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SPECTRAL CHARACTERIZATION AND ANTIBACTERIAL STUDIES OF ARENE-RUTHENIUM (II) COMPLEXES LIGATED WITH PHOSPHINE, ARSINE AND HETEROCYCLIC THIOAMIDES

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ABSTRACT

New cationic half-sandwich organometallic complexes of ruthenium (II) composition [(η^6-p-cymene) $RuE\phi_3L]^+$ BPh_4^- (L = Bidentate monoanionic thioamide, E = P/As;) have been synthesized and characterized as their tetraphenylborate salts. All the synthesized ruthenium (II) arene complexes are stable solids and are fully identified by elemental analysis, spectral (IR, UV-vis, ^{1}H NMR) and conductance data. An octahedral structure of complexes are deduced and thioamide ligand acts as N, S-chelating bidentate. The *in vitro* antibacterial screening of thioamide ligands and their respective complexes were tested against *S. aureus*, *B. Subtilis* and *E. coli*. The coordination of thioamide ligands to ruthenium (II) exhibited enhance activity.

Key words: Arene ruthenium (II), Half-sandwich, Thioamides, Structure.

INTRODUCTION

The study of arene-ruthenium complexes has been subject of recent interest[1-3] and receiving a lot of attention due to catalytic[4-6] and applications as anticancer drugs[7-9]. Mohr and Co-workers[10-12] have examined reactions, structures, and anti-tumor activity of various gold (I), platinum (II) and palladium (II) complexes with thioamide ligands. As a part of our going efforts to synthesize novel ruthenium complexes[13-15] and to study their physico-chemical and structural properties, we present here the synthesis, spectroscopic properties and bioactivity of some cationic arene ruthenium (II) complexes containing N, S-chelating heterocyclic thioamide ligands (I) incorporating $As\phi_3$ or $P\phi_3$.

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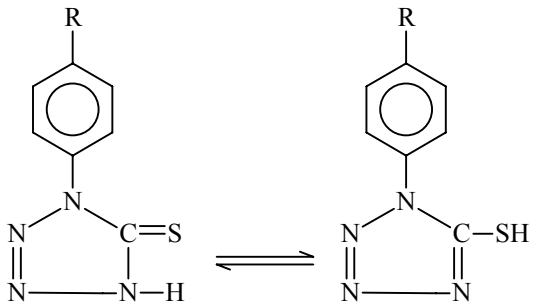


Structure 1: (R = H, CH_3, CH_3O)

EXPERIMENTAL

All chemical used were either CP grade or AR grade. Solvents were distilled and dried before use. All the chemicals were used as purchased without further purification. The ligand, 1-substituted-tetrazoline-5-thione[16] and precursor complex, $[Ru(\eta^6\text{-p-cymene})Cl_2]_2$[17] were prepared by reported literature methods. All complexes were prepared using a general method.

Preparation of complexes

To a solution of precursor complex (1 mmol) in dry benzene (30 mL) was added to 1 mmol of ligand in the same solvent containing $P\phi_3$ or $As\phi_3$ (1 mmol) MeOH (15 mL) and Et_3N (1 mL) was stirred on magnetic stirrer for 20 min. and further refluxed on water bath for two hrs. To the hot solution was added solid $NaBPh_4$ (1 mmol) and the yellow to light brown products were isolated by filtration, washed with H_2O, a little cold MeOH, Et_2O and were subsequently dried in vacuum (yield = 65-67%).

