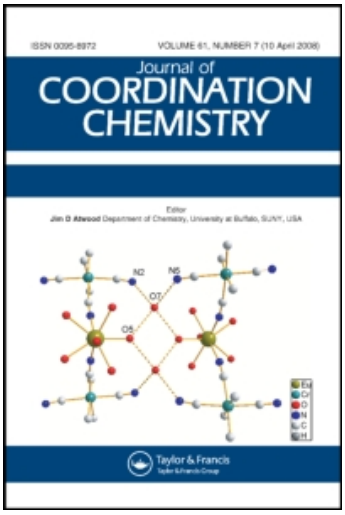

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STUDIES OF MIXED LIGAND COMPLEXES OF CHLOROGLYCYL-*D,L*-METHIONINATO-PLATINUM(II) AND CHLOROGLYCYL-*D,L*-METHIONINATOPALLADIUM(II) WITH PURINES AND NUCLEOSIDES

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The binary complex chloroglycyl-*D,L*-methioninatoplatinum(II) was synthesised and characterised. Subsequently, mixed ligand complexes of chloroglycyl-*D,L*-methioninatoplatinum(II) and chloroglycyl-*D,L*-methioninatopalladium(II) with purines adenine, guanine, hypoxanthine, and nucleosides adenosine, guanosine, inosine and cytidine were synthesised and characterised. Based on spectroscopic data it was found that adenine (Pt and Pd complexes), hypoxanthine (Pt), adenosine (Pt and Pd) and inosine (Pt) form binuclear complexes. Adenine coordinates through N_1 and N_7 in Pt complex and through N_3 and N_9 in the Pd complex, whereas hypoxanthine coordinates through N_3 and N_9 in the Pt complex. The corresponding Pd complex is insoluble. Adenosine (Pt and Pd) and inosine (Pt) coordinate through N_1 and N_7. Guanine, guanosine and cytidine form mononuclear complexes, the first two ligands coordinating to the metal ion through N_7 and the third (cytidine) through N_3.

KEYWORDS: purines, nucleosides, glycyl-*D,L*-methionine, chloroglycyl-*D,L*-methionine platinum(II), palladium(II)

INTRODUCTION

Binding of metal ions to peptides has been a subject of increasing interest, as many of these reactions provide simple models for much more complex enzymes.[1–3] Binary or ternary complexes with amino acids, peptides or nucleic acids, constitute simple models for more complex DNA-protein interactions.[4–6] Complexes of platinum group metals with these ligands have also been widely studied because of their antibacterial and antitumour activity.[7–12] Several mixed ligand complexes of platinum group metals with amino acids and nucleic acid constituents have been reported.[13–17] Recently, mixed ligand complexes of platinum(II) and palladium(II) with the amino acids ethionine and methionine and nucleic acid constituents have been reported.[18–21] Few of these complexes have been found to be biologically

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active towards human pathogens and tumors.[22] Considerable work has been carried out on complexes of dipeptides with 3d metal ions.[23–25] The X-ray crystal structure of chloroglycyl-*D,L*-methioninatoplatinum(II)[26] and chloroglycyl-*D,L*-methioninato palladium(II) monohydrate has been reported[27] where glycylmethionine is a terdentate ligand coordinating to the metal ion through amino nitrogen, peptide nitrogen and sulphur atoms. Few complexes of platinum(IV) with glycylmethionine are reported,[28] where the latter acts as a bidentate ligand. Very few ternary complexes of platinum, palladium or other transition metals with glycyl-*D,L*-methionine as primary ligand and other secondary ligands were reported.[29–30] The present paper, therefore, deals with studies of mixed ligand complexes of platinum(II) and palladium(II)-glycylmethionine with purines and nucleosides.

EXPERIMENTAL

Materials

Chromatographically pure glycyl-*D,L*-methionine, purines and nucleosides were purchased from Sigma Chemical Company. Pure samples of potassium tetrachloroplatinate(II) and potassium tetrachloropalladate(II) were purchased from Aldrich Chemical Company, U.S.A. Solvents used were of high purity and distilled before use.

Synthesis

Chloroglycyl-*D,L*-methioninatopalladium(II) monohydrate was prepared by the reported procedure.[27]

Physical Measurements

Elemental analyses of the complexes were obtained from Central Drug Research Institute, Lucknow. The conductivity data were measured on a digital conductivity meter No. DL 909. Molecular weight measurements were carried out using an osmometer. IR and UV spectra of the complexes were recorded on Shimadzu IR 435 and UV-160 instruments, respectively. Far infrared spectra were recorded at RSIC, Indian Institute of Technology, Madras. ^{1}H nmr spectra were recorded on Bruker 300 and 270 MHz and Varian 200 MHz spectrometers at the Centre for Cellular and Molecular Biology, Hyderabad, Indian Institute of Science, Bangalore and Indian Institute of Chemical Technology, Hyderabad. ^{13}C nmr were recorded at the Indian Institute of Science, Bangalore and Central Salt and Marine Chemicals Research Institute, Bhavnagar, Gujarat.

Preparation of Complexes

1. Chloroglycyl-*D,L*-methioninatoplatinum(II) monohydrate, [Pt(gly-*D,L*-meth) Cl]·H_2O

Potassium tetrachloroplatinate(II) (1.2 mM) was dissolved in water (10 cm^3) and added to an aqueous solution of glycyl-*D*,*L*-methionine (1.2 mM in 10 cm^3). The solution was heated on a water bath for 30 minutes, when the colour of the solution changed from red to orange and then to pale yellow. The pH of the solution was between 2 and 3. The solution was concentrated to half its volume, cooled and kept in a refrigerator overnight when pale yellow crystals were obtained. The crystals were filtered, washed with water, alcohol and acetone and vacuum dried.

