

# Supplementary Material

## Chapter 6

June 18, 2016

The SAMPL0 molecular information and the predicted solvation free energy with different charge method and atomic radius force field parametrization are listed in Table 1-4. The SAMPL1-SAMPL4 results are listed in Tables 5-20, respectively. For the Sampl0-Sampl2 test sets, the root mean squared error (RMSEs) that inside and outside the parenthesis denote that when the molecules contain Br atom are included and excluded, respectively. The mean error (ME) for different force field parametrization are also included.

Table S1: The experimental and predicted solvation free energy for the SAMPL0 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber6 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
1,1-diethoxyethane	-3.28	-3.30	-1.32	-3.30	-0.28
dimethoxymethane	-2.93	-3.66	-1.91	-3.40	-1.96
1-acetoxyethyl acetate	-4.97	-6.63	-6.40	-5.79	-5.51
diethyl propanedioate	-6.00	-8.27	-6.58	-6.17	-7.14
2-acetoxyethyl acetate	-6.34	-7.95	-7.16	-6.72	-6.93
2,3-diacetoxypentyl acetate	-8.84	-11.70	-10.34	-9.41	-9.89
1,2-diethoxyethane	-3.54	-3.34	-3.77	-3.30	-3.61
1,4-dioxane	-5.06	-5.10	-4.58	-4.62	-4.98
benzyl chloride	-1.93	-2.90	-2.38	-1.77	-1.79
N,N-4-trimethylbenzamide	-9.76	-9.50	-12.32	-13.04	-10.44
ethylsulfanyethane	-1.46	-1.56	-1.16	-1.37	-1.59
1-chloro-2-(2-chloroethoxy)ethane	-4.23	-6.13	-4.52	-4.76	-4.02
4-methoxy-N,N-dimethyl-benzamide	-11.01	-11.28	-10.73	-10.74	-9.95
phenyl formate	-3.82	-5.46	-5.34	-5.29	-4.13
m-bis(trifluoromethyl)benzene	1.07	1.45	1.04	2.01	1.29
imidazole	-9.63	-9.01	-7.18	-6.71	-8.61
benzyl bromide	-2.38	-2.78	-1.55	-2.05	NA
RMSE		1.30 (1.26)	1.27 (1.25)	1.23 (1.20)	0.99 (NA)
ME		0.78 (0.76)	-0.18 (-0.12)	-0.16 (-0.13)	0.13 (NA)

Table S2: The experimental and predicted solvation free energy for the SAMPL 0 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber bondi force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
1,1-diethoxyethane	-3.28	-3.58	-1.50	-3.75	-1.13
dimethoxymethane	-2.93	-3.90	-2.08	-3.77	-2.59
1-acetoxyethyl acetate	-4.97	-6.63	-6.46	-5.80	-5.41
diethyl propanedioate	-6.00	-8.34	-6.63	-6.21	-7.83
2-acetoxyethyl acetate	-6.34	-8.03	-7.28	-6.75	-7.23
2,3-diacetoxypentyl acetate	-8.84	-11.99	-10.56	-9.43	-8.67
1,2-diethoxyethane	-3.54	-3.29	-3.64	-3.41	-4.09
1,4-dioxane	-5.06	-5.24	-4.75	-4.73	-5.44
benzyl chloride	-1.93	-3.02	-2.48	-1.80	-2.17
N,N-4-trimethylbenzamide	-9.76	-9.43	-12.38	-13.28	-11.40
ethylsulfanyethane	-1.46	-1.54	-0.99	-1.41	-1.70
1-chloro-2-(2-chloroethoxy)ethane	-4.23	-6.40	-4.71	-4.95	-4.11
4-methoxy-N,N-dimethyl-benzamide	-11.01	-11.34	-10.84	-10.90	-10.75
phenyl formate	-3.82	-5.55	-5.41	-5.29	-3.69
m-bis(trifluoromethyl)benzene	1.07	1.36	0.92	2.07	1.06
imidazole	-9.63	-9.01	-7.09	-6.64	-8.49
benzyl bromide	-2.38	-2.85	-1.55	-2.09	NA
RMSE		1.40 (1.37)	1.30 (1.27)	1.30 (1.27)	0.93 (NA)
ME		0.88 (0.86)	-0.26 (-0.20)	-0.27 (-0.24)	-0.12 (NA)

Table S3: The experimental and predicted solvation free energy for the SAMPL 0 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber mbondi2 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
1,1-diethoxyethane	-3.28	-3.58	-1.50	-3.75	-1.13
dimethoxymethane	-2.93	-3.90	-2.08	-3.77	-2.59
1-acetoxyethyl acetate	-4.97	-6.63	-6.46	-5.80	-5.41
diethyl propanedioate	-6.00	-8.34	-6.63	-6.21	-7.83
2-acetoxyethyl acetate	-6.34	-8.03	-7.28	-6.75	-7.23
2,3-diacetoxypropyl acetate	-8.84	-11.99	-10.56	-9.43	-8.67
1,2-diethoxyethane	-3.54	-3.29	-3.64	-3.41	-4.09
1,4-dioxane	-5.06	-5.24	-4.75	-4.73	-5.44
benzyl chloride	-1.93	-3.02	-2.48	-1.80	-2.14
N,N-4-trimethylbenzamide	-9.76	-9.78	-12.60	-13.41	-12.31
ethylsulfanylethane	-1.46	-1.54	-0.99	-1.41	-1.70
1-chloro-2-(2-chloroethoxy)ethane	-4.23	-6.40	-4.71	-4.95	-4.12
4-methoxy-N,N-dimethyl-benzamide	-11.01	-11.55	-10.97	-10.97	-11.28
phenyl formate	-3.82	-5.55	-5.41	-5.29	-3.69
m-bis(trifluoromethyl)benzene	1.07	1.36	0.92	2.07	1.06
imidazole	-9.63	-8.87	-6.98	-6.59	-7.86
benzyl bromide	-2.38	-2.85	-1.55	-2.09	NA
RMSE		1.41 (1.37)	1.34 (1.32)	1.33 (1.29)	1.10 (NA)
ME		0.91 (0.88)	0.27 (0.21)	-0.28 (-0.25)	-0.17 (NA)

Table S4: The experimental and predicted solvation free energy for the SAMPL 0 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The ZAP9 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
1,1-diethoxyethane	-3.28	-2.27	-0.72	-2.58	-0.82
dimethoxymethane	-2.93	-2.44	-1.25	-2.40	-2.21
1-acetoxyethyl acetate	-4.97	-6.26	-6.39	-5.66	-5.38
diethyl propanedioate	-6.00	-7.87	-6.63	-5.97	-8.06
2-acetoxyethyl acetate	-6.34	-7.47	-7.09	-6.43	-7.07
2,3-diacetoxypropyl acetate	-8.84	-11.03	-10.34	-9.07	-9.53
1,2-diethoxyethane	-3.54	-3.19	-3.52	-3.39	-4.07
1,4-dioxane	-5.06	-5.00	-4.77	-4.49	-5.69
benzyl chloride	-1.93	-2.67	-2.23	-1.74	-3.15
N,N-4-trimethylbenzamide	-9.76	-9.94	-12.14	-13.14	-10.30
ethylsulfanylethane	-1.46	-1.41	-1.05	-1.41	-1.85
1-chloro-2-(2-chloroethoxy)ethane	-4.23	-6.08	-4.60	-4.58	-4.97
4-methoxy-N,N-dimethyl-benzamide	-11.01	-11.00	-10.66	-10.78	-9.95
phenyl formate	-3.82	-5.65	-5.51	-5.21	-3.93
m-bis(trifluoromethyl)benzene	1.07	3.86	2.42	3.73	2.35
imidazole	-9.63	-10.39	-7.24	-6.83	-10.57
benzyl bromide	-2.38	-2.85	-1.55	-2.09	NA
RMSE		1.33 (1.29)	1.39 (1.37)	1.37 (1.33)	1.08 (NA)
ME		0.44 (0.44)	0.00 (0.05)	0.11 (0.12)	-0.21 (NA)

Table S5: The experimental and predicted solvation free energy for the SAMPL 1 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber6 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
lindane	-5.44	-6.72	-4.65	-2.88	-4.40
isobutyl nitrate	-1.88	-1.87	-1.80	-1.85	-1.77
butyl nitrate	-2.09	-1.95	-1.87	-1.90	-1.42
[(2S)-butan-2-yl] nitrate	-1.82	-2.19	-1.97	-1.78	-0.98
1,2-dinitroxyethane	-5.73	-3.45	-4.30	-4.01	-4.31
1,2-dinitroxypropane	-4.95	-5.58	-4.69	-4.63	-5.02

