



Synthesis of some Novel Halogenated Platinum (II) Complexes of Active Schiff's Base Ligand Derived from 5-Bromo Isatin and Evaluation of their Antibacterial Activity

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ABSTRACT

This paper presents the synthesis and antibacterial studies some novel halogenated Platinum (II) complexes of active Schiff's base ligands of the type $[Pt(L_1H)_2]Cl_2$, $[Pt(L_2H)_2]Cl_2$ and $[Pt(L)_2]$ derived from 5-Bromo Isatin. Where L_1H = hydrazinecarbothiamide of 5-bromoindolinedione and L_2H = hydrazinecarboxamide of 5-bromoindolinedione. All complexes reported here had been characterised by 1H NMR and IR spectral studies. Molar conductance studies support the 1:2 natures of these complexes. Pt (II) complexes are diamagnetic in nature and showing square planer geometry. The IR spectral data reveals that both the Schiff's bases (L_1H and L_2H) behave as bidentate ligands and are co-ordinated to Pt (II) metal through the sulfur and hydrogenic nitrogen atom. All the new synthesized compounds were screened for antibacterial activity against four of the test organisms like *Bacillus pumilus*, *Micrococcus Lutes*, *E. coli* and *Salmonella abony*

Keywords: Schiff's base, Semicarbazone, Thiosemicarbazone, 5-bromo Isatin, *Bacillus pumilus*, *Micrococcus Lutes*, *E. Coli*, *Salmonella abony*

1. INTRODUCTION

Schiff's bases are an important class of ligands in co-ordination chemistry [1-2]. A large number of Schiff's bases and their metal complexes have been found to possess important biological and catalytic activity. Due to their great flexibility and diverse structural aspects, a wide range of Schiff bases have been synthesized and their complexation behaviour was studied [3-12].

Several studies have shown a growing interest in transition metal complexes of Schiff base ligands in past few decades. Co-ordination compounds are compounds containing one or more coordinate bonds, which is a link between a pair of electrons in which both electrons are donated by one of the atoms.

The metal complexes of semicarbazones and thiosemicarbazones have aroused considerable interest in view of their industrial and biological importance [13-17]. Many of these compounds possess a wide spectrum of medicinal properties.

Thiosemicarbazides and thiosemicarbazones react as chelating agents with transition metals ions by bonding through the sulfur and hydrogenic nitrogen atom. In the present investigation we have synthesized and characterized some new biologically active Schiff's base complexes of Platinum metals complexes in order to evaluate their antibacterial activity.

2. EXPERIMENTAL

2. 1. Preparation of Chalcones

The mixture of 0.1 M 5-Bromo Isatin and 50mL ethanol were stirred for 1 h [18-20]. Meanwhile the 25mL of 20% caustic soda solution was mixed with 0.1mol aromatic ketone. The above prepared solution was added slowly to ethanolic solution of bromoisatin maintaining the temperature of 15-20 °C.

The reaction mass was refluxed on water bath for 2-3 h. The progress of reaction was monitored by Thin Layer Chromatography (TLC) method. After completion of the reaction, the mixture was cooled on ice salt bath. It was filtered and washed with water and the resulting chalcone was re-crystallized with ethyl acetate.

2. 2. Preparation of Ligands

The ligands of hydrazinecarbothiamide (L_1H) of 5-Bromo Isatin and hydrazine-carboxamide (L_2H) of 5-Bromo Isatin are prepared as follows:

2. 2. 1 Preparation of hydrazinecarbothiamide (L_1H) of 5-bromoindolinedione

The 0.01 mol of chalcone was added to 25 mL of THF and 0.012 mol of thiosemicarbazide was added along with 5 g of sodium acetate [21-28]. The reaction mixture was then refluxed on water bath for 2-3 h.

The progress of reaction was monitored by TLC method. After completion of the reaction, the mixture was cooled on ice-salt mixture; it was then filtered and re-crystallized with alcohol.

2. 2. 2. Preparation of hydrazine-carboxamide (L₂H) of 5-bromoindolinedione

The mixture of 0.01 mol chalcone and 0.012 mol semicarbazide hydrochloride was added to 50 mL THF. To that 5g of sodium acetate was added. The reaction mixture was refluxed on water bath for 2-3 h.

The progress of reaction was monitored by TLC method. After completion of the reaction, the reaction mixture was cooled, filtered and the product obtained was re-crystallized by alcohol. The crystallized powder was further subjected to Silicagel column chromatography (2% EtoAc- Hexane) to get purified product.

