Does the Mode of Dioxygen Binding to Dinuclear Copper Complexes Depend on the Spectator Nitrogen-Containing Ligands? An ab Initio Theoretical Study

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Ab initio two-determinants GVB computations (required to get the appropriate representation of the lowest singlet states of such systems) have been carried out for $(Cu^+(NH_3)_n)_2-O_2$ ($n = 0-3$) and $[Cu_2(\mu\text{-pydz})_2(cnge)_2]^{2+}-O_2$. Different dioxygen binding modes (ranging from perpendicular to parallel with respect to the Cu−Cu direction) on these complexes have been examined. The results obtained show unambiguously that the parallel arrangements are always the less stable ones. In the especially important case of $(Cu^+(NH_3)_3)_2-O_2$ complexes, both staggered and eclipsed conformations have been considered. They are found almost isoenergetic, and the optimized geometrical parameters are, for a perpendicular O_2 binding onto a staggered complex, in fine agreement with corresponding experimental data obtained from either oxyhemocyanin or its synthetic models. In the case of a $(Cu^+(NH_3)_4)_2-O_2$ complex, taken as a model for Karlin's $[\{(TMPA)Cu\}_2-O_2]^{2+}$ complex, the computations tend to show that the experimental end-on (trans μ-1,2) O_2 binding is due to the presence of four nitrogens in the copper's coordination shell. Regarding the complexes with $[Cu_2(\mu\text{-pydz})_2(cnge)_2]^{2+}$, the results indicate that the dioxygen binding mode remains perpendicular even if the fixation of a third pyridazine is known to occur in a parallel manner on this complex.

Introduction

Reversible dioxygen binding to various classes of transition metal complexes is at the origin of sustained attention because of its implications in metal-catalyzed oxidation chemistry[1] and in industrial air separation and dioxygen-removal processes.[2] Among those, several dicopper complexes are also of biological relevance because of their relation with important non-heme proteins such as tyrosinase (widely spread phenols and catechols oxidizer) or hemocyanin (Hc, dioxygen carrier in molluscs and arthropods). The mild and efficient dioxygen activation performed by these systems has triggered off a sustained interest for their oxygenated adducts, both on experimental[3] and theoretical[4] grounds.

In most crystallographical studies of dicopper oxygenated complexes available, the dioxygen molecule has been found roughly perpendicular to the Cu−Cu direction. This statement holds for the recently crystallized *Limulus polyphemus* oxyhemocyanin,[5] as well as for oxygenated model complexes.[6] Theoretical studies have also led to the conclusion that the side-on μ:η^2-η^2 peroxo binding is energetically favored over the end-on cis μ-1,2 peroxo in the case of $(Cu^+)_2O_2$[7] and $[Cu^+(NH_3)_2]_2-O_2$.[8] The $[\{(TMPA)Cu\}_2-O_2]^{2+}$ complex characterized by Karlin and colleagues[9] is somewhat different since the O−O bond makes an angle of 55° with respect to the Cu−Cu direction, leading to an end-on trans μ-1,2 coordination. Such an arrangement can stem either from Cu−Cu distances larger than 3.4 Å, as shown by previous computations on Cu_2-O_2,[7] or from the larger number of ligands involved in this case (4 coordinating nitrogens around each Cu). Interestingly, the ligands surrounding the copper cations adopt a staggered arrangement in most of these species (Chart 1). By contrast, Hubberstey *et al.*[10] have synthetized and characterized a bis-

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(1) See for instance: (a) Jones, R. D.; Summerville, D. A.; Basolo, F. *Chem. Rev.* **1979**, *79*, 139. (b) Spodine, E.; Manzur, J. *Coord. Chem. Rev.* **1992**, *119*, 171. (c) Pecoraro, V. L.; Baldwin, M. J.; Gelasco, A. *Chem. Rev.* **1994**, *94*, 807. (d) Que, L., Jr.; True, A. E. *Prog. Inorg. Chem.* **1990**, *38*, 97.

(2) Ramprasad, D.; Gilicinski, A. G.; Markley, T. J.; Pez, G. P. *Inorg. Chem.* **1994**, *33*, 2841.

(3) The whole 1994 issue no. 3 of *Chem. Rev.* was dedicated to this problem. See also: (a) Karlin, K. D. *Science* **1993**, *261*, 701. (b) Kitajima, N.; Moro-oka, Y. *J. Chem. Soc., Dalton Trans.* **1993**, 2665. (c) Della Longa, S.; Ascone, I.; Bianconi, A.; Bonfigli, A.; Congiu Castellano, A.; Zarivi, O.; Miranda, M. *J. Biol. Chem.* **1996**, *271*, 21025.

(4) For an excellent review on theoretical aspects, see: Bytheway, I.; Hall, M. B. *Chem. Rev.* **1994**, *94*, 639.

(5) (a) Magnus, K. A.; Ton-That, H.; Carpenter, J. E. (1993) In *Bioinorganic Chemistry of Copper*; Karlin, K. D.; Tieklar, Z., Eds.; Chapman & Hall: New York, 1993; pp 143−150. (b) Magnus, K. A.; Ton-That, H.; Bonaventura, C.; Bonaventura, J.; Hol, W. G. J. *Proteins* **1994**, *19*, 302. (c) Magnus, K. A.; Ton-That, H.; Carpenter, J. E. *Chem. Rev.* **1994**, *94*, 727.

(6) (a) Kitajima, N.; Fujisawa, K.; Fujimoto, C.; Moro-oka, Y.; Hashimoto, S.; Kitagawa, T.; Toriumi, K.; Tatsumi, K.; Nakamura, A. *J. Am. Chem. Soc.* **1992**, *114*, 1277. (b) Sanyal, I.; Karlin, K. D.; Strange, R. W.; Blackburn, N. J. *J. Am. Chem. Soc.* **1993**, *115*, 11259.

