Metal Complexes of Cobalt(II), Copper(II) and Nickel(II) with some Dithiooxamide Derived Ligands - Their Synthesis, Structural Determination and Antibacterial Properties

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Summary: The complexes of cobalt(II), copper(II) and nickel(II) with some dithiooxamide derived ligands have been synthesised and characterised on the basis of their elemental analysis, molar conductance, magnetic moment, electronic, NMR and IR spectral data. These prepared complexes have been subjected to screening against bacterial species staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae and Tuberculi bacilli. These studies have shown the metal complexes to be more antibacterial than those of the parent ligands.

Introduction

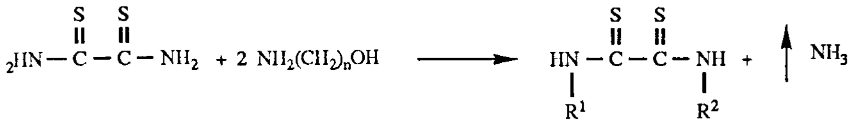
Dithiooxamides are weak acids in which the thiooxamide moiety interact with various metal ions through its nitrogen and sulphur groups. These chelates, therefore have utility in various spectrophotometric determinations [1,2] and spot reactions [3]. Their usefulness as fungicides [4] and bactericides [5] have also been studied by some research workers. In line with our current research programme of investigating the coordinating properties and pharmacological behaviour we intend to report the synthesis of biologically active derivatives ($2L_{1\text{-}3}$) of this versatile ligand (1) and their various metal complexes of the type ML_2X_2 where, M = Co(II), Cu(II) and Ni(II); L = $[CSNH(CH_2)_2OH]_2$ L = $[CSNH(CH_2)_3OH]_2$ and L = $CSNH(CH_2)_4OH]_2$ and X = Cl. The spectroscopic structural determination and antibacterial properties of these prepared metal chelates against various bacterial species is also reported in this paper.

Results and Discussion

Metal complexes summarised in Table 2 are stable amorphous solids which decompose between 160-190°C. The solubility data also show that they are appreciably soluble in common organic solvents but completely soluble in butanol and DMF.

All the complexes have low value of molar conductance (8.5-15.8 $ohm^{-1}\ cm^{-2}\ mol^{-1}$) in DMF solution ($10^{-3}$M) suggesting them to be non-electrolytic [6] which in turn indicate that the ligand and anions are covalently bonded to the metal atom [7].

On examining the IR spectra of complexes (Table 3) in comparison to those of free ligands in the solid state give clues regarding the donor sites of the ligand molecule. The free ligand shows certain characteristic bands in its spectrum.



$$ {}_{2}HN-\overset{\overset{S}{\|}}{C}-\overset{\overset{S}{\|}}{C}-NH_2 + 2\ NH_2(CH_2)_nOH \longrightarrow \underset{\underset{R^1}{|}}{HN}-\overset{\overset{S}{\|}}{C}-\overset{\overset{S}{\|}}{C}-\underset{\underset{R^2}{|}}{NH} + \uparrow NH_3 $$

(1)

(2)

$L_1 = R_1 = R_2 = -(CH_2)_2OH$
$L_2 = R_1 = R_2 = -(CH_2)_3OH$
$L_3 = R_1 = R_2 = -(CH_2)_4OH$

Table 1: IR, NMR and elemental analysis data of the ligands

No.	M.P .(°C)	IR (cm^{-1})	^{1}H-NMR ($CDCl_3$)δ-	% Calc (Found C	H	N
L_1	92-93	1105, 1385, 2975, 3600.	8.3(2H, s, NH exchange withD_2O), 2.6 (4H, t, 2xCH_2N), 3.8 (4H, q, 2zCH_2O), 4.1(2H, s, OH exchange with D_2O).	34.61 (34.50)	5.76 (5.70)	13.44 (13.43)
L_2	108	1115, 1380 3210, 3375.	8.45 (2H, s, 2xNH exchange with D_2O), 2.6 (4H, t, 2xCH_2N), 2.2 (4H, m, 2xCH_2), 3.85 (4H, q,2xCH_2O), 4.15 (2H, s, OH exchange with D_2O).	40.90 (40.93)	6.77 (6.73)	11.86 (11.02)
L_3	115-117	1120, 1365, 3300, 3540	8.5 (2H, s, 2xNH exchange with D_2O), 2.65 (4H, t, 2xCH_2N), 2.65(8H, s, 4 x CH_2), 3.9 (4H, q, 2xCH_2O), 4.2 (2H, s, OH exchange with D_2O).	45.45 (45.44)	7.57 (7.56)	10.60 (10.61)

