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Amine Deprotonation in Copper(III)–Peptide Complexes

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Copper(III)–peptide complexes react rapidly with base, changing color from yellow to red (or to blue with a prolyl group at the amine terminal), prior to their redox decomposition. The initial Cu(III) complexes have three deprotonated peptide groups, and the proposed reaction with base is a deprotonation of the coordinated amine terminal of the peptide. Complexes in which the amine group has been N-formylated or dimethylated do not exhibit the effect and therefore it cannot be attributed to hydroxide addition to the metal. The reaction occurs only with the +3 oxidation state of copper. The pK_a values determined for complexes of eight peptides and peptide amides vary from 11.3 to 12.3.

Introduction

Coordination of deprotonated peptide nitrogens and deprotonated amide nitrogens to metal ions is well-known and occurs commonly with both copper(II)[1-4] and nickel(II)[1,5,6] complexes. This has been confirmed by a combination of potentiometric,[1,2,4,5] spectrophotometric,[4,6] and crystallographic[7] data. Similar reactions are found with cobalt(II)[8,9] and palladium(II).[10,11] The pH at which the metal-assisted deprotonation occurs varies according to the sequence Co(II), above pH 10 > Ni(II), pH 7–9 > Cu(II), pH 5–7 > Pd(II), pH 2–4.

In these studies the deprotonation of coordinated amine nitrogens has not been observed. Amine hydrogens are, of course, much less acidic than hydrogens on peptide or amide nitrogens. Deprotonation of amines coordinated to cobalt(III) has been proposed in the conjugate-base mechanism of cobalt(III) substitution reactions,[12,13] but the pK_a values are estimated to be well above 14.[14,15] On the other hand, gold(III)[16,17] and platinum(IV)[18] complexes have been observed to lose amine protons at much lower pH. In this work we find that copper(III)–peptide complexes undergo deprotonation of amine groups at pH 11–12.

The trivalent oxidation state of copper is stabilized in aqueous solution by peptide coordination.[19] Whereas other copper(III) species generated by electrochemical methods,[20] by pulsed radiolysis,[21] or by hypohalites[22] are relatively short-lived, copper(III)–peptide complexes can be kept from minutes to weeks, depending upon the peptide and the solution conditions.[23] The tetraglycine (G_4) complex of copper(II) reacts spontaneously with dioxygen[24] to generate $Cu^{III}(H_{-3}G_4)^-$, a complex with three deprotonated peptide groups coordinated to copper(III).[25] This complex and many other peptide complexes can be generated easily with oxidizing agents or by electrochemical means.[26]

The typical yellow color of the copper(III)–tetraglycine complex changes to red upon the addition of base. We propose that the reaction (eq 1) occurs with the loss of a fourth proton

$$\underset{\text{yellow}}{Cu^{III}(H_{-3}G_4)^-} + OH^- \rightleftarrows \underset{\text{red}}{Cu^{III}(H_{-4}G_4)^{2-}} + H_2O \quad (1)$$

from tetraglycine, caused by deprotonation of the coordinated amine group. The reaction is reversible with the addition of acid. Since base also catalyzes the oxidation of the ligand by copper(III), most of the copper(III) is destroyed after shifting back and forth between yellow and red several times. The products and stoichiometry of the oxidation–reduction reaction with tetraglycine are discussed elsewhere.[27] In order to be certain that the spectral changes are due to the loss of amine hydrogens and not to the addition of hydroxide ion to Cu(III), several *N*-formyl peptide complexes were prepared. These complexes have four deprotonated nitrogens coordinated (one formyl and three peptide groups) but they do not undergo the characteristic spectral shift in base. Spectra are obtained rapidly for all the complexes using a stopped-flow vidicon system.[28,29] The pH dependence of the electrode potential for the Cu(II)–Cu(III) reaction measured by cyclic voltammetry confirms the stoichiometry and equilibrium constant for eq 1. The nature of the observed spectral shifts suggests interesting changes in the nature of the bonding for the amine-deprotonated copper(III) complexes.

