Synthesis and characterization of some heterocyclic including oxazoles,Thiazoles, Pyridazines, phthalizines and Pyrazoles with evaluating of biological activity.

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Abstract:

A series of new compounds including ***p***-bromo methyl pheno acetate [2]. N-(aminocarbonyl)–***p***-bromo pheno acetamide [3] ، N-(aminothioyl) -***p***-bromo phenoacetyl amide [4]، N-[4-(***p***-di phenyl)-1,3-oxazol-2-yl]-***p***-bromopheno acetamide [5],N-[4-***p***-di phenyl]-1,3-thiazol-2-yl-***p***-bromo phenoacet amide [6], ***p***-bromopheno acetic acid hydrazide [7] , 1-N-(***p***-bromo pheno acetyl)-1,2-dihydro-pyridazin-3,6-dione [8], 1-N-(***p***-bromo pheno acetyl)-1,2-dihydro-phthalazin-3,8- dione[9], 1-(***p***-bromo pheno acetyl)-3-methylpyrazol-5-one [10] and 1-(***p***-bromo phenol acetyl)- 3,5-dimethyl pyrazole [11] have been synthesized. The prepared compounds were characterized by m.p.,FT-IR and ^{1}H-NMR spectroscopy. Also ,the biological activity was evaluated .

Key words:- oxazol,Thiazole,Pyridazine,Phthalizine,Pyrozole.

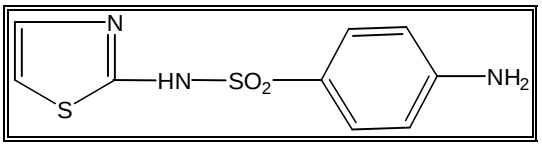
Introduction:

It has been reported [(1)] that heterocycles such as oxadiazoles are themselves important chemotherapeutic agents and exhibit antitubercular, bacteriostatic, hypoglycemic, antiviral, antifungal, antithyroid, carcinostatic and strong herbicidal activities when properly substituted in 2- and 5- positions.

Various 2, 5-diaryl-2, 5-dialkyl-, and 2-alkyl-5-aryl-1, 3, 4-oxadiazoles show herbicidal effect, especially against broad leafed weeds and grasses in crops such as rice and corn [(2)].

Thiazole compounds are regarded as a class of heterocyclic compounds. It was found that numerous aromas contained thiazole derivatives such as tomato, roasted coffee and roasted peanuts [(3)].

William and Coworkers[(4)] in 1935 demonstrated existence of simple thiazole ring in vitamin B_1 (thiamine). Thiazole and its derivatives were used as chemotherapeutic agent for the treatment of bacterial infections.



Gabriel[(5)] found that the reaction of α-acylaminoketone with phosphourous pentaoxide gave thiazole derivatives .

Thiazole was also found in the structure of numerous pesticides, fungicides, herbicides and nematocides [(6)].

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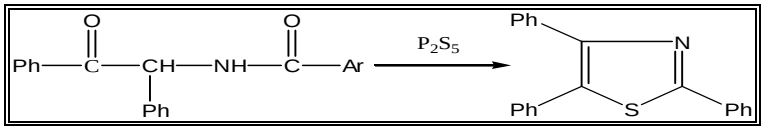
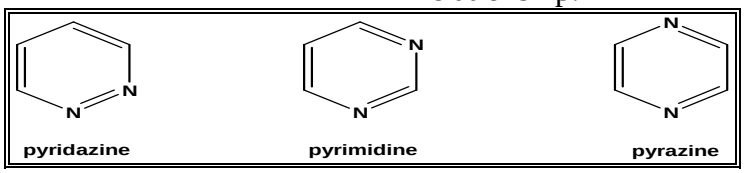


In addition to these, thiazoles were reported to be of commercial interest. For example, 2-mercapto thiazole was found to have wide use as
Accelerators in rubber vulcanization, anti-oxidant, photo-chromics, and dyestuffs [7], so because of these, they have been extensively studied.
Pyridazine is a member of a diazine group. There are three possibly isomeric diazines with the nitrogen atoms in a 1,2-; 1,3- or 1,4-relationship:



Pyridazine ring can be fused on to a benzene ring in two ways giving phthalazine or cinnoline [8].

