Article

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Synthesis , Identification some of new heterocyclic Compounds Derivatives and study of the biological Activity

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Abstract:

This research includes prepeared of some new heterocyclic compounds from 2-hydroxy napthaldehyde with 2-amino thiazol , 2-amino thiazol reacted with 2-hydroxy napthaldehyde , to produce shiff base derivative (R),(R) using to synthesis of some new heterocyclic derivatives by reactions and reactant with types solvent and materials to synthesis heterocyclic membered ring , first step : Involved synthesis of seven heterocyclic compounds by reacting (R) with phthalic ,succinic and malic anhydride to prepeared oxazepine compounds (R_1,R_2,R_3) . Second step involves preparing of five-heterocyclic derivatives by reacting (R) with amino acid glycine and thyrocine in tetra hydro furan to prepare (R_4,R_5).Third step includes preparing of heterocyclic compounds β-lactam(R_6). All the compounds were characterized by FT-IR ,H^1NMR,^{13}CNMR .Also compounds were studied the measurement antibacterial activity.

Introduction :

Schiff bases are known as organic compounds that contain azo methene group (CH=N)[(1)], were prepared an from the condensation that occurred between an amine and Primary with an active carbonyl group, whether aldehydes or ketones (aliphatic or aromatic)[(2)], the azo methene group is an effective and very important group Such as antioxidants and anti-inflammatory[(3)], four membered ring are heterocyclic tetracyclic compounds that contain a heteroatom of the nitrogen atom, where the β-lactam contains a lactam group, which is a seminal ring in which the nitrogen atom is linked to the carbon atom with the beta position

relative to the carbonyl group[4].Five membered ring It is one of the types of heterocyclic compounds that contain one, two, or more heteroatoms. It is classified according to the type and number of heteroatoms present in the ring. The pentagonal ring may include a heterogeneous monoatomic such as furan, thiophene, and pyrrole[5].seven membered ring Oxazepine is an unsaturated heterocyclic compound that contains two heteroatoms: an oxygen atom at position (1) and a nitrogen atom at position (3), in addition to five carbon atoms[6], oxazepine and its derivatives have some important issues, and commercial companies such as "Amoxapine" are a group of medications called tricyclic antidepressants and their effects are significant on the central nervous system [7]. It also has other things against different types of bacteria, some of which are... These derivatives act as inhibitors of the activity of some enzymes[8,9] . The effect of organic chemical compounds on the microorganisms that cause many common diseases has become noticeable, which has led to the interest of many researchers to study the inhibitory effectiveness of arriving at antibiotics that work to inhibit disease-causing bacteria[10].

Keyword:Schiff beses ,oxazepine derivatives ,Imidazolidine derivatives ,oxazepine ,biological activity.

MATERIALS AND METHODS

The chemicals compounds have high purity as supplied by sigma and GCC company,Melting point of the compounds recorded by electro thermal 9300,melting point engineering LTD,All measurments synthesis compounds were recorded by :FTIR spectra ,fourier transform infrared shimadzu(8400),H^1NMR and C^1NMR –spectra in (ppm) in DMSO solvent by Bruker –AVANCE AQS-300MH_Z ,Iran, Thin layer chromatography used silica gel in (Benzene :methanol) solvent.

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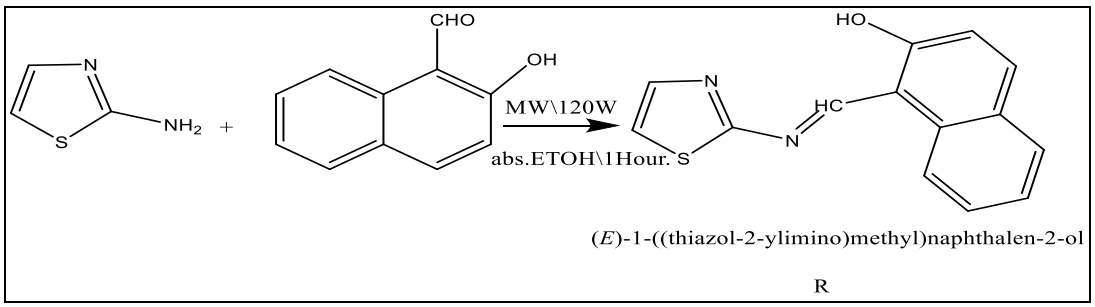
Experimental

Synthesis of Schiff base derivative [11] of compound (R)

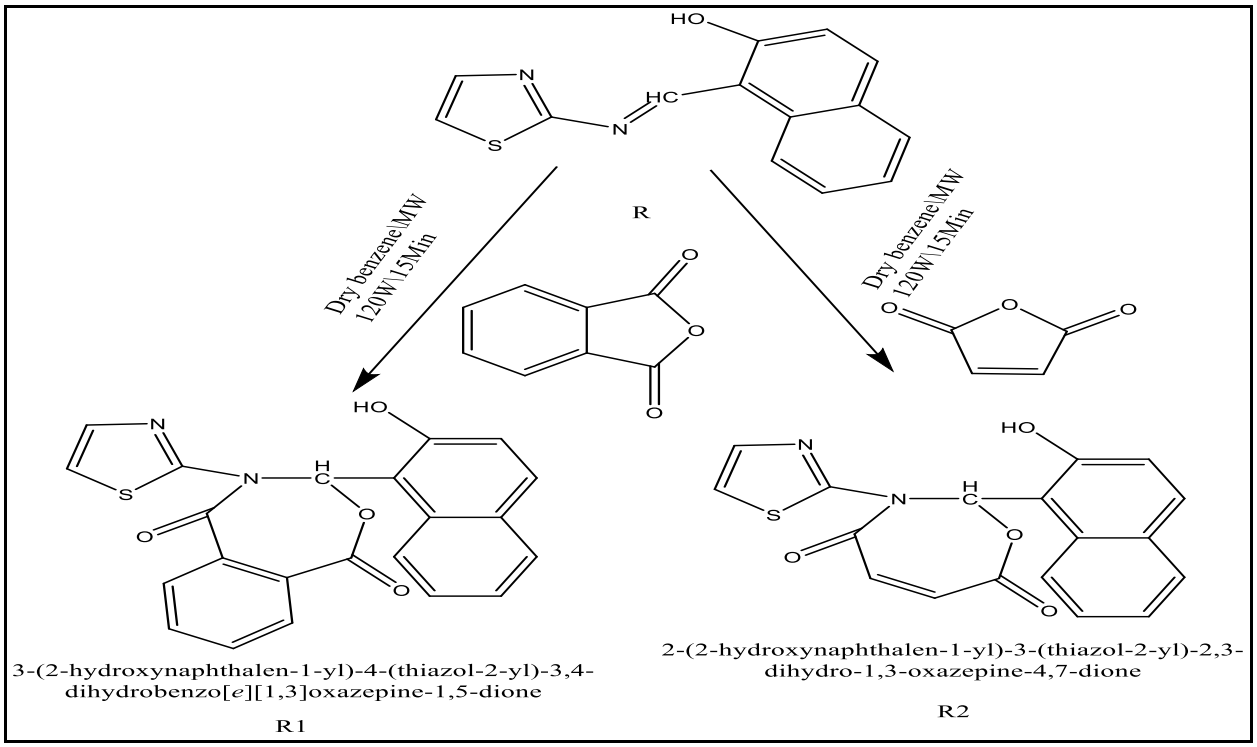
The 2-hydroxy napthaldehyde substance (0.344 g, 0.002 mol) was crushed well, then layered in a 25 ml ceramic jar, then absolute ethanol was added to it as a solvent, then with the amine colors 2-amino thiazole (0.2g, 0.002 mol), after it was crushed well and mixed. Sufficiently suitable mixture on a homogeneous paste, then irradiate it by placing the ceramic lid in the microwave oven and applying it (1hr.) at (120 w).. The resulting mixture was dried and recrystallized using absolute ethanol.



