	VS	BLYP	VBP	PW91
Cu–His44	1.99	2.07	2.07	2.07
Cu–His46	2.01	2.07	2.07	2.07
Cu–His61	1.98	2.03	2.04	2.04
Cu–His118	1.99	2.05	2.06	2.05
Cu–water	2.38	2.56	2.59	2.57
Zn–His61	2.00	2.05	2.07	2.05
Zn–His69	2.04	2.09	2.11	2.10
Zn–His78	2.05	2.10	2.12	2.10
Zn–O(Asp81)	1.97, 2.45	2.01, 2.49	2.02, 2.48	2.01, 2.50
His44–Cu–His61	88.2	89.1	88.8	88.8
His61–Cu–His46	89.6	89.5	90.0	89.8
His46–Cu–His118	93.1	93.2	93.2	93.0
His118–Cu–His44	92.9	92.8	92.4	92.7

Table S1: Calculated gometrical parameters for the oxidized form of CuZnSOD (Ox) using the local (VS) and non-local (BLYP, VBP and PW91) potentials.

	VS	BLYP	VBP	PW91
Cu–His44	1.93	2.00	2.00	2.00
Cu–His46	1.91	1.98	1.98	1.98
Cu–His61	3.15	3.39	3.46	3.38
Cu–His118	2.03	2.07	2.07	2.08
Cu–water	2.81	3.02	3.09	3.04
Zn–His61	2.02	2.08	2.09	2.08
Zn–His69	2.02	2.08	2.08	2.08
Zn–His78	2.04	2.10	2.10	2.09
Zn–O(Asp81)	2.02, 2.32	2.05, 2.45	2.06, 2.50	2.06, 2.45
His44–Cu–His61	74.9	75.3	73.2	75.0
His61–Cu–His46	84.5	83.3	84.6	83.6
His46–Cu–His118	110.1	110.2	111.0	110.1
His118–Cu–His44	100.9	102.0	102.7	101.9

Table S2: Calculated geometrical parameters for the oxidized protonated form of CuZnSOD (Ox^+) using the local (VS) and non-local (BLYP, VBP and PW91) potentials.

	VS	BLYP	VBP	PW91
Cu–His44	1.92	1.98	1.97	1.97
Cu–His46	1.91	1.98	1.97	1.97
Cu–His61	3.20	3.37	3.39	3.39
Cu–His118	2.15	2.28	2.30	2.31
Cu–water	2.84	3.00	3.03	3.02
Zn–His61	2.03	2.08	2.10	2.10
Zn–His69	2.04	2.11	2.12	2.12
Zn–His78	2.05	2.11	2.12	2.12
Zn–O(Asp81)	2.00, 2.31	2.03, 2.36	2.04, 2.37	2.04, 2.37
His44–Cu–His61	75.4	76.3	76.1	74.6
His61–Cu–His46	81.3	81.4	82.7	84.1
His46–Cu–His118	102.5	108.0	106.4	105.5
His118–Cu–His44	110.1	103.7	104.6	105.2

Table S3: Calculated geometrical parameters for the reduced protonated form of CuZnSOD (Red) using the local (VS) and non-local (BLYP, VBP and PW91) potentials.

	VS	BLYP	VBP	PW91
Cu–His44	1.98	2.01	2.01	2.01
Cu–His46	1.98	1.99	1.98	1.98
Cu–His61	2.35	2.96	2.95	2.94
Cu–His118	2.09	2.19	2.18	2.18
Cu–water	2.88	3.06	3.09	3.08
Zn–His61	1.97	2.00	2.01	2.01
Zn–His69	2.05	2.11	2.11	2.12
Zn–His78	2.08	2.14	2.15	2.15
Zn–O(Asp81)	2.02, 2.37	2.04, 2.41	2.04, 2.42	2.04, 2.41
His44–Cu–His61	89.0	86.5	86.8	86.9
His61–Cu–His46	88.4	84.3	84.2	84.4
His46–Cu–His118	104.6	114.1	114.0	113.7
His118–Cu–His44	97.6	96.2	96.4	94.4

Table S4: Calculated geometrical parameters for the reduced non-protonated form of CuZn-SOD (Red^-) using the local (VS) and non-local (BLYP, VBP and PW91) potentials.

