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A Five-coordinate Pt(II) Complex of Pyridylmethylaminediacetate

JOHN A. WINTER, FU-TYAN LIN
and REX E. SHEPHERD*

*Department of Chemistry, University of Pittsburgh,
Pittsburgh, PA 15260, U.S.A.*

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Square-planar coordination is generally the strongly favored coordination geometry of d^8 complexes of Pt(II), Pd(II) or Au(III). Their five-coordinate species are not particularly common unless the geometry is forced by the presence of tripodal ligands having P and As donors [1, 2]. Square-pyramidal coordination is rare; it has been observed in sparingly few cases with stiff or bulky ligands**: with Au(phen)I_3 [3] and Pt(tpas)I^+ [4]. Phen is known to occupy both the apical and one in-plane position of Au(phen)$(CN)_2$X (X = Br^- or Cl^-) [5]. Potentially bidentate ligands including phen, bipy and napth have been shown by Dixon to form square-planar $[Pt(PEt_3)_2Cl(L)]BF_4$ salts [6]. These rapidly equilibrate the pendant non-coordinated nitrogen donor via five-coordinate intermediates having both N-donors associated with the Pt(II) center in solution [6]. We have in progress studies which show that the polyaminocarboxylate ligand, uedda^{2-}, also forms Pt(II) complexes which are not simple square-planar species in solution [7]†. The Pt(II)(uedda)X (X = Cl^-, OH^- or H_2O) complexes appear to have either a square-pyramidal or a trigonal-bipyramidal isomer in solution [7] although more complete studies may be necessary to assure that these species are not dimeric in solution†.

An interest in the possible coordination geometries of simple Pt(II) chelates stems in large part from the antitumor activity exhibited by *cis*-Pt$(NH_3)_2Cl_2$ [8] and the elegant studies of the research groups of Lippard *et al.* [9], Reedijk *et al.* [10], and Lippert *et al.* [11] on the binding of *cis*-Pt$(NH_3)_2$ or ethylenediamine-based complexes of the general formula Pt(II)(AA)X_2 (AA = bidentate amine, X^- = leaving group anion) with DNA base pairs or other nitrogen base stand-ins for DNA bases. Geometries other than square-planar which might react more rapidly or with different base pairs along a DNA chain are of interest for antitumor properties or metal labelling of DNAs.

We have examined the pyridylmethylaminediacetate (pida^{2-}) complex of Pt(II) as a parallel study to the Pt(uedda)(H_2O) case. Co(III) [12], first row transition metal ions [13] and lanthanide [14] complexes of pida^{2-} have been characterized previously. In every case to date the typical coordination of polyaminecarboxylates analogous to uedda^{2-} has been observed for pida^{2-} [12–15]. In the case of Pt(II), a five-coordinate complex of C_{2v} symmetry is implicated by ^{1}H NMR in solution while the infrared evidence supports a square-planar structure in the solid state (*vide infra*). It is of interest that the tripodal ligand Me_6tren exhibits a pH-dependent interconversion between square-planar and trigonal-bipyramidal coordination for the d^8 Pd(II) center [16]. Therefore five-coordination for d^8 low-spin complexes with flexible tripodal ligands of nitrogen and oxygen donors may be more common than has been assumed previously.

Experimental

H_2pida ligand

2-Pyridine-2-methylaminediacetate was obtained as the barium salt after addition of 2 moles of bromoacetate to 1.0 mole of 2-methylaminopyridine at 35 °C [17]††. $BaCl_2$ was added to induce precipitation of the Ba(pida) complex. The free ligand was then prepared from the salt by adding H_2SO_4 to precipitate $BaSO_4$, filtering the solution and reducing the volume *in vacuo*. The product (H_2pida) was characterized by ^{1}H NMR (see main text) and by IR spectroscopies.

