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Research Article

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Synthesis, characterization and biological studies of N-(1-morpholino-4-methyl benzyl)-benzamide and its transition metal complexes

Suba Sharma (1) **and Shamim Ahmad** (2)

(1) Research Scholar, Singhania University, Pacheri Bari, Jhunjhunu, Rajasthan, India

(2) Department of Chemistry, Bareilly College, Bareilly, U.P., India

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ABSTRACT

The Mannich base -N-[1-morpholino-4-methyl benzyl]-benzamide was synthesized by reported method and characterized by elemental analyses, I.R. and NMR spectral data. The complexes of the Mannich base with a number of transition metals were prepared and characterized by elemental analyses, molar conductance, mangentic susceptibility, electronic, IR and NMR spectral studies. TGA was also performed in a number of complexes. The biological screening of the Mannich base and few of metal complexes was also carried out.

Key words: Mannich base, NMR & biological screening.

INTRODUCTION

Mannich bases have played a vital role in the development of synthetic organic Chemistry. It is well known from the literature that the compounds containing amide moiety as a functional group have been found to possess donor properties and exhibit a wide range of biological activities (1-6).

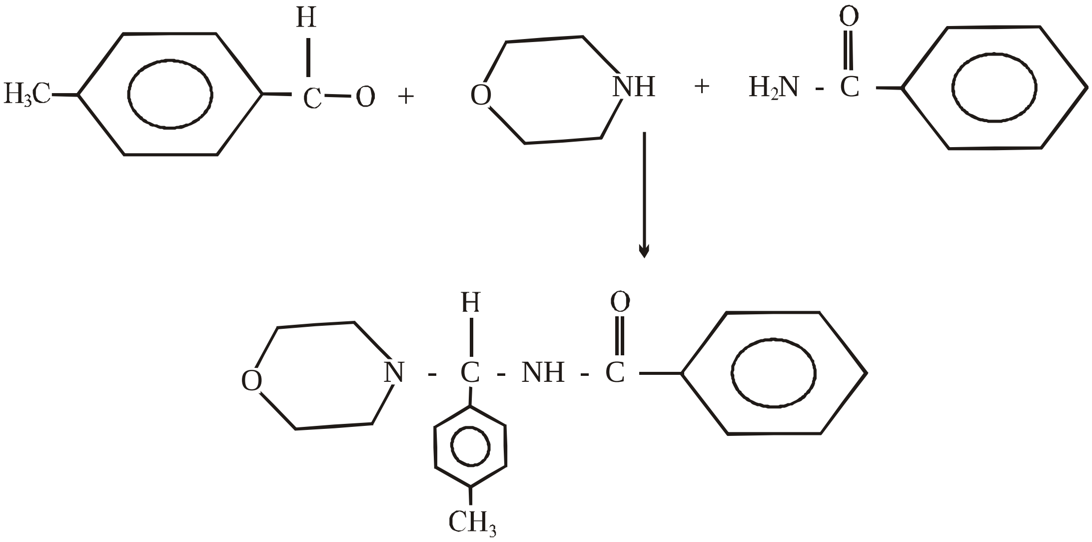
Metal Chelates of Mannich bases form an interesting class of compounds, which find extensive applications in various fields (7-8). Among the very few number of and variety of transition metal complexes of Mannich bases are of particular interest, because of their synthetic flexibility structure diversities, bonding interaction, biological significance and other multiple applications (9-11). Keeping these facts in view this work has been carried out.

EXPERIMENTAL SECTION

All the reagents and chemicals used were of A.R. grade or equivalent purity, 4-methyl Benzaldehyde, benzamide, morpholine and all the metal salts were procured from the reputed firms, while Titanium (III) Chloride was prepared in the lab by the reported method. Ethanol was purified by double distillation before use, while all other solvents were used as procured.

Preparation of the Ligand

The Mannich base was prepared by mixing ethanolic solution of benzamide with morpholine and treated with benzaldehyde in the molar ratio of 1:1:1. The reaction mixture was stirred under ice bath condition. A yellow solid was separated by filtration & washed with distilled water.



The Mannich base was characterized by the determination of melting point, elemental analyses, IR and NMR spectra.