Experimental Section

Reagents. Chromatographically pure peptides were used in this work. Tetraglycine (G_4), pentaglycine (G_5), hexaglycine (G_6), and tetra-L-alanine (A_4) were obtained from Biosynthetika (Oberdorf, Switzerland). Triglycinamide (G_3a), tetraglycinamide (G_4a), L-prolylglycylglycinamide (PGGa), and L-phenylalanylglycylglycinamide (FGGa) were supplied as hydrochlorides from Vega-Fox (Tucson, Ariz.). The *N*-formyl peptides were prepared by dissolving 0.2 g of the parent peptide in 2.3 mL of formic acid and adding dropwise a twofold excess of acetic anhydride (~0.2 g). The *N*-formyl derivatives crystallized readily during 2–3 h of stirring of this mixture. The crystals were washed several times with ethanol and ether and dried. Anal. Calcd for *N*-fG_3 ($C_7H_{11}N_3O_5$): C, 38.5; H, 5.07; N, 19.4. Found: C, 38.7; H, 5.22; N, 19.3. Calcd for *N*-fG_4 ($C_9H_{14}N_4O_6$): C, 39.4; H, 5.11; N, 20.4. Found: C, 39.1; H, 5.15; N, 19.7. (*N*-f = *N*-formyl.)

Copper(II) perchlorate solutions were prepared from the twice-recrystallized salt and were standardized by EDTA titration using Murexide as an indicator. The copper(II)–peptide complexes were prepared in solution using 5–10% stoichiometric excess of the peptide. The pH was adjusted to about 10.8 to form the triply deprotonated complexes $Cu^{II}(H_{-3}L)$ or, in the case of *N*-fG_3a and *N*-fG_4, the quadruply deprotonated complexes $Cu^{II}(H_{-4}L)$. High pH (>10) is needed to form the copper(II) complexes of the *N*-formyl peptides; otherwise the mixture tends to precipitate. Table I summarizes some of the spectral and electrochemical data for the copper–peptide complexes. Most of the visible absorption maxima for the copper(II) complexes occur at slightly lower wavelength than that predicted by

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Table I. Spectral and Electrochemical Characteristics of the Copper–Peptide Complexes

	Cu(II)[a]				
				Cu(III) λ_{max}, nm	
Cu(II) complex	λ_{max} nm	ϵ, M^{-1} cm^{-1}	$E°$,[b] V (at pH 10)	pH 6–9	~pH 13
$Cu(H_{-3}G_3a)^-$	517	144	0.64	365 (ϵ 7200)[d]	300, 525
$Cu(H_{-3}G_4)^{2-}$	520	145	0.63	250, 365	325, 525
$Cu(H_{-3}G_4a)^-$	511	162	0.68		
$Cu(H_{-3}G_5)^{2-}$	510	135	0.66	248, 367	300, 520
$Cu(H_{-3}G_6)^{2-}$	513	145	0.67	376[d]	320, 515
$Cu(H_{-3}FGGa)^-$	514	140	0.66	355[d]	
$Cu(H_{-3}PGGa)^-$	509	158	0.62	365[d]	285, 600
$Cu(H_{-4}\text{-}N\text{-}fG_4)^{3-}$	523	147	0.55[c]	357 (pH 10)[d]	357
$Cu(H_{-4}\text{-}N\text{-}fG_3a)^{2-}$	508	104	0.49[c]	345 (pH 9.4)[d]	
$Cu(H_{-3}\text{-}N\text{-}fG_3)^{2-}$	538	148	0.75[c]	365 (pH 9.4)[d]	

[a] For species at high pH. [b] Vs. NHE. [c] pH 11.5. [d] Also a λ_{max} at ~250 nm.

Billo[30] where the expected maxima are 524 nm for one amine and three deprotonated peptides, 516 nm for four deprotonated peptides, and 557 nm for three deprotonated peptides and one carboxylate group. The electrode potentials for the reduction of the Cu(III) complex to the Cu(II) complex also are given in Table I. The $E°$ values for the FGGa and PGGa complexes are consistent with previous results.[26] The $E°$ value for the N-fG_4 complex which is close to that for the N-fG_3a complex strongly suggests that it has four deprotonated peptide groups coordinated to copper. On the other hand, the visible absorption maxima for N-fG_4 is closer to the behavior of N-fG_3 with three deprotonated peptides and one carboxylate group. The solution may consist of a mixture of these coordinated forms.

