

Complexity with simplicity: a steric continuum of chelating diamines with copper(I) and dioxygen †

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Copper(I) complexed by simple peralkylated diamines reacts with O₂ at low temperature in aprotic solvents to create a diverse set of thermally sensitive, polynuclear copper products. Structural and spectroscopic characterization of several complexes provides keen insights into the complexity of this ostensibly simple, yet important, biological and industrial reaction. A correlation of a series of closely related copper(I) complexes with their oxygenated products highlights the preminent, though not absolute, role of the ligand in these multi-step formation reactions. A steric continuum of diamine ligands provides a sensitive probe into this copper(I)/O₂ reactivity. The diverse product distribution is interpreted through a single unifying mechanism.

1. Introduction

The reactivity of Cu^I complexes with O₂ and the subsequent oxidative reactivity of the formed Cu–O₂ species have attracted much interest over the past two-decades due to their potential relevance to biological systems and synthetic oxidative catalysis.^{1–5} These investigations have produced a wealth of spectroscopic, structural and mechanistic data covering the formation and oxidative reactivity of synthetic Cu–O₂ species, many of which are directly related to the species operative in biological systems.^{1–5} The structural diversity of the Cu–O₂

species formed in a homogeneous solution is quite remarkable. Cu^I : O₂ stoichiometries of 4 : 1 to 1 : 1 are known for these complexes, and different isomers within a particular stoichiometry are possible.⁶ The subsequent reactivity of these Cu–O₂ complexes is equally diverse motivating a better understanding of the variables controlling the species distribution. In all this chemistry, the ligand plays a preminent, though not absolute role. The ligand structure dictates the Cu–O₂ specie(s) that potentially may form and the subsequent oxidative reactivity with exogenous substrates. A series of closely related ligands that are systematically varied to create a steric continuum provides a sensitive probe into the Cu^I–O₂ chemistry and is the focus of this Perspective.

The majority of synthetic Cu^I complexes examined for bioinspired O₂ reactivity predominantly employ aromatic, trinitrogen-based ligands based on the well-characterized binuclear copper protein hemocyanin (**Hc**) that reversibly binds O₂.⁷ In both reduced and oxidized **Hc**, three nitrogen atoms derived from imidazole groups of histidine residues ligate each copper (Fig. 1). The reduced Cu^I centers are ligated in a trigonal-planar geometry, a coordination consistent with all other known biological Cu^I sites that directly activate O₂.^{8–14} In O₂ oxidized **Hc**, each Cu^{II} center adopts a square-pyramidal coordination by side-on ligation of the nascent peroxide and axial positioning of a nitrogen ligand. The axial nitrogen ligand is positioned along the Jahn–Teller axis of the d⁹ Cu^{II} center and is only weakly associated (Fig. 1).⁷ Similar distortions are found in structurally characterized model complexes of the oxygenated form of **Hc**.^{15–18} Though not structurally characterized, the oxygenated form of the binuclear copper enzyme tyrosinase (**Ty**) is spectroscopically congruent with **Hc** suggestive of a similar coordination.³ The ability of **Ty** to hydroxylate exogenous phenolate rings while **Hc** only reversibly binds O₂ is attributed to differences in the physical access of substrate to the oxygenated intermediate.¹⁹ The oxidative reactivity of **Ty** continues to motivate many synthetic investigations.

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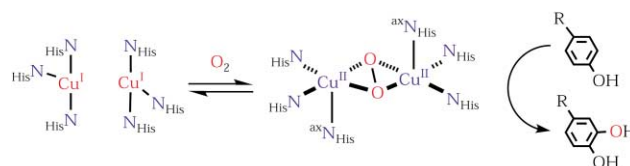


Fig. 1 Oxygenated form of the binuclear copper enzymes. The axial histidine ligands (^{ax}N_{His}) in the μ₂-η²:η²-peroxo-Cu(II)₂ species are weakly associated with the copper suggesting that chelating diamine ligands should suffice to stabilize the oxygenated form. Oxygenated tyrosinase performs 2e⁻/2H⁺ chemistry such as the hydroxylation of phenols to catechols.

The structure and reactivity of **Hc** and **Ty** provide insights into the ligand features necessary for a copper complex to activate O₂ and react with exogenous substrates. The trigonal ligation in reduced **Hc** provides facile access of O₂ to the copper centers; an associative, inner-sphere O₂ activation mechanism is necessary given that tris-imidazole ligation of Cu^I only creates a weak reducing agent. One-electron reduction of O₂ to superoxide by an outer-sphere electron transfer would be energetically prohibitive.^{5,20} The weak axial association by the axial

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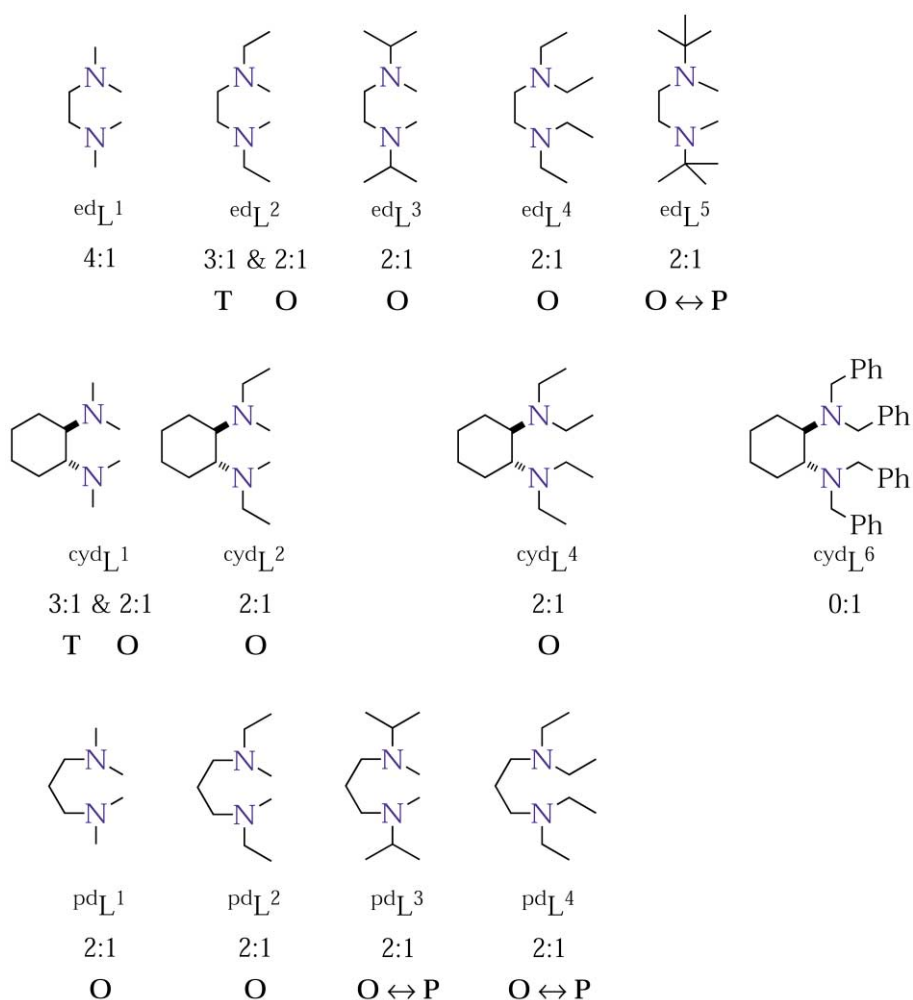


