

SYNTHESIS AND CHARACTERIZATION OF FIVE-MEMBERED HETEROCYCLIC COMPOUNDS OF TETRAZOLE DERIVATIVES AND THEIR BIOLOGICAL ACTIVITY

Sara L. Khalil*, Neam H. Saleem

College of education for Pure Science, Mosul University, Mosul, Iraq

*e-mail: sarah.23esp136@student.uomosul.edu.iq

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Abstract: The aim of this study is to synthesize five-membered heterocyclic compounds containing four nitrogen atoms and one carbon atom in their structure. These compounds are known as tetrazoles, derived from 4-aryl-2-amino-1,3-thiazole (4-1), which were synthesized by reacting acetophenone or its derivatives (4-CH₃, 3-NO₂, 2-Cl) with thiourea in the presence of iodine as a catalyst to initiate the reaction. The amine was used to prepare Schiff bases (5-13) by reacting with acetophenone or its derivatives (4-NO₂, 4-Cl, 4-CH₃, 2-Cl, 3-NO₂). The prepared Schiff bases (5-13) were then used to synthesize tetrazoles by reacting with sodium azide. Thin-layer chromatography (TLC) was employed to confirm the completion of the reaction and ensure the absence of unreacted materials. The newly synthesized compounds were characterized using physical methods, including melting point measurements and color determination, along with spectral techniques such as infrared spectroscopy (IR) and proton nuclear magnetic resonance (¹H-NMR), (¹³C-NMR) and their biological activity.

Keywords: 4-aryl-2-amino-1, 3-thiazole, Schiff bases, tetrazolate, biological activities.

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Introduction

Heterocyclic compounds contain one or more heteroatoms within their ring structure. The most common heteroatoms are oxygen, nitrogen, sulfur, phosphorus, and silicon [1]. Due to the significance of these compounds, researchers have focused on synthesizing them through various methods. One common approach involves the reaction of Schiff bases with various compounds. Schiff bases are of great importance because they contain the (R-C=N-) bond, known as the azomethine group, formed by the condensation of aldehydes or ketones with primary amines [2]. These compounds were first synthesized by the Italian chemist Hugo Schiff in 1864 [3]. Among the compounds that hold

significant importance in various fields are tetrazoles, which are five-membered heterocyclic compounds. Their structure contains four nitrogen atoms, one carbon atom, and two hydrogen atoms, with a molecular formula of (CN₄H₂) [4]. The interest in researching and developing this compound chemically and biologically has increased, as it has been used in the production of explosives, photography, pharmaceutical chemistry, and drug development [5], due to its low toxicity, high lipophilicity and metabolic stability [6]. It also exhibits various biological activities such as antiviral, antibacterial, anticancer, antifungal, and antioxidant properties [7-11].

Experimental part

Materials and methods. All chemicals and solvents directly from reliable and accessible sources, without any additional purification were used. We confirmed the IR spectra ($\nu_{\max}$ in cm⁻¹) using a Bruker Alpha FTIR Tensor_27 (Germany). Furthermore, ¹H-NMR spectroscopy

was performed at 400 MHz using a Bruker instrument, with DMSO-d₆ as solvent and TMS as reference standard for chemical shifts.

Synthesis of 4-aryl-2-amino-1,3-thiazole (1-4). A mixture of 0.0043 moles of acetophenone or its derivatives with 0.0065

moles of thiourea and 1.5 g of iodine was placed in a 50 mL glass conical flask equipped with an air condenser. The reaction mixture was heated in a solid phase, without solvent, in a sand bath at 150°C for 2 hours [12]. After cooling, hot water was added to the solid mass, and the product was filtered and washed multiple times with hot water. The filtrate was neutralized by adding ammonia, and the resulting precipitate was filtered and dried. The product was recrystallized using absolute ethanol [13].

Synthesis of Schiff Bases (5-13). Schiff bases were synthesized using the traditional method by reacting equimolar amounts (0.01 mol) of the prepared amines (1-4) with acetophenone or its derivatives, dissolved in 20 mL of absolute ethanol for four hours at a temperature of 170°C. After the reaction was complete, the solution was concentrated under reduced pressure, and the resulting precipitate was filtered and recrystallized using absolute ethanol [14].

Synthesis of Substituted Tetrazole (14-22). Equivalent moles (0.006 mol) of the prepared Schiff bases (S14-6) were mixed with of sodium azide (0.006 mol) dissolved in 25 mL of dry tetrahydrofuran (THF) for twelve hour at a temperature of 190°C. After the escalation was completed, the solution was concentrated under vacuum pressure, and then the resulting solution was left at laboratory temperature to form a precipitate. Then the solution was filtered, the precipitate was dried, and it was recrystallized using absolute ethanol.

Biological Study. A study was done on four distinct types of bacteria to look at the

antibacterial properties of numerous produced chemicals (S_{1,3,7,11,15,20}). One of the bacterial strains was Gram-positive [ve+Gr], *Staphylococcus aureus*, while the other three were Gram-negative [ve-Gr], including *Streptococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*. These bacterial strains were obtained at the Advanced Microbiology Research Laboratory at Department of Life Sciences of College of Pure Sciences (University of Mosul).