Table 5 – continued from previous page

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G^{\text{pred}}_{\text{AM1-BCC}}$	$\Delta G^{\text{pred}}_{\text{Mulliken}}$	$\Delta G^{\text{pred}}_{\text{Gasteiger}}$	$\Delta G^{\text{pred}}_{\text{SIESTA}}$
ethion	-6.10	-6.87	-12.72	-11.38	-12.20
captan	-9.01	-7.60	-6.99	-4.56	-7.13
trichloro(nitro)methane	-1.45	-0.90	-2.32	-1.93	-3.89
heptachlor	-2.55	-4.78	-4.46	-2.44	-5.05
chlordane	-3.44	-6.83	-5.88	-2.61	-4.03
dichlobenil	-4.71	-3.63	-2.33	-3.72	-5.51
fenuron	-9.13	-9.78	-8.32	-8.26	-8.25
N-(3,4-dichlorophenyl)propanimidic acid	-7.78	-8.22	-6.24	-7.10	-10.35
alachlor	-8.21	-7.57	-7.14	-3.25	-5.86
pebulate	-3.64	-4.93	-4.51	-0.93	-5.69
N,N-dipropyl(propylsulfanyl)formamide	-4.13	-4.80	-4.22	-0.59	-5.57
dicamba	-9.86	-13.10	-7.08	-7.89	-13.94
bensulfuron	-17.17	-24.05	-32.80	-30.70	-22.30
3,5,5-trimethylcyclohex-2-en-1-one	-5.18	-3.99	-2.61	-2.68	-4.29
1,4,5,8-tetramino-anthraquinone	-8.94	-14.62	-10.12	-12.97	-10.82
5-Amino-4-chloro-2-phenylpyridazin-3(2H)-one	-16.43	-10.35	-16.16	-16.72	-8.92
1-amino-4-anilino-anthraquinone	-7.44	-9.90	-7.81	-11.46	-8.94
4-amino-4'-nitroazobenzene	-11.24	-7.95	-9.95	-10.19	-10.73
1-N,1-N-diethyl-2,6-dinitro-4-(trifluoromethyl)benzene-1,3-diamine	-5.66	-3.83	-5.10	-10.12	-7.03
terbacil	-11.14	-11.48	-6.52	-5.91	-8.68
simazine	-10.22	-10.29	-10.24	-5.79	-8.95
aldicarb	-9.84	-9.49	-6.79	-6.18	-9.39
carbofuran	-9.61	-9.95	-9.22	-7.13	-8.24
trifluralin	-3.25	-1.17	-2.69	-9.49	-5.00
nitralin	-7.98	-11.34	-17.79	-16.11	-9.29
dinoseb	-6.23	-9.67	-7.61	-9.87	-12.93
nitroxyacetone	-5.99	-9.84	-8.43	-8.39	-8.14
2-(nitrooxy)ethan-1-ol	-8.18	-3.31	-9.26	-7.72	-2.85
N-butyl-N-ethyl-2,6-dinitro-4-(trifluoromethyl)aniline	-3.51	-1.34	-2.77	-9.51	-7.93
profluralin	-2.45	-0.55	-2.29	-9.60	-5.27
pirimor	-9.41	-11.73	-11.70	-8.92	-7.60
4-dimethylamino-azobenzene	-6.66	-5.52	-9.75	-10.59	-7.32
endrin	-4.82	-7.79	-6.20	-5.24	-4.90
endrin	-4.82	-8.03	-7.05	-5.17	-3.73
trichlorfon	-12.74	-14.89	-21.45	-3.32	-11.91
chlorfenvinphos	-7.07	-5.17	-11.99	-0.59	-2.33
azinhosmethyl	-10.03	-14.31	-25.20	-19.17	-15.70
malathion	-8.15	-7.89	-11.10	-8.38	-5.75
dialifor	-5.74	-11.78	-14.83	-2.20	-3.46
carbophenothion	-6.50	-13.81	-17.18	-1.96	-5.61
parathion	-6.74	-7.22	-12.74	-9.29	-7.38
methyparathion	-7.19	-5.45	-13.67	-8.36	-3.35
chlorpyrifos	-5.04	-7.89	-6.71	-11.87	-7.45
diazinon	-6.48	-7.90	-9.73	-9.35	-8.44
phorate	-4.37	-12.76	-9.48	6.76	-2.95
2-N-ethyl-6-(methylsulfanyl)-4-N-(propan-2-yl)-1,3,5-triazine-2,4-diamine	-7.65	-7.46	-15.88	-12.55	-8.62
terbutryn	-6.68	-6.26	-14.56	-8.79	-7.97
prometryn	-8.43	-5.53	-14.33	-8.63	-7.76
oxamyl	-10.18	-17.08	-15.80	-14.00	-15.03
naphthalen-1-yl N-methylcarbamate	-9.45	-7.93	-10.97	-8.20	-6.33
thifensulfuron	-16.23	-9.92	-20.52	-25.30	-16.30
sulfometuron-methyl	-20.25	-15.78	-17.70	-25.08	-21.81
chlorimuronethyl	-14.01	-21.38	-13.55	-16.75	-16.46
metsulfuronmethyl	-15.54	-15.68	-20.28	-19.84	-24.38
methomyl	-10.65	-10.29	-11.80	-9.98	-10.70
endosulfan alpha	-4.23	-10.07	-5.22	-19.99	-5.49
bromacil	-9.73	-13.28	-15.94	-16.63	NA
RMSE		3.26 (3.27)	4.74 (4.77)	4.92 (4.96)	2.92 (NA)

**Table 5 – continued from previous page**

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G^{\text{pred}}_{\text{AM1-BCC}}$	$\Delta G^{\text{pred}}_{\text{Mulliken}}$	$\Delta G^{\text{pred}}_{\text{Gasteiger}}$	$\Delta G^{\text{pred}}_{\text{SIESTA}}$
ME		0.83 (0.88)	-2.22 (-2.28)	-0.93 (-1.02)	-0.52 (NA)

Table S6: The experimental and predicted solvation free energy for the SAMPL 1 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G^{\text{pred}}_{\text{AM1-BCC}}$ ,  $\Delta G^{\text{pred}}_{\text{Mulliken}}$ ,  $\Delta G^{\text{pred}}_{\text{Gasteiger}}$ , and  $\Delta G^{\text{pred}}_{\text{SIESTA}}$  are the predicted solvation free energy with four different types of charges. The Amber Bondi force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G^{\text{pred}}_{\text{AM1-BCC}}$	$\Delta G^{\text{pred}}_{\text{Mulliken}}$	$\Delta G^{\text{pred}}_{\text{Gasteiger}}$	$\Delta G^{\text{pred}}_{\text{SIESTA}}$
lindane	-5.44	-7.35	-5.20	-3.08	-5.82
isobutyl nitrate	-1.88	-1.83	-1.73	-1.85	-1.67
butyl nitrate	-2.09	-1.91	-1.83	-1.89	-2.27
[(2S)-butan-2-yl] nitrate	-1.82	-2.15	-1.92	-1.77	-1.28
1,2-dinitroxyethane	-5.73	-3.47	-4.35	-4.02	-4.23
1,2-dinitroxypropane	-4.95	-5.60	-4.70	-4.63	-4.17
ethion	-6.10	-6.79	-13.14	-18.19	-10.20
captan	-9.01	-7.43	-7.03	-4.39	-7.04
trichloro(nitro)methane	-1.45	-0.80	-2.16	-1.81	-3.28
heptachlor	-2.55	-5.08	-4.71	-2.53	-5.51
chlordane	-3.44	-7.21	-6.19	-2.82	-5.11
dichlobenil	-4.71	-3.57	-2.38	-3.68	-5.33
fenuron	-9.13	-9.60	-8.26	-8.33	-8.95
N-(3,4-dichlorophenyl)propanimidic acid	-7.78	-8.36	-6.31	-7.09	-10.48
alachlor	-8.21	-8.38	-8.35	-4.30	-8.71
pebulate	-3.64	-4.92	-4.22	-0.45	-5.27
N,N-dipropyl(propylsulfanyl)formamide	-4.13	-4.80	-4.10	-0.47	-5.06
dicamba	-9.86	-9.90	-5.88	-7.04	-8.14
bensulfuron	-17.17	-24.85	-32.86	-40.60	-26.99
3,5,5-trimethylcyclohex-2-en-1-one	-5.18	-3.77	-2.44	-2.79	-4.71
1,4,5,8-tetramino-anthraquinone	-8.94	-13.96	-9.87	-12.56	-9.90
5-Amino-4-chloro-2-phenylpyridazin-3(2H)-one	-16.43	-12.98	-17.00	-17.34	-13.30
1-amino-4-anilino-anthraquinone	-7.44	-9.39	-7.71	-11.06	-9.75
4-amino-4'-nitroazobenzene	-11.24	-7.82	-10.06	-10.23	-10.50
1-N,1-N-diethyl-2,6-dinitro-4-(trifluoromethyl)benzene-1,3-diamine	-5.66	-3.08	-4.70	-10.17	-4.92
terbacil	-11.14	-11.10	-6.30	-5.98	-9.27
simazine	-10.22	-10.19	-10.01	-5.64	-8.94
aldicarb	-9.84	-9.27	-6.83	-6.30	-9.11
carbofuran	-9.61	-9.60	-9.08	-7.09	-8.21
trifluralin	-3.25	-0.75	-2.48	-9.57	-4.20
nitralin	-7.98	-11.29	-18.24	-7.62	-8.76
dinoseb	-6.23	-7.63	-6.47	-9.28	-9.35
nitroxyacetone	-5.99	-9.96	-8.60	-8.45	-9.19
2-(nitrooxy)ethan-1-ol	-8.18	-5.41	-10.48	-9.02	-9.19
N-butyl-N-ethyl-2,6-dinitro-4-(trifluoromethyl)aniline	-3.51	-0.96	-2.58	-9.58	-7.93
profluralin	-2.45	-0.15	-2.11	-9.65	-4.66
pirimor	-9.41	-11.61	-11.48	-9.29	-8.82
4-dimethylamino-azobenzene	-6.66	-5.32	-9.77	-10.80	-8.25
endrin	-4.82	-8.05	-6.48	-5.46	-5.24
endrin	-4.82	-8.21	-7.23	-5.34	-3.99
trichlorfon	-12.74	-12.86	-21.20	-2.67	-8.41
chlorfenvinphos	-7.07	-8.79	-13.54	-1.20	-9.00
azinthosmethyl	-10.03	-14.83	-16.05	-19.48	-14.72
malathion	-8.15	-8.22	-11.77	-8.51	-6.92
dialifor	-5.74	-15.11	-7.26	-2.98	-9.41
carbophenothion	-6.50	-12.90	-8.53	-2.87	-6.04
parathion	-6.74	-7.56	-13.06	-9.35	-7.06
methyparathion	-7.19	-7.53	-14.54	-8.89	-6.07
chlorpyrifos	-5.04	-7.56	-5.73	-11.72	-6.51

Table 6 – continued from previous page					
Solute Name	$\Delta G^{\text{exp}}$	$\Delta G^{\text{pred}}_{\text{AM1-BCC}}$	$\Delta G^{\text{pred}}_{\text{Mulliken}}$	$\Delta G^{\text{pred}}_{\text{Gasteiger}}$	$\Delta G^{\text{pred}}_{\text{SIESTA}}$
diazinon	-6.48	-7.82	-10.45	-9.19	-6.92
phorate	-4.37	-13.69	-9.84	7.18	-5.07
2-N-ethyl-6-(methylsulfanyl)-4-N-(propan-2-yl)-1,3,5-triazine-2,4-diamine	-7.65	-7.29	-15.13	-12.50	-9.18
terbutryn	-6.68	-6.09	-13.76	-9.11	-8.26
prometryn	-8.43	-5.34	-13.44	-9.12	-8.27
oxamyl	-10.18	-16.60	-15.54	-14.10	-14.79
naphthalen-1-yl N-methylcarbamate	-9.45	-8.88	-11.23	-8.33	-8.26
thifensulfuron	-16.23	-15.64	-29.47	-21.85	-23.46
sulfometuron-methyl	-20.25	-17.84	-19.19	-26.40	-24.56
chlorimuronethyl	-14.01	-14.64	-15.46	-19.14	-21.11
metsulfuronmethyl	-15.54	-16.98	-21.29	-20.51	-24.56
methomyl	-10.65	-10.20	-11.56	-9.88	-11.03
endosulfan alpha	-4.23	-9.90	-15.64	-20.47	-5.26
bromacil	-9.73	-13.13	-16.11	-17.12	NA
RMSE		3.06 (3.07)	4.65 (4.68)	5.52 (5.55)	2.89 (NA)
ME		0.96 (0.99)	-2.22 (-2.28)	-1.16 (-1.26)	-1.15 (NA)

