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Studies on Synthesis, Spectral Properties and Antimicrobial Activity of Biologically Potent Manganese(II) Complexes

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The synthesis, spectroscopic characterization and antimicrobial activities of some unsymmetrical manganese(II) complexes of thioazomethines including benzothiazolines having NS donor set have been described. The 1 : 1 : 1 reactions of hydrated manganese chloride with monobasic bidentate azomethines resulted in the formation of coloured solids which have been characterized by elemental analysis, molecular weight determination, conductance and magnetic measurements. The infrared, electronic and electron spin resonance spectral studies indicated tetrahedral geometry for the resulting complexes. These thio ligands along with their complexes have been screened *in vitro* against a number of pathogenic fungi and bacteri to assess their growth inhibiting potential.

Key Words: Synthesis, Spectral properties, Antimicrobial activities, Manganese(II) complexes.

INTRODUCTION

Metal complexes of thiosemicarbazones and benzothiazolines have aroused considerable interest in view of their industrial and biological importance. Many of these compounds possess a wide spectrum of medicinal properties including activity against tuberculosis[1], leprosy[2], bacterial and viral infections[3, 4]. They have also been found to be active against influenza, protozoa, small pox, psoriasis, rheumatism, trypanosomiasis, coccidiosis, malaria and certain kinds of tumours and have been suggested as possible pesticides[5] and fungicides[6]. Their activity has frequently been thought to be due to their ability to chelate trace metals. Thiosemicarbazones and benzothiazolines react as chelating ligands with transition metal ions by bonding through the sulphur and nitrogen atoms, although in a few cases they behave as monodentate ligands and bonded through the sulphur atom only.

Azomethines constitute one of the most important classes of sulfur, nitrogen as well as oxygen donor ligands. They have made spectacular progress in the field of coordination and bioinorganic chemistry. Azomethines and transition metal complexes are encouragingly patented on account of their practical uses in various applied fields. To illustrate a few examples, they are patented as NMR contrast agents[7], corrosion inhibitors for aqueous coating composition[8], high temperature stabilizers for luhricants[9], in food packaging materials and oxygen-absorbing complexes[10]. These complexes are also patented in multifunctional additive packages for disel fuels and fuel oils[11]. Azomethines and their transition metal complexes have remarkable potential for inhibiting growth of various pathogenic microorganisms[12] and this property has been exploited in pharmacological

applications[13]. In continuation of our work on such metal complexes of biologically active ligands, we report herein the synthesis and structures of some unsymmetrical complexes of manganese(II) along with their bioefficacy.

EXPERIMENTAL

All the chemicals were dried and purified before use and the reactions were carried out with a ratio head (distillation assembly) fitted with condenser. Thiosemicarbazones were prepared by the condensation of 2-thiophene carbaldehyde, acetone and cinnamaldehyde with hydrazine carbothioamide in 1 : 1 molar ratio. The benzothiazolines were prepared by the condensation of [1-(2-naphthenyl)ethanone], [1-(2-thienyl)ethanone], [1-(2-pyridinyl)ethanone] and indole-3-carbaldehyde with 2-mercaptoaniline in unimolar ratio in ethanol. The thiosemicarbazones were refluxed and benzothiazolines were stirred for 7–8 h. The coloured solid products were separated out, filtered off, recrystallized from ethanol and dried *in vacuo*.

Synthesis of Unsymmetrical Manganese(II) Complexes

Complexes of manganese(II) were prepared by the reactions of $MnCl_2 \cdot 4H_2O$ with [2-(2-thienylmethylene)hydrazine carbothioamide] and different thiosemicarbazones or benzothiazolines in 1 : 1 : 1 molar ratio in dry methanol. After the addition of both the ligands with hydrated $MnCl_2$, the solution was shaken thoroughly, refluxed for 6–8 h and then cooled to room temperature. The solvent was removed and the residue was dried *in vacuo*. The physical properties and analytical data of the complexes are given in Table-1.

