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Research Article

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Synthesis of 3-[{(3-(2'-Nitrophenyl)}-prop-2-enoyl]-4-hydroxy-6-methyl-2H-chromene-2-one and its metal complexes as an antimicrobial agent

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ABSTRACT

*Compound 3-[{(3-(2'-Nitrophenyl)}-prop-2-enoyl]-4-hydroxy-6-methyl-2H-chromene-2-one (III) has been synthesized by the condensation of 3-acetyl-4-hydroxymethyl-coumarin with 2-benzaldehyde in presence of piperidine. Compound(**III**) was further reacted with transition metal salts to prepare metalchelates compd.(**IVa** to compd. **IVe**).The constitution of the product has been supported by elemental analysis, IR spectra and conductivity measurements. The products have been screened for their in vitro growth inhibitory activity against several microorganisms. In-vitro anti microbial activity of all synthesized compounds and standard drugs have been evaluated against four strains of bacterial culture and one fungus, which includes two gram +ve bacterial culture and two gram -ve bacterial culture, which show net enhancement in activity on co-ordination of metals with ligand but moderate activity as compare to standard drugs.*

Key Words: Antimicrobial activity, Coumarin, Metal Complexes , Structural study.

INTRODUCTION

Chalcones bearing an active keto-ethylinic linkage and therefore reactive towards a number of reagents and act as an intermediate compounds for the synthesis of some naturally occurring heterocyclic compounds. Chalcones are useful for the detection of Fe(II)[1] and Ca (II)[2] ions in presence of Ba and Sr as it reacts with a number of metal ions. Furthermore 4-hydroxy coumarins give sensitive color reaction and can be made selective by appropriate variation in pH or alcohol concentration and the use of suitable masking agent.

Some 3-acetyl/acetoacetyl-4-hydroxy coumarins have been reported as an anti-HIV agent[3]. V. V. Mulwad et al.[4] have prepared some chalcones from coumarin derivatives which possess significant antimicrobial activity. *In-vitro* antibacterial, antifungal and cytotoxic activities of some coumarin and their metal complexes also have been reported[5,6] . Some researchers synthesized copper(II), cobalt(II), nickel(II), Zinc(II) and cadmium(II) complexes of 7-hydroxy-4-methyl coumarin and studied their antimicrobial activities[7].

The growing potent literature of recent years demonstrate that the chalcone bearing a very active synthon and metal complexes of coumarin derivatives possess significant biological activities viz. Antifungal[8], antibacterial[9] and antitumor[10] activity prompted us to synthesize some new chalcones bearing 4-hydroxy-6-methyl coumarin and their metal complexes to study their antimicrobial activity.

EXPERIMENTAL SECTION

All the reagents were of AR grade. All the melting points were determined in open capillary tubes and are uncorrected. Infrared spectra (KBr)(νmax, cm^{-1}) were recorded on a Shimadzu 435 –IR Spectrophotometer. The metal and anions are estimated using standard procedure[11]. Elemental analyses are quite comparable with their structure. Elemental analyses of metal complexes indicates that the metal: ligand (M:L) ratio is 1:2 for all the divalent metal ions. The conductivity of metal complexes were determined using Thoshniwal Conductivity Bridge.

Preparation of a ligand compound(III)

3-[{3-(2'-Nitrophenyl)}-prop-2-enoyl] -4-hydroxy-6-methyl-2H-chromen-2-one were prepared according to the reported method(III)[12].

A mixture of 3-acetyl-4-hydroxy-6-methyl coumarin (2.52 gm, 0.01M); 2'-nitrobenzaldehyde (0.025 M) and piperidine (1 ml) were added into enthanol (50 ml). The reaction mixture was refluxed on water bath for 4 hrs., cooled and solid was separated. Then it was crystallized from suitable solvent, lemon yellow colored compound was obtained yield 72% M.P. 192º C. Found : C, 64.95%, H,3.6%, O,15.54, N, 3.8% for $C_{19}H_{13}O_6N_2$ required : C,64.95%, H,3.70%, O,15.76, N, 3.98%.

Preparation of metal complexes compound(IV)

Bis3-[{3-(2'-Nitrophenyl)}-prop-2-enoyl]-4-hydroxy-6-methyl-2H-chromen-2-one]copper(II)complex; $[Cu(C_{19}H_{12}O_6N_2)_2(H_2O)_2]$

Copper chloride solution (10.0 ml, 0.1M) diluted to 50 ml. and excess of ammonium hydroxide was added to get the pH between 10.5 – 11.0 It was refluxed with excess of alcoholic solution of 3-[{3-(9'-Nitrophenyl)}-prop-2-enoyl]-4-hydroxy-6 methyl-2H-chromen-2-one (0.1 M) on a water bath for half an hour when cinnamon brown precipitates of copper complex were obtained. The precipitates were filtered, washed with distilled water and dried at 100º C. The complex was crystallized from DMF. Yield : 63% Found : C,56.9%, H,3.4%, O,17.51%, N, 3.4, Cu,7.8% for $[Cu(C_{19}H_{12}O_6N_2)_2(H_2O)_2]$ required C,57.03%, H,3.50%, O,17.63%, N, 3.50, Cu,7.94%.

Similarly other metal complexes were prepared. The complexes did not show clear melting point.

Conductivity

The conductivity of metal complexes was determined using Thoshniwal Conductivity Bridge. It was dissolved in DMF and conductivity was measured.

