

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF SOME OXAZEPINE AND OXAZINANE DERIVATIVES FROM REACTION OF SCHIFF BASES WITH SOME CYCLO ANHYDRIDE.



KAISS R.IBRAHEEM* ,MOHAMMED A.AL-HADITHI* AND WALEED F. AL-HITY*

*Chem.Dept.College of Science, University of Al-Anbar

**Chem.Dept.College of Education for women, University of Al-Anbar

ARTICLE INFO

Received: 21 / 4 /2007

Accepted: 2 / 8 /2007

Available online: 14/6/2012

DOI: [10.37652/juaps.2007.15287](https://doi.org/10.37652/juaps.2007.15287)

Keywords:

Synthesis,
Characterization,
Oxazepine,
Oxazepane,
Biological activity.

ABSTRACT

Schiff bases [2-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-5,5-diethyl-dihydro-pyrimidine-4,6-dione and 2,6-Bis-(1,5 Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-5,5-diethyl-tetrahydro-pyrimidin-4-one] were prepared by condensation of 5,5-Diethyl-pyrimidine-2,4,6-trione with one equivalent and tow equivalent of 4-Amino-1,5-dimethyl-2-phenyl-1,2-dihydro-pyrazol-3-one in ethanol (as solvent). These Schiff-base were reacted with one equivalent of maleic , succinic and malonic anhydride in absolute ethanol to give 7-membered heterocyclic ring system 12(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3,3-diethyl-7-oxa-1,5,12-triaza-spiro[5.6]dodecane-2,4,8,11-tetraone. and 6- membered heterocyclic ring system of 5-(1,5-Dimethyl -3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-9,9-diethyl-1-oxa-5,7,11-triaza-spiro[5.5]undecane-2,4,8,10-tetraone.Than , the product were reacted with tow equivalent of maleic , succinic and malonic anhydride in same solvent give 2 (7-membered) heterocyclic ring system of 8,15-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-18,18-diethyl-1,10-dioxa-6,8,15,16-tetraza-dispiro[6.1.6.3]octadeca-3,12-diene-2,5,11,14,17-pentaone.(9) and 2 (6-membered) heterocyclic ring system of 7,13-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-16,16-diethyl-1,9-dioxa-5,7,13,14-tetraza-dispiro[5.1.5.3]hexadecane-2,4,12,15-pentaone.

The final organic products were identified by there m.ps, elemental analyses,IR, and UV-Visible spectra.

INTRODUCTION:

The synthesis of 2-phenyl -1,3-oxazepine ⁽¹⁾ and the discovery of the central nervous system (CNS)

activity of 1,4-benzodiazepine ⁽²⁾ by irradiation of 4-phenyl-2-oxa-3-aza bicyclo [3,2,0] hepta-3,6- dione, encouraged the chemists to look for other ways to build up the 7-membered heterocyclic ring system.

* Corresponding author at: Chem.Dept.College of Science, University of Al-Anbar, Iraq.
E-mail address: Mohamed_alhadithi@yahoo.com

One of these ways which was discovered recently, involves direct addition of maleic anhydride to the (N=C) double bond of Schiff bases, a number of 2,3-diaryl-2,3-dihydro-1,3-oxazepine-4,7-dione and 2-aryl-3-(1,5-dimethyl-2-phenylpyrazolonyl)-2,3-dihydro-1,3-oxazepine-4,7-diones were prepared and characterized^(3,4).

The six-membered heterocyclic ring system: 1,3-oxazine has already been reported and thoroughly reviewed in the literature⁽¹⁻⁴⁾. Maleic arylmaleic and substituted maleic anhydrides react with trimethylsilylazide to give 4- and 5-substituted "oxauraciles": dihydro-1,3-oxazine-2,6-diones⁽⁵⁻⁶⁾

Both 2-methoxypyrroline and 2-methoxypiperidine react with diketene under neutral conditions at 0°C to give the corresponding, 2-methoxydihydro-1,3-oxazine-4-ones⁽⁷⁻⁸⁾.

Diketene reacts with N,N-diphenyl guanidine to give the tranquilizer ketazolam and N-substituted tetrahydro-1,3-oxazine-4-one respectively⁽⁹⁻¹⁰⁾.

The reaction of diketene with isocyanic acid, cyanamides and fluoro-sulphinyl isocyanate afforded the corresponding 1,3-oxazine-2,4-diones⁽¹¹⁻¹³⁾.

Ethyl benzimidate, and ethyl butyrimidate react with diketene to give 2-ethoxy-1,3-oxazine-4-ones⁽¹⁴⁾. Imines and N-acyl imines react with diketene to give tetrahydro-1,3-oxazine-4-ones⁽¹⁵⁻¹⁶⁾.

