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Synthesis, Characterization and Antifungal Activity of a Series of Schiff's bases of 2-(2-Oxo-2-Aryl) Ethyl Pyridazin-3-Thione derivatives

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Abstract
In the present investigation, a new series *of Schiff bases* of *2-(2-Oxo-2-Aryl) Ethyl Pyridazin-3-Thione derivatives were synthesized and screened for their antifungal activity. An efficient method is described for the synthesis of Schiff's bases of a* series *2-(2-Oxo-2-Aryl)Ethyl Pyridazin-3-Thione derivatives by the nucleophilic addition reactions of 1-Aryl-2-(3-Phenyl-6-thioxo-4,5-Dihydropyridazin-4H-1yl)ethanones which were inturn obtained from the corresponding Pyridazinones by using Phase transfer catalysis. The synthesized compounds were characterized by spectral analysis and then were screened for their antifungal activity against Candida albicans and Aspergillus flavus using agar diffusion method. The results indicated that all the compounds are potential therapeutic candidates and could be used for the treatment of various fungal infections.*

Keywords
Pyridazin-3-Thione derivatives, Phase transfer catalysis, antifungal activity

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I. INTRODUCTION

The novel trends in Experimental organic chemistry have always been aimed at the generation of new compounds on one side and the development of new reactions on the other. The purpose of developing new reactions is usually simplification of existing methods of preparation. During the last two centuries of organic synthesis [1], new techniques for faster, simpler and cheaper methods of synthesis have been constantly emerging. One such technique which came into vogue about two decades ago is phase transfer catalysis [2].

Reactions involving two substances located in different phases of a reaction mixture are often inhibited due to the reagents inability to come into contact with each other. In such reactions, conventional techniques are environmentally and industrially unattractive. Nevertheless, these reactions can be successfully promoted by a popular catalysis methodology *viz.,* phase-transfer catalysis (PTC) under mild operating conditions [3]. Now a days, PTC is a matured technology used in more than 600 synthesis application covering pharmaceuticals, perfumes, agrochemicals, flavors, dyes, polymer industries, pollution control technologies etc. PTC has proved as a better insight than traditional synthesis [4] method because of its mild operating condition, use of cheaper reagents, high selectivity of

product in shorter time and suppression of unwanted side reactions.

On the other hand, the pyridazine derivatives are reported for their therapeutic potential as antihypertensive cardiotonic and as antifungal agents essentially. Prompted by these observations the synthesis of pyridazin-3-thione derivatives by phase transfer catalysis is achieved with the aim to evaluate their antifungal activities [5-13].

II. MATERIALS AND METHODS

Synthetic grade solvents and all the chemicals used were of synthetic grade obtained from SD fine, Merck and Sigma Aldrich chemicals. The solvents received from vendors were purified as per the prescribed methods and used for the synthesis. Reactions were monitored by using pre-coated Silica Gel TLC plates and the spots were visualized under UV light and in iodine chamber. The synthesized compounds were purified by recrystallization and purity was determined by measuring in Kofler hot stage melting point apparatus and are uncorrected. The IR spectrums were recorded on Shimadzu FTIR spectrophotometer by using 1% KBR discs. Proton NMR was recorded on Bruker Advance II 400 MHz NMR spectrophotometer with TMS as internal standard mass spectrum was recorded using Agilent 1100.

III. RESULTS AND DISCUSSION

3.1 Synthesis

The synthesis of Schiff bases of 2-(2-Oxo-2-Aryl) Ethyl Pyridazin-3-Thione derivatives VIII-XI (a-i) was achieved from the synthetic route depicted in **figure 5**. The β-Aroyl propanoic acids (IIIa-i) have been synthesized by the reaction of substituted benzenes with succinic anhydride (II), the reaction progress was monitored by TLC and the formation of the compounds was confirmed by melting point and spectral data. The obtained β-Aroyl propanoic acids were inturn condensed with Hydrazine hydrate using ethanol under reflux conditions to yield 6-Aryl-4,5-Dihydropyridazin-3-ones(IVa-i).The IR spectra of (**IVd**) showed the characteristic absorption peak at 1670 cm^{-1} corresponds to C=O stretching of a cyclic amide which confirms the formation of compound . In the next step each of the 6-Aryl-4,5-Dihydropyridazin-3-ones (IVa-i) was subjected to N-alkylation with phenacyl bromide (V) in the presence of sodium hydride in toluene. The reaction conditions have been found to yield a single product in each case. The products have been characterized as 2-[2-phenyl-2-oxo] ethyl-6-aryl-4,5-dihyropyridazin-3(2H)-Ones(VI a-i) All the compounds were obtained in good yields and were characterized by melting point, proton NMR, FTIR and mass spectral data. Each of these 2-(2-oxo-2-aryl)-ethyl-6-aryl-4,5-dihydropyridazine-2H-pyridazine-3-ones have been subjected to a reaction with phosphorous pentasulphide over potassium carbonate and a PTC catalyst tetrabutyl ammonium bromide(TBAB) and Polyethylene glycol-4000 in ethylene dichloride by heating under reflux for about 45min,while monitoring the reaction on TLC to yield of 2-(2-Oxo-2-Aryl)Ethyl Pyridazin-3-Thione derivatives(VII a-i). These were inturn condensed with the nucleophilic reagents selected are hydrazine hydrate, phenylhydrazine and semicarbazide hydrochloride and hydroxylamine hydrochloride to yield 2-phenylhydrazono-2aryl-ethyl, 2-semicarbazone, 2-aryl-ethyl, & 2-hydrazono-2-aryl-ethyl derivatives of 2-(2-Oxo-2-Aryl)Ethyl Pyridazin-3-Thione derivatives(VIII-XI a-i) The formation of title compound(VIIId) was confirmed by FTIR with the characteristic CH deformations(730,680cm^{-1}), N-N stretching(979.84cm^{-1}), C-N stretching(1274cm^{-1}), C=N stretching(1560cm^{-1}), C=S stretching(1170cm^{-1}), NH-CO-NH_2(amide-3468.01 cm^{-1}), the characteristic singlet of NH proton at δ 9.71 and another characteristic –CH_2 singlet at δ 3.41 were observed in proton NMR spectra and mass peak is observed at m/z of 366.16.

3.2 Anti Fungal Activity

The synthesized Schiff bases of 2-(2-Oxo-2-Aryl)Ethyl Pyridazin-3-Thione derivatives were evaluated for antifungal activity against the fungal strains *Candida albicans* and *Aspergillus flavus* at a concentration of 500µg/ml. Agar gel diffusion method was employed for the anti fungal screening and compared with the standard Clotrimazole(100µg/ml in DMSO). The agar media for antifungal screening was prepared by the standard protocol. The Sabouraud Dextrose Agar medium was prepared by adding appropriate quantity of Dextrose (40gm), petone(12gm), Agar(15gm) to distilled water(1000ml) and the pH of the media was adjusted to 5.6±0.2. The czapex dox agar medium was prepared by dissolving appropriate quantity of Sucrose (3gm), Agar (18gm) Di potassium hydrogen phosphate(1gm), Magnesium sulphate(0.5gm), KCl (0.5gm) and Ferrous sulphate (0.01gm) in Distilled water- 1000ml. The media prepared was sterilized.

The petriplates were inoculated with the fungal strains aseptically then filter paper discs containing test and standard solutions (Clotrimazole100µg/ml) were placed on the petriplates and later petriplates were kept undisturbed for 1hr for proper diffusion of the solution in the media. Then plates were

incubated for 24hrs at 25°C ± 1°C. The diameter of the zone of inhibition was measured for test and standard compounds and the results are presented in tables I-IV

The synthesized compounds were evaluated for their antifungal activity [14,15], from the results it was concluded that the compounds showed higher sensitivity towards fungi *Candida albicans than Aspergillus flavus*. CompoundsVIIId, IXd, IXh, Xf, XId and XIh were exhibited remarkable inhibition on the growth of fungal strains respectively. Apparently, all the remaining compounds demonstrated moderate anti fungal activity. It was evident from the above results that the Schiff bases of 2-(2-Oxo-2-Aryl) Ethyl Pyridazin-3-Thione derivatives could be used as better alternatives for the treatment of fungal diseases.

Table I Antifungal activity of 2-[2-(phenylhydrazono)-2-aryl]-ethyl-6-aryl-4,5 dihydro-2H-pyridazine-3-thione (VIIIa-i and IXa-i)

 # Each experiment was carried out in triplicate and* Zone of inhibition *values are presented as Mean± S.D (mm)

Compound	Zone of inhibition(mm) Mean ± SD		Compound	Zone of inhibition(mm) Mean ± SD	
	C. albicans	*A.flavus*		*C. albicans*	*A.flavus*
VIIIa	9±0.1	11±0.1	IXa	-	11±0.1
VIIIb	-	12±0.2	IXb	10±0.2	10±0.3
VIIIc	10±0.1	12±0.1	IXc	-	11±0.1
VIIId	12±0.2	13±0.2	**IXd**	**16±1.1**	**14±0.2**
VIIIe	12±0.1	12±0.3	IXe	12±0.2	12±0.1
VIIIf	10±0.1	11±0.1	IXf	14±0.1	12±0.3
VIIIg	12±0.2	14±0.1	IXg	14±0.2	12±0.1
VIIIh	**14±0.5**	**11±0.2**	**IXh**	**16±0.4**	**12±0.12**
VIIIi	9±0.1	10±0.2	IXi	10±0.3	09±0.2
Standard	18±0.2	17±0.2	***Clotrimazole***	18±0.6	17±0.1

