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Biologically Active Thioamides as Ligands for Some Toxic and Non-Toxic Metal Ions

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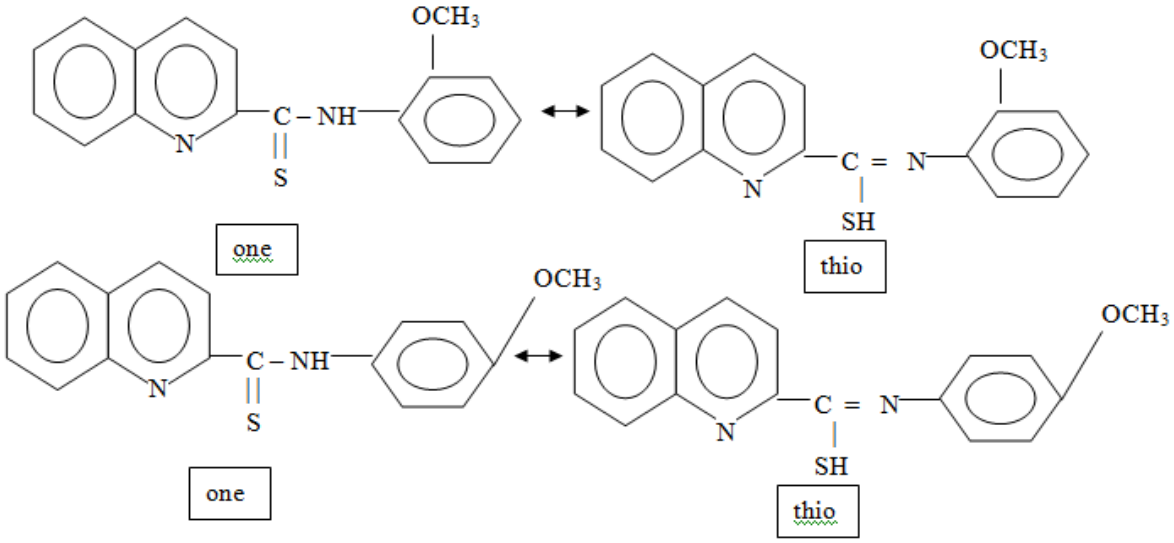
Abstract: ***Sulphur compounds have been the subject of interest for the chemist all over the world due to their chemotherapeutic use for the mankind and animals. In recent few years coordination chemists have shown their interest in synthesizing organo-metallic compounds mainly chelates of metals ions with sulphur and nitrogen containing organic molecules. The ability of nitrogen and sulphur based donors to stabilize different metal ions has sparked interest in bioinorganic systems. They are now a day widely explored owing to their versatile biological activity and prospective use as drugs. So, in the present investigations an attempt is made in the direction of seeking such a co-relation between different physico chemical properties of complexes with ligands (thioamides) having sulphur and nitrogen atoms as potential donors. For this, 2' – methoxy – 2 thioquinaldine anilide ligand has been prepared by Willgerdort reaction. In the present study, complexes of the ligand with Cu(II), Ni(II) have been prepared and investigated. From the studies of magnetic behaviour, electronic & IR spectra it is concluded that ligand behaves in bidentate manner utilizing sulphur and nitrogen donor atoms.***

Keywords: Cu(II),Complexes, 2-Thioquinaldine Anilide, bidentate, potential donor.

1. Introduction

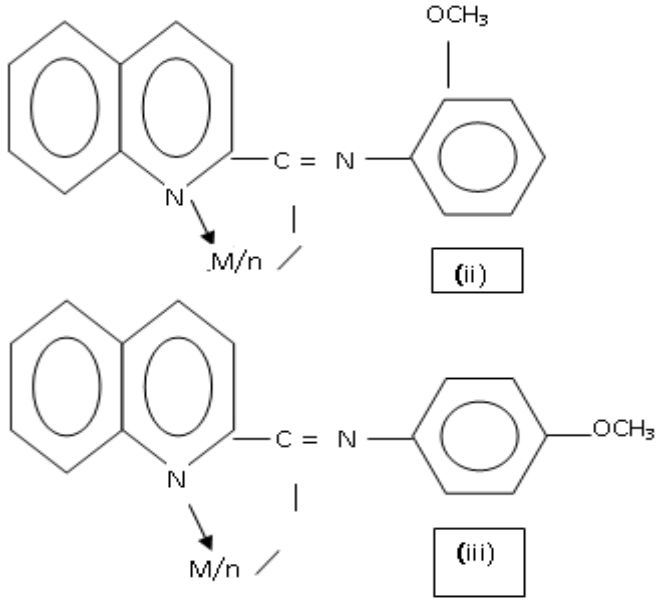
The proper functioning of biological activities, a definite amount of a particular element is essential. Anything may be toxic if its level is higher than required and on the other hand its deficiency is also harmful.**1-6** Some heavy metal ions, such as Zn(II), Cu(II), Ni(II) are essential for the maintenance of human metabolism. However, high concentrations of these ions can lead to many adverse health effects.**1, 2, 7-20** It is also a fact that others such as Hg(II), Pb(II), and As(III) are among the most toxic ions known that lack any vital or beneficial effects .Accumulation of these over time in the bodies of humans and animals can lead to serious debilitating illnesses.**2,21-30**

