

1,5-Bis(*N*-phenylamino)-9-(2-pyridyl)-4,8-nonadiene-1,3,7-trione and its Metal Complexes

MUHAMMED BASHEER UMMATHUR

Department of Chemistry, KAHM Unity Women's College, Manjeri, Kerala-676122, India
mbummathur@gmail.com

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Abstract: Condensation of pyridine-2-carbaldehyde with acetoacetanilide under specified conditions yielded a conjugated diketoanilide (HL) in which the keto groups are attached to olefinic linkages. The existence of one keto group of the compound in the intramolecularly hydrogen bonded enol form and others in the β -diketo form have been well demonstrated from its analytical and spectral data. Analytical, IR, ^1H NMR and mass spectral data revealed neutral bidentate coordination of the compound in $[\text{Co}(\text{HL})(\text{OAc})_2(\text{H}_2\text{O})_2]$ and $[\text{M}(\text{HL})(\text{OAc})_2]$ complexes $[\text{M} = \text{Ni}(\text{II}), \text{Zn}(\text{II}), \text{Cd}(\text{II})$ and $\text{Pd}(\text{II})]$. The Cu(II) complex conform to $[\text{Cu}_2(\text{L})(\text{OAc})_3]$ stoichiometry having both neutral bidentate and monobasic tridentate coordination. The Cd(II), Ni(II), Pd(II) and Zn(II) chelates are diamagnetic while Co(II) and Cu(II) complexes showed normal paramagnetic moment. The antimicrobial studies revealed significant activity against the tested organisms (*Aspergillus niger*, *Aspergillus parasiticus* and *Rhizopus oryzae*) and the activity of free ligand is more than its metal complexes.

Keywords: Tricarbonyl compounds, Metal complexes, IR, ^1H NMR, Mass spectra, Antifungal studies.

Introduction

The higher homologues of 1,3-dicarbonyl compounds have considerable importance in the design and synthesis of multidentate ligand systems that can function as model compounds in various bioinorganic studies¹. Thus a large number of polycarbonyl compounds and their derivatives have been synthesized and characterized^{2,3}. Many of these compounds are known to exhibit certain important biological functions due to their ability to form complexes with various metal ions⁴. Therefore studies on the coordination behavior of polyketones have tremendous importance in modern coordination chemistry. Polycarbonyl compounds in which carbonyl groups are attached to olefinic linkages are the active chemical principle of biologically important medicinal plants^{5,6} like curcuminoids (*Curcuma longa*), piperine (*Piper nigrum*) and cassumunin (*Zingiber cassumunar*). The natural curcuminoids were reported to possess anticancer⁷, antitumour⁸, antioxidant^{8,9}, anti-inflammatory¹⁰, antiviral and immunomodulatory activities¹¹. Synthetic curcuminoids are reported to be more potent anticarcinogenic and antimutagenic¹² agents. However structural aspects of many of these products and their metal derivatives have received only scanty attention. In continuation of

the studies on such biologically important unsaturated polycarbonyl compounds and their metal complexes¹³⁻¹⁷, the present communication reports the synthesis and characterization of a new type of conjugated diketoanilide compound obtained by condensing pyridine-2-carbaldehyde with acetoacetanilide. Typical Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Pd(II) complexes of the compound were also synthesized and characterized.

Experimental

Carbon, hydrogen and nitrogen contents 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 (10^{-4} 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 ($\sim 10^{-3}$ mol/L) at $28 \pm 1^\circ\text{C}$. Magnetic susceptibilities were determined at room temperature on a Guoy type magnetic balance, Sherwood Scientific Ltd., England, at room temperature ($28 \pm 1^\circ\text{C}$) using Hg[Co(NCS)₄] as standard. The chemicals used were of AR grade, purchased from Merck, Germany.

Synthesis of conjugated diketoanilide (HL)

Claisen-Schmidt reaction of aromatic aldehydes with β -diketones containing acetyl groups like acetylacetone and benzoylacetone yield unsaturated β -diketones^{6,13,14}. Boric oxide and tri(*sec*-butyl)borate in the reaction prevent the Knoevenagel condensation by the formation of a boron complex⁶. The unsaturated tricarbonyl compound (HL) was synthesized by the method reported earlier¹⁶. The purity of the compound was checked by TLC (on silica gel, solvent was chloroform). The compound is stable, show sharp melting point and is soluble in common organic solvents.

