coordinating atoms of the bidentate base. As the temperature is raised, the inequivalent BH_3CH_3 groups exchange rapidly, leading to coalescence of the peaks. For $U(BH_3CH_3)_4$·dme, coalescence of methyl peaks occurs at ~-40 °C; for $U(BH_3CH_3)_4$·tmed, ~25 °C; for $U(BH_3CH_3)_4$·bmte, ~-20 °C, and for $U(BH_3CH_3)_4$·dmpe, ~10 °C.[2] The chemical shift difference between cis and trans CH_3 protons is ~126 ppm at -78 °C for $U(BH_3CH_3)_4$·dme, ~104 ppm at -59 °C for $U(BH_3CH_3)_4$·tmed, ~150 ppm at -78 °C for $U(BH_3CH_3)_4$·bmte, and ~63 ppm at -20 °C for $U(BH_3CH_3)_4$·dmpe.[2] From these data a free energy of activation of ~10 kcal/mol can be obtained for all four complexes. It is not possible to establish a unique mechanism with the present data.

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Registry No. $U(BH_3CH_3)_4$·dme, 97201-93-9; $U(BH_3CH_3)_4$·tmed, 109391-53-9; $U(BH_3CH_3)_4$·bmte, 97201-96-2.

Supplementary Material Available: Tables S1-S7, listing thermal parameters, distance restraints on hydrogen atoms, and hydrogen positions (7 pages); tables of calculated and observed structure factors (33 pages). Ordering information is given on any current masthead page.

Contribution from the Chemistry Department, Technion-Israel Institute of Technology, Haifa 32000, Israel

Ruthenium(III)-Promoted Hydrolysis of Chelated Glycinamide in Acidic Solution

Yigal Ilan* and Ariela Kfir

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(Glycinamide-*N*,*O*)tetraammineruthenium(III) reacts in dilute aqueous acid solution (pH 1-3) to give a mixture of (glycinato)tetraammineruthenium(III) and *cis*-diaquotetraammineruthenium(III). The yields of the products were calculated and compared to yields of NH_4^+. The yields are pH dependent contrary to the rate, which is pH independent: $k = (4.9 \pm 0.4) \times 10^{-5}$ s^{-1} (μ = 0.1 M, 23 ± 1 °C). A mechanism that involves a rate-determining nucleophilic attack of a water molecule on the carbonyl of chelated glycinamide is suggested. For the analogous chelates of ethyl glycylglycinate and of *N'*-ethylglycinamide, the rate is at least 2 orders of magnitude slower than that for the glycinamide chelate. This is the first demonstration of a significant promotion of a chelated amino acid amide hydrolysis by a metal ion at room temperature, in a solution of acidic pH.

Introduction

Metal ion promoted hydrolysis of amino acid esters and peptides has been a subject of numerous studies for many years.[1-4] These include studies of activation by labile metal ions such as Cu(II), Zn(II), Ni(II), Cd(II), Hg(II), and Pb(II),[1-3] as well as studies of activation by the inert metal ions Co(III)[4] and Ru(III).[5] Hydrolysis is rendered facile by chelation of the amino acid derivative through the amino nitrogen and the carbonyl oxygen. Attachment of the carbonyl group to the metal ion makes the carbon atom more susceptible toward nucleophilic attack.

The reactivity of the kinetically inert Co(III) complexes of amino acid derivatives has been thoroughly studied by the groups of Buckingham and Sargeson.[4,6] Analogous complexes of another kinetically inert metal ion—Ru(III)—were prepared and studied more recently.[5,7,8] By studying systems that contain inert metal ions rather than labile metal ions, one has the advantage of knowing the structure and properties of the starting reactants and the ability to define more unequivocally intermediates and mechanisms.

Chelation of esters, as well as of amides and peptides of amino acids to Co(III), enhances their hydrolysis under basic conditions. In acidic solutions, hydrolysis of Co(III)-chelated amino acid esters is also enhanced significantly.[4] In contrast, Co(III)-chelated amino acid amides and peptides are stable toward hydrolysis at low pH.[9] Similarly, the effect of other metal centers on the hydrolysis of amino acid amides and peptides in acid solution is small, and elevated temperatures are needed in order to study it.[1-3]

The chemistry of Ru(III) complexes of amino acid derivatives shows significant deviations from the chemistry of the analogous Co(III) complexes.[5,7,8] Thus, contrary to the stability of Co(III)-chelated glycinamide in acidic pH, Ru(III)-chelated glycinamide undergoes parallel hydrolysis and aquation in acid solution.

The results of studies of the reactivity of Ru(III)-chelated glycinamide and its derivatives in the pH range 1-3 are presented here.

