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Copper(I)/NO_(g) Reductive Coupling Producing a *trans*-Hyponitrite Bridged Dicopper(II) Complex: Redox Reversal Giving Copper(I)/NO_(g) Disproportionation

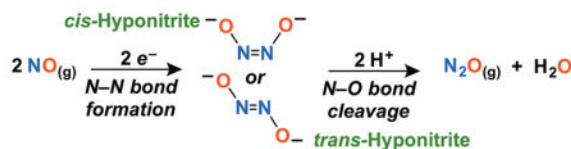
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Abstract

A copper complex, [Cu^I(tmpa)(MeCN)]⁺, effectively reductively couples NO_(g) at RT in methanol (MeOH), giving a structurally characterized hyponitrito-dicopper(II) adduct. Hydrogen-bonding from MeOH is critical for the hyponitrite complex formation and stabilization. This complex exhibits the reverse redox process in aprotic solvents, giving Cu^I + NO_(g), leading to Cu^I-mediated NO_(g)-disproportionation. The relationship of this chemistry to biological iron and/or copper mediated NO_(g) reductive coupling to give N₂O_(g) is discussed.

The interactions and reactivity of redox active metal ions with nitrogen oxides (NO_x) have widespread implications/importance in environmental, practical, and biological chemistries. Iron and copper provide for facile redox shuttling and one and/or the other in the presence of proton sources chemically or enzymatically facilitates reactions such as reduction of nitrite (NO₂⁻) to nitrogen monoxide (NO_(g)); nitric oxide), reductive coupling of NO_(g) to nitrous oxide (N₂O_(g)), and reduction of N₂O_(g) to N_{2(g)}.¹



Biological roles of NO_(g) include it as a signaling agent, yet, it can be toxic under oxidative conditions; NO_(g) is utilized in the human immune response, produced in elevated levels to effect invading pathogen biomolecule destruction (e.g., by oxidation or nitration).² Fighting back, bacteria/pathogens can upregulate NO-reductase (NOR) activity to eliminate toxic

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Notes

The authors declare no competing financial interest.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b07808.

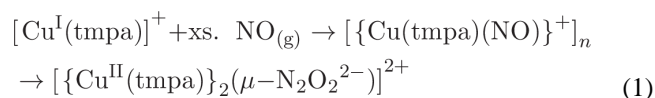
Synthetic and analytical details (methodologies and UV-vis, EPR, NMR, and FT-IR spectra; gas chromatograms); X-ray diffraction data collection details (PDF) Data for C₃₆H₃₆Cl₂Cu₂N₁₀O₁₀ (CIF)

$\text{NO}_{(\text{g})}$ by its reductive coupling to give benign $\text{N}_2\text{O}_{(\text{g})}$.³ Bacterial NOR's^{1d,4} possess heme/nonheme diiron active sites, effecting the coupling through a putative hyponitrito ($\text{N}_2\text{O}_2^{2-}$) intermediate;⁵ the metal ion centers provide electrons (diagram above). Evolutionarily related heme-Cu oxidases (HCO's) effect this reaction, albeit with lower efficiency.⁶

Our own interests encompass hemes and/or Cu,^{2a,7} and in this report we focus on the latter. In addition to HCO $\text{NO}_{(\text{g})}$ reductive coupling, copper nitrite reductases may also couple excess $\text{NO}_{(\text{g})}$ present to give $\text{N}_2\text{O}_{(\text{g})}$.^{1a} Further, in the presence of $\text{O}_{2(\text{g})}$, Cu-NO reactivity can lead to peroxyxynitrite ($\text{O}=\text{NOO}^-$).^{2b,8} Also, copper(I) complexes are efficient at $\text{NO}_{(\text{g})}$ -disproportionation, $3\text{NO}_{(\text{g})} + \text{Cu}^{\text{I}} \rightarrow \text{N}_2\text{O}_{(\text{g})} + \text{Cu}^{\text{II}}(\text{NO}_2^-)$, possibly also involving hyponitrite-type intermediates.^{1b,9} As well, copper ion loaded zeolites are effective catalysts to decompose NO_x to $\text{N}_2(\text{g})$ and $\text{O}_2(\text{g})$; automobile catalytic converters may utilize Cu as a catalyst for $\text{NO}_{(\text{g})}$ reduction to $\text{N}_2\text{O}_{(\text{g})}$.¹⁰