TABLE-1
PHYSICAL PROPERTIES AND ANALYTICAL DATA OF MANGANESE(II) COMPLEXES

Compound	Colour and m.p. (°C)	Analysis %, found (calcd.)			m.w. found (calcd.)
		Mn	N	S	
[Thiop.(TSCZ)Mn(Ac.TSCZ)]	Off white 170	14.79 (14.87)	22.67 (22.72)	25.97 (26.04)	347.81 (369.38)
[Thiop.(TSCZ)Mn(Cinn.TSCZ)]	Mustard 165	12.61 (12.67)	18.91 (18.95)	21.62 (21.69)	414.65 (443.46)
[Thiop.(TSCZ)Mn(2- Ac.naph. Bzt)]	Sparkling yellow 68	10.58 (10.65)	10.81 (10.86)	18.57 (18.65)	496.65 (515.58)
[Thiop.(TSCZ)Mn(2- Ac.thiop.Bzt)]	Reddish brown 225	11.61 (11.65)	11.81 (11.88)	27.13 (27.20)	449.32 (471.53)
[Thiop.(TSCZ)Mn(Indole.carb.Bzt)]	Brown > 300	11.17 (11.22)	14.26 (14.31)	19.58 (19.65)	466.26 (489.51)
[Thiop.(TSCZ)Mn(2-Ac.pyd.Bzt)]	Light Brown 185	11.41 (11.45)	14.96 (15.01)	20.57 (20.62)	446.99 (466.49)

Nitrogen and sulfur were estimated by Kjeldahl's and Messenger's methods, respectively. Manganese was estimated complexometrically with EDTA using Eriochrome Black-T as an indicator. The conductance was measured with a conductivity bridge type 304 systronics model and the molecular weights were determined by Rast-camphor method. Infrared spectra with KBr were obtained using Perkin-Elmer 557 grating spectrophotometer. The electron spin resonance spectra were recorded at IIT, Chennai.

Biological Studies

The antifungal activities were evaluated against *Macrophomina phaseolina* and *Fusarium oxysporum* by the agar plate technique. The compounds were dissolved in 100 and 200 ppm concentrations in methanol and then mixed with the medium. The linear growth of the fungus was obtained by measuring the diameter of the colony after 96 h. and percentage inhibition was calculated as (C – T) × 100/C, where C and T are the diameters of the fungus colony in the control and test plates, respectively. Bavistin was used as a standard.

The antibacterial activities were evaluated by the paper disc plate method. The nutrient agar medium (peptone, beef extract, sodium chloride and agar-agar) and 5 mm diameter paper discs (Whatman No. 1) were used. The compounds were dissolved in methanol in 500 and 1000 ppm concentrations. The filter paper discs were soaked in different solutions of the compounds, dried and then placed in the petriplate previously seeded with the test organisms (*E. coli and K. aerogenous*). The plates were incubated for 24–30 h at 28 ± 2°C and the inhibition zone around each disc was measured. Streptomycin was used as a standard for comparing the results (Tables 2 and 3).

TABLE-2
ANTIBACTERIAL SCREENING DATA OF COMPLEXES, INHIBITION (mm) AFTER 24 h (CONC. IN ppm)

Compound	*E. coli*		*K. aerogenus*	
	500	1000	500	1000
[Thiop.(TSCZ)Mn(Ac.TSCZ)]	5	8	6	7
[Thiop.(TSCZ)Mn(Cinm.TSCZ)]	6	9	7	9
[Thiop.(TSCZ)Mn(2-Ac.naph. Bzt)]	8	11	9	11
[Thiop.(TSCZ)Mn(2-Ac.thiop.Bzt)]	10	12	11	12
[Thiop.(TSCZ)Mn(Indole.carb.Bzt)]	9	10	10	11
[Thiop.(TSCZ)Mn(2-Ac.pyd.Bzt)]	7	9	8	10
Standard (Streptomycin)	17	18	13	14

TABLE-3
FUNGICIDAL SCREENING DATA OF COMPLEXES. INHIBITION (%) AFTER 96 HOURS (CONC. IN PPM.)

