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1,3,4-Thiadiazole: Their sugar and isoindole derivatives and Biological activities.

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Abstract: Heterocycles are compounds containing five triple or quaternary cyclic atoms of N, O, S. They have distinctive features that show their importance in many pharmaceutical formulations used in medicinal chemistry. Therefore, heterocycles are of great importance to chemists working in medicine for the development of the chemical field as well. 1,3,4-Thiadiazole has become an important building block in organic synthesis due to its wide range of natural substances. Therefore, scientists have paid attention and studied the biological activity of 1,3,4-thiadiazole. 1,3,4-Thiadiazoles derivatives and their activity against cancer and also against microbes were evaluated as 1,3,4-thiadiazole sulfonamides, as an example, which were evaluated extensively, and it was found that compounds containing the sulfonamide part are effective as virus inhibitors.

Keywords: 1,3,4-Thiadiazole; Heterocyclic compounds; anticancer activity; antimicrobial activity; glycosides; MCF -7

1.1 Heterocycles compounds

Five membered heterocyclic compounds consist of five cyclic atoms with three or four N, O, S heteroatoms.[1] Heterocyclic compounds constitute about 65% of the organic chemistry literature because of their great importance in our life.[2] Recently, interest in heterocyclic chemistry has increased because of its great importance in various fields, including medicine, pharmacology, agricultural chemistry, biology, and chemical industries[3] Examples of heterocyclic compounds are furan derivatives, thiophenes isoandoles pyrroles, isoxazoles thiazoles, imidazoles, oxadiazoles, triazoles and tetrazole[4]. Where some of these compounds were studied and gave biological activity against cancer, antibacterial and antimicrobial[5].

1.2. 1,3,4-Thiadiazole compounds

Thiadiazoles are among the important classes of heterocyclic compounds, which have become of great interest in research due to their biological activity. Thiadiazoles are a pentacyclic system that contains a hydrogen bonding domain, a sulfur atom, and a two-electron donor nitrogen system that exhibits a range of biological activities that occur in four types. Naturally compatible forms are 1, 2, 3-thiadiazole, 1, 2, 5-thiadiazole, 1, 2, 4-thiadiazole and 1, 3, 4-thiadiazole[6] Fig

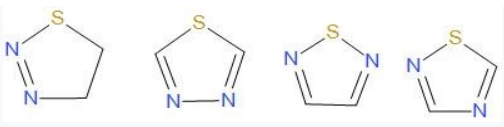


Fig.1. Thiadiazole structures.

On the other hand, indazole scaffolds were found it was found that the compounds of indazole are clear with a wide range of drugs Recently, a series of indazole derivatives have been described with remarkable biological activities. In addition, the indazole moieties constitute a class of pharmacologically active molecules that appear with a wide range of biological actions, including anti-inflammatory, antimicrobial, antibacterial, antifungal activity and antitumor activities, inhibition of the protease enzyme of HIV and anticancer activitie. In this part, the activity of thiadiazole and indazoles in medicinal chemistry was discussed[7-11] Fig

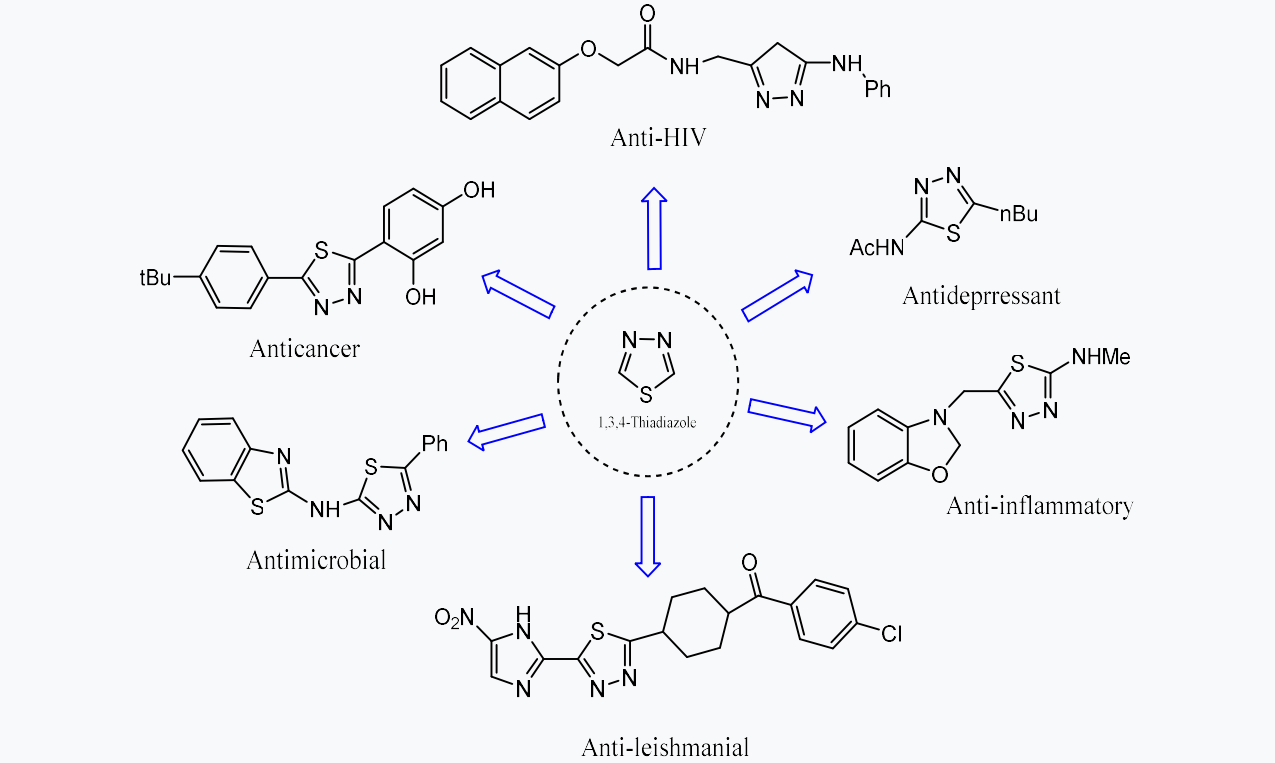


Fig.2. Importance of 1,3,4-thiadiazole cores

1.3. Carbohydrates

1.3.1 Carbohydrates classification:

Carbohydrates are important in various areas and their important role is evident in a variety of biological processes [12]. It is also characterized by its abundance in nature.[13] Carbohydrates are divided into two types: simple and complex carbohydrates, which contain starches and fiber. Examples of monosaccharides are glucose, fructose, galactose, and thedisaccharides lactose, sucrose, and maltose. Polysaccharides are divided according to the number of carbohydrate units, which are two categories of monosaccharides, tetra and pentose[14] an example of them is D-ribose, hexoses, D-glucose 2, heptoses, etc[15] Fig

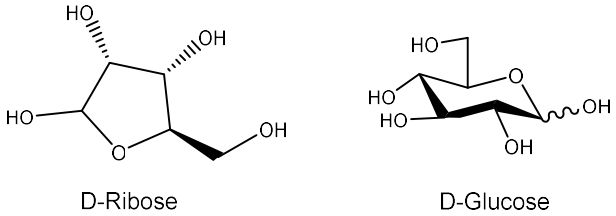


Fig.3.Biologically important monosaccharides

1.3.2 Carbohydrates and their biological activities:

Carbohydrates are the most basic source of energy and are among the most important, most abundant and structurally complex biomolecules in nature[16] Carbohydrates are characterized by their ability to bind to the surface of the cell, where the monosaccharide units are linked by glycosidic bonds forming multiple sugars that have biological activities, as they began to be developed on a large scale due to their great importance in the pharmaceutical industry[17] and in how important they are in the field of medicine, including antimicrobial[18,19], antitumor[20,21]and antioxidant[22] and anti-inflammatory[23].

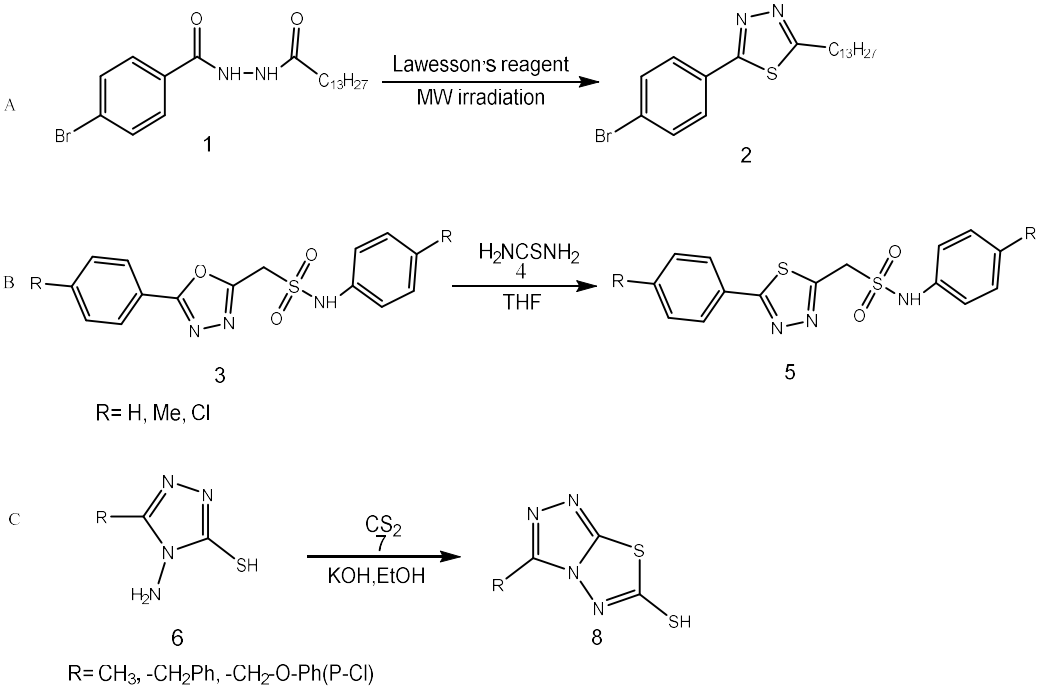
1.4 Synthesis of 1,3,4-Thiadiazole:

There are many ways to prepare 1,3,4-thiadiazole, including:

1.4.1 *From* Acylhydrazines:

