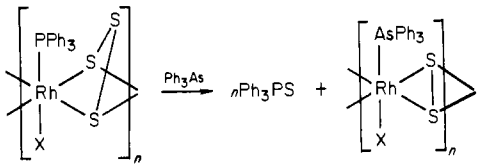

Registry No. **1**, 47898-17-9; **2**, 82522-17-6; **3**, 82522-18-7; **4**, 82522-19-8; **5**, 82522-20-1; **6**, 82522-22-3; **7**, 82522-23-4; **8**, 82522-24-5; **9**, 82544-26-1; **10**, 82522-25-6; **11**, 82536-82-1; **12**, 82522-27-8; **13**, 82522-29-0; **14**, 82522-31-4; **15**, 82522-33-6; **16**, 82522-35-8; **17**, 82522-36-9; **18**, 82522-37-0; **19**, 82536-84-3; **20**, 82522-38-1; **21**, 31168-83-9; **22**, 82522-39-2; **23**, 74472-62-1; **24**, 82522-40-5; **25**, 82522-41-6; **26**, 82522-42-7; $[Ir(Se_2)(dppe)_2]Cl\cdot H_2O\cdot 0.5C_6H_6$, 82522-43-8; S_8, 10544-50-0; $[Ir(dppe)_2]Cl$, 15390-38-2; Se_8, 12597-33-0; $[Ir(dmpe)_2]Cl$, 60314-45-6; $[Rh(dppe)_2]Cl$, 15043-47-7; $[Rh(dmpe)_2]Cl$, 16884-41-6; $[IrCl(CO)(PPh_3)_2]$, 14871-41-1; $[IrBr(CO)(PPh_3)_2]$, 14970-06-0; $[IrCl(CO)(AsPh_3)_2]$, 15682-62-9; $RhCl(PPh_3)_3$, 14694-95-2; $RhBr(PPh_3)_3$, 14973-89-8; $[RhCl(AsPh_3)_3]$, 14973-92-3; $Pt(PPh_3)_3$, 13517-35-6; $Pt(PEtPh_2)_3$, 36464-08-1; $[Ir(Se)_2(dppe)_2]BPh_4$, 82522-45-0; $[Pt(PEtPh_2)_4]$, 70163-52-9; $[IrCl(CO)(PEt_2Ph)_2]$, 27488-97-7; $[\{RhSCl(PPh_3)\}_n]$, 82536-86-5; $PEtPh_2$, 607-01-2; PPh_3, 603-35-0; Hg, 7439-97-6.

Supplementary Material Available: Tables of observed and calculated structure factors and thermal parameters (14 pages). Ordering information is given on any current masthead page.

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Tetraglycine Complexes of Cobalt(III): Preparations, ^1H and ^{13}C NMR Spectra, Absorption Spectra, and Reactions in Acid

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The preparations of three cobalt(III) complexes of tetraglycine are reported. In one complex, $[Co(NH_3)_2(H_{-3}GGGG)]^-$, the peptide is coordinated as a quadridentate through the terminal NH_2 and three peptide nitrogens. In the other two complexes, $[Co(NH_3)_3(H_{-2}GGGG)]$ and $[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$, the peptide is a terdentate chelate coordinated in the former through the terminal NH_2 and two peptide nitrogens and in the latter through the terminal NH_2, the adjacent peptide nitrogen, and a peptide oxygen. The ^1H and ^{13}C NMR spectra are given for the free peptide in its anionic, zwitterionic, and cationic forms and for the cobalt(III) complexes. The chemical shift data are analyzed in terms of the effects of protonation and coordination. In acid the free carboxylate in $[Co(NH_3)_2(H_{-3}GGGG)]^-$ is protonated with a pK_a at 278 K of 4.40 ± 0.08. At higher acid concentrations the terminal peptide nitrogen of the quadridentate chelate is protonated (pK_a at 298 K and I = 0.25, 1.7) and the nitrogen dissociates with a rate constant of 7.2×10^{-3} s^{-1} at 298 K (I = 0.25). The resultant diammineaqua complex with the chelate bound through the terminal NH_2 and two peptide nitrogens and the analogous triammine complex undergo a coordination rearrangement reaction in acid that involves an initial protonation (pK_a at 298 K and I = 0.25, 1.0) followed by the interchange of the Co–N to Co–O bonding for the peptide group trans to the NH_2 group with rate constants of 1.6×10^{-5} and 2.5×10^{-5} s^{-1}, respectively.

Introduction

The only cobalt(III) tetrapeptide complex in the literature, $[Co(dien)((H_{-1}GGGG)OEt)]^{2+}$, has the peptide coordinated as a terdentate chelate coordinated via the NH_2 group, a deprotonated peptide nitrogen, and a peptide oxygen.[1,2] The first quadridentate peptide complex of cobalt(III) was reported recently for a series of tripeptides.[3] In the present paper, the preparations are given for $[Co(NH_3)_2(H_{-3}GGGG)]^-$, in which the tetrapeptide is coordinated as a quadridentate through the NH_2 and three peptide nitrogens, and for triammine complexes where the peptide is a terdentate through the NH_2 and two peptide nitrogens, and through the NH_2, one peptide nitrogen, and one peptide oxygen. The UV–visible absorption and ^1H and ^{13}C NMR spectra of these complexes are also presented, and the NMR spectra are compared to those of the free peptide to determine the effects of coordination.

Margerum and his co-workers have studied the reactions with acid of a series of labile peptide complexes.[4-6] The peptide donor groups were found to be progressively removed from the metal. Because of the lability of the complexes, the various intermediates have not been isolated. However, the inertness of the present cobalt(III) system allows the isolation of complexes with the intermediate structures. The kinetics of the reactions with acid of the cobalt(III) tetraglycine complexes are also reported in this study.