2. 3. Preparation of [Pt (LH)₂]Cl₂ complexes

The 0.001 mol PtCl₂ was added to 0.002 mol ethanolic solution of ligand [29-31]. The reaction mixture was then heated under reflux for about 6 h in presence of few drops of concentrated HCl.

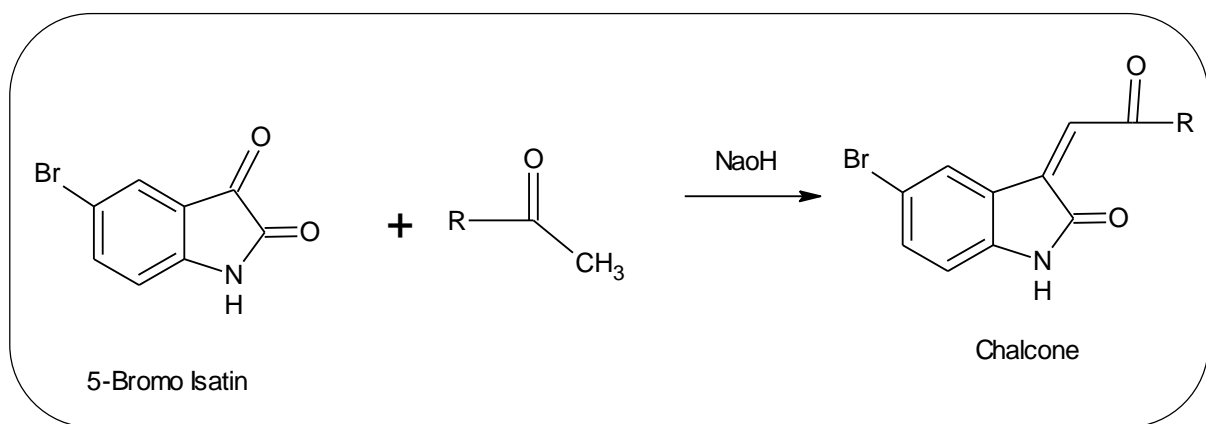
The reaction mixture was then cooled and filtered. The crystals obtained were washed several times with ice cold alcohol and dried in vacuum.

