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PALLADIUM (II) AND PLATINUM (II) COMPLEXES OF 1-METHYL-2-IMIDAZOLECARBOXALDEHYDE THIOSEMICARBAZONE, SYNTHESIS CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY

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ABSTRACT

Schiff bases are the most widely used organic compounds. They have been shown to exhibit a broad range of biological activities, including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral and antipyretic properties. These compounds are very important in medicinal and pharmaceutical fields because of their wide spectrum of biological activities. Such an attempt made here to synthesis; 1-methyl-2-imidazolecarboxaldehyde thiosemicarbazone by reacting equimolar amounts of thiosemicarbazide and the corresponding imidazolecarbaldehyde. The resulting ligand and its transition metal complexes with Platinum(II) and Palladium(II) were characterized by different spectroscopic techniques (IR, UV-Vis, Ms, NMR and X-ray). The ligand and its metals complexes were exhibit a moderate antimicrobial activity against four bacteria; *Bacillus cereus*, *Staphylococcus aureus* (Gram-positive). *Escherichia coli* and *Salmonella typhimurium* (Gram-negative) and one Fungi; *Candida albicans.*

Key words: Thiosemicarbazone, Synthesis, X-ray crystal structure, IR, UV-Vis, NMR and antimicrobial activity.

INTRODUCTION

The synthesis and structural investigations of thiosemicarbazone and their metal Complexes are of considerable centre of attention because of their potentially beneficial pharmacological properties and a wide variation in their modes of bonding and stereochemistry. Interest in metal complexes with thiosemicarbazone and semicarbazone ligands has been stimulated because biological activities are often enhanced on complexation. [1-4].

Thiosemicarbazones are very good ligands[5] in particular, that contain imidazole moiety which is known to play an important role in biological systems as a part of the histidyl residue in peptides and proteins[6] and it has been shown that their biological activities[7,8] are related to their ability to coordinate to metal centers in enzymes. There are some studies about imidazole

thiosemicarbazone derivatives and their metals complexes such as West et al[9] they have reported the N(1) substituted imidazole-2- carbaldehyde thiosemicarbazone and some of their complexes. Also, J.S. Casas et al. are synthesized imidazole-2-carbaldehyde thiosemicarbazone ligand and some of its diorganotin(IV) complexes as well as, group of M. C. Rodri guez-Arguelles[10] they were continuing and prepared other complex from 2-carbaldehyde thiosemicarbazone ligand and compared their coordinative behaviours beside their antimicrobial activities. In this paper preparation and characterization of new derivative of imidazole carboxaldehydes thiosemicarbazone and its metal complexes were described

MATERIALS AND METHODS

All chemicals and solvents of highest analytical grade were used as received form Sigma-Aldrich and Alfa-Aesar. X-ray crystallographic analysis of the synthesized thiosemicarbazone ligand was carried out using a Bruker, ABEX-IICCD diffractometer. Infrared spectra of the ligand and its metal complexes were recorded on Vertex-183387000 FT-IR spectrometer by using KBr disk in the range 4000-400 cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV-III 600 by using DMSO-$d_{6\ as}$ a solvent. UV-Vis spectra in solid state were recorded on a Cary-4000. EL05123055 UV-Vis spectrophotometer.

Synthesis of 1-methyl-2-imidazolecarboxaldehyde thiosemicarbazone (1-Me-2-ITSC).

