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Synthesis, characterization and antimicrobial activities of Cu(II), Mn(II) and Zn(II) ions complexes with 2-(8-quinolinol-5-yl) - amino methyl-3-(4- nitro phenyl)-5-(4-chloro phenyl)-pyrazoline

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ABSTRACT

Complexes of 2-(8-quinolinol-5-yl)-amino methyl-3-(4-nitro phenyl)-5-(4-chloro phenyl)-pyrazoline with Cu(II), Mn(II) and Zn(II) have been synthesized and characterized using elemental analysis, IR spectra, PMR spectra, Reflectance spectra, Conductivity measurements and antimicrobial activity. These studies revealed that they are having octahedral geometry of the type $[ML_2(H_2O)_2]$. The compounds show net enhancement in activity on coordination of metals with ligand but moderate activity as compared to standard drugs.

KEYWORDS

Pyrazoline;
Hydrazinehydrate;
Chalcones;
Chelates.

INTRODUCTION

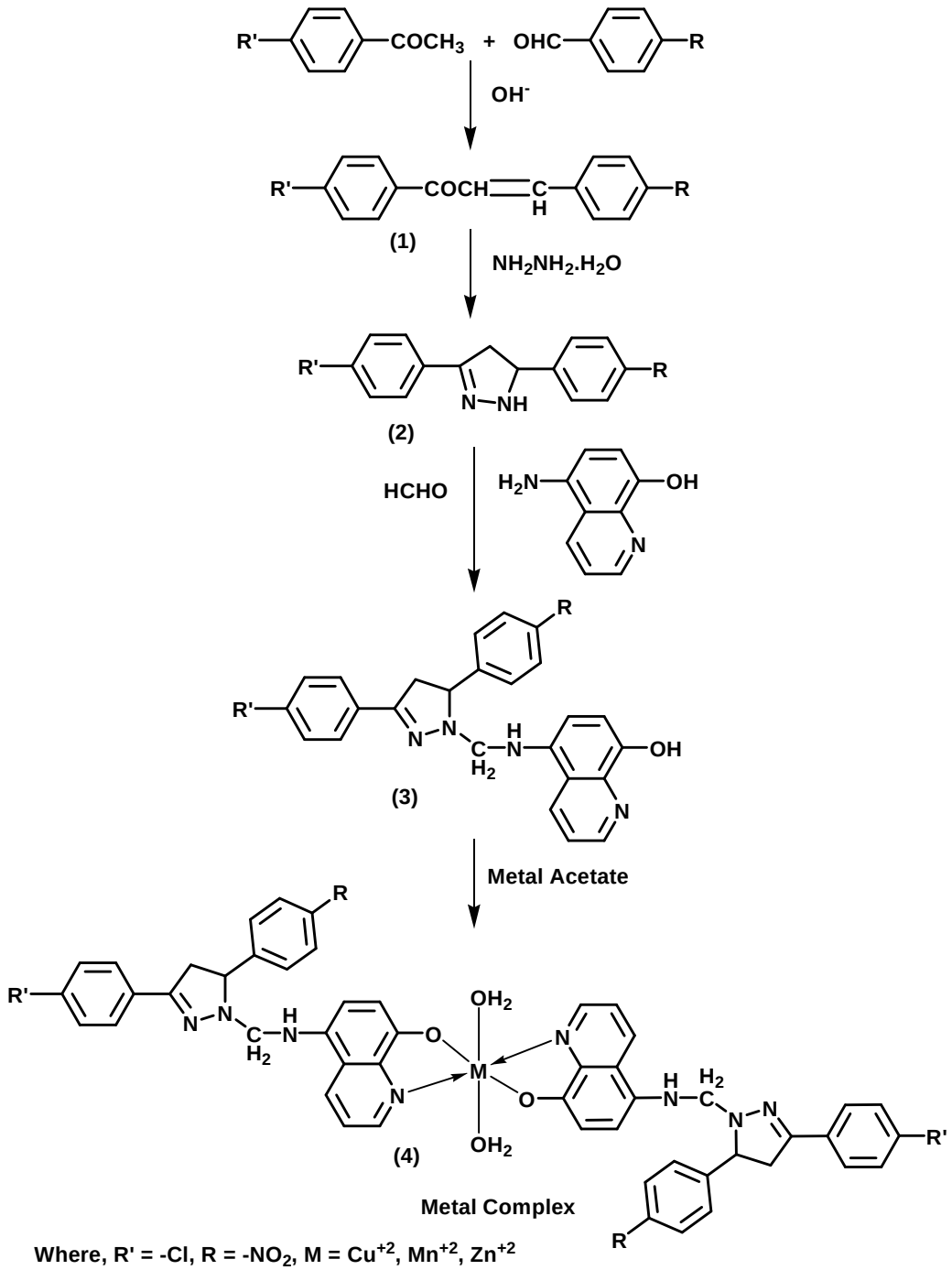
With a variety of biological activity, chalcones are useful in pharmaceuticals. They are associated with different biological activities like insecticidal[1], anticancer[2], anti-inflammatory[3], bactericidal[4], fungicidal[5], antiviral[6], antitumor[7] and antiulcer[8]. Synthesis of pyrazolines has been also stimulated by the fact that some of their derivatives were found to possess important bioactivities. Especially their antimicrobial[9], immunosuppressive[10] and central nervous system activity[11] should be emphasized.