Experimental Section

Materials. Tetraglycine was purchased from ICN Pharmaceuticals, Inc., and was used without further purification. All other reagents were of AnalaR grade. Stock solutions of perchloric acid were standardized by titration with standard CO_2-free sodium hydroxide solutions using an E.I.L. Vibron 39A pH meter. For the kinetics a constant ionic strength of 0.25 was maintained by the addition of appropriate amounts of dry sodium perchlorate. Adsorption properties of the complexes on ion-exchange cellulose papers were used to determine the sign of the charge on the complexes. Carboxymethyl cation-exchange cellulose CM 82 and aminoethyl anion-exchange cellulose AE 81 were used for this work. The pK_a value for the terminal carboxylate group was determined at 298 K by titration with standard acid using the above pH meter.

(1) The ligand abbreviations are as follows: dien, diethylenetriamine; GGGG, tetraglycinate; GGG, triglycinate; GG, diglycinate. For a peptide X, HX represents the peptide in the zwitterionic form, XH represents the peptide with the carboxylate protonated, and $H_{-n}X$ represents the peptide with n peptide nitrogens deprotonated. With use of this nomenclature, and with the premises that the amine group is preferentially coordinated, the deprotonated nitrogens are coordinated, and a coordinated peptide oxygen can only be a terminal group in the coordination, a formula $[CoA_3(H_{-1}GGGG)]^{n+}$ would depict a complex in which the amine, a peptide nitrogen, and a peptide oxygen are coordinated in that order.
(2) Wu, Y.; Busch, D. H. *J. Am. Chem. Soc.* **1972**, *94*, 4115.
(3) Evans, E. J.; Grice, J. E.; Hawkins, C. J.; Heard, M. R. *Inorg. Chem.* **1980**, *19*, 3496.
(4) Paniago, E. G.; Margerum, D. W. *J. Am. Chem. Soc.* **1972**, *94*, 6704.
(5) Pagenkopf, G. K.; Margerum, D. W. *J. Am. Chem. Soc.* **1968**, *90*, 6963.
(6) Cooper, J. C.; Wong, L. F.; Margerum, D. W. *Inorg. Chem.* **1978**, *17*, 261.

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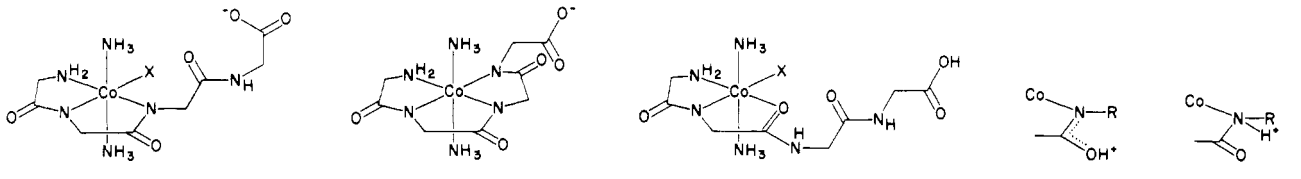
Table I. ^{1}H Chemical Shifts[a] of Tetraglycine and Its Cobalt(III) Complexes

compd	CH_2-1	CH_2-2	CH_2-3	CH_2-4	other
GGGG[b]	3.44	4.02	3.98	3.77	
HGGGG[c]	3.90	4.05	3.98	3.79	
$HGGGGH^+$ [d]	3.91	4.06	4.01	4.03	
$[Co(NH_3)_3(H_{-2}GGGG)]$[c]	3.56 (t)[e]	3.94	3.89	3.76	2.72 (6 H),[f] 3.62 (3 H),[f] 4.61 (2 H, t)[e,g]
$[Co(NH_3)_2(H_{-3}GGGG)]^-$ [c]	3.56 (t)[h]	4.03	3.99	3.92	2.31 (6 H),[f] 4.65 (2 H, t)[g,h]
$[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ [d]	3.50 (t)[e]	4.59	4.14	4.00	3.35 (6 H),[f] 4.2 (5 H)[e-g]

[a] In ppm from sodium 3-(trimethylsilyl)propane-1-sulfonate. [b] In dilute NaOD at pH 9.5. [c] In D_2O. [d] In D_2O acidified to pH 1 with perchloric acid. [e] $J_{HH} = 6.8$ Hz. [f] NH_3 resonance. [g] NH_2 resonance. [h] $J_{HH} = 6.6$ Hz.

Chart I



1 2 3 4 5

1a X = NH_3

1b X = H_2O

3a X = NH_3

3b X = H_2O

Preparation of $[Co(NH_3)_3(H_{-2}GGGG)]\cdot 2H_2O$. The peroxo dimer $[(NH_3)_5Co(O_2)CO(NH_3)_5](NO_3)_4\cdot 2H_2O$[7] (1.0 g, 0.0017 mol) was added with constant stirring to a solution of tetraglycine (0.84 g, 0.0034 mol) in aqueous ammonia (10 mL) at pH 9 kept at below 278 K. These conditions were maintained for 1.5 h, after which the solution was stored in a refrigerator for 16 h. The solution was filtered, and the filtrate was chromatographed on a Bio-Gel P2 column (50–100 mesh, 3 × 800 cm) with dilute aqueous ammonia (pH 7–8) as eluant. Four components were observed on the column. These were as follows in order of elution: fraction 1, a pink band (10–15% yield); fraction 2, an orange band (10–15% yield), which was incompletely separated from fraction 1; fraction 3, a broad orange band (~60% yield); fraction 4, a pink band (<10% yield), which strongly adhered to the top of the column.

The major band, fraction 3, was collected in a flask seated in an ice–salt–water mixture. After collection, the solution was frozen by immersing the flask in liquid nitrogen to prevent any further reaction. The frozen solution was then freeze-dried. The product was further purified by chromatography down a Sephadex DEAE A-25 column, followed by additional chromatography down the above Bio-Gel P2 column. The freeze-dried orange product's analysis and spectroscopic properties were consistent with the formula $[Co(NH_3)_3(H_{-2}GGGG)]\cdot 2H_2O$. Anal. Calcd for $C_8H_{24}CoN_7O_7$: C, 24.7, H, 6.2; N, 25.2. Found: C, 24.2; H, 6.1; N, 25.3.

