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Synthesis, Identification, and Antibacterial Effect Study of Some New Benzoxazepindions using Thiazolylimines

Asmaa Thamer Abdulrahman[1], Shakhawan Abdulrahman Omer[2*]

[1,2] Chemistry Department, College of Science, University of Kirkuk, Kirkuk, 36001, Iraq.

***Corresponding Author:**

Email ID: Sccm22001@uokirkuk.edu.iq

Email ID: sh.beebany@uokirkuk.edu.iq

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ABSTRACT

In this work, thiazolidinone scaffolds were condensed with different aromatic amines in 100% ethanol under reflux for six hours to create a novel series of Schiff base derivatives [A_1–A_8]. Benzoxazepine derivatives [A_9–A_{16}] were obtained by cyclizing these intermediates with phthalic anhydride in anhydrous benzene. FT-IR spectroscopy and physicochemical characterization were used to accomplish structural elucidation. Selected compounds were further validated by ^{1}H-NMR and ^{13}C-NMR with DMSO-d^6 as the solvent. Thin-layer chromatography was used to evaluate purity (TLC). Using Ciprofloxacin as a reference, the synthetic compounds' antibacterial effectiveness was evaluated against Gram-positive Staphylococcus aureus and Staphylococcus epidermidis, as well as Gram-negative Escherichia coli and Pseudomonas aeruginosa. Their potential as bioactive compounds was .highlighted by the results, which showed substantial inhibitory activity.

Keywords: *Schiff base, Aromatic amines, Ketones, Benzoxazipine.*

1. INTRODUCTION

Benzoxazepindione derivatives are a class of heterocyclic compounds that have garnered significant attention in medicinal chemistry due to their diverse pharmacological activities [1]. These compounds belong to the broader category of oxazepines, which are seven-membered unsaturated heterocycles containing nitrogen and oxygen as heteroatoms [2]. The fusion of a benzene ring with an oxazepine ring enhances their biological activity, making them promising candidates for drug development [3].

The synthesis of benzoxazepindione derivatives often involves cycloaddition reactions, similar to those used in the synthesis of oxazepine derivatives, where Schiff bases react with phthalic or maleic anhydrides [4]. This process allows for the creation of a wide range of derivatives by varying the starting materials and reaction conditions. The chemical structure of these compounds includes a benzene ring fused to an oxazepine ring, which can be further modified by incorporating different functional groups to enhance their pharmacological properties [5].

Benzoxazepindione derivatives exhibit a broad spectrum of biological activities, which are crucial for their application in therapeutic medicine [6]. While specific data on benzoxazepindione derivatives are limited, related compounds like benzoxazepines have shown potent anticonvulsant, antidepressant, CNS depressant, antipsychotic, and neuroleptic activities [7]. The versatility of these heterocyclic compounds makes them valuable in the design of novel drugs targeting various neurological disorders. Given their structural similarity to other pharmacologically active compounds like benzodiazepines and benzothiazepines, benzoxazepindione derivatives hold vast potential [8]. Benzodiazepines are widely used for treating anxiety, insomnia, and seizures, while benzothiazepines have been explored for their anticancer, antidiabetic, and anti-inflammatory properties [9]. By modifying the chemical structure of benzoxazepindione derivatives, researchers can tailor their biological activities to target specific therapeutic needs, making them promising candidates for future drug development [10].

As research continues to uncover the pharmacological potential of benzoxazepindione derivatives, advanced synthetic methodologies and computational tools will play a crucial role in optimizing their design [11]. The integration of computer-aided drug design approaches, similar to those used for benzothiazepines, can help predict and enhance the biological interactions of these compounds, thereby streamLining the drug development process [12]. With ongoing advancements in medicinal chemistry, benzoxazepindione derivatives are poised to contribute significantly to the development of novel therapeutic agents [13].

This article concerns the synthesis and characterization of a series of benzoxazepine derivatives and studying their biological activities against selected gram-positive and gram-negative bacteria types.

2. MATERIALS AND METHODS

2.1. Chemicals

All the chemicals were used in this research have been purchased from (CDH, Thomas Baker, Picaso - China, Loba – Chemie, Scharlau, and Aldrich) companies.

2.2. Instruments

The melting point was determined by using electrothermal melting point apparatus model SMP40. For the purity of the prepared compounds, we used the TLC techniques. The FT-IR spectra were recorded using the FT-IR 600 Shimadzu spectrophotometer scale (4000-400) cm^{-1}, in the Department of Chemistry, College of Science, University of Kirkuk, Iraq, ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Varian operating at 400 MHz instrument using DMSO-d^{6} as a solvent in the university of Basra.

2.3. Synthesis

2.3.1. Preparation of Thiazole Schiff Bases Derivatives (A_1-A_8) [14,15]

In a round bottomed flask with a capacity of (100) mL, (0.022 mol, 2.4 g) of thiazole – 2 – carbaldehyde were dissolved in absolute ethanol, followed by addition of (3-4) drops of glacial acetic acid, then (0.022) moles of various aromatic amines were dissolved in (25) mL of absolute ethanol and after obtaining complete dissolution, two mixture were mixed and refluxed for six houres, and the reaction was followed up using TLC technology, after the end of the reaction by cooling the mixture, filtering the precipitate, dried and recrystallized with absolute ethanol

2.3.2. Preparation of Oxazepinediones Derivatives (A_9-A_{16}) [15]

In a round bottomed flask of (50) mL, (0.0021) moles of one of the derivatives of the prepared Schiff bases (A_1-A_8) were dissolved in (20) mL of dry benzene and (0.0021 mol, 0.3 g) of phthalic anhydride were added to it, then the mixture was refluxed for 24 houres in water bath, and the reaction was followed up using TLC technology, the mixture was cooled, and the precipitate was filtered, dried and recrystallized with absolute ethanol

2.4. Biological Activity Study

2.4.1. Solution Preparations [15,16]

The chemical concentrations (25 %, 50 %, and 75 %) mg/mL of some of the prepared compounds were prepared using a DMSO solvent for each of these solid derivatives.