Table 2: Magnetic moment and elemental analysis data of the complexes

Molecular formula	M. Moment μ_{eff}(BM)	Elemental analysis, % Calc. (Found) C	H	N
1. $Co(L_1)_2Cl_2$	4.12	26.38 (26.41)	4.39 (4.36)	10.25 (10.28)
2. $Co(L_2)_2Cl_2$	4.26	31.91 (31.92)	5.31 (5.28)	9.30 (9.33)
3. $Co(L_3)_2Cl_2$	4.55	36.49 (36.46)	6.00 (6.09)	8.51 (8.46)
4. $Cu(L_1)_2Cl_2$	1.78	26.18 (26.16)	4.36 (4.35)	10.17 (10.17)
5. $Cu(L_2)_2Cl_2$	1.88	31.66 (31.65)	5.27 (5.25)	9.23 (9.24)
6. $Cu\ (L_3)_2\ Cl_2$	1.92	36.23 (36.21)	6.03 (6.01)	8.45 (8.43)
7. $Ni\ (L_1)_2Cl_2$	3.12	26.42 (26.43)	4.40 (4.39)	10.27 (10.25)
8. $Ni(L_2)_2Cl_2$	2.98	31.92 (31.91)	5.31 (5.33)	9.30 (9.29)
9. $Ni(L_3)_2Cl_2$	3.20	36.50 (36.48)	6.07 (6.05)	8.51 (8.51)

A strong band covering the region 3540-3600 cm^{-1} and at 2975-3300 cm^{-1} are attributed to (-NH) and (-OH) stretching frequencies in the free ligand. The bands appearing around 1385 and 1105 cm^{-1} may be assigned to (C=S) and (C-N) vibrations. The position of vibrations around 1385 and 1105 cm^{-1} are shifted to higher frequency side 1385-1420 cm^{-1} and 1105-1135 cm^{-1} upon chelation in the free ligands. Regarding the participation of thiooxamide moiety in complexation, however, all metal complexes exhibit two new characteristic bands (not observable in the free ligand) in the region 430-450 cm^{-1} and 280-340 cm^{-1} expected for (M-S) and (M-N) stretching modes respectively [8,9] which confirm the coordination of ligand to the metal atom through nitrogen and sulphur atoms. A new band indicating the bonding (M-Cl) in the region 340-370 cm^{-1} was also observed in all the spectra.

The room temperature effective magnetic moment (μ_{eff}) (Table 2) for all metal complexes lie well within the range for their observed geometries [10]. The μ_{eff} for Co(II) complexes fall in the range 4.12- 4.55 B.M. expected to contain odd number of electron (d^7-system). The μ_{eff} value for Cu(II) and Ni(II) complexes also lie within the range consistent to their spin-free octahedral geometries [11,12].

The electronic spectra of all the metal complexes exhibit bands due to d-d transitions (Table 3). Co(II) complexes exhibit bands around 29,900-31,900, 19,300-19,320, 17,550-17, 655, 10,300- 13,320 and 10,1150-10,120 cm^{-1} of which the first one is assigned to metal $\longrightarrow$ ligand charge transfer band. The band around 19,300-19,320 cm^{-1} is assigned to the transition $^4T_{1g}(F) \longrightarrow {}^4T_{1g}(P)$ for Co(II) ions in octahedral environment and rest of the bands were assigned to the transition $^4T_{1g}(F) \longrightarrow {}^4A_{2g}$ (ν_2), $^4T_{2g}(F) \longrightarrow {}^4T_{2g}(F)$ and $^4A_{2g} \longrightarrow {}^4T_{2g}$ respectively. The Ni(II) complexes exhibit three typical bands around 26, 110-26, 280, 15,480-15,650 and 9390-9600 cm^{-1} corresponding to the transitions $^3A_{2g} \longrightarrow {}^3T_{2g}(F)$ (ν_3), $^3A_{2g} \longrightarrow {}^3T_{1g}(F)$ (ν_2) and $^3A_{2g} \longrightarrow {}^3T_{2g}$ (ν_1) respectively in octahedral fields [13]. The Cu(II) complexes showed a broad band around 14,250-15,110 cm^{-1} arising from $^2E_g \longrightarrow {}^2T_{2g}$ transitions in octahedral field [14,15] with distorted geometry. Based on the above observations pseudo- octahedral structure is proposed for these complexes.

Antibacterial activity

Many studies have revealed [16-19] that the metal ions are known to display antimicrobial activity. Antibacterial action of these complexes was investigated in comparison with the uncomplexed

