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Design, Characterization & Biological Investigation Of Metal Complexes Of 1-(2-Hydroxy- Phenyl)-3-(2,4-Dichlorophenyl) Propane-1,3-Dione

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Abstract

A novel β-diketone 1-(2-hydroxy phenyl)-3-(2, 4-dichlorophenyl) propane-1,3-dione & its transition metal complexes have been synthesized by conventional as well as ultrasound method. Using Baker venkat raman rearrangement this diketone was prepared .UV-vis, IR, ^{1}H- NMR, ^{13}C- NMR, mass, XRD characterization and Elemental analysis has been done for newly synthesized ligand & its transition metal complexes. The newly synthesized ligand and its metal complexes were also studied by Antimicrobial & Antioxidant screening.

Key-Words: Baker venkat raman rearrangement, metal complexes, XRD, Antimicrobial & Antioxidant study.

Introduction

β-diketones and its metal complexes have played a vital role in co-ordination chemistry[1-] & are being extensively studied in various aspects of industries such as organic electroluminescent technology, luminescent materials[2], biological processes & serve as a suitable models for valuable information in the elucidation of enzymatic processes of biological relevance.[4-6] β-diketones and its metal complexes also show antimicrobial, antimalaerial, antitumour, antioxidant & insecticidal activity.[7-8]It has been also used as anti sun-screen agent..[9.]β-diketone and its metal complexes have been used as a model compound in the studies of physical chemistry. For the transition metal, they have been used as chelating agents.[10]Owing to β-diketone having such varying pharmacological activities, we were interested to design a novel β-diketone and its metal complexes[11]

Experimental

Synthesis of 2-acetyl-phenyl 2,4-dichloro benzoate (A) In the mixture of 2-hydroxyacetophenone & 2,4-dichloro benzoic acid a dry pyridine & $POCl_3$ were added drop wise with constant stirring at 0 ^{0}C . Then the reaction mixture was stirred for 7-8 hrs. The progress of reaction was monitored by TLC. After the completion of reaction, reaction mixture was poured on 50 gm of crushed ice & acidified with 100 ml 1MHCl.The obtained product was filtered on buckner funnel & washed with water & recrystallized from ethanol, filtered & dried. Yield 80% (M.P.174^{0}C)

Synthesis of 1-(2-hydroxy phenyl)-3-(2,4-dichlorophenyl)propane-1,3-dione (B) Compound A was dissolved in 20 ml pyridine (5 gm, 0.01 mol) & to this solution KOH (3gm, 0.04mol) was added. The reaction mixture was stirred for 3 hrs. & completion of reaction was checked by TLC .At this step, a yellow solid precipitate of potassium salt of β-diketone formed. After completion of reaction, reaction mixture was poured on crushed ice and acidified with 1MHCl.The obtained solid yellow product was filtered and recrystalised from ethanol to get pure product. Yield 80%(M.P.158^{0}C)

Preparation of Metal Complex –Bis-(diketonato) Cu (II) Complex To an alcoholic solution of compound B, hot alcoholic solution of copper nitrate solution was added and refluxed for 8 to 9 hours, where upon the green coloured precipitation occurs. After addition of alcoholic ammonia solid mass was filtered, washed with ethanol and dried .Yield 80% (M.P.222^{0}C)