Analysis

S. No. 1: $[Ru(\eta^6\text{-p-cym})(P\phi_3)L]BPh_4$ (yellow): Calculated (%) for $RuC_{59}H_{54}N_4PSB$ (992.81) : C = 71.31; H = 5.43; N = 5.61; Ru = 10.17; Found (%) : C = 71.36; H = 5.50; N = 5.70; Ru = 10.30;

S. No. 2: $[Ru(\eta^6\text{-p-cym})(As\phi_3)(L)]BPh_4$ (yellow): Calculated (%) for $RuC_{59}H_{54}N_4$ AsSB (1036.81): C = 68.28; N = 5.20; N = 5.40; Ru = 9.74; Found (%): C = 68.20; H = 5.32; N = 5.55; Ru = 9.80;

S. No. 3: $[Ru(\eta^6\text{-p-cym})(P\phi_3)(P\text{-}CH_3\text{-L})]BPh_4$ (yellow): Calculated (%) for $RuC_{60}H_{56}N_4SPB$ (1007.81) : C = 71.44; H = 5.55; N = 5.55; Ru = 10.02; Found (%) : C = 71.50; H = 5.60; N = 5.60; Ru = 10.11;

S. No. 4: [Ru(η^6-p-cym)(Asϕ_3)(P-CH_3-L)]BPh_4 (yellow): Calculated (%) for $RuC_{60}H_{56}N_4SAsB$ (1051.81): C = 68.45; H = 5.32; N = 5.32; Ru = 9.61; Found (%): C = 68.50; H = 5.35; N = 5.35; Ru = 9.86;

S. No. 5: [Ru(η^6-p-cym)(Pϕ_3)(P-CH_3O-L)]BPh_4 (yellow-brown): Calculated (%) for $RuC_{60}H_{56}N_4OSPB$ (1022.81): C = 70.39; H = 5.47; N = 5.47; Ru = 9.87; Found (%): C = 70.40; H = 5.50; N = 5.56; Ru = 10.00;

S. No. 6: [Ru(η^6-p-cym)(Asϕ_3)(P-CH_3O-L)]BPh_4 (yellow-brown): Calculated (%) for $RuC_{60}H_{56}N_4OSAsb$ (1066.81): C = 67.49; H = 5.24; N = 5.24; Ru = 9.46; Found (%): C = 67.54; H = 5.34; N = 5.10; Ru = 9.60.

Elemental analysis, Magnetic measurements, molar conductance, IR, UV-vis, ^{1}H NMR spectral data were obtained, as we have reported earlier[13].

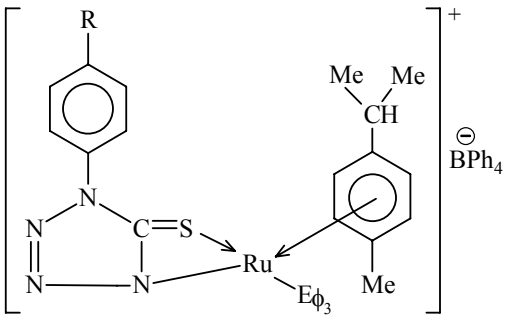
RESULTS AND DISCUSSION

All the newly synthesized η^6-p-cymene ruthenium (II) thioamide containing triphenylphosphine (Pϕ_3) or triphenylarsine (Asϕ_3) complexes are stable solid, non-hygroscopic, soluble in DMF, DMSO and CH_3CN. The molar conductance value of all the complexes is in the range of 89.80-102.6 $\wedge^{-1}cm^2mol^{-1}$ in acetonitrile solution at room temperature indicates 1:1 electrolyte nature[18-20]. The analytical data are in good agreement with the compositions proposed for all the complexes. All complexes display three intense absorptions in the range 500-200 nm. The absorption spectra of the arene ruthenium (II) thioamide containing phosphine or arsine complexes exhibited intense very broad bands around 303-305 nm and 268-270 nm are assigned to ligand-centered (LC) π-π^* and n $\rightarrow$ π^* transitions of coordinated arene, thioamide, Pϕ_3 or Asϕ_3 ligands. The lowest energy absorption bands in complexes at 405-410 nm are ascribed to metal ligand charge transfer (MLCT) Ru(T_{2g}) $\rightarrow$ π^* transition are consistent with octahedral structure reported for other ruthenium (II) complexes having similar composition in literature.[21-22]

