Synthesis and Characterization of some new Heterocyclic Compounds Prepared from Benzoimidazole Derivatives and Study of the Biological Activity

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Abstract

This research Included the preparation and characterization some novel five and seven member Heterocyclic Compounds (imidazolidine,Thiazolidine,oxazepine.) .The first step in clude react 4-chloro-o.phenylene amine with Anthranillic acid to get benz imidazolidined erivative (1). And the step second react (1) with 3-hydroxy benzaldehyde to get schiff base (2). And The three step react P.anisidine with derived (2) to get Azo dye derivative(3), derivative.react (3) with (alanine, glycine,thioglycoliacid, phthalic anhydride ,maleic anhydride)to get imidazoildine (4,5), Thiazolidine (6), oxazepine(7,8). Properties of the prepared; These Compounds. Were Identification (FT-IR),('H NMR) and (^{13}C-NMR) by spectroscopy thene study their biological effect on two types of bacteria Staphylococcus aureuses (Gram positive) and Escherichia coli (Gram Negative).

1. Introduction

The Benzimidazoles of living systems, which are in command of their many biological functions, can easily interact with benzolimidazoles. Particularly, the antibacterial properties of benzimidazole derivatives [1-3]. Many benzimidazole-containing medicines show effective biological features like antiviral activity, and the benzimidazole nucleus is gaining prominence in medicinal chemistry research [4]. Schiff bases are regarded as a preferred organic compound structure, particularly in the medical and pharmaceutical industries. Therefore, the creation of novel Schiff base derivatives as possible chemotherapeutics continues to catch the interest of researchers studying organic and pharmaceutical compounds and a variety of biological processes, including antibacterial ones [5]. Azo compounds are frequently employed as pigments and dyes. Analytical chemistry is another use. However, azo compounds with biological activity that include an antibacterial [6]. Structures like Schiff bases and azo compounds are crucial in the medical and pharmaceutical industries [7] Benzimidazole is a connected aromatic imidazole ring system wherever a benzene ring is fused to an imidazole ring as indicated within the structure for benzimidazole.

2. The Method of Work

"(FTIR) Spectra (400 -4000 cm-1) in KBr disk were recorded on SHIMADZU FTIR-8400S Fourier transform. 13C-NMR and 1HNMR were recorded on Varian Agilent USA at (500MHz) with (DMSO-d6) measurements were made at Department of Chemistry, basra University, Iraq."

Preparation methods of compound [1] (Benzimidazole) [8]

Compound No. (1) prepares by react Mix equal quantities (0.003 mol) of 4-chloro-o-phenylene amine (0.42777g) and Anthranillic acid (0.41142g) in a circular flask containing (20 ml) of absolute ethanol and stir the mixture at room temperature. Until the melting process is complete, add to the above mixture (20 ml). Of hydrochic acid 4n and the mixture was ascended for (6) hours, temperature (85) until the reaction was completed, the reaction was followed by TLC technology, then the mixture was cooled and the product was filtered

Preparation methods of compound [2, 9]

The compound (2) Schiff base was prepared by reacting Equal molar amounts (0.001 mol) each of the derivative (1)(0.2316g), 3-hydroxy benzaldehy(0.12212 g) de were mixed in a circular flask fitted with a magnetic compound containing 30 ml absolute ethanol, then three drops of glacial acid were added to the mixture. The mixture was prepared for 19hour, cooled, reacted, and kept. It was kept for 24 hours, the precipitate was filtered, washed, and recrystallized with absolute ethanol. Press follow interaction.

Preparation methods of compound [2, 10]

Preparation Compound (3), prepares by react (0.002) mol of P. anisidine (0.2463g)is taken and dissolved in (40 mL) of distilled water and (4 mL) of concentrated hydrochloric acid, then the reaction mixture is cooled in a refrigerator at a temperature, (0-5 Co) of (3 ml) of (0.002 mole) of sodium nitrite solution was added. Gradually with continuous stirring for 20 minutes at a temperature (5-0) to obtain diazonium salts, Then dissolve (0.002 mol) of the (2) derivative (0.680g) in (50 ml) of all absolute ethanol and (40 ml) of (5% sodium hydroxide). Then add diazonium salt from the first step slowly with continuous stirring at a temperature of (0 - 5 co) for one hour, then equalize the mixture by adding dilute hydrochloric acid and leave the solution until the next day.