Scheme (1): synthesis of compound (R)

Synthesis of the oxazepine derivatives [12] (R_1 ,R_2).

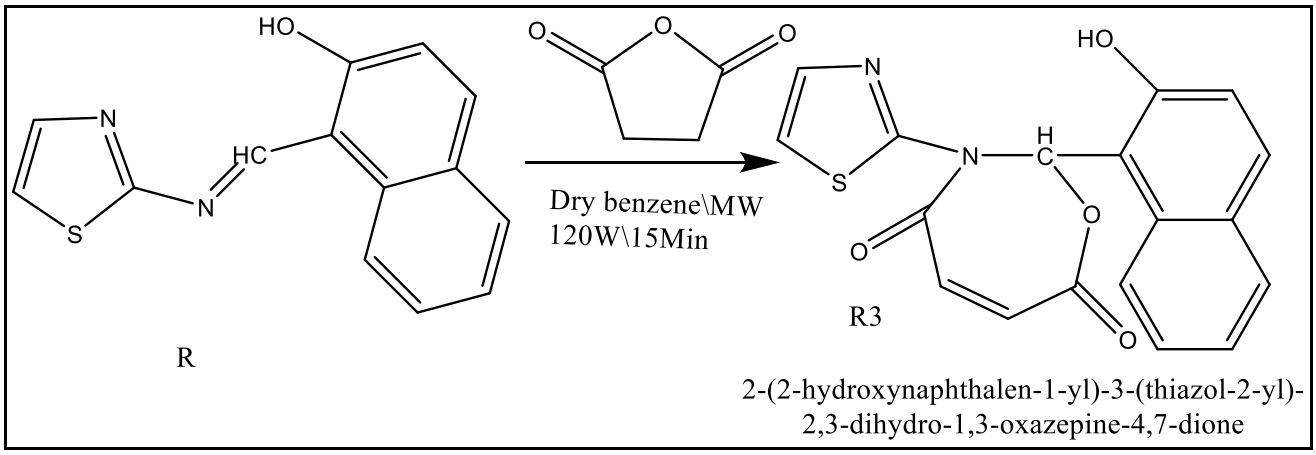
The compound was prepared by linking the previously prepared Schiff base preparation (0.0008mol.) mol) with pthalicand maleic anhydride (0.0008 mol respectly and crushing the material well with a mortar to the end of the layer in a ceramic shell, where it was exposed to microwave radiation at (120 watts) with intermittent periods. For a period (15 minutes) and after the end of the ramification, the laboratory temperature was cooled. The material was consumed with gasoline, and the reaction process was followed using the TLC technique, using the mobile phase (ethanol: dry gasoline) with a ratio of (2;4), and recrystallization was done using absolute ethanol.



Scheme (2): synthesis of compound (R1,R2)

Synthesis of the oxazepane derivative[13] (R_3).

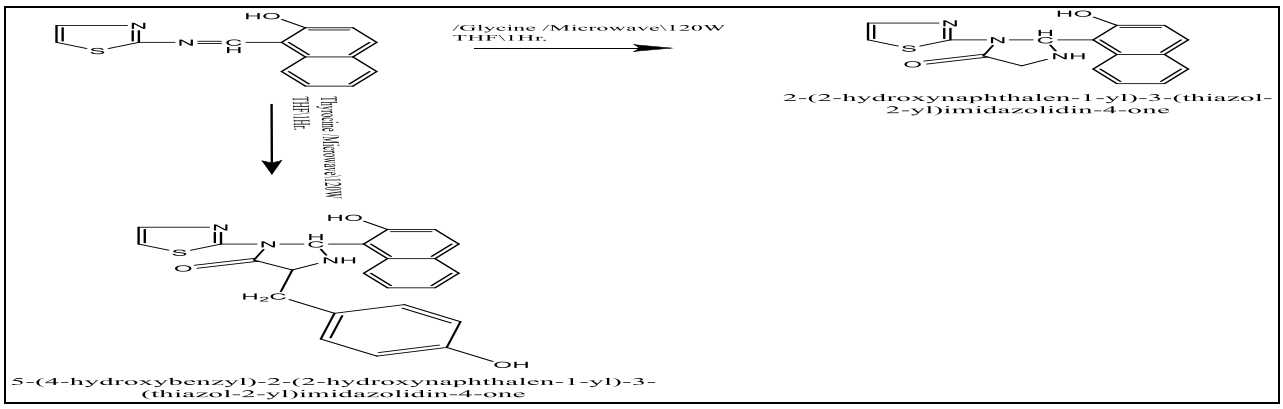
The compound (R_3) was prepared by linking the previously prepared Schiff base preparation (0.0008mol.) mol) succinic anhydride (0.0008 mol) and crushing the material well with a mortar to the end of the layer in a ceramic shell, where it was exposed to microwave radiation at (120 watts) with intermittent periods. For a period (15 minutes) and after the end of the ramification, the laboratory temperature was cooled. The material was consumed with gasoline, and the reaction process was followed using the TLC technique, using the mobile phase (ethanol: benzene) with a ratio of (2;4), and recrystallization was done using absolute ethanol.



Scheme (5): synthesis of compound (R3)

Synthesis of the Imidazolidine derivatives[14] (R_4,R_5)

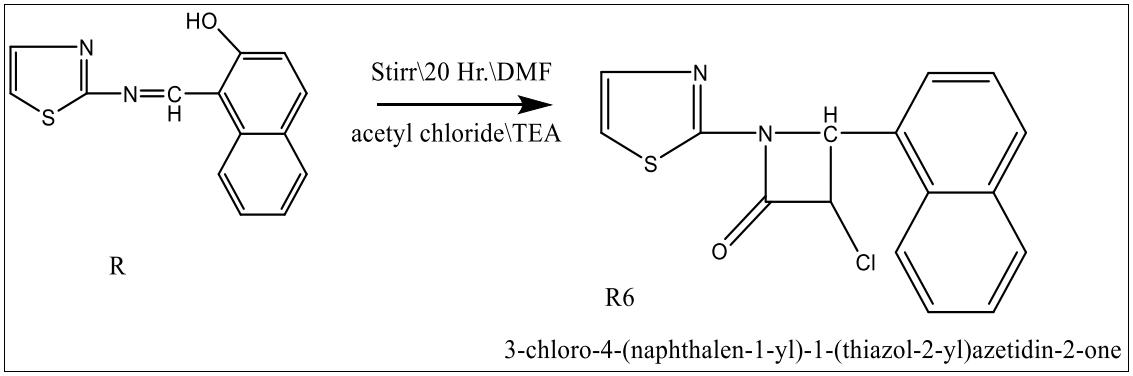
The compounds (R4,R5)) were prepared by the reaction between (R) (0.02mol,0.014gm) with amino acid (glycine and thyrocine) (0.02 mol) respectively in THF as solvent and the mixture was heated in lid in the microwave oven and applying it (1hr.) at (120 w).. The resulting mixture was dried and recrystallize using absolute ethanol.



