Supporting Information for:

SM6: A Density Functional Theory Continuum Solvation Model for Calculating Aqueous Solvation Free Energies of Neutrals, Ions, and Solute-Water Clusters

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Description of Charge Model 4 (CM4).

Charge Model 4 (CM4), as well as our previously developed charge models,[1-8] begins with wave function-dependent charges and empirically maps them to reproduce experimental or converged theoretical charge-dependent observables. The function we use for mapping these charges is

$$q_k = q_k^0 + \sum_{k \neq k'} T_{k,k'}(B_{k,k'}) \tag{S1}$$

where q_k^0 is the partial atomic charge from either a Löwdin population analysis (LPA)[9-12] for nondiffuse basis sets or a redistributed Löwdin population analysis (RLPA)[13] for diffuse basis sets, and $T_{kk'}(B_{kk'})$ is a quadratic function of the Mayer [14-16] bond order, $B_{kk'}$, between two atoms k and k':

$$T_{kk'}(B_{kk'}) = (D_{ZZ'} + C_{ZZ'}B_{kk'})B_{kk'} \tag{S2}$$

where $C_{ZZ'}$ and $D_{ZZ'}$ are parameters that depend on the atomic numbers Z and Z'. Because the total charge remains constant, the charge transferred from k' to k should be equal but opposite to the charge transferred from k to k'. This conservation of charge is maintained by the following relations:

$$C_{ZZ'} = -C_{Z'Z} \tag{S3}$$

$$D_{ZZ'} = -D_{Z'Z} \tag{S4}$$

As shown in earlier work, for a given basis set, the optimum $C_{ZZ'}$ and $D_{ZZ'}$ parameters for an arbitrary percentage X of Hartree-Fock exchange can be written to a good approximation as

$$P_{ZZ'} = b_{ZZ'} + \sum_{i=1}^{1 or 2} X^i m_{ZZ'}^{[i]} \tag{S5}$$

where $P_{ZZ'}$ is either $C_{ZZ'}$ or $D_{ZZ'}$. The above function is especially useful because different percentages of Hartree-Fock exchange are optimal for various applications. We have optimized $b_{ZZ'}$, $m_{ZZ'}^{[1]}$, and $m_{ZZ'}^{[2]}$, values for the MIDI!6D, 6-31G(d), 6-31+G(d), and 6-31+G(d,p) basis sets. These parameters were optimized using the MPW*X* functional, although they can be used with other density functionals, provided the given functional

delivers a reasonably accurate charge distribution for the molecule of interest. The CM4 parameters for the MIDI!6D, 6-31G(d), 6-31+G(d), and 6-31+G(d,p) basis sets are listed in Tables S2-S5, respectively, and the procedure we used to obtain them is described below.

For each of the four basis sets, $C_{ZZ'}$ and $D_{ZZ'}$ parameters were optimized for five different percentages of HF exchange: 0, 25, 42.8, 60.6, and 99.9 according to the procedure described below. First, a single D_{HC} parameter was optimized against the following error function:

$$\chi^{[1]} = \sum_k \left(q_k^{\mathrm{CM4}} - q_k^{\mathrm{target}} \right)^2 \tag{S6}$$

where q_k^{CM4} is the CM4 charge of atom *k* and q_k^{target} is the target value for the partial atomic charge on atom *k*. For q_k^{target}, we used partial atomic charges for 19 different hydrocarbons obtained from Jorgenson et al.'s OPLS force field.[17] The above procedure differs from previous parametrizations,[2,4,5,8] in which C–H parameters were determined by requiring that the average charge on H in benzene and ethylene be 0.11, a value that had been justified in a previous paper.[2] We used the procedure described above because some of our previous charge models gave C–H bonds that were too polar, and this, in turn, had a negative impact on the performance of our solvation models. The remaining $C_{ZZ'}$ and $D_{ZZ'}$ parameters were optimized using molecular dipole moment data taken from our most recent CM3 training set,[8] which includes 397 gas-phase dipole moments for 389 molecules containing H, Li, C, N, O, F, Si, P, S, Cl and/or Br, against the following error function

$$\chi^{[2]} = \sum_{i=1}^{397} (\mu_i^{\mathrm{CM4}} - \mu_i^{\mathrm{target}})^2 \tag{S7}$$

where μ_i^{target} is the molecular dipole moment taken from the training set. The CM4 point-charge-derived dipole moment, μ_i^{CM4} is calculated from the partial atomic charges according to