The copper(III) complexes were generated by electrochemical oxidation using a flow-through system. This allowed the oxidation to be performed quickly at the desired potential and minimized the introduction of other chemical species. The absorption spectra of all the copper(III) peptides have a strong charge-transfer band in the vicinity of 360–370 nm. There is another strong band for these complexes in the vicinity of 250 nm as shown for the G_4 and G_5 complexes. Table I also gives the spectral characteristics of several copper(III)–peptide complexes at high pH.

Apparatus. The electrolysis unit constructed for this work is a modification of earlier units.[31,32] It has a flow-through column of coarse graphite powder packed in contact with a platinum wire inside of a porous Vycor tube (5-mm i.d., 7-cm length) obtained from Dow-Corning. A second platinum wire is wound around the outside of the tubing as an auxiliary electrode, and the outer chamber is filled with 0.1 M $NaClO_4$ in contact with a Ag/AgCl reference electrode. The potential applied to the cell is controlled by a three-electrode potentiostat (Bioanalytical Systems Inc., West Lafayette, Ind.). The copper(II)–peptide solution is forced through the working electrode by means of a compact infusion pump (Harvard Apparatus). Flow rates of 1–2 mL/min are achieved. The potential applied to the cell is maintained at least 200 mV greater than the $E°$ value determined for the complex by cyclic voltammetry. Normally the pH of an unbuffered copper–peptide solution will decrease from 10.8 to between 5 and 8 upon electrolysis and 98–100% of the copper is converted to copper(III).

Cyclic voltammetry was performed at 25 °C with a three-electrode system consisting of a carbon-paste working electrode, a platinum-wire auxiliary electrode and a saturated calomel reference electrode. A Bioanalytical Systems, Inc., CV-1 instrument was used with a Hewlett-Packard HP7035B X-Y recorder. The voltammograms of the copper(II)–peptide solutions were run at a scan rate of 100 mV s^{-1}.

A vidicon rapid-scanning stopped-flow spectrometer[28,29] was used to obtain the spectra of the short-lived copper(III)–peptide complexes at high pH. A Durrum stopped-flow spectrometer interfaced to a HP2115A computer was used for the pK_a determinations. Other spectral measurements were obtained with a Cary 14 spectrophotometer.

For all measurements, the ionic strength was maintained at 1.0 M using $NaClO_4$, and the temperature was controlled at 25.0 ± 0.1 °C. A Radiometer Model PHM26 pH meter was used for pH measurements, and hydrogen ion concentrations were obtained by calibrating the electrode system against standard sodium hydroxide solutions maintained at μ = 1.0 M ($NaClO_4$) using a pK_w value of 13.8.[33]

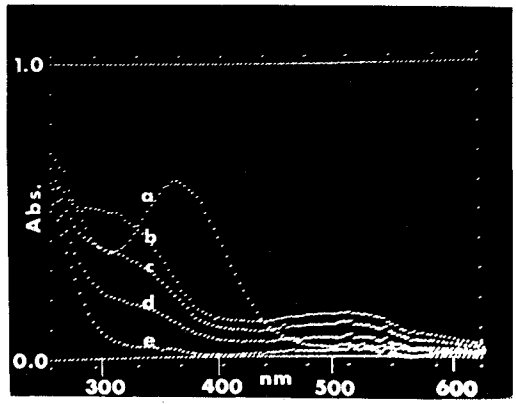

Figure 1. Vidicon spectra of (a) $Cu^{III}(H_{-3}G_3a)$ at pH 8 and $Cu^{III}(H_{-4}G_3a)^-$ after mixing with 0.5 M OH^- at times (b) 0.5 s, (c) 2.5 s, (d) 7.5 s, and (e) 28.0 s.

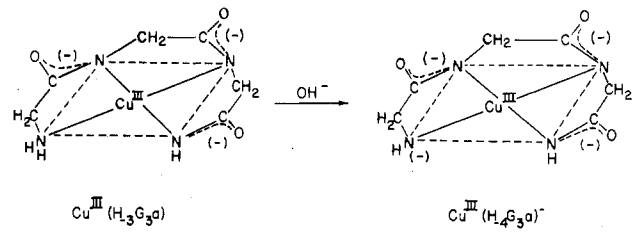

Figure 2. Proposed ionization of the amine hydrogen causing the yellow-to-red color change when base is added to copper(III)–peptide complexes.