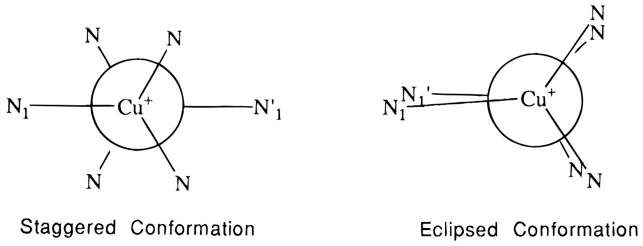
(7) Maddaluno, J.; Giessner-Prettre, C. *Inorg. Chem.* **1991**, *30*, 3439.

(8) Ross, P. K.; Solomon, E. I. *J. Am. Chem. Soc.* **1991**, *113*, 3246.

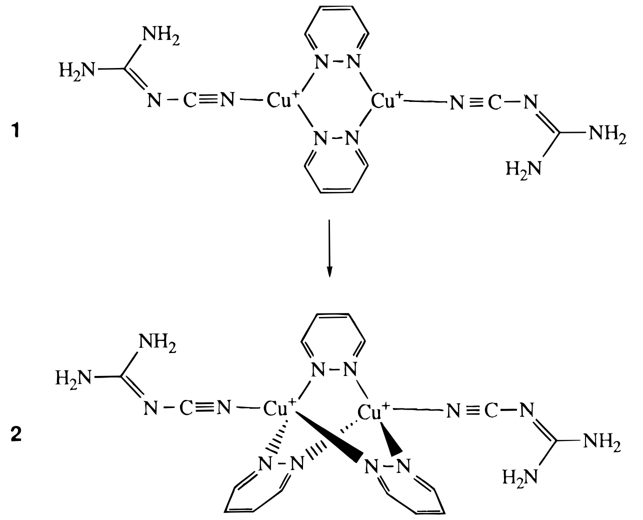
(9) (a) Jacobson, R. R.; Tyeklar, Z.; Farooq, A.; Karlin, K. D.; Liu, S.; Zubieta, J. *J. Am. Chem. Soc.* **1988**, *110*, 3690. (b) Tyeklar, Z.; Karlin, K. D. *Acc. Chem. Res.* **1989**, *22*, 241. (c) Tyeklar, Z.; Jacobson, R. R.; Wei, N.; Murthy, N. N.; Zubieta, J.; Karlin, K. D. *J. Am. Chem. Soc.* **1993**, *115*, 2677. (d) Karlin, K. D.; Lee, D. H.; Kaderli, S.; Zuberbülher, A. D. *J. Chem. Soc., Chem. Commun.* **1997**, 475. (e) Karlin, K. D.; Kaderli, S.; Zuberbülher, A. D. *Acc. Chem. Res.* **1997**, *30*, 139.

(10) Begley, M.; Hubberstey, P.; Russel, C. E.; Walton, P. H. *J. Chem. Soc., Dalton Trans.* **1994**, 2483.

Chart 1



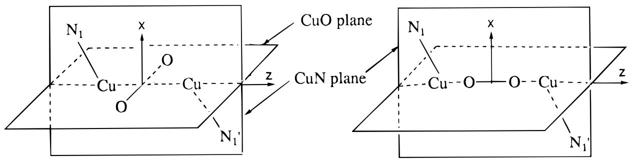
Scheme 1



(μ-pyridazine)bis(1-cyanoguanidine)dicopper(I) cation ([$Cu_2(\mu$-pydz$)_2$(cnge$)_2]^{2+}$, **1**) that presents a drastically different arrangement of its bidentate rigid ligands but still reversibly binds dioxygen. Albeit no geometrical data on the **1**$-O_2$ complex is available to our knowledge, it has been shown that the fixation of a third pyridazine ligand on **1** leads to the formation of complex **2** of which single-crystal X-ray analysis exhibits an eclipsed arrangement and an approximate C_3 symmetry (Scheme 1). Other eclipsed situations have also been observed for a functional model of dopamine β-hydroxylase[11] as well as in the active site of zucchini ascorbate oxidase.[12] Last but not least, extended Hückel Theory (EHT) results on a model have confirmed the absence of a significant energy gap between eclipsed and staggered conformations of $[Cu^+(NH_3)_3]_2-O_2$.[6a] A somewhat larger difference has very recently been obtained from *ab initio* computations for the eclipsed and staggered ("anti") conformations of the $(\mu$-O$)_2$ form of this complex.[13]

This large variety of situations prompted us to investigate the following: (i) the eventual influence of the number of nitrogen ligands (taking NH_3 as model) surrounding each copper cation on the geometry of the corresponding oxygenated complex (*i.e.* the O−O bond perpendicular or parallel to the Cu−Cu direction, leading respectively to a trans μ-1,2/μ:η^2-η^2 or a cis μ-1,2 situation); (ii) the possibility of a relationship between staggered/eclipsed conformations of the nitrogen ligands and this same dioxygen binding mode; (iii) the particular case of complex **1** which could be a likely candidate to a cis μ-1,2 dioxygen binding since this type of situation is obtained upon bridging of a third pyridazine.[10]