IR Spectra

IR bands of free ligands and complexes are elaborated and elucidated for comparison which indicates formation of simultaneous Ru-N and Ru-S bond in all complexes with thioamide ligands (Str. II). The ν SH (2550 cm^{-1}) and ν NH (3145 cm^{-1}) bands of ligands disappeared from the spectra of complexes indicating deprotonation of imino proton of thiioamide group and formation of Metal-N bond during complexation. New bands in far IR of complexes at 465-445 cm^{-1} assigned due to Ru-N stretching mode confirmed these

observations.[22] The normal coordinate analysis (NCA) of thioamide group is performed by Agarwala and Rao[23] and Suzuki[24] suggested that all four thioamide bands are mixed bands having contributions from ν C⎓S, ν C⎓N, δ C-H and δ N-H modes. The blue shift of thioamide band II to higher frequency about 25-30 cm^{-1} and red shift of band IV (35-40 cm^{-1}), band III (15-20 cm^{-1}) and band II (25-30 cm^{-1}) to lower frequency suggest simultaneous Ru-N and Ru-S bond considering our previous observations[25-27] and other workers.[28-30] New bands of weak intensity at 430-420 cm^{-1} also supports the formation of metal-S bond and assigned to ν Ru-S mode.[22] New bands around 532, 690, 740 and 1550 cm^{-1} ($As\phi_3$) and at 542, 695, 745 and 1445 cm^{-1} ($P\phi_3$) in complexes may be due to coordinated $As\phi_3/P\phi_3$ ligands[31-33].



(E = P/As; R = H, CH_3-; CH_3O-)
Octahedral Structure
(Structure II)

^{1}H NMR Spectra

Supplementary data have been obtained by ^{1}H NMR spectroscopy recorded for the ligands and metal complexes to substantiate further metal-ligand bonding and proton chemical shift are given in Table 2.

The deprotonation of thioamide ligand is confirmed by the absence of an N-H signal in the ^{1}H NMR spectra of the complexes. The broad multiplet in the region δ = 7.42-7.74 ppm due to phenyl protons of thioamide ligand in complexes. The broad nature of peak may be due to large quadrupole resonance broadening effect of tetrazoline nitrogen atoms.[34] The methoxy protons observed as a sharp singlet at δ = 3.74 ppm in complexes concides with that of methoxy group protons in literature.[35] The signal at δ = 2.60 ppm assigned to methyl protons of coordinated ligand. The two isopropyl methyl protons of the p-cymene appeared as doublet in the region δ = 0.70-0.90 ppm and the methine proton in the range of δ = 0.9-2.1 ppm as septet and the methyl group of the p-cymene comes as singlet around the region of δ = 1.48-1.76 ppm. The arene protons exhibited a down field as compared with

that in the precursor complex[36]. All the complexes show multiplets δ = 6.18-8.42 ppm for the presence of thioamide ligand, $E\phi_3$ (E = P/As) and the tetraphenylborate aromatic protons.

Antibacterial property

The *in vitro* antibacterial screening of ligands and their complexes have been tested against *S. Aureus*, *B. Subtilis* and *E. Coli* using a nutrient agar medium by Disc diffusion method using streptomycin as standard[37]. The results (Table 3) showed that the complexes exhibited moderate activity and the toxicity of ruthenium complexes increases on increasing the concentration[38]. Metal complexes are more active than thioamide ligans but lesser than standard drug streptomycin. The coordination of 1-substituted tetrazoline-5-thione to ruthenium (II) results enhanced activity[39-41] may be explained on the basis of Tweeds Chelation Theory.[42]