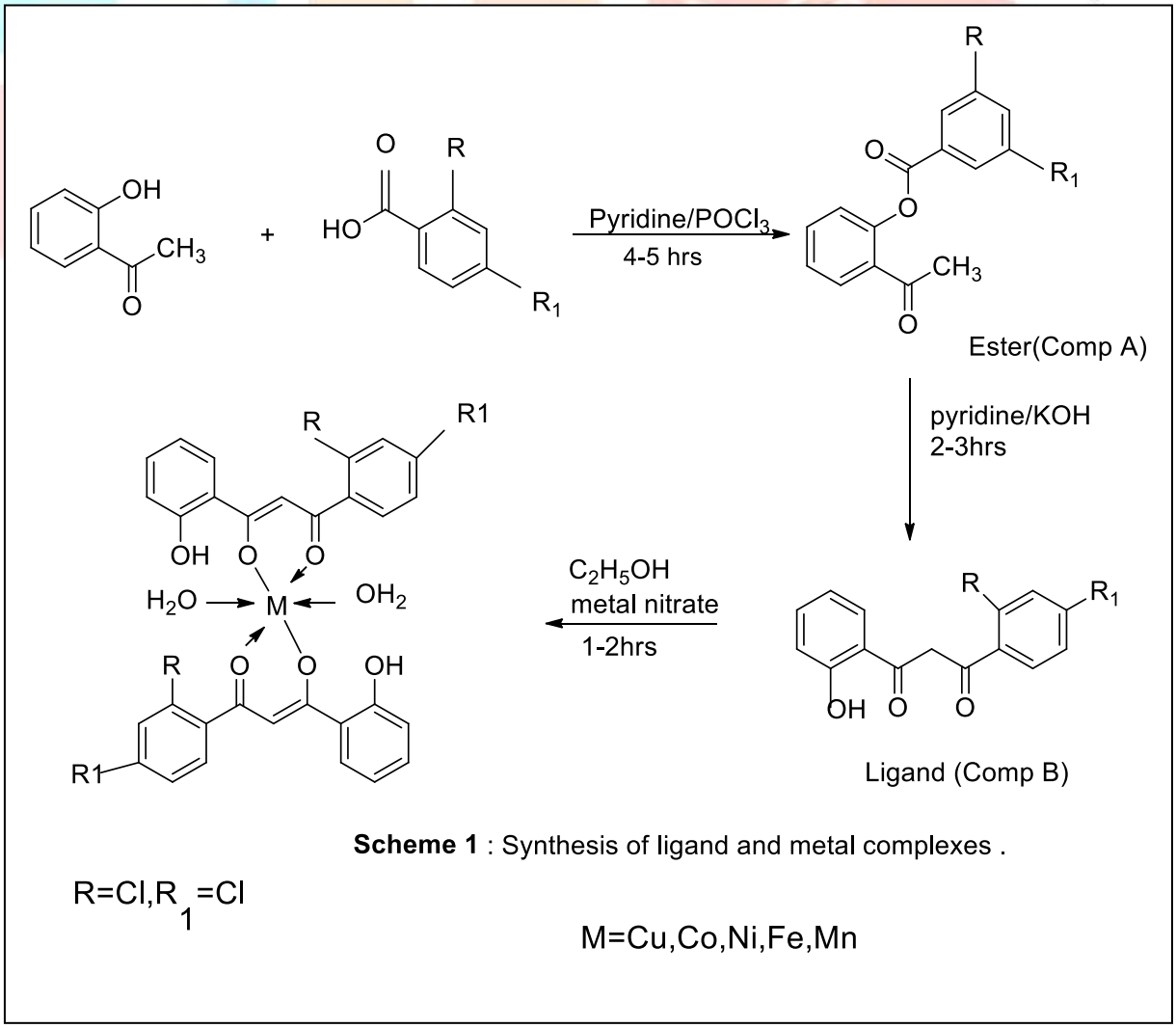
Characterization Of Ligand

FT-IR (KBr) cm^{-1}(C=O) 1598, (C-O) 1455, (O-H) 3054,(Ar-H) 2311, (Ar, C=C) 1512,(C-H) 1274

^{1}H- NMR (500mHz,DMSO)^{1}H(=CH)-δ 6.62,1H(Ar-H)- 7.01,1H(Phenolic O-H)-11.01,1H(enolic O-H)-14.01,6H(m,Ar-H)-.15-7.31

^{13}C-NMR(500mHz,DMSO)C_1-190.78,C_2-91.31,C_3-185.61,C'_1-102.02,C'_2-159.24,C'_3-126.09,C'_4-127.68,C'_5-130.15C_1"-131.10,C_2"-131.23,C_3"-132.14,C_4"-158.05,C_5"-131.98,C_6"-130.15

UV-Vis (DMSO) nm-370,410 **Mass** LS,MS-309.0(M^{+1})



Scheme 1 : Synthesis of ligand and metal complexes .