Chart 2



Computational Procedures and Input

For all different $(Cu^+(NH_3)_n)_2-O_2$ complexes considered, the two-reference-determinants closed-shell SCF calculations (ROHF-GVB) have been carried out using Gaussian 92[14] and/or Hondo 95.6.[15] This procedure was adopted because previous results[7,16] on $(Cu^+)_2-O_2$ have shown that, in the lowest singlet state, there is a large mixing of two closed-shell determinants when the calculated complex corresponds to an energy minimum. The highest occupied orbital of these two electronic configurations is either the symmetric or the antisymmetric combination of the two d_{yz} atomic orbitals (see Chart 2 for definition of the axes), a choice based on CASSCF results discussed below. Such a large two-determinants mixing is constantly found in these complexes. All intermolecular parameters and the O−O bond length have been optimized at the two-determinants GVB level. The geometrical arrangements used as starting points for the optimization of the parallel and the perpendicular oxygen binding modes rely on data concerning experimentally characterized related complexes. The optimization of the bond lengths and bond angles within the model ligand NH_3 did not appear necessary. Except when dealing with our model of Karlin's complex,[9] we will restrict our comments to the parallel and perpendicular cases, since the optimization of all intermolecular parameters has led to these two limit situations when starting from intermediate arrangements. The 3-21G basis set was used for the copper cation[17] with 3d, 4sp, and 4sp′ exponents modified as in ref 7. For the oxygen, we used the 3-21G basis set plus a polarization function with exponent 0.8. Dunning's diffuse p function was further added since superoxide/peroxide anions are to be considered in the oxygenated complexes under study. A minimal basis was used for all the nitrogen-containing ligand's atoms.[18] This set will hereafter be referred to as basis I. In addition, the consistency of the computational procedure adopted here was checked by carrying out some CAS/CASMP2[15,19] calculations on Cu_2-O_2 not only with basis I but also with a somewhat larger basis set (DZVP2[20] plus diffuse p on oxygen referred to as basis II). In these computations, the active space is made of molecular orbitals 33−38. It includes dioxygen's σ (10ag), σ^* (11ag), and the two π^* ($8b_{1u}$, $2b_{1g}$) orbitals plus the odd (5_{b2u}) and even ($4b_3g$) combinations of the copper d_{yz} (and d_{xz} in the case of the parallel arrangement) orbitals at the origin of the Cu → O charge transfer, that is those involved in the two-determinants GVB treatment. The limitation to 6 active orbitals in the CAS/CASMP2 treatment, imposed by the software used, gets support from previous more extended CI computations (all single and double excitations concerning orbitals 27−42) on this system.[7]

The size of the $[Cu_2(\mu$-pydz$)_2$(cnge$)_2]^{2+}-O_2$ system precludes the use of the GVB level of calculation to perform the optimization of all

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(11) Itoh, S.; Kondo, T.; Komatsu, M.; Ohshiro, Y., Li, C.; Kanehisa, N.; Kai, Y.; Fukuzumi, S. *J. Am. Chem. Soc.* **1995**, *115*, 4714.

(12) Messerschmidt, A.; Rossi, A.; Ladenstein, R.; Huber, R.; Bolognesi, M.; Gatti, G.; Marchesini, A.; Petruzzelli, R.; Finassi-Agro, A. *J. Mol. Biol.* **1989**, *206*, 513.

(13) Mahapatra, S.; Halfen, J. A.; Wilkinson, E. C.; Pan, G.; Wang, X.; Young, V. G.; Cramer, C. J.; Que, L., Jr.; Tolman, W. B. *J. Am. Chem. Soc.* **1996**, *118*, 11555.

(14) Gaussian 92: Frisch, M. B.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gonperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. Gaussian, Inc., Pittsburgh PA, 1992.

(15) Dupuis, M.; Johnston, F.; Marquez, A. *Hondo 8.5 from CHEM-Station*; IBM Corp.: Neighborough Rd, Kingston, NY 12401, 1994.

(16) (a) Bernardi, F.; Bottoni, A.; Casadio, R.; Fariselli, P.; Rigo, A. *Int. J. Quantum Chem.* **1996**, *58*, 109. (b) Bernardi, F.; Bottoni, A.; Casadio, R.; Fariselli, P.; Rigo, A. *Inorg. Chem.* **1996**, *35*, 5207.

(17) Dobbs, K. D.; Hehre, W. J. *J. Comput. Chem.* **1987**, *8*, 861.

(18) Clementi, E. J. M.; Andre, M. C. L.; Klint, D.; Hahn, D. *Acta Phys. Acad. Sci. Hung.* **1969**, *27*, 493.

(19) Kozlowski, P. M.; Davidson, E. R. *J. Chem. Phys.* **1994**, *100*, 3672.

(20) Godbout, N.; Salahub, D. R.; Andzelm, J.; Wimmer, E. *Can. J. Chem.* **1992**, *70*, 560.

Table 1. Variation of Energy (au), Geometrical Parameters (Å), and Wave Function Characteristics of $Cu^{+}{}_2-O_2$ with the Basis Set and Computational Level

O_2 binding	comput level	basis I							basis II						
		E	d_{Cu-Cu}	d_{Cu-O}	d_{O-O}	q_O[a]	coeff occupancy		E	d_{Cu-Cu}	d_{Cu-O}	d_{O-O}	q_O	coeff occupancy	
perp	GVB	−3410.0431	3.35	1.84	1.51	−0.599	0.7672 222200	−0.6414 222020	−3426.0220	3.45	1.88	1.48	−0.630	0.7722 222200	−0.6354 222020
	CAS	−3410.0467	3.35	1.84	1.50	−0.596	0.7774 222200	−0.6276 222020	−3426.0253	3.45	1.88	1.47	−0.616	0.8131 222200	−0.5800 222020
	CASMP2[b]	−3410.8600	3.35	1.84	1.50	−0.596	0.6903 222110 −0.6903 222110	−0.1503 212120 0.1503 212120	−3426.5821	3.45	1.88	1.47	−0.616	0.7069 222110	−0.7069 222110
par	GVB	−3409.9270	4.73	2.46	1.36	−0.628	0.7335 222200	−0.6797 222020							
	CAS	−3409.9604	4.77	2.49	1.40	−0.635	0.7298 222200	−0.6339 222020							
	CASMP2[b]	−3410.8291	4.77	2.49	1.40	−0.635	0.7032 221210	0.7032 221210							

[a] Mulliken net charges. [b] The CASMP2 computations were carried out using the CAS geometries.