Inhibition Activity Test. The Vandyke approach [15] was modified to create the Levene method [16]. This entails introducing individual bacterial colonies into a nutrient-saline medium and allowing them to grow. For 18 to 24 hours, the bacteria were cultured at 37°C. After that, 10⁸ cells/mL was achieved by a series of dilutions using regular saline, and this concentration was compared to the concentration in tube 1 (standard McFarland tubes). Using a sterile glass spreader, the bacterial suspension was applied to the surface of regular nutrition agar plates. After that, the plates were incubated for 30 minutes to permit diffusion. Filter paper discs with a 6 mm diameter were made in order to test the synthetic compounds' antibacterial capabilities. The precise concentrations of the chemicals were then soaked into these discs. dissolved in DMSO, or dimethyl sulfoxide. The discs were deposited onto the surface of the agar plates using sterile tweezers and incubated at 37°C for 18-24 hours. Following incubation, the inhibitory zones were assessed, and certain discs were contrasted with controls made of ampicillin, a common antibiotic [17].

Results and discussion

Substituted 4-aryl-2-amino-1,3-thiazoles were synthesized by reacting acetophenone and its derivatives with thiourea in the presence of

iodine [18]. Table 1 shows the most important physical properties of 4-aryl-2-amino-1,3-thiazole and its derivatives.

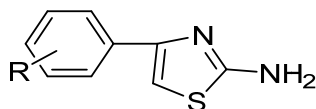


Table 1. The most important physical properties of 4-aryl-2-amino-1,3-thiazole and its derivatives

Comp. No	R	Molecular formula	M/Wt, gm/mol	M.P., °C	Yield, %	Color
S ₁	H	C ₉ H ₈ N ₂ S	176	85-87	76	Yellow

S ₂	4-CH ₃	C ₁₀ H ₁₀ N ₂ S	190	165-167	88	Yellow
S ₃	3-NO ₂	C ₉ H ₇ N ₃ O ₂ S	221	142-144	90	Yellow
S ₄	2-Cl	C ₉ H ₇ ClN ₂ S	210	122-124	66	Yellow

4-phenylthiazol-2-amine (S₁). This compound result in FT-IR (KBr, ν , cm⁻¹): 3434, 3249 (N-H), 1596 (C=N), 1157 (C-S-C asym), 1022 (C-S-C sym). ¹H-NMR (ppm): (DMSO d₆, 400 MHz) δ : 7.66–7.36 (m, 5H), 6.70 (s, 1H), 5.42 (s, 2H).

4-(4-methylphenyl) thiazol-2-amine (S₂). This compound result in FT-IR (KBr, ν , cm⁻¹): 3450, 3290 (N-H), 1519 (C=N), 1120 (C-S-C asym), 824 (C-S-C sym). ¹H-NMR (ppm): (DMSO d₆, 400 MHz) δ : 7.62–7.30 (m, 4H), 6.67 (s, 1H), 2.35 (s, 2H), 5.47 (s, 2H).

4-(3-Nitrophenyl) thiazol-2-amine (S₃). This

compound result in FT-IR (KBr, ν , cm⁻¹): 3447, 3289 (N-H), 1633 (C=N), 1514 (C-NO₂ asym), 1337 (C-NO₂ sym), 1128 (C-S-C asym), 972 (C-S-C sym) (Fig. 1). ¹H-NMR (ppm): (DMSO d₆, 400 MHz) δ : 8.58–8.05 (m, 2H), 7.70–8.00 (m, 2H), 6.73 (s, 1H), 5.48 (s, 2H).

4-(2-Chlorophenyl) thiazol-2-amine (S₄). This compound result in, FT-IR (KBr, ν , cm⁻¹): 3398, 3243 (N-H), 1638 (C=N), 1098 (C-S-C asym), 780 (C-S-C sym), 717 (C-Cl). ¹H-NMR (ppm): (DMSO d₆, 400 MHz) δ : 7.64–7.33 (m, 4H), 6.44 (s, 1H), 5.45 (s, 2H).

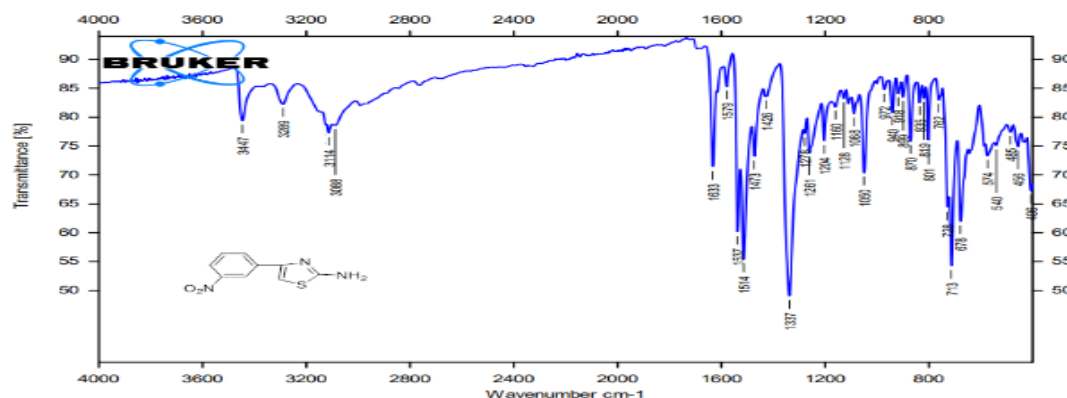


Fig.1. The infrared spectrum for (S₃)