Sener [9] found that 3,4-diphenyl-2H-pyrazol [3,4-d] pyridazin-7-one was obtained from the reaction of hydrazine with 4-benzoyl-5-phenyl-1,2,3-dihydro-2,4-furandione.
Some imidazole [1,2-b] pyridazine derivatives are reported to possess antiasthmatic and analgesic activities [10]. It has been reported that a considerable number of 3(2H)-pyridazine derivatives bear analgesic activity as Emorfazone (4-ethoxy-2-methyl-5-morpholino-3(2H) pyridazinone [11].
From their structure-activity relationship, it may be expected that hydrazinepyrazoleo [3,4-d] pyridazines, which are formed by replacement of the benzene ring in hydrazine with a pyrazole nucleus can exhibit interesting biological activity [12].

Reaction of acid hydrazide and its derivatives reacted with ethylaceto acetate or acetyl acetone or diethyl malonate produced pyrazole derivatives [13].

Various ring systems containing the –(NH_2)-N- moiety as a part of the ring have been found to condense with α-bromoketones to yield condensed imidazoheterocyclic systems; the ring nitrogen attacks the CH_2Br unit rather than the primary exocyclic amino group [14].

The incorporation of the imidazole nuclei is an important synthetic strategy in drug discovery [15]. The high therapeutic properties of the related drugs have encouraged the medicinal chemists to synthesize a large number of novel chemotherapeutic agents [16].

Materials and methods:

1- Melting points were recorded using hot stage Gallen Kamp melting point apparatus and were uncorrected.

2- Infrared spectra were recorded using Fourier Transform infrared ***SHIMADZU*** (8400) and (8300)

(F.T.IR) infrared spectrophotometer, KBr disc or thin film was performed by Chemistry Department ,AL-Nahrain University .

3- Thin layer chromatography (TLC) was carried out using Fertigfollen precoated sheets type polygram Silg, and the plates were developed with iodine vapour.

4-^{1}H-NMR spectra ($CDCl_3$) were recorded on a BRUKER- 400 MHz instrument with tetramethyl silane (TMS) as internal standard in $CDCL_3$ d.Measurments were made at Chemistry Department , Al-Baath University ,Syria and a BRUKER -300 MHz in $CDCL_3$,Chemistry Department , Jordan University .

5- The biological activity was performed by Biology Department, Tikret University.

1-Preparation of p-bromo methyl pheno acetate [2].

A mixture of ***p***- bromo phenol (10g, 0.05mol) and (6.6g,0.05mol) of chloroethyl acetate in ethanol(20ml) in presence of (2.8g,0.02mol) K_2CO_3 was refluxed for (3hours), and then cooled to room temperature . The mixture was extracted with ethyl acetate and washed with water ,dried with $MgSO_4$ and filtered off . The solvent was evaporated m.p for [2] (55 ^{0}C), yield (70 %) .

2-Preparation of N-(aminocarbonyl) –*p*-bromo pheno acetamide [3][(17)].

A mixture of ***p***-bromo methyl pheno acetate compound [2] (0.2g,0.0007mol)in absolute ethanol (20ml), urea (0.2g, 0.0033mol) was added. The mixture was refluxed for (5hours). After cooling and filtering, the white precipitate was obtained, m.p. for [3] (300 dec.), yield (85%).

3-Preparation of N-(aminothioyl) – *p*-bromo phenoacetyl amide [4][(17)].

Compound [4] was prepared by the same method described for the preparation of compound [3], white precipitate was obtained, m.p. for [4] (260 ^{O}C), yield(97.7%).

4- Preparation of N-[4-(*p*-di phenyl)-1,3-oxazol-2-yl]-*p*-bromopheno acetamide [5][(18)].

A mixture of compound [3] (0.54g, 0.002mol) and absolute ethanol (15ml),p-phenylphenacylbromide (0.55g, 0.002mol) was added. The mixture was refluxed for (8hours), cooled and neutralized with ammonium hydroxide solution. The precipitate was filtered off, washed with water, and petroleum ether was used for re-crystallization, the m.p. for [5] is (110^{0}C), yield (80%) .

5- Preparation of N-[4-*p*-di phenyl]-1,3-thiazol-2-yl-*p*-bromo phenoacet amide [6][(18)].

Compound [6] was prepared by the same method described for the compound [5]. Yellow precipitate was obtained, m.p. for [6] (120 ^{0}C) yield (90.7%).

6 - Preparation of p-bromopheno acetic acid hydrazide [7] [(19)].