Results

The trivalent copper–peptide complexes exhibit properties quite different from those of the corresponding divalent complexes. The copper(III) species are slow to dissociate in acid, they have no ESR signal, and they will oxidize a variety of substrates including ascorbate, sulfite, iodide, and cysteine. They exhibit strong charge-transfer bands in their UV–visible spectra with maxima centered near 250 and 365 nm (Table I). Typically yellow in acid or neutral solutions, the copper(III) peptides (except for the N-formyl derivatives) turn bright red, and in one case blue, in base. This spectral change in base is very rapid but the base also catalyzes self-redox reactions which give copper(II) and oxidized ligand as products.[27] Half-lives of only a few seconds are typical for the copper(III) species in 1 M NaOH. Thus, a rapid mixing and scanning technique is needed to obtain the spectra in base. Figure 1 shows vidicon spectra of $Cu^{III}(H_{-3}G_3a)$ before and after its reaction with 0.5 M NaOH. The triply deprotonated reactant has a molar absorptivity (ϵ) of 7200 M^{-1} cm^{-1} at 365 nm. Immediately after reaction with base the 365-nm peak disappears and two new bands appear, one at 300 nm ($\epsilon_{300} \simeq 5000$ M^{-1} cm^{-1}) and one at 525 nm ($\epsilon_{525} \simeq 2000$ M^{-1} cm^{-1}). This is seen in the spectrum after 0.5 s in Figure 1. Other stopped-flow experiments at fixed wavelength show that the change is complete within the mixing time of a few milliseconds. Subsequent spectra in Figure 1 show the decomposition of the Cu(III) complex which is complete after about 30 s. Figure 2 gives the proposed reaction in which the terminal amine has lost a proton and a quadruply deprotonated Cu(III) complex is formed. This red complex still has oxidizing power and it can be converted back to the original complex if base and acid are added in rapid sequence. Hence, it is a Cu(III) complex and not a Cu(II) complex with an oxidized ligand. This is confirmed by electrochemical data as seen later. Similar spectral features in base are observed for all the Cu(III) complexes studied where a primary amine group is present.

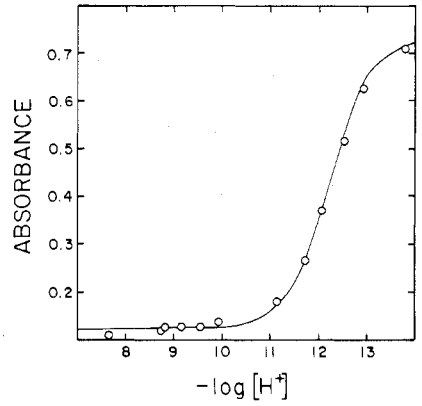

Figure 3. Absorbance (525 nm) vs. $-\log [H^+]$ for amine hydrogen ionization from $Cu^{III}(H_{-3}G_3a)$. The calculated best fit for a K_a value of $10^{-12.3}$ M is shown.

Table II. Ionization Constant for the Loss of Coordinated Amine Hydrogens from $Cu^{III}(H_{-3}L)$ Complexes (25 °C, $\mu = 1.0$ M $NaClO_4$) Determined Spectrophotometrically at 525 nm

ligand	pK_a[a]	ligand	pK_a[a]
G_3a	12.3 ± 0.2	PGGa	11.7 ± 0.2[b]
G_4	12.1 ± 0.2	G_5	11.6 ± 0.1
A_4	12.0 ± 0.1	G_4a	11.4 ± 0.2
FGGa	11.9 ± 0.2	G_6	11.4 ± 0.2

[a] The $[H^+]$ is calculated from standardized $[OH^-]$ using $pK_w = 13.8$ at $\mu = 1.0$ M $NaClO_4$.[33] [b] Measured at 600 nm.

