Supporting Information

for

Solvation Thermodynamics in Different Solvents – Water-Chloroform Partition Coefficients from Grid Inhomogeneous Solvation Theory

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Table S1: Calculated reference Energies and densities for CHCl3, OPC, and OPC3.

SOLVENT MODEL	$\mathbf{E_{VV}}$**-REF** $\frac{kcal}{mol}$	$\boldsymbol{\rho_0}$ $\frac{particles}{A^3}$
$CHCl_3$	-8.099	0.00768
OPC	-12.266	0.03325
OPC3	-11.720	0.0333

Table S2: Enthalpic contributions to the differences in solvation free energy between water and chloroform. All values are given in kcal/mol.

	SOLVENT	**A**	**G**	**C**	**T**	**U**	**W**	**Y**	**F**
GAFF2	**TIP3P**	13.7	11.4	13.9	8.5	9.1	3.2	4.3	2.7
	TIP4P	10.1	11.3	13.3	8.6	9.3	2.8	5.0	3.1
	TIP5P	10.7	12.2	11.3	6.1	7.1	6.4	8.5	4.0
	OPC	9.5	9.3	11.2	7.2	7.3	3.4	3.6	1.4
	OPC3	9.3	8.3	9.4	6.4	5.8	0.5	1.8	1.4
	SPCE	13.3	13.6	15.9	10.6	11.1	4.7	6.5	5.6

Table S3: Entropic contributions to the differences in solvation free energy between water and chloroform. All values are given in kcal/mol.

	SOLVENT	**A**	**G**	**C**	**T**	**U**	**W**	**Y**	**F**
GAFF2	**TIP3P**	11.8	7.9	8.5	8.1	7.1	7.0	6.8	5.6
	TIP4P	11.5	9.6	9.2	9.0	8.0	8.1	8.4	7.1
	TIP5P	13.5	13.4	10.6	9.0	8.1	10.1	11.1	6.8
	OPC	14.0	12.3	11.4	11.3	9.9	11.4	10.6	10.4
	OPC3	14.4	11.5	11.1	11.8	9.9	10.3	9.9	9.5
	SPCE	14.1	11.2	12.0	11.3	9.6	9.8	9.9	8.7