An equimolar amount of of thiosemicarbazide (0.091g 0.001 mol) and (1-Me-2-ITSC) (0.11g (0.001 mol) was dissolved in 40ml of ethanol: water (60:40 %) and refluxed for 7 hrs in an oil bath at 78°C [11]. The solution was allowed to cool at room temperature and left for slow solvent evaporation. After Several days white crystals were obtained. The crystals were separated, washed with cold ethanol and dried under vacuum; Yield: 72%; mp 217°C. The pure crystals were suitable for X-ray analysis; data collection and structure refinement results are summarized in Table 1. For the ligand $C_6H_9N_5S$: FT-IR (KBr cm^{-1}); *ν*(NH_2) 3404, 3306; *ν*(NH) 3104; *ν*(C=N) 1643; *ν*(C=S) 854; *ν*(N-N) 1101. *ν*(N-N) 1103. NMR spectrum (600 MHz for ^{1}H and 151 MHz for ^{13}C, DMSO-*d_6*, ppm): ^{1}H NMR; δ=3.9 (3H, s, CH_3); 7.4-7.5 (2H, CH ring), 7.0-7.3(2H, s, NH_2), 8.3(1H, s, =N-NH); 11.5 (1H, s, NH); ^{13}C NMR; δ=35.42 (CH_3);140.89 (Cq ring); 125.54-129.03(2C-H ring), 135.69(HC=N); 177.80(C=S). Ms (ESI.m/z): M^{+} 184.1; Analysis for $C_6H_9N_5S$ (Mw 183.24). UV-Vis spectrum (λ_{max} nm): 311.

Synthesis of [Pd(1-Me-2-ITSC)$_2$]Cl$_2$.

1.632 x 10^{-2} g (5.0 x 10^{-5} mol) of K_2PdCl_4 was dissolved in hot ethanol, and then mixed with a hot ethanolic solution containing 1.83 x10^{-2}g (1.0 x 10^{-4} mol) of (1-Me-2-ITSC). The mixture was refluxed for 7 hrs at $78^{O}c$ in an oil bath and then allowed to cool at room temperature and left for slow solvent evaporation for several days. The colored precipitate was obtained filtered off, washed with cold ethanol and dried in air and a vacuum oven. An orange solid precipitate was obtained, Yield: 97%; mp Dec. > 238°C. For the complex $C_{12}H_{18}N_{10}S_2PdCl_2$: FT-IR (KBr cm^{-1}); *ν*(NH_2) 3338, 3302; *ν*(NH) 3091; *ν*(C=N) 1640; *ν*(C=S) 854; *ν*(N-N) 1106. NMR spectrum (600 MHz for ^{1}H and 151 MHz for ^{13}C, DMSO-*d_6*, ppm): ^{1}H NMR; δ=3.9 (3H, s, CH_3); 7.6 (2H, CH ring), 6.9-7.3(2H, s, NH_2), 8.7 (1H, s, HC=N); 12.1(1H, s, NH);

^{13}CNMR; δ=34.60(CH_3); 140.05(Cq ring); 124.76-128.17 (2C-H ring), 151.62 (HC=N); 178.77 (C=S).UV-Vis spectrum (λ_{max} nm): 221, 236, 436.

Synthesis of [Pt(1-Me-2-ITSC)$_2$]Cl$_2$.

2.075 x 10^{-2} g (5.0 x 10^{-5} mol) of K_2PtCl_4 was dissolved in hot ethanol, and then mixed with a hot ethanolic solution containing 1.83 x10^{-2}g (1.0 x 10^{-4} mol) of (1-Me-2-ITSC). The mixture was refluxed for 7 hrs at 78^{o}C in an oil bath and then allowed to cool at room temperature and left for slow solvent evaporation for several days. The colored precipitate was obtained filtered off, washed with cold ethanol and dried in air and a vacuum oven. Red solid precipitate was obtained, Yield: 76%.mp244^{o}C. For the complex $C_{12}H_{18}N_{10}S_2PtCl_2$: FT-IR (KBr cm^{-1}); *ν*(NH_2) 3395, 3260; *ν*(NH) 3039; *ν*(C=N) 1641; *ν*(C=S) 861; *ν*(N-N) 1067. NMR spectrum (600 MHz for ^{1}H and 151MHz for ^{13}C, DMSO-*d6*, ppm): ^{1}H NMR; δ=3.9 (3H, s, CH_3); 7.6(2H, CH ring), 7.9-8.1(2H, s, NH_2), 8.8(1H, s, HC=N);12.1 (1H, s, NH); ^{13}C NMR; δ=35.80(CH_3); 1 40.04 (Cq ring); 123.43-126.45(2C-H ring), 148.66(HC=N); 178.94 (C=S). UV-Vis spectrum (λ_{max} nm): 216, 346, 499.