Preparation methods of compound [4, 5, 11]

The derivative(imidazolidine), derivative react (3), was prepared by reaction (0.46993g, 0.001mol) of compound (3), with (0.07507g,0.001 mol), (glycine), (0.0891g,0.001 mol), (alanine) each dissolved in (1.4 dioxane) (15 ml).

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Sublimation was carried out from (30) hours at a temperature (50°C), after which the solution was left to cool for (24 hours), after which it was filtered and recrystallized with ethanol.

Preparation methods of compound [6, 12]

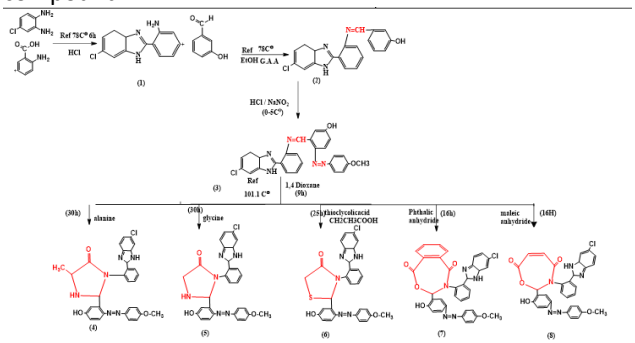
The derivative (Thiazolidine), derivative.reast (3), prepares by react (0.001 mol,0.09212g), of (thiogly coli acid) was added to (0.46993g,0.001 mol) of compound (3), each of them dissolved in (20 ml) of (1.4 dioxane) in a circular flask with continuous stirring, then added to The mixture (0.5 g) of (anhydrous zinc) with continuous stirring was then solidified for (25) hours at a temperature of (50 ° C), then the solution was left to cool for (24 hours), after which it was filtered and recrystallized with ethanol.

Preparation methods of compound [6, 7]

The two derivative (Oxazepine), derivative.reast (3), prepared by reacting (0.46993 g, 0.001mol) of compound (3with each of (0.4812g, 0.001 mol), (phathalic anhydride), (0.09806g, 0.001 mol) (maleic anhydride) ,each dissolves in (20 ml) of dry benzene. The escalation was done from (20) hours at a temperature of (50 Co) after that the solution is left to cool down for a period of (16 hours), after that, it is filtered and recrystallized with ethanol.

Preparation of Microbiology Culture Media [13]

38 g of nutrient agar is dissolved in (1L) of distill water, after that place it in an autoclave for 15 minutes at 121 C◦ for the purpose of sterilizing. After the media reached 37 C◦, it is poured into petri dishes made ready for bacteria streaking. It was acquiring isolated bacteria (Eschericia coli) and (Staphylococcous aurous) from hospital. It was cultivated, and the plates were incubatd at 37 C◦ for 24 hours for both type of bacteria, DMSO was used as a solvent to prepare solution of the various compounds were tested (0.02 g of compounds in 5 ml DMSO) after that the inhibition zones were calculated for each compound.



Scheme (1): preparation of compounds (1-8)

3. Results and Discussion

Compound (1) 2-(6-chloro-3a, 4-dihydro-1H-benzo[d]imidazol-2-yl) aniline.

The infrared spectrum data of the compound (1) showed band at (3232.46-3325.03cm-1) broad for (OH), (1697.24 cm-1) for (C=N) for imidazole ring, and (1558.38 cm-1) due to aromatic (C=C). The 1H-NMR (DMSO) spectrum data of compound (1) show: 6.98-6.73(m, 6H, Ar-H), 4.28 (S, 2H, NH_2), 9.66 (S, H, NH)

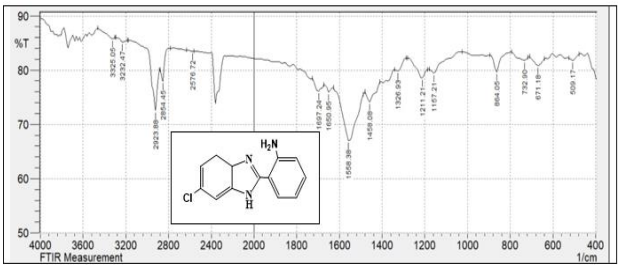


Fig. 1: FT-IR spectrum of compound (1)