Scheme (4): synthesis of compounds (R_4,R_5)

Synthesis of β-lactam derivative[15] (R_6)

B- lactam derivatives(R_6) was prepared by reaction between the compound(S) (0.02 mol) and tri ethyl amine(0.02 mol) and acetyl chloride (0.02) in 1,4-dioxane ,The mixture was stirred at1(15-20)C^0 for 17 hrs, to produce the compound R_6 , The products ,which crystallized from absolute ethanol.



Scheme (5): synthesis of compound (R6)

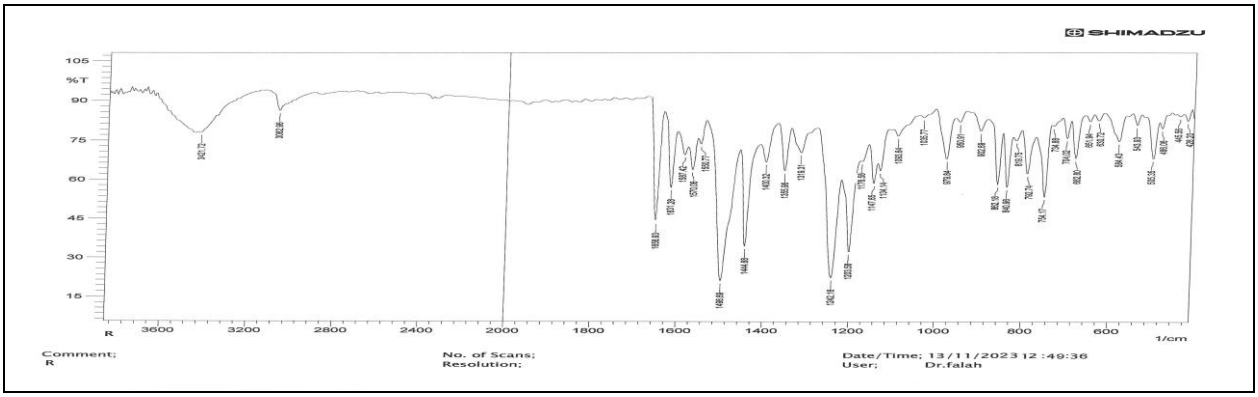


Fig. (1): FTIR Spectrum of the compound (R)

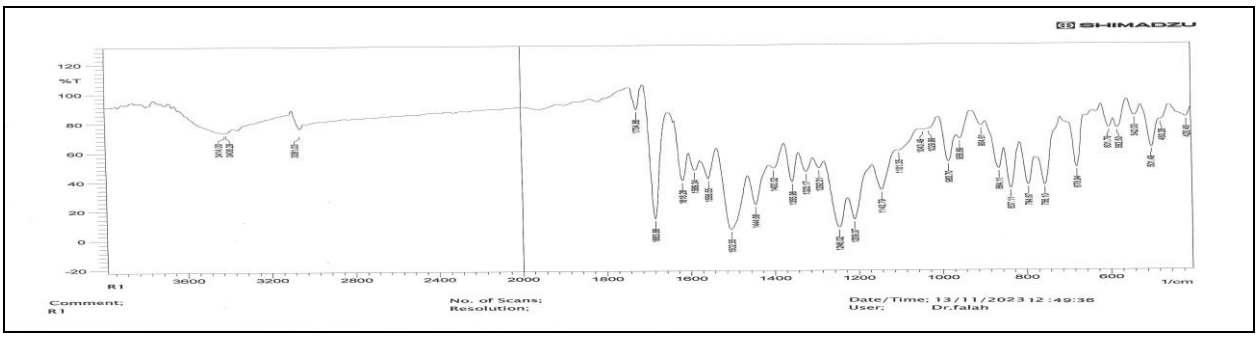


Fig. (2): FTIR Spectrum of the compound (R_1)

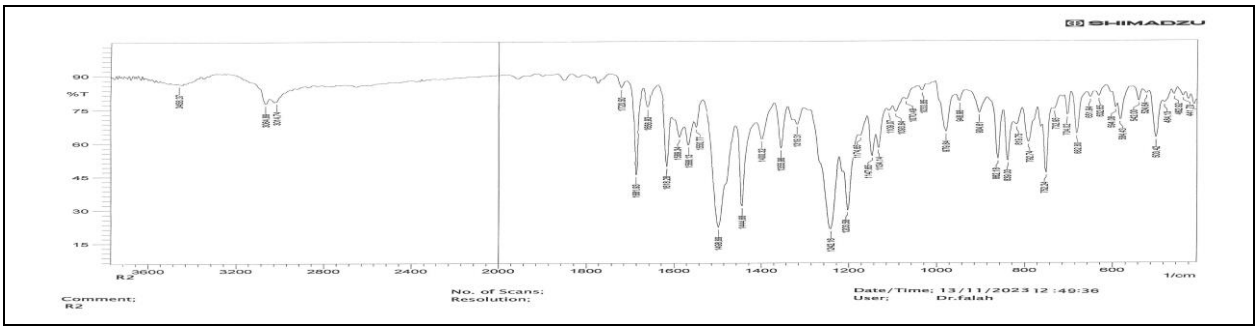


Fig.(3): FTIR Spectrum of the compound (R_2)

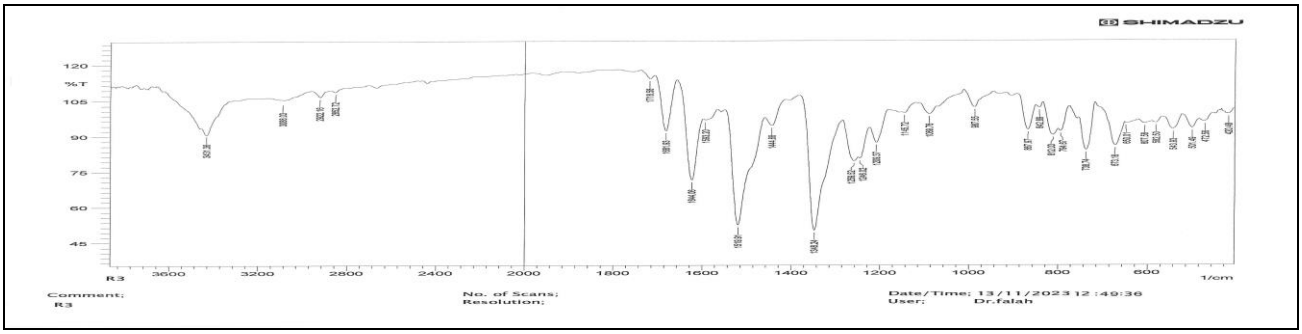


Fig. (4): FTIR Spectrum of the compound (R_3)

