Synthesis ,Characterization and Study Biological Activity of Some New 1, 3, 4-Thiadiazole and Pyrazolone Derivatives Containing Indole Ring

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Received in: 12 june 2014,Accepted in: 29 September 2014

Abstract

This work involves synthesis and characterization of some new 1, 3, 4-thiadiazole or pyrazoline derivatives heterocyclic containing indole ring. The new 2-amino-1, 3, 4-thiadiazole derivatives[IV] and $[V]_{a, b}$ were synthesized by cyclization reaction of 2-methyl-1H-indole-carbothiosemicarbazide[III] in H_2SO_4 acid or by reaction of indole-3-acetic acid or indole-3-butanoic acid with thiosemicarbazide in the presence of phosphorous oxychloride, respectively. Amide derivatives [VI]-[VIII] were synthesized by the reaction equimolar of 2-amino-1, 3, 4-thiadiazoles and (acetyl chloride, benzoyl chloride, anisoyl chloride and heptanoyl chloride) in DMF and pyridine as accepter. The new pyrazolone derivatives $[XI]_{a, b}$ were synthesized from heating under reflux equimolar from a mixture of acid hydrazides $[X]_a$ or $[X]_b$ and ethylacetoacetate in absolute ethanol. Acetyl pyrazolone compounds$[XII]_{a, b}$ were synthesized by the reaction of pyrazolone derivatives $[X]_a$ or $[X]_b$ with acetyl chloride in 1,4-Dioxane in present of calcium hydroxide to give 4-acetyl pyrazolone derivatives$[XI]_{a, b}$. The new aryl hydrazone derivatives of pyrazoline [XIII] and [XIV] were synthesized by the reaction of one mole of compounds $[XII]_a$ or $[XII]_b$ with one mole of phenyl hydrazine or substituted phenyl hydrazine in ethanol. All the synthesized compounds have been characterized by melting points , FTIR, ^{1}HNMR and Mass spectroscopy (of some of theme).

Key Words : 1,3,4-thiadiazole, pyrazole, pyrazolone, Indole, hydrazone.

Introduction

The indole ring system has become an important structural requirement in many pharmaceutical agents[1]. Indole and its derivatives occupied a unique place in the chemistry of nitrogen heterocyclic compounds because of their varied biodynamic properties [2]. Most of the Indole derivatives are biologically active chemicals present in microorganisms, plants and animals representing an important class of therapeutic agent in medicinal chemistry [3]. The five-member heterocyclic compounds particularly nitrogen and sulphur heterocyclic: thiadiazole, contains the five membered unsaturated ring structure composed of two nitrogen atoms and one sulfur atom. There are four isomeric types: 1,2,3-thiadiazole; 1,3,4-thiadiazole; 1,2,4-thiadiazole and 1,2,5-thiadiazole[4].

In view of the standard reference work shows that more work has been carried out on the 1,3,4-thiadiazole than all other isomers combined[5]. 1,3,4-Thiadiazole moiety in which sulfur present at position-1, and two nitrogen atom at position-3 and position-4. Thiadiazoles are an important class of heterocyclic compounds that exhibit diverse applications in organic synthesis, pharmaceutical and biological applications, among them 2,5-disubstituted-1,3,4-thiadiazoles are associated with divers biological activities probably by the virtue (-N=C-S-) grouping[6]. 1,3,4-Thiadiazole derivatives possessed a wide range of therapeutic activities [7-14].

Pyrazoles represent one of the most active classes of compounds possessing wide spectrum of biological activities[15]. Hydrazones possessing an azomethines -NH-N=CH- proton constituent an important class of compounds for new drug development. Therefore, many researchers have synthesized these compounds as target structures and evaluated their biological activities[16].

In view of these facts, we decided to synthesize new 1,3,4-thiadiazole, pyrazoline and their hydrazone derivatives containing indole ring.

Experimental

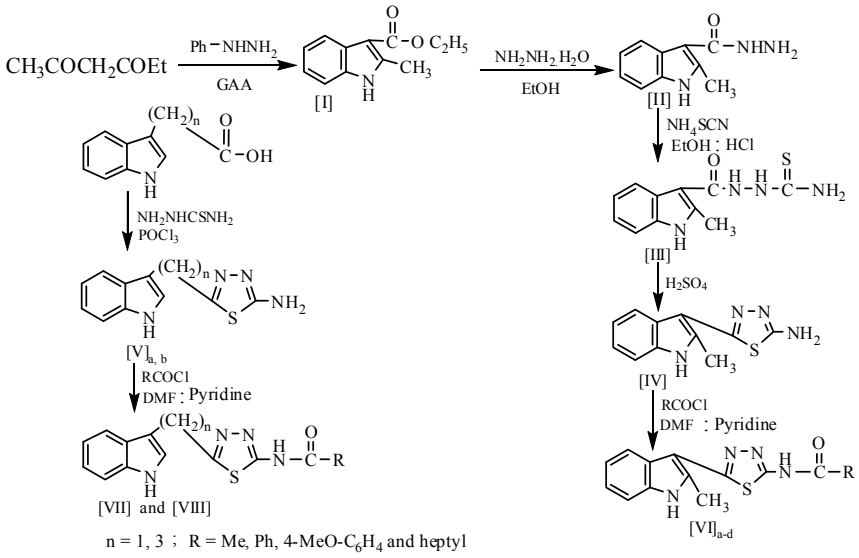
Materials

All chemicals were supplied from Merck, GCC and Aldrich Chemicals Co. and used as received.

