III. The quadrupole splitting for the high-spin state is almost independent of pressure and has a small negative slope (Table III). In contrast, the quadrupole splitting in the low-spin state, which is dominated by the lattice contribution to the ECG tensor, increases by a factor of at least 3 between 3 and 70 kbar. The applied pressure apparently has a significant influence upon the symmetry of the "packing" of the ligands about the iron(II) ion. In the high-spin state a difference in sign for the pressure dependence of the valence and lattice contribution to the EFG tensor may account for the small change in the quadrupole splitting with pressure.

A study of the pressure dependence of the spin state in Fe[HB(3,4,5-$(CH_3)_3$pz$)_3]_2$ provides a nice contrast to the above work. For this compound, the low-temperature results (see Table I) indicate that it is always completely high spin, at least down to 1.7 K. In this case, the thermal contraction upon cooling is not significant enough to increase the crystal field and promote the population of the low-spin state. The spectra obtained for Fe[HB(3,4,5-$(CH_3)_3$pz$)_3]_2$ at 4.2 K in an applied field are shown in Figure 6. In this case, because of the large quadrupole interaction, the applied field results clearly indicate a negative quadrupole interaction and a small asymmetry parameter. As expected for a paramagnetic material, the internal field is equal to the applied field. The quadrupole interaction is virtually independent of temperature, and the isomer shift shows values typical of high-spin iron(II) with a temperature dependence that is typical of the second-order Doppler shift.

The Mössbauer effect spectra of Fe[HB(3,4,5-$(CH_3)_3$pz$)_3]_2$, obtained at various pressures and illustrated in Figure 7, indicate that, as expected, a much higher pressure is required to observe the low-spin state in this compound. In fact, as illustrated in Figure 5, approximately 12 times higher applied pressures are required to produce the same fraction of the low-spin state in Fe[HB(3,4,5-$(CH_3)_3$pz$)_3]_2$ as is found in Fe[HB(3,5-$(CH_3)_2$pz$)_3]_2$. Once again the conversion to the low-spin state is gradual, and the results indicate that at 24 kbar the low-spin state is 200 cm^{-1} above the high-spin ground state. The two spin states are equivalent in energy at ca. 55 kbar and the low-spin state is 75 cm^{-1} below the high-spin state at 86 kbar. These results are an indication that the application of high pressure is sufficient to produce a spin-state change in iron(II) even when no such change is indicated at low temperature. The pressure dependence of the hyperfine parameters are reasonable for Fe[HB(3,4,5-$(CH_3)_3$pz$)_3]_2$ in that the isomer shift decreases with increasing temperature, whereas the quadrupole interaction decreases for the high-spin state and increases for the low-spin state with increasing pressure. This latter difference again may indicate a different pressure dependence for the valence and lattice contribution to the EPG tensor in the high-spin state.

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Registry No. Fe[HB(pz$)_3]_2$, 16949-45-4; Fe[HB(3,4,5-$(CH_3)_3$pz$)_3]_2$, 16949-44-3; Fe[HB(3,5-$(CH_3)_2$pz$)_3]_2$, 17567-19-0.

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Oxidation of a Dinuclear Platinum(II) Complex with Hydrogen Peroxide

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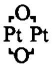
The oxidation of a dinuclear Pt(II) complex with hydrogen peroxide is described. The dinuclear complex ion [*cis*-Pt^{II}($^{15}NH_2CH_2CH_3)_2(\mu$-$OH)]_2^{2+}$ undergoes oxidation in aqueous H_2O_2 to produce dinuclear Pt(IV) ions of the type [*cis*-Pt^{IV}($^{15}NH_2CH_2CH_3)_2(OH)_2(\mu$-$OH)]_2^{2+}$. Following the reaction by using ^{195}Pt NMR spectroscopy and isolation of the major product revealed that oxidation primarily yields a D_{2h}-symmetry dinuclear compound having a four-membered  ring. However, the fact that the reaction also yields lower symmetry dinuclear Pt(IV) compounds possessing this ring indicates that the oxidation, at least in part, proceeds through an "open-ring" intermediate that allows isomerization to occur. The ^{195}Pt NMR chemical shifts and $^1J(^{195}Pt$–$^{15}N)$ values, the latter measured by using both ^{195}Pt and ^{15}N NMR spectroscopies, were used to examine the effects of the four-membered ring and the various ligands on the electronic properties of the platinum ion.

