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Article

Synthesis and Characterization of Some New Pyrazole and Pyrimidine Derivatives From Chalcones and Evaluation of Their Biological Effectiveness

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Abstract: This study includes the preparing a new series of pyrazolin and pyrimidine derivatives that are expected to have promising biological properties. The preparation process was achieved through cyclization reactions and optimized reaction conditions to ensure high purity and yield of the target compounds. The first step includes the synthesis of (E)-3-(4-aminophenyl)-1-(2-chloroquinolin-3-yl)prop-2-en-1-one (M1) from the reaction between 2-chloroquinoline-3-carbaldehyde and 1-(4-aminophenyl)ethan-1-one. The second step includes the synthesis of (E)-N-(4-(3-(2-chloroquinolin-3-yl)-3-oxoprop-1-en-1-yl)phenyl)benzamide(M2) via reaction a mixture of (E)-3-(4-aminophenyl)-1-(2-chloroquinolin-3-yl)prop-2-en-1-one (M1) and benzoyl chloride in the presence of pyridine. The third step includes the synthesis of pyrazole compounds (M3-M6) via the reaction of compounds (M2) with phenylhydrazine, hydrazine hydrate 80%, thiosemicarbazide, and hydrazine carboxamide, and finally, the production of pyrimidine compounds (M7-M8) via the condensation of compounds (M2) with thiourea and urea. The structures of the prepared compounds were confirmed using advanced analytical techniques, including (13C-NMR and 1H-NMR) spectroscopy, as well as infrared (IR) spectroscopy. These spectroscopic techniques provided detailed structural data that contributed to identifying and confirming the chemical structures of the new compounds. Furthermore, the biological activity of the prepared compounds was evaluated against a variety of microorganisms, including bacteria Escherichia coli, pseudomonas, and Staphylococcus aureus, The antibacterial activity of compounds (M3, M4, M6 and M7) showed a significant effect as inhibitors of bacterial growth, while the rest of the compounds showed a weak to moderate effect compared to antibiotics. The results of this research contribute to expanding the library of biologically important heterocyclic compounds and open new horizons for the development of potential drugs with improved efficacy and fewer side effects.

Keywords: Pyrozoline, Pyrimidine, Quinolones, Biological Activity.

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1. Introduction

The nitrogen-containing heterocyclic aromatic form quinoline, also called benzo[b] benzo, pyridine, has a weak tertiary base and may form salts with acids as well as undergo electrophilic substitution reactions and reactions that resemble those between pyridine and benzene. The biological effects of quinolines include antibacterial antifungal, antituberculosis, antiprotozoal anti-cholesterol medicine, painkiller, and anti-disease Alzheimer's pharmaceutical [1], [2]. Pyrazolines are heterocyclic rings containing two nitrogen atoms and five members. There are three isomeric forms of them: 1-pyrazoline,

2-pyrazoline, and 3-pyrazoline, as shown in Figure 1. One In order to investigate the biological potential of 2-pyrazolines, medicinal chemists made two or three replacements [3], [4]. They also function as isosteres for a number of heterocyclic rings, such as oxazole, thiazole, and imidazole.As noticed in Figure 1.

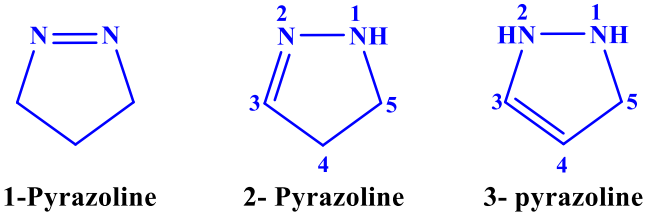


Figure 1: Different pyrazoline isomers and substitutions at positions 1, 3, and 5 on 2-pyrazoline

Pyrazoline and its derivatives have demonstrated significant biological activity and are regarded as neutrophil compounds [5] [6]. As a result, they play a significant role in a variety of pharmacological actions, including anti-inflammatory and anti-microbial[7], [8], [9]. The heterocyclic aromatic chemical molecule pyrrimidine, which has similarities with pyridine and benzene, has two nitrogen atoms at positions 1 and 3 of its six-member ring. It shares isomeric bonds with two more diazine forms [9].Because of its broad spectrum of chemical and biological relevance in medicinal chemistry, nitrogen-containing heterocyclic rings, such as pyrimidine, have been mentioned[10]. In addition, pyrimidine demonstrated its use in industrial and agricultural chemicals. Posticides and plant magnification regulators are also pyrimidine derivative, with a broad range of biological and pharmacological properties, including antibacterial, analgesic, antiviral, anti-inflammatory, antitubercular, antitumor, and antimalarial agent[11], [12]. This study aims to prepare a number of pyrazole and pyrimidine derivatives by reacting chalcones with phenyl hydrazine, hydrazine hydrate, thiosemicarbazide, semicarbazide, thiourea, and urea to form pentacycles and hexacycles and to test the sensitivity of these compounds against two types of Gram-positive and Gram-negative bacteria [13], [14].

Experimental

All the chemicals were supplied by BDH and fluka – chemical company. Using the Electro-Thermal 9300 melting point apparatus from Engineering, Ltd., U.K., we determined the melting points of the generated compounds. Then, using KBr pellets, we analyzed them using the Shimadzu FTIR-8400 Fourier transform infrared spectrophotometer and recorded their 1H NMR and 13C NMR in DMSO-d6 on the Bruker spectroscopic ultra-shield magnet 300 MHz instruments, using tetramethyl silane (TMS) as an internal standard. The measurements were conducted privately in organics at the University of Kashan, Iran [15].

2. Materials and Methods

Synthesis of chalcone:

Preparation of : (E)-3-(4-aminophenyl)-1-(2-chloroquinolin-3-yl)prop-2-en-1-one (M1).

A mixture of 2-chloroquinoline-3-carbaldehyde (1.91 g, 0.01 mol) and 4-aminobenzophenone (1.35 g, 0.01 mol) was stirred in 40 mL of ethanol. Subsequently, 1 mL of 40% NaOH was added. The mixture underwent HCl acetification. The solids were separated from the ethanol and recrystallized using the same solvent, as illustrated in Scheme 1 and Table 1.

Synthesis of benzamide:

Preparation of N-(4-(3-(2-chloroquinolin-3-yl)-3-oxoprop -1-en-1-yl)phenyl) benzamide (M2).

Compound (M1) was dissolved (0.308 g, 0.001 mol) in 10 ml of pyridine and allowed to cool before adding (0.14 g, 0.001 mol) of benzoyl chloride drop by drop while stirring continuously for 8 hours. The reaction mixture was then placed on ice that had been acidified with hydrochloric acid, and the precipitate was collected by filtering, The precipitate was then recrystallized with ethanol to afford compound M2, as shown in Scheme 1 and Table 1.

A general method for synthesizing compounds (M3-M4).

Chalcone (M2) (0.41 g, 0.01 mol) and two dipoles, phenylhydrazine and hydrazine hydrate (0.01 mol), were mixed with 25 mL of ethanol and heated at reflux for 8 hours. Following the reaction's conclusion, the mixture was concentrated by allowing the solvent to evaporate under low pressure before being placed in ice water. Compounds M3 and M4 were produced by filtering out the precipitate, washing it with water, and then recrystallizing it from ethanol, as shown in Scheme 1 and Table 1.

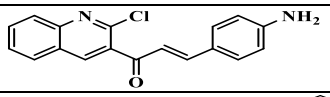
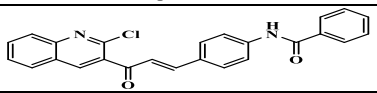
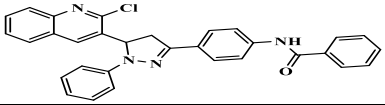
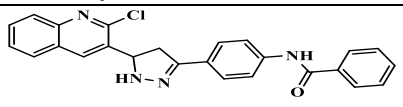
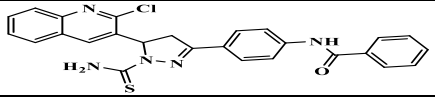
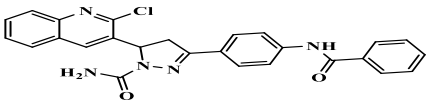
A general method for synthesizing compounds (M5-M6).

