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Preparation, characterization, and evaluation of the biological activity of new 2,3-dihydroquinazoline-4-one derivatives

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Abstract:
This study included the preparation of a new six-ring derivative of hydroquinazoline by reacting one mole of Schiff bases with two moles of anthralic acid in the presence of triethylamine as a catalyst and dioxane as a solvent. Its biological effectiveness was tested against two types of Gram-positive and Gram-negative bacteria. The validity of the structures was confirmed using physical measurements. From the melting point, color change, and product percentage, spectroscopic measurements were used, such as infrared spectroscopy and nuclear magnetic resonance spectroscopy for the proton and carbon.

Key words: *Heterocyclic, dihydroquinazoline-4-one, biological activity*

Introduction

In addition to carbon atoms, heterocyclic molecules also contain atoms of nitrogen, oxygen, and sulfur [1, 2]. Heterocyclic rings are considered very important due to their spread in nature. They are involved in the synthesis of many organic compounds necessary for the basic structure of life, and they are also found in many forms in sugars and their derivatives [3]. 2,3-dihydroquinazoline-4-one It is a hexagonal ring containing two nitrogen atoms and a carbonyl group and when the -4 position contains a carbonyl group it is called dihydroquinazoline-4-one [4].
Hydroquinazoline compounds have great biological and pharmacological importance because they are closely related to medicinal chemistry and are involved in the preparation of many drugs and antimicrobials [5]. 1,2-

Dihydroquinazoline derivatives are also useful as insecticides and antibacterial agents. It acts as an anti-inflammatory, sedative, anti-apoptotic, and anti-cancer agent in the central nervous system [6],

2.1. Material: Without additional purification, all the compounds utilized in this investigation were acquired from BDH, Fluka, and Aldrich.

2.2. Devices used: Melting points were measured with a thermoelectric melter 9300. KBr disk at 400–4000 cm-1 scale, Shimadzu FT-IR 8400S spectrophotometer; Bruker equipment running at 400 MHz for 1H-NMR and 13C-NMR spectra. Fluka silica gel plates, with a thickness of 0.2 mm, were used in thin-layer chromatography (TLC). UV light achieved visibility after fluorescent silica gel G activated the plates.

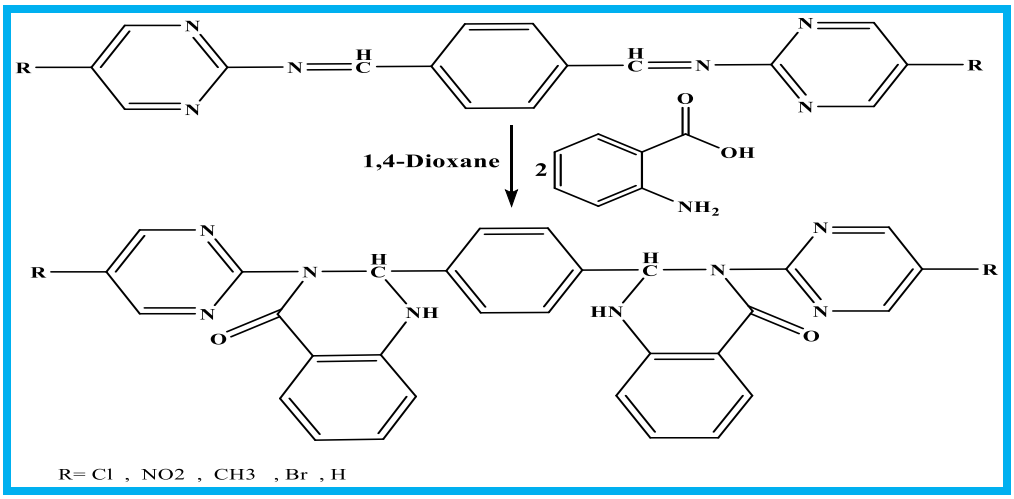
2.3. Preparation of 3,2-dihydroquinazoline-4-one derivatives (M_6-M_{10}) .[7]

Mix (0.0004mole) of the previously prepared Schiff bases[M1-M6] with (10ml) of dioxane in a round flask, add to it (0.0008mole) of anthranilic acid, and gradually add to it a few drops of triethylamine (Et3N), then escalate the mixture in a water bath for (8-12) hours, then cool the mixture, neutralize it with sodium bicarbonate solution, collect the precipitate, dry it and recrystallize it, and its physical characteristics are shown in Table 1.