Introduction

Recent interest in platinum coordination chemistry has been greatly stimulated by the finding that the simple square-planar complex *cis*-$Pt(NH_3)_2Cl_2$, cisplatin, is a potent anticancer agent.[1] Studies on the mechanism of action of the compound have suggested that its cytotoxic effects are related to its ability to bind to cellular DNA.[2] In addition to complexes of Pt(II), many Pt(IV) compounds have been found to be effective as anticancer agents.[3–5] Since Pt(IV) complexes are generally slow to undergo substitution reactions,[6] it has been suggested that their ability to kill tumor cells requires reduction to active Pt(II) compounds.[7] Supporting this hypothesis is the observation that divalent platinum complexes have been found in the urine and plasma of cancer patients receiving the Pt(IV) antitumor agent iproplatin, *cis,-cis,trans*-$Pt^{IV}(NH_2CH(CH_3)_2)_2Cl_2(OH)_2$. Moreover, chemical reduction of iproplatin using Fe(III) salts or ascorbate has been shown to produce a Pt(II) complex that is known to be active as

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an antitumor agent and is also capable of binding to and unwinding supercoiled DNA.[3,9]

In attempting to identify new types of antitumor-active Pt(IV) complexes, we examined the ability of hydrogen peroxide to oxidize dinuclear Pt(II) complexes of the type $[cis\text{-Pt}^{II}L_2(\mu\text{-OH})]_2^{2+}$, where L is a monodentate amine, to dinuclear Pt(IV) species. In a previous report[10] we demonstrated that, for L = NH_3, $NH_2CH_2CH_3$, and $NH_2CH(CH_3)_2$, it is possible to oxidize the Pt(II) dimers to Pt(IV) compounds possessing the bis(μ-hydroxo) linkage. Although Pt(IV) dimers have been previously synthesized via dimerization of mononuclear[11] or breakdown of tetranuclear[12] Pt(IV) complexes, hydrogen peroxide oxidation of dimeric Pt(II) compounds provides a synthetic route to new materials possessing the antitumor-active *cis*-diamine geometry. In this work, we focus on a group of compounds containing ^{15}N-enriched $NH_2CH_2CH_3$ and examine the solution chemistry leading to divalent and tetravalent dimer formation using ^{195}Pt NMR spectroscopy. In addition, the ^{195}Pt NMR chemical shifts and coupling constant values, $^1J(^{195}\text{Pt}-^{15}\text{N})$, the latter measured by using both ^{195}Pt and ^{15}N NMR spectroscopy, have been used to examine the effects of the ligands and the four-membered ring present in the compounds on the electronic properties of the platinum ion.

Experimental Section

Reagents and Instrumental Techniques. Unless otherwise noted, all of the compounds used in the syntheses were reagent grade. The ^{15}N-enriched ethylamine hydrochloride was purchased from MSD Isotopes.

Proton-decoupled ^{195}Pt NMR spectra at 53.7 MHz were obtained (25 °C) by using a homemade spectrometer having a tunable 10-mm multinuclear probe. The data were collected by employing a typical spectral width of 20–30 kHz with a total delay of 1.0 s between 10-μs pulses. Good spectral data on solutions containing 50–60 mM total platinum could be obtained with (3–5) × 10^4 scans. All shifts reported as negative were located on the high-field side of external Na_2PtCl_6. Proton-decoupled ^{15}N NMR spectra were obtained at 25 MHz by using a 10-mm probe. The spectral conditions for the measurements were as follows: 20–25-kHz spectral width, 8K data ports, and broad-band proton-noise decoupling. Chemical shifts were initially determined by using external $HCONH_2$ and ultimately referenced to liquid NH_3 by using the expression $\delta = \delta_{obsd} + 112.6$ ppm.

Although the value of the coupling constant $^1J(^{195}\text{Pt}-^{15}\text{N})$ could be obtained from either ^{195}Pt or ^{15}N NMR data, where possible, the latter were used to obtain the value. The significant temperature dependence of ^{195}Pt NMR chemical shifts gave rise to relatively broad lines having widths that varied widely from run to run (30–200 Hz). In light of the relative intensities of many of the multiplets observed, i.e. 1:2:1, line broadening had the effect of yielding an observed coupling constant that was less than its true value.

Infrared spectra were recorded on a Perkin-Elmer 4220 spectrometer, with Nujol mulls in KBr disks or with KBr pellets. Microanalyses were carried out either by the Bristol Myers Co., Syracuse, NY, or by Atlantic Microlab, Atlanta, GA.

Synthesis. Since ethylamine was used for all of the syntheses, it is referred to as L in the procedures given below.

***cis*-Bis(nitrato)bis(ethylamine)platinum(II), *cis*-$Pt^{II}L_2(NO_3)_2$ (1).** The following, a modification of an earlier reported procedure,[13] involved two silver halide precipitations.

To a filtered solution containing 10.0 g (24.1 mmol) of potassium tetrachloroplatinate in 80 mL of water was added a solution containing 80 g (482 mmol, 5-fold excess) of KI in 50 mL of H_2O. The resulting solution was left stirring at room temperature for 10 min, after which time 3.10 g (68.8 mmol) of a 70% aqueous solution of ethylamine was added dropwise. After the mixture was stirred for 1 h, the crude yellow precipitate, *cis*-$Pt^{II}L_2I_2$, was removed by filtration, washed with small amounts of water, ethanol, and ether, and air-dried. Yield: 12 g (92%).

