



Antimicrobial Potentials of 1,1-Hydrazine-1,2-Diphenylbis(Methanylidene) Bis(Naphthalene-2-Ol) and its Mn^(II), Fe^(II) and Cu^(II) Complexes

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ABSTRACT

1,1-Hydrazine-1,2-Diphenylbis(methanylidene)bis(naphthalene-2-ol) and its M(II) (M = Mn^(II), Fe^(II) and Cu^(II)) complexes were synthesized by refluxing the ligand and corresponding aqueous solution of metal(II) chloride in hot ethanol. The precipitates obtained were recovered by filtration, purified by recrystallization in absolute methanol and later dried. The ligand and all the M(II) complexes were characterized based on Fourier Transform Infrared (FT-IR) spectroscopy, elemental analysis, magnetic susceptibility, solubility, conductivity and melting/decomposition temperature. Sharp melting temperature obtained indicates the purity of the compounds. Peaks; 1655cm⁻¹, 1599cm⁻¹, 1600cm⁻¹ and 1612cm⁻¹ corresponding to the azomethine (-C=N-) group vibration frequencies for the ligand and metal(II) complexes were observed respectively, The shift in the bands observed in the spectra of the complexes indicates coordination of the azomethine nitrogen to the metals. Elemental analysis results showed 1:1 ligand to M(II) ratio. Magnetic susceptibility results revealed that the complexes are paramagnetic while molar conductance values showed that they are non-electrolytes. The antimicrobial potentials of the compounds were tested against four (4) bacterial isolates; Staphylococcus aureus (S. aureus), Escherichia coli (E.coli), Klebsiella pneumoniae (K. pneumoniae), Proteus mirabilis (P. mirabilis) and three (3) fungal isolates; Candida albicans (C. albicans), Fusarium solani (F. solani) and Aspergillus fumigates respectively using disc diffusion technique. The test compounds were found to be active against most of the test organisms. The highest activity was observed against S. aureus at 1000µg/disc. All the compounds show promising application as antibacterial and antifungal.

Keyword: C Schiff base, Azomethine, Reflux, Complex and Antimicrobial

1.0 INTRODUCTION

Schiff bases are nitrogen analog of an aldehyde or ketone in which the carbonyl group (C=O) has been replaced by an imine or azomethine group. Aromatic aldehydes, especially with an effective conjugation system, form stable Schiff bases, whereas those aliphatic aldehydes are unstable and readily polymerize. Generally Schiff bases with aldehyde are formed more readily than with ketones. Schiff bases are very flexible and have different structures (Chandra *et al.* 2012).

Phenolic Schiff bases and their derivatives behave as flexidentate ligands and commonly coordinate through the O atom of the deprotonated phenolic group and the N atom of azomethine group. Schiff bases have significant importance in chemistry; especially in the development of Schiff base metal complexes. Schiff bases are capable of forming stable complexes with metal ions, they have been reported to possess biological properties such as antibacterial and antifungal activities (Williams 1972; Campos *et al.* 1999; Sari *et al.* 2003; Nair *et al.* 2006). Metal complexes of Schiff base have been widely studied because they have

anticancer and herbicidal applications (Kozi *et al.* 2004; Muhammad *et al.* 2011). They

2.0 MATERIALS AND METHODS

All the reagents used were obtained from Sigma Aldrich and were used without further purification.

2.1 Bacterial Species

The isolates used in this study were obtained Aminu Kano Teaching Hospital and identified at Microbiology Laboratory, Department of Microbiology, Bayero University Kano. The isolates were *Staphylococcus aureus* (*S. aureus*), *Escherichia coli* (*E.coli*), *Klebsiella pneumoniae* (*K. pneumoniae*), *Proteus mirabilis* (*P. mirabilis*), *Candida albicans* (*C. albicans*), *Fusarium solani* (*F. solani*) and *Aspergillus fumigates* (*A. fumigates*). Nutrient Agar (NA) and Potato Dextrose Agar (PDA) were used as bacterial and fungal media respectively.

2.2 Synthesis of the Ligand

The ligand was prepared according to the method described by Aliyu and Sani (2012). 20mmol (3.44 g) 2-hydroxy-1-naphthaldehyde and 10mmol equivalent hydrazine monohydrate were condensed in refluxing ethanol for two (2) hours. The resulting precipitate was cooled, filtered, washed with ethanol and diethyl ether and dried in a desiccator over CaCl_2 .

