Synthesis and characterization of some new triazine-1-one derivatives with studying its biological activity

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Abstract:

This work includes synthesis a series of some new derivatives of triazine from reaction between the sulfur amino acid (L-cysteine) and different aldehydes in dry ethanol to obtain thiazolidine ring as diastereo isomers (Cis and Trans)- 2- alkylthiazolidine-4- carboxylic acids (**1**).

The thiazolidine derivatives (1) suffered esterfication reaction of carboxylic acid in presence of drops of concentrated sulfuric acid as a catalyst to give the esters **:**
ethyl 2- alkylthiazolidine -4 - carboxylates (**2**), which reacted with hydrazine hydrate in (addition- elimination) reaction to give acid hydrazides **:** 2-alkylthiazolidine-4-carbohydrazides (**3**). Acid hydrazides (3) were reacted with acetyl chloride by (NH) acetylation reaction to form**:** 3- acetyl-2-alkylthiazolidine -4 - carbohydrazides (**4**).

The last step includes cyclization reaction of compound (4) to yeild triazine-1-one derivatives (**5**), which undergo tautomerization phenomena**:** triazine -1- ol (6)**.** Triazine derivatives were expected to be biologically active.

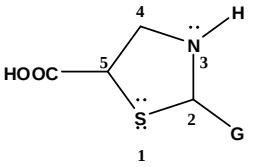
The prepared compounds were characterized by spectral methods (FT.IR, H^1NMR, and UV. -Vis.) , melting points and measurement of some of its physical properties ; and the reaction was followed by TLC. Some of these compounds were tested against becteria , Escherchia coli and Staphococcus aureus.

Key word: Heterocyclic compounds, Thiazolidine, Triazine ring, Sulfur amino acids **.**

Introduction:

Thiazolidine or tetrahydrothiazole is α- amino acid derivatives having interesting biological properties, especially with respect to their possible anti proliferative action ,certain cancer cells have an absolute requirement for cystein [1,2]. They have played a pivotal role in organic, bio-organic, medicinal, and natural products chemistry since most of the antimicrobial substance such as penicillins,cephalosporins,narcodicins, thienamicyn have been prepared from thiazolidines [3-6].

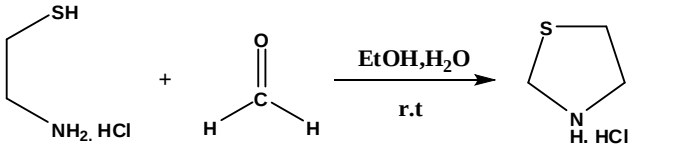
2-Substituted thiazolidine -4- carboxylic acids are used as hepatoprotective drugs and are known to be excellent substrate for antibiotics[7-11].



G = group

2-Substituted thiazolidine -4- carboxylic acids

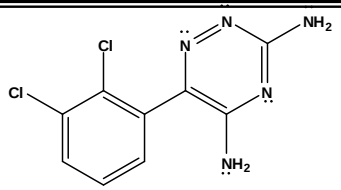
The parent compound ,thiazolidine (1) is obtained in very high yield as the hydrochloride, by the reaction of cysteamine hydrochloride with aqueous formaldehyde at ambient temperature [12-17].



cysteamine hydrochloride **formaldehyde** **thiazolidine hydrochloride**

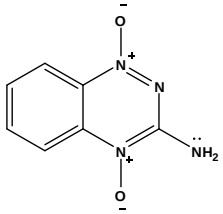
(1)

The biological activities of 1,2,4-triazines have attracted the attention of many chemists because numerous 1,2,4-triazines are biologically active [18-23] ,they are used in medicine, especially as anti AIDS agents, anticancer agents [24,25], drugs (e.g., the effective anticonvulsant lamotrigine and anticancer drug tirapazamine)[24,25], anti tubercular agents [26,27], cathepsin K inhibitors [28], and for their anti-anxiety and anti-inflammatory activities [29,30], as well as in agriculture in various herbicides [31-34], luminescent materials, dyes, specific ligands for complexation with metals, and other compounds based on 1,2,4-triazines[34,35].



6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine

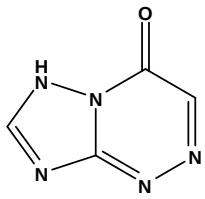
(LAMOTRIGINE DRUG)



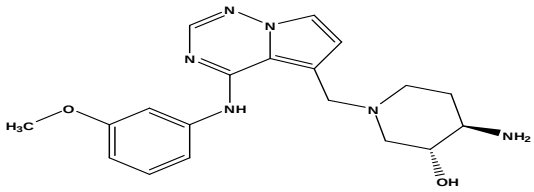
3-aminobenzo[*e*][1,2,4]triazine 1,4-dioxide

(TIRAPAZAMINE DRUG)

Fused 1,2,4-triazine systems have also attracted considerable interest in their biological activity., For example 1,2,4-triazolo[5,1-c][1,2,4]triazinones and their sodium salts, which express the high activity against different kinds of viruses, including influenza and bird flu (type H5N1) [36-38], and several pyrrolotriazine derivatives were identified as potentially active anticancer agents acting on vascular endothelial growth factor receptor (VEGFR) tyrosine kinases [39].

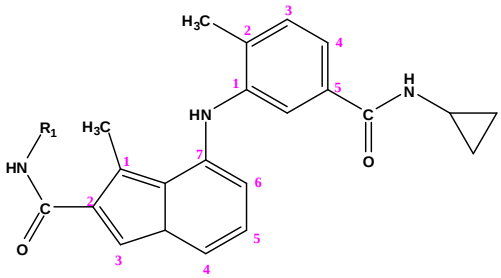


1,2,4-triazolo[5,1-c][1,2,4]triazinone



(3*R*,4*R*)-4-amino-1-((4-(3-methoxyphenylamino)pyrrolo[1,2-*f*][1,2,4]triazin-5-yl)methyl)piperidin-3-ol

(pyrrolotriazine derivative)



where R1 is lower alkyl or aryl,

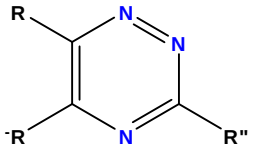
7-(5-(cyclopropylcarbamoyl)-2-methylphenylamino)-*N* -alkyl(or aryl),1-methyl-3-*H* -indene-2-carboxamide

(pyrrolotriazine derivative such as amide II)

On the other hand, thiophene -containing compounds are also well known to exhibit various biological effects as BACE1 inhibitors [40], anti-HIV PR inhibitors [41], anti-breast cancer [42], anti-inflammatory [43-45], anti-protozoal [46] or anti- tumor agents [47,48], and anti- tubercular with anti-mycobacterial activity [49].

In light of this we planned to synthesize a series of new 1,2,4-triazines carrying thiophene moieties in the hope of obtaining new products of superior biological activity such as anticancer activity[48, 49].

Orientation of heterocyclization reactions of functionalized 1,2,4-triazenes were studied by effect of substituents in 1,2,4- triazene moieties, type of the solvent used in the reaction and the temperature effect.Also, it was found that cyclization process depended mainly on the chemoselective and regioselectivity states of the parent substrate as well as preferring cite of ring closure[50].



Experimental;

A- Tehniques :

1- Melting points were measured by digital MP 161 MSRS melting point apparatus and
were uncorrected.

2- FT.IR spectra were recorded by SHIMADZU FT.IR 8300 spectrophotometer in the range (4000-400) cm^{-1} using KBr disk.

3- ^{1}HNMR spectra were recorded by BRUKER-400 MHz operating at 300 MHz with tetra methyl silane as internal standard in DMSO-d^{6} as a solvent at Chemistry Department , AL- Bayt University, Jordan.

4- UV- Vis. spectra were recorded by SHIMADZU UV spectrophotometer - 1800 using DMSO as solvent.

5- Thin Lyer Chromatography (T.L.C.) was carried out using Fertigfollen precoated sheets type Polygram silg, and the plates were developed with iodine vapor.

6- The biological activity was performed by environmental laboratory, Baghdad University.

B- Materials :

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

Synthesis of : 2- alkylthiazolidine-4- carboxylic acids (1) [15,16].

A solution of aldehyde (0.01 mol.) in absolute ethanol (15 mL) was added at $0C^{o}$ to a stirred solution of L-cysteine hydrochloride (0.01 mol.,1.575 gm) and potassium acetate (0.01 mol.,98 gm) in absolute ethanol (20 mL). After stirring for (5 hrs.) at $0C^{0}$,the solvent was evaporated to crystalline residue, the crystals were filtered, washed and dried to gave bright yellow- brown crystals; Re-crystallized from ethanol.

Synthesis of : ethyl 2- alkylthiazolidine - 4 - carboxylates (2) [51].

2- alkylthiazolidine-4- carboxylic acid (1) (0.005 mol.) was refluxed with (15 mL) of absolute ethanol and few drops of conc. H_2SO4 (sulfuric acid) for (5 hrs.). The mixture was left to cool and filtered to give crystals., Re-crystallized from ethanol.

Synthesis of : 2- alkylthiazolidine -4- carbohydrazides (3) [52].

To a solution of (0.01 mol.) of ethyl 2- alkylthiazolidine- 4- carboxylate (2) in (15 mL) absolute ethanol was added (0.0 1mol, 0.5 gm, 0.485 mL)of hydrazine hydrate (90%).The mixture was refluxed under anhydrous conditions for (4 hrs.) ; Then the mixture was allowed to cool and crystals were filtered, washed and dried., Re-crystallized from ethanol.

Synthesis of : 3- acetyl-2-alkylthiazolidine-4 -carbohydrazides (4) [53].

To a solution of (0.01 mol.) of 2- alkylthiazolidine -4- carbohydrazide (3) in (15 mL) of dry benzene was added drop wise a solution of (0.01 mol, 0.785 gm, 0.711 mL) of acetyl chloride in (10 mL) dry benzene., The mixture was stirred for (1 hr), then refluxed for (2 hrs.)**.** The mixture was allowed to cool and crystals were filtered , washed and dried ., Re-crystallized from ethanol.

Synthesis of : triazin -1-one (5) [50].

