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SYNTHESIS, STRUCTURAL AND BIOLOGICAL SCREENING OF SOME ORGANORHODIUM (I) COMPLEXES LIGATED BY HETEROCYCLIC THIOAMIDE

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ABSTRACT

Organorhodium (I) complexes ligated by substitution at various locations in phenyl group of 1-phenyl tetrazoline-5-thione have been prepared and the identities of complexes are deduced by elemental analysis, magnetic conductivity measurements, electronic, IR and ^{1}H NMR spectral studies. The *in vitro* antimicrobial activity of the investigated compounds was tested against the bacteria such as *S. aureus*, *B. Subtilis* and *E. Coli* and fungi *A. niger* and *F. heterosporium*. The data reveal that all complexes are more active than free ligand molecules.

Key words: Organorhodium (I), Heterocyclic thioamides, Antimicrobial activity.

INRODUCTION

Tetrazoles are well known for their varied spectrum of pharmacological activities[1]. Antimicrobial activities of tetrazoles having thioamide group (HNCS) against *staphylococcus aureus* and *Escharichia coli* have been reported by Cowper et al.[2] The present investigation aims at structural, spectral and biological evaluation of some organorhodium (I) complexes ligated by 1-substituted phenyl-tetrazoline-5-thione. The phenyl ring was substituted at various locations with methyl and chloro groups to correlate the electronic effect of such substituents on the magnitude of the antimicrobial activity and antifungal activity. The identities of all organorhodium (I) complexes have been established on the basis various physicochemical studies and IR, UV-Vis and ^{1}H NMR spectral analysis.

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EXPERIMENTAL

Melting points are uncorrected. All the chemicals used were of AR or CP grade. 1-substituted tetrazoline-5-thione was prepared by the method of Liebere et al.[3] and organorhodium (I) complexes were prepared by our previous method reported in literature[4]. Elemental analysis, magnetic measurements, molecular weight determination, IR, UV-Vis and ^{1}H NMR spectral data were obtained as reported in our previous work[5]. Oxidation state of rhodium in complexes was verified by titrating complexes with ceric ammonium sulphate using ferroin as indicator[6]. All compounds were titrated for two electron charge.

Analysis

S. No. 1: [RhCl(CO)(Pϕ_3)(O-CH_3-L) : Yellowish Brown (M. Pt = 157^{o}C)

Calculated (%) for **$RhC_{27}H_{23}N_4OPSCl$** : C, 52.21; H, 3.70; N, 9.02; Rh, 16.59;

Found (%) : C, 52.02; H, 3.73; N, 9.30; Rh, 16.80.

S. No. 2: [RhCl(CO)(Pϕ_3)(m-CH_3-L) : Yellowish Brown (M. Pt = 185^{o}C)

Calculated (%) for **$RhC_{27}H_{23}N_4OPSCl$** : C, 52.21; H, 3.70; N, 9.02; Rh, 16.59;

Found (%) : C, 52.31; H, 3.72; N, 9.31; Rh, 16.78;

S. No. 3: [RhCl(CO)(Pϕ_3)(P-CH_3-L) : Brown (M. Pt = 190^{o}C) :

Calculated (%) for **$RhC_{27}H_{23}N_4OPSCl$** : C, 52.21; H, 3.70; N, 9.02; Rh, 16.59;

Found (%) : C, 52.32; H, 3.72; N, 9.30; Rh, 16.68;

S. No. 4: [RhCl(CO)(Pϕ_3)(2,6-Me_2-L) : Brown (M. Pt = 201^{o}C) :

Calculated (%) for **$RhC_{27}H_{23}N_4OPSCl$** : C, 52.21; H, 3.70; N, 9.02; Rh, 16.59;

Found (%) : C, 52.25; H, 3.69; N, 9.11; Rh, 16.56;

