Table S1. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **keto-OxyLH$_2$**. High pH model with Q^{AMP}=-2.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	-0.41	-0.41	0.00	0.00	0.00
S201	0.38	0.38	0.00	0.00	0.00
R220	-0.45	0.54	0.04	-0.25	-0.78
N231	-0.02	-0.02	0.00	0.00	0.00
H247	-4.13	-4.24	5.24	-1.83	-3.30
G248	-0.53	0.02	0.18	-0.09	-0.64
F249	-11.55	-3.34	7.16	-2.35	-13.01
F252	-0.45	0.18	0.00	-0.16	-0.48
T253	-1.58	-0.76	2.16	-0.39	-2.59
Y257	0.00	0.00	0.00	0.00	0.00
I288	-1.38	-0.15	0.17	-0.30	-1.11
E313	0.24	0.24	0.00	0.00	0.00
A315	-0.50	-0.08	0.03	-0.11	-0.33
S316	-0.10	0.14	0.00	-0.03	-0.21
G317	-0.63	-0.82	3.07	-0.75	-2.13
G318	-2.08	-0.61	0.15	-0.58	-1.04
A319	-0.01	-0.01	0.00	0.00	0.00
R339	-0.37	-0.19	0.00	-0.02	-0.16
Q340	-0.33	0.21	0.01	-0.11	-0.44
G341	-1.16	-3.14	7.30	-1.35	-3.97
Y342	-1.23	-0.34	0.07	-0.12	-0.85
G343	-0.84	0.02	0.06	-0.15	-0.78
L344	-2.18	-0.90	1.16	-0.69	-1.75
T345	-2.73	-1.41	0.41	-0.54	-1.20
E346	-1.22	-1.22	0.00	0.00	0.00
T348	0.02	0.19	0.00	-0.02	-0.16
S349	-6.32	-2.84	1.85	-1.80	-3.54
A350	-3.00	-1.50	3.89	-1.03	-4.35
I353	-0.70	-0.01	0.01	-0.14	-0.56
T529	-1.39	-1.02	0.00	-0.19	-0.19
K531	-10.38	-9.52	0.00	-0.38	-0.48
AMP	-3.46	0.27	8.24	-4.35	-7.61
WAT2001	-9.65	-18.74	19.67	-5.67	-4.91
WAT2002	-0.16	-0.16	0.00	0.00	0.00
WAT2011	-0.19	-0.19	0.00	0.00	0.00
WAT2017	0.23	0.46	0.00	-0.09	-0.14
WAT2026	-0.13	-0.13	0.00	0.00	0.00
WAT2031	-0.44	-0.24	0.00	-0.11	-0.10
WAT2048	0.15	0.22	0.00	-0.06	-0.02
WAT2112	-0.01	-0.01	0.00	0.00	0.00
WAT2155	-0.33	-0.33	0.00	0.00	0.00
WAT2228	0.53	0.53	0.00	0.00	0.00
WAT2325	-11.77	-12.35	5.42	-2.55	-2.29
WAT2336	0.39	0.39	0.00	0.00	0.00
WAT2470	-0.55	-0.21	0.08	-0.13	-0.30
WAT2575	0.14	0.18	0.00	-0.01	-0.02

Table S2. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **keto-OxyLH$_2$**. Low pH model with Q^{AMP}=-1.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	-0.06	-0.06	0.00	0.00	0.00
S201	0.58	0.58	0.00	0.00	0.00
R220	-0.31	0.75	0.04	-0.29	-0.81
N231	0.10	0.10	0.00	0.00	0.00
H247	-4.62	-4.39	4.84	-1.78	-3.30
G248	-0.41	0.16	0.18	-0.11	-0.64
F249	-10.98	-3.45	7.96	-2.39	-13.10
F252	-0.49	0.12	0.00	-0.14	-0.46
T253	-1.58	-0.70	2.22	-0.37	-2.73
Y257	-0.10	-0.10	0.00	0.00	0.00
I288	-1.99	-0.71	0.32	-0.35	-1.25
E313	-0.73	-0.73	0.00	0.00	0.00
A315	-0.64	-0.19	0.11	-0.12	-0.45
S316	-0.35	-0.11	0.00	-0.03	-0.22
G317	-1.12	-0.73	2.24	-0.59	-2.04
G318	-2.09	-0.29	0.21	-0.77	-1.25
A319	0.02	0.02	0.00	0.00	0.00
R339	-0.46	-0.27	0.00	-0.02	-0.17
Q340	-0.28	0.24	0.01	-0.12	-0.41
G341	-0.92	-2.44	6.29	-1.08	-3.69
Y342	-1.27	-0.40	0.07	-0.11	-0.83
G343	-0.97	-0.10	0.07	-0.14	-0.80
L344	-1.35	-0.42	1.39	-0.58	-1.74
T345	-1.16	0.28	0.43	-0.54	-1.33
E346	-0.84	-0.84	0.00	0.00	0.00
T348	-0.10	0.06	0.00	-0.01	-0.14
S349	-2.34	0.07	1.88	-1.37	-2.91
A350	-2.99	-1.42	3.75	-1.01	-4.31
I353	-0.78	-0.12	0.01	-0.13	-0.54
T529	-0.35	-0.07	0.00	-0.04	-0.23
K531	-10.95	-10.47	0.00	-0.26	-0.23
AMP	-7.39	-3.63	8.41	-4.20	-7.97
WAT2001	-7.90	-16.59	20.34	-6.53	-5.11
WAT2002	-0.07	-0.07	0.00	0.00	0.00
WAT2011	0.42	0.42	0.00	0.00	0.00
WAT2017	-0.75	-0.55	0.00	-0.08	-0.13
WAT2026	-0.03	-0.03	0.00	0.00	0.00
WAT2031	0.07	0.18	0.00	-0.04	-0.07
WAT2048	-0.97	-0.92	0.00	-0.04	-0.02
WAT2112	0.07	0.07	0.00	0.00	0.00
WAT2155	0.13	0.13	0.00	0.00	0.00
WAT2228	1.04	1.04	0.00	0.00	0.00
WAT2325	-11.30	-11.41	4.61	-2.25	-2.26
WAT2336	0.01	0.01	0.00	0.00	0.00
WAT2470	-0.31	0.47	0.15	-0.41	-0.53
WAT2575	0.21	0.27	0.00	-0.02	-0.03

