Study of the Biological Activity of Some new Heterocyclic Compounds Prepared from Benzoimidazole Derivatives

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Abstract

This study synthesised and characterised new five- and seven-member heterocyclic compounds (imidazolidine, Thiazolidine and oxazepine). The first step in clude react o-phenylene diamine with salicylic acid to get Benz imidazolidine derivative (1). and the second step react p-amino acetophenone with Sodium nitrite to get diazonium salts after this add the mixture to derived (1) to get Azo dye derivative (2) the three steps react (2) with 2_amino pyridine to get schiff base (3) derivative. (3) wit with (alanine, glycine, thioglycolic acid, phthalic anhydride, maleic anhydride) to get imidazolidine (4,5), Thiazolidine (6), oxazepine(7,8) derivatives. These compounds' properties; their composition. Staphylococcus aureus (Gram-positive) and Escherichia coli (13C-NMR) were used for identification, ('H NMR), (13C-NMR) and (FT-IR), and their biological effects were studied (Gram Negative).

Keywords: Schiff base, Azo dye, Oxazepine. imidazolidine, Thiazolidine

1. Introduction

The benzimidazole group, known for its wide range of therapeutic uses (including antimicrobial, anti-inflammatory, anti-cancer, etc.), and the chalcones, which are biologically active due to the presence of the unsaturated carbonyl system, are the two biological components that we hope to combine in this research. They have demonstrated antibacterial activity against a variety of bacteria, including S.aureus, E.coli, C.albicans, T.utilis, S.sake, and W.anomala (1). Schiff's base derivatives are employed as antibiotics, antibacterial, antimalarial, anti-inflammatory, antifungal, anticancer, and anthelminthic agents, among other things (2) azo compounds. These materials stand out due to their resistance to light, the elements, water, and other solvents. The groups on either side of the N atom of the azo group are essential for color detection (3), The crucial role that imidazolidine plays in the synthesis of molecules with biological activity is what gives it its significance. The biological effects of the imidazolidine derivatives are interesting; they include anti-inflammatory, antiviral, antifungal, hypotensive, and antibiotics for the digestive system (4). Thiazolidine compounds due to their use as anti-inflammatory agent, thiazolidine chemicals have a high biological activity (5). an anticancer (6).

Oxazepine derivatives are an organic compound widely used in chemistry, Due to the chemical formula of these molecules, which contains two heterogeneous atoms, oxygen and nitrogen, medicine and pharmacology. Therefore, this compound has a very high biological activity (7). It is also used as anti-cancer agent (8).

2. The Method of Work

A SHIMADZU Fourier transform was used to record FT-IR spectra, (400-4000-cm-1) in the KBr disk. DMSO-d6 was used to record the 1H-NMR and 13C-NMR data on a Varian Agilent USA (500MHz) at Basra University, Iraq," according to the study.

Preparation methods of compound (1) (Benzimidazole) (9)

Compound No. (1) prepares by reacting Mix equal quantities (0.003 mol) of Phenylene diamine (0.324g) and Salicylic acid (0.414g) 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 Hydrochloric acid 4n and the mixture was ascended for (5) 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) (10)

Compound No. (2) prepares by react (0.002) mol of p-amino aceto phenon (0.270g) 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 mile) 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 first derivative (0.420g) 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, equalize the mixture by adding dilute hydrochloric acid and leave the solution until the next day.

Preparation methods of compound (3) (11)

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The compound (3) Schiff base was prepared by reacting Equal molar amounts (0.001 mol) each of the derivative (2) (0.0941g) and amino acid 2-aminopyridine (0.356g) 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 3 hr., 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 (4,5) (12)

The derivatives (imidazolidine), derivative react (3), was prepared by reaction (0.43239g, 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). Sublimation was carried out for (16) 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) (13)

