

Synthesis and Antimicrobial Screening of Metal Complexes of 1-(5-Chloro-2-Hydroxyphenyl)-3-(2,4-Dichlorophenyl) Propane-1,3-Dione

D. D. Suryawanshi¹, A. D. Suryawanshi², A. S. Padampalle³, A. S. Rajbhoj¹

¹Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, India

² Department of Physics, B. J. College Ale., Pune, Maharashtra, India

³ Department of Physics, S. C. S. College Omerga., Osmanabad, India

ABSTRACT

1-(5-Chloro-2-Hydroxyphenyl)-3-(2,4-Dichlorophenyl) Propane-1,3-Dione and its metal complexes have been synthesized by conventional method. The diketone is offered by employing Baker- Venkatraman rearrangement. The synthesized compounds were confirmed by the spectroscopic analysis such as UV, IR, ¹H-NMR, ¹³C-NMR, mass, elemental analysis, magnetic susceptibility, XRD and evaluated for antibacterial screening.

Keywords: Baker-Venkatraman rearrangement, metal complexes, XRD, thermal study.

I. INTRODUCTION

β -diketones and relative derivatives are considered as a class of very important ligands in the growth of coordination Chemistry. The Chemistry of 1,3-diketones has attracted the attention of scientists for almost century[1]. Due to the presence of two oxygen donor atoms and facile keto-enol tautomerism[2], they easily coordinate with metal ions after deprotonating the enolic hydrogen atom and provides stable metal complexes. They have been used as ligands for coordination of transition metals and have been investigated for use as potential antiviral agents[3]. Those are important class of organic compounds frequently encountered in synthetic chemistry[4-6]. As a result of their usability, the biological transformation of these compounds have recently arised interest[7-8]. 1,3-diketones have gained a lot of interest due their importance as good ligands[9], for the chelation with metals, as intermediate in the synthesis of core heterocycles such as pyrazole[10], flavones[11], isoxazole[12], triazole[13], benzodiazepine[14] and pyrimidine[15]. Those have pharmacological activities like antioxidant[10], prophylactic antitumor[16], systematic insecticidal[17] and antibacterial[18]. Recently, it is known that they have the important pharmacophores for the HIV-integrase(1N) inhibitors[19]. It has been used as anti-sunscreen agent[20].

Owing to β -diketones having such varying pharmacological activities, we were interested to synthesize a novel β -diketone and its transition metal complexes

II. Experimental

Synthesis of 2-acetyl-4-chlorophenyl 2,4-dichloro benzoate (A):

To The mixture of 5-chloro-2-hydroxyacetophenone and 2,4-dichlorobenzoic acid, a dry pyridine and POCl₃ were added dropwise with constant stirring at 0°C. Then the reaction mixture was stirred for about 7-8 hours. After completion of the reaction, the reaction mixture was poured into 100ml 1M HCl containing 50 gm of crushed ice and solid obtained was filtered and washed with 10 ml of water. It was recrystallized from ethol, filtered and dried. Yield: 80%.

Synthesis of 1-(5-chloro-2-hydroxyphenyl)-3-(2,4-dichlorophenyl) propane-1,3-dione (B):

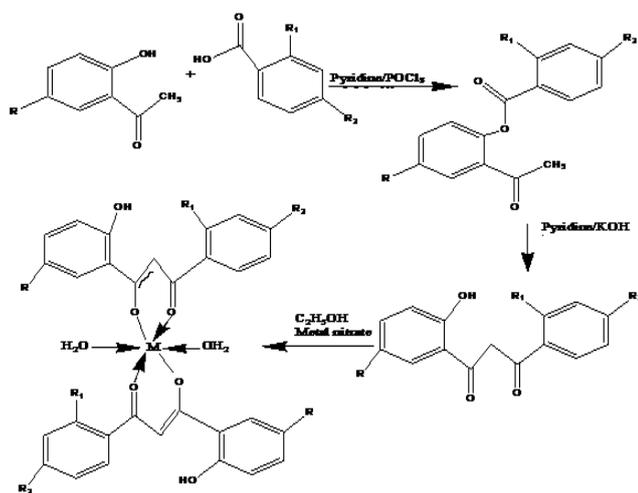
Compound (A) was dissolved in dry pyridine. To this powdered KOH was added and the reaction mixture was stirred for about 3-4 hours. After completion of the reaction, the reaction mixture was poured on ice cold water and acidified with conc. HCl. The yellow solid was filtered off and crystallized from absolute ethanol to obtain pure product. Yield: 80%.

