

Synthesis, Characterization and Antimicrobial studies of 1-(2,4-dichlorophenyl)-3-(2-hydroxyphenyl)propane-1,3-dione and its transition metal complexes

D. D. SURYAWANSHI¹, A. D. SURYAWANSHI², A. S. RAJBHOJ¹, S. T. GAIKWAD¹.

¹ Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad.

² Department of Physics B. J. College, Ale(Pune) (M.S.)

Corresponding Author: ddschem84@gmail.com

Abstract

The solid complexes of Cu(II), Ni(II), Co(II), Cr(III), Fe(III) were prepared from ligand 1-(2,4-dichlorophenyl)-3-(2-hydroxyphenyl)propane-1,3-dione. The ligand is offered by employing Baker-Venkatraman rearrangement on ester. The synthesized compounds were confirmed by the spectroscopic analysis such as ¹H-NMR, ¹³C-NMR, Mass, elemental analysis, magnetic susceptibility, XRD and evaluated for antimicrobial screening.

Keywords: β -diketone ligand, Baker-Venkatraman rearrangement, metal complexes, magnetic susceptibility, X-ray diffraction, antimicrobial screening.

Introduction

Literature survey revealed that β -diketones and their metal complexes are associated with various pharmacological and biological properties and thus find importance in medicine. In recent years a number of β -diketones in which carbonyl function (s) have gained considerable importance because of the fact that such compounds structurally related to active chemical constituents of several traditional medicinal plants. β -diketones are important class of organic compounds frequently encountered in synthetic chemistry[1-3]. They have been used as ligands for coordination of transition metals[4] and have also been investigated for use as potential antiviral agents[5]. β -diketones are also encountered in nature as both metabolic intermediates in the microbial metabolism of aromatics and terpenes and also as anthropogenic environmental contaminants. As a result of their ubiquity, the biological transformation of these compounds has recently aroused interest[6-7].

β -diketones are versatile metal coordinating agents and have played a significant role in coordination chemistry. 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[8]. These are most widely used ligands in coordination chemistry[9][10]. β -diketones have gained a lot of interest due to their importance as good ligands[11], for the chelation with metals, as intermediate in the synthesis of core heterocycles such as pyrazole[12], flavones[13] isoxazole[14], triazole[15], benzodiazepine[16], and pyrimidine[17]. β -diketones have been pharmacological activities like antioxidant[18], prophylactic antitumor[19], systematic insecticidal[20]

and antibacterial[21]. It has been used as an anti-sunscreen agent[22]. β -diketones are well known to have keto-enol tautomerism[23]. Recently it is known that they have the important pharmacophores for the HIV-integrase(1N) inhibitors[24].

Owing to β -diketones having such varying pharmacological activities, we were interested to synthesize a novel β -diketone and its transition metal complexes.

Materials and methods:

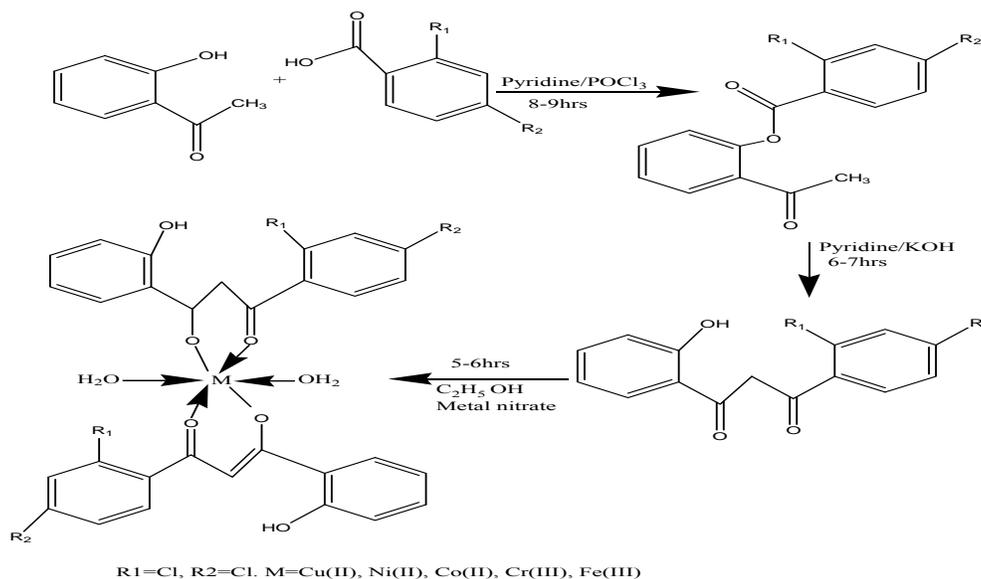
Experimental section:

2-acetylphenyl 2,4-dichlorobenzoate(A):

To the mixture of 2-hydroxyacetophenone(1.36g, 0.01mol) and 2,4-dichloro benzoic acid(1.91g, 0.01 mol), a dry pyridine and POCl_3 (11ml) were added drop wise with constant stirring at 0°C . Then reaction mixture was stirred on magnetic stirrer for 8-9hours. 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 10 ml of water. It was recrystallized from ethanol, filtered and dried. Yield: 80%. m.p.105 $^\circ\text{C}$.

