Evaluation of CM5 Charges for Non-Aqueous Condensed Phase Modeling

Supporting Information

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Table S1. Comparison of Previous and Recomputed OPLS-AA Heats of Vaporization (kcal/mol) and Densities (g/cm^3) for 22 Organic Liquids at 25ºC.

	ΔH_{vap}			Density		
Molecule Name	**OPLS-AA**	**Previous**	**Expt.[a]**	**OPLS-AA**	**Previous**	**Expt.[a]**
acetic acid	12.26	12.51	12.49	1.066	1.059	1.044
acetone	7.23	7.24	7.48	0.797	0.795	0.784
acetonitrile	7.57	7.59	8.01	0.759	0.765	0.776
aniline	11.88	12.78	12.60	1.013	1.036	1.017
benzonitrile	12.52	12.55	12.54	0.994	0.995	1.001
cyclohexane	7.56	7.80	7.86	0.752	0.755	0.774
diethylamine	7.68	7.84	7.48	0.706	0.709	0.699
diethyl ether	6.90	6.80	6.56	0.707	0.708	0.708
N,N-dimethylacetamide	13.44	11.99	11.75	0.963	0.911	0.936
ethanethiol	6.67	6.79	6.58	0.859	0.855	0.833
ethanol	10.29	10.29	10.11	0.798	0.799	0.785
furan	6.91	6.77	6.56	0.935	0.943	0.931
hexane	7.54	8.07	7.54	0.640	0.677	0.661
methanol	9.00	8.95	8.95	0.779	0.779	0.786
methyl acetate	7.99	7.74	7.72	0.943	0.929	0.928
nitroethane	9.78	9.99	9.94	1.024	1.029	1.040
N-methylacetamide[b]	13.87	13.55	13.30	0.917	0.907	0.894
phenol	14.58	14.09	13.82	1.052	1.050	1.058
propylamine	7.90	7.80	7.47	0.719	0.717	0.711
pyridine	9.76	9.80	9.61	0.968	0.977	0.978
pyrrole	10.32	10.60	10.80	0.971	0.987	0.966
tetrahydrofuran	7.52	7.49	7.61	0.853	0.855	0.884
MUE	**0.35**	**0.20**		**0.014**	**0.013**	

[a] Refs. 32-40. [b] At 100ºC.

Table S2. Mean Unsigned Errors in Computed Liquid Properties from CM5 Scale Factors Optimized Independently for Each Molecule.

Molecule	Independent Scale Factor	MUE ΔH_{vap}(kcal/mol)	MUE ρ(g/cm^3)
acetic acid	1.16	0.05	0.04
aniline	1.12	0.09	0.01
benzonitrile	0.93	0.25	0.01
acetonitrile	1.14	0.04	0.02
cyclohexane	0.39	0.08	0.02
diethylamine	1.30	0.13	0.00
N,N-dimethylacetamide	0.97	0.20	0.00
diethyl ether	0.87	0.09	0.02
methyl acetate	0.92	0.18	0.01
ethanol	1.27	0.08	0.00
ethanethiol	1.23	0.01	0.03
furan	0.99	0.00	0.00
hexane	0.79	0.03	0.02
acetone	1.08	0.04	0.03
methanol	1.29	0.27	0.02
nitroethane	1.09	0.06	0.01
N-methylacetamide	1.01	0.07	0.03
phenol	1.25	0.07	0.01
propylamine	1.34	0.68	0.01
pyridine	1.01	0.06	0.02
pyrrole	1.16	0.08	0.01
tetrahydrofuran	1.12	0.43	0.03

Table S3. Computed Heats of Vaporization (kcal/mol) and Densities (g/cm^3) for 1.14*CM5 and 1.20*CM5 charges at 25ºC.

