Amino Acid Complexes of Palladium(II). 1. NMR Study of the Reactions of the Diaqua(ethylenediamine)palladium(II) Cation with Ammonia, Betaine, and the Amino Acids $^{+}NH_3(CH_2)_nCO_2^-$ (n = 1–3)[1]

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^{15}N NMR spectra were obtained for solutions of $[Pd(en\text{-}^{15}N_2)(H_2O)_2]^{2+}$ (**1**) and the complexes formed from it on addition of alkali, $[\{Pd(en\text{-}^{15}N_2)(\mu\text{-}OH)\}_n]^{n+}$ (n = 2, 3), and $[Pd(en\text{-}^{15}N_2)(OH)_2]$. In the presence of weak donor anions, NO_3^-, SO_4^{2-}, and ClO_4^- and dioxane, the ^{15}N NMR peak from **1** was broadened at 298 K, owing to exchange between H_2O and these ligands. When betaine ($^{+}(CH_3)_3NCH_2CO_2^-$, bet) reacted with **1**, the major ^{15}N NMR peaks at 277 K were assigned to $[Pd(en)(bet\text{-}O)(H_2O)]^{2+}$ and $[Pd(en)(bet\text{-}O)_2]^{2+}$. At higher temperatures, the peaks broadened and coalesced, until by 353 K there was a broad singlet, indicating that intermolecular exchange of betaine between the free ligand and these complexes was rapid. The products of reactions of **1** with ammonia depended on pH. $[Pd(en)(NH_3)(H_2O)]^{2+}$, $[Pd(en)(NH_3)_2]^{2+}$, $[Pd(en)(NH_3)(OH)]^{+}$, and $[\{Pd(en)(NH_3)\}_2(\mu\text{-}OH)]^{3+}$ were characterized in solution by ^{15}N NMR. Reaction of **1** (in excess) with glycine (Hgly) gave $[Pd(en)(gly\text{-}N,O)]^{+}$ as the dominant complex over the pH range 4–10. Above pH 10, $[Pd(en)(gly\text{-}N)(OH)]$ formed. With excess glycine, at high pH, $[Pd(en)(gly\text{-}N)_2]$ was the dominant complex. Near pH 2, $[Pd(en)(Hgly\text{-}O)(H_2O)]^{2+}$ was in equilibrium with the N,O-chelate complex, free glycine, and **1**. *cis*-$[Pd(NH_3)_2(H_2O)_2]^{2+}$ with glycine, without addition of acid or base to adjust pH, gave initially $[Pd(NH_3)_2(gly\text{-}N,O)]^{+}$, but with standing, reaction with the acid liberated gave the isomer of $[Pd(NH_3)(H_2O)(gly\text{-}N,O)]^{+}$ with ammine trans to glycinate O, as well as $[Pd(H_2O)_2(gly\text{-}N,O)]^{+}$. Reactions of β-alanine ($^{+}NH_3(CH_2)_2CO_2^-$, Hβala) with **1** were generally similar to those of glycine, except that the N,O-chelate complex was less stable relative to $[Pd(en)(H\beta ala\text{-}O)(H_2O)]^{2+}$ at low pH. Reaction of **1** with γ-aminobutyric acid ($^{+}NH_3(CH_2)_3CO_2^-$, Hγaba) gave a mixture over the pH range 4–8 of the chelate complex $[Pd(en)(\gamma aba\text{-}N,O)]^{+}$ with the isomers of $[\{Pd(en)(\mu\text{-}\gamma aba)\}_2]^{2+}$.

Introduction

In introducing their review on palladium(II) complexes with amino acids and peptides,[2] Pettit and Bezer commented that interest in platinum(II) amino acid complexes had been stimulated by the discovery of anticancer properties of platinum(II) compounds. They remarked that the kinetic inertness of platinum(II) complexes makes them difficult to study, so that "due to the similarities in the general chemistry of Pt(II) and Pd(II), as well as the increased rates of reaction of Pd(II) ions (on average approximately 10^3 times faster than platinum), palladium analogues are studied instead of, or as well as, the platinum compounds". Even in 1985, their view of the prospects of elucidating platinum(II) amino acid chemistry was probably unduly pessimistic, and since then, there has been considerable progress in the chemistry of platinum(II) complexes with amino acids and peptides.[3-8] Much of our own work has focused on reactions of *cis*-$[Pt(NH_3)_2(H_2O)_2]^{2+}$ with these ligands.[6-8] Our results, and those of others,[5] have shown that amino acids frequently react with platinum(II) to give an initial product which is "metastable", a kinetically-preferred product which must overcome a significant energy barrier to rearrange to the thermodynamically-preferred compound. Specific examples are mentioned below in the context of comparisons between the reactions of the two metal ions with particular ligands. Our aim on embarking on the present study was to carry out reactions with a palladium species which would, as much as possible, be analogous to those we had studied with *cis*-$[Pt(NH_3)_2(H_2O)_2]^{2+}$. We expected that with the more labile palladium species we would obtain the thermodynamically-preferred species. As well as being of some interest in themselves, these results would then throw some light on the kinetic and thermodynamic factors which work together to give specific compounds as products from the reactions of platinum compounds.

A major tool in our investigations of the reactions of *cis*-$[Pt(NH_3)_2(H_2O)_2]^{2+}$ has been multinuclear NMR spectroscopy. As well as ^1H and ^{13}C NMR from nuclei present in the amino acid ligands, we have used ^{15}N NMR with the ammine ligands highly enriched in ^{15}N ($I = {}^1/_2$). In ^{15}N NMR spectra, a separate peak (with "satellites" from coupling to ^{195}Pt, $I = {}^1/_2$, 34% abundance) is observed for each distinct ammine ligand, and δ_N and $^1J(^{195}Pt\text{–}^{15}N)$ can both provide information about the nature of the ligand trans to that ammine.[9] The only naturally-occurring isotope of palladium with nuclear spin is ^{105}Pd, $I = {}^5/_2$, 22.2% abundance. With its large quadrupole moment, this nucleus is expected to relax rapidly in square planar Pd(II) complexes.[10] There is therefore no information available from coupling constants to the metal nucleus. In a ^{15}N NMR study of palladium(II) ammine complexes,[11] we showed that δ_N does depend primarily on the nature of the ligand trans to ammine. We were able to confirm

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earlier suggestions from UV spectroscopy[12,13] that the preferred isomer of $[Pd(NH_3)_2(H_2O)_2]^{2+}$ in aqueous solution is the cis isomer. However, our results also showed that the ammine ligands bound to palladium are very labile, so that, for example, the isomerization of *trans*-$[Pd(NH_3)_2(H_2O)_2]^{2+}$ to the cis isomer proceeds by reactions in which ammine ligands dissociate, rather than by intramolecular rearrangement. It was therefore clear that it would be difficult to make useful comparisons between the reactions of *cis*-$[Pt(NH_3)_2(H_2O)_2]^{2+}$ and its palladium analogue, because the products in the latter reactions would arise largely from ammine redistribution reactions. We therefore used $[Pd(en)(H_2O)_2](NO_3)_2$ (**1**) (en = 1,2-diaminoethane) as our palladium(II) starting complex, with the expectation that the chelate effect would sufficiently hinder redistribution reactions of this ligand to allow a useful exploration of the reactions of **1** with amino acids and derivatives to be carried out. Recent papers[14-16] described reactions of **1** with various ligands, in which the $Pd(en)^{2+}$ moiety retained its integrity.

In this paper we describe the reactions of **1** with the amino acids $^+NH_3(CH_2)_nCO_2^-$ with $n = 1$ (glycine, Hgly), $n = 2$ (β-alanine, Hβala), and $n = 3$ (γ-aminobutyric acid, Hγaba). We also include the results of one study of the reactions of *cis*-$[Pd(NH_3)_2(H_2O)_2]^{2+}$ (**2**), with glycine, to show similarities and differences from the reactions of **1**. To assist us in our interpretation of NMR results obtained with the amino acids, we have also studied the reactions of **1** with betaine ($^+(CH_3)_3NCH_2CO_2^-$, bet) as a model for the carboxylate end of an amino acid and with ammonia as a model for the amine end.

Experimental Section

Starting Materials. Ethylenediamine highly enriched in ^{15}N (en-$^{15}N_2$) is commercially available, but is expensive, and so was prepared from ^{15}N-labeled potassium phthalimide. Details are given in the supplementary material. Ammonium sulfate, glycine, and potassium phthalimide highly enriched (99%) in ^{15}N and glycine 99% enriched in ^{13}C at the carboxyl group, produced by Cambridge Isotopes Ltd., were supplied by Novachem (Melbourne, Australia). Amino acids, Hgly, Hβala, and Hγaba, were used as supplied by Sigma, and betaine monohydrate was used as supplied by Aldrich. Solutions containing $[Pd(en)(H_2O)_2]A_2$ ($A^- = ClO_4^-, NO_3^-, CF_3SO_3^-, BF_4^-$) were obtained by the method used by Hohmann and van Eldik[14] to prepare solutions of the perchlorate salt, by reaction of $[PdCl_2(en)]$ with an aqueous solution of the appropriate silver salt. An aqueous solution of $[Pd(en)(H_2O)_2](NO_3)_2$ was taken to dryness in a stream of air to give $[Pd(ONO_2)_2(en)]$ as a pale yellow solid. Satisfactory microanalyses were obtained. The IR spectrum showed strong bands at 1495, 1471, 1300, and 1274 cm^{-1} (*cf.* bands assigned to nitrate in *cis*-$[Pt(ONO_2)_2(NH_3)_2]$ at 1510 (sh), 1485, 1275 (sh), and 1260 cm^{-1} [17]). A solution containing predominantly *cis*-$[Pd(NH_3)_2(H_2O)_2](NO_3)_2$ was prepared as previously described.[11]

NMR Spectra. The 20.2-MHz ^{15}N, 200-MHz ^1H, and 50.2-MHz ^{13}C NMR spectra were obtained with the use of a Bruker AC-200F spectrometer equipped with a 5-mm quad probe ($^1H/^{13}C/^{15}N/^{19}F$). Some ^1H (400-MHz) and ^{13}C (100.4-MHz) spectra were run on a JEOL GX-400 instrument with a 5-mm dual $^1H/^{13}C$ probe. ^{15}N spectra were obtained in ^1H_2O without instrument lock. Some were obtained with the use of a DEPT pulse sequence.[18,19] Other ^{15}N spectra were run with broad band ^1H decoupling. In the latter case, negative nuclear Overhauser enhancement gives rise to negative (emission) peaks, but phase was adjusted so that all spectra were presented in conventional absorption mode. Peaks are referenced relative to the $^{15}NH_4^+$ signal ($\delta_N = 0$) from 5 M $^{15}NH_4NO_3$ in 2 M HNO_3 in a coaxial capillary.[20] ^{13}C spectra were obtained in ^1H_2O (for ^{15}N-enriched substances) without instrument lock or in ^2H_2O (for substances not enriched in ^{15}N) with deuterium lock. The reference was internal dioxane ($\delta_C = 67.73$[21]). A delay of at least 3.5 s was allowed between pulses to allow carboxylate carbon spins to relax. ^1H spectra were obtained in ^2H_2O and are referenced relative to the methyl signal of 3-(trimethylsilyl)propanesulfonate (TSS) ($\delta_H = 0$). The 21.4-MHz ^{195}Pt NMR spectra were obtained with a JEOL FX-100 instrument, as previously described.[6-9] All shifts are positive to lower nuclear shielding (higher frequency). Spectra of nuclei other than ^1H were ^1H-decoupled.