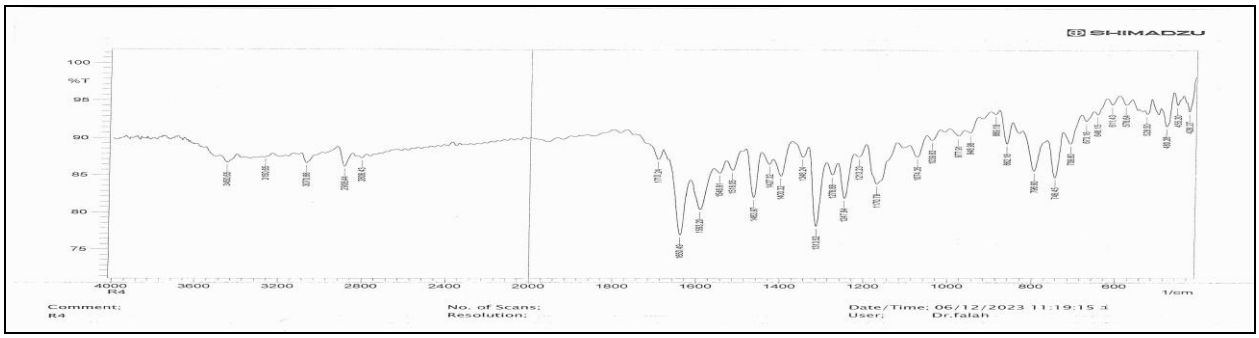


Fig. (5): FTIR Spectrum of the compound (R_4)

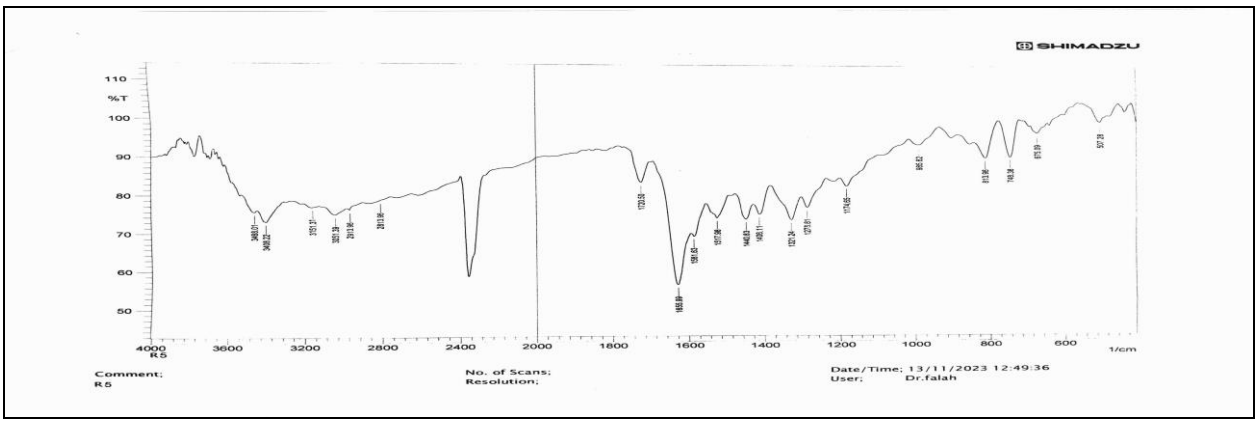


Fig. (6): FTIR Spectrum of the compound (R_5)

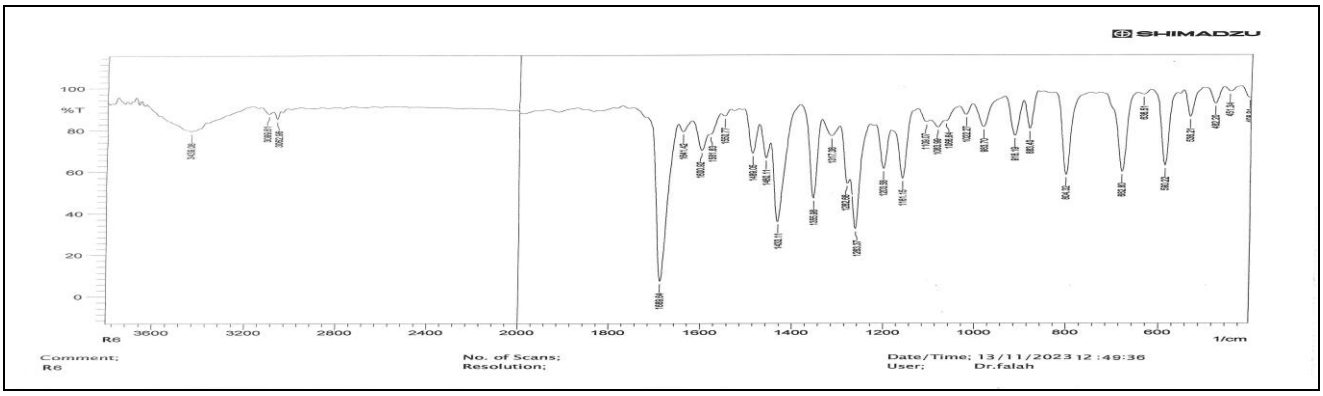


Fig.(7): FTIR Spectrum of the compound (R_6)

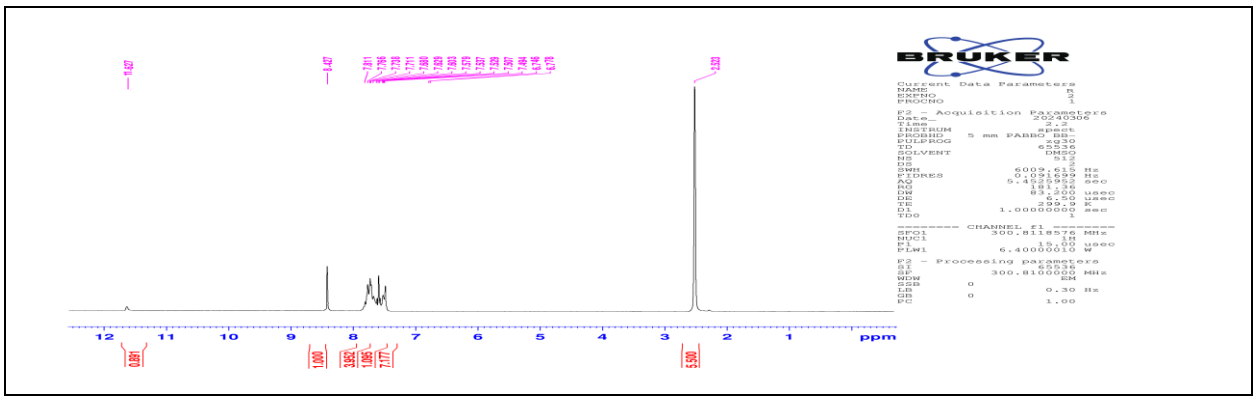


Fig.(8):[1] HNMR Spectrum of the compound (R)

