Direct Evidence for an S_N1CB Mechanism. II. Aminoacidate Dechelation in the bis(N,N-bis(2-hydroxyethyl)glycinato)copper(II) Chelate upon Hydroxyl Group Ionization

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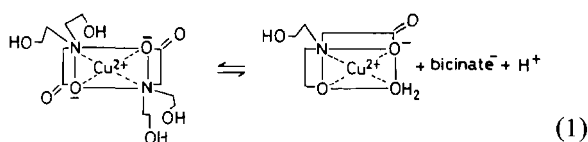
In the previous paper [1] the bis[N-acetamido)-iminodiacetato]copper(II) chelate was shown to lose an aminoacidate ligand upon amide proton ionizattion. We now report a similar reaction upon hydroxyl proton ionization in bis(N,N-bis(2-hydroxyethyl)-glycinato)copper(II) $[Cu(bicine)_2]$ (eqn. 1):



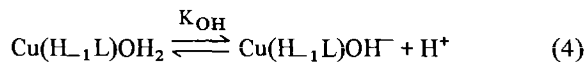
(1)

Potentiometric formation curves (not shown)** of 2:1 bicine to Cu(II) have three buffer zones with inflections at $a = 0.5$ and 1.0 mol of base per mol of ligand. The 1:1 and 2:1, bicine to Cu(II), chelates are formed in the first and second buffer zones (eqns. 2 and 3), respectively:

$$Cu^{2+} + L^- \underset{}{\overset{K_1}{\rightleftharpoons}} CuL^+ \quad (2)$$

$$CuL^+ + L^- \overset{K_2}{\rightleftharpoons} CuL_2 \quad (3)$$

Computer treatment of the data from the third buffer region indicates that concomitant loss of aminoacidate binding occurs with coordination of a deprotonated alcohol group (eqn. 1) which is then followed by hydroxo complex formation (eqn. 4):***



$$Cu(H_{-1}L)OH_2 \overset{K_{OH}}{\rightleftharpoons} Cu(H_{-1}L)OH^- + H^+ \quad (4)$$

Visible spectra (not shown)† of 2:1 bicine to Cu(II) solutions from $a = 0$ to $a = 2.0$, show a monotonic shift in λ_{max} and ϵ_{max} from $a = 0$ to $a = 1.0$, indicating the formation of $[Cu(bicine)_2]$. The λ_{max} value at $a = 1.0$ is 610 nm in accord with a variety of other bis(aminoacidato)copper(II) chelates ($\lambda_{max} \simeq 605$ nm) [2]. From $a = 1.0$ to $a = 2.0$, λ_{max} shifts monotonically to lower energy ($\lambda_{max} = 724$ nm at $a = 2.0$), which indicates the loss of an aminoacidate ligand (eqn. 1). The λ_{max} and ϵ_{max} values of 1:1 and 2:1 bicine to Cu(II) solutions at $a = 3.0$ and 2.0, respectively, are both 724 nm and 64 M^{-1} cm^{-1}, indicating that both solutions contain the same species, $[Cu(H_{-1}$ bicine$)OH^-]$.

