

Full Proceeding Paper

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL STUDIES OF M(II) COMPLEXES WITH 2,3-BUTANEDIONE-3-MONOXIME

VAISHALI H. RAJURKAR

D. G. Ruparel college of Arts, Science and Commerce, Mahim, Mumbai University, Mumbai, India. Email: vaishali.rajurkar@ruparel.edu

Received: 25 January 2020, Revised and Accepted: 17 March 2020

ABSTRACT

Objective: Various Schiff bases and their metal complexes have wide applications in various fields such as pharmaceuticals, analytical, clinical, biological etc due to their biological activity such as antibacterial, antifungal, anticancer, antidiuretic, antioxidant etc.

Materials and Methods: Reaction between 2,3-Butanedione-3-monoxime, 3/4-hydroxyphenyl and some hydrated metal salts of Mn^{II} gives complexes of the type [MnL₂(H₂O)]. The ligands and the complexes were characterized by elemental analysis, magnetic susceptibility measurements and spectral (I.R., U.V.-Vis., N.M.R.) analysis. Anti-bacterial and anti-fungal activity of the Schiff base ligands and their metal complexes have been studied using the agar well diffusion method and ditch diffusion method.

Results: Spectroscopic study shows bidentate ligands and coordination occurs through oxime oxygen after deprotonation and nitrogen of azomethine group. Ligands and metal complexes shows activity against *S. aureus* (gm positive), *P. aeruginosa* (gm negative), *Aspergillusniger* and *Candidaalbicans*.

Conclusion: The spectral and magnetic study suggests octahedral geometry for metal complexes. Metal complexes acts as most promising antifungal and antibacterial against *Staphylococcus aureus* and *Pseudomonas aeruginosa* as compared to Schiff bases.

Keywords: Antifungal and antibacterial agents. Bidentate ligands

INTRODUCTION

Metal complexes with various donor groups had attracted by many workers [1-3] due to their biological, pharmacological, clinical and analytical importance. Thiophene derivatives exhibit an array of biological activity such as antibacterial and antifungal activity [4-6]. Piperonylamine Schiff bases metal complexes are most potent antimicrobial agents as compared to its Schiff bases [7]. Macrocyclic Schiff base metal complexes derived from 1,4-dicarbonylphenyl dihydrazide and pentane-2,4-dione also acts as growth inhibiting agents against some bacteria and fungi [8]. There is enormous interest presently in the field of coordination chemistry of '3d' transition metals with Schiff bases. They have also been used as biological models [9], oxygen carriers and antifertility agents on male albino rats [10]. Some studies of metal complexes of diacetylmonoxime and their related ligands have been reported [11-12]. We have already reported the antibacterial and antifungal properties of 2-nitroaniline 2,3-Butanedione 3-monoxime and 3-nitroaniline 2,3-Butanedione 3-monoxime and their metal complexes [13]. In this paper we reported the study of 3-hydroxyphenyl 2,3-Butanedione 3-monoxime (L¹) and 4-hydroxyphenyl 2,3-Butanedione 3-monoxime (L²) and their Mn^{II} complexes. The main interest in this ligand originates in its oxime group containing -N-O- donor atoms.

Materials and method

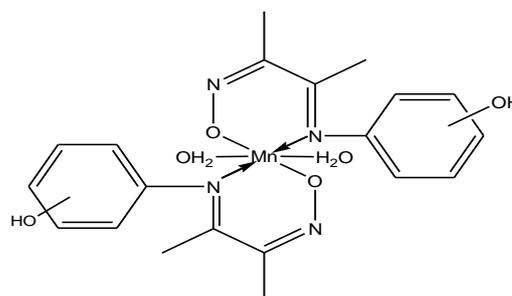
L¹ and L² were prepared according to the literature method [12,14]. All the chemicals used for synthesis were analytical grade. 2,3-Butanedione 3-monoxime was obtained from Thomas Baker, 3-hydroxyphenyl and 4-hydroxyphenyl were obtained from Aldrich.

Synthesis of Ligand and metal complexes

2,3-Butanedione 3-monoxime and 3/4-hydroxyphenyl in 1:1 proportion were dissolved separately in absolute alcohol, mixed and refluxed for 4 hrs. in water bath. After heating insoluble materials removed by filtration and cooled. A dark brown needle shaped L¹ and L² formed.

The prepared ligand and metal salts in 2:1 proportion were mixed and refluxed for 4 hrs. in water bath. After cooling insoluble materials removed by filtration, coloured crystalline metal complexes formed, recrystallized and dried over anhydrous CaCl₂. The physical and analytical data listed in table 1.

