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Effects of Tris(pyrazolyl)borato Ligand Substituents on Dioxygen Activation and Stabilization by Copper Compounds

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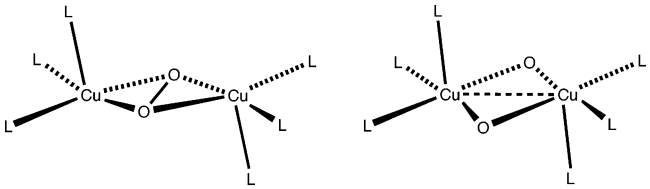
Dinuclear $[Cu_2(\mu\text{-}O)_2(Tp^{R,R'})_2]$ complexes, analogues of the active site of oxyhemocyanin, are theoretically studied, and the effect of the substituents of the tris(pyrazolyl)borate ligands, $Tp^{R,R'}$, is analyzed. Density functional theory calculations reveal that the type of bridging oxygen, peroxo, or bisoxo is strongly influenced by the nature and position of the R substituents because of variable substituent···bridging oxygen interactions, as well as electronic effects. The electronic effects of ligands at the 5 position are not significant, but peroxo complexes are favored by electron-withdrawing groups at the 3 position while bisoxo ones are strongly sterically disfavored.

Introduction

One of the most active fields of biocoordination chemistry stems from the discovery of the presence of copper in the active site of hemocyanin,[1,2] an oxygen transport protein found in molluscs and arthropods, as well as its role in the tyrosine-catalyzed oxidation of phenols to catechols and catechols to quinones.[3−6] Not less interesting are the intense and fruitful efforts to model the dinuclear copper enzymes using copper compounds of the type $[Cu_2(\mu\text{-}O)_2L_6]$.[7,8] These models are also believed to play a key role in the oxidation of alcohols[9] and C−H bonds,[5,10] as well as oxidative polymerizations[11] and nitrogen oxide decomposition.[12] Moreover, these model complexes provide evidence for the existence of an equilibrium between the limiting peroxo and bisoxo isomers **1a** and **1b**, respectively (Chart 1).[13,14] While the isomer **1a**, a $\mu\text{-}\eta^2\text{:}\eta^2$-peroxodicopper(II) complex, contains the form of oxygen present in oxyhemocyanin and tyrosinase, the bis-μ-oxodicopper(III) **1b** might be involved in the phenol hydroxylation reaction performed by tyrosinase.[15]

Chart 1



The Cu_2O_2 core of **1a** exhibits short, through-ring O−O distances, but long, nonbonding O···O distances are present in **1b**.[16−18] A recent example of a molecule containing a Cu_2O_2 core is $[Cu_2(\mu\text{-}O)_2(Tp^{CF_3,CH_3})_2]$ where $Tp^{R,R'}$ stands for

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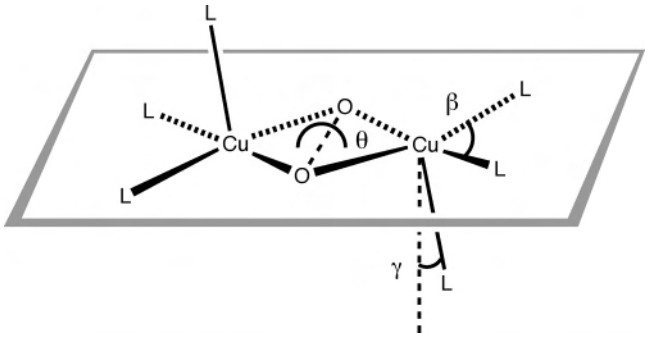
Chart 2



the tris(pyrazolyl)borato anion, with the R and R′ substituents located at the 3 (close to the metal) and 5 (close to the boron) positions, respectively. In $[Cu_2(\mu\text{-}O)_2(Tp^{CF_3,CH_3})_2]$, the substituents of the pyrazolyl rings seem to stabilize the peroxo form, **1a**, relative to the bisoxo one, **1b**.[19,20]

We have shown previously that the existence of bonding interactions between antipodal atoms (either metal−metal or bridge−bridge) in dinuclear complexes obeys simple rules.[21] These rules, applied to the model compound $[Cu_2(\mu\text{-}O)_2(NH_3)_6]^{2+}$, allowed us to understand the role of the electronic structure in the **1a** ↔ **1b** interconversion process, in which a reorganization of the coordination sphere of the copper atoms takes place simultaneously with the cleavage of the O−O bond.[22] Hence, the two copper atoms of isomer **1a** can be described as having a tetrahedral environment, formed by three ammonia and one *side-on*-bonded peroxide ligand. On the other hand, isomer **1b** can be described as a bis-square-pyramidal complex, in which two ammonia and two oxo bridges are in a basal plane while a third ammonia is weakly bonded in an apical position.

The rearrangement of the coordination sphere of the copper atoms can be described quantitatively by the angular parameters defined in Chart 2:[21,22] Thus, in **1a**, the copper tetrahedral environment corresponds to $\beta \approx 109°$ and $\gamma \approx 19°$, with three equivalent Cu−N bonds. In **1b**, the copper is nearly square-planar, having $\beta \approx 90°$ and $\gamma \approx 0°$ with two short and one long Cu−N distances.

