How to Cite:
Jebur, M. H., Albdere, E. A., Al-Hussainawy, M. K., & Alwan, S. H. (2022). Synthesis and characterization of new 1,3-Oxazepine-4,7-dione compounds from 1,2-diaminobenzene. *International Journal of Health Sciences*, *6*(S4), 4578–4589. https://doi.org/10.53730/ijhs.v6nS4.9123

Synthesis and characterization of new 1,3-Oxazepine-4,7-dione compounds from 1,2-diaminobenzene

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***Abstract*---**In this research, done synthesized a series of new 1,3-oxazepine-4,7-dione derivatives as D1-D3 compounds via using [2+5] cycloaddition reaction. Synthesized compounds that have been bis azo groups [B1-B3] from 1,2-diaminobenzene via coupling its diazonium salt with phenoxide anion of 4-alkoxybenzaldehyde which Alkoxy was as pentyl, hexyl, and Heptyl groups. These compounds B1-B3 are condensed with 4-Bromoaniline in Schiff bases reactions to give bisazoimine derivatives C1-C3. The compounds C1-C3 were produced by cycloaddition reaction to produce 1,3-oxazepine-4,7-dione derivatives D1-D3. The structures of the synthesized compounds are characterized by spectroscopic methods, such as FTIR, and 1HNMR spectra with the elemental composition analysis. The compounds D1-D3 that are synthesized play a big role in the inhibition of growth.

