تحضير وتشخيص بعض المشتقات الجد يدة لمركبات قواعد شف ودراسة تاثيراتها البايولوجية .

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المستخلص :

تم تحضير سلسلة من مركبات قوعدشف الجديدة المحتوية على اصرة الازو ميثان والتي من المتوقع ان تكون فعالة حيويا. تم تشخيص المركبات المحضرة بالطرق الفيزياوية والطيفية (مطيافية الاشعة تحت الحمراء والاشعة فوق البنفسجية/المرئية) وتم متابعتها بواسطة كروماتوغرافيا الطبقة الرقيقة (TLC) كما تمت دراسة الفعالية البايولوجية للمركبات المحضرة ضد نوعين من البكتريا.

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Synthesis and Identification of Some New Derivatives of Schiff bases Compounds and study their Biological avtivity.

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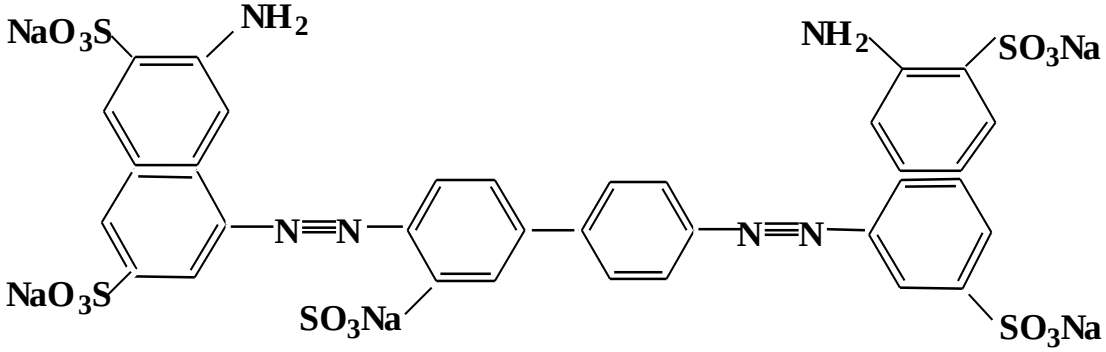
ABSTRACT :

A new series of Schiff bases compounds , containing an azomethine linkage was synthesized and expected to be biologically active .The structures of these compounds were identified by IR , Uv/vis spectra , melting points and followed by T.L.C.The biological activity of these compounds was studied.

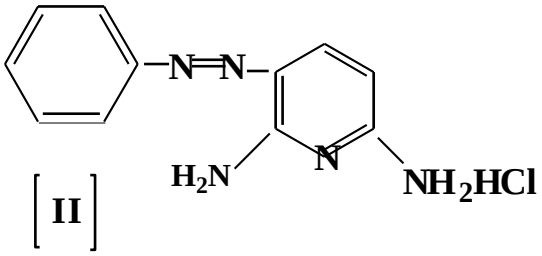
INTRODUCTION:

Various compounds containing an azo group have been shown to possess biological activity ,Wilson [(1)] found that the compound [1] Tryparned possessed activity against typhus .



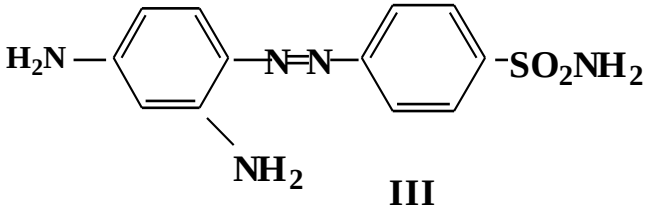
I

2,6-diamino-3-(phenylazo) pyridine monohydrochloride which is known as pyridium [(2)] has been used as antiseptic and antibacterial agent .



