



“Synthesis, Characterization and Biological Importance of Inner Transition Metal complexes of Schiff base Benzilmonoximethiocarbohydrazide derivative”: a Review

Dr. Sharad Sankhe¹, Mr. Pratik Sarvade²

¹ Research Guide & Asst. Prof., Dept. of Chemistry, Patkar-Varde College, Mumbai.

² Ph.D. Scholar, Dept. of Chemistry, Patkar-Varde College, Mumbai.

ABSTRACT

Schiff base with an additional oxime group have been considered as ligand both on account of synthetic flexibility and sensitivity towards metal ion as well as wide range of application ranging from analytical to biological activities. Many biologically important Schiff base complexes of transition and inner-transition metal ions have been reported in the literature possessing antimicrobial, antibacterial, antifungal, anti-inflammatory, antitumor, anti HIV activities, etc. The Schiff bases with sulphur, oxygen and nitrogen donor atoms in their structures act as superior chelating agents for transition, inner transition metal ions.

It has been seen that the ligands containing both oxygen and nitrogen donor atoms behaves as a good building blocks for formation of various lanthanoid co-ordination compounds. The pharmacological properties of N-donor ligands of Schiff bases and their derivatives have attracted worldwide attention in the last few decades because of their wide occurrence in natural products and drugs.

Benzilmonoximehydrazone-p-hydroxybenzaldehyde acts a tridentate ligand coordinating to the metals through the azomethine nitrogen atom, the nitrogen atom of oximino group. The metal complexes will be synthesized in a suitable medium and characterized on the basis of various physicochemical techniques such as Elemental analysis, Solubility in various solvents, Conductance measurements, investigation of UV-Vis, FT-IR, PMR, powder XRD, ESR spectra as may be necessary.

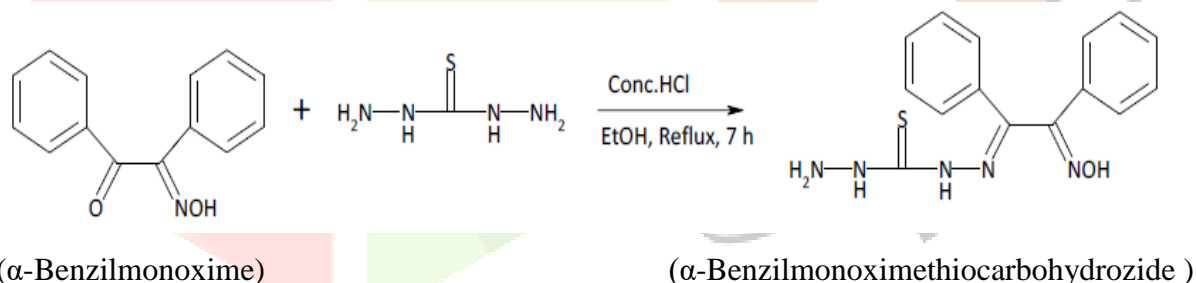
Key Words: Schiff base complexes, biological activities, Azomethine nitrogen, Lanthanoids.

Introduction

In view of this, many literature surveys have been done for Schiff bases derived from the reaction of aldehyde or ketone with amino acid are an excellent class of ligands which have a variety of applications including biological, clinical, industrial, analytical, as well as in catalysis and organic synthesis.[1]. Hydrazone Schiff base complexes are an area of increasing attention, it has been reported that they possess anticarcinogenic, antimicrobial, antitumor activity and anti HIV activities, etc.[2]. This is by no means of an exhaustive review, nor can it be taken as a definitive guide, as the nature of the described. It is, however, hoped that the information provided will permit educated choices of systems to use, and potentially limit the inappropriate use and interpretation of data obtained from these work. In this paper many biologically important Schiff base complexes of transition and inner-transition metal complexes of Benzilmonoximethiocarbohydrazone derivative were studied. The purpose of this review is to study the literature and to understand further scope for Inner Transitions Metal complexes of Benzilmonoximethiocarbohydrazone derivative and its biological importance.