1.4.1.1 From diacylhydrazine:

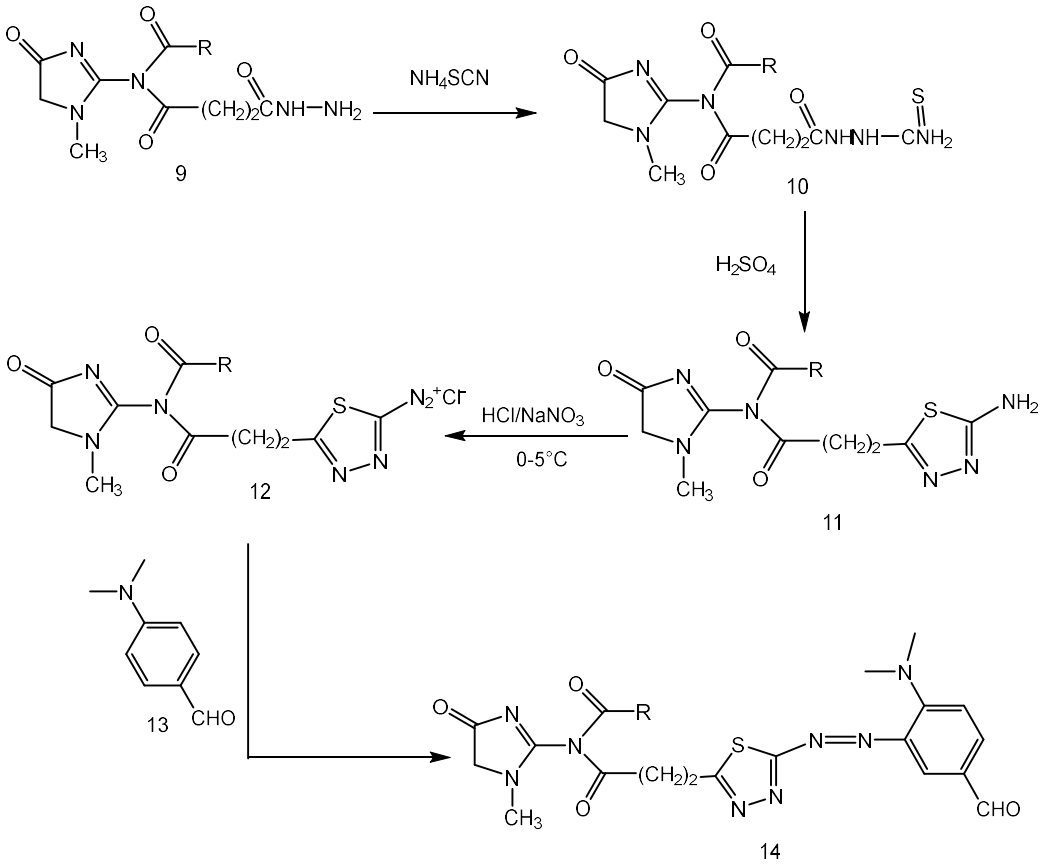
Synthesis of 1,3,4-thiadiazole by a one-pot reaction between a diacylhydrazine using Lawesson's reagent by microwave- irradiation see Sch.1A. Besides, 1,3,4-oxadiazole was reacted with thiourea in the presence of THF to obtain 1,3,4-thiadiazole which is a simple and high yield method Sch.1B. In addition, compound 8 was prepared from the reaction of 4-amino-5-mercapto-1,2,4-triazole with CS_2 [24] see Sch.1C.



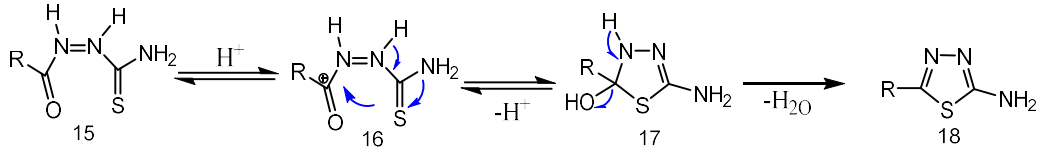
Sch.1. Illustrative methods for synthesis of thiadiazoles

1.4.1.2 From acid hydrazides:

Compound **10** is prepared by from ammonium hydrazide thiocyanate in the presence of concentrated hydrochloric acid using ethanol solvent and reflux for 20 hours and the mechanism of synthesis 1,3,4-thiadiazole[25] Sch.3.



Sch. 2. All synthesis compounds **1-3**

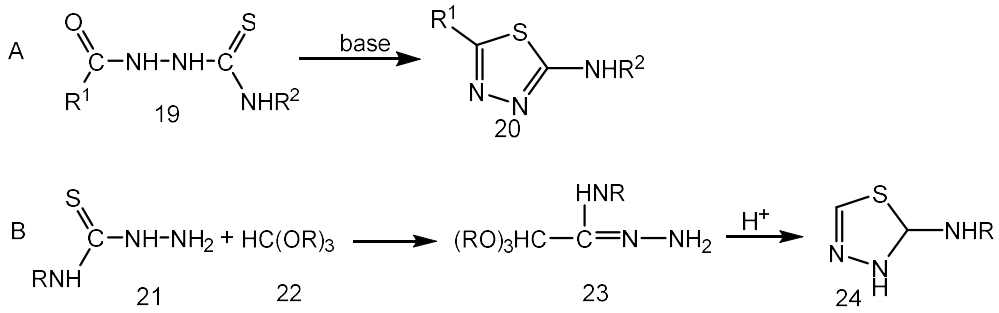


Sch. 3. The mechanism of synthesis 1,3,4-thiadiazole

1.4.2 From Thiohydrazines:

1.4.2.1 From thiosemicarbazide:

The thiadiazole derivative **20-25** was prepared by the cyclization of a acylated thiosemicarbaziin the presence of an base medium, which in turn forms a single bond to cycle the compound see Sch.4. The synthesis of other simple mercapto-thiadiazoles is outlined in[26-28] Fig



Sch.4. Synthesis of thiadiazoles

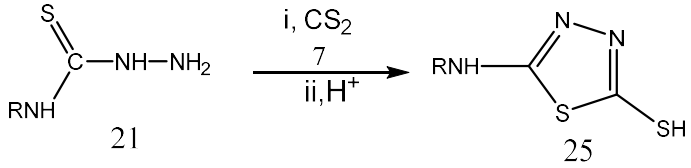
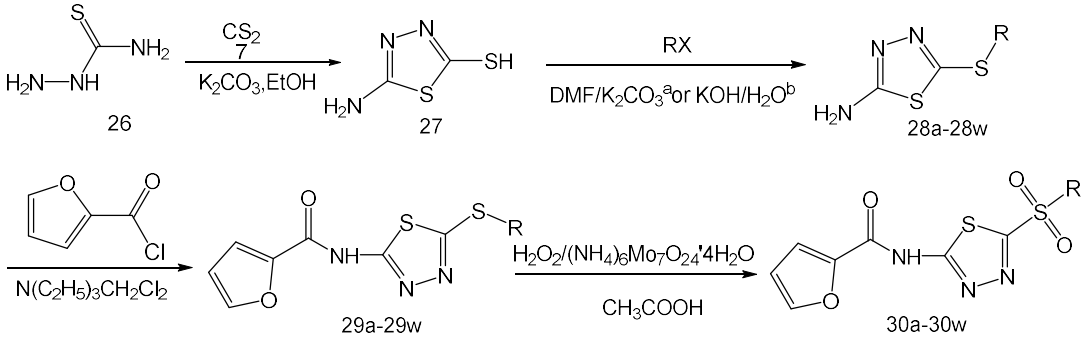


Fig.4. Synthesis of mercapto-thiadiazoles

Compound **27** was prepared by mixing anhydrous ethanol with an amount of thiosemicarbazide in the presence of K_2CO_3. then reacted with N, N -dimethylformamide and added with K_2CO_3 with types of alkyl halogens. In another way, compound **27** was reacted by dissolving it in water, then adding a certain amount of KOH with types of halogenated hydrocarbons[29-33] Sch.5.

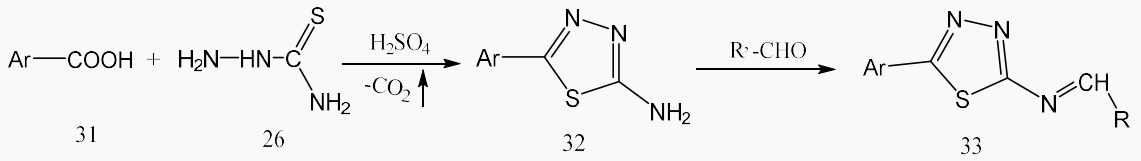


X=Cl,Br,I
a:R=CH_3
b:R=C_2H_5
c:R=$CH_2CH_2CH_3$
d:R=$CH(CH_3)_2$
e:R=$CH_2CH=CH_2$
f:R=$CH_2CH_2CH_2CH_3$
g:R=$CH(CH_3)CH_2CH_3$
h:R=$CH_2CHCH_3CH_2CH_3$
i:R=$CH_2CH_2CH_2CH_2CH_3$
j:R=$CH_2CH_2CH_2OCH_3$
k:R=$COOC_2H_5$
l:R=$C_6H_5CH_2$
m:R=$_2$-$CH_3C_6H_4CH_2$
n:R=$_3$-$CH_3C_6H_4CH_2$
o:R=$_4$-$CH_3C_6H_4CH_2$
p:R=3-$CH_3OC_6H_4CH_2$
q:R=$_2$-F-$C_6H_4CH_2$
r:R=$_3$-F-$C_6H_4CH_2$
s:R=$_4$-F-$C_6H_4CH_2$
t:R=$_4$-Cl-$C_6H_4CH_2$
u:R=$_4$-CN-$C_6H_4CH_2$
v:R=$_3$-CN-$C_6H_4CH_2$
w:R=$_4$-CF_3-$C_6H_4CH_2$

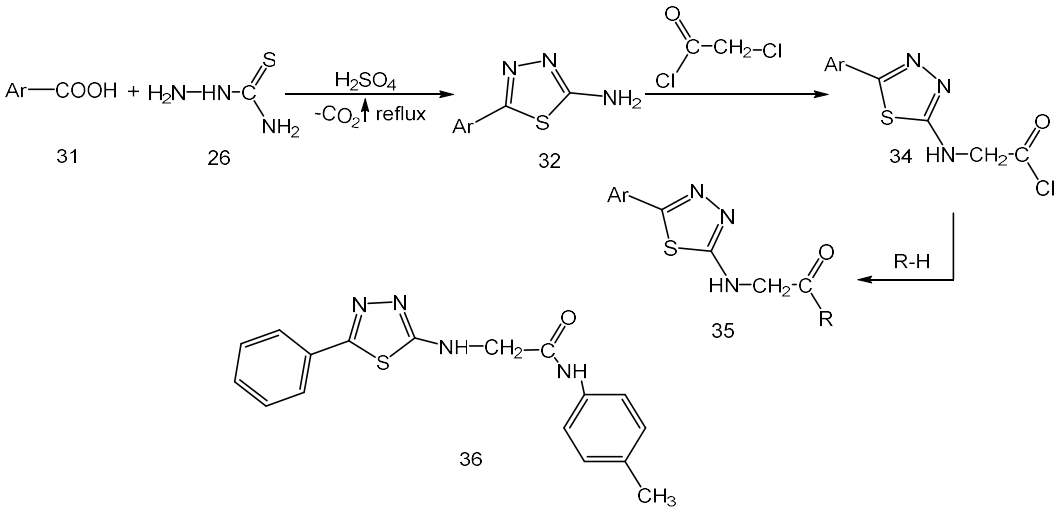
a.DMF/K_2CO_3: d, h, i, j: b.KOH/H_2O :a-c, e-g, k-w.

Sch.5.The synthetic route of the target compounds

In the first step, 2-amino-5-aryl-1,3,4-thiadiazole was prepared by reacting thiosemicarbazide with aryl carboxylic acid in the presence of a certain amount of concentrated sulfuric acid and reflexing it for 2 hours and then following it up with TLC, Sch.6. and 7. Synthesis of (5-aryl-1, 3, 4-thiadiazole-2-yl) acetamide by reacting the product of step 1(5-aryl-1, 3, 4-thiadiazole-2-amine) with acetyl chlorideusing irradiated in a microwave oven for 3 minutes at a strength of 40% at intervals of every 30 seconds after the end of the reaction. (5-phenyl-1, 3, 4-thiadiazole-2-ylamino)-N-p- tolylacetamide was also synthesized. Sch.7. It was taken from step 2 with a small amount of alcohol for an aryl derivative and reflexed it for 4 hours, then purified and recrystallized with water alcohol[34] Sch.7.