.2.4. Biological activity study [8, 9]

Gram-positive Staphylococcus aureus and Gram-negative Escherichia coli were the two pathogenic bacterial species employed in this investigation. Both the College of Pure Science Education and the Department of Life Sciences employ Molter Hinton agar as a bacterial growth medium. Chemical solutions of M6, M8, and M10 were prepared using dimethyl sulfoxide (DMSO) at concentrations of (0.01, 0.001, 0.0001) mg/mL. This process determines and monitors the minimum inhibitory concentration (MIC) [8, 9]. Mueller-Hinton agar was utilized as a nutrient medium, and the diffusion technique was performed to assess the susceptibility of the bacterial isolates used in the investigation. Once the culture medium is ready, it is sterilized, distributed among plates, and given time to solidify. Next, make four small holes in each panel. They were then incubated at 37°C for a full day. Derivatives used. Clarifying the sensitivity of the derivatives used. As the diameter increases, these derivatives depend on the damping diameter of the plate surrounding the hole used. When the chemical produced shows an inhibitory effect, its biological activity increases, and this can be compared to the inhibitory diameter of an antibiotic. [10, 11].

3. Results and discussions shown in Scheme 1, a 1:2 reaction took place between derivatives of Schiff bases with anthranilic acid with the presence of trimethylamine as a catalyst and dioxane
as a solvent.



Scheme (1): Path of the Ready Compounds (M6-M10)

3.1. Characterization of 2,3-dihydroquinazoline-4-one derivatives (M6-M10)

The stretching of the carbonyl amide resulted in an absorption band in the region of (1656-1629) cm-1 in the infrared spectra of molecules (M6-M10). A band resulting from the amine's stretching in the region of (3289-3226) cm-1, and a band caused by aromatic (C-H) sphincter stretching in the region (3091-3030) cm-1., and two bands in the range (2965-2921) cm-1 and (2843-2889) cm-1 due to aliphatic (C-H) sphincter stretching, and two absorption bands in the range (1563- 1521) cm-1 and (1485-1440) cm-1 due to the stretching of the aromatic sphincter (C=C), in addition to an absorption band caused by the sphincter (C=N) in the pyrimidine ring extending at the region of (1591-1599) cm-1[12]. As in Table 2 and Figure 1,2

Compound M9's 1H-NMR spectra revealed a signal at the site (5.62) ppm that was ascribed to the quinazoline's (C-H) group protonation. and a signal dating back to the amine group at the site (6.40) ppm, as well as a multiple signal dating back to the aromatic ring at The range is (7.91-6.99) ppm, and a signal at (2.47) ppm is attributed to solvent (DMSO-d6). As in Figure 3

Compound M9's 13C-NMR spectra revealed a signal at position (89.37) ppm that was ascribed to the (C-H) group's carbon. a signal that is attributable to the carbon of the carbonyl group at position (162.13) ppm and a signal at (169.55) ppm that is ascribed to the connected pyrimidine ring's isomethene group's carbon. Having the ring of quinazoline, as well as a multiple signal in the ppm range (40.58-39.33) attributed to the solvent (DMSO-d6). As in Figure 4

3.2. Evaluation of the Biological Activity of Prepared Compounds

This research uses Escherichia coli and Staphylococcus aureus bacteria to study the biological activity of the compounds produced. Different biological actions are displayed by heterocyclic compounds against both Gram-positive and Gram-negative bacteria. These bacteria were chosen because they are known to cause a variety of diseases. Moreover, the resistance patterns of these microorganisms to antibiotics vary [13]. The bioactivity of the resulting compounds was evaluated by measuring the width of the inhibition zone and using the agar well diffusion method [14]. The results showed that the prepared compounds can inhibit the growth of Gram-positive and Gram-negative bacteria to varying degrees. This substance has significant inhibitory activity against Escherichia coli and extraordinary inhibitory effects against Staphylococcus aureus [15,16]. A concentration of 0.01 mg/mL increases inhibition in a dose-dependent manner. As shown in Table 3.

