$(phen)(CN)Br]^+$ intermediate (**2**), is due to this, the trihalo complexes undergoing this change rapidly. However, the subsequent behavior can be accounted for only if the released CN^- displaces Br^- from **2** before it leaves its environment, with formation of $[Au(phen)(CN)_2]^+$ (**3**). The isolation of some $[Au(phen)(CN)Br]^+$ is not inconsistent with this mechanism, but in view of the lability of the reaction products, it is not compelling evidence. Alternatively, the rate-determining step might be an intramolecular rearrangement of **1** that allows CN and Br to exchange sites (**4**), which is followed rapidly by loss of Br^- in a classic fashion to give **3**.

A very rapid reaction between the released Br^- and the unreacted 5-coordinate substrate will lead to the formation of *trans*-$[Au(CN)_2Br_2]^-$ and free phenanthroline by a normal substitution pathway that is the reverse of the entry of the first nitrogen of the chelate. As a result, only half of the substrate is converted to $[Au(phen)(CN)_2]^+$ while the rest goes to *trans*-$[Au(CN)_2Br_2]^-$. The very rapid reaction between $[Au(phen)(CN)_2Br]$ and Br^- in DMF to give *trans*-$[Au(CN)_2Br_2]^-$ has been examined qualitatively and shown to be complete before the first spectrum could be measured. $[Au(phen)(CN)_2]^+$ also reacts rapidly with Br^- (as might be expected from the strong trans effect of cyanide), but the product appears to be the trans isomer as well. These reactions are now being studied in detail.

The rate constants at a common temperature and the activation parameters are collected in Table III. The rate constants appear to be markedly dependent upon the nature of the solvent, the reaction in Me_2SO being significantly faster than that in DMF, which in turn is faster than the reactions in butanone and *sym*-dichloroethane. The reaction could not be studied in water, but addition of water to DMF leads to a large increase in reactivity. A plot of k_{obsd} against percent by volume of water is almost linear and extrapolates smoothly to the value measured in pure DMF. The general tendency for the rate constant to parallel the dielectric constant of the medium suggests that there is charge separation on going to the transition state of the rate-determining step and thus favors the successive displacement mechanism. However, one should bear in mind that this type of reasoning may lead to false conclusions as it did in the case of the PR_3-catalyzed cis–trans isomerization of $[Pt(PR_3)_2Cl_2]$, where an ionization mechanism has been demonstrated[18] even though the rate is much retarded in polar solvents.[19]

The difference in the reactivities of 1,10-phenanthroline and 5-methyl-1,10-phenanthroline complexes is too small to be considered significant, but the 5-coordinate complex of 2,9-dimethyl-1,10-phenanthroline reacts very slowly indeed ($t_{1/2} > 100$ h at 50 °C in DMF). This is to be expected since the methyl substituents offer a considerable increase in steric hindrance on going to any trigonal-bipyramidal transition state for substitution (for the same reason that orthomethylation in the cis ligands, R, decreases the substitutional lability of *cis*-$[Pt(PEt_3)_2RCl]$[20,21]). There will also be strong hindrance between the methyl groups and the adjacent ligands in the square-planar chelated product.

The difference in the reactivities of the chloro and bromo complexes is small, and either may be the more reactive species. Such a similarity is not uncommon in square-planar substitution when these ligands are leaving groups or are cis to them.[22]

Acknowledgment. We thank the Italian Ministry of Education, the CNR (Rome), and NATO (Grant No. 593/84) for Financial support and S. Boesso for technical assistance.

Registry No. **1**, 105250-54-2; **3**·ClO_4, 108189-79-3; $[Au(5\text{-}Mephen)(CN)_2Br]$, 108189-74-8; $[Au(phen)(CN)_2Cl]$, 108189-75-9; $[Au(5\text{-}Mephen)(CN)_2Cl]$, 108189-76-0; $[Au(2,9\text{-}Me_2phen)(CN)_2Cl]$, 108212-07-3; $[Au(2,9\text{-}Me_2phen)(CN)_2Br]$, 108189-77-1; *trans*-$K[Au(CN)_2Br_2]$, 30643-42-6; *trans*-$K[Au(CN)_2Cl_2]$, 30643-41-5; $[AsPh_4]$-[*trans*-$Au(CN)_2Br_2$], 108189-80-6; $[Au(phen)(CN)(Br)_2]$, 108189-81-7.

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Deprotonation of the α-Carbon in Amino Acid Amides and Peptides Chelated to Ruthenium(III)

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Deprotonations of chelates of $NH_2CH_2CONR^1R^2$ N,O-bound to Ru(III) (R^1 = H, R^2 = H, C_2H_5, CH_2COO^-; R^1 = CH_3, R^2 = CH_2COO^-) after they were mixed with buffer solutions (pH 6.3–8.5) were followed spectrophotometrically and electrochemically: $k = 0.055 \pm 0.004$ s^{-1} ($R_1 = R_2 = H$); $k = 0.057 \pm 0.004$ s^{-1} (R_1 = H, $R_2 = CH_2COO^-$); $k = 0.032 \pm 0.002$ s^{-1} ($R_1 = CH_3$, $R_2 = CH_2COO^-$); μ = 0.1 M, 23 ± 2 °C. The chelate of glycylsarcosine ($R_1 = CH_3$, $R_2 = CH_2COO^-$) was prepared for the first time and showed a $pK_a = 6.5 \pm 0.1$, similar to pK_a's observed before for similar chelates. It is suggested that the site of deprotonation is the chelate ring methylene group, and not the dangling amido group as suggested before. Extra stabilization of the deprotonated species is ascribed to π interaction that involves the half-filled t_{2g} orbital of Ru(III) and p orbitals of the two sp^2-hybridized carbon atoms and the oxygen atom. This is consistent with NMR results in which full exchange of the methylene protons with deuterium is observed at neutral pH within a few minutes. The deprotonation process is thought to be slow because of a configuration change of the chelate ring from a nonplanar strain-free configuration to a planar strained configuration of the enolate anion produced.

