



## Study of Some Biorelevant Complexes of Transition Metals with Active Imines

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### ABSTRACT

The reactions of transition metal salts with monofunctional bidentate thiosemicarbazone (TSCZH) derived from the condensation of 6-nitro-1H-indole 2-3 dione with thiosemicarbazide have been carried out in 1:2 molar ratio. Derivatives of the type  $[M(TSCZH)_2 \cdot xH_2O] Cl$  (where  $M=Ti(III), V(III), Mn(III), Co(III), Ru(III), Fe(III), MoO_2(V)$  and  $MoO_2(VI)$ ) have been obtained. All these complexes are coloured solids and monomeric in nature. Octahedral geometry has been proposed for these complexes based on elemental analyses, molar conductance, magnetic susceptibility and spectral studies. Antimicrobial effects of the ligand and its complexes on different species of pathogenic fungi and bacteria have been recorded.

**Key words :** Transition metal, Octahedral fungi, antimicrobial & biorelevant.

### INTRODUCTION

There is substantial interest in the therapeutic activities of the co-ordination compounds as drugs<sup>1-3</sup>. In recent years some important Schiff base complexes derived from<sup>2,3</sup>-diaminopyridine and O-vanillin were synthesized and their antibacterial activity has also been studied<sup>4</sup>. Schiff bases act as intermediate in biological processes. Examples of such processes are reactions involving pyridoxal enzyme, aldol condensation, decarboxylation, transmutation and visual processes.

A lot of work is reported on the Schiff base hydrolysis, but the mechanism of the hydrolysis has not been worked out in detail<sup>5-6</sup>. Several Schiff base complexes have been synthesized as models for some of metalloproteins<sup>7-9</sup>. Schiff base complexes

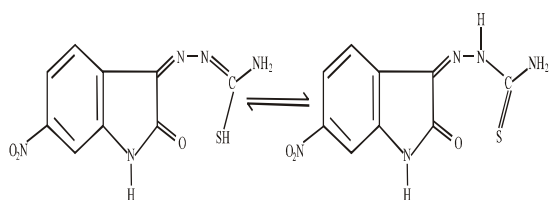
have gained additional importance due to their possible applications as superoxide dismutase mimics<sup>10-11</sup> and their catalytic role in the epoxidation of olefins<sup>12</sup>.

Transition metals form some specific and important drugs with diphenyl pyridine and isothipendyl<sup>1</sup>. These drugs are found to be antiserotherine, antihistaminic, anticonvulsants and antifungal in nature and hence used in medicinal chemistry<sup>13-15</sup>. It has been well established that certain platinum and palladium<sup>16-17</sup> complexes are of biological importance due to their carcinostatic activity and interest in biological chemistry. Chalson *et al.*,<sup>18</sup> have reported that cesium cis-dichlorosreinetopalladate (II) induces filament growth in *E. coli*. The complexes of palladium (II) with amino acids such as glycine, serine and glutamine have also been reported<sup>19-20</sup>

to be active against certain tumors. It is also well known that carcinostatic action<sup>21-24</sup> of drugs is due to their interaction with nuclear D.N.A. Keeping these facts in view, the present research work was carried out.

## EXPERIMENTAL

The transition metal salts and *m*-nitroaniline were purchased from Lobochemie and used as such. 6-Nitroisatin was prepared in the laboratory. All the solvents were dried and distilled before use.



6-Nitroisatin was synthesised by Sandmeyer isonitrosoacetanilide synthesis method.<sup>25</sup> The ligands TSCZH was prepared by the condensation of 6-nitroisatin with hydrazinecarbothioamide in presence of sodium acetate in 1:1 molar ratio, in absolute alcohol. The reaction mixture was refluxed over a water bath for 4h and allowed to stand overnight. The product was recrystallized from ethanol and dried in vacuo. It may be represented by following structure.

### Synthesis of Metal Complexes

The ethanolic solution of metal salts and ligand was mixed in 1:2 molar ratio. Aqueous  $\text{NH}_4\text{OH}$  was added dropwise in the reaction mixture till the solution became basic (pH 8.0). The mixture was then stirred on a magnetic stirrer for 2-3 h and the resulting product was recovered by filtration, washed with ethanol and dried in vacuo.

The ligand and its metal complexes were subjected to elemental analyses for C, H and N, while metal was estimated gravimetrically in the lab (Sulphur was estimated by Messengers method). The melting points were determined by open capillary method and are uncorrected. The molar conductance was determined by Systronics (model 305) conductivity bridge. Magnetic susceptibility was determined by Gouy's method, using  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$

as calibrant. The electronic spectra were recorded by Beckman -DU Spectrophotometer. The IR spectra were recorded in KBr pellets at CDRI Lucknow.

