

Synthesis, Characterization and Biological Activity of Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) Complexes of Tridentate Thiosemicarbazones

M. ADHARVANA CHARI^{1,2,*}, D. SHOBHA², K.M.M.S. PRAKASH² and K. SYAMASUNDAR¹

¹Department of Chemistry, Jawaharlal Nehru Technological University, Kukatpally, Hyderabad-500 072, India

²Dr. MACS Bio-Pharma Pvt. Ltd., Plot-32/A, Western Hills, Kukatpally, Hyderabad-500 085, India

*Corresponding author: Fax: +91 40 40206647; E-mail: drmac_s@yahoo.com

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Metal complexes of divalent *d*-block metal ions with different thiosemicarbazones have been synthesized. These thiosemicarbazone ligands forms complexes with iron(II), cobalt(II), nickel(II), copper(II), zinc(II), cadmium(II) and mercury(II). The structural study of the complexes have been characterized by elemental analysis, conductance, IR, NMR and Mass spectral data. The physico-chemical and spectral data suggests octahedral and tetrahedral geometry for various complexes. The ligand and metal chelates have been screened *in vitro* for antimicrobial activity against some of the fungal and bacterial. The screening have revealed that metal complexes exhibit enhanced activity than their parent ligand-against both the fungal and bacterial strains used.

Key Words: Divalent metal ions, Tridentate azomethine ligand, Oxime-thiosemicarbazones, Synthesis, Metal chelates.

INTRODUCTION

Thiosemicarbazone metal chelates have broad applications in biological and industrial fields¹⁻⁴. Thiosemicarbazone and their metal chelates find important applications in the fields like pharmacology as well as medicine⁵⁻⁶. It is observed that biological activity of ligand increases on complexation with different metal ions. Metal complexes of ligands containing both oximes and thiosemicarbazones are pharmacophores much less investigated. In view of this the synthesis, characterization, antibacterial and antifungal studies of Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) complexes of biacetylmonoxime thiosemicarbazone (BAMOT) and 4-methylbiacetylmonoxime thiosemicarbazone (MBAMOT) are reported.

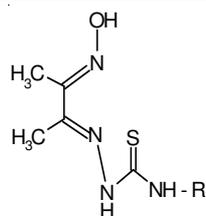
EXPERIMENTAL

All chemicals and solvents used were of A.R. grade. The elemental analysis were performed at HCU, Hyderabad by using micro analytical techniques. Metals are estimated by using AAS model Z-6100 (Hitachi Ltd.,). Chlorine is estimated by using standard procedure⁷. The IR spectra were recorded in the range 4000 - 200 cm⁻¹ using KBr discs with Perkin-Elmer model 1430 and 337. The electrical conductivity measurements were made in DMF (10⁻³ M) at room temperature (27 ± 2 °C) using a Digisun digital conductivity meter (DI-909 model). The NMR spectra were recorded in DMSO-*d*₆ on

NMR spectrophotometer model JEOL Ex-90 FT using TMS as the reference. The mass spectra of the ligand and metal chelates were recorded using VG autospec. Mass spectrometer operating under liquid secondary ion mass spectral (LSIMS) conditions. In a 100 mL round-bottomed flask, the corresponding ligand⁸ (50 mmol) was taken in methanol (50 mL) and to each of this was added thiosemicarbazide (4.55 g, 50 mmol) in a mixture of 50 mL water and 10 mL glacial acetic acid. The reaction mixture was boiled under reflux for 2 - 4 h. The reaction mixture was cooled and the compound obtained was recrystallized from methanol. Pure white needles of BAMOT and MBAMOT was obtained. Metal complexes were prepared by mixing hot aqueous solution of hydrated metal salts and ligand in the molar ratio of 1: 1 (metal being in slight excess). To the boiling solution of ligand (10 mmol) in methanol (100 mL) was added to hydrated metal salts (10 mmol) dissolved in minimum quantity of water and heated under reflux for 1-2 h in the neutral conditions. Crystalline complexes which separated out were collected by filtration washed with hot water, small quantity of methanol and hexane dried *in vacuo*.

