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

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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-1*H*-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-1*H*-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-1*H*-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-1*H*-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.

Key wards: Synthesis, Characterization, Oxazepine, Oxazepane, Biological activity .

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. 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-di hydro-1,3-oxazepine-4,7-dione and 2-aryl-3-(1,5-dimethyl-2-phenyl pyrazolonyl)-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 trimethylsilyl azide to give 4- and 5-substituted "oxauraciles": dihydro-1,3-oxazine-2,6-diones [5-6]

Both 2-methoxypyrroline and 2-methoxypiperdine react with diketene under netural conditions at 0c 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 flourosulphinyl isocyanate afforded the corresponding 1,3-oxazine-2,4-diones [11-13].

Ethyl benzimideate,and ethyl butyrimidate react with diketene to give 2-ethoxy-1,3-oxazine-4-ones [14].

Imines and N-acyl imines react with diketen to give tetrahydro-1,3-oxazine-4-ones [15-16].

N-acyl imines undergo [4+2] cycloaddition with both-C=C- and hetrodienes. 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-3-3(1,5-dimethyl-2-phenylpyrazolo)-1-(5) spirocyclopentyltetra hydro-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 , tautomerizeation 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 Schimadza Reco- 160 Spectrophotometer.

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

To a solution of o.o5 mole of 4-Amino-1,5-dimethyl-2-phenyl-1,2-dihydro-pyrazol-3-one in 30 ml of absolute ethanol o.o5 mole or o.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 evapouration 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
Staphylococcus aureus	stool	Blood agar
Proteus merabilis	urine	Blood agar
Pseudomonas aeruginosa	Ear infection	Nutrient agar
Klebsiella pneumoniae	burns	MacConkey agar
Salmonella typhi	urine	S.S. agar
Shigella Sonni	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 deferent 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 37c° 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 ,Succinc , 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-dioxa-6,8,15,16-tetraza-dispiro[6.1.6.3]octadeca-3,12-diene-2,5,11,14,17-pentaone. (9) and5-(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.(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 olefen 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-dioxa-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 .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-dioxa-6,8,15,16-tetraza-dispiro[6.1.6.3]octadeca-3,12-diene-2,5,11,14,17-pentaone. and5-(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.ps,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 towared 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 de activation 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 abvious 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 spacimen of bacteria. Bacteria is known to be anti-toxic and enjoys a resistance to anti-biotic for blasma.

The results indicate that some compounds with the concentration (10) compounds are not able to pentrate to their target area in the cell , because of a barrier, like the external tissue in the cellular wall of the negative bacteria of Grame Co lour . 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 environumental problems and are very expensive.

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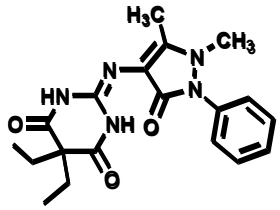
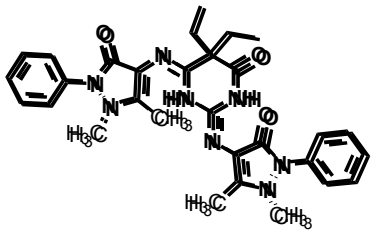
Table (1) : Melting point, percentage yield, molecular formula and elemental analysis of antipyrine-Schiff-bases





Comp.	M.P/C°	Yield %	M.F (M .Wt)	Calc.			Found		
				C	H	N	C	H	N
1	190-192	60	C19H23N5O3 (373.45)	61.77	6.28	18.96	61.65	6.23	18.84
5	206-208	51	C29H31N8O3 (554.64)	64.55	5.79	20.77	64.51	5.72	20.65

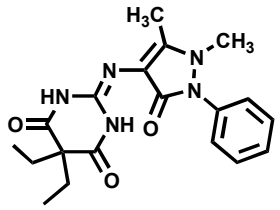
Table (2): major IR absorptions (cm^{-1}) of antipyrine-Schiff-bases.

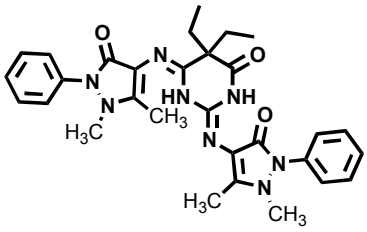
Comp.	C-H str. Aromatic	C-H str. Alkane	C=O str	C=N Imine	C=C str. Aromatic	C-H bending Alkane
1	3025	2850	1685	1620	1580,1520	1460,1350
5	3040	2860	1690	1610	1590,1540	1480,1410

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

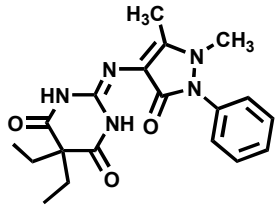
Table (4) : Some physical of experimental properties of Oxazepine and Oxazepane compounds.

