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Synthesis and Characterization of Some New Compounds Including Heterocyclic Units

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ABSTRACT

New compounds of 5-(***p***-florophenyl)- 2-amino-1,3,4-thiadiazole [2], 2-(substituted benzylidene)-1,3,4-Thiadiazole -5-(***p***-florophenyl [3-10], 2-(substituted amino phenyl)- 1,3,4-Thiadiazole -2-yl)-)imidazolidine-4-one-3-[5-(***p***-florophenyl] [11-18],Schemes 1, 2 and **(**E)-3(3(4-nitro or 4-N,N-dimethyl aminophenyl) acryloyl)-(3--nitrophenyl)[19,20], 3-(6-***p***-Nitrophenyl or***p***-N,N-Dimethylaminophenyl)-2-thioxo-1,2,5,6-tetrahydropyrimidine-4-yl)-(Nitrophenyl) [21,22], 3(5-4(3-nitrophenyl)-1-phenyl 4,5-dihydro-1H-pyrazol-3-yl)phenyl)-4-nitrophenyl or 4-N,N-Dimethyl aminophenyl): [23,24] and 3-(2-amino-4-(4-Nitrophenyl or 4-N,N-Dimethylaminophenyl)-5,6-dihydro-2H-1,3-oxazine-6-yl)-3-Nitrophenyl[25,26]have been synthesized. The prepared compounds have synthesized from chalcone [19,20]. The structures of these compounds were identified by FT-IR,H-NMR,Uv spectra and checked by TLC.

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INTRODUCTION

1, 3, 4-thiadiazoles are known for their broad-spectrum of biological activity such as antifungal (Mishra and Tewari, 1991 andTasaka*et al.*,1993), antibacterial (Abdon and Amin, 1990), herbicidal (Khal and Nizamuddin, 1997), antiviral (Bonina *et al.*, 1982), and analgesiceffect (Zhang*et al.*, 1993 and Gupta *et al.*, 1996). Chalcones are an aromatic ketone and an enone that forms the central core for a variety of important biological compounds, which are known collectively as chalcones. Aldolcondensation represents an important class of carbon–double bond carbon formation reactions both in nature and in synthetic chemistry. Compounds called chalcones(Jayapal andSreedhar, 2010), can prepare by aldol condensation of an aromatic ketone and aldehyde. In a chalcone, two aromatic rings are joined by a 3-carbon α,β-unsaturated carbonyl compounds system. The compounds with the backbone of chalcones have been reported to possess various biological activities such as antimicrobial (Nowakowska*et al.*,2008; Narenderand Papi,2007 and Mishra *et al.*, 2008), anti-inflammatory (Li *et al.*,2002), antimalarial (Karthikeyan*et al.*,2007 and Rateb,2007), antilieshmanial(Dhar, 1981), antioxidant(Go *et al.*, 2005) and antitubercular (Azarifar and Ghasemn, 2003). Pyrazole also, is one of a class of organic heterocyclic compounds containing a five member aromatic ring structure composed of two nitrogen atoms and three carbon. But pyrazoline it is a class of organic heterocyclic compounds containing a five member not aromatic ring structure composed of two nitrogen atoms and three carbon(Echeverra*et al.*, 2009).
The aim of the present work was to form chalcones from the reaction of substituted acetophenone with different substituted aromatic aldehyde and then converted to pyrimidine,oxazine and carbothioamide.

MATERIALS AND METHODS

Chemicals:

All chemicals used in the present work were analytical reagent grade (produced by Merck, Germany; Fluka, Germany and BDH, England).

Experimental:

Synthesis of 5-(p-floro phenyl)- 2-amino-1,3,4-thiadiazole [2]:

A mixture of (0.01mol) of thiosemicarbazide and (0.01mol) of*p*- fluoro benzoic acid with (5ml) of phosphorousoxy chloride. The mixture was refluxed for 3 hrs., and then cold to room temperature. The mixture

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was diluted with 20 ml of water and refluxed, then cold and neutralized with KOH. The precipitate was filtered and recrystallized from ethanol.

