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PREPARATION, DIAGNOSIS AND EVALUATION OF THE BACTERIAL EFFICACY OF A NEW DERIVATIVE OF THE 2, 3-DIHYDROQUINAZOLINE-4-ONE RING

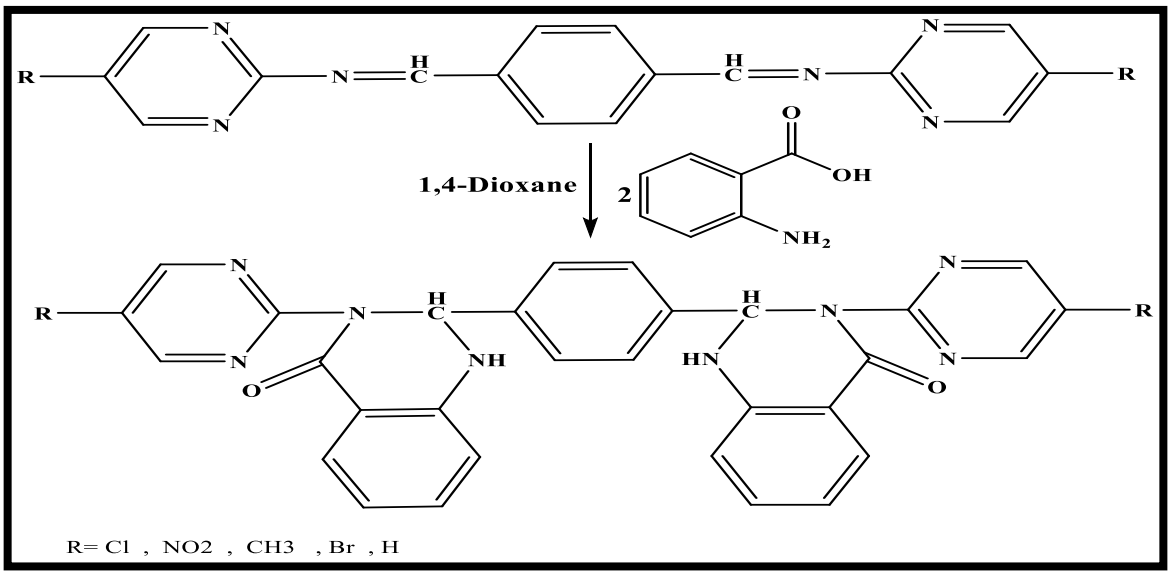
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Abstract: This research included the preparation of Schiff bases (Z1-Z5(from the reaction one mole of (terephthalaldehyde) with two mole of aniline derivatives, and then the preparation of 2, 3-dihydroquinazoline-4-one derivatives(Z6-Z10(from the reaction of Schiff bases(Z1-Z5(with 2-aminobenzoic acid. Using physical and spectroscopic methods (mp, color and nuclear magnetic resonance spectroscopy (1H-NMR), (13C-NMR) and FT-IR) to confirm the compounds' structure and evaluate their biological activity on two types of bacteria, Escherichia coli and Staphylococcus aureus.

Key words: Quinazoline, Schiff bases, Biological activity.

1. Introduction

Quinazoline is a six ring containing two nitrogen atoms and a carbonyl group. When it contains a carbonyl group in the -4-position, it is called dihydroquinazoline -4-oxo[1]. Many researchers have prepared the metabolites of these rings in various ways, where the researcher (**Talluh**)[2] prepared the binary derivatives of 2, 3-dihydroquinazoline-4-one from the reaction of derivatives of Schiff bases with anthralenic acid as in the following equation.



These compounds are of wide activity and are considered interesting. This is because it has important medicinal properties, as it was found to give a high Biological activity as anticancer[3], antioxidant[4], anti-inflammatory[5],[6] , antimalarial[7],[8] , Antiviral[9], and It also showed antimicrobial activity[10].

2. Experimental

2.1. Material: All chemicals were used through this work purchased from Fluka, BDH Companies.

2.2. Devices used: Melting points are uncorrected and were recorded in an open capillary tube on Stuart melting point apparatus. Infrared spectra have been recorded on a Shimadzo FTIR-8100 spectrophotometer using KBr discs–and ^{1}H-NMR Spectra have been measured on a MH_Z spectrometer using DMSO-d^6) as solvent. reaction monitoring and verification of the purity of the compounds was done by TLC on silica gel-percolated alumni sheets (type 60 F254 Merck, Darmstadt, Germany).

