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Coordination Behavior and Biopotency of N and S/O Donor Ligands with their Palladium(II) and Platinum(II) Complexes

R.V. Singh*, N. Fahmi and M.K. Biyala
Department of Chemistry, University of Rajasthan, Jaipur-302004, India

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Some metal complexes of Schiff bases have been prepared by the interactions of palladium(II) and platinum(II) chloride with 5-chloro-1,3-dihydro-3-[2-(phenyl)-ethylidene]-2H-indol-2-one-hydrazinecarbothioamide(L^1H) and 5-chloro-1,3-dihydro-3-[2-(phenyl)-ethylidene]-2H-indol-2-one-hydrazinecarboxamide(L^2H), in bimolar ratios. All the new compounds have been characterized by elemental analyses, conductance measurements, molecular weight determinations, IR and ^1H NMR spectral studies. The spectral data are consistent with a square planar geometry around Pd(II) and Pt(II) in which the ligands act as neutral bidentate and monobasic bidentate ligands, coordinating through the nitrogen and sulfur/oxygen atoms. Free ligands and their metal complexes were screened for their antimicrobial activity on different species of pathogenic fungi and bacteria and their biopotency has been discussed.

Keywords: Schiff bases, Palladium(II) and Platinum(II) chlorides, Fungicidal and bactericidal activities

INTRODUCTION

The discovery of the anticancer activity of *cis*-dichlorodiammine platinum(II) (cisplatin) and subsequently its use as a drug in the treatment of several human tumors [1,2], stimulated many research groups to synthesize new platinum group metal complexes and test them for their anti-tumor activity. Several researchers are trying to synthesize less toxic analogous of cisplatin with molecules found in the biological systems [3-4]. Although much attention has been directed to study the metal complexes of the Schiff base ligands derived from isatin [5-6], no investigations have appeared in the literature to describe the metal complexes of the Schiff bases derived from isatin with acetophenone. Several binary and ternary complexes of Pd(II) and Pt(II) were reported with nucleic acid constituents, amino acids and other nitrogen containing ligands [7-9]. Metal complexes of semicarbazones and thiosemicarbazones have aroused considerable interest in view of their industrial and biological importance. Many of these compounds possess a wide spectrum of medicinal properties, including activity against tuberculosis, leprosy, and bacterial and viral infections. They have also been found to be active against influenza, protozoa, smallpox, psoriasis, rheumatism, trypanosomiasis, coccidiosis, malaria and certain kinds of tumors and have been suggested as possible pesticides and fungicides. Their activity has frequently been thought to be due to their ability to chelate trace metals [10].

In view of the versatile importance of isatins [11-12] and in continuation of our previous work dealing with the metal complexes of thiosemicarbazones and semicarbazones, we herein describe the synthesis and identification of the Pd(II) and Pt(II) complexes of the Schiff bases 5-chloro-1,3-dihydro-3-[2-(phenyl)-ethylidene]- 2H-indol-2-one-hydrazinecarbothioamide(L^1H) and 5-chloro-1,3-dihydro-3-[2-

* Corresponding author. E-mail: kudiwal@datainfosys.net

(phenyl)-ethylidene]-2H-indol-2-one- hydrazinecarboxamide (L^2H), prepared by condensation of isatin derivatives with acetophenone.

EXPERIMENTAL

The palladium and platinum compounds, $PdCl_2$ and $PtCl_2$, isatin, and acetophenone were purchased from Lancaster and Lobachemie and used as such. 5-Chloroisatin was prepared in the laboratory. All the solvents were dried and distilled before use.

Preparation of the Ligands

The ligands (L^1H) and (L^2H) were prepared by the condensation of 5-chloroisatin and acetophenone in equimolar (1:1) ratio and the resulting mixture was condensed with hydrazinecarbothioamide and hydrazincarboxamide in presence of sodium acetate in 1:1 molar ratio, in absolute alcohol. The reaction mixture was then refluxed over a water bath for 3-4 h and allowed to stand over night. The products were recrystallized from the solvent ethanol and dried *in vacuum*. Their physico-chemical properties and analytical data are given in Table 1.

Preparation of $[Pd(LH)_2]Cl_2$ Complexes

These complexes were prepared by dissolving $PdCl_2$ (0.001 mol, 0.177 g) in ethanol and then adding an ethanolic solution of the ligand (0.002 mol) to this solution in 1:2 molar ratio. The reaction mixture was heated under reflux for about one hour in the presence of few drops of concentrated HCl. On cooling, the complexes separated out, which were filtered and washed several times with alcohol and dried *in vacuum*.