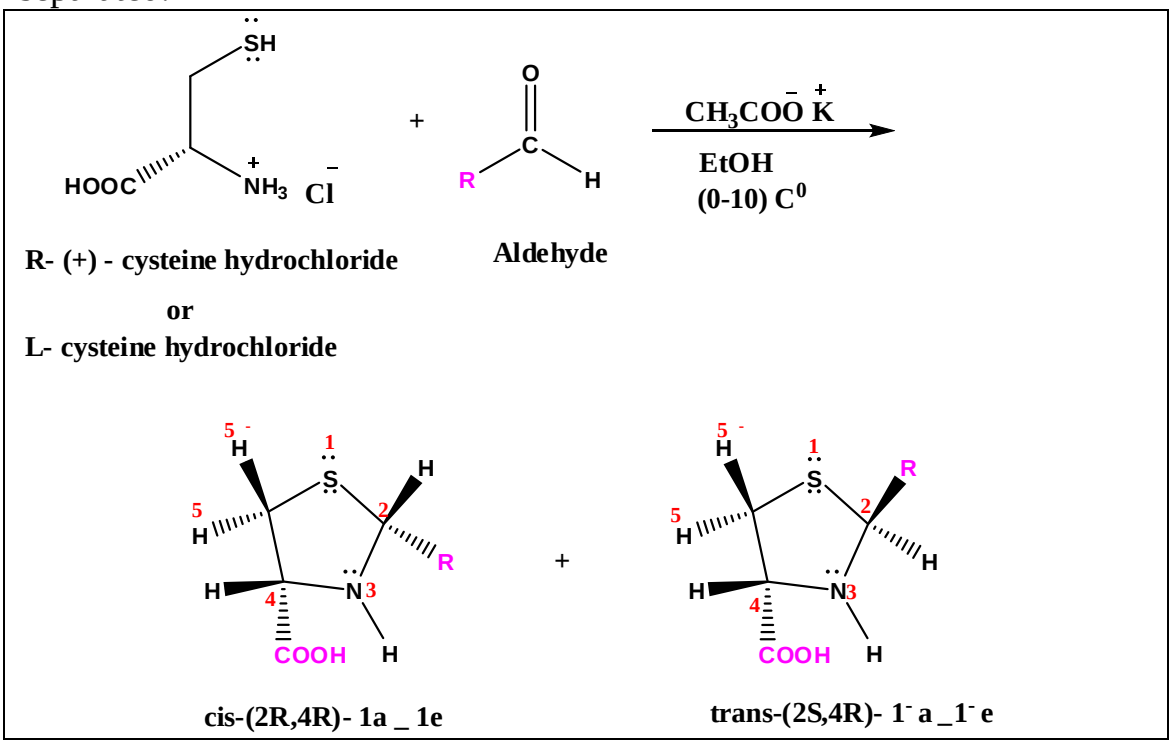
The compound 3- acetyl-2-alkylthiazolidine - 4 - carbohydrazide (4) (0.005 mol) in (15 mL) absolute ethanol was refluxed with stirring for (7-8 hrs.) in intermolecular cyclization reaction, cooled**.** The precipitate was filtered off, dried and re-crystallized from ethanol.

Results and Discussion:

Cysteine provides both nitrogen and sulfur atoms as important building block for heterocyclic compounds such as thiazolidine and its derivatives. The chirality of this amino acid offers the advantage of asymmetric introduction into heterocyclic systems [54].

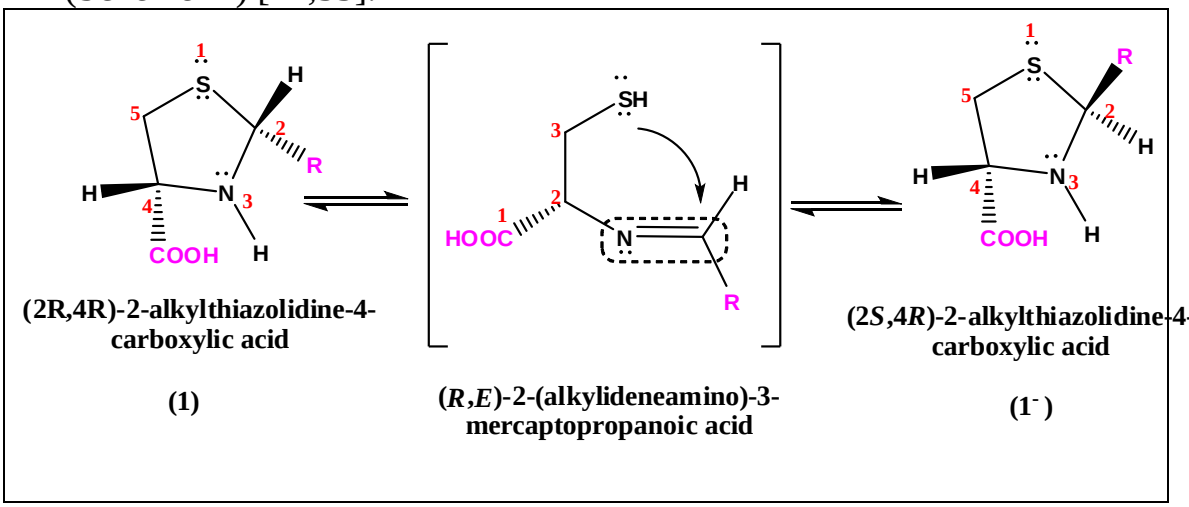
The most widely used method for the preparation of thiazolidine and its derivatives involves the reaction of carbonyl compounds with α-aminoacids [7,8]. Aldehydes has been used to react with L - or (R) - cysteine hydrochloride under slightly basic conditions [15,16]. This condensation reaction affored compound (1) as a mixture of diastereomers,

cis-(2R,4R)-1 and trans-(2S,4R)-1^{-} (Scheme -1) which could not be separated.



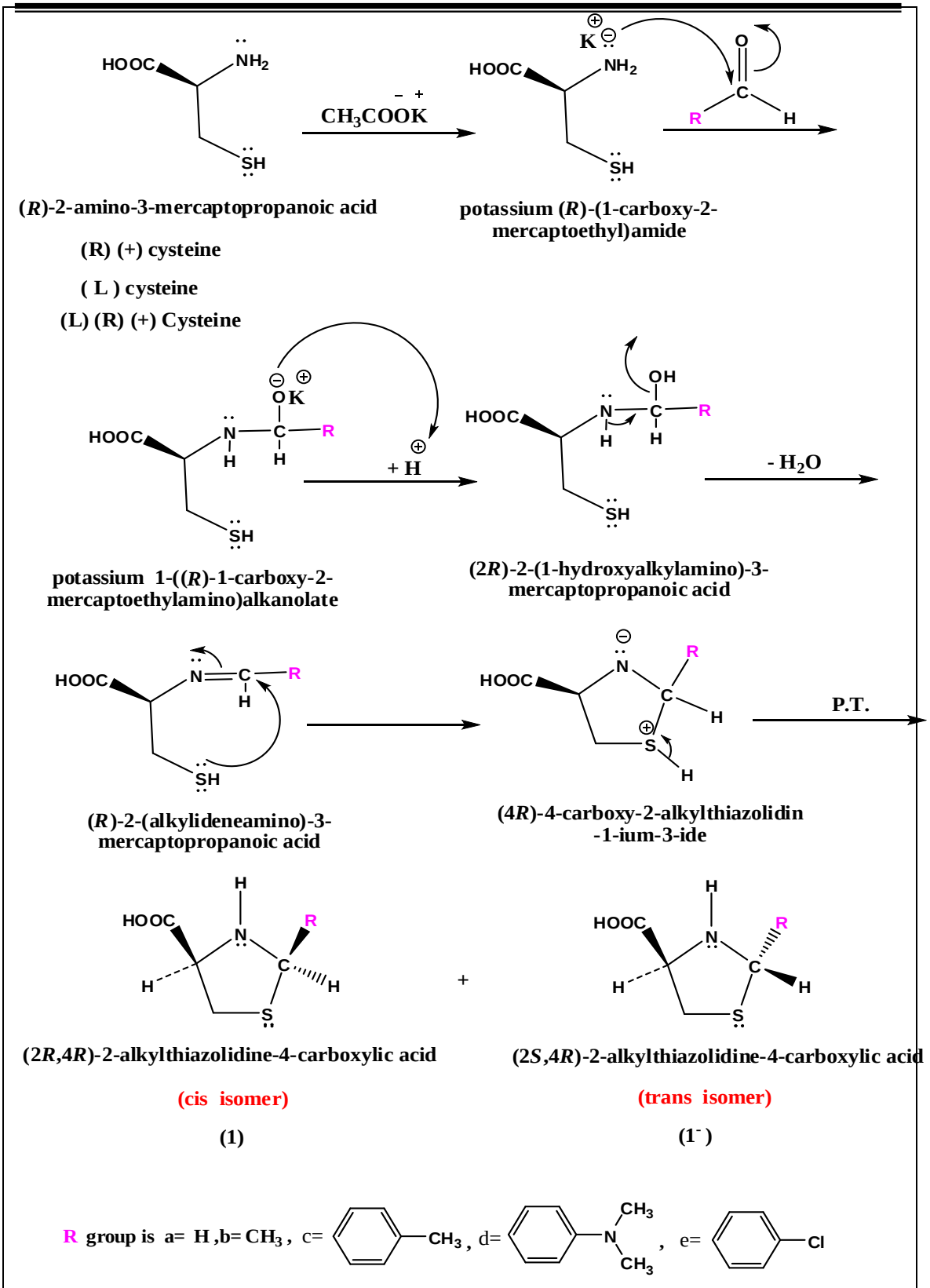
Scheme -1

An equilibrium resulting from epimerization at C(2) occurs between 1 and 1^{-} (Scheme -2) [17,55].



Scheme -2

The suggested mechanism of the reaction is shown in scheme below:


HOOC
NH2
SH
CH3COOK
K
O
R
H
OK
+ H
OH
- H2O
P.T.
S
(R)-2-amino-3-mercaptopropanoic acid
potassium (R)-(1-carboxy-2-mercaptoethyl)amide
(R) (+) cysteine
(L) cysteine
(L) (R) (+) Cysteine
potassium 1-((R)-1-carboxy-2-mercaptoethylamino)alkanolate
(2R)-2-(1-hydroxyalkylamino)-3-mercaptopropanoic acid
(R)-2-(alkylideneamino)-3-mercaptopropanoic acid
(4R)-4-carboxy-2-alkylthiazolidin-1-ium-3-ide
(2R,4R)-2-alkylthiazolidine-4-carboxylic acid
(cis isomer)
(1)
(2S,4R)-2-alkylthiazolidine-4-carboxylic acid
(trans isomer)
(1-)
R group is a= H ,b= CH3 , c=
CH3 , d=
e=
Cl

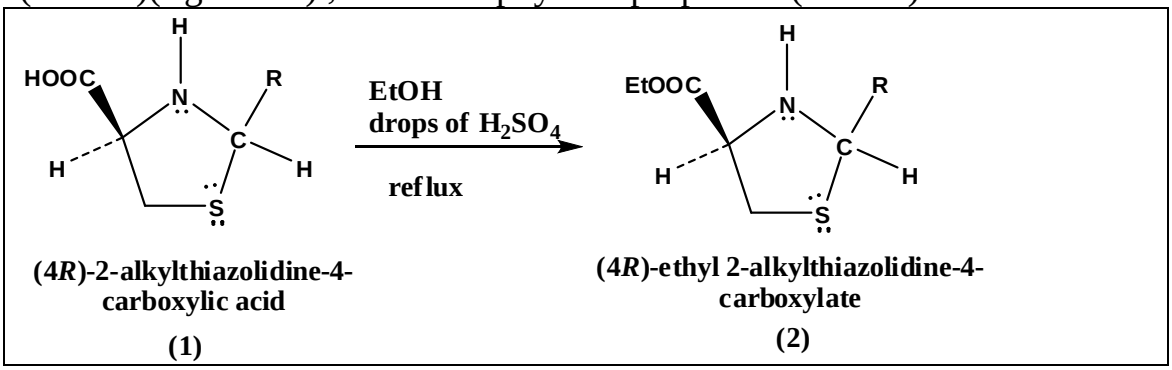
Scheme -3

The reaction was followed by TLC., and the compounds were characterized through FT.IR spectra, and other physical properties (table-2).

The FT.IR spectra of compounds (1) , showed disappearances of stretching bands of (NH_2) , (SH), and (C=O) of aldehyde, and appearance of stretching band of (NH) which interference with (OH) of carboxylic acid at (3372-3341) cm^{-1} , (table -3) (figs.1-5) [56].

Thiazolidine-4-carboxylic acid derivatives (1) were converted to esters (2) by reaction with absolute ethanol in presence of H_2SO_4 drops by (esterfication reaction)[51,57]

The FT.IR spectra of compounds (2) showed disappearance of (OH) bands , the products were characterized by FT.IR spectroscopy (table-4)(figs. 6-10) , and other physical properties (table-2).



