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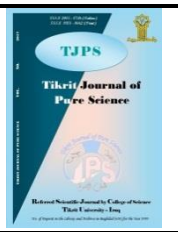

Synthesis, diagnosis and biological activity study of some heterocyclic compounds derived from 2-aminobenzothiazole

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Abstract

This study includes synthesis of some benzothiazole derivatives from treatment 2 -aminothiazole with choroacyle chloride to form 1-hydrogen-benzothiazole-2yl-2-chloroastiamide (1).the last one was reacted with urea, thiurea, thiosymigarizaide, 2- amibenzothiazole and para-aminoaniline, respectively to form the compounds (2,6). Some shiff bases for 2-aminobenzothiazole (7,8) were prepared from the reacting with aromatic aldehydes and it was cycled by reaction with glycine to form two derivatives of amidazolidine (9,10). The prepared compounds were diagnosed by IR spectra and H^1NMR for proton, then, the bacterial susceptibility towards some prepared compounds (1,2,5,6,7) were estimated against *E.coli* and *Proteus mirabilis* .

1- Introduction

Thiazole derivatives occupy an im portant position among heterocycle that are containing N and S atoms [1,2], several of thiazole derivatives are charachterized by their biological and pharmacological activity[3,4], therefore, it was studied at a wide range including several fields. thiazole cycle plays an important role in medicine [5] due to using it as antibiotic drugs against microbes [6], tuberculosis[7], viruses[8], malaria [9] and HIV[10] also in development of allergy [11] and in synthesis of sulfonylamide[12]. Benzothiazoles are used as anticancer [13] with mixture of amino acids complexes that introduced into the transference and replacement mechanisms of trace elements ions in human body [14]. The nucleus of benzothiazole are linkaged with various activities of antihistamine[15], some of chloride-cobalt complexes which contain benzothiazole were also showed high activity in increasing of agriculture production[16]. the functional benzothiazole was reported to show the reverse applications as light stabilizer and complexity factors with metal [17] .

2- Experment & Methods

2-1 Methods

General procedure for Synthesis of benzothiazole-2yl-2chloroastiamide[18] (1)

(0.01 mol) (1.5 gm) 2-aminobenzothiazole, that dissolved in 15 ml of dry benzene, and was mixed with (0.01 mol) (1ml) chloroacytle chloride, that dissolved in (5ml) from the same solvent. drops from triethyleamine were added to mixture then, refluxed in water bath for 3 hr., left the mixture to cool then filtered and using distill water to wash the precipitant, finally, it was recrystallized from ethanol.

General procedure for Synthesis of benzothiazole-2yl- oxazole/thiazole-2,5-diamine[19] (2- 3)

(0.01mol)(2.19gm) from compound (1) was dissolved in (60ml) ethanol, then (0.01mol) (1.6gm) urea and (0.76gm) thiurea were added gradually . the mixture was refluxed in water bath for24 hr. and left to cool, after that, drops of 10%NaOH were added to it, then, the precipitant was filtered and recrystallized from ethanol .

General procedure for Synthesis of benzothiazole-2yl(3-thiosymicarbizide) acetamide [19] (4)

(0.01mol) (2.9fm) from compound (1) was dissolved in (30ml) ethanol, then (0.01mol) (0.91gm) thiosinicarbazide was added gradually, and after addition some drops of pyridine, the mixture was refluxed for 24 hr., then the precipitant was cooled, filtered and recrystallized from ethanol.

General procedure for Synthesis of 2-(benzothiazole-2-yl) amino(benzothiazole-2-yl) acetamide [20] (5)

(0.01mol)(2.19gm) from compound (1) was dissolved in (20ml) ethanol, then, (0.01mol) (1.5gm) from 2-

aminobenzothiazole was added gradually . the mixture was refluxed for 6hr. and cooled. And it was neutralized with 10% sodium bicarbonate, then, the precipitant was filtered and washed by distill water, finally, it was recrystallized from ethanol.

General procedure for Synthesis of 2-(4-anilineo)(benzothiazole-2yl) acetamide [20] (6)

(0.01mol) (2.19gm) from compound (1) was dissolved in (20ml) ethanol, then (0.01mol) (1.08gm) p-phenylene diamine was added gradually. The mixture was refluxed for 6hr. then, it was concentrated to one-third the volume, and calibrated by 10% sodium bicarbonate. The precipitant was filtered and washed with distill water, and recrystallized from ethanol .