Sch.6. Synthesis of thiadiazole derivative



Sch.7. Synthesis of compound **35** and **36**

Preparation of 5-(4-fluoro-phenyl)-1, 3, 4-thiadiazole-2-yl) amine by reacting an equal amount of 4-fluorobenzoic acid with thiosemicarbazide in the presence of $POCl_3$ and reflexing it for 5 hours[35]

Fig

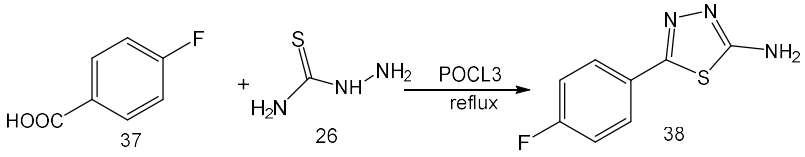


Fig.5.Synthesis [5-(4- fluoro-phenyl) - [1,3,4] thiadiazol-2-yl]-amine

1.4.2.2 From hydrazine hydrate:

Synthesis 1, 3, 4-thiadiazole-2,5-dithiol by reacting hydrazine hydrate with CS_2 using sodium hydroxide and sulfuric acid with good yield[36]

Fig

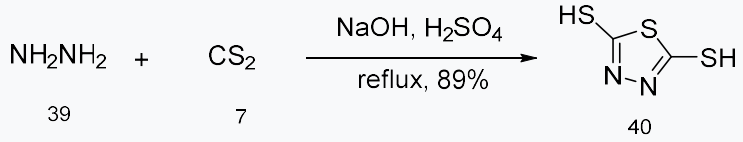
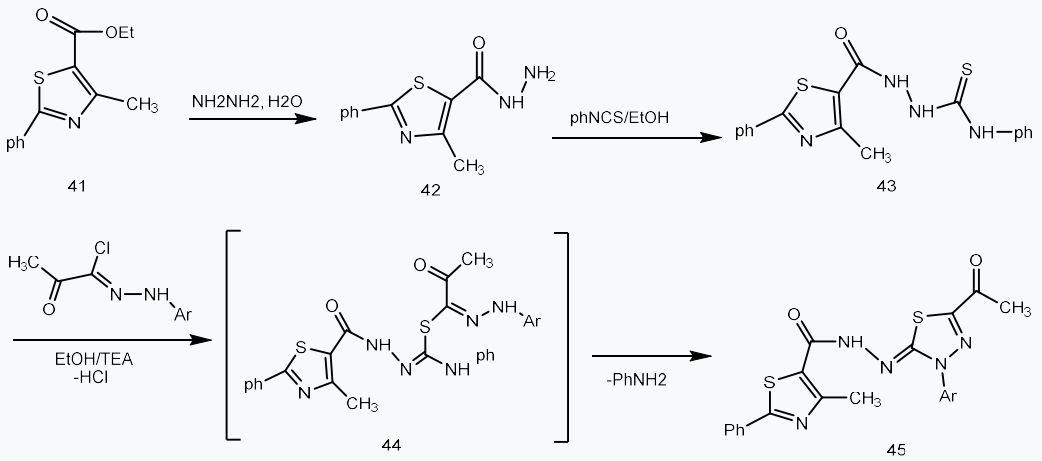


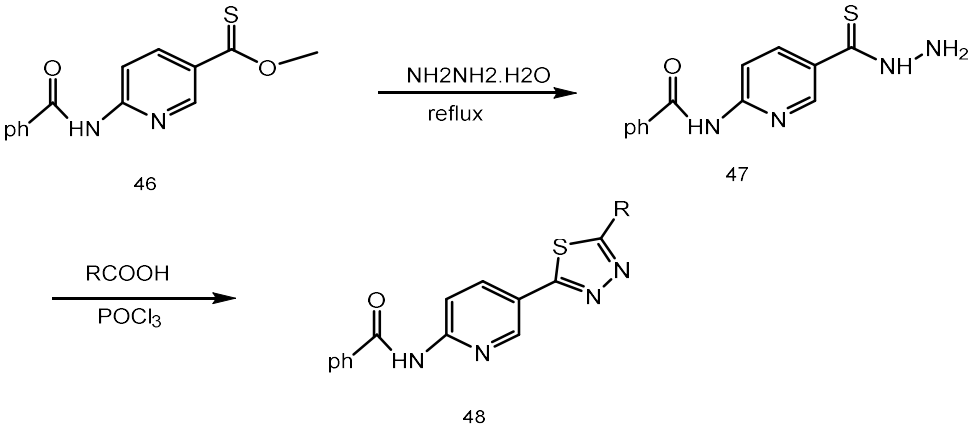
Fig.6. Synthesis 1,3,4-thiadiazole -2,5-dithiol

2-(4-Methyl-2-phenylthiazole-5-carbonyl)-N-phenylhydrazine carbothioamide **43** was prepared by the reaction of 4-methyl-2-phenylthiazole-5-carbohydrazide 42 with phenyl isothiocyanate using ethanol as a solvent. Compound **43** contains a hydrazine thioamide moiety as a side chain, which in turn reacts with many hydrazonoyl chlorides by deacetylation of hydrochloric acid in the presence of ethanol and TEA to give an unstable intermediate **44** followed by intramolecular cyclization and elimination of aniline molecule to give the respective thiadiazole derivatives45[37] Sch.8.



Sch.8. Synthesis of 1,3,4-thiadiazole derivatives from hydrazine hydrate.

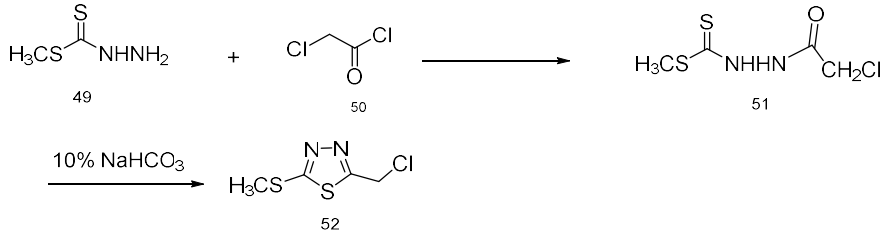
O-Methyl-6-(benzamido)pyridine-3-carbothioate **46** was reacted with hydrazine hydrate and methanol and refluxed for 5 hours to give compound47. Then compound b was treated with aryl acid in the presence of phosphoryl chloride to give compound **48** [38] Sch.9.



Sch. 9. Synthesis of Pyridine-based-thiadiazole analogues

1.4.2.3 From Dithiocarbazate:

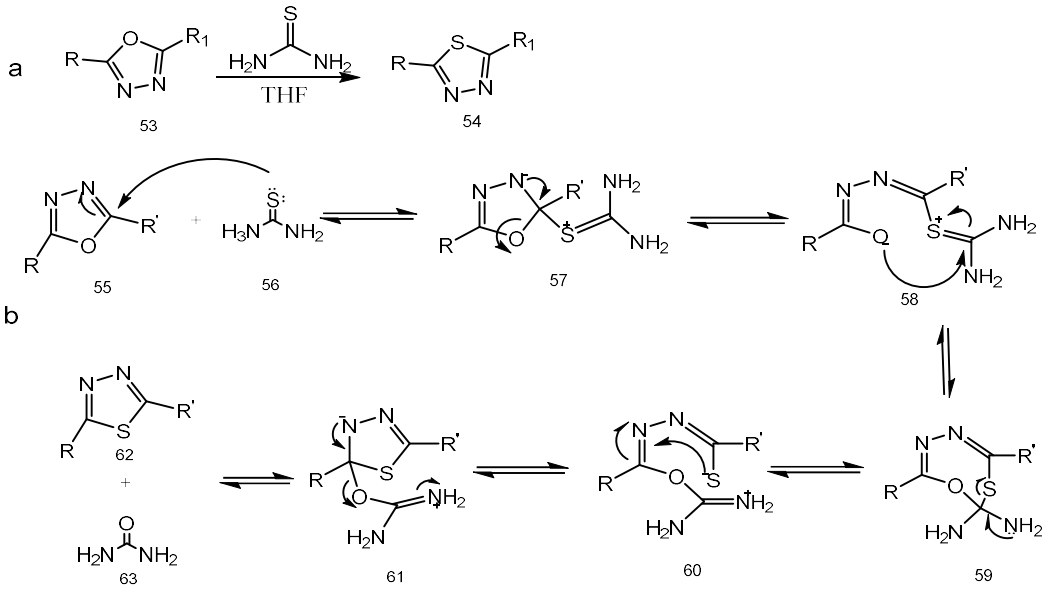
The preparation of 1, 3, 4-thiadiazole by dithiocarbazate was afforded with chloroacetylchloride at -15 °C. since the reaction mixture was stirred for 1 hour at 10 °C to generate compound 51 which was cyclized in 10 % sodium bicarbonate to give the desired compound 52 [39] **Error! Reference source not found.**



Sch. 10. Synthesis 1, 3, 4-thiadiazole from dithiocarbazate

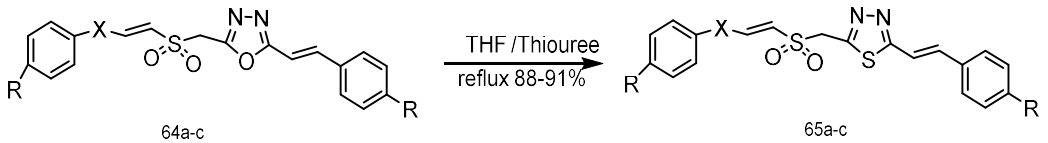
1.4.3 From 1, 3, 4-Oxadiazole:

In this method, the oxadiazole has been converted to thiadiazol. The oxadiazole reacted with thiourea in tetrahydrofuran at refluxed for 24-36 hours the authors reported yields of 55–69 % Sch.11a. The mechanism of this interaction can be explained by thiourea attacking 1, 3, 4-oxadiazole, reasoning the ring opening as shown in[40] Sch.11b.



Sch. 11. Synthesis of compound **54** and mechanism of this interaction

The acetohydrazide has been reacted with compound 64a-c in THF. It was heated and stirred for 13-16 hours, and it gave higher yields[41] Fig.