[Pt(pidaH$_2$)Cl$_2$] and [Pt(pidaH)Cl]

K_2PtCl_4 (1.00 g; 1.69×10^{-3} mol) and 0.384 g H_2pida (1.71×10^{-3} mol) were placed into a round-bottom 3-neck flask. Distilled water (70 ml) was added and the solution was stirred for 5 min. NaOH (42 ml, 0.1 M) was added over a 5-h period while the system was under reflux at a temperature of 90–95 °C in the absence of light. The mixture was then cooled and allowed to stand overnight. The solution was reduced *in vacuo* to 50 ml. HCl (10 ml, 0.6 M) was then added. The mixture was centrifuged to removed a small amount of black material from

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*Author to whom correspondence should be addressed.

**Ligand abbreviations: phen = *ortho*-phenanthroline; tpas = *o*-phenylenebis[(*o*-dimethylarsinophenyl)methylarsine]; napth = naphthyridine; uedda^{2-} = ethylenediamine-*N*,*N*-diacetate; edda^{2-} = ethylenediamine-*N*,*N'*-diacetate; pida^{2-} = pyridylmethylaminediacetate.

†The ^{195}Pt NMR spectra of Pt(II)(edda), Pt(II)(uedda)X and other Pt(II) polyaminocarboxylates are being examined in order to deduce the effects of R substituents on ethylenediamine derivatized units and chelation on the chemical shift of ^{195}Pt(II) species. Details will be reported in ref. 7.

††The procedures follow the synthesis designed by Martell *et al.* [17] for ethylenediamine-*N*,*N*-diacetic acid.

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the yellow liquid. The solvent H_2O was removed *in vacuo* and the solid phase was placed into a vacuum oven to dry. Purification was afforded by dissolving in a minimum of hot distilled water. Yellow needle-like crystals of Pt(pidaH_2)Cl_2 formed upon cooling. Heating of the complex in more dilute solution yielded a different solid, shown here to be Pt(pidaH)Cl.

IR Spectra

Spectra were obtained with an IBM IR/32 FTIR instrument on KBr pellets, collecting an average of 64 scans. Pellets were pressed at 9 tons.

^1H NMR Spectra

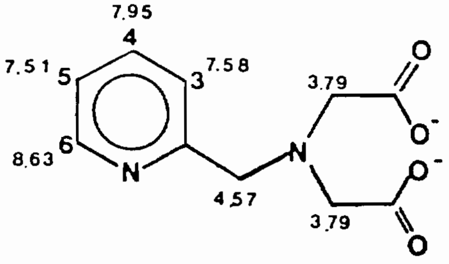
^1H NMR spectra were recorded on a Bruker/IBM AF 300 NMR spectrometer at a magnetic field strength of 70.46 kG, employing a radio frequency of 300.13 MHz. All spectra were obtained in D_2O with = 0.10 phosphate buffer present (pD = 7.20) against a DSS reference (0.00 ppm) with $\mu = 0.10$ M phosphate buffer present (pD = 7.20).

^{195}Pt NMR Spectra

^{195}Pt NMR spectra were obtained at 21 °C on a Bruker/IBM AF 300 NMR spectrometer at 64.5 MHz using procedures of Dabrowiak and Al-Baker [18]. K_2PtCl_4 was used as an external reference ($\delta = -1620$ ppm) [19]. Only one singlet at $\delta = -1937$ ppm was observed for the complex. This shows that only one Pt(II) complex is present in solution because the shift of the ^{195}Pt NMR signal is widely dependent on the geometry of the Pt(II) complex and the nature of the donor ligands [19–24].

Results and Discussion

The proper synthesis of the H_2pida ligand was confirmed by ^1H NMR. The numbering system for H_2pida is shown here together with the ^1H shifts:



H_2pida was dissolved in D_2O phosphate buffer to give a pD of 7.2. The singlets at 3.79 and 4.51 ppm can be assigned to the equivalent glycinate and 2-methylene hydrogens, respectively. It was necessary to perform a decoupling experiment in order to assign the aromatic portion of the spectrum.

