$\pm 1.5\sigma$. The poorest correspondence, though still within this limit, is the Re-C(4) distance.

A comparison of the intra-chelate ring bond distances of similar type within **5** indicates a slightly unsymmetrical rhenaacetylacetonate ring. The difference between the two Re-C distances, the two C-O distances, and the two O-H(2A) distances is consistent with a slight distortion toward structure **2**. Furthermore, a partial difference Fourier map, phased with all the atoms but with H(2A) excluded from the structure factor calculation, also exhibits an asymmetric O···H···O bond consistent with **5** and **2**. However, it must be noted that structure **5** is symmetrical, as shown in **3** within the $\pm 1.5\sigma$ limit. Also, the numerical asymmetry shown in **4** (as determined by X-ray diffraction) is not consistent with **2** and might indicate that any observed asymmetry in the neutron structure is not significant because of the relatively large standard deviations.

Both structural determinations give an O(1)···O(2) bite distance of 2.40 (2) Å. The corresponding bite distance in tetraacetylethane, which exists as the dienolic tautomer, is 2.42 Å.[16] In one survey of structures containing O-H···O hydrogen bonds, it was concluded that an observed O···O distance of less than 2.47 Å indicates a probable symmetrical hydrogen bond.[17] In the neutron structure **5** reported here, the position of the enolic hydrogen atom, H(2A), is determined. The O(1)-H(2A)-O(2) angle of 172 (2)° indicates a slightly bent hydrogen bond. The two O-H(2A) distances are numerically nonequivalent by 0.11 Å, although this difference is within $\pm 1.5\sigma$ and might not be significant. Large thermal motion, also observed in the X-ray structure, apparently prevents the precise location of the enolic hydrogen atom. Oscillation between two closely spaced enolic hydrogen atom positions, as might be expected if a double-minimum asymmetric hydrogen bond exists,[18] might account for the directional feature of this thermal motion.

A more recent analysis of very short O···H···O hydrogen bonds (defined as having an O···O nonbonding distance in the range of 2.40-2.50 Å) that have been studied by neutron diffraction reveals that centered or symmetric hydrogen bonds and asymmetric hydrogen bonds are observed with nearly equal frequency.[19] Of those bonds previously considered to be symmetric, recent findings indicate that many are actually disordered or asymmetric.[20] These observations further complicate the classification of the O···H···O hydrogen bonding observed in **1** since the very short O(1)···O(2) distance of 2.40 (3) Å does not require that a centered O···H···O hydrogen bond be present. The effectively centered O···H···O hydrogen bond observed in potassium hydrogen chloromaleate reveals O···H distances of 1.199 (5) and 1.206 (5) Å, an O-H-O angle of 175.4 (4)° and an O···O distance of 2.403 (3) Å.[19] Pyridine-2,3-dicarboxylic acid has an asymmetrical O-H···O hydrogen bond having O-H distances of 1.163 (5) and 1.238 (5) Å, an O-H···O angle of 174.4 (4)°, and an O···O distance of 2.398 (3) Å.[21] Relative to these structural extremes, the O(2)-H(2A) and O(1)-H(2A) distances in **5** of 1.15 (4) and 1.26 (4) Å are numerically quite consistent with an asymmetrical O-H···O hydrogen bond. However, the large standard deviations on these distances prevents a conclusive structural definition of the type of hydrogen bonding within the rhenaacetylacetone molecule.[22]

Conclusion

This paper reports one of the first molecular structure determinations obtained by single-crystal time-of-flight neutron diffraction. The existence of a strong intramolecular O···H···O bond in the rhenaacetylacetone molecule, [*cis*-$(OC)_4Re(CH_3CO)_2H$], is established unambiguously. Although large thermal motion prevents a conclusive definition of the bonding in the rhena chelate ring, the neutron diffraction results appear to be consistent with a localized π-electron system and an asymmetric O···H···O bond.

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Registry No. 1, 59299-78-4; $CH_3C(O)Re(CO)_5$, 23319-44-0; methyllithium, 917-54-4.

Supplementary Material Available: Tables of structure factors and thermal parameters (7 pages). Ordering information is given on any current masthead page.

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Polypeptide Complexes of Silver(III)

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Abstract: Trivalent silver complexes of triglycine (G_3) and tetraglycine (G_4) have been prepared by direct reaction of the ligand with $Ag(OH)_4^-$ in aqueous alkali media. The multistep formation reaction of $Ag^{III}G_4$ is accompanied by a silver ion catalyzed path and a competing redox path. These complexes have characteristic spectra and, except for the method of preparation, are strikingly similar to the analogous Cu(III) system studied by Margerum and co-workers. The region of maximum stability ($k_d \sim 7 \times 10^{-3}$ s^{-1} for $Ag^{III}G_4$) is at pH 5-10. The pK_a for the interconversion of $Ag^{III}(H_{-3}G_4)^-$ and $Ag^{III}(H_{-4}G_4)^{2-}$ is about 12.5. Above pH 10 both species decompose mainly by a path involving abstraction of a methylenic proton by OH^- followed by reduction of the metal to Ag^I. The net activation energy for $Ag^{III}G_4$ decomposition is about 16 kcal/mol. $Ag^{III}G_3$ is considerably less stable than the tetraglycine complex at lower pH.

Peptide complexes of trivalent copper and nickel have been studied extensively by Margerum and co-workers.[1-7] The tetraglycine complex, $Cu^{III}G_4$,[8] has significant stability in aqueous solution and decomposes by one-electron processes that are both

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acid and base catalyzed.[4] This complex is most stable ($t_{1/2}$ = 5.4 h) in a neutral medium. A similar pH dependence is observed for the Ni(III) complex,[7] but decomposition is faster (maximum half-life of about 5 min). The oxidation of the peptide ligand results in different products in the Ni(III) and Cu(III) systems.[4] Kirksey et al.[6] found that $Cu^{III}(H_{-3}G_4)^-$ has a pK_a = 12.1. The high positive charge of the central metal accounts for the rather facile loss of the proton from the terminal amine group. This deprotonation causes a marked change in the electronic spectrum, which is seen as a yellow-to-red conversion on making the medium strongly alkaline.

Although the most stable oxidation states of copper and silver are +2 and +1, respectively, the analogous M(III) complexes have been prepared for both metals with, for example, periodate and tellurate as ligands. The electronic spectra of bis(periodato)- and bis(tellurato)copper(III) and -silver(III) are similar.[9]

Cu(III) and Ni(III) complexes are usually prepared by chemical or electrochemical oxidation of the corresponding M(II) species.[10] Chemical oxidation with one-electron oxidants ($IrCl_6^{2-}$ or $S_2O_8^{2-}$) is rapid. For Cu(II) compounds, these syntheses are facilitated by the increase in crystal-field stabilization energy, which accompanies the removal of an antibonding electron.[3] The oxidation of Ag(I) compounds to Ag(III) or Ag(II) by peroxodisulfate is often difficult[11] and may be complicated by the insolubility of the reactants as well as the electronic stability of the completed 4d shell. The oxidation of silver salts in strong acid in the presence of an appropriate ligand (e.g., 1,10-phenanthroline or bipyridine) has some applicability for the preparation of Ag(II) complexes. However, with the exception of some nitrogen-donor macrocycles, the conversion of Ag(II) complexes to Ag(III) is not a generally useful synthetic route.[12]

We have been studying the reactions of the square-planar d^8 system $Ag(OH)_4^-$, which is prepared by the electrochemical oxidation of a silver anode in strong base.[13] Direct combination of the tetrahydroxoargentate(III) ion with potential ligands has successfully yielded kinetically stable Ag(III) complexes such as with periodate and tellurate.[13] Indeed, replacement of bound hydroxyls to give intermediate Ag(III) complexes commonly occurs in $Ag(OH)_4^-$ redox reactions.[14,15]

Because of the great deal of interest in the Cu(III) and Ni(III) peptide systems, we decided to see if Ag(III) peptides could be prepared by direct reaction of the ligands with $Ag(OH)_4^-$. This paper reports on the results of this study for triglycine and tetraglycine, which yield complexes having strikingly similar behavior to the analogous copper(III) and nickel(III) systems.