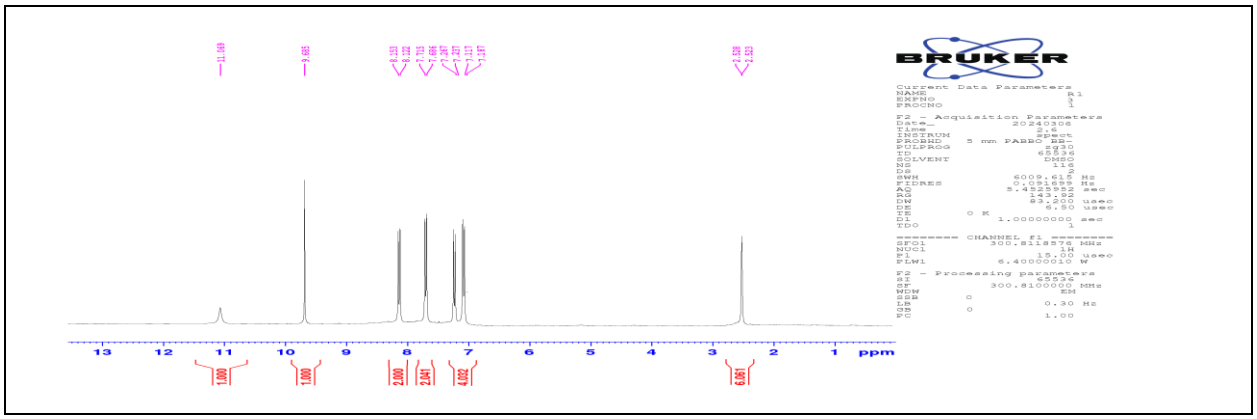


Fig.(9):[1] HNMR Spectrum of the compound (R1)

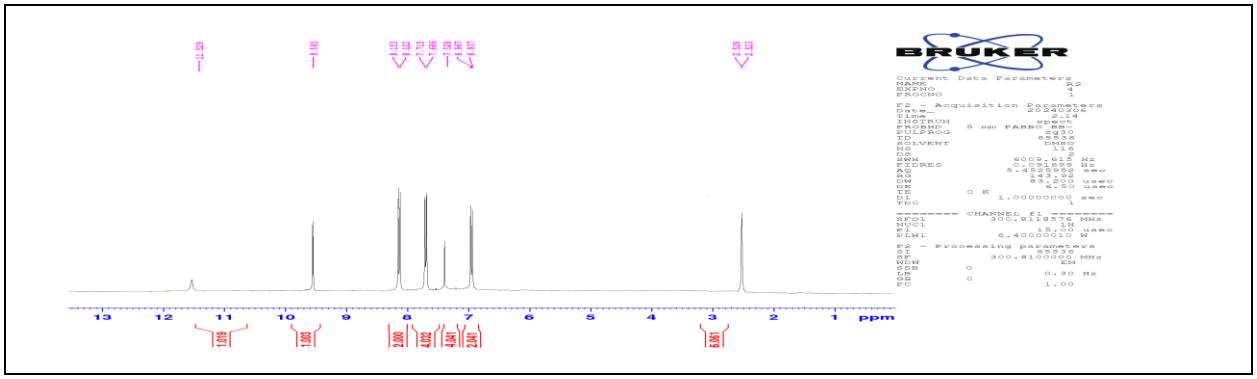


Fig.(10):[1] HNMR Spectrum of the compound (R2)

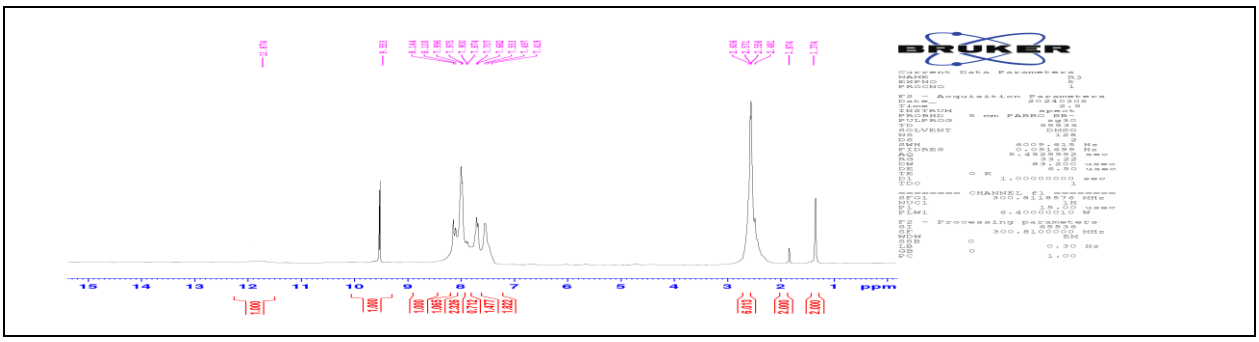


Fig.(11):[1] HNMR Spectrum of the compound (R3)

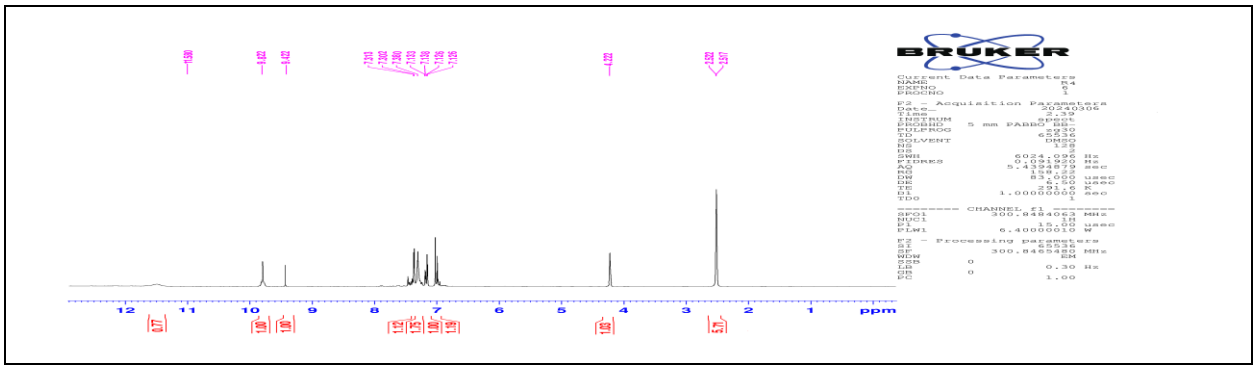


Fig.(12):[1] HNMR Spectrum of the compound (R4)

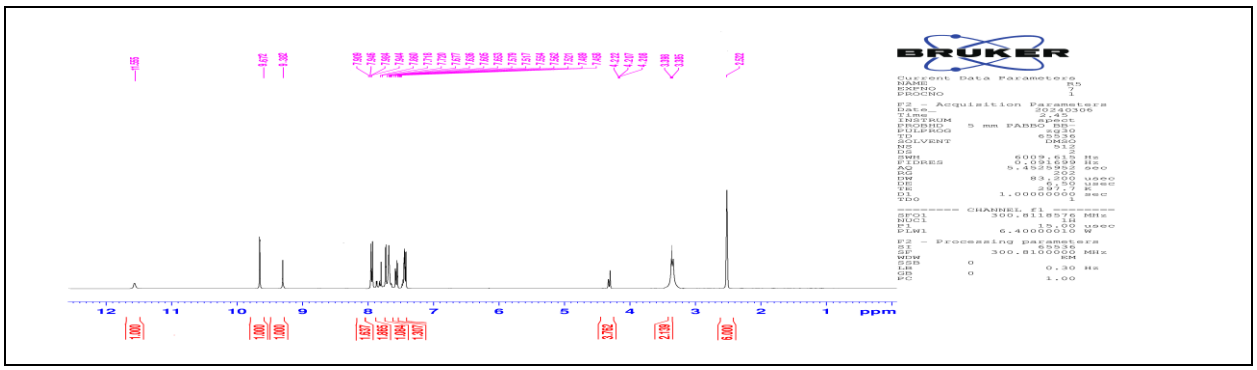


Fig.(13):[1] HNMR Spectrum of the compound (R5)

