Supporting Information

Extension of the CHARMM General Force Field to Sulfonyl-Containing Compounds and Its Utility in Biomolecular Simulations

Wenbo Yu, Xibing He, Kenno Vanommeslaeghe and Alexander D. MacKerell, Jr.*

Department of Pharmaceutical Sciences, School of Pharmacy, University of Maryland, Baltimore, Maryland 21201

* Corresponding author email: alex@outerbanks.umaryland.edu

Table of Contents: **Page Number**

Table S1. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of MSAM – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-5.36	-5.04	0.32	2.08	1.83	-0.25
O11...HOH	270	-5.20	-5.31	-0.11	2.10	1.82	-0.28
N2...HOH	270	-3.50	-3.39	0.11	2.24	2.07	-0.17
N2H…OHH	0	-6.18	-5.95	0.23	2.02	1.85	-0.17

Table S2. Gas phase dipole moment (Debye) of MSAM calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-1.7042	-2.2275
Y	2.8347	2.7365
Z	0.0297	0.0276
Total	3.3076	3.5286

Table S3. MM and MP2/6-31G(d) level equilibrium geometry of MSAM

Coordinate	QM	MM	Difference	Coordinate	QM	MM	Difference
Bond length (Å)				Angles (°)			
S1-N2	1.684	1.621	-0.062	N2-S1-C3	101.9	101.5	-0.4
S1-O11	1.464	1.431	-0.033	O11-S1-N2	107.5	106.7	-0.9
S1-O12	1.464	1.431	-0.033	O12-S1-N2	107.5	106.7	-0.9
S1-C3	1.776	1.770	-0.006	O11-S1-C3	107.9	109.0	1.1
N2-H21	1.019	1.015	-0.004	O12-S1-C3	107.9	109.0	1.1
N2-H22	1.019	1.015	-0.004	O11-S1-O12	122.3	122.0	-0.2
C3-H31	1.091	1.108	0.016	S1-N2-H21	109.5	108.7	-0.8
C3-H32	1.090	1.108	0.018	S1-N2-H22	109.5	108.7	-0.8
C3-H33	1.090	1.108	0.018	H21-N2-H22	110.9	111.2	0.3
				S1-C3-H31	107.2	108.3	1.1
				S1-C3-H32	108.9	108.8	-0.1
Dihedrals (°)				S1-C3-H33	108.9	108.8	-0.1
N2-S1-C3-H31	180.0	180.0	0.0	H31-C3-H32	110.4	110.2	-0.2

H21-N2-S1-C3	-119.1	-119.4	-0.3	H31-C3-H33	110.4	110.2	-0.2
				H32-C3-H33	110.9	110.5	-0.4

Table S4. Scaled MP2/6-31G(d) and MM level vibrational spectra of MSAM.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
152.4	tS1-N2	78	iSO2	17			180.5	tS1-N2	97				
230.6	tC3-S1	96					239.6	tC3-S1	100				
280.9	cNSC	85					338.3	cNSC	89				
313.5	iSO2	68	rSO2	15			344.1	wSO2	79				
381.2	rSO2	72					361.3	iSO2	93				
452.6	cSO2	45	wSO2	42			384.5	rSO2	92				
477.1	wSO2	38	cSO2	37			454.6	cSO2	82				
679.1	wNH2	50	sS1-N2	44			643.1	sC3-S1	39	sS1-N2	28		
720.8	sC3-S1	67	wNH2	15			752.4	sC3-S1	38	sS1-N2	36		
874.5	sS1-N2	35	wNH2	31			892.6	wNH2	77				
968.8	rCH3'	81					949.4	rCH3	81				
982.8	rCH3	76					949.6	rCH3'	90				
1071.0	rNH2	81					1044.2	rNH2	92				
1112.2	sS1-O12	43	sS1-O11	43			1119.6	sS1-O12	41	sS1-O11	41		
1324.6	sS1-O11	43	sS1-O12	43			1321.8	sS1-O11	44	sS1-O12	44		
1347.4	dsCH3	98					1378.4	dsCH3	93				
1431.0	daCH3'	93					1441.6	daCH3	94				
1431.3	daCH3	93					1445.6	daCH3'	93				
1558.9	cNH2	101					1533.2	cNH2	99				
2960.1	sC3-H31	38	sC3-H32	31	sC3-H33	31	2843.9	sC3-H31	33	sC3-H33	33	sC3-H32	33
3067.0	sC3-H31	62	sC3-H32	19	sC3-H33	19	2915.3	sC3-H31	66	sC3-H32	17	sC3-H33	17
3076.1	sC3-H33	50	sC3-H32	50			2916.6	sC3-H32	50	sC3-H33	50		
3332.2	sN2-H22	50	sN2-H21	50			3341.2	sN2-H22	50	sN2-H21	50		
3443.6	sN2-H21	50	sN2-H22	50			3420.5	sN2-H22	50	sN2-H21	50		

Only vibrational modes with 15% or more contributions are shown here, but if no vibrational mode for a frequency higher than 15% contribution can be found, then the one with the highest contribution is shown. Notations for PED are: t6RNG and d6RNG are six member ring torsion and deformation; BFLY is bicyclic ring butterfly; s stands for bond stretching; ss and sa stand for group symmetric and asymmetric stretching; r for rocking; i for twisting; w for wagging; c for scissoring; t for torsions. Same notations are adopted in the following tables of vibrational spectra.

Table S5. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of BSAM – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-5.32	-5.18	0.14	2.08	1.83	-0.25

O11...HOH	270	-5.42	-5.56	-0.14	2.08	1.81	-0.27
N2...HOH	270	-2.37	-2.62	-0.25	2.42	2.08	-0.34
N2H…OHH	0	-5.96	-5.99	-0.03	2.03	1.85	-0.18

Table S6. Gas phase dipole moment (Debye) of BSAM calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-1.8213	-1.8975
Y	-1.2688	-1.4018
Z	2.8815	2.9933
Total	3.6373	3.8112

Table S7. MM and MP2/6-31G(d) level equilibrium geometry of BSAM

Coordinate	QM	MM	Difference	Coordinate	QM	MM	Difference
Bond length (Å)				Angles (°)			
S1-N2	1.684	1.637	-0.046	N2-S1-CZ	103.2	104.0	0.9
S1-O11	1.465	1.435	-0.030	O11-S1-N2	107.2	107.5	0.3
S1-O12	1.465	1.435	-0.030	O12-S1-N2	106.8	107.5	0.7
S1-CZ	1.775	1.781	0.007	O11-S1-CZ	107.5	107.0	-0.5
N2-H21	1.019	1.015	-0.004	O12-S1-CZ	107.6	107.0	-0.7
N2-H22	1.019	1.015	-0.004	O11-S1-O12	122.7	122.5	-0.2
CZ-CE1	1.396	1.411	0.015	S1-N2-H21	109.7	109.5	-0.3
CZ-CE2	1.396	1.411	0.015	S1-N2-H22	109.4	109.5	0.1
CE1-CD1	1.395	1.401	0.006	H21-N2-H22	111.2	111.4	0.1
CE2-CD2	1.395	1.401	0.005	S1-CZ-CE1	119.1	120.7	1.6
CG-CD1	1.397	1.400	0.003	S1-CZ-CE2	119.1	120.7	1.6
CG-CD2	1.397	1.400	0.003	CE1-CZ-CE2	121.8	118.6	-3.2
CE1-HE1	1.086	1.081	-0.006	CZ-CE1-CD1	118.7	120.7	2.0
CE2-HE2	1.086	1.081	-0.006	CZ-CE2-CD2	118.7	120.7	2.0
CD1-HD1	1.087	1.081	-0.006	CG-CD1-CE1	120.3	119.9	-0.3
CD2-HD2	1.087	1.081	-0.006	CG-CD2-CE2	120.3	119.9	-0.3
CG-HG	1.087	1.081	-0.006	CD1-CG-CD2	120.2	120.1	0.0
Dihedrals (°)				CZ-CE1-HE1	120.0	119.8	-0.2
N2-S1-CZ-CE1	-88.1	-89.4	-1.3	CD1-CE1-HE1	120.0	119.8	-0.2

CZ-S1-N2-H21	-116.1	-118.8	-2.7	CD2-CE2-HE2	121.2	119.5	-1.7
S1-CZ-CE1-CD1	179.2	179.3	0.1	CE1-CD1-HD1	121.3	119.5	-1.8
CZ-CE1-CD1-CG	-0.1	-0.2	-0.1	CE2-CD2-HD2	119.6	120.1	0.4
CE1-CD1-CG-CD2	0.6	0.0	-0.6	CG-CD1-HD1	119.6	120.1	0.4
S1-CZ-CE2-CD2	-179.2	-179.3	-0.1	CG-CD2-HD2	120.1	120.0	-0.1
CZ-CE2-CD2-CG	0.1	0.2	0.1	CD1-CG-HG	120.1	120.0	-0.1
CE2-CD2-CG-CD1	-0.6	0.0	0.6	CD2-CG-HG	119.9	119.9	0.0

Table S8. Scaled MP2/6-31G(d) and MM level vibrational spectra of BSAM.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
4.4	tCZ-S1	87					24.0	tCZ-S1	98				
86.7	tS1-N2	73					113.1	tS1-N2	98				
112.4	wCZH	64	cNSC	20	ta6RNG1	15	124.0	wCZH	66	cNSC	16	ta6RNG1	15
182.9	dCZH	65	rSO2	24			218.6	dCZH	67	rSO2	17		
259.5	cNSC	51	ta6RNG1	43			252.0	cNSC	43	sCZ-S1	19	ta6RNG1	17
299.3	sCZ-S1	41	da6RNG1	23			292.1	wSO2	37	ta6RNG1	19	cNSC	17
								sCZ-S1	15				
341.9	iSO2	74					324.4	iSO2	68	dCZH	15		
374.5	ta6RNG1a	116					375.0	rSO2	68	iSO2	19		
411.4	cSO2	37	ta6RNG1	37			384.7	wSO2	30	cSO2	24	sCZ-S1	16
417.8	rSO2	67	dCZH	17			413.5	ta6RNG1a	118				
485.0	tp6RNG1	63	cSO2	20			482.5	ta6RNG1	63	wCZH	21		
532.0	wSO2	24	cSO2	20	da6RNG1	17	498.1	cSO2	68				
547.3	wSO2	31	tp6RNG1	29	wCZH	17	652.3	tp6RNG1	106				
590.2	da6RNG1a	90					685.5	da6RNG1a	82				
662.2	wNH2	51	sS1-N2	36			699.4	sS1-N2	46	da6RNG1	17	wNH2	16
686.5	da6RNG1	44	sCZ-S1	24			745.7	da6RNG1	32				
702.8	wCGH	31	wCD1H	18	wCD2H	18	752.2	wCGH	22				
794.8	wCE1H	31	wCE2H	30	wCD2H	20	850.0	wCE1H	27	wCE2H	27	wCD2H	23
	wCD1H	19						wCD1H	23				
842.5	wCE1H	37	wCE2H	37	wCGH	27	869.4	wNH2	74	sS1-N2	19		
853.7	wCGH	47	wCD1H	31	wCD2H	27	916.1	wCE1H	39	wCE2H	39	wCGH	28
857.1	sS1-N2	42	wNH2	35			949.3	dt6RNG1	68				
860.2	wCD2H	37	wCD1H	33	wCE2H	25	975.9	sCG-CD1	38	sCD2-CG	38		
	wCE1H	22	ta6RNG1a	-17									
958.5	dt6RNG1	65					991.2	wCD2H	32	wCD1H	32	wCE1H	27
								wCE2H	27	ta6RNG1a	-18		
1003.0	sCG-CD1	29	sCD2-CG	29			1006.1	wCGH	53	wCD2H	31	wCD1H	31
								tp6RNG1	-18				
1061.2	rNH2	18	sCD1-CE1	17			1018.6	sCD1-CE1	25	sCE2-CD2	25		

1063.6	sS1-O11	20	sS1-O12	20			1050.5	rNH2	92				
1069.1	rNH2	68					1068.9	sCZ-S1	13				
1121.4	sS1-O11	27	sS1-O12	25	sCZ-S1	15	1118.1	sS1-O11	31	sS1-O12	31		
1149.9	dCGH	40	dCD2H	21	dCD1H	20	1198.7	dCE2H	14	dCE1H	14		
1162.6	dCD1H	21	dCD2H	20	dCE1H	18	1210.3	dCGH	26	dCD1H	19	dCD2H	19
	dCE2H	18											
1277.1	dCE1H	29	dCE2H	29			1312.6	sS1-O12	39	sS1-O11	39		
1313.7	sS1-O12	44	sS1-O11	43			1352.6	sCE1-CZ	20	sCZ-CE2	20	dCE1H	19
								dCE2H	19				
1391.7	sCZ-CE2	17	sCE1-CZ	17	sCD2-CG	16	1419.1	dCGH	36	dCD2H	16	dCD1H	16
	sCG-CD1	15											
1417.0	dCGH	30					1442.5	sCE2-CD2	17	sCD1-CE1	17		
1449.9	dCE1H	17	dCE2H	17	dCD2H	16	1468.9	dCD2H	28	dCD1H	28		
	dCD1H	16											
1550.7	cNH2	101					1487.6	dCGH	25				
1566.6	sCG-CD1	20	sCD2-CG	19	sCZ-CE2	18	1509.4	dCE1H	24	dCE2H	24		
	sCE1-CZ	17											
1569.6	sCD1-CE1	23	sCE2-CD2	23			1542.6	cNH2	98				
3045.4	sCG-HG	47	sCD1-HD1	24	sCD2-HD2	24	3054.0	sCE2-HE2	38	sCE1-HE1	38		
3055.5	sCD1-HD1	43	sCD2-HD2	43			3054.7	sCG-HG	46	sCE2-HE2	24	sCE1-HE1	24
3063.8	sCG-HG	46					3056.1	sCD1-HD1	37	sCD2-HD2	37		
3072.8	sCE1-HE1	55	sCE2-HE2	31			3056.7	sCG-HG	39	sCD2-HD2	24	sCD1-HD1	24
3074.2	sCE2-HE2	49	sCE1-HE1	22			3059.7	sCD1-HD1	23	sCD2-HD2	23	sCE1-HE1	20
								sCE2-HE2	20	sCG-HG	15		
3326.5	sN2-H22	50	sN2-H21	50			3340.6	sN2-H21	50	sN2-H22	50		
3441.1	sN2-H21	50	sN2-H22	50			3420.7	sN2-H22	50	sN2-H21	50		

Table S9. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of MMSM – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-5.93	-5.69	0.24	2.05	1.82	-0.23
O11...HOH	270	-5.51	-5.95	-0.44	2.08	1.81	-0.27
O12...HOH	180	-5.62	-5.35	0.27	2.06	1.83	-0.23
O12...HOH	90	-5.36	-5.55	-0.19	2.09	1.82	-0.27
N2...HOH	270	-3.69	-3.47	0.22	2.23	2.10	-0.13
N2H...OHH	0	-5.32	-5.10	0.22	2.04	1.85	-0.19

Table S10. Gas phase dipole moment (Debye) of MMSM calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-1.5631	-2.1943
Y	3.2715	3.4892
Z	-1.0665	-1.2668
Total	3.7793	4.3121

Table S11. MM and MP2/6-31G(d) level equilibrium geometry of MMSM

Coordinate	QM	MM	Difference
Bond length (Å)			
S1-N2	1.681	1.630	-0.051
S1-O11	1.466	1.435	-0.031
S1-O12	1.465	1.434	-0.031
S1-C3	1.778	1.771	-0.007
N2-H21	1.020	1.020	0.000
N2-C4	1.470	1.478	0.009
C3-H31	1.091	1.108	0.017
C3-H32	1.091	1.108	0.017
C3-H33	1.089	1.108	0.019
C4-H41	1.091	1.112	0.021
C4-H42	1.091	1.113	0.022
C4-H43	1.093	1.113	0.020
Dihedrals (°)			
N2-S1-C3-H31	178.9	-178.4	2.7
C4-N2-S1-C3	-98.2	-97.1	1.1
H41-C4-N2-S1	179.8	177.0	-2.7

Coordinate	QM	MM	Difference
Angles (°)			
N2-S1-C3	101.8	103.1	1.3
O11-S1-N2	110.1	109.3	-0.8
O12-S1-N2	105.6	106.2	0.7
O11-S1-C3	107.4	108.2	0.8
O12-S1-C3	108.6	107.6	-0.9
O11-S1-O12	121.7	120.9	-0.7
S1-N2-H21	106.8	106.0	-0.8
S1-N2-C4	116.6	116.7	0.0
H21-N2-C4	113.5	114.2	0.7
S1-C3-H31	107.3	108.3	1.0
S1-C3-H32	109.1	108.8	-0.3
S1-C3-H33	108.7	108.7	0.0
H31-C3-H32	110.0	110.2	0.3
H31-C3-H33	110.8	110.2	-0.6
H32-C3-H33	110.9	110.5	-0.4
N2-C4-H41	107.3	110.7	3.4
N2-C4-H42	109.2	111.2	2.0
N2-C4-H43	113.4	111.1	-2.3
H41-C4-H42	108.2	107.8	-0.4
H41-C4-H43	110.0	108.0	-2.0
H42-C4-H43	108.7	107.9	-0.7

Table S12. Scaled MP2/6-31G(d) and MM level vibrational spectra of MMSM.