Synthesis of 2-(substituted benzylidene)-1,3,4-Thiadiazole -5- (p-florophenyl [3-10]:

A mixture of compound [2] (0.01mol) and substituted benzaldehyde (0.01mol) was refluxed in absolute ethanol (15ml) containing few drops of glacial acetic acid for 3hrs. After cooling to room temperature the precipitate was filtered and dried. The products were re-crystallized from ethanol,yield (80%).

Synthesis of 2-(substituted phenyl)-1,3,4-Thiadiazole-2-yl)-)imidazolidine-4-one -3-[5- (p-florophenyl] [11-18]:

A mixture of Schiff base (0.01) mole and glycine (0.01) mole in (15 ml) of THF was refluxed for (12) hours then cold to room temperature and the formed precipitate was filtrated and recrystallized from ethanol and THF,yield (70-80%).

Synthesisof (E)-3(3(4-nitro or 4-N,N-dimethyl aminophenyl) acryloyl)- (3nitrophenyl) [19,20]:

To astirredmixtureof3-nitroacetophenone(0.01mol)andsubstituted benzaldehyde(0.01 mol) in absolute ethanol (5 ml) and NaOH in ethanol (30%) and continue stirring for two hoursatroomtemperature.Allowto stand reactionmixturefor12 hours.Precipitate thereactionmixturebyadditionofwater, acidified with diluted HCl. Filter the product,washwithcold ethanoland allowed to afford. (Dighade and Dighade, 2012).

Synthesis of 3-(6-p-Nitrophenyl or p-N,N-Dimethyl aminophenyl)-2-thioxo-1,2,5,6-tetrahydropyrimidine-4-yl)-(3-Nitrophenyl)[21,22]:

A mixture of compounds [19] or [20] (0.01mol) was added to a mixture of thiourea (0.01mol) in ethanol (20 ml) and concentrated HCl (0.3ml), them refluxed for 6 hrs. The mixture was concentrated to half its volume, cold and neutralized with diluted NaOH. The precipitate solid was filtered off, washed with water, dried and recrystallized from ethyl acetate.

Synthesis of 3-(5-4(3-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)-4-nitrophenyl or 4-N,N-Dimethyl aminophenyl) [23,24]:

Chalcone [19,20] (0.01mol) was dissolved in ethyl alcohol 95% (20ml) and refluxed with excess of phenyl hydrazine and drops of acetic acid for 12hrs ,the reaction mixture was diluted with cold water (50ml) and the precipitate formed was filtered off and recrystallized with ethyl alcohol.

Synthesis of 3-(2-amino-4-(4-Nitrophenyl or 4-N, N-Dimethylaminophenyl)-5, 6-dihydro-2H-1, 3-oxazine-6-yl)-3-Nitrophenyl [25,26]:

A mixture of compounds [19] or [20] (0.01mol),thiourea (0.01mol) was dissolved in ethanolic sodium hydroxide (0.01mol) in (20ml) was stirred for 2-3 hrs. The mixture was poured into 100 ml of cold water with continues stirring for 60 minute,the precipitate obtained was filtered off, washed water and recrystallized.

Synthesis of 5-(4-Nitrophenyl or 4-N,N-Dimethylaminophenyl)-4, 5-dihydro-1H-pyrazole-1-carbothioamide)-3-(3-Nitrophenyl) [27, 28]:

A mixture of the chalcone [19,20] (0.01mol), thiosemicarbazide (0.02mol)and (0.02mol) of potassium hydroxide in ethanol (40ml) was refluxed for 14hrs. the progress of reaction was monitored by TLC. After the completion of the reaction, the mixture was poured onto acidic ice water and the solid was filtered off.

Table 1: Physical properties of compounds [3-10].