General procedure for Synthesis of (4-chloro/4-hydroxy) benzlydine-2-aminobenzothiazole [21] (7-8)

(0.01mol) (2.19gm) from 2-aminobenzothiazole was mixed with (0.01mol) aromatic aldehyde in (30ml) ethanol. The mixture was refluxed for 6 hr., then, the solution was cooled for 24 hr. at 0°C. The precipitant was filtered and recrystallized from ethanol.

General procedure for Synthesis of [3-(benzothiazole-2-yl)-2-(4-chloro/4-hydroxy)phenyl] amidazolldine-on [21] (9-10)

(0.01mol) from compound (7,8), that dissolved in THF, was mixed with (0.01mol) glycine ,which dissolved in (15ml) THF,. The mixture was refluxed for 24hr.. the precipitant was cooled, filtered and recrystallized from ethanol.

2-2 Bacterial susceptibility test for some prepared compounds (1- 2- 5- 6-7)

Two species of pathogenic bacteria, that resistance to antibiotics, were used , which were *E.coli* and *Proteus Mirabilis.* the bacterial isolates were taken ready and diagnosed from laboratory of biology department in education collage of pure science / Tikrit university.

2-2-1 culture media

a- Nutrient broth: it was prepared and used according to the company's instructions, it sterilized by autoclave at 121°C for 15 min. under 15bar/inch^2 . then, poured in petri dishes or special tubes and left to cool [22]

b- Muller Hinton agar: this medium is used to measure the biological activity for antibiotics and pharmacological, also is used to measure the diameter of inhibition zone [23].

2-2-2 Chemical solutions

The chemical solutions for some prepared compounds were prepared at concentration (0.01-0.1 gm/5ml) and sterilized by autoclave at 121°C for 15 min under 15 bar/inch^2, then left to cool before used .

2-2-3 Estimation of biological activity by diffusion methods

The biological activity was estimated by followed a Kirby Bauer method ; it has been spread (0.1ml) from bacterial suspension on the petri dishes that containing muller hinton agar and left for 5 min. to diffuse into medium. after that, 4 pores in each dishes were done using sterilize cort porer (5mm diameter). (0.1 ml) from prepared solutions were added to each pores while the fourth pore filled by DMSO as control sample. All dishes were incubated for 24 hr. at 37°C [24-25]. The inhibition diameter was measured around each pore in Mm according to Preslott method [26]

Results and discussion:

The amino group in 2-aminobenzothiazole reacted with chloroacetyl chloride to form the compound (1) as shown in table (1) and figure(5). The IR spectra for this compound showed absorption band at 3506cm^{-1} for stretch of (NH) bond and the absorption band at 1693 cm^{-1} for stretch of(C=O)bond, and also at 715 cm^{-1} for (C=C) bond. The H-NMR spectra of this compound was showed a dual signal at frequency (4.46-4.51 δ ppm) attributed to (2H,CH_2) protons, and a signal at (8δ ppm) to (H, NH)proton, as well as, a signal showed at range (7.24-7.98 δppm) attributed to (4H, phenyl group) as shown in figure (1).

The compound (1) was reacted with urea and thiurea to formed oxazole and thiazole (2-3) respectively . IR spectra for these compounds showed absorption band at (3465 cm^{-1}) attributed to stretch (NH_2) bond , and at (1155cm^{-1}) to stretch of(C-O) band . as shown in table (1).

The compound (1) was reacted with thiocymicambarzide and 2- aminobenzothiazole and para aminoaniline to form compounds (4-5-6). IR spectra for these compounds showed absorption band at range (3506-3382 cm^{-1}) attributed to stretch of (N-H) bond , also at (1666-1616cm^{-1}) to stretch of (C=O) bond, and at (1242 cm^{-1}) to (C=S) bond, as shown in table (2). H-NMR spectra was showed a dual signal for compound (5) at range (3.59-3.66δppm) attributed to (2H-CH_2) proton, and a single signal at (4.15 δppm) to (H, CH_2 –NH) proton, and at (7.96δ ppm) to (H, NH-CO) proton, also H-NMR showed a signal at (6.99-7.68 δppm) attributed to (8H,phenyl group), as shown in figure (2).