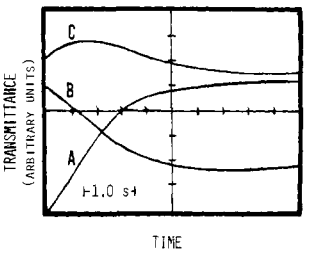

Figure 1. Oscilloscope trace of $Ag^{III}G_4$ formation reaction. $[Ag(OH)_4^-]_0 = 1 \times 10^{-4}$ M, $[G_4] = 1 \times 10^{-3}$ M, $[OH^-] = 0.6$ M. (A) = 300 nm; (B) = 318 nm; (C) = 420 nm.

Experimental Section

Chemicals. Tetraglycine (G_4) and triglycine (G_3) were used as received from Vega and Sigma. The purity of these materials was checked by comparison of the infrared spectra with literature data.[16] The proton NMR spectrum of tetraglycine also showed satisfactory correspondence with published data.[17] Since relatively small amounts of peptide fragments would be difficult to detect by these methods, the peptides were chromatographed on filter paper, using an 80% phenol eluant. While the G_4 did not contain detectable amounts of ninhydrin-active impurities, the G_3 did contain trace quantities of what were probably lower peptides. Solutions of the peptides were prepared in doubly distilled water or 1.2 M $NaClO_4$ adjusted to neutral pH and used the same day to minimize the effects of hydrolysis.

Solutions of $Ag(OH)_4^-$ were prepared as described elsewhere.[13,18] A silver foil anode is oxidized electrochemically in a 1.2 M NaOH solution until the desired amount of the tetrahydroxoargentate(III) ion has formed. Solutions containing up to approximately 5×10^{-4} M Ag(III) can be obtained by this method and quantified by the absorption spectrum of the complex (λ_{max} = 267 nm, $\epsilon = 1.17 \times 10^4$ M^{-1} cm^{-1}). Ag(III) solutions were bubbled with N_2 during the electrolysis to minimize the absorption of CO_2.

Acid solutions (1.2 M $HClO_4$) were prepared directly from Baker Reagent 70% solutions. NaOH preparations were made from low-carbonate 50% solution (Baker-Adamson or Mallinckrodt). Reagent grade boric acid and sodium phosphate salts were used in all buffer preparations.

Kinetics. Kinetic measurements at $[OH^-] > 0.1$ M were made in an Aminco-Morrow stopped-flow apparatus.[13] Most such runs were done at an ionic strength of 1.2 M and a temperature of 25 °C. As demonstrated in Figure 1, qualitative differences in stopped-flow traces at different wavelengths allowed us to distinguish a multistep formation reaction from the decomposition of Ag(III) polypeptide complex. Kinetic measurements of the decomposition reaction at pH ≤13 were carried out in a Varian DMS-90 UV–vis spectrophotometer with thermostated cells. Solutions of $Ag^{III}G_4$ or $Ag^{III}G_3$ were prepared for these runs by mixing the reactants in strong base and then quenching the rapid decomposition of complex by reducing the pH of the medium with 1.2 M $HClO_4$ containing the appropriate pH buffer. These solutions were placed immediately in the sample compartment. (When practical, solutions were filtered to remove precipitates of the reduced complex.) Concentrations of the $Ag^{III}(H_{-3}G_4)^-$ on which kinetic runs were made generally did not exceed 5×10^{-5} M after thermal equilibration in the sample cell. Initial ligand concentrations were 5×10^{-4} M in these runs.

In solutions where an accurate limiting absorbance could be determined, first-order rate constants were determined conventionally. At lower pH, however, continued precipitation and settling of the precipitate required that the infinity of the reaction be estimated from its initial behavior. Under these circumstances, reactions were followed through at least 2 half-lives. First-order rate constants thus obtained generally are reliable to within about 20%.

Spectra. The Ag(III) complexes were prepared as described above and immediately placed in the quartz cell of a Cary 15 spectrophotometer. Rapid scanning over a 100–200-nm range on separate solutions and comparison with stopped-flow data allowed the accumulation of an entire spectrum even when the half-life was less than 20 s. Solutions of the complexes prepared in strong base were adjusted to various pHs with

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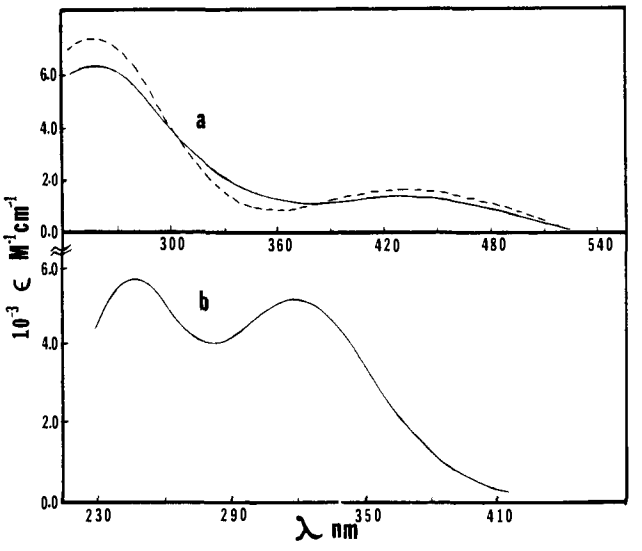


Figure 2. (a) Absorption spectra of $Ag^{III}(H_{-4}G_4)^{2-}$ (—) and intermediate, I_S (---) obtained from stopped-flow traces. $[Ag(III)]_0 = 1 \times 10^{-4}$ M, $[G_4] = 1 \times 10^{-3}$ M, $[OH^-] = 0.6$ M. (b) Absorption spectrum of $Ag^{III}(H_{-3}G_4)^-$ measured at pH 7. $[NaClO_4] = 0.6$ M, [phosphate] = 0.05 M.

$HClO_4$ or with concentrated (0.5 M) phosphate buffers. The separate solutions were generally kept cold prior to mixing to minimize decomposition.

In the case of $Ag^{III}(H_{-4}G_4)^{2-}$ a point-by-point spectrum of the complex (and an intermediate of the formation reaction) was obtained from stopped-flow kinetic traces of the reaction between $Ag(OH)_4^-$ and $H_{-3}G_4^{4-}$ in basic solution. Extinction coefficients for this complex were calculated from the absorbance at selected wavelengths after the reaction of a known amount of $Ag(OH)_4^-$ with a large excess of the ligand. Conversion of the $Ag^{III}(H_{-4}G_4)^{2-}$ to the protonated form by neutralization with acid or concentrated buffers and subsequent recording of the spectrum involve a significant loss of the Ag(III) initially present as $Ag(OH)_4^-$, which can only be accounted for approximately. The extinction coefficients of the absorption spectrum were therefore estimated on the basis of the rate of decomposition of $Ag^{III}(H_{-4}G_4)^{2-}$ prior to acidification. $Ag^{III}G_4$ spectra are shown in Figure 2.