Preparation of NMR Samples. For all experiments, approximately 0.08 g of $[Pd(ONO_2)_2(en)]$ (with either ^{14}N or ^{15}N present) was dissolved in 0.75 mL of water (^1H_2O or D_2O as appropriate) and approximately 0.8 mol equiv of the amino acid was added. The mixture was warmed briefly, to dissolve all solids, and NMR spectra were obtained from solutions in which the pH was adjusted by addition of 1 M HNO_3 or KOH solutions (in ^1H_2O) or D_2SO_4 or NaOD solutions in D_2O. Reversibility of changes in spectra as pH was changed was frequently checked. An additional 0.8 mol equiv of the ligand was then added, and spectra were again run at various pH values. The pH was measured on a JENCO 6072 pH meter with a Sensorex combination electrode.

Preparation of [Pd(gly-*N,O*)$_2$]. The preparation of crystals of the isomers of $[Pd(gly-N,O)_2]$ from $K_2[PdCl_4]$ and glycine in aqueous solution was described by Coe and Lyons.[22] They added no base to remove protons generated by chelation of glycine, so that the yield when their procedure was followed was low. The following adaptation of their method was used. $K_2[PdCl_4]$ (0.1994 g, 0.61 mmol) and glycine (0.1017 g, 1.36 mmol) were dissolved in 5 mL of water. The pH of the solution was adjusted to 4–5 by the addition of 6 M NaOH solution. The pale yellow solid which precipitated was filtered off, washed with a small volume of cold water, and air-dried. Yield: 0.0662 g (42%). Satisfactory microanalyses were obtained. Similar procedures were used for glycine containing either ^{14}N or ^{15}N.

Results

Selected NMR data are listed in Table 1.

NMR Spectra of Palladium(II) Ethylenediamine Complexes. Since $[PdCl_2(en)]$ is only sparingly soluble in water, the ^{15}N NMR spectrum of the ^{15}N-enriched complex was obtained in *N,N'*-dimethylformamide (dmf). The spectrum showed a single sharp peak at −18.7 ppm. The low nuclear shielding compared with that of ^{15}N in *cis*-$[PdCl_2(^{15}NH_3)_2]$ (δ_N −57.5 in dmf[11]) was expected, in view of the analogous deshielding of the ^{15}N nucleus in a five-membered chelate ring in platinum(II) complexes.[23] A solution containing $[Pd(en)_2]^{2+}$ (**3**) was obtained by addition of $(H_2en)(NO_3)_2$ to a solution of $[Pd(en)(H_2O)_2](NO_3)_2$, followed by the quantity of KOH solution required to deprotonate the ligand. When the ethylenediamine ligand was ^{15}N enriched, the ^{15}N NMR spectrum showed a single sharp peak ($\Delta\nu_{1/2} = 1$ Hz) at −20.0 ppm. The ^1H NMR spectrum of a solution of $[Pd(en)_2]^{2+}$ which had been allowed to stand in D_2O solution (to replace NH by ND) showed a singlet at 2.75 ppm.[24] The corresponding spectrum of $[Pd(en\text{-}^{15}N_2)_2]^{2+}$ did not show any resolvable ^{15}N–C–^1H coupling. The ^{13}C NMR spectrum of the compound containing ^{14}N showed a singlet at 47.0 ppm. When ^{15}N was present, the signal appeared as a doublet ($^1J(^{13}C\text{–}^{15}N) = 3.5$ Hz).

Dissolution of $[Pd(ONO_2)_2(en)]$ in water would, by analogy with platinum compounds,[17,25,26] be expected to give predominantly $[Pd(en)(H_2O)_2](NO_3)_2$. The ^1H and ^{13}C NMR spectra of the ^{14}N-containing compound, in D_2O at pD 1.3, each showed the expected sharp singlet (^1H, 2.64 ppm; *cf.* 2.63 ppm reported for the perchlorate salt by Zhu and Kostic,[16] ^{13}C, 48.39 ppm). The ^{15}N NMR spectrum (298 K) of a 0.2 M solution of $[Pd(en\text{-}^{15}N_2)(H_2O)_2](NO_3)_2$ in ^1H_2O at pH 2.2 showed a moderately broad peak ($\Delta\nu_{1/2} = 3.7$ Hz) at −27.4 ppm. The broadness of the

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Table 1. Selected NMR Data for Ethylenediamine–Palladium Complexes[a]

complex	pH	δ_N[b] en	δ_N[b] trans ligand	δ_N[b] other ^{15}N	δ_C ($-CO_2^-$)
$[Pd(en)(OH_2)_2]^{2+}$ (**1**)	4	−27.4	H_2O		
$[Pd(en)(OH)_2]$ (**6**)	12.3	−27.9	OH^-		
$[\{Pd(en)(\mu\text{-}OH)\}_2]^{2+}$ (**4**)	9.6	−29.0	μ-OH^-		
$[\{Pd(en)(\mu\text{-}OH)\}_3]^{3+}$ (**5**)	9.6	−27.0	μ-OH^-		
$[Pd(en)_2]^{2+}$ (**3**)	4	−20.0	en		
$[Pd(en)(NH_3)(OH_2)]^{2+}$ (**9**)	1	a −16.8 (d)	NH_3	c −56.7 (d)	
		b −28.7 (s)	H_2O		
$[Pd(en)(NH_3)_2]^{2+}$ (**10**)	1	a −18.7 (d)	NH_3	b −58.2 (d)	
$[\{Pd(en)(NH_3)\}_2(\mu\text{-}OH)]^{3+}$ (**12**)	7.2	a −16.0 (d)	NH_3	c −53.8 (d)	
		b −27.3 (s)	μ-OH^-		
$[Pd(en)(NH_3)(OH)]^+$ (**11**)	12.5	a −20.0 (d)	NH_3	c −56.2 (d)	
		b −27.0 (s)	OH^-		
$[Pd(en)(bet\text{-}O)(OH_2)]^{2+}$ (**7**)[c]	4	a −26.2	O(bet)		171.53[d]
		b −29.5	H_2O		
$[Pd(en)(bet\text{-}O)_2]^{2+}$ (**8**)	4	−28.2	O(bet)		
$[Pd(en)(Hgly\text{-}O)(OH_2)]^{2+}$ (**16**)	2	a −26.4[d]	O(Hgly)	c +9.17 (s)	174.8[e]
		b −29.2[d]	H_2O		
$[Pd(en)(gly\text{-}N,O)]^+$ (**13**)	4	a −18.7 (d)	N(gly^-)	c −45.8 (d)	187.4
		b −28.1 (s)	O(gly^-)		
$[Pd(en)(gly\text{-}N)(OH)]$ (**14**)	12	a −20.1 (d)	N(gly^-)	c −38.6 (d)	
		b −24.9 (s)			
$[Pd(en)(gly\text{-}N)_2]$ (**15**)	10	a −16.9 (d)	N(gly^-)	b −39.6 (d)	177.1
$[Pd(en)(\beta ala\text{-}N,O)]^+$ (**20**)	4	a −14.1	N(βala^-)		181.8
		b −28.7	O(βala^-)		
$[Pd(en)(\beta ala\text{-}N)(OH)]$ (**24**)	12	a −19.6	N(βala^-)		
		b −25.2	OH^-		
$[Pd(en)(\beta ala\text{-}N)_2]$ (**25**)	10	−16.4	N(βala^-)		180.8
$[Pd(en)(\gamma aba\text{-}N,O)]^+$ (**28**)	7.9	a −19.2	N(γaba^-)		183.7
		b −26.5	O(γaba^-)		
$[\{Pd(en)(\mu\text{-}\gamma aba\text{-}N,O)\}_2]^{2+}$ (**29**)	7.9	a −19.2	N(γaba^-)		
		b −26.0	O(γaba^-)		
$[\{Pd(en)(\mu\text{-}\gamma aba\text{-}N,O)\}_2]^{2+}$ (**30**)	7.9	a −16.0	N(γaba^-)		
		b −27.6	O(γaba^-)		
$[Pd(en)(\gamma aba\text{-}N)_2]$ (**26**)	7.9	−16.4	N(γaba^-)		183.3
$[Pd(en)(\gamma aba\text{-}N)(OH)]$ (**27**)	12	a −19.7	N(γaba^-)		183.5
		b −25.3	OH^-		

[a] Recorded at 20.2 MHz for ^{15}N and 50.2 MHz for ^{13}C, in H_2O. [b] All compounds have ethylenediamine highly enriched in ^{15}N. Letters in parentheses indicate multiplicity when all other N atoms present are also ^{15}N: d = doublet; s = singlet. "a", "b", "c" labels correspond to those in structural drawings and schemes and to peak labels in figures. [c] ^{15}N spectrum recorded at 277 K. [d] Peak broad at 298 K. [e] Spectrum obtained from ^{13}C-enriched complex.

line contrasted with the sharpness of the line from $[Pd(en\text{-}^{15}N_2)_2]^{2+}$ (**3**) mentioned above. The NMR spectra of solutions prepared from $[Pd(ONO_2)_2(en)]$ usually also showed relatively weak peaks from $[Pd(en)_2](NO_3)_2$, presumably due to a small amount of redistribution of ethylenediamine ligands during the preparation of the solid dinitrato complex ($[Pd(H_2O)_4]^{2+}$ would also be formed but would not be detected by NMR).[27] The sharp peak due to $[Pd(en\text{-}^{15}N_2)_2]^{2+}$ (**3**) impurity provided a useful check that line broadening was not due to poor instrument tuning. If excess $(H_2en\text{-}^{15}N_2)(NO_3)_2$ was added, it also showed a sharp singlet at 9.91 ppm. The broadening was therefore not due to a reaction in which ethylenediamine exchanged between palladium ions. The line width was significantly dependent on concentration of the compound, becoming narrower for more dilute solutions. Addition of $NaNO_3$ caused an increase in line width, to 11.2 Hz in saturated $NaNO_3$ solution. These data are all consistent with the existence of an exchange between water and nitrate ions as ligands which was not fast enough on the NMR time scale to completely average the environments of the ^{15}N nuclei. With *cis*-diammineplatinum(II) complexes, separate ^{15}N NMR peaks are observed for the diaqua and aqua nitrato complexes, but the latter are relatively weak unless the nitrate concentration is high.[26] To produce the observed effect with the palladium complex, there must be a greater tendency for nitrate, relative to water, to coordinate to palladium than to platinum. Addition of Na_2SO_4 had a similar broadening effect. The ^{15}N NMR peak from a 0.5 M solution of $[Pd(en\text{-}^{15}N_2)(H_2O)_2](ClO_4)_2$ (prepared *in situ* by reaction of $[PdCl_2(en)]$ and 2 mol of $AgClO_4$) at pH 2.6 was also relatively broad ($\Delta\nu_{1/2}$ = 3.5 Hz) and became broader on addition of $NaClO_4$. In contrast to the case of platinum analogues,[26,28] there must be significant coordination of perchlorate to palladium. The addition of dioxane, which could also act as an O-donor ligand, also caused significant broadening. The ^{15}N NMR peaks obtained under comparable conditions from solutions where the counterion was $CF_3SO_3^-$ or BF_4^- were significantly sharper (<2-Hz width) than for nitrate or perchlorate salts. These anions would be expected to be very weakly coordinating indeed.