$$\mu^{\mathrm{CM4}} = \sqrt{\left(\sum_k q_k^{\mathrm{CM4}} x_k\right)^2 + \left(\sum_k q_k^{\mathrm{CM4}} y_k\right)^2 + \left(\sum_k q_k^{\mathrm{CM4}} z_k\right)^2} \quad \text{(S8)}$$

where q_k^{CM4} is the CM4 partial atomic charge, and x_k, y_k, and z_k are the Cartesian coordinates of atom k in a barycentric coordinate system, that is, a coordinate system with the center of mass at the origin. (However, since all of the molecules used to parametrize CM4 set are neutral, the dipole moment is independent on the location of the origin). The application of eq S7 was carried out in several stages. First, the parameters for molecules containing at most H, C, N, and O were determined with fixed D_{HC}. Then, with the parameters for H, C, N, and O fixed, the parameters for bonds between C–F, C–Cl, and C–Br were optimized. Then, these parameters were fixed, and the parameters involving sulfur were determined. Then the parameter optimization for Si was carried out in two steps. First, the D_{HSi} and the D_{CSi} parameters were optimized using the subset of the training set that contains at most C, H, and Si. Second, these parameters were held fixed, and the remaining Si parameters (C_{OSi}, D_{OSi}, D_{FSi}, and D_{SiCl}) were optimized using the rest of the Si training set. Finally, with all of these parameters fixed, the parameters for Li and P were optimized.

With the $C_{ZZ'}$ and $D_{ZZ'}$ parameters determined for each percentage of HF exchange, the parameters in eq S5 were then determined through a linear or quadratic regression. Note that in tables S2-S5, an entry of 0.0000 in the column labeled $m_{ZZ}^{[2]}$, implies that a linear regression was used for the particular parameter, whereas a nonzero value implies that a quadratic regression was used.

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Table S1. Experimental aqueous solvation free energies (kcal/mol) of neutral solutes used in this work. All data are for a temperature of 298 K.

No.	Solute	ΔG_S^*
1	ammonia	-4.29
2	hydrogen	2.33
3	methane	2.00
4	ethane	1.83
5	*n*-propane	1.96
6	*n*-butane	2.08
7	*n*-pentane	2.33
8	*n*-hexane	2.49
9	*n*-heptane	2.62
10	*n*-octane	2.89
11	2-methylpropane	2.32
12	2,2-dimethylpropane	2.50
13	2-methylpentane	2.52
14	2,4-dimethylpentane	2.88
15	2,2,4-trimethylpentane	2.85
16	cyclopropane	0.75
17	cyclopentane	1.20
18	cyclohexane	1.23
19	methylcyclohexane	1.71
20	cis-1,2-dimethylcyclohexane	1.58
21	ethane	1.27
22	propene	1.27
23	*s-trans*-1,3-butadiene	0.61
24	2-methylpropene	1.16
25	1-butene	1.38
26	cyclopentene	0.56
27	1-pentene	1.66
28	*E*-2-pentene	1.34
29	1-hexene	1.68
30	ethyne	-0.01
31	propyne	-0.31
32	1-butyne	-0.16
33	1-pentyne	0.01
34	1-hexyne	0.29
35	benzene	-0.87
36	toluene	-0.89
37	ethylbenzene	-0.80
38	*o*-xylene	-0.90
39	*m*-xylene	-0.84
40	*p*-xylene	-0.81
41	naphthalene	-2.39
42	anthracene	-4.23
43	methanol	-5.11
44	ethanol	-5.01
45	1,2-ethanediol	-9.30