2.4 Synthesis of the Metal (II) Complexes

Solution of metal (II) chloride (10mmol) in boiling ethanol was added to 10mmol (2.12g) ethanol solution of the Schiff base. The mixture was refluxed for three (3) hours. The resulting precipitates were filtered, washed successively with ethanol, diethyl ether and dried in desiccator over CaCl_2 for five (5) days (Aliyu and Sani, 2012).

2.5 Antimicrobial Studies

Antimicrobial activity of the ligand and its metal (II) complexes was tested against *S. aureus*, *E.coli*, *K. pneumoniae*, *P. mirabilis*, *C. albicans*, *F. solani* and *A. fumigates* using

serve as models for many biologically important species (Muhammad *et al.* 2011) Disc Diffusion Method (Cohan *et al.* 2004). Autoclave sterilized aliquots of Nutrient Agar (NA) and Potato Dextrose Agar (PDA) were used for the antibacterial and antifungal studies respectively. The prepared Agar were poured into 90mm petri-dishes. Once these plates were cooled, the microbial suspensions were spread on the agar media using sterile swab. Discs of 6mm diameter were punched and serial dilution of the test compounds were prepared to give 1000, 500 and 250 $\mu\text{g}/\text{disc}$. These prepared discs were placed on the plates and incubated at suitable optimum temperatures for 24hrs.

3.0 RESULTS AND DISCUSSION

A ligand (H_2L) and its Metal (II) complexes were successfully synthesized by condensing 2-hydroxy-1-naphthaldehyde and hydrazine monohydrate in absolute ethanol. The Schiff base was obtained as yellow crystals in good yield (Table 1). The Schiff base was then chelated to Mn^{2+} , Fe^{2+} and Cu^{2+} ions to obtain the complexes as brown, green and blue crystals respectively (Table 1). The complexes showed improved thermal stability compared to the Schiff base as indicated by the melting/ decomposition temperatures. All the metal (II) complexes were non electrolyte (Geary, 1971) as indicated by the molar conductivity values (Table 1). The magnetic susceptibility results showed that all the complexes are paramagnetic while the elemental analysis data revealed 1:1 Schiff base to metal ratio in all the complexes. Solubility results showed that all the compounds are soluble in dimethylsulfoxide and protonic solvents such as methanol and ethanol, insoluble in distilled water, ether, acetonitrile, nitrobenzene and carbontetrachloride while slightly soluble in acetone and dimethylformamide. These solubilities/insolubilities may be attributed

to the ability/inability of the test compounds to form hydrogen bond with the respective solvents used.

Table 1: Physical and Analytical Data of the Schiff base and its Metal (II) Complexes

Compound	% Yield	Colour	Melting Temp. (°C)	Elemental Analysis Calc. (Found)			Magnetic (μ_{eff} Temp. (K))	Molar Conduct. ($\Omega^{-1}\text{cm}^2\text{mol}^{-1}$)
				%C	%H	%N		
H ₂ L	78	Yellow	236	77.64 (77.21)	4.70 (4.53)	8.23 (8.11)	-	-
[MnL ₂]	69	Brown	260	67.19 (67.01)	3.56 (3.41)	7.13 (6.97)	4.41	11.00
[FeL ₂]	57	Green	245	67.03 (66.89)	3.55 (3.53)	7.11 (6.91)	5.26	19.00
[CuL ₂]	80	Blue	278	65.75 (64.01)	3.49 (3.15)	6.97 (6.88)	2.12	7.50

KEY: L= N,N'-Bis(2-hydroxy-1-naphthyl) Hydrazine

Table 2: Solubility of the Schiff base and the metal (II) complexes

Solvent	H ₂ L	[MnL ₂]	[FeL ₂]	[CuL ₂]
Distilled Water	IS	IS	IS	IS
Methanol	S	S	S	S
Ethanol	S	S	S	S
Acetonitrile	IS	IS	IS	IS
Nitrobenzene	IS	IS	IS	IS
Acetone	SS	SS	SS	SS
Ether	IS	IS	IS	IS
CCl ₄	IS	IS	IS	IS
DMF	SS	SS	SS	SS
DMSO	S	S	S	S

KEY: L= N,N'-Bis(2-hydroxy-1-naphthyl) Hydrazine

S= Soluble, SS= Slightly Soluble and IS= Insoluble

Arrangement of the solvents: Distilled water, MeOH, EtOH, Acetonitrile, Nitroben, Acetone, Ether, CCl₄, DMF, DMSO.

