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Some unsaturated β -diketones and their metal chelates

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ABSTRACT

A new series of β -diketones, in which the keto group attached to an olefinic linkage, have been synthesized by the reaction of acetylacetone with aromatic aldehydes (furfural, salicylaldehyde and 2-hydroxynaphthaldehyde) under specified conditions. The existence of these compounds predominantly in the intramolecularly hydrogen bonded enol forms has been well demonstrated from their IR, ¹H NMR and mass spectral data. Details on the formation of their [ML₂] complexes [M = Ni(II), Cu(II) and Zn(II)] and their nature of bonding has been established on the basis of analytical and spectral data. © 2009 Trade Science Inc. - INDIA

KEYWORDS

Unsaturated β -diketones;
Metal complexes;
IR spectra;
¹H NMR spectra;
Mass spectra.

1. INTRODUCTION

In continuation of our studies on unsaturated polycarbonyl compounds and their metal complexes^[1-3], we here report the synthesis and characterization of three new unsaturated β -diketones (HL¹-HL³) and their typical metal complexes. Such unsaturated carbonyl compounds have gained considerable importance in recent years^[1-4] because these structural types constitute the major biologically active compounds present in the traditional Indian medicinal plant turmeric^[5] (*Curcuma longa*, Linn, Zingiberacea family).

2. EXPERIMENTAL

2.1. Materials and methods

Carbon and hydrogen percentages were determined by microanalyses (Heraeus Elemental analyzer) and metal contents of complexes by AAS (Perkin Elmer

2380). The electronic spectra of the compounds in methanol (10⁴ mol/L) were recorded on a 1601 Shimadzu UV-Vis. spectrophotometer, IR spectra (KBr discs) on an 8101 Shimadzu FTIR spectrophotometer, ¹H NMR spectra (CDCl₃ or DMSO-d₆) on a Varian 300 NMR spectrometer and mass spectra on a Jeol/SX-102 mass spectrometer (FAB using Argon and *meta*-nitrobenzyl alcohol as the matrix). Molar conductance of the complexes was determined in DMF (~10⁻³ mol/L) at 28±1°C. Magnetic susceptibilities were determined at room temperature on a Guoy type magnetic balance.

2.2. Synthesis of unsaturated β -diketones (HL¹, HL² and HL³)

A well established synthetic route to 'unsaturated' β -dicarbonyl compounds is based on the synthesis of curcuminoids by Pabon^[5] using the reaction of aromatic aldehydes and β -dicarbonyl compounds containing at least one acetyl group in presence of boric oxide, tri(*sec*-

butyl)borate and *n*-butylamine. The use of boric oxide and tri(*sec*-butyl)borate is to prevent Knoevenagel type condensation and facilitate Claisen type condensation by the formation of a boron complex of the diketone. This method was employed with suitable modifications for the synthesis of unsaturated β -diketones considered in the present investigation.

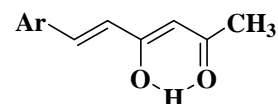
The aldehydes used for the condensation reaction were furfural, salicylaldehyde and 2-hydroxyphthalene-1-carbaldehyde. A typical procedure for the synthesis is given below.

A mixture of acetylacetone (0.075 mol) and boric oxide (0.055 mol) were made into a paste with dry ethylacetate and stirred on a magnetic stirrer for ~1 h at room temperature. To this mixture kept at 0°C, a solution of aromatic aldehyde (0.025 mol) and tri(*sec*-butyl)borate (0.1 mol) dissolved in dry ethylacetate (15 mL) was added and stirred for ~3 h with the slow addition of *n*-butylamine (0.5 mL in 5 mL dry ethylacetate) and the reaction mixture was kept overnight. Hot (~70°C) HCl (0.4 M, 20 mL) was added and again stirred for ~1 h. The mixture was extracted repeatedly with ethylacetate and the combined extracts were evaporated to dryness on a water bath to get a pasty mass. To this 10 mL of 2 M HCl were added and the resulting mixture was again stirred for ~1 h. The precipitate formed was filtered. The TLC of the products revealed the presence of two compounds and were quantitatively separated by column chromatography as outlined below.

