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Supporting Information

Fragments as Novel Starting Points for tRNA-Guanine Transglycosylase Inhibitors Found by Alternative Screening Strategies

Engi Hassaan, Per-Olof Eriksson, Stefan Geschwindner, Andreas Heine, and Gerhard Klebe*

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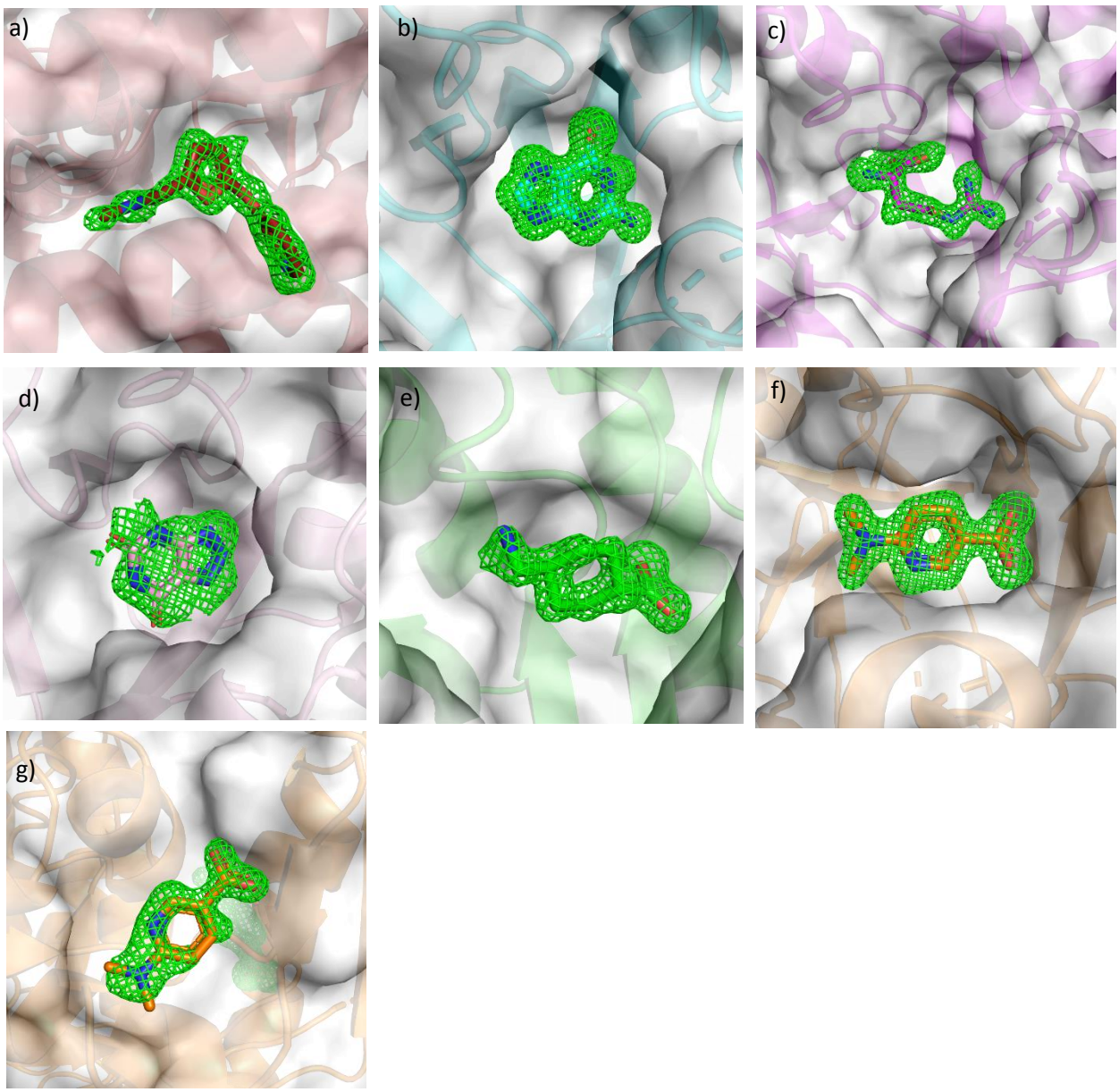