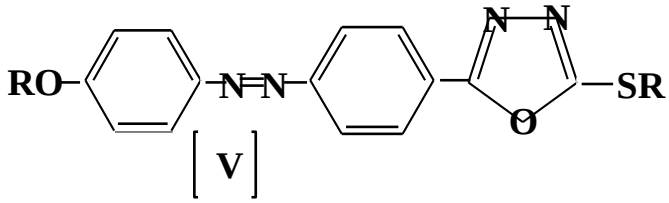
[II]

Irik [3] found that pronstil , is used as a medical compound against typhus and as antibacterial .

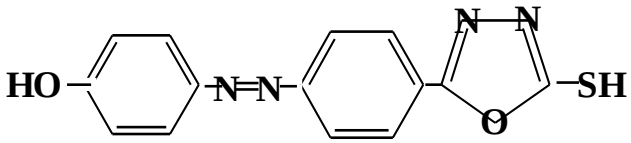


III

Also ,Fadel [4] , has condensed azo compounds with heterocyclic units in order to know the effects of the presence of heterocyclic units on the activity of the azo compounds . These compounds which containe oxadiazole ring are known to have biological activity .

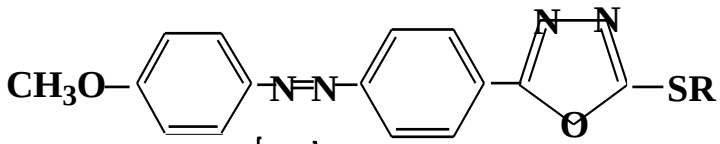


V



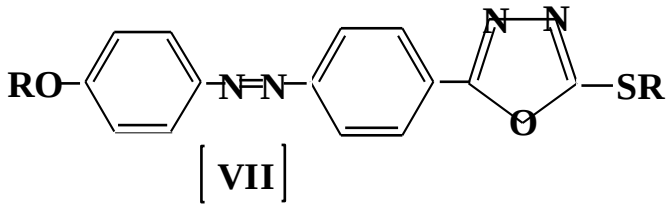
IV

Ali [5] also synthesized azo compounds with oxadiazole ring by the reaction of diazonium salts .



VI

Hussein [6] synthesized azo compounds with oxadiazoke ring and different substituents to study the effect of length of alkyl chain on the physical properties of azo compounds .

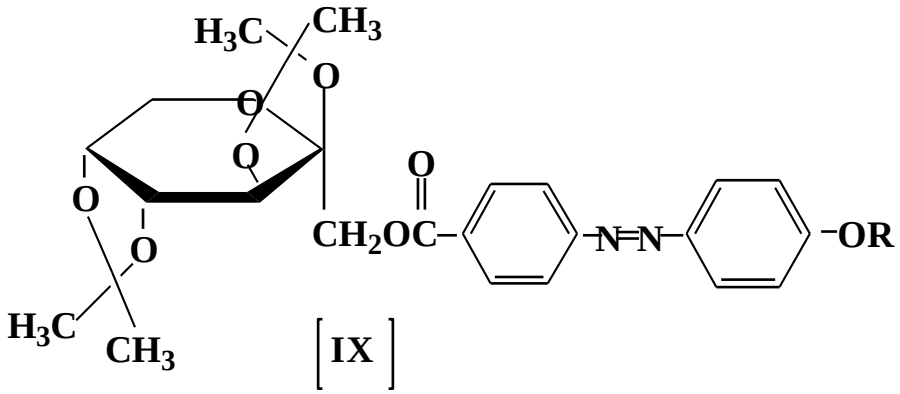


[VII]

R= C_nH_{2n+1} ; n=1,2-6

$R^{/}=C_4H_9$

Also, Jassim [7] synthesized azo compounds condensed with carbohydrate unit in order to study the effect of carbohydrate unit on the biological activity of azo compounds ,and found that these compounds still have biological activity against styphylococcus and Escherichia Coli.