The crude product was dissolved in a minimum quantity of dry ethylacetate and the resulting solution was placed over a column (2×100 cm) densely packed with silica gel (mesh 60-120) and eluted with a 5:1 v/v chloroform-acetone mixture at a uniform flow rate of 2 mL per min. As the elution proceeds, two bands were developed in the column, a pale yellow lower band and an orange red upper band. The lower region was collected as 10 mL aliquots in separate tubes and in each case the purity was established by TLC. The combined eluates after evaporation gave the pure unsaturated β -diketone (Figure 1).

2.3. Synthesis of Cu(II), Ni(II) and Zn(II) complexes

To a refluxing solution of the compound in methanol



Compound	Ar-
HL ¹	2-Furyl
HL ²	2-Hydroxyphenyl
HL ³	2-Hydroxy-1-naphthyl

Figure 1: Structure of the unsaturated β -diketones

(0.02 mol, 20 mL) an aqueous solution of the metal(II) acetate (0.01 mol, 15 mL) was added and the reaction mixture was refluxed for ~3 h. The solution was concentrated to half the volume and then cooled to room temperature. The precipitated complex was filtered, washed several times with water, then with ethanol, re-crystallized from hot methanol and dried in vacuum.

2.4. Determination of antifungal activity

The antifungal activity of the compounds were studied by the disk diffusion technique using agar nutrient as the medium^[6,7]. A 1000 ppm solution of nystatin was used as the standard. Stock solutions (10⁻³ M) were prepared by dissolving the compounds in DMSO and sterilized in an autoclave at 121°C for 20 min. The nutrient medium was prepared by adding 2 g glucose and 1.5 g agar in to a paste of potato (20 g) in 100 ml distilled water. The pH was adjusted to 5.7 using 10% HCl and autoclaved for 20 min. When the temperature became 35-40°C, the fungal spores were scrapped and added to the medium. Mixed well and carefully poured into petridishes and allowed to cool. Using an agar punch, wells (10 mm) were cut on these plates. In each well two drops of 1000 ppm solution of the compound was added along with DMSO and standard nystatin in separate wells and incubated at 35°C for 24 h. During this period, the test solution diffused and growth of the inoculated microorganism was affected. The antifungal activity was measured by noting the diameter of the inhibition zone around each well (mm). The three different fungal strains used were *Aspergillus niger*, *Aspergillus parasiticus* and *Rhizopus oryzae*.

3. RESULTS AND DISCUSSION

Analytical (TABLE 1), IR, ¹H NMR and mass

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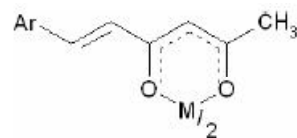
TABLE 1: Physical and analytical data of the unsaturated β -diketones and their metal complexes

