



## Original Research Article

# Synthesis and Characterization of Some New Heterocyclic Compounds Derived from Thiosemicarbazide (A Response Surface Methodology Approach)

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Thiosemicarbazide

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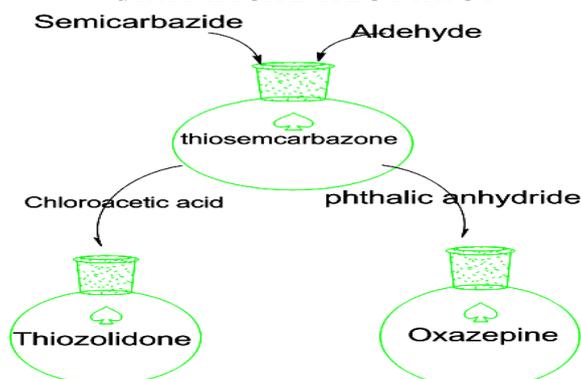
Thioxoimidazolidin-4-one ring

[1,3] oxazepin -4(3H)-yl)thiourea

## ABSTRACT

In this work new thiosemicarbazide derivatives were synthesized to obtain the intermediate of thiosemicarbazone compounds (1-5) by thiosemicarbazide reaction with several aromatic aldehydes, following treatment of compounds (1-5) with 2-chloroethanoic acid with sodium acetate, a series of compounds (6-8) was prepared. There were 1,3-oxazepine-4,7-dione derivatives compounds (9,10) with phthalic anhydride. By heating thiosemicarbazide with carbon disulfide and anhydrous sodium carbonate in absolute ethanol, 5-amino-1,3,4-thiadiazole-5-thiol compound (11) was prepared. The azomethines synthesized by reaction of compound (11) with aromatic aldehyde compounds (12-14), then processed to obtain mercaptoacetic acid as compounds (15-17). The compound (18) was made with ethylchloroacetate from the cyclization thiosemicarbazone compound (2) in the presence of fused sodium acetate. The reaction of compound (11) with chloroacetylchloride produced compound (19) then treated with urea to obtained compound (20) followed by 4- phenyl phenacyl bromide to prepare compound (21). The characterization outcomes for the prepared compounds verified their chemical structures using IR spectroscopy, NMR, and melting points.

## GRAPHICAL ABSTRACT



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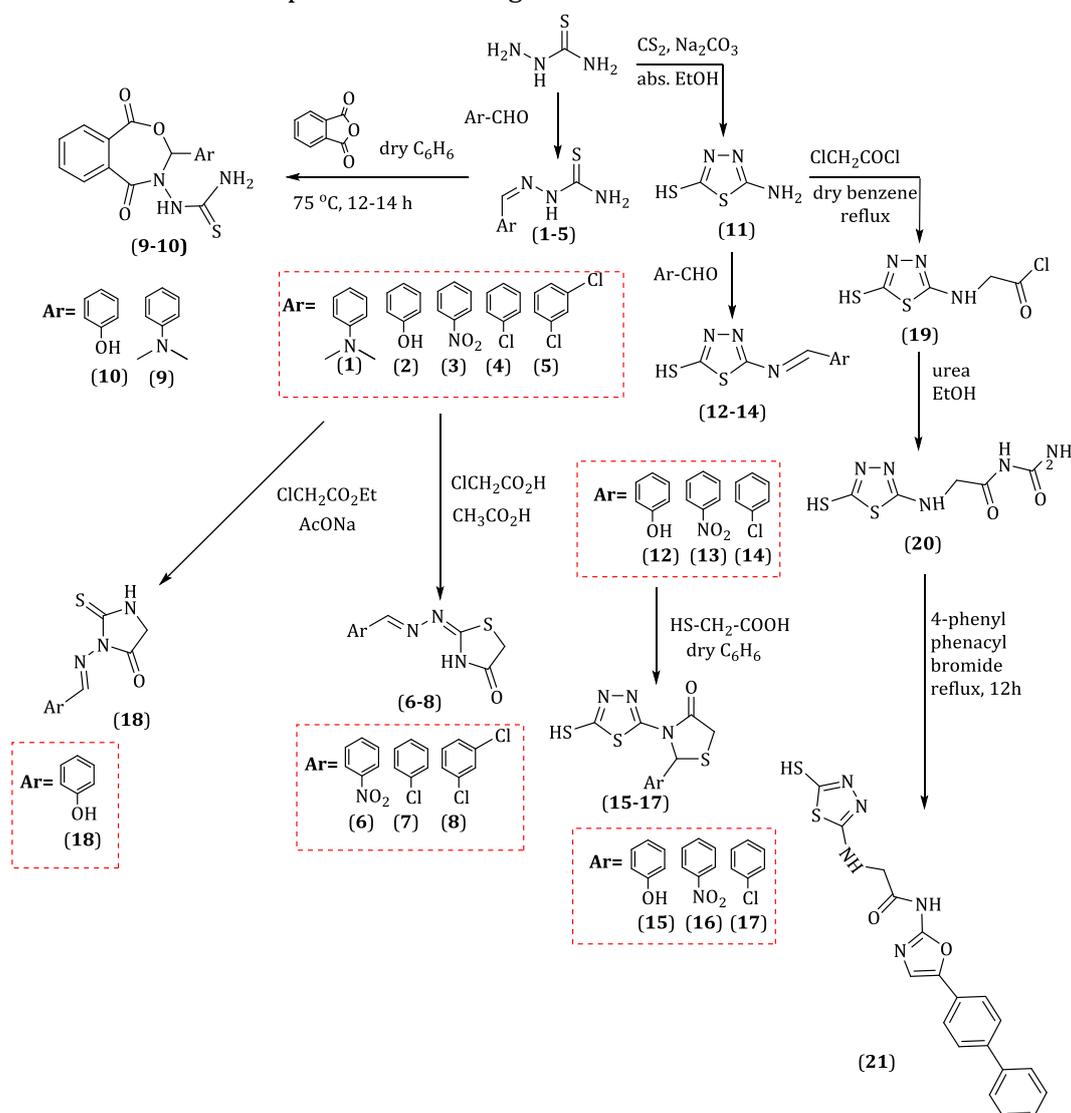
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## Introduction