QM (scaled by a factor 0.943)						
Freq	Assignment	%	Assignment	%	Assignment	%
75.7	tS1-N2	91				

MM						
Freq	Assignment	%	Assignment	%	Assignment	%
69.7	tS1-N2	100				

162.3	tN2-C4	85					179.2	tN2-C4	91				
215.4	tC3-S1	65					215.3	tC3-S1	93				
237.5	tC3-S1	32	iSO2	25	dSNC	24	270.3	rSO2	26	dSNC	22	wNH	22
								iSO2	20				
294.4	cNSC	68					314.4	cNSC	83				
307.0	iSO2	53	rSO2	25			334.4	wSO2	47	iSO2	22		
408.8	rSO2	37	wSO2	23			371.6	iSO2	46	rSO2	36		
448.5	cSO2	64					429.5	cSO2	34	wSO2	17	rSO2	15
488.3	wSO2	48	sC3-S1	15			475.7	cSO2	54				
604.6	sS1-N2	35	wNH	21			635.3	dSNC	36	sC3-S1	28	wNH	20
713.8	sC3-S1	59					691.5	wNH	35	sS1-N2	22	sC3-S1	15
833.0	sS1-N2	26	sC3-S1	20			752.3	sS1-N2	37	sC3-S1	34	wSO2	12
968.3	rC3H3'	75					944.3	rC3H3	87				
978.6	rC3H3	69					946.9	rC3H3'	90				
1046.0	sN2-C4	73					1043.0	sN2-C4	53	rNH	22		
1101.5	sS1-O12	35	sS1-O11	25	rC4H3'	22	1088.0	rC4H3'	65				
1111.7	rC4H3'	55					1110.3	rC4H3	30	sS1-O11	19	sN2-C4	15
1118.7	rC4H3	58					1124.6	rC4H3	30	sS1-O12	28	sS1-O11	17
1297.6	sS1-O11	44	sS1-O12	40			1306.6	sS1-O11	46	sS1-O12	40		
1341.6	dsC3H3	96					1376.9	dsC3H3	90				
1380.5	rNH	73					1386.7	rNH	65	sN2-C4	15		
1422.0	dsC4H3	80					1424.0	daC4H3	81				
1430.5	daC3H3	92					1435.5	daC4H3'	82	rC4H3'	16		
1433.0	daC3H3'	76					1439.2	daC3H3	93				
1462.8	daC4H3'	80					1442.6	daC3H3'	93				
1481.8	daC4H3	75					1453.5	dsC4H3	99				
2940.4	sC4-H43	49	sC4-H41	27	sC4-H42	25	2843.8	sC3-H33	33	sC3-H32	33	sC3-H31	33
2957.3	sC3-H31	36	sC3-H32	36	sC3-H33	28	2915.3	sC3-H31	67	sC3-H33	17	sC3-H32	16
3027.0	sC4-H43	51	sC4-H42	27	sC4-H41	22	2916.4	sC3-H32	50	sC3-H33	50		
3043.8	sC4-H41	51	sC4-H42	49			2974.8	sC4-H41	37	sC4-H43	32	sC4-H42	31
3061.3	sC3-H31	51	sC3-H32	50			3020.6	sC4-H41	62	sC4-H43	27		
3076.0	sC3-H33	72					3022.6	sC4-H42	58	sC4-H43	41		
3357.9	sN2-H21	100					3339.3	sN2-H21	100				

Table S13. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of MBSM – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-5.54	-5.48	0.07	2.07	1.83	-0.24
O11...HOH	270	-5.63	-6.01	-0.39	2.07	1.80	-0.27
O12...HOH	180	-5.76	-5.57	0.19	2.06	1.82	-0.24
O12...HOH	90	-5.64	-5.75	-0.11	2.09	1.81	-0.28

N2...HOH	270	-1.65	-1.60	0.04	3.43	2.99	-0.44
N2H…OHH	0	-5.47	-5.55	-0.08	2.04	1.83	-0.21

Table S14. Gas phase dipole moment (Debye) of MBSM calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-0.1504	-0.5223
Y	-4.2033	-4.3775
Z	1.3805	1.8830
Total	4.4268	4.7939

Table S15. MM and MP2/6-31G(d) level equilibrium geometry of MBSM

Coordinate	QM	MM	Difference	Coordinate	QM	MM	Difference
Bond length (Å)				Angles (°)			
S1-N2	1.680	1.641	-0.039	N2-S1-CZ	100.7	101.8	1.1
S1-O11	1.468	1.439	-0.030	O11-S1-N2	111.2	109.7	-1.4
S1-O12	1.465	1.437	-0.028	O12-S1-N2	104.9	108.3	3.4
S1-CZ	1.776	1.778	0.002	O11-S1-CZ	107.3	107.4	0.1
N2-H21	1.022	1.020	-0.002	O12-S1-CZ	109.7	105.7	-3.9
N2-C3	1.469	1.478	0.009	O11-S1-O12	121.2	122.0	0.8
CZ-CE1	1.398	1.411	0.013	S1-N2-H21	107.0	106.0	-1.0
CZ-CE2	1.395	1.411	0.016	S1-N2-C3	115.7	116.4	0.6
CE1-CD1	1.394	1.400	0.007	H21-N2-C3	113.7	113.1	-0.6
CE2-CD2	1.397	1.401	0.004	S1-CZ-CE1	118.8	120.1	1.3
CG-CD1	1.399	1.400	0.001	S1-CZ-CE2	119.3	121.3	2.0
CG-CD2	1.396	1.400	0.004	CE1-CZ-CE2	121.9	118.6	-3.3
CE1-HE1	1.087	1.081	-0.006	CZ-CE1-CD1	118.7	120.7	2.0
CE2-HE2	1.086	1.081	-0.006	CZ-CE2-CD2	118.7	120.7	2.0
CD1-HD1	1.087	1.081	-0.006	CG-CD1-CE1	120.3	119.9	-0.3
CD2-HD2	1.087	1.081	-0.006	CG-CD2-CE2	120.2	119.9	-0.3
CG-HG	1.087	1.081	-0.006	CD1-CG-CD2	120.2	120.1	-0.1
C3-H31	1.091	1.113	0.022	CZ-CE1-HE1	120.1	119.6	-0.5
C3-H32	1.094	1.113	0.019	CZ-CE2-HE2	119.6	119.8	0.2
C3-H33	1.092	1.112	0.021	CD1-CE1-HE1	121.2	119.7	-1.5

Dihedrals (°)			
N2-S1-CZ-CE1	-66.6	-74.1	-7.5
CZ-S1-N2-C3	-82.2	-80.6	1.6
S1-N2-C3-H31	178.3	179.0	0.6
S1-CZ-CE1-CD1	-179.1	179.2	-1.7
CZ-CE1-CD1-CG	-0.1	-0.1	0.0
CE1-CD1-CG-CD2	0.3	0.0	-0.3
S1-CZ-CE2-CD2	179.2	-179.2	1.7
CZ-CE2-CD2-CG	0.1	0.1	0.0
CE2-CD2-CG-CD1	-0.3	0.0	0.2

CD2-CE2-HE2	121.7	119.5	-2.2
CE1-CD1-HD1	119.7	120.0	0.3
CE2-CD2-HD2	119.7	120.1	0.4
CG-CD1-HD1	120.0	120.0	0.0
CG-CD2-HD2	120.1	120.0	-0.1
CD1-CG-HG	119.9	119.9	0.1
CD2-CG-HG	119.9	119.9	0.0
N2-C3-H31	107.6	110.6	3.0
N2-C3-H32	113.3	111.2	-2.1
N2-C3-H33	108.5	111.2	2.7
H31-C3-H32	110.0	108.0	-2.1
H31-C3-H33	108.3	107.7	-0.6
H32-C3-H33	109.0	108.1	-0.9

Table S16. Scaled MP2/6-31G(d) and MM level vibrational spectra of MBSM.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
18.2	tCZ-S1	99					29.4	tCZ-S1	97				
62.9	tS1-N2	54	cNSC	22	wCZH	20	67.2	tS1-N2	75	wCZH	15		
129.9	wCZH	43	tS1-N2	32			122.3	wCZH	44	tN2C3	18		
167.8	dCZH	41	tN2C3	22			184.0	tN2C3	65				
187.2	tN2C3	56	dCZH	21			215.0	dCZH	61	rSO2	20		
214.2	dSNC	29	iSO2	27	wNH	27	247.6	dSNC	16	cNSC	16	iSO2	16
281.0	ta6RNG1	37	cNSC	21	iSO2	18	274.4	wSO2	24	sCZ-S1	23		
295.7	sCZ-S1	42	da6RNG1	23			288.1	iSO2	29	ta6RNG1	23	cNSC	19
								wSO2	19				
348.0	iSO2	32	dCZH	16			328.3	iSO2	26	rSO2	22	dCZH	17
371.9	ta6RNG1a	113					375.7	cSO2	17	rSO2	16	sS1-N2	15
								wSO2	15				
420.1	ta6RNG1	35	cSO2	32			413.6	ta6RNG1a	118				
445.8	rSO2	35					452.6	dSNC	26	wSO2	17		
487.8	tp6RNG1	67					489.1	ta6RNG1	41	cSO2	18		
521.5	tp6RNG1	20	wSO2	17	cSO2	17	500.5	cSO2	54				
545.5	wSO2	27					653.5	tp6RNG1	103				
590.0	da6RNG1a	88					685.2	da6RNG1a	79				
614.6	sS1-N2	27	wNH	21			692.2	dSNC	36	wNH	31		
683.3	da6RNG1	44	sCZ-S1	23			725.1	sS1-N2	37	wNH	22		
697.9	wCGH	28	wCE1H	22	wCD1H	18	746.1	da6RNG1	29				
	wCD2H	16											
789.8	wCE1H	44	wCD2H	24	wCE2H	21	753.3	wCGH	20				

816.9	sS1-N2	34	dSNC	16			850.3	wCE2H	28	wCE1H	27	wCD1H	23
								wCD2H	23				
837.7	wCE2H	33	wCE1H	33	wCD1H	24	916.5	wCE1H	39	wCE2H	39	wCGH	28
	wCGH	18											
853.2	wCGH	58	wCD1H	40			949.3	dt6RNG1	68				
859.5	wCD2H	52	wCE2H	43			975.8	sCG-CD1	39	sCD2-CG	36		
958.3	dt6RNG1	66					991.5	wCD2H	32	wCD1H	31	wCE1H	28
								wCE2H	27	ta6RNG1a	-18		
1001.9	sCG-CD1	30	sCD2-CG	27			1006.2	wCGH	53	wCD1H	32	wCD2H	31
								tp6RNG1	-18				
1039.4	sN2-C3	72					1018.7	sCE2-CD2	25	sCD1-CE1	25		
1058.8	sCD1-CE1	16	dCE2H	15			1042.1	sN2-C3	50	rNH	19		
1063.9	sCE2-CD2	19					1069.5						
1105.4	rCH3'	45					1093.1	rCH3'	66				
1113.2	rCH3	52	rCH3'	23			1112.7	rCH3	39				
1126.1	sS1-O11	19	rCH3	18			1122.1	sS1-O12	26	rCH3	25	sS1-O11	16
1149.7	dCGH	40	dCD2H	24	dCD1H	17	1198.3	dCE1H	16				
1161.4	dCD1H	25	dCE1H	18	dCE2H	16	1210.3	dCGH	25	dCD2H	20	dCD1H	17
	dCD2H	16											
1276.4	dCE1H	25	dCE2H	25			1302.2	sS1-O11	44	sS1-O12	39		
1287.9	sS1-O11	40	sS1-O12	39			1351.5	sCZ-CE2	22	dCE1H	20	sCE1-CZ	20
								dCE2H	19				
1367.3	rNH	76					1380.9	rNH	68	sN2-C3	16		
1392.7	sCZ-CE2	17	sCE1-CZ	17	sCD2-CG	16	1419.1	dCGH	36	dCD1H	17	dCD2H	16
1416.4	dCGH	29					1422.8	daCH3	82				
1418.7	dsCH3	93					1437.3	daCH3'	83	rCH3'	16		
1449.3	dCE1H	18	dCD2H	16	dCD1H	16	1442.5	sCD1-CE1	17	sCE2-CD2	17		
	dCE2H	15											
1462.7	daCH3'	85					1455.9	dsCH3	100				
1482.2	daCH3	82					1468.9	dCD1H	29	dCD2H	26		
1565.6	sCG-CD1	22	sCZ-CE2	22			1487.7	dCGH	24	sCD2-CG	15		
1569.0	sCD1-CE1	24	sCE2-CD2	21			1509.8	dCE2H	28	dCE1H	20		
2934.0	sCH2	51	sCH3	25	sCH1	23	2974.7	sCH1	36	sCH2	32	sCH3	31
3020.9	sCH2	48	sCH3	36	sCH1	16	3020.2	sCH1	63	sCH2	21	sCH3	16
3040.4	sCH1	60	sCH3	39			3022.6	sCH3	53	sCH2	47		
3045.2	sCG-HG	48	sCD1-HD1	24	sCD2-HD2	23	3054.0	sCE2-HE2	45	sCE1-HE1	27	sCD1-HD1	15
3055.3	sCD1-HD1	42	sCD2-HD2	42			3054.7	sCG-HG	48	sCE1-HE1	28	sCE2-HE2	17
3063.1	sCG-HG	43	sCE1-HE1	21	sCD2-HD2	21	3056.1	sCD2-HD2	40	sCD1-HD1	31		
3070.9	sCE1-HE1	64	sCD1-HD1	25			3056.7	sCG-HG	36	sCD1-HD1	31	sCD2-HD2	19
3075.0	sCE2-HE2	80					3059.7	sCD2-HD2	22	sCE1-HE1	22	sCD1-HD1	22
								sCE2-HE2	19				
3338.9	sN2-H21	100					3338.8	sN2-H21	100				

Table S17. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of EESM – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-6.15	-5.68	0.47	2.04	1.82	-0.22
O11...HOH	270	-5.66	-6.01	-0.35	2.08	1.81	-0.27
O12...HOH	180	-5.81	-5.39	0.42	2.06	1.83	-0.23
O12...HOH	90	-5.49	-5.66	-0.16	2.08	1.81	-0.27
N2...HOH	270	-3.93	-3.41	0.53	2.24	2.14	-0.10
N2H...OHH	0	-5.22	-5.22	0.00	2.06	1.85	-0.21

Table S18. Gas phase dipole moment (Debye) of EESM calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-1.5921	-2.1139
Y	3.2270	3.5884
Z	-1.2104	-1.2655
Total	3.7965	4.3528

Table S19. MM and MP2/6-31G(d) level equilibrium geometry of EESM

Coordinate	QM	MM	Difference	Coordinate	QM	MM	Difference
Bond length (Å)				Angles (°)			
S1-N2	1.683	1.629	-0.054	N2-S1-C3	101.8	102.2	0.4
S1-O11	1.468	1.436	-0.032	O11-S1-N2	110.3	109.2	-1.1
S1-O12	1.468	1.435	-0.033	O12-S1-N2	105.7	106.3	0.6
S1-C3	1.787	1.799	0.012	O11-S1-C3	107.5	108.3	0.8
N2-H21	1.022	1.018	-0.004	O12-S1-C3	108.7	107.8	-0.8
N2-C4	1.474	1.476	0.002	O11-S1-O12	121.3	121.3	0.1
C3-H31	1.094	1.108	0.014	S1-N2-H21	106.8	107.0	0.2
C3-H32	1.092	1.108	0.016	S1-N2-C4	117.0	117.7	0.6
C3-C5	1.524	1.540	0.016	H21-N2-C4	112.8	112.8	0.0
C4-H41	1.093	1.114	0.021	S1-C3-H31	106.6	106.6	0.0
C4-H42	1.096	1.115	0.019	S1-C3-H32	106.1	106.6	0.5
C4-C6	1.520	1.526	0.006	S1-C3-C5	110.4	110.9	0.5

C5-H51	1.093	1.110	0.018
C5-H52	1.092	1.112	0.020
C5-H53	1.092	1.112	0.020
C6-H61	1.093	1.111	0.018
C6-H62	1.094	1.111	0.017
C6-H63	1.092	1.112	0.020

Dihedrals (°)			
N2-S1-C3-C5	178.1	-179.1	2.8
S1-C3-C5-H51	179.1	180.0	0.9
C4-N2-S1-C3	-98.9	-100.1	-1.2
C6-C4-N2-S1	177.7	178.9	1.2
H61-C6-C4-N2	-178.5	-179.2	-0.7

H31-C3-H32	108.9	110.1	1.2
H31-C3-C5	112.0	111.2	-0.8
H32-C3-C5	112.6	111.2	-1.3
N2-C4-H41	107.6	110.3	2.7
N2-C4-H42	111.8	110.3	-1.4
N2-C4-C6	108.9	108.7	-0.2
H41-C4-H42	107.1	107.9	0.8
H41-C4-C6	110.2	109.8	-0.4
H42-C4-C6	111.2	109.8	-1.4
C3-C5-H51	109.6	110.5	1.0
C3-C5-H52	110.5	110.5	0.0
C3-C5-H53	110.6	110.5	-0.1
H51-C5-H52	108.6	108.5	-0.1
H51-C5-H53	108.8	108.5	-0.3
H52-C5-H53	108.8	108.3	-0.5
C4-C6-H61	110.2	110.3	0.1
C4-C6-H62	111.0	110.9	-0.1
C4-C6-H63	110.6	110.6	0.0
H61-C6-H62	107.8	108.2	0.4
H61-C6-H63	108.9	108.3	-0.6
H62-C6-H63	108.4	108.5	0.1

Table S20. Scaled MP2/6-31G(d) and MM level vibrational spectra of EESM.

