JBAAR

Journal of Bioscience and Applied Research

https://jbaar.journals.ekb.eg

SPBH

Study of Some Types of Bacteria and application of biological activity for some new Heterocyclic Compounds containing nitrogen Derivatives

Eman Abdul Wahab. A. ALKuwaity[1], Rajaa Abdulameer Ghafil[2]

[1]Department of Biochemistry, Jabir ibn Hayyan University, for medical and pharmaceutical sciences, Iraq

[2] Department of Chemistry, Faculty of Education for Girls, University of Kufa, Iraq.

DOI: 10.21608/jbaar.2025.360107.1153

Abstract:

This broadside includes a preparation of certain bioheterocyclic multifaceted derivatives starting: 6-bromo-2-hydroxy napthaldehyde, by the reaction between 2-amino-5-bromo pyrimidine with 6-bromo-2-hydroxy napthaldehyde, to produce a Schiff base derivative (S). The latter compound was used as an important substance to prepare six new heterocyclic derivatives that have a pyrimidine ring. Also, newly synthesized compounds were characterized by spectral data (FTIR, ^{1}H NMR, ^{13}C NMR), and all the prepared derivatives were studied on four types of bacteria ***(Staphylococcus aureus and Escherichia coli, Enterococcus faecalis, Pseudomonas aeruginosa)***, by paper technique disks. Biological capacity tests for these derivatives revealed favorable findings.

Keywords: Bacteria, microwave irradiation, Schiff bases, oxazepine, Imidazolidine derivatives.

Introduction:

Pyrimidine is widely found in nature as a component of nucleic acids (cytosine, thymine, and uracil) and many other natural and synthetic compounds, including pharmaceuticals, and has become known over time as a powerful pharmacophore **(1)**. Also, Pyrimidine can be considered a cyclic amine **(2)**. Pyrimidine is also known as 1,3-diazine. It is the fundamental substance of a large group of heterocyclic compounds and plays a vital role in many biological processes **(3)**. Schiff bases are an important group of organic medicinal chemical compounds. They contain an azomethine group (-CH=N-) **(4)** and are prepared from the condensation that occurs between a Primary aromatic or aliphatic amine with an active carbonyl group, either aldehydes or ketones (aliphatic or aromatic) **(5)**. They have been used to treat cancers, including skin cancer and brain cancer **(6,7)**. They are also considered antifungal, antibacterial, antiviral, and immune modulatory (8) and are able to bind to DNA(9) Imidazolidine is generally a five-ring non-exocyclic ring (10), Imidazolidine, also known as tetra hydrimidazole, is a bioactive nitrogen containing a non-imported cyclic moiety which provides a wide range of important biological effects such as antioxidants ,antibacterial, antiphrastic, oral anti diabetic activities (11-14), Oxazepine is one of the carbon atoms that contains two oxygen atoms at position (1) and a nitrogen atom located at position (3), in addition to five carbon atoms (15), 1,3-Oxazepine pathways were prepared by closing reactions that result in the condensation of the sheaf residues with different anhydrides such as maleic anhydride and phaleic anhydride(16), Oxazepine derivatives have gained great importance and have been used in a number of fields due to their diverse biological activity, including antibacterial (17), anticancer (18), and antifungal (19), so most of their applications have been in the biological and pharmaceutical fields (20,21). Beta-lactams (2-azetidinones) are saturated heterocyclic compounds

Received: February 12, 2025. Accepted: July 25, 2025. Published: September 18, 2025

with a four-membered ring that includes three carbon atoms, a nitrogen atom, and a carbonyl group. The name "β-lactam" is given to the cyclic amides because the nitrogen atom is connected to the β carbon atom relative to the carbonyl group (22). β-Lactams, as a structural unit found in the most commonly used antibiotics, have held a fundamental position in medicinal chemistry for about a century. With bacterial resistance to conventional antibiotics through β-lactamases, the need for modern antibiotics is emerging, making the synthesis of newer β-lactams more necessary. In addition to their use as antibiotics, β-lactams are increasingly used as basic compounds for other biologically important molecules (23-25). It has been found that beta-lactams act as inhibitors of acylcholesterol transferase, thrombin inhibitors, inhibitors of human cytomegalovirus protease, matrix metalloprotease inhibitors, cysteine protease inhibitors, and apoptosis inducers. Biological activity is usually linked to the nature of the groups connected to N-1, C-3, and C-4 of the beta-lactam molecules (26). 2-azetidinone derivatives that contain a beta-lactam core have a wide range of pharmacological activity and have become an essential part of the chemical therapeutic arsenal available to medical practitioners today (27).

EXPERIMENTAL

Experimental Apparatus All the chemicals used were of the highest grade and were obtained from Fluka and Merck. For melting point measurements, an Electro-Thermal 9300 apparatus from Melting Point Engineering Ltd, UK, was used. Thin-layer chromatography (TLC) was performed on silica gel, and spots were visualized using iodine vapor. FTIR spectra were obtained using a Shimadzu 8400 Fourier transform infrared spectrophotometer with potassium bromide (KBr) discs, and measurements are reported in cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra, expressed in ppm, were obtained in DMSO-d_6 as a solvent using an Agilent Varian 300 MHz and 75 MHz spectrometer at the University of Tehran, Iran. Microwave irradiation was used at 120 W and 280 W.

Combination of Schiff base derivative of compound (S)[28]

The 6-bromo- 2-hydroxy-1- naphthaldehyde substance (0.344 g, 0.002 mole) 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-5-bromo pyrimidine (0.188 g, 0.002 mole), 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 (1 hr.) at (120 w). Following (TLC) at a ratio of (2:4) and then cooling. The resulting mixture was recrystallized and dried using absolute ethanol

Combination of oxazepine derivatives (S_1, S_2)[28].

The compound was prepared by linking the previously prepared Schiff base preparation (0.0008 mol.) with phthalic and maleic anhydride (0.0008 mole 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 of 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

Combination of the oxazepane derivative (S_3).

The compound (S_3) was prepared by linking the previously prepared Schiff base preparation (0.0008 mol.), succinic anhydride (0.0008 mole), 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 of 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

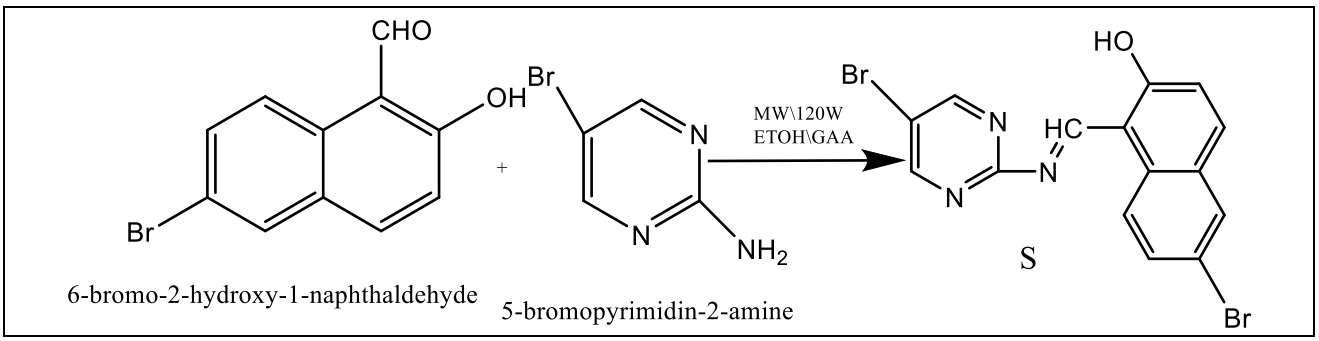
(ethanol: benzene) with a ratio of (2; 4), and recrystallization was done using absolute ethanol.

Combination of the Imidazolidine derivatives (S_3).