Thiosemicarbazide is one of the *N*-amino thiourea compounds and is considered an effective control for rice bacterial leaf blight as a ketone reagent, some metals as arodenticide. Antibiotics have been used in organic chemistry to condense aldehyde or ketone with semicarbazide to form semicarbazone derivatives such as nitrofurazone [1]. Due to their antineoplastic action, thiosemicarbazone derivatives from related aldehydes and 2- formyl pyridine have been of considerable interest [2]. Thiosemicarbazone derivatives are of the broad pharmaceutical interest and exhibit various biological activities such as anticancer, antifungal, Leprosy, and antiviral [3-4].

For various pathological states [15-12] (including antibacterial, and anti-inflammatory, the therapeutic effect of a compound containing

1,3,4-thiadiazole ring has been well studied. Because of their numerous applications as agricultural insecticidal, antidepressants, thiadiazole gained widespread attention. The 4-thiazolidinone class is an essential analogue of heterocyclic thiazolidine compounds. 4-thiazolidinone derivatives have been synthesized by various methods. Enaminones reactions with ethyl-2-bromo propionate [13] are included in this method. Thiosemicarbazones bearing aromatic heterocyclic moiety tends to have improved the biological activities [14,15]. On the other hand, due to their therapeutic and pharmacological activities, heterocyclic compounds containing the dole ring are of considerable importance [16-22].



## Methods and Materials

### General procedures

#### Preparation of Thiosemicarbazones compounds (1-5)

A mixture of aromatic aldehyde [0.01 mole], thiosemicarbazide [0.01 mole] in 20 mL of ethanol, and four drops of glacial acetic acid were heated under reflux for 5 h. The product was cooled to room temperature, and the solid was filtered, dried, and purified to provide compounds (1-5) via recrystallization with ethanol.

#### Synthesis of 2-(4-substituted-benzylidene hydrazono)-1,3-thiazolidine-4-one compounds (6-8)

A mixture of thiosemicarbazide derivatives compounds (1-3) was prepared by heating and continuous stirring for 0.01 mole chloroacetic acid (0.01 mole), and anhydrous sodium acetate (0.01 mole) in 20 mL glacial acetic acid under reflux for 8 h. The produced mixtures for compounds (6-8) were left to cool via poured into ice cold water, and the separated solid was filtered off, washed with water, dried, and recrystallized by absolute ethanol.

#### Synthesis of 1-(3-(derivative)-1,5-dioxo-1,5-dihydrobenzo[e][1,3]oxazepin-4(3H)-yl) thiourea compounds (9-10)

A 0.0025 mole from thiosemicarbazone derivatives (1-2) compounds and 0.0025 mole from phthalic anhydride in 20 mL from dry benzene was mixed, refluxed, and stirring on a water bath at 75 °C for 12-14 h.