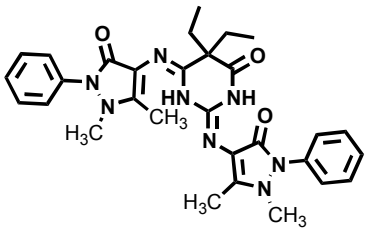




Compounds	M.P/C°	Yield %	M.F	Calc.			Found		
				C	H	N	C	H	N
2	180-182	58	C23H27N5O6	58.84	5.80	14.92	58.93	5.88	14.78
3	170-172	64	C23H25N5O6	59.09	5.39	14.98	59.00	5.42	14.87
4	166-168	54	C22H25N5O6	58.01	5.53	15.38	58.12	5.51	15.27
6	220-222	67	C34H38N8O6	62.37	5.85	17.11	62.30	6.00	17.02
7	198-200	52	C38H42N8O9	60.47	5.61	14.85	60.36	5.67	14.73
8	177-179	55	C34H36N8O6	62.57	5.56	17.17	62.44	5.51	17.05
9	162-164	58	C38H38N8O9	60.79	5.10	14.93	60.63	5.04	14.81
10	188-190	60	C33H36N8O6	61.86	5.66	17.49	61.80	5.55	17.34
11	150-152	62	C36H38N8O9	59.50	5.27	15.42	59.45	5.30	15.36
12	175-177	50	C38H40N8O9	60.63	5.36	15.36	60.57	5.29	15.23
13	194-196	63	C37H40N8O9	59.99	5.44	15.13	59.87	4.42	15.00
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.





Comp	C-H str. aromatic	C-H str. Olefin	C=O str. Lacton, lactam	C=C str. Olefin	C=C str. Aromatic	C-O str. lacton	C-H bend Aromatic	C-N str.
2	3060		1680	-	1580,1540	1330	1020,870	1430
3	3050	3150	1670	1620	1570, 1535	1320	1030,900	1420
4	3030		1660	-	1580,1530	1320	1010,800	1440
6	3070		1670	-	1575,1540	1330	1020,850	1435
7	3080		1680	-	1580,1545	1310	1030,860	1450
8	3060	3160	1675	1610	1570,1540	1320	1010,780	1450
9	3050	3180	1680	1625	1570,1535	1325	1020,880	1440
10	3090		1685	-	1580,1530	1320	1030,770	1445
11	3075		1670	-	1585,1540	1330	1025,860	1450
12	3080	3145	1660	1610	1570,1550	1330	1030,900	1440
13	3040		1680	-	1580,1545	1325	1020,870	1435
14	3060	3170	1670	1620	1570,1530	1320	1010,850	1445

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

compound	UV-Visible absorption maxima λ/nm
2	320,300,266,230.221
3	333,265,251,243,223
4	325,278,239,224
6	329,269,241,236,222
7	335,300,265,237,220
8	329,261,245,221
9	319,258,238,223
10	320,255,238,220
11	315,267,240,226
12	314,262,242,228
13	309,266,240,222
14	312,305,265,222

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

B.Isolated						concentration	Compounds No.
Shigella sonni	Salmonella typhi	Pseudomonas aeruginosa	Proteus	Klebsiella	Staphylococcus		
Diameters of deactivation (mm)						ml / mg	
0	0	0	0	0	0	10	1
8.1	7.5	6.0	4.0	4.0	4.5	25	
10.3	10.0	9.2	7.0	6.7	6.2	50	
11.5	10.9	10.7	8.9	8.4	8.0	75	
15.2	14.8	14.5	12.0	12.4	12.5	1000	
0	0	0	0	0	0	10	2
5.4	4.9	5.0	3.0	3.3	3.2	25	
9.1	8.8	7.5	5.0	4.7	5.1	50	
10.5	11.0	10.1	8.0	8.1	7.7	75	
12.4	13.5	12.7	105	100.9	11.2	1000	
0	0	0	0	0	0	10	3
9.1	8.4	7.2	4.5	4.9	5.0	25	

