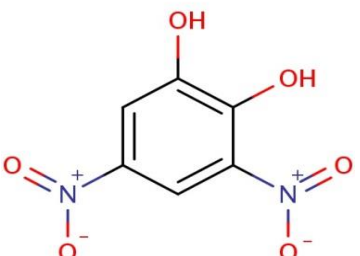
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
59		609-40-5	2-Nitrothiophene	129,14	45,82	1,70	NA	
60		62-23-7	4-Nitrobenzoic acid	167,12	83,12	1,52	< 59.8 mM	
61		3316-09-4	4-Nitrocatechol / 1,2-Dihydroxy-4-nitrobenzene	155,11	86,28	1,26	NA	

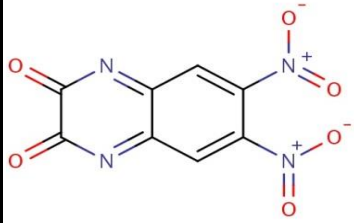
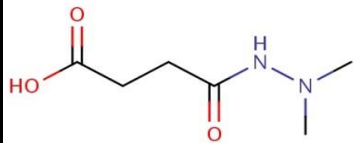
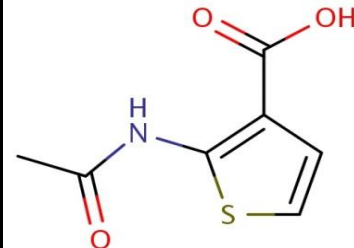
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) _a [[]	Solubility ^[b]	LD50 [mg/kg]
62		157837-31-5	3-(1,3-Oxazol-5-yl)aniline	160,18	52,05	0,75	NA	
63		1953-54-4	5-Hydroxyindole	133,15	36,02	2,00	NA	
64		20535-83-5	6-O-Methylguanine / 2-Amino-6-methoxypurine	165,16	89,71	-0,43	soluble in DMSO and water	

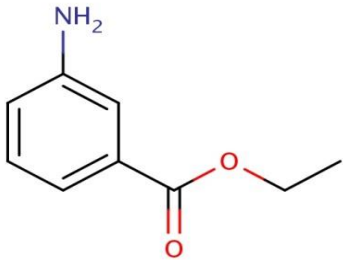
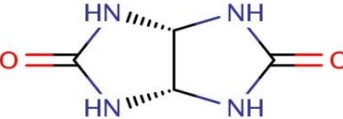
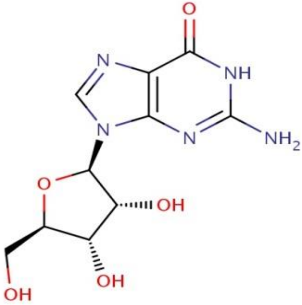
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
65		60-32-2	6-Aminocaproic acid	131,17	63,32	0,29	381.1 mM	
66		51-43-4	(-)-Epinephrine / (R)-(-)-3,4-Dihydroxy- α - (methylaminomethyl)benzyl alcohol	183,21	72,72	0,53	< 545.9 μ M / 272.9 mM in 0.5 M HCl	
67		3544-24-9	3-Aminobenzamide	136,15	69,11	0,21	183.6 mM / 367.1 mM in EtOH	

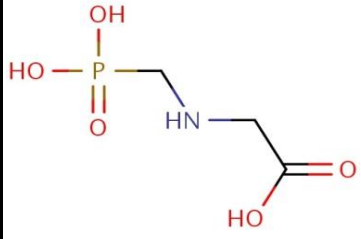
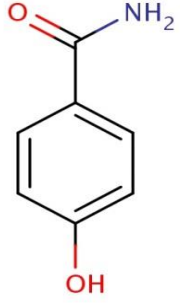
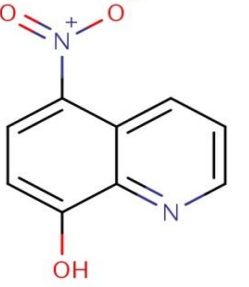
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
68		504-88-1	3-Nitropropionic acid	119,08	83,12	-0,22	839.6 mM in alcohol	
69		1197-18-8	trans-4-(Aminomethyl)cyclohexanecarboxylic acid	157,21	63,32	0,53	318.1 mM	
70		22150-76-1	6-Biopterin / (1'R,2'S)-Biopterin, 2-Amino-4-hydroxy-6-(1,2-dihydroxypropyl)pteridine	237,22	134	-2,0	3.0 mM	