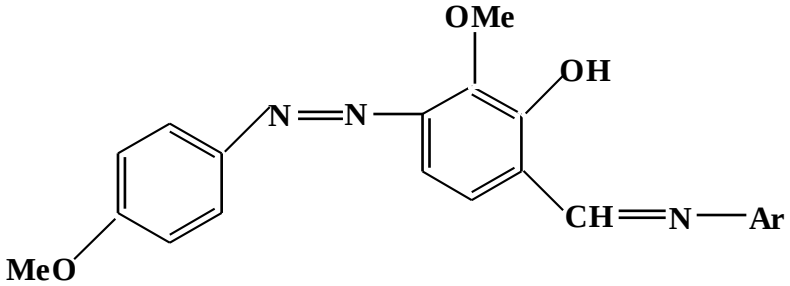


[IX]

VIII

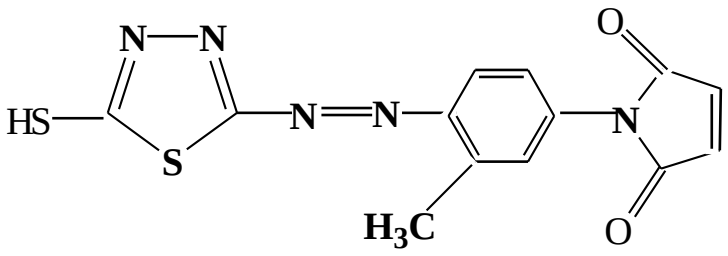
R= $C_nH_{2n+1;}$ n=1-12 .

It is also known that the presence of an azo moiety in different types of Schiff bases can lead them to exhibit pesticidal activities .Both Schiff bases azo compounds are important structures in the medicinal and pharmaceutical fields [8] and it has been suggested that the azomethine linkage might be responsible for biological activities displayed by Schiff bases . In the light of the interesting variety of biological activities seen in compounds containing azo and azomethine linkage , Jarrahpour et., al,[9] prepared eight new azo Schiff bases via condensation of different aromatic amines and new azoablehydes :



IX

Also ,a series of mono azo disperse dyes based on 2-amino-5-mercapto -1,3,4-thiadiazole was prepared by coupling with various N-aryl maleimides [10].



X

These dyes have been found to give a wide range of couter shades [11] with very good depth and levelness on fabric[12] .

Experimental Part :

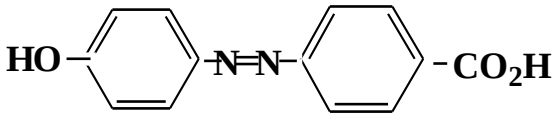
A-Tehniques:

Melting points were determined by using an "Electrothermal " melting red -apparatus IR spectra were recorded on a Perkin Elmer 1310 infra spectrophotometer in the 4000-200 cm^{-1}range using KBr disc . Elemental analysis were performed with a (ARLO-ERBA) instrumental EA 1108 ELEMENTAL ANALYZER .

B-Materials :

Chemicals employed were of analytical reagent and used without further purification .

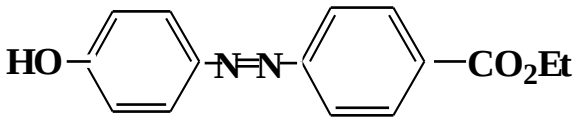
1-Preparation of 4-(*p*-hydroxy phenyl azo) benzoic acid [6] (1).



4-amino benzoic acid (0,02mol) was added to a mixture of hydrochloric acid and sodium nitrite ($NaNO_2$) ccled in an ice bath with stirring .Then (0.02mol) of phenol, dissolved in alkaline medium was added to the mixture . The mixture was left for two hours with cooling then acidified with hydrochloric acid whereby a precipitated of red separated out. These crystals were filtered washed with cold water ,dried and re-crystallized from ethanol[6].

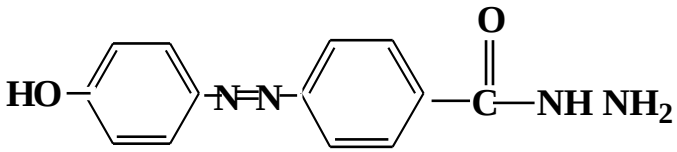
Melting point =(264-266 ^{0}C), yield 95%.

