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Research Article

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Synthesis and physico-chemical characterisation of new mannich base and its metal complexes

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ABSTRACT

A new Mannich base, N-(morpholino-N, N-dimethyl-4-aminobenzyl) benzamide, formed by the condensation of morpholine, benzamide and N, N-dimethyl-4-amino benzaldehyde and its Fe(II), Fe(III), Mn(III),Co(III),Ti(III),V(III),V(IV),MoO(V),Ru(II) and Ru(III) complexes have been Synthesized. Their probable structures have been proposed on the basis of their microanalytical, IR, UV-vis. ^{1}H NMR spectral data. All the complexes exhibit octahedral geometry. The biological activities of the ligand and its metal chelates against the bacteria E.coli, Staphylococcus aureus, Klebsiella pneumonia, Salmonella typhi, Pseudomonas aeruginosa and Shigella flexnri are also being reported. The complexes have higher activity than that of the free Mannich base and the control.

Key words: N-(morpholino-N, N-4 aminobenzyl) benzamide, Morpholine, Benzamide, Mannich base and biological activity.

INTRODUCTION

It is well known from the literature that the compounds containing amide moiety have a strong ability to form metal complexes and exhibit a wide range of biological activities[1-4] .The coordination chemistry of amide group has received much attention due to its diverse coordinating behaviour and the role it plays in biological process[5].An amide group offers two potential sites, i.e., through oxygen and nitrogen for complexation with protons and metal ions. It is now generally accepted that for neutral amide groups, both protonation and metal ion binding will be at the amide oxygen[6].Upon deprotonation the binding shifts to the amide nitrogen[7] .But, for certain reasons, like bit size and steric hindrance, the coordination may also take place at amide nitrogen.

Keeping these facts in view, an attempt has been made to synthesize and characterized the complexes of metals a new Mannich Base, N-(morpholino-N, N-dimethyl-4-aminobenzyl) benzamide which also contains amide moiety. The synthesis of N-(morpholino-N, N-dimethyl-4-aminobenzyl) benzamide and its complexation characteristics with Fe(II), Fe(III), Mn(III),Co(III),Ti(III), V(III),V(IV), MoO(V), Ru(II) and Ru(III) salts and the antibacterial activity of the complexes are described in this note.

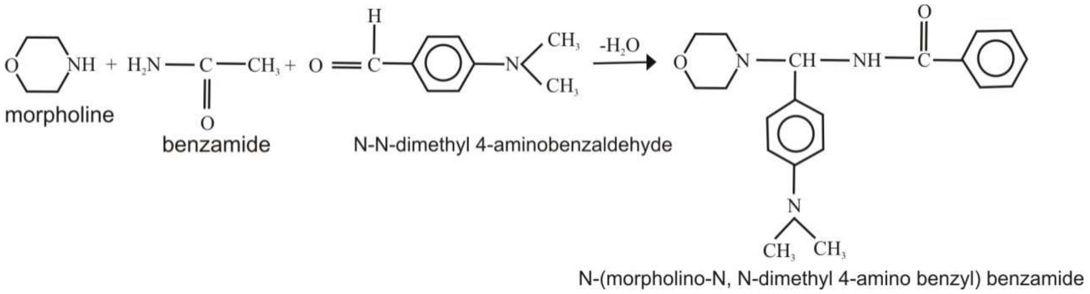
EXPERIMENTAL SECTION

All the chemicals and reagents used were of AR grade or equivalent purity, Spectroscopic grade solvents were used for spectral analysis. The carbon, hydrogen, and nitrogen were analysed at CDRI, Lucknow.Conductivity

measurements were carried out with Philips conductivity Bridge Model PR 9500 at room temperature and 10^{-3} M dilution. Magnetic susceptibility was determined by Gouy's balance. Copper sulphate was used as the calibrant.
The IR spectra were recorded in KBr pellets using a Perkin-Elmer 783 spectrophotometer. The UV-vis spectra of the complexes were recorded On a Shimadzu UV-1601 spectrophotometer. Ti (III)was prepared by the standard procedure while the other metal salts were used as procured.