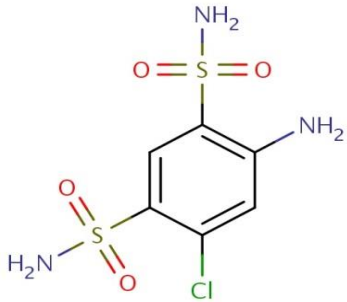
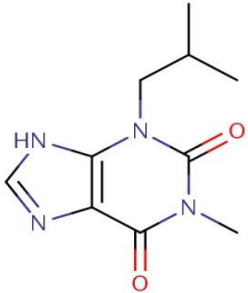
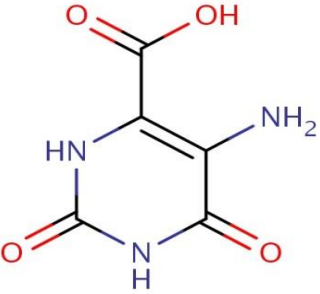
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
71		58-85-5	Biotin / Vitamin B7	244,31	78,43	0,32	204.7 mM in 2 M NH ₄ OH	
72		30411-84-8	4-methylsulfanyl-2-ureido-butyrlic acid	192,24	92,42	-0,55	NA	
73		95-25-0	Chlorzoxazone / 5-Chloro-2(3H)-benzoxazolone	169,57	38,33	1,80	294.8 mM in MeOH	763 (rat oral)

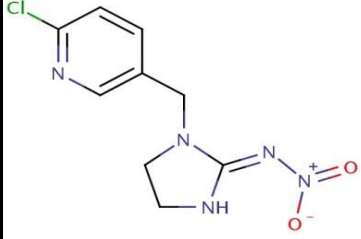
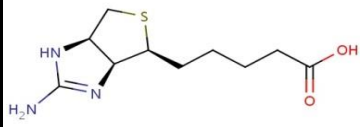
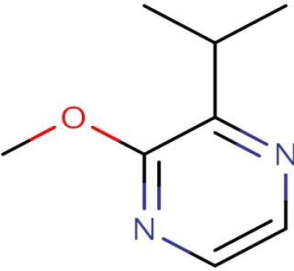
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
74		79831-76-8	Castanospermine / (1S,6S,7R,8R,8aR)-1,6,7,8-Tetrahydroxyoctahydroindolizidine	189,21	84	-2,3	105.7 mM in 1 N HCL	
75		660-88-8	5-Aminovaleric acid	117,15	63,32	-0,15	NA	
76		7659-29-2	3,5-Dinitrocatechol / 3,5-Dinitro-1,2-benzenediol	200,11	132,10	1,23	5.0 mM	

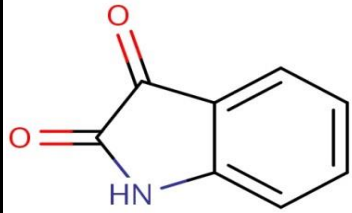
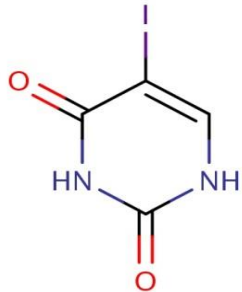
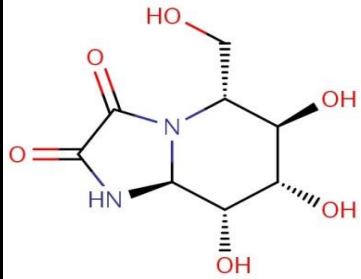
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) _a [[]	Solubility ^[b]	LD50 [mg/kg]
77		2379-57-9	DNQX / 6,7-Dinitroquinoxaline-2,3(1H,4H)- dione	250,13	150,50	0,32	1.2 mM / 38.9 – 40.5 mM in DMSO	
78		1596-84-5	Daminozide / Succinic acid mono(2,2- dimethylhydrazide)	160,17	69,64	-1,35	624.2 mM	
79		50901-18-3	3-(Acetylamino)thiophene-2-carboxylic acid	185,20	66,40	0,74	NA	

