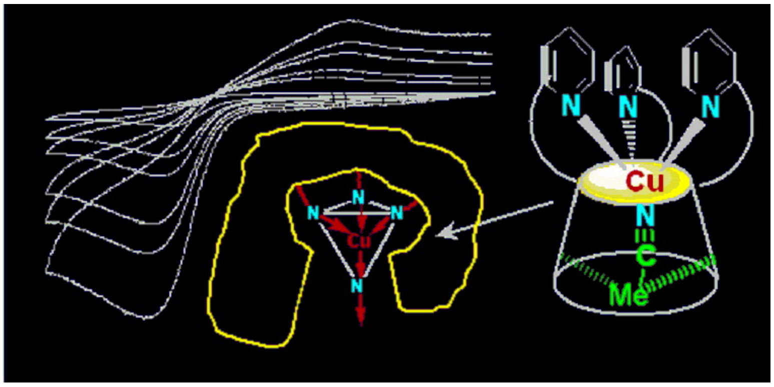
Communication

Electrochemical Behavior of the Tris(pyridine)–Cu Funnel Complexes: An Overall Induced-Fit Process Involving an Entatic State through a Supramolecular Stress

Nicolas Le Poul, Morgan Campion, Guillaume Izzet, Bndicte Douziech, Olivia Reinaud, and Yves Le Mest

J. Am. Chem. Soc., **2005**, 127 (15), 5280-5281• DOI: 10.1021/ja043073h • Publication Date (Web): 19 March 2005



Journal of the American Chemical Society is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

J|A|C|S
COMMUNICATIONS

Electrochemical Behavior of the Tris(pyridine)−Cu Funnel Complexes: An Overall Induced-Fit Process Involving an Entatic State through a Supramolecular Stress

Nicolas Le Poul,† Morgan Campion,† Guillaume Izzet,‡ Bénédicte Douziech,† Olivia Reinaud,‡ and Yves Le Mest*,†

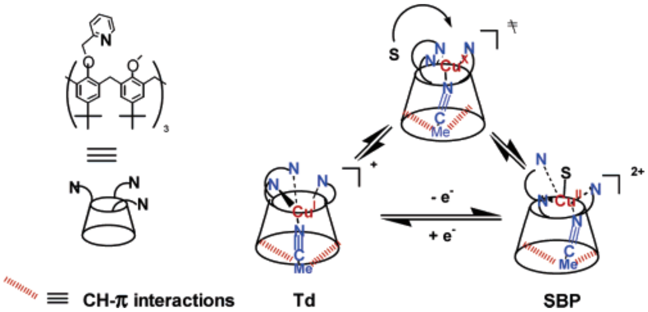
Laboratoire de Chimie, Electrochimie Moléculaires et Chimie Analytique, UMR CNRS 6521, Université de Bretagne Occidentale, 6 av. Le Gorgeu, 29238 Brest Cedex 3, and Laboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques, UMR CNRS 8601, Université René Descartes, 45 rue des Saints Pères, 75270 Paris Cedex 06, France

Received November 17, 2004; E-mail: yves.lemest@univ-brest.fr

The entatic state and induced-fit mechanism are two concurrent theories proposed as crucial tools for nature to regulate the function of an active site by exerting a strain on its electronic/geometric conditions by means of the surrounding protein matrix.[1,2] The functionality of the redox Cu proteins based on the Cu(II)/Cu(I) process is considered as an ultimate candidate for taking advantage of this effect.[1] The geometry of the Cu(I) d^{10} ion is dictated by the surrounding ligands mostly through steric repulsions leading to a tetrahedral (Td) geometry. Conversely, due to crystal field force, for the prototypical Jahn−Teller Cu(II) d^9 ion, the metal itself tends to enforce its geometric square-based pyramid (SBP) preferential pattern.[3] Thus, the Cu(II)/Cu(I) process involves a reorganizational barrier depending on the constraint exerted by the coordination environment. Such a behavior has been theorized by Rorabacher in terms of a square-scheme mechanism involving two metastable Cu(I) SBP and Cu(II) Td species.[4] The electrochemical behavior of low molecular weight complexes supports this mechanism, showing that, except in rare cases,[5] the topological reorganization takes place at the Cu(I) state owing to its geometrical adaptability in the absence of crystal field force.[4] The metallic N_3-calix[6]arene derivatives, so-called funnel complexes, have demonstrated their biomimetic coordinating ability as structural models that integrate a protein-like pocket encapsulating one of their binding sites.[6] Herein, we propose that the Cu(II)/Cu(I) redox process of the tris(pyridine)−Cu complexes[7] (Scheme 1) is regulated by an overall induced-fit mechanism constituting a dynamic electrochemical model for the topological reorganization of the Cu environment involving a real entatic energized state.