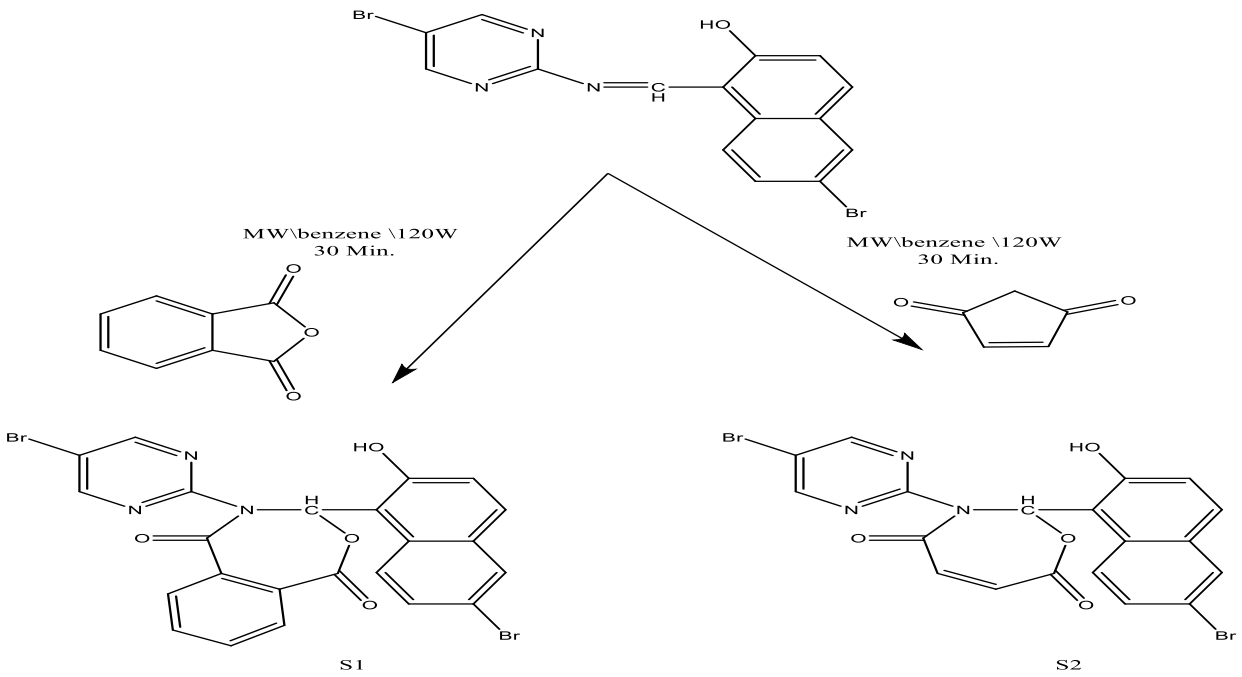
This compound (0.02 mol, 0.014 g) was mixed with glycine and tyrosine (0.02 mol) separately in tetrahydrofuran as a solvent, and the mixture was heated under a cap in a microwave oven and using it (1 hour) at 120 watts. This was followed by (TLC) at a ratio of (2:4), then cooling. The resulting mixture was then dried and crystallized using absolute ethanol.

Combination of β-lactam derivative (S_6)

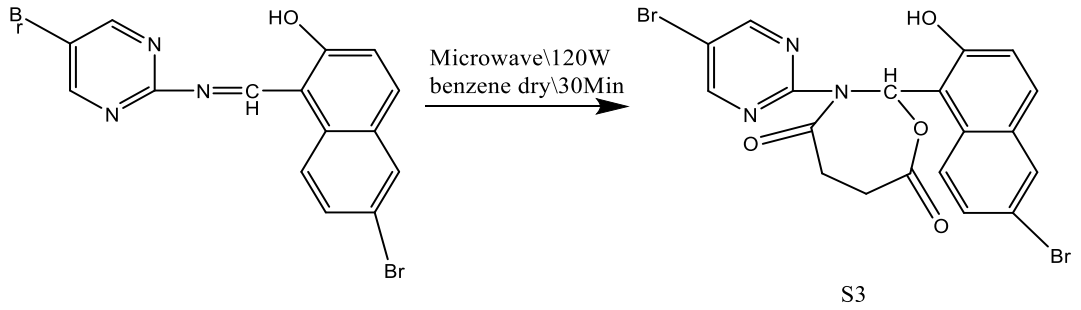
Beta-lactam derivatives (S7) were prepared by reacting compound (S) (0.02 mol) with triethylamine (0.02 mol) and acetyl chloride (0.02 mol) in 1,4-dioxane. The mixture was stirred at 1(15-20) °C for 17 hours to create chemical R6. The products were crystallized from absolute ethanol



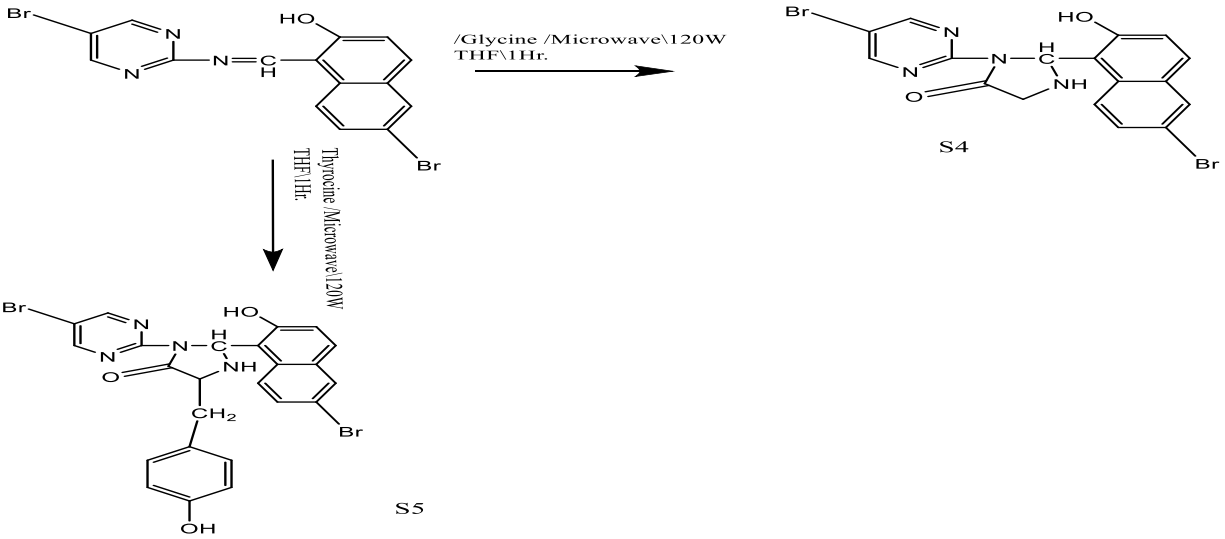
Scheme (1): Combination of compounds (S)



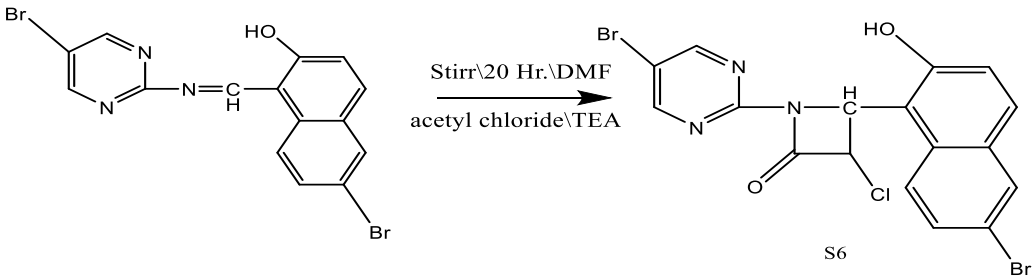
Scheme (2): Combination of compounds (S1, S2)



Scheme (3): Combination of compounds (S3)



Scheme (4): Combination of compounds (S_4, S_5)



Scheme (5): Combination of compounds (S6)

Study of the biological activity of the compound by paper technique disks (19)

The antibacterial activity on four types of bacteria ***(Staphylococcus aureus and Escherichia coli, Enterococcus faecalis, Pseudomonas aeruginosa)*** was measured using a filter paper type (Whiteman NO. 1) to prepare 200 tablets after purification. Subsequently, the tablets were placed in test tubes with an average of (5) tablets per tube, and (1 ml) of the synthetic compound solution was added. Weights of (5 mg, 10 mg, 20 mg) of the synthetic compounds were used. The standard used was ciprofloxacin 10. Forceps were sterilized using a flame.

Results and Discussion:

S: (Z)-1-(5-bromo pyrimidin-2-ylimino)methyl)naphthalen-2-ol, I.R : ,ν3421(OH),ν3082($CH_{aromatic}$), ν1657(C=N),ν1570(C=C)$_{aromatic}$, (DMSO), δ 11.5 (s, hydroxyl,1H)$_{hydroxyl\ group}$, 8.3(s, C=N)$_{Imine\ group}$, δ7.0-7.3(m, Benzene group $_{group}$, (DMSO), δ 160.486 (C of C=N)$_{pyrimidine\ ring}$, δ 158 (C of C=N)$_{imine\ group}$, δ 156.486 (C of C=N)$_{pyrimidine\ ring}$, δ 153.486 (C of C-OH)$_{hydroxylgroup}$105-130(C, Benzene group).