Table 2. Energy (au) and Geometrical Parameters (Å) for $(Cu^{+}(NH_3)_n)_2-O_2$ ($n = 0, 1, 2, 3$) and $(Cu_2(\mu\text{-pydz})_2(cnge)_2{}^{2+}-O_2)$ Complexes with the O−O Bond Perpendicular or Parallel to the Cu−Cu Direction

O_2 complex	perpendicular						parallel					
	E	d_{Cu-Cu}	d_{Cu-N}[a]	d_{O-O}	d_{Cu-O}	x[b]	E	d_{Cu-Cu}	d_{Cu-N}[a]	d_{O-O}	d_{Cu-O}	x[b]
$(Cu^{+})_2$	−3409.7287	3.46		1.52	1.89	0.00	−3409.6636	4.68		1.36	1.66/3.02	0.00
$(Cu^{+}(NH_3))_2$	−3522.0192	3.38	1.97	1.49	1.84	0.00	−3521.9211	4.72	2.00	1.35	1.68/3.04	0.00
$(Cu^{+}(NH_3)_2)_2$	−3634.1863	3.42	2.07	1.48	1.86	0.00	−3634.0856	4.59	2.06	1.37	1.71/3.03	0.58
$(Cu^{+}(NH_3)_3)_2$ eclipsed	−3746.2697	3.48	2.13/2.21	1.48	1.89	0.07	−3746.1729	4.56	2.11/2.19	1.38	2.03/3.23	1.26
$(Cu^{+}(NH_3)_3)_2$ staggered	−3746.2702	3.48	2.13/2.21	1.48	1.89	0.00	−3746.1675	4.87	2.11/2.20	1.38	1.74/3.12	0.00
$Cu_2(\mu\text{-pydz})_2(cnge)_2{}^{2+}$	−4522.6187	2.88	2.27/1.93	1.50	1.89	0.96	−4522.5448	3.12	2.10/1.95	1.40	1.76/2.73	1.53

[a] When two values are given, the first corresponds to the two equivalent distances. [b] Chart 2.

intermolecular parameters. We thus first run RHF optimizations on the $(Cu^{+}(NH_3)_2)-O_2$ complex to check the reliability of the geometrical parameters given by this computational level. The values obtained[21] differ from the GVB ones by less than 0.1 Å or 0.1°, except for the O−O distance since this level of computation is unable to account for the Cu → O electron transfer.[7] Thus in the case of the $[Cu_2(\mu\text{-pydz})_2(cnge)_2]^{2+}-O_2$ complexes, the calculations were carried in the following manner. Using the bond lengths and angles taken from the crystallographic data, the intermolecular metric parameters around each copper center were optimized at the RHF level. Finally, dioxygen location and the O−O bond length were optimized at the GVB level. Since it has been observed that the bond lengths and angles of the pyridazine and cyanoguanidine ligands do not vary upon the fixation of a third pyridazine,[10] we can reasonably expect that a similar situation will be encountered upon dioxygen complexation.

Results and Discussion

$(Cu^{+}(NH_3)_n)_2-O_2$ Complexes. The results obtained for the perpendicular arrangement of $(Cu^{+})_2-O_2$ with the two basis sets and the different computational levels considered are reported in Table 1. The four geometry optimizations lead to an arrangement in which the O−O bond is perpendicular to the Cu−Cu direction, the four atoms being coplanar. Therefore the four Cu−O distances are equal. The tabulated values show that the two-determinants GVB and CAS (8,6) optimizations give results which are quite similar and the total energy is the only quantity which varies significantly when going from basis I to basis II. In particular, it is clear that the lowest singlet state of these systems cannot be accounted for by a single determinant as also reported very recently by Bernardi *et al.*[16] Moreover with both basis sets, the same molecular orbitals, *viz.* those built mainly from the copper d-orbitals, concerned by the Cu → O charge transfer are found to be the most important at the CASMP2 level. When dynamic correlation is taken into account we obtain, also with both basis sets, the open-shell singlet instead of the GVB singlet as the lowest one. This result is consistent with previous CI calculations[7] which have shown that the correlation contribution is larger for the open-shell than for the GVB singlet.

For the parallel arrangement of $(Cu^{+})_2-O_2$, the results obtained with basis I show that this situation is less favorable than the perpendicular one, for every computational level. Moreover the evolution of the calculated values with the degree of refinement of the method is totally similar to that found in the perpendicular case. With basis II, the optimization leads invariably, at the GVB and CAS computational levels, to dissociation of the complex into $O_2 + 2\ Cu^{+}$. These results, which by themselves show the mediocre stability of the parallel arrangement, can be used to indicate the preference for the perpendicular arrangement. At this point it is worth noticing that with basis I, the two binding modes give complexes more stable than the isolated species (which have a total energy of −3409.8974 au at the SCF level). With basis II, the situation is reverse; the energy of the isolated species is of −3426.2070 au in this case. The perpendicular complex thus corresponds only to a local minimum.

