Supporting Information for

Comparison of the active-site design of molybdenum oxo-transfer enzymes by quantum mechanical calculations

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Figure S1. Relaxed potential-energy surfaces scan for the DMSOR-Xan and SO-Xan reactions with neutral xanthine protonated either on the N_1, N_7, and N_9 (H7) or on the N_1, N_3, and N_7 atoms (H3) along the C_8–O(Mo) reaction coordinate (RC →IM reaction; for the XO model, RC, TS1 and IM are found at C_8–O distances of 2.72, 1.75, and 1.43 Å, respectively). The reference energy is that of the RC state.

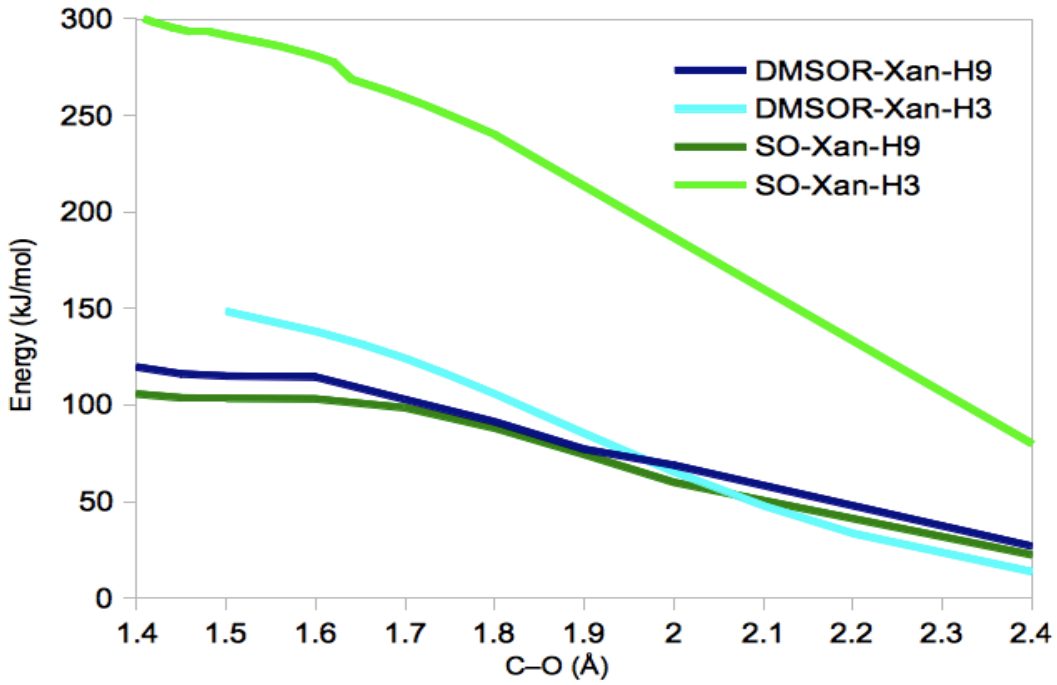


Table S1. Reaction free energies (kJ/mol) of the general OAT reaction in Eqn. 2, calculated with TPSS functional (corresponding to the data in Table 1).

X	*Y*		*Z* =	
		DMS	SO_3^{2-}	Xan
DMDT	OMe	104.1	-87.3	9.9
DMDT	SMe	111.7	-79.8	17.5
DMDT	OH	100.0	-91.4	5.8
O	OMe	183.1	-8.3	89.0
O	SMe	180.2	-11.3	86.0
O	OH	182.9	-8.5	88.7
S	OMe	199.5	8.0	105.3
S	SMe	195.0	3.6	100.9
S	OH	188.9	-2.6	94.7
S	O	183.2	-8.2	89.0

Table S2. The four reduction potentials (V) in Scheme 3 for the ten models, calculated with TPSS functional (corresponding to the data in Table 2).