Discussion

1] In the paper 'Synthesis and Characterization of Novel Coordination Compound of Cr (III), Fe (III) with α -Benzilmonoximethiocarbohydrazone.' the α -Benzilmonoximethiocarbohydrazone ligand was prepared by their previous reported work as [3],



The results obtained were as follows:

FTIR spectra:

The band due to $\nu(\text{O-H})$ of oxime group at 3288cm^{-1} , is absent in complexes suggesting the deprotonation of the hydroxyl group of the oxime in the complex formation. The band due to the $\nu(\text{C=N-N})$ of the azomethine group which is observed at 1600cm^{-1} in HBMOTCH is shifted to higher frequency in the region $1650\text{-}1675\text{cm}^{-1}$ in complexes, indicating the participation of the azomethine group in coordination. Also the band at 1580cm^{-1} due to $\nu(\text{C=NO})$ oxime group is observed at a higher frequency at $1603\text{-}1627\text{cm}^{-1}$ in the complexes which shows the involvement of the oxime group in the coordination.

Magnetic susceptibility measurements and Electronic spectra:

The electronic spectra of HBMOTCH ligand shows $\pi \rightarrow \pi^*$ transition in the range 239-251nm are not significantly altered on complex formation. The $n \rightarrow \pi^*$ transitions associated with nitrogen of the azomethine and oxime group in free ligand are found in the range 222nm and 271nm. In the complexes results indicate that the nitrogen atoms of the oxime group are coordinated to the metal ions..

The octahedral complexes of Cr(III) have $(t_{2g})^2$ configuration. It was confirmed by magnetic moments value 3.40 B.M. Fe (III) complex shows a room temperature magnetic moment of 4.93BM , which is higher than the spin only magnetic moment of 4.89BM expected for the four unpaired electrons in high spin Ferrous complexes. However, term for the high spin octahedral complexes of Fe(III) is expected to contribute significantly to the room temperature magnetic moment and the observed moment for most high spin complexes of Fe(III) is expected to be greater than the spin only moment and are often observed in the range between 5.1-5.7BM. Tetrahedral complexes of Fe(III) are expected to reveal moment in the range between 5.00-5.20BM. Where, the orbital contribution to the observed moment is expected to be lower than for octahedral complexes.

¹H NMR Spectra:

The ¹H NMR Spectra of HBMOTCH and its complexes, show the singlet peak due to the N-OH proton at 10.53ppm is absent in complexes, suggesting the deprotonation of the hydroxyl group of the oxime ligand. The bands at 8.00, 8.66 and 7.45-7.95 ppm were assigned to $-\text{NH}_2$, $-\text{NH}-$, phenyl ring respectively in HBMOTCH ligand. These peaks are also observed in complexes without any change in their positions, indicating no participation in coordination.

2] In the paper entitled "Synthesis, Characterization and Physico-chemical Studies of Metal Complexes of Schiff Base derived from p-hydroxybenzaldehyde and benzilmonoximehydrazone"[4] Complexes obtained from the reaction of benzilmonoximehydrazone-p-hydroxybenzaldehyde Schiff base with metal (II) salt of Mn, Cu, Cd, Pd and Zn are stable at room temperature exhibiting variety of colors with good yields.

The results obtained were as follows:

FTIR spectra:

All the complexes absent broad bands in the range of 3200–3300 cm^{-1} , which is reported at 3295 cm^{-1} , in the benzilmonoximehydrazone-p-hydroxybenzaldehyde ligand, indicated oximino group deprotonated during coordination. A sharp band at 1526 cm^{-1} in free the benzilmonoximehydrazone-p-hydroxybenzaldehyde ligand (HL) is due to azomethine $\nu \text{C}=\text{N}-\text{N}-$ vibration. The shifting of this band to lower frequency (1500-1512 cm^{-1}) in the metal complexes suggests the coordination of metal ion through nitrogen atom of azomethine group.

Electronic spectra:

The observed magnetic moment for Mn(II) complex was 5.75 B.M which is observed in the expected range (5.7-6.0 B.M) for a high spin octahedral geometry of Mn(II) complex.

The Cu(II) complexes appear to be in the octahedral geometry. The Pd(II) complex is diamagnetic, therefore the square planar arrangement of the HBMHpHB molecules around Pd(II) is assigned to this complex. The electronic spectrum of this complex shows absorption bands at 325 and 280nm due to the metal-ligand charge transfer transition. The Zn(II) and Cd(II) complexes show high energy band at the region 340-398nm and 265-299nm due to ligand to metal charge transfer transition.

Study of a biological activity:

Six choice species of bacteria were used in this study *K. pneumonia*, *P. aeruginosa*, *E. coli* gram negative and *S. aureus*, *B. subtilis*, *S. typhi* as a gram positive bacteria, in nutrient agar medium against HL ligand and their Mn(II), Pd(II), Cu(II), Cd(II) and Zn(II) complexes.

