Supporting Information

Neutralization of Reactive Oxygen Species at Dinuclear Cu(II) Cores: Tuning the Anti-Oxidant Manifold in Water by Ligand Design

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1. General Information

1.1 Materials
Commercially available reagents were used directly, unless otherwise noted. Copper (II) perchlorate hydrate, xanthine, xanthine oxidase from bovine milk, cytochrome c from horse heart, catalase from bovine liver, morin, di-2-pyridyl ketone, hydroxylamine hydrochloride, pyridine, ammonium acetate, sodium bromide, zinc powder, salicylaldehyde, 2-hydroxy-5-nitrobenzaldehyde, sodium borohydride, sodium triacetoxyborohydride, formaldehyde aqueous solution 37 % wt, hydrogen peroxide solution 30% wt, triethylamine, diethyl ether, dichloromethane, 1,2-dichloroethane, methanol, acetonitrile, magnesium sulphate, sodium dihydrogen phosphate, boric acid, were purchased by Sigma-Aldrich. Silica gel (particle size 0.040-0.064 mm, 230-400 mesh) was purchased by Macherey-Nagel. Milli-Q water was used to prepare all of the buffer solutions. The ligands 2-[[di(2-pyridyl)methyl](methyl)amino]methyl) phenol (HL1) and 2-(((di(pyridin-2-yl)methyl)amino)methyl)-4-nitrophenol (HL3) were synthesized according to the literature procedures.[S1,S2]

1.2 Instrumentation
UV-Vis spectra were recorded with an UV-Vis Varian Cary 100 for the SOD activity determination and an UV-Vis Varian Cary 50 for other measures. FT-IR spectra of the KBr pellets of the compounds were recorded on a Nicolet 5700 FT-IR instrument. Cyclic voltammetry experiments were performed using a BAS Cell C3 EC-epsilon potentiostat. A standard three-electrode electrochemical cell was used. Glassy carbon electrode (3 mm diameter, geometric surface area = 7 mm²) from BAS and a Pt wire were used respectively as working and auxiliary electrode. Potentials were referred to an Ag/AgCl/(3 M NaCl) reference electrode. Prior to each experiment, the electrode was polished with 1 µm alumina, rinsed with deionised water and wiped with a paper tissue. Potential were then reported vs NHE. ESI-MS measurements were carried out by using an Agilent Technologies MSD SL Trap mass spectrometer with ESI source. Sample solutions in water with 0.1 % v/v HCOOH were injected into the ion source without the addition of any other solvent at a flow rate of 50 µL/min. For electrospray ionization, the drying gas (nitrogen) was heated at 325 °C. Each species is indicated with the m/z value of the first peak of its isotopic cluster. The peaks in ESI-MS spectra were assigned by comparing the experimental isotopic patterns with the corresponding simulated profiles. EPR spectra were recorded on an ELEXSYS E580 spectrometer equipped with a rectangular cavity, ER4102ST, both from Bruker, Germany, and fitted with a cryostat (ESR900) and a variable-temperature controller (ITC503S), both from Oxford Instruments, UK. All experiments were performed at 50 K on samples frozen in dry ice and sealed under vacuum in quartz tubes (i.d. 3 mm, o.d. 4 mm). The experiments were performed using the following parameters: microwave frequency 9.35 GHz, microwave power 6.4 mW (attenuation 15
dB), sweep width 150 mT, center field 300 mT, conversion time 82 ms, time constant 82 ms, modulation amplitude 0.95 mT, 1024 points, 3 averages.

2. Synthetic Procedures

2.1. Synthesis of Cu$_2$L$_1$

185 mg (0.5 mmol) of Cu(ClO$_4$)$_2$·6H$_2$O and ligand 2-[[di(2-pyridyl)methyl]methylene[amino]methyl]phenol (150 mg, 0.5 mmol) were dissolved in 10 mL of methanol. After all solids were dissolved, an excess of triethylamine was added (80 µL, 0.6 mmol) and the solution turned dark green. After stirring, a formation of a green precipitate occurred. The solution was heated until boiling and gradually acetonitrile was added until complete dissolution of the solid. The solution was then let cool down. After a week green crystals were obtained, washed with methanol and ether and finally dried under vacuum. Yield: 153 mg, 56 %. UV-Vis (H$_2$O): $\lambda_{\text{max}}$/nm ($\varepsilon$/M cm$^{-1}$) 269 (2.1·10$^4$), 410 (1.0·10$^3$). FT-IR (KBr): $\nu$ (cm$^{-1}$) 3089(w), 3024(w), 3005(w), 2926(w), 2906(w), 2867(w), 2855(w), 2819(w), 1614(m), 1603(m), 1598(sh), 1574(w), 1480(s), 1453(s), 1448(sh), 1426(w), 1292(m), 1264(m), 1246(m), 1234(m), 1093(s), 984(m), 893(m), 885(m), 781(m), 768(s), 758(s), 623(s), 554(w), 543(w). ESI(+) - MS m/z calcd. for (C$_{38}$H$_{36}$Cu$_2$N$_6$O$_2$·2+·HCO$_2$) (M+HCO$_2$) 779.1, found 779.0 and (C$_{38}$H$_{36}$Cu$_2$N$_6$O$_2$·2+·ClO$_4$) (M+ClO$_4$) 833.1, found 833.0. Elemental Analysis, calcd. for C$_{38}$H$_{36}$Cl$_2$Cu$_2$N$_6$O$_{10}$: C = 48.83, H = 3.88, N = 8.99; found C = 48.65, H = 3.92, N = 8.85.

2.2. Synthesis of Cu$_2$L$_2$

75 mg (0.2 mmol) of Cu(ClO$_4$)$_2$·6H$_2$O and ligand 2-[[di(2-pyridyl)methyl]amino]methyl)phenol (60 mg, 0.2 mmol) were dissolved in 5 mL of ethanol. After all solids were dissolved, an excess of triethylamine was added (35 µL, 0.25 mmol) and the solution turned dark green. After stirring, the formation of a green precipitate occurred. The solution was heated until boiling and gradually acetonitrile was added until complete dissolution of the solid. The solution was then let cool down. After a week green crystals were obtained, washed with methanol and ether and finally dried under vacuum. Yield: 50 mg, 55 %. UV-Vis (H$_2$O): $\lambda_{\text{max}}$/nm ($\varepsilon$/M cm$^{-1}$) 265.1 (2.3·10$^4$), 397.4 (3.6·10$^3$), 667.5 (6.2·10$^2$). FT-IR (KBr): $\nu$ (cm$^{-1}$) 3239(w), 3094(w), 3070(w), 3034(sh), 2925(w), 2870(w), 1680(sh), 1658(s), 1610(s), 1597(s), 1573(m), 1482(s), 1471(s), 1452(s), 1441(s), 1389(m), 1291(w), 1273(w), 1248(m), 1098(s), 1002(m), 928(w), 882(m), 868(w), 791(w), 778(m), 758(m), 699(w), 640(w), 625(m), 598(w), 551(w), 473 (w). ESI(+) - MS m/z calcd. for (C$_{38}$H$_{32}$Cu$_2$N$_6$O$_2$·2H$^+$) (M-H$^+$) 705.1, found 705.0 (C$_{38}$H$_{32}$Cu$_2$N$_6$O$_2$·2H$^+$·HCO$_2$) (M+HCO$_2$) 751.1, found 751.0 and (C$_{38}$H$_{32}$Cu$_2$N$_6$O$_2$·2H$^+$·ClO$_4$) (M+ClO$_4$) 805.1, found 805.0. Elemental Analysis, calcd. for C$_{38}$H$_{32}$Cl$_2$Cu$_2$N$_6$O$_{10}$·DMF: C = 47.81, H = 4.01, N = 10.01; found C = 47.62, H = 4.23, N = 10.24.
2.3. Synthesis of Cu\textsubscript{2}L\textsubscript{3}\textsubscript{2}