Antimicrobial Screening

In vitro antimicrobial screening was performed by agar disk diffusion method. All the test organisms were obtained from microbial type culture collection MTCC. Nutrient agar growth media was prepared according to the instruction of MTCC[12].

Antibacterial Screening

The antibacterial activity of the synthesized thiosemicarbazone and its metal complexes were tested by using agar disk diffusion method against four bacteria; *Bacillus cereus* and *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* and *Salmonella typhimurium* (Gram-negative). The compounds having concentrations 100μg/ml and 200μg/ml. Twenty-five milliliter nutrient agar media was poured in Petri-plates. After solidification, 0.1 ml of test bacteria spread over the medium using a spreader. The disks of whatman No.1 filter paper having diameter 5.00mm were placed at four equidistant places at a distance of 2cm from the centre. The Petri-plates were incubated at 37°C for 26 hrs. The zone of inhibition was calculated and compared with that of DMSO to evaluate the zone of inhibition due to tested compounds [12].

Antifungal Screening

The antifungal activity of ligand and its corresponding metal complexes were tested against one fungi; *Candida albicans*. The compounds having concentrations 100 and 200μg/ml were poured in Petri-plates and similar experiment were repeated and zones of inhibition formed were measured and compared with that of DMSO to evaluate the zone of inhibition due to tested compounds[12].

RESULTS AND DISCUSSION

Crystal structures of 1-methyl-2-imidazolecarboxaldehydethiosemicarbazone

Crystallized with one molecule per asymmetric unit in to Monoclinic crystal system with a space group of $P2_1/n$ *as* shown in Table 1. The structure reveals that the ligand exists in the thione form. S1 and N3 are at trans-conformation (E configuration) to each other with respect to the N2—C1 bond (Figure 1). This is confirmed by the torsion angle of 177.64 (14) of the S1—C1—N2—N3 moiety, which is close to that reported for salicylaldehyde thiosemicarbazone [**13**] thus, the N1 atom lies cis to N3. The thione form in the solid state is strongly confirmed by the observed bond lengths: C1—S1 [1.689(2) Å] and C1—N2 [1.347(3) Å]. The C1—S1 distance of 1.689(2) Å is closer to the C=S bond length [1.62 Å] than to the C—S bond length [1.81 Å], and the C1—N2 distance of 1.347(3) Å is in the range of 1.349(6)—1.386(4) Å for other thiosemicarbazones having the C—N single bond reported earlier[**13, 15**].

Mass-spectra

The electrospray ionization mass spectra (ESI-Mass) of the synthesized thiosemicarbazone (1-Me-2-ITSC) shows molecular ion (M^+) Peak at m/z 184.1a.m.u corresponding to the species $[C_6H_9N_5S]^+$ confirming the empirical formula of the synthesized thiosemicarbazone. The spectra also show series of peaks corresponding to various fragments in the compound.

Infra-red spectra

The infrared absorption bands become very useful for determining the mode of coordination of the ligands to metal. In the IR spectra, the broad band at 3104cm^{-1} in ligand due to -NH vibration. In both complexes, the presence of a band in this region corresponds to -NH vibration which indicates that the ligand is coordinated in the neutral form[2]. The strong band observed at 1643 cm^{-1} in the free ligand have been assigned to ν(C=N) stretching vibrations [16]. As shown in Table 2.

On complexation this bands were observed to be shifted to lower frequencies (1640-1641 cm^{-1}), which are in agreement with the wave numbers for other bis-chelate complexes[17, 18]. These results indicate that the imine nitrogen is coordinated to the metal ion. The ligand showed medium band at 854cm^{-1} ascribed to ν(C=S) vibrations. These absorption band shift 4-49 cm^{-1} to lower frequencies on the coordination of the thiocarbonyl sulfur to palladium(II) or platinum(II) ion. These results are in agreement with other thiosemicarbazone complexes. In addition the vibrational frequencies of the $-NH_2$ groups remain unchanged for the ligand and the metal complexes. This evidence indicates the non-coordination of the $-NH_2$ group to metal ion.