ESR analysis was done on a Bruker ER-200 spectrometer by using frozen aqueous solutions of the tetraglycine complex. The decomposition of the complex was quenched by plunging the ESR tubes containing the freshly mixed solutions into liquid nitrogen. Accumulated scans were run on the protonated and deprotonated complexes and at varying stages in their decomposition. Under similar conditions, prepared solutions of Ag(II) species (the bipyridyl and pyrophosphate complexes) gave distinctive ESR spectra, and it was estimated that Ag(II) in concentrations less than about 1.0×10^{-6} M would have been detectable in these experiments.

Product Analysis. The untreated product mixtures from the reduction of the Ag(III) peptides were tested for carbonyl groups with 2,4-dinitrophenylhydrazine.[19] After acid hydrolysis of the product (reflux for 12 h in 2 M HCl), the chromotropic acid test for detection of formaldehyde was used.[20] The reduction of sodium periodate was used as a selective test for the presence of a 1,2-dioxo organic compound.[21]

For infrared analysis, separation of the Ag(I) product was accomplished by centrifuging the reaction mixture. Alternatively, Ag(III) peptides were decomposed in KOH solution, which was then neutralized with HBr. After evaporation of the solvent at reduced pressure, KBr pellets containing the reaction products were made. However, owing to the apparent photosensitivity of the product, not enough could be obtained for reliable infrared analysis although precautions were taken to protect the sample from direct light.

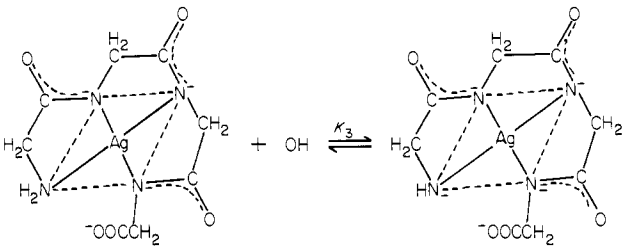
Results and Discussion

Preparation and Identification. The complexation of Ag(III) by tetraglycine and triglycine in aqueous alkaline media occurs immediately on mixing of $Ag(OH)_4^-$ solutions with the polypeptide. The kinetics of the formation reactions (eq 1 and 2) are complex (see Figure 1) and involve multiple steps.

$$Ag(OH)_4^- + H_{-3}G_4^{4-} \rightarrow Ag^{III}(H_{-4}G_4)^{2-} + 3OH^- + H_2O \quad (1)$$

$$Ag(OH)_4^- + H_{-2}G_3^{3-} \rightarrow Ag^{III}(H_{-3}G_3)^- + 3OH^- + H_2O \quad (2)$$

Because of its greater stability in neutral solution, the tetraglycine complex was studied in more detail than the triglycine species. The possibility of spontaneous reduction of Ag(III) on complexation was considered. The absence of an ESR signal from a frozen solution of the tetraglycine complex rules out the presence of Ag(II) while monovalent silver–polypeptide solutions are colorless. Structures A and B for the protonated and deprotonated forms, $Ag^{III}(H_{-3}G_4)^-$ and $Ag^{III}(H_{-4}G_4)^{2-}$ are proposed in eq 3.



(3)

These structures are analogous to those of the Cu(III) and Ni(III) species.[1,2] This identification is supported by the spectral similarities exhibited by the Ag(III) and Cu(III) systems.

The spectra of the silver(III) tetraglycine complexes are shown in Figure 2. At high pH, a broad absorption at longer wavelengths, which gives the complex an orange color, is due to the deprotonation of the terminal amine. The pK_a, which was determined kinetically (vide infra), is 12.5 ± 0.2, which also accords with visual observations (an orange-to-pale yellow color change). The spectrum of the protonated form, which persists in the range $3 < pH < 12.5$, shows two charge-transfer bands of nearly equal intensity at 248 and 315 nm. $Cu^{III}(H_{-3}G_4)^-$ has a similar spectrum[4] except that the second peak is at 360 nm. As shown in Table I, the second and third charge-transfer bands are typically shifted ~50 nm toward the UV for Ag(III) compared to Cu(III) complexes. Because of factors mentioned above, the extinction coefficients for $Ag^{III}(H_{-3}G_4)^-$ are probably lower limits. The deprotonated silver(III) triglycine, $Ag^{III}(H_{-3}G_3)^-$, has a spectrum similar to $Ag^{III}(H_{-4}G_4)^{2-}$ except that the broad band peaks at 480 nm. A similar (brown to yellow) spectral change upon lowering the pH to about 12 is seen, but the complete spectrum of the protonated form was not obtained. Observations at wavelengths shorter than 250 nm are hindered by the presence of reduction products.

The spectrum of $Ag^{III}(H_{-3}G_4)^-$ was unaffected by the presence of phosphate ions even at high concentrations, indicating that axial coordination of Ag(III) by this anion is negligible. This is as would be expected of a low-spin d^8 system.

Attempts to prepare $Ag^{III}G_4$ by alternate methods were unsuccessful. The colorless silver(I) peptide was precipitated from

Table I. Spectral Correlations for Ag(III) and Cu(III) Complexes

complex	charge transfer band λ_1, nm	λ_2, nm	λ_3, nm	ref
$Cu(H_2TeO_6)_2^{5-}$	274	402		9
$Ag(H_2TeO_6)_2^{5-}$	267	347		9
$Cu(HIO_6)_2^{5-}$	262	340	421	9
$Ag(HIO_6)_2^{5-}$	254	295	362	9
$Cu^{III}(H_{-3}G_4)^-$	259	365		4
$Ag^{III}(H_{-3}G_4)^-$	245	315		this work
$Cu^{III}(H_{-2}G_3)$	275	390		4
$Ag^{III}(H_{-2}G_3)$	260–290[a]	336 ± 3		this work

[a] Peak is partially obscured by reduction products.

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equimolar solutions of $AgNO_3$ and peptide. This material is photosensitive but did not undergo a disproportionation to Ag(II) such as reported for Ag(I) tetraaza compounds.[22] The compound was insoluble in common solvents (e.g., DMF and CH_3CN) and was used as a suspension. The suspension was made basic with 1 M NaOH containing 0.2 M $(NH_4)_2S_2O_8$ and left for 12 h in the dark. At the end of this time no changes could be observed that might be attributed to either ligand oxidation (e.g., formation of silver(I) oxide) or the formation of Ag(II) or Ag(III) species.

Cyclic voltammograms of Ag^IG_4 suspensions, in both neutral and acidic media, over the range 0 to +2 V vs. Ag/AgCl gave no indication of oxidation. Electrolysis in the range +2 to +4 V resulted in ligand oxidation only with eventual formation of a brown precipitate. The lack of reducible products was confirmed by cathodic scans of the electrolyzed solutions.

Formation Kinetics. The formation kinetics of $Ag^{III}(H_{-4}G_4)^{2-}$ are very complex and could not be analyzed fully. In Figure 1 the trace at 420 nm shows the distinctly biphasic formation reaction.[23] An isosbestic point between the product and the spectral intermediate (I_S) occurs at 300 nm. Kinetics at 320–340 nm were first order in one portion (k = 2.0 s^{-1}) and were essentially independent of $[Ag(III)]_0$, $[G_4]$, and $[OH^-]$. This can be attributed to the final phase in the formation of $Ag^{III}(H_{-4}G_4)^{2-}$.