	ΔH_{vap}			Density		
Molecules	**1.14*CM5**	**1.20*CM5**	**Expt.[a]**	**1.14*CM5**	**1.20*CM5**	**Expt.[a]**
acetic acid	12.10	13.16	12.49	1.072	1.082	1.044
aniline	12.89	13.69	12.60	0.816	0.828	0.784
benzonitrile	14.28	14.81	12.54	0.760	0.785	0.776
acetonitrile	7.97	8.80	8.01	1.013	1.023	1.017
cyclohexane	7.69	7.56	7.86	1.008	1.011	1.001
diethylamine	6.88	7.22	7.48	0.755	0.750	0.774
N,N-dimethylacetamide	13.83	14.73	11.75	0.684	0.692	0.699
diethyl ether	7.03	7.14	6.56	0.707	0.710	0.708
methyl acetate	9.17	9.56	7.72	0.962	0.981	0.936
ethanol	7.91	8.96	10.11	0.852	0.854	0.833
ethanethiol	6.41	6.47	6.58	0.758	0.774	0.785
furan	6.86	7.03	6.56	0.934	0.942	0.931
hexane	7.40	7.44	7.54	0.640	0.640	0.661
acetone	7.91	8.36	7.48	0.727	0.747	0.786
methanol	6.73	7.71	8.95	0.973	0.984	0.928
nitroethane	10.35	10.96	9.94	1.041	1.053	1.040
N-methylacetamide[b]	15.99	17.16	13.30	0.950	0.952	0.894
phenol	12.47	13.13	13.82	1.040	1.045	1.058
propylamine	6.14	6.49	7.47	0.675	0.684	0.711
pyridine	10.38	10.78	9.61	0.971	0.983	0.978
pyrrole	10.38	11.37	10.80	0.969	0.983	0.966
tetrahydrofuran	7.62	7.83	7.61	0.848	0.856	0.884
MUE	**0.89**	**1.06**		**0.022**	**0.023**	

[a] Refs. 32-40. [b] At 100ºC.

Table S4. MUE in GB/SA Free Energies of Hydration Calculated Using CM1A and CM5 Charges Scaled by Different Scale Factors.[a]

CM1A		CM5	
Scale Factor	**MUE**	**Scale Factor**	**MUE**
1.00	1.19	1.00	1.82
1.03	1.15	1.09	1.37
1.04	1.14(4)	1.18	1.08
1.05	**1.14(3)**	1.19	1.08
1.06	1.15	1.20	1.07
1.07	1.16	**1.21**	**1.06**
1.08	1.17	1.22	1.06
1.09	1.20	1.23	1.07
1.18	1.55	1.24	1.07
1.27	2.10	1.27	1.10
1.36	2.88	1.36	1.37

[a] Optimal Scale Factors are highlighted in bold.

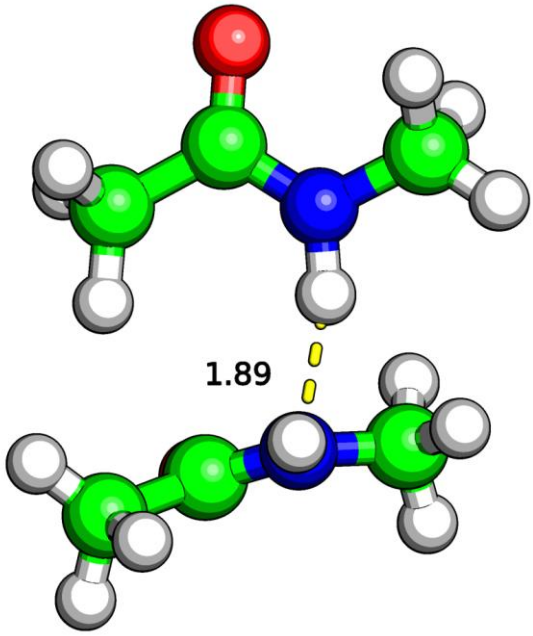

Figure S1. Dimers of *N*-methylacetamide with π-type hydrogen bonds observed in 1.14*CM1A pure liquid simulations.

