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Synthesis, Characterization and Antibacterial Activity of Mixed Ligand Complexes of Pd(II) Ions with Oxalic Acid and Heterocyclic Amines

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Abstract

The present work has been designed for the characterization and antibacterial studies of mixed ligand complexes of Pd(II) ions with phthalic acid and heterocyclic amines. The general formula of the complexes is (MLL′) [where, M = Pd(II); L = Oxalic acid, C_2O_4, L′ = Quinoline, $C_9H_7N(1)$; *iso*-Quinoline, $C_9H_7N(2)$]. The complexes were prepared in the solid form and characterized by elemental analysis, conductivity & magnetic measurements and infrared & electronic spectroscopic studies. The infrared spectra of the complexes confirmed the coordination of metal ion with ligands. Their antibacterial activity has been evaluated by the disc diffusion method against seven pathogenic bacteria (three gram positive and four gram negative). The complexes were shown to exhibit mild to moderate antibacterial activity against the tested bacteria.

Key words: Pt(IV) complexes, oxalate, antibacterial activity.

Introduction

Mixed ligand complexes with metal ion bound to two different and biochemically important ligands have gained interest as model for metallo-enzymes (Bowen *et al*., 2009; Navarro *et al*., 2010, 2011). The physiologically interesting mixed ligand complexes of transition metals with heterocyclic amines play an important role in biological systems and have been a subject of great interest for researchers (Reza *et al*., 2003; Hossain *et al*., 2012). Platinum(II) complexes and its derivatives have been widely recognized as potent anticancer agents, effective against different types of cancer *in vitro* (Lin *et al*., 2011; Neves *et al*., 2010). After the discovery of its activity, thousands of platinum complexes have been synthesized and tested so far. In a recent study, new Pt based agents have been reported to have distinct features from marketed platinum drugs in several critical aspects (Gao *et al*., 2009). Cisplatin has become a standard drug for the treatment of patients with non-small cell lung cancer. However, it is one of the most frequently used chemotherapeutic drugs (Lottner *et al*., 2002; Brow *et al*., 2002; Liao *et al*., 2008). Palladium(II) complexes on the other hand, have been reported to possess antitumor activity at least comparable to cisplatin (Gao *et al*., 2010). The metal complexes of malonic and succinic acid and their activities have been reported (Reza *et al*., 2003; Islam *et al*., 2003). All of these experimental works and evidences prompted us in the formation of dibasic acid complexes with metal atoms. Keeping these facts in view, the present work describes some mixed ligand complexes of palladium (II) with oxalic acid (OXH_2) as primary agents and heterocyclic bases, *viz*., quinoline (Q), *iso*-quinoline(IQ) as secondary ligands have been prepared and their antibacterial studies have been performed, which may help in the primary selection of these complexes as therapeutic agents.

Materials and Methods

Chemicals and reagents: All the chemicals were of reagent grade and unless otherwise specified, were used as received. The solvents were purified using conventional methods.

Physical measurements: Infrared spectra were recorded on FTIR spectrophotometer (IR-Prestrige-21) in the region 4500-400 cm-1 at the Department of Chemistry, University of Dhaka, Bangladesh. Carbon, hydrogen and nitrogen analyses were carried out by LECO CHEN-932, Organic Elemental Analyzer, University Kebangsaan Malaysia. Metal was determined by weighing as the oxide produced by direct ignition. The molar conductance of

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10^{-3} M solutions of the metal complexes in DMF was measured at 30°C using a Jenway 4310 Conductivity meter having a dip-cell with platinized electrode. Melting points were determined using an electrothermal digital melting point apparatus. Magnetic susceptibility was measured with Magnetic Susceptibility Balance (Model: Mk1, Sherwood Scientific, Cambridge, England) at the Department of Chemistry, University of Dhaka, Bangladesh at 298 °K. All susceptibilities were corrected for diamagnetic contribution using Pascal's constant (Vogel, 1961).

