Redox-linked Pyrrole NH Deprotonation in a Dicopper Azacryptate System

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The pyrrole-based cryptand L, has asymmetric conformation when coordinated to dicopper(I); one-electron oxidation yields a localized mixed-valence dicopper cryptate of the singly deprotonated ligand and two-electron oxidation a dicopper(II) cryptate of the triply deprotonated ligand; single crystal X-ray structure determination shows two different irregular sites for $\mathrm{Cu^{II}}$.

In many bioinorganic systems,[1] $\mathrm{Cu^{II}}$ is coordinated by anionic donors, *e.g.* $\mathrm{SR^-}$, $\mathrm{His^-}$, $\mathrm{TyrO^-}$, $\mathrm{RN^-}$ (CO), $\mathrm{O_2^{2-}}$ *etc.* Indeed the recent successful modelling of the haemocyanin active site[2] utilized the anionic ligand, trispyrazolylborate. The frequent biological use of potentially anionic ligands in conjunction with $\mathrm{Cu^{II}}$ emphasises the importance of minimising charge build-up; this approach to electroneutrality is especially important in dicopper systems. Coupling of protonation/deprotonation equilibria to redox change is seen in the cytochrome oxidase system, where proton translocations associated with redox at copper constitute the basis of the redox-linked proton pump[3] mechanism for the four electron reduction of dioxygen to water. The recent development[4,5] of a facile synthetic route [eqn. (1)] to azacryptand ligands

$$2\,\mathrm{N(CH_2CH_2NH_2)_3} + 3\mathrm{OCH{\cdot}R{\cdot}CHO} \xrightarrow{\mathrm{Cu^+}} \mathrm{N(CH_2CH_2N{=}CHRCH{=}NCH_2CH_2)_3N}\ (\mathrm{R} = \text{pyrrole-2,5-diyl}) \quad (1)$$

furnishes a range of hosts for dicopper(II) with donor set and coordination geometry similar to those in copper metalloenzymes. None of the dicopper(I) cryptates of the series so far studied[6–8] react with atmospheric oxygen, despite the favourable thermodynamics evident[9] in many cases. We were interested to discover whether an ionizable ligand such as L would generate such inertness in its dicopper(I) cryptates in basic solution; deprotonation of pyrrole NH is general upon coordination of the highly delocalized porphyrin ligand to divalent cations, and has been reported[10,11] for several non-porphyrin pyrrole-containing macrocycles.

The dicopper(I) complex† of L: $\mathrm{[Cu_2L](BF_4)_2}$ **1** is easily made in >60% yield by template synthesis on the appropriate $\mathrm{Cu^I}$ salt, under inert atmosphere conditions; **1** is air-stable for hours <–> days which permits the observation of solution properties. The complex ^{1}H NMR spectrum (Table 1) of $\mathrm{[Cu_2L]^{2+}}$ has been assigned by a combination of NOE and COSY 45 experiments. Three pyrrole CH signals (each of intensity corresponding to two protons) appear, of which two ($\mathrm{H_f}$ and $\mathrm{H_g}$) are coupled to each other. This shows that, as far as these protons are concerned, the two ends of the macrobicycle are different, and indeed two separate sets (d,j,m,p,q) and (b,h,k,n,s) of imine and methylene signals related (through NOE and COSY) to $\mathrm{H_f}$ and $\mathrm{H_g}$ protons respectively, are observed. The third strand of the cryptand ligand does not show any coupling or differentation of the pyrrole CH protons, so it looks as though the cryptate may have a 'basket' conformation where the third strand ('handle') is remote from any coordination effects. In agreement with this idea, a relatively sharp signal is seen for one (NH″) of the three pyrrole NH protons, together with (most easily observable in acid solution) a much broader low field signal corresponding to the other two protons.