The compound 2-aminobenzothiazole was also reacted with aromatic aldehydes to form shiff bases of compounds (7-8), IR spectra showed absorption band for these compounds at range (1631-1643 cm^{-1}) attributed to stretch (C=O) bond, also at (744 cm^{-1}) to stretch (C-Cl) bond and (3392 cm^{-1}) to stretch (C-OH) bond as shown in table (3)and figure (6). H-NMR spectra for compound (7) showed a signal at (10δ ppm) attributed to (H-CH) proton, as well as, a signal at range (6.97-7.95δppm) to (8H-phenyl group), as shown in figure (3), while compound (8) was showed a signal at (3.39δ ppm) attributed to (H,OH) proton and a signal at range (7.64 δppm) to (H-CH) proton, as well as, a signal showed at range (6.62-6.97δ ppm) attributed to (8H, phenyl group) proton , as shown in figure (4).

The compound (7-8) were cycled using glycine and THF as solvent to formation amideazoldine-4-on

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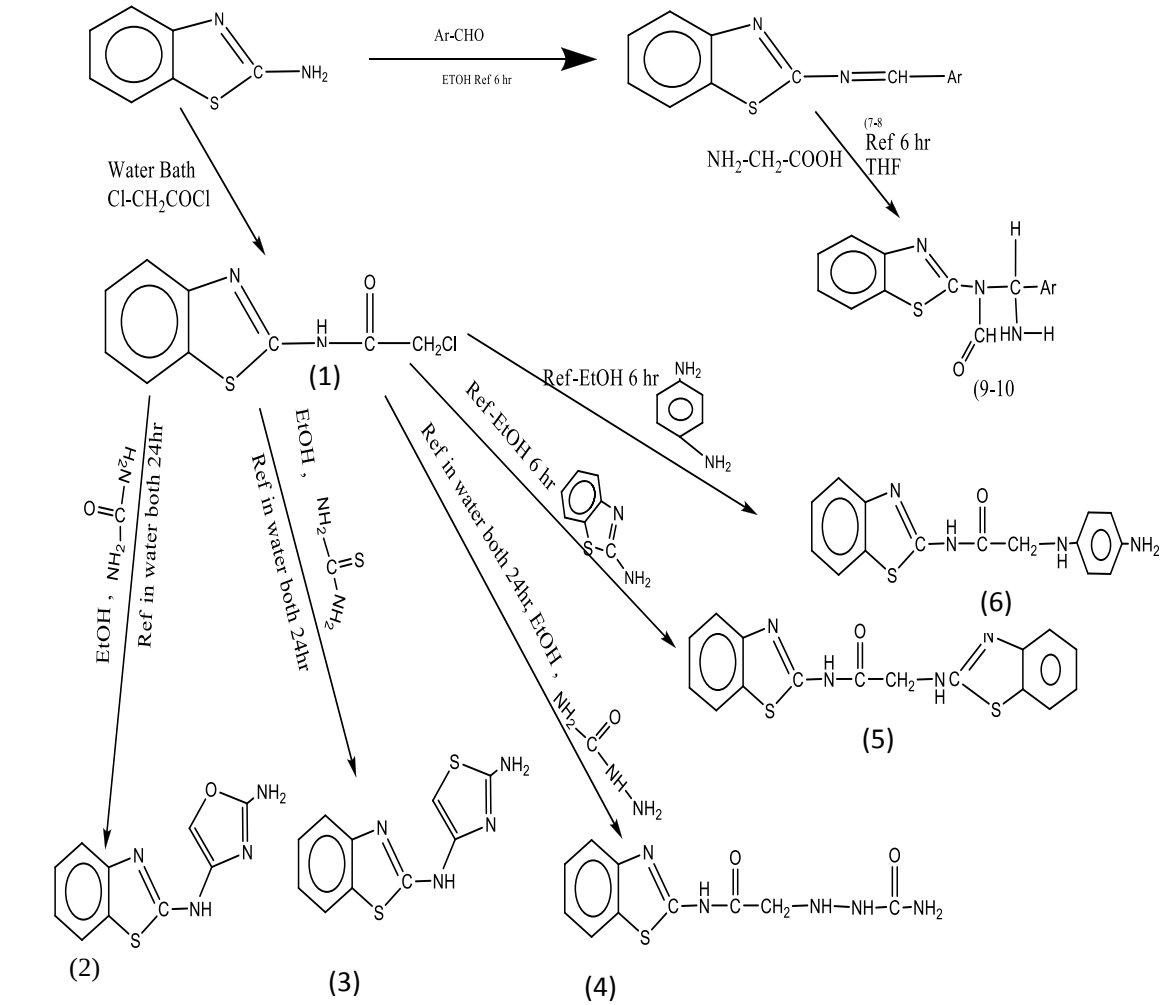
compounds that represent by compounds (9-10). IR spectra for these compounds was showed absorption band at range (1633-1683 cm^{-1}) attributed to stretch of (C=O) bond , also at (3332-3402 cm^{-1}) to stretch of (N=H) bond as shown in table (4) .