#### Synthesis of 2-amino-1,3,4-thiadiazole-5-thiol compound (11)

Exact 0.02 mole, 1.82 (g) from thiosemicarbazide suspended in 15 mL ethanol was added to anhydrous sodium carbonate (0.02 mole, 2.12 g) and 3 mL carbon disulphide, the produced mixture was warmed with stirring under reflux for 1 h., then heated on the steam bath for 4 h. The most solvent was removed, and the residue was dissolved in ice-water and acidified with concentrated hydrochloric acid [7].

#### Synthesis of E-4-((5-mercapto-1,3,4-thiadiazol-2-yl) imino derivatives compounds (12-14)

A suspension of p-hydroxybenzaldehyde (0.01 mole) in 40 mL ethanol and 2-amino-1,3,4-thiadiazole-5-thiol compound (11) (0.01 mole) were mixed with two drops of glacial acetic acid and heated under reflux for 4h. The product was collected after cooling and recrystallized using ethanol, in the same way for preparation compounds (13,14).

#### The preparation of thiazolidine-4-one compounds (15-17) [8]

0.01 mole of Schiff bases compounds (12-14) was mixed with 0.04 mole (0.26 mL) from mercaptoacetic acid in 30 mL from dry benzene, and then refluxed for 10 h. The mixture has been concentrated and recrystallized by absolute methanol.

#### Synthesis of 3-((4-hydroxybenzylidene) amino)-2-thioxoimidazolidin-4-one compound (18) [9]

A mixture of 0.01 mole from compound (2), 0.01 mole of ethyl chloroacetate and 0.03 mole from sodium acetate in 30 mL ethanol were heated under reflux for 4h, then cooled and poured in water.

#### Synthesis of 2-chloro-N-(5-mercapto-1,3,4-thiadiazole-2-yl) acetamide compound (19)

Freshly 2.5 mL of distilled chloroacetyl chloride was dissolved in 100 mL dry benzene, and gradually added to a mixture of 0.033 mole (4.3 g) from 2-amino-1,3,4-thiadiazole-5-thiol in 30 mL dry benzene. The mixture was refluxed via a water bath for 4 h. and benzene solvent was distilled off. The product was washed with distilled water, dried, and recrystallized using absolute ethanol.

#### Synthesis of N-(5-mercapto-1,3,4-thiadiazole-2-yl)-2-ureidoacetamide compound (20)

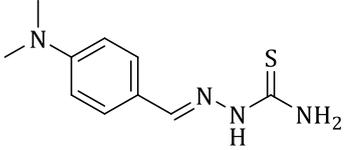
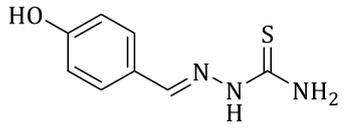
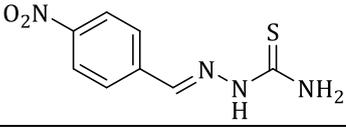
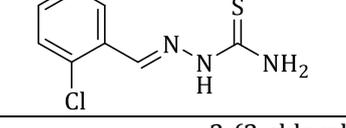
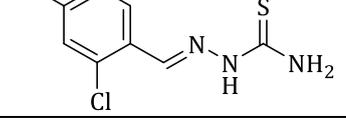
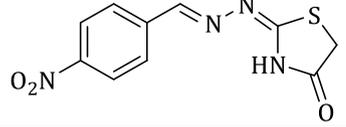
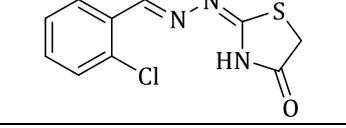
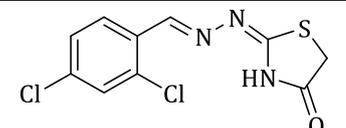
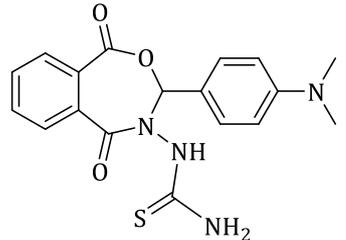
Exact 0.01mole (4.18 g) from compound (19) was refluxed with 0.02 mole, (1.2 g) from urea for 14h. In 20 mL from absolute ethanol. Then the reaction mixture was filtered, recrystallized the product by ethanol, and dried to give the final product.