46	*trans*-1-propanol	-4.83
47	2-propanol	-4.76
48	1-butanol	-4.72
49	2-methyl-2-propanol	-4.51
50	cyclopentanol	-5.49
51	1-pentanol	-4.47
52	1-hexanol	-4.36
53	1-heptanol	-4.24
54	1-octanol	-4.09
55	phenol	-6.62
56	*o*-cresol	-5.87
57	*m*-cresol	-5.49
58	*p*-cresol	-6.14
59	dimethyl ether	-1.92
60	tetrahydrofuran	-3.47
61	1,4-dioxane	-5.05
62	diethyl ether	-1.76
63	methyl propyl ether	-1.66
64	methyl isopropyl ether	-2.01
65	1,2-dimethoxyethane	-4.84
66	*t*-butyl methyl ether	-2.21
67	anisole	-2.45
68	isopropyl ether	-0.53
69	tetrahydropyran	-3.12
70	ethyl phenyl ether	-2.22
71	ethanal	-3.50
72	propanal	-3.44
73	butanal	-3.18
74	pentanal	-3.03
75	benzaldehyde	-4.02
76	octanal	-2.29
77	acetone	-3.85
78	2-butanone	-3.64
79	cyclopentanone	-4.68
80	2-pentanone	-3.53
81	3-pentanone	-3.41
82	2-hexanone	-3.29
83	3,3-dimethylbutanone	-2.89
84	2-heptanone	-3.04
85	4-heptanone	-2.93
86	methyl phenyl ketone	-4.58
87	5-nonanone	-2.67
88	2-octanone	-2.88
89	acetic acid	-6.70
90	propanoic acid	-6.47
91	butanoic acid	-6.36
92	pentanoic acid	-6.16
93	hexanoic acid	-6.21
94	methyl methanoate	-2.78
95	trans ethyl methanoate	-2.65

96	methyl ethanoate	-3.32
97	methyl propanoate	-2.93
98	ethyl ethanoate	-3.10
99	methyl butanoate	-2.83
100	propyl ethanoate	-2.86
101	methyl pentanoate	-2.57
102	butyl ethanoate	-2.55
103	methyl hexanoate	-2.49
104	pentyl ethanoate	-2.45
105	methyl octanoate	-2.04
106	methyl benzoate	-3.91
107	2-propen-1-ol	-5.08
108	2-methoxyethanol	-6.77
109	butenyne	0.04
110	*m*-hydroxybenzaldehyde	-9.51
111	*p*-hydroxybenzaldehyde	-10.48
112	hydrogen peroxide	-8.58
113	methyl peroxide	-5.28
114	ethyl peroxide	-5.32
115	ethylamine	-4.50
116	dimethylamine	-4.29
117	azetidine	-5.56
118	propylamine	-4.39
119	trimethylamine	-3.23
120	pyrrolidine	-5.48
121	piperazine	-7.40
122	butylamine	-4.29
123	diethylamine	-4.07
124	*N*-methylpiperazine	-7.77
125	pentylamine	-4.10
126	*N*,*N*'-dimethylpiperazine	-7.58
127	dipropylamine	-3.66
128	piperidine	-5.11
129	methylamine	-4.56
130	aniline	-5.49
131	2-methylaniline	-5.56
132	3-methylaniline	-5.67
133	4-methylaniline	-5.55
134	*N*-methylaniline	-4.68
135	*N*-ethylaniline	-4.62
136	*N*,*N*-dimethylaniline	-3.58
137	pyridine	-4.70
138	2-methylpyridine	-4.63
139	3-methylpyridine	-4.77
140	4-methylpyridine	-4.94
141	2,4-dimethylpyridine	-4.86
142	2,5-dimethylpyridine	-4.72
143	2,6-dimethylpyridine	-4.60
144	3,4-dimethylpyridine	-5.22
145	3,5-dimethylpyridine	-4.84

146	4-ethylpyridine	-4.74
147	2-methylpyrazine	-5.57
148	2-ethylpyrazine	-5.51
149	hydrazine	-6.26
150	methylhydrazine	-5.31
151	1,1-dimethylhydrazine	-4.48
152	ethanonitrile	-3.89
153	propanonitrile	-3.85
154	butanonitrile	-3.64
155	benzonitrile	-4.10
156	9-methyladenine	-13.60
157	3-aminoaniline	-9.92
158	1,2-ethanediamine	-9.72
159	acetamide	-9.71
160	*E*-*N*-methylacetamide	-10.00
161	*Z*-*N*-methylacetamide	-10.00
162	benzamide	-10.90
163	1,1-dimethyl-3-phenylurea	-9.63
164	urea	-13.80
165	nitroethane	-3.71
166	1-nitropropane	-3.34
167	2-nitropropane	-3.14
168	1-nitrobutane	-3.08
169	nitrobenzene	-4.12
170	2-methyl-1-nitrobenzene	-3.59
171	nitromethane	-3.95
172	2-methoxyethanamine	-6.55
173	morpholine	-7.17
174	*N*-methylmorpholine	-6.34
175	1-methylthymine	-10.40
176	fluoromethane	-0.22
177	1,1-difluoroethane	-0.11
178	tetrafluoromethane	3.16
179	hexafluoroethane	3.94
180	octafluoropropane	4.28
181	fluorobenzene	-0.78
182	chloromethane	-0.56
183	dichloromethane	-1.36
184	trichloromethane	-1.07
185	chloroethane	-0.63
186	1,1,1-trichloroethane	-0.25
187	1,1,2-trichloroethane	-1.95
188	1-chloropropane	-0.27
189	2-chloropropane	-0.25
190	1,1,1,2-tetrachloroethane	-1.15
191	hexachloroethane	-1.40
192	2-chlorobutane	0.07
193	1-chloropentane	0.07
194	2-chloropentane	0.07
195	chloroethene	-0.59