Table 1: Characterization IR bands (cm^{-1}) of ligands and complexes

Compounds	Thioamide bands[Ψ]				Stretching modes		
	Band I	Band II	Band III	Band IV	Ru-N	Ru-S	Ru-P
LH (ligand)	1512 s	1280 s	1058 s	785 ms	-	-	-
S. No. 1 (Complex) ($RuC_{59}H_{54}N_4PSB$)	1495 (m)	1315 (s)	1025 (m)	777 (m)	465 (m)	430 (w)	503 (m)
S. No. 2 (Complex) ($RuC_{59}H_{54}N_4AsSB$)	1490 (s)	1316 (s)	1020 (m)	765 (m)	445 (m)	420 (w)	495 (m)
P-CH_3-L (ligand)	1500 (m)	1280 (s)	1044 (m)	810 (m)	-	-	-
S. No. 3 (Complex) ($RuC_{60}H_{56}N_4SPB$)	1480 (m)	1310 (m)	1025 (m)	785 (m)	460 (m)	422 (w)	490 (m)
S. No. 4 (Complex) ($RuC_{60}H_{56}N_4SAsB$)	1480 (m)	1315 (m)	1030 (m)	780 (m)	462 (m)	430 (w)	495 (m)
P-CH_3-O (ligand)	1505 (s)	1290 (s)	1050 (m)	800 (m)	-	-	-
S. No. 5 (Complex) ($RuC_{60}H_{56}N_4OSPB$)	1485 (m)	1322 (s)	1035 (m)	782 (m)	465 (m)	425 (w)	505 (m)
S. No. 6 (Complex) ($RuC_{60}H_{56}N_4OSAsB$)	1480 (m)	1310 (m)	1305 (m)	780 (m)	465 (m)	420 (w)	500 (m)

Ψ: Mixed Bands: Band I-δNH + δCH + νC=N; Band II = νC—N + δNH + δCH + νCS, Band III = νC-N + νC-S; Band IV = νC=S

Table 2: ^{1}H NMR Spectra of ligands and complexes$^{\psi}$

Compds.	P-Cymene (δ PPM)				Thioamide ligand				$E\phi_3$
	Ar-H	-CH $(CH_3)_2$	$-CH_3$	-CH	Phenyl proton	$-CH_3$ proton	CH_3O- proton	N-H Proton	
LH (ligand)	-	-	-	-	7.52-7.74	-	-	1.25	-
S. No. 1	5.0-5.70	0.90	1.48	1.9	7.42-7.35	-	-	-	8.22
S. No. 2	4.98-5.8	0.75	1.38	1.9	7.40-7.30	-	-	-	6.82
P-CH_3-L (ligand)	-	-	-	-	7.58-7.78	2.66	-	1.28	-
S. No. 3	5.00-5.90	0.70	1.70	1.9	7.38-7.46	2.63	-	-	8.18
S. No. 4	5.10-5.82	0.80	1.50	1.9	7.48-7.58	2.60	-	-	6.92
P-CH_3O-L (ligand)	-	-	-	-	7.67-7.70	-	3.60	-	-
S. No. 5	5.2-5.9	0.90	1.76	1.9	7.66-7.70	-	3.59	-	8.52
S. No. 6	5.1-5.6	0.82	1.73	2.10	7.65-7.78	-	3.61	-	6.98

ψ : E = P/As; LH = $C_7H_6N_4S$; P-CH_3-L = $C_8H_7N_4S$; P-CH_3O-L = $C_8H_7ON_4S$

Table 3: Antibacterial activity of ligands and ruthenium (II) complexes at different concentration (ppm)

Compounds	Diameter of inhibition (mm)								
	S. Aureus			*B. Subtilis*			*E. Coli*		
	25	50	100	25	50	100	25	50	100
LH (ligand)	-	+	+	-	-	+	-	-	+
S. No. 1	+	++	++	+	+	++	+	+	++
S. No. 2	+	++	++	NT	NT	NT	NT	NT	NT
P-CH_3-L (ligand)	+	++	++	-	+	+	-	-	+
S. No. 3	++	++	+++	+	++	++	+	+	++
S. No. 4	++	++	+++	+	++	+++	+	++	++
P-CH_3O-L (ligand)	+	+	++	+	++	++	-	+	+

Cont…

Compounds	Diameter of inhibition (mm)								
	S. Aureus			*B. Subtilis*			*E. Coli*		
	25	**50**	**100**	**25**	**50**	**100**	**25**	**50**	**100**
S. No. 5	++	++	+++	NT	NT	NT	NT	NT	NT
S. No. 6	++	+++	++++	+	++	+++	+	++	+++
Streptomycin (stand.)	++	+++	+++	++	+++	++++	++	+++	++++

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

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