QM (scaled by a factor 0.943)						
Freq	Assignment	%	Assignment	%	Assignment	%
56.1	tN2-C4	44	tS1-N2	24		
63.1	tN2-C4	43	tS1-N2	39		
85.4	tC3-S1	60	tS1-N2	25		
170.6	dSNC	36	wNH	18		
196.6	cCCS	38	cNSC	32		
212.0	tC4-C6	71				
260.2	tC3-C5	87				
311.3	cCCN	45	sS1-N2	19		
311.4	iSO2	67				
341.4	cNSC	36	cCCS	20		
400.5	rSO2	59				
458.4	cSO2	71				
546.1	wSO2	50				

MM						
Freq	Assignment	%	Assignment	%	Assignment	%
49.4	tS1-N2	61	tN2-C4	31		
63.2	tN2-C4	58	tS1-N2	37		
89.7	tC3-S1	86				
186.2	cCCN	25	dSNC	17		
216.4	cNSC	27	cCCS	26		
225.6	tC4-C6	71				
255.0	tC3-C5	69				
265.8	cCCN	22	sS1-N2	19		
297.4	cNSC	43	wSO2	18		
350.3	iSO2	79				
382.7	rSO2	61				
446.2	cSO2	41	wSO2	24	cCCS	17
476.0	cSO2	47	wSO2	18		

617.6	wNH	34	sS1-N2	19			626.3	sC3-S1	32	wNH	27	dSNC	25
695.9	sC3-S1	59					684.1	sC3-S1	33	wNH	26		
772.0	rC3H2	54	rC5H3'	32			775.8	sS1-N2	65				
783.0	rC4H2	46	rC6H3'	36			812.0	rC3H2	75	rC5H3'	15		
857.2	sS1-N2	23	dSNC	18			864.1	rC4H2	61	rC6H3'	28		
917.0	sC4-C6	28	rC6H3	22	sN2-C4	19	923.7	rC6H3	51	sN2-C4	23		
	sS1-N2	19											
966.1	sC3-C5	45	rC5H3	27	wC3H2	17	986.8	rC5H3	43	sC3-C5	34		
1042.4	iC3H2	24	rC5H3'	20	rC3H2	18	1029.0	rC5H3'	70				
1046.1	sC4-C6	21					1034.1	sC4-C6	70				
1056.2	sC4-C6	27	sC3-C5	19	rC5H3	19	1040.2	sC3-C5	47	rC5H3	40		
	sN2-C4	15											
1093.5	sS1-O12	37	sS1-O11	37			1065.5	rC6H3'	60	rC4H2	27		
1110.5	rC6H3	32	sN2-C4	29			1113.6	sS1-O12	44	sS1-O11	41		
1129.4	rC4H2	39	rC6H3'	25			1128.2	sN2-C4	47	rC6H3	28		
1227.7	iC3H2	48	rC5H3'	28			1198.2	iC3H2	87				
1253.1	iC4H2	55	rC6H3'	19			1302.3	iC4H2	70				
1285.9	wC3H2	71					1310.6	sS1-O11	34	sS1-O12	31	iC4H2	23
1296.7	sS1-O11	33	sS1-O12	32			1334.2	wC3H2	79				
1328.7	wC4H2	60	rNH	15			1377.3	wC4H2	44	rNH	31		
1382.8	dsC5H3	66					1415.9	dsC5H3	73				
1387.3	dsC6H3	39	dsC5H3	28	rNH	22	1416.5	dsC6H3	61				
1393.1	dsC6H3	42	wC4H2	22	rNH	21	1422.9	daC6H3	37	dsC6H3	20	wC4H2	16
1431.2	cC3H2	99					1423.7	daC5H3	72				
1467.6	daC5H3'	87					1426.0	daC6H3	46	rNH	15		
1468.1	daC6H3'	73					1430.0	daC5H3'	91				
1472.5	daC6H3	64	cC4H2	16			1433.7	daC6H3'	82				
1480.9	daC5H3	92					1455.1	cC3H2	88				
1491.0	cC4H2	81	daC6H3	15			1459.5	cC4H2	77	wC4H2	17		
2934.3	sC6-H62	42	sC6-H61	29	sC6-H63	24	2851.6	sC3-H32	49	sC3-H31	49		
2936.7	sC4-H42	71	sC4-H41	23			2892.5	sC3-H31	50	sC3-H32	49		
2947.3	sC5-H51	38	sC5-H52	33	sC5-H53	29	2902.7	sC6-H61	31	sC6-H62	29	sC6-H63	28
2959.7	sC3-H31	64	sC3-H32	35			2902.8	sC5-H51	31	sC5-H53	28	sC5-H52	28
2991.4	sC4-H41	67	sC4-H42	23			2957.5	sC6-H61	63	sC6-H62	20		
3016.9	sC6-H62	46	sC6-H61	44			2958.8	sC5-H51	65	sC5-H52	19	sC5-H53	17
3023.6	sC3-H32	57	sC3-H31	31			2959.8	sC6-H63	53	sC6-H62	44		
3033.9	sC5-H51	60	sC5-H52	30			2959.9	sC5-H53	50	sC5-H52	49		
3034.5	sC6-H63	69	sC6-H61	23			2972.6	sC4-H42	48	sC4-H41	46		
3046.2	sC5-H53	55	sC5-H52	31			2998.0	sC4-H41	51	sC4-H42	48		
3334.8	sN2-H21	100					3339.2	sN2-H21	100				

Table S21. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of PMSM – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-4.74	-4.43	0.31	2.12	1.88	-0.24
O11...HOH	270	-5.26	-5.24	0.02	2.10	1.84	-0.26
O12...HOH	180	-4.62	-4.93	-0.31	2.11	1.86	-0.25
O12...HOH	90	-5.31	-5.66	-0.35	2.09	1.83	-0.26
N2...HOH	270	-1.60	-1.62	-0.02	2.44	2.22	-0.22
N2H...OHH	0	-6.51	-6.47	0.04	2.04	1.85	-0.19

Table S22. Gas phase dipole moment (Debye) of PMSM calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	2.5421	2.1314
Y	1.4102	2.1082
Z	4.2351	5.4936
Total	5.1368	6.2583

Table S23. MM and MP2/6-31G(d) level equilibrium geometry of PMSM

Coordinate	QM	MM	Difference	Coordinate	QM	MM	Difference
Bond length (Å)				Angles (°)			
S1-N2	1.683	1.639	-0.044	N2-S1-C3	105.1	103.7	-1.5
S1-O11	1.462	1.435	-0.027	O11-S1-N2	104.6	106.8	2.2
S1-O12	1.461	1.436	-0.024	O12-S1-N2	108.0	110.6	2.6
S1-C3	1.785	1.777	-0.008	O11-S1-C3	108.7	106.5	-2.2
N2-H21	1.020	1.015	-0.005	O12-S1-C3	106.9	107.5	0.6
N2-C4	1.424	1.404	-0.020	O11-S1-O12	122.4	120.5	-1.9
C4-C51	1.401	1.404	0.003	S1-N2-H21	109.7	110.2	0.5
C4-C52	1.401	1.404	0.003	S1-N2-C4	120.8	121.7	0.9
C51-C61	1.395	1.402	0.007	H21-N2-C4	115.1	115.4	0.3
C52-C62	1.395	1.403	0.008	N2-C4-C51	119.9	121.5	1.6
C7-C61	1.397	1.401	0.004	N2-C4-C52	119.8	118.9	-0.8
C7-C62	1.396	1.401	0.005	C51-C4-C52	120.3	119.5	-0.8
C51-H51	1.085	1.081	-0.004	C4-C51-C61	119.2	120.3	1.1
C52-H52	1.089	1.080	-0.009	C4-C52-C62	119.9	120.3	0.4
C61-H61	1.087	1.081	-0.006	C7-C61-C51	120.8	119.9	-0.9

C62-H62	1.087	1.081	-0.006
C7-H7	1.087	1.081	-0.006
C3-H31	1.092	1.109	0.017
C3-H32	1.091	1.108	0.017
C3-H33	1.091	1.109	0.018

Dihedrals (°)			
N2-S1-C3-H31	-177.1	177.9	-5.1
C3-S1-N2-C4	52.4	65.0	12.6
S1-N2-C4-C51	60.1	67.9	7.8
N2-C4-C51-C61	179.2	179.0	-0.2
C4-C51-C61-C7	-1.8	-0.5	1.2
C51-C61-C7-C62	0.6	-0.1	-0.7
N2-C4-C52-C62	-177.5	-179.0	-1.5
C4-C52-C62-C7	-1.6	0.5	2.1
C52-C62-C7-C61	1.1	0.1	-1.0

C7-C62-C52	120.2	119.9	-0.3
C61-C7-C62	119.6	120.1	0.5
C4-C51-H51	119.4	119.7	0.2
C4-C52-H52	119.9	120.3	0.4
C61-C51-H51	121.3	120.0	-1.3
C62-C52-H52	120.3	119.4	-0.8
C51-C61-H61	119.2	120.0	0.8
C52-C62-H62	119.5	120.2	0.6
C7-C61-H61	120.0	120.2	0.2
C7-C62-H62	120.2	119.9	-0.3
C61-C7-H7	120.2	119.9	-0.3
C62-C7-H7	120.2	120.0	-0.1
S1-C3-H31	107.2	108.2	1.0
S1-C3-H32	109.2	109.3	0.1
S1-C3-H33	108.9	109.0	0.1
H31-C3-H32	110.3	109.9	-0.3
H31-C3-H33	110.2	109.8	-0.4
H32-C3-H33	111.0	110.6	-0.5

Table S24. Scaled MP2/6-31G(d) and MM level vibrational spectra of PMSM.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
35.3	tNC	61	tS1-N2	35			41.1	tNC	52	tS1-N2	44		
62.0	wNH	38	tS1-N2	27	wC4N	19	66.0	wNH	35	wC4N	20	tNC	19
								tS1-N2	17				
114.5	dSNC	26	tNC	24	tS1-N2	16	115.2	wC4N	25	tNC	24	dSNC	18
205.8	ta6RNG1	37	cNSC	32			226.4	tC3-S1	46				
216.8	tC3-S1	89					227.7	tC3-S1	47	ta6RNG1	16		
256.4	iSO2	39	dC4N	27			263.7	cNSC	21				
272.7	iSO2	29	cNSC	17			283.8	iSO2	33	dC4N	26	rSO2	17
334.7	rSO2	50					369.7	cNSC	39	wSO2	26		
350.5	wSO2	18	cNSC	16	rSO2	15	374.6	iSO2	46	rSO2	43		
378.9	ta6RNG1a	115					412.9	wSO2	34				
444.4	tp6RNG1	74	ta6RNG1	25			417.6	ta6RNG1a	114				
469.9	cSO2	59					457.7	ta6RNG1	40	cSO2	33		
481.1	wSO2	27					482.4	cSO2	44	ta6RNG1	23		
492.7	wC4N	30	cSO2	18			572.2	da6RNG1	30	wNH	15		
532.2	wNH	31	wSO2	16			631.8	tp6RNG1	35	wNH	26		
596.0	da6RNG1a	73					656.8	tp6RNG1	64				

601.7	da6RNG1	39	dSNC	16			678.5	da6RNG1a	52	sC3-S1	17			
691.0	wC52H	25	wC7H	25	wC62H	18	696.0	da6RNG1a	24	sC3-S1	18	dSNC	17	
731.8	sC3-S1	61					747.1	wC7H	18					
765.9	wC52H	55	wC51H	23			772.0	sS1-N2	16					
798.3	dSNC	14	sC4-C51	14			809.6	sS1-N2	23	dt6RNG1	18			
805.3	wC51H	36	wC62H	24	wC52H	18	857.5	wC61H	28	wC52H	28	wC62H	23	
	wC7H	18						wC51H	20					
836.8	wC62H	57	wC7H	31			928.2	wC52H	40	wC51H	39	wC7H	27	
848.6	wC61H	73	wC51H	19	wC7H	16	945.8	rC3H3	86					
853.6	sS1-N2	40					952.3	rC3H3'	83					
965.5	dt6RNG1	47					952.8	dt6RNG1	51	sC4-C51	15	sC52-C4	15	
968.3	rC3H3'	62					975.8	sC7-C62	36	sC61-C7	35			
974.8	rC3H3	58					998.2	wC62H	40	wC51H	29	wC52H	29	
								ta6RNG1a	-17	wC61H	17			
1008.7	sC61-C7	29	sC7-C62	29			1007.2	wC7H	48	wC61H	42	wC62H	20	
								tp6RNG1	-18					
1064.6	sC62C52	20	sC51C61	16			1021.6	sC62C52	26	sC51C61	23			
1113.9	sS1-O11	45	sS1-O12	40			1119.4	sS1-O11	44	sS1-O12	40			
1147.4	dC7H	39	dC62H	24	dC61H	18	1155.9	sC51C61	23	sC62C52	21			
1162.1	dC52H	22	dC51H	21	dC61H	19	1207.5	dC61H	23	dC7H	20			
1204.6	sN2-C4	37					1225.7	dC52H	18	rNH	17			
1256.0	rNH	19	dC51H	18			1302.2	sS1-O12	41	sS1-O11	36			
1312.7	sS1-O12	22	sS1-O11	18			1343.1	dC51H	30	sC4-C51	19			
1336.8	dsC3H3	99					1387.2	dsC3H3	93					
1353.8	rNH	24	sS1-O11	17			1404.8	dC52H	31	rNH	21	dC7H	18	
1397.6	sC51C61	17	sC62C52	16			1434.9	rNH	20	dC7H	18	dC61H	17	
1428.8	daC3H3	86					1437.0	daC3H3	86					
1432.5	daC3H3'	81					1441.3	sC51C61	15					
1441.7	dC7H	22	rNH	16			1444.1	daC3H3'	85					
1465.8	dC61H	17					1470.7	dC61H	29	dC62H	29			
1570.1	sC61-C7	19	sC52-C4	18	sC7-C62	17	1488.1	dC7H	22					
	sC4-C51	16												
1579.7	sC51C61	22	sC62C52	22			1548.6	sN2-C4	18	dC51H	17	dC52H	17	
2952.1	sC3-H32	34	sC3-H31	33	sC3-H33	33	2844.1	sC3-H32	34	sC3-H33	34	sC3-H31	32	
3029.0	sC52H52	89					2914.5	sC3-H31	67	sC3-H33	22			
3046.1	sC7-H7	38	sC61H61	38	sC62H62	17	2915.9	sC3-H32	55	sC3-H33	44			
3054.2	sC62H62	50	sC61H61	42			3054.6	sC52H52	36	sC61H61	31	sC62H62	21	
3060.3	sC3-H31	67	sC3-H33	18	sC3-H32	15	3055.2	sC7-H7	56	sC62H62	20			
3063.9	sC3-H32	51	sC3-H33	49			3056.4	sC62H62	41	sC52H52	29	sC7-H7	24	
3066.2	sC7-H7	59	sC62H62	22	sC61H61	15	3057.2	sC61H61	53	sC51H51	34			
3086.0	sC51H51	95					3060.5	sC51H51	45	sC52H52	19			
3360.6	sN2-H21	100					3332.9	sN2-H21	100					