From earlier data of Erickson, Sarneski *et al.* [25] and the 2,2'-bipy assignments [26], the doublet at 8.63 ppm is assigned to the H_6 of the ring. Therefore, the doublet at 7.58 ppm must be due to the H_3. Using this as a guide, decoupling was used to aid the other multiplet assignments. Figure 1 shows the ^1H NMR spectra generated from decoupling. Figure 1a is the uncoupled H_2pida spectrum. When the peak due to H_6 was irradiated, the triplet at 7.51 ppm collapsed into a doublet (Fig. 1b). Therefore this peak is assigned to H_5. As a check for H_4, the suspected peak at 7.95 ppm (H_4) was irradiated and, as expected, both the H_3 and H_5 peaks collapsed (see Fig. 1c).

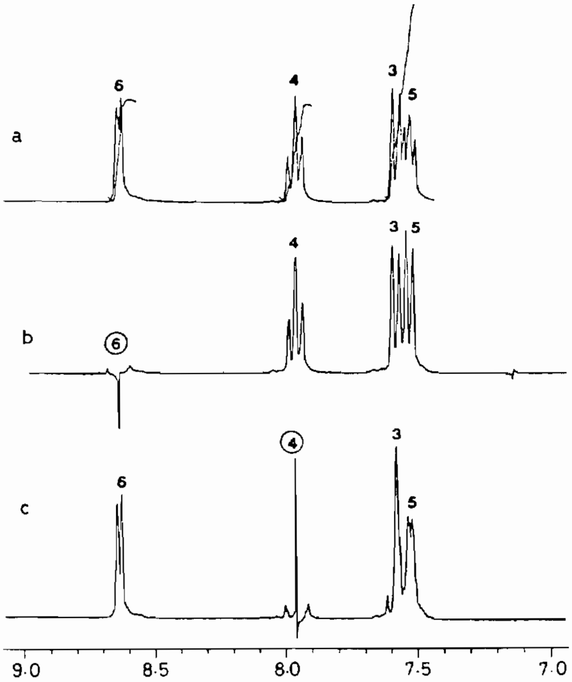
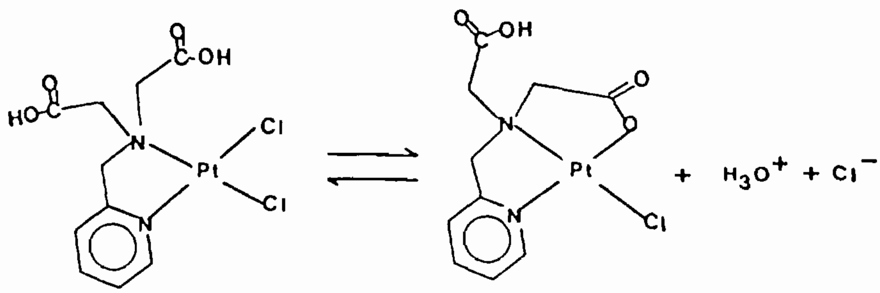


Fig. 1. Aromatic ring assignments for H_2pida from ^1H NMR decoupling experiments: (a) ^1H NMR of H_2pida aromatic region; (b) ^1H NMR of H_2pida irradiated at resonance 6; (c) ^1H NMR of H_2pida irradiated at resonance 4.

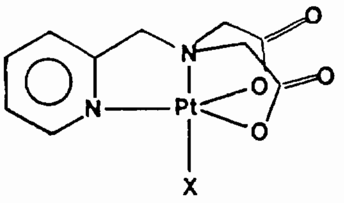
The IR spectrum of Pt(pidaH_2)Cl_2 shows two distinctive carbonyl stretches at 1720 and 1751 cm^{-1} (see Fig. 1a). In the solid, both glycinate groups are pendant and protonated. However, two different stretches due to geometrical factors are exhibited. Pt(pidaH)Cl results after mild heating in water. One of the glycinate groups becomes coordinated (1650 cm^{-1}) and the other moiety remains pendant and protonated (1720 cm^{-1}) (see Fig. 2B). These changes are consistent with equilibrium (1).