68 mg (0.18 mmol) of Cu(ClO\textsubscript{4})\textsubscript{2}·6H\textsubscript{2}O and ligand 2-(((di(2-pyridyl)methyl)amino)methyl)-4-nitrophenol (60 mg, 0.18 mmol) were dissolved in 5 mL of ethanol. After all solids were dissolved, an excess of triethylamine was added (35 µL, 0.25 mmol) and the solution turned dark green. After stirring, the formation of a green precipitate occurred. The solution was heated until boiling and gradually DMF was added until complete dissolution of the solid. The solution was then let cool down. After a week green crystals were obtained, washed with methanol and ether and finally dried under vacuum. Yield: 80 mg, 45 %. UV-Vis (H\textsubscript{2}O): \(\lambda_{\text{max}}/\text{nm} (\varepsilon/M^{-1} \text{cm}^{-1})\) 255.9 (2.1\times10\textsuperscript{4}), 375.8 (2.3\times10\textsuperscript{3}), 652.1 (2.4\times10\textsuperscript{2}). FT-IR (KBr): \(\nu (\text{cm}^{-1})\) 3228(w), 3089(w), 2971(w), 2921(w), 1599(s), 1575(m), 1504(sh), 1478(s), 1442(m), 1332(s), 1297(s), 1263(s), 1119(sh), 1096(s), 1056(m), 1006(w), 934(w), 903(w), 840(w), 789(w), 760(w), 652(w), 624(m), 559(w), 467(w).

ESI(+)-MS \(m/z\) calcd. for \((C_{36}H_{31}Cl_{2}Cu_{2}N_{7}O_{14})^{2+} + HCO\textsubscript{2}^{-}\) 841.1, found 841.1 and \((C_{36}H_{31}Cl_{2}Cu_{2}N_{7}O_{14})^{2+} + ClO\textsubscript{4}^{-}\) 895.1, found 895.0. Elemental Analysis, calcd. for \(C_{36}H_{31}Cl_{2}Cu_{2}N_{7}O_{14}\): C = 43.38, H = 3.03, N = 11.24; found C = 43.09, H = 3.16, N = 10.92.

**Caution**: Although the salts and the complexes reported do not appear to be mechanically sensitive, perchlorates should be treated with due caution.

3. X-Ray Diffraction Analysis

Diffraction data from single crystals of dinuclear complexes [Cu\textsubscript{2}L\textsubscript{2}L\textsubscript{2}], [Cu\textsubscript{2}L\textsubscript{2}L\textsubscript{2}] and [Cu\textsubscript{2}L\textsubscript{3}L\textsubscript{2}] were collected by the rotating crystal method using synchrotron radiation at the XRD1 beam-line of the Elettra Synchrotron, Trieste, Italy. In all cases, a single crystal of the complex was dipped in the paratone cryoprotectant and flash-frozen to 100 K in a stream of N\textsubscript{2} vapour. Diffraction images were indexed and integrated using the XDS package and the resulting data sets were scaled using XSHELL.\textsuperscript{[S3,S4]} The structure of [Cu\textsubscript{2}L\textsubscript{2}L\textsubscript{2}] was solved in space group P-1 with SHELXS (Direct Methods); while the structures of complexes [Cu\textsubscript{2}L\textsubscript{2}L\textsubscript{2}] and [Cu\textsubscript{2}L\textsubscript{3}L\textsubscript{2}] were solved in space groups P-1 and P2\textsubscript{1}/a, respectively, with SIR-2014 (VLD and Patterson Phasing, respectively). Refinements were implemented with SHELXL-14, operating through the WinGX GUI, by full-matrix least-squares (FMLS) methods on F\textsuperscript{2}.\textsuperscript{[S5-S7]} Thermal parameters of all non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed at the geometrically calculated positions and refined using the riding model. Crystal data and final refinement details for the three complexes are reported in Table S1. The asymmetric unit of [Cu\textsubscript{2}L\textsubscript{2}L\textsubscript{2}] contains one half of the dinuclear dimer, a perchlorate ion and two acetonitrile solvent molecules. Extinction correction was applied using the card EXTI in SHELXL-14.\textsuperscript{[S6]} The asymmetric unit of [Cu\textsubscript{2}L\textsubscript{2}L\textsubscript{2}] contains one half of the dinuclear dimer, which includes a DMF molecule to complete the coordination sphere, a perchlorate anion and half an ethanol molecule. All atoms of the perchlorate anion are disordered in two positions and the occupancies were refined freely to 0.73/0.27. DFIX and DANG restraints were applied, using idealised tetrahedral bond lengths and angles as targets, to maintain the tetrahedral
geometry. The ethanol molecule lays on an inversion centre and was refined at half occupancy. DFIX and DANG instructions were used to restrain distances and angles. EADP restraints were used to restrain the thermal parameters of selected atoms of the perchlorate ions and DMF molecule, while thermal parameters of the ethanol molecule were restrained with RIGU, SIMU and ISOR instructions. A FLAT instruction was used to maintain all the non-hydrogen atoms of the DMF molecule on a single plane. Analogously to $[\text{Cu}_2\text{L}_2^2]$, the asymmetric unit of $[\text{Cu}_3\text{L}_3^2]$ contains one half of the dinuclear dimer, which includes a dimethylformamide (DMF) molecule to complete the coordination sphere, a perchlorate anion and half an ethanol molecule. During refinement restraints were applied to disordered and/or partially occupied atoms, as outlined below. The DMF molecule in the coordination sphere is disordered in two positions, with the coordinating oxygen atom common to both disordered fragments at full occupancy. The occupancies of the disordered atoms were freely refined to 0.54/0.46. Bond lengths and angles were restrained with DFIX and DANG instructions using the idealised values as targets. The perchlorate anion is disordered in two positions around a 3-fold common axis and the occupancies of the disordered atoms were freely refined to 0.74/0.26. Bond lengths and angles were restrained with DFIX instructions using the idealised values as targets. Finally, the ethanol molecule lays on an inversion centre and was refined at half occupancy. Distances and angles were restrained with DFIX and DANG instructions using idealised values as targets. EADP instructions were used to restrain thermal parameters of selected disordered atoms of the perchlorate and DMF fragments.