2. Bis[glycyl-*D*,*L*-methioninatoplatinum(II)]-μ-adenine chloride, $\{[Pt(gly\text{-}D,L\text{-}meth)]_2(ade)\}Cl_2$
3. Bis[glycyl-*D*,*L*-methioninatopalladium(II)]-μ-adenine chloride, $\{[Pd(gly\text{-}D,L\text{-}meth)]_2(ade)\}Cl_2$
4. Glycyl-*D*,*L*-methioninatoguanineplatinum(II) chloride, [Pt(gly-*D*,*L*-meth)(gua)]Cl
5. Glycyl-*D*,*L*-methioninatoguaninepalladium(II) chloride, [Pd(gly-*D*,*L*-meth)(gua)]Cl
6. Bis[glycyl-*D*,*L*-methioninatoplatinum(II)-μ-hypoxanthine chloride $\{[Pt(gly\text{-}D,L\text{-}meth)]_2(hypo)\}Cl_2$
7. Glycyl-*D*,*L*-methioninatohypoxanthinepalladium(II) chloride, [Pd(gly-*D*,*L*-meth)(hypo)]Cl
8. Bis[glycyl-*D*,*L*-methioninatoplatinum(II)]-μ-adenosine chloride, $\{[Pt(gly\text{-}D,L\text{-}meth)]_2(ado)\}Cl_2$
9. Bis[glycyl-*D*,*L*-methioninatopalladium(II)]-μ-adenosine chloride, $\{[Pd(gly\text{-}D,L\text{-}meth)]_2(ado)\}Cl_2$
10. Glycyl-*D*,*L*-methioninatoguanosineplatinum(II) chloride monohydrate, $[Pt(gly\text{-}D,L\text{-}meth)(guo)]Cl\cdot H_2O$
11. Bis[glycyl-*D*,*L*-methioninatoplatinum(II)]-μ-inosine chloride, $\{[Pt(gly\text{-}D,L\text{-}meth)]_2(ino)\}Cl_2$
12. Glycyl-*D*,*L*-methioninatoinosinepalladium(II) chloride, [Pd(gly-*D*,*L*-meth)(ino)]Cl
13. Glycyl-*D*,*L*-methioninatocytidineplatinum(II) chloride monohydrate, $[Pt(gly\text{-}D,L\text{-}meth)(cyd)]Cl\cdot H_2O$

Chloroglycyl-*D*,*L*-methioninatoplatinum(II)/chloroglycyl-*D*,*L*-methioninato palladium(II)(1.2 mM) dissolved in water (10 cm^3) was added to an aqueous solution of the ligand (1.2 mM in 10 cm^3; adenine, guanine, hypoxanthine, adenosine, guanosine, inosine and cytidine). The pH of the solution (between 2 and 3) was adjusted to 8.0 with 0.1 N KOH wherever necessary to obtain a clear solution. The resulting solution was heated on a water bath for 5–8 hrs, when the colour of the solution changed from pale yellow to colourless (complex 2), orange to yellow (complex 3), greenish yellow (complex 5), colourless (complexes 4, 6, 7, 8, 10, 11, 12 and 13) and yellow (complex 9), respectively. The solution was concentrated to half its volume, the product precipitated with ice-cold acetone and kept in the refrigerator overnight. The solid was filtered, washed with ice-cold acetone and vacuum dried.

RESULTS AND DISCUSSION

Analytical and conductivity data for the complexes are presented in Table 1.

Table 1 Analytical and conductivity data for the complexes.

	Complex	Colour	Analysis*				Molar Conductivity at 30°C in DMSO (mhos cm^{-2})
			C%	H%	N%	Cl%	
1.	[Pt(gly-*D*,*L*-meth)Cl]H_2O	Pale Yellow	18.47 (18.50)	3.30 (3.33)	5.86 (6.10)	—	0
2.	{[Pt(gly-*D*,*L*-meth)]$_2$(ade)}Cl_2	White	23.73 (22.65)	3.25 (3.10)	13.15 (12.52)	6.74 (7.04)	42
3.	{[Pd(gly-*D*,*L*-meth)]$_2$(ade)}Cl_2	Yellow	28.12 (27.55)	3.85 (3.77)	14.68 (15.21)	8.34 (8.55)	44
4.	[Pt(gly-*D*,*L*-meth)(gua)]Cl	White	23.74 (24.49)	3.08 (3.09)	15.85 (16.66)	6.18 (6.02)	27
5.	[Pd(gly-*D*,*L*-meth)]$_2$(gua)]Cl	Yellow	29.15 (28.91)	3.47 (3.64)	20.05 (19.66)	6.99 (7.11)	27
6.	{[Pt(gly-*D*,*L*-meth)]$_2$(hypo)}Cl_2	White	22.79 (22.64)	3.08 (3.00)	11.84 (11.12)	7.00 (7.04)	43
7.	[Pd(gly-*D*,*L*-meth)(hypo)]Cl[a]	Pale Yellow	28.56 (29.80)	3.72 (3.54)	17.98 (17.38)	7.08 (7.33)	
8.	{[Pt(gly-*D*,*L*-meth]$_2$(ado)}Cl_2	White	24.95 (25.30)	3.23 (3.45)	12.05 (11.12)	6.36 (6.23)	45
9.	{[Pd(gly-*D*,*L*-meth)}$_2$(ado)}Cl_2	Pale Yellow	30.12 (29.90)	3.97 (4.08)	12.68 (13.08)	7.06 (7.36)	55
10.	[Pt(gly-*D*,*L*-meth)(guo)]Cl.H_2O	White	23.70 (24.20)	3.46 (3.38)	14.70 (14.30)	6.20 (6.80)	29
11.	{[Pt(gly-*D*,*L*-meth)]$_2$(ino)}Cl_2	White	26.00 (25.30)	3.38 (3.34)	10.01 (9.86)	6.30 (6.25)	40
12.	[Pd(gly-*D*,*L*-meth)(ino)]Cl[a]	Pale Yellow	32.52 (33.16)	3.96 (4.09)	12.87 (13.65)	5.23 (5.76)	
13.	[Pt(gly-*D*,*L*-meth)(cyd)]Cl.H_2O	White	27.29 (27.56)	3.94 (4.04)	9.67 (10.04)	5.18 (5.08)	27

*Calculated value in parentheses. [a]Insoluble complex.