To a solution of (2.59g,0.01mole) of compound[2] in absolute ethanol (50ml) , was added to (10ml) of (99-100%) hydrazine hydrate , and the mixture was refluxed under anhydrous conditions , for (3 hours). a white solid mass, which separated on cooling , was collected by filteration and re-crystallized from ethanol into white crystalline solid, m.p for [7] (150 ^{O}C), yield (80).

7 -Preparation of 1-N-(p-bromo phenol acetyl)-2-hydro-pyridazine-3,6-dione [8][(20)].

Compound [7] (0.53g ,0.0023mole,) was mixed with maleic anhydride (0.22g,0.0023mole) in acetic acid (20ml), the mixture was refluxed for (7 hours) then cooled and added into crushed ice, the precipitate was filtered off, washed with water and re-crystallized to give the final product, m.p for [8] (80 ^{o}C). yield (60%) .

8 -Preparation of 1-N-(p-bromo pheno acetyl)-1,2-dihydro-phthalazin-3,8- dione[9] [(20)] .
Compound [7] (0.53g,0.0023mole) was mixed with phthalic anhydride (0.34g,0.0023mole) in acetic acid (20mL), the mixture was refluxed for (7 hours) then cooled and added to crushed ice. The precipitate was filtered off, washed with water and re-crystallized to give the final product, m.p for [9] (88-92 ^{o}C) , yield (84%).

9- Preparation of 1-(*p*-bromo pheno acetyl)-3-methylpyrazol-5-one [10] [(21)].

A mixture of carbohydrazide [7] (0.53g,0.0023mole) and ethylacetoacetate (0.29g,0.0023mole) in absolute ethanol (20mL) was heated at reflux temperature for (5hours), the reaction mixture was cooled and the precipitate was filtered off and re-crystallized to give the compound [10], m.p for [10] .(88-92 ºC), yield(83%).

10 Preparation of 1-(*p*-bromo phenol acetyl)- 3,5-dimethyl pyrazole [11] [(22)] : -

A mixture of compound[7] (0.69g, 0.003mol) was treated respectively with acetyl acetone (0.32ml, 0.003mol) and acetic acid (0.5ml) in abs. ethanol (15ml) was heated under reflux for (7hours).After concentration and cooling, the solid product that formed was filtered off, and re-crystallized from ethanol , the m.p. for [11] (116 ^{o}C) yield (99.51%) .

Results and Discussion

1 Preparation of p-bromo methyl pheno acetate [2].

To synthesize ***p***-bromo phenyl hydrazide derivatives , we used ***p***-bromo phenol .

p-bromo phenol was first converted to ester compound [2] by using K_2CO_3 ,acetone and chloro ethyl acetate . The ester was identified by FT-IR spectrum which showed the disappearance of a wide absorption band in the range (3160-3020) cm^{-1} which belongs to stretching vibration of the (-OH) group of ***p***- bromo phenol. The FT-IR spectrum also , showed the appearance of the characteristic absorption band at (1737) cm^{-1} due to the stretching vibration of the (C=O) of the forming ester .

2- Preparation of N-(aminocarbonyl)*p*-bromo phenoacetyl amide [3].

The FT-IR spectrum showed a split broad bands at (3400-3085) cm^{-1}due to the asymmetric and symmetric bands of υ (NH_2) and υ (NH) groups , other band at (1595.02) cm^{-1} for the carbonyl group and bands at (2960-1483.16) cm^{-1}which were due to υ (C-H) and υ (C=C) stretching of aromatic system , respectively , and band at (823) cm^{-1} for(Br-C).

3- Preparation of N-(aminothioyl) –*p*-bromo phenoacetyl amide [4].

The FT-IR spectrum showed a band at (3033-3091) cm^{-1} which was assigned to the asymmetric and symmetric bands of (NH_2) and (NH) groups , at (1604) cm^{-1} for υ (C=O) , at (1016) cm^{-1} for υ (C=S)[(23)] and bands at (3956,1487) cm^{-1} which were due to υ (C-H) and υ (C=C) stretching of aromatic system , respectively, and at (1419) cm^{-1} for δ (NH).

4- Preparation of N-[4-(*p*-phenyl)-1,3-oxazol-2-yl]-*p*-bromopheo acetamide [5].

The compound [5] was synthesized according to reaction of N-(amino thioyl)-***p*** bromo pheno acetyl amid and ***p***-phenyl phencyl bromide .

The reaction of compound [3] with ***p***- phenyl phenacyl bromide under refluxing condition affected on intermolecular cyclization through SN_2 mechanism giving the desired oxazole derivative compound [5].