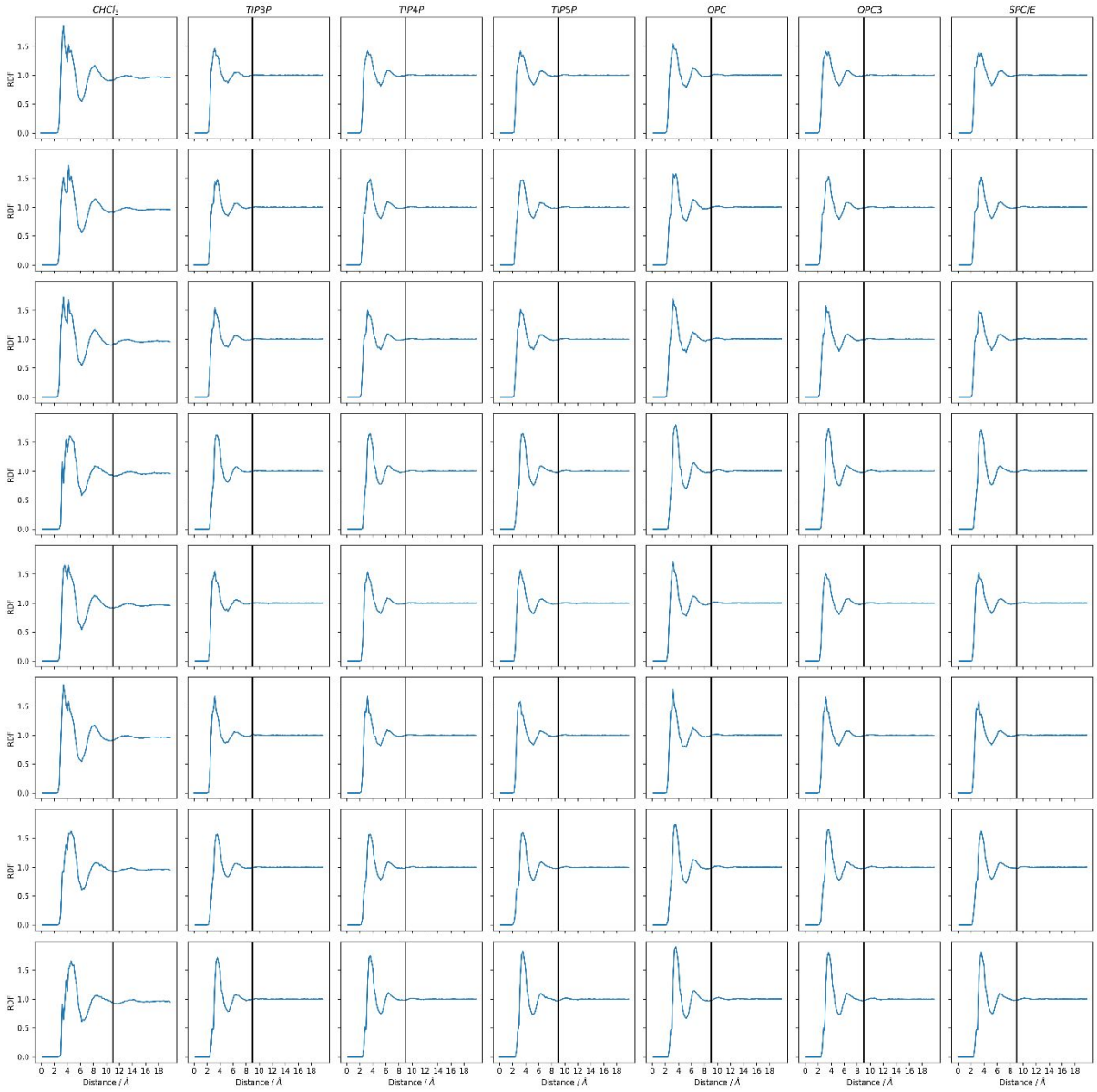

Figure S1: The different RDFs for the different compounds. On the left, the RDF of the compound in Chloroform is shown. On the right hand, the RDF for the compounds in water (TIP3P model) is shown. For both sides our chosen cutoff is shown as a black line (11 Å for Chloroform, and 9 Å for water). For chloroform, the heavy atom (compounds) to C (chloroform) distance was used, and for water the heavy atom (compounds) to O (water) distance was used. From left to right, the plots depict the RDFs for CHCl3, TIP3P, TIP4P, TIP5P, OPC, OPC3, SPC/E. And the different compounds are ordered from top to bottom: Cytosine, Thymine, Uracil, Tryptophane, Adenine, Guanine, Tyrosine, Phenylalanine.

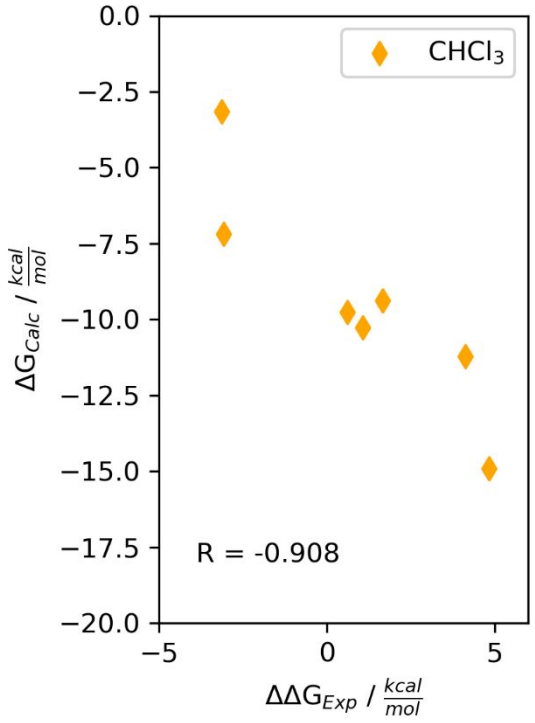

Figure S2: Solvation free energy of the different compounds in chloroform, compared with the experimentally determined difference in solvation free energy between water and chloroform. The Pearson correlation coefficient (R) is given within the graph.

