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Synthesis, characterisation and Biological Activities of some bivalent Platinum and Palladium Complexes with ThioSemicarbazone Ligands derived from some chalcones.

Sharad T Tajane^{1,2} , and Ashok N Patange^{1*}.

¹Department of Chemistry, Bhavan's College, Munshi Nagar, Andheri (West), Mumbai, Maharashtra 400058, India

²Research Scholars, University of Mumbai, Mumbai 400001,

ABSTRACT

The therapeutic importance of thiosemicarbazone group containing ligands has promoted the selection of this class of ligands and their complexes for the study. The present work describes the synthesis, characterisation and biological investigations of Pd(II) and Pt(II) complexes with the active Schiff's base ligands derived from some chalcone. All complexes reported here had been characterised on the basis of elemental analysis, molecular weight determinations and spectral studies by ¹H NMR and FTIR spectra. The complexes are diamagnetic in nature and showing square planar geometry. The IR spectral data reveals that the Schiff's bases behave as a bidentate ligands and are coordinated to Pd(II) and Pt(II) metal through the sulfur and hydrogenic nitrogen atom. All the new synthesized compounds were screened for antibacterial activity against the test organism viz *Escherichia coli* NCIM 2641, *Staphylococcus aureus* MTCC 1144

Keywords: Schiff's base, Thiosemicarbazone, *Escherichia coli* NCIM 2641, *Staphylococcus aureus* MTCC 1144.

*Corresponding author

INTRODUCTION

The synthesis and structural investigation of some Thiosemicarbazones metal complexes are of significant attention because of their pharmacological, antibacterial [1], antifungal [2], antitumor [3], antiarthritic antiamebic, antiviral, antimalarial properties and modes of bonding and stereochemistry and some have been found to possess anti-HIV activity [4]. In the last two decades sulphur and nitrogen-based containing thiosemicarbazones ligands have emerged as important and were most widely studied. The importance and significance of these complexes due to their diverse chemical and structural characteristics with a wide spectrum of activities as biologically active molecules. Most of metal complexes of Thiosemicarbazones were colored and used as analytical reagents [5] for selective and sensitive determinations of metal ions. The geometry of the studied metal complexes were greatly influenced by the nature of the ligand and a variation of charge density around the coordination site and by the type of metal salts used in their preparation. The synthesized ligands and complexes were characterized and identified by using $^1\text{H-NMR}$ spectroscopy and FTIR spectroscopy, elemental analysis, molar conductivity measurements. The ligand has two nitrogen and Sulphur/ oxygen donor sites, which can effectively coordinate to a metal ion in a tetra dentate fashion. Palladium (II) and Platinum (II) complexes of hydrazine carbothiamide (T_1H) of (2E)-1,3-bis-(4-bromophenyl)prop-2-en-1-one, hydrazine carbothiamide (T_2H) of (2E)-1-(4-chlorophenyl)-3-(4-nitrophenyl) prop-2-en-1-one have been prepared and screened for their antibacterial activity against the test organism viz *Escherichia coli* NCIM 2641, *Staphylococcus aureus* MTCC 1144 by paper disc diffusion technique. The antibacterial data reveals that that the complexes were superior to the free ligands [6-7]. In the present investigation we have synthesized and characterize some new active Schiff's base complexes of Palladium and Platinum metals in order to evaluate their antibacterial activity.

EXPERIMENTAL

All chemicals used were of A.R Grade and purchased from S.D Fine and Lobachem chemicals (Mumbai) and were used further purification. This experimental part divided in to three parts,

Preparation of Chalcones

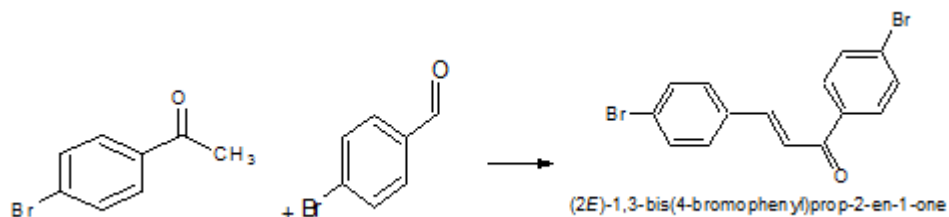
(2E)-1,3-bis-(4-bromophenyl)prop-2-en-1-one [B_1]:

Procedure: In the three necked round bottom flask a mixture of 4-bromo benzaldehyde (0.05mole) and 40mL ethanol were taken and stirred for one hour. Meanwhile the solution of 20% caustic soda solution (20ml) mix with 4-bromo Acetophenone (0.05mole) was prepared, Above prepared solution was added slowly to ethanolic solution of 4-bromo benzaldehyde maintaining temp. 15-20°C, then the reaction mass was refluxed on water bath for 3-4 hrs. After the reaction reached completion (monitored by TLC), the mixture was cooled on ice salt bath. It was filtered and washed with water & Chalcone obtained was recrystallized with ethyl acetate. Similarly the chalcone [B_2] (2E)-1-(4-chlorophenyl)-3-(4-nitrophenyl)prop-2-en-1-one also prepared as the above procedure.