Preparation of the Complexes

The solution of the Mannich base was added to the solution of the respective metal salt. A solid complex was obtained in each case. It was filtered washed and dried in vacuum dessicator over fused $CaCl_{2.}$

RESULTS AND DISCUSSION

The complexes are coloured solids except those of MoO_2 (VI) and UO_2(VI). The elemental analyses of the complexes revealed 1:2 metal ligand ratio. The molar conductance values in DMSO at 25^0 and 10^{-3} M dilution, suggested 1:1 electrolytic nature for Ti (III), Mn (III), V (III), Fe (III), Co (III), Ru (III) and MoO (V) complexes while the complexes of Ru (II), MoO_2 (VI) and UO_2 (VI) were non electrolytes.

The measurement of magnetic moment by Gouy's balance suggested paramagnetic nature for Ti (III), V (III), Fe (III), Mn (III), Ru (III) and MoO (V) complexes while the complexes of Ru (II), Co (III), MoO(VI) and UO_2 (VI) were diamagentic in nature.

Magnetic Moment and Electronic Spectra :

The Ti (III) complex shows magentic moment of 1.70 B.M. This value is close to the calculated value for d^1 system (1.71 B.M.) like Ti (III) and show paramagentic character for the complex. The electronic spectrum of the complex shows a single band at 19600 cm^{-1}, which may be assigned to $^2T_{2g} \rightarrow ^2E_g$ transition[15]. This is characteristic of Ti (III) octahedral complex.

The magnetic moment of the vanadium (III) complex is 2.94 B.M. which is nearly equal to the calculated value for d^2 system like V (III). The electronic spectrum of V (III) complex exhibited band at 16200 cm^{-1} and shoulder at 20800 cm^{-1}. The low energy band may be assigned to the $^3T_{1g}(f) \rightarrow ^3T_{2g}(f)$ transition in octahedral symmetry and high energy band to $^3T_{1g}(f) \rightarrow ^3T_{1g}(p)$ transition (16).

The magnetic moment of Ru (III) complex is 1.96 B.M. The electronic spectrum shows bands at 10330, 16129, 24390 and 35087 cm^{-1} which may be assigned to the transition $^2T_{2g}\rightarrow ^4T_{1g}$, $^2T_{2g}\rightarrow ^4T_{2g}$, $^2T_{2g}\rightarrow ^2A_{2g}$, $^2T_{1g}$ and $\pi\rightarrow T_{2g}(\pi^*)$respectively(17). These are characteristic of an octahedral geometry.

The Ru (II) complex is diamagnetic in nature. The electronic spectrum of the complex in CH_2Cl_2 shows a band assigned to the charge transfer transition arising from the excitation of an electron from the metal t_{2g} level to the unfilled molecular orbitals derived from the π^* level of the ligand in accordance with the assignments made for other similar octahedral ruthenium (II) complexes (18-20).

The magnetic moment of Mn (III) complex is 4.96 B.M. which is in expected range for d^4 system like Mn (III) and suggested paramagnetic nature for the complex and revealed high spin nature of the complex. It supported octahedral symmetry. Unusually Mn (III) has ^5D electronic ground state and in an octahedral symmetry, a single absorption band is expected due to spin allowed transition $^5E_g \longrightarrow {}^5T_{2g}$ however even for symmetrical ligand field, they are subject to Jahn-Teller distortion for high spin d^4 configuration (21).

The complex shows two bands assignable to $^5B_{1g} \longrightarrow {}^5T_{2g}$ at 18500 cm^{-1} transition and other band at 25000 cm^{-1} may be assigned to Mn$\longrightarrow$ ($d\pi$) - $\pi*$(22).

The magnetic moment of Fe (III) complex is 5.97 B.M. corresponding to five unpaired electron and high spin state of Fe(III) ion. Three bands have been observed in the electronic spectrum of the complex at 11235, 21740 and 27780 cm^{-1} assignable to $^6A_{1g} \longrightarrow {}^4T_{1g}$, $^6A_{1g} \longrightarrow {}^4T_{2g}$ and $^6A_{1g} \longrightarrow {}^4E_g$ transitions respectively suggesting an octahedral geometry (23).