Schiff bases (S₅₋₁₃). Schiff bases were synthesized from the prepared amines (S₄₋₁) with acetophenone or its derivatives [19]. Table

2 shows the most important physical properties of the Schiff bases.

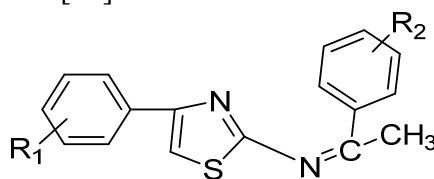


Table 2. The most important physical properties of Schiff bases.

Comp. No	R ₁	R ₂	Molecular formula	M/Wt, gr/mol	M.P., °C	Yield, %	Color
S ₅	4-CH ₃	4-Cl	C ₁₈ H ₁₅ ClN ₂ S	326	78-82	60	White
S ₆	H	4-CH ₃	C ₁₈ H ₁₆ N ₂ S	292	146-148	54	White
S ₇	3-NO ₂	H	C ₁₇ H ₁₃ N ₃ O ₂ S	323	124-126	87	Brown
S ₈	2-Cl	4-NO ₂	C ₁₇ H ₁₂ ClN ₃ O ₂ S	357	90-92	67	Yellow
S ₉	4-CH ₃	2-Cl	C ₁₈ H ₁₅ ClN ₂ S	326	50-53	78	Brown
S ₁₀	H	4-Cl	C ₁₇ H ₁₃ ClN ₂ S	312	74-75	65	Yellow
S ₁₁	4-CH ₃	3-NO ₂	C ₁₈ H ₁₅ N ₃ O ₂ S	337	173-177	56	Pale yellow

S ₁₂	H	2-Cl	C ₁₇ H ₁₃ ClN ₂ S	312	49-51	55	Yellow
S ₁₃	3-NO ₂	4-Cl	C ₁₇ H ₁₂ ClN ₃ O ₂ S	357	74-77	52	Dark yellow

1-(4-Chlorophenyl)-N-(P-tolyl)thiazol-2-yl)ethane-1-imine (S₅). This compound result in FT-IR (KBr, ν , cm^{-1}): 3060 (C-H arom.), 2975(C-H aliph), 1615 (C=N), 1164 (C-S-C asym), 1005 (C-S-C sym), 732 (C-Cl). ¹H-NMR (ppm): (DMSO d₆) δ : 7.28- 7.55 (m, 8H), 7.45(S, 1H) 2.36, 2.56 (S, 6H).

1-(4-phenylthiazol-2-yl)-1-(P-tolyl)thiazol-2-yl)ethane-1-imine (S₆). This compound result in FT-IR (KBr, ν , cm^{-1}): 3058 (C-H arom.), 2980(C-H aliph), 1598(C=N), 1150 (C-S-C asym), 1008 (C-S-C sym). ¹H-NMR (ppm): (DMSO d₆) δ : 7.58- 7.33 (m, 9H), 7.51 (S, 1H).

N-(4-(3-nitrophenyl) thiazol-2-yl)-1-phenyl ethane-1-imine (S₇). This compound result in IR (KBr, ν , cm^{-1}): 3046 (C-H arom.), 2970 (C-H aliph)1641 (C=N), 1162 (C-S-C asym), 1004 (C-S-C sym). ¹H-NMR (ppm): (DMSO d₆) δ : 8.55 (S, 1H), 7.50- 8.21 (m, 9H), 7.63 (S, 1H), 2.57 (S, 3H).

(4-(2-Chlorophenyl) thiazol-2-yl)-1-(4-nitrophenyl)ethane-1-imine (S₈). This compound result in FT-IR (KBr, ν , cm^{-1}): 3080 (C-H arom.), 2987 (C-H aliph), 1603 (C=N), 1130 (C-S-C asym), 1013 (C-S-C sym), 735(C-Cl). ¹H-NMR (ppm): (DMSO d₆) δ : 8.04 (S, 1H),7.51- 8.02 (m, 8H), 7.85 (S, 1H), 2.46 (S, 3H).

1-(2-Chlorophenyl)-N-(4-(4-tolyl) thiazol-2-yl)ethane-1-imine (S₉). This compound result in FT-IR (KBr, ν , cm^{-1}): 3080 (C-H arom.), 2987

(C-H aliph), 1617 (C=N), 1164 (C-S-C asym), 1012 (C-S-C sym), 785 (C-Cl) (Fig. 2). ¹H-NMR (ppm): (DMSO d₆) δ : 7.23- 7.54 (m, 8H), 7.54 (S, 1H), 2.34, 2.61(S, 6H).