EXPERIMENTAL

Melting points were taken in open capillary tube and were uncorrected. IR spectra (KBr) were recorded on Nicollet FT-IR 760 and PMR spectra were recorded on Bruker NMR spectro-photometer. PMR chemical shifts are recorded in δ value using TMS as an internal standard in $CDCl_3/D_6$-DMSO. Purity of the compounds were checked by TLC on silica-G plates. The fungicidal activity of all the compounds was studied at 1000ppm concentration in vitro. Plant pathogenic organisms used were Penicillium expansum, Botrydepladia thiobromine, *Nigrospora Sp.*, *Trichothesium Sp.*, and *Rhizopus nigricum*. Anti bacterial activities were tested by Agar Cup method.

Preparation of chalcone (1)

To a well stirred solution of p-nitro benzaldehyde (0.01 mole) And p-Chloro acetophenone (0.01 mole) in ethanol (25ml), 40% KOH added till the solution become basic. The reaction mixture was stirred for 24 hrs. the contents were poured into ice, acidified, filtered and crystallized from ethanol. The yield of the



Scheme 1

TABLE 1 : Characterization of metal chelates of ligand

Metal complexes	Molecular formula	M.W	Yield %	Elemental analysis							
				%Metal analysis		%C		%H		%N	
				Cald.	Found	Cald.	Found	Cald.	Found	Cald.	Found
$(HL)_2\ Cu^{+2}$	$C_{50}H_{38}N_{10}O_6Cl_2Cu^{+2}.2H_2O$	1044.5	88	6.0	6.0	57.4	57.4	4.0	4.0	13.4	13.3
$(HL)_2\ Mn^{+2}$	$C_{50}H_{38}N_{10}O_6Cl_2Mn^{+2}.2H_2O$	1036	83	5.3	5.2	57.9	57.8	4.0	4.0	13.4	13.4
$(HL)_2\ Zn^{+2}$	$C_{50}H_{38}N_{10}O_6Cl_2Zn^{+2}.2H_2O$	1046	78	6.2	6.1	57.3	57.3	4.0	3.9	13.3	13.3

IR (KBr); $(HL)_2$-Zn^{+2} : (cm^{-1}): 3500-2600 broad (-OH), 1638,1459,3108 (Aromatic), 1638,1509, 1459 (8-HQ Moiety), 1282 (C-N), 2838,2958,1459 (>CH_2)

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TABLE 2 : Experimental data of magnetic moment and conductivity of metal chelate of ligand

Metal complexes	$\chi_r \times 01^{6-}$ (cgs)	$\chi_\mu \times 01^{6-}$ (cgs)	Magnetic moment μ_{eff}(BM)	$\mu_{eff}=\sqrt{n(n+2)}$ BM	μ_{eff}(BM) Expected	Λ_M^a
$(HL)_2Cu^{+2}$	1.48	1551	1.94	1.73	1.7-2.2	9.21
$(HL)_2Mn^{+2}$	14.13	14638	5.96	5.91	5.2-6.0	10.90
$(HL)_2Zn^{+2}$	-	-	-	-	D(*)	8.21

TABLE 4 : Antifungal activity of ligand HL and their metal chelate

Sample	Zone of inhibition at 1000 ppm (%)				
	Penicillium expansum	*C.Albicans*	*Nigras pora Sp.*	*Trichothesium Sp.*	*A.niger*
HL	66	70	70	64	64
$(HL)_2Cu^{+2}$	81	86	87	86	87
$(HL)_2Mn^{+2}$	58	56	57	56	57
$(HL)_2 Zn^{+2}$	80	80	84	81	84

product was 84 % .Found: C(62.60%) H(3.47%) Cl(12.30%) N(4.84%).,Calcd. for $C_{15}H_{10}ClNO_3$: C(62.62%) H(3.50%) Cl(12.32%) N(4.87%).