Electronic spectra

The electronic spectra of 1-Me-2-ITSC, showed strong absorption band at 312 nm; this band assigned to $\pi\rightarrow\pi^*$ transition of the azomethine group[10]. The electronic absorption bands are shown in Table3. The energy of intraligand bands slightly changed upon complexation due to the involvement of C=S bond and azomethine nitrogen atom in coordination [1]. The intraligand transitions of the Pd(II) and the Pt(II)complexes are observed in the range (210 to 499) nm and these bands are mainly due to $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ transitions.

^{1}H and ^{13}C NMR Spectra

The ^{1}H and ^{13}C NMR spectrum and chemical shift values (δ, ppm) of the ligand and corresponding metal complexes were record in DMSO-d_6 solvent.

The ^{1}H NMR of 1-Me-2-ITSC ligand and its metal complexes show signal at δ11.5-12.1 have been assigned to δ(NHCS) proton and the signal at 6.9-8.1δ have been assigned to δ($CSNH_2$) proton. Signals at δ8.3-8.8 ppm assignable to azomethine proton [CH=N]. The downfield in the spectra of Pd(II) and Pt(II) complexes indicated coordination through the azomethine nitrogen to the metal atom resulting in the formation of a coordinate M‹—N linkage. Signals at 3.8-3.9are assigned to methyl group (-CH_3). And all imidazole ring protons were observed in the expected regions [17].

The ^{13}C NMR spectra revealed the presence of expected number of signals corresponding to different types of carbon atoms present in the compounds. The Schiff base ligand shows the signal at δ 34.60-35.42 ppm due to carbon atoms of methyl groups. The spectra of the Schiff base ligand exhibits a strong band at δ177.8 ppm due to C=S group. On complex formation the position of this band undergoes up field shift [17] to δ 178.8-178.9 ppm. This indicates that sulphur is involved in coordination ((M‹—S linkage).

Thermal analysis (DTA and TG) of Pd(II) and Pt(II) complexes.

Generally, not much was known about the thermal properties of transition metal complexes of imidazolecarboxaldehyde thiosemicarbazones. The thermal behavior of the Pd(II) and Pt(II) complexes of the synthesized imidazole-carboxaldehyde thiosemicarbazones were studied under argon atmosphere using thermal analyzer (DTA-TG) the results shown in Table4. The thermal decomposition of the complexes was recorded from ambient temperature to 1000^{o}C. The results showed that the complexes, generally decomposed in several thermal events (decomposition steps). The complexes loss moisture around 100^{o}C, and then started to decompose at a temperature above this limit. The total weight loss around 1000ºC is nearly 70-80% and this equals the loss of two moles of ligand in agreement with the proposed metal:ligand ratio of 1:2 of the complex. The remaining weights correspond to the metallic residue.

Antimicrobial activity

The synthesized compounds were screened in vitro for their antibacterial activity against four pathogenic bacteria; *Bacillus cereus, Staphylococcus aureus, Escherichia coli, Salmonella typhimurium* and one fungi; *Candida albican* at a concentration of 100 and 200µg/ml with DMSO as the solvent. The activity data is given in Table 5. The results showed that the tested compounds possess moderate antimicrobial activity against most of the tested organism.

Table 1. Crystal data and structure refinement for (1-Me-2-ITSC)

Chemical formula	$C_6H_9N_5S$
M_r	183.24
Temperature (K)	200
Crystal system	Monoclinic
Space group	$P2_1/n$
A	12.0701 (5) Å
B	5.8341 (3) Å
C	12.3586 (5) Å
(α)	-
(β)	91.011 (2)°
(γ)	-
V	870.13 Å3
Z	4
Radiation type, μ(mm^{-1})	Mo *K*α, 0.32
Crystal size (mm)	0.24 × 0.16 × 0.04
Diffractometer	Bruker*APEX*-IICCD
Absorption correction	Numerical*SADABS* 2014/5
T_{min}, T_{max}	0.950, 0.997
Measured, independent and observed reflections.	16022, 2679, 2122
R_{int}	0.030
$(\sin \theta/\lambda)_{max}$ ($Å^{-1}$)	0.717
$R[F^2> 2\sigma(F^2)]$, $wR(F^2)$, S	0.033, 0.090, 1.01
No. of reflections	2679
No. of parameters	117
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$)	0.29,-0.22