The first part of the reaction was monitored at 267, 300, and 420 nm. At 267 and 300 nm, $Ag(OH)_4^-$ absorbs more strongly than I_S or $Ag^{III}(H_{-4}G_4)^{2-}$. At 420 nm, the absorbances of I_s and $Ag^{III}(H_{-4}G_4)^{2-}$ are comparable and that of $Ag(OH)_4^-$ is almost negligible. The reaction was studied over the following concentration ranges: 5×10^{-4} M $\leq [G_4] \leq 2 \times 10^{-2}$ M, 2×10^{-5} M $\leq [Ag(OH)_4^-] \leq 2 \times 10^{-4}$ M, and $[OH^-]$ = 0.15–0.6 M. The following features were noted:

(i) Both the total increase in absorbance at 420 nm, ΔA_{420}, and the decrease, ΔA_{300}, at 300 nm level off as $[G_4]$ increases, indicating complete complexation at $[G_4]$ between 10^{-3} and 10^{-2} M. However, ΔA_{300} actually increases as $[G_4]$ decreases, apparently due to a loss of Ag(III) in a competing redox reaction. Thus, we are unable to accurately determine a stability constant for the overall reaction.

(ii) The reaction obeys first-order kinetics only for $[Ag(III)]_0 \leq 7 \times 10^{-5}$ M. Observed rate constants, k_f (Table IIa), were independent of wavelength and $[OH^-]$. A rate dependence proportional to $A[G_4]/(1 + B[G_4])$ is found even in the range where complex formation is essentially complete. A plot of $1/k_f$ vs. $1/[G_4]$ yielded A = 1370 ± 40 M^{-1} s^{-1} and B = 160 ± 10 M^{-1}.

(iii) For $[Ag(OH)_4^-]_0 > 7 \times 10^{-5}$ M, deviations from first-order behavior were large near the beginning of the reaction, and in some runs a short induction period was observed. Plots of absorbance vs. time at 300 nm were nearly linear for this portion of the reaction and the dependence of the slopes, $\Delta A/\Delta t$, on the initial concentration of Ag(III) was measured. Values of $(\Delta A/\Delta t)/[Ag(III)]_0$ (Table IIb) increased linearly, indicating that the first phase of the formation reaction contains contributions from terms both first and second order in $[Ag(III)]_0$. At 420 nm, varying $[Ag(III)]_0$ while maintaining a constant ligand concentration showed that the amount of the intermediate, I_S, attained was disproportionately greater at higher $[Ag(III)]_0$, although the final absorbance change after complete reaction was in proportion to the amount of Ag(III) used (Table IIc). Thus, these variations do not result from the parallel reduction of Ag(III).

A wavelength study of the reaction of triglycine with $Ag(OH)_4^-$ was made at $[G_3] = 1.0 \times 10^{-3}$ M and $[Ag(III)]_0 = 1.4 \times 10^{-2}$ M. At corresponding wavelengths in the ranges $\lambda < 300$ nm and $\lambda > 400$ nm, traces were qualitatively the same as those of the tetraglycine reaction with similar rates. However, at $300 < \lambda < 400$ nm, oscilloscope traces showed only monotonic changes in transmittance.

For lower concentrations of Ag(III), where second-order effects appear to be negligible, a three-step mechanism can account for the reaction of $Ag(OH)_4^-$ with $H_{-3}G_4^{4-}$. The sequence of reactions, eq 4–6, seems most likely.[24] K_4 and k_5 were calculated from the results of the ligand dependence: $K_4 = B$ = 160 ± 10 M^{-1}, $k_5 = A/K_4$ = 8.60 ± 0.5 s^{-1}, and k_6 = 2.0 ± 0.1 s^{-1}.

$$Ag(OH)_4^- + H_{-3}G_4^{4-} \underset{}{\overset{K_4}{\rightleftharpoons}} I_1 \quad (4)$$

$$I_1 \xrightarrow{k_5} [(OH)Ag(NH^-)(N^-)_2N^-]^{3-} + (2 \text{ or } 3)OH^- \quad (5)$$

$$[(OH)Ag(NH^-)(N^-)_2N^-]^{3-} \xrightarrow{k_6} Ag^{III}(H_{-4}G_4)^{2-} + OH^- \quad (6)$$

Equation 4 involves the attack on $Ag(OH)_4^-$ by the amine group of tetraglycine. Although appreciable quantities of the intermediate (I_1) accumulate in the early stages of the reaction if $[G_4]$ is large, no distinct spectral changes could be attributed to its formation. The implied similarity of its spectrum to that of the reactant and the absence of a hydroxide dependence suggest that two cases must be considered: (a) I_1 is a monosubstituted species in which one hydroxyl is replaced by an amido group with the net elimination of H_2O or, (b) I_1 is a five-coordinate species with the amine coordinated axially to $Ag(OH)_4^-$. If case a is correct, deprotonation of the coordinated amine by OH^- increases the stability of I_1 both to redox (vide infra) and the displacement of G_4 by OH^-. The stability constant of I_1 (K_4 = 180 M^{-1}) is intermediate between that of the monoazido Ag(III) species (0.4 M^{-1})[15a,c] and that of the monothiosulfato complex (~1 × 10^4 M^{-1}).[15b] The reversibility of its formation accounts for the saturation in rate with respect to $[G_4]$. In case b, the stability of

Table II. Data for $Ag^{III}G_4$ Formation

(a) Ligand and Hydroxyl Ion Dependence[a]

$10^3[G_4]$, M	k_f, s^{-1} [OH^-] = 0.6 M	[OH^-] = 0.3 M	[OH^-] = 0.15 M
0.50		0.63	
1.0	1.25	1.3	1.1
2.0	1.8	2.0	
3.0		3.2	
5.0	3.8	3.8	
6.0	4.4		
10.0	4.9	5.1	
20.0	6.5	6.2	

(b) Total Absorbance Change, ΔA_{tot}, at 420 nm[b]

$10^4[Ag(III)]_0$, M	ΔA_{tot}	$10^{-2}\Delta A_{tot}/[Ag(III)]_0$, M^{-1}
1.9	0.12	6.3
1.7	0.107	6.3
1.2	0.087	7.2
1.15	0.071	6.2
0.61	0.037	6.1
0.48	0.030	6.2

(c) Rate of Absorbance Change at 300 nm[b]

$10^4[Ag(III)]_0$, M	$\Delta A_{300}/\Delta t$, s^{-1}	$10^{-3}(\Delta A_{300}/\Delta t)/[Ag(III)]_0$, M^{-1} s^{-1}
1.95	1.18	5.9
1.35	0.64	4.7
0.60	0.17	2.8
0.38	0.102	2.6

[a] $[Ag(III)]_0 < 7 \times 10^{-5}$ M; μ = 1.2 M; T = 25 °C. [b] $[OH^-]$ = 0.6 M; $[G_4] = 1 \times 10^{-3}$ M; T = 25 °C.