Table (1): Some physical properties of 2,3-dihydroquinazoline-4-one derivatives.

Comp. No.	R	Molecular formula	m.p. °C	Yield%	Color
M_6	4-Cl	$C_{30}H_{20}Cl_2N_8O_2$	−215 213	57	White
M_7	4-NO_2	$C_{30}H_{20}Br_2N_{10}O_6$	231-233	63	Yellow
M_8	4-CH_3	$C_{32}H_{26}N_8O_2$	−229 227	68	Orange
M_9	4-Br	$C_{30}H_{20}Br_2N_8O_2$	−247 245	74	Brown
M_1	4-H	$C_{16}H_{11}BrCl_2N_2$	−253	67	White

Table (2): FT-IR absorption results for 2,3-dihydroquinazoline-4-one derivatives (M6-M10)

Comp. No.	R	ν(C-H) Aliph.	ν(C-H) Arom.	ν(N-H)	ν(C=O)	ν(C=C) Arom.	Others
M_6	4-Cl	2889,2947	3091	3267	1656	1516,1471	ν (C-Cl) 663
M_7	4-NO_2	2872,2965	3065	3289	1643	1533,1465	ν (N-O) 1381
M_8	4-CH_3	2843,2926	3041	3226	1638	1563,1451	--
M_9	4-Br	2877,2921	3039	3272	1651	1527,1485	ν (C-Br) 591
M_{10}	4-H	2881,2935	3030	3236	1629	1521,1440	--

Table (3): Biological efficacy of produced substances and control methods (measured in millimeters of inhibition).

Comp. No.	E. Coil Conc. mg/ml			Staph. Aureus Conc. mg/ml		
	0.01	0.001	0.0001	0.01	0.001	0.0001
M6	20	13	5	15	10	10
M8	18	12	10	15	15	10
M10	15	10	10	10	5	--
Amoxicillin	22	17	16	20	19	15

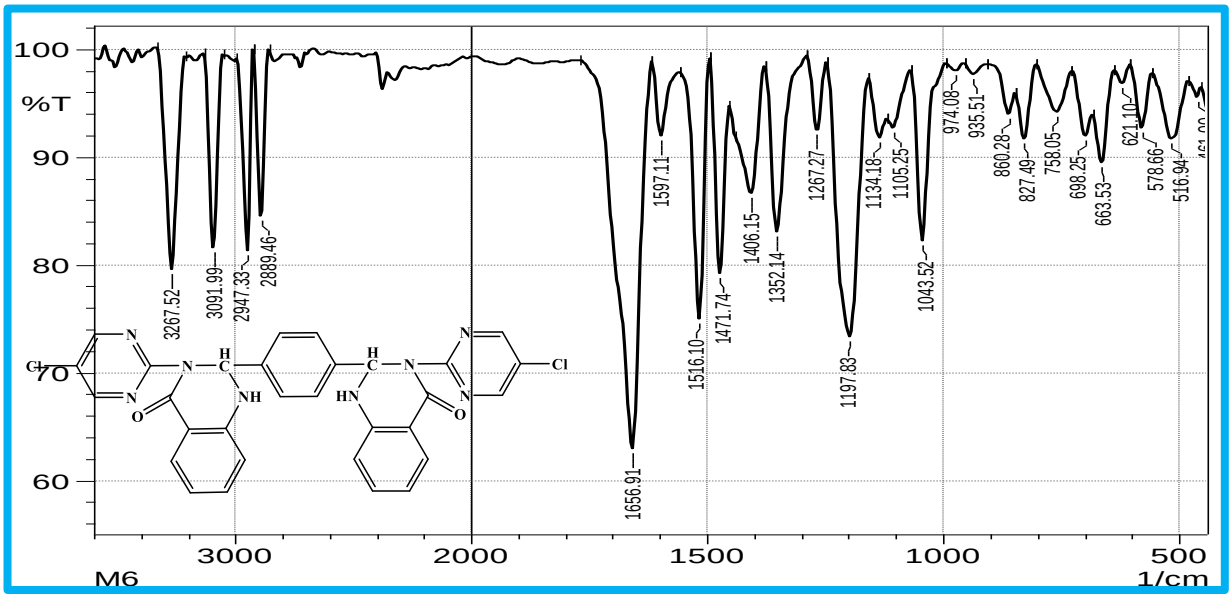


Figure (1): The compound's FT-IR spectra (M6).

