A possible reason for this changeover of oxidation pattern of the Mo(IV) complexes from a single- to a two-electron process is still not clear to us. Initially when we first observed this phenomenon in the butyl derivative (**5c**), we were under the impression that the size of the alkyl group had a possible role to play for this two-electron process. This has prompted us to investigate the *n*-hexyl derivative (**5d**), which only produced a one-electron-oxidation wave.

Concluding Remarks. Oxygen-transfer reactions have been successfully employed here to get a number of molybdenum compounds in the oxidation states VI, V, and IV. The sequential abstraction of oxygen atoms in going from $MoO_2(L\text{-}R)_2$ to $Mo(L\text{-}R)_2(L\text{-}H)_2$ is clearly manifested in their IR spectra (Figure 1). Mo(IV) compounds constitute the first reported example of a series of complexes with an MoS_8 chromophore having a spin triplet ground state. Electron-transfer behavior of the reported complexes show a complete changeover from an initial irreversible to a perfectly reversible type via a quasi-reversible stage as the oxygen atoms are depleted successively from the *cis*-O_2 Mo^{VI} moiety. Alkyl substitution in the ligand framework appears to have very little effect upon their magnetic, spectroscopic, and electrochemical properties except in the redox behavior of $Mo(L\text{-}Bu)_2(L\text{-}H)_2$, where a single-step two-electron reversible oxidation (Mo(IV)-(Mo(VI)) is observed. Similar redox behavior involving simultaneous two-electron transfer is well-known for many biochemical reactions catalyzed by molybdenum enzymes.[51]

Acknowledgment. Thanks are due to Dr. K. Nag for many helpful suggestions and to Dr. P. Ghosh for assistance in the electrochemical experiments. I am indebted to Professor A. Chakravorty for use of the electrochemical equipment.

Registry No. **2a**, 97316-06-8; **2b**, 97316-07-9; **3a**, 97316-08-0; **3b**, 97316-09-1; **3c**, 97316-10-4; **3d**, 97316-11-5; **4a**, 97316-12-6; **4b**, 97316-13-7; **4c**, 97316-14-8; **4d**, 97316-15-9; **5a**, 97316-16-0; **5b**, 97316-17-1; **5c**, 97316-18-2; **5d**, 97316-19-3; $MoO_2(acac)_2$, 17524-05-9; $MoO_2(L\text{-}Et)_2$, 89742-19-8; $MoO_2(L\text{-}Bu)_2$, 89742-20-1; $Mo^VO_2(L\text{-}Pr)_2^-$, 97316-20-6; $Mo^VO_2(L\text{-}Hx)_2^-$, 97316-21-7; $Mo^VOCl_2(L\text{-}Et)_2^-$, 97316-22-8; $Mo^VOCl_2(L\text{-}Pr)_2^-$, 97316-23-9; $Mo^VOCl_2(L\text{-}Bu)_2^-$, 97316-24-0; $Mo^VOCl_2(L\text{-}Hx)_2^-$, 97316-25-1; $Mo^{III}(L\text{-}Et)_2(L\text{-}H)_2^-$, 97316-26-2; $Mo^{III}(L\text{-}Pr)_2(L\text{-}H)_2^-$, 97316-27-3; $Mo^{III}(L\text{-}Hx)_2(L\text{-}H)_2^-$, 97316-28-4; $Mo^V(L\text{-}Et)_2(L\text{-}H)_2^+$, 97316-29-5; $Mo^V(L\text{-}Pr)_2(L\text{-}H)_2^+$, 97316-30-8; $Mo^V(L\text{-}Hx)_2(L\text{-}H)_2^+$, 97316-31-9; $Mo^{VI}(L\text{-}Bu)_2(L\text{-}H)_2^{2+}$, 97316-32-0.

Supplementary Material Available: A listing of analytical data for the compounds (Table I) (1 page). Ordering information is given on any current masthead page.

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Formation and NMR Spectra of Platinum(II)-Tripeptide Complexes

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Triglycine (G_3^-) reacts with $PtCl_4^{2-}$ to give complexes with two deprotonated-N(peptide) bonds to Pt(II). Three species, with relative concentrations $Pt^{II}(H_{-2}G_3)Cl^{2-} > Pt^{II}(H_{-2}G_3)^- > Pt^{II}(H_{-2}G_3)(OH)^{2-}$, are identified from ^{13}C, ^1H, and ^{195}Pt NMR and the measurement of released Cl^- and H^+. These complexes cause an enormous upfield shift of −7144 to −7517 ppm in ^{195}Pt NMR peaks (relative to $PtCl_6^{2-}$). This shift is much larger than that caused by cyanide ion in $Pt(CN)_4^{2-}$ and indicates the high donor strength of the deprotonated-N(peptide) group. The pK_a of the peptide group, when it bonds to Pt(II), is between 1 and 2 in the presence of $\sim 4 \times 10^{-4}$ M Cl^-. The acid dissociation rate constant of the $Pt^{II}(H_{-2}G_3)Cl^{2-}$ complex increases from 6×10^{-5} s^{-1} in 0.10 M acid to 3×10^{-3} s^{-1} in 2.5 M acid. The CD spectra of complexes with GAG^- and GGA^- (A = L-alanyl) also indicate the coordination of two deprotonated peptide nitrogens to platinum.

