PLATINUM(II) COMPLEXES OF HETEROCYCLIC LIGANDS OF BIOLOGICAL IMPORTANCE

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Abstract

The synthetic, spectroscopic and biological studies of some heterocyclic complexes derived from 3,8-dimethyl-4,6-diazadecane-3,7-diene-2,9-dione and 3,9-dimethyl-4,8-diazaundecane-3,8-diene-2,10-dione and platinum(II) chloride with various type of diamines (1,2-phenylenediamine, naphthalene-1,8-diamine,2,6-diaminopyridine or 2,2'-diaminodiethyl amine) have been carried out. These complexes have been characterized on the basis of elemental analysis, molecular weight determinations and spectral studies including IR, ^{1}H NMR, mass and electronic spectra. The resulting coloured products are electrolytic in nature. On the basis of above studies and X-ray diffraction studies square planar geometry has been proposed for the resulting complexes. The possibility of potential uses of these complexes as fungicides and bactericides have also been explored.

Introduction

The heterocyclic compounds having metal-nitrogen bonding occupy an important position amongst the recent developments related to bioinorganic systems. Metal ion recognition is of fundamental importance to broad areas of both chemistry and biochemistry. The importance of metal ion in biological systems as heterocyclic compounds is well established because of their catalytic behaviour in a number of redox reactions of biological significance. Heterocyclic ligands are relatively rigid in nature and impose a specific coordination geometry on the metal ions. Thus much of the current interest in heterocyclic coordination chemistry arises from the hope that the unusual geometrical relationship imposed into metal ions by the nitrogen donor set may be transformed on to unusual bonding situation.

The recognition of a metal ion by a heterocyclic ligand and modification of the properties of the resulting complexes is controlled to a large extent by a match between the size of the ligand hole and that of the metal ions[2]. Apart from more obvious parameters such as donor atom, radius and type of hybridisation, a range of other structural factors, including chelate ring size, extent of ligand rigidity and the presence or absence of ring substituents can all influence the geometry of the binding cavity[3]. In view of the versatile chelating ability, wide spread applications[4,5] and lack of data involving heterocyclic derivatives of platinum, it has been considered worth while to examine these reactions. The focus of our present communication is on the exploration of the studies on synthetic, structural and biological aspects of such platinum complexes.

Experimental

All the glass apparatus with standard quick fit joints was used throughout. Adequate precautions were taken to exclude moisture from the system. The chemicals and solvents used were dried and purified by standard methods.

Preparation of the Ligands

3,8-Dimethyl-4,6-diazadecane-3,7-diene-2,9-dione and 3,9-dimethyl-4,8-diazaundecane-3,8-diene 2,10-dione were prepared by the condensation of 2,3-butanedione with 1,2-diaminoethane and 1,3-diaminopropane in ethanol in presence of acidic medium. The reaction was carried out in 2:1 molar ratio and heated under reflux for 12 hours. The reaction mixture was cooled and the product was purified by recrystallisation from ethanol and finally from cyclothexane.

Preparation of the Complexes

The reaction mixture containing ligand, platinum (II) chloride and one of the diamines (1,2-phenylenediamine, naphthalene-1,8-diamine, 2,6-diaminopyridine or 2,2'-diaminodiethyl amine) in 1:1:1 molar ratio in methanol was heated under reflux for 36-38 hours. The solution was cooled, transferred to an evaporating dish and set aside for a few hours, where upon a dark coloured complex separated out. The

product formed was washed and dried under reduced pressure. The complex was repeatedly washed with dry cyclohexane so as to ensure its purity and again dried under reduced pressure. The important properties and analytical data of the complexes have been reported in Table 1.