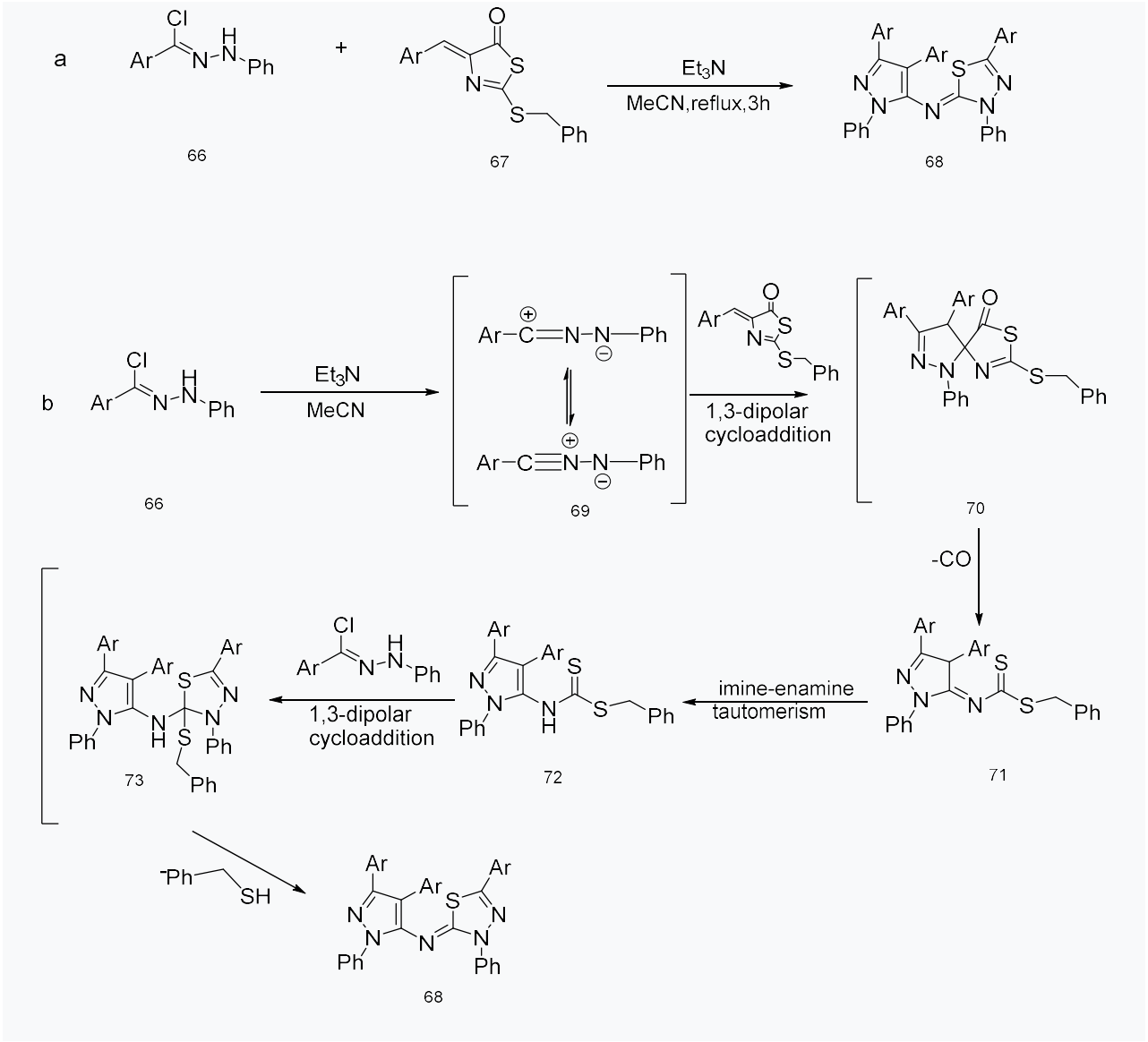


X=C=O
R= a) H, b) CH_3,C) Cl

Fig.7. Formation of **64a-c** and **65a-c**

1.4.4 From N-phenylbenzohydrazonoyl chloride:

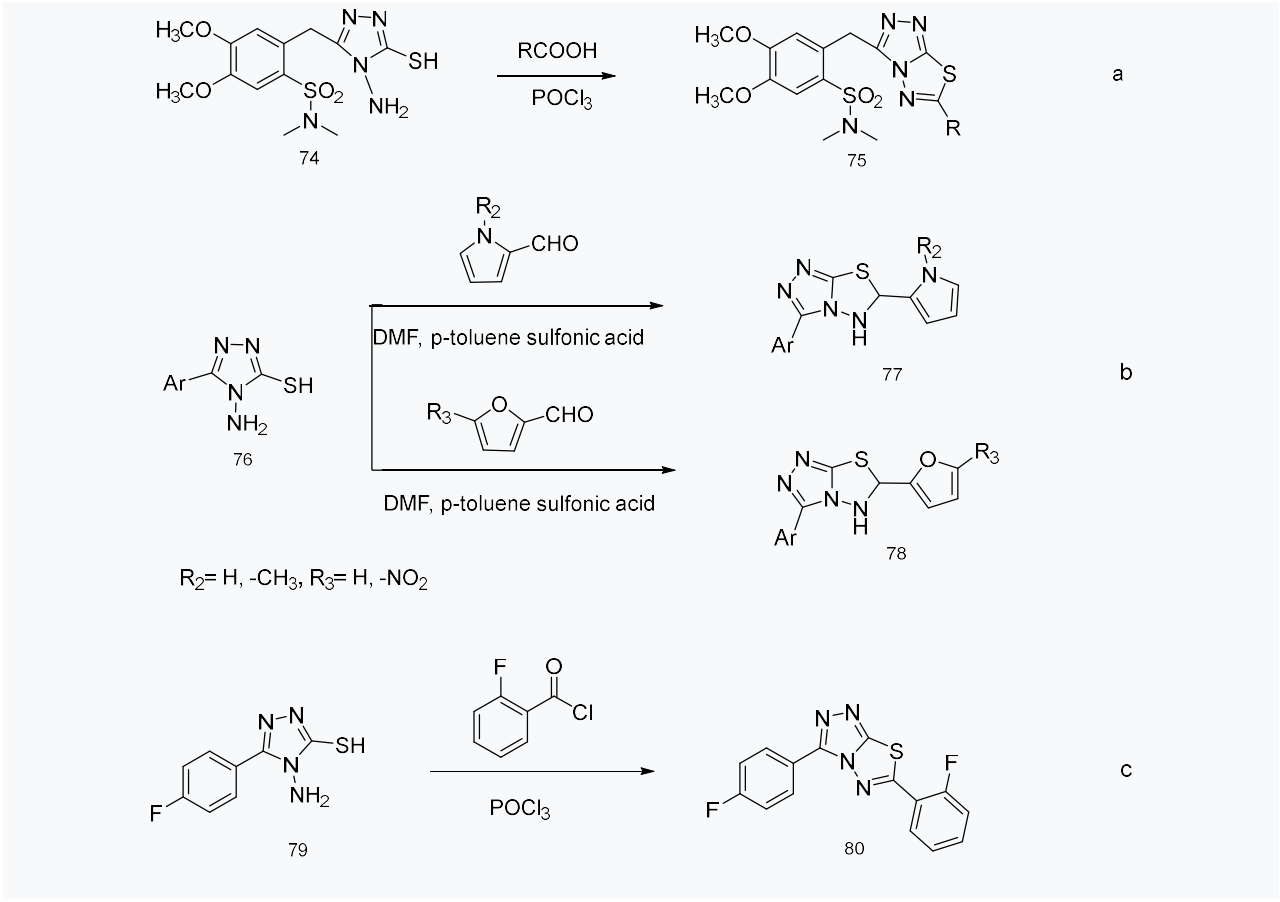
Yavar al. reported a synthesis of 1, 3, 4-thiadiazole from reaction between N-phenylbenzohydrazonoyl chloride and 4-benzylidene-2-(benzylthio) thiazol-5(4H)-one in the presence of Et3N in MeCN reflex for three hours and follow up the reaction by TLC. Where the compound reaction gave a yield of 98% Sch.12a. The reaction mechanism is a 1-3 dipolar cycloaddition, in the beginning the formation of nitrile imine trapped by an external cyclic bond C = C, which forms an intermediate cyclic compound **70** that removes -CO to form compound **71** that turns into an aromatic compound 72 by imine–enamine tautomerism then C=S reacts to form compound **73**, an intermediate compound that removes phenylmethane to give compound **68**[42] Sch.12b.



Sch.12. Synthesis N-(3,5-diphenyl-1,3,4-thiadiazol-2(3H)-ylidene)-1,3,4- triphenyl-1H-pyrazol-5-amine

1.4.5 From 4-Amino-1,2,4-triazolyl-3-thiol:

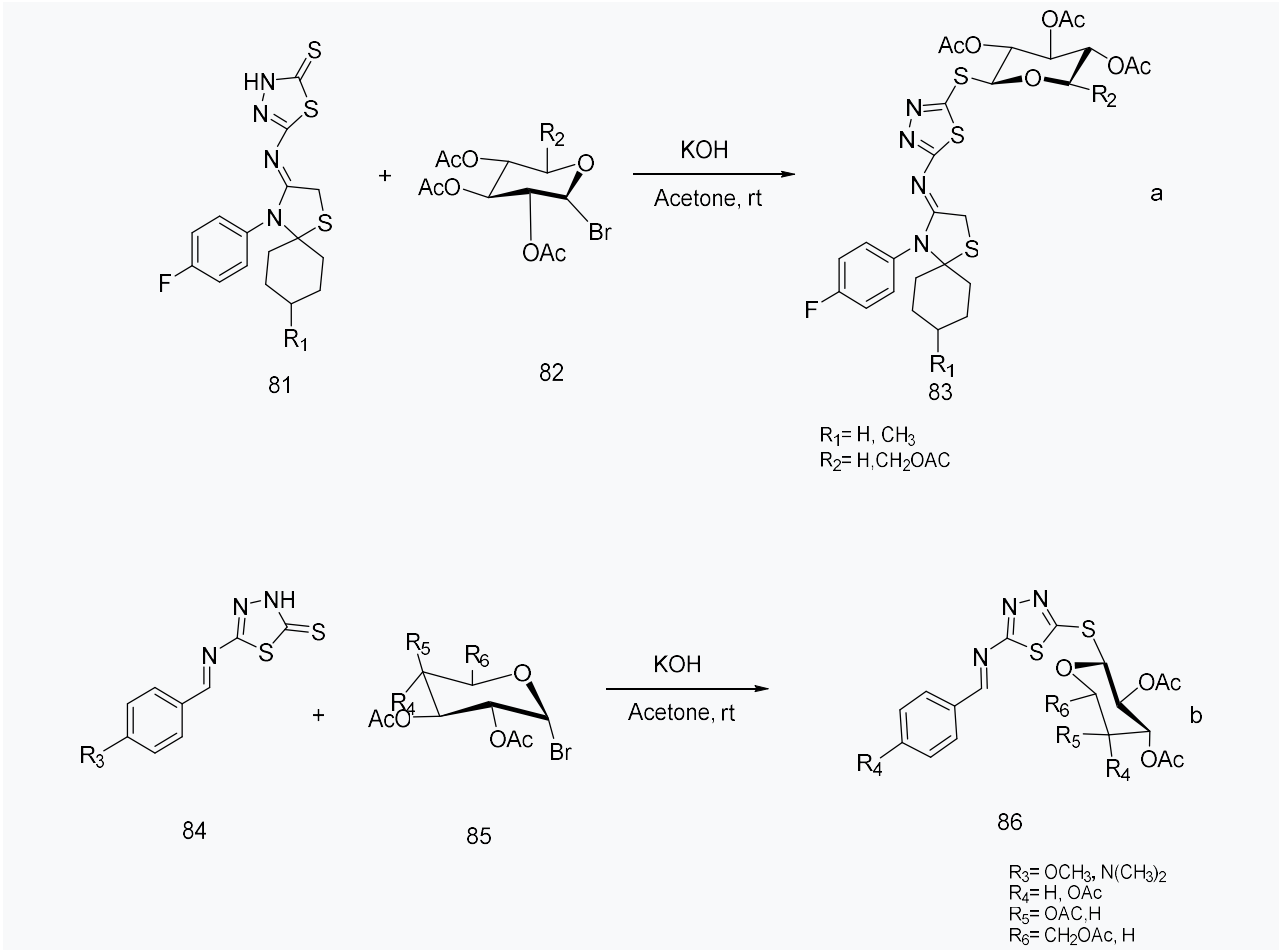
The compound 1, 2, 4-Triazolo [3, 4-b]-1, 3, 4-thiadiazole was prepared, via the reaction of 5-[2-(N,N-dimethylsulfamoyl)-4,5-dimethoxybenzyl]-3-mercapto-4-amino-1, 2, 4-triazole and acids in the presence of phosphorus oxychloride[43] Sch .13a. Another interaction is between amino-triazolethiol and aldehydes[44] Sch. 13b and acyl chlorides [45,46]Sch.13c.



Sch.13. preparation of compound 75, 77, 78, 80

1.5 Synthesis of 1,3,4-thidaiazol attached with Glycosides*:*

The glycosylated bromide compounds were dissolved using acetone with a 1, 3, 4-thiadiazole derivative in the presence of a KOH solution, and stirred for 5-6 hours at room temperature and gave a yield of 65%-75% [47] Sch.14a. With the same steps compound 86 can be synthesized[48] Sch.14b.



Sch.14. Synthesis of 1,3,4-thiadiazole thioglycoside.

Compound **88** was prepared by reacting 2-mercaptothiodiazole with NaOH in water, then benzyltriethylammonium bromide and glucosyl bromide or galactosyl bromide were added using dimethylformamide as a solvent, and the reaction was stirred at room temperature for 10 hours[49] Fig.1.

