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GREEN AND CONVENTIONAL SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL STUDIES OF SOME NEW MN (II) COMPLEXES DERIVED FROM N⌒O AND N⌒S DONOR AZOMETHINES

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Abstract

Series of new Mn (II) complexes of biologically potent (N⌒O and N⌒S) donor azomethines are synthesized by classical thermal and microwave-irradiation techniques and characterized by the elemental analysis, IR, UV and EPR spectral and X-ray powder diffraction studies. The azomethine ligands have been prepared from the condensation of 2-acetyl-5-methyl furan and 3-acetyl coumarin with semicarbazide hydrochloride and thiosemicarbazide in 1:1 molar ratio, respectively. The Mn (II) complexes of azomethine ligands have been prepared by mixing $MnCl_2.4H_2O$ *in 1:1 and 1:2 molar ratios with azomethine ligands (*L^1H, L^2H, L^3H *and* L^4H*) in methanol. The synthesized ligands and their new metal complexes have also been screened for biological activity.*

The spectral data suggested that complexes have tetra-coordinated environment around the central metal ion. Thus tetrahedral geometry of the said complexes has been proposed.

Keywords: Schiff base ligands, Transition metal complexes, antifertility activity, cyclic voltametric study, Microwave-assisted synthesis.

1.INTRODUCTION

Environmental concerns in research, academia and industries are increasing with the increasing pressure of pollutants in atmosphere. This requires a new approach, which will minimize or eliminate the dispersion of harmful chemicals in the environment in a way that enhances the industrially benign approach and meets the challenges of green chemistry (Chanshetti, 2014). Microwave chemistry is the science of applying microwave irradiation to chemical reactions (Gude et al. 2013). This implies a considerable saving in energy (Yamgar et al. 2014).

In recent years, transition metal complexes of Schiff bases containing oxygen, sulfur and nitrogen donar atoms have received great attention as a consequence of their biological properties (Sirajuddin et al. 2014). Many of the metal complexes of Schiff base ligands containing N⌒O and N⌒S donor atoms, such as semicarbazones thiosemicarbazones and their metal chelates have been found to exhibit fungicidal, bactericidal, antiviral, and antitubercular activities and their abilities to coordinate with the transition metal ions, it is highly desirable to synthesize and characterize the transition metal complexes with such Schiff base ligands (Maurya et al. 2010).

Therefore, in the present investigation some potent N⌒O and N⌒S donar azomethines and their Mn (II) complexes have been synthesized, characterized and screened against a variety of pathogenic fungal and bacterial strains.

2. EXPERIMENTAL

2.1. Methods and instrumentation

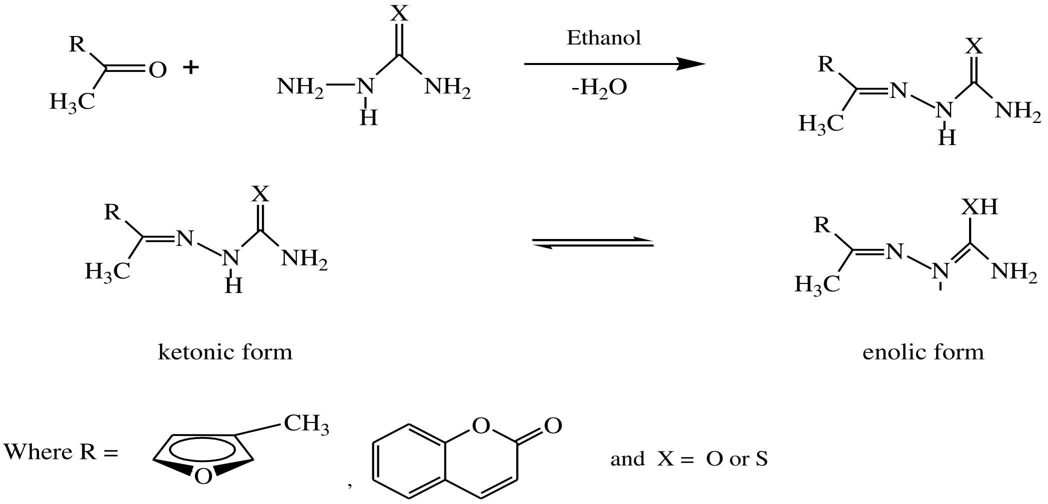
All the chemicals and reagents were used of AR grade and dried and distilled before use. The $MnCl_2.4H_2O$ was purchased from Alfa Aesar. 2-Acetyl-5-methyl furan, 3-acetyl coumarin (Sigma Aldrich) semicarbazide hydrochloride and thiosemicarbazide (Spectrochem) were purchased and used as such. Apparatus fitted with Quickfit interchangeable joints was used to carry out the reactions under completely anhydrous conditions. The molecular weights were determined by the Rast Camphor method (Vogel, 2004). The metal contents were analyzed gravimetrically. Sulfur and nitrogen were determined by Messenger's (Vogel, 2006) and Kjeldahl's methods (Vogel, 2000) respectively. Carbon and hydrogen analyses were performed at the CDRI, Lucknow. Infrared spectra were recorded on a Perkin elmer FTIR-spectrum two spectrophotometer using KBr pellets. The electronic spectra and were recorded on a Shimadzu UV-2450 spectrophotometer at SAIF, IIT, Madras. EPR spectra of the complexes were recorded on Varian E-4X band spectrometer at SAIF, IIT Madras.

