

SYNTHESIS AND ANTIBACTERIAL STUDIES OF SOME Pt(II) AND Ni(II) COMPLEXES OF SEMICARBAZONE SCHIFF'S BASE DERIVED FROM SOME CHALCONES

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ABSTRACT

The therapeutic importance of semicarbazone and thiosemicarbazone group containing Schiff's base ligands has promoted the selection of this class of ligands and their complexes for the study. The present study describes the synthesis, characterisation and antibacterial investigations of Pt(II) and Ni(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 Pt(II) and Ni(II) metal through the oxygen 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, semicarbazone, *Escherichia coli* NCIM 2641, *Staphylococcus aureus* MTCC 1144

Introduction

The synthesis and structural investigation of some Platinum complexes with Semicarbazone and Thiosemicarbazones based active Schiff's base ligands as well as their coordination complexes are useful because of their versatile properties such as pharmacological, antibacterial [1], antifungal [2], antitumor [3] and antimalarial activities. Numbers of Schiff bases ligands and their respective complexes have been synthesized for studying their complexation behaviour and evaluation various activities such as antimicrobial, biological [4]. Most of the quinazoline derivatives possessing wide range of biological and antimicrobial activities were investigated and reported in various research studies [5]. Taking into consideration all above points and especially the important of quinazoline moiety in the present research work we have synthesized various semicarbazone and thiosemicarbazone 3-phenylquinazoline-2,4(1H,3H)-dione active

Schiff's base ligands and their Pt(II) and Ni(II) complexes in order to explore the biological activities and importance as ligands for various transition metal complexes.

Materials and Methods

All chemicals used were of A.R. grade purchased from S.D Fine chemicals (Mumbai) and were used further purification. This experimental part divided into six parts,

A) Preparation of 3-phenylquinazoline-2,4(1H,3H)-dione(L₁):

In the two necked round bottom flask, a mixture of Anthranilic acid (0.1 mole) and Phenyl isocyanate (0.1 mole) in 40 mL ethanol were taken and stirred on the magnetic stirrer at room temperature for about 30 minutes and the resultant reaction mass was refluxed on water bath for 3 hrs. The completion of reaction was monitored by TLC and the crude product obtained was recrystallized with ethanol.

B) Preparation of Chalcones of 3-phenylquinazoline-2,4(1H,3H)-dione(C-1) from 4-nitroacetophenone:

In the three necked round bottom flask, a mixture of 3-phenylquinazoline-2,4(1H,3H)-dione[7-10] (0.1M) in 40mL ethanol were taken and stirred for one hour. Meanwhile the solution of 20% NaOH(30ml) added separately in 4-nitro Acetophenone(0.11M) and temperature of system was maintained at 0-4 °C, the prepared solution was then added slowly to ethanolic solution of 3-phenylquinazoline-2,4(1H,3H)-dione maintaining temperature 15-20°C and the reaction mass was refluxed on water bath for 2-3 hrs., the completion of reaction was monitored by TLC. The product obtained was filtered and washed with water. Chalcones of 3-phenylquinazoline-2,4(1H,3H)-dione[C-1] obtained was recrystallized with ethanol.

C) Preparation of hydrazinecarbothiamide (L₁T) of (2E)-2-[-(4-substituted Phenyl)-2-oxoethylidene]-3-2,3-dihydroquinazoline-4(1H)-one :

The chalcones [C-1] [13-16] (0.01mol) was added to 40 ml of THF & thiosemicarbazide (0.012mol) was added along with sodium acetate (5gm) reaction mixture was then refluxed on water bath for 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.