Table S7: The experimental and predicted solvation free energy for the SAMPL 1 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G^{\text{pred}}_{\text{AM1-BCC}}$ ,  $\Delta G^{\text{pred}}_{\text{Mulliken}}$ ,  $\Delta G^{\text{pred}}_{\text{Gasteiger}}$ , and  $\Delta G^{\text{pred}}_{\text{SIESTA}}$  are the predicted solvation free energy with four different types of charges. The Amber mbondi2 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G^{\text{pred}}_{\text{AM1-BCC}}$	$\Delta G^{\text{pred}}_{\text{Mulliken}}$	$\Delta G^{\text{pred}}_{\text{Gasteiger}}$	$\Delta G^{\text{pred}}_{\text{SIESTA}}$
lindane	-5.44	-7.35	-5.20	-3.08	-5.55
isobutyl nitrate	-1.88	-1.83	-1.73	-1.85	-1.67
butyl nitrate	-2.09	-1.91	-1.83	-1.89	-2.27
[(2S)-butan-2-yl] nitrate	-1.82	-2.15	-1.92	-1.77	-1.28
1,2-dinitroxyethane	-5.73	-3.47	-4.35	-4.02	-4.23
1,2-dinitroxypropane	-4.95	-5.60	-4.70	-4.63	-4.17
ethion	-6.10	-6.79	-13.14	-18.19	-10.20
captan	-9.01	-7.77	-7.37	-4.67	-7.60
trichloro(nitro)methane	-1.45	-0.80	-2.16	-1.81	-3.28
heptachlor	-2.55	-5.08	-4.71	-2.53	-5.12
chlordane	-3.44	-7.21	-6.19	-2.82	-4.57
dichlobenil	-4.71	-3.57	-2.38	-3.68	-5.30
fenuron	-9.13	-9.57	-8.28	-8.38	-9.40
N-(3,4-dichlorophenyl)propanimidic acid	-7.78	-8.21	-6.19	-6.98	-9.92
alachlor	-8.21	-8.38	-8.35	-4.30	-8.71
pebulate	-3.64	-5.06	-4.31	-0.55	-5.71
N,N-dipropyl(propylsulfanyl)formamide	-4.13	-4.93	-4.19	-0.56	-5.49
dicamba	-9.86	-9.90	-5.88	-7.04	-8.04
bensulfuron	-17.17	-21.47	-32.66	-21.88	-24.75
3,5,5-trimethylcyclohex-2-en-1-one	-5.18	-3.77	-2.44	-2.79	-4.71
1,4,5,8-tetramino-anthraquinone	-8.94	-13.10	-8.88	-11.48	-7.76
5-Amino-4-chloro-2-phenylpyridazin-3(2H)-one	-16.43	-12.93	-16.88	-17.20	-12.96
1-amino-4-anilino-anthraquinone	-7.44	-8.91	-7.42	-10.83	-8.71
4-amino-4'-nitroazobenzene	-11.24	-7.44	-9.82	-9.96	-9.92
1-N,1-N-diethyl-2,6-dinitro-4-(trifluoromethyl)benzene-1,3-diamine	-5.66	-2.58	-4.27	-9.79	-4.10
terbacil	-11.14	-10.80	-6.08	-5.85	-8.59
simazine	-10.22	-9.43	-9.43	-5.21	-7.87
aldicarb	-9.84	-9.09	-6.71	-6.20	-9.24
carbofuran	-9.61	-9.46	-9.01	-7.05	-7.81
trifluralin	-3.25	-0.78	-2.46	-9.49	-4.20
nitralin	-7.98	-11.32	-18.23	-7.56	-8.75
dinoseb	-6.23	-7.63	-6.47	-9.28	-9.35
nitroxyacetone	-5.99	-9.96	-8.60	-8.45	-9.19

Table 7 – continued from previous page					
Solute Name	$\Delta G^{\text{exp}}$	$\Delta G^{\text{pred}}_{\text{AM1-BCC}}$	$\Delta G^{\text{pred}}_{\text{Mulliken}}$	$\Delta G^{\text{pred}}_{\text{Gasteiger}}$	$\Delta G^{\text{pred}}_{\text{SIESTA}}$
2-(nitrooxy)ethan-1-ol	-8.18	-5.41	-10.48	-9.02	-9.19
N-butyl-N-ethyl-2,6-dinitro-4-(trifluoromethyl)aniline	-3.51	-0.99	-2.55	-9.49	-7.93
profluralin	-2.45	-0.18	-2.08	-9.56	-4.64
pirimor	-9.41	-11.68	-11.55	-9.31	-9.21
4-dimethylamino-azobenzene	-6.66	-5.49	-10.00	-10.95	-9.34
endrin	-4.82	-8.05	-6.48	-5.46	-4.71
endrin	-4.82	-8.21	-7.23	-5.34	-3.53
trichlorfon	-12.74	-12.86	-21.20	-2.67	-8.41
chlorfenvinphos	-7.07	-8.79	-13.54	-1.20	-9.00
azinthosmethyl	-10.03	-14.92	-16.09	-19.47	-14.82
malathion	-8.15	-8.22	-1.77	-8.51	-6.92
dialifor	-5.74	-15.11	-7.26	-2.98	-9.41
carbophenothion	-6.50	-12.90	-8.53	-2.87	-6.04
parathion	-6.74	-7.56	-3.06	-9.35	-7.06
methyparathion	-7.19	-7.53	-4.54	-8.89	-6.07
chlorpyrifos	-5.04	-7.56	-15.73	-11.72	-6.51
diazinon	-6.48	-7.82	-10.45	-9.19	-6.92
phorate	-4.37	-13.69	-9.84	7.18	-5.07
2-N-ethyl-6-(methylsulfanyl)-4-N-(propan-2-yl)-1,3,5-triazine-2,4-diamine	-7.65	-7.78	-15.38	-13.12	-10.85
terbutryn	-6.68	-6.05	-13.80	-9.39	-8.86
prometryn	-8.43	-5.36	-13.50	-9.45	-8.93
oxamyl	-10.18	-16.49	-15.43	-14.05	-14.71
naphthalen-1-yl N-methylcarbamate	-9.45	-9.00	-11.29	-8.40	-8.48
thifensulfuron	-16.23	-25.73	-28.92	-24.53	-23.85
sulfometuron-methyl	-20.25	-27.46	-28.96	-17.81	-24.05
chlorimuronethyl	-14.01	-14.22	-25.18	-8.44	-20.75
metsulfuronmethyl	-15.54	-16.84	-31.13	-19.87	-24.39
methomyl	-10.65	-10.17	-11.48	-9.79	-11.03
endosulfan alpha	-4.23	-9.90	-15.64	-20.47	-5.26
bromacil	-9.73	-13.55	-16.54	-17.47	NA
RMSE		3.29 (3.30)	5.39 (5.41)	4.76 (4.82)	2.82 (NA)
ME		1.17 (1.22)	-2.32 (-2.39)	-0.56 (-0.67)	-1.05 (NA)

Table S8: The experimental and predicted solvation free energy for the SAMPL 1 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G^{\text{pred}}_{\text{AM1-BCC}}$ ,  $\Delta G^{\text{pred}}_{\text{Mulliken}}$ ,  $\Delta G^{\text{pred}}_{\text{Gasteiger}}$ , and  $\Delta G^{\text{pred}}_{\text{SIESTA}}$  are the predicted solvation free energy with four different types of charges. The ZAP9 field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G^{\text{pred}}_{\text{AM1-BCC}}$	$\Delta G^{\text{pred}}_{\text{Mulliken}}$	$\Delta G^{\text{pred}}_{\text{Gasteiger}}$	$\Delta G^{\text{pred}}_{\text{SIESTA}}$
lindane	-5.44	-7.29	-5.26	-3.27	-5.99
isobutyl nitrate	-1.88	-1.84	-1.74	-1.83	-2.44
butyl nitrate	-2.09	-1.90	-1.83	-1.88	-2.63
[(2S)-butan-2-yl] nitrate	-1.82	-2.15	-1.95	-1.72	-1.43
1,2-dinitroxyethane	-5.73	-3.47	-4.26	-4.06	-3.73
1,2-dinitroxypropane	-4.95	-5.50	-4.61	-4.64	-4.50
ethion	-6.10	-12.14	-12.52	-18.74	-9.43
captan	-9.01	-8.27	-6.85	-5.65	-6.04
trichloro(nitro)methane	-1.45	-0.90	-1.74	-1.41	-0.76
heptachlor	-2.55	-5.18	-4.61	-2.73	-4.40
chlordan	-3.44	-6.98	-5.92	-3.14	-6.89
dichlobenil	-4.71	-3.85	-2.53	-3.61	-2.33
fenuron	-9.13	-7.28	-7.30	-7.68	-8.23
N-(3,4-dichlorophenyl)propanimidic acid	-7.78	-8.32	-6.46	-6.69	-9.77
alachlor	-8.21	-8.75	-7.86	-5.64	-9.14
pebulate	-3.64	-5.30	-4.06	1.45	-5.66
N,N-dipropyl(propylsulfanyl)formamide	-4.13	-5.21	-3.90	1.56	-5.81

