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Studies on Structural Aspects of Biologically Active Oxygen Donor Ligands of Oxazolines and Copper Metal Complexes

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Abstract

Tri Chloro/Tri Acetato And Trinitrato Tris (2-Imino Phenyl -3-Phenyl -4- (P-Methoxy/Ethoxy Phenyl) -Δ^4-Oxazoline Cu(II) Complexes were synthesized and characterized for antifungal activity against *Phoma- exigua, Macrophomia phaseoli and Colletotrichum-Capsici* at different concentrations of 100,50&20 ppm. The copper complexes show good antifungal activity

Keywords: Transition Metals, Copper, Oxazolines, Active Oxygen.

Introduction

A number of heterocyclic compounds are known which form complexes with various transition metal ions. These metal complexes have shown importance is the field of medicine and analytical chemistry. Metal ion plays an important role is the biological system specially in maintaining the osmotic balance in multiphase system and as necessary component in various enzymatic reactions. Metal complexes of various heterocyclic compounds are used in cancer chemotherapy. Metal complexes with sulphur and Oxygen donor ligands have been reported[2] to possess antitumour activity.

The chemistry and the various activities of oxazole class of compounds have attracted the attention of many workers. A large number of pharmaceutical applications of oxazolines and its derivatives have been reported in literature like hypertensive,[3] analgesic, antinflamatory[4,5], antibacterial, antiviral[6] , antirubercular[7] anticonvulsent[8] , urinary tract their structural and biological activity.

Review of Literature

Survey of literature revealed that no systematic work have been done on the structural and fungicidal aspect of transition metal complexes of oxazoline. In this chapter preparation and characterisation of complexes of 2-Imino-phenyl -3-phenyl-4 (p-methoxy/ethoxy phenyl) - Δ^4 - oxazoline with various metal ions have been dealt.

Aim of the Study

The complexes formed are screened for anti fungal activity. The active oxygen of oxazoline class of compound with transition metals are good anti fungal agent.

Experimental

The I.R., magnetic and elemental analysis were carried out as described earlier. All the chemicals used were of B.D.H. (A.R) grade otherwise used after distillation.

Synthesis Of The Ligands

2-Imino phenyl -3-phenyl -4- (p -methoxy / ethoxy phenyl)-Δ^4 – Oxazoline : The ligand 2-Imino phenyl-3-phenyl-4-(p- methoxy / ethoxy) -Δ^4-Oxazoline was synthesized according to the literature procedure[21]. To a solution of methoxy / ethoxy acetophenone (3.09 g) in benzene (10 ml), bromine (3.2 g) in dry benzene (30 ml) was added drop wise with constant stirring when the reaction was complete, symm - dipheny] urea (4.25 g) was added and the reaction on a water bath for 30 hours. The mixture was refluxed solvent distilled off, and then the product was triturated with ether for overnight. The ether decanted off, the residue obtained was boiled with water and the water was decanted hot. The product was basified with strong ammonia, by this a gummy mass was obtained, which solidified gradually. The product was crystallized from ethanol acidified with acetic acid. Their formation was confirmed by m.p.. elemental analysis and I.R. spectral studies.

Ligand	% found / calculated		
	C	H	N
$C_{22}H_{18}N_{2}0_{2}$	77.20 (77.19)	5.28 (5.26)	8.20 (8.19)
$C_{23}H_{20}N_{2}0_{2}$	77.54 (77.53)	5.64 (5.62)	7.86 (7.87)

Preparation and Isolation of Complexes

DICHLORO/DINITRATO AND DIACETATO BIS (2-IMINO PHENYL -3-PHENYL -4- (p-METHOXY/ETHOXY PHENYL) -Δ^{4}- OXAZOLINE.

Cu (II) COMPLEXES

An alcoholic solution of ligand (0.02 mole) was mixed with an aqueous solution of corresponding Cu (II) salts (0.01 mole). After gradual addition of ammonia, the reaction mixtures were refluxed for one hour on water bath. On cooling ppt were obtained which were filtered, washed with water, ethanol and finally with ether and then dried in vacuum.