1-(4-Chlorophenyl)-N-(4-phenyl thiazol-2-yl)ethane-1-imine (S₁₀). This compound result in FT-IR (KBr, ν , cm^{-1}): 3076 (C-H arom.), 2921 (C-H aliph), 1596 (C=N), 1164 (C-S-C asym), 1012 (C-S-C sym), 771 (C-Cl). ¹H-NMR (ppm): (DMSO d₆) δ : 8.23 (S, 1H), 7.33- 7.56 (m, 9H), 7.52 (S, 1H), 2.56(S, 3H).

1-(2-Chlorophenyl)-N-(4-phenyl thiazol-2-yl)ethane-1-imine (S₁₁). This compound result in FT-IR (KBr, ν , cm^{-1}): 3056 (C-H arom.), 2924 (C-H aliph), 1620 (C=N), 1134 (C-S-C asym), 1012 (C-S-C sym). ¹H-NMR (ppm): (DMSO d₆) δ : 7.30-7.65 (m, 9H), 7.80 (S, 1H), 2.83(S, 3H).

1-(3-nitrophenyl)-N-(4-(4-tolyl) thiazol-2-yl)ethane-1-imine (S₁₂). This compound result in FT-IR (KBr, ν , cm^{-1}): 3087(C-H arom.), 2978(C-H aliph), 1599(C=N), 1154 (C-S-C asym), 1022 (C-S-C sym), 785 (C-Cl). ¹H-NMR (ppm) (Fig. 3): (DMSO d₆) δ : 8.51(S, 1H), 7.28- 7.71 (m, 8H), 7.47 (S, 1H), 2.34, 2.61(S, 6H).

1-(4-Chlorophenyl)-N-(4-(3 nitrophenyl) thiazol-2-yl)ethane-1-imine (S₁₃). This compound result in FT-IR (KBr, ν , cm^{-1}): 2961 (C-H arom.), (C-H aliph), 1682 (C=N), 1162 (C-S-C asym), 1012 (C-S-C sym), 732 (C-Cl). ¹H-NMR (ppm): (DMSO d₆) δ : 8.23 (S, 1H), 7.32- 8.63 (m, 8H), 7.60 (S, 1H), (2.76-2.29) (S, 6H).

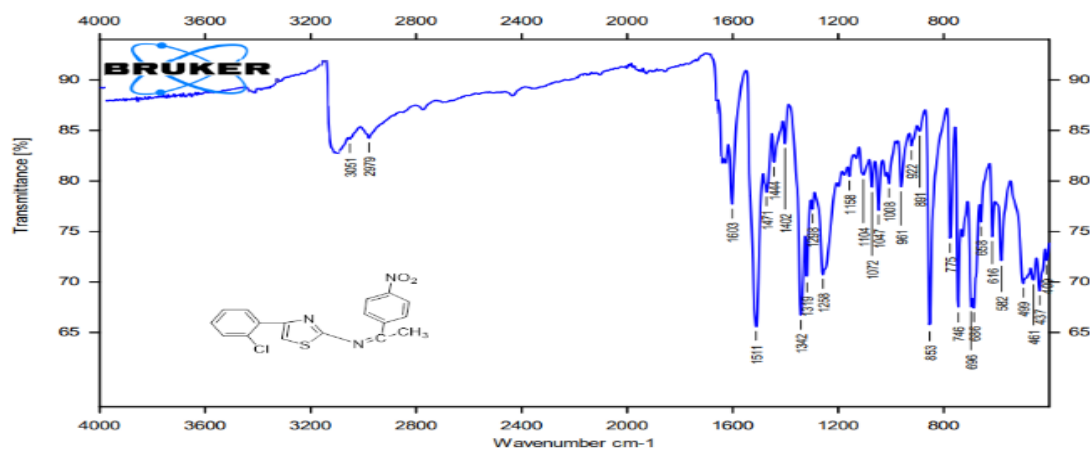


Fig. 2. The infrared spectrum for (S₉)

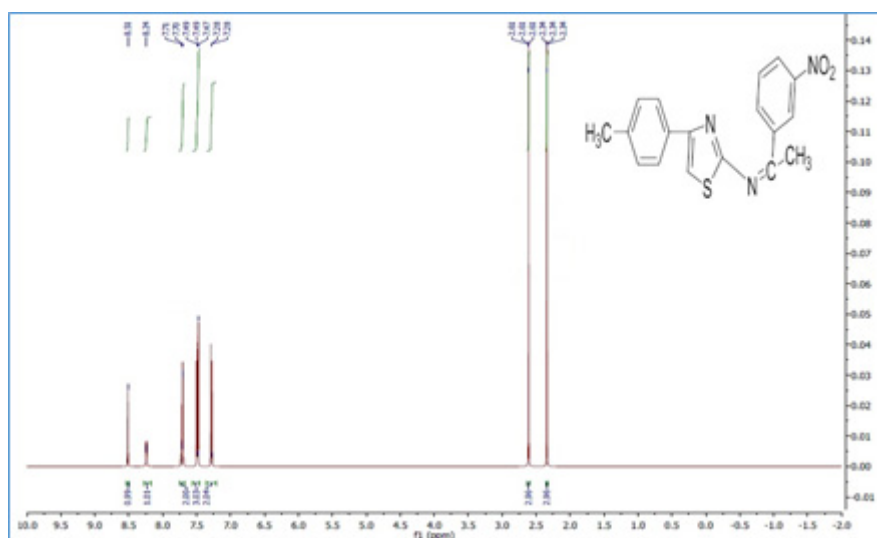


Fig. 3. ^1H -NMR spectrum for (S₁₂)

