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Synthesis of β-Diketone and its Metal Complexes

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Abstract: 1-(2', 4' dihydroxyphenyl)-3-phenyl-propane-1, 3-dione and its transition metal complexes have been synthesized. The β-diketone is afforded by employing Baker-Venkataraman rearrangement on 4-hydroxy-2-benzoyloxyacetophenone. The synthesized compounds were characterized by analytical techniques viz: IR, NMR, Mass and elemental analysis. The thermal stability and antibacterial activity of the newly synthesized metal complexes have been studied.

Key words: β-diketones · Baker-Venkataraman rearrangement · Metal complexes · Antibacterial activity.

INTRODUCTION

β-diketones are used as ligands for almost 120 years. These derivatives were synthesized for the first time in 1887. The nature of bonding and chelation was elucidated by Werner and Morgan. [1-2]

In the last decades, β-diketones and their metal complexes have been used as model compounds in physical chemistry studies. They have also been used as chelating ligands for lanthanides and transition metals. [3] They are bidentate ligands with the possibility of complexation with almost all the metal ions. [4] A wide variety of β-diketones with different substituents and their 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 pressures and enantioselective catalytic property have been studied. [5] β-diketones have a wide range of uses in metal extraction by chelation. 1,3-Diketones are very important compounds in organic chemistry, because they exhibits some biological activities, such as antioxidants, antitumor and antibacterial activities and are also key intermediates to various heterocyclic compounds. [5-8] β-diketone like Anabaena β-diketone hydrolase also possesses some enzymatic activities [9], Europium (III) β -diketonates have excellent luminescent property. [10]

β-diketones like (4-*tert*-butyl-4'-methoxydibenzoylmethane) and 1-(4-t-butyl phenyl) propane-1,3-dione and 1-p-cumenyl-3-phenyl-propane-1,3-dione are used in UV sunscreen cosmetics that filters certain ultraviolet rays to protect skin. [11] β-diketone in its keto-enol form is also a important pharmacophores of HIV-1 integrase inhibitors. [12] It is also used as chelating agents in some process based on supercritical CO_2 [13] It is used as extractants for lanthanide ions. [14]

In present work, we have synthesized and studied some properties of 1-(2', 4'-dihydroxyphenyl)-3-phenyl-propane-1, 3-dione and its metal complexes. The title compound was synthesized from 4-hydroxy-2-benzoyloxyacetophenone by employing Baker-Venkataraman rearrangement [15,16] which was previously synthesized by Resacetophenone. The synthesized compounds were characterized by analytical techniques and screened for antibacterial study.

MATERIALS AND METHOD

All the elemental analyses were done using the Perkin Elmer 2400 CHN analyzer. FT-IR spectra were recorded using (KBr) disc on Perkin-Elmer spectrum Rx-I spectrometer. ^1H NMR were recorded on Brucker AC-300 F (300 MHz) NMR spectrometer by using DMSO-d^6 and $CDCl_3$ as solvent and tetramethylsilane as an internal standard. Mass spectra were recorded on 70-S Mass spectrometer using m-nitro benzyl alcohol (NBA) matrix.

4-hydroxy-2-benzoyloxyacetophenone 2: .8g (0.025mol) of resacetophenone was taken in a flask along with 4.9g (4ml, 0.035mol) benzoyl chloride and 5ml dry distilled pyridine.

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After 20min, the reaction mixture was poured into 120ml of 1M hydrochloric acid containing 50g of crushed ice with constant stirring. The product obtained after sometimes was filtered and washed with 10ml of ice-cold methanol and then with 10ml of water. It was recrystallized from ethanol, filtered and dried. Yield: 81%; m.p. 99°C.

1-(2', 4' Dihydroxyphenyl)-3-phenyl-propane-1, 3-dione 3: 5.1g (0.02mol) of 4-hydroxy-**2**-benzoyloxyacetophenone 2 was dissolved in 18ml of dry pyridine in a 50ml bolt-necked flask and heated to 50°C. With mechanical stirring 1.7g (0.03mol) of potassium hydroxide was added which was powdered rapidly in a mortar preheated in an oven at 100°C and was stirred for 15min. The reaction mixture was cooled to room temperature and acidified by adding with stirring 25ml of 10% aqueous acetic acid. The pale yellow precipitate was collected by filtration and dried in an oven at 50°C and was recrystallized from ethanol. Yield: 79%; m.p.164°C.

