



Synthesis and characterization of some conjugated β -ketoesters and their Cu(II) complexes

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Abstract

Five conjugated β -ketoesters (HL^1 to HL^5) with the keto group connected to carbon-carbon double bond have been prepared through the condensation of methyl acetoacetate with aromatic aldehydes (4-nitrobenzaldehyde; 4-methoxybenzaldehyde; 3,4-dihydroxybenzaldehyde; 3,4-dimethoxybenzaldehyde and indole-3-carbaldehyde). Structural characterization by physicochemical techniques indicated the occurrence of HL^1 in the keto form and HL^2 to HL^5 in the intra-molecularly hydrogen bonded enol form. Details on the formation and nature of bonding in the $[Cu(HL)(OAc)_2]$ complex of HL^1 and $[CuL_2]$ complexes of HL^2 to HL^5 are confirmed by analytical and spectral techniques.

Keywords: Conjugated β -ketoesters, metal complexes, keto form, enol form, spectral data.

Introduction

As a part of our investigation on conjugated carbonyl ligands and their metal chelates, this paper includes the preparation and structural identification of five conjugated β -ketoesters and their Cu(II) complexes¹⁻⁶. Such synthetic carbonyl compounds with the carbonyl group attached to olefinic linkages have received much attention recently because many naturally occurring biologically active compounds like curcumin (in turmeric), piperine (black pepper), Cassumunin (ginger), etc contain these type of structural units which are responsible for their biological and medicinal properties⁷⁻¹⁰. Metal complexes of these structural types have gained a prominent place in modern coordination chemistry because in most of the cases metal chelation considerably enhances their medicinal properties^{4,8,11}.

Materials and methods

Instruments and methods: Elemental analysis was carried out by microanalyses (HERAEUS CHNO rapid analyzer). Metal percentage of Cu(II) chelates was determined by AAS (PERKIN ELMER 2380) after decomposing with concentrated sulphuric acid and nitric acid mixture.

The UV-VISIBLE spectra of the compounds were measured using a JASCO V-550 UV-VISIBLE spectrophotometer in methanol (10^{-6} mol/L) solvent, IR spectra (KBr discs) using a JASCO FT/IR 4100 spectrophotometer, ¹HNMR spectra (CDCl₃ or DMSO-d₆) using a JEOL 400 NMR spectrometer and mass spectra using a JEOL JMS 600H mass spectrometer (FAB using argon and *meta*-nitrobenzyl alcohol as the matrix). DMF was used for determining the molar conductance of the complexes

($\sim 10^{-3}$ mol/L) at $28 \pm 1^\circ\text{C}$. A Guoy type magnetic balance at room temperature was used to determine the magnetic susceptibilities of the Cu(II) complexes.

Synthesis of conjugated β -ketoesters, (HL^1 - HL^5) and their Cu(II) complexes:

The conjugated β -ketoesters were prepared by reacting methyl acetoacetate with aromatic aldehydes as reported in our previous work⁶. Use of boric oxide and tri (*sec*-butyl) borate block the condensation of aldehydes at the active methylene group of ester. The condensing agent used was *n*-butylamine⁶. The aldehydes used for the synthesis were: 4-nitrobenzaldehyde; 4-methoxybenzaldehyde; 3,4-dihydroxybenzaldehyde; 3,4-dimethoxybenzaldehyde and indole-3-carbaldehyde. The Cu(II) complexes were also synthesized by the reported method⁶.

Results and discussion

All the ligands are stable with finite melting points. The CHN analysis of the ligands (Table-1) confirms the 1:1 stoichiometric reaction between methyl acetoacetate and aromatic aldehydes. The specific conductance of 10^{-3} M solution of Cu(II) complexes in DMF was found as $<10 \Omega^{-1}\text{cm}^{-1}$. This, along with elemental and metal percentages, indicate the $[CuL_2]$ stoichiometry for all the complexes except that of HL^1 which agree with $[Cu(HL)(OAc)_2]$ composition (Table-1).

The results obtained from various spectral data were in agreement with the Figures-1 and 2 of the conjugated β -ketoesters and Figures-3 and 4 of their Cu(II) complexes.

Table-1: Analytical results and physical constants of conjugated β -ketoesters and Cu(II) chelates.