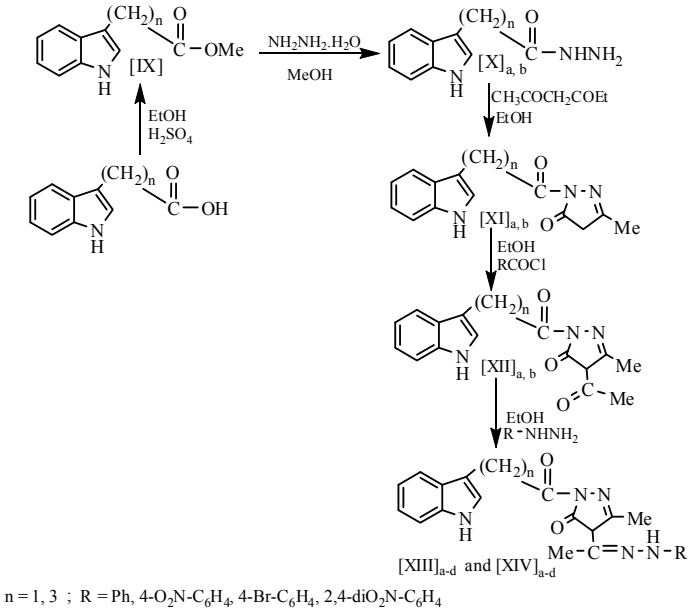
Techniques

FTIR spectra were recorded using potassium bromide discs on a Shimadzo (Ir prestige-21) FTIR spectrophotometer. ^{1}HNMR spectra were carried out by company: Bruker, model: ultra-shield 300 MHz origin: Switzerland, and Bruker model: ER-av-400 MHz, origin: Switzerland are reported in ppm(δ), DMSO was used as solvents with TMS as an internal standard . Measurements were made at Chemistry Department, Al-albyat University and University of Science and Technology, respectively in Jordan. Uncorrected melting points were determined by using Hot-Stage, Gallen Kamp melting point apparatus. The mass spectrum was recorded on Shimadzo model: 6CMS QD 1000 EX, made in Japan.

New compounds are synthesized according to scheme1 and scheme 2:



Scheme(1)



Schems (2)

Method Procedure

Ethyl-2-methyl-1H-indole-3-carboxylate [I]

This compound was prepared according to the let. [17].

2-methyl-1H-indole-3-carbohydrazide [II]

This compound was prepared according to the procedure method in let. [18]. Yield 84%, m.p = (144-146) ^{0}C.

2-(2-methyl-1H-indole-3-carbonyl)hydrazine carbothioamide[III]

This compound was prepared according to the procedure method in let. [19], Yield 90 %; m.p.: (200-202) ^{0}C.

2-Amino-5-(2-methyl-1H-indol-3-yl)-1,3,4-thiadiazole [IV]

This compound was prepared according to the procedure method in let. [10], Yield 65 %; m.p.: (190-192) ^{0}C.

2-Amino-5-(substituted-(1H-indol-3-yl)alkyl)-1,3,4-thiadiazole [V]$_{a, b}$

A mixture of 1H-indole-3-acetic acid or 1H-indole-3-butanoic acid (0.01 mol), thiosemicarbazide (0.91g, 0.01mol) , phosphorus oxy chloride (5 mL) was refluxed gently for 6 hrs. After cooling, ice water (50 mL) was added in portions with stirring at (0-4) ^{0}C . The precipitate was filtered, washed with water , dried and recrstalization from ethanol.

Synthesis of Amide Derivatives [VI]$_{a-d}$, [VII]$_{a-d}$ and [VIII]$_{a-d}$

2-Amino-1,3,4-thiadiazoles, (0.001 mol) was dissolved in mixture of pyridine and DMF (1:2 mL) on ice bath then different acid chloride (0.001 mol) was added, the mixture was stirred for 3 hrs at room temperature , afterward 10% HCl was added, the precipitate was filtered and washed with water, dried and recrystalized from ethanol.

Methyl Substituted-(1H-indol-3-yl) alkyloate [IX] $_{a, b}$

This compound was prepared according to the procedure method in let. [20], compound [II]$_a$; yield 94%, m.p. oily. compound [IV]$_a$; yield 94%, m.p. (82-84) ^{0}C.

Substituted-(1H-indol-3-yl)alkylhydrazide[X]$_{a, b}$

These compounds was prepared according to the procedure method in let. [19], compound[IV]$_a$, Yield 97%; m.p.= (142-144) ^{0}C. compound[IV]$_b$ Yield 92%; m.p. = (151-153) ^{0}C.

Synthesis of 1-(substituted-(1H-indol-3-yl)alkanoyl)-3-methyl-pyrazol-5(4H) -one[XI]$_{a, b}$

The acid hydrazides (0.0028 mol) and ethyl acetoacetate (0.364g, 0.0028 mol) in absolute ethanol(20mL) was refluxed for 3 hrs. The reaction mixture was allowed to cool and the formed precipitate was filtered off and recrystallized from methanol to give new compounds.

Synthesis of 1-[substituted-(1H-indol-3-yl)alkanoyl]-4-acetyl-3-methyl-pyrazol-5(4H)-one [XII]$_{a, b}$

1,4-Dioxane solution (25 mL) of compounds[XI]$_a$ or [XI]$_b$ (0.013 mol) and acetyl chloride (1.027g, 0.013 mol) was refluxed for 4 hrs on oil bath with calcium hydroxide (1.397g) and cooled to room temperature. The resulting reaction mass is added to the dilute hydrochloric acid (4.5mL Conc. in 20 mL water), the cured product was collected by filtrations and washed several times with water and recrystallized from acetone.

Synthesis of 1-[substituted-(1H-indol-3-yl)alkanoyl]-3-methyl-4-[1-(2-arylhydrazono) ethyl]-4-hydro-pyrazol-5-one[XIII]$_{a-d}$ and [XIV]$_{a-d}$

A mixture of compounds [XII]$_{a, b}$ (0.001 mol) and phenyl hydrazine or substituted phenyl hydrazine (0.001mol) in ethanol (5mL) was refluxed for 3 hrs. Cool, pour onto water. The formed solid, was collected by filtrations and crystallized from chloroform.
The physical properties of the synthesized compounds[V]-[XIV] are given in Table(1).

Results and Discussion

Ethyl-2-methyl-1H-indole-3-carboxylate [I] was obtained by Fischer indole synthesis from the reaction of phenyl hydrazine with ethyl acetoacetate in glacial acetic acid, following the procedure described by P. Kumar et al[20]. This structure was identified by melting point and FTIR spectroscopy. The characteristic FTIR spectrum of compound[I], showed the disappearance of absorption stretching bands of NH_2 group of phenyl hydrazine and C=O of ketone group of ethyl acetoacetate together with the appearance of a new stretching band at 1714cm^{-1} which is assigned to υ C═O of ester moiety in addition, two stretching bands at 1620$cm^{-1}$and 3392 cm^{-1} due to the υ C=N(endocyclic) and N-H of indole ring, respectively. On the other hand methyl substituted-(1H-indol-3-yl) alkyloate $[II]_{a, b}$ were obtained by esterification of indole-3-acetic acid or indole-3-butanoic acid in absolute methanol using conc. H_2SO_4 as a catalyst, following the procedure described by Vogel[21]. These compounds were identified by melting points and FTIR spectroscopy. The FTIR absorption spectra showed the disappearance of absorption stretching bands of O─H and C═O groups of (carboxylic moiety) in indole-3-acetic acid and indole-3-butanoic acid together with the appearance of a stretching bands at 1732cm^{-1} which is assigned to C═O of ester moiety of compound$[IX]_a$ and at 1722cm^{-1} of compound$[IX]_b$, respectively.

