

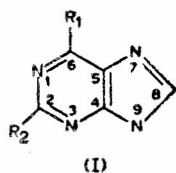
Complexes of Platinum(II & IV) with Adenine & Guanine

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Metal complexes of adenine and guanine with platinum(II & IV) chlorides have been prepared. Different types of complexes are obtained in different pH ranges. The complexes have been characterised on the basis of elemental analyses, IR, FMR and electronic spectral and conductivity data. The results indicate that in acidic and neutral media, adenine behaves as a monodentate ligand and coordinates through N₍₇₎. In acidic medium, guanine also behaves as a monodentate ligand and coordinates through N₍₇₎. In basic medium, adenine acts as a bridging ligand coordinating through N₍₆₎ and N₍₉₎ whereas guanine acts as a bidentate ligand coordinating through N₍₇₎ and C₆-O.

THE coordination of nucleosides and nucleotides and their constituent bases to platinum has been a subject of much recent interest¹⁻³. The discovery of the antitumour activity of *cis*-[Pt(NH₃)₂Cl₂] (refs. 4,5) has created much interest in the synthesis of complexes of the type *cis*-[Pt(L)₂Cl₂] which could be used against a variety of tumours. We report here the preparation and isolation of Pt(II) and Pt(IV) complexes of adenine and guanine (structure I) in different pH ranges. It has been observed that in acidic and neutral media, adenine acts as a monodentate ligand coordinating through N₍₇₎ and in basic medium it acts as a bidentate bridging ligand coordinating through N₍₃₎ and N₍₉₎. Guanine acts as a monodentate ligand in acidic medium coordinating through N₍₇₎ and as a bidentate ligand in basic medium coordinating through N₍₇₎ and hydroxy oxygen at C₆.



(I)
R₁ = NH₂, R₂ = H: Adenine
R₁ = OH, R₂ = NH₂: Guanine

Materials and Methods

Chloroplatinic acid, adenine and guanine were obtained from M/s Alfa Ventron (USA). Chloroplatinic acid was converted to K₂PtCl₆ and K₂PtCl₄ by standard procedures⁶. The IR spectra were recorded in KBr on a Perkin Elmer spectrophotometer (337). The PMR spectra were recorded on a JOEL 100 MHz spectrometer. The electronic spectra were recorded on a Beckmann (model DB) spectrophotometer. Microanalyses were performed at CSIRO, Australia and at CDRI, Lucknow. Chlorine was estimated by Styermerk method. The conductivity data were obtained in DMSO using an Elico

conductivity bridge. The electronic spectra and conductivity of a few complexes could not be recorded due to their insolubilities.

1. *Pentachloroadeniniumplatinum(IV)* — Potassium hexachloroplatinate(IV) (0.195 g, 0.4 mM) was dissolved in 15 ml of water and to this a solution of adenine (0.056 g, 0.4 mM) in 10 ml of 3N HCl was added. The resulting mixture was stirred for 4 hr when a yellow precipitate was obtained. The precipitate was filtered, washed with water and dried at 110° in *vacuo*. Its molar conductivity in DMSO was found to be 26.32 mho cm² mol⁻¹.

2. *Trichlorotriadenineplatinum(IV) chloride pentahydrate* — Potassium hexachloroplatinate(IV) (0.195 g, 0.4 mM) was dissolved in 15 ml of water and to this a solution of adenine (0.167 g, 1.2 mM) in 20 ml of water was added. The solution was stirred for 8 hr when a buff coloured precipitate was obtained. The precipitate was filtered, washed with water, acetone and dried. Its molar conductivity in DMSO was found to be 106 mho cm² mol⁻¹.

3. *Hexachlorodiaquo-μ-chloro-μ-adeninatodiplatinum(IV) hydrate* — Potassium hexachloroplatinate(IV) (0.195 g, 0.4 mM) was dissolved in 15 ml of water and to this adenine (0.056 g, 0.4 mM) in 10 ml of 0.1N KOH was added. The resulting solution was refluxed for 6 hr and concentrated when a yellow coloured precipitate was formed. The precipitate was filtered, washed with methanol, acetone and dried in *vacuo*.

4. *Trichloroadeniniumplatinum(II) trihydrate* — Potassium tetrachloroplatinate(II) (0.166 g, 0.4 mM) was dissolved in 15 ml of water and to this a solution of adenine (0.056 g, 0.4 mM) in 10 ml of 3N HCl was added. The resulting solution was refluxed for 8 hr when it gave a buff coloured precipitate. The precipitate was filtered, washed with water and acetone and dried.