N-acyl imines undergo [4+2] cycloaddition with both C=C- and heterodienes. For instance, isolable bis(trifluoromethyl)acyl imine, reacts with 2,2-dimethylethylene to give 1,3-oxazine.

N-acyl immonium ions have been the most commonly used dienes to effect [4+2] cycloaddition as 4π components with substituted 1,3-butadienes. It is found that N-acylimines or immonium ions that are capable of tautomerization undergo intramolecular Diels-Alder reaction to give dihydro-1,3-oxazines⁽¹⁷⁾.

The reaction of N-Benzylidene 1,5-dimethyl-2-phenylpyrazolonamines (Schiff bases with Cyclopentane-1,1-dicarboxylic anhydride to give 2-aryl-3-(1,5-dimethyl-2-phenylpyrazolo)-1(5)-spirocyclopentyltetrahydro-1,3-oxazine-4,6-diones⁽¹⁸⁾.

Extensive synthesis and testing of the barbiturates over a long time span has produced well-defined structure – activity relationships. Which have been summarized.⁽²⁵⁾

Both hydrogen atoms at the 5-position of barbituric acid must be replaced. If one hydrogen is available at position 5, tautomerization to a highly acidic trihydroxypyrimidine (pKa = 4) can occur. Consequently, the compound is largely in the anionic form at physiologic pHs, with little nonionic lipid-soluble compound available to cross the blood-brain barrier.⁽²⁶⁾

EXPERIMENTAL:-

Melting points were recorded on Gallenkamp melting points Apparatus and were uncorrected. Elemental analysis was carried out in Mutah University on Perkin-Elmer 2400 CHN Elemental analyzer . FT-IR spectra were recorded on FT-IR spectrophotometer -8400s Shimadza (KBr) and UV-Visible spectra were recorded (in ethanol) On Shimadza Reco- 160 Spectrophotometer.

Preparation of 2-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-5,5-diethyl-dihydro-pyrimidine-4,6-dione (Schiff-base):-

To a solution of 0.05 mole of 4-Amino-1,5-dimethyl-2-phenyl-1,2-dihydro-pyrazol-3-one in 30 ml of absolute ethanol 0.05 mole or 0.1 mole of 5,5-Diethyl-pyrimidine-2,4,6-trione was added and the mixture was refluxed for one hour. Where by a yellow crystalline solid separated out . The solid was filtered and recrystallized from ethanol and their spectral features were discussed .

Preparation of 12(1,5-Dimethyl -3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3,3-diethyl-7-oxa-1,5,12-triaza-spiro[5.6]dodecane-2,4,8,11-tetraone:-(3)

In a 100 ml round bottom flask equipped with double surface condenser fitted with calcium chloride guard tube was placed. A mixture of 0.01 mole of 2-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-5,5-diethyl-dihydro-pyrimidine-

4,6-dione and 0.01mole maleic anhydride in 20 ml of absolute ethanol.

The reaction mixture was refluxed in water bath at 78C° for 3 hrs., the solvent was then removed and the resulting solid was recrystallized from anhydrous THF.

Preparation of 8,15-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-18,18-diethyl-1,10-dioxa-6,8,15,16-tetraza-dispiro[6.1.6.3]octadeca-3,12-diene-2,5,11,14,17-pentaone:- (9)

A mixture of (0.01 mole) of 2,6-Bis-(1,5 Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-5,5-diethyl-tetrahydro-pyrimidin-4-one and (0.002 mole) of maleic anhydride in absolute ethanol was refluxed on a water bath for 3hr. The solvent was then removed by evaporation and the crystalline solid was recrystallized from anhydrous 1,4-dioxan.

This experiment was repeated using the same amounts of the reactance to obtain other derivatives. The spectral features of products were discussed

BIOLOGICAL ACTIVITY

MATERIAL & METHODS;

1-Preparation of concentration ;

Five diluted solutions were prepared from the compounds under study. These were (10,25,50,75,100) mg/mm. Disks of filtering paper were saturated with each dilution in order to decide the deactivating

capacity of these compounds the isolated specimen of pathological bacteria.