Figure 1: **Graphical Representation of Antifungal activity of 2-[2-(phenylhydrazono)-2-aryl]-ethyl-6-aryl-4,5 dihydro-2H-pyridazine-3-thione (VIIIa-i)**

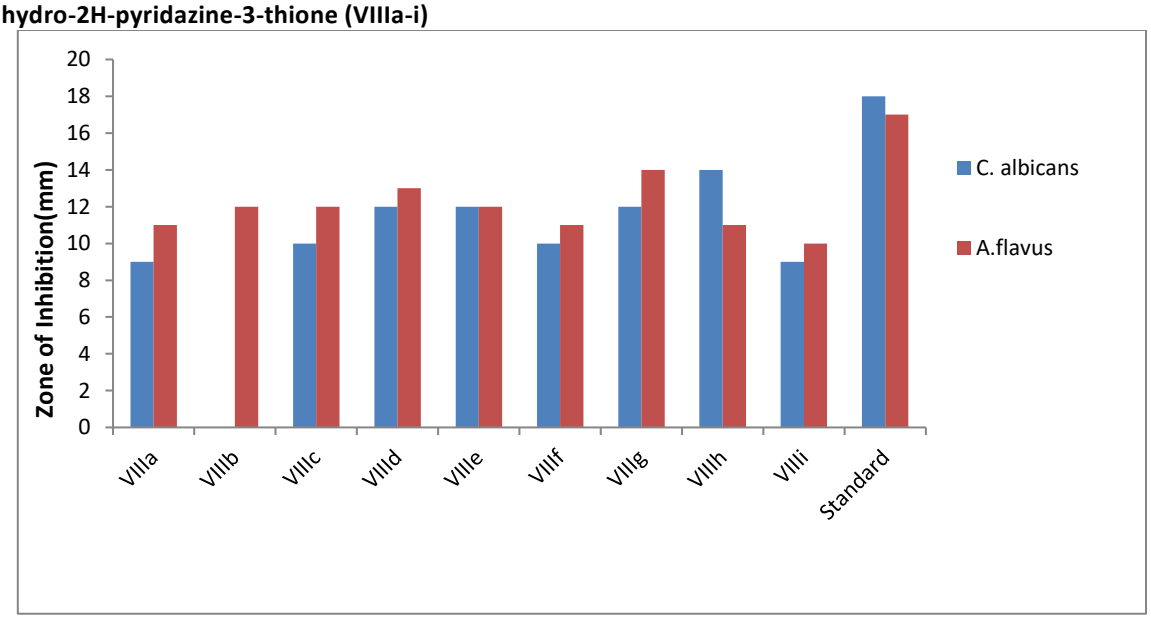


Figure2: **Graphical Representation of 2-[2-(semicarbozono)-2-aryl]-ethyl-6-aryl-4,5-dihydro-2H-pyridazine-3-Thiones (IXa-i)**

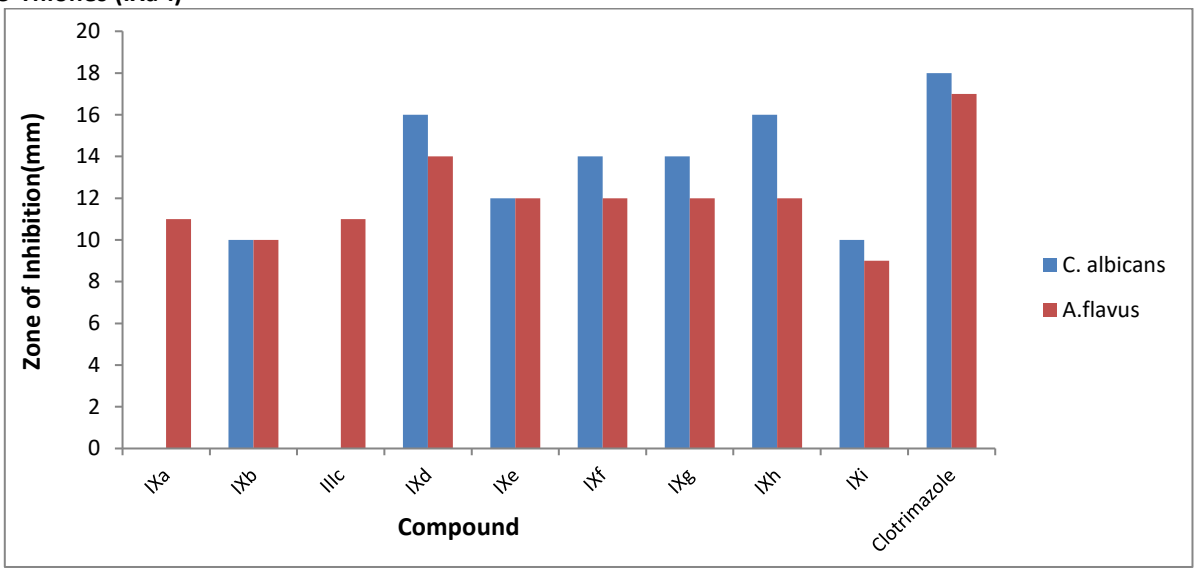


Table II: Antifungal activity of 2-(2-(hydroxyimino)-2-phenylethyl)-6-phenyl-4,5-dihydropyridazine-3(2H)-thione (Xa-i and XI a-i)

Compound	Zone of inhibition(mm) Mean ± SD		Compound	Zone of inhibition(mm) Mean ± SD	
	C. albicans	*A.flavus*		*C. albicans*	*A.flavus*
Xa	9±1.2	-	XIa	11±0.2	-
Xb	11±1.2	-	XIb	10±0.2	-
Xc	11±0.1	-	XIc	11±0.2	12±0.2
Xd	14±0.1	12±0.2	XI**d**	**16±0.3**	10±0.1
Xe	12±0.2	12±0.2	XIe	12±0.1	10±0.3
X**f**	**12±0.3**	**16±0.5**	XIf	14±0.5	14±0.1
Xg	**16±0.1**	14±0.4	XIg	14±0.1	14±0.5
Xh	14±0.4	14±0.2	XI**h**	**14±0.5**	**16±0.4**
Xi	10±0.5	-	XIi	12±0.5	-
Clotrimazole	18±0.1	17±0.1	***Clotrimazole***	18±0.2	17±0.1

 # Each experiment was carried out in triplicate and Zone of inhibition values are presented as Mean± S.D (mm)

Figure 3: **Graphical Representation of 2-(2-(hydroxyimino)-2-phenylethyl)-6-phenyl-4,5-dihydropyridazine-3(2H)-thione (Xa-i)**

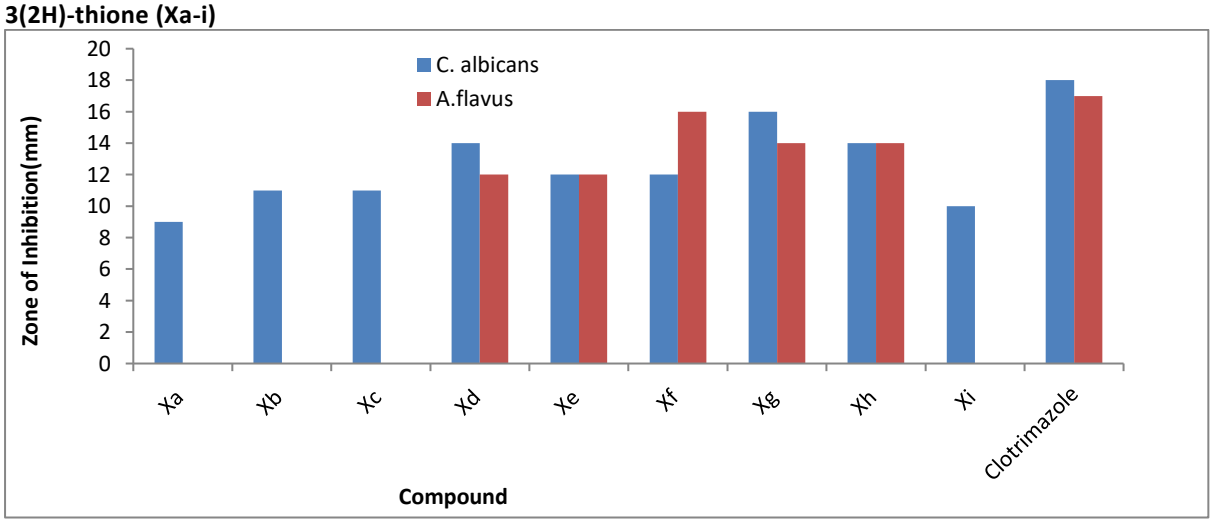
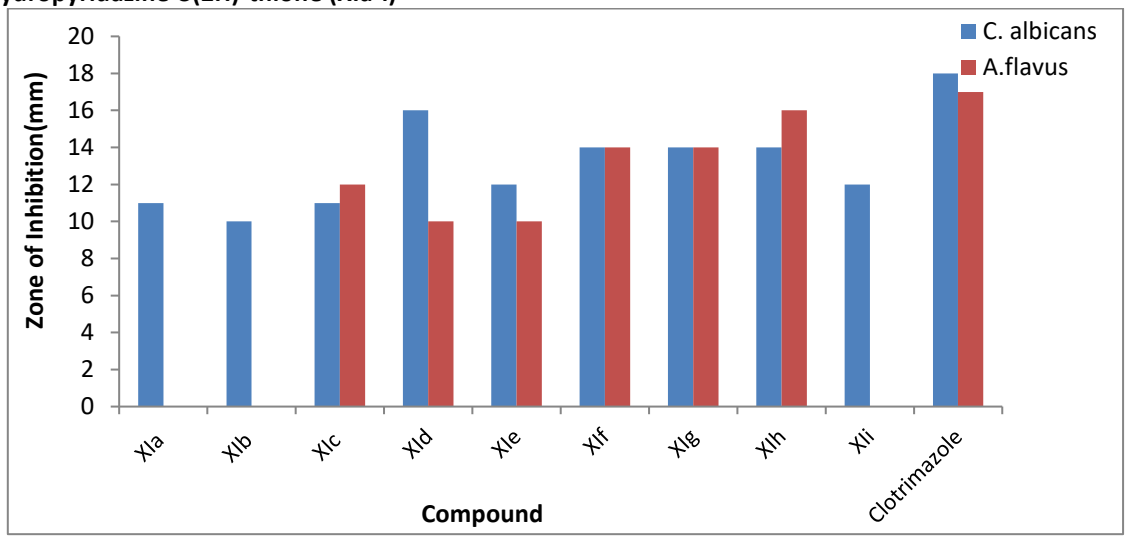