### Antimicrobial Activity

The antifungal activity was evaluated against *Macrophomina phaseolina* and *Fusarium oxysporum* using standard food poisoning technique and a procedure recommended for testing new chemicals<sup>26</sup>. The linear growth of the fungus was recorded by measuring the diameter of the fungus colony after 96h and the percentage inhibition was calculated as  $10^2 (d_c - d_t)/d_c$ . Where  $d_c$  and  $d_t$  are the diameters of the fungus colony in the control and test plates, respectively.

Antibacterial activity was tested against *Bacillus subtilis* and *Salmonella* species using the Paper disc plate method.<sup>27</sup>

## RESULTS AND DISCUSSION

The analytical data suggested 1:2 (M:L) stoichiometry for the synthesized complexes. The vast difference in melting point of the ligand and its complexes indicated their formation. The determination of molar conductance suggested 1:1 electrolytic nature for all the M(III) & Mo(V) complexes except those of Ru(II) &  $\text{MoO}_2(\text{VI})$  which are non electrolytes.

The I.R. spectrum of free ligand shows bands at  $3284, 1612$  and  $995 \text{ cm}^{-1}$  which may be assigned to  $\nu(\text{N-H})$ ,  $\nu(\text{C=N})$  and  $\nu(\text{C=S})$  respectively. The band due to N-H vibration disappears in IR spectrum of the complexes indicating deprotonation of the functional group upon complexation<sup>28</sup>. The band at  $1612 \text{ cm}^{-1}$  shifted to higher wave number by  $10-15 \text{ cm}^{-1}$  in the metal complexes, which suggested coordination through azomethine nitrogen atom. The band at  $995 \text{ cm}^{-1}$  is shifted towards lower frequencies indicating involvement of C=S group in co-ordination. The band at  $3430 \text{ cm}^{-1}$  attributed to asymmetric and symmetric mode of  $\text{NH}_2$  group remain almost at the same position in the spectra of the complexes, suggesting non-involvement of these groups in bonding<sup>29</sup>. In the far IR region of the complexes, some non ligand bands have appeared in the region of  $440-445$  and  $365-375$  which may be assigned to  $\nu(\text{M-N})$  and  $\nu$

Table 1: Analytical and Physical Data of Ligand and Complexes

S. No	Compound	Colour	m.p. °C	Elemental analyses				Magnetic Moments	Molar Conductance in (B.M.) ohm <sup>-1</sup> cm <sup>2</sup> mole <sup>-1</sup>
				% C	% H	% N	% S		
1	(TSCZH)	Grey	221	40.90 (40.85)	2.27 (2.25)	26.51 (26.49)	12.12 (12.09)	-	-
2	[Ti (C <sub>9</sub> H <sub>6</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> .2H <sub>2</sub> O] Cl	Yellow	275	33.35 (33.31)	2.47 (2.41)	21.62 (21.59)	9.88 (9.82)	1.68 (7.39)	65
3	[V(C <sub>9</sub> H <sub>6</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> .2H <sub>2</sub> O] Cl	Yellow	278	33.20 (33.18)	2.46 (2.44)	21.52 (21.45)	9.84 (9.80)	2.92 (7.81)	70
4	[Mn (C <sub>9</sub> H <sub>6</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> .2H <sub>2</sub> O] Cl	Brown	280	33.00 (32.96)	2.43 (2.42)	21.39 (21.35)	9.77 (9.71)	4.93 (8.37)	75
5	[Fe (C <sub>9</sub> H <sub>6</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> .2H <sub>2</sub> O] Cl	Dark Brown	276	32.95 (32.90)	2.44 (2.41)	21.35 (21.31)	9.76 (9.74)	5.87 (8.52)	65
6	[Co (C <sub>9</sub> H <sub>6</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> .2H <sub>2</sub> O] Cl	Brown	281	32.80 (32.78)	2.42 (2.40)	21.46 (21.23)	9.71 (9.69)	Diamagnetic (8.91)	70
7	[MoO (C <sub>9</sub> H <sub>6</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> .H <sub>2</sub> O] Cl	Redish Brown	295	30.36 (30.33)	1.96 (1.94)	19.67 (19.60)	8.99 (8.95)	1.78 (13.45)	75
8	[MoO <sub>2</sub> (C <sub>9</sub> H <sub>6</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> ]	White	286	32.92 (32.87)	1.82 (1.79)	21.34 (21.30)	9.75 (9.71)	Diamagnetic (14.58)	Non Electrolyte
9	[Ru(C <sub>9</sub> H <sub>6</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> .2H <sub>2</sub> O] Cl	Green	310	30.83 (30.80)	2.28 (2.25)	19.98 (19.95)	9.14 (9.12)	1.98 (14.39)	80
10	[Ru(C <sub>9</sub> H <sub>6</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> .2H <sub>2</sub> O]	Green	305	42.48 (42.45)	2.40 (2.38)	21.05 (21.00)	9.62 (9.60)	15.18 (15.12)	Non electrolyte

Figures in parenthesis are observed values.