FT-IR: (KBR) cm⁻¹: 3001.96 (OH), 1680.26 (C=O), 1480.18 (Ar C=C). ¹H-NMR (300 MHz, CDCl₃-d₆);

$\delta=6.8$ (s, 1H, =CH-), 7.1 (s, 1H, Ar-H), 7.4-7.7 (m, 5H, Ar-H), 11.9 (s, 1H, OH), 15.1 (s, 1H, Enolic-OH), ¹³C-NMR (300MHz, CDCl₃); $\delta=187.3$ (s, C-1, C=O), 94.1 (s, C-2, -CH=), 185.6 (d, C-3), 115.2 (s, C-1'), 160.4 (s, C-2'), 119.2 (d, C-3'), 129.5 (d, C-4'), 125.5 (s, C-5'), 128.3 (d, C-6'), 135.2 (s, C-1''), 136.5 (d, C-2''), 131.5 (d, C-3''), 141.3 (s, C-4''), 127.2 (s, C-5''), 132.6 (s, C-6''). UV/Vis (DMSO)nm: 370,415. EC-MS: 344.91 (M+1).

Bis-(diketonato) Fe(III) complex:

The mixture of (3.43gm, 0.01 mol) of compound B and (4.04 gm, 0.01 mol) of anhydrous Fe(III) nitrate and 20 ml of anhydrous ethanol were added and refluxed for about 8-9 hrs. The brown solid which precipitated was washed with boiling ethanol and recrystallised from ethyl acetate to give brownish crystals of Fe(III) β -diketonate. Yield: 85%.



$R_1, R_2 = Cl, R_3 = Cl, R_4 = Cl$
 $M = Cu, Ni, Co, Cr, Fe$. In all these cases water of coordination is present.
 Scheme I. Synthesis of ligand and metal complexes.

III. Results and discussion

2-acetyl-4-chlorophenyl 2,4-dichlorobenzoate was prepared by the esterification of 5-chloro, 2-hydroxyacetophenone with 2,4-dichlorobenzoic acid in the presence of POCl₃. 2-acetyl-4-chlorophenyl 2,4-dichlorobenzoate undergoes Baker-Venkatraman transformation to offered pale yellow needle of ligand (B). The negative test for ester confirms the absence of ester group. The structure was further confirmed by spectral analysis.

The ¹H-NMR spectra gives characteristic peak at $\delta 15.1$ which corresponds to enolic proton and at $\delta 11.9$ which is due to phenolic proton adjacent to the carbonyl group. It confirms the formation of β -diketone. The compound in enolic form is more stable than that of ketonic one. The complex of synthesized compound(B) gives browned coloured Fe(III) in high yield. The structure was then confirmed by spectral analysis.

The C=O bond in complexes of shifted to lower frequency as compared to that of free ligand which indicates the coordination of metal atom with the carbonyl group of diketone[21].

Similarly, other metal complexes were prepared by the same method. The ligand and its metal complexes are quite stable. All the complexes are insoluble in water but soluble in DMSO and DMF. The complexes are non-electrolytic in nature[22].

Table 1. Molar conductivity, magnetic and Infrared spectral data of synthesized compounds.

Compound	Meff(BM)	Molar Conductance	IR (cm ⁻¹)				
			$\nu(C=O)$	$\nu(C-O)$	$\nu(-OH)$	$\nu(M-O)$	$\nu(OH)$ Coordinated H ₂ O Molecule
Ligand			1680	1480	3001	--	---
Cu(II) complex	2.12	29.40	1657	1501	3016	527	3255
Ni(II) complex	2.73	54.22	1655	1505	3017	505	3258
Co(II) Complex	4.45	35.45	1666	1522	3020	505	3248
Cr(III) Complex	3.82	37.23	1663	1518	3018	520	3244
Fe(III) Complex	6.11	61.65	1656	1523	3015	512	3260