Comp.No.	Yield %	Molecular Formula	Recrystallization solvent
[3]	80	$C_{17}H_{14}N_4SF$	EtOH
[4]	70	$C_{15}H_{10}N_3SOF$	MeOH
[5]	80	$C_{15}H_{15}N_4O_2SF$	EtOH
[6]	80	$C_{15}H_{10}N_3O_2SF$	EtOH
[7]	75	$C_{15}H_9N_3O_4SFBr$	EtOH
[8]	90	$C_{15}H_9N_4O_2SF$	MeOH
[9]	70	$C_{15}H_9N_3SFCl$	EtOH
[10]	75	$C_{15}H_{12}N_3O_2SF$	MeOH
[11]	65	$C_{15}H_{10}N_7O_2SF$	EtOH
[12]	60	$C_{15}H_{11}N_6OSF$	EtOH
[13]	70	$C_{15}H_{10}N_6SClF$	EtOH
[14]	57	$C_{15}H_{10}N_7O_2SF$	EtOH
[15]	67	$C_{15}H_{10}N_6SBrF$	EtOH
[16]	64	$C_{18}H_{16}N_7SF$	EtOH
[17]	69	$C_{15}H_{11}N_6O_2SF$	EtOH
[18]	67	$C_{16}H_{13}N_6O_2SF$	EtOH

Table 2: Physical properties of compounds [19-28].

Comp. No.	Molecular formula	Yield %
[19]	$C_{15}H_{10}N_2O_5$	80
[20]	$C_{17}H_{16}N_2O_3$	73
[21]	$C_{16}H_{12}N_4O_4S$	67
[22]	$C_{18}H_{18}N_4O_2S$	78
[23]	$C_{21}H_{16}N_4O_4$	68
[24]	$C_{23}H_{22}N_4O_2$	77
[25]	$C_{16}H_{12}N_4O_4S$	62
[26]	$C_{18}H_{18}N_4O_2S$	74
[27]	$C_{16}H_{13}N_5O_4S$	69
[28]	$C_{18}H_{19}N_5O_2S$	85

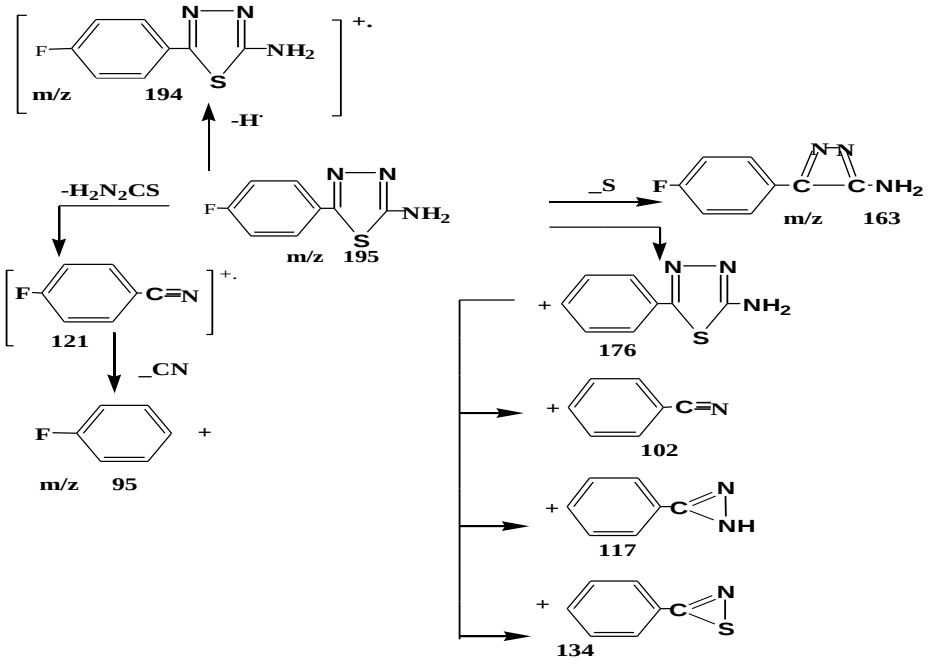
RESULTS AND DISCUSSION

Compound [2] Thiadiazoleis characterized by FT.IR, Mass and Uv spectroscopy, the melting point is recorded and the purity of this compound is checked by T.L.C. technique.

The FT-IR spectrum of the compound [2] in general, exhibited significant two bands in the region 3251-3097 cm^{-1}, which could be attributed to asymmetricand symmetric stretching vibration ofNH_2 group. In addition to a band at about 1610 cm^{-1} due to cyclic (C=N)stretching is also observed, with symmetrical stretching near 1080 cm^{-1}, in addition to a band at 837 cm^{-1},due to *p*-substituted group. UV spectrum, shows the transionsn→л and л→л* which confirmed the presence of the un-bonded pair of electrons on sulfur atom and aromatic system (double bond).