Table S3. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **phenolate-keto-OxyLH**$^-$. High pH model with Q^{AMP}=-2.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	-1.22	-1.22	0.00	0.00	0.00
S201	0.26	0.32	0.00	-0.01	-0.05
R220	-46.23	-45.25	0.06	-0.31	-0.73
N231	-1.15	-1.15	0.00	0.00	0.00
H247	-2.95	-2.56	4.80	-1.84	-3.36
G248	-0.15	0.42	0.18	-0.11	-0.65
F249	-10.42	-2.21	7.71	-2.45	-13.47
F252	-1.00	-0.33	0.00	-0.17	-0.49
T253	-3.76	-2.74	2.31	-0.53	-2.80
Y257	0.99	0.99	0.00	0.00	0.00
I288	-2.76	-1.04	0.13	-0.74	-1.11
E313	38.10	38.10	0.00	0.00	0.00
A315	-2.27	-1.08	0.03	-0.63	-0.60
S316	-0.15	0.11	0.00	-0.04	-0.22
G317	-1.37	-0.80	2.16	-0.65	-2.08
G318	-2.64	-0.68	0.21	-0.84	-1.32
A319	-0.06	-0.06	0.00	0.00	0.00
R339	-39.44	-39.21	0.00	-0.04	-0.19
Q340	-2.98	-2.27	0.01	-0.24	-0.48
G341	-3.07	-3.76	6.14	-1.41	-4.04
Y342	-1.61	-0.67	0.07	-0.15	-0.85
G343	-0.84	0.08	0.06	-0.16	-0.82
L344	-0.95	0.00	1.40	-0.61	-1.74
T345	-2.67	-1.28	0.38	-0.56	-1.21
E346	21.39	21.39	0.00	0.00	0.00
T348	-0.56	-0.40	0.00	-0.02	-0.14
S349	-1.31	1.31	1.91	-1.50	-3.03
A350	-4.35	-2.27	3.50	-1.12	-4.47
I353	-2.59	-1.76	0.01	-0.26	-0.57
T529	-1.93	-1.48	0.00	-0.18	-0.27
K531	-39.20	-38.69	0.00	-0.25	-0.27
AMP	54.41	58.40	8.95	-4.79	-8.15
WAT2001	-15.55	-25.48	23.23	-7.85	-5.45
WAT2002	1.02	1.02	0.00	0.00	0.00
WAT2011	1.11	1.11	0.00	0.00	0.00
WAT2017	-0.67	-0.48	0.00	-0.07	-0.12
WAT2026	0.57	0.57	0.00	0.00	0.00
WAT2031	1.19	1.28	0.00	-0.05	-0.04
WAT2048	0.10	0.14	0.00	-0.04	-0.01
WAT2112	-0.87	-0.87	0.00	0.00	0.00
WAT2155	-1.04	-1.04	0.00	0.00	0.00
WAT2228	0.34	0.34	0.00	0.00	0.00
WAT2325	-13.01	-12.97	4.47	-2.23	-2.29
WAT2336	0.16	0.16	0.00	0.00	0.00
WAT2470	-4.35	-3.70	0.20	-0.43	-0.42
WAT2575	1.54	1.52	0.00	-0.02	0.04