Preparation of $NH_4[Co(NH_3)_2(H_{-3}GGGG)]\cdot 2H_2O$. $[Co(NH_3)_3(H_{-2}GGGG)]\cdot 2H_2O$ (30 mg) was dissolved in a minimum of aqueous ammonia at pH 9. The solution was heated at 313 K for 20 h and then chromatographed on a Bio-Gel P2 column as described above. Two orange bands were observed on the column: fraction 1 (~40% yield) was the desired product; fraction 2 (~60% yield) was the starting material. Both fractions were freeze-dried. Fraction 1 had the same chromatographic and spectroscopic properties as the second fraction in the previous preparation. The orange solid from fraction 1, which absorbs on an anion-exchange paper but not on a cation-exchange paper, has an analysis and spectroscopic properties consistent with the formula $NH_4[Co(NH_3)_2(H_{-3}GGGG)]\cdot 2H_2O$. Anal. Calcd for $C_8H_{24}CoN_7O_7$: C, 24.7; H, 6.2; N, 25.2. Found: C, 24.8; H, 6.0; N, 25.4.

Preparation of $[Co(NH_3)_3(H_{-3}GGGGH)](NO_3)_2$. $[Co(NH_3)_3(H_{-2}GGGG)]\cdot 2H_2O$ (30 mg) was dissolved in a minimum of dilute nitric acid at pH 1, and the solution was warmed at 313 K for 1 day. The pink solution that formed was chromatographed on the above Bio-Gel P2 column with dilute nitric acid (pH 2) as eluant to give a single broad pink band. The solution containing this fraction was reduced to about one-tenth its original volume by vacuum rotary evaporation. A pink solid was precipitated from the solution by the addition of acetone and was dried in a vacuum desiccator over P_2O_5. The complex absorbed to a cation-exchange paper but not to an anion-exchange paper. The product's analysis and spectroscopic properties are consistent with the formula $[Co(NH_3)_3(H_{-1}GGGGH)](NO_3)_2$. Anal. Calcd for $C_8H_{22}CoN_9O_{11}$: C, 20.1; H, 4.6; N, 26.3. Found: C, 20.3; H, 4.8; N, 25.9.

Spectroscopic Studies. The UV–visible absorption spectra were measured on a Cary 17 spectrophotometer. For the kinetic studies a 2- or 10-cm flow-through cell was thermostated in a jacketed holder kept at a constant temperature (±0.1°C) with a Colora thermostat. All reactions were monitored at constant wavelength. For systems involving two simultaneous reactions, the kinetics of the reaction to be considered were monitored at the wavelength of an isosbestic point of the other reaction. The isosbestic points were obtained by repetitive scans of the spectrum during the course of the reaction. The kinetic data were processed on the Department's PDP 1134 computer.

The ^{1}H and ^{13}C NMR spectra were recorded on a JEOL FX100 FT NMR spectrometer with a 5-mm $^1H/^{13}C$ dual probe using D_2O as solvent and sodium 3-(trimethylsilyl)propane-1-sulfonate and dioxane (δ 67.4), respectively, as internal references.

Results

Characterization of the Complexes. The major product from the initial preparation of the cobalt(III) tetraglycine complex has an analysis consistent with $[Co(NH_3)_3(H_{-2}GGGG)]\cdot 2H_2O$. The ^{1}H NMR spectrum (Table I) when measured in D_2O acidified to pH 4 with perchloric acid shows that two ammonia molecules give degenerate resonances whereas the third ammonia resonates 0.9 ppm to lower shielding, a chemical shift difference similar to that observed for $[Co(NH_3)_3(H_{-1}GG)]^+$ ($\Delta\delta$ 0.86),[8] in which the three ammonia molecules have a meridional configuration with the central ammonia trans to a peptide nitrogen. The NH_2 group is observed as a triplet in the ^{1}H NMR spectrum with coupling to CH_2-1. If the NH_2 was not coordinated, the protons would exchange too rapidly with the deuterium from the solvent to be observed. The fact that the complex passes freely down an anionic cellulose column and moves with the solvent front on both cation- and anion-exchange papers shows that the complex is neutral. As the complex gives a neutral solution in distilled water, the terminal carboxylate group must be deprotonated, and hence two peptide nitrogens must be deprotonated to balance the charge of cobalt(III). The ^{1}H and ^{13}C NMR data (see below) are consistent with this. The above evidence shows

(7) Davies, R.; Mori, M.; Sykes, A. G.; Weil, J. A. *Inorg. Synth.* **1971**, *12*, 197.

(8) Evans, E. J.; Hawkins, C. J.; Heard, M. R., unpublished results.

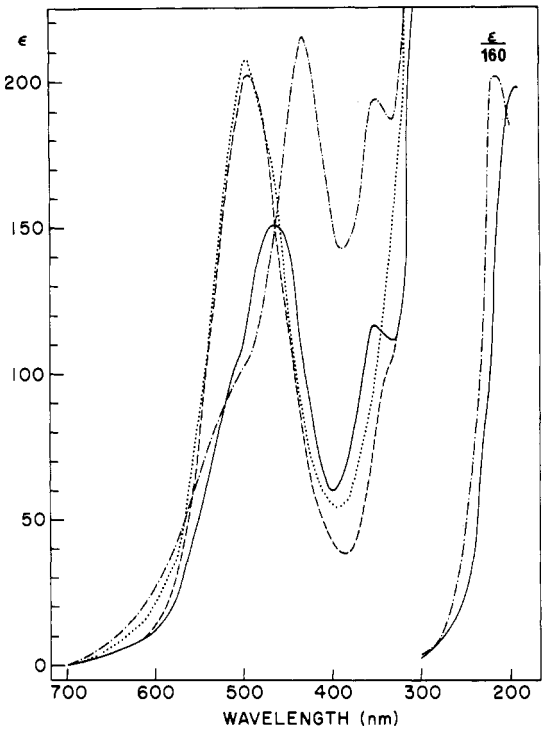


Figure 1. Absorption spectra of (—) $[Co(NH_3)_3(H_{-2}GGGG)]$ in H_2O, (---) $[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ in dilute $HClO_4$ at pH 1, (-·-·) $[Co(NH_3)_2(H_{-3}GGGG)]^-$ in H_2O, and (···) $[Co(NH_3)_2(OH_2)(H_{-1}GGGGH)]$ in dilute $HClO_4$ at pH 1.

that this complex has structure **1a** (see Chart I), in which the terminal NH_2 and two peptide nitrogens are coordinated with three ammonia molecules completing the octahedral coordination in a meridional configuration. Its UV–visible absorption spectrum is given in Figure 1.