2- The Isolated bacteria specimen;

Specimen of bacteria were obtained from different cases from the Labs of Ramadi Central Hospital that cover wounds., burns , stolls, urine and ear infections. These specimen were diagnosed and cultured on a nutrient agar medium for use in the experiment, and in measuring the deactivating capacity of the prepared compounds. The following shows the sources of the bacteria obtained and their media.

bacteria	sources	Culture
<i>Staphylococcus aureus</i>	stool	Blood agar
<i>Proteus mirabilis</i>	urine	Blood agar
<i>Pseudomonas aeruginosa</i>	Ear infection	Nutrient agar
<i>Klebsiella pneumoniae</i>	burns	MacConkey agar
<i>Salmonella typhi</i>	urine	S.S. agar
<i>Shigella Sonni</i>	urine	S.S. agar

3- Test of deactivating capacity of the prepared compounds;

The deactivating capacity agent of the isolated bacteria of these compounds was tested by using the method of the spread over the discs as described by Bauer, *et al* in (1966).⁽¹¹⁾ This method uses discs of filtering paper saturated with five different concentrations (10,25,50,75,100) of the given compound after culturing this bacteria on dishes on the hard Muller–Hinton medium. Discs of filtering paper, that were saturated with these different prepared compounds , were placed on the medium and then incubated at 37°C for 24 hours.

ANTI-BIOTICS

(Tetracycline,Amoxicillin,Nalidixic acid, Gentamycin) were used to control the bacteria specimen. The deactivation diameters were measured by special ruler designed for this purpose.

DISCUSSTION:-

It is known that Schiff bases react smoothly with acid chlorides and anhydrides to give the corresponding addition products.^(5,6,10)

In this paper, the reaction of the Maleic Succinic and Malonic anhydrides with 2-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-5,5-diethyl-dihydro-pyrimidine-4,6-dione to gives the intermediate [11A] and [111A] which collapses to the

7- membered and 6- membered heterocyclic ring system (11C) and [111C] is presented.

It is known that Schiff bases react smoothly with acid chlorides and anhydrides to give the corresponding addition products ⁽⁵⁻⁷⁾ .

In this paper , the reaction of the cyclic anhydride (maleic , succinic and malonic) anhydride with 2,6-Bis-(1,5 Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-5,5-diethyl-tetrahydro-pyrimidin-4-one can be presented as follows:

This is indicated by the appearance of the characteristic C=O (lacton-lactam) absorption band at 1700cm⁻¹ in the IR spectra of addition products [11B] and [111B]

It is impressive to note that the two absorption band at (1800-1950)cm⁻¹ in the IR spectra of pure Maleic , Succinic , and malonic anhydride have disappeared when the anhydride became part of the 7-membered ring system of the 8,15-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-18,18-diethyl-1,10-dioxo-6,8,15,16-tetraza-dispiro[6.1.6.3]octadeca-3,12-diene-2,5,11,14,17-pentaone. (9) and 5-(1,5-Dimethyl -3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-9,9-diethyl-1-oxa-5,7,11-triaza-spiro[5.5]undecane-2,4,8,10-tetraone.(4)

The (C=O) group in the IR spectra of the addition products ,1,3-oxazepine-4,7-diones and 2-aryl-3-methyl-5,6-dihydro-7H-pyrrolo[1,2-d]

[1,4]benzodiazepine-6-ones(8,9) is absorbed in the same region (1670-1700) cm⁻¹, This conforms the assigned 7-membered ring system structure. The cycloaddition reaction is classified as 2+5—7, and it is the first cycloaddition of this type, although in principle, one would predict that the pentadienyl cation might add to an olefin through a (4n+2) transition state to yield the cycloheptenyl cation ⁽¹⁰⁾.

Structure [11B] and [111B] is a combination of both lactone and lactam in a 7- heterocyclic ring. This is indicated by the appearance of the characteristic(C=O) (lactone/lactam) absorption band at (1660-1680)cm⁻¹ in their IR spectra. Furthermore, structure (3,8,9,12,14) still maintains the (cis-CH=CH) double bond of maleic and anhydride as indicated by the absorption band at (1600-1610) cm⁻¹ .

The UV spectra of 8,15-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-18,18-diethyl-1,10-dioxo-6,8,15,16-tetraza-dispiro[6.1.6.3]octadeca-3,12-diene-2,5,11,14,17-pentaone and 5-(1,5-Dimethyl -3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-9,9-diethyl-1-oxa-5,7,11-triaza-spiro[5.5]undecane-2,4,8,10-tetraone .show absorption maxima at (240-310)nm , and at (310-445)nm due to charge transfer of the aryl group and the cyclic 6-membered structure [11B]and [111B]

8,15-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-18,18-diethyl-1,10-dioxo-

6,8,15,16-tetraza-dispiro[6.1.6.3]octadeca-3,12-diene-2,5,11,14,17-pentaone. and 5-(1,5-Dimethyl -3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-9,9-diethyl-1-oxa-5,7,11-triaza-spiro[5.5] undecane-2,4,8,10-tetraone. are identified by their m.p., elemental analysis (table 4), IR spectra (table 5) and UV spectra (table 6). It is noticeable that the values of C-Hstr. (benzylic) absorption bands are rather high. This is in fact explained by the shift toward longer wavelength, that takes place when the benzylic carbon is linked to three electron-withdrawing groups, phenyl, O and N in the title compounds.