Complex 1 is a non-electrolyte; complexes 2, 3, 6, 8, 9 and 11 are 1:2 electrolytes, and complexes 4, 5, 10 and 13 are 1:1 electrolytes.[31]

Infrared data for the complexes are given in Table 2. The IR spectra of the complexes, in general, show a broad band in the region 3400–3100 cm^{-1} which is assigned to νOH, νNH and νCH stretching frequencies of coordinated purine or nucleoside and glycylmethionine.[32] A sharp peak at 1710 cm^{-1} is assigned to the free COOH group of glycylmethionine and to νC=O of guanine, guanosine, cytidine which are not involved in coordination to the metal ion. A peak at 1650 cm^{-1} is due to NH_2 deformation of adenine, guanine, adenosine, guanosine and cytidine. An intense peak at 1560 cm^{-1} is assigned to the coordinated amide group of glycyl-*D*,*L*-methionine. The important purines and nucleoside νC=C and νC=N frequencies are observed in the region 1600 to 1350 cm^{-1} and on complexation are shifted to lower frequencies by about 40–70 cm^{-1}, indicating that ring nitrogens are involved in coordination to the metal ion.[32] The peaks observed at 550 and 480 cm^{-1} are assigned to νM-N and νM-S stretching frequencies, respectively. Electronic spectra data for the complexes are given in Table 3.

^1H nmr and ^{13}C nmr data for the complexes are given in Tables 4 and 5, respectively. The spectra were very helpful in determining the binding sites of the ligand to the metal ion. The ^1H nmr spectrum of complex 1 shows a singlet at 2.4

Table 2 Infrared data for the complexes.

	Ligand/Complex	νM-N	νM-S	νC=C	νC=N	ν-C(=O)-N-	δ NH_2	ν>C=O
	Glycyl-*D,L*-methionine					1530(s)	1590(m)	1680(s)
1.	[Pt(gly-*D,L*-meth)Cl]H_2O	570	490			1540(s)	1640(m)	1700(s)
			350	(νM-Cl)				
	Adenine			1600(m)	1440(m)		1650(m)	
				1570(m)				
2.	{[Pt(gly-*D,L*-meth)]$_2$(ade)}Cl_2	550	480	1510	1400(m)	1560(s)	1650(s)	1710(s)
3.	{[Pd(gly-*D,L*-meth)]$_2$(ade)}Cl_2	525	460	1520	1385(m)	1560(s)	1650(m)	1700(m)
	Guanine			1500(m)	1380(s)		1620(b)	1700(s)
4.	[Pt(gly-*D,L*-meth)(gua)]Cl	530	480	1490(m)	1350(s)	1580(m)	1630(m)	1700(s)
				1405(s)				
5.	[Pd(gly-*D,L*-meth)(gua)]Cl	545	460	1470(m)	1350(s)	1560(m)	1630(m)	1700(s)
				1390(s)				
	Hypoxanthine			1570(m)	1425(s)			1680(s)
6.	Pt(gly-*D,L*-meth)]$_2$(hypo)}Cl_2	540	475	1500(s)	1400(m)	1580(s)		1690(s)
7.	[Pd(gly-*D,L*-meth)(hypo)]Cl	570	465	1510(m)	1390(m)	1580(m)		1690(s)
	Adenosine			1600	1470(m)		1660(s)	
				1570(s)				
8.	{[Pt(gly-*D,L*-meth)]$_2$(ado)}Cl_2	560	490	1490(m)	1400(m)	1580(s)	1650(s)	1710
9.	{[Pd(gly-*D,L*-meth)]$_2$(ado)}Cl_2	535	475	1495(s)	1410(m)	1580(s)	1650(s)	1700
	Guanosine			1580(s)	1470(s)		1620(s)	1700(s)
10.	[Pt(gly-*D,L*-meth)(guo)]Cl.H_2O	550	480	1500(s)	1410(m)	1580(s)	1625(m)	1690(s)
	Inosine			1600(s)	1480(m)			1700(s)
				1565(s)	1435(s)			
11.	{[Pt(gly-*D,L*-meth)]$_2$(ino)}Cl_2	545	480	1510	1410(m)	1580(s)		1700(s)
12.	[Pd(gly-*D,L*-meth)(ino)]Cl	560	470	1520	1430(m)	1560(s)		1700(s)
	Cytidine			1560(s)	1470(s)		1640(m)	1700(s)
13.	[Pt(gly-*D,L*-meth)(cyd)]Cl.H_2O	550	465	1500(s)	1410(m)	1580(s)	1640(m)	1720(m)

ppm due to *S*-CH_3 protons and a triplet centred at 4.46 ppm due to the α-CH proton. These protons are shifted downfield by 0.25 ppm and 0.11 ppm, respectively, as compared to the free ligand, thus indicating the involvement of the sulphur and amide nitrogen atoms in coordination to the metal ion. The peaks observed in the region 2.86 to 3.0 ppm are assigned to β-CH_2 and γ-CH_2 protons of methionine, respectively. The peak corresponding to the methylene protons of the glycine arm is shifted upfield by 0.4 ppm indicating coordination of the NH_2 group of glycine arm to the metal ion. It is, therefore, inferred that the sulphur, the amide nitrogen and amino group (NH_2) of glycylmethionine are coordinated to the metal ion. This is confirmed by the X-ray crystal structure of the complex.[27]

The ^{1}H nmr spectrum of 2 (Fig. 1) shows two main peaks at 8.38 and 8.5 ppm due to C_2H and C_8H protons of coordinated adenine. The C_2H and C_8H protons of adenine in 2 are nearer to platinum and couple with ^{195}Pt to give two overlapping triplets (^{J195}Pt-C_2H = 60Hz, ^{J195}Pt-C_8H = 70Hz). The peak which is observed between two main peaks is due to overlapping of two ^{195}Pt satellites corresponding to the two triplets and appears with double the intensity as compared to the other satellites. The C_2H and C_8H protons are shifted equally dowfield by 0.18 ppm as compared to the free ligand indicating the involvement of N_1 and N_7 of adenine in coordination to the metal ion.[33] In 3 the binding of the metal ion to adenine is different as compared to complex 2. The ^{1}H nmr spectrum of 3 exhibits an upfield shift of C_2H and C_8H protons by 0.30 and 0.17 ppm respectively,

Table 3 Electronic absorption data for the complexes.