Experimental Section

Chemicals and Reagents. Chloropentaammineruthenium(III) chloride was prepared from ruthenium trichloride[10] and was purified by recrystallization from 0.1 M HCl. *cis*-Diaquotetraammineruthenium(III) trifluoromethanesulfonate was prepared from chloropentaammineruthenium(III) chloride as described before.[8a,11]

Glycinamide hydrochloride and ethyl glycylglycinate (Sigma) were used without further purification. *N'*-Ethylglycinamide hydrochloride was prepared as described before.[8a]

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 the resulting product in a vacuum desiccator over NaOH.

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*)tetraammineruthenium(II) hexafluorophosphate ($[(NH_3)_4\overline{RuNH_2CH_2CONH_2}](PF_6)_2$, I) was prepared as described.[8a] Solutions of (ethyl glycylglycinate-*N*,*O*)tetraammineruthenium(III) (II) and of (*N'*-ethylglycinamide-*N*,*O*)tetraammineruthenium(III) (III) were prepared by oxidizing the corresponding ruthenium(II) pentaammine complexes, isolated as the

(1) Hay, R. W.; Morris, P. J. In *Metal Ions in Biological Systems*; Sigel, H., Ed.; Marcel Dekker: New York and Basel, 1976; Vol. 5, pp 173-243.
(2) Satchell, D. P. N.; Satchell, R. S. *Annu. Rep. Prog. Chem., Sect. A: Phys. Inorg. Chem.* **1978**, *75*, 25-48.
(3) Sigel, H.; Martin, R. B. *Chem. Rev.* **1982**, *82*, 385-426.
(4) Buckingham, D. A. In *Biological Aspects of Inorganic Chemistry*; Addison, A. W., Cullen, W. R., Dolphin, D., James, B. R., Eds.; Wiley: New York, 1977; pp 141-196.
(5) Yeh, A.; Taube, H. *J. Am. Chem. Soc.* **1980**, *102*, 4725-4729.
(6) The latest papers: (a) Baraniak, E.; Buckingham, D. A.; Clark, C. R.; Moynihan, B. H.; Sargeson, A. M. *Inorg. Chem.* **1986**, *25*, 3466-3478. (b) Buckingham, D. A.; Clark, C. R. *Inorg. Chem.* **1986**, *25*, 3478-3483.
(7) Diamond, S. E.; Taube, H. *J. Am. Chem. Soc.* **1975**, *97*, 5921-5923.
(8) (a) Ilan, Y.; Taube, H. *Inorg. Chem.* **1983**, *22*, 1655-1664. (b) Ilan, Y.; Taube, H. *Inorg. Chem.* **1983**, *22*, 3144-3151. (c) Ilan, Y.; Kapon, M. *Inorg. Chem.* **1986**, *25*, 2350-2354. (d) Ilan, Y. *Inorg. Chem.*, in press.
(9) Buckingham, D. A.; Davis, C. E.; Foster, D. M.; Sargeson, A. M. *J. Am. Chem. Soc.* **1970**, *92*, 5571-5579.
(10) Ferguson, J. E.; Love, J. L. *Inorg. Synth.* **1972**, *13*, 208-212.
(11) Diamond, S. E. Ph.D. Thesis, Stanford University, 1975.

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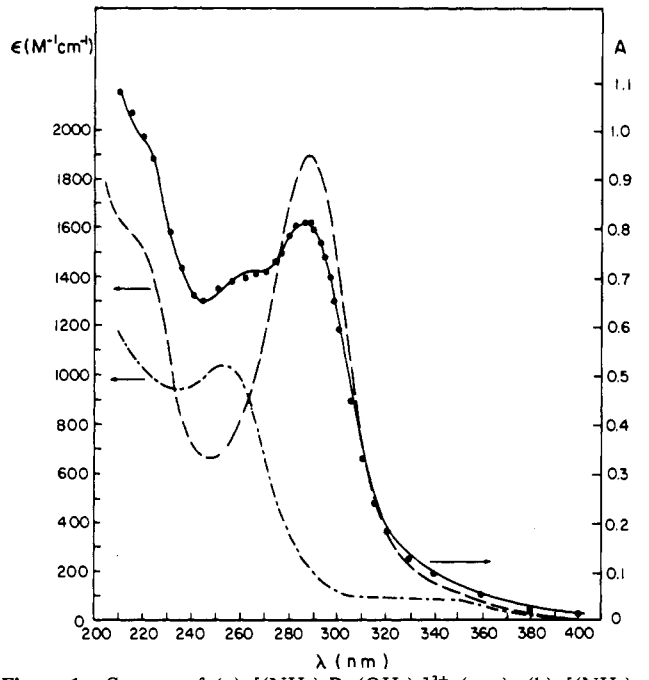


Figure 1. Spectra of (a) $[(NH_3)_4Ru(OH_2)_2]^{3+}$ (-·-), (b) $[(NH_3)_4\overline{RuNH_2CH_2COO}]^{2+}$ (--), and (c) the product solution after hydrolysis of 7.9×10^{-4} M $[(NH_3)_4\overline{RuNH_2CH_2CONH_2}]^{3+}$ (—). All spectra were recorded at 0.1 M CF_3SO_3H. The circles are calculated absorption values for a mixture of 4.0×10^{-4} M $[(NH_3)_4Ru(OH_2)_2]^{3+}$ and 3.8×10^{-4} M $[(NH_3)_4\overline{RuNH_2CH_2COO}]^{2+}$.