Introduction

Ruthenium-modified proteins have been used to study electron transfer between ruthenium ions and metal centers of metalloproteins.[1-3] The ruthenium moiety has also been attached to several proteins as a probe of various effects on the structure of proteins.[4] We have been studying the interaction between am-

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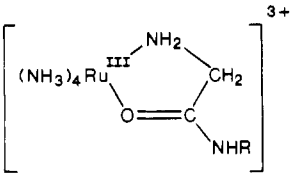
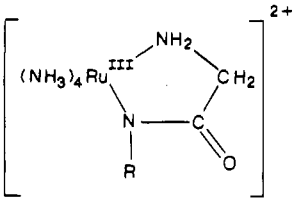
mineruthenium ions and constituents of proteins, namely amino acids, amino acid amides, and peptides.[5] These systems serve as models of the interaction between metal centers of hydrolytic metalloenzymes and the amido group of their peptide substrates, which is susceptible to cleavage. Our studies are undertaken in the hope that a better understanding of the interaction between ruthenium species, and more generally transition-metal ions, and proteins will be achieved.

In previous work, chelates of $(NH_3)_4Ru^{III}$ and ligands of the NH_2CH_2CONHR type were prepared and characterized.[5] These ligands can be bound either via the amino nitrogen and the amido oxygen (N,O-bound chelates)



I

or via the amino nitrogen and the deprotonated amido nitrogen (N,N′-bound chelates)



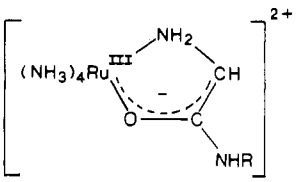
II

The N,O-bound chelates I undergo reversible protonation–deprotonation equilibria with pK_a's in the range 5.0–6.2.[5a] These equilibria were ascribed to the dangling amido NH_2 group, in spite of the fact that the pK_a values are ~10 units lower than those of the free ligands[6] and ~6 units lower as compared to those of analogous chelates of Co(III).[7] An explanation for these large differences between the chelates of the two metal centers could not be offered.

Here we present the results of a detailed study of these equilibria using spectroscopic, electrochemical, and kinetic methods.

Proton dissociation is observed to be slow for a deprotonation process ($t_{1/2}$ = 12–22 s). Such a slow rate is inconsistent with simple deprotonation of the dangling amido NH_2 group.

We suggest that proton dissociation takes place from the chelate ring methylene group. If this is the case, a planar sp^2-hybridized carbanion is produced and the whole chelate ring becomes planar. As a consequence, a π interaction that involves p orbitals of the two sp^2-hybridized carbon atoms and of the oxygen atom and the half-filled t_{2g} orbital of Ru(III) is made possible:



III

This interaction statilizes the deprotonated species considerably, as indicated by the low pK_a values.

The deprotonation is slow because it involves a transition of the chelate ring from a nonplanar strain-free configuration, similar to that found by X-ray crystallography for the related chelates of glycinate and of N,N′-bound glycinamide,[5c] to a planar strained configuration, where the π interaction is possible.

The suggestion of deprotonation from the α-carbon of the chelated ligands is consistent with the results for the chelate of glycylsarcosine $NH_2CH_2CON(CH_3)CH_2COOH$. No protons are bound to the amido nitrogen of this ligand, yet its chelate features a pK_a of 6.5, similar to that of the other N,O-bound chelates.

Experimental Section

Chemicals and Reagents. Chloropentaammineruthenium(III) chloride was prepared from ruthenium trichloride[8] and was purified by recrystallization from 0.1 M HCl. *cis*-Diaquotetraammineruthenium(III) trifluoromethanesulfonate was prepared from chloropentaammineruthenium(III) chloride as described before.[5a,9]

Glycylglycine, glycylsarcosine, and glycinamide hydrochloride (Sigma) were used without further purification. *N*′-Ethylglycinamide hydrochloride was prepared according to the published procedure.[5a]

CF_3SO_3H (Fluka, purum) was distilled under reduced pressure in an ungreased apparatus and kept in a desiccator at ~4 °C. $CF_3SO_3Na\cdot H_2O$ was prepared by neutralizing CF_3SO_3H with NaOH (~10 M) and drying in a vacuum desiccator over NaOH.

D_2O (99.8% D) was obtained from Sigma. NaOD (40 wt % in D_2O, 99+ atom % D) and D_2SO_4 (98 wt % in D_2O, 99.5+ atom % D) were purchased from Aldrich.

All other chemicals were reagent grade and were used as received. Deionized water that was distilled from an all-glass apparatus was used throughout.