The structure of oxazole derivative was confirmed by FT-IR . The FT-IR spectrum showed a broad band of (N-H) at (3261.4) cm^{-1}, carbonyl group

shifted to higher frequency (1735.8) cm^{-1} due to disappearance of possibility of hydrogen bonding . Sharp absorption band at (1670.2) cm^{-1} due to υ (C=N) group the aromatic (C=C) at (1515.9) cm^{-1} , stretching band of (C-O-C) at (1207.4) cm^{-1},band of (C-Br) at (815.8) cm^{-1},and at (1593) cm^{-1} for δ (-NH) .

5-Preparation of N-[4-(*p*-di phenyl)-1,3-thiazol-2-yl]-*p*-bromo phenoacetamide [6].

The reaction of compound [4]with ***p***-phenyl phenacyl bromide under refluxing condition affected on intermolecular cyclization through SN_2 mechanism giving the desired thiazole derivative compound [6] . The FT-IR spectrum of compound [6]showed the disappearance of the (C=S) band of compound [6] at (1110) cm^{-1} , carbonyl group shifted to higher frequency (1602) cm^{-1} due to disappearance of possibility of hydrogen bonding . Sharp absorption band at (1643.24) cm^{-1} and (3307.69) cm^{-1} due to υ(C=N) and υ (N-H) cm^{-1}, respectively , the aromatic (C=C) at (1538) cm^{-1}, stretching band of υ (C-S-C) cm^{-1} at (709.76.) cm^{-1}, and band of (C-Br) at (848) cm^{-1}, and band of δ (NH) at (1496.66) cm^{-1}.The ^{1}H-NMR spectrum of compound [6] showed δ(4 .5)ppm due to aliphatic protons (CH_2) δ (4.8) ppm due to cyclic protons δ (5.5) ppm due to (N-H) protons δ (6.9-8.2) ppm due to aromatic protons .

6 - Hydrazide derivative [7].

The reaction of hydrazide hydrate with ester is one of the most common reaction to synthesize the acid hydrazide , it is a tetrahedral nucleophilic[(24))] substitution reaction.

FT.IR of the hydrazide derivative compound [7]showed the appearance of the characteristic absorption bands in the region (3084-3220) cm^{-1}due to the asymmetric and symmetric stretching vibration of the (-NH-NH_2) group , the FT.IR for the compound [7] showed the disappearance of absorption bands at (1737) cm^{-1}due to the stretching vibration of carbonyl group of ester , while showed appearance of absorption band at (1677) $cm^{-1(25)}$ of the compound [7] due to stretching vibration of amide I band and appearance of amide II bending vibration band at (1581.45) cm^{-1}. The ^{1}H-NMR spectrum of compound [7], showed δ (6.8-7.8) ppm due to aromatic protons δ (3) ppm due to (N-H) protons δ (4.6)) ppm due to(NH_2) protons .

7- phthalazin and pyridazine –dion derivatives :[9] ,[8] .

Six membered heterocyclic rings compound [8] and compound [9] were synthesized by the reaction of hydrazide compound [7] with maleic and phthalic anhydride respectively in the presence of acetic acid as a solvent and catalyst .

The IR spectrum of compound [8], shows band at (3303) cm^{-1} was assignable to (-NH) stretching vibration . The band at (1735) $cm^{-1}$was due to υ(C=O) moiety of pyridazine ring. Band at (1672) $cm^{-1}$was due to υ (C=O) of amide I. From the above mentioned results we can say that the compound [8]can be exit in two tautomeric forms , keto (I) and enol (II) forms.

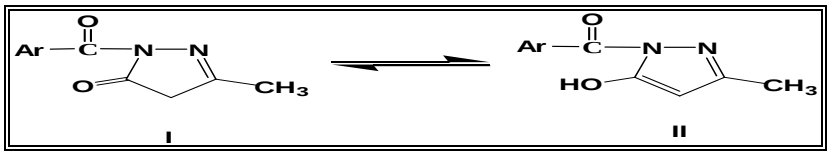
Also, the FT-IR spectrum of compound [9], showed the disappearance of two bands of (-NH_2) group of starting material compound [7] at (3309) $cm^{-1}$and (3221) cm^{-1}, appearance of a band due to (-NH) group at (3350.12) cm^{-1}. Two carbonyl group of compound [9] appeared at (1731.96) $cm^{-1}$and (1691.46) $cm^{-1}$for phthalazine ring and at (1604.66) $cm^{-1}$for the amide carbonyl . The ^{1}H-NMR spectrum , of the above compound [9] shows the signals δ (6.8 – 8) ppm due to aromatic protons δ (8.7) ppm due to (N-H) protons δ (4.7) ppm due to (CH_2) aliphatic protons .