(22) Barefield, E. K.; Mocella, M. T. *Inorg. Chem.* **1973**, *112*, 2829.
(23) Changes at $t > 4$ s correspond to the decomposition reaction.
(24) Groups that are coordinated to Ag(III) are enclosed in parentheses. The symbols N^- and NH^- refer respectively to the deprotonated peptide and amine nitrogens of tetraglycine. In this notation, the alternate formulations of I_1 are $[(OH)_3Ag(NH^-)N_3^-]^{5-}$ or $[(OH)_4Ag(NH_2)N_3^-]^{5-}$, depending on the interpretation of eq 4.

the five-coordinate adduct might arise from hydrogen bonding between the amine group and the hydroxyl ligands. The rate laws for the oxidations of HO_2^-[25] and ethylenediamine[14] by $Ag(OH)_4^-$ contain terms that are third order overall, being first order in hydroxyl ion concentration. This has been interpreted as the attack of hydroxide on a five-coordinated Ag(III) species. In neither system was there indication of a tendency to rate saturation, implying that the steady-state concentrations of these intermediates were small.

In eq 5, I_1 undergoes ring closure with loss of two (case a) or three (case b) hydroxyl ligands. The product of this step is I_S. For case b, the loss of the first hydroxyl would not be expected to be rate determining if this process is initiated by a fast proton transfer from amine to hydroxyl and the subsequent displacement of water by NH^-. The slowness of ring closure may be due in part to the poor leaving-group character of OH^-[26] and the absence of protons on the peptide nitrogens to assist their departure. Unlike the complexation reaction of $Ni(H_2O)_6^{2+}$ with G_4,[27] in which the rate is determined by the initial attack on the metal ion, ring closure is slower than the initial entry of the ligand into the primary coordination sphere of Ag(III).

The rising absorbance at 420 nm indicates that the chelate ring containing the amido group is closed in this step. The deprotonated amine is expected to be strongly trans-labilizing.[26] Its effect on cis substitutions in a square-planar system is unknown, although the rate of the ring-closure steps suggests that it does not strongly labilize cis ligands. Recent work on the substituion reactions of $Au^{III}(NH_3)_4^{3+}$ suggests that amine groups have a strong cis effect.[28] However, NH^- has quite different chemical properties, particularly the ability to rehybridize and π-bond with the empty $5p_z$ orbitals of the metal.[6] In addition to stabilizing the positive charge on silver, the transfer of electron density to this orbital probably makes axial attack by a nucleophiles more difficult.

Substitution of the last hydroxyl group (eq 6) proceeds more slowly than the second hydroxyl replacement, which probably controls the rate of the preceding step. A possible cause is the reduction of positive charge on the Ag(III) ion by the peptide ligands.[29] The spectral changes that are associated with this step are not seen in the triglycine reaction.

The Ag(III) dependence in the absorbance/time behavior of the formation reaction seems to require the interaction of two Ag(III) moieties. The relatively constant proportion of $[Ag(III)]_0$ to total absorbance change shown in Table IIc indicates that both first- and second-order paths yield only one product. Numerical integrations of the differential equations arising from several potential pathways were used to simulate the kinetic behavior. The closest approach to the experimental kinetic curves at $[Ag(III)]_0 > 1.0 \times 10^{-4}$ M was obtained by postulating a reaction between $Ag(OH)_4^-$ and the intermediate of eq 4, which catalyzes the ring-closure step of eq 5. A rate constant of at least 1×10^5 M^{-1} s^{-1} for the reaction between the Ag(III) species is necessary to account for the importance of this pathway. The reaction is not simple, and an induction period indicates that at least one weakly absorbing intermediate complex is formed prior to ring closure.

The reduction of Ag(III), which accompanies the formation reaction (see (i) above), appears to arise from a parallel reaction of $Ag(OH)_4^-$ rather than the instability of one of the intermediates. A plausible explanation is that G_4 is oxidized by the Ag(III) species, $Ag(OH)_3H_2O$, which is much less stable to redox[30] than

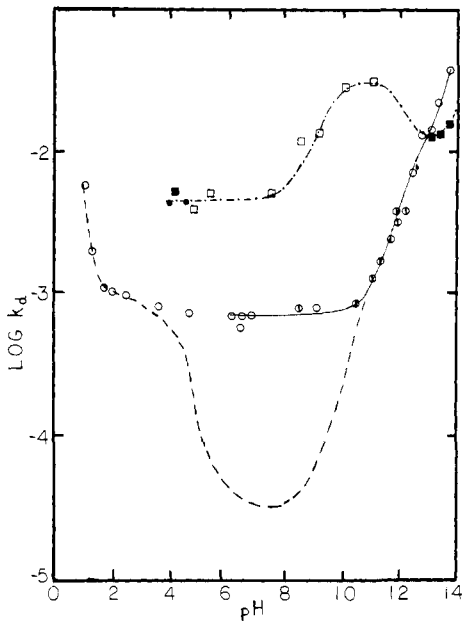

Figure 3. pH profile of the rate of decomposition of $Ag^{III}G_4$ and $Ag^{III}G_3$ in aqueous media at 20 °C and μ = 1.0 M. $Ag^{III}G_4$: (○) phosphate, 0.01 M; (⊖) borate, 0.01 M. $Ag^{III}G_3$: (□) phosphate, 0.015 M, (●) borate 0.03 M, (■) unbuffered. Solid line at pH >6 is calculated from eq 10; dashed line is for $Cu^{III}G_4$ from ref 4.

$Ag(OH)_4^-$. The aquation of $Ag(OH)_4^-$ occurs at a rate of about 0.6 s^{-1}.[14,15b] The slowness of the complexation reaction at lower $[G_4]$ (Table IIa) thus accounts for the competitive reduction of Ag(III).

Decomposition Kinetics. The rate of disappearance of $Ag^{III}G_4$ in the range $2 < pH < 14$ is first order in complex and independent of the monitoring wavelength. The pH profile is shown in Figure 3. The rate constant, k_d, has a first-order dependence on $[OH^-]$ except in the region $0.01 \leq [OH^-] \leq 0.1$ M, which corresponds to a region of changing speciation (eq 3). From the variation of k_d with $[OH^-]$ outside of this region, the second-order rate constants for the base-catalyzed reductions of $Ag^{III}(H_{-3}G_4)^-$ and $Ag^{III}(H_{-4}G_4)^{2-}$ were estimated. The rate constant for the uncatalyzed path was obtained from the intercept of these plots.

At pH <11 the rate of reduction of the tetraglycine complex was sufficiently slow that precipitation of the Ag(I) product interfered. Thus it was necessary to estimate an absorbance infinity, which resulted in a constant half-life being obtained over the first 75% of the reaction. There was no indication of catalysis by products at any pH.

Between pH 5 and 3, the decrease in stability of $Ag^{III}(H_{-3}G_4)^-$ is first order in $[H^+]$, and the rate increases abruptly at pH <2, and, in this region, shows at least a second-order dependence on $[H^+]$. The rate law and mechanism for acid-catalyzed reduction of $Ag^{III}(H_{-3}G_4)^-$ appears to be similar to that for the Cu(III) system.[2,4] A summary of decomposition modes in the neutral and basic regions is given by eq 7–9. The rate law for the reduction

$$Ag^{III}(H_{-3}G_4)^- \xrightarrow{k_7} Ag^{I}G_4(ox) \quad (7)$$

$$Ag^{III}(H_{-3}G_4)^- + OH^- \xrightarrow{k_8} Ag^{I}G_4(ox) \quad (8)$$

$$Ag^{III}(H_{-4}G_4)^{2-} + OH^- \xrightarrow{k_9} Ag^{I}G_4(ox) \quad (9)$$

of silver(III) tetraglycine for $6 < pH < 14$ is given by eq 10

$$-\frac{d[Ag(III)]}{dt} = (k_7 + k_8[OH^-])[Ag^{III}(H_{-3}G_4)^-] + k_9[OH^-][Ag^{III}(H_{-4}G_4)^{2-}] = k_d[Ag^{III}G_4] \quad (10)$$

(25) Borish, E. T.; Kirschenbaum, L. J. *J. Chem. Soc., Dalton Trans.* **1983**, 749.