Table I. Platinum-195 and Nitrogen-15 NMR Data in Aqueous Solution

complex[a]	$\delta(^{195}\text{Pt})$[b]	$\delta(^{15}\text{N})$[c]	$^1J(^{195}\text{Pt}-^{15}\text{N})$, Hz
cis-$[Pt^{II}L_2(H_2O)_2]^{2+}$ (**1**)[d]	−1721	−34.8	435[e]
cis-$Pt^{II}L_2(OH)_2$[f]	−1695		333
$[cis\text{-}Pt^{II}L_2(\mu\text{-OH})]_2^{2+}$ (**2**)	−1326	−34.6	370[e]
$[cis\text{-}Pt^{II}L_2(\mu\text{-OH})]_3^{3+}$	−1680		
cis-$Pt^{IV}L_2(OH)_4$ (**4**)[f]	+1745		269
$[cis\text{-}Pt^{II}L_2(H_2O)(\mu\text{-OH})\text{-}cis\text{-}Pt^{II}L_2(H_2O)]^{3+}$	−1623		
D_{2h}-$[cis\text{-}Pt^{IV}L_2(OH)_2(\mu\text{-OH})]_2^{2+}$ (**3**)	+1925	−7.8	317[e]
C_2,C_s-$[cis\text{-}Pt^{IV}L_2(OH)_2(\mu\text{-OH})]_2^{2+}$	+1977		265, 317
C_2,C_s-$[cis\text{-}Pt^{IV}L_2(OH)_2(\mu\text{-OH})]_2^{2+}$	+1980		265, 317
C_1-$[cis\text{-}Pt^{IV}L_2(OH)_2(\mu\text{-OH})]_2^{2+}$	~+1947		

[a] L = $^{15}NH_2CH_2CH_3$. [b] ^{195}Pt NMR chemical shifts in H_2O relative to external Na_2PtCl_6 in D_2O. [c] ^{15}N NMR chemical shifts in H_2O relative to liquid NH_3. [d] The complex ion obtained by dissolution of *cis*-$Pt^{II}L_2(NO_3)_2$ (**1**) in water. [e] Measured from ^{15}N NMR spectral data; ±2 Hz. [f] pH 13.2.

To 10.0 g (18.6 mmol) of *cis*-diiodobis(ethylamine)platinum(II) in 25 mL of water was added 6.15 g (30.2 mmol, 1.95 equiv) of $AgNO_3$ in 10 mL of water. The suspension was left stirring overnight in a flask wrapped with aluminum foil. The AgI that formed was removed by filtration, and an excess of KCl (or 1 M HCl) was added to the yellow filtrate, resulting, after cooling to 5 °C, in the crystallization of *cis*-PtL_2Cl_2.

To a stirred aqueous solution containing 5.58 g (1.95 equiv) of $AgNO_3$ in 35 mL of water was added 6.0 g (16.185 mmol) of *cis*-$Pt^{II}L_2Cl_2$. Stirring for 20 h in the dark resulted in the precipitation of AgCl, which was removed by filtration and washed with 2 × 3 mL of water. The pale yellow filtrate was reduced under vacuum to induce crystallization. The crude product was recrystallized once from a small amount of hot water that had been acidified with 1 N HNO_3. The compound (**1**) was recovered by filtration, washed with a small amount of cold water, ethanol, and ether, and air-dried. Yield: 5.38 g, 78%. Anal. Calcd for $C_4H_{14}N_4O_6Pt$: C, 11.73; H, 3.42; N, 13.70. Found: C, 11.68; H, 3.25; N, 12.92. IR (cm^{-1}): 3300 vs, 3280 vs, 3190 vs, 1510, 1275 s, 985 m, 825 m.

Bis(μ-hydroxo)-*cis*-bis(ethylamine)platinum(II) Nitrate or Perchlorate, $[cis\text{-}Pt^{II}L_2(\mu\text{-OH})]_2X_2$ (X = NO_3^-, ClO_4^-) (2). *Caution! Perchlorate salts are potentially explosive, and due care should be taken in preparing and handling them.* The following is a modification of the procedure reported earlier by Faggiani et al.[14] To 2.0 g of **1** dissolved in 20 mL of water was added sufficient aqueous 3 N NaOH to adjust the pH to 6.2. After the mixture was allowed to stand at 5 °C for 10 h, colorless needles of the title compound crystallized from solution. A second crop was obtained by readjusting the pH of the filtrate to 6.2 and reducing the volume at reduced pressure (35–40 °C) to 2 mL. The two crops were combined and recrystallized twice from water to give pale yellow needles. Yield: 82%. Anal. Calcd for $C_8H_{30}N_6O_8Pt_2$: C, 13.18; H, 4.12; N, 11.54. Found: C, 13.10; H, 4.15; N, 11.54. IR (cm^{-1}): 3400 s, br, 3240 s, 3140 s, 1035 m, 535 m, 520 m, 500 m.