The reaction of 2-Oxa-spiro[3.4] octane-1,3-dione with various Schiff bases is a sort of cycloaddition reaction. Cycloaddition is a ring formation that results from the addition of bonds to either δ or π with formation of new δ bonds. This class of reactions and its reverse encompasses a large number of individual types. Huisgen ⁽¹⁹⁾ has formulated a useful classification of diverse cycloaddition in terms the number of the new δ bond. the ring size of the product, and the number of atoms in the components taking part in the cycloaddition. This cycloaddition reaction is classified as a 2 + 5-7, and it is the first cycloaddition of this type, although in principle, one would predict that the butadienyl cation might add to an olefin through a $(4n+2)$ transition state to yield the cyclohexenyl cation⁽²⁰⁾.

RESULTS;

Table(8) show the deactivation capacity against the bacteria specimen of the prepared compounds under study. The results show that the lowest which is (10) concentrations did not have any deactivation capacity against the bacteria specimen, and this applies to all B. isolated and all compounds deactivation capacity. The concentration 25-100 shows deactivation. The difference in deactivation was obvious through the difference in concentration, the highest deactivation is 75-100.

DISCUSSION;

The results of the present study show that some of the prepared compounds have a relatively strong deactivating capacity against the specimen of bacteria. Bacteria is known to be anti-toxic and enjoys a resistance to anti-biotic for plasma.

The results indicate that some compounds with the concentration (10) compounds are not able to penetrate to their target area in the cell, because of a barrier, like the external tissue in the cellular wall of the negative bacteria of Gram Colour. This may prevent the extracted access to the center of vital effect in the cell. The lack of deactivation areas for some compounds may be due to the lack of the suitable

carrier in the cell or the necessary energy to have access to the internal target⁽²²⁾ .on the hand.

The results, on the other hand, show that some compounds have a good deactivating capacity against the isolated bacteria specimen. This is due to the percentage of active material solved in the water . Water is known to be the most common solvent in nature. It can solve many compounds.

The study showed also many evidences of other active anti-biotics that can be put to further use in the system of Bioresistense against the causes of several plant diseases in order to avoid the excessive use of the chemical pasteyciedes that cause environmental problems and are very expensive.

Acknowledgments:

The authors would like to thank Dr.mohammed Qais Al-Ani – biology dept. in help to isolation of bacteria in microbiology lab .

REFERENCES:

- [1]-Toshio Makai, Tsutomu Kumagai, and Osamu Sashimoto, (photochemical and thermal reactions of some heterocyclic containing C=N-O and N=C-O group) Pure and Appl. Chem. Vol. 49, pp. 287-308, 1977
- [2]-Cheesman, G.W. H. and Greenberg, S.G., (Synthesis of 5,6-dihydro-4H-pyrrolo[1,2- α] [1,4]

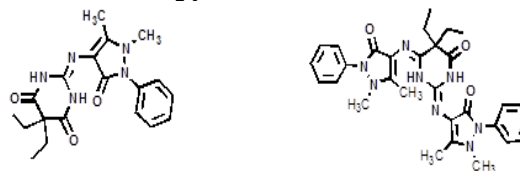
enzodiazepines) J.Heterocyclic Chem. 16,241, 1979

- [3]- Schiff ,H.,Ann, 131,118, 1864
- [4]- Clifford J.Crewell, Olaf, A.Rungvist,and Malcolm M.Campbell, (spectral analysis of organic compounds) ,2nd ed., Longman, 1972
- [5]- Hussein F.A . Obaid,H.,A; (synthesis of N-substituted saccharins via Schiff Bases) ., Iraqi Journal of Chemistry , Vol 26,No.(1),pp.42-50, 2000
- [6]- Hussein F.A. Obaid,H., A; (synthesis of N-substituted saccharins via Schiff Bases) Iraqi Journal of Chemistry , Vol 26,No.(1) pp.35-41, 2000,
- [7]- Hussein F.A. Obaid,H.,A; 1, (synthesis of some Barbiturates via Schiff bases). Iraqi Journal of Chemistry, Vol 26,No.(1) pp.216-274, 2000
- [8]-Enrico Aiello, Gaetano Dattolo, Cirrincione,, (polycondensed Nitrogen Heterocycles . V11.5,6-dihydro-7H-pyrrolo [1,2- α] [1,4] benzodiazepines-6-ones), J.Heterocyclic Chem., 16,209, 2000
- [9]-John.R.Dyer, (Applications of absorption spectroscopy of Organic Compounds) Prentice-Hall, Inc.,Englewood Chiff,S,N.J., 2000
- [10]-Robert M.Moriarty and charless w.Jefford, (Organic chemistry A problms : An Approach,) W.A.Bengamine,Inc,p 526, ,,

