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RESEARCH PAPER

Synthesis and Antibacterial Studies of new mixed ligand transition metal complexes of thioester (1, 3, 4-Oxadiazole) derivative (phozbt) and dppe Ligands.

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A B S T R A C T:
Complexes of transition palladium(II) and platinum(II) metals that possessing two kinds of ligands: S-5-phenyl -1, 3, 4-oxadiazole-2-yl benzothioate (phozbt) and tertiary diphosphine (dppe), were synthesized. The thioester (phozbt) ligand was synthesized by reaction between 2-mercapto-5-phenyl-1,3,4-oxadiazole (PhozSH) with benzoyl chloride and using sodium hydroxide. The synthesized ligand and complexes were described by C, H, N, S analysis, infrared spectra, molar conductivity, UV-visible and magnetic susceptibility measurements. The (dppe) act as bidentate chelate that linked to the metals on both P-donor atoms. According to the spectral analysis of the complexes, a square planer structure were suggested for both metal complexes. The ligand and complexes were studied for antibacterial activity by using agar diffusion method. This study showed positive inhibition zone results, for both ligand and complexes with *S*. aureus and *P*. aeruginosa bacteria.

KEY WORDS: Pd(II), Pt(II), Oxadiazole derivatives, Dppe, Antibacterial activity
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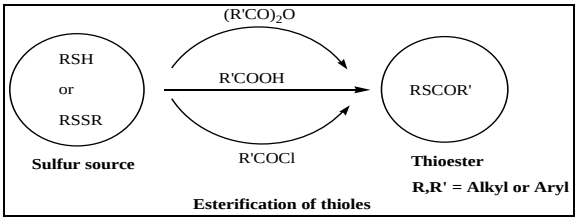
INTRODUCTION :

The chemistry of heterocyclic substance is a fascinating field of study since a long time (Pangal and Shaikh, 2013).
Compounds containing the (C-S-CO-C) functionality are identified as thioesters**.** A thioester is an ester with S atom instead of the O atom between the acyl and alkyl groups. Thioesters are a significant section of organosulfur compounds that have an essential role in the manufacture of pharmaceutical, biological, industrial and natural products.

In this consideration, preparation of thioesters is one of the most imperative assignments in organosulfur chemistry. The esterification of thiol groups is the main and most frequent strategy for the synthesis of thioesters (Scheme 1) (Kazemi and Shiri). Thioesters are the most usual type of activated carboxylic acids in a cell (Bruice, 2006).



Scheme 1: Preparation of thioester compounds

Oxadiazole is a five member heterocyclic compound containing one O and two N atoms, in

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older literature it was referred as furadiazoles which attracted wide attention of chemist for preparation of different biological active drugs. The biological behavior of oxadiazole are attributable to the presence of -N=C – O linkage (Shubhangi and Pravina, 2013).

This work, reports, the synthesis and Identification of new transition metal Pd(II) and Pt(II) complexes containing both (dppe) and (phozbt) ligands.

1. MATERIALS AND METHODS

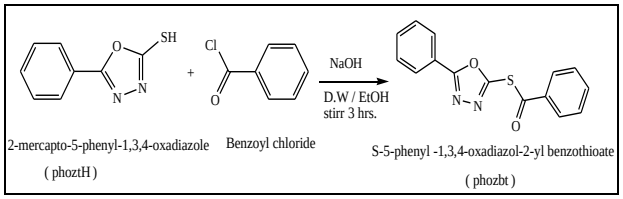
2.1. MATERIALS

The (Platinum (II) chloride, Paladium(II) chloride, PhozSH and dppe) (commercial products) were used as supplied. Melting points and decomposed degrees were determined on an electrothermal MPD-100. Infrared spectra were taken on Brooker-ALPHA infrared appliance using potassium bromide disc. Proton and carbon thirty- NMR were recorded in chloroform solution on a Bruker Ac 400 MHz spectrometer using d^6-DMSO as solvent. Uv.-Vis. spectra were acquired using a Perkin-Elmer Lamda 9 spectrophotometer. Conductivity measurements were executed on 10^{-3}M solutions using a conductivity meter type CDM 83 70. Elemental analyses were taken on Carlo-

Erba elemental analyzer, type 1106. Magnetic measurements were measured on a Bruker BM6 appliance at room temperature following the Faraday method.

