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RESEARCH ARTICLE

Preparation, Characterization and Antibacterial Study of Schiff Base Derivatives

Ayat Abdulkareem Ibrahim[1], Sarah Alaa Muhi[2*], Dhifaf Handhal Bandar[1]

[1]Department of Chemistry, College for Sciences, University of Kerbala, Iraq.

[2]Department of Biology, College for Sciences, University of Kerbala, Iraq.

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Corresponding author:

Sarah Alaa Muhi

Email: biologistsara9@gmail.com

Department of Biology, College for Sciences, University of Kerbala, Iraq.

ABSTRACT

Recently developed Schiff base derivative, specifically designated as G1, was synthesized and meticulously analyzed through fourier transform infrared (FTIR) spectroscopy. Compound G1 is identified as (E)-N,1-bis(4-chlorophenyl) methenamine. The *in-vitro* antibacterial efficacy of these substances was thoroughly assessed in relation to *Escherichia coli, Streptococcus faecalis*, and *Staphylococcus aureus* bacterial strains. The results indicate a noteworthy antibacterial activity of compound G1, exhibiting minimum inhibition concentration (MIC) values of 16, 13, and 10 µg/mL, respectively, when compared to the established standard.

INTRODUCTION

In light of the escalating rate of resistance observed in prevailing antibacterial therapies, there is a pressing need for the exploration and development of novel, selective,[1] and non-toxic[2] antibacterial agents within the realm of medicinal chemistry. The persistence and emergence of drug resistance among pathogenic bacteria, despite the existence of diverse classes of antibacterial agents, pose significant challenges. The inherent chemical diversity and myriad mechanisms of action further complicate the identification of definitive strategies for the discovery of new drugs. Consequently, the treatment of infectious diseases has become increasingly intricate, contributing to the resurgence of diseases previously believed to have been managed, like malaria.

To tackle this pressing medical issue, novel antimicrobial agents must be discovered, or the bioactivity of already available medications must be improved.[3] Consequently, contemporary research endeavors are increasingly directed toward the creation of novel halogens and metal complexes to create antibacterial agent compounds to counteract bacterial resistance to available drugs. Globally, the synthesis, characterization, and exploration of the structural-activity relationships of Schiff bases have gained prominence, given the established significance of the C=N linkage in Schiff bases for

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bioactivity.[4] The pronounced bioactivity of these compounds predominantly stems from alkyl/aryl/heteroaryl groups with multi-substituents appended to the C=N moiety.

Schiff bases have garnered attention for their noteworthy antibacterial,[5] antifungal,[6] anticancer,[7] urease inhibition,[8] antioxidant,[9-14] and antiglycation[15-17] activities. Prior studies have documented the potent antibacterial efficacy of Schiff bases against a range of harmful microorganisms.[13-25] As a result, the current study is concentrated on the synthesis and evaluation of novel derivatives of Schiff base compounds, incorporating additional donor-acceptor groups (Cl). This structural modification renders them promising candidates for creating an additional active site and emulating biological systems. The synthesized compound is systematically evaluated against pathogenic bacteria, namely *Escherichia coli, Streptococcus faecalis*, and *Staphylococcus aureus*, with the aim of elucidating the impact of Schiff base on their antibacterial effects.

MATERIAL AND METHODS

General

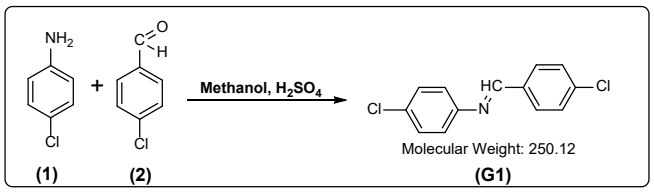
Chemicals and solvents were procured from commercial vendors and used straight out of the package without further filtration processes. The FTIR spectrum was acquired utilizing a Tensor II Bruker-Optics FTIR spectrophotometer (Bruker, Germany).

Synthesis of (G1)

The synthesis of (E)-N,1-bis(4-chlorophenyl) methanimine (G1) was conducted following a previously reported procedure.[23] In a 50 mL flask with a round bottom, 4-chloro Aniline (0.75 gm, 3.0 mmol) was combined with 4-chloro benzaldehyde (3.0 mmol) and dissolved in methanol (20 mL). After adding a catalytic quantity of sulfuric acid, the mixture was refluxed for five hours. The mixture proceeded to cool to room temperature, and filtering was used to gather the precipitated solid. After the collected material was thoroughly cleaned with heated methanol, it was dried., yielding white solid materials denoted as G1, as depicted in Scheme 1.

Solution preparation

A stock solution containing G1 at a concentration of 1.00 mM was meticulously produced by combining 0.283 g of the ingredients with 2 mL of dimethyl sulfoxide. (DMSO), followed by adjusting the volume to 1000 mL. Subsequently, various concentrations ranging from 5 to 30 µm/mL were derived from the stock solution through dilution with the test solution.



Scheme 1: Preparation of the studied Schiff base

Antibacterial tests

Bacterial subcultures of *E. coli*, *S. aureus* and *S. faecalis* were sourced from the biological department of the Holy Karbala Health Department. Approximately Aseptically, 1.5 cm^3 of a 24-hour broth culture with around 106 CFU/cm^3 was added to sterile petri plates. The Mueller-Hinton agar (20 cm^3) was then added to the petri dishes and left to harden at a temperature of around 45°C. After solidification, the test solutions (at the investigated concentrations in DMSO) were carefully poured into 7 mm diameter holes that had been painstakingly punched using a sterile cork borer. The zone of growth inhibition for each sample was determined using the mean value that was found for the two holes.