8- Pyrazolone derivative : 1-(p-bromopheno acetyl)-3methyl pyrazol-5-one [10] .

Compound [10]was synthesized from reacting the hydrazide with ethyl aceto acetate in absolute ethanol , compound [10] was characterized by FT-IR spectrum .

The suggested mechanism for this reaction involves the nucleophilic attack of nitrogen atom of the hydrazide on the ketonic carbonyl of ethyl acetoacetate followed by the formation of Schiff 's base as intermediate compound, then another intramolecular nucleophilic attack occur between the other nitrogen atom of hydrazide and the esteric carbonyl of ethyl aceto acetate.

The FT-IR spectrum of compound [10], showed the presence of bands at (3992) $cm^{-1}$and (1743) cm^{-1} which were due to the υ(-OH) and υ(C=O) moieties of pyrazole ring, respectively , while the (C=O) stretching band of amide I occur at (1693) cm^{-1}. From the above mentioned facts , we can say that compound [10] can exist in equilibrium between keto (I) and enol (II) forms. Also a new band appeared at (3029-3062) cm^{-1}due to the stretching vibration of the (-C-H) group.



9- Preparation 1-(p-bromo phenol acetyl)-3,5-dimethyl pyrazole [11].

The route for the preparation compound involves the reaction of acid hydrazide with acetylaceton. The suggested mechanism for this reaction is the nucleophilic attack of nitrogen atom of hydrazide on the ketonic carbonyl of acetyl acetone followed by the formation of Schiff base as intermediate compound , then another nucleophilic attack occurs between the other nitrogen atom of hydrazide and the esteric carbonyl of acetyl acetone .

The derivative compound[11] was identified by FT-IR spectrum which showed the disappearance of two absorption bands of ($-NH_2$)group of the starting material [7] at (3304-3220) $cm^{-1}$and appearance of carbonyl group shifted to higher frequency (1753) cm^{-1}. The aromatic (C=C) appeared at (1579) cm^{-1}.

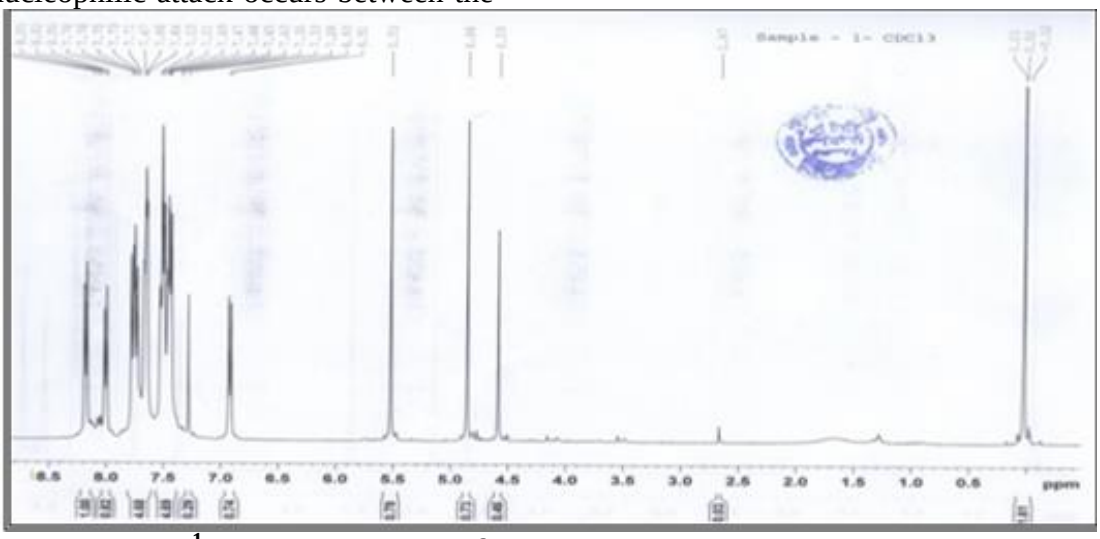


Fig (1): ^{1}H-NMR spectrum of compound [6].