	Ligand/Complex	λ_{max}(nm)	ε_{max}*	Transition
	Glycl-*D,L*-methionine	291	0.58×10^2	$\eta - \pi^*$
1.	[Pt(gly-*D,L*-meth)Cl]H_2O	293	2.28×10^2	$\eta - \pi^*$
	Adenine	268	1.13×10^4	$\pi - \pi^*$
2.	{[Pt(gly-*D,L*-meth)]$_2$(ade)}Cl_2	246	3.22×10^3	$\pi - \pi^*$
3.	{[Pd(gly-*D,L*-meth)]$_2$(ade)}Cl_2	248	6.24×10^3	$\pi - \pi^*$
	Guanine	246	9.40×10^3	$\pi - \pi^*$
4.	[Pt(gly-*D,L*-meth)(gua)]Cl	280	8.10×10^3	$\pi - \pi^*$
5.	[Pd(gly-*D,L*-meth)(gua)Cl	281	2.12×10^3	$\pi - \pi^*$
	Hypoxanthine	250	1.05×10^4	$\pi - \pi^*$
6.	{Pt(gly-*D,L*-meth)]$_2$(hypo)}Cl_2	247	1.72×10^4	$\pi - \pi^*$
	Adenosine	259	1.10×10^4	$\pi - \pi^*$
8.	{[Pt(gly-*D,L*-meth)]$_2$(ado)}Cl_2	249	1.50×10^4	$\pi - \pi^*$
9.	{[Pd(gly-*D,L*-meth)]$_2$(ado)}Cl_2	248	1.23×10^4	$\pi - \pi^*$
	Guanosine	259	9.47×10^3	$\pi - \pi^*$
10.	[Pt(gly-*D,L*-meth)(guo)]Cl.H_2O	249	1.60×10^4	$\pi - \pi^*$
	Inosine	248	1.41×10^4	$\pi - \pi^*$
11.	{[Pt(gly-*D,L*-meth)]$_2$(ino)}Cl_2	246	1.67×10^4	$\pi - \pi^*$
	Cytidine	271	1.07×10^4	$\pi - \pi^*$
13.	[Pt(gly-*D,L*-meth)(cyd)]Cl.H_2O	276	1.68×10^4	$\pi - \pi^*$

*$M^{-1}cm^{-1}$.

indicating that N_3 and N_9 of adenine are involved in coordination to the metal ion.[34,35] The peaks corresponding to the protons of glycyl-*D,L*-methionine are observed in the region 2.10 to 4.41 ppm. The $^{13}C[^1H]$ nmr spectra of 2 and 3 support the above coordination of the ligand to the metal ion. The ^{13}C nmr spectrum of 2 shows a downfield shift in C_2, C_5, C_6 and C_8 carbons by 4.4, 3.0, 1.4 and 2.2 ppm, respectively, as compared to the ^{13}C nmr spectrum of the free ligand. There is no shift for C_4, indicating that adenine coordinates to the metal ion through N_1 and N_7. The ^{13}C nmr spectrum of 3 shows an upfield shift for C_2 and C_8 by 7.3 and 4.7 ppm, respectively, and a downfield shift for C_4 by 3.8 ppm. There is no shift for C_5 or C_6. It is inferred that in complex 3 the metal ion binds to adenine through N_3 and N_9. ^{13}C nmr spectra of the complexes show peaks due to free carboxylic carbon, amide carbonyl carbon and *S*-CH_3, γ-CH_2, β-CH_2, CH_2 of glycine and CH carbons of glycylmethionine. The ^1H nmr spectrum of 4 shows a doublet at 8.36 ppm with two ^{195}Pt satellites. The doublet is due to the coupling of C_8H with N_9H (^JC_8H-N_9H = 40 Hz). This coupling arises due to the slow exchange of NH D_2O. The C_8H proton further couples with platinum to give two ^{195}Pt satellites (^{J195}Pt-C_8H = 60 Hz) and is shifted downfield by 0.68 ppm as compared to the ligand, indicating that guanine coordinates to the metal ion through N_7.[27] The ^1H nmr spectrum of 5 shows a downfield shift for the C_8H proton by 0.42 ppm indicating that guanine coordinates to the metal ion through N_7. The glycylmethionine protons resonate between 2.1 and 4.8 ppm in both complexes. The $^{13}C[^1H]$ nmr spectrum of 5 supports coordination of guanine to the metal ion through N_7. This spectrum shows a downfield shift in C_5 and C_8 carbons by 2.4 and 4.2 ppm, respectively. As there is a shift in C_5 and C_8 carbons it is inferred that guanine coordinates to the metal ion through N_7.[27] Peaks due to free carboxylic carbon, amide carbonyl carbon and *S*-CH_3, γ-CH_2, β-CH_2, CH_2 of glycine arm and CH carbons of glycylmethionine are also observed.

Table 4 ^{1}H NMR data for the complexes (D_2O solution).

	Ligand/Complex	Purine		$J^{195}Pt-H_2$	$J^{195}Pt-H_8$	Glycyl-*D,L*-methionine				
		C_2H	C_8H			S-CH_3	γ-CH_2	β-CH_2	-CH_2-	α-CH
	Glycyl-*DL*-methionine					2.15	2.50	2.70	3.90	4.35
1.	[Pt(gly-*D,L*-meth)Cl]·H_2O					2.40	2.86	3.00	3.50	4.46
	Adenine	8.20	8.32							
2.	{[Pt(gly-*D,L*-meth)]$_2$(ade)}Cl_2	8.38	8.50	60 Hz	70 Hz	2.26	2.30	2.52	3.36	4.41
3.	{[Pd(gly-*D,L*-meth)]$_2$(ade)}Cl_2	7.90	8.15			2.10	2.35	2.50	3.50	4.10
	Guanine		7.68							
4.	[Pt(gly-*D,L*-meth)(gua)]Cl		8.36		60 Hz	2.15	2.26	2.53	3.66	4.76
5.	[Pd(gly-*D,L*-meth)(gua)]Cl		8.10			2.10	2.20	2.50	3.55	4.10
	Hypoxanthine	7.87	8.08							
6.	{[Pt(gly-*D,L*-meth)]$_2$(hypo)}Cl_2	8.28	8.70	75 Hz	70 Hz	2.20	2.29	2.50	3.60	4.40