When $[Co(NH_3)_3(H_{-2}GGGG)]$ is heated at 313 K in dilute aqueous ammonia at pH 9, a second orange compound is produced with an analysis consistent with $NH_4[Co(NH_3)_2(H_{-3}GGGG)]\cdot 2H_2O$. The complex's anionic character was confirmed by its strong adsorption to a Sephadex DEAE A-25 anion-exchange column and to anion-exchange paper. In the ^1H NMR spectrum (Table I) a peak corresponding to two ammonia molecules was observed at δ 2.31 in a position similar to those of the axial NH_3 resonances in $[Co(NH_3)_2(H_{-2}GGG)]$ (δ 2.50)[3] and in $[Co(NH_3)_3(H_{-2}GGGG)]$ (δ 2.72). The NH_2 group is again observed as a triplet in the ^1H NMR spectrum (Table I) and therefore remains coordinated to cobalt(III). These NMR results taken together with the anionic nature of the complex suggest that the complex has structure **2** with the peptide coordinated through the terminal NH_2 group and three peptide nitrogens. The complete analysis of the ^1H and ^{13}C NMR spectra (see below) supports this structure. The UV–visible absorption spectrum is given in Figure 1. The complex is a base with a pK_a of 4.40 ± 0.08 consistent with the free terminal carboxylate group.

When heated at 313 K in dilute nitric acid at pH 1, $[Co(NH_3)_3(H_{-2}GGGG)]$ yields a pink cationic complex, which absorbs strongly to cation-exchange paper and which has an analysis consistent with $[Co(NH_3)_3(H_{-1}GGGGH)](NO_3)_2$. The isolation of the complex from acid results in the carboxylate being protonated. The change in the UV–visible spectrum (Figure 1) during the reaction with acid is consistent with the replacement of a coordinated nitrogen by an oxygen. Previous work with other metals has shown that when terdentate peptide complexes with structure **1** react with acid the terminally coordinated peptide nitrogen interchanges with its carbonyl with the concomitant protonation of the peptide nitrogen.[4-6] The ^1H and ^{13}C NMR spectra (see below) are also consistent with this occurring here. The coordination of the three ammonia molecules and the NH_2 group is maintained during the reaction. This complex has structure **3a**.

Table II. ^1H Chemical Shift Differences[a] on Protonation and Chelation

compd	CH_2-1	CH_2-2	CH_2-3	CH_2-4
HGGGG[b]	+0.46	+0.03	0.00	+0.02
$HGGGGH^+$ [c,d]	+0.01	+0.01	+0.03	+0.24
$[Co(NH_3)_3(H_{-2}GGGG)]$[b]	+0.12	−0.08	−0.09	−0.01
$[Co(NH_3)_2(H_{-3}GGGG)]^-$ [b]	+0.12	+0.01	+0.01	+0.15
$[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ [c]	+0.06	+0.57	+0.16	+0.23

[a] In ppm from the corresponding resonance for GGGG. [b] In D_2O. [c] In D_2O acidified to pH 1 with perchloric acid. [d] Shift difference is taken relative to the resonance for HGGGG.

^1H NMR Spectra. The ^1H NMR data for the free peptide in its anionic, zwitterionic, and cationic forms and for the three cobalt(III) complexes are given in Table I, and the shifts of the various proton resonances on protonation of the NH_2 and CO_2^- groups and coordination are given in Table II. The data for the free peptide are in good agreement with those published by Beecham and Ham.[9]

Protonation of the free peptide's NH_2 group causes only one resonance to shift significantly. This resonance at δ 3.44 in the anion and δ 3.90 in the zwitterion is assigned to CH_2-1, which is adjacent to the site of protonation. On protonation of the CO_2^- group this resonance does not shift (δ 3.91 for the cation), but the resonances at δ 3.77 and 3.79 in the anion and zwitterion, respectively, shift to δ 4.03 and hence have been assigned to CH_2-4, which is adjacent to the CO_2^- group. The resonance at δ 3.98 in the anion does not shift on protonation of the NH_2 group but shifts 0.03 ppm on protonation of the CO_2^- group. The resonance at δ 4.02 in the anion shifts 0.03 ppm on protonation of the NH_2 and only a further 0.01 ppm on protonation of the CO_2^-. Hence the former resonance is assigned to CH_2-3 and the latter to CH_2-2.

The assignments of the NH_3 and NH_2 resonances in the complexes (Table I) are based on the integrated band intensities, the facility with which the resonances diminish in intensity upon deuteration, and the coupling of the NH_2 resonance to CH_2-1. This coupling also enables CH_2-1 to be assigned to the triplet at approximately δ 3.5. The coupling is confirmed by the observation of a singlet for the NH_2 group when CH_2-1 is irradiated. For $[Co(NH_3)_3(H_{-2}GGGG)]$ and $[Co(NH_3)_2(H_{-3}GGGG)]^-$ the other CH_2 resonances are assigned from the similarity of their positions to those of the free anion. The largest shift ($\Delta\delta$ ±0.15) is experienced by CH_2-4 in the second complex. For $[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ at pH 1 the CO_2^- group is protonated, and the adjacent CH_2-4 should resonate at a position similar to that of the analogous CH_2 in the free cation (δ 4.03). The peak at δ 4.00 is therefore assigned to CH_2-4. The remaining two CH_2 resonances' assignments are based on the premise that the CH_2 in the chelate ring adjacent to the coordinated carbonyl (CH_2-2) should experience a greater shift from its free peptide position than CH_2-3, which is adjacent to the exocyclic NH. The peaks at δ 4.59 and 4.14 are hence assigned to CH_2-2 and CH_2-3.