1-(2,4-dichlorophenyl)-3-(2-hydroxyphenyl)propane-1,3-dione(B):

Compound (A) was dissolved in dry pyridine. To this powdered KOH was added and reaction mixture was stirred on magnetic stirrer for about 4-5hrs. After completion of the reaction (monitored by TLC), 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:130 $^\circ\text{C}$.



Scheme: Synthesis of ligand and metal complexes.

FT-IR: (KBR) cm^{-1} : 3050 (OH), 1685 (C=O), 1498 (Ar C=C), $^1\text{H-NMR}$ (300 MHz, $\text{CDCl}_3\text{-d}_6$): δ =6.8-7.2 (m, 3H,Ar-H), 7.3-7.7 (m, 5H, Ar-H), 12.2 (s, 1H, OH), 15.6 (s,1H, Enolic-OH). $^{13}\text{C-NMR}$ (300MHz, CDCl_3); δ =191.3 (s, C-1, C=O), 94.1 (s, C-2, -CH=), 184.6 (s,C-3), 112.2 (d, C-1'), 162.3 (d,C-2'), 118.3 (s, C-3'), 128.4 (d, C-4'), 122.6 (d,C-5'), 126.6 (s, C-6'), 134.2 (d, C-1''), 135.6 (s, C-2''), 131.2(s, C-3''), 145.2 (s, C-4''), 125.6 (s, C-5''), 130.3 (s, C-6''). UV/Vis(DMSO)nm: 372,410. EC-MS: 310.05 (M+1).

Bis(-diketonato) Fe(III) complex: The mixture of (3.09g, 0.02mol) of compound (B) and (4.04g, 0.01mol) of anhydrous Fe(III) nitrate and 20ml anhydrous ethanol was added and refluxed for about 8-9 hrs. 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:349°C.

Results and discussion:

2-acetylphenyl 2,4-dichlorobenzoate was prepared by the esterification of 2-hydroxy acetophenone with 2,4-dichloro benzoic acid in presence of POCl_3 . 2-acetylphenyl 2,4-dichlorobenzoate undergoes Baker-Venkataraman transformation[25] 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 $^1\text{H-NMR}$ spectra it gives characteristic peak at δ 15.6 which corresponds to enolic proton and at δ 12.2 which is being due to phenolic proton adjacent to carbonyl group. It confirms the formation of β -diketone and in the $^{13}\text{C-NMR}$ spectra it gives characteristic peak at δ 191.3, δ 94.1 and δ 184.6 confirms the formation of β -diketone. The compound in enolic form is more stable than that of ketonic one. 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[26].

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[27].

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 Cu(II) complex is 1.94BM, Ni(II) complex is 3.09BM, Co(II) complex is 4.08BM, Cr(III) complex is 3.65BM and Fe(III) complex is 5.68BM at room temperature has octahedral geometry[28-29].

Powder X-ray diffraction analysis:

The X-ray diffractograms of the Cu(II), Ni(II) and Fe(III) complexes were scanned in the range 5-85° at a wavelength of 1.543 Å. The diffractograms and associated data depict the 2 θ values for each peak, the relative intensity and inter-planar spacing (d-values). The X-ray diffraction pattern of these complexes with respect to major peaks of relative intensity greater than 10% were indexed using a computer programme[30]. This indexing method also yields Miller indices (hkl), the unit cell parameters and the

unit cell volume. The unit cell of Cu(II) complex yielded values of lattice constant: $a=21.51 \text{ \AA}$, $b=5.16 \text{ \AA}$ and $c=7.3 \text{ \AA}$ and a unit cell volume $V=810.23 \text{ \AA}^3$. The unit cell of the Co(II) complex yielded values of lattice constant: $a=8.71 \text{ \AA}$, $b=9.95 \text{ \AA}$ and $c=7.79 \text{ \AA}$ and a unit cell volume $V=675.11 \text{ \AA}^3$. In concurrence with these cell parameters conditions such as $a \neq b \neq c$ and $\alpha = \gamma = 90^\circ \neq \beta$ required for a monoclinic sample were tested and found to be satisfactory. Hence, it can be concluded that the Cu(II) and Co(II) complexes were monoclinic crystal systems. The experimental density values of the complexes were determined using the specific gravity method[31] and found to be 3.5 g cm^{-3} , 3.7 g cm^{-3} for the Cu(II) and Co(II) complexes respectively. Comparison of experimental and theoretical density values shows good agreement within the limits of experimental error[32].

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 ₂ O molecule
Ligand			1685	1498	3050		
Cu(II) complex	1.94	28.7	1655	1515	3061	521	3210
Ni(II) complex	3.09	51.2	1663	1501	3069	516	3315
Co(II) complex	4.08	27.9	1650	1507	3071	505	3237
Cr(III) complex	3.65	22.1	1656	1515	3068	515	3327
Fe(III) complex	5.68	58.9	1665	1518	3066	508	3265

Antimicrobial Screening:

Antimicrobial screening[33] 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 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.

