Direct Evidence for an S_N1CB Mechanism I. Aminoacidate Dechelation Upon Amide Deprotonation in bis[N-2-acetamidoiminodiacetato] copper(II)

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There has been much indirect evidence for the S_N1CB mechanism [1] (eqn. 1) developed by Basolo and Pearson [2] explain accelerated substitution rates in octahedral Co(III) amine complexes in the presence of hydroxide ions; however, there has been no direct evidence [1]. In a continuing study of unusual

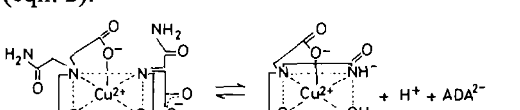
$$[Co(NH_3)_5X^{2+}] \underset{-OH^-}{\overset{+OH^-}{\rightleftharpoons}} [Co(NH_3)_4(NH_2)X^+] +$$

$$+ H_2O \rightleftharpoons [Co(NH_3)_4(NH_2)^{2+}] + X^-$$

$$\uparrow -H_2O \qquad H_2O \downarrow$$

$$[Co(NH_3)_5OH^{2+}] \rightleftharpoons [Co(NH_3)_4(NH_2)(OH_2)^{2+} \quad (1)$$

deprotonation reactions in metal chelates [3], the bis(N-2-acetamidoiminodiacetato)copper(II) chelate, $[Cu(ADA)_2^{4-}]$, was found to undergo loss of an aminoacidate ligand upon amide proton ionization (eqn. 2).



(2)

Potentiometric formation surves (not shown) of 2:1 $ADAH_2$ to Cu(II) solutions show three buffer zones: a low pH one terminated by an inflection at $a = 1.5$ (moles of base per mole of ligand), a mid pH one with an inflection at $a = 2.0$, and a high pH one*. In the low pH region, the following reactions take place,

$$Cu^{2+} + ADA^{2-} \rightleftharpoons Cu(ADA) \quad (3)$$

$$H_2ADA + OH^- \rightleftharpoons HADA^- + H_2O \quad (4)$$

while in the mid-pH region $[Cu(ADA)_2^{2-}]$ is formed (eqn. 5). In the high pH

$$Cu(ADA) + ADA^{2-} \rightleftharpoons Cu(ADA)_2^{2-} \quad (5)$$

region reactions 2 and 6 occur.

$$Cu(H_{-1}ADA)(H_2O)^- \rightleftharpoons Cu(H_{-1}ADA)OH^{2-} + H^+ \quad (6)$$

Visible spectral data (not shown)** support the above. From $a = 0$ to $a = 1.5$, there is no shift in λ_{max} (780 nm), which has previously been assigned to $[Cu(ADA)OH_2]$ [4]. From $a = 1.5$ to $a = 2.0$, λ_{max} shifts from 780 nm to 699 nm, indicating the coordination of a stronger σ-donor than OH_2, *i.e.*, the formation of $[Cu(ADA)_2^{2-}]$. From $a = 2.0$ to $a = 3.0$, λ_{max} shifts monotonically from 699 nm to 745 nm indicating the loss of one aminoacidate ligand and coordination of an ionized amide group and subsequent hydroxo complex formation (eqns. 2 and 6). The λ_{max} and ϵ_{max} values for the Cu(II) species at $a = 3.0$ (2:1, H_2ADA to Cu(II)) and $a = 4.0$ (1:1 H_2ADA to Cu(II)) are identical, indicating that the same species is in both solutions [4].

While the visible data support the above, ESR spectra*** were obtained since such data are extremely sensitive to the environment about Cu(II). The ESR spectra (Fig. 1, spectra 3 and 6) of 1:1 and 2:1 $ADAH_2$ to Cu(II) solutions are identical at $a = 4.0$ (1:1 system) and $a = 3.0$ (2:1 system), respectively, indicating that the species in the solutions are identical, *i.e.*, $[Cu(H_{-1}ADA)OH^{4-}]$. Similarly, spectra 1 and 4 are identical indicating that 1:1 and 2:1 $ADAH_2$ to Cu(II) solutions at $a = 2.0$ and $a = 1.5$, respectively, contain the same species, $[Cu(ADA)OH_2]$. The ESR spectrum of $[Cu(ADA)_2^{2-}]$ is shown as spectrum 3; no similar spectrum was found in any 1:1 $ADAH_2$ to Cu(II) solution from $a = 0$ to $a = 4.0$. Therefore, the ESR data are fully in agreement with the potentiometric and visible data, which indicate loss of aminoacidate chelation upon amide proton ionization (eqn. 2) in the 2:1 H_2ADA to Cu(II) system.