Preparation of $[Pd(L)_2]$ Complexes

The ethanolic solution of $PdCl_2$ (0.001 mol, 0.177 g) was mixed with an ethanolic solution of ligand (0.002 mol) in 1:2 molar ratios. Aqueous NH_4OH was added drop wise to the reaction mixture until it was weakly alkaline (pH *ca*. 8.0). The mixture was then stirred on a magnetic stirrer for 2-3 h and the resulting product was recovered by filtration, washed with ethanol and dried *in vacuo*.

Preparation of $[Pt(LH)_2]Cl_2$ Complexes

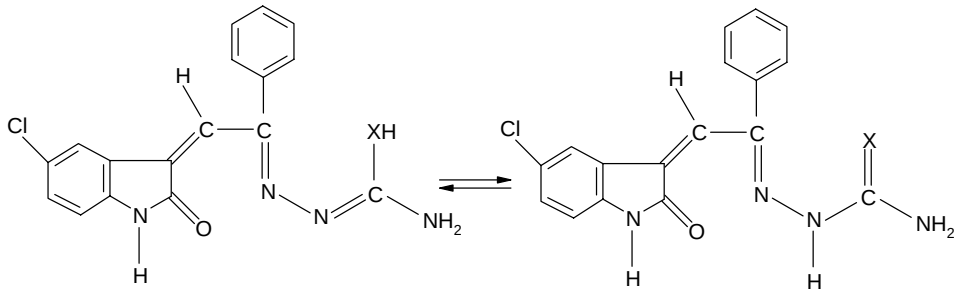
These complexes were prepared by dissolving $PtCl_2$ (0.001 mol, 0.265 g) in a 1:1 mixture of water and ethanol and then adding an ethanolic solution of the ligand (0.002 mol) to this solution in 1:2 molar ratios. The reaction mixture was heated under reflux for about one hour in the presence of few drops of concentrated HCl. On cooling, the complexes separated out which were filtered and washed several times with a mixture of water and ethanol and dried *in vacuo*.

Preparation of $[Pt(L)_2]$ Complexes

The 1:1 water-ethanol solution of $PtCl_2$ (0.001 mol, 0.265 g) was mixed with an ethanolic solution of ligand (0.002 mol) in 1:2 molar ratios. Aqueous NH_4OH was added drop wise to the reaction mixture until it was weakly alkaline (pH *ca*. 8.0). The mixture was then boiled under reflux for 2-3 h and the resulting product was recovered by filtration, washed with ethanol and dried *in vacuo*.

Analytical Methods and Physical Measurements

Conductivity measurements were made with a Systronics Model 305 Conductivity Bridge. Molecular weights were determined by the Rast Camphor method. IR spectra of the



ligands and their complexes were recorded with the help of Nicolet-Megna FT-IR 550 spectrophotometer in 1" KBr pellets. The electronic spectra were recorded on a Varian-Cary/2390 spectrophotometer at RSIC, I.I.T., Chennai. ^{1}H NMR spectra were recorded on a Hitachi Perkin Elmer spectrometer in DMSO-d_6 at 300 MHz using TMS as the internal standard at Delhi University, New Delhi. Pd and Pt were estimated gravimetrically. Nitrogen was determined by the Kjeldahl's method and sulfur was estimated by the Messenger's method.

The antifungal activity was evaluated against *Macrophomina phaseolina* and *Fusarium oxysporum* using standard food poisoning technique and a procedure recommended for testing new chemicals [13]. The linear growth of the fungus was recorded by measuring the diameter of the fungus colony after 96 h and the percentage inhibition was calculated as 100 (C-T)/C, where C and T are the diameters of the fungus colony in the control and test plates,respectively.

Antibacterial activity was done by the paper-disc plate method. The nutrient agar medium (peptone, beef extract, NaCl and agar-agar) and 5-mm diameter paper discs (Whatman No. 1) were used. The compounds were dissolved in DMSO in 500 and 1000 ppm concentrations. The filter-paper discs were soaked in different solutions of the compounds, dried and then placed in the petri dishes previously seeded with the test organisms (*Escherichia coli, Klebseila aerogenous and Xanthomonas compestris*). The plates were incubated for 24-30 h at 28 ± 2 °C and the inhibition zone around each disc was measured.

