

Dichloro- & monochloro-oxovanadium(V) complexes of benzothiazolines

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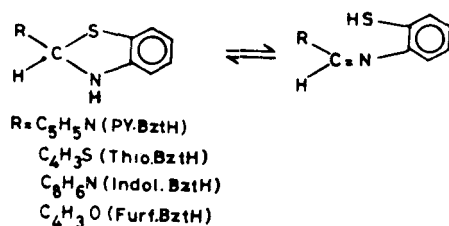
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Synthetic and structural features of some oxovanadium(V) complexes with biologically active benzothiazolines obtained by the condensation of 2-pyridinecarboxaldehyde, 2-thiophene carboxaldehyde, indole-3-carboxaldehyde and furfuraldehyde with 2-mercaptoaniline have been described. The new complexes $[(VOCl_2)(Bzt)]$ and $[(VOCl)(Bzt)_2]$ ($BztH$ = benzothiazoline) have been characterized by elemental analyses, conductance measurements, molecular weight determinations and magnetic studies. Based on IR, ^1H NMR, ^{13}C NMR and electronic spectral studies, trigonal-bipyramidal and octahedral geometries have been assigned to the resulting complexes. A few representative compounds have been screened for their fungicidal activity and found to be quite active against *Helminthosporium graminum* and *Rhizopus oryzae*.

Recently, much interest has been shown in the synthesis of metal chelates with sulphur containing ligands as these possess cytotoxic activity¹. Benzothiazolines, obtained by the condensation of 2-mercaptoaniline with the carboxyl compounds, constitute an important series of sulphur donor ligands². The condensation of 2-mercaptoaniline with an aldehyde does not normally lead to the isolation of the corresponding schiff base, but rather to a thiazoline or benzothiazoline^{3,4}. However, it has been shown that in the presence of the metal ion, which acts as a template, formation of the schiff base is favoured in comparison with the bis-thiazolidinyl form⁵.

In previous communications from our laboratories, considerable amount of work with transition as well as non-transition metals⁶⁻⁹ has been reported with oxygen, nitrogen and/or sulphur containing ligands. The marked biological activity of vanadium complexes with thio ligands and the role of vanadium as a trace element with inhibitory effects on the enzymes in the bio-systems¹⁰ prompted us to study the oxovanadium(V) complexes with the following benzothiazolines, derived from the condensation of 2-mercaptoaniline with heterocyclic aldehydes.



Materials and Methods

All the chemicals used were of AR grade and the reactions were carried out under strictly anhydrous conditions.

Benzothiazolines were prepared by the condensation of 2-pyridine carboxaldehyde, 2-thiophene carboxaldehyde, indole-3-carboxaldehyde and furfuraldehyde with 2-mercaptoaniline taken in equimolar ratio in benzene. The solution was stirred for 2-3 hr and the excess of the solvent was removed *in vacuo*. The crude solid obtained was recrystallised from the same solvent. 2-Pyridine carboxaldehyde benzothiazoline, yellow solid m.p. 81°C; 2-thiophene carboxaldehyde benzothiazoline, yellow solid m.p. 91°C; indole-3-carboxaldehyde benzothiazoline, yellow solid m.p. 154°C; furfuraldehyde benzothiazoline, yellow solid m.p. 72°C.

For the preparation of metal complexes, to a weighed amount (0.006-0.007 mol) of trichlorooxovanadium(V) in 40 cm³ of dry MeOH, the requisite amount (0.004-0.006 mol) of the sodium salt of the benzothiazoline was added. The resulting mixture was refluxed for 12-14 hr on an oil-bath at 120°C. After the completion of the reaction, the sodium chloride formed during the reaction was filtered off and the residue was dried *in vacuo* at 40-60°C/.05 mm for 3 hr. The important physical properties and analytical data of the complexes are given in Table 1.

Vanadium was estimated as V_2O_5 after hydrolysing the compound in a platinum crucible with dilute NH_4OH solution. The product was subsequently oxidised by conc. HNO_3 and finally ignited to get the pentoxide. Carbon and hydrogen analyses were performed at the Microanalytical Laboratory of our dep-