Table S25. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of PBSM – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-4.71	-4.45	0.26	2.13	1.87	-0.26
O11...HOH	270	-5.44	-5.50	-0.06	2.09	1.82	-0.27
O12...HOH	180	-4.97	-4.92	0.04	2.08	1.85	-0.23
O12...HOH	90	-5.71	-5.92	-0.21	2.07	1.82	-0.25
N2...HOH	270	-2.32	-2.23	0.08	2.34	2.12	-0.22
N2H...OHH	0	-6.16	-6.05	0.12	2.05	1.87	-0.18

Table S26. Gas phase dipole moment (Debye) of PBSM calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-2.0777	-2.0116
Y	-0.8324	-0.6319
Z	5.4978	6.0991
Total	5.9359	6.4533

Table S27. MM and MP2/6-31G(d) level equilibrium geometry of PBSM

Coordinate	QM	MM	Difference	Coordinate	QM	MM	Difference
Bond length (Å)				Angles (°)			
S1-N2	1.694	1.648	-0.046	N2-S1-CZ	104.9	102.2	-2.7
S1-O11	1.463	1.438	-0.025	O11-S1-N2	104.7	108.2	3.5
S1-O12	1.461	1.439	-0.022	O12-S1-N2	106.9	111.6	4.7
S1-CZ	1.777	1.783	0.006	O11-S1-CZ	108.5	105.1	-3.4
N2-H21	1.022	1.015	-0.007	O12-S1-CZ	107.5	105.9	-1.6
N2-C3	1.428	1.403	-0.024	O11-S1-O12	123.1	121.9	-1.2
CZ-CE1	1.398	1.412	0.014	S1-N2-H21	108.5	109.4	0.8
CZ-CE2	1.397	1.412	0.014	S1-N2-C3	117.4	120.6	3.3
CE1-CD1	1.395	1.400	0.005	H21-N2-C3	114.0	114.5	0.4
CE2-CD2	1.395	1.401	0.005	S1-CZ-CE1	119.2	120.4	1.2
CG-CD1	1.397	1.400	0.002	S1-CZ-CE2	119.0	121.0	2.1
CG-CD2	1.397	1.400	0.002	CE1-CZ-CE2	121.7	118.5	-3.2

CE1-HE1	1.086	1.081	-0.005
CE2-HE2	1.087	1.081	-0.006
CD1-HD1	1.087	1.081	-0.006
CD2-HD2	1.087	1.081	-0.006
CG-HG	1.087	1.081	-0.006
C3-C41	1.400	1.403	0.003
C3-C42	1.400	1.403	0.004
C41-C51	1.395	1.403	0.008
C42-C52	1.395	1.402	0.007
C51-C6	1.397	1.401	0.005
C52-C6	1.398	1.401	0.003
C41-H41	1.089	1.080	-0.009
C42-H42	1.085	1.081	-0.005
C51-H51	1.087	1.081	-0.006
C52-H52	1.087	1.081	-0.006
C6-H6	1.087	1.081	-0.006

Dihedrals (°)			
N2-S1-CZ-CE1	-82.4	-88.5	-6.1
CZ-S1-N2-C3	54.2	64.5	10.3
S1-CZ-CE1-CD1	176.3	177.8	1.5
CZ-CE1-CD1-CG	-0.5	-0.1	0.4
CE1-CD1-CG-CD2	0.7	0.0	-0.7
S1-CZ-CE2-CD2	-176.6	-177.9	-1.2
CZ-CE2-CD2-CG	1.1	0.3	-0.8
CE2-CD2-CG-CD1	-1.0	-0.1	0.9
S1-N2-C3-C41	-107.8	-109.9	-2.1
N2-C3-C41-C51	-178.6	-179.8	-1.2
C3-C41-C51-C6	-1.7	0.4	2.1
C41-C51-C6-C52	1.1	0.1	-1.0
N2-C3-C42-C52	-179.8	179.8	-0.4
C3-C42-C52-C6	-1.5	-0.4	1.1
C42-C52-C6-C51	0.5	-0.1	-0.6

CZ-CE1-CD1	118.7	120.8	2.1
CZ-CE2-CD2	118.8	120.7	1.9
CG-CD1-CE1	120.4	119.9	-0.4
CG-CD2-CE2	120.3	120.0	-0.3
CD1-CG-CD2	120.2	120.1	0.0
CZ-CE1-HE1	120.1	119.7	-0.4
CZ-CE2-HE2	119.8	119.9	0.1
CD1-CE1-HE1	121.2	119.5	-1.7
CD2-CE2-HE2	121.4	119.4	-2.0
CE1-CD1-HD1	119.6	120.0	0.4
CE2-CD2-HD2	119.7	120.1	0.4
CG-CD1-HD1	120.1	120.1	0.0
CG-CD2-HD2	120.1	120.0	-0.1
CD1-CG-HG	119.9	119.9	0.0
CD2-CG-HG	119.9	119.9	0.0
N2-C3-C41	120.6	119.2	-1.5
N2-C3-C42	118.9	121.2	2.3
C41-C3-C42	120.5	119.6	-0.9
C3-C41-C51	119.7	120.2	0.5
C3-C42-C52	119.3	120.3	1.0
C41-C51-C6	120.2	119.9	-0.3
C42-C52-C6	120.6	119.9	-0.7
C51-C6-C52	119.8	120.1	0.3
C3-C41-H41	119.9	120.2	0.4
C3-C42-H42	119.2	119.6	0.4
C51-C41-H41	120.4	119.6	-0.9
C52-C42-H42	121.6	120.1	-1.4
C41-C51-H51	119.6	120.1	0.5
C42-C52-H52	119.4	120.0	0.6
C6-C51-H51	120.2	120.0	-0.2
C6-C52-H52	120.0	120.2	0.2
C51-C6-H6	120.1	120.0	-0.1
C52-C6-H6	120.1	119.9	-0.2

Table S28. Scaled MP2/6-31G(d) and MM level vibrational spectra of PBSM.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
24.3	tS1-N2	47	tCZ-S1	24			27.3	tS1-N2	53	tCZ-S1	27		
36.3	tNC	46					33.9	tCZ-S1	55	tNC	31		
45.9	tCZ-S1	64					44.6	tNC	30	wNH	17		
99.6	wCZH	40	wC4N	16			106.2	wC4N	32	dSNC	21		
105.6	tNC	34	tS1-N2	17			117.1	wCZH	35	tNC	23		
178.4	dCZH	62	rSO2	22			218.2	dCZH	20	cNSC	17		
209.9	ta6RNG1	29	ta6RNG1	22	cNSC	19	227.7	dCZH	44				
251.6	dC4N	18	iSO2	16			248.4	wSO2	22				
269.8	iSO2	41					270.9	iSO2	62	dC4N	15		
296.1	sCZ-S1	36	da6RNG1	20			306.3	sCZ-S1	22	wSO2	18		
354.4	ta6RNG1	24	dC4N	20			340.7	rSO2	43	dCZH	19		
374.6	ta6RNG1a	111					350.1	dC4N	35				
377.8	ta6RNG1a	107					414.1	ta6RNG1a	117				
392.8	rSO2	30	dCZH	20			417.5	ta6RNG1a	116				
437.1	tp6RNG1	27	ta6RNG1	22	ta6RNG1	17	448.5	wSO2	22				
442.7	tp6RNG1	42					473.5	ta6RNG1	48	wC4N	17		
470.0	tp6RNG1	26	wC4N	25			492.4	ta6RNG1	41	cSO2	17		
500.6	tp6RNG1	45	cSO2	29			503.3	cSO2	52				
524.2	tp6RNG1	19	wNH	16	wSO2	15	583.2	da6RNG1	34	tp6RNG1	15		
552.4	tp6RNG1	28	wSO2	21			651.5	tp6RNG1	66	tp6RNG1	28		
580.1	da6RNG1	19	wNH	18			657.9	tp6RNG1	71	tp6RNG1	26		
589.5	da6RNG1a	89					674.3	da6RNG1a	67				
596.6	da6RNG1a	82					686.3	da6RNG1a	81				
626.4	sS1-N2	23	da6RNG1	20			710.3	wNH	35	dSNC	21		
688.6	wC52H	22	wC7H	20			726.5	sS1-N2	26	da6RNG1	19		
698.5	da6RNG1	18					744.3	da6RNG1	29				
706.5	wCGH	22					751.5	wCGH	26	wCD1H	17	wCD2H	17
762.6	wC52H	53	wC51H	28			768.3	wC7H	18				
795.3	wCE1H	36	wCE2H	25	wCD2H	23	806.6	dt6RNG1	20	sS1-N2	18		
	wCD1H	15											
802.4	wC7H	29	wC51H	29	wC52H	17	851.2	wCE2H	27	wCE1H	26	wCD1H	23
	wC62H	17						wCD2H	23				
805.9	dSNC	15					856.7	wC52H	28	wC61H	28	wC62H	23
								wC51H	21				
834.1	wC62H	53	wC7H	24			917.4	wCE1H	40	wCE2H	39	wCGH	28
843.3	wCE1H	41	wCGH	29	wCE2H	28	927.2	wC52H	40	wC51H	40	wC7H	27
844.7	wC61H	63	wC51H	22			949.4	dt6RNG1	68				
849.3	sS1-N2	28					952.6	dt6RNG1	56	sC4-C72	16	sC52-C4	16
854.1	wCD1H	44	wCGH	43			975.5	sC7-C62	36	sC61-C7	35		
861.7	wCD2H	48	wCE2H	42	wCD1H	16	976.5	sCG-CD1	37	sCD2-CG	37		
957.5	dt6RNG1	66					992.1	wCD2H	32	wCD1H	31	wCE1H	28
								wCE2H	27	ta6RNG1a	-18		

967.0	dt6RNG1	65					997.4	wC62H	39	wC51H	30	wC52H	29	
								wC61H	19	ta6RNG1a	-18			
1001.9	sCD2-CG	29	sCG-CD1	29			1006.4	wCGH	53	wCD1H	32	wCD2H	31	
								tp6RNG1	-18					
1006.4	sC61-C7	28	sC7-C62	28			1006.9	wC7H	49	wC61H	40	wC62H	22	
								tp6RNG1	-18					
1059.2	sCD1-CE1	15					1019.7	sCD1-CE1	25	sCE2-CD2	25			
1061.2	sC62C73	19	sC51C61	16			1020.7	sC62C73	26	sC51C61	23			
1063.8	sCE2-CD2	21					1071.4	sCZ-S1	14					
1122.9	sS1-O11	32	sS1-O12	29			1118.2	sS1-O11	34	sS1-O12	31			
1146.6	dC7H	40	dC62H	21	dC61H	20	1155.0	sC51C61	23	sC62C73	21			
1149.7	dCGH	39	dCD2H	24	dCD1H	18	1200.8	dCE1H	15					
1158.0	dC52H	23	dC51H	21	dC62H	18	1206.4	dC61H	22	dC7H	18			
	dC61H	16												
1162.5	dCD1H	24	dCE1H	18	dCE2H	17	1210.4	dCGH	25	dCD2H	19	dCD1H	18	
	dCD2H	17												
1201.7	sN2-C3	41					1223.7	dC52H	17	rNH	17			
1248.8	rNH	25	dC51H	16			1297.3	sS1-O12	40	sS1-O11	36			
1277.9	dCE1H	30	dCE2H	28			1337.4	dC51H	28	sC4-C72	17			
1305.0	sS1-O12	22	sS1-O11	18			1354.5	sCZ-CE2	20	sCE1-CZ	19	dCE2H	18	
								dCE1H	18					
1344.0	rNH	29	sS1-O11	19	sS1-O12	17	1400.7	dC52H	33	rNH	25			
1393.3	sCE1-CZ	18	sCZ-CE2	17			1419.5	dCGH	36	dCD1H	17	dCD2H	16	
1398.8	sC62C73	16	sC51C61	15			1431.9	dC7H	23	rNH	20			
1415.5	dCGH	28					1440.2	sC51C61	18					
1436.5	dC7H	25					1443.3	sCD1-CE1	16	sCE2-CD2	16			
1446.8	dCE1H	18	dCE2H	17	dCD2H	16	1469.4	dCD1H	25	dCD2H	25			
	dCD1H	15												
1463.5	dC61H	17					1470.3	dC61H	27	dC62H	26			
1562.6	sCD2-CG	22	sCE1-CZ	18	sCG-CD1	17	1487.3	dC7H	23					
	sCZ-CE2	15												
1566.3	sCE2-CD2	23	sCD1-CE1	23			1488.5	dCGH	24					
1569.6	sC52-C4	22	sC61-C7	22			1511.2	dCE2H	25	dCE1H	24			
1577.2	sC51C61	21	sC62C73	20			1547.0	sN2-C3	18	dC52H	17	dC51H	17	
3031.2	sC52H73	84					3053.8	sCE2-HE2	53	sCE1-HE1	25			
3044.5	sCG-HG	47	sCD2-HD2	27	sCD1-HD1	21	3054.6	sCG-HG	41	sCE1-HE1	33			
3044.8	sC7-H7	42	sC61H61	35			3054.7	sC61H61	33	sC52H73	30	sC62H62	24	
3053.6	sC62H62	47	sC61H61	43			3055.2	sC7-H7	63					
3054.4	sCD1-HD1	43	sCD2-HD2	41			3056.0	sCD2-HD2	44	sCD1-HD1	33			
3062.5	sCG-HG	43	sCE2-HE2	22	sCD1-HD1	21	3056.6	sC62H62	44	sC52H73	32	sC7-H7	18	
3064.4	sC7-H7	54	sC62H62	25	sC61H61	16	3056.6	sCG-HG	40	sCD1-HD1	30	sCD2-HD2	16	
3069.5	sCE2-HE2	63	sCD2-HD2	25			3057.2	sC61H61	52	sC51H51	36			
3074.5	sCE1-HE1	81					3059.7	sCD1-HD1	23	sCD2-HD2	23	sCE1-HE1	21	
								sCE2-HE2	17					

3081.7	sC51H51	93				3060.5	sC51H51	43	sC52H73	21	
3334.3	sN2-H21	100				3333.1	sN2-H21	100			