- [11]-Gunav,V.I.;Mikhailopulo,I-A;Ovechkina,L.F
andZavyalov,S.I;Chem.Abst.,67,5497, 1967[12]
- ficini,J .and Gene t,J. P; Soc. Chim .Fr., 2086,
1967
- [13]ietch, H.;Glauss,K.;Schmidt,E and Jensen, H.;
Chem. Abst.,,84,13568f, 1967
- [14]Kato,T.;Ymamota,Y.,Chem.Pharm.Bull.,,15,1334
, 1967
- [15]-Kato, T. and Sakamoto, T.,Chem.Abst., ,68,
11452, 1968
- [16]- Matsuda,I.,;Yamato,S.,and Ishii,Y.;J.Chem.Soc.
perkin Trans. (1) ,1933, 1976
- [17]-Eckhardt,H.H and Perst,H .; Tet.Lett. , ,23 2125,
1979
- [18]- Obaid,H.,A; National J.,Chem. Vol(7),446-460,
2002.
- [19]-Huisgen R., Angew; Chem. Internt.,Edit.7,321,
1968 .
- [20]-Robert M.Moriarty and charless w.Jefford
(Organic chemistry A problms : An Approach,)
W.A.Bengamine,Inc,p 526 ,1975 .

- [24]- Robert M.Moriarty and charless w.Jefford
(Organic chemistry A problems):
- [25]- Hou,J.P.,and Poole,J.W.: J. Pharm.Sci.
58:1150,1969
- [26]- Wilson and Gisold,s (Textbook of organic
medical and pharmaceutical chemistry) Tenth
Edition , ippincott Williams & wilkins P 444 -
446 .

Table (1) : Melting point, percentage yield, molecular formula and elemental analysis of antipyrine-Schiff-bases



Comp.	M.P/C ^o	Yield%	M.F (M .Wt)	Calc.			Found		
				C	H	N	C	H	N
1	190-192	60	C ₁₉ H ₂₃ N ₅ O ₃ (373.45)	61.77	6.28	18.96	61.65	6.23	18.84
5	206-208	51	C ₂₉ H ₃₁ N ₈ O ₃ (554.64)	64.55	5.79	20.77	64.51	5.72	20.65

Table (2): major IR absorptions (cm⁻¹) of antipyrine-Schiff-bases.

Comp.	C-H str. Aromatic	C-H str. Alkane	C=O str	C=N Imine	C=C str. Aromatic	C-H bending lkane

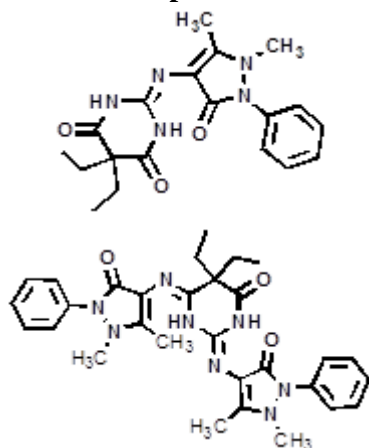
- [21] رويحة'أمية'1973 التداوي بالإعشاب بطريقة علمية تشمل الطب
الحديث والقديم.
- [22] الزبيدي، زهير نجيب بابان، هدى عبد الكريم و فليح كاظم فارس
1997 دليل العلاج بالإعشاب الطبية العرقية- شركة آب للطباعة
المحدودة. بغداد-العراق
- [23]-Huisgen R., Angew; Chem. Internt. ,Edit.7,321
,1968 .

1	5
3025	3040
2850	2860
1685	1690
1620	1610
1580,1520	1590,1540
1460,1350	1480,1410

Table (3): The UV-Visible absorption maxima λ /nm of antipyrine-Schiff-bases.

compound	UV-Visible absorption maxima λ /nm
1	380,300,266,225,220
5	370,310,275,226

Table (4) : Some physical of experimental properties of Oxazepine and Oxazepane compounds.