Table 2. IR spectral data of (1-Me-2-ITSC) and its Pd(II) and Pt(II) complexes

Compounds	$\nu(NH_2)cm^{-1}$	$\nu(NH)cm^{-1}$	$\nu(C=N)cm^{-1}$	$\nu(C=S)cm^{-1}$	$\nu(N-N)cm^{-1}$
1-Me-2-ITSC	3404, 3306	3104	1643	854	1101
$Pd(1\text{-Me-2-ITSC})_2Cl_2$	3338, 3302	3091	1640	850	1106
$Pt(1\text{-Me-2-ITSC})_2Cl_2$	3395, 3260	3039	1641	805	1067

Table 3. UV-Vis spectrum and physical properties of (1-Me-2-ITSC) and its Pd(II) and Pt(II) complexes

Compounds	Color	Yield %	M.P °C	UV-Vis absorption bands
1-Me-2-ITSC	White	72	217	311
$Pd(1\text{-}Me\text{-}2\text{-}ITSC)_2Cl_2$	Orange	97	238	221, 236, 436
$Pt(1\text{-}Me\text{-}2\text{-}ITSC)_2Cl_2$	Red	76	244	216, 246, 499

Table 4: Thermoanalytical results (DTA-TG) of of (1-Me-2-ITSC) and its Pd(II) and Pt(II) complexes

Complexes	TG (^oC) Range	DTA (^oC) Range	Mass loss %	Total mass loss %	Metallic residue %
$Pd(1\text{-}Me\text{-}2\text{-}ITSC)_2Cl_2$	30-1000	102(-) 621(-)	3.50, 12.07, 27.20 5.66, 9.69, 4.68, 6.91, 06.57, 7.91	84.19 (80.43)	Pd 15.84 (19.56)
$Pt(1\text{-}Me\text{-}2\text{-}ITSC)_2Cl_2$	30-1000	256(-) 305(-) 557(-) 841(-)	1.96, 13.91, 18.57 11.92, 9.38, 4.07, 3.14, 07.93	70.88 (69.15)	Pt 29.31 (30.84)

Found (Calculated), (-) exothermic

Table 5: Antimicrobial activity of two synthesized thiosemicarbazones

Compounds	Con. $\mu g \cdot ml^{-1}$	Diameter of Inhibition Zone (mm) (conc. in $\mu g \cdot ml^{-1}$) *Gram+ve: Bacteria Gram-ve: Bacteria Fungi* *B. cereus*	*S. aureus*	*E. coli*	*S. typhi*	*C. Albicans*
1-Me-2-ITSC	100	10	09	10	07	10
	200	11	13	10	10	11
$Pd(1\text{-}Me\text{-}2\text{-}ITSC)_2Cl_2$	100	11	13	12	12	15
	200	14	15	11	12	13
$Pt(1\text{-}Me\text{-}2\text{-}ITSC)_2Cl_2$	100	13	13	10	10	11
	200	11	14	11	12	12