2.2. Synthesis of thioester (phozbt)

Sodium hydroxide (0.003mol, 0.132g) was dissolved in water (15 ml) and (PhoztH) (0.0033mol, 0.587g) was inserted. After stirring for (15 minutes), a solution of appropriate benzoyl chlorides (0.0033mol, 0.463g) in ethanol (5 ml) was inserted drop-wise. The resultant mixture was stirred at room temperature for 3 hours; the observed precipitate was filtered, then recrystallized in methanol to obtain pure target compounds (Scheme 2) (Gurrala *et al.*, 2010). (Formula: $C_{15}H_{10}N_2O_2S$; Yield: 0.7 g, 75.2%; melting point: 138-139 °C; Colour: Off-white).



Scheme 2: Preparation of (phozbt) ligand

2.3. Synthesis of [Pd(κ^1-phozbt)Cl(κ^2-dppe)]Cl (1)

This compound can be synthesized by the following steps:

First step: Preparation of [$PdCl_2$(κ^2-dppe)]

Solution of dppe (0.25 mmol, 0.0994 g) in dichloromethane (13 ml) was inserted to a solution of palladium chloride (0.25 mmol, 0.0443 g) that dissolved in a mixture of warm concentrated hydrochloric acid (3 ml) and ethanol (10 ml). The final solution was stirred under reflux about 3hrs. The hot yellow solution was filtered. The resulting yellow colour precipitate was collected when the solvent evaporated (Lassahn *et al*., 2003). (Formula: $C_{26}H_{24}Cl_2PdP_2$; Yield: 0.137g, 95.3%; decomposition point: 294°C; Colour: Yellow).

Second step: Addition of (phozbt) ligand to the prepared [$PdCl_2$(κ^2-dppe)]

A warm ethanolic solution (10 ml) of (phozbt) (0.13 mmol, 0.0367 g) was inserted to a solution of [$PdCl_2$(κ^2-dppe)] (0.13 mmol,0.0747 g) in dichloromethane (10 ml). The resultant mixture was heated to a reflux for 4 hours. After a few days, when the solvent was evaporated a yellow-brown precipitate was obtained (Formula: $C_{41}H_{34}Cl_2N_2PdO_2P_2S$; Yield: 0.096 g, 86.2%; melting point: 236-239 °C; Colour: Yellow-brown).

2.4. Synthesis of [Pt(κ^1-phozbt)Cl(κ^2-dppe)]Cl (2)

This compound was synthesized by the following steps

First step one: Synthesis of [$PtCl_2$(κ^2-dppe)]

The complex was synthesized as a Light-brown precipitate, by similar mode that applied for preparation of [$PdCl_2$(κ^2-dppe)] complex. (Formula: $C_{26}H_{24}Cl_2PtP_2$; Yield: 0.120 g, 90.5%;

decomposition point: 255 °C; Colour: Light-brown).

Second step: Addition of (phozbt) ligand to [$PtCl_2(\kappa^2$-dppe)] complex

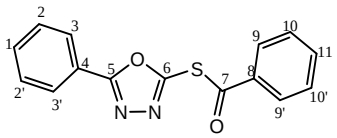
(0.12 mmol, 0.0796 g) of [$PtCl_2(\kappa^2$-dppe)] dissolved in (10 ml) of CH_2Cl_2 solvent, then a hot ethanolic (10 ml) solution of (phozbt) ligand (0.12 mmol, 0.0338 g) was inserted and refluxed for 4 hours and filtered. After a few days when the solvent evaporated at room temperature, the light brown solid was observed (Formula: $C_{41}H_{34}Cl_2N_2PtO_2P_2S$; Yield: 0.085 g, 74.9%; melting point: 232-235 °C; Colour: Light-brown).