The structural reorganization of the copper coordination spheres can be more simply gauged by means of continuous shape measures[23,24] relative to ideal tetrahedron, $S(T_d)$, and square-planar, $S(D_{4h})$, geometries. Briefly, a zero value of a given shape measure indicates a perfect match with the symmetry under consideration, while larger values reflect increasing deviations from it. Thus, for the isomer **1a** of $[Cu_2(\mu\text{-}O)_2(NH_3)_6]^{2+}$, one can calculate $S(T_d) = 0.76$ for the N_3-(η^2-O_2 centroid) set and $S(D_{4h}) = 7.33$ for the $N(basal)_2O_2$ donor set of each copper atom, disregarding in the latter case the apical NH_3 ligand in order to estimate deviations from square planarity. These values indicate that isomer **1a** is nearly tetrahedral. Similarly, because for isomer **1b** the $S(T_d)$ and $S(D_{4h})$ values are 1.85 and 1.24, respectively, its geometry is closer to that of a square-planar complex with an additional fifth axial ligand, consistent with the angular parameter analysis. The reorganization of the copper coordination sphere also implies some degree of electron transfer from copper to oxygen atoms, consistent with the following oxidation states: Cu^I/O_2 prior to the oxygen binding step, Cu^{II}/O_2^{2-} in peroxo complexes of type **1a**, and $Cu^{III}/(O^{2-})_2$ in bisoxo complexes of type **1b**.

The electronic structure of the ligands that promote/prevent oxygen binding is naturally expected to influence the copper oxidation states and type of bridging oxygen.[25] This was the basis for our experimental consideration[19] of quasi-isostructural variations in the Tp series and the current DFT theoretical search for understanding the theoretical foundations of the dioxygen molecule formation/cleavage process because the six ammonia ligands in $[Cu_2(\mu\text{-}O)_2(NH_3)_6]^{2+}$ are substituted by two tridentate Tp anions to yield $[Cu_2(\mu\text{-}O)_2(Tp^{R,R'})_2]$ complexes. The effects of the R electron-withdrawing fluorinated groups on the O−O bond splitting are of particular interest and are examined in depth in this paper. While in a previous study the role of substituent−substituent steric repulsions was analyzed,[26] herein we will discuss some cases in which substituent-bridging oxo interactions may influence the oxo−peroxo equilibrium. To that end, we have explored a variety of $[Cu_2(\mu\text{-}O)_2(Tp^{R,R'})_2]$ complexes with different R and R′ substituents, some of them as yet unprepared.

The accurate calculation of the energy differences between the peroxo- and bisoxo-bridged isomers of copper complexes is still a matter of debate, and several authors have reported theoretical studies at the pure DFT,[27] CASPT2,[28] MRCI,[29] and CR-CCSD(T)[30] levels. Although it is generally assumed that DFT-B3LYP calculations somewhat underestimate the stability of the **1b** isomer, this method allows one to treat the large systems studied in this work and is expected to reveal correctly the trends in the energy difference between the two isomers upon changes in the substitution pattern of the Tp ligand.

Results and Discussion

Geometrical Features. DFT calculations were performed on complexes of the general formula $[Cu_2(\mu\text{-}O)_2(Tp^{R,R'})_2]$

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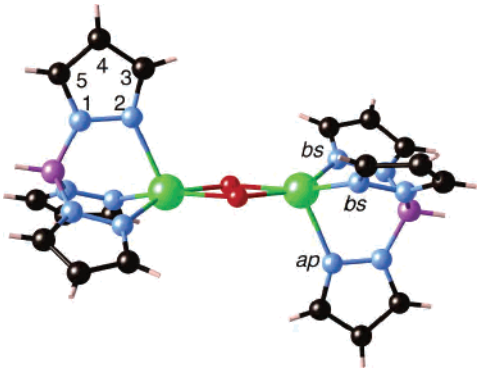

Figure 1. Basic structure for $[Cu_2(\mu\text{-}O)_2Tp_2]$ compounds, with identification of basal (bs) and apical (ap) Cu−N bonds and the numbering scheme for the pyrazolyl atoms. Color code: Cu, green; O, red; N, blue; C, black.

corresponding to the geometry shown in Figure 1. The main geometrical parameters are presented in Table 1. Atomic coordinates of the optimized geometries are supplied as Supporting Information.

For the compound with the unsubstituted Tp ligand, $[Cu_2(\mu\text{-}O)_2(Tp^{H,H})_2]$, two energy minima are found, similarly to previous results for a simpler model with monodentate ligands, $[Cu_2(\mu\text{-}O)_2(NH_3)_6]$. One minimum corresponds to structure **1a**, with an O−O distance of 1.41 Å, clearly indicative of a bond intermediate between those in O_2^{2-} and O_2, together with a long Cu···Cu distance of 3.66 Å. The second minimum has structure **1b**, with no through-ring bonding interaction, having O···O and Cu···Cu distances of 2.25 and 2.83 Å, respectively. The Cu−O distances in the Cu_2O_2 core are significantly longer in **1a** (1.97 Å) than in **1b** (1.81 Å), as expected according with a previous qualitative bonding analysis.[21] The $Cu-N_{bs}$ and $Cu-N_{ap}$ distances are consistent with a tridentate (κ^3) coordination mode of the Tp ligand. Note that, in going from **1a** to **1b**, $Cu-N_{bs}$ decreases by only 0.06 Å, whereas $Cu-N_{ap}$ increases by 0.20 Å, consistent with a change from tetrahedral to nearly square-planar coordination of the copper atoms and as indicated by the corresponding symmetry measures, $S(T_d)$ and $S(D_{4h})$ (Table 1).