Table S4. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **phenolate-keto-OxyLH$_2$**. Low pH model with Q^{AMP}=-1.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	-1.04	-1.04	0.00	0.00	0.00
S201	0.55	0.55	0.00	0.00	0.00
R220	-44.34	-43.38	0.06	-0.31	-0.72
N231	-1.04	-1.04	0.00	0.00	0.00
H247	-3.77	-3.34	4.85	-1.85	-3.43
G248	-0.29	0.28	0.19	-0.11	-0.65
F249	-10.61	-2.54	8.09	-2.61	-13.56
F252	-1.16	-0.56	0.00	-0.13	-0.47
T253	-3.18	-2.24	2.32	-0.47	-2.79
Y257	1.25	1.25	0.00	0.00	0.00
I288	-2.56	-0.83	0.13	-0.75	-1.11
E313	37.54	37.54	0.00	0.00	0.00
A315	-2.19	-0.98	0.04	-0.64	-0.61
S316	-0.02	0.24	0.00	-0.04	-0.23
G317	-1.30	-0.75	2.16	-0.64	-2.08
G318	-2.55	-0.60	0.21	-0.84	-1.32
A319	0.00	0.00	0.00	0.00	0.00
R339	-38.61	-38.38	0.00	-0.04	-0.19
Q340	-2.87	-2.15	0.01	-0.25	-0.49
G341	-2.98	-3.62	6.11	-1.41	-4.06
Y342	-1.61	-0.68	0.07	-0.15	-0.86
G343	-0.92	0.00	0.06	-0.16	-0.83
L344	-0.80	0.17	1.43	-0.60	-1.79
T345	-1.73	-0.31	0.44	-0.51	-1.35
E346	22.72	22.72	0.00	0.00	0.00
T348	-0.54	-0.39	0.00	-0.02	-0.14
S349	-6.18	-3.37	2.25	-1.55	-3.51
A350	-4.25	-2.07	3.50	-1.12	-4.56
I353	-2.34	-1.51	0.01	-0.26	-0.57
T529	-2.72	-2.15	0.00	-0.27	-0.30
K531	-40.83	-40.26	0.00	-0.28	-0.29
AMP	26.04	30.10	8.41	-4.29	-8.17
WAT2001	-1.81	-6.51	11.65	-2.91	-4.05
WAT2002	0.95	0.95	0.00	0.00	0.00
WAT2011	1.21	1.21	0.00	0.00	0.00
WAT2017	-0.63	-0.43	0.00	-0.08	-0.12
WAT2026	0.65	0.65	0.00	0.00	0.00
WAT2031	1.17	1.24	0.00	-0.05	-0.03
WAT2048	0.19	0.27	0.00	-0.04	-0.05
WAT2112	-0.80	-0.80	0.00	0.00	0.00
WAT2155	-0.87	-0.87	0.00	0.00	0.00
WAT2228	1.05	1.05	0.00	0.00	0.00
WAT2325	-14.50	-14.52	4.89	-2.46	-2.41
WAT2336	-0.54	-0.54	0.00	0.00	0.00
WAT2470	-4.08	-3.44	0.19	-0.43	-0.40
WAT2575	1.50	1.47	0.00	-0.02	0.05

Table S5. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **enol-OxyLH$_2$**. High pH model with Q^{AMP}=-2.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	0.23	0.23	0.00	0.00	0.00
S201	0.01	0.05	0.00	0.00	-0.04
R220	-6.40	-5.32	0.05	-0.29	-0.84
N231	-0.15	-0.15	0.00	0.00	0.00
H247	-1.51	-0.23	3.77	-1.44	-3.61
G248	-0.44	0.14	0.21	-0.12	-0.68
F249	-11.57	-2.88	7.06	-2.50	-13.26
F252	-0.48	0.13	0.00	-0.13	-0.48
T253	-1.63	-0.52	2.12	-0.44	-2.79
Y257	0.34	0.34	0.00	0.00	0.00
I288	-1.85	-0.50	0.28	-0.38	-1.26
E313	2.20	2.20	0.00	0.00	0.00
A315	-0.38	0.00	0.12	-0.06	-0.44
S316	-0.05	0.20	0.00	-0.04	-0.21
G317	-0.96	-0.68	2.24	-0.53	-1.99
G318	-1.11	-0.06	0.21	-0.30	-0.97
A319	0.04	0.04	0.00	0.00	0.00
R339	-3.25	-3.07	0.00	-0.02	-0.17
Q340	-0.06	0.49	0.01	-0.15	-0.41
G341	-1.79	-1.15	3.07	-0.70	-3.01
Y342	-0.66	0.23	0.07	-0.12	-0.83
G343	-1.10	0.04	0.16	-0.27	-1.02
L344	-1.10	0.28	0.55	-0.35	-1.59
T345	-1.24	0.14	0.43	-0.54	-1.27
E346	-3.09	-3.09	0.00	0.00	0.00
T348	-0.11	0.05	0.00	-0.02	-0.14
S349	-6.85	-3.84	1.78	-1.43	-3.37
A350	-2.96	-1.72	4.31	-1.07	-4.47
I353	-0.93	-0.24	0.01	-0.14	-0.56
T529	-0.74	-0.47	0.00	-0.06	-0.21
K531	4.54	4.92	0.00	-0.15	-0.24
AMP	-21.38	-18.61	10.59	-5.17	-8.19
WAT2001	-5.44	-12.16	16.17	-4.44	-5.00
WAT2002	0.42	0.42	0.00	0.00	0.00
WAT2011	-0.14	-0.14	0.00	0.00	0.00
WAT2017	0.33	0.55	0.00	-0.05	-0.17
WAT2026	0.20	0.20	0.00	0.00	0.00
WAT2031	0.32	0.44	0.00	-0.04	-0.09
WAT2048	-0.29	-0.25	0.00	-0.02	-0.02
WAT2112	-0.15	-0.15	0.00	0.00	0.00
WAT2155	-0.13	-0.13	0.00	0.00	0.00
WAT2228	0.32	0.32	0.00	0.00	0.00
WAT2325	-3.45	-2.25	4.28	-2.86	-2.63
WAT2336	0.07	0.07	0.00	0.00	0.00
WAT2470	-0.89	-0.12	0.17	-0.40	-0.54
WAT2575	0.52	0.58	0.00	-0.02	-0.04