2.1.1. Preparation of the azomethine ligands (L^1H, L^2H, L^3H and L^4H)

Two different routes were used for the synthesis of azomethine ligands (L^1H, L^2H, L^3H and L^4H)

(A) Microwave method: In microwave assisted synthesis of the ligands, 2-acetyl-5-methyl furan hydrazine carboxamide (L^1H), 3-acetyl coumarin hydrazine carboxamide (L^2H), 2-acetyl-5-methyl furan hydrazine carbothioamide (L^3H) and 3-acetyl coumarin hydrazine carbothioamide (L^4H) were obtained by the condensation of 2-acetyl-5-methyl furan and 3-acetyl coumarin with semicarbazide hydrochloride (in presence of sodium acetate) and thiosemicarbazide in 1:1 molar ratio using microwave oven by taking 5 mL ethanol as solvent, respectively. The reactions were completed in a short period of 10–12 min. The solution was then concentrated under reduced pressure, which on cooling gave dark yellow/whitish creamy/creamy colored crystalline precipitates (80-94 % yield). These were washed and recrystallized in alcohol.

(B) Thermal method: Above mentioned ligands were synthesized by conventional thermal method to compare with microwave synthesis. 2-Acetyl-5-methyl furan and 3-acetyl coumarin was mixed separately with hot ethanolic solution (30 mL) of semicarbazide hydrochloride (in presence of sodium acetate) and thiosemicarbazide in 1:1 molar ratio. The contents were refluxed for about 3–4 hrs on a water bath. The solution was then concentrated under reduced pressure, which on cooling gave dark yellow/whitish creamy/creamy colored crystalline precipitates (65-77 % yield). These were washed and recrystallized in alcohol.



2.1.2. Preparation of the complexes

The metal complexes of the synthesized ligands were prepared by both thermal and microwave method.

Manganese chloride tetrahydrate ($MnCl_2.4H_2O$) in dry methanol was mixed with a methanolic solution of the ligands (L^1H, L^2H, L^3H and L^4H) in 1:1 and 1:2 molar ratios. The reaction mixture was subjected under both energy sources; thermal as well as microwave. The reaction mixture was refluxed for 8-10 hours in thermal method and for 7-9 minutes in microwave method. The thermal method required a large amount of solvent ~50 mL but the microwave method required only ~5 mL of solvent as reaction media. The resulting mixture was then concentrated under reduced pressure. The resulting compounds were washed with methanol followed by drying in *vacuum* for about one hour to get the final products. The monomeric nature of these products has been confirmed by the molecular weight determinations

