Japanese Journal of Gastroenterology and Hepatology

Research Article ISSN 2435-1210 |Volume 6

Synthesis, Characterization, Biological Evaluation of Some Heterocyclic Oxazepine Derivatives

Kezhal MS*

Pharmaceutical Chemistry department, College of Pharmacy/ Hawler medical University, Iraq

***Corresponding author:**

Kezhal Mahmood Salih,
Pharmaceutical Chemistry department,
College of Pharmacy/ Hawler medical University, Iraq,
E-mail: kezhalsalih@yahoo.com

Received: 15 July 2021
Accepted: 05 Aug 2021
Published: 10 Aug 2021

Citation:

Kezhal MS,. Synthesis, Characterization, Biological Evaluation of Some Heterocyclic Oxazepine Derivatives. Japanese J Gstro Hepato. 2021; V6(22): 1-9

Keywords:

Schiff base; Wiliamson Ether synthesis; Oxazipine

1. Abstract

The new serious of pentyloxy and aryloxy benzaldehyde (3a-e) were synthesized from the substitution reaction of 4-hydroxy benzaldehyde with different aryl bromide and alkyl bromide, on the basis of Williamson ether synthesis in the presence of Potassium carbonate using absolute ethanol as a solvent. The second step was the synthesis of 2-amino-5-(p-tolyl)1,3,4-thiadiazole.

The new serious of Schiff bases were synthesized from the reaction of new carbonyl compounds with 4-aminodiphenylamine and 2-amino-5-(p-tolyl)1,3,4-thiadiazole, in absolute ethanol to form compounds (4a-g) and (5a-d).

The new derivatives of 1,3-Oxazepine derivatives were synthesized from the reaction of new serious of imines with maleic anhydride, in dry benzene to form compounds (6a-g).and (7a-c).

All of the synthesized compounds have been characterized by FTIR and some of them were characterized using ^{1}H-MNR and ^{13}C-NMR spectroscopy which supported the formation of the products of the desired compounds. The synthesized compounds have been tested for bactericidal against Gram- negative.*P. aeruginosa* and Gram -positive bacteria *Staphylococcus aureus.*

2. Introduction

Heterocyclic compounds are widely distributed in nature and essential for life. Heterocyclic compounds have great role in the synthesis of Drugs, that contains two heteroatoms (Sulfur and Nitrogen). They play a vital role in the metabolism of all living cells. Numerous reactions of imines, are extensively developed over the years, describe the synthetic procedures for the preparation of different organic molecules, especially heterocyclic compounds which they possess biological activity.

Schiff bases has different pharmacological activity is used as antibacterial [1], anticancer [2] antioxidant and antifungal activities [3] the azomethine linkage (N=CH) imine which is important in biological systems display the activity of Schiff bases.

Many researchers have synthesized these compounds as well as their metal complexes as target structures and evaluated their biological activities, and it has application in various field of science [4-5] Imines undergo cyclization reactions under different conditions and techniques. It is preferable to classify them according to size of their heterocyclic products to four, five, six member's heterocyclic rings and macrocyclic compounds [6].

Hetrocyclic compounds have great role in the synthesis of Drugs, 1,3-Oxazepines is seven-member ring, that contains two heteroatoms (Oxygen and Nitrogen). Oxazepines has different pharmacological activity is used as antibiotics, enzyme inhibitors and as antidepressant. Synthesis of 1,3- Oxazepine -4,7-dione from the reaction of Schiff bases with maleic or phthalic anhydride were recorded in the literature, [7-8] we tried to convert some of these Schiff bases to Oxazepine derivatives through cyclization of the Azomethins bond with Maleic anhydride [9].

Amino-1,3,4- Thiadiazole system is an important starting material in the synthesis of biologically active compound and important heterocyclic, which constitute an important class of organic compounds in synthesis of Drugs. The synthesis of Thiadizoles bonded to another ring has attracted particular attention due to their diverse applications as antibacterial, antidepressant, antiviral,

antitumor and anti-inflammatory agents [10-18].

In the recent year's number of scientific research focused on the Thiadiazole in their research, considered as an important moiety for the synthesis of new derivatives, so in this work we combine thiadiazole moiety with 1,3-Oxazepine moiety and study their biological activity.

3. Materials and Methods

3.1. Instruments

Melting points were determined by using electro thermal melting point apparatus from stuart scientific. Infrared Spectra were recorded on a Bio - Rad Merlin, FT-IR Spectroscopy Mod Special for spectroscopy ^{1}H- and ^{13}C-NMR spectrum were measured using a Bruker ultra-shield 300 MHz with internal TMS (Central Lab. University of Jordon); chemical shifts are given in ppm.

3.2. Experimental

3.2.1. Synthesis of 4-Ethers derivatives of benzaldehyde (3a-e)

A mixture of 4- hydroxybenzaldehyde (0.05 mole) and K_2CO_3 (0.11 mole) were dissolved in 10 ml of absolute ethanol and stirred at room temperature for 2 hours. 0.05 mole of aryl halides were added to the mixture and heated under reflux for 7 hours. The mixture was powered in to ice, and filtered. Products were recrystallized from appropriate solvent (Table 2).

