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Original Article

Synthesis and evaluation of antimicrobial activity of two Schiff bases derived from cyclohexylamine

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ABSTRACT

Design and development of novel materials with outstanding antimicrobial properties has transpired to hinder and regulate the growth of microorganisms. Indubitably, Schiff bases are the magic bullet that have efficient antimicrobial properties against various pathogenic strains. The Schiff bases, L^1 and L^2 reported herein were respectively synthesized by equimolar condensation of benzophenone with cyclohexylamine and 2,4-dihydroxybenzophenone with cyclohexylamine. The products were obtained in excellent yield of 66 and 75 %. The Schiff bases were subjected to solubility test, melting point determination and FT-IR spectroscopic analysis. They were found to show relative thermal stability with melting points of 220 and 195 ^{o}C and solubility in methanol, acetone and dimethylformamide of the solvents used. The FT-IR confirmed the formation of the Schiff bases with appearance of azomethine (C=N) peak at 1652 and 1592 cm^{-1}. The *in vitro* antimicrobial activity of the Schiff bases was tested against two gram positive bacteria (*Staphylococcus aureus* and *Streptococcus pyogens*) and two gram negative (*Pseudomonas aureginosa* and *Escherichia coli*) as well as two fungi strains (*Aspergillus niger* and *Candida albicans*). The results reveal that the Schiff base L^2 shows promising activity against all the pathogen under investigation. However, no activity was observed for L^1 against the microbes except *Streptococcus pyogens.*

1. Introduction

Schiff bases occur from reaction of primary amines and carbonyl compounds (aldehydes or ketones) and were first reported in 1864 by German chemist Hugo Schiff [1]. The bond formed by reaction with aldehydes is called azomethine or aldimine while the bond formed by reaction with ketone is called imine or ketimine [2]. Schiff bases are an important class of organic compounds and a great number of Schiff base compounds have been studied due to their facile synthesis, biological applications, chelating properties and stability [3]. These compounds have received considerable attention in development of inorganic biochemistry and pharmacological fields because of their excellent biological activities as antibacterial, antifungal [4], antioxidant and anticancer [3,5]. Several studies showed that the presence of a lone pair of electrons in nitrogen atom of azomethine group is of considerable chemical and biological importance [6].

Since prehistoric times, microbial infections are one of the most common diseases known to humanity and mortality due to these infections with even antimicrobial therapy is still unacceptable on the increase. Therefore, the development of new antimicrobial agents targeting bacterial and fungal structures is being actively pursued [7].

In the present study, the antimicrobial activity of two Schiff bases derived from benzophenone with cyclohexylamine (L^1) and 2,4-dihydroxybenzophenone with cyclohexylamine (L^2) have been reported.

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2. Materials and Methods

2.1. Material

All chemicals used were of analytical grade and used without further purification. These include cyclohexylamine (BDH), benzophenone, 2,4-dihydroxybenzophenone (Aldrich), ethanol, glacial acetic acid, methanol, ethanol, acetone, benzene, dimethylformamide, tetrachloromethane, distilled water.

2.2. Instrumentation

The FT-IR spectra of the Schiff bases were recorded at the Department of Pure and Industrial chemistry, Bayero University, Kano, Nigeria using FTIR- Fourier transform infrared spectrophotometer, Agilent Technologies with a resolution of 8 cm^{-1} in the region 4000-650 cm^{-1}. Melting points were determined on Electrothermal 9200 apparatus at the Department of Pharmaceutical Chemistry, University of Maiduguri, Nigeria.

2.3. Synthesis of Schiff base ligands

Benzophenone (24 mmol) dissolved in 30 ml of ethanol was added to cyclohexylamine (24 mmol) diluted in isochoric ethanol with continuous stirring. To the resulting mixture, 1 ml of acetic acid was added as catalyst. The reaction mixture was refluxed for 3 hours at 70 ^{o}C in 100 ml flask equipped with condenser on a magnetic stirrer. The resulting solution was evaporated and cooled to ambient temperature, then refrigerated for crystallization to occur. The product obtained (L^1) was filtered, washed with cold ethanol and dried in a desiccator that contains silica gel as moisture adsorbent [8]. The procedure was repeated for L^2 with 2,4-dihydroxybenzophenone in place of benzophenone using methanol as medium. The reaction is depicted in Fig. 1.