Therefore, in recent few years co-ordination chemists have shown their interest in synthesizing the coordination compounds of transition metal ions with the ligand having S & N atoms (thioamides) as ligands.In view of the growing interest of thioamide ligand and their complexes in this work presentation the synthesis and characterization of , 2' – methoxy – 2 thioquinaldine anilide and its complexes with Cu(II) and Ni(II) ions are reported.The ligand exists in the one-thio tautomeric form as shown:



Structure (i): the one-thio tautomeric form of Ligand

This is bidentate monobasic and form five membered chelate ring with various metal ions (structure-ii and iii).



Structure (ii) & (iii): Metal – Ligand Complexes

2. Experimental

2.1 Preparation of 2'-Methoxy 2-Thioquinaldine anilide

The ligand 2' – Methoxy 2 – Thioquinaldine anilide was synthesised by Willgerdort reaction.[31] Meta-toluidine (distilled 1 mol.) quinaldine (distilled 1 mole) and sulphur (powder 1 mole) were mixed in a 250 cc flask fitted with reflux condenser. The mixture was refluxed at 160°C for six hours . The reaction mixture was kept overnight. The solid red crystals obtained were filetered and recrystallised twice from ethanol. The deep yellow compounds obtained were dried in vaccuum (0.1 mm of Hg) for 24 hours.

2.2 Preparation of [Cu (L_2).2H_2O complex:

LH = 2' – Methoxy 2 –thioquinaldine anilide
The alcoholic solution of hydrated copper (II) chloride was treated with ligand (1:2 proportion) dissolved in the same solvent with proper shaking and stirring. Blackish brown product formed immediately was digested on steam bath. Cooled, filtered, washed with alcohol and dried in air.

Table 1: Results of Elemental Analysis of Complexes:

Compound	*% of metal Theo.*	*Found*	*% of C Theo.*	*Found*	*% of H Theo.*	*Found*	*% of O Theo.*	*Found*	*% of N Theo.*	*Found*	*% of S Theo.*	*Found*
[Cu $(L)_2$2H_2O	9.28	9.32	59.57	59.60	4.38	4.42	9.34	9.37	8.17	8.24	9.34	9.40

3. Results and Discussion

3.1 Magnetic Behaviour of Copper II complexes-

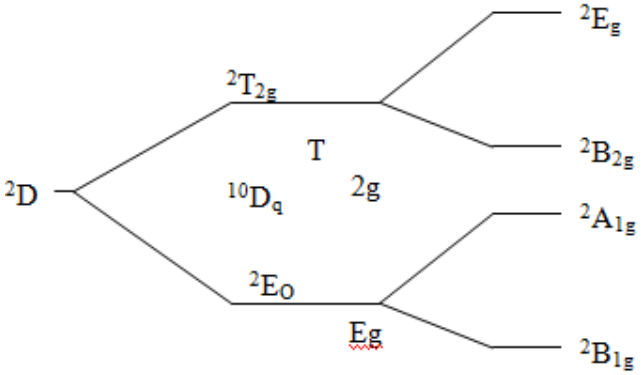
Magnetic behaviour of certain metal ions show important role in structural determination of complexes. The reflectance or absorption spectral studies of the complexes under the present investigations are of little significance, since the strong charge transfer transition originating from π back bonding of thiomide sulphur to copper atom obscures the expected d-d bands of Copper-II complexes. The important bands are given in the following table and some reflectance spectral curves are given in figure ES1, ES2, ES3, ES4.

In Nujol mull the copper (II) complexes display three or four bands to charge transfer and intra ligand –n →π or π → π electronic transitions. All other band are either shoulders or weak and broad except the charge transfer band which absorbs as strong band near 400 to 435 mm. The reflectance spectra of some copper (II) complexes show shoulders or weak and broad bands near 400 nm due to charge transfer. The broad shoulder observed near 645-685 nm in the electronic spectra of mono nuclear Copper (II) complexes fall in the range of spectral band assignable to $E_g \rightarrow T_{2g}$ transition for octahedral or disturbed octahedral Copper (II) complexes.