Table S5. Coordinates and ESP charges of oxidized cluster Ox.

Atom				X	Y	Z	Charge	Radius
ATOM	1	1C	NONE 1	1.229	1.347	1.653	-0.095	1.700
ATOM	2	2C	NONE 1	1.218	-0.278	3.111	-0.044	1.700
ATOM	3	3C	NONE 1	2.536	1.081	1.948	-0.162	1.700
ATOM	4	4C	NONE 1	-4.826	3.221	1.436	-0.009	1.700
ATOM	5	5C	NONE 1	-4.583	1.016	1.449	0.002	1.700
ATOM	6	6C	NONE 1	-3.589	2.897	1.925	-0.337	1.700
ATOM	7	7C	NONE 1	-1.238	0.973	-1.953	-0.042	1.700
ATOM	8	8C	NONE 1	-0.419	-0.301	-0.401	0.065	1.700
ATOM	9	9C	NONE 1	-1.947	1.200	-0.799	-0.406	1.700
ATOM	10	10C	NONE 1	2.491	-3.348	-2.517	-0.274	1.700
ATOM	11	11C	NONE 1	3.255	-2.046	-0.951	0.150	1.700
ATOM	12	12C	NONE 1	3.359	-4.101	-1.774	-0.014	1.700
ATOM	13	13C	NONE 1	1.333	-0.361	-5.787	-0.199	1.700
ATOM	14	14C	NONE 1	-0.222	-1.698	-5.048	0.045	1.700
ATOM	15	15C	NONE 1	0.687	-0.854	-6.887	-0.135	1.700
ATOM	16	16C	NONE 1	4.474	2.356	-2.306	-0.250	1.700
ATOM	17	17C	NONE 1	3.331	1.381	-2.248	0.317	1.700
ATOM	18	18C	NONE 1	-1.629	0.327	6.460	-0.183	1.700
ATOM	19	19C	NONE 1	-3.018	-0.108	4.787	-0.054	1.700
ATOM	20	20C	NONE 1	-1.040	0.667	5.273	-0.095	1.700
ATOM	21	21N	NONE 1	0.420	0.503	2.388	-0.116	1.550
ATOM	22	22N	NONE 1	2.508	0.055	2.867	-0.166	1.550
ATOM	23	23N	NONE 1	-5.434	2.021	1.145	-0.346	1.550
ATOM	24	24N	NONE 1	-3.453	1.524	1.928	0.025	1.550
ATOM	25	25N	NONE 1	-0.275	0.017	-1.691	-0.356	1.550
ATOM	26	26N	NONE 1	-1.426	0.380	0.187	0.117	1.550
ATOM	27	27N	NONE 1	2.429	-2.074	-1.992	-0.218	1.550
ATOM	28	28N	NONE 1	3.825	-3.260	-0.790	-0.377	1.550
ATOM	29	29N	NONE 1	0.759	-0.895	-4.649	-0.140	1.550
ATOM	30	30N	NONE 1	-0.287	-1.696	-6.399	-0.249	1.550
ATOM	31	31N	NONE 1	-2.874	-0.158	6.128	-0.194	1.550
ATOM	32	32N	NONE 1	-1.912	0.383	4.238	-0.156	1.550
ATOM	33	33H	NONE 1	0.910	-1.060	3.794	0.155	1.200
ATOM	34	34H	NONE 1	3.321	-0.364	3.319	0.347	1.200
ATOM	35	35H	NONE 1	3.454	1.507	1.564	0.221	1.200
ATOM	36	36H	NONE 1	0.830	2.059	0.940	0.146	1.200
ATOM	37	37H	NONE 1	-6.377	1.908	0.770	0.402	1.200
ATOM	38	38H	NONE 1	-4.798	-0.037	1.309	0.172	1.200
ATOM	39	39H	NONE 1	-2.803	3.558	2.272	0.220	1.200
ATOM	40	40H	NONE 1	-5.314	4.175	1.281	0.212	1.200
ATOM	41	41H	NONE 1	0.215	-1.008	0.120	0.044	1.200
ATOM	42	42H	NONE 1	-2.775	1.874	-0.616	0.244	1.200
ATOM	43	43H	NONE 1	-1.354	1.418	-2.935	0.150	1.200
ATOM	44	44H	NONE 1	3.459	-1.165	-0.351	0.121	1.200
ATOM	45	45H	NONE 1	4.514	-3.503	-0.078	0.398	1.200
ATOM	46	46H	NONE 1	3.691	-5.128	-1.862	0.202	1.200
ATOM	47	47H	NONE 1	1.930	-3.632	-3.398	0.220	1.200
ATOM	48	48H	NONE 1	-0.887	-2.270	-4.413	0.136	1.200
ATOM	49	49H	NONE 1	-0.950	-2.227	-6.964	0.372	1.200
ATOM	50	50H	NONE 1	0.829	-0.687	-7.948	0.231	1.200