Before discussing the results concerning the systems including the nitrogen-containing ligands, we wish to point out that the 6 Cartesian d-orbitals have been used for the calculations reported in Table 1, while for the forthcoming results we resorted to the five spherical harmonic d-functions. This explains the numerical differences between the values of Table 1 obtained with basis I/GVB and the corresponding results in Table 2. This choice in Table 1 has been made for the sake of consistency with our own previous results.[7]

Table 2 reports the results regarding $(Cu^{+}(NH_3)_n)_2-O_2$ for $n = 0-3$ while Figure 1 show the geometries of these complexes for $n = 1-3$. For each value of n, two coordination modes of

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(21) Data for perpendicular $(Cu(NH_3)_2)_2-O_2$ at the RHF level: $d_{Cu-Cu} = 3.31$ Å, $d_{Cu-N} = 1.97$ Å, $d_{O-O} = 1.35$ Å, $d_{Cu-O} = 1.73/1.85$ Å; see Table 2 for corresponding GVB values.

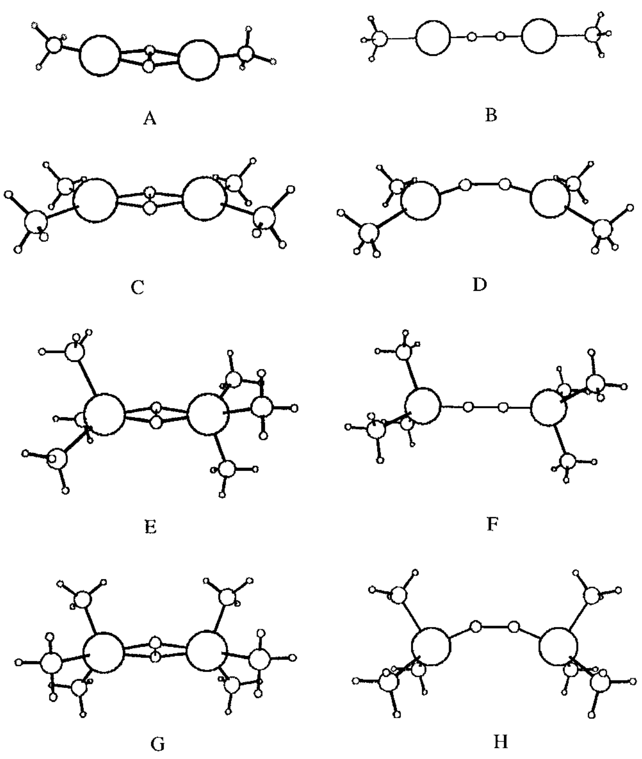

Figure 1. Theoretical optimized parallel and perpendicular arrangements for the $(Cu^+(NH_3)_n)_2{-}O_2$ complexes with $n = 1$ (A, B), 2 (C, D), and 3 (E−H). Large circles = Cu, medium circles = N, and small circles = O.

O_2 have been considered, the μ:η^2-η^2 (O_2 perpendicular to the Cu−Cu direction) and the cis μ-1,2 (O_2 parallel to the Cu−Cu direction) ones.

From the values of the first five entries in Table 2 it appears that the perpendicular dioxygen arrangement is in all cases more stable than the parallel one. The energy difference increases with the number of NH_3 in the complex from about 40 ($n = 0$) to 75 ($n = 3$) kcal/mol. For O_2 perpendicular to the Cu−Cu axis and $n = 1$, the two NH_3 ligands are in a cis relationship with respect to the Cu−Cu axis, the N−Cu−Cu angle being equal to 157° (C_{2v} symmetry). For $n = 2$ and 3, the CuO and CuN planes are found to be perpendicular (Figure 1 and Chart 2). In these three cases, all Cu−O distances are found equal as in the $Cu_2{-}O_2$ complex. For O_2 parallel to the Cu−Cu axis, there is a preference for the linear Cu−O−O−Cu for $n = 0$, 1, and 3 (with staggered ligands in this last case). In the other cases, the O−O and Cu−Cu axes do not coincide and O_2 moves increasingly away from the Cu−Cu axis (along x, Chart 2) with increasing number of NH_3 ligands. In addition, for any value of n, the Cu−Cu distance is shorter when O_2 and Cu−Cu are perpendicular: In the experimental cases Cu−Cu is about 3.5 Å[3b] while for our model calculations Cu−Cu varies between 3.4 and 3.5 Å. Moreover, the O−O distance is more stretched (1.48−1.50 Å) in the perpendicular case than in the parallel situation (1.35−1.39 Å). In particular, this distance is larger than in superoxide (1.347 Å)[22] and identical to that deduced from Raman spectra for peroxide (1.49 Å) in anhydrous Na_2O_2[23] while the oxygen net molecular charge is intermediate between the two situations (Table 3). This feature clearly indicates a predissociative state for bonded O_2, as expected along a tyrosinase mechanistic cycle. As mentioned earlier,[7] calculated d_{O-O} appears somewhat overstretched when compared to experimental data on various complexes (1.4,[5b] 1.412,[6a] 1.432 Å [9]). This difference may be due to the lack of dynamic correlation in the present computations.[24]

