



SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF COPPER (II) COMPLEXES OF SOME 2-HYDROXY-4, 5-DIMETHYL SUBSTITUTED CHALCONES

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ABSTRACT

The present paper deals with synthesis and characterization of metal complex of some novel 2-hydroxy-4,5-dimethyl substituted chalcones. The substituted chalcones were prepared by reacting 2-hydroxy-4,5-dimethyl acetophenone with corresponding aromatic aldehydes like 2-chlorobenzaldehyde, 3-bromobenzaldehyde, 4-fluorobenzaldehyde and 4-cyanobenzaldehyde. The Copper(II) metal complexes of general formula ML_2 with newly prepared chalcones synthesized and characterized by several physicochemical techniques like Melting point, Elemental analysis, molar conductance, magnetic susceptibility, Electronic absorption and Infrared spectral studies. The analytical data confirmed 1:2 stoichiometry of M: L and the electronic spectral data suggest that all Cu (II) complexes have distorted octahedral geometry. The conductivity data show that all these complexes are non-electrolytes. Furthermore, biological activities of complexes with selected bacterial strain carried and the results have been compared with commercial standards.

KEY WORDS: Transition metal complexes, Chalcones, Spectral characterization and biological activities

INTRODUCTION

The chemistry of chalcones generated intensive scientific studies throughout the world, specially interesting for their biological applications. Chalcones are coloured compounds¹ because of the presence of the chromophore and auxochromes. Chalcones are of a great interest because they have a unique structural feature² of having a $>C=O$ functional group in conjugation with $>C=C<$ and the whole molecule is in conjugation. The chalcones are α,β -unsaturated ketones containing the reactive keto ethylene group $-CO-CH=CH$ which makes it biologically active. Some substituted chalcones and their derivatives have been reported to possess some interesting³ biological properties such as antibacterial, antifungal, insecticidal, ulcerogenic, anticancer, anti-inflammatory, anaesthetic, analgesic, antimalarial, antioxidant etc.

Chalcones are also key precursor^{4,5} in the synthesis of many biologically important heterocycles. Transition metal ions are found in several biological species and are reported to play an important role in different enzymatic and physiological reactions, the interaction of chalcones

with metal ions may also change the antioxidant properties and also biological effects of the chalcones⁶.

MATERIALS

All the chemicals and reagents were of AR grade and used without further purification. Ethanol, DMF, CuSO₄.5H₂O, 2-hydroxy-4, 5-dimethyl acetophenone, 2-chorobenzaldehyde, 3-bromobenzaldehyde, 4-fluorobenzaldehyde and 4-cyanobenzaldehyde etc were used in this work.

METHODS

1) Synthesis of transition metal complexes

The substituted chalcones were prepared⁷ by reacting 2-hydroxy-4,5-dimethyl acetophenone with corresponding aromatic aldehydes like 2-chorobenzaldehyde, 3-bromobenzaldehyde, 4-fluorobenzaldehyde and 4-cyanobenzaldehyde in presence of alkaline medium at room temperature.

The transition metal complexes were prepared by mixing corresponding chalcone ligands with copper sulphate in the ratio of 1:2. A warm ethanolic solution of CuSO₄.5H₂O (0.01mole) was added to ethanolic solution (0.02 mole) of corresponding chalcone ligands. The pH of solution adjusted to 7-8 using aqueous ammonia Solution. The mixture was heated under reflux for 2-3 hrs. The complex thus obtained was filtered and washed with excess of ethanol and dried at room temperature.

2) Biological Studies

The complexes were screened for antibacterial activity against gram positive *Staphylococcus aureus*, gram negative *Escherichia coli* and for antifungal activity against *Aspergillus niger* by following methods.

a) Antibacterial activity

The minimum inhibitory concentration (MIC) of the chalcone ligands and their complexes was carried using Broth dilution method⁸. The stock solution of all the complexes was prepared by dissolving 10 mg of complex in 10 ml DMF. The complex solution was serially diluted to give a concentration of 512, 256, 128, 64, 32 and 16 µg/ml in test tubes containing 1 ml sterile nutrient broth. Then, the tubes were inoculated with 100 µl of bacterial suspension in the saline and incubated at 37°C for 24 hrs. A tube containing nutrient broth only was seeded with the test organism to serve as control. All the tubes were then incubated at 37°C for 24 h and then examined for growth by observing O.D. at 600nm.

b) Antifungal activity by Disc Transfer Technique

The measurement of antifungal activity by disk transfer technique was carried using 6 mm diameter disks. Single disc was aseptically inoculated with sabouraud's dextrose agar medium containing desired concentration of the test complex. Test and control (without complex) were inoculated for 3-4 days at 28°C and zone of inhibition was calculated using standard technique.