IV. Powder X-ray diffraction analysis

The X-ray diffractograms of the complexes were scanned in the range 5-85° at a wavelength of 1.543Å. The diffractograms and associated data depict the 2θ values for each peak, the relative intensity and inter-planar spacing (d-values). The X-ray diffraction pattern of these complexes with respect to major peaks of relative intensity greater than 10% were indexed using a computer programme[23]. This indexing method also yields Miller indices (hkl), the unit cell parameters and the unit cell volume. The unit cell of Cu(II) complex yielded values of lattice constant: a=21.543 Å, b=8.532Å and C= 7.592 Å and a unit cell volume V=1395.4 Å³. The unit cell of the Co(II) complex yielded values of lattice constant: a=14.511, b=5.130 and c=13.087 and a unit cell volume V=974.29. In concurrence with these cell parameters conditions such as a≠b≠c and α≠γ≠β required for a monoclinic sample were tested and found to be satisfactory. Hence, it can be concluded that the Cu(II) and Co(II) complexes were monoclinic crystal systems. The experimental density values of the complexes were determined using the specific gravity method[24] and found to be 3.24 g cm⁻³, 4.83 g cm⁻³ for the Cu(II) and Co(II) complexes respectively. Comparison of experimental and theoretical density values shows good agreement within the limits of experimental error[25].

V. Thermo Gravimetric Analysis

Cu (II) complex:

The simultaneous TG/DTA analysis of a representative metal complex of Cu (II) was studied from ambient temperature to 1000°C in nitrogen atmosphere using α-Al₂O₃ as reference. The thermogram curve of Cu(II) complex shows weight loss 8.11% (cal. 8.20) in the temperature range 190-215°C and sharp endotherm at 195°C which clearly indicate a removal of two coordinated water molecules[26].

The anhydrous complex first showed decomposition from 265-570°C with a 20.16% (cal. 20.50) mass loss and a broad exothermic peak with 390°C in the DTA which may be attributed to the removal of the non-coordinated part of the ligand. The second step of the decomposition from 580-865°C with a mass loss of 55.10% (cal. 51.79) corresponded to the decomposition of the coordinated part of the ligand. A broad endotherm in DTA was observed for this. The mass of final residue corresponds to stable CuO, 17.95% (17.10) which is in agreement with earlier workers[27].

VI. Antimicrobial Screening

Antimicrobial screening[28] of prepared compounds were tested against bacteria as Staphylococcus aureus and Bacillus subtilis (Gram +ve); Escherichia coli (Gram -ve) and against fungi, Aspergillus niger and Fusarium Oxysporum by Kirby Baur's disc diffusion technique using dimethyl sulfoxide as a solvent. The streptomycin was used as reference in case of antibacterial and antifungal activity. A uniform suspension of test organism of 24 hrs old cultures was prepared in test tube containing sterile saline solution. A sterile nutrient agar was then added in each of the petri plates. The plates were related to ensure the uniform mixing of the micro organism in the agar medium which was then allowed to solidify. Sterile Whatmann filter paper disc were dipped in the solution of each compound and placed on the labeled plates. The DMSO was used as a control of the solvent. The streptomycin was used as a standard compound for comparison. Plates were kept in refrigerator for half an hour for diffusion and then incubated at 37°C for 24hrs. After incubation the inhibitory zones around the discs were measured in terms of mm. The observed data of antimicrobial activity of compounds and the standard drugs are given in table.

Table 2. Antimicrobial activity of synthesized compounds

Compound No.	Conc. (ppm)	Antibacterial activity (inhibition in mm)			Antifungal activity	
		Bacillus subtilis	E. coli	Staphylococcus aureus	Aspergillus niger	Fusarium oxysporum

Ligand		12	11	9	9	8
Cu -B	100	16	14	10	17	10
Ni-B	100	13	13	12	18	11
Co-B	100	12	15	14	13	16
Cr-B	100	14	12	10	10	13
Fe-B	100	12	11	11	11	12

VII. CONCLUSION

In the present work Ligand and its transition metal complexes were synthesized and their structures elucidated on the basis of spectral analysis. ¹H-NMR and ¹³C-NMR spectra revealed that the prepared diketone possess characteristic peaks due to the presence of enolic proton (enol form of β -diketone) and phenolic proton adjacent to carbonyl group. These synthesized compounds were screened for in vitro antibacterial and antifungal activity and found to be promising candidates as new antibacterial and antifungal agents.

VIII. REFERENCES

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