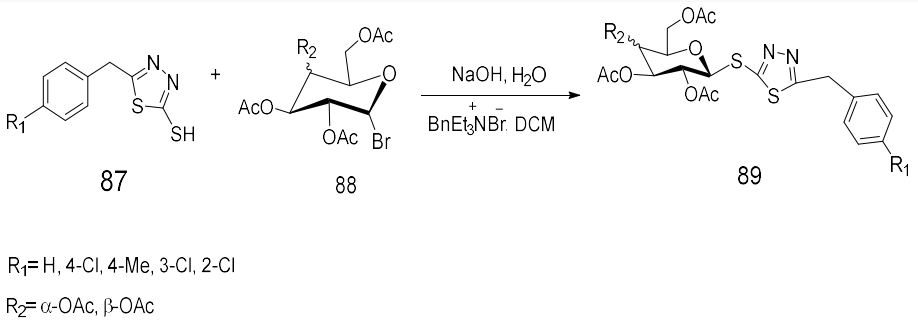
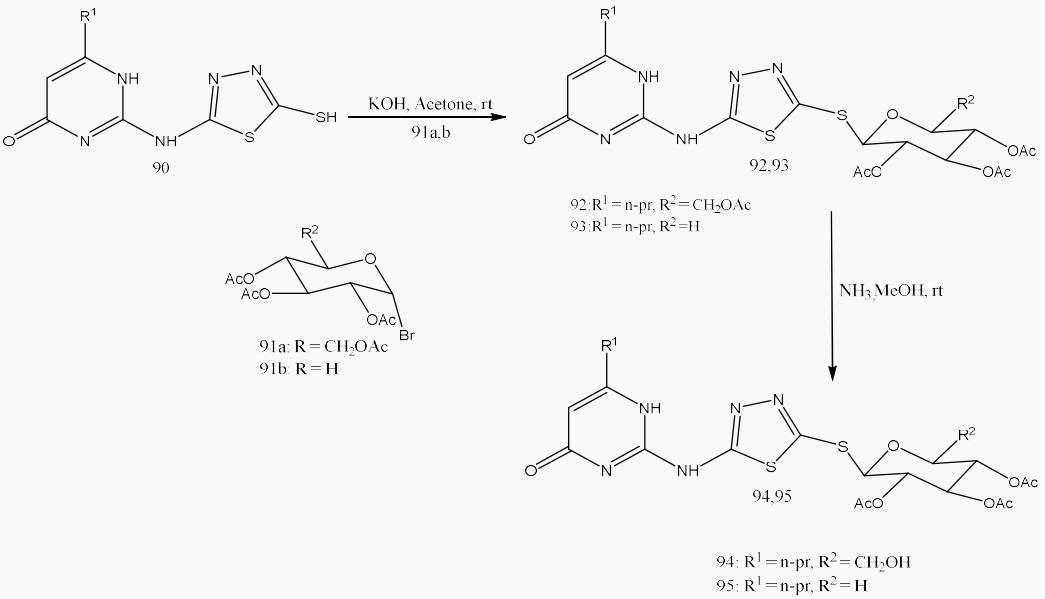


Fig.1. Synthesis of 1,3,4-thidaiazol attached with Glycosides.

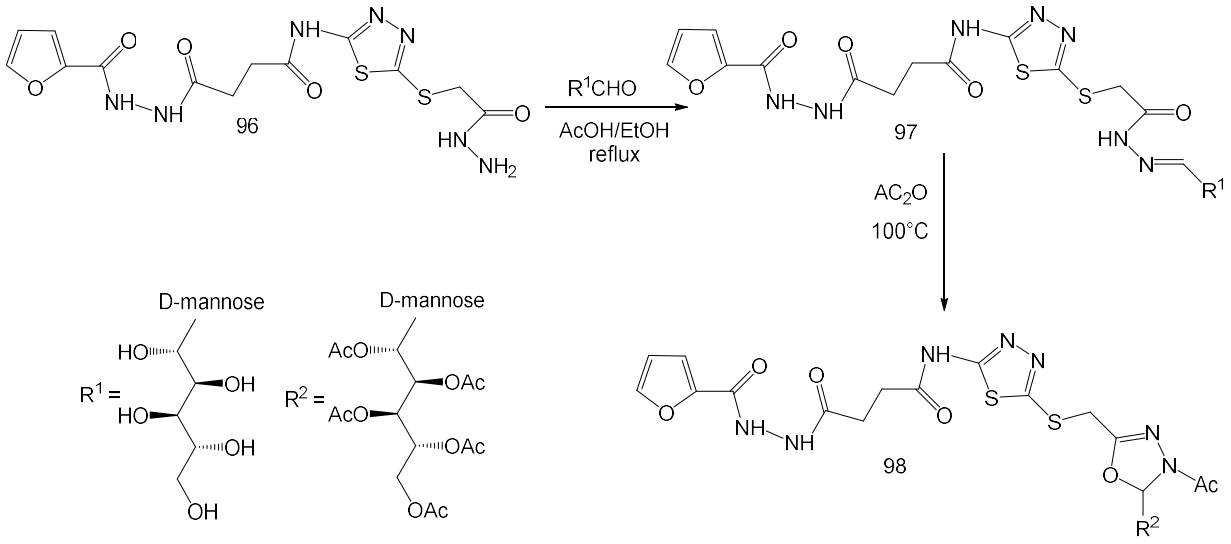
The 1, 3, 4-thiadiazole derivative reacts with O-acetyl-α-D-gluco D-xylopyranosyl bromide compounds in the presence of potassium hydroxide solution and using acetone as solvent. The reaction is stirred at

room temperature to give derivatives of 1, 3, 4-thiadiazole thioglycosides with a good yield of 76-78%. 1, 3, 4-thiadiazole-thioglycosides are produced by removing the acetyl group using ammonia solution[50] Sch.15.



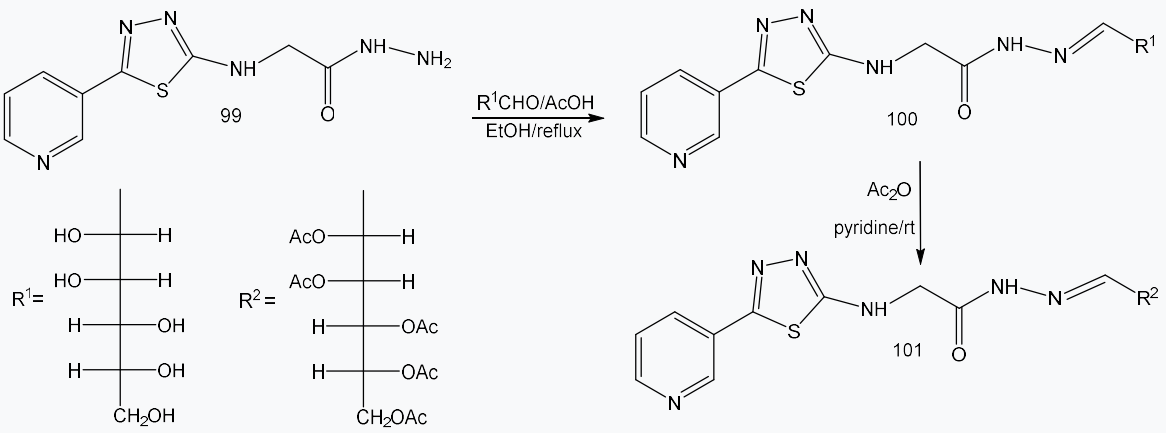
Sch.15. Synthetic rout for the new 1, 3, 4-thiadiazole thioglycosides.

The hydrazide acid derivative reacts with O-acetylated-sugar derivatives in the presence of ethanol to give compound 97. It is refluxed at a temperature of 100 °C using acetic anhydride to give oxadiazole sugar derivatives[51] Sch.16.



Sch.16. Synthesis of ((Furyl)thiadiazolyl) oxadizole Sugar dderivatives

In 2013, the synthesis of the target compound **100** was developed by adding a solution of 1, 3, 4-thiadiazole in ethanol to D- galactose in water in the presence of acetic acid, then the reaction was stirred with acetic anhydride and pyridine at room temperature to give compound 101[52] Sch.17.



Sch.17. Preparation of thiadiazole derivatives with sugars

1.6 Isoindole

consists of a benzene ring attached to a pyrrole ring[53] are structurally unstable isomers that are Isoandoles relatively unstable.They exist in two isomers, 1H isoandole and 2H isoandole Fig They are widely used as multiple building blocks useful in materials science, laser dyes, and various devices. They are also used in pharmacology as antibiotics and enzyme inhibitors. Examples of this are lenalidomide anticancer multiple e myeloma, apremilast antiinflammatory, and pomalidomide anticancer multiple myeloma[54]

Fig

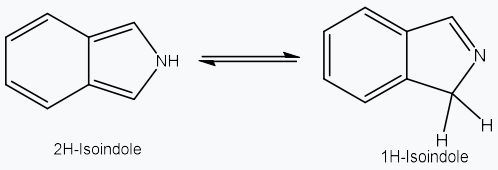


Fig.9. The isomers isoandole

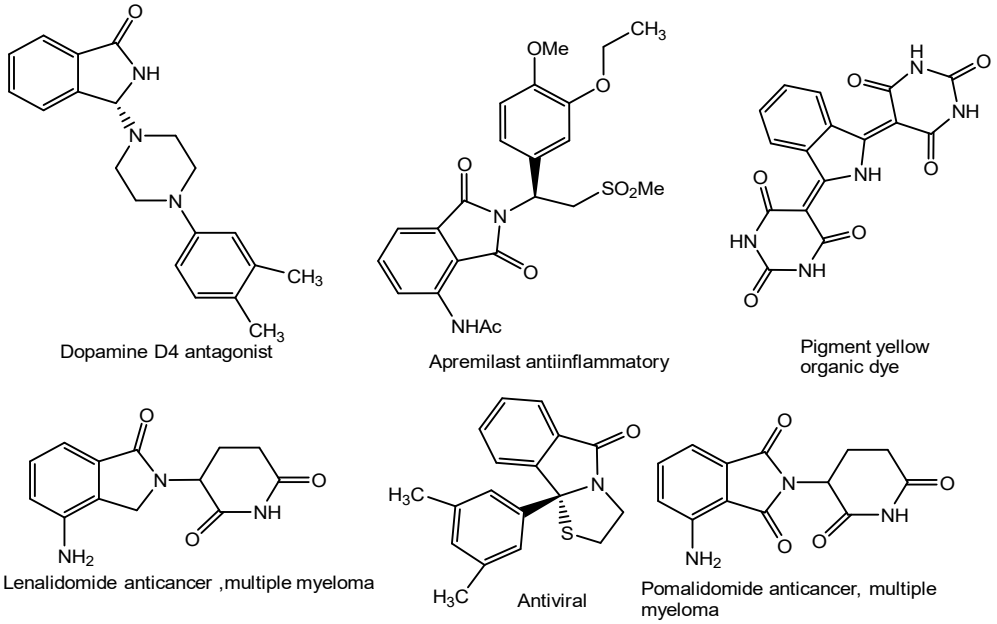
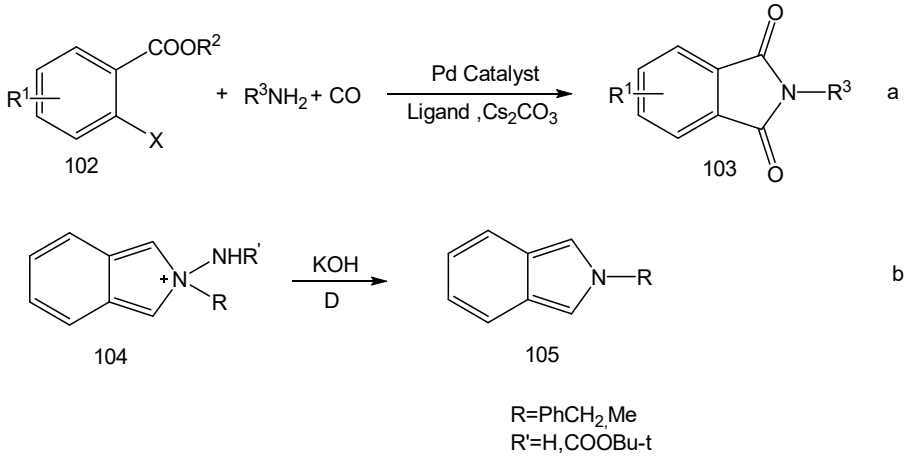


Fig.10.Structures of isoandole derivative

1.7 Synthesis of Isoindole

Isoindole 1, 3-diones were prepared by reacting aminocarbonylation with halopenzoates in the presence of palladium as a catalyst and it gave a good yield. This protocol can be used with different functional groups including methoxy, carbonyl, nitro and hydroxy Sch.18a. Another approach to the synthesis of isoindole derivatives under basic conditions, the disposal of 2-aminoisoindolinium salts to the production of N-substituted isoindoles. This method is considered good for the production of isoindole when the a tert-butoxycarbonyl group is attached to the nitrogen ring[54] Sch.18b.