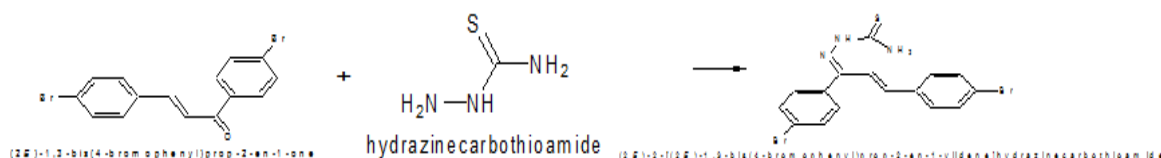
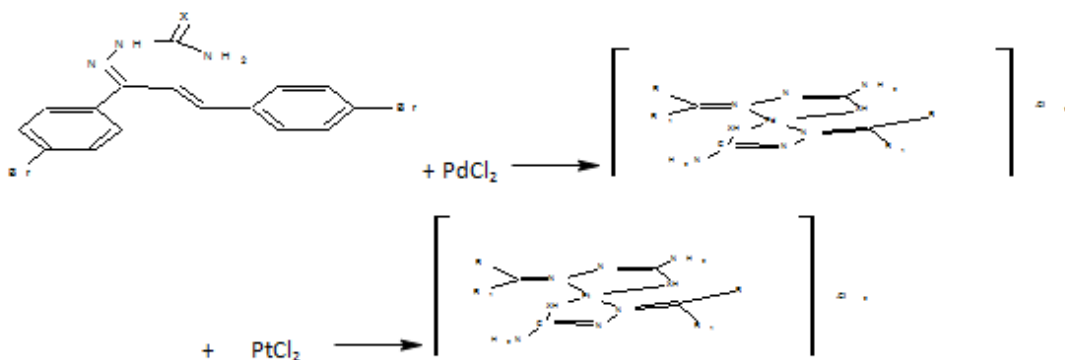
Preparation of Preparation of Ligands: The ligands of hydrazine carbothiamide (T_1H) of (2E)-1,3-bis-(4-bromophenyl)prop-2-en-1-one, hydrazinecarbothiamide (T_2H) of (2E)-1-(4chlorophenyl)-3-(4 nitrophenyl)prop-2-en-1-one, were prepared as

Preparation of hydrazine carbothiamide (T_1H) of (2E)-1,3-bis-(4-bromophenyl)prop-2-en-1-one The chalcone (2E)-1,3-bis-(4-bromophenyl)prop-2-en-1-one [8-12] (0.005mol) was added to 20 ml of THF & thiosemicarbazide (0.0061mol) was added along with sodium acetate (3gm) reaction mixture was then refluxed on water bath for 2-3 hrs. After the reaction reached completion (monitored by TLC); the mixture was cooled on ice-salt mixture, it was then filtered and recrystallized with alcohol. Similarly the ligand (L_2H) of (2E)-1-(4-chlorophenyl)-3-(4-nitrophenyl)prop-2-en-1-one as above method

Preparation of [$\text{Pt}(\text{T}_1\text{H})_2$]Cl₂ complexes: PtCl₂ (0.0005mol.) was added to an ethanolic [13] solution of ligands [T_1H] (0.001mol.). The reaction mixture was than heated under reflux for about 5-6 hrs in presence of few drops of concentrated HCl. The reaction mixture was than cooled and filtered. The crystal obtained were washed several times with ice cold alcohol and dried in vacuum. Similarly the [$\text{Pt}(\text{T}_2\text{H})_2$]Cl₂, [$\text{Pd}(\text{T}_1\text{H})_2$]Cl₂ and [$\text{Pd}(\text{T}_2\text{H})_2$]Cl₂ complexes were prepared as discussed the above procedure.



