



Research Article

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Studies on novel hydrazone compounds and their metal complex

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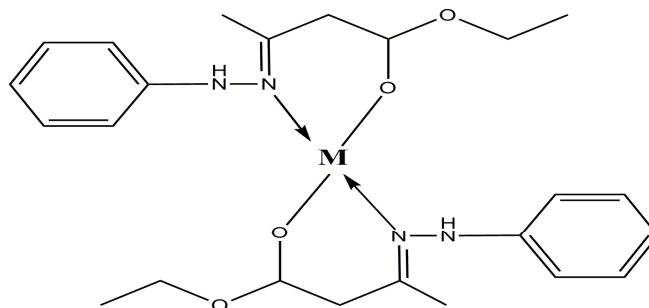
ABSTRACT

Ethyl acetoacetate react with phenyl hydrazine in the presence of acid was gave ethyl-3-(2-phenylhydrazono)butanoate (EP), which was characterized by elemental analysis and spectral studies. The transition metal chelates viz. Cu^{2+} , Ni^{2+} , Co^{2+} , Mn^{2+} and Zn^{2+} of EP were prepared and characterized by metal-ligand (M:L) ratio, IR and reflectance spectroscopies and magnetic properties. The antifungal activity of EP and its metal chelates was screened against various fungi. The results show that all these samples are good antifungal agents.

Keywords: ethyl-3-(2-phenylhydrazono)butanoate, Spectroscopies study, Magnetic moment, Antifungal properties.

INTRODUCTION

Hydrazides containing compounds have not found wide application in organic synthesis, but several of these molecules display significant biological activity [1-4]. In recent year extensive study of hydrazides and their derivatives show diverse biological activities like antibacterial, antifungicidal, analgesic, chemotherapeutic agent and anti-inflammatory properties [5-15]. Hydrazides play an important role in inorganic chemistry, as they easily form stable complexes with most transition metal ions. The development of the field of bioinorganic chemistry has increased the interest in hydrazone complexes, since it has been recognized that many of these complexes may serve as models for biologically important species [16-20]. Coordination compounds derived from aroylhydrazones have been reported to act as enzyme inhibitors and are useful due to their pharmacological applications [21-25]. In view of the importance of such hydrazones, we describe here the synthesis and characterization of Cu^{+2} , Ni^{+2} , Co^{+2} , Mn^{+2} and Zn^{+2} complexes of ethyl-3-(2-phenylhydrazono)butanoate (EP) (Scheme-1).



Metal C complex of ethyl-3-(2-phenylhydrazono)butanoate
Where $\text{M} = \text{Cu}^{+2}, \text{Co}^{+2}, \text{Ni}^{+2}, \text{Mn}^{+2}, \text{Zn}^{+2}$

Scheme-I

EXPERIMENTAL SECTION

All other chemicals used were of laboratory grade.

Synthesis of ethyl-3-(2-phenylhydrazono)butanoate (EP): In a Erlenmeyer flask, Ethyl acetoacetate (0.1 mol) and phenyl hydrazine(0.12mol) was mixed in presence of conc.HCl(0.5ml) and stand overnight. The resulting mass was add to 50ml dry ether and washed with water. Then evaporation of ether gave product. Crystallized the product by Ethanol. It's melts at 123°C.

Analysis:

| | | C% | H% | N% |
|---|-------------|-------|------|-------|
| Elemental Analysis | Calculated: | 65.45 | 7.27 | 12.72 |
| C ₁₂ H ₁₆ N ₂ O ₂ (220) | Found : | 65.40 | 7.23 | 12.68 |

IR Spectral Features (cm⁻¹): 3310 (NH), 1615(C=O), 1589(C=N), 1061(N-N)

NMR Signals: δ ppm 6.83-7.41 (m, 5H, Ar-H), 6.89 (s, NH, 1H), 4.16(q, O-CH₂, 2H), 2.74(s, CH₂, 2H), 1.32(t, 3H, CH₃, 3H), 1.98(s, 3H, CH₃, 3H).

Synthesis of metal chelates of EP:

The metal chelates of EP with Cu²⁺, Co²⁺, Zn²⁺, Mn²⁺, and Ni²⁺ metal ions were prepared in two steps. All the metal chelates were prepared in an identical procedure.

Preparation of EP solution:

EP (0.05 mol) was taken in 500 ml beaker and formic acid (85% v/v) was added up to slurry formation. To this slurry water was added till the complete dissolution of EP. It was diluted to 100 ml.