Table 1 - Physical properties and analytical data of Platinum (II) complexes

Compound	Colour	M.P. (°C)	Analysis (%)[a]			Mol. Wt.[a]
			Pt	N	Cl	
$C_{10}H_{16}N_2O_2$	Wine red	155-157	-	12.96 (14.27)	-	189 (196)
$[Pt(C_{16}H_{20}N_4)]Cl_2$	Brown	108 (d)	36.23 (36.51)	10.00 (10.49)	12.69 (13.27)	515 (534)
$[Pt(C_{15}H_{19}N_5)]Cl_2$	Coke	142-144	35.93 (36.44)	12.56 (13.08)	12.66 (13.24)	508 (535)
$[Pt(C_{14}H_{25}N_5)]Cl_2$	Grey	174 (d)	36.57 (36.85)	12.72 (13.23)	12.82 (13.39)	504 (529)
$[Pt(C_{20}H_{22}N_4)]Cl_2$	Dark red	138 (d)	33.10 (33.38)	9.08 (9.59)	11.65 (12.13)	559 (584)
$C_{11}H_{18}N_2O_2$	Reddish brown	167-169	-	12.01 (13.32)	-	186 (210)
$[Pt(C_{17}H_{22}N_4)]Cl_2$	Dark brown	152-154	35.50 (35.58)	9.78 (10.22)	12.37 (12.93)	520 (548)
$[Pt(C_{16}H_{21}N_5)]Cl_2$	Light brown	107-109	35.28 (35.51)	12.22 (12.75)	12.33 (12.91)	533 (549)
$[Pt(C_{15}H_{27}N_5)]Cl_2$	Mustard	136-138	33.72 (35.90)	11.68 (12.89)	11.74 (13.05)	553 (543)
$[Pt(C_{21}H_{24}N_4)]Cl_2$	Green	225-227	32.32 (32.60)	8.84 (9.36)	11.27 (11.85)	574 (598)

[a]Found (Calcd.)

Analytical Methods and Physical Measurements

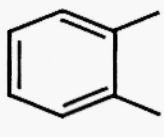
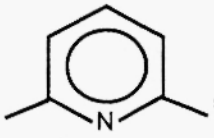
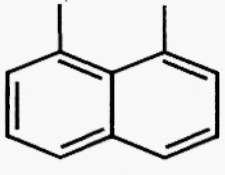
Conductivity measurements in dry DMF were performed with a Systronics Conductivity Bridge type 305 and molecular weights were determined by the Rast camphor method. IR spectra were recorded on Perkin-Elmer 577 Grating Spectrophotometer. ^1H NMR spectra were recorded on a Jeol FX-90Q Spectrometer in methanol and DMSO-d_6 using TMS as the internal standard. Electronic spectra were recorded on a Hitachi U-2000 Spectrophotometer. ^{13}C NMR spectra were recorded in methanol, using TMS as the standard. Mass spectral study was performed at CDRI, Lucknow. Nitrogen and chlorine were estimated by Kjeldahl's and Volhard's method[6], respective,ly. The analytical and physical data of the isolated ligands and their complexes are summarised in Table 1.

Results and Discussion

The reactions involved in the preparation of these derivatives may be depicted as shown below :

$$C_{10}H_{16}N_2O_2 + PtCl_2 + H_2N\text{–}R\text{–}NH_2 \longrightarrow [Pt(C_5H_8N_2)_2(R)]Cl_2 + 2H_2O$$

$$C_{11}H_{18}N_2O_2 + PtCl_2 + H_2N\text{–}R\text{–}NH_2 \longrightarrow [Pt(C_{11}H_{18}N_4)(R)]Cl_2 + 2H_2O$$

R =  ,  , $-(CH_2)_2-NH-(CH_2)_2-$ and 

These reactions are quite facile and the resulting complexes are coloured solids, sparingly soluble in methanol and ethanol and readily soluble in DMF and DMSO. Molecular weight determinations revealed the monomeric nature of the resulting complexes. The molar conductance values of 10^{-3}M solutions (210-240 Ω^{-1} cm^2 mol^{-1}) of the complexes in dry DMF, show them to be strong electrolytes. A square planar

environment around platinum has been proposed which get strengthened from the spectral studies discussed below.