2.3. Preparation 2, 3-dihydroquinazoline-4-one (Z_6-Z_{10}) [11]

These compounds were prepared by dissolving (0.0004 mole) of previously prepared schiff bases in 1-4 dioxane and adding to it (0.0008 mole) of anthranilic acid ASD and gradually adding to it a few drops of triethylamine(Et_3N) then escalating the mixture in a water bath for (8-12) hours and then cooling the mixture and neutralizing it with sodium bicarbonate hydrogen solution, collecting the precipitate[11], drying and recrystallizing physical recipes shown in Table(1).

Table (1) Physical properties of the prepared compounds (Z_6-Z_{10})

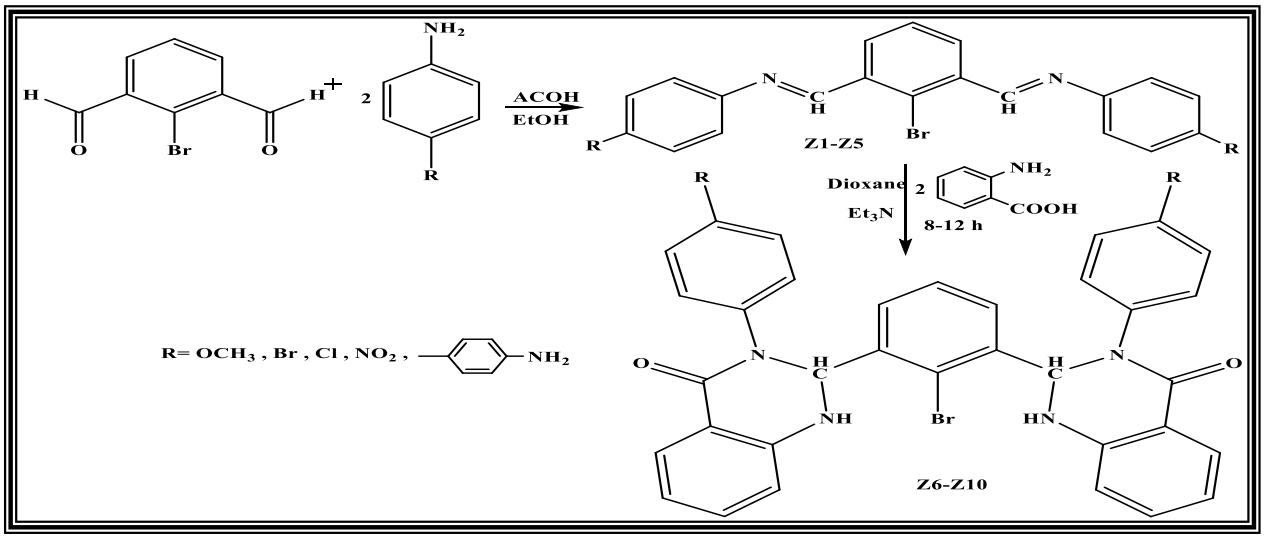
Comp. No.	X	Molecular Formula	M.p (C ^{0})	Yield %	Powder Color
Z_6	4-OCH_3	$C_{36}H_{29}N_4O_4Br$	218-220	70	White
Z_7	4-Br	$C_{34}H_{23}N_4O_2Br_3$	238-240	61	Yellow light
Z_8	4-Cl	$C_{34}H_{23}N_4O_2Cl_2Br$	186-188	62	White
Z_9	4-No_2	$C_{34}H_{23}N_6O_6Br$	177-180	60	Yellow dark
Z_{10}	C_6H_6N	$C_{46}H_{35}O_2N_6Br$	223-225	70	Yellow dark

2.4. Evaluation of biological activity

The biological activity has been estimated by using the propagation method whereas the biological activity has been estimated by the Kirby Bauer method[12], [13], where 0.1 ml of bacterial suspension has spread to the ager Muller Hinton dishes and left for 5 minutes to absorb the suspension[14],[15]. After that, holes were prepared for each dish using a Cork Porer and a diameter of (5) mm per hole (0.1 ml) of the prepared solutions of the fourth hole using (Ciprofloxacin) as a control sample and incubated the dishes for (24) hours at 37 ℃. The inhibition zone diameters around each hole has been measured in milmeter, depending on the method of Prescott[16],[17].