		Nucleoside		$J^{195}Pt-H_2$	$J^{195}Pt-H_8$	Ribose protons					Glycyl-DL-methionine				
		C_2H	C_8H			C'_1H	C'_2H	C'_3H	C'_4H	C'_5H	S-CH_3	γ-CH_2	β-CH_2	-CH_2-	α-CH
	Adenosine	8.15	8.36			6.40	6.25	4.63	4.19	3.90					
8.	{[Pt(gly-*D,L*-meth)]$_2$(ado)}Cl_2	8.42	8.70	70 Hz	65 Hz	6.10	2.28	4.40	3.90	3.65	2.20	2.36	2.55	3.60	4.30
9.	{[Pd(gly)-*D,L*-meth)]$_2$(ado)}Cl_2	8.45	8.65			6.15	2.75	4.45	3.90	3.50	2.15	2.30	2.50	3.60	4.36
	Guanosine		7.88			5.86	4.72	4.43	4.35	3.92					
10.	{[Pt(gly-*D,L*-meth)(guo)]Cl·H_2O		8.60		90 Hz	6.00	4.68	4.40	3.30	3.91	2.20	2.30	2.53	3.60	4.20
	Inosine	8.11	8.22			6.03	4.41	4.28	3.99	3.75					
11.	{Pt(gly-*D,L*-meth)]$_2$(ino)}Cl_2	8.33	9.02	75 Hz	70 Hz	6.20	4.40	4.30	3.93	3.67	2.22	2.27	2.57	3.87	4.41
		C_5H	C_6H												
	Cytidine	5.70	7.78			5.91	4.32	4.32	3.65	3.96					
13.	[Pt(gly-*D,L*-meth)(cyd)]Cl·H_2O	6.20	8.00			6.00	4.30	4.30	3.80	3.90	2.20	2.30	2.50	3.60	4.20

Table 5 $^{13}C[^{1}H]$ NMR data for the complexes (D_2O Solution).

Ligand/Complex	Purine/Pyrimidine Nucleoside					Ribose					Glycyl-*D,L*-methionine						
	C_2	C_4	C_5	C_6	C_8	C'_1	C'_2	C'_3	C'_4	C'_5	S-CH_3	γ-CH_2	β-CH_2	-CH_2-	α-CH	-C(=O)-N-	COOH
Adenine	150.5	160.4	121.0	155.0	153.7												
2. {[Pt(gly-*D*,L-meth)]$_2$(ade)]}Cl_2	154.9	160.0	124.0	156.4	155.9						22.20	26.60	30.87	46.10	53.00	174.30	184.1
3. {[Pd(gly-*D*,*L*-meth)]$_2$(ade)]}Cl_2	143.2	164.2	121.7	154.8	149.0						23.00	30.20	34.20	51.00	59.00	182.00	186.5
Guanine	160.0	162.2	119.6	168.8	150.1												
5. [Pd(gly-*D*,*L*-meth)(gua)]Cl	160.2	162.5	122.0	169.1	154.3						25.45	29.49	45.60	53.24	64.24	177.09	181.3
Adenosine	152.3	149.0	119.3	154.0	140.1	88.00	76.00	74.40	85.90	63.60							
8. {[Pt(gly-*D*,*L*-meth)]$_2$(ado)}Cl_2	150.0	149.3	122.3	157.5	145.2	91.00	77.00	73.00	87.00	64.00	24.00	31.00	34.00	43.70	56.00	179.60	188.5
Guanosine	153.8	151.5	116.7	157.1	136.1	86.70	73.90	70.60	85.50	61.60							
10. [Pt(gly-*D*,*L*-meth)(guo)]$Cl \cdot H_2O$	153.9	151.5	120.3	156.9	140.4	89.14	74.22	70.19	85.75	61.18	22.09	27.36	30.93	47.19	55.10	176.72	182.4
[Pd(gly-*D*,*L*-meth)(guo)]Cl	153.8	151.4	118.2	156.4	138.9	86.65	68.80	72.64	84.30	61.40	22.64	28.02	34.64	45.40	59.12	178.05	182.5
Inosine	145.8	148.2	124.5	155.2	138.7	89.82	78.40	73.96	90.00	64.68							
11. {[Pt(gly-*D*,*L*-meth)]$_2$(ino)}Cl_2	152.3	147.9	127.0	160.2	144.0	94.40	79.10	74.45	90.36	65.38	25.42	31.68	35.08	44.40	51.63	180.79	192.0
Cytidine	155.3	165.3	93.5	141.3		89.00	69.30	73.90	84.00	60.50							
13. [Pt(gly-*D*,*L*-meth)(cyd)]$Cl \cdot H_2O$	157.5	165.73	95.4	141.2		90.01	69.05	74.08	84.02	60.51	21.43	26.46	28.21	46.87	54.30	177.16	185.0

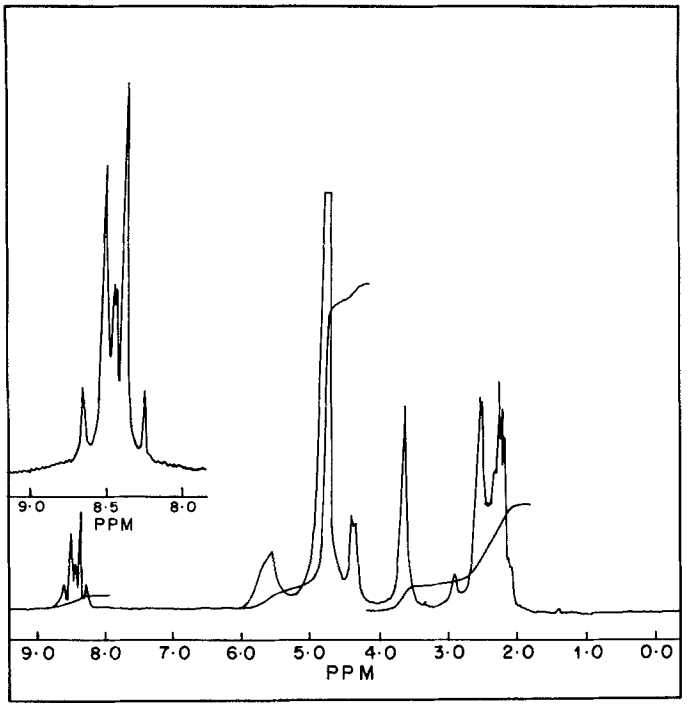

Figure 1 ^{1}H nmr spectrum of {[Pt(gly-*D*,*L*-meth)]$_2$(ade)}Cl$_2$.

