Formation and Interconversion of End-on and Side-on μ-Peroxo−Dicopper(II) Complexes

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Investigations of copper(I)−dioxygen reactivity of relevance to oxidative chemical processes and/or metalloenzyme active site chemistry have lead to the characterization of a number of discrete Cu_n−O_2 (n = 1, 2) products.[1] For Cu/O_2 = 2:1 peroxo−dicopper(II) complexes, two structural types are well described; end-on (*trans*) μ-1,2-O_2^{2-} coordination[2] is exemplified by $[\{(TMPA)Cu\}_2(O_2)]^{2+}$ (TMPA = tris(2-pyridylmethyl)amine),[2a] while μ-η^2:η^2 side-on peroxo binding was validated for $\{Cu[HB(3,5\text{-}i\text{Pr}_2\text{pz})_3]\}_2(O_2)$ ($HB(3,5\text{-}i\text{Pr}_2\text{pz})_3$ = hydrotris(3,5-diisopropylpyrazolyl)borate anion),[1a,3] is found in other cases,[4,5] and has been confirmed in the oxygenated forms of arthropodal and molluscan hemocyanins (Hc's).[6] Here, we report on dioxygen binding to $[(N4)Cu^I_2]^{2+}$ (**1**), previously shown to give rise to $[(N4)Cu_2(O_2)]^{2+}$ (**2**), described as a peroxo-dicopper(II) complex with bent side-on μ-η^2:η^2-peroxo ligation.[4a,b,7] Stopped-flow kinetic studies confirm the reversible oxygenation chemistry[4b] but also reveal that *both* end-on and side-on Cu_2−O_2 structures form in this system, providing important new insight into the relative stabilities and reactivities of these two structural types and fundamental information concerning the dynamics of Cu_n−O_2 interconversions.

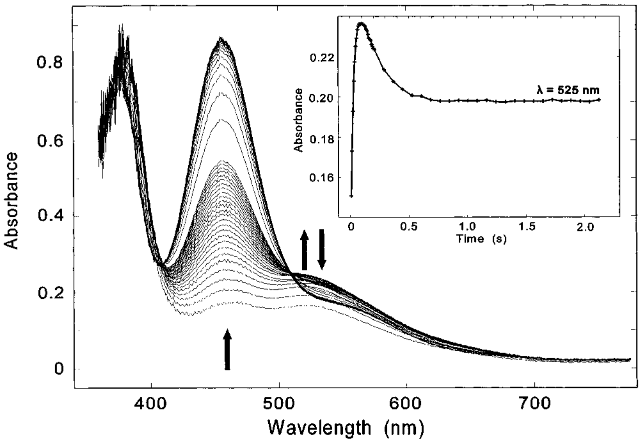

Figure 1. Spectral changes in the reaction of $[(N4)Cu^I_2]^{2+}$ (**1**) with O_2. See text for conditions.

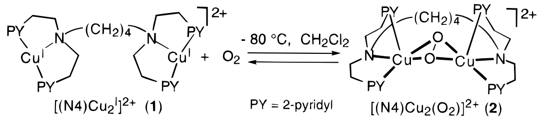

Figure 1 illustrates spectrophotometric changes (complete scans initially repeated every 8 ms, ca. 2 s total; 360−780 nm) observed for the reaction of **1** with O_2 in CH_2Cl_2 at 179 K ([(**1**)] = 8.5 × 10^{-4} M; [O_2] = 1.9 × 10^{-3} M).[9] An initial increase in absorbance at λ = 525 nm is followed by a decrease after ca. 100 ms (inset), while a peak at λ = 456 nm steadily builds up. Spectroscopic evidence for the intermediate essentially disappears above 190 K. The final product (**2**) is quite stable at these reduced temperatures and begins to decay appreciably only above ca. 223 K. Analysis[9] of data taken over the range T = 179−203 K leads to a simple and consistent picture (Scheme 1), allowing calculation of kinetic−thermodynamic parameters.[10] Spectra associated with the final product **2** (λ_{max} = 456 nm, comparable to that previously observed by benchtop UV−vis spectroscopy),[4b] plus a new initially formed adduct, **Init**, with λ_{max} = 525 nm, could also be determined.[10b]

The kinetics show that **Init** has the composition $[(N4)Cu_2(O_2)]^{2+}$, i.e., it is an isomer of the previously characterized peroxo species **2**; **Init** is formed rapidly with $k_{\mathbf{Init}}$ = (1.1 ± 0.1) × 10^4 M^{-1} s^{-1} and $K_{\mathbf{Init}}$ = (4.5 ± 0.4) × 10^2 M^{-1} at 183 K (Table 1), values in fact quite close to those observed for the 1:1 superoxo complex $[(TMPA)Cu^{II}(O_2^-)]^+$ (1.8 × 10^4 M^{-1} s^{-1} and 1.9 × 10^3 M^{-1}, respectively).[9b] However, formulation of **Init** as a superoxo−Cu(II) species[11] is precluded for several reasons. First, MePY2 (= bis(2-pyridylethyl)methylamine), a tridentate mononucleating analogue of N4, shows no buildup of any adduct such as $[(MePY2)Cu(O_2)]^+$, as determined by benchtop UV−vis as well as stopped-flow kinetic monitoring.[12] Also, the UV−vis absorption characteristics of **Init** (vide supra)