The perchlorate was isolated by dissolution of the nitrate in water followed by addition of saturated $LiClO_4$ to induce crystallization. The crude product was recrystallized once from water. Anal. Calcd for $C_8H_{30}Cl_2N_4O_{10}Pt_2$: C, 11.95; H, 3.73; N, 6.97. Found: C, 12.04; H, 3.78; N, 6.93.

D_{2h}-Bis(μ-hydroxo)-*cis*-bis(ethylamine)dihydroxoplatinum(IV) Nitrate or Perchlorate, D_{2h}-$[cis\text{-}Pt^{IV}L_2(OH)_2(\mu\text{-OH})]_2X_2$ (X = NO_3^-, ClO_4^-) (3). To 0.77 g of **2** dissolved in 3 mL of water was added 2 mL of 30% aqueous H_2O_2. The yellow solution was left stirring overnight, during which time a small amount of a pale yellow precipitate formed. After the precipitate was removed by filtration, the filtrate volume was reduced under vacuum to 1 mL. The pale yellow product that formed was removed from solution, washed with small amounts of cold water followed by ethanol and ether, and finally air-dried. The crude yellow complex was recrystallized twice from water. Yield: 0.74 g (88%). Anal. Calcd for $C_8H_{34}N_6O_{12}Pt_2$: C, 12.06; H, 4.27; N, 10.55. Found: C, 11.99; H, 4.33; N, 10.53. IR (cm^{-1}): 3420 s, br, 3170 s, 3065 s, 1020 m, 580 m, 540 s, 510 m. Anal. Calcd for $C_8H_{34}Cl_2N_4O_{14}Pt_2$: C, 11.02; H, 3.90; N, 6.43. Found: C, 11.08; H, 3.94; N, 6.41.

***cis*-Tetrahydroxobis(ethylamine)platinum(IV), *cis*-$Pt^{IV}L_2(OH)_4$ (4).** This compound was synthesized in situ by dissolution of 100 mg of **1** in 2.5 mL of water, adjustment of the pH to 12–13 (3 N, NaOH), and addition of 0.5 mL of 30% H_2O_2. A ^{195}Pt NMR spectrum showed the reaction to be complete within 10 min and to produce a single product

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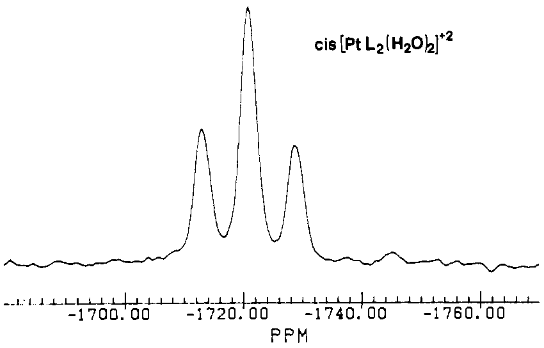

Figure 1. Platinum-195 NMR spectrum of *cis*-$[\mathrm{Pt^{II}}(^{15}\mathrm{NH_2CH_2CH_3})_2(\mathrm{H_2O})_2](\mathrm{NO_3})_2$ in aqueous solutions at pH 2.5.

having the NMR properties given in Table I.

Results and Discussion

The Divalent Compounds. As has been previously shown, adjustment of the pH of the solution containing the complex cation $[cis\text{-}\mathrm{Pt^{II}}(^{15}\mathrm{NH_3})_2(\mathrm{H_2O})_2]^{2+}$ to ~7 results in the formation of dinuclear and trinuclear Pt(II) compounds containing μ-OH bridges.[2b,15-18] The oligomerization process appears to be initiated by deprotonation of one of the coordinated water molecules of the mononuclear species, which in turn reacts with a second complex to initially yield an "open ring" μ-OH-bridged dinuclear compound. This compound either reacts via water displacement with itself to yield a dinuclear Pt(II) complex possessing a four-membered $\mathrm{Pt}\underset{\mathrm{O}}{\overset{\mathrm{O}}{\ }}\mathrm{Pt}$ ring, referred to as the dimer, or reacts with an additional mononuclear complex, referred to as the monomer, via water displacement with itself and ring closure to produce a trinuclear species, the trimer. In the case of coordinated ammonia, the dimer and trimer have been characterized by X-ray analysis,[14,19-21] and the oligomerization process has been investigated by using ^{15}N-enriched compounds and ^{195}Pt and ^{15}N NMR spectroscopies.[2b,15-18] It appears that this general sequence of events is common for a variety of *cis*-diaquo Pt(II) compounds, and dimers, as well as trimers, containing a number of different mono- and bidentate amine ligands have been prepared.[10,22-25]