(4*R*)-2-alkylthiazolidine-4-carboxylic acid

(1)

(4*R*)-ethyl 2-alkylthiazolidine-4-carboxylate

(2)

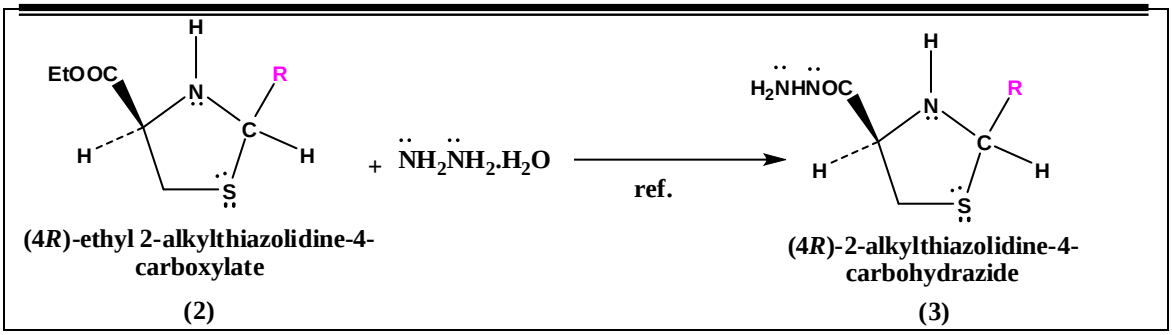
Scheme -4

The mechanism of this condensation is known and is acid catalyzed [58,59].

The reaction of hydrazine hydrate with ester is one of the most common reaction to synthesize the acid hydrazide , it is a tetrahedral nucleophilic substitution reaction[60,61].

FT.IR spectra of the hydrazide derivative compounds (3) showed the appearance of the characteristic absorption bands in the region (3482-3220) cm^{-1} due to the asymmetric and symmetric stretching vibration of the (-HN-NH_2) group , and disappearance of absorption bands at (1770-1716) cm^{-1} due to the stretching vibration of carbonyl group of ester , while showed appearance of absorption band at (1683-1674) cm^{-1} of the compound (3) due to stretching vibration of amide II band [56,61], (table-5) (figs.11-15). The ^{1}HNMR spectrum of compound [3c], showed δ (6.52-7.14) ppm due to aromatic protons,δ (2.54 , and 9.27) ppm due to (N-H amine) protons, δ (4.64) ppm due to(NH_2) protons , δ (3.32) ppm due to methyl group (CH_3) protons, δ (3.54) ppm due to methylene group (CH_2) protons, δ (4.13 , and 5.27) ppm due to methine group (CH) protons (fig.26).

The physical properties of these compounds are shown in (table-2).



(4*R*)-ethyl 2-alkylthiazolidine-4-carboxylate

(2)

(4*R*)-2-alkylthiazolidine-4-carbohydrazide

(3)

Scheme -5

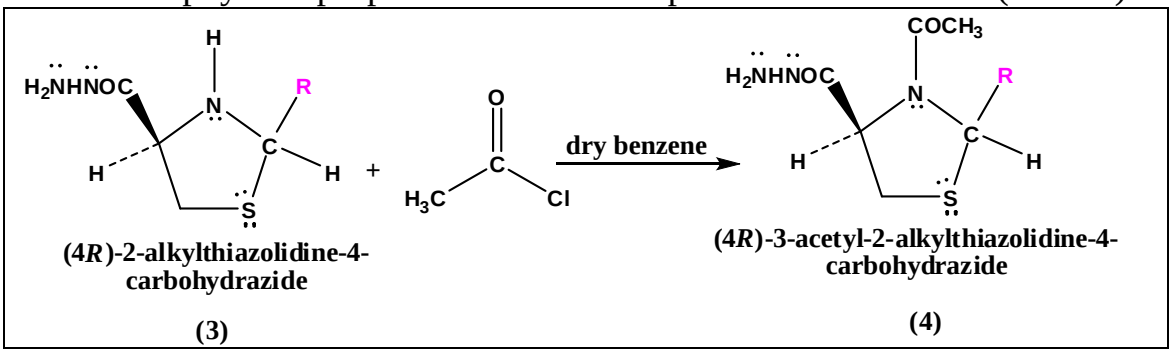
The mechanism of this reaction is known [61].

The N-acetylation of compounds (3) with acetyl chloride in refluxing dry benzene gives tertiary amide (4) , it is an electrophilic substitution reaction[62,63].

FT.IR of compound (4) showed the appearance of the characteristic absorption bands in the region (1681-1625) cm^{-1} due to the stretching vibration of the (C=O) group , of tertiary amide[56], (table-6) (figs.16-20).

The ^{1}HNMR spectrum of compound [4e], showed δ (7.27-7.33) ppm due to aromatic protons, δ (3.92) ppm due to amine group (NH_2) protons, δ (8.25) ppm due to sec. amide (NH) protons , δ (1.36) ppm due to methyl group (CH_3) protons, δ (2.5) ppm due to methylene group (CH_2) protons, δ (4.43 , and 4.39) ppm due to methine group (CH) protons (fig.27).

The physical properties of these compounds are shown in (table-2).



(4*R*)-2-alkylthiazolidine-4-carbohydrazide

(3)

(4*R*)-3-acetyl-2-alkylthiazolidine-4-carbohydrazide

(4)

Scheme -6

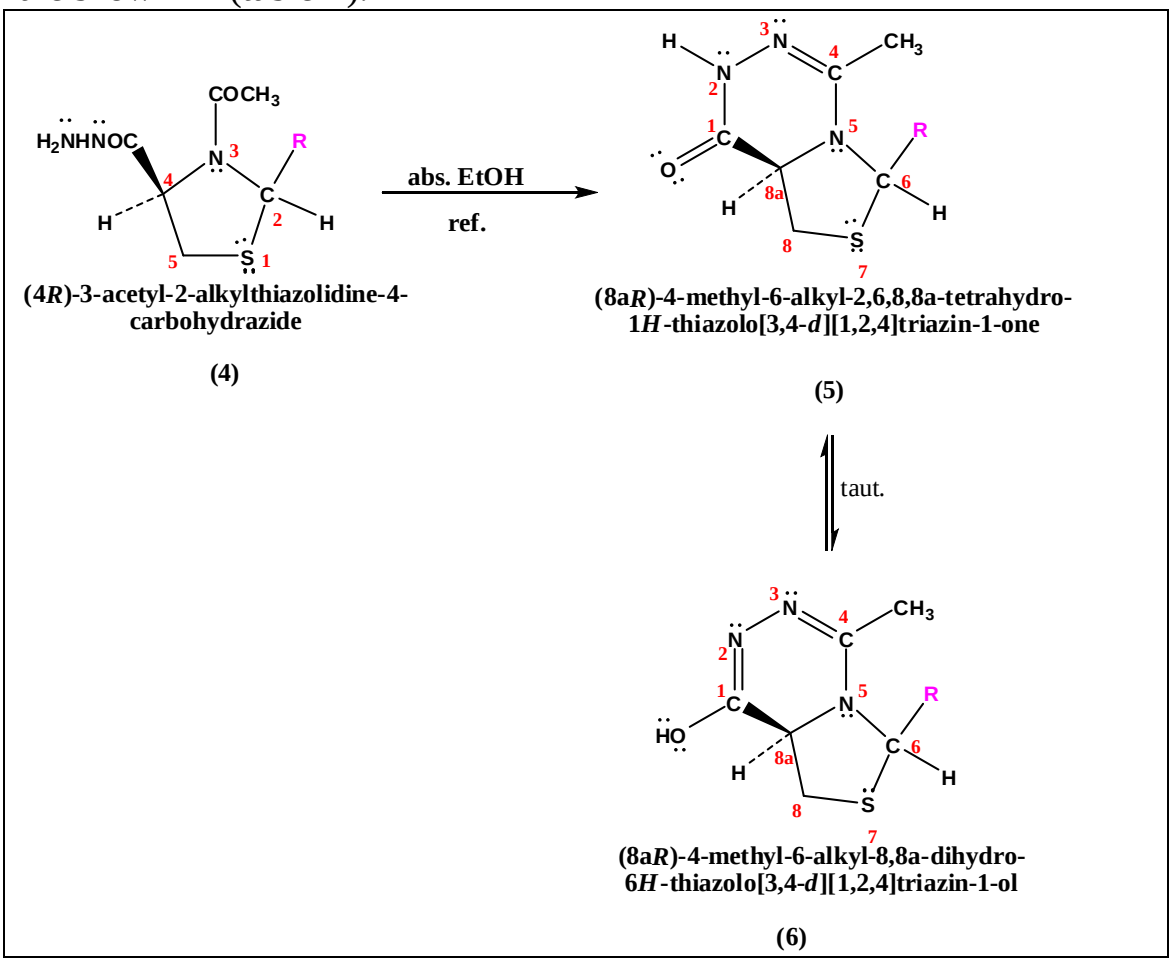
The mechanism of this acetylation reaction is known [62].

Compounds (4) in absolute ethanol was stirring for (7-8 hrs.) under refluxing condition affected on intermolecular cyclization through S_N2 mechanism giving the desired triazine derivative compounds (5) which suffered tautomerization phenomena(6).

The FT.IR spectra of compounds (5) , showed disappearances of stretching bands of (NH_2) , and (C=O) of tertiary amide, and appearance of the characteristic absorption bands in the region (1721-1710) cm^{-1} due to the stretching vibration of the (C=O) group , of six membered cyclic

ketone , and endo (C=N) group at (1654-1609) cm^{-1}., [56], (table-7) (figs. 21-25).

The ^{1}HNMR spectrum of compound [5e], showed δ (7.74-8.58) ppm due to aromatic protons, δ (10.45) ppm due to (NH) proton in azine cycle, δ (2.5) ppm due to methyl group (CH_3) protons, δ (3.33) ppm due to methylene group (CH_2) protons, δ (4.42 , and 5.54) ppm due to methine group (CH) protons, (fig.28). The physical properties of these compounds are shown in (table-2).