PF_6^- slats,[8b] by $Na_2S_2O_8$ 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 complexes were converted into the tetraammine chelates.[8b,12]

Analytical Methods. UV spectra were recorded on a Perkin-Elmer 555 recording spectrophotometer. pH was measured with a homemade digital pH meter, using a Metrohm EA 147 combined electrode.

Analyses for NH_4^+ were done after separating the complex on a column of Sephadex SP-C25-120 strongly acidic cation-exchange resin (Sigma). Ammonium ion was eluted with either 0.1 M $HClO_4$, or 0.1 M $LiClO_4$ at pH 3 ($HClO_4$), elution being continued until no more ammonium came off the column. The determination was performed with use of Nessler's reagent[13] against a calibration curve based on NH_4Cl solutions in $HClO_4$ and $LiClO_4$.

Electrochemical Measurements. Square-wave and cyclic voltammograms were recorded by using a homemade multipurpose polarographic analyzer and a Hewlett-Packard Model 7045B X-Y recorder. The electrochemical cell and the deaeration system for samples containing Ru(III) complexes were part of a PARC automatic voltammetric electrode, Model 309.[14] For samples containing Ru(II) complexes, 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 ~1×10^{-3} M, and the ionic strength was kept at ~0.1 M. Potentials were converted to normal hydrogen scale by adding 0.197 V.

Kinetic Measurements. Kinetics were followed spectrophotometrically at 23 ± 1 °C, by recording spectra as a function of time. Rate constants were calculated at several wavelengths.

Results

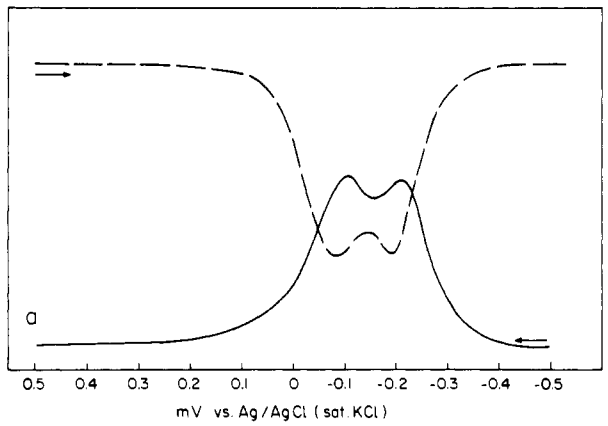
Products of the Reaction of Chelated Glycinamide. After oxidation of I by $Na_2S_2O_8$ (~5% excess) in acidic solution (pH 1–3), spectroscopic changes were observed. The final spectrum of the solution depended on pH, but it was always a superposition of the spectra of two Ru(III) ions: $[(NH_3)_4Ru(H_2O)_2]^{3+}$ (IV) and $[(NH_3)_4\overline{RuNH_2CH_2COO}]^{2+}$ (V).

The spectra of these two ions were recorded separately under the same conditions, and were compared to that of the product solution. The relative amounts of the two products were calculated at each pH by using their extinction coefficients at several wavelengths. The results of these calculations are given in Table I. Figure 1, which shows the spectra of IV and V and compares the spectrum of the product solution at pH 1 with the calculated spectrum of a mixture of IV and V, is typical of the results obtained.

Table I. Yields of the Products of (Glycinamide-*N*,*O*)tetraammineruthenium(III) Hydrolysis as a Function of H^+ Concentration

$[H^+]$	% $[(NH_3)_4\overline{RuNH_2CH_2COO}]^{2+}$ [a]	% $[(NH_3)_4Ru(H_2O)_2]^{3+}$ [a]	% NH_4^+ [b]
0.1	49	51	55
0.08	53	47	
0.05	58	42	
0.04	60	40	
0.03	61	39	
0.02	64	36	
0.01	65	35	65
0.001	72	28	70

[a] ±2%. Mean value of at least four experiments. [b] ±3%. Mean value of at least two determinations.