The proton-decoupled ^{195}Pt NMR spectrum of *cis*-$[\mathrm{Pt^{II}}(^{15}\mathrm{NH_2CH_2CH_3})_2(\mathrm{NO_3})_2]$ (**1**) in aqueous media is shown in Figure 1. Earlier studies have shown that dissolution of this type of complex in water results in loss of the coordinated nitrate ligands and production of the diaquo species *cis*-$[\mathrm{Pt^{II}L_2(H_2O)_2}]^{2+}$.[17] Coupling of the two symmetry-equivalent ($I = {}^1/_2$) ^{15}N nuclei with ^{195}Pt ($I = {}^1/_2$, 34% abundance) yields a 1:2:1 triplet centered at −1721 ppm having a coupling constant $^1J(^{195}\mathrm{Pt}-^{15}\mathrm{N})$ of 435 Hz (Table I). Rapidly adjusting the pH to 13.2 by addition of 3 N NaOH resulted in only a slight change in the position of the resonance but a significant decrease in the value of the coupling constant (Table I). By analogy with the ammonia-containing analogue, the species present in solution at high pH is the dihydroxo complex *cis*-$\mathrm{Pt^{II}}(^{15}\mathrm{NH_2CH_2CH_3})_2(\mathrm{OH})_2$. As has been previously noted, the decrease in the value of ^1J upon substitution of water with hydroxide ion has its origins in the stronger trans-directing ability of the latter compared to that of H_2O.[26]

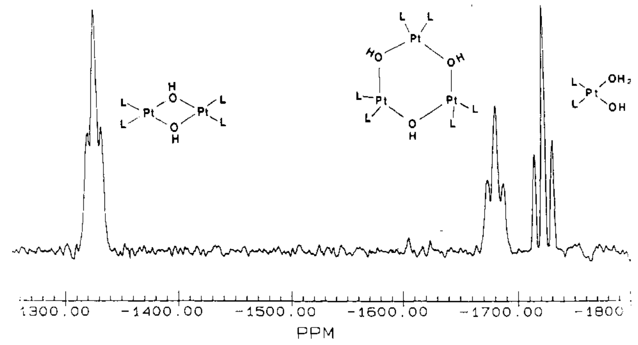

Figure 2. Platinum-195 NMR spectrum showing the monomer *cis*-$[\mathrm{Pt^{II}}(^{15}\mathrm{NH_2CH_2CH_3})_2(\mathrm{OH})(\mathrm{H_2O})]^+$, dimer $[cis\text{-}\mathrm{Pt^{II}}(^{15}\mathrm{NH_2CH_2CH_3})_2(\mu\text{-OH})]_2^{2+}$, and trimer $[cis\text{-}\mathrm{Pt^{II}}(^{15}\mathrm{NH_2CH_2CH_3})_2(\mu\text{-OH})]_3^{3+}$. The spectrum is that of the filtrate obtained after removal of a significant amount of the dimer from solution (Experimental Section).

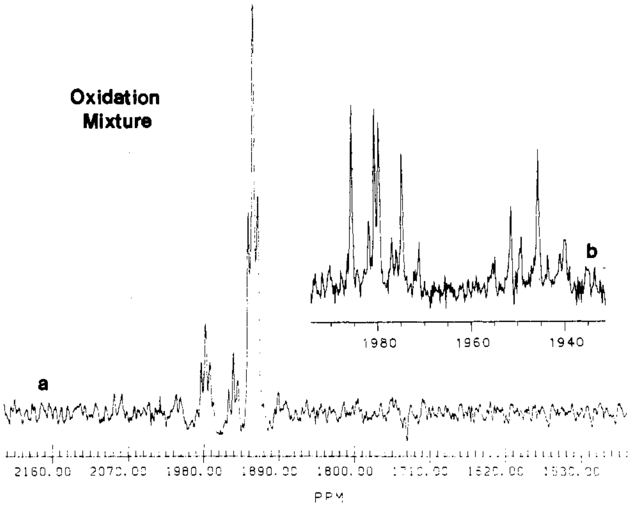

Figure 3. Platinum-195 NMR spectra showing the Pt(IV) products obtained in the oxidation of $[cis\text{-}[\mathrm{Pt^{II}}(^{15}\mathrm{NH_2CH_2CH_3})_2(\mu\text{-OH})]_2^{2+}$ (**2**) with H_2O_2. The regions 1500–2100 ppm (a) and 1930–1990 ppm (b) are shown.

When the pH of a solution containing **1** was adjusted to 6.2 by the addition of alkali, the ^{195}Pt NMR signal due to **1** was observed to decrease in intensity and three new species formed. The first, which appeared during the early part of the oligomerization process (within 15 min), occurred at −1623 ppm. Although its low intensity and transient nature precluded recording of reliable coupling constant data, analogy with the ammonia system suggests that this signal is due to an "open-ring" dinuclear structure, i.e. $[cis\text{-}\mathrm{Pt^{II}L_2(H_2O)}(\mu\text{-OH})\text{-}cis\text{-}\mathrm{Pt^{II}L_2(H_2O)}]^{3+}$ or its monodeprotonated form. As the oligomerization proceeded, a strong signal was observed at −1326 ppm, subsequently associated with the dimer $[cis\text{-}\mathrm{Pt^{II}L_2}(\mu\text{-OH})]_2^{2+}$ (**2**), while a somewhat weaker signal associated with the trimer $[cis\text{-}\mathrm{Pt^{II}L_2}(\mu\text{-OH})]_3^{3+}$ appeared at −1680 ppm. A ^{195}Pt NMR spectrum of a solution containing the monomer, dimer, and trimer is shown in Figure 2.