Figure S1: Electron density maps of the fragment hits found by X-ray crystallography in addition to the fragment coordinates a) J14, b) J64, c) J72, d) J79, e) J86, f) J14, pocket binder and g) J14, surface binder. The m|Fo|-|Fc| density map shown (green) is contoured at a sigma level of 3σ.

Table S1: Structures of fragments not included in SPR fragment screen.

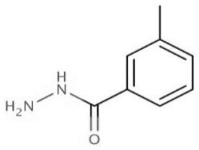
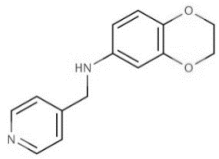
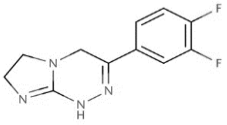
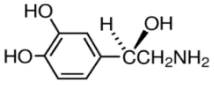
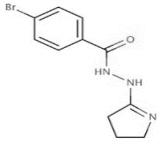
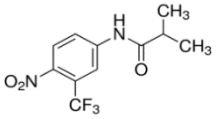
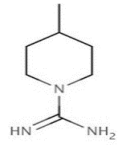
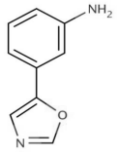
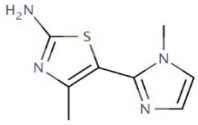
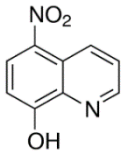
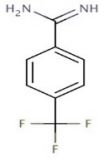
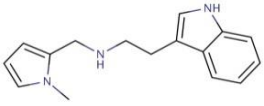
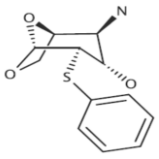
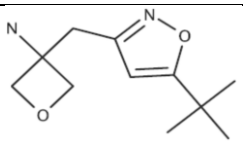
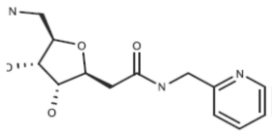
Jena Plate ID	Fragment	Jena Plate ID	Fragment
J1		J48	
J11		J74	
J16		J75	
J21		J83	
J26		J90	
J33		J35	
J53		J54	
J57			

Table S2: Structures of fragments not included in NMR fragment screen.

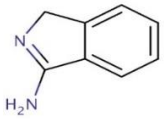
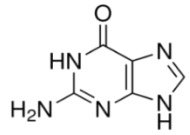
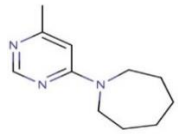
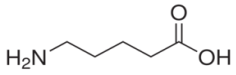
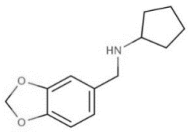
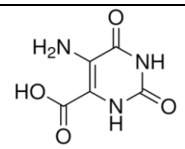
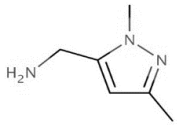
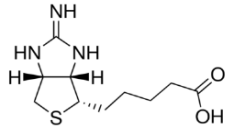
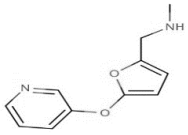
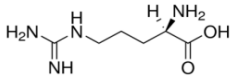
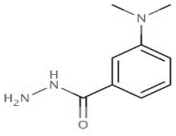
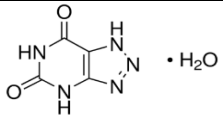
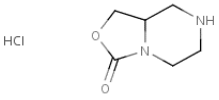
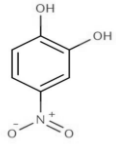
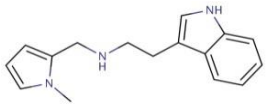
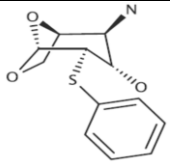
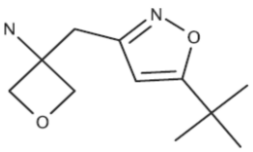
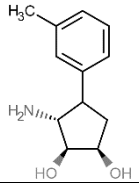
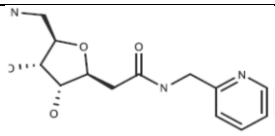
Jena Plate ID	Fragment	Jena Plate ID	Fragment
J2		J64	
J4		J67	
J6		J69	
J13		J73	
J14		J77	
J17		J79	
J59		J82	
J35		J53	
J54		J55	
J57			