Sch.18. Preparation of compound **103** and **105**

Products was prepared by adding a certain amount of 2-iodobenzamides with 2-alkynylanilines in the presence of DMF as a solvent, where aqueous copper sulfate was used as a catalyst. This reaction was carried out at a temperature of 100 ° C for an hour and gave a yield of 65-88% [55]
Fig

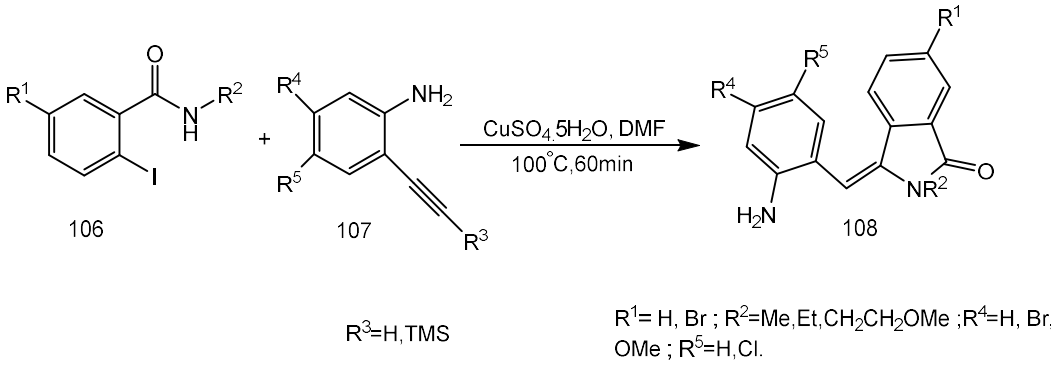
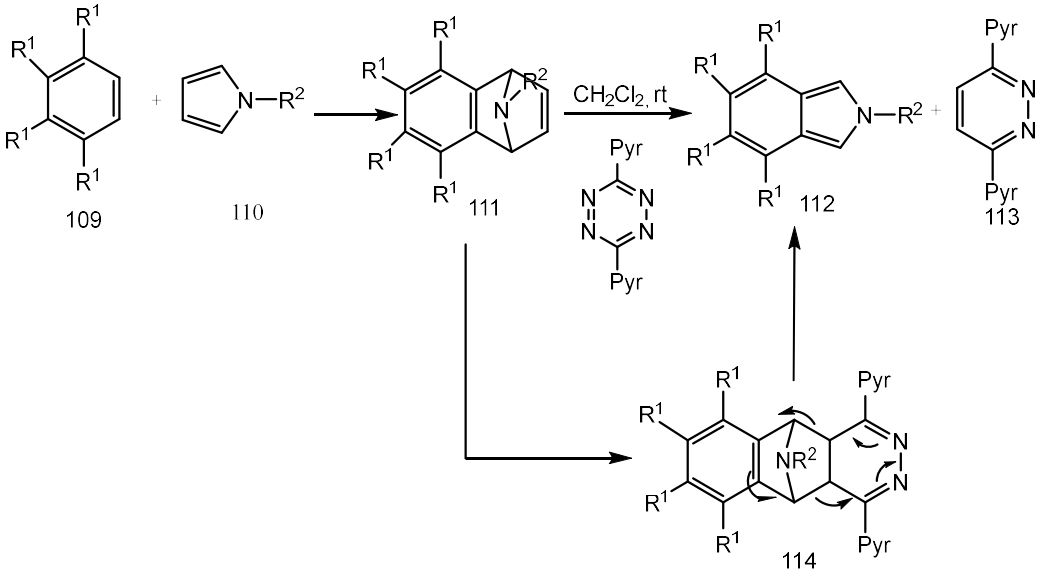


Fig.11. Structures of compound **108**

1.7.1diels-AlderInteractions

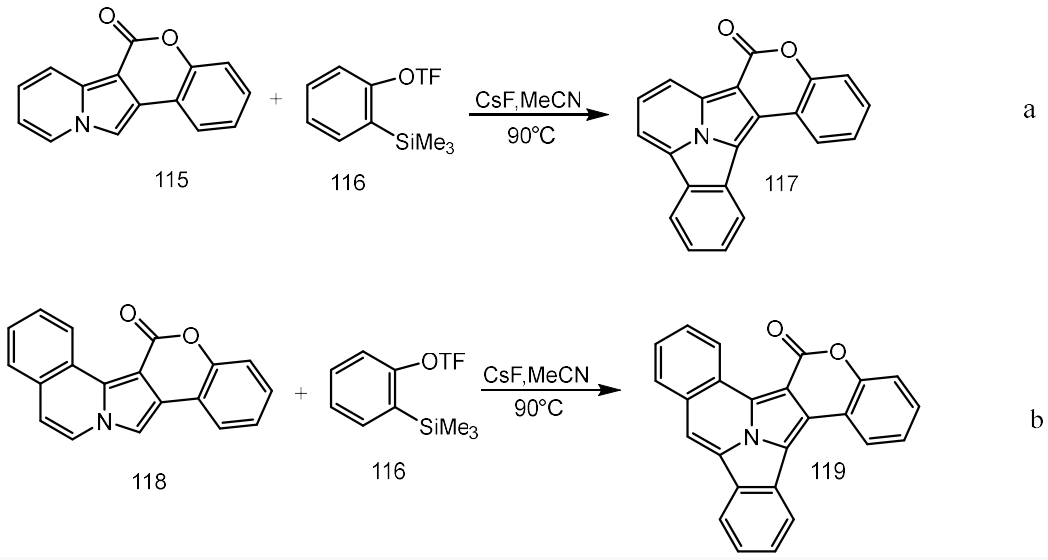
Stevensa et al. reported the preparation of isoindoles derivatives by using Diels Alder reactions, which consists of the reaction of the benzene ring with the pyrrole ring, where a wide range of isoindoles derivatives were prepared[56] Sch.19.



Sch.19. Prepartion diels -Alder Interactions

1.7.2 From Cesium fluoride catalyst

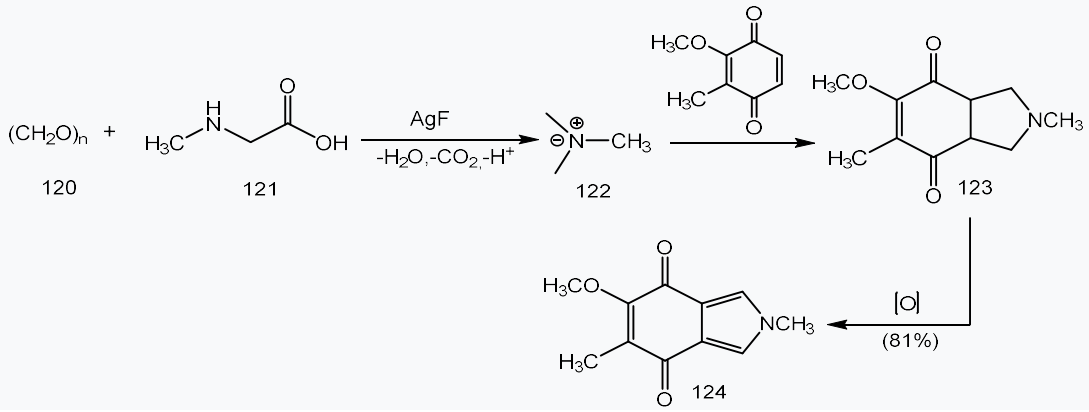
6H-[1]benzopyrano[3,4-a]indolizin-6-one and 6H-[1]benzopyrano- [3,4 :3,4] pyrrolo[2,1-a] isoquinolin-6-one reacts with compound **116** under the same conditions where the compound **117** gave a yield of 93% and the compound 119 gave a yield of 62%[57] Sch.20.



Sch.20. Preparation of an isoindoles derivative Cesium fluoride

1.7.3 1, 3-dipolar cycloaddition:

This reaction was done by heating paraformaldehyde with sarcosine, where a molecule of water and carbon dioxide was removed. This reaction was carried out in a 1,3-dipolar cycloaddition between azomethinylide and benzoquinone, then the product was oxidation to give isoazandol[58] Sch.21.



Sch.21.Synthesis of isoindole

1.7.4 ImmPd-IL reaction:

This reaction is carried out by cyclization of 2-iodobenzoic acid and a primary amine to form *N*-substiuted isoindole 1, 3- dione derivatives at a temperature of 100 for 4-6 hours using toluene as a solvent and gave a good yield 75-95%. Various other derivatives were used to prepare *N*-substiuted isoindole 1,3-dione [59] Fig.

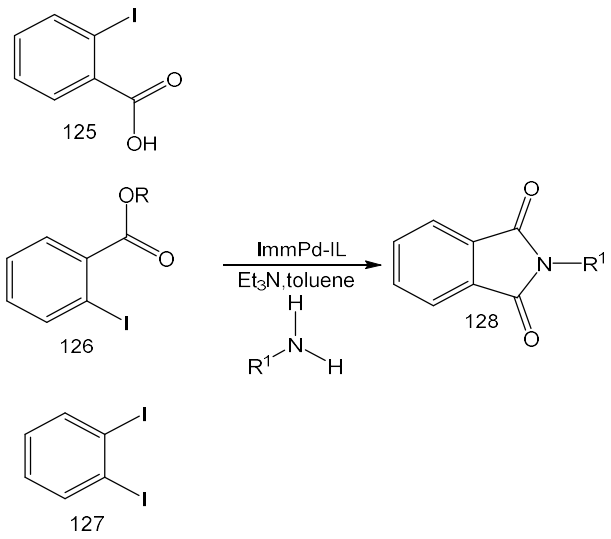


Fig. 12. Structures of isoindole 1,3-dione

1.7.5 5-Bromo-2-(5-aryl-1, 3, 4-thiadiazol-2-yl) isoindoline-1, 3-dione derivatives:

A mixture of 5-Aryl-1, 3, 4-thiadiazol-2-amine with 4-bromophthalic anhydride using glacial acetic acid at a temperature of 120 ° C followed by reflux for 12-24 hours was applied for the preparation which was followed by recrystallization with ethanol. This reaction gave a good yield between 45-95% [60] Fig.13.