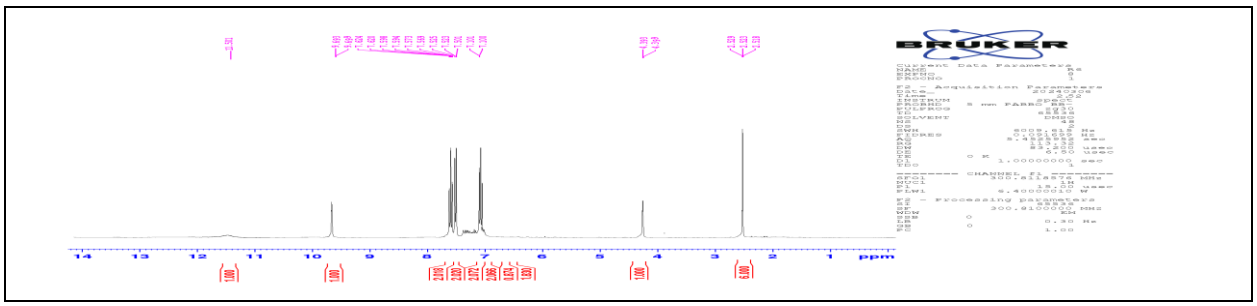


Fig.(14):[1] HNMR Spectrum of the compound (R6)

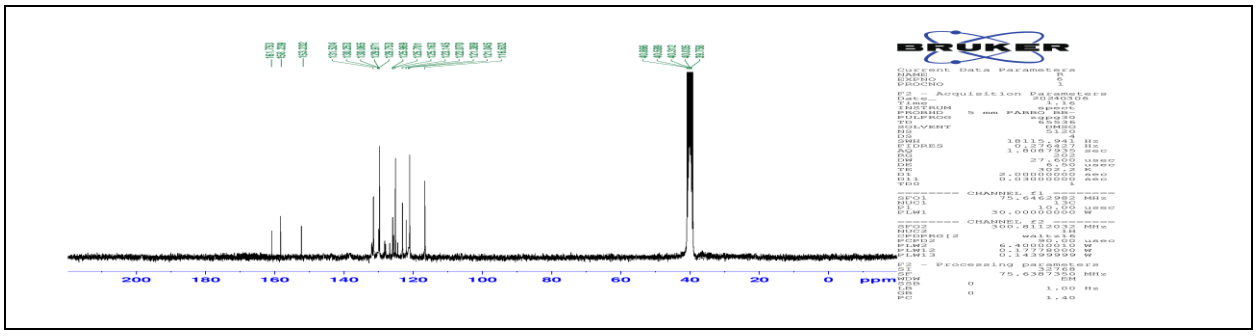


Fig.(15):[13] CNMR Spectrum of the compound (R)

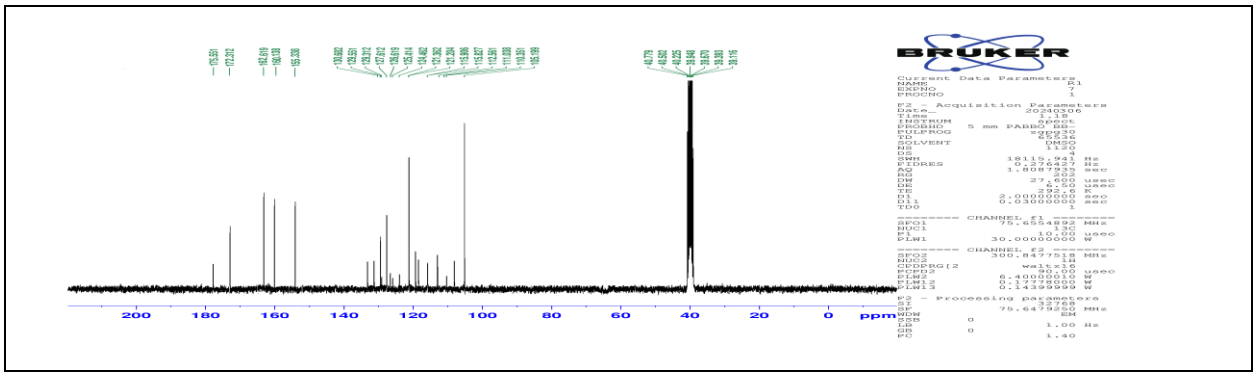


Fig.(16):[13] CNMR Spectrum of the compound (R_1)

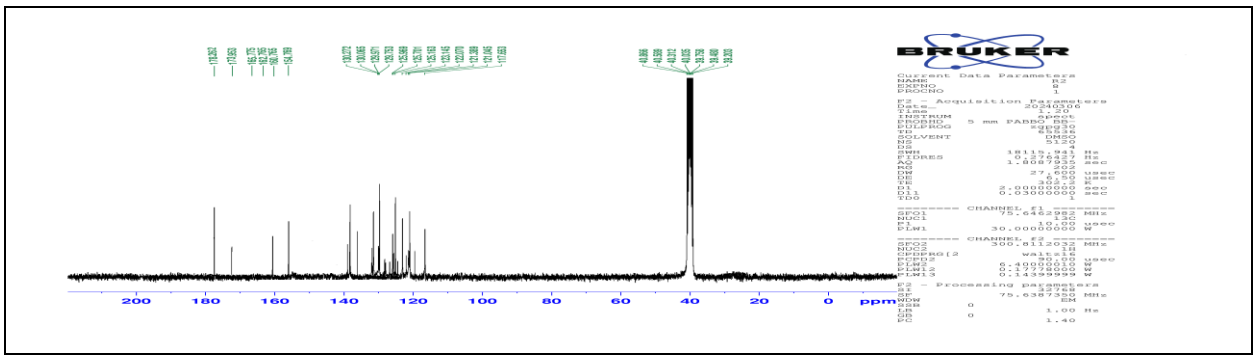


Fig.(17):^{13} CNMR Spectrum of the compound (R_2)

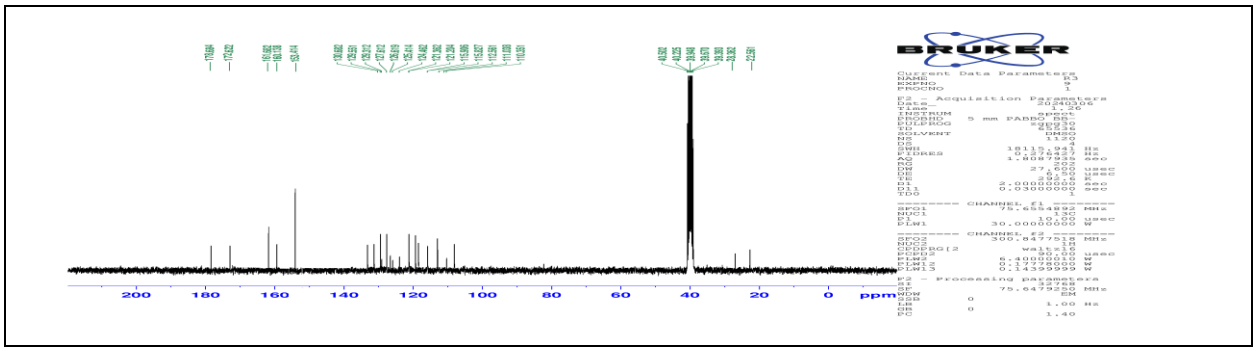


Fig.(18):^{13} CNMR Spectrum of the compound (R_3)