Table S3: Data Collection and Refinement Statistics

PDB Code [a]	6FSO	5SW3	5N6F
Fragment Jena ID	J14	J41	J64
A) Data Collection and Processing			
Wavelength	0.9184	1.000	0.9184
Beamline	BESSY BEAMLINE 14.1	ELETTRA BEAMLINE 5.2R	BESSY BEAMLINE 14.1
Detector	PILATUS 6M	DECTRIS PILATUS 2M	PILATUS 6M
Resolution range (Å)	43.29 - 1.45 (1.54 - 1.45)	44.46 - 1.38 (1.46 - 1.38)	44.28 - 1.12 (1.19 - 1.12)
Space group	C 1 2 1	C 1 2 1	C 1 2 1
Unit cell parameters (a,b,c Å)	90.9 64.9 70.8	89.0 64.1 70.5	88.7 64.9 70.7
Unit cell parameters (α, β, γ °)	90.0 95.7 90.0	90.0 92.8 90.0	90.0 93.4 90.0
Matthews coefficient [b] Å^3/Da)	2.5	2.4	2.5
Solvent content [b] (%)	51.1	49.4	50.8
Total reflections	183142 (27068)	303178 (47561)	537838 (59077)
Unique reflections	68249 (10718)	81197 (12961)	149008 (20548)
Multiplicity	2.7	3.7	3.6
Completeness (%)	94.8 (92.3)	99.7 (98.9)	97.1 (83.2)
Mean I/sigma(I)	9.8 (2.2)	12.4 (2.5)	10.3 (2.0)
Wilson B-factor (Å^2)	11.5	13.6	10.9
R-sym [c] (%)	7.3 (48.6)	6.0 (49.3)	6.1 (48.7)
R-meas (%)	9.0 (60.8)	6.9 (57.7)	7.1 (59.2)
CC1/2	99.6 (76.3)	99.8 (79.7)	99.7 (72.0)
B) Refinement			
Resolution range (Å)	43.29 - 1.45	44.46 - 1.38	44.28- 1.12
Total reflections used in refinement	68178	81188	148997
Reflections used for R-work	64769	77129	141547
Reflections used for R-free	3409	4059	7450
Final R value for R-work (%)	16.6	13.3	13.6
Final R value for R-free (%)	18.6	16.2	15.4
No. of Protein residues	368	371	365
No. of Water molecules	252	223	280
No. of Ligand molecules	1	2	1
No. of Other ligand molecules	8	6	4
RMSD bond lengths (Å)	0.008	0.007	0.007
RMSD bond angles (°)	1.0	0.9	1.0
Ramachandran plot [d]			
Residues in most favored regions (%)	93.9	95	96.1
Residues in additionally allowed regions (%)	5.4	4.7	3.6
Residues in generously allowed regions (%)	0.3	0.3	0.3
Residues in disallowed regions (%)	0	0	0
Average B-factor all atoms [e] (Å^2)	16.2	17.9	16.1
Protein main chain	13.4	15.7	13.7
Protein side chain	16.6	18.2	16.1
Protein all atoms	15.1	17.0	15.0
Ligand	21.6	30.1	12.2
Water molecules	25.5	26.4	27.4
Other ligands	36.3	36.3	33.5
Number of TLS groups	6	N/A	N/A