13.0	**11.1**	**10.2**	**8.1**	**7.7**	**7.9**	**50**	
14.2	**12.8**	**12.1**	**10.1**	**9.1**	**9.7**	**75**	
16.2	**15.1**	**16.0**	**15.2**	**14.0**	**14.2**	**100**	
0	**0**	**0**	**0**	**0**	**0**	**10**	**4**
5.5	**5.1**	**5.0**	**4.1**	**3.0**	**3.2**	**25**	
7.0	**6.8**	**6.1**	**4.9**	**5.0**	**5.1**	**50**	
8.9	**9.7**	**10.0**	**7.8**	**7.4**	**7.4**	**75**	
11.1	**12.4**	**12.0**	**9.0**	**9.7**	**9.9**	**100**	
0	**0**	**0**	**0**	**0**	**0**	**10**	**5**
4.9	**4.0**	**2.0**	**3.1**	**4.0**	**4.4**	**25**	
5.9	**6.4**	**5.1**	**6.0**	**6.3**	**6.1**	**50**	
7.9	**8.0**	**7.1**	**7.4**	**8.4**	**8.0**	**75**	
12.7	**13.9**	**14.0**	**12.8**	**13.7**	**14.5**	**100**	
0	**0**	**0**	**0**	**0**	**0**	**10**	**6**
5.2	**5.0**	**5.5**	**4.5**	**5.1**	**5.0**	**25**	
7.5	**8.7**	**8.0**	**6.9**	**7.3**	**7.0**	**50**	

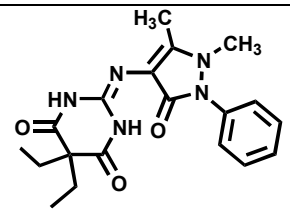
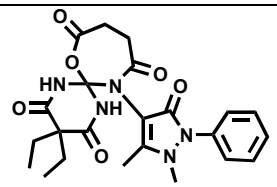
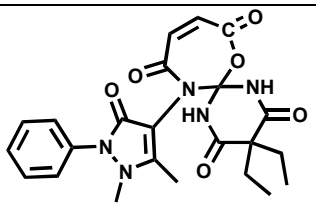
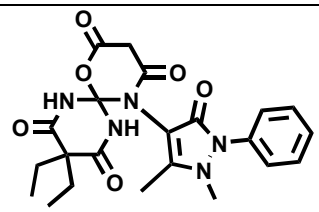
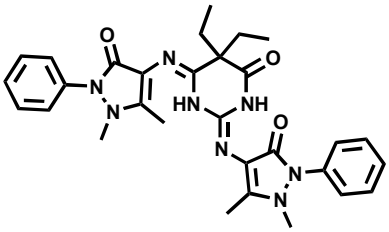
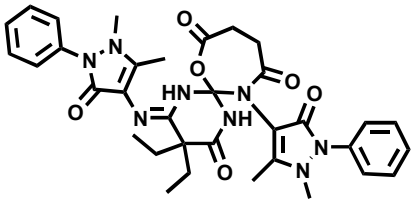
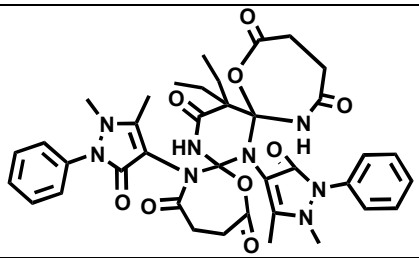
12.4	12.0	11.4	9.7	10.8	10.1	75	
15.4	14.8	13.1	11.6	12.7	12.8	1000	
0	0	0	0	0	0	10	7
4.9	3.0	4.4	3.6	3.0	3.5	25	
7.7	5.5	6.2	4.4	4.7	5.0	50	
10.0	7.8	9.1	8.0	7.3	7.0	75	
13.4	10.2	12.1	10.4	9.4	8.8	1000	
B.Isolated							
Shigella sonni	**Salmonella typhi**	**Pseudomonas aeruginosa**	**Proteus**	**Klebsiella**	**Staphylococcus**	**Compound No. ml / mg**	
Diameters of deactivation (mm)							
0	0	0	0	0	0	10	8
7.6	6.8	5.0	3.0	3.7	3.8	25	
8.1	6.2	6.0	5.7	4.1	4.0	50	
9.4	8.1	8.2	7.7	7.0	6.8	75	