5. *Dichloroaquoadenineplatinum(II) hydrate* — Potassium tetrachloroplatinate(II) (0.166 g, 0.4 mM) was dissolved in 15 ml of water and a solution of adenine (0.056 g, 0.4 mM) in 20 ml of water was added. The resulting solution was stirred for 8 hr

when an yellow precipitate was obtained. It was filtered, washed with water and acetone and dried.

6. *Pentachloroguaniniumplatinum(IV) hydrate* — Potassium hexachloroplatinate (IV) (0.2 g, 0.41 mM) was dissolved in 20 ml of water and to this a solution of guanine (0.62 g, 0.41 mM) in 2N HCl (15 ml) was added. The resulting solution was stirred for 2 hr at room temperature. On cooling, yellow crystals were obtained. The crystals were washed with water and acetone. The conductivity of the complex in DMA was found to be 25.58 mho cm² mol⁻¹.

7. *Trichlorotriguanineplatinum (IV) chloride dihydrate* — Potassium hexachloroplatinate(IV) (0.2 g, 0.41 mM) was dissolved in 20 ml of water and to this a solution of guanine (0.186 g, 1.28 mM) in 20 ml of 2N KOH was added. The resulting solution was stirred at room temperature for 15 hr. The solution was concentrated and the pH was adjusted to 6 when a cream-coloured precipitate was obtained. It was washed with water and acetone and dried.

8. *Trichloroguaniniumplatinum(II) methanolate* — Potassium tetrachloroplatinate(II) (0.20 g, 0.41 mM) was dissolved in 20 ml of water and to this a solution of guanine (0.70 g, 0.46 mM) in 20 ml of 2N HCl was added. The resulting solution was stirred at room temperature for 14 hr when an yellow coloured complex was obtained. It was filtered, washed with water, methanol and dried.

9. *Bisguaninato-μ-dichlorodiplatinum(II) heptahydrate* — Potassium tetrachloroplatinate(II) (0.2 g, 0.4 mM) was dissolved in 20 ml of water and to this a solution of guanine (0.07 g, 0.46 mM) in 20 ml of 2N KOH was added. The resulting solution was stirred when a dark-green precipitate was obtained. The precipitate was filtered, washed with water and methanol.

Results and Discussion

The analytical data of the complexes are in conformity with the stoichiometries shown in Table 1. The IR, PMR and electronic spectral data support these formulations.

The IR spectra of adenine and guanine exhibit a strong band around 1600 cm⁻¹ due to δNH₂ mode. This band remains unaffected in the spectra of all the complexes indicating that NH₂ group is not involved in coordination. The ν C = N and ν C = C frequencies observed as strong bands around 1350 and 1400 cm⁻¹ respectively in the free ligands, are shifted in the complexes to the higher frequency side by about 70–100 cm⁻¹ indicating the involvement of ring nitrogen atoms in bonding. The coordination of the ring nitrogen to the metal ion is also indicated by a band due to ν M-N observed around 500–600 cm⁻¹ in all the complexes.

Complexes 1 and 6 exhibit two ν M-Cl modes indicating the presence of two different types of M-Cl bonds. The ν M-Cl mode due to *trans* chlorides in the axial positions is exhibited at 395 and 380 cm⁻¹ respectively and ν M-Cl due to the chloride *trans* to adeninium and guaninium ions is exhibited at 345 and 350 cm⁻¹, respectively.

TABLE 1 — ANALYTICAL DATA OF THE COMPLEXES

Sl. No.	Complex	m.p. (°C) (decomp)	Found (Calc.), %		
			C	H	Cl
1	[Pt(AdH ⁺)Cl ₃]	300	12.30 (12.79)	1.30 (1.19)	34.5 (34.9)
2	[Pt(Ad) ₂ Cl ₂]Cl.5H ₂ O	210	22.20 (21.62)	3.10 (3.00)	17.2 (17.7)
3	[Pt ₂ Ad ⁻ (H ₂ O) ₂ Cl ₇].H ₂ O	200	7.30 (7.20)	1.10 (1.08)	29.28 (30.01)
4	[Pt(AdH ⁺)Cl ₃].3H ₂ O	250	12.70 (12.20)	2.60 (2.41)	20.80 (21.60)
5	[Pt(Ad)(H ₂ O)Cl ₂].H ₂ O	200	13.70 (13.72)	2.21 (2.06)	16.73 (16.25)
6	[Pt(GuH ⁺)Cl ₃].H ₂ O	230	11.53 (11.70)	1.80 (1.80)	33.3 (32.6)
7	[Pt(Gu) ₂ Cl ₃]Cl.2H ₂ O	210	22.50 (21.80)	2.65 (2.90)	16.5 (17.1)
8	[Pt(GuH ⁺)Cl ₃].CH ₃ OH	250	14.7 (14.8)	2.40 (2.28)	22.3 (21.9)
9	[Pt ₂ (Gu ⁻) ₂ Cl ₂].7H ₂ O	250	13.30 (13.10)	2.50 (2.46)	7.47 (7.57)