The energetic profile for the cleavage of the O−O bond in going from **1a** to **1b** is shown in Figure 2. The two minima are separated by 16.7 kcal·mol^{-1}, with the more stable structure being **1a**, as expected from previous studies.[21,26] The two minima are connected by a transition state, located at O···O ≈ 1.94 Å, with an estimated energy of ∼19 kcal·mol^{-1} above that of **1a**. This value is within the 17−19 kcal·mol^{-1} range previously reported for $[Cu_2(\mu\text{-}O)_2(NH_3)_6]^{2+}$ (O···O ≈ 1.85 Å).[22,31]

Substitution Effects. To estimate the contributions of electronic and steric effects of the fluoro substituents to the extra stability of the peroxo isomer, we have examined several $Tp^{3R,5R'}$ ligand substitution schemes, by independently varying both the nature of the substituents and their position. As mentioned above and shown in Figure 1, for the 3-substituted ligand R is close to the Cu_2O_2 core while for the 5-substituted ligand R′ is away from it. These ligands are abbreviated as $Tp^{R,R'}$, and for the sake of clarity, we will also include hydrogen atoms in case substituents are missing. Thus, the unsubstituted Tp ligand is abbreviated $Tp^{H,H}$. We group the ligands for subsequent discussion into five categories: (a) 3-halo derivatives $Tp^{X,Z}$ where X = F, Cl, Br, and I; (b) 5-fluoro derivatives $Tp^{Z,F}$; (c) 3-methyl, $Tp^{CH_3,Z}$, and related 3-trifluoromethyl, $Tp^{CF_3,Z}$, derivatives; (d) mixed ligands having trifluoromethyl groups in some pyrazolyl rings (pz) such as $HB(pz)(pz^{CF_3,Z})_2$ and $HB(pz)_2(pz^{CF_3,Z})$; and (e) hydrogen donor groups, such as amino or hydroxyl, $Tp^{NH_2,Z}$ and $Tp^{OH,Z}$. In these formulas, Z stands for any atom or group, including H.

(a) 3-Halo-Substituted Ligands. Unlike the complexes of the unsubstituted Tp ligand, the optimized structures for compounds with the $Tp^{X,Z}$ ligands (X = F, Cl, Br, and I; Z = H) present only one minimum with a short O−O distance of about 1.40 Å (**1a**), whereas the isomer **1b** is estimated to be about 26 kcal·mol^{-1} higher in energy, as illustrated in Figure 2 for the case of $Tp^{F,H}$. Only small variations in bonding parameters are found for the four members of this family, with the main difference appearing in the $Cu-N_{ap}$ distance, which increases from 2.276 Å for F to 2.316 Å for I.

The additional destabilization of the bisoxo-bridged isomer **1b** upon introduction of fluorine atoms into the optimized geometry of unsubstituted **1b**-$Tp^{H,H}$ to give $Tp^{F,H}$ can be attributed to the $O\cdots F_{bs}$ repulsions within the set of the four basally coordinated pyrazolyl rings; see Figure 3. Thus, the $O\cdots F_{bs}$ distance in optimized peroxo **1a**-$[Cu_2(\mu\text{-}O)_2(Tp^{F,H})_2]$ is 3.57 Å, but this value is reduced to only 2.73 Å in the hypothetical bisoxo isomeric structure **1b** (calculated by fixing the O···O distance at 2.255 Å, as in $[Cu_2(\mu\text{-}O)_2(Tp^{H,H})_2]$ and optimizing the rest of the structure). Thus, the O···F steric interactions contribute very significantly to the destabilization of the bisoxo isomer **1b** of $[Cu_2(\mu\text{-}O)_2(Tp^{F,H})_2]$. Similarly, the O···X nonbonding contacts decrease from 3.63−3.73 to 2.72−2.76 Å for the other halogenated ligands when going from the **1a** to **1b** type structures. Distances between halogen atoms at the basal pyrazolyl rings of the $Tp^{X,H}$ ligands coordinated to each copper atom in excess of 4.80 and 3.66 Å for **1a** and **1b** isomers, respectively, rule out any significant $X_{bs}\cdots X_{bs}$ steric interaction.

(b) 5-Fluoro Derivatives. The copper complexes of $Tp^{H,F}$ and $Tp^{F,F}$ ligands have been studied in order to analyze the effect of placing substituents in position 5 of the pyrazolyl rings and compared with the complexes of the $Tp^{H,H}$ and $Tp^{F,H}$ pair discussed above. The results indicate that substitution of H by F at the 5 position has a negligible influence on the relative stabilities of the two isomeric forms. Hence, the two optimized structures obtained for $Tp^{H,F}$ (**1a** and **1b**) are equivalent to those calculated for the unsubstituted $Tp^{H,H}$ analogue and have similar relative energies, whereas the complex with the $Tp^{F,F}$ ligand presents only one minimum, structure **1a**, whose bond distances and angles are identical with those of **1a**-$Tp^{F,H}$ within 0.003 Å and 0.4°, respectively. We can conclude that the substituents in the 5 position of the pyrazolyl rings (if not too bulky to interact with the B−H group or with themselves) do not affect electronically the

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Table 1. Relative Energies and Geometrical Parameters[a] for Optimized Dinuclear Complexes of the Type $[Cu_2(\mu\text{-}O)_2(L)_2]$ and Related Compounds (L = Tripodal Ligand)[b]