Fig. 2 Series of related peralkylated diamine ligands (L^{PDA}) listed from least to most sterically demanding; ^{ed}L, 1,2-diaminoethane; ^{cyd}L, 1R,2R-diaminocyclohexane; ^{pd}L, 1,3-diaminopropane. The Cu^I : O₂ reaction ratios (200 K, 1 atm O₂, CH₂Cl₂, CF₃SO₃⁻) are indicated below each ligand. The 3 : 1 and 2 : 1 designation indicate that a trinuclear copper bis(μ₃-oxo) complex (**T**) forms at a high initial [L^{PDA}Cu^I]⁺ (>10 mM) and a binuclear copper bis(μ₂-oxo) complex (**O**) forms at low initial [L^{PDA}Cu^I]⁺ (< 1 mM). Systems that create an optically detectable equilibrium mixture of dicopper bis(μ₂-oxo) (**O**) and (μ₂-η²:η²-peroxo) (**P**) are given an **O** ↔ **P** designation.

nitrogen ligand in the oxidized form of **Hc** suggests that bidentate nitrogen ligation should suffice to stabilize the oxygenated form. While the close proximity of the Cu^I centers in **Hc** and **Ty** provides the possibility for a simultaneous two-electron reduction of O₂ to a peroxide-level species,²⁰ this type of O₂-activation mechanism is generally not supported in synthetic binucleating Cu^I complexes. Such complexes generally react through two sequential one-electron steps through the intermediacy of a superoxide complex to form a peroxide-level complex.²¹

While many of the models of **Hc** and **Ty** are binucleating, our interest has focused on simple mononuclear Cu^I-complexes. Our focus on bidentate nitrogen chelation is driven by an overarching goal of creating simple metal-based organic oxidants. Not only are bidentate diamine ligands readily available, but we reasoned that the Cu–O₂ complexes formed would provide greater physical access to substrates thereby increasing the possibility of creating a useful oxidant. The reduction in the ligand denticity from three to two requires an additional exogenous ligand, such as MeCN or CO, to stabilize a Cu^I center in a geometry that is reactive with O₂. An emerging trend within the area of synthetic Cu^I–O₂ chemistry is the use of bidentate nitrogenous ligands. Such ligation does not adversely effect the stability of the nascent Cu–O₂ complexes.^{22–28} In fact, a greater diversity of Cu–O₂ species is created with such ligands. What could not be anticipated in this chemistry was the important role of Cu^{III} in the oxygenation reactions. The simplicity of bidentate diamine ligands in conjunction with the accessibility

of both Cu^{II} and Cu^{III} oxidation states provides many reactivity avenues that are only now being appreciated.

2. Peralkylated diamine ligands (L^{PDA})

Simple peralkylated diamines form a large class of readily modifiable bidentate ligands, a small subset of which is presented in Fig. 2. Apart from their occasional use with Cu^I and atmospheric O₂ for organic oxidations involving unknown active species,^{29–32} these ligands have been largely ignored in the context of examining Cu^I–O₂ reactivity. The thermal instability of the oxygenated intermediates certainly has impeded their characterization. Most of the Cu–O₂ products with these and related ligands have appreciable first-order decay rates above 230 K.^{23,24,26,33–37} The complexity of the problem is compounded by the ligand, solvent, and counteranion dependence of the Cu^I–O₂ reactivity and product stability.^{24,33,38,39} Not all these variables were initially appreciated. In the early 1980s, a Cu^{II}-peroxo intermediate was reported from the reaction of [^{ed}L⁴Cu^I](ClO₄) and O₂ at 298 K in MeOH.^{40,41} This complex decomposes with hydroxylation of an alkyl substituent of the ligand. Motivated by this potent oxidative reactivity along with the synthetic flexibility afforded by peralkylated diamine ligands, L^{PDA}, we decided to explore the reactivity of a series of [L^{PDA}Cu^I]⁺ complexes with O₂ at lower temperatures (~200 K), in aprotic solvents (CH₂Cl₂, THF, acetone), with weakly coordinating counteranions (CF₃SO₃⁻, SbF₆⁻, BF₄⁻, ClO₄⁻). Unless explicitly stated otherwise, the solvent and counteranion

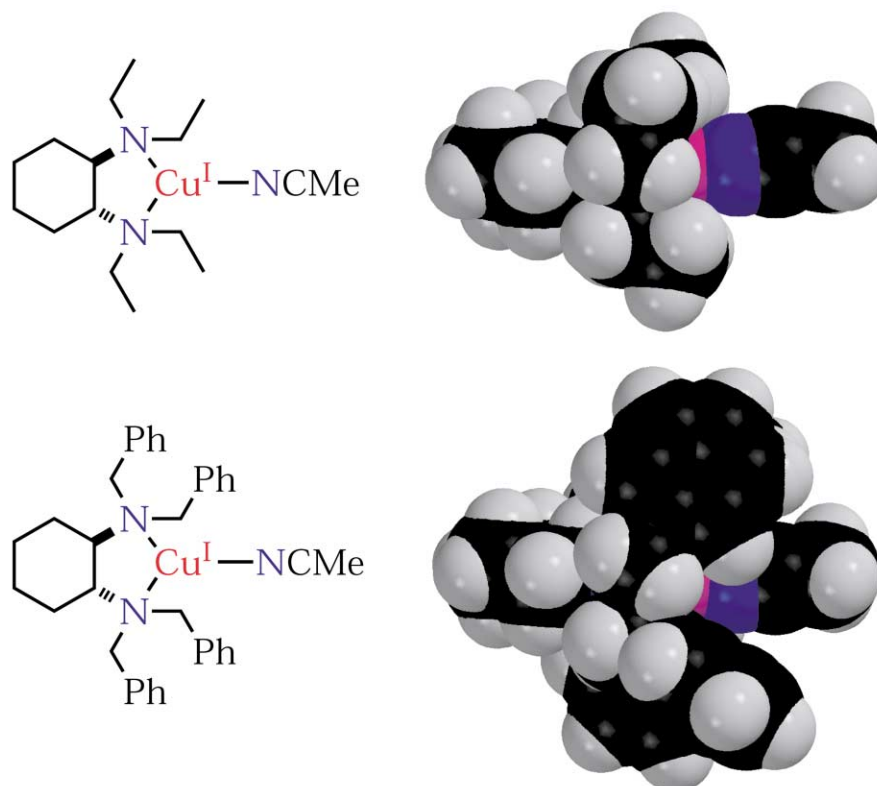


Fig. 3 Space-filling representations of the X-ray structures of $[\text{cydL}^4\text{Cu}^{\text{I}}(\text{MeCN})]^{1+}$ (top) and $[\text{cydL}^6\text{Cu}^{\text{I}}(\text{MeCN})]^{1+}$ (bottom).

used in the studies described below are CH_2Cl_2 and CF_3SO_3^- , respectively. In several instances, new $\text{Cu}-\text{O}_2$ species were observed with spectroscopic features distinct from those of any characterized $\text{Cu}-\text{O}_2$ intermediates at the time.^{26,33,34,38}