2-Preparation of Ethyl 4-(*p*-hydroxy phenyl azo) benzoate[6] (2) .



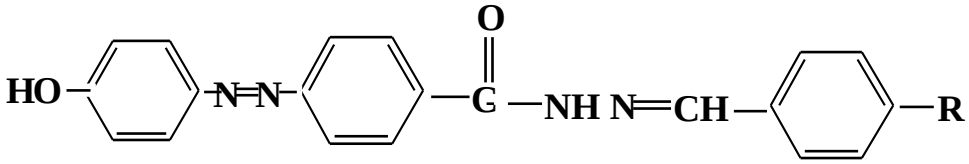
4-(*p*-hydroxy phenyl azo) benzoic acid (0.01 mol) was refluxed with 25ml. of ethanol and few drops of cnc. H_2SO4 (sulfuric acid)for four hours . The mixture was left to cool and filtered to give crystals [7].

3-Preparation of 4-(*p*-hydroxy phenyl azo) benzoic acid hydrazide (3).[5]



To a solution of (0.01 mole) of ethyl4-(*p*-hydroxy phenyl azo) benzoate in 20 ml. of ethanol was added (0.02 mole) of hydrazine hydrate . The mixture was refluxed for four hours. Then the mixture was allowed to cool and crystals were filtered ,washed and dried .
M.P.==155-158^{0}C ,yield 80%.

4-Preparation of Schiff bases (4-12) :

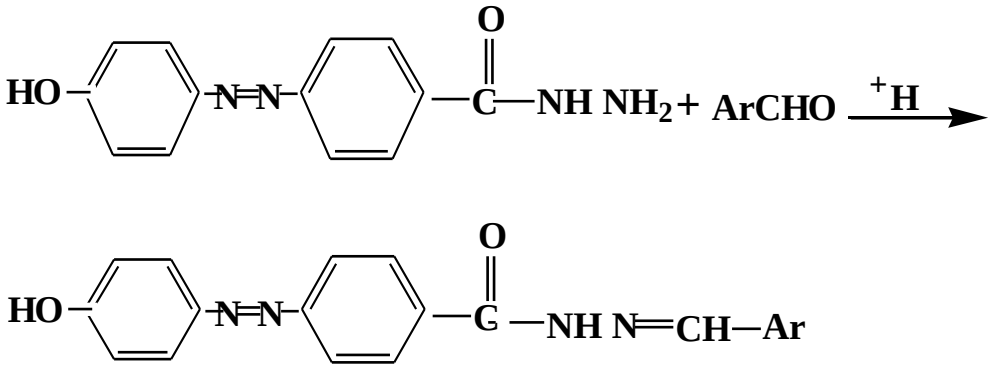


R=H, ***p***-OCH_3, ***p***-Cl, ***p***-N $(CH_3)_2$, ***p***-NO_2 , ***p***-CH_3 , ***m***-CH_3, ***p***-OH ,***m***-NO_2

The hot ethanol solution of 4-(*p*-hydroxy phenyl azo) benzoic hydrazide (0.01 mole) mixed with a solution of the corresponding substituted benzaldehyde (0.01 mole) in 10 ml. in absolute ethanol with some drops of glacial acetic acid .The mixture was refluxed for 30 minutes .The product was separated by filtration .