Table 29. Scaled MP2/6-31G(d) and MM level vibrational spectra of OBTZ.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
63.6	ta6RNG1a	74					86.6	ta6RNG1a	71				
111.6	BFLY	36	ta6RNG1	33			124.5	BFLY	41	ta6RNG1	25		
196.5	ta6RNG2a	26	ta6RNG1	23	BFLY	16	208.8	ta6RNG1	31	BFLY	19		
235.5	sC10-S1	25	da6RNG2	24			225.5	wS1O	35	sC10-S1	22		
249.5	iS1O	40	tp6RNG1	18			279.8	iS1O	44	tp6RNG1	17		
304.5	ta6RNG2a	21	da6RNG1a	18	cS1O	16	306.5	da6RNG1a	22	rS1O	16		
319.3	da6RNG1a	30	ta6RNG2a	19			326.4	da6RNG1a	35				
375.5	da6RNG1	33					362.4	da6RNG1	32	wS1O	22		
401.1	da6RNG1	24	iS1O	20			384.4	sC10-S1	12	ta6RNG1	12		
450.6	tp6RNG2	32	ta6RNG2a	29			422.6	ta6RNG2a	51	wN4H	19		
452.9	tp6RNG2	52	ta6RNG2	15			449.8	wS1O	22	da6RNG1	15	sC10-S1	15
478.5	wN4H	36	cS1O	20	da6RNG1a	15	467.5	cS1O	25	ta6RNG2a	21		
482.2	rS1O	21	wS1O	20			497.5	ta6RNG2	54				
502.4	wN4H	20					528.8	cS1O	29	wN4H	16	dt6RNG1	16
552.0	cS1O	22	da6RNG2a	21			554.3	da6RNG2a	19	wN4H	19		
563.4	tp6RNG1	30	ta6RNG2	19			634.8	dt6RNG1	35	wN4H	16		
648.0	da6RNG2a	23					683.1	tp6RNG2	80				
667.4	dt6RNG1	23	da6RNG2	18			721.0	sS1-N2	51				
705.7	wC6H	22	wC8H	19	wC7H	16	735.7	da6RNG2	26	da6RNG2a	23	sC5-C10	16
712.5	sS1-N2	22					771.5	wC8H	33	wC7H	32	wC9H	17
								wC6H	15				
769.2	wC6H	59	wC9H	25	wC8H	18	798.9	dt6RNG2	31	da6RNG2	18		
789.0	dt6RNG2	23	wN2H	15			861.3	wN2H	74				
833.9	wC9H	67	wC8H	28			876.8	wC9H	43	wC6H	42		
836.4	wC7H	70	wC8H	29			966.1	wC6H	40	wC9H	39	wC8H	19
								wC7H	17				
844.4	wN2H	28	sS1-N2	17			989.1	sC8-C7	48	sC9-C8	19	sC7-C6	17
992.5	sC3-N4	34	sN2-C3	18	dt6RNG2	18	997.4	rC3H2	43	dt6RNG2	17		
1015.1	sC8-C7	31	sC7-C6	17			1004.2	wC8H	49	wC7H	49		
1041.6	dt6RNG2	13					1045.8	sC7-C6	18	sC6-C5	15		
1054.0	sC3-N4	24	rC3H2	17	sN2-C3	16	1059.9	sC3-N4	43	rC3H2	24		
1089.0	sN2-C3	36	rC3H2	33			1084.8	sC9-C8	20				
1113.6	ssS1O	39					1096.1	sN2-C3	41	ssS1O	16		
1130.5	ssS1O	38					1119.8	ssS1O	55				
1151.5	dC8H	33	dC7H	33			1177.9	sC10-C9	17	sN4-C5	17	sC7-C6	15
1213.3	iC3H2	48					1230.0	dC8H	19	dC9H	15	dC7H	15
1234.6	sN4-C5	35					1264.0	dC6H	21	sC6-C5	18	dN4H	15

1243.2	dC6H	19	iC3H2	19	dC9H	18	1301.2	saS1O	76			
1302.2	saS1O	56					1324.1	iC3H2	76			
1317.9	wC3H2	46	saS1O	25			1384.4	dN2H	53			
1375.0	dN2H	25					1403.3	wC3H2	17			
1388.5	dN2H	31	wC3H2	16			1427.1	wC3H2	39	dC8H	16	dC7H 16
1403.3	sC10-C9	21	dC7H	19			1429.7	wC3H2	19	sC5-C10	16	dC7H 16
1454.2	dN4H	33					1454.2	dN4H	23	dC6H	21	dC8H 16
1459.8	sN4-C5	14					1474.5	dC9H	22	sC9-C8	21	
1481.7	cC3H2	83					1478.2	cC3H2	84			
1559.0	sC8-C7	25	sC5-C10	21			1482.0	dC9H	24	dC7H	22	sC8-C7 15
1586.1	sC7-C6	23	sC10-C9	15			1546.5	sN4-C5	19	dC6H	18	sC6-C5 16
2922.9	ssC3H2	85					3035.4	ssC3H2	90			
3000.8	saC3H2	85					3055.3	sC6-H6	40	sC8-H8	25	sC9-H9 23
3031.2	sC6-H6	88					3056.1	sC7-H7	50	sC8-H8	23	sC9-H9 16
3049.4	sC9-H9	47	sC8-H8	23	sC7-H7	23	3057.1	sC8-H8	40	sC7-H7	22	sC9-H9 19
								sC6-H6	19			
3055.0	sC7-H7	53	sC9-H9	41			3059.5	sC9-H9	42	sC6-H6	30	sC7-H7 15
3071.0	sC8-H8	75					3059.7	saC3H2	90			
3324.6	sN2-H2	100					3339.0	sN2-H2	99			
3383.8	sN4-H4	100					3353.9	sN4-H4	99			

Table S30. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of DMSN – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	90	-5.11	-5.19	-0.07	2.09	1.83	-0.26
O11...HOH	180	-7.24	-7.54	-0.30	2.00	1.78	-0.22

Table S31. Gas phase dipole moment (Debye) of DMSN calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-2.9295	-3.8470
Y	3.5790	4.6999
Z	0.0000	0.0000
Total	4.6250	6.0736

Table S32. MM and MP2/6-31G(d) level equilibrium geometry of DMSN

Coordinate	QM	MM	Difference
Bond length (Å)			
S1-O11	1.469	1.437	-0.033
S1-O12	1.469	1.437	-0.033
S1-C2	1.785	1.781	-0.004
S1-C3	1.785	1.781	-0.004
C2-H21	1.092	1.110	0.018
C2-H22	1.091	1.109	0.018
C2-H23	1.091	1.109	0.018
C3-H31	1.092	1.110	0.018
C3-H32	1.091	1.109	0.018
C3-H33	1.091	1.109	0.018
Dihedrals (°)			
C2-S1-C3-H32	61.3	60.6	-0.8
C3-S1-C2-H22	61.3	60.6	-0.8

Coordinate	QM	MM	Difference
Angles (°)			
C2-S1-C3	103.6	103.6	0.0
O11-S1-C2	107.7	107.7	0.0
O12-S1-C2	107.7	107.7	0.0
O11-S1-C3	107.7	107.7	0.0
O12-S1-C3	107.7	107.7	0.0
O11-S1-O12	121.1	121.1	0.0
S1-C2-H21	106.2	108.3	2.1
S1-C2-H22	109.7	109.4	-0.4
S1-C2-H23	109.7	109.4	-0.4
H21-C2-H22	109.9	109.6	-0.2
H21-C2-H23	109.9	109.6	-0.2
H22-C2-H23	111.4	110.5	-0.9
S1-C3-H31	106.2	108.3	2.1
S1-C3-H32	109.7	109.4	-0.4
S1-C3-H33	109.7	109.4	-0.4
H31-C3-H32	109.9	109.6	-0.2
H31-C3-H33	109.9	109.6	-0.2
H32-C3-H33	111.4	110.5	-0.9

Table S33. Scaled MP2/6-31G(d) and MM level vibrational spectra of DMSN.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
190.2	tS1-C2	50	tS1-C3	50			217.2	tS1-C3	50	tS1-C2	50		
219.6	tS1-C3	49	tS1-C2	49			222.6	tS1-C3	50	tS1-C2	50		
261.9	cSCC	88					319.8	cSCC	95				
275.8	iSO2	94					363.8	iSO2	98				
347.5	rSO2	87					379.8	wSO2	86				
429.8	wSO2	79					382.1	rSO2	94				
462.1	cSO2	87					454.2	cSO2	85				
674.5	sS1-C2	44	sS1-C3	44			652.0	sS1-C2	37	sS1-C3	37		
744.9	sS1-C3	37	sS1-C2	37			734.2	sS1-C2	39	sS1-C3	39		
931.9	rC2H'	45	rC3H'	45			939.7	rC3H	42	rC2H	42		
943.4	rC3H	34	rC2H	34	wSO2	16	943.0	rC3H	44	rC2H	44		
986.8	rC3H'	39	rC2H'	39			947.1	rC2H'	46	rC3H'	46		
997.9	rC2H	35	rC3H	35			948.6	rC2H'	44	rC3H'	44		
1113.4	sS1-O11	37	sS1-O12	37			1118.8	sS1-O11	42	sS1-O12	42		

1296.1	sS1-O11	45	sS1-O12	45	1312.5	sS1-O12	45	sS1-O11	45
1330.2	dsC2H	49	dsC3H	49	1388.9	dsC3H	45	dsC2H	45
1346.4	dsC3H	49	dsC2H	49	1389.9	dsC3H	46	dsC2H	46
1422.4	daC3H'	48	daC2H'	48	1433.9	daC3H	46	daC2H	46
1426.3	daC2H	47	daC3H	47	1436.0	daC3H	46	daC2H	46
1434.9	daC3H	47	daC2H	47	1437.8	daC3H'	47	daC2H'	47
1438.0	daC2H'	46	daC3H'	46	1439.6	daC2H'	47	daC3H'	47
2950.7	sC4-H	50	sC3-H	50	2843.9	sC4-H	50	sC3-H	50
2952.5	sC3-H	50	sC4-H	50	2844.4	sC4-H	50	sC3-H	50
3058.7	sC4-H	50	sC3-H	50	2913.2	sC4-H	50	sC3-H	50
3059.6	sC3-H	50	sC4-H	50	2914.9	sC3-H	50	sC4-H	50
3062.2	sC4-H	50	sC3-H	50	2915.2	sC4-H	50	sC3-H	50
3065.4	sC3-H	50	sC4-H	50	2915.4	sC3-H	50	sC4-H	50

Table S34. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of EMSN – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-7.32	-7.66	-0.34	1.99	1.78	-0.21
O11...HOH	90	-5.30	-5.27	0.03	2.08	1.83	-0.25

Table S35. Gas phase dipole moment (Debye) of EMSN calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-3.3538	-4.2179
Y	3.0097	4.3589
Z	0.0000	0.0000
Total	4.5062	6.0655

Table S36. MM and MP2/6-31G(d) level equilibrium geometry of EMSN

Coordinate	QM	MM	Difference	Coordinate	QM	MM	Difference
Bond length (Å)				Angles (°)			
S1-O11	1.472	1.438	-0.034	C2-S1-C3	103.8	103.6	-0.2
S1-O12	1.472	1.438	-0.034	O11-S1-C2	107.7	107.6	-0.1
S1-C2	1.786	1.781	-0.005	O12-S1-C2	107.7	107.6	-0.1
S1-C3	1.794	1.798	0.004	O11-S1-C3	107.8	107.7	-0.1

C2-C3	1.524	1.535	0.010	O12-S1-C3	107.8	107.7	-0.1
C2-H21	1.092	1.110	0.018	O11-S1-O12	120.8	121.3	0.5
C2-H22	1.091	1.109	0.018	S1-C2-H21	106.2	108.3	2.0
C2-H23	1.091	1.109	0.018	S1-C2-H22	109.6	109.4	-0.3
C3-H31	1.094	1.109	0.015	S1-C2-H23	109.6	109.4	-0.3
C3-H32	1.094	1.109	0.015	H21-C2-H22	109.9	109.6	-0.3
C4-H41	1.092	1.110	0.018	H21-C2-H23	109.9	109.6	-0.3
C4-H42	1.092	1.112	0.020	H22-C2-H23	111.4	110.5	-0.8
C4-H43	1.092	1.112	0.020	S1-C3-H31	107.1	107.5	0.3
				S1-C3-H32	107.1	107.5	0.3
				H31-C3-H32	109.3	110.5	1.1
Dihedrals (°)				S1-C3-C4	109.5	108.8	-0.7
C2-S1-C3-C4	-180.0	-180.0	0.0	C4-C3-H31	111.8	111.2	-0.5
C3-S1-C2-H22	-61.3	-60.6	0.7	C4-C3-H32	111.8	111.2	-0.5
S1-C3-C4-H42	60.2	59.7	-0.4	C3-C4-H41	110.4	110.7	0.3
				C3-C4-H42	111.8	111.2	-0.5
				C3-C4-H43	111.8	111.2	-0.5
				H41-C4-H42	108.8	108.6	-0.3
				H41-C4-H43	108.8	108.6	-0.3
				H42-C4-H43	108.8	108.1	-0.7

Table S37. Scaled MP2/6-31G(d) and MM level vibrational spectra of EMSN.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
73.7	tS1-C3	94					91.4	tS1-C3	96				
187.0	cSCC	53	cC3CS	40			211.6	tS1-C2	91				
197.7	tS1-C2	89					220.0	cC3CS	50	cSCC	35		
209.5	tC3-C4	73					232.5	tC3-C4	81				
281.8	iSO2	86					306.8	cSCC	57	cC3CS	16		
301.5	cSCC	34	cC3CS	32	wSO2	16	359.1	iSO2	92				
355.3	rSO2	78					380.7	rSO2	87				
454.7	cSO2	87					410.6	wSO2	63	cC3CS	18		
485.6	wSO2	58	sS1-C2	20			454.3	cSO2	85				
659.4	sS1-C3	64					650.9	sS1-C3	55				
750.8	sS1-C2	66					714.9	sS1-C2	65				
774.4	rC3H	56	rC4H'	31			824.0	rC3H	74	rC4H'	17		
951.2	rC2H	42	rC4H	25			940.2	rC2H	87				
952.9	rC2H'	80					948.0	rC2H'	90				

973.7	sC3-C4	39	rC2H	27			983.2	rC4H	40	sC3-C4	36
1043.2	iC3H	32	rC4H'	27	rC3H	24	1030.6	rC4H'	67		
1050.5	sC3-C4	38	rC4H	36			1044.1	sC3-C4	44	rC4H	43
1104.2	sS1-O12	36	sS1-O11	36			1116.8	sS1-O12	42	sS1-O11	42
1231.5	iC3H	46	rC4H'	29			1180.7	iC3H	86		
1286.0	wC3H	79					1314.5	sS1-O11	45	sS1-O12	45
1291.9	sS1-O11	39	sS1-O12	39			1319.6	wC3H	80		
1335.6	dsC2H	98					1389.6	dsC2H	91		
1383.6	dsC4H	96					1416.4	dsC4H	62	daC4H	29
1428.4	daC2H	70	cC3H	25			1426.9	daC4H	59	dsC4H	33
1429.9	daC2H'	93					1432.3	daC4H'	90		
1434.4	cC3H	75	daC2H	24			1434.0	daC2H	91		
1466.5	daC4H'	91					1438.0	daC2H'	94		
1481.4	daC4H	92					1457.9	cC3H	91		
2949.1	sC4-H	53	sC3-H	29	sC2-H	18	2844.2	sC2-H	100		
2949.5	sC2-H	43	sC4-H	43			2850.1	sC3-H	98		
2952.5	sC3-H	57	sC2-H	39			2892.2	sC3-H	99		
3014.6	sC3-H	95					2903.1	sC4-H	99		
3037.1	sC4-H	100					2914.1	sC2-H	100		
3047.3	sC4-H	95					2915.2	sC2-H	100		
3058.1	sC2-H	100					2959.0	sC4-H	100		
3063.4	sC2-H	100					2960.1	sC4-H	99		

Table S38. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of MMST – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-4.79	-4.73	0.06	2.11	1.86	-0.25
O12...HOH	90	-4.70	-4.81	-0.10	2.12	1.85	-0.27
O3...HOH	0	-2.40	-2.16	0.23	2.15	1.89	-0.26
O3...HOH	90	-2.81	-2.99	-0.18	2.12	1.85	-0.27

Table S39. Gas phase dipole moment (Debye) of MMST calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	0.9540	1.2846
Y	1.6462	2.1155
Z	2.1677	2.6453
Total	2.8843	3.6226

Table S40. MM and MP2/6-31G(d) level equilibrium geometry of MMST

Coordinate	QM	MM	Difference
Bond length (Å)			
S1-C2	1.771	1.778	0.007
S1-O11	1.461	1.438	-0.023
S1-O12	1.461	1.438	-0.023
S1-O3	1.638	1.601	-0.037
O3-C4	1.453	1.436	-0.017
C2-H21	1.091	1.109	0.018
C2-H22	1.089	1.109	0.019
C2-H23	1.089	1.109	0.019
C4-H41	1.088	1.110	0.023
C4-H42	1.091	1.113	0.021
C4-H43	1.091	1.113	0.021
Dihedrals (°)			
C2-S1-O3-C4	-180.0	-180.0	0.0
H22-C2-S1-O3	60.7	60.1	-0.6
H42-C4-O3-S1	61.1	60.4	-0.8