Table S5. (continued)

Atom				X	Y	Z	Charge	Radius
ATOM	51 51H	NONE	1	2.158	0.339	-5.722	0.226	1.200
ATOM	52 52H	NONE	1	5.200	2.024	-3.060	0.111	1.200
ATOM	53 53H	NONE	1	4.103	3.339	-2.631	0.126	1.200
ATOM	54 54H	NONE	1	4.965	2.456	-1.333	0.082	1.200
ATOM	55 55H	NONE	1	-3.579	-0.491	6.788	0.373	1.200
ATOM	56 56H	NONE	1	-3.908	-0.425	4.259	0.194	1.200
ATOM	57 57H	NONE	1	-0.067	1.109	5.100	0.166	1.200
ATOM	58 58H	NONE	1	-1.286	0.392	7.485	0.243	1.200
ATOM	59 59H	NONE	1	-2.611	-1.496	0.818	0.197	1.200
ATOM	60 60H	NONE	1	-2.746	-2.575	1.941	0.346	1.200
ATOM	61 61O	NONE	1	2.947	0.879	-1.154	-0.384	1.400
ATOM	62 62O	NONE	1	2.767	1.069	-3.369	-0.455	1.400
ATOM	63 63O	NONE	1	-2.950	-1.636	1.733	-0.571	1.400
ATOM	64 64Zn	NONE	1	1.473	-0.346	-2.736	0.801	1.500
ATOM	65 65Cu	NONE	1	-1.644	0.549	2.206	0.445	1.500

Table S6. Coordinates and ESP charges of reduced cluster Red-.