Elemental analysis corresponds to the following molecular formulae:

Complex	% found / Calculated			
	C	H	N	Cu
$[Cu(C_{22}H_{18}N_{2}O_{2})_{2}Cl_{2}]$	64.48 (64.47)	4.40 (4.39)	6.85 (6.84)	7.82 (7.81)
$[Cu(C_{22}H_{18}N_{2}O_{2})_{2}(NO_{3})_{2}]$	60.56 (60.55)	4.18 (4.13)	9.68 (9.63)	7.38 (7.34)
$[Cu (C_{22}H_{18}N_{2}O_{2})_{2} (CH_{3}COO)_{2}]$	66.52 (66.51)	4.86 (4.85)	6.48 (6.47)	7.38 (7.39)
$[Cu(C_{23}H_{20}N_{2}O_{2})_{2}Cl_{2}]$	65.18 (65-17)	4.74 (4.72)	6.66 (6.61)	7.6O (7.56)
$[Cu(C_{23}H_{2}oN_{2}O_{2})_{2}(NO_{3})_{2}]$	61.38 (61.33	4.46 (4.44)	9.38 (9.33)	7.12 (7.11)
$[Cu (C_{23}H_{2}ONO_{3})_{2} (CH_{3}COO)_{2}]$	67.12 (67.11)	5.16 (5.15)	6.28 (6.26)	7.18 (7.16)

Result and Discussion

From the elemental analysis data, the stoichiometry ratio of the metal complexes, the ratio of metal and ligand was found to be 1: 2

Infra Red Spectral Studies

In the infra red spectral studies attempts were made to assign various frequencies obtained in the I.R. spectra of metal and ligand. A comparison is also made between the spectra of metal complexes and ligand to assign the group or atom involve in coordination. The spectra of the metal complexes and the ligand are quite complicated due to presence of a number of groups in the molecule and there is a very little difference between the spectra of free ligand with that of the metal complexes. The band appearing in the region 3055 and -1615 are assigned toY(C-H) andY(C=C) vibrations respectively and are suggestive of the aromatic character of the ligand and its complexes. The ligand has a greater steric hindrance due to the presence of phenyl group. The band appearing in the region 1590, 1610, 1230 cm^{-1} are due to presence of phenyl groupY(C=N) andY(C-N) vibration mode respectively. A band appeared in the region 1650-1680 cm^{-1} in the ligand assignable toY(C-O) frequencies. In all the metal complex a considerable shift in this frequency is observed. From the shift in Y (C-0) stretching frequency it can be concluded that the lone pair of oxygen is involved in coordination i.e. (C-O -> M) bond formation takes place. In the metal complexes a band appeared in the region 400-470 cm"^{1} which is assigned toY (M-O) band similar observation were also observed by number of workers[22]

Infra Red Spectra of Chloro Complexes

The spectra show frequencies around 275, 285 cm^{-1} characteristic to six- coordinated halide bridge vibration due to Y(Mn-Cl) andY(Co-Cl) respectively, while the bands at 280 cm^{-1} assigned toY(Ni-Cl) and at 290 cm^{-1} due toY(Cu-Cl) are indicative of halide bridged nature

Infra-Red Spectra of Nitrato Complex

In the present metal nitrato complexes absorption bands are observed in the region 1400-1430, 1300-1330, 990-1020, 790-880 cm^{-1} which are assigned to asymmetric NO_2 stretching, symmetric NO_2, stretching, NO stretching and out of plane NO_2 rocking vibrations respectively. These are suggesting monodentate coordination of nitrato groups.[26]

Infra-Red Spectra of Acetato Complexes

Asymmetric and symmetricY(C=O) stretching frequencies of free acetate ion reported at 158.0-1425 cm^{-1} are observed around 1575-1535 and 1450-1420 cm^{-1} respectively in acetato complexes. The seperation of 132-110 cm^{-1} in these mode on complexation suggest that the acetate group is behaving as unidentate ligand in these complexes.

Magnetic and Electronic Spectral Studies

Cu (II) Complexes

Copper (II) has one unpaired electron in the 3d sub-shell and its compounds are considered to have magnetic moments close to spin-only value (1.73 BM) irrespective of the band involved. The observed magnetic moment value 1.82 BM is very close to the value predicted for spin only which indicate the orbital contribution is almost quenched by the crystal field. Three brand have been obtained in the electronic spectra of copper (II) complex at due to the transition Big —> *A\g* -> Eg and charge 16100, 20300 and 2.2.600 cm^1 transfer respectively which corresponds to the square planar stereo chemistry.