Introduction

There has been a great deal of interest in the bioinorganic complexes of platinum(II)[1] since the first report[2] of the antitumor activity of *cis*-diamminedichloroplatinum(II). Much of the work has concerned platinum(II) complexes of nucleotides,[3-5] amino acids,[6] and peptide esters.[7]

Several dipeptide complexes have been found that contain deprotonated peptide nitrogens bound to platinum. The crystal structure[8,9] of $Pt^{II}(H_{-1}GM)Cl^-$ shows that the amine nitrogen, peptide nitrogen, and thioether sulfur are coordinated. On the basis of IR and elemental analysis data, a similar complex forms with L-alanyl-L-methionine (AM^-).[10] Diglycine (G_2^-) forms a bis complex, *trans*-$[Pt(G_2)_2Cl_2^{2-}]$, which on the addition of hot KOH solution yields *trans*-$[Pt^{II}(H_{-1}G_2)_2^{2-}]$.[11] Dipeptides have also been shown to bridge two Zeise's salt ($K[PtCl_3(C_2H_4)]$) residues. Coordination is through the amine nitrogen and peptide oxygen to one platinum(II) and through the peptide nitrogen and carboxylate oxygen to the second platinum(II).[12]

Is is surprising, given the work with dipeptide complexes, that no tripeptide (L^-) complexes of the form, $Pt^{II}(H_{-2}L)^-$, have been reported. Deprotonation of the peptide nitrogen to form Pt^{II}-

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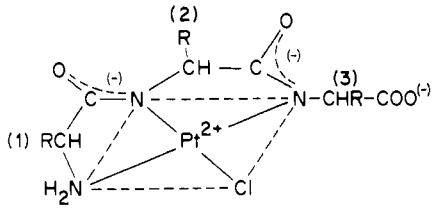
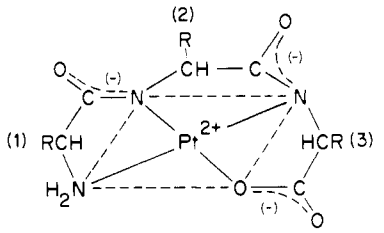
$(H_{-1}GM)Cl^-$ occurs below pH 2.5 in the presence of Cl^- ion.[8] The peptide N-coordination with Pt(II) thus appears to be more favorable than other metal peptides where the deprotonation pH is higher: Pd(II), pH 2.5–3.5;[13,14] Cu(II), pH 5–6;[15–17] Ni(II), pH 8–9.[18–20] The effective ionic radii of four-coordinate, square-planar M(II) ions are as follows: Pt(II), 74 pm; Pd(II), 78 pm; Cu(II), 71 pm; Ni(II), 63 pm.[21] Since Pd(II), Cu(II), and Ni(II) form strong complexes with tripeptides[13–20,22] and their ionic radii are comparable to that of Pt(II), we felt that similar complexes should form with Pt(II). The sluggish nature of the substitution reactions may have hindered previous investigations, because hydrolysis of the peptides as well as hydrolysis of platinum can interfere with the formation of $Pt(H_{-2}L)^-$ species.

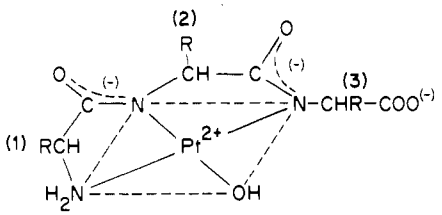
Evidence is given in this work for the formation of 1:1 tripeptide complexes with two deprotonated-N peptide bonds to platinum(II). The proposed structures of the triglycine (G_3^-) complexes (in order of their abundance in solution) are $Pt^{II}(H_{-2}G_3)Cl^{2-}$ (I), $Pt^{II}(H_{-2}G_3)^-$ (II), and $Pt^{II}(H_{-2}G_3)OH^{2-}$ (III). All have cis-deprotonated-N peptide bonds to platinum. Assignment of these structures is based on ^{195}Pt, ^{13}C, and ^1H NMR spectra, circular dichroism (CD) spectra of GAG^- and GGA^- complexes, and measurements of the concentration of Cl^- and H^+ released when the complexes form from $PtCl_4^{2-}$.