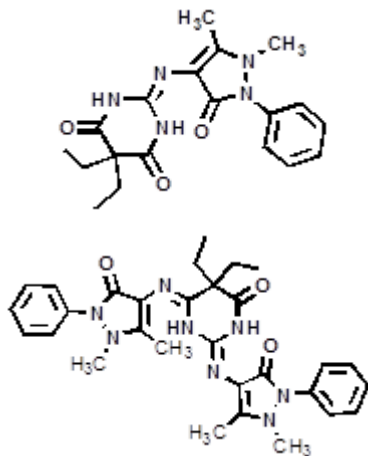


3	2	Compounds	
		M.P/C ^o	Yield%
170-172	180-182		
64	58		
C23H25N5O6	C23H27N5O6		
59.09	58.84		
5.39	5.80		
14.98	14.92		
59.00	58.93		
5.42	5.88		
14.87	14.78		
		Calc.	
		C	H
		N	
		C	H
		N	
		Found	

13	12	11	8	7	6	4
194-196	175-177	150-152	177-179	198-200	220-222	166-168
63	50	62	55	52	67	54
C37H40N8O9	C38H40N8O9	C36H38N8O9	C34H36N8O6	C38H42N8O9	C34H38N8O6	C22H25N5O6
59.99	60.63	59.50	62.57	60.47	62.37	58.01
5.44	5.36	5.27	5.56	5.61	5.85	5.53
15.13	15.36	15.42	17.17	14.85	17.11	15.38
59.87	60.57	59.45	62.44	60.36	62.30	58.12
4.42	5.29	5.30	5.51	5.67	6.00	5.51
15.00	15.23	15.36	17.05	14.73	17.02	15.27

14
210-212
52
C37H38N8O9
60.16
5.18
15.17
60.03
5.10
15.13

Table (5) : major IR absorptions (cm⁻¹) of Oxazepine and Oxazepane compounds.



7	6	4	3	2	Comp
3080	3070	3030	3050	3060	C-H str. aromatic
1680	1670	1660	1670	1680	C-H str. Olefin
-	-	-	1620	-	C=O str. Lacton, lactam
1580,1545	1575,1540	1580,1530	1570, 1535	1580,1540	C=C str. Olefin
1310	1330	1320	1320	1330	C=C str. Aromatic
1030,860	1020,850	1010,800	1030,900	1020,870	C-O str. lacton
1450	1435	1440	1420	1430	C-H bend Aromatic
					C-N str.

14	13	12	11	10	9	8
3060	3040	3080	3075	3090	3050	3060
3170		3145			3180	3160
1670	1680	1660	1670	1685	1680	1675
1620	-	1610	-	-	1625	1610
1570,1530	1580,1545	1570,1550	1585,1540	1580,1530	1570,1535	1570,1540
1320	1325	1330	1330	1320	1325	1320
1010,850	1020,870	1030,900	1025,860	1030,770	1020,880	1010,780
1445	1435	1440	1450	1445	1440	1450

Table (6) : The UV-Visible absorption maxima λ /nm of Oxazepine and Oxazepane compounds.

3	2	compound	UV-Visible absorption maxima λ /nm
333,265,25 1,243,223	320,300,26 6,230,221		

14	13	12	11	10	9	8	7	6	4
312,305,26 5,222	309,266,24 0,222	314,262,24 2,228	315,267,24 0,226	320,255,23 8,220	319,258,23 8,223	329,261,24 5,221	335,300,26 5,237,220	329,269,24 1,236,222	325,278,23 9,224

Table (8) Diameters of deactivation of Bacteria by use (1-14) compound in different concentration

B.Isolated

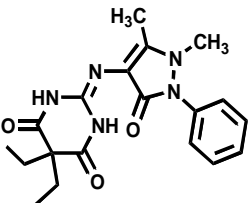
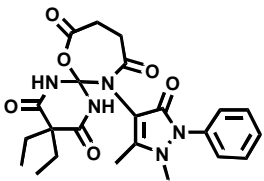
mg / ml	Diameters of deactivation (mm)																		
	4			3			2			1									
	75	50	25	100	75	50	25	10	100	75	50	25	10	100	75	50	25	10	
Staphylococcus aureus	7.4	5.1	3.2	0	14.2	9.7	5.0	0	11.2	7.7	5.1	3.2	0	12.5	8.0	6.2	4.5	0	
pneumonia Klebsiella	7.4	5.0	3.0	0	14.0	9.1	7.7	4.9	0	10.9	8.1	4.7	3.3	0	12.4	8.4	6.7	4.0	0
merabilis Proteus	7.8	4.9	4.1	0	15.2	10.1	8.1	4.5	0	10.5	8.0	5.0	3.0	0	12.0	8.9	7.0	4.0	0
Pseudomonas aeruginosa	10.0	6.1	5.0	0	16.0	12.1	10.2	7.2	0	12.7	10.1	7.5	5.0	0	14.5	10.7	9.2	6.0	0
Salmonella typhi	9.7	6.8	5.1	0	15.1	12.8	11.1	8.4	0	13.5	11.0	8.8	4.9	0	14.8	10.9	10.0	7.5	0
Shigella sonni	8.9	7.0	5.5	0	16.2	14.2	13.0	9.1	0	12.4	10.5	9.1	5.4	0	15.2	11.5	10.3	8.1	0