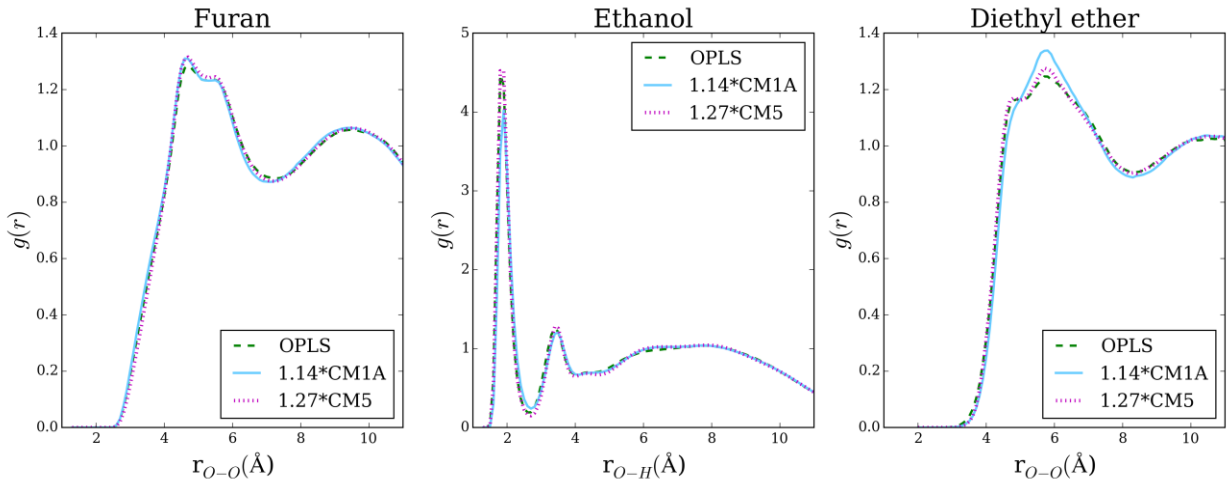

Figure S2. Radial distribution functions from OPLS-AA, OPLS/1.14*CM1A and OPLS/1.27*CM5 pure liquid simulations.

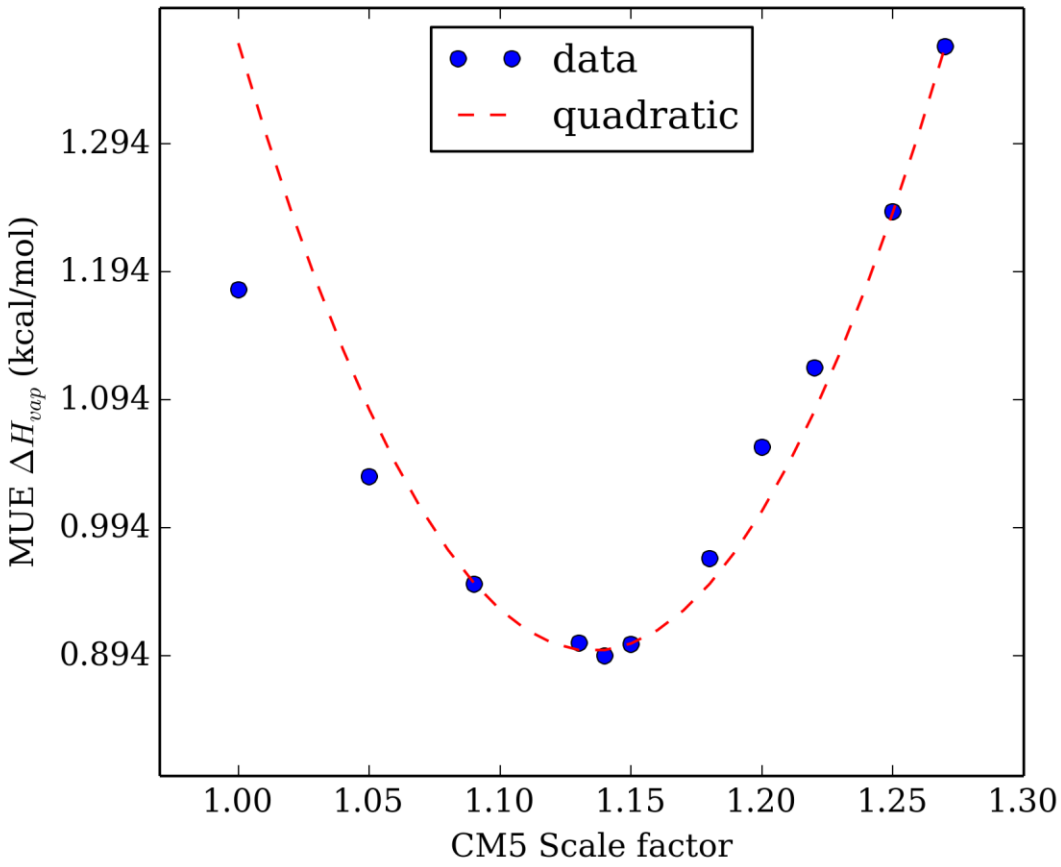

Figure S3. Interpolated MUEs for heats of vaporization to determine an optimal CM5 scale factor. The red dashed line represents a quadratic fit of the data.