(M-S) respectively. The appearance of these bands further support the bonding of the ligand to the metal atom through nitrogen and sulphur atom. Thus the ligand is behaving in mono basic bidentate manner. In the case of Mo O(V) complex a band has appeared at  $950\text{ cm}^{-1}$  due to Mo =O stretching frequency. The strong band exhibited by the dioxomolybdenum (VI) complexes in the region  $950\text{-}970$  and  $910\text{ cm}^{-1}$  are attributed to  $\nu_{\text{sym}}(\text{O}=\text{Mo}=\text{O})$  and  $\nu_{\text{sym}}(\text{O}=\text{Mo}=\text{O})$  respectively of Cis Mo O<sub>2</sub> configuration due to the maximum utilization of the available p orbitals for bonding with oxogroups. The I.R. spectra of the complexes show non-ligand bands in the region of  $3480\text{-}3510\text{ cm}^{-1}$  due to n O-H and  $840\text{-}850\text{ cm}^{-1}$  assignable to rocking mode of coordinated water molecules. TGA also supported the coordinated nature of water molecules.

The H<sup>1</sup> NMR spectrum of the ligand shows, multiplets at 6.70 ppm due to aromatic protons which remain in same position in the metal complexes. The free ligand exhibit sharp singlet at 11.25 ppm due to -NH proton, which disappear in the metal complexes, suggesting deprotonation during complexation.

### Electronic Spectra

The electronic spectrum of Ti (III) complex shows a single broad band at  $19560\text{ cm}^{-1}$  due to transitions for O<sub>h</sub> symmetry<sup>30</sup>. The value of magnetic moment of this complex is 1.68 B.M. which is in the expected range for d<sup>1</sup> system like Ti(III) and shows paramagnetic character of the complex. It also shows that Ti (III) has not been oxidised to Ti (IV) during or after complexation, although it is very sensitive to oxidation.

The Mn (III) complex shows a magnetic moment of 4.93 B.M., corresponding to the presence of four unpaired electrons and high spin state of the complex. This value also suggests the absence of any kind of exchange interaction<sup>31</sup>. The electronic spectrum of complex shows an intense and sharp charge transfer band at  $22000\text{ cm}^{-1}$  and a spin allowed d-d transition at  $18540\text{ cm}^{-1}$  characteristic of octahedral geometry<sup>31</sup>.

The study of magnetic properties of the Co (III) complex indicated diamagnetic nature, as expected for a low spin d<sup>6</sup> ion. The electronic

spectrum of the chelate displays bands at 15230, 21195 and  $23410\text{ cm}^{-1}$  assignable to  $t_{2g} \rightarrow e_g$  and transitions respectively. These are characteristic of low spin octahedral complexes of Co (III)<sup>32</sup>.

The observed value of effective magnetic moment of the complex is 2.92 B.M., as expected for d<sup>2</sup> system like V (III). The electronic spectrum of the complex exhibits a band at  $16110\text{ cm}^{-1}$  with a shoulder at  $20530\text{ cm}^{-1}$ . The low energy band may be assigned to  $t_{2g} \rightarrow e_g$  and the high energy band to  $t_{2g} \rightarrow t_{2g}$ . These are characterized of octahedral geometry<sup>33</sup>.

The Ru (III) complex shows a magnetic moment of 1.98 B.M. and three bands in its electronic spectrum at 13650, 17600 and  $22500\text{ cm}^{-1}$ . These bands are assigned to  $t_{2g} \rightarrow e_g$ ,  $t_{2g} \rightarrow t_{2g}$ , and  $e_g \rightarrow e_g$ , respectively, and are similar to those reported for other Ru (III) octahedral complexes<sup>34</sup>.

The electronic spectrum of oxomolybdenum (V) complex suggested that the complex may be considered as octahedral with a strong tetragonal distortion resulting from Mo=O bond. The spectrum exhibited three distinct absorption bands in the ligand field region. The low intensity band at  $13000\text{ cm}^{-1}$  in the long wavelength region is possibly due to first crystal field transition ( $d_{xy}, d_{yz}, d_{zx}$ ). The second crystal field transition at  $19000\text{ cm}^{-1}$  is assignable to  $(d_{xy}, d_{x^2-y^2})$ . The third peak was observed at  $3000\text{ cm}^{-1}$  assignable to  $(d_{xy}, d_{z^2})$ .

The electronic spectrum of Mo O<sub>2</sub> (VI) complex has a single band due to charge transfer transition. Its complex is diamagnetic in nature as expected for d<sup>0</sup> configuration.