Table 1: Antibacterial activity of (4a-g) (5a-d) and oxazepinens derivatives measured by the disc diffusion method.

Compound	*Pseudomonas aeruginosa*	*Staphylococcus. aureus*
4a	+++	++
4b	+++	++
4c	+++	++
4d	+++	+++
4e	++	+++
4g	+++	+++
5a	+++	+++
5b	+++	+++
5c	+	+++
5d	++	+++
6b	+++	+++
6c	+++	++
6d	+++	+++
6f	+++	+++
7b	+++	+++

Key:

(-) Inactive (<5mm)

(+) Slightly active (10-12mm)

(++) Moderatly active (15-20mm)

(+++) Highly active (>20m)

Table 2: Some physical properties of compounds (3a-d) and 4a-e

Compounds	R-	Chemical Formula	M.p.	color	Yield%
3a	$C_6H_5CH_2$-	$C_{14}H_{12}O_2$	63-65	whight	93
3b	3-NO_2-$C_6H_4CH_2$-	$C_{14}H_{11}NO_4$	53-59	yellow	87
3c	4-Br-C_6H_4-$COCH_2$-	$C_{15}H_{11}O_3Br$	96-98	brown	90
3d	3-ClC_6H_4-CH_2-	$C_{14}H_{11}O_2Cl$	53-55	white	85
3e	C_5H_{11}-	$C_{12}H_{16}O_2$	58-60	white crystal	85
4a	$C_6H_4CH_2$-	$C_{26}H_{22}N_2O$	145-146	green	98
4b	3-NO_2-$C_6H_4CH_2$-	($C_{26}H_{22}N_3O_3$	139-140	green	90
4c	4-Br-$C_6H_4COCH_2$-	($C_{27}H_{22}N_2O_2Br$	219-220	brawn	92
4d	3-Cl$C_6H_4CH_2$-	$C_{26}H_{22}N_2OCl$	259-261	green	85
4e	C_5H_{11}-	$C_{24}H_{26}N_2O$	212-214	green	75
4f	$(CH_3O)_2C_4H_6$	$C_{22}H_{22}N_2O_2$	215-218	Greenish yellow	90
4g	2-Cl	$C_{19}H_{14}N_2Cl$	220-222-	green	95
5a	$C_6H_5CH_2$-	$C_{23}H_{19}N_3OS$	164-168	yellow	80
5b	3-NO_2-$C_6H_4CH_2$-	$C_{23}H_{18}N_4O_3S$	221-223	yellow	92
5c	4-Br-$C_6H_4COCH_2$-	$C_{24}H_{18}N_3O_2SBr$	169-170	yellow	85
5d	3-Cl$C_6H_4CH_2$-	$C_{23}H_{18}N_3OSCl$	164-167	yellow	88
6a	$C_6H_5CH_2$-	$C_{30}H_{24}N_2O_4$	183-185	Orange	75
6b	3-NO_2-$C_6H_4CH_2$-	$C_{30}H_{24}N_3O_6$	188-190	orange	85
6c	4-Br-$C_6H_4COCH_2$	$C_{31}H_{24}N_2O_5Br$	200- 202	orange	75
6d	3-Cl$C_6H_4CH_2$	$C_{30}H_{24}N_2O_4Cl$	165-167	orange	80
6f	$(CH_3O)_2$ C_4H_6	$C_{26}H_{24}N_2O_5$	180-181	Greenish yellow	70
6g	2-Cl	$C_{23}H_{17}N_2O_3Cl$	193-	green	88
7b	3-NO_2-$C_6H_4CH_2$	$C_{27}H_{20}N_4O_6S$	160-162	yellow	80

3.2.2. Synthesis of 2-amino-5-(p-tolyl) 1,3,4- thiadiazole

Was prepared according to the procedure described in the literature [4].

3.2.3. General Procedure for the Synthesis of Schiff bases (4a-g) [4]

4-aminodiphenyl amine (0.01mole) was dissolved in 10 ml of absolute ethanol, appropriate aldehyde (0.01 mole) was added to the mixture. The reaction mixture was refluxed for 5 hours and then cooled. The products were precipitated and filtered off, recrystallized from absolute ethanol. The physical properties are listed in (Table 2).

3.3. General procedure for the Synthesis of Schiff bases (5a-d) [4]

3.3.1. 2-amino-5-(p-tolyl) 1,3,4-thiadiazole: (0.01mole) was dissolved in 10 ml of absolute ethanol, appropriate aldehyde (0.01 mole) was added to the mixture. The reaction mixture was refluxed for 5 hours and then cooled. The products were precipitated and filtered off, recrystallized from absolute ethanol. The physical properties are listed in (Table 2).

3.3.2. General procedure for preparation of substituted (1,3) Oxazepine [10-18]:

Mixture of corresponding Schiff bases (0.001 mol) and (0.001 mol) of Maleic anhydride in dry benzene (30 ml) was refluxed for (5 hr) The reaction mixture cooled and filtered and recrystallized from appropriate solvent.