The above is the first example of a base assisted substitution reaction in which a species containing the conjugate base has been observed. The above result could be of biochemical importance in that an ionized amide group has been shown to labilize ami-

*All potentiometric measurements were made at 25 °C and $\mu = 0.1$ *M* (KNO_3); $[Cu^{2+}]$ were 2.5×10^{-3} *M*. The following equilibrium constants were determined: $Cu(ADA) + ADA^{2-} \rightleftharpoons Cu(ADA)_2^{2-}$, $K = 10^{3.12\pm0.02}$ in good agreement with the literature [5]. $Cu(ADA)_2^{2-} \rightleftharpoons Cu(H_{-1}ADA)^- + ADA^{2-} + H^+$, $K = 10^{-11.34\pm0.02}$, and $[Cu(H_{-1}ADA)^{3-}] \rightleftharpoons Cu(H_{-1}ADA)OH^{4-} + H^+$, $K_{OH} = 10^{-9.98\pm0.02}$. The latter constant is the same as that determined from 1:1 H_2ADA to Cu^{2+} data, $K_{OH} = 10^{-9.95\pm0.02}$ [4].

**All visible spectral data were obtained on a Bausch and Lomb Spectronic 2000 spectrophotometer at ambient temperatures and $\mu = 0.1$ *M* (KNO_3).

***ESR spectra were obtained on a Brucker ER200D SRC spectrometer at ambient temperatures.

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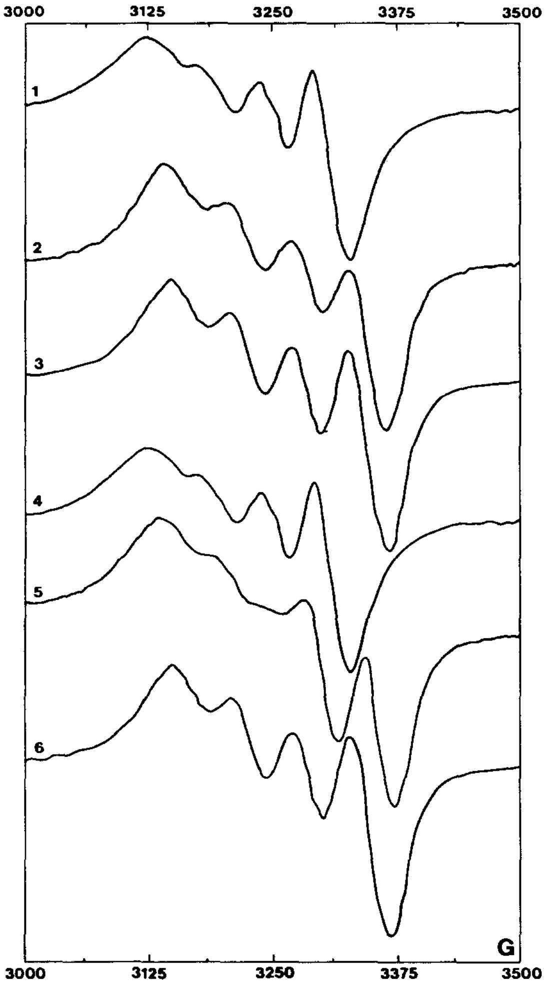

Fig. 1. Electron Spin Resonance Spectra of 1:1 H_2ADA to Cu(II) Solutions at a = 2.0(1), 3.0(2), and 4.0(3), moles of base per mole of ligand and 2:1 H_2ADA to Cu(II) solutions at a = 1.5(4), 2.0(5), and 3.0(6).

noacidate binding to a metal ion. Since equilibria in the above system were instantaneous, substrate removal at the active site of metalloenzymes could be assisted by coordination of an ionized peptide (amide) group. The dechelation of an aminoacidate group from Cu(II) is remarkable in that such binding is quite strong, $K = 10^{8.2}$ (eqn. 7) [5] and that it has been

$$Cu^{2+} + L^- \rightleftharpoons CuL^+ \quad (7)$$

shown [6] to prevent complete (tetradentate) chelate formation in bis(3-[(2-aminoethyl)thio-*L*-alaninato]- and bis(3-[(carboxymethyl)thio-*L*-alaninato] copper-(II) chelates.

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