With this background, we highlight the need to elucidate fundamental aspects of $\text{NO}_{(\text{g})}$ reductive coupling, details/requirements for (i) N-N bond formation and (ii) N-O bond cleavage for hyponitrite formation and $\text{N}_2\text{O}_{(\text{g})}$ elimination, respectively. Even though hyponitrite intermediates have been proposed/observed within enzymatic systems, details pertaining to their binding mode within the binuclear active site, protonation state(s), and the metal oxidation states, all remain elusive.¹¹ In this report, employing the copper(I) complex $[\text{Cu}^{\text{I}}(\text{tmpa})(\text{MeCN})](\text{B}(\text{C}_6\text{F}_5)_4)$ ($\text{MeCN} = \text{CH}_3\text{CN}$; $\text{TMPA} = \text{tris}(2\text{-pyridylmethyl})\text{amine}$), we describe (i) the first example of a copper(I) complex whose $\text{NO}_{(\text{g})}$ reactivity leads to efficient reductive coupling to give the hyponitrite complex $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$, (ii) the first structurally characterized Cu-only hyponitrite complex, and (iii) the effective reversal of $\text{NO}_{(\text{g})}$ reductive coupling occurring for the hyponitrite complex in tetrahydrofuran (THF), i.e., formation of a putative $\{\text{Cu}^{\text{I}}(\text{tmpa})\}^+ + \text{NO}_{(\text{g})}$ solution mixture, followed by $\text{NO}_{(\text{g})}$ -disproportionation (Figure 1).

When excess $\text{NO}_{(\text{g})}$ is bubbled through a RT MeOH solution of $[\text{Cu}^{\text{I}}(\text{tmpa})(\text{MeCN})]^+$, the initial pale yellow solution immediately transforms to forest green giving electronic absorption features: $\lambda_{\text{max}} = 310$ ($\epsilon = 3800 \text{ M}^{-1} \text{ cm}^{-1}$), 675 ($\epsilon = 250 \text{ M}^{-1} \text{ cm}^{-1}$), and 870 nm ($\epsilon = 340 \text{ M}^{-1} \text{ cm}^{-1}$) (Figure 2). An EPR spectrum of the green solution reveals a classic reverse axial pattern ($g_{\perp} > g_{\parallel}$) indicating a d_{z^2} ground state, with a single type of mononuclear copper(II) environment occurring in a trigonal bipyramidal (TBP) geometry; this also indicates that the copper(II) ions are electronically site-isolated, i.e., no magnetic/electronic interaction between the two copper(II) ions occurs. Upon solvent removal, this new complex was obtained in near stoichiometric yields (>97%), and it is the hyponitrito complex $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})](\text{B}(\text{C}_6\text{F}_5)_4)_2 \cdot 2\text{H}_2\text{O} \cdot 2\text{MeOH}$ (eq 1).¹²



With the intention of further supporting our complex formulation, we probed the $\text{Cu}^{\text{I}}/\text{NO}_{(\text{g})}$ stoichiometry; $[\text{Cu}^{\text{I}}(\text{tmpa})(\text{MeCN})]^+$ was titrated with varying amounts of $\text{NO}_{(\text{g})}$ from a

