Kirkuk Journal of Science Vol. 18, Iss. 3, p 21-31, 2023 doi:10.32894/kujss.2023.143144.1119

Synthesis, Characterization of New Phenylene Bis Tetrazole and Bis Benzoxazepinedione Derivatives from some Bis Imines with its Biological Activity Assessment

Shakhawan Beebany

Department of Chemistry , College of Sciences, University of Kirkuk, Kirkuk, Iraq.
*Corresponding author : sh.beebany@uokirkuk.edu.iq

Article Information

Article Type:
Research Article

Keywords:
Bistetrazole; Bisbenzoxazepinedione; Schiff cyclization; Bisimines; Sodium azide.

History:
Received: 1 September 2023
Revised: 25 September 2023
Accepted: 27 September 2023
Published: 30 September 2023

Citation: Shakhawan Beebany, Synthesis, Characterization of New Phenylene Bis Tetrazole and Bis Benzoxazepinedione Derivatives from some Bis Imines with its Biological Activity Assessment., Kirkuk Journal of Science, 18(3), 21-31, 2023, https://doi.org/10.32894/kujss.2023.143144.1119

Abstract

Some new phenylene bis tetrazole (T1-3) and bis benzoxazepinedione (B1-3) derivatives have been successfully synthesized through cyclization reaction for some bisimines (S1-3). The bisimines were transferred to heterocyclic compounds by adding sodium azide and phthalic anhydride to form bistetrazoles and bisbenzoxazepinediones respectively. The structures of the prepared compounds have been identified using infrared spectroscopy technique (FT-IR), the proton nuclear magnetic resonance (^{1}HNMR) and the carbon nuclear magnetic resonance ^{13}CNMR. Antibacterial effect of the novel compounds has been evaluated against *Staphylococcus aureus* (gram-positive bacteria) and *Escherichia coli* (gram-negative bacteria). The results indicated that bistetrazole T1 and bisbenzoxazepinedione B1 showed the highest inhibition zone against the growth of the applied bacteria. This may relate to presence of dimethyl amino group $(CH_3)_2N$ increasing the potential of bacterial cell attack by the tested compound as this substituent can behave as donating group. This leads to less resistivity from bacteria to the tested compound resulting in an increase in the inhibition zone. Thus, tetrazole and oxazepine derivatives bearing dimethyl amino group should be considered as antibacterial agents for drug industry application field.

1. Introduction:

Schiff bases are organic compounds that contain an Imine bond (C=N). These compounds are versatile and have wide applications in industrial, biological, analytical, and inorganic pharmaceutical fields [1]. Schiff bases have attracted the interest of researchers in the field of medicinal and pharmaceutical chemistry because of their biological efficacy [2]. Schiff bases are also promising compounds in antiviral drug design and discovery [3]. They have been shown to possess antibacterial, anticonvulsant, antidepressant, anticancer, antihypertensive, antipyretic, analgesic, sedative, hypnotic, and anti-HIV properties [4]. Schiff bases are typically obtained by facile condensation between an aldehyde or a ketone with primary amines [1].

The imine group can undergo cyclization reaction with some compounds to give heterocyclic derivatives. Imine compounds can be converted to cyclic product by treating it with maleic anhydride resulting in oxazepinediones [5]. Additionally, imines transferred to Benzoxazepinediones when phthalic anhydride reacted with it [6], [7]. Another cycliza-

tion reaction is the dealing imines with mercaptobenzoic acid or aminobenzoic acid to form benzothiazinones and quinazolinones respectively [8], [9]. Tetrazoles also prepared from imines reaction with addition sodium azide to it [10], [11]. The academic community has shown considerable interest in the synthesis of new heterocyclic compounds from Schiff bases through cyclization on the imine group and the assessment of their antibacterial action [12], [13].

The aim of this research is to synthesize a novel series of heterocyclic compounds through cyclization reaction for some imines. The newly synthesized compounds are phenylene bis tetrazole and bis benzoxazepinedione derivatives attached to substituted phenyl ($N(CH_3)_2$, Br and $NHCOCH_3$. In addition to the novel products antibacterial effect evaluation against some types of gram-positive and gram-negative bacteria. The design, synthesis, and assessment of novel organic compounds will persist valuable scientific academically.

2. Materials and Methodology:

2.1 Chemicals:

All chemicals for this research were used without any purification. Melting points determined using with Stuart melting point instrumental and infrared spectra (FT-IR) were scanned by Shimadzu FT-IR-3800 Spectrophotometer. The ^{1}HNMR and ^{13}CNMR spectra were recorded on a Bruker Ultra Shield – 400 MHz with and DMSO-d_6 as a solvent. The microbials were isolated and identified by laboratory facilities at biology department, science college in Kirkuk university.

2.2 Methods:

2.2.1 Synthesis of *N,N′* - (1,4-phenylene) bis (1- phenylmethanimine) (S1-3)[14].

Phenyl-1,4-diamine (0.108 g, 0.001 mole) and different benzaldehydes (0.002 mole) were dissolved in absolute ethanol (30 mL) with three drops of glacial acetic acid. The mixture was refluxed for 6 hours. After cooling, it filtered and dried then recrystallized from ethanol. Some physical properties of compounds (S1-3) are available in Table Table 1.

Table 1. Physical properties of imines (S1-3).

Comp. No.	R	Molecular Formula/M.Wt g/mol	Color	M.P (^{0} C)	Time (h.)	Yield (%)
S 1	$(CH_3)_2N$	$C_{24}H_{26}N_4$ 370	White	138-140	6	78
S 2	CH_3CONH	$C_{24}H_{22}N_4O_2$ 398.29	Dark Brown	132-134	6	80
S 3	Br	$C_{20}H_{14}N_2Br_2$ 442.042	Yellow	125-127	6	85

2.2.2 Synthesis of 1,4-bis(5-phenyl-4,5-dihydro-1H-tetrazol-1-yl) benzene (T1-3) [11]:

(0.001 mole) of imines (S1-3) dissolved in tetrahydrofuran (10 mL). To the imine solutions, (0.002 mole) of sodium azide was added after that the mixture refluxed for 10 h and left overnight. The precipitate was filtered and dried then recrystallized using absolute ethanol. Table Table 2 exhibits some physical characteristics of tetrazoles (T1-3).

