RESEARCH ARTICLE

New Benzohydrazide Schiff Base: Synthesis, Characterization and Biological Studies

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ABSTRACT

In this study, two new Schiff bases are produced via condensation reaction of 2-hydroxy-3-methoxy benzaldehyde and 2-hydroxy benzaldehyde compounds with benzohydrazide compound. The products are investigated by fourier-transform infrared spectroscopy (FTIR), proton nuclear magnetic resonance (H-NMR), carbon-13 nuclear magnetic resonance (^{13}C-NMR), and mass spectroscopy. Antibacterial activities of synthesized compounds are scanned versus *Staphylococcus aureus* (gram-positive) and *Escherichia coli* (gram negative) strains. The results showed that the Schiff bases compounds illustrated weak effectiveness against *S. aureus*. At the same time, these compounds are found inactive against *E. coli*.

Keywords: Antibacterial activity, Benzohydrazide, Schiff base.

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INTRODUCTION

Schiff bases are organic compounds created using the condensation reaction of the prime amines and carbonyl compounds.[1] First, they were found by the German scientist Hugo Schiff in 1864.[2] The joint structural configuration of such materials is the azomethine categories with the general formula $R_1R_2C{=}NR_3$, where R_1 is an alkyl or aryl group, R_2 is a hydrogen atom, and R3 is either an aryl or alkyl group.[3] The ary substitutes Schiff bases, which are more stable in contrast with alkyl-substituted Schiff bases.[4] Contagious diseases which are caused by bacteria resist antibiotics. This has led to a high mortality rate in elderly people and children nearly (17 million deaths per year) across the globe.[5] Several types of research proved that the availability of the lone pair of electrons in an sp^2 hybridized orbital of the nitrogen atom (i.e., C=N) group represents chemical and biological significance.[6] They form as dyes, catalysts, polymer stabilizers, intermediate compounds in the organic synthesis, pigments,[7] corrosion inhibitors,[8] antioxidants,[9] anti-cancer,[10,11] anti-tubercular,[12] anti-inflammatory,[13,14] anti-malaria,[15] anti-helminthic,[16] anti-hypertensive,[17] anti-depressant,[18] and anti-bacterial.[19] Several important biological Schiff base derivatives include pyrimidines, imidazoles, hydrazines, and hydrazides.[20,21] Hydrazide compounds were considered to act against a wide range of bacteria and were used in oral medication to cure genetic disorders such as thalassemia.[22,23]

Schiff bases are considered antibacterial. Therefore we investigate the synthesis of two hydrazides Schiff bases: benzohydrazide with 2-hydroxy-3-methoxybenzaldehyde or 2-hydroxybenzaldehyde using reflux methods as chemotherapeutic agents with biological characteristics such as antibacterial. The synthesized compounds were investigated by FTIR, H-NMR,13C-NMR, and Mass spectroscopy.

METHODS AND MATERIALS

Chemicals and Equipment

Methyl benzoate was bought from B.DH, hydrazine, 2-hydroxy-3-methoxy benzaldehyde, and 2-hydroxybenzaldehyde and all solvents were purchased from B.DH. Melting points were observed on the SMP31 melting point device. The FTIR was recorded on 250 to 4000 cm^{-1} at Chemistry Department, College of Science, Thi-Qar University, Iraq. 1H-NMR and 13C-NMR spectra were observed on Bruker 499.67 MHz and 125.66 MHz, respectively whereas mass spectra on Agilent Technology Model: 5973 Network Mass Selective Detector and Ion source: Electron Impact (EI) 70eV.

Synthesis of Benzohydrazide

The Benzohydrazide compound shown in Figure 1 was produced by mixing methyl benzoate (14 mL, 0.1 mol) and hydrazine (14 mL, 0.1mol) in absolute ethanol (100 mL). The reflux was achieved in the mixture for 5 hours and evaporated

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until half volume. Light white crystals were generated after cooling. Filtration and washing processes were carried out for the generated product.[24] An excellent yield of 93% was achieved by recrystallization from ethanol (Figure 1).

Synthesis of Schiff Base (LR1R)

"N'-[(Z)-(2-hydroxy-3-methoxyphenyl)methylidene] benzohydrazide"

In a round-bottomed flask with a capacity of 500 mL, (0.02 mole–2.72 gm) of benzohydrazide was dissolved into 30 mL of ethanol. Then gradually add (0.02 mole-3.04 gm) of 2-hydroxy-3-methoxy benzaldehyde dissolved in 10 mL of ethanol. The mixture was enforced to reflux process for 5 hours at the refluxing temperature. The recrystallization procedure was carried out on the product from ethanol,[25] and the result of the reaction was 62.1%. Schiff base synthesis is schematically presented in Figure 2.