196	3-chloropropene	-0.57
197	*Z*-1,2-dichloroethene	-1.17
198	*E*-1,2-dichloroethene	-0.76
199	trichloroethene	-0.39
200	tetrachloroethene	0.05
201	chlorobenzene	-1.12
202	1,2-dichlorobenzene	-1.36
203	1,4-dichlorobenzene	-1.01
204	chlorotoluene	-1.92
205	ortho-chlorotoluene	-1.15
206	2,2'-dichlorobiphenyl	-2.73
207	2,3-dichlorobiphenyl	-2.45
208	2,2',3'-trichlorobiphenyl	-1.99
209	bromomethane	-0.82
210	dibromomethane	-2.11
211	tribromomethane	-1.98
212	bromoethane	-0.70
213	1-bromopropane	-0.56
214	2-bromopropane	-0.48
215	1-bromobutane	-0.41
216	1-bromopentane	-0.08
217	1-bromoisobutane	-0.03
218	3-bromopropene	-0.86
219	bromobenzene	-1.46
220	*p*-dibromobenzene	-2.30
221	bromotoluene	-2.37
222	*p*-bromotoluene	-1.39
223	bromotrifluoromethane	1.79
224	chlorofluoromethane	-0.77
225	chlorodifluoromethane	-0.50
226	1-bromo-1-chloro-2,2,2-trifluoroethane	-0.13
227	1-bromo-2-chloroethane	-1.95
228	1-bromo-1,2,2,2-tetrafluoroethane	0.52
229	1-chloro-2,2,2-trifluoroethane	0.06
230	1,1,2-trichloro-1,2,2-trifluoroethane	1.77
231	difluorodichloromethane	1.69
232	fluorotrichloromethane	0.82
233	bromotrichloromethane	-0.93
234	chloropentaflouroethane	2.86
235	2,2,2-trifluoroethanol	-4.31
236	1-chloro-2,2,2-trifluoroethyl difluoromethyl ether	0.11
237	1,1,1-trifluoropropan-2-ol	-4.16
238	1,1,1,3,3,3-hexafluoropropan-2-ol	-3.77
239	2,2,2-trifluorethyl vinyl ether	-0.12
240	*p*-bromophenol	-7.13
241	3,5-dibromo-4-hydroxybenzonitrile	-9.00
242	2,6-dichlorobenzonitrile	-5.22
243	4-amino-3,5,6-trichloropyridine-2-carboxylic acid	-11.96
244	methanethiol	-1.24
245	ethanethiol	-1.30

246	1-propanethiol	-1.05
247	thiophenol	-2.55
248	dimethyl sulfide	-1.54
249	diethyl sulfide	-1.43
250	dipropyl sulfide	-1.27
251	thioanisole	-2.73
252	hydrogen sulfide	-0.70
253	dimethyl disulfide	-1.83
254	diethyl disulfide	-1.63
255	thiophene	-1.42
256	bis(2-chloroethyl)sulfide	-3.92
257	2,6-dichlorothiobenzamide	-10.81
258	phosphine	0.60
259	trimethylphosphate	-8.70
260	triethylphosphate	-7.80
261	tripropylphosphate	-6.10
262	methyl 3-methyl-4-thiomethoxyphenyl thiophosphate	-6.92
263	dimethyl 4-nitrophenyl thiophosphate	-7.62
264	diethyl 4-nitrophenyl thiophosphonate	-6.27
265	2,2-dichloroethenyl dimethyl phosphate	-6.61
266	dimethyl 5-(4-chloro)bicyclo[3.2.0]heptyl phosphate	-7.28
267	diethyl 2,4-dichlorophenyl thiophosphate	-3.86
268	O-ethyl,O'-4-bromo-2-chlorophenyl,S-propyl,phosphorothioate	-4.09
269	dimethyl 2,4,5-trichlorophenyl thiophosphate	-5.06
270	dimethyl 4-bromo-2,5-dichlorophenyl thiophosphate	-5.70
271	ethyl 4-cyanophenyl phenylthiophosphonate	-5.10
272	water	-6.31
273	water dimer	-14.29

Table S2. CM4/MIDI!6D parameters, slopes ($m^{[2]}_{ZZ'}$ and $m^{[1]}_{ZZ'}$), and intercepts ($b_{ZZ'}$) for various percentages of Hartree-Fock exchange, *X*, obtained using the MPW*X* functional.