3. Results and Discussion

3.1. Proton-NMR spectrum of (phozbt)

The ^{1}H-NMR spectral band of the thioester (phozbt) ligand in d_6-dimethyl sulfoxide solvent displayed two doublets at δ (7.99 and 7.65) ppm which referred to (H9 and H3) protons correspondingly. The two triplets appearing at (7.71, 7.62, 7.54 and 7.28) ppm corresponding to the proton of (H11, H10 , H2 and H1) respectively (Dalia and Faiq, 2018).

The dissaperance of the SH band at (2.5) ppm that remarked in (phoztH) ligand indicates the formation of the thioester (phobt) ligand (figure 1) (Husain and Ajmal, 2009)(Kumar *et al.*, 2014).



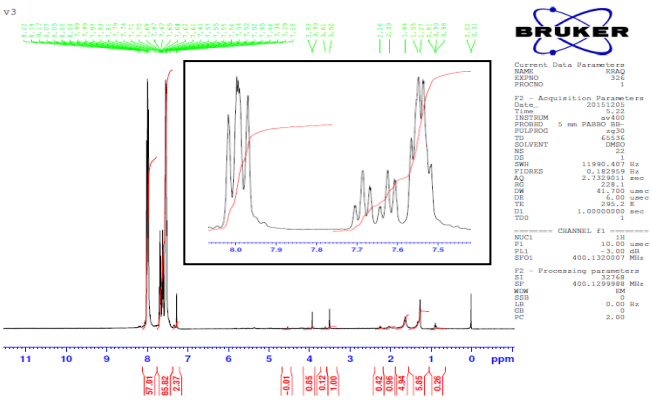
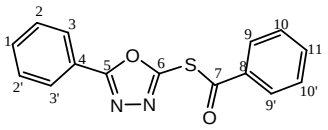


Figure 1: ^{1}H-NMR spectrum of (phozbt) ligand

3.2 ^{13}C-NMR spectrum of (phozbt)

The carbon-NMR spectrum of (phozbt) was recorded in dimethyl sulfoxide solvent. The carbonyl carbon band displayed at (174.43) ppm; C_7 (Joshi *et al.*, 2015).The two carbon atom (C_6 and C_5) of oxadiazole ring occurred at (164.55 and 157.64) ppm respectively (Kumar *et al.*, 2014). The peaks observed at (133.62, 132.81, 130.53 and 128.09) ppm were correspondingly ascribed to aromatic benzo carbon of (C_8, C_{11}, C_{10} and C_9) (Almajan *et al.*, 2008). The aromatic phenyl carbons of (C_2, C_1, C_3 and C_4) were correspondingly observed at signals (130.61, 128.94, 126.74 and 121.31) ppm (figure 2) (Aydoğan *et al.*, 2002)(Aras and Hassan, 2018).



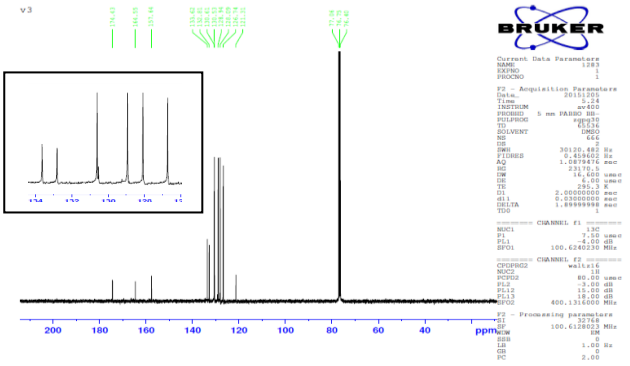


Figure 2: ^{13}C-NMR spectrum of (phozbt) ligand

3.3. CHNS analysis for the synthesized complexes

The elemental analysis of all the complexes are coherent with the proposed stoicheometries (Table 1). Some physical data for the synthesized complexes are also recorded.