Antimicrobial activity
The in vitro biological screening effects of the investigated compounds were tested against the bacteria, S. aureus, S. typhi, K. pneumoniae, S. flexneri, P. aeruginosa, E. coli by the well diffusion method using agar nutrient as the medium. The test solutions were prepared by dissolving the compounds in DMSO. In a typical procedure[8], a well was made on the agar medium inoculated with microorganisms. The well was filled with the test solution using micropipette and the plate was incubated at 35°C for 25 h., during this period, the test solution was diffused and the growth of the inoculated micro organisms was affected. The inhibition zone developed on the plate was measured. Here ampicillin was used as the control.

Synthesis of mannich base
Benzamide (1.21 g, 10 mmol) in 20 ml of ethanol was mixed with morpholine (0.9 ml, 10 mmol) with stirring to get a clear solution under ice cold condition. To the contents N,N-dimethyl-4-amino benzaldehyde (1 ml, 10 mmol) was added drop wise using dropper with stirring for 15-20 min.The reaction mixture was then kept at room temperature for 5 days. The colourless solid obtained was filtered and recrystallized from ethanol. (Yield: 70%; m.p. 85 °C).



Synthesis of metal complexes
A solution of 5 mmol of metal salts and the Mannich base (10 mmol, 2.92 g) in 40 ml ethanol and chloroform mixture (1:6, v/v) was boiled under reflux at 58 °C (b.p. of azeotropic mixture) for 3 h. The resulting solution was concentrated and then cooled to 0 °C for 12 h and the precipitated complexes were filtered, washed with ethanol and dried in vacuo.

RESULTS AND DISCUSSION

The analytical data of the synthesized complexes is given in table. The data suggested 1:2 (M:L) stetiometry for all the complexes. The molar conductance values determined at 10^{-3} M dilution and 25^{0}C in both DMF and DMSO suggested 1:1 electrolytic nature for Fe(III), Mn(III),Co(III),Ti(III), V(III),MoO(V), and Ru(III)complexes where as Fe(II)and Ru(II) complexes were non electrolytic in nature. The V (IV) complex is 1:2 electrolytes.

IR spectrum of the ligand shows bands at 3380,1600 and 1100 cm^{-1} which have been assigned to ν(NH),amide ν(C=O) and ν(C-N-C) of morpholine group respevtively[9].In all the complexes, the ν(N-H) band appeared in the region 3330-3425 cm^{-1}.The amide ν(C=O)and ν(C-N-C) of morpholine bands displayed substantial negative shifts with fairly low intensity indicating coordination through the oxygen of amide moiety and nitrogen of morpholine entity present in the ligand.Some new bands were found around 420-400 cm^{-1} and 540-520 cm^{-1} assignable to υ_{M-N} and υ_{M-O} vibration respectively which further supported these proposed coordination sites. The MoO (v) complex showed a band at 855 cm^{-1}assignable to Mo=O moiety.

^{1}H NMR spectra of the ligand and its Ti (III) complex were recorded in DMSO-d_6 solution. The spectrum of the ligand shows the signals as follows: a broad absorption around 6.2 δ due to the NH proton; morpholine N-CH_2 at 2.2 δ and morpholine O-CH_2 at 3.7 δ; the methyline proton appeared in 6.7 δ; the multiplet observed around 7.2 to 8.2 δ is assignable to the phenyl group. In the ligand spectrum, one absorption peak at 10.1 δ was observed which can be assigned to N=C-OH proton. The disappearance of the peaks at 10.1 δ and 6.2 δ in the spectrum of Ti (III) complex indicates that the coordination is taking place via the dissociation of the –OH proton also shifted downfield and appeared at 2.6 δ in the complex. This is an indication of the coordination of morpholine nitrogen. In the case of Mn (III) complex the sixth position is occupied by the water molecule. This was indicated by appearance of two non ligand bands in their IR spectra in the range of 3310 – 3400 cm^{-1} to ν (OH) group of coordinated water molecule[10]. The magnetic moment of Fe (III) complex is 6.04 B.M. The electronic spectrum of the complex showed bands at 14705, 16949 and 26315 cm^{-1} corresponding to ${}^6A_{1g} \rightarrow {}^4T_{1g}$ (G), ${}^6A_{1g} \rightarrow {}^4T_{1g}$ (P) and ${}^6A_{1g} \rightarrow {}^4T_{2g}$ (2D) trasition respectively are observed in the electronic spectrum of Fe (III) complex suggesting an octahedral geometry[11].