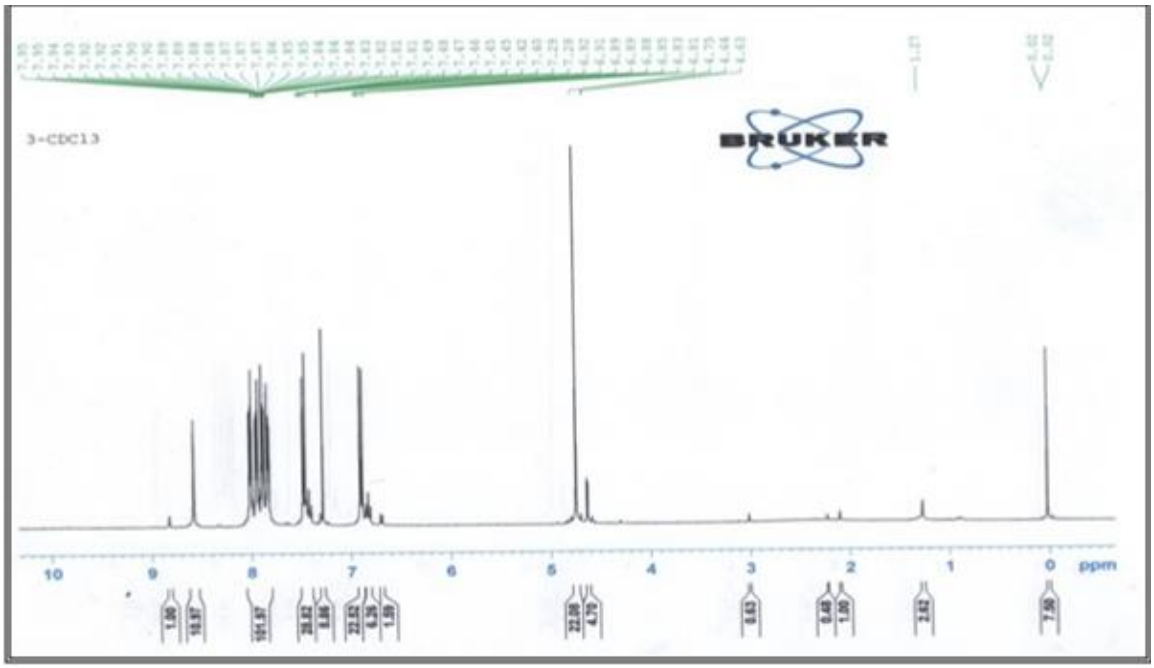


Fig (2): ^{1}H.N.M.R spectrum of compound [9].

Results and Discussion:

The biological activity of compounds was determined by measuring the diameter of the empty region around the well (Inhibition zone). The results of preliminary screening tests are listed in table (4).

Table (4): Antibacterial Activities of the synthesized compounds.