Biological activity for some compounds (1- 2-5-6-7)

The biological activity of some compounds (1-2-5-6-7) was measured ,where compounds (1-2) showed a high efficiency towards *Proteus mirabilis* (susceptibility), also compound (6) showed an efficiency towards E.coli, while the rest compounds were ineffective towards these species of bacteria but compound (5) was had a low efficiency towards E.coli. as shown in table (5).



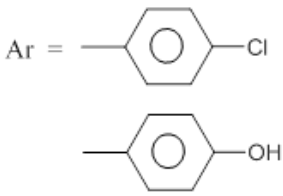


Table (1) The results of IR spectra for (1-2-3) compounds

No. Comp	Ar – H	N – H	C = O	C - S	C-Cl	NH_2	C – O
(1)	3047	3506	1693	—	755	—	—
(2)	3050	—	—	—	—	3465	1155
(3)	3065	—	—	1080	—	3450	—

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Table (2) The results of IR spectra for (4-5-6)compounds

No. Comp	Ar – H Orma	N – H	CH_2 Aleph	C = O	C = S
(4)	3070	3360	2929	1641	1242
(5)	3035	3382	2925	1622	—
(6)	3052	3313	2889	1616	—

Table (3) The results of IR spectra for (7-8) compounds

No. of comp	νA – H arom	νC = N	N=C – H Aleph	C – Cl	C-OH
(7)	3077	1637	2935	744	—
(8)	3053	1643	2927	—	3392

Table (4)Tthe results of IR spectra for (9-10) compounds

No. of comp	νAr – h arom	ν N – H	C – N	C=O
(9)	3063	3332	1591	1683
(10)	3037	3402	1541	1633

Table (5) The results of biological activity for (1-2-5-6-7) compounds

No.comp	E.coil	Proteus
(1)	M	S
(2)	M	D
(5)	R	M
(6)	S	M
(7)	M	M

Comparative with ciprofloxacin

Sensitive	intermediate	Resistant
⩾ 21 MM	15 – 20	⩽ 14

Table (6) The physical properties for (1-10) compounds

No . of comp	Format	Colour	Yiled%	Mp	Solvent
(1)	$C_9H_7N_2SOCl$	Off -yellow	90 %	187 – 190	Benzene
(2)	$C_{10}H_8N_4SO$	White	93 %	228 – 230	Ethanol
(3)	$C_{10}H_8N_4S_2$	White	34 - %	238 – 340	Ethanol
(4)	$C_{10}H_{11}N_5S_2O$	White	62 %	250 – 252	Ethanol
(5)	$C_{16}H_{12}N_4S_2O$	White	72 %	243 - 245	Ethanol
(6)	$C_{15}H_4N_4SO$	Grey	19 %	110-112	Ethanol
(7)	$C_{14}H_9N_2SCl$	Off- green	59 %	115 – 118	Ethanol
(8)	$C_{14}H_{10}N_2SO$	Orange	35 %	105 – 107	Ethanol
(9)	$C_{16}H_{12}N_3SCl$	Yellow	40%	185 – 188	THF
(10)	$C_{16}H_{13}N_3SO_2$	Yellow	____	Oily	THF