IR Spectral Studies

A comparative study of the IR spectra of the ligands and their complexes show that the bands due to $-NH_2$ and >C=O at 3150 cm^{-1} and 1685 cm^{-1} disappear in all the complexes due to the elimination of two water molecules, resulting in the formation of >C=N bond. The band due to ν(>C=N) at 1620-1630 cm^{-1} registers a substantial decrease in the metal complexes as a result of chelation[7]. The bands characteristics of the methyl moiety appeared in all the complexes at 3035 cm^{-1} (ν_{asy} CH_3) and 2825 cm^{-1} (ν_{sy} CH_3). All the complexes and ligands show two distinct sharp bands occurring at *ca* 2810 and 1425 cm^{-1} assigned to C-H stretching and bending vibrations[8], respectively.

^{1}H NMR Spectral Studies

A broad signal exhibited by the diamines due to NH_2 protons at δ 4.25-5.12 ppm disappears in the unsymmetrical complexes suggesting the coordination of nitrogen to the metal atoms. A singlet appeared at δ 3.09-3.60 ppm in the complexes as well as ligands assigned to methylene protons adjacent to nitrogen. The shift of the signals towards lower field suggesting the coordination of the ligand. A sharp singlet also observed at δ 2.21-2.32 ppm due to the middle methylene protons. The complexes show multiplets in the region δ 7.18-8.64 ppm attributable to aromatic protons[9]. The ^{1}H NMR spectra of the ligands and their complexes have been recorded in Table 2.

Table 2 - ^{1}H NMR Spectral data (δ, ppm) of ligands and their Pt (II) complexes

Compound	-N-CH_2 (bs)	-CH_2-	- R -		-CH_3(s)
$C_{10}H_{16}N_2O_2$	3.09	-	-	-	1.29
$[Pt(C_8H_{10}N_2)_2]Cl_2$	3.41	-	8.46 ($H_{2,5}$s)	7.25($H_{3,4}$d)	1.76
$[Pt(C_{15}H_{19}N_5)]Cl_2$	3.22	-	8.11 ($H_{2,4}$d)	7.18 (H_3d)	1.23
$[Pt(C_{14}H_{25}N_5)]Cl_2$	3.52	-	-	-	1.31
$[Pt(C_{10}H_{11}N_2)_2]Cl_2$	3.40	-	8.28 ($H_{2,7}$bs)	7.67 ($H_{3,6}$d) 7.32 ($H_{4,5}$d)	1.82
$C_{11}H_{18}N_2O_2$	3.41	2.21	-	-	1.36
$[Pt(C_{17}H_{22}N_4)]Cl_2$	3.60	2.26	8.23 ($H_{2,5}$d)	7.41 ($H_{3,4}$d)	1.42
$[Pt(C_{16}H_{21}N_5)]Cl_2$	3.47	2.29	8.16 ($H_{2,5}$s)	7.36 (H_3d)	1.69
$[Pt(C_{15}H_{27}N_5)]Cl_2$	3.52	2.22	-	-	1.70
$[Pt(C_{21}H_{24}N_4)]Cl_2$	3.57	2.32	8.64 ($H_{2,7}$bs)	7.92 ($H_{3,6}$d) 7.52 ($H_{4,5}$d)	1.51

Electronic Spectral Studies

The electronic spectra of the ligands, consist of a band around 380 nm due to n-π* transitions of the >C=N chromophore which shifted to *ca* 10 nm in the complexes. This shifting suggests the formation of azomethine grouping on complexation and subsequent isomerization of the carbonyl group into azomethine. The band around 278nm and 305nm in the complexes are assigned to π-π* transitions within the benzenoid ring[10].