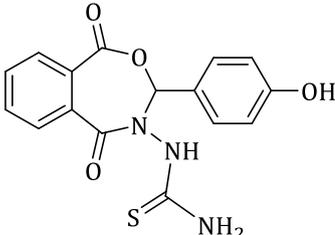
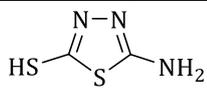
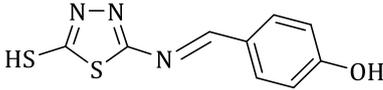
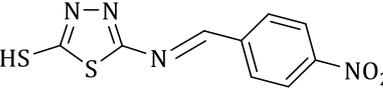
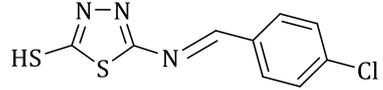
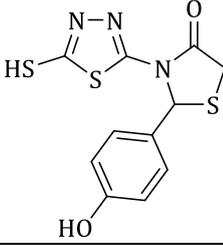
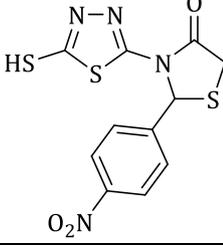
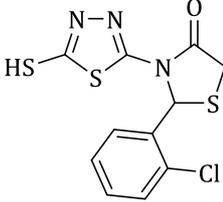
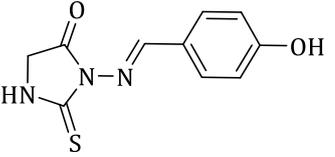
#### Synthesis of 2-((5-([1,1'-biphenyl]-4-yl)-2-yl) amino)-N-(5-mercapto-1,3,4-thiadiazol-2-yl) acetamide compound (21)

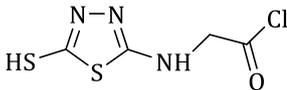
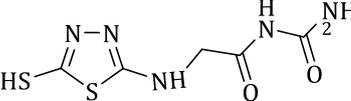
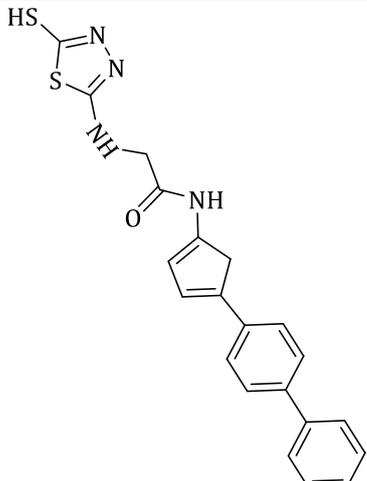
A mixture of 0.01 mole (2.33 g) compounds (20) and 0.01 mole (2.75 g) from 4-phenyl phenacyl

bromide in 20 mL of ethanol. The reaction was filtered off and recrystallized using absolute ethanol. The precipitate ethanol.