Magnetic moment for Mn (III) complex is 4.93 B.M. revealing the high spin nature of the complex, corresponding to four unpaired electrons. Electronic spectrum shows a strong band at 19680-20000 cm^{-1} which can be assigned due to ligand to metal charge transfer and a shoulder at 18000-180540 cm^{-1} may be assigned to the ${}^5E_g \rightarrow {}^5T_{2g}$ transition[12, 13].

The Co (III) complex is diamagnetic (at 27^0C) as expected for a low spin d^6 ion. The electronic spectrum of Co(III) complex displays band at 15350,21530 and 23470 cm^{-1} .These are similar to those reported for other six coordinated Co(III) complex[12-15] and may be assigned to ${}^1A_{1g} \rightarrow {}^3T_{2g}$, ${}^1A_{1g} \rightarrow {}^4T_{1g}$ and ${}^1A_{1g} \rightarrow {}^1T_{2g}$ transitions respectively.

The Ti (III) complex shows magnetic moment of 1.68 B.M. for one unpaired electron. The higher value may be due to the orbital contribution. A single broad band has been observed at 20110 cm^{-1} for Ti(III) complex derived from the transition ${}^2A_{2g} \rightarrow {}^2E_g$ for an octahedral symmetry[16].

The electronic spectrum of V(III)complex exhibited a band at 17100 cm^{-1} with a shoulder at 21750 cm^{-1}.The low energy band has been assigned to ${}^3T_{1g} \rightarrow {}^2T_{2g}$ and the high energy band to ${}^3T_{1g} \rightarrow {}^3T_{2g}$ (P) transition respectively. These bands are characterised of octahedral geometry[17].The electronic spectrum of V (IV) complex exhibited a single band at 12820 cm^{-1}.In the absence of finely resolved spectra, it was therefore, not appropriate to judge the geometry of the complex as regular octahedral[18].

The electronic spectrum of MoO (V) complex suggested that the complex may be considered as octahedral with a strong tetragonal distortion resulting from Mo=O band[19].The spectrum exhibited three distinct absorption bands in the ligand field region. The low intensity band at 14000 cm^{-1} in the long wavelength region, is possibly due to first crystal field transition ${}^2B_2 \rightarrow {}^2E(dxy_{\rightarrow}dyz,dxz)$.The second crystal field transition at 20000 cm^{-1} is assignable to ${}^2B_2 \rightarrow {}^2B_1(dxy_{\rightarrow} dx^2-y^2)$.The third peak was observed at 23500 cm^{-1} assignable to ${}^2B_2 \rightarrow {}^2A_1(dxy_{\rightarrow}dz^2)$.

The μ_{eff} for this complex was found to be 1.82 BM.as expected for an octahedral complex with t_{2g}^5 configuration. Its electronic spectrum in complex displayed band at 13700,17600 and 22650 cm^{-1},which may be assigned to ${}^2T_{2g} \rightarrow {}^4T_{1g}$, ${}^2T_{2g} \rightarrow {}^4T_{2g}$, ${}^2T_{2g} \rightarrow {}^2A_{2g}$, ${}^2T_{1g}$ transition respectively. These are similar to those reported to octahedral Ru (III) complex[20].