2.4.2. Diffusion Method in Drilling

The agar medium was prepared and sterilized in an autoclave at 121°C and 1 atm for 25 minutes after 25 mL of nutritional agar was added to each dish. Next, using a sterile spreader, 0.1 mL of bacterial culture containing 1.5×10^{8} cells/mL was put onto the nutrient agar to inoculate it. At 0.5 mg/mL, the bacterial concentration was standardized using the McFarland standard. Each plate was divided into three wells, and the dishes were allowed to air dry at room temperature. The plates were then incubated for 24 hours at 37°C after 0.2 mL of each produced concentration (25%, 50%, and 75%) was added using a tiny pipette. Three degrees of antibacterial activity were identified based on the measurement of the inhibition zone widths in millimeters using a transparent ruler: mild (7–10 mm), moderate (10–20 mm), and strong (>20 mm).

2.4.3. Antioxidant Effect Test [18-20]

2,2-Diphenyl-1-picrylhydrazine (DPPH) Antioxidant Assay Kit (ab289847, K2078) has been used as free radical activity to evaluate its radical scavenging toward synthesized compounds (A_9-A_{16}).

2.4.3. Antioxidant Measurement Procedure

Following the prescribed procedure, the percentage of antioxidant activity (% Radical Scavenging Activity, RSA) was calculated as follows:

The reference ascorbic acid solution was prepared in a range of graded concentrations alongside the DPPH solution. The test

substance was then synthesized in a spectrum of three different concentrations, with three replications of each dilution to guarantee experimental accuracy. Maintaining a volumetric ratio of 15:10, equal aliquots of the purple DPPH reagent were added to each test dilution, replication, reference solution, and control.

After that, the reaction mixtures were incubated for 30 minutes in total darkness, during which time a chromatic transition was noticed. If the studied substance demonstrated antioxidant activity, the solution changed from purple to one of several colors (yellow or transparent), indicating its capacity to reduce oxidative processes. In contrast, the combination and the control sample both maintained their purple hue in the absence of antioxidant activity.

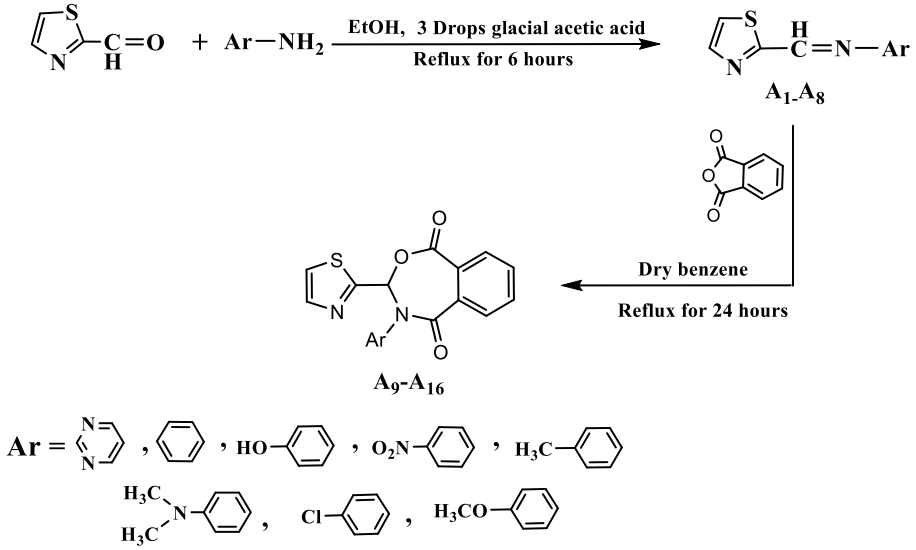
Following incubation, a microplate reader set at 517 nm was used to record the absorbance of all experimental treatments, including controls and synthetic compounds. It was determined that absorbance intensity and antioxidant efficacy were inversely correlated, with lower absorbance values indicating a higher capacity for radical scavenging. The conventional mathematical equation was then used to calculate radical scavenging activity (RSA%) is then calculated using the following equation:

$$\mathrm{RSA}(\%) = \left[\frac{(\mathrm{Ac} - \mathrm{As})}{\mathrm{Ac}}\right] \times 100 \text{ or } \mathrm{RSA}(\%) = \left[1 - \frac{\mathrm{Ac}}{\mathrm{As}}\right] \times 100$$

Where: (Ac) represents the absorbance of the control, and (As) represents the absorbance of the sample.

3. RESULTS AND DISCUSSIONS

Some new series of bezoxazepines derivatives has been synthesized, as shown in Scheme (1). All the new prepared compounds were characterized by FT-IR, ^{1}H-NMR and ^{13}C-NMR spectra.



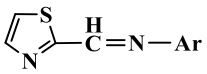
Scheme (1): Rout shows all the prepared compounds (A_1-A_{16})

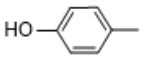
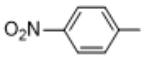
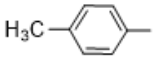
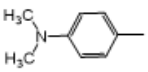
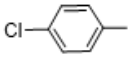
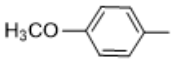
3.1. Characterization of Schiff Base Derivative Compounds (A_1-A_8).

Schiff bases compounds (A_1-A_8) were prepared from the reaction of equimolar of thiazole – 2 – caraldehyde (0.022 mol, 2.48 g) with (0.022 mol) of different aromatic amines in absolute ethanol as a solvent in the presence of (3-4) drops of glacial acetic acid as a catalyst and refluxed for six hours, as shown in Scheme (1).