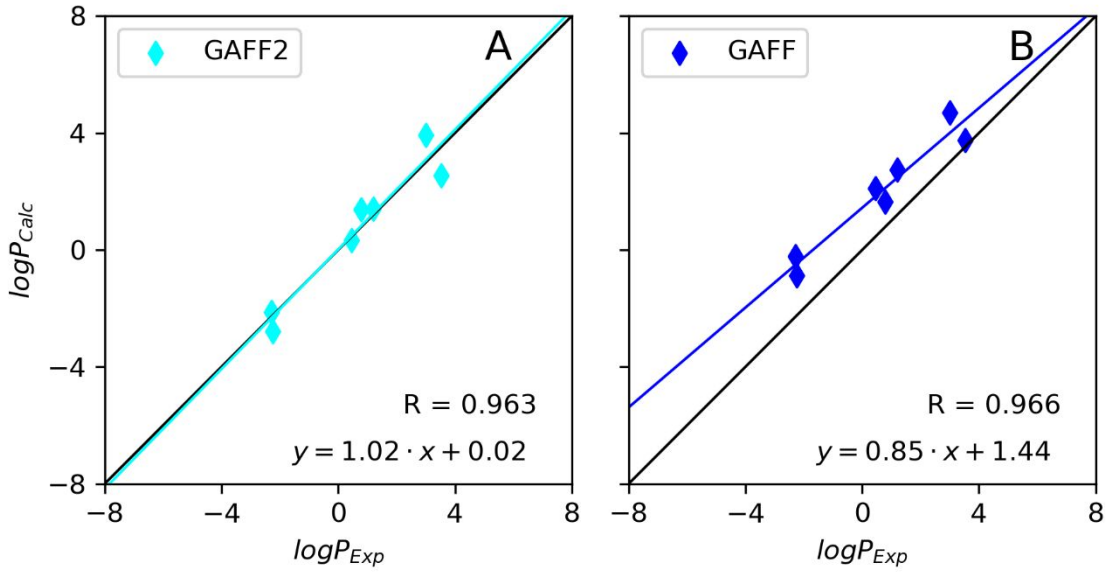

Figure S3: Values of the partition coefficients between chloroform and TIP3P water calculated with GAFF2 and GAFF are plotted against the experimental values. The Pearson correlation coefficient and the parameters for the linear fit are given within the graph.

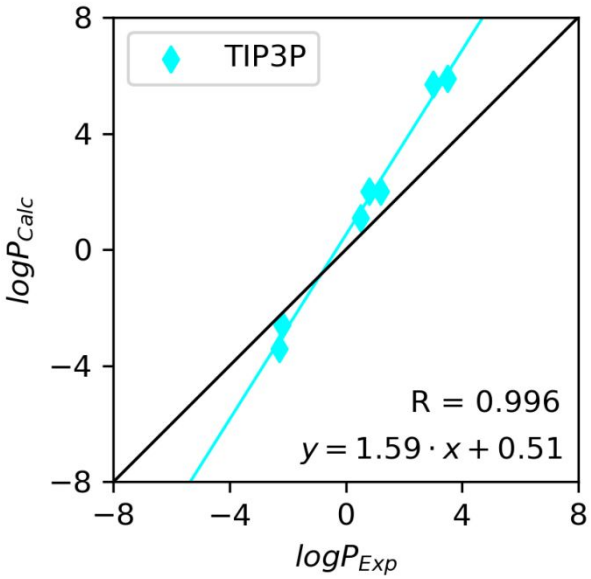

Figure S4: Values of the partition coefficients calculated by Wolf and Groenhof are plotted against the experimental values. The Pearson correlation coefficient and the parameters for the linear fit are given within the graph.