Synthesis of Schiff Base (LR2)

"N'-[(Z)-(2-hydroxyphenyl)methylidene]benzohydrazide"

Here, the same capacity of 500 mL flask and same quantities as shown in the previous section were used (0. 02 mole-2.72 gm) of benzohydrazide was dissolved by 30ml of ethanol. After that, adding (0.02 mole-2.44 gm) of 2-hydroxybenzaldehyde dissolved in 10 mL of ethanol. The refluxing process to the reaction mixture was done for 5 hours at the refluxing temperature. Recrystallized the product from ethanol25 with a reaction result of (61.11%). The synthesis of the Schiff base is schematically detailed in Figure 3.

Antibacterial Activity

The biological activity is studied by the agar distribution method, where two types of bacteria, Staphylococcus aureus, and *Escherichia coli* strains, are adopted. The agar distribution method is used to calculate the effect of chemical compound inhibition as follows, an amount of 36 gm of agar is dissolved in 1L of distilled water and mixed, then heated. After that, the mixture is put in an autoclave for 15 minutes. Then the mixture was put into plastic dishes and let to be solidified. The bacteria are grown up in a nutrient broth and left for 24 hours in an incubator at 37°C. At the moment, Schiff bases solutions are prepared by dissolving 0.02 gm in 1-mL of dimethyl sulfoxide (DMSO) solvent. Then, holes are located in each plate using a sterile cork borer (1-mL). Then, 0.1ml of solutions are added to the wells. Finally, the inhibition zones are measured to scrutinize the inhibition activity.[26]

RESULTS AND DISCUSSION

The reflux approach was adopted to synthesize two Schiff bases of benzohydrazide with 2-hydroxy benzaldehyde and 2-hydroxy-3-methoxy benzaldehyde. Their structures were characterized on the bases of spectroscopic data. The antibacterial activities of the prepared bases were assessed against *s*taphylococcus and *E. coli* strains.

Structure Illustration

SB1(L_1): "N'-[(Z)-(2-hydroxy-3-methoxyphenyl) methylidene]benzohydrazide."

M.P:185˚C; yield (62.1); Molecular mass: 270.1; IR (KBr):