4. Biological Study

The sensitivity of Oxazipine and Schiff bases derivatives were carried out against two kinds of bacteria, Gram-positive *S. aureus* and Gram-negative Bacteria *P. aeruginosa* using disc agar diffusion method. The tests were performed using Muller Hinton agar, the medium was prepared using nutrient agar for preservation of pure culture, then sterilized by autoclave, and poured in Petri dish to a depth of 4 mm. Activation of each type of bacteria Gram-positive and Gram-negative was done before culturing on the nutrient agar in a nutrient broth which was used for dilution of bacterial and cultivation of culture isolates for 24 h in 37°C, then inoculation of the plates. The discs of the synthesized compounds were prepared by mixing a compound with KBr powder (1:3). The mixture was pressed under pressure KBrwhich has been used as a blank disc. The dried surface of the Muller Hinton agar plate was streaked; tow dried discs were placed on the surface of the cultured media per petri dish. The plates were then incubated at 37℃ for 18 to 24 h. Microbial growth was indicated by measuring the diameter of the zone of inhibition (Table 1).

5. Discussion

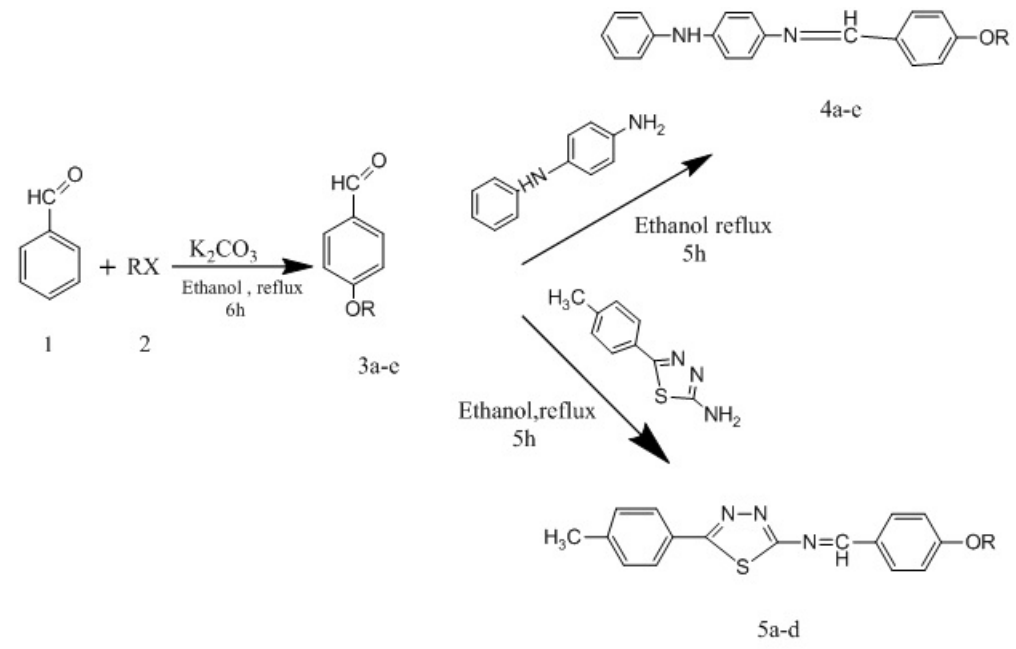
The first stage of the present work involves the synthesis of Ether derivatives of benzaldehyde (3a-e) from *p* -hydroxyl benzaldehyde using the Williamson ether synthesis method. The Reaction were proceeding under reflux –condition using potassium carbonate and the nucleophilic substitution reactions were progressed smoothly and products were obtained in very good yields and in high purity for the alkyloxy and aryloxy benzaldehyde. The structure of the synthesized compounds was confirmed from the physical and chemical properties and also from the spectroscopic data. The IR spectra of these compounds showed the disappearance of the OH band of para hydroxyl benzaldehyde that appeared at (3400 cm^{-1}), also the appearance of a new band at (1217-1352 cm^{-1}) due to the new C-O bond vibration indicated the formation of the desired compound, ether derivatives of benzaldehyde and substitution takes place successfully using the described condition by heating under reflux in the presence of K_2CO_3 as a catalyst [5] (Scheme 1).

The ^{1}H-NMR spectrum of the compound (3b) (Figure 1) showed the presence of a signal related to CH_2 group at chemical shift 5.3 ppm with appearance of multiplet for 8 protons at δ 7-8.3 ppm, and a singlet at δ 7-8.3 ppm due to the CH=O proton. Also the formation of the aryloxy compounds Identified by ^{13}C-NMR spectrum from the appearance of signal at δ 68, ppm for CH_2 group, with 10 signal for 10 carbons in aromatic region and a signal attributed to CH=O carbon at δ191 ppm Figure (4). $DMSOd^6$ used as solvent in this analysis which showed three signal at δ 2, δ 2.5 and δ 3.3 ppm for water molecule in the solvent.

The Synthesized aryloxy and alkyloxy benzaldehyde used as a starting material for preparation of a new series of Schiff bases (imines) using condensation method without catalyst. The structure of the synthesized compounds were elucidated from the physical and chemical properties (Table 2) and from various spectroscopic techniques. The infrared as well as ^{1}H- and ^{13}C-NMR spectral data of some of the synthesized compounds were consistent with expected structures. The Infrared spectra of the synthesized imines compounds showed the disappearance of vibration frequency of C=O groups at (1710) cm^{-1} for derivative of aldehydes and appearance of a new band for azomethines bond (–N=CH-) in the regain between (1582-1642) cm^{-1}. (Table 3).