RESULTS AND DISCUSSION

The reactions of 5-chloro-1,3-dihydro-3-[2-(phenyl) ethylidene]-2H-indol-2-one-hydrazine carbothioamide (L^1H) and 5-chloro-1,3-dihydro-3-[2-(phenyl)ethylidene]-2H-indol-2-one-hydrazinecarboxamide (L^2H) with $PdCl_2$ and $PtCl_2$ have been carried out in 1:2 molar ratios in ethanol and in 1:1 water

Table 1. Physical Properties and Analytical Data of L^1H and L^2H and their Complexes

Compound	Colour	M.P. (ºC)	Elemental Analysis (%)			
			M Found (Calcd.)	N Found (Calcd.)	S Found (Calcd.)	Mol. Wt. Found (Calcd.)
L^1H	Light Brown	222	-	15.98 (15.70)	8.72 (8.98)	359 (356.82)
L^2H	Dirty Yellow	239	-	16.03 (16.44)	-	338 (340.76)
$[Pd(L^1H)_2]Cl_2$	Reddish Brown	257	11.70 (11.94)	12.73 (12.57)	7.39 (7.19)	894 (890.98)
$[Pd(L^1)_2]$	Dark Brown	253	12.86 (13.00)	13.92 (13.69)	8.12 (7.83)	822 (818.06)
$[Pd(L^2H)_2]Cl_2$	Grey	278	12.57 (12.39)	13.32 (13.04)	-	859 (858.85)
$[Pd(L^2)_2]$	Brown	274	13.49 (13.54)	13.96 (14.25)	-	783 (785.93)
$[Pt(L^1H)_2]Cl_2$	Reddish Brown	255	19.72 (19.91)	11.29 (11.43)	6.28 (6.54)	977 (979.64)
$[Pt(L^1)_2]$	Dark Brown	249	21.62 (21.51)	11.68 (12.35)	7.24 (7.07)	909 (906.72)
$[Pt(L^2H)_2]Cl_2$	Reddish Brown	280	20.41 (20.58)	11.73 (11.82)	-	943 (947.51)
$[Pt(L^2)_2]$	Grey	276	21.98 (22.30)	12.63 (12.81)	-	873 (874.59)

ethanol solution, respectively. The metal chloride interacts to with the ligands in presence of few drops of concentrated HCl to form complexes of the type $[M(LH)_2]Cl_2$. However, complexes of the $[M(L)_2]$ type were obtained when the reaction was carried out in the presence of aqueous ammonium hydroxide.

$$MCl_2 + 2LH \longrightarrow [M(LH)_2]Cl_2$$

$$MCl_2 + 2LH + 2NH_4OH \longrightarrow [M(L)_2] + 2NH_4Cl + 2H_2O$$

(Where, **M** = Pd(II) and Pt(II) and **LH** is the ligand molecule)

These reactions proceed easily and all the complexes are soluble in DMF, DMSO and chloroform. The complexes are monomers as revealed by their molecular weight determinations. The molar conductance values of 10^{-3} M solutions of $[M(L)_2]$ type of complexes lie in the range 10-15 ohm^{-1} cm^2 mol^{-1} in dry DMF indicating their non-electrolytic behavior. However, the $[M(LH)_2]Cl_2$ complexes are 1:2 electrolytes, with conductance values of 200-220 ohm^{-1} cm^2 mol^{-1}. The analytical data of the ligands and their complexes are given in Table 1.

Spectral Studies

UV-Vis spectra. The electronic spectra of the ligands and their metal complexes were recorded in distilled DMSO. The electronic spectra of these complexes show three d-d spin allowed transitions. These are corresponding to the transitions from the three lower lying 'd' levels to the empty $d_{x^2-y^2}$ orbital. The ground state is $^1A_{1g}$ and exited states corresponding to the above transitions are $^1A_{2g}$, $^1B_{1g}$ and ^1E_g in order of increasing energy. Three d-d bands are observed in the region 472-521 nm, 405-448 nm and 347-394 nm. These bands are attributed to $^1A_{1g} \rightarrow {}^1A_{2g}$, $^1A_{1g} \rightarrow {}^1B_{1g}$ and to $^1A_{1g} \rightarrow {}^1E_g$ transitions, respectively. The electronic spectra of these complexes indicate the square planar geometry and the values obtained correspond to those reported earlier for the square planar complexes [15-16] (Table 2).

IR spectra. The IR spectra of the free ligands display two sharp bands at *ca* 3442 and 3325 cm^{-1}, assignable to asymmetric and symmetric NH_2 group modes, respectively, which remain at almost the same positions in the metal complexes, suggesting that the amino group is not involved in chelation. In the IR spectra of the free ligands, a band at *ca* 3286 cm^{-1} assigned to NH vibrations of the functional group which disappear in the corresponding $[M(L)_2]$ type of complexes, indicating possible deprotonation of the functional group upon complexation.