2. 4. Preparation of [Pt(L)₂] complexes

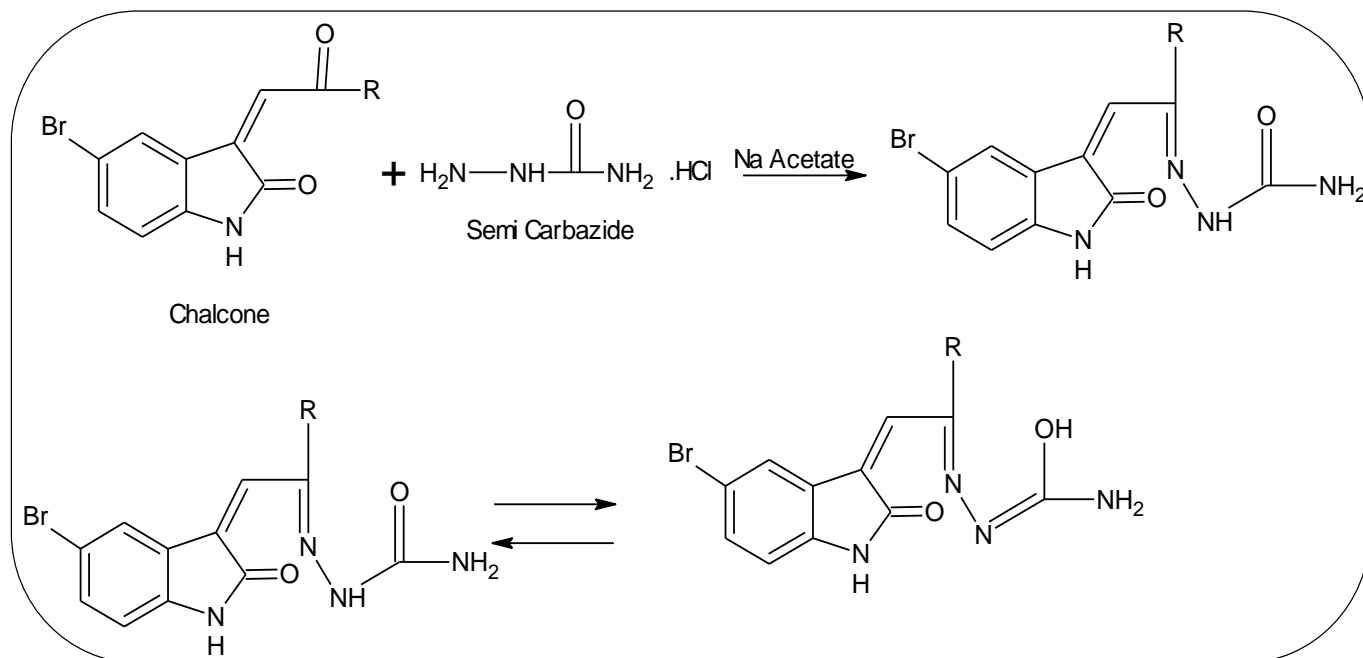
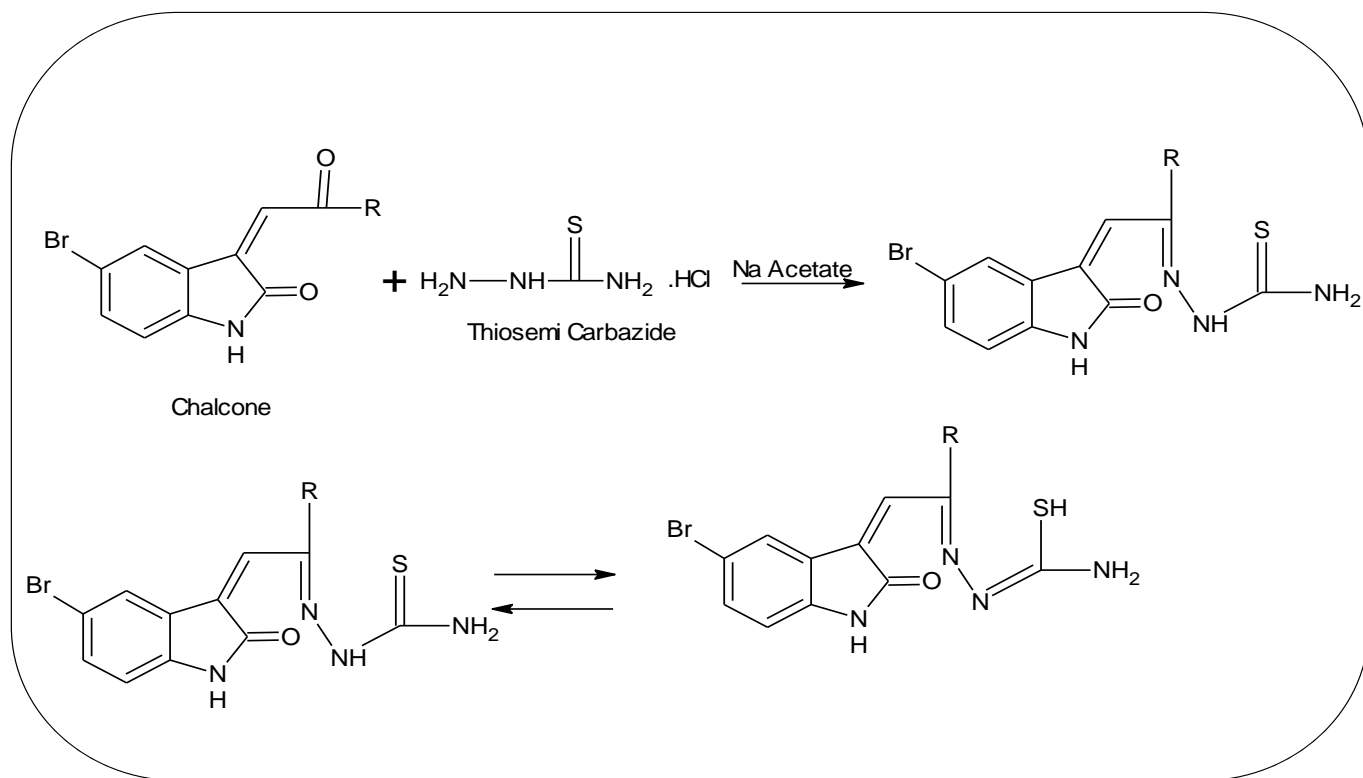
The 0.001 mol ethanolic solution of PtCl₂ was mixed with 0.002 mol ethanolic solution of ligands in 1:2 molar ratio [32]. NH₄OH was added drop wise to reaction mixture until it was weakly alkaline (pH 8.0).

The mixture was then stirred for 2-3 h and heated at 40 °C for 45 minutes. On cooling the complexes separated out were filtered, washed several times with alcohol and dried in vacuum.

