



SYNTHESIS, CHARACTERISATION OF N-(3-(FURAN-2-YL)-3-OXO-1-PHENYLPROPYL) BENZOHYDRAZIDE AND ITS CHLORO COMPLEXES

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Article Received on 01/02/2018

Article Revised on 22/02/2018

Article Accepted on 12/03/2018

ABSTRACT

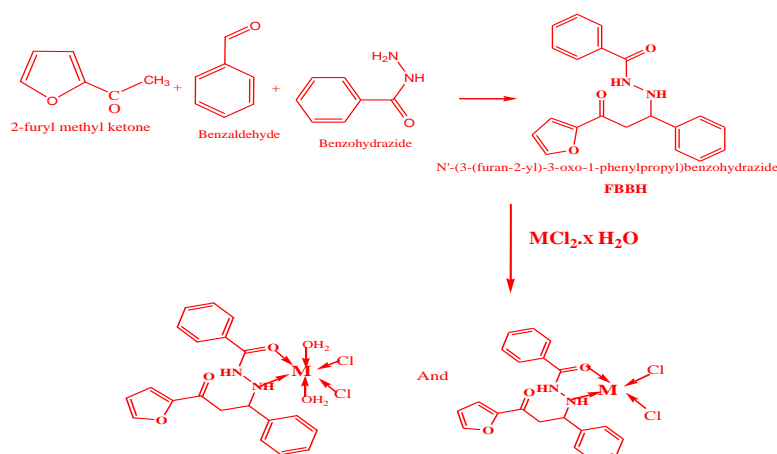
The present study deals with the structure and antimicrobial properties of some complexes of Mn(II), Co(II), Ni(II) and Zn(II) with a new Mannich base N¹-(3-(furan-2-yl)-3-oxo-1-phenylpropyl)benzohydrazide. All the compounds were characterized through spectral and analytical data. The transition metal complexes of resultant Mannich bases have been synthesized and well characterized by elemental analyses, spectral studies, magnetic moment determination, molar conductivity measurement and thermogravimetric analysis. Experimental results showed that metal complexes act as bi-dentate ligands. The in-vitro antibacterial and antifungal activity of Mannich bases and their metal (II) complexes was assayed against different pathogens using MIC method. All the compounds and their metal complexes showed good potency against various microorganisms.

KEYWORDS: Mannich bases, Benzohydrazide, Metal complexes, Anti-microbial agents.

INTRODUCTION

From the survey of existing literature, it appears that metal complexes of Mannich bases have played a vital role in the development of coordination chemistry.^[1-5] 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. Earlier work reported that some drugs showed increased activity when administered as metal chelates rather than as organic compounds. Keeping the above facts in mind and as part of our continuing efforts to

investigate transition metal(II)^[6-9] complexes using Mannich bases, in this paper we describe the synthesis, characterization and antimicrobial studies of Mn(II), Co(II), Ni(II) and Zn(II) complexes containing bidentate Mannich base derived by condensing benzohydrazide, benzaldehyde and 2-furyl methyl ketone. The ligand system coordinates to the metal ion in a bidentate manner through the amide carbonyl oxygen and the terminal hydrazine nitrogen atom. The proposed structure of the complexes is shown below.



Scheme - 1: Synthesis of the ligand and its complexes

MATERIALS AND METHODS

Chemicals

Reagents such as 2-Furyl methyl ketone, benzaldehyde, Benzohydrazide and various Metal(II) chlorides were of Merk product. Spectroscopic grade solvents were used for the spectral measurements. The carbon, hydrogen and nitrogen contents in each samples were done at the Regional Sophisticated Instrumentation Centre, Central Drug Research Institute, Lucknow. The ^1H NMR and ^{13}C NMR spectra of the samples were measured in Bruker 300 MHz Instrument using DMSO as solvent. Mass spectra were recorded on a JEOL-8X102. The IR spectra were recorded with KBr pellets using FT-IR Shimadzu Instrument. Molar conductivity was measured using 10^{-3}M solution of complexes in DMSO on Systronic Conductivity Bridge. UV-Visible spectra of the complexes were recorded on Perkin Elmer Lambda EZ 301 spectrometer in DMSO solutions. Magnetic susceptibility was measured with Gouy balance at room temperature. $\text{Hg}[\text{Co}(\text{SCN})_4]$ was used as a standard. Nutrient agar was used for testing the susceptibility of microorganisms to antimicrobial agents using the *Disc-diffusion* technique. *Ciprofloxacin* was used as standard for antibacterial activity and *Nystatin* for antifungal activity.