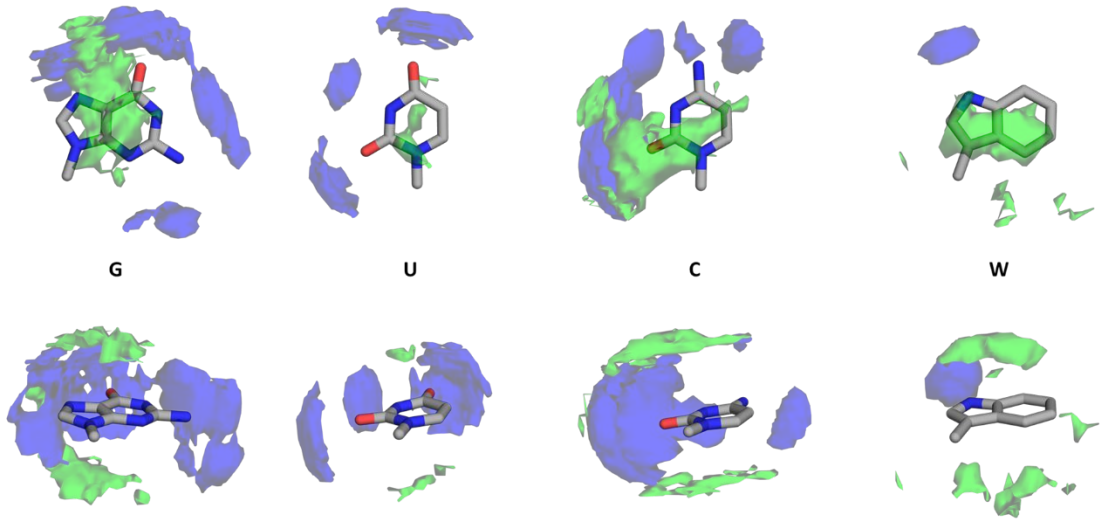

Figure S5: Difference in solvation free energy between water and chloroform. Blue regions are favorable water interaction sites (<-0.05 kcal/mol/Å^3), green regions are favorable chloroform interaction sites (>0.05 kcal/mol/Å^3). (**G**) 9-methylguanine, (**U**) 1-methyluracil, (**C**) 1-methylcytosine, (**W**) 3-methylindole.

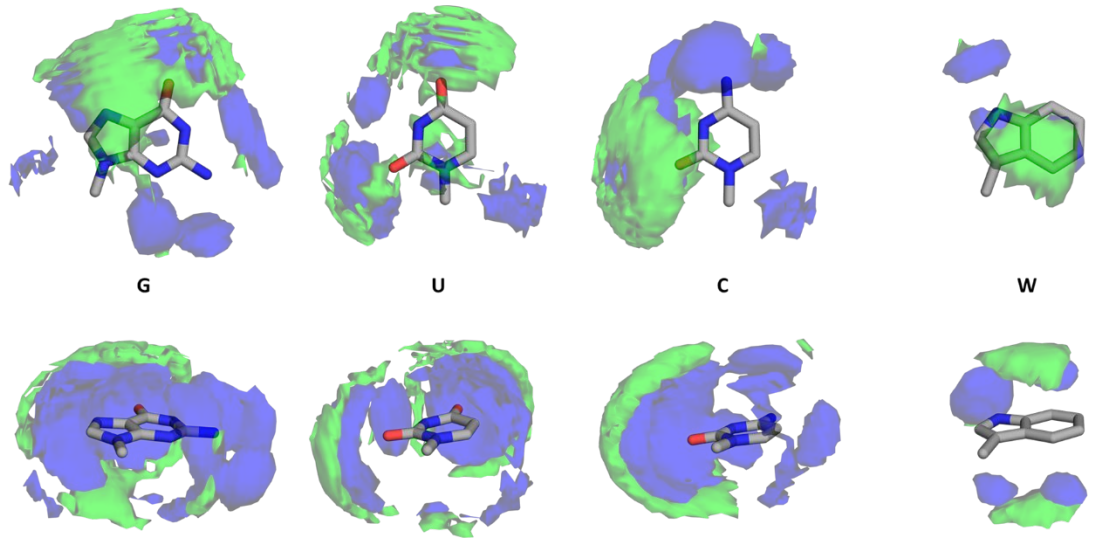

Figure S6: Difference in the enthalpic contributions to solvation free energy between water and chloroform, visualized as a grid. Blue regions are favorable water interaction sites (-0.05 kcal/mol/Å^3), green regions are favorable chloroform interaction sites (0.05 kcal/mol/Å^3). (**G**) 9-methylguanine, (**U**) 1-methyluracil, (**C**) 1-methylcytosine, (**W**) 3-methylindole.