Compound/ Molecular formula	MP (°C)	Yield (%)	μ_{eff} BM	Elemental Analysis: Found (Calculated) %			
				C	H	N	Cu
HL ¹ C ₁₂ H ₁₁ NO ₅	54	67	-	57.78 (57.83)	4.40 (4.42)	5.59 (5.62)	-
HL ² C ₁₃ H ₁₄ O ₄	49	71	-	66.46 (66.67)	5.92 (5.98)	-	-
HL ³ C ₁₂ H ₁₂ O ₅	84	75	-	61.15 (61.02)	5.06 (5.08)	-	-
HL ⁴ C ₁₄ H ₁₆ O ₅	61	68	-	63.55 (63.64)	6.03 (6.06)	-	-
HL ⁵ C ₁₄ H ₁₃ NO ₃	87	78	-	68.99 (69.14)	5.38 (5.35)	5.74 (5.76)	-
Cu[(HL ¹)(OAc) ₂] C ₁₆ H ₁₇ NCuO ₉	192	72	1.74	44.57 (44.60)	4.02 (3.95)	3.32 (3.25)	14.70 (14.76)
[CuL ²] ₂ C ₂₆ H ₂₆ CuO ₈	208	67	1.76	58.82 (58.92)	5.02 (4.91)	-	11.92 (12.00)
[CuL ³] ₂ C ₂₄ H ₂₂ CuO ₁₀	196	74	1.75	53.87 (53.98)	4.15 (4.12)	-	11.84 (11.91)
[CuL ⁴] ₂ C ₂₈ H ₃₀ CuO ₁₀	205	72	1.75	57.12 (56.99)	4.99 (5.09)	-	10.83 (10.78)
[CuL ⁵] ₂ C ₂₈ H ₂₄ N ₂ CuO ₆	242	75	1.73	61.24 (61.37)	4.34 (4.38)	4.98 (5.11)	11.59 (11.60)

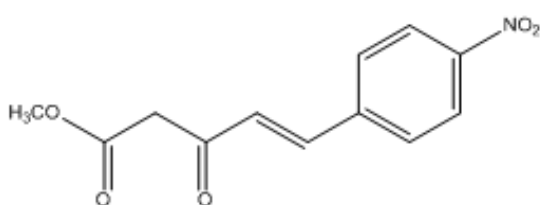


Figure-1: Structure of the conjugated β -ketoester (HL¹).

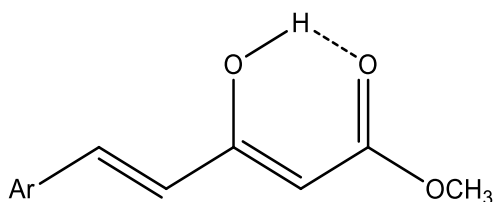


Figure-2: Structure of the conjugated β -ketoesters (HL²-HL⁵).

Ar = 4-Methoxyphenyl (HL²); 3,4-dihydroxyphenyl (HL³); 3,4-dimethoxyphenyl (HL⁴) and 3-Indolyl (HL⁵).

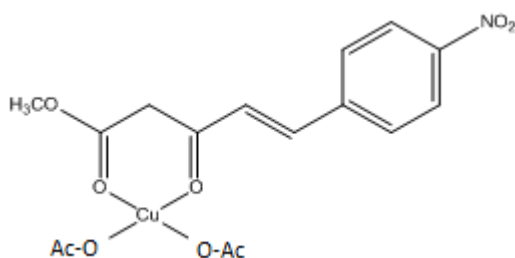


Figure-3: Structure of the Cu(II) chelate of HL¹.

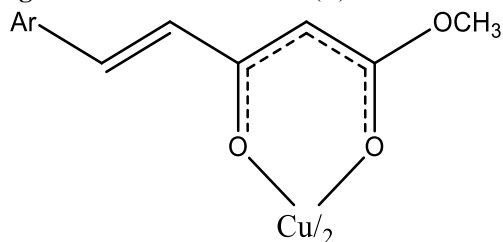


Figure-4. Structure of the Cu(II) chelates of HL² to HL⁵.

IR spectra: The keto-enol equilibrium of methyl acetoacetate shifts into the keto form⁶. The compound displays two intense bands at ~ 1750 and $\sim 1720\text{cm}^{-1}$ due to the ester and acetyl carbonyl functions respectively^{6,12-14}. The carbonyl stretching frequency of the enol tautomer is observed at around 1650cm^{-1} . Strong bands are observed at 1740 and 1640cm^{-1} in the IR spectrum of HL¹ due to the stretching of ester and cinnamoyl carbonyl groups respectively. No other strong bands are observed in the $1600-1800\text{cm}^{-1}$ and $2500-3500\text{cm}^{-1}$ regions of the spectrum. These observations suggest that the compound exists in the keto form as in Figure-1. This may be due to the electron withdrawing effect of the nitro group at para position of the aryl substituent. The trans orientation of $-\text{CH}=\text{CH}-$ group¹⁴ is confirmed by a band at 972cm^{-1} .