Preparation of Complexes. (Glycinamide-*N*,*O*)- and (*N*′-ethylglycinamide-*N*,*O*)tetraammineruthenium(II) hexafluorophosphate were prepared as described.[5a] (Glycylglycine-*N*,*O*)tetraammineruthenium(II) was precipitated as the $[Cr(NH_3)_2(SCN)_4]^-$ salt.[5a] Solutions of (glycylglycine-*N*,*O*)tetraammineruthenium(III) not containing the $[Cr(NH_3)_2(SCN)_4]^-$ anion, which absorbs strongly in the UV region, were prepared by oxidizing (glycylglycine)pentaammineruthenium(II) hexafluorophosphate[5b] with $S_2O_8^{2-}$ at pH ~3 (10^{-3} M CF_3SO_3H, μ = 0.1 M, CF_3SO_3Na) and waiting for ~2.5 h, after which all of the pentaammine complex is converted into the tetraammine chelate.[5b] Solutions of (glycylsarcosine-*N*,*O*)tetraammineruthenium(III) were prepared similarly from (glycylsarcosine)pentaammineruthenium(II) hexafluorophosphate, which was obtained by the same route used for the preparation of pentaammineruthenium(II) complexes with NH_2CH_2CONHR ligands.[5b]

Analytical Methods. UV spectra were recorded on a Perkin-Elmer 555 recording spectrophotometer. The pH was measured with a homemade digital pH meter using a Metrohm EA 147 combined electrode. Microanalysis was performed by the Microanalytical Laboratory of the Hebrew University, Jerusalem, Israel.

Electrochemical Measurements. Cyclic voltammograms were recorded with a homemade multipurpose polarographic analyzer and a Hewlett-Packard Model 7045B X-Y recorder. The electrochemical cell was of the conventional two-compartment design, in which the reference cell was isolated from the test solution by means of a glass frit. A carbon-paste working electrode, platinum-wire auxiliary electrode, and Ag/AgCl in saturated KCl reference electrode were used. All experiments were performed in argon-saturated solutions. The concentrations of complexes were (1–2) × 10^{-3} M, and the ionic strength was kept at ~0.1 M. Potentials were converted to the normal hydrogen scale by adding 0.197 V.

Kinetic Measurements. The kinetics were followed spectrophotometrically at ambient temperature (23 ± 2 °C). The rapid deprotonation reactions were studied with a rapid-mixing device. This consisted of a small hand-operated stopped-flow mixer, which introduced the solution into a quartz flow-through cell (1.00 cm) via two syringes (delivery volume 2 mL each). One solution contained the Ru(III) chelate solution at pH 3 (10^{-3} M CF_3SO_3H) and an ionic strength of 0.1 M (CF_3SO_3Na). This solution was mixed with a 0.2 M solution of either Tris–CF_3SO_3H buffer (Tris = tris(hydroxymethyl)aminomethane, pH 7.5–8.5) or MOPS–NaOH buffer (MOPS = 3-(*N*-morpholino)propanesulfonic acid, pH 6.3–7.5). The pH of the mixed solutions was checked and found to be within 0.05 pH unit of the pH of the original buffer. Solutions of the glycinamide chelate were prepared by dissolving the solid hexafluorophosphate Ru(II) salt in a solution that contained a slight (~5%) excess of $Na_2S_2O_8$, shortly before use, since the amide group is hydrolyzed with a half-lifetime of ~4 h.[10]

NMR Spectra and H Exchange. ^1H NMR spectra were recorded at 400 MHz, with a Bruker AM400WB spectrometer. The NMR signals

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Table I. Spectral and Electrochemical Features of Pentaammineruthenium Complexes and Tetraammine Chelates of $NH_2CH_2CONRCH_2COOH$ (R = H, Glycylglycine; R = CH_3, Glycylsarcosine)

	$(NH_3)_5RuNH_2CH_2CONRCH_2COOH$			$(NH_3)_4\overline{RuNH_2CH_2CO}N(R)CH_2COOH$					
		$\lambda_{max}{}^b$ (ϵ)^c			$\lambda_{max}{}^b$ (ϵ)^c				
R	$E_{1/2}{}^a$	Ru(II)	Ru(III)	$E_{1/2}{}^a$	pH 1	pH 3	pH 8.5	$pK_a{}^{1\,d}$	$pK_a{}^{2\,e}$
H[f]	+0.16	265 (7.3×10^2)	275 (5.2×10^2)	+0.13	306 (1.1)	316 (1.0)	300 (1.8)	2.2	6.2
CH_3	+0.15	265 (7.0×10^2)	265 (sh) ($\sim 6 \times 10^2$)	+0.09	326 (1.2)	336 (1.1)	300 (1.7)	1.6	6.5

[a] In volts vs. NHE. [b] In nm. [c] In M^{-1} cm^{-1}. [d] For the carboxylic group. [e] For the methylene group. [f] Reference 5a,b.

were recorded in ppm positive downfield from tetramethylsilane, with the HOD signal as an internal reference (4.6 ppm). The Ru(II) chelate was dissolved in an argon-saturated 0.07 M D_2SO_4 solution in D_2O (pD ~0.9) to give a concentration of $\sim 5 \times 10^{-3}$ M. This solution was transferred under Ar to an NMR tube, and its NMR spectrum was recorded. A similar solution was oxidized by solid $Na_2S_2O_8$ (5% excess), and its pD was raised to ~7 by using NaOD solutions (2, 0.1 M) in D_2O. After about 10 min, the pD was decreased to ~1 by using a 0.9 M solution of D_2SO_4 in D_2O. The solution was reduced with zinc amalgam for about 20 min and transferred to an NMR tube under Ar, and its NMR spectrum was recorded.