L	isomer	energy	Cu···Cu	O···O	Cu−O	Cu−N_{bs}	Cu−N_{ap}	β	γ	$S(T_d)$	$S(D_{4h})$
$(NH_3)_3$[22]	**1a**	0.0	3.668	1.515	1.985	2.055	2.220	104.4	8.3	0.76	7.33
	1b	+17.0	2.869	2.288	1.835	2.003	2.381	99.3	9.3	1.85	1.24
$Tp^{H,H}$	**1a**	0.0	3.659	1.412	1.961	2.032	2.256	93.8	24.2	2.20	7.69
	1b	+16.7	2.828	2.255	1.808	1.976	2.460	92.0	26.0	3.07	0.98
$Tp^{F,H}$	**1a**		3.647	1.403	1.954	2.044	2.276	92.3	20.7	2.61	7.68
$Tp^{Cl,H}$	**1a**		3.657	1.399	1.958	2.052	2.285	92.7	21.3	2.50	7.77
$Tp^{Br,H}$	**1a**		3.667	1.398	1.962	2.057	2.293	93.1	22.9	2.40	7.83
$Tp^{I,H}$	**1a**		3.683	1.397	1.970	2.064	2.316	93.9	23.9	2.28	7.91
$Tp^{H,F}$	**1a**	0.0	3.656	1.411	1.960	2.031	2.257	93.9	22.6	2.20	7.64
	1b	+17.0	2.826	2.254	1.808	1.975	2.448	92.2	25.4	3.01	0.98
$Tp^{F,F}$	**1a**		3.646	1.402	1.953	2.043	2.273	92.4	20.3	2.61	7.68
$Tp^{CH_3,H}$	**1a**	0.0	3.690	1.409	1.975	2.033	2.246	93.8	21.9	2.15	7.75
	1b	+22.0	2.966	2.117	1.822	2.014	2.388	91.4	18.5	2.60	1.63
$Tp^{CF_3,H}$	**1a**		3.633	1.428	1.952	2.068	2.336	91.3	19.9	2.70	7.49
$Tp^{bs-CF_3,H}$ [c]	**1a**		3.657	1.398	1.958	2.059	2.205	90.7	19.8	2.58	7.86
$Tp^{ap-CF_3,H}$ [c]	**1a**	0.0	3.627	1.414	1.946	2.017	2.319	93.9	15.1	2.63	7.36
	1b	+15.4	2.812	2.255	1.802	1.969	2.469	91.7	20.2	3.13	0.84
$Tp^{NH_2,H}$	**1a**	0.0	3.677	1.475	1.981	2.000	2.224	93.1	26.2	2.20	7.20
	1b	+15.9	2.850	2.323	1.838	1.977	2.429	91.3	23.3	2.89	0.78
$Tp^{OH,H}$	**1a**	0.0	3.689	1.426	1.978	2.001	2.237	94.4	26.2	2.08	7.62
	1b	−8.0	2.858	2.485	1.893	1.976	2.549	92.0	22.5	3.80	0.55

[a] For the definition of angles, see Chart 2. [b] Energies are in kcal·mol^{-1}, distances in Å, and angles in deg. [c] $Tp^{bs-CF_3,H}$ and $Tp^{ap-CF_3,H}$ are tris(pyrazolyl)borato ligands in which only basal or apical pyrazolyl rings contain a substituent, respectively.

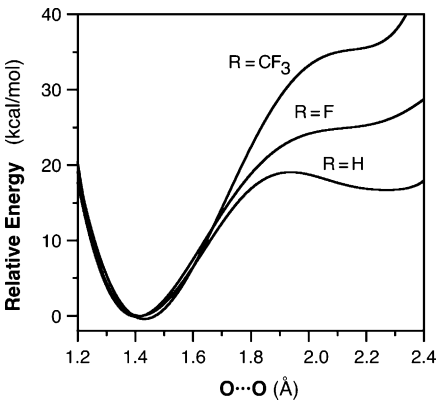

Figure 2. Energetic profiles for the O−O bond splitting/formation in $[Cu_2(\mu\text{-}O)_2(Tp^{R,H})_2]$ compounds with R = H, F, and CF_3.

structural choice of the $\{Cu_2O_2\}^{2+}$ core and that the molecular geometry of the 5-substituted complexes is well reproduced by related ligands in which that position remains unsubstituted.

(c) 3-Methyl and 3-Trifluoromethyl Derivatives. Compound $[Cu_2(\mu\text{-}O)_2(Tp^{CH_3,H})_2]$ has two energy minima corresponding to structures **1a** and **1b**. The former isomer presents geometric parameters close to those of the related $[Cu_2(\mu\text{-}O)_2(Tp^{H,H})_2]$ complex, thus indicating that the methyl substituents have little effect on the molecular geometry, despite the short contacts between the bridging oxygen atoms and the methyl groups (O···H = 2.59 Å). In contrast, the **1b** isomer presents clear differences with respect to the unsubstituted analogue because the $Tp^{CH_3,H}$ ligand is accommodated in the molecular geometry by a lengthening of the Cu−N_{bs} bond distance and a shortening of the Cu−N_{ap} bond distance by 0.03 and 0.07 Å, respectively. Moreover, short contacts between the bridging oxygen atoms and the methyl groups of basal pyrazolyl rings (shortest O···H distance = 2.21 Å, with O···H−C angle = 142°) are shorter than those of the unsubstituted $Tp^{H,H}$ analogue (2.76 Å) and can be considered as weakly attractive hydrogen-bonding interactions.[32] Longer distances have been found for Me_{bs}···Me_{bs} contacts (C···C ≥ 4.73; H···H ≥ 3.28 Å), again indicating that steric interactions between pyrazolyl rings have a minor role in determining the relative stability of the two isomers. Because in the $Tp^{iPr,iPr}$ compound first reported by Kitajima and coworkers[33,34] the methyl groups of the *i*Pr substituents in the 3 position are pointing away from the Cu_2O_2 core, this compound should be well represented by $[Cu_2(\mu\text{-}O)_2(Tp^{CH_3,Z})_2]$, as verified by the similar bond distances and angles found in their experimental and calculated structures, respectively. Also the greater calculated stability of isomer **1a** for $[Cu_2(\mu\text{-}O)_2(Tp^{CH_3,Z})_2]$ is in excellent agreement with the structure found for the $Tp^{iPr,iPr}$ analogue.

Importantly, in contrast with $[Cu_2(\mu\text{-}O)_2(Tp^{CH_3,H})_2]$, $[Cu_2(\mu\text{-}O)_2(Tp^{CF_3,H})_2]$ exhibits only one energy minimum, corresponding to the peroxo structure **1a** (Figure 4). Notably, the Cu−N_{ap} distance, 2.34 Å (Table 1), is the second longest (after the complex containing the $Tp^{OH,H}$ ligand). The O···F−C contacts (O···F_{bs} = 3.04 Å) are too long for interatomic interactions (Chart 3).