The chemical shift differences between the various O-donor complexes present were apparently small enough for the different environments of ^1H and ^{13}C nuclei to be completely averaged.

For convenience, solid $[Pd(ONO_2)_2(en)]$ was used as a starting material for our reactions, with the ^{15}N NMR peak at −27.4 ppm from an aqueous solution referred to as being from the diaqua complex **1**, and dilute HNO_3 was frequently used to decrease pH. The higher shielding of the ^{15}N nucleus trans to water (plus nitrate) in **1**, compared with that trans to N in $[Pd(en\text{-}^{15}N_2)_2]^{2+}$, was as expected from comparison with the influence of trans ligands on δ_N in ammine–palladium complexes.[11]

$[Pd(ONO_2)_2(en\text{-}^{15}N_2)]$ dissolved readily in dmf, with gentle warming. The ^{15}N NMR spectrum of the resultant solution showed a broad peak ($\Delta\nu_{1/2}$ = 21.4 Hz) at −28.1 ppm, which would be due to the incomplete averaging of the ^{15}N environments in $[Pd(ONO_2)_2(en\text{-}^{15}N_2)]$, $[Pd(ONO_2)(en\text{-}^{15}N_2)(dmf\text{-}O)]^+$, and $[Pd(en\text{-}^{15}N_2)(dmf\text{-}O)_2]^{2+}$. When *cis*-$[Pt(ONO_2)_2(^{15}NH_3)_2]$ was

(27) We propose that this redistribution occurred during the isolation of solid $[Pd(ONO_2)_2(en)]$, since the spectrum of $[PdCl_2(en)]$ in dmf did not show any peaks from $[Pd(en)_2]^{2+}$ and solutions of $[Pd(en)(H_2O)_2](NO_3)_2$ prepared directly from reaction of $[PdCl_2(en)]$ with aqueous $AgNO_3$ solution showed only a very weak peak.

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dissolved in dmf, separate sharp ^{15}N NMR peaks were observed for the analogues of these species.[29]

When the pH of an aqueous solution of $[Pd(en\text{-}^{15}N_2)(H_2O)_2]^{2+}$ (**1**) was increased to a value in the range 6–9.5, the ^{15}N NMR spectrum of the solution showed two sharp peaks, at −27.0 and −29.0 ppm, in the approximate intensity ratio 2.8:1. Within this pH range, *cis*-$[Pt(NH_3)_2(OH)(H_2O)]^+$ rapidly oligomerizes to $[\{Pt(NH_3)_2(\mu\text{-}OH)\}_n]^{n+}$ (n = 2, 3).[25,26,30-33] The ammine ^{15}N nucleus is more shielded for the dimer than for the trimer. ^{195}Pt NMR has shown that similar (ethylenediamine)platinum(II) oligomers exist.[34,35] The crystal structure of a compound containing the tetrameric cation $[\{Pt(en)(\mu\text{-}OH)\}_4]^{4+}$ has been published,[36] but this species appears to be at most a minor component in solution. The two peaks observed in our spectrum were assigned to the oligomers $[\{Pd(en)(\mu\text{-}OH)\}_n]^{n+}$, with that at −29.0 ppm corresponding to the cation with n = 2 (**4**) and that at −27.0 ppm to n = 3 (**5**). Lim and Martin[37] interpreted their potentiometric data for titration of $[Pd(en)(H_2O)_2]^{2+}$ in terms of rapid formation of such oligomers. NMR spectra have shown that dinuclear platinum complexes with a single hydroxo bridge, $[\{PtL_2(H_2O)\}_2(\mu\text{-}OH)]^{3+}$ (L = NH_3, $^1/_2$(en)), are present under some conditions. Peaks due to a palladium analogue $[\{Pd(en)(H_2O)\}_2(\mu\text{-}OH)]^{3+}$ were not observed in our spectra (unlike **4** and **5**, which each gave a single sharp peak, this complex would be expected to show two ^{15}N NMR peaks of equal intensity).

When the pH was increased to 12.3, the peaks due to the oligomers disappeared, to be replaced by a sharp singlet at −27.9 ppm, assigned to $[Pd(en\text{-}^{15}N_2)(OH)_2]$ (**6**). At pH 4.0, peaks due to the oligomers were present (somewhat broadened), together with a peak from **1**. If the pH was decreased still further, the peaks due to the oligomers disappeared. These changes in the spectra were all fully reversible as pH of the solution was increased or decreased.

Reactions of $[Pd(en)(H_2O)_2]^{2+}$ (1) with Betaine. When betaine (0.9 mol equiv) was added to an aqueous solution of $[Pd(en\text{-}^{15}N_2)(H_2O)_2]^{2+}$ (**1**) and the pH of the solution adjusted to 4.0, the 20.2-MHz ^{15}N NMR spectrum of the resultant solution at 277 K was as shown in Figure 1a. There were several relatively sharp well-resolved peaks. Two peaks, at −26.2 and −29.5 ppm, were of equal intensity in all spectra and so were assigned to the nonequivalent ^{15}N nuclei of $[Pd(en\text{-}^{15}N_2)(bet\text{-}O)(H_2O)]^{2+}$ (**7**). For the diammineplatinum complexes *cis*-$[Pt(^{15}NH_3)_2(O_2CCH_3)(H_2O)]^+$ [26] and *cis*-$[Pt(^{15}NH_3)_2(Hgly\text{-}O)(H_2O)]^{2+}$,[6] the lower ^{195}Pt–^{15}N coupling constant for the ^{15}N trans to carboxylate compared with that for the ^{15}N trans to water allowed the ^{15}N peaks to be assigned. In each case, the ^{15}N nucleus trans to carboxylate was less shielded. By analogy, the peak at −26.2 ppm in our spectrum was assigned to ethylenediamine ^{15}N trans to betaine carboxylate, and that at −29.5 ppm, to ^{15}N trans to water. A broad peak was also present, due to **1**, as were weak peaks due to the hydroxo-bridged oligomers **4** and **5**. The peak at −28.2 ppm, which increased in relative intensity when the betaine:palladium ratio was increased, was assigned to $[Pd(en\text{-}^{15}N_2)(bet\text{-}O)_2]^{2+}$ (**8**).

In reactions between *cis*-$[Pt(NH_3)_2(H_2O)_2]^{2+}$ and acetate[26] or amino acids $^+NH_3(CH_2)_2CO_2^-$ (n = 2, 3)[7] under mildly acidic conditions, peaks were observed in NMR spectra which were assigned to dinuclear complexes containing bridging carboxylate, such as $[\{Pt(NH_3)_2\}(\mu\text{-}OH)(\mu\text{-}O_2CR)]^{n+}$. It is possible that the broad peak at approximately −23.5 ppm in our spectra was due to a dinuclear complex, possibly with a counterpart peak in the region −26 to −30 ppm obscured by other peaks. It was not possible, on the basis of the information available, to make a more definite assignment.

When the temperature was increased, all of these peaks broadened and coalesced, until by 353 K a single broad peak was

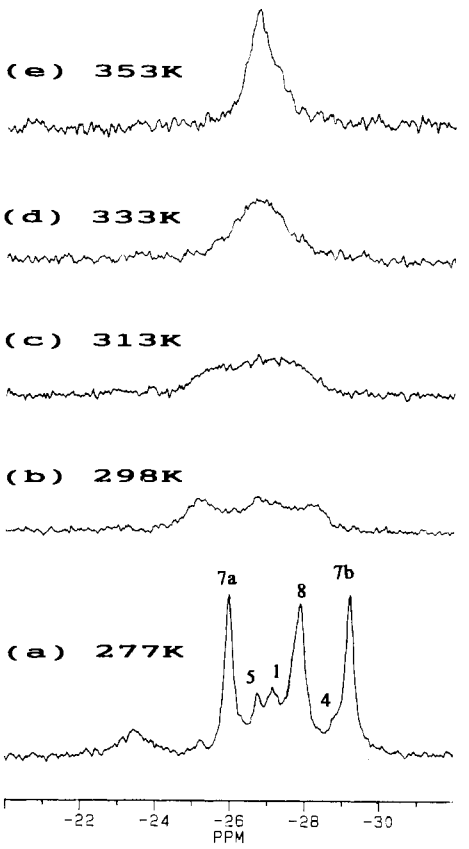
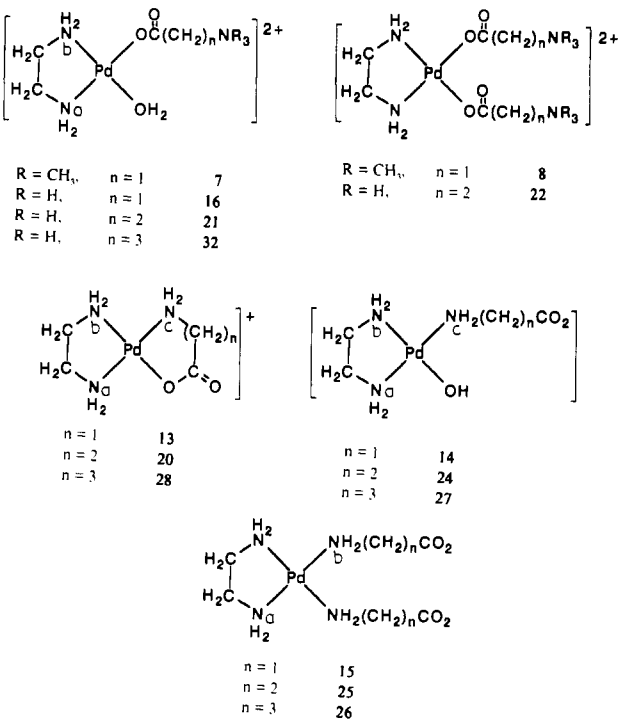


Figure 1. Variable-temperature 20.2-MHz ^{15}N NMR spectra of a solution obtained by addition of 0.9 mol equiv of betaine to $[Pd(en\text{-}^{15}N_2)(H_2O)_2](NO_3)_2$ in ^1H_2O at pH 4.0. Peak labels correspond to the numbers used in structural diagrams and in Table 1.