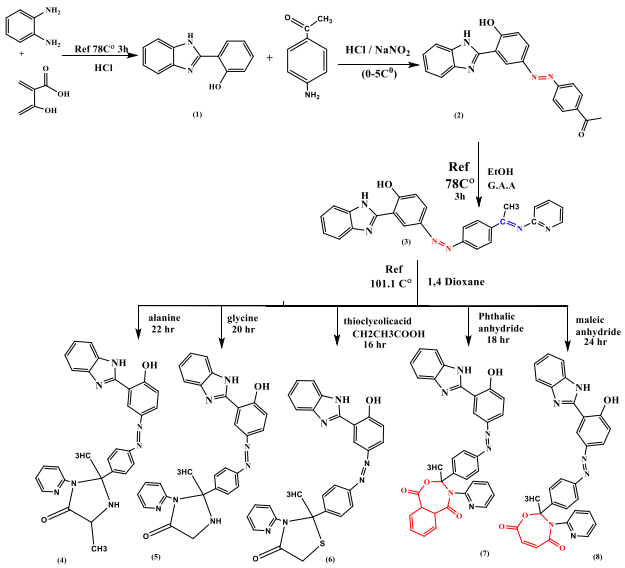
The derivatives (Thiazolidine) , derivative react(3), by reacting (0.001 mol,0.09212g), of (thioglycolic acid) was added to (0.432g,0.001 mol) of compound (3), each of them dissolved in (20 ml) of (1.4 dioxane) in a circular flask with continuous stirring, then (0.5 g) added to the mixture of (Zn anhydrous) with continuous stirring was then solidified for (16) hours at a temperature of (50°C). The solution was left to cool for (24 hours), after which it was filtered and recrystallized with ethanol.

Preparation methods of compound (7,8) (14)

The two derivatives (Oxazepine), derivative react (3), prepared by reacting (0.432 g, 0.001mol) of compound (3with each of (0.4812g, 0.001 mol), (phthalic anhydride), (0.09806g, 0.001 mol) (maleic anhydride), each dissolvecompound 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 (24 hours), After that, it is filtered and recrystallized with ethanol.

Culture media for microbiology research (15)

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 reaches 37 C◦, it is poured into petri dishes ready for bacteria streaking. It was acquiring isolated bacteria (Eschericia coli) and (Staphylococcous aurous) from hospital. DMSO was used to prepare a solution of the various compounds tested (0.02 g in 5 mL of the solvent). After 24 hours of incubation at 37°C, each compound's inhibition zones were calculated.



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

3. Results and Discussion

Compound (1), 2-(1H-benzo[d]imidazol-2-yl) phenol

The infrared spectrum data of the compound (1) showed band at (3417.63-3209.33cm^{-1}) broad for (OH), (C=N) at (1612.38 cm^{-1}) for for imidazole ring, and (1512.09 cm^{-1}) due to (C=C) aromatic. Compound (1)'s 1H-NMR DMSO spectra show: 6.9-778 (m,6H, Ar-H), 10.84 (S, 2H, NH_2), 8.15 (S, H, OH)

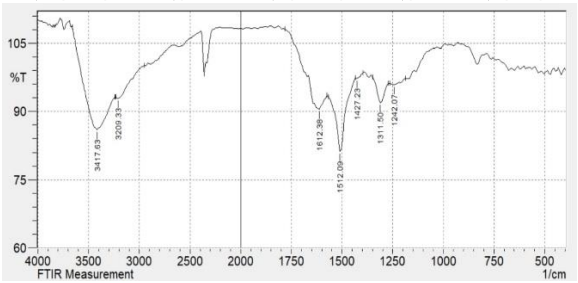


Fig. 1: FT-IR spectrum of compound (1)

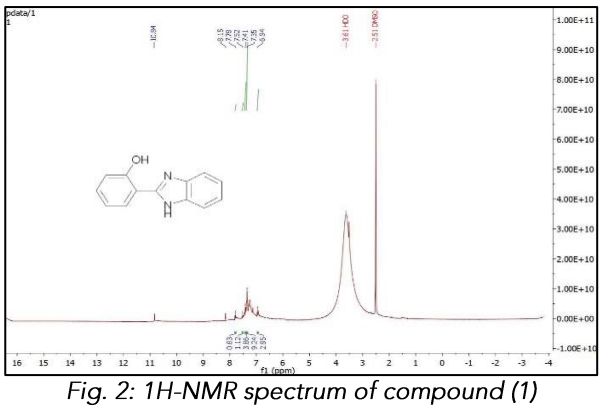


Fig. 2: 1H-NMR spectrum of compound (1)

Compound (2): 1-(4-3-1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl) ethan-1-one
The infrared spectrum data of the compound (2), (3417.63cm-1) for (OH) band, (1566.09 cm-1) for (C=N) and (1627.81cm-1) for(C=O).1H-NMR (DMSO) spectrum data of compound (2) show δ:6.5-8.5(m,8H, Ar-H), 1.64(S,3H, CH3), 9.55(S,1H, OH) ,12.69(S,1H, NH)