Compound/ empirical formula	Yield %	M.P. °C	Elemental Analysis: Found (Calculated)%		
			C	H	M
HL ¹	60	140	67.30 (67.42)	5.64 (5.62)	-
C ₁₀ H ₁₀ O ₃					
HL ²	54	92	70.68 (70.59)	5.88 (5.88)	-
C ₁₂ H ₁₂ O ₃					
HL ³	65	89	75.64 (75.59)	5.58 (5.51)	-
C ₁₆ H ₁₄ O ₃					
[NiL ¹ ₂]	60	>300	58.17 (58.15)	4.32 (4.36)	14.26 (14.22)
C ₂₀ H ₁₈ NiO ₆					
[NiL ² ₂]	50	280	61.75 (61.97)	4.74 (4.73)	12.56 (12.63)
C ₂₄ H ₂₂ NiO ₆					
[NiL ³ ₂]	55	>300	68.04 (68.00)	4.64 (4.60)	10.41 (10.40)
C ₃₂ H ₂₆ NiO ₆					
[CuL ¹ ₂]	70	>300	57.34 (57.48)	4.32 (4.31)	15.30 (15.22)
C ₂₀ H ₁₈ CuO ₆					
[CuL ² ₂]	55	>300	61.55 (61.33)	4.63 (4.69)	13.60 (13.53)
C ₂₄ H ₂₂ CuO ₆					
[CuL ³ ₂]	65	>300	67.50 (67.42)	4.40 (4.57)	11.22 (11.16)
C ₃₂ H ₂₆ CuO ₆					
[ZnL ¹ ₂]	70	228	57.38 (57.23)	4.24 (4.29)	15.64 (15.59)
C ₂₀ H ₁₈ O ₆ Zn					
[ZnL ² ₂]	60	242	61.28 (61.10)	4.66 (4.67)	13.74 (13.87)
C ₂₄ H ₂₂ O ₆ Zn					
[ZnL ³ ₂]	65	198	67.38 (67.21)	4.46 (4.55)	11.34 (11.44)
C ₃₂ H ₂₆ O ₆ Zn					

TABLE 2: Characteristic IR stretching bands (cm⁻¹) of the unsaturated β -diketones and their metal complexes

Compound	C=O		CH=CH <i>trans</i>	M-O
	acetyl	cinnamoyl		
HL ¹	1670	1630	974	-
[NiL ¹ ₂]	1625	1588	970	480, 418
[CuL ¹ ₂]	1620	1586	974	478, 418
[ZnL ¹ ₂]	1618	1582	976	460, 424
HL ²	1668	1634	978	-
[NiL ² ₂]	1625	1591	978	490, 418
[CuL ² ₂]	1634	1587	970	467, 428
[ZnL ² ₂]	1632	1584	972	470, 420
HL ³	1674	1628	971	-
[NiL ³ ₂]	1623	1590	975	485, 416
[CuL ³ ₂]	1628	1592	967	460, 418
[ZnL ³ ₂]	1636	1586	968	464, 422

spectral data of the compounds suggest that the condensation has occurred in the 1:1 ratio as in figure 1. The analytical data (TABLE 1) together with non-electrolytic nature in DMF (specific conductance <10 $\Omega^{-1}\text{cm}^{-1}$; 10⁻³M solution) suggest [ML₂] stoichiometry of the complexes. The Ni(II) and Zn(II) chelates are diamagnetic while Cu(II) complexes showed normal paramagnetic moment. The observed electronic, IR, ¹H



M = Ni(II), Cu(II), Zn(II)

Figure 2: Structure of the metal complexes of unsaturated β -diketones

NMR and mass spectra of the complexes are fully consistent with the figure 2.

3.1. Infrared spectra

The spectra of all the unsaturated β -diketones show two intense bands at ~1670 and ~1630 cm⁻¹ assignable respectively to the intramolecularly hydrogen bonded acetyl and cinnamoyl carbonyl stretching vibrations. The observed position and intensity of these bands indicate that the compounds exist entirely in the enolic form and enolised towards the cinnamoyl function^[3,8] as in figure 1. The broad band in the region 2500-3500 cm⁻¹ also suggests the existence of the compounds predominantly in the intramolecularly hydrogen bonded enolic form. The spectra of all the compounds showed a prominent band at ~980 cm⁻¹ typical of *trans* - CH=CH- group^[8].

In the IR spectra of all the complexes, no band of appreciable intensity observed in the region 1650-1800 cm⁻¹ assignable to free or hydrogen bonded acetyl and cinnamoyl groups. Instead, two strong bands are observed in the 1580-1640 cm⁻¹ region due to metal bonded acetyl and cinnamoyl carbonyl functions^[2,9] as in figure 2. The broad band in the region 2500-3500 cm⁻¹ cleared up in the spectra of metal complexes indicating the replacement of enolic proton by the metal cation during complexation. That the carbonyl groups are involved in bonding with the metal ion is further supported by the appearance of two medium intensity bands at ~420 and ~470 cm⁻¹ assignable to $\nu_{\text{M-O}}$ ^[9] (TABLE 2).