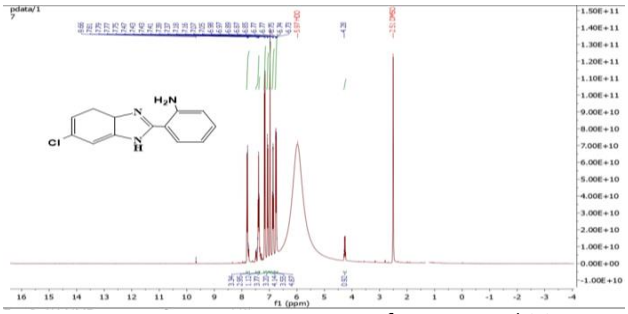


Fig. 2: 1H-NMR spectrum of compound (1)

Compound (2). (E)-3-(((2-(6-chloro-3a, 4-dihydro-1H-benzo[d]imidazol-2yl) phenyl)imino)methyl)phenol

The infrared spectrum data of the compound (2) showed band (334.19 cm-1) for (OH) band, (2869.88-2962.46 cm-1) for (C-H) in aliphtic, (1473.51cm-1) for (N=N) and (1596.95 cm-1) due to aromatic (C=C), (1681.81 cm-1) for (C=O). 1H-NMR (DMSO) spectrum data of compound (2) show δ: 6.36-7.83 (m, 10H, Ar-H), 9.72 (S, 1H, OH), 8.50(S, H, CH), 12.34(S, 1H, NH).

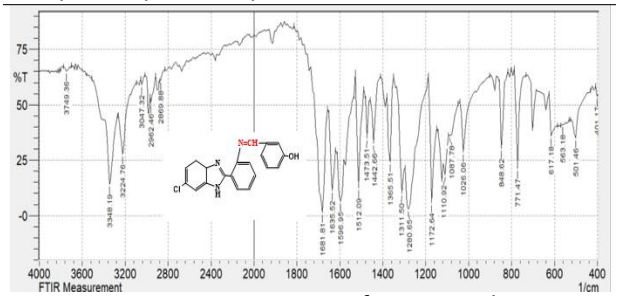


Fig. 3: FT-IR spectrum of compound (2)

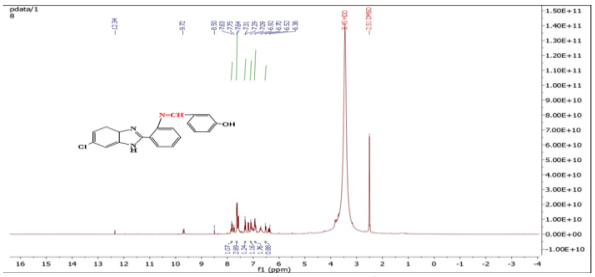


Fig. 4: 1H-NMR spectrum of compound (2)

Compound (3): 3-(2-(6-chloro-3a, 4-dihydro-1H-benzo[d]imidazol-2-yl) phenyl) imino) methyl)-4-((Z)-(4-methoxyphenyl)diazenyl)phenol

The infrared spectrum data of the compound (3),(3417.63cm-1) for (OH) band, (1589.23 cm-1) for (C=N), and (1697.24cm-1) (C=O),(1442.66 cm-1)for(N=N).1H-NMR (DMSO) spectrum data of compound (3) show δ:8.79(S,H,CH), 1.2(S,3H,CH3), 9.5(S,1H,OH) ,9.8(S,1H,NH).

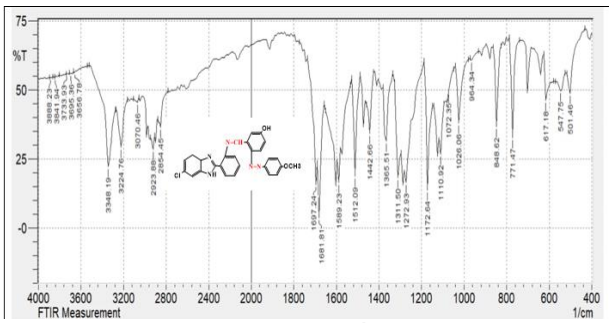


Fig. 5: FT-IR spectrum of compound (3)