The IR spectra of the ligand and the M(II) complexes were recorded on a Shimadzu 4800S FT-IR spectrophotometer in the range 4000-400 cm^{-1} and presented in Table 3. Sharp bands at 1655 cm^{-1} and 3434 cm^{-1} were observed in the spectra of the ligand which is attributed to the azomethine (-HC=N-) and phenolic -OH stretching vibrations respectively (Aliyu and Sani, 2011). The ν (-HC=N-) stretching vibrations appear at lower frequencies in the spectra of

the M(II) complexes which indicates coordination of N to the metals. The ν (-OH) stretching vibration disappeared in the spectra of the M(II) complexes. This indicates deprotonation and covalent bond formation between the phenolic O and the metal ions (Byeon Goo *et al.* 1996). Two more new bands were observed at lower region (776-778 cm^{-1} and 406-430 cm^{-1}) in the spectra of the complexes corresponding

to M-N and M-O bond formation respectively.

Table 3: Selected Vibration Frequencies of the Schiff base and the M(II) Complexes

Compound	$\nu(\text{O—H}) \text{ cm}^{-1}$	$\nu(\text{C=N}) \text{ cm}^{-1}$	$\nu(\text{M—N}) \text{ cm}^{-1}$	$\nu(\text{M—O}) \text{ cm}^{-1}$
H ₂ L	3434	1655	—	—
[MnL ₂]	—	1599	776	421
[FeL ₂]	—	1600	778	430
[CuL ₂]	—	1612	776	406

KEY: L= N,N'-Bis(2-hydroxy-1-naphthyl) Hydrazine

The *in-vitro* antibacterial activity of the ligand and its M(II) complexes showed that all the compounds were active against the gram positive bacterium (*S. aureus*) and unicellular fungus (*C. albicans*), in active against gram negative bacterium (*K. pneumoniae*), at all concentrations (Table 4). Highest activity was observed in Cu(II) complex against *S. aureus* at 1000 $\mu\text{g}/\text{disc}$ while the least activity was observed in the Schiff base against *E. coli* at same concentration. The test compounds were inactive against the gram negative bacterium (*K. pneumoniae*). It was observed that the gram positive bacteria are more susceptible

to the test compounds compared to the gram negative bacteria used, which could be attributed to the complex structure of the gram negative bacteria. The improved activity in all the M(II) complexes than in the free Schiff base ligand may be attributed to chelation (Cohan *et al.* 2006) which reduces polarity of the metal ion by partial sharing of the positive charge by donor atoms of the ligand. This increases the lipophilic character, favouring the permeation through lipid layers of the bacterial membrane.

Table 4: Antibacterial Activities of the Ligand and the M(II) Complexes

Compound	Conc. (µg/disc)	<i>E. coli</i>	<i>S. aureus</i>	<i>P. aeruginosa</i>	<i>K. pneumoniae</i>	<i>P. mirabilis</i>
Zone of Inhibition (mm)						
H ₂ L	1000	07	17	08	NZI	17
	500	06	09	06	NZI	11
	250	NZI	07	NZI	NZI	08
[MnL ₂]	1000	09	19	11	NZI	20
	500	08	16	08	NZI	14
	250	06	11	06	NZI	08
[FeL ₂]	1000	08	17	13	NZI	11
	500	06	15	09	NZI	11
	250	06	09	06	NZI	08
[CuL ₂]	1000	18	22	09	NZI	20
	500	14	18	09	NZI	14
	250	09	11	06	NZI	11
Ciproflaxacin (Control)	05	15	21	11	06	18

KEY: L= N,N'-Bis(2-hydroxy-1-naphthyl) Hydrazine NZI= No Zone of Inhibition

Table 5: Antifungal Activity of the Ligand and the M(II) Complexes

Compound	Conc. (µg/disc)	<i>C. albicans</i>	<i>F. solani</i>	<i>A. fumigates</i>
Zone of Inhibition (mm)				
H ₂ L	1000	09	11	10
	500	06	09	07
	250	NZI	06	NZI
[MnL ₂]	1000	12	08	09
	500	11	NZI	06
	250	07	NZI	06
[FeL ₂]	1000	10	12	10
	500	08	11	09
	250	07	08	07
[CuL ₂]	1000	13	11	07
	500	11	09	07
	250	NZI	08	NZI
Mancozef (Control)	10	24	19	22

