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Synthesis and Biological Activities of Oxine Containing Aurones

KEYWORDS: oxine hydroxyl acetophenones, aurone, metal complex, magnetic properties, fungicidal activity

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ABSTRACT *Oxine (i.e. 8-hydroxy quinoline) containing aurone derivatives (2a-e) have been prepared by condensation reaction of -iodoacetophenone derivatives and 5-formyl- 8-hydroxy quinoline. All the aurones have been characterized by elemental and spectral analysis. One of the aurone derivatives (2b) has been utilized for transition metal : ligand ratio, magnetic properties, and spectral analysis. All the aurones metal chelates were also screened for antifungal activity.*

Introduction
Aurones i.e. 2-benylidne coumaran-3-one are synthesized by different ways. Reaction of manganese acetate or mercuric acetate with 2- hydroxyl acetophenones in either acetic acid or DMSO solvent afford aurones[1-3]. The bromoclromone in alkali also yields aurones[4-5]. The hydroxyl substituted alkali or in non-aqueous base catalyst afford aurones[6-9]. The area in which the aurones containing oxine (i.e. 8-hydroxy quinoline) has not been reported so far such type of compound may have microbial as well as complexion properties. Hence it was thought interesting to study the oxine containing aurones. The present paper comprises the synthesis, characterization and chelating properties of oxine containing aurones. The work is scanned in the scheme-1.

Experimental
Materials
All the chemicals have been obtained from SDS chemicals, boisar, India. 5-formyl- 8-hydroxy quinoline was prepared by the method reported in literature[10]. Preparation of –iodo-2-hydroxy substituted acetophenone.

To a solution of each of acetophenone (0.1 mol) (Scheme-1) in tetrahydrofuran (THF) solvent a solution of lcl in forming acid was added drop wise with constant stirring. It was than refured for an hour. The resulting mixture was poured in to water and ether extracted. The solid mass was obtained on evaporation and then crystallized from tetrahydrofuran (THF). The details of all (1a-e) are given in table – 1.

Preparation of 2-(quinolinolyidene) coumaran-3-ones. (2a-e)
Each iodide compound (3a-f) and 5-formyl- 8-hydroxy quinoline was suspended in THF. The suspension was then added in 40% NaOH with constant stirring till dark brown color persists. The resultant mixture was then neutralized by 50% HCL and separated solid was filtered off, washed by THF and air dried. The details of all aurones (2a-e) are furnished in Table – 2.

Synthesis of Metal complexes of aurone 2d:
The aurone 2d (0.01 mole) was dissolved in formic acid and diluted by water. This solution was added drop wise to metal acetate (0.05 mole) in water. The resultant mixture was added by sodium acetate up to the precipitates exist. The precipitates were then digested on the boiling water bath. The metal complex was filtered, washed and air dried. The details of metal complexes are given in Table – 3.

Measurement
C, H, N content of all compounds (2a-e) and metal complexes of 2d were determined on C-H-N-O elemental analyzer, carlo Erba, Italy. The metal contents of metal complexes were estimated by analytical method[11].The IR spectra of all the sample were scanned in KBr pellets on perkin elmer IR spectrometer. The NMR spectra of DMSO soluble sample were scanned on 60 MHz spectrophotometer using TMS as an internal standard. Magnetic susceptibility measurements of all the metal complexes of 2d compound were carried out Guay Method. Mercury tetrathiocynatocobaltet (II), $Hg[Co(NCS)_4]$ was used as a calibrant. The diffusion reflectance spectra of all metal complexes were recorded on DK-2A spectrometer with a solid reflectance attachment MgO was employed as reference compound.

Antimicrobial activity of all the compounds and metal complexes (Table -2 & Table – 3) were screened for their antibacterial activities in "in vitro" at doses of 100 mg in 0.1 ml of DMF against gram negative bacterium Escherichia coil and the gram positive bacterium bacilas ciroflagallous and for their antifungal activity in vitro agents the fungi aspergills niger and candida ablicans. DMF was used as a solvent control. PDA (potato-dextrose-agar) medium was used as a culture medium and method employed was cup method[12]. The zones of inhibition was measured in mm and are represented by (+), (++), (+++) depending upon the diameter and clarity.

