Structural Barriers to the Rates of Electron Transfer of Copper Complexes. Oxidation of Cytochrome c (II) by Copper(II) Complexes

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Summary The rates of oxidation of cytochrome c (II) by a number of copper(II) complexes are found to be indicative of a large structural barrier to electron transfer in these complexes.

DESPITE the obvious importance of copper redox reactions in many chemical and biochemical catalytic processes, few studies of the rates of oxidation or reduction, and in particular electron transfer reactions,[1,2] of copper complexes have been published. Electron transfer between copper(II) and copper (I) is unusual in that the two oxidation states differ, at least for 'simple' complexes, in both stereochemistry and co-ordination number. This paper demonstrates for the first time that these differences in structure contribute significantly to the activation energy barrier to electron transfer between copper(II) and copper(I) complexes. Vallee and Williams[3] have argued that the co-ordination sphere stereochemistry of copper enzymes is intermediate between square-planar and tetrahedral in order to facilitate electron transfer in these enzymes, in comparison to electron transfer between 'normal' tetrahedral copper(I) and square-planar copper(II) complexes. We feel, however, that the most important difference between such complexes is the difference in co-ordination number. Nevertheless both factors are likely to result in a significant structural barrier to electron transfer because of the rearrangement energy required to reach a transition state of intermediate co-ordination number and stereochemistry.

In an attempt to assess the magnitude of such a structural barrier we have compared the rates of the electron transfer reactions of bis(1,10-phenanthroline)copper(II), $Cu(phen)_2^{2+}$, and bis(5-nitro-1,10-phenanthroline)copper(II), $Cu(nitrophen)_2^{2+}$, ions with those of the distorted bis(2,9-dimethyl-1,10-phenanthroline)copper(II) ion,[4] $Cu(dmp)_2^{2+}$. Co-ordinated water molecules are not included in these formulations. All the complexes oxidize ferrocytochrome c in a simple electron transfer reaction, as judged largely by changes in the visible absorption spectrum of the cytochrome. The oxidation by $Cu(dmp)_2^{2+}$ goes effectively to completion as anticipated from the known redox potentials.[5] Pseudo-first-order rate constants measured on a stopped flow apparatus gave the second-order rate constant listed in the Table. $Cu(phen)_2^{2+}$ oxidation of cytochrome proceeds, in the absence of oxygen, to a measurable equilibrium position. The value of the equilibrium constant (Table) is within experimental error of the equilibrium constant calculated from the published redox potentials.[5] In the presence of molecular oxygen, $Cu(phen)_2^{+}$ is rapidly reoxidized to $Cu(phen)_2^{2+}$, thus setting up a catalytic cycle which results in the complete oxidation of ferrocytochrome c to ferricytochrome c. We have clearly established, by comparison of the rates of oxidation of cytochrome c in the absence and in the presence of oxygen, that the rate determining step in the $Cu(phen)_2^{2+}$ system is the one-electron oxidation of ferrocytochrome c by $Cu(phen)_2^{2+}$, Pseudo-first-order rates for this reaction and the analogous $Cu(nitrophen)_2^{2+}$ reaction were slow enough to be determined with a conventional visible absorption spectrophotometer. The derived second-order rate constants are given in the Table. All three reactions have been shown to be independent of pH between pH 5 and 7, and to be unaffected by the presence of 10% excess ligand.

Simple outer sphere electron transfer through the edge of the haem[6] most probably occurs in these systems. Therefore the Marcus cross relationship[7] may be used to derive redox potential independent rate constants (k_{22}, see Table) for electron exchange between the various Cu^{II}–Cu^{I} couples.

We have also examined the kinetics of oxidation of cytochrome c by a number of other copper complexes including aquocopper(II), 1,10-phenanthrolinecopper(II), bis(dipyridylammine)copper(II), (1,2-dihydroxybenzene 3,5-disulphonate)copper(II), bis(dimethylviolurate)copper(II), and (salicylaldehydesulphonate)copper(II). All of these presumably five- or six-co-ordinate complexes (including the co-ordinated water molecules) catalyse the autoxidation of cytochrome c (II) at rates less than that found for Cu-nitrophen$_2^{2+}$.

The striking feature of all of these rates is the relative slowness of both the reactions with cytochrome c and of the calculated rates of electron exchange. As $Cu(dmp)_2^{2+}$ is probably four- or at most five-co-ordinate, since the steric hindrance of the adjacent methyl groups prevents the formation of six-co-ordinate complexes,[4] the faster rates of electron transfer and exchange found with this complex are consistent with a significant structural barrier to electron transfer for 'normal' copper complexes. Data reported for some four-co-ordinate copper(II) systems also support this contention. Thus, exchange between the presumably tetrahedral copper chloro-complexes present in concentrated hydrochloric acid was found[2] to be very rapid (5×10^8 l mol^{-1} s^{-1}). Similarly, electron transfer and exchange for 'blue' copper proteins is comparatively fast (2×10^5 l mol^{-1} s^{-1} for stellacyanin), at least for copper centres which are 'kinetically accessible.'[8]

TABLE. Observed and calculated rate and equilibrium constants (K_{12}) for the reaction $L_2Cu^{II} + Cytc(II) \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} L_2Cu^{I} + Cytc(III)$ and related rate constants for self exchange of the copper complexes, (k_{22}) at 25 °C, pH 6·1 (2-(*N*-morpholino)ethanesulphonic acid buffer), and ionic strength 0·1.

Copper complex	K_{12}	k_{12}/l mol^{-1} s^{-1}	k_{22}/l mol^{-1} s^{-1}
$Cu(dmp)_2^{2+}$	$(4{\cdot}5) \times 10^5$ [a]	$(1{\cdot}00 \pm 0{\cdot}04) \times 10^6$	$1{\cdot}8 \times 10^4$
$Cu(phen)_2^{2+}$	$(5{\cdot}2 \pm 1{\cdot}2) \times 10^{-2}$ [b]	$(2{\cdot}72 \pm 0{\cdot}26) \times 10$	$7{\cdot}4 \times 10$
	$(3{\cdot}5 \pm 2) \times 10^{-2}$ [a]		
$Cu(nitrophen)_2^{2+}$ ..	$0{\cdot}81 \pm 0{\cdot}1$ [b]	$(1{\cdot}57 \pm 0{\cdot}06) \times 10^2$	$1{\cdot}0 \times 10^2$
	$0{\cdot}89$ [a]		

[a] Calculated. [b] Observed.

Another simple, but interesting illustration of the presence of a structural barrier to electron transfer is provided by our studies on the reduction of the clearly six-co-ordinate tris(1,10-phenthroline)copper(II) ($k_2 < 0{\cdot}2$ l mol^{-1} s^{-1}) and tris(2,2′-bipyridyl)copper(II) ions ($k_2 < 0{\cdot}5$ l mol^{-1} s^{-1}). Only upper limits to the rate of reduction of these complexes by ferrocytochrome c could be obtained, since reduction of solutions of these complexes occurred *via*

the low equilibrium concentration of the bis complexes present in solution. It is apparent, however, that, as expected, the rate of reduction of these complexes is slow compared to the bis complexes, which can more easily reach the transition state.

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