Above pH 12 they all have absorption bands at 310 ± 15 and 510 ± 15 nm. By following the spectral change as a function of hydroxide ion concentration we were able to measure the acidity of the coordinated amine proton. The absorbance of the $Cu^{III}(H_{-4}L)$ species at 525 nm was measured with the Durrum stopped-flow instrument in order to obtain data immediately after mixing before a significant amount of decomposition to Cu(II) occurred. These amine-deprotonation rate constants are too large ($k_{OH} > 10^6$ M^{-1} s^{-1}) to be observed by stopped-flow experiments and hence the acid–base equilibrium is established upon mixing. The resulting absorbance vs. $-\log [H^+]$ data are fitted by a nonlinear program to give the optimum pK_a value. Figure 3 shows the plot for the G_3a complex reaction given in Figure 2, and a pK_a value of 12.3 is found. Table II summarizes the spectrophotometrically determined pK_a values for a variety of copper(III)–peptide complexes.

The prolylglycylglycinamide complex $Cu^{III}(H_{-3}PGGa)$ has the typical 365-nm absorption band in neutral solution, but in base it forms a blue complex with absorption bands at 285 and 600 nm (Figure 4) rather than the red complex.

In addition to the spectrophotometric measurements, the pK_a values can be determined electrochemically using cyclic voltammetry. The current–voltage behavior is consistent with the redox couple in eq 2 where the electroactive forms of

$$Cu^{III}(H_{-3}G_4)^- + e^- \rightleftarrows Cu^{II}(H_{-3}G_4)^{2-} \quad (2)$$

Cu(II) and Cu(III) are the triply deprotonated species. The pH will affect both the copper(II) and copper(III) equilibria as given in eq 3 and 4. The $E°$ value obtained depends upon

$$Cu^{II}(H_{-2}G_4)^- \overset{K_1}{\rightleftarrows} Cu^{II}(H_{-3}G_4)^{2-} + H^+ \quad (3)$$

$$Cu^{III}(H_{-3}G_4)^- \overset{K_2}{\rightleftarrows} Cu^{III}(H_{-4}G_4)^{2-} + H^+ \quad (4)$$

eq 5, where $Cu_T^{II} = [Cu^{II}(H_{-2}G_4)^-] + [Cu^{II}(H_{-3}G_4)^{2-}]$ and

$$E = E° - 0.0591 \log \left(\frac{Cu_T^{II}}{Cu_T^{III}} \right) \left(\frac{K_1K_2 + K_1[H^+]}{K_1[H^+] + [H^+]^2} \right) \quad (5)$$

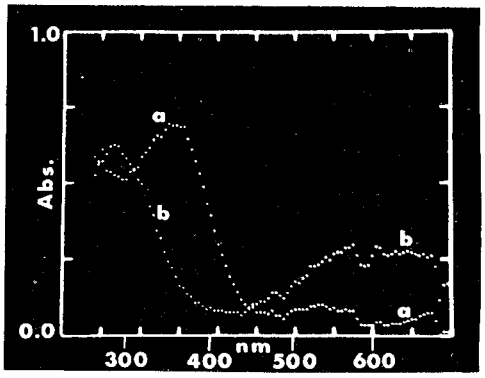

Figure 4. Vidicon spectra of $Cu^{III}(H_{-3}PGGa)$ and $Cu^{III}(H_{-4}PGGa)^-$: (a) $Cu^{III}(H_{-3}PGGa)$ at pH 8, (b) $Cu^{III}(H_{-4}PGGa)^-$ 100 ms after mixing with 0.2 M OH^-. (Note: The glitch at ~580 nm is due to light source artifacts.)

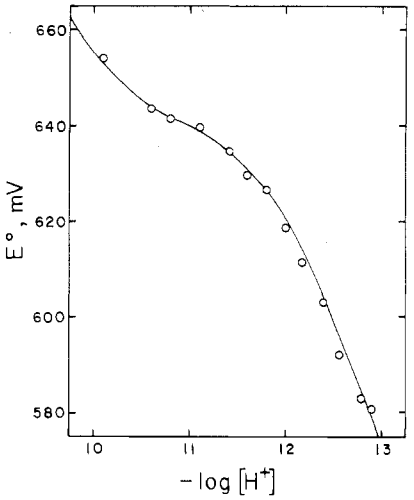

Figure 5. Dependence of $E°$ on $-\log [H^+]$ for $Cu^{II,III}(H_{-3}G_4)$. The solid line is calculated on the basis of eq 5 ($[Cu^{II}(H_{-3}G_4)] = 2.5 \times 10^{-3}$ M; $\mu = 1.0$ M $NaClO_4$, 25 °C; scan rate 100 mV s^{-1}).