The Cd(II), Mn(II) and Zn(II) complexes gave a similar zone of inhibition 5mm for all bacterial strains. The Pd(II) and Cu(II) complexes showed more activity against gram positive bacteria than gram negative bacteria. The HL ligand and its Mn(II), Pd(II), Cu(II), Cd(II) and Zn(II) complexes act as potent bacterial agents. Further work with analogs is needed.

3] In the paper "To Study the Biological Activity of Some Inner-Transition Metal Coordination Compounds of Oximino Hydrazones"[5] La(III), Sm(III), Nd(III), Gd(III), Tb(III), Dy(III) complexes of ligand L1 diacetylmonoximehydrazide-*o*-hydroxybenzaldehyde (HDMHoHB), ligand L2 diacetylmonoximehydrazide -*m*-hydroxybenzaldehyde (HDMH*m*HB), and ligand L3 diacetylmonoximehydrazide -*p*-hydroxybenzaldehyde (HDMHpHB) were synthesized and its biological activity study reported.

4] In the paper 'Synthesis and Characterization of Novel Compound derived from α -Benzilmonoximehydrazone with 4,4-dimethylaminobenzaldehyde and its Fe(II), Ni(II) and Pd(II) Complexes'[6-7] data show that metal to ligand ratio is 1:2 corresponding to the general formula ML_2 . They are insoluble in water, soluble in common organic solvents. The low molecular conductance value of the complexes reveals their non-electrolytic nature. High melting points of all metal complexes suggest strong metal-ligand bond.

5] In the paper 'Synthesis and Characterization of Transition Metal Coordination Compound of Oxime Hydrazone'[8-9] novel ligand (1-(2-hydroxyphenyl) ethylidene) hydrazono)-1-phenylpropan-2-one oxime (HHPEHPPPO) have synthesized, characterized first time. Ligand of this type are also known for their antibacterial activity. The synthesized ligand HHPEHPPPO acts as a bidentate or tridentate ligand and have a good chelation ability to yield stable coordination compounds.

6] In the paper 'Synthesis and Characterization of Novel Benziloxime Ligand and its Fe(II) and Ni(II) Complexes' 4,4-dibromobenzilmonoxime (DBBOH) and its complexes $[\text{Fe}(\text{DBBO})_3]$ and $\text{Na}[\text{Ni}(\text{DBBO})_3]$ [10] are described. The ligand (DBBOH) was prepared by MeOH from the reaction of 4,4-dibromobenzil with hydroxylamine hydrochloride in the presence of sodium acetate.

7] In the paper 'Synthesis and Characterization of (1E,2E)-1,2-diphenylethane-1,2-dienehydrazone oxime ligand and its Fe(II) and Pd(II) metal complexes'[11] the reaction of HBMOH with FeSO_4 gave $[\text{Fe}(\text{BMOH})_2]$ as ink blue, PdCl_2 gave $[\text{Pd}(\text{BMOH})_2]$ has green complex respectively. The singlet peak due to the N-OH proton at δ 12.45 in HBMOH is absent in its Pd(II) complex, suggesting the deprotonation of the hydroxyl group of the oxime in the ligand.

8] The paper entitled with 'Synthesis, Characterization and Antimicrobial Studies on Some Trivalent Lanthanide metal complexes with a Bidentate O,N Donor mixed Ligands'[12] a new divalent mixed ligand Schiff base and some lanthanides (III) complexes such as La (III) , Pr(III) , Ce(III) , Nd(III) , Gd(III) , Sm(III) , Dy(III) and Tb(III) complexes were synthesized derived from condensation of salicylaldehyde with 4-methoxyphenylamine and 2-hydroxy-3-methoxybenzaldehyde with 4-methoxyphenylamine in alcoholic medium . The characteristic data of these mixed ligands and lanthanides(III) complexes revealed that ligand coordinates with central lanthanide(III) ions by its two imines nitrogen atom and two phenolic oxygen atom and two water molecule. The general formula of the complex is $[\text{LnL}^1 \text{ and } \text{L}^2(\text{H}_2\text{O})_2 \text{NO}_3]$. The ligand metal complex obtained by (1:1:1) (L^1 : metal : L^2) molar ratio.