RESULTS AND DISCUSSION

All the metal complexes are stable at room temperature non-hygroscopic, sparingly soluble in methanol or ethanol and fairly soluble in DMF and DMSO. The analytical data for both thiosemicarbazones and their metal chelates are consistent with



R = H (BAMOT) or CH₃ (MBAMOT)

their proposed molecular formulae. The molar conductivity data (Table-1) of Fe, Co, Ni, Cu, Zn, Cd and Hg complexes of BAMOT and MBAMOT indicates that all the metal complexes are electrolytes⁹ and are monomers. The presence of chloride is evident only after the chemical decomposition of metal complexes suggesting the presence of chloride in the complex. The magnetic moment values indicate the paramagnetic nature for Fe, Co, Ni, Cu complexes. The magnetic moment values are observed as zero for Zn, Cd and Hg complexes and thus show the diamagnetic nature of these complexes.

The magnetic moment value of [Fe(BAMOT)(H₂O)₂]₂SO₄ and [Fe(MBAMOT)(H₂O)₂]₂SO₄ is observed as 4.8 and 4.9 BM, which is in good agreement with the reported value of high spin octahedral Fe(II) complexes¹⁰. The magnetic moment value is obtained for [Co(BAMOT)(H₂O)₂]₂Cl₂ is 4.88 and for [Co(MBAMOT)(H₂O)₂]₂Cl₂ is 5.0. In the present study, the μ_{eff} value of these complexes indicates the paramagnetic in nature such an observation confirms the Co(II) in high spin octahedral

environment. The actual μ_{eff} value for octahedral complexes depends upon the extent of orbital angular momentum contribution associated with the ⁴T_g ground state and the values usually lie in the range 4.7-5.2 BM¹¹. Generally octahedral complexes show magnetic moment value in the range 2.9-3.4 BM depending on the magnitude of orbital contribution. In the present study the μ_{eff} values of Ni(BAMOT)₂Cl₂ and Ni(MBAMOT)₂Cl₂ are found to be in good agreement with the reported values of tetrahedral geometry¹². The magnetic moment values of Cu(BAMOT)₂Cl₂ and Cu(MBAMOT)₂Cl₂ are in good agreement with the reported value of tetrahedral geometry¹³. The magnetic moment values of BAMOT and MBAMOT complexes of iron, cobalt are in good agreement with octahedral geometry and Ni, Cu are with tetrahedral geometry.

IR spectra: The ligand IR bands around at 3400 and 3290 cm⁻¹ are assigned to the asymmetric and symmetric stretching of free NH₂ group. These bands remained unaltered in the spectra of the complexes, which indicate non-participation of NH₂ in coordination¹⁴. A strong band appearing at 1175 and 1134 cm⁻¹ in the spectra of BAMOT and MBAMOT is shifted to lower frequency indicating the involvement of thio-keto sulphur in coordination. A strong band observed at 3420 and 3410 cm⁻¹ in the IR spectra of BAMOT and MBAMOT disappeared in the spectra of all complexes suggesting deprotonation of oxime OH in the complex formation. The >C=N (imine band) is observed at 1600 and 1615 cm⁻¹ in the