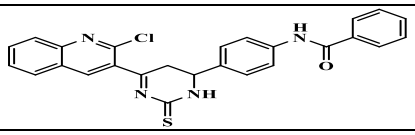
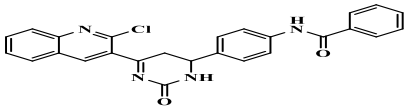
Chalcone (M2) (0.308 g, 0.001 mol), thiosemicarbazide, and semicarbazide (0.001 mol) were each added to the mixture, along with 12 mL of absolute ethanol and 0.5 g of NaOH dissolved in 10 mL of ethanol. The mixture was heated at reflux for 14 hours, transferred to a beaker filled with ice and cold water, and stirred again. Drops of diluted hydrochloric acid were then added to the mixture to neutralize the base. The precipitate was filtered and recrystallized with ethanol to yield compounds M5 and M6, as shown in Scheme 1 and Table 1.

A general method for synthesizing compounds (M7-M8).

Equivalent moles (0.41 g, 0.001 mol) of chalcone (M2) were mixed with (0.001 mol) of thiourea and urea in 20 mL of absolute ethanol in a conical flask. (0.5 g) of NaOH was dissolved in (10 mL) of ethanol and added to it. The mixture was heated at reflux for 10 hours, and thin-layer chromatography (TLC) was used to monitor the reaction. The contents of the beaker were transferred to a beaker with ice and cold water after the reaction was complete. The mixture was stirred, and then drops were added to it. To neutralize the base, dilute hydrochloric acid was used, followed by filtration and washing of the precipitate with distilled water. The precipitate was then recrystallized with ethanol to afford compounds M7 and M8, as shown in Scheme 1 and Table 1. \

Table 1: The physical properties of compounds (M_1-M_8)

Comp. No.	Structure formula	Molecular formula	M.P (C°)	Yield (%)	Colour
M_1		$C_{18}H_{13}ClN_2O$	235-237	71	yellow
M_2		$C_{25}H_{17}ClN_2O_2$	240-242	82	Orange
M_3		$C_{31}H_{23}ClN_4O$	220-222	63	Greenish yellow
M_4		$C_{25}H_{19}ClN_4O$	236-238	56	Light yellow
M_5		$C_{26}H_{20}ClN_5OS$	581-187	59	Orange
M_6		$C_{26}H_{20}ClN_5O_2$	230-232	68	Greenish yellow

M_7		$C_{26}H_{19}ClN_4OS$	215-217	59	Light yellow
M_8		$C_{26}H_{19}ClN_4O_2$	240-242	69	Orange

3. Results and Discussion

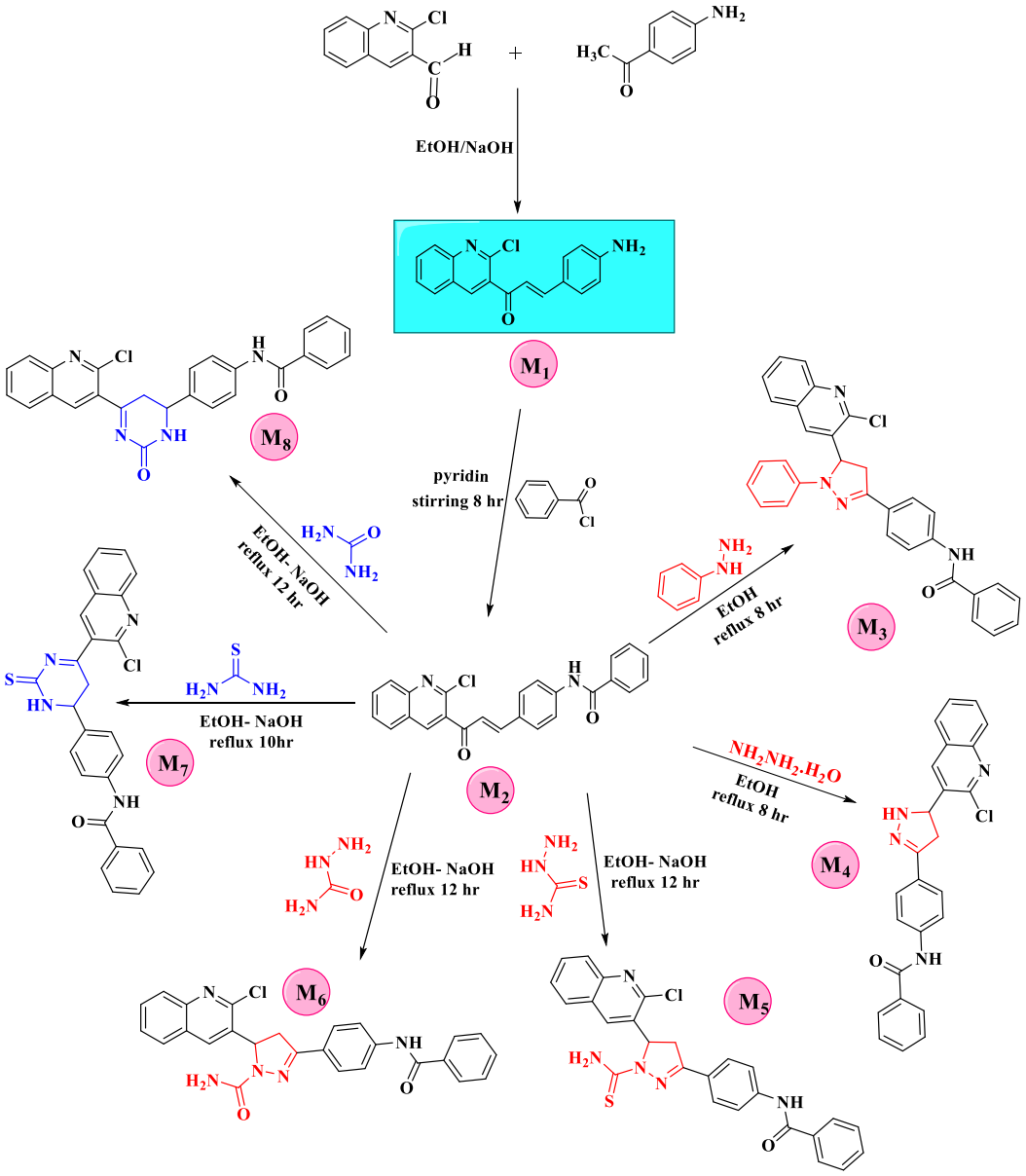


Figure 2: Synthesis of compounds (M_1-M_8).

Discussion of (IR) spectra.

Identificatio of compound (M_1).

compound (M1) were prepared via reaction of 2-chloroquinoline-3-carbaldehyde and 1-(4-aminophenyl)ethan-1-one in absolute ethanol. The compound (M1) was identified using FT-IR spectra and its melting point [16], [17]. The stretching vibrations of the υ(NH2) amine, υ(C-H) of aromatic, υ(C=O) of ketone, υ(C=C) of aliphatic, υ(C=C) of aromatic, and υ(C-N) of the amine group are shown by the bands at (3382, 3334) cm^{-1}, (3070) cm^{-1}, (1697)

cm^{-1}, (1666) cm^{-1}, and (13442) cm^{-1} in the compound (M1)'s infrared spectrum. See Table 2, Figure 2.

Identificatio of compound (M_2).

Compound (M2) was produced by reacting benzoyl chloride with pyridine with a mixture of (E)-3-(4-aminophenyl)-1-(2-chloroquinolin-3-yl)prop-2-en-1-one (M1). Compound (M2) has bands in its FTIR spectrum at (3359) cm-1 and (3154) cm-1 that show the stretching vibration of the (NH) group and the stretching vibration of the υ(C-H) of aromatic [18], [19]. Other absorptions were seen at (1683) cm-1 and (1656) cm-1, (1589) cm-1, (1525,1515) cm-1, and (1344) cm-1, and this indicate the υ(C=O) of the ketone group, the υ(C=C) of the amide group, the υ(C=C) of the aliphatic, the υ(C=C) of the aromatic, the υ(C=C) of aromatic, when the υ(C-N) respectively. Note Table 2, Figure 3.

Identificatio of pyrazolines (M_3 – M_6).

compounds (M3- M6) were prepared via reaction of compounds(M2) with phenylhydrazine, hydrazine hydrate 80%, thiosemicarbazide and hydrazinecarboxamide in the presence of ethanol [20]. The prepared compounds(M3-M6) were characterized by the infrared spectrum, as it showed an absorption band within the range IR: (3454, 3377-3422,33266) cm-1, ,(3390-3293)cm-1, (1704-1676)cm-1, (1656-1652) cm-1, indicates the υ(NH2) amin stretching vibration, υ(NH) amide, υ(C=O) of amide group and υ(C=N) respectively, Note Table 2, Figure 4 and 5.