However, the CF_3 groups play a significant regulatory role. Thus, if the formation of isomer **1b** is attempted by elongating the O···O bond, the distance between the CF_3 groups and the bridging O atoms, O···F_{bs}, shortens to ∼2.0 Å, resulting in strong steric repulsions, in sharp contrast with the methyl analogue, whose weak attractive interaction with the metal−oxo groups was discussed above. These terminal-

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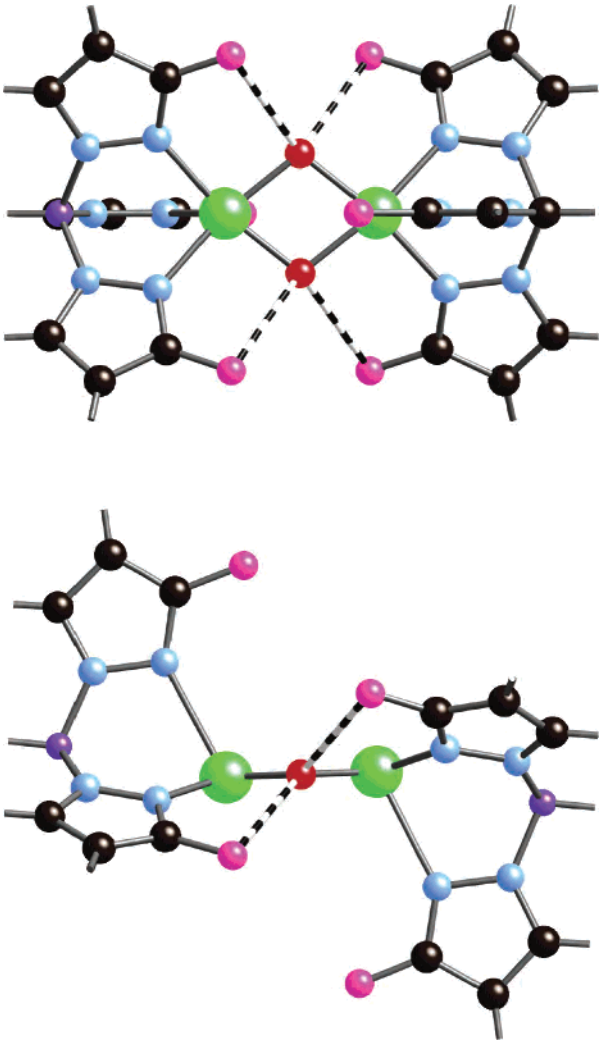


Figure 3. Perpendicular (top) and parallel (bottom) views of the optimized structure of the bisoxo isomer **1b** of the Cu_2O_2 ring of $[Cu_2(\mu\text{-}O)_2(Tp^{F,H})_2]$. In the parallel view, one basal pyrazolyl group of each Tp ligand is omitted for the sake of clarity. Hydrogen atoms have been omitted. Color code: Cu, green; O, red; N, blue; C, black; F, purple. The O···F contacts, 2.73 Å, are shown as discontinuous lines.

bridging ligand repulsions provide a steric rationale for the energy increase of the **1b** isomer relative to **1a** along the series $[Cu_2(\mu\text{-}O)_2(Tp^{R,H})_2]$ [R = H < F < CF_3 (see Figure 2)]. Note that the energetic cost of elongating the O−O bond up to ∼1.65 Å appears similar for the above three complexes, with the R = CF_3 complex exhibiting a slightly more shallow minimum. Stretching the O−O bond beyond ∼1.65 Å results in the steep destabilization of the bisoxo complexes. Only for R = H is a slightly shallow minimum noticed for O···O ≈ 2.3 Å, consistent with the onset of a bisoxo, **1b** structure. Assuming that the destabilization of the bisoxo form relative to the peroxo structure is due essentially to the interactions between the 3 substituent and the oxygen atoms, one can estimate these repulsions in $[Cu_2(\mu\text{-}O)_2(Tp^{R,H})_2]$ to increase by ∼21 kcal·mol^{-1} from R = H to R = F and by ∼12 kcal·mol^{-1} from R = F to R = CF_3. The energy required for opening of the Cu_2O_2 ring in the $[Cu_2(\mu\text{-}O)_2(Tp^{CF_3,H})_2]$ derivative (∼33 kcal·mol^{-1}) is thus consistent with the high experimentally observed stability of the peroxo isomer

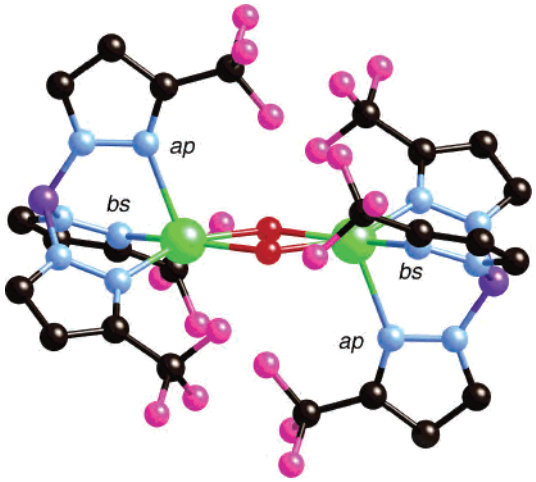
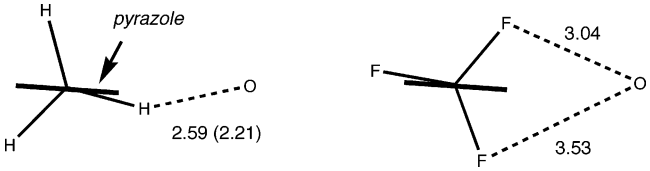


Figure 4. Optimized peroxo structure **1a** of $[Cu_2(\mu\text{-}O)_2(Tp^{CF_3,H})_2]$ viewed along the O−O vector. The closest O···F contacts (2.89 Å) correspond to the CF_3 group of the apical pyrazolyl rings (see also Chart 3). Apical (ap) and basal (bs) nitrogen donor atoms are indicated; all hydrogen atoms are omitted for the sake of clarity. Color code: Cu, green; O, red; N, blue; C, black; F, purple.

