Inorganica Chimica Acta, 46 (1980) L43–L45
©Elsevier Sequoia S.A., Lausanne – Printed in Switzerland

Studies on Complexes of 4-(5'-Phenyl-1',3',4'-Oxadiazole-2'-YL) Thiosemicarbazide with Some First Transition Series Metal Ions

R. S. SRIVASTAVA

Department of Chemistry, M. G. Degree College, Gorakhpur, 273001, India

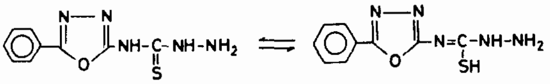
Received December 17, 1979

Oxidiazole derivatives have been reported to be biologically versatile compounds, having bactericidal [1], fungicidal [2], herbicidal [3], analgesic [4], hypoglycemic [5] and antipyretic [4] activities. Further, the compounds synthesised in the present communication, possess—N—C—S—linkage, which is possible toxophore in many pesticides [6]. Several metal chelates are known to possess bactericidal [7], fungicidal [8] and antiviral [9] activities. Some metal chelates are known to inhibit tumour growth [10] and during treatment of cancer with thiosemicarbazones it has been shown that the active species is not the thiosemicarbazone itself but its metal chelates [11, 12]. Recently the examination of the antitumour properties of α (N)-heterocyclic carboxaldehyde thiosemicarbazones has been extended to the consideration of some of their first-row transition metal complexes [13]. Previously other bis(thiosemicarbazonato) copper and zinc chelates had been shown to have substantial inhibitory effect against tumour cells [11, 14]. It has been shown that the mode of action of these complexes is at the genetic level through the formation of inter or intra-strand links in DNA chain, thus inhibiting its replication [15–17].

In view of the above, it was presumed that the title complexes might have enhanced anticancer and antifungal activities. The anticancer activity of these complexes will be published elsewhere.

Experimental

All chemicals used were of analytical grade or equivalent quality. The ligand (POT), 4-(5'-phenyl-1',3',4'-oxadiazol-2'-yl) thiosemicarbazide (i) was prepared according to the method of Kozakov *et al.* [18]. (MP 232 °C as reported by Singh and Yadav [19]).



(i)

The appropriate metal salt and sodium salt of the ligand (1:2 molar ratio) were refluxed in ethanol for 4–5 hours. The reaction mixture on cooling gave the desired product which was filtered, washed with water followed by ethanol and dried in a vacuum desiccator for constant weight. The analytical data are listed in Table I.

Electrical conductance was measured with the help of Toshniwal's conductivity bridge (type CL01/01), using a dip type cell at room temperature.

Magnetic susceptibility of the complexes was determined by Gouy's method using $Co[Hg(SCN)_4]$ as a calibrant. The experimental magnetic susceptibilities were corrected for diamagnetism [20].

The electronic spectra of the complexes and the chelating agent were recorded, in acetone, on a Unicam SP 8000 UV Spectrophotometer.

TABLE I. Analytical and Magnetic moment Data of the Complexes.[a]

Complex	Metal %	Nitrogen %	Sulphur %	μ_{eff} (B.M.)	M.P. (°C)
$Mn[POT(H_2O)]_2$	9.10 (9.15)	13.86 (13.97)	20.98 (21.29)	5.90	>250
$Fe[POT(H_2O)]_2$	9.26 (9.30)	13.90 (13.95)	21.40 (21.26)	4.90	>250
$Co[POT(H_2O)]_2$	9.70 (9.75)	13.76 (13.88)	21.10 (21.15)	4.79	230
$Ni[POT(H_2O)]_2$	9.71 (9.75)	13.90 (13.88)	20.97 (21.15)	3.05	236
$Cu[POT]_2$	10.46 (11.14)	14.47 (14.63)	22.20 (22.29)	1.73	218

[a]Calculated values are given in parentheses.

TABLE II. Fungicidal Screening.

Compound serial, as in Table I	Average percentage inhibition after 96 hours					
	Organism-*Paecilomyces Variotii* concentrations used			Organism-*Curvularia lunata* concentrations used		
	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
1	56.2	42.1	30.2	52.4	47.2	27.4
2	60.5	42.2	31.0	59.6	49.3	30.0
3	78.2	50.0	37.0	66.7	53.4	36.3
4	90.0	52.4	40.6	79.9	56.6	40.4
5	100.2	66.6	50.0	98.9	62.5	48.6
Ligand	40.7	36.2	25.5	42.0	35.4	25.5

Infrared spectra of the ligand and complexes were recorded on a Perkin–Elmer (model 337) Spectrophotometer in KBr in the range 400–4000 cm^{-1}.