X	*Y*	$\Delta G^{\text{redox}}_{6\rightarrow5,O}$	$\Delta G^{\text{redox}}_{6\rightarrow5,OH}$	$\Delta G^{\text{redox}}_{5\rightarrow4,OH}$	$\Delta G^{\text{redox}}_{5\rightarrow4,Wat}$
DMDT	OMe	-3.06	-0.94	-2.96	-0.51
DMDT	SMe	-2.79	-0.72	-2.81	-0.74
DMDT	OH	-2.73	-0.84	-2.93	-0.50
O	OMe	-3.39	-0.88	-3.50	-1.24
O	SMe	-3.08	-0.57	-3.08	-1.05
O	OH	-3.42	-0.66	-3.38	-1.19
S	OMe	-2.96	-1.38	-3.51	-1.20
S	SMe	-2.59	-1.20	-3.50	-1.08
S	OH	-2.94	-1.10	-3.47	-1.20
S	O	-5.28	-2.94	-5.54	-2.53

Table S3. The four acidity constants (pK_a units) in Scheme 3 for the ten models, calculated with TPSS functional (corresponding to the data in Table 3).

X	*Y*	$\Delta G^{\text{pKa}}_{6,OH\rightarrow O}$	$\Delta G^{\text{pKa}}_{5,OH\rightarrow O}$	$\Delta G^{\text{pKa}}_{5,Wat\rightarrow OH}$	$\Delta G^{\text{pKa}}_{4,Wat\rightarrow OH}$
DMDT	OMe	11.7	47.6	14.9	56.4
DMDT	SMe	9.7	44.8	12.1	47.0
DMDT	OH	13.1	45.0	12.5	53.5
O	OMe	11.8	54.3	10.4	48.5
O	SMe	10.1	52.5	7.9	42.2
O	OH	9.3	56.0	9.5	46.6
S	OMe	10.4	37.0	18.9	57.9
S	SMe	9.4	32.9	16.9	57.8
S	OH	6.0	37.2	18.3	56.7
S	O	43.1	82.7	39.6	90.4

Table S4. Reaction energies of the two hydrogen-atom transfer reactions in Scheme 3 (diagonal reactions; V) for the ten models, calculated with TPSS functional (corresponding to the data in Table 4).

X	*Y*	$\Delta G_{6\to5}^{\mathrm{diag}}$	$\Delta G_{5\to4}^{\mathrm{diag}}$
DMDT	OMe	-0.24	0.38
DMDT	SMe	-0.14	-0.02
DMDT	OH	-0.06	0.24
O	OMe	-0.18	-0.63
O	SMe	0.03	-0.59
O	OH	-0.11	-0.62
S	OMe	-0.77	-0.08
S	SMe	-0.64	-0.09
S	OH	-0.74	-0.12
S	O	-0.39	-0.19

Table S5. Gibbs free energies (kJ/mol) for the water-binding reaction in Eqn. 3 calculated with TPSS functional (corresponding to the data in Table 5).

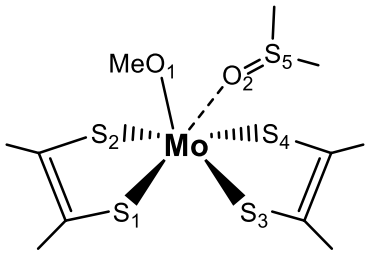
X	*Y*	ΔG
DMDT	OMe	10.6
DMDT	SMe	33.6
DMDT	OH	17.3
O	OMe	16.9
O	SMe	0.5
O	OH	11.9
S	OMe	7.1
S	SMe	0.0
S	OH	15.1
S	O	2.2

Table S6. Relative enthalpies (kJ/mol) along the reaction paths for the studied reactions calculated with TPSS functional (corresponding to the data in Table 6).