Results and Discussion :

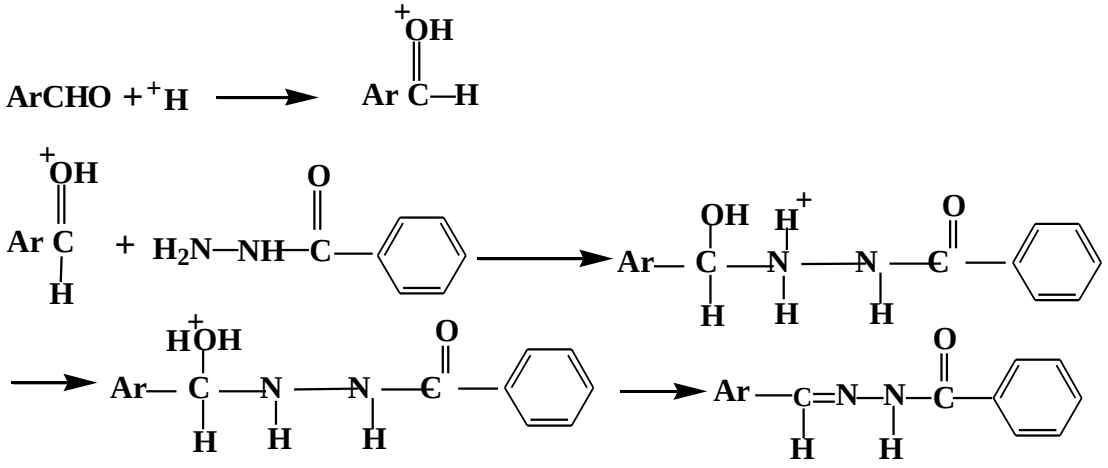
The resulting 4-(***p***-hydroxy phenyl) azo benzoic acid hydrazide is condensed with some selected benzaldehydes to give the corresponding Schiff bases ,i.e. N^2 [4-(***p***-hydroxy phenyl) azobenzoyl –N^1 – benzaldehyde hydrazone .



The reaction is initiated by protonation of the benzaldehyde carbonyl group which is attached by the nitrogen of the unsubstituted (A) which suffers a proton transfer from nitrogen to oxygen to give the final products :

N^2 [4-(***p***-hydroxy phenyl) azobenzoyl –N^1-benzaldehyde hydrazone .

These Schiff bases are identified by their m.ps ,elemental analysis (Table 1) and IR-UV/vis spectra Table (2).



B

Table (1) :Physical properties of the Schiff bases .

Compound No.	R	Melting point ^0C	Color	Yield percentage
4	H	320	Orange	70
5	***p***-OH	190	Red	75
6	***p***-NO_2	240	Yellow	90
7	***m***-NO_2	210	Yellow	80
8	***p***-Me	307-309	Orange	95
9	***m***-Me	150	=	90
10	***p***-Cl	210	=	75
11	***p***-OCH_3	129-130	=	90
12	***p***-$N(CH_3)_2$	258-260	Red	60

The IR spectrum of compound (1) 4-(***p***-hydroxy phenyl azo) benzoic acid showed principle bands at (3290-3350) ,1600 and 1670 cm^{-1} due to stretching vibration of O-H, N=N and C=O acid group (Benzoic acid) and the compound (2) ethyl 4-(*p*-hydroxy phenyl azo) benzoate showed band at 1760 cm^{-1}due to (C=O) ester group instead of 1670 cm^{-1} due to (C=O) acid group .

The hydrazide compound (3) ethyl 4-(***p***-hydroxy phenyl azo) benzoic acid hydrazide , showed the appearance of bands at 1620,(3350-3400) cm^{-1}due to (C=O)amide and N-H respectively and disappearance of (C=O) ester group while the IR bands of the new derivatives show disappearance of N-H (NH_2) stretching band, the new strong bands appear near 1620 cm^{-1} ,(800-850) cm^{-1} due to characterized to (C=N) Schiff bases **(13)** ,and *p,m*-substituted terminated respectively besides the fundamental bands Table (2).

Table (2): IR,UV/vis spectral data for the prepared compounds.