R=Cl,R$_1$=Cl

M=Cu,Co,Ni,Fe,Mn

Result & Discussion

2-acetyl-phenyl,2,4-dichloro benzoate was prepared by esterification of 2- hydroxy-acetophenone & 2,4-dichloro Benzoic acid in presence of pyridine & $POCl_3$. 2-acetyl-phenyl-2,4-dichloro benzoate undergoes Baker venkat raman transformation to offered yellow coloured ligand .The structure was further confirmed by spectral analysis.[1]H-NMR spectra gives characteristic peak at δ14.1 which corresponds to enolic proton & at δ11.01 which is due to phenolic proton adjacent to the carbonyl group. It confirms that formation of β-diketone. The enolic form of β-diketone is more stable than that of ketonic form. The Cu(II) complex of synthesized compound gives green coloured in high yield. The structure was confirmed by spectral analysis. The C=O bond in complexes shifted to lower frequency as compared to that of free ligand which indicates the co-ordination of metal atom with the carbonyl group of diketone.[12]Similarly,other transition metal complexes were prepared by same method. The ligand and its metal complexes are quite stable. All synthesized metal complexes are insoluble in water but they are soluble in organic solvent DMSO. The synthesized metal complexes are non-electrolytic in nature.[13]

Table:1 Analytical data of synthesized compounds are listed.

Sr.No.	Compounds	M.W	M.P.	Yield	Analytical data (calculated)				
					%C	%H	%O	%Cl	%M
1	Ligand (A)	308	158	85	55.26 (58.28)	3.01 (3.26)	22.36 (22.97)	14.95 (15.53)	--------
2	A_1	715	222	85	50.02 (50.19)	3.24 (3.37)	17.20 (17.83)	18.56 (19.75)	8.23 (8.65)
3	A_2	714	228	75	50.21 (50.52)	2.89 (3.39)	17.01 (17.95)	19.63 (19.88)	7.96 (8.26)
4	A_3	713	286	87	49.33 (50.54)	2.89 (3.39)	16.90 (17.95)	18.69 (19.89)	7.89 (8.23)
5	A_4	707	312	70	49.58 (50.74)	3.21 (3.41)	19.02 (18.02)	19.02 (19.97)	7.56 (7.86)
6	A_5	709	278	80	49.25 (50.80)	3.56 (3.41)	17.93 (18.05)	18.77 (19.99)	8.96 (7.75)

The data of Magnetic moments & IR spectra is depicted in Table 2

Table: 2 Magnetic moments & IR Spectral data of synthesized compound

Sr.No.	Compounds	Magnetic moment μ(B.M.)	(C=O)	(C-O)	(O-H)	(M-O)	(O-H) Co-ordinated with H2O	Ar-H	Ar (C=C)
1	Ligand (A)	-----	1598	1455	3054	----	3250	2311	1512
2	A_1	1.73	1740	1320	2970	702	3338	2364	1530
3	A_2	3.12	1775	1330	3051	522	3250	2421	1581
4	A_3	2.15	1740	1371	2963	655	3025	2363	1512
5	A_4	5.29	1733	1370	2950	668	3025	2365	1522
6	A_5	5.57	1919	1362	2657	588	3337	2345	1614

Powder X- Ray Diffraction Analysis

The X-ray diffractograms of synthesized complexes were scanned in the range of 298^{0}C at a wavelength of 1.675 A^0.The diffractograms & associated data depict the 2θ values for each peak, the relative intensity & interplanar spacing (d-value)[14] .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.

This indexing method also yields miller indices (h,k,l) the unit cell parameters & the unit cell volume. The unit cell of Cu(II) complex yielded values of lattice constant, a= 13.68 A^0,b=5.168 A^0, c =10.70 A^{0}In concurrence with above unit cell parameters conditions such as edge-length a≠b≠c required for monoclinic sample were tested & found to be satisfactory.

Table: 3 Unit cell data and crystal lattice parameter of Cu-complex

Cryastallographic parameters	
Crystal system	Monoclinic
Space group	I2/a
Space group number	15
a (A^0)	13.68
b (A^0)	5.168
c (A^0)	10.70
Alpha (α)	90
Beta (β)	110.10
Gamma (μ)	90
Calculated density	1.7
Measured density	1.61
Volume of cell	710.49
Z	4

Antimicrobial Screening

3.1 Antibacterial and antifungal Screening

The complexes and the ligands were screened for their in vitro antibacterial activity against Staphylococcus aureus ,Bacillus megaterium, E. coli,P. areugenosa,and antifungal activity against Aspergillums Niger, Aspergillums oryzae ,Rhizopus, C.albicans at 100ppm. By Kirby Bauer's disc diffusion techniques using dimethyl sulphoxide as a solvent. The streptomycin & Flucanozole were used as references drugs.[15-18]