Table 1: Molecular weight, melting points and C,H,N,S analysis for the synthesized complexes

No.	Complexes	M.Wt g/mol	M.P. (°C)	(Calculated) Found % C	H	N	S
1	[Pd(κ^1-phozbt)Cl(κ^2-dppe)]Cl	857.33	236-239	(57.38) 56.88	(3.96) 4.07	(3.26) 2.65	(3.74) 2.88
2	[Pt(κ^1-phozbt)Cl(κ^2-dppe)]Cl	946.00	232-235	(52.01) 52.68	(3.59) 4.10	(2.96) 3.22	(3.39) 3.39

3.3 FT-IR spectra for the synthesized complexes

The ν(C-S) stretching vibration of complex (1 and 2) occurred at (704 and 707) cm^{-1} and a new peak was detected at (430 and 437) cm^{-1} were attributed to ν(M-S) stretching vibration correspondingly, which signify of the linkage of S-atom of oxadiazole to the metal center (Al-Jibori *et al.*, 2002). In addition, the ν(P-Ph) vibration in (1 and 2) complexes were occurred at (1435) cm^{-1}, on the other hand, the ν(P-C) vibration displayed at (530 and 511) cm^{-1} correspondingly (Jensen and Nielsen, 1963)(Al-Jibori *et al.*, 2015). These data suggest participation of sulfur atom of (phozbt) and phosphorous of (phosphines) ligands in bonding.

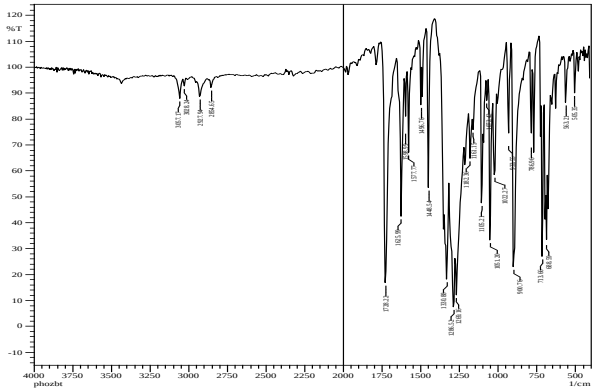


Figure 3: Infrared spectrum of (phozbt) ligand

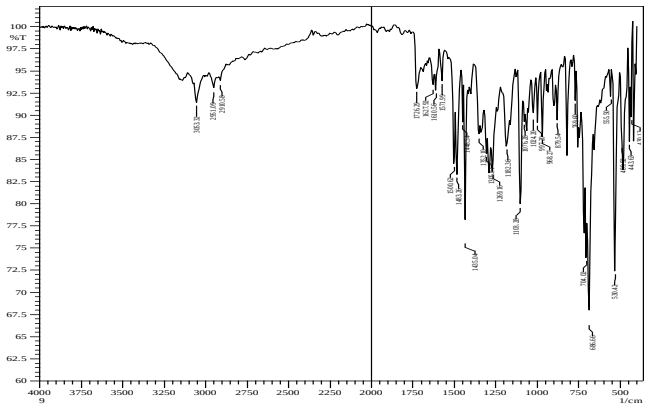


Figure 4: IR spectrum of [Pd(κ^1-phozbt)Cl(κ^2-dppe)]Cl complex (1)

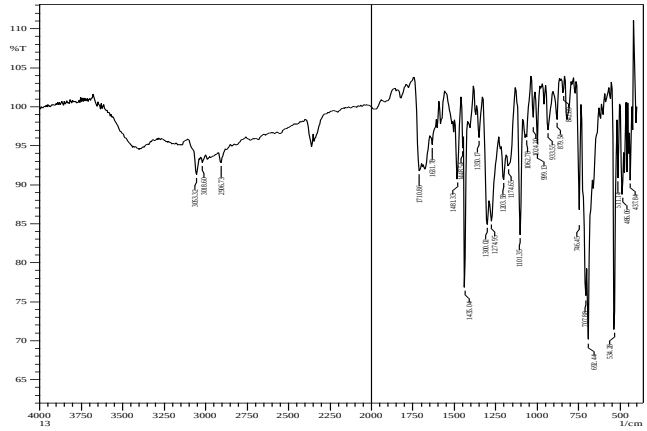


Figure 5: IR spectrum of [Pt(κ^1-phozbt)Cl(κ^2-dppe)]Cl complex (2)