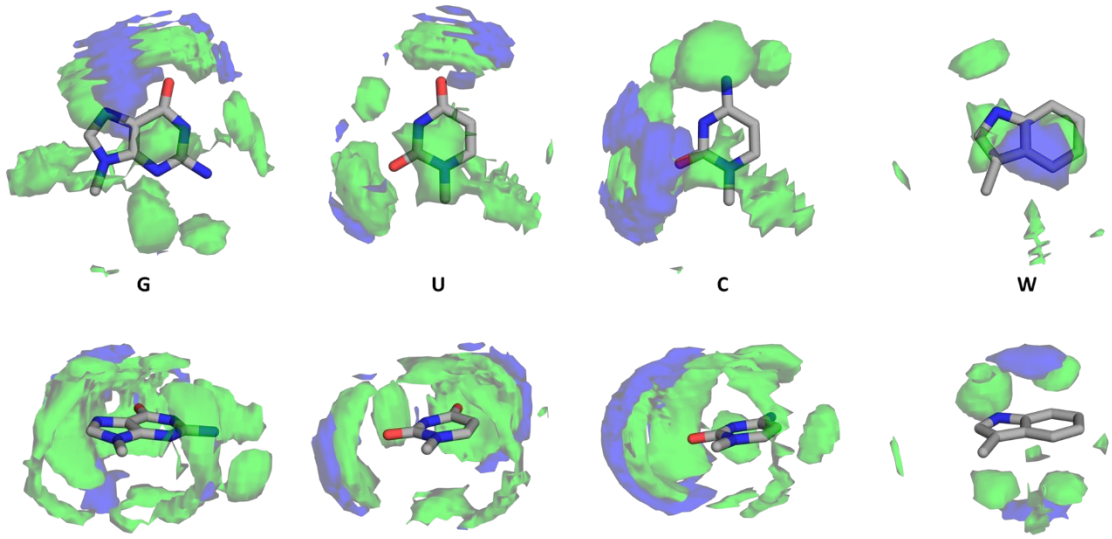

Figure S7**:** Difference in the entropic contributions to solvation free energy between water and chloroform, visualized as a grid. Note that for the entropic contributions, -TΔS is visualized. Blue regions are favorable water interaction sites (-0.05 kcal/mol/Å^3), green regions are favorable chloroform interaction sites (0.05 kcal/mol/Å^3). (**G**) 9-methylguanine, (**U**) 1-methyluracil, (**C**) 1-methylcytosine, (**W**) 3-methylindole.

TI calculations

For the calculation of the solvation free energy with TI, we used the equilibrated structures of the GIST calculations. We then performed 10 ns of simulation on the 11 lambda windows from 0.0 to 1.0, with a 0.1 spacing between these lambda windows. We used the softcore potentials implemented in the CUDA accelerated version of pmemd in AMBER. The solvation free energy was then calculated by using the trapezoid integration scheme. The logP was then calculated as described in the main manuscript. The solute was simulated unrestrained, but all other simulations parameters are identical as stated in the Methods section in the main text.

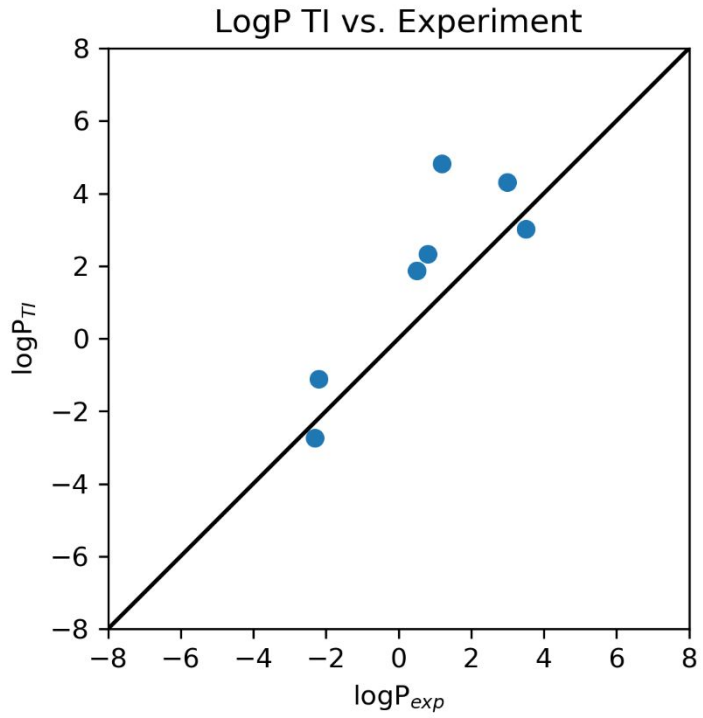

Figure S8 Values of the partition coefficient between chloroform and TIP3P water are plotted against the experimentally determined values.