Synthesis of Substituted Tetrazole (S₁₄₋₂₂): physical properties of Tetrazole and its synthesized Schiff bases (S₅₋₁₃) of Sodium azide derivatives. [20-21]. Table 3 shows the most important

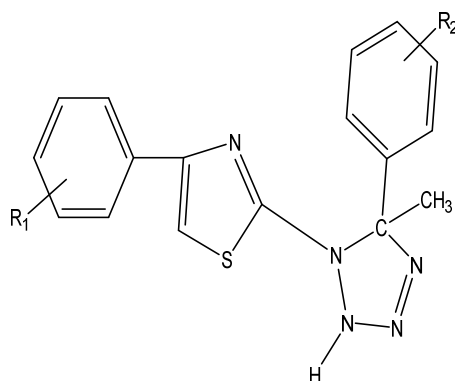


Table 3. The most important physical properties of Tetrazole and its derivatives.

Comp. No	R ₁	R ₂	Molecular formula	MWt, gm/mol	M.P., °C	Yield, %	Color
S ₁₄	H	4-CH ₃	C ₁₈ H ₁₇ N ₅ S	336	217-219	86	White
S ₁₅	4-CH ₃	4-Cl	C ₁₈ H ₁₆ ClN ₅ S	369	80-82	75	White
S ₁₆	3-NO ₂	H	C ₁₈ H ₁₇ N ₆ O ₂ S	381	187-189	65	Brown
S ₁₇	2-Cl	4-NO ₂	C ₁₈ H ₁₅ ClN ₆ O ₂ S	414	70-72	56	Orange
S ₁₈	4-CH ₃	2-Cl	C ₁₈ H ₁₆ ClN ₅ S	369	138-139	50	Black
S ₁₉	H	4-Cl	C ₁₇ H ₁₄ ClN ₅ S	355	120-122	54	Pale brown
S ₂₀	H	2-Cl	C ₁₇ H ₁₄ ClN ₅ S	355	130-132	45	Brown
S ₂₁	4-CH ₃	3-NO ₂	C ₁₈ H ₁₆ N ₆ O ₂ S	380	190-192	56	White
S ₂₂	3-NO ₂	4-Cl	C ₁₈ H ₁₅ ClN ₆ O ₂ S	414	98-100	53	Yellow

2-(5-methyl-5-(p-tolyl)-2,5-dihydro-1H-tetrazol-1-yl)-4-phenylthiazole (S₁₄). This

compound result FT-IR (KBr, ν , cm^{-1}): 3391 (N-H tetrazol), 1664 (C=N), 1683 (N=N), 1126 (C-

S-C asym), 1103 (C-S-C sym). $^1\text{H-NMR}$ (ppm): (DMSO- d_6) δ 7.16-7.61 (m, 9H), 7.41 (s, 1H), 6.53 (s, 1H), 2.34-1.81 (s, 6H). $^{13}\text{C-NMR}$ (ppm): (DMSO- d_6 , 400 MHz) δ : 149.81, 144.15, 139.01, 134.62, 134.05, 129.65, 129.09, 127.65, 127.07, 124.32, 111.19, 21.13, 19.43.

2-(5-(4-chlorophenyl)-5-methyl-2,5-dihydro-1H-tetrazol-1-yl)-4-(p-tolyl)thiazole (S_{15}). This compound result in FT-IR (KBr, ν , cm^{-1}): 3378 (N-H tetrazol), 1663 (C=N), 1448 (N=N), 1126 (C-S-C asym), 1109 (C-S-C sym). $^1\text{H-NMR}$ (ppm): (DMSO- d_6) δ 7.24-7.56 (m, 8H), 7.62 (s, 1H), 6.53 (s, 1H), 1.82-2.34 (s, 6H). $^{13}\text{C-NMR}$ (ppm): (DMSO d_6 , 400 MHz) δ 149.81, 144.15, 138.54, 136.07, 135.68, 134.29, 130.38, 129.73, 128.18, 127.71, 111.19, 21.13, 19.43