Table S1: Crystallographic data for complexes $[\text{Cu}_2\text{L}_2^2]$, $[\text{Cu}_4\text{L}_2^2]$ and $[\text{Cu}_3\text{L}_3^2]$.

| Property                      | $[\text{Cu}_2\text{L}_2^2]$ | $[\text{Cu}_4\text{L}_2^2]$ | $[\text{Cu}_3\text{L}_3^2]$ |
|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Formula                       | $\text{C}_{38}\text{H}_{36}\text{N}_6\text{O}_2\text{Cu}_2$ | $\text{C}_{42}\text{H}_{44}\text{N}_{10}\text{O}_8\text{Cu}_2$ | $\text{C}_{42}\text{H}_{46}\text{N}_8\text{O}_4\text{Cu}_2$ |
| Temperature (K)               | 100                           | 100                           | 100                           |
| Wavelength (Å)                | 0.8                           | 0.7                           | 0.7                           |
| Crystal system                | Triclinic                     | Triclinic                     | Monoclinic                    |
| Space group                   | P-1                           | P-1                           | P21/a                         |
| a (Å)                         | 8.911 (2)                     | 8.704 (3)                     | 12.048 (9)                    |
| b (Å)                         | 11.282 (2)                    | 12.259 (2)                    | 18.859 (6)                    |
| c (Å)                         | 13.011 (3)                    | 12.347 (1)                    | 12.560 (10)                   |
| α (°)                         | 111.76 (3)                    | 108.18 (2)                    | 90                            |
| β (°)                         | 95.18 (3)                     | 97.25 (3)                     | 116.69 (6)                    |
| γ (°)                         | 101.80 (3)                    | 101.81 (3)                    | 90                            |
| V (Å³)                        | 1169.2 (5)                    | 1199.3 (5)                    | 2550 (3)                      |
| Z, ρcalc (g.mm⁻³)             | 1, 1.561                      | 1, 1.522                      | 2, 1.549                      |
| μ (mm⁻¹)                      | 1.446                         | 1.025                         | 0.976                         |
| F (000)                       | 566                           | 568                           | 1224                          |
| Data collection θ range       | 3.359 – 29.966                | 1.747 - 25.993                | 2.080 – 33.042                |
| Refl. Collected / unique      | 7080 / 3992                   | 15469 / 4503                  | 25463 / 8639                  |
| Rint                          | 0.0112                        | 0.0650                        | 0.0379                        |
| Completeness (%)              | 84.1                          | 91.5                          | 85.5                          |
| Data/Restraints/Parameters    | 3992 / 0 / 320                | 4503 / 64 / 338               | 8639 / 39 / 369               |
| GooF                          | 1.185                         | 1.074                         | 1.029                         |
| $R_1$, wR₂ (|>2σ(I)|)        | 0.0328 / 0.0903               | 0.0784 / 0.2122               | 0.0569 / 0.1637               |
| $R_1$, wR₂ all data           | 0.0328 / 0.0904               | 0.0916 / 0.2273               | 0.0772 / 0.1842               |
Figure S1. Crystallographic structures of [CuL2]\(2\) (a), [CuL2]\(2\) (b) and [CuL2]\(2\) (c). For clarity, counter ions and solvent molecules which are not part of the Cu coordination spheres have been omitted. The atom numbering scheme for [CuL2]\(2\) and [CuL2]\(2\) is the same as that shown for [CuL2]\(2\), with the exception of oxygen atoms O4 and the inversion related O4’ of the perchlorate ions and the O2 and O2’ atoms of the DMF molecules.
Table S2: Bond lengths, bond angles and interatomic distances around the Cu – Cu sites in complexes \([\text{Cu}_2\text{L}^1_2]\), \([\text{Cu}_2\text{L}^2_2]\) and \([\text{Cu}_2\text{L}^3_2]\). Atom numbering scheme is reported in Figure S1.

| Distances (Å) and Angles (°) | \(\text{Cu}_2\text{L}^1_2\) | \(\text{Cu}_2\text{L}^2_2\) | \(\text{Cu}_2\text{L}^3_2\) |
|-------------------------------|------------------|------------------|------------------|
| **Equatorial Distances**      |                  |                  |                  |
| \(\text{Cu}1 – \text{N}1\)   | 1.9993(18)       | 2.020(4)         | 2.018(3)         |
| \(\text{Cu}1 – \text{N}2\)   | 2.0315(16)       | 1.998(4)         | 1.980(2)         |
| \(\text{Cu}1 – \text{O}1\)   | 1.9614(17)       | 1.988(3)         | 2.011(2)         |
| \(\text{Cu}1 – \text{O}1’\)  | 1.9578(14)       | 1.951(3)         | 1.952(2)         |
| \(\text{Cu}1 ----- \text{Cu}1’\) | 3.0072(10)       | 3.015(1)         | 3.033(3)         |
| **Cis Angles**                |                  |                  |                  |
| \(\text{N}1 – \text{Cu}1 – \text{N}2\) | 81.16(7)         | 80.72(16)        | 81.52(11)        |
| \(\text{O}1 – \text{Cu}1 – \text{O}1’\) | 79.78(7)         | 80.09(14)        | 80.14(9)         |
| \(\text{N}1 – \text{Cu}1 – \text{O}1’\) | 105.09(7)        | 106.01(16)       | 106.19(10)       |
| \(\text{N}2 – \text{Cu}1 – \text{O}1\) | 93.88(6)         | 93.40(14)        | 92.50(10)        |
| \(\text{N}3 – \text{Cu}1 – \text{N}1\) | 86.10(7)         | 81.64(17)        | 82.94(9)         |
| \(\text{N}3 – \text{Cu}1 – \text{N}2\) | 78.93(6)         | 74.23(16)        | 76.35(8)         |
| \(\text{N}3 – \text{Cu}1 – \text{O}1\) | 102.06(6)        | 100.65(15)       | 101.47(7)        |
| \(\text{N}3 – \text{Cu}1 – \text{O}1’\) | 102.31(6)        | 103.29(15)       | 101.83(8)        |
| \(\text{“O”} – \text{Cu}1 – \text{O}1\) b | 92.58 (7)        | 92.07 (17)       | 89.24 (9)        |
| \(\text{“O”} – \text{Cu}1 – \text{O}1’\) b | 90.20 (7)        | 91.53 (17)       | 95.31 (9)        |
| \(\text{“O”} – \text{Cu}1 – \text{N}1\) | 78.27 (7)        | 84.27 (19)       | 84.32 (10)       |
| \(\text{“O”} – \text{Cu}1 – \text{N}2\) | 90.05 (7)        | 92.30 (18)       | 88.15 (11)       |
| \(\text{Cu}1-\text{O}1-\text{Cu}1’\) | 100.22(7)        | 99.91(14)        | 99.86(9)         |
| **Axial Distances**           |                  |                  |                  |
| \(\text{Cu}1-\text{N}3\)     | 2.3265(14)       | 2.525 (4)        | 2.438(2)         |
| \(\text{Cu}1-“\text{O”}\) b  | 2.9893(19)       | 2.446 (5)        | 2.485 (3)        |
| **Trans Angles**              |                  |                  |                  |
| \(\text{N}1 – \text{Cu}1 – \text{O}1\) | 169.54(6)        | 172.92(16)       | 171.33(8)        |
| \(\text{N}2 – \text{Cu}1 – \text{O}1’\) | 173.65(5)        | 172.55(14)       | 171.80(9)        |
| \(\text{N}3 – \text{Cu}1 – “\text{O”}\) b | 162.19 (6)       | 161.87 (18)      | 161.20 (8)       |

a Symmetry related atoms are distinguished by the prime symbol.