State	DMSOR–DMSO	SO–DMSO	XO–DMSO	XOH–DMSO	SO–SO_3^{2-}	DMSOR–SO_3^{2-}	XO–SO_3^{2-}	XOH–SO_3^{2-}	XO–Xan	XO_3[b]–Xan
SR	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
TS1	11.2	1.6	19.1	-71.4	134.0	146.6	441.5	154.7	46.8	62.6
IM	4.0	-50.5	-6.4	-196.5	35.3	66.0		93.1	45.5	52.5
TS2	23.2	-55.0	-10.3	-17.5	151.9	56.7		158.9	47.4	105.7
SP	-102.5	-180.7	-182.2	-181.4	-13.8	-88.0	-7.8	-9.3	-11.4	32.6

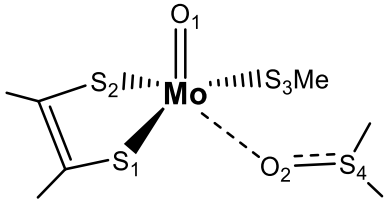
[a] preR (with XOH); RC is at 12.7 kJ/mol. [b] preR; RC is at 6.8 kJ/mol.

Table S7. Mo–ligand bond lengths (Å), angles and dihedrals (°) for the DMSOR–DMSO reaction, obtained at the B3LYP-D2/def2-TZVPP+ZORA+COSMO level.



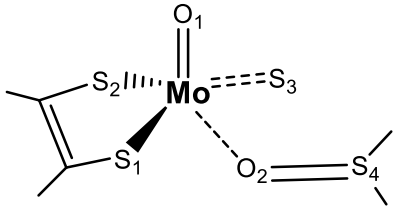
	M-O$_2$	M-O$_1$	M-S$_1$	M-S$_2$	M-S$_3$	M-S$_4$	O$_2$-S$_5$	MO$_2$S$_5$	S$_2$MS$_3$	S$_1$S$_2$S$_3$S$_4$
SR		1.86	2.34	2.34	2.36	2.36	1.50			
TS1	2.62	1.94	2.37	2.35	2.36	2.38	1.51	116.6	140.1	177.6
IM	2.31	1.99	2.38	2.37	2.37	2.39	1.53	121.4	140.2	175.5
TS2	1.91	1.99	2.43	2.42	2.42	2.44	1.89	121.3	151.5	143.7
SP	1.71	1.94	2.45	2.43	2.61	2.42				

Table S8. Mo–ligand bond lengths (Å), angles and dihedrals (°) for the SO–DMSO reaction, obtained at the B3LYP-D2/def2-TZVPP+ZORA+COSMO level.



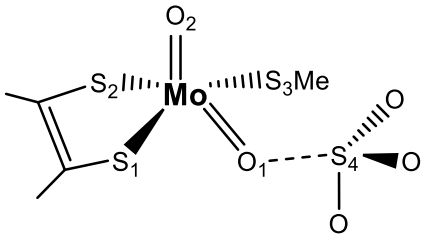
	M-O$_2$	M-O$_1$	M-S$_1$	M-S$_2$	M-S$_3$	O$_2$-S$_4$	MO$_2$S	S$_1$MS$_2$S$_3$
R	6.19	1.71	2.32	2.32	2.35	1.51		-112.1
TS1	3.20	1.69	2.35	2.31	2.39	1.51	98.2	-122.3
IM	2.24	1.70	2.39	2.37	2.42	1.54	126.9	-137.1
TS2	1.95	1.70	2.42	2.42	2.42	1.84	129.1	-140.7
P	1.71	1.72	2.46	2.47	2.44	5.01	83.7	168.5

Table S9. Mo–ligand bond lengths (Å), angles and dihedrals (°) for the XO–DMSO reaction, obtained at the B3LYP-D2/def2-TZVPP+ZORA+COSMO level.