Compound	*Macrophomina phaseolina*		*Fusarium oxysporum*	
	100	200	100	200
[Thiop.(TSCZ)Mn(Ac.TSCZ)]	59	66	51	60
[Thiop.(TSCZ)Mn(Cinm.TSCZ)]	60	72	53	62
[Thiop.(TSCZ)Mn(2-Ac.naph.Bzt)]	77	83	67	74
[Thiop.(TSCZ)Mn(2-Ac.thiop.Bzt)]	86	89	83	86
[Thiop.(TSCZ)Mn(Indole.carb.Bzt)]	81	87	74	79
[Thiop.TSCZ)Mn(2-Ac.pyd.Bzt)]	68	77	56	69
Standard (Bavistin)	100	100	100	100

The experimental data from Tables 2 and 3 suggest that the metal complexes are more potent in inhibiting the growth of microorganisms than the original biologically relevant ligands. The enhanced antimicrobial activity of the metal complexes over their corresponding chelating agents may conveniently be explained by exploiting chelation theory[14]. Chelation reduces the polarity of the metal ion mainly because of the partial sharing of its positive charge with the donor groups and possible π-electron-delocalization over the whole chelate ring. Since the plasma membrane in general is more permeable to non-polar compounds than to polar compounds, it is natural to hypothesize that the more lipoid-soluble compounds are more toxic simply because they enter the cell more rapidly[15].

RESULTS AND DISCUSSION

Reactions of hydrated manganese(II) chloride with monobasic bidentate unsymmetrical benzothiazolines and thiosemicarbazones in 1 : 1 : 1 molar ratio in methanol may be represented by the following equations:

$$MnCl_2 \cdot 4H_2O + \text{Thiop.TSCZH} + \text{2-Ac·TSCZH} \rightarrow \text{Mn (Thiop·TSCZ)(2-Ac.TSCZ)} + 4H_2O + 2HCl.$$

$$MnCl_2 \cdot 4H_2O + \text{Thiop.TSCZH} + \text{2-Acnaph·BztH} \rightarrow \text{Mn(Thiop. TSCZ)(2-Acnaph.Bzt)} + 4H_2O + 2HCl.$$

The resulting complexes have been obtained as coloured solids which are soluble in DMF, DMSO and CCl_4. These reactions are quite facile and can be completed within 8–10 h of refluxing. The yields of these reactions are almost quantitative. The methods used for the preparation and isolation of the resulting complexes give materials of good purity as supported by their analysis. The

complexes are monomeric as indicated by the molecular weight determinations. The low molar conductance value in dry DMF (10–15 ohm^{-1} cm^2 mol^{-1}) reveals the non-electrolytic nature of the synthesized complexes.

In the IR spectra of the free ligands, the —NH stretching bands appear at 3370–3200 cm^{-1}. On complexation these vibrations of ligands disappear and a new band at *ca.* 1600 cm^{-1} is observed due to ν(C=N) vibrations. In the IR spectra of benzothiazolines, the absence of ν(SH) at 2600–2500 cm^{-1} and presence of ν(C=N) is strong evidence for a ring structure. The appearance of azomethine bands in the complexes suggests that the complexes are metal Schiff base derivatives as in presence of metal ion the cyclic structure of benzthiozolines rearranges to give the Schiff base metal chelates. The coordination of ligands through azomethine nitrogen and thiosulfur further get support by the appearance of new bands of medium to weak intensity in the regions 400–390 cm^{-1} and 340–270 cm^{-1} attributable to ν(Mn—N) and ν(Mn—S) vibrations, respectively[18]

Manganese(II) complexes show a maximum absorption band at *ca.* 435 nm and a charge transfer band at *ca.* 280 nm indicating a tetrahedral geometry[19] for these complexes. In tetrahedral fields, the transitions are spin forbidden and are no longer parity forbidden. Thus the tetrahedral compounds are somewhat more intensely coloured[20].

The electron spin resonance spectral studies of Mn(II) complexes at the room temperature show only one isotropic signal centred at 2.0273 g and which once again sugest a tetrahedral geometry for these complexes[21].

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