S1 : 3-(6-bromo2-hydroxynaphthalen-1-yl)-4-(5-bromo pyrimidin-2-yl)-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione, FT-IR(KBr) cm^{-1},ν3421(OH),ν3021($CH_{aromatic}$), ,ν1722 (O-C=O)lacton,ν1687(N-C=O)lactam, ν1627 (C=C)$_{aromatic}$, ^{1}H-NMR(DMSO), δ 11.7 (s, OH,1H)$_{hydroxyl\ group\ group}$, δ 9.3(s, CH-N)$_{Oxazipne}$ ring, δ7.0-7.4(m, Benzene group, ^{13}C NMR(DMSO): δ 176.3(C, C=O)$_{Lactone\ ring}$, δ 172.1(C, C=O)$_{Lactam\ group}$, δ 162 (C of CH-N)$_{Oxazepine\ ring}$, δ 160 (C of C=N)$_{imine\ group}$, δ 155 (C of C=N)$_{pyrimidine\ ring}$, δ 153.486 (C of C-OH)$_{hydroxylgroup}$106-111(C, Benzene group).

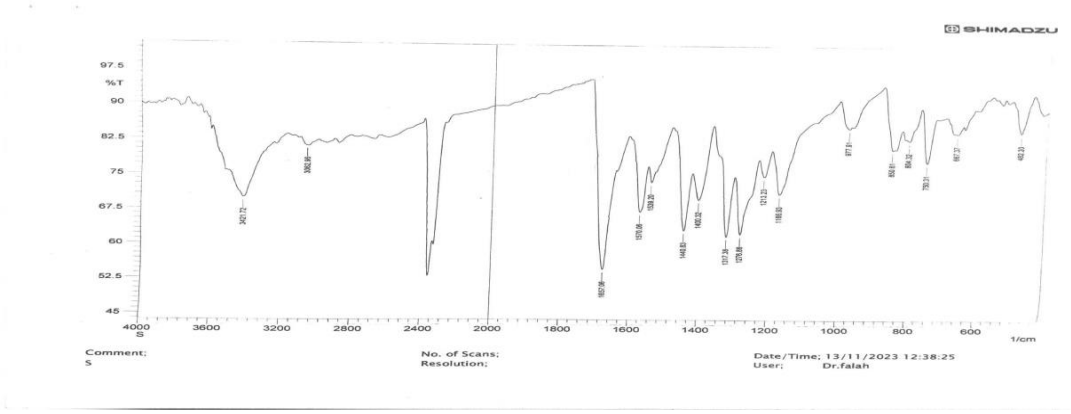
S2: 2-(6-bromo 2-hydroxynaphthalen-1-yl)-3-(5-bromo pyrimidin-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione:
, I.R (KBr) cm^{-1},ν3489(OH),ν3064($CH_{aromatic}$), ,ν1714 (O-C=O)lacton,ν1680(N-C=O)lactam, , ν1635 (C=C)$_{olfine}$ ν1579 (C=C)$_{aromatic}$ (DMSO), δ 11.2 (s, OH,1H)$_{hydroxyl\ group\ group}$, δ 9.2(s, CH-N)$_{Oxazipne}$ ring, δ7.0-7.4(m, Benzene group, δ6.76-6.78 (d,2H, CH_2)$_{Methene\ group}$, (DMSO): δ 177(C, C=O)$_{Lactone\ ring}$, δ 172.1(C, C=O)$_{Lactam\ group}$, δ 162 (C of CH=CH)$_{Methene\ group}$ δ 161 (C of CH-N)$_{Oxazepine\ ring}$, δ 160 (C of C=N)$_{pyrimidine\ ring}$, δ 157 (C of C=N)$_{pyrimidine\ ring}$, δ 155.486 (C of C-OH)$_{hydroxylgroup}$112-130(C, Benzene group).

S3: 2-(6-bromo2-hydroxynaphthalen-1-yl)-3-(5-bromo pyrimidin-2-yl)-1,3-oxazepane-4,7-dione, I.R (KBr) cm^{-1},ν3408(OH),ν3015($CH_{aromatic}$), ν2927-2864 ($CH_{aliphatic}$),ν1720 (O-C=O)lacton,ν1685(N-C=O)lactam, ν1527 (C=C)$_{aromatic}$, (DMSO), δ 11.3 (s, OH,1H)$_{hydroxyl\ group\ group}$, δ 9.2(s , CH-N)$_{Oxazipne}$ ring, δ7.0-7.5(m, Benzene group), δ1.9 (s, CH2COO)$_{Lactone\ group}$, δ1.3 (s, CH2CO)$_{Lactam\ g\ oup}$, (DMSO): δ 175(C, C=O)$_{Lactone\ ring}$, δ 173.1(C, C=O)$_{Lactam\ group}$, 161 (C of CH-N)$_{Oxazepine\ ring}$, δ 161 (C of C=N)$_{pyrimidine\ ring}$, δ 156 (C of C=N)$_{pyrimidine\ ring}$, δ 152. (C of C-OH) $_{hydroxyl\ group}$121-131(C, Benzene group).

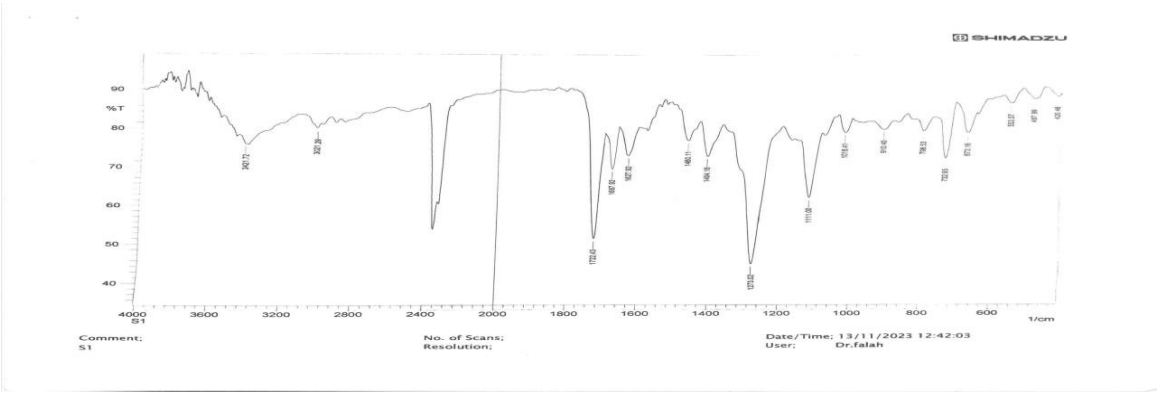
S4: 2-(6-bromo2-hydroxynaphthalen-1-yl)-3-(5-bromopyrimidin-2-yl)imidazolidin-4-one FT-IR(KBr) cm^{-1},ν3475(OH) ν3288($NH_{imidazolidine\ ring}$),ν3015($CH_{aromatic}$), ν1716(C=O)$_{imidazolidine\ ring}$, ν1624-1579 (C=C)$_{aromatic}$, (DMSO), δ 11.4 (s, OH,1H)$_{hydroxyl\ group\ group}$, δ 9.6(s, NH)$_{Iidazolidine\ ring}$, δ 9.3(s, CH-N)$_{Iidazolidine\ ring}$, , δ7.2-7.7(m, Benzene group), δ4.7 (s, CH2) $_{Iidazolidine\ ring}$, (DMSO): δ 175(C, C=O)$_{Imidazolidine\ ring}$, δ, 161 (C of CH-N)$_{Imidazolidine\ ring}$, δ 160 (C of C=N)$_{pyrimidine\ ring}$, δ 157 (C of C=N)$_{pyrimidine\ ring}$, δ 153. (C of C-OH)$_{hydroxyl\ group}$105-130(C, Benzene group), δ, 63 (C of CH2) $_{Imidazolidine\ ring}$.