b In the case of \(\text{Cu}_2\text{L}^1_2\) “O” is an oxygen atom of a perchlorate ion, while for the other two complexes it is the oxygen atom of a DMF molecule.
Figure S2. ORTEP views of the structures of \([\text{Cu}_2\text{L}_2]\) (a), \([\text{Cu}_2\text{L}_2]\) (b) and \([\text{Cu}_2\text{L}_2]\) (c). Carbon atoms are depicted as grey ellipsoids, oxygen atoms as red ellipsoids, nitrogen atoms as pink ellipsoids, chlorine atoms as green ellipsoids and copper atoms as orange ellipsoids. Ellipsoid probability is set to 50%. Hydrogen atoms have been omitted for clarity.
4. UV-Vis Spectra

**Figure S3.** UV-Vis spectra of Cu$_2$L$_2$, in phosphate buffer 50 mM, pH 7.8 (red line), in CH$_3$CN (black line).

**Figure S4.** UV-Vis spectra of Cu$_2$L$_2$ in phosphate buffer 50 mM pH = 7.8, $\lambda_{max}$/nm ($\varepsilon$/M·cm$^{-1}$) 410 (1.3·10$^3$) (LMCT band) and 675 (2.9·10$^2$) (d-d band) (red line), in CH$_3$CN (black line) 391 (2.9·10$^3$) (LMCT band) and 670 (3.7·10$^2$) (d-d band).
Figure S5. UV-Vis spectra of \( \text{HL}^2 \), \( \lambda_{\text{max}}/\text{nm} \) \( (\varepsilon/\text{M}^{-1} \text{cm}^{-1}) \) 261.5 (7.1 \times 10^3), 266.7 (6.5 \times 10^3) (\text{red line}) and \( \text{HL}^3 \) 261.9 (7.1 \times 10^3), 410.9 (1.0 \times 10^4) (\text{black line}) in phosphate buffer 50 mM pH 7.8.

Figure S6. UV-vis spectrum of \( \text{Cu}_2\text{L}^2 \) in phosphate buffer 50 mM pH = 7.8, \( \lambda_{\text{max}}/\text{nm} \) \( (\varepsilon/\text{M}^{-1} \text{cm}^{-1}) \) 265 (2.3 \times 10^4), 397 (1.7 \times 10^3) (LMCT band) and 668 (2.9 \times 10^2) (d-d band). The inset highlights the LMCT and d-d bands.
Figure S7. UV-vis spectrum of $\text{Cu}_2\text{L}_2$ in phosphate buffer 50 mM pH = 7.8, $\lambda_{\text{max}}$/nm ($\varepsilon$/M cm$^{-1}$) 256 (2.1·10$^4$), 376 (2.3·10$^4$) and 670 (1.7·10$^2$) (d-d band). The inset highlights the LMCT and d-d bands.

Figure S8. Comparison of the UV-Vis spectra of $\text{Cu}_2\text{L}_1^1$, $\text{Cu}_2\text{L}_2^2$, and $\text{Cu}_2\text{L}_3^3$ in phosphate buffer 50 mM pH 7.8. The inset highlights the LMCT and d-d bands.
5. FT-IR Spectra

Figure S9. FT-IR spectrum (KBr pellet) of 2-[[di(2-pyridyl)methyl](methyl)amino]methyl]phenol (HL1).

Figure S10. FT-IR spectrum (KBr pellet) of 2-[[di(2-pyridyl)methyl]amino]methyl]phenol (HL2).
Figure S11. FT-IR spectrum (KBr pellet) of the complex \([\text{Cu}_2\text{L}^2](\text{ClO}_4)_2\).

Figure S12. FT-IR spectrum (KBr pellet) of the complex \([\text{Cu}_2\text{L}^2](\text{ClO}_4)_2\).
Figure S13. FT-IR spectrum (KBr pellet) of 2-((di(2-pyridyl)methylamino)methyl)-4-nitrophenol (HL).

Figure S14. FT-IR spectrum (KBr pellet) of the complex CuL2(ClO4)2.
6. Cyclic Voltammograms

CV experiments were performed using a three-electrode setup system in a small volume cell. Glassy carbon electrode (3 mm diameter, geometric surface area = 7 mm$^2$) from BAS and a Pt wire were used respectively as working and auxiliary electrode. Potentials were referred to an Ag/AgCl/(3 M NaCl) reference electrode; scan rate of 50 mV/s. Prior to each experiment, the electrode was polished with 1 μm alumina, rinsed with deionised water and wiped with a paper tissue. In a typical experiment, a 0.5-1 mM solution of the copper compound in 0.05 M phosphate buffer, pH = 7.8, with 0.1 M NaCl as support electrolyte was purged with nitrogen and then analysed. Potential were then reported vs NHE.

Figure S15. CV of 2-[[di(2-pyridyl)methyl](methyl)amino]methyl)phenol (HL$^1$) (1 mM) in CH$_3$CN (TBACIO$_4$ 0.1 M); $E^1_c$ = -1285 mV, $E^1_a$ = -772 mV, $E^2_c$ = -599 mV, $E^2_a$ = 197 mV, $E^3_c$ = 654 mV, $E^3_a$ = 1133 mV and $E^4_a$ =1690 mV.$^{[58]}$
Figure S16. CV of Cu$_2$L$_2$(0.5 mM) in CH$_3$CN (TBACIO$_4$ 0.1 M), $E_c$ = -136 mV.

Figure S17. CV of Cu$_2$L$_2$(0.5mM) in phosphate buffer 50 mM (pH = 7.8, TEABF$_4$ 0.1 M), $E_{1/2}$ = -161 mV, $\Delta E$ =350 mV.
Figure S18. Cyclic voltammetry of Cu₂L₂ (1mM) in acetonitrile (TBAClO₄ 0.1M), E₁c = 296 mV, E₂c = 635 mV, E₁a = 1060 mV, mV, E₂a = 1380 mV, and E₃a = 1780 mV (vs NHE).

Figure S19. CV of the oxidation of Cu₂L₂ (1 mM) in CH₃CN (TBAClO₄ 0.1 M) with increasing aliquots of water.
Figure S20. CV of the oxidation of Cu₂L₁ \( (1 \text{ mM}) \) in phosphate buffer 50 mM (pH 7.8, TEABF₄ 0.1 M), \( E_a = 1.11 \text{ V} \).

Figure S21. CV of 2-\{[(2-pyridyl)methyl]amino|methyl|phenol (HL₂) \( (1 \text{ mM}) \) in CH₃CN (TBACIO₄ 0.1 M); \( E^{1c} = -758 \text{ mV}, E^{1a} = -573 \text{ mV}, E^{2a} = 231 \text{ mV}, E^{1} = 621 \text{ mV}, E^{1a} = 1079 \text{ mV} \) and \( E^{2a} = 1635 \text{ mV} \).
Figure S22. CV of Cu$_2$L$_2$(0.5 mM) in CH$_3$CN (TEABF$_4$ 0.1 M), $E^1_c$ = -96 mV and $E^2_c$ = -465 mV.

