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

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Abstract: ***1-(5-chloro-2-hydroxyphenyl)-3-(2,4-dichlorophenyl) propane-1,3-dione and its metal complexes Cu(II), Ni(II), Co(II), Cr(III) and Fe(III) have been synthesized by ultrasound irradiation method. The diketone is offered by employing Baker-Venkatraman rearrangement. The synthesized compounds were confirmed by the spectroscopic analysis such as IR, ^{1}H-NMR, ^{13}C-NMR, mass, elemental analysis, magnetic susceptibility and evaluated for antibacterial screening.***

Keywords: β-diketone, Baker-Venkatraman rearrangement, metal complexes, magnetic susceptibility, antimicrobial screening, ultrasound irradiation.

I. INTRODUCTION

β-diketones have gained a lot of interest due to their importance as good ligands[1], for the chelation with metals, as intermediate in the synthesis of core heterocycles such as pyrazole[2], flavones[3], benzodiazepine[4],isoxazole[5] and pyrimidine[6]. They have also been used as an antisunscreen agent[7]. β-diketones have shown pharmacological activities like prophylactic antitumor[8], antioxidant[9], antibacterial[10]. β-diketones are well known to have keto-enol tautomerism[11] and recently it is reported that they have the important pharmacophores for the HIV-integrase (1N) inhibitors[12]. Further, it has been reported that a number of β-diketones has warrant examination as breast cancer chemopreventive blocking agent[13], antiestrogenic agent[14] and anticarcinogenic agent[15]. β-diketones with different substituents and their metal complexes have been synthesized and their properties such as volatility, Lewis acidity or aggregation state, standard molar enthalpies of formation, standard molar enthalpies of sublimation, vapour pressure and enatioselective catalytic property have been studied[16]. Ultrasound irradiation assisted organic synthesis is an efficient and eco-friendly synthetic strategy. The reaction conducted by sonication provides improved yields and increased selectivities[17]. Here we have developed an environmently benign and novel approach for the synthesis of1-(5-chloro-2-hydroxyphenyl)-3-(2,4-dichlorophenyl) propane-1,3-dione and its transition metal complexes.

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II. EXPERIMENTAL SECTION

The solvents and reagents used in the synthetic work were of analytical grade. Melting points of synthesized compounds were determined in open capillary and were uncorrected. 5-Chloro,2-hydroxy acetophenone was prepared by fries reaction from 4-chloro phenol and acetic anhydride. All the elemental analysis were done using the perkin Elemer 2400 CHN analyzer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a varian-NMR-mercury 300 using tretra methyl silane as an internal standard and $CDCl_3$ as solvent. FT-IR spectra were recorded using (KBr) disc on Bruker spectrophotometer. Mass spectra were taken on a macro mass spectrometer. The magnetic susceptibility of the complexes were measured at room temperature using a Gouy balance.

2-acetyl-4-chlorophenyl 2,4-dichloro benzoate(E_6):

To the mixture of 5-chloro, 2-hydroxyacetophenone and 2,4-dichloro benzoic acid, a dry pyridine and $POCl_3$ were added dropwise with constant stirring at 0°C. Then the reaction mixture was irradiated for about 4-5 hours under ultrasound. After completion of the reaction (monitored by TLC), the reaction mixture was poured into 100ml 1M HCl containing 50gm of crushed ice and solid obtained was filtered and washed with 10ml of water. It was recrystallized from ethanol, filtered and dried. Yield:80%, m.p.:90°C.

1-(5-chloro-2-hydroxyphenyl)-3-(2,4-dichlorophenyl)propane-1,3-dione(L_6): Compound(E_6) was dissolved in dry pyridine. To this powered KOH was added and the reaction mixture was irradiated for about 2-3 hrs. After completion of the reaction , the reaction mixture was poured on ice cold water and acidified with conc.HCl. The yellow solid obtained was filtered off and crystallized from absolute ethanol to obtain pure product. Yield:80%, m.p.160°C.

L_6: FT-IR: (KBR) cm^{-1}: 3001.96 (OH), 1680.26 (C=O), 1480.18 (Ar C=C). ^{1}H-NMR (300 MHz, $CDCl_3$-d_6); δ=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), ^{13}C-NMR (300MHz, $CDCl_3$); δ=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).

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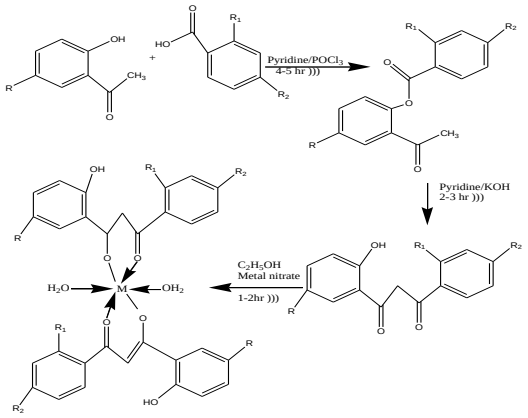
Bis-(diketonato) Fe(III) complex:

To the mixture of (3.43gm, 0.01mol) of compound L_6 and (4.04 gm, 0.01mol) of anhydrous Fe(III) nitrate and 20ml of anhydrous ethanol were added and irradiated for about 1-2 hours under ultrasound. The brown solid which precipitated was washed with boiling ethanol and recrystallized from ethyl acetate to give brownish crystals of Fe(III) β-diketonate Yield:89%, m.p.348°C.