***Keywords*---**1,3-oxazepine, Schiff bases synthes, Cyclo addition, biological activity.

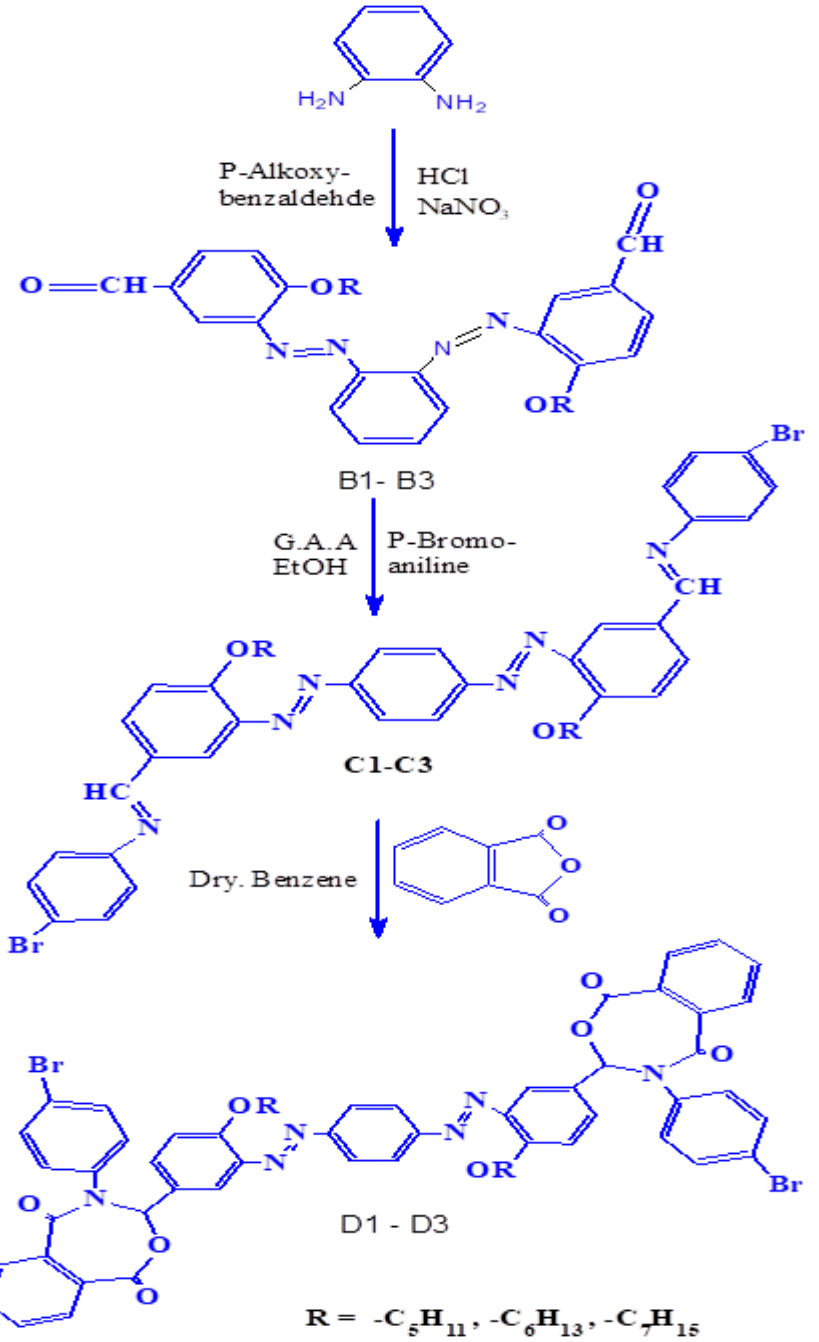
Introduction

Azo compound, any organic compound, diverse set of both natural and synthetic molecules containing at least one double-bonded nitrogen group. Though there is an extremely wide range of azo compounds, the most common are pigments and dyes (Aljamali, 2015). Oxazepine is a heterocyclic molecule that consists of a seven-membered ring and includes oxygen and nitrogen atoms (Prakash et al., 2021). The biological activity of oxazepine compounds include anticonvulsant (Sharma et al., 2008), antiviral (Campiani et al., 1996), antifungal (Kumar & Joshi, 2009), and other uses in many applications. Cycloaddition reaction is the kind of reaction used in the production of the 1,3-oxazepine chemical ring classed as (2+5) to create seven cycloaddition reactions. Two imine groups were added to a five-membered component, such as phthalic anhydrides, to form a heterocycle with seven members (Carruthers, 2013; Jørgensen, 2002). The antibacterial and antiviral functions of a molecule are entirely dependent on chemicals that target viruses and bacteria biologically, limit their rate of growth, and are damaging to injured tissue. Recently produced antibacterial agents include natural compounds that have been chemically modified (Aftan et al., 2021; Kanichar et al., 2014).

Experimental Part

Characterization

The FTIR spectra use an FT-IR instrument that has model 8300 Shimadzu. 1HNMR spectra that were used Brüker ACF 400 spectrometer. The chemicals used were obtained from different such as, Fluka, BDH, and Merck companies.



Scheme 1. Synthesis of substituted 1,3-oxazepine-4,5-dione D1-D3.

General procedure for the synthesis of Azo compounds (B1-B3)

In cooling bath, added %10 HCl solution (5 mL) to 1,2-diaminobenzene (0.01 mol) then add (2-3) drops of Conc. HCl into test tube No.1. On the other hand, prepare $NaNO_2$ (0.02 mole, 1.379 g) in distilled water (5 mL) in test tube No.2.When the

temperature of the solution in test tube No. 1 became (0-5 ℃), added test tube No. 2 to test tube No.1. Prepare each solution 4-pentoxybenzadehyde as R1 (0.02 mole), 0.02 mole 4-hexoxylbenzaldehyde R2, 0.02 mole 4-heptoxylbenzaldehyde R3, in (10 ml) %10 NaOH into test tube No.3. Finally, added the mixture of solutions into test tube No. 3 (Zhang et al., 2020). Then filtration of the solution, and collected the precipitate.

General procedure for the synthesis of Schiff's base compounds (C1-C3) (Ye et al., 2018).

(2-3) drops of glacial acetic acid were added to each compound (B1-B3) (0.01 mol), then mixture with 4-bromoaniline (0.02 mole) in a solvent, such as 20 ml of EtOH. Refluxed the mixture of solution for 3 hours. Finally, the precipitates were formed, collected by filtration, dried, and recrystallized. Listed in Table 1.