Table 8 – continued from previous page

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G^{\text{pred}}_{\text{AM1-BCC}}$	$\Delta G^{\text{pred}}_{\text{Mulliken}}$	$\Delta G^{\text{pred}}_{\text{Gasteiger}}$	$\Delta G^{\text{pred}}_{\text{SIESTA}}$
dicamba	-9.86	-9.96	-6.54	-6.68	-6.74
bensulfuron	-17.17	-26.51	-32.14	-41.69	-20.94
3,5,5-trimethylcyclohex-2-en-1-one	-5.18	-3.47	-2.53	-2.22	-4.47
1,4,5,8-tetramino-anthraquinone	-8.94	-17.00	-10.66	-10.73	-8.06
5-Amino-4-chloro-2-phenylpyridazin-3(2H)-one	-16.43	-12.95	-14.96	-14.70	-12.38
1-amino-4-anilino-anthraquinone	-7.44	-9.73	-8.06	-10.03	-5.16
4-amino-4'-nitroazobenzene	-11.24	-9.35	-10.29	-9.56	-9.64
1-N,1-N-diethyl-2,6-dinitro-4-(trifluoromethyl)benzene-1,3-diamine	-5.66	0.44	-1.54	-7.64	5.31
terbacil	-11.14	-7.63	-5.85	-5.12	-5.16
simazine	-10.22	-12.35	-9.62	-4.52	-7.43
aldicarb	-9.84	-6.80	-6.33	-5.47	-7.32
carbofuran	-9.61	-8.01	-8.52	-6.86	-7.34
trifluralin	-3.25	2.33	0.16	-7.52	6.82
nitralin	-7.98	-8.06	-10.88	-16.91	-3.83
dinoseb	-6.23	-8.41	-6.55	-8.59	-6.54
nitroxyacetone	-5.99	-10.33	-9.32	-8.86	-7.61
2-(nitrooxy)ethan-1-ol	-8.18	-6.53	-10.14	-9.10	-8.13
N-butyl-N-ethyl-2,6-dinitro-4-(trifluoromethyl)aniline	-3.51	2.16	0.09	-7.54	5.02
profluralin	-2.45	2.86	0.47	-7.69	6.76
pirimor	-9.41	-9.57	-9.86	-7.84	-6.34
4-dimethylamino-azobenzene	-6.66	-4.93	-9.24	-10.49	-6.71
endrin	-4.82	-7.35	-5.91	-5.20	-5.60
endrin	-4.82	-7.87	-6.80	-5.25	-5.26
trichlorfon	-12.74	-11.29	-16.22	-3.50	-9.32
chlorfenvinphos	-7.07	-8.36	-18.50	-3.41	-8.58
azinthosmethyl	-10.03	-15.99	-18.71	-19.79	-13.95
malathion	-8.15	-8.59	-15.42	-8.18	-6.23
dialifor	-5.74	-14.48	-20.25	-4.48	-9.40
carbophenothion	-6.50	-12.13	-18.47	-2.09	-3.59
parathion	-6.74	-8.20	-17.80	-9.26	-8.07
methyparathion	-7.19	-7.63	-18.93	-9.05	-6.44
chlorpyrifos	-5.04	-5.38	-9.98	-10.56	-5.70
diazinon	-6.48	-7.90	-15.19	-9.49	-7.66
phorate	-4.37	-12.68	-15.88	3.85	-5.39
2-N-ethyl-6-(methylsulfanyl)-4-N-(propan-2-yl)-1,3,5-triazine-2,4-diamine	-7.65	-5.07	-14.11	-12.56	-7.95
terbutryn	-6.68	-4.17	-13.16	-9.35	-7.41
prometryn	-8.43	-3.20	-13.05	-9.40	-8.46
oxamyl	-10.18	-17.63	-15.41	-13.74	-14.82
naphthalen-1-yl N-methylcarbamate	-9.45	-8.93	-10.88	-8.63	-9.52
thifensulfuron	-16.23	-29.08	-28.50	-23.14	-21.81
sulfometuron-methyl	-20.25	-28.98	-30.86	-17.47	-25.88
chlorimuronethyl	-14.01	-24.75	-25.29	-6.96	-20.37
metsulfuronmethyl	-15.54	-20.18	-23.92	-20.91	-26.29
methomyl	-10.65	-11.47	-11.39	-10.28	-9.47
endosulfan alpha	-4.23	-9.83	-17.67	-14.11	-5.88
bromacil	-9.73	-13.52	-15.80	-20.25	NA
RMSE		4.26 (4.35)	6.16 (6.16)	5.33 (5.45)	3.76 (NA)
ME		1.26 (1.30)	-3.01 (-3.06)	-0.66 (-0.82)	0.31 (NA)



Table S9: The experimental and predicted solvation free energy for the SAMPL 2 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber6 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
(+)-ibuprofen	-7.00	-4.86	-9.88	-8.47	-5.73
glycerol	-13.43	-13.97	-13.28	-14.57	-14.67
hexachloroethane	-0.64	-1.36	-1.92	-0.43	-1.29
hexachlorobenzene	-2.33	-0.64	-1.62	-3.28	-3.70
Trimethyl phosphate	-8.70	-8.88	-3.20	-3.82	-6.35
phthalimide	-9.61	-10.84	-9.60	-10.33	-10.68
pentachloronitrobenzene	-5.22	-1.00	-2.61	-6.66	-8.86
caffeine	-12.64	-14.07	-13.31	-10.36	-12.01
Ketoprofen	-10.78	-11.90	-13.91	-11.49	-8.92
Flurbiprofen	-8.42	-3.88	-5.12	-2.67	-3.87
naproxen	-10.21	-11.71	-12.36	-9.84	-9.17
diflunisal	-9.40	-13.30	-12.20	-12.47	-15.30
acetylsalicylic acid	-9.94	-10.39	-10.58	-9.34	-9.37
octafluorocyclobutane	3.43	5.29	4.42	5.20	3.73
Uracil	-16.59	-16.77	-12.89	-11.10	-15.13
5-fluorouracil	-16.92	-16.22	-11.52	-10.51	-13.21
5-chlorouracil	-17.74	-14.53	-9.63	-4.37	-10.32
6-chlorouracil	-15.83	-12.96	-8.81	-5.24	-10.32
5-trifluoromethyluracil	-15.46	-17.22	-8.39	-4.85	-9.89
cyanuric acid	-18.06	-16.90	-13.34	-10.06	-9.20
D-xylose	-20.52	-16.88	-19.95	-18.57	-17.44
D-glucose	-25.47	-22.61	-23.96	-25.26	-22.44
1,1,1-trifluoro-2,2,2-trimethoxyethane	-0.80	1.27	-2.14	-1.92	2.09
propyl paraben	-9.37	-9.14	-6.56	-7.30	-10.79
butyl paraben	-8.72	-9.31	-6.75	-7.28	-9.70
methyl paraben	-9.51	-10.22	-7.11	-7.93	-11.70
ethyl paraben	-9.20	-9.73	-6.87	-7.50	-11.30
sulfolane	-8.61	-8.58	-10.99	-7.01	-9.04
5-bromouracil	-18.17	-15.70	-12.74	-11.49	NA
RMSE		2.09 (2.11)	3.51 (3.59)	4.78 (4.86)	3.46 (NA)
ME		-0.59 (-0.65)	1.56 (1.65)	2.51 (2.65)	1.18 (NA)

Table S10: The experimental and predicted solvation free energy for the SAMPL 2 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber bondi force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
(+)-ibuprofen	-7.00	-7.71	-10.96	-9.25	-7.03
glycerol	-13.43	-14.62	-13.10	-14.40	-13.22
hexachloroethane	-0.64	-1.24	-1.87	-0.39	-1.01
hexachlorobenzene	-2.33	-0.34	-1.40	-3.19	-3.22
Trimethyl phosphate	-8.70	-9.00	-3.30	-3.96	-7.27
phthalimide	-9.61	-10.87	-9.63	-10.30	-10.31
pentachloronitrobenzene	-5.22	-0.68	-2.29	-6.52	-8.04
caffeine	-12.64	-14.15	-13.41	-10.31	-12.60
Ketoprofen	-10.78	-12.71	-14.17	-11.35	-9.53
Flurbiprofen	-8.42	-3.52	-5.90	-3.38	-3.77
naproxen	-10.21	-11.90	-12.43	-9.76	-9.39
diflunisal	-9.40	-11.30	-9.55	-11.23	-11.07
acetylsalicylic acid	-9.94	-10.33	-10.46	-9.03	-8.01
octafluorocyclobutane	3.43	5.47	4.57	5.30	3.86
Uracil	-16.59	-16.84	-13.14	-11.37	-14.57
5-fluorouracil	-16.92	-17.46	-12.22	-11.39	-14.72
5-chlorouracil	-17.74	-16.91	-10.17	-4.21	-14.36
6-chlorouracil	-15.83	-15.35	-9.30	-5.15	-14.44
5-trifluoromethyluracil	-15.46	-18.76	-8.82	-5.16	-11.67
cyanuric acid	-18.06	-20.74	-13.99	-11.38	-17.59
D-xylose	-20.52	-17.11	-19.44	-18.48	-17.99
D-glucose	-25.47	-23.50	-24.00	-25.33	-24.40
1,1,1-trifluoro-2,2,2-trimethoxyethane	-0.80	-0.63	-2.30	-1.79	-2.34
propyl paraben	-9.37	-8.08	-6.17	-6.92	-7.70
butyl paraben	-8.72	-8.42	-6.43	-6.96	-7.33
methyl paraben	-9.51	-8.82	-6.61	-7.48	-7.85
ethyl paraben	-9.20	-8.56	-6.43	-7.13	-7.55
sulfolane	-8.61	-8.73	-11.37	-8.47	-10.17
5-bromouracil	-18.17	-15.61	-12.69	-11.29	NA
RMSE		1.95 (1.97)	3.38 (3.47)	4.62 (4.72)	1.90 (NA)
ME		-0.17 (-0.26)	1.55 (1.69)	2.45 (2.61)	0.87 (NA)

Table S11: The experimental and predicted solvation free energy for the SAMPL 2 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber mbondi2 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
(+)-ibuprofen	-7.00	-7.71	-10.96	-9.25	-7.03
glycerol	-13.43	-14.62	-13.10	-14.40	-13.22
hexachloroethane	-0.64	-1.24	-1.87	-0.39	-1.00
hexachlorobenzene	-2.33	-0.34	-1.40	-3.19	-3.18
Trimethyl phosphate	-8.70	-9.00	-3.30	-3.96	-7.27
phthalimide	-9.61	-10.87	-9.65	-10.32	-10.11
pentachloronitrobenzene	-5.22	-0.68	-2.29	-6.52	-7.93
caffeine	-12.64	-14.32	-13.50	-10.30	-12.77
Ketoprofen	-10.78	-12.71	-14.17	-11.35	-9.53
Flurbiprofen	-8.42	-3.52	-5.90	-3.38	-3.77
naproxen	-10.21	-11.90	-12.43	-9.76	-9.39
diflunisal	-9.40	-11.30	-9.55	-11.23	-11.07
acetylsalicylic acid	-9.94	-10.33	-10.46	-9.03	-8.01
octafluorocyclobutane	3.43	5.47	4.57	5.30	3.86
Uracil	-16.59	-16.39	-12.89	-11.36	-13.70
5-fluorouracil	-16.92	-16.85	-11.89	-11.32	-13.52
5-chlorouracil	-17.74	-15.79	-9.49	-4.00	-12.48
6-chlorouracil	-15.83	-14.32	-8.71	-4.95	-12.73
5-trifluoromethyluracil	-15.46	-17.98	-8.39	-5.06	-10.22
cyanuric acid	-18.06	-19.32	-13.63	-11.82	-15.41
D-xylose	-20.52	-17.11	-19.44	-18.48	-17.99
D-glucose	-25.47	-23.50	-24.00	-25.33	-24.40
1,1,1-trifluoro-2,2,2-trimethoxyethane	-0.80	-0.63	-2.30	-1.79	-2.34
propyl paraben	-9.37	-8.08	-6.17	-6.92	-7.70
butyl paraben	-8.72	-8.42	-6.43	-6.96	-7.33
methyl paraben	-9.51	-8.82	-6.61	-7.48	-7.85
ethyl paraben	-9.20	-8.56	-6.43	-7.13	-7.55
sulfolane	-8.61	-8.73	-11.37	-8.47	-10.17
5-bromouracil	-18.17	-15.02	-12.13	-10.90	NA
RMSE		1.90 (1.96)	3.55 (3.66)	4.65 (4.76)	2.35 (NA)
ME		-0.36 (-0.46)	2.46 (2.62)	1.64 (1.79)	1.21 (NA)