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(36) Rochon, F. D.; Morneau, A.; Melanson, R. *Inorg. Chem.* **1988**, *27*, 10.
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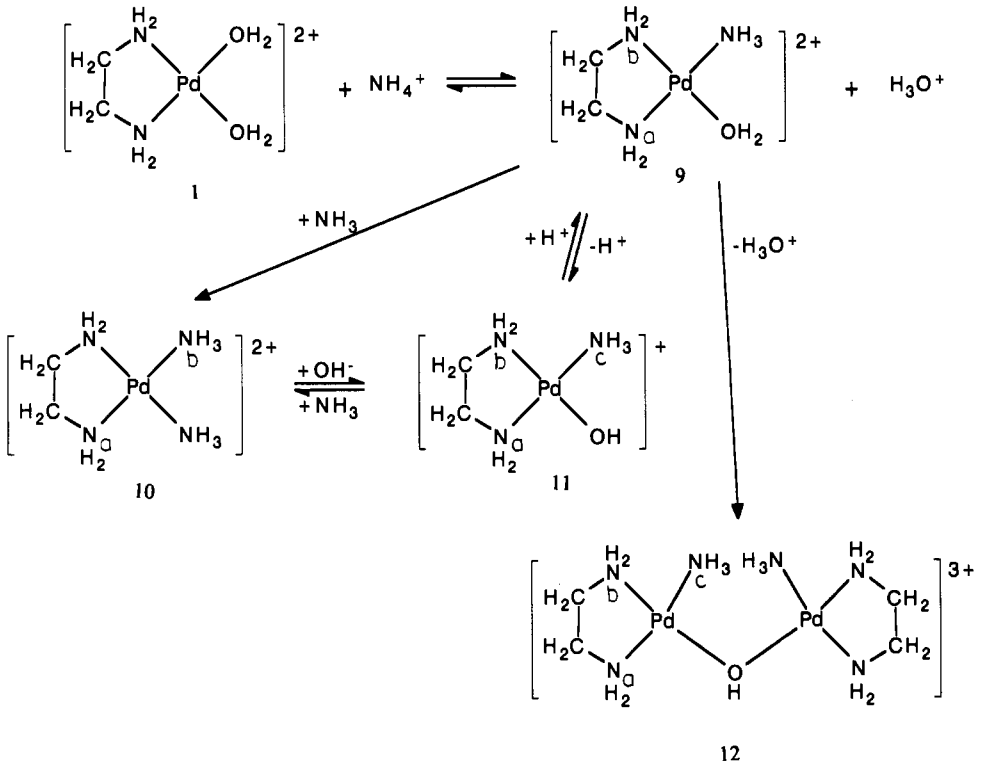
Scheme 1



observed (Figure 1e). There was therefore exchange between **1**, **7**, and **8** (*i.e.*, between free betaine and betaine coordinated in **7** and **8**), which became rapid on the NMR time scale as the temperature was increased.

In strongly acid solution (pH 0.2), the ^{15}N NMR spectrum showed only the peak due to **1**. At pH 0.8, peaks due to **7** were present but were much less intense than that due to **1**. At pH 10.2, the ^{15}N NMR spectrum showed only peaks due to [Pd(en)$(OH)_2$] (**6**) and $[\{Pd(en)(\mu\text{-}OH)\}_n]^{n+}$ (**4** and **5**).

The ^{13}C NMR spectra at 298 K were consistent with the betaine-exchange reactions discussed above. In the 50.2-MHz ^{13}C NMR spectrum of free betaine, the resonances from the methyl carbon (54.48 ppm) and the methylene carbon (67.29 ppm) were split into 1:1:1 triplets by coupling with ^{14}N (15.4 and 12.6 Hz, respectively). There was no resolvable coupling for the carboxylate carbon (170.2 ppm, $\Delta\nu_{1/2}$ = 0.6 Hz at pH 4). In the spectrum run under similar conditions of a solution from **1** with 0.9 mol equiv of betaine at pH 4.2, no separate resonances were observed for free and coordinated betaines. The splittings from ^{14}N–^{13}C couplings were not resolved, and the peaks had shifted significantly from their positions for free ligand: methyl, 54.63 ppm; methylene, 66.18 ppm; carboxyl, 171.53 ppm. The peaks were all broader than those for the free ligand, especially that from the carboxylate carbon ($\Delta\nu_{1/2}$ = 18.5 Hz).

Reactions of $[Pd(en)(H_2O)_2]^{2+}$ (1) with Ammonia (Scheme 1). One mole equivalent of $^{15}NH_4^+$ (in the form of $(^{15}NH_4)_2SO_4$) was added to a solution of $[Pd(en\text{-}^{15}N_2)(H_2O)_2](NO_3)_2$ (**1**), and the pH of the solution was adjusted by addition of NaOH or HNO_3 solution. The ^{15}N NMR spectrum at 298 K of a solution at pH 1 is shown in Figure 2a. In addition to the sharp singlet from $[Pd(en\text{-}^{15}N_2)_2]^{2+}$ (**3**) impurity (see above), the spectrum showed a singlet (A) from $^{15}NH_4^+$, a large, broad peak from **1**, and two sets of weaker peaks assigned to $[Pd(en\text{-}^{15}N_2)(^{15}NH_3)(H_2O)]^{2+}$ (**9**) and to $[Pd(en\text{-}^{15}N_2)(^{15}NH_3)_2]^{2+}$ (**10**). Three resonances were observed from **9**, which were readily assigned to the ammine ^{15}N (N_c), to ethylenediamine ^{15}N trans to ammine (N_a), and ethylenediamine ^{15}N trans to H_2O (N_b). As previously observed with platinum(II)[6,9] and rhodium(III)[38] complexes,

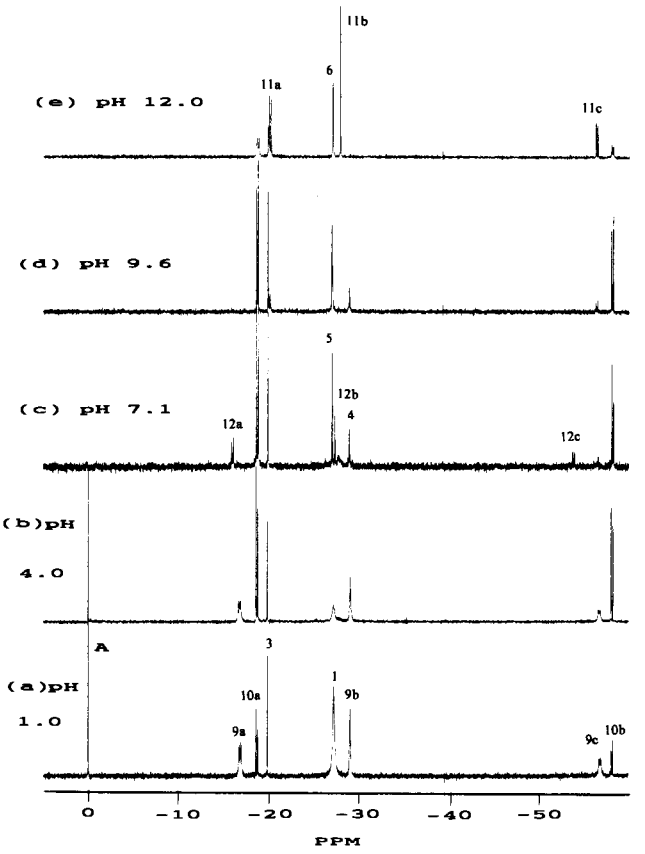


Figure 2. Effect of pH on the 20.2-MHz ^{15}N NMR spectrum at 298 K of a solution obtained by addition of 0.5 mol equiv of $(^{15}NH_4)_2SO_4$ to a ^1H_2O solution of $[Pd(en\text{-}^{15}N_2)(H_2O)_2](NO_3)_2$. Peak labels correspond to the numbers in Scheme 1 and Table 1, except for A, $^{15}NH_4^+$.

mutually trans nonequivalent ^{15}N nuclei coupled with each other, to split each of the signals from N_a and N_c into a doublet ($^2J(^{15}N_a$–Pd–$^{15}N_c)$ = 4.2 Hz). The peak from N_b was not split by coupling with cis ^{15}N nuclei but was broadened, presumably due to exchange between H_2O, NO_3^-, and SO_4^{2-} at the trans coordination site.

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Two doublets were assigned to **10**, from ethylenediamine ^{15}N (N_a) and from $^{15}NH_3$ (N_b).

When the temperature was lowered to 277 K, the peaks from **9** all broadened significantly, consistent with slower exchange between H_2O and nitrate. With an increase in temperature from 298 to 343 K, the only changes were slight sharpenings of all of the peaks as exchange of these labile ligands cis to NH_3 became faster. The specific $^{15}N_a$–Pd–$^{15}N_c$ couplings remained. There was no coalescence of peaks from N_a and N_b. There were no coalescence of ethylenediamine peaks from **1**, **9**, and **10** and no coalescence between ammine peaks from NH_4^+, **9**, and **10**. There was therefore no rapid exchange between free and bound ammonias or between mono- and diammine complexes, even under these acidic conditions. There was also no process which rapidly interchanged the environments of the two nonequivalent ethylenediamine N atoms N_a and N_b in **9**.