KEY: L= N,N'-Bis(2-hydroxy-1-naphthyl) Hydrazine NZI= No Zone of Inhibition

The *in vitro* antifungal activities (Table 5) of the Schiff base and the metal (II) complexes were studied as described by Cohan *et al.* (2004). The test compounds were found to be active against all the test fungi at high (1000µg/disc) concentration with the highest activity for Cu(II) complex against *Candida albicans* fungus. It can also be observed that the metal (II) complexes showed more activity compared to the free ligand. The high activity may be attributed to chelation [18] and extra stability of the complexes when compared to the unchelated ligand.

4.0 CONCLUSION

A Schiff base ligand 1,1-Hydrazine-1,2-Diphenylbis(methanylidene)bis(naphthalene-2-ol) and its M(II) (M = Mn^(II), Fe^(II) and Cu^(II)) complexes were successfully synthesized and characterized. Both the Schiff base and the complexes were coloured and thermally stable. The antibacterial and antifungal study out comes showed that all the test compounds are promising antimicrobial agents.

5.0 REFERENCES

- Aliyu H. N. and Sani U.: Synthesis, Characterization and Biological Activity of Manganese (II), Iron(II), Cobalt(II), Nickel(II) and Copper(II) Schiff base Complexes Against Multidrug Resistant Bacterial and Fungal Pathogens, International Research Journal of pharmacy and Pharmacology, 2012; 2(2), 40 – 44
- Aliyu H. N. and Sani U.: Synthesis, Physicochemical Characterization and Microbial Activity of N,N bis(2-hydroxyl-1-naphthalyl)propylenediiminato Metal (II) Complexes, Journal of Asian Scientific Research, 2011, 1(8), pp 300 – 406
- Byeon Goo J., Chae-Pyong R., Hee-Nam C., Ki-Hyung C., Yohng-Koo C., Synthesis and Characterization of Schiff base derived from 2-Hydroxy-1-naphthaldehyde and Aliphatic Diamines, Bull. Korean Chem. Soc. 1996, 17(8), pp 687 – 693
- Campos A. Anacona JR and Campos-Vallette M M. Main group Metal chem. 1999; 22: 283.
- Chandra S., Raizada S. and Verma R.: Synthesis, Characterization and Biological Activities of Copper (II) Complexes with Semicarbazones and thiosemicarbazones, Journal of Chemical and Pharmaceutical Research, 2012, 4(3), pp 1612 – 1618
- Cohan Z. H., Perez H., Rauf A., Khan K. M., Supuran C.T.: Antibacterial Study of Copper(II), Cobalt(II), Nickel(II) and Zinc(II) Complexes of Mercaptothiszole derived from furanyl, thienyl, pyrrolyl, salicyl and pyridinyl Schiff bases, J. Enzyme Inhib. Med. Chem. 2006, Vol. 21 pp 193 – 201
- Cohan Z.H., Pervez H., Rauf A., Khan K.M., Maharvi G.M., Supuran C.T.: Antibacterial and Antifungal Mono and Di-substituted Symmetrical and Unsymmetrical Triazine derived from Schiff bases and their Transition Metal complexes, J. Enzyme inhib. Med. Chem. 2004, Vol. 19, pp 161 – 168
- Cozzi PG. (2004): Metal-salen Schiff base complexes in catalysis: Practical aspects. Chem. Soc. Rev.; 33: 410.
- Geary W. J.: The Use of Conductivity Measurements in Organic Solvents for Characterization of Coordination Compounds, Coord. Chem. Review, 1971, 7(1), pp 81 – 122
- Muhammad AA. Abdul W. Mahmood K. Mohd. J M and Ismail Y. Spectral Investigation of the Activities of Amino Substituted Bases. Oriental

- Journal of Chemistry. 2011; 27: 363-372.
- Nair R. Shah A. Baluja S. and Chanda S. Synthesis and antibacterial activity of some Schiff bases Complexes. J. Serb. Chem. Soc. 2006; 71: 733–744.
- Sari N. Arslan S. Logoglu E and Sakiyan I. Antibacterial activities of some Amino acid Schiff bases. G. U. J. Sci. 2003; 16: 283.
- Williams DR. (1972): Metals, Ligand and Cancer. Chem. Rev., 72: 1972.