Figure S23. CV of Cu$_2$L$_2$(0.5 mM) in phosphate buffer 50 mM (pH = 7.8, TEABF$_4$ 0.1 M), $E_{1/2}$ = -55 mV, $\Delta E = 116$ mV.
Figure S24. Cyclic voltammetry of $\text{Cu}_2\text{L}_2^1$ (1 mM) in acetonitrile (TEABF$_4$ 0.1M), with $E_{1_a}^1 = 1281$ mV and $E_{2_a}^2 = 1620$ mV. $E_{3_a}^3 = 1775$ mV.

Figure S25. CV of the oxidation of $\text{Cu}_2\text{L}_2^1$ (1 mM) in CH$_3$CN (TEABF$_4$ 0.1 M) with increasing aliquots of water.
Figure S26. CV of the oxidation of Cu$_2$L$_2$ (1 mM) in phosphate buffer 50 mM (pH 7.8, TEABF$_4$ 0.1 M), $E_a = 1.07$ V.

Figure S27. CV of 2-([(di(2-pyridyl)methyl]amino)methyl)-4-nitrophenol (HL$_3$) (1 mM) in CH$_3$CN (TEABF$_4$ 0.1 M); $E^4_c = -1600$ mV, $E^4_a = -1499$ mV, $E^1_c = -916$ mV, $E^1_a = 1299$ mV, $E^2_a = 1452$ mV and $E^3_a = 1727$ mV.
Figure S28. CV of Cu\(_2\)L\(_3\) (0.5 mM) in CH\(_3\)CN (TEABF\(_4\) 0.1 M), \(E^1_c = 62\) mV and \(E^2_c = -273\) mV.

Figure S29. CV of Cu\(_2\)L\(_3\) (0.5 mM) in phosphate buffer 50 mM (pH = 7.8, TEABF\(_4\) 0.1 M), \(E_{1/2} = 60\) mV, \(\Delta E = 450\) mV.
Figure S30. Cyclic voltammetry of Cu$_2$L$_3^2$ (1 mM) in acetonitrile (TEABF$_4$ 0.1M), with $E^1_a = 1.56$ V and $E^2_a = 2.19$ V (vs NHE).

Figure S31. CV of the oxidation of Cu$_2$L$_3^2$ (1 mM) in CH$_3$CN (TEABF$_4$ 0.1 M) with increasing aliquots of water.
Figure S32. CV of the oxidation of Cu$_2$L$_2$ (1 mM) in phosphate buffer 50 mM (pH 7.8, TEABF$_4$ 0.1 M), $E^1_a = 1.31$ V and $E^2_a = 1.71$ V (vs NHE).

7. ESI-MS

Figure S33. ESI-MS spectrum of Cu$_2$L$_2$ in acetonitrile, where 833.0 m/z correspond to the molecular ion [Cu$_2$L$_2$+ClO$_4$]$^+$ and 367.1 m/z to the fragment [CuL]$^+$. 
Figure S34. ESI-MS spectrum of CuL12 in acetonitrile 90 min after the addition of H2O2 30 mM, where 833.0 m/z correspond to the molecular ion [CuL12+ClO4]+ and 367.1 m/z to the fragment [CuL]1+ (* eluent impurity).

Figure S35. ESI-MS spectrum of CuL12 in water, where 779.0 correspond to the molecular ion [CuL12+HCO2]+, 751.1 to [CuL12+OH]+ and 833.0 m/z [CuL12+ClO4]+ and 367.1 m/z to the fragment [CuL]1+.
Figure S36. ESI-MS spectrum of CuL₂ in borate buffer 50 mM, 25 min after the addition of H₂O₂ 30 mM, where 657.0 m/z correspond to the dinuclear copper specie \([\text{Cu}_2\text{L}^2\text{O}_x\text{L}^2\text{Cl}^\text{O}_x]\)⁺ and 384.0 to the inactive mononuclear copper(III) specie \([\text{CuL}^3\text{OH}]^\text{+}\)⁺.

Figure S37. ESI-MS spectrum of CuL₂ in borate buffer 50 mM, 240 min after the addition of H₂O₂ 30 mM, where 384.0 correspond to the inactive mononuclear copper(III) specie \([\text{CuL}^3\text{OH}]^\text{+}\)⁺.
Figure S38. ESI-MS spectrum of Cu_L_2 in borate buffer 50 mM with NaBr 50 mM, where 813.0 m/z correspond to the molecular ion \([\text{Cu}_2L_2+\text{Br}]^+\) and 367.1 m/z to the fragment \([\text{CuL}]^+\).

Figure S39. ESI-MS spectrum of Cu_L_2 in borate buffer 50 mM with NaBr 50 mM, 80 min after the addition of \(\text{H}_2\text{O}_2\) 30 mM where 657.0 and 784.9 m/z correspond respectively to the molecular ions \([\text{Cu}_2L_2L_2^{\text{Cl}_2}+2\text{Br}]^+\) and \([\text{Cu}_2L_2L_2^{\text{O}_2}\text{Cl]}^+\) and 420.9 m/z correspond to the inactive specie \([\text{Cu}^{\text{O}}(\text{H}_2\text{O})_2+\text{Br}+\text{HCO}_2\text{H}]^+\).
Figure S40. ESI-MS spectrum of CuL$_2$ in borate buffer 50 mM with NaBr 50 mM, 240 min after the addition of H$_2$O$_2$ 30 mM where 784.9 m/z correspond to the molecular ion [CuL$^2$Cl$^2$+2Br]$^+$ and 420.9 m/z to the inactive specie [CuL$^2$(H$_2$O)$_2$+Br+HCO$_2$H]$^+$. 

Figure S41. ESI-MS spectrum of CuL$_2$ in acetonitrile, where 805.0 m/z correspond to the molecular ion [CuL$^2$Cl$^2$+ClO$_4$]$^+$, 705.0 m/z to [CuL$^2$-H]$^+$ and 353.1 m/z to the fragment [CuL]$^+$. 
Figure S42. ESI-MS spectrum of CuL$_2$ in water, where 805.0 m/z correspond to the molecular ion [CuL$_2$+ClO$_4$]$^+$, 751.0 m/z to [CuL$_2$+HCO$_2$]$^+$ and 353.1 m/z to the fragment [CuL]$^+$.

Figure S43. ESI-MS spectrum of CuL$_3$ in acetonitrile, where 895.0 m/z correspond to the molecular ion [CuL$_3$+ClO$_4$]$^+$, 841.1 m/z to [CuL$_3$+HCO$_2$]$^+$ and 398.1 m/z to the fragment [CuL]$^+$. 
Figure S44. ESI-MS spectrum of Cu$_2$L$_3$ in water, where 895.0 m/z correspond to the molecular ion [Cu$_2$L$_3$+ClO$_4$]$^+$, 841.2 m/z to [Cu$_2$L$_3$+HCO$_3$]$^+$ and 398.1 m/z to the fragment [CuL]$^+$.