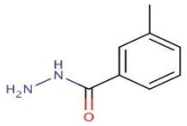
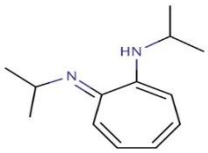
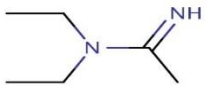
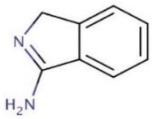
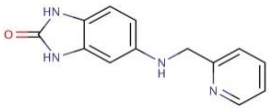
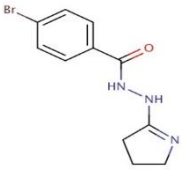
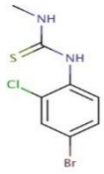
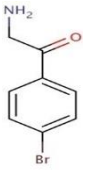
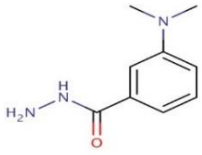
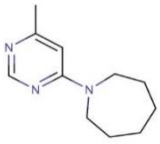
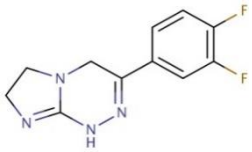
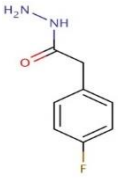
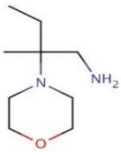
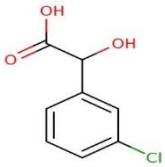
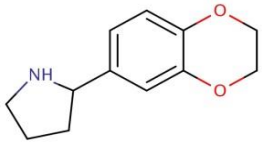
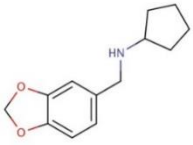
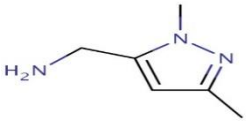
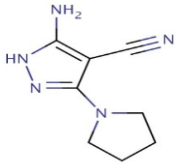
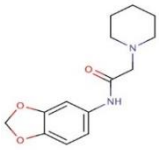
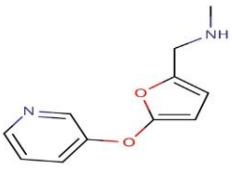
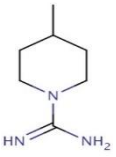
a) Statistics for the highest-resolution shell are shown in parenthesis, b) calculated with *Matthews_coef* program from *CCP4* suite version 7.0.047[1], c) calculated by the equation: (SUM(ABS(I(h,i)-I(h))))/(SUM(I(h,i))) d) calculated with *PROCHECK*[2], e) calculated with *MOLEMAN*[3], f) other ligands include DMSO, PEG, Glycerol, 1PE, ACT, PG4, Zn.