The effects on the 20.2-MHz ^{15}N NMR spectra of increasing the pH of this solution are illustrated in Figure 2. In the spectrum run at pH 4.0 (Figure 2b), the peaks from the ammine complexes, especially the diammine complex **10**, were larger relative to that from **1**. At pH 7.1 (Figure 2c), the strongest peaks in the ^{15}N NMR spectrum were from **10**. Other moderately strong peaks in the spectrum were due to the oligomers $[\{Pd(en\text{-}^{15}N_2)(\mu\text{-}OH)\}_n]^{n+}$ (**4** and **5**). A very weak set of broadened peaks were still present due to $[Pd(en\text{-}^{15}N_2)(^{15}NH_3)(H_2O)]^{2+}$ (**9**) (in rapid equilibrium with $[Pd(en)(NH_3)(OH)]^+$ (**11**)). The remaining peaks in the spectrum were doublets at −16.0 and −53.8 ppm ($^2J(^{15}N\text{–Pd–}^{15}N$ = 4.2 Hz) and a sharp singlet at −27.3 ppm. From the chemical shifts, it was evident that this species contained ethylenediamine ^{15}N nuclei trans to ammine (−16.0 ppm) and trans to an O-donor (−27.3 ppm). Given the limited number of complexes possible in this system, and the tendency for complexes containing bridging hydroxide to form near pH 7, these peaks were assigned to $[\{Pd(en\text{-}^{15}N_2)(^{15}NH_3)\}_2(\mu\text{-}OH)]^{3+}$ (**12**), analogous to $[\{Pt(NH_3)_3\}_2(\mu\text{-}OH)]^{3+}$ [39] and $[\{Pt(dien)\}_2(\mu\text{-}OH)]^{3+}$.[40] There was no longer any peak from $^{15}NH_4^+$.

At pH 12.0 (Figure 2e), the peaks from **12** and from $[\{Pd(en)(\mu\text{-}OH)\}_2]^{2+}$ (**4**) had disappeared from the spectrum. It would be expected from our previous results with hydroxo complexes (outlined above) that $[\{Pd(en)(\mu\text{-}OH)\}_3]^{3+}$ (**5**) would also no longer be present at this pH. The strong sharp singlet at −27.0 ppm in this spectrum was therefore not assigned to the hydroxo-bridged trimer, **5**. Together with a doublet at −20.0 ppm (partly overlapping with the signal from $[Pd(en)_2]^{2+}$ (**3**) impurity) and a doublet at −53.8 ppm ($^2J(^{15}N\text{–Pd–}^{15}N$) = 4.1 Hz), this peak was assigned to $[Pd(en\text{-}^{15}N_2)(^{15}NH_3)(OH)]^+$ (**11**). Peaks due to $[Pd(en\text{-}^{15}N_2)(^{15}NH_3)_2]^{2+}$ (**10**) were also present but were not as intense as at pH 7–10. At the intermediate pH 9.6, the species present were **10**, **11**, and the hydroxo-bridged oligomers **4** and **5**, with the peak from $[\{Pd(en)(\mu\text{-}OH)\}_2]^{2+}$ (**4**) and the peak from N_b in **11** coincident.

From these results, it is clear that $[Pd(en)(NH_3)(H_2O)]^{2+}$ (**9**) (with its deprotonated form, **11**) is not very stable in the mid-pH range 7–10 with respect to the ammine redistribution reaction which produces $[Pd(en)(NH_3)_2]^{2+}$ (**9**) and hydroxo-bridged oligomers $[\{Pd(en)(\mu\text{-}OH)\}_n]^{n+}$. At higher pH, where hydroxo-bridged complexes are less stable, the monoammine complex $[Pd(en)(NH_3)(OH)]^+$ (**11**) becomes more stable relative to **10** and $[Pd(en)(OH)_2]$ (**6**).

Bis(glycinato)palladium(II), [Pd(gly-*N,O*)$_2$], Isomers. Because there was some indication that small amounts of *cis*- and *trans*-$[Pd(gly\text{-}N,O)_2]$ were produced as byproducts in the reactions of **1** with glycine, solid $[Pd(gly\text{-}^{15}N,O)_2]$, a mixture of the geometric isomers, was prepared. The solid was sparingly soluble in water, and the ^{15}N NMR spectrum of the solution showed two sharp peaks, at −55.7 and −47.4 ppm, in the intensity ratio 1.7:1. Since glycinate ^{15}N trans to O would be expected to be more shielded than that trans to N, the former peak may be assigned to the cis isomer, which would be expected to be thermodynamically preferred on the basis of the general rule that the most stable isomer has ligands with strongest trans influence trans to those with weakest trans influence.[41] The ^{13}C NMR spectrum of this solution was also obtained. Two sets of peaks were observed, and from their relative intensities, they were assigned to cis and trans isomers (cis 48.45, 186.39 ppm; trans 48.51, 186.37 ppm).

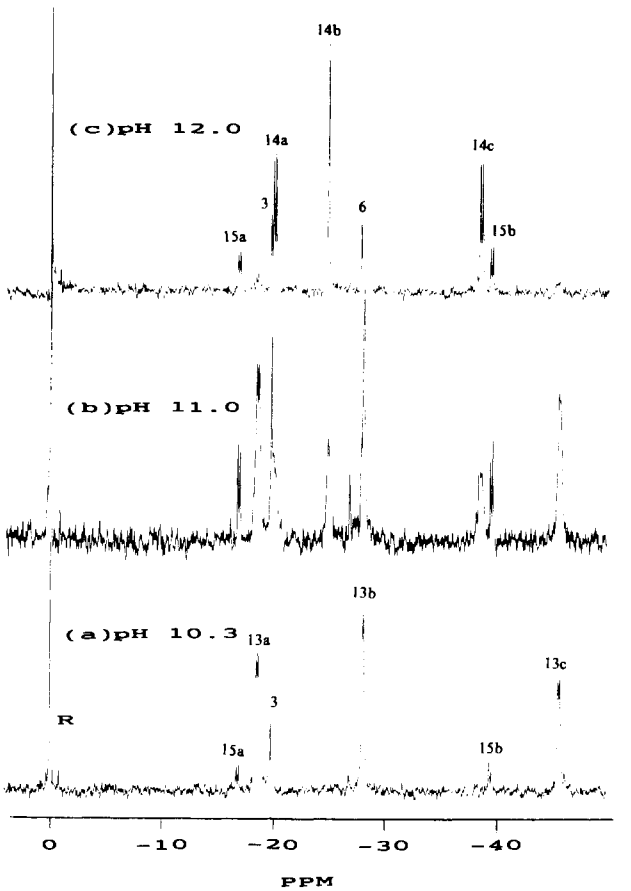


Figure 3. Effect of pH on the 20.2-MHz ^{15}N NMR spectrum of a ^1H_2O solution of $[Pd(en\text{-}^{15}N_2)(gly\text{-}^{15}N,O)](NO_3)$ (**13**) with a small excess of [^{15}N]glycine over the pH range 10.3–12.0. Peak labels correspond to the numbers in structural diagrams and Table 1, except for R, $^{15}NH_4^+$ in reference capillary.

Reactions of $[Pd(en)(H_2O)_2]^{2+}$ (1) with Glycine. When glycine (Hgly) (0.8 mol equiv) was added to an aqueous solution of **1** and the pH of the solution was adjusted to 4.0 by addition of KOH, no NMR peaks from free glycine were observed, and it was evident from ^{15}N and ^{13}C NMR spectra that the only glycine-containing species present in detectable amounts was the chelate complex $[Pd(en)(gly\text{-}N,O)]^+$ (**13**). The low shielding of the carboxylate carbon (187.4 ppm) indicated that this atom was incorporated in a five-membered chelate ring[7,42] (*cf.* 190.0 ppm for $[Pt(NH_3)_2(gly\text{-}N,O)]^+$ [6]). The ^{15}N NMR spectrum of $[Pd(en\text{-}^{15}N_2)(gly\text{-}^{14}N,O)]^+$ showed the two sharp peaks expected, at −18.7 ppm ($^{15}N_a$ trans to glycinate N_c) and −28.1 ppm ($^{15}N_b$ trans to glycinate O). The ^{15}N spectrum of $[Pd(en\text{-}^{14}N_2)(gly\text{-}^{15}N,O)]^+$ showed a sharp peak from chelated glycinate $^{15}N_c$ at −45.8 ppm. This represents a large coordination shift from free glycine (+9.53 ppm at pH 4), although smaller in magnitude than that for the platinum complex $[Pt(^{14}NH_3)_2(gly\text{-}^{15}N,O)]^+$ (δ_N −54.4[6]). In the ^{15}N NMR spectrum of $[Pd(en\text{-}^{15}N_2)(gly\text{-}^{15}N,O)]^+$ (Figure 3a), $^{15}N_a$–Pd–$^{15}N_c$ coupling caused the ^{15}N NMR peaks from glycinate

(39) Appleton, T. G.; Hall, J. R.; Ralph, S. F.; Thompson, C. S. M. *Inorg. Chem.* **1989**, *28*, 1989.
(40) Erickson, L. E.; Erickson, H. L.; Meyer, T. Y. *Inorg. Chem.* **1987**, *26*, 997.
(41) Appleton, T. G.; Clark, H. C.; Manzer, L. E. *J. Organomet. Chem.* **1974**, *65*, 275.
(42) Appleton, T. G.; Hall, J. R.; Prenzler, P. D. *Inorg. Chem.* **1989**, *28*, 815.

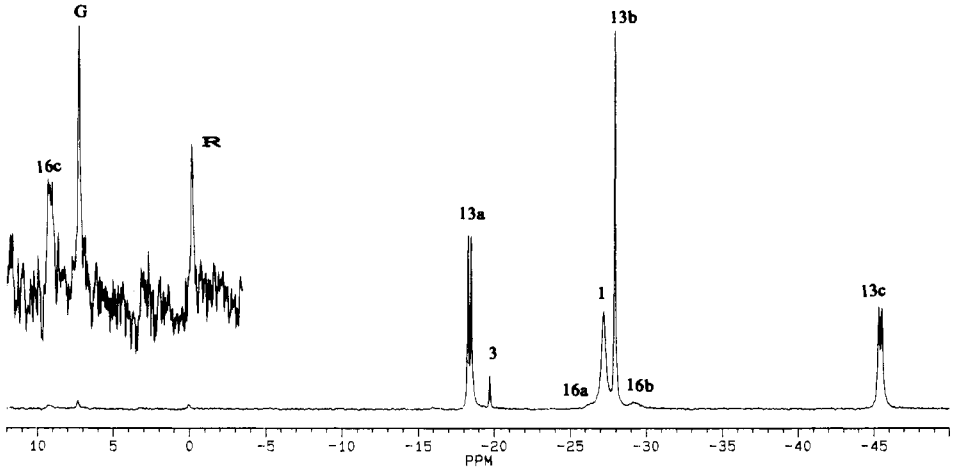


Figure 4. 20.2-MHz ^{15}N NMR DEPT spectrum of a solution obtained by addition of 0.8 mol equiv of [^{15}N]glycine to a $^{1}H_2O$ solution of [Pd(en-$^{15}N_2$)(H_2O)$_2$](NO_3)$_2$, with pH adjusted to 1.0. Peak labels correspond to those in structural diagrams and Table 1, except for R, $^{15}NH_4^+$ in reference capillary, and G, free glycine.

nitrogen (N_c) and the ethylenediamine nitrogen trans to it, N_a, each to be split into a doublet (4.0 Hz). The ethylenediamine ^{15}N nucleus trans to glycinate oxygen (N_b) showed no coupling. These couplings are analogous to those observed for [Pt($^{15}NH_3$)$_2$-(gly-^{15}N,O)]$^+$.[6]

At pH 10 (still with an excess of palladium over glycinate), the spectra run soon after the pH was adjusted showed that **13** was the only glycinate complex present. However, with longer standing at this pH, redistribution of ligands slowly occurred, so that peaks due to [Pd(en)$_2$]$^{2+}$ (**3**) slowly grew. When [^{15}N]glycine was used, ^{15}N NMR peaks due to *cis*- and *trans*-[Pd(gly-^{15}N,O)$_2$] were also observed, and small amounts of solid [Pd(gly-N,O)$_2$] precipitated from these solutions.