**Table 1:** physical properties of the prepared compounds (1-21)

NO	Structure and nomenclature	Yield	color	M.P/ °C	FT-IR
1		77%	yellow	217-215	3390 (ν <sub>as</sub> (N-H)), 3240 (ν <sub>S</sub> (N-H)) 3186 (ν <sub>N-H</sub> ), 3048 (ν <sub>S</sub> (C-H)benzene ring), 2907 (ν <sub>as</sub> (C-H, CH <sub>3</sub> )), 2853 (ν <sub>S</sub> (C-H, CH <sub>3</sub> )), 1612 (ν <sub>C=N</sub> ), 1220 (ν <sub>C=S</sub> ).
2-(4-(dimethylamino)benzylidene)hydrazine-1-carbothioamide					
2		84%	yellow	231-230	3388 (ν <sub>as</sub> (N-H)), 3238 (ν <sub>S</sub> (N-H)) 3182 (ν <sub>N-H</sub> ), 3040 (ν <sub>S</sub> (C-H)benzene ring), 3222 (ν <sub>OH</sub> ), 3080 (ν <sub>S</sub> (C-H)benzene ring), 1225 (ν <sub>C=S</sub> ), 1614 (ν <sub>C=N</sub> ).
2-(4-hydroxybenzylidene)hydrazine-1-carbothioamide					
3		91%	yellow	246-244	3384 (ν <sub>as</sub> (N-H)), 3234 (ν <sub>S</sub> (N-H)) 3184 (ν <sub>N-H</sub> ), 3042 (ν <sub>S</sub> (C-H)benzene ring), 1513 (ν <sub>as</sub> C-NO <sub>2</sub> ), 1332 (ν <sub>S</sub> C-NO <sub>2</sub> ).
2-(4-nitrobenzylidene)hydrazine-1-carbothioamide					
4		98%	White	221-220	3380 (ν <sub>as</sub> (N-H)), 3235 (ν <sub>S</sub> (N-H)) 3180 (ν <sub>N-H</sub> ), 3041 (ν <sub>S</sub> (C-H)benzene ring), 1080 (ν <sub>C-Cl</sub> ).
2-(2-chlorobenzylidene)hydrazine-1-carbothioamide					
5		74%	White	201-199	3377 (ν <sub>as</sub> (N-H)), 3233 (ν <sub>S</sub> (N-H)) 3177 (ν <sub>N-H</sub> ), 3039 (ν <sub>S</sub> (C-H)benzene ring), 1082 (ν <sub>C-Cl</sub> ).
2-(2,4-dichlorobenzylidene)hydrazine-1-carbothioamide					
6		87%	yellow	218 (dec.)	1512 (ν <sub>as</sub> C-NO <sub>2</sub> ), 1332 (ν <sub>S</sub> C-NO <sub>2</sub> ), 1601 (ν <sub>C=N</sub> ), 3432 (ν <sub>N-H</sub> ), 3060 (ν <sub>S</sub> (C-H)benzene ring), 2925 (ν <sub>as</sub> (C-H, CH <sub>2</sub> )), 2852 (ν <sub>S</sub> (C-H, CH <sub>2</sub> )).
(2Z)-2-(4-nitrobenzylidene)hydrazono)thiazolidin-4-one					
7		77%	White	293 (dec.)	3430 (ν <sub>N-H</sub> ), 3050 (ν <sub>S</sub> (C-H)benzene ring), 2924 (ν <sub>as</sub> (C-H, CH <sub>2</sub> )), 2850 (ν <sub>S</sub> (C-H, CH <sub>2</sub> )), 720 (ν <sub>C-Cl</sub> ).
(2Z)-2-(2-chlorobenzylidene)hydrazono)thiazolidin-4-one					
8		82%	brown	214-211	3435 (ν <sub>N-H</sub> ), 3053 (ν <sub>S</sub> (C-H)benzene ring), 2920 (ν <sub>as</sub> (C-H, CH <sub>2</sub> )), 2853 (ν <sub>S</sub> (C-H) CH <sub>2</sub> ), 722 (ν <sub>C-Cl</sub> ).
(2Z)-2-(2,4-dichlorobenzylidene)hydrazono)thiazolidin-4-one					
9		65%	yellow	215-213	3015 (ν <sub>S</sub> (C-H)benzene ring), 2939 (ν <sub>as</sub> (C-H, CH <sub>3</sub> )), 2836 (ν <sub>S</sub> (C-H) CH <sub>3</sub> ), 3240 (ν <sub>N-H</sub> ), 3419 (ν <sub>as</sub> (N-H 2)), 3276 (ν <sub>S</sub> (N-H <sub>2</sub> )), 1220 (ν <sub>C=S</sub> ), 1714 ((ν <sub>C=O</sub> ), O=C-O, oxazepine), 1639 ((ν <sub>C=O</sub> ), O=C-N, oxazepine).
1-(3-(4-(dimethylamino)phenyl)-1,5-dioxo-1,5-dihydrobenzo[e][1,3]oxazepin-4(3H)-yl)thiourea					