1,2-Diaminoethane ($^{\text{ed}}\text{L}$), *trans*-1*R*,2*R*-diaminocyclohexane ($^{\text{cyd}}\text{L}$) and 1,3-diaminopropane ($^{\text{pd}}\text{L}$) provide convenient, modular synthetic access to a homologous series of very simple Cu^{I} -complexing ligands that provide nearly equivalent electron-donating characteristics (Fig. 2). Systematic variation of the proximal substituents on these three diamine backbones creates a series of ligands that span a steric continuum. The smooth variation of the spatial demands of these ligands allows for a systematic study of the effects of ligand structure on the formation, stability, and reactivity of these copper complexes. In this context, $^{\text{cyd}}\text{L}$ affords several advantages over $^{\text{ed}}\text{L}$, both five-atom chelating diamine ligands. The chair conformation of $^{\text{cyd}}\text{L}$ is thermodynamically preferred in which the two amine groups are equatorially positioned. This creates a highly predisposed binding pocket with an attendant increase in the metal binding affinity.⁴² The enantiomeric purity of $^{\text{cyd}}\text{L}$ used in these studies is also advantageous in the self-assembly process of polynuclear $\text{Cu}-\text{O}_2$ complexes, as the probability of forming diastereomeric products is significantly reduced.^{26,33,43-45} In the three series of ligands, the greatest difference is the lesser metal bite-angle of the five-atom chelating ligands, $^{\text{ed}}\text{L}$ and $^{\text{cyd}}\text{L}$, as compared to the six-atom chelate ligands, $^{\text{pd}}\text{L}$.

As with many reported tridentate $\text{Cu}-\text{O}_2$ systems, the peripheral substituents of the diamine ligands are used to destabilize or preclude 2 : 1 $\text{L}^{\text{PDA}} : \text{Cu}$ complexes with Cu^{I} or Cu^{II} . The former creates a tetrahedrally ligated Cu^{I} center that is generally inert to O_2 . Indeed, the simplest $^{\text{cyd}}\text{L}$ forms a structurally characterized, colorless complex, $[\text{cydL}_2\text{Cu}^{\text{I}}](\text{CF}_3\text{SO}_3)$, that does not react with O_2 in solution at ambient temperatures.⁴⁶ Other substituent combinations in the ligands of Fig. 2 prove sufficiently bulky to preclude formation of such 2 : 1 complexes. The 2 : 1 $\text{L}^{\text{PDA}} : \text{Cu}^{\text{II}}$ complexes are also destabilized by interligand steric clashes of the substituents thus significantly reducing the tendency of the Cu^{I} starting materials to disproportionate.

3. $\text{Cu}^{\text{I}}-\text{L}^{\text{PDA}}$ Complexes

An equimolar reaction of L^{PDA} with $[\text{Cu}^{\text{I}}(\text{MeCN})_4]^{1+}$ usually yields a discrete Cu^{I} complex with a single MeCN bound as a labile auxiliary. In the solid state, the Cu atom in $[\text{cydL}^4\text{Cu}^{\text{I}}(\text{MeCN})]^{1+}$ and $[\text{cydL}^6\text{Cu}^{\text{I}}(\text{MeCN})]^{1+}$ is ligated in a trigonal-planar coordination with the third site occupied by an MeCN molecule.^{33,46} The space-filling models accentuate how the proximal substituents congest the area near the metal center (Fig. 3). In solution, ^1H NMR evidence for both complexes suggests that the bound MeCN is in fast exchange on the NMR time-scale with MeCN in solution. Stronger Cu^{I} ligands such as phosphines stoichiometrically displace the auxiliary MeCN to create related trigonal-planar complexes.^{33,46} While a four-coordinate tetrahedral complex $[\text{L}^{\text{PDA}}\text{Cu}^{\text{I}}(\text{MeCN})_2]^{1+}$ can not be excluded in solution with *in situ* preparations,³⁵ all spectroscopic and reactivity data suggest that a three-coordinate, trigonal-planar structure is the predominant species. It is this species that is necessary, in our view, for a facile associative activation of O_2 ; the oxidation potential of these $[\text{L}^{\text{PDA}}\text{Cu}^{\text{I}}(\text{MeCN})]^{1+}$ complexes are all in excess of +1.2 V versus NHE, effectively precluding an outer-sphere electron transfer as a first step in the O_2 activation.

4. Ambient temperature $\text{Cu}^{\text{I}}-\text{L}^{\text{PDA}}$ reactivity with O_2

The oxygenation of $[\text{L}^{\text{PDA}}\text{Cu}^{\text{I}}(\text{MeCN})]^{1+}$ is dependent on the subtle interplay of several variables including temperature, ligand, counteranion, and solvent. The latter two are generally subordinate to the former two in aprotic polar solvents. At 298 K, the reaction of O_2 with $[\text{L}^{\text{PDA}}\text{Cu}^{\text{I}}(\text{MeCN})]^{1+}$ results in the formation of a blue or green Cu^{II} complex without a detectable accumulation of an intermediate species. A 4 : 1 $\text{Cu}^{\text{I}} : \text{O}_2$ stoichiometry is usually measured indicating full reduction of O_2 to the oxide level (O^{2-}) and full oxidation of Cu^{I} to Cu^{II} . With weakly coordinating anions, the copper products generally lack intense ligand to metal charge transfer (LMCT) bands at wavelengths above 300 nm. The most commonly

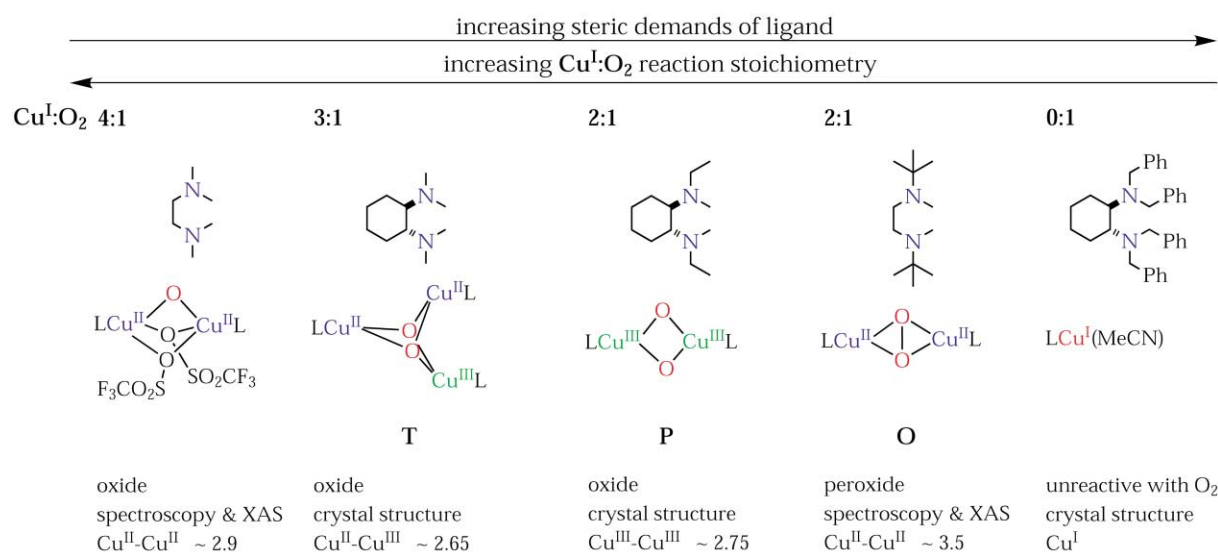


Fig. 4 A continuum of Cu–O₂ products formed in the reaction of [L^{PDA}Cu^I]⁺ with O₂ at 200 K. A representative L^{PDA} that forms a particular type of Cu–O₂ product is given. Note that increasing the steric demands of the ligands reduces the Cu^I–L^{PDA} : O₂ reaction ratio.

characterized product is a bis(μ₂-OH) Cu^{II} dimer, an example of which is presented in Fig. 6. Adventitious water is usually the source of the required protons, though oxidation of the ligands is also possible.