Atom					X	Y	Z	Charge	Radius
ATOM	1	1C	NONE	1	1.175	1.336	1.281	-0.140	1.700
ATOM	2	2C	NONE	1	1.147	0.119	3.081	-0.092	1.700
ATOM	3	3C	NONE	1	2.478	1.008	1.541	-0.162	1.700
ATOM	4	4C	NONE	1	-4.788	3.379	1.239	0.038	1.700
ATOM	5	5C	NONE	1	-4.445	1.203	1.535	0.218	1.700
ATOM	6	6C	NONE	1	-3.514	3.164	1.694	-0.327	1.700
ATOM	7	7C	NONE	1	-1.183	0.834	-1.922	-0.139	1.700
ATOM	8	8C	NONE	1	-0.603	-0.799	-0.613	-0.109	1.700
ATOM	9	9C	NONE	1	-2.189	0.600	-1.012	-0.317	1.700
ATOM	10	10C	NONE	1	2.366	-3.342	-2.447	-0.242	1.700
ATOM	11	11C	NONE	1	3.257	-2.082	-0.913	0.040	1.700
ATOM	12	12C	NONE	1	3.138	-4.165	-1.671	-0.075	1.700
ATOM	13	13C	NONE	1	1.510	-0.527	-5.765	-0.174	1.700
ATOM	14	14C	NONE	1	-0.236	-1.512	-4.918	0.047	1.700
ATOM	15	15C	NONE	1	0.755	-0.954	-6.824	-0.171	1.700
ATOM	16	16C	NONE	1	4.531	2.499	-2.575	-0.261	1.700
ATOM	17	17C	NONE	1	3.462	1.448	-2.432	0.338	1.700
ATOM	18	18C	NONE	1	-1.890	0.082	6.688	-0.253	1.700
ATOM	19	19C	NONE	1	-2.694	-0.800	4.818	-0.106	1.700
ATOM	20	20C	NONE	1	-1.231	0.593	5.600	-0.053	1.700
ATOM	21	21N	NONE	1	0.358	0.785	2.248	-0.147	1.550
ATOM	22	22N	NONE	1	2.441	0.233	2.683	-0.190	1.550
ATOM	23	23N	NONE	1	-5.358	2.128	1.141	-0.479	1.550
ATOM	24	24N	NONE	1	-3.310	1.808	1.872	-0.160	1.550
ATOM	25	25N	NONE	1	-0.167	-0.064	-1.663	-0.127	1.550
ATOM	26	26N	NONE	1	-1.816	-0.433	-0.180	-0.094	1.550
ATOM	27	27N	NONE	1	2.448	-2.053	-1.964	-0.155	1.550
ATOM	28	28N	NONE	1	3.689	-3.348	-0.706	-0.298	1.550
ATOM	29	29N	NONE	1	0.885	-0.885	-4.588	-0.124	1.550
ATOM	30	30N	NONE	1	-0.343	-1.578	-6.268	-0.253	1.550
ATOM	31	31N	NONE	1	-2.816	-0.799	6.168	-0.157	1.550
ATOM	32	32N	NONE	1	-1.738	0.037	4.442	-0.250	1.550
ATOM	33	33H	NONE	1	0.821	-0.449	3.944	0.187	1.200
ATOM	34	34H	NONE	1	3.245	-0.150	3.174	0.327	1.200
ATOM	35	35H	NONE	1	3.386	1.226	0.993	0.196	1.200
ATOM	36	36H	NONE	1	0.773	1.908	0.454	0.165	1.200
ATOM	37	37H	NONE	1	-6.307	1.925	0.833	0.402	1.200
ATOM	38	38H	NONE	1	-4.604	0.127	1.540	0.083	1.200
ATOM	39	39H	NONE	1	-2.737	3.889	1.901	0.203	1.200
ATOM	40	40H	NONE	1	-5.328	4.284	0.990	0.175	1.200
ATOM	41	41H	NONE	1	-0.012	-1.591	-0.164	0.125	1.200
ATOM	42	42H	NONE	1	-3.136	1.116	-0.899	0.223	1.200
ATOM	43	43H	NONE	1	-1.111	1.563	-2.722	0.113	1.200
ATOM	44	44H	NONE	1	3.542	-1.213	-0.333	0.166	1.200
ATOM	45	45H	NONE	1	4.337	-3.641	0.024	0.369	1.200
ATOM	46	46H	NONE	1	3.350	-5.226	-1.721	0.193	1.200
ATOM	47	47H	NONE	1	1.777	-3.584	-3.323	0.205	1.200
ATOM	48	48H	NONE	1	-0.976	-1.899	-4.227	0.120	1.200
ATOM	49	49H	NONE	1	-1.114	-1.999	-6.783	0.362	1.200
ATOM	50	50H	NONE	1	0.891	-0.865	-7.895	0.223	1.200

Table S6. (continued)

Atom				X	Y	Z	Charge	Radius
ATOM	51 51H	NONE	1	2.438	0.033	-5.751	0.202	1.200
ATOM	52 52H	NONE	1	5.257	2.181	-3.337	0.099	1.200
ATOM	53 53H	NONE	1	4.077	3.433	-2.937	0.116	1.200
ATOM	54 54H	NONE	1	5.046	2.681	-1.625	0.078	1.200
ATOM	55 55H	NONE	1	-3.487	-1.339	6.712	0.335	1.200
ATOM	56 56H	NONE	1	-3.294	-1.392	4.135	0.205	1.200
ATOM	57 57H	NONE	1	-0.436	1.330	5.576	0.142	1.200
ATOM	58 58H	NONE	1	-1.788	0.259	7.752	0.227	1.200
ATOM	59 59H	NONE	1	-2.715	-1.201	0.996	0.147	1.200
ATOM	60 60H	NONE	1	-3.283	-2.565	1.565	0.274	1.200
ATOM	61 61O	NONE	1	3.225	0.893	-1.322	-0.412	1.400
ATOM	62 62O	NONE	1	2.796	1.142	-3.494	-0.439	1.400
ATOM	63 63O	NONE	1	-3.294	-1.603	1.746	-0.563	1.400
ATOM	64 64Zn	NONE	1	1.570	-0.257	-2.652	0.682	1.500
ATOM	65 65Cu	NONE	1	-1.638	0.908	2.445	0.444	1.500