Preparation of 3-(4-nitro phenyl)-5-(4-chloro phenyl) -2H- Pyrazoline (2)

A mixture of Chalcones (0.01 mole) in 25ml of absolute alcohol, add hydrazine hydrate (0.5gm, 0.01 mole) was refluxed in water bath at temp. 80-90°C for 8 hrs. The reaction mixture was poured into ice. The product was isolated and crystallized from ethanol. The yield of the product was 91 %. Found: C(59.68%) H(4.00%) N(13.91%) Cl(11.73%), Calcd. for $C_{15}H_{12}ClN_3O_2$: C(59.71%) H(4.01%) N(13.93%) Cl(11.75%).

Preparation of 2-(8-quinolinol-5-yl)-amino methyl-3-(4-nitro phenyl)-5-(4-chloro phenyl)-pyrazoline, **[HL](3)**.

A mixture of 3-(4-nitro phenyl)-5-(4-chloro phenyl) -2H-pyrazoline (0.01 mole) and formaldehyde (40%, 1.5ml) in ethanol (20ml) was stirred at room temp. With a solution of 5-amino-8-quinolinol (0.01 mole) in ethanol (10ml) for 30 min. The solid product that separated out on standing for a 1 hrs was collected by filtration, washed with ethanol & dried. It was recrystallized from ethanol to yield the ligand compounds having m.p.: 251°C (Uncorrected). The yield of the product was 55% .Found: C(63.2%) H(4.2%) N(14.7%) Cl(7.4%), Calcd. for $C_{25}H_{20}N_5O_3Cl$: C(63.4%) H(4.2%) N(14.8%) Cl(7.5%); IR (KBr); [HL]: (cm^{-1}): 3815-2600 (-OH), 1598, 1507, 3028 (Aromatic), 1638, 1575,1698 (8-HQ Moiety), 1275-1298 (C-N), 2849,2918,1448 (>CH_2); PMR; [HL]: δppm 7.1 to 7.64 Multiplet, quinoline, δppm 8.5 to 9.2 Singlet of phenolic- OH, δppm 4.75 to 4.95 - CH_2-, δppm 3.45 - CH_2-.

TABLE 3 : Reflectance spectral data of metal complexes of ligand

Metal complex	Absorption, cm^{-1}	Transional
$(HL)_2 Cu^{+2}$	23872	CT
	15294	$^2B_{1g} \rightarrow {}^2A_{1g}$
$(HL)_2 Mn^{+2}$	23999	$^6A_{1g} \rightarrow {}^4A_{1g}$ ($4E_g$)
	18780	$^6A_{1g} \rightarrow {}^4T_{2g}$(4G)
	16534	$^6A_{1g} \rightarrow {}^4T_{1g}$ (4G)

TABLE 5 : Antibacterial activity of ligands HL and their metal chelate

Sample	Zone of inhibition (in mm)			
	Gram + Ve		Gram -Ve	
	B.Cereus	*Micrococcus*	*P. Aeruginosa*	*E-Coli*
HL	16	20	16	05
$(HL)_2 Cu^{+2}$	17	21	20	15
$(HL)_2 Mn^{+2}$	10	16	09	06
$(HL)_2 Zn^{+2}$	15	19	14	14

Preparation of metal chelates of 2-(8-quinolinol-5-yl) - amino methyl-3-(4-nitro phenyl)-5-(4-chloro phenyl)-pyrazoline. (P-4)

Formation of Cu^{2+} chelates

The reagent solution of each ligand (0.01 mole) was added drop wise to a solution of cupric nitrate hexahydrate (0.005 mole) in 100ml. of water with rapid stirring. The pH of the resultant solution was maintained at 4.5 by NH_3. A greenish blue solid precipitated out. It was allowed to settle. Then it was digested on water bath at 70°C for about 2 hours. The solid mass was filtered, washed with 1:1 mixture of water- ethanol and finally with acetone, and the yield of complex 74%. The resulting complex was powdered well and further dried at 70°C over a period of 24 hrs.

Formation of Mn^{2+} chelates

The reagent solution of ligand (0.005 mole) was stirred in a solution of manganese chloride hexahydrate (0.005 mole) in 100ml. of water. The final pH adjusted was 5.6. The yield of complex was 68%.

Formation of Zn^{2+} chelates

The reagent solution of each ligand (0.01 mole) was

added to that of zinc nitrate hexahydrate (0.005 mole) in 100ml of water. The resultant pH was 5.6. The product was purified in the same manner described earlier. The dried complex was in pale yellow powder. The yield was 72%.

RESULT AND DISCUSSION

All the complexes are toxic more or less to fungi. The substitution of phenyl rings does not have more effect on the fungicidal activity of complexes. In each series the Cu-complexes have much toxicity. This is expected because the copper salts are mostly used as fungicides. Most of the complexes inhibit the growth of the above organisms which cause decease in many plants. Out of all metal complexes, Cu^{+2} metal complexes are more toxic than others and the order for is $Cu^{+2} > Zn^{+2} > Mn^{+2}$.

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