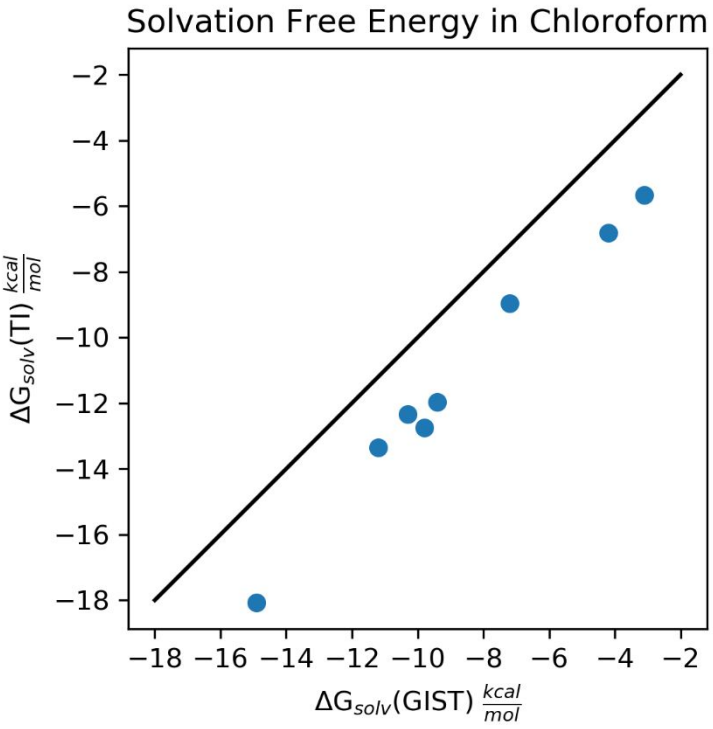

Figure S9 The solvation free energy calculated with TI against the solvation free energy calculated with GIST of the different compounds in chloroform.

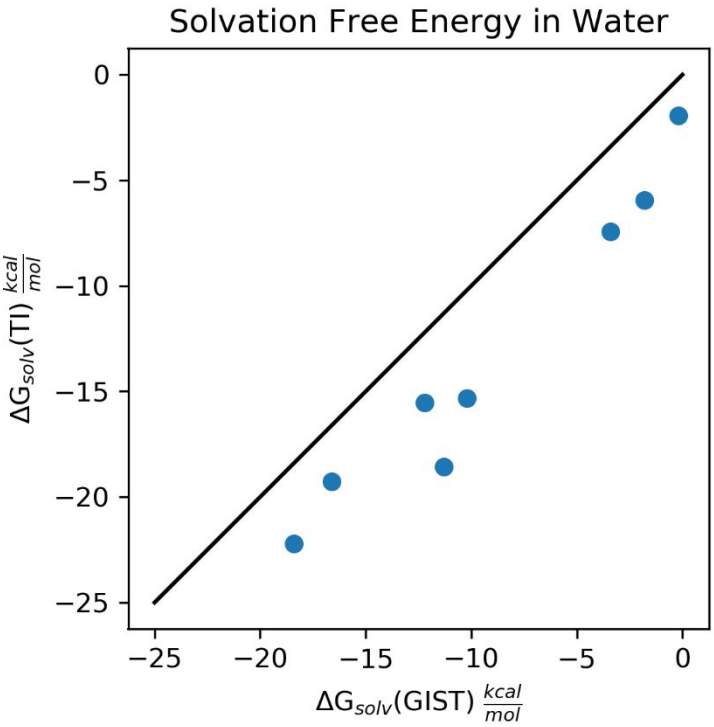

Figure S10 The solvation free energy calculated with TI against the solvation free energy calculated with GIST of the different compounds in TIP3P water.