$\text{NO}_{(\text{g})}$ -saturated MeOH solution $\{[\text{NO}_{(\text{g})}] = 14.5 \text{ mM at RT}\}$.¹² The data clearly indicates that the $\text{Cu}^{\text{I}}/\text{NO}_{(\text{g})}$ stoichiometry, as measured in this manner, lies between 1 and 1.5, very close to the expected 1:1 stoichiometry.^{12,13} It is presumed that $\text{NO}_{(\text{g})}$ reaction with $[\text{Cu}^{\text{I}}(\text{tmpa})(\text{MeCN})]^+$ initially gives a $\text{Cu}^{\text{I}}\text{-NO}$ adduct, perhaps like that previously reported on (but in EtCN),¹⁴ prior to $\text{NO}_{(\text{g})}$ -coupling in the present case to give the hyponitrito-dicopper(II) complex (eq 1).⁵

$[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ can also be generated by a metathesis reaction involving the $\text{Cu}^{\text{II}}\text{-OH}$ complex, $[\text{Cu}^{\text{II}}(\text{tmpa})(\text{OH})]^+$, generated and isolated by reaction of tetrabutylammonium hydroxide with $[\text{Cu}^{\text{II}}(\text{tmpa})(\text{MeCN})\text{-(ClO}_4)_2]$ in MeCN at RT ($\nu_{\text{O-H}} = 3533 \text{ cm}^{-1}$).¹² Freshly generated $[\text{Cu}^{\text{II}}(\text{tmpa})(\text{OH})]^+$ mixing with 1/2 equiv $\text{Ag}_2\text{N}_2\text{O}_2$ in MeOH, with sonication, gave a color change from light green to forest green. The UV-vis changes correspond with those seen for the hyponitrito-dicopper(II) complex obtained via the $\{[\text{Cu}^{\text{I}} + \text{NO}_{(\text{g})}]\}$ reaction.¹² Isolation of the solid product and redissolution into a MeOH/EtOH = 1:1 solution also gives the same EPR spectrum (20 K).¹²

X-ray quality crystals of $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})](\text{ClO}_4)_2$ could be obtained from MeOH at $-35 \text{ }^\circ\text{C}$, and the structure of the dicationic portion is shown in Figure 3.¹² The complex possesses a dicopper-bridged $\eta^1\text{-O-trans}$ -hyponitrite species with a $\text{Cu}\cdots\text{Cu}$ distance of $5.5648(7) \text{ \AA}$; the dication possesses a centrosymmetric structure. Each copper(II) ion is pentacoordinate, with the four *N* atoms from the TMPA chelate plus the anionic hyponitrito *O* atom (O1 or $\text{O1}'$; Figure 3). However, there also exists a clear interaction of Cu ions with the distal *N* atom of the $\text{N}_2\text{O}_2^{2-}$ moiety, ($\text{Cu-N} = 2.851(2) \text{ \AA}$), i.e., Cu1 interacts with $\text{N5}'$, with $\text{Cu1}'$ interacting with N5 (Figure 3, shown in broken lines). See the SI (page S10) for information and arguments in support of this point. We hypothesize that this weak interaction transforms into a “true” metal–ligand bond when $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ is put into aprotic solvents (*vide infra*; Scheme 1).

Thus, the copper(II) ions in this structure are distorted octahedrally ligated (six-coordinate), which contrasts greatly with other many well characterized $[\text{Cu}^{\text{II}}(\text{tmpa})(\text{X})]^{n+}$ species such as those with $\text{X} = \text{Cl}^-$ ($n = 1$),¹⁵ $\text{X} = \text{nitrito} (\text{NO}_2^-, \text{Obound}; n = 1)$ ¹⁶ and $\text{X} = \text{NCCCH}_3$ ($n = 2$).¹⁷ Recall that methanolic solutions of $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ possess a well-defined TBP coordination geometry, as distinctly and unambiguously observed from frozen solution EPR spectra (*vide supra*). In fact, this hyponitrito-dicopper(II) complex, $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$, is only stable in alcoholic solvents; we thus conclude that the latter observation indicates that MeOH hydrogen-bonds to the $\text{N}_2\text{O}_2^{2-}$ ligand of the complex, probably with the lone pairs on the central *N* atoms. Such an interaction has recently been suggested by Liaw and co-workers¹⁸ although in that case H-bonding to the $\text{Co}^{\text{II}}\text{-NO}$ *O* atom is proposed, which aids the formation of a hyponitrite metastable species. Such H-bonding in solution would “relieve” the structurally observed weak interaction between N5 or $\text{N5}'$ with the copper(II) ions, leaving only the O1 -to-Cu1 (and $\text{O1}'$ -to-Cu1') bond interaction in addition to N4 ligation from TMPA, allowing for strict TBP coordination (as expected from EPR spectra).