The condensation ester compounds with hydrazine hydrate produce the acid hydrazide [II], $[X]_a$ and $[X]_b$ which are characterized by higher melting points and the FTIR spectra revealed stretching vibration of (N-H, NH_2) groups as well as stretching absorption at of C═O (amid) group between (3323-3200)cm^{-1} and (1681-1649)cm^{-1}, respectively and disappearance of absorption stretching band due to C═O of ester moiety.

Neucleophilic addition reaction of acid hydrazide [II] to ammonium thiocyanate in ethanol using hydrochloric acid as a catalyst to give 2-(2-methyl-1H-indole-3-carbonyl) hydrazine carbothioamide[III]. The structure of this compound was identified by melting point , FTIR spectroscopy. FTIR spectrumindicated absorption stretching band at 1288cm^{-1} that could be assigned to C=S group in addition to new bands which could be attributed to asymmetric and symmetric stretching vibration of NH_2 and N-H groups appear between (3356-3169)cm^{-1}, also showed shifting of C═O (amid) group to 1637cm^{-1}.

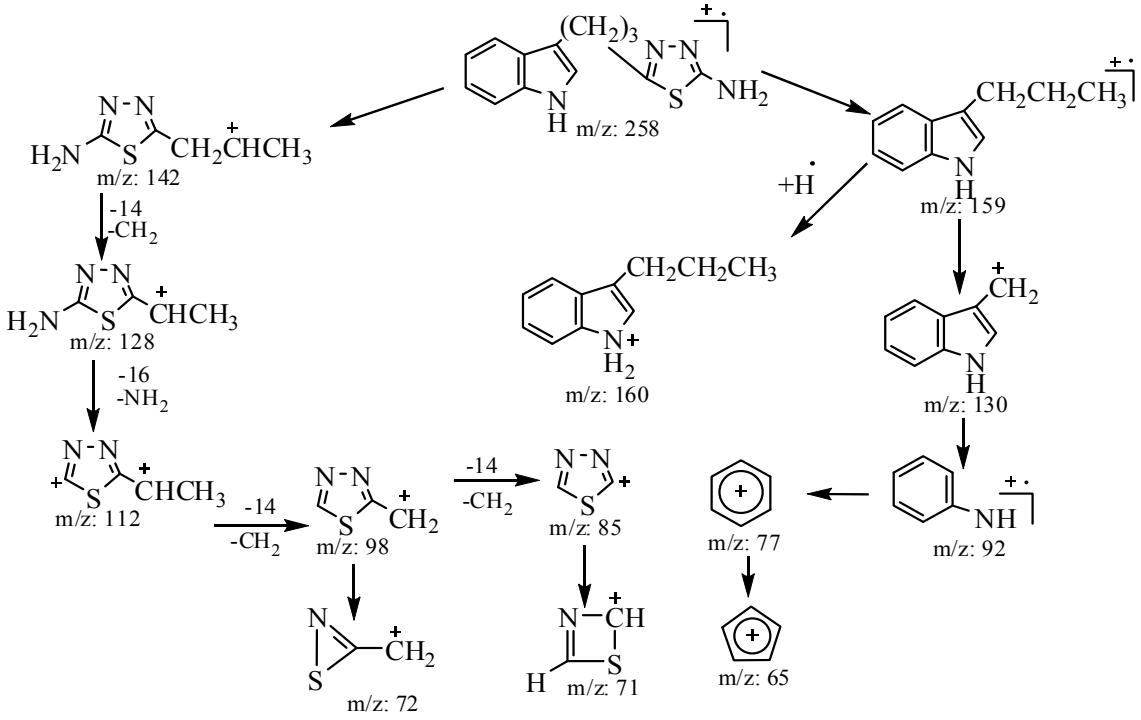
Cyclization 2-(2-methyl-1H-indole-3-carbonyl)hydrazine carbothioamide [III] is carried out in conc. H_2SO_4 followed by neutralized with liquid ammonia yielded 2-amino-5-(2-methyl-1H-indol-3-yl)-1,3,4-thiadiazole[IV], this compound is identified by melting point and FTIR spectroscopy. The FTIR absorption spectrum of this compound showed two peaks at 3296 and 3155 for stretching bands of NH_2, also show the disappearance of the characteristic bands of starting material[III], in addition of new peak at 690 for C-S-C bond.

^{1}HNMR spectrum (in DMSO as a solvent) for compound [IV], showed that the singlet signal at δ2.2 ppm could be attributed to three protons of CH_3 group. Also, the spectrum show many signals in the region δ(6.93-7.69)ppm due to four aromatic protons and two protons of NH_2 group which is in toutomerism forms (NH_2↔NH) therefore NH_2 protons appeared as very weak a broad peak in the region δ(3.06-5.0)ppm, while the protons NH forms appeared as a singlet signal at δ7.69 ppm. Finally signal at δ11.21 ppm for one proton of N-H indole ring.

The new 2-amino-1, 3, 4-thiadiazole derivatives$[V]_{a, b}$, were synthesized by the reaction of indole-3-acetic acid or indole-3-butric acid with thiosemicarbazide in the presence of phosphorous oxychloride under reflux for 6 hrs. These compounds were identified by melting points , FTIR, ^{1}HNMR and Mass spectroscopy. The FTIR absorption spectra of compounds$[V]_{a, b}$ showed two peaks in the region (3400-3178) cm^{-1} that attributed to the NH_2 group, peak at 1635 cm^{-1} or at 1630cm^{-1} of compounds$[VII]_{a, b}$, respectively due to C=N of thiadiazole ring, also show new peak around 710cm^{-1} for C-S-C group. The FTIR spectral data for these compounds are listed in Table (2).

The ^{1}HNMR spectrum (in DMSO as a solvent) for compound $[V]_a$, showed the following signals: a singlet signal at δ9.82 ppm for one proton of N-H indole ring, signals in region δ(6.7-8.1) ppm that could be attributed to the five aromatic protons, Also, the spectrum shows signals between δ(4.04-4.95) ppm for two protons of the NH_2 group. Finally, a singlet signal at δ(3.44)ppm for two protons of CH_2 group.