Identificatio of pyrimidines. (M_7 – M_8).

compounds (M3- M6) were prepared via reaction of compounds(M2) with thiourea and urea in the presence of ethanol. The prepared compounds(M7-M8) were characterized by the infrared spectrum, as it showed an absorption band within the range IR: (3451- 3312) cm-1, (1670-1652)cm-1, (1650-1602) cm-1 and (1220)cm-1 denotes to stretching vibration of υ(NH) amide, υ(C=O) of amide group, υ(C=N) and (C=S) cm-1 respectively, Note Table 2, Figure 6.

Table (2): characterization of absorption bands in FT-IR spectrum data in cm^{-1}

Comp No.	IR(KBr) υ . (cm^{-1})							
	(NH_2) sy , asy	(NH) amide	(C-H) aromatic	(C=O) amide ketone	υ (C=C) Aliphatic	(C=N) stretch	(C=C) aromatic	Other bond
M_1	3382, 3334	-	3070	1693	1666	1644	1591,1407	(C-Cl) 848
M_2	-	3359	3154	1656 1683	1552	1589	1515,1463	(C-N) 1197
M_3	-	3290	3058	1704	-	1652	1512, 1411	(C-N) 1218
M_4	-	3376	3018	1675	-	1656	1568, 1435	(C-Cl) 748
M_5	3454, 3377	-	3043	1676	-	1656	1585, 1514	(C=S) 1255
M_6	3422, 3256	-	3049	1668	-	1651	1576, 1446	(C-Cl) 654
M_7	-	3461	3074	1652	-	1602	1552, 1483	(C=S) 1220

M_8	-	3381	3036	1671	-	1637	1592, 1455	(C-Cl) 758

The Figure 3 IR spectrum of compound M_1 exhibits characteristic absorption bands at 3369 and 3201 cm^{-1} corresponding to N-H stretching, and a sharp peak at 1667 cm^{-1} indicative of C=O stretching. Additional bands between 1600–600 cm^{-1} represent aromatic C=C and C–N vibrations, confirming the presence of aromatic and amide functionalities.

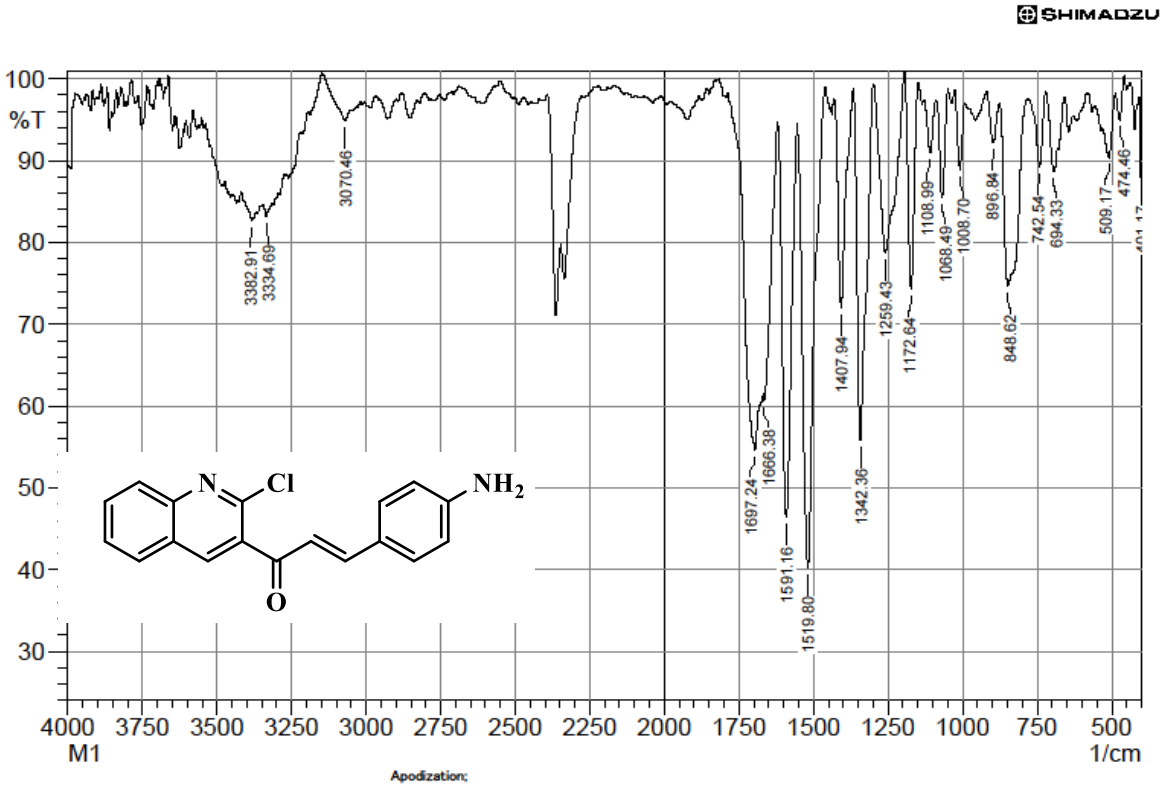


Figure 3: Show the IR for compound (M_1)

The Figure 4 IR spectrum of compound M_2 reveals broad N–H stretching bands at 3388–3127 cm^{-1} and a strong C=O stretching peak at 1688 cm^{-1}, characteristic of amide functionality. Aromatic C=C and C–N vibrations appear between 1600–600 cm^{-1}, confirming aromatic substitution and structural consistency with the depicted molecular framework.

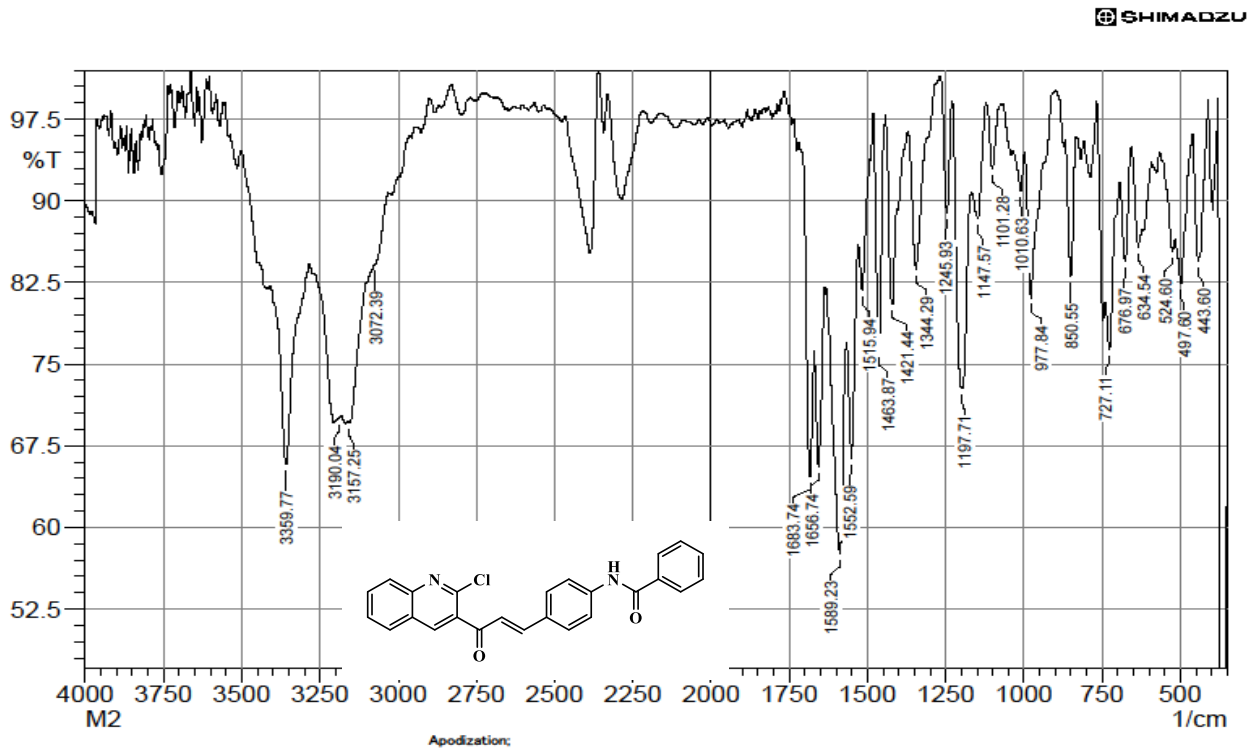


Figure 4: Show the IR for compound (M2)

The Figure 5 IR spectrum of compound M_3 shows broad N–H and secondary amide stretches at 3290–3098 cm^{-1} and a strong C=O stretch at 1693 cm^{-1}. Peaks in the 1600–600 cm^{-1} region correspond to aromatic C=C and N=N bond vibrations, consistent with the triazole and aromatic functional groups in the structure.