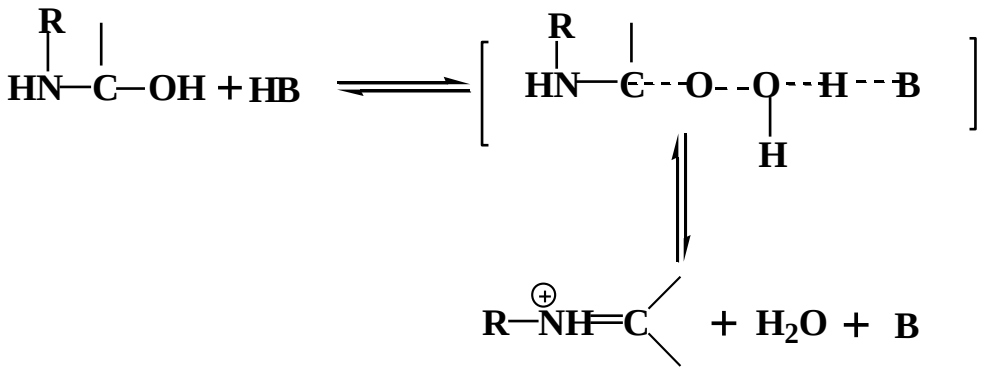
Comp. No.	R	ν C=C(Ar)	ν C-H(Ar)	ν C=N	ν C-Haliph	$\lambda_{max.}$
4	H	1560	3100	1600	2880	260
5	***P***-OH	1580	3080	1610	2900	250
6	***P***-NO_2	1565	3090	1620	2880	288
7	***m***-NO_2	1590	3100	1600	2890	240
8	***p***-Me	1590	3089	1630	2900	260

9	***m***-Me	1585	3090	1610	2900	240
10	***p***-Cl	1560	3089	1625	2880	265
11	***p***-OCH_3	1500	3100	1620	2900	270
12	***p***-$N(CH_3)_2$	1560	3090	1600	2890	280

These compounds were found through the addition of substituted benzaldehydes to 4-(***p***-hydroxy phenyl azo) benzoic acid hydrazide in absolute ethanol using catalytic amount of glacial acetic acid . There are two step mechanism consisting of an initial addition of the amine to the carbonyl to form a carbinol amine followed by dehydration to give the –C=N- bond .

Carbinal amine intermediate derived from strongly basic amines may be dehydrate by expelling hydroxide ion without the acid catalyst .Intermediates derived from weakly basic amine require acid or base catalysts for dehydration to occur .

The mechanism , below involving addition of a proton from a general acid to the leaving hydroxyl group , appears to be the most satisfactory for the acid catalyzed dehydration step .



Biological activity :

Here, in this work the anti-microbial test was performed according to agar well diffusion method[14].

The prepared compounds were tested against two pathogenic microorganism ,staphylococcus Aurus and E. Coli. In the solidified media (Nutrient agar) , suitable spaced apart holes were made (6mm in diameter) these holes were filled with (0.1 ml) of prepared compounds concentration that dissolve in DMSO (Dimethyl sulphoxide) after spread the bacteria on agar .these plates were incubated at 37 ^{0}C for 24 hour , the zone of inhibition of bacteria growth around the hole was observed

and measured in mm and are represented by (+),(++), and (-) depending upon the diameter and clarity as in Table (3). ***Staphylococcus aureus*** is gram positive cluster form, non-motil, non-spore forming. It is leading cause of soft tissue inflection ,as well as toxic shock syndrome and scalded skin syndrome. It has been found to be the causative agent in such illness as pneumonia, meningitis, boils, arthritis and osteomyelities (chroic bpne infection) [(15)].

Table (3): Antibacterail activity of the prepared derivatives (4-12).

Comp. No.	Staph.aureus	E. Coli
4	+ +	+
5	+	-
6	-	+
7	+	+
8	-	+ +
9	+ +	+
10	+	-
11	+	+
12	+	+

Key to symbols :
(-) = No inhibition , (+) = 10-14 mm , (+ +) = 15-22 mm .

The screening results reveal that most of the prepared compounds exhibited biological against both of these organisms ,while the others showed low or no activity against both organisms .

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