Coordinate	QM	MM	Difference
Angles (°)			
C2-S1-O3	96.1	96.7	0.6
O11-S1-C2	110.0	108.8	-1.2
O12-S1-C2	110.0	108.8	-1.2
O11-S1-O3	109.1	109.1	0.0
O12-S1-O3	109.1	109.1	0.0
O11-S1-O12	120.0	121.6	1.6
S1-O3-C4	113.1	114.0	0.9
S1-C2-H21	106.8	108.6	1.8
S1-C2-H22	108.8	108.9	0.1
S1-C2-H23	108.8	108.9	0.1
H21-C2-H22	110.5	110.0	-0.5
H21-C2-H23	110.5	110.0	-0.5
H22-C2-H23	111.2	110.2	-1.0
O3-C4-H41	104.7	109.7	5.0
O3-C4-H42	110.0	110.5	0.6
O3-C4-H43	110.0	110.5	0.6
H41-C4-H42	110.8	108.5	-2.3
H41-C4-H43	110.6	108.5	-2.1
H42-C4-H43	110.6	109.0	-1.7

Table S41. Scaled MP2/6-31G(d) and MM level vibrational spectra of MMST.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
35.1	tS1-O3	93					73.9	tS1-O3	85				
140.0	tO3-C4	93					146.2	tO3-C4	84				
201.9	tS1-C2	99					195.0	tS1-C2	98				
207.2	iO3	47	cSOC	47			231.4	iO3	52	cSOC	34		
284.8	iSO2	81					324.5	cSOC	51	wSO2	26		
317.8	cSOC	37	iO3	29	wSO2	23	366.9	iSO2	78	rSO2	20		
430.7	rSO2	77					427.5	wSO2	41	iO3	19	sS1-C2	19
464.8	cSO2	84					449.0	rSO2	72	iSO2	21		
511.3	wSO2	47	sS1-C2	23	iO3	16	468.9	cSO2	74				
675.5	sS1-O3	72					686.9	sS1-O3	38	sS1-C2	24		

782.0	sS1-C2	64					723.0	sS1-C2	48	sS1-O3	29					
970.2	rC2	43	sO3-C4	41			944.0	rC2'	90							
978.8	rC2'	84					945.3	rC2	86							
998.4	sO3-C4	49	rC2	35			1026.5	sO3-C4	77							
1127.1	sS1-O12	38	sS1-O11	38			1113.3	sS1-O11	33	sS1-O12	33	rC4	20			
1133.1	rC4'	95					1128.0	rC4'	76	daC4H3'	23					
1152.8	rC4	79					1150.2	rC4	57							
1310.7	sS1-O11	46	sS1-O12	46			1312.6	sS1-O12	46	sS1-O11	46					
1348.4	dsC2H3	98					1384.5	dsC2H3	93							
1423.6	dsC4H3	97					1432.8	daC4H3	82	rC4	18					
1428.5	daC2H3'	93					1434.1	daC2H3	94							
1433.9	daC2H3	90					1436.1	daC2H3'	93							
1461.7	daC4H3'	95					1458.8	daC4H3'	76	rC4'	24					
1479.1	daC4H3	94					1594.6	dsC4H3	88							
2950.5	sC4-H42	40	sC4-H43	40	sC4-H41	19	2844.1	sC2-H22	33	sC2-H23	33	sC2-H21	33			
2964.3	sC2-H21	39	sC2-H23	30	sC2-H22	30	2851.5	sC4-H41	35	sC4-H43	32	sC4-H42	32			
3046.3	sC4-H43	50	sC4-H42	50			2913.2	sC4-H41	64	sC4-H43	18	sC4-H42	18			
3070.8	sC2-H21	61	sC2-H22	20	sC2-H23	20	2914.9	sC2-H21	66	sC2-H22	17	sC2-H23	17			
3077.0	sC4-H41	81					2915.6	sC4-H42	41	sC4-H43	41					
3082.8	sC2-H23	50	sC2-H22	50			2915.6	sC2-H23	41	sC2-H22	41					

Table S42. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of PMST – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-4.64	-4.76	-0.12	2.12	1.87	-0.25
O11...HOH	90	-4.96	-5.19	-0.23	2.11	1.84	-0.27
O3...HOH	0	-2.46	-2.10	0.36	2.19	1.95	-0.24
O3...HOH	90	-2.69	-2.70	-0.01	2.15	1.87	-0.28

Table S43. Gas phase dipole moment (Debye) of PMST calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-1.6853	-2.0895
Y	1.8837	2.9529
Z	-0.0099	0.0000
Total	2.5276	3.6174

Table S44. MM and MP2/6-31G(d) level equilibrium geometry of PMST

Coordinate	QM	MM	Difference
Bond length (Å)			
S1-C2	1.772	1.778	0.006
S1-O11	1.459	1.438	-0.021
S1-O12	1.459	1.438	-0.021
S1-O3	1.663	1.607	-0.056
O3-CZ	1.413	1.388	-0.024
C2-H21	1.091	1.109	0.018
C2-H22	1.089	1.109	0.019
C2-H23	1.089	1.109	0.019
CZ-CE1	1.393	1.404	0.012
CZ-CE2	1.393	1.404	0.012
CE1-CD1	1.396	1.402	0.006
CE2-CD2	1.396	1.402	0.006
CG-CD1	1.397	1.402	0.004
CG-CD2	1.397	1.402	0.004
CE1-HE1	1.086	1.079	-0.006
CE2-HE2	1.086	1.079	-0.006
CD1-HD1	1.087	1.081	-0.006
CD2-HD2	1.087	1.081	-0.006
CG-HG	1.087	1.081	-0.006
Dihedrals (°)			
C2-S1-O3-CZ	-179.9	-180.0	-0.1
O3-S1-C2-H22	-60.6	-60.2	0.5
S1-O3-CZ-CE1	91.3	92.2	0.9
O3-CZ-CE1-CD1	177.0	177.1	0.1
CZ-CE1-CD1-CG	0.3	-0.8	-1.1
CE1-CD1-CG-CD2	0.0	0.0	0.0
O3-CZ-CE2-CD2	-177.0	-177.1	-0.1
CZ-CE2-CD2-CG	-0.3	0.8	1.1
CE2-CD2-CG-CD1	0.0	0.0	0.0

Coordinate	QM	MM	Difference
Angles (°)			
C2-S1-O3	95.4	96.3	0.9
O11-S1-C2	110.0	108.1	-1.9
O12-S1-C2	110.0	108.1	-1.9
O11-S1-O3	108.9	109.8	0.9
O12-S1-O3	108.9	109.8	0.9
O11-S1-O12	120.6	121.7	1.1
S1-O3-CZ	113.5	113.2	-0.2
S1-C2-H21	106.9	108.6	1.8
S1-C2-H22	108.7	109.0	0.2
S1-C2-H23	108.7	109.0	0.2
H21-C2-H22	110.6	110.0	-0.6
H21-C2-H23	110.6	110.0	-0.6
H22-C2-H23	111.2	110.2	-1.0
O3-CZ-CE1	118.7	120.2	1.5
O3-CZ-CE2	118.8	120.2	1.4
CE1-CZ-CE2	122.5	119.5	-3.0
CZ-CE1-CD1	118.4	120.3	2.0
CZ-CE2-CD2	118.4	120.3	2.0
CG-CD1-CE1	120.3	119.8	-0.5
CG-CD2-CE2	120.3	119.8	-0.5
CD1-CG-CD2	120.1	120.2	0.1
CZ-CE1-HE1	119.7	119.1	-0.5
CZ-CE2-HE2	119.7	119.1	-0.5
CD1-CE1-HE1	122.0	120.5	-1.5
CD2-CE2-HE2	122.0	120.5	-1.5
CE1-CD1-HD1	119.5	120.1	0.6
CE2-CD2-HD2	119.5	120.1	0.6
CG-CD1-HD1	120.1	120.1	0.0
CG-CD2-HD2	120.1	120.1	0.0
CD1-CG-HG	119.9	119.9	0.0
CD2-CG-HG	119.9	119.9	0.0

Table S45. Scaled MP2/6-31G(d) and MM level vibrational spectra of PMST.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
12.3	tO3-CZ	51	tS1-O3	47			18.4	tO3-CZ	68	tS1-O3	30		
53.4	tS1-O3	51	tO3-CZ	50			62.2	tS1-O3	67	tO3-CZ	35		
81.9	iO3	48	wCZH	41			89.9	wCZH	52	iO3	37		
198.8	tS1-C2	99					194.3	tS1-C2	99				
216.6	cSOC	32	ta6RNG1a	31			237.1	iO3	35	ta6RNG1a	24		
241.2	cSOC	44					252.5	cSOC	71				
251.1	iSO2	74	dCZH	22			326.3	iSO2	48	dCZH	34		
331.9	rSO2	47	dCZH	31			377.8	rSO2	55	iSO2	31		
382.0	ta6RNG1	87	ta6RNG1a	29			398.3	wSO2	72				
423.6	ta6RNG1a	32	cSO2	18			415.0	ta6RNG1	89	ta6RNG1a	30		
450.1	wSO2	37	cSO2	20			449.6	ta6RNG1a	39	cSO2	31		
462.7	rSO2	43	dCZH	30			486.3	cSO2	51				
463.4	tp6RNG1	81					525.7	dCZH	34	rSO2	34	iSO2	21
490.8	cSO2	47					576.6	da6RNG1a	27				
578.6	da6RNG1a	20	iO3	20			646.1	tp6RNG1	103				
593.1	da6RNG1	61	da6RNG1a	20			677.8	da6RNG1	62	da6RNG1a	21		
657.2	sS1-O3	46					695.6	sS1-C2	51				
713.7	wCGH	24	wCZH	16			738.0	sS1-O3	24	sS1-C2	15		
762.1	sS1-C2	61					763.7	wCGH	22				
763.7	wCE1H	40	wCE2H	40			809.5	sS1-O3	20	dt6RNG1	18		
807.1	wCE1H	29	wCE2H	29	wCGH	17	854.0	wCE1H	25	wCE2H	25	wCD2H	25
								wCD1H	25				
819.7	sCZ-O3	20	sS1-O3	16			924.4	wCE1H	40	wCE2H	40	wCGH	27
840.8	wCD1H	44	wCD2H	44			944.7	rC2H'	90				
844.2	wCGH	52	wCD2H	28	wCD1H	27	946.0	rC2H	84				
966.9	dt6RNG1	64					951.3	dt6RNG1	47				
978.0	rC2H'	84					978.8	sCG-CD2	30	sCD1-CG	30		
981.8	rC2H	70					995.6	wCD1H	30	wCD2H	30	wCE2H	29
								wCE1H	29				
1001.8	sCD1-CG	26	sCG-CD2	26			1006.4	wCGH	51	wCD2H	31	wCD1H	31
								tp6RNG1	-18				
1054.7	sCE1-CD1	19	sCD2-CE2	19			1030.9	sCD2-CE2	23	sCE1-CD1	23		
1120.7	sS1-O12	29	sS1-O11	29			1123.0	sS1-O12	41	sS1-O11	41		
1143.4	dCE1H	19	dCE2H	19			1157.0	sCE1-CD1	21	sCD2-CE2	21		
1146.0	dCGH	42	dCD2H	19	dCD1H	19	1214.9	dCGH	25	dCD2H	19	dCD1H	19
1169.5	sCZ-O3	30					1267.7	sCZ-O3	37	dCE1H	19	dCE2H	19
1275.1	dCE2H	26	dCE1H	26			1313.2	sS1-O11	46	sS1-O12	46		
1319.0	sS1-O11	46	sS1-O12	46			1359.2	dCE2H	29	dCE1H	29		
1345.9	dsC2H3	98					1385.3	dsC2H3	93				
1388.0	sCE2-CZ	17	sCZ-CE1	17	sCD1-CG	16	1427.2	dCGH	25	sCZ-CE1	20	sCE2-CZ	20
	sCG-CD2	16											
1424.5	dCGH	30					1434.2	daC2H3	94				

1427.5	daC2H3'	92					1436.2	daC2H3'	93					
1432.4	daC2H3	93					1437.9	dCD2H	20	dCD1H	20	sCE1-CD1	17	
								sCD2-CE2	17					
1457.1	dCD1H	16	dCD2H	16			1467.4	dCD1H	30	dCD2H	30			
1569.9	sCD2-CE2	23	sCE1-CD1	23			1486.3	dCGH	23					
1576.0	sCZ-CE1	20	sCE2-CZ	20	sCG-CD2	18	1542.1	dCE2H	16	dCE1H	16			
	sCD1-CG	17												
2963.2	sC2-H	100					2844.2	sC2-H	100					
3046.1	sCG-HG	43	sCD1-HD1	27	sCD2-HD2	27	2915.0	sC2-H	100					
3055.6	sCD2-HD2	46	sCD1-HD1	46			2915.6	sC2-H	100					
3065.4	sCG-HG	54	sCD2-HD2	17	sCD1-HD1	17	3054.7	sCD1-HD1	28	sCD2-HD2	28	sCE1-HE1	22	
								sCE2-HE2	22					
3070.2	sC2-H	100					3055.2	sCG-HG	71					
3078.4	sCE1-HE1	52	sCE2-HE2	41			3056.8	sCE1-HE1	28	sCE2-HE2	28	sCD1-HD1	22	
								sCD2-HD2	22					
3079.0	sCE2-HE2	48	sCE1-HE1	37			3057.0	sCD2-HD2	33	sCD1-HD1	33	sCG-HG	16	
3082.5	sC2-H	100					3060.2	sCE2-HE2	28	sCE1-HE1	28	sCD2-HD2	15	
								sCD1-HD1	15					

Table S46. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of MSNA – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-11.86	-11.66	0.20	1.90	1.73	-0.17

Table S47. Gas phase dipole moment (Debye) of MSNA calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	3.5340	3.1044
Y	0.0000	0.0000
Z	0.0000	0.0000
Total	3.5340	3.1044

Table S48. MM and MP2/6-31G(d) level equilibrium geometry of MSNA

Coordinate	QM	MM	Difference	Coordinate	QM	MM	Difference
Bond length (Å)				Angles (°)			
S1-O11	1.488	1.447	-0.041	O11-S1-C2	104.0	103.8	-0.2

S1-O12	1.488	1.447	-0.041	O12-S1-C2	104.0	103.8	-0.2
S1-O13	1.488	1.447	-0.041	O13-S1-C2	104.0	103.8	-0.2
S1-C2	1.804	1.804	-0.001	O11-S1-O12	114.4	114.5	0.1
C2-H21	1.092	1.106	0.015	O11-S1-O13	114.4	114.5	0.1
C2-H22	1.092	1.106	0.015	O12-S1-O13	114.4	114.5	0.1
C2-H23	1.092	1.106	0.015	S1-C2-H21	109.1	109.1	0.0
				S1-C2-H22	109.1	109.1	0.0
				S1-C2-H23	109.1	109.1	0.0
Dihedrals (°)				H21-C2-H22	109.8	109.8	0.0
O11-S1-C2-H21	-180.0	-180.0	0.0	H21-C2-H23	109.8	109.8	0.0
				H22-C2-H23	109.8	109.8	0.0

Table S49. Scaled MP2/6-31G(d) and MM level vibrational spectra of MSNA.