The spectrum shown in Figure 3a was run at pH 10.3 with a slight excess of [^{15}N]glycinate. In addition to peaks from **13**, it showed two relatively weak doublets, at −16.9 and −39.6 ppm. If a larger excess of glycinate (total 1.6 mol equiv) was added, these peaks became much more intense. They were assigned to [Pd(en-$^{15}N_2$)(gly-^{15}N)$_2$] (**15**). The ^{13}C peak for the carboxylate carbon in **15** occurred at 177.1 ppm, which may be compared with 179.3 ppm for free glycine in the same solution. When acid was added to decrease the pH to 4.2, the NMR peaks due to **15** decreased in intensity but did not entirely disappear. Peaks due to the chelate complex, **13**, and free glycine then dominated.

For the solution with a slight excess of glycinate, at pH 12 (Figure 3c), the ^{15}N NMR peaks from **13** were very weak. A new set of peaks was assigned to [Pd(en-$^{15}N_2$)(gly-^{15}N)(OH)] (**14**). At pH values intermediate between 10 and 12 (pH 11.0, Figure 3b), peaks due to both **13** and **14** were present. Under these conditions, the rate of interconversion between **13** and **14** was fast enough to cause some peak broadening. This behavior is reminiscent of the rapid exchange between carboxylate in chelated glycinate and hydroxide at labile coordination sites in methylplatinum(IV) complexes.[43,44] These pH-dependent changes in the spectra were all reversible.

The ^{15}N NMR spectrum of a solution obtained from [Pd(en-$^{15}N_2$)(H_2O)$_2$]$^{2+}$ (**1**) and [^{15}N]glycine (0.8 mol equiv), with the pH adjusted to 1.0, is shown in Figure 4. The major peaks were due to the chelate complex **13** and to the starting material, **1**. However, the spectrum also clearly showed two weak broad peaks at −26.4 and −29.2 ppm. These chemical shifts could correspond only to ethylenediamine ^{15}N trans to O-donors. From comparison with the spectra discussed above for [Pd(en-$^{15}N_2$)(bet-O)(H_2O)]$^{2+}$ (**7**), such peaks would be expected from a complex in which glycine was carboxylate-bound, [Pd(en-$^{15}N_2$)(Hgly-O)(H_2O)]$^{2+}$ (**16**). The ^{15}N NMR spectrum also showed weak peaks at +7.1 and (slightly broadened) +9.3 ppm. The former peak corresponded to that for free glycine at this pH (labeled G in Figure 4). As we have seen, coordination of glycine nitrogen to palladium causes a large coordination shift (approximately −50 ppm). The peak at +9.3 ppm must therefore be due to N_c in a complex in which glycine is bound to the metal through oxygen, as in **16**.[45] The broadening would be expected if exchange was occurring between free and O-bound glycine.

These results clearly showed that a small proportion of **16**, with glycine bound only through carboxylate oxygen, was present in equilibrium with **1**, free glycine, and the chelate complex **13**. Weak peaks from **16** were present in spectra run at pH 2 or below but were not detectable at pH 4. These spectroscopic changes were all reversible when pH values were cycled. To allow the ^{13}C peak from the carboxylate carbon atom in **16** to be detected, glycine with this carbon atom enriched in ^{13}C was added to a solution of **1** in D_2O, and the pD was adjusted to 1.0. In the ^{13}C NMR spectrum, strong peaks were observed from the carboxyl carbon atom in the chelate complex **13** (187.2 ppm) and from free glycine (171.2 ppm) and a weaker peak was observed at 174.8 ppm which was assigned to **16**. In the ^{1}H NMR spectrum of a D_2O solution prepared from **1** and glycine, at pD 1.0, a broad singlet was observed at 3.88 ppm. The methylene protons from free glycine and **16** were therefore close enough in chemical shift that only an averaged signal was observed.

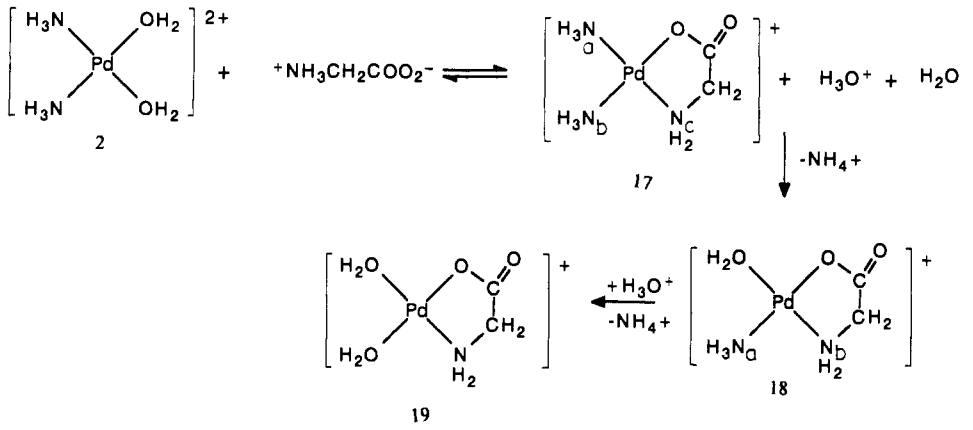
Reaction of [Pt(en)(H_2O)$_2$]$^{2+}$ with Glycine. We previously reported[6,7] that *cis*-[Pt(NH_3)$_2$(H_2O)$_2$]$^{2+}$ reacts with glycine to form initially *cis*-[Pt(NH_3)$_2$(Hgly-O)(H_2O)]$^{2+}$, which then slowly undergoes chelate ring closure to form [Pt(NH_3)$_2$(gly-N,O)]$^+$. In view of the finding presented above, that small amounts of carboxylate-bound complex were present in acid solution in the palladium system, in equilibrium with the chelate complex, we considered the possibility that a similar equilibrium could exist with the platinum complexes but that small amounts of carboxylate-bound complex were not detected. We decided therefore to re-examine carefully the platinum–glycine system. To counter the slight possibility that ethylenediamine complexes might behave differently from cis-diammine ones, we examined the reaction of [Pt(en)(H_2O)$_2$]$^{2+}$ rather than the diammine complexes. The pH of the solution was maintained at ≤1.8 throughout, because the equilibrium constant would certainly strongly favor the chelate complex at higher pH values, and once formed, the chelate complex cannot be converted to a carboxylate-O complex by treatment with acid.[6,7] The behavior of the complexes was similar to that of the diammine complexes, in that [Pt(en-$^{15}N_2$)(Hgly-O)-

(43) Agnew, N. H.; Appleton, T. G.; Hall, J. R. *Inorg. Chim. Acta* **1980**, *41*, 71.

(44) Agnew, N. H.; Appleton, T. G.; Hall, J. R. *Inorg. Chim. Acta* **1980**, *41*, 85.

(45) The peak at +9.3 ppm was not due to small amounts of H_2(en-$^{15}N_2$)$^{2+}$, since it was observed only when ^{15}N-labeled glycine was present and the measured δ_N for H_2(en-$^{15}N_2$)$^{2+}$, +9.9, was significantly different.

Scheme 2



$(H_2O)]^{2+}$ was formed initially (^{15}N NMR spectrum, singlets with satellites for ethylenediamine ^{15}N trans to glycine O (–44.6 ppm) and trans to H_2O (–48.5 ppm) and a singlet for glycine ^{15}N (+9.1 ppm)). Peaks due to $[Pt(en\text{-}^{15}N_2)(gly\text{-}^{15}N,O)]^+$ appeared within 3 h (^{195}Pt spectrum doublet of doublets of doublets at –2448 ppm, ^{15}N spectrum doublet for ethylenediamine ^{15}N trans to glycinate N at –29.1 ppm (J(Pt–N) = 327 Hz, $J(^{15}N\text{–}Pt\text{–}^{15}N)$ = 3.5 Hz), singlet for ethylenediamine ^{15}N trans to glycinate O (–46.5 ppm, J(Pt–N) = 361 Hz), glycinate ^{15}N doublet at –53.0 ppm (J(Pt–N) = 263 Hz)). In this strongly acidic solution, approximately 2 weeks was required for all of the complex with glycine O-bound to react, but after this time, there were no detectable peaks from this complex. With an initial small excess of diammineplatinum over glycine (1:0.8), all of the glycine present was in the form of the chelate complex. The equilibrium concentration of the complex with glycine bound monodentately through oxygen was therefore undetectably small.

Reaction of *cis*-$[Pd(NH_3)_2(H_2O)_2]^{2+}$ (2) with Glycine (Scheme 2). For glycine only, of the ligands studied, the reaction with a solution containing predominantly *cis*-$[Pd(^{15}NH_3)_2(H_2O)_2]^{2+}$ (**2**) (in equilibrium with small amounts of $[Pd(^{15}NH_3)_3(H_2O)]^{2+}$ and $[Pd(NH_3)(H_2O)_3]^{2+}$, prepared as described previously[11]) was studied by ^{15}N NMR. When [^{15}N]glycine was added to a solution containing excess **2**, the ^{15}N NMR spectrum run immediately showed two doublets at –57.1 and –46.4 ppm ($J(^{15}N\text{–}Pd\text{–}^{15}N)$ = 4.0 Hz) and a singlet at –68.8 ppm, which were easily assigned to $[Pd(^{15}NH_3)_2(gly\text{-}^{15}N,O)]^+$ (**17**) (respectively, ammine N_a, glycinate N_c, and ammine N_b). Protons were released by the chelation of glycinate, so the pH of this solution immediately after mixing was low (approximately 1.0). There was then a slow reaction as this acid reacted with coordinated ammonia. Within 10 min of mixing, weaker peaks were present: singlets at –68.2 and –59.8 ppm. In parallel experiments with [^{14}N]-glycine, the peak at –59.8 ppm was absent, so it could be assigned to glycinate $^{15}N_b$ in the isomer of $[Pd(^{15}NH_3)(H_2O)(gly\text{-}^{15}N,O)]^+$ with this N atom trans to H_2O, **18**. The peaks from **18** continued to grow for several hours, becoming the dominant peaks in the spectrum. No confident assignment could be made for peaks from the other isomer of $[Pd(^{15}NH_3)(H_2O)(gly\text{-}^{15}N,O)]^+$, with the N-donor atoms trans. If present, these peaks were very much weaker than those due to **18**. Once again, the more stable isomer was, as predicted, that in which ligands of highest trans influence are trans to those of weakest trans influence. After several hours, equilibrium was established, and there was no further change in the spectrum. As well as strong peaks from **18**, and weak peaks from **2** and **17**, there was also a weak peak at –64.4 ppm. When dilute HNO_3 was added to the solution, this peak grew more intense at the expense of those from **17** and **18**. It was assigned to $[Pd(H_2O)_2(gly\text{-}^{15}N,O)]^+$ (**19**).