From the study of FT-IR Spectral absorption, all the spectra of the prepared compounds (A1-A8) indicated the disappearance of the aldehyde carbonyl group stretch peak (C=O), and the disappearance of the symmetrical and asymmetrical stretch peak of the amine group, it was observed that a strong peak due to the elastic vibration of the azomethene group (C=N) was observed at (1586-1627) cm-1, and the appearance of absorption peak at the range (3104-3238) cm-1 belonging to the elastic stretch (C-H) aromatic, with the appearance of two absorption peaks at the range (1528-1594) cm-1 and (1498-1524) cm-1 for stretching (C=C) aromatic. Table (1) shows the physical properties with infrared spectra of the prepared compounds.

Table 1. Some physical properties and IR spectral data of Schiff base derivatives (A_1-A_8).



No.	Substituents group	Physical properties			IR (KBr) cm^{-1}				
	Ar	Yield %	Color	M. P. ^{o}C	ν (C-H) Arom.	ν (C-H) Aliph.	ν (C=N)	ν (C=C) Arom.	Others
A_1		75	Yellowish white	170-172	3238	2990 2949	1586	1528 1511	-----
A_2		65	Yellowish white	71-72	3107	2991 2897	1624	1594 1498	-----
A_3		65	Light brown	153-155	3111	2950 2817	1623	1587 1512	υ (OH) 3469
A_4		69	Yellowish orange	204-206	3130	2926 2855	1607	1581 1515	υ (NO_2) Sym. (1342) Asy. (1515)
A_5		70	Shiny cotton white	86-87	3118	2974 2867	1627	1580 1512	υ CH_3 Sym. (2867) Asy. (2929)
A_6		72	Light brown	136-138	3115	2991 2899	1620	1567 1524	υ $N(CH_3)_2$ Sym. (2899) Asy. (2991)
A_7		73	Greenish white	110-112	3104	2973 2915	1622	1576 1499	υ (C-Cl) 832
A_8		73	Blakish green	83-85	3127	2971 2846	1621	1594 1499	υ (C-O-C) Sym. (2846) Asy. (2971)

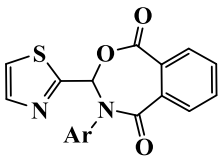
3.2 Characterization of the 1, 3 - Oxazepinediones Derivatives (A_9-A_{16}).

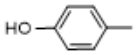
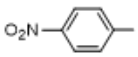
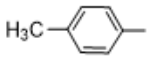
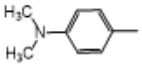
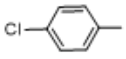
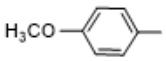
Oxazepinediones derivatives compounds (A9-A16) were prepared from the reaction of (0.0021) mol one of the derivatives of the prepared Schiff bases (A1-A8) with (0.0021 mol, 0.3 g) of phthalic anhydride, then the mixture was refluxed for 24 houres, and the reaction was followed up using TLC technology, as shown in Scheme1.

The infrared spectra for oxazepine (A9-A16) revealed the appearance of the strong peaks at the range (1566-1495) cm-1 attributed to the stretching of the bond (C-N), and the absorption peak at range (3333-3011) cm-1 belonging to stretching, aromatic (C-H), as well as the appearance of two peaks at the range (2952-2818) cm-1 and (2901-2820) cm-1 for the symmetrical and asymmetrical stretching aliphatic (C-H), and new peaks observed at the range (1717-1600) cm-1 and (1787-1695)due to the vibration of the (-CO-N-) and (-CO-O-) for lactams and lactones respectively.

It was also observed that two peaks appeared at the range (1680-1599) cm^{-1} and (1616-1532) cm^{-1} due to the vibration of the aromatic (C=C). Table (2) shows the physical properties with infrared spectra of the prepared compounds The synthesis of thiazolidine-4-one derivatives was confirmed and compared to the literature [21].

Table 2. Some physical properties and IR spectral data of thiazolidine-4-one derivatives compounds (N_{22}-N_{36}).



No.	Substituents group	Physical properties			IR (KBr) cm^{-1}						
	Ar	Yield %	Color	M. P. ^{o}C	ν (C-H) Arom.	ν (C-H) Aliph.	ν (C=O) Lactam, Lactone	ν (C=N)	ν (C=C) Arom.	ν (C-O-C) Asym. Sym.	Others
A_9		76	Yellowish white	233-235	3235	2991	1787	1702	1680 1616	Asy. (1285) Sym. (1074)	ν (C-N) 1524
A_{10}		78	Yellowish white	166-168	3069	2974	1695	1600	1599 1583	Asy. (1271) Sym. (1076)	ν (C-N) 1519
A_{11}		73	Dark brown	170-172	3297	2929	1765	1717	1657 1606	Asy. (1249) Sym. (1111)	ν (C-N) 1540 ν (O-H) 3422
A_{12}		75	Dark brown	178-180	3085	2992	1707	1673	1623 1602	Asy. (1272) Sym. (1080)	ν (C-N) 1566 ν(NO_2), Asy. (1508) Sym. (1339)
A_{13}		79	Yellow	167-169	3129	3011	1712	1658	1605 1547	Asy. (1245) Sym. (1075)	ν (C-N) 1547
A_{14}		75	Redish brown	265-266	3011	2991	1739	1704	1622 1532	Asy. (1231) Sym. (1103)	ν (C-N) 1532 υ (CH_3) Asy. (2901) Sym. (2818)
A_{15}		72	White	193-195	3333	2992	1711	1643	1599 1582	Asy. (1242) Sym. (1075)	ν (C-N) 1495 (C-Cl), 762
A_{16}		67	Dark brown	142-143	3147	2975	1723	1643	1604 1581	Asy. (1243) Sym. (1074)	ν (C-N) 1549 Asy.CH_3 (2820) Sym.CH_3 (2952)