The PMR spectrum (δ scale) of free adenine exhibits two singlets centred around 8.2 and 8.31 ppm due to protons at C₂ and C₈, respectively. The PMR spectrum of complex 1 shows the C₂ proton at 8.7 ppm and C₈ proton at 9.2 ppm. The C₈ proton is thus shifted to a greater extent (0.9 ppm) as compared to the C₂ proton, indicating N₍₇₎ of the adeninium ion as the binding site to the metal ion⁷.

The multiplet due to the NH₂ protons centred at 7.4 ppm is not shifted in the complex indicating the non-participation of NH₂ group in coordination. The adeninium proton at N₍₁₎ is observed around 6.4 ppm in the complex.

The PMR spectrum of free guanine gives a singlet at 7.68 ppm due to C₈ proton. The PMR spectrum of complex 6 shows a down field shift of the C₈ proton peak by about 0.52 ppm. This supports N₍₇₎ as the coordination site to the metal ion. The site of proton association however cannot be ascertained from PMR studies. It may be N₍₁₎, as in the adeninium ion.

Complexes 2 and 7 are similar in structure. In these complexes the ν M-Cl mode is observed as two strong bands in the region 350–395 cm⁻¹, corresponding to meridional arrangement of the chlorides in the complexes. The ν M-Cl due to *trans* chlorides is observed at 395 and 390 cm⁻¹ respectively and ν M-Cl due to the chloride *trans* to adenine and guanine is observed at 350 and 370 cm⁻¹ respectively in complexes 2 and 7. The ν C-O of guanine is not shifted in complex 7 indicating that guanine is coordinated as a monodentate group through N₍₇₎ and OH group at C₆ is not involved in bonding. The PMR spectrum of complex 7 exhibits a peak at 6.64 ppm assignable to C₈ proton. The peak is shifted upfield by about 1.04 ppm due to the coordination of neutral guanine at N₍₇₎ to the metal ion.

Complex 3 was prepared in basic medium. In this complex adenine acts as a bridging anionic ligand coordinating to two platinum(IV) ions through $N_{(3)}$ and $N_{(9)}$ (ref. 8-10). The bridging chloride exhibits a ν M-Cl peak around 320 cm^{-1} . The ν M-O frequency of coordinated water is observed around 410 cm^{-1} . Complexes 4 and 5 were obtained from platinum(II) in acidic and neutral media, respectively. The ν M-Cl mode in complex 4 is observed at 300 and 360 cm^{-1} . The band at 360 cm^{-1} may be assigned to ν M-Cl due to *trans* chlorides and the one at 335 cm^{-1} to the chloride *trans* to adeninium ion in the square-planar complex. The ν M-Cl modes of complex 5 are observed around 340 and 350 cm^{-1} which may be due to the presence of *cis* chlorides. The ν M-O frequency of coordinated water is observed at 410 cm^{-1} (ref. 11). Complex 8 exhibits a strong ν M-Cl band around 395 cm^{-1} due to *trans* chlorides and a band around 345 cm^{-1} which may be assigned to ν M-Cl frequency due to the chloride *trans* to guaninium ion. In complex 8, the ν C-O frequency not shifted indicating that this group is not involved in coordination.

A dimeric structure is proposed for complex 9 where guanine binds to platinum (II) as a bidentate anionic ligand and the two platinum(II) ions are bridged by chlorides, at pH 10, the OH group at C_8 is deprotonated facilitating the bonding of C_8O to the metal ion. The ν C - O frequency shifts of a lower value by about 100 cm^{-1} indicating coordination through C_8O and $N_{(7)}$ and chelate formation. Possibility of such a chelated structure has been proposed earlier^{12,13}. The peak due to bridging chlorides is observed around 330 cm^{-1} . Complex 9 has been proposed as a dimer on the basis of its insolubility in water. The complex dissolves in basic medium because of the cleavage of the chloro bridges. A monodentate structure with the composition $[\text{Pt}(\text{Gu})(\text{H}_2\text{O})\text{Cl}]$ is expected to go in solution because of the displacement of the chloro group by strong *trans* directing guaninato ion. The dimeric structure of 9 is also supported by the occurrence of ν M-Cl at 330 cm^{-1} which is typical of chloro bridged square-planar platinum(II) complexes. The ν M-Cl for a coordinated chloro end group is usually observed around 390 cm^{-1} .