RESULT AND DISSCUSSION

1) Characterisation of complexes

All the complexes are stable at room temperature insoluble in water and most of the common organic solvents but soluble in DMF and DMSO. The elemental analysis data of its complexes

are in good agreement with proposed molecular formulas. The thermogram of Cu (II) complexes shows the absence of hydrated water molecule. The analytical data of the complexes (Table-1) indicates that their stoichiometry may be represented as 1:2 metal to ligand ratio. The molar conductance values of the complexes in DMF solvents suggesting their non-electrolytic nature.

The μ_{eff} values at room temperature for Cu(II) complexes have magnetic moment values in the range of 1.45 to 1.85 B.M. These values are expected for distorted octahedral geometry of Cu(II) complexes at room temperature and further supported by electronic spectral data.

Table-1 Elemental Analysis, Magnetic Susceptibility and Physical Properties of Cu(II)-Chalcone Complexes

Complex	Molecular Formula	Mol. Wt. (gm/mol)	Color	M.P. °C	Yield (%)	% Elemental found(Calculated)			analysis		μ_{eff} [BM]	Molar Conductance (mho.cm ² .mol ⁻¹)
						Carbon	Hydrogen	Halogen	Metal			
Cu(II)-2-Chloro Complex	[Cu(C ₁₇ H ₁₄ O ₂ Cl) ₂]	635.04	Green	>300	62	64.31 (64.39)	4.44 (4.51)	11.17 (11.13)	10.01 (9.96)	1.61	0.003	
Cu(II)-3-Bromo Complex	[Cu(C ₁₇ H ₁₄ O ₂ Br) ₂]	723.94	Brown	>300	69	56.41 (56.46)	3.90 (3.93)	22.07 (22.01)	8.78 (8.71)	1.83	0.002	
Cu(II)-4-Fluoro Complex	[Cu(C ₁₇ H ₁₄ O ₂ F) ₂]	602.13	Blue	>300	58	67.82 (67.88)	4.69 (4.73)	6.31 (6.35)	10.55 (10.46)	1.71	0.001	
Cu(II)-4-Cyano Complex	[Cu(C ₁₈ H ₁₄ O ₂ N) ₂]	616.16	Brown	>300	52	70.17 (70.21)	4.58 (4.62)	-	10.31 (10.24)	1.67	0.006	