Results

Properties of the Glycylsarcosine Complexes. The (glycylsarcosine)pentaammineruthenium(II) complex has not been prepared hitherto. Its preparation and properties resemble those of the other pentaammineruthenium(II) complexes with $NH_2CH_2CONR^1R^2$ type ligands (for glycylsarcosine, $R^1 = CH_3$ and $R^2 = CH_2COOH$).[5b] The complex features a single reversible couple in cyclic voltammetry with $E_{1/2} = +0.15 \pm 0.005$ V vs. NHE (0.1 M CF_3SO_3H), and its UV spectrum shows a broad peak at 265 nm ($\epsilon = 7.0 \times 10^2$ M^{-1} cm^{-1}). Immediately after oxidation by a slight excess (~5%) of $Na_2S_2O_8$, the UV absorption shifts and exhibits a shoulder near 265 nm ($\epsilon \approx 6 \times 10^2$ M^{-1} cm^{-1}). Later on, a slower change in absorption occurs, which shifts the absorption to longer wavelengths. The final spectrum of the solution depends on pH. It features a peak at 326 nm ($\epsilon = 1.2 \times 10^3$ M^{-1} cm^{-1}) at pH 1, whereas the peak appears at 336 nm ($\epsilon = 1.1 \times 10^3$ M^{-1} cm^{-1}) at pH 3. A spectroscopic titration of the solution with either dilute acid or dilute base gave a pK_a of 1.6 ± 0.1 for this spectral change, which is reversible. Isosbestic points are observed during the titration, at 291 nm and at 337 nm.

In analogy to the case for the NH_2CH_2CONHR complexes,[5b] the reaction after oxidation is ascribed to the formation of a tetraammine N,O-bound chelate. The observed pK_a is that of the carboxylic group of the sarcosine residue of glycylsarcosine.

First-order plots of the spectral change caused by the chelate formation process are linear. The rate constant calculated from these plots is $(1.1 \pm 0.1) \times 10^{-3}$ s^{-1} and is independent of the concentration of the complex (4×10^{-4}–1.2×10^{-3} M) and of pH in the range 1–3 (μ = 0.1 M, $CF_3SO_3H + CF_3SO_3Na$ or $HClO_4 + LiClO_4$).

Cyclic voltammetry of the product solution in the pH range 1–3 (μ = 0.1 M) shows only one quasi-reversible (peak separation 0.075–0.085 V) couple with $E_{1/2} = +0.090 \pm 0.005$ V vs. NHE.

When the pH of the product solution is increased, by either addition of dilute base, or mixing with an appropriate buffer solution (phosphate, MOPS, or Tris), a further spectral change is observed. At pH 8.5, the peak is shifted to 300 nm and increases in intensity ($\epsilon = 1.7 \pm 0.1) \times 10^3$ M^{-1} cm^{-1}). A pK_a of 6.5 ± 0.1 was calculated from a spectroscopic titration. At pH >6, a further slow change (hours) also occurs. This reaction is currently under investigation. It is too slow to interfere significantly with the titration. Isosbestic points at 271 nm and at 340 nm are maintained during the titration.

Table I summarizes the spectral and electrochemical features of the glycylsarcosine complexes and compares them with the analogous features of the glycylglycine species.

Electrochemistry of the N,O-Bound Chelates at pH >7. Figure 1 illustrates the electrochemical behavior of the reduced, N,O-bound glycinamide chelate at pH 7.0 (0.2 M MOPS buffer). The cyclic voltammogram displays two quasi-reversible pairs of peaks

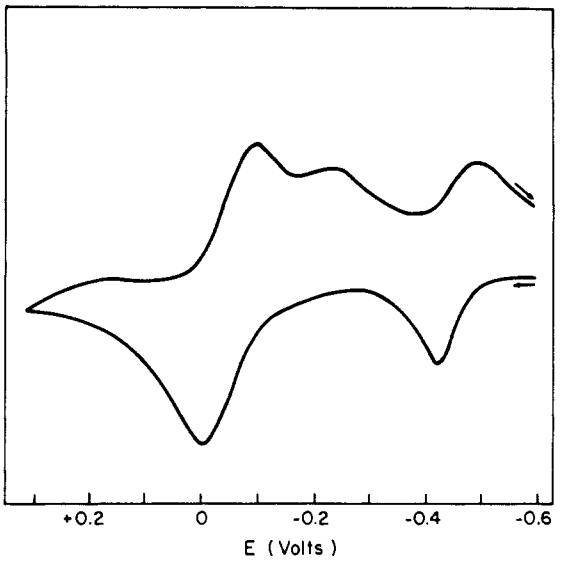


Figure 1. Cyclic voltammogram of (glycinamide-*N,O*)tetraammineruthenium(II) hexafluorophosphate in 0.2 M MOPS–NaOH buffer (pH 7.0; potential vs. Ag/AgCl (saturated KCl); sweep rate 0.1 V s^{-1}).

and an additional single peak in the reduction wave. One couple has a half-wave potential of –0.267 V vs. NHE, which equals that of the N,N′-bound isomer at this pH.[5a] The other couple features an $E_{1/2}$ value of +0.143 V vs. NHE—the same value featured by the N,O-bound chelate in acid solution, where it is protonated in both oxidation states.[5a]