	0	25	42.8	60.6	99.9	$m^{[2]}_{ZZ'}$	$m^{[1]}_{ZZ'}$	$b_{ZZ'}$
C – O	0.069	0.076	0.080	0.084	0.091	-0.0070	0.0290	0.0690
O – Si	-0.063	-0.066	-0.068	-0.069	-0.071	0.0060	-0.0130	-0.0630
O – P	-0.033	-0.029	-0.026	-0.025	-0.021	-0.0050	0.0160	-0.0330
P – S	-0.032	-0.041	-0.043	-0.045	-0.054	0.0060	-0.0250	-0.0340
H – C	-0.034	-0.039	-0.042	-0.045	-0.051	0.0000	-0.0170	-0.0340
H – N	0.086	0.083	0.081	0.079	0.074	-0.0010	-0.0110	0.0860
H – O	0.001	-0.006	-0.010	-0.015	-0.026	0.0000	-0.0270	0.0010
H – Si	0.003	0.010	0.015	0.020	0.030	0.0000	0.0270	0.0030
H – P	-0.070	-0.072	-0.071	-0.070	-0.067	0.0100	-0.0060	-0.0710
H – S	-0.119	-0.117	-0.115	-0.114	-0.110	0.0000	0.0080	-0.1190
Li – C	-0.033	-0.119	-0.182	-0.245	-0.389	0.0000	-0.3580	-0.0300
Li – N	0.151	0.129	0.106	0.083	0.033	-0.0250	-0.0970	0.1530
Li – O	0.200	0.138	0.099	0.063	-0.014	0.0360	-0.2480	0.1990
Li – F	0.290	0.258	0.237	0.218	0.175	0.0120	-0.1260	0.2890
Li – P	0.026	-0.012	-0.039	-0.064	-0.116	0.0000	-0.1420	0.0240
Li – Cl	-0.059	-0.094	-0.117	-0.140	-0.190	0.0000	-0.1310	-0.0600
C – N	0.033	0.027	0.022	0.017	0.006	0.0000	-0.0280	0.0340
C – O	-0.097	-0.125	-0.143	-0.161	-0.199	0.0110	-0.1120	-0.0970
C – F	0.007	-0.030	-0.056	-0.081	-0.138	0.0000	-0.1450	0.0070
C – Si	0.057	0.068	0.076	0.083	0.100	0.0000	0.0430	0.0570
C – P	-0.039	-0.040	-0.039	-0.039	-0.037	0.0050	-0.0020	-0.0390
C – S	-0.001	-0.005	-0.008	-0.011	-0.017	0.0000	-0.0160	-0.0010
C – Cl	0.006	0.000	-0.003	-0.007	-0.013	0.0040	-0.0230	0.0060
C – Br	0.051	0.044	0.039	0.033	0.023	0.0000	-0.0290	0.0510
N – O	0.026	0.006	-0.014	-0.028	-0.062	0.0030	-0.0950	0.0280
N – P	-0.085	-0.081	-0.078	-0.076	-0.069	0.0000	0.0160	-0.0850
O – Si	0.046	0.069	0.085	0.100	0.133	0.0000	0.0870	0.0470
O – P	0.025	0.025	0.033	0.041	0.060	0.0320	0.0070	0.0230
O – S	-0.006	0.018	0.035	0.053	0.092	0.0000	0.0980	-0.0070
F – Si	-0.058	-0.025	-0.001	0.023	0.078	0.0000	0.1360	-0.0590
F – P	-0.041	-0.018	0.002	0.021	0.065	0.0000	0.1070	-0.0430
Si – Cl	-0.027	-0.037	-0.044	-0.051	-0.066	0.0000	-0.0390	-0.0270
P – S	0.092	0.105	0.105	0.106	0.114	-0.0170	0.0340	0.0950
P – Cl	0.034	0.072	0.069	0.065	0.058	-0.1090	0.1170	0.0420

Table S3. CM4/6-31G(d) parameters, slopes ($m_{ZZ'}^{[2]}$ and $m_{ZZ'}^{[1]}$), and intercepts ($b_{ZZ'}$) for various percentages of Hartree-Fock exchange, *X*, obtained using the MPW*X* functional.