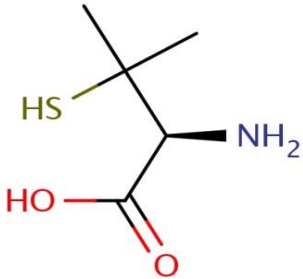
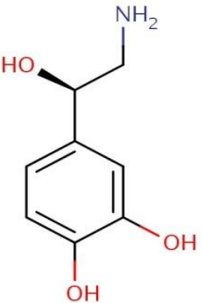
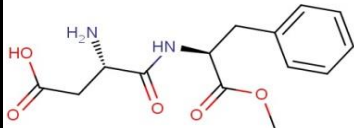
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
80		582-33-2	Ethyl 3-aminobenzoate	165,19	52,32	1,55	NA	
82		496-46-8	Glycoluril / Tetrahydroimidazo[4,5-d]imidazole-2,5-dione	142,12	82,26	-2,22	NA	
83		118-00-3	Guanosine / 9-(β-D-Ribofuranosyl)guanine	283,24	155,22	-2,89	2.7 mM /176.6 mM in acid:water (1:1)	

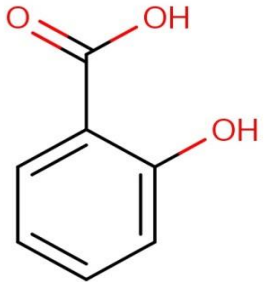
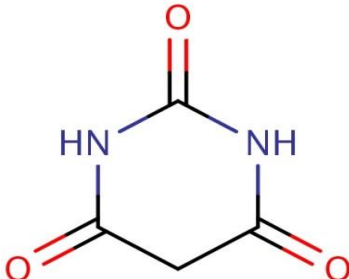
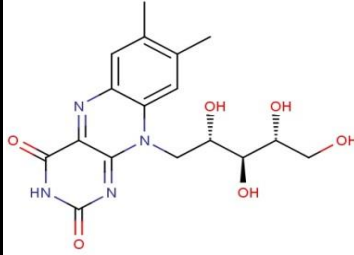
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
84		1071-83-6	Glyphosate / N-(phosphonomethyl) glycine	169,07	106,86	-2,21	71.0 mM	5000 (rat oral)
85		619-57-8	4-Hydroxybenzamide	137,14	63,32	0,54	NA	
86		4008-48-4	8-Hydroxy-5-nitroquinoline	190,16	78,94	1,73	NA	

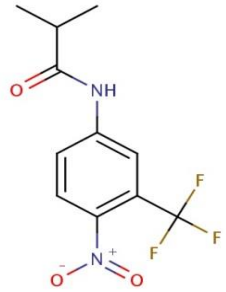
Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) _a [[]	Solubility ^[b]	LD50 [mg/kg]
87		121-30-2	4-Amino-6-chloro-1,3-benzenedisulfonamide	285,73	146,34	-1,25	NA	
88		28822-58-4	3-Isobutyl-1-methylxanthine	222,25	69,30	0,32	225.0 mM in warm MeOH	
89		7164-43-4	5-Aminoorotic acid	171,11	121,52	-1,64	NA	

Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) _a [[]	Solubility ^[b]	LD50 [mg/kg]
90		138261-41-3	Imidacloprid	255,66	86,34	2,16	2.4 mM	
91		13395-35-2	2-Iminobiotin	243,33	87,71	0,72	205.5 mM in 1 M HCl	
92		25773-40-4	2-Isopropyl-3-methoxypyrazine	152,20	35,01	1,10	NA	

Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) _a [[]	Solubility ^[b]	LD50 [mg/kg]
93		91-56-5	Isatin / 2,3-Dioxo-2,3-dihydroindole	147,13	46,17	0,44	12.9 mM	
94		696-07-1	5-Iodouracil / 2,4-Dihydroxy-5-iodopyrimidine	237,98	58,20	0,18	soluble in cold Water or 1 M NaOH	
95		109944-15-2	Kifunensine / Hexahydro-6R,7S,8aS-trihydroxy-5R- (hydroxy-methyl)-imidazo[1,2-a] pyridine-2,3-dione	232,19	130	-4,1	4.3 mM	

Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) ^[a]	Solubility ^[b]	LD50 [mg/kg]
96		52-67-5	D-Penicillamine / 3,3-Dimethyl-D-cysteine	149,21	102,12	-1,73	744.0 mM	6170 (rat oral)
97		51-41-2	(-)-Norepinephrine / (R)-4-(2-Amino-1-hydroxyethyl)-1,2-benzenediol	169,18	86,71	0,01	295.5 mM	
98		22839-47-0	Aspartame / N-(L-α-Aspartyl)-L-phenylalanine methyl ester	294,31	118,72	-0,02	NA	>10000 (rat oral)

Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) _a [[]	Solubility ^[b]	LD50 [mg/kg]
99		69-72-7	Salicylic acid / 2-Hydroxybenzoic acid	138,12	57,53	1,27	1M in EtOH	
100		67-52-7	Barbituric acid / 2,4,6-Trihydroxypyrimidine, Malonylurea	128,09	75,27	-1,38	1.1 M	> 5000 (rat oral)
101		83-88-5	(-)-Riboflavin / Vitamin B2	376,37	155,05	-1,21	26.6 mM in 0.1 M NaOH	

Fragment ID	Molecule	CAS #	Name	MW [Da] ^[a]	tPSA [Å ²] ^[a]	logP(o/w) _a ^[a]	Solubility ^[b]	LD50 [mg/kg]
102		13311-84-7	Flutamide / 2-Methyl-N-(4-nitro-3- [trifluoromethyl]phenyl)propanamide	276,21	74,92	2,95	181.1 mM in EtOH	

[a] calculated by MOE (Chemical Computing Group Inc.)
version 2014.09.

[b] in water at room temperature, if not stated otherwise

Table S2. Crystallographic fragment-screening campaigns reported in the literature.

Fragment library	No. of fragments	Screening method	Target protein	Hit rate (no. of hits)	Availability of library/ individual compounds	Reference
Self assembled	800	80 cocktails of 10 fragments	Soluble epoxide hydrolase	1% (8)	Not known	Amano <i>et al.</i> (2015)
Fragments of life (15% randomly selected)	200	25 cocktails of 8 fragments	Leukotriene A4 hydrolase	6% (13)	Yes	Davies <i>et al.</i> (2009)
Focused fragment library	80	-	Thrombin	2.5% (2)	Not known	Howard <i>et al.</i> (2006)
Virtual library of ring scaffolds with side chains a)	347	Cocktails of 6 fragments	β -Secretase	0.6% (2)	Not known	Murray <i>et al.</i> (2007)
The fragment based screening library from ActiveSight (a Rigaku company) b)	376	96 cocktails of 4 compounds	Phenylethanol amine N-methyltransferase	3.2% (12)	Yes	Drinkwater <i>et al.</i> (2010)
ActiveSight fragment library 1	384	96 cocktails of 4 fragments	Wild type HIV protease	~0.8% (3)	Possibly from ActiveSight	Perryman <i>et al.</i> (2010)
Inhouse assembled c)	775	143 cocktails of 4 to 8 fragments	HIV-1 reverse transcriptase	4.4% (34)	Partly	Bauman <i>et al.</i> (2012, 2013)
Small organic brominated molecules d)	18	6 cocktails of 3 fragments	Elongation factor Tu	5.6% (1)	Not known	Groftenhauge <i>et al.</i> (2013)

Compounds with at least one Br atom e)	68	Individual soaking	HIV-1 protease	3-6% (2-4)	Yes	Tiefenbrunn <i>et al.</i> (2014)
Inhouse assembled c)	775	143 cocktails of 4 to 8 fragments	Influenza endonuclease	1% (8)	Partly	Bauman <i>et al.</i> (2013)
Drug fragment set and focused phosphatase set	327 and 264	Cocktails of 2 to 8 fragments	P38 MAP kinase, CDK2, thrombin, ribonuclease A, PTP1B	0.5-10%	Not known	Hartshorn <i>et al.</i> (2005)

- a) based on the small number of commonly appearing ring scaffolds and side chains in drugs
- b) 384 compounds in total, X-ray diffraction data were collected for 94 cocktails
- c) 500 compounds purchased from Maybridge (Cornwall, UK), 175 individual compounds purchased based on recommendations of Christophe Verlinde and Wim Hol (Verlinde *et al.*, 2009), 100 compounds gifted by James Williamson (The Scripps Research Institute, La Jolla, unpublished)
- d) A library for organic synthesis (Department of Chemistry, Aarhus University) e) selected by Maybridge Hit Finder

The program Marvin was used for drawing, displaying and characterizing chemical structures (Marvin 6.3.1, 2014, Chemaxon; <http://www.chemaxon.com>)