(1)

Similar equilibria are known for the $Pt(edta)^{2-}$ and Pt(edda) complexes [27–32].

$Pt(pidaH_2)Cl_2$ was dissolved in D_2O phosphate buffer at pD = 7.1. The resulting ^1H NMR spectrum is shown in Fig. 3A; the free ligand at pD = 7.1 is shown in Fig. 3B. The pattern resembles the H_{ab} pattern found for Pt(edda) [7]. Due to complexation with Pt(II), the H_a and H_b hydrogens of the glycinato moieties, comprising a singlet in the free ligand at 3.79 ppm, are now different. Chemical shifts centered at 3.84 and 3.71 ppm with a J_{ab} coupling of 16 Hz are observed. The H_3, H_4 and H_5 protons in the aromatic portion of the spectrum are shifted from free ligand values. The H_4 and H_3 resonances are shifted downfield by 0.16 and 0.05 ppm, respectively, while H_5 experiences a slight 0.05 ppm upfield influence. Due to steric restraints, Pt(II)(pida) cannot adopt a square-planar configuration as does Pt(edda). To satisfy the H_{ab} pattern indicative of a C_{2v} symmetry, a trigonal bipyramidal structure is required.



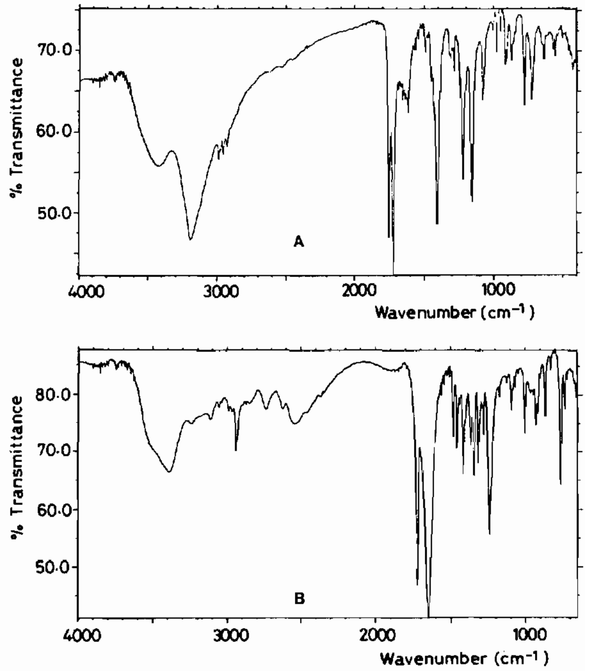


Fig. 2. Infrared spectra of Pt(II)(pida) complexes in KBr: (A) $[Pt(pidaH_2)Cl_2]$; (B) [Pt(pidaH)Cl].

