# Synthesis of Some New Schiff Bases and Reaction with Urea & Thiourea Derivatives from 2-Amino -1,3,4-thiadiazole-5-thiol

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## Abstract:

In this paper new Schiff bases and tetrazole derivatives of 2-Amino-1,3,4-thiadiazole- 5-thiol have been prepared.2-Amino-1,3,4-thiadiazole-5-thiol was prepared by the reaction of thiosemicarbazide with carbon disulfide in alcoholic sodium carbonate solution .The new Schiff bases derivatives [2_5] were prepared by condensation of aldehyde group with 2-Amino-1,3,4-thiadiazole-5-thiol (P-Nitrobenzeldehyde ,M-Nitrobenzeldehyde, P-Hydroxybenzeldehyde, , 4-Hydroxy 3-Methoxy benzeldehyde) . The resulting Shiffbase were

Reaction with acetic anhydride [6-9] and this derivatives reaction with urea and thiourea intetrahydrofuran{10-17}.

All new synthesized derivatives were identified by their melting points, and FT-IR,U.V spectra. Some products were identified in elemental analysis and Chledal analysis .They have long been known to possess hypnotics activities and it is hoped that our compounds would do so.

## Introduction

Thiadiazole represents a group of heterocyclic whose derivative are very important in industrial, medicine, and agriculture (1,2). These compounds contain a five member diunsaturated ring structure consisting of two nitrogen atoms and one sulfur atom.

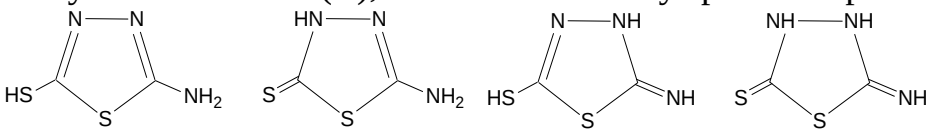
Thiadiazole present almost in four parent compounds as below:-

[1,3,4]Thiadiazole [1,2,5]Thiadiazole [1,2,4]Thiadiazole [1,2,3]Thiadiazole

Fig(1-1)

These compounds have a considerable published work and best intensive study (3,4).

AMT is capable of existing in four tautomeric forms and exist predominately in thione form (II), as demonstrated by spectroscopic study.



I II III IV

Fig (1-2) The four tautomeric forms of AMT

The chemical shift of the C-2 (13C-NMR) represents the chemical shift characterstic of carbon atom of a thione group, and also in the HNMR spectrum, NH can be observed as NH of thioamide (13.2-14 ppm) instead of thiol (SH) group (2.0 - 4.0 ppm).(5,6,7)

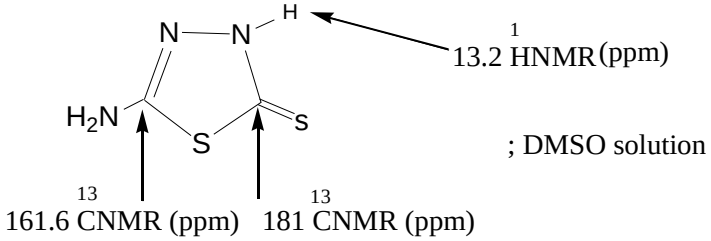
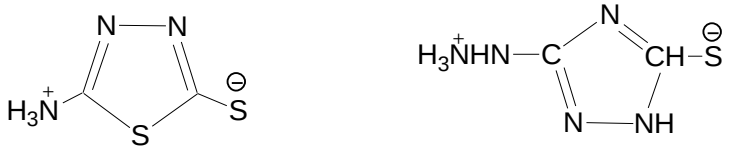



Fig (1-3)

The structure of AMT can also be represented by zwitter ionic form such as (V) since the reviews of hydrogen bonding showed the capabilities of sulfur to exist in zwitter ionic tautomeric forms(8) (VI).



**V** **VI**

In the literature (5,6,7), 2- amino -5- mercapto -1,3,4- thiadizole (AMT) possesses other chemical names such as 5-amino-1,3,4- thiadiazol-2-thiol (I) and 5- amino-3H-1,3,4- thiadiazole-2- thione (II), with molecular formula of C2H3N3S2 .

Schiff bases are prepared by the acid-catalyzed condensation of primary amines , with aldehydes.These derivatives are well known to have a wide range of biological activities such as antiviral, antibacterial, antifungal, anticonvulsant and anticancer [9]. Urea was the first synthesized organic compound, it was artificially synthesized in synthetic laboratory by Wohler

in 1828. Urea is synthesized in the body of many organisms as part of the urea cycle. Urea production occurs in the
liver and found in the urine of mammals, dissolved in blood, plants, birds, yeast and many microorganisms.[10]

## Experimental Chemicals

The following chemicals have been used in this work according to their manufactures .