2-(5-methyl-5-phenyl-2,5-dihydro-1H-tetrazol-1-yl)-3-nitrothiazole (S_{16}). This compound result in FT-IR (KBr, ν , cm^{-1}): 3260 (N-H tetrazol), 1615 (C=N), 1420 (N=N), 1134 (C-S-C asym), 1117 (C-S-C sym). $^1\text{H-NMR}$ (ppm) (Fig. 4): (DMSO d_6) δ 8.33 (s, 1H), 7.23-8.33 (m, 9H), 7.76 (s, 1H), 6.65 (s, 1H), 1.84 (s, 3H). $^{13}\text{C-NMR}$ (ppm) (Fig. 5): (DMSO d_6 , 400 MHz) δ : 149.81, 148.37, 142.31, 135.92, 135.53, 134.34, 130.56, 129.54, 128.90, 128.90, 126.30, 124.97, 124.97, 124.30, 113.09, 19.43

Synthesis of 4-(2-chlorophenyl)-2-(5-methyl-(4-nitrophenyl)-2,5-dihydro-1H-tetrazol-1-yl)thiazole (S_{17}). This compound result in FT-IR (KBr, ν , cm^{-1}): 3152 (N-H tetrazol), 1665 (C=N), 1456, (N=N), 1137 (C-S-C asym), 1102 (C-S-C sym). $^1\text{H-NMR}$ (ppm): (DMSO- d_6) δ 8.04 (s, 1H), 7.27-7.52 (m, 8H), 6.99 (s, 1H), 6.56 (s, 1H), 1.82 (s, 3H). $^{13}\text{C-NMR}$ (ppm): (DMSO- d_6 , 400 MHz) δ 150.10, 147.54, 139.87, 139.36, 135.34, 133.51, 131.00, 128.99, 128.48, 127.44, 123.11, 123.02, 118.55, 19.43

2-(5-(2-chlorophenyl)-5-methyl-2,5-dihydro-1H-tetrazol-1-yl)-4-(p-tolyl)thiazole (S_{18}). This compound result in FT-IR (KBr, ν , cm^{-1}): 3388 (N-H tetrazol), 1620 (C=N), 1487 (N=N), 1129 (C-S-C asym), 1113 (C-S-C sym). $^1\text{H-NMR}$ (ppm): (DMSO d_6) δ 7.15-7.58 (m, 8H), 6.92 (s, 1H), 6.40 (s, 1H), 1.92, 2.35 (s, 6H). $^{13}\text{C-NMR}$ (ppm): (DMSO d_6 , 400 MHz) δ : 149.81,

144.15, 138.54, 134.29, 133.99, 131.49, 130.44, 128.00, 127.86, 126.91, 111.19, 21.13, 19.81

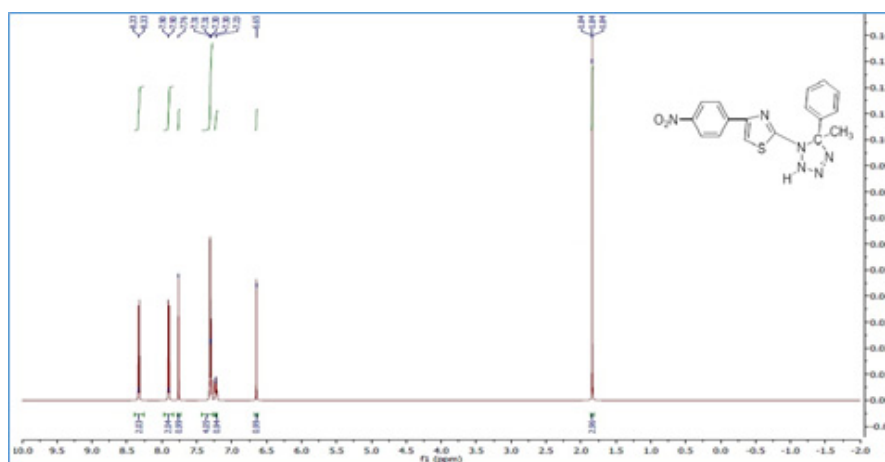
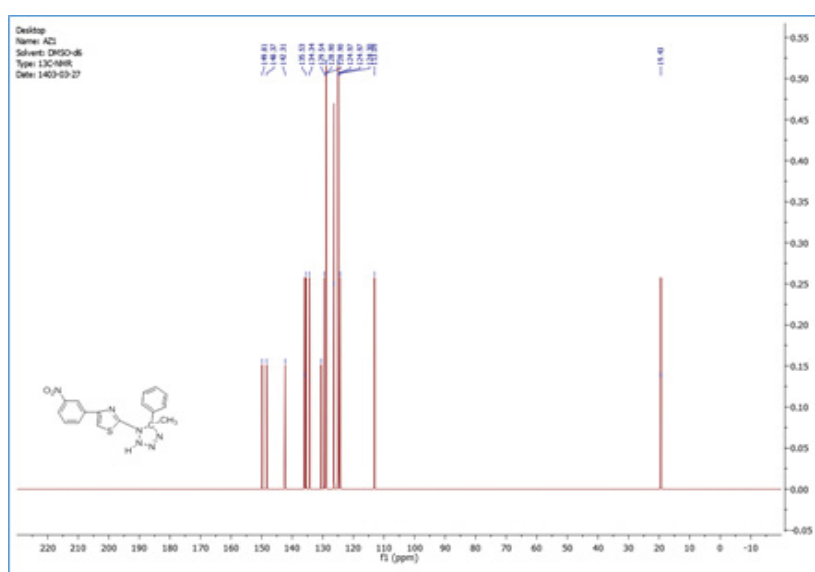
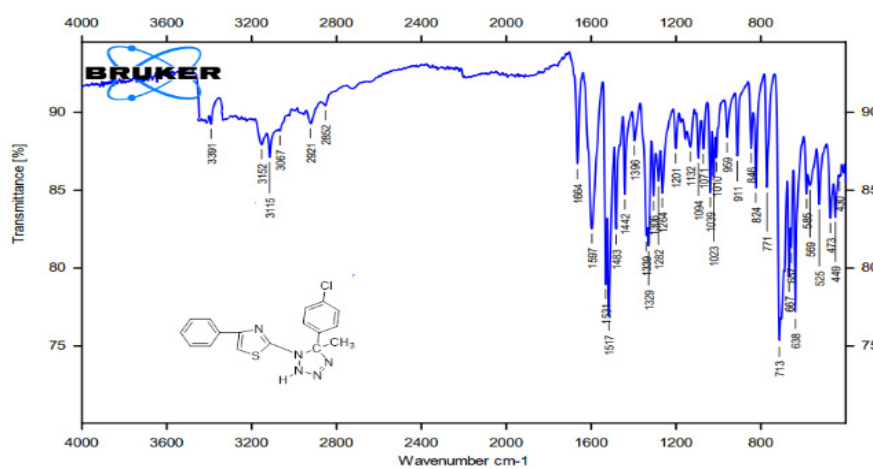
Synthesis of 2-(5-(4-chlorophenyl)-5-methyl-2,5-dihydro-1H-tetrazol-1-yl)-4-