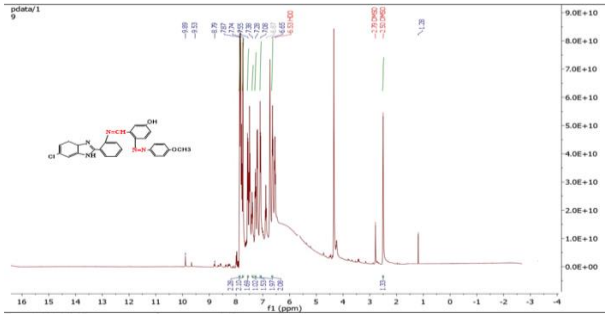


Fig. 6:1H-NMR spectrum of compound (3)

Compound (4) (E)-3-(2-(6-chloro-2, 7a-dihydro-1H-benzo[d]imidazol-2-yl) phenyl)-2-(5-hydroxy-2-((4-methoxyphenyl) diazenyl) phenyl)-5-methylimidazolidin-4-one

The infrared spectrum data of the compound (4) showed band at (2869.98) for (Ar-C-H), (1512.09cm-1) for (C=N) inside imidazole ring, (2769.99-2615.29 cm-1) for (C-H) in (CH3), (3348.19 cm-1) for (OH) band, (1697.24cm-1) for (C=O) and (1473.51 cm-1) due to aromatic (N=N). 1H-NMR (DMSO) spectrum data of compound (4) show δ: 6.65-7.78 (m, 10H, Ar-H), 9.95 (S, 1H, OH), 9.98(S, 1H, NH), 8.79(S, 1H, CH),

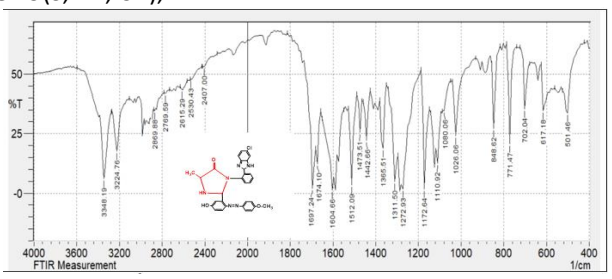


Fig. 7: FT-IR spectrum of compound (4)

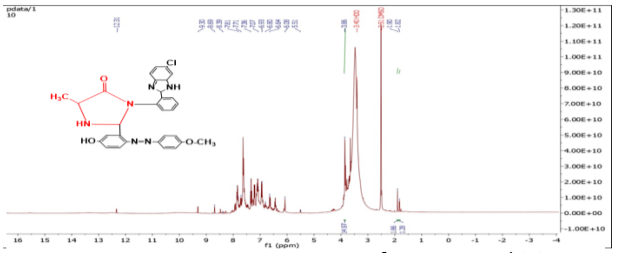


Fig. 8: 1H-NMR spectrum of compound (4)

Compound (5): (E)-3-(2-(6-chloro-2, 7a-dihydro-1H-benzo[d]imidazol-2-yl) phenyl)-2-(5-hydroxy-2-((4-methoxyphenyl) diazenyl) phenyl) imidazolidin-4-one

The infrared spectrum data of the compound (5) showed band at (3132.16 -3232.47cm-1) for (Ar-C-H), (1589.23 cm-1) for (C=N) inside imidazole ring, (2993.32cm-1) for (C-H) in (CH3), (3517.92cm-1) for (OH) band, (1385.51 cm-1) for (N=N) and (1612.38 cm-1) due to aromatic (C=C), (1712.67cm-1) for C=O imide,. 1H-NMR (DMSO) spectrum data of compound (5) show δ: 6.07-7.86(m, 10H, Ar-H), 9.28 (S, 1H, OH), 1.36(S, 3H, CH3), 12.18(S, 1H, NH). 1.92(S, 2H, CH2),

