Table S1. New OLYP calculations on large DNC Models with neutral protonated Y237 sidechain.[a]

State [b]	Geometry						*E*	Q	S^2	Net Spin			
	Fe-N (H384)	Fe-O1	Cu-O2	O1···O2	Fe···Cu	O···O (Y237)				Fe^{3+}	O1	O2	Cu^{2+}
$Fe^{3+,LS}$-$OH^-\cdots H_2O$-Cu^{2+} ($H376H^+$,H282H,Y237H)(F) [c]	2.06	1.83	2.26	2.68	5.54	3.32	–151.68	2	2.03	1.27	0.15	0.03	0.38
$Fe^{3+,LS}$-$OH^-\cdots H_2O$-Cu^{2+} ($H376H^+$,H282H,Y237H)(AF) [c]	2.06	1.85	2.16	2.62	5.49	3.32	–146.82	2	1.00	0.82	0.11	–0.06	–0.46
$Fe^{3+,LS}$-$OH^-\cdots H_2O$-Cu^{2+} (H376,H282H,Y237H)(F) [d]	2.07	1.83	2.22	2.68	5.47	3.37	–151.28	1	2.03	1.24	0.14	0.03	0.40
$Fe^{3+,LS}$-$OH^-\cdots H_2O$-Cu^{2+} (H376,H282H,Y237H)(AF) [d]	2.07	1.86	2.14	2.62	5.41	3.33	–147.26	1	1.00	0.82	0.12	–0.06	–0.47
$Fe^{3+,LS}$-$OH^-\cdots H_2O$-Cu^{2+} ($H376H^+$,$H282^-$,Y237H)(F) [e]	2.07	1.84	2.26	2.66	5.51	3.28	–147.43	1	2.02	1.05	0.14	0.03	0.41
$Fe^{3+,LS}$-$OH^-\cdots H_2O$-Cu^{2+} ($H376H^+$,$H282^-$,Y237H)(AF) [e]	2.07	1.85	2.20	2.63	5.48	3.31	–146.55	1	1.02	0.95	0.13	–0.04	–0.43

a. OLYP calculations have been performed on the larger model. The calculated properties given here include energies (*E*, –28000 kcal mol^{-1}), S^2 expectation value, net charge of the cluster (Q), the Mulliken net spin polarizations for Fe, Cu, O1 and O2 atoms, and the key geometric data (distances in Angstrom).
b. LS represents low-spin, (F) stands for ferromagnetically-coupling, and (AF) for antiferromagnetically-coupling.
c. This is formally state **13**+H_2O+H^+, where H_2O is scalar water on Cu^{2+} and H^+ is on Y237.
d. This is formally state **14**+H_2O+H^+, where H_2O is scalar water on Cu^{2+} and H^+ is on Y237.
e. This is formally state **1**+H_2O+H^+, where H_2O is scalar water on Cu^{2+} and H^+ is on Y237.

Table S2. New calculations on Modified smaller 2008 DNC Models of **11**-**1** in the Cycle with the scalar water on $Cu^{+/2+}$.

State	*E*(PW91)	*E*(B3LYP*)
11_2_2H [b]	–26902.90	–28300.30
12_H_2O [c]	–27011.72	–28405.55
13_H_2O_H [d]	–27009.64	–28410.97
14_H_2O_H [e]	–27349.22	–28766.61
1_H_2O_H [f]	–27006.19	–28402.81
13_H_2O [g]	–27019.56	–28417.51
14_H_2O [h]	–27357.54	–28770.82
1_H_2O [i]	–27011.06	–28403.19

[a.] Geometries were optimized with PW91 potential the same way described in the 2008 JACS paper. B3LYP* single-point energy calculations were performed on the PW91 optimized geometries. Electronic energy (*E*) in kcal mol^{-1}. Fe^{3+} and Cu^{2+} are F-coupled.

[b.] State $Fe^{3+,LS}$-$OH^{-}\cdots H_2O$-Cu^{2+}(H376H^{+},H282H,Y237$^{\bullet}$)(F).