Table S7. Coordinates and ESP charges of reduced, protonated cluster Red.

Atom				X	Y	Z	Charge	Radius
ATOM	1 1C	NONE	1	0.992	1.314	1.406	-0.067	1.700
ATOM	2 2C	NONE	1	1.116	-0.038	3.107	-0.102	1.700
ATOM	3 3C	NONE	1	2.286	0.875	1.455	-0.227	1.700
ATOM	4 4C	NONE	1	-4.893	3.237	1.249	0.000	1.700
ATOM	5 5C	NONE	1	-4.441	1.133	1.785	0.107	1.700
ATOM	6 6C	NONE	1	-3.617	3.149	1.736	-0.259	1.700
ATOM	7 7C	NONE	1	-1.018	0.874	-1.848	-0.060	1.700
ATOM	8 8C	NONE	1	-0.418	-0.891	-0.729	0.004	1.700
ATOM	9 9C	NONE	1	-2.001	0.634	-0.923	-0.292	1.700
ATOM	10 10C	NONE	1	2.412	-3.430	-2.477	-0.213	1.700
ATOM	11 11C	NONE	1	3.429	-2.139	-1.048	-0.011	1.700
ATOM	12 12C	NONE	1	3.246	-4.237	-1.747	-0.089	1.700
ATOM	13 13C	NONE	1	1.519	-0.372	-5.848	-0.165	1.700
ATOM	14 14C	NONE	1	-0.147	-1.511	-5.027	0.016	1.700
ATOM	15 15C	NONE	1	0.770	-0.790	-6.913	-0.152	1.700
ATOM	16 16C	NONE	1	4.581	2.544	-2.495	-0.271	1.700
ATOM	17 17C	NONE	1	3.535	1.469	-2.443	0.383	1.700
ATOM	18 18C	NONE	1	-1.911	0.165	6.893	-0.206	1.700
ATOM	19 19C	NONE	1	-3.314	-0.343	5.257	-0.134	1.700
ATOM	20 20C	NONE	1	-1.277	0.267	5.686	-0.180	1.700
ATOM	21 21N	NONE	1	0.269	0.746	2.442	-0.191	1.550
ATOM	22 22N	NONE	1	2.341	0.021	2.533	-0.138	1.550
ATOM	23 23N	NONE	1	-5.392	1.955	1.284	-0.381	1.550
ATOM	24 24N	NONE	1	-3.344	1.834	2.067	-0.170	1.550
ATOM	25 25N	NONE	1	-0.034	-0.086	-1.716	-0.180	1.550
ATOM	26 26N	NONE	1	-1.604	-0.487	-0.229	-0.104	1.550
ATOM	27 27N	NONE	1	2.533	-2.128	-2.030	-0.147	1.550
ATOM	28 28N	NONE	1	3.870	-3.401	-0.849	-0.276	1.550
ATOM	29 29N	NONE	1	0.940	-0.831	-4.679	-0.164	1.550
ATOM	30 30N	NONE	1	-0.275	-1.508	-6.374	-0.232	1.550
ATOM	31 31N	NONE	1	-3.200	-0.222	6.598	-0.156	1.550
ATOM	32 32N	NONE	1	-2.155	-0.061	4.662	-0.082	1.550
ATOM	33 33H	NONE	1	0.887	-0.655	3.965	0.176	1.200
ATOM	34 34H	NONE	1	3.178	-0.443	2.885	0.345	1.200
ATOM	35 35H	NONE	1	3.123	1.072	0.792	0.244	1.200
ATOM	36 36H	NONE	1	0.535	1.987	0.691	0.159	1.200
ATOM	37 37H	NONE	1	-6.330	1.674	0.998	0.396	1.200
ATOM	38 38H	NONE	1	-4.563	0.063	1.907	0.146	1.200
ATOM	39 39H	NONE	1	-2.888	3.938	1.874	0.214	1.200
ATOM	40 40H	NONE	1	-5.478	4.079	0.899	0.203	1.200
ATOM	41 41H	NONE	1	0.132	-1.749	-0.362	0.128	1.200
ATOM	42 42H	NONE	1	-2.923	1.157	-0.706	0.249	1.200
ATOM	43 43H	NONE	1	-0.956	1.661	-2.591	0.151	1.200
ATOM	44 44H	NONE	1	3.782	-1.259	-0.527	0.183	1.200
ATOM	45 45H	NONE	1	4.582	-3.682	-0.175	0.384	1.200
ATOM	46 46H	NONE	1	3.447	-5.301	-1.791	0.213	1.200
ATOM	47 47H	NONE	1	1.762	-3.692	-3.303	0.203	1.200
ATOM	48 48H	NONE	1	-0.849	-1.990	-4.356	0.142	1.200
ATOM	49 49H	NONE	1	-1.025	-1.954	-6.901	0.368	1.200
ATOM	50 50H	NONE	1	0.885	-0.646	-7.981	0.237	1.200