^1H NMR spectra were recorded on a Varian A-60D spectrometer.

The complexes were analysed for their metal content employing standard literature procedures after destroying the organic residue with a mixture of concentrated nitric and hydrochloric acid.

The water content of the complexes was determined by heating them in the range 150–300 °C and determining the loss in weight.

Fungicidal activity was evaluated against *Paecilomyces variotii* and *Curvularia lunata* by the agar-plate technique [21] at three concentrations, *viz.* 1000 ppm, 100 ppm and 10 ppm, and the number of replications in each case was three. The percentage inhibitions by various compounds are included in Table II.

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

where,

C = Diameter of fungus colony in control plates after 96 hours.

T = Diameter of fungus colony in treated plates after 96 hours.

Results and Discussion

The analytical data included in Table I show that deprotonated complexes are formed in 1:2 metal to ligand stoichiometries. The complexes have a molar conductance of ~2 mho $cm^2 \times 1 \times mol^{-1}$ and these may, therefore, be classed as non-electrolytes. The absence of anions in the above complexes suggests the formation of covalent bond between sulphur of SH group and metal. The loss of water at relatively high temperature (170–285 °C) indicated that these are coordinated and not lattice held.

Magnetic Moments

The corrected magnetic moment data (Table I) indicate high-spin octahedral geometry for Mn(II), Fe(II), Co(II), Ni(II) complexes and square planar structure for Cu(II) complex.

Electronic Spectra

The spectrum of the Mn(II) complex gives three peaks at 16000, 24620 and 35210 cm^{-1} which are compatible with the octahedral geometry of Mn(II) complex.

The electronic spectrum of Fe(II) complex shows a weak absorption band at 11500 cm^{-1} which is due to the $^5T_{2g} \rightarrow {}^5E_g$ transitions and is characteristic of high spin octahedral Fe(II) complex.

The spectrum of Co(II) complex gives two absorption bands at 9000 and 18150 cm^{-1} with the transitions: $^4T_{1g}(F) \rightarrow {}^4T_{2g}(\nu_1)$ and $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ (ν_3) respectively in octahedral environment of Co(II). With the help of these values of ν_1 and ν_3, Dq, B′ and ν_2 work out as 900, 1120 and 18000 cm^{-1} respectively. The ν_2/ν_1 ratio is found to be 2.01 which lies well within the limit reported for distorted octahedral Co(III) complexes [22].

The Ni(II) complex exhibits three spin-allowed transitions (cm^{-1}) at 11000, $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$ (ν_1); 17800, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ (ν_2) and 30000, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ (ν_3). The ratio ν_2/ν_1 is equal to ≈1.62 usually accepted for octahedral Ni(II) complexes [23]. The frequencies ν_1, ν_2 and ν_3 denote the first, second and third spin transitions respectively. Using these frequencies the values of Dq, B′ and β have been calculated, which are 1100 cm^{-1}, 1080 cm^{-1} and 0.50 respectively. These values are in accordance with the O_h symmetry around the Ni(II) ion.

The visible spectrum of the Cu(II) complex showed a broad band at 15384 cm^{-1} corresponding to a combination of ${}^2B_{1g} \rightarrow {}^2A_{1g}$, ${}^2B_{1g} \rightarrow {}^2B_{2g}$ and ${}^2B_{1g} \rightarrow {}^2E_{1g}$ transitions in the D_{4h} symmetry, most probably showing square planar arrangement.

Infrared Spectra

The positions of the absorption bands due to –NH and –N=C modes remain practically unchanged in the spectra of the complexes, indicating that the nitrogen of oxadiazole ring is not taking part in coordination. However, a negative shift of 20–30 cm^{-1} in cyclic –CO, a positive shift of 10–15 cm^{-1} N–N and complete disappearance of the SH bands taken together in the spectra of complexes as compared to the spectrum of the free ligand indicate that oxygen of the cyclic –CO group involved in coordination and sulphur of the –SH group is covalently bonded with metal.

The IR spectra clearly indicate that all the complexes except that of copper contain coordinated water molecule.