**Table(1) : Chemicals and their manufactures**

| Chemicals | Supplied |
|---|---|
| Thiosemicarbazide | Fluka |
| Sodium carbonate(anhydrous) | BDH |
| Carbon disulfide | Fluka |
| Conc.Hydrochloric acid | Merck |
| Acetic anhydride | BDH |
| Sodium hydroxide | BDH |
| Ethanol(absolute) | BDH |
| Glacial acetic acid | BDH |
| P-Nitrobenzeldehyde | Fluka |
| Urea | BDH |
| Thiourea | BDH |
| M- Nitrobenzeldehyde | Fluka |
| 4-Hydroxy 3- Methoxy | Merck |
| Tatrahydrofuran | BDH |

**General Notes**

All solvents used were redistilled. Thin layer chromatography were performed on asilica-gel SG - 40 (Merck). Spots were visualized with iodine vapour. The melting points were determined with Stuart Melting Point Apparatus. The FT-IR spectra were recorded on FT - IR - 8000S, Schimadzu-Spectrophotometer and using KBr discs.Elemental analysis measured on EA7708 University of Kufa elemental analyzer.

## Preparation Methods:

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

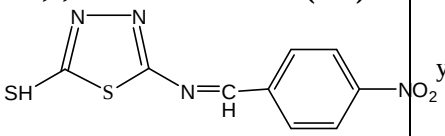
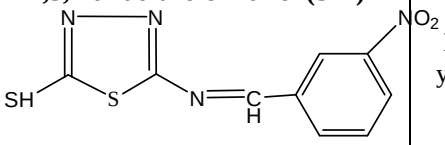
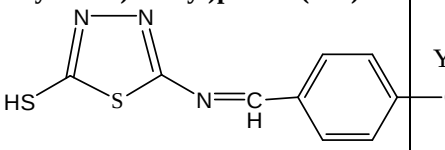
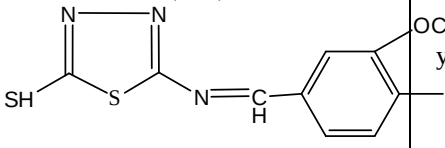
A solution of thiosemicarbazide (2g , 0.021 mol) and any sodium carbonate (1.059 g , 0.01 mol) in ethanol was placed in 250cm 3round bottomed flask fitted with reflux condenser. Carbon disulfide (4.712 g, 0.02 mol) was then added and the mixture was stirred for 1h. at room temp. after being refluxed for 7h , the reaction mixture was then allowed to cool and most of the solvent removed via evaporization under reduced pressure by rotary evaporator. Water (60cm3) was added to the residue and the mixture

acidified carefully by conc hydrochloric acid. The crude pale yellow residue was filtered and washed with distil. Cold water , then recrystallized from ethanol to give pale greenish-yellow needs of 2-amino- 5-mercapto – 1,3,4 - thiodiazole (1.6 g . 80%) m.p. 230 – 232C˚

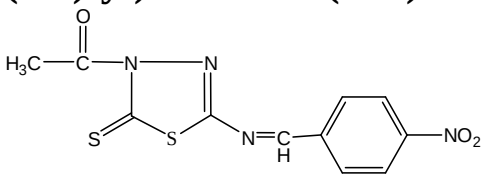
## General Synthesis of compound 2-5

An ethanolic solution (20 cm3) of aldehyde (0.01 mol) catalyzed by a few drops of acetic acid was stirred in a round bottomed flask equipped with reflux condenser compound (No.1) (0.01mol) was added and reaction mixture was refluxed for 7h , the solvent was reduced by evaporation and the reaction mixture was filtered then recrystallized from ethanol to get crystals of the desired compound .

The following table No.(2) shows the physical properties and %ylede

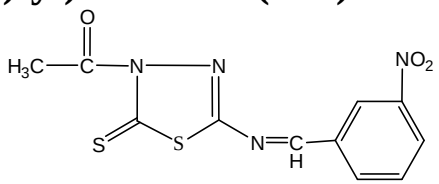
| No. of compound | Carbonyl compound / weight | Structure product | Color product | ylide % | MP C˚ |
|---|---|---|---|---|---|
| 2 | P-Nitrobenzeldehyde (1.87g , 0.01mol) | **5-(4-nitrobenzylideneamino)-1,3,4-thiadiazole-2-thiol (S21)**  | Dark yellow | 1.6g , 85% | 135-137C˚ |
| 3 | M-Nitrobenzeldehyde (1.87g , 0.01mol) | **5-(3-nitrobenzylideneamino)-1,3,4-thiadiazole-2-thiol (S22)**  | Light yellow | 1.68g, 89% | 118-120 C˚ |
| 4 | P-Hydroxybenzeldehyde (1.22g , 0.01mol) | **4-((5-mercapto-1,3,4-thiadiazol-2-ylimino)methyl)phenol (S23)**  | Yellow | 1g , 81% | 88-90 C˚ |
| 5 | 4- Hydroxy-3-Methoxy benzeldehyde (1.52g , 0.01mol) | **4-((5-mercapto-1,3,4-thiadiazol-2-ylimino)methyl)-2-methoxyphenol (S26)**  | Dark yellow | 1.2g , 78% | 184-186 C˚ |