(4*R*)-3-acetyl-2-alkylthiazolidine-4-carbohydrazide

(4)

(8a*R*)-4-methyl-6-alkyl-2,6,8,8a-tetrahydro-1*H*-thiazolo[3,4-*d*][1,2,4]triazin-1-one

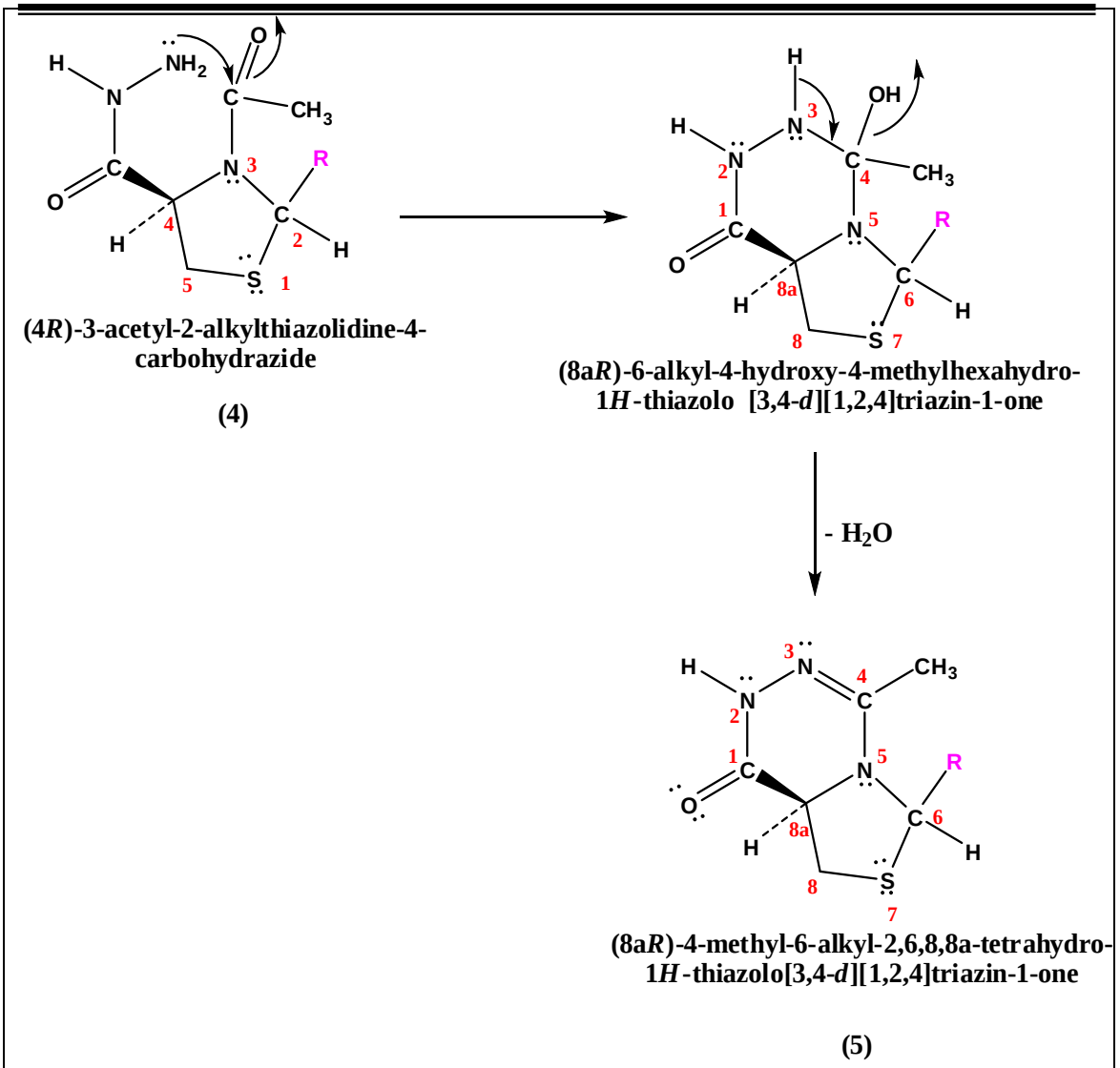
(5)

(8a*R*)-4-methyl-6-alkyl-8,8a-dihydro-6*H*-thiazolo[3,4-*d*][1,2,4]triazin-1-ol

(6)

Scheme -7

The mechanism of cyclization reaction was shown in scheme (8) below:



Scheme -8

UV-Vis. absorption peaks values for compounds (1c, 2e, 3a, 4b, 5d) were shown in (table-8).

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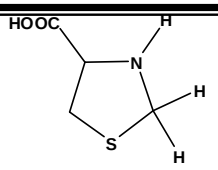
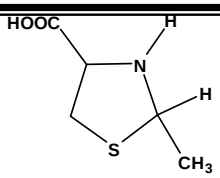
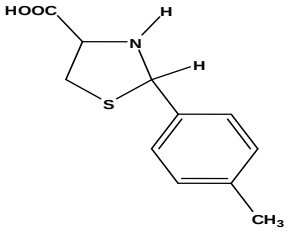
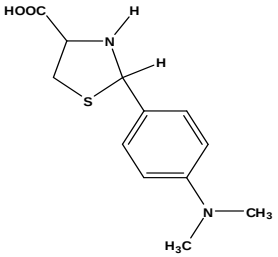
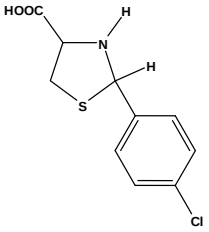
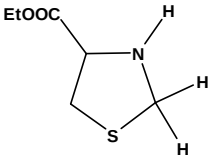
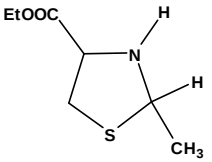
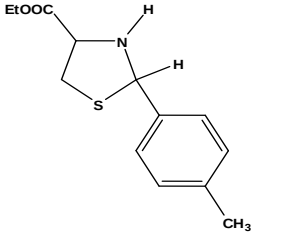
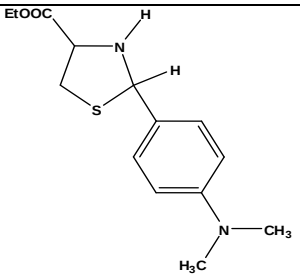
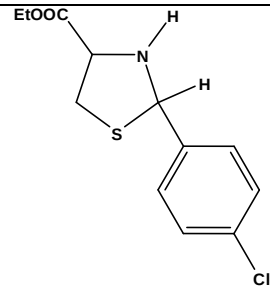
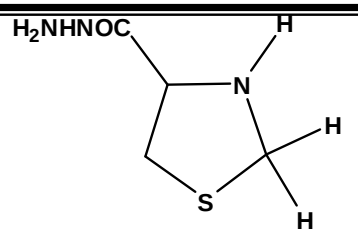
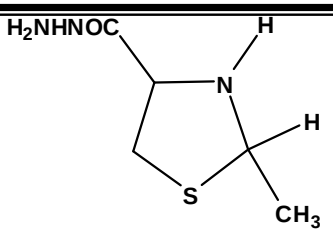
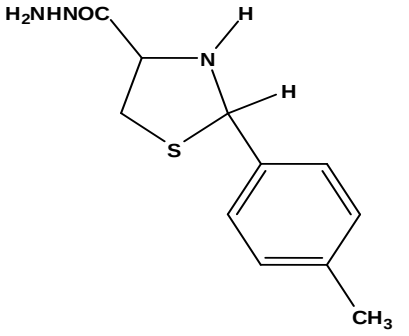
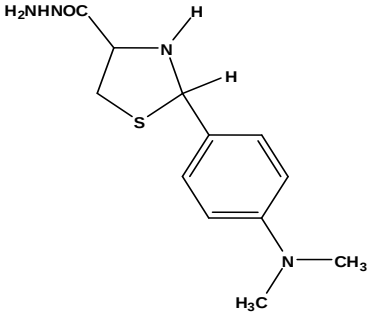
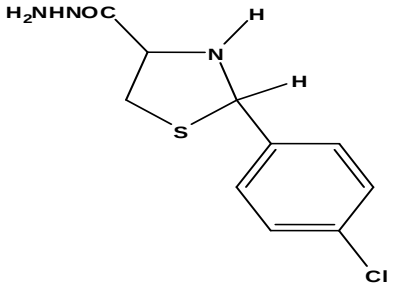
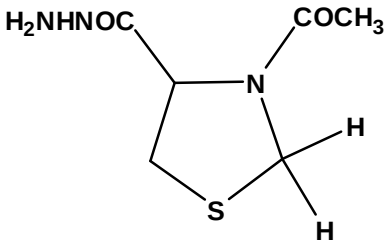
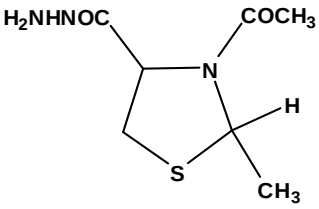
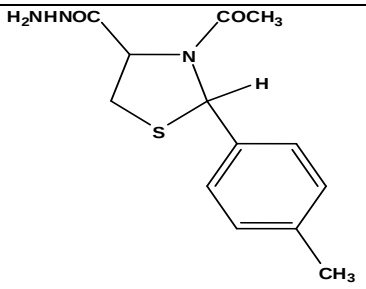
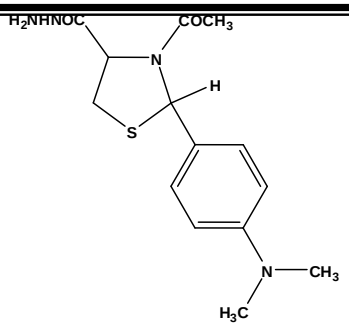
Table no. (1): Structure and nomenclature of the prepared compounds.

 **thiazolidine-4-carboxylic acid** 1a	 **2-methylthiazolidine-4-carboxylic acid** 1b
 **2-*p*-tolylthiazolidine-4-carboxylic acid** 1c	 **2-(4-(dimethylamino)phenyl)thiazolidine-4-carboxylic acid** 1d
 **2-(4-chlorophenyl)thiazolidine-4-carboxylic acid** 1e	 **ethyl thiazolidine-4-carboxylate** 2a
 **ethyl 2-methylthiazolidine-4-carboxylate** 2b	 **ethyl 2-*p*-tolylthiazolidine-4-carboxylate** 2c
 **ethyl 2-(4-(dimethylamino)phenyl)thiazolidine-4-carboxylate** 2d	 **ethyl 2-(4-chlorophenyl)thiazolidine-4-carboxylate** 2e

 **thiazolidine-4-carbohydrazide** 3a	 **2-methylthiazolidine-4-carbohydrazide** 3b
 **2-*p*-tolylthiazolidine-4-carbohydrazide** 3c	 **2-(4-(dimethylamino)phenyl)thiazolidine-4-carbohydrazide** 3d
 **2-(4-chlorophenyl)thiazolidine-4-carbohydrazide** 3e	 **3-acetylthiazolidine-4-carbohydrazide** 4a
 **3-acetyl-2-methylthiazolidine-4-carbohydrazide** 4b	 **3-acetyl-2-*p*-tolylthiazolidine-4-carbohydrazide** 4c



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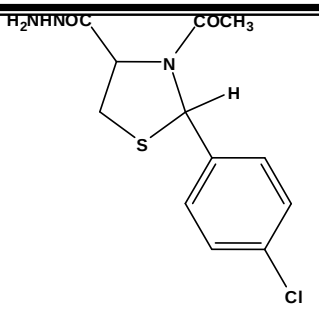
4d



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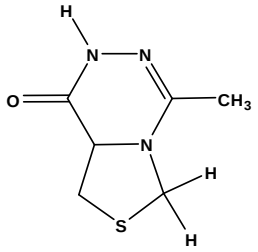

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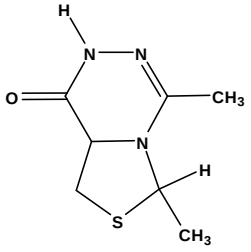
5a



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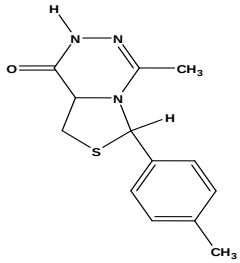
5b



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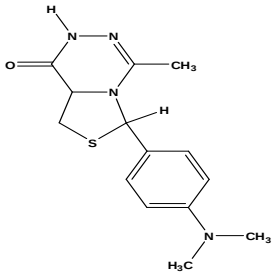
5c



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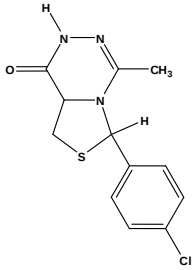
5d



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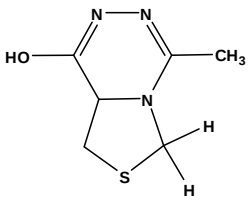
5e



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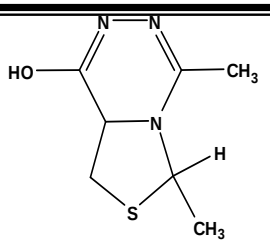
6a



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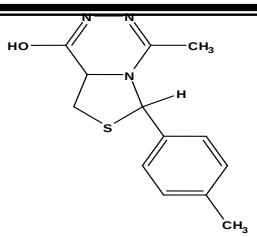
6b



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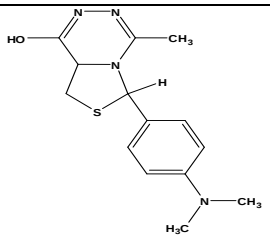
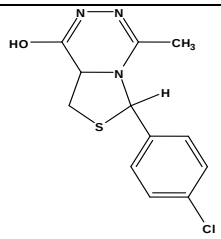
6c



6-(4-(dimethylamino)phenyl)-4-methyl-8,8a-dihydro-6*H*-thiazolo[3,4-*d*][1,2,4]triazin-1-ol

6d



6-(4-chlorophenyl)-4-methyl-8,8a-dihydro-6*H*-thiazolo[3,4-*d*][1,2,4]triazin-1-ol 6

e

Table no. (2): Physical properties of the prepared compounds.