I $Pt^{II}(H_{-2}G_3)Cl^{2-}$ for R=H



II $Pt^{II}(H_{-2}G_3)^-$ for R=H



III $Pt^{II}(H_{-2}G_3)OH^{2-}$ for R=H

Experimental Section

Chromatographically pure peptides were obtained from Bachem (GGA and GAG) and United States Biochemical Corp. (G_3).

Solutions of platinum(II)–peptide complexes were prepared by addition of 2–100% excess tripeptide to slightly acidic solutions of K_2PtCl_4 (Strem Chemicals). The pH was adjusted with NaOH and maintained between pH 6 and 7 for 24 h, after which time hydroxide was no longer consumed. It was important to keep the pH below 7 to minimize hydrolysis of the platinum. All measurements were performed between 24 and 30 h after reaction was begun and without separation of the product mixture.

Chloride determinations were based on a spectrophotometric method where the absorbance of $FeCl^{2+}$, formed by the reaction of Fe^{3+} with Cl^-, was monitored at 348 nm.[23] The platinum(II)–tripeptide complexes decompose ($k_{obsd} = 3 \times 10^{-3}$ s^{-1} for the triglycine complex) in the 2.5 M $HClO_4$ required for this determination. Therefore, the reactions were carried out on a stopped-flow spectrophotometer, and the absorbance values were extrapolated back to the mixing time. Neglecting decomposition and performing determinations on a spectrophotometer gave Cl^- concentrations 12% lower than those obtained on the stopped-flow apparatus.

The number of moles of hydroxide ion consumed due to formation of the platinum(II)–triglycine complexes was determined by potentiometric titration. Equilibrium was not always fully established prior to the addition of each increment of titrant, so this experiment could not be used to calculate exact pK values. The apparatus consisted of an Orion Research Model 701A digital ion analyzer equipped with a Corning 476051 combination electrode. Due to the sluggish formation of the platinum(II)–tripeptide complexes, titrant (NaOH) was added slowly, over a period of 24–26 h, by means of an infusion pump (Harvard Apparatus No. 975). The titration vessel was thermostated at 25.0 ± 0.2 °C, and a stream of Ar saturated with H_2O was blown over the top of the solution to minimize carbonate error. Sufficient titrant was added during the course of the titration to bring the solution to pH 9, 1 pH unit above the pK_a value of 7.88 for the triglycine ligand.[20]

The concentration of unreacted triglycine present in solutions of platinum(II)–triglycine was measured chromatographically on a Sephadex A-25 anion-exchange column (10 × 1.5 cm) using a 0.020 M phosphate buffer (pH 6.0) eluent and a UV detector (λ = 210 nm). The triglycine eluted well before the platinum(II) complexes.

Circular dichroism measurements were made on a Cary Model 61 CD spectropolarimeter. UV–vis spectra were recorded on a Perkin-Elmer 320 spectrophotometer equipped with a Perkin-Elmer 3600 data station. Kinetics were measured at 25.0 ± 0.2 °C (λ = 235 nm) on a Cary Model 16 spectrophotometer.

FT-NMR spectra were recorded on a Varian XL-200 (^{13}C and ^{195}Pt) and a Nicolet NT-200 (^1H) spectrometer. In all cases, D_2O was the solvent and the total concentration of platinum was 0.25 M. Tetramethylsilane (Me_4Si) was used as an external reference for ^{13}C NMR. Deuterated TSP, $(CH_3)_3Si(CD_2)_2CO_2Na$, was added as a reference for ^1H NMR. The ^{195}Pt NMR lines were referenced to $PtCl_6^{2-}$. Spectrometer frequencies were 200.066 927, 50.3090, and 42.7359 MHz for ^1H, ^{13}C, and ^{195}Pt NMR, respectively. Pulse widths of 8.0 μs with a delay of 0.5 s produced well-resolved ^{195}Pt spectra after 1000 transients.

The number of platinum(II)–triglycine products indicated by ^{195}Pt NMR was confirmed chromatographically. Products were first separated from reactants by size-exclusion chromatography on a Bio-Gel P-2 column (100–200 mesh, 60 × 2.5 cm) with H_2O elution. A Varian Techtron 635 series UV–vis spectrophotometer with flow cell was used as a detector (λ = 230 nm). Further separation of the platinum complexes was performed by ion-pair chromatography on an IBM Instruments LC/9533 liquid chromatograph equipped with a LC/9523 variable-wavelength UV detector (set at 206 nm) and a Hewlett-packard 3390A integrator. The column was a Waters Associates Radial-PAK 10μ C_{18} μ-Bondapak cartridge in a Waters Associates RCM-100 radial compression unit. The eluent was Waters Associates PIC B-8 ion-pairing reagent (1.0×10^{-3} M).