^{1}H NMR Spectra

The ^{1}H NMR spectrum of ligand in DMSO-d_6 + $CDCl_3$ shows the following signals: aromatic proton (5H) between 7.2–7.7 δ, –$NHNH_2$ (3H) at 6.4 δ and –SH (1H) at 4.42δ. Complexes were studied by looking at the phenyl proton –$NHNH_2$ and –SH resonances. The observed spectra are consistent in all the cases with maintenance of the ligand chemical structure.

The proton spectrum of the title complexes shows practically no shift in phenyl group and the disappearance of resolution at 4.42 δ corresponding to –SH, indicates binding of the ligand to metal ion under study through the sulphur of –SH group. This is in accordance with the various workers [24].

The rather small shift of the –$NHNH_2$ proton resonance observed upon coordination and the relative intensity of the signal are in agreement with lack of direct interaction between the metal and amide nitrogen.

Fungitoxicity

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.

Our studies indicate that in the case of Cu(II) complex studied, the arrangement of the chelate ring is square planar. In all the other cases the complexes are hexacoordinated, involving covalent bonding through the sulphur of –SH group and coordination through the oxygen of the oxadiazole ring.

Acknowledgement

The author thanks the authorities of M. G. Degree College, Gorakhpur for providing laboratory facilities. Thanks are also due to the Director Central Drug Research Institute, Lucknow for elemental and spectral analyses. The financial support from the University Grants Commission, New Delhi is also gratefully acknowledged.

References

1 I. Hirao, Y. Kato and T. Hirota, *Bull. Chem. Soc. (Japan), 44,* 1923 (1971).
2 A. Sugihara and M. Ito, *Jap. Pat.* 11743 (1967); *Chem. Abstr., 68,* 78292 V (1968).
3 Rhône-Poulenc S.A., *Brit. Pat.* 1110500 (1968); *Chem. Abstr., 69,* 52143 t (1968).
4 E. Wilder Smith, *U.S. Pat.* 3127410; *Chem. Abstr., 61,* 3118 (1964).
5 Tohoku Yakka Daigaku, *Kenkyu Nempo, 17,* 43 (1970).
6 B. C. Dash and G. N. Mahapatra, *J. Indian Chem. Soc., 44,* 939 (1967).
7 K. K. Chaturvedi and R. Kaushal, *Indian J. Pharm., 37,* 85 (1975).
8 J. G. Horsfall, 'Fungicides and their Action', Chronica Botanica Co., Waltham (Mass) (1945) p. 1–8 and 14–41.
9 F. P. Dwyer and D. P. Mellor, 'Chelating agents and Metal Chelates', Academic Press, London (1964).
10 F. P. Dwyer, E. Mayhew, E. M. F. Roe and A. Shulman, *Brit. J. Cancer., 19,* 195 (1965).
11 J. A. Crim and H. G. Petering, *Cancer Res., 27,* 1278 (1967).
12 H. G. Petering and G. J. Van-Giessen, 'The Biochemistry of Copper', Academic Press, New York (1966) p. 197–208.
13 W. E. Anthrholine and D. H. Petering, *Proc. Am. Assoc. Cancer Res., 15,* 63 (1974).
14 G. J. Van-Giessen, J. A. Crim, D. H. Petering and H. G. Petering, *J. Natl. Cancer Inst., 51,* 139 (1973).
15 H. C. Harder and B. Rosenberg, *Int. J. Cancer, 6,* 207 (1970).
16 J. A. Howle and G. R. Gale, *Biochem. Pharmacol., 19,* 2757 (1970).
17 A. J. Thomson, R. J. P. Williams and S. Reslova, *Str. Bonding (Berlin), 11,* 1 (1972).
18 V. Ya. Kazakov and I. Ya. Postovskii, *Izvest. Vysshikh Ucheb. Zavedenii, Khim i Khim Tekhnol, 4,* 238 (1961).
19 H. Singh and L. D. S. Yadav, *Agr. Biol. Chem., 40* (4) 759 (1976).
20 B. N. Figgis and J. Lewis, in 'Modern Coordination Chemistry', Edited by J. Lewis and R. G. Wilkins, Interscience, New York (1960) p. 403.
21 U.S.D.A. Circular No. 198 (1931).
22 K. C. Patel and D. E. Goldberg, *J. Inorg. Nucl. Chem., 34,* 637 (1972).
23 L. Sacconi, *Trans. Metal Chem., 4,* 199 (1968).
24 R. Ettorre, V. Guantieri, A. M. Tamburro and L. De Nardo, *Inorg. Chim. Acta Letters, 32,* L38 (1979) and references therein.