Synthesis, Characterization of Schiff Base Derived from 2-Aminobenzothiazole and Evaluation of its Anti-Bacterial Efficacy

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Abstract
This study includes the preparation of derivatives of Schiff bases (R6-R10) from isotonic reactance of substituents of para-benzaldehyde (4-bromobenzaldehyde, 4-chlorobenzaldehyde, 4-nitrobenzaldehyde, 4-methoxy benzaldehyde, 4-dimethylaminobenzaldehyde) with 2-aminobenzothiazole, using ethanol as a solvent. Physical properties such as melting point, colour, and molecular weight and spectroscopic measurements such as the infrared spectrum, [1H-NMR], [13C-NMR] spectrum were used to confirm the accuracy of the prepared compounds' compositions. The biological activity of various produced compounds was investigated in two species of pathogenic bacteria, one of which is Gram-positive, Staphylococcus aureus, and the other, Gram-negative, Pseudomonas aeruginosa. Chemical solutions for the compounds (R6, R8, and R9) with concentrations (0, 01, 0.001, and 0.0001) mg /ml were created using a solvent DMSO and Multer Hinton Agar growth medium. The antibiotic Ciprofloxacin was utilized as a control sample for the diffusion sensitivity test of the bacterial isolates used in the investigation.
Keywords: 2-Aminobenzothiazole, Schiff base, Staphylococcus aureus, Pseudomonas aeruginosa.

1. Introduction

Schiff's bases are those compounds that contain the azomethine group (-HC=N-) and are often characterized by a yellow colour [1]. They are named after the chemist Hugo Schiff [2]. Schiff's rule has the general formula (R1R2C=N-R3) [3, 4]. The azomethine group possesses basic properties; Because of the presence of a single electron double on the nitrogen atom [5], as well as the double bond of the azomethine group (C=N) [6], and are also used in the preparation of a large number of heterocyclic compounds and their complexes that are used to prepare special conjugated polymers [7]. Schiff's bases were prepared by an escalation of an equal number of moles of carbonyl compounds (aldehyde or ketones) with the aromatic amine, and then the product was isolated and purified by recrystallization under low pressure. In the amine group [8]. Schiff's bases and their metal complexes are a class of compounds that have been studied because of their chemical activity and physical properties [9], as they were used as corrosion inhibitors and catalysts [10] and in the preparation of polymers [11], and Schiff's base complexes are used as oxidizing agents [12]. Schiff's bases are also used in the dyes industry [13], and Schiff's bases form-colored complexes with many transition metal ions. Containing carbonyl aggregates [14]. Schiff's bases have a wide biological activity because the compounds contain azomethine group (HC=N), which has a wide biological activity [15], and for this reason, it is used as an antidote for many diseases, including antispasmodics, blood pressure reducers, and tuberculosis [16]. Bacterial activity against some bacteria, including E. coli, B. subtilis and S. aureus, and against several fungi [17] such as Aspergillus, Candida glabrata and Saccharomyces. Many of Schiff's bases showed a distinctive efficacy against tuberculosis [18], as they were used in the preparation of several drugs, such as isonicotinic hydrazide, which is effective against tuberculosis, as the amine group shows a certain degree of toxicity, so it is removed This toxicity is by converting the compound to hydrazone by condensing it with ketones or aldehydes [19], as well as it was proved that some Schiff bases containing the heterocyclic ring have medicinal properties as cardio-stimulants and diuretics [20], and Schiff bases showed clear efficacy against leukemia [21], and brain cancer [22], as the compound 2-(4-hydroxybenzidine amino) benzoic acid prepared from condensation of anthranilic acid with para-hydroxybenzaldehyde showed better anti-inflammatory and anticonvulsant effects than the drugs used in the treatment of these two cases [23].

2. Experimental

2.1. Material

All chemicals used in this work were purchased from Fluka, Aldrich, and BDH and used without further purification.

Devices used

The melting points were measured using Electrothermal Melting Apparatus 9300. The FT-IR spectra were captured using a Shimadzu FT-IR 8400S spectrophotometer with a scale of (400-4000) cm-1 by KBr disc. DMSO-d6 as solvents were used to capture 1H-NMR and 13C-NMR spectra on Bruker instruments running at 400 MHZ.

