Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2010, 2(1): 295-300
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X

Synthesis, characterization and antimicrobial activity of metal chelates of 2-(8-Quinolinol-5-yl)-amino methyl-3(4-methyl phenyl)-5-(phenyl)-pyrazoline

B. N. Patel,[1] P. S. Patel[2] and V. G. Patel[1]

[1]*Department of Chemistry, Municipal Arts and Urban Bank Science College, Mehsana*
[2]*Department of Chemistry, Sheth L.H. Science College, MANSA, India*

Abstract

Complexes of 2-(8-Quinolinol-5-yl)-amino methyl-3(4-methyl phenyl)-5-(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.

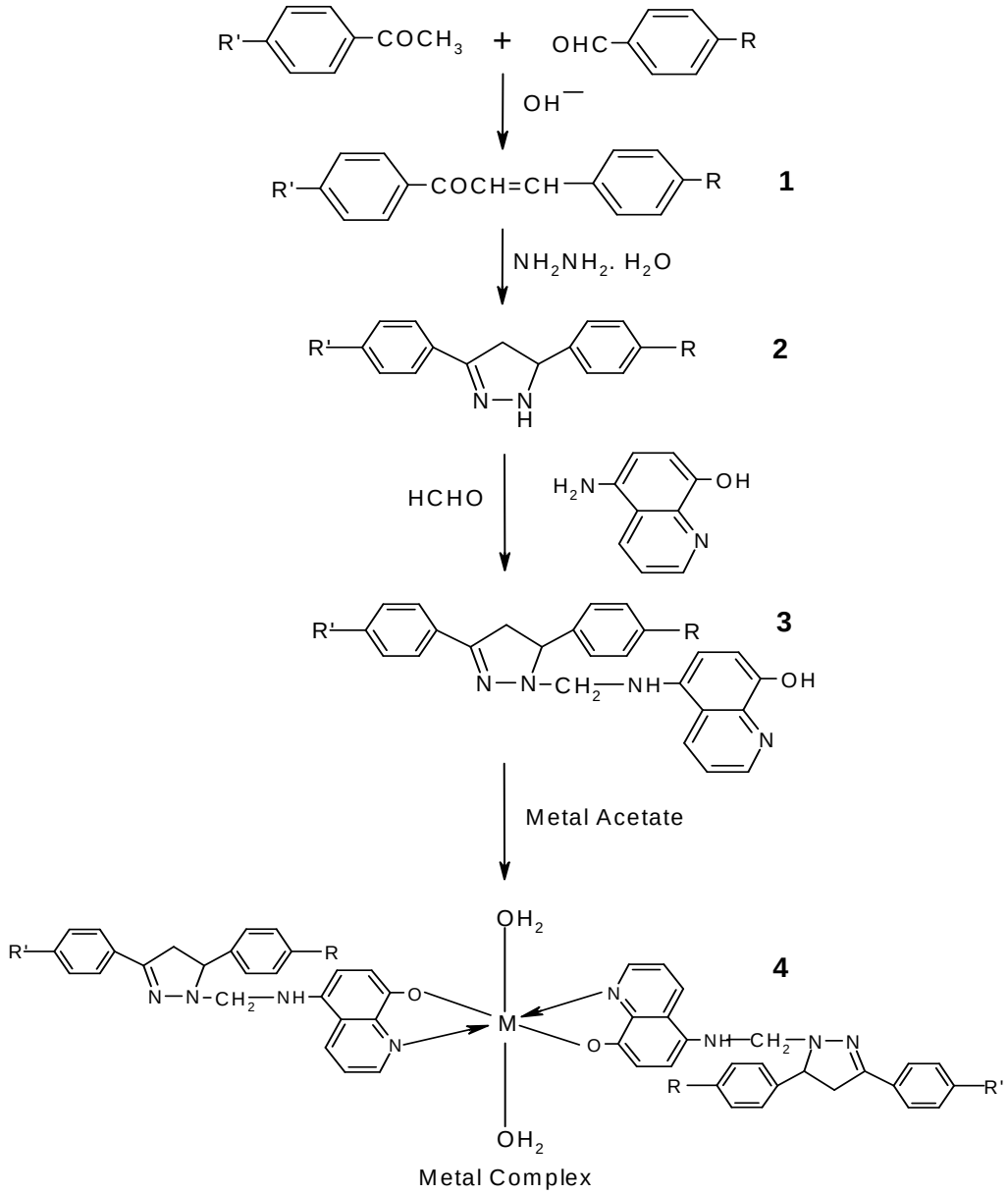
Key Words : pyrazoline, hydrazinehydrate, chalcones, Chelates.