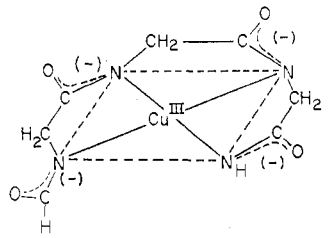

Figure 6. $Cu^{III}(H_{-4}$-*N*-$fG_3a)^-$.

$Cu_T^{III} = [Cu^{III}(H_{-3}G_4)^-] + [Cu^{III}(H_{-4}G_4)^{2-}]$. Figure 5 shows the best fit of eq 5 to the potentials and gives values of $E° = 0.64$, $K_1 = 10^{-9.40}$ M, and $K_2 = 10^{-11.9}$ M. The $E°$ and K_1 values are in excellent agreement with previous experimental values. The K_2 value is within the experimental uncertainty of the pK_a value of 12.1 obtained spectrophotometrically. It is interesting that the reduction potential of this copper(III) complex is predicted to be as low as 0.51 V in 1 M OH^-, but the base-catalyzed self-redox reaction interferes with observations in such strong base. Nevertheless, the electrochemical behavior provides strong supporting evidence that copper(III) species are still present immediately after the first reaction with base.

Several experiments were performed to confirm that deprotonation of an amine group is taking place rather than the addition of hydroxide ion to copper(III) in base. The *N*-formyl peptides have no amine groups (Figure 6) and their copper(III)

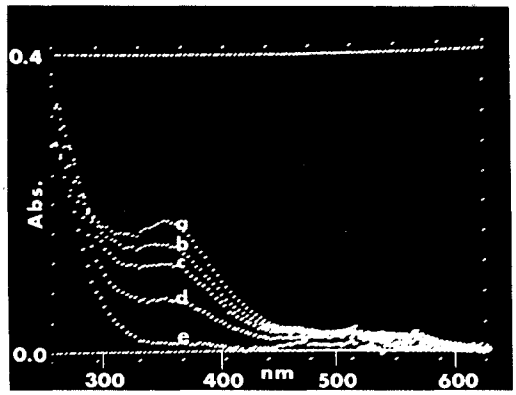

Figure 7. Vidicon spectra of $Cu^{III}(H_{-4}$-*N*-$fG_4)^{2-}$ (a) at pH 9 and after mixing with 0.5 M OH^- at times (b) 0.5 s, (c) 2.5 s, (d) 7.5 s, and (e) 28.0 s.

complexes fail to show significant shift in changing from neutral solution to 0.1 M NaOH as seen in the vidicon spectra in Figure 7. There is a decay of the Cu(III) species in base but the absorption maximum remains at 357 nm. The same behavior was found for the copper(III) complexes of *N*-fG_3a and *N*-fG_3. In addition, qualitative tests on a solution of the $Cu^{III}(H_{-3}N,N$-dimethyl$G_4)^-$ complex show no formation of the red intermediate. Other studies show that the substitution reactions of copper(III)–peptide complexes are exceedingly slow.[23] Hence, the rapid reactions of the yellow copper(III) species with base cannot be attributed to hydroxide ion displacement of the coordinated amine group. Nor is the rapid reversibility with acid in eq 1 compatible with a substitution reaction mechanism. On the other hand, these fast reactions are to be expected in the proposed proton-transfer mechanism.

Discussion

Coordination to copper(III) decreases the pK_a values for the amine deprotonation to a much greater extent than does the coordination of amines to cobalt(III). It is interesting that the pK_a values are as low as they are despite the fact that the copper(III) complexes are neutral or negative and that there are already three deprotonated peptide donor groups coordinated to the copper. We have examined corresponding copper(II)– and nickel(II)–peptide complexes in 1 M NaOH and have seen no spectral evidence of amine deprotonation. On the other hand, gold(III)–polyamine complexes readily ionize amine hydrogens. Hence, it appears that a square-planar geometry, a d^8 electronic configuration, and a high metal oxidation state may all contribute to the ease of amine deprotonation.