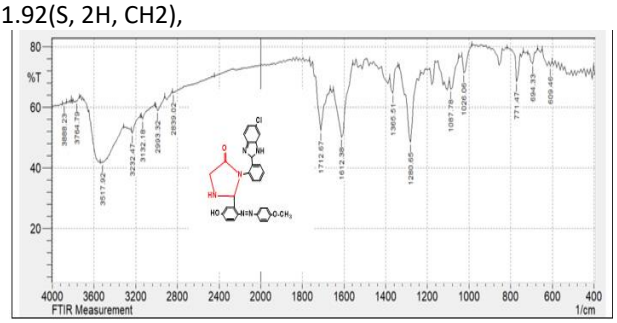


Fig. 9: FT-IR spectrum of compound (5)

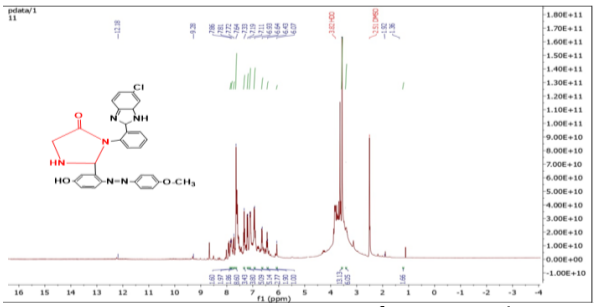


Fig. 10: 1H-NMR spectrum of compound (5)

Compound (6): (E)-3-(2-(6-chloro-2, 7a-dihydro-1H-benzo[d]imidazol-2-yl) phenyl)-2-(5-hydroxy-2-((4-methoxyphenyl) diazenyl) phenyl) thiazolidin-4-one

The infrared spectrum data of the compound (6) showed band at (3078.18cm-1) for (Ar-C-H), (1712.67 cm-1) for (C=N) for ring, (2988.60 cm-1) for (C-H) in (CH3), (3348.19 cm-1) for (OH), (1411.80cm-1) for (N=N) and (1596.95 cm-1) due to aromatic (C=C), and the band of ester carbonyl(O-C=O) is disappear, (1689.53 cm-1) for amide carbonyl group(N-C=O), (3224.76 cm-1) for (NH).1H-NMR (DMSO) spectrum data of compound (6) show δ: 6.57-7.85(m,15H,Ar-H), 9.26 (S, 1H, OH), 3.03(S,3H,CH3), 10.36(S, 1H, NH), 4.97(S, 4H, CH2).

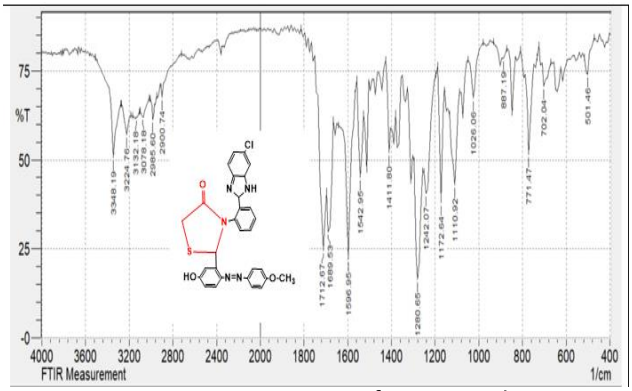


Fig. 11: FT-IR spectrum of compound (6)

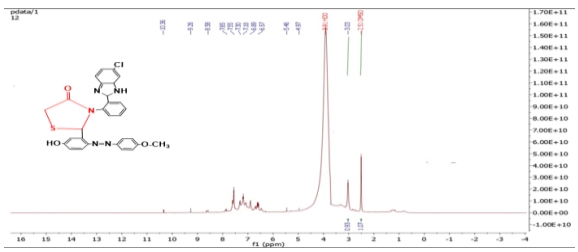


Fig. 12: 1H-NMR spectrum of compound (6)

Compound (7) (E)-4-(2-(6-chloro-2, 7a-dihydro-1H-benzo[d]imidazol-2-yl) phenyl)-3-(2-hydroxy-5-((4-methoxyphenyl) diazenyl) phenyl)-3, 4-dihydrobenzo[e]

oxazepine-1, 5-dione

The infrared spectrum data of the compound (7) showed band at (3116.76 cm-1) for (Ar-C-H), (1588.23 cm-1) for (C=N) inside imidazole ring, (2977.89 cm-1) for (C-H) in (CH3), (3425.43 cm-1) for (OH) band, (1542.75 cm-1) due to aromatic (C=C), (2576.72 cm-1) and (1635.52cm-1) for C=O imide (N-C=O) and (1280.65 cm-1) for (C-N) group inside oxazepine ring. 1H-NMR (DMSO) spectrum data of compound (7) show δ: 6.28-7.78(m, 10H, Ar-H), 10.29 (S, 1H, OH), 2.8(S, 3H, CH3), 11.47 (S, 1H, NH)