Figure 4: **Graphical Representation of Antifungal activity of 2-(2-hydrazono-2-phenylethyl)-6-phenyl-4,5-dihydropyridazine-3(2H)-thione (XIa-i)**



IV. EXPERIMENTAL

4.1 Synthesis of Schiff bases of 2-(2-Oxo-2-Aryl) Ethyl Pyridazin-3-Thione derivatives:

General procedure for the synthesis of β -Aroyl Propionic Acids (IIIa-i):

METHOD (A): To a 1 litre round bottomed flask with a mechanical stirrer and condenser carrying a gas outlet connected to scrubbing system aromatic hydrocarbon (R=H or CH_3, 2.25 moles) and succinic anhydride (0.34 moles) were added. The reaction mixture was stirred and powdered anhydrous aluminiumchloride (6.75 moles) was added in installments. After the addition, the reaction mixture was heated under reflux in an oil bath for one hour. The reaction mixture was cooled, and the contents were slowly added to a mixture of ice 150gm and concentrated hydrochloric acid 50ml. The separated organic layer was subjected to steam distillation. The residue after steam distillation was cooled, separated solid was filtered off and washed with cold dilute HCl 100ml followed by cold water. The crude product was taken in aqueous Na_2CO_3 solution (prepared by dissolving 40gm of Na_2CO_3 in 250ml of water) and heated under reflux for 10-15 minutes to get a clear solution, which was treated with charcoal(2g) and filtered. The filtrate was cooled to room temperature and acidified with 60-70-ml of concentrated HCl and the mass was cooled at 10°C for 1hour. The separated solid was filtered and washed with cold water(100ml) and dried to yield β-aroyl propionic acid.

METHOD(B): To a round bottomed flask with a mechanical stirrer and condenser, aromatic compound (R=Cl, Br or-OCH_3; 2.143 and 0.8 moles respectively) and succinic anhydride(0.5, 0.5, 0.4 moles respectively) were added. To this reaction mixture , while stirring at 10°C in an ice bath, powdered aluminium chloride (0.87, 0.87and 0.71 moles respectively)was added during half-an-hour. Reaction temperature was brought to room temperature and stirring was continued for 4 hours. Finally , the temperature of reaction mass was maintained at 35°C for one hour. The contents were slowly added to a mixture of ice(200gm) and 60ml of dil HCl. Separated organic layer was subjected to steam distillation, the product obtained was cooled and separated solid was filtered, washed with cold dilute hydrochloric acid(120ml) and then with ice cold water. The crude product was taken in aqueous Na_2CO_3(40gm Na_2CO_3 in 250 ml of water) and heated until the product dissolved(15minutes), charcoal (2-4gm) was added to the solution and filtered. The filtrate was cooled to room temperature, acidified with concentrated HCl(50ml) and cooled to 0°C. The product was filtered, washed with cold water and dried to get substituted aryl propionic acids.

General Procedure for the synthesis Of 6-Aryl-4,5-Dihydropyridazin-3(2H)-Ones(IVa-i): A mixture of appropriate β-aroyl propionic acid(0.1 moles) and hydrazine hydrate (0.21 moles) in ethanol(100ml) were placed in a round bottomed flask and was heated under reflux for 3 hours on a water bath. The reaction mixture was concentrated under vaccum and cooled to room temperature to afford a crystalline product.

General procedure for the synthesis Of 2-(2-Oxo-2-Phenyl)-Ethyl-6-Aryl-4,5-Dihyropyridazine-3(2H)-Ones (VIa-i): To a stirred solution of 6-aryl-4,5-dihydropyridazin-3(2H)-one (0.05 moles) and sodium hydride(0.08 moles) in toluene (50ml) at room

temperature, phenacyl bromide (0.05 moles) in toluene was added dropwise. Stirring was continued and the progress of the reaction was monitored by TLC on silica gel plate using hexane: ethylacetate (6:4) as solvent. After completion of reaction, toluene was removed under vaccum distillation to yield crude product. The crude product was purified by recrystallisation from suitable solvents like methanol, chloroform, or acetone.

General Procedure for the Synthesis Of 2-[(2-Oxo-2-Aryl-)]Ethyl-6-Aryl-4,5-Dihydropyridazine-3(2H)-Thione Using Phase Transfer Catalysis (VIIa-i): A mixture of Phosphorous Pentasulphide(0.055mole), anhydrous potassium carbonate(0.075mole) and TBAB/and PEG4000(0.00025mole each) in ethylene dichloride(125ml) was heated under reflux for about 45min and then cool the reaction mixture to 60˚c and then add 6-aryl-4,5dihydro-2H-pyridazine-3-one(0.05mole) and the reaction is continued. when the reaction is completed, filter the mixture while hot. Distill off the solvent, ethylene dichloride. The product resulted was purified by recrystallization from ethanol to obtain and yellow crystalline solid. MP: 200˚c

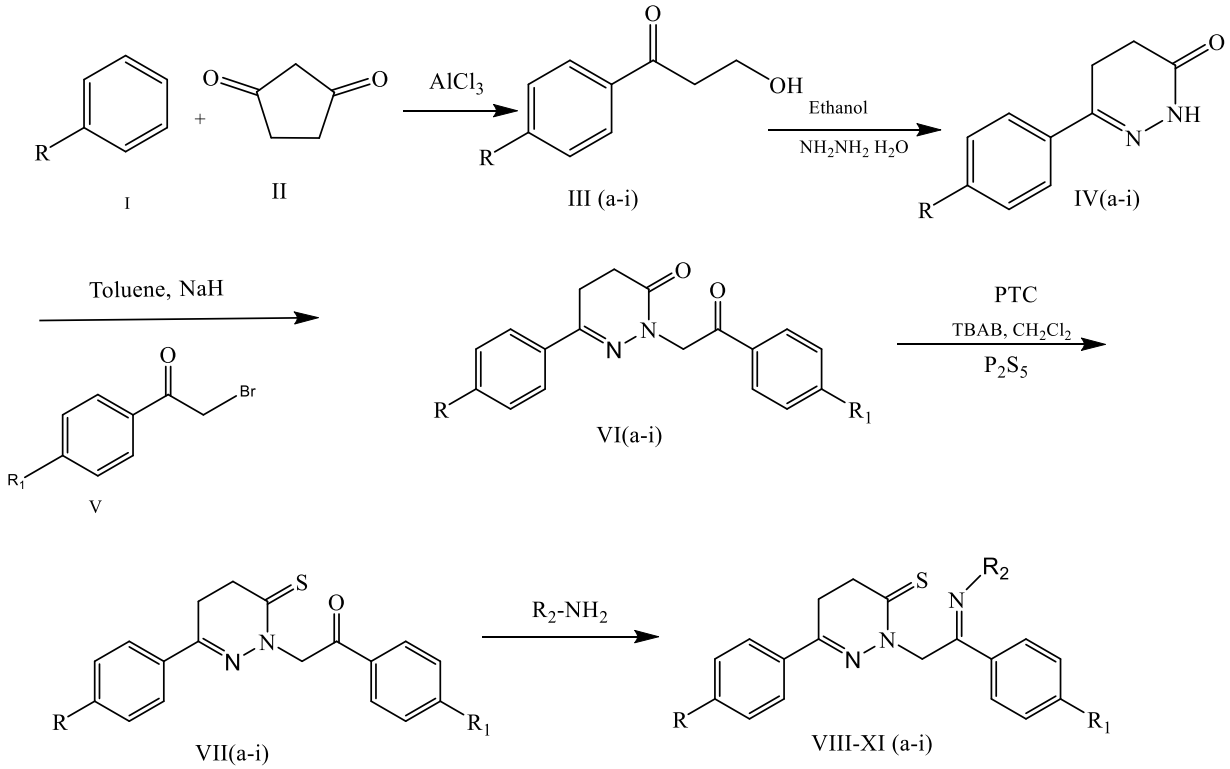
General Procedure For The Synthesis Of Schiff's Bases Of 2-[(2-Oxo-2-Aryl-)]Ethyl-6-Aryl-4,5-Dihydropyridazine-3(2H)-Thione:

i) Synthesis of 2-[2-(phenylhydrazono)-2-aryl]-ethyl-6-aryl-4,5 dihydro-2H-pyridazine-3-thione (VIIIa-i): To solution of 2-[(2-oxo-2-aryl)]-ethyl-6-aryl-4,5-dihydro-2H-pyridazine-3-thione (X, 0.005 mole) in acetic acid (25ml) was added a solution of phenylhydrazine (0.005 mole) in aqueous acetic acid (5ml). The reaction mixture was stirred while scratching the walls of the container for about 30 min. During this period, the solution slowly got warmed up and the product started forming, rapidly. Later, the reaction mixture was cooled to room temperature and the product was filtered, washed with dilute HCl and finally with cold water. The product was purified by recrystallization from a suitable solvent to obtain a colorless crystalline compound [16-18].

