Redox Behaviour of Novel Copper(II) Crown Ether–Pyrazole Complexes

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A novel dinuclear copper(II) diazacrown ether complex reduces in solution to the copper(I) state; the related mononuclear copper(II) monoazacrown ether complex undergoes reduction, when K^+-ions are added.

One of the most challenging themes in bioinorganic chemistry is the mimicking of the dinuclear copper sites in copper proteins such as haemocyanin and dopamine-β-hydroxylase.[1] The former protein is responsible for dioxygen transport in arthropods and molluscs,[2] the latter enzyme is vital for the biosynthesis of noradrenaline.[3] The binding of dioxygen to haemocyanin occurs through the cooperative action of both copper ions present in the active centres[4] and can be influenced by pH,[5] anions[6] and cations.[7] Model systems mimicking this behaviour could provide insight into the mechanistic action of these biomolecules.

In the literature only a few examples are known of dinuclear

copper(II) complexes that reduce to the copper(I) state.[8] We present here a novel dinuclear copper(II) crown ether–dimethylpyrazole complex **1**, which in methanol solution is reduced to the copper(I) state, even in the presence of air. The related complex **2** undergoes a much slower reduction under these conditions. This process, however, can be enhanced and controlled by the addition of alkali metal ions.

The ligands from which **1** and **2** are derived were synthesized by treating α-bromo-α′-{bis[2-(3,5-dimethyl-1-pyrazolyl)ethyl]amino}-*m*-xylene† with the corresponding diaza- and aza-crown ethers in dimethylformamide (DMF). The yield after column chromatography (silica 60H, eluent $CHCl_3$–MeOH–triethylamine, 97.5:2:0.5, v/v/v) for both ligands was approximately 55%. The ligands were mixed with 2 equiv. (for **1**) and 1 equiv. (for **2**) of $Cu(ClO_4)_2 \cdot 6H_2O$ in methanol to give the di- and mono-nuclear complexes **1** and **2** in 77 and 80% yield, respectively.‡ During the synthesis of **2** a dark-green colour developed, typical for this type of copper(II) complex. The homogeneous solution of **1**, however, decolorized rapidly, indicating the formation of a copper(I) complex. Proof that **1** indeed had reduced to the copper(I) state came from electrochemical experiments on samples of **1** and **2**, obtained from these reactions. A solution of **2** in acetonitrile [0.1 mol dm^{-3} $(Bu^n)_4PF_6$, Pt-electrode] showed a reversible wave with $E_{1/2} = 0.29$ V (*vs.* Fc^+/Fc, $\Delta E_p = 0.12$ V, $i_b/i_f = 1$). The equilibrium potential (E_{eq}) of the solution was 0.50 V, proving that **2** indeed is a Cu^{II} complex. Complex **1** also showed a reversible wave at approximately the same potential ($E_{1/2} = 0.31$ V, $\Delta E_p = 0.18$ V, $i_b/i_f = 1$) as found for **2**. The equilibrium potential of this solution was 0.15 V, clearly indicating that **1** was present in the form of a reduced complex. In view of the broad forward oxidation peak and the presence of two copper atoms, it is clear that **1** can be oxidized in two consecutive one-electron steps following an EE-reaction path. The half-wave potentials of these steps were calculated by the method of Richardson and Taube and amounted to $E_{1/2}$ (**1**) = 0.29 V and $E_{1/2}$ (**2**) = 0.32 V.[9]

For the reaction $Cu^{I,I} + Cu^{II} \rightleftarrows 2Cu^{I,II}$ we can calculate from the $\Delta E_{1/2}$ (30 mV) a comproportionation constant $K_c = 4$.§ This value suggests that there is hardly any interaction between the two copper centres in the electrochemical reduction of **1**. This is not unexpected in view of the large metal–metal distance [~18 Å from Corey–Pauling–Koltun (CPK) models] in the complex. The chemical reduction reaction follows a pathway different from the electrochemical oxidation/reduction of **1**. We assume that in the former case a cooperative action between the two copper(II)-centres is necessary to achieve the observed reduction of complex **1**. This is based on our observation that formaldehyde is produced during the reaction (fuchsine test): a two electron oxidation of methanol requires two copper(II) ions as electron acceptors. This reaction probably takes place in a μ-alkoxo (or μ-hydroxo) bridged complex, as described by Nelson and Drew.[8a] Subsequent electron transfer and liberation of the aldehyde will yield the dinuclear copper(I) complex.