The preeminent role of the ligand in controlling O₂ reactivity is highlighted by [cy^dL⁶Cu^I(MeCN)]⁺, a Cu^I complex inert to O₂ in solution at ambient temperatures (Fig. 3). The four proximal benzyl substituents of cy^dL⁶ create a very congested area around the trigonally ligated Cu^I center. Replacement of two benzyl substituents of cy^dL⁶ with two methyl substituents creates a Cu^I complex that reacts immediately upon exposure to O₂.

Most investigations into the oxygenation reaction support the initial formation of a 1 : 1 Cu^{II} : superoxide complex. Subsequent reactions with additional equivalent(s) of the Cu^I complex create the polynuclear Cu–O₂ products. The inert behavior of [cy^dL⁶Cu^I(MeCN)]⁺ to O₂ suggests an inhibition of either superoxide formation or the subsequent reactions. As the MeCN of [cy^dL⁶Cu^I(MeCN)]⁺ rapidly exchanges with CO or MeCN in solution, inhibition of the subsequent reactions of the superoxide species is the more probable explanation. Cu^{II} superoxide complexes have strong LMCT bands, yet oxygenation of a solution of [cy^dL⁶Cu^I(MeCN)]⁺ does not result in any visible change. A thermodynamic instability of the superoxide intermediate relative to the starting materials is consistent with the absence of any distinct superoxide spectroscopic features.^{38,47} Stabilization of 1 : 1 Cu : O₂ superoxide complexes formed from Cu^I and O₂ is certainly possible with synthetic nitrogenous ligands.^{22,23,48–51} Yet, these ligands are either anionic or polydentate tetramines. The former significantly increases the reducing ability of the Cu^I complexes,^{22,23,50} and the latter provides a very electron-rich Cu^I center in a trigonal monopyramidal coordination.^{49,51}

5. Low temperature Cu^I–L^{PDA} reactivity with O₂

The oxygenation reaction of [L^{PDA}Cu^I(MeCN)]⁺ appears very different at ~200 K as new, yellow to purple species rapidly accumulate with intense LMCT bands in the 300–450 nm range. While such species likely form at ambient temperatures, their accumulation is precluded by rapid subsequent reactions. The low-temperature stabilized intermediates decay at higher temperatures to green and blue complexes similar to the products of oxygenation at ambient temperatures. The intense LMCT bands of the thermally sensitive intermediates derive from oxygen ligation of the copper centers and are often characteristic of the type of Cu–O₂ species formed.³ At ~200 K, Cu^I : O₂ reaction ratios of 4 : 1, 3 : 1, and 2 : 1 can be

manometrically measured for various [L^{PDA}Cu^I(MeCN)]⁺ complexes. These stoichiometries inversely correlate to the steric demands of the L^{PDA}; the structural diversity of the products formed is presented in Fig. 4.

5.1. 4 : 1 Cu^I : O₂

Of all the Cu^I–L^{PDA} complexes examined, only [e^dL¹Cu^I(MeCN)]⁺, the least sterically demanding complex, reacts in 4 : 1 ratio at 200 K by manometry.⁵² Optical monitoring of the LMCT feature at 340 nm indicates that product formation is invariant to the initial Cu^I concentration.⁵³ Crystalline material is accessible, but its thermal and moisture sensitivity has precluded an X-ray structure. Extensive spectroscopic and chemical characterization of the microcrystalline solid provides some insights into the complex. EPR and variable field, variable temperature magnetic susceptibility measurements are consistent with an *S* = 1 electronic ground state.⁵⁴ The Cu K-edge X-ray absorption spectrum (XAS) supports a Cu^{II} formulation through its characteristic feature at 8979 eV,⁵⁵ and the extended fine structure (EXAFS) model has two Cu–N/O distances at 1.94 Å, two Cu–N/O distances at 2.03 Å, and a Cu–Cu distance of 2.90 Å.⁵² While the optical spectrum and *S* = 1 electronic ground state are reminiscent of a structurally and spectroscopically characterized 3 : 1 Cu^I : O₂ species (*vide infra*), the chemical reactivity differences and absence of any short Cu–O/N or Cu–Cu distances in the EXAFS model support a different structural motif. While a tetrameric complex is appealing to match the 4 : 1 stoichiometry, a simpler postulated model is a Cu^{II} μ₂-oxo dimer with one or two μ₂-CF₃SO₃[−] counteranions, [(^edL¹Cu^{II})₂(μ₂-O)(CF₃SO₃)_{*n*}]²⁺ (*n* = 1 or 2). In this model, the short Cu–O/N distances (1.94 Å) at each copper center are associated with the μ₂-oxo ligand and one nitrogen atom of the ligand. Ferromagnetic coupling to give the triplet ground state would result from a Cu–O–Cu bridge of less than ~98°. ^{56,57} Of the limited reports of μ₂-oxo Cu^{II} dimers, none have been structurally characterized, and all have moderately intense LMCT features in the 340 nm region.^{58,59} A fuller understanding of this complex awaits a crystal structural determination.

5.2. 3 : 1 Cu^I : O₂

Remarkably minor alterations within a ligand structure can lead to a dramatic change in the oxygenation reaction. cy^dL¹ is very similar to e^dL¹ with four proximal methyl substituents. Yet, [cy^dL¹Cu^I(MeCN)]⁺ reacts with O₂ (30 mM, 200 K) in a 3 : 1 ratio to form a brown product chemically distinct from the 4 : 1 complex described above. A crystal structure confirms the