ii) Synthesis of 2-[2-(semicarbozono)-2-aryl]-ethyl-6-aryl-4,5-dihydro-2H-pyridazine-3-Thione(IXa-i): A mix of powdered semicarbazide HCl (0.005 moles) and anhydrous sod acetate (0.045 mole) in water (2.5 ml) was warmed gently to get a clear solution then added a solution of 2-(2-oxo-2-aryl)-ethyl-6-aryl-4,5-dihydro-2H-pyridazin-3-thione(X) in ethanol. The reaction mixture was heated gently under reflux on a water bath for 15-20 min. The product started crystallizing out while the reaction mixture was still hot. It was cooled and the product was filtered and washed thoroughly with cold water and drained well. It was purified by recrystallization from appropriate solvent.

iii) Synthesis of 2-(2-(hydroxyimino)-2-phenylethyl)-6-phenyl-4,5-dihydropyridazine-3(2H)-thione (Xa-i): Two different conical flasks were taken and labelled as A and B. The hydroxylamine hydrochloride (0.014mole) was dissolved in water and mixed well properly to obtain a clear solution which was labelled as A.In another conical flask sodium hydroxide(0.05mole) dissolved in water was prepared and it is labelled as B. Both the prepared solutions were cooled, later the sodium hydroxide solution was added to the flask containing hydroxylamine hydrochloride solution by maintaining the temperature between 5 & 10˚c. To the prepared mixture of solution, the 2-(2-oxo-2-aryl)ethyl pyridazine-3-thione was added slowly by gently mixing the solution under cold conditions and to be observed that the temperature should not rise to 15˚c during addition.The product starts to crystallize when half of the solution was added. After the complete addition of compound the flask was kept aside for about 15min and allow it to cool. The obtained product was filtered at the pump and recrystallized by the specific solvent.

iv) Synthesis of 2-(2-hydrazono-2-phenylethyl)-6-phenyl-4,5-dihydropyridazine-3(2H)-thione(Xia-i): To the synthesized compound of 2-(2-oxo-2-aryl)ethyl pyridazine-3-thione(0.003moles) which was dissolved in ethanol, the hydrazine hydrate(0.019mole) in ethanol was added and these mixed solutions were taken into a three necked round bottomed flask fitted to a condenser, the contents of the flask was kept for reflux for about 2-3 hours. After completion of the reaction, the product was obtained on evaporation of the solvent. It was purified by recrystallization with ethanol.



R	R_1	R_2
H	H	-NHPh (VIII)
CH_3	Cl	-$NHCONH_2$ (IX)
OCH_3		-OH (X)
Cl,		-NH_2 (XI)
Br		

Scheme: Synthesis of Schiff bases of 2-(2-Oxo-2-Aryl)Ethyl pyridazin-3-thione derivatives

VIIIa: 6-phenyl-2-(2-phenyl-2-(2-phenylhydrazono) ethyl)-4,5-dihydropyridazine-3(2H)-thione(R=R_1=H, R2 = NHPh): Recrystallized from ethanol to get colorless crystals. Yield :2g(75%),M.P(˚C): 122-128, IR(KBr)(cm-1):730&680**(**aromatic CH), 977.91 **(**N-N stretching), 1325(C-N stretching), 1290(C=Sstretching), 2904 (CH_2 stretching), 1591.27(C=N), 3527(N-H,aromatic), ^{1}H NMR (DMSO) δ (ppm): 2.64 (2H, ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.79 (2H, ddd, *J* = 14.2, 4.2, 1.8 Hz), 4.65 (2H, s), 7.08 (1H, tt, *J* = 7.8, 1.2 Hz), 7.13-7.31 (4H, 7.21 (tt, *J* = 7.5, 1.3 Hz), 7.16 (dtd, *J* = 8.2, 1.2, 0.5 Hz), 7.26 (tt, *J* = 7.4, 1.3 Hz)), 7.31-7.42 (4H, 7.36 (dddd, *J* = 7.9, 7.5, 1.9, 0.5 Hz), 7.37 (dddd, *J* = 8.2, 7.4, 1.9, 0.5 Hz)), 7.58 (2H, dddd, *J* = 8.2, 7.8, 1.5, 0.5 Hz), 8.17-8.27 (4H, 8.23 (dddd, *J* = 7.9, 1.8, 1.3, 0.5 Hz), 8.20 (dddd, *J* = 8.2, 1.9, 1.3, 0.4 Hz).

VIIIb:6-(4-Chlorophenyl)-2-(2-phenyl-2-(2-phenylhydrazono) ethyl)-4,5-dihydropyridazine 3(2H)-thione(R= Cl, R_1=H, R2 = NHPh): Recrystallized from ethanol to get colorless crystals. Yield: 2g (75%), M.P:123-124˚c. IR(KBr)(cm-1): 725&679 **(**aromatic C-H), 986.8 **(**N-N stretching), 1315(C-N stretching), 1285(C=Sstretching), 2916 (CH_2 stretching), 1576.1(C=N), 3497(N-H,aromatic),658(C-Cl stretching)^{1}H NMR (DMSO) δ (ppm): 2.61-2.84 (4H, 2.68 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.79 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.65(2H,s), 7.08 (1H, tt, *J* = 7.8, 1.2 Hz), 7.16 (2H, dtd, *J* = 8.2, 1.2, 0.5 Hz), 7.21-7.42 (5H, 7.37 (dddd, *J* = 8.2,7.4, 1.9, 0.5 Hz), 7.33 (ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.26 (tt, *J* = 7.4, 1.3 Hz)), 7.52-7.63 (4H, 7.58 (dddd, *J* =8.2, 7.8,1.5, 0.5 Hz), 7.56 (ddd, *J* = 8.6, 1.4, 0.6 Hz)), 8.20 (2H, dddd, *J* = 8.2, 1.9, 1.3, 0.4 Hz).

VIIIc:(4-methoxyphenyl)-2-(2-phenyl-2-(2-phenylhydrazono) ethyl)-4,5-dihydropyridazine-3(2H)-thione (R=OCH3, R_1=H, R2 = NHPh): Recrystallized from ehanol to get colorless crystals. Yield:2g (75%),M.P:123-128.˚c. IR(KBr) (cm-1): 729&683(aromatic C-H), 987.6 (N-N stretching), 1296(C-N stretching), 1197(C=Sstretching), 2896 (CH_2 stretching), 1610.5(C=N), 3415(N-H,aromatic), ^{1}H NMR (DMSO) δ (ppm): 2.62-2.84 (4H, 2.69 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 3.82 (3H, s), 4.65 (2H, s), 7.08 (1H, tt, *J* = 7.8, 1.2 Hz), 7.16 (2H, dtd, *J* = 8.2, 1.2, 0.5 Hz), 7.21-7.31 (3H, 7.26 (tt, *J* = 7.4, 1.3 Hz), 7.25 (ddd, *J* = 8.8, 1.2, 0.5 Hz)), 7.32-7.42 (4H, 7.37 (dddd, *J* = 8.2, 7.4, 1.9, 0.5 Hz), 7.38 (ddd, *J* = 8.8, 1.8, 0.5 Hz)), 7.58 (2H, dddd, *J* = 8.2, 7.8, 1.5, 0.5 Hz), 8.20 (2H, dddd, *J* = 8.2, 1.9, 1.3, 0.4 Hz).

VIIId: 2-2-phenyl-2-(2-phenylhydrazono) ethyl)-6-(p-tolyl)-4,5-dihydropyridazine-3(2H)-thione (R=CH3, R_1=H, R2 = NHPh): Recrystallized from ethanol to get colorless crystals. Yield: 2.5g(78%) M.P:124-128.˚c,m/z ratio: 410, IR(KBr) (cm-1): aromatic C-H deformations(730,680),N-N stretching(977.91), C-N strecthing((1325), C=S stretching((1290), CH_2 stretching((2904), C=N(1591.27), 3511(N-H,aromatic), ^{1}H NMR (DMSO) δ (ppm): 1.54(t,2H-Ar-H),2.68(t,2H-Ar-H), 2.07(s, 2H-CH_2- at position 2), 6.81 (t,1H- Ar-H), 2.34 (s, 3H-CH_3 para position of aromatic ring at position 6), 7.0(s, 1H- N-H), 7.28(d,d 2H-Ar-H), 7.71(d,d 2H-Ar-H), 7.94(d,d 2H-Ar-H),7.52(d,d,d 3H-Ar-H), 7.20(d,d 2H-Ar-H), 7.35(d,d 2H-Ar-H).

VIIIe:6-(4-bromophenyl)-2-(2-phenyl-2-(2-phenylhydrazono) ethyl)-4, 5 dihydropyridazine-3(2H) thione (R=Br, R_1=H, R2 = NHPh): Recrystallized from ethanol to get colorless crystals. Yield:2.5g(78%) M.P:124-128.˚c. . IR(KBr)(cm-1): 734&686 (aromatic C-H), 989.1 (N-N stretching), 1333.2(C-N stretching), 1286(C=Sstretching), 2941 (CH_2 stretching), 1617.8(C=N), 3489(N-H,aromatic), .545.4(C-Br stretching) ^{1}H NMR (DMSO) δ (ppm): 2.59-2.84 (4H, 2.67 (ddd, *J* = 13.6, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.65 (2H, s), 7.08 (1H, tt, *J* = 7.8,1.2 Hz), 7.16 (2H, dtd, *J* = 8.2, 1.2, 0.5 Hz), 7.26 (1H, tt, *J* = 7.4, 1.3 Hz), 7.37 (2H, dddd, *J* = 8.2, 7.4, 1.9, 0.5 Hz), 7.45 (2H, ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.48-7.63 (4H, 7.58 (dddd, *J* = 8.2, 7.8, 1.5, 0.5 Hz), 7.51 (ddd, *J* = 8.6, 1.4, 0.6 Hz)), 8.20 (2H, dddd, *J* = 8.2, 1.9, 1.3, 0.4 Hz).