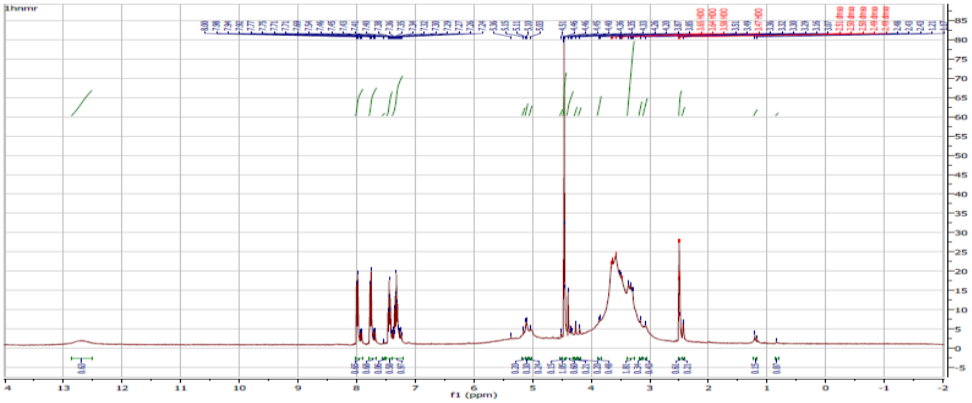

Figure (1) H^1 NMR for compound (1)

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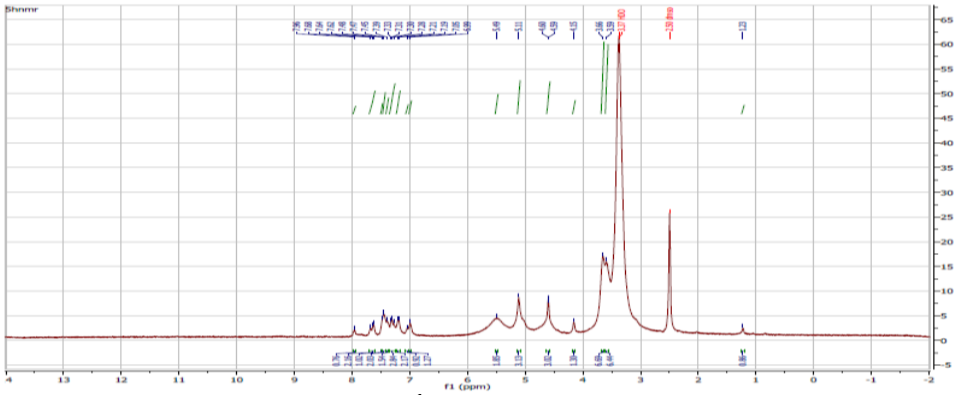

Figure (2) H^1 NMR for compound (5)

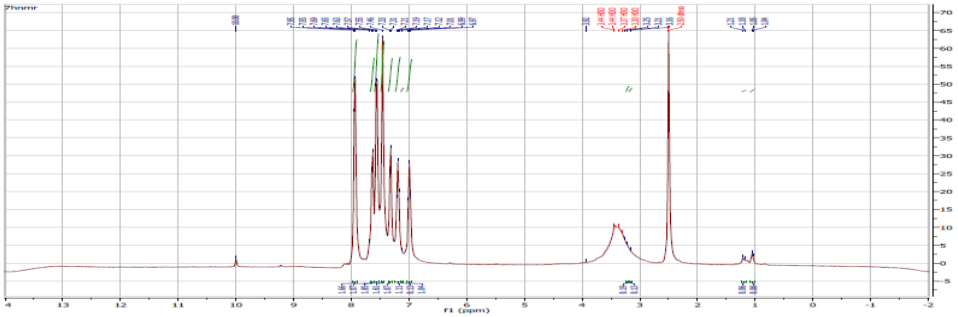

Figure (3) H^1 NMR for compound (7)

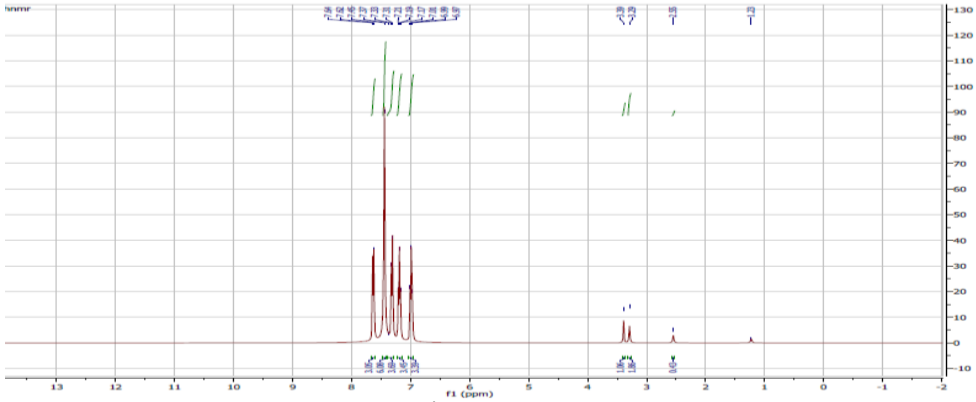

Figure (4) H^1 NMR for compound(8)