As outlined in the Experimental Section, the dimer **2** can be isolated in good yield from the solution containing the mixture of compounds. The complex is stable in the solid state and, as

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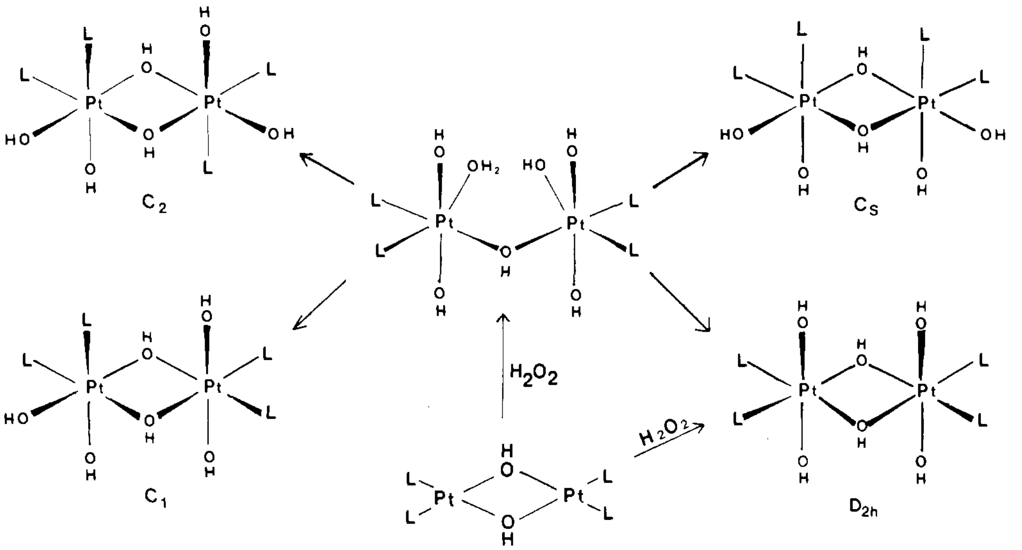
Scheme I



shown by ^{195}Pt NMR, also in aqueous solution (weeks, pH 4–7). As with other μ-OH-bridged Pt(II) dimeric species,[14,19,21] the strain present in the four-membered $\overset{O}{\underset{O}{\mathrm{Pt\ Pt}}}$ ring of **2** significantly deshields the platinum nucleus, causing the resonance of the compound to occur ~400 ppm to lower field relative to those of the strain-free monomer and trimer. The presence of this ring is also evident from the infrared spectrum of the compound, while exhibits a band diagnostic of this feature at 1035 cm^{-1}.

Oxidation of 2 with Hydrogen Peroxide. After consideration of a number of observations pertaining to the oxidation and by reference to the events that are believed to occur in the breakdown of certain tetranuclear Pt(IV) complexes in solution,[12] the oxidation of **2** with hydrogen peroxide appears to proceed according to Scheme I.

Monitoring the oxidation of ^{15}N-labeled **2** by using ^{195}Pt NMR revealed that the oxidation is rapid and that more than one Pt(IV) product is produced in the reaction. Within 15 min after the addition of H_2O_2 to a solution of **2**, the signal at −1326 ppm due to the dimer disappears and a number of new signals in the general region for Pt(IV) having an N_2O_4 donor set appear. One of the signals is transient and weak (+1750 ppm) and appears only in the early time course of the oxidation. The spectrum at the end of the oxidation is shown in Figure 3a. The intensity and pattern of the signals were found to be invariant with time (days) at room temperature and upon heating the NMR sample to 90 °C. Although its relative intensity changed somewhat in the various oxidation reactions carried out, the triplet centered at +1925 ppm accounted for ~70% of the total ^{195}Pt NMR signal intensity in the mixture at the end of the oxidation. Isolation of the compound producing the signal and subsequent characterization of it using X-ray analysis[10] identified the material as the dinuclear Pt(IV) complex ion having D_{2h} symmetry shown in Scheme I, i.e. D_{2h}-[*cis*-Pt^{IV}L$_2$(OH)$_2$(μ-OH)]$_2^{2+}$ (**3**). The structural analysis also revealed that, as for [*cis*-Pt^{II}(NH$_3$)$_2$(μ-OH)]$_2^{2+}$,[14,19,20] the four-membered $\overset{O}{\underset{O}{\mathrm{Pt\ Pt}}}$ ring in the compound is highly strained, having an O–Pt–O angle of 81.8°. The infrared absorption diagnostic of the ring occurred at 1020 cm^{-1}.