Table 2. Physical characteristics of tetrazole (T1-3).

Comp. No.	R	Molecular Formula/M.Wt g/mol	Color	M.P (^{0} C)	Time (h.)	Yield (%)
T 1	$(CH_3)_2N$	$C_{29}H_{22}N_{10}$ 456.334	Pole Yellow	129-131	10	65
T 2	CH_3CONH	$C_{24}H_{24}N_{10}O_2$ 484.332	Brown	125-127	10	87
T 3	Br	$C_{20}H_{16}N_8Br_2$ 528.084	Yellow	113-115	10	85

2.2.3 Synthesis of 4,4′-(1,4-phenylene) bis(3-phenyl-3,4-dihydrobenzo[e][1,3] oxazepine-1,5-dione) (B1-3) [15].

A mixture of imines (S1-3) (0.001 mole) and (0.002 mole) of phthalic anhydride was dissolved in dry benzene (25 mL). The mixture was refluxed for 8 h and it cooled down to the room temperature. The precipitate was collected by filtration. The precipitate was dried and purified by crystallization it from absolute ethanol. Some physical properties of benzoxazepinedione (B1-3) are listed in Table Table 3.

Table 3. Physical properties of benzoxazepinediones (B1-3).

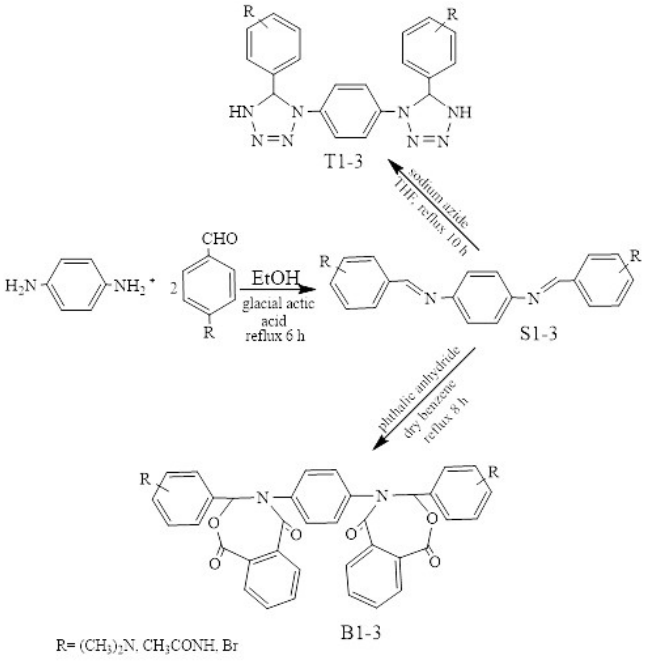
Comp. No.	R	Molecular Formula/M.Wt g/mol	Color	M.P (^{0} C)	Time (h.)	Yield (%)
B 1	$(CH_3)_2N$	$C_40H_{46}N_4O_6$ 678.462	White	123-125	8	70
B 2	CH_3CONH	$C_{40}H_{42}N_4O_8$ 706.46	Light	119-121	8	73
B 3	Br	$C_{36}H_{34}N_2O_6Br_2$ 750.212	Light White	110-112	8	85

2.2.4 Antibacterial effect study [16]:

The antibacterial activity effect of the final novel compounds (T1-3 and B1-3) was tested against gram-positive bacteria (*Staphylococcus Aureus*) and gram-negative bacteria (*Escherichia Coli*). This was performed by using the agar diffusion method. To prepare the disks, Whatman number 1 was utilized and remained for period of 24 h along with the new tested derivatives (0.0001, 0.001, and 0.01) mg L^{-1}. The inhibition diameter area was measured to each microbials for analysis purposes. Ciprofloxacin was applied as blank and control antibodies with concentration of (0.01 mg mL^{-1}).

3. Results and Discussion:

In this research paper, bisimines (S1-3) were synthesized from reaction between aldehydes and amines, using absolute ethanol as solvent. These imines have been transformed into heterocyclic derivatives via cyclocondensation reaction of imines with phthalic anhydride (dry benzene as solvent) and sodium azide (THF as solvent) as shown in Scheme Scheme 1. The addition of sodium azide to the bisimines resulting in forming bistetrazoles (T1-3), while in the case of phthalic anhydride addition, bisbenzoxazepinediones (B1-3) leading to be produced. For details about the mechanisms for synthesis of the bisimines, the bisbenzoxazepinediones and the bistetrazoles, see [15], [17] respectively.



Scheme 1. Describes the synthesis steps of bisimines (S1-3), bistetrazoles (T1-3) and bisbenzoxazepinediones (B1-3).

3.1 Characterization:

In the IR spectrum of bisimines S2, clearly a stretching band observed at 1631 cm^{-1} for the (C=N) group with disappearance of the (N-H vibration band in phenylamine's primary amine group. Additionally, asymmetrical and symmetrical vibration bands for CH3 noticed at frequency (2945 cm^{-1} and 2839 cm^{-1}) respectively. A single absorbance band realized at (3287 cm^{-1}) referring to (N-H) amide and another band at (1764 cm^{-1}) for carbonyl in amide group as shown in Figure Figure 1. The IR spectral data of the bisimines S1 and S3 is collected in Table Table 4.

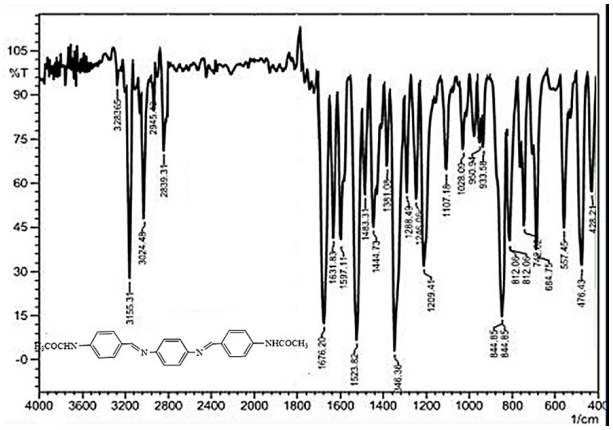


Figure 1. IR spectrum for bisimine S2.