Comp. no.	Molecular Formula	Molecular Weight (gm/mol)	Yield %	M.P. C^0	Color
1a	$C_4H_7NO_2S$	133	92	197-199	Pale yellow
1b	$C_5H_9NO_2S$	147	85	220- 223	Light yellow
1c	$C_{11}H_{13}NO_2S$	223	80	231-234	Light yellow
1d	$C_{12}H_{16}N_2O_2S$	252	86	254-255	Brown
1e	$C_{10}H_{10}NO_2SCl$	243	90	225-227	Light brown
2a	$C_6H_{11}NO_2S$	161	85	163-166	Yellow
2b	$C_7H_{13}NO_2S$	175	79	177-179	Yellow
2c	$C_{13}H_{17}NO_2S$	251	69	193-195	Light brown
2d	$C_{14}H_{20}N_2O_2S$	280	77	127-129	Brown
2e	$C_{12}H_{14}NO_2SCl$	271	76	146-148	Yellowish brown
3a	$C_4H_9N_3OS$	147	75	151-154	Yellow
3b	$C_5H_{11}N_3OS$	161	75	155-157	Dark yellow
3c	$C_{11}H_{15}N_3OS$	237	61	169-171	Dark brown
3d	$C_{12}H_{18}N_4OS$	266	67	163-165	Reddish brown
3e	$C_{10}H_{12}N_3OSCl$	257	59	171-173	Greenish brown
4a	$C_6H_{11}N_3O_2S$	189	63	143-145	Dark yellow
4b	$C_7H_{13}N_3O_2S$	203	65	165-168	Dark yellow
4c	$C_{13}H_{17}N_3O_2S$	279	57	219-221	Brown
4d	$C_{14}H_{20}N_4O_2S$	308	69	231-233	Brown
4e	$C_{12}H_{14}N_3O_2SCl$	299	55	227-230	Brown
5a	$C_6H_9N_3OS$	171	57	233-235	Brown
5b	$C_7H_{11}N_3OS$	185	54	228-231	Brown
5c	$C_{13}H_{15}N_3OS$	261	59	203-205	Light brown
5d	$C_{14}H_{18}N_4OS$	290	63	290-292	Dark brown
5e	$C_{12}H_{12}N_3OSCl$	281	61	267-269	Dark brown

Table no. (3): FT.IR spectral data of the prepared compounds (1a - e).

	CH υ	CH υ	C=O υ	OH υ	C=C υ	

Comp.	aro.	ali.	acid	acid	aro.	Others
1a	-	2926	1733	3342	-	C-O 1216 C-S 715 C-N 1266 N-H bend. 1585
1b	-	2970	1750	3344	-	C-O 1224 C-S 715 C-N 1283 N-H bend. 1611
1c	3053	2922	1795	3372	1535	C-O 1307 C-S 720 C-N 1358 N-H bend. 1634
1d	3070	2926	1764	3341	1523	C-O 1324 C-S 725 C-N 1365 N-H bend. 1640
1e	3059	2931	1776	3346	1554	C-O 1364 C-S 730 C-N 1343 N-H bend. 1610 C-Cl 764

Table no. (4): FT.IR spectral data of the prepared compounds (2a - e).

Comp.	CH^{υ} aro.	CH^{υ} ali.	$C{=}O^{\upsilon}$ ester	NH^{υ}	$C{=}C^{\upsilon}$ aro.	Others
2a	-	2942	1716	3322	-	C-O 1033 C-S 769 C-N 1176 N-H bend. 1589
2b	-	2957	1749	3365	-	C-O 1097 C-S 703 C-N 1185 N-H bend. 1621
2c	3084	2924	1751	3319	1575	C-O 1123 C-S 721 C-N 1251 N-H bend. 1645
2d	3053	2992	1765	3354	1555	C-O 1155 C-S 726 C-N 1354 N-H bend. 1669
2e	3051	2962	1770	3351	1558	C-O 1211 C-S 733 C-N 1373 N-H bend. 1607 C-Cl 755

Table no. (5): FT.IR spectral data of the prepared compounds (3a - e).

Comp.	CH$^{\upsilon}$ aro.	CH$^{\upsilon}$ ali.	C=O$^{\upsilon}$ amide II	NH_2 , N-H$^{\upsilon}$	C=C$^{\upsilon}$ aro.	Others
3a	-	2922	1683	3447- 3354	-	C-S 622 C-N 1234 N-H bend. 1591
3b	-	2927	1674	3446- 3350	-	C-S 619 C-N 1221 N-H bend. 1585
3c	3055	2918	1681	3448- 3220	1587	C-S 634 C-N 1257 N-H bend. 1633
3d	3054	2952	1676	3469- 3236	1571	C-S 716 C-N 1255 N-H bend. 1656
3e	3082	2968	1681	3482- 3219	1587	C-S 719 C-N 1265 N-H bend. 1622 C-Cl 751

Table no. (6): FT.IR spectral data of the prepared compounds (4a - e).

Comp.	CH$^{\upsilon}$ aro.	CH$^{\upsilon}$ ali.	C=O$^{\upsilon}$ tert. amide	C=O$^{\upsilon}$ sec. amide	NH_2 , N-H$^{\upsilon}$	C=C$^{\upsilon}$ aro.	Others
4a	-	2846	1654	1724	3442-3255	-	C-S 645 C-N 1213 N-H bend. 1592
4b	-	2855	1625	1720	3423-3250	-	C-S 643 C-N 1210 N-H bend. 1600
4c	3093	2933	1628	1718	3441-3269	1581	C-S 721 C-N 1211 N-H bend. 1632
4d	3068	2943	1681	1766	3441-3268	1583	C-S 735 C-N 1254 N-H bend. 1623
4e	3051	2970	1677	1710	3476-3251	1527	C-S 741 C-N 1323 N-H bend. 1665 C-Cl 756

Table no. (7): FT.IR spectral data of the prepared compounds (5a - e).

Comp.	CHᵛ aro.	CHᵛ ali.	C=Oᵛ cyclic ketone	C=Nᵛ endo	N-Hᵛ	C=Cᵛ aro.	Others
5a	-	2931	1710	1641	3446	-	C-S 633 C-N 1211 N-H bend. 1625
5b	-	2924,2854	1713	1633	3420	-	C-S 704 C-N 1234 N-H bend. 1622
5c	3030	2924	1713	1609	3421	1555	C-S 728 C-N 1273 N-H bend. 1615
5d	3055	2981, 2933 , 2854	1716	1654	3418	1560	C-S 732 C-N 1267 N-H bend. 1634
5e	3054	2924	1721	1636	3422	1585	C-S 755 C-N 1375 N-H bend. 1677 C-Cl 756

Table no. (8): UV.-Visible spectral data of the prepared compounds.

Comp.	λ_{Max} (nm)
1c	202
2e	226
3a	245
4b	298, 307
5d	340, 361

Table no. (9): Antibacterial activities of some of the synthesized compounds.

Comp. no.	*E*scherichia coli	*S*taphococcus aureus
1a	+ +	+ +
2c	-	-
3e	-	-
4b	+	-
5d	-	+

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

Conclusion:

1. For *St* . (G+), compound (1a) showed moderate activity, while compounds (2c,3e,4b) showed
no activity on this bacteria. Compound (5d) showed slightly activity.
2. For *E.coli* (G-), compounds (2c,3e,5d) have no effect on this bacteria because this bacteria is highly resistant to a wide range of antibiotic because of the slim polysaccharides in cell wall which blocked antibiotics from bacteria and also there are genetic factor., While compounds (1a,4b) have effect on this bacteria.

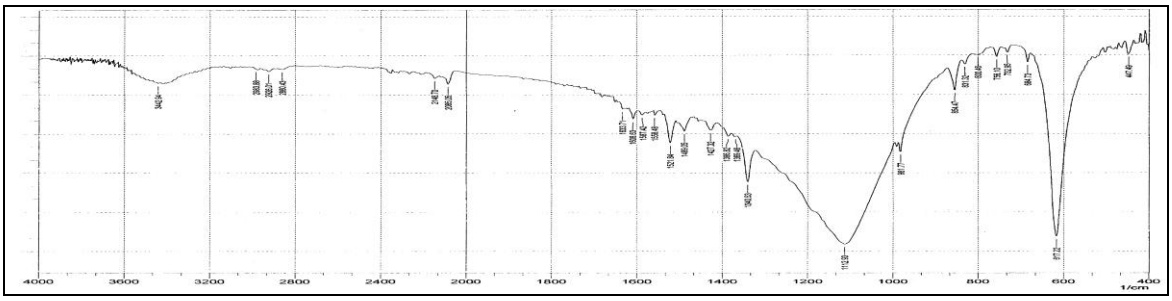


Fig.(1): FT.IR spectrum of compound (1a).

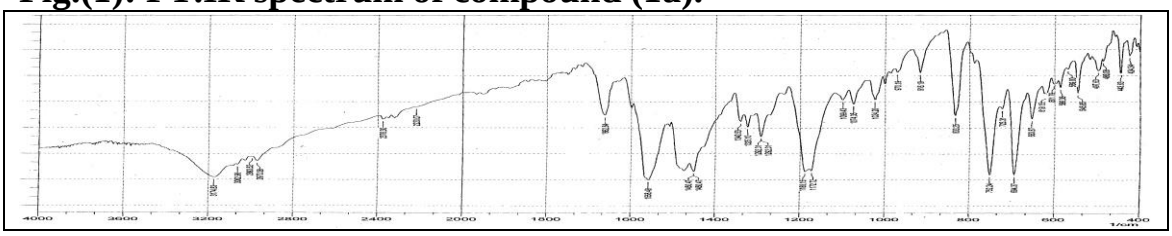


Fig.(2): FT.IR spectrum of compound (1b).

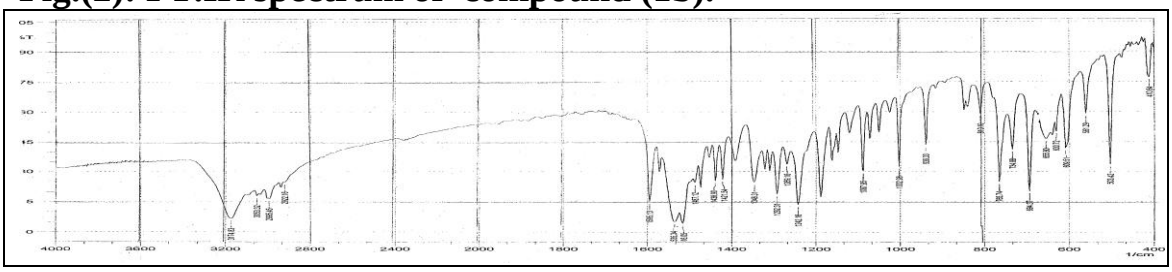


Fig.(3): FT.IR spectrum of compound (1c).