3.2. ¹H NMR spectra

The ¹H NMR spectra of the unsaturated β -diketones displayed a one proton signal at ~ δ 16 ppm due to the intramolecularly hydrogen bonded enolic proton^[10,11]. The spectra of HL² and HL³ displayed signals at δ 13.95 and 12.80 ppm due to the phenolic OH groups. The *trans* orientation of the -CH=CH- group is evident from their observed *J* values (~16 Hz). Inte-

TABLE 3: ^1H NMR spectral data (δ , ppm) of the unsaturated β -diketones and their Ni(II) and Zn(II) complexes

Compd.	Enolic OH	Methyl	Methine	CH=CH	Aryl	Phenyl substituent
HL ¹	16.08	2.41	5.96	8.26, 8.08	7.24-7.87	-
[NiL ₂] ¹	-	2.36	6.56	8.24, 8.14	7.22-7.82	-
[ZnL ₂] ¹	-	2.42	6.56	8.24, 8.06	7.28-7.92	-
HL ²	15.98	2.50	5.92	8.32, 8.07	7.26-7.82	13.95
[NiL ₂] ²	-	2.48	6.50	8.32, 8.12	7.22-7.90	13.91
[ZnL ₂] ²	-	2.46	6.46	8.34, 8.09	7.26-7.82	13.90
HL ³	15.85	2.60	5.86	8.31, 8.13	7.24-7.80	12.80
[NiL ₂] ³	-	2.51	6.44	8.36, 8.12	7.30-7.96	12.76
[ZnL ₂] ³	-	2.55	6.54	8.33, 8.17	7.26-7.78	12.72

TABLE 4: Mass spectral data of the unsaturated β -diketones and their Cu(II) complexes

Compound	Mass spectral data (m/z)
HL ¹	178, 163, 135, 121, 93, 85
HL ²	204, 189, 161, 147, 119, 85
HL ³	254, 239, 211, 197, 169, 85
[CuL ₂] ¹	419, 417, 376, 374, 333, 331, 326, 324, 233, 231, 178, 163, 121, 93
[CuL ₂] ²	471, 469, 428, 426, 385, 383, 352, 350, 233, 231, 204, 189, 147, 85
[CuL ₂] ³	571, 569, 528, 526, 485, 483, 402, 400, 233, 231, 254, 211, 197, 169

grated intensities of all the protons agree well with the figure 1 of the compounds.

In the ^1H NMR spectra of the diamagnetic Ni(II) and Zn(II) complexes the low field signal due to the enol proton of the ligands is absent indicating its replacement by the metal ion during complexation. The methine proton signal shifted appreciably to low field compared to the shift in the olefinic protons. This may be due to the aromatic character that might have been imparted to the $\text{C}_3\text{O}_2\text{M}$ ring system of the chelates by the highly conjugated groups attached to the dicarbonyl moiety. The integrated intensities of various signals agree well with the $[\text{ML}_2]$ stoichiometry of the complexes as in figure 2. That the phenolic OH group of HL² and HL³ are not involved in bonding with the metal ion is clearly indicated^[12] in the spectra of their Ni(II) and Zn(II) complexes where the phenolic signal remains unaltered. The assignments of various proton signals observed are assembled in TABLE 3.

3.3. Mass spectra

Mass spectra of all the unsaturated β -diketones

showed intense molecular ion peak, thereby confirming the formulation of the compounds^[13]. Peaks due to $(\text{Ar-CH=CH-CO})^+$, $(\text{P-CH}_3)^+$, $(\text{P-CH}_3\text{CO})^+$, $(\text{P-ArC}_2\text{H}_2)^+$, etc. are characteristic of all the spectra. The FAB mass spectra of the Cu(II) complexes showed molecular ion peaks corresponding to $[\text{CuL}_2]$ stoichiometry. Peaks correspond to $[\text{CuL}]^+$, L^+ and fragments of L^+ are also present in the spectra. The spectra of all the chelates contain a number of fragments containing copper in the 3:1 natural abundance of ^{63}Cu and ^{65}Cu isotopes (TABLE 4).