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF THE LIGANDS (BAMOT, MBAMOT) AND THEIR METAL CHELATES

Ligand/complex (yield (%)/colour)	m.p. (°C)	m.w.	Magnetic momentum (B.M.)	Conductance (mhos cm ² mol ⁻¹)	Element analysis (%): Found (calcd.)				
					C	H	N	M	Cl
BAMOT (90/Yellowish white)	165	174.0	–	–	34.96 (35.00)	4.86 (5.10)	31.80 (32.20)	–	–
[Fe(BAMOT)(H ₂ O) ₂] ₂ SO ₄ (70/Reddish)	235-237	625.7	4.8	35.0	19.10 (19.16)	4.12 (4.15)	17.80 (17.89)	17.78 (17.80)	–
[Co(BAMOT)(H ₂ O) ₂] ₂ Cl ₂ (65/Reddish)	232-235	607.0	4.88	45.0	19.73 (19.76)	4.25 (4.28)	18.36 (18.40)	19.37 (19.41)	11.60 (11.60)
[Ni(BAMOT)] ₂ Cl ₂ (60/Light green)	220-222	534.4	3.5	25.0	22.45 (22.50)	3.38 (3.41)	20.89 (20.91)	21.88 (21.92)	12.97 (13.21)
[Cu(BAMOT)] ₂ Cl ₂ (85/Green)	189-191	544.0	2.0	48.0	22.00 (22.05)	3.20 (3.30)	20.50 (20.58)	23.25 (23.35)	12.90 (13.05)
[Zn(BAMOT)] ₂ Cl ₂ (75/Light yellow)	240-242	547.8	–	20.0	21.87 (21.92)	3.27 (3.31)	20.39 (20.45)	23.81 (23.84)	13.12 (13.0)
[Cd(BAMOT)] ₂ Cl ₂ (80/Yellow)	250-252	641.8	–	25.0	18.69 (18.72)	2.90 (2.87)	17.48 (17.51)	35.25 (35.32)	11.91 (11.10)
[Hg(BAMOT)] ₂ Cl ₂ (85/Dark yellow)	264-268	818.2	–	33.0	14.68 (14.71)	2.19 (2.23)	30.68 (30.73)	49.07 (49.13)	8.69 (8.71)
MBAMOT (75/Light yellow)	172	188.0	–	–	38.18 (38.20)	6.38 (6.43)	29.80 (29.82)	–	–
[Fe(MBAMOT)(H ₂ O) ₂] ₂ SO ₄ (65/Reddish)	239-241	653.7	4.9	28.0	21.90 (22.00)	4.53 (4.58)	17.06 (17.10)	17.05 (17.10)	–
[Co(MBAMOT)(H ₂ O) ₂] ₂ Cl ₂ (62/Reddish)	236-238	634.8	5.0	45.0	22.58 (22.60)	4.69 (4.70)	17.48 (17.50)	18.45 (18.50)	11.18 (11.20)
[Ni(MBAMOT)] ₂ Cl ₂ (60/Light green)	224-226	562.4	3.7	24.0	25.58 (25.60)	3.87 (3.90)	19.86 (19.90)	20.85 (20.90)	12.56 (12.60)
[Cu(MBAMOT)] ₂ Cl ₂ (80/Light green)	193-195	572.1	2.1	50.0	25.09 (25.10)	3.77 (3.80)	19.58 (19.60)	22.18 (22.2)	12.35 (12.40)
[Zn(MBAMOT)] ₂ Cl ₂ (70/Light yellow)	244-246	575.8	–	24.0	24.97 (25.00)	3.77 (3.80)	19.38 (19.40)	22.67 (22.70)	12.18 (12.30)
[Cd(MBAMOT)] ₂ Cl ₂ (75/Yellow)	254-256	670.0	–	30.0	21.46 (21.50)	3.17 (3.30)	16.68 (16.70)	33.46 (33.50)	10.58 (10.60)
[Hg(MBAMOT)] ₂ Cl ₂ (80/Dark yellow)	268-270	846.0	–	32.0	16.95 (17.00)	2.46 (2.50)	13.17 (13.20)	47.36 (47.40)	8.34 (8.40)