Figure S45. ESI-MS spectrum of Cu$_2$L$_2$ in borate buffer 50 mM, 30 min after the addition of H$_2$O$_2$ 30 mM, where 353.2 and 444.1 and correspond to the inactive mononuclear copper species. For details see Table S3 and Figure S51.
Figure S46. ESI-MS spectrum of Cu$_2$L$_2$ in borate buffer 50 mM, 30 min after the addition of H$_2$O$_2$ 30 mM, where 396.1 and 489.1 correspond to the inactive mononuclear copper species. For details see Table S3 and Figure S51.

Figure S47. Comparison between the experimental (left) and calculated (right) isotopic pattern for [Cu$_2$L$_2$O$^\text{aq}$]+ (m/z = 657.0).
Figure S48. Comparison between the experimental (left) and calculated (right) isotopic pattern for $[\text{Cu}_2\text{L}\text{L}^\text{O} + 2\text{Br}]^+ \quad (m/z = 784.9)$.

Figure S49. Comparison between the experimental (left) and calculated (right) isotopic pattern for $[\text{CuL}^\text{O}](\text{OH})^+ \quad (m/z = 384.0)$.

Figure S50. Comparison between the experimental (left) and calculated (right) isotopic pattern for $[\text{CuL}^\text{O}(\text{H}_2\text{O}) + \text{Br} + \text{HCO}_2\text{H}]^+ \quad (m/z = 420.9)$. 

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Figure S51. Schematic representation of the ligand oxidation during the reaction of \(\text{Cu}_2\text{L}_2^{2+}\) and \(\text{Cu}_2\text{L}_3^{2+}\) (200 \(\mu\text{M}\)) with \(\text{H}_2\text{O}_2\) (30 mM) in BBS 50 mM.

Table S3. ESI-MS(+) molecular peaks for the \(\text{Cu}_2\text{L}_2^{2+}\) molecular ions.

| Molecular ions | Assignment | Calculated (m/z) | Found (m/z) |
|----------------|------------|------------------|-------------|
| \([\text{Cu}_2\text{L}_2^{2+}]^{2+}\) (1) | \([\text{Cu}_2\text{L}_2^{2+} + \text{OH}]^{+}\) | 751.2 | 751.1 |
| | \([\text{Cu}_2\text{L}_2^{2+} + 
\text{HCO}_2]^{+}\) | 779.2 | 779.1 |
| | \([\text{Cu}_2\text{L}_2^{2+} + \text{Br}]^{+}\) | 813.1 | 813.0 |
| | \([\text{Cu}_2\text{L}_2^{2+} + \text{ClO}_4]^{+}\) | 833.1 | 833.0 |
| \([\text{Cu}_2\text{L}_2^{2+}]^{3+}\) (2) | \([\text{Cu}_2\text{L}_2^{2+} + \text{OH}]^{+}\) | 657.1 | 657.0 |
| \([\text{Cu}_2\text{L}_2^{2+}]^{3+}\) (2) | \([\text{Cu}_2\text{L}_2^{2+} + 2\text{Br}]^{+}\) | 785.0 | 784.9 |
| \([\text{Cu}_2\text{L}_2^{2+}]^{3+}\) (3) | \([\text{Cu}_2\text{L}_2^{2+} + \text{OH}]^{+}\) | 384.1 | 384.0 |
| \([\text{Cu}_2\text{L}_2^{2+}]^{3+}\) (3) | \([\text{Cu}_2\text{L}_2^{2+} + \text{HCO}_2]^{+}\) | 420.9 | 421.0 |
| \([\text{Cu}_2\text{L}_2^{2+}]^{2+}\) | \([\text{Cu}_2\text{L}_2^{2+} + \text{HCO}_2]^{+}\) | 751.1 | 751.0 |
| | \([\text{Cu}_2\text{L}_2^{2+} + \text{ClO}_4]^{+}\) | 805.1 | 805.0 |
| \([\text{Cu}_2\text{L}_2^{2+}]^{+}\) | \([\text{Cu}_2\text{L}_2^{2+} + \text{OH}]^{+}\) | 353.1 | 353.2 |
| | \([\text{Cu}_2\text{L}_2^{2+} - 2\text{H}]^{+}\) | 351.1 | 351.1 |
| \([\text{Cu}_2\text{L}_2^{2+}]^{+}\) | \([\text{Cu}_2\text{L}_2^{2+} + \text{Br}-2\text{H}]^{+}\) | 444.0 | 444.1 |
| \([\text{Cu}_2\text{L}_2^{2+}]^{+}\) | \([\text{Cu}_2\text{L}_2^{2+} - 2\text{H}]^{+}\) | 396.1 | 396.1 |
| \([\text{Cu}_2\text{L}_2^{2+}]^{+}\) | \([\text{Cu}_2\text{L}_2^{2+} + \text{OH} + \text{H}_2\text{O} - 2\text{H}]^{+}\) | 431.1 | 431.1 |

Exact mass calculated for the molecular ions: \([\text{Cu}_2\text{L}_2^{2+}] = 734.2; [\text{Cu}_2\text{L}_2^{2+} + \text{OH}]^{+} = 641.1; [\text{Cu}_2\text{L}_2^{2+} + \text{Br}]^{+} = 627.1; [\text{Cu}_2\text{L}_2^{2+} + \text{ClO}_4]^{+} = 260.0; [\text{Cu}_2\text{L}_2^{2+}] = 706.1; [\text{Cu}_2\text{L}_2^{2+} + \text{H}_2\text{O} - 2\text{H}]^{+} = 353.1; [\text{Cu}_2\text{L}_2^{2+} + \text{Br}]^{+} = 398.1; [\text{Cu}_2\text{L}_2^{2+} + \text{OH} + \text{H}_2\text{O} - 2\text{H}]^{+} = 412.1. The subtraction of two protons (-2H) indicates the formation of the corresponding ligand imine.
8. SOD-like Activity

SOD-like activity of the complexes was measured by using the cyt c assay, described by McCord and Fridovich, with some modifications.\(^{[59]}\) Screening of catalysts as SOD-mimicking systems was performed by spectrophotometric analysis of the inhibition of the superoxide-dependent reduction of the cyt c chromophore to ferricythocrome (Figure S52).

![Diagram of cytchrome c assay for SOD activity](image)

The superoxide radical anions was generated by the xanthine/xanthine oxidase system. In all experiments, the reaction mixture was prepared with 40 µM xanthine, 10 µM cyt c, catalase 15 µg/ml, 50 mM phosphate buffer (pH=7.80) and xanthine oxidase 0.0053 U/ml. Catalyst solutions (64-550 nM) were prepared upon dilution of a stock solution in water. Possible interference through inhibition of the xanthine/xanthine oxidase reaction by test compounds was examined by following the rate of urate accumulation at 295 nm in the absence of cyt c.\(^{[59]}\) The concentration of the stock catalyst solutions was chosen in order to obtain approximately an inhibition interval of the superoxide-dependent reduction of the cyt c between 40-60 %. Among standard conditions the apparent rate constant, \(k_{McF}\), can be determined from the IC\(_{50}\) value as \(k_{McF} = k_{cyt}[cyt]/IC_{50}\) (where \(k_{cyt}\) is \(2.6 \times 10^5\) M\(^{-1}\) s\(^{-1}\)). Each experiment was performed in triplicate.
Figure S53. Plot of inhibition of cyt c reduction versus $[\text{CuL}_2^1]$ in 50 mM phosphate buffer at pH 7.8, 25°C, 40 μM xanthine, 2 nM xanthine oxidase.