The net positive charge on Cu cations, although still indicative of a d^9 configuration, decreases with increasing number of NH_3 (which carry a global positive charge as can be seen from Table 3), while the oxygen negative charge increases with one exception. For the perpendicular binding mode, when going from $n = 1$ to $n = 2$ the Cu → O charge tranfer decreases. However the difference between the Cu → O charge transfer and the oxygen electronic population increases regularly for both arrangements since it is of 0.000, 0.187, 0.276, and 0.325/0.328 in the perpendicular case and 0.000, 0.172, 0.289, and 0.350/0.358 in the parallel case for $n = 0$, 1, 2, and 3, respectively. Thus the ligand also contributes to the anionic character of complexed dioxygen and therefore to the weakening of the O−O bond,[25] and Cu^+ may be considered as a relay to transfer electronic charges from the nitrogen-containing ligands to the coordinated O−O unit. The results obtained by Mandal *et al.*[26] from diagrammatic valence bond studies on $[Cu_2O_2]$ and $[Cu_2O_2N_4]^{2+}$ do not indicate this feature. It has been verified that the electronic density on the oxygen is very similar with the larger basis set II. Thus for a staggered $(Cu^+(NH_3)_3)_2{-}O_2$ the net charges are −0.737, 0.993, 0.282, and 0.180 for O, Cu, and close and remote NH_3, respectively. Interestingly, this same trend is found for parallel dioxygen coordination. We can also notice that, for each individual ligand, the L → Cu → O charge transfer decreases when the number of ligands increases. This suggests that the ligand charge is function of the amount of electrons which are transferred to the O_2 substrate.

In the case of the six coordinated NH_3 ligands, both staggered and eclipsed situations have been considered. The staggered conformer is found to be about 0.3 kcal/mol more stable for the perpendicular binding mode, in good agreement with previous EHT results.[6a] This indicates that both conformations are possible as indeed experimentally found in dicopper complexes.[5,6,9−11] When considering the parallel O_2 binding mode, the energy difference beween the two conformations is larger (11 kcal/mol). As expected, the Cu−N distances increase with the number of NH_3 ligands. Furthermore, with the exception of $n = 1$, going from the perpendicular to the parallel binding mode somewhat decreases the Cu−N distances. For $n = 3$, our findings are in good agreement with the experimental data about the oxyhemocyanin active site[5] and several model systems[3b,6b,c,24] since the C−N bond length for the NH_3 perpendicular to the $Cu_2{-}O_2$ plane (Chart 2) increases (2.2 instead of 2.1 Å). The results obtained for the staggered and eclipsed conformations of $(Cu^+(NH_3)_3)_2{-}O_2$ differ significantly from those very recently published by Mahapatra *et al.*[27] using a smaller basis set and limited to a single determinant wave function[28] since the O−O bond is cleaved at this lower level of computation. Furthermore optimizations (at the GVB level with basis I) of the $(Cu^+(NH_3)_3)_2{-}O_2$ staggered conformation, using as starting point their experimental data for the $Cu^+{}_2{-}O_2$ core, lead to the structure reported in Table 2. This result, which

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(22) Travers, M. J.; Cowles, D. C.; Ellison, G. B. *Chem. Phys. Lett.* **1989**, *164*, 449.

(23) Evans, J. C. *Chem. Commun.* **1969**, 682.

(24) We thank a reviewer for suggesting this explanation.

(25) Solomon, E. J.; Teczck, F.; Root, D. E.; Brown, C. A. *Chem. Rev.* **1994**, *94*, 827.

(26) Mandal, P. K.; Manoharan, P. T.; Sinha, B.; Ramasesha, S. *Theor. Chim. Acta* **1996**, *96*, 1.

(27) Mahapatra, S.; Halfen, J. A.; Wilkinson, E. C.; Pan, G.; Cramer, C. J.; Que, L., Jr.; Tolman, W. B. *J. Am. Chem. Soc.* **1995**, *117*, 8865.

(28) When optimizing this system using the STO-3G basis set, we find geometrical parameters in agreement with these authors but the energy, calculated at the STO-3G* level, is considerably poorer (−3724.0736/−3720.2796 au for the $(\mu\text{-O})_2$ and μ-η^2:η^2-O_2 binding modes, respectively) than the corresponding one in Table 2.

Table 3. Atomic Charges (Mulliken) on Cu, O, and the Ligands for $(Cu^+(NH_3)_n)_2-O_2$ ($n = 0, 1, 2, 3$) and $(Cu_2(\mu\text{-pydz})_2(cnge)_2{}^{2+}-O_2)$ Complexes with the O−O Bond Perpendicular or Parallel to the Cu−Cu Direction

	perpendicular			parallel		
O_2 complex	q_{Cu}	q_O	q_L[a]	q_{Cu}	q_O	q_L[a]
$(Cu^+)_2$	1.723	−0.724		1.688	−0.688	
$(Cu^+(NH_3))_2$	1.593	−0.780	0.187	1.612	−0.784	0.172
$(Cu^+(NH_3)_2)_2$	1.456	−0.732	0.138	1.496	−0.785	0.145
$(Cu^+(NH_3)_3)_2$ eclipsed	1.492	−0.817	0.113/0.098	1.472	−0.822	0.114/0.110
$(Cu^+(NH_3)_3)_2$ staggered	1.484	−0.812	0.113/0.101	1.477	−0.835	0.121/0.116
$Cu_2(\mu\text{-pydz})_2(cnge)_2{}^{2+}$	1.476	−0.623	0.00/0.147	1.402	−0.659	0.09/0.148

[a] When two values are given, the first one corresponds to the two equivalent ligands.

does not agree with the double minimum found by Cramer *et al.*[29] at the RHF-STO-3G level, suggests that the exact structure of the ligands should be taken into account in order to reproduce the experimental data at all computational levels. Mahapatra *et al.*[13] have reached a similar conclusion.