## 6. Synthesis of 1-(5-(4-nitrobenzylideneamino)-2-thioxo-1,3,4-thiadiazol-3(2H)-yl)ethanone (S59)



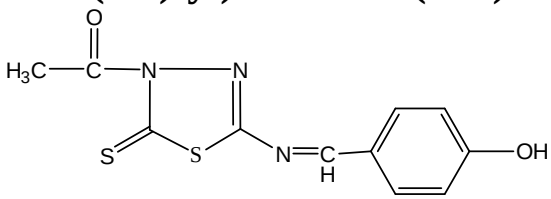
A mixture compound No. (2) (2.66g , 0.01mol ) with acetic anhydride (1.00g, 0.01mol) in THF (20cm3) was refluxed with stirring for 3h. Then the reaction mixture was concentrated by evaporation part of the solvent and cooled to room temperature filtered of and recrystallization from ethanol gave yellow crystals of compound (No. 59) 1.5 g ,59% , M.P.86 - 88 C˚.

## 7. Synthesis of 1-(5-(3-nitrobenzylideneamino)-2-thioxo-1,3,4-thiadiazol-3(2H)-yl)ethanone (S60)



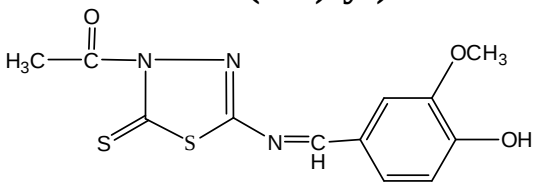
A mixture compound No. (3) (2.66g, 0.01mol ) with acetic anhydride (1.00g, 0.01mol) in THF (20cm3) was refluxed with stirring for 3h. Then the reaction mixture was concentrated by evaporation part of the solvent and cooled to room temperature filtered of and recrystallization from ethanol gave brown crystals of compound (No. 60) 1.6g ,60% , M.P. 180C˚.

## 8. Synthesis of 1-(5-(4-hydroxybenzylideneamino)-2-thioxo-1,3,4-thiadiazol-3(2H)-yl)ethanone (S61)



A mixture compound No. (4) (2.73g, 0.01mol ) with acetic anhydride (1.00g, 0.01mol) in THF (20cm3) was refluxed with stirring for 3h. Then the reaction mixture was concentrated by evaporation part of the solvent and cooled to room temperature filtered of and recrystallization from ethanol gave a yellow crystals of compound (No. 61) 1.65g , 61% , M.P. 110-112C˚.

## 9. Synthesis of 1-(5-(4-hydroxy-3-methoxybenzylideneamino)-2-thioxo-1,3,4-thiadiazol-3(2H)-yl)ethanone (S62)

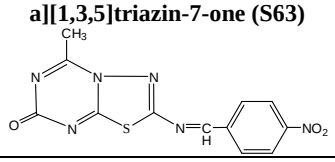
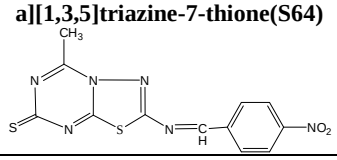
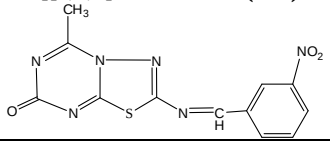


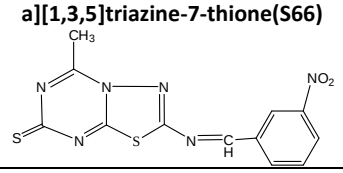
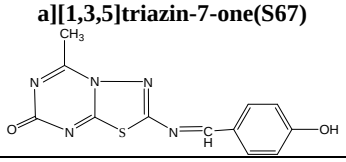
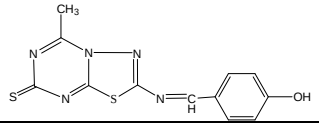
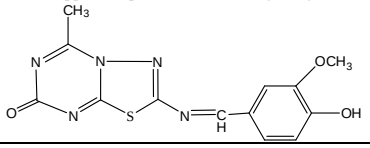
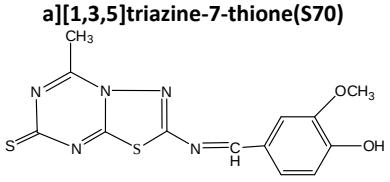
A mixture compound No. (5) (2.67g, 0.01mol ) with acetic anhydride (1.00g, 0.01mol) in THF (20cm3) was refluxed with stirring for 3h. Then the reaction mixture was concentrated by evaporation part of the solvent and cooled to room temperature filtered of and recrystallization from ethanol gave a brown crystals of compound (No. 62) 1.0 g , 75% , M.P. 120-122C˚.