Further aspects of the solid-state structure of $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ are as follows:

(a) The N-N and N-O distances of the *trans*-hyponitrite moiety are $1.257(3) \text{ \AA}$ and $1.361(2)$

Å, respectively, which compare well with the N=N double bond (1.256(2) Å) and N–O single bond (1.3622(11) Å) distances of *trans*-sodium hyponitrite.^{5c} (b) The Cu...Cu distance of 5.565 Å is much shorter compared with the Fe–Fe distance (6.7 Å) in [(OEP)Fe^{III}-ONNOFe^{III}(OEP)] (OEP = octaethylporphyrinate), with extended hyponitrito; *O,O'* bonding to iron(III) occurs, but there are no Fe...N_(hyponitrite) interactions.^{20c} (c) The Cu...Cu distance here is virtually identical to that (5.566 Å) of the Agapie's¹⁹ copper–yttrium complex with bridged copper-bound hyponitrite adduct. (d) A number of differing structures have been proposed based on computational analyses for HCO, NOR or other protein hyponitrite species (see diagram below; M = Fe or Cu).^{4e,6d,20}



When solid samples of $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ (as $(\text{B}(\text{C}_6\text{F}_5)_4)^-$ or ClO_4^- salts) are dissolved in THF, or excess THF is added to the complex already dissolved in MeOH, a reaction takes place, and a mixture of products are formed (Figure 1), which we hypothesize to arise from a rearrangement of electron density on the bridging $\text{N}_2\text{O}_2^{2-}$ ligand,²¹ followed by transformations leading to the products seen from reaction of $[\text{Cu}^{\text{I}}(\text{tmpa})]^+ + \text{NO}_{(\text{g})}$ in nonalcoholic solvents, namely $\text{NO}_{(\text{g})}$ -disproportionation, $3\text{NO}_{(\text{g})} + \text{Cu}^{\text{I}} \rightarrow \text{N}_2\text{O}_{(\text{g})} + \text{Cu}^{\text{II}}\text{-NO}_2^-$. We speculate that either THF effects a “reverse” reaction to give a $\{\text{Cu}^{\text{I}}(\text{tmpa})\}^+ + \text{NO}_{(\text{g})}$ solution, or $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ reacts to give $\text{N}_2\text{O}_{(\text{g})}$ and the Cu^{II} -nitrito complex by an as yet undetermined mechanism. However, because there is only one equiv of $\text{NO}_{(\text{g})}$ per $\text{Cu}(\text{I})$ ion present, excess $\{\text{Cu}^{\text{I}}(\text{tmpa})\}^+$ is left over, giving the mixture of products described by Scheme 1.

Experiments carried out on the final product solution confirm the identity, yields and relative-yields of the transformation of $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ originally formed by the $\{\text{Cu}^{\text{I}} + \text{NO}_{(\text{g})}\}$ reaction (*vide supra*) (with stoichiometry of Scheme 1). (a) Cooling the decay product mixture in THF to -80°C and bubbling with $\text{O}_2_{(\text{g})}$ led to the formation of the well-known *trans*-peroxo-dicopper(II) complex, $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-O}_2^{2-})]^{2+}$; with known molar absorptivities, one could relate back to the finding of a 96% yield of $[\text{Cu}^{\text{I}}(\text{tmpa})]^+$.^{12,22} (b) Previously published methodologies¹⁶ were followed to determine and quantify the nitrite content in the final decay mixture, giving >85% yields,¹² and (c) the headspace of the decay product mixture was sampled by gas chromatographic analysis for the identification and quantitation of product $\text{N}_2\text{O}_{(\text{g})}$; yields of ~85% were obtained.¹² The decay of $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ originally formed by the $\{\text{Cu}^{\text{II}}\text{-OH} + \text{Ag}_2\text{N}_2\text{O}_2\}$ method (*vide supra*), gave 96% $[\text{Cu}^{\text{I}}(\text{tmpa})]^+$, > 85% yield of nitrite and 98% yield $\text{N}_2\text{O}_{(\text{g})}$,¹² again all based on the Scheme 1 reaction stoichiometry.