The synthesis, crystal structure, and spectroscopic features of the Cu(I)−tris(pyridine) complex have been previously described.[7a] This complex displays in CD_2Cl_2 solution ^1H NMR spectra attesting to a lack of symmetry,[7d] due to an undefined geometrical pattern. The addition of an organonitrile RCN leads to the formation of a new species in which the Cu(I) center resides in a Td N_4 environment secured by the global organization of the system involving (i) coordination of Cu by the three pyridine groups and the RCN ligand buried inside the cavity of the calix[6]arene, and (ii) CH−π second sphere interactions between the methyl group of the nitrile and the phenyl units of the cavity.[7d] This geometry has been confirmed in the crystal structure of $[Cu(X_6Me_3Pic_3)(EtCN)](PF_6)$.[7a] We have now synthesized and characterized the Cu(II) complex.[8] In a noncoordinating solvent, the EPR spectra display a broad rhombic signal indicating an ill-defined structure. In MeCN, the EPR parameters ($A_{\|} = 148$ G, $g_{\|} = 2.34$, $g_{\perp} = 2.07$) and UV−vis data ($\lambda_{max} = 727$ nm) are typical of a mononuclear Cu(II) lying in a distorted SBP geometry. This geometry was established by X-ray studies with two Cu(II)−N_3-calixarene complexes (Scheme 1);[7b,c] the Cu(II) ion is coordinated to the N_3 ligand, a guest RCN molecule buried inside the calixarene cavity and a water molecule (S) sitting outside. One nitrogen arm is the apical site. Thus, also for the Cu(II) complex, a small nitrile inside the cavity is necessary to maintain the architecture of the system.

Scheme 1. Tris(pyridine) N_3-Calixarene Ligand ($X_6Me_3Pic_3$), the Structures of the Cu(I)[7a] and Cu(II) Complexes,[7b,c] and the Reorganization at the Cu(II)/Cu(I) Process



In noncoordinating solvents, the electrochemical behavior of the Cu(I) and Cu(II) complexes is totally impossible to interpret, giving rise to undefined electrochemically and chemically irreversible peaks. Similar behavior was reported for the rare cases of Cu complexes in a hydrophobic environment.[9] In PhCN, the Cu(II)/Cu(I) process is chemically reversible, but extremely slow. The cyclic voltammetry (CV) behavior could only be rationalized in the presence of a nonsterically encumbered nitrile, such as MeCN. Figure 1 displays the CV of the Cu(II) and Cu(I) complexes in the bulk at different scan rates (v). Both forms can be interconverted by electrolysis ($n = 1\ e^-$), indicating, with corroboration of the spectroscopic features, a full chemical reversibility. Figure 1a shows that, at low scan rate, a quasi-reversible system is observed ($E_{pa}^B \cong +0.80$ V, $E_{pc}^B \cong +0.50$ V; $i_{pa}/i_{pc} \approx 1$), defined as "system B" along Rorabacher's formalism (Scheme 2).[4] As v is increased, a cathodic peak at $E_{pc}^A \cong +0.18$ V, with a peak current i_{pc}^A becoming predominant over i_{pc}^B, reveals the existence of an equilibrium in solution (CE process). A fourth peak, $E_{pa}^A \cong +0.34$ V, corresponding to the reverse peak at E_{pc}^A of "system A", has been detected only at higher scan rates ($v > 1$ V s^{-1}). The behavior of the Cu(I) complex (Figure 1b) is similar to that of the Cu(II) complex except that the two cathodic peaks, E_{pc}^A and E_{pc}^B, appear not deconvoluted in these scanning conditions. The intensity i_{pa}^B is linear with $v^{1/2}$, and even at very low scan rates, the peak at E_{pa}^A could not be detected. On the basis of the structural characterizations, this demonstrates qualitatively that the Cu(I) derivative is strongly stabilized in a Td configuration, with a single oxidation peak at E_{pa}^B, and not adjustable to a SBP geometry at low v through the

---

† Université de Bretagne Occidentale.
‡ Université René Descartes.