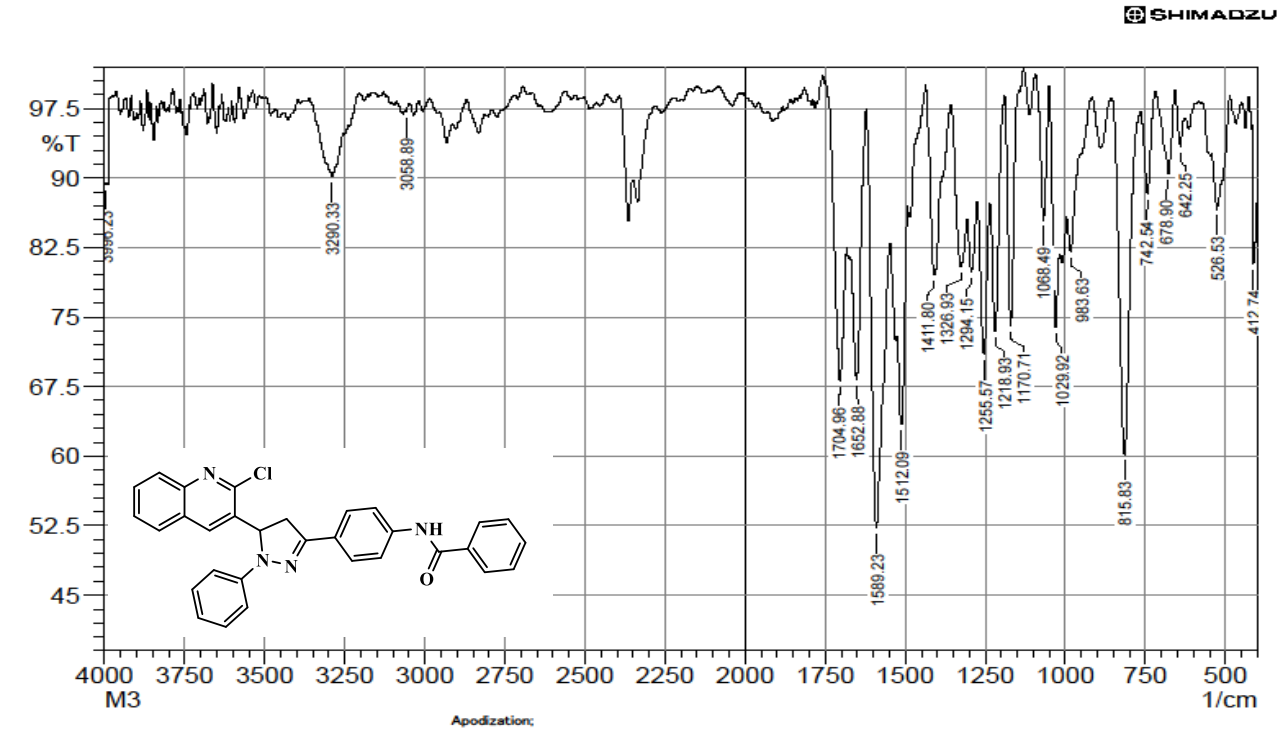


Figure 5: Show the IR for compound (M_3)

The Figure 6 IR spectrum of compound M_5 shows broad N–H stretching bands at 3444–3088 cm^{-1} and a distinct amide C=O stretch at 1678 cm^{-1}. Peaks at 1585 and 1514 cm^{-1} correspond to C=N and C=C stretches, while strong absorptions between 1300–500 cm^{-1} confirm aromatic rings and heterocyclic thiosemicarbazone presence.

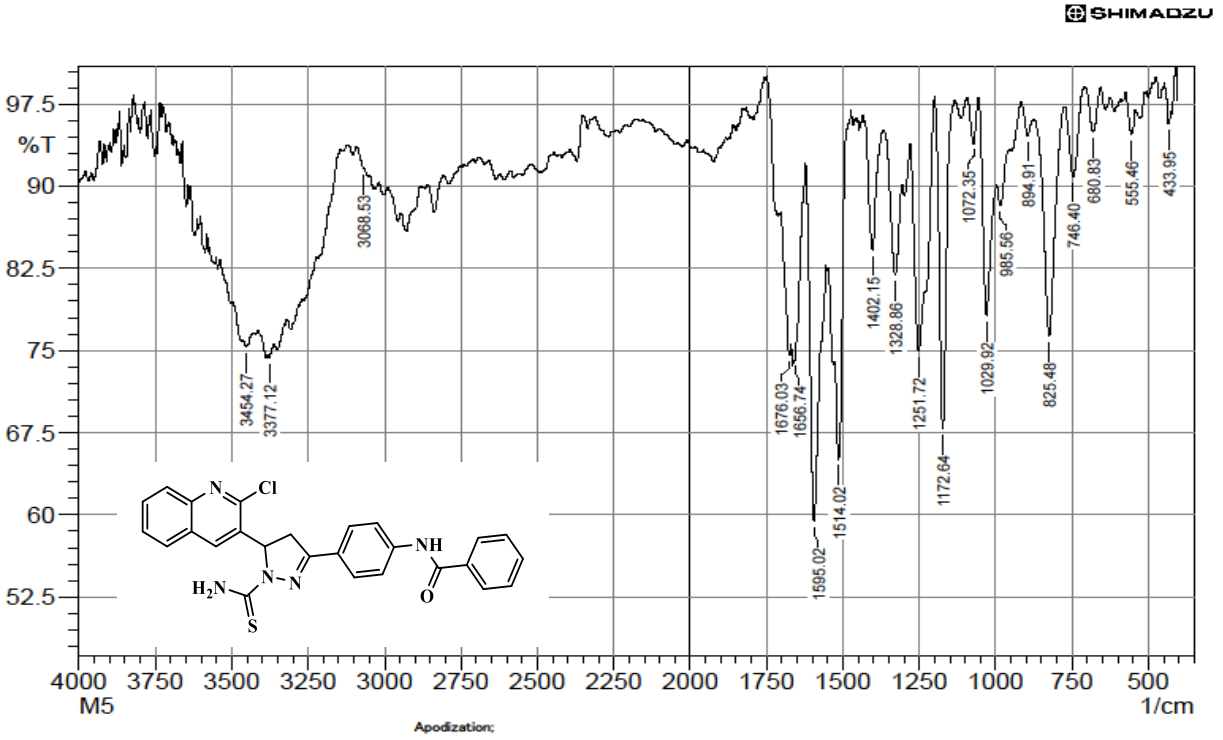


Figure 6: Show the IR for compound (M_5)

The Figure 7 IR spectrum of compound M_7 displays broad N–H stretching bands at 3461–3021 cm^{-1} and a prominent C=O stretching peak at 1652 cm^{-1}, indicating amide functionality. Strong absorptions at 1380–1238 cm^{-1} reflect C–N and C=S bonds, while multiple peaks between 1100–500 cm^{-1} confirm aromatic and heterocyclic structural features.