3. Results and Discussion

The diagram shows the prepared vehicles:



Scheme (1): Route of prepared compounds (Z_1-Z_{10})

3.1. Characterization of 2, 3-dihydroquinazoline-4-one (Z_6-Z_{10})

As for studying the FT-IR infrared spectrum, the appearance of a new medium-intensity beam at the range (3212-3178) cm-1 was observed due to the elastic sphincter (NH) in the 3,2-hydroquinosoline-4-on ring formed, and the appearance of a strong beam at the frequency range (1661-1645) cm-1 was attributed to the amide carbonyl (C=O) elastic formed in the hexagonal ring, and the spectra showed absorption beams at the range (3212-3178) cm-1 3091-3024) cm-1 belongs to the aromatizing (c-h) sphincter as well as the appearance of two absorption beams at the range (2871-2912) cm-1, (2921-2854) cm-1 belongs to the aliphatic (Ch) sphincter, the appearance of two beams at the range (1584-1534) cm-1 and (1515-1447) cm-1 belongs to the elastic sphincter (C=C) aromatics[18]. Note Table (2) and figure (1,2).

Table (2): FT-IR data of prepared compounds (Z_6-Z_{10}) cm^{-1}

Comp. No.	R	IR (KBr) cm^{-1}					
		ν(C-H) Aliph.	ν(C-H) Arom.	ν (C=O)	ν(C=C) Arom.	ν(N-H)	Others
Z_6	4-OCH_3	2943 2892	3032	1656	1534 1447	3185	ν (C-O) 1286
Z_7	4-Br	2912 2854	3049	1647	1575 1479	3191	ν (C-Br) 603
Z_8	4-Cl	2950 2919	3024	1661	1567 1515	3212	ν (C-Cl) 614
Z_9	4-NO_2	2972 2871	3070	1645	1584 1456	3178	ν(NO_2).*asy*.(1406) *sym*.(1375)
Z_{10}	4-C_6H_6N	2961 2921	3091	1658	1547 1486	3208	ν (NH_2) *asy*.3352 *sym*. 3331

When studying the 1H-NMR NMR spectrum of the compound [Z7] using a solvent (DMSO-d6), the appearance of a multiple signal was observed in the range ppm(7.26-7.77) attributed to the protons of aromatic rings, the appearance of a single signal at the chemical displacement ppm (5.96) attributed to the Proton of two groups (CH) in the quinazoline ring, and the appearance of a single signal at the chemical

displacement ppm (6.68) the two groups (NH) in the QUINAZOLINE ring are attributed to the proton, and the appearance of a signal at the PPM (2.55) site is attributed to the protons of the solvent (DMSO-D6), as in figure (3).

When studying the NMR spectrum of carbon 13C-NMR of the compound [Z7] using a solvent (DMSO-d6), it was observed the appearance of a signal at the chemical displacement ppm (156.87) attributed to the carbon of the two carbonyl Groups (C=O), the appearance of a multiple signal at the chemical displacement ppm (117.19-143.67) attributed to the aromatic ring carbon atoms, and the appearance of a signal at the chemical displacement ppm (75.95) is attributed to the carbon of the two groups (CH) in the quinazoline ring, and a signal appeared at the chemical displacement ppm (39.08-40.75) is attributed to the solvent carbon (DMSO-D6), the spectrum is shown in Figures (4).

3.3. Evaluation of Biological activity:

Some of the synthesized compounds (Z6 ,Z8 ,Z9) were tested against various strains of bacteria: gram-positive bacteria ***Staphylococcus aureus***, and gram-negative bacteria ***Escherichia coli*** by cup plate agar diffusion method[19],[20]. The microbial cultures were incubated at (37 ^{0}C for 8 hours) and diluted with 0.8% sterile saline[21]. The solution concentration for used drugs in DMSO was kept at 100µg/mL. Ciprofloxacin as a negative control was used. The biological activity was measured by measuring the inhibition diameter of the growth of bacteria around the disk in use[22]. as shown in Table (3) and figures (9).