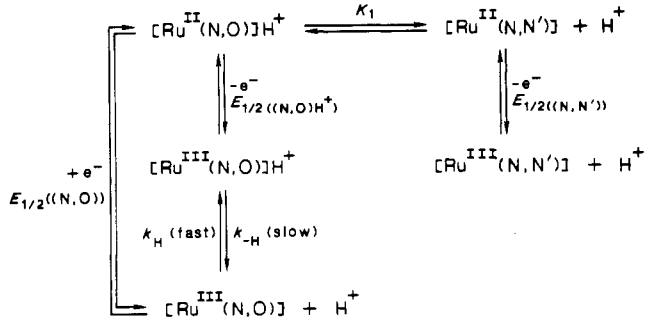
In the Ru(II) state, the N,O- and N,N′-bound isomers are in a pH-dependent equilibrium:

$$[Ru^{II}(N,O)]H^+ \rightleftarrows [Ru^{II}(N,N')] + H^+ \qquad (1)$$

The pK of this equilibrium is 8.1 for the glycinamide chelate.[5a] Therefore, at pH 7.0 both isomers should be present, with the N,O isomer as the dominant form. The presence of two oxidation peaks and the relative areas under these peaks are consistent with the pK value of equilibrium 1. But, at pH 7—two units above the pK_a value of the oxidized N,O-bound species[5a] and below the pK_a value of the reduced species—the half-wave potential should be negatively shifted by ~0.14 V relative to its value at low pH. This is not observed. Instead, a new peak appears in the reduction wave. These phenomena can be interpreted by assuming that deprotonation of the N,O-bound Ru(III) chelate is slow compared to the heterogeneous electron exchange with the electrode. If this is the case, the electrode interacts with two independent oxidized species—the protonated and the deprotonated N,O-bound Ru(III) chelate. Protonation of the chelate is a fast process in both oxidation states, so that only one reduced species—the protonated chelate—exchanges electrons with the electrode. Scheme I represents the relevant equilibria. $k_{-H} = 0.055$ s^{-1} for glycinamide (vide infra)—slow compared to the rate of electron exchange with the electrode.

If this interpretation is correct, a change in the scan rate should affect the relative areas of the two reduction peaks that belong to the protonated and deprotonated N,O-bound chelates. This is indeed the case, as demonstrated (Figure 2) by the cyclic voltammograms of the *N*′-ethylglycinamide chelate at pH 8.4. As the scan rate is increased, the amount of chelate that is deprotonated before being reduced decreases significantly, and its

Scheme I



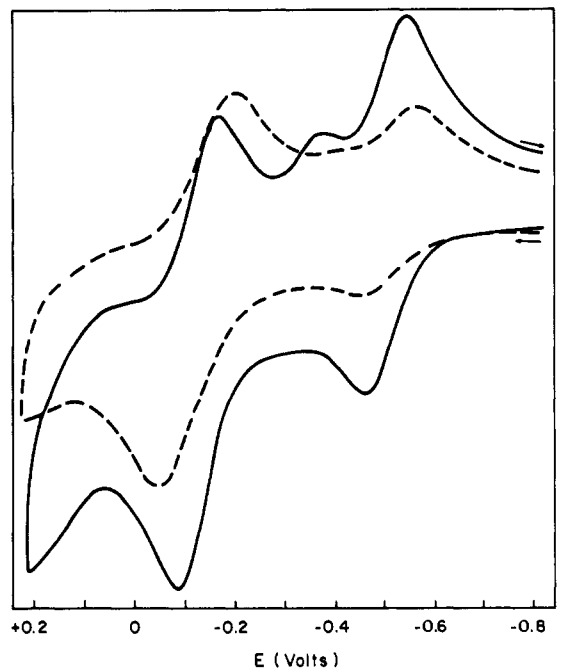


Figure 2. Cyclic voltammogram of (*N'*-ethylglycinamide-*N,O*)tetraammineruthenium(II) hexafluorophosphate in 0.2 M Tris–CF_3SO_3H buffer (pH 8.4; potential vs. Ag/AgCl (saturated KCl); sweep rate 0.05 V s^{-1} (solid line) and 0.5 V s^{-1} (dashed line)).

negative reduction peak is almost absent.

From Figures 1 and 2, the rate of deprotonation of the Ru(III) chelates can be estimated to be in the range 0.03–0.07 s^{-1}.

The chelates of glycinamide, *N'*-ethylglycinamide, and glycylglycine were isolated as the Ru(II) solid salts, and all display similar electrochemical behavior. The glycylsarcosine chelate was produced in solution in the Ru(III) state. At pH 8 (Tris buffer), it exists as the deprotonated species and the first scan in cyclic voltammetry shows its (single) reduction peak, together with a single oxidation peak of the protonated Ru(II) species. In the second and later scans, a second reduction peak appears, while the original reduction peak is diminished in intensity. Only a single oxidation peak is still present. The new reduction peak pairs with the oxidation peak, and a value of +0.090 V vs. NHE is calculated for this couple. In situ electrochemical oxidation of the Ru(II) species produces the protonated Ru(III) chelate, which deprotonates slowly compared to the heterogeneous electron transfer, and therefore two reduction peaks are observed in the second and later scans.