IR spectra of all other conjugated β -ketoesters (HL²-HL⁵) showed two strong bands at ~ 1740 and $\sim 1640\text{cm}^{-1}$ due to the ester and cinnamoyl carbonyl stretching vibrations respectively^{6,14}. Unlike in the IR spectrum of HL¹, the spectra of HL²-HL⁵ displayed a strong band at $\sim 1670\text{cm}^{-1}$ due to the carbonyl stretching of the enol tautomer. This, together with the presence of broad band in the $2800-3500\text{cm}^{-1}$ region, confirms the intra-molecularly H-bonded enol structure of these ligands in as in Figure-2. The presence of trans- $\text{CH}=\text{CH}-$ group is confirmed by a prominent band at $\sim 970\text{cm}^{-1}$.

IR spectrum of the Cu(II) complex of HL¹ exhibited bands at 1585 and 1625cm^{-1} due to the stretching of cinnamoyl and metal coordinated ester carbonyl groups respectively^{6,15}. Monodentate coordination of acetate groups can be identified by two bands observed at $\sim 1620\text{cm}^{-1}$ and $\sim 1310\text{cm}^{-1}$. These bands arise from the antisymmetric and symmetric stretching of acetate group respectively¹⁵. The band at $\sim 1620\text{cm}^{-1}$ could not be identified in the spectrum since the stretching of the coordinated ester carbonyl also appeared in this region. But the existence of a band of medium intensity at 1320cm^{-1} confirmed that the acetate groups are monodentate in the chelate¹⁶. Thus IR spectral data of HL¹ are in conformity with neutral bidentate coordination as in Figure-3.

IR spectra of the Cu(II) complexes of all other conjugated β -ketoesters showed a slightly broadened intense band at $\sim 1630\text{ cm}^{-1}$ due to metal coordinated carbonyl functions^{6,15}. The coordination of cinnamoyl carbonyl function with the metal cation is clear from the creation of a new strong band at $\sim 1590\text{ cm}^{-1}$. The broad band in the $2800\text{-}3500\text{ cm}^{-1}$ region of the ligands vanished in the IR spectra of all the chelates, which indicate that the enolic proton of the ligands are substituted by metal cation during chelate formation as in Figure-4. The participation of carbonyl groups in metal coordination as in Figures-3, 4 are further confirmed by the presence of two bands of medium intensity at $\sim 420\text{ cm}^{-1}$ and $\sim 480\text{ cm}^{-1}$ due to $\nu_{\text{M-O}}$. The IR spectral data are shown in Table-2.

¹H NMR spectra: All the ligands (except HL¹) showed a slightly broadened one proton signal in the range δ 13-14 ppm of their ¹H NMR spectra. Based on earlier reports this signal arises due to the intra-molecularly hydrogen bonded enol proton^{6,17}. The methine proton signal of HL² to HL⁵ appeared at $\sim \delta$ 6ppm confirming the enol form of the ligands. ¹H NMR spectrum of HL¹ does not display any signal above δ 10ppm. This, together with the absence of methine proton signal and presence of methylene proton signal at δ 3.7ppm, suggests its existence in the keto form¹⁷. All the compounds showed a three proton signal in the range $\sim \delta$ 3ppm due to the OCH₃ group of ester. The alkenyl proton signals are observed at $\sim \delta$ 8.1-8.5ppm¹⁸. The *J* values ($\sim 16\text{ Hz}$) indicate the trans orientation of $-\text{CH}=\text{CH}-$ group.

Aryl proton signals were observed in the range $\sim \delta$ 7-8ppm as a multiplet. The aryl substituent proton chemical shifts were observed as expected¹⁷. Integrated intensities and position of all the signals observed are in agreement with Figures-1 and 2 of the conjugated β -ketoesters. The various proton signals found in the spectra of the ligands are shown in Table-3.

Mass spectra: The intense molecular ion peaks observed in the mass spectra of all conjugated β -ketoesters confirm their existence as in Figures-1 and 2. Peaks due to $(\text{Ar}-\text{CH}=\text{CH}-\text{CO})^+$ is observed in the spectra of all the ligands. Presence of this fragment confirms the Claisen-Schmidt condensation of the acetyl group of ester with carbonyl group of aromatic aldehydes^{6,19}. Mass spectra of the ligands also contain peaks due to the removal OCH₃, COOCH₃ and ArC₂H₂ groups from the molecular ion.

[Cu(HL)(OAc)₂] stoichiometry of the Cu(II) complex of HL¹ as in Figure-3 is confirmed by the presence of molecular ion peak in its mass spectrum. Peaks due to the removal of one or both acetate groups are also an important characteristic of the spectrum. The mass spectra of the Cu(II) complexes of HL² to HL⁵ showed relatively intense molecular ion peaks confirming their [CuL₂] stoichiometry as in Figure-4. Peaks assignable to [CuL]⁺, L⁺ and ligand fragments are also observed in the spectra^{6,20}. Peaks assignable to the natural abundance of Cu isotopes are a characteristic feature of all the spectra⁵. Fragments observed in the mass spectra are shown in Table-4.

Table-2: IR spectral data of the conjugated β -ketoesters and Cu(II) chelates.