Table 1
Physical properties of Schiff's base compounds (C1-C3)

ComP. No.	Yield %	Colour	m.p.℃
C1	67	Brown	165-170
C2	66	Brown	168-172
C3	70	Dark brown	166-171

General procedure for the synthesis of Oxazepine compounds (D1-D3) (Alfatlawi et al., 2018; Ayfan et al., 2019)

The mixture of each Schiff's bases (C1-C3) (0.01mol) with 0.02-mole phthalic anhydride in 20 ml of dry benzene. Then, refluxed the mixture. Finally, filtration of solution and collected the precipitate and recrystallized via dry 1,4-dioxan.

Table 2
Physical properties of 1,3-Oxazepine-4,7-Dione derivative(D1-D3)

ComP. No.	Yield %	Colour	m.p.℃
D1	69	Light brown	230-235
D2	63	Brown	228-232
D3	68	Brown	219-224

Results and Discussion

The compounds 4-Alkoxybenzaldehyde as start materials were prepared from the reaction of 4-hydroxybenzaldehyde with appropriate alkyl halides (1-Bromo pentane and 1-Bromo hexane, 1-Bromo heptane) (Sleevi et al., 1991). The azo compounds form from a diazonium salt and a coupling component. The aryl diazonium ion is directed to the meta position with respect to the carbonyl group and ortho site with respect to the alkoxy group (Du & Huang, 2019). The titled compounds were synthesized from the reaction of previously synthesized compounds (B1 - B3) with 4-Bromoaniline through the condensation reaction.

FT-IR spectra for compounds C1-C3 showed in Figures (1, 3) the disappearance of the -NH_2 group and on other hand the appearance of a new imine group in the range (1636 -1642 cm^{-1}) (Nolte et al., 2021). The bands at the range (3062 – 3081cm^{-1}) for the C–H aromatic stretching. (2984 – 2870 cm^{-1}) for asymmetrical and symmetrical C - H aliphatic stretching, while the azo groups appeared at (1541-1453cm^{-1}) and bands at (1593-1606cm^{-1}) returned to C = C aromatic stretching (Ozaki et al., 2021).

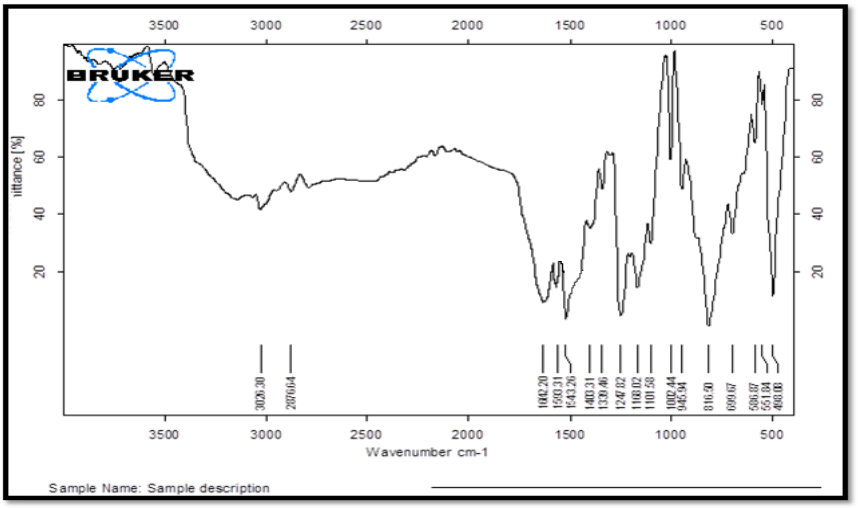


Figure 1. FT-IR spectra of compound C1.