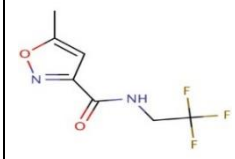
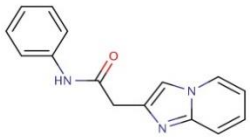
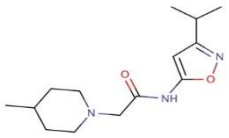
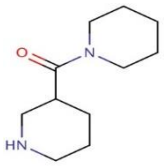
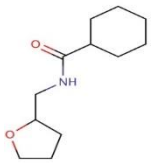
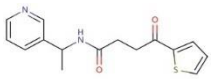
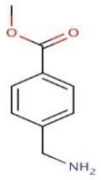
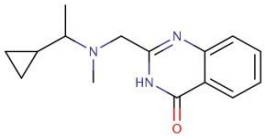
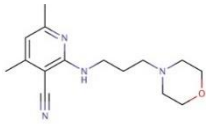
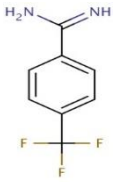
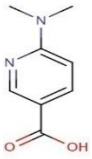
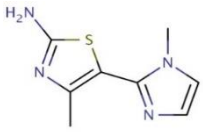
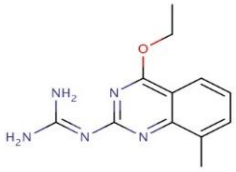
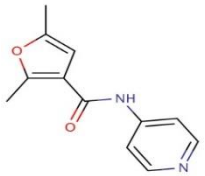
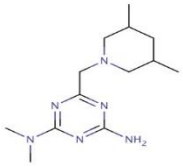
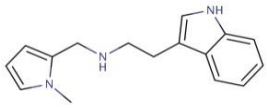
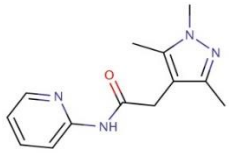
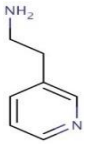
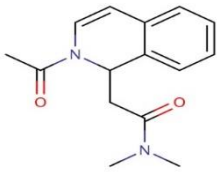
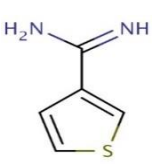
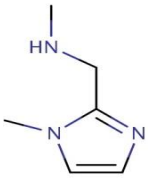
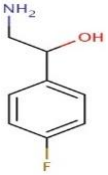
Table S4: Data Collection and Refinement Statistics.