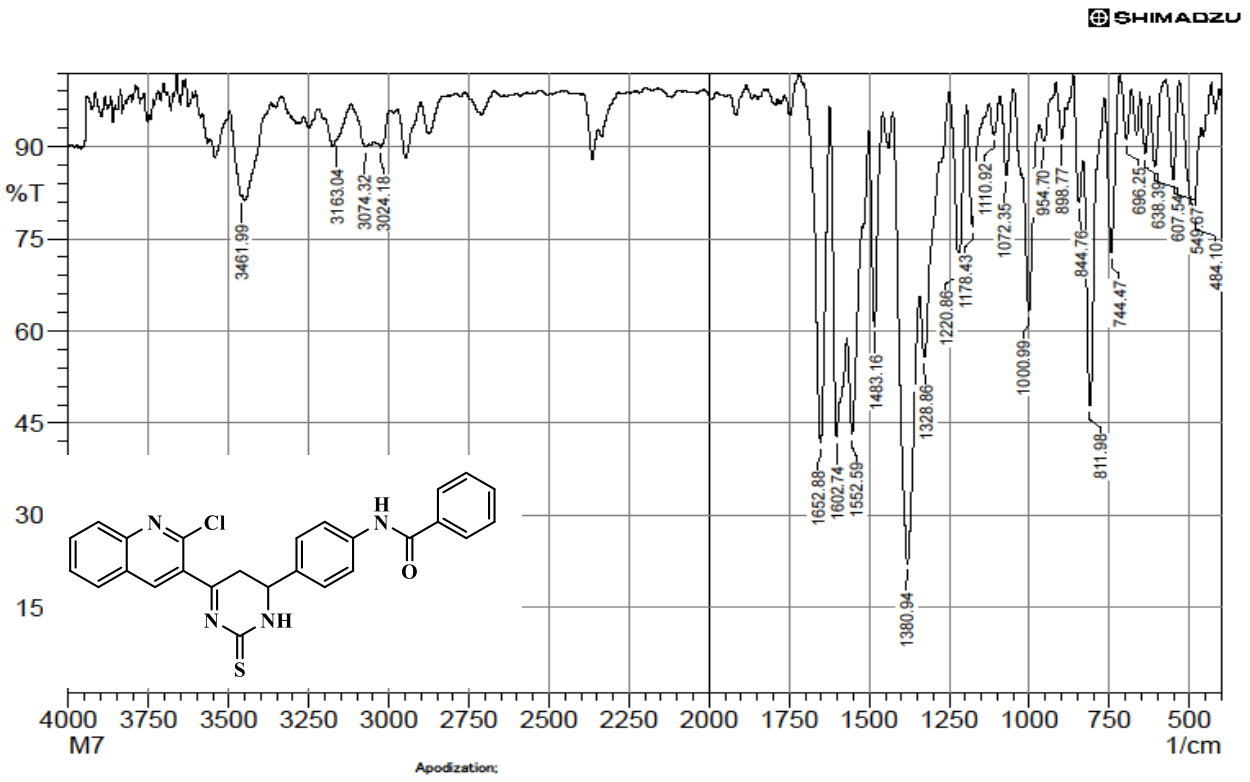


Figure 7: Show the IR for compound (M_7)

Discussion of (1H-NMR and 13C-NMR) spectra.

The 1H-NMR and 13C-NMR spectra were acquired on a 400 MHz spectrometer in DMSO using tetramethylsilane as an internal reference. The data are given as follows: Chemical shift in parts per million (ppm) with multiple (s = single, d = double, t = triple, q = quadruple, m = multiple).

Compound **M_1** was identified by H-NMR spectrum and showed 5.62(d,2H , NH_2), 9.51(s,1H, C_{15}), 7.5(d,2H, C=Colefin), 7.59-8.13(m,8H, aromatic) . $_1$H-NMR compound **M_2** Show up; 10.94(s,1H,NH) , 6.34(m,2H,H alphatic), 7.12-7.83(m , $_{14}$H, Ar-H) . Show the compound **M_3** signal 11.57(s,$_1$H,NH) , 3.34 (m,2H,CH_2) methylene ,3.95 (m,1H,CH) methine, 7.2-8.32(d , 18H, Ar-H . And show up compound **M_4** signs 11.16(s,$_1$H,NH amid) 10.11(s,$_1$H,NH pyrazole), 4.57(m,1H,CH) methine, 3.59(m,2H,CH_2) methylene, 7.15-7.89(m , $_{14}$H, Ar-H). As for the compound M_5, there are signs; 10.95(s,1H,NH)amide, 9.40(m,2H,NH_2) thiourea,3.98(m,2H,CH_2) methylene, 3,90(m,1H,CH)methine, 7.04-7.87(m , 20H, Ar-H). As for the compound **M_6**, there are signs 10.77(s,1H,NH)amide, 6.45(s,2H,NH2)urea ,4.4(m,1H,CH)methine, 3.73(m,2H,CH2)methylene, 7.10-7.81(m , 20H, Ar-H). And show up compound M7 signs; 10.33(s,1H,NH)amide 9.47(s,1H,NH)benamide , 3.67(m,1H,CH_1)methine, 2.7(m,2H,CH_2), 7.2-8.3(m , $_{18}$H, Ar-H). And show up compound M_8 signs; 9.99(s,1H,NH)amide , 8.78(s,$_1$H,NH)benzamide , 5.23(m,$_1$H,CH1)methine, 2.47(m,$_2$H,CH_2), 7.21-8.09(d , $_{19}$H, Ar-H) . Note Figures 8-11.

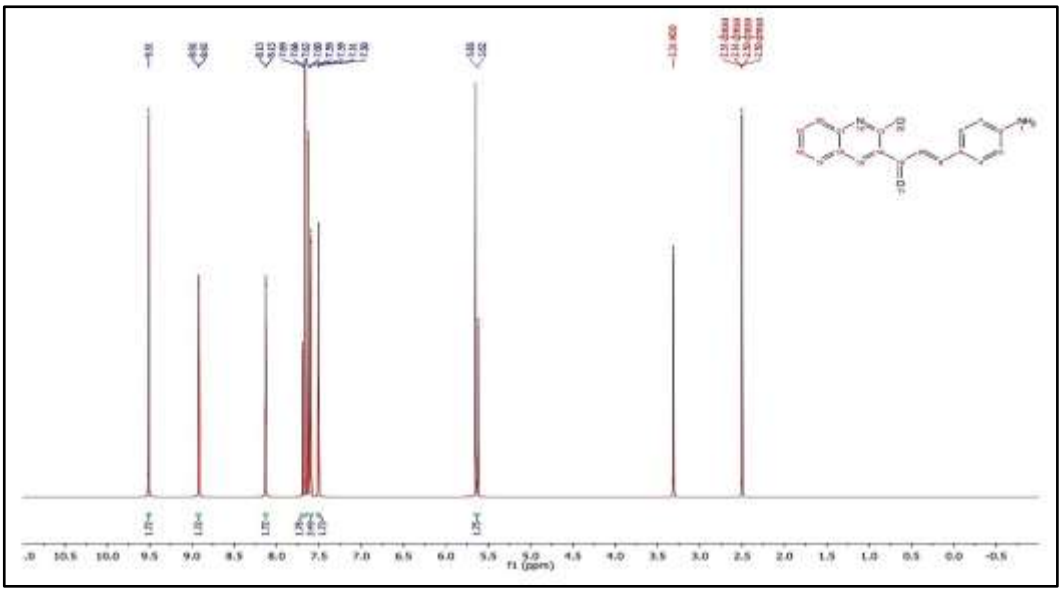


Figure 8: 1H NMR spectra for the compound M_1

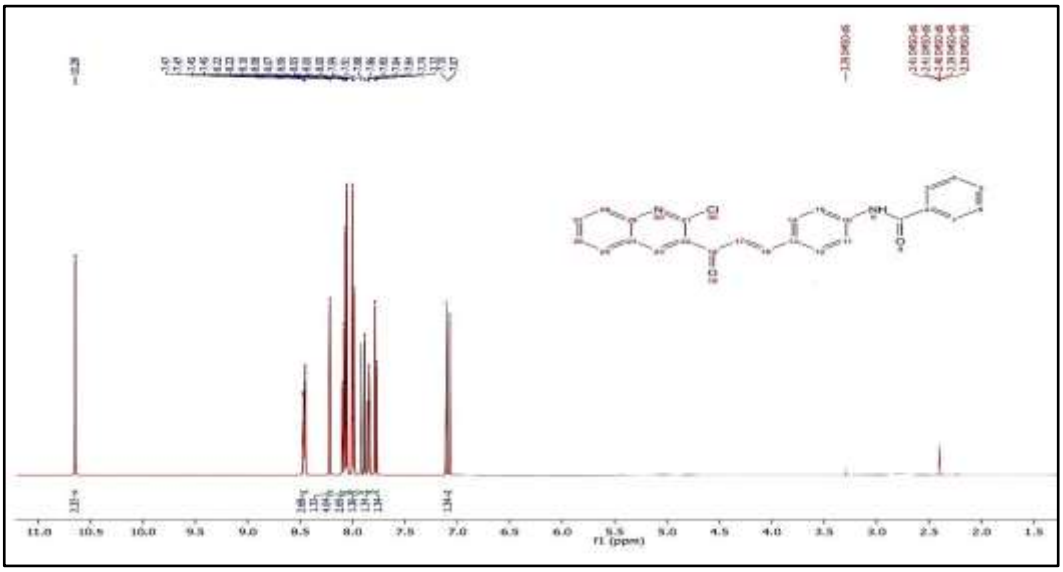


Figure 9: 1H NMR spectra for the compound M_2.