Table S6. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **enol-OxyLH$_2$**. Low pH model with Q^{AMP}=-1.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	0.97	0.97	0.00	0.00	0.00
S201	-0.29	-0.29	0.00	0.00	0.00
R220	-4.97	-3.90	0.05	-0.30	-0.82
N231	-0.02	-0.02	0.00	0.00	0.00
H247	0.40	1.77	4.06	-1.62	-3.81
G248	-0.28	0.30	0.17	-0.11	-0.64
F249	-10.90	-2.78	7.58	-2.44	-13.26
F252	-0.53	0.10	0.00	-0.16	-0.48
T253	-1.78	-0.87	2.23	-0.39	-2.75
Y257	0.17	0.17	0.00	0.00	0.00
I288	-1.88	-0.58	0.32	-0.36	-1.26
E313	1.88	1.88	0.00	0.00	0.00
A315	-0.60	-0.14	0.11	-0.12	-0.46
S316	-0.24	0.02	0.00	-0.03	-0.23
G317	-1.04	-0.64	2.24	-0.59	-2.05
G318	-1.67	-0.15	0.21	-0.56	-1.18
A319	0.02	0.02	0.00	0.00	0.00
R339	-3.07	-2.88	0.00	-0.02	-0.17
Q340	-0.29	0.23	0.01	-0.12	-0.41
G341	-0.96	-2.47	6.20	-1.06	-3.63
Y342	-0.94	-0.07	0.07	-0.11	-0.83
G343	-0.89	0.04	0.07	-0.18	-0.82
L344	-0.88	0.65	0.65	-0.43	-1.75
T345	-3.68	-2.07	0.43	-0.69	-1.34
E346	-6.05	-6.05	0.00	0.00	0.00
T348	-0.10	0.05	0.00	-0.01	-0.14
S349	-2.01	0.60	1.84	-1.41	-3.03
A350	-3.17	-1.51	3.69	-1.02	-4.34
I353	-0.90	-0.21	0.01	-0.14	-0.56
T529	-0.67	-0.20	0.00	-0.18	-0.29
K531	2.15	2.58	0.00	-0.19	-0.24
AMP	-42.77	-42.33	19.06	-9.41	-10.08
WAT2001	-11.00	-19.73	20.81	-6.77	-5.30
WAT2002	0.16	0.16	0.00	0.00	0.00
WAT2011	-0.04	-0.04	0.00	0.00	0.00
WAT2017	-0.80	-0.57	0.00	-0.10	-0.13
WAT2026	0.16	0.16	0.00	0.00	0.00
WAT2031	0.29	0.40	0.00	-0.04	-0.07
WAT2048	-0.95	-0.90	0.00	-0.02	-0.03
WAT2112	-0.11	-0.11	0.00	0.00	0.00
WAT2155	0.20	0.20	0.00	0.00	0.00
WAT2228	0.33	0.36	0.00	-0.01	-0.02
WAT2325	-5.13	-6.31	5.28	-2.07	-2.03
WAT2336	0.52	0.52	0.00	0.00	0.00
WAT2470	-0.60	0.13	0.16	-0.39	-0.51
WAT2575	0.42	0.47	0.00	-0.02	-0.03