$[Cu_2(\mu\text{-pydz})_2(cnge)_2]^{2+}-O_2$ Complexes. There are fundamental differences between complex **1** ($Cu_2(\mu\text{-pydz})_2(cnge)_2$) and the hemocyanin active site since the model complex contains bidentate ligands restraining the Cu−Cu distance. For this reason, comparing Cu−Cu distances could be hazardous. However, because there is an identical number of Cu−N bonds in **1** and the Hc active site, it was important to establish if, for this last complex, the binding mode of dioxygen is similar to that found for the models of oxyhemocyanin. Our calculations indeed suggest that the trends are very similar, in particular the perpendicular binding mode is more stable by 46 kcal/mol (Table 2). The comparison of the optimized configurations displayed in Figure 2 with the X-ray structure of $[Cu_2(\mu\text{-pydz})_2(cnge)_2]^{2+}$ shows that dioxygen binding displaces significantly the bidentate pyridazines. This displacement is larger in the perpendicular arrangement where it leads to an angle of 88° between the pyridazine planes (Figure 2). The data in Table 2 show also that the Cu−Cu distance in the perpendicular case is much shorter than in **1** (2.88 Å instead of 3.33 Å).[10] On the other hand, both the Cu−Cu distance and the angle between the pyrazine planes are, in the O_2 parallel arrangement, very close to those measured for complex **2** (3.12 vs 3.10 Å and 116 vs 122°, respectively).[10]

Switching from NH_3 to pyridazine ligands gives rise to significant changes in the Cu−Cu distances which, in turns, influence other structural parameters. Thus, the x distance (Chart 2) is, as expected,[7,30] dramatically increased in the pydz−cnge complexes. The Cu−O distances are in both $[Cu_2(\mu\text{-pydz})_2(cnge)_2]^{2+}-O_2$ species very similar to those obtained for the $(Cu^+(NH_3)_n)_2-O_2$ cases. The electron density on O is smaller in complex **1** than in the $(Cu^+(NH_3)_n)_2-O_2$ complex while the electron populations of the coppers are very similar. However the total ligand net charge is smaller than in the ammonia case. Furthermore the ligand which is closer to the Cu cation is more positive. These results are thus consistent with a smaller L → Cu → O charge transfer in complex **1**.

Karlin's $[\{(TMPA)Cu\}_2-O_2]^{2+}$ Complex. The dichotomy between the perpendicular/parallel O_2 binding modes obtained from the present results seems in contradiction with Karlin's experimental data for the $[\{(TMPA)Cu\}_2-O_2]^{2+}$ complex (TMPA = tris(2-pyridylmethyl)amine), which exhibits an end-on (trans) μ-1,2-$O_2{}^{2-}$ coordination.[9] In order to investigate the origin of this discrepancy we undertook an optimization of the intermolecular geometrical parameters of the $(Cu^+(NH_3)_4)_2-O_2$ system. We took, as starting point, the values measured for the Cu_2-O_2 core of the aforementioned complex and four equal Cu-N distances. Two of the eight ammonia ligands have been placed, as in Karlin's complex, collinear to the Cu−Cu direction. The optimal arrangement obtained, depicted on Figure 3A, presents three striking differences with the experimental arrangement: (i) The perpendicular binding mode is preferred (by about 35 kcal/mol). (ii) The Cu−Cu distance is noticeably shortened (3.477 Å). (iii) Two ammonia molecules are expelled from the complex ($d_{Cu-N} = 5.89$ Å). Since this last phenomenon cannot occur in TMPA because of the tethers linking the

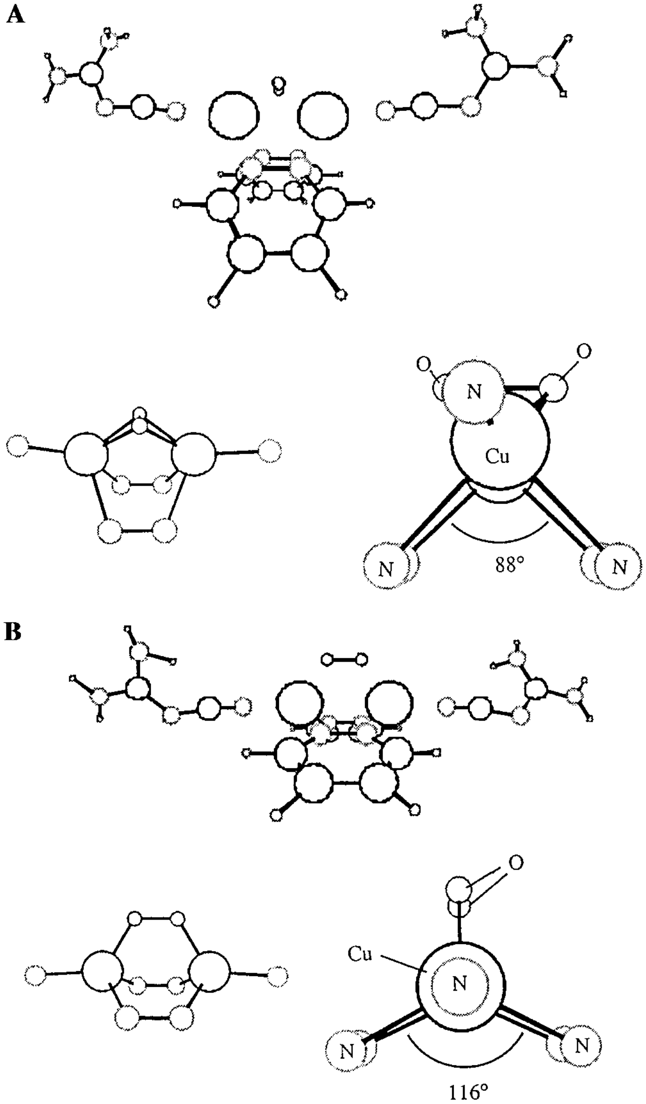

Figure 2. Top parts of (A) and (B): Optimized geometries for the $[Cu_2(\mu\text{-pydz})_2(cnge)_2]^{2+}-O_2$ complex (see Scheme 1). Bottom parts of (A) and (B): Same as above but limited to the Cu^+ coordination sphere for sake of clarity. (A) O_2 perpendicular to the Cu−Cu direction. (B) O_2 parallel to the Cu−Cu direction.