Reaction Scheme:



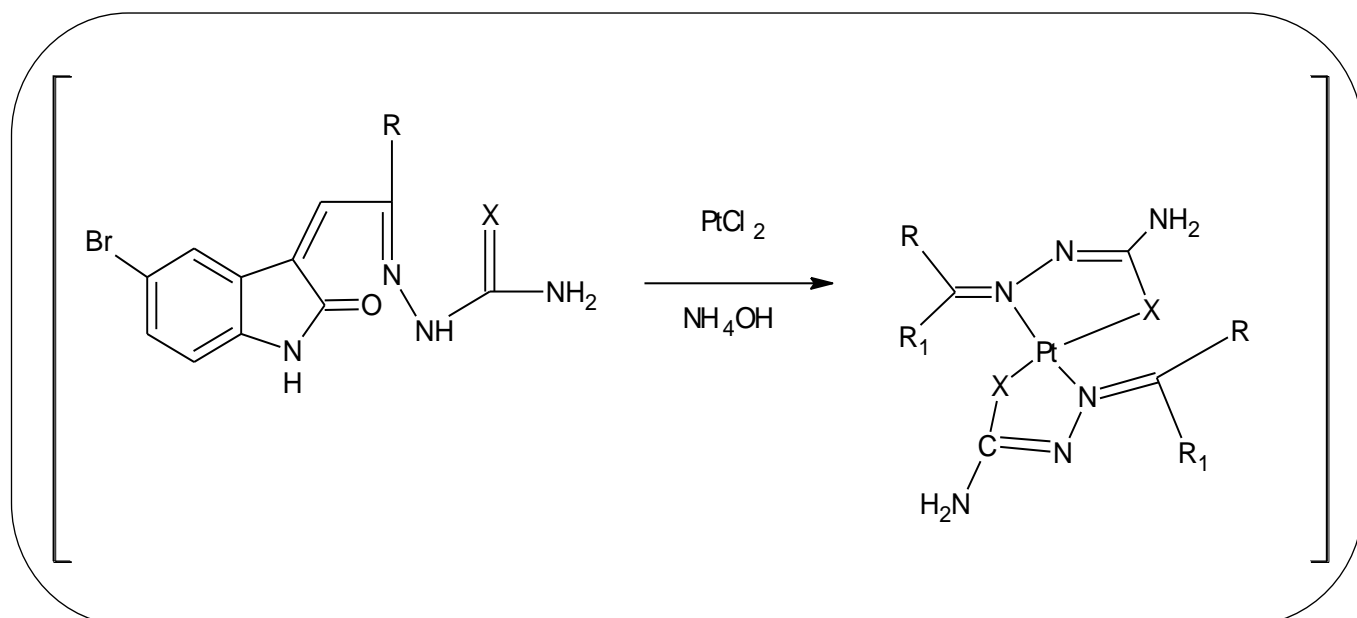
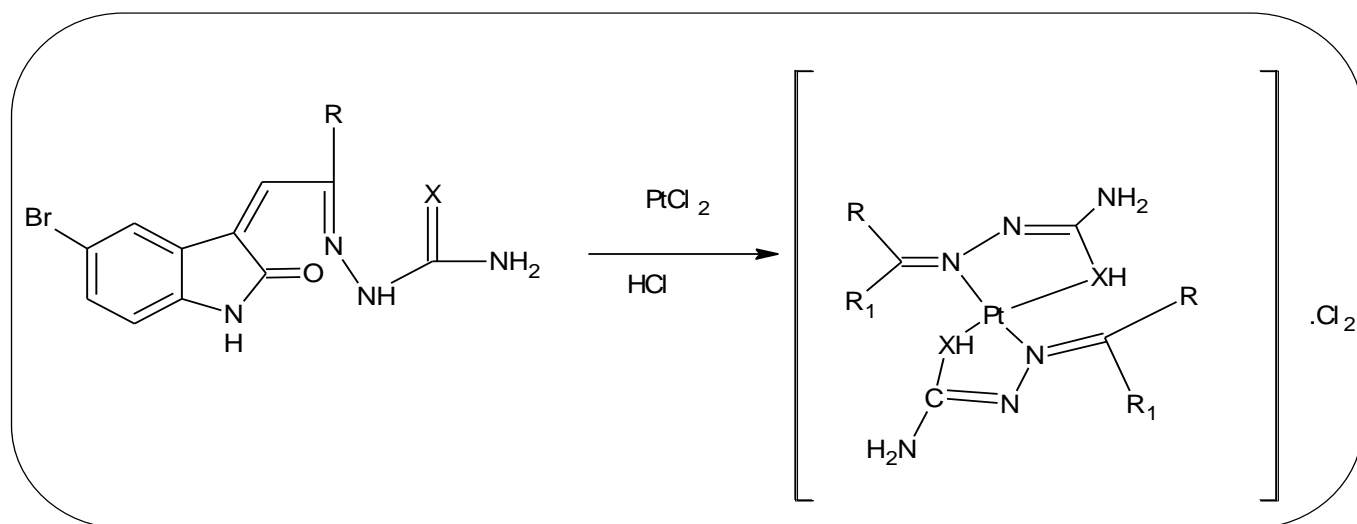
Scheme 1. Preparation of chalcones:
Where R = C₆H₅, C₆H₄CH₃, C₆H₄Cl, C₆H₄OCH₃