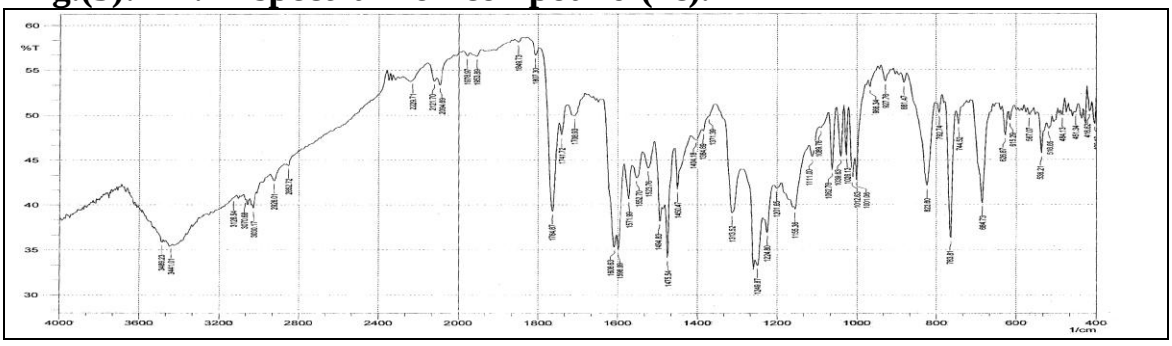


Fig.(4): FT.IR spectrum of compound (1d).

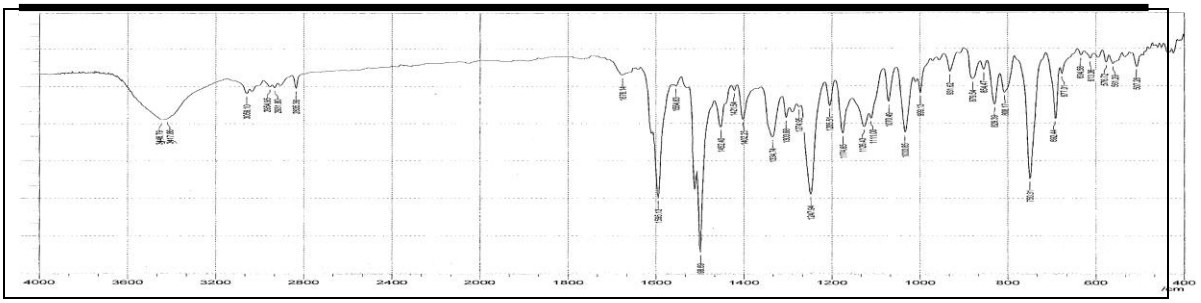


Fig.(5): FT.IR spectrum of compound (1e).

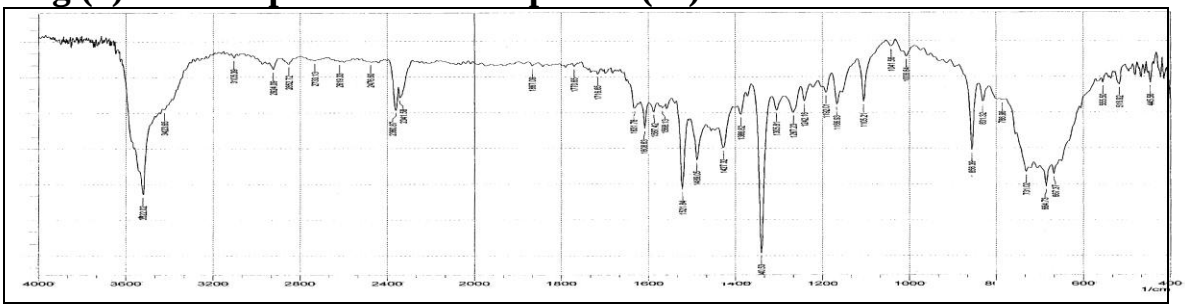


Fig.(6): FT.IR spectrum of compound (2a).

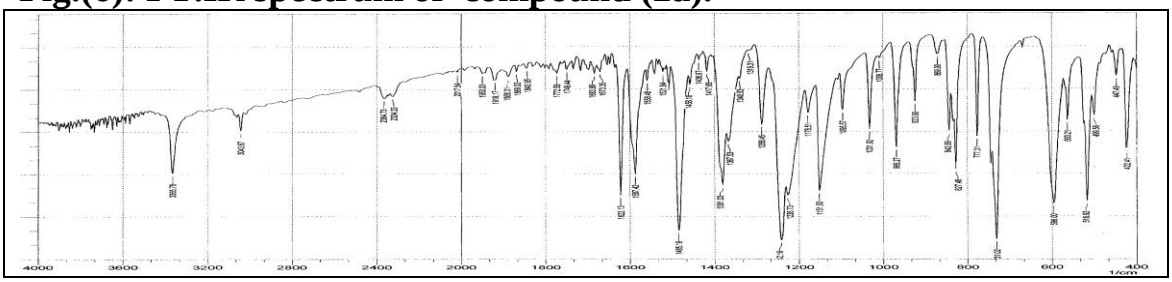


Fig.(7): FT.IR spectrum of compound (2b).

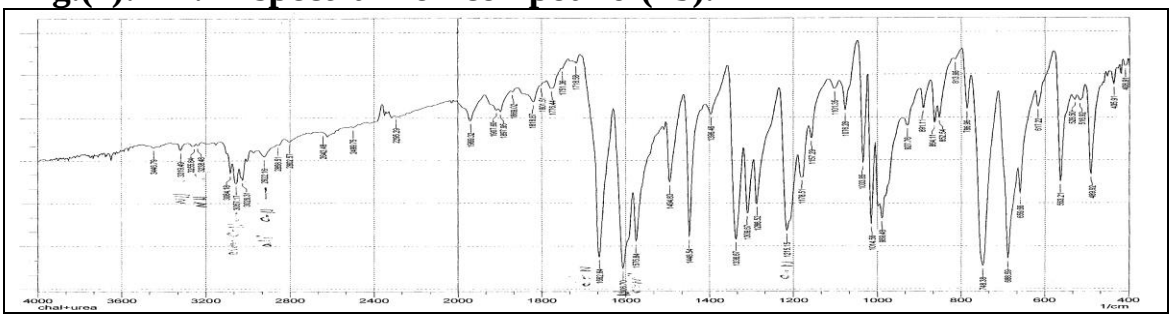


Fig.(8): FT.IR spectrum of compound (2c).

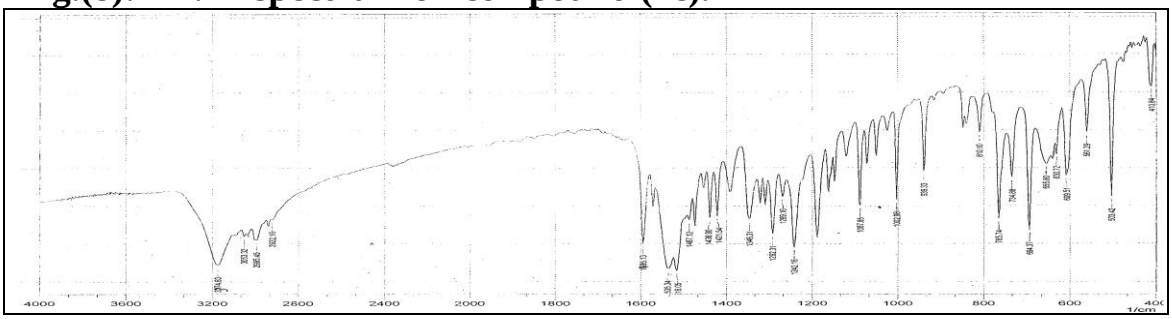


Fig.(9): FT.IR spectrum of compound (2d).

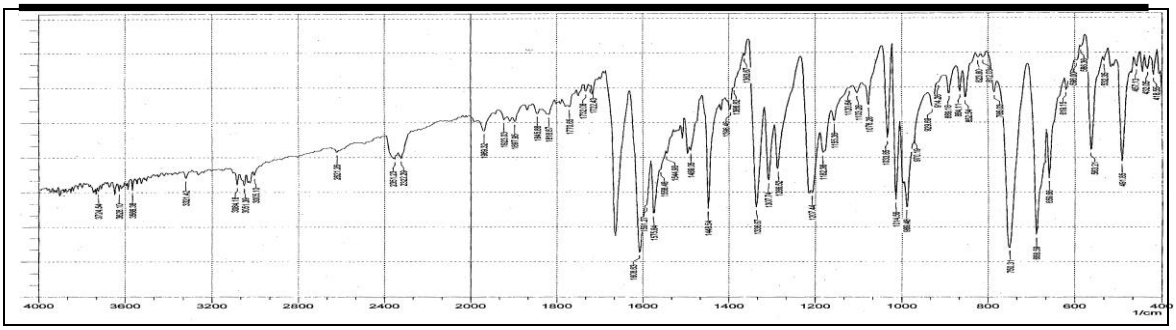


Fig.(10): FT.IR spectrum of compound (2e).

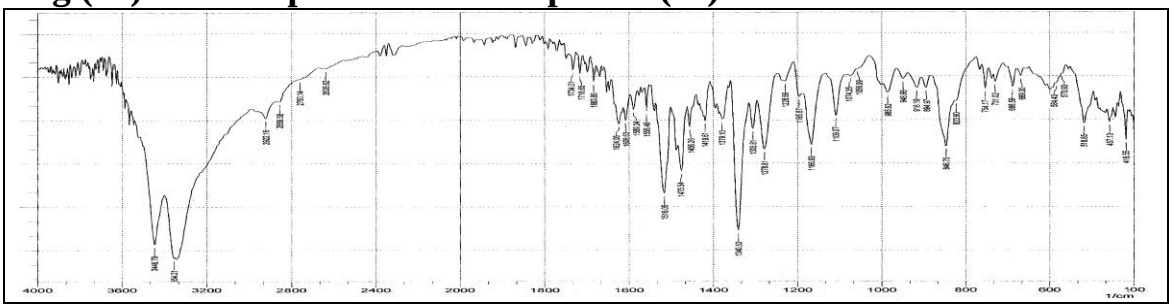


Fig.(11): FT.IR spectrum of compound (3a).

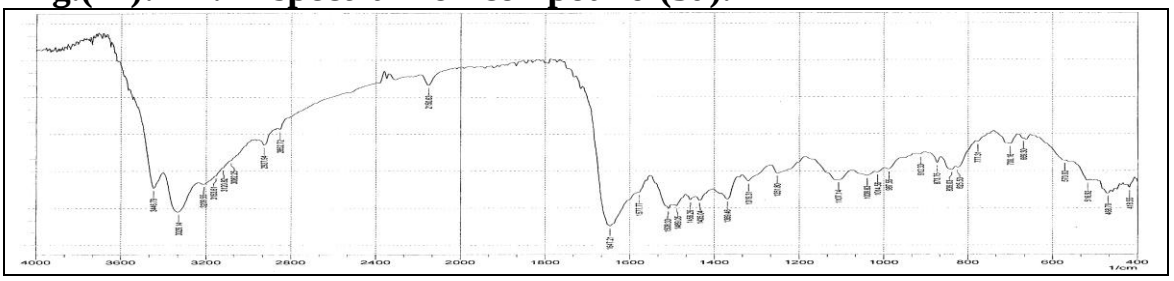


Fig.(12): FT.IR spectrum of compound (3b).

