SYNTHESIS, CHARACTERIZATION, AND BIOLOGICAL ACTIVITY OF VARIOUS NEW SCHIFF BASES ASSOCIATED WITH THE 9,10-DIHYDRO-9,10-[3,4]FURANOANTHRACENE-12,14-DIONE GROUP

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Abstract: *A series of novel Schiff bases linked to Furanoanthracene-12,14-Dione (5-10) were synthesized. The first step involved the reaction of anthracene with maleic anhydride, which produced dione (1). The next step was treated the dione with aniline to produce the imide (2). In the third step, the prepared imide was reacted with chlorosulfonic acid, leading to produce epipyrroloanthracen benzenesulfonyl chloride (3). The fourth step was amination of (3) with hydrazine hydrate to give epipyrroloanthracen benzenesulfono hydrazide (4). Ultimately, this hydrazine derivative underwent a condensation reaction with various aromatic aldehydes and ketones, resulting in the formation of the desired Schiff bases (5-10). The structures of the synthesised compounds were confirmed by spectroscopic methods. The biological activities were assessed against four bacterial strains. Furthermore, compounds (5-10) underwent molecular docking studies targeting the Penicillin Binding Protein (PDB ID: 3vsl), with Penicillin G (PNM) used as a control for comparison. The newly synthesised Schiff bases are expected to exhibit biological activity, especially due to their initial synthesis from biologically relevant components.*

Keywords: *Anthracene, Sulfone amide, Sulfonyl hydrazine, Molecular Docking*
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1. Introduction

Cyclic imides are a significant category of bioactive compounds known for their diverse pharmacological properties, including the capacity to antagonize androgen receptors [1]. Imines are synthetically accessible and structurally diverse compounds, typically generated through the straightforward condensation of an aldehyde or ketone with primary amines, commonly known as Schiff bases [2]. Preparation of bulky novel imides have azo methene group will enrich the biological active properties [3]. Schiff bases are versatile compounds with a wide range of therapeutic applications, including antibacterial (such as antimycobacterial), antifungal, antiviral, antimalarial, anti-inflammatory, antioxidant, pesticidal, cytotoxic, enzyme inhibitory, and anticancer activities [4-9]. Nowadays, molecule docking became a successful strategy to predict the biological activity properties.

2. Experimental part

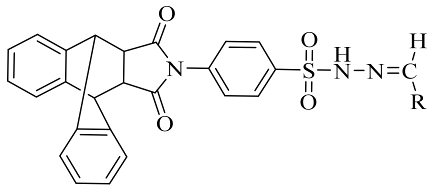
2.1. Materials and methods

The solvents and chemicals were all purchased from reliable commercial suppliers and were utilized without additional purification. The IR spectra (ν_{max} in cm^{-1}) were performed using a Bruker FT-IR 8400 spectrophotometer with KBr discs. Tetramethylsilane (TMS) was used as the standard for chemical shift reference and DMSO-d6 as the solvent in ^{1}H-NMR spectroscopy, which was performed on a Bruker apparatus running at 400 MHz. The compounds (1), (2), (3), and (4) were prepared according to the literature [10-14].

2.2. Synthesis of Schiff Bases (5-10) [15, 16]. A mixture containing (0.25 mmol, 0.11 g) of (4), (0.25 mmol) of substituted aromatic aldehyde, and 2-3 drops of glacial acetic acid in 20 mL of absolute ethanol were used. The mixture was refluxed for 6 hours. After cooling, the resulting precipitate was filtered, washed with cold ethanol, dried, and recrystallized from an appropriate solvent (Table 1).

Table 1. Physical properties of compounds (5-10)

No.	R	Color	Melting Point, ˚C	Yield, %	Recrystallization Solvent
5	-Ph	Pale yellow	218-220	72%	Acetone
6	4-Cl-Ph	Pale orange	245-248	78%	Acetone
7	4-Br-Ph	Yellow	198-201	83%	Ethanol
8	3-NO_2-Ph	White	231-235	86%	Acetone
9	4-OH-Ph	White	105-108	53%	Ethanol
10	4-OCH_3-Ph	Brown	224-227	65%	Ethanol



[5-10]Schiff bases

Below the obtained FT-IR, ^{1}H-NMR and ^{13}C-NMR analysis data for all synthesized compounds (1-5).

N'-benzylidene-4-(12,14-dioxo-9,10-dihydro-9,10-[3,4]epipyrroloanthracen-13-yl)benzenesulfo nohydrazide (5). *FT-IR (KBr, ν_{max}, cm^{-1}):* 3184 (N-H), 3075 (=C-H), 2969 (C-H), (1771, 1693) the asymmetric and symmetric ν(C=O) of the imide, 1610 (C=N), (1382, 1165) the asymmetric and symmetric ν (SO_2), 1337 (C-N).

^{1}H-NMR (ppm): (DMSO d^6, 400 MHz) δ: 8.11-7.18 (m, 17H), 8. 58 and 8. 31 (s, 1H), NH, (-CH=N-) imine protons, respectively, 4.62 (t, 2H) 2CH, 3.36 (t, 2H) 2CH.

^{13}CNMR (ppm): (DMSO d^6, 400 MHz) δ: 172.34, 149.08, 141.85, 139.97, 139.75, 134.73, 129.07, 128.74, 127.03, 124.87, 123.80, 123.37, 41.60, 39.04.