2.2. Biological activity

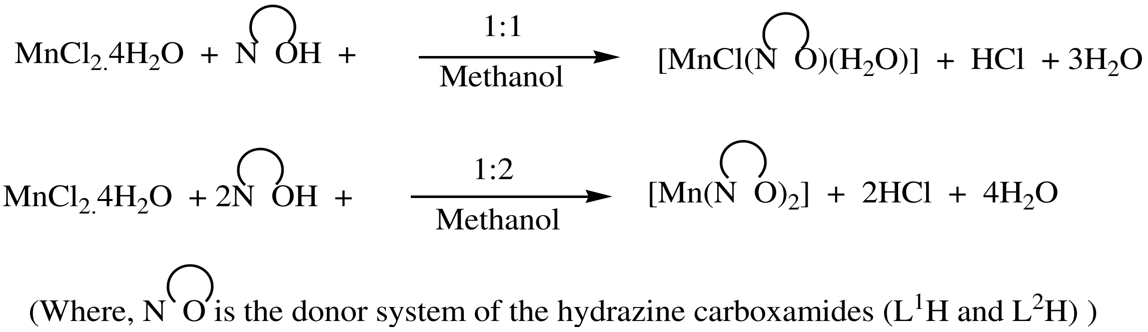
2.2.1 Determination of minimum inhibitory concentration (MIC)

Minimum Inhibitory Concentration, MIC, is the lowest concentration of test agent that inhibited visible growth of bacteria after 24 hrs incubation at 37°C. The determination of the MIC involves a semi quantitative test procedure, which gives an approximation to the least concentration of an antimicrobial needed to prevent microbial growth. The minimum inhibitory concentration was determined by liquid dilution method (Vogel, 2000).

Stock solutions of Mn(II) complexes with 5-50 µg/mL concentrations were prepared with aqueous methanol as solvent. Inoculum of the overnight culture was prepared. In a series of tubes, 1mL of each of Mn (II) complex solution with varying concentration were taken in a series of tubes & top up with 0.5 mL of the inoculum. Further 5 mL of the sterile water was added to each of the test tubes. These test tubes were incubated for 24 hrs and observed for the presence of turbidity.

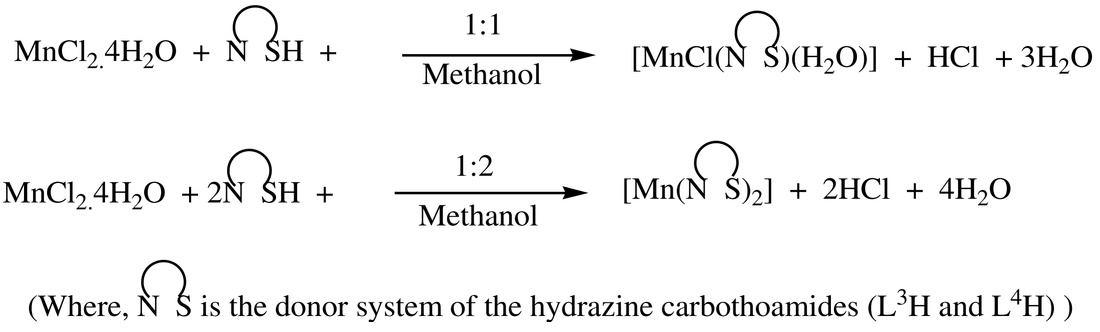
3.RESULTS AND DISCUSSION

The elemental analysis and spectral data are consistent with the formulation of compounds as [MnCl(L)(H_2O)] and [Mn$(L)_2$]. Molecular weight determinations indicate their monomeric nature is shown in Table 1. The reactions proceed as shown in (Scheme 1 and 2).



(Where, N O is the donor system of the hydrazine carboxamides (L^1H and L^2H))

Scheme 1



(Where, N S is the donor system of the hydrazine carbothoamides (L^3H and L^4H))

Scheme 2

Metal complexes were prepared by both microwave and conventional methods. The reaction time is brought from hours to seconds and a small amount of solvent is required in microwave method.

Enhancement in the yield of the resulting products is also observed under microwave exposure (Singh et al. 2009).