[c.] State $Fe^{4+,IS}$=O$\cdots H_2O$-Cu^{+}(H376H^{+},H282H,Y237H).

[d.] State $Fe^{3+,LS}$-$OH^{-}\cdots H_2O$-Cu^{2+}(H376H^{+},H282H,Y237H)(F).

[e.] State $Fe^{3+,LS}$-$OH^{-}\cdots H_2O$-Cu^{2+}(H376,HOH,H282H,Y237H)(F).

[f.] State $Fe^{3+,LS}$-$OH^{-}\cdots H_2O$-Cu^{2+}(H376H^{+},H282^{-},Y237H)(F).

[g.] State $Fe^{3+,LS}$-$OH^{-}\cdots H_2O$-Cu^{2+}(H376H^{+},H282H,Y237^{-})(F).

[h.] State $Fe^{3+,LS}$-$OH^{-}\cdots H_2O$-Cu^{2+}(H376,HOH,H282H,Y237^{-})(F).

[f.] State $Fe^{3+,LS}$-$OH^{-}\cdots H_2O$-Cu^{2+}(H376H^{+},H282^{-},Y237^{-})(F).

Table S3. Absolute zero kelvin energies in eV (energies in parentheses are in kcal/mol) of the individual compounds obtained for the smaller models.

Compound	Exchange correlation potential	
	PW91	**B3LYP***
1{H376H$^+$,Fe3OH_Cu2,H282$^-$,Y´O$^-$,ups=2,184,Q=0}	−1156.5514 (−26670.48)	−1216.1144 (−28044.02)
2{H376H$^+$,Fe2_Cu1,H282H,Y´O$^-$,ups=4,183,Q=0}	−1150.0376	−1209.5118
2H{H376H$^+$,Fe2_Cu1,H282H,Y´OH,ups=4,184,Q=+1}	−1150.3103	−1209.2909
3{H376H$^+$,Fe2-O_2,H_2O-Cu1,H282H,Y´OH,ups=0,189,Q=+1}	−1175.7395	−1236.0939
4{H376,HOH,Fe3-O-O-Cu2,H282H,Y´OH,ups=2,188,Q=0}	−1176.4647	−1236.9466
5{H376H$^+$,Fe3-O-O-Cu2,H282H,Y´O$^-$,ups=2,185,Q=0}	−1161.6314	−1221.2326
5_2{H376H$^+$,Fe3-O-O-Cu2,H282$^-$,Y´OH,ups=2,185,Q=0}	−1161.4193	−1221.2580
6{H376H$^+$,Fe3-O-OH-Cu2,H282H,Y´O$^-$,ups=2,186,Q=+1}	−1161.5300	−1221.4689
6_2{H376H$^+$,Fe3-O-O-Cu2,H282H,Y´OH,ups=2,186,Q=+1}	−1161.7892	−1221.9196
6_3{H376H$^+$,Fe3-O-OH-Cu2,H282$^-$,Y´OH,ups=2,186,Q=+1}	−1161.2242	−1221.3505
7{H376,HOH,Fe4=O,HO-Cu2,H282H,Y´O$^•$,ups=4,188,Q=0}	−1176.0769	−1236.8902
7_2{H376,HOH,Fe4=O,H_2O-Cu2,H282$^-$,Y´O$^•$,ups=4,188,Q=0}	−1176.2470	−1236.8659
8{H376H$^+$,Fe4=O,HO-Cu2,H282$^-$,Y´O$^•$,ups=4,185,Q=0}	−1160.9090	−1220.4212
$8H_1${H376H$^+$,Fe4=O,HO-Cu2,H282H,Y´O$^•$,ups=4,186,Q=+1} [a]	−1161.4331	−1221.5749
$8H_2${H376H$^+$,Fe4=O,H_2O-Cu2,H282$^-$,Y´O$^•$,ups=4,186,Q=+1} [a]	−1161.6013	−1221.6329
9{H376H$^+$,Fe4O,H_2O-Cu2,H282$^-$,Y´OH,ups=3,187,Q=+1}	−1166.3966	−1226.6185
9_2{H376H$^+$,Fe4O,H_2O-Cu2,H282H,Y´O$^-$,ups=3,187,Q=+1}	−1166.9517	−1227.1210
9_3{H376H$^+$,Fe4O,HO-Cu2,H282H,Y´OH,ups=3,187,Q=+1}	−1166.2602	−1226.6891
10{H376,HOH,Fe4=O,H_2O-Cu2,H282$^-$,Y´OH,ups=3,189,Q=0}	−1181.1346	−1242.0818
10_2{H376,HOH,Fe4=O,H_2O-Cu2,H282H,Y´O$^-$,ups=3,189,Q=0}	−1181.7404	−1242.2962
10_3{H376,HOH,Fe4=O,HO-Cu2,H282H,Y´OH,ups=3,189,Q=0}	−1181.1518	−1242.3326
11{H376H$^+$,Fe4=O,Cu2,H282$^-$,Y´O$^-$,ups=3,183,Q=0}	−1152.0253	−1211.1518
11_2{H376H$^+$,Fe4=O,H_2O-Cu2,H282$^-$,Y´O$^-$,ups=3,186,Q=0} [b]	−1166.6995	−1226.6947
11_3{H376H$^+$,Fe4=O,HO-Cu2,H282H,Y´O$^-$,ups=3,186,Q=0} [b]	−1166.3661	−1226.7129
11_4{H376H$^+$,Fe4=O,HO-Cu2,H282$^-$,Y´OH,ups=3,186,Q=0} [b]	−1165.9874	−1226.1545
12{H376H$^+$,Fe4=O,Cu1,H282H,Y´OH,ups=2,185,Q=+1}	−1156.9845 (−26680.47)	−1216.8226 (−28060.36)
13{H376H$^+$,Fe3-OH,Cu2,H282H,Y´O$^-$,ups=2,185,Q=+1}	−1157.0116 (−26681.09)	−1216.5724 (−28054.59)
13_2{H376H$^+$,Fe3-OH,Cu2,H282$^-$,Y´OH,ups=2,185,Q=+1}	−1156.7243	−1216.3119
14{H376,HOH,Fe3-OH,Cu2,H282H,Y´O$^-$,ups=2,187,Q=0}	−1171.8059 (−27022.25)	−1232.0310 (−28411.07)
14_2{H376,HOH,Fe3-OH,Cu2,H282$^-$,Y´OH,ups=2,187,Q=0}	−1171.5138	−1231.6896