Table-1: ANALYSIS OF EP LIGAND AND ITS METAL CHELATES

| Empirical Formula | Mol. Wt. gm/mole | Yield (%) | Elemental Analysis | | | | | | | |
|--|------------------|-----------|--------------------|-------|------|-------|-------|-------|-------|-------|
| | | | C% | | H% | | N% | | M% | |
| | | | Cald | Found | Cald | Found | Cald | Found | Cald | Found |
| C ₁₂ H ₁₆ N ₂ O ₂ | 220 | 78 | 65.45 | 65.40 | 7.27 | 7.23 | 12.72 | 12.68 | - | - |
| C ₂₄ H ₃₂ N ₄ O ₂ Cu ²⁺ | 471.54 | 74 | 61.08 | 61.05 | 6.79 | 6.76 | 11.88 | 11.86 | 13.47 | 13.45 |
| C ₂₄ H ₃₂ N ₄ O ₂ Co ²⁺ | 466.94 | 70 | 61.68 | 61.66 | 6.85 | 6.82 | 11.99 | 11.97 | 12.62 | 12.59 |
| C ₂₄ H ₃₂ N ₄ O ₂ Ni ²⁺ | 466.71 | 67 | 61.71 | 61.69 | 6.86 | 6.84 | 12.00 | 11.97 | 12.58 | 12.56 |
| C ₂₄ H ₃₂ N ₄ O ₂ Mn ²⁺ | 462.94 | 71 | 62.21 | 62.18 | 6.91 | 6.89 | 12.10 | 12.07 | 11.87 | 11.85 |
| C ₂₄ H ₃₂ N ₄ O ₂ Zn ²⁺ | 473.38 | 69 | 60.84 | 60.82 | 6.76 | 6.74 | 11.83 | 11.82 | 13.81 | 13.77 |

Synthesis of EP-metal-chelates:

In an ethanolic solution of metal chloride (0.005 mol) and 20 ml of above mentioned EP solution (i.e. containing 0.01 M EP) was added with vigorous stirring at room temperature. The appropriate pH was adjusted by addition of sodium acetate for complete precipitation of metal chelate. The precipitates were digested on a boiling water bath. The precipitates of chelate were filtered off, washed by water and air-dried.

MEASUREMENTS

The elemental contents were determined by Thermo Finigen Flash1101 EA (Italy) the metals were determined volumetrically by Vogel's method [26]. To a 100 mg chelate sample, each 1 ml of HCl, H₂SO₄ and HClO₄ were added and then 1 g of NaClO₄ was added. The mixture was evaporated to dryness and the resulting salt was dissolved in double distilled water and diluted to the mark. From this solution the metal content was determined by titration with standard EDTA solution. Infrared spectra of the synthesized compounds were recorded on Nicolet 760 FT-IR spectrometer. NMR spectrum of EP was recorded on 60 MHz NMR spectrophotometer. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy Balance at room temperature. Mercury tetrathiocyanatocobaltate (II) Hg [Co(NCS)₄] was used as a calibrant. The electronic spectra of complexes in solid were recorded on at room temperature. MgO was used as reference. Antifungal activity of all the samples was monitored against various fungi, following the method reported in literature [27].

RESULTS AND DISCUSSION

The synthesis of ethyl-3-(2-phenylhydrazono)butanoate (EP) was made by a simple condensation reaction of ethyl acetoacetate and phenyl hydrazine. The resulted EP ligand was white crystalline powder. The C,H,N contents of EP

(Table-1) are consistent with the structure predicted (Scheme-1). The IR spectrum of EP comprises the important bands of C=N at 1589 cm^{-1} .

TABLE-2: SPECTRAL FEATURUES AND MAGNETIC MOMENT OF EP METAL CHELATES

| Metal Chelates | μ_{eff} (BM) | Electronic spectral data (cm^{-1}) | Transition |
|---------------------|-------------------------|---|---|
| EP-Cu ²⁺ | 1.85 | 23447 13209 | Charge transfer ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$ |
| EP-Ni ²⁺ | 3.69 | 22592 15366 | ${}^3\text{A}_{1g} \rightarrow {}^3\text{T}_{1g}(\text{P})$ ${}^3\text{A}_{1g} \rightarrow {}^3\text{T}_{1g}(\text{F})$ |
| EP-Co ²⁺ | 4.72 | 23729 19099 8918 | ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$ ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}$ ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{P})$ |
| EP-Mn ²⁺ | 5.53 | 23229 19038 16836 | ${}^6\text{A}_{1g} \rightarrow {}^6\text{A}_{2g}$ ${}^4\text{E}_g$ ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}$ (4G) ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}(\text{PG})$ |
| EP-Zn ²⁺ | Diamag. | ----- | ----- |