Finally, to further verify the solvent effect for the $\{[\text{Cu}^{\text{I}}(\text{tmpa})]^+ + \text{NO}_{(\text{g})}\}$ reaction, we carried out separate experiments. When $[\text{Cu}(\text{tmpa})(\text{MeCN})]^+$ is subjected to excess $\text{NO}_{(\text{g})}$ in THF solution at RT, the pale yellow solution immediately turns to an olive green color exhibiting the UV-vis features corresponding to the nitrito complex $[\text{Cu}^{\text{II}}(\text{tmpa})\text{-(NO}_2\text{)}]^+$ (96% yield) $\lambda_{\text{max}} = 303$ ($\epsilon = 3360 \text{ M}^{-1} \text{ cm}^{-1}$), 420 ($\epsilon = 1340 \text{ M}^{-1} \text{ cm}^{-1}$) nm. $\text{N}_2\text{O}_{(\text{g})}$ is also produced, so we can conclude that $\text{NO}_{(\text{g})}$ -disproportionation occurs.^{1b} As described in detail above, in MeOH as solvent, the hyponitrito-dicopper (II) complex forms. It is remarkable how the reactivity between $[\text{Cu}^{\text{I}}(\text{tmpa})]^+$ and $\text{NO}_{(\text{g})}$ modify to such great extent merely by altering the solvent properties.

In summary, herein we report the first Cu-only system that mediates the reductive coupling of $\text{NO}_{(\text{g})}$, stoichiometrically yielding the corresponding hyponitrito-dicopper(II) complex in MeOH at RT. We suggest that H-bonding to the $\text{N}_2\text{O}_2^{2-}$ ligand is key to its stabilization and this course of reaction. Unlike other synthetic bioinspired examples,^{5a,7b,19,23} this reaction does not require any low-temperature conditions, and is independent of the equiv of added $\text{NO}_{(\text{g})}$. The new hyponitrito complex possesses versatile synthetic pathways, and is characterized by X-ray crystallography. Dissolution in aprotic solvents triggers its decay with essentially the reversal of $\text{NO}_{(\text{g})}$ coupling, leading to products of Cu^{I} -mediated $\text{NO}_{(\text{g})}$ -disproportionation. We should also note that addition of HCl to $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ in MeOH gives rise to the release of $\text{N}_2\text{O}_{(\text{g})}$.¹² Such unique redox behavior involving copper and $\text{NO}_{(\text{g})}$ is unprecedented, and may have implications in metalloenzyme related $\text{NO}_{(\text{g})}/\text{NO}_x$ biochemistry. A deeper understanding is needed as pertains to the $\text{NO}_{(\text{g})}$ -coupling mechanism (N-N bond formation), the oxidation and/or protonation state of the N_2O_2 -type intermediate formed,^{6a,9,11,24} and the mechanism of (N-O bond cleavage) $\text{N}_2\text{O}_{(\text{g})}$ formation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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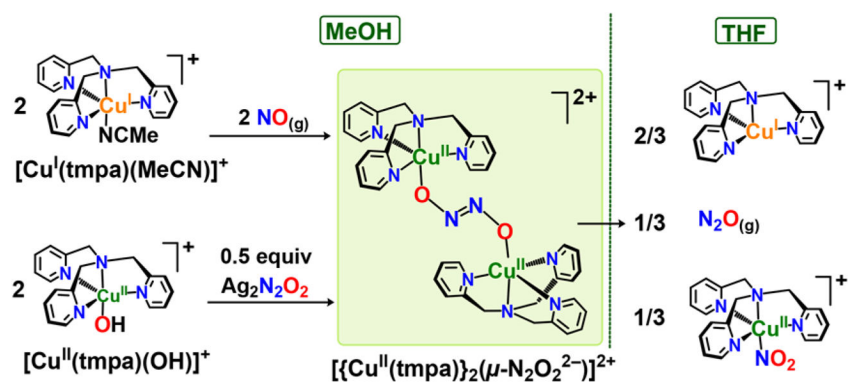