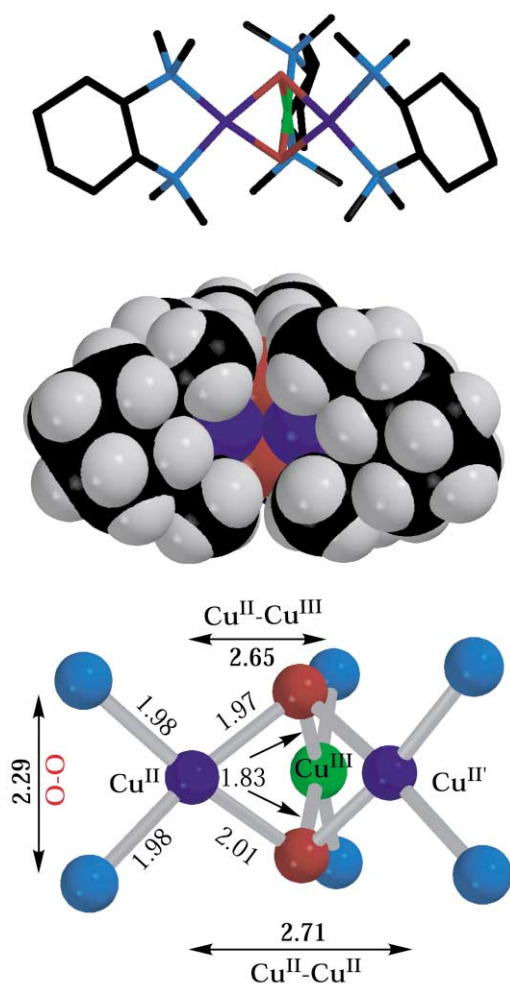


Fig. 5 A line (top) and space filling (middle) drawing of the crystal structure of the valence localized $\text{Cu}^{\text{III}}\text{-Cu}^{\text{II}}\text{-Cu}^{\text{II}}$ trinuclear cluster (**T**), $[(^{\text{cyd}}\text{L})_3\text{Cu}_3(\mu_3\text{-O})_2]^{3+}$. The space-filling model highlights the extreme crowding of the methyl substituents. The metrical distances (\AA) of the $\text{N}_6\text{Cu}_3\text{O}_2$ core of one of the two unique clusters in the asymmetric unit are shown in the diagram (bottom). All drawings view along the crystallographically imposed two-fold axis with the unique copper center positioned behind.

trinuclear composition, $[(^{\text{cyd}}\text{L}^1\text{Cu})_3(\mu_3\text{-O})_2]^{3+}$, with three non-ligated CF_3SO_3^- anions (Fig. 5).³³ Two independent cations exist in each asymmetric unit, each with slightly different metrical parameters. The bond of the O_2 molecule is fully cleaved to give two μ_3 -oxide ligands, and all three coppers are ligated in a square-planar N_2O_2 coordination. The crystallographically imposed two-fold symmetry of each copper cluster requires a unique and symmetry-related pair of copper centers. The unique copper center has significantly shorter Cu–O distances (Cu–O; 1.83 \AA versus 1.97 \AA) than the symmetry related one. These large disparities are consistent with a higher oxidation state for the unique copper center. The short Cu–Cu and Cu–O distances to the unique copper are readily observed in the Cu K-edge EXAFS in both solution and solid state.⁶⁰ In addition, the pre-edge region exhibits a feature characteristic of Cu^{III} .^{60,61} The asymmetry of the structure and the XAS data fully support a formal description as a localized valence $\text{Cu}^{\text{III}}\text{-Cu}^{\text{II}}\text{-Cu}^{\text{II}}$ cluster. This valence accounting provides the four electrons needed to fully reduce one O_2 molecule. The stabilization of the less-frequently observed Cu^{III} oxidation state is consistent with the strongly anionic bis-oxide ligation in a square-planar environment. Such ligation can significantly attenuate the reduction potential of Cu^{III} .⁶² Though electrochemical characterization of this thermally sensitive complex is not currently available, all reactivity studies suggest that the trinuclear complex is only a mild oxidant.

Solid-state magnetic susceptibility, EPR, and MCD (magnetic circular dichroism) support an $S = 1$ electronic ground state for the trinuclear complex (**T**).⁶³ In an anionic square-planar coordination, Cu^{III} will be low-spin and diamagnetic. The remaining two square-planar Cu^{II} centers each possess one unpaired electron. The superexchange pathway between these centers through the oxide bridges is poor due to the acute $\text{Cu}^{\text{II}}\text{-O-Cu}^{\text{II}}$ angles ($\sim 87^\circ$). The triplet ground state ($S = 1$) is consistent with the weak ferromagnetic coupling ($J = +7 \text{ cm}^{-1}$) between these two Cu^{II} centers. Electronic structure calculations support a localized-valence description of the asymmetric Cu_3O_2 core and suggest that its stabilization over a symmetric delocalized core (three $\text{Cu}^{2.33+}$) is a result of a Jahn–Teller distortion.⁶³

The formation of the trinuclear species is dependent on a number of variables including the ligand and, remarkably, the ratio of initial concentrations of Cu^{I} and O_2 . Only a slight alteration in the ligand structure changes the stoichiometry of the reaction and the Cu– O_2 product; $[(^{\text{cyd}}\text{L}^2\text{Cu}^{\text{I}}(\text{MeCN}))]^{1+}$, with two ethyl and two methyl substituents rather than four methyl substituents, oxygenates in a 2 : 1 $\text{Cu}^{\text{I}} : \text{O}_2$ stoichiometry rather than 3 : 1 under all conditions examined. $[(^{\text{cyd}}\text{L}^1\text{Cu}^{\text{I}}(\text{MeCN}))]^{1+}$ oxygenates to a spectroscopically similar 2 : 1 product if the concentration of dissolved O_2 is greater than that of Cu^{I} . If the concentration of O_2 is significantly less than that of Cu^{I} ,⁶⁴ the 3 : 1 species preferentially forms. Intermediate ratios lead to mixtures of the two products. Thus, high $\text{Cu}^{\text{I}} : \text{O}_2$ concentration ratios favor the 3 : 1 product, while low ratios favor the 2 : 1 product assuming that the ligand used is capable of assembling to the trinuclear structure. Formation of a spectroscopically pure 3 : 1 species is experimentally difficult, and in all cases, some of the 2 : 1 complex is spectroscopically detectable. Consequently, the characterization of the **T** species has relied predominantly on crystalline material. These experimental complications do not detract from the amazing result that the **T** species is a kinetic rather than a thermodynamic product and suggests a complexity to Cu– O_2 reactions not previously appreciated.

The 3 : 1 stoichiometry in the $[(^{\text{cyd}}\text{L}^1\text{Cu}^{\text{I}}(\text{MeCN}))]^{1+}$ mediated reduction of O_2 was unique among synthetic metal complexes when initially observed. The characteristic spectroscopic features of $[(^{\text{cyd}}\text{L}^1\text{Cu})_3(\mu_3\text{-O})_2]^{3+}$ has now allowed characterization of other systems. The oxygenation behavior of $[(^{\text{pd}}\text{L}^2\text{-Cu}^{\text{I}}(\text{MeCN}))]^{1+}$ is similar to $[(^{\text{cyd}}\text{L}^1\text{Cu}^{\text{I}}(\text{MeCN}))]^{1+}$: at high and low $\text{Cu}^{\text{I}} : \text{O}_2$ concentration ratios, a 3 : 1 and 2 : 1 product are formed, respectively. The compact nature of the trinuclear cluster suggests that only the least sterically demanding ligands are capable of stabilizing the complex (Fig. 5). Yet, the steric demands of $^{\text{pd}}\text{L}^1$, the simplest 1,3-diaminopropane ligand, are apparently too large as its Cu^{I} complex oxygenates to form a 2 : 1 complex under all conditions examined.⁶⁵ A slight reduction in the steric demands of $^{\text{pd}}\text{L}^1$ can be achieved by substituting one of the permethylated amine groups with a 2-pyridyl group. The Cu^{I} complex of *N,N*-dimethyl-2-(2-pyridyl)ethylamine has recently been reported by Itoh to form a trinuclear cluster in acetone at 180 K.²⁴