The ^{1}H nmr spectrum of 6 shows two doublets at 8.28 and 8.70 ppm due to C_2H and C_8H protons. The doublets are due to the coupling of C_2H and C_8H protons with N_1H and N_7H protons ($^JH_1$-H_2 = 15 Hz; $^JH_7$-H_8 = 26 Hz) as was observed in complex 4. In addition, four ^{195}Pt satellites were observed, two for C_2H and two for C_8H protons indicating that both the C_2H and C_8H protons are closer to the metal ion. These protons couple with ^{195}Pt to give in each case two ^{195}Pt satellites with (^{J195}Pt-C_2H = 75 Hz) and (^{J195}Pt-C_8H = 70 Hz) and are shifted downfield by 0.41 and 0.62 ppm respectively, inferring that hypoxanthine coordinates to the metal ion through N_3 and N_9.[13] The peaks due to coordinated glycyl-*D*,*L*-methionine resonate between 2.2 to 4.4 ppm. Complex 7 is insoluble; nmr spectra could not be recorded.

The ^{1}H nmr spectrum of 8 shows two triplets for C_2H and C_8H protons centred at 8.42 and 8.70 ppm due to coupling with ^{195}Pt (^{J195}Pt-C_2H = 70 Hz) and (^{J195}Pt-C_8H = 65 Hz) and are shifted downfield by 0.27 ppm and 0.34 ppm, respectively, inferring that adenosine coordinates to the metal ion through N_1 and N_7.[13,36] The ^{1}H nmr spectrum of 9 shows an equal downfield shift in C_2H and C_8H protons by 0.29 ppm, inferring that adenosine binds through N_1 and N_7 to palladium(II).[13] The ribose protons resonate between 3.5 to 6.4 ppm and those due to coordinated glycylmethionine between 2.15 and 4.36 ppm. The ^{13}C nmr spectrum of 8 (Fig. 2) supports coordination of adenosine to the metal ion through N_1 and N_7. There is an upfield shift for the C_2 carbon by 2.32 ppm and a downfield shift for C_5, C_6 and C_8 carbon resonances by 3.0, 3.5 and 5.15 ppm, respectively. As there is no shift in the C_4 carbon resonance, it is inferred that adenosine

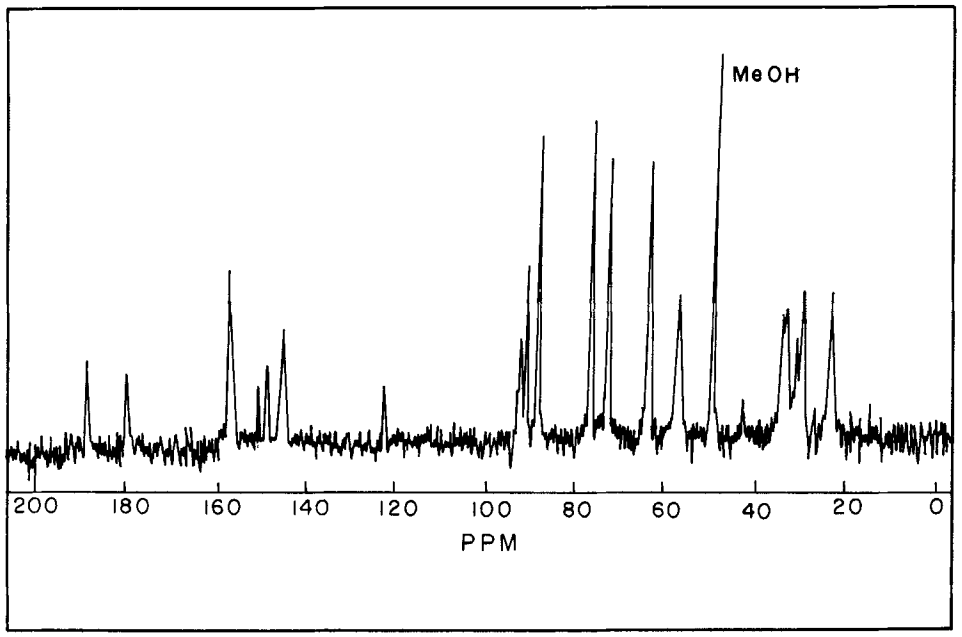

Figure 2 $^{13}C[^1H]$ nmr spectrum of {[Pt(gly-*D*,*L*-meth)]$_2$(ado)}Cl_2.

coordinates to the metal ion through N_1 and N_7. Resonances due to ribose carbons and coordinated glycylmethionine carbons are observed between 64 and 91 ppm, and 24 and 56 ppm, respectively. The carboxylic carbon and the amide carbonyl carbon of glycylmethionine are observed at 188.5 and 179.6 ppm, respectively. A few low intensity ^{13}C nmr peaks found in Figure 2 may be due to the presence of diastereomers. The ^1H nmr spectrum of 10 shows a peak with two platinum satellites (^{J195}Pt-C_8H = 90 Hz) due to the C_8H proton; this proton couples with ^{195}Pt and is shifted downfield by 0.72 ppm indicating that guanosine coordinates to the metal ion through N_7.[27] Ribose protons are observed between 3.9 to 6.0 ppm and those due to coordinated glycylmethionine between 2.2 to 4.2 ppm.