Bis(β-diketonato) Cu(II) Complex 4a: mixture of 2.56g (0.01 mol) of β-diketone compound **3** and 0.9g (0.005 mol) anhydrous Cu (II) acetate and 5ml anhydrous ethanol was stirred for 3h at room temperature. The pale green solid which precipitated was washed with boiling ethanol and recrystallized from ethyl acetate to give pale green crystals of Cu (II) β-diketonate **4a.** Yield: 92%.

Similarly, the complexes of Cobalt, Nickel, Manganese and Zinc were prepared by the same method.

RESULTS AND DISCUSSION

4-hydroxy-2-benzoyloxyacetophenone **2** undergoes Baker-Venkataraman rearrangement to afford pale yellow needles of 1-(2', 4' dihydroxyphenyl)-**3**-phenyl-propane-1, 3-dione 3. The negative test for ester confirms that it is devoid of ester group. The structure was further confirmed by the spectral analysis: IR (KBr): 3450 (-OH); 3061 (=C-H); 1744 (-C=O); 1606 (C=C); 735 (Ar-H); ^{1}H NMR (DMSO-d_6)ä: 15.72 (s, 1H), 12.02 (s, 1H), 4.76(s, 1H), 8.89(s, 1H), 8.84 (d, 2H), 7.10-8.17 (m,3H), 7.26 (d, 1H), 6.92 (d, 1H), 7.02 (s, 1H); MS (EI, 70eV): m/z (%) 256 (M$^+$, 100), 257 (M^{+1},16.5), 69 (50) Anal. Calcd. for $C_{15}H_{12}O_4$: C, 70.31; H, 4.68. Found: C, 70.12; H, 4.81. In the ^{1}H NMR Spectra it gives characteristic peak at ä 15.72 which corresponds to enolic proton and at ä 12.02 which is being due to phenolic proton adjacent to carbonyl group. It confirms the formation of β-diketones. The compound in enolic form is more stable than that of ketonic one.

The complex of synthesized compound **3** gives green coloured Cu (II) β-diketonate **4a** in high yield. The structure was then confirmed by the spectral analysis: IR (KBr): 3336 (-OH), 3050 (=C-H), 1735 (-C=O), 1609 (C=C), 701 (Ar-H); ^{1}H NMR (DMSO-d_6): ä 12.56 (s, 2H), 4.99(s, 2H), 8.79(s, 2H), 8.78 (d, 4H), 7.67-8.21 (m,6H), 7.67 (d, 2H), 7.02 (d, 2H), 7.09 (s, 2H); MS (EI, 70eV): m/z(%) 612 (M$^+$, 100); Anal. Calcd for $C_{30}H_{28}O_{10}Cu$: C, 58.82; H, 4.57; Cu, 10.38; Found: C, 58.43; H, 4.76; Cu, 10.89. The $v_{C=O}$ band in complex **4a** shifted to lower frequency as compared to that of free ligand which indicates the coordination of metal atom with the carbonyl group of diketone.

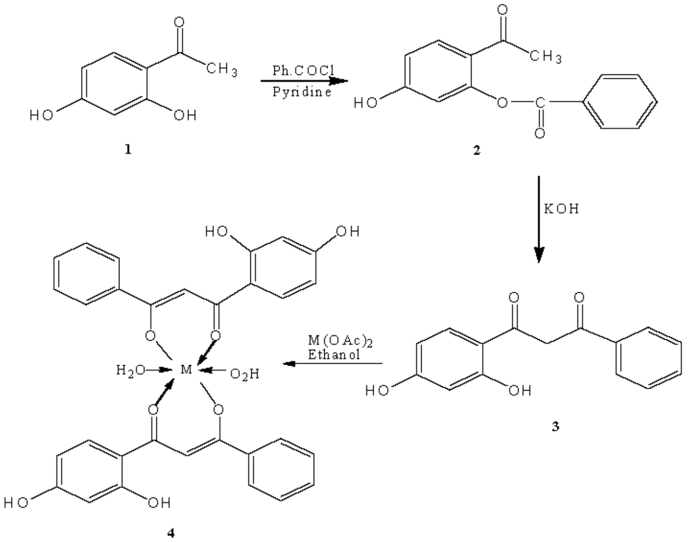
Similarly, other transition metal complexes were prepared by the same method. The ligand and its metal complexes are quite stable. All the complexes are insoluble in water but soluble in acetone, Methanol and DMSO. The complexes are non-electrolytic in nature. [17]