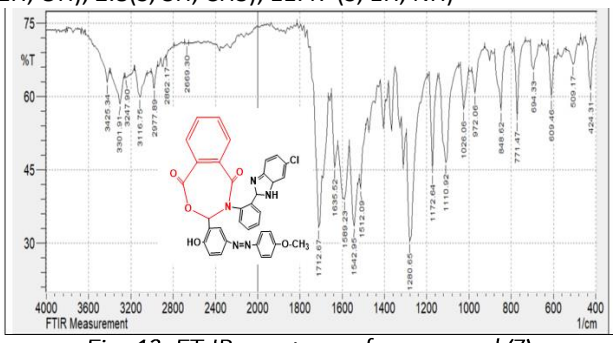


Fig. 13: FT-IR spectrum of compound (7)

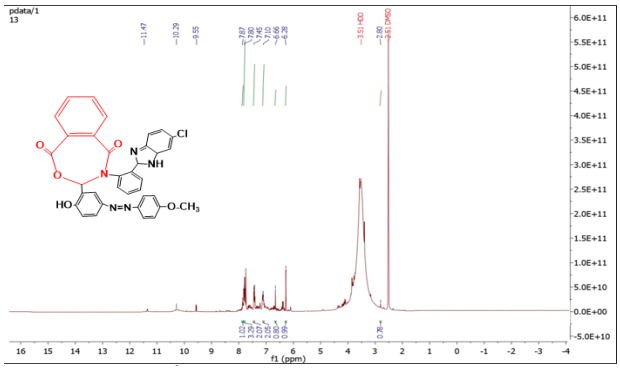


Fig. 14: 1H-NMR spectrum of compound (7)

Compound (8) (E)-3-(2-(6-chloro-2, 7a-dihydro-1H-benzo[d]imidazol-2-yl) phenyl)-2-(2-hydroxy-5-((4-methoxyphenyl) diazenyl) phenyl)-2, 3-dihydro-1, 3-oxazepine-4,7-dione

The infrared spectrum data of the compound (8) showed band at (3201.61 cm-1) for (Ar-C-H), (1542.95 cm-1) for (C=N) inside imidazole ring, (3039.60 cm-1) for (C-H) in (CH3), (332.76cm-1) for (OH) band, (1504.37cm-1) for (N=N) and (14 cm-1) due to aromatic (C=C), (1604.66 cm-1) for amide carbonyl group(N-C=O),and (1234.36cm-1) for (C-N) group inside oxazepine ring,. 1H-NMR (DMSO) spectrum data of compound (8) show δ: 6.5-8.1(m, 10H, Ar-H), 10.34 (S, 1H, OH), 2.8(S, 3H, CH3),), 5.56(t, 2H, (CH2), 11.56(S, 1H, NH), 9.9 (S, 1H, CH).

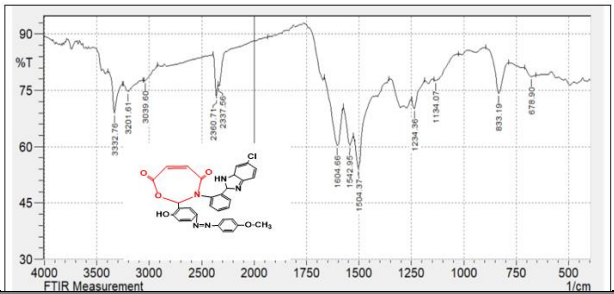


Fig. 15: FT-IR spectrum of compound (8)