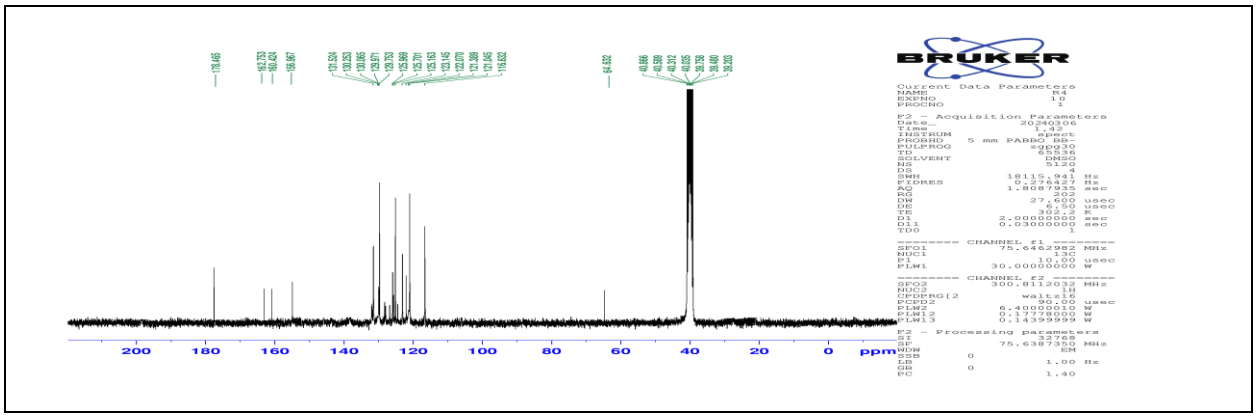


Fig.(19):^{13} CNMR Spectrum of the compound (R_4)

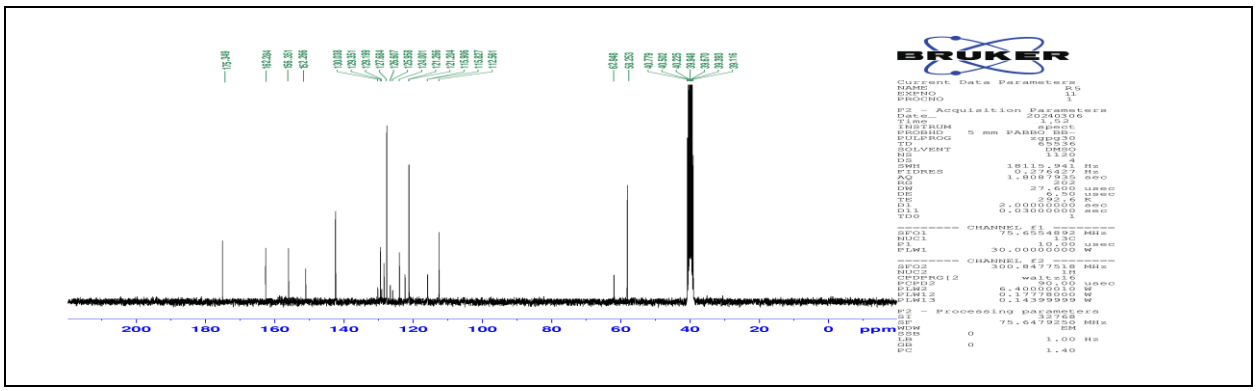


Fig.(20):[13] CNMR Spectrum of the compound (R_5)

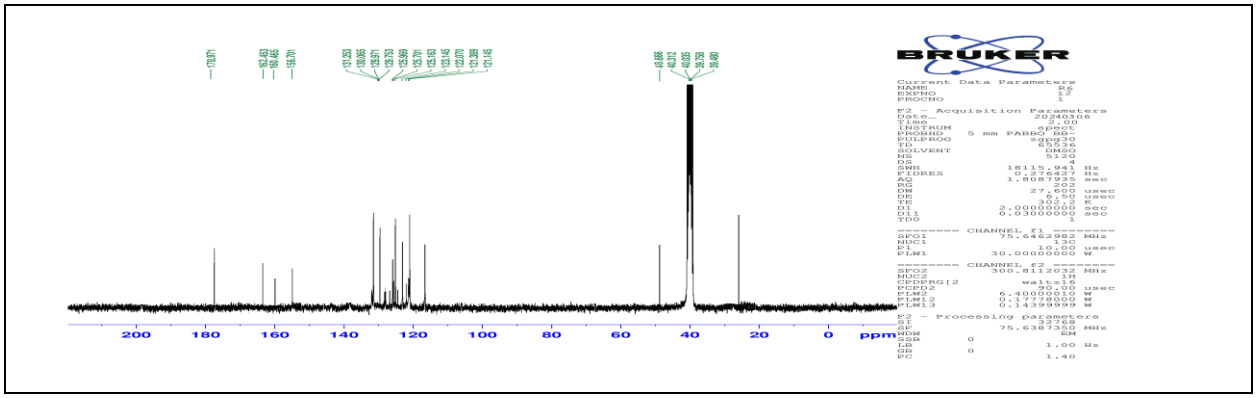


Fig.(21):[13] CNMR Spectrum of the compound (R_6)

Study of the biological activity of the compound by paper technique disks[16].

Antibacterial activity was measured by using filtering paper type (whiteman NO.1) to prepared (120) pills after purification, after that ,the pills put in the test tube average (5) pills for every tube and added (1 mml) from syntheses compounds solution .were used weight of (5mg,10 mg,20mg) from the synthesis compounds.

Result and discussion:

R: (Z)-1-((Thiazol-2-ylimino)methyl)naphthalen-2-ol , FT-IR(KBr) cm^{-1} ,ν3421(OH),ν3082($CH_{aromatic}$), ν1657(C=N),ν1570(C=C)$_{aromatic}$,^{1}H-NMR(DMSO), δ 11.5 (s,OH,1H)$_{hydroxyl\ group}$, 8.3(s ,C=N)$_{Imine\ group}$, δ7.0-7.3(m, phenyl group $_{group}$,

^{13}CNMR(DMSO), δ 158 (C of C=N)$_{\text{imine group}}$, δ 156.486 (C of C=N)$_{\text{thiazol ring}}$, δ 153.486 (C of C-OH)$_{\text{hydroxylgroup}}$105-130(C ,phenyl group) .