Schme-1 Preparation of chalcones


 Schme-2 Preparation of Ligands (T₁H)

 Schme-4 Preparation of [Pd(T₁H)₂]Cl₂ & [Pd(T₂H)₂]Cl₂ complexes Product Code

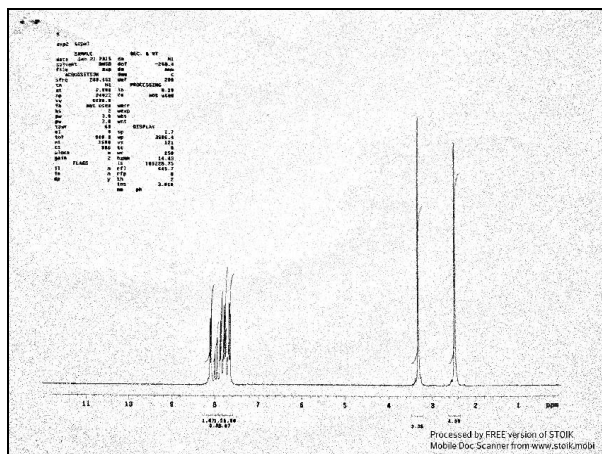
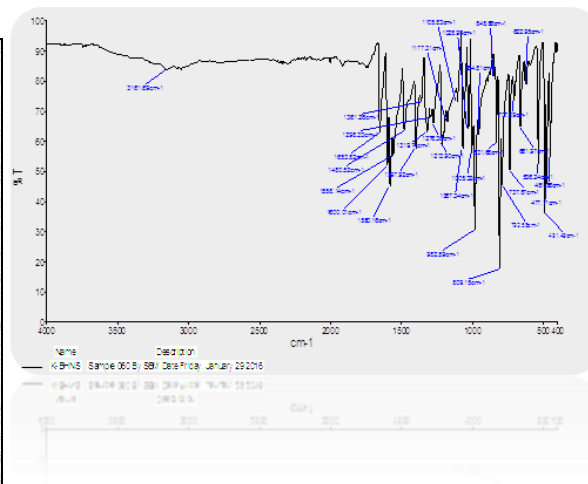
X=S Where R = C₇H₄Br, R₁ = C₈H₆Br, Pd(L₁H)₂Cl₂, Pt(L₁H)₂Cl₂

RESULT AND DISCUSSION

The ¹H NMR spectra were recorded on Hitachi PerkinElmer spectrophotometer in CDCl₃ Using TMS as internal standard. FTIR spectra (in 4000–450 cm⁻¹ range) of Ligands as well as complexes were recorded in KBr pellets (2 mg / 200 mg KBr) using a FTIR PerkinElmer 1750 spectrophotometer. Molecular weights were determined by the Rast Camphor method. Molar conductivities Measurements of the complexes were made with a Equiptronics Model-305. Nitrogen was determined by the Kjeldahls method and sulphur was estimated by the messengers method. Pd and Pt were estimated gravimetrically. The molar conductance values of 10⁻³M solutions of [M(TH)₂]Cl₂ type complexes lie in the rage of 195-185 Sm²mol⁻¹ in dry DMF indicating 1:2 electrolytes nature. the analytical data of the ligands and complexes are given in Table-3

NMR Spectra of [Pt(T₁H)₂]Cl₂ complex (in 400 MHz, CDCl₃) δ_{ppm} :-

In the ¹H NMR spectrum of complex the most common [14] NMR multiplets for Aromatic rings protons are found to be resonating around δ 7.8-δ 8.0 whereas the broad singlet for -NH₂ group protons appeared around δ 3.4. a sharp doublet peak for olefinic protons (>C=C-H) group of the complexes were observed in the range of δ 7.6- δ 8.15. The distinguishing singlet peak around δ 9.2 (>C=N-group) for azomethine protons observed in ligands was completely disappears in the complexes due to co-ordination through >C=N- group indicates the formation of Platinum complex.


 Figure:1 NMR spectrum of $[Pt(T_1H)_2]Cl_2$ complex

 FTIR:2IR spectrum of $[Pt(T_1H)_2]Cl_2$ complex

FTIR Spectra of $[Pt(T_1H)_2]Cl_2$ complex

IR (KBr) cm^{-1} : -3227-3161(>NH, NH_2), 2963 (CH), 809 (>C=S), 1600 (Aromatic Stretching), $\nu(C=N)$ groups 1558 cm^{-1}

The band appears at 3161 cm^{-1} indicates that >NH, NH_2 group [15] were not involved in co-ordination, on Complexation the bands corresponding to $\nu(C=N)$ and $\nu(C=S)$ (in case of thiosemicarbazone) are shifted towards lower side 1558 cm^{-1} and 809 cm^{-1} (ca.20-30 cm^{-1}). This suggest that the ligand acts as a bidentate chelating agent coordinating to Pt (II) metal ion through nitrogen of $\nu(C=N)$ group and sulphur of $\nu(C=S)$ group.