In vitro antibacterial and antifungal assay

The biological activities of synthesized Mannich base and its Mn(II), Co(II), Ni(II) and Zn(II) complexes have been studied for their antibacterial and antifungal activities by *Disc diffusion* test using Nutrient agar (NA) and S,abouraud Dextrose Agar(SDA). The antibacterial and antifungal activities were done at $10\ \mu\text{g}/\text{mL}$ concentrations in DMSO solvent using bacteria (*S aureus*, *B substillis*, *E.coli* and *P.aeruginosa*) and fungi(*C.albicans*, *A.niger*) at the minimum inhibitory concentration (MIC) method. These bacterial strains were incubated for 24 h at $37\ ^\circ\text{C}$ and fungi strains were incubated for 48 h at $37\ ^\circ\text{C}$. Standard antibacterial (*ciprofloxacin*) and antifungal drug (*Nystatin*) were used

for comparison under similar conditions. Activity was determined by measuring the diameter of the zone showing complete inhibition (mm).

Synthesis of Mannich base

For the preparation of FBBH, benzohydrazide, 2-furyl methyl ketone and benzaldehyde were taken in 1:1:1 mol ratio. A solution of benzohydrazide (5.6 g, 0.05 mol) in 20 mL ethanol was neutralized with 20 mL of aqueous ammonia. To this solution 2-furyl methyl ketone (5.5 ml, 0.05 mol) was added and stirred well to get a clear solution. Benzohydrazide (4.3 mL0.05 mol) was added to the reaction mixture. The resulting colloidal solution was kept at room temperature for 48 h. Compound formed was filtered and then recrystallised from ethanol. Purity of the compound was checked by TLC and the melting point of the compound was determined in an open capillary tube and was uncorrected. Yield: 79%, M.P: $95\ ^\circ\text{C}$.

Synthesis of metal complexes

Hot ethanolic solution of ligand (1 equivalent) was slowly mixed with hot methanolic solution of the metal chloride (2 equivalent) under reflux condition with constant stirring. The mixture was refluxed for 1-2 hours and after that it was cooled under ice cold condition, the colored solid complex separated out in each case. It was filtered, washed with 50% ethanol and finally dried.

RESULTS AND DISCUSSION

Molar conductance

The complexes prepared are various colored, powder like, air stable, soluble in dimethylformamide (DMF) and dimethylsulfoxide (DMSO). The analytical data and some physical properties of the metal complexes were listed in table 1 and synthetic scheme of complex is given in scheme 1. The molar conductivities values showed that all the complexes are non-electrolytes nature with $\Lambda_m = 30\text{-}45\ \Omega^{-1}\text{cm}^2\text{mol}^{-1}$ in 10^{-3} in DMSO solutions at room temperature.

Table-1: Physical characterization, Analytical, Molar conductance Magnetic susceptibility data.

Compound	Colour	Found/Calculated					Yield %	$\Lambda_m\ \text{Mho cm}^2\ \text{mol}^{-1}$	$\mu\text{-eff B.M}$
		M%	C%	H%	N%	Cl%			
FBBH $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_3$	Colourless	-	71.84 (71.85)	5.43 (5.48)	8.38 (8.39)	-	78	-	-
Mn(II) Complex	pink	10.31 (10.34)	45.06 (45.07)	4.59 (4.62)	5.12 (5.14)	26.29 (26.33)	64	14.25	5.82
Co(II) Complex	pink	11.06 (11.08)	45.02 (45.05)	3.37 (3.39)	5.25 (5.27)	26.26 (26.28)	68	12.36	4.58
Ni(II) Complex	green	11.09 (11.12)	45.11 (45.17)	3.38 (3.49)	5.32 (5.34)	26.29 (26.32)	68	33.75	4.5 4
Zn(II) Complex	Colourless	12.05 (12.07)	43.52 (43.68)	3.33 (3.36)	5.19 (5.21)	25.67 (25.68)	61	16.74	--