N'-(4-chlorobenzylidene)-4-(12,14-dioxo-9,10-dihydro-9,10-[3,4]epipyrroloanthracen-13-yl) benzenesulfonohydrazide (6). *FT-IR (KBr, ν_{max}, cm^{-1}):* 3313 (N-H), 3041 (=C-H), 2955 (C-H), (1766, 1709) the asymmetric and symmetric ν(C=O) of the imide, 1629 (C=N), (1345, 1180) the asymmetric and symmetric ν (SO_2),1292 (C-N), 763, (C-Cl).

^{1}H-NMR (ppm): (DMSO d6, 400 MHz) δ: 7. 91-6.81 (m, 16H), 8.24 and 8.06 (s, 1H), NH, (-CH=N) imine protons, respectively, 4.42 (t, 2H) 2CH, 3.49 (t, 2H) 2CH.

^{13}C-NMR (ppm): (DMSO d6, 400 MHz) δ: 172.34, 149.08, 141.85, 139.97, 139.75, 135.13, 134.11, 129.41, 129.07, 129.06, 124.87, 123.80, 123.37, 41.60, 39.04.

N'-(4-bromobenzylidene)-4-(12,14-dioxo-9,10-dihydro-9,10-[3,4]epipyrroloanthracen-13-yl)benzenesulfonohydrazide (7) *FT-IR (KBr, ν_{max}, cm^{-1}):* 3296 (N-H), 3049 (=C-H), 2981 (C-H), (1776, 1701) the asymmetric and symmetric ν(C=O) of the imide, 1620 (C=N), (1327, 1197) the asymmetric and symmetric ν (SO_2), 1378 (C-N), 759, (C-Br).

^{1}H-NMR (ppm): (DMSO d6, 400 MHz) δ: 8.11-7.07 (m, 16H), 8.22 and 7.92 (s, 1H), NH, (-CH=N-) imine protons, respectively, 4.66 (t, 2H) 2CH, 3.60 (t, 2H) 2CH.

^{13}CNMR (ppm): (DMSO d6, 400 MHz) δ: 172.34, 149.08, 141.85, 139.97, 132.49, 132.38, 129.31, 129.07, 124.87, 123.99, 123.80, 123.37, 41.60, 39.04.

4-(12,14-dioxo-9,10-dihydro-9,10-[3,4]epipyrroloanthracen-13-yl)-N'-(3-nitrobenzylidene)ben zenesulfonohydrazide (8) *FT-IR (KBr, ν_{max}, cm^{-1}):* 3212 (N-H), 3038 (=C-H), 2935 (C-H), (1744, 1694) the asymmetric and symmetric ν(C=O) of the imide, 1614 (C=N), (1379, 1177) the asymmetric and symmetric ν (SO_2), 1536 asym.,1343 sym., (C-NO_2), 1355 (C-N).

^{1}H-NMR (ppm): (DMSO d6, 400 MHz) δ: 8.07-7.25 (m, 16H), 8.78 and 8.02 (s, 1H), NH, (-

CH=N-) imine protons, respectively, 4.78 (t, 2H) 2CH, 3.21 (t, 2H) 2CH.

^{13}CNMR (ppm): (DMSO d6, 400 MHz) δ: 172.34, 172.34, 149.35, 147.42, 141.85, 139.97, 139.75, 137.76, 132.63, 129.94, 129.07, 124.87, 124.15, 123.80, 123.37, 122.33, 41.60, 39.04.

4-(12,14-dioxo-9,10-dihydro-9,10-[3,4]epipyrroloanthracen-13-yl)-N'-(4-hydroxybenzylidene) benzenesulfonohydrazide (9) *FT-IR (KBr, ν_{max}, cm^{-1}):* 3448(OH) Phenolic, 3218 (N-H), 3088 (=C-H), 2970 (C-H), (1745, 1717) the asymmetric and symmetric ν(C=O) of the imide, 1609 (C=N), (1372, 1159) the asymmetric and symmetric ν (SO2) ,1325 (C-N).

^{1}H-NMR (ppm): (DMSO d6, 400 MHz) δ: 7.92-6.84 (m, 16H), 8.69 and 7.96 (s, 1H), NH, (-CH=N-) imine protons, respectively, 4.82 (t, 2H) 2CH, 3.73 (t, 2H) 2CH, 4.19 (s, 1H) OH.

^{13}CNMR (ppm): (DMSO d6, 400 MHz) δ: 172.34, 158.32, 149.08, 141.85, 139.97, 129.72, 129.07, 126.92, 124.87, 123.80, 123.37, 115.60, 41.60, 39.04.

4-(12,14-dioxo-9,10-dihydro-9,10-[3,4]epipyrroloanthracen-13-yl)-N'-(4-methoxybenzylidene) benzenesulfonohydrazide (10) *FT-IR (KBr, ν_{max}, cm^{-1}):* 3317 (N-H), 3081 (=C-H), 2967 (C-H), (1756, 1712) the asymmetric and symmetric ν(C=O) of the imide, 1639 (C=N), (1377, 1160) the asymmetric and symmetric ν (SO$_2$), 1265 asym., 1115 asym. (C-O-C), 1325 (C-N).

^{1}H-NMR (ppm): (DMSO d^{6}, 400 MHz) δ: 8.03-6.67 (m, 16H), 8.91 and 8.17 (s, 1H), NH, (-CH=N-) imine protons, respectively, 4.36 (t, 2H) 2CH, 3.47 (t, 2H) 2CH, 3.85 (s, 3H) CH3.