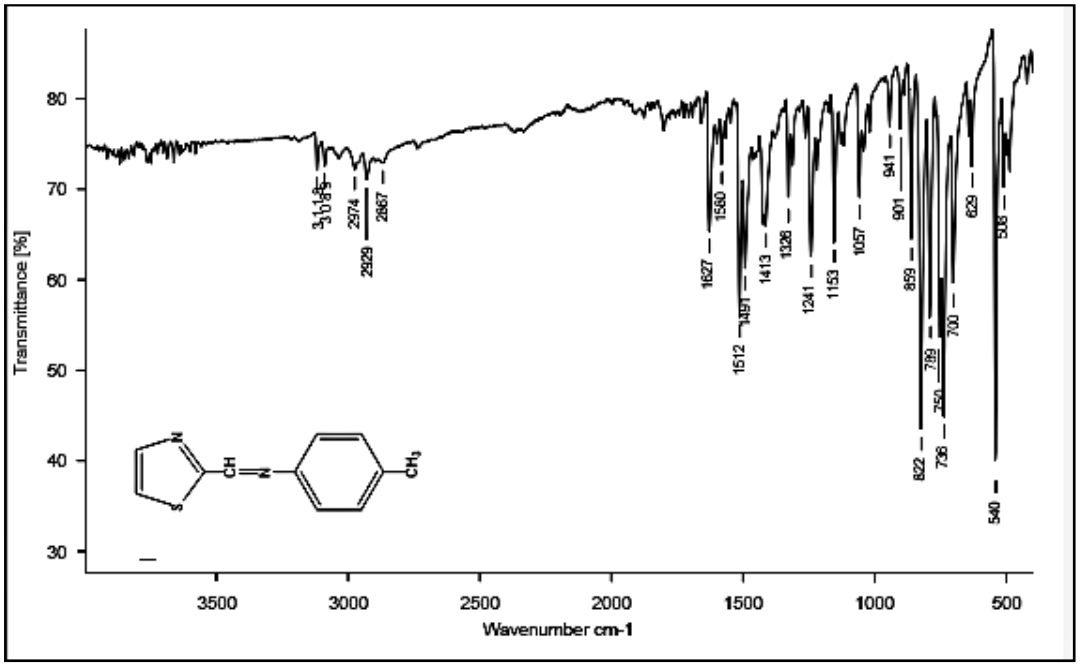


Fig. 1. FT-IR spectrum for Schiff base compound (A_5).

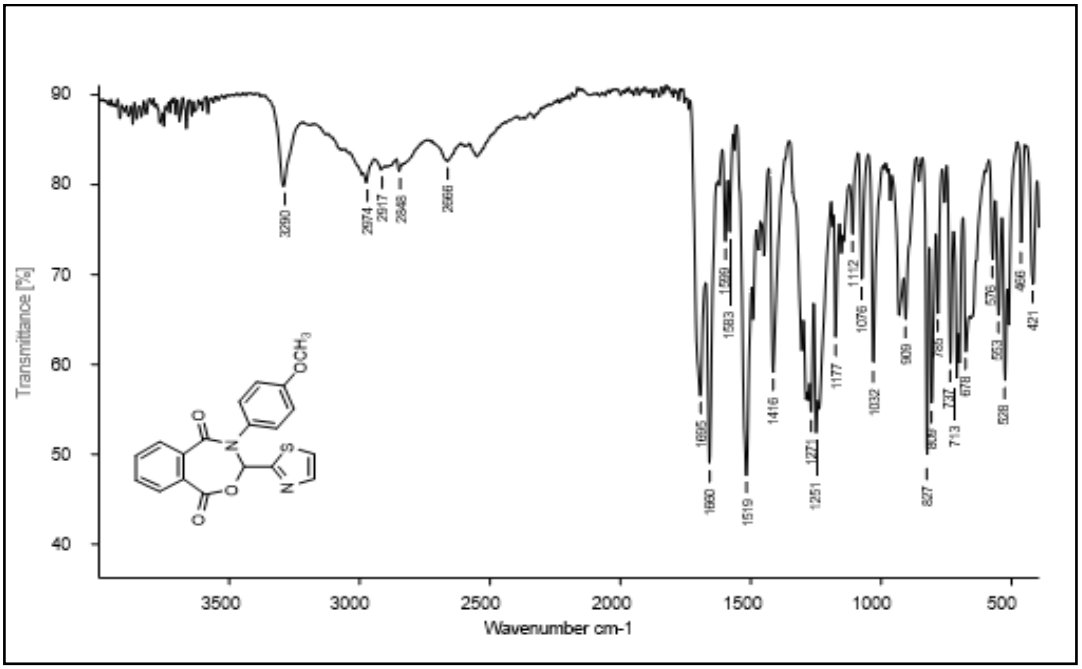


Fig. 2. FT-IR spectrum for oxazepine compound (A_{16}).

When studying the proton NMR spectrum of the prepared benzoxazepindione compounds (A_{13}) using solvent (DMSO-d^6) and (TMS) as a reference, it was observed that a singlet signal appeared at (2.27) ppm attributable to (CH_3) group protons, and appearance of a multiple signals at (7.65 – 7.98) ppm due to the protons of the aromatic ring labeled (2), and the appearance of a singlet signal at (8.10) ppm due to (CH_3) for Oxazepindione ring labeled (3), other spectra are shown in figure (3) and table (3).

