

ULTRASOUND IRRADIATION ASSISTED SYNTHESIS AND ANTIMICROBIAL SCREENING OF NOVEL CYCLIC B-DIKETONES AND ITS TRANSITION METAL COMPLEXES

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ABSTRACT

1-(5-chloro, 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 5-chloro, 2-acetylphenyl, 4-methoxy benzoate. The synthesized compounds were confirmed by the spectroscopic analysis such as IR, ¹H-NMR, ¹³C-NMR, Mass, Elemental analysis, magnetic susceptibility and were employed for antimicrobial screening.

KEYWORD: 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 anti sunscreen agent.^[8] 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-(5-chloro, 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 Elmer 2400 CHN analyzer. Melting points were determined in open glass capillaries and were uncorrected. ¹H-NMR and ¹³C-NMR spectra were recorded on Varian –NMR-mercury 300 using tetra methyl silane as an internal standard and CDCl₃ 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 5-chloro,2-acetylphenyl, 4-methoxy benzoate (1)

To the mixture of 5-chloro, 2-hydroxyacetophenone (1.70g, 0.01mol) and 4-methoxy benzoic acid (1.52g, 0.01mol), a dry pyridine (5mL) and POCl₃ (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:84%; mp: 88°C

Preparation of 1-(5-chloro, 2-hydroxyphenyl)-3-(4-methoxyphenyl) propane-1, 3-dione (2)

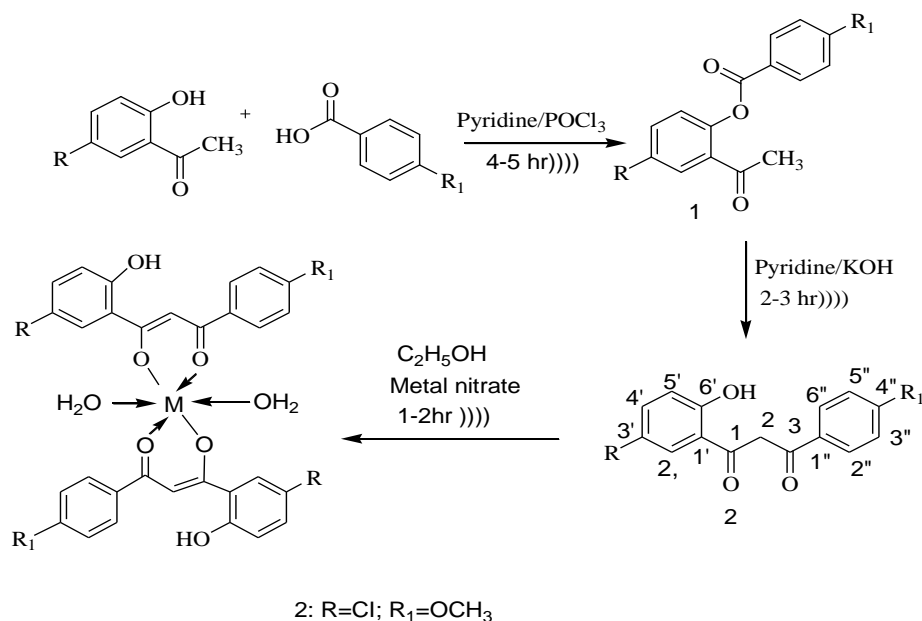
Compound 1 (3.04 g, 0.01mol) was dissolved in dry pyridine (10 ml). To this powdered KOH (1.12 g, 0.02mol) was added and the reaction mixture was irradiated in ultrasound for 1-2 hrs.