UV Spectra. In previous work,[5a] the pK_a values of the Ru(III) N,O-bound chelates of glycinamide, *N'*-ethylglycinamide, and glycylglycine were determined spectroscopically as 5.0, 6.2, and 6.2, respectively. We have now determined the corresponding pK_a value of the glycylsarcosine chelate as 6.5 (vide supra). These values were calculated from spectroscopic titrations by recording the spectra of the chelate solutions at several pH values, 2–5 min after the pH change. No significant spectral changes were observed within several minutes after the pH change, except at the higher pH values (>6), where very slow (hours) changes were observed. All titrations showed isosbestic points and were reversible. These results indicate that the equilibrium studied is a simple deprotonation process and are consistent with the suggestion that the unpaired reduction peak in the cyclic voltammograms does not belong to a new species that is formed by some chemical reaction after oxidation but rather to the deprotonated Ru(III) chelate.

Table II. Rate Constants for Deprotonation of $(NH_3)_4\overline{Ru^{III}NH_2CH_2CONR^1R^2}$ Chelates[a]

ligand	R^1	R^2	k, s^{-1}
glycinamide	H	H	0.055 ± 0.004
glycylglycine	H	CH_2COO^-	0.057 ± 0.004
glycylsarcosine	CH_3	CH_2COO^-	0.032 ± 0.002

[a] 23 ± 2 °C.

Rapid Kinetics after pH Increase. Spectral changes were monitored at 300 nm, where the absorption increases (all deprotonated N,O-bound chelates feature a peak near 300 nm (Table I and ref 5a)), and at 230 nm, where the absorption decreases. The absorption change was somewhat more complicated at 300 nm, where a slow increase in absorption follows the fast spectral change. At 230 nm, an isosbestic point occurs in the spectra of the deprotonated chelate, and of the product of the slow consecutive reaction. This enables an accurate kinetic analysis of the results of this wavelength.

First-order plots were linear for at least 4 half-lifetimes (results at 230 nm were used in order to get accurate values for the absorption at the end of the fast reaction at 300 nm). The calculated rate constants (Table II) are independent of pH (6.3–8.5), wavelength, and the concentration of the chelate (4×10^{-4}–1.2×10^{-3} M).

NMR Spectra and H–D Exchange. The ^1H NMR spectrum of the Ru(II) chelate of glycinamide demonstrates a series of broad lines, at 1.6 ppm (3 protons), 2.2 and 2.4 ppm (overlapping, both asymmetric, 11 protons together), and at 4.0 ppm (slightly structured, 2 protons).

The peak at 1.6 ppm is assigned to the NH_3 ligand that is trans to the glycinamide oxygen. All other ammonia ligands and the NH_2 group of glycinamide are in positions cis to this oxygen atom, are trans to nitrogen donor atoms (either NH_3 or NH_2), and therefore have similar chemical shifts: 2.2–2.4 ppm. This chemical shift is similar to that observed for $[(NH_3)_6Ru]^{2+}$: 2.1 ppm.[11] The peak at 4.0 ppm is assigned to the methylene group of glycinamide. This peak is somewhat structured due to coupling with the two protons of the neighboring NH_2 group. The chemical shift of the methylene group is similar to that observed for glycinamide chelated to $(en)_2Co^{III}$[12] and for dipeptides and N-alkylated glycinamides, both by themselves and as chelates with $(en)_2Co^{III}$ and with $(trien)Co^{III}$.[13]

After a cycle of oxidation, pH increase to neutral pH, pH decrease, and reduction, as described in the Experimental Section, all of the peaks of the original spectrum disappeared. The hydrogen atoms of the ammonia ligands and the NH_2 group are expected to undergo rapid exchange with the solvent, since the rate of exchange for the ammonia hydrogens in $[(NH_3)_6Ru]^{3+}$ was measured as 2.0×10^9 M^{-1} s^{-1} at 25 °C.[14] Assuming a similar value for the glycinamide chelate, the half-lifetime for the exchange at neutral pH is in the millisecond range. The NMR spectra show that the methylene hydrogens exchange with solvent deuterons, as expected if this group undergoes deprotonation in the Ru(III) state at neutral pH.

Discussion

Both the electrochemical and kinetic results show that the proton dissociation process observed for Ru(III) chelates of

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N,O-bound $NH_2CH_2CONR^1R^2$ type ligands is slow. The sluggishness of this process is inconsistent with the assignment of the pK_a's observed for deprotonation of the dangling amido group. This group is sterically unhindered, and its deprotonation should not involve any slow step.

The pK_a of 6.5 observed for the glycylsarcosine chelate in spite of the fact that there are no protons attached to the amido nitrogen in this case is also inconsistent with deprotonation taking place from the amido group.

Chelates of glycinamide and glycylglycine derivatives N,O bound to $(en)_2Co^{III}$ and to $(trien)Co^{III}$ feature pK_a values in the range 10–12.5.[7] These equilibria were assigned by Buckingham et al. to the deprotonation of the amido nitrogen, an assignment consistent with the fact that the chelate of *N'*-dimethylglycinamide shows no proton dissociation in the pH range 9–14.[7]

The pK_a values of the Co(III) chelates represent an enhancement of the amido group acidity by 3–5 orders of magnitude as compared to the free ligands.[6] The pK_a value for deprotonation of the water molecule in the complex $[(NH_3)_5Co(OH_2)]^{3+}$ is 6.2.[15] This represents an enhancement of about 10 orders of magnitude in the acidity of water by Co(III). This effect can be regarded as an induction effect, and as such it is commonly attenuated by about 10^3 for every atom that intervenes between the acid-promoting center and the site of deprotonation. Thus, in the case of the amido group of Co(III)-chelated glycinamide and glycylglycine derivatives, the observed enhancement of acidity by 3–5 orders of magnitude is expected.