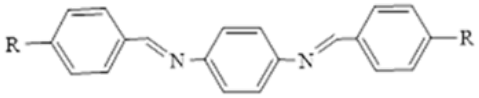


Table 4. IR data for bisimines S1 and S3.

Comp. No.	R	υ C−N cm^{-1}	υ C=N cm^{-1}	υ =C−H Arom cm^{-1}	υ ArC=C cm^{-1}	Other absorptions cm^{-1}
S1	$(CH_3)_2N$	1220	1656	2330	1528 1467	asym. $\upsilon(C-H)$2923 sym.$\upsilon(C-H)$2854
S3	Br	-	1668	3010	1556 1489	$\upsilon(C-Br)$754

The ^{1}HNMR spectrum of bisimine S1 obviously showed a singlet band for the imine group (CH=N) at δ 8.8 with the disappearance of amine proton signal compare to the starting materials. Furthermore, aromatic protons signals appeared at δ 7.52-8.40 and singlet for methyl protons at δ 2.52 and this is correlated with the literature [18]. According to the integral calculation results, the ratio of methyl protons ($4CH_3$) to imine proton (CH=N) is 12:1 as shown in Figure Figure 2. This is strong evidence for imine formation from an amine. The spectral data for bisimines S2 and S3 summarized in Table Table 5. The protons of DMSO-d6 as a solvent appeared at δ 3.37-3.39.

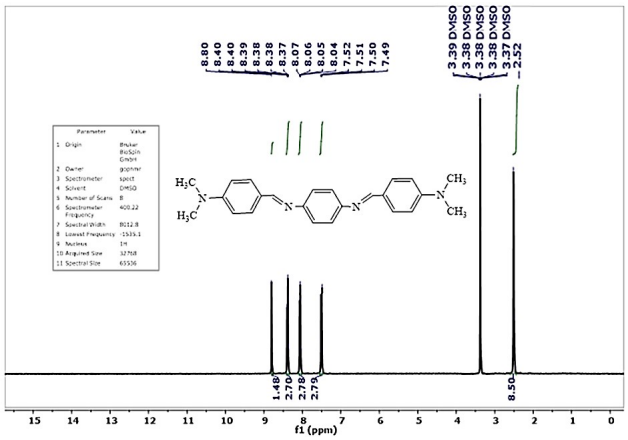


Figure 2. ^{1}HNMR spectrum for bisimine S1.

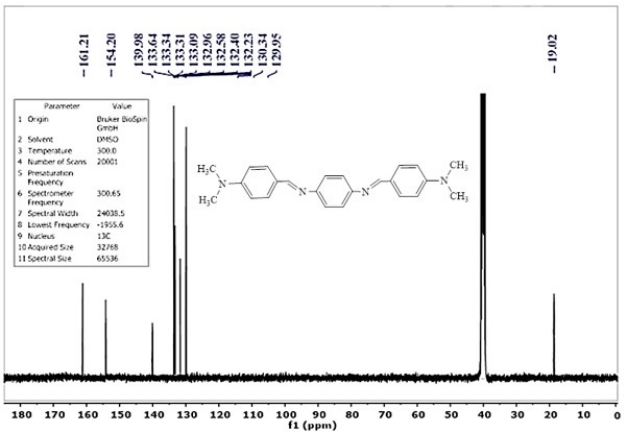


Figure 3. ^{13}CNMR spectrum for bisimine S1.

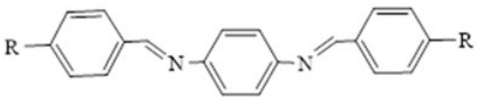


Table 5. ^{1}HNMR data spectra for bisimines S2 and S3.

Comp. No.	R	^{1}HNMR data in δ ppm
S2	$NHCOCH_3$	2.53 (s, 6H, $2CH_3$), 7.75-8.92 (m, 12H aromatic CH), 9.15 (s, 2H, imine), 10.83 (s, 2H, amide).
S3	Br	123.15-142.18 (12 aromatic carbons), 159.42 (imine carbon).

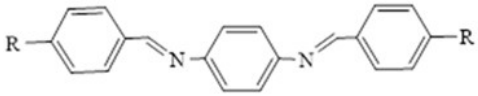


Table 6. ^{13}HNMR data spectra for bisimines S2 and S3.

Comp. No.	R	^{13}HNMR data in δ ppm
S2	$NHCOCH_3$	19.81 ($2CH_3$), 126.04-151.12 (12 aromatic carbons), 162.02 (2 imine carbon), 171.13 (2 amide carbon).
S3	Br	123.15-142.18 (12 aromatic carbons), 159.42 (imine carbon).

The ^{13}C NMR spectrum of bisimine S1 appeared ten aromatic carbons at the range of δ 129.95-133.64 and two aromatic carbons in benzene connected to nitrogen atom out of the benzene ring at 154.20 and 139.98 for C-N and C-N= respectively. Moreover, a singlet observed at δ 19.02 for carbon in methyl group and this is in agree with the literature [18]. The interesting band appeared at δ 161.21 for carbon in C=N and this good evidence for imine formation. Consequently, the combined spectroscopic data is consistent with the formation of imine compound S1see Figure Figure 3. The spectral data for bisimines S2 and S3 collected in Table Table 6.

The IR spectrum of bistetrazole T2 exhibited two diagnostic vibrational bands for N=N and N-N in the tetrazole ring at 1452 cm^{-1} and 1130 cm^{-1} respectively with the disappearance of CH=N band. This can be taken as evidence for cyclization transferal of CH=N compared to the IR spectrum of the bisimine S2. As well as, it clearly indicated stretching vibrational bands at 3211 cm^{-1}, 3124 cm^{-1} for the N-H vibration amide and NH vibration absorbance band in tetrazole respectively see Figure Figure 4. The remaining IR data is appeared at the expected regions. Table Table 7 collets the IR data of bistetrazoles T1 and T3.