Fungicidal Activity

Metal ions are important in fungicidal action, since many of them form complexes with ligands containing sulphur, nitrogen or oxygen as electron donors. However, the quantities of various ligands in cells of different species, vary and the biological effects of metals are not so simple that more consideration of metal binding capacity will suffix to predict such effect Mathew (1904) suggested that the toxic action of the metal ion is due to the formation of unionized complexes between anions present at some surface and metal ions. Later Danielli and Dauris (1951) proposed that tightness of covalent bonding of the ion to the surface ionic groups of cell was the important factor. The toxic action of heavy metal is based upon the properties of these ion for denaturing the protein. Anti metabolites produced by pest cells may repress synthesis of catabolic and biosynmetic enzymes. Activity of endogeneous enzymes may be stimulated by fungicides that act in place of cofactors in the enzyme system.

The zone of inhibition in 100, 50,20 ppm of the test complexes against phoma- exigua, Macrophomia phaseoli and Colletotrichum-Capsici are given in table- 1.

Because of the oxazoline ring the ligand may compete with histidine and purines for enzymic binding sites. The ligand is fungistatic in action and has a steep dosage response. The presence of nitrogen as well as the phenyl groups augments, the greater fungicidal activity. The results are however indicative of the fact that the growth of the fungi are inhibited by almost all the complexes but the inhibitory effect of the free ligand is undoubtedly greater in comparison to the complexes. The complexes are inherently toxic to fungi and inhibit synthesis of protein and deoxyribo-nucleic acid. Analysis of the data showed that Cu (II) complexes acts as most active fungicides. The binding of these complexes with the cell surface of fungi results in a disturbance of semi permeability while some of the metal may enter the cell and be distributed among the cell contents. Thus the factors concerned with the accessibility of metal sensitive locii, rather than their chemical affinity.

Conclusion

Analysis of the data showed that Cu (II) complexes acts as most active fungicides. The binding of these complexes with the cell surface of fungi results in a disturbance of semi permeability while some of the metal may enter the cell and be distributed among the cell contents. Thus the factors concerned with the accessibility of metal sensitive locii, rather than their chemical affinity.

Table 1 : Fungicidal screening; Growth responses of Phoma-exiqua, Macro phomina- phaseoli and ColletoW-chum capcici (After 168 hours at 25 ± 1° on Czepecks Dose Agar Medium) at different concentration (in ppm) in relation to the ligand. 2-Inino phenyl-3-phenyl-4-(p-Methoxy phenyl) - A^4 oxazoline (IPPM PO)

Test Samples	Phoma-exigna			Macro phomia-phaseoli concentration used in ppm			Colletotrichum-capsici			
	100	50	20	100	50	20	100	50	20	
Ligand	87.0	74.0	50.0	80.0	65.2	50.0	85.0	70.2	50.2	
[Cu (L)$_2$ C1$_2$]	67.8	45.2	30.1	50.2	35.2	20.2	57.6	57.6	38.4	25.3
[Cu(L)$_2$ (N0$_3$)$_2$]	66.0	45.0	29.8	49.8	34.8	20.0	55.3	55.3	38.2	25.1
[Cu (L)$_2$ (CH$_3$ C00)$_2$]	66.4	45.2	30.0	50.0	35.0	20.4	55.1	55.1	38.3	25.2

Table 2 : Fungicidal screening; Growth responses of phoma-exiqua, Macro phomina- phaseoli and colletoWchum capxici (After 168 hours at 25 ± 1° on Czepecks dose agar medium) at different concentration (in ppm) in relation to the ligend 2-Iminophenyl-3-phenyl-4-(p-ethoxy phenyl)-A^4-oxazoline (IPPE PO).Average Percentage Inhibition after 168 hours

Test Samples	Phoma-exigna			Macro phomia-phoscoli concentration used in ppm			Colletotrichum-capsici		
	100	50	20	100	50	20	100	50	20
Ligand	86.0	73.0	49.0	79.0	64.0	48.0	82.0	68.0	48.0
[Cu (L)$_2$ C1$_2$]	66.8	44.2	29.1	49.2	34.2	19.2	54.3	37.2	24.3
[Cu (L$_2$)$_2$ (N0$_3$)$_2$]	65.0	44.0	28.8	48.8	33.8	19.0	54.1	37.0	24.1
[Cu(L$_2$)(CH$_3$COO)$_2$	65.4	44.2	29.0	49.0	34.0	19.4	54.2	37.1	24.2

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