



Efficient Ultrasound Synthesis of 1-(2- Hydroxyphenyl)-3-P-Tolylpropane-1,3-Dione and its Transition Metal Complexes

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Abstract:

1-(2- hydroxyphenyl)-3-p-tolylpropane-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, ¹H-NMR, ¹³C-NMR, mass, elemental analysis, and magnetic susceptibility and evaluated for biological screening.

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

Introduction

 β -diketone and its metal complexes have been used in diverse areas because of their unique structural features, chemical functionalities and toughness for light and heat as electroluminescence materials[1]. β diketones are versatile metal coordinating agents and have played a significant role in coordination chemistry. These are most widely used ligands in coordination chemistry[2][3]. β -diketones have gained a lot of interest due to their importance as good ligands[4],for the chelation with metals, as intermediate in the synthesis of core heterocycles such as pyrazole[5], flavones[6] isoxazole[7], triazole[8], benzodiazepine[9], and pyrimidine[10]. β -diketones have been pharmacological activities like antioxidant[11], prophylactic antitumor[12], systematic insecticidal[13], antibacterial[14] and antiviral[15]. It has been used as an anti-sunscreen agent[16]. β -diketones are well known to have keto-enol tautomerism[17]. Recently it is known that they have the important pharmacophores for the HIV-integrase(1N) inhibitors[18].

Owing to β -diketones having such varying pharmacological activities, we were interested to synthesize a novel β -diketone and its transition metal complexes. However, in most cases, synthesis of β -diketone and its transition metal complexes by ultrasound irradiation method has received less attention. With this view here we report the synthesis of 1-(2-hydroxyphenyl)-3-p-tolylpropane-1,3-dione and its transition metal complexes by ultrasound irradiation method and evaluated for 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[19]. Therefore ultrasound irradiation has been established as an important technique in organic synthesis.

Materials and methods

Experimental section

2-acetylphenyl4-methylbenzoate(A)

To the mixture of 2-hydroxyacetophenone (1.36g, 0.01mol) and 4-methyl benzoic acid (1.36g, 0.01mol), a dry pyridine (5ml) and POCL₃ (11ml) were added drop wise with constant stirring at 0°C. Then reaction mixture was irradiated for about 4-5 hrs under ultrasound. After completion of the reaction (monitored by TLC), the reaction mixture was poured into 100ml 1M HCl containing 50 g of crushed ice and solid obtained was filtered and washed with 10 ml ice-cold methanol and then with 10ml of water. It was recrystallized from ethanol, filtered and dried.

1-(2-hydroxyphenyl)-3-p-tolylpropane-1,3-dione(B)

Compound A was dissolved in dry pyridine. To this powdered KOH was added and then 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% mp.120°C

 L_2

FT-IR: (KBR) cm⁻¹:3096.25 (OH), 1715.20 (C=O), 1497.11(Ar C=C). ¹H-NMR (300 MHz, CDCl₃-d₆); δ =2.3 (s, 3H, CH₃) 6.8-7 (m, 3H, Ar-H), 7.2-7.4 (m, 3H, Ar-H), 7.5-7.9 (m, 3H, Ar-H). 12.2 (s, 1H, OH), 15.6 (s, 1H, Enolic-OH). ¹³C-NMR (300MHz, CDCl₃); δ =194.1 (s, C-1, C=O), 92.4 (s, C-2, -CH=), 180.2 (s, C-3), 112.5 (s, C-1'), 161.1 (s, C-2'), 117.3 (s, C-3'), 128.4 (d, C-4'), 120.2 (d, C-5'), 126.4 (s, C-6'), 135.4 (d, C-1''), 131.4 (d, C-2'',C-6''), 143.1 (s, C-4''), 130.3 (,C-3'',C-5''), 22.6 (s,C7'',CH₃). UV/Vis (DMSO)nm: 380,420. EC-MS: 255.13 (M+1). Elemental analysis:C,75.42; H,5.41.

Bis(-diketonato) Fe(III) complex(C₅)

The mixture of (2.54g, 0.02mol) of compound B and (4.04g, 0.01mol) of anhydrous Fe(III) nitrate and 20ml anhydrous ethanol was added and irradiated for about 1-2 hrs under ultrasound. 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%, mp:320°C.

Results and Discussion

2-acetylphenyl4-methylbenzoate was prepared by the esterification 2-hydroxy acetophenone with 4-methyl benzoic acid in presence of POCl₃ (scheme 1). 2-acetylphenyl4-methylbenzoate undergoes Baker-Venkataraman transformation[20] to offered pale yellow needles of ligand. The negative test for ester confirms the absence of ester group. The structure was further confirmed by spectral analysis.



In the ¹H-NMR spectra it gives characteristic peak at $\delta 15.6$ which corresponds to enolic proton and at $\delta 12.2$ which is being due to phenolic proton adjacent to carbonyl group. It confirms the formation of β -diketone and in the ¹³C-NMR spectra it gives characteristic peak at $\delta 193.1$, 92.4 and 180.2 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) diketonate(C₅) in high yield. The structure was then confirmed by spectral analysis. The C=O bond in complexes 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 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[22]. It was observed that the reaction under ultrasonic irradiation had significantly improved yield[23].

Compound	µeff(BM)	Molar		IR(cm	ī ⁻¹)		
		conductance	υ(C=O)	υ(C-O)	υ(-OH)	υ(M-O)	υ(-OH)
		ohm ⁻¹ cm ⁻					coordinated
		² mol ⁻¹					H2O
							molecule
Ligand			1715	1497	3096		
Cu(II)	1.83	20	1690	1501	3116	510	3290
complex							
Ni(II)	2.62	39	1680	1509	3118	495	3288
complex							
Co(II)	4.73	31	1670	1504	3119	524	3286
complex							
Cr(III)	4.15	26	1682	1514	3112	518	3270
complex							
Fe(III)	5.65	62	1675	1512	3116	505	3275
complex							

Table-1: Molar conductivity, Magnetic and Infrared spectral data of synthesized compounds

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) complex is 5.65BM. Co(II) complex is 4.73BM, Ni(II) complex is 2.62BM, Cu(II) complex is 1.83BM and Cr(III) complex is 4.15BM at room temperature has octahedral geometry[24-25].





Antimicrobial Screening

Antimicrobial screening[26] of prepared compounds were tested against bacteria such 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. 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.

Compound	Conc.	Antibacterial	Activity (inhib	oition in mm)	Antifungal	Activity
No.	(ppm)				(inhibition in a	mm)
		Bacillus	E. coli	Staphylococcus	Aspergillus	Fusarium
		subtilis		aureus	niger	oxysporum
Ligand	100	12	9	7	7	8
Cu complex	100	13	10	8	9	9
Ni complex	100	12	10	9	11	13
Co complex	100	14	11	8	13	12
Cr complex	100	12	12	11	8	13
Fe complex	100	13	11	13	8	20
streptomycin	100	6	7	6	6	6

1 abic-2. Anumuci ubiai activity of synthesized compounds







R=CH₃, M=Cu(II), Ni(II), Co(II), Cr(III), Fe(III) Scheme1: synthesis of ligand and metal complexes

Conclusion

In the present work 1-(2-hydroxyphenyl)-3-p-tolylpropane-1,3-dione 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 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 agents.

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