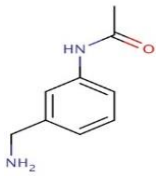
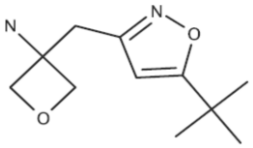
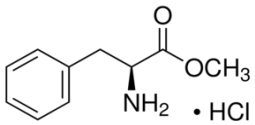
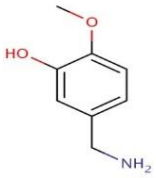
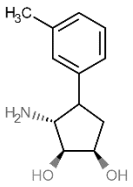
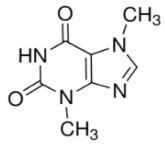
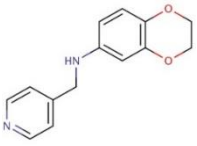
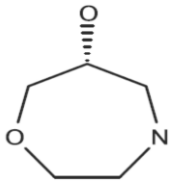
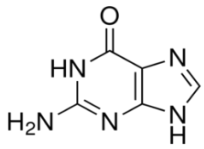
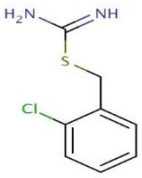
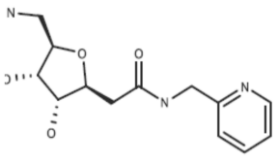
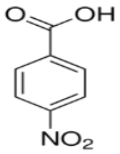
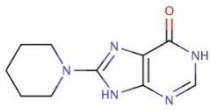
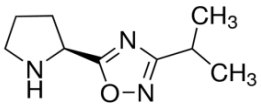
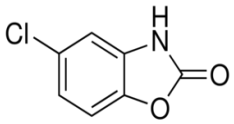
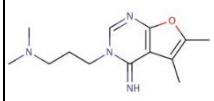
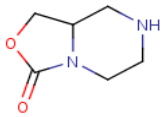
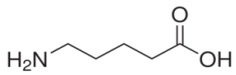
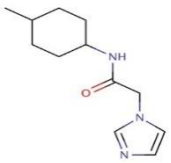
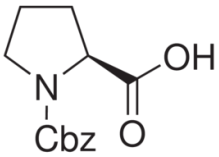
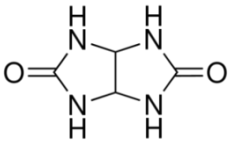
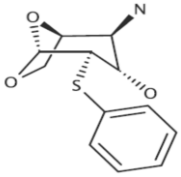
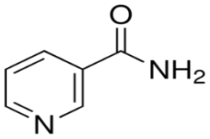
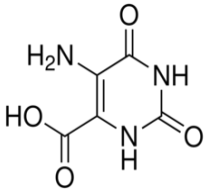
PDB Code [a]	5UTI	5UTJ	5V3C
Fragment Jena ID	J72	J79	J86
A) Data Collection and Processing			
Wavelength	1.000	0.9184	0.9184
Beamline	ELETTRA BEAMLINE 5.2R	BESSY BEAMLINE 14.1	BESSY BEAMLINE 14.1
Detector	DECTRIS PILATUS 2M	PILATUS 6M	PILATUS 6M
Resolution range (Å)	44.51 - 1.36 (1.44 - 1.36)	44.50 - 1.55 (1.64 - 1.55)	44.33 - 1.42 (1.51 - 1.42)
Space group	C 1 2 1	C 1 2 1	C 1 2 1
Unit cell parameters (a,b,c Å)	89.2 64.3 70.9	89.1 64.8 70.5	88.8 63.7 70.4
Unit cell parameters (α, β, γ °)	90.0 93.1 90.0	90.0 93.2 90.0	90.0 92.6 90.0
Matthews coefficient [b] ($Å^3$/Da)	2.5	2.5	2.4
Solvent Content [b] (%)	50.1	51.0	48.8
Total reflections	239209 (38188)	219498 (34906)	276359 (43372)
Unique reflections	81480 (12780)	58079 (9314)	73712 (11753)
Multiplicity	2.9	3.8	3.8
Completeness (%)	95.0 (92.5)	99.7 (99.4)	99.4 (98.4)
Mean I/sigma(I)	11.6 (2.3)	15.4 (2.0)	15.6 (2.0)
Wilson B-factor ($Å^2$)	15.4	18.0	15.7
R-sym [c] (%)	5.0 (44.5)	5.2 (55.6)	4.6 (55.1)
R-meas (%)	6.1 (54.2)	6.0 (64.7)	5.4 (64.3)
CC1/2	99.8 (81.6)	99.9 (77.4)	99.9 (74.1)
B) Refinement			
Resolution range (Å)	44.51 - 1.36	44.50 - 1.55	44.33 - 1.42
Total reflections used in refinement	81466	58069	73705
Reflections used for R-work	77393	55166	70020
Reflections used for R-free	4073	2903	3685
Final R value for R-work (%)	13.5	14.7	13.4
Final R value for R-free (%)	15.8	17.7	15.5
No. of Protein residues	371	364	373
No. of Water molecules	269	322	359
No. of Ligand molecules	1	1	1
No. of Other ligand molecules	4	4	6
RMSD bond lengths (Å)	0.007	0.008	0.007
RMSD bond angles (°)	0.9	0.9	0.9
Ramachandran plot [d]			
Residues in most favored regions (%)	94.6	94.2	94
Residues in additionally allowed regions (%)	5	5.5	5.6
Residues in generously allowed regions (%)	0.3	0.3	0.3
Residues in disallowed regions (%)	0	0	0
Average B-factor all atoms [e] ($Å^2$)	20.5	24.6	22.1
Protein main chain	17.9	22.1	19.7
Protein side chain	20.9	25.9	22.5
Protein all atoms	19.5	24.1	21.1
Ligand	27.1	57.5	26.8
Water molecules	29.8	30.4	31.2
Other ligands	44	36.4	46
Number of TLS groups	N/A	N/A	N/A