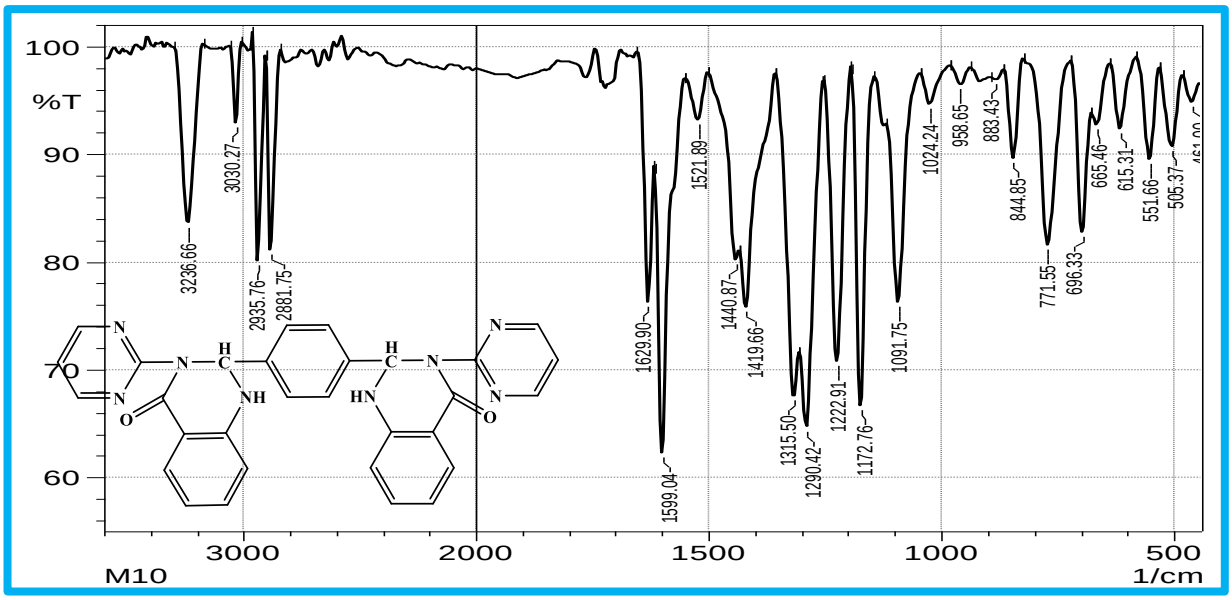


Figure (2): The compound's FT-IR spectra (M10).