With the use of ^{13}C-enriched glycine under comparable conditions, the carboxylate carbon resonances for the complexes **17** and **18** could be observed (187.5 and 186.4 ppm, respectively).

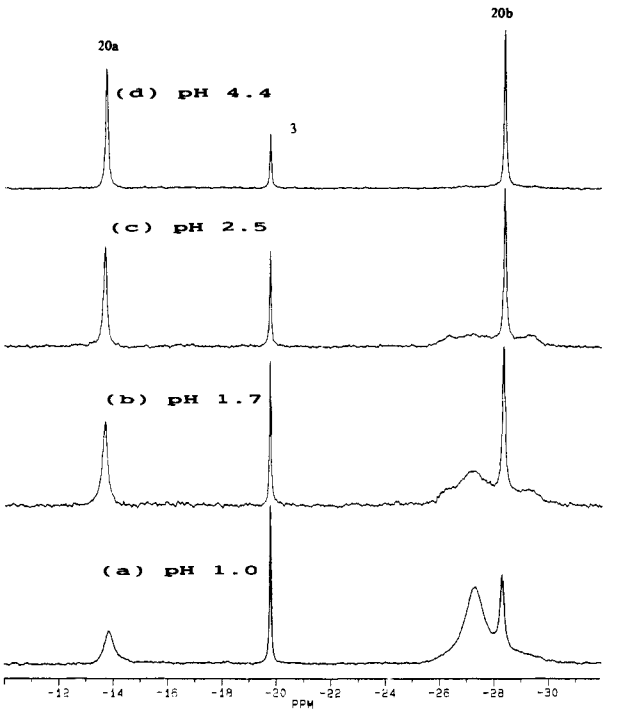


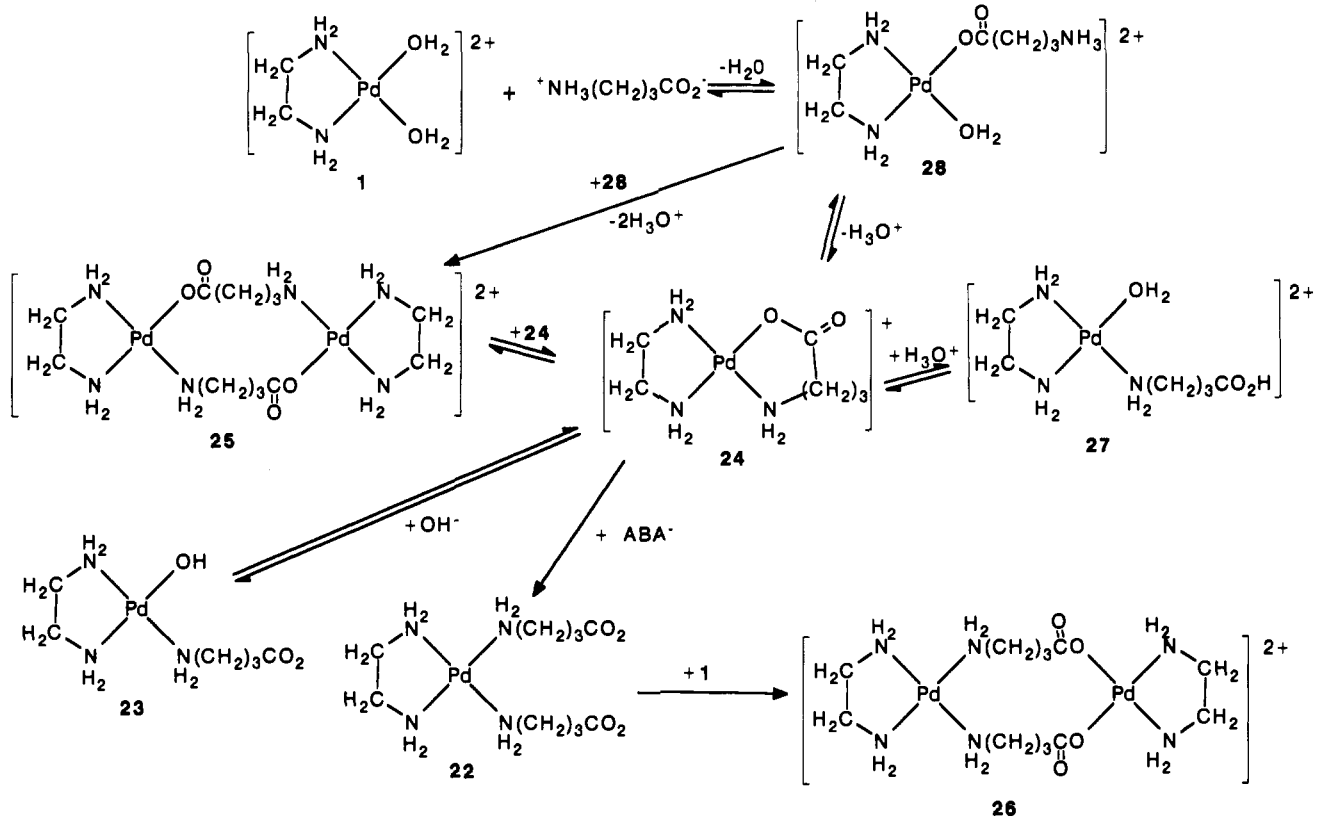
Figure 5. Effect of pH on the 20.2-MHz ^{15}N NMR spectrum of a solution prepared from $[Pd(en\text{-}^{15}N_2)(H_2O)_2](NO_3)_2$ and 0.8 mol equiv of β-alanine in ^1H_2O. Peak labels correspond to those in structural diagrams and Table 1.

When acid was added to produce **19**, a strong peak was observed at 187.5 ppm (coincident with the peak from **17**).

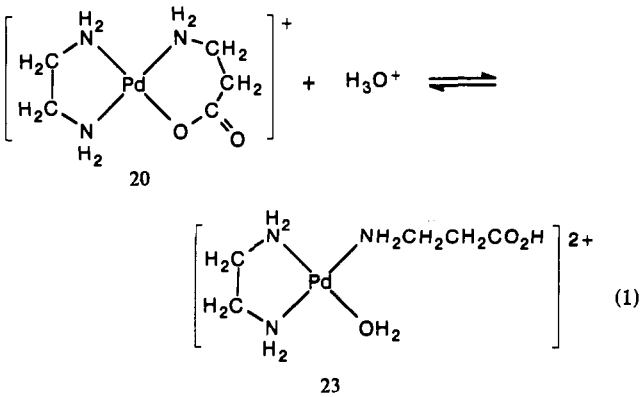
If an excess of [^{15}N]glycine was used, peaks due to **17** were observed initially, but peaks from the isomers of $[Pd(gly\text{-}^{15}N,O)_2]$ and free $^{15}NH_4^+$ grew over several hours. If the glycine:Pd ratio was >2, these (and a peak from excess free glycine) eventually were the only peaks in the ^{15}N NMR spectrum.

Reactions of $[Pd(en)(H_2O)_2]^{2+}$ (1) with β-Alanine. When β-alanine (Hβala) (0.8 mol equiv) was added to an aqueous solution of $[Pd(en\text{-}^{15}N_2)(H_2O)_2]^{2+}$ (**1**) and the pH adjusted to 4.4, the ^{15}N NMR spectrum of the resultant solution (Figure 5d) showed two sharp singlets which were assigned to ethylenediamine N atoms N_a and N_b trans respectively to N and O of chelated β-alaninate in $[Pd(en\text{-}^{15}N_2)(\beta ala\text{-}N,O)]^+$ (**20**). The ^{13}C NMR spectrum of this solution showed the expected peaks from two methylene carbon atoms of the ethylenediamine ligand (each showing 3.5 Hz coupling to ^{15}N) and the two methylene carbon atoms and the carboxylate carbon of the β-alaninate ligand. The carboxylate carbon nucleus was more shielded (181.8 ppm) than for the glycinate analogue, as expected with a six-membered rather than a five-membered ring.[7,41] When acid was added to decrease the pH to 2.5, an envelope of peaks in the ^{15}N NMR spectrum

Scheme 3



between −25 and −30 ppm (Figure 5c) was similar to that for the betaine system at 298 K (Figure 1b) and clearly was due to complexes in which β-alanine was coordinated only through the carboxylate oxygen, $[Pd(en\text{-}^{15}N_2)(H\beta ala\text{-}O)(H_2O)]^{2+}$ (**21**) and $[Pd(en\text{-}^{15}N_2)(H\beta ala\text{-}O)_2]^{2+}$ (**22**), in equilibrium with **1**. These peaks were much more intense, relative to those from the chelate complex, than the corresponding peaks under the same conditions for the glycinate system. As well, there was significant broadening of the peaks due to the chelate complex, especially the peak from N_a, in strongly acidic solutions (Figure 5a,b). This broadening was not due to any rapid exchange of β-alanine between **21** and **20**, as the peak from N_b in **20** would then be expected to broaden more than the peak from N_a and to coalesce with the nearby peaks from **21**. The reaction responsible was more likely to be a rapid reaction in which the Pd–N bond remains intact but the Pd–O bond in the six-membered chelate ring opens, to form $[Pd(en)(H\beta ala\text{-}N)(H_2O)]^{2+}$ (**23**), and closes again (eq 1). Analogous broadening was not observed for the peaks from the glycinate chelate complex **13** in acid solution.



(1)

The chelate complex **20** was dominant over the pH range 4–10, but by pH 10 (still with Pd in excess), the peaks from **20** had begun to broaden, as $[Pd(en)(\beta ala\text{-}N)(OH)]$ (**24**) began to form, and exchange with **20** (with the glycinate complexes, broadening began at higher pH). By pH 12, the peaks from the chelate had disappeared, and there were sharp peaks at −19.6 and −25.2 ppm from **24**. There was also the expected peak at −27.9 ppm from $[Pd(en)(OH)_2]$ (**6**) and a weak peak at −16.4 ppm from $[Pd(en)(\beta ala\text{-}N)_2]$ (**25**).