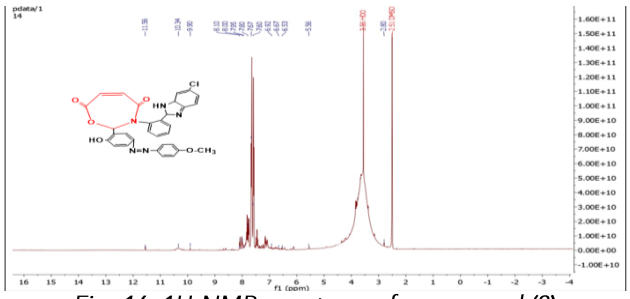


Fig. 16: 1H-NMR spectrum of compound (8)

4. Conclusions

According to the above studies it can be concluded that the synthesized compounds have substantial antibacterial activity against bacteria Staphylococcus aureas and Escherichia Coli, the compounds that appeared good activity are (3,5,7) against (Staphylococcus aureas) on other hand, compounds (3,4.5) show good activity against (Escherichia Coli), the results of the antibacterial activity are shown in the Fig.(16)

Table 1: Show Biological activity for compounds (1-9)

Compounds No.	E. Coli	Staph. Aureus
1	_	_
2	++	++
3	_	+
4	++	_
5	++	+
6	+	+
7	+	+
8	+	++
DMSO Solvent	_	_
Amoxicillin	+	+++

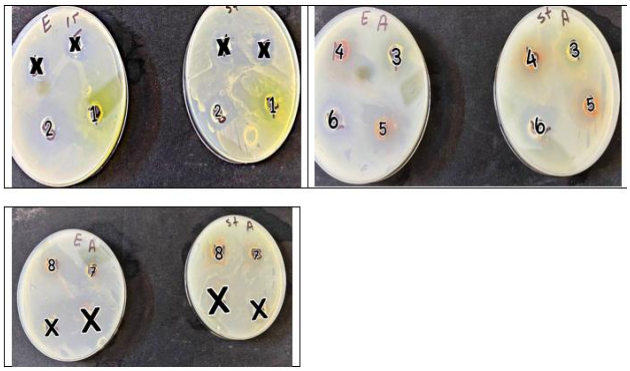


Fig. 16: Biological activity of compounds prepared against (St aureas, E Coli) bacteri

- = No inhibition = inactive, + = (5-10) mm = slightly active, ++= (11-20) mm = moderately active, +++ = (more than 20) mm = Good active.

Table 2: Physical properties of compounds (1-8)

NO	Name of comp	M.F	M.W	M.P	RF	%
1	2-(6-chloro-3a,4-dihydro-1H-benzo[d]imidazol-2-yl)aniline	C13H12ClN3	245.71	183-185	0.5	77

2	(E)-3-(((2-(6-chloro-3a,4-dihydro-1H-benzo[d]imidazol-2-yl)phenyl)imino)methyl)phenol	C20H16ClN3O	349.82	287-290	0.73	71
`3	3-(((2-(6-chloro-3a,4-dihydro-1H-benzo[d]imidazol-2-yl)phenyl)imino)methyl)-4-((Z)-(4-methoxyphenyl)diazenyl)phenol	C27H22ClN5O2	483.96	220-222	-	87
4	(E)-3-(2-(6-chloro-2,7a-dihydro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(5-hydroxy-2-((4-methoxyphenyl)diazenyl)phenyl)-5-methylimidazolidin-4-one	C30H27ClN6O3	555.04	208-210	0.52	85
5	(E)-3-(2-(6-chloro-2,7a-dihydro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(5-hydroxy-2-((4methoxyphenyl)diazenyl)phenyl)imidazolidin-4-one	C29H25ClN6O3	541.01	264-266	0.57	89
6	(E)-3-(2-(6-chloro-2,7a-dihydro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(5-hydroxy2-((4methoxyphenyl)diazenyl)phenyl)thiazolidin-4-one	C29H24ClN5O3S	557.13	170-173	0.7	88
7	(E)-4-(2-(6-chloro-2,7a-dihydro-1H-benzo[d]imidazol-2-yl)phenyl)-3-(2-hydroxy-5-((4-methoxyphenyl)diazenyl)phenyl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione	C35H26ClN5O5	631.16	198-200	0.42	73
8	(E)-3-(2-(6-chloro-2,7a-dihydro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(2-hydroxy-5-((4-methoxyphenyl)diazenyl)phenyl)-2,3-dihydro-1,3-oxazepine-4,7-dione	C31H24ClN5O5	582.15	219-221	0.37	86

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