Table (3): Inhibitory effectiveness of some prepared compounds (Z6, Z8, Z9) and control treatments (antibiotics) on the growth of a number of positive and negative bacteria

Com. No.	Escherichia coli			Staphylococcus aureus		
	25%	50%	100%	25%	50%	100%
Z6	0	0	0	0	0	0
Z8	0	0	0	0	0	0
Z9	0	0	0	0	0	0
Ciprofloxacin	0.5	0.5	0.5	0.8	0.8	0.8

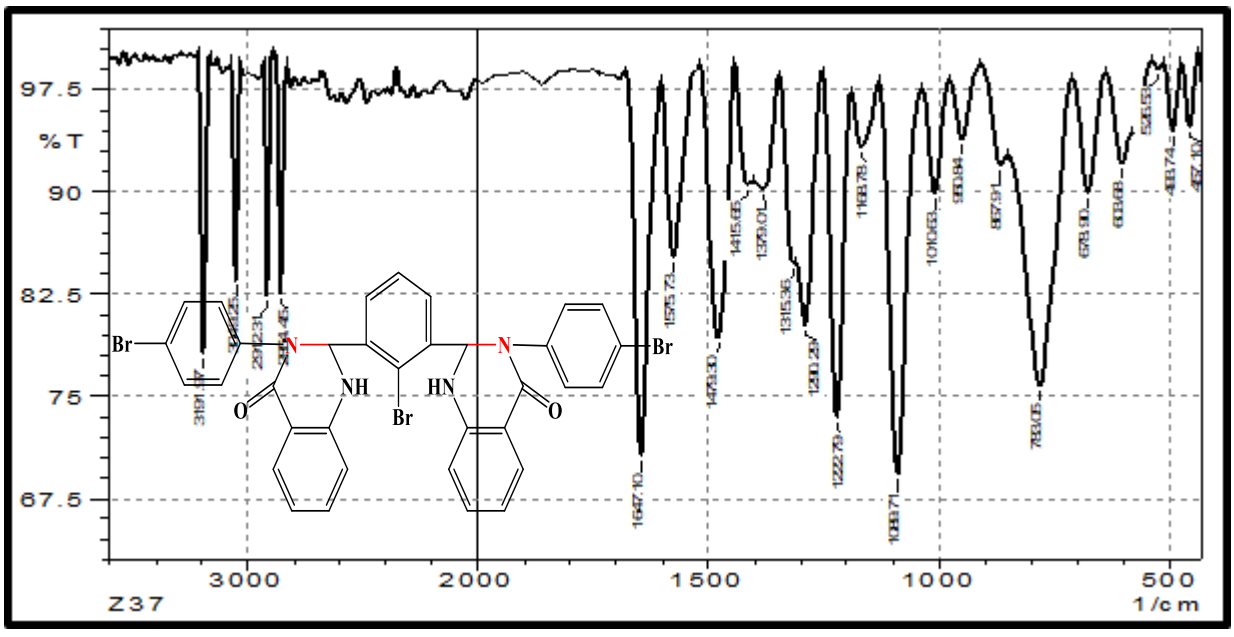


Figure (1): The infrared spectrum of the compound (Z7)

