Electronic Supplementary Material (ESI) for Medicinal Chemistry Communications
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Table S1. Key distances and RMSDs for molecular fragments found in the best ranked docking pose for compounds 1 to 3 compared to those in crystal structures. All values are in Å. Entries coloured green are within 1 Å for distances or 2 Å for RMSDs. Entries coloured amber are RMSDs slightly above 2 Å.

Protein being docked into:	P1							P2							P3							
Compound being docked and geometric parameter:	Gold			Glide				Gold			Glide				Gold			Glide				
1	1	2	3	SP1	XP1	SP2	XP2	1	2	3	SP1	XP1	SP2	XP2	1	2	3	SP1	XP1	SP2	XP2	Expt
Fe-N	5.74	6.36	9.58	6.47	2.48	4.83	4.13	6.65	6.36	5.03	8.46	4.02	2.51	7.04	11.2	4.83	11.5	9.13	14.5	4.79	4.01	2.178
O-NH	12.4	10.3	8.03	4.21	3.88	4.14	5.62	8.5	10.5	14.7	7.99	5.53	3.67	9.31	12.2	11.6	8.15	14	6.47	16.6	14.6	3.79
C-O=C	13.9	13.5	6.22	6.72	3.23	7.36	8.35	11.5	13.7	14	6.37	8.39	3.1	12.5	14.7	14.6	6.27	16.6	4.87	16.5	14.6	2.974
Pyrimidine-Imidazole RMSD	4.2	4.41	7.1	3.91	0.66	3.01	3.56	4.69	4.27	3.14	4.95	3.75	0.73	4.57	6.52	2.46	6.46	4.59	9.53	2.71	3.32	
Benzdioxolane RMSD	8.75	8.83	4.46	4.37	1.97	6.99	8.04	7.76	8.79	8.92	4.21	8.29	0.64	8.07	9.11	9.11	5.01	11	4.15	10.8	9.14	
2																						
Fe-N	12.4	6.86	12.7	4.16	10.3	6.71	4.14	12.5	6.7	12.4	8.58	2.61	2.64	14.8	15.1	6.36	5.72	5.71	9.49	12.2	11.5	2.262
O-NH	8.04	5.99	8.05	15.3	5.59	12.6	9.59	7.99	6.35	8.05	3.65	3.92	3.2	7.17	8.49	13.8	11.9	18.8	19.2	8.93	8.11	3.53
C-O=C	6.27	9.64	6.3	16.3	9.6	14.6	12.8	6.24	9.27	6.28	2.64	3.22	3.52	5.73	6.51	14	14.2	19	19.2	6.89	6.17	3.147
Pyrimidine-Imidazole RMSD	6.96	4.37	7.22	2.36	5.49	4.4	3.39	7.13	4.24	7.04	4.35	0.46	0.39	9.96	8.72	4.3	4.43	2.52	3.99	6.56	6.19	
Benzdioxolane RMSD	4.87	6.83	4.91	10.3	5.53	8.87	9.08	4.92	6.91	5.03	1.75	0.88	0.82	4.34	5.81	8.06	8.63	13.6	13.7	5.87	5.59	
Kalypsys1																						
NHLig-O=C	5.36	9.77	6.79	10.8	10.5	3.11	9.2	4.92	9.56	6.92	8.34	9.15	9.61	9.21	2.82	2.98	2.83	3.09	3.12	3.1	3.07	3.042
C=Olig-NH	4.34	8.44	8.48	9.74	9.6	2.68	8.74	9.58	9.06	8.59	9.32	9.1	9.12	8.63	2.88	2.85	2.89	2.96	2.99	2.97	2.97	2.883
quinoline RMSD	2.68	5.61	3.74	6.7	6.36	2.38	5.74	4.07	5.16	3.8	5.48	6.33	6.21	5.75	2.12	2.08	2.13	2.09	2.1	2.09	2.09	
5,6_het_cyclobutyl	4.64	4.97	4.7	6.06	6.08	5.52	6.33	4.72	5.13	4.72	4.74	6.22	6.18	6.24	4.97	0.5	4.98	0.23	0.37	0.71	0.46	

Table S2. Docking scores for the highest ranking pose obtained for docking each compound into each protein structure/