When β-alanine was in excess, the spectra of acid solutions were qualitatively similar to those discussed above. At pH 10.2, a single peak was observed, from **25**, at −16.5 ppm.

In summary, the chemistry of the β-alanine complexes was overall similar to that of the glycinate analogues, but the N,O-chelate complex was less stable relative to nonchelate species than for glycinate.

Reactions of $[Pd(en)(H_2O)_2]^{2+}$ (1) with γ-Aminobutyric Acid (Scheme 3). The spectra for this system were overall much more complicated than with glycine or β-alanine. The simplest spectra were obtained at high pH. When *excess* Hγaba was added to $[Pd(en\text{-}^{15}N_2)(H_2O)_2]^{2+}$ (**1**) and the pH was adjusted to any value >4, the dominant peak in the ^{15}N NMR spectrum was a sharp singlet at −16.4 ppm, which was assigned to $[Pd(en\text{-}^{15}N_2)(\gamma aba\text{-}N)_2]$ (**26**).

With a ratio of Hγaba:**1** = 0.8:1 the effect of pH on the ^{15}N NMR spectrum is illustrated in Figure 6. The simplest spectrum in this series was that run at pH 12.0 (Figure 6e). It showed two strong sharp peaks with chemical shifts corresponding to ethylenediamine ^{15}N trans to an N-donor and an O-donor, respectively. In such a strongly alkaline solution, in both the glycinate and β-alaninate systems, the dominant complex was $[Pd(en)(NH_2(CH_2)_nCO_2)(OH)]$ (**14** for n = 1, **24** for n = 2). These peaks were therefore assigned to the analogous γaba complex (n = 3, **27**). The only other peaks in the spectrum were relatively weak peaks from $[Pd(en)_2]^{2+}$ (**3**) impurity, $[Pd(en)(OH)_2]$ (**6**), and $[Pd(en)(\gamma aba\text{-}N)_2]$ (**26**). When the pH was decreased to 10 (Figure 6d), the peaks from $[Pd(en)(\gamma aba\text{-}N)(OH)]$ (**27**) were still strong, but the peak from $[Pd(en)(\gamma aba\text{-}N)_2]$ (**26**) was much stronger, and peaks from the oligomers $[\{Pd(en)(\mu\text{-}OH)\}_n]^{n+}$ (**4** and **5**) were also quite strong. This behavior contrasted with that observed with glycinate and β-alaninate, where peaks from the

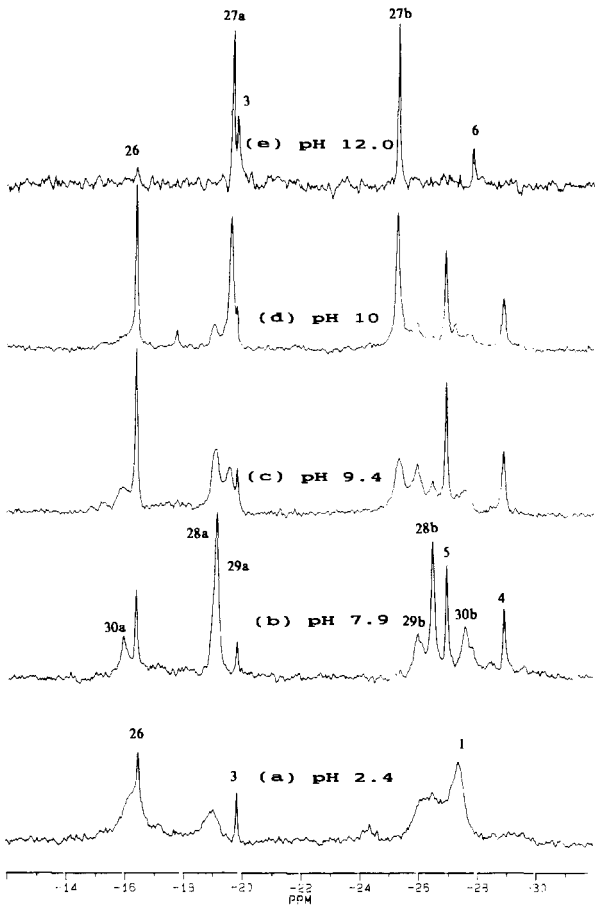


Figure 6. Effect of pH on the 20.2-MHz ^{15}N NMR spectrum of a solution prepared from [Pd(en-$^{15}N_2$)(H_2O)$_2$](NO_3)$_2$ and 0.8 mol equiv of γ-aminobutyric acid in ^1H_2O. Peak labels correspond to those in structural diagrams, Scheme 3, and Table 1.

chelate complex were dominant at this pH. A number of weak peaks were observed in this spectrum, which became more intense as the pH was decreased further.

The ^{15}N NMR spectrum at pH 7.9 (Figure 6b) showed, apart from peaks already discussed above, two strong relatively sharp peaks with chemical shifts corresponding to ethylenediamine nitrogen trans to N and O, respectively. For the other amino acids, peaks from the N,O-chelate complex were always sharp under these conditions, so these peaks have been assigned to [Pd(en)(γaba-*N*,*O*)]$^+$ (**28**). There were also three weaker, broader peaks, which all had the same intensities, 1 in the region for ^{15}N trans to N and 2 in the region for ^{15}N trans to O. The simplest complexes that would give such a set of peaks would be the isomers **29** and **30** of [{Pd(en-$^{15}N_2$)(μ-γaba)}$_2$]$^{2+}$, in which each γaba ligand binds to one Pd atom through N and to a second through O. The environments of the ethylenediamine nitrogen atoms in isomer **29** should be similar to those in the chelate complex **28**, so a peak close to peak 28b has been assigned to N_b trans to carboxylate in **29**. It appears that the peak from N_a in **29** was coincident with peak 28a. In isomer **30**, the ethylenediamine N atoms bound to one Pd atom (N_a) are in an environment similar to that in [Pd(en)(γaba-*N*)$_2$] (**26**) and the ethylenediamine N atoms bound to the other Pd atom (N_b) are in an environment similar to that in [Pd(en)(bet-*O*)$_2$]$^{2+}$ (**8**). The shifts of peaks labeled 30a and 30b, respectively, are consistent with these expectations. The broadening of the peaks would be due to the effects of reactions in which the palladium–carboxylate bonds of **29** and **30** were broken. Although the assignments of these peaks in Figure 6b remain tentative, they are self-consistent. At pH 9.4 (Figure 6c), these peaks were all present, together with the peaks assigned to [Pd(en)(γaba-*N*)(OH)] (**27**).

Apart from the disappearance of peaks due to the hydroxo-bridged oligomers **4** and **5** and the growth of a peak due to **1**, there were few changes in the ^{15}N NMR spectrum when the pH was decreased to 4. With further addition of acid (*e.g.*, to pH 2.4, Figure 6a), the peaks due to **1** and to complexes with the ligand bound only through carboxylate O (*e.g.*, **32**) grew, and the peaks due to the chelate and amino acid-bridged complexes became broad, presumably due to rapid equilibrium with [Pd(en)(Hγaba-*N*)(H_2O)]$^{2+}$ (**31**). Even in this strongly acid solution, a peak with significant intensity was still present due to [Pd(en)(Hγaba-*N*)$_2$]$^{2+}$ (**26**).

Discussion

In the reactions of *cis*-[$Pt(NH_3)_2(H_2O)_2$]$^{2+}$ with amino acids $^+NH_3(CH_2)_nCO_2^-$ in mildly acidic solution, complexes with the amino acid bound monodentately only through carboxylate oxygen form initially.[6,7] We have described these complexes as "metastable". They are kinetic products which are thermodynamically unstable relative to N,O-chelates, at least for n = 1 and 2. *cis*-[$Pt(NH_3)_2$(Hgly-*O*)(H_2O)]$^{2+}$ spontaneously slowly reacts, even in quite strongly acidic solution, to give [$Pt(NH_3)_2$(gly-*N*,*O*)]$^+$.[6,7] To ensure that the presence of ethylenediamine, rather than two ammine ligands, coordinated to the metal does not affect this aspect of the chemistry, we have studied by ^{15}N NMR the reaction of [Pt(en)(H_2O)$_2$]$^{2+}$ with glycine in a solution with pH maintained near 1.7. As expected, [Pt(en)(Hgly-*O*)(H_2O)]$^{2+}$ formed initially but, after 2 weeks, converted entirely to [Pt(en)(gly-*N*,*O*)]$^+$. In the reaction of β-alanine with *cis*-[$Pt(NH_3)_2(H_2O)_2$]$^{2+}$ (n = 2), the conversion of *cis*-[$Pt(NH_3)_2$(Hβala-*O*)(H_2O)]$^{2+}$ to [$Pt(NH_3)_2$(βala-*N*,*O*)]$^+$ requires heating at pH 5.5, but the reaction is irreversible, and the chelate complex is clearly thermodynamically preferred.

Our results have shown that [Pd(en)(Haa-*O*)(H_2O)]$^{2+}$ exists together with [Pd(en)(aa-*N*,*O*)]$^+$ in acid solution (Haa = amino acid). The carboxylate-bound complexes are therefore not just kinetic products but are present in equilibrium under these conditions. The difference in the relative thermodynamic stabilities of monodentate O-bound Haa and N,O-chelated aa$^-$ between the two metal ions may be due to a smaller preference for N-donors over O-donors generally for Pd^{2+} compared with Pt^{2+}. The expectation that palladium(II) chemistry will be similar to that of platinum(II), except that reactions will be faster (see Introduction), has not, at least in this instance, been entirely fulfilled.

Only with γ-aminobutyric acid were complexes other than the N,O-chelate complex important over the pH range 4–10. Clearly the seven-membered chelate ring in **28** was much less stable relative to the complexes with bridging amino acid (**29**, **30**) than with glycinate and β-alaninate. The hydroxo complex [Pd(en)(aa-*N*)(OH)] was also present at lower pH values for aa = γaba than with the other amino acids. The differences in stability between the five-membered glycinate chelate ring and the six-membered β-alaninate chelate ring were most evident in acid solution (pH <4), both in the greater concentration of complex with the amino acid bound only through carboxylate and in the broadening of peaks due to the N,O-chelate complex as the equilibrium with [Pd(en)(Hβala-*N*)(H_2O)]$^{2+}$ became important.

The clear decrease in the thermodynamic stability of the N,O-chelate palladium complex relative to nonchelate complexes as the chelate ring size increased from 5 to 6 to 7 mirrors the differences in the kinetics of chelate ring closure with the platinum complexes.[7]

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Supplementary Material Available: Details of the preparation of ^{15}N-labeled ethylenediamine, Table S1, giving ^1H and ^{13}C NMR data, and Table S2, giving analytical data (4 pages). Ordering information is given on any current masthead page.