Supporting Information for: A Systematic Analysis of the Binding Affinity Between the Pim-1 Kinase and Its Inhibitors Based on the MM/3D-RISM/KH Method

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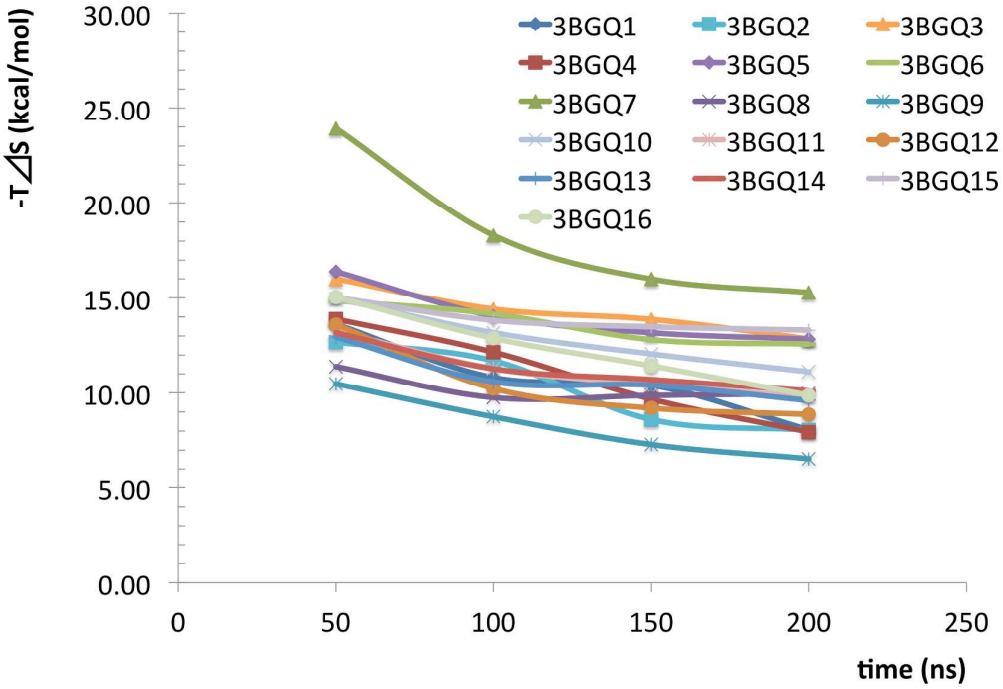

Figure S1. Running average of $-T\Delta S_{solute}$ over the elapsed time during the simulation that provide the rate of convergence. The figures indicate that $-T\Delta S_{solute}$ seems to be hardly converged, and is still decreasing for most of ligands.