Structure of metal complex



Antibacterial activity and Antifungal activity

The synthesized ligands and complexes were screened for in vitro growth inhibitory activity against gram-positive bacteria *Staphylococcus aureus* and gram-negative bacteria *Pseudomonas aeruginosa* by well diffusion method and fungi against *Aspergillusniger* and *Candidaalbicans* by ditch diffusion method. [6, 15].

The lowest concentration of compounds, which completely inhibited visible microbial growth, was recorded as the Minimum inhibitory concentration (MIC, µg/ml) [5, 8]. Subsequent dilutions (80%, 60%, 40%, and 20%) made by using DMF. Under aseptic conditions, the diluted test solution with different concentration was poured into the disc and ditch placed on the numbered plates. Then the plates incubated at room temperature for 24 hr. During this period, the test solution diffused and the growth of the inoculated microorganisms affected.

Antibacterial activity indicated by the presence of clear inhibition zone around the well and antifungal activity indicated by the presence of inhibition zone nearer to the ditch. The zones of inhibition exhibited by the ligands and complexes matched with ciprofloxacin as an antibiotic and fluconazol as an antifungal at the same concentrations.

RESULTS AND DISCUSSION

The complexes are stable in air but decomposed at high temperature. Easily soluble in dimethylformamide (DMF) and dimethylsulphoxide (DMSO). The physical and elemental analysis of ligands and metal complexes listed in table 1.

Table 1: Physical and elemental analysis

| Name of the compounds | % Yield | Molecular formula (mol. Wt.) | Melting point | Elemental Analysis found (calculated) % | | | |
|--|---------|--|---------------|---|-------------------|------------------|------------------|
| | | | | C % | H % | N % | Mn % |
| L ¹ (brown) | 90 | C ₁₀ H ₁₂ N ₂ O ₂ (192.1) | 375K | 51.898 (54.319) | 3.6806 (4.974) | 18.292 (19.0) | - |
| Mn-L ¹ .2H ₂ O (dark red brown) | 70 | [MnC ₂₀ H ₂₇ N ₂ O ₂] | < 573K | 50.74 (50.74) | 5.51 (5.53) | 11.80 (11.83) | 11.61 (11.60) |
| L ² (dark red brown) | 90 | C ₁₀ H ₁₂ N ₂ O ₂ (192.1) | 415K | 51.898 (54.319) | 3.6806 (4.974) | 18.292 (19.0) | - |
| Mn-L ² .2H ₂ O (dark red brown) | 65 | [MnC ₂₀ H ₂₇ N ₂ O ₂] | < 573K | 50.71 (50.74) | 5.50 (5.53) | 11.84 (11.83) | 11.58 (11.60) |

Electronic Spectra and Magnetic moment

The electronic spectrum of ligands and complexes helps to indicate the geometry. The important electronic spectral bands recorded in table 2. The spectra of the ligand shows strong absorption bands in the region 260 to 280nm but in complexes they are slightly shifted to lower frequency [16] which are $\pi \rightarrow \pi^*$ charge transfer transitions. The bands in the region 360 to 430nm can be assigned to the $n \rightarrow \pi^*$ transitions of the azomethine group. In the spectra of both metal complexes in which the bands of the azomethine chromophore $n \rightarrow \pi^*$ transitions are shifted to lower frequencies indicating that the imine nitrogen atom is involved in coordination to the metal ion [17]. Mn^{II} complexes show low intensity absorption bands associated with d-d transition supports the coordinated geometry of the Mn-complexes [18] similarly spin allowed transition for Mn^{II} in octahedral field [6] are ${}^6A_{1g} \rightarrow {}^4T_{2g}$ (D) (500-515nm), ${}^6A_{1g} \rightarrow {}^4T_{2g}$ (D) (600-625nm), ${}^6A_{1g} \rightarrow {}^4T_{1g}$ (700-720nm) indicates octahedral geometry.

The room temperature magnetic moment values also help to indicate the geometry. The magnetic moment value of Mn^{II} in range 5.7 to 6.0 BM is close to theoretical spin only value ($\mu_{\text{eff}} = 6.4$ to 6.5 BM for Mn²⁺ (d⁵ system)) indicates octahedral geometry of the complexes [19].