## General Synthesis of compound 10 -17

A mixture compound (0.01mol) with urea 0.01mol and thiourea 0.01mol in THF (20cm3) was refluxed with stirring for 3h. Then the reaction mixture was concentrated by evaporation part of the solvent and cooled to room temperature filtered of and recrystallization from ethanol gave crystals of desired compound.

The following table No.(3) shows the physical properties and %ylede

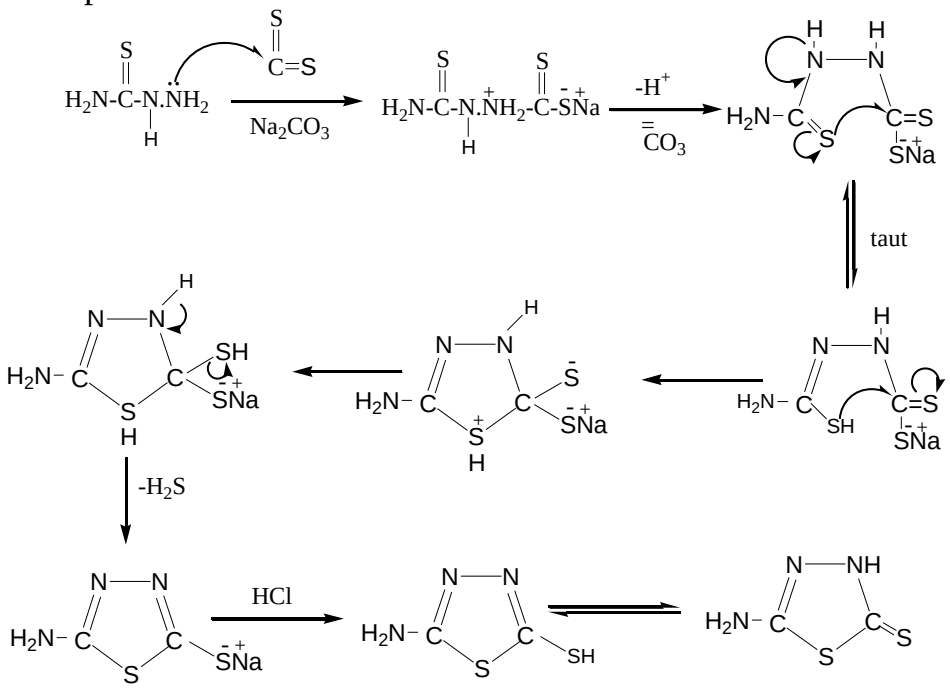
| No. | Starting material /Weight | Urea weight | Thiourea weight | Structure product | Color product | Solvent recrystallization | MP C˚ |
|---|---|---|---|---|---|---|---|
| 10 | 6 3.08g – 0.01mol | 6.0g 0.01mol | | **5-methyl-2-(4-nitrobenzylideneamino)-7H-*[1,3,4]*thiadiazolo[3,2-a][1,3,5]triazin-7-one (S63)**  | Light Yellow | Ethanol | 118-120 |
| 11 | 6 3.08g – 0.01mol | | 7.6g 0.01mol | **5-methyl-2-(4-nitrobenzylideneamino)-7H-[1,3,4]thiadiazolo[3,2-a][1,3,5]triazine-7-thione(S64)**  | White | Ethanol | 125 |
| 12 | 7 3.08g – 0.01mol | 6.0g 0.01mol | | **5-methyl-2-(3-nitrobenzylideneamino)-7H-[1,3,4]thiadiazolo[3,2-a][1,3,5]triazin-7-one(S65)**  | Brown | Ethanol | 108-110 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 13 | 7<br>3.08g –<br>0.01mol | | 7.6g<br>0.01mol | **5-methyl-2-(3-nitrobenzylideneamino)-7H-[1,3,4]thiadiazolo[3,2-a][1,3,5]triazine-7-thione(S66)**  | Light Brown | Ethanol | 170-172 |
| 14 | 8<br>2.79g –<br>0.01mol | 6.0g<br>0.01mol | | **2-(4-hydroxybenzylideneamino)-5-methyl-7H-[1,3,4]thiadiazolo[3,2-a][1,3,5]triazin-7-one(S67)**  | Light yellow | Ethanol | 98-100 |
| 15 | 8<br>2.79g –<br>0.01mol | | 7.6g<br>0.01mol | **2-(4-hydroxybenzylideneamino)-5-methyl-7H-[1,3,4]thiadiazolo[3,2-a][1,3,5]triazine-7-thione(S68)**  | Yellow | Ethanol | 124-126 |
| 16 | 9<br>3.09g –<br>0.01mol | 6.0g<br>0.01mol | | **2-(4-hydroxy-3-methoxybenzylideneamino)-5-methyl-7H-[1,3,4]thiadiazolo[3,2-a][1,3,5]triazin-7-one(S69)**  | Light Green | Ethanol | 120-122 |
| 17 | 9<br>3.09g –<br>0.01mol | | 7.6g<br>0.01mol | **2-(4-hydroxy-3-methoxybenzylideneamino)-5-methyl-7H-[1,3,4]thiadiazolo[3,2-a][1,3,5]triazine-7-thione(S70)**  | Light yellow | Ethanol | 158-160 |