Chart 3



of $[Cu_2(\mu\text{-}O)_2(Tp^{CF_3,CH_3})_2]$.[19,20] Finally, we note that the Cu···F_{ap} contacts, ∼3.0 Å, are too long to give significant through-space metal···F−C interaction such as that recently found for vanadium complexes by electron paramagnetic resonance (EPR).[35]

To put the numerical values of such contacts in context, we carried out a structural database search for O···F nonbonded distances shorter than 3.0 Å (see the Appendix). The only contact shorter than 2.8 Å found corresponds to a case[36] in which a BF_4^- anion is weakly coordinated to copper at an axial position (Cu···F = 2.17 Å) that imposes a relatively short contact to a basally coordinated oxygen atom (2.36 Å). The available structural data thus support the idea that the calculated value for the O···F contact in **1b**-$[Cu_2(\mu\text{-}O)_2(Tp^{CF_3,H})_2]$, 2.0 Å, represents a strongly repulsive situation.[37]

To obtain a rough estimate of the importance of the O···F_{bs} contacts for the destabilization of the bisoxo isomer **1b** in $[Cu_2(\mu\text{-}O)_2(Tp^{R,H})_2]$ complexes (R = CH_3 and CF_3), we have calculated the intermolecular interaction energy between H_2O and F_3CH, with the oxygen and carbon atoms fixed in the same geometry as the O···F_3C (or H_3C) fragment in optimized **1b**-$[Cu_2(\mu\text{-}O)_2(Tp^{R,H})_2]$ (R = CH_3) and in the hypothetical **1b** structure of the R = CF_3 analogue. From

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the peroxo to bisoxo form, the calculated interaction energies (corrected for the basis set superposition error) change by −0.1 and +4.4 kcal·mol^{-1} per oxygen atom in the R = CH_3 and CF_3 geometries, respectively. Because there are two such interactions in the full complex, an estimated interaction energy between the CF_3 groups and the bridging oxo ligands of +9 kcal·mol^{-1} is in excellent agreement with the increased instability of **1b**-[$Cu_2(\mu\text{-}O)_2(Tp^{R,H})_2$] (R = CF_3) compared to the analogous compound with R = CH_3 (∼11 kcal·mol^{-1}) and confirms the crucial role that the repulsive steric interactions between the 3-CF_3 group and the bridging oxygen atoms have in rendering structure **1b** unstable.

Another structural aspect of [$Cu_2(\mu\text{-}O)_2(Tp^{CF_3,H})_2$] that is of interest is the Cu_2O_2 ring preference for planarity, as found in all compounds mentioned above (Table 1). An estimation of the Cu_2O_2 ring bending energy can be obtained when its geometry is partially optimized by fixing the bending angle between the two CuO_2 planes, θ, to 150° (Chart 2). The bent structure is destabilized by about 8 kcal·mol^{-1} relative to the planar geometry, θ = 180°, and is accompanied by changes in the geometric parameters of the Cu_2O_2 core, specifically, the interatomic distances O−O = 1.37 Å and Cu−O = 2.01 Å, to be compared with the values obtained for the planar optimized structure, 1.43 and 1.95 Å, respectively.

Because the two copper atoms in the optimum **1a** peroxo structure of [$Cu_2(\mu\text{-}O)_2(Tp^{CF_3,H})_2$] are formally copper(II), the exchange interaction between the two unpaired electrons is an important aspect of their electronic and magnetic properties. Therefore, we have investigated the exchange interaction between the two copper(II) atoms, in an attempt to evaluate the relative energies of the singlet (antiferromagnetic coupling) and triplet (ferromagnetic coupling) states. Broken-symmetry DFT calculations indicate a stabilization of the singlet relative to the triplet state by −7178 and −5271 cm^{-1} for the [$Cu_2(\mu\text{-}O)_2(Tp^{CF_3,H})_2$] and [$Cu_2(\mu\text{-}O)_2(Tp^{CH_3,H})_2$] complexes, respectively. Such strong antiferromagnetic interactions should render these complexes diamagnetic at room temperature. Our calculations are consistent with the experimental behavior reported for alkyl-substituted analogous complexes[34] and with previous theoretical calculations that give values between −2500 and −7600 cm^{-1}.[38−41] These results are also fully consistent with the observed diamagnetism and EPR-silent behavior at room temperature of [$Cu_2(\mu\text{-}O)_2(Tp^{CF_3,CH_3})_2$],[19] as well as with the facile observation of solid-state NMR signals from this complex.[42] Notably, the effect of ligand fluorination is to increase significantly the singlet−triplet gap.

(d) Mixed Ligands. To determine the importance of the $Tp^{CF_3,H}$ ligand for the molecular geometry of the $\{Cu_2O_2\}^{2+}$ core, we have also studied two complexes having different pyrazolyl rings: $HB(pz)(pz^{3CF_3})_2$ and $HB(pz)_2(pz^{3CF_3})$. In these complexes, the CF_3 groups are attached to rings either basally (two groups) or apically (one group) bonded to copper atoms. The complexes are abbreviated as $Tp^{bs-CF_3,H}$ and $Tp^{ap-CF_3,H}$, respectively.

The complex having the two pz^{3CF_3} rings of the Tp ligand in basal positions, [$Cu_2(\mu\text{-}O)_2(Tp^{bs-CF_3,H})_2$], exhibits the same trends as those found above for the analogous complex with all three pyrazolyl rings carrying CF_3: only one energy minimum is obtained, with an O−O distance of about 1.40 Å (peroxo structure **1a**). We notice that by removal of the CF_3 group Cu−N_{ap} decreases from 2.34 to 2.21 Å, probably because of a relaxation in the steric congestion of the $F_{bs}\cdots F_{ap}$ contacts of 2.79 Å found in [$Cu_2(\mu\text{-}O)_2(Tp^{CF_3,H})_2$]. In addition, the enhanced basicity of the pz ligand that lost its CF_3 group may contribute to the shortening of its Cu−N bonds.