VIIIf:2-(2-(4-chlorophenyl)-2-(2-phenylhydrazono)ethyl)-6-phenyl-4,5-dihydropyridazine-3(2H)-thione (R=H, R_1=Cl, R2 = NHPh): Recrystallized from ethanol to get colorless crystals.Yield:2.5g(78%) M.P: 124-128.˚c. IR(KBr) (cm-1): 730&685(aromatic C-H), 979.9 (N-N stretching), 1325.1(C-N stretching), 1291(C=Sstretching), 2941 (CH_2 stretching), 1646.1(C=N), 3497(N-H,aromatic),797.6(C-Cl stretching) ^{1}H NMR (DMSO) δ (ppm): 2.59-2.84 (4H, 2.67 (ddd, *J* = 13.6, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.61 (2H, s), 7.08 (1H, tt, *J* = 7.8, 1.2 Hz), 7.16 (2H, dtd, *J* = 8.2, 1.2, 0.5 Hz), 7.32 (2H, ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.45 (2H, ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.48-7.63 (6H, 7.58 (dddd, *J* = 8.2, 7.8, 1.5, 0.5 Hz), 7.51 (ddd, *J* = 8.6, 1.4, 0.6 Hz), 7.54 (ddd, *J* = 8.6, 1.5, 0.6 Hz))

VIIIg:6-(4-chlorophenyl)-2-(2-(4-chlorophenyl)-2-(2-phenylhydrazono) ethyl)-4,5-dihydro pyridazine-3(2H)-thione (R=R_1=Cl, R2 = NHPh): Recrystallized from ethanol to get colorless crystals. Yield:2.5g(78%), M.P: 124-128.˚C, IR(KBr)(cm-1): 729&684 (aromatic C-H), 980.1 (N-N stretching), 1319.1(C-N stretching), 1198(C=Sstretching), 2948.4 (CH_2 stretching), 1656.1(C=N), 3397(N-H,aromatic),791.6& 689.6(C-Cl stretching) ^{1}H NMR (DMSO) δ (ppm): δ 2.62-2.84 (4H, 2.70 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.79 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.63 (2H, s), 7.08 (1H, tt, *J* = 7.8, 1.2 Hz), 7.16 (2H, dtd, *J* = 8.2, 1.2, 0.5 Hz), 7.28-7.37 (4H, 7.32 (ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.33 (ddd, *J* = 8.6, 1.9, 0.6 Hz)), 7.51-7.63 (6H, 7.58 (dddd, *J* = 8.2, 7.8, 1.5, 0.5 Hz), 7.56 (ddd, *J* = 8.6, 1.4, 0.6 Hz), 7.54 (ddd, *J* = 8.6, 1.5, 0.6 Hz)).

VIIIh:6-(4-bromophenyl)-2-(2-(4-chlorophenyl)-2-(2-phenylhydrazono) ethyl)-4,5-dihydropyridazine-3(2H)-thione (R=Br, R_1=Cl, R2 = NHPh): Recrystallized from ethanol to get colorless crystals. Yield:2.5g(78%) M.P:124-128˚C. IR(KBr) (cm-1): 761&695(aromatic C-H), 983.4 (N-N stretching), 1321.5(C-N stretching), 1284.1(C=Sstretching), 2903.1 (CH_2 stretching), 1587.6(C=N), 3526(N-H,aromatic),581.4(C-Br stretching) ^{1}H NMR (DMSO) δ (ppm): δ 2.59-2.84 (4H, 2.67 (ddd, *J* = 13.6, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.61 (2H, s), 7.08 (1H, tt, *J* = 7.8, 1.2 Hz), 7.16 (2H, dtd, *J* = 8.2, 1.2, 0.5 Hz), 7.32 (2H, ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.45 (2H, ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.48-7.63 (6H, 7.58 (dddd, *J* = 8.2, 7.8, 1.5, 0.5 Hz), 7.51 (ddd, *J* = 8.6, 1.4, 0.6 Hz), 7.54 (ddd, *J* = 8.6, 1.5, 0.6 Hz)).

VIIIi: 2-(2-(4-chlorophenyl)-2-(2-phenylhydrazono) ethyl)-6-(p-tolyl)-4,5-dihydropyridazine-3(2H)-thione (R=CH3, R_1=Cl, R2 = NHPh): Recrystallized from ethanol to get colorless crystals.Yield:2.5g(78%) M.P:124-128˚c. IR(KBr) (cm-1): 728&683(aromatic C-H), 979.8 (N-N stretching), 1326.1(C-N stretching), 1289.4(C=Sstretching), 2903.9 (CH_2 stretching), 1590.6(C=N), 3526.7(N-H,aromatic),591.6(C-Cl stretching) ^{1}H NMR (DMSO) δ (ppm): δ 2.20 (3H, s), 2.61-2.84 (4H, 2.68 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.79

(ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.66 (2H, s), 7.03-7.20 (5H, 7.16 (dtd, *J* = 8.2, 1.2, 0.5 Hz), 7.11 (ddd, *J* = 8.0, 1.3, 0.5 Hz), 7.08 (tt, *J* = 7.8, 1.2 Hz)), 7.32 (2H, ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.40 (2H, ddd, *J* = 8.0, 1.8, 0.5 Hz), 7.51-7.63 (4H, 7.58 (dddd, *J* = 8.2, 7.8, 1.5, 0.5 Hz), 7.54 (ddd, *J* = 8.6, 1.5, 0.6 Hz)).

IXa:2-(1-phenyl-2-(3-phenyl-6-thioxo-5,6-dihydropyridazin-1(4H)-yl)ethylidene) hydrazinecarboxamide:(R=R_1=H, R_2 = $NHCONH_2$) Recrystallized from chloroform to get colorless compound..Yield:1.5g(75%) M.P:190-194˚c**,** **,** IR(KBr) (cm-1): 730.6&680 (Aromatic C-H deformations), 979.84(N-N stretching), 1274(C-N stretching), 1560 (C=N stretching), 1170(C=S stretching), 3468.01(NH-CO-NH_2,amide), 2916(CH2-stretching,) ^{1}H NMR (DMSO) δ (ppm): 2.62-2.84 (4H, 2.69 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 3.82 (3H, s), 4.66 (2H, s), 7.08 (1H, tt, *J* = 7.8, 1.2 Hz), 7.16 (2H, dtd, *J* = 8.2, 1.2, 0.5 Hz), 7.22-7.35 (4H, 7.25 (ddd, *J* = 8.8, 1.2, 0.5 Hz), 7.32 (ddd, *J* = 8.6, 1.9, 0.6 Hz)), 7.38 (2H, ddd, *J* = 8.8, 1.8, 0.5 Hz), 7.51-7.63 (4H, 7.58 (dddd, *J* = 8.2, 7.8, 1.5, 0.5 Hz), 7.54 (ddd, *J* = 8.6, 1.5, 0.6 Hz)).

IXb:2-(2-(3-(4-chlorophenyl)-6-thioxo-5,6-dihydropyridazin-1(4H)-yl)-1-phenyl ethylidene) hydrazine carboxamide: (R=Cl, R_1=H, R_2 = $NHCONH_2$) Recrystallized from chloroform to get colorless compound.Yield:1.5g(75%)M.P:190-194˚c**,** IR(KBr)(cm-1):729.6&676 (Aromatic C-H deformations), 976.84(N-N stretching), 1274(C-N stretching), 1560 (C=N stretching), 1170(C=S stretching), 3468.01(NH-CO-NH_2,amide), 2916(CH2-stretching,), 690(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.62-2.84 (4H, 2.70 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.79 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.63 (2H, s), 7.33 (2H, ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.36-7.49 (3H, 7.45 (dddd, *J* = 8.1, 7.4, 1.9, 0.4 Hz), 7.38 (tt, *J* = 7.4, 1.3 Hz)), 7.56 (2H, ddd, *J* = 8.6, 1.4, 0.6 Hz), 8.37 (2H, dddd, *J* = 8.1, 1.9, 1.3, 0.4 Hz).

IXc:2-(2-(3-(4-bromophenyl)-6-thioxo-5,6-dihydropyridazin-1(4H)-yl)-1-phenyl ethylidene) hydrazine carboxamide:(R=Br, R_1=H, R_2 = $NHCONH_2$) Recrystallized from chloroform to get colorless compound.Yield:1.5g(75%) M.P:194˚c. **,** IR(KBr) (cm-1): 732.6&684 (Aromatic C-H deformations), 978.8(N-N stretching), 1289.4(C-N stretching), 1560 (C=N stretching), 1179(C=S stretching), 3465.01(NH-CO-NH_2,amide), 2896(CH2-stretching,), .545.4(C-Br stretching) ^{1}H NMR (DMSO) δ (ppm): δ 2.62-2.84 (4H, 2.69 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 3.82 (3H, s), 4.60 (2H, s), 7.25 (2H, ddd, *J* = 8.8, 1.2, 0.5 Hz), 7.35-7.49 (5H, 7.45 (dddd, *J* = 8.1, 7.4, 1.9, 0.4 Hz), 7.38 (ddd, *J* = 8.8, 1.8, 0.5 Hz), 7.38 (tt, *J* = 7.4, 1.3 Hz)), 8.37 (2H, dddd, *J* = 8.1, 1.9, 1.3, 0.4 Hz).