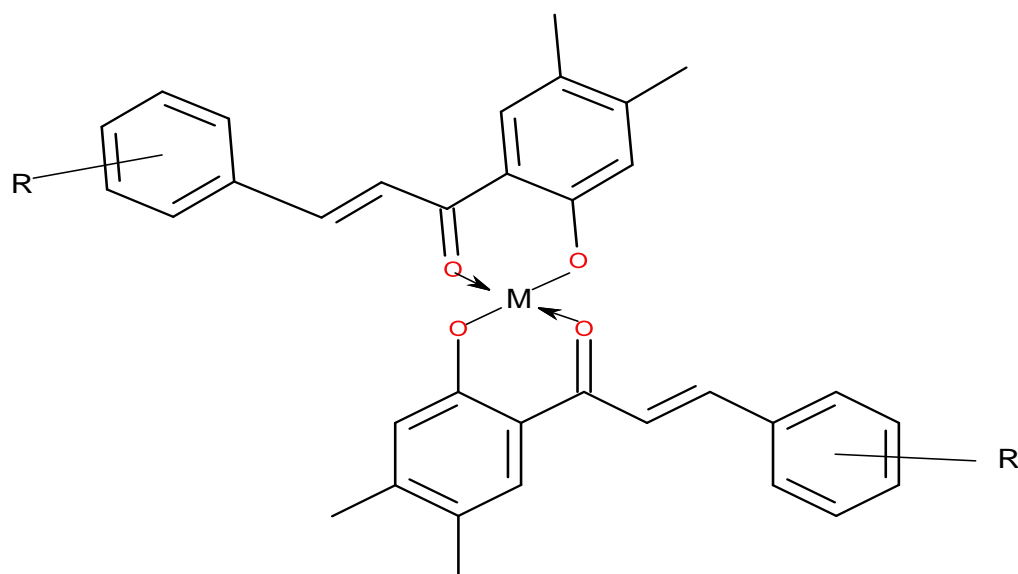
Infra-Red

The IR Spectra of all the Cu (II) –Chalcones Complexes have been recorded in KBr pellets in the region of 4000-400 cm⁻¹. On FTIR Spectrophotometer Shimadzu (Model).The IR spectral data along with the possible assignments of chalcone complexes are presented in Table 2.

The evidence drawn for the formation of complexes has been done by using their analytical data, spectral techniques and magnetic studies. Thus on the basis of above results the possible geometry around the metal ion was evidently confirmed in such a way that the Cu (II) complexes form distorted octahedral geometries

Table-2 : : Some Important IR Bands in cm⁻¹ of the Cu (II) chalcones-Metal Complexes

Complex	$\nu(\text{O-H})$ (H ₂ O)	$\nu_{\text{C-H}}$ (CH ₃) str.	$\nu_{\text{C-O}}$ (Phenol)	$\nu_{\text{Ph-C=C}}$	$\nu_{\text{C=O}}$	$\nu_{\text{M-O}}$
Cu(II)-2-Chloro Chalcone Complex [Cu (II) (C ₁₇ H ₁₄ O ₂ Cl) ₂ .]	-	2945	1188	1572	1641	450
Cu(II)-3-Bromo Chalcone Complex [Cu (II) (C ₁₇ H ₁₄ O ₂ Br) ₂ .]	-	3305	1188	1577	1647	520
Cu(II)-4-Fluoro Chalcone Complex [Cu (II) (C ₁₇ H ₁₄ O ₂ F) ₂ .]	-	3250	1190	1575	1653	468
Cu(II)-4-Cyano Chalcone Complex [Cu (II) (C ₁₈ H ₁₄ O ₂ N) ₂ .]	-	2975	1188	1573	1641	496



Where M – Copper, R – 2- Chloro, 3-Bromo, 4-Fluoro, 4-Cyano Chalcone.

Figure 1: Proposed structure of the complexes

Table-3 : Antimicrobial activity of synthesized Ligands and Cu(II)Complexes			
Samples	Antibacterial		Antifungal
	E. coli	S. aureus	A. Niger
	(MIC- $\mu\text{g/ml}$)		(ZOI- mm)
DMF	-	-	-
Ampicillin	4	8	-
Fluconazole	-	-	30 \pm 02
2-hydroxy-4,5-dimethyl-2-chloro chalcone	>512	>512	-
2-hydroxy-4,5-dimethyl-3-bromo chalcone	16	128	-
2-hydroxy-4,5-dimethyl-4-fluoro chalcone	16	256	08 \pm 0.2
2-hydroxy-4,5-dimethyl-4-cyano chalcone	128	218	09 \pm 0.2
Cu(II)-2-chloro chalcone Complex	256	32	12 \pm 02
Cu(II)-3-bromo chalcone Complex	>512	32	06 \pm 0.2
Cu(II)-4-fluoro chalcone Complex	128	128	07 \pm 01
Cu(II)-4-cyano chalcone Complex	64	128	07 \pm 0.2

In addition to this keeping in view of the increasing problems of antimicrobial resistance complexes were screened for their antibacterial and antifungal activities.

The antimicrobial activity of all the complexes is less than that of standard Ampicillin and Fluconazole, Shown in (Table-3).

CONCLUSION

The elemental analysis, magnetic susceptibility, IR, ^1H NMR and Physical Properties observations suggest the distorted octahedral geometry for the Cu (II) complexes and also exhibit the antimicrobial activity.

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