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(7) The structure assignment is based on the stoichiometry of O_2 binding, presence of an intense peroxo-to-Cu(II) charge-transfer absorption (λ_{max} = 360 nm; ϵ = >14 000 mol^{-1} cm^{-1}) characteristic of this side-on bridged structure,[8] and X-ray absorption properties which verify the presence of the Cu(II) oxidation state and give a Cu···Cu distance of 3.4 Å.[4a] Recent studies by Tolman and co-workers[7b] reveal cases on side-on μ-η^2:η^2-peroxo−dicopper(II) complexes which form also in rapid equilibrium with bis(μ-oxo)dicopper(III) structures, i.e., with a cleaved O−O bond. We cannot exclude the possibility of such a mixture describing **2**. (b) Halfen, J. A.; Mahapatra, S.; Wilkinson, E. C.; Kaderli, S.; Young, V. G., Jr.; Que, L., Jr.; Zuberbühler, A. D.; Tolman, W. B. *Science* **1996**, *271*, 1397−1400.

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(10) (a) **Init** and **2** *both* form in parallel from **1**, and **Init** is *not* an intermediate leading to **2**. If it were, formation of **2** would have an induction period; this is not observed. The schemes fitting the data are **1** + O_2 ⇄ **Init**, **1** + O_2 ⇄ **2** (or **1** + O_2 ⇄ **Tr**, **Tr** ⇄ **Init**, **Tr** ⇄ **2**, where **Tr** is a nonobservable steady state species). For these reaction models, no induction period would be seen. (b) Calculated final spectra of **Init** and **2** are given in the supporting information.

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Scheme 1

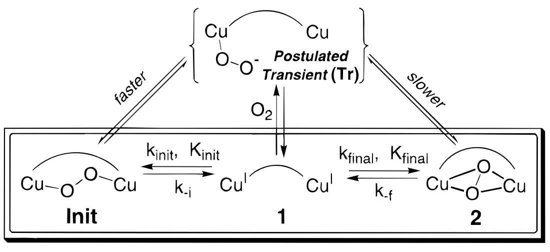
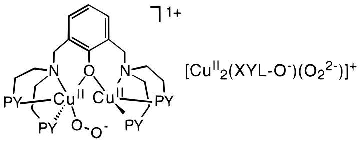


Table 1. Kinetic/Thermodynamic Parameters for Formation of **Init** and **2** by oxygenation of **1**

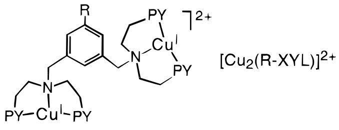
	Init	**2**
k (M^{-1} s^{-1}) 183 K	$k_{\mathbf{Init}} = (1.1 \pm 0.1) \times 10^4$	$k_{final} = (8.5 \pm 0.2(4)) \times 10^3$
223 K	$k_{\mathbf{Init}} = (1.4 \pm 0.6) \times 10^4$	$k_{final} = (8 \pm 2) \times 10^4$
$\Delta H^‡$ (kJ mol^{-1})	0 ± 3	18 ± 2
$\Delta S^‡$ (J K^{-1} mol^{-1})	-162 ± 18	-70 ± 9
K_{eq} (M^{-1}) 183 K	$K_{\mathbf{Init}} = (4.5 \pm 0.4) \times 10^2$	$K_{final} = (7 \pm 3) \times 10^7$
223 K	$K_{\mathbf{Init}} = 18 \pm 8$	$K_{final} = (7.8 \pm 1.1) \times 10^5$
$\Delta H°$ (kJ mol^{-1})	-28 ± 3	-58 ± 2
$\Delta S°$ (J K^{-1} mol^{-1})	-101 ± 19	-165 ± 8

are not compatible with those of other superoxo−Cu(II) species[2b,9b,11] but remarkably resemble the pattern seen for terminally coordinated peroxo−dicopper(II) complexes such as $[\{(TMPA)Cu\}_2(O_2)]^{2+}$,[2a] its closely related quinolyl-containing analogues,[9b,13] and $[Cu^{II}_2(XYL-O^-)(O_2^{2-})]^{2+}$ (λ_{max} = 505 (6300), 610 (2400) nm).[14] Thus, the kinetically preferred adduct, **Init**, must be formulated as a peroxo−dicopper(II) complex with end-on coordination, $Cu^{II}-O-O-Cu^{II}$ (Scheme 1).