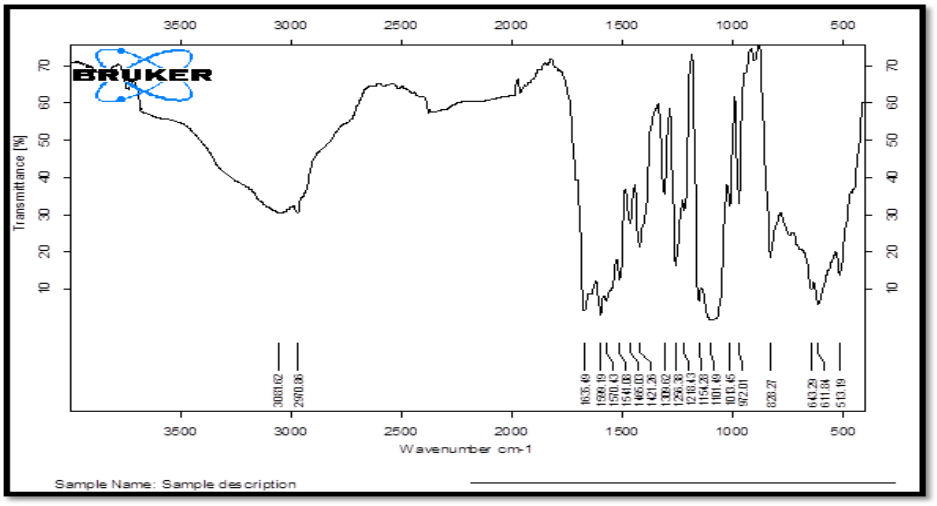


Figure 2. FT-IR spectra of compound C2.

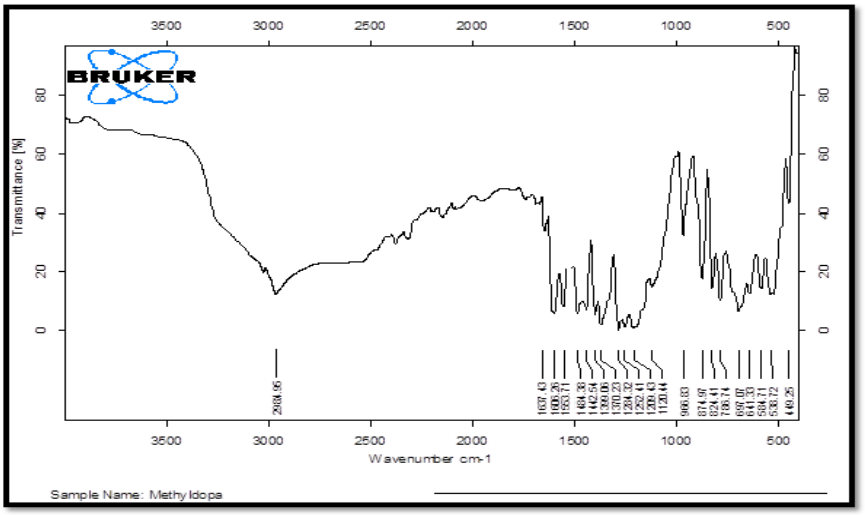
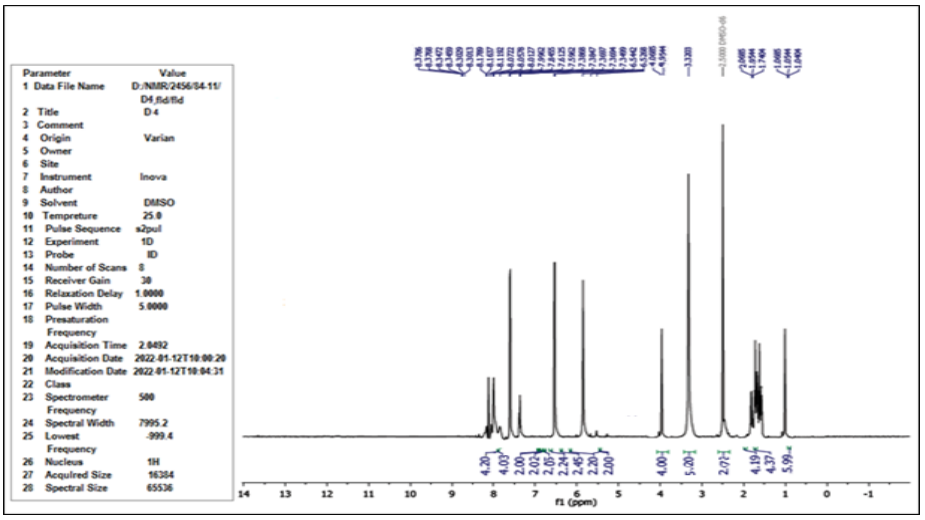


