Platinum(II) Complexes with Glycine as an Oxygen-bound Unidentate Ligand

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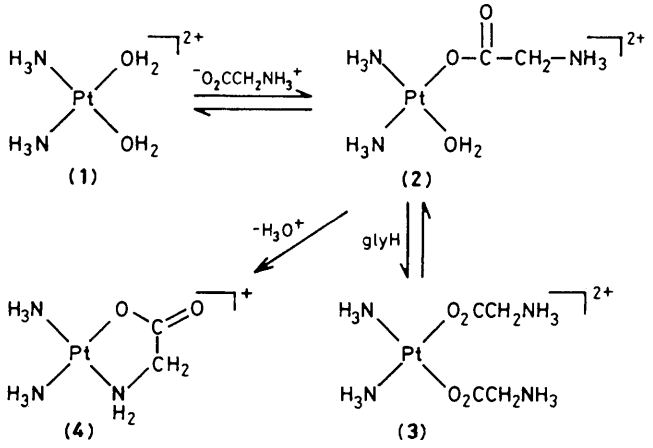
Reaction of glycine (glyH) with *cis*-$Pt(NH_3)_2(H_2O)_2^{2+}$ in water gives *cis*-$Pt(NH_3)_2(O\text{-glyH})(H_2O)^{2+}$, in which glycine co-ordinates through oxygen only, and which converts only slowly into the chelate complex, $Pt(NH_3)_2(N,O\text{-gly})^+$.

Many complexes of platinum with bidentate amino acids, NH_2CHRCO_2H, have been reported.[1] All of these contain the ligand bound either as a chelate bidentate ligand, through nitrogen and oxygen, or as a unidentate ligand, through

Table 1. N.m.r. data.[a]

Compound	CH_2 and CH_3 groups $\delta_H(J$[Pt–H])	$\delta_C(J$[Pt–C])	Carboxy group $\delta_C(J$[Pt–C])	δ_{Pt}[b]	δ_N[c](J[Pt–N])	*trans*-Ligand
cis-$Pt(NH_3)_2(H_2O)_2^{2+}$ (**1**)(refs. 4, 5)				−1583.7(t)	−85.83 (390.6)	H_2O
cis-$Pt(NH_3)_2(O_2CMe)(H_2O)^+$ (ref. 5)	1.99 (<2)	23.09 (32.3)	183.47 (30)	−1585.0(dd)	−87.19 (393.6) −81.67 (348.1)	H_2O O_2CMe^-
cis-$Pt(NH_3)_2(O_2CMe)_2$ (ref. 5)	1.97 (<2)	23.24 (31)	183.10 (24.4)	−1581.5(t)	−83.12 (349.6)	O_2CMe^-
cis-$Pt(NH_3)_2$(*O*-glyH)$(H_2O)^{2+}$ (**2**)	3.74 (<2)	42.15 (32)	175.34 (11.6)	−1582.2(dd)	−87.19 (392.1) −82.64 (358.4)	H_2O $-O_2C-$
cis-$Pt(NH_3)_2$(*O*-glyH)$_2^{2+}$ (**3**)	3.70 (<2)	42.15 (32)	175.57 (12)	−1573.8(t)	−83.85 (359)	$-O_2C-$
$Pt(NH_3)_2$(*N*,*O*-gly)$^+$ (**4**)	3.61 (32.0)	47.57 (28.3)	190.04 (39.0)	−2130.8(br.)	−84.91 (331.1) −64.93 (301.3)	$-O_2C-$ $-NH_2-$

[a] The ^{15}N and ^{195}Pt n.m.r. spectra were run with 99% ^{15}N ammine. The ^{15}N, ^{195}Pt, and ^{13}C n.m.r. spectra were run in H_2O, and were ^1H-decoupled. The ^1H n.m.r. spectra were run in D_2O. Chemical shifts in p.p.m., lower shielding positive. Coupling constants in Hz. [b] Relative to aqueous Na_2PtCl_6; t = triplet; dd = doublet of doublets; br. = broad. [c] Relative to $^{15}NH_4^+$, 5 M NH_4NO_3 in 2 M HNO_3.



nitrogen alone (with the carboxy group either protonated or deprotonated). Co-ordination of an amino acid through oxygen alone is well known for some other metals ions (*e.g.*, Co^{III})[2] which are 'harder' or more 'class a' than Pt^{II}. Using ^{15}N and ^{195}Pt n.m.r. spectra with ^{15}N-substituted ammine complexes,[3,4] we have characterized the first platinum(II) complex with an amino acid bound in this way.

When equimolar quantities of glycine (glyH) and *cis*-[Pt$(NH_3)_2(H_2O)_2$]$(NO_3)_2$ (**1**) are mixed in aqueous solution, n.m.r. peaks from a new species, (**2**), grow rapidly (see Table 1). Complex (**2**) was assigned as *cis*-$Pt(NH_3)_2$(*O*-glyH)$(H_2O)^{2+}$ for the following reasons:

(i) Since the ^{195}Pt n.m.r. spectrum (Figure 1) shows a doublet of doublets, and the ^{15}N spectrum two singlets with 'satellites', the two ammine ligands are non-equivalent.

(ii) The ^{195}Pt chemical shift corresponds to a complex with two *N*-donors and two *O*-donors [*cf.* δ_{Pt} for (**1**)]. Co-ordination of the additional *N*-donor ligands in place of *O*-donors would be expected to increase nuclear shielding [*e.g.*, δ_{Pt} for $Pt(NH_3)_4^{2+}$ is −2579 p.p.m.[4]].