Conductivity of the DMF along was measured and solution of the complexes in DMF with different concentration was measured.

The molar conductivity was calculated using the formula.

$$\text{Molecular conductivity} = \frac{1000 \times K}{C}$$

Where, K=Conductivity of the sol. of the complexes in DMF. C = Concentration of the complexes(10^{-3} M). The conductivity data are in (**Table-I**) and the data indicates that the complexes are non- electrolyte in nature[13].

IR Spectral analyses

The Infrared spectra of the metal complexes were recorded on Shimadzu 435-IR Spectrophotometer between 4000-400 cm^{-1}.

The examination of the IR spectra of all the complexes reveals that

(I) All the IR spectra have identical bands at their respective positions.

(II) Most of the bands appeared in the spectra of ligand are observed at the similar position in the IR spectra of metal complexes.

(III) Only the discermible difference in the IR spectra of metal complexes has been appeared. The band between 3200 - 3400 cm^{-1} due to - OH group in the spectra of ligands is less broader in the spectra of all the metal complexes. This might be due to complexation of metal ion. The less broadness might be due to water molecules associated with complex formation.

(IV) In addition the IR spectra of complexes showed new bands between 590-500 cm^{-1} assigned to metal-ligand vibration (M-O).

Antimicrobial activity

The antimicrobial activity was assayed by Cup-plate agar diffusion method[14] by measuring inhibition zones in mm. *In vitro* antimicrobial activity of all synthesized compounds and standard drugs have been evaluated against four strains of bacteria which includes two Gram +ve bacteria such as *Staphylococcus aureus***,** *Bacillus megaterium* and two Gram-ve bacteria such as *Escherichia coli, Proteus vulgaris* and one fungi *Aspergillus nige*r. The cups (10 mm in diameter) were formed by the help of borer in agar medium and filled with 0.04 ml (40 µg/ml) solution of sample in DMF.

The plates were incubated at 37^{O}C for 24 hrs. and the control was also maintained with 0.04 ml of DMF in similar manner and the zones of inhibition of the bacterial/ fungal growth were measured in millimeter and recorded in (**Table- III**). .

The antibacterial activity was compared with standard drugs viz. Amoxycillin, Ampicillin, Ciprofloxacin, Erythromycin and antifungal activity was compared with standard drug viz. Griseofulvin. Most of the compounds inhibit the growth of the above organism, which cause decease in many plants. Hence such type of compounds may find as agricultural and garden bactericides and fungicides.

TABLE - I : Elemental and metal analysis of metal (II) complexes

Sr.	Molecular Formula	M.W.	% of Carbon		% of Hydrogen		% of Oxygen		% of Metal		Conductivity
			Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	
IVa	$Cu[C_{19}H_{12}O_6N_2]_2(H_2O)_2$	907.54	71.40	71.30	4.18	4.10	17.63	17.51	7.00	6.80	7.90
IVb	$Ni[C_{19}H_{12}O_6N_2]_2(H_2O)_2$	902.71	71.78	71.50	4.20	4.10	17.72	17.60	6.50	6.30	8.50
IVc	$Co[C_{19}H_{12}O_6N_2]_2(H_2O)_2$	902.93	71.76	71.60	4.20	4.00	17.72	17.64	6.52	6.40	9.20
IVd	$Fe[C_{19}H_{12}O_6N_2]_2(H_2O)_2$	901.85	71.85	71.60	4.65	4.50	17.74	17.68	6.19	6.10	10.60
IVe	$Mn[C_{19}H_{12}O_6N_2]_2(H_2O)_2$	894.93	72.40	72.30	4.24	4.10	17.87	17.75	6.13	6.00	10.50

TABLE - II : IR spectral data of metal (II) complexes

Sr.	Metal Complexes	N=O	Alkane $-CH_3$	Aromatic -CH	Ketone -C=O	Alkene CH=CH	M-O Band	Ether C-O-C
IVa	$Cu[C_{19}H_{12}O_6N_2]_2(H_2O)_2$	1550	2928 2834 1443 1383	1511 1249 832	1650 1710	1609	590-500	1112
IVb	$Ni[C_{19}H_{12}O_6N_2]_2(H_2O)_2$	1555	2920 2858 1456 1384	1562 821 1222	1697 1715	1612	590-500	1130
IVc	$Co[C_{19}H_{12}O_6N_2]_2(H_2O)_2$	1545	1922 2853 1460 1375	1554 1222 833	1689 1715	1584	590-500	1138
IVd	$Fe[C_{19}H_{12}O_6N_2]_2(H_2O)_2$	1556	2920 2850 1418 1376	1584 1223 819	1669 1710	1608	590-500	1137
IVe	$Mn[C_{19}H_{12}O_6N_2]_2(H_2O)_2$	1541	2933 2858 1464 1383	1562 1227 821	1661 1732	1602	590-500	1072

TABLE - III : Microbiological evaluation of synthesised compounds

Micro Organism	Compounds						Standard drugs				
	III	**IVa**	**IVb**	**IVc**	**IVd**	**IVe**	Ampicillin	Amoxycillin	Ciprofloxacin	Erythromycin	Griseofulvin
E. coli	19	22	24	18	23	25	16	17	26	22	0
P. vulgaris	19	21	25	20	22	23	24	21	28	18	0
B. megaterium	20	19	23	22	19	21	20	22	23	10	0
S. aureus	22	21	20	23	18	19	25	29	24	22	0
A. niger	18	20	24	17	22	23	0	0	0	0	21

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