Table S12: The experimental and predicted solvation free energy for the SAMPL 2 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The ZAP9 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
(+)-ibuprofen	-7.00	-8.88	-10.41	-8.36	-6.06
glycerol	-13.43	-14.05	-13.27	-14.32	-13.87
hexachloroethane	-0.64	-0.92	-1.56	-0.58	-1.29
hexachlorobenzene	-2.33	-0.08	-1.15	-2.87	-0.82
Trimethyl phosphate	-8.70	-6.85	-3.30	-3.66	-7.85
phthalimide	-9.61	-10.48	-10.60	-11.23	-9.75
pentachloronitrobenzene	-5.22	-0.70	-1.90	-5.40	-3.16
caffeine	-12.64	-13.12	-13.12	-10.78	-11.18
Ketoprofen	-10.78	-13.98	-14.16	-10.85	-7.80
Flurbiprofen	-8.42	-3.93	-5.66	-3.72	-4.73
naproxen	-10.21	-13.04	-12.54	-9.28	-8.46
diflunisal	-9.40	-12.59	-10.32	-10.31	-11.86
acetylsalicylic acid	-9.94	-10.80	-10.44	-8.70	-7.38
octafluorocyclobutane	3.43	3.81	3.49	3.12	3.32
Uracil	-16.59	-16.43	-14.02	-12.37	-14.56
5-fluorouracil	-16.92	-17.66	-12.88	-10.74	-14.00
5-chlorouracil	-17.74	-15.10	-9.53	-3.86	-13.83
6-chlorouracil	-15.83	-13.54	-8.88	-4.86	-14.09
5-trifluoromethyluracil	-15.46	-16.97	-9.81	-5.48	-13.25
cyanuric acid	-18.06	-19.16	-15.64	-13.05	-17.07
D-xylose	-20.52	-17.24	-19.75	-18.87	-18.27
D-glucose	-25.47	-23.57	-24.11	-25.45	-24.73
1,1,1-trifluoro-2,2,2-trimethoxyethane	-0.80	-0.83	-1.08	-1.33	-2.68
propyl paraben	-9.37	-7.93	-6.48	-6.86	-8.05
butyl paraben	-8.72	-8.32	-6.75	-6.84	-7.32
methyl paraben	-9.51	-8.46	-6.81	-7.08	-8.09
ethyl paraben	-9.20	-8.31	-6.68	-6.94	-8.81
sulfolane	-8.61	-8.10	-7.76	-11.02	-10.48
5-bromouracil	-18.17	-16.88	-18.69	-15.54	NA
RMSE		2.05 (2.03)	3.19 (3.15)	4.56 (4.51)	1.93 (NA)
ME		-0.37 (-0.41)	2.36 (2.37)	1.52 (1.45)	1.13 (NA)

Table S13: The experimental and predicted solvation free energy for the SAMPL 3 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber6 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
dibenzo-p-dioxin	-3.15	-2.04	-3.76	-2.66	-4.13
ethane	1.83	1.34	1.48	1.20	1.15
biphenyl	-2.70	-2.49	-2.02	-2.76	-2.36
1,1,1,2-tetrachloroethane	-1.43	-2.84	-2.40	-1.28	-0.70
1,1,1,2,2-pentachloroethane	-1.23	-2.83	-2.58	-1.39	-1.08
hexachloroethane	-0.64	-0.64	-0.64	-0.64	-0.64
chloroethane	-0.63	-0.70	-0.42	-0.25	-0.17
1,2-dichloroethane	-1.79	-3.11	-2.07	-1.44	-2.24
1,1-dichloroethane	-0.84	-1.80	-1.35	-0.65	-0.36
1,1,2-trichloroethane	-1.99	-3.82	-2.72	-2.01	-1.79
1,1,2,2-tetrachloroethane	-2.37	-3.90	-2.89	-2.05	-0.92
1,2,3,4,5-pentachloro-6-(2,3,4,5,6-pentachlorophenyl)benzene	-2.98	-1.88	-3.38	-5.85	-2.85
1-chloro-2-phenyl-benzene	-2.69	-2.15	-1.53	-2.00	-1.47
1,4-dichloro-2-phenyl-benzene	-2.46	-2.00	-1.64	-2.12	-1.23
1,3,5-trichloro-2-phenyl-benzene	-2.16	-1.87	-1.78	-2.53	-1.36
1,3-dichloro-2-(2,6-dichlorophenyl)benzene	-2.28	-3.28	-3.39	-2.66	-0.82
1,2,3,4-tetrachloro-5-phenyl-benzene	-3.48	-1.61	-1.84	-3.06	-1.33
1,2,3-trichloro-5-(2,5-dichlorophenyl)benzene	-3.61	-2.11	-2.31	-2.92	-2.11
1,3,5-trichloro-2-(2,6-dichlorophenyl)benzene	-1.96	-2.81	-3.23	-2.85	-1.06
1,2,3,4-tetrachloro-5-(3,4-dichlorophenyl)benzene	-3.04	-2.15	-2.46	-3.71	-2.89
1,2,4,5-tetrachloro-3-(3,4-dichlorophenyl)benzene	-4.38	-2.32	-2.63	-3.69	-2.79
1,2,3,4-tetrachloro-5-(2,3,4-trichlorophenyl)benzene	-4.40	-2.46	-3.01	-4.21	-1.88
1,2,3,4-tetrachloro-5-(3,4,5-trichlorophenyl)benzene	-3.17	-2.02	-2.45	-4.24	-1.79
1,2,3,4-tetrachloro-5-(2,3,4,6-tetrachlorophenyl)benzene	-4.61	-2.26	-3.09	-4.61	-3.54
1,1,1-trichloroethane	-0.19	-1.64	-1.61	-0.44	-0.06
1-chlorodibenzo-p-dioxin	-3.52	-2.82	-2.03	-3.02	-3.11
2-chlorodibenzo-p-dioxin	-3.10	-2.28	-1.80	-2.81	-3.17
2,3-dichlorodibenzo-p-dioxin	-3.56	-2.13	-1.71	-3.18	-3.65
2,7-dichlorodibenzo-p-dioxin	-3.67	-2.22	-1.70	-3.04	-3.20
1,2,4-trichlorodibenzo-p-dioxin	-4.05	-2.79	-1.84	-4.04	-4.06
2,3,7,8-tetrachlorodibenzo-p-dioxin	-3.37	-2.13	-1.53	-3.96	-4.39
1,2,3,4-tetrachlorodibenzo-p-dioxin	-3.81	-2.57	-1.78	-4.79	-4.46
1,2,3,7-tetrachlorodibenzo-p-dioxin	-3.84	-2.43	-1.67	-4.24	-4.31
1,2,3,4,7,8-hexachlorodibenzo-p-dioxin	-3.71	-2.62	-1.53	-5.75	-5.49
1,2,3,4,7-pentachlorodibenzo-p-dioxin	-4.15	-2.61	-1.64	-5.17	-5.33
1,2,3,4,6,7,8,9-octachlorodibenzo-p-dioxin	-4.53	-3.21	-1.57	-7.88	-6.66
RMSE		1.28	1.42	0.97	1.08
ME		0.38	0.72	-0.16	0.34

Table S14: The experimental and predicted solvation free energy for the SAMPL 3 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred0}}$  are the predicted solvation free energy with four different types of charges. The Amber bondi force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
dibenzo-p-dioxin	-3.15	-2.88	-3.68	-2.49	-4.26
ethane	1.83	1.35	1.49	1.03	1.23
biphenyl	-2.70	-2.56	-2.07	-2.71	-2.79
1,1,1,2-tetrachloroethane	-1.43	-2.94	-2.50	-1.37	-1.06
1,1,1,2,2-pentachloroethane	-1.23	-2.85	-2.61	-1.49	-1.39
hexachloroethane	-0.64	-0.64	-0.64	-0.64	-0.64
chloroethane	-0.63	-0.75	-0.43	-0.32	-0.40
1,2-dichloroethane	-1.79	-3.29	-2.21	-1.55	-3.04
1,1-dichloroethane	-0.84	-1.90	-1.39	-0.75	-0.81
1,1,2-trichloroethane	-1.99	-4.05	-2.88	-2.18	-2.24
1,1,2,2-tetrachloroethane	-2.37	-4.12	-3.03	-2.23	-1.86
1,2,3,4,5-pentachloro-6-(2,3,4,5,6-pentachlorophenyl)benzene	-2.98	-1.03	-2.63	-5.65	-1.59
1-chloro-2-phenyl-benzene	-2.69	-2.19	-1.52	-1.92	-1.91
1,4-dichloro-2-phenyl-benzene	-2.46	-1.99	-1.56	-2.05	-1.76
1,3,5-trichloro-2-phenyl-benzene	-2.16	-1.82	-1.71	-2.44	-1.76
1,3-dichloro-2-(2,6-dichlorophenyl)benzene	-2.28	-3.18	-3.26	-2.59	-0.62
1,2,3,4-tetrachloro-5-phenyl-benzene	-3.48	-1.39	-1.59	-2.94	-1.88
1,2,3-trichloro-5-(2,5-dichlorophenyl)benzene	-3.61	-1.95	-2.12	-2.81	-2.03
1,3,5-trichloro-2-(2,6-dichlorophenyl)benzene	-1.96	-2.67	-3.08	-2.77	-0.78
1,2,3,4-tetrachloro-5-(3,4-dichlorophenyl)benzene	-3.04	-1.85	-2.15	-3.58	-1.56
1,2,4,5-tetrachloro-3-(3,4-dichlorophenyl)benzene	-4.38	-2.05	-2.37	-3.57	-1.67
1,2,3,4-tetrachloro-5-(2,3,4-trichlorophenyl)benzene	-4.40	-2.05	-2.60	-4.05	-1.08
1,2,3,4-tetrachloro-5-(3,4,5-trichlorophenyl)benzene	-3.17	-1.62	-2.06	-4.09	-1.10
1,2,3,4-tetrachloro-5-(2,3,4,6-tetrachlorophenyl)benzene	-4.61	-1.76	-2.63	-4.46	-2.69
1,1,1-trichloroethane	-0.19	-1.65	-1.59	-0.50	-0.12
1-chlorodibenzo-p-dioxin	-3.52	-2.84	-2.04	-2.73	-2.97
2-chlorodibenzo-p-dioxin	-3.10	-2.33	-1.84	-2.53	-3.23
2,3-dichlorodibenzo-p-dioxin	-3.56	-2.08	-1.67	-2.80	-3.63
2,7-dichlorodibenzo-p-dioxin	-3.67	-2.25	-1.73	-2.66	-3.31
1,2,4-trichlorodibenzo-p-dioxin	-4.05	-2.63	-1.68	-3.59	-3.68
2,3,7,8-tetrachlorodibenzo-p-dioxin	-3.37	-1.97	-1.42	-3.40	-4.16
1,2,3,4-tetrachlorodibenzo-p-dioxin	-3.81	-2.28	-1.51	-4.25	-3.97
1,2,3,7-tetrachlorodibenzo-p-dioxin	-3.84	-2.24	-1.51	-3.69	-3.95
1,2,3,4,7,8-hexachlorodibenzo-p-dioxin	-3.71	-2.19	-1.16	-5.04	-4.73
1,2,3,4,7-pentachlorodibenzo-p-dioxin	-4.15	-2.26	-1.31	-4.54	-4.77
1,2,3,4,6,7,8,9-octachlorodibenzo-p-dioxin	-4.53	-2.41	-0.85	-6.97	-5.45
RMSE		1.47	1.58	0.82	1.16
ME		-0.56	0.85	-0.09	0.45