General methods for complexes preparation: A 25 ml of ethanolic solution of the metal salt ($PdCl_2$) (1 mmole) and oxalic acid (1 mmol) were mixed in the calculated ratio with constant stirring at 70°C. No precipitate was observed. Then 25 ml of an ethanolic solution of heterocyclic amine bases, e.g. 2 mmol of Q (for complex 1), IQ (for complex 2) were added with constant stirring. The volume of the solution was reduced to 50% and allowed to cool. The precipitate formed was filtered, washed several times with ethanol and then dried a in desiccator over anhydrous $CaCl_2$.

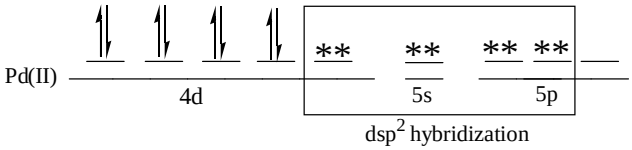
Antimicrobial screening: Seven pathogenic bacteria viz *Psudomonas aeruginosa* (Gram negative), *Salmonella bovismorbificans* (Gram negative), *Salmonella typhi* (Gram negative), *Escherichia coli* (Gram negative), *Listeria monocytogenes* (Gram positive), *Staphylococcus aureus* (Gram positive), and *Enterococcus faecalis* (Gram positive) were collected from the Fish Inspection & Quality Control Section, Department of Fishery, Boyra, Khulna. Nutrient agar was used as the bacteriological media. The complexes were dissolved separately in acetonitrile to get a concentration of 50-μg $disc^{-1}$. Then *in vitro* anti-bacterial activity of these complexes was assessed by the disc diffusion method (Rios *et al*., 1988; Bauer *et al.*, 1966). The diameter of the zone of inhibition produced by the complexes was compared with that of Kanamycin (30 μg $disc^{-1}$).

Results and Discussion

Elemental analysis and conductivity measurement: The analytical data and their physical properties of the complexes are summarized in Table 1. The analytical data are in good agreement with the proposed empirical formula of the present complexes.

The molar conductance were measured in *N,N′*-dimethyl formamide. The conductance values of the Pt(IV) complexes were in the range (10.75 – 12.40) Ω^{-1} cm^2 $mole^{-1}$, which indicated that these complexes were non-electrolyte in nature (Sukalpa *et al*., 2003; Islam *et al*., 1991).

Magnetic moment: The observed magnetic moment of the complexes at room temperature is given in Table 1. The magnetic moment values of the complexes indicated that these complexes are diamagnetic. This diamagnetism was supported by the small negative values obtained for their magnetic susceptibility. It appears from the magnetic moment data that the complexes of Pd(II) ion display diamagnetic property and an square planar geometry with dsp^2 hybridization which are consistent with the published structure (Sukalpa *et al*., 2003; Islam *et al.*, 1991).



Infrared spectral studies: In the infrared spectra strong bands between ~ 1692.56 and ~ 1441.81 cm^{-1} revealed the presence of carboxylic group in oxalic acid due to $\nu_{C=O}$ and $\nu_{C-O,}$ which were shifted to 1610.0 ~ 1610.5 cm^{-1} and 1379.1 ~ 1379.1 cm^{-1} in the spectra of all the complexes. This indicates the coordination of oxalic acid through the carboxylic acid group.

The characteristic ring vibration of the heterocyclic amines in the range 1400-1600 cm^{-1} generally show significant changes on complexation but in our present complexes these bands could not be distinguished because of overlapping with $\nu_{C=O}$ and ν_{C-O} stretching bands. The in-plane and out of plane ring deformation modes of the heterocyclic amines observed at ~ 520 and ~ 720 cm^{-1}, respectively underwent a positive shift in mixed ligand complexes conforming thereby a co-ordination through nitrogen and presence of M-O bonding is evident from the appearance of ν_{M-O} modes at 500.5 – 510.0 cm^{-1} in the spectra of the complexes. The presence of M-N bonding in the complexes is evident for the appearance of ν_{M-N} modes at 450.0 – 460.0 cm^{-1} in the spectra of the complexes (Hossain *et al*., 2004; Islam *et al*., 2004; Hossain *et al*.,

2012a, b). Key I.R. spectral data for the complexes are given in Table 2.