In contrast, but consistent with the basal steric hindrance mentioned above, the complex with the single CF_3 substituent at the apically coordinated pyrazolyl rings has two minima corresponding to the **1a** and **1b** isomers, whose molecular geometries are practically the same as that in the unsubstituted analogue. In other words, the presence of the CF_3 groups on the apical pyrazole prevents the formation of either the peroxo or bisoxo isomer.

(e) Hydrogen Donor Derivatives. According to our conclusion that for [$Cu_2(\mu\text{-}O)_2(Tp^{CF_3,H})_2$] the **1b** isomer is destabilized by F···O repulsions whereas it is somewhat stabilized by C−H···O weak hydrogen bonding in the case of [$Cu_2(\mu\text{-}O)_2(Tp^{CH_3,H})_2$], one would expect that the presence of better hydrogen donor groups at position 3 of the pyrazolyl rings would significantly stabilize that isomer. We have thus selected amino and hydroxo groups as hydrogen donors and performed calculations on [$Cu_2(\mu\text{-}O)_2(Tp^{NH_2,H})_2$] and [$Cu_2(\mu\text{-}O)_2(Tp^{OH,H})_2$]. As predicted, both complexes present two minima corresponding to isomers **1a** and **1b**. Furthermore, as the hydrogen-bond formation ability of the R group increases (i.e., $CH_3 < NH_2 < OH$), the energy of **1b** relative to that of **1a** decreases, finally resulting in a reversal of their relative stability for [$Cu_2(\mu\text{-}O)_2(Tp^{OH,H})_2$] (see Table 1). The isomers **1b** show important differences in their O···O distances, which parallel the ligand-induced increase in the stability of the bisoxo isomer: $Tp^{CH_3,H}$ (2.12 Å) < $Tp^{NH_2,H}$ (2.32 Å) < $Tp^{OH,H}$ (2.48 Å). Both the increased bisoxo isomer stability and O···O distances are undoubtedly related to the increasing strength of the hydrogen bonds, as revealed by the decreasing (Cu)O···H(ligand) distances (2.21, 1.96, and 1.59 Å, respectively). Finally, the hydrogen-bond-enhanced stability of the bisdioxo isomer is also correlated with a significant approach to square-planar coordination-sphere geometry for the copper atoms, as indicated by a progressive lengthening of the Cu−N_{ap} bond distances, 2.39, 2.43, and 2.55, respectively, as well as by the overall progressive approach to an ideal square-planar geometry as measured by the $S(D_{4h})$ shape parameters: 1.63, 0.78, and 0.55, respectively (Table 1). We note here that, as one moves from peroxo to bisoxo complexes, copper(II) becomes copper(III), a process favored by electron-rich ligands and which also likely favors the limiting square-planar coordination geometry.

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Table 2. Metal Coordination-Sphere Parameters[a] for Experimental Structures Having a General Formula $[Cu_2(\mu\text{-}O)_2(L)_2]$, Where L = Tripodal Ligand[b]

L[c]	Cu···Cu	O···O	Cu···O	Cu- -N_{bs}	Cu- -N_{ap}	β	γ	θ	$S(T_d)$	$S(D_{4h})$	ref
					Structure **1a**						
oxyhemocyanin	3.59	1.41	1.98	2.08	2.42	96.2	9.3	156	2.10	9.53	43
$Tp^{iPr,iPr}$	3.556	1.413	1.913	1.997	2.260	92.6	24.7	180	2.40	7.42	33, 34
$TACD^{iPr}$	3.519	1.374	1.893	2.054	2.221	104.8	35.7	172	2.11	10.52	26
$-CH_2$(6-TPYM)	3.477	1.486	1.908	1.995	2.201	91.6	19.0	163	2.32	7.55	44
$-CH_2$(6-TPYE)	3.520	1.488	1.919	1.984	2.188	91.5	18.0	168	2.47	7.52	45
Tp^{CF_3,CH_3}											
A	3.366	1.728	1.892	2.005	2.420	96.6	18.4	180	2.62	4.38	20
B	3.366	1.496	1.890	2.004	2.420	96.6	18.7	151	3.44	8.07	
					Structure **1b**						
$TACN^{Bz}$	2.796	2.287	1.806	1.986	2.297	88.9	16.9	180	3.15	0.76	13, 14
ETPY	2.866	2.287	1.833	1.991	2.412, 2.592	99.2	11.6, 11.1	180	3.23, 3.77	1.02	46
TPYA	2.759	2.323	1.803	1.940	2.478, 2.545	87.0	15.7, 13.1	180	4.44, 4.65	0.53	47
$-CH_2(TACN^{iPr})$	2.782	2.352	1.827	1.991	2.310	88.0	12.0	168	3.21	0.98	48

[a] For the definition of angles, see Chart 2. [b] Distances are in Å and angles in deg. [c] Abbreviations: ETPY = 1,1,1-(2-pyridylmethyl)bis[(6-methyl-2-pyridyl)ethyl]amine; TACD = 1,4,7-triazacyclodecane; TACN = 1,4,7-triazacyclononane; TPYA = 1,1,1-(2-pyridylmethyl)bis[(6-methyl-2-pyridyl)-methyl]amine; TPYE = bis(6-methyl-2-pyridyl)(2-pyridyl)ethane; TPYM = bis(6-methyl-2-pyridyl)(2-pyridyl)methane.

Structural Comparison with Experimental Data. The main structural parameters for compounds having Cu_2O_2 rings are shown in Table 2.