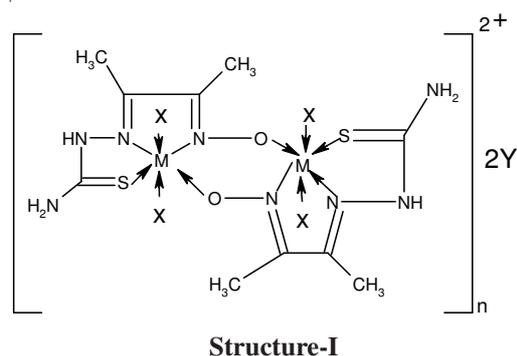
IR spectra of BAMOT and MBAMOT respectively. These peaks are shifted by 10-20 cm^{-1} in the metal chelates indicating coordination through azomethine nitrogen¹⁵. The appearance of strong and broad bands at 3500-3400 cm^{-1} region suggest the presence of coordinated water molecules for Fe(II) and Co(II). The bands at 830-800 cm^{-1} region are assigned to wagging modes of water molecules in Fe(II) and Co(II) complexes. Additional bands are observed in far IR spectra of metal complexes at 500-485 cm^{-1} and 360-340 cm^{-1} regions due to $\nu(\text{M-N})$ and $\nu(\text{M-S})$ modes respectively and these absorptions support the coordination^{4,8} of azomethine nitrogen and thio enol sulfur.

NMR spectra: The study of the NMR spectrum of Cu, Zn, Cd and Hg metal chelates illustrates the presence of methyl protons ligand moiety, NH_2 protons of thiosemicarbazide moiety, N-H imino protons and C-methyl protons. The NMR spectrum of ligand shows different signals at δ 10.45 (imino protons), δ 7.53 ppm (NH_2 protons) of thiosemicarbazide moiety⁸ and a singlet at δ 2.48 ppm corresponds to C-methyl. These signals are not changed in the nmr spectra of the metal complexes. The nmr spectrum of metal chelates confirms the non participation of NH_2 group and imino NH group in the coordination with metal ions.

Mass spectra: The mass spectrum of ligand and metal complexes is recorded under liquid secondary ion mass spectral conditions¹⁶⁻¹⁸. The ligands BAMOT and MBAMOT are gave the peaks at m/z 166 and 173 Da_1 and these values confirms the molecular weight of the ligands.

The LSIM spectrum of the Fe complex of BAMOT ligand showed abundant ions at m/z 175 and 626 are corresponding to ligand and metal chelate *i.e.*, $[(\text{ligand} - \text{H})]^+$ and $[(2 \text{ ligand} + 2\text{Fe} - 2\text{H})]^+$ respectively. This ion is resulted from the complex by the decomposition process to get a species with one charge because mono positive ion only detected under the mass spectral conditions. The ion at 627 having more abundance than other peaks which supports $[\text{ML}]_2\text{X}_2$ composition. The LSIM spectrum of the Fe complex of MBAMOT ligand showed abundant ions at m/z 189 and 655 along with the characteristic isotopic clusters of iron atom. The peak corresponding to the complex at m/z 189 is due to ligand and 655 is due to metal chelate *i.e.*, $[(2 \text{ ligand} + 2\text{Fe} - 2\text{H})]^+$ ion. The ion at 655 having more abundance than other peaks, which supports $[\text{ML}]_2\text{X}_2$ composition. The LSIM spectrum of the Co complex of BAMOT ligand showed abundant ions at m/z 175 and 608 are corresponding to ligand and metal chelate *i.e.*, $[(\text{ligand} - \text{H})]^+$ and $[(2 \text{ ligand} + 2\text{Co} - 2\text{H})]^+$ ions respectively. The ion at 608 having more abundance than other peaks which supports $[\text{ML}]_2\text{X}_2$ composition. The LSIM spectrum of the Co complex of MBAMOT ligand showed abundant ions at m/z 189 and 636. The peak corresponding to the complex at m/z 189 is due to ligand and 636 is due to metal chelate *i.e.*, $[(2 \text{ ligand} + 2\text{Co} - 2\text{H})]^+$ ion. The ion at 636 having more abundance than other peaks which supports $[\text{ML}]_2\text{X}_2$ composition. In the LSIM spectrum of the nickel complex of BAMOT ligand showed abundant ions at m/z 175 and 536 corresponding to $[(\text{L} - \text{H})]^+$ and $[(2\text{L} + 2\text{Ni} - 2\text{H})]^+$ ion. The LSIM spectrum of the Ni complex of MBAMOT ligand showed abundant ions at m/z 189 and 564 corresponding to $[(\text{L} - \text{H})]^+$ and $[(2\text{L} + 2\text{Ni} - 2\text{H})]^+$ ion. The ion at 564 having more abundance than