## Results and Discussion

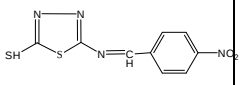
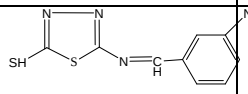
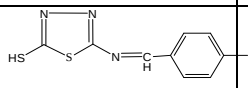
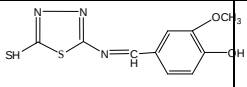
Schiff bases can be prepared via a condensation reaction between primary amines with aldehydes, therefore we prepared 2-Amino-1,3,4-thiadiazole-5-thiol, by the reaction of thiosemicarbazide with carbon disulfide in alcoholic sodium carbonate solution . The new Schiff bases derivatives [2-5] were prepared by condensation of aldehyde group with 2-Amino-1,3,4-thiadiazole-5-thiol, P-Nitrobenzeldehyde ,M-Nitrobenzeldehyde, P-Hydroxybenzeldehyde, , 4-Hydroxy 3-Methoxy benzeldehyde) .

Compound [1] showed identical melting point also characterized with FT-IR spectrum which showed the following characteristic bands: the two bands at 3398cm-1 and 3278cm-1 were due to asymmetric and symmetric stretching vibrations of (-NH2) group respectively an absorption band at 3089cm-1 was due to the (-NH) stretching vibration (tautomeric form). The absorption bands at 2916cm-1 and 2773cm-1 were attributable to the intramolecularly hydrogen bonded of (-NH) group The (-SH) stretching band found as very weak shoulder at 2600cm-1. A band at 1600cm-1 was due to the (C=N) stretching vibration of the thiadiazole ring moiety. The sharp bands at 1535cm-1 and1496cm-1 are due to the (-NH) bending and (C-N) stretching vibrations respectively. Also, the absorption bands at (1226, 1172)cm-1 are due to the presence of (=N-N-C-) cyclic grouping (28 ). Moreover, the absorption band at 1070cm-1 for the (C=S) group stretching vibration gives evidence that compound [1] can exist in two tautomeric forms, thiol form and thion form Beside this, the band at 750cm-1due to (C-S) bond stretching is good evidence for the structure given to the product.

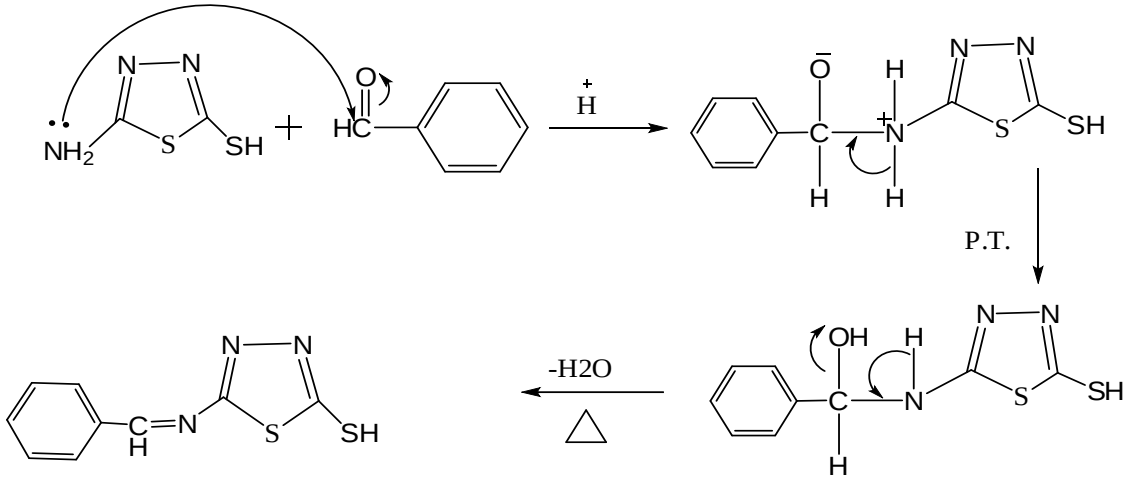



Scheme (1)