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: 81%; mp: 164°C. FT-IR (KBr) cm^{-1} : 2919.67(-OH), 1743.31 (C=O), 1465.02 (Ar C=C). $^1\text{H-NMR}$ (300MHz, $\text{CDCl}_3\text{-d}_6$); δ =7.0 (t,3H, Ar-H), 7.99 (d, 2H, Ar-H), 7.85 (s, 1H, Ar-H), 7.31 (m,1H, Ar-H), 6.9 (q, 1H,=CH-), 3.9 (s, 3H,-OCH₃), 12.1 (s, 1H,OH), 17.7 (s,1H,Enolic -OH), $^{13}\text{C-NMR}$ (300MHz, CDCl_3); δ 192.5(s,C-1,C=O). 91.2(s,C-2,-CH=), 179(s,C-3), 124.5(s,C-1'), 161.0(d,C-2',C-4''), 120.0(s,C-3'), 134.9(s,C-4'), 128.4(t,C-5',C-2'',C-6''), 131.5(s,C-6'),128.0(s,C-1'')114.2(d,C-3'',C-5''),55.1(s,C-7'',OCH₃), UV/Vis(DMSO)nm:374,412; EC-MS : 304.73 (M+23). Elemental analysis. For $\text{C}_{16}\text{H}_{13}\text{O}_4\text{Cl}$: Calcd.: C,63.06; H,4.30. Found: C,62.98; H,4.11

Bis (-diketonato) Fe(III) complex

The mixture of compound 2 (6.08g, 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: 85%; mp: 319°C.

A similar procedure was adopted to prepare Co(II), Ni(II), Cu(II), and Cr(III) complexes of 1-(5-chloro,2-hydroxyphenyl)-3-(4-methoxyphenyl)propane-1,3-dione.



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

5-chloro, 2-acetylphenyl, 4-methoxybenzoate (1) undergoes Baker-Venkatraman transformation.^[11] to give pale yellow needles of 1-(5-chloro,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 1670.16 cm^{-1} which normally appears at 1743.31 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 resonance spectra

The $^1\text{H-NMR}$ spectra gives characteristic peak at δ 17.7 and 12.1 which corresponds to enolic proton and phenolic proton adjacent to carbonyl group which confirms the formation of β -diketone. The $^{13}\text{C-NMR}$ spectra gives characteristic peak at δ 192.5, 91.28 and 179 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 dimethyl formamide and values were observed between $27.5\text{-}63.1\text{ ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ 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 5.92, 4.28, 3.02, 2.22 and 4.08 BM at room temperature. From the above values we can deduce that the complexes have octahedral geometry.^[15-16]

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

compound	$\mu_{\text{eff}}(\text{BM})$	Molar conductance $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$	IR(cm^{-1})				
			$\nu(\text{C}=\text{O})$	$\nu(\text{C}-\text{O})$	$\nu(-\text{OH})$	$\nu(\text{M}-\text{O})$	$\nu(-\text{OH})$ coordinated H_2O molecule
Ligand (Comp 2)			1743.31	1465.02	2919.67	---	---
Fe (III) complex	5.92	63.1	1670.16	1494.88	3000.78	767.90	3216.25
Co (II) complex	4.28	27.5	1686.19	1498.48	3353.24	827.38	3325.18
Ni(II) complex	3.02	47.6	1678.43	1494.61	3175.20	792.80	2916.85
Cu(II) complex	2.22	35.6	1688.35	1502.83	3311.47	824.88	---
Cr(III) complex	4.08	39.4	1683.53	1535.38	3312.87	830.04	---

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] 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°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)	
		<i>Bacillus subtilis</i>	<i>E. coli</i>	<i>Staphylococcus aureus</i>	<i>Aspergillus. niger</i>	<i>Fusarium oxysporum</i>
Ligand (Comp 2)	100	10	7	10	11	11
Fe Complex	100	9	8	7	9	9
Co Complex	100	8	7	10	8	7
Ni Complex	100	10	9	8	8	9
Cu Complex	100	9	8	9	9	6
Cr Complex	100	8	9	8	8	9
<i>Streptomycin</i>	100	6	7	6	6	6

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

CONCLUSION

In the present work 1-(5-chloro, 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 ¹H-NMR and ¹³C-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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REFERENCES

1. Aromi G, Gamez P, Reedijk M. Poly beta-diketones: Prime ligands to generate supramolecular metaloclusters J. Coordination Chemistry Reviews, 2008; 252: 8.
2. Anjali Rajbhoj, Nanda Korde, Suresh Gaikwad, Jayprakash Dargad. Efficient ultrasound synthesis and biological screening of metal complexes of 1-(2-hydroxyphenyl)-3-(4-