Table 1—Analytical data and physical properties of metal complexes

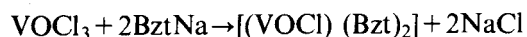
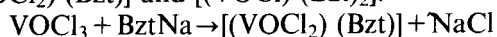
Complex	Colour and state (MP, °C)	Found (Calc.), %						Mol. Wt. Found (Calc.)
		V	C	H	N	Cl	S	
[(VOCl ₂) (PyBzt)]	Brown solid (110)	14.60 (14.57)	41.00 (41.03)	2.60 (2.56)	7.63 (7.97)	20.10 (20.23)	9.30 (9.11)	329.45 (350.94)
[(VOCl) (PyBzt) ₂]	Brown solid (124)	9.70 (9.63)	54.61 (54.50)	3.48 (3.40)	10.50 (10.59)	6.69 (6.71)	12.21 (12.11)	542.40 (528.44)
[(VOCl ₂) (ThioBzt)]	Green solid (130)	14.20 (14.31)	37.02 (37.08)	2.26 (2.24)	3.90 (3.93)	20.01 (19.94)	18.12 (17.98)	315.69 (355.94)
[(VOCl) (ThioBzt) ₂]	Dark Green solid (65)	9.56 (9.46)	49.23 (49.03)	3.05 (2.97)	5.30 (5.20)	6.72 (6.59)	23.44 (23.77)	522.75 (538.44)
[(VOCl ₂) (IndolBzt)]	Dark Red solid (95)	12.90 (13.09)	46.20 (46.27)	2.90 (2.82)	7.34 (7.19)	18.05 (18.25)	8.29 (8.22)	413.52 (388.94)
(VOCl) (IndolBzt) ₂	Reddish brown solid (140d)	8.49 (8.42)	59.50 (59.55)	3.84 (3.63)	9.20 (9.26)	5.80 (5.87)	10.23 (10.58)	569.16 (604.44)
[(VOCl ₂) (FurfBzt)]	Bright Green solid (88)	14.93 (14.98)	38.12 (38.33)	2.45 (2.35)	4.10 (4.11)	10.37 (10.44)	9.49 (9.41)	362.17 (339.9)
[(VOCl) (FurfBzt) ₂]	Green solid (75)	10.12 (10.05)	52.32 (52.12)	3.17 (3.15)	5.50 (5.52)	7.23 (7.00)	12.81 (12.63)	536.23 (506.44)

artment and sulphur was estimated by Messenger's method.

Electronic spectra were recorded in MeOH on a Pyeunicam SP8-100 spectrophotometer and the IR spectra on a Perkin Elmer 577 grating spectrophotometer in KBr pellets. ¹H and ¹³C NMR spectra at 90 MHz and 22.49 MHz, respectively, were recorded on a Jeol FX 90Q spectrometer with TMS as the internal standard. Magnetic measurements were carried out at the room temperature (303K) by the Gouy's method using NiCl₂ solution as the calibrant. Conductivity measurements were made using a conductivity bridge Systronics 305 and molecular weights were measured by the Rast Camphor method.

Results and Discussion

Reactions of trichlorooxovanadium(V) with the sodium salts of benzothiazolines in anhydrous methanol gave 1:1 and 1:2 molar products of the type [(VOCl₂) (Bzt)] and [(VOCl) (Bzt)₂].



The reactions in 1:3 molar ratio were also attempted but even on prolonged heating the reactions did not proceed beyond the replacement of two chlorine atoms by the ligand moieties and [(VOCl) (Bzt)₂] type of derivatives were the end products.

The resulting complexes were soluble in methanol, DMF and DMSO and were recrystallized from a mixture of methanol and solvent ether. Their purity was checked by thin layer chromatography. They were found to be monomers and non-electrolytes (molar conductances: 15-20 ohm⁻¹cm²mol⁻¹ in dry DMF).

In the IR spectra of ligands, the absence of νSH at 2500-2600 cm⁻¹ and νC=N at 1600-1650 cm⁻¹ clearly indicated the benzothiazoline rather than the schiff base structure¹¹. In the spectra of complexes, ligand bands at 3370-3200 cm⁻¹ due to NH stretching vibrations, disappeared indicating the chelation of nitrogen to vanadium; a new band at ~ 1600 cm⁻¹ was observed due to νC=N vibrations. The appearance of this band is a strong evidence that the complexes are metal schiff base derivatives as the benzothiazoline ring rearranges to give the schiff base derivative in presence of vanadium. The chelation of ligands through azomethine nitrogen and thiolosulphur gets further support from the appearance of new bands in the regions 445-410 and 330-300 cm⁻¹ due to νV←N and νV—S vibrations, respectively¹². However, the bands in the region 380-360 cm⁻¹ are assigned to νV—Cl vibrations. Further, the appearance of strong bands in the region 940-980 cm⁻¹ in the complexes is due to V=O stretching vibrations¹³.

The ¹H NMR spectrum of 2-thiophenecarboxaldehyde benzothiazoline showed the NH proton signal

Table 2 ^{13}C NMR spectral data (δ , ppm) of benzothiazoline and its vanadium (V) complexes.