(iii) Co-ordination of ^{14}N from 'natural' glycine would cause broadening or greater complexity in the ^{195}Pt n.m.r. spectrum.

(iv) ^{195}Pt–^{15}N Coupling constants correspond to ammine *trans* to water and carboxylate [*cf.* values for *cis*-$Pt(^{15}NH_3)_2$-$(O_2CMe)(H_2O)^+$,[5] given in Table 1 for comparison].

(v) No coupling is observed between ^{195}Pt and the methylene protons. When glycine co-ordinates as a chelate or *N*-bound unidentate ligand to Pt^{II}, $^3J(Pt–N–CH_2)$ is in the range 30—45 Hz.[6]

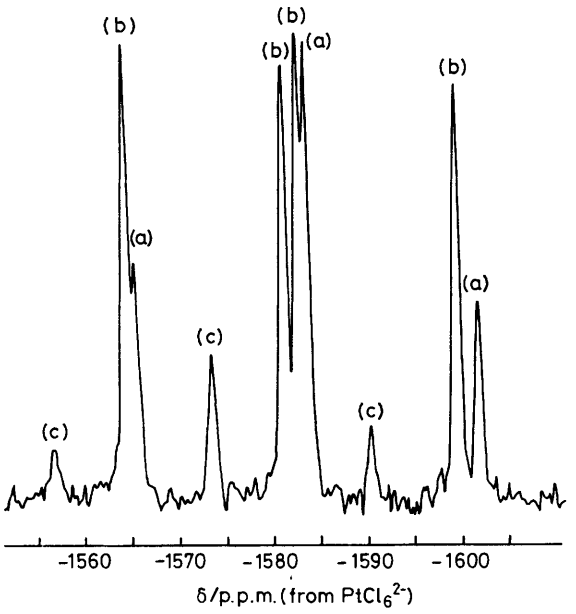


Figure 1. ^1H-Decoupled 21.4 MHz ^{195}Pt n.m.r. spectrum of the solution obtained from mixing *cis*-[Pt$(^{15}NH_3)_2(H_2O)_2$]$(NO_3)_2$ (**1**) and glycine in water. Peaks marked (a) are from $Pt(NH_3)_2(H_2O)_2^{2+}$ (**1**), (b) $Pt(NH_3)_2$(*O*-glyH)$(H_2O)^{2+}$ (**2**), and (c) $Pt(NH_3)_2$(*O*-glyH)$_2^{2+}$ (**3**).

(vi) There are no changes in the spectra over the pH range 4.5—1.5 consistent with the co-ordinated ligand remaining protonated over this range.

Even when equimolar quantities of (**1**) and glycine are used, additional peaks, of lower intensity than those from (**2**), are observed in the n.m.r. spectra. They become more intense if more glycine is added. The n.m.r. parameters (Table 1) are consistent with the assignment of these peaks to *cis*-$Pt(NH_3)_2$-(*O*-glyH)$_2^{2+}$ (**3**), analogous to *cis*-$Pt(NH_3)_2(O_2CMe)_2$.[5]

Complex (**2**) remains as the major component in solution for several hours at 25 °C, but peaks slowly grow from the chelate complex $Pt(NH_3)_2$(*N*,*O*-gly)$^+$ (**4**). Although this is a known compound,[7] the n.m.r. parameters are reported here for the first time (Table 1). One of the ^{195}Pt–^{15}N coupling constants, 301.3 Hz, is now in the region expected for ammine *trans* to N [*cf.* 283 Hz in $Pt(^{15}NH_3)_4^{2+}$ [4]], while the other, 331.1 Hz, is slightly smaller than the coupling for ammine *trans* to carboxylate in (**2**), with the Pt–O bond now incorporated in a

chelate ring. The ^{195}Pt n.m.r. spectrum shows a broad, complex multiplet at higher shielding. ^{3}J(Pt–N–CH_2) is consistent with a chelate structure.[6]

Conversion of (**2**) into (**4**) is irreversible, and there is no doubt that the chelate complex is thermodynamically preferred. Complex (**2**) is formed first because, in the glycine zwitterion, the carboxylate end of the ligand is more nucleophilic. Once (**2**) is formed, ring closure to (**4**) requires deprotonation of the NH_3^+ group. As this reaction proceeds, the pH decreases from an initial value of 4.5 to 1.5, so that the reaction is self-inhibiting, requiring about 24 h to approach completion at 25 °C. If alkali is added to a solution of (**2**), to increase the pH to 8, the reaction is rapid. Ring closure is also faster if the solution is heated.

For an *O*-bound glycine complex to form, the leaving group on the platinum starting material must be sufficiently labile for it to be displaced under conditions mild enough that the *O*-bound complex will not rearrange. Pt–Cl bonds, for example, are probably insufficiently labile. On the other hand, if a co-ordination site is too labile [*e.g.*, the sites *trans* to methyl in *fac*-$PtMe_3(H_2O)_3^+$ [8]], exchange between the *O*-bound complex and the aqua complex may be fast on the n.m.r. time scale, making the *O*-bound complex difficult to detect in the absence of large chemical shift changes.

We have found that analogous reactions occur between (**1**) and more complex amino acids. For example, *N*-methyliminodiacetic acid, $MeN(CH_2CO_2H)_2$ gives initially a complex with the ligand binding in a unidentate manner through one of the carboxy O-atoms, with slow subsequent formation of a complex where the ligand is bidentate (through the N-atom and one O-atom).

When platinum aqua complexes interact with complex ligands, including some of biological significance, the possibility of 'metastable' binding to *O*-donor sites should not be ignored, even when such complexes would certainly not be the most preferred thermodynamically.

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