Table S7. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **phenolate-enol-OxyLH**$^-$. High pH model with Q^{AMP}=-2.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	0.24	0.24	0.00	0.00	0.00
S201	0.98	1.04	0.00	0.00	-0.06
R220	-52.23	-51.19	0.07	-0.32	-0.80
N231	-1.42	-1.42	0.00	0.00	0.00
H247	1.79	3.24	4.10	-1.63	-3.92
G248	-0.30	0.30	0.22	-0.14	-0.68
F249	-12.03	-2.79	7.00	-2.65	-13.58
F252	-1.49	-0.81	0.00	-0.18	-0.50
T253	-2.16	-0.99	2.21	-0.53	-2.84
Y257	1.67	1.67	0.00	0.00	0.00
I288	-3.34	-1.50	0.13	-0.78	-1.19
E313	40.74	40.74	0.00	0.00	0.00
A315	-2.48	-1.14	0.03	-0.75	-0.62
S316	-2.60	-2.32	0.00	-0.05	-0.23
G317	-1.45	-1.04	2.22	-0.62	-2.02
G318	-1.65	-0.39	0.16	-0.41	-1.01
A319	-0.08	-0.08	0.00	0.00	0.00
R339	-42.35	-42.12	0.00	-0.04	-0.19
Q340	-3.48	-2.61	0.01	-0.33	-0.55
G341	-4.50	-2.82	3.22	-1.50	-3.39
Y342	-1.53	-0.57	0.08	-0.17	-0.87
G343	-1.17	0.00	0.15	-0.29	-1.03
L344	-0.25	1.39	0.67	-0.50	-1.81
T345	0.04	1.89	0.47	-0.82	-1.51
E346	16.48	16.48	0.00	0.00	0.00
T348	-0.67	-0.51	0.00	-0.02	-0.14
S349	-8.13	-5.04	1.94	-1.53	-3.51
A350	-4.51	-2.85	4.09	-1.12	-4.63
I353	-2.91	-2.06	0.01	-0.28	-0.57
T529	-1.16	-0.79	0.00	-0.12	-0.25
K531	-25.05	-24.62	0.00	-0.18	-0.25
AMP	1.42	1.99	20.38	-10.55	-10.40
WAT2001	-12.79	-24.24	23.24	-6.37	-5.42
WAT2002	2.00	2.00	0.00	0.00	0.00
WAT2011	0.21	0.21	0.00	0.00	0.00
WAT2017	-0.33	-0.10	0.00	-0.06	-0.18
WAT2026	0.66	0.66	0.00	0.00	0.00
WAT2031	1.48	1.56	0.00	-0.05	-0.04
WAT2048	0.69	0.76	0.00	-0.02	-0.05
WAT2112	-1.13	-1.13	0.00	0.00	0.00
WAT2155	1.83	1.83	0.00	0.00	0.00
WAT2228	0.85	0.92	0.00	-0.02	-0.06
WAT2325	-6.00	-6.74	4.49	-1.81	-1.95
WAT2336	0.46	0.46	0.00	0.00	0.00
WAT2470	-4.88	-4.18	0.21	-0.44	-0.48
WAT2575	1.73	1.76	0.00	-0.02	-0.01

Table S8. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **phenolate-enol-OxyLH**$^-$. Low pH model with Q^{AMP}=-1.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	0.11	0.11	0.00	0.00	0.00
S201	-0.33	-0.33	0.00	0.00	0.00
R220	-47.41	-46.50	0.06	-0.27	-0.70
N231	-0.90	-0.90	0.00	0.00	0.00
H247	0.62	2.00	3.94	-1.48	-3.84
G248	-0.38	0.21	0.20	-0.13	-0.66
F249	-11.94	-2.81	6.65	-2.45	-13.33
F252	-1.30	-0.69	0.00	-0.15	-0.46
T253	-3.82	-2.88	2.26	-0.52	-2.68
Y257	-0.46	-0.46	0.00	0.00	0.00
I288	-2.80	-0.94	0.13	-0.82	-1.17
E313	40.27	40.27	0.00	0.00	0.00
A315	-2.61	-1.20	0.04	-0.78	-0.66
S316	-1.31	-1.02	0.00	-0.04	-0.26
G317	-1.55	-1.28	2.85	-0.90	-2.23
G318	-2.01	-0.35	0.21	-0.66	-1.21
A319	0.07	0.07	0.00	0.00	0.00
R339	-42.27	-42.03	0.00	-0.05	-0.19
Q340	-3.34	-2.50	0.01	-0.31	-0.54
G341	-3.86	-4.77	6.86	-1.72	-4.22
Y342	-1.86	-0.90	0.08	-0.16	-0.88
G343	-0.98	0.01	0.07	-0.24	-0.82
L344	-1.13	0.74	0.68	-0.62	-1.93
T345	-1.63	0.02	0.46	-0.71	-1.41
E346	17.84	17.84	0.00	0.00	0.00
T348	-0.53	-0.36	0.00	-0.02	-0.15
S349	1.35	3.32	1.68	-0.94	-2.71
A350	-4.70	-2.74	3.59	-1.10	-4.45
I353	-2.53	-1.72	0.01	-0.26	-0.56
T529	-2.77	-2.21	0.00	-0.25	-0.32
K531	-27.45	-26.89	0.00	-0.26	-0.30
AMP	-3.65	-3.67	18.15	-8.50	-9.64
WAT2001	-13.82	-23.44	21.78	-6.90	-5.27
WAT2002	1.49	1.49	0.00	0.00	0.00
WAT2011	0.59	0.59	0.00	0.00	0.00
WAT2017	-0.21	0.09	0.00	-0.10	-0.20
WAT2026	1.08	1.08	0.00	0.00	0.00
WAT2031	0.12	0.18	0.00	-0.05	-0.02
WAT2048	0.57	0.64	0.00	-0.02	-0.05
WAT2112	1.80	1.80	0.00	0.00	0.00
WAT2155	-0.38	-0.38	0.00	0.00	0.00
WAT2228	0.54	0.63	0.00	-0.02	-0.07
WAT2325	-9.64	-11.17	6.24	-2.47	-2.24
WAT2336	0.56	0.56	0.00	0.00	0.00
WAT2470	-2.11	-1.93	0.12	-0.10	-0.20
WAT2575	1.10	1.07	0.00	-0.02	0.05