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2.3. Preparation of derivatives of Schiff bases (R6-R10) [24]

(0.006 mol) of different para-benzaldehyde substitutes (4-bromobenzaldehyde, 4-chloro benzaldehyde, 4-nitrobenzaldehyde, 4-methoxy benzaldehyde, 4-dimethylaminobenzaldehyde) was dissolved in (10 ml) absolute ethanol in a Circular flask, and after completion of dissolution, (4) drops of glacial acetic acid were added to the mixture and then dissolved in (10 ml) of absolute ethanol in another flask (0.006 mol, 1 g) of (2-Aminobenzothiazole) In another beaker, after the dissolution was completed, it was added to the contents of the first beaker and the mixture was ascended for (9-13) hours, and the completion of the reaction was confirmed using thin layer chromatography (TLC) technology. It was dried until stable weight and recrystallized with ethanol, and dried again, and the table (1) shows some physical properties, percentage, reverse sublimation time and flow rate of Schiff base derivatives (R6-R10).

Table (1): Physical properties of Schiff bases derivatives (R6-R10)

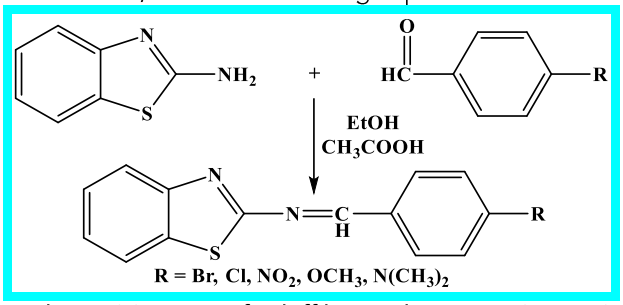
Rf	Yield (%)	T. Ref. (h.)	M.P. (0C)	Color	Molecular Formula/ M.Wt g/mol	R	Comp. No.
0.80	80	9	108-110	Yellow	C14H9BrN2S 317.20	Br	R6
0.78	78	10	112-114	Light yellow	C14H9ClN2S 272.75	Cl	R7
0.75	75	11	225-227	Light orange	C14H9N3O2S 283.31	NO2	R8
0.85	85	12	140-142	Dark yellow	C15H12N2OS 268.33	OCH3	R9
0.82	82	13	186-188	Orange	C16H15N3S 281.38	N(CH3)2	R10

2.4. Biological activity study

This research employed two kinds of harmful bacteria, one of which is Gram-positive, Staphylococcus aureus, and the other of which is Gram-negative, Pseudomonas aeruginosa; and these microorganisms. It is essential in medicine because it is resistant to antibiotics. These bacteria were collected from the Department of Life Sciences at the College of Education for Pure Sciences. The culture medium was utilized as a form of Multer Hinton Agar, which is used to test the biological activity of antibiotics and other chemicals. Chemicals have therapeutic potential. Chemical solutions of (R6, R8, R9) were prepared in concentrations of (0, 01, 0.001, 0.0001) mg/ml and using a solvent Dimethyl sulfoxide to measure and determine the minimum inhibitory concentration (MIC) (DMSO). The bacteria isolates used in the study were sensitivity tested using the diffusion method in the nutrient medium Mueller- Hinton agar, which is a transparent food medium with a dark yellow color that is useful in testing the sensitivity of microorganisms to antibiotics because it contains casein and starch extracted from an animal infusion. It allows most bacteria and germs to thrive. The medium was prepared and sterilized in an autoclave, then distributed in dishes, and allowed to harden before making four small pits in each plate. It was then incubated for 48 hours at 37 degrees Celsius (24 hrs). The results were read the next day to show the sensitivity derivatives used, which are dependent on the diameter of the inhibition visible in the dishes around the holes used as the diameter of the inhibition increases. Inhibition refers to the rise in the biological activity of the prepared compounds, as opposed to antibiotics' diameter of inhibition [25, 26].

