Stereochemistry and Fungitoxicity of Complexes of *p*-Anisaldehydethiosemicarbazone with Mn(II), Fe(II), Co(II) and Ni(II)

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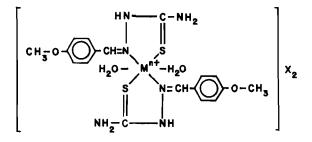
Received August 7, 1984

Abstract

The complexes of p-Anisaldehydethiosemicarbazone (PAT) with Mn(II), Fe(II), Co(II) and Ni(II) have been isolated and characterised on the basis of elemental analyses, molar conductance, magnetic moment and spectral studies. Fungicidal activity has been evaluated against *Alternaria* (Sp.), *Paecilomyces* (Sp.) and *Pestalotia* (Sp.).

Introduction

Since Domagk's original discovery [1] of their antitubercular activity, thiosemicarbazones have been shown to be pharmacologically active against viruses, protozoa, smallpox and certain kinds of tumor [2]. It has been suggested that the fungicidal activity of thiosemicarbazones is due to their ability to chelate the essential metals which the fungus needs in its metabolism [3, 4]. On the basis of chelation theory, the fungicidal activity of compounds containing the -SH group adjacent to nitrogen has been well explained [5, 6]. It has already been suggested by various authors that the metal chelates are more potent than the chelating agents themselves [7, 8]. Thimmaiah et al. have proposed PAT as a selective and sensitive spectrophotometric reagent for nickel(II) [9], copper-(II) and palladium(II) [10] and as a chelating agent for Cu(II), Zn(II), Hg(II) and Cd(II) [11]. In the present paper, the authors report the isolation and characterization of Mn(II), Fe(II), Co(II) and Ni(II) complexes with PAT and the fungitoxicity of the complexes on pathogenic fungi. The following is the proposed structure of the complexes of the type [M- $(PAT)_2(H_2O)_2 | X_2$, where M = Mn(II), Fe(II), Co(II) and Ni(II) and $X = CI^{-}$.



Experimental

Synthesis

All chemicals used were AR grade. PAT was prepared and purified by the recommended method [12]. The complexes were all prepared by the following method.

A solution of the metal salt in ethanol was added with stirring to an ethanolic solution of PAT and the pH of the solution was increased to 7.0 by adding dilute ammonia. The reaction mixture was refluxed for about 1 h. This was cooled, filtered off, washed with water followed by ethanol and dried in a vacuum desiccator.

Physical Measurements

Mn, Fe, Co and Ni contents of the complexes were estimated by standard methods. Carbon, hydrogen, nitrogen, oxygen and sulphur were determined using Buehler Apparatus for Microstructural Analysis, Stroehlein, West Germany. The analytical results are given in Table I.

Conductance measurements were made on 10^{-3} M solution of the complexes in nitromethane using a Toshniwal conductivity bridge.

The magnetic susceptibility of the complexes was determined by Gouy's method at room temperature. The experimental magnetic susceptibilities were corrected for diamagnetism.

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Complex	М.Р. (°С)	C% Calc. (found)	H% Calc. (found)	N% Calc. (found)	S% Calc. (found)	M% Calc. (found)	Ω	μ _{eff} (BM) (27 °C)
Mn(PAT) ₂ (H ₂ O) ₂ Cl ₂	260	37.25 (37.18)	4.48 (4.45)	14.48 (14.43)	11.04 (11.09)	9.47 (9.49)	4.0	5.90
Fe(PAT) ₂ (H ₂ O) ₂ Cl ₂	360	37.18 (37.09)	4.48 (4.46)	14.46 (14.39)	11.02 (11.00)	9.62 (9.60)	5.6	4.90
Co(PAT) ₂ (H ₂ O) ₂ Cl ₂	170	36.99 (36.72)	4.45 (4.39)	14.38 (14.39)	10.96 (10.70)	10.09 (10.20)	6.8	4.80
Ni(PAT) ₂ (H ₂ O) ₂ Cl ₂	210	37.00 (37.10)	4.45 (4.49)	14.39 (14.29)	10.96 (10.88)	10.06 (10.02)	8.0	3.05

TABLE I. Analytical Data, Melting Point, Magnetic Moment and Conductance Data of the Complexes.

TABLE II. Fungicidal Screening Data of Complexes and Ligand.

Compound	Average percentage inhibition after 8 days									
	Organism Alternaria S Conen used	p.	Organism <i>Paecilomyces Sp.</i> Conen used		Organism Pestalotia Sp. Conen used					
	0.01%	0.1%	0.01%	0.1%	0.01%	0.1%				
Mn(PAT) ₂ (H ₂ O) ₂ Cl ₂	43.2	58.3	45.3	60.4	45.4	65.3				
$Fe(PAT)_2(H_2O)_2Cl_2$	55.1	64.7	50.2	79.7	52.4	78.9				
Co(PAT) ₂ (H ₂ O) ₂ Cl ₂	60.4	75.8	60.4	80.9	64.2	86.8				
$Ni(PAT)_2(H_2O)_2Cl_2$	65.6	89.8	70.8	95.9	85.1	98.2				
PAT	36.2	40.7	38.7	42.2	43.1	44.5				

The electronic spectra of the complexes and the chelating agent were recorded on a Varian Cary, Model 219, spectrophotometer.

Infrared spectra of the ligand and complexes were recorded on a Perkin-Elmer model 983 G spectrophotometer in CsI pellets in the range 4000-180 cm⁻¹.