Since it is known that cis-$(NH_3)_2PtCl_2$ and (en)-$PtCl_2$ undergo displacement of Cl^- by H_2O and H_2O by PO_4H^{2-} or HO^- [18–21], it has not been unambiguously established whether X = H_2O or HO^- or PO_4H^{2-} in the D_2O phosphate buffer. The absence of a yellow color, diagnostic of Cl^- association, suggests the Cl^- anions have dissociated upon coordination of the carboxylates. This is also known for the Pt(II)(edda) and Pt(II)(uedda) complexes [7]. Appleton *et al.* state that platinum-blue bridged complexes form readily with the $Pt(NH_3)_2^{2+}$ and $Pt(en)^{2+}$ system in phosphate media above pH ~ 3 [21, 33]. No such oxidation (and polymerization) has been observed by us, as evidenced by the absence of "platinum blues" in solutions of Pt(II) ligated by $edda^{2-}$, $uedda^{2-}$ or $pida^{2-}$. Therefore it appears that X is not PO_4H^{2-}. Square-planar complexes are insensitive as to whether oxygen donors such as H_2O, HO^- or PO_4H^{2-} are coordinated to Pt(II) unless the ligands are bridging between the Pt(II) centers [18, 19, 21]. The presence of two anionic donors probably renders the pK_a of a coordinated H_2O molecule higher than the 5.6 exhibited by cis-$Pt(NH_3)_2(OH_2)_2^{2+}$ [8a, 34]. Therefore X is most probably D_2O in the solutions for ^1H NMR. The important result is that the Pt(II) complex of $pida^{2-}$ must be a five-coordinate trigonal bipyramidal complex in order to possess C_{2v} symmetry. If the complex had been square-planar, one unique glycinato singlet would be required for the pendant moiety. If the complex were square-pyramidal, two distinctly different types of glycinates, one in-plane or G ring and one axial or R ring would be observed, as has been found for the Pt(uedda)X case [7] or for the octahedral Co(III) complex [12].

Supporting evidence for the existence of a single Pt(pida)X complex in solution was obtained from ^{195}Pt NMR, as described in the 'Experimental' sec-

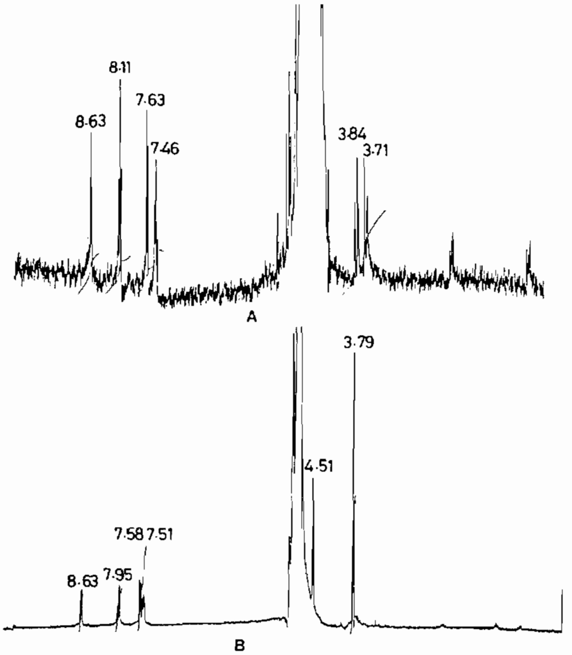


Fig. 3. ^1H NMR spectra of $Pt(pida)(H_2O)$ and free ligand $pida^{2-}$ at pD = 7.1 in D_2O: (A) $Pt(pida)(D_2O)$; (B) $pida^{2-}$ ligand.

tion. Only one Pt(II) species exists with $\delta = -1937$ ppm. This shift is consistent with the existence of a donor to Pt(II) having one en-like chelate, two glycinato donors, two 'R-releasing' substituents on one of the 'en-chelate' nitrogens and a trigonal bipyramidal geometrical correction. Such a complex gives a predicted ^{195}Pt shift of -1936 ppm; details of the ^{195}Pt spectra of polyaminocarboxylate chelates are reported elsewhere [7]. When the Pt(II)(pida) complex was isolated from strongly acidic solution (0.6 M HCl concentrated in the rotary evaporator) only $Pt(pidaH_2)Cl_2$ was obtained. Under less acidic conditions and at lower Cl^- concentration, Pt(pidaH)Cl is obtained. This is analogous to the $[PdCl(Me_6trenH]X_2$ salts obtained by Senoff which revert to five-coordination using all four donors of Me_6-tren at higher pH (~12) [16]. The lower pK_a values of carboxylates allow coordination of $pida^{2-}$ at a much lower pD value.

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