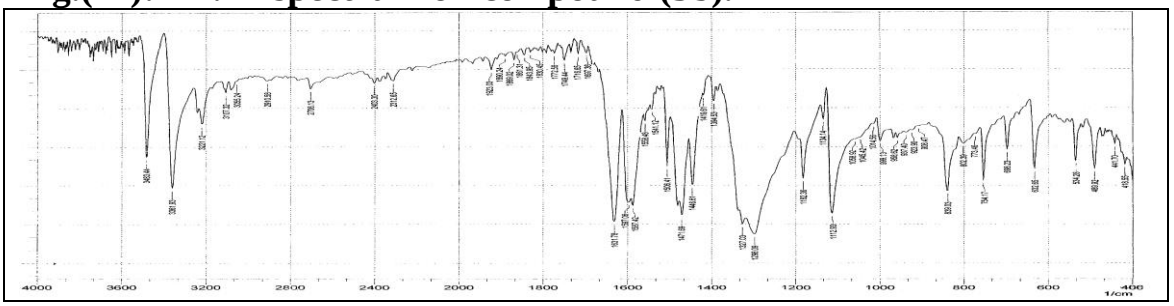


Fig.(13): FT.IR spectrum of compound (3c).

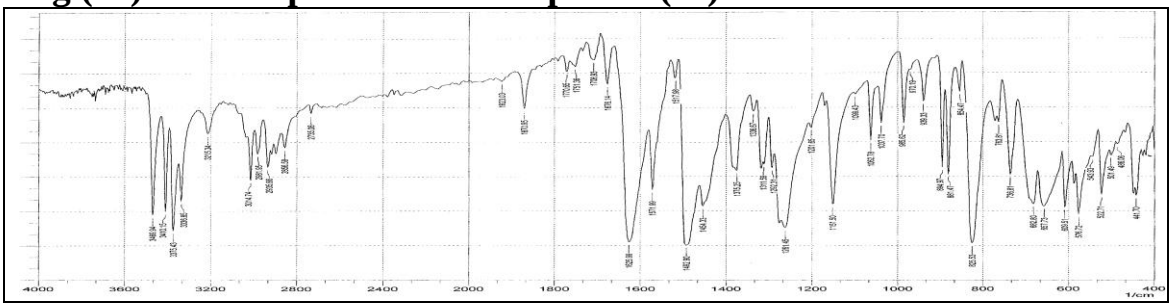


Fig.(14): FT.IR spectrum of compound (3d).

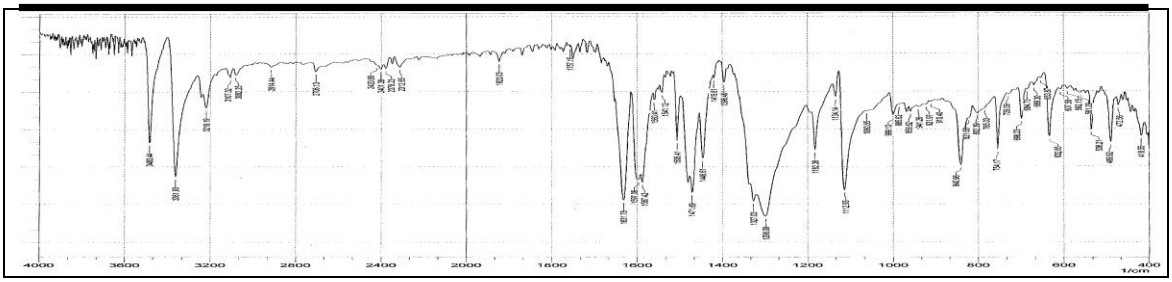


Fig.(15): FT.IR spectrum of compound (3e).

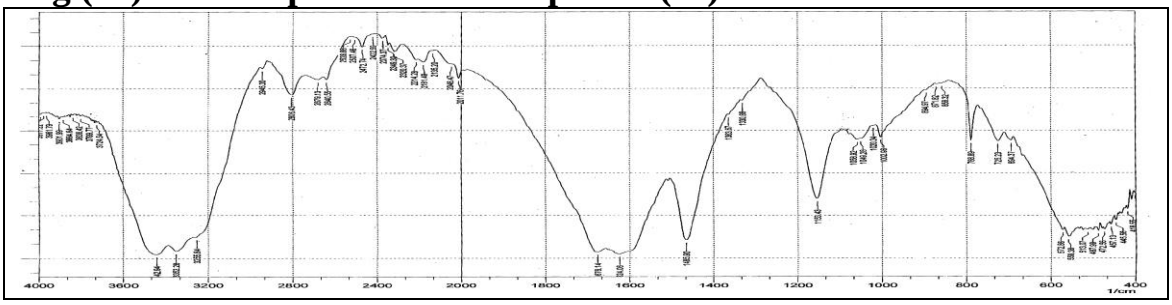


Fig.(16): FT.IR spectrum of compound (4a).

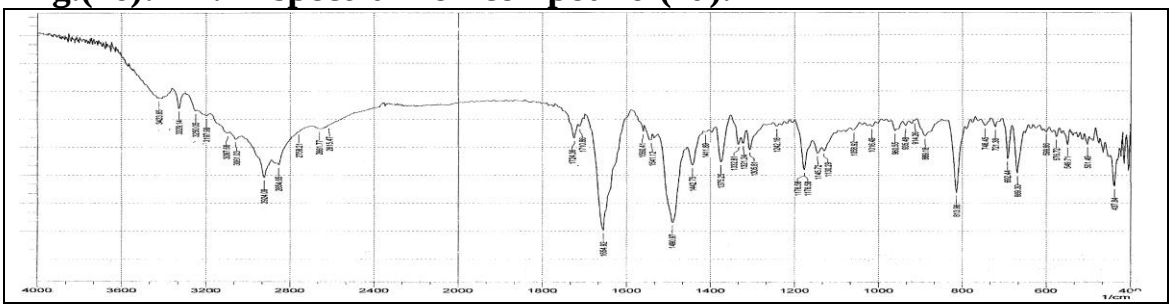


Fig.(17): FT.IR spectrum of compound (4b).

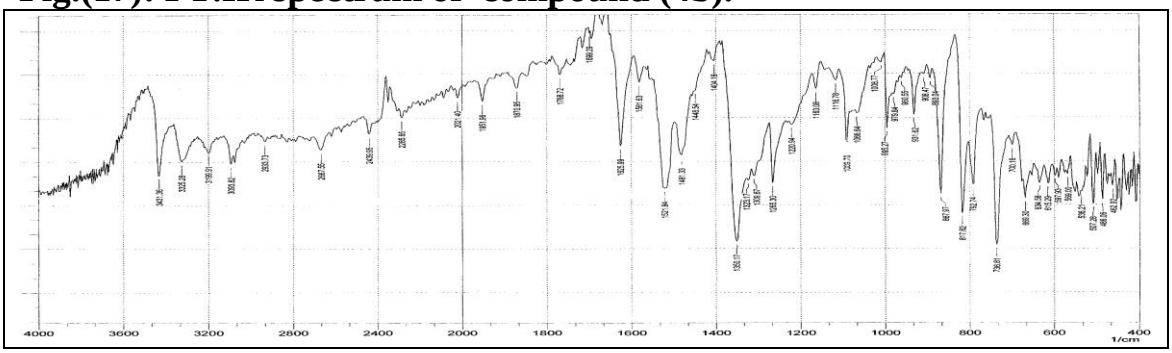


Fig.(18): FT.IR spectrum of compound (4c).

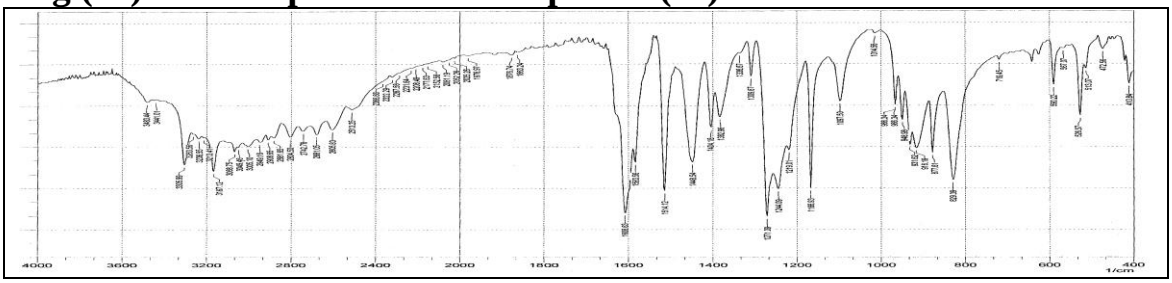


Fig.(19): FT.IR spectrum of compound (4d).

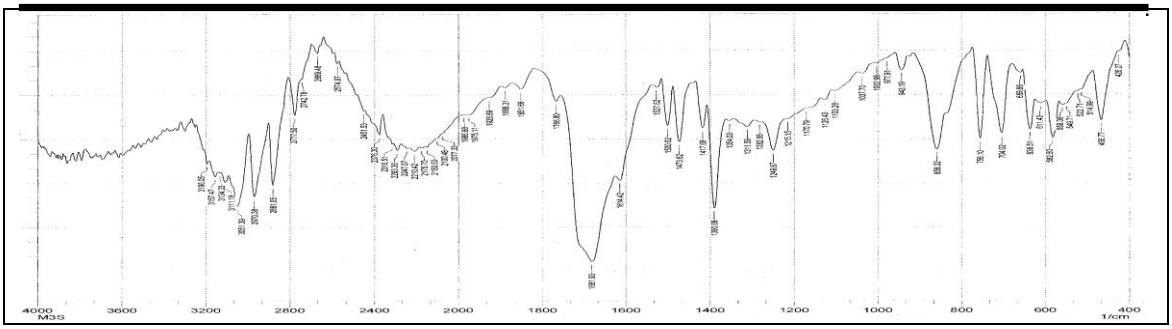


Fig.(20): FT.IR spectrum of compound (4e).

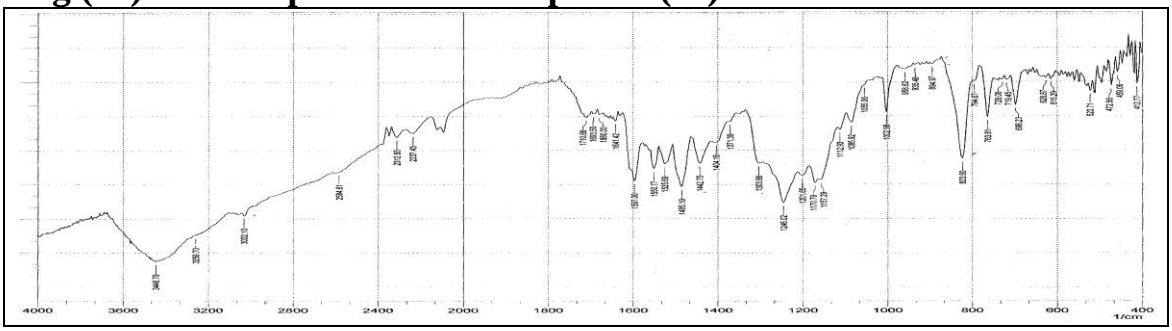


Fig.(21): FT.IR spectrum of compound (5a).