Mass spectrum (Fig. 3) of the compound [2] exhibits prominent molecular ion at 212 m/z which corresponds to the molecular weight of compound. According to these data the expected molecular formula of this compound is $C_8H_6N_3SF$.

The fragmentation of the compound [2], can be illustrated by the following mechanism:



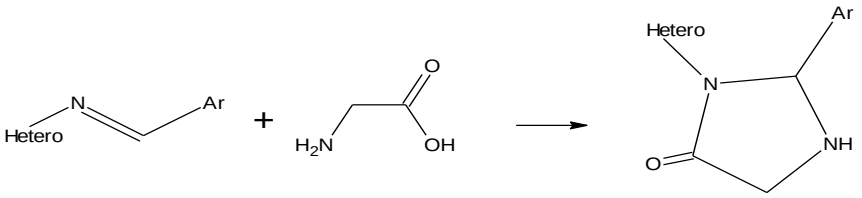
Scheme 1: The fragmentation rout specific of compound [2].

The mass spectrum of this compound [2] gave the molecular ion at m/z 194 which is equal to molecular weight of the structure given to this compound. Condensation of compound [2] with different substituted benzaldehyde in absolute ethanol afforded the corresponding Schiff bases [3-10], scheme (2), Table (3).

TheFT-IR spectrum of the Schiff base [3-10] was devoid of characteristic stretching frequencies of (C=N) groups. The vibration bands of N-N=C was in the region 1200-1280 cm^{-1}, C=N was in the region 1590-1680 cm^{-1}. ^{1}H-NMR spectrum of compound [4] showed the signals at (2.49) ppm for DMSO also at (3-3.3) ppm for (S,1H,-CH-); (6.7- 7.3-7.9) ppm for aromatic protons, at (8.7) ppm(1H,-NH)and at (9.66) (2H,OH).

Table 3: FT-IR and Uv/Vis spectral data for compounds [3-10].

Comp. No.	UV,λmax (nm),DMSO	νas. CH_2 νs CH_2	ν=C-H Ar.	ν C=C Ar.	ν C=N	ν C-N	N-N	Others
[3]	260	2910 2880	3110	1593,1485	1660	1396	1110	(N-CH_3) 1371
[4]	250	2900 2870	3097	1600,1470	1650	1400	1145	OH 3450
[5]	269	2980,2850 2860	3089	1600,1490	1681	1397	1150	NO_2 1438,1413
[6]	295	2900 2870	3112	1590,1480	1648	1395	1170	2OH 3450
[7]	274	2940 2870	3099	1600,1490	1691	1400	1120	Br 873
[8]	269	2960 2860	3095	1600,1495	1610	1389	1160	NO_2 1550,1350
[9]	270,350	2940 2860	3100	1598,1485	1650	1497	1150	Cl879
[10]	296	2914 2883	3167	1600,1478	1666	1496	1160	OCH_3 1288,1030



Imidazolidine derivatives [11-18] prepared by the heating of Schiff base derivative with glycine (α-amino acetic acid) in THF the products were identified by the FTIR spectra which show the appearance of NH vibration in 3320 cm^{-1} and the disappearance of C=N band in 1600cm^{-1}.The proposed mechanism of this reaction described below.

^{1}H-NMR spectrum of compound [17] showed the signals at (2.47) ppm for DMSO also at (3.5) ppm for (S,2H,-CH_2 -); (6.7- 7.3-7.9) ppm for aromatic protons, at (8.7) ppm(1H,-NH)and at (9.64-9.65) (2H,OH). ^{1}H-NMR spectrum of compound [12] showed the signals at(2.5) ppm for DMSO also at (3.5-3.9) ppm for (S,2H,-CH_2 -); (6.9,7.1, 7.7-8.2) ppm for aromatic protons, at (8. 85) ppm(1H,-NH) and at (9.7-9.98) (1H,OH).