Scheme 2. Preparation of Ligands (L₁H) and (L₂H)
Product Codes

where: R = C₆H₅ L₂H-1
 R = C₆H₄CH₃ L₂H-2
 R = C₆H₄Cl L₂H-3
 R = C₆H₄OCH₃ L₂H-4

where: R = C₆H₅ L₁H-1
 R = C₆H₄CH₃ L₁H-2
 R = C₆H₄Cl L₁H-3
 R = C₆H₄OCH₃ L₁H-4



Scheme 3. Preparation of [Pt(LH)₂]Cl₂ and [Pt(L)₂] complexes

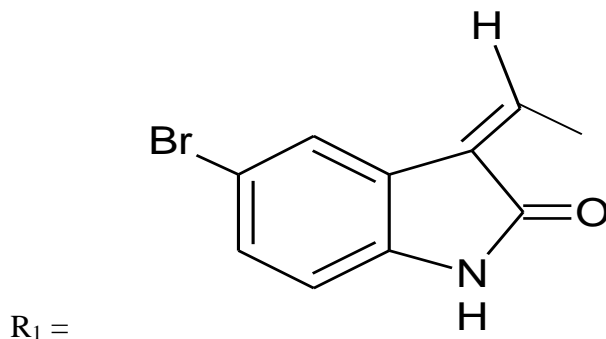
Product Code

X = S

X = O

where:

R = C ₆ H ₅	Pt(L ₁ H) ₂ Cl ₂ -1	Pt(L ₂ H) ₂ Cl ₂ -1
R = C ₆ H ₄ CH ₃	Pt(L ₁ H) ₂ Cl ₂ -2	Pt(L ₂ H) ₂ Cl ₂ -2
R = C ₆ H ₄ Cl	Pt(L ₁ H) ₂ Cl ₂ -3	Pt(L ₂ H) ₂ Cl ₂ -3
R = C ₆ H ₄ OCH ₃	Pt(L ₁ H) ₂ Cl ₂ -4	Pt(L ₂ H) ₂ Cl ₂ -4



For the entire experimental work the chemicals used were of analytical reagent (A.R.) grade purchased from S.D Fine chemicals (Mumbai) and were used after purification.

3. RESULT AND DISCUSSION

The ligand (L₁H): In the IR spectrum of ligand (L₁H) bands corresponding to -NH₂ and -NH groups appeared at 3463 and 3263 cm⁻¹ respectively [33]. The bands corresponding to ν(C = S) and ν(C=N) groups appeared at 818 and 1587 cm⁻¹. In the ligand (L₂H): the band corresponding to ν(C=O) appeared at 1711 cm⁻¹. On complexation the bands [34] corresponding to ν(C=N) and ν(C = S) (in case of thiosemicarbazone) are shifted towards lower side (ca.20-30 cm⁻¹).

This suggest that the ligand acts as a bidentate chelating agent coordinating through nitrogen of ν(C=N) group and sulphur of ν(C = S) group. In case of semicarbazone the bands corresponding to ν(C=N) and ν(C = O) are shifted towards lower side (ca.20-30 cm⁻¹) suggest that the ligand acts as a bidentate chelating agent coordinating through nitrogen of ν(C=N) group and oxygen of ν(C = O) group.

In the ¹H NMR spectrum of ligands and complexes the most common NMR multiplets for aromatic rings protons are found to be resonating around δ7.5-δ8.4 whereas the broad singlet for >NH and -NH₂ group protons appeared around δ3.3- δ3.6. A sharp singlet peak for olefinic protons (>C=C-H) group in ligands as well as in the complexes are observed in the range of δ7.1- δ7.4.

The distinguishing singlet peak around δ9.0 in ligands are due to (>C=N- group) azomethine protons but in the complexes this singlet was shifted to downfield and appears at δ9.3 due to co-ordination thorough >C=N-group.