Figure 1. Divergent synthetic routes to $[\{Cu^{II}(tmpa)\}_2(\mu-N_2O_2^{2-})]^{2+}$ in MeOH, and its unique redox behavior in THF, effecting Cu^I -mediated $NO(g)$ -disproportionation.

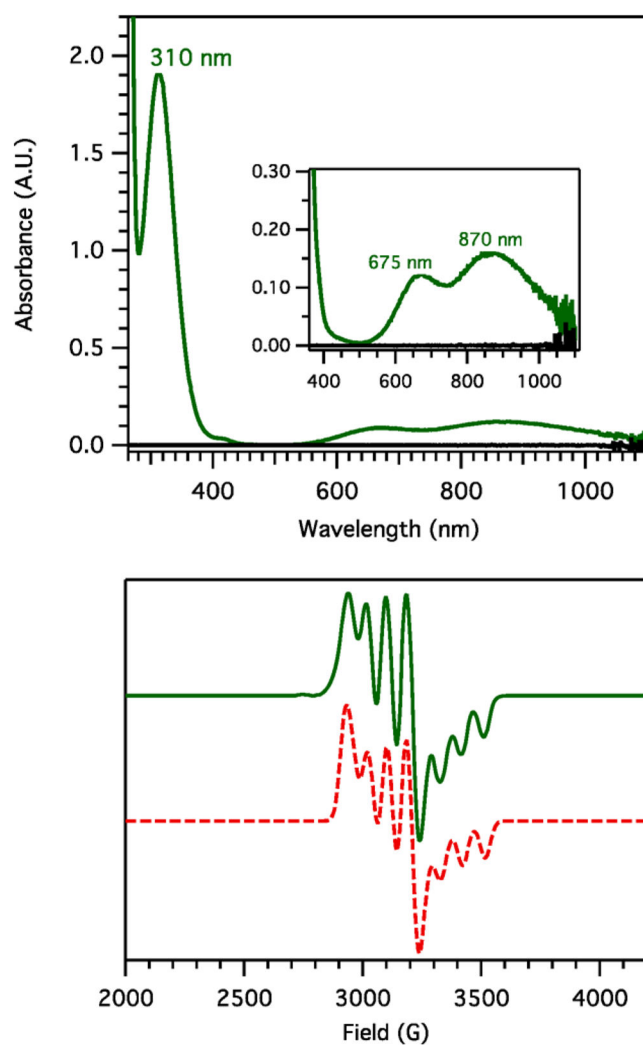


Figure 2. Top: Electronic absorption spectrum resulting from the $\text{NO}_{(\text{g})}$ reactivity with 1 mM $[\text{Cu}^{\text{I}}(\text{tmpa})(\text{MeCN})]^+$ in MeOH at RT. Bottom: EPR spectra (experimental (green) and simulated (red)) of $[\{\text{Cu}^{\text{II}}(\text{tmpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ (2 mM in MeOH/EtOH = 1:1 glass) at 20 K ($g_{\perp} = 2.18$, $g_{\parallel} = 1.99$; $A_{\perp} = 82$ G, $A_{\parallel} = 90$ G).