Table S7. (continued)

Atom				X	Y	Z	Charge	Radius
ATOM	51 51H	NONE	1	2.415	0.236	-5.827	0.211	1.200
ATOM	52 52H	NONE	1	5.342	2.268	-3.239	0.121	1.200
ATOM	53 53H	NONE	1	4.129	3.484	-2.841	0.123	1.200
ATOM	54 54H	NONE	1	5.056	2.692	-1.520	0.092	1.200
ATOM	55 55H	NONE	1	-3.930	-0.423	7.282	0.366	1.200
ATOM	56 56H	NONE	1	-4.227	-0.660	4.766	0.191	1.200
ATOM	57 57H	NONE	1	-0.260	0.583	5.491	0.201	1.200
ATOM	58 58H	NONE	1	-1.570	0.330	7.907	0.252	1.200
ATOM	59 59H	NONE	1	-2.335	-1.269	3.002	0.211	1.200
ATOM	60 60H	NONE	1	-2.709	-2.629	2.303	0.347	1.200
ATOM	61 61H	NONE	1	-2.076	-0.926	0.583	0.258	1.200
ATOM	62 62O	NONE	1	3.308	0.808	-1.384	-0.467	1.400
ATOM	63 63O	NONE	1	2.873	1.227	-3.523	-0.442	1.400
ATOM	64 64O	NONE	1	-2.710	-1.656	2.169	-0.574	1.400
ATOM	65 65Zn	NONE	1	1.753	-0.307	-2.790	0.721	1.500
ATOM	66 66Cu	NONE	1	-1.641	1.119	2.756	0.385	1.500