^{13}C NMR Spectral Studies

The conclusions drawn from the IR and ^{1}H NMR spectra are parallel with the carbon-13 spectral data regarding the authenticity of the proposed structures. The shift of the carbons attached to the nitrogen further support to proposed coordination in the complexes (Table 3).

X-Ray Diffraction

The X-ray diffraction studies of a representative complex, $[Pt(C_{14}H_{25}N_5)]Cl_2$ have been carried out to determine its molecular symmetry. The observed interplanar spacing values, d (A°) and the miller indices h, k and l are given in Table 4. The data suggest a "Orthorhombic" lattice to this derivative having unit cell dimensions a = 20.240, b = 34.450, c = 6.560 and $\alpha = \beta = \gamma = 90^\circ$.

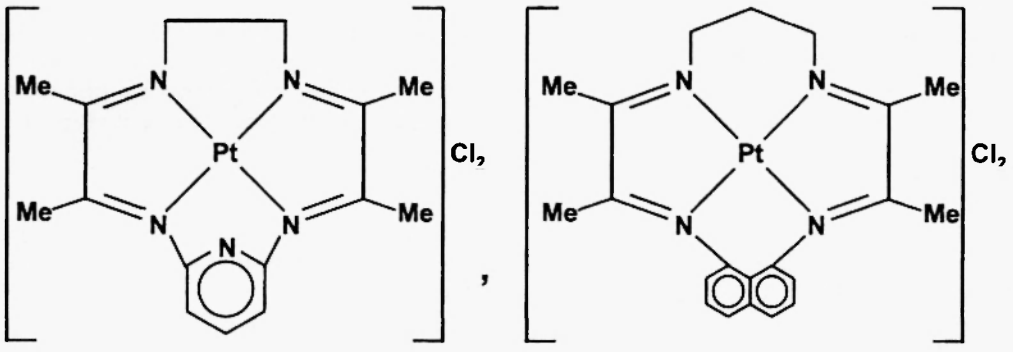
Table 3 - ^{13}C NMR Data (δ, ppm) of ligands and their complexes

Compound	>C=O	>N-CH_2	>C=N	-CH_3	-R	-CH_2-
$C_{10}H_{16}N_2O_2$	169.34	41.71	165.31	12.22	-	-
$[Pt(C_8H_{10}N_2)_2]Cl_2$	-	45.53	158.32	16.62	$C_{1,6}$128.87; $C_{2,5}$126.43; $C_{3,4}$125.92	-
$[Pt(C_{15}H_{19}N_5)]Cl_2$	-	43.99	162.63	13.27	$C_{1,5}$136.82; $C_{2,5}$127.19; $C_3$120.21	-
$[Pt(C_{14}H_{25}N_5)]Cl_2$	-	39.61	154.28	19.01	-	-
$[Pt(C_{10}H_{11}N_2)_2]Cl_2$	-	49.50	163.43	12.63	$C_{2,7}$129.72; $C_{3,6}$126.81; $C_{4,5}$124.51	-
$C_{11}H_{18}N_2O_2$	163.92	42.39	160.12	11.47	-	34.27
$[Pt(C_{17}H_{22}N_4)]Cl_2$	-	40.61	164.39	19.81	$C_{1,6}$132.19; $C_{2,5}$129.44; $C_{3,4}$123.42	-
$[Pt(C_{16}H_{21}N_5)]Cl_2$	-	43.38	157.89	11.51	$C_{1,5}$128.12; $C_{2,4}$122.51; $C_3$121.59	29.81
$[Pt(C_{15}H_{27}N_5)]Cl_2$	-	51.90	169.51	11.94	-	28.61
$[Pt(C_{21}H_{24}N_4)]Cl_2$	-	49.28	159.32	11.95	$C_{2,7}$128.21; $C_{3,6}$125.31; $C_{4,5}$121.82	36.52