Infrared spectra

The IR spectra of the Mannich base ligand (FBBH) and its complexes are recorded. The IR spectra of the complexes were compared with those of the free ligand in order to determine the coordination sites that may be

involved in coordination.^[10-12] The free ligand FBBH exhibits absorption bands at 3343 , 3171 and $3027\ \text{cm}^{-1}$ which may be due to N-NH of symmetric stretching. The bands appearing at 1644 and $1141\ \text{cm}^{-1}$ are due to C=O group of the ligand $\nu_{(\text{C}=\text{O})}$ and $\nu_{(\text{C}-\text{O}-\text{C})}$ of furan

respectively. The bands of $\nu_{(C=O)}$ adjacent to $-NH-$ and hydrozinic N-H attached to methine $\nu_{(N-H)}$ viz. 1644 cm^{-1} and 3171 cm^{-1} have been shifted to lower frequencies in the spectra of complexes. These shifts are indicative of the involvement of oxygen atom and nitrogen of benzohydrazide group in coordination with central metal

ion. Hence the ligand acts as a neutral bidentate one. The presence of coordinated water molecular in Mn(II) chloro complex is determined by the appearance of band at $3200\text{--}3400\text{ cm}^{-1}$ and a peak at 884 cm^{-1} is assignable to the $-OH$ stretching and rocking mode of coordinated water molecule.

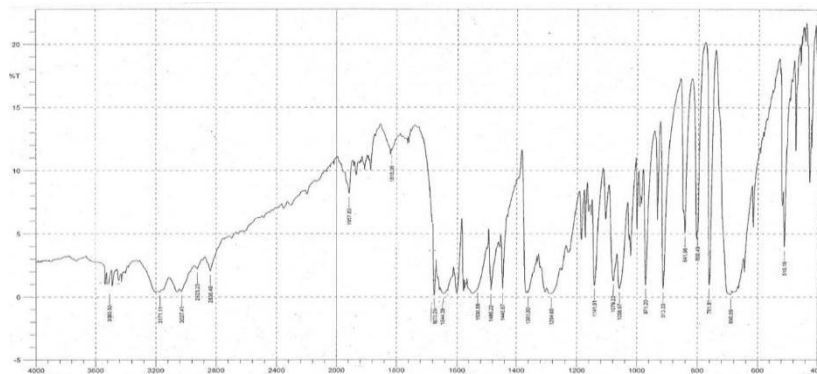


Fig. 1: IR Spectra of ligand using KBr pellets.

Magnetic moment and UV-Visible spectra

Electronic spectra and magnetic measurements were recorded in order to obtain information about the geometry of the complexes. The μ_{eff} (5.82) value of the Mn (II) representing an octahedral geometry of the ligand around the central metal ion. The four coordinated Co(II) complex shows μ_{eff} value of 4.58 which indicates the presence of three unpaired electrons, supports tetrahedral geometry. The observed zero magnetic moment value confirms the square planar environment for the Ni (II). The Zn (II) complex is found to be diamagnetic as expected for d^{10} configuration. The electronic spectra of the ligand and its complexes were recorded in DMSO solution. The Mn (II) complex under the present study exhibits a broad band in the region $22,752 - 24,649\text{ cm}^{-1}$. The broadness of the band may be due to Jahn-Teller distortion. These observations indicate that the complexes have distorted octahedral structure. Co (II) complex displays a band at $14,916\text{ cm}^{-1}$ which assigned to ${}^4A_2 \rightarrow {}^4T_1$ for tetrahedral geometry. The Ni (II) complex is a diamagnetic suggesting a square planar geometry. It showed a broad band at 14588 cm^{-1} which is assigned to ${}^1A_{1g} \rightarrow {}^1B_{1g}$. The spectra of this complex consistent

with this assignment. The spectra of Zn (II) complex exhibited band assigned to $L \rightarrow M$ charge transfer. It is diamagnetic as expected.

1H NMR and ${}^{13}C$ NMR spectra

1H NMR spectrum of FBBH was recorded in DMSO solvent. The compound exhibits multiplet at δ 7.3-7.4 ppm due to protons of furan. A broad band at δ 6.73 ppm is assigned to N-H proton adjacent to C=O and a sharp band at 2.73 ppm is assigned to N-H proton of terminal hydrazine. A multiplet between at δ 7.49-7.57 ppm is assigned to C-H of benzene rings. The methine proton is not split up by the adjacent N-H proton which appear at δ 3.2 ppm.

The ${}^{13}C$ -NMR spectrum exhibits the resonance of ketonic carbonyl carbon at δ 163.15 ppm and amide carbon at δ 147.79 ppm. The chemical shift of aromatic carbon appears between δ 130.06 and 133.29 ppm. The peaks at 134.29 and 13.5.43 ppm may be assigned to the substituted carbons in benzene and furyl ring respectively. The methine carbon which is directly bonded to benzene ring exhibits signal at δ 38.62 ppm. Methylene carbon exhibits peak at δ 39.73 ppm.