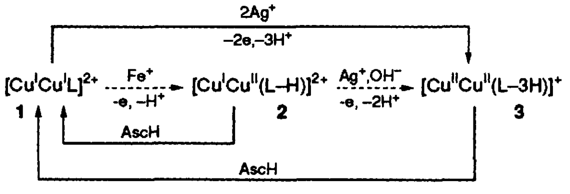
Table 1 ^{1}H NMR spectrum[a] of **1**

Pyrrole NH	Imino CH	Pyrrole CH	Methylene $\mathrm{CH_2}$			
NH		CH				
NH′	$\mathrm{H_d}$	$\mathrm{H_f}$	$\mathrm{H_j}^f$	$\mathrm{H_m}^f$	$\mathrm{H_p}^f$	$\mathrm{H_q}^f$
12.9^b br	8.08	6.69 d^c	3.51 tr^g	3.23 d^d	3.01^g	2.75^g
NH″	$\mathrm{H_c}$	$\mathrm{H_e}$	$\mathrm{H_i}$	$\mathrm{H_l}$	$\mathrm{H_o}$	$\mathrm{H_r}$
11.67	8.11	6.74 s	3.54 tr^g	3.26 d^d	3.06^g	2.72^e
NH′	$\mathrm{H_b}$	$\mathrm{H_g}$	$\mathrm{H_h}$	$\mathrm{H_k}$	$\mathrm{H_n}$	$\mathrm{H_s}$
12.9^b br	8.29	6.65 d^c	3.58 tr^g	3.34 d^d	3.10^g	2.70^e

[a] In $\mathrm{CD_3CN}$ at 345 K, shifts in δ from $\mathrm{Me_4Si}$; all signals[2H] intensity, (except NH″, which is [1H]). [b] Broad singlet seen in acid soln. [c] Coupled, $^3J \approx 4$ Hz. [d] Assigned on the basis of NOE irradiation from the appropriate pyrrole CH. [e] Assigned from the multiplet on the basis of COSY 45 alone. [f] $^2J \approx 12$; ^3J: ≈ 13 Hz (ax/ax′) : ≈ 4 Hz (ax/eq′ or eq/eq′). [g] Signal selected from the spectrum with assistance of COSY 45.

The electrochemical properties of **1**[9] suggest that one-electron oxidation with $\mathrm{Fc^+}$ should be possible, and indeed this reaction generates the mixed-valence cryptate† $\mathrm{[Cu_2(L\text{-}H)](BF_4)_2{\cdot}H_2O}$ **2**. The IR spectrum of **2** still shows ν_{NH} absorption,‡ at 3130 cm^{-1} red-shifted by ≈ 150 cm^{-1} and intensified relative to that of **1**. This suggests involvement of pyrrole NH protons in intramolecular H-bonding. Complex **2** has a temperature-independent solid-state magnetic moment of ≈ 2.0 μ_B per formular unit, and polycrystalline or MeCN glass EPR spectra alike take the form of a poorly resolved $g \approx 2$ signal lacking hyperfine structure.§ Such broadening of the EPR spectra indicates involvement of the paramagnetic ion in some dynamic process, *e.g.* dynamic Jahn–Teller distortion. The absence of hyperfine coupling hinders assessment of the degree of electron delocalisation between the pair of copper sites; however, on the basis of the lack of intense near-IR absorption attributable to intervalence transfer, the compound is classified as Class 1[12] localized mixed-valence. In the absence of base, no perceptible oxidation of **2** by $\mathrm{Ag^+}$ or $\mathrm{O_2}$ occurs over a period of days; however at pH > 7, such oxidation takes place within hours, as shown by development of the electronic spectrum associated with the dicopper(II) cryptate **3**.

Fig. 1(*a*) shows that the more negative redox process, E^1, shifts by ≈ 500 mV to negative potential when **1** is oxidised to **2** in MeCN solution, leaving the potential of the more positive process, E^2, unaffected. This suggests that the deprotonated pyrrole anion coordinates copper(II) at the site generating E^1, which rationalises the localization of the unpaired spin at this site. The site generating E^2 is presumably unaffected by the oxidation. However, cyclic voltammograms (CV) of **2** run in basic MeCN¶ solution show shifting of E^2 to negative potential (together with loss of reversibility) which implies that further deprotonation affects the second copper coordination site. Oxidation of both **2** (in basic solution) and **1** with $\mathrm{AgClO_4}$ generates a dark-brown solution from which black