FT.IR & U.V spectrum of compound [2-5] showing in the table (4)

| No. of com. | Structure | C=N cm-1 | N-H | C=C | C-H cm-1 Aram. | C-H cm-1 Aliph. | S-H cm-1 | C-S cm-1 | Other | Peak | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | λmax nm | Abs |
| 2 |  | 1517 | 3415 | 1442 | 2968 | 2773 | 2364 | 661-617 | NO2 1442-1300 | 218 249-288-370 | 3.641-0.721-1.450-0.210 |
| 3 |  | 1703-1614 | 3263 | 1481 | 3082 | 2059 | 2362 | 725-690 | NO2-1481-1317 | 210-255-391 | 3.54-0.762-o.213 |
| 4 |  | 1670-1643 | 3251 | 1562 | 3178 | 2607 | 2808 | 667-664 | OH-3410 | 210-260-340 | 2.44-0.75-0.312 |
| 5 |  | 1700-1610 | 3109 - 3089 | 1587 - 1554 | 3000 | 2775 | 2790 | 750-640 | OH-3450 | 215-250-295-350 | 2.16-065-0.45-0.27 |

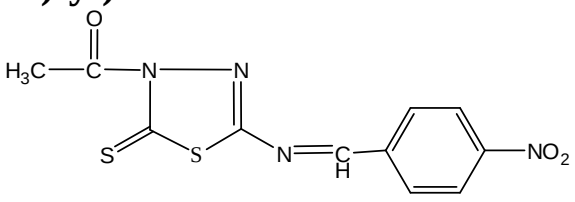
Chledal analysis N%ForComp.3,Caicd.21,05%.Found;21,49%.



Scheme (2)

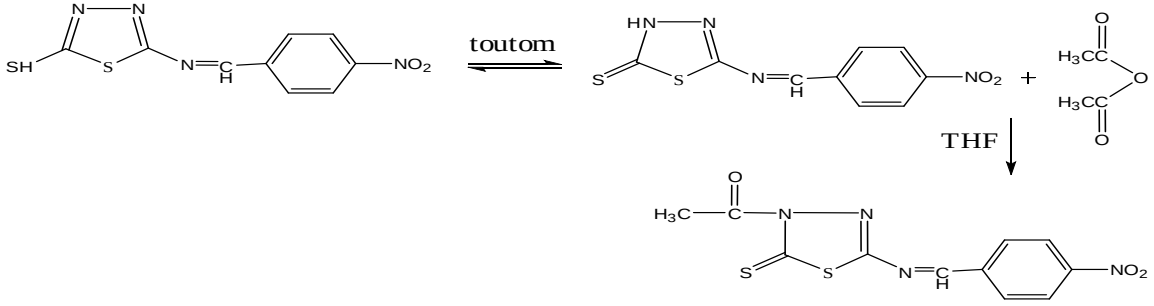
FT-IR spectrum of Schiff bases derivatives of compounds [2-5] showed appearance of absorption bands due to the exocyclic imine group stretching vibration υ(C=N) at (1517cm-1703cm-1,1670cm-1, 1700cm-) respectively .

## 6. Synthesis of 1-(5-(4-nitrobenzylideneamino)-2-thioxo-1,3,4-thiadiazol-3(2H)-yl)ethanone.



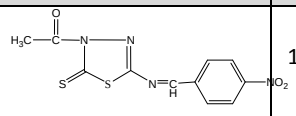
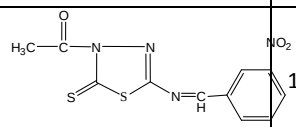
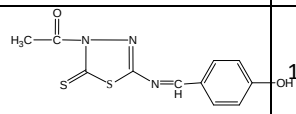
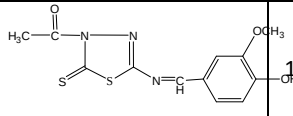
On following:

- The reaction of compound No.(2) with 1mol acetic anhydride to give the compound [6]
- The reaction of compound No.(3) with 1mol acetic anhydride to give the compound [7]
- The reaction of compound No.(4) with 1mol acetic anhydride to give the compound [8]
- The reaction of compound No.(5) with 1mol acetic anhydride to give the compound [9].
- The mechanistic path of this reaction is discussion as in scheme (59)