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where

$$k_d = \frac{k_7 + k_8[OH^-]}{1 + K_3[OH^-]} + \frac{k_9 K_3 [OH^-]^2}{1 + K_3[OH^-]}$$

Final refinements of the values for the rate and equilibrium constants appearing in eq 10 were made by a nonlinear least-squares fit. Values of k_7, k_8 and k_9 were in good agreement with the graphical analysis. At μ = 1.2 M, T = 20 °C, and [buffer] = 0.01 M, $k_7 = (7.0 \pm 0.3) \times 10^{-4}$ s^{-1}, $k_8 = 0.34 \pm 0.1$ M^{-1} s^{-1}, $k_9 = 4.7 \pm 2.5$ M^{-1} s^{-1}, and $K_3 = K_a/K_w = 30 \pm 14$. Therefore, $pK_a = 12.5 \pm 0.2$ for amine deprotonation.

The decomposition of $Ag^{III}G_3$ is first order in [complex] in the range 4 < pH < 14. The pH profile is also shown in Figure 3. The reaction is base catalyzed, although the rate levels off and actually decreases between pH 10 and 13, where the triglycine equilibrium analogous to eq 3 occurs. The maximum half-life for $Ag^{III}(H_{-2}G_3)$ is 150 s at pH 4–7.

Buffer, Ionic Strength, and Temperature Dependences. The influence of buffer concentration on the rate of decomposition of $Ag^{III}G_4$ was found to be important only when [OH$^-$] was small, i.e., when eq 7 was the principal mode of reduction. At neutral pH, increasing [phosphate] 60-fold at constant ionic strength brought about a doubling of the rate. At [OH$^-$] = 0.3 M, addition of 0.3 M PO_4^{3-} had an insignificant effect. Substitution of borate for phosphate above pH 10 had no noticeable effect (cf. Figure 3). The decomposition of $Ag^{III}G_3$ was also independent of these ions at less than 0.03 M concentrations. The acid dissociation of nickel(II) triglycine is catalyzed by $H_2PO_4^-$ and HCO_3^-,[31] which may coordinate axially and transfer a proton to the peptide, but not by borate. Absence of axial coordination is a common feature in the chemistry of Cu(III) and Ag(III) (low-spin d^8) in contrast to that of d^7 Ni(III).[2,32]

Variation of the ionic strength, μ, from 1.2 to 0.12 M with [OH$^-$] = 0.12 M incurred an approximately 20% reduction in the rate of $Ag^{III}G_4$ decomposition. Since [OH$^-$] is close to K_a, this result is somewhat ambiguous, owing to the possible effects of μ on eq 3. However, the method of preparation of the complexes did not allow this experiment to be run at a more favorable pH. Calculation of the expected effect of the ionic strength on the protonic equilibrium,[33,34] assuming that the extended-Debye–Hückel law could be applied with reasonable accuracy to both rate (eq 7–9) and equilibrium (eq 3) expressions, predicted that the change in speciation would largely compensate for the reduction in rate expected at lower ionic strengths for the reaction between anions. The slight decrease in the observed rate is consistent with these opposing factors.

For $Ag^{III}G_4$ the temperature dependence of k_d was studied at [OH$^-$] = 0.3 M. The net activation energy was equal to 16.5 kcal/mol. At pH 6.5 and 3.7 the temperature effect is of similar magnitude, the rate of decomposition doubling for each 6–7 deg. For $Ag^{III}G_3$, at [OH$^-$] = 0.6 M, the activation energy was 12.5 kcal/mol. Data for the buffer, ionic strength, and temperature effects are summarized in Table III.

Product Identification. The decomposition products of $Ag^{III}G_4$ and $Ag^{III}G_3$ are Ag(I) compounds of the oxidized peptides, $Ag^IG_{3,4}$(ox), present as white solids in suspension. These resemble the precipitates obtained from $AgNO_3$ and the peptides, both in color and in photosensitivity. Attempts to isolate the tetraglycine reaction products for IR analysis were unsuccessful.

If a suspension of Ag^IG_4(ox) is made basic, the solid slowly dissolves, giving a yellow or orange product. The source of this color is uncertain although a charge-transfer complex containing Ag(I) and the hydrolyzed peptide product is possible. The visible spectrum of the solution depends on the buffer and alkali metal ion present but not on whether the Ag(III) complex had decomposed under acidic or basic conditions. Ag^IG_3(ox) formed Ag_2O under the same conditions. Ag^IG_4 itself is insoluble in base. The color of product solutions disappears rapidly upon the addition of sodium periodate, which is consistent with the presence of a 1,2-dioxo function in the hydrolyzed peptide.[35] Unoxidized tetraglycine does not react with periodate.

Acid hydrolyses of the G_3 and G_4 product suspensions were performed as described in ref 5. Formaldehyde was detected in the triglycine hydrolysate only. The presence of formaldehyde indicates an *N*-methoxyamide precursor, which is the immediate product of oxidative decarboxylation of the ligand. A summary of these observations and those for other metal peptides is given in Table IV.[36]

Table III. Variation of $Ag^{III}G_4$ and $Ag^{III}G_3$ Decomposition Rates with Solution Conditions[a]

(a) $Ag^{III}G_4$ Buffer Dependence

[phosphate], M	[OH$^-$] or pH	T, °C	$10^3 k_d$, s^{-1}
	0.6 M OH$^-$	25	80
0.02	0.6 M OH$^-$	25	70
0.10	0.6 M OH$^-$	25	70
0.18	0.6 M OH$^-$	25	80
0.004	pH 6.8	20	0.80
0.05	pH 6.9	20	0.90
0.234	pH 6.5	20	2.0

(b) $Ag^{III}G_4$ Temperature Dependence

[buffer]	[OH$^-$] or pH	T, °C	$10^2 k_d$, s^{-1}
—	0.6 M OH$^-$	18	1.8
—	0.6 M OH$^-$	25	3.6
—	0.6 M OH$^-$	30	5.8
—	0.6 M OH$^-$	35	8.8
0.234 (P)	pH 6.5	20	0.20
0.234 (P)	pH 6.5	26	0.38
0.01 (B)	pH 3.7	20	0.078
0.01 (B)	pH 3.6	32.5	0.17

(c) $Ag^{III}G_3$ Temperature Dependence

[buffer]	[OH$^-$], M	T, °C	$10^2 k_d$, s^{-1}
—	0.6	20	7.9
—	0.6	25	4.9
—	0.6	33	3.2
—	0.3	20	2.8
—	0.3	25	4.2

(d) $Ag^{III}G_4$ Ionic Strength Dependence[d]

μ, M	$10^2 k_d$, s^{-1}
1.2	2.2
0.72	2.0
0.24	1.6
0.12	1.5

[a] μ = 1.1 ± 0.2 M except in (d); (P) = phosphate; (B) = borate. [b] [OH$^-$] = 0.12 M; T = 25 °C.