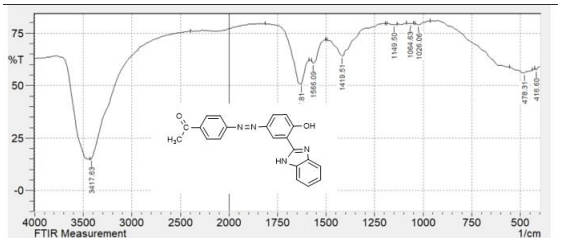


Fig. 3: FT-IR spectrum of compound (2

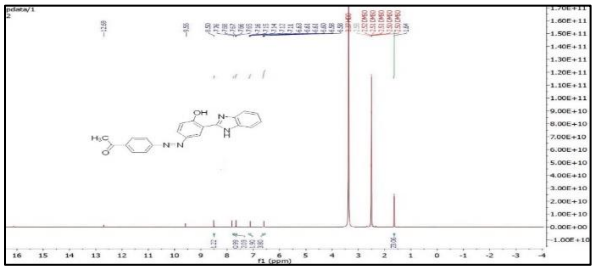


Fig. 4: 1H-NMR spectrum of compound (2)

Compound(3):2-(1H-benzo[d]imidazol-2-yl)-4-((Z)-(4-((E)-1-(pyridin-2-ylimino) ethyl) phenyl) diazenyl) phenol

The infrared spectrum data of the compound (3) showed band (3417.63 cm^{-1}) for (OH) band, (2854.45-2923.88 cm-1) for (C-H) in aliphatic, (1427.23 cm^{-1}) for (N=N) and (1535.23 cm^{-1}) due to aromatic (C=C), (1604.66 cm-1) for (C=O). 1H-NMR (DMSO) spectrum data of compound (3) show δ: 6.3-8.7 (m,10H, Ar-H) , 9.43 (S, 1H, OH) , 1.70(S,3H,CH3), 10.23(S,1H,NH).

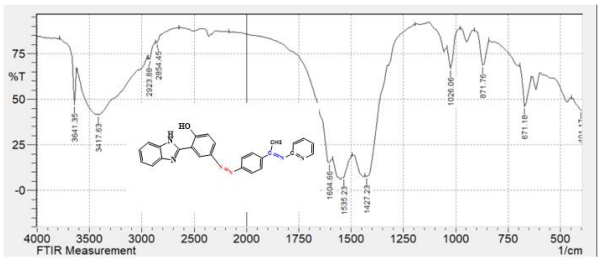


Fig. 5: FT-IR spectrum of compound (3)

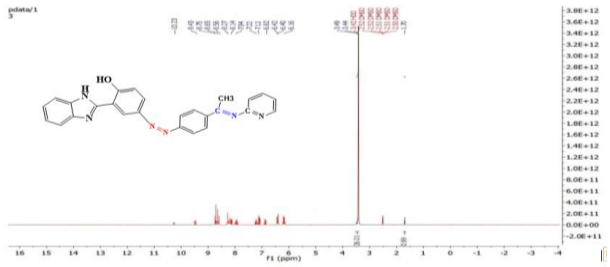


Fig. 6: 1H-NMR spectrum of compound (3)

Compound (4) :2-(4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl)-2,5-dimethyl-3-(pyridin-2-yl) imidazolidin-4-one

The infrared spectrum data of the compound (4) showed band at (3085.59) for (Ar-C-H), (1589.23cm-1) for (C=N) inside imidazole ring, (2923.88-2854.43 cm-1) for (C-H) in (CH3), (3425.43 cm-1) for (OH) band, (1620.09cm-1) for (C=O) and (1419.51 cm-1) due to aromatic (N=N). 1H-NMR (DMSO) spectrum data of compound (4) show δ: 6.20-8.00 (m,10H, Ar-H), 8.56 (S, 1H, OH), 1.74(S,3H, CH3), 4.05(t, 1H, CH), 2.09(S, 2H, (CH2), 1.7(t, 2H, (CH_3).