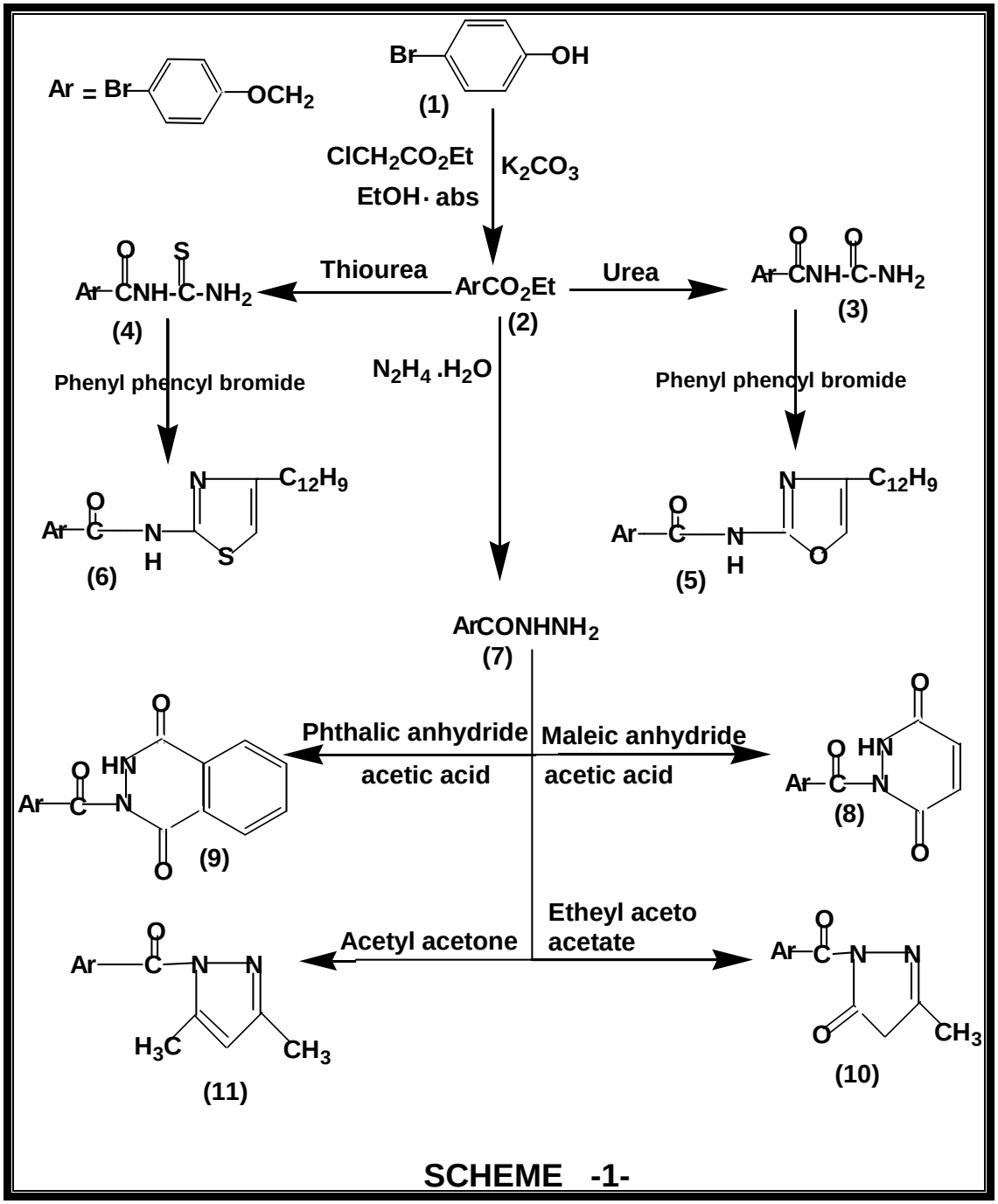
Compd.No.	St.	E .coli	Sal.	Ps.
[8]	++	-	-	±
[3]	±	-	++	-
[4]	±	-	±	±
[10]	-	-	±	-
[11]	±	±	-	±

Notes :

- = No inhibition = inactive, + = (5-10) mm= active, ++ = (11-20) mm = high active.
± = slightly active

Conclusion:

1. For *St* . (G^+), compound [8] showed highest activity, while compound [10] showed no activity on this bacteria.
2. For *Pseudomonas aeuroginosa* (G^-), compounds [3 ,10]have no effect on this bacteria because this bacteria is highly resistant to a wide range of antibiotic because of the slim poly saccharides in cell wall which blocked antibiotics from bacteria and also there are genetic factor.
3. For *E. coli* (G^-), [11] compounds have moderate effect on this bacteria.
4. For Sal . (G^-), all compounds have moderate effect but compounds [8,12,11] have no effect on these bacteria .


Ar = Br OCH2
Br OH
(1)
ClCH2CO2Et
EtOH. abs
K2CO3
Thiourea
ArCO2Et
(2)
Urea
Ar CNH-C-NH2
(4)
Ar CNH-C-NH2
(3)
Phenyl phencyl bromide
N2H4 .H2O
Phenyl phencyl bromide
C12H9
(6)
C12H9
(5)
ArCONHNH2
(7)
Phthalic anhydride
acetic acid
Maleic anhydride
acetic acid
(9)
(8)
Acetyl acetone
Etheyl aceto acetate
H3C
CH3
(11)
CH3
(10)

SCHEME -1-

References

1- Ladva K., Patel P.,. Upadhyay P and Parekh H., 1966 *Ind. J. Chem.* ,**35B**, 1062.

2-. Frump J. A, 1971*Chem. Rev.*, **71,** 483

3- JMetzge. V. r, 1985 "Thiazole and its Derivatives", John Wiley and Sons, New York, pp.395-399.

4-. Williams R. R,. Coworkers, A. A 1935 , *J. Am. Chem. Soc*., **57** (53), 224.