Introduction

The chemistry of chalcones has generated intensive scientific studies throughout the world. Especially interest has been focused on the synthesis and biodynamic activities of chalcones.The name “chalcones”was given by kostanecki and tambor [1]. The most convenient methods are the claisen-schimdt condensation of equimolar quantities of a arylmethylketones with aryl aldehyde in the presence of alcoholic alkali [2]. Chalcone are used to synthesize several derivatives like cyanopyridines, pyrazolines isoxazoles, pyrimidines, having different heterocyclic ring systems [3-6].

It was more than a hundred years ago that Fischer and Knovenagel described the synthesis of a pyrazoline by the reaction of phenyl hydrazine and acrolein [7]. This report is probably the first example of pyrazoline formation by the reaction of a α,β-unsaturated carbonyl compound with a hydrazine derivative. Formation of 1-phenyl-2-pyrazoline in this way was corroborated by Auwers et al. [8,9].
Synthesis of pyrazolines has been also stimulated by the fact that some of their derivatives were found to possess important bioactivities. Especially their antimicrobial [10],

immunosuppressive [11] and central nervous system activity [12] should be emphasized. Although pyrazolines are useful substances in drug research and are well-known five-membered nitrogen-containing heterocyclic compounds, a comprehensive review on their synthesis was published thirty years ago [13].



Where, R' = -H, R = $-CH_3$

M = Cu^{+2}, Mn^{+2}, Zn^{+2}

Results 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 $Cu^{+2} > Zn^{+2} > Mn^{+2}$.

Materials and Methods

Melting points were taken in open capillary tube and were uncorrected. IR spectra (KBr) were recorded on Nicollet FTIR 760 and PMR spectra were recorded on Bruker NMR spectro-photometer. PMR chemical shifts are recorded in δvalue 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 1000 ppm 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-methyl benzaldehyde (0.01 mole) And acetophenone (1.2 gm, 0.01 mole) in ethanol (25 ml), 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 product was 82 % .Found: C(86.41%) H(5.31%), Calcd. for $C_{16}H_{14}O$: C(86.45%) H(5.35%) .

Preparation of 3-(4-methyl phenyl)-5-(phenyl)-2H-pyrazoline (2).
A mixture of Chalcones (0.01 mole) in 25 ml of absolute alcohol, add hydrazine hydrate (0.5 gm, 0.01 mole) was refluxed in water bath at temp. 80-90 ^{0} 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 84 %. Found: C(81.29%) H(6.78%) N(11.83%), Calcd. for $C_{16}H_{16}N_2$: C(81.32%) H(6.82%) N(11.85%)

Preparation of 2-(8-quinolinol-5-yl)-aminomethyl-3(4-methylphenyl)-5-phenyl)-pyrazoline. [HL] (3).
A mixture of 3-(4-methyl phenyl)-5-(phenyl) -2H- Pyrazoline (0.01 mole) and formaldehyde (40%, 1.5 ml) in ethanol (20 ml) was stirred at room temp. With a solution of 5-Amino-8-Quinolinol (0.01 mole) in ethanol (10 ml) 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- 269°C. (Uncorrected).

The yield of the product was 92 % .Found: C(76.3%) H(5.8%) N(13.6%) , Calcd. for $C_{26}H_{24}N_4O$: C(76.5%) H(5.9%) N(13.7%); IR (KBr); [HL]: (cm^{-1}): 3810-2710 (-OH), 1599,1507,3028 (Aromatic), 1634, 1575,1698,1470 (8-HQ Moiety), 1275-1298 (C-N), 2850,2921,1450 (>CH_2) ; PMR ; [HL]: δ ppm 7.1 to 7.64 Multiplet, quinoline, δ ppm 8.53 to 8.95 Singlet of phenolic- OH, δ ppm 4.75 - CH_2-, δ ppm 3.52 - CH_2-, δ ppm 1.05, – CH_3

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

Formation of Cu^{2+} Chelates :
The reagent solution of ligand (0.01 mole) was added drop wise to a solution of cupric nitrate hexahydrate (0.005 mole) in 100 ml. 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 70^0C 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 70 %. The resulting complex was powdered well and further dried at 70^0C over a period of 24 hrs.

Characterization of Metal Chelates of Ligand

Metal Complexes	Molecular formula	M.Wt Gm/mole	Yield %	% Metal analysis		Elemental analysis					
						%C		%H		%N	
				Cald.	Found	Cald.	Found	Cald.	Found	Cald.	Found
$(HL)_2$ Cu^{+2}	$C_{52}H_{48}N_8O_2$ $Cu^{+2}.2H_2O$	913.5	73	6.9	6.8	68.3	68.2	5.4	5.4	12.2	12.2
$(HL)_2$ Mn^{+2}	$C_{52}H_{48}N_8O_2$ $Mn^{+2}.2H_2O$	905	82	6.0	6.0	68.9	68.8	5.5	5.5	12.3	12.3
$(HL)_2$ Zn^{+2}	$C_{52}H_{48}N_8O_2$ $Zn^{+2}.2H_2O$	915	75	7.1	7.0	68.2	68.1	5.4	5.3	12.2	12.2

IR (KBr); $(HL)_2$-Mn^{+2}: (cm^{-1})**:** 3500-2600 broad (-OH), 1610,1497,2928 (Aromatic), 1610,1577,1509,1466 (8-HQ Moiety), 1270 (C-N), 2847,2928,1466 (>CH_2).