Table-2: Antimicrobial activity of synthesized compounds

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

Conclusion:

In the present work ligand 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 characteristics 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.

Acknowledgement:

Department of Chemistry acknowledges the financial assistance of UGC (SAP). The authors are grateful to the, Head, Department of Chemistry, Pune university, Pune for providing spectral analysis.

References:

- [1] Fargeas V, Baglouch M, Metay E, Baffreau J, Mehard D, Gosselin P, Berge J P, Barthomeuf C Tetrahedron 60, 2004, 10359.
- [2] Christoffers J, Oertling H, Fischer P and Frey W Tetrahedron 59, 2003, 3769.
- [3] Katritzky A. R. , Wang Z, Wang M, Wilkerson C R, Hall D and Akhmedor N G, J Org Chem. 69, 2004, 6617.
- [4] Garnovskii A D, Kharixov B. I. Blanco L M, Garnouskii D A, Burlov A S Vasilchenko Is and Bondarenko G I J coord. Chem. 46, 1999, 365.
- [5] Dinna G D, Carabateas P M, Johnson R E, Williams G L, Pancic F and Collins J C J med Chem. 21, 1978, 889.
- [6] Pokormy D, Striner W and Ribbons D W Biotechnol 15, 1997, 291-296.



- [7] Grogan G, J mol Catal B Enzym 19, 2002, 73.
- [8] Aromi G, Gamez P and Reedijk J Coordination Chemistry Reviews, 2008, vol. 252, no. 8-9 pp. 964.
- [9] Meldola R, Kuntzen H. S, Brightman R., J. Chem. Soc., 97, 456 (1910).
- [10] Maurya R. Rajput C. S, J. Mo.. Struct. 687, 35, (2004).
- [11] A. Siedle in comprehensive Coordination chem..., 1987, Wilkinson, pergamon press, Oxford, vol. 2 cha 15,4 pp 365.
- [12] Nishiyama T, Shiotsu S, T Polym. Degrad & Stab, 2002, 76, 435-439.
- [13] Heller S.T, Natrajan S. R, Org. Lett. 2006, 8, 2675.
- [14] Simoni D, Invidita F, Rondanin R, Grimaudo S, Cannizzo G, Barbusca E, Porretto F, Alessandro N and Tolomeo M, J Med Chem., 1999, 42, 4961.
- [15] Alekseev V V, Zelenin K N and Yakimovich S I, Russ J Org Chem., 1995, 31, 868.
- [16] Kumar R and Joshi C Y, Arkivoc, 2007, 9, 142.
- [17] Kuzueva O, Burgart Y, Saloutin V and Chupakhin O, Chemistry of Heterocyclic compounds, 2001, 37, 1130.
- [18] Nishiyama T, Shiotsu S and Tsujita H, Polym Degrad Stab., 2002, 76, 435.
- [19] Acton N, Brossi A, Newton D L and Sporn M B, J Med Chem., 1980, 23, 805-809.
- [20] Crouse G, McGowan M and Boisvenue R, J Med Chem., 1989,32, 2148.
- [21] Bennett I, Broom N J, Cassels R, Elder J S, Masson N D and O' Hanlon P L, Nioorg Med Chem Lett., 1999, 9, 1847-1852.
- [22] Andrae I, Bringham A, Bohm F, Gonzenbach H, Hill T, Mulroy L and Truscott T G, J Photochem Photobiol B: Biol., 1997, 37, 147-150.
- [23] Dziemboska T and Rozwadowski Z, Curr Org Chem., 2001, 5, 289-313.
- [24] Chate A. V, Bhagat S. S and Gill C. H, J. Heterocyclic Chem, 2011, DOI.1002/955.
- [25] Prasad R. N, Agrawal M and Sharma M, J. Indian Chem. Soc., 2002, 79:531
- [26] Varma P. N, Sheikh J. I and Juneja H. D, World Applied Sciences Journal, 2011, 14(8):1154.
- [27] Chate A. V, Joshi R. S, Badadhe V and Gill C. H, Bull. Korean Chem. Soc, 2011., vol 32, 11, 3887.
- [28] Oluwatola Omoregie, International J. of Chem, 2011, vol.3 no. 1 Feb.
- [29] Chohan Z. H, Arif M, Akhtar M. A and Supuran C. T, J. Bioinorganic Chemistry and Applications, 2006, vol. 2006, Article ID 83131,13 pages.
- [30] Carvajal J. R, Roisnel T, Winplotr, A graphic Tool for Powder Diffraction, Laboratoire Leon Brillouin (ceal/cnrs) 91191 Gif sur Yvette Cedex, France, 2004.
- [31] Shoemaker D. P, Garland C. W, Experiments in Physical Chemistry, 5th ed., McGraw-Hill International Edition, New York, 1989.
- [32] Deshmukh M. B, S. Dhongade-Desai, Chavan S. S, Indian J. Chem. 44 (2005) 1659.
- [33] Sharma O, Singla R, Shrivastava B, Bhat V, Shenoy G, Sreenivasan K, Indo Globl J. of Pharmaceutical Sciences; 2012; 2(1), 70-75.