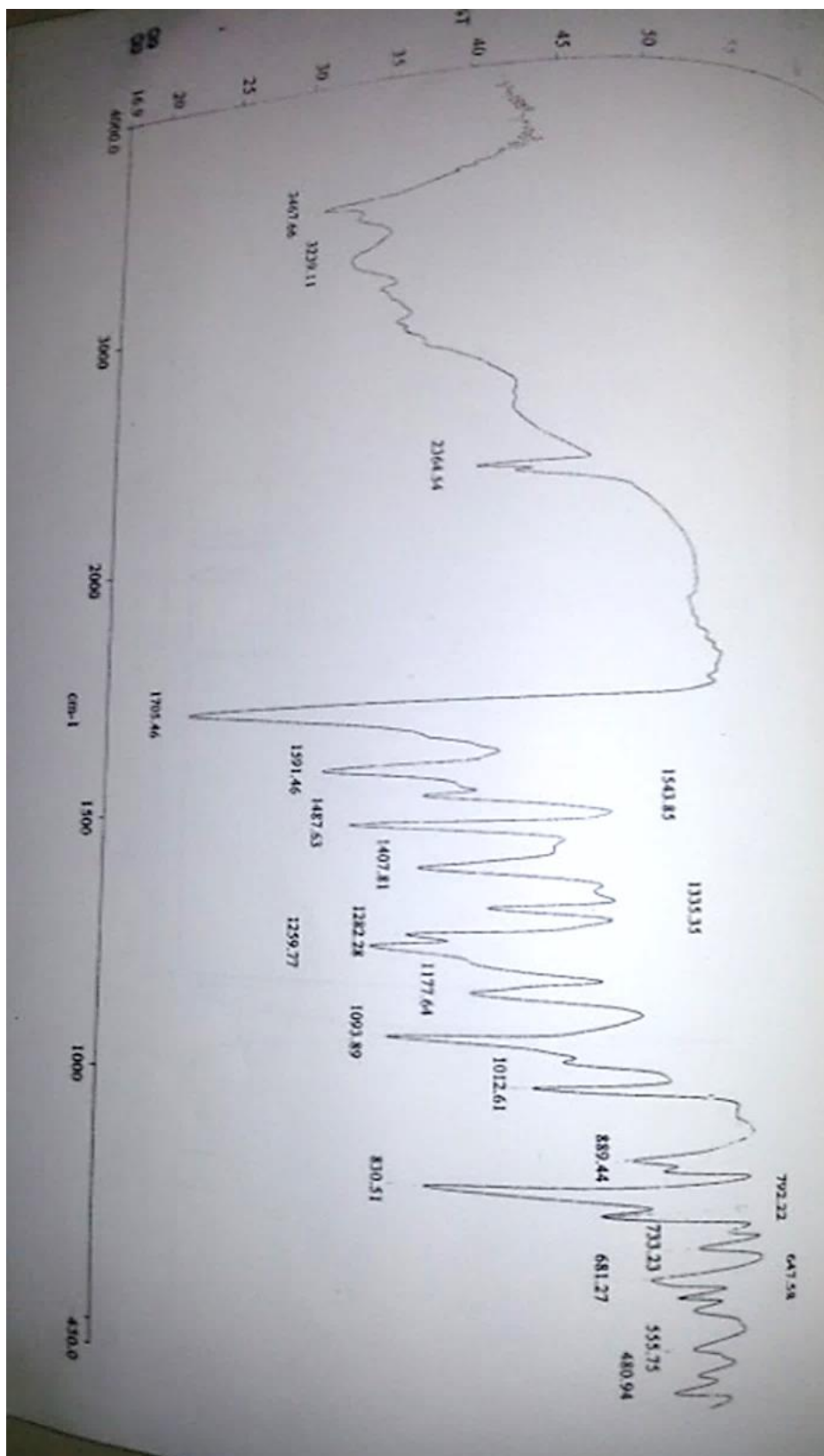


Figure 1. IR spectrum of Ligands L₂H

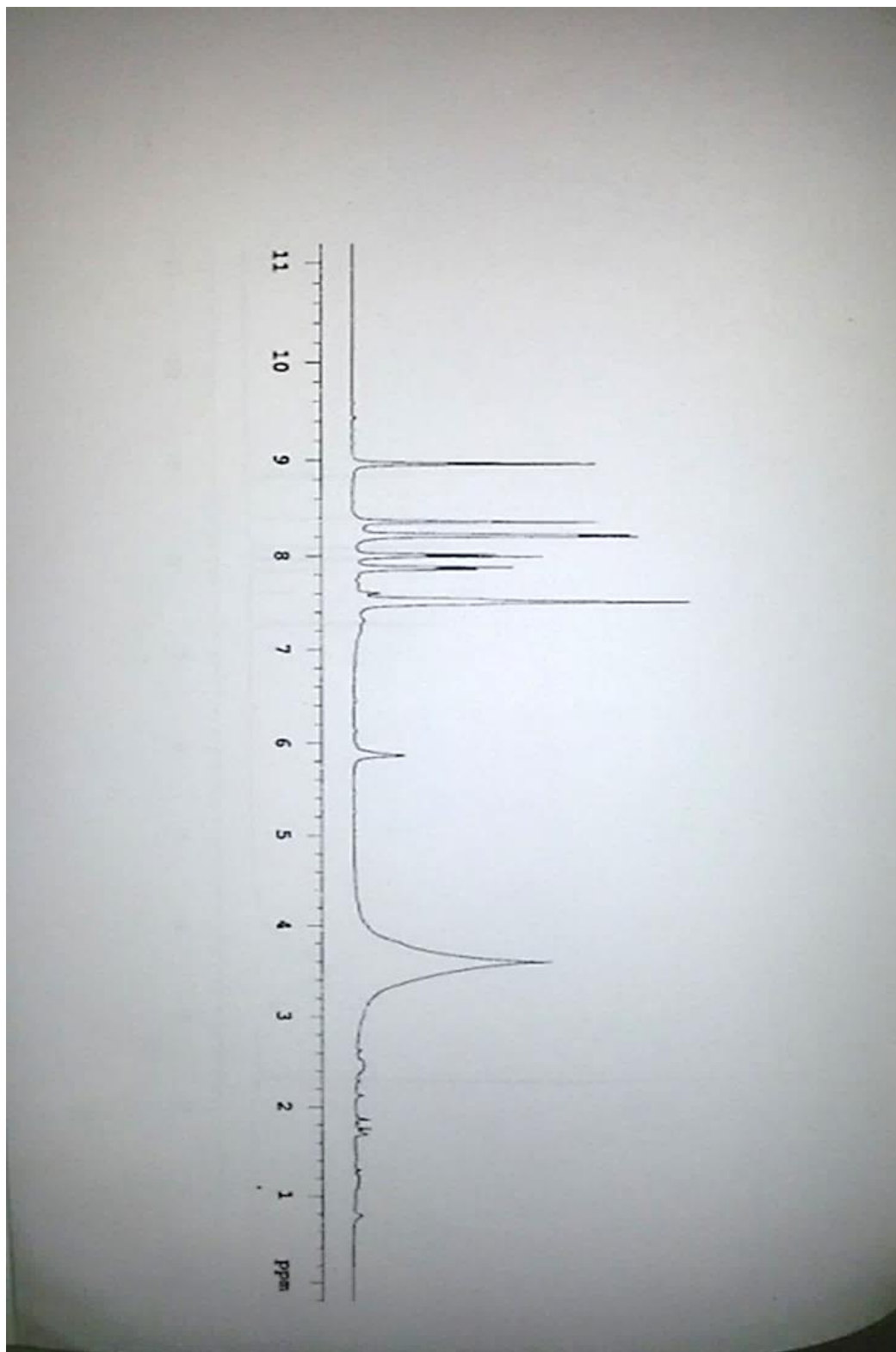


Figure 2. NMR spectrum of Ligands L₂H

^1H NMR (400 MHz, CDCl_3) δ_{ppm} of Chalcone:

$-\delta 3.6$ Brs S ($>\text{NH}$), $\delta 7.5$ S (1H olefinic proton), $\delta 7.2-8.2$ M (7H aromatic ring proton).

^1H NMR (400 MHz, CDCl_3) δ_{ppm} of Lingand (L_1H):