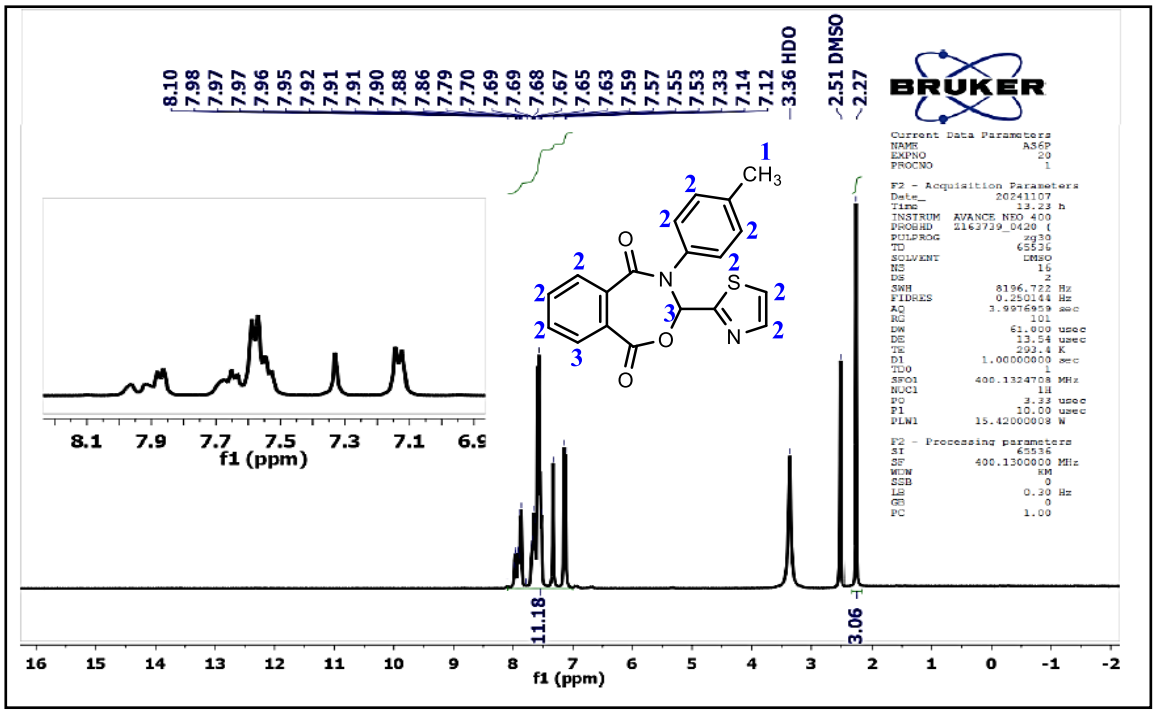


Fig. 3. ^{1}H-NMR spectrum for compound (A_{13}).

The ^{13}C-NMR spectrum of compound (A_{13}) clearly gives a singlet peak at (20.97) ppm belongs to methyl group labeled (a), peak at (119.95) ppm refers to labeled carbon (b), peak at (127.72) ppm corresponds to carbo (C) in thiazole ring, peaks at (128.24) ppm for benzene carbons labeled (d), peaks at the region (127.72-130.47) ppm for four aromatic carbons labeled (e), peaks at the range (131.23) ppm for aromatic carbons briged withoxazepine ring labeled (f), peak at the region (135.13) ppm for benzene ring attached to nitrogen in oxazepane ring labeled (h), peak at (139.40) ppm for another carbon of the thiazole ring, peaks at (167.59) ppm for the carbonyl carbon (lactone) and finally peak at (169.13) ppm for another carbonyl carbon (lactam), the spectra are shown in figure (4) and table (3).

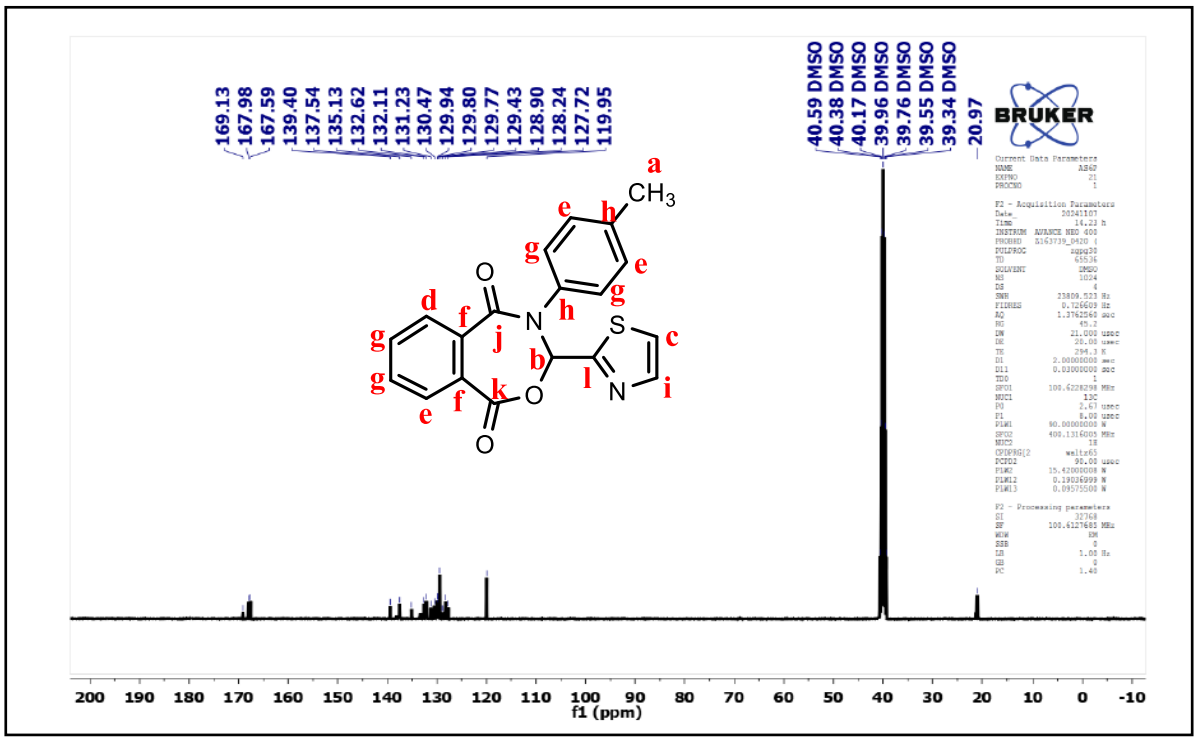
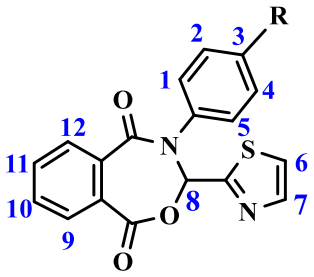


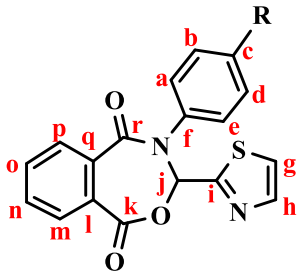
Fig. 4. ^{13}C-NMR spectrum for compound (A_{13}).