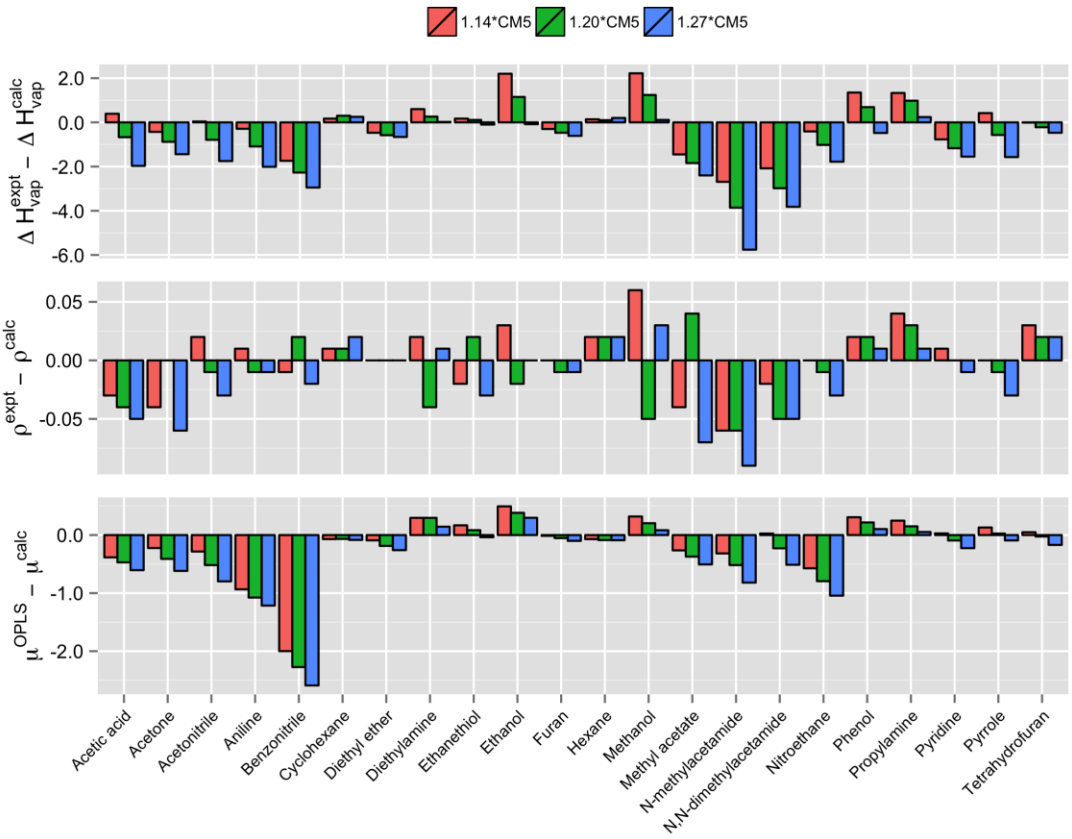

Figure S4. Signed errors of computed liquid properties comparing 1.14*CM5 (orange), 1.20*CM5 (green) and 1.27*CM5 (blue) scaled CM5 charge models.