Table 3: IR and electronic spectral data of the complexes

Complex	IR (cm^{-1})	λ_{max} (cm^{-1})
$Co(L_1)_2Cl_2$	435 (M-S), 280 (M-N), 1130 (C-N), 1420 (C=S) 360 (M-Cl).	10150, 13010, 17550, 19310, 31900.
$Co(L_2)_2$	Cl_2 440 (M-S), 285 (M-N), 1125 (C-N), 1410 (C=S) 365 (M-Cl).	10200, 10320, 17655, 19320, 30300.
$Co(L_3)_2Cl_2$	430(M-S), 295 (M-N), 1115 (C-N), 1410 (C=S), 360 (M-Cl).	10200, 10315, 17650, 19300, 29900.
$Cu(L_1)_2Cl_2$	430 (M-s), 320 (M-N), 1135(C-N), 1400 (C=S) 345 (M-Cl).	15100, 29910
$Cu(L_2)_2Cl_2$	435 (M-S), 325 (M-N), 1130 (C-N), 1400 (C=S) 340 (M-Cl).	15200, 30100.
$Cu(L_3)_2Cl_2$	440 (M-S), 320 (M-N), 1110 (C=N), 1410 (C=S) 340 (M-Cl).	15120, 3015,
$Ni(L_1)_2Cl_2$	445 (M-S), 340 (M-N), 1120 (C-N), 1415 (C=S) 365 (M-Cl).	9390, 15500, 26200.
$Ni(L_2)_2Cl_2$	455 (M-S), 335 (M-N), 1125 (C-N), 1415 (C=S) 370 (M-Cl).	9600, 15480, 26110.
$Ni(L_3)_2Cl_2$	450 (M-), 335 (M-N), 1120 (C-N), 1420 (C=S). 370 (M-Cl).	9520, 15650, 26820.

Table 4: Antibacterial activity data of the complexes and the ligands

Ligand/complex	Microbial species			
	S.aureus	E.coli	K.pneumoniae	T.bacilli
$L_1 = [CSNH(CH_2)_2OH]_2$	++	+	++	++
L_2 $[CSNH(CH_2)_3OH]_2$	++	++	++	++
$L_3 = [CSNH(CH_2)_4OH]_2$	++	++	++	++
$Co(L_1)_2Cl_2$	++	++	++	+++
$Co(L_2)_2Cl_2$	+++	+++	+++	+++
$Co(L_3)_2Cl_2$	+++	+++	+++	+++
$Cu(L_1)_2Cl_2$	+++	+++	+++	++
$Cu(L_2)_2Cl_2$	+++	++	+++	+++
$Cu(L_3)_2Cl_2$	+++	+++	+++	++
$Ni(L_1)_2Cl_2$	+++	++	+++	+++
$N9L_2)_2Cl_2$	+++	+++	+++	+++
$Ni(L_3)_2Cl_2$	+++	+++	+++	++

L_1, L_2 and L_3 = Uncomplexed ligands. Microbial effect (+ Inhibition). Zone diameter; (+)=6-8 mm, (++)=8-10 mm, (+++)= 10 mm.

ligands against bacterial species (a), (b), (c) and (d). All the complexes were tested at concentration 30μg/0.01 ml in DMF using paper disc diffusion method already reported [20]. The zone of inhibition (in mm) was measured. The result of these studies (Table 4) are reproduced which indicate that metal complexes have shown a significant antibacterial activity against all bacteria. This enhanced activity is may be, due to the chelation which reduces the polarity of the metal ions in the complexes. This may increase, in turn the hydrophobic character of the chelate favouring its easy permeation through lipoid layer of the microorganism.

Experimental

All chemicals and solvents used in this work were AR grade. IR spectra were recorded on Perkin-Elmer 598 spectrophotometer. NMR spectra were recorded on Perkin-Elmer R_{14}(90 MHz) spectrometer in deuteriated solvent using TMS as an internal standard. Electronic spectra were studied with a Beckman spectrophotometer model DU using glass cells of 1 cm thickness.

Magnetic measurements were done on solid complexes using Gouy balance method. Elemental analysis of CHN were carried out on a coleman automatic analyser.

Preparation of phosphate buffer pH-7 solution

It was prepared by adding aqueous solution of sodium dihydrogen phosphate (0.2 M, 40 ml) into an aqueous solution of disodium hydrogen phosphate (0.2M, 60 ml). The pH was then adjusted to pH- 7 by adding ammonium hydroxide solution.

Preparation of ligands

To an ethanolic solution (30 ml) of dithiooxamide (1) (10.3m) in ammonium hydroxide solution (10 ml) was mixed ethanolic solution of corresponding ligands (L_1), (L_2) and (L_3) (0.06M). The contents were refluxed for 2h. The mixture was then reduced to a small volume (20 ml) and left overnight at room temperature. Yellow crystals were formed which were filtered and recrystallised from dichloromethane (70% yield).

Preparation of metal complexes

A solution of metal salt (1 mmol) in distilled water was added with stirring to a solution of ligand (2 mmol) in acetone:phosphate buffer solution (80:20) (15 ml). The mixture was stirred for 4h during which the solid complex was formed, filtered, washed with dil.HCl several times, finally washed with diethyl ether and recrystallised from aqueous ethanol mixture.

Preparation of discs

A solution of metal complex (30 μg) in dimethylformamide (DMF) (0.01 ml) was applied on the disc, prepared from blotting paper (3 mm size) with the help of a micropipett. These were then put in an incubator at 30°C for 27h and applied on bacterial species grown on nutrient agar medium. The zone of inhibition of bacterial growth around the disc was measured in diameter after 24h.

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