Table S15: The experimental and predicted solvation free energy for the SAMPL 3 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber mbondi2 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
dibenzo-p-dioxin	-3.15	-2.88	-3.68	-2.49	-4.26
ethane	1.83	1.35	1.49	1.03	1.23
biphenyl	-2.70	-2.56	-2.07	-2.71	-2.79
1,1,1,2-tetrachloroethane	-1.43	-2.94	-2.50	-1.37	-1.06
1,1,1,2,2-pentachloroethane	-1.23	-2.85	-2.61	-1.49	-1.39
hexachloroethane	-0.64	-0.64	-0.64	-0.64	-0.64
chloroethane	-0.63	-0.75	-0.43	-0.32	-0.40
1,2-dichloroethane	-1.79	-3.29	-2.21	-1.55	-3.04
1,1-dichloroethane	-0.84	-1.90	-1.39	-0.75	-0.81
1,1,2-trichloroethane	-1.99	-4.05	-2.88	-2.18	-2.24
1,1,2,2-tetrachloroethane	-2.37	-4.12	-3.03	-2.23	-1.86
1,2,3,4,5-pentachloro-6-(2,3,4,5,6-pentachlorophenyl)benzene	-2.98	-1.03	-2.63	-5.65	-1.59
1-chloro-2-phenyl-benzene	-2.69	-2.19	-1.52	-1.92	-1.91
1,4-dichloro-2-phenyl-benzene	-2.46	-1.99	-1.56	-2.05	-1.76
1,3,5-trichloro-2-phenyl-benzene	-2.16	-1.82	-1.71	-2.44	-1.76
1,3-dichloro-2-(2,6-dichlorophenyl)benzene	-2.28	-3.18	-3.26	-2.59	-0.62
1,2,3,4-tetrachloro-5-phenyl-benzene	-3.48	-1.39	-1.59	-2.94	-1.88
1,2,3-trichloro-5-(2,5-dichlorophenyl)benzene	-3.61	-1.95	-2.12	-2.81	-2.03
1,3,5-trichloro-2-(2,6-dichlorophenyl)benzene	-1.96	-2.67	-3.08	-2.77	-0.78
1,2,3,4-tetrachloro-5-(3,4-dichlorophenyl)benzene	-3.04	-1.85	-2.15	-3.58	-1.56
1,2,4,5-tetrachloro-3-(3,4-dichlorophenyl)benzene	-4.38	-2.05	-2.37	-3.57	-1.67
1,2,3,4-tetrachloro-5-(2,3,4-trichlorophenyl)benzene	-4.40	-2.05	-2.60	-4.05	-1.08
1,2,3,4-tetrachloro-5-(3,4,5-trichlorophenyl)benzene	-3.17	-1.62	-2.06	-4.09	-1.10
1,2,3,4-tetrachloro-5-(2,3,4,6-tetrachlorophenyl)benzene	-4.61	-1.76	-2.63	-4.46	-2.69
1,1,1-trichloroethane	-0.19	-1.65	-1.59	-0.50	-0.12
1-chlorodibenzo-p-dioxin	-3.52	-2.84	-2.04	-2.73	-2.97
2-chlorodibenzo-p-dioxin	-3.10	-2.33	-1.84	-2.53	-3.23
2,3-dichlorodibenzo-p-dioxin	-3.56	-2.08	-1.67	-2.80	-3.63
2,7-dichlorodibenzo-p-dioxin	-3.67	-2.25	-1.73	-2.66	-3.31
1,2,4-trichlorodibenzo-p-dioxin	-4.05	-2.63	-1.68	-3.59	-3.68
2,3,7,8-tetrachlorodibenzo-p-dioxin	-3.37	-1.97	-1.42	-3.40	-4.16
1,2,3,4-tetrachlorodibenzo-p-dioxin	-3.81	-2.28	-1.51	-4.25	-3.97
1,2,3,7-tetrachlorodibenzo-p-dioxin	-3.84	-2.24	-1.51	-3.69	-3.95
1,2,3,4,7,8-hexachlorodibenzo-p-dioxin	-3.71	-2.19	-1.16	-5.04	-4.73
1,2,3,4,7-pentachlorodibenzo-p-dioxin	-4.15	-2.26	-1.31	-4.54	-4.77
1,2,3,4,6,7,8,9-octachlorodibenzo-p-dioxin	-4.53	-2.41	-0.85	-6.97	-5.45
RMSE		1.47	1.58	0.82	1.16
ME		-0.56	0.85	-0.09	0.39

Table S16: The experimental and predicted solvation free energy for the SAMPL 3 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The ZAP9 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
dibenzo-p-dioxin	-3.15	-2.32	-4.31	-3.43	-4.23
ethane	1.83	1.29	1.41	1.00	1.35
biphenyl	-2.70	-2.56	-2.14	-2.91	-2.79
1,1,1,2-tetrachloroethane	-1.43	-2.72	-2.38	-1.49	-2.30
1,1,1,2,2-pentachloroethane	-1.23	-2.60	-2.41	-1.68	-2.20
hexachloroethane	-0.64	-0.64	-0.64	-0.64	-0.64
chloroethane	-0.63	-0.64	-0.36	-0.35	-0.90
1,2-dichloroethane	-1.79	-3.05	-2.10	-1.56	-4.88
1,1-dichloroethane	-0.84	-1.78	-1.40	-0.79	-1.18
1,1,2-trichloroethane	-1.99	-3.81	-2.77	-2.24	-3.32
1,1,2,2-tetrachloroethane	-2.37	-3.92	-2.93	-2.37	-2.97
1,2,3,4,5-pentachloro-6-(2,3,4,5,6-pentachlorophenyl)benzene	-2.98	-0.90	-2.47	-5.38	-3.45
1-chloro-2-phenyl-benzene	-2.69	-2.15	-1.50	-1.94	-1.71
1,4-dichloro-2-phenyl-benzene	-2.46	-2.10	-1.71	-2.10	-2.21
1,3,5-trichloro-2-phenyl-benzene	-2.16	-1.97	-1.85	-2.48	-2.39
1,3-dichloro-2-(2,6-dichlorophenyl)benzene	-2.28	-3.52	-3.39	-2.87	-3.14
1,2,3,4-tetrachloro-5-phenyl-benzene	-3.48	-1.48	-1.67	-2.90	-2.98
1,2,3-trichloro-5-(2,5-dichlorophenyl)benzene	-3.61	-2.31	-2.47	-2.90	-2.34
1,3,5-trichloro-2-(2,6-dichlorophenyl)benzene	-1.96	-3.04	-3.30	-2.99	-3.29
1,2,3,4-tetrachloro-5-(3,4-dichlorophenyl)benzene	-3.04	-2.15	-2.42	-3.62	-2.34
1,2,4,5-tetrachloro-3-(3,4-dichlorophenyl)benzene	-4.38	-2.38	-2.66	-3.64	-2.82
1,2,3,4-tetrachloro-5-(2,3,4-trichlorophenyl)benzene	-4.40	-2.32	-2.76	-4.11	-2.49
1,2,3,4-tetrachloro-5-(3,4,5-trichlorophenyl)benzene	-3.17	-1.91	-2.33	-4.09	-2.49
1,2,3,4-tetrachloro-5-(2,3,4,6-tetrachlorophenyl)benzene	-4.61	-1.95	-2.77	-4.45	-2.57
1,1,1-trichloroethane	-0.19	-1.51	-1.57	-0.59	-1.10
1-chlorodibenzo-p-dioxin	-3.52	-2.45	-2.90	-3.59	-1.94
2-chlorodibenzo-p-dioxin	-3.10	-1.98	-2.82	-3.33	-1.77
2,3-dichlorodibenzo-p-dioxin	-3.56	-1.77	-2.53	-3.51	-1.97
2,7-dichlorodibenzo-p-dioxin	-3.67	-2.01	-2.69	-3.39	-1.92
1,2,4-trichlorodibenzo-p-dioxin	-4.05	-2.21	-2.41	-4.20	-1.85
2,3,7,8-tetrachlorodibenzo-p-dioxin	-3.37	-1.70	-2.25	-3.92	-2.37
1,2,3,4-tetrachlorodibenzo-p-dioxin	-3.81	-1.74	-2.00	-4.67	-2.17
1,2,3,7-tetrachlorodibenzo-p-dioxin	-3.84	-1.90	-2.24	-4.20	-1.87
1,2,3,4,7,8-hexachlorodibenzo-p-dioxin	-3.71	-1.66	-1.79	-5.25	-2.34
1,2,3,4,7-pentachlorodibenzo-p-dioxin	-4.15	-1.75	-1.90	-4.87	-2.14
1,2,3,4,6,7,8,9-octachlorodibenzo-p-dioxin	-4.53	-1.53	-1.15	-6.84	-2.69
RMSE		1.55	1.28	0.78	1.33
ME		-0.68	-0.37	0.31	-0.59