3. Results and Discussion

The Schiff bases derivatives (R6-R10) were prepared by reacting a mole of different para-benzaldehyde substitutes (4-bromobenzaldehyde, 4-chloro benzaldehyde, 4-nitrobenzaldehyde, 4-methoxy benzaldehyde, 4-dimethylaminobenzaldehyde) with a mole of 2-aminobenzothiazole and using ethanol as a solvent, as in the following equation:



Scheme (1): Route of Schiff bases derivatives (R6-R10)

3.1. Diagnosis of Schiff bases derivatives (R6-R10)

The reaction of the Schiff bases derivatives was confirmed by observing the changes in the melting point's physical properties and the large colour change. Also, the Schiff bases derivatives were diagnosed by measurements of ultraviolet spectra and infrared (IR) spectra, and nuclear magnetic resonance spectrum (1H, 13C-NMR).

When studying the UV-Vis spectra of the prepared compounds (R6-R10) using ethanol (95%) as a solvent and at a concentration of (10-3) molar, an absorption band appeared. At (219-261) nm, respectively, is due to (π→π*) transitions, and an absorption beam at (288-360) nm, respectively, is due to (n→π*) electronic transitions [27].

When studying the infrared (IR) spectrum of the prepared Schiff base derivatives (R6-R10), it was noticed that the two bands of the amine group (NH2) disappeared, and an absorption band appeared at the frequency (3032-3095) cm-1 this is due to the stretching of the aromatic (CH) bond, and an absorption band appeared at the frequency (1637-1660) cm-1 due to the stretching of the azomethine bond (HC=N), and two absorption bands appeared at the frequency (1579-1602) cm-1 and (1483-1493) cm-1 due to the stretching of the aromatic (C=C) bond, in addition to the appearance of an absorption band at

frequency (669-711) cm-1 due to the stretching of the (C-S) bond [28]. As shown in table (2).

Table (2): Results of the infrared absorption (cm-1) and the values of the absorptions in the UV spectrum for the derivatives of Schiff bases (R6-R10)

IR (KBr) cm-1					λ1 max λ2 max EtOH	R	Comp. No.
Others	ν C-S	ν C=C Arom.	ν C=N	ν C-H Arom.			
ν C-Br 642	695	1598 1493	1648	3065	234 297	Br	R_6
ν C-Cl 765	669	1602 1481	1637	3072	261 351	Cl	R_7
ν (NO_2). *asy.* (1539) *sym.*(1371)	711	1579 1491	1660	3032	219 288	NO_2	R_8
ν (CH_3) *asy.*(2964) *sym.*(2870)	690	1588 1493	1654	3095	227 302	OCH_3	R_9
ν (CH_3) *asy.*(2986) *sym.*(2844)	678	1583 1489	1646	3081	226 360	$N(CH_3)_2$	R_{10}

When studying the 1H-NMR spectrum of the compound (R7) using a solvent (DMSO-d6), it was observed that a single signal appeared at a frequency of (8.79) ppm belonging to a group proton (CH =). The appearance of a multiple signal in the range (7.51-8.18) ppm attributed to the protons of the aromatic rings, as well as the appearance of a single signal at frequency (3.58) ppm attributed to water protons, and the appearance of a signal at frequency (2.51) ppm. Of the million is attributed to the protons of the solvent (DMSO-d6) [29], as shown in figure (2).

When studying the nuclear magnetic resonance spectrum of the carbon of the compound (R7), it was observed that a signal appeared in the range (166.06) ppm attributed to the group carbon (C=N), as well as the appearance of a signal in the range (162.77) ppm. The ppm is attributed to the carbon of the azomethine group (HC=N), the signs in the range (116.26-159.17) ppm are attributed to the aromatic cyclic benzene carbons, and the signs in the range (39.17-40.83) ppm are attributed to Solvent carbonate (DMSO-d6) [29], as shown in figure (3).

3.2. Biological activity of some prepared compounds

The compounds with heterocyclic rings showed different inhibitory activity against five types of Gram-positive (Staphylococcus aureus) and Gram-negative (Pseudomonas aeruginosa). The inhibitory activity of some prepared compounds was tested using the well-diffusion method, and measuring the diameter of the inhibition zone. Some compounds of the preparation used to study the inhibitory activity against bacteria, and three concentrations were used, which are of (0, 01, 0.001, 0.0001) mg/ml, and the standard antibiotic was used for comparison purposes in the effectiveness of inhibition, which is an amoxicillin antagonist at one concentration. Which is (30 mg/ml); the results showed that the prepared compounds have good inhibitory activity against bacteria [30], as shown in table (3).