10.1021/ja043073h CCC: $30.25

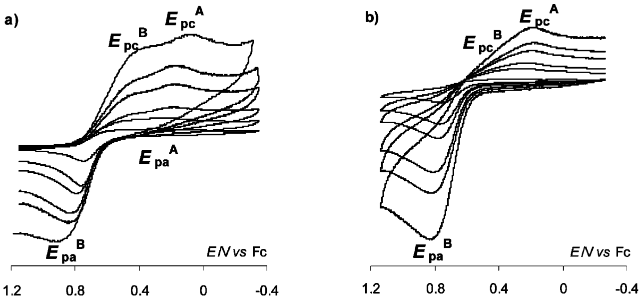
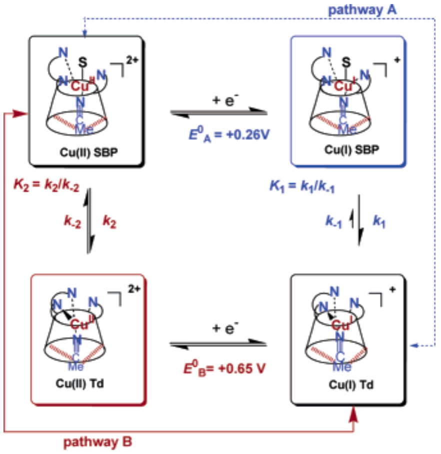


Figure 1. CVs of the Cu(II) (a) and Cu(I) (b) complexes; CH_3CN/NBu_4PF_6; $v = 0.01, 0.05, 0.1, 0.3, 0.5$, and 1 V s^{-1}; $T = 293$ K.[8]

Scheme 2. Square-Scheme Redox Mechanism



classical CE process for Cu(I). Conversely, the Cu(II) species, stable in solution in a SBP configuration, is reduced at E_{pc}^{A} at high scan rates; at lower rates, an interconversion SBP → Td (CE process) is observed, with the complex being reduced at the potential of the Td species, E_{pc}^{B}. This behavior results from the crossing of geometry (SBP ↔ Td) at the electron transfer and can be interpreted in terms of the square-scheme double $C_{rev}E$ mechanism (Scheme 2).[4] The adequacy of this model has been confirmed by a simulation of the CVs using the Digisim program on the basis of a first-order approximation by a fitting procedure. The appearance of the simulated voltammograms satisfactorily reproduced the trends displayed in the experimental curves and gave an estimation of the thermodynamic and kinetic constants.[8] Particularly striking was that (i) the value of $K_1 \approx 3.5 \times 10^5$ reflects a Cu(I) strongly secured in a Td configuration and nonadjustable to a SBP geometry; (ii) the value of $K_2 \approx 0.07$ reveals a Cu(II) complex more stable as a SBP but fluxional between a SBP and Td geometry.

The electrochemical behavior of the tris(pyridine) calix[6]arene Cu adducts is remarkable as compared to that of most of the classical Cu complexes in a strain-free environment;[4,5] (i) the presence of MeCN buried inside the cavity is a prerequisite for a quasi-reversible behavior in a dynamic mode; (ii) the coordination adaptability of the two redox states is completely reversed and enforced toward the Td geometry. These unusual properties emphasize the key role played by the intrapocket ligand, which dictates the coordination of the copper ions by combination of the Cu−N (nitrile) bond and second-sphere interactions. The organization is largely favored by the relatively low donor effect of the pyridine and steric crowding on the upper rim. The fitted MeCN ligand is thus proposed to act as a “shoetree” molecule, which induces defined conformations to the cone and controls, by transmission of the forces to the upper rim, the N_3 coordination of the metal adapted to the Cu(II) and Cu(I) redox states. This effect is postulated to maintain a coherent host−guest interaction at the transient state by the means of the lone CH−π interactions whether the metal is or is not coordinated to the *N*-nitrile at the reorganization process (Scheme 1).[10] These interactions generate a supramolecular stress resulting in a driving force pulling the Cu inside the cavity, strongly favoring the Td geometry at every stage of the redox process, including the metastable species. The electron transfer is thus gated through the pathway B, kinetically closed along the pathway A. This determines an enhanced oxidizing power equalized to the more anodic $E°_B$ potential, which rationalizes the ability of the tris(pyridine)−Cu complex to electrocatalyze phenol oxidation.[7b] Pathway B has been scarcely established, especially when involving an entatic state[5a−c] or with a minimized ligand reorganization.[5d]

This is the first example of a Cu complex where the supramolecular control of the coordination by a protein-like pocket determines the dynamics of the electron transfer process, its thermodynamics, and the kinetics of the reorganizational barrier and generates a preorganization state for oxidation. This phenomenon evidences an overall induced-fit redox process enforcing, by a protein-like strain, a highly oxidizing Cu(II) state. This corresponds to a definitive entatic state as originally stated by Vallee and Williams,[1] which is now recognized as an operative means for nature to modulate the redox properties of proteins.[11,12] This observation is tangible evidence that the Cu(II/I) systems can be considered as truly biomimetic processes and provide relevant information for our understanding of the more complex proteins,[4] especially when involving a hydrophobic channel modeling their secondary coordination sphere.[9a,11,13]

Acknowledgment. We acknowledge support from the CNRS, Ministère de la Recherche (G.I.), Conseil Régional de Bretagne (M.C.), and Conseil Général du Finistère (N.L.P.). Dr. E. Levillain is thanked for free access to Digisim and valuable discussions.

Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Williams, R. J. P. *Eur. J. Biochem.* **1995**, *234*, 363. (b) Vallee, B. L.; Williams, R. J. P. *Proc. Natl. Acad. Sci. U.S.A.* **1968**, *59*, 498.
(2) (a) Comba, P. *Coord. Chem. Rev.* **2000**, *200−202*, 217. (b) Comba, P.; Schiek, W. *Coord. Chem. Rev.* **2003**, *238−239*, 21.
(3) Hathaway, B. J. *Struct. Bonding (Berlin)* **1984**, *57*, 55.
(4) For leading refs, see: Rorabacher, D. B. *Chem. Rev.* **2004**, *104*, 651.
(5) (a) Bernardo, M. M.; Robandt, P. V.; Schroeder, R. R.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1989**, *111*, 1224. (b) Xie, B.; Wilson, L. J.; Stanbury, D. M. *Inorg. Chem.* **2001**, *40*, 3606. (c) Koshino, N.; Kuchiyama, Y.; Ozaki, H.; Funahashi, S.; Takagi, H. D. *Inorg. Chem.* **1999**, *38*, 3352. (d) Ambundo, E. A.; Yu, Q.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **2003**, *42*, 5267.
(6) See refs in: Seneque, O.; Campion, M.; Giorgi, M.; Le Mest, Y.; Reinaud, O. *Eur. J. Inorg. Chem.* **2004**, 1817.
(7) (a) Blanchard, S.; Le Clainche, L.; Rager, M.-N.; Chansou, B.; Tuchagues, J.-P.; Duprat, A. F.; Le Mest, Y.; Reinaud, O. *Angew. Chem., Int. Ed.* **1998**, *37*, 2732. (b) Le Clainche, L.; Rondelez, Y.; Seneque, O.; Blanchard, S.; Campion, M.; Giorgi, M.; Duprat, A. F.; Le Mest, Y.; Reinaud, O. *C. R. Acad. Sci., Ser. IIc: Chim.* **2000**, *3*, 811. (c) Le Clainche, L.; Giorgi, M.; Reinaud, O. *Inorg. Chem.* **2000**, *39*, 3436. (d) Rondelez, Y.; Rager, M.-N.; Duprat, A.; Reinaud O. *J. Am. Chem. Soc.* **2002**, *124*, 1334.
(8) See Supporting Information.
(9) (a) Kuzelka, J.; Mukhopadhyay, S.; Spingler, B.; Lippard, S. J. *Inorg. Chem.* **2004**, *43*, 1751. (b) Carrier, S. M.; Ruggiero, C. E.; Houser, R. P.; Tolman, W. B. *Inorg. Chem.* **1993**, *32*, 4889.
(10) (a) Arduini, A.; Giorgi, G.; Pochini, A.; Secchi, A.; Ugozzoli, F. *Tetrahedron* **2001**, *57*, 2411. (b) Bonechi, C.; Donati, A.; Martini, S.; Rossi, C.; Arduini, A.; Pochini, A.; Lonetti, B.; Baglioni, P. *J. Phys. Chem. B* **2004**, *108*, 7603.
(11) Gray, H. B.; Malmström, B. G.; Williams, R. J. P. *J. Biol. Inorg. Chem.* **2000**, *5*, 551.
(12) (a) DeBeer G. S.; Basumallick, L.; Szilagyi, R. K.; Randall, D. W.; Hill, M. G.; Nersissian, A. M.; Valentine, J. S.; Hedman, B.; Hodgson, K. O.; Solomon, E. I. *J. Am. Chem. Soc.* **2003**, *125*, 11314. (b) Li, H.; Webb, S. P.; Ivanic, J.; Jensen, J. H. *J. Am. Chem. Soc.* **2004**, *126*, 8010.
(13) Izzet, G.; Douziech, B.; Prangé, T.; Tomas, A.; Jabin, I.; Le Mest, Y.; Reinaud, O. Submitted.

JA043073H