Table S17: The experimental and predicted solvation free energy for the SAMPL 4 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber 6 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
cyclohexene	0.14	1.07	0.87	1.15	1.29
1,1-diphenylethene	-2.78	-2.78	-2.42	-2.08	-1.87
2-methylbenzaldehyde	-3.93	-2.97	-4.41	-3.43	-3.80
hexyl acetate	-2.26	-2.36	-2.52	-2.46	-2.55
(2S,5R)-2-isopropyl-5-methylcyclohexanone	-2.53	-3.03	-3.03	-3.20	-3.12
piperidine	-5.11	-3.72	-3.69	-3.77	-3.42
(1R,2S,5R)-2-isopropyl-5-methylcyclohexanol	-3.20	-3.32	-3.61	-4.03	-3.70
(2R,3R,4R,5R)-Hexan-1,2,3,4,5,6-hexol	-23.62	-29.50	-23.82	-21.93	-29.82
2-ethylphenol	-5.66	-5.74	-5.75	-5.79	-6.10
tetrahydropyran	-3.12	-2.12	-1.92	-2.32	-1.87
1,4-dioxane	-5.06	-4.97	-4.45	-4.79	-4.75
diphenyl ether	-2.87	-1.68	-2.33	-1.82	-2.84
1,2-dimethoxybenzene	-5.33	-4.92	-4.58	-6.83	-4.38
dibenzo-p-dioxin	-3.15	-2.04	-3.76	-2.66	-4.13
anthracene	-3.95	-4.12	-3.68	-4.10	-3.91
1-ethyl-2-methylbenzene	-0.85	-0.73	-0.97	-0.84	-0.70
9,10-dihydroanthracene	-3.78	-3.23	-3.58	-3.08	-2.95
HEXYL NITRATE	-1.66	-1.08	-1.29	-1.65	-2.24
3-nitrooxypropyl nitrate	-4.80	-5.71	-5.69	-5.83	-5.58
1,3-bis-(nitrooxy)butane	-4.29	-4.84	-5.09	-4.83	-5.03
4-(1-Methylethenyl)-1-cyclohexene-1-carboxaldehyde	-4.09	-3.44	-3.08	-2.83	-3.34
2-hydroxybenzaldehyde	-4.68	-4.80	-6.04	-4.80	-5.04
2-chlorosyringaldehyde	-7.78	-8.58	-9.46	-9.41	-7.27
2,6-dichlorosyringaldehyde	-8.68	-7.64	-8.77	-10.19	-7.79
2-(2,3-dimethylphenyl)aminobenzoic acid	-6.78	-7.81	-8.43	-8.44	-6.23
(3R)-3,7-Dimethylocta-1,6-dien-3-yl acetate	-2.49	-2.87	-2.38	-1.97	-2.84
2-ethoxyethyl acetate	-5.31	-4.84	-4.78	-4.48	-5.38
1,4-diamino-9,10-anthracenedione	-11.85	-11.81	-8.29	-10.18	-10.31
1-amino-9,10-anthracenedione	-9.44	-9.38	-7.86	-8.97	-9.45
2-amino-9,10-anthraquinone	-11.53	-11.34	-8.64	-8.76	-11.64
1-(2-hydroxyethylamino)-9,10-anthraquinone	-14.21	-13.52	-13.37	-14.28	-13.33
1-amino-4-hydroxy-9,10-anthracenedione	-9.53	-9.80	-8.61	-11.62	-9.43
(2R,5R)-2-methyl-5-(1-methylethenyl)-cyclohexanone	-3.75	-3.32	-3.40	-2.78	-3.65
6-isopropyl-3-methyl-1-cyclohex-2-enone	-4.51	-3.43	-3.52	-2.39	-3.75
Amitriptyline	-7.43	-6.29	-4.93	-6.25	-3.90
[2-benzhydryloxyethyl]-dimethyl-amine	-9.34	-10.01	-7.64	-8.97	-6.01
(1S,5R)-2-methyl-5-(1-methylethenyl)-2-cyclohexen-1-ol	-4.44	-4.84	-5.39	-4.82	-4.70
(2E)-3,7-dimethylocta-2,6-dien-1-ol	-4.45	-5.80	-6.21	-5.30	-6.02
(2Z)-3,7-dimethylocta-2,6-dien-1-ol	-4.78	-2.98	-5.91	-5.00	-3.66
1-butoxy-2-propanol	-5.73	-5.09	-6.05	-5.47	-4.08
3,4-dichlorophenol	-7.29	-6.64	-5.65	-7.26	-9.19
2-methoxyphenol	-5.94	-6.30	-5.82	-4.34	-5.87
4-methyl-2-methoxyphenol	-5.80	-8.71	-6.55	-6.70	-6.55
4-propylguaiaicol	-5.26	-7.02	-6.05	-5.18	-5.40
2,6-dimethoxyphenol	-6.96	-8.87	-7.03	-8.34	-7.68
3,5-dichloro-2,6-dimethoxyphenol	-6.44	-6.83	-5.62	-7.31	-5.09
1-benzylimidazole	-7.63	-9.50	-10.04	-7.91	-8.63
RMSE		1.28	1.20	1.08	1.41
ME		-0.14	0.11	0.18	0.15

Table S18: The experimental and predicted solvation free energy for the SAMPL 4 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber bondi force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
cyclohexene	0.14	0.99	0.78	1.15	1.27
1,1-diphenylethene	-2.78	-2.83	-2.39	-1.97	-1.58
2-methylbenzaldehyde	-3.93	-2.92	-4.48	-3.35	-3.47
hexyl acetate	-2.26	-2.45	-2.58	-2.44	-2.22
(2S,5R)-2-isopropyl-5-methylcyclohexanone	-2.53	-2.95	-3.02	-3.23	-2.92
piperidine	-5.11	-3.82	-3.79	-3.72	-3.33
(1R,2S,5R)-2-isopropyl-5-methylcyclohexanol	-3.20	-3.59	-3.89	-4.15	-4.44
(2R,3R,4R,5R)-Hexan-1,2,3,4,5,6-hexol	-23.62	-25.61	-22.46	-20.52	-24.15
2-ethylphenol	-5.66	-5.61	-5.71	-5.75	-5.54
tetrahydropyran	-3.12	-2.25	-2.10	-2.29	-1.78
1,4-dioxane	-5.06	-5.12	-4.62	-4.97	-5.16
diphenyl ether	-2.87	-1.72	-2.40	-1.52	-2.39
1,2-dimethoxybenzene	-5.33	-4.89	-4.57	-6.68	-3.70
dibenzo-p-dioxin	-3.15	-2.88	-3.68	-2.49	-4.26
anthracene	-3.95	-4.11	-3.67	-3.96	-4.43
1-ethyl-2-methylbenzene	-0.85	-0.69	-0.92	-0.88	-0.75
9,10-dihydroanthracene	-3.78	-3.20	-3.58	-3.01	-4.63
HEXYL NITRATE	-1.66	-1.08	-1.33	-1.65	-1.60
3-nitrooxypropyl nitrate	-4.80	-5.73	-5.69	-5.85	-6.77
1,3-bis-(nitrooxy)butane	-4.29	-4.83	-5.08	-4.80	-4.47
4-(1-Methylethenyl)-1-cyclohexene-1-carboxaldehyde	-4.09	-4.32	-3.11	-2.77	-4.15
2-hydroxybenzaldehyde	-4.68	-5.93	-7.66	-3.94	-7.05
2-chlorosyringaldehyde	-7.78	-5.86	-9.67	-8.87	-9.31
2,6-dichlorosyringaldehyde	-8.68	-9.17	-8.80	-9.60	-9.06
2-(2,3-dimethylphenyl)aminobenzoic acid	-6.78	-8.84	-7.13	-8.36	-8.06
(3R)-3,7-Dimethylocta-1,6-dien-3-yl acetate	-2.49	-3.57	-2.39	-2.12	-2.76
2-ethoxyethyl acetate	-5.31	-4.85	-5.04	-4.48	-6.75
1,4-diamino-9,10-anthracenedione	-11.85	-10.22	-8.10	-9.84	-9.21
1-amino-9,10-anthracenedione	-9.44	-8.58	-7.93	-8.59	-8.51
2-amino-9,10-anthraquinone	-11.53	-10.59	-7.98	-8.83	-10.81
1-(2-hydroxyethylamino)-9,10-anthraquinone	-14.21	-12.14	-10.57	-13.77	-14.37
1-amino-4-hydroxy-9,10-anthracenedione	-9.53	-9.37	-8.21	-11.08	-10.23
(2R,5R)-2-methyl-5-(1-methylethenyl)-cyclohexanone	-3.75	-3.55	-3.32	-3.54	-3.95
6-isopropyl-3-methyl-1-cyclohex-2-enone	-4.51	-3.61	-3.46	-3.17	-4.41
Amitriptyline	-7.43	-6.14	-4.97	-6.58	-5.79
[2-benzhydryloxyethyl]-dimethyl-amine	-9.34	-9.87	-8.04	-8.99	-7.91
(1S,5R)-2-methyl-5-(1-methylethenyl)-2-cyclohexen-1-ol	-4.44	-3.84	-5.42	-4.86	-4.01
(2E)-3,7-dimethylocta-2,6-dien-1-ol	-4.45	-4.56	-6.22	-5.24	-3.88
(2Z)-3,7-dimethylocta-2,6-dien-1-ol	-4.78	-3.29	-5.82	-5.11	-3.57
1-butoxy-2-propanol	-5.73	-4.89	-5.48	-5.46	-5.01
3,4-dichlorophenol	-7.29	-5.78	-5.26	-6.89	-7.06
2-methoxyphenol	-5.94	-5.88	-5.32	-3.39	-4.41
4-methyl-2-methoxyphenol	-5.80	-8.26	-6.00	-5.59	-6.75
4-propylguaiaicol	-5.26	-7.36	-5.69	-4.02	-4.68
2,6-dimethoxyphenol	-6.96	-8.79	-6.43	-7.38	-7.16
3,5-dichloro-2,6-dimethoxyphenol	-6.44	-6.65	-5.07	-6.24	-5.86
1-benzylimidazole	-7.63	-9.66	-10.07	-7.87	-9.60
RMSE		1.12	1.41	1.10	1.07
ME		0.06	0.31	0.33	0.10