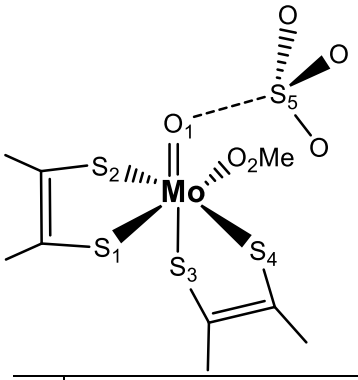
	M-O$_2$	M-O$_1$	M-S$_1$	M-S$_2$	M-S$_3$	O$_2$-S$_4$	MO$_2$S$_4$	S$_1$MS$_2$S$_3$
R	8.84	1.72	2.36	2.36	2.24	1.50	70.7	-114.1
TS1	2.35	1.72	2.37	2.39	2.35	1.53	118.8	-123.1
IM	2.10	1.71	2.41	2.41	2.38	1.62	121.5	-134.6
TS2	2.01	1.71	2.44	2.43	2.35	1.74	120.7	-139.7
P	1.74	1.72	2.57	2.52	2.27	4.17	101.4	-163.6

Table S10. Mo–ligand bond lengths (Å), angles and dihedrals (°) for the SO–SO_3^{2-} reaction, obtained at the B3LYP-D2/def2-TZVPP+ZORA+COSMO level.



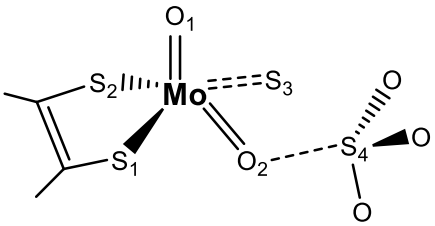
	M-O_1	M-O_2	M-S_1	M-S_2	M-S_3	O1-S_4	MO_1S_4	$S_1MS_2S_3$	$S_1S_2O_1S_3$
SR	1.71	1.72	2.46	2.48	2.44				
TS1	1.78	1.72	2.50	2.5	2.43	2.51	135.4	-153.2	-176.1
IM	2.13	1.70	2.43	2.41	2.43	1.55	140.7	-144.0	173.8
TS2	3.60	1.69	2.37	2.33	2.37	1.49	147.2	-128.7	152.4
SP		1.70	2.33	2.32	2.35	1.50		-113.17	

Table S11. Mo–ligand bond lengths (Å), angles and dihedrals (°) for the DMSOR–SO_3^{2-} reaction, obtained at the B3LYP-D2/def2-TZVPP+ZORA+COSMO level.



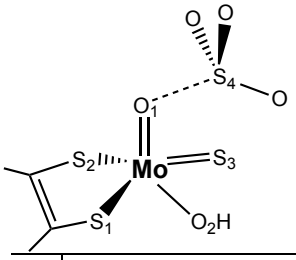
	M-O_1	M-O_2	M-S_1	M-S_2	M-S_3	M-S_4	O1-S_5	MO_1S_5	S_2MS_4	$S_1S_2S_3S_4$
SR	1.71	1.95	2.46	2.43	2.62	2.44		132.8	159.0	-46.7
TS1	1.80	1.98	2.53	2.47	2.54	2.46	2.26	127.5	157.2	-40.6
IM	2.13	1.96	2.48	2.37	2.41	2.40	1.54	135.7	152.3	-28.9
TS2	2.75	1.87	2.41	2.30	2.34	2.40	1.50	146.9	157.3	-29.4
SP	**5.37**	1.85	2.39	2.39	2.33	2.34	1.49		146.3	-0.95

Table S12. Mo–ligand bond lengths (Å), angles and dihedrals (°) for the XO–SO_3^{2-} reaction, obtained at the B3LYP-D2/def2-TZVPP+ZORA+COSMO level.