QM (scaled by a factor 0.943)					MM				
Freq	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%
253.0	tS1-C2	100			267.5	tS1-C2	100		
300.4	rS1O	60	rS1O'	26	359.6	rS1O	88		
300.4	rS1O'	60	rS1O	26	359.6	rS1O'	88		
485.3	daS1O'	89			409.1	dsS1O	80	sS1-C2	19
485.3	daS1O	89			616.7	daS1O'	80		
513.9	dsS1O	69	sS1-C2	30	616.7	daS1O	80		
730.8	sS1-C2	66	dsS1O	26	689.1	sS1-C2	72	dsS1O	20
944.8	rC2H	74			905.2	rC2H	56	rC2H'	34
944.8	rC2H'	74			905.2	rC2H'	56	rC2H	34
986.1	sS1-O	91			1013.9	sS1-O	97		
1195.4	sS1-O	89			1221.3	sS1-O	90		
1195.4	sS1-O	89			1221.3	sS1-O	90		
1317.1	dsC2H	98			1360.2	dsC2H	94		
1447.1	daC2H	72	daC2H'	24	1443.1	daC2H'	86		
1447.1	daC2H'	72	daC2H	24	1443.1	daC2H	86		
2939.3	sC2-H	100			2845.9	sC2-H	100		
3040.9	sC2-H	100			2914.6	sC2-H	100		
3040.9	sC2-H	100			2914.6	sC2-H	100		

Table S50. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of ESNA – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-11.73	-11.65	0.08	1.90	1.73	-0.17

O12...HOH	180	-11.76	-11.79	-0.03	1.90	1.73	-0.17

Table S51. Gas phase dipole moment (Debye) of ESNA calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-4.3135	-4.4230
Y	-1.6972	-1.4640
Z	-0.0001	0.2289
Total	4.6354	4.6646

Table S52. MM and MP2/6-31G(d) level equilibrium geometry of ESNA

Coordinate	QM	MM	Difference
Bond length (Å)			
S1-O11	1.488	1.449	-0.040
S1-O12	1.491	1.449	-0.042
S1-O13	1.491	1.449	-0.042
S1-C2	1.809	1.811	0.002
C2-H21	1.094	1.107	0.013
C2-H22	1.094	1.107	0.013
C2-C3	1.521	1.545	0.025
C3-H31	1.092	1.112	0.019
C3-H32	1.092	1.112	0.019
C3-H33	1.097	1.109	0.012
Dihedrals (°)			
O12-S1-C2-C3	59.9	60.2	0.3
S1-C2-C3-H32	-59.2	-59.7	-0.5

Coordinate	QM	MM	Difference
Angles (°)			
O11-S1-C2	103.9	103.4	-0.4
O12-S1-C2	104.0	104.4	0.4
O13-S1-C2	104.0	104.4	0.4
O11-S1-O12	114.4	114.2	-0.3
O11-S1-O13	114.4	114.2	-0.3
O12-S1-O13	114.2	114.5	0.3
S1-C2-H21	106.7	106.9	0.2
S1-C2-H22	106.7	106.9	0.2
S1-C2-C3	111.9	112.0	0.2
C3-C2-H21	111.5	110.7	-0.8
C3-C2-H22	111.5	110.7	-0.8
H21-C2-H22	108.2	109.3	1.1
C2-C3-H31	109.5	110.2	0.7
C2-C3-H32	109.5	110.2	0.7
C2-C3-H33	111.6	110.5	-1.1
H31-C3-H32	108.1	108.2	0.1
H31-C3-H33	109.0	108.8	-0.2
H32-C3-H33	109.0	108.8	-0.2
O11-S1-C2	103.9	103.4	-0.4
O12-S1-C2	104.0	104.4	0.4
O13-S1-C2	104.0	104.4	0.4

Table S53. Scaled MP2/6-31G(d) and MM level vibrational spectra of ESNA.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
103.2	tS1-C2	93					113.2	tS1-C2	94				
207.4	dC2CS	50	rS1O'	35			240.3	dC2CS	50	rS1O	41		
216.9	tC2-C3	77					241.8	tC2-C3	84				
316.3	rS1O	53	rS1O'	18			347.3	rS1O	44	dsS1O	21	sS1-C2	16
356.3	dC2CS	26	rS1O'	26			358.1	rS1O'	85				
484.4	daS1O	65	daS1O'	22			452.2	dsS1O	57	dC2CS	27		
485.6	daS1O'	41	dsS1O	23	sS1-C2	16	615.6	daS1O'	94				
541.8	dsS1O	37	daS1O'	17			616.4	daS1O	92				
707.4	sS1-C2	52	dsS1O	29			680.5	sS1-C2	62	dsS1O	18		
769.9	rC2H	51	rC3H	25			822.4	rC2H	74				
960.2	sC2-C3	31	rC3H'	22	sS1-O	18	987.2	sC2-C3	34	rC3H'	28		
	wC2H	16											
983.3	sS1-O	75					1017.2	sS1-O	83				
1018.6	iC2H	38	rC2H	23	rC3H	19	1036.8	rC3H	52	rC3H'	17		
1054.6	sC2-C3	51	rC3H'	25			1051.5	sC2-C3	41	rC3H'	35		
1178.1	sS1-O	80					1192.0	iC2H	46	sS1-O	43		
1182.0	sS1-O	91					1213.7	sS1-O	90				
1244.4	iC2H	56	rC3H	20			1244.0	iC2H	48	sS1-O	47		
1281.4	wC2H	73					1374.0	wC2H	80				
1366.9	dsC3H	95					1413.7	dsC3H	78				
1444.2	cC2H	97					1429.1	daC3H'	56	daC3H	19	dsC3H	16
1463.4	daC3H	70	daC3H'	23			1436.8	daC3H	67	daC3H'	22		
1487.1	daC3H'	70	daC3H	23			1458.6	cC2H	91				
2917.2	sC3-H	99					2852.6	sC2-H	98				
2943.1	sC2-H	98					2890.6	sC2-H	99				
2999.3	sC2-H	94					2902.7	sC3-H	99				
3002.8	sC3-H	99					2959.5	sC3-H	100				
3034.4	sC3-H	94					2960.5	sC3-H	99				

Table S54. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of PSNA – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-11.67	-11.64	0.03	1.90	1.73	-0.17
O12...HOH	180	-11.72	-11.75	-0.03	1.90	1.73	-0.17

Table S55. Gas phase dipole moment (Debye) of PSNA calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	6.2863	6.6515
Y	-1.1324	-1.0656
Z	0.0000	0.0000
Total	6.3875	6.7363

Table S56. MM and MP2/6-31G(d) level equilibrium geometry of PSNA

Coordinate	QM	MM	Difference
Bond length (Å)			
S1-O11	1.488	1.449	-0.040
S1-O12	1.490	1.449	-0.042
S1-O13	1.490	1.449	-0.042
S1-C2	1.810	1.807	-0.003
C2-H21	1.096	1.107	0.011
C2-H22	1.096	1.107	0.011
C2-C3	1.520	1.544	0.024
C3-H31	1.095	1.115	0.020
C3-H32	1.095	1.115	0.020
C3-C4	1.527	1.531	0.003
C4-H41	1.096	1.110	0.014
C4-H42	1.0957	1.11092	0.015
C4-H43	1.0957	1.11092	0.015
Dihedrals (°)			
O12-S1-C2-C3	59.9	60.2	0.3
S1-C2-C3-C4	180.0	180.0	0.0
C2-C3-C4-H42	59.8	59.8	0.0

Coordinate	QM	MM	Difference
Angles (°)			
O11-S1-C2	103.9	103.5	-0.4
O12-S1-C2	104.0	104.4	0.4
O13-S1-C2	104.0	104.4	0.4
O11-S1-O12	114.5	114.2	-0.2
O11-S1-O13	114.5	114.2	-0.2
O12-S1-O13	114.3	114.4	0.2
S1-C2-H21	106.9	107.0	0.1
S1-C2-H22	106.9	107.0	0.1
S1-C2-C3	112.3	112.3	0.0
C3-C2-H21	111.1	110.6	-0.6
C3-C2-H22	111.1	110.6	-0.6
H21-C2-H22	108.2	109.3	1.0
C2-C3-H31	108.1	108.9	0.8
C2-C3-H32	108.1	108.9	0.8
C2-C3-C4	112.8	112.9	0.1
H31-C3-H32	106.7	107.3	0.6
C4-C3-H31	110.4	109.4	-1.1
C4-C3-H32	110.4	109.4	-1.1
C3-C4-H41	111.6	110.5	-1.1
C3-C4-H42	111.0	110.1	-0.9
C3-C4-H43	111.0	110.1	-0.9
H41-C4-H42	107.8	108.8	1.1
H41-C4-H43	107.8	108.8	1.1

H42-C4-H43	107.6	108.5	1.0

Table S57. Scaled MP2/6-31G(d) and MM level vibrational spectra of PSNA.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
83.4	tC2-C3	75	tS1-C2	15			94.1	tC2-C3	76				
96.5	tS1-C2	76					106.0	tS1-C2	76				
153.9	dC2CS	57	rS1O	29			184.9	dC2CS	59	rS1O	27		
247.0	tC3-C4	90					241.1	tC3-C4	90				
296.3	dC3CC	53	sS1-C2	24			274.9	dC3CC	35	sS1-C2	26	dsS1O	17
311.5	rS1O'	77					354.1	rS1O'	90				
333.8	rS1O	52	daS1O	16			363.8	rS1O	64	dC3CC	20		
483.9	daS1O'	88					471.8	dsS1O	71				
493.2	daS1O	75					615.7	daS1O'	94				
570.8	dsS1O	66					616.6	daS1O	93				
732.0	rC3H	49	rC2H	19			724.3	sS1-C2	63				
752.7	sS1-C2	56					756.8	rC3H	53	rC2H	27		
843.2	rC2H	40	rC4H'	33	iC3H	16	856.7	rC2H	54	rC3H	22	rC4H'	17
886.8	rC4H	34	sC2-C3	26	sC3-C4	24	915.9	rC4H	46	sC2-C3	31		
979.6	sS1-O	90					1014.5	sS1-O	96				
1031.2	sC3-C4	61					1028.1	rC4H'	67	rC3H	16		
1033.6	iC2H	45					1033.8	sC3-C4	70				
1085.4	sC2-C3	43	rC4H	24	wC3H	15	1090.3	sC2-C3	40	rC4H	33		
1180.4	sS1-O	82					1152.2	iC2H	74	sS1-O	18		
1181.1	sS1-O	87					1211.7	sS1-O	88				
1215.4	rC4H'	30	iC2H	26	rC3H	25	1226.3	iC3H	64	sS1-O	28		
1231.5	wC2H	60	wC3H	15			1236.7	sS1-O	45	iC3H	27	iC2H	19
1281.8	iC3H	62	iC2H	24			1305.4	wC2H	61	wC3H	29		
1336.4	wC3H	60	wC2H	18			1361.3	wC3H	46	wC2H	18		
1376.7	dsC4H	93					1401.3	dsC4H	93				
1440.7	cC2H	96					1425.1	daC4H	70	cC3H	19		
1472.9	daC4H	53	cC3H	43			1427.8	daC4H'	92				
1475.1	daC4H'	94					1440.8	cC3H	66	daC4H	22		
1485.0	cC3H	56	daC4H	41			1447.8	cC2H	94				
2907.7	sC4-H	100					2852.6	sC2-H	98				
2929.9	sC2-H	96					2889.7	sC2-H	98				
2945.2	sC3-H	94					2897.2	sC4-H	66	sC3-H	33		
2979.9	sC3-H	38	sC4-H	35	sC2-H	27	2907.4	sC3-H	65	sC4-H	34		
2985.1	sC4-H	98					2932.0	sC3-H	94				
2988.2	sC2-H	57	sC4-H	43			2959.5	sC4-H	100				
3007.4	sC3-H	62	sC4-H	21	sC2-H	17	2959.7	sC4-H	96				

Table S58. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of MSMT – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference
O11...HOH	180	-3.99	-4.09	-0.10	2.17	1.91	-0.26
O11...HOH	270	-3.95	-3.97	-0.03	2.16	1.88	-0.28
O3...HOH	0	-2.25	-1.98	0.26	2.12	1.86	-0.26
O3...HOH	90	-3.08	-3.18	-0.11	2.09	1.80	-0.29
N2...HOH	180	-1.25	-0.04	1.21	2.45	2.50	0.05
N2H..OHH	90	-7.26	-7.19	0.07	2.00	1.82	-0.18

Table S59. Gas phase dipole moment (Debye) of MSMT calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-1.6294	-1.9325
Y	-0.8514	-1.0213
Z	-3.4157	-4.0984
Total	3.8790	4.6448

Table S60. MM and MP2/6-31G(d) level equilibrium geometry of MSMT

Coordinate	QM	MM	Difference	Coordinate	QM	MM	Difference
Bond length (Å)				Angles (°)			
S1-N2	1.647	1.642	-0.004	N2-S1-O3	99.7	99.9	0.2
S1-O11	1.453	1.435	-0.018	O11-S1-N2	108.1	108.9	0.8
S1-O12	1.453	1.435	-0.018	O12-S1-N2	108.1	108.9	0.8
S1-O3	1.642	1.594	-0.047	O11-S1-O3	108.2	108.1	-0.1
N2-H21	1.017	1.014	-0.003	O12-S1-O3	108.2	108.1	-0.1
N2-H22	1.017	1.014	-0.003	O11-S1-O12	122.2	121.0	-1.2
O3-C4	1.452	1.436	-0.016	S1-N2-H21	112.2	111.3	-0.8
C4-H41	1.088	1.110	0.022	S1-N2-H22	112.2	111.3	-0.8
C4-H42	1.092	1.112	0.021	H21-N2-H22	112.7	110.2	-2.5
C4-H43	1.092	1.112	0.021	S1-O3-C4	113.2	114.0	0.8
				O3-C4-H41	104.8	109.7	4.8
				O3-C4-H42	110.0	110.6	0.6

Dihedrals (°)				O3-C4-H43	110.0	110.6	0.6
O3-S1-N2-H21	-64.0	-61.7	2.3	H41-C4-H42	110.6	108.5	-2.1
O11-S1-O3-C4	-67.2	-66.3	0.9	H41-C4-H43	110.6	108.5	-2.1
S1-O3-C4-H42	-61.1	-60.4	0.8	H42-C4-H43	110.8	108.9	-1.9

Table S61. Scaled MP2/6-31G(d) and MM level vibrational spectra of MSMT.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
51.1	tS1-O3	89					80.2	tS1-O3	78	tO3-C4	21		
148.7	tO3-C4	91					154.1	tO3-C4	78	tS1-O3	21		
215.2	iO3	49	dS1ON	42			240.8	iO3	53	dS1ON	32		
253.1	tS1-N2	64	iSO2	27			279.5	tS1-N2	88				
339.8	dS1ON	38	iO3	29			334.1	dS1ON	53	wSO2	19		
389.9	iSO2	65	tS1-N2	34			391.1	iSO2	78				
453.8	rSO2	87					430.6	wSO2	39	cSO2	24	sS1-N2	19
475.0	cSO2	80					450.8	rSO2	77				
533.3	wSO2	59	iO3	17			464.1	cSO2	64	wSO2	16		
641.3	wN2S1	49	sS1-O	31			698.8	sS1-O	59				
738.3	sS1-O	49	wN2S1	25			724.7	sS1-N2	44	wN2S1	18	sS1-O	18
860.9	sS1-N2	66					918.7	wN2S1	77	sS1-N2	16		
986.7	sO3-C4	92					1028.8	sO3-C4	77				
1081.4	dN2S1	87					1064.7	dN2S1	92				
1133.5	rC4H'	94					1115.8	sS1-O	69	rC4H	20		
1139.8	sS1-O	66	rC4H	24			1129.3	rC4H'	76	daC4H'	24		
1154.2	rC4H	67	sS1-O	22			1150.7	rC4H	57	sS1-O	24		
1353.5	sS1-O	88					1318.8	sS1-O	89				
1424.6	dsC4H	100					1432.5	daC4H	82	rC4H	18		
1462.3	daC4H'	94					1460.8	daC4H'	76	rC4H'	24		
1479.1	daC4H	94					1569.2	dN2H21	97				
1562.0	dN2H21	98					1596.5	dsC4H	88				
2949.0	sC4-H	100					2851.5	sC4-H	100				
3045.1	sC4-H	100					2913.1	sC4-H	100				
3074.2	sC4-H	100					2915.6	sC4-H	100				
3351.3	sN2-H	100					3339.8	sN2-H	100				
3467.5	sN2-H	100					3415.5	sN2-H	100				

Table S62. MM and HF/6-31G(d) level interaction energies (kcal/mol) and distances (Å) of PSMT – water complexes.

Interaction	Orientation	ΔE (QM)	ΔE (MM)	Difference	r (QM)	r (MM)	Difference

O11...HOH	180	-3.85	-4.14	-0.29	2.18	1.91	-0.27
O11...HOH	90	-4.57	-4.87	-0.30	2.14	1.86	-0.28
O3...HOH	180	-2.42	-2.10	0.32	2.14	1.89	-0.25
O3...HOH	90	-2.86	-2.87	-0.01	2.12	1.82	-0.30
N2...HOH	180	-1.13	0.02	1.15	2.45	2.52	0.07
N2H..OHH	90	-7.42	-7.33	0.09	2.00	1.82	-0.18

Table S63. Gas phase dipole moment (Debye) of PSMT calculated at the MP2/6-31G(d) and MM level of theory.