5.3. 2 : 1 $\text{Cu}^{\text{I}} : \text{O}_2$

5.3.1. Bis(μ_2 -oxo) dimers. While the simplest $\text{Cu}^{\text{I}}\text{-L}^{\text{PDA}}$ react with O_2 in 4 : 1 or 3 : 1 ratios, almost all others react in a 2 : 1 ratio to form a bis(μ_2 -oxo)dicopper(III) species, **O** (Figs. 2 and 4). Even though the initial characterization of this species lagged behind the more traditional 2 : 1 Cu– O_2 peroxo-species, more spectroscopically and structurally characterized examples of **O** now exist than any other Cu– O_2 type. This proliferation results in part from the diversity of ligands capable of stabilizing an **O** species including diamines,^{22–24,26,35,37,39,65–68} triamines,^{34,38,69–71} and even tetraamines.^{72,73} The six reported crystal structures all show very compact Cu_2O_2 cores with

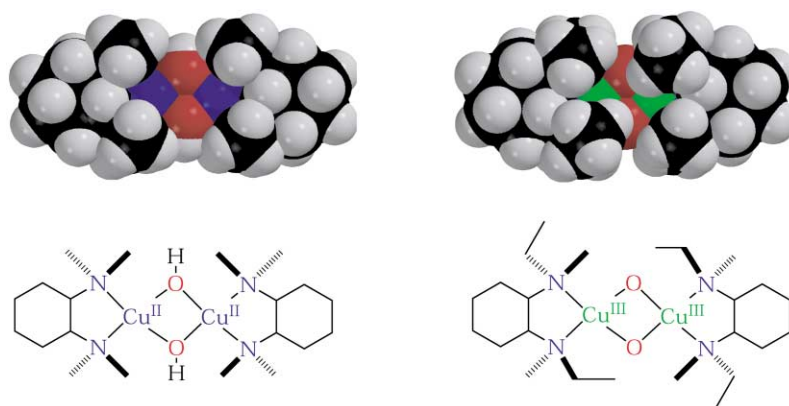


Fig. 6 A space-filling drawing of the crystal structure of the bis(μ_2 -hydroxy)dicopper(II) dimer, $[(\text{C}^{\text{vd}}\text{L}^{\text{I}}\text{Cu}^{\text{II}})(\mu_2\text{-OH})_2]^{2+}$ (left) and of the bis(μ_2 -oxo)dicopper(III) dimer, $[(\text{C}^{\text{vd}}\text{L}^{\text{II}}\text{Cu}^{\text{III}})(\mu_2\text{-O})_2]^{2+}$ (right). Note the highly ordered, pseudo- C_2 -symmetric alternation of the ethyl and methyl substituents within the bis(μ_2 -oxo)dicopper(III) dimer. Metrical parameters for the bis(μ_2 -hydroxy) {bis(μ_2 -oxo)} structures: Cu–Cu, 2.992 {2.743}; Cu–O_{ave}, 1.91 {1.81}; Cu–N_{ave}, 2.01 {1.96}; O–O 2.38 {2.34} Å; Cu–O–Cu 102 {99}°.

characteristically short Cu–O and Cu–Cu distances.^{22,26,38,68,72,74} These distances are dependent on the charge of the overall complex, with the dicationic complexes exhibiting the most contracted distances (Cu–O ~ 1.80 Å; Cu–Cu ~ 2.75–2.80 Å). Of these crystal structures, $[(\text{C}^{\text{vd}}\text{L}^{\text{II}}\text{Cu}^{\text{III}})(\mu_2\text{-O})_2]^{2+}$ contains the least sterically demanding ligand and correspondingly, the shortest Cu–Cu distance at 2.74 Å.²⁶ A space-filling model of the crystal structure clearly shows that the potentially destabilizing steric interactions between substituents on opposing ligands are minimized (Fig. 6). An increase in the spatial demands of these substituents increases intraligand steric interactions thereby decreasing the relative stability of an **O** complex (*vide infra*).

Though now commonly accepted, the formation of a Cu^{III} center in the reaction of O₂ with Cu^I chelated by a neutral amine ligand was a radical departure from conventional wisdom. The 3+ oxidation state of the Cu centers in **O** species cannot be deduced directly from the metrical parameters of the crystal structures, since no substantially disparate Cu–O bond distances are present to allow for an internal comparison as was the case for the **T** cluster. Short Cu–O distances are not sufficient evidence, as similarly short Cu–O bond distances are known among Cu^{II} complexes.^{75–77} The pre-edge feature in the Cu K-edge XAS currently provides the sole experimental basis for definitive assignment of the Cu valence in this class of compounds. This low intensity feature at ~8981 eV for all **O** species examined corresponds to a $1s \rightarrow 3d_{x^2-y^2}$ transition and is a characteristic signature for the copper 3+ oxidation state.^{60,78}

Bis(μ_2 -oxo)dicopper(III) species exhibit spectroscopic features that allow an unambiguous characterization. These diamagnetic complexes exhibit two characteristically intense features at ~300 nm ($\epsilon = \sim 10\text{--}20 \text{ mM}^{-1} \text{ cm}^{-1}$) and ~400 nm ($\epsilon = \sim 10\text{--}30 \text{ mM}^{-1} \text{ cm}^{-1}$) in their electronic absorption spectra. On the basis of electronic structure calculations, the ~300 nm band has been assigned to the oxygen in-plane $\pi_{\sigma}^* \rightarrow \text{Cu } d_{xy}$ LMCT and the ~400 nm band to the oxygen $\sigma_{\text{u}}^* \rightarrow \text{Cu } d_{xy}$ LMCT.⁷⁹ These intense LMCT features are almost solely diagnostic for this 2 : 1 species, as the maxima for other 2 : 1 species appear at different energies. The intensity of these absorptions indicates substantial covalency in the Cu–O bonds.⁷⁹ The **O** species also exhibit a characteristically intense resonance Raman feature (rR) in the ~600 cm^{-1} region assigned as an A_g-symmetric Cu₂O₂ breathing mode.^{79,80} As substantial Cu–O bond elongation is associated with this vibration, the 600 cm^{-1} is sensitive to ¹⁶O to ¹⁸O substitution ($\Delta\nu_{\text{Cu}_2\text{O}_2} = \sim 26 \text{ cm}^{-1}$). Analogous rR features have been assigned for other metal bis(μ_2 -oxo) M₂O₂ cores (M = Ni, Co, Fe and Mn).⁸¹

5.3.2. Bis(μ_2 -oxo) to μ_2 - η^2 : η^2 peroxo equilibrium, **O** \leftrightarrow **P**.

The structure of the μ_2 - η^2 : η^2 -peroxodicopper(II) intermediate

of **Hc** and **Ty** provided the initial motivation to examine the O₂ reactivity of simple Cu^I-L^{PDA} complexes. Yet, the characterized products described above are very different, calling into question the initial hypothesis concerning the stabilization of a μ_2 - η^2 : η^2 -peroxodicopper(II) species, **P**, with simple diamine ligands. Tolman's work with Cu^I complexes of peralkylated triamine ligands based on triazacyclononane (TACN) provided key insights into this issue.^{38,82} Using a sterically demanding TACN derivative, an equilibrium mixture of **O** and **P** could be obtained. This result indicated that stabilization of a **P** species required significant steric demands within a ligand, but that aromatic ligation was not a necessary requirement. Our interest in finding a L^{PDA} that could stabilize a **P** isomer was heightened by the potential opportunity of exploring other equilibrating **O** and **P** systems. As this **O** \leftrightarrow **P** equilibrium formally involves forming and cleaving an O–O bond, it has important chemical and mechanistic implications.