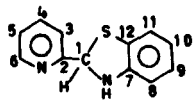
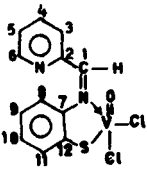
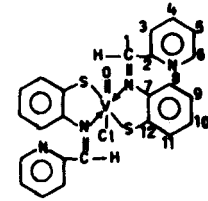
Structure	1	2	3	4	5	6	7	8	9	10	11	12
 (Ligand)	149.57	125.52	121.19	120.64	121.09	123.46	126.17	125.95	125.61	125.42	126.77	136.92
 (1 : 1 complex)	160.96	125.57	121.83	120.94	122.72	124.36	126.27	126.29	125.71	125.31	127.83	146.98
 (1 : 2 complex)	158.31	124.31	121.17	120.05	122.31	123.56	126.56	126.18	125.22	125.38	125.53	148.18

Table 3—Fungicidal screening data of benzothiazoline and its oxovanadium(V) complexes

Compounds

Av. percentage inhibition after 96 hr.

	<i>Helminthosporium graminum</i>			<i>Rhizopus oryzae</i>		
	25 ppm	50 ppm	75 ppm	25 ppm	50 ppm	75 ppm
ThioBztH	82	86	89	30	39	47
$[\text{VOCl}_2(\text{ThioBzt})]$	85	89	91	37	43	54
$[\text{VOCl}(\text{ThioBzt})_2]$	86	95	98	45	49	58

at δ 4.36 ppm, which disappeared in the corresponding vanadium complexes. The azomethine proton signal observed at δ 7.84 ppm in the benzothiazoline got shifted downfield in the spectra of vanadium(V) complexes indicating the formation of a coordinate bond.

^{13}C NMR spectra of 2-pyridine carboxaldehyde benzothiazoline and its vanadium complexes were also recorded (Table 2). The shifts of the carbons attached to S and N indicate their coordination^{14,15} to vanadium atom.

The electronic spectra of ligands showed two bands at 250-265 and 300-320 nm characteristic of benzothiazolines¹⁶. These bands arising out of $\phi - \phi^*$ benzenoid¹⁴⁻¹⁷ transitions remained unaltered in all the vanadium complexes, whereas an additional band was observed around 380-400 nm due to $n - \pi^*$ electronic transitions of the azomethine, which indic-

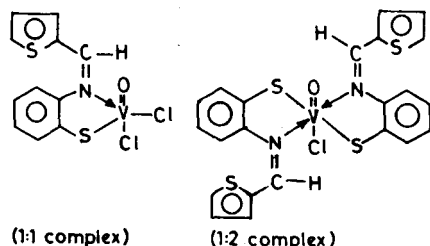
ates isomerization of the ligands on complexation. However, in the visible region, the metal complexes showed an absorption maximum at 545 nm which is too strong to be accounted for by a $d-d$ transition and presumably arises from the ligand $\rightarrow$ metal charge-transfer ($L \rightarrow M$) as reported earlier⁷.

The specific susceptibility measurements at 303 K have been found to be in the range of 0.5021 to 0.6832 ($\chi_s \times 10^{-6}$ c.g.s. units) confirming the diamagnetic nature of the complexes.

On the basis of above evidences distorted trigonal bipyramidal and octahedral geometries have been proposed for the 1:1 and 1:2 derivatives, respectively.

Biological screening

For evaluating the antifungal activity of the ligand and metal complexes, these were incorporated in the



Agar medium at a fixed pH (6-7) against *Helminthosporium graminum* and *Rhizopus oryzae*. The growth inhibition percentage was calculated on the basis of average diameter of the fungal colony.

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

where C = diameter of the fungus colony of the control plate after 96 hr and T = diameter of the fungus colony in the tested plates after the same period.

The average diameters (mm) for blank (after same period) reading were 48 and 80 for *Helminthosporium graminum* and *Rhizopus oryzae*, respectively, at 25°C. It is clear from the fungicidal screening data (Table 3) that the metal complexes are more fungitoxic than the chelating agent itself. Further, it can be noted that the toxicity of the metal chelates decreases on lowering the concentration.

The observed toxicity can be explained in the light of the chelation theory¹⁸. The chelation reduces polarity of the metal ion mainly because of partial sharing of its positive charge with the donor groups and electron delocalisation over the whole chelate ring. This increases the lipophilic character of the metal, which subsequently favours its permeation through lipid

layer of the fungus membranes. Furthermore, the mode of action of the compounds may involve the formation of a hydrogen bond through the $-N=C<$ group with the active centers of the cell constituents which may interfere with the normal cell process.

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