Result and Discussion
All aurone derivatives listed table – 2 were dark brown amorphous powder. All these compounds are sparingly soluble in DMF, DMSO solvents. They did not melt up to 230° C. the C, H, N content of all these compounds are consistent with their predict structure. IR spectra (not shown) of all the aurone derivatives are almost identical in most of the aspects. The broad band extending from 3500 to 2800 cm^{-1} is due to –OH of oxine unit. The bands at 3030, 1800, 1600, 810, 860 cm^{-1} arises from C=O stretching of 5 membered ring. The band due to ether is appeared at 1180 cm^{-1}. The other bands are appeared at their respective portions. The PMR of soluble sample show the signal at δ = 4.0 ppm due to =CH groups. The signals for aromatic ring are appeared in downfield area (i.e. δ = 7.4 ppm).

The C, H, N of all the metal complexes are also consistent with their predicted structure. The metal contents of each complex suggest the M:L ratio is 1:2. The magnetic properties of all these complexes are agreed with their structure.

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This is also supported by reflectance spectra. Examination of magnetic moment (μ_{eff}) of all the complexes except Zn^{2+} is di-amagnetic. The diffuse electronic spectrum of Cu^{2+} complex shows two broad bands 15872 cm^{-1} and 22985 cm^{-1} 2Eg ◊ $2T_{2g}$ translation and charge transfer respectively. The Ni^{2+} and Co^{2+} complexes gave two absorption bands at 15625 cm^{-1}, 22470 cm^{-1}, 16530 cm^{-1} correspoding to $4T_1g$ ◊$2T_1g$ and to $4T_1g$ ◊$4T_1g$(p) translations[14]. This data and μ_{eff} of complexes suggest octahedral centrifugal for both complexes. The Mn^{2+} complex also the bands at 14660 cm^{-1}, 19755 cm^{-1}, 25570 cm^{-1} suggest the $6A_1g$ ◊$4T_1g$(4G), $6A_1g$ ◊$4T_1g$(4G) and $6A_1g$ ◊$4T_1g$(4G) translation. This indicates the octahedral structure. The microbial activity of all the compounds (2a-e) and metal complexes is presented in table – 3. The result reveal that the

1. The chloro bromo containing compounds are more toxic against the bacterial and fungi.
2. The metal complexes are more toxic than parent ligand
3. The copper complex is more toxic than other metal chelats.

Table – 1
Synthesis and Characterization of ω-iodo-4- substituted acctophenones

Sample No.	R	M. Pc	Yield %	I content	
				Calc	Found
1a	H	45-6	76	48.84	48.5
1b	CH_3	43-4	55	46.35	46.2
1c	OCH_3	55-6	66	43.79	43.6
1d	Cl	76-7	50	42.83	42.6
1e	Br	93-4	50	37.24	37.1

Table - 2
Characterization of oxine containing aurones

Aurone Derivative	Molecular Formula	Yield %	Elemental Analysis						Clor For	
			C		H		N			
			Clac	Found	Clac	Found	Clac	Found	Clac	Found
2a	$C_{18}H_{11}NO_3$	75	74.74	74.6	3.8	3.7	4.84	4.7		
2b	$C_{19}H_{13}NO_3$	70	75.24	75.1	4.29	4.1	4.62	4.5		
2c	$C_{19}H_{13}NO_4$	80	71.47	71.3	4.07	4.0	4.38	4.2		
2d	$C_{18}H_{10}ClNO_3$	65	64.96	64.8	3.00	2.8	4.2	4.1	10.67	10.5
2e	$C_{18}H_{10}BrNO_3$	65	68.69	68.5	2.71	2.6	3.8	3.7	21.73	21.6