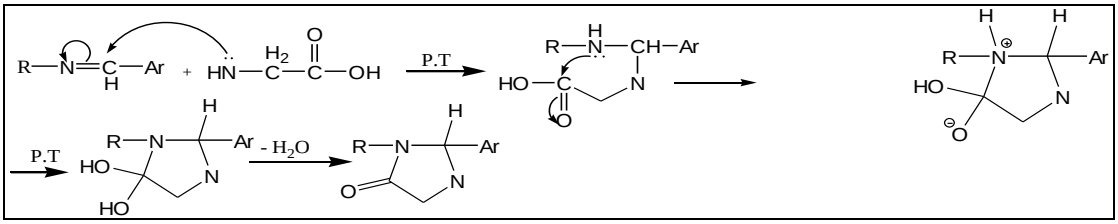


Table 4: FT-IR and UV/Vis spectral data for compounds [11-18].

Comp. No.	UV,λmax (nm)DMSO	νN-H	ν = C-H Ar.	ν C=O	ν C=C Ar.
[11]	225,350	3394-3274	3091	1654	1590
[12]	250	3345	3091	1630	1600
[13]	220,350	3280	3100	1640	1590
[14]	260	3350	3100	1600	1580
[15]	256,340	3254	3100	1630	1575
[16]	260	3320	3109	1680	1589
[17]	270,350	3345	3110	1620	1580
[18]	260,350	3345	3100	1600	1590

Compounds [19,20] containing carbon-carbon double bond (C=C) and a carbonyl group (C=O) in conjugation are known as α,β-unsaturated carbonyl compounds. A large number ofα,β-unsaturated carbonyl compounds (1,3-disubstituted-2-propene-1-one) were prepared and were considered the principle nucleus for the synthesis of many important heterocyclic organic compounds through their reaction with different compounds.

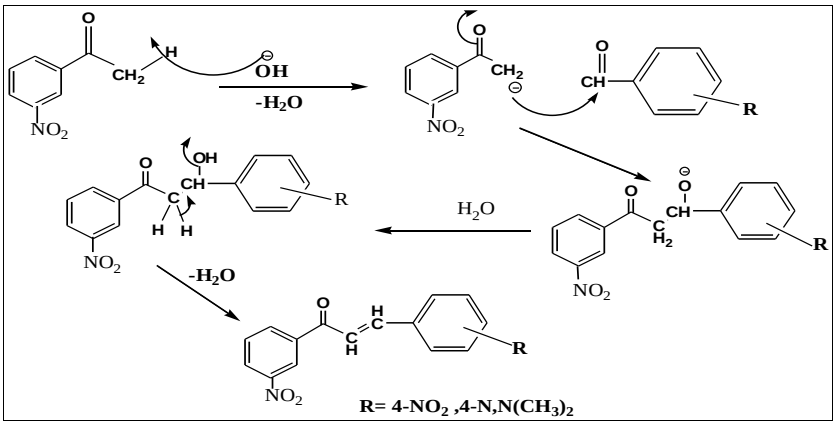
All the compounds give the characteristic FT-IR bands that proved the presence of particular functional groups, Table (5)and ^{1}H-NMR, Uv/visspectros copy helps to find the molecular weight structures of the synthesized compounds, Table (5). The band at 1778cm^{-1} suggesting the presence of (C=O)group, at 1631cm^{-1} due to (C=C) group compound [19]. Also,FT-IR spectrum of (20) gives a strong absorption at about 1716 cm^{-1}

which belongs to conjugated carbonyl group. Another strong absorption belonging to carbon-carbon double bondappears at 1647 cm^{-1}. It is worth mentioning that the intensity of C=C band is generally more than C=O band for most of the chalcones.

Table 5: FT-IR spectral data of compounds (19-28).