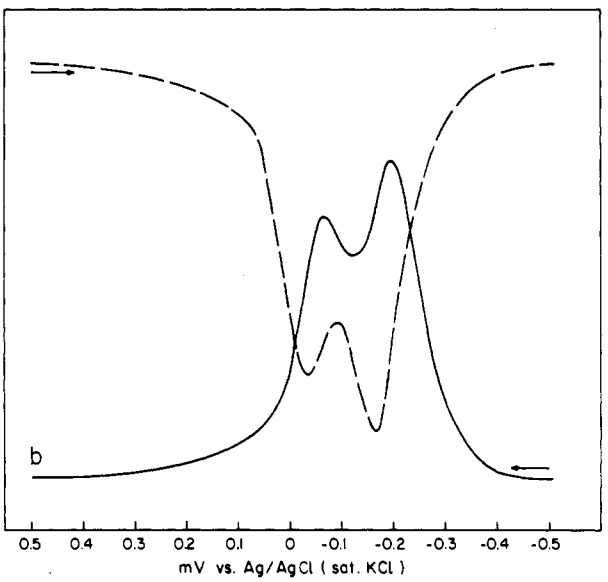


Figure 2. Square-wave voltammograms of solutions obtained after eaction of (glycinamide-N,O)tetraammineruthenium(III): (a) pH 1; (b) pH 3. Conditions: sweep rate, 0.1 V s^{-1}; pulse amplitude, 0.05 V; pulse width, 0.01 s.

(12) The Ru(II) chelates of these two ligands are easily isolated only as the $[Cr(NH_3)_2(SCN)_4]^-$ salts. This anion absorbs strongly in the UV region, where the hydrolysis reaction is monitored. Therefore, an in situ method of preparation of these chelates was employed.

(13) Basset, J.; Denney, R.; Jefferey, G. H.; Mendham, J. *Vogel's Textbook of Quantitative Analysis*, 4th ed.; Longmans, Green and Co: New York, 1978; p 730.

(14) Yarnitzky, Ch. *Anal. Chem.* **1985**, *57*, 2011–2015.

Electrochemical experiments show that the product solutions contain two electrochemically active species with relative concentrations that depend on pH (Figure 2). The two products feature $E_{1/2}$ values that correspond to those of IV and V: +0.10[15] and −0.010 V[11] vs. NHE at pH 1, respectively. The $E_{1/2}$ values of the products are anodically shifted as the pH is increased. The same shifts are also featured by genuine samples of IV and V.

The glycinato chelate (V) produced by hydrolysis of oxidizied I was isolated as a solid salt. This was achieved by dissolving 50 mg of I in 2 mL of 0.001 M CF_3SO_3H solution that contained an equivalent amount of solid $Na_2S_2O_8$, and 0.07 g of NH_4PF_6. The solution was filtered and left in a desiccator over dry silica. After 5 days a crystalline precipitate was formed. This solid exhibited spectral and electrochemical features identical with those of a genuine sample of V.[8a]

(Glycinato)pentaammineruthenium(III), in which the amino acid is O-bound, features an absorption spectrum similar to that of V. A possibility exists that *cis*-aquo(glycinato)tetraammineruthenium(III) in which glycine is bound to Ru(III) through the carboxylate is also produced. In order to examine this possibility, the product solution was partially reduced after saturation with argon by using zinc amalgam. About 20 min later, the solution was reoxidized with air, and its spectrum was recorded and compared to the spectrum of the same solution before reduction. No change was detected. Carboxylato complexes of ruthenium are known to be very labile in the Ru(II) state, and Ru(II)–Ru(III) electron transfer is fast.[16] Therefore, it is expected that any glycinate bound through the carboxylato group monodentately would dissociate in the presence of Ru(II). The identical spectra before and after partial reduction show that glycinate is bound to ruthenium only as a bidentate ligand.

Ammonium Ion Determination. Table I compares the yields of NH_4^+ and of V, which are produced from I after its oxidation, at three pH values. At pH 2 and 3, the yields are equal within the experimental error. The difference in the yields at pH 1 is somewhat larger and is out of the experimental error (see discussion).

Kinetic Experiments. I ($(2–4) \times 10^{-4}$ M) was dissolved in a solution of the desired pH (CF_3SO_3H, μ = 0.1 M, CF_3SO_3Na) containing a small (~5%) excess of $Na_2S_2O_8$. Spectra of the solution were recorded immediately after oxidation (dissolution) and later until no further spectral changes could be detected. First-order plots of the absorption changes at several wavelengths were linear for at least 3 half-lives. The rate constant calculated from these plots is $(4.9 \pm 0.4) \times 10^{-5}$ s^{-1}, and is independent of the concentration of the complex, the wavelength, and the pH (1–3).

Experiments with N,O-Bound Ethyl Glycylglycinate, and *N'*-Ethylglycinamide. Solutions of II and of III were followed spectrophotometrically for about a week. No changes indicating either hydrolysis to form bound glycinate, or aquation to form mono- or diaquo complexes could be detected. Irreproducible absorption increases were detected in some of the experiments in the wavelength range 350–400 nm, but the species responsible for this absorption was of very low concentration, as indicated by an electrochemical analysis of the solutions.