^{13}CNMR (ppm): (DMSO d6, 400 MHz) δ: 172.34, 160.10, 149.08, 141.85, 139.97, 139.75, 129.12, 129.07, 127.06, 124.87, 123.80, 123.37, 114.32, 56.04, 41.60, 39.04.

The Biological Activity Study. The biological activity of Schiff bases was evaluated against four types of bacteria, specifically Gram -positive *(Staphylococcus aureus and Gram-negative strains such as Escherichia coli, Pseudomonas aeruginosa, and Salmonella typhi*), utilizing a nutrient medium. The Schiff bases and their complexes were dissolved in a DMSO solvent for preparation.

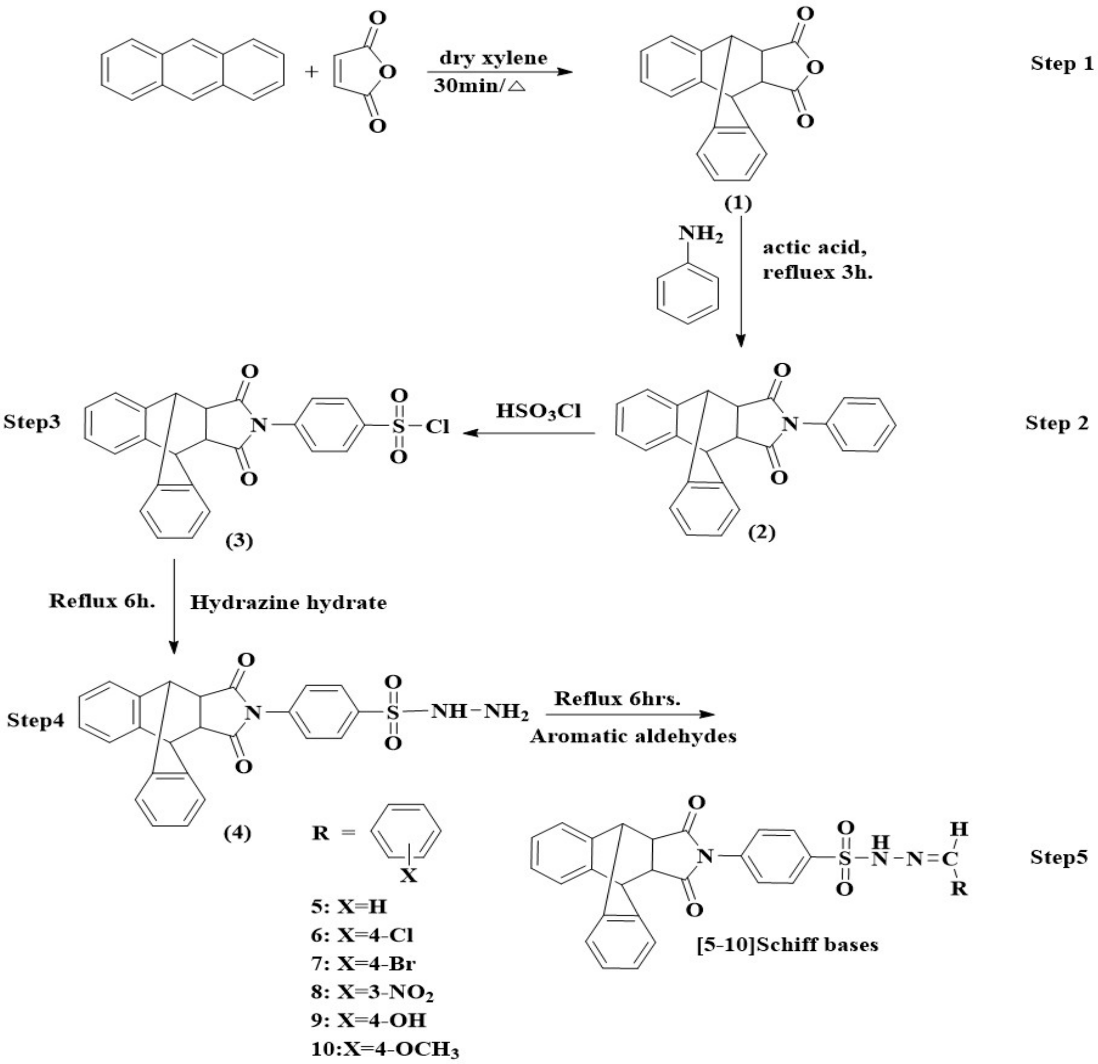
In this study, the agar-well diffusion method was employed to assess the compounds' ability to inhibit bacterial growth by measuring a 6 mm diameter zone on the surface of the nutrient medium. Following this, the plates were incubated at 37°C for 24 hours. The effectiveness of each compound was determined by measuring the diameter of the inhibition zone [17].

3. Results and discussion

N-substituted cyclic imides and Schiff bases belong to a wide range of important intermediates used in the production of multiple types of drugs and have diverse biological applications; the aim of this work is to develop new molecules containing these two active compounds. The newly synthesized compounds incorporate both cyclic imides and Schiff base moieties, interconnected through a phenyl sulfonamide component. This objective was achieved through a multistep synthesis, as detailed in the following **Scheme 1.**

The synthesis started with the formation of dione (1) by reacting equivalent amounts of anthracene and maleic anhydride. In the subsequent step, imide (2) was synthesized by reacting compound (1) with aniline. The third step involved exposing imide (2) to chlorosulfonic acid, yielding epipyrroloanthracen benzenesulfonyl chloride (3). In the fourth step, (3) was reacted with hydrazine hydrate to form benzenesulfonohydrazide (4). Finally, the synthesized hydrazine (4) underwent a condensation reaction with substituted aldehydes to produce the desired new Schiff bases (5-10) [18].