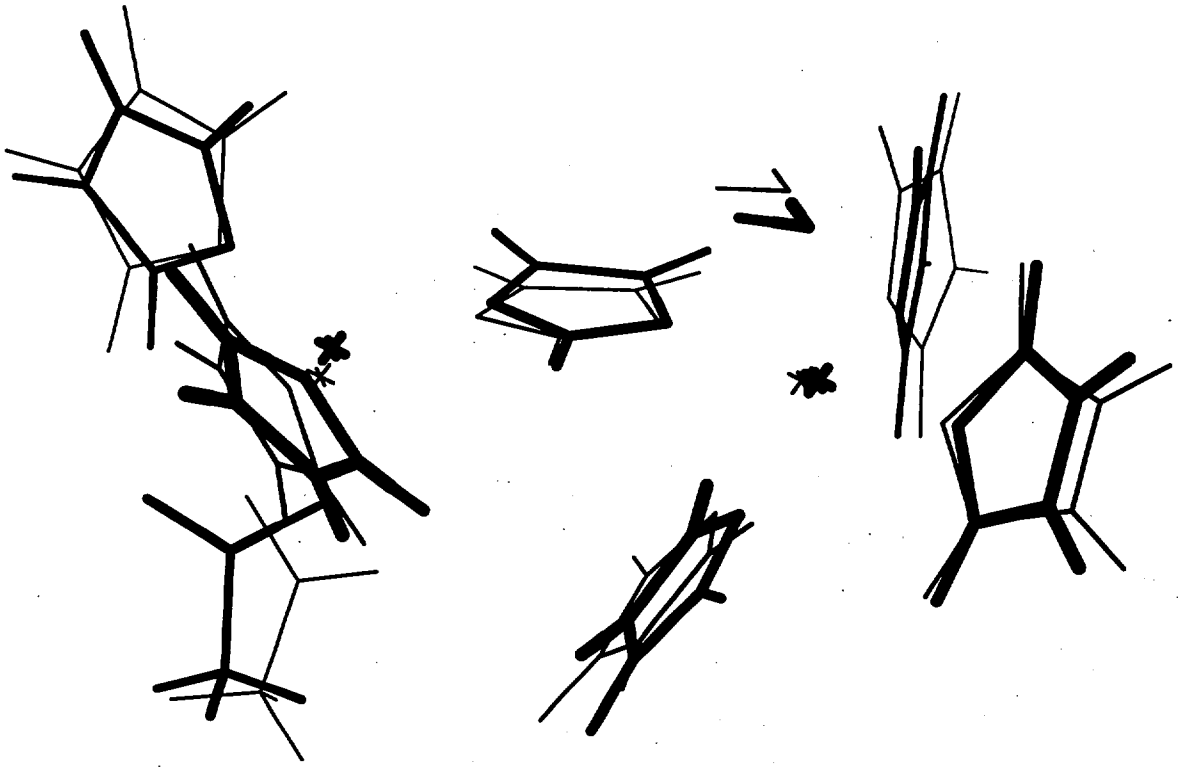

Figure S1. Overlay of experimental (bold line) and optimized (thin line) structures for oxidized active site.