Table (3): The inhibitory activity of the compounds (R6, R8, R9) in the growth of several positive and negative bacteria (the diameter of inhibition is measured in mm)

Biological activity of Pseudomonas aeruginous (Inhibition zone/mm)	Biological activity of Staphylococcus aureus (Inhibition zone/mm)					
Concentration	Concentration					Compounds
0.1	0.01	0.001	0.1	0.01	0.001	
30	22	13	32	13	16	R6
31	26	17	35	15	11	R8
32	25	14	17	12	10	R9
12	11					Amoxicillin (30 mg)

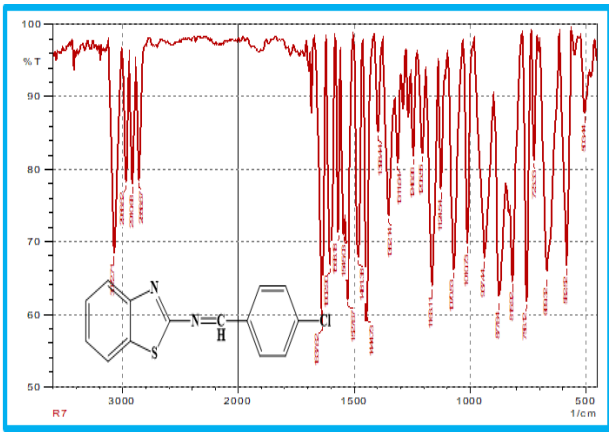


Figure (1): Infrared spectrum of the compound (R7)

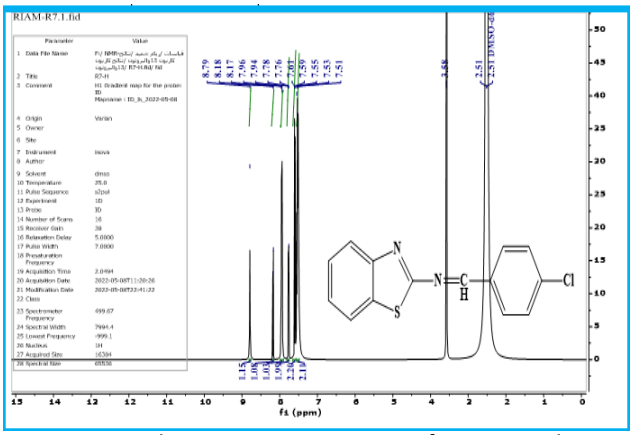


Figure (2): The 1H- NMR spectrum of compound (R7)

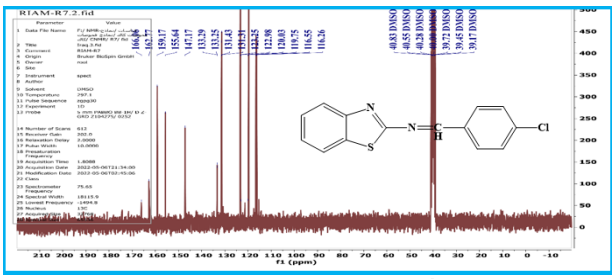


Figure (3): The 13C- NMR spectrum of compound (R7)

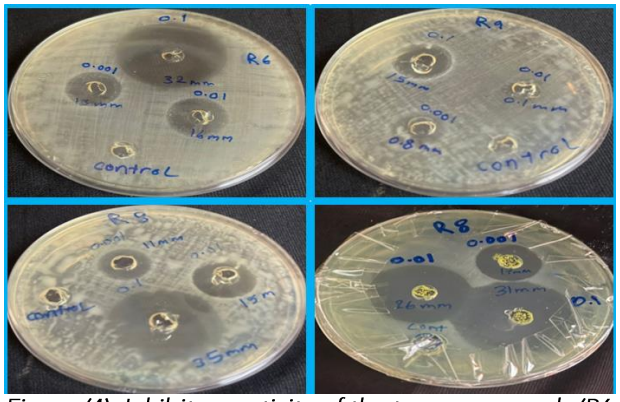


Figure (4): Inhibitory activity of the two compounds (R6, R8, R9) against Staphylococcus aureus and Pseudomonas aeruginosa bacteria

4. Conclusions

Through spectroscopic and physical measurements, it was found that the accuracy and validity of the prepared compounds. The biological activity study showed that the compounds had the effect of good inhibiting compared to the control sample.

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