- ethoxyphenyl) propane-1, 3- dione . International Journal of Green and Herbal chemistry, 2012; 1(3): 226-231.
3. N. S. Korde, S. T. Gaikwad, B. C. Khade, A. S. Rajbhoj. Efficient Ultrasound synthesis, characterizations and antimicrobial screening of novel cyclic β diketones. Chemical Science Transactions, 2013; 2(2).
 4. Heller S, Natarajan, S. 1, 3-Diketones from Acid Chlorides and Ketones: A Rapid and General One-Pot Synthesis of Pyrazoles. Org. Lett, 2006; 8: 2675.
 5. Anjali S. Rajbhoj, Nanda S. Korde, Suresh T. Gaikwad, Seema S. Korde. Efficient ultrasound syntjesis of β -diketones & its metal complexes. Der pharma Chemica, 2012; 4(5): 1868-1872.
 6. Sato K, Yamazoe S, Yamamoto R, Ohata S.,Ando A. Direct Synthesis of 1,3-Diketones by Rh-Catalyzed Reductive α -Acylation of Enones . Org Lett, 2008; 10: 2405-2408.
 7. Bennett I, Broom J., Cassels R., Eleder J, Masson N, Hanlon. Synthesis and antibacterial properties of β -diketone acrylate bioisosteres of pseudomonic acid A. J. Bioinorganic and Medicinal Chem Lett, 1999; 9: 1847.
 8. D. D. Suryawanshi, A. D. Suryawanshi, A.S. Rajbhoj, S. T. Gaikwad. Synthesis, characterization and antimicrobial studies of 1-(2,4-dichlorophenyl)-3-(2hydroxyphenyl) propane-1,3-dione and its transition metal complexes International Journal of Chemical and Physical Sciences, Jan-Feb 2015; 4: 2.
 9. Tchertanov L, Mouscadet J. Raltegravir: molecular basis of its mechanism of action J. Med. Chem, 2007; 50: 1133.
 10. Chate A, Bhagat S, Gill C. Synthesis and Antimicrobial Activity of 2- (Pyridine-3-yl) -4H-chromen-4-one Derivatives J. Heterocyclic Chem, 2013; 50(1): DOI:10.1002/jhet.955.
 11. Baker, W. Molecular rearrangement of some o-acyloxyacetophenones and the mechanism of the production of 3-acylchromones. J.Chem.Soc, 1933; 1381.
 12. Chate A, Joshi R, Badadhe V, Gill C. Efficient Ultrasound Enhance Novel Series of 2- ((E)-2, 3-Dihydro-2-(4-(phenylthio)phenyl)benzo[b][1,4]thiazepin-4-yl) phenol as an Antimicrobial Agent . Bull. Korean Chem. Soc, 2011; 32(11): 3887.
 13. Nanda S. Korde, Suresh T. Gaikwad, Seems S. Korde, Anjali S. Rajbhoj. Ultrasound synthesis, characterization and thermal study of some transition metal complexes of β -diketone ligand. International Journal of Recent Technology and Engineering, Sept. 2013; 2: 4.

14. Verma P, Sheikh J, Juneja H. Synthesis of β -diketone and its Metal Complexes World Applied Sciences Journal, 2011; 14(8): 1154.
15. Singh K, Barwa S, Tyagi P. Synthesis, characterization and biological studies of Co (II), Ni(II), Cu(II) and Zn(II) complexes with bidentate Schiff bases derived by heterocyclic ketone European Journal of Medicinal Chemistry, 2006; 41: 1. 147.
16. Oluwatola O. Synthesis and Physicochemical Studies of Some 2-substituted-1-phenyl-1,3-butanedionato Nickel(II) and Copper(II) Complexes And Their 2,2'-Bipyridine and 1,10-Phenanthroline Adducts International J. of Chem, 2011; 3.
17. Chohan Z, Arif M, Akhtar A, Supuran C. Metal-Based Antibacterial and Antifungal Agents: Synthesis, Characterization, and In Vitro Biological Evaluation of Co(II), Cu(II), Ni(II), and Zn(II) Complexes with Amino Acid-Derived Compounds J. Bioinorganic Chemistry and Applications, 2006, Article ID 83131, 13.