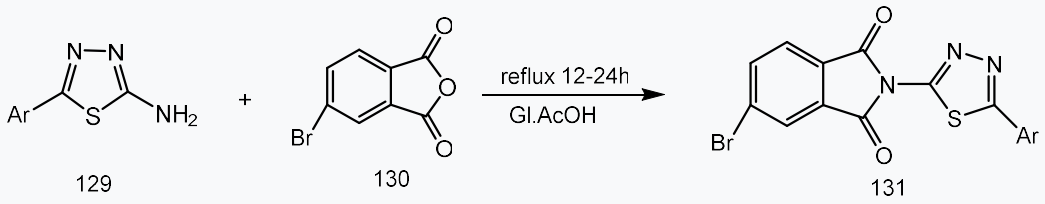


Fig.13. Synthesis of compounds **131**

1.7.6 3-Alkylsubstituted 2,5-Diamino-1, 3, 4-thiadiazoles with 1, 1-Dimethoxy-3-iminoisoindoline:

This product was prepared by reacting certain moles of 2,5-diamino-1, 3, 4-thiadiazoles with 1,1-dimethoxy-3-iminoisoindo. The reaction was continued via reflux for 15 hours at a temperature of 40-45 °C using methyl hydroxychloroquine[61] Fig

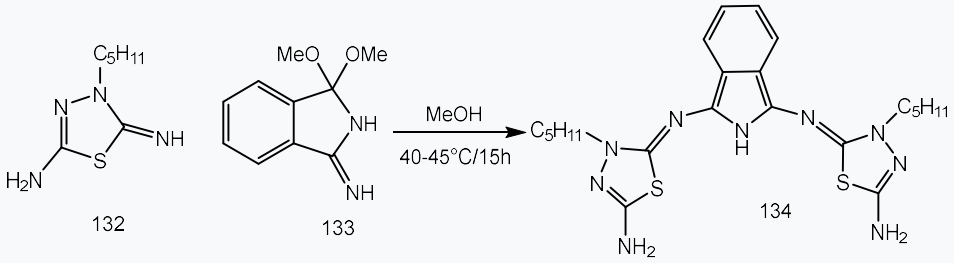


Fig.14. Preparation of compound **134**

1.7.7 Synthesis 2-(5-(4-methoxyphenyl)-1, 3, 4-thiadiazole -2-yl) isoindoline-1, 3-dione:

This reaction is done by reflux of the thiadiazole derivative in the presence of CH_3CN with the use of TEA to give the compound136[62] Fig

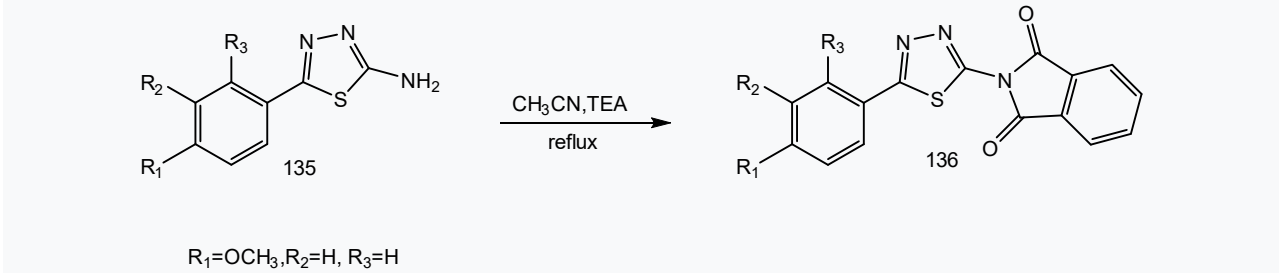


Fig.15. Synthesis of compound **136**

1.7.8 Nickel catalyzed:

This reaction was performed by using 2,5-diamino-1,3,4-thiadiazole and 3,6-diisopropyloxyphthalonitrile using a nickel complex for 24 hours gave a good yield[63] Fig

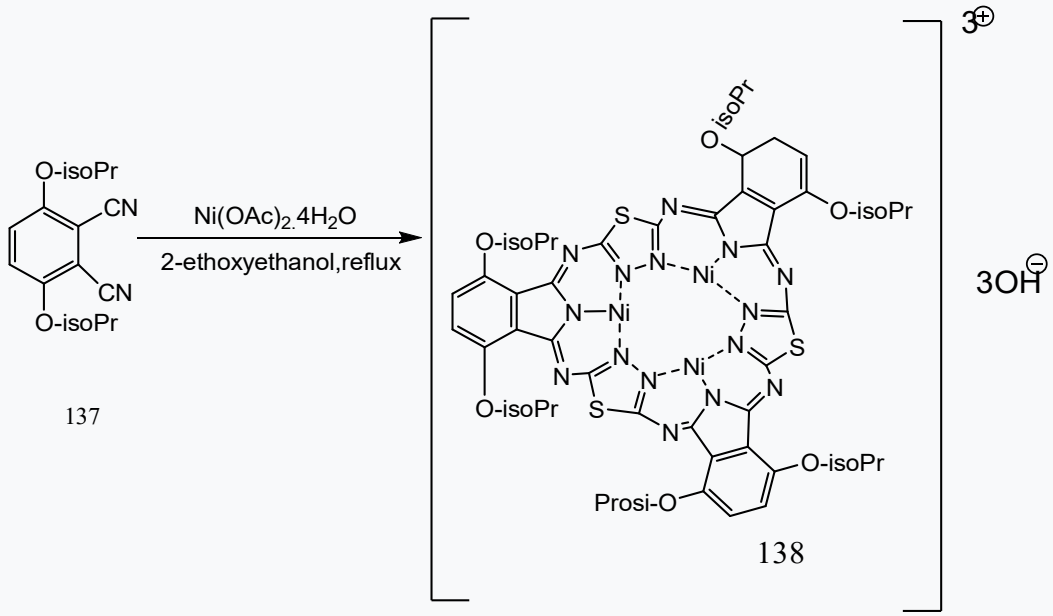
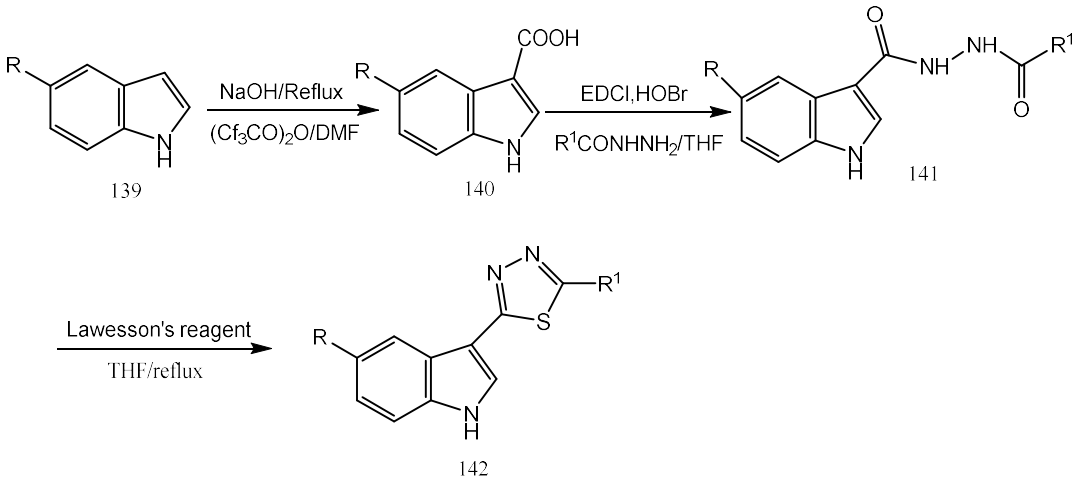


Fig.16. Preparation of an isoindole derivative using nickel

1.8 Biological activity:

1.8.1 Compounds of 1, 3, 4- Thiadiazole anticancer:

Kumar et al. studied 1, 3, 4-thiadiazole derivatives and evaluated their activity against cancer. They showed toxicity to cell lines, but not to normal cells. The compounds were screened using a single concentration. The substitution on the 2-carbon atom of the thiadiazole ring plays an important role in transmitting the cytotoxic activity of the compound[64] Sch. 22. Whereas, when the phenyl ring is substituted at the benzyl carbon 2 position, 4-(dimethylamino) phenyl 3, 4-dimethoxyphenyl and 4-benzyloxy group gave high anti-proliferative activity, while when replacing the phenyl group with chlorophenyl, the introduction of the third methoxy group reduced the biological activity of compound 142 Fig



Sch.22. Synthesis of compound 142

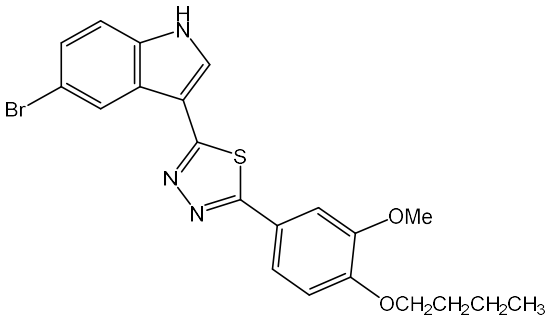
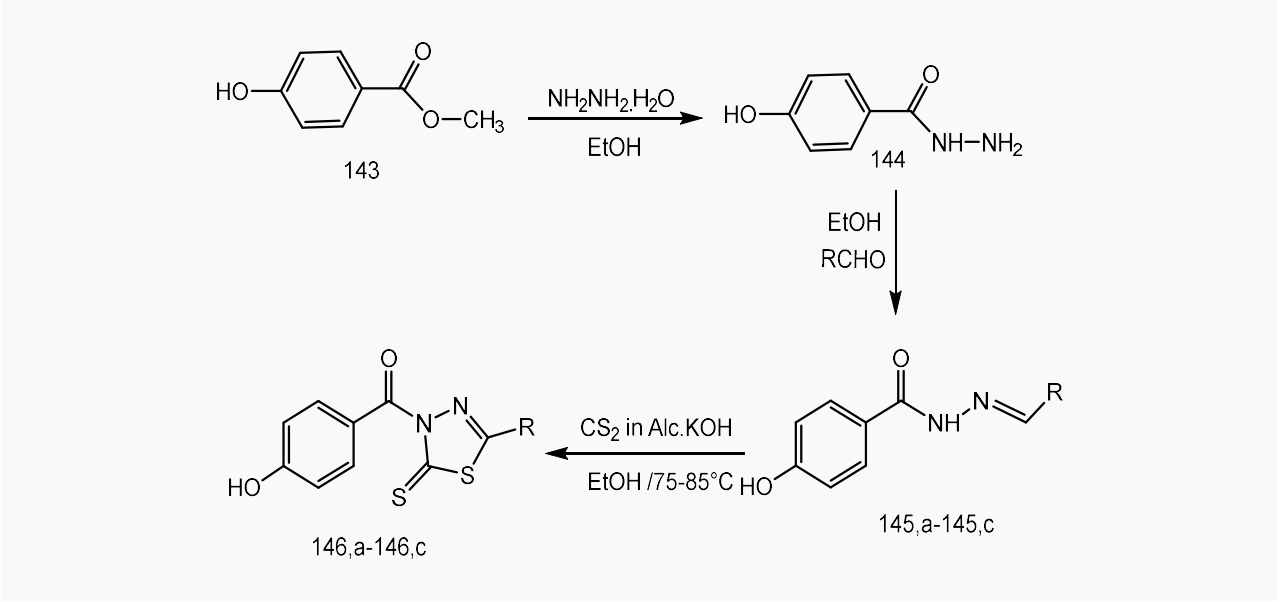


Fig.17. Biologically potent compounds containing thiadiazole anticancer drugs

	R	R^1
a	H	C_6H_5
b	H	$CH_2C_6H_5$
c	H	$4\text{-}ClC_6H_4$
d	H	4-N, N'$(CH_3)_2C_6H_4$
e	H	$3,4\text{-}(OCH_3)_2C_6H_3$
f	H	$3,4,5\text{-}(CH_3O)_3C_6H_2$
g	H	$3,4\text{-}(OCH_2O)\ C_6H_3$
h	H	$4\text{-BnO-}3\text{-}OCH_3C_6H_3$
i	H	3-Pyridyl
j	H	4-Pyridyl
k	Br	4-N, N'$(CH_3)_2C_6H_4$
l	Br	$3,4,5\text{-}(CH_3O)_3C_6H_2$
m	Br	$4\text{-BnO-}3\text{-}OCH_3C_6H_3$

Table 1-1. The compounds demonstrated anticancer activity

4-Hydroxyphenyl) [5-(2,6-dichloro)-2-thioxo 1, 3, 4-thiadiazole -3-yl] methanone Fig has been shown to have broad activity against cancer cells in humans, including lung cancer. (HOP92), which gave a Log Gl50 value of -6.49 and also gave activity against colon cancer (HCC-2998) with a Gl50 value of 5.31 and against prostate cancer (PC-3) with a Gl50 value of -5.48[65] Sch.23.