	0	25	42.8	60.6	99.9	$m_{ZZ'}^{[2]}$	$m_{ZZ'}^{[1]}$	$b_{ZZ'}$
C – O	0.052	0.054	0.055	0.056	0.056	-0.0060	0.0100	0.0520
O – Si	-0.059	-0.062	-0.064	0.030	0.041	0.0450	0.1200	-0.0910
O – P	-0.073	-0.072	-0.071	-0.070	-0.069	-0.0010	0.0060	-0.0730
P – S	0.016	0.007	0.000	-0.008	-0.027	-0.0090	-0.0340	0.0160
H – C	-0.094	-0.097	-0.099	-0.102	-0.106	0.0000	-0.0130	-0.0940
H – N	0.041	0.035	0.031	0.027	0.017	0.0000	-0.0240	0.0410
H – O	-0.027	-0.035	-0.041	-0.047	-0.060	0.0000	-0.0330	-0.0270
H – Si	-0.003	0.006	0.013	0.019	0.031	0.0000	0.0340	-0.0020
H – P	0.078	0.083	0.085	0.088	0.093	-0.0040	0.0180	0.0780
H – S	-0.011	-0.009	-0.007	-0.006	-0.003	0.0000	0.0070	-0.0110
Li – C	0.470	0.478	0.478	0.479	0.483	-0.0130	0.0230	0.4720
Li – N	-0.609	0.001	-0.026	-0.053	0.751	0.1300	0.8380	-0.4130
Li – O	0.677	0.691	0.705	0.723	0.772	0.0500	0.0450	0.6770
Li – F	0.595	0.607	0.619	0.634	0.675	0.0410	0.0390	0.5950
Li – P	0.540	0.542	0.544	0.547	0.554	0.0070	0.0070	0.5400
Li – Cl	0.577	0.589	0.600	0.612	0.643	0.0220	0.0440	0.5770
C – N	0.095	0.090	0.086	0.082	0.072	-0.0040	-0.0190	0.0950
C – O	-0.004	-0.021	-0.032	-0.043	-0.065	0.0080	-0.0690	-0.0040
C – F	0.060	0.033	0.014	-0.004	-0.045	0.0000	-0.1060	0.0600
C – Si	-0.043	-0.033	-0.026	-0.020	-0.006	0.0000	0.0370	-0.0430
C – P	0.063	0.063	0.064	0.065	0.065	-0.0010	0.0040	0.0630
C – S	0.140	0.138	0.137	0.136	0.132	-0.0020	-0.0050	0.1400
C – Cl	0.106	0.101	0.097	0.093	0.085	0.0000	-0.0210	0.1060
C – Br	0.066	0.059	0.054	0.049	0.037	0.0000	-0.0290	0.0660
N – O	0.008	-0.017	-0.032	-0.046	-0.078	0.0120	-0.0960	0.0070
N – P	-0.017	-0.011	-0.006	-0.002	0.009	0.0000	0.0260	-0.0170
O – Si	0.105	0.130	0.148	-0.034	-0.010	-0.0580	-0.1940	0.1730
O – P	0.185	0.201	0.214	0.227	0.254	0.0000	0.0700	0.1840
O – S	0.091	0.119	0.140	0.160	0.206	0.0000	0.1160	0.0900
F – Si	0.028	0.064	0.090	0.117	0.177	0.0000	0.1490	0.0270
F – P	0.124	0.157	0.180	0.203	0.253	0.0000	0.1290	0.1240
Si – Cl	0.039	0.025	0.016	0.007	-0.013	0.0000	-0.0520	0.0390
P – S	-0.037	-0.030	-0.024	-0.017	0.003	0.0170	0.0230	-0.0370
P – Cl	-0.065	-0.076	-0.083	-0.090	-0.105	0.0000	-0.0400	-0.0650

Table S4. CM4/6-31+G(d) parameters, slopes ($m_{ZZ'}^{[2]}$ and $m_{ZZ'}^{[1]}$), and intercepts ($b_{ZZ'}$) for various percentages of Hartree-Fock exchange, *X*, obtained using the MPW*X* functional.