IXd:2-(1-phenyl-2-(6-thioxo-3-(p-tolyl)-5,6-dihydropyridazin-1(4H)-yl) ethylidene) hydrazine carboxamide:(R=CH3, R_1=H, R_2 = $NHCONH_2$) Recrystallized from chloroform to get colorless compound.Yield:1.5g(75%) M.P:190˚c. IR(KBr) (cm-1): 731.6&682 (Aromatic C-H deformations), 979.1(N-N stretching), 1290.2(C-N stretching), 1568 (C=N stretching), 1169(C=S stretching), 3475.01(NH-CO-NH_2,amide), 2931.4(CH2-stretching,) ^{1}H NMR (DMSO) δ (ppm): 2.20 (3H, s), 2.61-2.84 (4H, 2.68 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.79 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.57 (2H, s), 7.11 (2H, ddd, *J* = 8.0, 1.3, 0.5 Hz), 7.36-7.49 (5H, 7.45 (dddd, *J* = 8.1, 7.4, 1.9, 0.4 Hz), 7.40 (ddd, *J* = 8.0, 1.8, 0.5 Hz), 7.38 (tt, *J* = 7.4, 1.3 Hz)), 8.37 (2H, dddd, *J* = 8.1, 1.9, 1.3, 0.4 Hz).

IXe: 2-(2-(3-(4-methoxyphenyl)-6-thioxo-5,6-dihydropyridazin-1(4H)-yl)-1 phenyl methylidene) hydrazine carboxamide:(R=OCH3, R_1=H, R_2 = $NHCONH_2$) Recrystallized from chloroform to get colorless. compound.Yield :1.5g(75%) M.P:190˚c. IR(KBr) (cm-1): 730&679 (Aromatic C-H deformations), 984.9(N-N stretching), 1273.9(C-N stretching), 1564 (C=N stretching), 1168.4(C=S stretching), 3469.6(NH-CO-NH_2,amide), 2914.4(CH2-stretching,) ^{1}H NMR (DMSO) δ (ppm): 2.59-2.84 (4H, 2.67 (ddd, *J* = 13.6, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.63 (2H, s), 7.36-7.54 (7H, 7.45 (dddd, *J* = 8.1, 7.4, 1.9, 0.4 Hz), 7.45 (ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.51 (ddd, *J* = 8.6, 1.4, 0.6 Hz), 7.38 (tt, *J* = 7.4, 1.3 Hz)), 8.37 (2H, dddd, *J* = 8.1, 1.9, 1.3, 0.4 Hz).

IXf:2-(1-(4-chlorophenyl)-2-(3-phenyl-6-thioxo-5,6-dihydropyridazin (4H) yl)ethylidene) hydrazine carboxamide :(R=H, R_1=Cl, R_2 = $NHCONH_2$) Recrystallized from chloroform to get colorless compound.Yield:1.5g(75%), M.P:180˚c **.** IR(KBr) (cm-1): 730.1.6&678 (Aromatic C-H deformations), 976.7(N-N stretching), 1271.6(C-N stretching), 1560 (C=N stretching), 1169(C=S stretching), 3469.01(NH-CO-NH_2,amide), 2914(CH2-stretching,), 696.4(C-Cl stretching)**..** ^{1}H NMR (DMSO) δ (ppm): 2.64 (2H, ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.79 (2H, ddd, *J* = 14.2, 4.2, 1.8 Hz), 4.55 (2H, s), 7.21 (1H, tt, *J* = 7.5, 1.3 Hz), 7.31-7.43 (4H, 7.36 (dddd, *J* = 7.9, 7.5, 1.9, 0.5 Hz), 7.40 (ddd, *J* = 8.6, 1.9, 0.5 Hz)), 7.59 (2H, ddd, *J* = 8.6, 1.4, 0.5 Hz), 8.23 (2H, dddd, *J* = 7.9, 1.8, 1.3, 0.5 Hz).

IXg: 2-(1-(4-chlorophenyl)-2-(3-(4-chlorophenyl)-6-thioxo-5,6-dihydropyridazin-1(4H)-yl) ethylidene) hydrazine carboxamide:(R=R_1=Cl, R_2 = $NHCONH_2$) Recrystallized from chloroform to get colorless compound. Yield:1.5g(75%) M.P:180˚c. IR(KBr) (cm-1): 729.8&680 (Aromatic C-H deformations), 986.9(N-N stretching), 1270.8(C-N stretching), 1566

(C=N stretching), 1169.4(C=S stretching), 3467.6(NH-CO-NH_2,amide), 2962.6(CH2-stretching,), 798.4&696.4(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.62-2.84 (4H, 2.70 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.79 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.69 (2H, s), 7.33 (2H, ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.40 (2H, ddd, *J* = 8.6, 1.9, 0.5 Hz), 7.52-7.62 (4H, 7.59 (ddd, *J* = 8.6, 1.4, 0.5 Hz), 7.56 (ddd, *J* = 8.6, 1.4, 0.6 Hz)).

IXh:2-(2-(3-(4-bromophenyl)-6-thioxo-5,6-dihydropyridazin-1(4H)-yl)-1-(4 chloro phenyl) ethylidene) hydrazine carboxamide:(R=Br,R_1=Cl, R_2 = NHCONH$_2$) Recrystallized from chloroform to get colorless compound.Yield:1.5g(75%) M.P:180˚c. IR(KBr) (cm-1): 729.&681 (Aromatic C-H deformations), 991.8(N-N stretching), 1291.6(C-N stretching), 1569 (C=N stretching), 1178.4(C=S stretching), 3467.6(NH-CO-NH_2,amide), 2963.6(CH2-stretching,), 596.8 (C-Br stretching). ^{1}H NMR (DMSO) δ (ppm): δ 2.59-2.84 (4H, 2.67 (ddd, *J* = 13.6, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.66 (2H, s), 7.40 (2H, ddd, *J* = 8.6, 1.9, 0.5 Hz), 7.42-7.54 (4H, 7.51 (ddd, *J* = 8.6, 1.4, 0.6 Hz), 7.45 (ddd, *J* = 8.6, 1.9, 0.6 Hz)), 7.59 (2H, ddd, *J* = 8.6, 1.4, 0.5 Hz).

IXi: 2-(1-(4-chlorophenyl)-2-(6-thioxo-3-(p-tolyl)-5,6-dihydropyridazin-1(4H)-yl)ethylidene) hydrazine carboxamide:(R=CH3, R_1=Cl, R_2 = NHCONH$_2$) Recrystallized from chloroform to get colorless compound.Yield:1.5g(75%), M.P:180˚c. IR(KBr) (cm-1): 734.8&681 (Aromatic C-H deformations), 983.4(N-N stretching), 190(C-N stretching), 1566 (C=N stretching), 1181.6(C=S stretching), 3467.6(NH-CO-NH_2,amide), 2962.6(CH2-stretching,), 798.4(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.20 (3H, s), 2.61-2.84 (4H, 2.68 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.79 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.61 (2H, s), 7.11 (2H, ddd, *J* = 8.0, 1.3, 0.5 Hz), 7.37-7.43 (4H, 7.40 (ddd, *J* = 8.6, 1.9, 0.5 Hz), 7.40 (ddd, *J* = 8.0, 1.8, 0.5 Hz)), 7.59 (2H, ddd, *J* = 8.6, 1.4, 0.5 Hz).

Xa:2-(2-(hydroxyimino)-2-phenylethyl)-6-phenyl-4,5-dihydropyridazine-3(2H)-thione: (R=R_1=H, R_2 = -OH) Recrystallized from chloroform to get colorless product.Yield:1.2g(75%), M.P:186˚c IR (KBr, Cm-1) at 730,680 (Aromatic C-H deformations), 950,979 (N-N stretching), 1348(C-N stretching), 1570 (C=N stretching), 1276(C=S stretching), 1629(C=N stretching oximes), 2916 (CH2-Stretching)^{1}H NMR (DMSO) δ (ppm): 2.62-2.84 (4H, 2.69 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 3.82 (3H, s), 4.63 (2H, s), 7.25 (2H, ddd, *J* = 8.8, 1.2, 0.5 Hz), 7.35-7.43 (4H, 7.40 (ddd, *J* = 8.6, 1.9, 0.5 Hz), 7.38 (ddd, *J* = 8.8, 1.8, 0.5 Hz)), 7.59 (2H, ddd, *J* = 8.6, 1.4, 0.5 Hz).

Xb:6-(4-chlorophenyl)-2-(2-(hydroxyimino)-2-phenylethyl)-4,5-dihydropyridazine-3(2H)-thione:(R=Cl, R_1=H, R_2 = -OH) Recrystallized from chloroform to get colorless product.Yield:1.2g(75%), , M.P:132-136˚c. IR (KBr, Cm-1) at 729,681 (Aromatic C-H deformations), 950,979 (N-N stretching), 1347(C-N stretching), 1569.8 (C=N stretching), 1278.4(C=S stretching), 1629(C=N stretching oximes), 2916 (CH2-Stretching), 696.4(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.62-2.83 (4H, 2.70 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.70 (2H, s), 7.33 (2H, ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.40-7.52 (3H, 7.47 (dddd, *J* = 7.7, 7.3, 1.6, 0.4 Hz), 7.43 (tt, *J* = 7.3, 1.4 Hz)), 7.56 (2H, ddd, *J* = 8.6, 1.4, 0.6 Hz), 8.28 (2H, dddd, *J* = 7.7, 1.7, 1.4, 0.4 Hz).