Presence of platinum in chromatographic bands was tested for by a spot test[24] based on the reaction of acidic $SnCl_2$ with platinum(II). A yellow-orange spot is a positive test.

Results and Discussion

In the course of the reaction of tripeptide with $PtCl_4^{2-}$, the color of the solution changes from red to yellow and the pH of the solution decreases. Absorbance spectra of the platinum(II)

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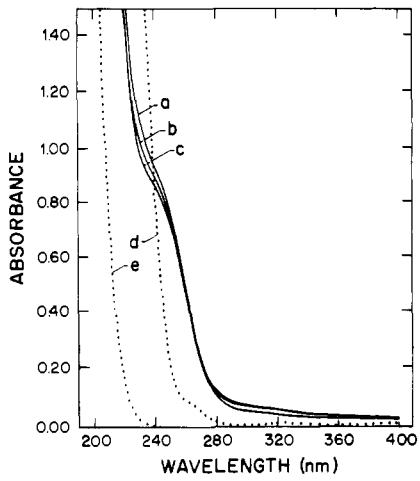

Figure 1. UV–vis spectra of the platinum(II) complexes of (a) G_3, (b) GAG, and (c) GGA, and of (d) $PtCl_4^{2-}$, and (e) G_3. $[Pt]_T = 2 \times 10^{-4}$ M, $[L] = 3 \times 10^{-4}$ M, pH = 6, and path length = 1.0 cm.

complexes of G_3^-, GAG^-, and GGA^- are shown in Figure 1. As is the case for the absorbance maxima of nickel(II)–tripeptide complexes,[25] the λ_{max} of the platinum(II) complexes is not particularly sensitive to the identity of the tripeptide. The shoulders in these spectra occur at approximately the same wavelength as the λ_{max} of $Pt^{II}(H_{-1}G_2)_2^{2-}$ (250 nm, $\epsilon = 9000$ M^{-1} cm^{-1}).[11] Molar absorptivities of the tripeptide complexes are approximately 5100 M^{-1} cm^{-1} (based on the total concentration of platinum present in solution).

Only one tripeptide is coordinated to each platinum(II) ion in solution. This was determined by the reaction of G_3^- with $PtCl_4^{2-}$ in the molar ratios (G_3:Pt) 1:1 and 2:1. After 24 h, the concentration of uncoordinated triglycine was determined chromatographically for each solution. In both cases, the amount of free G_3^- recovered was in agreement with a 1:1 platinum(II)–triglycine complex.

The number of platinum(II) complexes present in solution was determined chromatographically and by ^{195}Pt NMR spectroscopy. Chloride and excess triglycine were separated from the platinum-containing complexes by size-exclusion chromatography. The platinum complexes were further separated by ion-pair chromatography and gave three elution peaks (a large one at 2.1 min, a small peak at 2.5 min, and a very small peak at 3.2 min for flow rates of 1.0 mL/min). If similar molar absorptivities are assumed for each species, the first complex eluted contains ~84% of the platinum followed by complexes that contain ~15% and ~1% of the platinum. Attempts to separate these three complexes on a preparative scale in order to allow further characterization of each complex were not successful. Therefore, all studies were performed on mixtures of the three complexes.

Triglycine could act as a mono-, di-, tri-, or tetradentate ligand with platinum(II). The degree of coordination in each of the three platinum(II)–triglycine complexes was determined by the following methods.

Chloride Determination. Chloride ion selective electrodes, and titration with $AgNO_3$ or $Hg(NO_3)_2$ could not be used to determine the concentration of Cl^- released by $PtCl_4^{2-}$ during reaction with G_3^- because both Ag^+ and Hg^{2+} precipitate the platinum(II)–tripeptide products. However, a spectrophotometric method[16] based on formation of $FeCl^{2+}$ is effective. Appreciable concentrations of $FeCl^{2+}$ do not form in the reaction of $PtCl_4^{2-}$ with Fe^{3+}. Hence, Fe^{3+} is unlikely to abstract a Cl^- ion from the platinum(II)–tripeptide complexes during the time of the determination.

After reaction with G_3^- for 24 h, solutions that initially contained 9.68×10^{-4} M $PtCl_4^{2-}$, yielded 3.18×10^{-3} M Cl^-, which corresponds to a release of 3.29 Cl^- per Pt(II). This suggests that the platinum(II)–triglycine solution contains a mixture of 70% tri- and 30% tetradentate complexes. However, this is insufficient evidence alone since water or hydroxide may occupy some of the coordination sites vacated by Cl^-.