IR Spectral Data
1724 v cm^{-1} c=0 of 5mombered ring NMR : 2a

1576, 1463 cm^{-1} aromatic ring 4.5 δppm = CH

1180 cm^{-1} C-O stretching 6.9-8.1 δppm (Ar-H)

729 cm^{-1} C-Cl

Table – 3
Characteristics of Metal Complexes of compound 2d

Metal Complex of 2d	Molecular Formula	% elemental analysis (Calc.) (Found)										Magnetic Moment μeff B.M.
		%C		%H		%Cl		%N		%Metal		
		Calc	Found	Calc	Found	Calc	Found	Calc	Found	Calc	Found	
Cu2+	$C_{36}H_{18}C_{12}N_2O_6Cu$ (708.54)	60.97	60.8	2.54	2.55	10.02	10.00	3.95	3.88	8.96	8.99	2.01
Ni2+	$C_{36}H_{18}C_{12}N_2O_6Ni$ (703.72)	61.38	61.20	2.55	2.55	10.08	10.00	3.97	3.85	8.34	8.25	4.69
Co2+	$C_{36}H_{18}C_{12}N_2O_6Co$ (703.94)	61.28	61.25	2.53	2.55	10.08	10.10	3.97	3.85	8.34	8.33	3.11
Mn2+	$C_{36}H_{18}C_{12}N_2O_6Mn$ (699.94)	61.72	61.60	2.58	2.55	10.15	10.05	4.01	4.00	7.85	7.88	5.11
Zn2+	$C_{36}H_{18}C_{12}N_2O_6Zn$ (710.37)	60.81	60.70	2.53	2.45	9.99	9.88	3.94	3.80	9.20	9.11	Diamagnetic

Table – 4
Antibacterial and Antifungal activities of oxine containing aurones and metal complexes of 2d

	2a	2b	2c	2d	2e	2d-Cu2+	2d-Ni2+	2d-Co2+	2d-Mn2+	2d-Zn2+
E.Coil	++	++	+++	+++	+++	+++	+++	+++	++	++
B. Cirrofla Gallosus	++	++	+++	+++	+++	+++	+++	+++	+++	++
A. Niger	++	+++	+++	+++	+++	+++	+++	+++	++	++
C. Albicans	++	++	+++	+++	+++	+++	+++	+++	+++	++

(+) Poor active, (++) Active, (+++) More active

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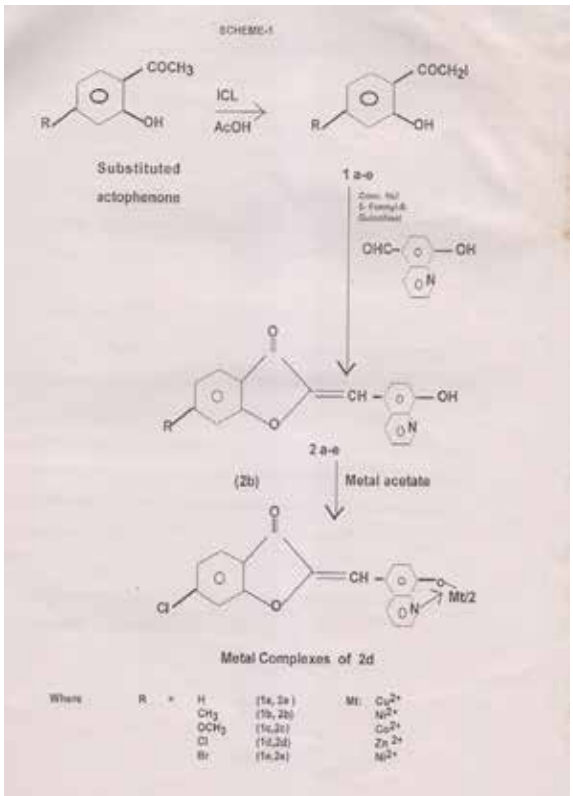

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