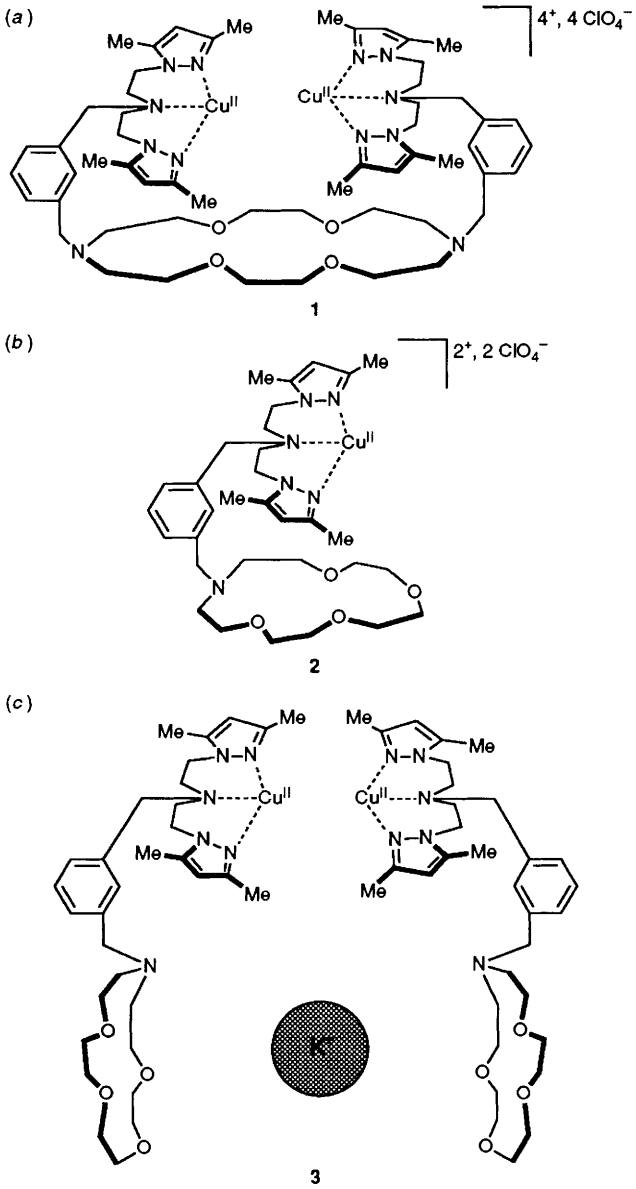

Fig. 1

The progress of the reduction of **1** (2.5 mmol dm^{-3}, acetonitrile–methanol 1:1, v/v) was followed by UV–VIS spectroscopy, measuring the decrease of the d–d absorption band at 700 nm as a function of time and temperature. Rate constants and equilibrium constants were obtained by standard procedures assuming the equilibrium Ox $\underset{k_{-1}}{\overset{k_1}{\rightleftarrows}}$ Red.¶ The following parameters were obtained: forward reaction $\Delta G^{\neq}_{333\,K} = 88$ kJ mol^{-1}, $\Delta H^{\neq} = 48$ kJ mol^{-1}, $\Delta S^{\neq} = -120$ J mol^{-1} K^{-1} and $E_a = 50.6$ kJ mol^{-1}; $\Delta G^{\circ} = -4$ kJ mol^{-1}, $\Delta H^{\circ} = 17$ kJ mol^{-1} and $\Delta S^{\circ} = 63$ J mol^{-1} K^{-1}. The negative entropy of activation points towards a highly ordered transition state, thus supporting our proposed mechanism. The overall reaction is entropy driven as can be seen from the

† This compound was synthesized from 1 equiv. of bis[2-(3,5-dimethyl-1-pyrazolyl)ethyl]amine and 3.5 equiv. of *m*-α,α′-dibromoxylene in tetrahydrofuran–benzene (1:1, v/v). Yield 51% after column chromatography (silica 60H, eluent 3% methanol in chloroform). $R_f = 0.22$. ^1H NMR ($CDCl_3$) δ 2.1 (s, 6H, CH_3), 2.2 (s, 6H, CH_3), 2.9 (t, 4H, NCH_2CH_2) 3.6 (s, 2H, $ArCH_2N$), 3.9 (t, 4H, NCH_2CH_2), 4.5 (s, 2H, $ArCH_2Br$), 6.8 (s, 2H, Pyrazole *H*), 7.1–7.4 (m, 4H, Ar*H*); Mass spectrometry (*m/z*) 364 (20%, M − Br).