Discussion

It is generally accepted that the mechanism of the slow hydrolysis of amides, observed in dilute aqueous acid solutions, involves a rate-determining attack of a water molecule on the conjugate acid of the amide to form a tetrahedral intermediate.[17] The proton that is bound to the amide oxygen exerts a polarizing effect on the carbon group and enhances the nucleophilic attack of a water molecule on the carbon. The kinetics is first order both in the amide and in the dilute acid. A similar mechanism operates in hydrolysis of esters, where the reaction is faster than in the case of amides.

Amides and esters of amino acids also undergo acid-catalyzed hydrolysis reactions that are promoted by transition-metal ions.[1-4] Rate acceleration is achieved by chelation of the substrate to the metal ion via the amino nitrogen and the carbonyl oxygen. Metal ions polarize the carbonyl group to a smaller extent than protons in spite of their larger positive charge[18] and are, therefore, less effective in promoting ester and amide hydrolyses.

Glycinamide, the amino acid amide studied here, is no exception. Buckingham et al.[9] calculated a first-order rate constant of 6×10^{-4} s^{-1} for the attack of water on protonated glycinamide at 25 °C. This rate is about an order of magnitude faster than the rate of hydrolysis of Ru(III)-chelated glycinamide observed in the present work and almost 7 orders of magnitude faster than the rate of ~10^{-10} s^{-1} estimated for glycinamide chelated to Co(III).[9]

The affinities of amino acid amides toward transition-metal ions are higher than their affinities towards protons. Therefore, transition-metal ions may become more effective than protons in promoting hydrolysis of amino acid amides in dilute acid solutions, or at higher pH values, where the hydroxide ion is the attacking nucleophile, instead of water.[1-4]

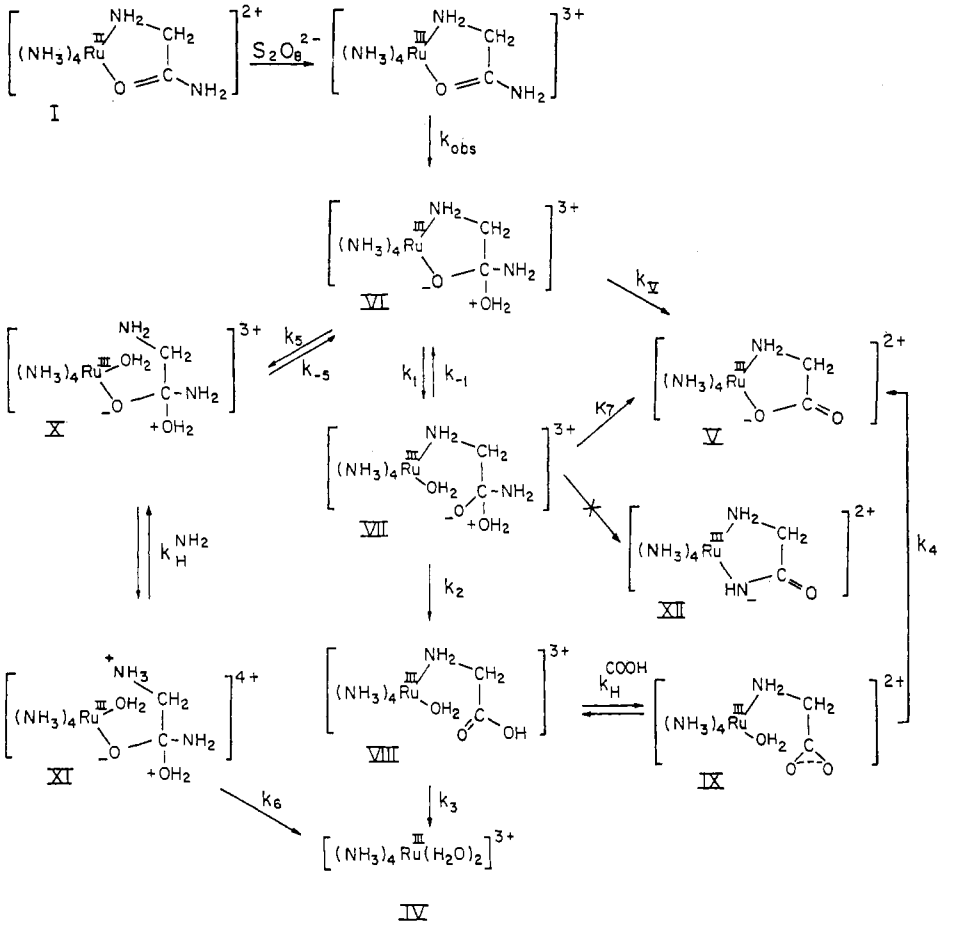
The susceptibility of amino acid amides and peptides toward hydrolysis is very low. For example, elevated temperatures and long periods of time (hours to days at 50–93 °C) are necessary in order to observe an appreciable amount of hydrolysis of the dipeptide glycylglycine.[19-22] Chelation of glycylglycine to the divalent metal centers Co(II), Ni(II), Zn(II),[21] and Cu(II)[22,23] by the amino nitrogen and amido oxygen enhances the cleavage of the peptide bond, but it is still slow and is observed only at high temperatures. Chelation of glycylglycine or glycinamide to Co(III) in the same way does not bring about any observable hydrolysis in acid solution at room temperature after several days.[9] Similarly, alanylethylenediamine chelated to Co(III) does not show significant hydrolysis in 0.01 M $HClO_4$ at 20 °C, giving an upper limit of 3×10^{-8} s^{-1} for the first-order rate constant.[24] Chelation of dipeptides via the amino nitrogen and the deprotonated amido nitrogen inhibits hydrolysis of the amido group.[3,22,23] The only case in which a very significant promotion of the hydrolysis of glycylglycine as well as of other glycinamide derivatives is observed at room temperature is when the amide derivative is bound to Co(III) as a monodentate ligand cis to a water molecule, which serves as an intramolecular nucleophile. The adjacent positions of the substrate and nucleophile brings about an enhancement by several orders of magnitude.[4,25]