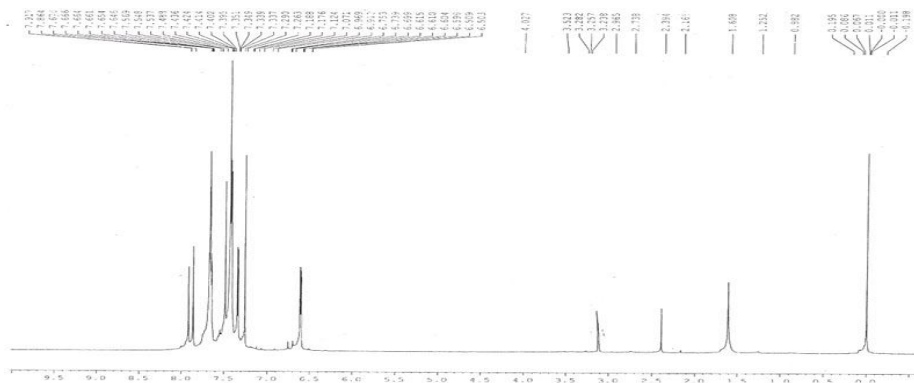


Fig. 2: 1H -NMR Spectra of ligand in DMSO-D6 solvent.

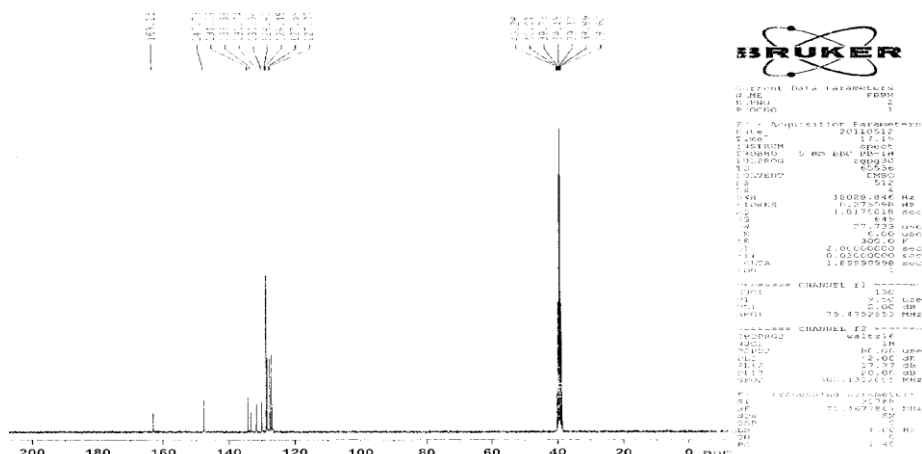


Fig. 3: ^{13}C -NMR spectra of ligand in DMSO-D6 solvent.

In vitro antibacterial assay

For in vitro antimicrobial activity, the synthesized compounds were tested against the bacteria *Bacillus Subtillis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* and fungi *Candidaalbicans* and *Aspergillus niger*. The minimum inhibitory concentration (MIC) values of the investigated compounds with the standard drugs are presented in Table 2. Antimicrobial activity of metal chelates can be explained on the basis of coordination theory/[13-16] 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 electrons over the whole chelate ring and enhances the presentation of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganism. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organism.

Table: 2 Antimicrobial Activities of Metal Complexes of FBBH

Compound	<i>Bacillus substillis</i>	<i>Staphylococcus Aureus</i>	<i>Escherichia Coli</i>	<i>Pseudomonas Aeruginosa</i>	<i>Candidaalbicans</i>	<i>Aspergillus niger</i>
FBBH	24	19	21	20	11	23
Mn(II) complex	20	17	22	19	12	17
Co(II) complex	20	21	20	22	15	18
Ni(II) complex	19	20	19	25	12	19
Zn(II) complex	20	19	28	18	18	20
Standard	30*	23*	31*	30*	33**	32**
Solvent(DMSO)	NI	NI	NI	NI	NI	NI

NI=No Inhibition, *Ciprofloxacin, **Nystatin

CONCLUSION

It may be concluded that the ligand behaves as bidentate chelating agent and the spectroscopic techniques were well supported to our proposed structure. The metal complexes showed good microbial activity than the ligand was observed.

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