Electronic spectra: The electronic spectra of the Pd(II) complex in DMSO showed three spin allowed d-d transitions and two charge transfer bands. The bands were obtained at 22,220-23,040, 28,155-28500, 31,050-31,115, 35,000-34,505 and 40,050-40,165 cm^{-1} corresponding to the transitions of $^1A_{1g} \rightarrow {}^1A_{2g}$, $^1A_{1g} \rightarrow {}^1B_{1g}$, $^1A_{1g} \rightarrow {}^1E_g$, $^1A_{1g} \rightarrow {}^1A_{2u}$ & $^1A_{1g} \rightarrow {}^1E_u$ respectively, which indicates square planar stereochemistry (Sukalpa *et al*., 2003; Islam *et al*., 1991). Electronic spectral data are presented in Table 3.

Antimicrobial activity: The Antibacterial activity of the ligand and its complexes have been studied against various microorganisms (both Gram-positive and Gram-negative bacteria) and the results have been compared with the standard drug, kanamycin and results have been presented in Table 4. Complex 1 showed the lowest inhibitory zones against *Psudomonas aeruginosa* corresponding to zone size of 11 mm. From the data it may be concluded that our synthesized complexes have shown mild to moderate antibacterial activity.

Table 1. Elemental analyses and physical properties of the complexes.

Com.No	Complexes (Colour)	Yields %	Metal %	Carbon %	Hydrogen %	Nitrogen %	Melting point (± 5°C)	A_M (ohm^{-1} cm^2 mol^{-1})	μ_{eff} (BM.)
1	$Pd(OX)(Q)_2$ (Yellow)	61	23.45 (23.51)	52.89 (53.05)	3.21 (3.12)	6.18 (6.19)	270	10.75	Dia
2	$Pd(OX)(IQ)_2$ (Apricot)	65	23.41 (23.51)	52.92 (53.05)	3.18 (3.12)	6.13 (6.19)	255	12.40	Dia

where, Dia = Diamagnetic, OX = Diprotonated oxalic acid, Q =quinoline, IQ= iso-quinoline.

Table 2. Infrared spectral data of the complexes (band maxima in cm^{-1}).

Com. No.	Complexes	ν(OH)	ν(N-H)	ν(C=O)	ν(C-O)	ν(M-O)	ν(M-N)
1	Pd(OX)(Q)	-	-	1610.5	1379.1	510.0	460.0
2	$Pd(OX)(IQ)_2$	-	-	1610.0	1379.1	500.5	455.0

* See table 1.

Table 3. Electronic spectral data (cm^{-1}) of palladium(II) complexes.

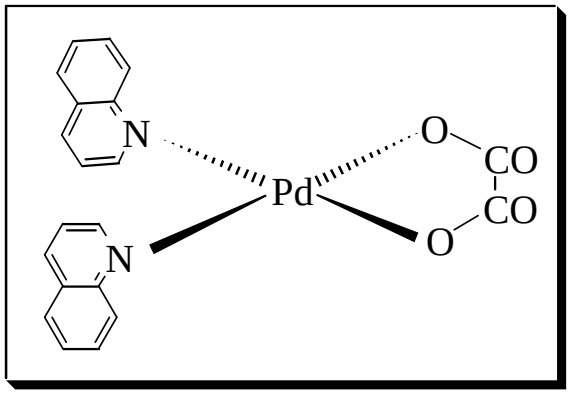
Com. No*	Spectral band (cm^{-1}) with assignment				
	$^1A_{1g} \rightarrow {}^1A_{2g}$	$^1A_{1g} \rightarrow {}^1B_{1g}$	$^1A_{1g} \rightarrow {}^1E_g$,	$^1A_{1g} \rightarrow {}^1A_{2u}$	$^1A_{1g} \rightarrow {}^1E_u$
1	22,220	28,500	31,115	35,000	40,165
2	23,040	28,155	31,050	34,505	40,050