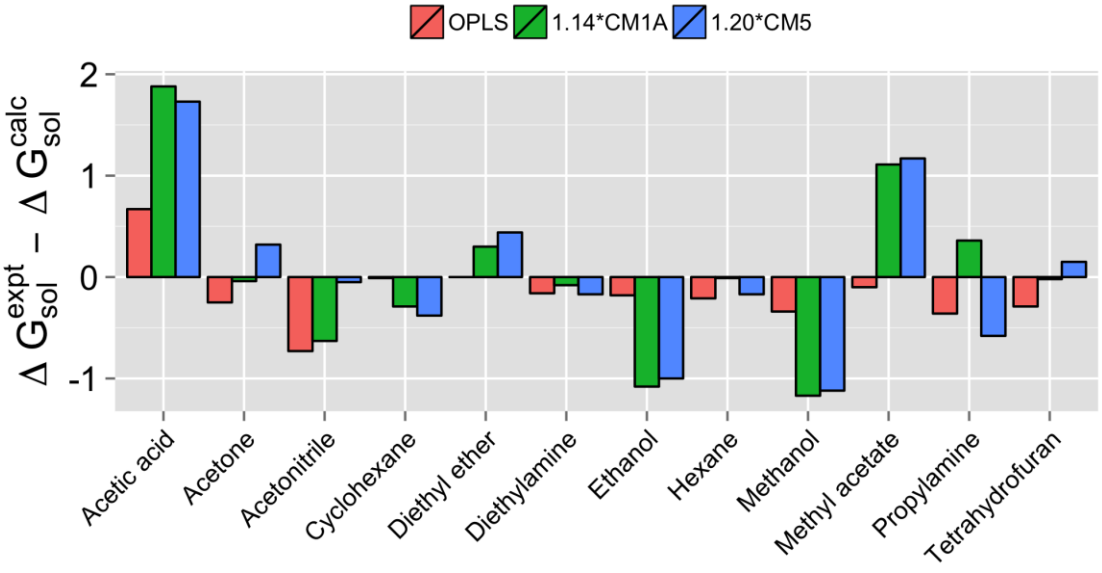

Figure S5. Signed errors in computed free energies of self-solvation with OPLS-AA (orange), 1.14*CM1A (green), and 1.20*CM5 (blue) charges.

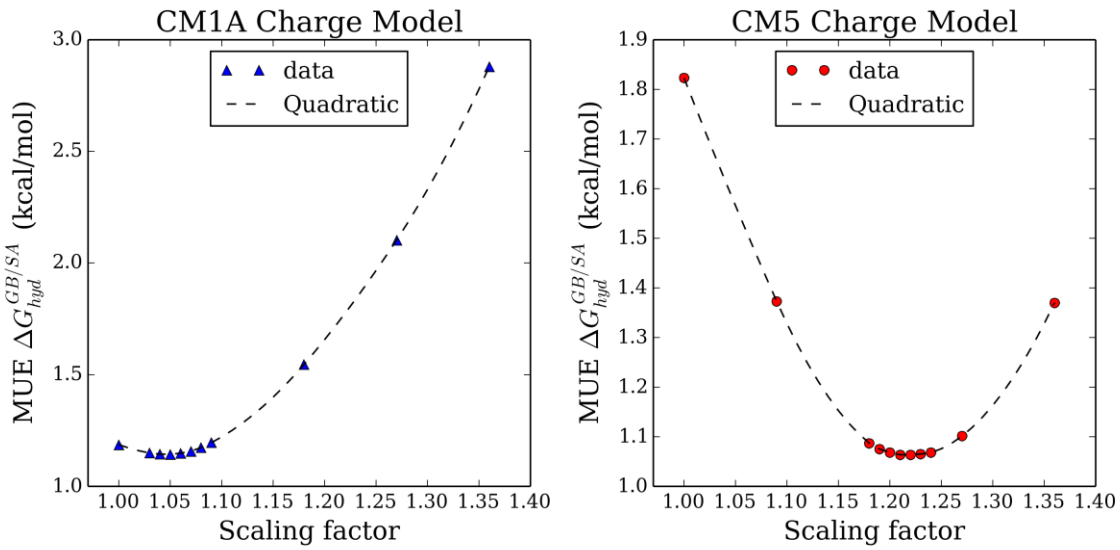

Figure S6. MUEs in free energies of hydration calculated using GB/SA methodology for CM1A and CM5 charge models with different scaling factors. Dashed lines represent quadratic fits of the data.

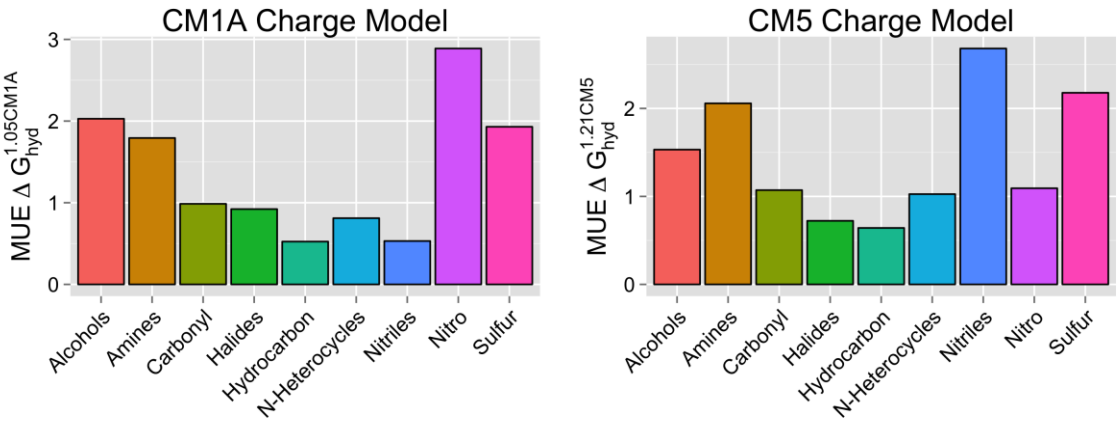

Figure S7. CM*x* MUEs in GB/SA free energies of hydration for compound classes.