Therefore, it is suggested that the copper (II) complexes have distorted octahedral structure. These values fall in the range required for planar or distorted tetrahedral or distorted octahedral Cu (II) Complexes. No definite geometry could be given to the complex on the basis of the present magnetic moment values. The absorption spectral studies of the complexes under the present investigations suggested that the Copper (II) complexes fall in the range of spectral band assignable to $E_g \rightarrow T_{2g}$ transition. Therefore, it is suggested that the copper (II) complexes have distorted octahedral structure.

3.2 Electronic Behaviour of Copper II complexes

Bivalent copper II ($3d^9$) forms tetrahedral, distorted octahehdral complexes and square planar. The free copper (ii) ion had d^2 ground state term and the degenerate d level s are split up in presence of octahehdral fields as shown below.



Only one absorption band arising form d-d transition E_g----------T_{2g} is observed in the spectra of octahedral complexes. In excited state, the three electrons in e_g could so range as to lead to the different possible configurations i.e. $(d_z2)^2$ $(d_x2\text{-}_y2)^1$ or $(d_z2)^1$ $(d_x2\text{-}y^2)^2$ in the former case the more repulsion is expected between metal ion and ligand electron along the d_z2 axis than along $d_x\text{-}y^2$ axis because there is high electron density in d_z2, therefore alongating the bond along z-axis. In the letter case, we can similarly predict four long bonds along $d_x2\text{-}_y2$ and two short ones along d_z2. The more common distortion involves lengthening of the

bonds along d_z2. Under such circumstances, the e_g and t_{2g} level no longer constitute degenerate sets and splitting of the do – orbitals occur to remove this degeneracy thus , more stable distorted complex results because metal ion electrons do not repel ligand electron density as much as in the undistorted structure. Hence, in the distorted crystal field the doubly degenerate ground state E_g as well the upper state T_{2g} are, each , split into two other components (Shown in Fig.)

The existence of a planar or distorted octahehdral ligands field results in the appearance of three transitions :

$^2B_{1g} \rightarrow {}^2B_{2g}$
$^2B_{1g} \rightarrow {}^2E_g$
$^2B_{1g} \rightarrow {}^2A_{1g}$

and these are generally every asymmetric . it is found that the d-d band due to planar or octahedral field appears generally at higher energy (around 19,000cm^{-1} for planar, and around 15,000-18,000 cm^{-1} for octaheral complexes) than those of pssude- tetrahedral arrangement (around 8,000-11,500cm^{-1}). In case of distorted tetragonal or week distorted octahedral field (0_4h aymmetry) an asymmetric contour is located in the range of 10,000-14,000cm^{-1}. Holmes and moclure by analysis of polarised absorption spectrum of $CuSO_4$-$5H_2$ showed that three transitions are found in the range of 10,000-14,000cm^{-1} . The absorption spectrum of (Cu $(H_2O)_6$ show one every asymmetric band which can resolved at least into two bands. It is believed that the asymmetric band is due to Jahn- Taller effect which causes distortion of the octahedral coordination of water molecules around Cu ion. Bjerrum etiel . and jrgensen have recorded spectral data of many Cu (II) complexes in solution. They observed that most of the distorted octahedral copper (II) complexes show one asymmetric band which, in some cases, has been resolved into two or three overlapping bands.

Table 2: Electronic spectra of ligand and its Cu (II) complexes (as Nujo1) mul

[Cu $(L)_{2'}$] $2H_2O$	220sh	262	332	380	409s

3.3 Infrared Spectroscopic Measurement of the Complex

The groups present in thioamides are (C = S), (C = N) and (n = H), whose characteristic vibrations are expected at 750, 1590, and (35U0 s, 3400 s) respectively. The characteristic bands of quinoline ring may also be expected. Several thioamide bands are also expected. It may be expected that thiomide bands should remain intact as (C = N) and thiol (C = S), (originating from the tautomerism of thioanilide group). The main shift can be expected in the position of i.r. bands originating from different modes of (C = S) and (C = N) vibrations, The bands of the spectra of the ligands and Metal complexes have been recorded in the following *j.r.* Tables (IR_1) The spectra of thioquinalide anilides (MTQA) and (MTQA') exhibit strong and broad bands at 3175 - 3170 cm-1 which is attributed to hydrogen bonded N - H stretching frequency of the unco-ordinated ligands. In netural and adduct complexes the strong and broad bands at almost the position N-H vibration is atttributed to Nujol vibrations.