The mass spectrum, Figure(1) of compound$[V]_b$, given molecular ion at m/z = 258, which is correspond to the molecular weight of structures suggested for this compound. The results obtained from the mass spectrum suggested that fission was more easily accomplished at the carbon- nitrogen bond rather than at the carbon-carbon bond such as fragments at m/z = 112, 72 and 71. This peak at m/z = 85 is characteristic for 1, 3, 4-thiadiazole ring in addition to peak at m/z= 71. This spectrum showed interesting peak at m/z = 130 due to the indole ring. The other important fragments given in scheme (3).



Scheme(3)

Amide derivatives [VI]-[VIII] were synthesized by the reaction equimolar of 2-amino-1,3,4-thiadiazoles[IV], $[V]_a$ and $[V]_b$ and different acid chlorides in DMF and pyridine as accepter. These compounds were identified by melting points , FTIR and ^{1}HNMR spectroscopy. The FTIR spectra of amide derivatives[VI]-[VIII], as in Figure(2) showed the disappearance of bands of NH_2 groups of starting material with the appearance of a new stretching band of NH group in the range (3408-3200)cm^{-1}, also the appearance of carbonyl amide (C=O) in the range (1690-1674) cm^{-1}, the characteristics FTIR absorption bands of these compounds are given in Table(2).

The ^{1}HNMR spectrum (in DMSO as a solvent) for compound $[VIII]_d$, Figure(3) showed the following signals: a weak singlet signal at δ (11.57) ppm for proton of NH indole ring, a broad signal at δ(3.49)ppm due to one proton of (NH-CO) group, signals in the region δ(7.08-7.68) ppm that could be attributed to the five aromatic protons, many signals in the region δ(0.84-2.95) ppm that could be attributed to the aliphatic protons.

The new pyrazolone derivatives $[XI]_{a, b}$ were synthesized from heating under reflux equimolar from a mixture of acid hydrazides $[X]_a$ or $[X]_b$ and ethylacetoacetate in absolute ethanol. These compounds were identified by melting points and FTIR spectroscopy. FTIR spectra of pyrazoline compounds$[XI]_{a, b}$ showed new stretching band due to C=O of

pyrazoline ring appear near 1700 cm^{-1}, in addition of the band of the (C=O amide) group. The appearance of new absorption band between1625 cm^{-1} is due to C=N group (endocyclic) of pyrazoline ring . The FTIR spectral data of pyrazolines $[XI]_{a, b}$ are listed in Table (3).

New 4-acetyl pyrazolone compounds$[XII]_{a, b}$ were synthesized by the reaction of pyrazolone derivatives$[XI]_a$ or $[XI]_b$ and acetyl chloride in 1,4-Dioxane in present of calcium hydroxide. The synthesized compounds were characterized by melting points, and FTIR spectroscopy. The FTIR spectra of acetyl pyrazolines as in Figure(4) showed new stretching band due to C=O (acetyl) group at 1735cm^{-1}. The FTIR spectral data of 4-acetyl pyrazolones$[XII]_{a, b}$ are listed in Table (3).

Aryl hydrazone derivatives $[XIII]_{a-d}$ and $[XIV]_{a-d}$ were synthesized by the reaction of one mole of acetyl compounds$[XI]_{a, b}$ with one mole of phenyl hydrazine or substituted phenyl hydrazine in ethanol. The structure of these compounds were studied by melting points , FTIR and ^{1}HNMR spectroscopy. The FTIR spectra, as in Figure(5) showed the disappearance of absorption band of the C=O(acetyl) group and appearance of new absorption stretching bands of NH and C=N groups in the regions(3408-3200) cm^{-1} and (1645-1618) cm^{-1}, respectively. The FTIR spectral data of aryl hydrazone derivatives $[XIII]_{a-d}$ and $[XIV]_{a-d}$ are listed in Table (3).

The ^{1}HNMR spectrum (in DMSO as a solvent), Figure(6)for compound $[XIII]_c$ showed: a singlet signal at δ10.90 ppm for one proton of NH indole ring, a singlet signal at δ9.90 ppm for one proton of (C=N-NH) group(264), another singlet signal at δ8.97 ppm for one proton of NH pyrazoline ring (the proton at C-4 is toutomerism with NH pyrazoline ring) as in scheme (3-20) (302) , signals in region δ(6.73-8.32) ppm that could be attributed to the nine aromatic protons, two signals at δ1.20 ppm and at δ1.80ppm for six protons of (CH_3-C=N) and CH_3 at C-3 of pyrazoline ring of pyrazoline ring. Finally a signal at δ(3.60) ppm for two protons of CH_2 group.

^{1}HNMR spectrum (in DMSO as a solvent), for compound$[XIV]_b$ showed: a singlet signal at δ10.18 ppm for one proton of NH indole ring, singlet signal at δ8.40 ppm for one proton of (C=N-NH) group, two doublets and mulitiple signals in region δ(6.90-7.48)ppm that could be attributed to the nine aromatic protons, singlet signal at δ(1.14-1.35)ppm for eight protons of CH_3 group at C-3 of pyrazolone ring, CH_3C=N and C-CH_2-C groups. Finally signals in the region δ(3.2-4.2) ppm for four aliphatic protons of two -CH_2- groups and the proton at C-4 of pyrazolone ring which is toutomerism with NH, the later proton appeared at δ7.83ppm for proton of NH form.

^{1}HNMR spectrum (in DMSO as a solvent), Figure(7)for compound $[XIV]_c$ showed: a singlet signal at δ(9.94)ppm for one proton of NH indole ring, singlet signal at δ(8.98)ppm for one proton of (C=N-NH) group, two doublets and mulitiple signals in region δ(6.58-7.95) ppm that could be attributed to the nine aromatic protons, singlet signal at δ(1.3-2.00) ppm for eight protons of CH_3 group at C-3 of pyrazolone ring, CH_3C=N and C-CH_2-C. Signals in the region δ(3.4-4.1) ppm for four aliphatic protons of two -CH_2- groups and a proton of C-4 of pyrazolone ring which is toutomerism with NH, the later proton appeared at δ8.07 ppm.

Biological Activity

The antibacterial activity of the synthesized compounds was performed according to the agar diffusion method[21]. The synthesized compounds were tested against E.coli and Staph. aureus. Each compound was dissolved in DMSO to give concentration 1ppm. The plates were then incubated at 37^0C and examined after 24 hrs. The zones of inhibition formed were measured in millimeter and are represented by (-), (+), (+ +) and (+ + +) depending upon the diameter and clarity as in Table (4). The synthesized compounds exhibit the highest, moderately or low biological activity or no active of some of them against one of the organisms. Compounds showed good inhibition against of the two types of the bacteria, this

could be related to the presence of the indole, 1,3,4-thiadiazole, amide or pyrazolone and hydrazone units.