Table 3. ^{1}H-NMR spectrum data for A_{11}-A_{16}.



Comp. No.	R	^{1}H-NMR data of (δ-H) in ppm
A_{11}	- OH	δ (6.71-6.84), (m, 2H, labeled 2, 4); δ (7.35-7.92), (m, 7H, labeled 1, 5, 6, 7, 10-12); δ (8.04-8.06), (m, 1H, labeled 3); δ (13.08, 1H, for phenol ring).
A_{12}	- NO_2	δ (7.67-7.96), (m, 7H, labeled 1, 5, 6, 7, 10-12); δ (8.01-8.33), (m, 4H, labeled 2, 4, 8, 9).
A_{13}	- CH_3	δ (2.27), (s, 3H, methyl); δ (7.12-7.97), (m, 9H, labeled 1, 2, 4, 5-7, 10-12); δ (7.98-8.10), (m, 2H, labeled 8, and 9).
A_{14}	- $(CH_3)_2$	δ (3.21), (s, 6H, dimethyl); δ (7.63-7.69), (m, 2H, labeled 2, and 4); δ (7.70-7.88), (m, 2H, labeled 1, and 5); δ (7.90-7.99), (5H, labeled 6, 7, 10-12); δ (8.15-8.18), (m, 1H, labeled 8).
A_{15}	- Cl	δ (7.39-7.93), (m, 9H, labeled 1, 2, 4-7, 10-12); δ (7.98-8.09), (m, 2H, labeled, 8, 9)
A_{16}	- OCH_3	δ (2.87), (s, 3H, methyl); δ (7.16-7.84), (m, 2H, labeled 2, and 4); δ (7.89-7.99), (m, 7H, labeled 1, 5-7, 10-12); (8.17), (m, 2H, labeled 8, 9)

Table 4. ^{13}C-NMR spectrum data for A_{11}-A_{16}.



Comp. No.	R	^{13}C-NMR data in ppm
A_{11}	- OH	δ (115.41), for phenolic ring labeled (a); δ (121.71), for phenolic ring labeled (b); δ (123.47), for phenolic ring labeled (c); δ (123.92), for phenolic ring labeled (d); δ (128.24), for phenolic ring labeled (e); δ (128.86), for phenolic ring labeled (f); δ (129.66-129.88), for thiazole ring labeled (g); δ (130.59), for thiazole ring labeled (h); δ (131.24), for thiazole ring labeled (i); δ (131.73), for oxazepine ring labeled (j); δ (132.01), for oxazepine ring labeled (k); δ (133.30), for oxazepine ring labeled (l); δ (139.50), for thiazole ring labeled (m); δ (139.50), for benzene ring attached to oxazepane ring labeled (m); δ (140.82), for benzene ring attached to oxazepane ring labeled (n); δ (145.04), for benzene ring attached to oxazepane ring labeled (o); δ (167.16), for benzene ring attached to oxazepane ring labeled (p); δ (168.10), for benzene ring attached to oxazepane ring labeled (q); δ (169.15), for benzene ring attached to oxazepane ring labeled (r);

A_{12}	**- NO_2**	δ (112.81), for nitro benzene ring labeled (j); δ (125.81), for nitro benzene ring labeled (g); δ (126.38), for nitro benzene ring labeled (p); δ (126.88), for nitro benzene ring labeled (b, d); δ (128.26), for benzene ring attached to oxazepane ring labeled (m); δ (128.55-128.82), for two benzene rings labeled (a, e, l, n, o, q); δ (136.02), for benzene ring attached to oxazepane ring labeled (c); δ (136.63-137.63), for carbones labeled (f, h); δ (138.73-152.60), for crbones in oxazepane ring labeled (r); δ (169.16), for oxazepane ring oxazpine ring labeled (k).
A_{13}	**- CH_3**	δ (20.97), for methyl group; δ (119.95), for carbon in oxazepane ring labeled (j); δ (127.72), for thiazole ring labeled (g); δ (128.24), for benzene ring attached to oxaepine ring labeled (p); δ (128.90), for toluene ring labeled (b, d, m); δ (129.43-130.47), for benzene ring labeled (l, q); δ (131.23-132.62), for benzene ring labeled (a, e, n); δ (135.13), for thiazole ring labeled (h); δ (137.54), for oxaepine ring labeled (r); δ (139.40), for oxaepine ring labeled (k); δ (167.59-167.98), for thiazole ring labeled (l).
A_{14}	**- $(CH_3)_2$**	δ (37.32), for methyl groups; δ (120.04), for oxazepane ring labeled (j); δ (128.43), for thiazole ring labeled (g); δ (129.95), for benzene ring labeled (p); δ (129.61), benzene ring labeled (f); δ (129.80-130.50) labeled (a, e, n, o, q); δ (137.56), for thiaole ring labeled (h); δ (139.44), benzene ring labeled (i); δ (167.96), oxazepine ring labeled (j); δ (168.48), for oxazepine ring labeled (k); δ (169.83), benzene ring labeled (l);
A_{15}	**- Cl**	δ (121.43), for oxazepane ring labeled (j); δ (123.96-125.82), for thiazole ring carbon labeled (g); δ (127.30-128.24), for benzene ring labeled (p); δ (129.02-129.98), for benzene ring labeled (a, e); δ (130.30-132.26), for benzene ring labeled (b, d); δ (135.23-138.96), for benzene ring labeled (l, n, o, q); δ (139.11), for benzene ring labeled (f); δ (167.98), for thiazole ring labeled (h); δ (169.40), for thiazole ring labeled (i).
A_{16}	**- OCH_3**	δ (37.32), for methyl groups; δ (120.04), for oxazepane ring labeled (j); δ (128.43-129.96), for benzene ring labeled (b, d); δ (130.50), for thiazole ring labeled (g); δ (131.26-132.62), for benzene rings labeled (a, e, p); δ (135.10), for benzene ring labeled (m); δ (137.56-139.44), for benzene rings labeled (f, l, n, o, q); δ (167.96), for thiazole ring labeled (h); δ (168.48), for benzene ring labeled (c); δ (169.83), for thiazole and oxazepane rings labeled (I, k, r)