In an effort to examine the effects of ring strain on the ^{195}Pt NMR resonance of **3** and also to shed further light on the nature of the other Pt(IV) products produced in the oxidation, the mononuclear Pt(IV) complex *cis*-Pt^{IV}L$_2$(OH)$_4$ (**4**) was synthesized through the reaction of *cis*-Pt^{II}L$_2$(OH)$_2$ with hydrogen peroxide in basic media. A ^{195}Pt NMR spectrum showed that the oxidation produced a single compound having a shift of +1745 ppm and a value for $^1J(^{195}\mathrm{Pt}-^{15}\mathrm{N})$ of 269 Hz. The observed ^{195}Pt NMR parameters were found to be similar to those reported for the related tetrahydroxo complex *cis*-Pt^{IV}(NH$_2$CH(CH$_3$)$_2$)$_2$(OH)$_4$, the structure of which has been determined via X-ray analysis.[26,27]

Comparison of the chemical shift value of the dimer **3** with that of the mononuclear tetrahydroxo species, **4**, revealed that the presence of the four-membered ring in the former deshields the platinum ion by ~200 ppm. Although comparisons are not numerous, this value is somewhat lower than that found for Pt(IV) mono- and dinuclear species involving coordinated CH$_3$ where the ring effect has been reported to be ~450 ppm.[12]

Reference to the value of $^1J(^{195}\mathrm{Pt}-^{15}\mathrm{N})$ for the tetrahydroxo species and **3** revealed that the presence of a terminal hydroxide rather than a bridging one lowers the coupling constant (269 Hz vs. 317 Hz). A similar trend is also revealed for *cis*-Pt^{II}L$_2$(OH)$_2$ and **2** (Table I), as well as their earlier studied ammonia analogues.[17] The decrease in the magnitude of $^1J(^{195}\mathrm{Pt}-^{15}\mathrm{N})$ as the platinum oxidation state is changed from +2 to +4 is probably due to a decrease in the s character of the bonding orbitals used in the tetravalent complex.[26]

The chemical shifts of the other compounds formed in the oxidation suggested that they, like **3**, are dinuclear and possess a four-membered $\overset{O}{\underset{O}{\mathrm{Pt\ Pt}}}$ ring. Although the minor products were not isolated and characterized via X-ray analysis, a number of factors point to their being the isomers shown in Scheme I. Reference to earlier work with Pt(II) dimers[17] and certain alkyl Pt(IV) dinuclear complexes[12] indicated that the minor products may be due to the presence on an open-ring intermediate of the type shown in Scheme I. The transient signal at +1750 ppm, observed during the early part of the oxidation, is likely due to this intermediate. Consideration of the number of ways the open-ring structure can close to give four-membered-ring products revealed that isomers having symmetries C_1, C_s, C_2, and D_{2h} can form. Were the oxidation to proceed exclusively through the open-ring intermediate, a statistical isomer distribution (assuming all possible ring closures are equally likely) of 4:2:2:1 would be expected for the C_1, C_2, C_s, and D_{2h} isomers, respectively. The large amount of the D_{2h} isomer produced strongly suggests that the bulk of the reaction proceeds without ring opening.

The structural assignments of the minor products are based on their ^{195}Pt NMR spectral data. The pattern of lines at lowest field, at +1980 and +1977 ppm, appears to be due to two compounds, each having *equivalent* platinum ions and values for $^1J(^{195}\mathrm{Pt}-^{15}\mathrm{N})$ of 316 and 265 Hz. From the magnitude of the coupling constants, both compounds have one nitrogen atom trans to a terminal OH group (265 Hz) and one nitrogen atom trans to a bridging OH group (316 Hz). Thus, these signals are most likely due to the C_s and C_2 isomers shown in Scheme I. The complex pattern of lines centered at ~+1947 ppm has been assigned to the C_1 isomer.

This isomer possesses *nonequivalent* platinum ions and contains the structural elements of both the D_{2h} isomer (nitrogens trans to a bridging OH group) and the C_s and C_2 isomers (nitrogens atoms trans to bridging and terminal OH groups). If the chemical shifts for the two platinum ions in the C_1 isomer are intermediate between those of the D_{2h} and C_s (C_2) isomers, a second-order pattern of the type found at ∼+1947 ppm would be expected for the compound. An alternative assignment, based on the NMR properties of the hydrogen peroxide oxidation products of *cis*-$[\mathrm{Pt^{II}(^{15}NH_3)_2(\mu\text{-}OH)}]_2^{+2}$,[28] is that the weak doublet of doublets at +1977 ppm and a triplet centered at ∼+1947 ppm are *both* due to the nonequivalent platinum ions of the C_1 isomer. However, in the case of the ethylamine compounds, this assignment seems less favorable since it does not account for one of the isomers, C_s (C_2), and it requires that the chemical shift of one of the platinums of C_1 be the same as the platinum ions of C_s (C_2) but that the other platinum of C_1 be significantly different from the platinum ions found in D_{2h}. Clearly, a definitive assignment will require additional information and most likely an X-ray structural analysis of one or more of the minor products produced in the reaction. Although a fifth isomer having C_i symmetry is theoretically possible, its formation would involve breaking and re-forming *both* μ-OH linkages of the four-membered $\mathrm{Pt}\overset{\mathrm{O}}{\underset{\mathrm{O}}{\ }}\mathrm{Pt}$ ring. Its presence, as well as other possible structures having trans ethylamine ligands (inconsistent with the coupling data[26]), is considered unlikely.