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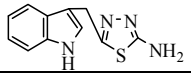
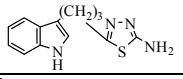
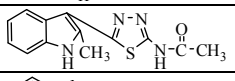
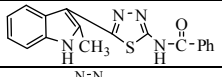
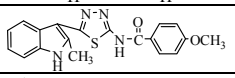
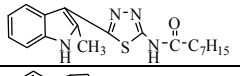
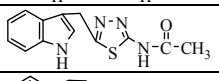
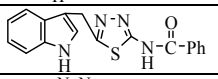
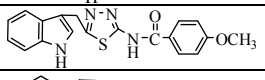
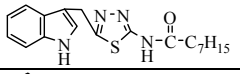
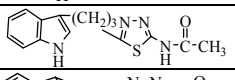
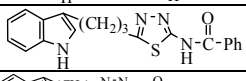
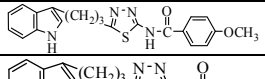
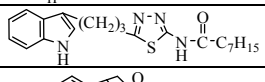
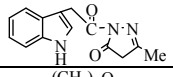
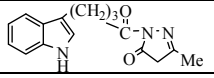
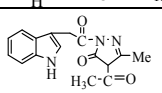
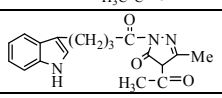
Table No.(1) : Physical properties of synthesized compounds [V]-[XIV]

Comp. No.	Nomenclature	Structural formula	Molecular formula	M.P °C	Yield%	Color
$[V]_a$	2-amino-5-[(1H-indol-3-yl)methyl]-1,3,4-thiadiazole		$C_{11}H_{10}N_4S$	210-212	93	Brown
$[V]_b$	5-(3-(1H-indol-3-yl)propyl)-1,3,4-thiadiazol-2-amine		$C_{13}H_{14}N_4S$	168-170	88	Red
$[VI]_a$	N-(5-(2-methyl-1H-indol-3-yl)-1,3,4-thiadiazol-2-yl) acetamide		$C_{13}H_{12}N_4OS$	170-172	81	Yellow
$[VI]_b$	N-(5-(2-methyl-1H-indol-3-yl)-1,3,4-thiadiazol-2-yl) benzamide		$C_{18}H_{14}N_4OS$	124-126	87	Pale yellow
$[VI]_c$	4-methoxy-N-(5-(2-methyl-1H-indol-3-yl)-1,3,4-thiadiazol-2-yl)benzamide		$C_{19}H_{16}N_4O_2S$	154-156	90	Pale brown
$[VI]_d$	N-(5-(2-methyl-1H-indol-3-yl)-1,3,4-thiadiazol-2-yl)octanamide		$C_{19}H_{24}N_4OS$	Gummy	63	brown
$[VII]_a$	N-(5-((1H-indol-3-yl)methyl)-1,3,4-thiadiazol-2-yl) acetamide		$C_{13}H_{12}N_4OS$	164-166	93	brown
$[VII]_b$	N-(5-((1H-indol-3-yl)methyl)-1,3,4-thiadiazol-2-yl)benzamide		$C_{18}H_{14}N_4OS$	175-177	87	pale brown
$[VII]_c$	N-(5-((1H-indol-3-yl)methyl)-1,3,4-thiadiazol-2-yl)-4-methoxybenzamide		$C_{19}H_{16}N_4O_2S$	158-160	89	brown
$[VII]_d$	N-(5-((1H-indol-3-yl)methyl)-1,3,4-thiadiazol-2-yl)octanamide		$C_{19}H_24N_4OS$	188-190	75	Orange
$[VIII]_a$	N-(5-(3-(1H-indol-3-yl)propyl) -1,3,4-thiadiazol-2-yl)acetamide		$C_{15}H_{16}N_4OS$	196-198	86	gray
$[VIII]_b$	N-(5-(3-(1H-indol-3-yl)propyl)-1,3,4-thiadiazol-2-yl)benzamide		$C_{20}H_{18}N_4OS$	122-124	71	yellow
$[VIII]_c$	N-(5-(3-(1H-indol-3-yl)propyl)-1,3,4-thiadiazol-2-yl)-4-methoxy benzamide		$C_{21}H_{20}N_4O_2S$	144-146	76	brown
$[VIII]_d$	N-(5-(3-(1H-indol-3-yl)propyl)-1,3,4-thiadiazol-2-yl)octanamide		$C_{21}H_{28}N_4OS$	128-130	81	Black
$[XI]_a$	1-(2-1H-indol-3-yl-acetyl)-3-methyl-4-hydro-pyrazol-5(4H)-one		$C_{14}H_{13}N_3O_2$	112-114	90	Brown
$[XI]_b$	1-(4-1H-indol-3-yl-butanoyl)-3-methyl-4-hydro-pyrazol-5-one		$C_{16}H_{17}N_3O_2$	1541-56	69	Red
$[XII]_a$	1-(2-1H-indol-3-yl-acetyl)-4-acetyl-3-methyl-4-hydro-pyrazol-5-one		$C_{16}H_{15}N_3O_3$	212-214	77	Brown
$[XII]_b$	1-(4-1H-indol-3-yl-butanoyl)-4-acetyl-3-methyl-4-hydro-pyrazol -5-one		$C_{18}H_{19}N_3O_3$	268-270	87	Brown