Init is generated with an activation enthalpy close to zero (Table 1), indicative that its formation is not an elementary process, consistent with the presence of a rapid preequilibrium. As a precursor, we thus postulate a superoxo−Cu(II) transient (**Tr**) (Scheme 1), which does not build up appreciably and is therefore not spectroscopically observable.[10] $Cu-O_2$ (1:1) species have been isolated[11] or characterized in stopped-flow kinetic studies.[2b,9b] Superoxo−copper(II) species could possess end-on $Cu^{II}-O-O^-$ coordination,[2b,13] and we propose this structure for **Tr**. Rapid attack of one more Cu(I) moiety on the uncoordinated (basic) superoxo oxygen atom leads to the terminally coordinated peroxo−dicopper(II) complex **Init**, as observed for $[\{(TMPA)Cu\}_2(O_2)]^{2+}$ and a quinolyl analogue.[9b,13] If **Tr** were to have a side-on η^2-superoxo−Cu(II) structure as observed in $\{Cu[HB(3\text{-Ph},5\text{-}i\text{Prpz})_3]\}(O_2)$, (Ph = phenyl),[11a] attack by the second Cu(I) ion within **1** should lead directly to **2** and not to the first reaction product observed, **Init**.

The end-on peroxo−dicopper(II) species **Init** is thermodynamically unstable with respect to the final side-on μ-η^2:η^2-peroxo product $[(N4)Cu_2(O_2)]^{2+}$ (**2**). For the overall reaction from **1** to **2**, $k_{final} = (8.5 \pm 0.2(4)) \times 10^3$ M^{-1} s^{-1} and $K_{final} = (7 \pm 3) \times 10^7$ M^{-1} at 183 K (Scheme 1 and Table 1). A reaction model where terminal peroxo **Init** directly rearranges to **2** is not accommodated by the data;[10] **2** must form by rearrangement via $[(N4)Cu^I_2]^{2+}$ or via the superoxo−Cu(II) transient **Tr**. With $\Delta H° = -28$ kJ mol^{-1}, **Init** is far less enthalpically stabilized than the end-on peroxo−dicopper(II) complex, $[\{(TMPA)Cu\}_2(O_2)]^{2+}$, $\Delta H_{form}° = -81$ kJ mol^{-1}.[2b,9b] However, $\Delta H°$ and $\Delta S°$ for formation of **2** (Table 1) approach values observed for quinolyl tripod-ligand analogues $[\{(L)Cu\}_2(O_2)]^{2+}$ [9b] and especially the closely related O_2 adducts of $[Cu_2(R-XYL)]^{2+}$ ($\Delta H° = -52$ to -74 kJ mol^{-1} and $\Delta S° = -156$ to -250 J K^{-1} mol^{-1}),[9a] having the same *tri*dentate ligand donor set as N4.



The considerable (more than double; Table 1) enthalpic stabilization of μ-η^2:η^2 side-on (in **2**) relative to end-on peroxo coordination (in **Init**) is noteworthy and may derive primarily from formation of a penta- rather than tetra-coordinated copper(II). Solomon and co-workers[8] have shown that having twice as many $Cu^{II}-O_{peroxo}$ bonds is responsible for the characteristic intense λ_{max} = 350−360 nm in side-on peroxo coordination (originating from peroxide oxygen $\pi^*_\sigma \rightarrow$ Cu(II) charge transfer), compared to having a single $Cu^{II}-O$ bond for end-on coordination.

Our study reveals the formation of two kinds of Cu_2-O_2 structures in the same system. End-on peroxo ligation occurs more rapidly, but subsequent rearrangement leads to the final side-on product; we have provided the first quantitative estimates of the relative stabilities of these two peroxo−dicopper(II) structures and the dynamics relating them. End-on peroxo bridging may generally occur first in metal ion−O_2 reactions. Depending on geometry and the nature or presence of other bridging ligands (e.g., RO^-, NH_2^-), peroxo−dimetal complexes may have M···M distances varying from ca. 3.1 to ∼4.4 Å for end-on (μ-1,2-) coordination,[15,16] but a μ-η^2:η^2 side-on structure will have M···M ≤ 3.7 Å.[3,4a,5a,17] We can therefore speculate/suggest that in hemocyanin, O_2 binding may initially lead to end-on coordinated transient $Cu-O_2$ and Cu_2-O_2 species,[18] since Cu(I)···Cu(I) = 4.6 Å in deoxy-Hc.[19] Our work suggests that subsequent rearrangement to the observed μ-η^2:η^2-peroxo−dicopper(II) oxy-Hc product is thermodynamically driven and must involve movement of copper ions (and/or protein-derived histidine ligands); the latter has been discussed[19] as a basis for initiating hemocyanin subunit−subunit cooperative O_2 binding interactions.

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Supporting Information Available: Calculated final spectra of **Init** and **2** (1 page). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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