D) Preparation of hydrazine-carboxamide (L₁C) of (2E)-2-[-(4-substituted Phenyl)-2-oxoethylidene]-3-2,3-dihydroquinazoline-4(1H)-one :

The mixture of chalcones [C-1] (0.01mol) & semicarbazide hydrochloride (0.012mol) was added to 40ml THF. To that sodium acetate (5gm) was added. The reaction mixture was refluxed on water bath for 3 hrs. After completion of reaction (monitored by TLC); the reaction mixture was cooled, filtered & the product obtained was recrystallized by alcohol. The crystallized powder was further subjected to Silicagel column chromatography (2% EtoAc- Hexane) to get purified product.

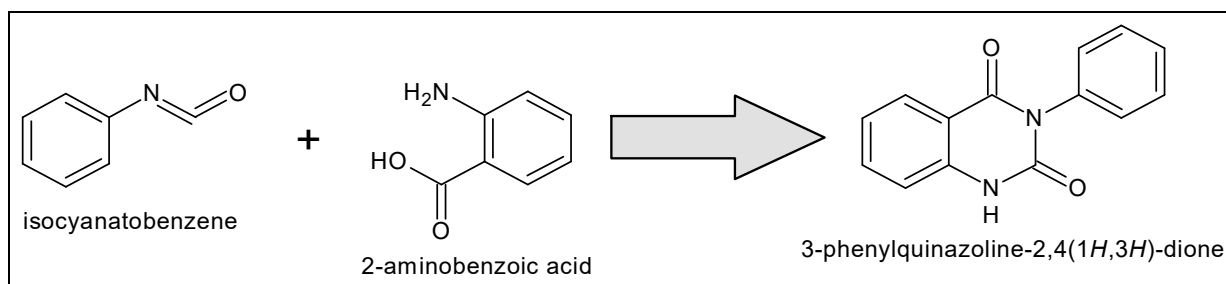
E) Preparation of [Pt(L₁T)₂]Cl₂ and [Pt(L₁C)₂]Cl₂ complexes:

PtCl₂ (0.001mol.) was added to an ethanolic [11-12] solution of ligands [L₁T] and [L₁C] (0.002mol.). The reaction mixture was then heated under reflux for about 6 hrs in presence of few drops of concentrated HCl. The reaction mixture was then cooled and filtered. The crystal obtained were washed several times with ice cold alcohol and dried in vacuum.

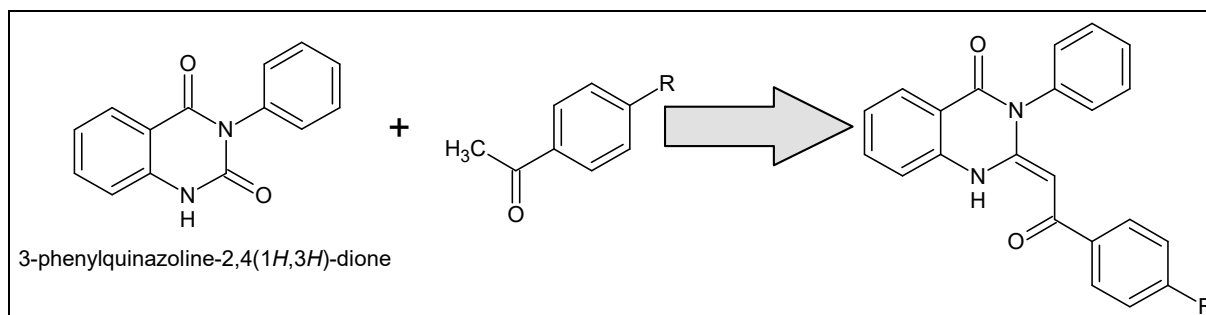
F) Preparation of [Ni(L₁T)₂]Cl₂ and [Ni(L₁C)₂]Cl₂ complexes:

PtCl₂ (0.001mol.) was added to an ethanolic solution of ligand [L₁T] and [L₁C] (0.002mol.). The reaction mixture was then heated under reflux for about 6 hrs in presence of few drops of concentrated HCl. The reaction mixture was then cooled and filtered. The crystal obtained were washed several times with ice cold alcohol and dried in vacuum.