	0	25	42.8	60.6	99.9	$m_{ZZ'}^{[2]}$	$m_{ZZ'}^{[1]}$	$b_{ZZ'}$
C – O	0.025	0.027	0.030	0.032	0.035	-0.0010	0.0120	0.0240
O – Si	-0.106	-0.110	-0.113	-0.115	-0.115	0.0130	-0.0230	-0.1060
O – P	-0.208	-0.226	-0.239	-0.254	-0.231	0.1080	-0.1410	-0.2030
P – S	-0.057	-0.076	-0.088	-0.101	-0.167	-0.0760	-0.0270	-0.0610
H – C	-0.094	-0.095	-0.096	-0.097	-0.099	-0.0010	-0.0050	-0.0940
H – N	0.061	0.054	0.049	0.043	0.032	0.0000	-0.0300	0.0610
H – O	0.007	-0.003	-0.010	-0.016	-0.028	0.0080	-0.0430	0.0070
H – Si	-0.023	-0.018	-0.014	-0.011	-0.007	-0.0080	0.0250	-0.0230
H – P	0.042	0.050	0.055	0.060	0.069	-0.0060	0.0330	0.0420
H – S	-0.047	-0.046	-0.044	-0.042	-0.035	0.0090	0.0030	-0.0470
Li – C	0.361	0.346	0.338	0.330	0.314	0.0130	-0.0590	0.3600
Li – N	0.478	0.465	0.456	0.448	0.430	0.0000	-0.0480	0.4770
Li – O	0.458	0.450	0.445	0.440	0.429	0.0000	-0.0290	0.4570
Li – F	0.516	0.522	0.526	0.528	0.533	-0.0090	0.0250	0.5160
Li – P	0.436	0.433	0.431	0.430	0.427	0.0040	-0.0120	0.4360
Li – Cl	0.432	0.426	0.422	0.418	0.408	0.0000	-0.0240	0.4320
C – N	0.093	0.089	0.085	0.080	0.070	-0.0060	-0.0180	0.0930
C – O	0.013	-0.005	-0.019	-0.033	-0.063	0.0000	-0.0770	0.0130
C – F	0.002	-0.032	-0.056	-0.080	-0.131	0.0000	-0.1330	0.0010
C – Si	0.020	0.028	0.033	0.037	0.044	-0.0110	0.0350	0.0200
C – P	0.177	0.176	0.176	0.176	0.175	0.0000	-0.0020	0.1770
C – S	0.169	0.167	0.166	0.164	0.158	-0.0060	-0.0040	0.1690
C – Cl	0.120	0.113	0.108	0.104	0.094	0.0000	-0.0270	0.1200
C – Br	0.113	0.109	0.105	0.102	0.094	0.0000	-0.0190	0.1130
N – O	-0.023	-0.044	-0.055	-0.067	-0.091	0.0150	-0.0810	-0.0240
N – P	0.050	0.056	0.060	0.064	0.073	0.0000	0.0230	0.0500
O – Si	0.282	0.310	0.329	0.346	0.378	-0.0230	0.1200	0.2820
O – P	0.516	0.570	0.607	0.646	0.632	-0.2050	0.3390	0.5070
O – S	0.151	0.186	0.211	0.236	0.290	0.0000	0.1390	0.1510
F – Si	0.179	0.216	0.243	0.269	0.324	0.0000	0.1460	0.1800
F – P	0.301	0.366	0.416	0.469	0.653	0.1650	0.1770	0.3060
Si – Cl	-0.019	-0.030	-0.037	-0.044	-0.057	0.0080	-0.0460	-0.0190
P – S	0.111	0.141	0.158	0.175	0.277	0.1180	0.0340	0.1180
P – Cl	-0.086	-0.095	-0.101	-0.106	-0.115	0.0100	-0.0390	-0.0860

Table S5. CM4/6-31+G(d,p) parameters, slopes ($m_{ZZ'}^{[2]}$ and $m_{ZZ'}^{[1]}$), and intercepts ($b_{ZZ'}$) for various percentages of Hartree-Fock exchange, *X*, obtained using the MPW*X* functional.