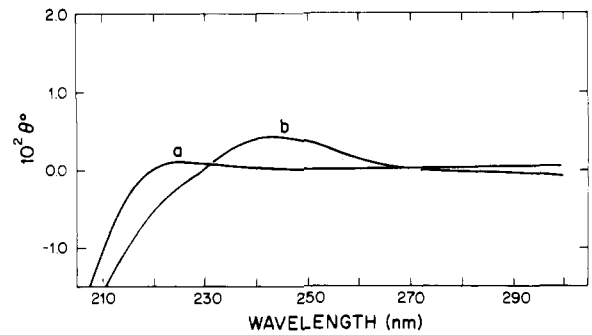

Figure 2. CD spectra of (a) GGA only and (b) the platinum(II) complex of GGA. $[Pt^{II}\text{-GGA}]_T = 1 \times 10^{-4}$ M, $[GGA] = 1.5 \times 10^{-4}$ M, and path length = 1.0 cm.

Table I. ^{13}C NMR Shifts for Free Triglycine and Triglycine Coordinated to Platinum(II)[a]

species	CH-1	CO-1	CH-2	CO-2	CH-3	CO-3
pH 6.0 triglycine	40.31	167.61	42.18	170.66	43.01	176.30
pH 6.0 Pt^{II}–G_3	48.49	171.18	50.81	180.03	49.68	185.15[b]
					43.41	176.10[c]

[a] Shifts given in ppm from Me_4Si. The nomenclature 1, 2, and 3 refers to carbons of the amine terminal, central, and carboxylate terminal peptide residues, respectively. [b] Coordinated carboxylate. [c] Noncoordinated carboxylate.

Consumption of Hydroxide Ion. In the reaction of $PtCl_4^{2-}$ with tripeptides, the pH of the solution drops unless base is added throughout the reaction. The amount of NaOH required for the reaction of $PtCl_4^{2-}$ with G_3^- was determined by potentiometric titration. The ratio of moles of OH^- consumed per mole of platinum(II)–triglycine is 2.13. A ratio of 2.0 is required to form the doubly deprotonated-N peptide complex. Some of the additional hydroxide ion consumed may be due to absorption of carbon dioxide (despite the Ar stream) over the course of the 24 h required for the titration. However, the excess may also be due to formation of a platinum(II)–peptide hydroxide similar to the $Ni^{II}(H_{-2}G_3)OH^{2-}$ complex previously reported.[20]

Estimated pK_a Values for Platinum(II)–Triglycine. No inflection points other than those due to triglycine were seen in a plot of pH vs. volume of NaOH. This indicates that reaction 1 takes place at a lower pH than the deprotonation of the carboxylic acid group of triglycine ($pK_a = 3.20$ for $H_2G_3^+$).[26]

$$PtCl_4^{2-} + H_2G_3^+ \rightleftarrows Pt^{II}(H_{-2}G_3)Cl^{2-} + 3Cl^- + 4H^+ \quad (1)$$

The pK_a of the peptide nitrogens was investigated further by study of the acid decomposition behavior of the platinum(II)–triglycine complexes. In 0.10 M acid, the complexes decomposed with an observed first-order rate constant of 6×10^{-5} s^{-1}. The absorbance change at 235 nm for this reaction was 0.025 (1.0-cm cell). In 0.010 M acid, the absorbance change was only 0.012, which indicated that reaction 1 was reversible at pH 2. The observed first-order rate constant in 0.010 M H^+ (a combination of the forward and reverse rate constants) was 1×10^{-4} s^{-1}. These data set limits for the pK_a of the peptide nitrogens between 1 and 2 in the presence of 3.7×10^{-4} M Cl^-.

It is important to realize that this pK_a value cannot be directly compared to the pK_a values of other metal–peptide complexes because Cl^- is replaced in the platinum(II) complexes vs. H_2O in the other metal peptides. Chloride is more difficult to displace from Pt(II) than is water. A possible correction to the pK_a value would be to subtract the value of $\log K_{3,4} = 1.90$[27] for the chloride complex (eq 2). This gives adjusted pK_a values of less than zero

$$Pt^{II}Cl_3(H_2O)^- + Cl^- \overset{K_{3,4}}{\rightleftarrows} PtCl_4^{2-} + H_2O \quad (2)$$

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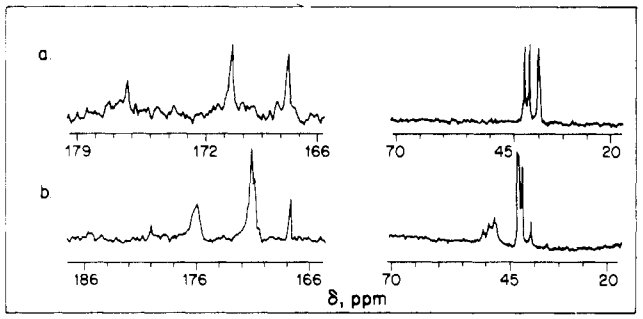

Figure 3. ^{13}C NMR spectra of (a) free G_3 and (b) the platinum(II)–G_3 mixture containing excess G_3 referenced to Me_4Si at 0 ppm. $[Pt]_T = 0.25$ M, $[G_3]_T = 0.38$ M in D_2O, and pD = 6.0.

for deprotonation of the peptide nitrogens, which indicates very strong metal–N(peptide) bonding.