In the evaluation of antifungal activity, the ligand and the metal complexes were incorporated in Czapecks medium against *Alternaria* (Sp.), *Paecilomyces* (Sp.) and *Pestalotia* (Sp.). Dimethyl sulphoxide was used as a solvent for preparing different concentrations (0.01% and 0.1%) of the chelating agent and metal complexes. The growth inhibition percentage was calculated on the basis of the average diameter of the fungal colony.

Percentage Inhibition =
$$\frac{(C-T) \times 100}{C}$$

C = diameter of the fungus colony in the control plates after 8 days, T = diameter of the fungus colony in the treated plates after 8 days. The values of percentage inhibition of various compounds are recorded in Table II.

Results and Discussion

The stoichiometries of the complexes are confirmed by the elemental analyses reported in Table I. All the complexes are soluble in acetone, methanol, nitromethane, DMF, DMSO, acetonitrile and chloroform. The molar conductivities range $4-8 \text{ cm}^2 \Omega^{-1} \text{ mol}^{-1}$ which clearly indicates that all the complexes behave as non-electrolytes.

Magnetic Moments

The corrected magnetic moment data (Table I) indicate high spin octahedral geometry for the Mn(II), Fe(II), Co(II) and Ni(II) complexes.

Electronic Spectra

The electronic spectrum of the Mn(II) complex gives three peaks of 16000, 25050 and 35100 cm⁻¹ which are compatible with the octahedral geometry of Mn(II) complexes.

The spectrum of the Fe(II) complex shows a weak absorption band at 11000 cm⁻¹ which is due to the ${}^{5}T_{2g} \rightarrow {}^{5}E_{g}$ transition and is characteristic of a high spin octahedral configuration around Fe(II). The spectrum of the Co(II) complex exhibits two absorption bands at 9250 and 18300 cm⁻¹ with the transitions ${}^{4}T_{1g}(F) \rightarrow {}^{4}T_{1g}$ and ${}^{4}T_{1g}(F) \rightarrow {}^{4}T_{1g}(P)$ respectively. These data are very much like those reported for other Co(II) complexes and are consistent with the assignment of distorted 6-coordinate geometry.

The Ni(II) complex exhibits three spin-allowed transitions (cm⁻¹) 11025, ${}^{3}A_{2g}(F) \rightarrow {}^{3}T_{2g}(F)$; 17900. ${}^{3}A_{2g}(F) \rightarrow {}^{3}T_{1g}(F)$ and 30100, ${}^{3}A_{2g}(F) \rightarrow {}^{3}T_{1g}(P)$. These data suggest an octahedral configuration around Ni(II).

Infrared Spectra

The infrared spectra of the complexes and the ligand were recorded in the range 4000 to 180 cm^{-1} and we will only discuss the selective infrared bands. The highest frequency band of PAT at 3425 cm^{-1} can be assigned to the asymmetric ν (N–H) vibration of the terminal NH₂ group. The other bands at 3250 and 3100 cm^{-1} may be due to the vibration of the imino group and the symmetric ν (N-H) vibration of the amino group. The C=N and C=C stretching vibrations are partially overlapping and the band at 1611 cm⁻¹ (doublet) is assigned to them. The band at 1589 cm⁻¹ can be assigned to δ (N–H) vibration of the NH₂ group. The C=N and C=C stretching vibrations are shifted from 1611 cm^{-1} (doublet) to 1620 cm^{-1} (doublet) on complex formation. This shift of 10 cm^{-1} is possibly due to the involvement of the C=N group in the complex formation. The δ (N-H) vibration of the NH₂ gorup is not shifted at all because it is not involved in bonding. The ν (C=S) vibration of the NH₂ group is not shifted at all downwards by about 40 cm⁻¹ in the spectra of the complexes suggesting the coordination of thiocarbonyl sulphur to the metal ion. The new bands which appeared in the spectra of the complexes in the regions 505-475 cm⁻¹, and 385-335 cm⁻¹ have been assigned to $\nu(M-N)$ and $\nu(M-S)$ respectively. In addition to these absorption bands, the complexes exhibited bands in the region 880-650 cm⁻¹ assignable to the coordinated water, which is absent in the free ligand. On the basis of this evidence, it is concluded that PAT is bidentate in nature.

Fungitoxicity

Alternaria (Sp.), Paecilomyces (Sp.), and Pestalotia (Sp.) were employed to check the antifungal activity of the ligand and its complexes. It is clear from the fungicidal screening data (Table II) that the metal chelates were found to be more fungitoxic than the chelating agent itself. Further, it was noted that the toxicity of the metal chelates increases as the radius of the metal ion decreases.

A possible mode of toxicity may be speculated in the light of chelation theory. Chelation reduces considerably the polarity of the metal ion mainly because of partial sharing of its positive charge with the donor groups and possible π -electron delocalisation over the whole chelate ring. This increases the lipophilic character of the metal chelate which favours its permeation through lipoid layers of fungus membranes. Furthemore, the mode of action of the compounds may involve the formation of hydrogen bond through the -N=C-group and/or hydroxyl group with the active centers of the cell constituents resulting in the interference with the normal cell process.

Acknowledgements

The authors thank the Microbiology Department of the Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina, U.S.A., for fungicidal screening experiments. One of the authors, GTC, gratefully acknowledges the University Grants Commission, New Delhi, for awarding a Junior Research Fellowship.

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