The FTIR spectrum of the synthesized Schiff bases (5-10) indicated the absence of the absorption band at 3334 cm^{-1}, which is characteristic of the NH$_2$ group in the hydrazine precursor. In contrast, a new absorption band appeared in the range of (1639-1604) cm^{-1}, attributed to the ν(C=N) stretching of the imine group, providing strong evidence for the successful formation of the Schiff base. Additionally, the FTIR spectra for Schiff bases (5-10) exhibited distinct absorption bands between (1776-1693) cm^{-1} corresponding to the ν(C=O) imide stretching. Other notable absorption bands were observed at ((1382-1327 cm^{-1} asymmetric ν(SO_2), 1197-1159 cm^{-1} (symmetric ν(SO_2)).



Scheme 1. Total prepared compounds (5-10)

Detailed FTIR spectral data for compounds (5-10) are compiled **in Table 2**.

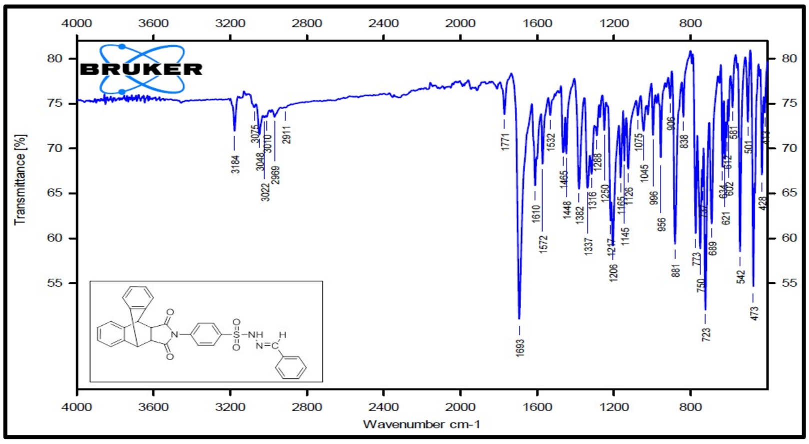
Table 2. FT-IR Spectral data (cm^{-1}) for the compounds (5-10)

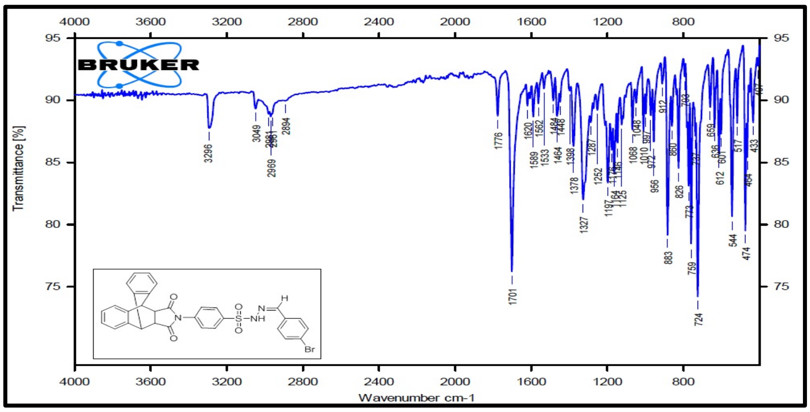
Comp. No.	**FT-IR spectral data, cm^{-1}**							
	□(N-H)	**□ (C-H) aromatic, aliphatic**	**□ (C=O) imide asym., sym**	**□ (C=N)**	**□ (C=C) aromatic**	**□ (SO_2) asym., sym.**	**□ (C-N) imide**	**Others**
5	3184	3075, 2969	1771, 1693	1610	1572	1382, 1165	1337	------------
6	3313	3041, 2955	1766, 1709	1629	1591	1345, 1180	1292	763, (C-Cl)
7	3296	3049, 2981	1776, 1701	1620	1589	1327, 1197	1378	759, (C-Br)
8	3212	3038, 2935	1744, 1694	1614	1601	1379, 1177	1355	1536 asym., 1343 sym. (C-NO_2)
9	3218	3088, 2970	1745,1717	1604	1592	1379, 1159	1364	3448, (O-H) Phenolic

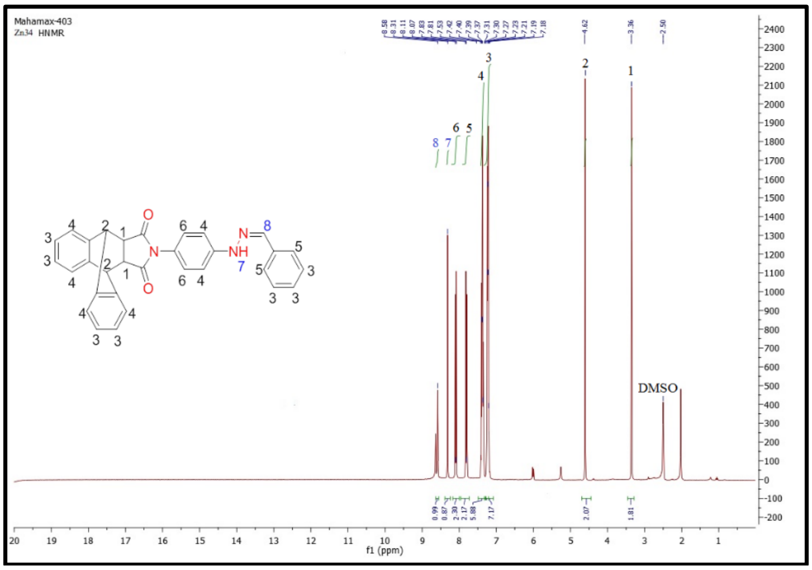
10	3317	3081, 2967	1756, 1712	1639	1611	1377, 1160	1325	1265 asym., 1115 asym. (C-O-C)