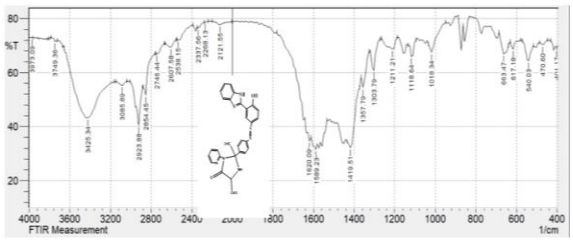


Fig. 7: FT-IR spectrum of compound (4)

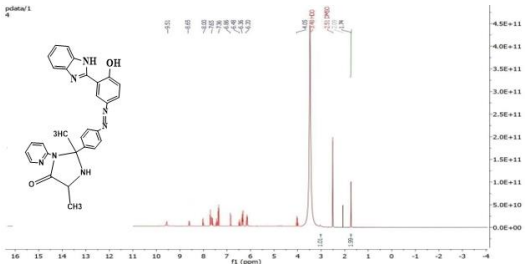


Fig. 8: 1H-NMR spectrum of compound (4)

Compound (5): 2-(4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl)-2-methyl-3-(pyridin-2-yl) imidazolidin-4-one

The infrared spectrum data of the compound (4) showed band at (3031.89 -3070.46 cm-1) for (Ar-C-H), (1589.23 cm-1) for (C=N) inside imidazole ring, (2931.60 cm-1) for (C-H) in (CH3), (3363.62 cm-1) for (OH) band , (1411.80 cm-1) for (N=N) and (1519.80 cm-1) due to aromatic (C=C), (1604.66cm-1) for C=O imide , . 1H-NMR (DMSO) spectrum data of compound (5) show δ: 6.46-7.71(m,10H, Ar-H), 7.95 (S, 1H, OH), 1.25(S,3H, CH3), 9.51 (S, 1H, NH), 4.55(S, 2H, CH_2).

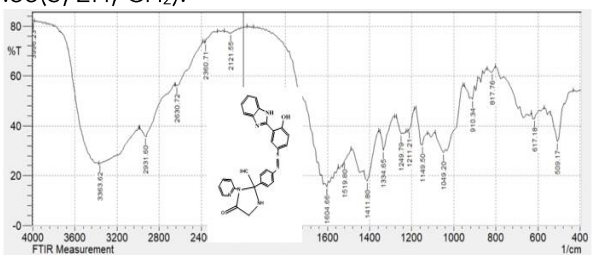


Fig. 9: FT-IR spectrum of compound (5)

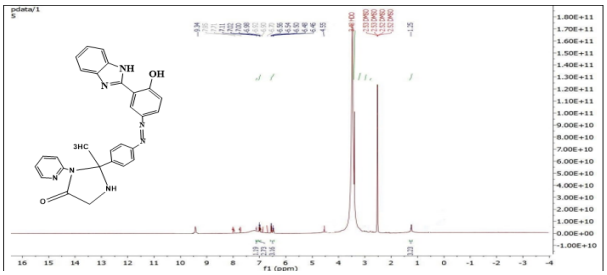


Fig. 9: FT-IR spectrum of compound (5)

Compound (6): (Z)-2-(4-((3-(1H-benzo[d]2970hiazolid-2-yl)-4-hydroxyphenyl) 2970hiazoli) phenyl)-2-methyl-3-(2970hiazoli-2-yl) 2970hiazolidine-4-one

The infrared spectrum data of the compound (6) showed band at (3016.46 cm-1) for (Ar-C-H), (1643.24. cm-1) for (C=N) for ring, (2923.88 cm-1) for (C-H) in (CH3), (3440.77 cm-1) for (OH) , (1496.66 cm-1) for (N=N) and (1573.81 cm-1) due to aromatic (C=C), and the band of ester carbonyl(O-C=O) is disappear , (1697.24 cm-1) for amide carbonyl

group(N-C=O), (3240.19 cm-1) for (NH).1H-NMR (DMSO) spectrum data of compound (6) show δ: 6.56-7.81(m,15H,Ar-H) , 8.13 (S, 1H, OH) , 2.9(S,3H,CH3), 9.39(S, 1H, NH), 3.94(S, 4H, CH2).