 Table-1: 1H NMR Ligands & complexes (400 MHz, $CDCl_3$) δ_{ppm}

Sr. No	Ligands & complexes	1H NMR peaks				
		- NH_2 δ_{ppm}	>NH δ_{ppm}	Olefinic Proton 1H doublet δ_{ppm}	Olefinic Proton 1H doublet δ_{ppm}	Aromatic ring 8H Proton δ_{ppm}
1	(T_1H)	3.4	9.7	7.4	8.2	7.6-7.9
2	(T_2H)	3.38	9.8	7.5	8.2	7.6-8.1
3	$Pd(T_1H)_2Cl_2$	3.4	Absent	7.6	8.1-8.15	7.8-8.0
4	$Pd(T_2H)_2Cl_2$	3.38	Absent	7.6	8.1	7.6-8.1
5	$Pt(T_1H)_2Cl_2$	3.35	Absent	7.7	8.2	7.8-8.1
6	$Pt(T_2H)_2Cl_2$	3.5	Absent	7.4	8.1	7.8-8.2

Table-2: FTIR Spectrum of Ligands & complexes (in KBr)

Sr. No	Ligands & complexes	- NH_2 , >NH Stretching frequency in cm^{-1}	(>C=S) Stretching frequency in cm^{-1}	(>C=O) Stretching frequency in cm^{-1}	(>C=N) Stretching frequency in cm^{-1}	Aromatic ring Stretching frequency in cm^{-1}
1	(T_1H)	3400-3250	810	----	1581	1603
2	(T_2H)	3330-3185	811	----	1581	1595
3	$Pd(T_1H)_2Cl_2$	3227-3161	809	----	1558	1600
4	$Pd(T_2H)_2Cl_2$	3250-3100	813	-----	1555	1606
5	$Pt(T_1H)_2Cl_2$	3270-3179	811	----	1555	1603
6	$Pt(T_2H)_2Cl_2$	3280-3170	810	---	1508	1608

Table-3: Analytical and Physical Data for T₁H, T₂H, and their complexes

Sr. No	Free Ligands & complexes	Yield (%)	Melting Point (°C)	Molar Conductance Sm ² mol ⁻¹	Found (calculated) (%)					
					M	C	H	N	S	Molecular weight Found(Calcd)
1	(T ₁ H)	66	255-260	--	--	63.48 (64.16)	4.22 (4.69)	16.67 (16.55)	9.62 (9.43)	428 (439)
2	(T ₂ H)	57	230-235	--	---	63.68 (64.56)	4.28 (4.59)	16.77 (16.65)	9.52 (9.48)	354 (360.5)
3	Pd(T ₁ H) ₂ Cl ₂	40	295-298	195.2	12.11 (12.47)	50.34 (50.77)	3.16 (3.83)	13.38 (13.15)	7.56 (7.44)	1027 (1055)
4	Pd(T ₂ H) ₂ Cl ₂	42	285-288	190.82	12.03 (12.45)	50.44 (50.87)	3.26 (3.93)	13.58 (13.35)	7.68 (7.49)	879 (898)
5	Pt(T ₁ H) ₂ Cl ₂	41	295-300	190.23	20.45 (20.63)	46.38 (46.10)	3.79 (3.48)	11.66 (11.88)	6.74 (6.88)	1135 (1144)
6	Pt(T ₂ H) ₂ Cl ₂	40	280-284	185.73	21.48 (21.57)	46.78 (46.30)	3.88 (3.67)	11.36 (11.78)	6.44 (6.78)	968 (987)

ANTIBACTERIAL ACTIVITY

All the new synthesized compounds were screened for antibacterial activity [16] against four of the test organism viz *Escherichia coli* NCIM 2641 and *Staphylococcus aureus* MTCC 1144. For this screening plate diffusion assay method was used [17] [Spooner and Skyes 1972]. The antibacterial activities of the test agents were determined by measuring the diameter of the zone of inhibition in millimetre. Results as per Table No. 4 shows average of diameter of zone of inhibition of triplicate set. Test cultures used for test are pathogenic and normal flora, one is of Gram positive and another is of Gram negative group. The antibacterial data reveals that that the complexes were superior to the free ligands [18].

Table- 4 Antibacterial activities of Ligands and their complexes

S.N.	Sample	Test Culture	
		<i>Escherichia coli</i> NCIM 2641	<i>Staphylococcus aureus</i> MTCC 1144
Diameter of zone of inhibition [mm]			
1	T ₁ H	20	14
2	T ₂ H	Nil	13.5
3	[Pd(T ₁ H) ₂]Cl ₂	10.5	8.5
4	[Pd(T ₂ H) ₂]Cl ₂	Nil	11
5	[Pt(T ₁ H) ₂]Cl ₂	8	6.5
6	[Pt(T ₂ H) ₂]Cl ₂	7	Nil
Solvent control	DMSO	Nil	Nil
Std. Antibiotic	Streptomycin [10ug/disc]	15	14
	Penicillin [10 U/disc]	16	18

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