Scheme 1

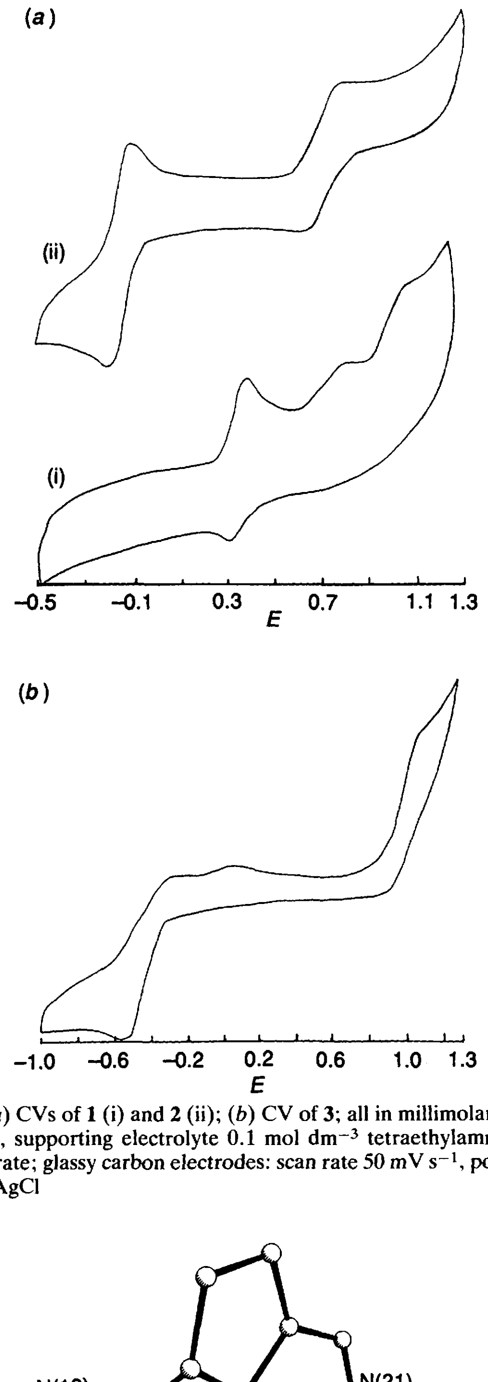


Fig. 1 (*a*) CVs of **1** (i) and **2** (ii); (*b*) CV of **3**; all in millimolar MeCN solution, supporting electrolyte 0.1 mol dm^{-3} tetraethylammonium perchlorate; glassy carbon electrodes: scan rate 50 mV s^{-1}, potentials *vs*. Ag/AgCl

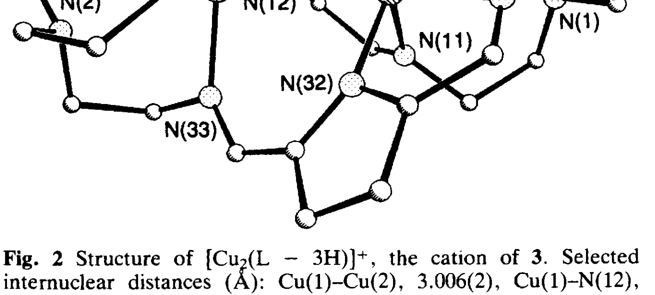


Fig. 2 Structure of $[Cu_2(L - 3H)]^+$, the cation of **3**. Selected internuclear distances (Å): Cu(1)–Cu(2), 3.006(2), Cu(1)–N(12), 2.009(5), Cu(1)–N(13), 2.058(6), Cu(1)–N(23), 2.031(6), Cu(1)–N(33), 1.981(6), Cu(2)–N(11), 1.999(6), Cu(2)–N(21), 2.039(6), Cu(2)–N(22), 2.151(6), Cu(2)–N(31), 2.205(6), Cu(2)–N(32), 2.029(6).

crystals of $[Cu_2(L\text{-}3H)]ClO_4$ **3**†,‖ can be isolated. The electronic spectrum** of this cryptate contains three intense UV absorptions, the shortest wavelength of which tails into the VIS and, together with broad d-d absorption centred at 700 and 900 nm, explains the black appearance of the crystals. In comparison with **2** the relative enhancement of absorption close to 700 nm suggests[13] that the additional Cu^{II} coordination site is four-coordinate distorted square-planar.

The dicopper(II) formulation suggested for **3** by stoichiometry and the absence of ν_{NH} IR absorption is confirmed by the virtually temperature-independent solid-state moment of ≈1.90 μ_B per Cu ion which also indicates that any interaction between the paramagnets is limited to the through-space dipolar mechanism. The MeCN glass EPR spectrum, like that of **2** is broad [($g \approx 2$ signal extending over 2000 G) (1 G = 10^{-4} T)] and poorly defined, lacking both hyperfine structure and any clear differentation of copper(II) sites; a poorly resolved half-band signal appearing with 1/10th intensity of the $g \approx 2$ absorption is evidence for at least weak interaction between copper(II) paramagnets.