Synthesis of metal complexes

The Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Pd(II) complexes were prepared by the following general method. To a refluxing solution of the compound in ethanol (0.001 mol, 20 mL) a solution of metal(II) acetate (0.001 mol) in minimum amount of water was added slowly with stirring. The reaction mixture was refluxed for ~ 3 h on a water bath and then cooled to $\sim 5^\circ\text{C}$ using an ice-salt bath. The precipitated complex was filtered, washed several times with water, then with methanol, recrystallized from hot ethanol and dried in vacuum. The complexes are well soluble in CH₃CN, DMSO and DMF and insoluble in carbon tetrachloride, chloroform and water.

Determination of magnetic susceptibility

A thin cylindrical glass tube, filled with the sample is vertically suspended from the beam of a balance in draught free enclosure in such a way that its lower end lies between the poles of an electromagnet. The weight of the sample is determined with the field off and with the field on. Corrections for diamagnetism of the constituents were made using Pascal's constants¹⁸. The effective magnetic moments were calculated using the formula $\mu_{\text{eff}} = 2.83 \times [\chi_M T]^{1/2} \times 9.274 \times 10^{-24} \text{ Am}^2$ where χ_M is the corrected molar susceptibility and T is the room temperature. The Ni(II), Zn(II), Cd(II) and Pd(II) chelates are diamagnetic while Co(II) and Cu(II) complexes showed normal paramagnetic moment.

Determination of antifungal activity

The antifungal activity of the compounds were studied by the disk diffusion technique^{19,20} using agar nutrient as the medium as reported earlier¹⁶. The three different fungal strains used were *Aspergillus niger*, *Aspergillus parasiticus* and *Rhizopus oryzae*.

Results and Discussion

The observed elemental analytical data of the conjugated diketoanilide, HL, (Table 1) indicate that the condensation between pyridine-2-carbaldehyde and acetoacetanilide has occurred in the 1:2 ratio. IR, ¹H NMR and mass spectral data of the compound are in agreement with Figure 1. The compound formed well defined and crystalline complexes with acetate salts of Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Pd(II) ions. The observed C, H, N and metal percentages suggest [M(HL)(OAc)₂] stoichiometry for the complexes except for the Co(II) and Cu(II) complexes which have [Co(HL)(OAc)₂](H₂O)₂] and [Cu₂(L)(OAc)₃] stoichiometries respectively (Table 1). All metal complexes are non-electrolytes in DMF (specific conductance <10Ω⁻¹cm⁻¹; 10⁻³ M solution). The observed IR, ¹H NMR and mass spectral data of the complexes are fully consistent with the Figure 2. Analytical and spectral data of the Cu(II) complex are in agreement with Figure 3.

Table 1. Physical and analytical data of HL and its metal complexes

Compound/ Empirical formula	M.P. °C	Yield %	Elemental Analysis Found (Calculated), %			
			C	H	N	M
HL C ₂₆ H ₂₃ N ₃ O ₃	52	70	73.28 (73.41)	5.40 (5.41)	11.26 (11.29)	-
[Co(HL)(OAc) ₂](H ₂ O) ₂] C ₃₀ H ₃₃ CoN ₃ O ₉	184	68	56.44 (56.43)	5.14 (5.17)	6.50 (6.58)	9.18 (9.24)
[Ni(HL)(OAc) ₂] C ₃₀ H ₂₉ N ₃ NiO ₇	188	70	59.92 (59.83)	4.77 (4.82)	6.88 (6.98)	9.78 (9.76)
[Cu ₂ (L)(OAc) ₃] C ₃₂ H ₃₁ Cu ₂ N ₃ O ₉	136	70	52.64 (52.74)	4.30 (4.26)	5.72 (5.77)	17.44 (17.45)
[Zn(HL)(OAc) ₂] C ₃₀ H ₂₉ N ₃ O ₇ Zn	170	68	59.02 (59.17)	4.76 (4.77)	6.80 (6.90)	10.72 (10.75)
[Cd(HL)(OAc) ₂] C ₃₀ H ₂₉ CdN ₃ O ₇	176	66	54.82 (54.93)	4.42 (4.42)	6.47 (6.41)	17.24 (17.15)
[Pd(HL)(OAc) ₂] C ₃₀ H ₂₉ N ₃ O ₇ Pd	182	68	55.51 (55.43)	4.44 (4.47)	6.40 (6.43)	16.42 (16.39)