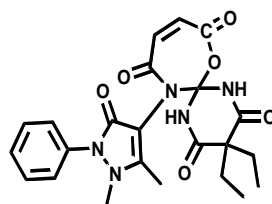
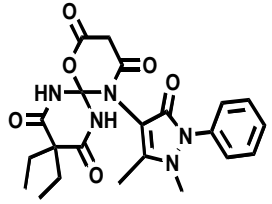
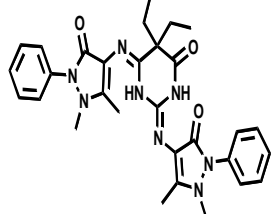
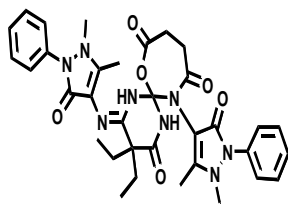
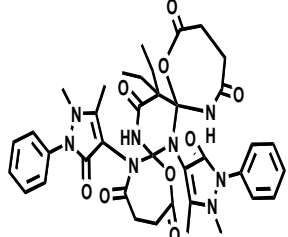
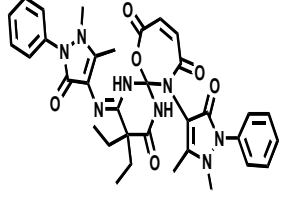
9			8			7			6			5					
75	50	25	100	75	50	25	10	100	75	50	25	10	100	75	50	25	10
7.8	5.1	4.1	7.1	6.8	4.0	3.8	0	8.8	7.0	5.0	3.5	0	12.8	10.1	7.0	5.0	0
7.4	5.0	5.3	8.4	7.0	4.1	3.7	0	9.4	7.3	4.7	3.0	0	12.7	10.8	7.3	5.1	0
8.1	5.5	4.6	10.0	7.7	5.7	3.0	0	10.4	8.0	4.4	3.6	0	11.6	9.7	6.9	4.5	0
9.4	6.2	6.2	11.1	8.2	6.0	5.0	0	12.1	9.1	6.2	4.4	0	13.1	11.4	8.0	5.5	0
10.8	7.1	6.9	9.5	8.1	6.2	6.8	0	10.2	7.8	5.5	3.0	0	14.8	12.0	8.7	5.0	0
12.2	7.9	8.0	11.2	9.4	8.1	7.6	0	13.4	10.0	7.7	4.9	0	15.4	12.4	7.5	5.2	0

14			13			12			11			10					
50	25	10	100	75	50	25	10	100	75	50	25	10	100	75	50	25	10
5.1	3.5	0	9.2	7.4	5.7	4.2	0	7.1	5.7	4.1	3.2	0	9.1	7.1	6.2	4.3	0
5.0	3.9	0	9.4	7.8	5.8	4.8	0	7.4	5.8	4.3	3.4	0	9.5	8.0	6.4	4.7	0
4.7	4.1	0	11.1	8.0	6.4	5.4	0	8.0	5.1	5.1	3.8	0	9.9	8.4	7.1	4.9	0
7.5	4.5	0	12.4	8.7	7.1	6.6	0	8.2	6.2	6.6	5.1	0	11.2	10.1	8.1	6.2	0
8.0	6.4	0	13.4	9.4	8.4	7.0	0	9.2	6.8	7.0	6.6	0	12.4	10.8	9.1	8.4	0
8.4	7.4	0	15.0	13.4	13.4	10.1	0	11.0	8.4	7.9	7.4	0	14.9	12.4	12.4	10.7	0

	Gentamycin	Amoxicillin	Nalidixic acid	Tetracycline		
					100	75
	30µg	20µg	30µg	300µg	100	75
	9.0	11.0	11.0	8.0	8.4	6.2
	6.0	6.0	13.0	9.0	8.9	6.0
	8.0	5.0	20.0	11.0	10.0	7.3
	0	12.0	13.0	12.0	11.4	7.9
	11.0	0	22.0	7.0	13.4	8.1
	20.0	0	12.0	11.0	15.7	9.7