L_6: R=Cl, R_1=Cl, R_2=Cl
M= Cu, Ni, Co, Cr, Fe. In all these cases water of coordination is present.

SchemeI: Scheme I. Synthesis of ligand and metal complexes.

III. RESULTS AND DISCUSSION:

2-acetyl-4-chlorophenyl 2,4-dichloro benzoate was prepared by the esterification of 5-Chloro, 2-hydroxyacetophenone with 2,4-dichloro benzoic acid in the presence of $POCl_3$ (scheme 1). 2-acetyl-4-chlorophenyl 2,4-dichloro benzoate undergoes Baker-Venkatraman transformation to offered pale yellow needles of ligand(L_6). The negative test for ester confirms the absence of ester group. The structure was further confirmed by spectral analysis.

The ^{1}H-NMR spectra gives characteristic peak at δ15.1which corresponds to enolic proton and at δ11.9 which is due to phenolic proton adjacent to the carbonyl group. It confirms the formation of β-diketone and in ^{13}CNMR it gives characteristic peak at δ187.3,94.1,185.6 which confirms the formation of β-diketone. The compound in enolic form is more stable than that of ketonic one. The complex of synthesized compound (L_6) gives browened coloured Fe(III) in high yield. The structure was then confirmed by spectral analysis.

The C=O bond in complex Fe(III) shifted to lower frequency as compared to that of free ligand which indicates the coordination of metal atom with the carbonyl group of diketone[18].

Similarly, other transition 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[19]. It was observed that the reaction under ultrasonic irradiation had significantly improved yield[20].

IV.MAGNETIC MEASUREMENTS:

Magnetic moments of complexes were measured at room temperature and values are given in table I. The observed magnetic moment value of Fe(III) complex is 6.11BM, Co(II) complex is 4.45BM, Ni(II) complex is 2.73BM, Cu(II) complex is 2.12BM and Cr(III) complex is 3.82 BM at room temperature has octahedral geometry[21]-[24].

The data of IR spectra of ligand and its metal complexes are listed in the table below.

Table-I: Molar conductivity, Magnetic and Infrared spectral data of synthesized compounds

Compound	μeff (BM)	Molar Conductance Ohm^{-1} Cm2mol^{-1}	IR(cm-1)				
			γ (C=O)	γ(C-O)	γ (-OH)	γ (M-O)	γ (-OH) Coordinated H2O molecule
Ligand			1680.26	1480.18	3001.96	- -	- -
Cu(II)complex	2.12	29.40	1657.15	1501.81	3016.12	527.56	3255.14
Ni (II)complex	2.73	54.22	1655.32	1505.10	3017.33	505.92	3258.89
Co(II)Complex	4.45	35.45	1666.42	1522.65	3020.18	505.92	3248.45
Cr(III)complex	3.82	37.23	1663.31	1518.28	3018.46	520.51	3244.90
Fe(III) Complex	6.11	61.65	1656.10	1523.20	3015.48	512.71	3260.16

V. ANTIMICROBIAL SCREENING:

Antimicrobial screening[25], 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 oxyporum* 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 labled plates. The DMSO was used as a control of the solvent. Plates were kept in refrigerator for half an hour for diffusion and then incubated at 37°C for 24 hrs. After incubation the inhibitory zones around the discs were observed. The diameter on inhibition zones were measured in terms of mm. Activity of each compound was compared with streptomycin as standard. The observed data of antimicrobial activity of compounds and the standard drugs are given in table below.

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Table:II

Compd No.	Conc. (ppm)	Antibacterial activity (inhibition in mm)			Antifungal activity (inhibition in mm)	
		Bacillus subtilis	E.coli	Staphylococcus aureus	Aspergillus. niger	Fusarium oxyporum
Ligand		12	11	9	9	8
Cu-L_6	100	16	14	10	17	10
Ni-L_6	100	13	13	12	18	11
Co-L_6	100	12	15	14	13	16
Cr-L_6	100	14	12	10	10	13
Fe-L_6	100	12	11	11	11	12
Streptomycin	100	6	7	6	6	6

Among all the compounds screened Co(II) and Cu(II) complexes showed highest antibacterial activity than other compounds whereas Co(II), Ni(II) and Cu(II) showed more antifungal activity. Although with respect to standard, all the tested compounds were found to be moderately active.

VI.CONCLUSION

In the present work 1-(5-chloro-2-hydroxyphenyl)-3-(2,4-dichlorophenyl)propane-1,3-dione and its transition metal complexes were synthesized and their structures elucidated on the basis of spectral analysis. The ^{1}H-NMR and ^{13}C-NMR spectra revealed that the prepared diketone possess charecterestic 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 agent.

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