Aliphatic amides undergo acid hydrolysis at 25 °C with a second-order rate constant of about 1×10^{-5} M^{-1} s^{-1}.[9,26] This gives an estimate of ~1×10^{-6} s^{-1} for the observed rate constant of the hydrolysis of glycinamide at 0.1 M acid, ~50 times slower than the rate observed for Ru(III)-chelated glycinamide. This ratio increases at higher pH, as the rate of hydrolysis of Ru(III)-chelated glycinamide is independent of pH in dilute acid solutions, whereas the rate of the acid-catalyzed reaction decreases as the pH is raised. Thus, Ru(III) chelated glycinamide demonstrates the first case where chelation of an amino acid amide to a transition-metal ion is observed to significantly enhance the hydrolysis of the amide at room temperature.

Scheme I represents possible mechanisms for the hydrolysis and aquation of Ru(III)-chelated glycinamide in acid solution. All possible routes have a common intermediate—VI—which is

(15) Elson, C. M.; Itzkovitch, I. J.; McKenney, J.; Page, J. A. *Can. J. Chem.* **1975**, *53*, 2922–2929.
(16) Stritar, J. A.; Taube, H. *Inorg. Chem.* **1969**, *8*, 2281–2292.
(17) O'Connor, C. *Q. Rev. Chem. Soc.* **1970**, *24*, 553–564.
(18) Martin, R. B. *J. Am. Chem. Soc.* **1967**, *89*, 2501–2502.
(19) Lawrence, L.; Moore, W. J. *J. Am. Chem. Soc.* **1951**, *73*, 3973–3977.
(20) Lee, R. G.; Long, D. A.; Truscott, T. G. *Trans. Faraday Soc.* **1969**, *65*, 503–508.
(21) Long, D. A.; Truscott, T. G.; Cronin, J. R.; Lee,. R. G. *Trans. Faraday Soc.* **1971**, *67*, 1094–1103.
(22) Grant, I. J.; Hay, R. W. *Aust. J. Chem.* **1965**, *18*, 1189–1195.
(23) Nakata, T.; Tasumi, M.; Miyazawa, T. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1599–1601.
(24) Buckingham, D. A.; Binney, G. S.; Clark, C. R.; Graham, B.; Simpson, J. *Inorg. Chem.* **1985**, *24*, 135–141.
(25) (a) Buckingham, D. A.; Keene, F. R.; Sargeson, A. M. *J. Am. Chem. Soc.* **1974**, *96*, 4981–4983. (b) Boreham, C. J.; Buckingham, D. A.; Keene, F. R. *J. Am. Chem. Soc.* **1979**, *101*, 1409–1421.
(26) Edwards, J. T.; Meacock, C. R. *J. Chem. Soc.* **1957**, 2000–2007.

Scheme I



produced by a rate-determining attack of a water molecule on the carbonyl carbon. This intermediate is analogous to the tetrahedral intermediate suggested for the acid-catalyzed hydrolysis of amides. VI can hydrolyze directly in a simple first-order reaction to produce V (k_V), or it can undergo two kinds of ring opening equilibria (path 1 and path 5). Assuming steady states for intermediates VII, VIII, and XI and fast proton equilibria for K_H^{COOH} and $K_H^{NH_2}$, the concentration ratio between IV and V is given by eq 1 (see Appendix).

$$\frac{[IV]}{[V]} = \left\{\left(\frac{k_1k_2k_3}{(k_{-1}+k_2+k_7)(k_3[H^+]+k_4K_H^{COOH})} + \frac{k_5k_6}{k_{-5}K_H^{NH_2}+k_6[H^+]}\right)[H^+]\right\} \Big/ \left\{k_V + \frac{k_1k_7}{k_{-1}+k_2+k_7} + \frac{k_1k_2k_4K_H^{COOH}}{(k_{-1}+k_2+k_7)(k_3[H^+]+k_4K_H^{COOH})}\right\} \quad (1)$$