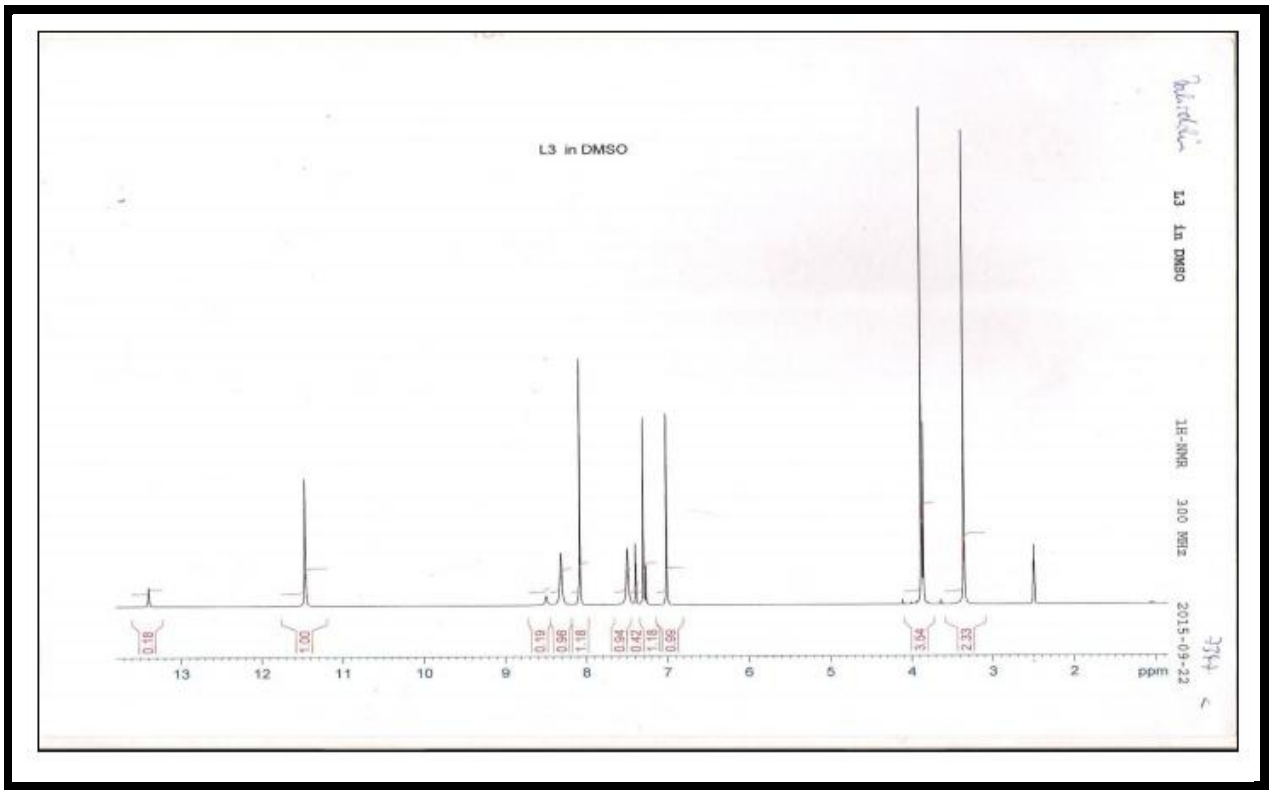

Figure 1. ^{1}H NMR spectrum of the ligand (1-Me-2-ITSC).