phenylthiazole (S_{19}). This compound result in FT-IR (KBr, ν , cm^{-1}) (Fig. 6): 3391 (N-H tetrazol), 1664 (C=N), 1438 (N=N), 1115 (C-S-C asym), 1100 (C-S-C sym). $^1\text{H-NMR}$ (ppm): (DMSO d_6) δ 7.21-7.59 (m, 9H), 7.30 (s, 1H), 6.64 (s, 1H), 1.84 (s, 3H). $^{13}\text{C-NMR}$ (ppm): (DMSO d_6 , 400 MHz) δ : 149.81, 144.15, 136.07, 135.68, 134.62, 129.73, 129.65, 128.18, 127.65, 111.19, 19.43.

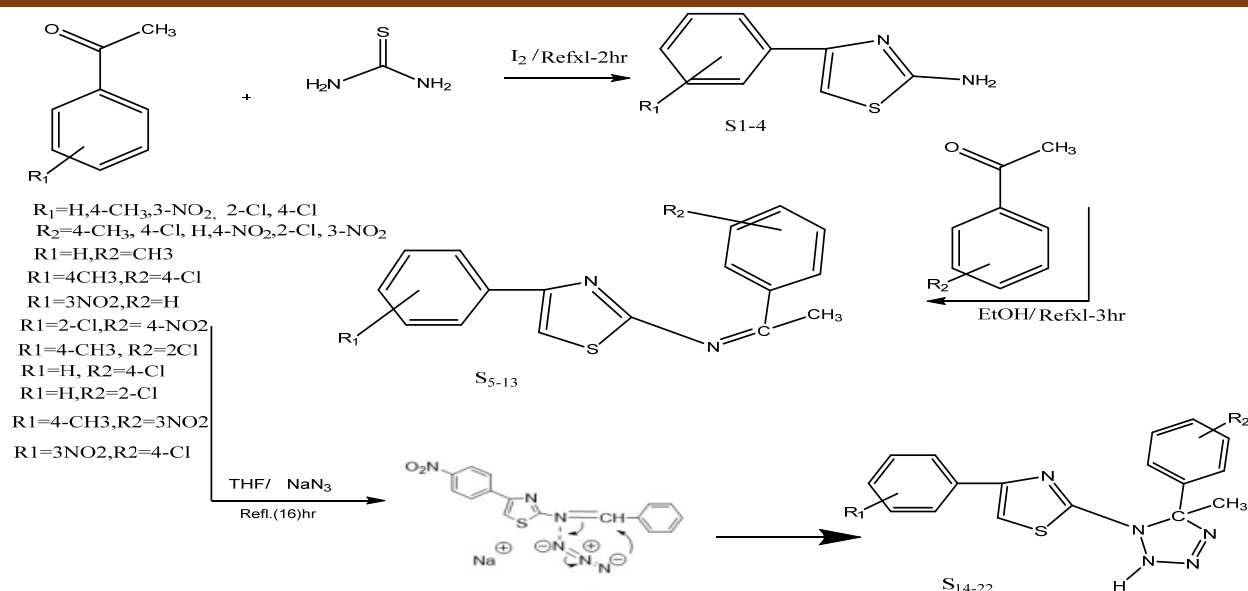
2-(5-(2-chlorophenyl)-5-methyl-2,5-dihydro-1H-tetrazol-1-yl)-4-phenylthiazole (S_{20}). This compound result in FT-IR (KBr, ν , cm^{-1}): 3389 (N-H tetrazol), 1645 (C=N), 1478 (N=N), 1146 (C-S-C asym), 1104 (C-S-C sym). $^1\text{H-NMR}$ (ppm): (DMSO d_6) δ 7.08-7.62 (m, 9H), 6.85 (s, 1H), 6.60 (s, 1H), 1.92 (s, 3H). $^{13}\text{C-NMR}$ (ppm): (DMSO d_6 , 400 MHz) δ : 149.81, 144.15, 134.62, 133.99, 131.49, 130.44, 129.65, 128.00, 127.86, 127.65, 126.91, 111.19, 19.81.