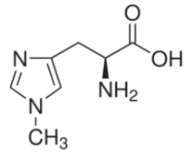
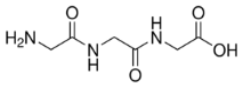
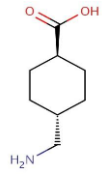
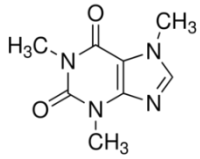
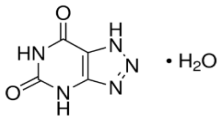
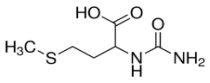
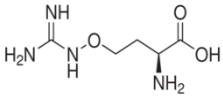
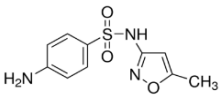
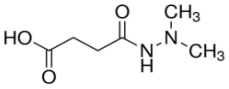
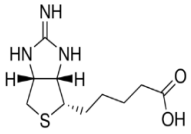
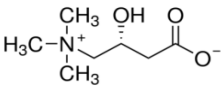
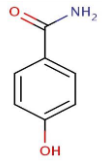
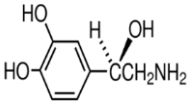
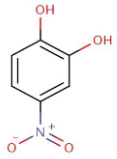
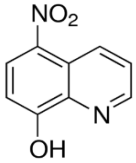
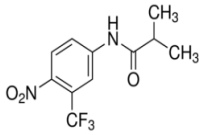
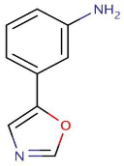
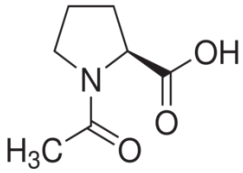
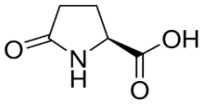
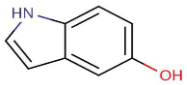
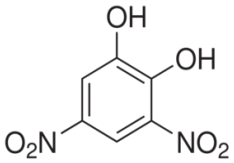
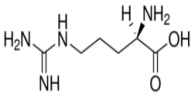
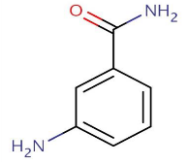
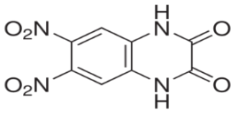
a) Statistics for the highest-resolution shell are shown in parenthesis, b) calculated with *Matthews_coef* program from *CCP4* suite version 7.0.047[1], c) calculated by the equation: (SUM(ABS(I(h,i)-I(h))))/(SUM(I(h,i))) d) calculated with *PROCHECK*[2], e) calculated with *MOLEMAN*[3], f) other ligands include DMSO, PEG, Glycerol, 1PE, ACT, PG4, Zn.

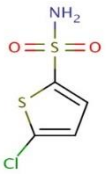
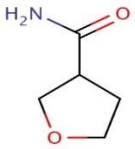
Table S5: Chemical Structures of the 96 fragments. Marvin was used for displaying chemical structures, Marvin 6.3.1, 2014, ChemAxon (http://www.chemaxon.com) and the web server chemicalize.com

Jena Plate ID	Fragment	Jena Plate ID	Fragment	Jena Plate ID	Fragment
1		8		15	
2		9		16	
3		10		17	
4		11		18	
5		12		19	
6		13		20	
7		14		21	

22		**30**		**38**	
23		**31**		**39**	
24		**32**		**40**	
25		**33**		**41**	
26		**34**		**42**	
27		**35**		**43**	
28		**36**		**44**	
29		**37**		**45**	

46		**54**		**62**	
47		**55**		**63**	
48		**56**		**64**	
49		**57**		**65**	
50		**58**		**66**	
51		**59**	HCl 	**67**	
52		**60**		**68**	
53		**61**		**69**	

70		**78**		**86**	
71		**79**		**87**	
72		**80**		**88**	
73		**81**		**89**	
74		**82**		**90**	
75		**83**		**91**	
76		**84**		**92**	
77		**85**		**93**	

94		**95**		**96**