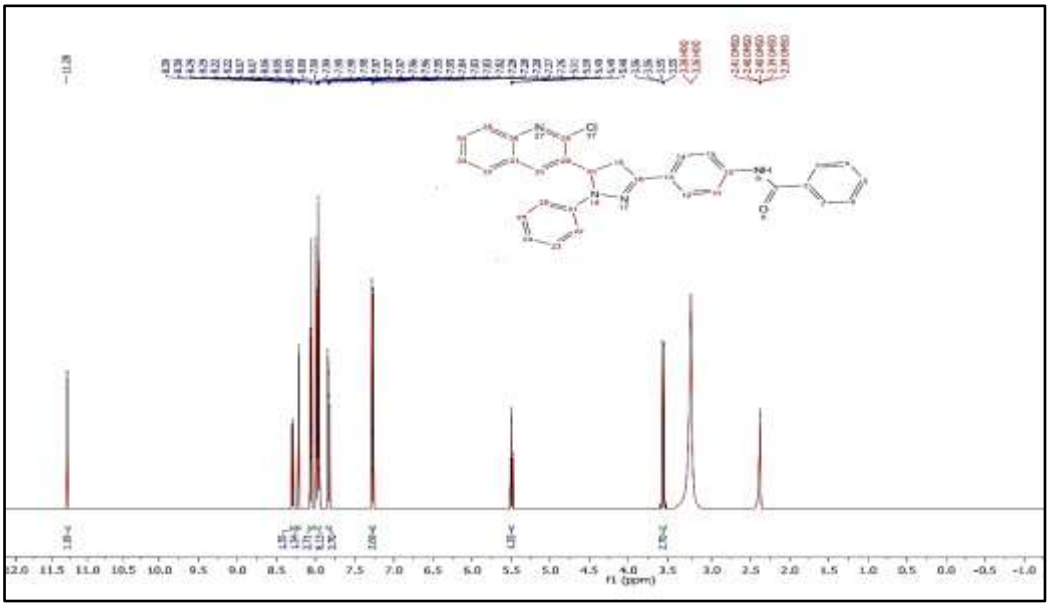


Figure 10: 1H NMR spectra for the compound

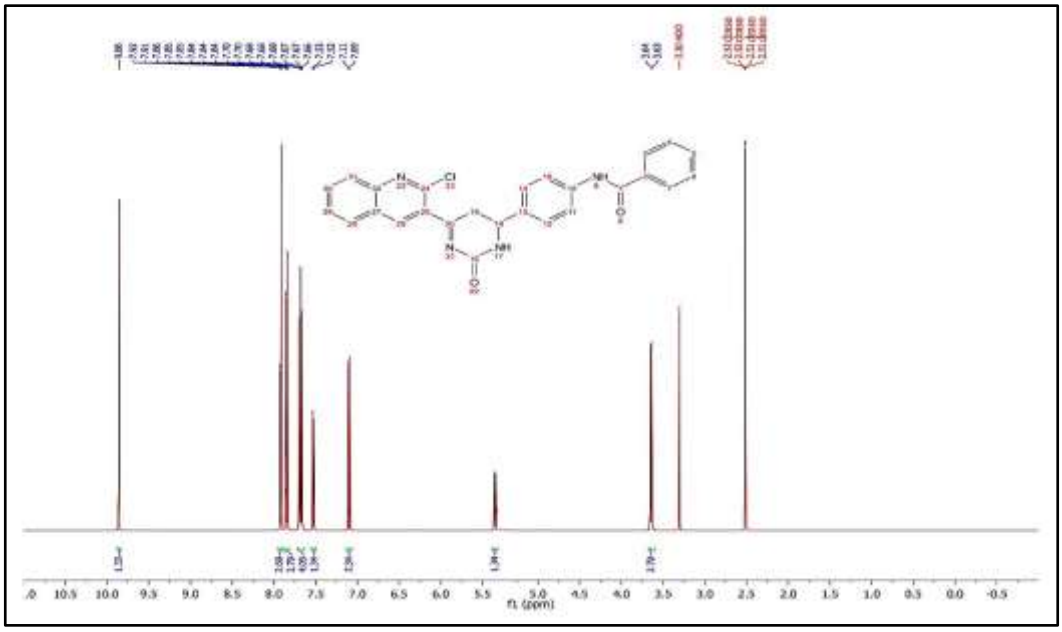


Figure 11: 1H NMR spectra for the compound

The 13CNMR spectra of compound M1 showed a distinct band at 189.48 ppm attributed to the carbonyl group C=O of the C1 carbon atom. While the carbon atoms C18-C20 showed a signal at (115.39-115.78) ppm [21], [22]. A packet appeared at (143.56) ppm, belonging to C3. Also, signal appeared at (121.78) ppm, which are related to the C2 carbon atom. While a signal group of (126.76-151.98) ppm appeared, which is attributed to carbon atoms (C6 to C21). As for the compound **M2** 150.34 (C_{21}), 148.62(C_6), 144.34(C_{16}), 138.34(C_{10}), 133.29 (C_2), 132.62(C_{27}), 132.23(C_{22}), 131.34(C_5), 130.78 (C_{13}), 129.56(C_{25}), 128.98(C_{14}), 128.22($C_{12,28}$) , 127.99 ($C_{6,4}$), 127.56(C_{24}), 127.22($C_{7,3}$), 126.43($C_{23,26}$) , 120.54 (C_{17}), 119.94($C_{11,15}$). Also the compound **M3** Show signs when 167.36 (C_1), 152.88(C_{18}), 149.23(C_{28}), 148.34(C_{36}), 144.46 (C_{21}), 138.89(C_{10}), 134.45(C_2), 132.90($C_{29,34}$), 132,65 (C_5), 131.11(C_{30}), 130.93($C_{25,23}$), 130.65($C_{12,6}$) , 129.91 (C_{33}), 129.72($C_{4,14}$), 128.85($C_{31,35}$), 128.43(C_{13}) , 127.78 ($C_{3,7}$), 124.84(C_{24}), 120.67($C_{11,15}$), 117.94($C_{22,26}$), 68.21(C_{20}) 39.76(C_{19}). While compound **M4** showed signs of 165.47 carbonyl (C_1), 158.52(C_{24}) 150.63(C_{18}), 148.44($C_{22,}$), 148.66(C_{30})145.75,(C_{10}),138.38(C_5),135.38(C_{10}), 133.75 (C_2), 133.62(C_{23}), 131.23(C_{28}), 130,11 ($C_{6,29}$), 129.91($C_{26,27}$), 129.52($C_{7,25}$), 129.18($C_{12,14}$) , 128.91 ($C_{3,4}$), 128.52(C_{31}), 127.22(C_7), 125.43(C_{13}) , 122.82 ($C_{11,15}$), 61.03(C_{20}), 39.97(C_{19}). Compound **M5** showed signs 175.94 (C_{32}), 165.01(C_1), 157.09($C_{18,12}$), 154.84 (C_{27}), 146.57(C_{22}), 150.54($C_{7,5}$) 146.90(C_{22}),142.91(C_{30}),140.10(C_{10}), 131.54(C_3), 131.17 ($C_{23,24}$), 129.09($C_{29,25}$), 127.94(C_{14}), 118.85(C_{28}) , 113.96 ($C_{15,13}$), 112.28(C_{26}), 10916(C_2), 106.82(C_4), 100.92(C_6) , 60.84(C_{20}), 39.46(C_{19}) . Compound **M6** showed signs of 167.76 (C_{26}), 156.00(C_6), 153.43(C_3), 149.07(C_{18}), 147.47 (C_{10}), 139.87(C_{23}), 135.59(C_{27}), 134.10(C_{11}), 131.83 ($C_{16,30}$), 131.11(C_{12}), 130.75(C_{15}), 129.97($C_{14,21}$) , 129.30 ($C_{25,29}$), 129.05(C_{31}), 128.00($C_{28,32}$), 127.93($C_{13,17}$) , 126.86 (C_{20}), 59.36(C_5), 39.75(C_4) .Compound **M7** showed signs of 181.76 (C_{16}), 173.07(C_{20}), 167.76(C_1), 148.84(C_{24}), 145.46 (C_{32}), 138.34($C_{10,13}$), 134.78(C_2), 133.06($C_{5,30}$), 131,47 ($C_{25,26}$), 130.31($C_{6,31}$), 129.43($C_{7,12}$), 129.05($C_{3,27}$) , 128.58 ($C_{4,6}$), 127.72(C_3), 126.47($C_{11,15}$), 55.43(C_{18}) , 37.67 (C_{19}). Compound **M8** showed signs of 169.12 (C_1), 163.18(C_{20}), 151.86(C_{16}), 149.91(C_{24}), 144.67 (C_{32}), 138.77(C_{10}), 137.64(C_{13}), 134.40(C_2), 132.09(C_{30}), 131.86(C_5), 129.47 ($C_{31,26}$), 128.93($C_{29,28}$), 128.23($C_{6,4}$), 128.05($C_{12,14}$) , 127.92 ($C_{3,7}$), 121.06($C_{11,15}$), 54.34(C_{18}) , 36.69. Note Figures 12-13.