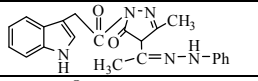
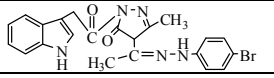
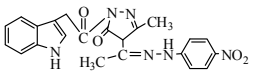
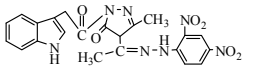
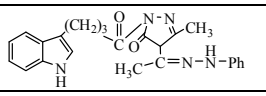
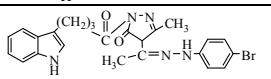
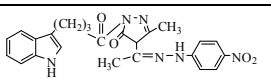
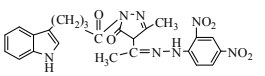
$[XIII]_a$	1-(2-(1H-indol-3-yl-acetyl)-3-methyl-4-[1-(2-phenylhydrazono)ethyl]-4-hydro-pyrazol-5-one		$C_{22}H_{21}N_5O_2$	162-164	83	Yellow
$[XIII]_b$	1-(2-(1H-indol-3-yl-acetyl)-3-methyl -4-{1-[(4-bromophenyl) hydrazono]ethyl}-4-hydro-pyrazol-5-one		$C_{22}H_{20}BrN_5O_2$	128-130	82	Brown
$[XIII]_c$	1-(2-1H-indol-3-yl-acetyl)-3-methyl-4-{1-[(4-nitrophenyl) hydrazono]ethyl}-4-hydro-pyrazol-5-one		$C_{22}H_{20}N_6O_4$	98-100	87	Dark red
$[XIII]_d$	1-(2-1H-indol-3-yl-acetyl) -3-methyl-4-{1-[(2,4-dinitrophenyl) hydrazono] ethyl}-4-hydro- pyrazol-5-one		$C_{22}H_{19}N_7O_6$	140-142	79	Red
$[XIV]_a$	1-(4-1H-indol-3-yl-butanoyl)-3-methyl-4-[1-(phenylhydrazono) ethyl]-4-hydro-pyrazol-5-one		$C_{24}H_{25}N_5O_2$	113-115	81	Pale orange
$[XIV]_b$	1-(4-1H-indol-3-yl-butanoyl)-3-methyl-4-{1-[(4-bromophenyl) hydrazono] ethyl}-4-hydro-pyrazol-5-one		$C_{24}H_{24}BrN_5O_2$	120-122	80	Brown
$[XIV]_c$	1-(4-1H-indol-3-yl-butanoyl)-3-methyl-4-{1-[(4-nitrophenyl) hydrazono] ethyl}-4-hydro-pyrazol-5-one		$C_{24}H_{24}N_6O_4$	108-110	76	Brown
$[XIV]_d$	1-(4-1H-indol-3-yl-butanoyl)-3-methyl-4-{1-[(2,4-dinitrophenyl) hydrazono]ethyl}-4-hydro-pyrazol -5-one		$C_{24}H_{23}N_7O_6$	194-192	70	Orange

Table No.(2): Characteristic FTIR absorption bands data of new amide compounds$[V]_a$-$[VIII]_d$

Comp. No.	νN-H	νC-H arom.	νC-H alipha.	νC=O Amide	νC=C arom.	νC-S-C
$[VI]_a$	3446, 3151	3012	2920-2850	1684	1595	698
$[VI]_b$	3412, 3190	3072	2950-2837	1689	1602	684
$[VI]_c$	3400, 3200	3070	2981-2843	1685	1604	684
$[VI]_d$	3400, 3170	3050	2956-2872	1690	1593	696
$[VII]_a$	3392, 3167	3057	2924-2858	1683	1590	680
$[VII]_b$	3407, 3159	3062	2926-2845	1666	1600	694
$[VII]_c$	3398-2178	3053	2953-2843	1685	1602	698
$[VII]_d$	3400-3180	3050	2953-2854	1683	1600	685
$[VIII]_a$	3400-2209	3055	2929-2850	1681	1600	680
$[VIII]_b$	3388-3201	3057	2927-2862	1674	1602	681
$[VIII]_c$	3398-3172	3050	2981-2843	1685	1602	698
$[VIII]_d$	3400-3184	3055	2953-2854	1689	1590	690

Table No.(3): Characteristic FTIR absorption bands data of new pyrazolone compounds[XI]-[XIX]

Com. No.	νN-H	νC-H arom.	νC-H alipha.	νC=O	νC=O amide	νC=N pyrazolone	νC=C arom.	Other
$[XI]_a$	3404,3287	3057	2970-2858	1795	1670	1625	1600	____
$[XI]_b$	3400,3273	3014	2983-2864	1701	1669	1625	1600	____
$[XII]_a$	342, 3280	3057	2933-2850	1735,1995	1662	1620	1591	____
$[XII]_b$	3400,3271	3055	2981-2866	1735,1705	1684	1638	1600	____
$[XIII]_a$	3400-3200	3055	2981-2850	1700	1670	1625	1602	mono-sub.: 694,746
$[XIII]_b$	3400-3205	3053	2956-2856	1693	1662	1622	1589	p-Br: 611
$[XIII]_c$	3400-3220	3055	2954-2854	1695	1670	1625	1597	p-NO_2 :1520,1323
$[XIII]_d$	3400-3250	3090	2929-2850	1699	1675	1645	1593	p-NO_2 :1517,1319
$[XIV]_a$	3406-3200	3080	2929-2856	1690	1670	1635	1602	mono-sub.:694, 752
$[XIV]_b$	3408-3263	3055	2950-2850	1699	1680	1640	1595	p-Br: 615
$[XIV]_c$	3400-3200	3055	2927-2872	1696	1665	1625	1597	p-NO_2 :1519,1325
$[XIV]_d$	3383-3267	3072	2929-2856	1701	1647	1618	1593	p-NO_2 :1519,1309

Table No. (4) : antibacterial activity of the synthesized compounds $[V]_a$ -$[XIX]_d$

Comp. No.	E.Coli(G-)	Staphlococcus aurus (G+)	Comp. No.	E.Coli(G-)	Staphlococcus aurus (G+)
DMSO	-	-	$[VII]_d$	-	+++
$[V]_a$	-	+++	$[VIII]_a$	-	+++
$[V]_b$	-	+++	$[VIII]_b$	-	++
$[VI]_a$	++	++	$[VIII]_c$	+++	+++
$[VI]_b$	+++	+++	$[VIII]_d$	-	++
$[VI]_c$	++	+	$[XI]_a$	-	++
$[VI]_d$	+++	++	$[XI]_b$	+++	+
$[VII]_a$	+	+++	$[XII]_b$	+++	-
$[VII]_b$	++	+++	$[XIII]_b$	+++	++
$[VII]_c$	++	+++	$[XIV]_d$	+++	+++

Key to symbols: Highly active = + + +(more than)15 mm. Moderately active = + +(11-15) mm. Slightly active = + (5-10) mm . (-)Zone of inhibition.