S5: 5-(6-bromo4-hydroxybenzyl)-2-(2-hydroxynaphthalen-1-yl)-3-(5-bromo pyrimidin-2-yl)imidazolidin-4-one FT-IR(KBr) cm^{-1},ν3475(OH) ν3288($NH_{imidazolidine\ ring}$),ν3015($CH_{aromatic}$), ν1716($C=O)_{imidazolidine\ ring}$, ν1624-1579 $(C=C)_{aromatic}$,: ^{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, Benzene group), δ4.32-4.30(trp,1H) $_{Iidazolidine\ ring}$, δ3.3-3.3(d,2H) $_{Iidazolidine\ ring}$, ^{13}C NMR(DMSO): δ 172(C, C=O)$_{Imidazolidine\ ring}$, δ, 162.145 (C of CH-N)$_{Imidazolidine\ ring}$, δ 159 (C of C=N)$_{pyrimidine\ ring}$, δ 155 (C of C-OH $_{hydroxylgroup}$), δ 151. (C of C-OH)$_{hydroxylgroup}$105-130(C, Benzene group), δ 62 (C of CH)$_{Imidazolidine\ ring}$ δ 58 (C of CH2)$_{thyrocine\ ring}$.,

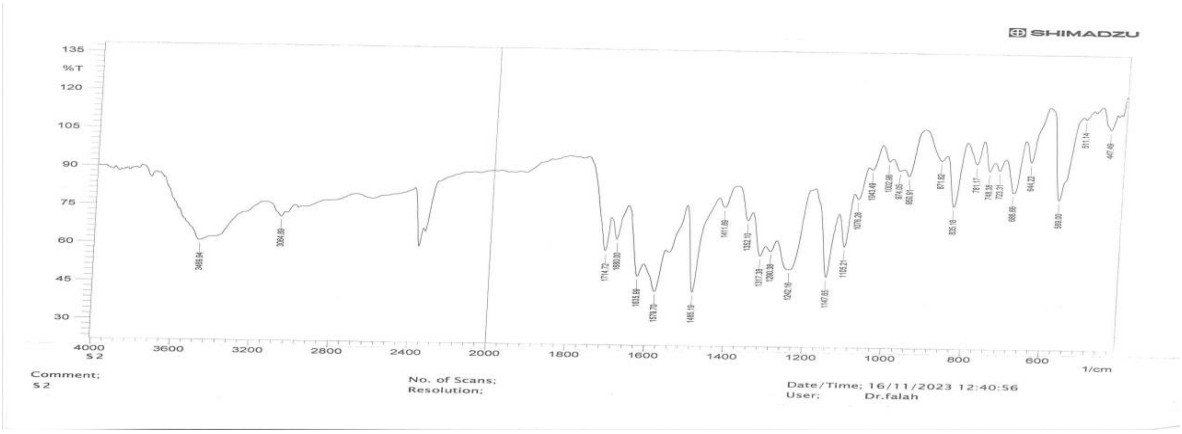
S6: 3-chloro-4-(6-bromo 2-hydroxynaphthalen-1-yl)-1-(5-bromo pyrimidin-2-yl)azetidin-2-one, FT-IR(KBr) cmν3408(OH),ν3064($CH_{aromatic}$) ν1672(C=O)lactam,1597-1548 $(C=C)_{aromatic}$, ν 800-600(C-Cl), ,: ^{1}H-NMR(DMSO), δ 11.8 (s, OH,1H)$_{hydroxyl\ group\ \ group}$, δ 9.4-9.4(d, CH-N)$_{lactam\ ring}$, , δ7.0-7.9(m, Benzene group), δ4.6-4.6(d,1H) $_{lactam\ ring}$, ^{13}C NMR(DMSO): δ 174(C, C=O)$_{lactam\ ring}$, δ, 163 (C of CH-N)$_{lactam\ ring}$, δ 159 (C of C=N)$_{pyrimidine\ ring}$, δ 157 (C of C=N)$_{pyrimidine\ ring}$, δ 153 (C of C-OH)$_{hydroxylgroup}$105-130(C, Benzene group), δ 47 (C of C-Cl)$_{lactam\ ring}$



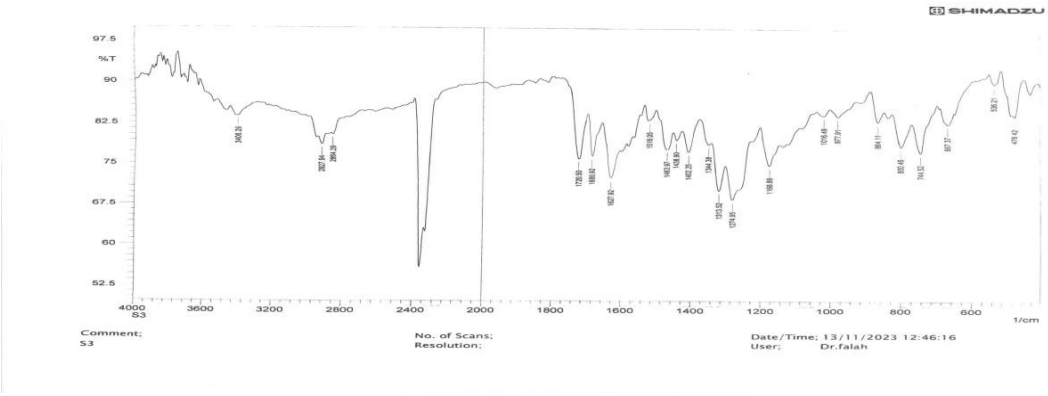
Sym. (1): IR - (S)



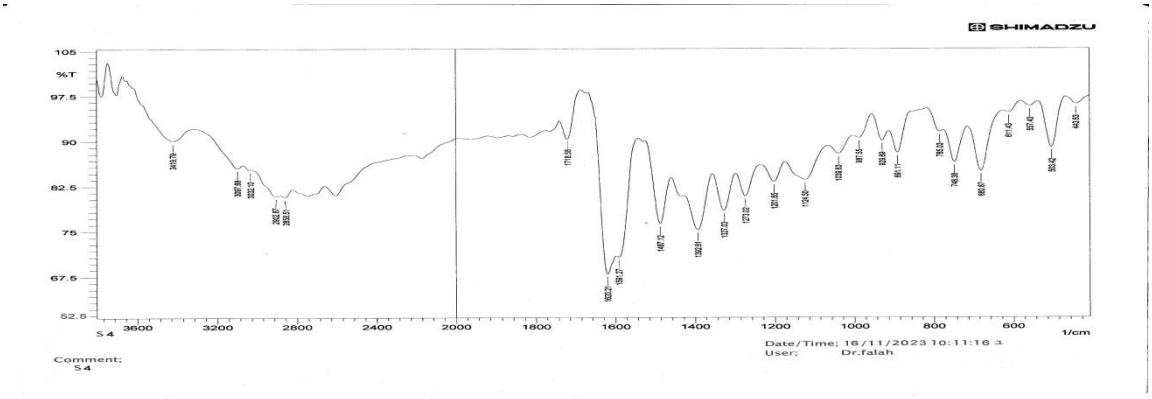
Sym. (2): IR - (S_1)



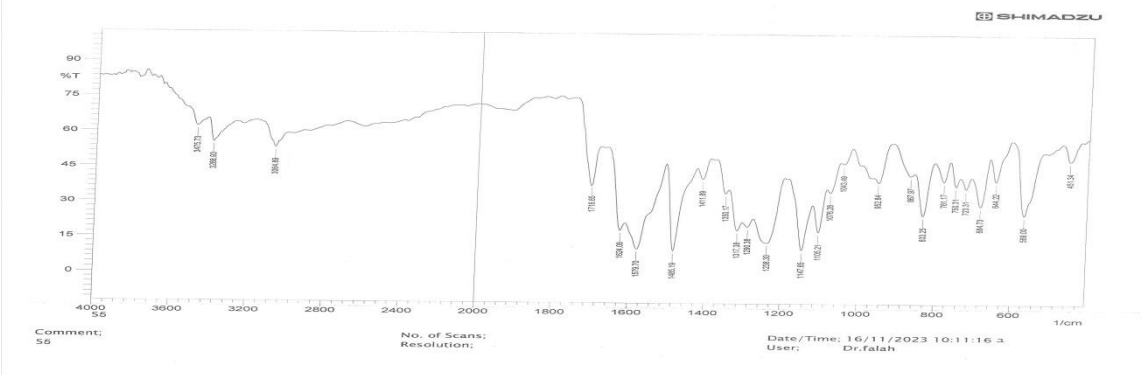
Sym. (3): IR -(S_2)



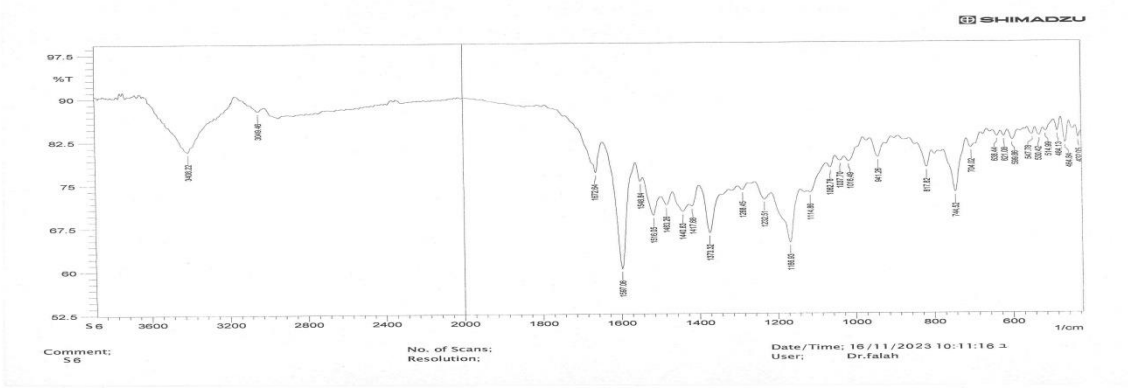
Sym. (4): IR - (S_3)