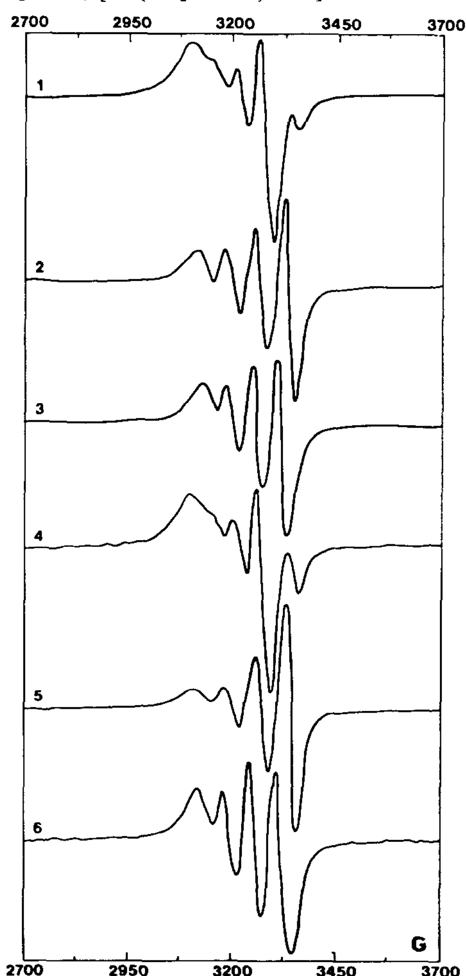


Fig. 1. Electron spin resonance spectra of 1:1 (spectra 1–3) and 2:1 (spectra 4–6) bicine to Cu(II) solutions at a (mol of base per mol of ligand) = 1.0(1), 2.0(2), 3.0(3), 0.5(4), 1.0 (5) and 2.0(6), respectively.

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**All potentiometric measurements were performed on a Corning 130 Research Model pH meter at 25.0 °C and $\mu = 0.10$ (KNO_3); $[Cu^{2+}] = 5.0$ to 7.5×10^{-3} M.

***The equilibrium constant for eqn. 1 is $10^{-12.36 \pm 0.02}$ while that for eqn. 4 is $10^{-10.42 \pm 0.02}$. The latter constant is the same as that determined from 1:1 bicine to Cu(II) solution data, $10^{-10.40 \pm 0.02}$.

†Visible spectra were determined with the aid of a Bausch and Lomb Spectronic 2000 spectrophotometer on 1:1 and 2:1 bicine to Cu(II) solutions at ambient temperatures.

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Due to the sensitivity of ESR spectra to the environment about Cu(II), spectra of both 1:1 and 2:1 bicine to Cu(II) solutions were obtained at various a values and are shown in Fig. 1.†† The ESR spectra of 1:1 and 2:1 bicine to Cu(II) solutions at $a = 3.0(3)$ and $a = 2.0(6)$, respectively, are the same, indicating that the same species, $[Cu(H_{-1}\,bicine)OH^-]$, is present in both solutions. Similarly, spectra 1 and 4 are identical indicating that the same species is present at $a \simeq 1$ (1:1) and $a \simeq 0.5$ (2:1). The ESR spectrum of $[Cu(bicine)_2]$ is shown as 5 and no similar spectrum was observed in 1:1 bicine to Cu(II) solutions from $a = 0$ to $a = 3.0$.

The above ESR data is wholly consistent with the potentiometric and visible spectral data indicating that 2:1 complex formation occurs in 2:1 bicine to Cu(II) solutions and that upon deprotonation of an alcohol group, dechelation of an aminoacidate moiety occurs.

The equilibrium constant for the reaction (eqn. 1) is $10^{-12.36 \pm 0.02}$ which is about 10 times smaller than that observed for dechelation of an aminoacidate ligand upon amide deprotonation in bis[(N-2-acetamino)iminodiacetato]copper(II) $[Cu(ADA)_2^{2-}]$. As in the $[Cu(ADA)_2^{2-}]$ system [1], the product $[Cu(H_{-1}\,bicine)OH_2]$ contains the conjugate base that assisted in the substitution reaction. Therefore, the ionization and coordination of an alcohol group has been shown to labilize aminoacidate binding in Cu(II). This result could be of biochemical importance in that alcohol groups can be present at the active site of enzymes (threonine, serine) and could be of assistance in the removal of substrates from the active sites. Both the ionization of amide and alcohol groups in $[Cu(ADA)_2^{2-}]$ and $[Cu(bicine)_2]$, respectively, occur just within the physiological pH region; if such reactions do occur in proteins, facile exchange may render it difficult to retain and detect.

†† Electron spin resonance spectra were obtained on a Brucker ER200D SRC spectrometer on 1:1 and 2:1 bicine to Cu(II) solutions at ambient temperatures.

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