Table 2. Electronic (UV-Vis) Spectral Data of the Palladium(II) and Platinum(II) Complexes

Complexes	nm	Assignment
$[Pd(L^2H)_2]Cl_2$	472	$^1A_{1g} \rightarrow {}^1A_{2g}$ (υ_1)
	444	$^1A_{1g} \rightarrow {}^1B_{1g}$ (υ_2)
	394	$^1A_{1g} \rightarrow {}^1E_{1g}$ (υ_3)
$[Pd(L^2)_2]$	478	$^1A_{1g} \rightarrow {}^1A_{2g}$ (υ_1)
	448	$^1A_{1g} \rightarrow {}^1B_{1g}$ (υ_2)
	391	$^1A_{1g} \rightarrow {}^1E_{1g}$ (υ_3)
$[Pt(L^1H)_2]Cl_2$	521	$^1A_{1g} \rightarrow {}^1A_{2g}$ (υ_1)
	405	$^1A_{1g} \rightarrow {}^1B_{1g}$ (υ_2)
	350	$^1A_{1g} \rightarrow {}^1E_{1g}$ (υ_3)
$[Pt(L^1)_2]$	518	$^1A_{1g} \rightarrow {}^1A_{2g}$ (υ_1)
	408	$^1A_{1g} \rightarrow {}^1B_{1g}$ (υ_2)
	347	$^1A_{1g} \rightarrow {}^1E_{1g}$ (υ_3)

The bands at 1610 cm^{-1} and 1606 cm^{-1} in L^1H and L^2H respectively, due to υ (C=N), are shifted to higher wave numbers (υ 10-20 cm^{-1}) in the metal complexes, suggesting coordination through the azomethine nitrogen. The bands at 1678 cm^{-1} and 1020 cm^{-1} due to υ (C=O) and υ (C=S), respectively, are shifted towards lower frequencies in the complexes, indicating coordination of oxygen or sulfur to the central metal atoms and formation of M-O or M-S type of bonding. In addition, new weak to strong intensity bands are observed in the far IR spectra of the complexes. Bands at *ca* 360-365, 440-448, 305-315 and 410-422 cm^{-1} can be assigned to υ (Pd-N), υ (Pt-N), υ (M-S) and υ (M-O), respectively. The appearance of these bands further supports bonding of the ligands to the metal through nitrogen, sulfur and oxygen. However, no υ (M-Cl) band is observed in the spectra of the $[M(LH)_2]Cl_2$ complexes, suggesting that the chloride is ionic (Table 3).

^{1}H NMR spectra. The ^{1}H NMR spectra of the free ligands and the metal complexes were recorded in DMSO-d_6. The free

Table 3. ^{1}H NMR and IR Spectral Data of the Ligands and their Complexes

Compound	^{1}H NMR (δ ppm)				IR (cm^{-1})			
	-NH_2	-NH (1)	-NH (2)	Aromatic Protons	υ (C=N)	υ (M-S)	υ (M-O)	υ (M-N)
L^1H	3.42	11.26	11.94	6.81-8.26	1610	-	-	-
L^2H	3.40	11.30	11.96	6.78-8.24	1606	-	-	-
$[Pd(L^1H)_2]Cl_2$	3.44	11.40	11.92	6.76-8.26	1626	307	-	360
$[Pd(L^1)_2]$	3.42	-	11.94	6.77-8.24	1624	305	-	362
$[Pd(L^2H)_2]Cl_2$	3.40	11.55	11.92	6.74-8.28	1620	-	410	361
$[Pd(L^2)_2]$	3.42	-	11.96	6.76-8.20	1625	-	418	364
$[Pt(L^1H)_2]Cl_2$	3.46	11.48	11.93	6.72-8.18	1628	312	-	444
$[Pt(L^1)_2]$	3.44	-	11.94	6.70-8.20	1624	308	-	443
$[Pt(L^2H)_2]Cl_2$	3.42	11.50	11.92	6.74-8.22	1626	-	416	448
$[Pt(L^2)_2]$	3.40	-	1196	6.76-8.24	1630	-	418	442