9] In the paper 'Synthesis and Characterization of Metal Complexes Schiff base Ligand Derived from Isonitrosoacetophenone and Hydrazine'[13] The complexes of Cr(III) , Mn(II) , Co(II) , Ni(II) Cu(II) , Zn(II) and Cd(II) with Schiff base ligand 1-phenyl-1-1-hydrazoneyl 2- oximino 1,2-ethanedione (HPHOED) have been synthesized *in situ* by the reaction of Isonitrosoacetophenone with Hydrazine sulphate and metal chloride. The complexes have been characterized by various physic-chemical methods. The analytical data corresponds to the general formula $\text{ML}_2 \cdot x\text{H}_2\text{O}$ where L is deprotonated ligand HPHOED, M is a divalent metal ion and x=nil or 2 while Cr(III) complexes of Schiff base ligand can be formulated as $\text{CrL}_2\text{Cl} \cdot \text{H}_2\text{O}$.

10] In the paper 'Antibacterial and Antifungal activities of (1E, 2E)- 1, 2-Diphenylethane-1, 2-Diene Hydrazone Oxime ligand and its Zn(II), Cd(II) and Hg(II) metal complexes'[14-15] Antibacterial activities of synthesized compounds were studied against six human pathogenic bacteria, viz. E. coli(G-), S. aureus(G+), S. typhi(G+), B. subtilis(G+), K. pneumoniqe(G+), P. aeruginosa(G+) . For the detection of antibacterial activities, the agar cup method. Nutrient agar (NA) was used as basal medium for test bacteria and Minimum Inhibitory Concentration (MIC) were determined against all six bacteria. Antifungal activities of synthesized compounds towards five plant pathogenic and mould fungi were studied, viz. *Colletotrichum Gloeosporiodes penz*, *Canilida Albicans*, *Aspergillus Niger*, *Aspergillus*

Flaves and *penicillium sp.* Antifungal activity was assessed by the poisoned food technique in a modified condition.

11] In the reported work of Chu et al. 'Synthesis and Biological Studies of Some Lanthanide Complexes of Schiff Base primary ligand in complexes'[16] is isoniazid furalcylylhydrazone(FLSY) and secondary ligand is sodium salicylate which is not only an important drug intermediate but also may increase the biocompatibility of these complexes. The DNA-binding and photo -cleavage properties are also investigated.

12] In the paper "Synthesis, Characterisation, and Biological Activity of Pd(II), Zn(II), Cd(II), and Hg(II) Metal Coordination Compounds of (4-(dimethylamino)benzylidene)hydrazono)butan-2-one oxime" [17] antimicrobial activity of the test compounds done by three methods viz. ditch plate method, plug diffusion method and cup diffusion method . [Cd(DABHBO)₂] and [Hg(DABHBO)₂] coordination compound showed biological activity towards *Escherichia coli*, *Staphylococcus aureus*, *Corynebacterium diphtheriae* and *Pseudomonas spp.* [Pd(DABHBO)₂] was biologically active towards *Staphylococcus aureus*, and *Corynebacterium diphtheriae*.

Conclusion:

From the above discussion, it is learnt that,

1] The stoichiometric reaction between HBMOTCH and metal salts [CrCl₃.6H₂O, FeCl₃] has yielded to monomeric complexes [Fe(BMOTCH)₃]. The title ligands is soluble in most of the organic solvents and dilute alkali, but its ternary metal complexes are insoluble in ethanol, dilute alkali and soluble in methanol, chloroform, DMF etc. All metal complexes are non-electrolytic nature. The ligand coordinates through its oximino and azomethine nitrogen atoms to the metal ions and acts as a neutral bidentate ligand. All complexes are non-electrolyte , high thermal stability and strong metal-ligand bond. On the basis of spectral and magnetic moment analysis, Fe(II) and Ni(II) complexes are high spin octahedral and Pd(II) is square planar geometry. The ligand coordinates through azomethine nitrogen , oxime nitrogen and phenolic oxygen in Co(II) , Ni(II) and Cu(II) complexes.

2] The preferred coordination number of Ln(III) metal ion is 7. All synthesized ligands and their lanthanide complexes shows remarkable biological activity over a certain range of concentrations towards specific pathogen.

3] The analysis of IR , ¹H- and ¹³ C-NMR spectral data of Fe(III) and Ni(II) complexes suggest that 4,4'-dibromobenzilmonoximate is bonded to Iron (III) and Ni(II) ions through the oxygen atom of the carbonyl, and the nitrogen atom of the imine groups. The Electronic spectral data the complexes in CHCl₃ are in good agreement with the octahedral coordination of Fe(III) and Ni(II) ions.

4] A significant feature of the IR spectrum of α-benzilmonoximehydrazone is the absence of band between 1720- 1680cm⁻¹ due to the νC = O vibration reported¹¹ at 1715cm⁻¹ in α-benzilmonoxime

indicating a successful replacement of the carbonyl oxygen by the hydrazone group during Schiff base formation. The spectral and magnetic data suggests that Fe(II) complex is high spin octahedral and Pd(II) complex is square planar geometry.