Table IV. Decomposition Products of Peptide/Amino Acid Complexes

metal	ligand	decomposition
Ni(III)	$H_{-3}G_4^{4-}$	Ni(II), decarboxylated peptide[a]
Cu(III)	$H_{-3}G_4^{4-}$	Cu(II), oxidized peptide[b] (without decarboxylation)
Ag(III)	$H_{-3}G_4^{4-}$	Ag(I), oxidized peptide[c] (without decarboxylation)
Ag(III)	$H_{-2}G_3^{3-}$	Ag(I), decarboxylated peptide[c]
Ag(III)	glycine	Ag(I), decarboxylation products (silver mirror indicates HCHO)[c]

[a] Reference 5. Products include peptide fragments, CO_2, NH_3, triglycyl-*N*-methoxyamide, and tetraglycine. [b] Reference 4. Products include peptide fragments, glyoxalglycine, and diglycinamide. [c] This work. [d] Reference 36.

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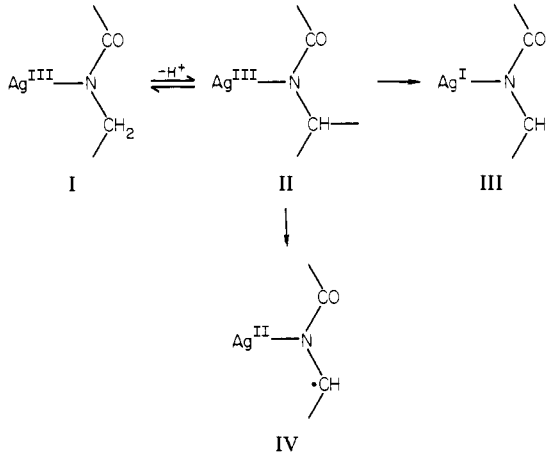
(36) Kumar, A.; Neta, P. *J. Am. Chem. Soc.* **1983**, *102*, 7284.

Scheme I



I II III IV

Decomposition Mechanism. Although the hydrolysis of uncoordinated peptides is catalyzed by both acid and base, complexation by metal ions often tends to inhibit cleavage of the peptide linkage.[37] The M(III) peptide complexes tend to be unusually inert to substitution.[1,2] An NMR study of the copper(II) diglycine complex in aqueous alkali has demonstrated that the methylene protons exchange rapidly with solvent.[38]

Oxidative dehydrogenation of macrocyclic complexes of Cu(III) and Ni(III) results in the increased unsaturation of the ligand and is frequently general base catalyzed.[10] In some cases the hydrolysis of coordinated imine groups results in ring cleavage and the insertion of a carbonyl function. In the present case a 1,2-dioxo species was detected after base hydrolysis of $Ag^{I}G_4(ox)$. Dehydrogenation followed by hydrolysis occurring at one of the peptide links would be expected to produce such a species. Indeed, the decomposition products of $Cu^{III}G_4$,[4,7] glyoxalglycine and diglycinamide, indicate that the carbon–nitrogen bond linking the second peptide nitrogen to the adjacent methylene group is oxidized. Therefore, the base-catalyzed reduction of $Ag^{III}G_4$ (eq 8 and 9), like that of $Cu^{III}G_4$,[7] is probably initiated by the abstraction of a methylene proton by hydroxide ion or by water. A mechanism that seems consistent with the hydroxide dependence in the kinetics and the product analysis of $Ag^{III}G_4$ decomposition is given in Scheme I. The deprotonated species II must be rapidly converted back to the protonated form or else undergo reduction to Ag(I). Although the overall stability of $Ag^{III}G_4$ is greater in neutral solution than at high pH (Figure 3), the second-order rate constant for the base-catalyzed reduction of $Ag^{III}(H_{-3}G_4)^-$ is approximately 5 times as great as that for $Ag^{III}(H_{-4}G_4)^{2-}$. Neglecting any small effects that may be due to the charge product of the reaction, I $\rightleftarrows$ II, the reasons for this must lie in the relative rates with which species II, derived from $Ag^{III}(H_{-3}G_4)^-$ or $Ag^{III}(H_{-4}G_4)^{2-}$, undergoes redox. The acidity of methylene protons in the chelate ring containing the amine group is probably enhanced by the protonation of the terminal amine. However, the loss of a proton results in a species tautomeric to $Ag^{III}(H_{-4}G_4)^{2-}$, and it seems unlikely that this can account for the observed reactivity. The acidity of the methylene protons in other chelate rings is probably not affected significantly.

With the exception of certain macrocyclic complexes, stable Ag(III) compounds generally contain four anionic donor atoms, which suggests that reduction of charge on the metal ion is essential to stabilizing the +3 oxidation state.[12,13] In the $Cu^{III}G_4$ system, for which the pH dependence of the Cu(III)/Cu(II) redox potential was measured, the deprotonation of the terminal amine in the oxidized form lowers this potential to 0.51 V (vs. NHE) from 0.63 V for the protonated complex.[6] The instability of $Ag^{III}(H_{-3}G_4)^-$ must also arise from a higher Ag(III)/Ag(I) reduction potential relative to $Ag^{III}(H_{-4}G_4)^{2-}$.

The validity of the proposed mechanism for the base-catalyzed path was tested in several ways. Although deprotonation of an acidic carbon in a chelate ring may result in an unstable species, owing to the high negative charge on the ligand, intermediate II may transfer one or two electrons rapidly to the metal. Such intermediates are present only in steady-state amounts, and at the highest base strength under which decomposition rates were measured, no deviations from first-order behavior were observed. The effect of ionic strength on the rate, although small, is suggestive of a reaction between OH^- and $Ag^{III}(H_{-4}G_4)^{2-}$. The rather large activation energy of the reaction seems significant and would be consistent with a rate-determining step which involves the breaking of a carbon–hydrogen bond.[39]

The reduction of $Ag^{III}(H_{-3}G_4)^-$ is catalyzed by both acid and base and, except in the region of pH between 4 and 9, the pH profiles for the reduction of $Ag^{III}G_4$ and $Cu^{III}G_4$ are nearly the same. This similarity extends to the individual rate constants for the base-catalyzed reactions.[4] The rates for the acid-catalyzed paths show the same correspondence. Such similarities are expected for metals of similar oxidation potential since decomposition is catalyzed by a reaction of the ligand rather than the metal. Unless there were a significant difference in the acid–base properties of the coordinated peptide (such as might occur if the metal ions had markedly different charge/radius ratios) reactions that are controlled by the rate of deprotonation should have similar rates. The amine deprotonations occur with a $pK = 12.1$ for the Cu(III) peptide and about 12.5 for Ag(III), suggesting that the properties of the ligand are not greatly affected by the difference in the metal.

The data for reduction of the $Ag^{III}G_4$ complex in acid seem consistent with a mechanism proposed by Paniago and Margerum[31] for the acid dissociation of deprotonated tetrapeptide complexes. The terminal carboxylate groups of Cu(III),[4] Co(III),[17] and Ni(II)[31] have pK_a's of 4.3, 4.4, and 4.2, respectively. Because this protonation does not result in the weakening of a metal–ligand bond, the rate of reduction of the metal does not increase markedly between pH 2 and 5. In both Cu(III) and Co(III) systems a second protonation occurs at lower pH (pK_a = 1.6 and 1.7, respectively). The similarity in the values of these equilibrium constants probably extends to the Ag(III) system. Although the carbonyl function of the terminal peptide group is protonated, resulting in an increase in the C–N double-bond character of the peptide link, transfer of the proton to the nitrogen with the resulting labilization of the metal–ligand bond is kinetically important.[2,4] The aquated metal(III) complex that results, having a higher redox potential, is reduced rapidly.