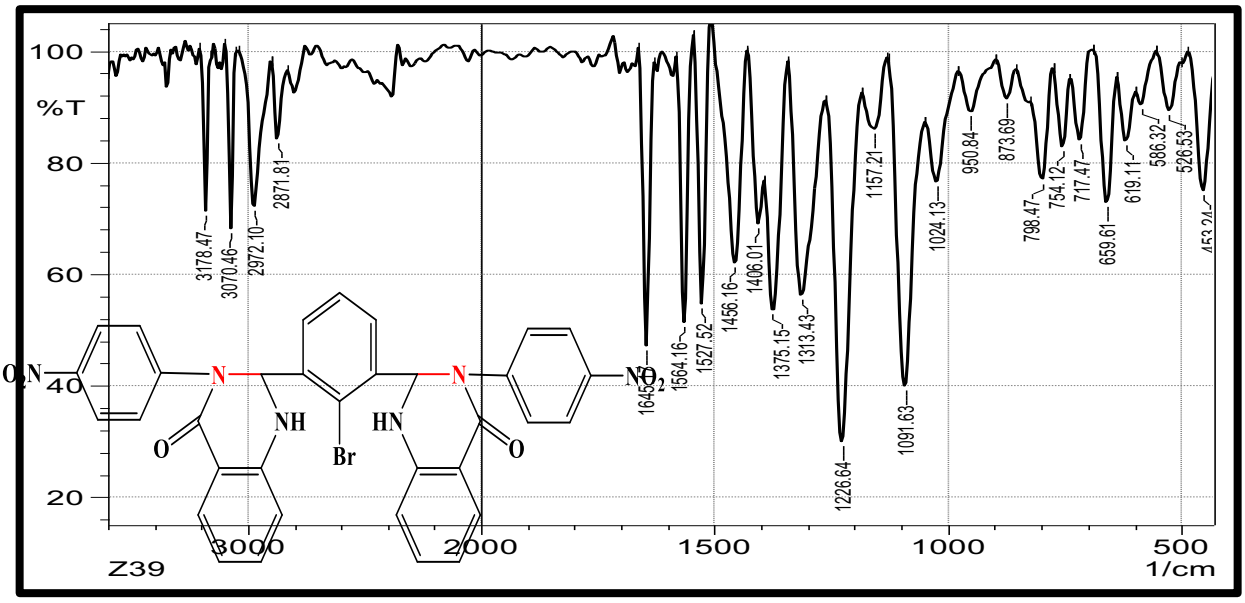


Figure (2): The infrared spectrum of the compound (Z9)

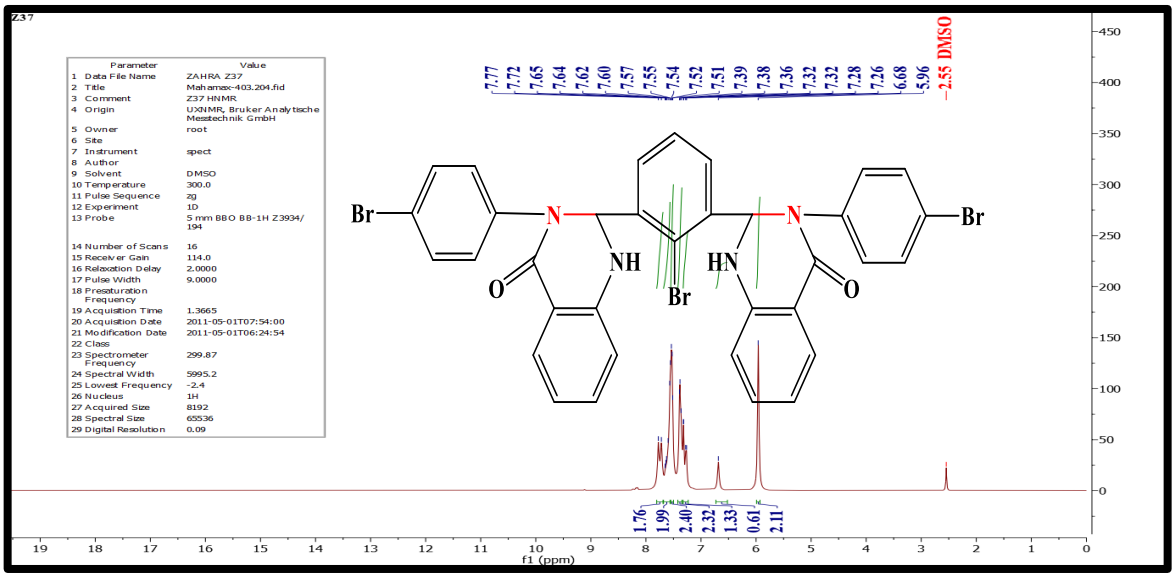


Figure (3): The ^{1}H-NMR spectrum of the compound (Z7)