other peaks which supports $[\text{ML}]_2\text{X}_2$ composition. In the LSIM spectrum of the copper, zinc, cadmium and mercury complexes of BAMOT ligand showed abundant ions at m/z 175 and 545, 549, 643, 819 corresponding to $[(\text{L} - \text{H})]^+$ and $[(2\text{L} + 2\text{M} - 2\text{H})]^+$ ions. The LSIM spectrum of the copper, zinc, cadmium and mercury complexes of MBAMOT ligand showed abundant ions at m/z 189 and 573, 577, 671, 847 corresponding to $[(\text{L} - \text{H})]^+$ and $[(2\text{L} + 2\text{M} - 2\text{H})]^+$ ions. The ions supports $[\text{ML}]_2\text{X}_2$ composition. On the basis of physicochemical and spectral data the metal chelates plausible **structure I** may be given as follows. Octahedral geometry is suggested for Fe(II) and Co(II) complexes. For other metal ions tetrahedral geometry is proposed.



where, X = water molecule present in Fe(II), Co(II) complexes; M = Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II); Y = $\frac{1}{2}\text{SO}_4$ in Fe(II); chloride ion in Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) complexes.

Biological activity: The ligands BAMOT, MBAMOT and their metal complexes were screened for their antifungal and antibacterial activity¹⁹ against some of the pathogenic fungi and bacteria *viz.* *Bacillus subtilis*, *E. schochia* and *Aspergillus niger*. The results of investigation have been presented in Table-2 and observed that the metal complexes showed more biological activity than the corresponding ligands.

TABLE-2
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES OF LIGANDS
(BAMOT, MBAMOT) AND THEIR METAL CHELATES

Compound	Zone of inhibition (mm)		
	<i>B. subtilis</i> (Gr. +ve)	<i>E. coli</i> (Gr.-ve)	<i>A. niger</i>
BAMOT	100	90	80
[Fe(BAMOT)(H ₂ O) ₂] ₂ SO ₄	70	0	0
[Co(BAMOT)(H ₂ O) ₂] ₂ Cl ₂	190	150	120
[Ni(BAMOT)] ₂ Cl ₂	100	90	80
[Cu(BAMOT)] ₂ Cl ₂	190	150	120
[Zn(BAMOT)] ₂ Cl ₂	170	160	160
[Cd(BAMOT)] ₂ Cl ₂	180	150	154
[Hg(BAMOT)] ₂ Cl ₂	200	185	162
MBAMOT	100	80	85
[Fe(MBAMOT)(H ₂ O) ₂] ₂ SO ₄	90	75	80
[Co(MBAMOT)(H ₂ O) ₂] ₂ Cl ₂	110	85	75
[Ni(MBAMOT)] ₂ Cl ₂	100	100	90
[Cu(MBAMOT)] ₂ Cl ₂	150	130	130
[Zn(MBAMOT)] ₂ Cl ₂	140	120	120
[Cd(MBAMOT)] ₂ Cl ₂	150	120	130
[Hg(MBAMOT)] ₂ Cl ₂	190	130	130

In summary, the ligands biacetyl-monoxime thiosemicarbazone (BAMOT), 4-methyl biacetylmonoxime thiosemicarbazone (MBAMOT) and their *d*-block complexes were synthesized. All the metal(II) complexes plausible structures are supported by LSI mass spectral data along with physico-chemical and IR, NMR spectral data. The ligands and their complexes were screened for their antifungal and antibacterial activity against some of the pathogenic fungi and bacteria and observed that the metal complexes are showed more biological activity than ligands. The authors have developed a simple, convenient and effective method for the synthesis of complexes.

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