Figure 3. FT-IR spectra of compound C3.

The structure of this group was identified by using ^{1}HNMR spectroscopy. The ^{1}HNMR spectrum of compound C3 is shown in Figure 5, the proton of the imine group CH=N (2H) generates a signal at 8.37 ppm, and the aromatic protons generate signals at 6.52 – 8.17 ppm (Mandal & Paul, 2022). At 1.04 - 1.06, six protons showed as a triplet, which could be referred to $–CH_3$, and 20 protons appeared as a multiplet, which could be referred to $–CH_2$- CH_2. At 3.32-4.06 (4H), the $–OCH_2$ groups of the heptyl group appeared as a triplet (Roduner et al., 2019).



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3 Comment	
4 Origin	Varian
5 Owner	
6 Site	
7 Instrument	Inova
8 Author	
9 Solvent	DMSO
10 Tempreture	25.0
11 Pulse Sequence	s2pul
12 Experiment	1D
13 Probe	ID
14 Number of Scans	8
15 Receiver Gain	30
16 Relaxation Delay	1.0000
17 Pulse Width	5.0000
18 Presaturation Frequency	
19 Acquisition Time	2.0492
20 Acquisition Date	2022-01-12T10:00:20
21 Modification Date	2022-01-12T10:04:31
22 Class	
23 Spectrometer Frequency	500
24 Spectral Width	7995.2
25 Lowest Frequency	-999.4
26 Nucleus	1H
27 Acquired Size	16384
28 Spectral Size	65536

Figure 5. 1HNMR spectrum of compound C3.

The synthesized compounds of Oxazepine produce via Schiff`s base compounds that reacted with phthalic anhydride (Jabar et al., 2020). Figures 6 showed absorption bands at (1722-1731) cm^{-1} that returned to (C=O of lactone stretching), (1664-1668) cm^{-1}, and (C=O of lactam stretching) (Zhang et al., 2020). The bands at (3078-3140) cm^{-1} that for (C– H) of the aromatic ring, then (2897-

2976) cm^{-1} for (ν C–H) of aliphatic chain, (1510-1524) cm^{-1} (ν N=N) (Sallal & Ghanem, 2018).