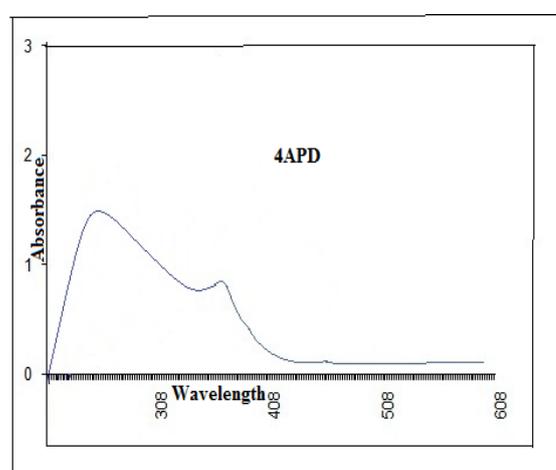


Fig. 1: Electronic absorption spectra of L²

Table 2: Electronic spectral data and magnetic values of the metal complexes

| Name of the compounds | μ_{eff} (BM) | $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions and charge transitions (nm) | d-d transitions |
|--------------------------------------|-------------------------|---|-----------------|
| L ¹ | - | 264, 425 | - |
| Mn-L ¹ .2H ₂ O | 6.400 | 275, 378 | 506, 624, 710 |
| L ² | - | 265, 396 | - |
| Mn-L ² .2H ₂ O | 6.500 | 276, 380 | 506, 625, 714 |

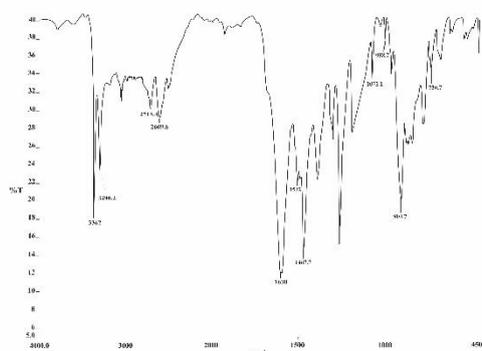


Fig. 2: IR Spectra of L¹

Infrared Spectra - The I.R. spectra (table 3) shows, complexes behave as bidentate coordinating ligand via the azomethine nitrogen (C=N*) and oxygen of oxime (-NOH) group by replacement of

hydrogen ion forming six-membered ring around metal ion [12]. In the ligand azomethine (C=N*) group is at high wavenumber but in metal complexes it shifts to lower wavenumber, this indicates the imine nitrogen atom involved in coordination to the metal ion [16, 20] while oxime (C=N) remains more or less at the same position. The N-O band in the ligand is observed at 998 cm⁻¹ but in metal complexes it shifts to a higher wavenumber, this indicates the oxygen atom is replaced by the oxime proton involved in coordination to the metal ion [12, 18]. A band observed in the ligand at about 3296 cm⁻¹ due to N-H stretching is rarely observed in metal complexes. Phenolic (O-H) in ligands and their metal complexes observed in the range 3360-2609 cm⁻¹ means (O-H) of hydroxyphenyl does not involve in coordination or ligand formation. A broad band observed in all the complexes in the range ~3396 cm⁻¹ due to (O-H) of the coordinated H₂O. This is supported by the appearance of an additional band in the range 950-900 cm⁻¹ for (O-H) rocking deformation and 800-750 cm⁻¹ for (O-H) wagging mode of coordination which is not observed in the ligand spectrum [18]. Thus, H₂O is coordinated in metal complexes. New bands appear in the

450-420 and 400-360 cm^{-1} assignable to the $\nu(\text{Mn-O})$ and $\nu(\text{Mn-N})$ resp. in metal complexes only [21, 22].

^1H N.M.R. analysis-The proton nuclear magnetic resonances for ligands recorded in deuterated CDCl_3 as a solvent. The chemical shifts in term of δ ppm tabulated in Table 4. In ligands a broad peak of -OH of oxime is not observed due to rapid exchange with the solvent CDCl_3 [11, 23]. There are two signals in between 1.70 to 2.00 ppm are due to presence of methyl protons in all Schiff bases. A peak of phenyl -OH for L^1 and L^2 observed at 9.73 and 9.59 ppm. Similarly, multiple signals in the region $\delta = 7.30$ -8.10 ppm are assignable to aromatic protons.

Antibacterial and Antifungal activity

The inhibitory zones are shown in table 5 & 6. It has been observed that the metal complexes have moderate antibacterial and antifungal activity than the free ligands but less activity as compared to standard drugs. Only L^2 shows inhibitory zone up to 37 mm for *Staphylococcus aureus* and moderate activity for

Pseudomonas aeruginosa at higher concentration. There is moderate activity for both the ligands and their complexes against *Aspergillus niger* and less activity against *Candida albicans*.

It has been suggested that the complexes having antimicrobial activity may act either by killing the microbes or by inhibiting multiplication of the microbes by blocking their active sites of enzymes [24]. This is also probably due to the greater lipophilic nature of the complexes. The lipid membrane that surrounds the cell favors the passage of only lipid soluble material, which controls the microbial activity.