S. No. 5: [RhCl(CO)(Pϕ_3)(P-Cl-L) : Yellowish Brown (M. Pt = 167^{o}C)

Calculated (%) for **$RhC_{26}H_{20}N_4OPSCl_2$** : C, 48.67; H, 3.12; N, 8.73; Rh, 16.06;

Found (%) : C, 48.85; H, 3.21; N, 8.78; Rh, 16.30;

S. No. 6: [RhCl(CO)(Pϕ_3)(m-Cl-L) : Yellowish Brown (M. Pt = 157^{o}C)

Calculated (%) for **$RhC_{26}H_2ON_4OPSCl_2$** : C, 48.67; H, 3.12; N, 8.73; Rh, 16.06;

Found (%) : C, 48.68; H, 3.14; N, 8.68; Rh, 16.02;

S. No. 7: [RhCl(CO)(Pϕ_3)(O-Cl-L) : Yellowish Brown (M. Pt = 175^{o}C)

Calculated (%) for **$RhC_{26}H_2ON_4OPSCl_2$** : C, 48.67; H, 3.12; N, 8.73; Rh, 16.06;

Found (%) : C, 48.66; H, 3.21; N, 8.80; Rh, 16.10;

RESULTS AND DISCUSSION

All solid products isolated after substitution reaction with $[RhCl(CO)(P\phi_3)_2]$[7] by 1-substituted tetrazoline-5-thione yielded the complexes having general formula [RhCl (CO) (Pϕ_3) (ligand)]. Analytical results were satisfactory and supported the proposed stoichiometry. All complexes were diamagnetic indicating Rh^+ (d^8) species in square planar structure and isostructural with precursor complex. The determination of univalent oxidation state of rhodium in complexes was further verified by titrating complexes with ceric ammonium sulphate using ferroin as indicator[6]. The molar conductance of complexes were found to be less than 10 $\wedge^{-1}$ cm^2 mol^{-1} suggesting non-electrolyte nature of complexes.

Electronic spectra of complexes display a very broad band of very strong intensity between 24690-24000 cm^{-1} assigned to charge transfer band ($T_{2g} \rightarrow \pi^*$). The other ligand field bands are obscured due to strong reducing character of Rh^+ species. These observations are in agreement with our previous work[8-10].

IR Spectra

All derivatives of 1-substituted tetrazoline-5-thione contain thioamide group (HNCS) and give rise to four characteristics band between 1500-805 cm^{-1}.[11-13] A comparison of the IR spectral bands of ligands and complexes and considering normal coordinate analysis (N.C.A) of thioamides[14], formation of strong Rh – S bond is indicated. Thioamide band IV of ligands mainly due to $\nu_{C\,S}$, undergoes red shift of 35-55 cm^{-1} in all complexes suggesting bonding through thione sulphur of ligand[15]. Bonding through sulphur is further supported by the presence of new bands at 355 ± 5 cm^{-1} (ν_{sym} ν_{Rh-S}) and 335 ± 5 ($\nu_{sym\ Rh-S}$) in the spectra of complexes.[15] New bands around 420-425 cm^{-1} in the spectra of complexes was assigned due to ν_{Rh-P} modes. Non-ligand bands due to coordinated Pϕ_3, CO and coordinated chlorine atom was also observed as our previous report[15].

The bonding through imino nitrogen atom of ligands was ruled out considering blue shift (~ 15-20 cm^{-1}) of thioamide band I and ν_{N-H} of ligands[11-13].

^{1}H NMR Spectra

The metal-ligand bonding is further substantiated by the comparison of ‘H NMR spectra of ligands and corresponding complexes.

The complexes display signals in the δ 8.12-8.88 ppm range due to aromatic proton of $P\phi_3$[16,25].

The phenyl protons of 1-substituted tetrazoline-5-thione appears as broad multiplet in region δ7.30-8.30 ppm on complexation (Table 1).