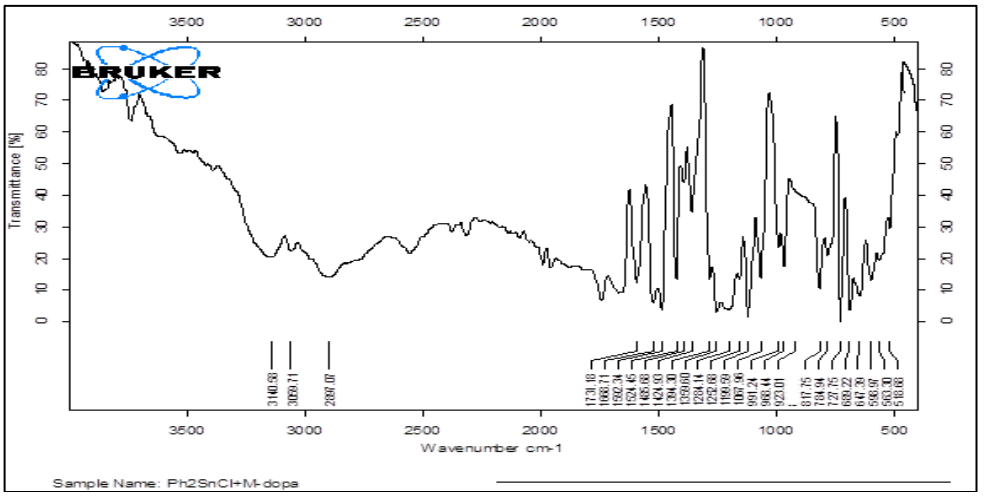

Figure 5. FT-IR spectra of compound D1

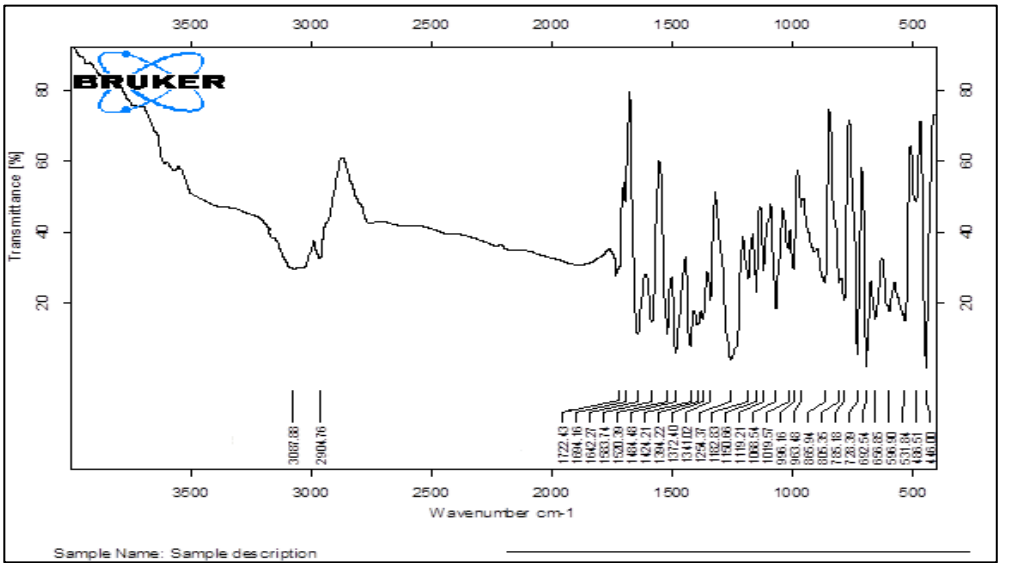

Figure *6.* FT-IR spectra of compound D2.

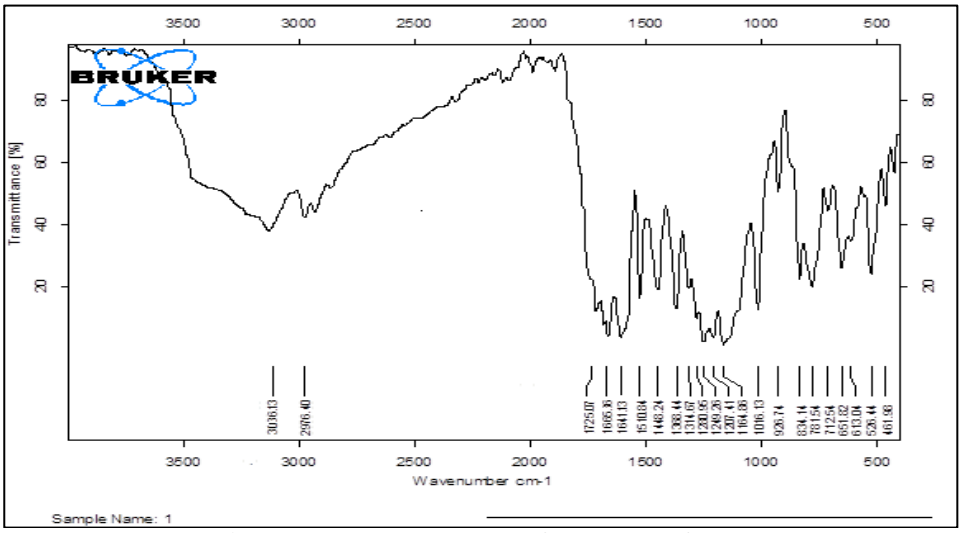

Figure *7*. FT-IR spectra of compound D*3*.