3.4. ^{31}P-{^{1}H}-NMR Spectrum of Complex (2)

The spectrum of [Pt(κ^1-phozbt)Cl(κ^2-dppe)]Cl displayed an AX splitting system comprising of two singlet at δPA(48.69) and δPX(42.50) ppm, each associated with platinum satellites, J(Pt-PA)=2355 Hz and , J(Pt-PX)=3563 Hz, correspondingly attributed to the coordination of S and Cl-coordinated to the platinum metal (figure 6)(Al-Jibori *et al.*, 2013).

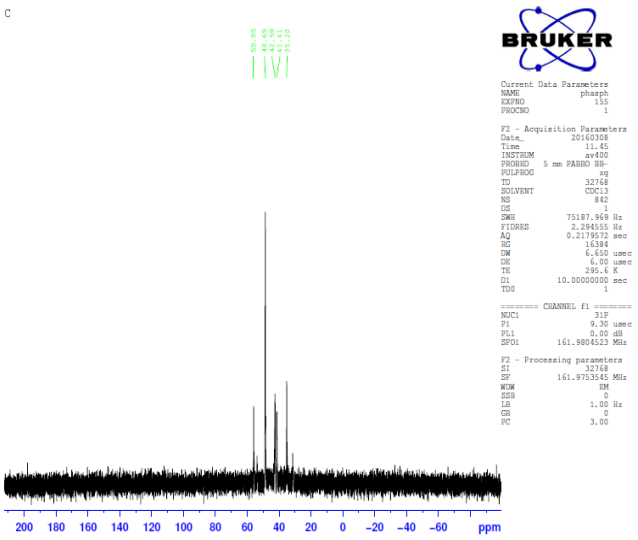


Figure 6: ^{31}P-{^{1}H}-NMR spectrum of [[Pt(κ^1-phozbt)Cl(κ^2-dppe)]Cl] complex

3.5. UV-Visible Spectra and Magnetic Susceptibility of the Synthesized Complexes

The UV-Vis. spectra of both the synthesized compounds were measured at room temperature in chloroform (10^{-3} M) solution in UV. and Vis. regions. The (phozbt) exhibited two transitions at (41666 and 34482) cm^{-1}, that correpondongly ascribed to the transitions; π- π* and n- π*.

The Pd(II) complex, demonstrated four absorption bands at (23809, 33333, 38461 and 45454) cm^{-1}, the former two transitions attributed to $^1A_1g \rightarrow {}^1B_1g$ and $^1A_1g \rightarrow {}^1Eg$ and the next two bands were attributed to C.T transitions. On the other hands, the Platinum (II) complex display three d-d with two C.T transitions. The d-d bands observed at (18181, 19607 and 32258) cm^{-1} that respectively assigned to $^1A_1g \rightarrow {}^3B_1g$, $^1A_1g \rightarrow {}^1A_2g$ and $^1A_1g \rightarrow {}^1Eg$ and the C. T. transitions appeared at (40000 and 43478) cm^{-1}.

The magnetic susceptibility for the prepared complexes were carried out at 25 °C and the effective magnetic moments data for the synthesized complexes are listed in Table 2.