In the region 1624 to 1430 cm-1 the ligands (MTQA) show first prominent absorption bands at 1680 cm-1, the broad bands is assigned to (C = N) stretching vibration on co-ordination tnese bands shifts to lower frequency by 1520 cm-$^{1.}$ In [Cu$(L)_2$] $2H_2O$ exhibit splitting of V(C110= N) vibration into two bands in which one band is located at original position 1600 $^{-5}$ and other band at lower frequencies by 20-25^{cm-1}.The splitting of (C = N) vibration indicates that only one (C = N) nitrogen is involved in co-ordination.

In the region 1545 - 1455 the ligands display three other bands located- at 1555, 1525 and 1495 cm^{-1}. It is well known that aromatic compounds; show characteristic vibration in several regions of spectrum. These are absorption bands in 1590 - 1425 cm^{-1} region and that are particularly diagnostic of aromatic structures. These four bands generally occur 1570,1540,1480 and 1445 cm^{-1} and are caused by (C = E) skeletal vibration. The second band is generaly observed as a shoulder of the first band. In case, the organic molecule contains C; N, N - H, and (C = N) groups, the phenyl ring vibration are overlapped by .√(C = NO, and (C - N) vibrations. The ligands (MTOA) under investigation exhibit phenyl ring skeletal . √ (C = C) , (N- H) and . √ (C = N) vibration 1555, 1525, 1485cm^{-1}. These bands expect N - H are not affected on Co-ordination, but these are observed with reduced intensities where as N - H disappears.

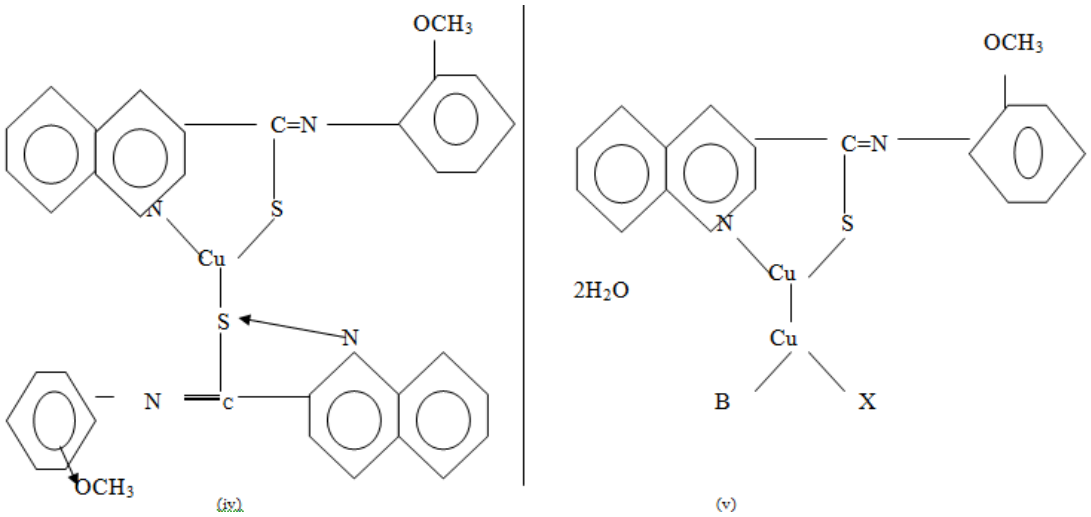
The aromatic compounds show a number of absorption bands of variable intensities in the region 1005 - 665 cm^{-1}. These absorption bands depend on the number of free adjacent hydrogen atoms that an aromatic compound contains. In present case, the ligands, MTOA exhibit a strong and sharp band due to (C = N) out of plane bending vibration 745 cm^{-1}. This band is observed in complexes 750+2cm^{-1}.

Table 3: IR_1Major I, R. absorption bands (cm^{-1}) of Copper (II) complexes as Nujol pull

Ligand	(Cu(L_2) } $2H_20$	Assignment
	3445 wb	ν OH of H_2O molecule
3175	-	ν NH
1610a	1605 w sp	
		ν C=C skeletal
		Thioamide band -1
		Thioamide band – II
		Characteristics os pyridine ring
		Thioamide band – III
		ν (C=S) + ν (C=H)
		Thioamide band – IV ν C=S
		C-H out of plane deform
		Characteristics of pyridine ring
		ν C-s
		ν M-O
		ν M-N
		ν M-S

S= strong; m = medium; w = week; sh=shoulder; sp – sharp= broad

Thus from the above studies the following structures are suggested for copper (II) complexes $[Cu(L)_2]2H_2O$.



Structure (iv and v): metal-ligand complex

4. Conclusion and Future Implications

The metal chelation significantly affects the antimicrobial behavior and the complex can be used as anti cancer drug On the basis of above discussion it is concluded that the ligand behaves in a bidentate manner utilizing S & N donor atoms.

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