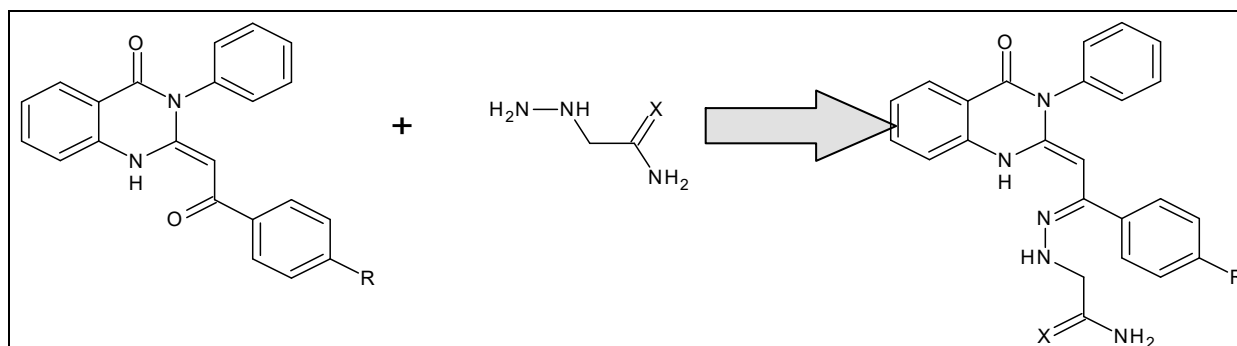
Reaction Scheme



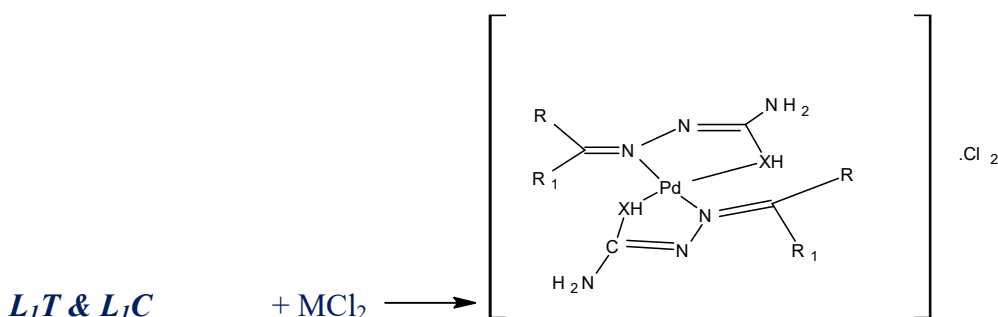
Schme-1 Preparation 3-phenylquinazoline-2,4(1H,3H)-dione(L₁)



Schme-2 Preparation of (2E)-2-[-(4-substituted Phenyl)-2-oxoethylidene]-3-2,3dihydroquinazoline-4(1H)-one (C-1)
Where R = H,NO₂



Schme-3 Preparation of (2E)-2-[-(4-substituted Phenyl)-2-oxoethylidene]-3-2,3dihydroquinazoline-4(1H)-one(L₁T) & (L₁C)
Where R = H,NO₂ and X=S, O



Schme-4 Preparation of $[M(L_1T)_2]Cl_2$ & $[M(L_1C)_2]Cl_2$ complexes
Product Code

X=S X=O
Where R = H,NO₂ M = Pt(II),Ni(II)
R₁ = 3-phenylquinazoline-2,4(1H,3H)-dione(L₁)