The ^{1}H-NMR spectrum of Schiff base (5) revealed a two signals at (δ =4.62, 3.36 ppm), (m, 4h) corresponding to the (2CHCH) protons, with additional signals in the range of (δ = 8.11-7.18) ppm attributed to aromatic protons, and signals at (δ = 8.31 and 8.58) ppm(s, 1H) representing the (NH) amide and (-CH=N-) imine protons, respectively.

In compound (7), the ^{1}H-NMR spectrum showed two signals at (δ = 4.66 and 3.60 ppm), (m, 4H) for (2CHCH), with further signals at (δ = 8.11-7.07 ppm), 7.92 ppm, and 8.22 ppm corresponding to aromatic protons, (NH) amide proton, and (-CH=N-) imine proton, respectively.







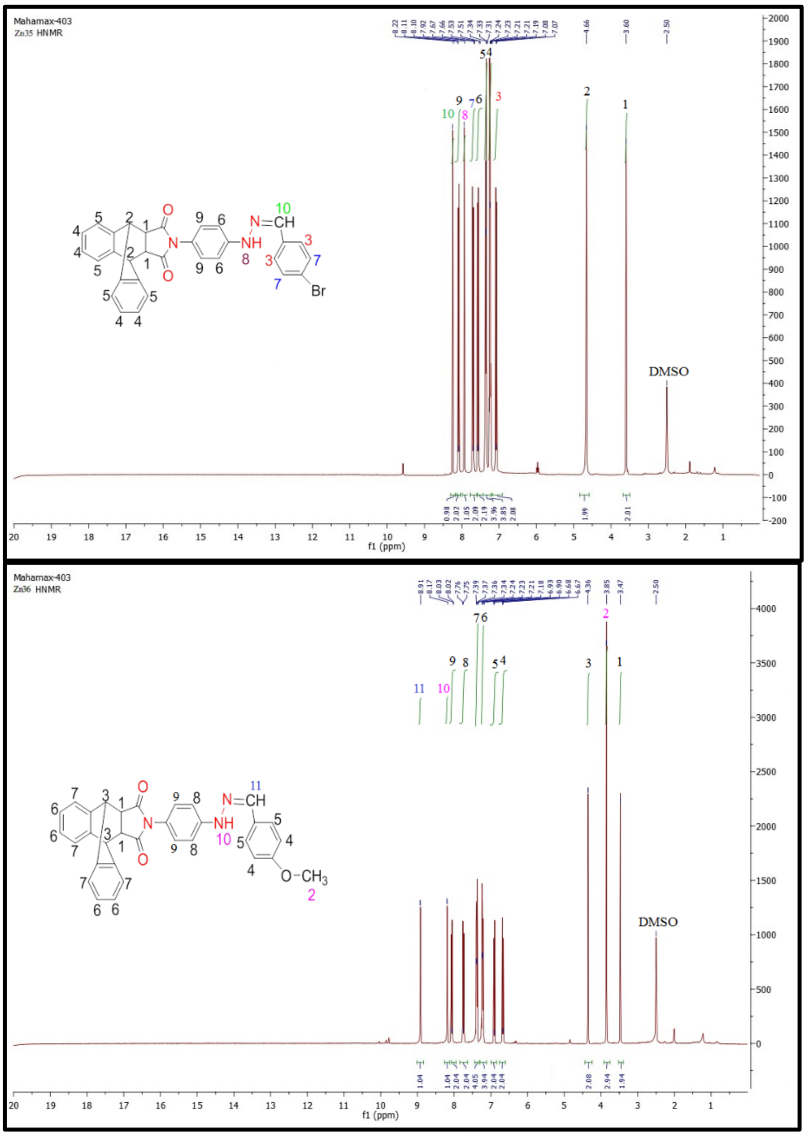


Fig. 1. FT-IR spectra for the compounds (5 and 7) and ^{1}H-NMR charts for the compounds (5, 7, and 10)

Lastly, the ^{1}H-NMR spectrum of compound (10) showed three signals at (δ =3.47, 4.36 and 3.85 ppm) belong to (2CHCH) protons and (OCH_3) protons. Other signals appeared at (8.03-6.67) ppm, (8.17and 8.91) ppm which belong to aromatic protons, (NH) amide proton and (-CH=N-) imine proton respectively (Fig. 1).

3.1. Biological Activity. The study examined the activity of several compounds (5, 6, 8, 9) on the growth of four distinct bacterial types, including both Gram-negative and Gram-positive strains. The results fluctuated from mostly highest to rarely moderate (see the Table 5). These compounds have the potential to inhibit bacterial growth. Based on the inhibition zones measured, compounds (8, 9) demonstrated remarkable effectiveness in suppressing *E. coli* and S. typhi compared to ampicillin, which served as a control. The effectiveness of the other compounds ranged from moderate to good (Fig. 2).