^{13}C NMR Spectra. The ^{13}C NMR chemical shifts are given in Table III, and the shifts in the positions of the resonances on protonation and chelation are given in Table IV. The ^{13}C NMR spectra of tetraglycine in acid and alkali are in close agreement with the spectra of Christl and Roberts.[10] Because the zwitterion was not previously studied, changes of chemical shift on protonation could not previously give unambiguous assignments for all ^{13}C resonances. However, with all three spectra, it has been possible to assign the resonances for the

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(10) Christl, M.; Roberts, J. D. *J. Am. Chem. Soc.* **1972**, *94*, 4565.

Table III. ^{13}C Chemical Shifts[a] of Tetraglycine and Its Cobalt(III) Complexes

compd	CH_2-1	CO-1	CH_2-2	CO-2	CH_2-3	CO-3	CH_2-4	CO-4
GGGG[b]	44.61	177.44	43.24	173.11	43.24	171.85	44.03	177.33
HGGGG[c]	41.34	168.90	43.33	172.65	43.21	171.80	44.00	177.33
$HGGGGH^+$ [d]	41.34	168.70	43.23	172.65	43.12	172.63	41.85	174.02
$[Co(NH_3)_3(H_{-2}GGGG)]$[c]	47.79	179.02	49.61	182.95	47.96	173.97	44.15	177.67
$[Co(NH_3)_2(H_{-3}GGGG)]^-$ [c]	50.08	178.85	51.19	180.16	50.67	180.66	48.64	178.09
$[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ [d]	50.08	178.82	50.32	185.58	43.94	171.15	42.01	174.08

[a] In ppm from Me_4Si. [b] In dilute NaOD at pH 9.5. [c] In D_2O. [d] In D_2O acidified to pH 1 with perchloric acid.

Table IV. ^{13}C Chemical Shift Differences[a] on Protonation and Chelation

compd	CH_2-1	CO-1	CH_2-2	CO-2	CH_2-3	CO-3	CH_2-4	CO-4
HGGGG[b]	−3.27	−8.54	+0.09	−0.46	−0.03	−0.05	−0.03	0.00
$HGGGGH^+$ [c,d]	0.00	−0.20	−0.10	0.00	−0.09	+0.83	−2.15	−3.31
$[Co(NH_3)_3(H_{-2}GGGG)]$[b]	+3.18	+1.58	+6.37	+9.84	+4.72	+2.12	+0.12	+0.34
$[Co(NH_3)_2(H_{-3}GGGG)]^-$ [b]	+5.47	+1.41	+7.43	+7.05	+7.95	+8.81	+4.61	+0.76
$[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ [c]	+5.47	+1.38	+7.08	+12.47	+0.70	−0.70	−2.02	−3.25

[a] In ppm from corresponding resonance for GGGG. [b] In D_2O. [c] In D_2O acidified to pH 1 with perchloric acid. [d] Shift difference is taken relative to the resonance for HGGGG.

free peptide by comparison with shifts induced in the corresponding resonances for triglycine. Protonation of the NH_2 group of the triglycine anion causes the resonances to shift as follows: CH_2-1, −3.35; CO-1, −8.69; CH_2-2, +0.08; CO-2, −0.45; CH_2-3, +0.03; CO-3, −0.02.[3] Hence for tetraglycine only one CH_2 resonance (CH_2-1) is expected to have a marked shift. The CH_2-1 resonance is therefore assigned to the peaks at δ 44.61 and 41.34 in the spectra of the anion and zwitterion, respectively. The corresponding peaks for triglycine are at δ 44.67 and 41.32.[3] In the carbonyl region for triglycine CO-1 and CO-2 shift 8.69 and 0.45 ppm, respectively, to higher shielding protonation, whereas CO-3, which is removed from the site of protonation, does not shift significantly.[3] For tetraglycine, two resonances, δ 171.85 and 177.33, do not shift significantly whereas another shifts 8.54 ppm and the fourth shifts 0.46 ppm to higher shielding on protonation of the anion. These latter two resonances are hence assigned to CO-1 and CO-2, respectively. The close correspondence in the shifts of CH_2-1, CO-1, and CO-2 for the two peptides suggests CH_2-2 should also have a similar shift for the two peptides. There are two possible assignments for CH_2-2 in the zwitterion, 43.33 or 43.21 ppm with shifts of +0.09 or −0.03 ppm. As the corresponding shift for triglycine is +0.08, CH_2-2 is assigned to the 43.33-ppm peak in the spectrum of the zwitterion.