Result and Discussion

The compounds (L₁T & L₁C) : In the IR spectrum [17-20] of ligand (L₁T) bands corresponding to -NH₂ & -NH groups appeared at 3464 and 3270 cm⁻¹ respectively. The bands corresponding to ν(C=S) and ν(C=N) groups appeared at 811 & 1585 cm⁻¹. In (L₁C): the

band corresponding to ν(C=O) appeared at 1710 cm⁻¹. In the ¹H NMR spectrum of (L₁T & L₁C) the most common NMR multiplets for aromatic rings protons are found to be resonating around δ 6.9-δ 8.7 whereas the broad singlet for >NH & -NH₂ group protons appeared around δ 3.4- δ 3.8. a sharp singlet peak for olefinic protons (>C=C-H) group in

are observed in the range of $\delta 7.3$ - $\delta 7.9$ while $>NH$ quinazoline ring singlet appears at $\delta 9.9$. The distinguishing singlet peak around $\delta 10.4$ ($>C=N$ -group) azomethine protons singlet was shifted to downfield. The distinguishing singlet peak around $\delta 9.9$ ($>C=N$ -group) for azomethine protons observed in ligands was completely disappears in the complexes due to co-ordination thorough $>C=N$ -group indicates the formation of Platinum and Nickel complex. The 1H NMR and FTIR spectrums and antibacterial activities of synthesized

compounds L_1 , C-1, L_1T and L_1C and their complexes were reported in Table -1, 2 & 3

Antibacterial Activity

All the new synthesized compounds were screened for antibacterial activity [21-24] against four of the test organisms viz *Escherichia coli* NCIM 2641 and *Staphylococcus aureus* MTCC 1144. For this screening plate diffusion assay method was used.

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

Sr. No	compounds	$-NH_2$ δ_{ppm}	$>NH$ or $>SH$ δ_{ppm}	Olefinic Proton 1H singlet δ_{ppm}	$>NH$ quinazoline ring singlet δ_{ppm}	Aromatic ring 8H Proton δ_{ppm}
1	L_1	--	--	--	---	7.0-7.9
2	C-1	---	--	7.8	9.8	6.9-7.7
3	L_1T	3.4	10.4	7.7	9.9	7.7-8.2
4	L_1C	3.8	10.4	7.6	9.8	7.0-7.8
5	$[Pt(L_1T)_2]Cl_2$	3.4	11.2	7.7	9.9	7.7-8.2
6	$[Pt(L_1C)_2]Cl_2$	3.4	11.4	7.5	9.8	7.6-8.1
7	$[Ni(L_1T)_2]Cl_2$	2.8	11.2	7.6	9.8	7.0-7.8
8	$[Ni(L_1C)_2]Cl_2$	2.5	absent	7.6	9.9	7.0-7.7

Table-2: FTIR Spectrum (in KBr):

Sr. No	compounds	$-NH_2, >NH$ Stretching frequency $incm^{-1}$	$(>C=S)$ Stretching frequency $incm^{-1}$	$(>C=O)$ Stretching frequency $incm^{-1}$	$(>C=N)$ Stretching frequency $incm^{-1}$	Aromatic ring Stretching frequency $incm^{-1}$
1	L_1	3400-3250	-----	1673	---	1603
2	C-1	3427-3279	----	1655	---	1591
3	C-2	3330-3185	-----	1680	---	1595
4	L_1T	3300-3195	811	1655	1580	1603
5	L_1C	3227-3161	----	1668	1558	1600

Table- 3 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	L_1T	5.7	8
2	L_1C	4.7	11.5
3	$[Pt(L_1T)_2]Cl_2$	7	7.5
4	$[Ni(L_1T)_2]Cl_2$	5.1	8
5	$[Pt(L_1C)_2]Cl_2$	7	Nil
6	$[Ni(L_1C)_2]Cl_2$	3.9	7
Solvent control	DMSO	Nil	Nil
Std. Antibiotic	Streptomycin [10ug/disc]	15	14
	Penicillin [10 U/disc]	16	18

Conclusion

The antibacterial studies of ligands and their complexes shows that the enhanced activity towards microorganism as compared to free ligands. We also observed that the sulphur containing ligands as well as their complexes were more reactive than their oxygen counterparts.

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