-OAc – Acetate

IR spectra

The IR spectrum of HL in the 1600-1800 cm⁻¹ region shows three strong bands at 1718, 1663 and 1620 cm⁻¹ assignable respectively to the stretching of the amide carbonyl (amide I), alkenyl carbonyl and the partially enolised cinnamoyl carbonyl functions [16,21] of Figure 1. Spectrum of the compound in the region below 1600 cm⁻¹ shows several medium intensity bands due to various C=C and C-N stretching and N-H and N-C=O bending vibrations. The spectrum also shows a prominent band at 970 cm⁻¹.

typical of *trans* –CH=CH– absorption. The broad band in the region 2800-3300 cm⁻¹ suggests the existence of the compound predominantly in the intramolecularly hydrogen bonded enolic form²¹.

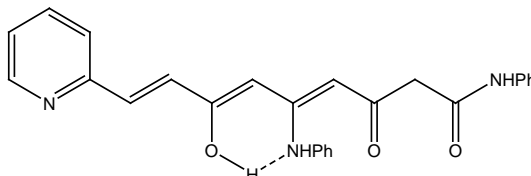
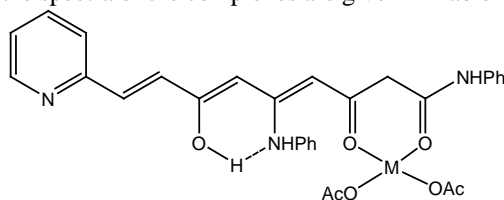


Figure 1. Structure of conjugated diketoanilide

The bands at 1718 and 1663 cm⁻¹ of the free ligand disappeared in the spectra of all the metal complexes and instead a comparatively broad and intense band appeared at ~1640 cm⁻¹. The partially enolised cinnamoyl carbonyl stretching of the free ligand at 1620 cm⁻¹ remained unaltered in the spectra of all the chelates. These indicate that the amide and alkenyl carbonyl groups are involved in coordination with the metal ion while the cinnamoyl carbonyl is excluded from coordination²². The broad band in the 2800-3300 cm⁻¹ region of the ligand remained almost unaffected in the spectra of the complexes, which indicate that the enolic OH is not replaced during complex formation. Monodentate acetate usually shows two bands at 1620 and 1310 cm⁻¹ due to antisymmetric and symmetric stretching respectively^{16,22}. Since carbonyl absorption of the compound also appeared in this region the band at 1620 cm⁻¹ could not be located. However a medium intensity band observed at ~1320 cm⁻¹ suggests the monodentate coordination of the acetate groups. The Co(II) complex showed bands at ~3400 cm⁻¹ indicating the presence of coordinated water molecules. That the carbonyl groups are involved in bonding with the metal as in Figure 2 is further supported by the appearance of two medium intensity bands in the region 420-480 cm⁻¹ assignable to ν_{M-O} vibrations²². Thus IR spectra of the complexes support the neutral bidentate coordination of HL. The important bands that appeared in the spectra of the complexes are given in Table 2.