Circular Dichroism. It has been observed that nickel(II)–tripeptide complexes that contain optically active amino acid residues exhibit CD signals at approximately the same wavelength as the absorbance maxima of the complexes.[28] Furthermore, the CD signal is greatly diminished or lost entirely when the optically active residue is no longer coordinated to the nickel.

CD spectra of GGA^- and its platinum(II) complex are shown in Figure 2. The corresponding CD spectra of GAG^- are very similar. Each complex has a CD maximum in the range 243–247 nm, which is the same region where their absorption maximum occurs. The $\Delta\epsilon$ ($\epsilon_L - \epsilon_R$) is approximately 1.36 M^{-1} cm^{-1} in both cases. On the basis of the observations with nickel(II) CD spectra,[28] the second peptide nitrogen in GGA^- must be directly coordinated to the platinum(II) ion in order to see a CD signal of magnitude similar to the GAG^- signal.

^{13}C NMR Spectra. The ^{13}C NMR chemical shifts of free triglycine and the platinum(II)–triglycine complexes are listed in Table I. Assignments of the NMR lines are analogous to those reported by Hawkins in studies of cobalt(III)–peptide complexes.[29-31] The nomenclature 1, 2, and 3 refers to carbons of the amine, central, and carboxylate residues, respectively.

In the study of tetraglycine complexes of Co(III), Hawkins found that the ^{13}C chemical shifts of carbons within several atoms of the Co(III) were significantly different from the chemical shifts of the free ligand. In the present study, all three CH_2 and CO chemical shifts move downfield of the free ligand values upon complexation with platinum(II) (Figure 3). This suggests that G_3^- acts as a tetradentate ligand in at least one of the platinum(II)–triglycine complexes. The most likely sites of coordination are the amine nitrogen, the two peptide nitrogens, and the carboxylate oxygen. While it is possible to argue from the ^{13}C NMR data alone that the peptide oxygens, rather than the peptide nitrogens, are coordinated, this is unlikely in light of the consumption of hydroxide during the formation of the complexes.

Not all of the G_3^- can be acting as a tetradentate ligand as indicated by the Cl^- determination. Comparison of the peak height ratios in the free G_3^- spectrum with the ratio of peak heights of excess G_3^- in the Pt^{II}–G_3 spectrum, Figure 3, shows that G_3^- is acting as a tridentate ligand in at least one of the complexes in the Pt^{II}–G_3 mixture. The CH-3 (43.01 ppm) and CO-3 (176.30 ppm) lines of the excess G_3^- ion are more intense than they should be if the carboxylate is coordinated to the same degree as the amine or central residues. This suggests that the platinum solution contains a mixture of coordinated and noncoordinated carboxylate, $Pt^{II}(H_{-2}G_3)^-$ and $Pt^{II}(H_{-2}G_3)X^{2-}$, respectively, where X = Cl^- or OH^-.

Table II. ^1H NMR Chemical Shifts for Free Triglycine and Triglycine Coordinated to Platinum(II)[a]

species	CH-1	CH-2	CH-3
pH 6.0 triglycine	3.91	4.05	3.79
pH 6.0 Pt^{II}–G_3	3.60	3.63	3.70[b]
			3.80[c]

[a] Shifts are given in ppm from TSP. The nomenclature 1, 2, and 3 refers to protons on the methylene carbons of the amine terminal, central, and carboxylate terminal residues, respectively. [b] Coordinated carboxylate. [c] Noncoordinated carboxylate.

Table III. ^{195}Pt NMR Chemical Shifts for Platinum(II) Complexes

complex	shift, ppm[a]	ref
K_2PtCl_4	−1650	4
cis-$[Pt(NH_3)_2Cl_2]$	−2161	4
$[Pt(NH_3)_4](ClO_4)_2$	−2610	33
$[Pt(en)_2]Cl_2$	−3015	33
$PtGCl_2^-$	−1602	34
cis-$[Pt(NH_3)_2(H_2O)_2]^{2+}$	−1584	35
$Pt(H_2O)_4^{2+}$	+25	36
$PtCl(H_2O)_3^+$	−350	36
$PtOAc(H_2O)_3^+$	−20	36
$Pt(OH)_4^{2-}$	−165	36
$Pt(CN)_4^{2-}$	−4725	34
$Pt(H_{-2}G_3)^-$	−7144	*b*
$Pt(H_{-2}G_3)OH^{2-}$	−7146	*b*
$Pt(H_{-2}G_3)Cl^{2-}$	−7517	*b*

[a] Shifts are relative to K_2PtCl_6. [b] This work.