The corresponding palladium complex [Pd(gly-*D*,*L*-meth)(guo)]Cl reported earlier[27] also shows coordination of guanosine through N_7. $^{13}C[^1H]$ nmr spectra of platinum complex 10 and the palladium complex also support coordination of guanosine through N_7 to the metal ion. In both complexes there is a downfield shift in C_5 and C_8 carbon resonances by 3.6 and 4.3 ppm in platinum complex 10 and by 1.5 and 2.8 ppm in the palladium complex, respectively.[27] There is no shift in C_2, C_4 and C_6 carbons, inferring that guanosine coordinates to the metal ion through N_7. Resonances due to ribose carbons and coordinated glycylmethionine are shown in Table 5.

The ^1H nmr spectrum of 11 shows peaks due to C_2H and C_8H protons at 8.33 and 9.02 ppm, respectively. These peaks are shifted downfield by 0.22 and 0.80 ppm, respectively, inferring that inosine coordinates to the metal ion through N_1 and N_7.[37,38] The C_2H and C_8H protons couple with ^{195}Pt to give two doublets (^{J195}Pt-C_2H = 75 Hz) and (^{J195}Pt-C_8H = 70 Hz). The $^{13}C[^1H]$nmr spectrum shows

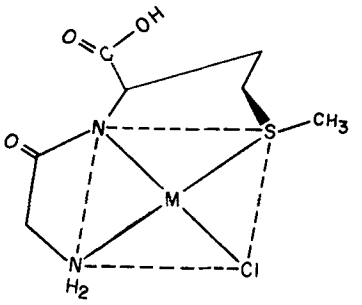

Figure 3 Structure of [Pt(gly-*D*,*L*-meth)Cl]H_2O.

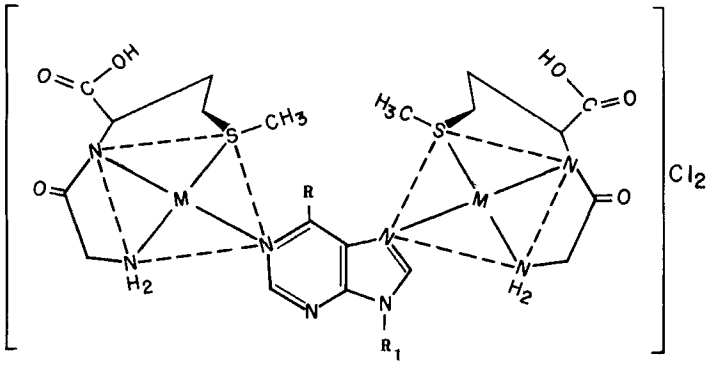

Figure 4 Structure of $[M(gly\text{-}D,L\text{-}meth)]_2(ade)\}Cl_2$, M=Pt, R=$NH_2$, R_1=H, $\{[M(gly\text{-}D,L\text{-}meth)]_2(ado)\}Cl_2$, M = Pt, Pd, R = NH_2, R_1 = ribose, and $\{[M(gly\text{-}D,L\text{-}meth)]_2(ino)\}Cl_2$, M = Pt, R = OH, R_1 = ribose.

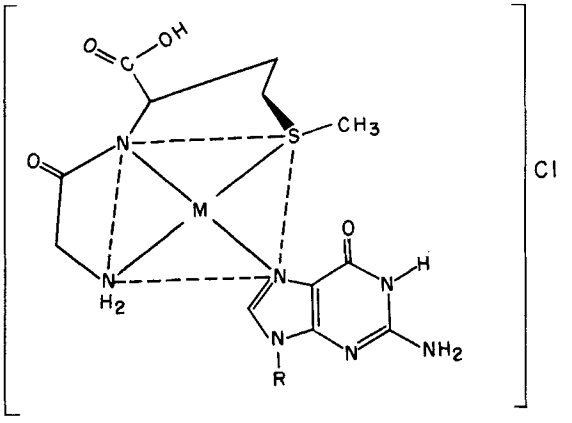

Figure 5 Structure of [M(gly-*D*,*L*-meth)(gua)]Cl, M = Pt(II), Pd(II), R = H, and M = Pt(II), R = ribose.

downfield shifts in C_2, C_5, C_6 and C_8 carbons by 6.5, 2.5, 5.0 and 5.29 ppm, respectively, and a negligible shift for the C_4 carbon, indicating that inosine coordinates to the metal ion through N_1 and N_7. Proton and carbon resonances for ribose and glycylmethionine are shown in Tables 4 and 5, respectively. Based on the ^1H nmr and ^{13}C nmr data, binding of the metal ion to inosine is through N_1 and N_7. The corresponding palladium complex, 12, [Pd(gly-*D*,*L*-meth)(ino)]Cl is insoluble and its nmr spectrum could not be recorded.

The ^1H nmr spectrum of 13 shows two peaks at 6.20 and 8.00 ppm due to C_5H and C_6H protons which are shifted downfield by 0.5 ppm and by 0.22 ppm, respectively. Since the downfield shift for the C_5H proton is more than for the C_6H proton, it is inferred that cytidine coordinates to the metal ion through N_3.[39] Platinum satellites were not observed as N_3 is distant from C_5H and C_6H protons. Ribose protons are observed between 3.9 and 6.00 ppm and coordinated glycylmethionine protons between 2.2 and 4.2 ppm. The $^{13}C[^1H]$ nmr spectrum also supports coordination of cytidine to the metal ion through N_3. It shows a downfield shift for C_2, C_4 and C_5 carbons by 2.2, 0.43 and 1.9 ppm, respectively. Ribose carbons are observed in the region 60 to 90 ppm and those due to glycylmethionine between 21 and 55 ppm. The amide carbonyl and carboxylic carbons of glycylmethionine are observed at 177.16 and 185 ppm, respectively. The corresponding palladium complex [Pd(gly-*D*,*L*-meth)(cyd)]Cl, reported earlier,[27] also shows coordination of cytidine through N_3.

Molecular weights of complexes 2, 3, 6, 8, 9 and 11 were found to correspond to the binuclear complex and complexes 4, 5, 7, 10, 12 and 13 to mononuclear complexes.