Table 3. The biological activity of prepared compounds

Comp. No	*S. aureus* 10(mg/ml) *ZI mm	*E. coli* 10(mg/ml) ZI mm	*P. aeruginosa* 10(mg/ml) ZI mm	*S. typhi* 10(mg/ml) ZI mm
5	17	18	23	12
6	19	18	16	20
8	18	19	18	20

9	15	17	17	15
Ampicillin 10mg/disk	20	15	18	14

** ZI= zone inhibiter in millimeter*

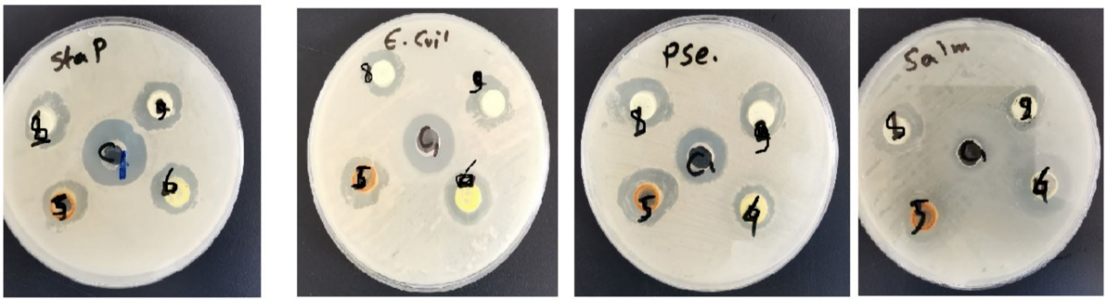


Fig. 2. The biological potency of compounds (5, 6, 8, and 9)

3.2. Study of Molecular Docking. The synthesized compounds underwent molecular docking studies targeting the Penicillin Binding Protein (PDB ID: 3vsl), with Penicillin G utilized as a control. The docking analyses were carried out using the online platform CB-dock2 [19], accessible at https://cadd.labshare.cn/cb-dock2/php/index.php.

Table 4. Docking result with the interactions

Compound	Docking Score	Hydrogen Bonding	Hydrophobic Interactions
5	-11.2	Asn487, Arg483	Asn501, Ser274, Ile507, Leu510, Pro509, Ala479, Ile381, Asp378, Tyr379, Gln480, Arg484, Lys273, Arg504, Tyr275
6	-11.6	Arg504, Tyr275, Leu510	Glu255, Arg484, Thr511, Pro509, Asp378, Asp380, Gly240, Arg239, Lys273 ,Ser274
7	-11.6	Asn487, Arg483	Arg504, Ser274, Arg484, Ala497, Ile507, Leu510, Ile381, Pro509, Asp378, Gln480, Tyr379, Asn501, Lys273, Tyr275
8	-3.1	Ser66	Arg270, Trp228, Asp227, His50
9	-11.2	Leu510, Arg504, Tyr275	Asn487, Thr511, Pro509, Asp380, Gly240, Leu238, Gly240, Arg239, Asp378, Ser274, Lys273
10	-10.4	Lys273, Arg504	Glu255, Leu256, Asn487, Arg484, Gln480, Arg483, Ile381, Asp378, Gly240, Lys275, Ser274, Asn501, Tyr278
PNM	-7.6	Arg484, Arg504	Lys273, Ser274, Asn501, Val493, Lys494, Leu256, Glu255

Docking scores presented in Table 4 are crucial for virtual screening and lead optimization in drug discovery, as they assist in prioritizing potential drug candidates based on their predicted binding affinities for further experimental validation [20]. However, it's important to recognize that docking scores are merely predictions and may not always align perfectly with actual experimental binding affinities. Therefore, they are typically utilized as an initial filtering step in the drug development process.

Additionally, understanding contact residues is vital for elucidating the molecular details of protein-ligand interactions. This knowledge provides insights into the binding interface and identifies the key amino acids involved in the interaction [21]. Fig. 3 shows the binding of compounds Z(5, 6, 7, 8, 9, and10) to the enzyme, highlighting the interacting amino acid residues.

The results from docking experiments suggest that these compounds interact with the Penicillin Binding Protein, which plays a significant role in the biosynthesis of aromatic amino acids. Given that this enzyme may serve as a molecular target in bacteria, these compounds could be valuable in the research and development of new antimicrobial drugs [22].