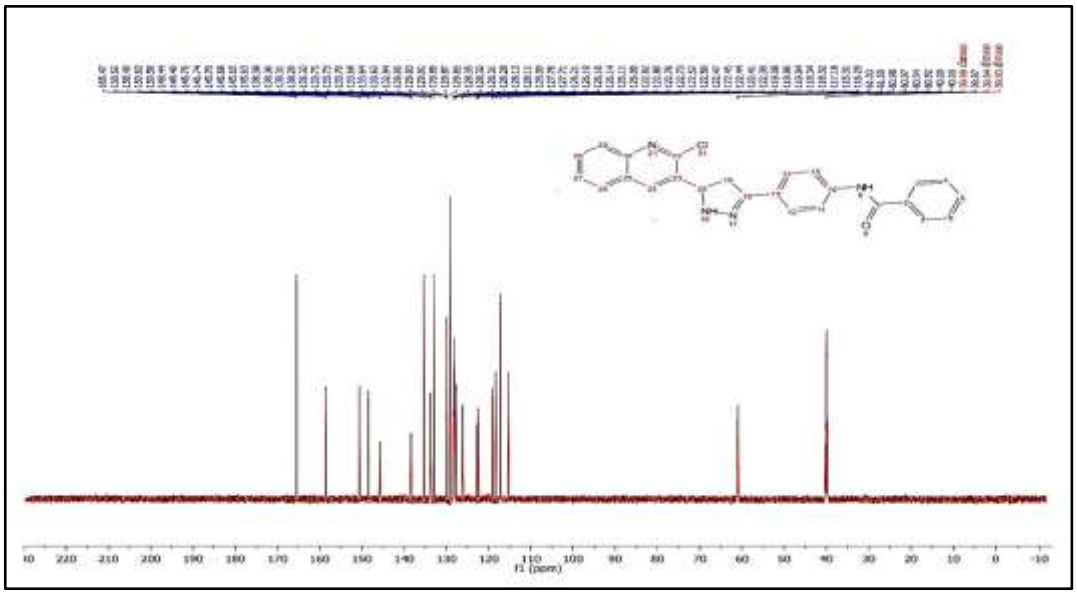


Figure 12: 13C-NMR spectra for the compound M_4

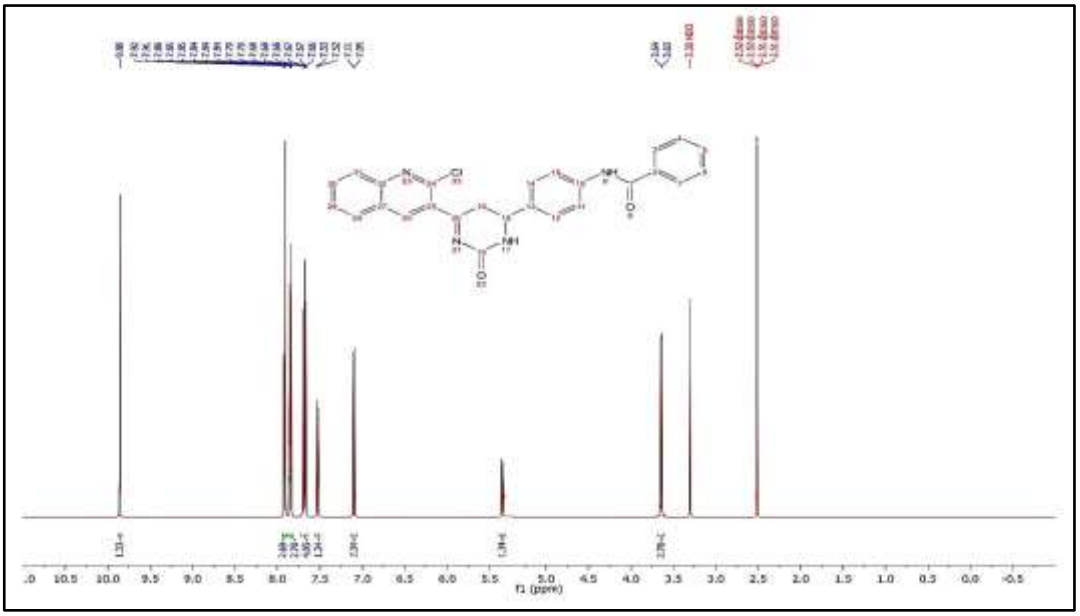
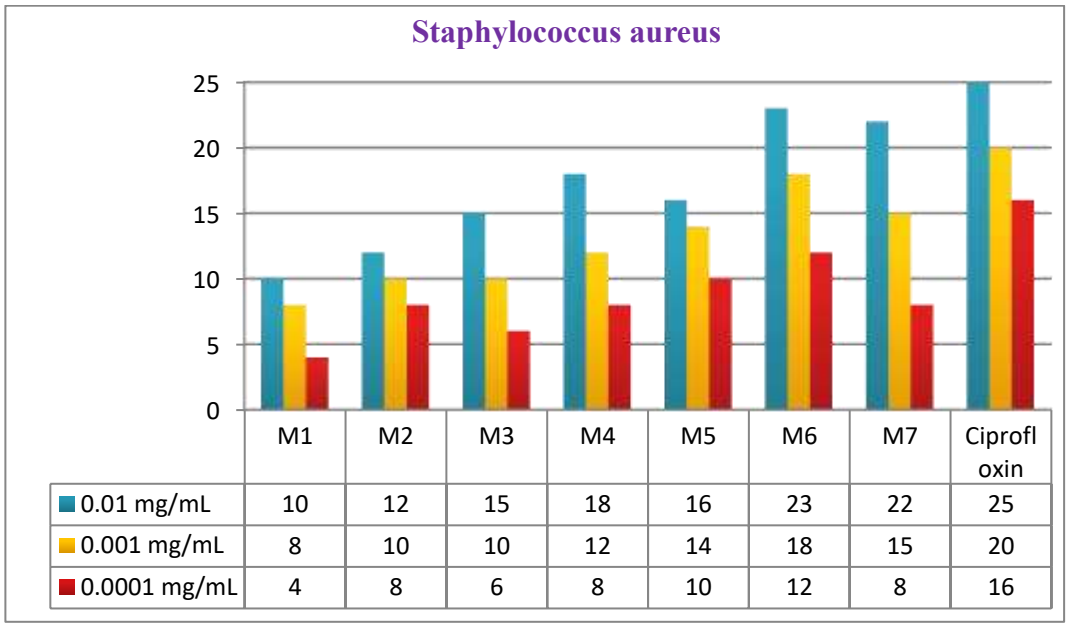


Figure 13: 13C-NMR spectra for the compound M_5.

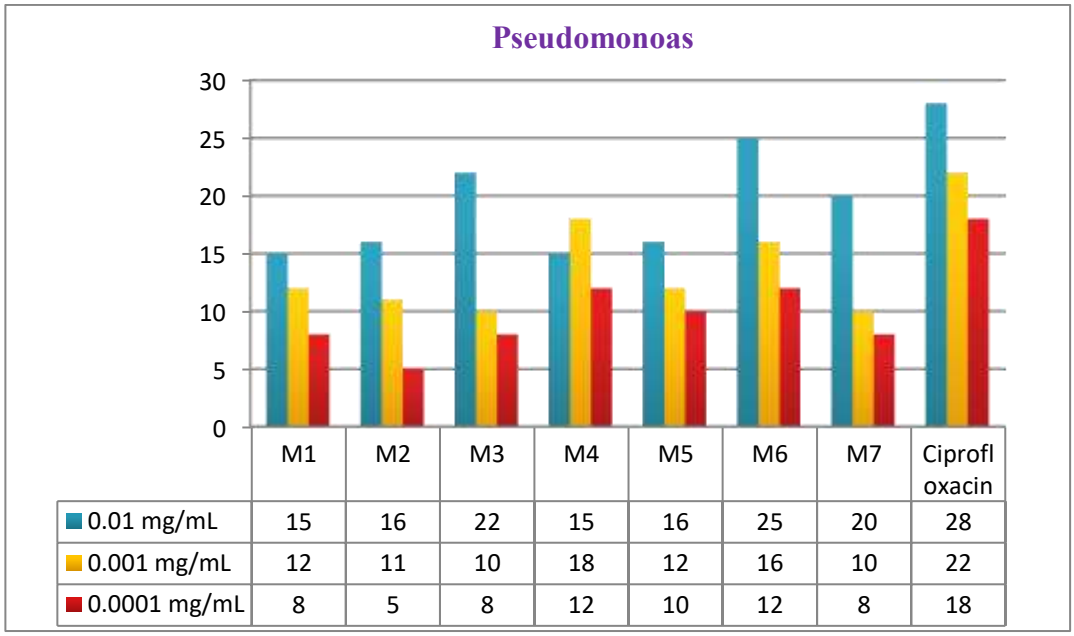
Biological effectiveness:

The antibacterial activities of the produced compounds were evaluated in vitro against a range of pathogenic representative pathogens, including Escherichia coli, pseudomonas, and Staphylococcus aureus, using the Agar well diffusion technique[23],[24]. Ciprofloxacin was employed as a conventional medication to investigate these compounds' possible actions. DMSO served as both a solvent and a control when all of the substances were evaluated at various concentration levels (0.01, 0.001, 0.0001 mg/ml).The antibacterial activity was measured using the inhibition zone diameter in millimeters (IZD). Minimum inhibitory concentration (MIC, μg/mL), which was established for each component and contrasted with the control, was the lowest concentration needed to stop the growth of bacteria[25, 26]. Comparing the synthetic compounds to the commonly used antibiotics. The bacterial activity against the latter compounds demonstrated a considerable effect as inhibitors of bacterial growth. Note Figures 14-18.