[a.] A proton was added to the original intermediate 8. [b.] A water molecule added to original intermediate **11**.

Gas-phase H_2 OLYP calculation:

E = −6.66667825 eV
= −153.74 kcal/mol

Zero-Point Energy : 0.010008 a.u.
=================== 0.272334 eV

temperature: 298.15

	Transl	Rotat	Vibrat	Total
Entropy (cal/mole-K):	28.080	3.091	0.000	31.171
Internal Energy (Kcal/mole):	0.889	0.592	6.280	7.761
Constant Volume Heat Capacity (cal/mole-K):	2.981	1.987	0.000	4.968

Gas-phase O2 OLYP calculation:

E = −9.60155 eV
= −221.42 kcal/mol

Zero-Point Energy : 0.003496 a.u.
=================== 0.095140 eV

Temperature: 298.15

	Transl	Rotat	Vibrat	Total
Entropy (cal/mole-K):	36.321	10.546	0.010	46.877
Internal Energy (Kcal/mole):	0.889	0.592	2.197	3.678
Constant Volume Heat Capacity (cal/mole-K):	2.981	1.987	0.066	5.034

Gas-phase OLYP calculation on a water molecule:

E = −13.7672 eV
= −317.48 kcal/mol

Zero-Point Energy : 0.020580 a.u.
=================== 0.559998 eV

Temperature: 298.15

	Transl	Rotat	Vibrat	Total
Entropy (cal/mole-K):	34.608	10.576	0.007	45.191
Internal Energy (Kcal/mole):	0.889	0.889	12.916	14.693
Constant Volume Heat Capacity (cal/mole-K):	2.981	2.981	0.051	6.012