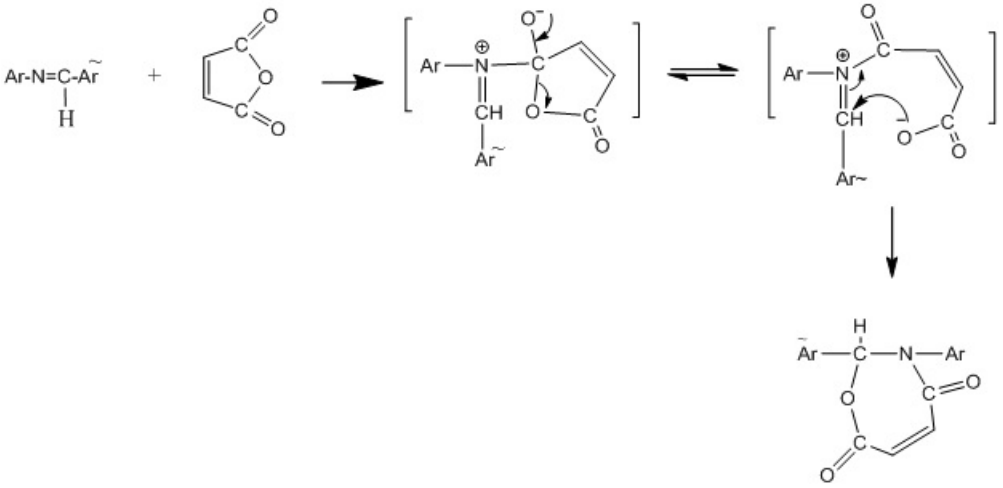
The two bands at 3460 and 3385 cm^{-1} related to amino group are assigned to N-H asymmetric and symmetric stretching vibrations disappeared in the IR spectrum of Schiff bases. The substituted benzene showed C-H stretching, C-H out-of-plane bending and C-H ln-plane bending. Normally, the bands around 3000 - 3100 cm^{-1} are assigned to C-H stretching vibration of aromatic hydrocarbons.

The ^{1}H-NMR supported the formation of the synthesized compounds(4a-g, 5a-d), which they characterized via appearance of a singlet signal at δ (8-10) ppm belongs to azomethin protons (-N=CH), and the observation of the presence of signals related to the substituted aldehyde in all of the products such as O-CH_2 group at δ 4-5.3 ppm, which indicate the presence of benzyloxy ($C_6H_5CH_2O$-) group in the structure of a new compounds and the multiple signals from δ 6-8 ppm characterized the protons of phenyl groups.Figure (7)



R= (a)$C_6H_4CH_2$-(b) 3-NO_2-$C_6H_4CH_2$-, (c) 4 -Br-$C_6H_4COCH_2$- ,(d) 3-$ClC_6H_4CH_2$ - , (e)C_5H_{11}-

Scheme 1: Synthetic pathway of the Schiff bases derivatives



Scheme 2: The synthetic pathway of Oxazepine derivatives

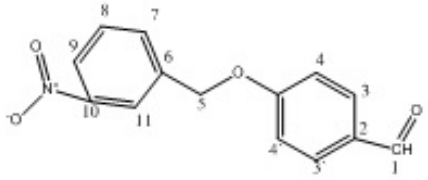


Figure 1: Compound 3b

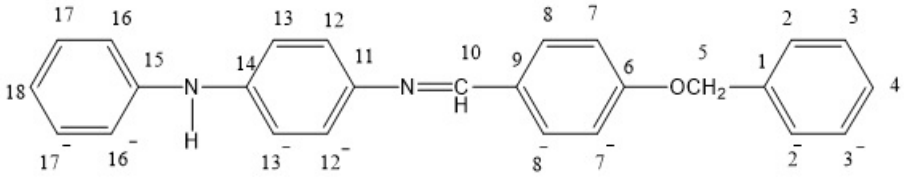


Figure 2: compound 4a

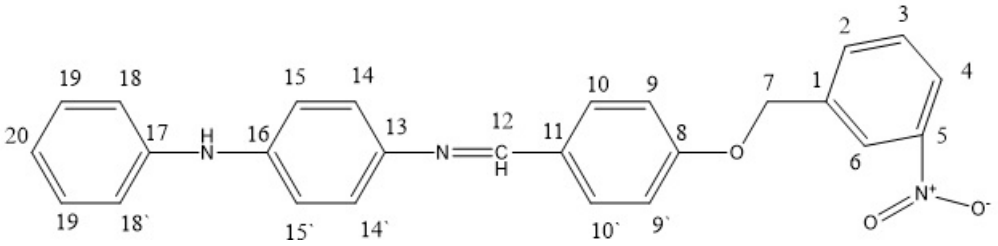


Figure 3: compound 4b

Compound (5d) showed a multiplet for 13 protons in aromatic regionwith a doublet at δ 5.2 ppm attributed to protons of O-CH_2 group, and appearance of a singlet at δ 9 ppm for azomethine (-N=CH) proton was a significant signal were distinguishable for condensation with benzaldehde, (Figure 7) (Table 5).