M = Co(II), Ni(II), Zn(II), Cd(II) and Pd(II) [The Co(II) complex contain two coordinated H₂O molecules]

Figure 2. Structure of the metal complexes of HL

Table 2. Characteristic IR stretching bands (cm⁻¹) of Co(II), Ni(II), Zn(II), Cd(II) and Pd(II) complexes of HL

Complex	(C=O) Cinnamoyl	(C=O) Metal chelated	(CH=CH) <i>trans</i>	(M-O)
[Co(HL)(OAc) ₂ (H ₂ O) ₂]	1620 s	1644 s	968 m	424 m 470 m
[Ni(HL)(OAc) ₂]	1618 s	1640 s	970 m	428 m 480 m
[Zn(HL)(OAc) ₂]	1620 s	1642 s	971 m	422 m 476 m
[Cd(HL)(OAc) ₂]	1616 s	1638 s	975 m	420 m 468 m
[Pd(HL)(OAc) ₂]	1622 s	1646 s	968 m	422 m 466 m

s = strong, *m* = medium

The IR spectrum of the Cu(II) complex showed significant difference from the spectra of other complexes. Thus the broad band observed in the ligand in the region 2800-3300 cm^{-1} due to the O-H...N hydrogen bonding disappeared and several bands due to NH, CH, *etc.* vibrations appeared in this region. The partially enolised cinnamoyl carbonyl stretching of the free ligand at 1620 cm^{-1} also disappeared and instead a strong band appeared at 1590 cm^{-1} . These indicate that the enol proton has been replaced by the metal ion. The bands at 1718 and 1663 cm^{-1} of the free ligand disappeared in the spectrum of the complex and instead a comparatively broad and intense band appeared at 1635 cm^{-1} . These indicate the involvement of all the three carbonyl groups in metal complexation. Further the region 1400-1600 cm^{-1} of the complex also showed appreciable deviation from the ligand spectrum. Thus the bands due to the various C=C, C=N, *etc.* shifted to lower frequency presumably due to the coordination as in Figure 3. The presence of new medium intensity bands in the 420-480 and 530-560 cm^{-1} region assignable to $\nu\text{M-O}$ and $\nu\text{M-N}$ in the spectrum of the complex²² also supports Figure 3.

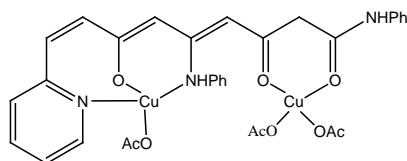


Figure 3. Structure of the Cu(II) complex of HL

¹H NMR spectra

The ¹H NMR spectrum of HL displayed a one proton singlet at δ 12.34 ppm due to the intramolecularly hydrogen bonded enolic proton^{23,24}. Two one-proton signals at δ 10.02 and 9.80 ppm indicate different electronic environment of the two NH protons¹⁶. The methine proton signals appeared at δ 6.04 and 5.93 ppm. The methylene proton signals appeared at δ 3.78 ppm and the alkenyl proton signals are observed in the range δ 8.00-8.35 ppm. Aryl protons appear in the range δ 7.00-8.00 ppm as a complex multiplet. Integrated intensities of all the protons agree well with the Figure 1 of the compound.

In the ¹H NMR spectra of the diamagnetic Ni(II), Zn(II), Pd(II) and Cd(II) complexes the enolic and NH proton signals of the free ligand remained almost unaffected indicating their non-involvement in complexation¹⁶. However the methylene proton signal shifted appreciably to downfield indicating the involvement of β -dicarbonyl function in complexation. Unlike in the spectrum of the ligand, the complexes showed a signal at $\sim\delta$ 2.50 ppm due to methyl protons of acetate groups. Integrated intensities of all the protons agree well with the Figure 2 of the complexes. The assignments of various proton signals observed are assembled in Table 3.

Table 3. ¹H NMR spectral data in δ /ppm of HL and its diamagnetic metal complexes

Compound	Enolic OH	NH	CH=CH	Methine	Methylene	Acetate
HL	12.34 s	10.02 s 9.80 s	8.22 d 8.06 d	6.04 s 5.93 s	3.78 s	-
[Ni(HL)(OAc) ₂]	12.28 s	9.98 s 9.77 s	8.30 d 8.04 d	6.09 s 5.98 s	4.34 s	2.54 s
[Zn(HL)(OAc) ₂]	12.38 s	10.04 s 9.76 s	8.30 d 8.18 d	6.06 s 5.96 s	4.28 s	2.58 s
[Cd(HL)(OAc) ₂]	12.32 s	9.99 s 9.74 s	8.22 d 8.04 d	5.99 s 5.87 s	4.40 s	2.53 s
[Pd(HL)(OAc) ₂]	12.40 s	10.06 s 9.69 s	8.34 d 8.08 d	6.02 s 5.90 s	4.28 s	2.56 s