[1]HNMR spectroscopy was used to confirm the structure of these compounds. Figure 8 shows the [1]HNMR spectrum of compound D1, the following characteristic chemical shifts (d6 -DMSO, ppm) appeared: signal observed at δ 6.9 – 7.4 ppm (18H). Four protons appeared as a doublet at δ 8.1 ppm. Six protons appeared as a triplet at δ 0.93-0.95 which could be assigned to $–CH_3$, protons appeared as a multiple at δ 1.6-1.9 ppm which could be assigned to $(-CH_2-)_6$ (24 H). The $-OCH_2$ groups of pentyl substituent appeared as a triplet at δ 3.80-3.83 ppm (Alfatlawi et al., 2018).

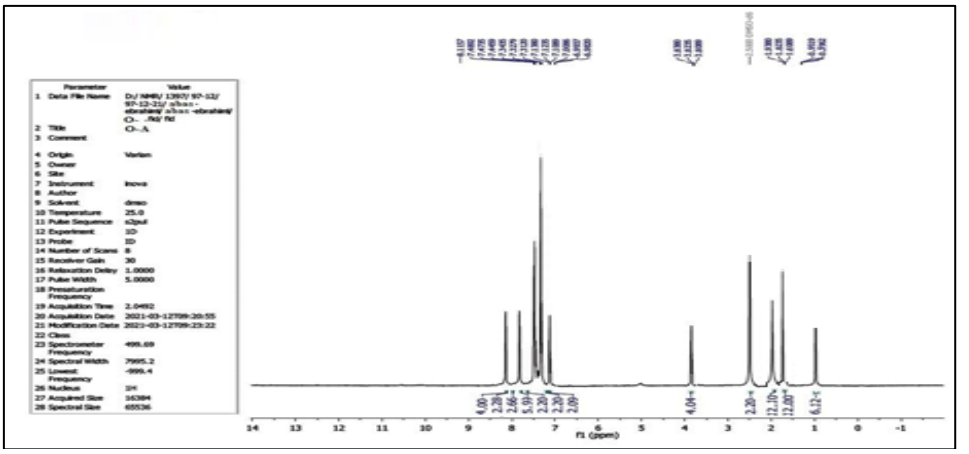

Figure 8. 1HNMR spectrum of compound D1.

Table 3
Elemental composition analysis for compounds D1-D3.

Compound	Measured % (Calculated; %)		
	C	H	N
D1	62.52(62.46)	5.97 (5.90)	4.50 (4.55)

D2	51.36 (51.28)	7.94 (7.82)	5.35 (5.44
D3	53.15 (53.03)	7.20 (7.12)	8.18 (8.25)

As seen in Figure 9, the EDX mapping of compounds D1-D3 including additives reveals the distribution and relative abundance of atoms within the mixes. The Figures clearly depict the uniform distribution of components inside these complexes. Bromine and carbon atoms are numerous and widely dispersed throughout the mixtures. In addition, the photos suggest that these molecules include additional elements (nitrogen and oxygen) (Scimeca et al., 2018).