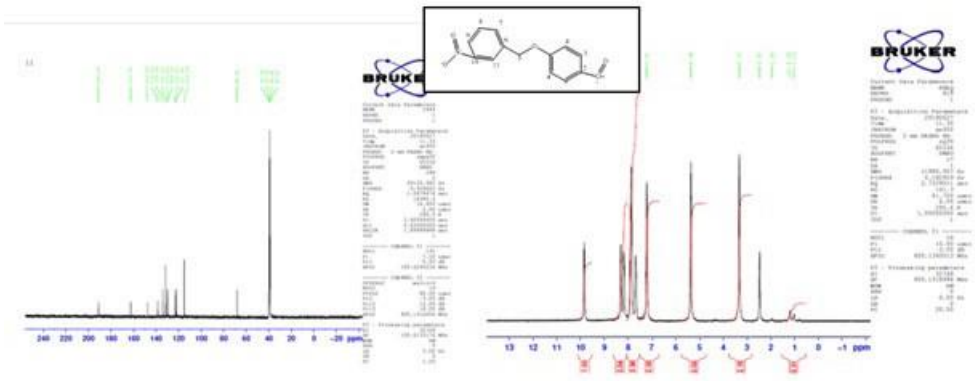


Figure 4: ^{13}C –NMR and ^{1}H-NMR spectrum of compound 3b

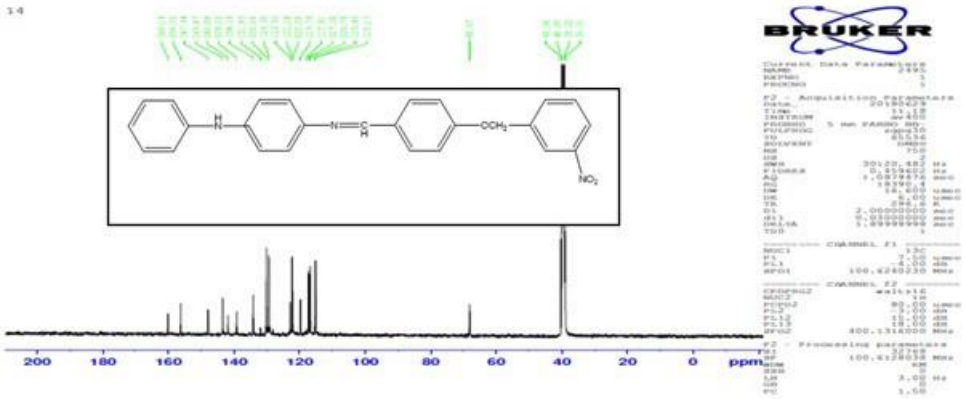


Figure 5: ^{13}C spectrum of compound (4b)

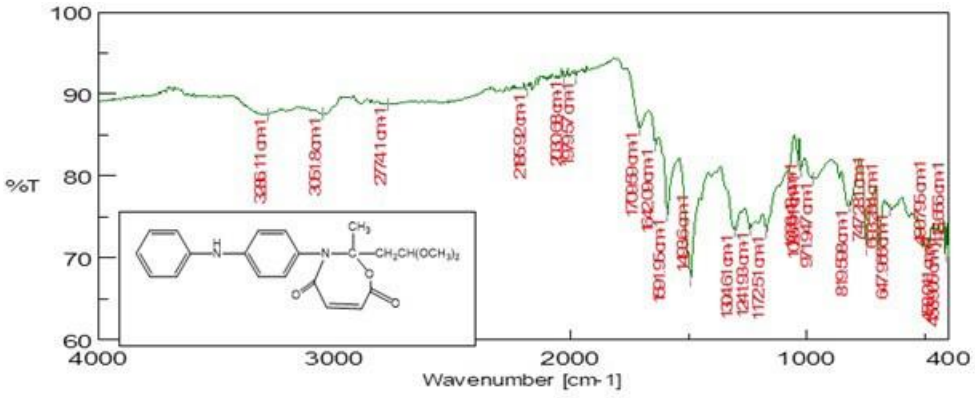


Figure 6: IR spectrum of Compound (6f)

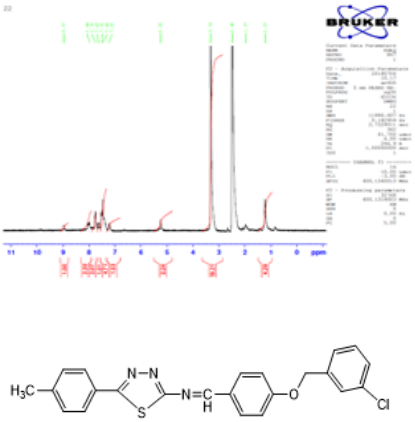


Figure 7: ^{1}H-NMR of Compound 5d

:

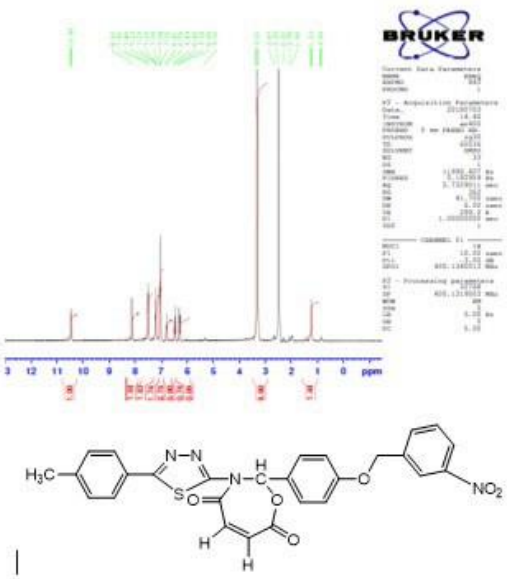


Figure 8:^{1}H-NMR of Compound 7b

Table 3: Assignments of characteristic frequencies (cm^{-1}) of IR spectra for the prepared compounds 4a-g5a-d:

compound	NH	CH (Ar.)	CH_2 alphatic	CH azomethin	CH=N	C=C (Ar.)	C-o Str.	N=Ostr.	N=Ostr.
4a	3380	3030	2980,2900	2859	1620	1593	1240		
4b	3383	3071	2987,2971	2890	1623	1596	1217	1347	1514
4c	3261	3057	2987,2901	2880	1585	1498	1225		
4d	3380	3000	2987,2901	2850	1583	1495	1220		
4e	3282	3020	2950,2932	2887	1600	1490	1230		
4f	3284	3033	2896,2922	2828	1640	1597	1225		
4g	3275	3029	2980,2900	2820	1644	1593	1225		
5a		3056	2961,2900	2800	1632	1462	1087		
5b		3062	2988,2921	2889	1570	1453	1241	1351	1516
5c		3056	2985,2900	2890	1585	1488	1240		
5d		3054	2988,2925	2898	1596	1514	1242		

Table 4: Assignments of characteristic frequencies (cm-1) of IR spectra for the prepared compounds 6a-g and 7a-d.

compound	N-H str.	C-Hstr. aromatic	C=O str.	C=C str.	C=O str. C-O str. Lacton	C=O str. Lac-tam	$N=O_{str.}$	$N=O_{str.}$
6b	3300	3058		1488	1701,1240	1630	1596	1397
6c	3286	3000	1690	1585	1771,1224	1656		
6d	3253	3056		1597	1686,1087	1632		
6e	3280	3056		1586	1701,	1632		
6f	3286	3051		1590	1709,1241	1642		
7a		3056		1597	1686,1087	1632		
7b		3056		1515	1734,1241	1630	1570	1351
7c		3050	1690	1585	1736,1223	1655		

Table 5: ^{1}H-NMR chemical shift assignment in ppm of some of the synthesized compounds.

Compound	1H-NMR Chemical Shifts in ppm
4b	^{1}H- NMR:, 8.54(s, 1H, Azomethine proton-CH=N-) 8.3 (s, 1H, -NH);6.8-7.8) (m, 17H, aromatic ring),5.2 (d 2H,CH_2)
4c	^{1}H-NMR: 8.54(s, 1H, Azomethine proton-CH=N-);8.2 (s, 1H, -NH); 6.8-7.8 (m, 17H, aromatic ring); 5.4 (d 2H,CH_2)
4d	^{1}H-NMR: 8.6 (s, 1H, Azomethine proton-CH=N-); 8.4 (s, 1H, -NH); 6.8-7.8 (m, 17H, aromatic ring); 5.2 (d 2H,CH_2)
4e	^{1}H-NMR: 8 (s, 1H, Azomethine proton-CH=N-); 7.9 (s, 1H, -NH); ; 68-7.5 (m, 17H, aromatic ring) ; 4 (t,CH_2O-); 1.3 (p, 2H (CH_2) ; 1.3 (p, 2H (CH_2) ; 0.9 (t, 3H (CH_3)
4g	^{1}H-NMR: 7-8 (m, 13H, aromatic ring), 8.3 (s, 1H, -NH)
5a	^{1}H-NMR: 9 (s, 1H, Azomethine proton-CH=N-); 7.3-8 (m, 13H, aromatic ring);
	5.24(d, 2H, CH_2O); 1.4(s, 3H CH_3)
5b	^{1}H-NMR: 9 (s, 1H, Azomethine proton-CH=N-); 7.2-8 (m, 13H, aromatic ring)
	5. 4(d, 2H, CH_2O); 1.4(s, 3H CH_3)
5c	^{1}H-NMR: 9 (s, 1H, Azomethine proton-CH=N-); 7.2-8 (m, 13H, aromatic ring)
	5. 3(d, 2H, CH_2O); 1.4(s, 3H CH_3)
5d	^{1}H-NMR: 9 (s, 1H, Azomethine proton-CH=N-); 7.3-8 (m, 12H, aromatic ring) ; 5. 3(d, 2H, CH_2O); 1.4(s, CH_3)
6:00 AM	^{1}H-NMR: 10.5 (s, 1H, CH-N-);7.3-8 (m, 16H, aromatic ring) 6.2,6.5 (d,d , 2H CH=CH Oxazepine ring) 5.3 (d, 2H, CH_2O);
7b	^{1}H-NMR: 10.5 (s, 1H, CH-N-);7.3-8 (m, 12H, aromatic ring) 6.3,6.5 (d,d , 2H CH=CH Oxazepine ring)

