

"STRUCTURE-REACTIVITY RELATIONSHIPS IN HOMOGENEOUS ELECTRON TRANSFER REACTIONS,"

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Any geometric rearrangement which accompanies a change in oxidation state is expected to produce a significant contribution to the activation energetics of electron-transfer processes. This "Franck-Condon" barrier is of particular significance in reactions involving metal complexes where the length of the coordinate bonds and, in some instances, the coordination number and the coordinate bond angles may change significantly as the metal oxidation number varies.

Vallee and Williams¹ incorporated these concepts into their proposal that the active center of redox-active enzymes must exist in a strained configuration which approximates the geometry of the transition state for corresponding unconstrained systems undergoing similar oxidation changes. This resultant strained (or "entatic") state would then be expected to reduce the activation barrier for electron transfer and would account for the kinetic efficiency of such enzyme systems.

In expanding upon the implications of this "entatic state" hypothesis, Vallee and Williams focused on metalloenzymes involving iron or copper, the two most common metal ions in redox active enzymes. For the former systems, Fe(III) normally exhibits shorter coordinate bonds than does Fe(II). In the absence of physical constraints, electron transfer would then be expected to involve a change in coordinate bond lengths which would be manifested in the activation barrier for Fe(III)/Fe(II) redox kinetics. For Cu(II)/Cu(I) systems, even larger barriers are anticipated since Cu(II) normally prefers a coordination number of 6 or 5 while Cu(I) has a preferred coordination number of 4 (or less). This implies that Cu(II)/Cu(I) electron-transfer processes must normally involve the rupture or formation of one or more coordinate bonds with a corresponding alteration in bond angles (and, possibly, bond lengths as well).

Despite the current wide-spread interest in structure-reactivity relationships in chemistry, few attempts have been made to explore the quantitative implications of Vallee and Williams' "entatic state" hypothesis for electron-transfer processes. In one of the few definitive studies reported to date, Endicott and coworkers² compared the structures and kinetic parameters of a series of macrocyclic complexes containing Co(III)/Co(II) (analogous to the Fe(III)/Fe(II) redox couple). From these studies they were able to demonstrate that constraints upon the flexibility of the cobalt-donor atom bond lengths did, indeed, impact the electron transfer kinetics. However, no similar studies have been conducted on metal complexes which do not retain octahedral geometries.

Much recent attention has been focused on a series of copper enzymes known as the "blue electron carriers." These enzymes exhibit relatively large self-exchange rate constants which have generally been attributed to an unusual "strained" (four coordinate) geometry of the copper site.³ However, the lack of systematic information for Cu(II)/Cu(I) systems involving other coordination geometries makes such an interpretation tenuous.

Nearly all reported studies on low molecular weight copper complexes involve the reduction of Cu(II) to Cu(I). In fact, for the few systems for which the kinetics of both Cu(II) reduction and Cu(I) oxidation have been determined independently, the calculated self-exchange rate constants differ drastically (i.e., by $\geq 10^4$) for the two processes.⁴ This discrepancy suggests that the theoretical treatments normally applied for the evaluation of self-exchange rate constants may not be valid for Cu(II)/Cu(I).⁵

In an attempt to characterize the relationship between structure and electron-transfer reactivity in Cu(II)/Cu(I) systems, we have undertaken a thorough investigation of a series of low molecular weight copper polythiaether complexes which mimic the potentials and spectral properties of the blue electron carriers.⁶ This work has incorporated a multi-faceted approach which includes (i) structural determinations, (ii) electrochemical measurements, (iii) nmr determinations of the apparent self-exchange rate constants, and (iv) kinetic studies on representative cross reactions.⁷ These studies

suggest that Cu(II)/Cu(I) redox reactions may involve two or more parallel pathways in which electron-transfer and structural rearrangements may occur sequentially rather than in a concerted manner. An analysis of available literature data suggests that a similar mechanism may also be operative in copper enzyme systems resulting in a biological "switch" to control the net direction of electron flow. The evidence for this electron-transfer mechanism and its implications will be discussed.

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