Table (9) : The name and structure of synthesis compounds

No.	Name	Structure
1	2-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-5,5-diethyl-dihydro-pyrimidine-4,6-dione	
2	12-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3,3-diethyl-7-oxa-1,5,12-triaza-spiro [5,6]dodecane-2,4,8,11-tetraone	

3	12-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3,3-diethyl-7-oxa-1,5,12-triaza-spiro [5,6]dodecane-9-ene-2,4,8,11-tetraone	
4	5-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-9,9-diethyl-1-oxa-5,7,11-triaza-spiro [5,5]undecane-2,4,8,10-tetraone	
5	2,6-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-5,5-diethyl-tetrahydro-pyrimidin -4-one	
6	12-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-3,3-diethyl-7-oxa-1,5,12-triaza-spiro[5,6]dodecane-2,8,11-trione	
7	8,15-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-18,18-diethyl-1,10-dioxo-6,8,15,16-tetraza-dispiro[6,1.6.3]octadecane-2,5,11,14,17-pentaone	
8	12-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-3,3-diethyl-7-oxa-1,5,12-triaza-spiro[5,6]dodecane-9-ene-2,8,11-trione	

9	<p>8,15-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-18,18-diethyl-1,10-dioxo-6,8,15,16-tetraaza-dispiro[6.1.6.3]octadeca-3,12-diene-2,5,11,14,17-pentaone</p>	
10	<p>5-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-10-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-ylimino)-9,9-diethyl-1-oxa-5,7,11-triaza-spiro[5.5]undecane-2,4,8-trione</p>	
11	<p>7,13-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-16,16-diethyl-1,9-dioxo-5,7,13,14-tetraaza-dispiro[5.1.5.3]hexadecane-2,4,10,12,15-pentaone</p>	
12	<p>8,15-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-18,18-diethyl-1,10-dioxo-6,8,15,16-tetraaza-dispiro[6.1.6.3]octadec-3-ene-2,5,11,14,17-pentaone</p>	

13	<p>5,7-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-15,15-diethyl-1,9-dioxo-5,7,14,17-tetraaza-dispiro[5.1.6.3]heptadecane-2,4,10,13,16-pentaone</p>	
14	<p>5,7-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-15,15-diethyl-1,9-dioxo-5,7,14,17-tetraaza-dispiro[5.1.6.3]heptadec-11-ene-2,4,10,13,16-pentaone</p>	

تحضير، تشخيص ودراسة الفعالية الحيوية لبعض مشتقات الاوكسازين والاوكسازينان من تفاعل قواعد شيف مع بعض الانهايديريدات الحلقية

قيس ارزيك إبراهيم- محمد عبد الكريم الحديثي - وليد فرج إلهيتي

Email : Mohamed_alhadithi@yahoo.com

الخلاصة:-

تم تحضير قواعد شيف 3، - (1، 5- ثنائي مثيل -3-اوكسو-2-فنييل -2,3-ثنائي هيدرو-1 H -بيرازول -4-يل امينو) -5,5-ثنائي اثيل-ثنائي هيدرو -بيراميدين - 4,6- دايون و 2,6-بس- (1، 5- ثنائي مثيل -3-اوكسو-2-فنييل -2,3-ثنائي هيدرو-1 H -بيرازول -4-يل امينو) -5,5-ثنائي اثيل -رباعي هيدرو -بيراميدين - 4- اون من تكثيف 5,5-ثنائي اثيل -بيرمدين -2,4,6-ترايون مع مول واحد ومولين من 4- أمينو -1,5-ثنائي مثيل -2-فنييل -1,2-ثنائي هيدرو - بيرازول-3-اون. فوعلت قواعد شيف هذه مع مول واحد من انهيديريدات كل من المالك والسكسنيك والمالونيك وتم الحصول على نظام حلقي غير متجانس (سباعي وسداسي الحلقة) وعند مفاعلة قواعد شيف مع مولين من الانهيديريدات أنفة الذكر أعطى نظام حلقي غير متجانس (بحلقتين سباعيتين او سداسيتين او خليط من السداسية والسباعية). وقد شخصت المركبات المحضرة بتعيين درجات انصهارها، تحليل العناصر، أطياف الأشعة فوق البنفسجية، أطياف الأشعة تحت الحمراء وقد أسهمت نتائج التشخيص بالطرق المختلفة في إثبات الصيغ التركيبية للمركبات المحضرة كما درست الفعالية البايولوجية لهذه المركبات مع عدد من البكتريا الموجبة والسالبة .