Table 4. Fungicidal Screening Data of the Ligands and their Metal Complexes

Compound	Percent Inhibition after 96 h (conc. in ppm)					
	Fusarium oxysporum			*Macrophomina phaseolina*		
	50	100	200	50	100	200
L^1H	43	52	58	42	53	57
L^2H	38	46	52	37	44	54
$[Pd(L^1H)_2]Cl_2$	48	56	64	47	57	63
$[Pd(L^1)_2]$	47	55	65	45	56	61
$[Pd(L^2H)_2]Cl_2$	42	49	56	41	48	56
$[Pd(L^2)_2]$	41	47	54	40	45	55
$[Pt(L^1H)_2]Cl_2$	46	52	60	44	53	59
$[Pt(L^1)_2]$	45	51	58	43	52	58
$[Pt(L^2H)_2]Cl_2$	41	46	53	41	45	53
$[Pt(L^2)_2]$	40	45	52	40	46	52
Bavistin	86	100	100	82	100	100

ligands and the complexes $[M(LH)_2]Cl_2$ exhibit a singlet at δ 11.26-11.30 ppm and δ 11.40-11.55 ppm, due to the -NH proton. The absence of this signal in the spectra of the complexes, $[M(L)_2]$, suggests that this proton has been lost *via* thioenolization and ketoenolization of > C=S and > C=O groups and coordination of the sulfur and oxygen atom to the metal atom, respectively. The complexes show multiplets in the region δ 6.70-8.18 ppm attributable to aromatic protons, which appear almost in the same position as in the respective ligands. The -NH_2 group gives singlet at δ 3.40-3.48 ppm in the free ligands as well as in the complexes. It shows that the -NH_2 group is not taking part in the complexation. The -NH of the ring gives singlet at δ 11.92-11.96 ppm in the free ligands as well as in the complexes. It also shows that the -NH group

of the ring is not taking part in the complexation (Table 3).

BIOCIDAL SCREENING

Antifungal Activity

The antifungal activity was evaluated against *Macrophomina phaseolina* and *Fusarium oxysporum* by the agar plate technique. Solutions of the compounds in different concentrations in DMF were then mixed with the medium. The linear growth of the fungus was recorded by measuring the diameter of colony after 96 h, and the percentage inhibition was calculated as 100 (C-T)/C, where C and T are the diameters of the fungus colony in the control and test plates, respectively (Table 4).

Antibacterial Activity

The antimicrobial screening data in Table 5 show that the compounds exhibit antimicrobial properties and it is important to note that the metal chelates exhibit more inhibitory effects than the parent ligands. The increased lipophilic character of these complexes seems to be responsible for their enhanced biological potency. It may be postulated that these compounds deactivate various cellular enzymes, which play a vital role in various metabolic pathways of these microorganisms. It has also been proposed that the ultimate action of the toxicant is the denaturation of one or more proteins of the cell, which, as a result, impairs normal cellular processes.

CONCLUSIONS

The present study revealed square planar geometry around Pd(II) and Pt(II) complexes, in which the ligands act as a neutral bidentate and monofunctional bidentate ligand, coordinating through nitrogen and sulfur/oxygen atoms.

The electronic spectra of Pd(II) and Pt(II) complexes show three d-d spin allowed transitions from the three lower lying 'd' levels to the empty $d_{x^2-y^2}$ orbital. The bands are attributed to $^1A_{1g} \rightarrow {}^1A_{2g}$, $^1A_{1g} \rightarrow {}^1B_{1g}$ and to $^1A_{1g} \rightarrow {}^1E_g$ transitions.

The results of antimicrobial activity show that the compounds exhibit antimicrobial properties and it is important to note that the metal chelates show more inhibitory effects than the parent ligands. The increased lipophilic character of these complexes seems to be responsible for their enhanced biological potency.

It has also been proposed that concentration plays a vital role in increasing the degree of inhibition; as the concentration increases, the activity increases.

It is interesting to note that the sulfur bonded ligands and their complexes are more active than the oxygen bonded ligands and their complexes.

Table 5. Antibacterial Screening Data of the Ligands and their Complexes

Compound	Diameter of Inhibition Zone (mm) (conc. in ppm)					
	E. coli		*K. aerogenous*		*X. campestris*	
	500	1000	500	1000	500	1000
L^1H	8	10	7	10	8	10
L^2H	6	8	5	9	6	9
$[Pd(L^1H)_2]Cl_2$	12	14	12	13	11	14
$[Pd(L^1)_2]$	10	12	10	11	9	12
$[Pd(L^2H)_2]Cl_2$	9	11	8	11	9	11
$[Pd(L^2)_2]$	8	10	9	10	8	10
$[Pt(L^1H)_2]Cl_2$	11	13	11	12	11	13
$[Pt(L^1)_2]$	10	11	10	11	10	12
$[Pt(L^2H)_2]Cl_2$	8	10	9	10	9	11
$[Pt(L^2)_2]$	7	9	8	9	8	10
Streptomycin	17	18	16	18	15	18

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