Table 4 - X-ray powder diffraction data of $[Pt(C_{14}H_{25}N_5)]Cl_2$

Peak No.	2θ(deg.) (obs.)	h	k	l	d-spacing (obs).
1.	11.50	2	1	0	9.669
2.	15.80	0	5	0	7.048
3.	19.80	2	5	0	5.634
4.	21.92	4	0	0	5.095
5.	25.80	3	3	1	4.339
6.	26.28	1	6	1	4.261
7.	27.20	3	4	1	3.695
8.	30.40	2	7	1	3.371
9.	33.40	3	9	1	2.968
10.	38.10	3	9	1	2.968
11.	43.40	5	10	0	2.626
12.	58.90	4	3	3	1.970

Thus on the basis of above evidences, the following structures can be assigned to these metal complexes.



Biological Studies

Antibacterial and antifungal activities data of the ligands and their respective complexes against pathogenic bacteria and fungi are given in Tables 5 and 6. A culture of the test organisms was grown on PDA media (starch, glucose, agar-agar and water) for fungi and agar media (Peptone, beef extract, agar-agar, NaCl and water) for bacteria for several days at the optimum temperature for growth. All the glasswares

used were sterilized in an autoclave before use. The radial growth method and paper disc-plate method were employed to evaluate the fungicidal (at 25±1°C) and bactericidal (at 30±1°C) activities, respectively.

Table 5 - Fungicidal screening data of ligands and their Pt(II) complexes

Compounds	(%) Inhibition after 96 h (conc. in ppm)					
	F. oxysporum			*M. Phaseolina*		
	50	100	200	50	100	200
$C_{10}H_{16}N_2O_2$	30	42	50	28	37	42
$[Pt(C_8H_{10}N_2)_2]Cl_2$	43	52	60	40	47	58
$[Pt(C_{15}H_{19}N_5)]Cl_2$	54	65	72	51	62	68
$C_{11}H_{18}N_2O_2$	35	49	58	33	46	49
$[Pt(C_{17}H_{22}N_4)]Cl_2$	49	66	78	44	55	62
$[Pt(C_{16}H_{21}N_5)]Cl_2$	68	71	80	50	68	73
$[Pt(C_{15}H_{27}N_5)]Cl_2$	37	48	69	38	48	57
$[Pt(C_{21}H_{24}N_4)]Cl_2$	73	77	85	58	69	83

Table 6 - Antibacterial screening data of ligands and their Pt (II) complexes

Compounds	Diameter of inhibition zone after 24 hours at 28± 2°C (mm) (conc. in ppm)			
	E- coli (-)		*S. aureus (+)*	
	500	100	500	1000
$C_{10}H_{16}N_2O_2$	3	4	3	6
$[Pt(C_8H_{10}N_2)_2]Cl_2$	7	8	8	9
$[Pt(C_{15}H_{19}N_5)]Cl_2$	9	10	12	13
$C_{11}H_{18}N_2O_2$	4	5	5	6
$[Pt(C_{17}H_{22}N_4)]Cl_2$	7	9	10	11
$[Pt(C_{16}H_{21}N_5)]Cl_2$	11	12	11	14
$[Pt(C_{15}H_{27}N_5)]Cl_2$	5	7	6	8
$[Pt(C_{21}H_{24}N_4)]Cl_2$	12	13	13	14

The results recorded in Tables, pointed out that these compounds are microbially active. The antifungal activity and antibacterial activity of these compounds may well be explained in the light of modern electronic theory as resonating rings also exert effects on fungitoxicity. Resonating structures[11], such as benzene ring, pyridine ring and other conjugated systems may serve as power houses to activate potentially reactive grouping.

Acknowledgement

The authors are thankful to CSIR, New Delhi for financial assistance. One of the authors Dr. Mukta Jain is extremely grateful for all types of help, cooperation and blessings by Kanti Kumar R. Podar and Shri Moti Chand Maloo and Shri Shailendra Sharma for their constant encouragement and moral support during this work.

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Received on March 9, 2004.