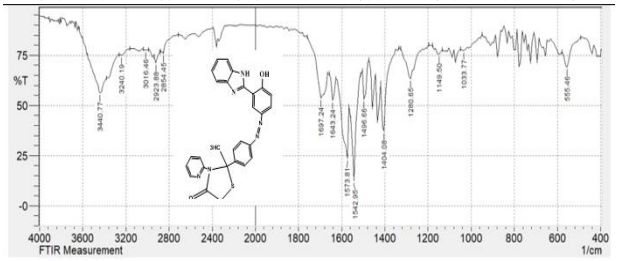


Fig. 11: FT-IR spectrum of compound (6)

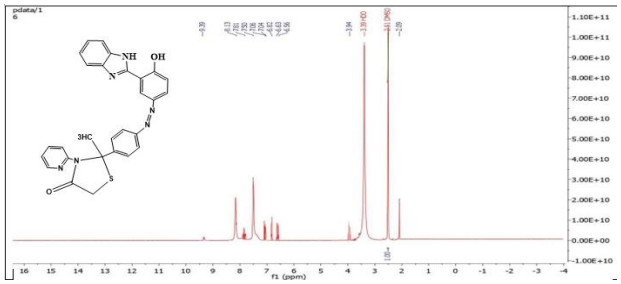


Fig. 12: 1H-NMR spectrum of compound (6)

Compound (7): 3-(4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl)-3-methyl-4-(pyridin-2-yl)-3,4,5a,9a-tetrahydrobenzo[e][1,3]oxazepine-1,5-dione

The infrared spectrum data of the compound (7) showed band at (3031.89 -3070.46 cm^{-1}) for (Ar-C-H), (1589.23 cm-1) for (C=N) inside imidazole ring, (2923.88 cm^{-1}) for (C-H) in (CH3), (3325.05 cm^{-1}) for (OH) band , (1458.08 cm-1) for (N=N) and (1558.38 cm^{-1}) due to aromatic (C=C), C=O at (1696.24 cm^{-1}) for imide (N-C=O) and (1326.93 cm-1) for (C-N) group inside oxazepine ring, (1211.21 cm^{-1}) for (C-O-C) group. 1H-NMR (DMSO) spectrum data of compound (7) show δ: 7.70-8.25(m,10H, Ar-H), 8.47 (S, 1H, OH), 1.23(S,3H,CH3), 9.70 (S, 1H, NH)

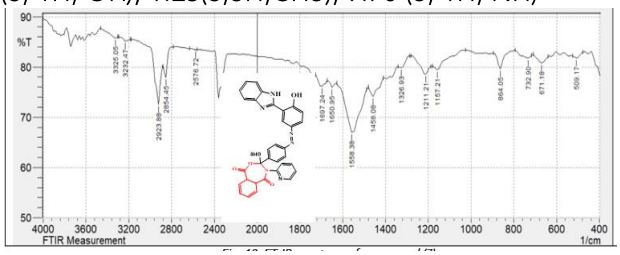


Fig. 12: FT-IR spectrum of compound (7)

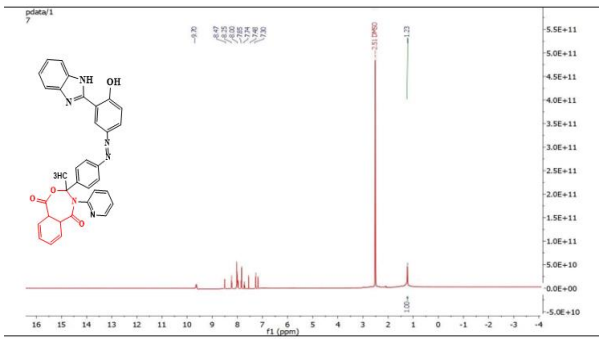


Fig. 13: 1H-NMR spectrum of compound (7) Compound (8) (E)-2-(4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl)-2-methyl-3-(pyridin-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione

The infrared spectrum data of the compound (8) showed band at (3047.32 -3224.76 cm-1) for (Ar-C-H), (1512.09 cm-1) for (C=N) inside imidazole ring, (2931.60 cm-1) for (C-H) in (CH3), (3749.36cm-1) for (OH) band , (1473.51cm-1) for (N=N) ,(1681.81 cm-1) for amide carbonyl group(N-C=O) and (1365.51 cm-1) for (C-N) group inside oxazepine ring, (1280.65 cm-1) for (C-O-C) group . 1H-NMR (DMSO) spectrum data of compound (8) show δ: 6.43-7.79 (m,10H, Ar-H), 8.33 (S, 1H, OH), 1.70(S,3H, CH3),),5.26(d, H, (CH) , 9.29 (S, 1H, NH).