Based on analytical and spectroscopic data, the structure shown in Figure 3 was proposed for 1. In this complex, glycylmethionine acts as a terdentate coordinating to the metal ion through sulphur, amide nitrogen and amino nitrogen atoms, and the fourth position is occupied by chloride. Complexes 2 and 3 are binuclear complexes where adenine acts as a bridging ligand between two [M(glymeth)] moieties coordinating to the two metal ions through N_1 and N_7 in complex 2 (Fig. 4) and through N_3 and N_9 in complex 3. Complexes 4 and 5 are mononuclear complexes where guanine coordinates to the metal ion through N_7 (Fig. 5). In complex 6 hypoxanthine acts as a bridging ligand between two [Pt(glymeth)] moieties, coordinating to the metal ion through N_3 and N_9. Complex 7 is insoluble. Complexes 8, 9 and 11 are binuclear (Fig. 4) where adenosine and inosine act as bridging ligands between two [M(glymeth)] moieties coordinating to the metal ion through N_1 and N_7. In complexes 10 and 13, guanosine (Fig. 5) and cytidine coordinate to the metal ion through N_7 and N_3, respectively.

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References

1. G.L. Eichhorn (Ed.), Inorganic Biochemistry, (Elsevier, Amsterdam, 1973).
2. H. Sigel (Ed.), In "Metal Ions in Biological Systems", Vol. 2, (Marcel Dekker, New York, 1979).

3. R.W. Hay and P.J. Morris, In "Metal Ions in Biological Systems" Vol. 5, (Marcel Dekker, New York, 1976).
4. C. Helene and J. Maurizot, *CRC Crit. Rev. Biochem.*, **10**, 213 (1981).
5. G.L. Eichhorn, In "Metal Ions in Biological Systems", Vol. 10, (Marcel Dekker, New York, 1980).
6. Y.A. Shin and G.L. Eichhorn, *Biopolymers*, **16**, 225 (1977).
7. B. Rosenberg, L. Van Camp, J.E. Troska and V.H. Manson, *Nature*, **22**, 385 (1969).
8. D.W. Brown, A.R. Khokkar, M.P. Hacker, J.J. McCormack and W.M. Statick, *Inorg. Chim. Acta*, **67**, 47 (1982).
9. R. Faggani, C.J.L. Lock and B. Lippert, *Inorg. Chim. Acta*, **106**, 75 (1985).
10. Badar Taqui Khan, G. Narsa Goud and S. Vijaykumari, *Inorg. Chim. Acta*, **80**, 145 (1983).
11. V.V. Lakshmi, Padma Sridhar, Badar Taqui Khan and H. Polasa, *J. Gen. Microbiol*, **134**, 1977 (1988).
12. W.I. Sundquist and S.J. Lippard, *Coord. Chem. Rev.*, **100**, 293 (1990).
13. Badar Taqui Khan, S. Vijaykumari and G. Narsa Goud, *J. Coord. Chem.*, **12**, 19 (1982).
14. S. Kasselouri, A. Garoufis and N. Hadjiliadis, *Inorg. Chim. Acta*, **L23**, 135 (1987).
15. G. Pneumatikakis, N. Hadjiliadis and T. Theophanides, *Inorg. Chem.*, **17**, 915 (1978).
16. N. Hadjiliadis and G. Pneumatikakis, *Inorg. Chim. Acta*, **46**, 255 (1980).
17. G. Pneumatikakis, *Polyhedron*, **3**, 15 (1984).
18. Badar Taqui Khan and K. Murali Mohan, *Trans. Met. Chem.*, **15**, 407 (1990).
19. Badar Taqui Khan, K. Najmuddin, S. Shamsuddin and S.M. Zakeeruddin, *Inorg. Chim. Acta*, **170**, 129 (1990).
20. Badar Taqui Khan, K. Venkatasumbramanian, K. Najmuddin, S. Shamsuddin and S.M. Zakeeruddin, *Inorg. Chim. Acta*, **179**, 117 (1991).
21. Badar Taqui Khan, K. Annapoorna, S. Shamsuddin and K. Najmuddin, *Polyhedron*, **11**, 2109 (1992).
22. Badar Taqui Khan, Jayshree Bhatt, K. Najmuddin, S. Shamsuddin, and K. Annapoorna, *J. Inorg. Biochem.* **44**, 55 (1991).
23. D.A. Buckingham and J.P. Collman, *Inorg. Chem.*, **6**, 1803 (1967).
24. D. Driver and W.R. Walker, *Aust. J. Chem.*, **21**, 671 (1968).
25. K.C. Tewari, J. Lee and C. LiNorman, *Trans. Faraday Soc.*, **66**, 2069 (1970).
26. H.C. Freeman and M.L. Golomb, *J. Chem. Soc. Chem. Commun.*, 1523 (1970).
27. Badar Taqui Khan, S. Shamsuddin and K. Venkatasubramanian, *Polyhedron*, **11**, 671 (1992).
28. C.A. Bear and H.C. Freeman, *Acta. Cryst.*, **B22**, 2534 (1976).
29. M.F. Mogilevkina, V.I. Rar and I.K. Korobeiwiekeva, *Z. Neorg. Chim.*, **25**, 1004 (1980).
30. D. Camboll, J. Besancon, J. Tirouflet, B. Gautheron and P. Meunier *Inorg. Chim. Acta*, **78**, L51 (1983).
31. W.J. Geary, *Coord. Chem. Rev.*, **7**, 81 (1971).
32. L.J. Bellamy, "The Infrared Spectra of Complex Molecules", (Wiley, New York, 1970), p. 234.
33. M.M. Chester, D. David, B. Domenick and M.K. Nicholas, *Inorg. Chim. Acta*, **93**, L9 (1984).
34. Badar Taqui Khan and K. Annapoorna, *Inorg. Chim. Acta*, **176**, 241 (1990).
35. Chin Hsuan Wei and K.B. Jacobson, *Inorg. Chem.*, **20**, 356 (1981).
36. W.M. Beck, J.C. Calabrese and N.D. Kottmair, *Inorg. Chem.*, **18**, 176 (1979).
37. G. Pneumatikakis, *Inorg. Chim. Acta*, **80**, 89 (1983).
38. K.H. Scheller, V. Scheller and R.B. Martin, *J. Am. Chem. Soc.*, **103**, 6833 (1981).
39. Badar Taqui Khan, S. Vijaya Kumari and K. Murali Mohan, *Indian J. Chem.*, **31A**, 28 (1992).