	0	25	42.8	60.6	99.9	$m_{ZZ'}^{[2]}$	$m_{ZZ'}^{[1]}$	$b_{ZZ'}$
C – O	0.023	0.026	0.028	0.029	0.032	-0.0040	0.0120	0.0230
O – Si	-0.098	-0.100	-0.100	-0.100	-0.096	0.0120	-0.0110	-0.0980
O – P	-0.197	-0.212	-0.224	-0.236	-0.248	0.0250	-0.0800	-0.1950
P – S	-0.064	-0.080	-0.091	-0.102	-0.144	-0.0350	-0.0410	-0.0660
H – C	-0.043	-0.043	-0.044	-0.044	-0.045	0.0000	-0.0020	-0.0430
H – N	0.147	0.144	0.141	0.138	0.131	0.0000	-0.0170	0.1480
H – O	0.143	0.140	0.138	0.136	0.134	0.0060	-0.0150	0.1430
H – Si	-0.005	0.000	0.004	0.007	0.013	-0.0040	0.0230	-0.0050
H – P	0.063	0.074	0.082	0.088	0.101	-0.0110	0.0480	0.0630
H – S	0.004	0.007	0.009	0.012	0.020	0.0070	0.0090	0.0040
Li – C	0.354	0.341	0.332	0.325	0.309	0.0090	-0.0530	0.3540
Li – N	0.467	0.454	0.445	0.436	0.418	0.0000	-0.0490	0.4670
Li – O	0.446	0.438	0.433	0.427	0.416	0.0000	-0.0300	0.4460
Li – F	0.515	0.521	0.525	0.528	0.532	-0.0110	0.0280	0.5150
Li – P	0.435	0.433	0.431	0.430	0.426	-0.0010	-0.0080	0.4350
Li – Cl	0.432	0.426	0.422	0.419	0.410	0.0000	-0.0220	0.4320
C – N	0.095	0.090	0.086	0.082	0.072	-0.0040	-0.0190	0.0950
C – O	0.016	-0.001	-0.014	-0.027	-0.054	0.0000	-0.0700	0.0160
C – F	0.007	-0.027	-0.051	-0.075	-0.125	0.0000	-0.1320	0.0060
C – Si	0.015	0.022	0.026	0.030	0.036	-0.0090	0.0300	0.0150
C – P	0.179	0.178	0.178	0.177	0.175	-0.0020	-0.0010	0.1790
C – S	0.162	0.161	0.159	0.157	0.153	-0.0040	-0.0060	0.1620
C – Cl	0.122	0.115	0.110	0.106	0.097	0.0000	-0.0250	0.1210
C – Br	0.114	0.110	0.106	0.103	0.095	0.0000	-0.0190	0.1140
N – O	-0.024	-0.043	-0.054	-0.065	-0.088	0.0120	-0.0750	-0.0250
N – P	0.050	0.056	0.060	0.064	0.073	0.0000	0.0230	0.0500
O – Si	0.268	0.290	0.305	0.319	0.343	-0.0210	0.0970	0.2680
O – P	0.500	0.550	0.585	0.620	0.670	-0.0590	0.2340	0.4980
O – S	0.155	0.189	0.214	0.238	0.291	0.0000	0.1370	0.1550
F – Si	0.175	0.212	0.237	0.263	0.316	0.0000	0.1410	0.1760
F – P	0.309	0.374	0.424	0.477	0.631	0.1020	0.2150	0.3110
Si – Cl	-0.017	-0.028	-0.035	-0.041	-0.054	0.0080	-0.0440	-0.0170
P – S	0.122	0.146	0.162	0.178	0.234	0.0390	0.0690	0.1240
P – Cl	-0.088	-0.097	-0.102	-0.108	-0.119	0.0040	-0.0340	-0.0880

Table S6. Mean unsigned errors (kcal/mol) in aqueous solvation free energies calculated using SM6, by data set.

	MPW25					
	MIDI!6D	6-31G(d)	6-31+G(d)	6-31+G(d,p)	B3LYP/ 6-31+G(d,p)[a]	B3PW91/ 6-31+G(d,p)[a]
neutrals[b]	0.50	0.47	0.55	0.54	0.55	0.54
unclustered ions[c]	5.26	4.72	4.27	4.19	4.37	4.22
selectively clustered ions[c]	4.24	3.80	3.28	3.21	3.37	3.25
all ions[d]	5.32	4.88	4.47	4.38	4.55	4.42
all data[e]	2.16	1.98	1.90	1.86	1.92	1.87

[a]Surface tension coefficients optimized for the MPW25/6-31+G(d,p) level of theory were used in these calculations.
[b]273 molecules. [c]112 ions. [d]143 ions. [e]416 data.

END OF SUPPORTING INFORMATION