Figure S54. Plot of inhibition of cyt c reduction versus $[\text{CuL}_2^2]$ in 50 mM phosphate buffer at pH 7.8, 25°C, 40 μM xanthine, 2 nM xanthine oxidase.
Figure S55. Plot of inhibition of cyt c reduction versus $[\text{Cu}_2\text{L}^3\text{]}_2$, in 50 mM phosphate buffer at pH 7.8 25°C, 40 μM xanthine, 2 nM xanthine oxidase.

9. CAT-like activity

CAT-like activity was determined by adding to a solution of $\text{H}_2\text{O}_2$ (30 mM) in BBS 50 mM (pH=7.8) or Krebs-Henseleit (KH) buffer (pH=7.4) (12 ml), 300 μL of a 8 mM acetonitrile solution of the $\text{Cu}_2\text{L}^x_2$ complex to start the dismutation reaction. The reactor was maintained at 25 °C by a circulating thermostat, and the progress of reaction was determined by monitoring the pressure developed by molecular oxygen generated from dismutation of hydrogen peroxide into a closed vessel. The amount of $\text{O}_2$ was determined by continuous detection of pressure variation, through a pressure transducer. Initial rates were calculated by linear regression of data within 10 % $\text{H}_2\text{O}_2$ conversion. Kinetic runs were performed in triplicate. Control experiments performed without the $\text{Cu}_2$-based catalyst, confirmed that no oxygen evolution is detected from the buffer solution in the presence of $\text{H}_2\text{O}_2$.\textsuperscript{[510]}
Figure S56. O₂ evolution kinetics by Cu₂L₁₂ (200 µM) upon incubation with H₂O₂ (30 mM) at 25°C in borate buffer (50 mM, pH=7.8).

Figure S57. O₂ evolution kinetics by Cu₃L₁₂ (200 µM) upon incubation with H₂O₂ (30 mM) at 25°C in KH buffer (pH = 7.4).
Figure S58. $O_2$ evolution kinetics by $\text{Cu}_2\text{L}_2^2$ (200 µM) upon incubation with $\text{H}_2\text{O}_2$ (30 mM) at 25°C in phosphate buffer (20 mM, pH = 7.8).

Figure S59. $O_2$ evolution kinetics by $\text{Cu}_2\text{L}_2^2$ and $\text{Cu}_2\text{L}_3^3$ (200 µM) upon incubation with $\text{H}_2\text{O}_2$ (30 mM) at 25°C in KH buffer (pH=7.4).
Figure S60. O₂ evolution kinetics by Cu²⁺ (400 µM) upon incubation with H₂O₂ (30 mM) at 25°C in borate buffer (50 mM, pH=7.8).

Figure S61. O₂ evolution kinetics by CuL₁₂ (200 µM) upon incubation with H₂O₂ (30 mM) at 25°C in acetonitrile.
Figure S62. Kinetics profile of Cu$_2$L$_1$ (200 µM) degradation with 30 mM H$_2$O$_2$ in acetonitrile, based on the molecular peak [Cu$_2$L$_1$ + ClO$_4$]$^-$ (m/z = 833.0).

Figure S63. O$_2$ evolution kinetics by incubation of H$_2$O$_2$ (30 mM) at 25°C in borate buffer (50 mM, pH=7.8) with different concentration of NaBr.
Figure S64. Initial lag phase in O$_2$ evolution kinetics by Cu$_2$L$_{12}$ (200 µM) upon incubation with H$_2$O$_2$ (30 mM) at 25°C in borate buffer (50 mM, pH = 7.8) in presence of different concentration of NaBr.

Figure S65. Kinetics profile of Cu$_2$L$_{12}$ (200 µM) degradation with 30 mM H$_2$O$_2$ in borate buffer (50 mM, pH = 7.8).
Figure S66. Dependence of the reaction rate of O$_2$ production with Cu$_2$L$_2^+$ (200 µM) in borate buffer (50 mM, pH 7.8) in presence of NaBr at different concentration.

Figure S67. O$_2$ evolution kinetics by Cu$_2$L$_2^+$ (200 µM) upon incubation with H$_2$O$_2$ (17 mM) at 25°C in borate buffer (50 mM, pH=7.8) with 0-100 NaBr.
Figure S68. O₂ evolution kinetics by Cu₂L₂² (200 µM) upon incubation with H₂O₂ (17 mM) at 25°C in borate buffer (50 mM, pH=7.8) with 0-100 NaBr.

Table S4. Dependence of the reaction rate of O₂ production with Cu₂L₂² and Cu₂L₃² (200 µM) in presence of NaBr at different concentrations in BBS (50 mM, pH 7.8), H₂O₂ (17 mM).

| [NaBr] (mM) | R_max* (uM O₂/s) | Yield (%) | TON |
|-------------|------------------|-----------|-----|
| Cu₂L₂²      |                  |           |     |
| 0           | 1.8              | 70        | 58  |
| 50          | 2.8              | 87        | 73  |
| 100         | 3.4              | 93        | 79  |
| Cu₂L₃²      |                  |           |     |
| 0           | 2.2              | 72        | 61  |
| 50          | 4.2              | 95        | 80  |
| 100         | 7.4              | >95b      | 83b |

*R_max were obtained by linear regression of data within 10% H₂O₂ conversion, the estimated errors are within ± 10%. A small overestimation of the Yield and TON values is attributed to the slow reaction occurring between Br⁻ and H₂O₂ (see Figure S63).
Figure S69. Effect of the \( \text{H}_2\text{O}_2 \) concentration on the disproportionation rate by CuL\(^{12} \) (200 µM) at 25 °C in a borate buffer (50 mM, pH=7.8).

Figure S70. \( \text{O}_2 \) evolution kinetics by CuL\(^{12} \) (200 µM) upon incubation with \( \text{H}_2\text{O}_2 \) (10 mM) at 25°C in borate buffer (50 mM, pH=7.8).
Figure S71. O₂ evolution kinetics by CuL₂ (200 µM) upon incubation with H₂O₂ (60 mM) at 25°C in borate buffer (50 mM, pH=7.8).

Figure S72. O₂ evolution kinetics by CuL₂ (200 µM) upon incubation with H₂O₂ (120 mM) at 25°C in borate buffer (50 mM, pH=7.8).
Figure S73. O₂ evolution kinetics by CuL₂ (200 µM) upon incubation with H₂O₂ (360 mM) at 25°C in borate buffer (50 mM, pH=7.8).

Figure S74. Comparison between the O₂ evolution kinetics by CuL₂ (200 µM) upon incubation with H₂O₂ (360 mM, black) and free copper (400 µM, red) upon incubation with H₂O₂ (30 mM) at 25°C in borate buffer (50 mM, pH=7.8).
Figure S75. Linear dependence of pseudo-first-order rate constants $k_{obs}$ on [H$_2$O$_2$], determined for hydrogen peroxide dismutation by Cu$_2$L$_2$ (black), Cu$_2$L$_3$ (red), Cu$_2$L$_3$ (blue) (200 µM) at 25°C in borate buffer (50 mM, pH 7.8). The second-order rate constants was determined from linear plots of the observed $k_{obs}$ vs [H$_2$O$_2$], $k_{obs} = k[H_2O_2]$. 