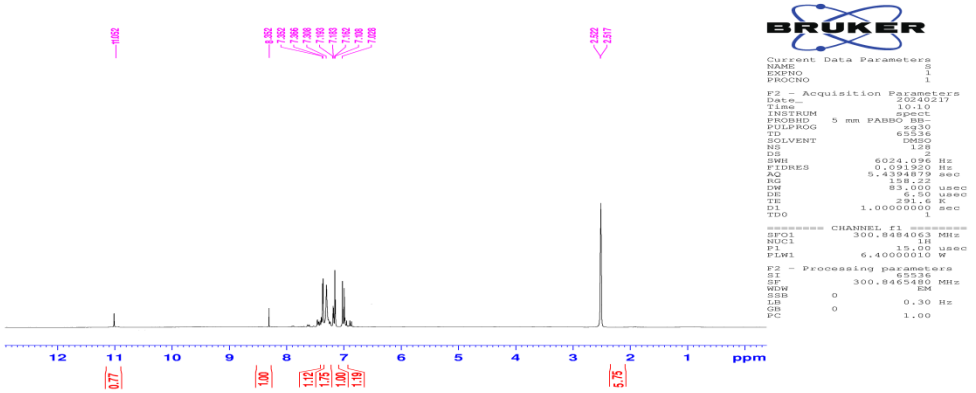
Sym. (5): IR -(S_4)



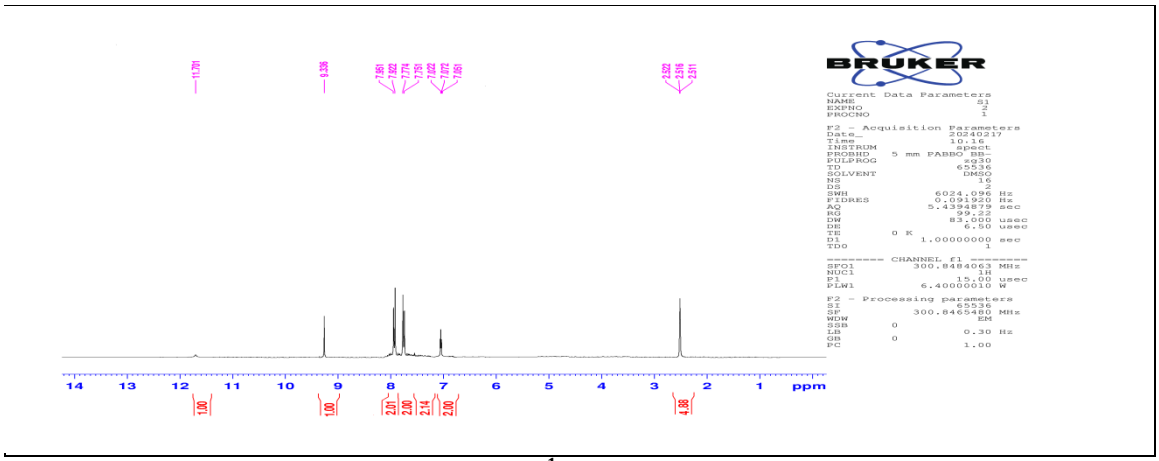
Sym. (6): IR -(S_5)



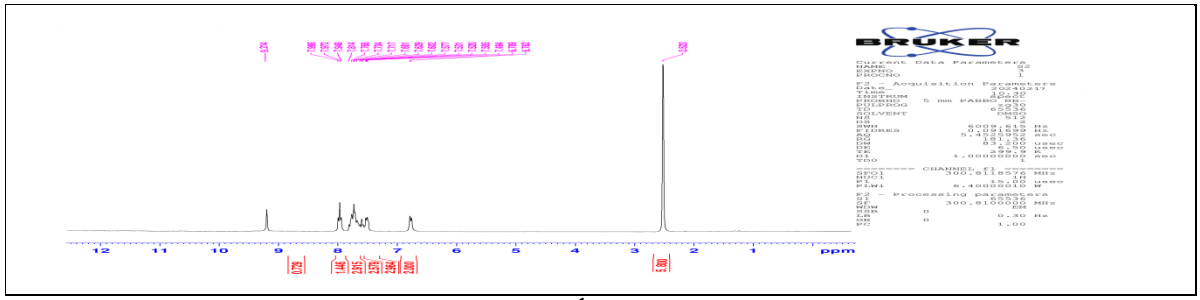
Sym. (7): IR -(S_6)



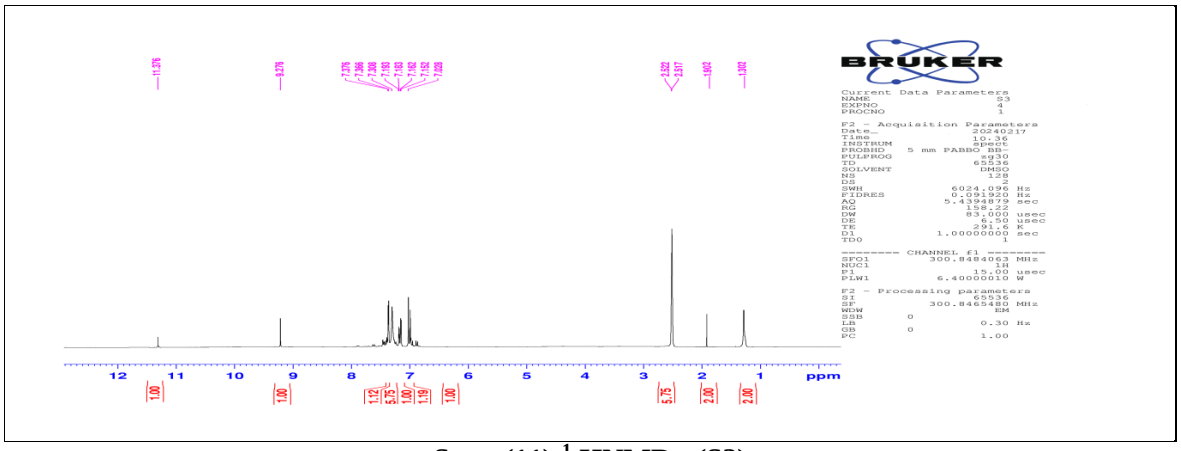
Sym. (8):[1] HNMR -(S)



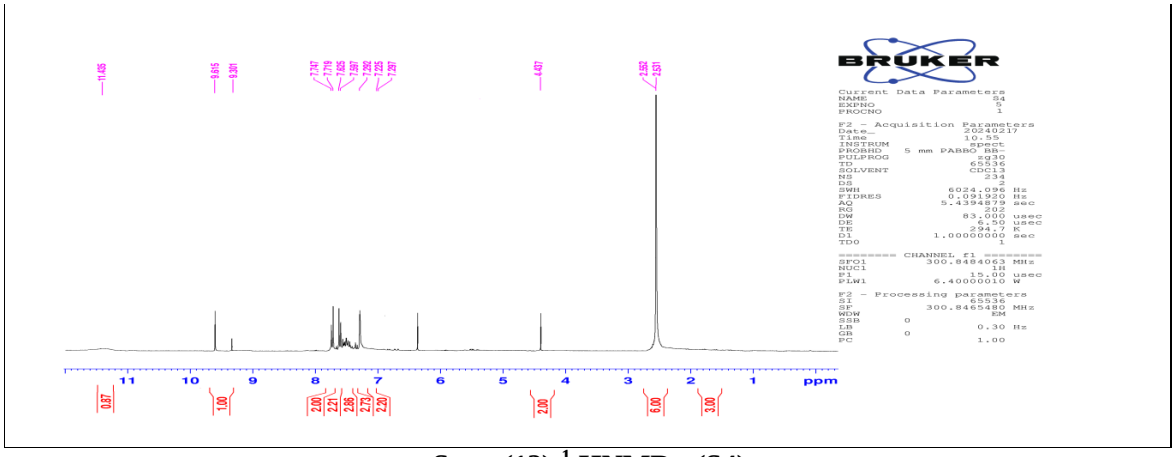
Sym. (9):[1] HNMR -(S1)