‡ *Selected spectral* data for complex **1**: UV–VIS (MeCN–MeOH, 1:1, v/v) $\lambda_{d\text{-}d}$/nm (ε) 695 (140); Λ = 253 μS cm^{-1} (1 mmol dm^{-3} in MeCN); FAB-MS: *m/z* (*m*-nitrobenzylalcohol) 1414 ($M^+ - ClO_4$), 1314 ($M^+ - 2\ ClO_4$); IR (CsI, ν/cm^{-1}) 1552 (pyrazole), 1097, 624 (ClO_4); satisfactory element analyses was obtained. For complex **2**: UV–VIS (MeCN–MeOH, 1:1, v/v) $\lambda_{d\text{-}d}$/nm (ε) 691 (80); Λ = 210 μS cm^{-1} (1 mmol dm^{-3} in MeCN); FAB-MS: *m/z* (*m*-nitrobenzylalcohol) 645 ($M^+ - 2\ ClO_4^-$); IR (CsI, ν/cm^{-1}) 1553 (pyrazole), 1097, 624 (ClO_4). No reproduceable elemental analysis could be obtained for oil **2**.

§ $K_c = \exp[n_1 n_2 F(\Delta E_{1/2})/RT] = \exp[\Delta E_{1/2}/25.69]$ at 298 K with $n_1 = n_2 = 1$.[9]

¶ The rate constants k_1 and k_{-1} follow from the equilibrium constant $K = k_1/k_{-1}$ and from $k = k_1 + k_{-1}$.[13] The latter *k* is obtained by fitting absorbance (A) − time (*t*) data points to the equation $A_t = [A_0/(K + 1)] \times [1 + (K \times \exp(-k \times t))]$.

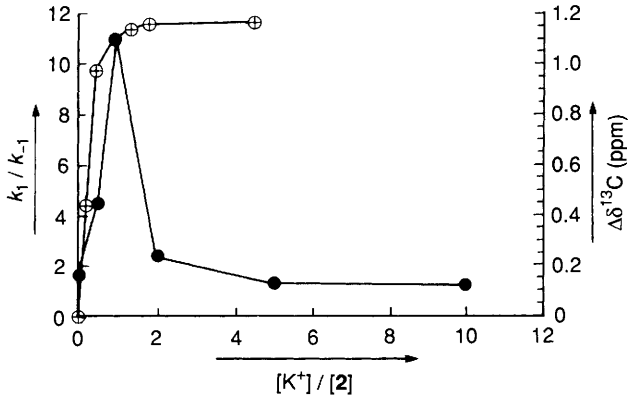

Fig. 2 Reduction of complex **2** as a function of the concentration of K^+ ions (●, ordinate on the left); ^{13}C NMR upfield shift displacement ($\Delta\delta$) for a ring CH_2 carbon atom of compound **2** as a function of K^+ ions (⊕, ordinate on the right)

positive value of $\Delta S°$. This can be rationalized from the fact that during the reduction solvent molecules surrounding the Cu^{II} centres are liberated.

15-Crown-5 is able to form sandwich complexes with a K^+ ion. It was, therefore, tempting to investigate whether this ion could induce the aggregation of **2** [see Fig. 1(*c*)] and influence the reduction of the copper(II) centre. Titration of the $ZnCl_2$ derivative of **2** with potassium picrate confirmed the predominant existence of sandwich complexes at low K^+ : **2** ratios and 1:1 complexes at high ratios (see Fig. 2).[10] We indeed observed that the addition of potassium picrate increased the reduction rate of **2** and caused a shift in the Ox ⇄ Red equilibrium in the direction of the Cu^I species. An optimum was found for a K^+ to **2** ratio of 0.5–1. The increase in $K_{eq} = k_1/k_{-1}$ was fivefold (see Fig. 2).

Alkali metal ions are known to control the aggregation of the subunits of haemocyanin to form the active protein.[11] We think that complexes of type **2** and the related pyridine complexes may be used to mimic this process. Work along this line is in progress.[12]

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