10. EPR investigation

Sample preparation. EPR spectra of all three complexes were recorded before and after addition of H$_2$O$_2$ at 50 K. A 200 µM solution in BBS (50 mM pH=7.8) of each complex (150 µL) was mixed with a large excess of hydrogen peroxide (30 mM), immediately transferred to a quartz EPR tube and frozen putting the tube in dry ice. The total time from mixing to the complete freezing of the solution can be estimated to be around 3 minutes. When present, NaBr was added at a concentration of 50 mM.

Simulations. Spectral simulations have been performed with Easyspin (version 5.2.20).

Spin Quantitation. Quantitative measurements were performed for all samples using identical instrumental conditions, volume and position of the sample tube. First, the spectra were corrected by subtracting the baseline obtained as the spectrum of a sample of buffer solution without complex. Then, quantitation of the absolute number of paramagnetic species in each sample was achieved by double integration of the first derivative EPR spectra. The absolute concentration was obtained by comparing the double integral of each sample with that of a freshly prepared copper standard (Cu:EDTA 1:3, [Cu(II)] = 246 µM, volume 150 µL).

EPR Spectra of Cu$_2$L$_2$ and Cu$_2$L$_3$. In Figure S76, the evolution of the EPR spectra of Cu$_2$L$_2$ and Cu$_2$L$_3$ are reported. Before the addition of hydrogen peroxide, both complexes are diamagnetic
and decompose to the monomeric form as reported for the parent Cu$_2$L$^1_2$ showing an analogous behaviour. In the presence of bromide, the breakdown to paramagnetic monomers is remarkably slowed down.

![EPR spectra](image)

*Figure S76.* EPR spectra of Cu$_2$L$^2_2$ (left) and Cu$_2$L$^3_2$ (right) in the absence (top) or in the presence (bottom) of NaBr (50 mM).

**11. Morin test**

Pro-oxidant activity of the complexes was measured by following the oxidative degradation of morin in the presence of hydrogen peroxide by UV-Vis spectroscopy.$^{[S11]}$

![Scheme 1](image)

*Scheme S1.* Morin bleaching with H$_2$O$_2$ catalysed by Cu$_2$L$^1_2$.

The reactions were carried out in borate buffer (50 mM, pH 7.8) at 25°C over a period of 3 hours. A freshly prepared morin solution in DMSO was diluted in borate buffer to obtain a morin solution of 0.12 mM in all the experiments. To this mixture, a stock catalyst solution (1 mM) was added in order to obtain the desired catalyst concentration (50 μM). Finally, a commercial H$_2$O$_2$ stock
solution (30% w/w) was added to get a concentration between 10-30 mM. The change in the absorption maximum of morin at 390 nm was monitored at intervals of 10 min, to evaluate the peroxidase-like activity of the complexes. Considering the excess of hydrogen peroxide employed in the experiments we can extrapolate a pseudo-first order kinetic constant $k_b$, where $v = k_{obs} \cdot [\text{morin}]$. The value of $k_b$ was obtained by linear regression of the initial rate of morin degradation at different hydrogen peroxide concentration (10-30 mM). Second-order rate constants were determined from linear regression of the observed pseudo-first-order rate constants vs $[\text{H}_2\text{O}_2]$.

Figure S7. UV–vis spectra over time of a 0.12 mM solution of morin in borate buffer (50 mM, pH 7.8) in the presence of 10 mM H$_2$O$_2$ and CuL$_2$ (50 μM).
Figure S78. UV–vis spectra over time of a 0.12 mM solution of morin in borate buffer (50 mM, pH 7.8) in the presence of 20 mM H$_2$O$_2$ and CuL$_2$ (50 μM).

Figure S79. UV–vis spectra over time of a 0.12 mM solution of morin in borate buffer (50 mM, pH 7.8) in the presence of 30 mM H$_2$O$_2$ and CuL$_2$ (50 μM).
Figure S80. Linear dependence of pseudo-first-order rate constants $k_{obs}$ on $[\text{H}_2\text{O}_2]$ varied in the range 10−30 mM, determined for oxidation of morin by Cu$_2$L$_2^+$ (50 µM) at 25°C in borate buffer (50 mM, pH 7.8). The second-order rate constant was determined from linear plots of the observed $k_{obs}$ vs $[\text{H}_2\text{O}_2]$, $k_b = k_0[\text{H}_2\text{O}_2]$.

Table S5. Pseudo-first order rate constant $k_{obs}$ and rate constant $k_b$ for oxidative degradation of morin with Cu$_2$L$_2^+$.

| [H$_2$O$_2$] (mM) | $k_{obs}$ (s$^{-1}$) | $k_b$ (M$^{-1}$s$^{-1}$) |
|------------------|---------------------|--------------------------|
| 10               | 1.0 × 10$^{-5}$     | 6.1 × 10$^{-4}$          |
| 20               | 1.6 × 10$^{-5}$     |                          |
| 30               | 2.2 × 10$^{-5}$     |                          |

Table S6. Pro-oxidant and anti-oxidant activity for catalytic anti-oxidants.

|          | $k_{\text{H}_2\text{O}_2}$ (M$^{-1}$s$^{-1}$) | $k_b$ (M$^{-1}$s$^{-1}$) | $p$ | Ref. |
|----------|---------------------------------------------|--------------------------|-----|------|
| Cu$_2$L$_2^+$ | 0.23 $^a$                                   | 6.1 × 10$^{-4}$        | 377 | this work |
| Mn$_2$L$_2$P2 | 1890 $^b$                                  | 116 $^e$               | 16  | [58] |
| [Cu(PBMPA)]$^+$ | 0.030 $^c$                              | 181 $^d$               | ~10$^{-4}$ | [511] |

Mn$_2$L$_2$P2 obtained by the self-assembly of Mn$_2$L$_2$ (HL = HL$^+$) and P2 (Mn-meso-tri(N-methylpyridinium-4-yl)mono(N-4-carboxybenzyl-4-pyridyl) porphyrin); HPBMPA = N-propanoate-N,N-bit-(2-pyridyl)methyl)amine (see also Table 1). $^a$ Based on oxygen evolution kinetics, monitored by a pressure transducer (see Table 1). $^b$ Based on oxygen evolution kinetics, monitored using a Clark electrode, [catalyst] = 10 µM, [H$_2$O$_2$] = 0.1−10 mM in BBS 50 mM pH 7.8 at 25 °C. $^c$ Based on morin bleaching monitored by UV-vis, [Cu$_2$L$_2^+$] = 50 µM and [Cu(PBMPA)] = 2.5 µM, [H$_2$O$_2$] = 10−30 mM. $^d$ Based on Mn-porphyrin bleaching monitored by UV-vis, [catalyst] = 10 µM, [H$_2$O$_2$] = 50−200 µM. $^e$ calculated from the reported pseudo-first order $k_{app} = k_0[\text{H}_2\text{O}_2] = 1.81$ s$^{-1}$ with [H$_2$O$_2$] = 0.01 M.
12. References

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