The first observation, as noted previously, is that there are clear differences between the geometric parameters of structures **1a** and **1b**. The computed structural data reproduce well the experimental trends regarding the interatomic distances and the shape parameters, clearly showing that, despite some variability from one compound to another, there is a clear-cut distinction between the peroxo-bridged structure, **1a**, and the bisoxo-bridged one, **1b**. The most distinctive differences appear in the nonbonding contacts: O···O distances of less than 1.73 Å for **1a** and larger than 2.12 Å for **1b** and Cu···Cu distances larger than 3.48 Å and shorter than 2.97 Å, respectively. The metal−ligand bond distances for **1a** and **1b** isomers are as follows: Cu−O, larger than 1.89 Å and shorter than 1.84 Å; Cu−N_{bs}, larger than 2.00 Å and shorter than 2.01 Å; Cu−N_{ap}, shorter than 2.42 Å and larger than 2.30 Å, respectively. Finally, the peroxo structures present small values of their *tetrahedral* shape parameters (0.76−3.44), whereas for **1b**, it is the *square-planar* shape parameters that have small values (0.53−1.63). These data illustrate that the peroxo−bisoxo isomerization is accompanied by a change in the coordination spheres of the copper ions from a distorted tetrahedral to a nearly square-planar (4 + 1) geometry. All compounds are planar with an O···O hinge angle θ of about 180°, except for two experimental structures that have tethers joining the terminal copper ligands.

The present results support the previous structural assignment of X-ray data as resulting from the cocrystallization of the peroxo isomer of $[Cu_2(\mu\text{-}O)_2(Tp^{CF_3,CH_3})_2]$ and a hydroxo-bridged complex. In effect, a long O···O distance of 1.73 Å and the concomitant bending of the Cu_2O_2 core that would be consistent with one of the positions of the disordered oxygen atoms can be ruled out on energetic grounds according to the present calculations. Furthermore, optimization of the analogous complex with a bis(hydroxo)-bridged copper(II) core reveals a O···O distance of 2.32 Å. Therefore, the previous explanation of the experimental distance as a weighted average of the population of crystallographic sites with oxo- and hydroxo-bridged species is a plausible one.

Conclusions

The present theoretical studies have allowed us to understand the structural choice of $[Cu_2(\mu\text{-}O)_2(Tp^{R,R'})_2]$ compounds with different tris(pyrazolyl)borato ligand substitution patterns. For the selected Tp ligands, the relative stability of the peroxo- and bisoxo-bridged isomers has been evaluated, and the presence of one or two minima is seen to strongly depend on the nature of the substituent at the 3 position of the pyrazolyl rings but not on the presence of substituents at the 5 position.

The energy profiles of compounds with several substitution patterns clearly indicate that upon fluorination of position 3 of the pyrazolyl rings (either directly or by attaching a fluoroalkyl group) it becomes harder to split the O−O bond. In other words, fluorination renders the bonded peroxo closer to free dioxygen. This conclusion is consistent with the position of the O−O stretching in the resonance Raman spectra, which is shifted from 741 cm^{-1} in the $[Cu_2(\mu\text{-}O)_2(Tp^{iPr,iPr})_2]$ derivative[34] to 765 cm^{-1} in its related fluorinated complex $[Cu_2(\mu\text{-}O)_2(Tp^{CF_3,CH_3})_2]$.[19]

These observations can be rationalized by considering the repulsive (R = F, Cl, Br, I, and CF_3) or attractive (R = CH_3, NH_2, and OH) interactions between 3-R groups and the bridging oxygen atoms. These interactions, along with the ligand electron-withdrawing ability, are responsible for the enhanced stability of a copper(II) peroxo-bridged isomer relative to copper(III) bisoxo complexes in the 3-substituted Tp ligand series.

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Finally, our calculations never exclude peroxo structures but reveal that bisoxo structures cannot form in certain cases for steric reasons. Thus, at least for this class of complexes, models for non-heme dinuclear copper enzymes, peroxocopper(II) units, may be present in equilibrium with potentially bisoxocopper(III) ones but only if the ligands are electron-rich.

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Appendix

Computational Details. DFT unrestricted calculations were performed with the *Gaussian 98* suite of programs.[49] The hybrid functional known as B3LYP was applied.[50,51] The basis set used in the calculations is LANL2DZ for copper and heavy halogen atoms (double-ζ valence and outermost core orbitals with effective core pseudopotentials for the innermost shells)[52,53] and 6-31G for light elements of the tris(pyrazolyl)borato ligands (C, N, B, H, and F),[54] which has been substituted by 6-31G* for the oxygen and nitrogen atoms directly attached to the metal.[55,56] The evaluation of the singlet−triplet energy gap has been carried out by nonprojected DFT calculations using the methodology described elsewhere,[57,58] with the exchange coupling constant corresponding to the Heisenberg spin Hamiltonian $H = -JS_1S_2$.

Structural Database Search. The structural data were obtained through a systematic search in the Cambridge Structural Database (version 5.26).[59] Our search included compounds with several Cu_2O_2 cores. Continuous shape measures have been carried out using the *Shape* program,[60] in which $Cu(N_{bs})_2(N_{ap})(O_2$ centroid) and $Cu(N_{bs})_2(O)_2$ cores have been considered as coordination polyhedra. For more information on shape measures of tetracoordinate transition metals, the reader is referred to a recent review.[24] A search for intermolecular O···F contacts was conducted on all Cu−O fragments not having hydrogen atoms, to exclude hydrogen bonding. The usual constraints on the quality of the structural data were applied: only structures with R < 10%, no disorder, and no errors were considered.

Supporting Information Available: Atomic coordinates of the optimized structures **1a** and **1b** (Tables S1 and S2). This material is available free of charge via the Internet at http://pubs.acs.org.

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