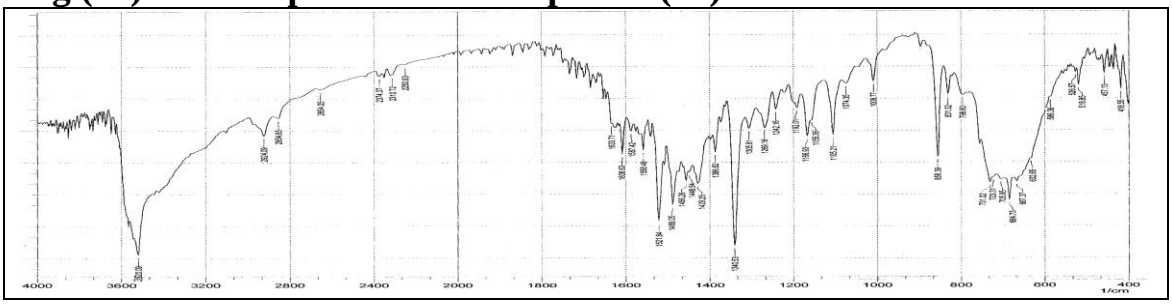


Fig.(22): FT.IR spectrum of compound (5b).

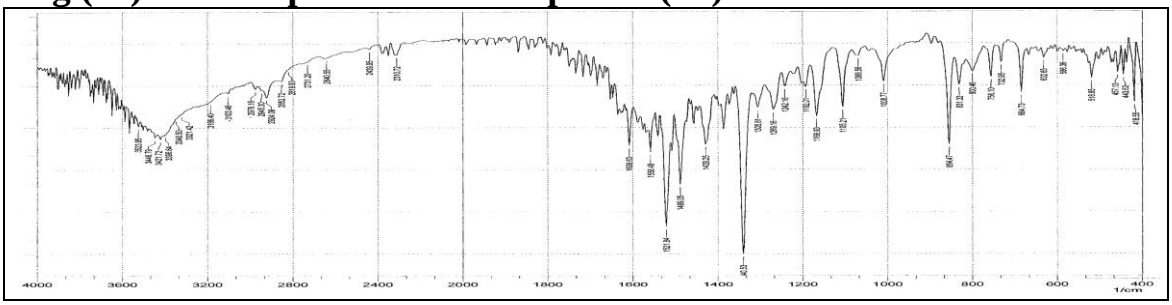


Fig.(23): FT.IR spectrum of compound (5c).

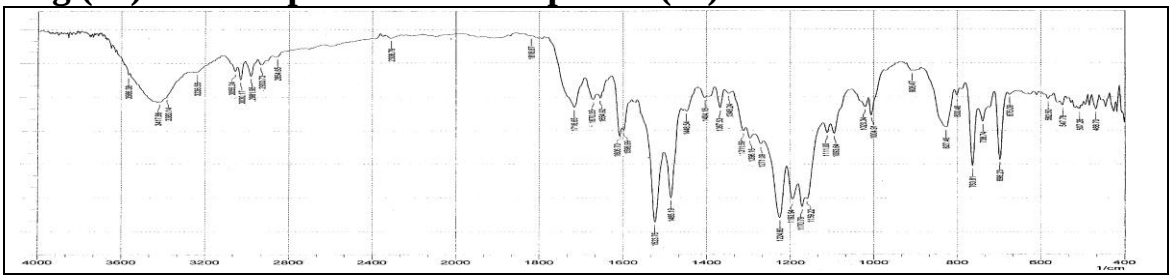


Fig.(24): FT.IR spectrum of compound (5d).

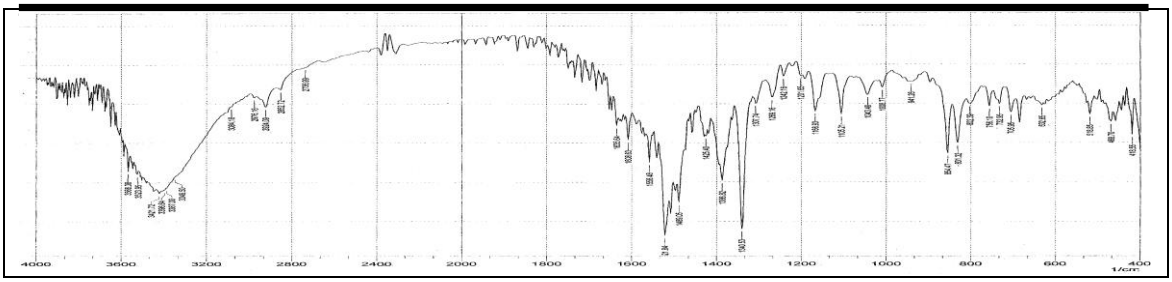


Fig.(25): FT.IR spectrum of compound (5e).

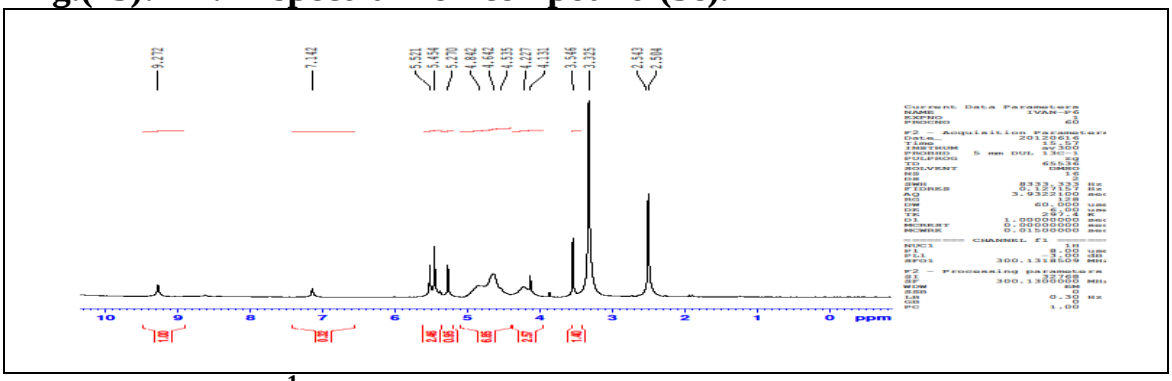


Figure no. (26): ^{1}HNMR spectrum of compound (3c).

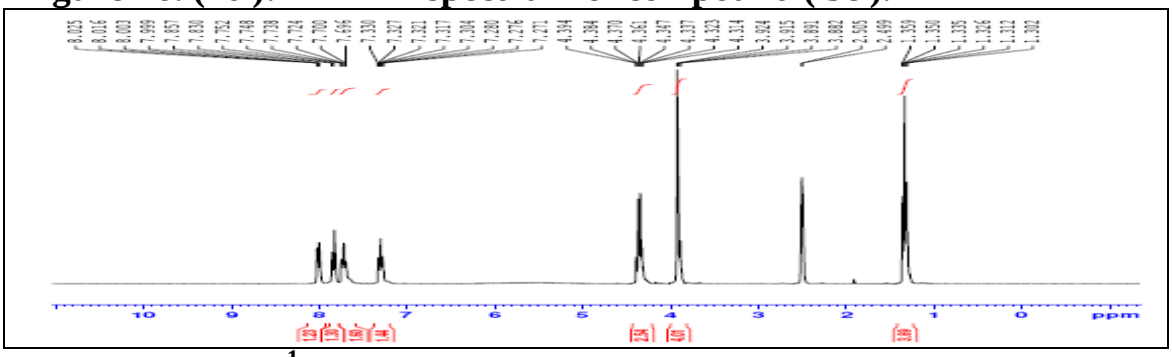


Figure no. (27): ^{1}HNMR spectrum of compound (4e).

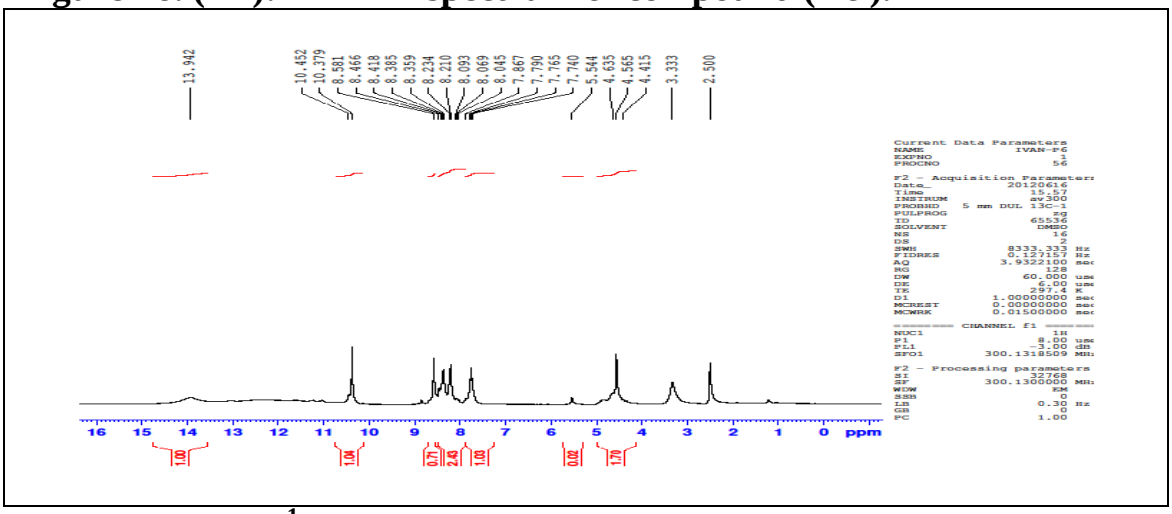


Figure no. (28): ^{1}HNMR spectrum of compound (5e).

تحضير و تشخيص بعض مشتقات جديدة للترايأزين –1– ون و دراسة الفعالية البيولوجية لها

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الخلاصة:

يتضمن البحث تحضير سلسلة من مشتقات الترايأزين الجديدة والتي من المتوقع أن تكون فعالة بيولوجيا وذلك من تفاعل الحامض الأميني الكبريتي L – سيستيئين مع الديهايدات مختلفة في الايثانول المطلق للحصول على حلقة ثايازوليدين بشكل أضداد بصرية (Cis و Trans) : 2 – ألكيل ثايازوليدين – 4– أحماض كاربوكسيلية.(1).

تعاني مشتقات الثايازوليدين (1) تفاعل أسترة الحامض الكاربوكسيلي بوجود قطرات من حامض الكبريتيك المركز كعامل مساعد ليعطي الأستر : أثيل 2– ألكيل ثايازوليدين –4– كاربوكسيلات(2)، يعاني الأستر تفاعل اضافة – حذف مع هيدرازين هيدريت ليعطي هيدرازيد الحامض : 2– ألكيل ثايازوليدين – 4– كاربوهيدرازيدات (3). تم مفاعلة المركب (3) مع كلوريد الأسيتيل بتفاعل أسيلة ذرة النتروجين (NH) ليعطي المركب :.3 – أسيتيل –2– ألكيل ثايازوليدين –4– كاربوهيدرازيدات (4).

حضرت مشتقات حلقة الترايأزينات من عملية الغلق الحلقي لتعطي المركب :

مشتقات ترايأزين –1– ون(5) . يعاني المركب (5) توتومرية ليعطي صيغة الأينول : ترايأزين –1– ول (6) .

تم تشخيص المركبات المحضرة بالطرق الفيزيائية و الطيفية (مطيافية الأشعة تحت الحمراء ، الرنين النووي المغناطيسي ، والأشعة فوق البنفسجية - المرئية). و تم متابعتها بوساطة كروموتوغرافيا الطبقة الرقيقة و قياس درجات الانصهار، كما أختيرت هذه المركبات ضد أنواع من البكتريا.

الكلمات المفتاحية : المركبات الحلقية غير المتجانسة ، ثايازوليدين ،حلقة ترايأزين ، أحماض أمينية كبريتية .