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ULTRASOUND IRRADIATION ASSISTED SYNTHESIS AND ANTIMICROBIAL SCREENING OF NOVEL TRANSITION METAL COMPLEXES OF B-DIKETONE

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ABSTACT

1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)propane-1,3-dione and its transition metal complexes have been synthesized by ultrasound irradiation method. The diketones are synthesized by using Baker-Venkatraman rearrangement on 2-acetylphenyl,4-methoxy benzoate. The synthesized compounds were confirmed by the spectroscopic analysis such as IR, ^{1}H-NMR, ^{13}C-NMR, Mass, Elemental analysis, magnetic susceptibility and were employed for antimicrobial screening.

KEYWORDS: Cyclic β-diketones, Baker-Venkatraman rearrangement, metal complexes, antimicrobial screening, ultrasound irradiation.

INTRODUCTION

β-diketone and its metal complexes have been widely used in diverse areas because of their unique structural features, chemical functionalities and electroluminescent materials[1] due to enhanced stability in heat and light. β-diketones have gained a lot of interest due to their high reactivity with to form chelates[2], as intermediate in the synthesis of core heterocycles such as flavones[3], pyrazole[4] and keto-enol tautomerism. They show pharmacological activities like prophylactic antitumor[5], antibacterial[6] and antioxidant[7] and recently it is reported that they have the important pharmacophores for the HIV-integrase(1N) inhibitors.[9]

As β-diketones are having such varied applications in pharmacology, we decided to synthesize a novel β-diketone and its transition metal complexes by ultrasound irradiation method. With this view here we reported the synthesis of 1-(2-hydroxyphenyl)-3-(4-

methoxyphenyl) propane-1,3-dione and its transition metal complexes by ultrasound irradiation method and determined their biological activities.

Ultrasound irradiation assisted organic synthesis is an efficient and eco-friendly synthetic strategy. Many homogeneous and heterogeneous reactions can be conducted smoothly by sonication to provide improved yields and increased selectivities[10]

MATERIALS AND METHODS

All the solvents and reagents used were of A. R. grade.

Analytical methods and physical measurements

All the elemental analyses were done using the Perkin Elmer2400 CHN analyzer. Melting points were determined in open glass capillaries and were uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian –NMR-mercury 300 using tetra methyl silane as an internal standard and $CDCl_3$ as solvent. FT-IR spectra were recorded using (KBr) disc on Bruker spectro-photometer. Mass spectra were taken on a Macro mass spectrometer. The magnetic susceptibility of the complexes were measured at room temperature using a Gouy's balance.

Preparation of 2-acetylphenyl, 4-methoxy benzoate (1)

To the mixture of 2-hydroxyacetophenone (1.36g, 0.01mol) and 4-methoxy benzoic acid (1.52g, 0.01mol), a dry pyridine (5ml) and $POCl_3$ (1ml) were added drop wise with constant stirring at 0°C. The reaction mixture was then irradiated in ultrasound for 4-5hrs. After completion of the reaction (monitored by TLC), the reaction mixture was poured into 100ml HCl (1M) containing 50g of crushed ice and solid obtained was filtered and washed with 10ml ice-cold methanol and then with distilled water. It was recrystallized from ethanol. Yield: 78%; mp: 102 °C

Preparation of 1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)propane-1,3-dione (2)