$-\delta 3.5$ Brs S 4H ($>\text{NH}$ & NH_2), $\delta 7.6$ S (1H olefinic proton), $\delta 7.1-9.1$ M (7H aromatic ring proton).

^1H NMR (400 MHz, CDCl_3) δ_{ppm} of complexes $[\text{Pt}(\text{L}_1\text{H})_2]\text{Cl}_2$:

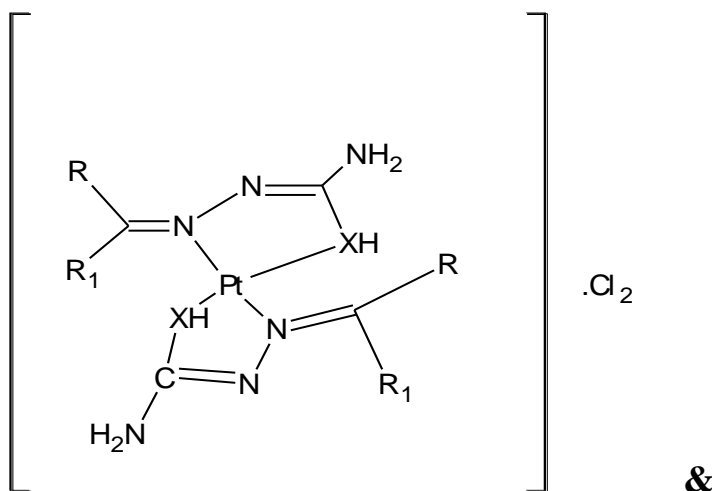
$\delta 3.5$ Brs S 4H ($>\text{NH}$ & NH_2), $\delta 7.6$ S (1H olefinic proton), $\delta 7.2-8.8$ M (7H aromatic ring proton). $\delta 9.3$ S 1H ($=\text{N}-\text{H}$, azomethine)