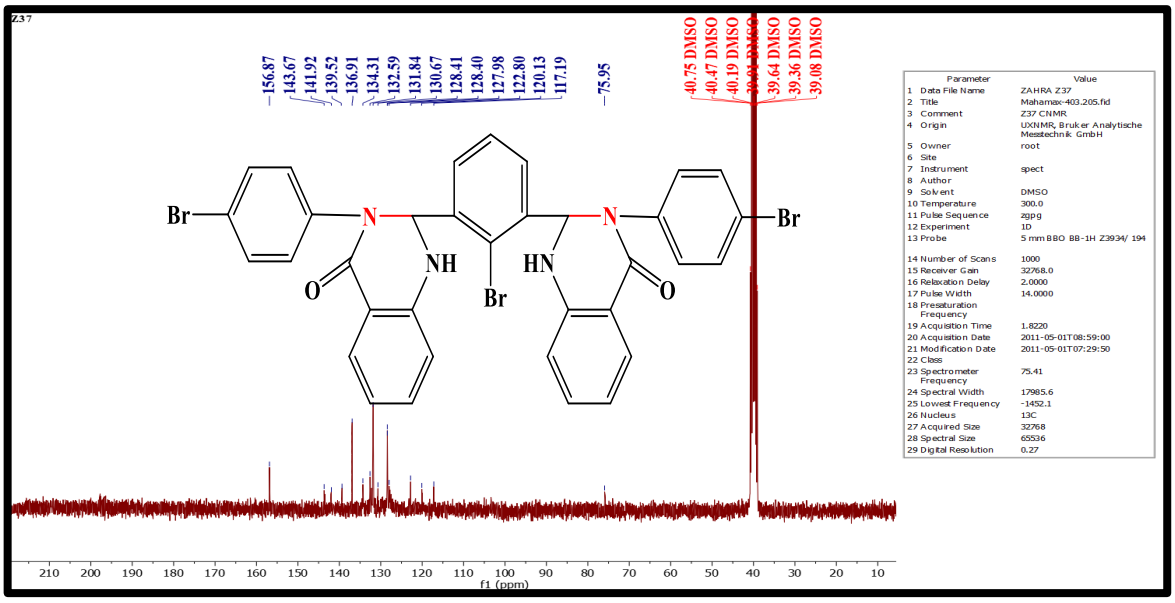


Figure (4): The ^{13}C-NMR spectrum of the compound (Z7)

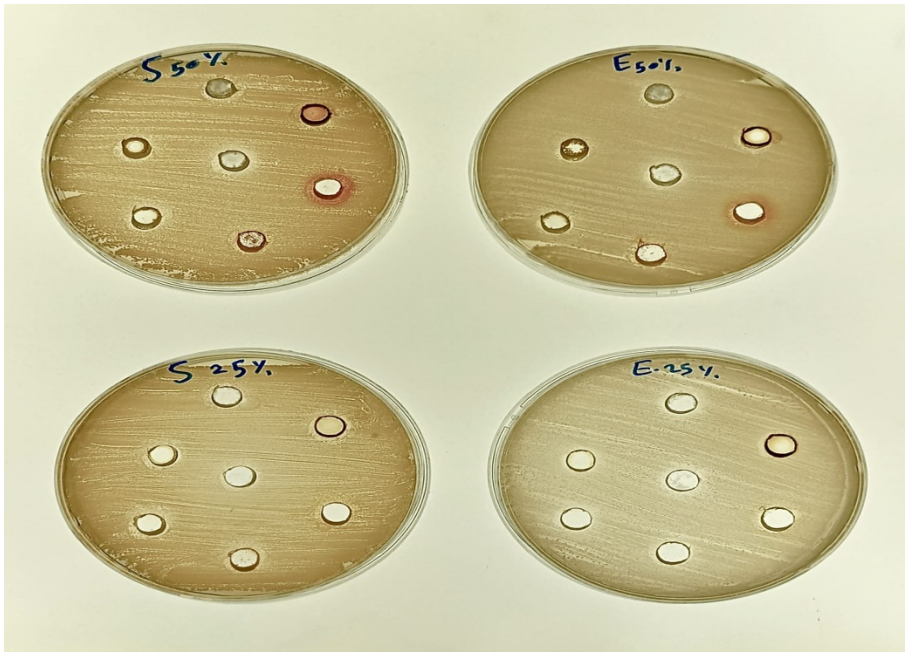


Figure (5) Biological effect and sensitivity test of compounds against bacteria

4. Conclusions:

The accuracy and validity of the prepared compounds were confirmed by spectroscopic and physical measurements, infrared and ultraviolet spectroscopy accurately proved the presence of active aggregates, and this confirmation increased the NMR spectrum of the proton and the carbon spectrum, accurately approving its validity. From the structures of prepared compounds. These compounds are stable at Laboratory temperature and do not decompose or change color. When studying the bioeffectiveness of these compounds against two types of negative and positive bacteria, the results were negative, as no inhibition was shown compared with the drug ***Ciprofloxacin***, which was used as a control sample.

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