Relative amounts of $Pt^{II}(H_{-2}G_3)^-$ and $Pt^{II}(H_{-2}G_3)X^{2-}$ present in solution were estimated on the basis of the assumption that the peak height of the NMR lines is proportional to concentration. In the free G_3^- spectrum, the ratio of the intensities of CO-3 and CO-2 is 0.34. The ratio should be similar for the excess G_3^- in the platinum sample. Therefore, the intensity of the CO-3 line should be 11.6, but it is actually 29. The difference is due to the CO-3 NMR line of $Pt^{II}(H_{-2}G_3)X^{2-}$, which is superimposed on the line of the free G_3^-. With the assumption that the metal also does not alter the intensity for the CO-3 signal for the uncoordinated carboxylate, the results indicate that ~78% of the platinum(II) mixture is $Pt^{II}(H_{-2}G_3)X^{2-}$ and that ~22% is $Pt^{II}(H_{-2}G_3)^-$.

It is proposed that of the ~78% $Pt^{II}(H_{-2}G_3)X^{2-}$, 70% is $Pt^{II}(H_{-2}G_3)Cl^{2-}$ (from Cl^- determination) and 7% is $Pt^{II}(H_{-2}G_3)OH^{2-}$ (from OH^- determination).

^1H NMR Spectra. The spectra of free triglycine ($[G_3]_T = 0.38$ in D_2O, pD 6.0) and the platinum(II)–triglycine complexes (0.25 M $[Pt]_T$) were obtained. Chemical shift data are contained in Table II relative to TSP. Assignment of the NMR lines to CH-1, CH-2, and CH-3 is by analogy to the cobalt(III)–tripeptide NMR data.[29,31] As was the case with Co(III) complexes, the ^1H lines move upfield on coordination to Pt(II) while the ^{13}C lines move downfield. This phenomenon is explained by changes in the hybridization and polarization of the C–H and CON bonds induced by coordination of the peptide nitrogens to the metal.[29,32]

Analysis of the ^1H NMR spectra is analogous to that of the ^{13}C spectra. The platinum solution is a mixture of complexes that have coordinated and noncoordinated carboxylates.

^{195}Pt NMR Spectra. Additional evidence that there are three platinum(II)–tripeptide complexes present in solution and that each contains two deprotonated peptide nitrogens is provided by ^{195}Pt NMR spectra. In general, ^{195}Pt chemical shifts are extremely sensitive to the σ-donor strength of the coordinated ligands. Representative chemical shifts for several platinum(II) complexes are contained in Table III.[4,33-36]

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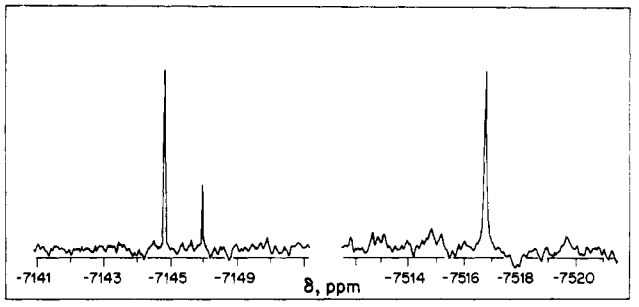

Figure 4. ^{195}Pt NMR spectrum of the Pt(II)–G_3 complexes. Referenced to K_2PtCl_6 at 0 ppm. $[Pt]_T$ = 0.25 M, $[G_3]_T$ = 0.38 M in D_2O, and pD = 6.0.

Cyanide is considered a very strong σ donor.[37] The chemical shift of $Pt^{II}(CN)_4^{2-}$ is −4725 ppm (upfield of K_2PtCl_6).[34] The three Pt^{II}–G_3 complexes appear at −7144, −7146, and −7517 ppm. This suggests coordination to donors much stronger than that of CN^-. The ^{195}Pt NMR spectrum of the three complexes is shown in Figure 4. No other ^{195}Pt lines were found in the range of 1000 to −10 000 ppm.

By comparison of the chemical shifts of $Pt^{II}Cl(H_2O)_3^+$, $Pt^{II}OAc(H_2O)_3^+$, and $Pt^{II}(OH)_4^{2-}$, (Table III), it is possible to assign the ^{195}Pt lines of the triglycine complexes to $Pt^{II}(H_{-2}G_3)^-$ (−7144 ppm), $Pt^{II}(H_{-2}G_3)OH^{2-}$ (−7146 ppm), and $Pt^{II}(H_{-2}G_3)Cl^{2-}$ (−7517 ppm).