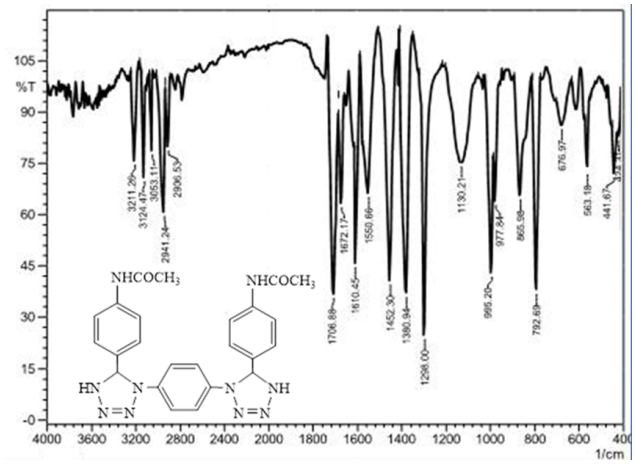


Figure 4. IR spectrum for bistetrazole T2.

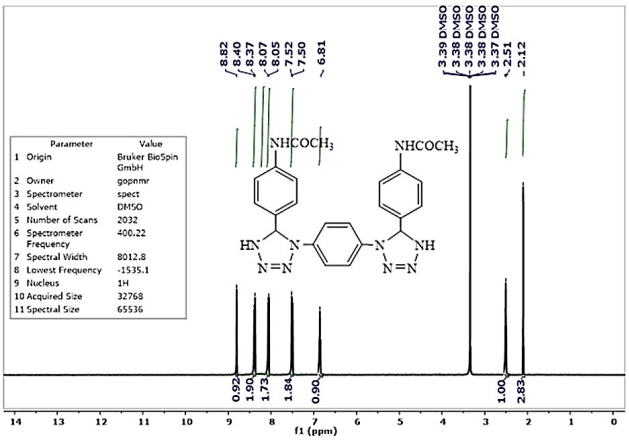


Figure 5. ^{1}HNMR spectrum for bistetrazole T2

Table 7. IR data for bistetrazoles T1 and T3.

Comp. No.	R	υ $C-N$ tetrazole cm^{-1}	υ $N=N$ cm^{-1}	υ $N-N$ cm^{-1}	$\upsilon N-H$ cm^{-1}	$\upsilon = C-HArom.$ $\upsilon C-HAliph.$ sym. asym. cm^{-1}	Other absorptions cm^{-1}
T1	$(CH_3)_2N$	1275	1450	1125	3216	3010 2854 2923	$\upsilon C-N$ 1245
T3	Br	1270	1430	1115	3290	3290 2878 2310	$\upsilon C-Br$ 768

The ^{1}HNMR spectrum of bistetrazole T2 showed a singlet at δ 2.12 for protons in the methyl group and aromatic protons signals at the range of (δ 7.50-8.40) for three benzene rings. Additionally, the proton signal of N-H amide in $NHCOCH_3$ appeared at δ 8.82 and two distinct signals observed at δ 2.51 for N-H proton in tetrazole ring and C-H of the tetrazole at δ 6.81 see Figure Figure 5. The integral calculation results indicated that the ratio of methyl protons ($2CH_3$) to N-H proton in the tetrazole ring is 6:1. This a confirmation for cyclization reaction of imine to tetrazole being formed. The spectral data for bistetrazoles T1 and T3 exhibited in Table Table 8.

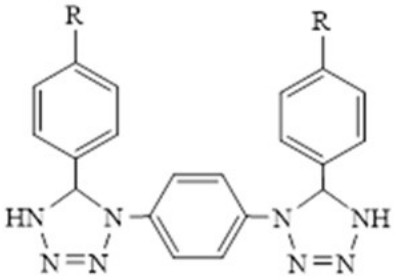


Table 8. HNMR spectrum for bistetrazoles T1 and T3.

Comp. No.	R	^{1}HNMR data in δ ppm
T1	$(CH_3)_2N$	2.48 (s, 12H, $4CH_3$), 2.77 (s, 2H, NH tetrazole), 7.13 (s, 2H, CH tetrazole), 7.71-8.85 (m, 12H aromatic CH).
T3	Br	2.73 (s, 2H, NH tetrazole), 6.92 (s, 2H, CH tetrazole), 7.62-8.25 (m, 12H aromatic CH).

The ^{13}CNMR spectrum of bistetrazole T2 indicated a diagnostic carbon signal for C-NH in the tetrazole ring at δ 116.78 with disappearance of the carbon signal for imine group compared to the started materials see Figure Figure 6. This is referring to achieve the cyclization reaction for the imine group. The carbonyl group signal noticed clearly at δ 170.07, in addition to the aromatic carbons signals at the range of δ 116.78-160.91 and this is reported in the literature [11]. It also showed the methyl group signal at δ 25.12. The spectral data for bistetrazoles series T1 and T3 is available in Table Table 9. Carbons signals for the DMSO-d6 as a solvent

appeared at δ 40. The IR spectrum of bisbenzoxazepine-

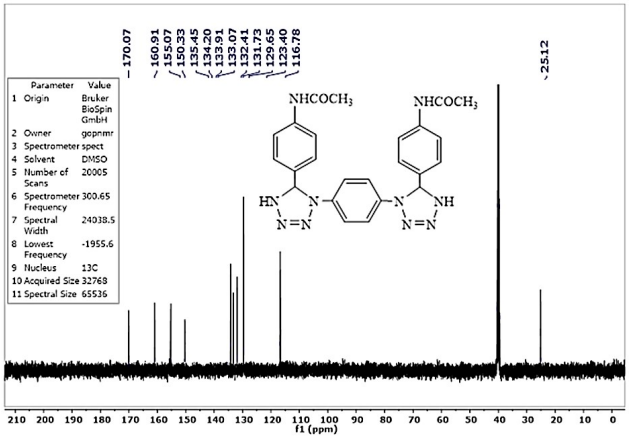


Figure 6. ^{13}CNMR spectrum for bistetrazole T2.