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(29) Cramer, C. J.; Smith, B. A., Tolman, W. B. J. *Am. Chem. Soc.* **1996**, *118*, 11283.

(30) Blackburn, N. J.; Strange, R. W.; Farooq, A.; Haka, M. S.; Karlin, K. D. *J. Am. Chem. Soc.* **1988**, *110*, 4263.

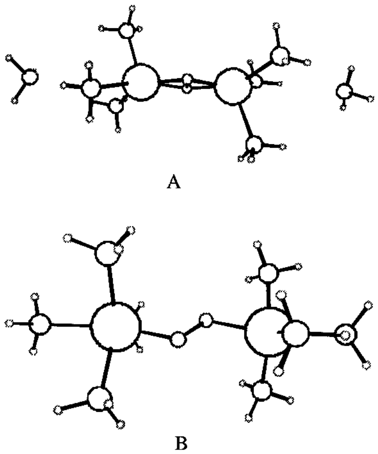

Figure 3. Theoretical optimized arrangements of the staggered conformation of the $(Cu^+(NH_3)_4)_2-O_2$ complex: (A) Cu−N distances optimized ($E = -3858.2935$ au); (B) fixed Cu−N distances ($E = -3858.2401$ au).

nitrogens, the optimization was rerun keeping the Cu−N distances fixed to 2.1 Å, a value close to those measured in the complex. In this case, and as can be seen from Figure 3B, the trans μ-1,2 binding mode is preferred (the Cu−Cu direction making an angle of 56.4° with the O−O bond) altogether with a longer Cu−Cu distance (4.30 Å).

These results tend to show that the trans μ-1,2 O_2^{2-} coordination is specific to the TMPA ligand structure and that the copper coordination sphere is saturated with five ligands. Therefore, the four nitrogens of TMPA prevent the side-on binding of O_2 which is energetically favored *in fine*. This hypothesis gets support from Karlin's very recent results indicating that the μ-1,2 side-on form is thermodynamically preferred over the the kinetic trans μ-1,2 "Init" species when the ligand is tridentate,[31] a situation more similar to that found in oxyhemocyanin and oxytyrosinase.[3c,5b]

Concluding Remarks

The results obtained from this study on dioxygen binding onto dinuclear copper complexes as a function of the number and arrangement of spectator nitrogen-containing ligands show that, for all the cases considered, the perpendicular binding mode leads to the formation of complexes much more stable than those derived from a parallel arrangement. When a comparison to experiment is possible (for the 6 ammonia complex and complex **1** with parallel O_2), we have a reasonable agreement for the geometrical features. The Cu_2O_2 central pattern reproduces well the experimental data with a proper stretch of the O−O bond and a correct Cu−Cu nonbonding distance. It is difficult to compare the Cu-N distance in the $(Cu^+(NH_3)_3)_2-O_2$ case to the experimental values since the experimental nitrogen-containing ligands are significantly different. However the observed trend in the C−N distance for close and remote ligands is correctly obtained from the calculations although the difference between these bonds is underestimated with respect to the real systems. In the case of complex **1**, when real ligands instead of models are used for the calculations, Cu-N distances are also reasonably close to experimental values. Because of the way complex **1** coordinates a third pyridazine, it was conceivable that O_2 binds in a parallel manner onto this complex which could have been a Hc model. Our study contradicts this expectation, and the greater stability of the perpendicular arrangement for the $[Cu_2(\mu\text{-pydz})_2(\text{cnge})_2]^{2+}-O_2$ complex renders the existence of a μ-1,2 dioxygen−dicopper complex unlikely. It also suggests that the preference for a perpendicular arrangement is due to the electronic affinity of the two half-filled dioxygen π^* molecular orbitals. Such a feature is definitely not encountered in pyridazine. In addition, because of its biological relevance, one specific aspect of our results concerning the $(Cu^+(NH_3)_3)_2-O_2$ complex is worth emphasizing: The staggered and eclipsed conformations are found almost isoenergetic, confirming previous EHT calculations[6a] and very recent ab initio ones concerning the $(\mu\text{-}O)_2$ form of this complex.[13] This indicates a versatility of the Cu^+ coordination sphere with respect to O_2 binding, as found in zucchini ascorbate oxidase (eclipsed) and hemocyanin (staggered). The particular case of the side-on $[\{(\text{TMPA})Cu\}_2-O_2]^{2+}$ complex appears to be due to the tetradentate character of the ligand. The results obtained for the $(Cu(NH_3)_4)-O_2$ system also suggest that the copper coordination sphere is saturated with five ligands, a feature implying that the oxytyrosinase active site will rapidly undergo major dioxygen binding alterations upon Cu docking of an incoming phenolic substrate. This hypothesis is in agreement with previously proposed mechanisms.[32]

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(31) Jung, B.; Karlin, K. D.; Zuberbühler, A. D. *J. Am. Chem. Soc.* **1996**, *118*, 3763.

(32) (a) Winkler, M. E.; Lerch, K.; Solomon, E. I. *J. Am. Chem. Soc.* **1981**, *103*, 7001. (b) Kitajima, N.; Moro-oka, Y. *Chem. Rev.* **1994**, *94*, 373. (c) Getlicherman, H.; Giessner-Prettre, C.; Maddaluno, J. *J. Phys. Chem.* **1996**, *100*, 6819.