				P1				P2				P3				P1			P2			P3		
Cpd	pIC50	clogP	LLE	SP1	XP1	SP2	XP2	SP1	XP1	SP2	XP2	SP1	XP1	SP2	XP2	GOLD1	GOLD2	GOLD3	GOLD1	GOLD2	GOLD3	GOLD1	GOLD2	GOLD3
1	9.0	1.75	7.3	-4.6	-5.4	-5.3	-6.1	-4.9	-7.2	-7.0	-4.4	-4.6	-5.5	-3.5	-4.1	74.7	67.6	72.6	39.3	42.2	35.3	75.8	69.9	69.6
2	9.5	2.28	7.3	-5.6	-6.7	-5.1	-5.8	-4.7	-6.6	-6.2	-6.1	-6.4	-6.9	-2.0	-5.3	81.9	82.7	74.6	41.5	41.1	37.1	80.9	84.5	74.9
3	7.0	1.41	5.6	-6.6	-5.4	-5.8	-5.4	-5.7	-5.5	-5.1	-5.2	-8.6	-9.1	-9.1	-9.2	64.4	62.3	74.3	41.8	41.0	46.4	60.0	63.7	74.2
4	8.0	3.93	4.0	-6.1	-7.1	-6.1	-6.9	-6.6	-7.9	-7.0	-7.1	-8.7	-9.3	-9.0	-10.	62.5	66.0	84.9	42.2	43.3	48.8	62.6	65.3	85.8

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5	4.0	2.26	1.7	-6.2	-6.1	-5.4	-6.8	-6.0	-7.2	-6.6	-7.5	-6.5	-8.0	-7.3	-7.6	62.1	64.5	70.7	41.2	41.2	42.2	62.8	61.4	72.7
6	5.9	3.83	2.1	-5.8	-7.7	-5.8	-7.5	-6.4	-7.7	-6.4	-7.5	-8.8	-9.4	-9.2	-10.6	64.9	64.7	75.1	42.3	45.2	51.2	65.3	68.1	75.7
7	5.7	4.39	1.3	-5.2	-7.3	-4.7	-6.7	-5.1	-7.9	-5.9	-7.1	-8.2	-8.8	-8.7	-9.4	61.0	64.7	80.8	43.0	42.3	45.8	59.0	64.0	81.7
8	4.0	5.85	-1.8	-5.8	-6.0	-5.0	-5.2	-6.3	-5.4	-5.4	-7.2	-5.5	-6.9	-7.3	-7.5	68.8	68.8	73.3	48.2	45.5	45.7	70.0	65.8	75.0
9	4.0	4.37	-0.4	.	.	.	.	.	-2.7	.	.	.	.	.	.	67.0	72.3	71.3	43.6	43.6	43.3	66.2	72.2	71.2
10	4.0	5.07	-1.1	-6.4	-7.0	-4.8	-6.6	-6.7	-5.6	-6.0	-8.0	-6.3	-7.6	-7.6	-8.7	61.0	65.1	80.2	47.6	47.6	50.9	62.3	65.3	80.1
11	6.1	4.86	1.3	-5.4	-6.2	-5.6	-6.4	-6.7	-6.9	-6.0	-8.0	-7.5	-7.7	-8.0	-9.7	67.7	65.0	77.1	47.7	47.2	49.5	66.4	66.3	77.7
12	7.1	3.24	3.8	-5.2	-6.7	-4.9	-6.6	-5.3	-7.3	-5.1	-6.2	-6.8	-7.5	-7.3	-8.1	68.5	64.5	81.8	47.1	44.7	49.0	67.4	65.3	82.3
13	8.7	4.06	4.6	-5.2	-7.3	-5.5	-6.6	-5.8	-7.8	-7.0	-6.9	-8.7	-9.5	-6.6	-10.6	62.8	63.7	85.1	40.4	41.1	46.0	62.3	64.2	85.8
14	6.1	4.46	1.6	-6.3	-6.7	-4.9	-6.9	-5.6	-7.7	-5.9	-7.3	-8.1	-8.8	-9.0	-9.8	61.0	65.6	80.3	43.2	42.9	43.2	61.2	65.0	81.6
15	6.7	4.95	1.7	-5.5	-6.7	-5.0	-6.5	-5.3	-6.5	-6.8	-6.3	-6.6	-7.8	-8.5	-9.1	67.1	66.0	77.0	46.5	43.1	49.0	68.7	66.6	77.5
16	7.7	3.43	4.3	-5.9	-6.9	-4.8	-6.6	-5.6	-6.0	-5.3	-6.3	-6.9	-7.3	-7.4	-8.9	66.1	64.9	83.3	44.3	42.6	46.2	67.6	67.9	83.6

Table S3. Distances found in QM optimized complexes for compounds 1, 2 and 13' compared to the experimental values found for 1 to 3. All values are in Å. Entries coloured green are within 0.1 Å and entries coloured amber are within 0.2 Å.