The pK_a values for the eight complexes in Table II are remarkably similar considering the changes in charge and the changes in the amino acid residues. One noticeable trend is the decrease in pK_a from G_4 to G_5 to G_6, despite the fact that the same groups are coordinated to copper(III) in all three complexes. This suggests hydrogen-bonding interactions between the uncoordinated segments of the peptide chain G_5 and G_6 and the coordinated amine group as depicted in Figure 8. Similar interactions have been observed in circular dichroism studies of copper(II)– and nickel(II)–peptide complexes.[34] Other hydrogen-bonding interactions between coordinated peptide groups and uncoordinated peptide groups have been proposed to explain infrared spectra.[35] Such an interaction might be expected to stabilize the deprotonated amine.

Spectral changes similar to those in the present study have been observed in the amine deprotonation of gold(III)–amine halide complexes.[16] The $[Au^{III}(dien)X]^{2+}$ complex, where dien is diethylenetriamine and X^- is Cl^- or Br^-, deprotonates in the pH range of 4–5 and the spectrum changes from a single band at 300 nm to two bands, one at 263 nm and one at 370 nm. Similar changes have been seen[17] with the tetraethyl derivative, $[Au^{III}(Et_4dien)X]^{2+}$. The lower energy band was attributed to a ligand-to-metal charge transfer involving the electron pair of the deprotonated amine nitrogen in a $2p_\pi$ orbital and an antibonding σ^* orbital of the complex. The higher energy band was attributed to a shift of a halide-to-metal band from 300 to 263 nm. Amine deprotonation observed with platinum(IV) complexes also is accompanied by spectral shifts to give a lower energy band. The $Pt^{IV}(NH_3)_5Cl^{3+}$ deprotonates at pH 8 to give $Pt^{IV}(NH_3)_4(NH_2)Cl^{2+}$; the band at 290 nm disappears and a band at 320 nm appears.[18]

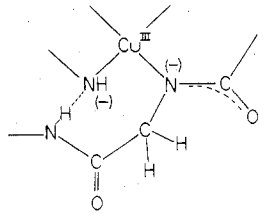

Figure 8. Proposed stabilization of deprotonated amine complex via intramolecular hydrogen bonding through an uncoordinated amide nitrogen.

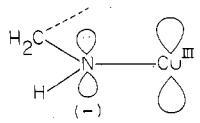

Figure 9. Proposed rehybridization at the amine nitrogen for the glycyl, alanyl, and phenylalanyl amine terminal copper(III)–peptide complexes.

The absorption band at 365 nm, characteristic of copper(III)–peptides, disappears upon deprotonation of the amine and two new bands appear, one as a shoulder at ~300 nm and one as a broad band centered ~525 nm. The large values for the molar absorptivities indicate that both are charge-transfer bands. The appearance of the low-energy band is consistent with Jorgensen's[36] optical electronegativity assignments for charge-transfer complexes. Anions containing lone pairs such as NH_2^-, RNH^-, or R_2N^- have a lower optical electronegativity than the protonated forms and can account for the long-wavelength bands seen for the deprotonated amine complexes of Cu(III) as well as those of Au(III) and Pt(IV). There are several possible reasons for the striking spectral difference for the deprotonated prolyl complex $Cu^{III}(H_{-4}PGGa)^-$, where the absorption band is shifted to 600 nm. Secondary amines R_2NH tend to have lower optical electronegativities than primary amines and this may also be true for R_2N^- compared to RNH^-. Alternatively, the prolyl ring may interfere with changes in ligand–metal bonding upon deprotonation.

Deprotonation of the amine nitrogen leaves a relatively unstable electron pair in an sp^3-type hybrid orbital, but the nitrogen could rehybridize to give a trigonal sp^2 geometry and place the free electron pair in a nitrogen $2p_z$ orbital suitable for π interaction with Cu(III) (Figure 9). Ligand-to-metal π bonding has been proposed for the amide nitrogen in the conjugate base of cobalt(III)–amine complexes.[37] Nitrogen-to-metal π bonding has been shown to be important in transition-metal dialkylamides, $M = N(CH_3)_2$, where M is Ti, V, and Mo.[38] In the Cu(III) complex π bonding between the N $2p_z$ orbital and the copper $4p_z$ orbital is possible. The energy levels of these orbitals would be brought closer together by the negative charge on the nitrogen and the high oxidation state of the metal. A similar type of π interaction has been discussed in the molecular orbital treatment of $Ni(CN)_4^{2-}$, $Pd(CN)_4^{2-}$, and $Pt(CN)_4^{2-}$ In these species bonding between the $(n + 1)p_z$ of the metal and the vertical π system of the