The Ru (II) complex is diamagnetic in nature which shows +2 oxidation state for Ru (II) in this complex. The electronic spectrum of the complex in CH<sub>2</sub>Cl<sub>2</sub> shows a band assigned to the charge transfer transition arising from the excitation of an electron from the metal t<sub>2g</sub> level to the unfilled molecular orbitals derived from the p\* level of the ligand in accordance with the assignments made for other similar octahedral Ru (II) complex<sup>35</sup>.

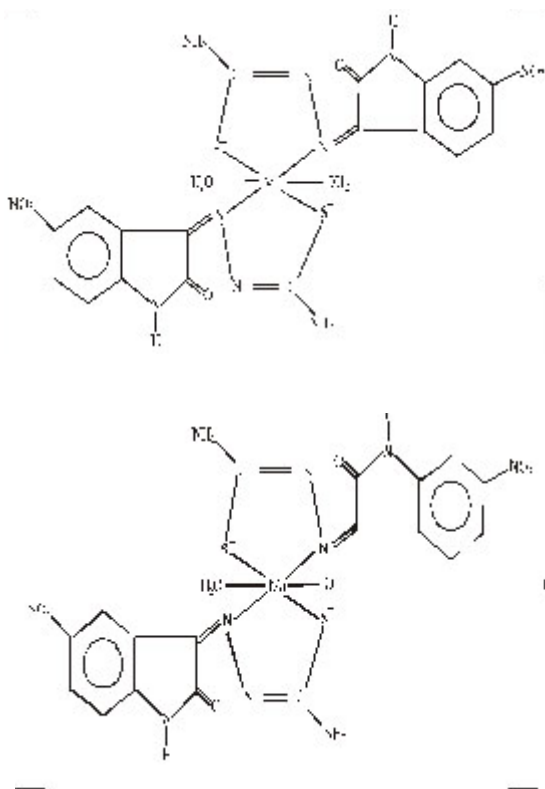
The magnetic moment of Fe (III) complex is 5.87 B.M. corresponding to the presence of five

unpaired electrons and high spin state of Fe (III) in this complex. The electronic spectrum of this complex shows three bands at 12720, 19600 and 25000  $\text{cm}^{-1}$  due to (G), (G) and (G) transition respectively in an octahedral symmetry.<sup>36</sup>

### CONCLUSION

On the basis of studies performed and discussed above octahedral geometry have been proposed for all the synthesized complexes.

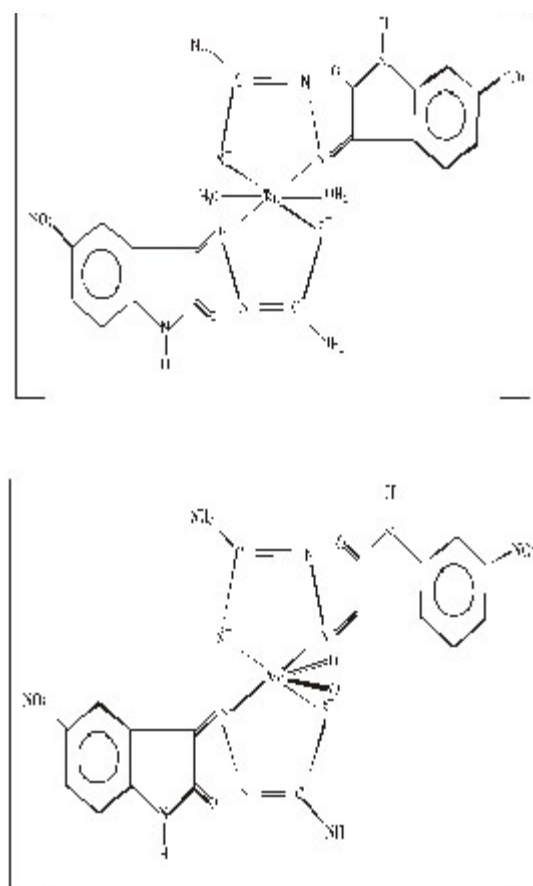
Where M = Ti (III), Mn(III), Co (III), V (III), Ru (III) and Fe (III)



arising due to chelation<sup>37</sup>. The toxicity increases as the concentration is increased. Mode of action of antimicrobials may involve various targets in microorganisms, e.g. interference with the cell wall synthesis, damage to the cytoplasmic membrane as a result of which cell permeability may be altered or they may disorganize the lipoprotein leading to the cell death<sup>38</sup>.

### Antifungal & Antibacterial Activities

The data for the antifungal and antibacterial activities of the ligands and their corresponding compounds evaluated against *Fusarium oxysporum* and *Alternaria alternata* and bacteria *Escherichia coli* and *Pseudomonas cepacicola* have been recorded. The results point out that the compounds are inhibiting the growth of fungus and bacteria to a greater extent as the concentration is increased. The enhanced activity of metal chelates may be ascribed due to the increased lipophilic nature of these complexes



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