The magnetic study of Co (III) complex indicated diamagnetic nature for the complex, as expected for low spin d^6 ion.

The electronic spectrum shows bands at 15140, 21110 and 23330 cm^{-1}. These bands have been assigned to $^1A_{1g} \longrightarrow {}^3T_{2g}$, $^1A_{1g} \longrightarrow {}^1T_{1g}$ and $^1A_{1g} \longrightarrow {}^1T_{2g}$ transitions respectively (24).

The magnetic moment of MoO(V) complex is 1.78 B.M. which is very near to calculated value for one unpaired electron. The electronic spectrum shows bands at 14200, 19610 and 25000 cm^{-1} which have been assigned to $^2B_2 \longrightarrow {}^2E$ (dxy$\longrightarrow$dxz - dyz), $^2B_2 \longrightarrow {}^2B_1$ (dxy$\longrightarrow$$dx^2$ - dz^2) and $^2B_2 \longrightarrow {}^2A_1$ (dxy - dz^2) transitions respectively. The complex can be best considered as octahedral with strong tetragonal distortion (C_{4r} symmetry) resulting from Mo=O bond (24).

The electronic spectrum of MoO_2(VI) & UO(VI) complexes show only charge transfer band.

Infra Red Spectra

The IR spectra of the ligand and its metal complexes were recorded in KBr phase and compared in order to find out the possible coordination sites. The IR spectrum of the ligand showed bands at 3380, 1600 and 1100 cm^{-1} assignable to ν(N-H), amide ν(C=O) and ν(C-N-C) of morpholine respectively. In the IR spectra of the complexes, the band due of ν (N-H) appeared almost unchanged, excluding the possibility the coordination through this group. The amide ν (C=O) and ν(C-N-C) bands showed substantial negative shifts, indicating coordination through oxygen atom of amide moiety and nitrogen of morpholine entity present in the ligand (8). These coordination sites were further supported by the appearance of non-ligand bands in the for IR region of the complex at 510 and 465 cm^{-1} assignable to ν M-O and ν M-N vibrations respectively. (25).

The IR spectra of the complexes showed some other non ligand bands in the region of 3490-3510 cm^{-1} attributable to νO-H of water molecule. The coordinated nature of these water molecules is suggested by two other non-ligand bands in the regions of 835-850 cm^{-1} and 740-750 cm^{-1} due to wagging and rocking modes. The coordinated nature of water molecules in further supported by TGA. The loss of water molecules occured in the temperature range of 170-190^{0}C. In UO_2(VI), bands at 910 and 930 cm^{-1} indicated linear character of UO_2group. In the case of MoO(V) complex, the bands at 950 cm^{-1} may be assigned to Mo = O moiety. The bands at 960 and 910 cm^{-1} in MoO_2 (VI) complex suggested cis nature of O=Mo=O moiety.

The NMR spectra of the ligand exhibited an absorption peak at 6.2δ and 10.1δ assignable to N-H proton and to N=C-OH proton respectively. The disappearance of these peaks in the complex indicated the coordination via the dissociation of -OH proton of the ligand. The signal due to morpholine ν-CH_2 proton at 2.6δ also shifted down field, suggesting coordination of morpholine nitrogen.

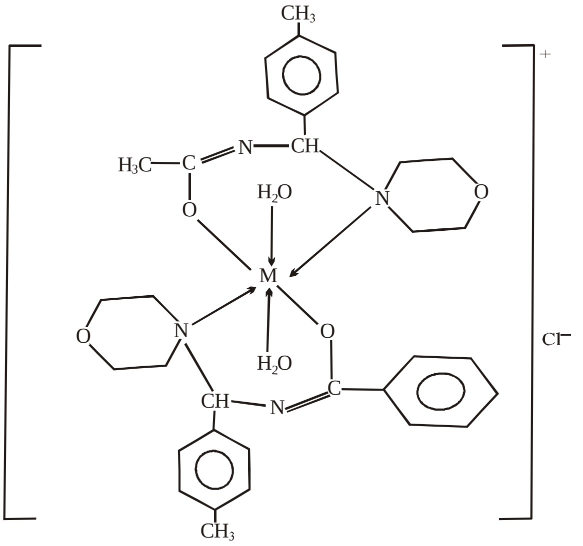
Table-1 : Physical Data of Ligand and its Complexes