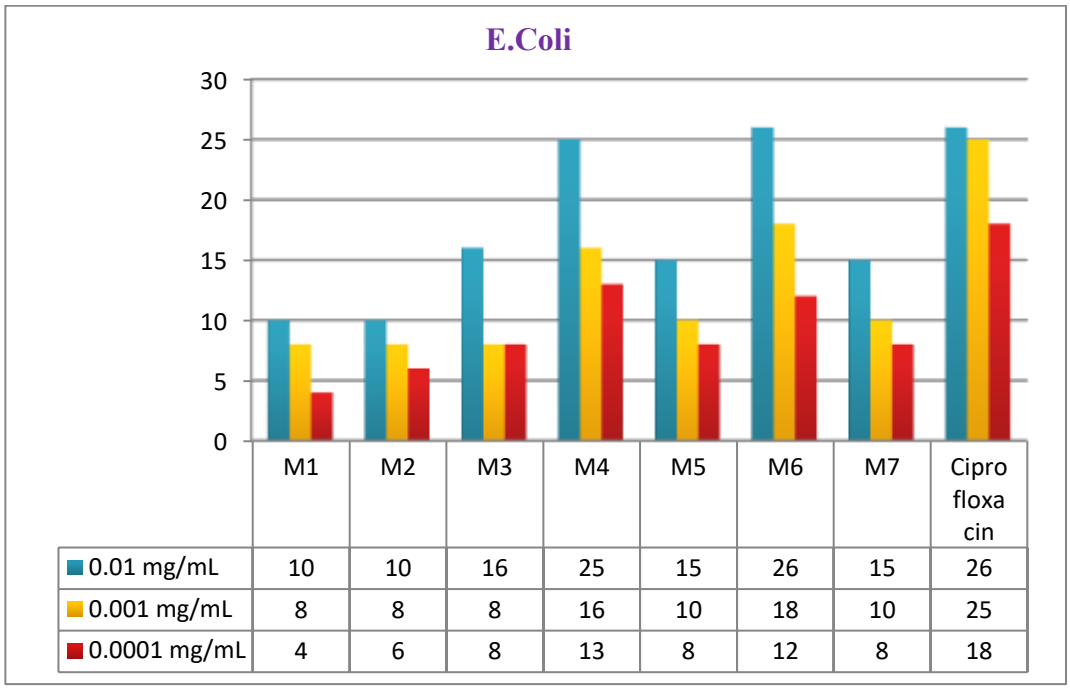
	M1	M2	M3	M4	M5	M6	M7	Ciprofloxin
0.01 mg/mL	10	12	15	18	16	23	22	25
0.001 mg/mL	8	10	10	12	14	18	15	20
0.0001 mg/mL	4	8	6	8	10	12	8	16

Figure 14: Inhibition activity data of prepared compounds against *staphylococcus aureus*.



	M1	M2	M3	M4	M5	M6	M7	Ciprofloxacin
0.01 mg/mL	15	16	22	15	16	25	20	28
0.001 mg/mL	12	11	10	18	12	16	10	22
0.0001 mg/mL	8	5	8	12	10	12	8	18

Figure 15: Inhibition activity data of prepared compounds against *pseudomonoas*



	M1	M2	M3	M4	M5	M6	M7	Ciprofloxacin
0.01 mg/mL	10	10	16	25	15	26	15	26
0.001 mg/mL	8	8	8	16	10	18	10	25
0.0001 mg/mL	4	6	8	13	8	12	8	18

Figure 16: Inhibition activity data of prepared compounds against *E.Coli*.

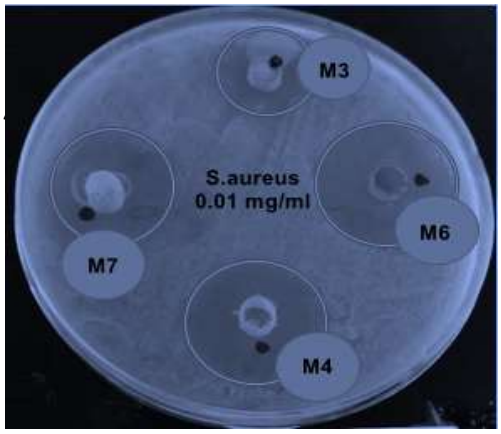


Figure 17a: Biological activity of compounds M_3,M_4, M_6 and M_7 agansit bacterial staph. aureus.

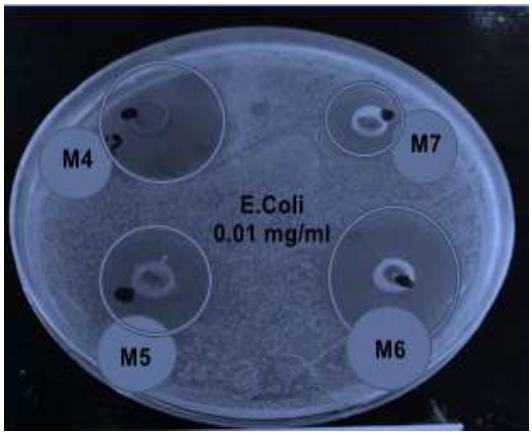


Figure 17b: Biological activity of compounds M_4,M_5, M_6 and M_7 agansit bacterial E. Coli.

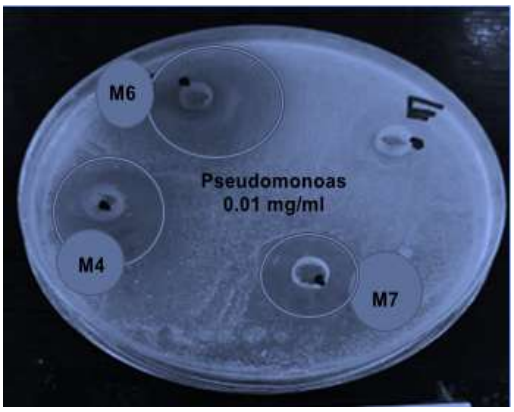


Figure 18a: Biological activity of compounds,M_4, M_6 and M_7 agansit bacterial Pseudomonas.

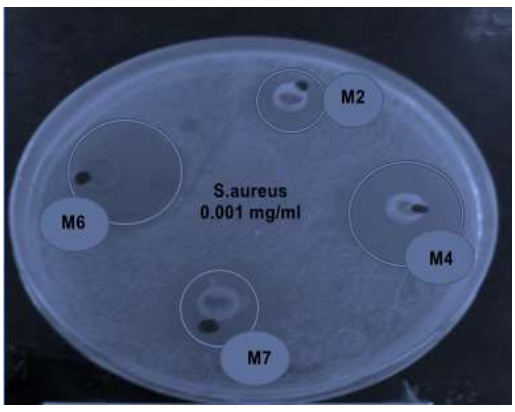


Figure 18b: Biological activity of compounds,M_4, M_6 and M_7 agansit bacterial staph. Aureus.

4. Conclusion

In this study , compound 1 was synthesized and characterized. It was synthesized and characterized by its good yield. It was then used as a basic compound for other ring-closure reactions with phenylhydrazine, hydrazine hydrate, thiosemicarbazide, semicarbazide, urea, and thiourea. The compounds were characterized by FT-IR, 13C NMR, and 1H NMR. The antibacterial activity of all produced compounds was assessed, with compounds M1, M2, M3, M5, and M8 exhibiting moderate activity against Escherichia coli, Pseudomonas, and Staphylococcus aureus, while compounds M4, M6 and M7 exhibited significant activity against certain bacteria. Finally, we concluded that the newly synthesized compounds exhibit strong to moderate antibacterial activity.

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