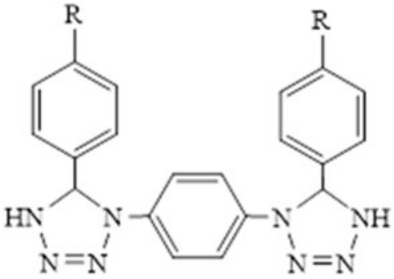


Table 9. HNMR spectrum for bistetrazoles T1 and T3.

Comp. No.	R	^{13}CNMR data in δ ppm
T1	$(CH_3)_2N$	24.20 ($4CH_3$), 119.23 (two tetrazole C), 127.15-162.17 (12 aromatic C).
T3	Br	120.43 (two tetrazole C), 129.37-161.06 (12 aromatic C).

diones B2 illustrated two distinguished vibrational bands for carbonyl group (O-C=O, N-C=O) in the oxazepine ring at 1693 cm^{-1} and 1660 cm^{-1} respectively, with the disappearance of CH=N band see Figure Figure 7. This described as evidence for cyclization reaction of imine group compared to the started materials. The remaining IR data realized in the expected regions. Table Table 10 shows the IR data of bisbenzoxazepinediones B1-3.

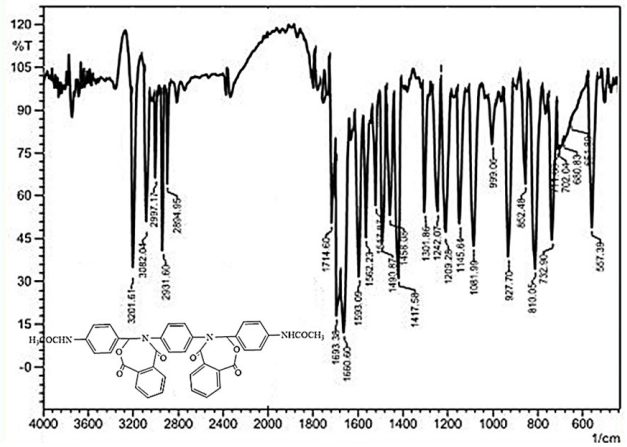


Figure 7. IR spectrum for bisbenzoxazepinedione B2.

Table 10. IR data for bisimines S1 and S3.

Comp. No.	R	υ $OC=O$ cm^{-1}	υ $N-C=O$ cm^{-1}	υ $C-N$ cm^{-1}	υ $=C-HArom.$ υ $C-HAliph.$ sym. asym. cm^{-1}	Other absorptions cm^{-1}
B1	$(CH_3)_2N$	1714	1693	1235	3070 2846 2909	υ $C-N$ 1221
B3	Br	1696	1694	1206	3290 2842 2928	υ $(C-Br)$ 757

The ^{1}HNMR spectrum of bisbenzoxazepinedione B3 exhibited a singlet signal for (CH-N) in the oxazepinedione ring at δ 9.68 with the disappearance of imine proton signal compare to the starting materials. Furthermore, aromatic protons signals appeared at δ 6.57-7.70 and this documented in the literature [18]. see Figure Figure 8. This is strong evidence for bisbenzoxazepinediones producing from an imine. The spectral data for bisbenzoxazepinediones B1and B2 is shown in Table Table 11.

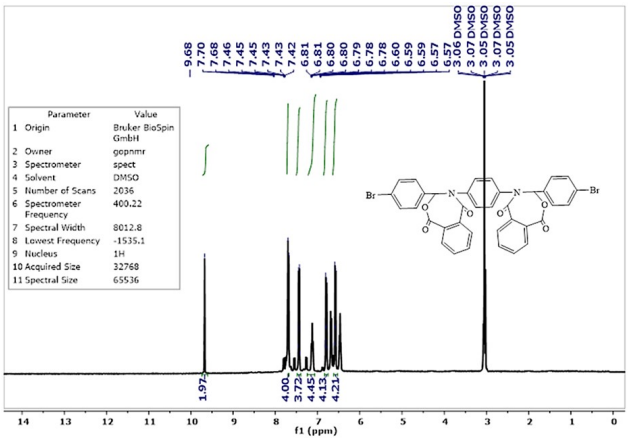


Figure 8. HNMR spectrum for bisbenzoxazepinedione B3.

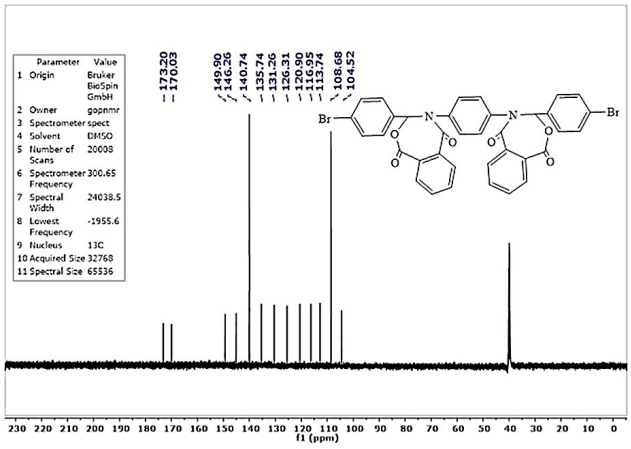


Figure 9. ^{13}CNMR spectrum for bisbenzoxazepinedione B3.

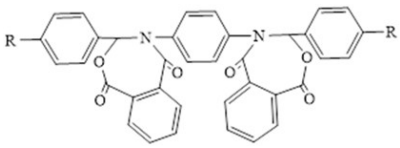


Table 11. HNMR spectrum for bisbenzoxazepinediones B1 and B2.