10		55%	brown	190-188	3013 (ν <sub>C-H</sub> benzene ring), 3222 (ν <sub>OH</sub> ), 3235 (ν <sub>N-H</sub> ), 3411 (ν <sub>as</sub> (N-H <sub>2</sub> )), 3270 (ν <sub>S</sub> (N-H <sub>2</sub> )), 1223 (ν <sub>C=S</sub> ), 1710 ((ν <sub>C=O</sub> ), O=C-O, oxazepine), 1635 (ν <sub>C=O</sub> ), O=C-N, oxazepine).
1-(3-(4-hydroxyphenyl)-1,5-dioxo-1,5-dihydrobenzo[e][1,3]oxazepin-4(3H)-yl)thiourea					
11		76%	White	186-184	3386 (ν <sub>as</sub> (N-H <sub>2</sub> )), 3270 (ν <sub>S</sub> (N-H <sub>2</sub> )), 2542 (ν <sub>S-H</sub> ), 1595 (ν <sub>C=N</sub> ), 1095 (ν <sub>C-S-C</sub> ).
5-amino-1,3,4-thiadiazole-2-thiol					
12		73%	yellow	226-224	2570 (ν <sub>S-H</sub> ), 3412 (ν <sub>O-H</sub> ), 1630 (ν <sub>C=N</sub> ), 3080 (ν <sub>S</sub> (C-H) benzene ring).
4-(((5-mercapto-1,3,4-thiadiazol-2-yl)imino)methyl)phenol					
13		81%	yellow	243-241	2560 (ν <sub>S-H</sub> ), 1620 (ν <sub>C=N</sub> ), 3071 (ν <sub>S</sub> (C-H) benzene ring), 1515 (ν <sub>as</sub> C-NO <sub>2</sub> ), 1333 (ν <sub>S</sub> C-NO <sub>2</sub> ).
5-((4-nitrobenzylidene)amino)-1,3,4-thiadiazole-2-thiol					
14		88%	yellow	226-224	2566 (ν <sub>S-H</sub> ), 1622 (ν <sub>C=N</sub> ), 3078 (ν <sub>S</sub> (C-H) benzene ring), 724 (ν <sub>C-Cl</sub> ).
5-((4-chlorobenzylidene)amino)-1,3,4-thiadiazole-2-thiol					
15		68%	White	243-241	2569 (ν <sub>S-H</sub> ), 3410 (ν <sub>O-H</sub> ), 1710 (ν <sub>C=O</sub> ), 3020 (ν <sub>S</sub> (C-H) benzene ring), 1609 (ν <sub>C=N</sub> ).
2-(4-hydroxyphenyl)-3-(5-mercapto-1,3,4-thiadiazol-2-yl)thiazolidin-4-one					
16		78%	yellow	233-231	2566 (ν <sub>S-H</sub> ), 1712 (ν <sub>C=O</sub> ), 1610 (ν <sub>C=N</sub> ), 3025 (ν <sub>S</sub> (C-H) benzene ring), 1512 (ν <sub>as</sub> C-NO <sub>2</sub> ), 1311 (ν <sub>S</sub> C-NO <sub>2</sub> ), 1709 (ν <sub>C=O</sub> ).
3-(5-mercapto-1,3,4-thiadiazol-2-yl)-2-(4-nitrophenyl)thiazolidin-4-one					
17		82%	White	260-256	2570 (ν <sub>S-H</sub> ), 1716 (ν <sub>C=O</sub> ), 1611 (ν <sub>C=N</sub> ), 3010 (ν <sub>S</sub> (C-H) benzene ring), 1513 (ν <sub>as</sub> C-NO <sub>2</sub> ), 1314 (ν <sub>S</sub> C-NO <sub>2</sub> ), 1710 (ν <sub>C=O</sub> ), 725 (ν <sub>C-Cl</sub> ).
2-(2-chlorophenyl)-3-(5-mercapto-1,3,4-thiadiazol-2-yl)thiazolidin-4-one					
18		91%	White	285 (dec.)	1240 (ν <sub>C=S</sub> ), 1613 (ν <sub>C=N</sub> ), 1628 (ν <sub>C=O,amide</sub> ), 3040 (ν <sub>S</sub> (C-H) benzene ring), 3416 (ν <sub>O-H</sub> ).
3-((4-hydroxybenzylidene)amino)-2-thioxoimidazolidin-4-one					

19		66%	yellow	140- 138	2561 ( $\nu_{\text{S-H}}$ ), 1612 ( $\nu_{\text{C=N}}$ ), 3270 ( $\nu_{\text{(N-H)}}$ ), 2924 ( $\nu_{\text{as(C-H), CH}_2}$ ), 2851 ( $\nu_{\text{S (C-H), CH}_2}$ ), 1620 ( $\nu_{\text{C=O,amide}}$ ), 750( $\nu_{\text{C-Cl}}$ ).
(5-mercapto-1,3,4-thiadiazol-2-yl)glycinoyl chloride					
20		58%	brown	246- 243	3270 ( $\nu_{\text{(N-H)}}$ ), 1650 ( $\nu_{\text{C=O,amide}}$ ), 3420 ( $\nu_{\text{as (N-H}_2)}$ ), 3266 ( $\nu_{\text{S (N-H}_2)}$ ), 2567 ( $\nu_{\text{S-H}}$ ), 1611 ( $\nu_{\text{C=N}}$ ).
N-carbamoyl-2-((5-mercapto-1,3,4-thiadiazol-2-yl)amino)acetamide					
21		71%	brown	230- 226	3269 ( $\nu_{\text{(N-H)}}$ ), 1645 ( $\nu_{\text{C=O,amide}}$ ), 3080 ( $\nu_{\text{(C-H)benzene ring}}$ ), 2567 ( $\nu_{\text{S-H}}$ ), 1596 ( $\nu_{\text{C=N}}$ ).
N-(4-([1,1'-biphenyl]-4-yl)cyclopenta-1,3-dien-1-yl)-2-((5-mercapto-1,3,4-thiadiazol-2-yl)amino)acetamide					