μ	QM	MM
X	-1.4223	-1.7721
Y	3.2020	4.3189
Z	0.0000	0.0000
Total	3.5037	4.6683

Table S64. MM and MP2/6-31G(d) level equilibrium geometry of PSMT

Coordinate	QM	MM	Difference	Coordinate	QM	MM	Difference
Bond length (Å)				Angles (°)			
S1-N2	1.647	1.643	-0.005	N2-S1-O3	99.1	99.5	0.4
S1-O11	1.452	1.436	-0.015	O11-S1-N2	108.2	108.2	0.1
S1-O12	1.452	1.436	-0.015	O12-S1-N2	108.2	108.2	0.1
S1-O3	1.665	1.601	-0.064	O11-S1-O3	108.0	108.8	0.8
O3-CZ	1.413	1.389	-0.023	O12-S1-O3	108.0	108.8	0.8
N2-H21	1.018	1.014	-0.003	O11-S1-O12	122.9	121.1	-1.8
N2-H22	1.018	1.014	-0.003	S1-O3-CZ	113.8	113.7	0.0
CZ-CE1	1.392	1.404	0.012	S1-N2-H21	112.1	111.5	-0.6
CZ-CE2	1.392	1.404	0.012	S1-N2-H22	112.1	111.5	-0.6
CE1-CD1	1.396	1.402	0.006	H21-N2-H22	112.7	110.3	-2.3
CE2-CD2	1.396	1.402	0.006	O3-CZ-CE1	118.8	120.2	1.4
CG-CD1	1.397	1.402	0.004	O3-CZ-CE2	118.8	120.2	1.4
CG-CD2	1.397	1.402	0.004	CE1-CZ-CE2	122.4	119.4	-3.0
CE1-HE1	1.086	1.079	-0.006	CZ-CE1-CD1	118.4	120.4	2.0
CE2-HE2	1.086	1.079	-0.006	CZ-CE2-CD2	118.4	120.4	2.0
CD1-HD1	1.087	1.081	-0.006	CG-CD1-CE1	120.3	119.8	-0.5

CD2-HD2	1.087	1.081	-0.006	CG-CD2-CE2	120.3	119.8	-0.5
CG-HG	1.087	1.081	-0.006	CD1-CG-CD2	120.1	120.2	0.1
Dihedrals (°)				CZ-CE1-HE1	119.7	119.1	-0.6
N2-S1-O3-CZ	180.0	180.0	0.0	CZ-CE2-HE2	119.7	119.1	-0.6
O3-S1-N2-H21	-63.9	-61.9	2.0	CD1-CE1-HE1	121.9	120.5	-1.4
S1-O3-CZ-CE1	91.4	92.3	0.9	CD2-CE2-HE2	121.9	120.5	-1.4
O3-CZ-CE1-CD1	176.9	177.0	0.1	CE1-CD1-HD1	119.5	120.1	0.6
CZ-CE1-CD1-CG	0.1	-0.8	-0.9	CE2-CD2-HD2	119.5	120.1	0.6
CE1-CD1-CG-CD2	0.1	0.0	-0.1	CG-CD1-HD1	120.1	120.1	0.0
O3-CZ-CE2-CD2	-176.9	-177.0	-0.1	CG-CD2-HD2	120.1	120.1	0.0
CZ-CE2-CD2-CG	-0.1	0.8	0.9	CD1-CG-HG	120.0	119.9	0.0
CE2-CD2-CG-CD1	-0.1	0.0	0.1	CD2-CG-HG	120.0	119.9	0.0

Table S65. Scaled MP2/6-31G(d) and MM level vibrational spectra of PSMT.

QM (scaled by a factor 0.943)							MM						
Freq	Assignment	%	Assignment	%	Assignment	%	Freq	Assignment	%	Assignment	%	Assignment	%
13.8	tO3-CZ	62	tS1-O3	37			21.7	tO3-CZ	70	tS1-O3	28		
57.6	tS1-O3	60	tO3-CZ	40			69.8	tS1-O3	69	tO3-CZ	32		
84.2	iO3	47	wCZH	41			91.9	wCZH	54	iO3	36		
220.3	ta6RNG1a	36	dSON	19	iO3	15	240.7	iO3	36	ta6RNG1a	23		
230.5	iSO2	43	tS1-N2	41			260.4	dSON	70				
254.3	dSON	53					275.4	tS1-N2	85				
317.3	tS1-N2	35	dCZH	35	rSO2	19	331.6	dCZH	36	iSO2	29	rSO2	16
381.7	ta6RNG1	87	ta6RNG1a	29			399.3	rSO2	42	iSO2	40		
405.7	iSO2	45	tS1-N2	23	rSO2	16	408.6	wSO2	69				
423.6	ta6RNG1a	29	cSO2	22			415.1	ta6RNG1	88	ta6RNG1a	29		
455.1	tp6RNG1	57	cSO2	26			447.5	cSO2	39	ta6RNG1a	34		
474.4	tp6RNG1	38	wSO2	31			484.0	cSO2	38	ta6RNG1a	17		
474.6	rSO2	56	dCZH	23			527.0	dCZH	34	rSO2	34	iSO2	21
507.2	cSO2	33	wSO2	20	da6RNG1a	15	574.3	da6RNG1a	26				
588.0	iO3	21	da6RNG1a	18	wSO2	16	646.8	tp6RNG1	104				
593.4	da6RNG1	61	da6RNG1a	20			678.0	da6RNG1	62	da6RNG1a	21		
642.1	wN2S1	34	sS1-O	27			708.5	sS1-N2	41	sS1-O	27		
695.8	wN2S1	23	wCGH	17			738.0	sS1-O	21				
731.5	sS1-O	30					763.5	wCGH	23				
763.2	wCE2H	41	wCE1H	41			811.7	sS1-O	19	dt6RNG1	18		
802.5	sCZ-O3	17					854.1	wCE2H	25	wCE1H	25	wCD1H	25
								wCD2H	25				
813.2	wCE1H	21	wCE2H	21			913.5	wN2S1	70	sS1-N2	16		
841.0	wCD2H	44	wCD1H	44			925.3	wCE1H	38	wCE2H	38	wCGH	26

844.1	wCGH	53	wCD1H	27	wCD2H	27	951.3	dt6RNG1	47			
860.1	sS1-N2	58	wN2S1	17			978.8	sCD1-CG	30	sCG-CD2	30	
968.6	dt6RNG1	66					995.7	wCD1H	30	wCD2H	30	wCE2H 29
								wCE1H	29			
1001.5	sCG-CD2	26	sCD1-CG	26			1006.6	wCGH	51	wCD1H	31	wCD2H 31
								tp6RNG1	-18			
1054.8	sCD2-CE2	19	sCE1-CD1	19			1031.0	sCE1-CD1	23	sCD2-CE2	23	
1081.7	dN2S1	88					1066.3	dN2S1	92			
1129.8	sS1-O	32	sCZ-O3	22			1124.3	sS1-O	90			
1146.1	dCGH	42	dCD2H	19	dCD1H	19	1157.1	sCD2-CE2	21	sCE1-CD1	21	
1147.1	sS1-O	36					1215.0	dCGH	25	dCD1H	19	dCD2H 19
1170.5	sCZ-O3	27	sS1-O	20			1268.1	sCZ-O3	37	dCE1H	19	dCE2H 19
1275.3	dCE2H	26	dCE1H	26			1319.4	sS1-O	88			
1360.8	sS1-O	89					1359.4	dCE1H	29	dCE2H	29	
1387.9	sCE2-CZ	17	sCZ-CE1	17	sCD1-CG	16	1427.4	dCGH	25	sCZ-CE1	20	sCE2-CZ 20
	sCG-CD2	16										
1424.6	dCGH	30					1437.9	dCD2H	20	dCD1H	20	sCD2-CE2 17
								sCE1-CD1	17			
1457.2	dCD2H	16	dCD1H	16			1467.4	dCD2H	30	dCD1H	30	
1561.2	dN2H	97					1486.4	dCGH	23			
1570.1	sCE1-CD1	23	sCD2-CE2	23			1542.3	dCE1H	16	dCE2H	16	
1576.2	sCE2-CZ	20	sCZ-CE1	20	sCD1-CG	18	1571.8	dN2H	97			
	sCG-CD2	18										
3046.2	sCG-HG	43	sCD1-HD1	27	sCD2-HD2	27	3054.7	sCD2-HD2	27	sCD1-HD1	27	sCE1-HE1 23
								sCE2-HE2	23			
3055.6	sCD2-HD2	46	sCD1-HD1	46			3055.2	sCG-HG	70			
3065.4	sCG-HG	54	sCD2-HD2	16	sCD1-HD1	16	3056.8	sCE2-HE2	27	sCE1-HE1	27	sCD1-HD1 23
								sCD2-HD2	23			
3077.6	sCE1-HE1	46	sCE2-HE2	46			3057.1	sCD2-HD2	33	sCD1-HD1	33	sCG-HG 16
3078.3	sCE2-HE2	41	sCE1-HE1	41			3060.3	sCE1-HE1	27	sCE2-HE2	27	sCD1-HD1 16
								sCD2-HD2	16			
3348.8	sN2-H	100					3339.4	sN2-H	100			
3465.0	sN2-H	100					3415.6	sN2-H	100			

Table S66. Parameters introduced to enable sulfonamide based peptide simulation.

Bond Parameter	Force constant	Equilibrium value
CG301 NH1	320.0	1.430

Angle Parameters	Force constant	Equilibrium value
C NH1 CG301	50.0	120.0
CG301 NH1 H	35.0	117.0

CG301	CG321	NG311	43.7	112.2
CG321	CG301	NH1	70.0	113.5
CG331	CG301	NH1	70.0	113.5

Dihedral Parameters				Force constant	Fold	Phase angle
CPD1	C	NH1	CG301	1.60	1	0.0
CPD1	C	NH1	CG301	2.50	2	180.0
O	C	NH1	CG301	2.50	2	180.0
NH1	CG301	CG321	HGA2	0.20	3	0.0
NH1	CG301	CG321	HGA3	0.20	3	0.0
CG321	CG301	NH1	C	1.80	1	0.0
CG321	CG301	NH1	H	0.00	1	0.0
CG331	CG301	NH1	C	1.80	1	0.0
CG331	CG301	NH1	H	0.00	1	0.0
CG301	CG321	NG311	SG3O2	0.10	1	0.0
CG301	CG321	NG311	SG3O2	0.70	2	0.0
CG301	CG321	NG311	SG3O2	0.10	3	0.0
CG301	CG321	NG311	HGP1	0.10	3	0.0
CG321	NG311	SG3O2	CG331	2.00	2	0.0
CG321	NG311	SG3O2	CG331	0.30	3	0.0
CG331	CG301	CG321	NG311	0.195	3	0.0
NH1	CG301	CG321	NG311	0.195	3	0.0

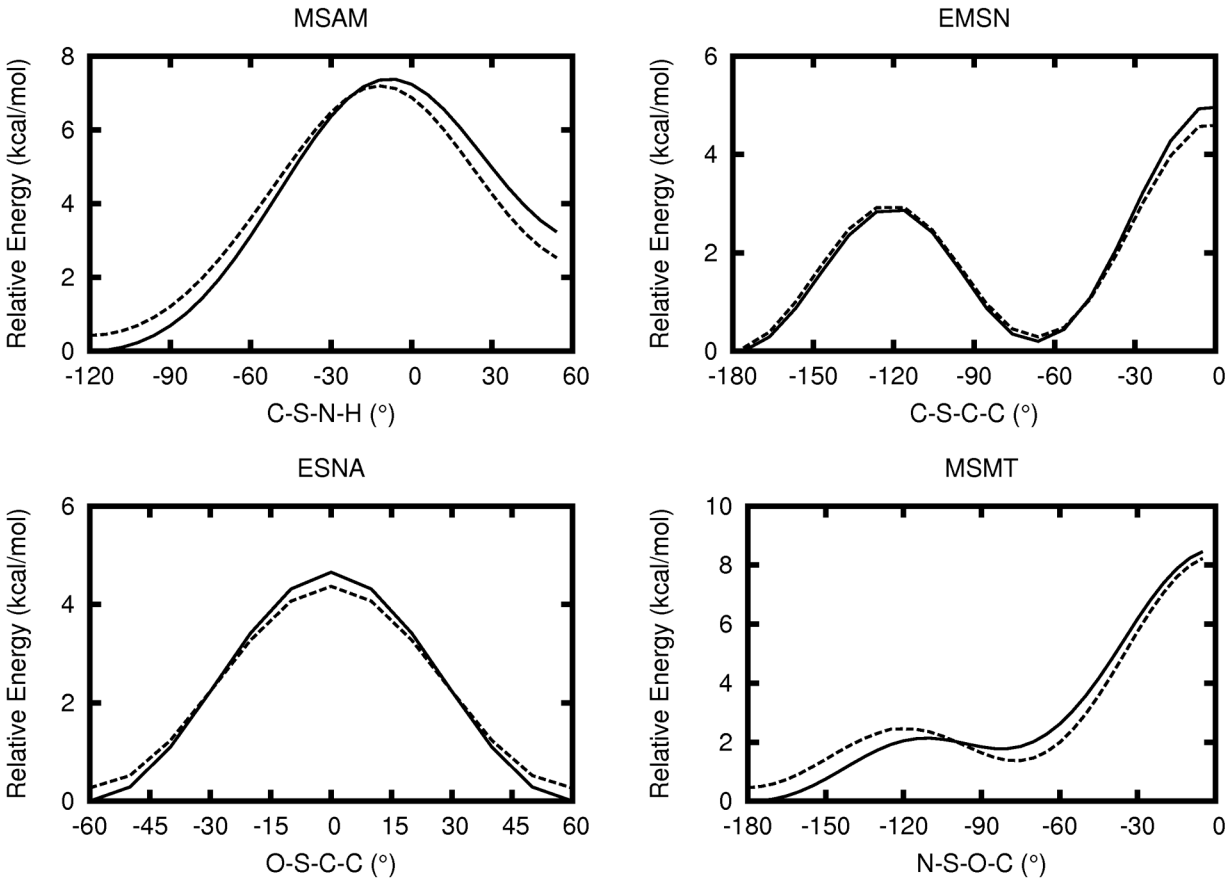
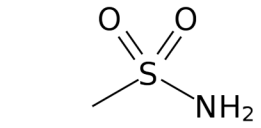


Figure S1. MP2/cc-pVTZ//MP2/6-31G(d) level PESs (dashed line) along with MP2/6-31G(d) level PESs (solid line) for the four model compounds containing the four sulfonyl moieties to test the basis set dependence.



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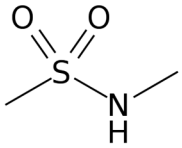

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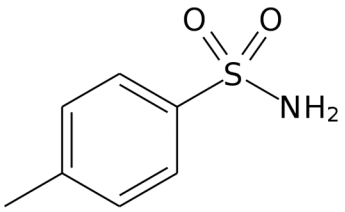

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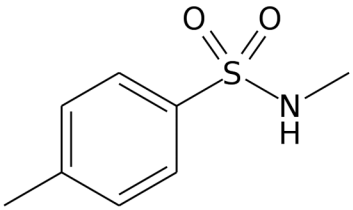

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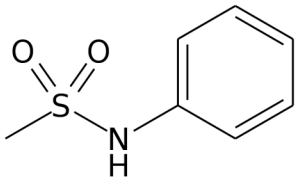

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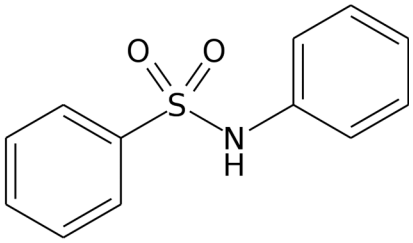

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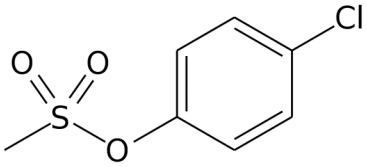

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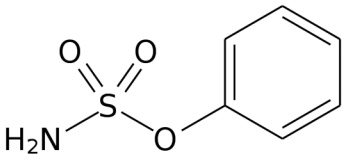

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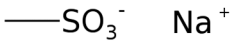

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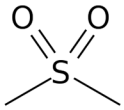

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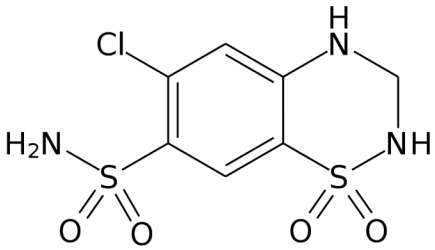

HCSBTZ04

Figure S2. Chemical structures of the compounds that were taken from the CSD and were used in the crystalline phase validations.