Comp. No.	R	^{1}HNMR data in δ ppm
B1	$(CH_3)_2N$	2.24 (s, 12H, $4CH_3$), 7.20-8.37 (m, 20H, aromatic CH), 9.73 (s, 2H, CH oxazepinedione),
B3	$NHCOCH_3$	2.31 (s, 6H, $2CH_3$), 7.26-8.86 (m, 20H, aromatic CH), 9.87 (s, 2H, CH oxazepinedione), 10.05 (s, 2H, amide).

The ^{13}C NMR spectrum of bisbenzoxazepinediones B3 indicated two diagnostic signals for carbonyl atoms (O-C=O, N-C=O) in the oxazepine ring at δ 173.20 and δ 170.03 respectively with disappearance of the carbon signal for imine carbon atoms compared to the started materials see Figure Figure 9. This refers to an indicator for converting the imine group to cyclic compound. It also showed the aromatic carbons signals at the range of δ 104.52-149.90. The spectral data for bisbenzoxazepinediones B1-3 series is collected in Table Table 12. Carbons signals for the DMSO-d6 as a solvent appeared at δ 39.85.

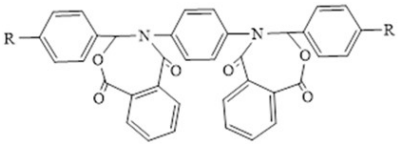


Table 12. ^{13}CNMR spectrum for bisbenzoxazepinediones B1 and B2.

Comp. No.	R	^{13}CNMR data in δ ppm
B1	$(CH_3)_2N$	23.40 ($4CH_3$), 106.12 (2C in oxazepinediones), 109.20-151.32 (15 aromatic C), 170.38 (2C, N-C=O), 172.92 (2C, O-C=O).
B2	$NHCOCH_3$	24.17 ($2CH_3$), 107.08 (2C in oxazepinediones), 110.61-157.18 (15 aromatic C), 171.49 (2C, N-C=O), 173.97 (2C, O-C=O), 174.16 (amide C).

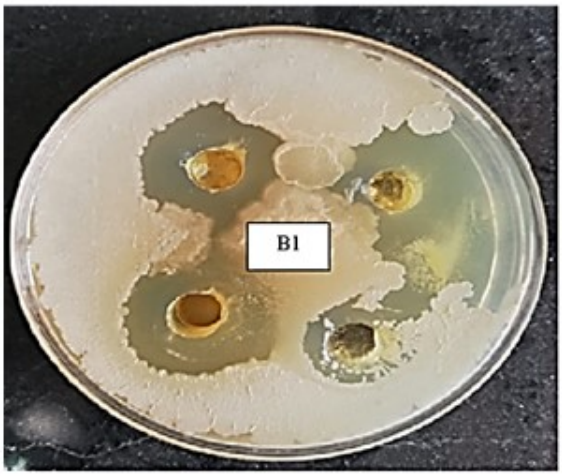
3.2 Antibacterial Activity:

The newly synthesized compounds (T1-3 and B1-3) were tested for antibacterial activity evaluation toward *Staphylococcus* aureus (gram-positive bacteria) and *Escherichia coli* (gram-negative bacteria). The results indicated that bistetrazole T1 and bisbenzoxazepinedione B1 showed the highest inhibition performance against the growth of the applied bacteria. Furthermore, both of T1 and B1 were behaved more active at high concentrations compared to the low concentrations due to the high concentration effect making to be the

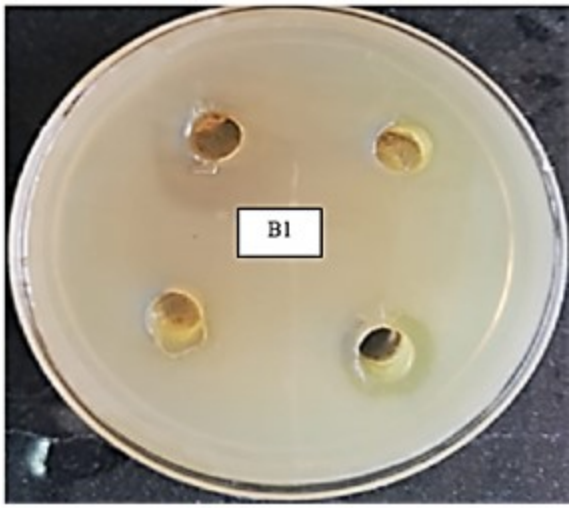
inhibition zone increased. However, the remaining of tested compounds gave low antibacterial activity against both of the applied bacteria. One of the reasons for these results is could be present of dimethyl amino group $(CH_3)_2N$ as this substituent can behave as donating group. This may increase the potential of bacterial cell attack by the tested compound leading to less resistivity from bacteria to the tested compound resulting in an increase in the inhibition zone. It also noticed that B1 behaved more active than T1 from high to low concentrations. This may relate to the different electronegativity of the oxygen atom availability in the oxazepinedione ring compared to the tetrazole ring having only nitrogen atom. Table Table 10 is collected the antibacterial effect results for the newly synthesized series on the tested bacteria in addition to some of disk images for the zone inhibition results are exhibited in Figures Figure 10 and Figure 11.

Table 13. ^{13}CNMR spectrum for bisbenzoxazepinediones B1 and B2.

Comp. No	Conc. mg mL^{-1}	Gram negative *Escherichia Coli*	Gram positive *Staphylococcus aureus*
T1	0.01	31	21
	0.001	16	15
	0.0001	12	13
T2	0.01	21	
	0.001	14	14
	0.0001	11	10
T3	0.01	18	19
	0.001	12	13
	0.0001	11	10
B1	0.01	28	25
	0.001	20	21
	0.0001	18	20
B2	0.01	20	18
	0.001	13	15
	0.0001	11	10
B3	0.01	16	15
	0.001	15	13
	0.0001	11	10
Ciprofloxacin	10 mg disk^{-1}	30	28