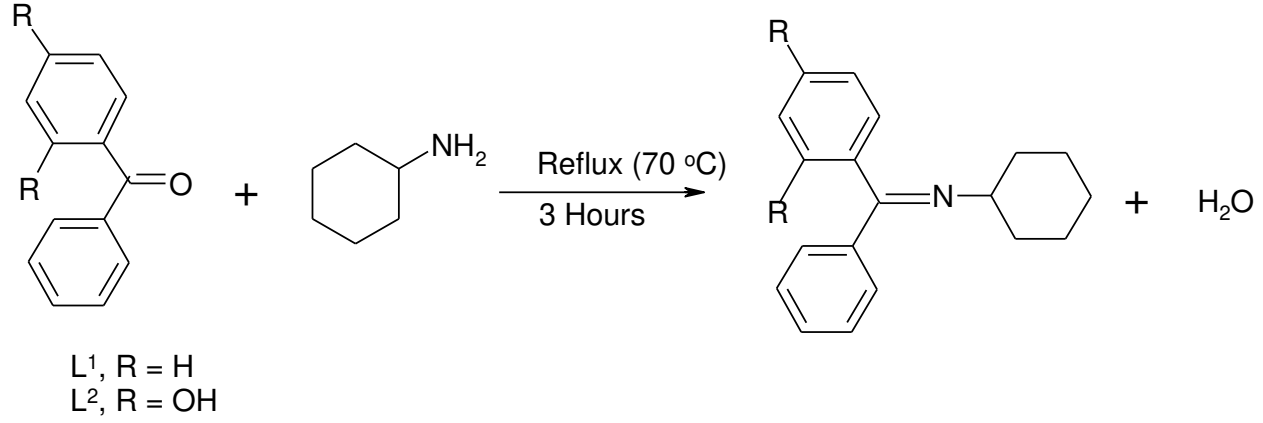


Fig. 1 Schematic Depiction of Synthesis of the Schiff base ligands

2.4. Antimicrobial screening

The antimicrobial assay of the Schiff bases was performed against two-gram positive (*Staphylococcus aureus*, *Streptococcus pyogenes*) and two-gram negative (*Escherichia coli, Pseudomonas aeruginosa*) bacteria using disc diffusion method. Sterilized petri dishes of 9 mm having autoclaved Muller Hinton agar (10 ml) was used. The solutions of the Schiff bases were prepared using dimethylsulphoxide (DMSO) solvent. Broth culture having used bacteria was incubated with autoclaved Muller Hinton agar at 38 ^{o}C. Further, the plates were kept for incubation for 24 and 72 hours for antibacterial and antifungal study respectively. The zones of inhibition present at each disc was carefully measured and recorded [9].

3. Results and Discussion

The two Schiff bases, L^1 and L^2 were respectively afforded in very good yield of 66 and 75 *% via* the condensation of benzophenone/2,4-dihydroxybenzophenone with cyclohexylamine in 1:1 mole ratio. The obtainment of these compounds in good yield might be attributed to optimization of reaction conditions such as temperature and solution concentration [10,11]. The Schiff bases, L^1 and L^2 were respectively white crystalline solid and brown jelly-like in appearance. They are non-hygroscopic, stable to air and light with sharp melting points of 220 ^{0}C and 195 ^{0}C respectively. These sharp and relatively high melting points is an indication of probable purity and thermo-stability [12-14]. The characteristics of the Schiff bases are furnished in Table 1. The formation of the Schiff bases was verified by determining the melting points and conducting infrared spectral studies [7]. The IR spectra data of the ligands, L^1 and L^2 show peak around 1592 and 1652 cm^{-1} conforming to the presence of azomethine (>C=N-) bond, thus confirming the formation of the Schiff base [15,16]. The FTIR spectra of L1 and L2 are respectively shown in Fig. 2 and 3.