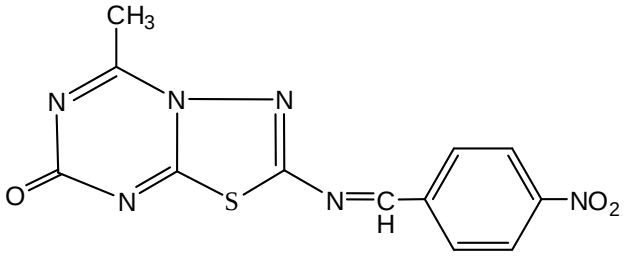

Scheme 3

**FT.IR & U.V spectrum of compound [59- 62] showing in the table (5 )**

| No. of com. | Structure | C=N str. | C=O str. | N-N Str. | C=C str. | C=S cm-1 | CH cm-1 Alip | C-H cm-1 Arm. | C-S cm-1 | Other | Peak | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | λmax nm | Abs |
| 6 |  | 1770 | 1740 | 1496 | 1404 | 1271 | 2652 2526 | 2987 | 675 | C-$NO_2$ 1200 | 234-237 | 1.5-0.36 |
| 7 |  | 1654 | 1597 | 1531 1504 | 1442 | 1273 1238 | 2939 2839 | 3008 2970 | 675 | C-$NO_2$ 1217 | 250-254 | 1.5- 0.2 |
| 8 |  | 1685 | 1637 | 1585 | 1404 | 1271 | 2998 | 2869 | 675 | C-OH 3200 | 266 275 | 2.2 0.2 |
| 9 |  | 1762 | 1654 | 1593 1504 | 1384 | 1238 | 2873 2839 | 3006 2966 | 675 | C-OH 3450 | 288-295 | 2.5 2.5 |

Anai.Calcd.for ,8, $C_{11}H_5N_2O_2S_2$:
C,50,57;H,1,91;N,10,72%;Found;C,50,00;H,2,05;N,10,06

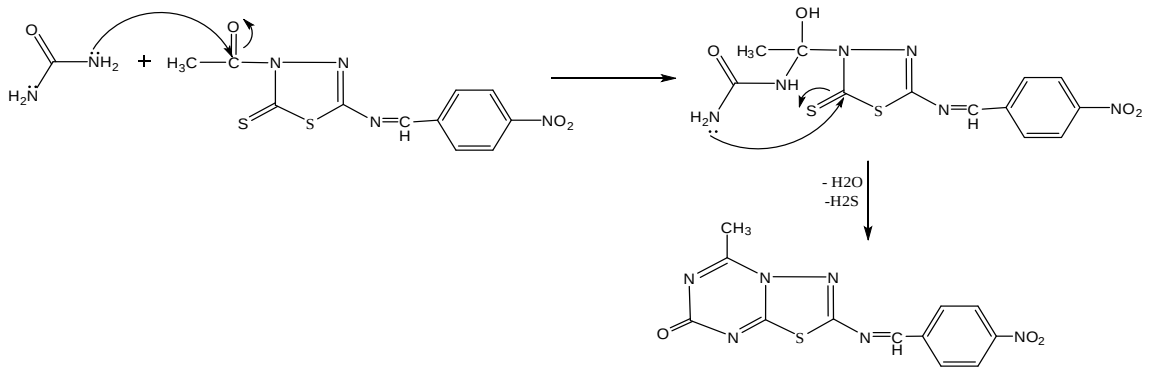
10 − **Synthesis of 5-methyl-2-(4-nitrobenzylideneamino)-7H-[1,3,4]thiadiazolo[3,2-a][1,3,5]triazin-7-one.**



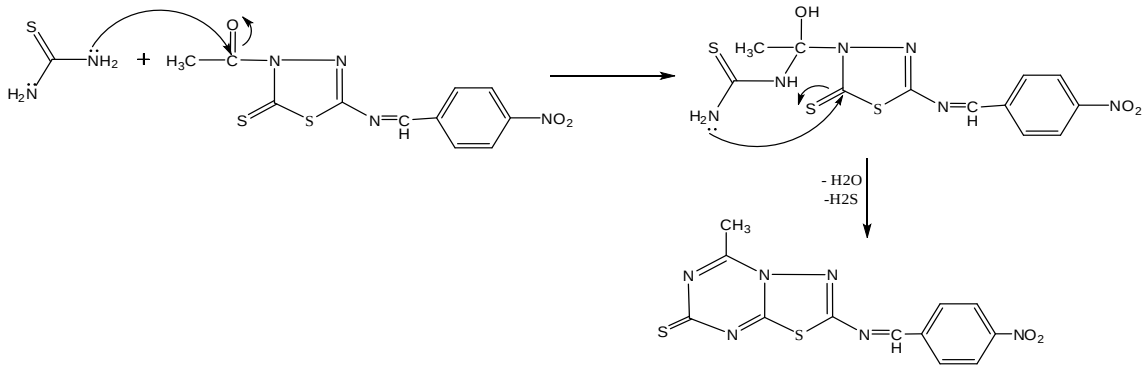

On following:

- The reaction of compound No.(6) with 1mol urea to give the compound [10]
- The reaction of compound No.(6) with 1mol thiourea to give the compound [11]
- The reaction of compound No.(7) with 1mol urea to give the compound [12]
- The reaction of compound No.(7) with 1mol thiourea to give the compound [13].
- The reaction of compound No.(8) with 1mol urea to give the compound [14].
- The reaction of compound No.(8) with 1mol thiourea to give the compound [15].
- The reaction of compound No.(9) with 1mol urea to give the compound [16].
- The reaction of compound No.(9) with 1mol thiourea to give the compound [17].
- The mechanistic path of this reaction is discussion as in scheme (4)