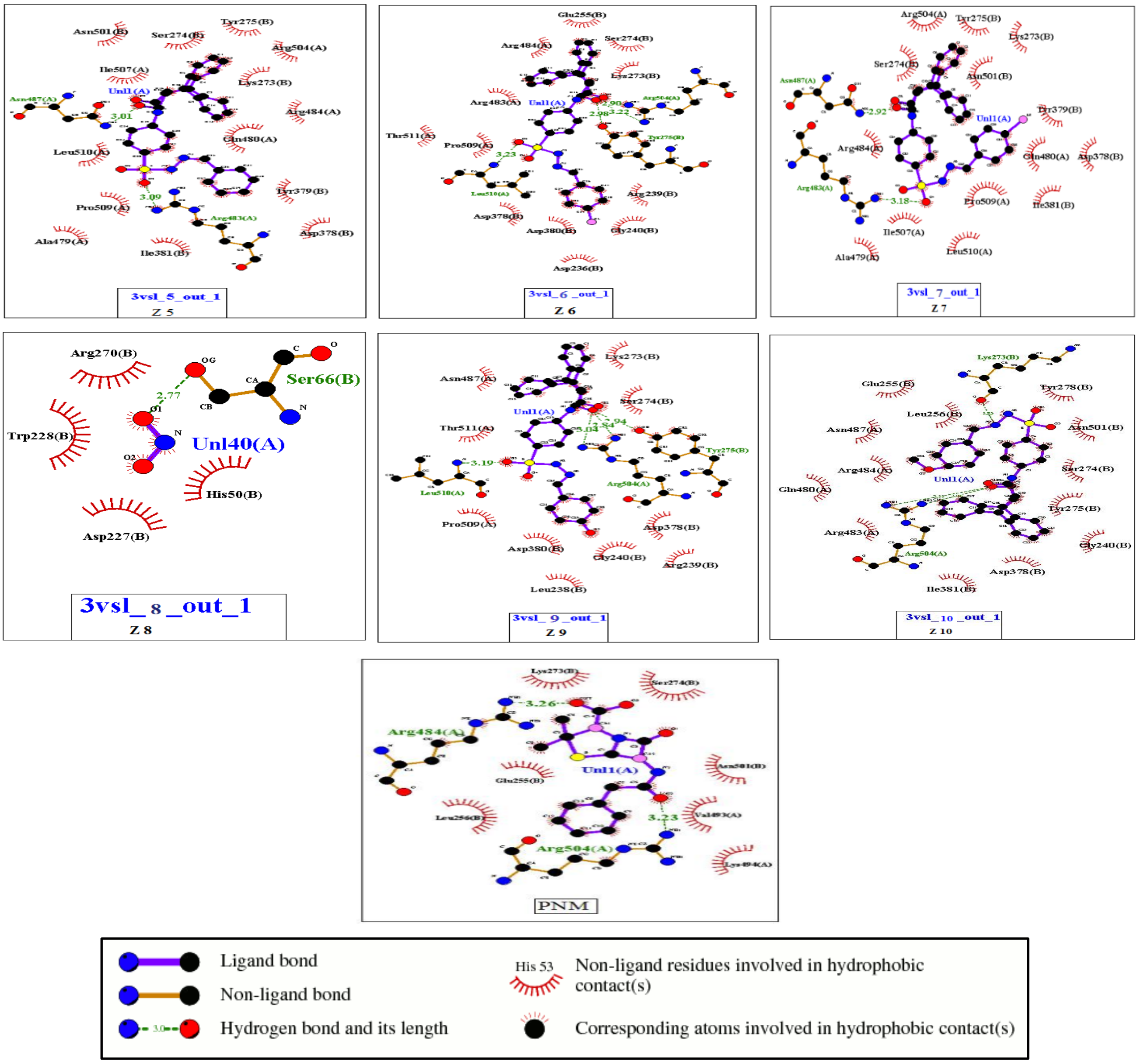


Fig. 3. Interaction of Penicillin Binding Protein (PDB ID: 3vsl) with (5, 6, 7, 8, 9, and 10)

Conclusion

A series of novel Schiff bases containing two biologically active components were successfully synthesized through a multi-step method. These newly developed compounds demonstrated significant biological activity, which can be attributed to the presence of three known bioactive entities. Compounds 8 and 9 exhibited strong inhibitory effects against the bacterial strains Escherichia coli and Salmonella typhi, while the other compounds displayed moderate sensitivity. The results regarding biological activity are promising, suggesting the potential use of these compounds as drugs or drug precursors. Furthermore, compounds (5, 6, 7, 8, 9, and 10) were shown to effectively bind to the target enzyme of the bacteria, as confirmed by docking studies have high binding affinity score.

References

1. El-Zahabi M., Amin Y., Sakr H., El-Hady O. An overview of imides and their analogues as

anticancer agents. *Al-Azhar Journal of Pharmaceutical Sciences*, 2022, **Vol. 66(2)**, p. 99-125. DOI: 10.21608/ajps.2022.268400