Table 2: Electronic spectral bands, Magnetic susceptibility and Molar conductivity of the prepared ligand and complexes

Complexes	Absorption band		Assignment Transition	Magnetic Susceptibility (μeff.)	Molar conductivity (cm^2. Ohm^{-1}. Mol^{-1})
	cm^{-1}	Nm			
Phozbt	41666 34482	240 290	π -*π n-π*	…	1
[Pd(κ^1-phozbt)Cl(κ^2-dppe)]Cl	45454 38461 33333 23809	220 260 300 420	C.T. C.T. $^1A_1g \rightarrow {}^1Eg$ $^1A_1g \rightarrow {}^1B_1g$	0.8 Sq. pl	44
[Pt(κ^1-phozbt)Cl(κ^2-dppe)]Cl	43478 40000 32258 19607 18181	230 250 310 510 550	C.T. C.T. $^1A_1g \rightarrow {}^1Eg$ $^1A_1g \rightarrow {}^1A_2g$ $^1A_1g \rightarrow {}^1B_1g$	1.0 Sq.pl	31

The results indicated a square planer geometry for both (1 and 2) complexes with magnetic moment (0.8 and 1.0) B.M. respectively. However, the electronic transition values are also indication for the formation of square planer geometry for both of the two complexes.

3.6. Molar conductivity measurements for the synthesized compounds

The molar conductivities of the synthesized compounds were taken at room temperature at (10^{-3} M) solution in dimethyl sulfoxide. It was deduced that both of the synthesized compounds are electrolyte that formed in (1:1) ratio.

4. Biological Activity of the Ligands and Complexes

The ligands and all the synthesized complexes were appraised for antibacterial activity toward gram positive *S. (Stophylococcus) aureus* and gram negative *P. (Pseudomonas) aeruginosa* bacteria by agar diffusion method.

4.1. Procedure

The sensitivity studies of 20 different chemical compounds against two kinds of bacteria determined according to NCCLS and CLSI standards. 20 ml of Muller Hinton agar melted and cooled at 45 °C was flowed into sterile petri dishes and ordered to solidify completely. A lawn

of tests pathogen was prepared by evenly spreading 100 µl inoculums ($1.5*10^8$ CFU/ml) (according to 0.5 McFarland standard solution) with the help of a sterilized swab onto the entire surface of Muller Hinton Agar plate (McFarland, 1907). The plates were permitted to dry before applying chemical compound disks. The disks were firmly applied to the surface of agar plates within 15 minutes of inoculation (Wikler *et al.*, 2007). After putting the chemical compound disks on plates incubated for 24 hrs. at 37 °C. Antibacterial activity was designated by measuring the diameter of inhibition zone. Activity of each compounds were compared with known antibiotics; Vancomycin and Impenem and their data are represented in Table (3).

The results of antimicrobial evaluation suggested that ligands and complexes have very good potential to act as antibacterial agents. All ligands and synthesized complexes were more active against gram negative bacteria as compared to gram positive one. Among the tested compounds, the ligands (phozbt and dppe) showed outstanding antibacterial activity against (*P. aeruginosa*) than (*S. aureus*) bacteria as compared to standard (Impenem and Vancomycin) antibiotics. Complex (2) showed comparatively good activity against (*P. aeruginosa*) as compared to the (*S. aureus*). Complex (1) displayed more active against (*P. aeruginosa*) bacteria, while they showed no activity against (*S. aureus*) and KBr was also inactive against both bacteria.

Table 3: The diameter of inhibition of the tested compounds on *S. aureus* and *P. aeruginosa* incubated for 24 hrs. at 37 °C

Complex No.	Structures	Inhibition diameter zone (mm)	
		P. aeruginosa	***S. aureus***
…	KBr	0	0
…	Phozbt	24	20
…	Dppe	17	…
1	[Pd(κ^1-phozbt)Cl(κ^2-dppe)]Cl	30	0
2	[Pt(κ^1-phozbt)Cl(κ^2-dppe)]Cl	34	17
…	Impenem	40	…
…	Vancomycin	…	21

5. Conclusion

This work comprises the synthesis of new thioester (phozbt) ligands and their mixed ligand palladium and platinum complexes with dppe ligands. With the aids of infrared, Electronic and magnetic susceptibility data, we deduced that both the Pd(II) and Pt(II) compounds have a square planer structure. With the aids of molar conductivity measurements, it has been proposed that all the compounds are electrolytes that formed in (1:1) ratio.

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