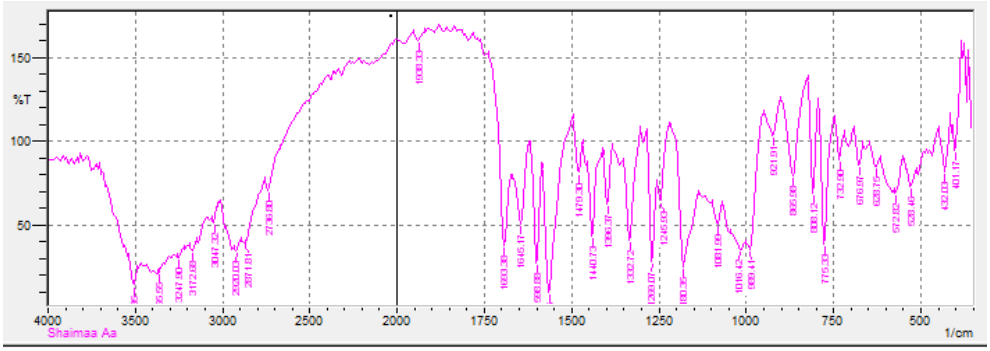

Figure (5) FTIR for compound(1)

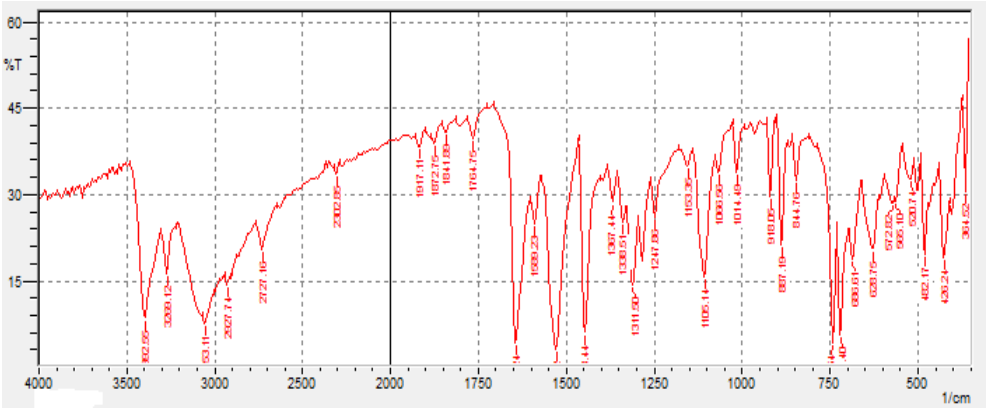

Figure (6) FTIR for compound (8)

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تحضير , تشخيص ودراسة الفعالة البايولوجية لبعض المركبات الحلقية غير المتجانسة المشتقة من 2- امينوبنزوثايازول

شيماء حاتم عبدالله

قسم الكيمياء ، كلية التربية للعلوم الصرفة ، جامعة تكريت ، تكريت ، العراق

الملخص

تضمن البحث تحضير بعض مشتقات البنزوثايازول من معاملة 2- أمينوثايارزول مع كلورو استيل كلورايد للحصول على (1- هيدروجين – بنزوثازول –2 يل) –2- كلورو أستمايد [1] فوعل الاخير مع كل من اليوريا والثايويوريا وثايو سيميكاربزايد و 2- أمينو بنزوثايازول و بارا – أمينو أنلين على الترتيب للحصول على المركبات [2-6]. حضرت بعض قواعد شف لـ 2- أمينو بنزوثايازول [8,7] من مفاعلته مع الاليهايدات الأروماتية تم حولقتها بالمفاعلة مع الكلايسين glycine للحصول على مشتقي الاميدازولدين المقابلة [10,9]. شخصت المركبات المحظرة بواسطة مطيافية الاشعة تحت الحمراء الرنين النووي المغناطيسي للبروتون تم تقييم الفعالية المضادة للبكتيريا لبعض المركبات المحضرة [7,6,5,2,1] ضد اشريشيا القالون (Escherichia Coli) و البكتيريا المتقلبة او بكتيريا المراحيض (Proteus Mirabilis).