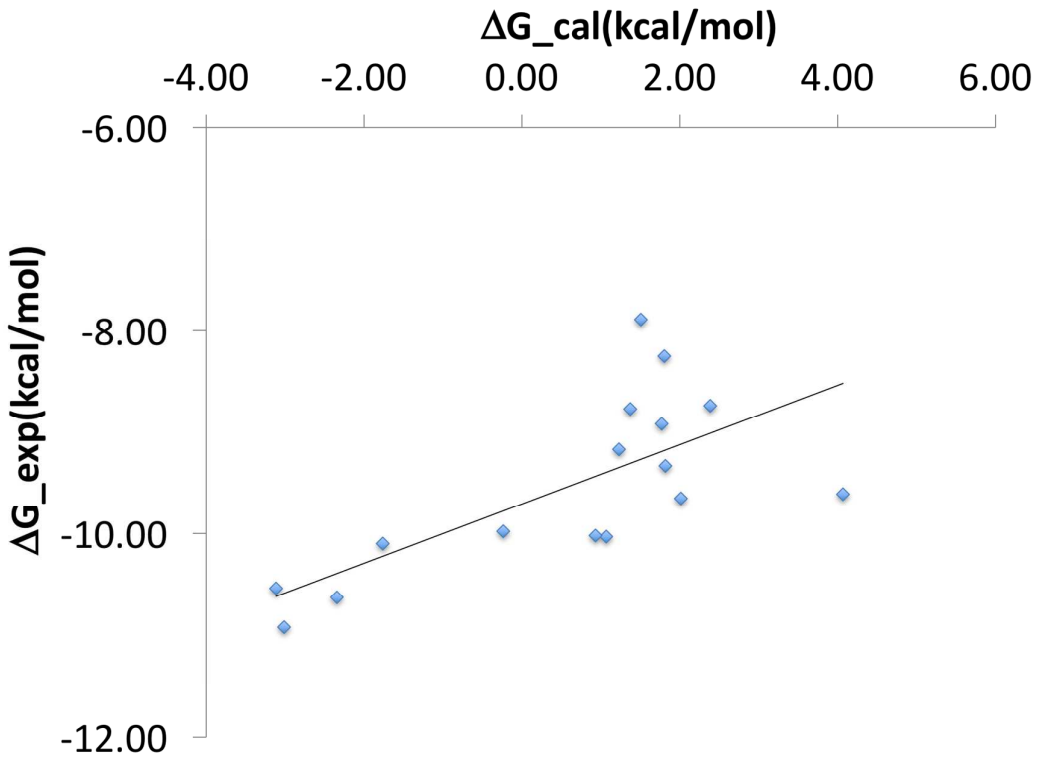

Figure S2 Correlation between calculated and experimental values of binding free energy for the all ligands. Theoretical values are estimated by means of the MM/3D-RISM method with the collection based on a partial molar volume. This collection brings the theoretical value to the lower side. Correlation coefficient R = 0.70.

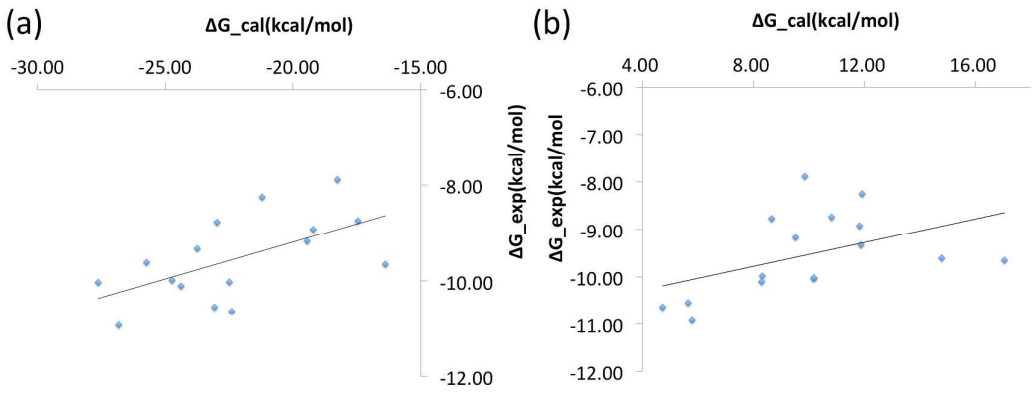

Figure S3. Correlation between experimental and calculated values of binding free energy for the all ligands by means of the MM/GBSA method (a) and MM/PBSA method (b). Quasi-harmonic method is applied for estimating the structural entropy. Correlation coefficient, R, between the experimental values and result of the MM/GBSA method is 0.59. Correlation coefficient, R, between the experimental values and result of the MM/PBSA method is 0.46.

Table S1. Local contribution around the ligand fragment of the desolvation free energy and interaction energy for each system.

Scaffold, Alkane, and Phenyl denote the triazolo[4.3-b]pyridazine scaffold , cyclo-alkane, and phenyl ring. ΔE and $\Delta G_{desolve}$ denote that the local contribution from the ligand fragments to the interaction energy for the residues in Class I and Class II and the desolvation free energy.

No.	Scaffold		Alkane		Phenyl	
	$\Delta G_{desolve}$ (kcal/mol)	ΔE (kcal/mol)	$\Delta G_{desolve}$ (kcal/mol)	ΔE (kcal/mol)	$\Delta G_{desolve}$ (kcal/mol)	ΔE (kcal/mol)
1	24.30	-6.50	49.34	-5.71	-4.54	-4.52
2	25.68	-7.22	52.78	-4.20	8.09	-3.94
3	17.16	-4.41	49.98	-2.52	23.99	0.68
4	18.28	-4.89	52.11	-6.01	4.92	-3.34
5	24.79	-7.94	51.76	-4.94	4.41	-4.58
6	7.41	-7.67	33.61	-5.59	-4.60	-4.77
7	4.69	-7.83	35.36	-5.53	0.10	-4.39
8	-1.42	-3.47	33.02	-1.00	19.42	-4.43
9	22.27	-4.70	38.18	-3.47	5.87	-3.06
10	22.22	-7.18	46.10	-2.93	4.28	-6.26
11	11.23	-4.28	36.27	-0.99	19.70	-4.25
12	10.92	-4.95	39.89	-2.16	13.96	-3.41
13	12.76	-7.29	46.50	-3.43	7.42	-5.55
14	11.52	-6.56	38.86	-2.54	9.56	-5.84
15	22.38	-8.01	44.19	-4.57	-6.11	-5.11
16	25.63	-6.89	51.41	-4.84	1.90	-4.27
average	16.24	-6.24	43.71	-3.78	6.77	-4.19