Table S9. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **phenol-enolate-OxyLH**$^-$. High pH model with Q^{AMP}=-2.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	-2.62	-2.62	0.00	0.00	0.00
S201	-0.42	-0.39	0.00	-0.01	-0.02
R220	-39.41	-38.32	0.05	-0.29	-0.86
N231	-0.84	-0.84	0.00	0.00	0.00
H247	-10.63	-8.15	3.40	-1.99	-3.89
G248	-0.82	-0.18	0.24	-0.17	-0.70
F249	-14.26	-5.02	7.10	-2.77	-13.56
F252	-2.62	-1.96	0.00	-0.17	-0.50
T253	-1.23	-0.10	2.14	-0.44	-2.83
Y257	0.78	0.78	0.00	0.00	0.00
I288	-1.96	-0.54	0.25	-0.40	-1.27
E313	23.82	23.82	0.00	0.00	0.00
A315	-0.25	0.14	0.11	-0.07	-0.43
S316	-0.92	-0.70	0.00	-0.04	-0.18
G317	-1.39	-1.17	2.28	-0.56	-1.95
G318	-2.58	-1.00	0.15	-0.66	-1.07
A319	-0.25	-0.25	0.00	0.00	0.00
R339	-25.39	-25.19	0.00	-0.02	-0.18
Q340	-2.52	-1.97	0.01	-0.16	-0.40
G341	-2.04	-1.33	3.09	-0.74	-3.06
Y342	-2.40	-1.47	0.07	-0.14	-0.87
G343	-1.72	-0.45	0.15	-0.35	-1.06
L344	-2.47	-0.67	0.54	-0.67	-1.68
T345	-3.58	-2.24	0.46	-0.55	-1.25
E346	33.35	33.35	0.00	0.00	0.00
T348	-1.22	-1.02	0.00	-0.03	-0.18
S349	-11.51	-7.90	1.97	-1.86	-3.71
A350	-4.01	-2.60	4.23	-1.08	-4.56
I353	-1.50	-0.80	0.01	-0.15	-0.55
T529	-4.34	-3.74	0.00	-0.28	-0.33
K531	-56.63	-55.99	0.00	-0.39	-0.26
AMP	92.67	97.94	9.41	-6.02	-8.66
WAT2001	-15.89	-26.57	23.45	-6.92	-5.85
WAT2002	1.61	1.61	0.00	0.00	0.00
WAT2011	1.45	1.45	0.00	0.00	0.00
WAT2017	-1.20	-0.94	0.00	-0.06	-0.21
WAT2026	0.60	0.60	0.00	0.00	0.00
WAT2031	1.22	1.35	0.00	-0.04	-0.08
WAT2048	1.37	1.35	0.00	-0.02	0.04
WAT2112	-0.83	-0.83	0.00	0.00	0.00
WAT2155	0.09	0.09	0.00	0.00	0.00
WAT2228	-0.59	-0.59	0.00	0.00	0.00
WAT2325	-21.66	-20.51	4.73	-3.19	-2.69
WAT2336	-0.39	-0.39	0.00	0.00	0.00
WAT2470	-1.75	-0.96	0.18	-0.40	-0.57
WAT2575	0.94	1.01	0.00	-0.02	-0.06