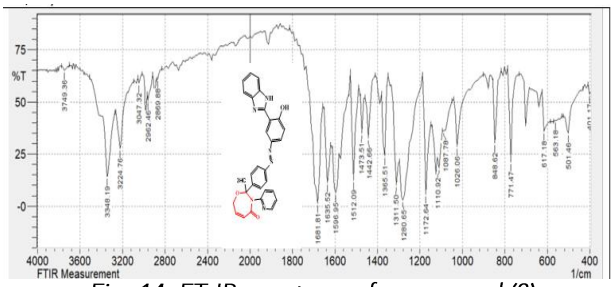


Fig. 14: FT-IR spectrum of compound (8)

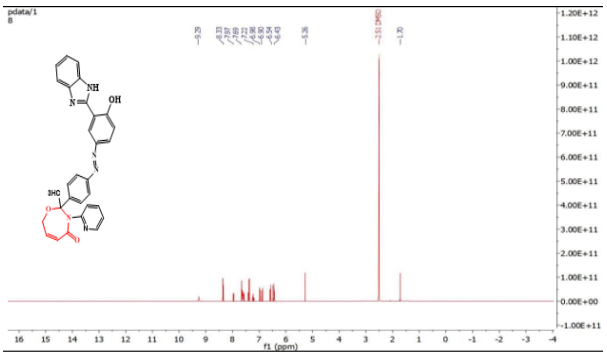


Fig. 15: 1H-NMR spectrum of compound (8)

Biological activity results

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

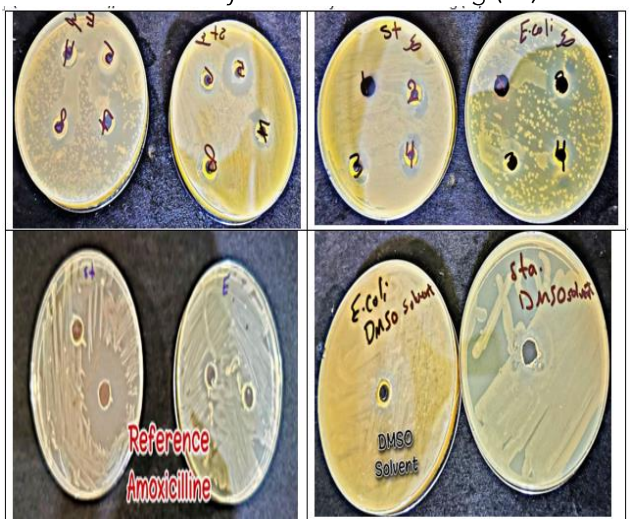


Fig. 16: Biological activity of compounds prepared against (St aureas , E Coli) bacteria

Table 1: Show Biological activity for compounds (1-9)		
Compounds No.	*E. Coli*	*S.aureus*
1	-	-
2	+	-
3	++	+
4	++	+
5	++	+
6	-	-
7	+	+
8	-	-
DMSO Solvent	-	-
Amoxicillin	+	+++
- = 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(^{O}C)	R.f	Color	%
1	2-(1H-benzo[d]imidazol-2-yl) phenol	C13H10N2O	210.24	240-242	0.38	Black	69
2	1-(4-3-1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl) ethan-1-one	C21H16N4O2	356.39	163-165	-	golden	73
3	2-(1H-benzo[d]imidazol-2-yl)-4-((Z)-(4-((E)-1-(pyridin-2-ylimino) ethyl) phenyl) diazenyl) phenol	C26H20N6O	434.50	190-192	0.42	white	77
4	2-(4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl)-2,5-dimethyl-3-(pyridin-2-yl) imidazolidin-4-one	C29H25N7O2	503.21	200-202	0.4	golden	63
5	2-(4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl)-2-methyl-3-(pyridin-2-yl) imidazolidin-4-one	C28H23N7O2	489.19	230-232	0.6	brouwn	84
6	(Z)-2-(4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl)-2-methyl-3-(pyridin-2-yl) thiazolidin-4-one	C28H22N6O2S	506.58	260-262	0.43	yellow	82
7	3-(4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl)-3-methyl-4-(pyridin-2-yl)-3,4,5a,9a-tetrahydrobenzo[e] [1,3] oxazepine-1,5-dione	C34H26N6O4	582.62	222-224	0.33	white	75
8	(E)-2-(4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl) phenyl)-2-methyl-3-(pyridin-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione	C30H22N6O4	530.17	232-234	0.36	Beige	87

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