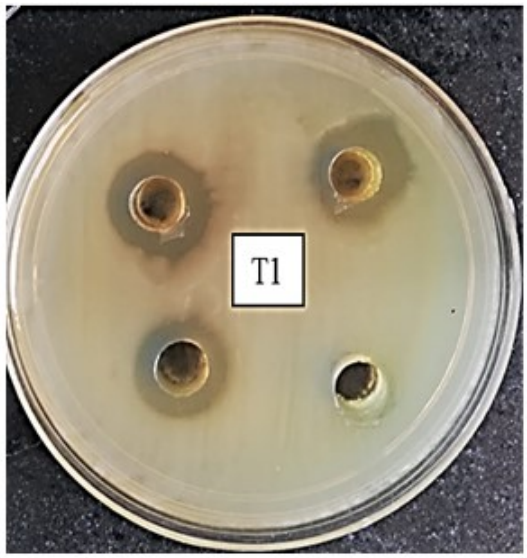


a

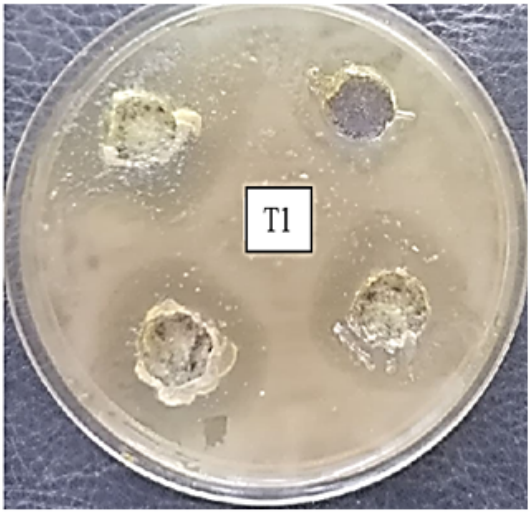


b

Figure 10. Images of the inhibition zone for B1 against (a): *Escherichia Coli* and (b): *Staphylococcus* aureus bacteria.



a



b

Figure 11. Images of the inhibition zone for T1 against (a): *Escherichia Coli* and (b): *Staphylococcus* aureus bacteria.

4. Conclusions:

Some new phenylene bistetrazole and bis benzoxazepinedione derivatives have been successfully synthesized from some bisimines and their structures were identified depending on the identification results. Antibacterial effect assessment results indicated that bistetrazole T1 and bisbenzoxazepinedione B1 were exhibited the highest inhibition performance against the growth of the applied bacteria and the both having higher activity at high concentration compared to the low concentrations as a result of the high concentration effect leading to increase the inhibition zone. However, the remaining of tested chemicals behaved with low antibacterial effect activity against the applied bacteria. This may contribute to present of dimethyl amino group $(CH_3)_2N$ as this substituent can behave as donating group leading to increase the potential of bacterial cell attack by the tested compound resulting in a less resistivity from bacteria to the tested chemicals. Furthermore, compound B1 is more active than T1 and this can be ascribed to the structure difference in terms of the high electronegativity of the oxygen atom for the oxazepinedione ring compared to the tetrazole ring containing nitrogen atom. As a result, tetrazole and oxazepine derivatives bearing dimethyl amino group $(CH_3)_2N$ should be regarded as antibacterial agents for pharmaceutical field.

Funding: None.

Data Availability Statement: All of the data supporting the findings of the presented study are available from corresponding author on request.

Declarations:

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: The manuscript has not been published or submitted to another journal, nor is it under review.

References

[1] C.M. Da Silva, D.L. da Silva, L.V. Modolo, R.B. Alves, M.A. de Resende, C.V. Martins, and Â. de Fátima. Schiff bases: A short review of their antimicrobial activities. *Journal of Advanced research*, 2(1):1–8, 2011, doi:10.1016/j.jare.2010.05.004.

[2] M. Horchani, H. Edziri, A.H. Harrath, H.B. Jannet, and A. Romdhane. Access to new schiff bases tethered with pyrazolopyrimidinone as antibacterial agents: Design and synthesis, molecular docking and dft analysis. *Journal of Molecular Structure*, 1248:131523, 2022, doi:10.1016/j.molstruc.2021.131523.

[3] S. Akkoc, H. Karatas, M.T. Muhammed, Z. Kökbudak, A. Ceylan, F. Almalki, H. Laaroussi, and T. Ben Hadda. Drug design of new therapeutic agents: Molecular docking, molecular dynamics simulation, dft and pom analyses of new schiff base ligands and impact of substituents on bioactivity of their potential antifungal pharmacophore site, 2023, doi:10.1080/07391102.2022.2111360.

[4] Z.H. Abood, Z.K. Chafcheer, and H.A. Suhail. Synthesis and antibacterial evaluation of 1, 3-benzoxazepine-1, 5-diones bearing Benzothiazole moiety. *Research Journal of Pharmacy and Technology*, 14(4):1905–1909, 2021, doi:10.52711/0974-360X.2021.00336.

[5] O.A. Nief, H.N. Salman, and L.S. Ahamed. Synthesis, characterization, biological activity studies of schiff bases and 1, 3-oxazipene derived from 1, 1-bis (4-aminophenyl)-4-phenyl cyclohexane. *Iraqi Journal of Science*, 58(4B):1998–2011, 2017, doi:10.24996/ijs.2017.58.4B.2.

[6] A. A Ahmed, A. Kh Ahmad, and N. G Ahmed. Synthesis of some new benzoxazepine compounds form derivatives of schiff bases. *Journal of Education and Science*, 29(1):218–232, 2020, doi:10.33899/edusj.2020.164374.

[7] A.A. Dawood, S.R. Mohammed, and M. Mahmoud. Synthesis, identification and biological activity of new heterocyclic compounds from reaction of new schiff-bases with phathalic anhydride. *Science Journal of University of Zakho*, 8(1):12–8, 2020, doi:10.25271/sjuoz.2020.8.1.641.

[8] M.G. Al-Khuzaie and S.M. Al-Majidi. Synthesis and characterization of some new benzothiazine, dihydroquinazolinone and oxazepine derivatives from 1, 8-naphthalic anhydride and evaluation of their antimicrobial activity. *Journal of Global Pharma Technology*, 10(11):415–423, 2018.