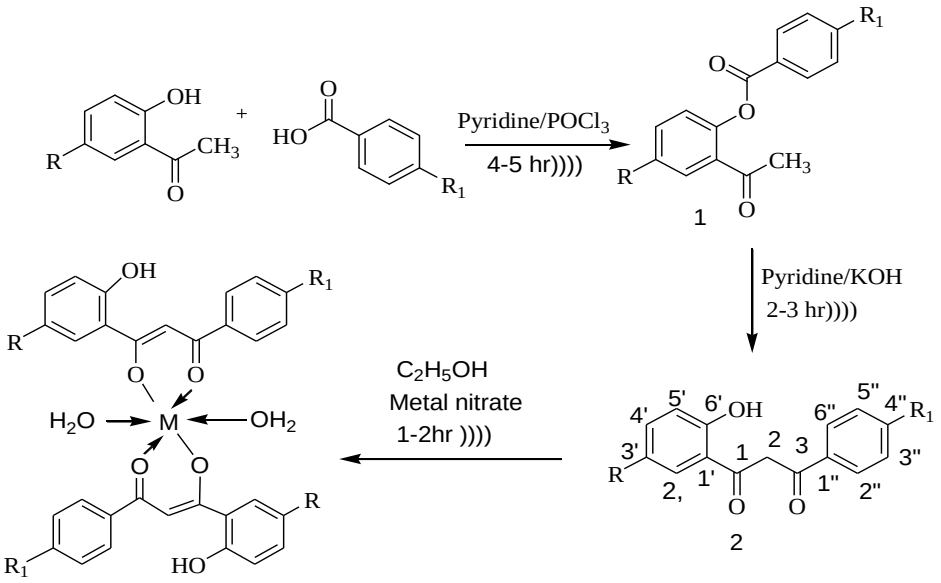
Compound 1 (2.70g, 0.01mol) was dissolved in dry pyridine (10 ml). To this powdered KOH (1.12 g, 0.02mol) was added and the reaction mixture was irradiated in ultrasound for 1-2 hrs. After completion of the reaction (monitored by TLC), the mixture was poured on ice cold water and acidified with conc.HCl. The yellow solid obtained was filtered off and crystallized from absolute ethanol. Yield: 85%; mp:115°C. FT-IR (KBr)cm^{-1}: (-OH), 1708(C=O), 1599 (Ar C=C). ^{1}H-NMR (300MHz, $CDCI_3$-d_6);δ =6.8 (t,3H, Ar-H), 7.9 (d, 2H, Ar-H), 7.85 (s,

1H, Ar-H), 7.31 (m,1H, Ar-H), 7.4 (q, 1H,=CH-), 3.98 (s, 3H,-0CH_3), 12.2 (s, 1H,OH), 15.9 (s,1H,Enolic-OH), ^{13}C-NMR(300MHz,$CDCl_3$);δ 190.0(s,C-1,C=O). 92.8(s,C-2,-CH=), 185.1(s,C-3), 126.0(s,C-1',c-1''), 162.8(d,C-2'), 118.4(s,C-3'), 135.8(s,C-4'), 119.3(s,C-5'), 128.7(s,C-6'),128.0(s,C-2'',C-6''),114.1(d,C-3'',C-5''),55.8(s,C-7'',OCH_3), V/Vis(DMSO)nm:370,410; EC-MS: 270.28 (M+23). Elemental analysis. For $C_{16}H_{14}O_4$: Cald.: C,71.10; H,5.22. Found: C,71.01; H,5.13

Bis(-diketonato) Fe(III) complex

The mixture of compound 2 (5.40g, 0.02mol), anhydrous Fe (III) nitrate (4.04g, 0.01mol) and 20 ml anhydrous ethanol was added and irradiated for 1-2 hrs under ultrasound. The precipitated solid was washed with boiling ethanol and recrystallised from ethyl acetate to give brownish crystals of Fe(III)β- diketonate. Yield: 78%; mp: 348°C.

A similar procedure was adopted to prepare Co(II), Ni(II), Cu(II), and Cr(III) complexes of 1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)propane-1,3-dione.



2: R=Cl; R_1=OCH_3

M : Fe(III), Co(II)and Ni(II),however in case of Cu(II)and Cr(III) water of coordination is absent

Scheme 1. Synthesis of ligand and metal complexes

RESULT AND DISCUSSION

2-acetylphenyl,4-methoxybenzoate (1) undergoes Baker-Venkatraman transformation[11] to give pale yellow needles of 1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)propane-1,3-dione (2).

It was observed that the reaction under ultrasonic irradiation had significantly improved yield.[12]

The metal complexes were synthesized under ultrasound irradiation using metal nitrates and β-diketone (1:2) in 20ml aq. ethanol. The reaction appears to proceed according to the given scheme 1.