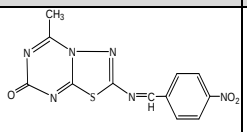
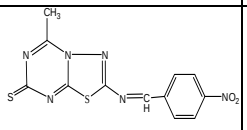
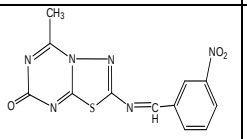
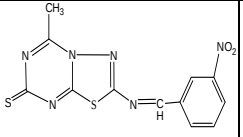
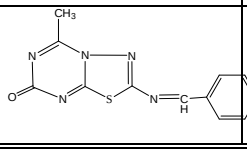
MECHANIZEM COPMOUND WIH UREA

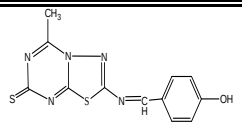
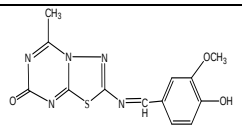
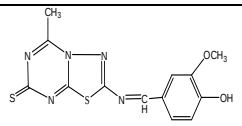


MECHANIZEM COPMOUND WIH THIOUREA



FT.IR & U.V spectrum of compound [10- 17] showing in the table (6 )

| No. of com. | Structure | C=N str. | C=O str. | N-N Str. | C=C str. | C=S cm-1 | CH cm-1 Alip | C-H cm-1 Arm. | C-S cm-1 | Other | Peak | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | λmax nm | Abs |
| 10 |  | 1683 | 1623 | 1465 | 1419 | 1155 | 2787 | 3253 3232 | 788 | C-NO2 1151 | 194- 305- 332 | 2.668 0.01. 0.01 |
| 11 |  | 1697 | 1694 | 1419 | 1311 | 1201 | 2879 2854 | 3170 2933 2906 | 638 | C-NO2 1176 | 210- 315 | 2.8 0.1 |
| 12 |  | 1718 1685 | 1647 1623 | 1583 1550 | 1492 1465 | 1377 1290 | 2802 | 3232 | 671 644 | C-NO2 1153 1128 | 259- 379 | 3.984 1.780 |
| 13 |  | 1616 | 1590 | 1473 | 1413 | 1300 | 3095 | 3172 | 632 | C-NO2 1085 | 266- 359 | 3.6 1.829 |
| 14 |  | 1683 | 1623 1600 | 1465 | 1419 | 1338 | 2767 | 3118 | 788 | C-OH 3440 3344 | 215- 219- 239- 285 | 3.68 3.275 1.259 1.293 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 15 |  | 1618 | 1550 | 1473 | 1411 | 1300 | 2968 | 3172<br>3062 | 730<br>630 | C-OH<br>3375<br>3271 | 244-<br>348 | 3.2<br><br>1.2 |
| 16 |  | 1676 | 1623<br>1604 | 1465 | 1400 | 1300 | 2800 | 3222 | 768 | C-OH<br>3436<br>3342 | 254<br><br>279 | 3.185<br>2.001 |
| 17 |  | 1618 | 1550 | 1473 | 1413 | 1300 | 2677 | 3176<br>3095<br>3026 | 730 | C-OH<br>3375<br>3278 | 233-<br>298-<br>309-<br>351 | 3.58<br>3.273<br>.2.08<br>0.8 |

Anai.Calcd.for ,14, $C_{12}H_9N_5O_2S_1$:
C,50,17;H,3, 13;N,24,39%;Found;C,50,00;H,2,98;N,25,00

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الخلاصة :

تم في هذه البحث تحضير قواعد شيف جديدة و المشتقات تترازول من 2 – امينو،1،3،4 – ثاياداياازول –5–ثايول تم تحضير المركب 2 – امينو،4،3،1 – ثاياداياازول –5–ثايول من تفاعل ثايوسيمي كاربازيد مع ثنائي كبريتد الكاربون في

محلول كحولي من كاربونات الصوديوم قواعد شف المحضرة من(2–5) بواسطة التكثيف مجموعة مع 2 – امينو،4،3،1 – ثاياداياازول –5 –ثايول (بارانتروبنزالديهيد ، ميتانتروبنزالديهيد ، بارهيدروكسي الدهايد بنزالديهيد ، ،4_هيدروكسي–3– ميثوكسي بنزالديهيد) قواعد شف الناتجة تم تفاعلها مع انهدريد الخليك (6–9) المشتقات الناتجه تدخل تفاعل مع اليوريا والثايويوريا في تتراهيدروفيوران المشتقات الناتجةتعطي المشتقات (10–17 ) تم تشخيص جميع المشتقات الناتجة عن طريق مطيافيه الأشعة تحت الحمراء ومطيافيه الأشعة فوق البنفسجية بعض المشتقات تم تشخيصها بواسطه تحليل العناصر وتحليل كليدال يتوقع ان تمتلك هذه المشتقات فعالية حيوية.