Table S10. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **phenol-enolate-OxyLH**$^-$. Low pH model with Q^{AMP}=-1.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	-2.00	-2.00	0.00	0.00	0.00
S201	0.62	0.62	0.00	0.00	0.00
R220	-36.18	-35.18	0.05	-0.26	-0.80
N231	-0.69	-0.69	0.00	0.00	0.00
H247	-12.42	-10.02	3.24	-1.85	-3.79
G248	-0.59	0.04	0.20	-0.15	-0.68
F249	-13.76	-4.51	6.71	-2.71	-13.25
F252	-2.11	-1.50	0.00	-0.15	-0.46
T253	-3.12	-2.23	2.21	-0.41	-2.68
Y257	-0.58	-0.48	0.00	-0.01	-0.09
I288	-1.45	-0.14	0.13	-0.35	-1.09
E313	22.99	22.99	0.00	0.00	0.00
A315	-0.53	0.06	0.05	-0.21	-0.42
S316	-0.33	-0.06	0.01	-0.03	-0.24
G317	-0.98	-1.04	2.83	-0.71	-2.06
G318	-4.07	-1.49	0.17	-1.28	-1.47
A319	-0.02	-0.02	0.00	0.00	0.00
R339	-23.59	-23.41	0.00	-0.02	-0.16
Q340	-2.16	-1.63	0.01	-0.10	-0.45
G341	-1.55	-3.60	7.40	-1.36	-4.00
Y342	-2.49	-1.55	0.08	-0.14	-0.87
G343	-1.50	-0.40	0.06	-0.34	-0.82
L344	-3.10	-0.65	0.56	-1.14	-1.87
T345	0.01	1.26	0.43	-0.52	-1.15
E346	35.72	35.72	0.00	0.00	0.00
T348	-1.05	-0.85	0.00	-0.03	-0.18
S349	-0.10	1.91	1.78	-1.01	-2.77
A350	-4.10	-2.16	3.43	-1.01	-4.37
I353	-1.25	-0.54	0.01	-0.17	-0.55
T529	-4.62	-3.90	0.00	-0.38	-0.35
K531	-58.77	-57.87	0.00	-0.61	-0.29
AMP	48.27	54.41	8.09	-5.58	-8.65
WAT2001	-15.85	-25.31	21.47	-6.71	-5.31
WAT2002	-0.32	-0.32	0.00	0.00	0.00
WAT2011	2.00	2.00	0.00	0.00	0.00
WAT2017	-1.83	-1.55	0.01	-0.08	-0.20
WAT2026	1.27	1.27	0.00	0.00	0.00
WAT2031	1.19	1.27	0.00	-0.05	-0.03
WAT2048	1.19	1.17	0.00	-0.02	0.04
WAT2112	0.59	0.59	0.00	0.00	0.00
WAT2155	-1.10	-1.10	0.00	0.00	0.00
WAT2228	-1.08	-1.14	0.00	-0.02	0.07
WAT2325	-22.48	-20.76	4.36	-3.36	-2.72
WAT2336	-1.47	-1.47	0.00	0.00	0.00
WAT2470	-1.41	-0.80	0.19	-0.34	-0.46
WAT2575	0.97	1.02	0.00	-0.01	-0.03

Table S11. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **$OxyL^{2-}$**. High pH model with Q^{AMP}=-2.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	-3.79	-3.79	0.00	0.00	0.00
S201	-0.62	-0.59	0.00	-0.01	-0.02
R220	-87.43	-86.29	0.08	-0.36	-0.87
N231	-2.31	-2.31	0.00	0.00	0.00
H247	-12.26	-9.68	3.53	-2.05	-4.06
G248	-1.06	-0.37	0.24	-0.21	-0.71
F249	-15.30	-5.58	7.00	-2.96	-13.76
F252	-4.06	-3.34	0.00	-0.21	-0.52
T253	-2.44	-1.12	2.22	-0.61	-2.93
Y257	1.55	1.55	0.00	0.00	0.00
I288	-4.46	-2.45	0.13	-0.88	-1.26
E313	61.89	61.89	0.00	0.00	0.00
A315	-3.12	-1.62	0.03	-0.86	-0.68
S316	-3.59	-3.33	0.00	-0.05	-0.22
G317	-2.01	-1.62	2.25	-0.65	-1.99
G318	-3.10	-1.36	0.15	-0.73	-1.16
A319	-0.45	-0.45	0.00	0.00	0.00
R339	-64.95	-64.71	0.00	-0.05	-0.19
Q340	-6.12	-5.21	0.01	-0.37	-0.55
G341	-5.14	-3.29	3.24	-1.62	-3.47
Y342	-3.58	-2.60	0.08	-0.18	-0.88
G343	-2.03	-0.71	0.14	-0.38	-1.07
L344	-3.22	-1.33	0.58	-0.72	-1.75
T345	-4.68	-3.33	0.49	-0.57	-1.28
E346	56.51	56.51	0.00	0.00	0.00
T348	-2.06	-1.86	0.00	-0.03	-0.17
S349	-13.46	-9.65	2.04	-2.03	-3.82
A350	-5.97	-4.16	4.06	-1.20	-4.68
I353	-4.07	-3.19	0.01	-0.31	-0.58
T529	-5.99	-5.34	0.00	-0.32	-0.33
K531	-86.42	-85.68	0.00	-0.44	-0.30
AMP	153.48	159.23	9.37	-6.19	-8.92
WAT2001	-20.97	-33.08	25.86	-7.76	-5.99
WAT2002	3.10	3.10	0.00	0.00	0.00
WAT2011	1.88	1.88	0.00	0.00	0.00
WAT2017	-2.03	-1.76	0.01	-0.06	-0.21
WAT2026	0.55	0.55	0.00	0.00	0.00
WAT2031	2.27	2.39	0.00	-0.06	-0.06
WAT2048	2.37	2.37	0.00	-0.02	0.02
WAT2112	-1.82	-1.82	0.00	0.00	0.00
WAT2155	1.79	1.79	0.00	0.00	0.00
WAT2228	-1.13	-1.13	0.00	0.00	0.00
WAT2325	-25.03	-23.45	4.82	-3.49	-2.91
WAT2336	-0.63	-0.63	0.00	0.00	0.00
WAT2470	-5.84	-5.11	0.24	-0.45	-0.52
WAT2575	2.08	2.14	0.00	-0.02	-0.04

Table S12. FMO2-MP2/6-311G(d,p) PIEDA interaction energies (kJ mol^{-1}) between active site components and **$OxyL^{2-}$**. Low pH model with Q^{AMP}=-1.