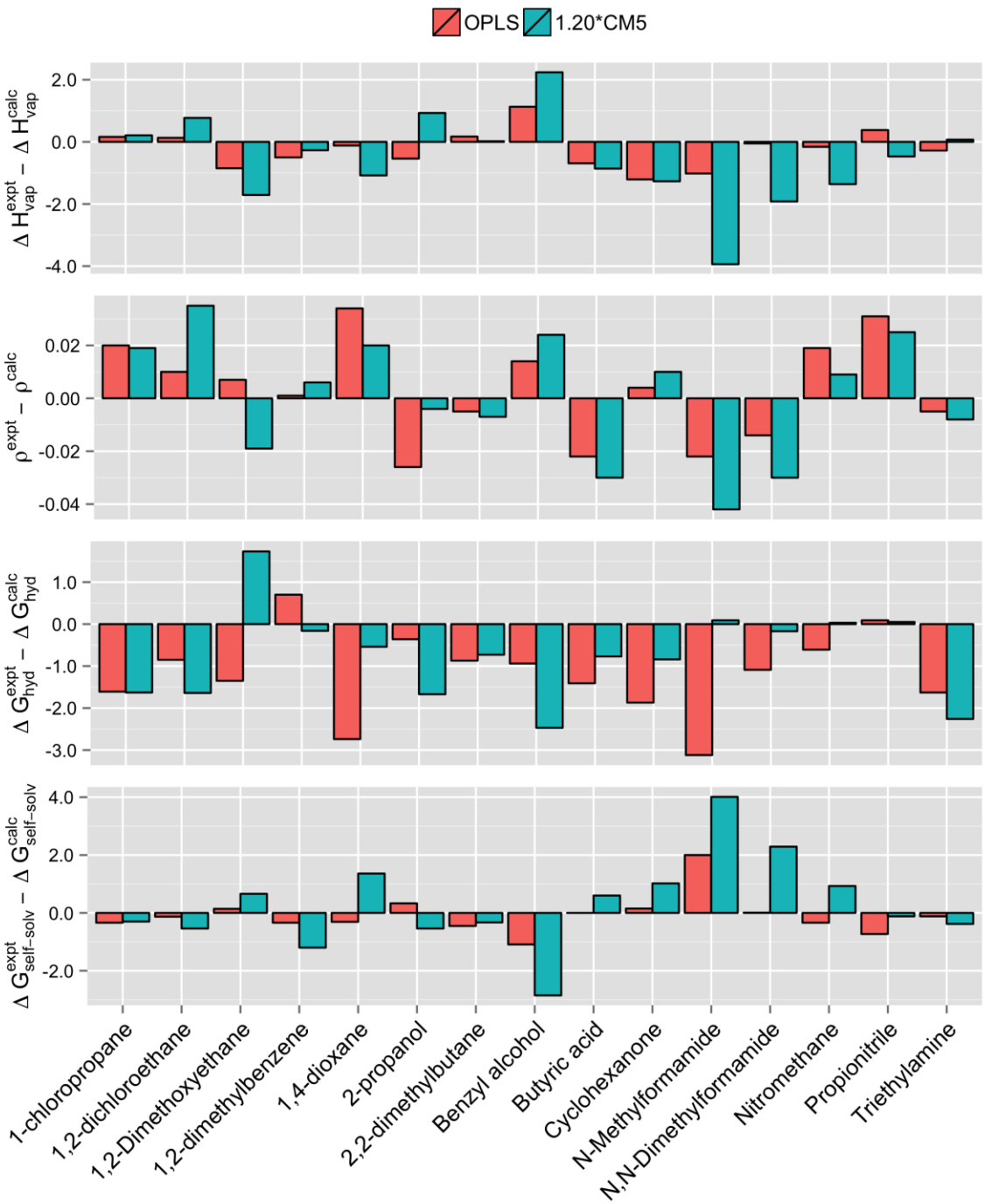

Figure S8. Signed errors in computed heats of vaporization (kcal/mol), density, free energies of hydration (kcal/mol) and free energy of self-solvation (kcal/mol) for molecules in the validation set with OPLS-AA (orange), and 1.20*CM5 (blue) charges.