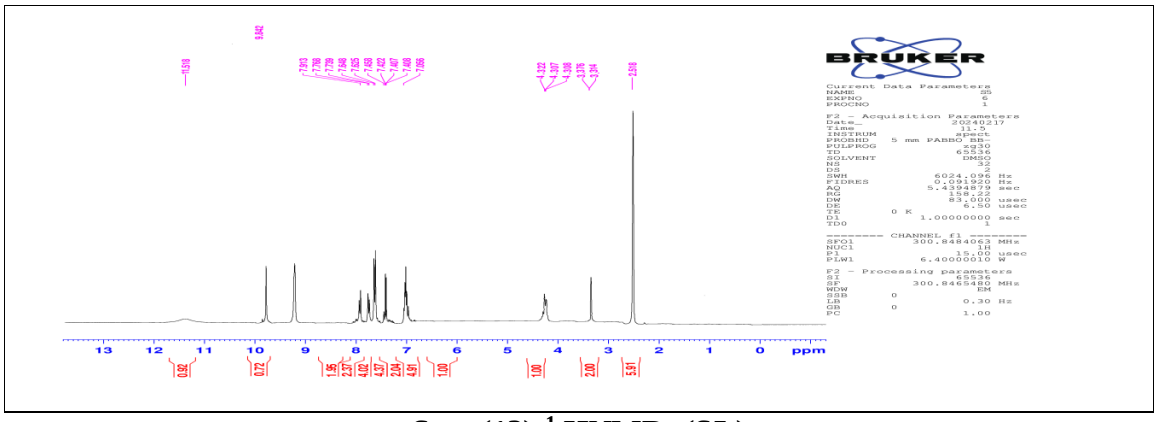
Sym. (10):[1] HNMR -(S2)



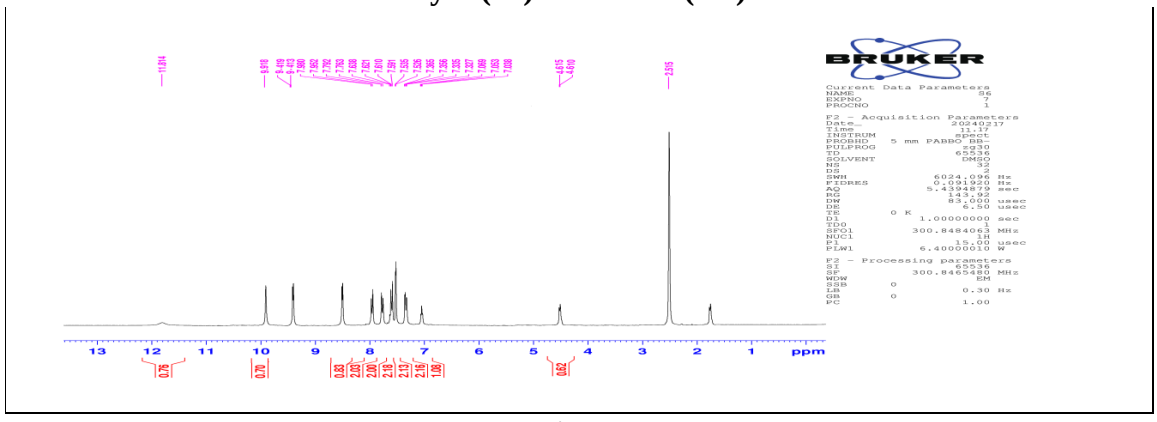
Sym. (11):[1] HNMR - (S3)



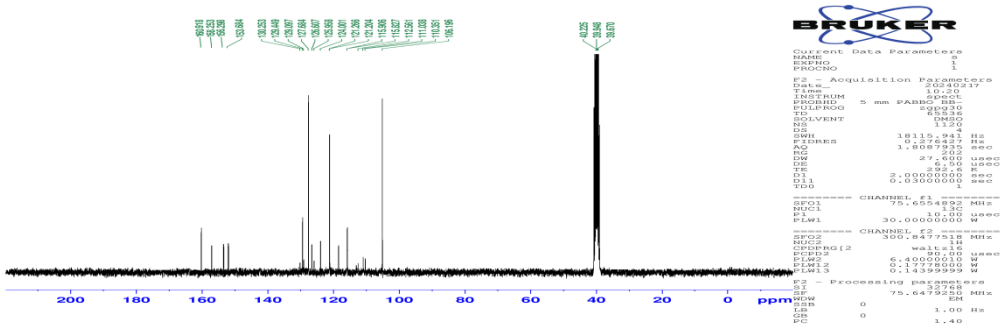
Sym. (12):[1] HNMR - (S4)



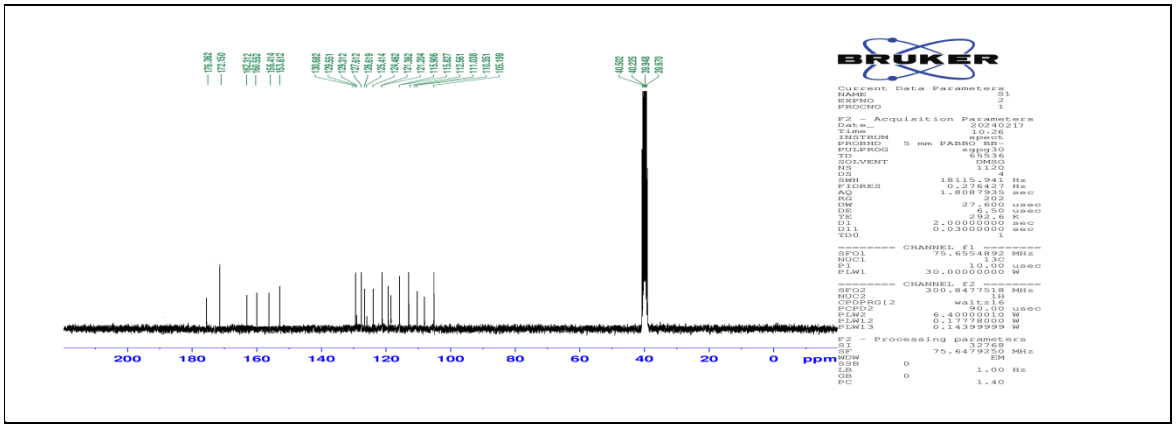
Sym.(13):[1] HNMR -(S5)



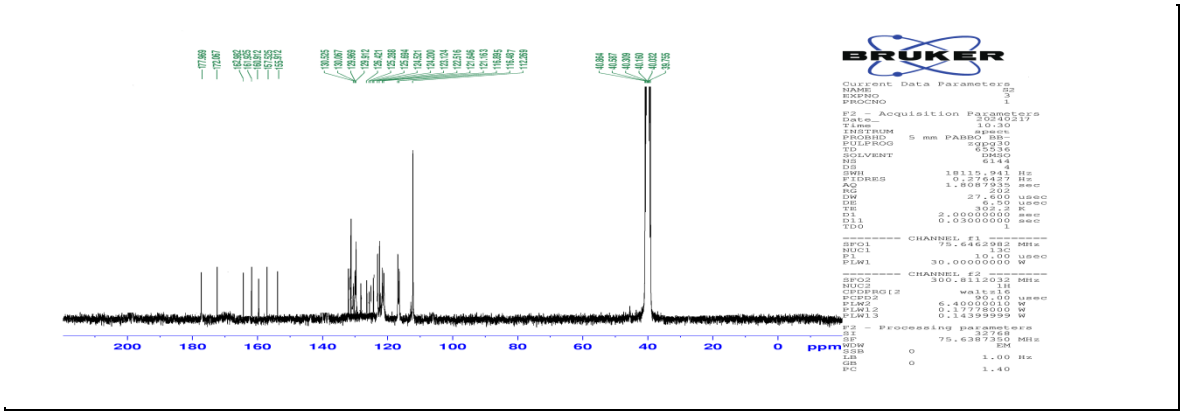
Sym. (14):[1] HNMR -(S6)