X-Ray crystallographic structure determination†† of **3** (Fig. 2) shows that the cation has no internal symmetry, and the geometry at each copper is irregular. Cu(1) is four-coordinate, distorted toward tetrahedral from square-planar while Cu(2) approximates to square pyramidal coordination geometry. Neither bridgehead N is coordinated to copper, but the three pyrrole nitrogens are: two with Cu lying more or less coplanar with the pyrrole ring having Cu–N distances ≈ 2.0 Å, and a third with Cu lying well out of the plane of the ring and a longer Cu–N distance of 2.15 Å. This pyrrole nitrogen also makes a long, weak >2.6 Å contact to the other copper ion. Such a distance is too long to represent a bond, so the paramagnetic centres may be considered unbridged, as the magnetic susceptibility results indicate. The Cu–Cu distance, at 3.006 Å is, to our knowledge, the shortest Cu^{II}–Cu^{II} contact unsupported by a bridge reported to date.

The electrochemistry of **3** is quite different from that of **2**, demonstrating that neither of the coordination sites revealed in the X-ray structure for **3** are identical with those used in **2**. The CV [Fig. 1(*b*)] shows very little reversibility; a feature consisting of two broad overlapping anodic waves (−290, +55 mV) and a single strong cathodic wave (−550 mV) appears. Irreversibility presumably derives from instability of the unprotonated reduced form of **3**. Chemical reduction of **3** with ascorbic acid generates **1**, while no reduction has so far been observed with non-acidic reductants such as $Cu(MeCN_4)^+$ or BPh_4^-. This indicates that chemical redox is linked to pH in both directions. Scheme 1 summarises the redox transformations observed.

The resistance of **2** to oxidation in the absence of base suggests that the two remaining pyrrolic nitrogens in this case may be involved in H-bonding, perhaps to imino-N (as has been confirmed for the analogous phenol-based cryptand[14]). The requirement to disturb H-bonding in the course of the redox process is an important element of redox-linked proton pumping mechanisms, which suggests that further work on proton translocations in this model system may prove worthwhile.

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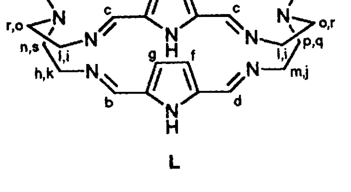

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access to services: 400 MHz NMR spectrometer at Warwick and FABMS at Swansea. We are grateful to Professor Allan White at University of Western Australia for X-ray data collection, and to Dr Charlie Harding (Open University) for magnetic susceptibility data.

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Footnotes

† Satisfactory elemental analyses were obtained for **1**, **2** and **3**. FAB MS data: **1** *m/z* 616 (75%); 743 (10%); **2** *m/z* 678 (100%); **3** *m/z* 678 (100%).

‡ KBr disc spectrum.

§ Dmf glass EPR spectra of **2** developed extensive hyperfine structure within 1–2 min; this was not further investigated as it clearly arises from some secondary process.

¶ Insolubility prevented measurements in aqueous solution.

‖ **CAUTION**: All perchlorates must be treated as potentially explosive.

** *Electronic spectral data* λ/nm (dm^3 mol^{-1} cm^{-1}): **1**: 282(62500), 340(25200), 375(16700); **2**: 306(71500), 390(4400), 610sh, 710(150), 885(185); **3**: 220(54000), 264(44000), 385sh, 342(48000), 550sh, 720(222), 904(228).

†† *Crystal data*: $C_{30}H_{37}ClCu_2N_{11}O_4$, brown, 0.35 × 0.32 × 0.15 mm, monoclinic, space group $P2_1/c$ $a = 10.597(5)$, $b = 17.554(9)$, $c = 17.560(12)$ Å, $\beta = 90.85(5)$, $U = 3266(3)$ Å^3, $Z = 4$, F(000) = 1604, $\mu = 1.44$ mm^{-1}. Data collected at room temp. on an Enraf-Nonius CAD-4 diffractometer using Mo-Kα radiation. The structure was solved by direct methods and refinement converged with $R = 0.045$, $R_w = 0.057$ for 2793 reflections $F > 6\sigma(F)$. Hydrogen atoms were inserted at calculated positions, and all non-hydrogen atoms were refined with anisotropic temperature factors. NRCVAX programs[15] were used in data reduction; solution and refinement programs are contained in the SHELXTL-PC package.[16] Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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