The broad band due to -NH group appeared at 3310 cm^{-1} . The band is observed at 1589 cm^{-1} vibration of C=N of EP. The NMR spectrum of EP in DMSO indicates that the singlet of 2 H at 2.74 for N-CH₂ and 4.16 O-CH₂ group. While the singlet at 6.89 δ ppm due to -NH group. The aromatic protons are appeared in multiplicity at 6.83-7.41 δ . It is m.p. is 123°C . Thus the structure of EP is confirmed as shown in Scheme-I.

The metal and C,H,N contents of metal chelates of EP (Table-I) are also consistent with the predicted structure. The results show that the metal: ligand (M:L) ratio for all divalent metal chelate is 1:2.

TABLE-3: ANTIFUNGAL ACTIVITY OF EP LIGAND AND ITS METAL CHELATES

| Sample | Zone of inhibition of fungus at 1000 ppm (%) | | | |
|---------------------|--|---------------------------------|-----------------------|---------------------------|
| | <i>Penicillium expansum</i> | <i>Botrydeplaia thiobromine</i> | <i>Nigrospora Sp.</i> | <i>Rhisopus Nigricans</i> |
| EP | 52 | 66 | 60 | 64 |
| EP-Cu ²⁺ | 74 | 81 | 82 | 70 |
| EP-Zn ²⁺ | 63 | 79 | 80 | 82 |
| EP-Ni ²⁺ | 74 | 78 | 67 | 76 |
| EP-Co ²⁺ | 74 | 80 | 73 | 73 |
| EP-Mn ²⁺ | 68 | 77 | 78 | 72 |

The infrared spectra of all the chelates are identical and suggest the formation of all the metalocyclic compound by the absence of band characteristic of free -OH group of parent EP. The other bands are almost at their respectable positions as appeared in the spectrum of parent-EP ligand. However, the band due to (M-O) band could not be detected as it may appear below the range of instrument used. The important IR Spectral data are shown in Table-2.

Magnetic moments of metal chelates are given in Table-2. The diffuse electronic spectrum of Cu²⁺ chelates shows two broad bands around 13209 and 23447 cm^{-1} . The first band may be due to a ${}^2\text{B}_{1g} \rightarrow {}^1\text{A}_{1g}$ transition. While the second band may be due to charge transfer. The first band shows structures suggesting a distorted octahedral structure for the Cu²⁺ metal chelates. The higher value of the magnetic moment of the Cu²⁺ chelate supports the same. The Co²⁺ metal chelate gives rise to two absorption bands at 23729 and 19099 cm^{-1} , which can be assigned ${}^4\text{T}_{1g} \rightarrow {}^2\text{T}_{2g}$, ${}^4\text{T}_{1g} \rightarrow {}^4\text{T}_{1g}(\text{P})$ transitions, respectively. These absorption bands and the μ_{eff} value indicate an octahedral configuration of the Co²⁺ metal chelate [28]. The spectrum of Mn²⁺ polymeric chelate comprised two bands at 19038 cm^{-1} and 23229 cm^{-1} . The latter does not have a very long tail. These bands may be assigned to ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g(\text{G})}$ and ${}^6\text{A}_{1g} \rightarrow {}^4\text{A}_{2g(\text{G})}$ transitions, respectively. The high intensity of the bands suggests that they may have some charge transfer character. The magnetic moment is found to be lower than normal range. In the absence of low temperature measurement of magnetic moment it is difficult to attach any significance to this. As the spectrum of the metal chelate of Ni²⁺ show two distinct bands at 22592 and 15366 cm^{-1} are assigned as ${}^3\text{A}_{1g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{P})$ and ${}^3\text{A}_{1g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$ transition, respectively suggested the octahedral environment for Ni²⁺ ion. The observed μ_{eff} values in the range 1.85-5.53 B.M are consistent with the above moiety^{28,29}.

The examination of antifungal activity of EP ligand and its all chelates (Table-3) reveals that the ligand is moderately toxic against fungi, while all the chelates are more toxic than ligand. Among all the chelates the Cu²⁺ chelate is more toxic against fungi.

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