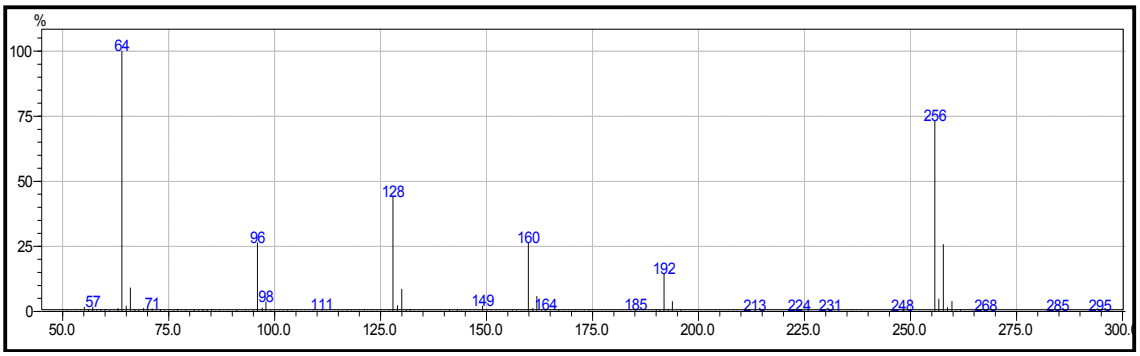


Figure No. (1) :Mass-spectrum of compound$[V]_b$

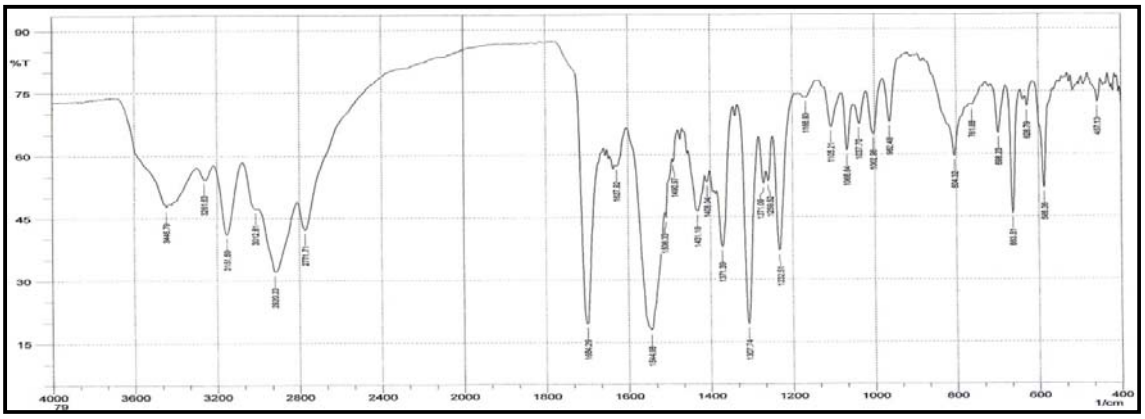


Figure No. (2): FTIR –spectrum of compound $[VI]_a$

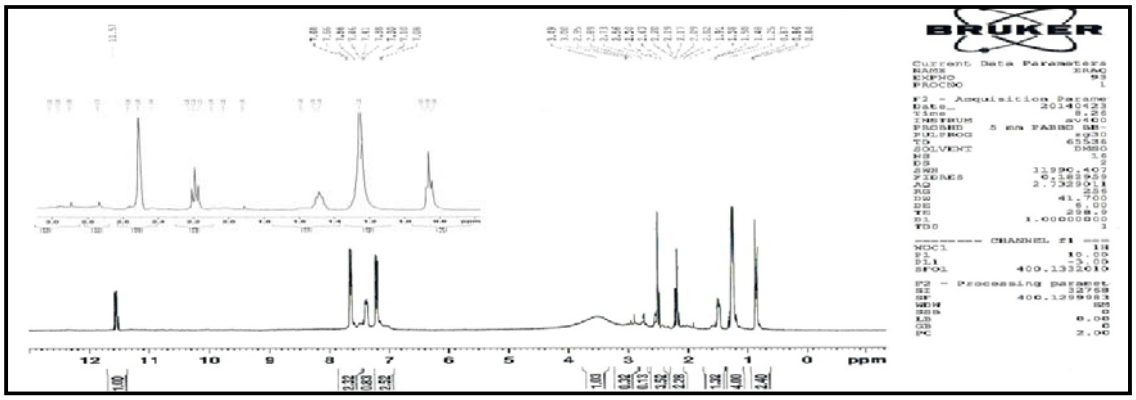


Figure No. (3) ^{1} HNMR - spectrum of compound[VIII]$_d$

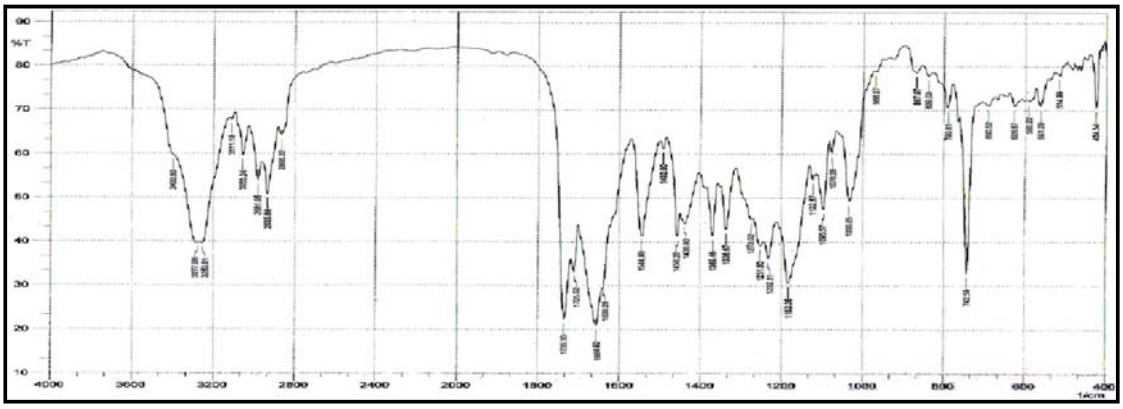


Figure No. (4): FTIR –spectrum of compound [XII]$_b$

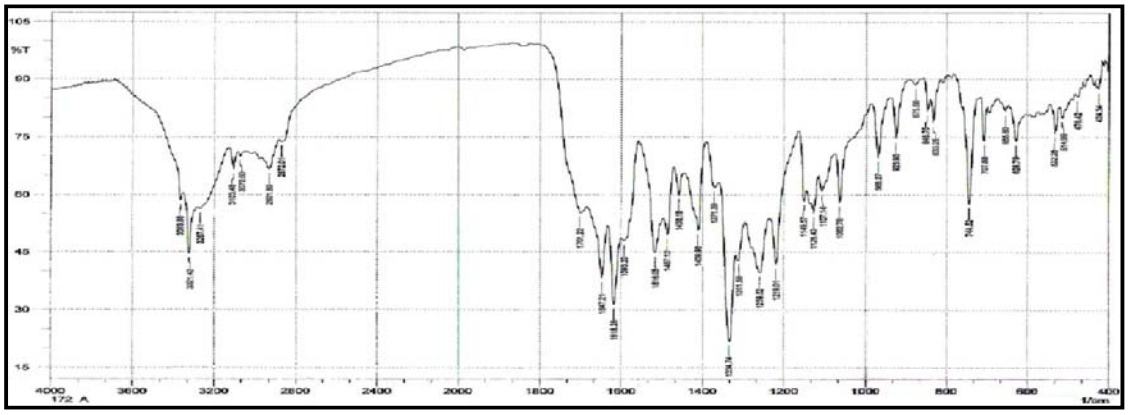


Figure No. (5): FTIR –spectrum of compound [XIV]$_d$

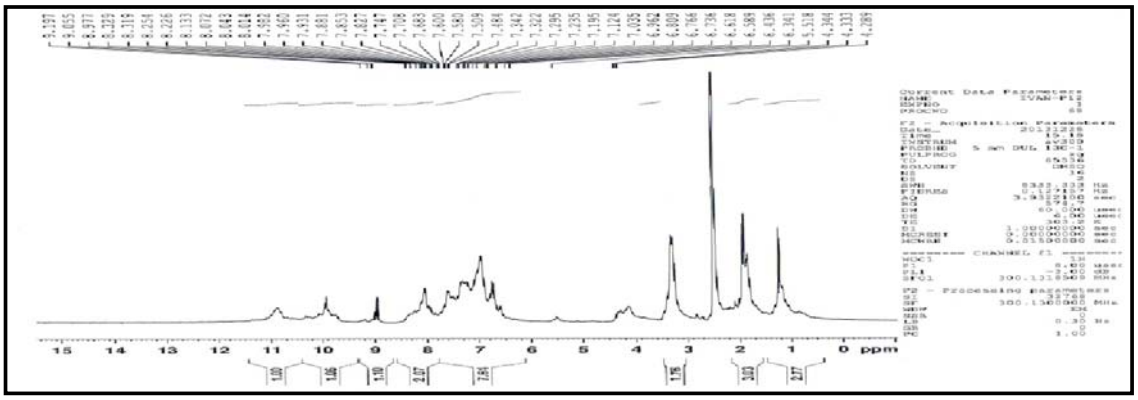


Figure No. (6) ^{1} HNMR - spectrum of compound[XIII]$_c$

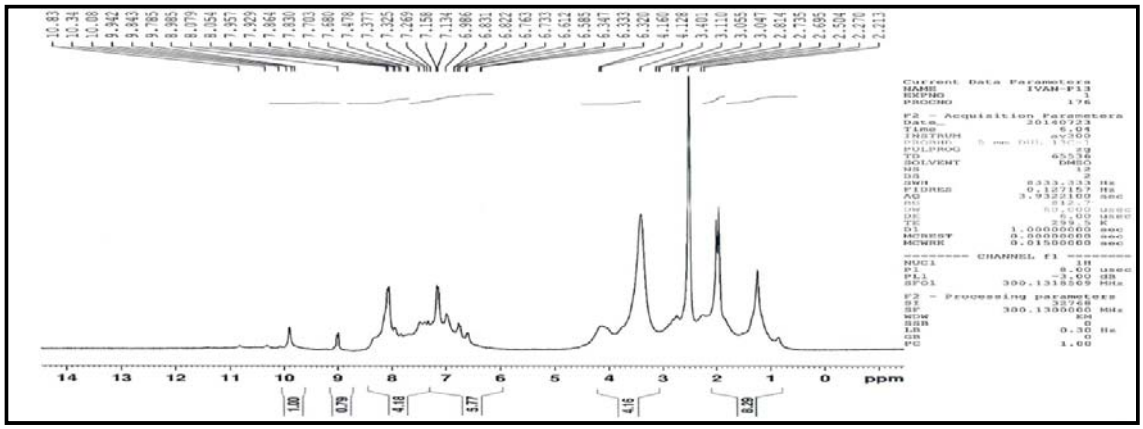


Figure No. (7) ^{1} HNMR - spectrum of compound[XIV]$_c$

مشتقات 1, 3 ,4- لبعض البايولوجي السلوك تحضير و تشخيص ودراسة ثايادايازول و البايرازولون الجديدة التي تحتوي على حلقة الاندول

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استلم البحث:12حزيران2014 ,قبل البحث في:29ايلول2014

الخلاصة

يتضمن هذا البحث تحضير مشتقات جديدة لـ3,1, 4-ثايادايازول أو البايرازولون تحتوي على حلقة الاندول إذ حضرت مركبات2-امينو- 3,1, 4-ثايادايازول [VII]a, b و[IV] من تحلق 2-(مثيل-1H-اندول-3-كاربونيل)-هايدرازين