The Ru(III) chelates of glycinamide and glycylglycine derivatives feature pK_a values that if considered to represent deprotonation of the amido nitrogen would imply an enhancement of acidity by 8–10 orders of magnitude. Thus, Ru(III) would be $\sim 10^5$ times more effective than Co(III) in promoting proton dissociation from the amido nitrogen. Part of the increased effect of Ru(III) as compared to that of Co(III) may come from a stronger inductive effect, as manifested also by a lower pK_a value of 4.1 for the dissociation of a proton from the water molecule in $[(NH_3)_5Ru(OH_2)]^{3+}$.[16] There is still left a factor of $\sim 10^3$ unaccounted for.

Deprotonation can then take place either from an ammine nitrogen or from the methylene group of the chelate ring.

Deprotonation of an amino group with a pK_a value in the range 5–6.5 is highly improbable since the hexaammineruthenium(III) ion features a much higher pK_a of 13.1.[17] We are left therefore with the possibility of deprotonation of the methylene group of the chelate ring. This possibility is sustained by the NMR results, which show that the methylene protons undergo exchange with the solvent within a few minutes, when the Ru(III) chelate is exposed to neutral pH.

It has been known for many years that metal ions increase the reactivity of the α-carbon atom of amino acids and their derivatives. Thus, aldehydes were condensed by means of a Knoevenagel type condensation with the methylene group of glycine chelated to Cu(II) and Co(III), almost 30 years ago.[18] Activation of the α-carbon and the protons bound to it toward reactions such as H–D exchange, racemization, and aldol condensation, by chelation to the metal ions Cu(II), Co(III), Mo(VI), Pt(II), and others, has been frequently studied since then.[19] These reactions take place at high pH and are slow even at elevated temperatures. They are presumed to take place via a planar enolate–carbanion intermediate.

Activation of the methylene group protons in the Ru(III) $NH_2CH_2CONR^1R^2$ chelate rings is consistent with the general phenomenon of activation of carbons of amino acid derivatives by chelation to transition-metal ions. Two questions arise in the case of Ru(III) chelates: (1) Why is the activation by this metal ion so much greater than that by other metal centers? (2) Why is the deprotonation process slow in spite of the stability of the deprotonated product? The answer to the first question is connected with two characteristics of the Ru(III) ion: its electronic configuration and its kinetic inertness. The low-spin d^5 configuration of Ru(III) leaves a half-filled t_{2g} orbital of π symmetry, which is available for interaction with ligand orbitals of the same symmetry. The deprotonated chelate ring of the N,O-bound chelates contains two sp^2-hybridized carbon atoms that should be coplanar with all of their substituents, a situation that forces the whole chelate ring to become planar. An electronic π interaction is now possible, involving p orbitals of the two carbon atoms and of the oxygen atom and the half-filled t_{2g} orbital of Ru(III) (structure III). Such an interaction superimposed on the inductive effect of a +3 charged ion may result in stabilizing the deprotonated chelate. This kind of interaction is impossible in Co(III) chelates because of the low-spin d^6 electronic configuration of this metal center, which does not leave a hole in the orbitals of π symmetry. In other metal centers such as square-planar Ni(II), Pd(II) and Pt(II) ions, an empty p_z orbital is available for π interaction,[5c] but in all of these cases, the deprotonated N,N'-bound isomers are stable and the systems are labile enough so that even if a N,O-bound chelate is produced, it is readily transformed into the N,N'-bound isomer. In the Ru(III) chelates, the N,N'-bound chelate is the more stable isomer at pH as low as 2, because of the high acidity of the Ru(III)-bound amido nitrogen, but the kinetic inertness of the Ru(III) center prevents isomerization from taking place.[5a]

Strong ligand to metal charge-transfer interactions are typical for Ru(III) complexes.[20] Strong π interactions between Ru(III) and the deprotonated amide nitrogen of *N,N'*-bound glycinamide and between Ru(III) and a carboxylic oxygen of chelated glycinate have been implicated recently in discussing the structures of these chelates and in rationalizing the structural differences between them and analogous Co(III) complexes.[5c] Similar π interactions were suggested for other metal centers with holes in their orbitals of π symmetry, such as square-planar Cu(III)[21] and Ni(II), Pd(II), and Pt(II),[22] trigonal-bipyramidal intermediates of Co(III),[23] and Ti, V, and Mo in $M{=}N(CH_3)_2$ complexes.[24]

The answer to the second question concerning the sluggishness of the deprotonation reaction involves the transition of the chelate ring from a nonplanar strain-free configuration into a strained planar structure in which the π interaction discussed above can take place. The exact structure of the N,O-bound Ru(III) chelates cannot be determined easily, because these chelates are not stable in solution for long enough periods that will allow good crystals to be formed.[10] The structures of two related chelates—of glycinate and of N,N'-bound glycinamide—were determined by X-ray crystallography[5c] and prove the chelate rings to be considerably nonplanar for both ligands. It is reasonable to assume that the chelate rings of the N,O-bound $NH_2CH_2CONR^1R^2$ ligands are also nonplanar. In order to attain the planar configuration that enables the suggested π interaction to take place after deprotonation, strain must be introduced into the ring. This slows down the whole deprotonation process.