Under our experimental conditions, $[H^+]$ is in the range 0.1–0.001 M. K_H^{COOH} was measured for a similar Co(III) complex, $[(NH_3)_5CoNH_2CH_2COOH]^{3+}$, as 2.43 at μ = 0.1 M and 25 °C, a value identical with that of protonated glycine.[27] Therefore, a similar value can be assumed for VIII. Thus, $[H^+]$ and K_H^{COOH} are of comparable values in our study. k_3—the rate of dissociation of the amino nitrogen from the inert Ru(III) center—is probably much smaller than k_4—the rate of intramolecular association of the deprotonated carboxylic end of Ru(III) nitrogen bound glycinate. It is reasonable therefore to assume that $k_4K_H^{COOH} \gg k_3[H^+]$. The value of $K_H^{NH_2}$ can be reasonably assumed to be similar to its value for free glycinamide, $10^{-8.1}$,[28] which is 5–7

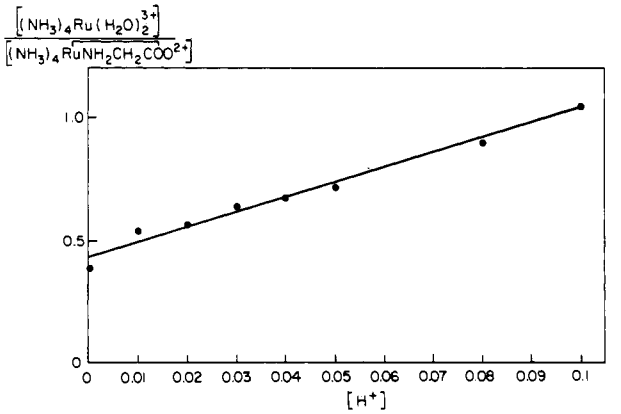


Figure 3. Concentration ratio of the products of hydrolysis of (glycinamide-*N*,*O*)tetraammineruthenium(III), $[(NH_3)_4Ru(H_2O)_2^{3+}]/[(NH_3)_4\overbrace{RuNH_2CH_2COO}^{2+}]$, as a function of H^+ concentration.

orders of magnitude smaller than $[H^+]$. It is difficult to estimate and compare k_6 and k_{-5}, but because of the large difference between $K_H^{NH_2}$ and $[H^+]$, assuming $k_6[H^+] \gg k_{-5}K_H^{NH_2}$ seems reasonable. If these two assumptions are inserted into eq 1, eq 2 is reached:

$$\frac{[IV]}{[V]} = \frac{k_1k_2k_3[H^+]}{(k_{-1}+k_2+k_7)k_4K_H^{COOH}k_V + k_1(k_2+k_7)k_4K_H^{COOH} + k_5/\left(k_V + \frac{k_1k_2}{k_{-1}+k_2+k_7}\right)} \quad (2)$$

(27) Buckingham, D. A.; Foster, D. M.; Sargeson, A. M. *J. Am. Chem. Soc.* **1969**, *91*, 3451–3456.

(28) Li, N. C.; Chien, M. C. M. *J. Am. Chem. Soc.* **1958**, *80*, 5678–5680.

The concentration ratio of the two products is expected to depend linearly on $[H^+]$, as is observed experimentally (Figure 3).

The open-ring intermediates VII, VIII, IX, X, and XI probably bind a solvent molecule in the sixth coordination site and are presented as such in Scheme I. The bound water molecule can attack the amido carbon intramolecularly (k_7), producing chelated glycinate (V).

As suggested in the scheme, the N,N′-bound isomer of the glycinamide chelate (XII), is not formed from intermediate VII. The N,N′-bound isomer features a strong absorption band around 360 mm and a negative redox potential (pH dependent),[8a] and it would be easily detected were it present in the solution. Under the experimental conditions, solutions of the N,N′-isomer, which is the thermodynamically stable isomer, remain unchanged for at least several days.[8a] The fact that it is not produced suggests that loss of NH_2 from VII (k_2) and/or the internal nucleophilic attack of bound H_2O on the carbonyl group (k_7) are much faster than the intramolecular binding of the amido nitrogen to Ru(III).

Three routes in Scheme I lead to formation of NH_4^+ in solution: direct hydrolysis of VI (k_V) and hydrolysis by the intramolecular attack of bound H_2O (k_7), in both of which one ion of V is produced for each NH_4^+ ion, and hydrolysis via equilibrium 1 and intermediates VII and VIII, in which either an ion of V or an ion of IV is produced, for each NH_4^+ ion. If production of IV from VIII (k_3) is significant, then $[NH_4^+]/[V] > 1$ is expected. Table I shows that the yields of NH_4^+ and V are equal within the experimental error at pH 2 and 3. At pH 1, the yield of NH_4^+ is somewhat larger than the yield of V. These results are explained by the fact that as the pH is decreased, more of the glycinato ligand of VIII is protonated and production of IV from VIII (k_3) becomes more significant. This is consistent with the assumption that $k_4K_H^{COOH} \gg k_3[H^+]$.