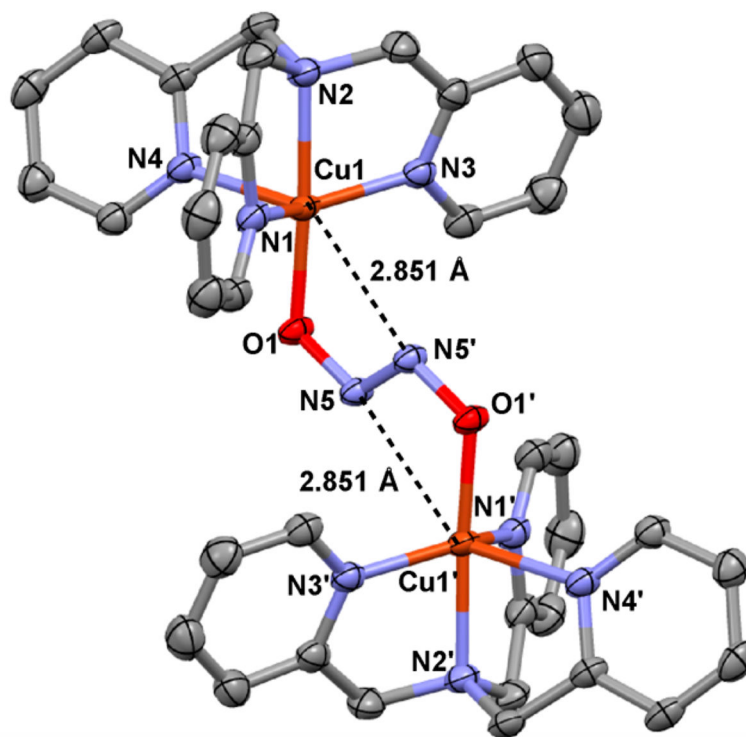
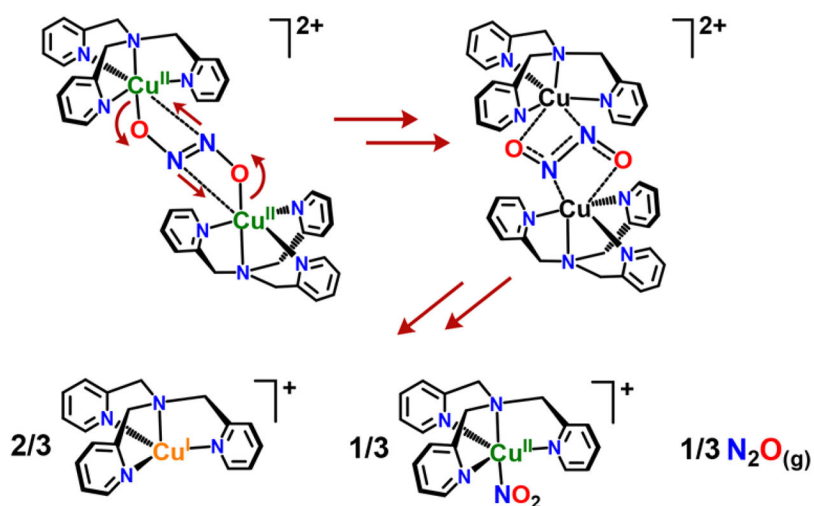


Figure 3. X-ray diffraction ORTEP diagram (50% probability thermal ellipsoids) of $[\{\text{Cu}^{\text{II}}(\text{tpa})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ along with the atom numbering scheme. Hydrogen atoms and noncoordinating perchlorate counteranions are omitted for clarity.¹²

**Scheme 1.**

Proposed Decay of $[\{\text{Cu}^{\text{II}}(\text{tpma})\}_2(\mu\text{-N}_2\text{O}_2^{2-})]^{2+}$ when Placed in THF, Giving a Final Product Mixture Consisting of $[\text{Cu}^{\text{I}}(\text{tpma})]^+$, $[\text{Cu}^{\text{II}}(\text{tpma})(\text{NO}_2)]^+$, and $\text{N}_2\text{O}_{(\text{g})}$