5-. Gabriel, S 1910 *Ber.*, **43**(134), 1283.

6-. Amad M. F,. Kamal M. D and. Abdou O. A, 1994 *Tetrahedron*, **53**, p.p 17461-17468.

7-Sulphur, Selenium and Tellurium, 2004 "Specialist Periodical Reports The chem., Soci., Lond., **1**, 9487.

8Alexander- E. R. 1960Principles of Ionic Organic Reactions", U.S.A. & U.K., **6**.

9-. Sener, A 2004 *Turk. J. Chem.*, **28**, 39.

10-. Coudert P,. Albusson E. Boire , J. Y and Bastide P., 1994*Eur. J. Med. Chem.*, **29**, 471.

11- Ostby O. B., gunderson L. L.,. Rise F and Bast, A. 1994 , *Arch. Pharm. Med. Chem.*, **29**, 471.

12- Contreras J., Rival y., Chayer S.and Wermuth C., 1999 *J. Med. Chem.*, **42**, 730.

13-. Danel A,. Chaczatuian K and. Tomasik P, 2001ARKIVOC, **1**(1), 51.

14--. Twnsend L. B, b1976,Chem. Rev. **67**, 533.

15-. Nezhad A. K, Soltani M. N., Mohabathkar H.and. Asrari Z, 2005 *Bioorg. & Med. Chem.*, **13**, 1931.

16-. Grimmet M. R, "Comprehensive Heterocyclic Chemistry, Five membered ring with two or more nitrogen atom",ed. By K. T. Potts, Vol. 5, Part UA, Pergaman Press, LFd., Oxford.

17- Ram V. J. and Haque N., 1996, *Ind. J. Chem*., **35B**, 238.

18-. El-Tamaty, E. S 1996 *Ind. J. Chem.* **35B**, 1067.

19.. Mohan, J. Anjaneyulu G and kiran, 1988 *Indian. J. Chem*., **27B**, 128.

20-. Wieg G. E. and. Bauer V. J, 1969 *J. Med. Chem*., **12**, 943.

21-.. El-masry, A. H. Fahmy H. H and. Abdelwahed . S. H. A ,2000M*olecules*, **5**, 1430.

22- Abdou A. I., Saleh A. M. and. Zohdi H. F, 2004 *Molecules*, **9**, 109.

23-. Sliverstien M and Webster X., 1999"*Spectrometric Identification of Organic Compounds"*, **Sixth Edition,** (a) 96,

24-. Hamdi J. J ,1999Ph. D. Thesis, Al-Mustansiria University.

25-.Wahe A,. Göker H,. Özden, S Karatas H.and Yildiz S., 2004 *Arch. Pharm. Med. Chem.*, **337**, 556.

تحضير وتشخيص بعض المركبات الغيرمتجانسة وتشمل الاوكسازول والثايازول والبيريدازين والفثالزين والبايرازول وتقييم الفعالية الحيوية.

وسام خليفة جاسم ***عبدالجبار مخلص**** ***ابتسام خليفة جاسم****

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الخلاصة :

تم تحضير سلسلة من المركبات الجديدة وتشمل بارا-بروموثيل فينو استيت(2)، ن-(امينوكاربونيل)-بار ابروموفينواستامايد(3)،ن-(امينوثايونيل)بارابروموفينواسيتايل امايد(4)،ن-(4-باراثنائي فنيل)1و3-اوكسازول-2-يل)-بارابروموفينواسيتامايد(5)، ن-(4-باراثنائي فنيل)1و3-اثايازولل-2-يل)-بارابروموفينو و اسيتامايد (6)، بارابروموفينواسيتك اسدهيدرازايد(7)، 1-ن-(بارابروموفينواسيتايل)1,2-ثنائي هيدروبيرادازين 6,3-ثنائي اون (8)، 1-ن-(بارابروموفينواسيتايل)1,2-ثنائي هيدروفثالزين 8,3-ثنائي اون (9)، 1-ن-(بارابروموفينو اسيتايل)-3-مثيل بايرازول-5-اون (10)، 1وكذلك 1-ن-(بارابروموفينواسيتايل)- 5,3 ثنائي مثيل بايرازول (11). تم تشخيص المركبات المحضرة بوسطة درجات الانصهار واطياف الاشعة تحت الحمراء والرنين النووي المغناطيسي.كذلك تم تقييم الفعالية الحيوية