For $[Co(NH_3)_3(H_{-2}GGGG)]$ CH_2-4 and CO-4 should not be shifted to any marked extent from their positions in the tetraglycine anion, and therefore the resonances at δ 44.15 and 177.67 are assigned to CH_2-4 and CO-4, respectively. The shifts on chelation for CH_2-1, CO-1, CH_2-2, and CO-2 should be similar to those for $[Co(NH_3)_2(H_{-2}GGG)]$, for which shifts of +3.18, +1.63, +7.93, and +6.90 ppm were found.[3] The predicted positions for the tetraglycine complex would be 47.79, 179.07, 51.17, and 180.01 ppm. The agreement with observed positions (47.79 and 179.02 ppm) is excellent for CH_2-1 and CO-1. On the basis of the predicted values CH_2-2 and CO-2 are assigned to the resonances at 49.61 and 182.95 ppm, respectively, and hence the remaining carbons, CH_2-3 and CO-3, are assigned to the peaks at δ 47.96 and 173.97. With use of the same technique to assign the peaks in the spectrum of $[Co(NH_3)_2(H_{-3}GGGG)]^-$, CO-1, CH_2-2, and CO-2 are assigned to δ 178.85, 51.19, and 180.16. With use of off-resonance decoupling of the CH_2-1 protons, the peak at 50.08 is assigned to $^{13}CH_2$-1. As CH_2-4 and CO-4 are not expected to shift markedly, these resonances have been assigned to δ 48.64 and 178.09, respectively. The remaining resonances, CH_2-3 and CO-3, are hence assigned to the peaks at δ 50.67 and 180.66. For $[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ the positions of CH_2-4 and CO-4 should be similar to those in the peptide cation, and therefore they are assigned to the peaks at δ 42.01 and 174.08. As two peaks occur at the same positions as CH_2-1 and CO-1 in the spectrum of $[Co(NH_3)_2(H_{-3}GGGG)]^-$, they are assigned to these resonances. Consistent with the carbons in the other chelate rings, CH_2-2 and CO-2 should show large shifts, and therefore they are assigned to peaks at δ 50.32 and 185.58, respectively. As CH_2-3 and CO-3 are not in a chelate ring and are not adjacent to a deprotonated peptide nitrogen, their resonances should not be markedly shifted from the free peptide positions. Consistent with this their resonances are assigned to the peaks at δ 43.94 and 171.15, respectively.

Kinetic Studies. (i) Coordination Rearrangement for $[Co(NH_3)_3(H_{-2}GGGG)]$. When a solution of $[Co(NH_3)_3(H_{-2}GGGG)]$ is placed in dilute perchloric acid, a slow, one-step reaction takes place. The repetitive-scan spectra of the reaction show two well-defined isosbestic points at 463 and 349 nm. The proposed reaction corresponds to the interconversion of structure **1a** to **3a**. The kinetics of the reaction were followed at 495.0 nm as a function of temperature with a constant acid strength of 0.115 M perchloric acid and as a function of acid concentration at 298 K, with a constant ionic strength of 0.25 for both experiments.

The rate of the reaction is given by

$$\text{rate} = k_{obsd}[\text{complex}] \quad (1)$$

The values of k_{obsd} were calculated from the slope of the linear plots of ln $(\epsilon_t - \epsilon_\infty)$ vs. time, where ϵ_t is the molar extinction coefficient at time t, and ϵ_∞ is the molar extinction coefficient observed when no further change in absorbance was observed. The values of k_{obsd} obtained for 0.115 M acid at 297.6, 302.0, 307.0, and 313.0 K are 1.28×10^{-5}, 2.14×10^{-5}, 4.23×10^{-5}, and 8.86×10^{-5} s^{-1}. The results for the acid-dependence study are given in Figure 2.

The reaction involves the rapid preliminary protonation of the peptide group followed by the slow replacement of the coordinated peptide nitrogen by the carbonyl group.[4,6] If the acid dissociation constant is K_a, and the rate of donor-group interchange is k, the observed rate constant, k_{obsd}, is given by

$$k_{obsd} = k[H^+]/(K_a + [H^+]) \quad (2)$$

A good fit to the experimental data determined at 298 K (Figure 2) is obtained with $k = 2.5 \times 10^{-5}$ s^{-1} and $K_a = 0.1$ M.

(ii) Ring-Opening Reaction for $[Co(NH_3)_2(H_{-3}GGGG)]^-$. When fully chelated $[Co(NH_3)_2(H_{-3}GGGG)]^-$ is placed in dilute acid, there is an initial fast change in the UV–visible absorption spectrum, and this is followed by a much slower

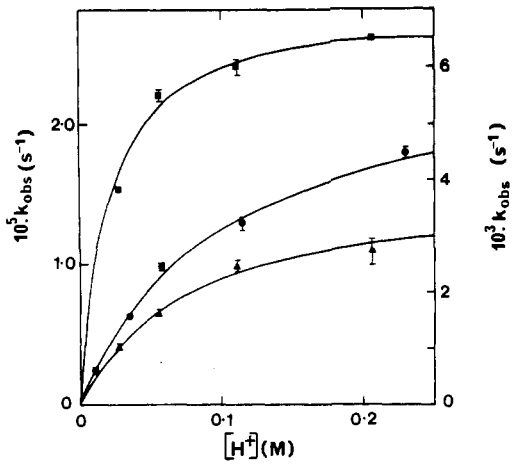

Figure 2. Plots of k_{obsd} vs. $[H^+]$ at 298 K and $I = 0.25$ for (i) the reaction of $[Co(NH_3)_3(H_{-2}GGGG)]$ with acid (●), (ii) the ring-opening reaction in acid of $[Co(NH_3)_2(H_{-3}GGGG)]^-$ (■), and (iii) the reaction of $[Co(NH_3)_2(OH_2)(H_{-2}GGGG)]$ with acid (▲). The solid lines are calculated from eq 2 with the following values for k and K_a: (i) 2.5×10^{-5} s^{-1}, 0.1 M; (ii) 7.2×10^{-3} s^{-1}, 0.02 M; (iii) 1.6×10^{-5} s^{-1}, 0.08 M. The left-hand ordinate relates to reactions i and iii, and the right-hand ordinate relates to reaction ii. The standard deviations are given by the error bars. For some points the errors are smaller than the symbol.

change with the formation of well-defined isosbestic points at about 350 and 484 nm. The proposed reaction is

$$\mathbf{2} \xrightarrow[H^+]{k_1\ (\text{fast})} \mathbf{1b} \xrightarrow[H^+]{k_2\ (\text{slow})} \mathbf{3b}$$

The kinetics of the initial reaction were followed with use of a stopped-flow apparatus at the wavelength corresponding to the isosbestic point at about 350 nm. This wavelength varied with the acid concentration. Values of k_1 were determined from the slope of the linear plots of ln $(\epsilon_t - \epsilon_\infty)$ vs. time. The kinetics were studied with a perchloric acid concentration of 0.115 M ($I = 0.25$) as a function of temperature. The values of k_1 obtained at 293.0, 298.2, 302.8, and 308.0 K were 0.38×10^{-2}, 0.60×10^{-2}, 1.15×10^{-2} and 1.95×10^{-2} s^{-1}. The stopped-flow kinetics were also studied as a function of acid concentration at 298 K ($I = 0.25$). The results are given in Figure 2.