Table S19: The experimental and predicted solvation free energy for the SAMPL 4 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The Amber mbondi2 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
cyclohexene	0.14	0.99	0.78	1.15	1.27
1,1-diphenylethene	-2.78	-2.83	-2.39	-1.97	-1.58
2-methylbenzaldehyde	-3.93	-2.92	-4.48	-3.35	-3.47
hexyl acetate	-2.26	-2.45	-2.58	-2.44	-2.22
(2S,5R)-2-isopropyl-5-methylcyclohexanone	-2.53	-2.95	-3.02	-3.23	-2.92
piperidine	-5.11	-3.80	-3.82	-3.77	-3.40
(1R,2S,5R)-2-isopropyl-5-methylcyclohexanol	-3.20	-3.59	-3.89	-4.15	-4.44
(2R,3R,4R,5R)-Hexan-1,2,3,4,5,6-hexol	-23.62	-25.61	-22.47	-20.52	-24.15
2-ethylphenol	-5.66	-5.61	-5.71	-5.75	-5.54
tetrahydropyran	-3.12	-2.25	-2.10	-2.29	-1.78
1,4-dioxane	-5.06	-5.12	-4.62	-4.86	-4.97
diphenyl ether	-2.87	-1.72	-2.40	-1.52	-2.39
1,2-dimethoxybenzene	-5.33	-4.89	-4.57	-6.68	-3.70
dibenzo-p-dioxin	-3.15	-2.88	-3.68	-2.49	-4.26
anthracene	-3.95	-4.11	-3.67	-3.96	-4.42
1-ethyl-2-methylbenzene	-0.85	-0.69	-0.92	-0.88	-0.75
9,10-dihydroanthracene	-3.78	-3.20	-3.58	-3.01	-4.63
HEXYL NITRATE	-1.66	-1.08	-1.33	-1.65	-1.60
3-nitrooxypropyl nitrate	-4.80	-5.73	-5.69	-5.85	-6.77
1,3-bis-(nitrooxy)butane	-4.29	-4.83	-5.09	-4.80	-4.47
4-(1-Methylethenyl)-1-cyclohexene-1-carboxaldehyde	-4.09	-3.56	-3.12	-2.77	-3.67
2-hydroxybenzaldehyde	-4.68	-6.76	-6.39	-3.94	-7.05
2-chlorosyringaldehyde	-7.78	-7.59	-6.71	-8.87	-7.07
2,6-dichlorosyringaldehyde	-8.68	-6.47	-8.81	-9.60	-6.74
2-(2,3-dimethylphenyl)aminobenzoic acid	-6.78	-8.61	-7.31	-8.45	-7.86
(3R)-3,7-Dimethylocta-1,6-dien-3-yl acetate	-2.49	-2.85	-2.39	-2.12	-2.47
2-ethoxyethyl acetate	-5.31	-4.85	-4.79	-5.08	-5.68
1,4-diamino-9,10-anthracenedione	-11.85	-10.31	-7.62	-10.68	-9.37
1-amino-9,10-anthracenedione	-9.44	-8.35	-7.43	-9.59	-9.49
2-amino-9,10-anthraquinone	-11.53	-10.31	-8.33	-9.87	-11.41
1-(2-hydroxyethylamino)-9,10-anthraquinone	-14.21	-12.40	-14.76	-13.67	-14.13
1-amino-4-hydroxy-9,10-anthracenedione	-9.53	-8.93	-7.95	-10.89	-9.57
(2R,5R)-2-methyl-5-(1-methylethenyl)-cyclohexanone	-3.75	-3.55	-3.32	-3.54	-3.95
6-isopropyl-3-methyl-1-cyclohex-2-enone	-4.51	-3.61	-3.46	-3.17	-4.41
Amitriptyline	-7.43	-6.34	-5.23	-6.82	-6.10
[2-benzhydryloxyethyl]-dimethyl-amine	-9.34	-9.87	-8.34	-10.62	-8.53
(1S,5R)-2-methyl-5-(1-methylethenyl)-2-cyclohexen-1-ol	-4.44	-3.84	-5.42	-5.65	-5.45
(2E)-3,7-dimethylocta-2,6-dien-1-ol	-4.45	-4.46	-6.22	-6.20	-5.64
(2Z)-3,7-dimethylocta-2,6-dien-1-ol	-4.78	-3.29	-5.82	-5.95	-5.06
1-butoxy-2-propanol	-5.73	-4.89	-5.48	-5.46	-5.01
3,4-dichlorophenol	-7.29	-5.78	-5.26	-6.89	-7.70
2-methoxyphenol	-5.94	-5.25	-6.92	-5.67	-5.39
4-methyl-2-methoxyphenol	-5.80	-7.64	-7.71	-8.05	-7.80
4-propylguaiaicol	-5.26	-6.95	-7.46	-6.61	-5.77
2,6-dimethoxyphenol	-6.96	-8.40	-8.64	-9.07	-7.80
3,5-dichloro-2,6-dimethoxyphenol	-6.44	-6.59	-6.95	-7.83	-5.89
1-benzylimidazole	-7.63	-9.76	-10.16	-7.87	-9.76
RMSE		1.09	1.33	1.13	1.04
ME		0.15	0.14	-0.08	0.00

Table S20: The experimental and predicted solvation free energy for the SAMPL 4 test set.  $\Delta G^{\text{exp}}$  is the experimental solvation free energy,  $\Delta G_{\text{AM1-BCC}}^{\text{pred}}$ ,  $\Delta G_{\text{Mulliken}}^{\text{pred}}$ ,  $\Delta G_{\text{Gasteiger}}^{\text{pred}}$ , and  $\Delta G_{\text{SIESTA}}^{\text{pred}}$  are the predicted solvation free energy with four different types of charges. The ZAP9 force field are employed for the atomic radius parametrization. The energy data are all in the unit of kcal/mol.

Solute Name	$\Delta G^{\text{exp}}$	$\Delta G_{\text{AM1-BCC}}^{\text{pred}}$	$\Delta G_{\text{Mulliken}}^{\text{pred}}$	$\Delta G_{\text{Gasteiger}}^{\text{pred}}$	$\Delta G_{\text{SIESTA}}^{\text{pred}}$
cyclohexene	0.14	1.02	0.81	1.03	1.10
1,1-diphenylethene	-2.78	-2.84	-2.43	-1.95	-1.57
2-methylbenzaldehyde	-3.93	-3.48	-4.55	-3.41	-4.48
hexyl acetate	-2.26	-2.50	-2.62	-2.41	-2.57
(2S,5R)-2-isopropyl-5-methylcyclohexanone	-2.53	-3.07	-3.13	-3.17	-2.09
piperidine	-5.11	-3.84	-3.85	-3.90	-3.04
(1R,2S,5R)-2-isopropyl-5-methylcyclohexanol	-3.20	-3.81	-4.28	-4.12	-3.65
(2R,3R,4R,5R)-Hexan-1,2,3,4,5,6-hexol	-23.62	-25.65	-24.63	-21.97	-23.66
2-ethylphenol	-5.66	-5.75	-5.75	-6.00	-5.62
tetrahydropyran	-3.12	-2.29	-2.21	-2.22	-1.94
1,4-dioxane	-5.06	-4.98	-4.74	-4.62	-5.38
diphenyl ether	-2.87	-2.11	-2.46	-1.67	-1.28
1,2-dimethoxybenzene	-5.33	-5.18	-4.85	-6.19	-4.01
dibenzo-p-dioxin	-3.15	-2.32	-4.31	-3.43	-4.23
anthracene	-3.95	-4.30	-3.93	-3.92	-2.92
1-ethyl-2-methylbenzene	-0.85	-0.59	-0.79	-0.90	-0.93
9,10-dihydroanthracene	-3.78	-3.14	-3.50	-3.08	-3.34
HEXYL NITRATE	-1.66	-1.19	-1.46	-1.71	-1.36
3-nitrooxypropyl nitrate	-4.80	-5.73	-5.66	-5.87	-5.80
1,3-bis-(nitrooxy)butane	-4.29	-4.85	-5.09	-4.80	-4.93
4-(1-Methylethenyl)-1-cyclohexene-1-carboxaldehyde	-4.09	-3.19	-3.30	-2.72	-3.55
2-hydroxybenzaldehyde	-4.68	-6.94	-7.61	-5.81	-6.48
2-chlorosyringaldehyde	-7.78	-7.48	-8.69	-9.75	-6.86
2,6-dichlorosyringaldehyde	-8.68	-6.87	-8.01	-10.52	-7.11
2-(2,3-dimethylphenyl)aminobenzoic acid	-6.78	-8.30	-6.74	-7.89	-7.26
(3R)-3,7-Dimethylocta-1,6-dien-3-yl acetate	-2.49	-2.71	-1.95	-1.74	-1.82
2-ethoxyethyl acetate	-5.31	-5.60	-5.04	-4.70	-5.44
1,4-diamino-9,10-anthracenedione	-11.85	-11.36	-9.37	-9.65	-9.04
1-amino-9,10-anthracenedione	-9.44	-9.15	-8.76	-8.61	-7.32
2-amino-9,10-anthraquinone	-11.53	-11.16	-9.63	-9.46	-9.46
1-(2-hydroxyethylamino)-9,10-anthraquinone	-14.21	-11.63	-13.43	-14.23	-11.37
1-amino-4-hydroxy-9,10-anthracenedione	-9.53	-9.81	-10.51	-10.54	-8.54
(2R,5R)-2-methyl-5-(1-methylethenyl)-cyclohexanone	-3.75	-3.24	-3.40	-3.37	-3.06
6-isopropyl-3-methyl-1-cyclohex-2-enone	-4.51	-3.34	-3.57	-3.07	-2.83
Amitriptyline	-7.43	-5.99	-4.53	-6.66	-8.84
[2-benzhydryloxyethyl]-dimethyl-amine	-9.34	-9.47	-7.45	-9.96	-9.80
(1S,5R)-2-methyl-5-(1-methylethenyl)-2-cyclohexen-1-ol	-4.44	-4.60	-5.49	-5.43	-4.51
(2E)-3,7-dimethylocta-2,6-dien-1-ol	-4.45	-5.36	-6.10	-6.01	-6.32
(2Z)-3,7-dimethylocta-2,6-dien-1-ol	-4.78	-3.64	-5.90	-6.05	-5.70
1-butoxy-2-propanol	-5.73	-4.98	-6.21	-5.52	-4.81
3,4-dichlorophenol	-7.29	-5.82	-5.61	-6.14	-4.50
2-methoxyphenol	-5.94	-5.92	-5.69	-5.67	-6.36
4-methyl-2-methoxyphenol	-5.80	-8.41	-6.49	-7.69	-6.70
4-propylguaiaicol	-5.26	-7.47	-6.12	-6.62	-6.65
2,6-dimethoxyphenol	-6.96	-8.73	-7.06	-8.70	-8.91
3,5-dichloro-2,6-dimethoxyphenol	-6.44	-6.59	-5.80	-7.67	-4.33
1-benzylimidazole	-7.63	-9.59	-9.77	-7.11	-9.08
RMSE		1.12	1.12	1.09	1.32
ME		-0.01	0.07	-0.04	0.36