## Result and Discussion

In the present work, new derivatives of carbothioamide, thiazolidin-4-one, [1,3]oxazepine-4(3H), 1,3,4-thiadiazole-2-thiol, 2-thioxoimidazolidin-4-one, Acetamide, were synthesis and outlined in Scheme 1. The first step of the reaction includes the removal of proton from NH group by sodium acetate that resulted from conversion of the produced intermediate partially or totally to thiol form. The second step represent that nucleophilic attack by thiol on carbon atom that bears an excellent leaving group (CH-Cl) will result in the formation of a new S-C bond. This step is followed by a nucleophilic attack by  $\text{NH}_2$  group on the carbon atom of carbonyl group resulted in the formation of five and a five-member heterocyclic ring. These steps have been demonstrated in changing physical properties (color and melting point) and FT-IR analysis in In the present work, new derivatives of carbothioamide, thiazolidin -4- one, [1,3]oxazepine-4(3H), 1,3,4-thiadiazole-2-thiol, 2-thioxoimidazolidin-4-one, Acetamide, were synthesis and outlined in Scheme 1. The first step of the reaction includes the removal of proton from NH group by sodium acetate that resulted from conversion of the produced intermediate

partially or totally to thiol form. The second step represent that nucleophilic attack by thiol on carbon atom that bears an excellent leaving group (CH-Cl) will result in the formation of a new S-C bond. This step is followed by a nucleophilic attack by  $\text{NH}_2$  group on the carbon atom of carbonyl group resulted in the formation of five and a five-member heterocyclic ring. These steps have been demonstrated in changing physical properties (color and melting point) and FT-IR analysis in Table 1. The FT-IR data were interpenetrated for conforming to the essential bonds generated in compounds synthesis (1-21) agree with the mention in references (23-24).  $^1\text{H-NMR}$  spectrum of compounds (7) in (DMSO as solvent) was pictured, a singlet signal appear at 3.9 ppm could be attributed to protons of methylene group (- $\text{CH}_2$ -) for thiazolidine -4-one ring. Aromatic protons appear at 7.5-7.7 ppm. Signal at 8.4 ppm could be attributed to proton of  $\text{CH=N}$  group. A singlet signal appears at 12.0 ppm referred to N-H group of 4-thiazolidineone ring. Shown  $^1\text{H-NMR}$  spectrum (400 MHz, in DMSO) of compounds (9). The singlet signal at 3.3 ppm was assigned to methyl groups protons (6H, 2  $\text{XCH}_3$ ). Aromatic protons appear at 6.6 - 8.0 ppm peaks as an amultiplate a signal at 5.0 ppm referred to

amine group (NH<sub>2</sub>), a singlet signal appear at 10.3 ppm are due to one proton of (-NH-) group (**25**). the <sup>1</sup>H-NMR spectrum (400 MHz, DMSO) of compound (**11**) explained that a singlet signal appears at 5.2 ppm due to two protons of NH<sub>2</sub> group, also the spectrum showed one sharp singlet signal at 13.2 ppm, which could be attributed to proton of -SH group. <sup>1</sup>H-NMR for compound (**15**) and found a quartet signal in the region (3.8- 3.9) ppm (2H) due to the protons of (CH<sub>2</sub>) in thiazolidin -4- one ring. The signal at 6.4 ppm, which belong to -CH- of thiazolidine-4- one ring, another multiple signal at (6.7- 7.6) ppm belong to aromatic protons. The board peak at 9.0 ppm (1H) was due to the proton of (-OH)

group. Also, the spectrum showed a signal at 13.2 ppm could be attributed to proton of -SH group. Other characteristic peaks with their interpretation were listed in Table 2. The <sup>1</sup>H-NMR spectrum of compound (**18**) at (400 NHZ, DMSO) obtained the following clear signals at ppm. The signal at 4.2 ppm (2H) due to the protons of (CH<sub>2</sub>) thioxoimidazolidin -4- one ring, and another multiple signal at 6.8- 7.2 ppm belong to aromatic protons; also the spectrum showed a signal at 8.5 ppm could be attributed to the proton of CH=N group. A signal at 9.6 ppm due to the proton of (-OH) group and the signal at 10.2 ppm referred to -NH of thioxoimidazolidin -4- one.