3.4. Electronic spectra

The UV spectra of the unsaturated β -diketones show two broad bands with maxima at ~ 370 nm and ~ 260 nm due to the various $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions. In complexes these absorption maxima shifted appreciably to low wave numbers. The Cu(II) complexes showed a broad visible band, λ_{max} at $\sim 15,000$ cm^{-1} . This, together with the measured μ_{eff} values (~ 1.76 BM) suggests the square-planar geometry^[14]. In agreement with this, spectra recorded in pyridine, a broad band centered at $\sim 11,000$ cm^{-1} was observed which indicates the formation of octahedral pyridine adducts. The observed diamagnetism and broad medium-intensity band at $\sim 17,800$ cm^{-1} in the spectra of the Ni(II) chelates suggest their square-planar geometry. In conformity, the spectra of the chelates in pyridine solution (10^{-3} M) showed three bands corresponding to configurational change to octahedral due to the association of pyridine. The three well-separated absorption bands at λ_{max} $\sim 8,000$, $\sim 13,500$ and $\sim 24,000$ cm^{-1} correspond to the transitions, $^3\text{A}_{2g} \rightarrow ^3\text{T}_{2g}$; $^3\text{A}_{2g} \rightarrow ^3\text{T}_{1g}(\text{F})$ and $^3\text{A}_{2g} \rightarrow ^3\text{T}_{1g}(\text{P})$ respectively.

3.5. Antifungal studies

Various biological activities exhibited by unsaturated β -diketones such as curcuminoids have been the subject of numerous physiological and clinical studies^[1-4]. In the present study the antifungal activity of the unsaturated β -diketones and their metal complexes were carried out. The data (TABLE 5) revealed that the compounds possess antifungal activity comparable to that of the drug nystatin. Among the compounds, HL² and HL³, which contain an OH group in the *ortho* position of the aryl ring were found to be highly active

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TABLE 5: Antifungal activities (diameter inhibition zone in mm) of the unsaturated diketones and their metal complexes

Compound	<i>Aspergillus niger</i>	<i>Aspergillus parasiticus</i>	<i>Rhizopus oryzae</i>
DMSO	10	10	10
Nystatin	12	12	11
HL ¹	12	12	10
HL ²	18	16	14
HL ³	22	20	15
[NiL ¹ ₂]	13	13	10
[NiL ² ₂]	19	14	12
[NiL ³ ₂]	16	21	12
[CuL ¹ ₂]	26	14	14
[CuL ² ₂]	26	18	15
[CuL ³ ₂]	29	22	16
[ZnL ¹ ₂]	14	11	10
[ZnL ² ₂]	14	12	14
[ZnL ³ ₂]	14	13	14

L=Deprotonated ligand

against all the three fungal strains studied, as in curcuminoids^[2]. In many cases metal complexation increased the activity of the compounds. Among the chelates, Cu(II) complexes are found to be highly active.

4. CONCLUSIONS

The reaction between acetylacetone and aromatic aldehydes under specified conditions yielded a new series of unsaturated β -diketones. The existence of these compounds in the intramolecularly hydrogen bonded enol form has been well demonstrated from their analytical and spectral data. Analytical, physical and spectral data of their [ML₂] complexes with Ni(II), Cu(II), and Zn(II) showed the monobasic bidentate coordination in which the intramolecularly hydrogen bonded enolic proton is replaced by metal cation. The antifungal studies reveal that the compounds possess significant activity against all the tested organisms. The compounds containing an OH group in the *ortho* position of the aryl ring were found to be highly active and in many cases metal complexation increased the activity.

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