As has been found for tetraglycine and tetraglycinamide complexes of other metals,[4,11,12] the acid dependence of the rate is consistent with an initial protonation followed by dissociation of the coordinated peptide group. With use of eq 2 a good fit to the experimental data is obtained with $k = 7.2 \times 10^{-3}$ s^{-1} and $K_a = 0.02$ M.

(iii) Coordination Rearrangement for $[Co(NH_3)_2(OH_2)(H_{-2}GGGG)]$. The ring-opened product from the reaction of $[Co(NH_3)_2(H_{-3}GGGG)]^-$ with acid undergoes a subsequent reaction as reported above for $[Co(NH_3)_3(H_{-2}GGGG)]$. The kinetics of the reaction were followed spectrophotometrically at an isosbestic point for the first reaction (~500 nm) as a function of acid concentration at 298 K. The results are given in Figure 2. A line calculated from eq 2 with $k = 1.6 \times 10^{-5}$ s^{-1} and $K_a = 0.08$ M gives a good fit to the experimental data.

Discussion

The visible absorption spectra of the three metal complexes (Figure 1) are consistent with the proposed structures. As the spectrochemical parameters for the donor groups have the order $\Delta_{N^-} > \Delta_{NH_2R} > \Delta_{NH_3} > \Delta_{CO_2^-}$,[13] it is expected that the position of the $^1A_{1g} \rightarrow {}^1T_{1g}$ absorption band for the cobalt(III) chromophore would be at increasing wavelengths for the complexes $[Co(NH_3)_2(H_{-3}GGGG)]^-$, $[Co(NH_3)_3(H_{-2}GGGG)]$, and $[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$. The λ_{max} values do follow this order: 433, 464, and 492 nm. Although the differences in the low-symmetry splitting of the $^1A_{1g} \rightarrow {}^1T_{1g}$ absorption complicate a quantitative comparison of the positions of this band, the positions of the total absorption bands are seen to follow the above order. The close similarity in the spectra of $[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ and $[Co(NH_3)_3(H_{-1}GG)]^+$ (λ_{max} 489 nm)[14] is further confirmation of the proposed structures. The spectrum of the product of the reaction of $[Co(NH_3)_2(H_{-3}GGGG)]^-$ with acid, $[Co(NH_3)_2(OH_2)(H_{-1}GGGGH)]^{2+}$ (structure **3b**) shows a maximum at 498 nm with an ill-defined shoulder above 550 nm. This spectrum is similar to the spectrum of the product of the reaction of $[Co(NH_3)_2(H_{-2}GGG)]$ with acid, $[Co(NH_3)_2(OH_2)(H_{-1}GGGH)]^{2+}$ (λ_{max} 503 nm),[8] which has the same donor groups bound to Co(III) as $[Co(NH_3)_2(OH_2)(H_{-1}GGGGH)]^{2+}$.

The protonations of the NH_2 and CO_2^- groups of tetraglycine cause the adjacent CH_2 ^1H resonances to shift about 0.5 and 0.2 ppm to lower shielding, respectively. These shifts correspond to the shifts found for the corresponding resonances in tripeptides.[3] The other CH_2 resonances shifted by 0.03 ppm or less by the protonations. Coordination of the terminal NH_2 in the Co(III) chelates has a much smaller effect ($\Delta\delta$ +0.1) than protonation. The effects of chelation on the other CH_2 resonances differ for the three complexes studied. In each complex CH_2-2 is adjacent to a deprotonated coordinated peptide nitrogen. In $[Co(NH_3)_3(H_{-2}GGGG)]$ this causes the resonance to shift to higher shielding by 0.1 ppm. In the quadridentate chelate the shift is only +0.01 ppm, but in the complex where CO-2 is coordinated, the shift is +0.57 ppm. Similar differences in shifts to those found for CH_2-2 occur for CH_2-3 except for $[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ ($\Delta\delta$ +0.16), where CH_2-3 is adjacent to an uncoordinated peptide NH.

For the ^{13}C NMR spectra the effects of the protonations of the terminal groups are again very similar to those for triglycine. For the protonation of the NH_2 group for both peptides the resonances are shifted as follows: CH_2-1, −3.3; CO-1, −8.6; CH_2-2, +0.1; CO-2, −0.45; other resonances, ≤±0.05 ppm. For the formation of the protonated carboxylate for both peptides, the C-terminal CO and CH_2 shift 3.3 and 2.2 ppm to higher shielding, respectively, whereas the adjacent CO resonates 0.8 ppm to lower shielding. All other shifts are 0.2 ppm or less in magnitude. Possible reasons for the changes on protonation have been discussed previously.[10,15-18] Whereas the major shifts on protonation of peptides are to higher shielding, coordination has a large deshielding effect on the various chelate ring carbons. There is correspondence again between the shifts experienced by tetraglycine and triglycine[3] for similar modes of coordination. Within the chelate rings the smallest effect is in the N-terminal residue. For $[Co(NH_3)_2(H_{-2}GGG)]$ and $[Co(HN_3)_3(H_{-2}GGGG)]$ CH_2-1 and CO-1 shift +3.2 and +1.6 ppm. For the other two tetraglycine complexes these resonances shift +5.5 and +1.4 ppm. The carbons in chelate rings with two peptide group donors show particularly large shifts: $[Co(NH_3)_2(H_{-2}GGG)]$, CH_2-2 +7.93, CO-2 +6.90;[3] $[Co(NH_3)_3(H_{-2}GGGG)]$, CH_2-2 +6.37,