^{13}C-NMR data were in agreement with the formation of the products, for example compound 4b Figure (3) showed a line at δ 68 ppm due to CH_2-O group and 18 lines for Aromatic carbons, CH=N observed at δ 158 ppm. ^{13}C-NMR: C : 160_8 19, C :158.30$_{12}$, C :147.34$_5$, C :143.47$_{17}$, C : $_1$ 141.86, C_{13}:139.22, C_{16}: 134. 18, C_2:131.94 , $C_{10,10`}$:130.4, $C_3$:129.28, $C_{19,19`}$: 122.9,C_{11}: 122.28 C_6: 122.16, $C_{14,14`}$:119.76, $C_{4`}$: 117.91,$C_{15,15}$`: 117.30, $C_{20}$: 116.78, $C_{18,18}$`:115.40 ,C_9: 115.17, C_7:68.17 Figure (5).

^{1}H-NMR spectra of compound 4g also exhibited a multiplet at δ 7-8 for 13H in aromatic position with two singlet signal at δ 8.3,8.75 for 1H (NH) and CH=N proton respectively. (Table 5) This compound characterized from the 13C–NMR spectrum data: $C_{13,13`}$ 117.03, $C_{15}$ 117.14, $C_{10,10`}$ 118.3, $C_{9,9}$:120.06, C_3:122 .65, C_2:128.95, C_5:129.091, C_4: 132.4.C_1:135.39, C_6: 135.53, C_{11}:140.9, C_8:142.61, C_{12}:143.24. C_7: 155.5.

The 1,3-oxazepine derivatives were obtained by addition reaction of Schiff bases with anhydride in dry benzene, Scheme 2, The new 1,3-oxazepine derivatives (6a-g) and [7a-d] were synthesized by refluxing imines compound with (maleic anhydride) in the presence

of dry benzene. The characteristic FTIR absorption bands of these compounds were confirmed from the disappearance of band due to C=N of Schiff bases and other peaks characterized of cyclic anhydride of the starting materials together with appearance of two characteristic bands of two carbonyl groups of Oxazepine ring at 1732 $cm^{-1}$and 1686 cm^{-1} respectively. Two bands around (1280 and 1103 cm^{-1}) was observed belong to asymmetric and symmetric(C-O-C) band.

The spectral data of FTIR for new Oxazepine compounds are listed in (Table 4) Figure 6. The ^{1}H-NMR spectrum), of compound 7b (in DMSOd6) showed a singlet signal of N-CH proton absorbed at δ 10.44 ppm, the aromatic ring protons appear as multiple in the region (δ 6.48-8.1) ppm for 12 hydrogen, and a signal related to CH_2-O at 5.3 ppm, with signals as two doublet attributed to CH=CH Oxazipine ring at (δ 6.28-6.31) [14], CH_3 group observed as a singlet at δ 1.2 ppm [15,16]. Figure (8)

6. Antimicrobial activities

Antibacterial activity of these compounds was determined by the ager diffusion method. Anti-microbial study was assessed by measuring the minimum inhibitory zone (using disk agar diffusion method).

The biological interest of Schiff base and Oxazipines derivatives were recorded in the literatures. Therefore, the antibacterial study was done and the activity was determined by the disc diffusion method at the concentration of 50 µg per disk. All the synthesized used compounds were tested for their antibacterial activity against both bacteria *S. aureus* and *P. aeruginosa*..

The synthesized Schiff bases 4a-c showed more activity against *Pseudomona*s than the *S. aureus* while compounds 4d and 4g showed the same activity against both the gram-positive and the gram-negative tested bacteria, this is may be due to the presence of Chlorine atom (Cl) in these compounds and the compound 4e was more active towards the *S. aureus* than the *Pseudomona*s *aeruginosa* The increased activity may be attributed to enhancement

of lipophilicity due to incorporation of aromatic benzene ring, stright chain alkanyl and substituent NO_2, Cl groups at meta positions with the presence of N-H groups.

Whereas the synthesized thiadiazole derivatives 5a and 5b also showed the same activity against both the gram-positive and the gram-negative tested bacteria. The compound 5d was moderately active against *Pseudomonas* if it compared with *S. aureus*, while 5c was slightly active against gram-negative bacteria. The increased activity may be attributed to enhancement of lipophilicity due to incorporation of aromatic benzene ring and substituent NO_2, Cl groups at meta and para positions with the presence of Ether groups with oxazipine moiety. antibacterial agent listed in (Table 1).