Compound	C=O Ester	C=O Cinnamoyl	C=O Olefinic	(C=C) Phenyl/ Alkenyl	Cu-O
HL ¹	1740	1640	-	1588, 1562, 1550, 1522	-
HL ²	1735	1638	1670	1587, 1564, 1546, 1520	-
HL ³	1737	1644	1663	1592, 1562, 1539, 1522	-
HL ⁴	1734	1642	1669	1590, 1559, 1543, 1524	-
HL ⁵	1736	1636	1668	1588, 1560, 1540, 1525	-
Cu(HL ¹)(OAc) ₂	1625	1585	-	1586, 1560, 1550, 1527	426, 470
[CuL ²] ₂	1631	1597	-	1588, 1560, 1538, 1522	418, 472
[CuL ³] ₂	1630	1596	-	1592, 1552, 1529, 1518	422, 473
[CuL ⁴] ₂	1635	1587	-	1590, 1561, 1547, 1524	418, 480
[CuL ⁵] ₂	1628	1589	-	1583, 1563, 1542, 1521	422, 482

Table-3: ¹H NMR spectral data (δ /ppm) of the conjugated β -ketoesters.

Compound	Enolic OH	Ester OCH ₃	Methine	Alkenyl	Aryl	Aryl substituent
HL ¹	-	3.1	-	8.1-8.3	7.2-8.0	-
HL ²	13.6	3.1	5.9	8.2-8.4	7.5-7.9	3.9
HL ³	13.7	3.1	6.0	8.1-8.3	7.4-8.3	10.1, 10.3
HL ⁴	13.1	3.2	6.1	8.3-8.5	7.2-8.0	3.8, 3.9
HL ⁵	13.2	3.1	5.9	8.2-8.5	7.5-7.9	-

Table-4: Important mass spectral fragments of the conjugated β -ketoesters and Cu(II) complexes.

Compound	Mass spectral data (m/z)
HL ¹	249, 234, 218, 190, 176, 148, 122, 101
HL ²	234, 219, 203, 175, 161, 147, 133, 101
HL ³	236, 221, 205, 177, 163, 135, 101
HL ⁴	264, 249, 233, 205, 191, 163, 151, 101
HL ⁵	243, 228, 212, 184, 170, 142, 101
Cu(HL ¹)(OAc) ₂	432, 430, 400, 398, 371, 346, 344, 313, 311, 249, 234, 218, 190, 176, 148, 122, 101
[CuL ²] ₂	531, 529, 500, 498, 469, 467, 398, 396, 367, 365, 334, 332, 317, 315, 265, 263, 234, 219, 203, 175, 147, 133, 127
[CuL ³] ₂	535, 533, 504, 502, 473, 471, 400, 398, 369, 367, 336, 338, 317, 315, 265, 263, 236, 205, 177, 163, 135, 127
[CuL ⁴] ₂	591, 589, 560, 558, 529, 527, 428, 426, 397, 395, 368, 366, 317, 315, 265, 264, 249, 205, 191, 163, 151, 127
[CuL ⁵] ₂	549, 547, 518, 516, 487, 485, 433, 431, 407, 405, 376, 374, 345, 343, 317, 315, 265, 263, 243, 228, 212, 184, 170, 142, 101

Electronic spectra: The $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions of the ligands are found at ~ 260 and ~ 390 nm in the UV spectra²¹. The values shifted to low wave numbers in the spectra of the complexes due to metal coordination using these groups²². A broad visible band is observed at $\lambda_{\max} \sim 15,000 \text{ cm}^{-1}$ in the electronic spectra of Cu(II) chelates. This, along with the calculated μ_{eff} values of $\sim 1.75 \text{ BM}$ (Table-1), suggests their square-planar geometry²⁰. The spectra recorded in pyridine displayed a broad band centered at $\sim 11,000 \text{ cm}^{-1}$ indicating their conversion to octahedral geometry due to the coordination with pyridine⁶.

Conclusion

Five new conjugated β -ketoesters with the carbonyl group connected to unsaturated linkage are prepared by the reaction of methyl acetoacetate with aromatic aldehydes. Spectral and analytical data revealed that the methyl group of the acetyl part of the ester and the carbonyl group of aromatic aldehydes condensed according to Claisen-Schmidt reaction. The existence of these conjugated β -ketoesters in the intra-molecularly hydrogen bonded enol form (except in HL¹) has been clearly explained from their analytical and spectral data. Analytical and spectral data of HL¹ suggests its existence in the keto form which may be due to the electron withdrawing effect of the nitro group. [CuL₂] chelates of HL² to HL⁵ showed the monobasic bidentate chelation in which the metal cation replaces the enolic proton. The existence of Cu(II) complex of HL¹ in the [Cu(HL)(OAc)₂] stoichiometry with neutral bidentate coordination is confirmed by analytical and spectral data.

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