Infrared spectra

The important bands of the infrared spectra for the complexes and β-diketone ligand are listed in Table 1.The Fe(III) complex exhibit C=O absorption around 1682 cm^{-1} which normally appears at 1708 cm^{-1} in free ligand. The C=O bond in complex shifted to lower frequency as compared to that of free ligand which indicates the coordination of metal atom with the carbonyl group of diketone.[13]

Nuclear magnetic reasonance spectra

The ^{1}H-NMR spectra gives characteristic peak at δ 15.9 and 12.2 which corresponds to enolic proton and phenolic proton adjacent to carbonyl group which confirms the formation of β-diketone. The ^{13}C-NMR spectra gives characteristic peak at δ 190, 92.8 and 185.1 confirms the formation of β-diketone. The compound in enolic form is more stable than in ketonic form.

Molar conductance measurements

The molar conductivity of all complexes were measured in dimethylformamide and values were observed between 12.8-61.3 $ohm^{-1}cm^{2}mol^{-1}$ indicating their non-electrolytic nature.[14]

Magnetic Measurements

Magnetic moments of complexes were measured at room temperature and the values are given in Table 1.The observed magnetic moment value of Fe(III), Co(II), Ni(II), Cu(II) and Cr(III) complexes were 5.55, 4.62, 2.42, 2.15 and 3.52 BM at room temperature. From the above values we can deduce that the complexes have octahedral geometry.[15-16]

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

Compound	μeff(BM)	Molar conductance ohm^{-1}cm^{2}mol^{-1}	IR(cm^{-1})				
			ν(C=O)	ν(C-O)	ν(-OH)	ν(M-O)	ν(-OH) coordinated H_2O molecule
Ligand (Comp 2)			1708	1465.02	2912	---	---
Fe (III) complex	5.55	61.3	16826	1494.88	3187	662	3290
Co (II) complex	4.62	12.8	1687	1498.48	3085	555	3487
Ni(II) complex	2.42	41.2	1663	1494.61	3157	570	3572
Cu(II) complex	2.15	20.3	16725	1502.83	3217	557	3387
Cr(III) complex	3.52	25.2	1678	1535.38	3058	569	3576

The ligand and its metal complexes showed antibacterial activity with respect to pathogenic bacteria like Bacillus subtilis and Staphylococcus aureus (Gram +ve); Escherichia coli(Gram -ve) and antifungal activity with fungi such as Aspergillus niger and Fusarium Oxysporum.

Antimicrobial Screening

Antimicrobial screening[17,18] of prepared compounds were tested against bacteria such as *Staphylococcus aureus* and *Bacillus subtilis* (Gram +ve); Escherichia coli(Gram -ve) and against *fungi,* eg. *Aspergillus niger* and *Fusarium Oxysporum* by Kirby Baur's disc diffusion technique using dimethyl sulfoxide as a solvent. The streptomycin was used as standard.

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 rotated 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. Plates were kept in refrigerator for half an hour for diffusion and then incubated at 37^{o}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. The observed data of antimicrobial activity of compounds and the standard are given in Table 2.

Table: 2 Antimicrobial activity of synthesized compounds

Compd No.	Conc. (ppm)	Antibacterial activity (inhibition in mm)			Antifungal activity (inhibition in mm)	
		Bacillus subtilis	***E. coli***	***Staphylococcus aureus***	***Aspergillus. niger***	***Fusarium oxysporum***
Ligand (Comp 2)	100	6	7	6	7	7
Fe Complex	100	8	8	7	9	7
Co Complex	100	10	11	11	11	10
Ni Complex	100	15	14	13	13	15
Cu Complex	100	19	19	20	19	18
Cr Complex	100	16	16	15	18	17
Streptomycin	100	6	7	6	6	6

Among all the compounds screened Ni(II), Cu(II) and Cr(III)complexes showed highest antibacterial and antifungal activity than other compounds. It was observed that the metal complexes showed highest antimicrobial activity than their parent ligand.

CONCLUSIONS

In the present work 1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)propane-1,3-dione ($4L_D$) and its transition metal complexes were synthesized and their structures were elucidated on the basis of spectral analysis. The ^{1}H-NMR and ^{13}C-NMR spectra revealed that the prepared diketone possess characteristic peaks due to the presence of enolic proton and phenolic proton adjacent to carbonyl group. These synthesized compounds were screened in vitro for antibacterial and antifungal activity and found to be promising candidates as new antibacterial and antifungal agents.

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