5] The newly synthesized ligand and mixed ligand metal complex like La(III) , Ce(III) , Pr(III) , Nd(III) , Sm(III) , Gd(III) , Dy(III) and Tb(III) complexes with bivalent N & O donor Schiff base ligand derived from 4-methoxyphenylalanine, Salicylaldehyde and 2-hydroxy-3-methoxybenzaldehyde were synthesized. The obtain by antimicrobial , antifungal activity indicates that the antifungal are highly active *Aspergillus Niger* at 500 ppm and at 250 ppm against *Fusarium Oxysporum* than that of antibacterial activity. All the complexes are low molar conductivity in nature. The x-ray diffraction study indicates that monoclinic crystal system for La(III) , Ce(III) complex and orthorhombic crystal system for Pr(III) , Nd(III) , , Gd(III) , Dy(III) and Tb(III) complexes and tetrahedral crystal system for Sm(III) complex.

6] Ligand HPHOED acts as a monobasic bidentate ligand, which lose oximino proton during formation of Schiff base complexes which is supported by infrared spectra. Electronic spectra & magnetic susceptibility measurement reveals octahedral geometry for Cr(III), Mn(II), Co(II), Ni(II), Zn(II) and Cd(II) complexes and square planar geometry for Cu(II) complexes.

7] Schiff base compounds and their metal complexes are very important as catalysts in various biological systems, polymers , dyes, medicinal and pharmaceutical field.

8] It has been concluded from this review that the lanthanides complexes with particular organic compounds can contribute the best in the development of new therapeutic agents. This review can be helpful to develop the drug/medicine for particular diseases caused by particular bacterial and/or fungal species.

References:

- 1] Anand Prakash , Devjani Adhikari, International journal of ChemTech Research , Vol. no.4 , 1891-1896, **2011**.
- 2] Prashant S. kamble PhD. Thesis; Mumbai University; **2019**.
- 3] Prashant S. kamble , Raj R. Badekar and Vinay H. Singh , International Journal of Research and Analytical Reviews, Volume 5, Issue 3, 910-913, **2018**
- 4] Nazar A Jafry ,Sharad Sankhe , Uttam Yadav ,Prashant Kamble, International Journal of Creative Research Thoughts, Volume 9, Issue 10, **2021**.
- 5] Sharad Sankhe, Sainath Bhavsar, Prashant S. Kamble, International Journal of All Research Education and Scientific Methods , Volume 9, Issue 10, October -**2021**.

- 6] Suryabhan Chaugule, Raj Badekar, Pradip Shimpi, Rama Lokhande , International Journal for Research in Applied Science & Engineering Technology, Volume 6,1233-1237, **2018**
- 7] Grey W.J.; Coord. Chem. Rev.; 7 81, **(1971)**.
- 8] Sharad S. Sankhe and Prashant S. Kamble , International Journal for Research in Applied Science & Engineering Technology, Volume 5 Issue IX,371-375, **2017**
- 9] S B Padhye and G B Kuffmann. Coordination Chemistry Reviews **(1985)**
- 10] Esmail Soleimani, Journal of Chinese Chemical Society, 57,332-337, **2010**.
- 11] Raj R. Badekar, R. S. Lokhande , S. W. Kulkarni, and R. M. Patil, Int.J.Adv.Res. 4(8), 796-800.**2016**.
- 12] V D Ingale , N R Dighore , A S Rajbhoj , S T Gaikwad , International journal of science and Research , Vol 4 issue 8, 1003-1009 , **2015**.
- 13] Jyoti v Patil and N B Laxmeshwar , Asian journal of chemistry, Vol.26, Suppl. Issue, S163-S166, **(2014)**.
- 14] Badekar R. R.; PhD. Thesis; Jaipur National University; **2017**.
- 15] Raj Badekar , Amol Thube, Santosh Kulkarni, and Rama Lokhande, International Journal for Research in Applied Science & Engineering Technology , Volume 6 Issue VI, **2018**.
- 16] Lian-Feng Chu, Yang Shi, Dong-Fang Xu, Hui Yu, Synthesis and Reactivity in Inorganic , Metal-Organic, and Nano-Metal Chemistry45, 1617-1626, **(2015)**.
- 17] Prashant S Kamble and Sharad S Sankhe , Journal of Emerging Technologies and Innovative Research , Volume 5, Issue 8 , 677-682 and 964-970, **2018**.