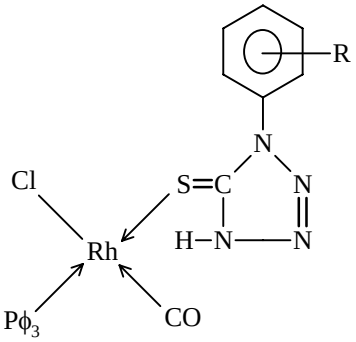
Table 1: Major spectral data of ligands and complexes

Compds.	IR (cm^{-1})		^1H NMR (ppm)			UV-Vis (cm^{-1})
	Thioamide band IV	**ν_{asym} Rh-S (ν_{sym} Rh-S)**	**Imino proton**	**Methyl protons**	**Phenyl protons**	**λ_{max} (assignment)**
O-CH_3-L (Ligand)	810 m	– (–)	1.25	2.40	7.30-7.95	33005 ($\pi \rightarrow \pi^*$) 24690 ($n \rightarrow \pi^*$)
Complex (S. No. 1)	780 m	355 w 335 w	1.25 + 2.50	2.94	7.3	37040 (CT Band) 26660 ($T_{2g} \rightarrow \pi^*$)
m-CH_3-L (ligand)	790 s	– (–)	1.20	2.25	7.5	33550 ($\pi \rightarrow \pi^*$) 24690 ($n \rightarrow \pi^*$)
Complex (S. No. 2)	755 m	350 w (340 w)	1.25	3.8	7.5	38460 (CT Band) 28570 ($T_{2g} \rightarrow \pi^*$)
P-CH_3-L (ligand)	810 m	– (–)	1.25	2.40	7.30-7.92	33330 ($\pi \rightarrow \pi^*$) 24875 ($n \rightarrow \pi^*$)
Complex (S. No. 3	750 m	360 w 340 w	1.50 + 2.50	2.95	7.4	36360 (CT Band) 26315 ($T_{2g} \rightarrow \pi^*$)
P-Cl-L (ligand)	780 m	– (–)	1.29	–	7.41-8.30	34445 ($\pi \rightarrow \pi^*$) 24815 ($n \rightarrow \pi^*$)
Complex (S. No. 5)	740 m	352 w 335 w	1.40	–	7.28-7.80	37735 (CT Band) 29410 ($T_{2g} \rightarrow \pi^*$)
O-Cl-L (ligand)	790 s	– (–)	1.25	–	7.50-9.75	32895 ($\pi \rightarrow \pi^*$) 24570 ($n \rightarrow \pi^*$)
Complex (S. No. 7)	755 m	355 w 340 w	1.50	–	7.4	37880 (CT Band) 28985 ($T_{2g} \rightarrow \pi^*$)
m-Cl-L (ligand)	785 s	– (–)	1.28	–	7.45	20890 ($\pi \rightarrow \pi^*$) 24660 ($n \rightarrow \pi^*$)
Complex (S. No. 6)	750 m	360 w 340 w	1.45	–	7.55-8.85	38450 (CT Band) 28580 ($T_{2g} \rightarrow \pi^*$)

L = 1-phenyl tetrazoline-5-thione

The broad nature of peak may be due to large quadrupole resonance broadening effect of tetrazole nitrogen atoms[17]. The imino proton of ligands remains almost at the same position on coordination to rhodium (I) and imino proton is intact on complexation (Table 1). The broad nature and splitting of imino proton signal indicate different magnetic environment in the complexes and close proximity of N-H group with coordinated chlorine atom. These observations are consistent with conclusion drawn from IR spectra.