**Table 2:** <sup>1</sup>H-NMR spectral data synthesis compounds (7, 9, 11, 15, and 18)

Compound NO.	<sup>1</sup> H-NMR ( DMSO) (δ, ppm)
7	3.9 (S, 2H, CH <sub>2</sub> ) 7.5- 7.7 (dd, 4H, Ar-H) 8.4 (S, 1H, CH=N) 12.0 (S, 1H, N-H)
9	3.3(S,6H,2XCH <sub>3</sub> ) 5.0 (m, 2H, NH <sub>2</sub> ) 6.6-8 (dd, 8H, Ar-H) 10.3 (m, 1H, NH)
11	5.2 (S, 2H, NH <sub>2</sub> ) 13.2 (S, 1H, SH)
15	3.8-3.9 (dd, 2H, CH <sub>2</sub> ) 6.4 (S, 1H, CH) 6.7-7.6 (dd, 4H, Ar-H) 9.0 (S, 1H, OH) 13.2 (S, 1H, SH)
18	4.2 (S, 2H, CH <sub>2</sub> ) 6.8-7.2 (dd, 4H, Ar-H) 8.5 (S, 1H, CH=N) 9.6 (S, 1H, OH) 10.2 (S, 1H, NH)

The <sup>13</sup>C-NMR of compound (**9**). The signal at 41.7 ppm assigned to methyl groups carbons (2C, 2 X CH<sub>3</sub>). The signal of carbon (C-N) of oxazepine ring appeared at the 94.3 ppm. The spectrum appeared at the range (123.5- 149.1) ppm attributed to carbon of methine group in Benzene ring. Moreover, the signal at 167.0 ppm was assigned to the carbon of (O-C=O) group inside the oxazepine ring. The signal at 172.5 ppm attributed to carbon of (O=C-N) group inside oxazepine ring. The signal at 182.5 ppm for the carbon of (C=S) group [25]. The <sup>13</sup>C- NMR spectrum of compound (**15**) in Figure A signal at 33.5 ppm referred to the carbon of methine

group inside thiazolidine-4-one. The signal at 72.3 ppm referred to -CH group in thiazolidine -4- one ring, in addition, another multiple signals at (115.8- 156.9) ppm referred to the carbon of CH<sub>2</sub> group in the benzene ring. Moreover, the signal at 163.4 ppm is for the carbon of (C=N) group for the thiadiazole ring. Also, the spectrum showed at 171.2 ppm referred to (N-C=O) group, and the signal at 184.0 ppm for (C=N) group inside thiadiazole ring, other characteristic peaks with their interpretation were listed in Table 3. The <sup>13</sup>C-NMR spectrum of compound (**18**), showed the following signals at ppm. The spectrum appeared a singlet signal at 55.5 ppm

for methylene group carbon inside thioxoimidazolidin-4-one. The aromatic carbons occurred at 154.1 ppm for the carbon of (CH=N)

group. Also, the spectrum showed one signal at 160.8 ppm that could be attributed to C=S group of thioxoimidazolidin-4-one ring (**25**).

**Table 3:**  $^{13}\text{C}$ -NMR spectral data synthesis compounds (9, 15, and 18)

Compound NO.	$^{13}\text{C}$ -NMR ( DMSO) ( $\delta$ , ppm)
9	41.7 (2C,2XCH <sub>3</sub> ) 94.3 (C-N) 123.5-149.1(CH <sub>2</sub> , Ar) 167.0 (O-C=O) 172.5 (O=C-N) 182.5 (C=S)
15	33.5 (CH <sub>2</sub> ) 72.3 (-CH -) 115.8- 156.9 (CH <sub>2</sub> , Ar) 163.4 (C=N) 171.2 (N-C=O) 184.0 (C=N)
18	55.5 (CH <sub>2</sub> , Ar) 154.1 (CH=N) 160.8 (C=S)

### Conclusion

The key results of this work are based on the synthesis of new compounds of carbothioamide, thiazolidin-4-one, [1,3]oxazepine-4(3H),1,3,4-thiadiazole-2-thiol, 2-thioxoimidazolidin-4-one, Acetamide, with good yields derived from carbothioamide or 5-amino-1,3,4-thiadiazole-2-thiol and they were characterized by various spectral analyses.

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### Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

### Conflict of Interest

We have no conflicts of interest to disclose.

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