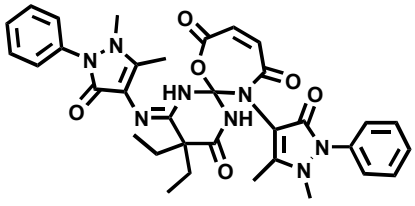
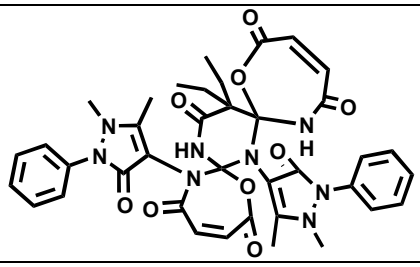
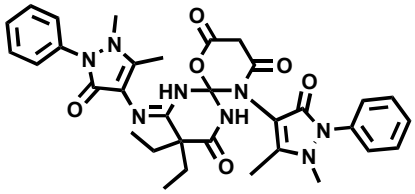
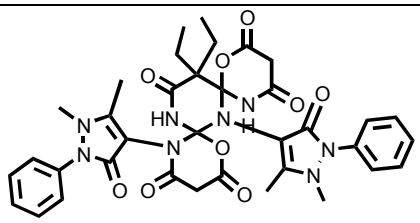
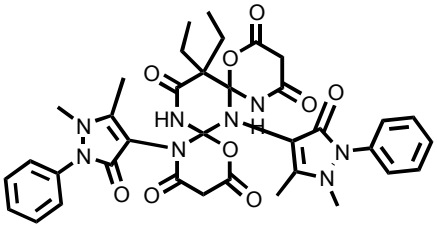
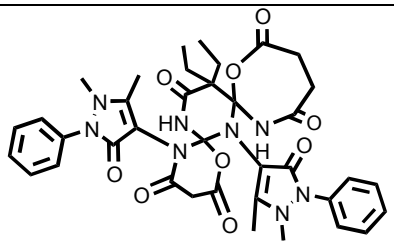
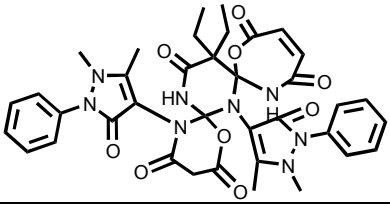
11.2	**9.5**	**11.1**	**10.0**	**8.4**	**7.1**	**100**	
0	**0**	**0**	**0**	**0**	**0**	**10**	
8.0	**6.9**	**6.2**	**4.6**	**5.3**	**4.1**	**25**	
7.9	**7.1**	**6.2**	**5.5**	**5.0**	**5.1**	**50**	**9**
12.2	**10.8**	**9.4**	**8.1**	**7.4**	**7.8**	**75**	
14.2	**12.8**	**12.1**	**11.4**	**10.5**	**10.1**	**100**	
0	**0**	**0**	**0**	**0**	**0**	**10**	
7.9	**7.4**	**6.8**	**6.0**	**4.7**	**5.1**	**25**	
9.1	**8.8**	**6.7**	**6.2**	**5.4**	**5.5**	**50**	**10**
12.8	**9.9**	**8.4**	**7.7**	**7.1**	**6.8**	**75**	
14.8	**12.8**	**11.7**	**9.7**	**8.4**	**8.1**	**100**	
0	**0**	**0**	**0**	**0**	**0**	**10**	
10.7	**8.4**	**6.2**	**4.9**	**4.7**	**4.3**	**25**	
12.4	**9.1**	**8.1**	**7.1**	**6.4**	**6.2**	**50**	**11**
12.4	**10.8**	**10.1**	**8.4**	**8.0**	**7.1**	**75**	
14.9	**12.4**	**11.2**	**9.9**	**9.5**	**9.1**	**100**	
0	**0**	**0**	**0**	**0**	**0**	**10**	**12**

7.4	**6.6**	**5.1**	**3.8**	**3.4**	**3.2**	**25**	**2**
7.9	**7.0**	**6.6**	**5.1**	**4.3**	**4.1**	**50**	
8.4	**6.8**	**6.2**	**5.1**	**5.8**	**5.7**	**75**	
11.0	**9.2**	**8.2**	**8.0**	**7.4**	**7.1**	**100**	
0	**0**	**0**	**0**	**0**	**0**	**10**	**13**
10.1	**7.0**	**6.6**	**5.4**	**4.8**	**4.2**	**25**	
13.4	**8.4**	**7.1**	**6.4**	**5.8**	**5.7**	**50**	
13.4	**9.4**	**8.7**	**8.0**	**7.8**	**7.4**	**75**	
15.0	**13.4**	**12.4**	**11.1**	**9.4**	**9.2**	**100**	
0	**0**	**0**	**0**	**0**	**0**	**10**	**14**
7.4	**6.4**	**4.5**	**4.1**	**3.9**	**3.5**	**25**	
8.4	**8.0**	**7.5**	**4.7**	**5.0**	**5.1**	**50**	
9.7	**8.1**	**7.9**	**7.3**	**6.0**	**6.2**	**75**	
15.7	**13.4**	**11.4**	**10.0**	**8.9**	**8.4**	**100**	
11.0	**7.0**	**12.0**	**11.0**	**9.0**	**8.0**	**300ug**	**Tetrac**

							ycline
12.0	**22.0**	**13.0**	**20.0**	**13.0**	**110**	**30µg**	**Nalidixic acid**
0	**0**	**12.0**	**5.0**	**6.0**	**110**	**20µg**	**Anoxicillin**
20.0	**11.0**	**0**	**8.0**	**6.0**	**9.0**	**30µg**	**Gentanycin**