Thus, on the basis of physico-chemical IR, UR-Vis and ^{1}H NMR spectral data the following tentative structure of complexes may be assigned:



Tentative square planar structure of [RhCl(CO)(Pϕ_3)(ligand)]
(R = o-CH_3-, m-CH_3-, p-CH_3-, o-Cl, m-Cl & P-Cl)

Antimicrobial activity

In vitro antimicrobial activity of lignads and metal complexes have been tested against the bacteria *s. aureus* and *bacillus* subtilis using streptomycin as standard drug for comparison under similar conditions using peptone beaf extract and agar medium. The synthesized compounds have also been evaluated for their antifungal activity against two fungi, *A. niger* and *F. heterosporium* by cup-plate method reported in literature[2] and Griscofulvin was used as standard drug. The results of antibacterial and antifungal are given in Tables 2 and 3, respectively.

The antibacterial value of ligands and their metal complexes reveal that the metal complexes are more active than ligands. The coordination of 1-substituted tetrazoline-5-thione to rhodium (I) results enhanced activity[19-21]. Bonding of thione ligand reduces the polarity of rhodium (I) ion and increases lipothilic character of central metal atom, which subsequently favours its permeation through the lipid layers of cell membrane[22-23]. The complexes possess lower activity than standard drug streptomycin. The variation in the effectiveness of the different compounds against different organism depend either on the impermeability of the cells or microbe of difference in ribosome of microbial cells[24].

Table 2: Antibacterial activity of ligands and complexes against various bacteria at different concentration (ppm)

Compounds	*S. aureus*		*Bacillus subtilis*		*E. coli*	
	25	**50**	**25**	**50**	**25**	**50**
P-CH_3-L (ligand)	+	++	+	++	+	++
[Rh(Cl(CO)(Pϕ_3)(P-CH_3-L)]	++	+++	++	+++	++	+++
m-CH_3-L (ligand)	-	+	-	+	-	+
[Rh(Cl(CO)(Pϕ_3)(m-CH_3-L)]	+	++	+	++	+	++
o-CH_3-L (ligand)	+	++	+	++	-	+
[Rh(Cl(CO)(Pϕ_3)(o-CH_3-L)]	++	+++	++	+++	NT	NT
o-Cl-L(ligand)	+	++	+	++	-	+
[Rh(Cl(CO)(Pϕ_3)(o-Cl-L)]	++	+++	++	+++	NT	NT
2,6-Me_2-L (ligand)	+	++	+	++	-	+
[Rh(Cl(CO)(Pϕ_3)(2,6-Me_2-L)]	++	+++	++	+++	NT	NT
Streptomycin (stand)	+++	++++	++	++++	NT	NT

Inhibition diameter in mm : (+) 15-20 mm; (++) 20-25 mm; (+++) 25-30 mm; (++++) 30-35 mm; (-) Inactive (inhibition zone < 10 mm); NT = not tested

Table 3: Antifungal activity of the complexes against fungi at different concentration (ppm)

Complex	*A. niger*			*F. heterosporium*		
	10	**50**	**100**	**10**	**50**	**100**
[RhCl(CO)(Pϕ_3)(P-CH_3-L)]	+	+	++	+	+	+++
[RhCl(CO)(Pϕ_3)(m-CH_3-L)]	-	+	++	-	++	++
[RhCl(CO)(Pϕ_3)(O-CH_3-L)]	-	++	+++	-	+	++
[RhCl(CO)(Pϕ_3)(O-Cl-L)]	+	++	+++	+	++	+++
[RhCl(CO)(Pϕ_3)(2,6-Me_2-L)]	++	++	++	+	++	+++
Griscofulvin (stand)	++	+++	++++	++	++	++++

Inhibition diameter in mm; (-) not effective; (+) 10-15 mm; (++) 15-20 mm; (+++) 20-25 mm; (++++) 25-30 mm

Fungicidal screening of the complexes by agar plate technique show them to be antifungal against *Aspergillus niger* and *F. heterosporium*. The result showed that most of compounds possess promising activity. Activity increases with increase in concentration of the complexes and presence of chlorine atom in ligand increases fungitoxicity. This observation is more or less in accordance with the observations of Horsfall and co-workers[26] and these compounds may serve as antifungal agents against the said organism.

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