2-(5-methyl-5-(3-nitrophenyl)-2,5-dihydro-1H-tetrazol-1-yl)-4-phenylthiazole (S_{21}). This compound result FT-IR (KBr, ν , cm^{-1}): 3387 (N-H tetrazol), 1668 (C=N), 1469 (N=N), 1163 (C-S-C asym), 1127 (C-S-C sym). $^1\text{H-NMR}$ (ppm): (DMSO d_6) δ 8.34 (s, 1H), 7.32-8.12 (m, 8H), 7.76 (s, 1H), 7.65 (s, 1H), 1.90, 2.35 (s, 6H). $^{13}\text{C-NMR}$ (ppm): (DMSO d_6 , 400 MHz) δ : 149.98, 146.35, 137.58, 135.98, 135.06, 133.48, 133.18, 129.20, 128.87, 128.87, 127.08, 126.64, 123.89, 121.55, 21.13, 19.43.

2-(5-(4-chlorophenyl)-5-(methyl)-2,5-dihydro-1H-tetrazol-1-yl)-4-(3-nitrophenyl)thiazole (S_{22}). This compound result in (KBr, ν , cm^{-1}): 3250 (N-H tetrazol), 1625 (C=N), 1425 (N=N), 1138 (C-S-C asym), 1101 (C-S-C sym). $^1\text{H-NMR}$ (ppm): (DMSO d_6) δ 8.64 (s, 1H), 7.26-8.24 (m, 8H), 7.76 (s, 1H), 6.61 (s, 1H), 1.84 (s, 3H). $^{13}\text{C-NMR}$ (ppm): (DMSO d_6 , 400 MHz) δ : 149.81, 148.37, 142.31, 136.07, 135.92, 135.68, 135.53, 130.56, 129.73, 128.18, 126.30, 124.30, 113.09, 19.43.

Fig. 4. ^1H -NMR spectrum for (S₁₆)Fig. 5. ^{13}C -NMR spectrum for (S₁₆)Fig. 6. The infrared spectrum for (S₁₉)

In this research, several five-membered heterocyclic compounds (tetrazol) were synthesized according to the following scheme:



Biological Activity. The biological activity of several synthesized compounds (S_{1,3,7,11,15,20}) was tested against four types of bacteria, including Gram-negative and Gram-positive bacteria: *Escherichia coli*, *Salmonella*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Using the disc diffusion method, these bacteria were selected due to their medical significance and their role in various infections, as well as their varying resistance to antibiotics and drugs. The inhibition results, as shown in the

table, indicate that some of the synthesized compounds have strong antibacterial activity. According to the inhibition zone, compounds (3, 15) exhibited excellent inhibition against *Pseudomonas aeruginosa*, while compounds (20, 19) demonstrated excellent inhibition against *Salmonella* and *Escherichia coli*, outperforming ampicillin as a control. Other compounds showed varying degrees of inhibition, ranging from moderate to good and weak. Table 4 shows the inhibition zones of tested compounds.

Table 4. Biological properties of tested compounds.

Comp No*	<i>Pseudomonas</i> 0.1(mg/ml) **ZI mm	<i>Escherichia coli</i> 0.1(mg/ml) ZI mm	<i>Salmonella</i> 0.1(mg/ml) ZI mm	<i>Staphylococcus aureus</i> 0.1(mg/ml) ZI mm
S ₁	16	18	20	19
S ₃	23	18	12	17
S ₇	12	17	20	13
S ₁₁	16	16	18	17
S ₁₅	25	20	23	15
S ₂₀	21	25	30	21
Ampicillin 0.1mg/disk	18	20	10	20

*Inhibition levels are categorized as follows: levels are between 12 to 15 mm are classified as Inhibition, those ranging from 16 to 20mm indicate moderate inhibition, and levels exceeding 20 mm are indicative of high impact and inhibition.
 **ZI - inhibition Zone.

Conclusion

In this research we have successfully synthesized substituted five membered heterocyclic compounds. 4-aryl-2-amino-1,3-thiazole was used as a primary ingredient. Schiff bases and tetrazole were prepared. The biological

study of some compounds revealed that number of compounds have excellent inhibition against the bacteria, while others showed moderate to weak activity.

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