2. Ahamed F.M., Ali A.M., Velusamy V., Manikandan M. Aminopyridine derived azomethines as potent antimicrobial agents. *Materials Today: Proceedings*, 2021, **Vol. 47**, p. 2053-2061. DOI: 10.1016/j.matpr.2021.04.424
3. Younus H.A., Saleem F., Hameed A., Al-Rashida M., Al-Qawasmeh R.A., El-Naggar M., Khan K.M. Part-II: an update of Schiff bases synthesis and applications in medicinal chemistry-a patent review (2016-2023). *Expert Opinion on Therapeutic Patents*, 2023, **Vol. 33(12)**, p. 841-864. DOI: 10.1080/13543776.2023.2297729
4. Shekhar S., Khan A.M., Sharma S., Sharma B., Sarkar A. Schiff base metallodrugs in antimicrobial and anticancer chemotherapy applications: a comprehensive review. *Emergent Materials*, 2022, **Vol. 5(2)**, p. 279-293. DOI: 10.1007/s42247-021-00234-1
5. Kaushik S., Paliwal S.K., Iyer M.R., Patil V.M. Promising Schiff bases in antiviral drug design and discovery. *Medicinal Chemistry Research*, 2023, **Vol. 32(6)**, p. 1063-1076. DOI: 10.1007/s00044-023-03068-0
6. Iacopetta D., Ceramella J., Catalano A., Saturnino C., Bonomo M. G., Franchini C., Sinicropi M.S. Schiff bases: Interesting scaffolds with promising antitumoral properties. *Applied Sciences*, 2021, **Vol. 11(4)**, 1877. DOI: 10.3390/app11041877
7. Ayaz F., Gonul I., Demirbag B., Ocakoglu K. Novel copper bearing schiff bases with photodynamic anti-inflammatory and anti-microbial activities applied Biochemistry and Biotechnology, 2020, **Vol. 191(2)**, p. 716-727. DOI: 10.1007/s12010-019-03223-7
8. Meena R., Meena P., Kumari A., Sharma N., Fahmi N. Schiff bases and their metal complexes: Synthesis, structural characteristics and applications. *In Schiff Base in Organic, Inorganic and Physical Chemistry*, 2023, Chapter 23 p. DOI: 10.5772/intechopen.108396
9. Uddin N., Rashid F., Ali S., Tirmizi S.A., Ahmad I., Zaib S., Haider A. Synthesis, characterization, and anticancer activity of Schiff bases. *Journal of Biomolecular Structure and Dynamics*, 2020, **Vol. 38(11)**, p. 3246-3259. DOI: 10.1080/07391102.2019.1654924
10. Madhurambal G., Ramasamy P., Srinivasan P., Mojumdar S. Synthesis and characterization of a novel non-linear optical (NLO) material: Endo anthracene maleic anhydride–Diel's–Alder adduct of anthracene. *Journal of thermal analysis and calorimetry*, 2006, **Vol. 86(3)**, p. 601-604. DOI:10.1007/s10973-006-7714-z
11. Weber E., Finge S., Csoeregh I. Modular design of hosts involving a rigid succinimide framework and N-bonded lateral groups. Crystalline inclusion properties and crystal structures of inclusion compounds with dioxane, methanol, and DMF. *Journal of Organic Chemistry*, 1991, **Vol. 56(26)**, p. 7281-7288. DOI: 10.1021/jo00026a018
12. Al-Azzawi A.M., Abdulrahman S. Synthesis, characterization and biological activity study of N-substituted sulfonamido maleimides substituted with different heterocycles. *Baghdad Science Journal*, 2010, **Vol. 7(1)**, p. 641-653. DOI: 10.21123/bsj.2010.7.1.641-653
13. Cunha M.R., Tavares M.T., Carvalho C.F., Silva N.A., Souza A.D., Pereira G.J., Parise-Filho R. Environmentally safe condition for the synthesis of aryl and alkyl sulfonyl hydrazones via one-pot reaction. *ACS Sustainable Chemistry & Engineering*, 2016, **Vol. 4(4)**, p. 1899-1905. DOI: 10.1021/acssuschemeng.6b00193
14. Fathi A.A., Al Jawaheri Y.A. Synthesis and characterization of new N-Aryl sulfonyl hydrazone compounds. *Egypt. J. Chem*. 2022, **Vol. 65**, p. 179-183. DOI: 10.21608/ejchem.2021.90637.4320
15. Al-Azzawi A.M., Hamed A.S. Synthesis of Several New Schiff Bases Linked to Sulfonamido Naphthalimide Moiety with Expected Biological Activity. *Journal of university of Anbar for Pure science*, 2014, **Vol. 8(2)**, p. 48-52. DOI: 10.37652/juaps.2014.123915
16. Fathi A., Al Jawaheri Y., Ismaeel S. Synthesis of some new substituted imines from aldehydes and ketones derived from quinolinic acid. *Eclet. Quim*. 2023, **Vol. 48**, p. 49-65. DOI: 10.26850/1678-4618eqj.v48.2.2023.p49-65

17. Shihab A.S. Synthesis Diagnosis, Evaluation of Biological Activity and Study of Molecular Docking for Furosemide Derivative and Its Coordination with Some Metals. *Chemical Problems*, 2024, **Vol. 22(3)**, p. 312-323. DOI: 10.32737/2221-8688-2024-3-312-323.
18. Johari N.L.S., Hassan N.H., Hassan N.I. A facile approach of Diels-Alder reaction in imidazolium-based ionic liquids at room temperature. *Oriental Journal of Chemistry*, 2014, **Vol. 30(3)**, p. 1191-1196. DOI: 10.13005/ojc/300333
19. Yang L., Xiaocong Y., Jianhong G., Shuang C., Zhi-Xiong X., Yang C., CB-Dock2: improved protein–ligand blind docking by integrating cavity detection, docking and homologous template fitting. *Nucleic Acids Research*, 2022, **Vol. 50**, p. 159-164. DOI:10.1093/nar/gkac394
20. Bhunia S.S., Saxena M., Saxena A.K. *Ligand-and structure-based virtual screening in drug discovery In Biophysical and Computational Tools in Drug Discovery*. In: Saxena, A.K. (eds) Biophysical and Computational Tools in Drug Discovery. Topics in Medicinal Chemistry, **Vol. 37**. Springer, Cham. 2021, p. 281-339. DOI:10.1007/7355_2021_130
21. Dhakal A., McKay C., Tanner J.J., Cheng J. Artificial intelligence in the prediction of protein–ligand interactions: recent advances and future directions. *Briefings in Bioinformatics*, 2022, **Vol. 23(1)**, 476. DOI: 10.1093/bib/bbab476
22. Yakobi S., Zuma L., Pooe O. Investigation into the Interaction between Penicillin-Resistant and Penicillin-Susceptible Gonococcal Penicillin-Binding Protein 2 and Target Phenolic Ligands through Molecular Docking Studies and Structure-Activity Relationship Analysis. *Advances in Pharmacological and Pharmaceutical Sciences*, 2024, **Vol. 20(1)**, p. 1-17. DOI: 10.1155/2024/2585922