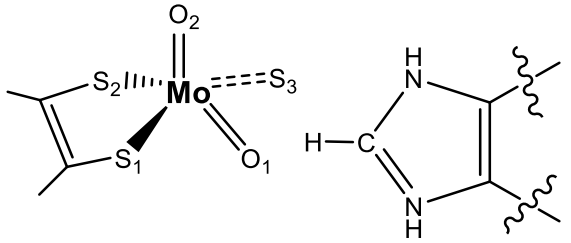
	M-O_2	M-O_1	M-S_1	M-S_2	M-S_3	O_2-S_4	MO_2S_4	$S_1MS_2S_3$	$S_1S_2O_2S_3$
R	1.74	1.72	2.53	2.57	2.26	14.86	161.3	-152.6	175.1
TS1	1.88	1.72	2.50	2.55	2.36	2.05	136.2	-141.8	163.2
P	19.04	1.73	2.36	2.36	2.24	1.49	172.8	-114.0	

Table S13. Mo–ligand bond lengths (Å), angles and dihedrals (°) for the XOH–SO_3^{2-} reaction, obtained at the B3LYP-D2/def2-TZVPP+ZORA+COSMO level.



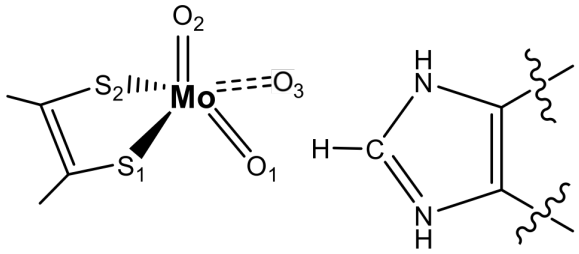
	M-O_2	M-O_1	M-S_1	M-S_2	M-S_3	O_1-S_4	MO_1S_4	$S_1MS_2S_3$	$S_1S_2O_1S_3$
R	1.95	1.71	2.48	2.45	2.16			112.6	-74.7
TS1	1.98	1.78	2.48	2.45	2.20	2.32	128.9	107.1	-67.6
IM	1.99	2.13	2.41	2.34	2.19	1.55	136.8	100.1	-54.9
TS2	1.93	3.01	2.31	2.31	2.17	1.50	172.0	104.3	-49.5
P	1.90		2.29	2.29	2.17			111.0	

Table S14. Mo–ligand bond lengths (Å), angles and dihedrals (°) for the XO–Xan reaction, obtained at the B3LYP-D2/def2-TZVPP+ZORA+COSMO level.



	M-O_1	M-O_2	M-S_1	M-S_2	M-S_3	O_1-C	C-H	S_3-H	MO_1C	$S_1MS_2S_3$	$S_1S_2O_1S_3$
RC	1.75	1.72	2.53	2.52	2.28	2.72	1.09	2.26	113.7	-158.3	-174.6
TS1	1.84	1.71	2.48	2.50	2.23	1.75	1.09	2.44	127.2	-145.3	169.0
IM	1.93	1.70	2.46	2.46	2.19	1.43	1.10	2.69	130.0	-140.3	162.7
TS2	2.00	1.70	2.43	2.43	2.27	1.35	1.32	1.69	129.2	-139.2	167.4
P	2.22	1.70	2.38	2.38	2.43	1.25	2.82	1.35	123.3	-135.6	159.5

Table S15. Mo–ligand bond lengths (Å), angles and dihedrals (°) for the $[MoO_3(DMDT)]^{2-}$–Xan reaction, obtained at the B3LYP-D2/def2-TZVPP+ZORA+COSMO level.



	M-O_1	M-O_2	M-O_3	M-S_1	M-S_2	O_1-C	C-H	O_3-H	MO_1C	$S_1MS_2O_3$	$S_1S_2O_1O_3$
RC	1.76	1.73	1.77	2.54	2.59	2.71	1.09	1.84	104.8	-146.4	171.4
TS1	1.85	1.72	1.74	2.51	2.53	1.75	1.09	2.21	122.5	-140.7	165.1
IM	1.93	1.71	1.72	2.49	2.48	1.43	1.09	2.46	128.1	-138.0	162.0
TS2	1.95	1.71	1.84	2.45	2.45	1.41	1.33	1.25	119.7	-140.0	173.5
P	2.27	1.70	2.01	2.37	2.38	1.25	3.00	2.23	134.3	-128.4	149.7