3.3. Evaluation of the Biological Activity of Some Prepared Compounds

3.3.1. Measurment of Biological Activity Against Positive and Negative Bacteria

A panel of clinically relevant bacterial strains, including Gram-positive Staphylococcus aureus (S. aureus) and Staphylococcus epidermidis (S. epidermidis), as well as Gram-negative Escherichia coli (E. coli) and Pseudomonas aeruginosa (P. aeruginosa), were used to rigorously evaluate the bacteriostatic activity of a few synthesized compounds. These microbial taxa were carefully selected because of their potential for pathogenicity and varying susceptibilities to antimicrobial treatments.

The main methodological technique used was the disk diffusion assay, in which the antibacterial potency was determined by carefully measuring the inhibition zone sizes in millimeters. The resulting results showed that the produced compounds had an inhibitory effect on both Gram-positive and Gram-negative bacteria that were dependent on concentration. Based on their inherent resistance mechanisms and virulence characteristics, the pathogenic strains were carefully chosen.

Additional bioactivity evaluations were carried out using the agar well diffusion technique, in which the widths of the growth suppression zones were measured to systematically estimate the inhibition efficiency, as shown in (Table 5.).

Table 5. Shows the inhibition zone diameters in (mm) around the prepared compounds.

Comp. No.	Gram-positive Bacteria						Gram-negative Bacteria					
	S. aureus			*S. epidermidis*			*E. coli*			*P. aeruginosa*		
	25%	50%	75%	25%	50%	75%	25%	50%	75%	25%	50%	75%
A_9	14	17	21	11	16	19	11	17	27	12	13	18
A_{10}	10	16	17	10	11	15	10	12	16	9	11	16

A_{11}	11	14	17	8	13	23	11	25	31	12	14	26
A_{12}	10	17	20	22	29	31	11	16	20	19	24	26
A_{13}	11	13	15	8	9	11	8	11	13	8	9	13
A_{14}	15	16	19	10	11	13	13	14	20	11	13	14
A_{15}	7	10	11	n.a	n.a	n.a	n.a	n.a	n.a	9	10	15
A_{16}	16	16	18	8	10	20	19	20	21	10	14	17
Ciprofloxacine	23	31	43	21	29	38	0	23	35	18	31	37

(Table 5.) evaluates the antibacterial efficacy of chemical compounds (A_9 to A_{16}) and Ciprofloxacin as a blank against Gram-positive (*S. aureus*, *S. epidermidis*) and Gram-negative (*E. coli*, *P. aeruginosa*) bacteria. Inhibition activity was assessed at 25%, 50%, and 75% concentrations, measured as inhibition zone diameters in (mm). Inhibition generally increases with concentration, as expected. Effectiveness varies among compounds, with (A_9, A_{12}, A_{13}, and A_{15}) showing notable activity, Gram-positive bacteria are generally more susceptible, likely due to structural differences in their cell walls. Ciprofloxacin serves as a control, exhibiting strong inhibition against Gram-positive bacteria and increasing inhibition against Gram-negative bacteria at higher concentrations.

Among the tested compounds, (A_9) shows some Gram-positive inhibition, increasing with concentration, whereas (A_{11}) exhibits no measurable activity. (A_{10}) moderately inhibits both Gram- positive and Gram-negative bacteria, with a marginal concentration-dependent increase. (A_{14}) displays moderate to strong inhibition across bacterial types, suggesting promising antibacterial potential, while (A_{16}) is particularly effective against *P. aeruginosa*, indicating potential selectivity. When compared to Ciprofloxacin, the antibiotic consistently outperforms most tested compounds against Gram-positive bacteria, particularly at higher concentrations. Against Gram-negative acteria, Ciprofloxacin shows minimal inhibition at 25% but increases at 50% and 75%, matching or exceeding the tested compounds.

Missing values limit full analysis, and single-experiment data necessitate further replication. Mechanistic studies are required to determine how these compounds inhibit bacterial growth. Overall, compounds (A_9, A_{12}, A_{13}, and A_{15}) exhibit antibacterial activity, though Ciprofloxacin remains superior, particularly against Gram-positive bacteria. The biological activity results of (A_9, A_{12}, A_{13}, and A_{15}) showed inhibition effects on similar gram-positive and gram-negative bacterias compared to the literature disregarding the concentrations of the solutions used by Beebany et al. [22,23]. Further studies should explore their mechanisms and optimize their antibacterial properties shown in (Fig. 5 and 6).

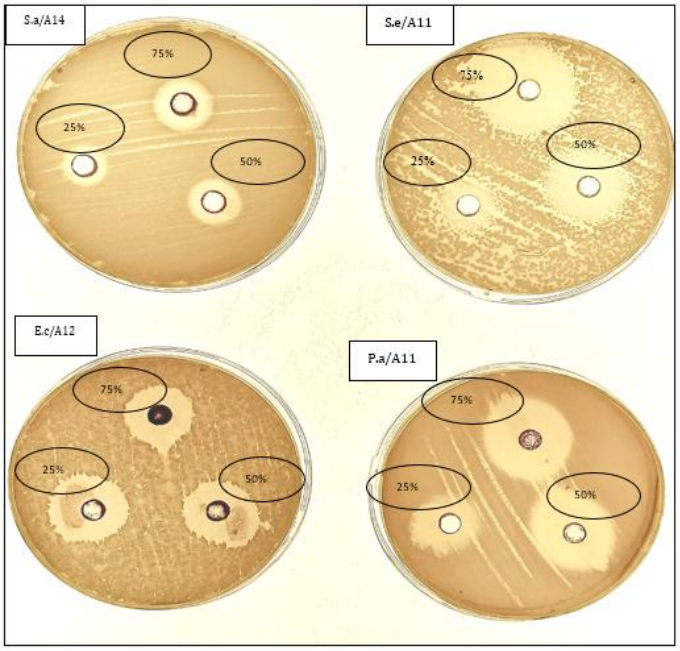


Fig. 5. Antibacterial activity of the compond (A_{12}).