The PMR spectrum of complex 9 exhibits a singlet for C_8 proton at 6.35 ppm , shifted upfield by about 1.52 ppm compared to position in the ligand spectrum. The upfield shift is due to the coordination of the guaninato ion which has higher electron density on the C_8 carbon atom.

It is of interest to compare the C_8 proton resonance frequencies of complexes 6, 7 and 9. Whereas C_8 proton in 6 undergoes a downfield shift of 0.5 ppm , in 7 and 9 it undergoes upfield shift of 1.04 ppm and 1.52 ppm , respectively. As the electron density on the C_8 proton increases, the upfield shift also increases in the order (neutral guanine < negative guaninato ion). Complex 6 shows a downfield shift of C_8 -H signal since guanine is coordinated as guaninium ion with a considerable deshielding of C_8 proton.

The electronic spectra of platinum(IV) complexes 1 and 6, with C_{4v} geometry show bands at 398 ,

TABLE 2 — ELECTRONIC SPECTRAL DATA OF THE COMPLEXES

Sl. No.	Complex	Geometry	λ_{max} (ϵ_{max})	Probable assignments
1	$[\text{Pt}(\text{AdH}^+)\text{Cl}_4]$	C_{4v}	398 (258) 364 (544) 260 (1.3×10^4)	$^1A_1 \rightarrow ^1B_2$ $^1A_1 \rightarrow ^1A_2$ $\pi \rightarrow \pi^*$
2	$[\text{Pt}(\text{Ad})_2\text{Cl}_2]\text{Cl} \cdot 5\text{H}_2\text{O}$	C_{2v}	400 (185) 332 (500) 274 (5.75×10^4)	$^1A_1 \rightarrow ^1A_2$ $^1A_1 \rightarrow ^1A_1(1)$ $\pi \rightarrow \pi^*$
6	$[\text{Pt}(\text{GuH}^+)\text{Cl}_4] \cdot \text{H}_2\text{O}$	C_{4v}	336 (480) 325 (540) 284 (8.0×10^4)	$^1A_1 \rightarrow ^1B_1$ $^1A_1 \rightarrow ^1A_2$ $\pi \rightarrow \pi^*$
7	$[\text{Pt}(\text{Gu})_2\text{Cl}_2]\text{Cl} \cdot 2\text{H}_2\text{O}$	C_{2v}	406 (300) 353 (700) 265 (4.9×10^4)	$^1A_1 \rightarrow ^1A_2$ $^1A_1 \rightarrow ^1A_1(1)$ $\pi \rightarrow \pi^*$
9	$[\text{Pt}_2(\text{Gu}^-)_2\text{Cl}_2] \cdot 7\text{H}_2\text{O}$	C_{2h}	380 (1.29×10^3) 348 (2.16×10^3) 278 (2.3×10^4)	$^1A_g \rightarrow ^1A_g(1)$ $^1A_g \rightarrow ^1A_g(1)$ $\pi \rightarrow \pi^*$

336 and 364 , 320 nm respectively. Based on a one electron ordering of energy levels for a $5d$ ion with C_{4v} geometry [$e(xz, yz) < b_2(xy) < b_1(x^2 - y^2) < a(z^2)$], the bands have been tentatively assigned to the transitions $^1A_1 \rightarrow ^1A_2$ and $^1A_1 \rightarrow ^1B_2$, respectively.

For complexes 2 and 7 with C_{2v} symmetry, two bands are observed around 400 , 406 and 332 , 350 nm respectively. Based on the ordering of the energy levels for a C_{2v} geometry [$b_1(xy) = b_2(yz) < a_2(xy) < a_1(x^2 - y^2, z^2)$], the bands are assigned to the transitions $^1A_1 \rightarrow ^1A_2$ and $^1A_1 \rightarrow ^1A_1(1)$. For the squareplanar complex with a geometry C_{2h} , the energy levels may be arranged as [$b_g(xy, yz) < a_g(z^2, x^2 - y^2, xz)$]. The bands at 380 nm and 348 nm may be assigned to the transitions $^1A_g \rightarrow ^1A_g(1)$ and $^1A_g \rightarrow ^1A_g(2)$, respectively. The electronic spectral data of complexes 1-7 are given in Table 2.

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