* See table 1**.**

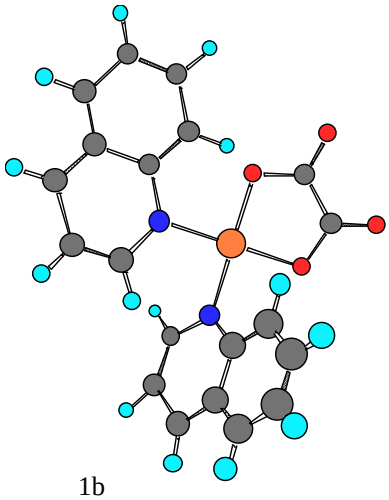
Table 4. Results of antibacterial activity of the complexes.

Test organism	Diameter of zone of inhibition complexes* (mm)		
	1	2	Kanamycin 30 µg/disc
Psudomonas aeruginosa (-ve)	11	23	22
Salmonella bovismorbificans (-ve)	18	16	22
S. typhi (-ve)	16	17	20
Escherichia coli (-ve)	23	19	20
Listeria monocytogenes (+ve)	31	26	25
Staphylococcus aureus (+ve)	23	22	23
Enterococcus faecalis (+ve)	15	21	21

*See table 1

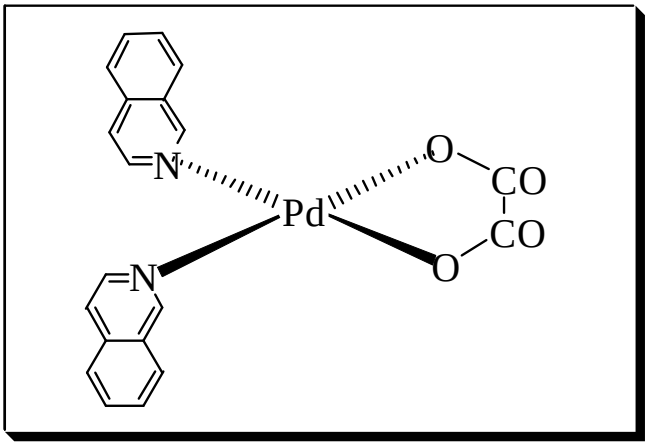


1a

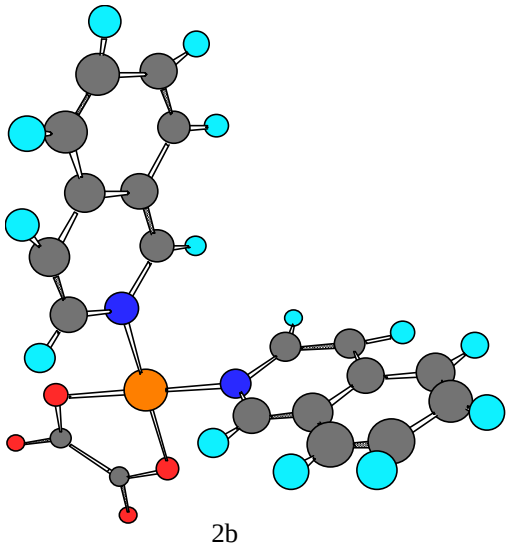


1b

Figure 1. (a) Probable structure of complex 1 [Pd(II)(OX)(Q)$_2$]. (b) Ball and stick model of complex 1 [Pd(II)(OX)(Q)$_2$].



2a



2b

Figure 2. (a) Probable structure of complex 2 [Pd(II)(OX)(IQ)$_2$]. (b) Ball and stick model of complex 2 [Pd(II)(OX)(IQ)$_2$].

Conclusion

From the above discussion, it is evident that the prepared Pd(II) complexes are square planar in structure and the probable structures of the complexes have been shown in figures 1-2. Antibacterial screening of our synthesized complexes have shown mild to moderate activity.

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