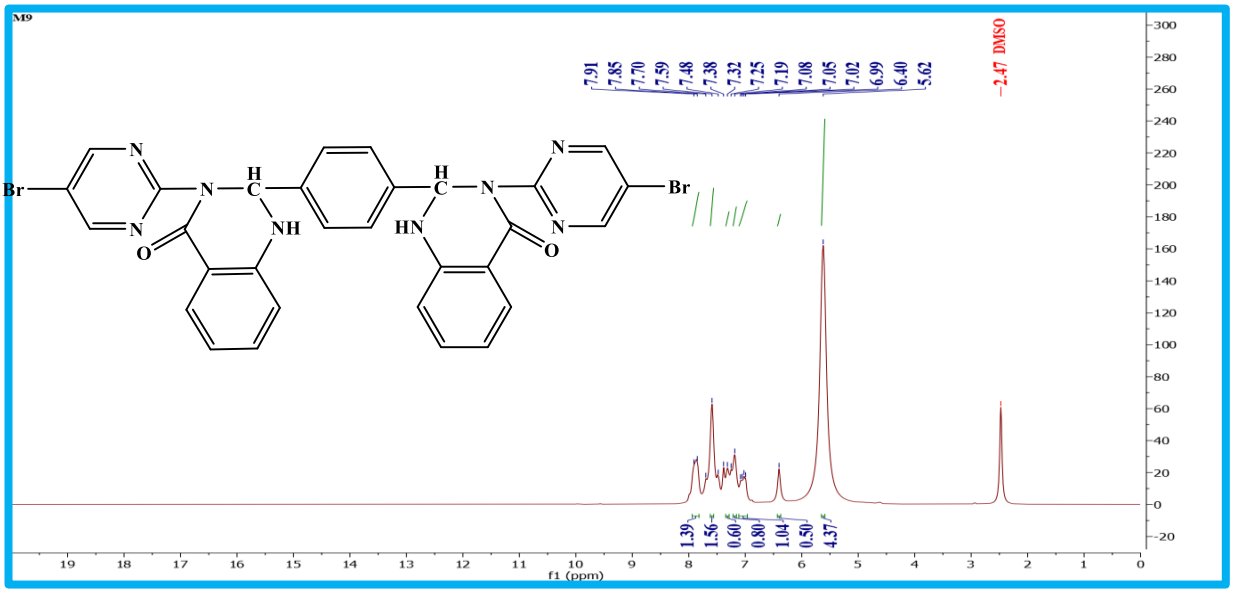


Figure (3): 1-H NMR spectra of the substance (M6).

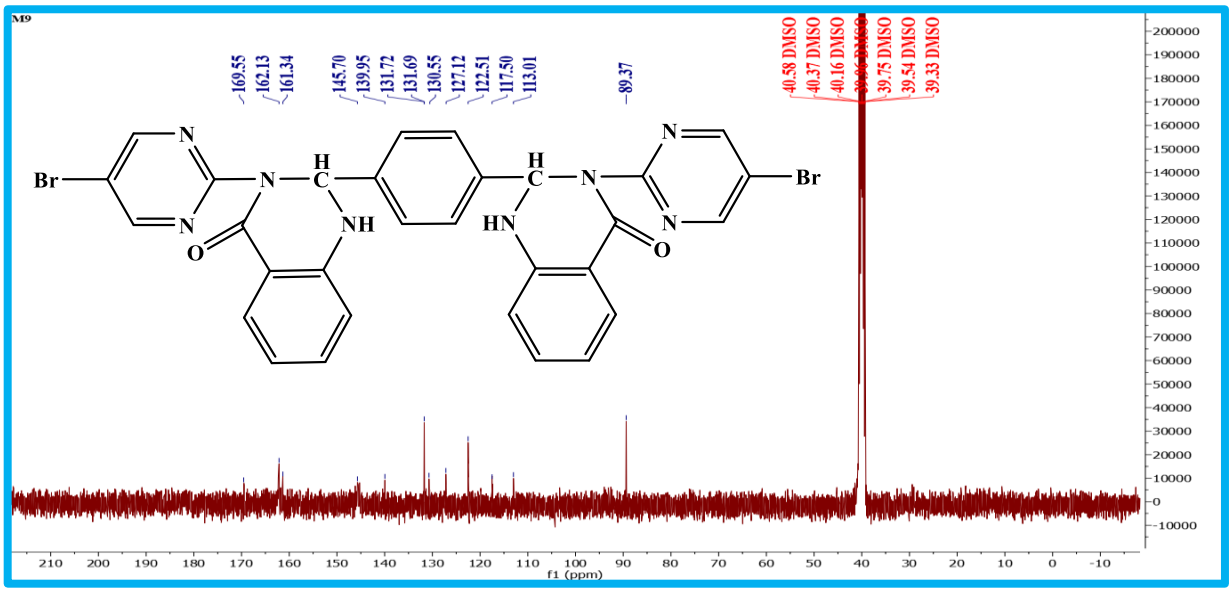


Figure (4): 13C-NMR spectrum of the compound (M6).

Conclusions

The reaction of Schiff bases with anthralic acid always gives a heterogeneous hexagonal ring. Physical and spectroscopic measurements indicate that the prepared compositions are correct and pure, in addition to their good biological activity against two types of gram-negative and gram-positive bacteria.

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