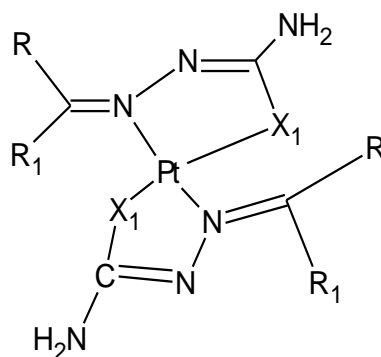
3. 1. Antibacterial Activity

All the new synthesized compounds were screened for antibacterial activity [35] against four of the test organisms like *Bacillus pumilus*, *Micrococcus Lutes*, *E. Coli* and *Salmonella* abony. For this screening plate diffusion method was used [36].

3. 2. Plate Diffusion Method

The 25mg compound was dissolved in methanol/DMF and phosphate buffer (2:8). The compounds were taken at 1000 mcg/mL per hole of petridish containing M. agar medium or antibiotic assay medium No.11. The hole in the medium should be more than 2.5 mm and 7.8 mm diameter. These holes in the petridish were then filled with antibacterial solution. The plates were then placed in refrigerator for 10 °C, at 15 °C for diffusion of the compounds and then incubated for 24 hrs at 37 °C. After the incubation period was over the zone of inhibitions were measured in mm as distance from source and are reported. Bacterial activity of the ligand and their metal complexes are recorded in the Tables 1 and 2 against Pathogenic bacteria. The free ligand and their respective metal chelates were screened against gram positive bacteria like *Bacillus Pumillius* and *Micrococcus*; gram negative bacteria like *E. colli* and *Salmonella* to evaluate their potential as antimicrobial agents. The results are quite promising. The antibacterial data reveals that complexes are ligands [37, 38]. It is also noted that sulphur containing ligand as well as their complexes are more active than their oxygen containing counterpart.





[Pt(LH)₂]Cl₂ and [Pt(L)₂] complexes

Table 1. Antibacterial activity of the ligand and their Pt-metal complexes.

Sr. No	R	X	Bacillus Pumillius	Micrococcus	E. colli	Salmonella
1	Pt(L ₁ H) ₂ Cl ₂ -1	S	4.10	3.40	2.90	1.70
2	Pt(L ₁ H) ₂ Cl ₂ -2	S	5.40	3.75	3.20	3.30
3	Pt(L ₁ H) ₂ Cl ₂ -3	S	5.80	3.95	3.90	2.85
4	Pt(L ₁ H) ₂ Cl ₂ -4	S	1.20	1	0.40	-
5	Pt(L ₂ H) ₂ Cl ₂ -1	O	3.30	3.70	2.45	1.90
6	Pt(L ₂ H) ₂ Cl ₂ -2	O	4.80	3.40	3.10	3.40
7	Pt(L ₂ H) ₂ Cl ₂ -3	O	3.90	3.60	3.80	3.60
8	Pt(L ₂ H) ₂ Cl ₂ -4	O	1.30	0.50	0.30	0.20

Table 2. Antibacterial activity of the ligand and their Pt-metal complexes.

Sr. No	R	X	Bacillus Pumillius	Micrococcus	E. colli	Salmonella
1	Pt(L ₂) ₂ -1	S	3.10	2.35	2.95	-
2	Pt(L ₂) ₂ -2	S	4.20	4.3	3.10	2.90
3	Pt(L ₂) ₂ -3	S	6.00	5.90	4.80	3.25
4	Pt(L ₁) ₂ -4	S	1-10	-	-	-
5	Pt(L ₂) ₂ -1	O	2.30	1.95	1.7	0.32

6	Pt(L ₂) ₂ -2	O	2.80	2.35	1.8	1.0
7	Pt(L ₂) ₂ -3	O	4.10	3.60	2.80	2.65
8	Pt(L ₂) ₂ -4	O	0.95	0.2	-	-

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