Comp. No.	υ(C-H) cm^{-1}	υ(C-H)Ar. cm^{-1}	υ(C=O)cm^{-1}	υ(C=C) alkene cm^{-1}	υ(C=C)Ar. cm^{-1}	Other bandscm^{-1}
[19]	2870	3082	1778	1631	1527, 1492	υ(NO_2) 1346- 1438 υ(C-N) 1184
[20]	2935, 2808	3082	1716	1647	1527, 1489	υ(N-CH_3) 1350 υ(NO_2) 1350- 1438 υ(C-N) 1168
[21]	2900	3090	1650	-	1487	NH(3250)
[22]	2930	3098	1678	-	1480	NH (3400)
[23]	2945	3100	1670	-	1478	NH (3250)
[24]	2900	3089	1636	-	1456	NH (3300)
[25]	2957	3080	1690	-	1478	NH (3368)
[26]	2945	3090	1654	-	1456	NH (3279)
[27]	2950	3100	1650	-	1458	NH (3400)
[28]	2900	3100	1670	-	1480	NH (3267)

The suggestion mechanism of synthesis of chalcones may be outlined as following in below:



The first step is proton abstraction from theα-carbon of the 3-Nitro acetophenone by the base catalyst. The reaction mixture of aldehydes and their enolate the carbonyl group of the aldehydes is electrophilic, the enolate is nucleophilic. This complementary reactivity leads to nucleophilic addition of the enolate to the carbonyl group in side of the aldehyde, this is a step in which the new carbon-carbon bond forms and its product is simply the alkoxide ion corresponding to the aldol, proton transfer from the solvent (water) . Finally the products of aldol undergo dehydration in the presence of the base, to yield α,β-unsaturated carbonyl compounds family.

UV spectrum, shows the transionsn→л and л→л* which confirmed the presence of the un-bonded pair of electrons on nitrogen atom and aromatic system (double bond). The product [19] is also, identified by the ^{1}H-NMR spectrum which shows the protons at (δ 7.5-8) ppm due to aromatic protons. Protons of (CH_2) of appeared at (δ 4.22).

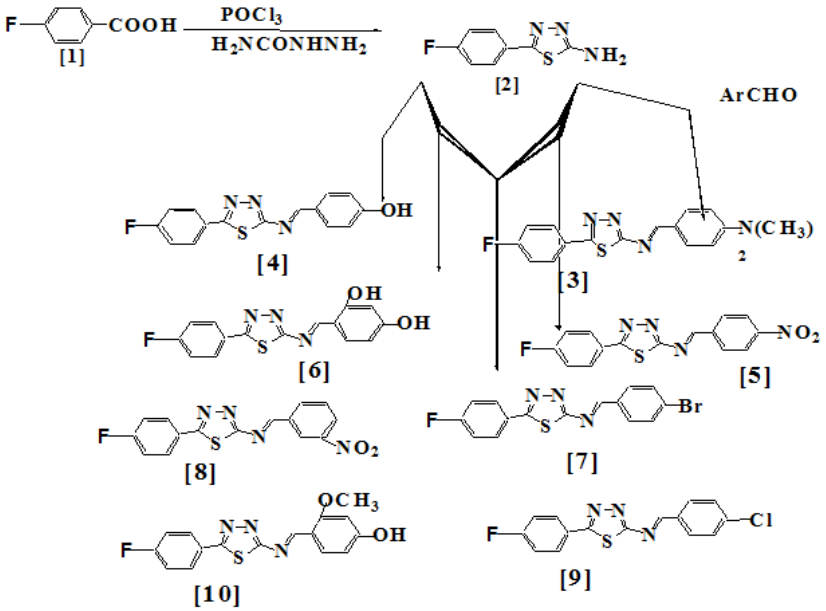
The FT-IR spectrum of compound [23], shows bands at 3250 cm^{-1}, 2924 and 2854 cm^{-1} are attributed to υ(C-H) aromatic, and (C-H) aliphatic stretching vibrations of (C-H) group. Other characteristic bands of aromatic system is the appearance ofυ(C=C) at about 1512 cm^{-1} besides the band at 1640 cm^{-1} due to (C=N).

The condensation reactions of phenyl hydrazine and few drops of glacial acetic acid with chalcone derivatives [19,20] gave compounds [23,24]. The FT-IR spectral data for these compounds (23,24) show the disappearance of the characteristic absorption at 1604-1606cm^{-1} for olefinic double bond of starting materials chalcone [19,20], which thus indicate that the reaction may be proceeded via Michael addition route.