R1 : 3-(2-hydroxynaphthalen-1-yl)-4-(thiazole-2-yl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione, FT-IR(KBr) cm^{-1} ,ν3421(OH),ν3021(CH$_{\text{aromatic}}$), ,ν1722 (O-C=O)lacton,ν1687(N-C=O)lactam, ν1627 (C=C)$_{\text{aromatic}}$, ^{1}H-NMR(DMSO), δ 11.7 (s,OH,1H)$_{\text{hydroxyl group group}}$, δ 9.3(s ,CH-N)$_{\text{Oxazipne}}$ ring, δ7.0-7.4(m, phenyl group, ^{13}C NMR(DMSO): δ 176.3(C , C=O)$_{\text{Lactone ring}}$, δ 172.1(C , C=O)$_{\text{Lactam group}}$, δ 162 (C of CH-N)$_{\text{Oxazepine ring}}$, δ 160 (C of C=N)$_{\text{imine group}}$, δ 155 (C of C=N)$_{\text{thazolring}}$, δ 153.486 (C of C-OH)$_{\text{hydroxylgroup}}$106-111(C ,phenyl group) .

R2: 2-(2-hydroxynaphthalen-1-yl)-3-(thiazol-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione: , FT-IR(KBr) cm^{-1} ,ν3489(OH),ν3064(CH$_{\text{aromatic}}$), ,ν1714 (O-C=O)lacton,ν1680(N-C=O)lactam, , ν1635 (C=C)$_{\text{olfine}}$ ν1579 (C=C)$_{\text{aromatic}}$^{1}H-NMR(DMSO), δ 11.2 (s,OH,1H)$_{\text{hydroxyl group group}}$, δ 9.2(s ,CH-N)$_{\text{Oxazipne}}$ ring, δ7.0-7.4(m, phenyl group, δ6.76-6.78 (d,2H,CH$_2$)$_{\text{Methene group}}$, ^{13}C NMR(DMSO): δ 177(C , C=O)$_{\text{Lactone ring}}$, δ 172.1(C , C=O)$_{\text{Lactam group}}$, δ 162 (C of CH=CH)$_{\text{Methene group}}$ δ 161 (C of CH-N)$_{\text{Oxazepine ring}}$, , δ 157 (C of C=N)$_{\text{thiazol ring}}$, δ 155.486 (C of C-OH)$_{\text{hydroxylgroup}}$112-130(C ,phenyl group) .

R3: 2-(2-hydroxynaphthalen-1-yl)-3-(thiazol-2-yl)-1,3-oxazepane-4,7-dione, FT-IR(KBr) cm^{-1} ,ν3408(OH),ν3015(CH$_{\text{aromatic}}$), ν2927-2864 (CH$_{\text{aliphatic}}$) ,ν1720 (O-C=O)lacton,ν1685(N-C=O)lactam, ν1527 (C=C)$_{\text{aromatic}}$, ^{1}H-NMR(DMSO), δ 11.3 (s,OH,1H)$_{\text{hydroxyl group group}}$, δ 9.2(s ,CH-N)$_{\text{Oxazipne}}$ ring, δ7.0-7.5(m, phenyl group), δ1.9 (s,CH2COO)$_{\text{Lactonegroup}}$, δ1.3 (s,CH2CO)$_{\text{Lactam g oup}}$

R4: 2-(2-hydroxynaphthalen-1-yl)-3-(thiazol-2-yl)imidazolidin-4-one FT-IR(KBr) cm^{-1} ,ν3475(OH) ν3288(NH$_{\text{imidazolidine ring}}$),ν3015(CH$_{\text{aromatic}}$), ν1716(C=O)$_{\text{imidazolidine ring}}$, ν1624-1579 (C=C)$_{\text{aromatic}}$, ^{1}H-NMR(DMSO), δ 11.4 (s,OH,1H)$_{\text{hydroxyl group group}}$, δ 9.6(s

,NH)$_{Iidazolidine\ ring,}$ δ 9.3(s ,CH-N)$_{Iidazolidine\ ring,}$, δ7.2-7.7(m, phenyl group), δ4.7 (s,CH2) Iidazolidine ring

R5: 5-(4-hydroxybenzyl)-2-(2-hydroxynaphthalen-1-yl)-3-(thiazol-2-yl)imidazolidin-4-one FT-IR(KBr) cm^{-1} ,v3475(OH) v3288($NH_{imidazolidine\ ring}$),v3015($CH_{aromatic}$), v1716(C=O)$_{imidazolidine\ ring}$, v1624-1579 (C=C)$_{aromatic}$,: ^{1}H-NMR(DMSO), δ 11.5 (s,OH,1H)$_{hydroxyl\ group\ \ group}$, δ 9.8(s ,NH)$_{Iidazolidine\ ring,}$ δ 9.3(s ,CH-N)$_{Iidazolidine\ ring,}$, δ7.2-7.7(m, phenyl group), δ4.32-4.30(trp,1H) $_{Iidazolidine\ ring}$, δ3.3-3.3(d,2H) $_{Iidazolidine\ ring}$,

R6: 3-chloro-4-(2-hydroxynaphthalen-1-yl)-1-(pyrimidin-2-yl)azetidin-2-one, FT-IR(KBr) cmv3408(OH),v3064($CH_{aromatic}$) v1672(C=O)lactam ,1597-1548 (C=C)$_{aromatic}$, v 800-600(C-Cl), ,: ^{1}H-NMR(DMSO), δ 11.8 (s,OH,1H)$_{hydroxyl\ group\ \ group}$, δ 9.4-9.4(d ,CH-N)$_{lactam\ ring,}$, δ7.0-7.9(m, phenyl group), δ4.6-4.6(d,1H) $_{lactam\ ring}$,

Table 1:physical properties of synthesis compounds

NO	M.F	M.WT gm.\mol	M.P	R_F	Color	yield %	solvent
R	C13H9N2OS	254.09	244-247	0.78	yellow	88	ethanol
R_1	C18H12N2O4S	352.11	260-261	0.9	orange	68	1,4-dioxane
R_2	C22H14N2O4S	402.09	255-256	0.66	Yellow	85	Dry benzene
R_3	C16H13N3O2S	354.11	270-271	0.75	yellow	83	Dry benzene
R_4	C17H14N4O2	306.11	198-199	0.79	yellow	83	Dry benzene
R_5	C22H17N3O3S	412.15	177-179	0.	Yellow	88	Tetra hydro furan
R_6	C16H11ClN2OS	325.75	233-234	0.73	yellow	83	Tetra hydro furan

Table 2: Results of biological activity

Type of bacteria / Comp.NO.	inhibition zone(mm) 5mg 10mg 20mg (mg\mol)			
	klebsiella pneumonia	***Staphylococcus***	***Enterococcus faecalis***	***pseudomonas aeruginosa***
R	**-,-,8**	**-, -, 10**	**-,-,5**	**-,-,8**
R_1	**-**	**-, - ,4**	**-,-,8**	**-,-,8**
R_2	**-, -, 8**	**-, 10, 8**	**-,-,-**	**-,-,6**
R_3	**-,-,6**	**-,-,10**	**8,10,15**	**-, -, 10**
R_4	**-**	**-,-,20**	**-,8,10**	**-,-,7**
R_5	**-**	**-**	**-,8,10**	**12,18,20**
R_6	**-,-,5**	**-,-,10**	**-,-,5**	**-,-,10**

Reference

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