A general structural comparison of the **O** and **P** isomers provides some insight into this equilibrium. The Cu₂O₂ metrical parameters of these two isomers are quite different. Overall, the **O** isomer is much more compact with a shorter Cu–Cu separation (**O** ~2.8 Å; **P**: ~3.6 Å) and shorter Cu–O bond distances (**O** ~1.8 Å; **P**: ~1.9 Å). Experimental data supports the notion that L^{PDA} preferentially stabilize the **O** isomer; the Cu^I-L^{PDA} complexes with the least sterically demanding ligands, that oxygenate in a 2 : 1 ratio, preferentially form **O** isomers (Fig. 2). High-level theoretical calculations support a preferential electronic stabilization of the **O** isomer.⁸³ At parity of ligand, intraligand steric interactions in the **O** dimer will be greater than the **P** dimer due to the more compact structure of **O**. Escalation of these intraligand interactions could potentially create a L^{PDA} that solely forms a **P** isomer.

While this two-state steric analysis is simplistic, it directly correlates with the oxygenation behavior of the Cu^I-L^{PDA} complexes (Fig. 2). Three of the most sterically demanding ligands (^{ed}L⁴, ^{pd}L³, ^{pd}L⁴) create optically detectable **O** \leftrightarrow **P** mixtures upon oxygenation of their Cu^I complexes in THF with CF₃SO₃[−] counteranions.³⁹ While the optical spectra clearly show two intense LMCT bands in the ~360 nm (**P**) and ~410–450 nm (**O**) regions (Figs. 8 and 9), the existence of both species has been verified by profiling the optical features by rR spectroscopy.^{84,85} Opposing and reversible changes in the intensity of these optical features with temperature indicates a facile equilibrium in each case. A variation of the equilibrium position ($K_{\text{eq}} = [\text{P}]/[\text{O}]$) with temperature consistently shows that the **P** isomer is entropically stabilized while the **O** isomer is enthalpically stabilized. The small magnitude and opposing nature of the entropic and enthalpic energies allows a detectable equilibrium mixture to develop at 200 K.

The position of the **O** \leftrightarrow **P** equilibrium is most sensitive to

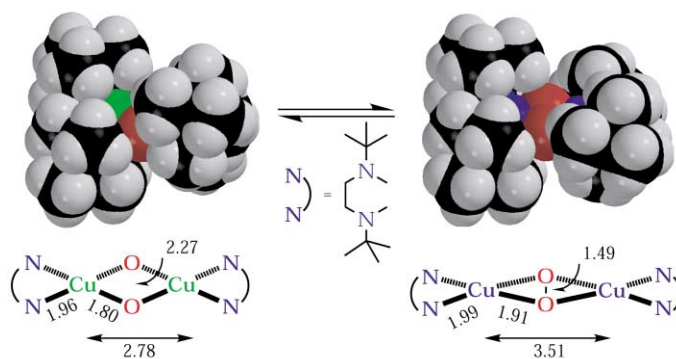


Fig. 7 Space-filling models for the geometry optimized DFT structures (B3LYP, 6-31G*) for the **O** ↔ **P** equilibrium, $[(^{\text{ed}}\text{L}^{\text{S}}\text{Cu}^{\text{III}})_2(\mu_2\text{-O})_2]^{2+} \leftrightarrow [(\text{edL}^{\text{S}}\text{Cu}^{\text{II}})_2(\mu_2\text{-}\eta^2\text{-}\eta^2\text{-O}_2)]^{2+}$. The overall twist in the **O** and **P** isomers is 38° and 6° , respectively, measured as the dihedral angle between the two N-Cu-N planes. Distances are in Å.

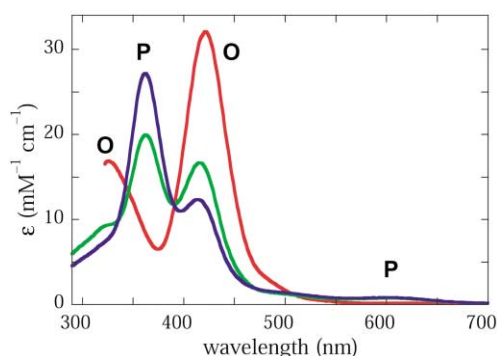


Fig. 8 Solvent effect on the **O** ↔ **P** equilibrium position for $[(^{\text{pd}}\text{L}^{\text{4}}\text{Cu})_2\text{O}_2](\text{CF}_3\text{SO}_3)_2$ (1 mM Cu, 187 K). A lower dielectric solvent (2-MeTHF, blue) biases the equilibrium towards the **P** isomer (~ 360 nm), while a higher dielectric solvent (acetone, red) biases the equilibrium towards the **O** isomer (~ 420 nm). The intermediate spectrum is in THF (green).

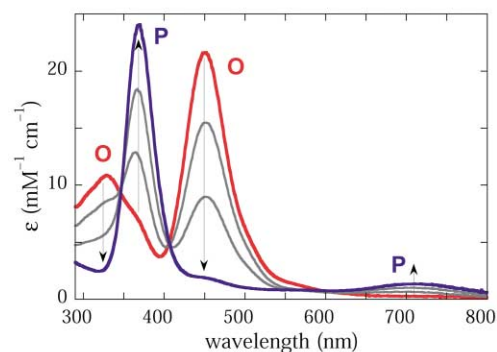


Fig. 9 A titration of $[(^{\text{ed}}\text{L}^{\text{5}}\text{Cu})_2\text{O}_2](\text{SbF}_6)_2$ with $0 \rightarrow 1.1$ equivalents of CH_3SO_3^- (THF, 1 mM Cu, 187 K). The initial equilibrium position favors the **O** isomer (~ 450 nm), while the more coordinating counteranion, CH_3SO_3^- , biases the equilibrium position towards the **P** isomer (~ 370 nm).

the ligand structure with the counteranion and solvent playing subordinate roles. Comparisons within several series of closely related L^{PDA} clearly indicate that the more sterically demanding ligand favors the formation of **P** over **O** resulting in a larger K_{eq} (Fig. 2). For the 1,3-diaminopropane series, $K_{\text{eq}}(\text{pdL}^4) > K_{\text{eq}}(\text{pdL}^3) > K_{\text{eq}}(\text{pdL}^2)$, and for the 1,2-diaminoethane series, $K_{\text{eq}}(\text{edL}^5) \gg K_{\text{eq}}(\text{edL}^4)$. These results are consistent with intraligand steric interactions within the **O** isomer as the dominant factor in positioning the equilibrium. Additional support of this conclusion is found by comparing the K_{eq} of the edL and pdL ligands. At parity of substituents, the pdL complexes are more effective in biasing the equilibrium to the **P** isomer; $K_{\text{eq}}(\text{pdL}^4) > K_{\text{eq}}(\text{edL}^4)$ and $K_{\text{eq}}(\text{pdL}^3) > K_{\text{eq}}(\text{edL}^3)$. These results can be attri-

buted to the larger metal bite-angle of pdL (N-Cu-N, $\sim 95^\circ$) in copper complexes compared to edL (N-Cu-N, $\sim 86^\circ$). This metal binding constraint results in a greater projection of the pdL substituents into the intervening space of the dimer. At parity of substituents, a pdL is more sterically demanding.