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

No.	Name	Structure
1	2-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro 1*H*-pyrazol-4-ylimino)-5,5-diethyl-dihydro -pyrimidine-4,6-dione	
2	12-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H* pyrazol-4-yl)-3,3-diethyl-7-oxa-1,5,12-triaza-spir [5.6]dodecane-2,4,8,11-tetraone	
3	12-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H* pyrazol-4-yl)-3,3-diethyl-7-oxa-1,5,12-triaza-spir [5.6]dodec-9-ene-2,4,8,11-tetraone	
4	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-spir [5.5]undecane-2,4,8,10-tetraone	
5	2,6-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3- dihydro-1*H*-pyrazol-4-ylimino)-5,5-diethy -tetrahydro-pyrimidin -4-one	
6	12-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H* pyrazol-4-yl)-4-(1,5-dimethyl-3-oxo-2-phenyl-2,3- dihydro-1*H*-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- 1*H*-pyrazol-4-yl)-18,18-diethyl-1,10-dioxa-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-1*H*-pyrazol-4-yl)-4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-ylimino)-3,3-diethyl-7-oxa-1,5,12-triaza-spiro[5.6]dodec-9-ene-2,8,11-trione**	
9	**8,15-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-18,18-diethyl-1,10-dioxa-6,8,15,16-tetraaza-dispiro[6.1.6.3] octadeca-3,12-diene-2,5,11,14,17-pentaone**	
10	**5-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-10-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-ylimino)-9,9-diethyl-1-oxa-5,7,11-triaza-spiro[5.5]undecane-2,4,8-trione**	
11	**7,13-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-16,16-diethyl-1,9-dioxa-5,7,13,14-tetraaza-dispiro[5.1.5.3]hexadecane-2,4,10,12,15-pentaone**	
12	**8,15-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-18,18-diethyl-1,10-dioxa-6,8,15,16-tetraaza-dispiro[6.1.6.3] octadec-3-ene-2,5,11,14,17-pentaone**	
13	**5,7-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-15,15-diethyl-1,9-dioxa-5,7,14,17-tetraaza-dispiro[5.1.6.3] heptadecane-2,4,10,13,16-pentaone**	
14	**5,7-Bis-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-15,15-diethyl-1,9-dioxa-5,7,14,17-tetraaza-dispiro[5.1.6.3]heptadec-11-ene-2,4,10,13,16-pentaone**	

تحضير ، تشخيص ودراسة الفعالية الحيوية لبعض مشتقات الاوكسازبين والاوكسازينان من تفاعل قواعد شيف مع بعض الانهايدريدات 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-فنيل -2,3-ثنائي هيدرو-1 *H* –بيرازول -4-يل امامينو) -5,5-ثنائي اثيل-ثنائي هيدرو –بيرامايدين – 4,6- دايون و 2,6-بس-((1، 5- ثنائي مثيل -3-اوكسو-2-فنيل -2,3-ثنائـي هـيدرو-1 *H* –بيرازول -4-يل امامينو) -5,5-ثنائي اثيل –رباعي هيدرو –بيرامايدين – 4- اون من تكثيف 5,5-ثنائـي اثيل –بيرمدين -2,4,6-ترايون مع مول واحد ومولين من 4- أمينو -1,5-ثنائي مثيل -2-فنيل -1,2-ثنائي هـيدرو – بيـرازول-3-اون . فوعلت قواعد شيف هذه مع مول واحد من انهيدريدات كل من الماليك والسكسنيك والمالونيك وتـم الحـصول علـى نظـام حلقي غير متجانس (سباعي وسداسي الحلقة) وعند مفاعلة قواعد شيف مع مولين من الانهيدريدات 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 تحـت الحمـراء وقـد أسـهمت نتائج التشخيص بالطرق المختلفة في إثبات الصيغ التركيبية للمركبات المحضرة كما درست الفعالية البايولوجية لهذه المركبات مع عدد من البكتريا الموجبة والسالبة .