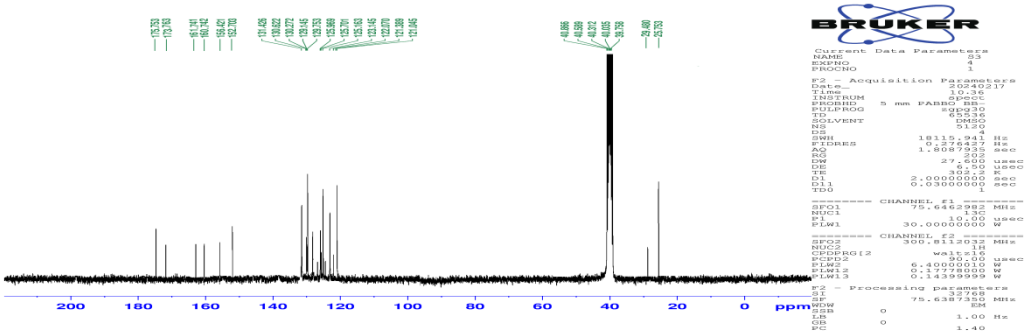
Sym. (15):^{13} CNMR - (S)



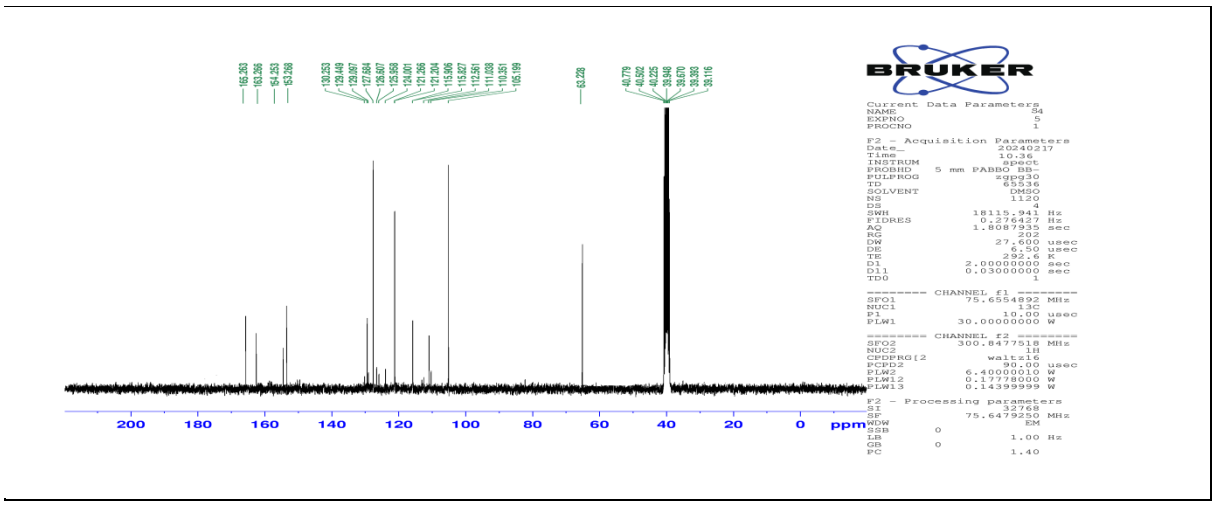
Sym. (16):^{13} CNMR -(S_1)



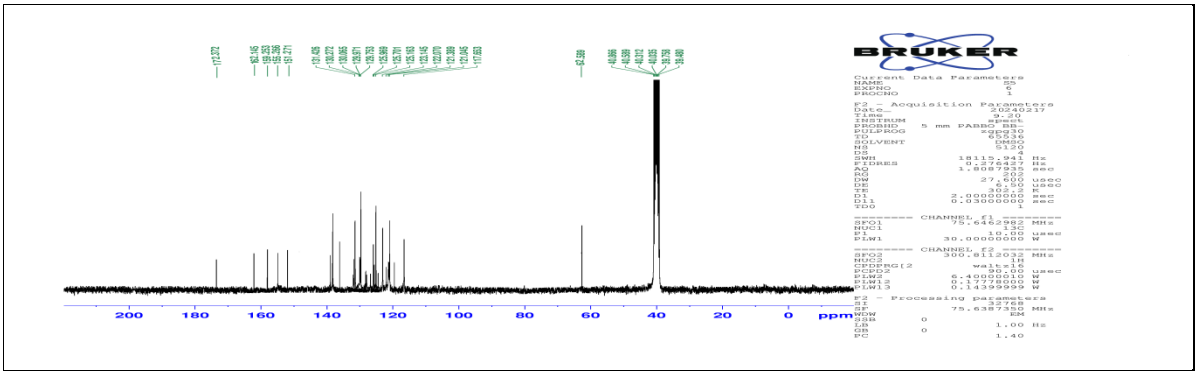
Sym. (17):^{13} CNMR -(S_2)



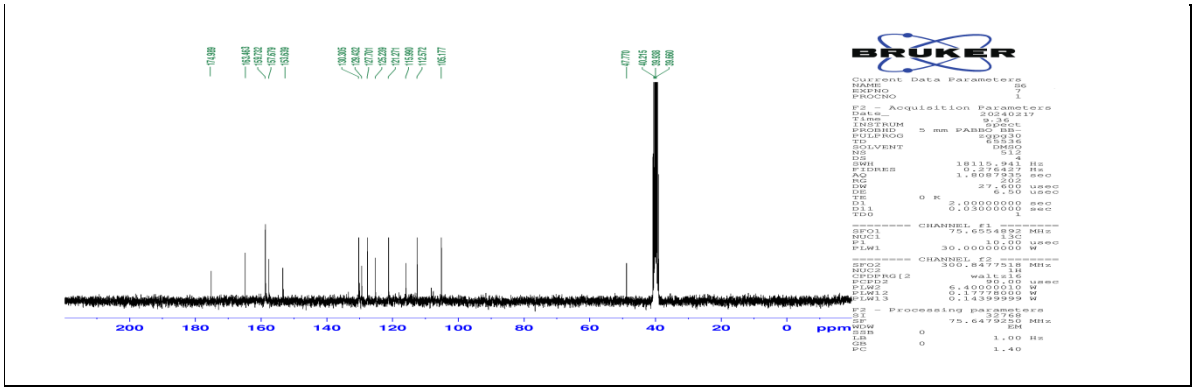
Sym. (18):^{13} CNMR - (S_3)



Sym. (19):^{13} CNMR -(S_4)



Sym. (20):^{13} CNMR - (S_5)



Sym. (21):^{13} CNMR -(S_6)

Stall. 1: Physical properties of Combination compounds

product	Struc.	MW	R_F	color	crop%	flush
S	C15H11Br2N3O	404.9	0.93	yellow	76	ethanol
S_1	C23H15Br2N3O4	584.9	0.91	orange	76	1,4-dioxane
S_2	C19H13Br2N3O4	502.9	0.82	Yellow	81	Dry benzene
S_3	C19H15N3O4	504.9	0.75	yellow	83	Dry benzene
S_4	C17H14N4O2	589.4	0.79	yellow	83	Dry benzene
S_5	C24H20N4O3	570.2	0.81	Yellow	88	Tetrahydrofuran
S_6	C17H12Br2ClN3O2	480.9	0.73	yellow	83	=

Stall 2: Results of Biological Commotion from Types of Bacteria

Sort of bacteria / Comp.NO.	reserve section (mm) 5mg 10mg 20mg (mg\mol)			
	klebsiella pneumonia	***Staphylococcus***	***Enterococcus faecalis***	***pseudomonas aeruginosa***
S	-,-,5	-, -, 5	,-,5-	,-,8-
S_1	-	-, - ,4	,-,8-	,-,8-
S_2	-, -, 8	-, 5, 8	,-,--	-,-,6
S_3	-,-,6	-,-,10	8,10,20	-, -, 10
S_4	-	-,-,10	,8,10-	,-,7-
S_5	-	-	,8,10-	12,18,20
S_6	-	-,5,10	-	-

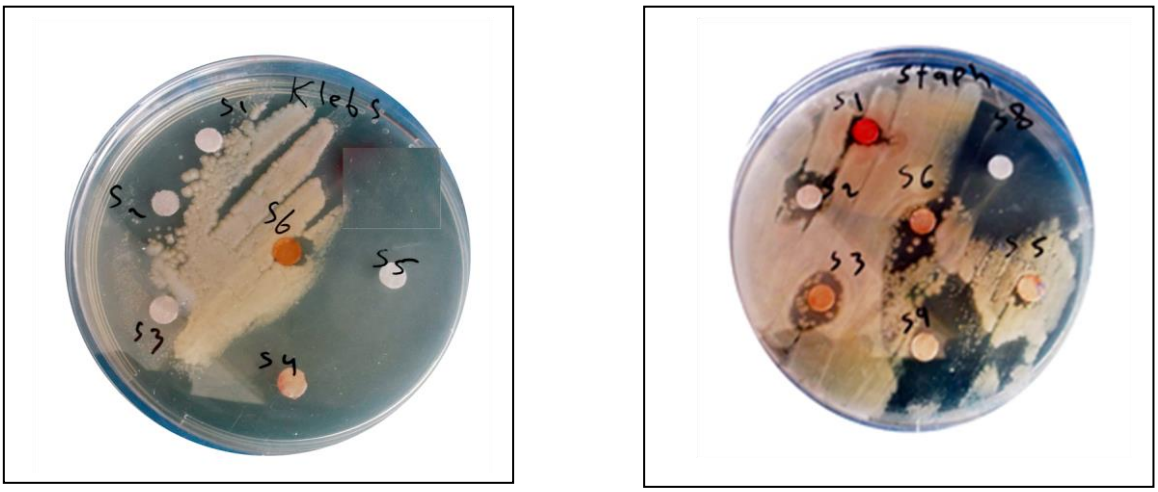


Fig. 1: The antimicrobial activity of compounds (S1-S6)