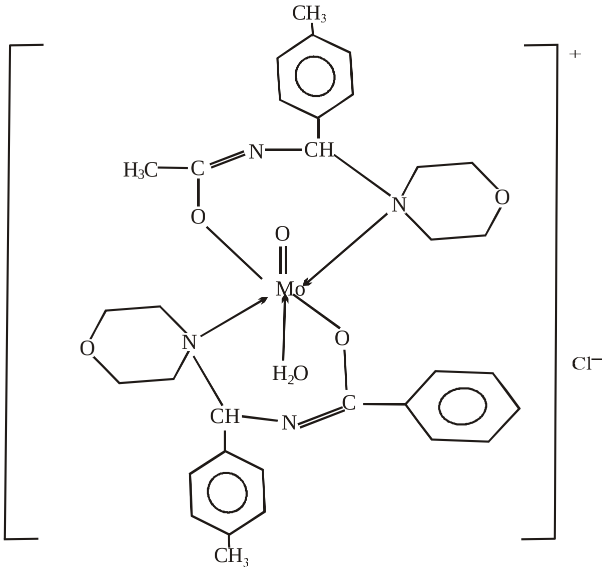
Sl No	**Molecular Formula of Ligand/Complex**	**M.P. ^{0}C**	**Colour**	**Elemental analyses**				**Magnetic Moments in (B.M.)**	**Molar Conductance**	**Electrolyte Type**
				% of C	**% of H**	**%of N**	**% of M**			
1	$C_{19}H_{22}O_2\ N_2$	138	Yellow	72.82 (72.97)	6.70 (6.75)	9.39 (9.45)	-	-	-	-
2	$[Ti(C_{19}H_{22}O_2N_2)_2.2H_2O]\ Cl$	181	Deep Yellow	60.79 (60.93)	5.89 (5.92)	7.82 (7.89)	6.70 (6.77)	1.71	65	1:1
3	$[V(C_{19}H_{22}O_2N_2)_2\ .2H_2O]\ Cl$	183	Dark Yellow	60.60 (60.67)	5.83 (5.89)	7.83 (7.86)	7.02 (7.16)	2.94	70	1:1
4	$[Mn(C_{19}H_{22}O_2N_2)_2\ .2H_2O]\ Cl$	186	Brown	60.28 (60.33)	5.80 (5.86)	7.79 (7.828)	7.60 (7.66)	4.96	70	1:1
5	$[Co(C_{19}H_{22}O_2N_2)_2\ .2H_2O]\ Cl$	188	Pink	59.92 (60.00)	5.79 (5.83)	7.71 (7.77)	8.08 (8.19)	Dia magnetic	65	1:1
6	$[Fe(C_{19}H_{22}O_2N_2)_2\ .2H_2O]\ Cl$	185	Dark brown	60.19 (60.25)	5.81 (5.85)	7.79 (7.81)	7.80 (7.81)	5.97	65	1:1
7	$[Ru(C_{19}H_{22}O_2N_2)_2\ .2H_2O]\ Cl$	205	Green	56.62 (56.69)	5.50 (5.51)	7.30 (7.34)	13.00 (13.25)	1.96	70	1:1
8	$[Ru(C_{19}H_{13}O_2N_2)_2\ .2H_2O]$	201	Dull White	59.39 (59.42)	5.70 (5.77)	7.70 (7.72)	13.81 (13.89)	Dia magnetic	Non electrolyte	-
9	$[MoO(C_{19}H_{22}O_2N_2)_2]\ .2H_2O]\ Cl$	199	Yellow	57.19 (57.21)	5.51 (5.56)	7.39 (7.41)	12.69 (12.71)	1.78	65	1:1
10	$[MoO_2(C_{19}H_{22}O_2N_2)_2$	200	White	60.00 (60.16)	5.81 (5.84)	7.70 (7.79)	13.30 (13.37)	Dia magnetic	Non-electrolyte	-
11.	$[UO_2(C_{19}H_{22}O_2N_2)_2]$	251	White	50.19 (50.23)	4.84 (4.88)	6.49 (6.51)	27.60 (27.67)	Dia magnetic	Non electrolyte	-

Cacld. values are given in brackets.