3.1. Infrared spectral analysis

A comparison of the characteristic IR absorption bands of the ligand with those of the corresponding metal complexes reveals important features for establishing the facts that the ligands (L^1H, L^2H, L^3H and L^4H) behave as monofunctional bidentate as $N^{\cap}O$ and $N^{\cap}S$ donor for bonding to the metal atom. The broad band due to νNH vibrations disappears in the spectra of manganese (II) complexes, indicating the deprotonation of this group on coordination with the metal atom (Sumrra et al. 2014). The IR spectra of the ligands (L^1H, L^2H, L^3H and L^4H), display absorption bands at 1620-1600 cm^{-1}, 1720-1710 cm^{-1} and 1035-1040 cm^{-1} which are assigned to ν(>C=N), ν(>C=O) and ν(C=S), respectively. These bands shift at lower frequency in the spectra of metal complexes, indicating the coordination of the azomethine nitrogen, ketonic-oxygen and thiolic sulfur atom to the manganese (II) atom. In the spectra of the ligand, L^5H & $L^{10}H$ the band at 1720 cm^{-1} is assigned to ν(C=O) of the lactone moiety. This band remains unchanged in the spectrum of metal complex indicating that the lactone oxygen is not involved in coordination. The spectra of the ligands display two sharp bands around 2850-2910 cm^{-1} and 3400-3350cm^{-1} assignable to ν_{sym} and ν_{asym} vibrations of the NH_2 group, respectively. These bands remain unchanged in the manganese (II) complexes of the ligands, indicating non-involvement of the NH_2 group in coordination. In the spectra of (1:1) manganese (II) complexes, a band observed at 800-880 cm^{-1} was assigned to the rocking mode of the coordinated water molecule. The band due to the ν (Mn−Cl) appears in the region 323-330 cm^{-1}. These bands are absent in the spectra of (1:2) manganese (II) complexes.

Some bands of low intensity appearing in the spectra of manganese (II) complexes in the region 440-421 cm^{-1}, 359–341 cm^{-1} and 600-585 cm^{-1} can be assigned to ν(Mn←N), ν(Mn-S) and ν(Mn-O) vibrations, respectively, which do not appear in the spectra of ligands confirming that the chelation takes place through the bidentate ($N^{\cap}S$) and ($N^{\cap}O$) donor system.

Electronic spectral analysis

Geometry of metal complexes is established by electronic spectral data along with supported by magnetic susceptibility measurements. The electronic spectra of the manganese (II) complexes have been recorded in methanol. The expected tetrahedral geometry in case of manganese (II) complexes was supported by the bands at 16000-16830 cm^{-1} and 19850-22340 cm^{-1} due to the $^6A_1 \rightarrow {}^4T_2(\nu_1)$ and $^6A_1 \rightarrow {}^4E(\nu_2)$ transitions, respectively which are characteristics of tetrahedral geometry (Daniel et al. 2008).

ESR spectral analysis and magnetic moment

The ESR spectrum of manganese (II) complexes was recorded at room temperature. The spectrum consists of a single broad peak from which the Lande splitting factor (‘g’ value) has been calculated Table 4. The ‘g’ value lie in the range 1.9920–2.0400, which is characteristic of tetrahedral geometry. Lande splitting factor (‘g’ values) has been calculated by the following formulae:

$$h\nu = g\beta H$$

$$g = h\nu/\beta H$$

Here: $h = 6.625 \text{ X } 10^{-34}$

$\nu = 9.38 \text{ X } 10^{9}$

$\beta = 9.27 \text{ X } 10^{-24}$

Where; h= Planck’s constant, *ν* = frequency, β = Bohr magneton

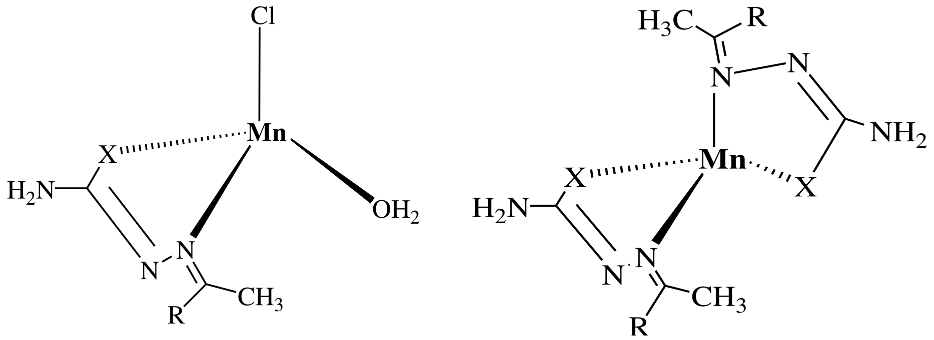
The effective magnetic moment recorded at room temperature for the manganese (II) complexes are close to the predicted values for five unpaired electrons in the metal ion. The observed magnetic moment value of 5.78-6.23 BM indicates that manganese (II) complexes are paramagnetic in nature consisting five unpaired electrons indicating the tetrahedral structure of the complexes.

3.2. X-ray powder diffraction study

The possible geometry of the finely powdered product has been deduced on the basis of X-ray powder diffraction studies. The observed interplanar spacing values (‘d’ in Å) for Mn(II) complex [Mn Cl $(L^3)(H_2O)$] have been measured from the diffractogram and the Miller indices h, k and l have been assigned to each d value and 2-Theta angles are reported in Table 2. The results show that the compound belongs to ‘Orthorhombic’ crystal system having unit cell parameters as a= 9.50,

b=17.30, c= 21.00 maximum deviation of 2-Theta=0.032° and Alpha= 90°, Beta= 90°, Gamma=90° .

On the basis of above studies, tetrahedral environment around the metal atoms has been proposed and the expected structures are as shown in Fig. 1.

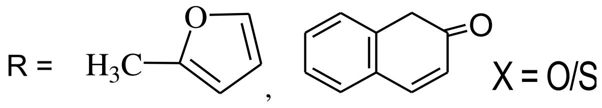


[MnCl(L)(H_2O)] Complex

(1:1)

[Mn($L)_2$] Complex

(1:2)



(L^1H, L^2H)(L^3H, L^4H)

Fig.1. Tetrahedral structures for Mn (II) complexes

3.3. Antimicrobial assay

Determination of minimum inhibitory concentration (MIC) for the ligands and their corresponding metal complexes synthesized by green chemical approach as well as conventional methods were carried out on selected fungi, *Candida albicans* and *Aspergillus niger* and two bacteria, Gram-positive (*Bacillus subtilis),* and Gram-negative (*Escherichia coli)*. The MIC values for the ligands and their manganese (II) complexes are shown in Table 3. The results indicated that the ligands and their metal complexes were the most active in inhibiting the growth of the tested organisms between 10-33 µg/mL minimum inhibitory concentration against selected bacteria and fungi.

The results showed that all the free ligands are less active as compared with their manganese (II) complexes. This indicated that the complexation to metal enhances the activity of the ligand. This may be explained by Tweedy's chelation theory (Tweedy, 1964).

4. CONCLUSION

- Microwave (MW) irradiation is an efficient and environmentally-benign method to accomplish various inorganic syntheses to afford products in higher yields in shorter reaction periods.
- Manganese (II) complexes synthesized in 1:1 and 1:2 molar ratios with both the ligands were found to possess tetra-coordinated tetrahedral structure.
- Biological data of the complexes and the ligands showed that the complexes are more active than the parent ligands

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Table 1. Analytical data and physical properties of the ligands and their complexes
d = decomposition