	B3LYP		HF	M06		M06-2X		M06HF	M06L		ωB976XD		
	DOUBLET	SEXTET	DOUBLET	DOUBLET	SEXTET	DOUBLET	SEXTET	DOUBLET	DOUBLET	SEXTET	DOUBLET	SEXTET	Expt.
1													
Fe-N	2.14	2.61		2.12	2.46	2.26	2.39		2.11	2.49	2.1	2.49	2.18
O-NH	3.11	3.11		3.32	3.33	3.3	3.3		3.4	3.33	3.36	3.26	3.79
C-O=C	3.57	3.6		3.16	3.16	3.11	3.11		3.2	3.19	3.18	3.15	2.97
Fe-S	2.24	2.38		2.21	2.34	2.49	2.35		2.21	2.37	2.21	2.32	2.08
2													
Fe-N	2.15	2.61		2.11	2.53	2.27	2.38		2.12	2.56	2.1	2.2	2.26
O-NH	3.1	3.12		3.38	3.13	3.44	3.47		3.64	3.19	3.45	3.58	3.53
C-O=C	3.57	3.54		3.07	3.27	2.98	2.96		2.97	3.21	3.04	3.04	3.15
Fe-S	2.24	2.38		2.21	2.34	2.5	2.35		2.21	2.37	2.21	2.39	2.17

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13'													
NHLig-O=C	3.13	3.13	3.01	2.99	3	2.96	2.96	2.92	3.02	3.03	3	3.01	3.04
C=Olig-NH	2.92	2.92	3.33	2.89	2.89	2.86	2.87	2.84	2.87	2.88	2.86	2.87	2.88
Fe-S	2.21	2.33	3.37	2.21	2.29	2.6	2.32	2.74	2.17	2.32	2.22	2.28	2.34
Summary													
MAE	0.26	0.35	0.24	0.13	0.22	0.18	0.18	0.08	0.13	0.22	0.13	0.17	
MAE excl Fe-S	0.30	0.38	0.24	0.15	0.22	0.14	0.16	0.08	0.14	0.21	0.14	0.16	
MAE Fe-S	0.12	0.17	0.34	0.10	0.16	0.33	0.16	0.13	0.11	0.17	0.10	0.17	

Table S4. Complexation energies in kcal/mol $E_{complex}$ computed for compounds with the QM model system.

	B3LYP		HF	M06		M06HF	M06L		M06-2X		ωB97XD	
Compound	Doublet	Sextet	Doublet	Doublet	Sextet		Doublet	Sextet	Doublet	Sextet	Doublet	Sextet
1	1.84	11.42	.	-4.26	3.95	.	-25.46	-14.82	-18.18	-14.88	-25.90	-16.21
2	-1.08	8.46	.	-6.31	2.73	.	-25.19	-13.37	-19.22	-15.78	-26.60	23.63
4'	-12.16	-11.94	-16.57	-27.03	-26.46	-35.10	-34.07	-32.71	-36.14	-35.07	-39.36	-38.16
5'	-15.44	-14.81	-15.34	-23.15	-22.87	-27.58	-26.73	-26.48	-28.51	-28.22	-31.57	-31.22
6'	-13.20	-13.36	-14.62	-26.10	-26.18	-29.65	-32.06	-32.23	-32.37	-32.40	-38.75	-38.34
7'	-6.11	-5.91	-12.53	-20.02	-19.43	-26.52	-27.51	-26.04	-28.08	-27.36	-31.08	-30.12
8'	-2.41	-3.46	-12.87	-13.82	-13.04	.	-21.82	-20.54	-22.17	-21.17	-26.13	-24.84
9'	-5.59	-4.06	.	-13.42	-13.88	-19.40	-21.76	-20.54	.	-22.64	-26.58	16.89
10'	-0.12	0.04	-11.32	-10.35	-9.41	-14.53	-18.01	-16.89	-17.50	-16.62	-21.38	31.08
11'	-5.60	-5.49	-14.98	-16.86	-16.10	-23.00	-24.19	-22.98	-24.65	-23.63	-28.50	28.32
12'	-9.02	-8.90	.	-23.59	-22.67	-32.72	-30.29	-29.02	-32.70	-31.69	-35.95	-34.85
13'	-12.37	-12.13	-15.37	-26.93	-26.20	-35.55	-33.91	-32.87	-36.17	-35.42	-39.00	-37.99
14'	-6.12	-5.95	-13.31	-19.48	-18.87	-26.68	-27.46	-26.21	-27.77	-27.36	-30.57	-29.77
15'	-5.28	-5.86	-14.80	-17.37	-16.97	-23.92	-24.64	-23.71	-25.14	-24.39	-28.94	-27.95
16'	-9.35	-9.20	-27.00	-23.64	-22.89	-33.25	-30.32	-29.26	-32.83	-32.20	-35.81	-34.90