Analytical data of the complexes

Compound/Complex	Colour	M	C	H	N	Cl	Mol Wt.	$^{\lambda}$M mho cm^2 mol^{-1}	μ_{eff} (B.M.)
$[(C_{20}H_{24}O_2N_3)_2Fe.2H_2O]Cl$	Brown	6.95	59.75	6.47	10.46	4.42	803.35	1:1	6.04
$[(C_{20}H_{24}O_2N_3)_2Mn.2H_2O]Cl$	Brown	6.85	59.82	6.48	10.47	4.42	802.44	1:1	4.93
$[(C_{20}H_{24}O_2N_3)_2Co.2H_2O]Cl$	Pink	7.31	59.52	6.45	10.42	4.40	806.43	1:1	Diamagnetic
$[(C_{20}H_{24}O_2N_3)_2Ti.2H_2O]Cl$	Yellow	6.02	60.35	6.54	10.56	4.46	795.36	1:1	1.68
$[(C_{20}H_{24}O_2N_3)_2V.2H_2O]Cl$	Yellow	6.38	60.12	6.51	10.52	4.45	798.44	1:1	2.91
$[(C_{20}H_{24}O_2N_3)_2MoO.H_2O]Cl$	Yellow	11.40	57.05	5.94	9.98	4.22	841.44	1:1	1.66
$[(C_{20}H_{24}O_2N_3)_2Ru.2H_2O]Cl$	Green	11.91	56.57	6.13	9.90	4.18	848.57	1:1	1.82
$[(C_{20}H_{24}O_2N_3)_2Ru.2H_2O]$	Green	12.43	59.04	6.40	10.33	-	813.07	Non-electrolyte	Diamagnetic
$[(C_{20}H_{24}O_2N_3)_2MoO_2.H_2O]$	White	11.67	58.40	6.08	10.22	-	821.94	Non-electrolyte	Diamagnetic
$[(C_{20}H_{24}O_2N_3)_2UO_2.2H_2O]$	White	24.24	48.88	5.30	8.55	-	982.03	Non-electrolyte	Diamagnetic

The determination of magnetic susceptibility of Ru (II) complex by Gouy's method indicated diamagnetic nature of the complex .The electronic spectrum of the complex showed a single band assignable to charge -transfer transition.

On the basis of above mention evidences octahedral geometry may be suggested for all the complexes with possible distortion in case of MoO(V) complex due to Mo=O moiety.

Antimicrobial Activity

The in vitro biological screening effects of the investigated compounds were tested against six bacteria: *Staphylococcus aureus, Klebsiella pneumoniae, Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli* and *Shigella flexneri* by the well diffusion method. The zone of inhibition values of the compounds against the growth of microorganisms .A comparative study of the ligand and its complexes indicates that the metal chelates exhibit higher activity than the free ligand and the control (ampicillin).The order of activity towards *Shigella flexneri* and *Staphylococcus aureus* is Fe>Mn>Co>Mo>Ru>V>Ti; *Psedomonas aeruginosa* is Fe>Co>Mn>Mo>Ru>V>Ti; *Klebsiella pneumoniae* and *Salmonella typhi* is Co>Fe>Mn>Mo>Ru>V>Ti; *Escherichia coli* is Fe>Co>Mo>Mn>Ru>V>Ti. The increase in antimicrobial activity is due to faster diffusion of metal complexes as a whole through the cell membrane or due to the combined activity effect of the metal and ligand. Such increased activity of the metal chelates can be explained on the basis of Overtone's concept. and the Tweedy's chelation theory. The lipid membrane that surrounds the cell favours the passage of only lipid soluble materials due to which liphophilicity is an important factor which controls the antimicrobial activity on chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further it increases the delocalization of π -electron over the whole chelate ring and enhances the liposolubility of the complexes. This increased liposolubility enhances the penetration of the complexes into the lipid membrane and blocks the metal binding sites in the enzymes of microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restrict further growth of the organisms.

Antibacterial Activity of the ligands and their complexes

Compound	*S. flexneri*	*S. typhi*	*P. aeruginosa*	*S. aureus*	*E. coli*	*K. pneumoniae*
Ampicillin	19	19	16	11	14	14
MBB	8	7	6	8	9	6
Fe (III) Complex	23	20	25	18	20	17
Mn (III) Complex	19	18	16	15	18	15
Co (III) Complex	15	11	13	11	14	12
Mo (III) Complex	20	23	12	17	17	20
Ru (III) Complex	14	16	15	14	17	19
V (III) Complex	13	15	14	13	16	17
Ti (III) Complex	12	14	13	11	14	15

CONCLUSION

In view of the analytical, conductometric, magnetic, thermal and spectral evidences cited above, an octahedral geometry may be proposed for this metal chelate.

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