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An interesting effect of ring conformation and strain was observed for the (ethylenediaminetetracetato)cobalt(III) ([Co(EDTA)]$^-$) chelate.[25] This chelate contains two types of glycinate-like chelate rings: one (in-plane rings) is strained and bent. The other type of rings (out-of-plane rings) is planar and strain-free. The two kinds of chelate rings undergo H–D exchange of their methylene groups with different rates: the planar nonstrained rings undergo the exchange much more readily than do the nonplanar strained rings. It was suggested that this difference in reactivity originates in the large energy required by the bent rings in order to become a planar enolate ion.[25]

Another example of differentiation of reactivity caused by flexibility variation of chelate rings, which affects their ability to assume a planar enolate intermediate is demonstrated by Co(III) chelates of aspartic acid, where the amino acid is a tridentate ligand.[19b] Two chelate rings are formed: a six-membered ring, which is relatively flexible, and a five-membered ring, which is less flexible, because of its smaller size and because of the coordination of the side chain. The 3-methylene protons of the six-membered ring exchange slowly with deuterium, whereas the 2-methyne proton of the five-membered ring exchanges with deuterium much more slowly, probably concurrent with opening of the six-membered ring.

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Registry No. $(NH_3)_5RuNH_2CH_2CON(CH_3)CH_2COOH^{3+}$, 108743-46-0; $(NH_3)_4RuNH_2CH_2CON(CH_3)CH_2COOH^{3+}$, 108743-47-1; $(NH_3)_4RuNH_2CH_2CONH_2^{3+}$, 85320-45-2; $(NH_3)_4RuNH_2CH_2CONHCH_2COOH^{3+}$, 85335-33-7; D_2, 7782-39-0.

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Synthesis, Electrochemistry, and Spectroelectrochemistry of Thallium(III) Porphyrins. Redox Properties of Five-Coordinate Ionic and σ-Bonded Complexes

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The synthesis and physicochemical characterization of 10 different metal–carbon σ-bonded thallium porphyrins are reported, and these data are compared to those of two different chlorothallium(III) porphyrins. The ligands σ-bonded to the thallium octaethyl- and tetraphenylporphyrin complexes were CH_3, C_6H_5, p-$CH_3OC_6H_4$, C_6F_4H, and C_6F_5. Each neutral complex was characterized by ^1H NMR, IR, and UV–visible spectroscopy and electrochemistry. Spectroelectrochemistry and ESR were used to characterize each oxidized and reduced complex. The singly and doubly oxidized Tl(III) complexes containing σ-bonded alkyl or aryl groups were stable. The electrooxidations were reversible, and the formation of a π radical cation in the first electron abstraction was observed by ESR spectroscopy. The electroreduction was also porphyrin ring centered, but the generated anion radical stability varied according to the nature of the axial and equatorial ligands. Spectroscopic data suggest the formation of a transient monothallium(I) porphyrin complex before demetalation, but the ultimate products of electroreduction were the reduced free-base porphyrin and a species that spectroscopically resembled a bis(thallium(I)) porphyrin.

Introduction

There are only two reports in the literature on thallium porphyrin electrochemistry. Fuhrhop, Kadish, and Davis demonstrated that (OEP)TlOH undergoes a reversible one-electron reduction in Me_2SO and two reversible one-electron oxidations in butyronitrile.[2] These reactions were postulated to involve formation of porphyrin π radical anions and π radical cations, but no spectroscopic monitoring of the products was reported. A later investigation of (OEP)Tl($OCOCF_3$) and (TPP)Tl($OCOCF_3$) demonstrated that these two compounds could be reduced by two steps in DMF.[3] The first reduction occurred at $E_{1/2} = -0.35$ V for the tetraphenylporphyrin (TPP) and at −0.47 V for the octaethylporphyrin (OEP). Both reactions involved an initial two-electron addition, which was followed by demetalation of the complex. Formation of an intermediate Tl(I) porphyrin was postulated,[3] but this species was not spectroscopically characterized nor was an overall reduction mechanism proposed. In addition, no information was given as to the oxidative behavior of these two Tl(III) complexes.

In the present paper we present the synthesis, electrochemistry, and solution characterization of (OEP)TlCl, (TPP)TlCl, and 10 different (P)Tl(R) complexes where R is a σ-bonded C_6F_5, C_6F_4H, p-$CH_3OC_6H_4$, C_6H_5, or CH_3 group and P is TPP or OEP. Until recently, the electrochemistry of σ-bonded porphyrins was limited to complexes of iron and cobalt.[4,5] However, it is now known that the σ-bonded alkyl complexes of indium[6,7] and gallium[8] can be oxidized by a single-electron-transfer step and that rapid cleavage of the metal–carbon bond may[6] or may not[7] occur depending upon the nature of the σ-bonded group. Electrochemical and spectroscopic data indicate that the least stable $[(P)In(R)]^{\bullet+}$ and $[(P)Ga(R)]^{\bullet+}$ complexes are those with R groups having the largest σ-bonding character.[6-8] Oxidized In(III) and Ga(III) porphyrins with σ-bonded aryl groups rapidly decompose to give the ionic In(III) or Ga(III) porphyrin species in solution. In contrast, oxidized In(III) porphyrins with σ-bonded perfluoroaryl groups are quite stable[7] and electron abstraction from the neutral complex can be characterized as involving the porphyrin π ring system.[7] As will be shown in this study, the oxidations of both σ-bonded alkylthallium and σ-bonded arylthallium porphyrins are reversible and a characterization of the stable singly and doubly

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