Unlike Ru(III)-chelated glycinamide, Ru(III)-chelated ethyl glycylglycinate and *N*′-ethylglycinamide are stable in acid solution for at least 1 week. Therefore, their rate of hydrolysis is at least 2 orders of magnitude slower than the rate of hydrolysis of oxidized I.

Secondary amides are generally more stable towards hydrolysis than primary amides. For example, *N*-methylacetamide is hydrolyzed ~20 times slower than acetamide, in 0.1 M HCl at 65 °C.[29] This retardation is attributed mainly to steric effects that inhibit the transformation of the planar sp^2-hybridized carbonyl carbon into a tetrahedral sp^3-hybridized carbon.

As mentioned above, Ru(III)-chelated glycinamide undergoes acid hydrolysis about 5 orders of magnitude faster than Co(III)-chelated glycinamide. This indicates a much stronger interaction of the carbonyl oxygen with Ru(III) than with Co(III), which can be explained by a significant ligand to metal π charge transfer from the oxygen to the half-filled t_{2g} orbital of Ru(III). Similar interactions are well-known for the Ru(III) metal center[8c,30] but are impossible in the d^6 Co(III) ion.

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Appendix

Derivation of Eq 1. (i) Steady-state assumption for VII:

$$\frac{d[VII]}{dt} = k_1[VI] - k_{-1}[VII] - k_2[VII] - k_7[VII] = 0$$

$$[VII] = \frac{k_1[VI]}{k_{-1} + k_2 + k_7}$$

(ii) Steady-state assumption for VIII:

$$\frac{d[VIII]}{dt} = k_2[VII] - k_3[VIII] - k_4[IX] =$$

$$k_2[VII] - k_3[VIII] - \frac{k_4K_H^{COOH}[VIII]}{[H^+]} = 0$$

$$[VIII] = \frac{k_2[VII]}{k_3 + k_4K_H^{COOH}/[H^+]} =$$

$$\frac{k_1k_2[VI]}{(k_{-1} + k_2 + k_7)(k_3 + k_4K_H^{COOH}/[H^+])}$$

(iii) Steady-state assumption for XI:

$$\frac{d[XI]}{dt} = k_5[VI] - k_{-5}[X] - k_6[XI] =$$

$$k_5[VI] - \frac{k_{-5}K_H^{NH_2}[XI]}{[H^+]} - k_6[XI]$$

$$[XI] = \frac{k_5[VI]}{k_{-5}K_H^{NH_2}/[H^+] + k_6}$$

$$\frac{d[IV]}{dt} = k_3[VIII] + k_6[XI] =$$

$$\frac{k_1k_2k_3[VI]}{(k_{-1} + k_2 + k_7)(k_3 + k_4K_H^{COOH}/[H^+])} +$$

$$\frac{k_5k_6[VI]}{k_{-5}K_H^{NH_2}/[H^+] + k_6}$$

$$\frac{d[V]}{dt} = k_V[VI] + k_4[IX] + k_7[VII] =$$

$$k_V[VI] + \frac{k_4K_H^{COOH}}{[H^+]}[VIII] + \frac{k_1k_7[VI]}{k_{-1} + k_2 + k_7} = k_V[VI] +$$

$$\frac{k_1k_2k_4K_H^{COOH}/[H^+]}{(k_{-1} + k_2 + k_7)(k_3 + k_4K_H^{COOH}/[H^+])}[VI] +$$

$$\frac{k_1k_7}{k_{-1} + k_2 + k_7}[VI]$$

$$\frac{[IV]}{[V]} = \frac{(d[IV]/dt)}{(d[V]/dt)} =$$

$$\left\{\left(\frac{k_1k_2k_3}{(k_{-1} + k_2 + k_7)(k_3[H^+] + k_4K_H^{COOH})} + \frac{k_5k_6}{k_{-5}K_H^{NH_2} + k_6[H^+]}\right)[H^+]\right\} \Big/ \left\{k_V + \frac{k_1k_7}{k_{-1} + k_2 + k_7} + \frac{k_1k_2k_4K_H^{COOH}}{(k_{-1} + k_2 + k_7)(k_3[H^+] + k_4K_H^{COOH})}\right\} \quad (1)$$

Registry No. (Glycinamide-*N*,*O*)tetraammineruthenium(III), 85320-45-2.

(29) Bolton, P. D. *Aust. J. Chem.* **1966**, *19*, 1013–1021.
(30) Hambley, T. W.; Lay, P. A. *Inorg. Chem.* **1986**, *25*, 4553–4558.