Experimental data of magnetic moment and conductivity of metal chelate of Ligand

Metal complexes	$\chi_\gamma \times 01^{6-}$ (cgs)	$\chi_\mu \times 01^{6-}$ (cgs)	Magnetic moment μeff (BM)	μeff = $\sqrt{n(n+2)}$ BM	μeff (BM) Expected	$\wedge_M^a$
$(HL)_2$ Cu+2	2.14	1958	2.18	1.73	1.7-2.2	9.29
$(HL)_2$ Mn^{+2}	16.28	14736	5.98	5.91	5.2-6.0	7.09
$(HL)_2$ Zn^{+2}	-	-	-	-	D(*)	9.81

Reflectance spectral data of metal complexes of ligand

Metal complex	**Absorption, cm^{-1}**	**Transional**
$(HL)_2$ Cu^{+2}	23985	CT
	15653	$^2B_{1g} \rightarrow {}^2A_{1g}$
$(HL)_2$ Mn^{+2}	23875	$^6A_{1g} \rightarrow {}^4A_{1g}$ ($4E_g$)
	18345	$^6A_{1g} \rightarrow {}^4T_{2g}$ (4G)
	16857	$^6A_{1g} \rightarrow {}^4T_{1g}$ (4G)

Formation of Mn^{2+} Chelates :

The reagent solution of each ligand (0.005 mole) was stirred in a solution of manganese chloride hexahydrate (0.005 mole) in 100 ml. of water. The final pH adjusted was 5.6. The yield of complex was 65%.

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 100 ml 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 75%.

Antifungal activity of ligand HL and their metal Chelate

Sample	Zone of inhibition at 1000 ppm (%)				
	Penicillium Expansum	C.Albicans	Nigras Pora Sp.	Trichothes ium Sp.	A. Niger
HL	55	56	55	60	59
$(HL)_2Cu^{+2}$	82	89	82	82	82
$(HL)_2\ Mn^{+2}$	58	60	60	58	57
$(HL)_2\ Zn^{+2}$	78	72	81	72	78

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	14	17	18	18
$(HL)_2\ Cu^{+2}$	21	20	21	19
$(HL)_2\ Mn^{+2}$	07	06	10	08
$(HL)_2\ Zn^{+2}$	20	12	19	17

Acknowledgements

The authors are thankful to Dr. D.R. Patel, principal, Municipal Arts and Urban Bank Science College, Mehsana for providing me with all possible research facilities. One of the author of this paper Pankaj S. Patel is thankful to UGC. Ganeshkhind, pune. for Teacher Research Fellowship.

References

[1] Kostanecki, S.V. and Tambor, *J.; Chem Ber.,* 32,**1921**(1899).
[2] Kazauki,K.; Hitayama,K.; Yokomor,S. and Soki, T.; *Chem Abstr.*, 85, 5913 (**1976**).
[3] El.Hashah,M.A.; El-Kady. M.; Saiyed, M.A. and Elaswy,A.A.; *Egypt.J.Chem.*, 27, 715(**1985**).
[4] Crawley,L.S. and Fanshawe,W.J., *J.Heterocyclic chem.*.,14,531(**1977**)
[5] Taylor,E.C and Morrison, R.W., *J.Org.Chem.*, 32,2379 (**1967**).
[6] Utale,P.S.; Raghuvanshi,P.B. and Doshi,A.G.; *AsianJ.Chem.*,10,597(**1998**).

[7] Fisher,E. and Knovengel.; *Ann.*,239,194(**1887**).
[8] Auwers,K.V. and Muller,K.; *Ber.*,41,4230(**1908**).
[9] Auwers,K.V. and Kreuder.A,; *Ber.*,58,1974(**1925**).
[10] P. S. Patel, R. A. Shah, D. K. Trivedi and P. J. Vyas; *Asian Journal of Chemical and Envrionmental Research.*, Vol.2(1-2), 6 (**2009**).
[11] Lombardino,J.G. and Otterness,I.G.; *J. Med. Chem.*, 830 (**1981**).
[12] U. S. Pat. 3,624,102; Brown,R.E. and Shavrel,J.; Jr.; *Chem. Abs.*, 76, 59618 (**1972**).
[13] Weissberger,A.; *The Chemistry of Heterocyclic Compounds*, Vol. 22, Wiley, New York, p. 180,(**1967**).