Compounds	**Colour**	**Melting Point(^{0}C)**	**Found (Calculated.) (%)**			**Mol. Wt. Found(Calculated)**
			N	**S**	**M**	
L^1H	Cream	160-165	22.74 (23.19)	-	-	176.53 (181.19)
L^2H	Whitish cream	199-205	17.28 (17.13)	-	-	235.48 (240.30)
L^3H	Cream	130-134	20.74 (21.26)	16.10 (16.27)	-	180.35 (195.19)
L^4H	Dark Yellow	220(d)	15.08 (16.06)	12.10 (12.27)	-	260.96 (261.39)
$[MnCl(L^1)(H_2O)]$	Light pink	273	14.27(14.56)	-	18.93 (19.03)	276.53 (288.58)
$[Mn(L^1)_2]$	Light pink	259(d)	20.90 (20.23)	-	13.49 (13.22)	386.58(415.29)
$[MnCl(L^2)(H_2O)]$	Light pink	175^{o}C(d)	12.16 (11.91)	-	15.43(15.57)	340.51(352.62)
$[Mn(L^2)_2]$	Light pink	168(d)	16.17 (15.43)	-	9.99 (10.10)	530.51 (543.36)
$[MnCl(L^3)(H_2O)]$	Light pink	226(d),	14.00 (13.79)	10.84 (10.52)	18.41 (18.03)	298.50(304.64)
$[Mn(L^3)_2]$	Light pink	246(d)	18.35 (18.78)	14.15 (14.33)	11.84(12.27)	444.23(447.42)
$[MnCl(L^4)(H_2O)]$	Light pink	181(d)	10.95 (11.39)	8.43 (8.69)	14.28 (14.89)	376.24 (368.68)
$[Mn(L^4)_2]$	Light pink	174(d)	16.47 (14.60)	8.22 (8.03)	10.00 (9.54)	562.81 (575.45)

Table- 2. X-ray diffraction data of [MnCl(L^3)(H_2O)]

h	k	l	2Theta (Exp.)	2Theta (Calc.)	2Theta (Diff.)	d (Exp.)	d (Calc.)	Intensity (Exp.)
1	1	2	27.306	27.316	-0.010	3.26339	3.26220	7.97
1	1	7	31.662	31.676	-0.014	2.82363	2.82242	62.32
2	5	3	34.475	34.507	-0.032	2.59940	2.59709	1.85
2	3	8	42.281	42.312	-0.030	2.13582	2.13435	0.91
4	4	3	45.412	45.416	-0.005	1.99559	1.99540	51.58
3	2	9	49.605	49.622	-0.017	1.83626	1.83568	4.55
4	7	4	56.451	56.477	-0.026	1.62873	1.62803	24.78
1	5	12	59.954	59.985	-0.031	1.54167	1.54094	5.00
0	6	13	66.242	66.267	-0.025	1.40975	1.40928	11.17

Table 3. Minimum inhibitory concentration (mg/mL) of the ligands and their complexes

Synthesized compounds	***Bacillus subtilis***	***Escherichia coli***	***Candida albicans***	***Aspergillusniger***
L^1H	31.0±0.3	30.0±0.2	29.0±0.1	28.0±0.2
L^2H	30.0±0.1	31.0±0.2	33.0±0.2	28.0±0.1
L^3H	29.0±0.3	31.0±0.2	33.0±0.4	30.0±0.3
L^4H	30.0±0.1	28.0±0.2	31.0±0.1	32.0±0.2
[MnCl(L^1)(H_2O)]	15.0±0.2	10.0±0.3	12.0±0.3	14.0±0.3
[Mn(L^1)$_2$]	10.0±0.2	14.0±0.2	11.0±0.2	16.0±0.1

[MnCl(L^2)(H_2O)]	20.0±0.1	22.0±0.2	18.0±0.1	23.0±0.1
[Mn(L^2)$_2$]	17.0±0.1	19.0±0.1	16.0±0.1	20.0±0.1
[MnCl(L^3)(H_2O)]	19.0±0.1	21.0±0.3	20.0±0.2	21.0±0.2
[Mn(L^3)$_2$]	20.0±0.4	23.0±0.3	22.0±0.3	22.0±0.2
[MnCl(L^4)(H_2O)]	19.0±0.2	20.0±0.3	22.0±0.3	22.0±0.3
[Mn(L^4)$_2$]	18.0±0.2	19.0±0.2	21.0±0.2	18.0±0.1
Streptomycin	10±0.2	09±0.2	-	-
Flucanazole	-	-	10±0.2	10±0.2