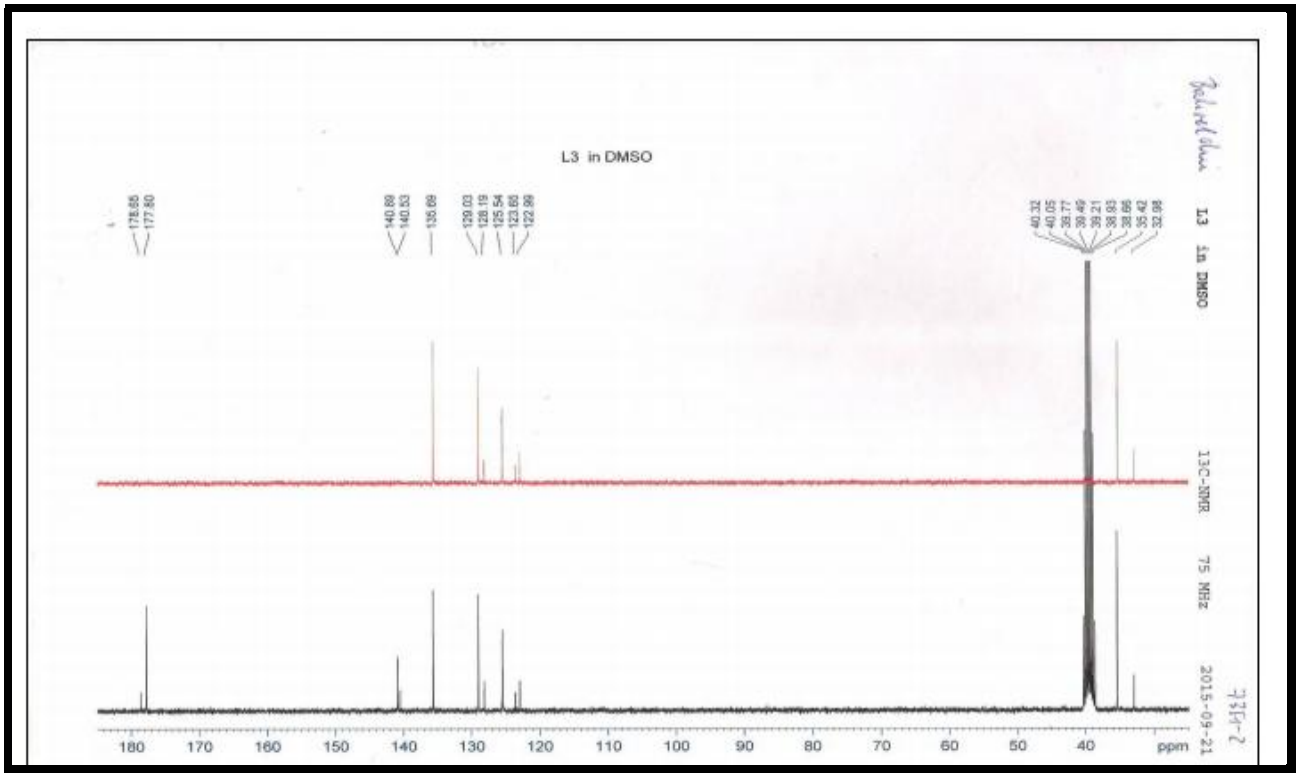

Figure 2. ^{13}C NMR spectrum of the ligand (1-Me-2-ITSC).

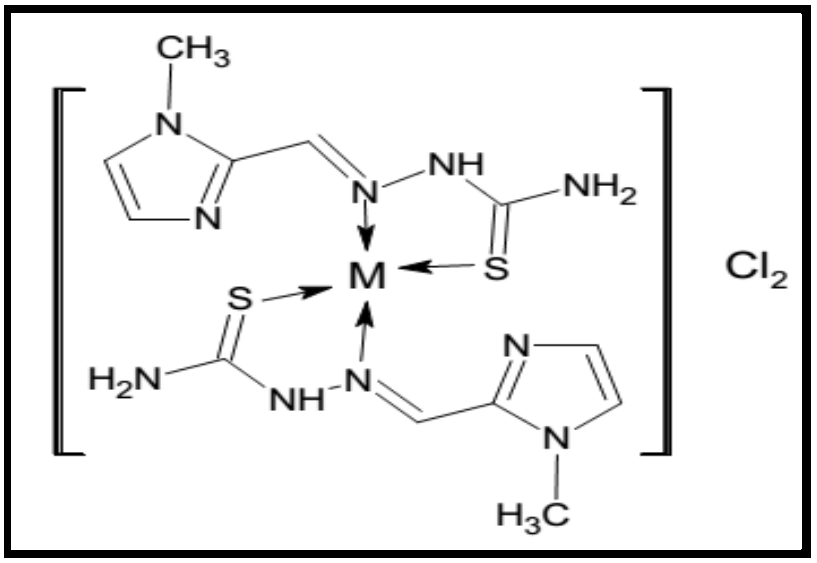

Figure 3. Proposed Structure of (1-Me-2-ITSC); Pd(II) and Pt(II) complexes

CONCLUSION

In this study condensation reaction was adopted for preparing new thiosemicarbazones;1-methyl-2-imidazolecarboxaldehyde thiosemicarbazone. The ligand was fully characterized by X-ray crystallographic analysis and the resulting complexes were studied by spectroscopic analysis and the antibacterial and antifungal activities were evaluated for the ligands and its metal complexes.

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CONFLICTS OF INTEREST

Authors declare that there is no conflict of interest.

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