Xc:6-(4-bromophenyl)-2-(2-(hydroxyimino)-2-phenylethyl)- 4,5-dihydropyridazine 3(2H)-thione: (R=Br, R_1=H, R_2 = -OH) Recrystallized from chloroform to get colorless product.Yield:1.2g(75%) M.P:134-136˚c. %), IR (KBr, Cm-1) at 729.1,682 (Aromatic C-H deformations), 949.1,978.1 (N-N stretching), 1348.1(C-N stretching), 1570 (C=N stretching), 1278.4(C=S stretching), 1631(C=N stretching oximes), 2915.9 (CH2-Stretching).545.4(C-Br stretching) ^{1}H NMR (DMSO) δ (ppm): 2.62-2.83 (4H, 2.69 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 3.82 (3H, s), 4.70 (2H, s), 7.25 (2H, ddd, *J* = 8.8, 1.2, 0.5 Hz), 7.38 (2H, ddd, *J* = 8.8, 1.8, 0.5 Hz), 7.40-7.52 (3H, 7.47 (dddd, *J* = 7.8, 7.3, 1.6, 0.4 Hz), 7.43 (tt, *J* = 7.3, 1.4 Hz)), 8.28 (2H, dddd, *J* = 7.8, 1.7, 1.4, 0.4 Hz).

Xd:2-(2-(hydroxyimino)-2-phenylethyl)-6-(p-tolyl)-4,5-dihydropyridazine-3(2H)-thione:(R=CH_3, R_1=H, R_2 = -OH) Recrystallized from chloroform to get colorless product.Yield:1.2g(75%), M.p=134˚c. IR (KBr, Cm-1) at 729.3,683 (Aromatic C-H deformations), 948,981 (N-N stretching), 1348.1(C-N stretching), 1581.8 (C=N stretching), 1280.4(C=S stretching), 1589(C=N stretching oximes), 2918 (CH2-Stretching).^{1}H NMR (DMSO) δ (ppm): 2.62-2.83 (4H, 2.69 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 3.82 (3H, s), 4.70 (2H, s), 7.25 (2H, ddd, *J* = 8.8, 1.2, 0.5 Hz), 7.38 (2H, ddd, *J* = 8.8, 1.8, 0.5 Hz), 7.40-7.52 (3H, 7.47 (dddd, *J* = 7.8, 7.3, 1.6, 0.4 Hz), 7.43 (tt, *J* = 7.3, 1.4 Hz)), 8.28 (2H, dddd, *J* = 7.8, 1.7, 1.4, 0.4 Hz).

Xe:2-(2-(hydroxyimino)-2-phenylethyl)-6-(4-methoxyphenyl)-4,5-dihydropyridazine-3(2H)-thione: (R=OCH3, R_1=H, R_2 = -OH) Recrystallized from chloroform to get colorless product.Yield:1.2g(75%), M.P=146˚c. IR (KBr, Cm-1) at 729.4,681.4 (Aromatic C-H deformations), 948,982 (N-N stretching), 1350.6(C-N stretching), 1584.5 (C=N stretching), 1286.4(C=S stretching), 1629(C=N

stretching oximes), 2916 (CH2-Stretching). ^{1}H NMR (DMSO) δ (ppm): 2.59-2.84 (4H, 2.67 (ddd, *J* = 13.6, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.71 (2H, s), 7.40-7.54 (7H, 7.47 (dddd, *J* = 7.7, 7.3, 1.6, 0.4 Hz), 7.45 (ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.51 (ddd, *J* = 8.6, 1.4, 0.6 Hz), 7.43 (tt, *J* = 7.3, 1.4 Hz)), 8.28 (2H, dddd, *J* = 7.7, 1.7, 1.4, 0.4 Hz).

Xf:2-(2-(4-chlorophenyl)-2-(hydroxyimino)ethyl)-6-phenyl-4,5-dihydropyridazine-3(2H)-thione:(R=H, R_1=Cl, R_2 = -OH) Recrystallized from chloroform to get colorless product.Yield:1.2g(75%),M.P=132-136˚c. IR (KBr, Cm-1) at 728.6,682 (Aromatic C-H deformations), 948,979 (N-N stretching), 1350.6(C-N stretching), 1584.1 (C=N stretching), 1278.4(C=S stretching), 1629(C=N stretching oximes), 2916 (CH2-Stretching), 696.4(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.63 (2H, ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.79 (2H, ddd, *J* = 14.2, 4.2, 1.8 Hz), 4.71 (2H, s), 7.21 (1H, tt, *J* = 7.5, 1.3 Hz), 7.36 (2H, dddd, *J* = 7.9, 7.5, 1.9, 0.5 Hz), 7.60-7.69 (4H, 7.63 (ddd, *J* = 8.7, 1.4, 0.5 Hz), 7.66 (ddd, *J* = 8.7, 1.7, 0.5 Hz)), 8.23 (2H, dddd, *J* = 7.9, 1.8, 1.3, 0.5 Hz).

Xg:6-(4-chlorophenyl)-2-(2-(4-chlorophenyl)-2-(hydroxyimino)ethyl)-4,5-dihydropyridazine-3(2H)-thione:(R=R_1=Cl, R_2 = -OH) Recrystallized from chloroform to get colorless product.Yield:1.2g(75%), M.P:138˚c. IR (KBr, Cm-1) at 727.98,683 (Aromatic C-H deformations), 950,979 (N-N stretching), 1347(C-N stretching), 1569.8 (C=N stretching), 1278.4(C=S stretching), 1628(C=N stretching oximes), 2916 (CH2-Stretching), 798.7&696.4(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.62-2.83 (4H, 2.70 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.72 (2H, s), 7.33 (2H, ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.56 (2H, ddd, *J* = 8.6, 1.4, 0.6 Hz), 7.60-7.69 (4H, 7.63 (ddd, *J* = 8.7, 1.4, 0.5 Hz), 7.66 (ddd, *J* = 8.7, 1.7, 0.5 Hz)).

Xh:6-(4-bromophenyl)-2-(2-(4-chlorophenyl)-2-(hydroxyimino)ethyl)-4,5-dihydropyridazine-3(2H)-thione:(R=Br, R_1=Cl, R_2 = -OH) Recrystallized from chloroform to get colorless product.Yield:1.2g(75%), M.P:166˚c. IR (KBr, Cm-1) at 728.4,683 (Aromatic C-H deformations), 948.4,980 (N-N stretching), 1339.6(C-N stretching), 1569.8 (C=N stretching), 1281(C=S stretching), 1629(C=N stretching oximes), 2916.4 (CH2-Stretching), 696.4(C-Br stretching), 696.4(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.59-2.84 (4H, 2.67 (ddd, *J* = 13.6, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.72 (2H, s), 7.42-7.54 (4H, 7.51 (ddd, *J* = 8.6, 1.4, 0.6 Hz), 7.45 (ddd, *J* = 8.6, 1.9, 0.6 Hz)), 7.60-7.69 (4H, 7.63 (ddd, *J* = 8.7, 1.4, 0.5 Hz), 7.66 (ddd, *J* = 8.7, 1.7, 0.5 Hz)).

Xi:2-(2-(4-chlorophenyl)-2-(hydroxyimino)ethyl)-6-(p-tolyl)-4,5-dihydropyridazine-3(2H)-thione: (R=CH_3, R_1=Cl, R_2 = -OH) Recrystallized from chloroform to get colorless product.Yield:1.2g(75%), **Chemical Formula**: $C_{19}H_{18}ClN_3OS$,M.P:156˚c, IR (KBr, Cm-1) at 728,682 (Aromatic C-H deformations), 948.4,981.4 (N-N stretching), 1340.4(C-N stretching), 1560.8 (C=N stretching), 1282.4(C=S stretching), 1648(C=N stretching oximes), 2917.1 (CH2-Stretching), 696.4(C-Cl stretching) . ^{1}H NMR (DMSO) δ (ppm): δ 2.20 (3H, s), 2.61-2.84 (4H, 2.68 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.67 (2H, s), 7.11 (2H, ddd, *J* = 8.0, 1.3, 0.5 Hz), 7.40 (2H, ddd, *J* = 8.0, 1.8, 0.5 Hz), 7.60-7.69 (4H, 7.63 (ddd, *J* = 8.7, 1.4, 0.5 Hz), 7.66 (ddd, *J* = 8.7, 1.7, 0.5 Hz)).

XIa:2-(2-hydrazono-2-phenylethyl)-6-phenyl-4,5-dihydropyridazine-3(2H)-thione:(R=R_1=H, R_2 = -NH_2) Recrystallized from chloroform to get colorless compound. yield:1.1g(60%), M.P:158˚c , IR (KBr, Cm-1) at 730,680 (Aromatic C-H deformations), 979.84(N-N stretching), 1274(C-N stretching), 1560 (C=N stretching), 1170(C=S stretching), 1648 (N-NH2 amine), 2916(CH2-stretching). ^{1}H NMR (DMSO) δ (ppm): 2.64 (2H, ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (2H, ddd, *J* = 14.2, 4.2, 1.8 Hz), 4.66 (2H, s), 7.15 (1H, tt, *J* = 7.5, 1.3 Hz), 7.21 (1H, tt, *J* = 7.5, 1.3 Hz), 7.28-7.41 (4H, 7.36 (dddd, *J* = 7.9, 7.5, 1.9, 0.5 Hz), 7.33 (dddd, *J* = 7.7, 7.5, 1.9, 0.4 Hz)), 8.02 (2H, dddd, *J* = 7.7, 1.8, 1.3, 0.4 Hz), 8.23 (2H, dddd, *J* = 7.9, 1.8, 1.3, 0.5 Hz).