[9] K.M. Fayyadh and I.H. Khudhair. Synthesis, Characterization and Spectroscopic Study of some Heterocyclic Compounds (2, 3-Dihydroquinazolin, Dzetidin-2-one) Derived from Schiff Bases and Evaluation Their Bacterial Activity. *Diyala Journal for Pure Science*, 15(1):38–53, 2019, doi:10.24237/djps.1501.451B.

[10] M.N. Khurshid, F.H. Jumaa, and S.S. Jassim. Synthesis, characterization, and evaluation of the biological activity of tetrazole compounds derived from the nitrogenous base uracil. *Materials Today: Proceedings*, 49(8):3630–3639, 2022, doi:10.1016/j.matpr.2021.08.203.

[11] Zanco Journal of Pure and Applied Sciences. B.s. abdulrahman and r.b. nadr. *Synthesis and Spectroscopic Characterization of a New Series of Tetrazole Compounds*, 34(6):217–229, 2022, doi:10.21271/ZJPAS.34.6.23.

[12] N.S. Majeed and F.N. Abdul-Hussein. Synthesis, characterization and studying of biological activity of some new six–membered compounds derived from schiff bases. *Research Journal of Pharmacy and Technology*, 16(5):2280–2286, 2023, doi:doi.org/10.52711/0974-360X.2023.00374.

[13] S.I.C. AL-Khazraji. Synthesis of and characterization of some Heterocyclic Compounds derived from Thiophenol. *Egyptian Journal of Chemistry*, 64(10):5655–5662, 2021, doi:doi.org/10.21608/ejchem.2021.70759.3559.

[14] S. Salim Jasim. Synthesis and Characterization of Some Bis-1, 3 Oxazepine-4, 7-dione and 1, 3–Diazepine-4, 7-dione Derivatives. *Kirkuk University Journal-Scientific Studies*, 13(2):149–165, 2018, doi:10.32894/kujss.2018.145725.

[15] J.H. Abdul–Wahid, A.S. Hameed, and A.K. Mohammed. Synthesis Characterization of Some New Heterocyclic Compounds Containing1, 3-Oxazepine Ring. *Kirkuk University Journal-Scientific Studies*, 11(3):237–247, 2016, doi:10.32894/kujss.2016.124651.

[16] L.B. Reller, M. Weinstein, J.H. Jorgensen, and M.J. Ferraro. Antimicrobial susceptibility testing: a review of general principles and contemporary practices. *Clinical infectious diseases*, 49(11):1749–1755, 2009, doi:10.1086/647952.

[17] H.M. Tawfeeq, R.F. Muslim, O.H. Abid, and M.N. Owaid. Synthesis and characterization of novel tetrazole derivatives and evaluation of their anti-candidal activity. *ACTA Pharmaceutica Sciencia*, 57(3):45–63, 2019, doi:10.23893/1307-2080.APS.05717.

[18] R.B. Nadr and B.S. Abdulrahman. Synthesis and characterization of a new series of [1, 3]-oxazepine compounds from heterocyclic schiff bases. *Zanco Journal of Pure and Applied Sciences*, 35(2):197–210, 2023, doi:10.21271/ZJPAS.35.2.21.

تحضير وتشخيص مشتقات ثنائي (تترازول وبنزوكسازبين ثنائي اون) فينيلين جديدة من بعض مركبات الثنائي أيمين وتقييم نشاطها البيولوجي

شاخوان بيباني

قسم الكيمياء، كلية العلوم، جامعة كركوك، كركوك، العراق.

* الباحث المسؤول: *sh.beebany@uokirkuk.edu.iq*

الخلاصة

حضرت بنجاح بعض من مشتقات جديدة لفنيل ثنائي تترازول $(T1-3)$ وثنائي بنزوكسازيبين ثنائي اون $(B1-3)$ من خلال التفاعل الحلقي لبعض من ثنائي إيمينات $(S1-3)$. حيث تم تحويل الإيمينات الثنائية $(S1-3)$ الى مركبات حلقية غير متجانسة بإضافة أزيد الصوديوم وأنهيدريد الفثاليك بوجود رباعي هيدروفيوران كمذيب لتكوين مشتقات ثنائي بنزوكسازيبين ثنائي اون وثنائي تترازول. شخصت تراكيب المركبات المحضرة باستخدام تقنية التحليل الطيفي للأشعة تحت الحمراء $(FTIR)$ والرنين النووي المغناطيسي للبروتون (^1HNMR) والرنين النووي المغناطيسي للكاربون $^{13}CNMR$. تم تقييم التأثير المضاد للبكتيريا للمركبات الجديدة ضد المكورات العنقودية الذهبية (البكتيريا موجبة الجرام) والإشريكية القولونية (البكتيريا سالبة الجرام). أشارت النتائج إلى أن المركب $(T1)$ والمركب $(B1)$ أظهرا أعلى أداء تثبيطي ضد نمو البكتيريا المطبقة. قد يكون هذا مرتبطًا بوجود مجموعة الثنائي ميثيل أميني $(CH_3)_2N$ مما يزيد من احتمالية هجوم الخلايا البكتيرية بواسطة المركب الذي تم اختباره حيث يمكن أن يتصرف هذا المعوض كمجموعة مانحة. وهذا يؤدي إلى مقاومة أقل من البكتيريا للمركب المستخدم مما يؤدي إلى زيادة منطقة التثبيط. وبالتالي يمكن اعتبار مشتقات التترازول والأوكسازيبين التي تحمل مجموعة ثنائي ميثيل امين كعوامل مضادة للجراثيم في مجال تطبيقات صناعة الأدوية.

الكلمات الدالة : ثنائي تترازول، ثنائي بينزوكسازبين ثنائي اون، حولقة .قواعد شف، ثنائي ايمين، أزيد الصوديوم

التمويل: لايوجد.

بيان توفر البيانات: جميع البيانات الداعمة لنتائج الدراسة المقدمة يمكن طلبها من المؤلف المسؤول.

اقرارات:

تضارب المصالح: يقر المؤلفون أنه ليس لديهم تضارب في المصالح.

الموافقة الأخلاقية: لم يتم نشر المخطوطة أو تقديمها لمجلة أخرى، كما أنها ليست قيد المراجعة.