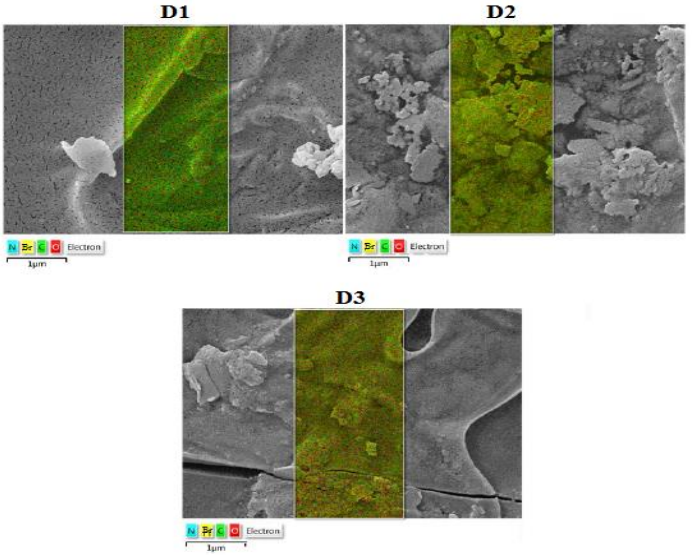

Figure 9. EDX mapping for 1,3-Oxazepine-4,5-dione compounds.

Oxazepine particle shape and size, amount of cross-sectioning, and homogeneity may be determined using FESEM analysis (Xie et al., 2007). FESEM images suggest that Oxazepine compounds are extremely homogenous and have relatively smooth surfaces, as shown in Figure 10.

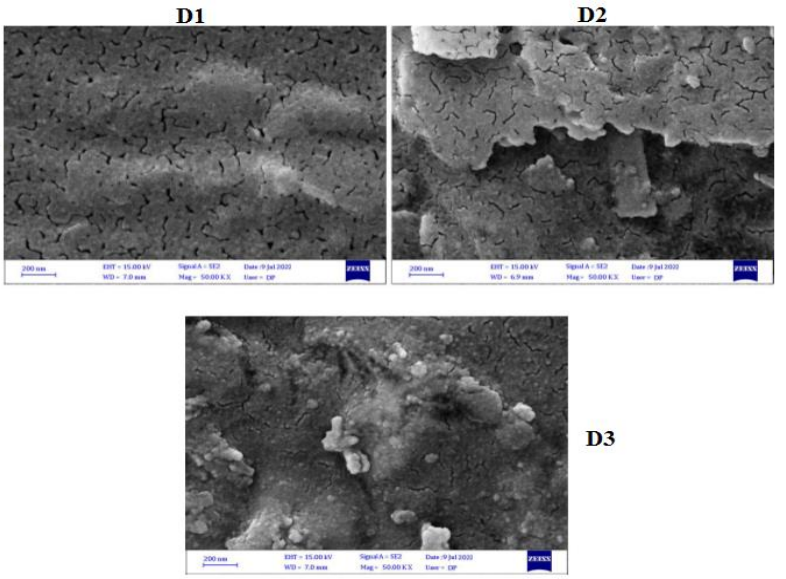

Figure 10. FESEM images for compounds D1-D3.

Biological activity

The synthesized compounds were tested against different types of gram-positive bacteria such as *Staphylococcus aureus,* in addition to gram-negative bacteria such as *Escherichia coli and Bacillus*. The compounds D1-D3 were used at a concentration of 10, 50, and 100 µg/ML via used the agar diffusion method (De et al., 2019). The results are shown in Table 4.

Table 4
Antibacterial activities of the compounds (D1-D3).

Sample	Staphylococcus aureus	Escherichia coli	Bacillus
D1	++	++	+
D2	+	+	-
D3	-	++	+

Note: (-) = No inhibition, (+) =10-14 mm, (++): 15-22 mm.

Conclusions

In conclusion, we have synthesized a series of new 1,3-oxazepine-4,7-dione derivatives using a Schiff's bases synthesis. In addition, all newly synthesized 1,3-oxazepine-4,7-dione were tested as antibacterial via the use of different types of bacteria such as *Staphylococcus aureus, escherichia coli, and bacillus,* these compounds that synthesized play a big role as an inhibition for growth of these bacterial via used different concentrations of Oxazepine compounds D1-D3.

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