A uniform suspension of test organism of 24 hrs old cultures were prepared in test tube contained sterile saline solution. A sterile nutrient agar was then added in each of the disk (Himedia Pvt. Ltd, Mumbai). The plates were related to ensure the uniform mixing of microorganism in the agar medium which was then allowed to solidify. Sterile Whatmann filter paper disc dipped in the solution of each compounds and placed on the labeled plates. The DMSO was used as a control of the solvent. The streptomycin & Flucanozole were used as a standard compound for the comparison.[19] Plate were kept in refrigerator for half an hour for diffusion and then incubated at 37 ^{0}C for 24 hrs. After incubation the inhibitory zone around the disc were observed. The diameter on inhibition zones were measured in terms of mm.[20] The activity of each compound was compared with streptomycin as standard.

The observed data of antimicrobial activity of compounds and standard drugs are given in table 4.

Table 4. Antimicrobial activity

Ligand/Metal Complex	Antibacterial Activity				Antifungal Activity				Antioxidant Activity	
	S Aureus	B. megaterium	E.coli	P.aeruginosa	A .niger	Rhizopus	A. oryzae	C. albicans	DPPH % radical scavenging activity	OH % radical scavenging activity
Concentration	100 ppm	100 ppm	100 ppm	100 ppm	100 ppm	100 ppm	100 ppm	100 ppm		
Ligand (A)	8	8	6	8	8	8	6	8	68.64	68.84
A_1	12	14	10	12	14	12	10	10	70.91	59.05
A_2	10	8	10	8	6	10	6	8	71.05	71.95
A_3	14	10	12	14	10	10	12	10	68.54	71.64
A_4	6	4	8	4	4	6	4	4	66.56	72.58
A_5	10	6	8	6	6	8	8	6	75.06	75.12
streptomycin	6	4	8	6	NA	NA	NA	NA	NA	NA
Flucanozole	NA	NA	NA	NA	10	8	6	4	NA	NA
Ascorbic acid	NA	NA	NA	NA	NA	NA	NA	NA	NA	67.45
α- tocopherol	NA	NA	NA	NA	NA	NA	NA	NA	62.45	NA

It is clear that, the results of antibacterial and antifungal activities of metal complexes are higher than free ligands against Staphylococcus aureus and Bacillus megaterium,E. coli,P. areugenosaand antifungal activity against Aspergillums Niger and Aspergillums oryzae ,Rhizopus, C.albicans at 100ppm.

3.2 Antioxidants Activities

DPPH(2,2-diphenyl-1-picrylhydrazyl radical scavenging assay

One of the key factor in the treatment of tuberculosis is free radical damage. In this spectrophotometric test, DPPH is a stable reagent [21-23]In summary, the assay was carried out by combining an equivalent amount of DPPH solution with the test substance to reach a final volume of 3 ml. The sample was then incubated for 20 minutes.and the absorbance at 517 nm was measured using a Shimadzu UV Vis-spectrophotometer. As a standard, 1mM α-tocopherol was utilized.

% radical scavenging activity= 1-T/C×100

OH (Hydroxyl radical assay)

The Fenton reaction was used to demonstrate the OH radical scavenging activity.In summary, the standard reaction mixture included 1.5 ml of the individual produced chemical (1mg/ml) , 60 µl of $FeCl_2$(1mM),90 µlof 1-10 phenanthroline (1mM),2.4 mL of phosphate buffer (0.2 M pH 7.8), and 150 µl of H_2O_2 (0.17)..H_2O_2 was added to begin the reaction.[24-27] The absorbance at 560 nm was measured following a 5 minute incubation period at room temperature. The reference was1 mM ascorbic acid

% radical scavenging activity= 1-T/C×100

Conclusion

In the present work, ligand & its transition metal complexes were synthesized & their structures elucidated on basis of spectral analysis ^{1}H- NMR & ^{13}C-NMR spectra revealed that the synthesized diketone ligand have a characteristic peak due to presence of enolic proton(enol form of β-diketone) & phenolic proton adjacent to carbonyl group[28] . These synthesized compounds were screened for in-vitro antibacterial & antifungal activity & antioxidant activity found to be promising candidates as new antibacterial, antifungal & antioxidant agents. All the tested compounds were found to be moderately active.

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