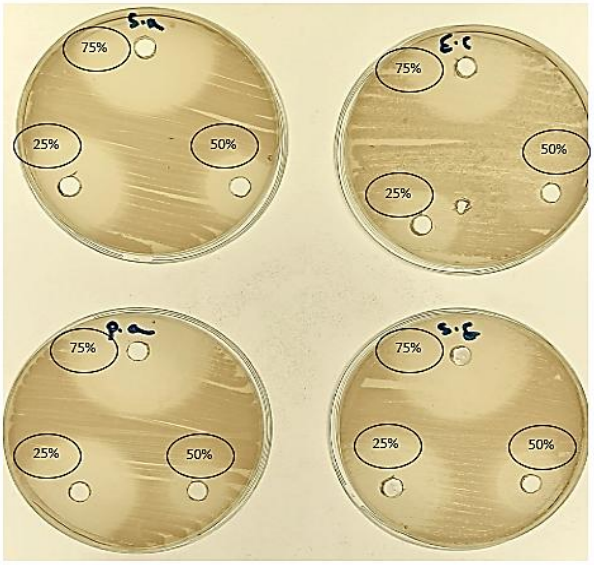


Fig. 6: Antibacterial activity of the control.

3.3.2. Measurment of Antioxidant Assay

The methodology described in references [24-26] was strictly followed when quantifying antioxidant activity, which is reported as the Radical Scavenging Activity percentage (RSA%). The reaction mixtures underwent regulated incubation after the purple-hued DPPH reagent was precisely added to the solutions in the microplate (MTP) for the evaluation of oxidative inhibition. Following incubation, spectrophotometric analysis was performed on all experimental treatments, including control and synthetic compounds, using a microplate reader set to an absorption wavelength of 517 nm. Absorbance intensity and antioxidative efficacy were shown to be directly inversely proportional, with lower absorbance levels indicating greater capacity for radical scavenging. The standardized computational formula was then used to calculate the RSA%.

Table 6. Antioxidant activity test results of the compounds against the DPPH reagent.

Compounds	**Radical Scavenging Activity Strength RSA %**		
	25 %	**50 %**	**75 %**
A9	70.16	81.66	**83.16**
A10	81.66	85.00	**86.33**
A11	57.33	69.50	**78.00**
A12	74.00	78.83	**87.50**
A13	75.00	83.33	**85.00**
A14	6.660	16.66	**33.33**
A15	75.16	85.16	**91.00**
A16	60.33	71.66	**73.33**
Ascorbic acid	94.00	95.50	**95.66**
Control (DPPH)	Negative	Negative	**Negative**

The results of the antioxidant activity test for sp.m compounds after a 30-minute incubation and it is observed that all compounds exhibited antioxidant activity across all concentrations and replicates.

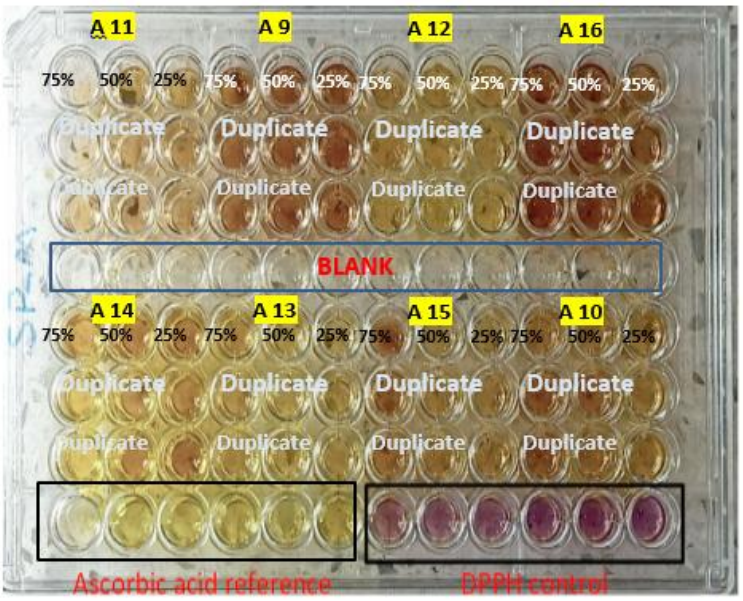


Fig. 7. Antioxidant activity of the some prepared componuds

4. CONCLUSIONS

This study synthesized and analyzed novel benzoxazepine compounds utilizing FT-IR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy. The spectrum investigation revealed the structural development of Schiff bases (A_1-A_8) and their subsequent conversion to oxazepinedione derivatives (A_9-A_{16}). The disappearance and reappearance of distinctive functional group peaks in FT-IR spectra, as well as the comprehensive NMR investigation, confirmed the chemical changes.

Promising antibacterial activity against both Gram-positive and Gram-negative bacteria was shown by the biological examination of certain chemicals. Significant inhibition was shown by compounds A_9, A_{12}, A_{13}, and A_{15}, especially against Gram-positive bacteria; nonetheless, Ciprofloxacin was still the more effective standard. The findings imply that certain chemicals exhibit selective activity and that structural variables affect antibacterial efficiency. To improve their antibacterial potential, more mechanistic research and optimization are required.

Furthermore, as demonstrated by their capacity to scavenge radicals in the DPPH assay, every evaluated molecule demonstrated antioxidant activity. These results demonstrate the potential of benzoxazepine derivatives as physiologically active substances possessing antioxidant and antibacterial qualities. Future studies should concentrate on examining their mode of action, possible pharmacological uses, and structural alterations for increased efficacy.

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