s = singlet, *d* = doublet

Mass spectra

The formulation of the compound (HL) as in Figure 1 is clearly supported from the presence of intense molecular ion peak in the mass spectrum²⁵ at m/z 425. Peaks due to $[\text{Ar-CH=CH-C=O}]^+$, $[\text{Ar-CH=CH(C=O)-CH}_2]^+$ and $[\text{P} - \text{C}_6\text{H}_5\text{NHCO}]^+$ confirm the condensation of the γ -methyl group of acetoacetanilide with pyridine 2-carbaldehyde (Table 4). The FAB mass spectra of the Ni(II) and Cu(II) complexes showed intense molecular ion peaks due to $[\text{Ni(HL)(OAc)}_2]$ and $[\text{Cu}_2\text{L(OAc)}_3]$ stoichiometries respectively as in Figures 2 and 3. Peaks due to the successive removal of acetate groups and fragments of L^+ are characteristic of the spectra. The spectra of the chelates contain a number of fragments containing metals in their natural isotopic abundance.

Table 4. Mass spectral data of HL and its Ni(II) and Cu(II) complexes

Compound	Mass spectral data (m/z)
HL	425, 333, 305, 291, 263, 241, 162, 134, 120, 116, 102, 92, 74
$[\text{Ni(HL)(OAc)}_2]$	602, 543, 528, 510, 500, 486, 484, 425, 418, 333, 305, 120, 116, 102
$[\text{Cu}_2\text{L(OAc)}_3]$	728, 669, 636, 610, 551, 382, 342, 333, 305, 120, 116, 102

Electronic spectra

The UV spectrum of HL shows two broad bands with maxima at 380 and 260 nm due to the various $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions. The absorption maxima of the metal chelates bear close resemblance with the free ligand which indicates that no structural alteration of the ligand has occurred during complexation. However the values shifted slightly to longer wavelength in the spectra of the metal complexes indicating the involvement of the carbonyl groups in metal complexation²⁶. In the Cu(II) complex, presence of a broad visible band at $15,000 \text{ cm}^{-1}$ and the measured μ_{eff} value ($16.8 \times 10^{-24} \text{ Am}^2$) support the square-planar structure²⁷. The visible spectrum of Co(II) complex showed a broad band with maxima at $19,100 \text{ cm}^{-1}$ with a shoulder at $20,800 \text{ cm}^{-1}$. These values along with the observed magnetic moment ($4.7 \times 10^{-24} \text{ Am}^2$) suggest the octahedral geometry. The observed diamagnetism and broad medium-intensity band at $17,800 \text{ cm}^{-1}$ in the visible spectrum of the Ni(II) chelate suggest its square planar geometry. In conformity, visible spectrum of the chelate in pyridine solution (10^{-3} M) showed three bands corresponding to configurational change from square planar to octahedral due to the association of pyridine. The three well-separated absorption bands at λ_{max} 8,230, 13,550 and $24,340 \text{ cm}^{-1}$ 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 $^3\text{A}_{2g} \rightarrow ^3\text{T}_{1g}(\text{P})$, respectively¹⁶.

Antifungal studies

The results (Table 5) reveal that the compounds possess significant activity against the tested organisms and the free ligand exhibited more activity than its metal complexes.

Table 5. Antimicrobial activity (diameter inhibition zone in mm) of HL and its metal complexes

Compound	<i>Aspergillus niger</i>	<i>Aspergillus parasiticus</i>	<i>Rhizopus oryzae</i>
Nystatin	10	10	10
HL	18	18	13
$[\text{Co(HL)(OAc)}_2(\text{H}_2\text{O})_2]$	12	12	11
$[\text{Ni(HL)(OAc)}_2]$	11	13	10
$[\text{Cu}_2\text{L(OAc)}_3]$	16	13	12
$[\text{Zn(HL)(OAc)}_2]$	12	13	11
$[\text{Cd(HL)(OAc)}_2]$	13	12	12
$[\text{Pd(HL)(OAc)}_2]$	12	13	11

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