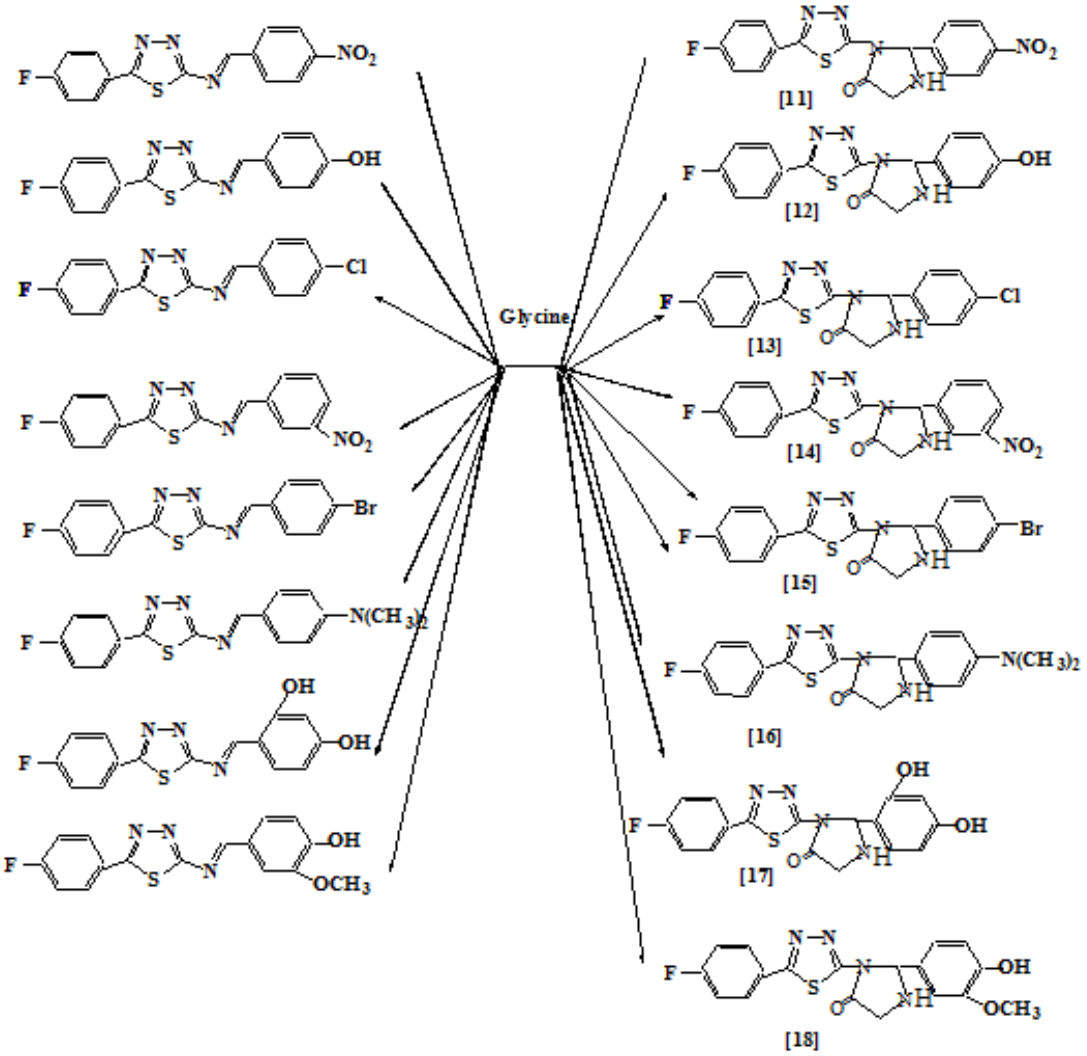
The appearance of absorption at 1641-1643 cm^{-1} are attributed to the (C=N) of pyrazoline fragment, absorption at 1590-1585 cm^{-1} due to the aromatic system (C=C). The reaction of chalcones [19,20] with thiourea gave the compounds [21,22] in presence of HCl and [25,26] in presence of NaOH (base). The FT-IR spectra for products [26,27] indicate the absence of the strong absorption band at 1603 cm^{-1} of the olefinic (C=C).