Thermogravimetric Analysis: All thermal analyses were done on Perkin Elmer SII, Diamond TG/DTA Thermogravimetric analyzer at VNIT, Nagpur. The Thermogravimetric curves of the synthesized complexes were recorded between 300C -10000C in air as medium. The TGA curves of all the complexes are almost similar and indicate a continuous weight loss till a stable metal oxide is formed. Weight loss of 5.73% - 6.01% between 150°C - 180°C has been observed for cobalt, Nickel and Manganese complex which indicate the presence of two molecules of water of coordination.

On further increasing the temperature, no weight loss takes place probably due to the formation of stable metal oxides.

Table 1: Thermal data of the complexes

Sr. No.	Complex	Coordination water (%) Obs (calc)	Decomposition Temperature (°C)	% Weight loss Obs (calc)	Residue comp
1.	$C_{30}H_{22}O_8Mn.2H_2O$	6.45 (5.98)	431.66	88.402 (88.21)	MnO
2.	$C_{30}H_{22}O_8Co.2H_2O$	6.294 (5.94)	396.31	71.98 (72.61)	Co_2O_3
3.	$C_{30}H_{22}O_8Ni.2H_2O$	5.702 (5.94)	475.99	87.014 (87.66)	NiO
4.	$C_{30}H_{22}O_8Cu$	----	360	85.246 (86.15)	CuO
5.	$C_{30}H_{22}O_8Zn$	----	421.51	85.249 (85.87)	ZnO



M = Co(II), Ni(II) and Mn(II), however in case of Cu(II) and Zn(II) water of coordination is absent

Scheme: Synthesis of ligand and its metal complexes

Table 2: Screening of antimicrobial activity of compounds:

		Inhibition in *mm*			
	Source	S. aureus	B. subtilis	E. coli	P. vulgaris
1.	Ligand 3	20.0	6.8	17.0	13.6
2.	Cu Complex	11.6	10.3	10.0	8.4
3.	Mn Complex	--	9.2	12.4	--
4.	Co complex	--	--	16.9	--
5.	Zn Complex	7.6	--	--	8.7
6.	Ni Complex	--	--	11.4	--

The antibacterial screening of ligand and its metal complexes shows that it possesses antibacterial activity with respect to pathogenic bacteria like Staphylococcus aureus, Bacillus substilis (Gram +ve); Escherichia coli and Proteus vulgaris (Gram -ve). From the antibacterial study it was observed that antimicrobial activity of ligand is higher than that of its metal complexes for most of the bacteria.

Antibacterial Screening: Antibacterial activities of the prepared compounds were tested against bacteria *Staphylococcus aureus, Bacillus substilis* (Gram +ve); *Escherichia coli* and *Proteus vulgaris* (Gram -ve) using filter paper disc diffusion method (Peach and Traey, 1950) using acetone as solvent. Antibiotic drugs such as Streptomycin and Amoxicillin were used as reference drugs. Selected pathogenic bacteria were maintained on nutrient agar medium for 36 hrs. Old bacterial culture were inoculated into nutrient broth and incubated at 37±2°c on a rotary shaker at 100 rpm. After 36 hrs incubation, the bacterial suspensions were used for further tests.

Antibacterial activity was then carried out using synthesized compounds. Filter paper disc soaked in solvent was used as negative controls while the discs soaked in standard broad-spectrum antibiotic solution (Streptomycin and Amoxicillin) were used as positive controls.

The results of tested compounds against these bacteria are shown in Table 2 given below. The ligand shows high antibacterial activity against *S.aureus, E.Coli and P.vulgaris* bacterium as compared to its complexes while in the case of *B.subtilis* ligand shows activity less than some of its complexes.

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