Supporting Information for "CHARMM Force Field Parameters for Simulation of reactive intermediates in native and thio-substituted systems"

Evelyn Mayaan[1], *Adam Moser*[1], *Alexander D. MacKerell, Jr.*[2,*] *and Darrin M. York*[1,*]

1. Department of Chemistry, University of Minnesota, 207 Pleasant St. SE, Minneapolis, MN 55455–0431, USA.

2. Department of Pharmaceutical Chemistry, School of Pharmacy, University of Maryland Baltimore, MD 21201, USA. E-mail: york@chem.umn.edu

Table S1: Weight factors for Parameter Fitting Function

Measurement	**σ Range**	**Tolerance**
HT–OW	5.0E2 - 1.0E5	4.4E-2 - 3.2E-3
MG· · ·OT	1.0E5	3.2E-3
MG· · ·OW	1.0E4 - 1.0E6	1.0E-2 - 1.0E-3
MG· · ·ON3	1.0E4 - 1.0E6	1.0E-2 - 1.0E-3
MG· · ·MG	1.0E2 - 5.0E3	1.0E-1 - 1.4E-2
MG· · ·OW· · ·MG	5.0E0 - 1.0E1	4.5E-1 - 1.0E-1
S· · ·OT	1.0E4	1.0E-2
S· · ·MG	1.0E4	1.0E-2
S· · ·HT	1.0E5	3.2E-3
MG· · ·S	1.0E0 - 1.0E4	1.0E0 - 1.0E-2
S-P	1.0E4	1.0E-2
ON2-P-S	1.0E1	3.2E-1
ON3-P-S	1.0E1	3.2E-1
S-P-S	1.0E1	3.2E-1
$(Mg(H_2O)_5 + H_2O) \rightarrow Mg(H_2O)_6$	1.0E2 - 1.0E3	1.0E-1 - 3.2E-2
DMP(oo)/(so):H_2O	5.0E1 - 1.0E3	1.4E-1 - 3.2E-2
DMP(oo)/(ss):H_2O	5.0E1 - 1.0E3	1.4E-1 - 3.2E-2
Mg(HOH)5(DMP)-(oo)/(so):H_2O	5.0E1 - 1.0E3	1.4E-1 - 3.2E-2
Mg(HOH)5(DMP)-(oo)/(ss):H_2O	5.0E1 - 1.0E3	1.4E-1 - 3.2E-2

The range of weight factor adjustments over the parameterization are shown in the table above. As discussed in the text, σ weight factors were adjusted somewhat empirically over the course of the parameter fitting. However, their purpose is to weight the fitting function tolerance for specific measurement types and so the ranges of these adjustments were made such that parameter searching could be kept within a desired range of deviation.

Table S2: Comparison of HF/6-31G* geometry results vs. B3LYP/6-31G++(d,p)

Complex	**DFT with TIP3P geometries**	**HF with TIP3P geometries**	**DFT without TIP3P geometries**	**HF without TIP3P geometries**
ON3/S· · ·OH2 distance				
DMP(oo)$^-$:H_2O	1.88	1.93	1.85	1.95
DMP(so)$^-$:H_2O	2.89 (1.01)	2.94 (1.00)	2.76 (0.91)	2.88 (0.93)
DMP(ss)$^-$:H_2O	2.94 (1.05)	2.99 (1.05)	2.76 (0.91)	2.90 (0.95)
ON3/S:MG distance				
$Mg(HOH)_5$:DMP(oo)$^-$	1.99	1.74	2.01	1.99
$Mg(HOH)_5$:DMP(so)$^-$	2.54 (0.55)	2.55 (0.81)	2.56 (0.56)	2.54 (0.59)
$Mg(HOH)_5$:DMP(ss)$^-$	2.53 (0.54)	2.54 (0.80)	2.54 (0.54)	2.53 (0.57)

Gas phase geometry optimizations with thio-substituted complexes. Numbers in parenthesis are differences in S binding distances relative to CHARMM OH2 or ON3 oxygen. Results showed that DFT calculations compared better with HF calculations (used in the original force field parameterization) when waters remained unconstrained to the TIP3P geometry.

Table S3: Summary of Parameterization Training Sets

Residue	Structure	New Atom Types	PES Scans
$Mg(H_2O)_6^{2+}$	Fig. 3a	MG	
$Mg(H_2O)_5^{2+}$	Fig. 3b	MG	
$Mg(H_2O)_5(OH^-)^{1+}$	Fig. 3c	MG, OW	
$Mg(H_2O)_5$:DMP^{1+}	Fig. 3d	MG	
$Mg(H_2O)_5 \cdot (OH^-) \cdot Mg(H_2O)_5^{3+}$	Fig. 3e	MG, OW	
$Mg(H_2O)_5 \cdot (OH^-) \cdot Mg(H_2O)_4$:$DMP^{2+}$	Fig. 3f	MG, OW	
ribose MeP^-	Fig. 2b	ONC	O2'-C2', O2'-C2'-C1', O2'-C2'-C3', O2'-C2'-H21'
ribose MeP^-:HOH		ONC	same as above
ribose $MePA^{2-}$	Fig.5a	PX, ONX,ONY	P-O2', P-O3', P-O5', P-O1P/O2P, O2'-C2', O5'-C5', O2'-P-O3', O2'-P-O5', O2'-P-O1P/O2P, O3'-P-O1P/O2P, O5'-P-O1P/O2P, C2'-O2'-P, C3'-O3'-P
ribose $MePA^{2-}$:HOH	Fig. 5b	PX, ONX, ONY	same as above
ribose MePA-so^{2-}	Fig. 5c	PX, ONX, ONY, SX, OX	same as above + P-S1P/S2P, O2'-P-S1P/S2P, O3'-P-S1P/S2P, O5'-P-S1P/S2P, S1P/O1P-P-O2P/S2P
ribose MePA-so^{2-}:HOH	Fig. 5d	PX, ONX, ONY, SX, OX	same as above
ribose MePA-ss^{2-}	Fig. 5e	PX, ONX, ONY, SX	same as above + P-S1P/S2P, O2'-P-S1P/S2P, O3'-P-S1P/S2P, O5'-P-S1P/S2P, S1P-P-S2P
ribose MePA-ss^{2-}:HOH	Fig. 5f	PX, ONX, ONY, SX	same as above
cyclic phosphate	Fig. 2d	PC	O2'-P, O3'-P, O1P/O2P-P, O2'-P-O1P/O2P, O3'-P-O1P/O2P, O2'-P-O3'
DMP-ss^-:HOH	Fig. 4a	SS	P-S1/S2
DMP-so^-:HOH	Fig. 4b	SO	P-S1, P-O3, S1-P-O3
DMP-so^-	Fig. 4c	SO	P-S1, S1-P-O3
DMP-$ss^-{}_{g-g}$	Fig. 4d	SS	P-S1/S2
DMP-$ss^-{}_{g-t}$	Fig. 4e	SS	P-S1/S2
DMP-so^-:$[Mg(HOH)_5]^{2+}$	Fig. 4f	SS, MG	P-S1, S1-P-O3
DMP-ss^-:$[Mg(HOH)_5]^{2+}$	Fig. 4g	SS, MG	P-S1/S2

PES column lists potential energy surface scans done for listed bond and angle force constants