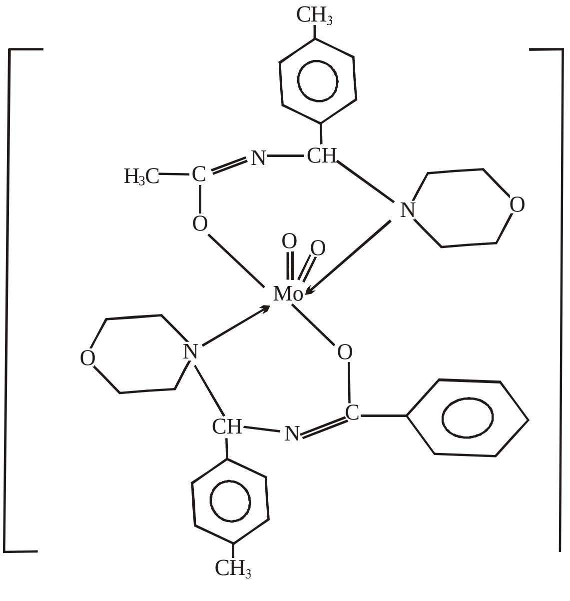
CONCLUSION

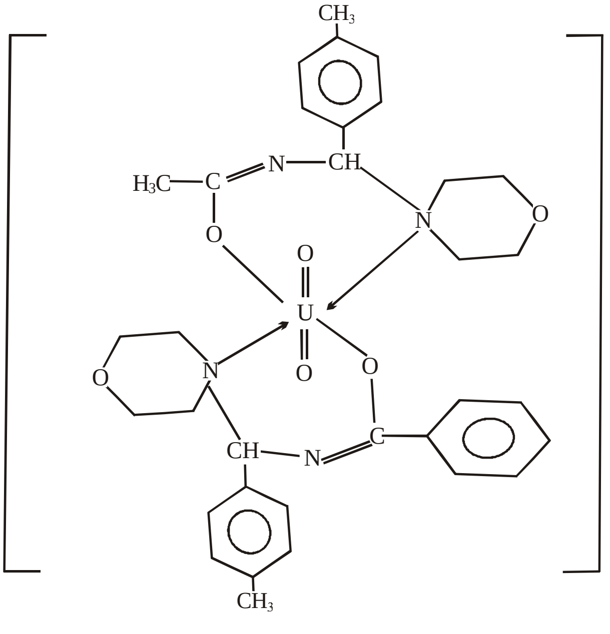
On the basis of studies performed an octahedral geometry may be proposed for all the synthesized complexes, with possible distortion due to Mo=O moiety in the case of MoO(V) complex.





M= Ti(III), V(III), Co(III), Fe(III), Ru(III) or Mn(III)





Antibacterial Activity:

The ligand and few of its metal complexes were tested for antibacterial activity. Muller Hinton agar was used for testing the susceptibility by well diffusion method (26) using DMSO as solvent, at a concentration of 0.01 M Gram positive and Gram negative bacteria. The zone of inhibition was determined at the end of incubation period of 24h at 37^0C. The metal complexes appeared to be more potent than the ligand (Table-2). Ampicelin was used as standard.

Table 2 : Antibacterial Activity of Mannich Base and its complexes

Compound	**Inhibition Zone (mm)**			
	S.aureus	***E. coli***	***P. auroginosa***	***B. subtitis***
Mannich Base	15	17	18	16
[Ti L_2] Cl	18	20	22	21
[V L_2] Cl	17	19	21	20
[Mn L_2] Cl	18	21	22	20
[Fe L_2] Cl	18	20	22	21
[Co L_2] Cl	18	21	22	20
[Ru L_2] Cl	19	22	23	21
[Ru L_2] Cl	18	20	21	20
[MoO(V) L_2] Cl	18	20	22	20

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