Residue	E(total)	E(electrostatic)	E(exchange)	E(charge-transfer)	E(dispersion)
S200	-3.75	-3.75	0.00	0.00	0.00
S201	-0.73	-0.69	0.00	-0.01	-0.03
R220	-83.43	-82.33	0.07	-0.34	-0.83
N231	-2.01	-2.01	0.00	0.00	0.00
H247	-13.63	-11.06	3.62	-2.07	-4.13
G248	-0.95	-0.30	0.19	-0.17	-0.67
F249	-14.97	-5.69	7.52	-2.95	-13.85
F252	-3.03	-2.29	0.00	-0.21	-0.53
T253	-6.30	-5.05	2.33	-0.65	-2.93
Y257	1.18	1.18	0.00	0.00	0.00
I288	-3.55	-1.79	0.12	-0.73	-1.15
E313	60.20	60.20	0.00	0.00	0.00
A315	-2.47	-1.31	0.03	-0.61	-0.58
S316	0.31	0.58	0.00	-0.04	-0.24
G317	-2.01	-1.42	2.21	-0.71	-2.10
G318	-4.61	-1.81	0.21	-1.39	-1.61
A319	-0.21	-0.21	0.00	0.00	0.00
R339	-62.55	-62.34	0.00	-0.03	-0.18
Q340	-5.41	-4.69	0.01	-0.23	-0.49
G341	-4.05	-4.74	6.18	-1.46	-4.03
Y342	-3.09	-2.11	0.07	-0.18	-0.87
G343	-1.64	-0.52	0.07	-0.31	-0.87
L344	-2.58	-0.76	0.63	-0.67	-1.77
T345	-5.45	-4.16	0.64	-0.57	-1.36
E346	59.17	59.17	0.00	0.00	0.00
T348	-1.79	-1.61	0.00	-0.02	-0.16
S349	-3.30	-0.28	2.06	-1.76	-3.32
A350	-6.29	-4.00	3.49	-1.23	-4.56
I353	-3.65	-2.79	0.01	-0.29	-0.57
T529	-5.86	-5.15	0.00	-0.36	-0.36
K531	-88.84	-88.00	0.00	-0.52	-0.32
AMP	76.28	82.50	9.05	-6.09	-9.18
WAT2001	-22.81	-32.97	24.68	-8.68	-5.84
WAT2002	1.76	1.76	0.00	0.00	0.00
WAT2011	2.69	2.69	0.00	0.00	0.00
WAT2017	0.17	0.39	0.00	-0.08	-0.14
WAT2026	0.93	0.93	0.00	0.00	0.00
WAT2031	2.21	2.33	0.00	-0.06	-0.07
WAT2048	3.29	3.28	0.00	-0.02	0.03
WAT2112	-1.71	-1.71	0.00	0.00	0.00
WAT2155	-2.40	-2.40	0.00	0.00	0.00
WAT2228	0.54	0.54	0.00	0.00	0.00
WAT2325	-27.28	-25.71	5.63	-4.04	-3.17
WAT2336	-2.39	-2.39	0.00	0.00	0.00
WAT2470	-5.39	-4.68	0.23	-0.44	-0.50
WAT2575	2.11	2.14	0.00	-0.02	-0.01

Table S13. FMO1:RHF-TDB3LYP S0→S1 excitation energies in eV for oxyluciferin species in the *L. cruciata* luciferase active site model. Oscillator strengths shown in parentheses.

	High pH[a]		Low pH[b]	
	6-311G(d,p)	6-311G(2d,2p)	6-311G(d,p)	6-311G(2d,2p)
keto-$OxyLH_2$	3.42 (0.399)	3.51 (0.387)	3.76 (0.353)	3.74 (0.353)
phenolate-keto-$OxyLH^-$	2.27 (0.349)	2.27 (0.341)	2.16 (0.354)	2.16 (0.351)
enol-$OxyLH_2$	3.11 (0.576)	3.09 (0.553)	3.25 (0.572)	3.22 (0.551)
phenolate-enol-$OxyLH^-$	2.41 (0.356)	2.41 (0.353)	2.32 (0.363)	2.31 (0.333)
phenol-enolate-$OxyLH^-$	2.02 (0.252)	2.03 (0.254)	2.19 (0.264)	2.20 (0.261)
$OxyL^{2-}$	2.27 (0.334)	2.27 (0.326)	2.74 (0.422)	2.46 (0.412)

a) Corresponding bioluminescence emission found at 2.2 eV.
b) Corresponding bioluminescence emission found at 2.0 eV.