8. Conclusion

An attempt to synthesize new series of ethers were carried out under reflux condition using alkyl and aryl halide via substitution on hydroxyl benzaldehyde, the products of the reaction used in the synthesis of new series of Schiff bases with two of amino compounds 2-amino-5 [-4-methylphenyl] thiadiazole and 4-aminodiphenyl amine, the products were obtained in very good yields. Another attempt was to study the Oxazepine derivatives of some the synthesized Schiff base compounds through the reaction of these compound with Maleic anhydride , the product were characterized by physical properties and by spectroscopic data the results were in agreement with formation of the desired compounds, The anti-microbial activities of the synthesized compounds were studied against two kinds of bacteria, Gram-positive *S. aureus* and Gram-negative bacteria *P. aeruginosa* all the synthesized Oxazipine derivatives were found to exhibit the sameactivity approximately toward both tested bacteria and in general were more active than some of synthesized Schiff bases.

References

1. Siddiqui L, Iqbal A, Ahmad S, George W. Weaver, Synthesis and Spectroscopic Studies of New Schiff Bases Hamid, Molecules. 2006; 11: 206-211.
2. Uddin, Faisal Rashid, Ali S, Tirmizi SA, Ahmad I, Sumera Zaib et al. Synthesis, characterization, and anticancer activity of Schiff bases, Journal of biomolecular Structure & Dynamics. 2019; 14: 1-14.
3. Siddappa k, Mayana NS. Synthesis, Spectroscopic Characterization, and Biological Evaluation Studies of 5-Bromo-3-(((hydroxy-2-methylquinolin-7-yl) methylene) hydrazono) indolin-2-one and Its Metal (II) Complexes, Bioinorg Chem. 2014; 12: 483282.
4. Yousif E, Majeed A, Khulood Al-Sammarrae , Nadia Salih c , Jumat Salimon , Bashar Abdullah, Metal complexes of Schiff base: Preparation, characterization and antibacterial activity, Arabian Journal of Chemistry. 2013; 5.
5. Brodowska K, Lodyga-Chruscinska E. Schiff basese-interesting range of applications in various fields of science, Cheminform.2015; 46(11). Review Article 1,3,4-THIADIAZOLE: A BIOLOGICALLY ACTIVE SCAFFOLD.
6. Jawdat H. Abdul – Wahid, Ayad S. Hameed, Aveen K. Mohammed, Synthesis Characterization of Some New Heterocyclic Compounds Containing1, 3-Oxazepine Ring, Kirkuk University Journal /Scientific Studies (KUJSS), 2016; 11: 237-247.
7. Mukhlus, MS. Al-Rawi, J. H. Tomma, A. H. Al-Dujaili, Synthesis and Characterization Of New Oxazepines Derived From D-Erythroascorbic Acid A, Ibn Al-Haitham Journal for Pure and Applied Science. 2012; 25: 2.
8. Azeez HJ, Qadir KM. Synthesis and spectroscopic characterization of a new series of benzo [E] [1,3] Oxazepine compounds from Schiff bases, Science journal of university of Zanko.2017 5: 101-106
9. Iman K. Naeem, Ezzat H. Zimam, Synthesis, Characterization and Study Antibacterial Activity of some New 1,3- oxazepine and 1,3-diazepine Derivatives, Der Pharma Chemica, 2017; 9: 86-93.
10. Khalilullah H, M U Khan, Danish Mahmood, Jawed Akhtar, Gamal Osman, 1,3,4 Thadiazole: Abiological Active, Scaffold,International

journal of Pharmacy and Pharmaceutical Sciences. 2014; 6

11. Abdyl Jabar, Kh, "Synthesis and Antibacterial Activities of New Metronidazole and Imidiazole Derivatives", Molecules. 2009; 14: 2431-2446.
12. ShukIa DK, Srivatava SD. "synthesis of new 5- [2-{(1, 2, 3)-benzotriazole)-1-yl-methyl}-1'-(4'-substituted aryl-3'-chloro-2'-oxo azetidine)] -amino-1, 3, 4-thiadizoles antifungal and Antibacterial agents, Journal Indian of Chemistry. 2008; 47: 463-469.
13. Atyaf AQ Younus, Nasreen R Jber. Synthesis and Characterization a New 1,3-Oxazepine Compounds from New Bis-4-Amino-3-mercapto-1,2,4-triazole Derivatives,Organic Chemistry. 2016; 12: 1-12A.
14. Mukhlus A, Al-Rawi MS, Tomma JH, Al-Dujaili AH, Synthesis and Characterization of New Oxazepines Derived from D-Erythroascorbic Acid, Ibn Al-Haitham Journal for Pure and Applied Science. 2012; 25.
15. Ruaa M. Al-Juburi, Synthesis and Characterization of Some Heterocyclic Compounds (Oxazepine, Tetrazole) Derived from Schiff Bases, Journal of Al-Nahrain University. 2012; 15: 60-67.
16. Yousif SA. Synthesis of substituted (oxazepine, Diazepine, tetrazde) via Schiff Bases for 2- Aminobenzo Thaizole Derivatives, Baghdad Science Journal. 2013; 10: 737.
17. Iman K. Naeem, Ezzat H. Zimam, Synthesis, Characterization and Study Antibacterial Activity of some New 1,3- oxazepine and 1,3-diazepine Derivatives, Der Pharma Chemica. 2017; 9: 86-93.
18. Jawdat H. Abdul – Wahid, Ayad S. Hameed, Aveen K. Moha, Synthesis Characterization of Some New Heterocyclic Compounds. 2016; 11: 237-247.