XIb:6-(4-chlorophenyl)-2-(2-hydrazono-2-phenylethyl)-4,5-dihydropyridazine-3(2H) thione (R=Cl, R_1=H, R_2 = -NH_2) Recrystallized from chloroform to get colorless compound. yield:1.1g(60%), M.P:156˚c. IR (KBr, Cm-1) at 729.6,681 (Aromatic C-H deformations), 979.8(N-N stretching), 1274(C-N stretching), 1538 (C=N stretching), 1169.4(C=S stretching), 1648.4 (N-NH2 amine), 2916(CH2-stretching), 796.4(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.62-2.84 (4H, 2.70 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.65 (2H, s), 7.15 (1H, tt, *J* = 7.5, 1.3 Hz), 7.28-7.38 (4H, 7.33 (dddd, *J* = 7.7, 7.5, 1.9, 0.4 Hz), 7.33 (ddd, *J* = 8.6, 1.9, 0.6 Hz)), 7.56 (2H, ddd, *J* = 8.6, 1.4, 0.6 Hz), 8.02 (2H, dddd, *J* = 7.7, 1.8, 1.3, 0.4 Hz).

XIc:6-(4-bromophenyl)-2-(2-hydrazono-2-phenylethyl)-4,5-dihydropyridazine-3(2H)-thione (R=Br, R_1=H, R_2 = -NH_2): Recrystallized from chloroform to get colorless compound. yield:1.1g(60%), M.P:158˚c. IR (KBr, Cm-1) at 730,681 (Aromatic C-H deformations), 979.8(N-N stretching), 1273.9(C-N stretching), 1538 (C=N stretching), 1180(C=S stretching), 1648.4 (N-NH2 amine), 2916.8(CH2-stretching), 576.4(C-Br stretching).^{1}H NMR (DMSO) δ (ppm): 2.62-2.83 (4H, 2.69 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.77 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 3.82 (3H, s), 4.66 (2H, s), 7.15 (1H, tt, *J* = 7.5, 1.3 Hz), 7.22-7.41 (6H,

7.33 (dddd, *J* = 7.7, 7.5, 1.9, 0.4 Hz), 7.38 (ddd, *J* = 8.8, 1.8, 0.5 Hz), 7.25 (ddd, *J* = 8.8, 1.2, 0.5 Hz)), 8.02 (2H, dddd, *J* = 7.7, 1.8, 1.3, 0.4 Hz).

XId:2-(2-hydrazono-2-phenylethyl)-6-(p-tolyl)-4,5-dihydropyridazine-3(2H) thione (R=CH_3, R_1=H, R_2 = -NH_2): Recrystallized from chloroform to get colorless compound. yield:1.1g(60%), M.P=159˚c. IR (KBr, Cm-1) at 729.8,680 (Aromatic C-H deformations), 979 (N-N stretching), 1273.9(C-N stretching), 1559 (C=N stretching), 1169.4(C=S stretching), 1648.1 (N-NH2 amine), 2917(CH2-stretching) ^{1}H NMR (DMSO) δ (ppm): δ 2.20 (3H, s), 2.61-2.84 (4H, 2.68 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.66 (2H, s), 7.08-7.18 (3H, 7.15 (tt, *J* = 7.5, 1.3 Hz), 7.11 (ddd, *J* = 8.0, 1.3, 0.5 Hz)), 7.28-7.43 (4H, 7.33 (dddd, *J* = 7.7, 7.5, 1.9, 0.4 Hz), 7.40 (ddd, *J* = 8.0, 1.8, 0.5 Hz)), 8.02 (2H, dddd, *J* = 7.7, 1.8, 1.3, 0.4 Hz).

XIe:2-(2-hydrazono-2-phenylethyl)-6-(4-methoxyphenyl)-4,5-dihydropyridazine-3(2H)-thione (R=OCH_3, R_1=H, R_2 = -NH_2): Recrystallized from chloroform to get colorless compound. yield:1.1g(60%), M.P:161˚c. IR (KBr, Cm-1) at 729.6,681 (Aromatic C-H deformations), 979.1(N-N stretching), 1274(C-N stretching), 1559.6 (C=N stretching), 1170(C=S stretching), 1648.8 (N-NH2 amine), 2916(CH2-stretching) ^{1}H NMR (DMSO) δ (ppm): 2.59-2.84 (4H, 2.67 (ddd, *J* = 13.6, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.67 (2H, s), 7.15 (1H, tt, *J* = 7.5, 1.3 Hz), 7.33 (2H, dddd, *J* = 7.7, 7.5, 1.9, 0.4 Hz), 7.42-7.54 (4H, 7.51 (ddd, *J* = 8.6, 1.4, 0.6 Hz), 7.45 (ddd, *J* = 8.6, 1.9, 0.6 Hz)), 8.02 (2H, dddd, *J* = 7.7, 1.8, 1.3, 0.4 Hz).

XIf:2-(2-(4-chlorophenyl)-2-hydrazonoethyl)-6-phenyl-4,5-dihydropyridazine-3(2H)-thione (R=H, R_1= Cl, R_2 = -NH_2): Recrystallized from chloroform to get colorless compound. yield:1.1g(60%), M.P:164˚c. IR (KBr, Cm-1) at 730,680 (Aromatic C-H deformations), 979.84(N-N stretching), 1274(C-N stretching), 1560 (C=N stretching), 1170(C=S stretching), 1648 (N-NH2 amine), 2916(CH2-stretching), 687.4(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): δ 2.64 (2H, ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (2H, ddd, *J* = 14.2, 4.2, 1.8 Hz), 4.62 (2H, s), 7.21 (1H, tt, *J* = 7.5, 1.3 Hz), 7.25-7.41 (4H, 7.36 (dddd, *J* = 7.9, 7.5, 1.9, 0.5 Hz), 7.28 (ddd, *J* = 8.5, 1.9, 0.6 Hz)), 7.47 (2H, ddd, *J* = 8.5, 1.5, 0.6 Hz), 8.23 (2H, dddd, *J* = 7.9, 1.8, 1.3, 0.5 Hz).

XIg:6-(4-chlorophenyl)-2-(2-(4-chlorophenyl)-2-hydrazonoethyl)-4,5-dihydropyridazine-3(2H)-thione (R=R_1=Cl, R_2 = -NH_2): Recrystallized from chloroform to get colorless compound. yield:1.1g(60%), M.P:161˚c. IR (KBr, Cm-1) at 730,680 (Aromatic C-H deformations), 979.84(N-N stretching), 1274(C-N stretching), 1560 (C=N stretching), 1170(C=S stretching), 1648 (N-NH2 amine), 2916(CH2-stretching), 696.4(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.62-2.84 (4H, 2.70 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.64 (2H, s), 7.25-7.37 (4H, 7.28 (ddd, *J* = 8.5, 1.9, 0.6 Hz), 7.33 (ddd, *J* = 8.6, 1.9, 0.6 Hz)), 7.47 (2H, ddd, *J* = 8.5, 1.5, 0.6 Hz), 7.56 (2H, ddd, *J* = 8.6, 1.4, 0.6 Hz).

XIh:6-(4-bromophenyl)-2-(2-(4-chlorophenyl)-2-hydrazonoethyl)-4,5-dihydropyridazine-3(2H)-thione (R=Br, R_1=Cl, R_2 = -NH_2): Recrystallized from chloroform to get colorless compound. yield:1.1g(60%), M.P:176˚c. IR (KBr, Cm-1) at 729,680 (Aromatic C-H deformations), 981.9(N-N stretching), 1281(C-N stretching), 1567.6 (C=N stretching), 1171(C=S stretching), 1648.4 (N-NH2 amine), 2916(CH2-stretching), 586.4(C-Br stretching) 786.5(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.59-2.84 (4H, 2.67 (ddd, *J* = 13.6, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.63 (2H, s), 7.28 (2H, ddd, *J* = 8.5, 1.9, 0.6 Hz), 7.42-7.54 (6H, 7.47 (ddd, *J* = 8.5, 1.5, 0.6 Hz), 7.45 (ddd, *J* = 8.6, 1.9, 0.6 Hz), 7.51 (ddd, *J* = 8.6, 1.4, 0.6 Hz)).

XIi:2-(2-(4-chlorophenyl)-2-hydrazonoethyl)-6-(p-tolyl)-4,5-dihydropyridazine-3(2H)-thione (R=CH_3, R_1=Cl, R_2 = -NH_2):`Recrystallized from chloroform to get colorless compound. yield:1.1g(60%), M.P:145˚c. IR (KBr, Cm-1) at 730,680 (Aromatic C-H deformations), 981.64(N-N stretching), 1276(C-N stretching), 1559 (C=N stretching), 1171(C=S stretching), 1648 (N-NH2 amine), 2916(CH2-stretching), 786.4(C-Cl stretching). ^{1}H NMR (DMSO) δ (ppm): 2.20 (3H, s), 2.61-2.84 (4H, 2.68 (ddd, *J* = 13.7, 9.9, 4.2 Hz), 2.78 (ddd, *J* = 14.2, 4.2, 1.8 Hz)), 4.63 (2H, s), 7.11 (2H, ddd, *J* = 8.0, 1.3, 0.5 Hz), 7.28 (2H, ddd, *J* = 8.5, 1.9, 0.6 Hz), 7.40 (2H, ddd, *J* = 8.0, 1.8, 0.5 Hz), 7.47 (2H, ddd, *J* = 8.5, 1.5, 0.6 Hz).

V. CONCLUSION

In the present investigation a new series of Schiff bases of 2-(2-Oxo-2-Aryl) Ethyl Pyridazin-3-Thione derivatives were synthesized and these compounds were characterized by FTIR, Mass and 1H NMR spectral data. All the title compounds were evaluated for the antifungal activity on *Candida albicans than Aspergillus flavus*. All the compounds tested were found to be moderately active on the tested fungal strains and these compounds could be considered as potential antifungal agents.

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