Sch.23. Synthesis of **146, a- 146, c**

Compd. No	R
145,146a	2,6 ClC_6H_4
145,146b	OHC_6H_4
145,146c	$CH_3OC_6H_4$

Table 1-2. The compounds demonstrated anticancer activity

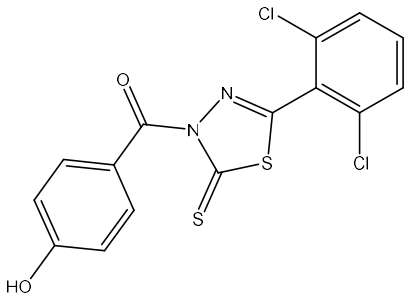


Fig.18. Examples of anticancer drugs

1.8.2 1,3,4-Thiadiazole as antiviral agents:

Viral diseases are among the most dangerous diseases that threaten human health. [66] Thus, there is a need to develop new compounds against viruses, where a study was done on 2-(naphthalen-2-yloxy)-N-((5-(phenylamino)-1,3,4-thiadiazol-2-yl)methyl); compound A acetamide and it gave activity as an anti-HIV (strain IIIB), as it gave an EC_{50} value of 0.96µg/ml. Also, 1, 3, 4-thiadiazole sulfonamides were evaluated, and it was found that compounds containing the sulfonamide part are effective as virus inhibitors with less cytotoxicity [67] Fig

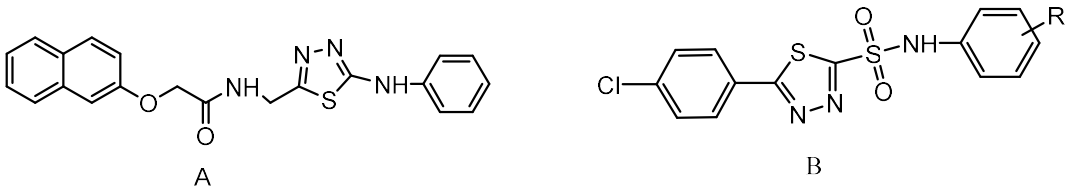
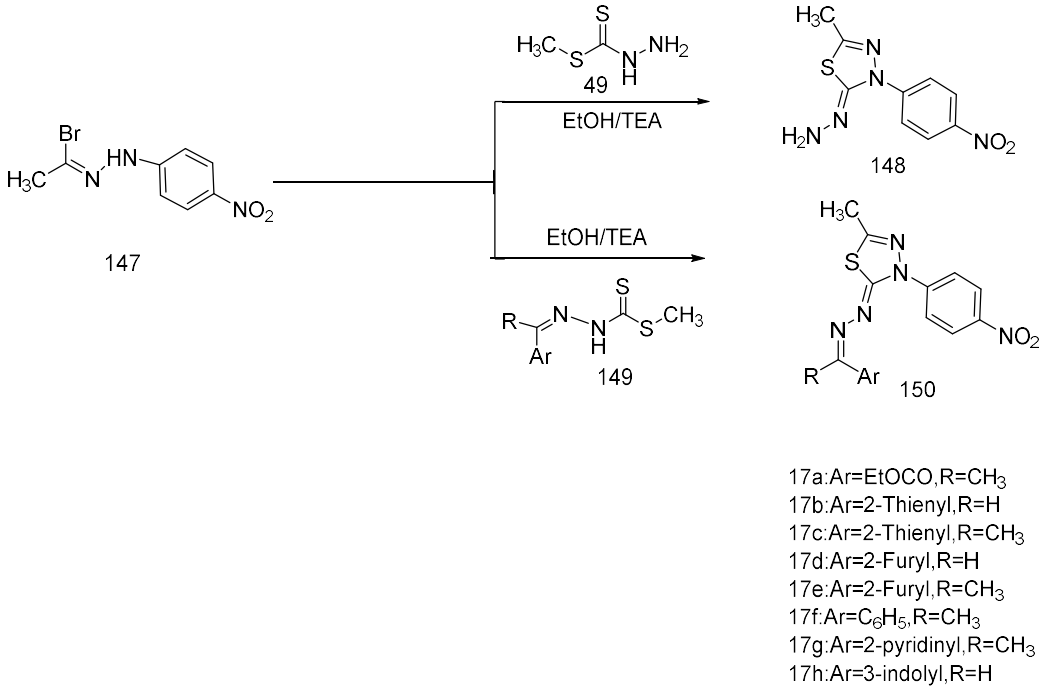


Fig.19. Formation of A and B

1.8.3 Compounds of 1,3,4-Thiadiazole as Antimicrobial:

Studying the biological activity of thiadiazole derivatives was of interest because of their great importance in the medical fields. In order to synthesize a new series of thiadiazole derivatives by reacting dithiocarbazate with N-(4-nitrophenyl) acetohydrazonoyl bromide using TEA, compound **148** gave distinct antimicrobial activity, while compound **150** gave less activity despite the use of a variable from compound 148[68] Sch.24.



Sch.24. Synthesis compound 148 and 150

Thiadiazole-related triazoles were screened for antimicrobial activities by combining an amino group with a thiol as in compound 1, as this combination resulted in enhanced antimicrobial activity against all bacterial strains at a MIC of 4-16 μg/mL[69] Fig

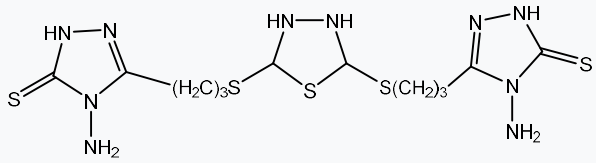


Fig.20. Thiadiazole derivatives which has a distinct antimicrobial activity

1.8.4 Compounds of 1,3,4-Thiadiazole as antibacterial*:*

Microorganisms constitute a dangerous factor for the medical community, so there was a need to prepare compounds and develop new antimicrobial agents.[70] Thiadiazole derivatives showed high activity against bacteria, and different substituting groups were used, where it was found when using the hydroxyl group in the naphthol ring in the meta position, as in compound 1A, it was found that its activity against bacteria was higher than in the para position, as in compound 1B[71] Fig

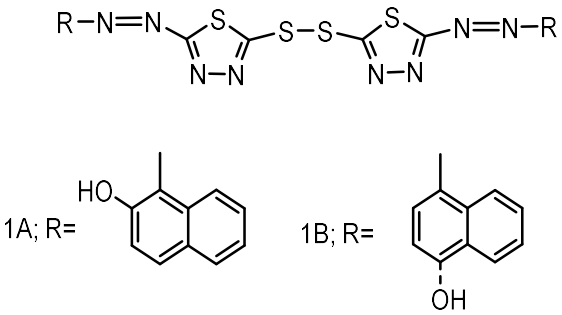


Fig.21.Thiadiazole derivative which has a distinct antibacterial activity

DHIAA et al. studied the antimicrobial activity that contains the thiadiazole ring, where they used ciprofloxacin as a reference drug, where a test was made for compounds C-F using gram, the compound gave 5,6 activity against Staphylococcus aureus, while compound C gave excellent activity against E. coli bacteria[72] Fig

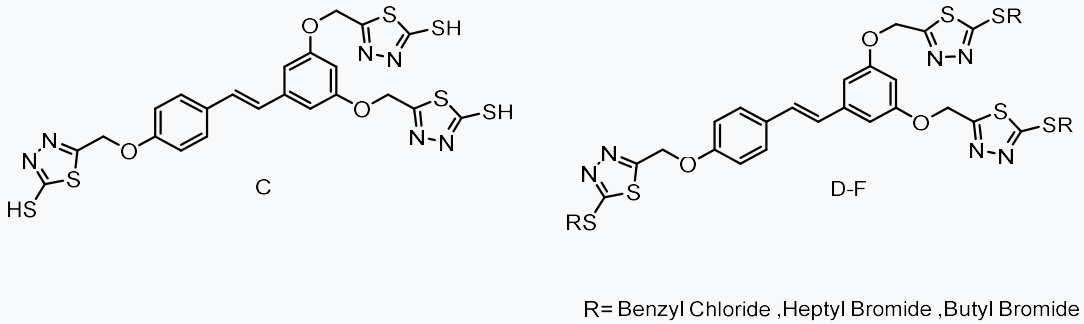


Fig.22. Formation of C and D-F

1.8.5 1,3,4- Thiadiazole compounds as antifungal agents:

Clinical drugs that contain the thiadiazole ring are among the most important antifungals, where the thiadiazole ring was combined with other derivatives and preparation of drugs that have antifungal activity and there are various examples of thiadiazole antifungal drugs[73] Fig

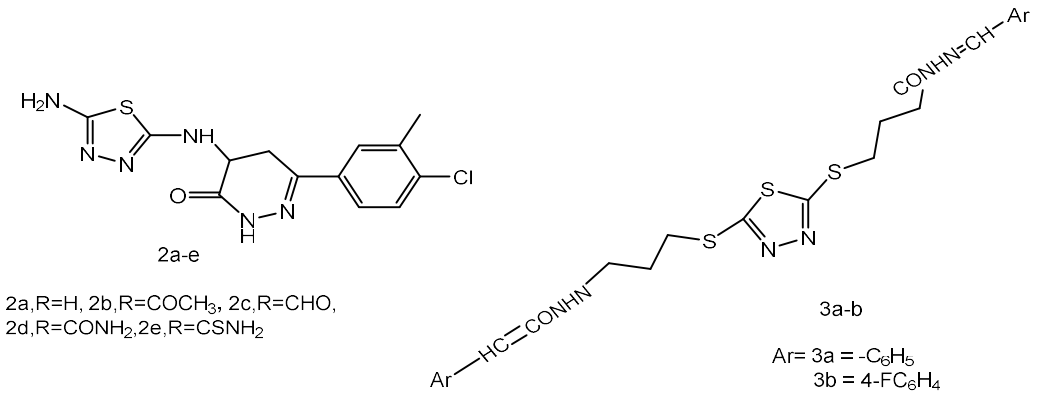


Fig.23. Formation of 2a-e and 3a-b

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الملخص العربي

4,3,1-الثياديازول: مشتقاتها من السكر والأيزواندول وأنشطتها البيولوجية.

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ملخص: المركبات الحلقية غير المتجانسة هي مركبات تحتوي على خمس ذرات حلقية ثلاثية أو رباعية هي N، O، S. ولها سمات مميزة تظهر أهميتها في العديد من التركيبات الصيدلانية المستخدمة في الكيمياء الطبية. ولذلك فإن الدورات غير المتجانسة لها أهمية كبيرة لدى الكيميائيين العاملين في الطب من أجل تطوير المجال الكيميائي أيضًا. أصبح 4،3،1-ثياديازول لبنة بناء مهمة في التركيب العضوي بسبب مجموعة واسعة من المواد الطبيعية. ولذلك فقد اهتم العلماء ودرسوا النشاط البيولوجي لمادة 4,3,1-ثياديازول. تم تقييم 4,3,1-ثياديازول وفعاليتها ضد السرطان وأيضا ضد الميكروبات كما تم تقييم 4,3,1-ثياديازول سلفونااميدات وتبين أن المركبات التي تحتوي على جزء السلفونااميد فعالة كمثبطات للفيروسات.

الكلمات المفتاحية: 4،3،1- ثياديازول؛ مركبات حلقية غير متجانسة. النشاط المضاد للسرطان. نشاط مضادات الميكروبات؛ جليكوسيدات MCF-7.