Geometry optimized models (DFT) of the **O** and **P** isomers of $[(^{\text{ed}}\text{L}^{\text{5}}\text{Cu})_2(\text{O})_2]^{2+}$ provide some structural insights into how the intraligand steric interactions are accommodated in each isomer. The metrical parameters of the symmetric cores are provided in the schematic drawings (Fig. 7). The Cu-Cu and Cu-O distances of the optimized structures are very close to those measured experimentally by Cu K-edge XAS. The **O** isomer is significantly twisted with each N-Cu-N plane rotated $+19^\circ$ and -19° relative to the Cu_2O_2 plane, for an overall 38° twist in the molecule. In contrast, the **P** isomer is nearly planar with an overall 6° twist in the molecule. The significant expansion of the Cu-Cu distance from **O** (2.78 Å) to **P** (3.51 Å) is associated with a decrease in the twist of the ligands as the intraligand steric interactions abate.

While this entire Perspective has focused on the dominant role of the amine ligand in controlling the type of species formed, the solvent and anions can also influence the species distribution. This is especially true in the case of the **O** ↔ **P** equilibria. Clear trends are observed with a change in the solvent dielectric with $[(^{\text{pd}}\text{L}^{\text{4}}\text{Cu})_2\text{O}_2]^{2+}$ (Fig. 8). Decreasing the dielectric of the solvent (acetone, THF, 2-MeTHF) progressively biases the equilibrium towards the **P** isomer.⁸⁶ Differential anion binding by the **P** isomer is a potential explanation of this trend. The calculated structures of $[(^{\text{ed}}\text{L}^{\text{5}}\text{Cu})_2(\mu_2\text{-O})_2]^{2+}$ (Fig. 7) clearly indicates that direct anion association with a copper center is not possible with the **O** isomer, while the more expanded core of the **P** isomer provides potential access for the anion(s) to bind to create a lesser charged species. Thus, lower dielectric solvent should preferentially stabilize the **P** isomer. This is observed for all three L^{PDA} systems that create measurable equilibrium mixtures. If anion ligation or tight ion-pairing to **P** is truly operative, then the equilibrium position should be very dependent on the nature of the anion. Indeed, changing the anion from SbF_6^- to ClO_4^- to CF_3SO_3^- influences the equilibrium position to a slight degree. A more spectacular change occurs when a “more coordinating” anion, CH_3SO_3^- , is employed. Titration of 1.1 equivalents of CH_3SO_3^- into an **O** ↔ **P** mixture of $[(^{\text{ed}}\text{L}^{\text{5}}\text{Cu})_2\text{O}_2](\text{SbF}_6)_2$ converts a **P** : **O** ratio of $\sim 10 : 90$ to a greater than $90 : 10$ ratio (Fig. 9). Thus, the counteranion role is far from innocent in these equilibria, and this behavior has important implications with respect to the relative reactivity of these oxidants with anionic substrates.⁸⁶

6. Summary

The reaction of Cu^{I} with O_2 is a deceptively simple reaction. This Perspective has detailed the use of a steric continuum of

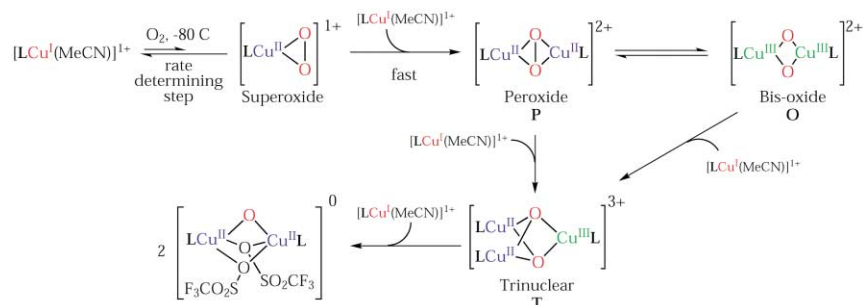


Fig. 10 A postulated reaction mechanism for the formation of the various products in the reaction of $[L^{\text{PDA}}\text{Cu}^{\text{I}}(\text{MeCN})]^{1+}$ with O_2 at low temperatures in aprotic solvents. The product formed is primarily determined by the steric demands of the ligands. Note that the structure of the final μ_2 -oxo dimer with bridging CF_3SO_3^- anions is only a postulated structure.

ligands to probe this reaction at low temperatures in aprotic solvents with weakly coordinating anions. Much of the reactivity can be explained through simple steric arguments and a realization that higher order polynuclear Cu– O_2 clusters are generally more compact. This is not to say that the electronic features of a ligand are unimportant, only that they are subordinate to the structure of the ligands. A working mechanistic scheme that summarizes the formation of the complexes with L^{PDA} is presented in Fig. 10. Note that many of the details have yet to be verified. However, the scheme provides an understanding and a predictive tool of how the diverse array of Cu– O_2 products might form. Whether these reactions are operative at ambient temperature will be the subject of future studies.

The initial step in all the oxygenation reactions of $\text{Cu}^{\text{I}}\text{-}L^{\text{PDA}}$ is the formation of a thermodynamically unfavorable 1 : 1 superoxide complex that reverts to starting materials if the second equivalent of the Cu^{I} complex is not readily available. The peroxide-level intermediate is presented in the scheme as a μ_2 - η^2 : η^2 -peroxide (**P**), as spectroscopic evidence for other peroxide forms with L^{PDA} is currently lacking. In our view, **P** resides at a critical juncture. If the steric demands of the ligand are sufficiently great to preclude the formation of a bis(μ_2 -oxo) dimer, **O**, then the **P** isomer can accumulate. No L^{PDA} are currently known to solely form a **P** isomer with CF_3SO_3^- counteranions, though examples of closely related ligands have recently appeared.^{24,25} An attenuation of the ligand steric demands can lead either to a **O** \leftrightarrow **P** equilibrium mixture or to a pure **O** species. The latter generally occurs. The energetic difference between these two species is relatively small. In the case of the least sterically demanding ligands, the 2 : 1 complexes can react with another equivalent of the Cu^{I} complex to form a **T** species. While attractive to postulate that the **T** formation proceeds directly from **O**,²⁴ our data does not allow us to distinguish between that path and another that involves an initial interconversion to the **P** isomer followed by the subsequent reaction with a Cu^{I} complex. The structural rearrangements necessary to proceed from the **O** isomer to the **T** species are equally unattractive to those required to proceed from the **P** isomer to the **T** species. If an inner-sphere process is operative in the formation of **T**, the path through the **P** isomer may be advantageous, as the Cu_2O_2 core is much more accessible. Finally, with the simplest of the $\text{Cu}^{\text{I}}\text{-}L^{\text{PDA}}$ complexes, we postulate that the trinuclear core reacts with a fourth and final Cu^{I} complex to give two equivalents of the bis(μ_2 -oxo) dimer, full reduction of O_2 , and oxidation of all the Cu^{I} centers to Cu^{II} .

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