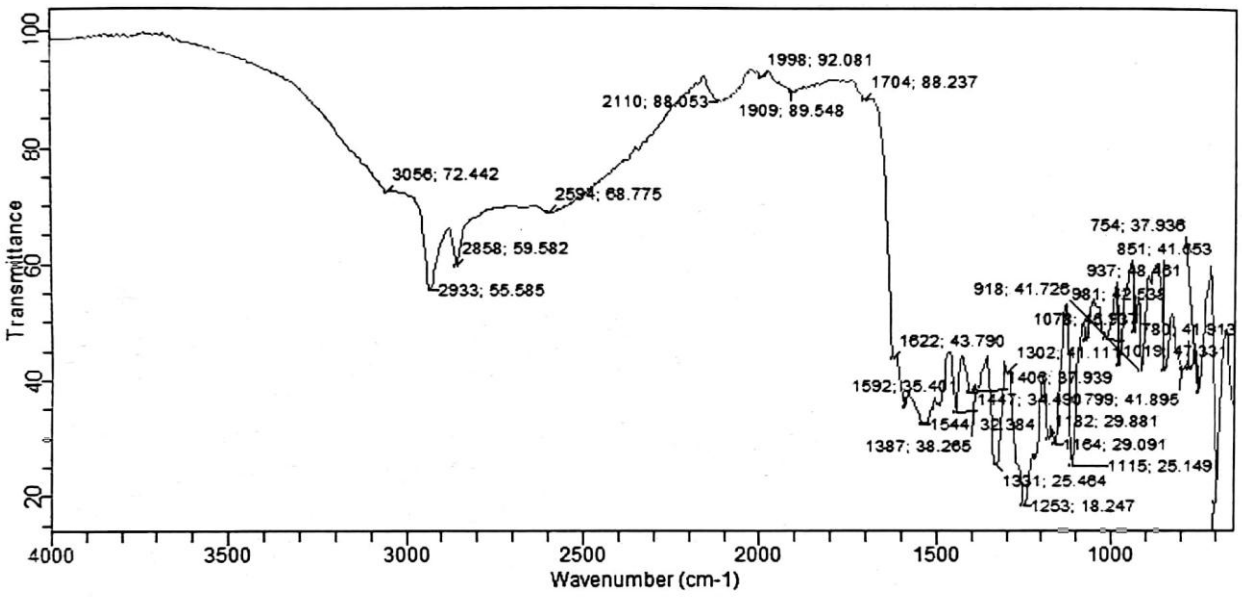


Fig. 2 FTIR spectrum of L^1

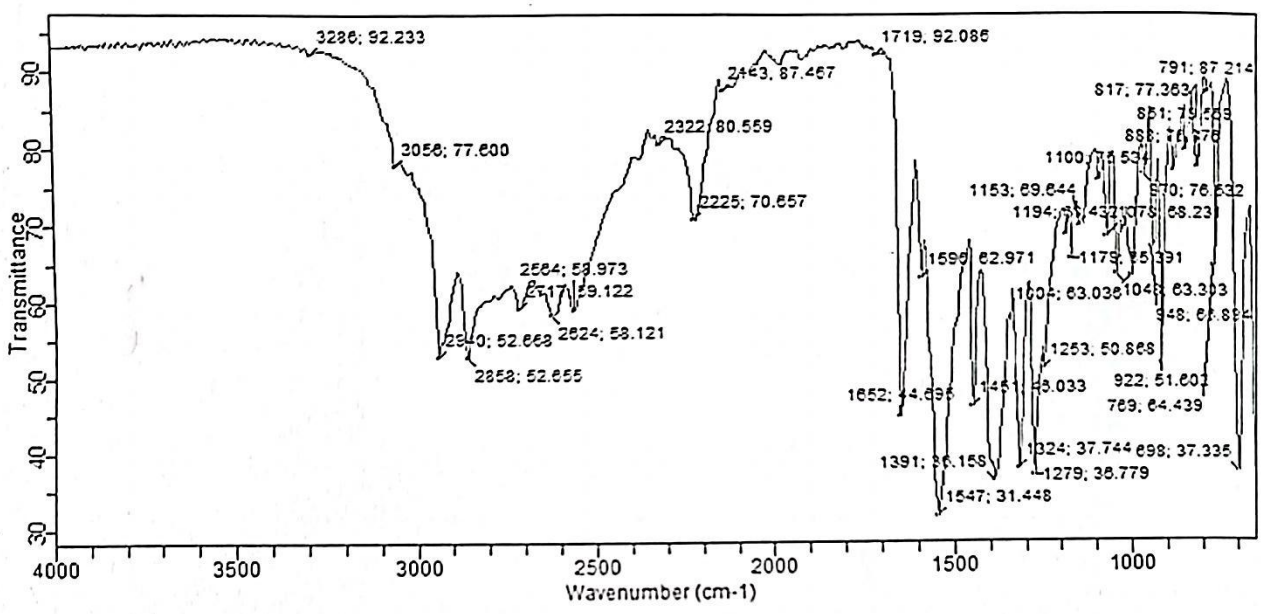


Fig. 3 FTIR spectrum of L^2

Table 1. Characteristics data of the Schiff bases

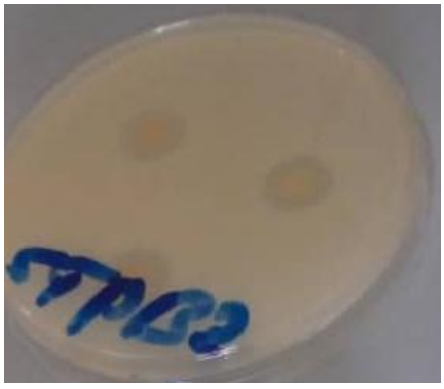
Schiff bases	Characteristics					FT-IR (cm^{-1})
	% Yield	Colour	Physical form	Melting point (^oC)	Solubility	ν(C=N)
L^1	66	Light brown	Crystalline	220	Water, methanol,	1592

					DMF, DMSO	
^{2}L	75	Brown	Jelly	195	Acetone, methanol, DMF, DMSO	1652

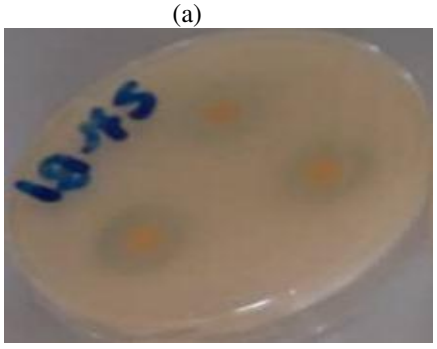
The antimicrobial activity of the synthesized Schiff bases was examined against some bacterial and fungal strains. The details of the antibacterial and antifungal assays are furnished in table 2 and Pictorial inhibition zones in plates 1 and 2. The result indicates that the microorganisms are resistant to the Schiff base ligand, L^1 at both concentrations except *Pseudomonas aeruginosa* which was moderately inhibited. The resistance of these microorganisms to the Schiff base could be attributed to the ability of the microbes to develop what is called genetic mutations. The mutation alters the antibiotic action via modification of the antimicrobial target sites that is decreasing the affinity for the drug and drug uptake, activation of efflux mechanisms to extrude the harmful molecule or genetic mutations might enable microbes to produce enzymes that deactivate antibiotics eliminating the target that the antibiotics are supposed to attack [17].

The Schiff base ligand, L^2 exhibits good activity against the following bacteria, viz: *Staphylococcus aureus, Streptococcus pyogenes* and *Pseudomonas aeruginosa* and all studied fungi, viz: *Candida albicans* and *Aspergillus niger*. The antimicrobial activity of these ligands increases with increase in the concentrations of the Schiff bases. The mechanisms of inhibition of the growth of the bacteria and fungi by these compounds are by:

- blockage of the synthesis of cell wall as a result the cell permeability may be altered or they may disorganize the lipoproteins leading to cell death [18];
- deactivation of various cellular enzymes which are important in the microorganism's metabolic pathways;
- formation of hydrogen bond through the azomethine group with the active centres of cell constituents resulting in interfering with the normal cell processes.
- Furthermore, denaturation of one or more proteins of the cell, as a result of which the normal cellular processes are impaired [7,17,19].



(a)



(b)

(c) (d)

Plate 1: Inhibition zone of (a) *Staphylococcus aureus* (b) *Streptococcus pyogene* (c) *Pseudomonas aeruginosa* (d) *Escherichia coli for* L^2

(a) (b)

Plate 2: Inhibition zone of (a) *Aspergillus niger* (b) *Candida albicans* for L^2

Table 2. Antimicrobial Assay of the Schiff bases

Schiff base	Concentration (ppm)	Diameter (mm) of zone of inhibition					
		Staphylococcus aureus	*Streptococcus pyogenes*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Aspergillus niger*	*Candida albicans*
L^1	100	0	0	0	7	0	0
	200	0	0	0	10	0	0
^2L	100	12	13	0	22	10	15
	200	16	17	0	26	20	22

4. Conclusion

Two Schiff base ligands obtained by condensation of cyclohexylamine with benzophenone and 2,4-dihydroxybenzophenone have been prepared and confirmed their formation by infrared spectroscopy and melting point determination. Furthermore, these compounds were investigated for their antibacterial and antifungal activity against some bacterial and fungal strains. With the exception of *Escherichia coli*, the results hold a great promise for the use of these Schiff bases as potential future antimicrobial agents. Further antimicrobial studies should be extended to other bacterial and fungal strains.

Conflict of Interest

The authors declare that they have no conflict of interest

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