كاربوثايوامايد [III] في حامض الكبريتيك أو من تفاعل حامض 3-اندول الايثانويك أو حامض 3-اندول البيوتانويك مع الثاياسيميكاربازايد بوجود كلوريد اوكسي الفسفور ($POCl_3$) بوصفه عامل مساعد. بينما حضرت مشتقات الاميد الجديدة [VIII]- [VI] من تفاعل الأمينات الاروماتية المحضرة [V]a,b- [IV] مع كلوريدات الحامض الكاربوكسيلي المختلفة بوجود البردين. كما تضمن البحث تحضير مشتقي البايرازول [XI]a, b من تفاعل مشتقي الهادرازايد [X]a أو [X]b مع اثيل اسيتواستيت باستعمال الايثانول المطلق مذيبا. ومن ثم تم إدخال مجموعة الاسيتايل على حلقة البايرازول في الموقع-4 عن طريق التفاعل مع كلوريد الاسيتايل في وسط قاعدي. أخيرا حضرت مشتقات والهايدرازون [XIII]a-h و [XIV]a-d من تفاعل مركبات البايرازولون [XII]a, b مع هايدرازينات اروماتية مختلفة باستعمال الايثانول المطلق مذيبا.
شخصت جميع المركبات المحضرة في هذ ا البحث من خلال قياس درجات أنصهارها فضلا عن الطرائق الطيفية المتمثلة بطيف الأشعة تحت الحمراء , وطيف الرنين النووي المغناطيسي البروتوني , وطيف الماس (للبعض منها) كما درست الفعالية البايولوجية لمعظم المركبات المحضرة ضد أنواع من البكتريا .هي كرام (+) وكرام(-).

الكلمات المفتاحية : 3,1, 4-ثايادايازول، بايرازول, بايرازولون، اندول و هايدرازون.