In summary, the oxidation of a bis(μ-hydroxo)-bridged Pt(II) dimer with hydrogen peroxide is described. Platinum-195 NMR spectroscopy and earlier X-ray structural data[10] indicated that the oxidation yields as a major product a D_{2h}-symmetry Pt(IV) dinuclear complex having a bis(μ-hydroxo) bridge. However, NMR spectra showed that lower symmetry, dinuclear, bis(μ-hydroxo)-bridged products are also produced, indicating that at least in part the reaction occurs through an open-ring intermediate that allows isomerization to occur.

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Notes

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Stereochemical Preferences of Methyl-Substituted Piperazines Chelated to Platinum(II)

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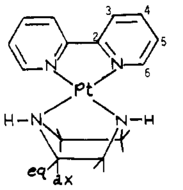
Chelated ligands can endow a metal complex with an ability to discriminate in its further reactions with other substrates. Such selectivity can arise from the conformational preferences of the chelated ligand, i.e. from the stereochemical disposition of substituents on the chelate rings.

Piperazine is an interesting diamine molecule that has been recognized as a chelating agent for some time.[1,2] Early workers saw that chelation would cast the normally chair conformation of the free piperazine ligand into a boat conformation anchored by the metal ion binding. X-ray crystallography has shown this to occur.[3]

Little is known about the stereochemical preferences of methyl substituents on the carbon skeleton of chelated piperazine ligands. We have prepared a series of methyl-substituted piperazine (ppz) complexes of the type **1** to study these preferences. The chelated boat moiety has axial and equatorial substituents, two of which are designated on **1**, ax and eq, respectively.



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Experimental Section

Diamines. All ligands were purchased from commercial sources (Aldrich Chemical Co.) and used without further purification. The commercial sample of 2,5-dimethylpiperazine (2,5-$\mathrm{Me_2}$ppz) was trans-rich (80–90%). To get the cis isomer of 2,5-$\mathrm{Me_2}$ppz, the initial amine mixture was converted to the dihydrochloride derivative and recrystallized from 95% ethanol. The *trans*-dihydrochloride is less soluble and is easily removed; an 80% cis-enriched sample was obtained after several recrystallizations. The NMR spectrum of the *cis*-dihydrochloride in $\mathrm{D_2O}$ shows a methyl doublet at 1.42 ppm (vs. external $\mathrm{Me_4Si}$), 0.07 ppm downfield from that of the *trans*-dihydrochloride isomer. However, eventually the 80:20 cis–trans mixture could not be purified further by fractional removal of the less soluble *trans*-dihydrochloride. At this stage 4.0 g of the 80:20 cis–trans dihydrochloride mixture was converted to an *N,N'*-dibenzoyl derivative.[4] The cis–trans derivative mixture was recrystallized from 95% ethanol several times to yield 0.7 g (10% yield) of white solid *N,N'*-dibenzoyl-*cis*-2,5-dimethylpiperazine, mp 148.5–152 °C (lit.[4] 147–148.5 °C). This solid was converted to the dihydrochloride by heating in 2 M HCl; after the solution was cooled, the solid benzoic acid was filtered off and the solution evaporated to give solid dihydrochloride. The cis amine was liberated in 5 M NaOH and ether extracted for reaction with $\mathrm{Pt(bpy)Cl_2}$ (bpy = 2,2'-bipyridine).

Platinum Complexes. $\mathrm{Pt(bpy)Cl_2}$ was reacted with the appropriate ligands in water at 80–90 °C as described earlier.[5]

NMR Spectra. Samples for NMR analysis were prepared in $\mathrm{D_2O}$ as described earlier.[5] ^{13}C NMR spectra were obtained on a Varian CFT-20 spectrometer at the University of Rhode Island through the generosity of Professor Elie Abushanab of the School of Pharmacy. The NMR spectra of the *cis*-2,5-$\mathrm{Me_2}$ppz ligand and its platinum complex were obtained at Yale University on a JEOL FX-90 (^{1}H and ^{13}C) spectrometer and on a Bruker WM-250 (^{1}H) spectrometer. ^{13}C spectra are referenced vs. internal dioxane, which has been found to have a shift of 67.73 ppm from $\mathrm{Me_4Si}$ sealed in an external capillary.[5]

Results

Carbon-13 NMR spectra which were used to characterize the complexes are summarized in Table I. All data are consistent with the formulation of a 1:1 mixed complex with both ligands being bound in a bidentate fashion. Some of the carbon resonances exhibit coupling to the ^{195}Pt nucleus (natural abundance 33%).

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