The condensation reaction of chalcones [19,20] with thiosemicarbazide gave the compounds [27,28]. The FT-IR spectra for [27,28] compounds exhibited significant two bands in the range 3371-3381cm^{-1} and (3157-3168) cm^{-1} which could be attributed to asymmetric and symmetric stretching vibrations of NH_2 group and a

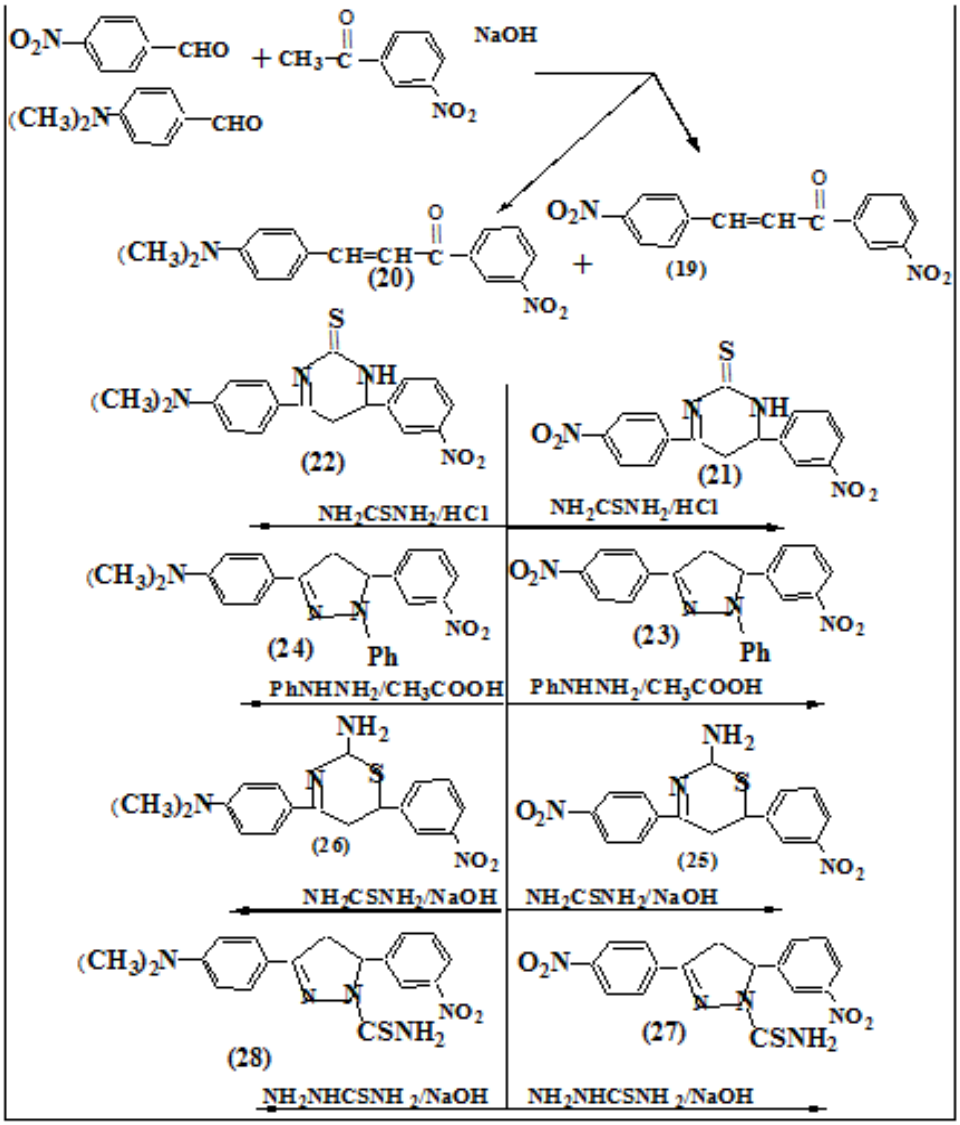
band at 1625-1630 cm^{-1} due to cyclic (C=N) stretching is also observed. Another band at 1093-1098 $cm^{-1}$for (C=S) thio group.



Scheme 3:



Scheme 4:



Scheme 5:

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