From the data in Table III, the chemical shift values (δ, in ppm from $PtCl_6^{2-}$) per donor group can be estimated on the basis of the assumption that chemical shift varies linearly with the number of equivalent donors.[36] The values are as follows: H_2O, +6; OH^-, −41; Cl^-, −368; peptide amine, −738; carboxylate, −39. Thus, the effect of deprotonated peptide nitrogen is −3184 ppm, which is much greater than the effect due to CN^-, −1181 ppm.

The predicted ^{195}Pt NMR chemical shifts of $Pt^{II}(H_{-2}G_3)OH^{2-}$ and $Pt^{II}(H_{-2}G_3)Cl^{2-}$ were calculated by using the above values and are −7147 ppm and −7474, respectively. These are in good agreement with the experimental values from Table III.

Conclusions

Reaction of tripeptides with $PtCl_4^{2-}$ produces complexes containing cis-deprotonated-N peptide bonds to platinum(II). Three products, as identified by HPLC and ^{195}Pt NMR, form when G_3^- is the tripeptide. The pK_a of the deprotonated peptide nitrogens is estimated to be between 1 and 2 in the presence of 3.7×10^{-4} M Cl^- ion.

Chloride determination of the G_3^- complexes indicates that 70% of the platinum is still coordinated to one Cl^- ion, so $Pt^{II}(H_{-2}G_3)Cl^{2-}$ is proposed as the major product.

NMR data (^1H and ^{13}C) show that 22% of the platinum is coordinated to the peptide carboxylate. Therefore, $Pt^{II}(H_{-2}G_3)^-$ is the next most abundant product.

The remaining species may have H_2O or OH^- coordinated in the fourth position. Titration data indicate that 7% excess hydroxide was consumed during formation of the complexes, suggesting that $Pt^{II}(H_{-2}G_3)OH^{2-}$ is the minor product.

The ^{195}Pt NMR data show that a deprotonated peptide nitrogen is a much stronger σ donor than cyanide ion.

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Volume Profile for the Trans ⇌ Cis Isomerization of the Chloroaquabis(ethylenediamine)cobalt(III) Ion

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Activation volume ($\Delta V^{\ddagger}$ = 5.1 ± 0.3 cm^3 mol^{-1} in 0.01 M $HClO_4$) and reaction volume (ΔV = −2.9 ± 0.2 cm^3 mol^{-1} in 0.039 M $HClO_4$) have been obtained at 31.5 °C for the trans ⇌ cis isomerization of $Co(en)_2Cl(OH_2)^{2+}$. These are almost independent of ionic strength or temperature. A tetragonal-pyramidal transition state with one water molecule outside the coordination sphere can be inferred on the basis of these $\Delta V^{\ddagger}$ and ΔV values. It has been also found that the partial molal volumes of the trans and the cis isomers are almost equal for $Co(en)_2(OH_2)_2^{3+}$, $Co(en)_2Cl(NO_2)^+$, and $Co(en)_2(NO_2)(OH_2)^{2+}$.

Introduction

Positive values (7–14 cm^3 mol^{-1}) of $\Delta V^{\ddagger}$ were known hitherto for four trans → cis isomerization reactions of Co(III) complexes:

$$trans\text{-}Co(en)_2(OH_2)_2^{3+} \rightarrow cis\text{-}Co(en)_2(OH_2)_2^{3+} \quad (1)^2$$

$$trans\text{-}Co(en)_2(SeO_3H)OH_2^{2+} \rightarrow cis\text{-}Co(en)_2(SeO_3H)OH_2^{2+} \quad (2)^3$$

$$trans\text{-}Co(en)_2(SeO_3)OH_2^{+} \rightarrow cis\text{-}Co(en)_2(SeO_3)OH_2^{+} \quad (3)^3$$

$$trans\text{-}Co(en)_2(CH_3COO)OH_2^{2+} \rightarrow cis\text{-}Co(en)_2(CH_3COO)OH_2^{2+} \quad (4)^3$$

These $\Delta V^{\ddagger}$ were interpreted according to the postulate given by Stranks that the intrinsic partial molal volume of the five-coordinate intermediate is equal to that of the six-coordinate precursor.[4] However, the inappropriateness of this postulate has been repeatedly pointed out in recent years.[5-7] On the other hand, ΔV was considered to be negligible for reactions 1 and 4 because the final spectra of these reactions were almost pressure independent.[2,3] This near-zero magnitude of ΔV might be just for reaction 4, where the final composition is 75% cis and 25% trans.[3] However, it is rather unreliable for reaction 1, where the final composition is one-sided (98.3% cis and 1.7% trans).[2]

In this work, $\Delta V^{\ddagger}$ and ΔV have been obtained for another isomerization:

$$trans\text{-}Co(en)_2Cl(OH_2)^{2+} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} cis\text{-}Co(en)_2Cl(OH_2)^{2+} \quad (5)^8$$

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