Conflict of interest: NIL
Funding: NIL

Reference

1. Lwona, B., Marcina, S., Aleksandra, M., Magdalene, K., Anna, P., Marcin, M., and Agnieszka, M., Pyrimidine Schiff Bases: Synthesis, Structural Characterization and Recent Studies on Biological Activities, *International Journal of Molecular Sciences*,**2024**,25, 1-27

2. Jumbad, H., Dhuha, F., M, and Nebras, M., Synthesis and Characterization of Some New Quinoline-2-one, Schiff bases, Pyrazole and Pyrazoline Compounds Derived from Hydrazide Containing Isoxazoline or Pyrimidine Cycles, *Iraqi Journal of Science***, 2016**, 57,1316-1332.

3. Bhavana, A., Jalpa, H., and Jayesh, J., Synthesis and Structure Elucidation of Some Newer Schiff Bases Derived from Pyrimidine-5-carbonitrile Moiety, *International Journal of Pharmaceutical Research and* Applications**,2022**,7, 894-906.

4. Andy, M., Abbas A, Waleed A. M. and Zinah H. A., Synthesis, Characterization and Bioactivity Evaluation for Some Metal Ions Complexes with New Ligand Derived from 2-hydroxy-1-naphthaldehyde, *Baghdad Science Journal*,**2024,** 21(4), pp. 1220- 1233.

5. Edyta, R., Justyne, S, and Januse, M., Different Schiff bases—Structure, importance and classification, *Molecule**s***, **2022**,27, 787.

6. Xavier, A. and Srividhya, N., Synthesis and Study of Schiff base Ligands, *Journal of Applied Chemistry*, **2014**,7, 6-15.

7. Sayed, S., Dawood, S., Ibrahim, K., Sajjad A., Umar, A. and Atiq, R., Synthesis and antioxidant activities of Schiff bases and their complexes: review, *Biointerface Research in Applied Chemistry*, **2020,**10, PP 6936–6963.

8. Bian, M., Wang, X., Sun, Y., and Liu, W., Synthesis and biological evaluation of gold (III) Schiff base complexes for the treatment of hepatocellular carcinoma through attenuating TrxR activity, *European Journal of Medicinal Chemistry*
, **2020**, 193, 112234

9. Hadi, M. and Kareem, I., Synthesis, Characterization and Spectral Studies of a new Azo-Schiff base Ligand Derived from 3, 4-diamino benzophenone and its Complexes with Selected Metal Ions, *Research Journal in Advanced Sciences*, **2020**,1,54-73.

10. Almehmadi, A., Ateyatallah, A., Shaya, Y., Imran A, Nadjet R, Mohamed, R., and Mohamed, H, synthesis, DNA binding, modeling, anticancer studies, and DFT calculations of Schiff bases tethering benzothiazole-1, 2, 3-triazole conjugates, *Journal of Molecular Structure*, **2021**,1225, 129-148.

11. Sharma, A., and Kumar, N., A review on "imidazoles": Their chemistry and pharmacological potentials, *International Journal of PharmTech Research*, **2011**,3, 268-282.

12. Husain, A., Ahmad, A., Alam, S., Asif, R, M., Rubina B., and Fahad, A., Synthesis, molecular properties, toxicity and biological evaluation of some new substituted Imidazolidine derivatives in search of potent anti-inflammatory agents, ***Sudi Pharmaceutical Journal***, 2015,24(1), pp 104-114**.**

13. Nahad, T., Synthesis of 1,3-Oxazepine Derivatives Derived from 2-(1H-Benzo[d][1,2,3]Triazol-1-yl) Acetohydrazide by Using Microwave Irradiation *International Journal of Organic Chemistry*, **2017,**7,219-228**.**

14. Rafat, H., Ahmed, M. and Laith, M. N., Bacitracin isolation from selected bacterial isolated and study 4 ITS inhibition zone against some pathogenic bacteria species, *Journal of Al-Anbar University for pure science*, **2007**,1,14-22

15. Wail, A., Abass, A., Susan, D., and Young, G., Synthesis, characterization and biological

activity of Schiff bases metal complexes, ***E****uropean Chemical Bulletin***, 2016**, 31,88-91

16. Haitham, D., Synthesis and Characterization of New Seven-Member heterocyclic Compounds from reaction of new Schiff bases with maleic and pthalic anhydride, *National Journal of Chemistry*,2011,41, p. 77- 89.
17. Shhar, A., Jumbad, T., and Ali, E., Synthesis And Characterization Of New Schiff Bases And Their 1, 3-Oxazepines Derived From Phthalic Anhydride, *Systematic Reviews in Pharmaceutical*, **2021**,12,260–265
18. Mohamd, G., Omar, M., Synthesis, characterization and antibacterial activities of new substituted (1, 3) oxazepine 1, 5-diones, *International Journal of New Chemistry*,10, 2023, 116-123.
19. Ruwaidah, S.S., Fadhel, S. M, and Ali, H.S., Chemical modification of PVA with four, five, and seven heterocyclic compounds and study anticancer activity, *Journal of Pharmaceutical Sciences and Research*, **2019**, 11,733–740
20. Rasim F., Hiba, F, and Mustafa, N., Synthesis, characterization, and evaluation of antifungal activity of seven-membered heterocycles, *ACTA Pharmaceutical Science*, **2018**,56,39-57.
21. Gilles, O., A review on Recent applications of seven-membered rings in drug design. *Bioorganic and Medicinal. Chemistry* **2022**,19, 116650.
22. Broccolo, F., Carnally, G., Caltabiano, G., Cocuzza, A., Fortuna, C., Galletti, G, D. Giacomini, Musumarra, P., Musumeci, R. and Quitavalla, A. Design, Synthesis, and Biological Evaluation of 4-Alkyliden-Beta Lactams: New Products with Promising Antibiotic Activity against resistant Bacteria, *Journal of Medicinal Chemistry*,**2006**, 49, 2804-2811
23. Alcaide, B., Almendros, P., Aragoncillo, C.m β-Lactams: Versatile Building Blocks for the Stereoselective Synthesis of Non-β-Lactam Products, *Journal of Chemical Reviews*.,**2007**, 107, 4437-4492.
24. 'Driscoll, M., Greenhalgh, K., Young, A., Turos, E., Dickey, S., and Lim, D., Studies on the Antifungal Properties of NThiolated β-Lactams. Bioorg, *Medicinal chemistry*,**2008**, 16, 7832-7837.
25. Turos, E., Reddy, G., Greenhalgh, K., Ramaraju, P., Abeylath, S., Jang, S., Dickey, S., and D. V. Lim, Penicillin-bound polyacrylate nanoparticles: restoring the activity of beta-lactam antibiotics against MRSA. Bioorg, *Medicinal Chemistry Letters*,**2007**, 17,3468-3472.
26. Bhalla, A., Bari, S., Berry, S.. Bhalla, S., Vats, S., Mandal, S., and S. Khullar, Facile synthesis of novel monocyclic trans- and cis-3-oxy/thio/seleno-4pyrazolyl-β-lactams, *ARKIVOC*, **2015**, vii, 10-27
27. Patel, J., Mistry, B., and Desai, K., Conventional and microwave induced synthesis of various azetidinone and thiazolidinone derivatives from 3[(1E)-1-aza-2-(2-chloro-7-methoxy-3-quinolyl)-vinyl]4-(aryldiazenyl) phenol and their antimicrobial screening, *Indian Journal of Chemistry*,**2008**, 47B, 16951700
28. Rusul, A., and Rajaa, A., G,. Synthesis, Identification some of new heterocyclic Compounds Derivatives and study of the biological Activity, *Journal of Kufa for Chemical Sciences*,**2024**,3,336-350.
29. Eman, A. Rajaa, A., Synthesis of new compounds derived from 5-chloroindole and the study of their biological activity, *Drug Invention Toda*, **2020**,14,79.