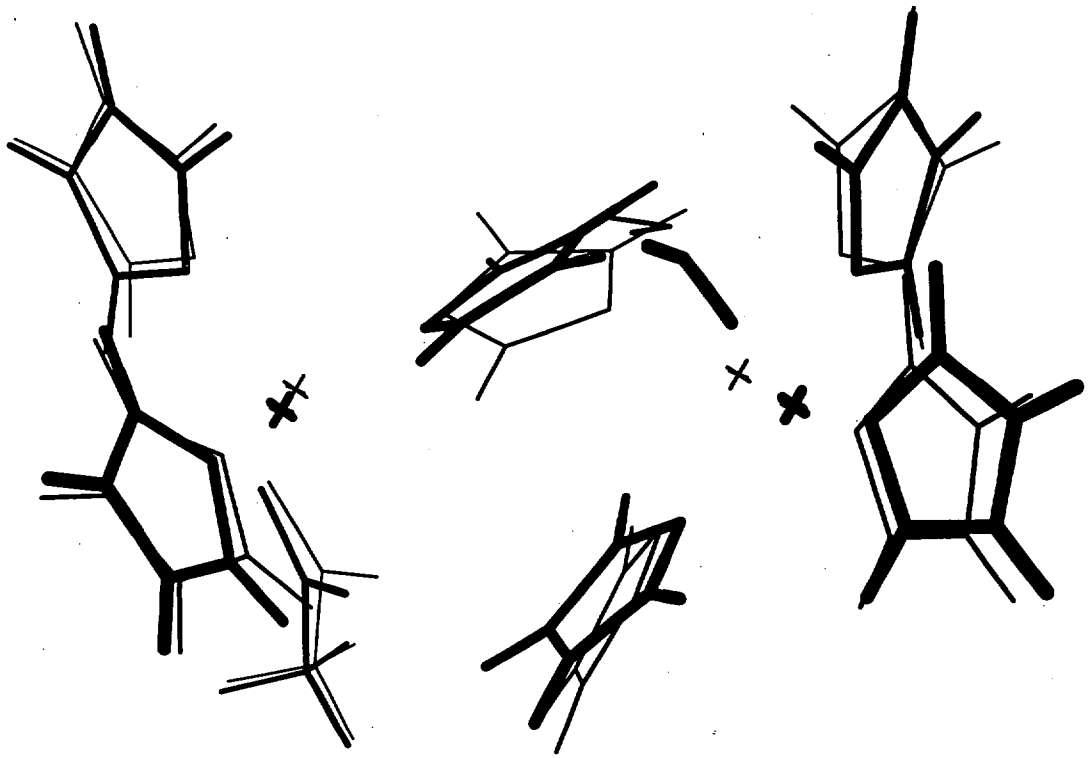

Figure S2. Overlay of optimized oxidized structure (thin line) and reduced, protonated structure (bold line).

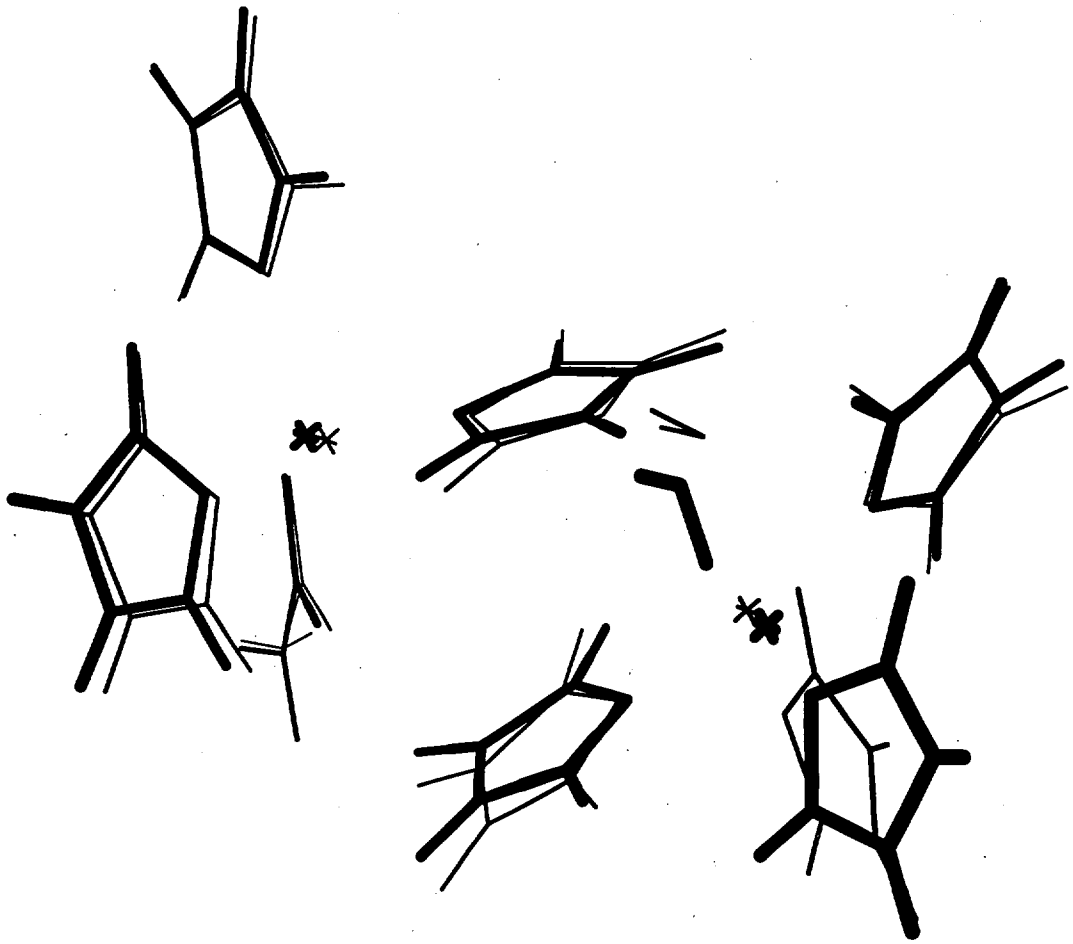

Figure S3. Overlay of optimized protonated (bold line) and non-protonated (thin line) structures of reduced active site.