On chelation, the metal ion will be reduced largely due to the overlap of the ligand orbital and partial sharing of positive charge of the metal ion with donor groups. Further, it increases the delocalization of π -electron over the completely chelate ring and enhances the lipophilicity of the complex [25]. This lipophilicity enhances the penetration of the complex into lipid membrane and blocks the metal binding sites on enzymes of microorganisms.

Table 3: I.R. bands of ligands and metal complexes

| Name of the compounds | $\nu(\text{C=N}^*)$ | $\nu(\text{C=N})$ | $\nu(\text{N-O})$ | $\nu(\text{M-O})$ | $\nu(\text{M-N})$ | $\nu(\text{O-H})$ phenolic |
|--|---------------------|-------------------|-------------------|-------------------|-------------------|----------------------------|
| L^1 | 1602 | 1531 | 998 | - | - | 3296 |
| Mn- $\text{L}^1 \cdot 2\text{H}_2\text{O}$ | 1609 | 1494 | 1116 | 521 | 456 | 3198 |
| L^2 | 1602 | 1532 | 998 | - | - | 3296 |
| Mn- $\text{L}^2 \cdot 2\text{H}_2\text{O}$ | 1610 | 1490 | 1101 | 520 | 450 | 3195 |

Table 4: NMR signal in (δ ppm) of L^1 and L^2 .

| Sr. no. | Schiff base | NMR signals in (δ ppm) |
|---------|--------------|---|
| 1 | L^1 | 7.2-8.0 (4H, multiplet, Ar-H), 1.9 (3H, S, -CH ₃) 2.20 (3H, S, -CH ₃), 10.00 (1H, S, -OH [Carboxylic]) |
| 2 | L^2 | 7.2-8.0 (4H, multiplet, Ar-H), 1.9 (3H, S, -CH ₃) 2.20 (3H, S, -CH ₃), 10.10 (1H, S, -OH [Carboxylic]) |

Table 5: Antibacterial activity

| S.NO. | Compound | <i>Pseudomonas aeruginosa</i> (mm) | | | | | <i>Staphylococcus aureus</i> (mm) | | | | |
|-------|--|------------------------------------|-------|-------|--------|----------|-----------------------------------|--------|--------|--------|--------|
| | | % | | | | | % | | | | |
| | | 20 | 40 | 60 | 80 | 100 | 20 | 40 | 60 | 80 | 100 |
| 1 | 3APD | - | - | - | - | +(16) | - | - | - | - | - |
| 2 | $[\text{Mn}(3\text{APD})_2(\text{H}_2\text{O})_2]$ | - | - | +(15) | +(20) | ++(23) | - | - | +(16) | +(20) | ++(23) |
| 3 | 4APD | - | +(20) | +(20) | ++(22) | +++ (37) | +(20) | ++(22) | ++(23) | ++(24) | ++(24) |
| 4 | $[\text{Mn}(4\text{APD})_2(\text{H}_2\text{O})_2]$ | - | - | +(17) | +(18) | +(20) | - | - | +(17) | +(20) | ++(22) |
| | Standard | +++ | +++ | +++ | ++++ | ++++ | +++ | +++ | +++ | ++++ | ++++ |

- less activity + 0 to 15mm ++ 15 to 30mm +++ 30 to 45mm ++++ above 45mm

Table 6: Antifungal activity

| Name of compounds | <i>Aspergillus niger</i> | | | | | <i>Candida albicans</i> | | | | |
|--|--------------------------|-----|-----|-----|------|-------------------------|-----|-----|-----|------|
| | 20% | 40% | 60% | 80% | 100% | 20% | 40% | 60% | 80% | 100% |
| L^1 | - | + | + | ++ | ++ | - | - | - | - | + |
| Mn- $\text{L}^1 \cdot 2\text{H}_2\text{O}$ | - | + | + | ++ | ++ | - | - | + | + | ++ |
| L^2 | - | + | + | ++ | ++ | - | - | - | - | + |
| Mn- $\text{L}^2 \cdot 2\text{H}_2\text{O}$ | - | + | + | ++ | ++ | - | + | + | + | ++ |
| Fluconazole | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ |

+ less activity, ++ moderate activity, +++ higher activity

CONCLUSION

The ligands 3-hydroxyphenyl 2,3-Butanedione 3-monoxime (L^1) and 4-hydroxyphenyl 2,3-Butanedione 3-monoxime (L^2) and their Mn(II) complexes had been synthesized and characterized. Both the complexes exhibit octahedral geometry by involvement of azomethine nitrogen and oxime oxygen. Metal complexes as compared to Schiff bases exhibited most potent antifungal activity and antibacterial activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

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