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CO-2 +9.84; $[Co(NH_3)_2(H_{-3}GGGG)]^-$, CH_2-2 +7.43, CO-2 +7.05, CH_2-3 +7.95, CO-3 +8.81; $[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$, CH_2-2 +7.08, CO-2 +12.47 ppm. The last resonance corresponds to a coordinated carbonyl. Coordinated peptide carboxylates also show large shifts.[3] The CH_2 resonances for groups adjacent to deprotonated peptide nitrogen donors that either are exocyclic or are in a terminal carboxylate chelate ring, as found in the tripeptide complexes, experience shifts of the order of +4.7 ppm. In $[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ the carboxylate is protonated and CH_2-4 and CO-4 show shifts to higher shielding similar to those experienced by the free peptide. The shift of the CO-3 resonance in this complex of 0.7 ppm to higher shielding is somewhat surprising as in the free peptide the protonation of the carboxylate causes this resonance to shift 0.83 ppm to lower shielding and all shifts caused by chelation are to lower shielding. This shift perhaps reflects a specific orientation of this group in the complex.

Paniago and Margerum[4] have proposed a general mechanism for the protonation of all metal peptide and amide complexes:

$$MH_{-n}L + HX \underset{K_a}{\rightleftharpoons} M(H_{-n}L)H + X^-$$

$$M(H_{-n}L)H \xrightarrow[k]{} M(H_{-n+1}L)$$

The species written as $M(H_{-n}L)H$ is an intermediate protonated complex formed without the cleavage of any M–N bonds. Its formation was termed "outside protonation". The reaction in this paper is consistent with this mechanism. Protonation of a coordinated peptide group is known to occur at the carbonyl oxygen,[19] giving rise to structure **4**, in which there is an increase in the C–N double-bond character and in which the M–N bond length has been lengthened. Margerum and his co-workers[4-6] suggest that, although **4** is thermodynamically preferred, structure **5** may be kinetically important.

The present study of the reaction of $[Co(NH_3)_3(H_{-2}GGGG)]$ in acid to yield $[Co(NH_3)_3(H_{-1}GGGGH)]^{2+}$ gives a quantitative measure of the acid dissociation constant for the protonation of the coordinated "terminal" peptide group for a terdentate peptide. The pK_a value of 1 is of a similar order of magnitude to the value of 0.5 found by Rabenstein[20] for the "central" peptide group in $[Co(H_{-1}GG)_2]^-$. The subsequent interchange between N and O coordination proceeds at a much slower rate than for the more labile metals that have been studied previously.[4-6,11,12]

The ligand cis to the interchanging peptide group has a small effect on the rate of reaction. In a comparison of the kinetic data for $[Co(NH_3)_3(H_{-2}GGGG)]$ and $[Co(NH_3)_2(OH_2)(H_{-2}GGGG)]$, in which this ligand is NH_3 and H_2O, respectively, it is seen that the K_a values for the protonation of the terminal peptide are similar (0.1 and 0.08 M, respectively) but the ammine complex (2.5×10^{-5} s^{-1}) reacts at a faster rate than the aqua complex (1.6×10^{-5} s^{-1}).

At the acid concentrations of these kinetic studies ($0.025 < [H^+] < 0.25$ M) the free carboxylate group is protonated, and the terminal peptide group (CO-2) is partially protonated. The carbonyl CO-1 might also be partially protonated although, if the value of the pK_a (0.5)[20] for the corresponding peptide group in $[Co(H_{-1}GG)_2]^-$ is a good indication of the basicity of CO-1, it would be much less protonated than CO-2. Of course, CO-1 is remote from the site of reaction and its protonation probably does not seriously affect the rate of this reaction.

The products of these reactions, in which the peptides are bound to Co(III) as a terdentate chelate via the NH_2, a peptide nitrogen, and a peptide oxygen, are inert to further reaction in dilute acid. This has been found by Rabenstein for a glycylglycine complex in which the terdentate chelate is bound to Co(III) via the NH_2, a peptide nitrogen, and the CO_2^-.[20] In contrast, in the corresponding complexes with the more labile metals such as Cu(II), Ni(II), and Pd(II), the peptide continues to unwrap from the metal in acid.[4-6,11,12]

For the quadridentate chelate $[Co(NH_3)_2(H_{-3}GGGG)]^-$ the M–N to M–O interchange reaction is not observed for the terminal peptide. Instead, the peptide group dissociates from the Co(III) rapidly in acid. The lability of this group could be associated with the trans coordination of a peptide nitrogen or with the strain in the 5,5,5 chelate ring system. Freeman and his co-workers have shown that for Cu(II)[21] and Ni(II)[22] the terminal $M-N^-$ bond for the quadridentate tetrapeptide complexes is significantly longer than the other two $M-N^-$ bonds. This increased bond length and the large size of the angle between the $M-NH_2$ and the terminal $M-N^-$ bonds in the quadridentate complexes (Cu(II) 109.8°;[21] Ni(II) 104.5, 103.2°[22]) reflect the strain in the terminal peptide chelate ring.

The complex $[Co(NH_3)_2(H_{-3}GGGG)]^-$ has a number of potential sites for protonation. The carboxylate group is uncoordinated and has a pK_a of 4.4 to be compared with 4.3[12] and 4.2[4] for the corresponding Cu(III) and Ni(II) complexes and with 3.2[23] for the free peptide. The terminal coordinated peptide group has a pK_a of 1.7, which is similar to that estimated for the corresponding Ni(II) complex.[11] In higher acid concentrations both CO-2 and CO-1 are protonated, but as these are remote from the site of the ring-opening reaction, these protonations are not expected to have a major effect on the rate of the dissociation of the terminal peptide group.

The rates of both types of reaction studied here are sensitive to temperature with an approximate doubling of the rate every 5 K increase in temperature.

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Registry No. **1a**, 82522-16-5; **2**, 82536-77-4; **3a**, 82536-80-9; $[(NH_3)_5Co(O_2)Co(NH_3)_5](NO_3)_4$, 16632-71-6.

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