Reduction potentials of Ag(III)/Ag(I) couples are difficult to measure reliably. However, in cases where Ag(III)/Ag(II)[40] couples can be compared with Cu(III)/Cu(II),[41] results indicate that the redox potential for silver is less than for copper. This is to be expected since the third ionization potential for silver is less than that of copper.[42] However, the complete irreversibility of the reduction of Ag(III) to Ag(I) undoubtedly increases the effective two-electron oxidizing power of Ag(III).

Silver(III) tetraglycine is at least an order of magnitude less stable than $Cu^{III}(H_{-3}G_4)^-$ in the range $4 < pH < 10$, where acid and base catalyses are insignificant. This is evidently related to the fact that the Ag(II) peptide is not formed from the decomposition of the Ag(III) species.

A metal(III) peptide from which the methylene proton is lost may undergo an internal two-electron reduction to a M(I) product (species III in Scheme I) or form an intermediate M(II) ligand radical (species IV). In the cases of nickel and copper decom-

(37) Bender, M. L. "Mechanisms of Homogeneous Catalysis"; Wiley-Interscience: New York, 1971; p 226.
(38) Williams, D. H.; Busch, D. H. *J. Am. Chem. Soc.* **1965**, *87*, 4644.
(39) Since this apparent activation energy remains high throughout the range of pH between 4 and 14 (Results), it does not seem likely that E_a has a large contribution from K_3 even though k_d is a composite quantity (eq 10. Activation energies measured for other silver(III) reductions[25,34] are, indeed, much smaller than those reported here.
(40) Barefield, E. K.; Mocella, M. T. *J. Am. Chem. Soc.* **1975**, *97*, 4238.
(41) Olson, D. C.; Vasilevskis, J. *Inorg. Chem.* **1971**, *10*, 463.
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position, where only the stable M(II) complexes result, reaction with a second M(III) complex ion has been postulated to account for the products and the stoichiometry.[5,7] Although a silver(II) tetraglycine complex should be stable under the conditions at which some of the decomposition experiments were carried out, none was detected either as intermediate or as product, indicating that $Ag^{III}G_4$ undergoes an intramolecular two-electron redox reaction. An Ag(II) ligand-radical was tentatively reported as an intermediate in the reduction of a Ag(III) tetraaza macrocycle[38] and Ag(II) can be an intermediate in redox reactions of Ag(III).[12] However, it is clear that in the present system Ag(II) intermediates either do not occur or they undergo self-redox very rapidly.

The circumstances under which the reaction of a deprotonated intermediate or a ligand-radical with a M(III) species affects the decomposition rate has been discussed by Kurtz et al.[7] It seems that the absence of a bimolecular step involving Ag(II) and Ag(III) is sufficient to account for the faster rate of decomposition in the Ag(III) system when both acid and base catalyses are unimportant. The decomposition rate rises sharply at pH 7 in the copper pH profile, owing to the presence of Cu(II) products, a feature that is absent in the $Ag^{III}G_4$ complex.

The lower stability of $Ag^{III}(H_{-2}G_3)$ relative to $Ag^{III}(H_{-3}G_4)^-$ at neutral pH is probably due to the reduction in CFSE that occurs when a strongly donating N^- group is replaced by COO^-. The redox potentials[1] of the corresponding Cu(III) complexes are 0.92 V (G_3) and 0.63 V (G_4). However, deprotonation of the amine group causes a marked increase in the ligand field stabilization of the triglycine complex, and $Ag^{III}(H_{-3}G_3)^-$ and $Ag^{III}(H_{-4}G_4)^{2-}$ have comparable stability.

The triglycine ligand is decarboxylated in a process that is base catalyzed. The products of ligand oxidation of triglycine and tetraglycine by Ag(III) appear to be the same as in the Cu(III) system. The decomposition products of the nickel(III) tetraglycine complex (Table IV) indicate that electron transfer to the metal occurs mainly through the terminal peptide group. The site of electron transfer in the triglycine and tetraglycine complexes of Cu(III) and Ag(III) is the peptide ligand trans to the amine group. In the absence of coordinating peptide groups, glycine is deaminated by Ag(II)[36] and Ag(III).

Registry No. G_3, 556-33-2; G_4, 637-84-3; $Ag(OH)_4^-$, 23172-26-1; Ag, 7440-22-4.

Dipole-Stabilized Carbanions: The α' Lithiation of Piperidides

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Abstract: The α' lithiations and subsequent electrophilic substitutions of two series of piperidides are reported. In the cases of 2,4,6-triisopropylbenzopiperidide (**5**) and 4-*tert*-butyl-2,4,6-triisopropylbenzopiperidide (**6**) lithiations and electrophilic substitutions give α'-substituted products, as shown in Table I, which cannot be cleaved. 2,2-Diethylbutanopiperidide (**19**), 4-phenyl-2,2-diethylbutanopiperidide (**20**), and *N,N*-diethyl-2,2-diethylbutanamide (**18**) undergo α' lithiation and electrophilic substitution as shown in Table II to give products that can be cleaved to the substituted amines. This sequence thus provides the (α-lithioalkyl)alkylamine synthetic equivalent from secondary amines. The addition of the α'-lithiated piperidides from **20** to aldehydes is shown to provide equatorial substitution with erythro and threo isomers of the amido alcohol **31** produced in a 1:1 ratio. Exclusive conversion to an equatorial threo amino ester **36t** is observed on treatment with strong acid. All four possible equatorial-axial and erythro-threo isomers of the amino alcohol **34** can be obtained by appropriate manipulations. The formation of the equatorially substituted products from **6** and **20** and of syn products from *N,N*-diethyl-2,4,6-triisopropylbenzamide (**4**) is noted to be consistent with oxygen-lithium complexation and dipole stabilization as important factors in α' lithiation.

The formation of a formally dipole-stabilized carbanion **1** by removal of the α' proton adjacent to nitrogen from a *N,N*-dialkyl amide is an interesting and useful reaction.[1] The synthetic value of the intermediate **1** in the conversion of an amine **2** to an electrophically substituted amine **3** is illustrated by Scheme I.[2-5] The possibilities of stabilization of **1** by complexation, by dipole stabilization, or by delocalization are shown by the contributors **a**, **b**, and **c**, respectively.[1] While the novel step in this approach is the α' metalation of the amide the utility of the sequence also depends on the facile preparation, electrophilic substitution, and hydrolysis of the amide. In this paper we give details of the methodology of the synthetic use of these species[13,6] and provide evidence that the formation of α'-lithiated amides is consistent with stabilization by complexation and dipole stabilization.

The methodology of Scheme I provides the (α-lithioalkyl)alkylamine synthetic equivalent and is representative of a strategy for amine elaboration which is frequently more efficient than classical approaches.[2] In addition to the carbon-oxygen double bond of amides,[3] carbon-nitrogen double bonds of formamidines[4] and nitrogen-oxygen double bonds of nitrosoamines[5] have been shown to be useful in providing activation for the formation of species analogous to **1**.

Results and Discussion

Sterically Hindered Aromatic Amides. The α' lithiations and subsequent electrophilic substitutions of *N,N*-dialkyl-2,4,6-triisopropylbenzamides have been reported from two laboratories.[6-8]

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