CN^- ligands leads to a "ring" π molecular orbital.[39]

The spectral difference between the $Cu^{III}(H_{-4}PGGa)^-$ complex and the other deprotonated complexes may be related to interferences of the prolyl ring in forming a N-to-metal π bond. However, if this is the case the effect does not seem to be reflected in the pK_a value for the prolyl complex.

In conclusion, the copper(III) oxidation state facilitates amine deprotonation, indicating very strong Cu(III)–N bonding in which ligand-to-metal π bonding could be important.

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Registry No. $Cu(H_{-3}G_{3a})$, 62801-36-9; $Cu(H_{-3}G_4)^-$, 57692-61-2; $Cu(H_{-3}A_4)^-$, 68628-66-0; $Cu(H_{-3}FGGA)$, 68550-42-5; $Cu(H_{-3}PGGA)$, 24212-63-3; $Cu(H_{-3}G_5)^-$, 68550-43-6; $Cu(H_{-3}G_{4a})^-$, 68550-44-7; $Cu(H_{-3}G_6)^-$, 68550-45-8; $Cu(H_{-3}$-*N*-$fG_4)$, 68550-46-9; $Cu(H_{-3}$-*N*-$fG_{3a})$, 68550-47-0; $Cu(H_{-3}$-*N*-$fG_3)$, 68550-48-1; Cu, 7440-50-8.

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Photoaquation of $[Cr(en)(NH_3)_4]^{3+}$, *cis*- and *trans*-$[Cr(en)_2(NH_3)_2]^{3+}$, and $[Cr(en)_3]^{3+}$. Relative Labilities of Ethylenediamine and Ammonia Ligands

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The total amine aquation yield and the free ammonia yield have been measured for photolysis of $[Cr(en)_x(NH_3)_{6-2x}]^{3+}$ complexes at 366 and 436 nm and at 10 °C in acidic aqueous solutions. For both the bis(ethylenediamine) complexes and the mono(ethylenediamine) complex the ethylenediamine yields were larger than the statistical expectations. The enhancement may involve the steric strain in the ethylenediamine ring; for the bis complexes the rate constant ratio for ethylenediamine to ammonia photoaquation is 2.83, while for the mono(ethylenediamine) complex the analogous ratio is 1.64. The systems provide unequivocal evidence for the importance of factors other than spectroscopic parameters in determining ligand labilities from excited states.

Introduction

Using *trans*-$[Cr(en)_2NH_3X]^{2+}$ compounds as models for the acidopentaamine series, the authors have in recent years carried out experiments[1-3] to try to determine the nature of the excited-state labilizations and ligands lost. Also studies of the wavelength and temperature dependence of these features as a probe of participation in reaction by more than one excited state were undertaken.

Up to this time we have assumed, largely of necessity, that the fact that ethylenediamine and ammonia are closely similar in ligand field spectroscopic parameters[4] gives reason to suppose that they would behave alike as leaving groups in the excited state. This expectation is implied by the currently existing theoretical models of chromium(III) photochemistry.[5,6] There is, however, some reason for uncertainty about this, not so much in regard to the spectroscopic aspect since for ethylenediamine and ammonia the spectroscopic parameters are as well defined as any existing but mainly as a result of the kinetic and structural dissimilarities. As an example, rate constants[7] for amine aquation by ground-state molecules for ethylenediamine complexes are generally greater than for the corresponding ammine complex and appear to arise from smaller activation energies. Also the rate constant for thermal aquation of the first end of an ethylenediamine ligand is larger than that for the second end, possibly due to steric strain in the five-membered chelate ring.

Unfortunately, photochemical evidence is difficult to obtain; comparisons of quantum yields for different molecules cannot be used reliably as a measure of relative leaving-group abilities because of the different excited-state lifetimes and properties

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