RESULTS

Synthesis of compound G1

The investigated compound was synthesized through a Schiff base reaction involving 3.0 mmol of 4-Bromoaniline and 3.0 mmol of 4-Chloroaniline, leading to the formation of compounds G1. The overall yield of the synthesized compounds reached approximately 86%.

Upon analysis of the FTIR spectra for synthesized compound G1, distinctive bands were noted. The band indicates a stretching action at 3096 cm^{-1}. of the sp2 aromatic (=CH) group. Additionally, the band at 1668 cm^{-1} is indicative of the imine (C=N) linkage, whereas the bands at 1573 and 1480 cm^{-1} are attributed to the aromatic (C=C) stretching vibrations, as illustrated in Figure 1.

Antibacterial tests

G1 was synthesized and assessed against three clinically significant, multidrug-resistant gram-positive bacterial pathogens, namely *E. coli*, *S. faecalis*, and *S. aureus*. Five different concentrations of the studied compound were employed, and the last-resort antibiotic, daptomycin, served as a control as shown in Figure 2. As depicted in Table 1, show the exhibited biological activity with MIC values of 20, 15, and 10 µg/mL. Despite the preliminary data, drawing definitive conclusions regarding the relationship between chemical

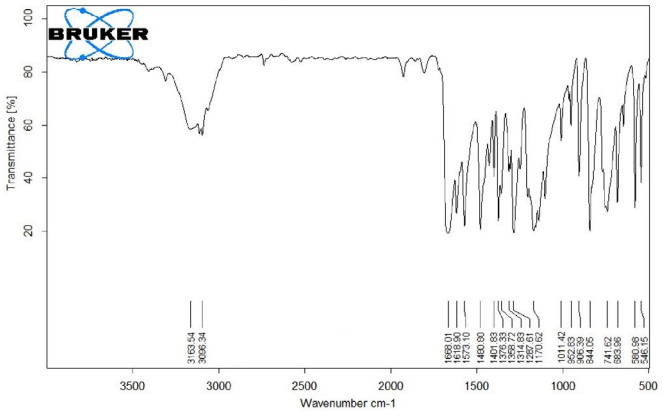


Figure 1: FTIR spectra for synthesized compound G1

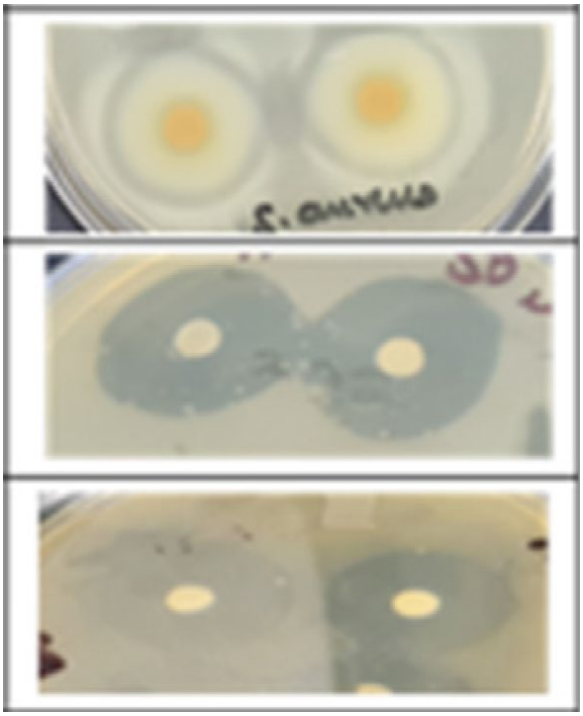


Figure 2: Antibacterial activity against the studied bacteria

Table 1: Antibacterial activity of the studied compound

Compound	*MIC (µg/mL)*		
	E. coli	*S. faecalis*	*S. aureus*
G1	20	15	10
Ciprofloxacin	5	8	3

substitutions and antibacterial activity requires more systematic investigations. Future studies will be essential to thoroughly elucidate the structure-activity relationship in this context.

CONCLUSION

In the present investigation, we have successfully demonstrated a novel and environmentally sustainable methodology for the synthesis of antibacterial imine derivatives. Our approach involved the utilization of 4-substituted amine to design compounds with enhanced structural stability. The synthesis of these imine derivatives was achieved through the Schiff reaction, and their chemical structures were substantiated using Fourier transform infrared spectroscopy (FTIR). Notably, a pronounced improvement in the antimicrobial activity of the synthesized Schiff bases was observed in their imine form. This enhancement can be ascribed to an augmented number of active sites, particularly the increased availability of -C=N- groups, facilitating interactions with the bacterial cell surface through hydrogen bonding and other chemical mechanisms. Consequently, these compounds exhibit considerable potential for diverse applications in the realms of life sciences and biomedicine.

RECOMMENDATIONS

We advocate for researchers to enhance the chemical structures of the investigated compounds through the incorporation of nanomaterials, such as nano-gold or other nanoparticles. Alternatively, employing these compounds as ligands to form complexes represents a promising avenue for further exploration.

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