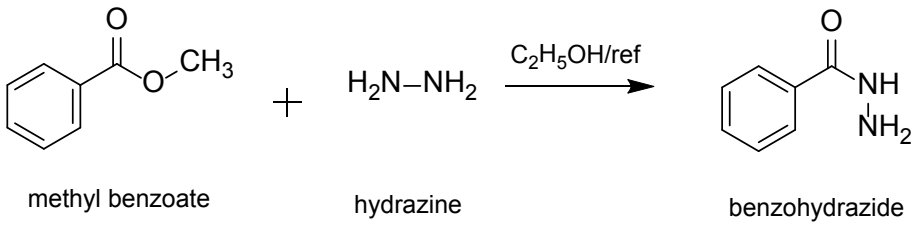

Figure 1: Synthesis of benzohydrazide

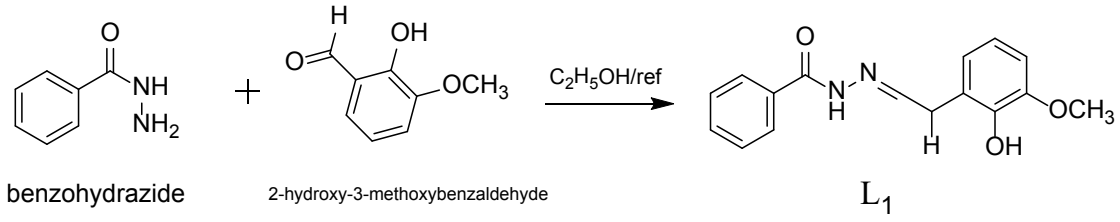

Figure 2: Condensation reaction for the preparation of the L_1

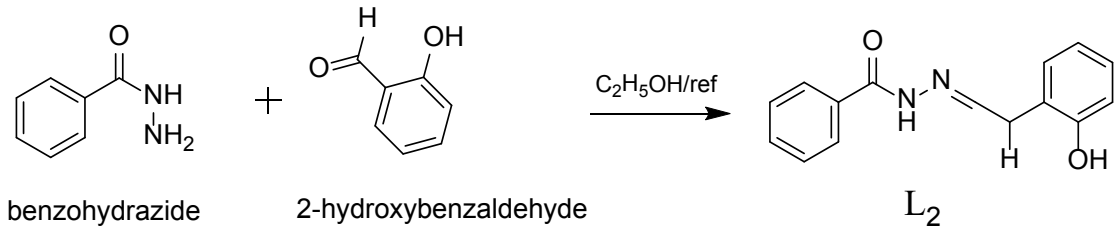

Figure 3: Condensation reactions for the preparation of the L_2

Table 1: Biological activity of the prepared compounds against some bacteria types.

Compound	*Staph (cm)*	*E. Coli*
L_1	0.8	No inhibition
L_2	0.5	No inhibition
Ab	2.6	2.4 cm

υ(cm^{-1}) =1622 (C=N), 1675 (C=O) , 1178 (C-O), 1447 (C=C), 2931 (C-H Aliphatic) and 3037 (C-H Aromatic), 3307 (O-H) , 3307 (N-H). ^{1}H-NMR (499.67 M_{HZ}, DMSO), (δppm):): 3.83 (s, 3H),), 6.87 (t, 1H), 7.04 (d, 1H), 7.15 (d, 1H), 7.54 (t, 2H), 7.61 (t, 1H), 7.94 (d, 2H), 8.67 (s, 1H), 10.99 (s, 1H), 12.1 (s, 1H) . MS(m/z): 270.1 [M^+], 149.1[$C_6H_3(OCH_3)(OH)C{\equiv}N^+$], 122.1[$C_6H_5(OH)C{=}NH_2^+$], 105.2 [$C_6H_5C{\equiv}O^+$], 77.1 [$C_6H_5^+$], 51.1 [$C_4H_3^+$].

SB2(L_2): "N'-[(Z)-(2-hydroxyphenyl)methylidene] benzohydrazide"

M.P: 217˚C; yield (61.11); Molecular mass: 240.2; IR (KBr): υ(cm^{-1}) =1624 (C=N), 1624 (C=O) , 1190 (C-O), 1469 (C=C), 3028 and 3053 (C-H Aromatic), 3202 (O-H) , 3176 (N-H). ^{1}H-NMR (499.67 M_{HZ}, DMSO), (δppm): 6,92-6.96 (m, 2H), 7.3 (t, 1H), 7.54 (t, 1H), 7.61 (t, 1H), 7.94 (d, 1H), 8.66 (s, 1H), 11.31 (s, 1H), 12.12 (s, 1H) . MS(m/z): 240.2 [M^+] , 122.1[$C_6H_5(OH)C{=}NH_2^+$], 105.2 [$C_6H_5C{\equiv}O^+$], 77.1 [$C_6H_5^+$], 51.1 [$C_4H_3^+$].

Anti-microbial Studies

Anti-microbial activities of the Schiff bases were investigated against some bacterial strains such as *Escherichia coli* and Staphylococcus. The microbial strains were obtained from Biology laboratories, Science College, Thi-Qar University, Thi-Qar.

Agar well diffusion method was applied to determine the zones of inhibition and solutions of the compounds prepared in DMSO. Firstly, (38 gm) of agar in (1-L) of the water, and the agar in The solution is heated until the agar dissolves. Then the culture medium is placed in a sterile apparatus (Autoclave) for 15 minutes, then pour the culture medium into sterilized plastic dishes and leave to indurate. Secondly, Bacteria were grown on a sterile liquid nutrient medium (Nutrient broth), which was left for (24 hours) in an incubator at 37°C. Finally, (0.02 gm) of ligands were dissolved in (1-mL) DMSO solvent. Then a hole was made in each dish using a pure cork with a diameter of 1-mL; then 0.1-mL of the solutions were placed in the holes of the acre planted with bacteria. The inhibition zone resulting from the effect of the prepared compounds was measured using a ruler A tabular development of the biological activity of the prepared compounds against bacteria.[27]

CONCLUSION

This study was undertaken to design some of the Schiff base compounds (L_1 and L_2) and diagnose them by Spectrophotometric techniques such as infrared, nuclear magnetic resonance, and mass spectrometry. Moreover, biological activity was conducted, as the ligands show less activity against selected microbial strains.

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