Chapter four

4-1 The biological activity

The biological activity of some prepared compound have been taken to evaluate there activity , some of these compound have high bioactivity on some bacteria while the same compounds don't have any effect on other bacteria .

The agar plates were surface inoculated uniformly from the broth culture of the tested microorganisms. In the solidified medium suitably spaced apart holes were made all 6mm in diameter. These holes were filled with 100µl of the prepared compounds (1mg of the compound dissolved in 1ml of DMSO solvent), DMSO was used as a solvent. These plates were incubated at 37C° for 24h for the bacteria.

4-1-1 Staphylococcus aurous

It is gram positive cluster form bacteria cause soft tissue infection as well as toxic shock syndrome and scalded skin syndrome it found to be causative agent to pneumonia , meningitis, boils, arthritis and chronic bone infection.[202]

4-1-2 Pseudomonas aeruginosa

It is gram negative rod bactirea it is major cause of hospital acquired ,infaction can occur at many site and can lead to urinary tract infections ,sepsis , pneumonia , pharyngitis, and wounda infection [(204)]

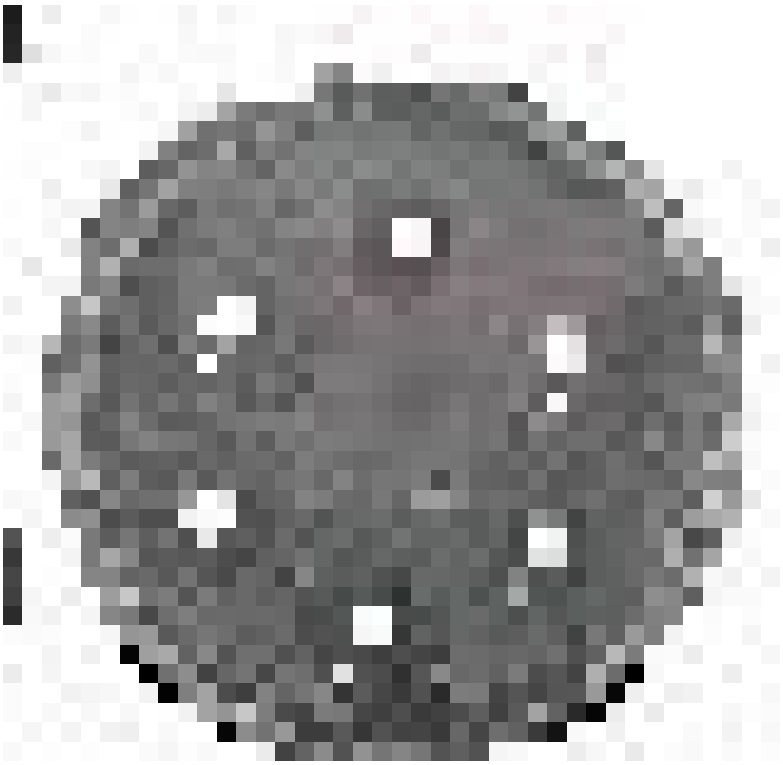
4-1-3 E.coli

E. coli O157:H7 is one of hundreds of strains of the gram negative bacterium *Escherichia coli*. Although most strains are harmless, this strain produces a powerful toxin that can cause severe illness. *E. coli* O157:H7 has been found in the intestines of healthy cattle, deer, goats, and sheep

4-14 Streptococcus

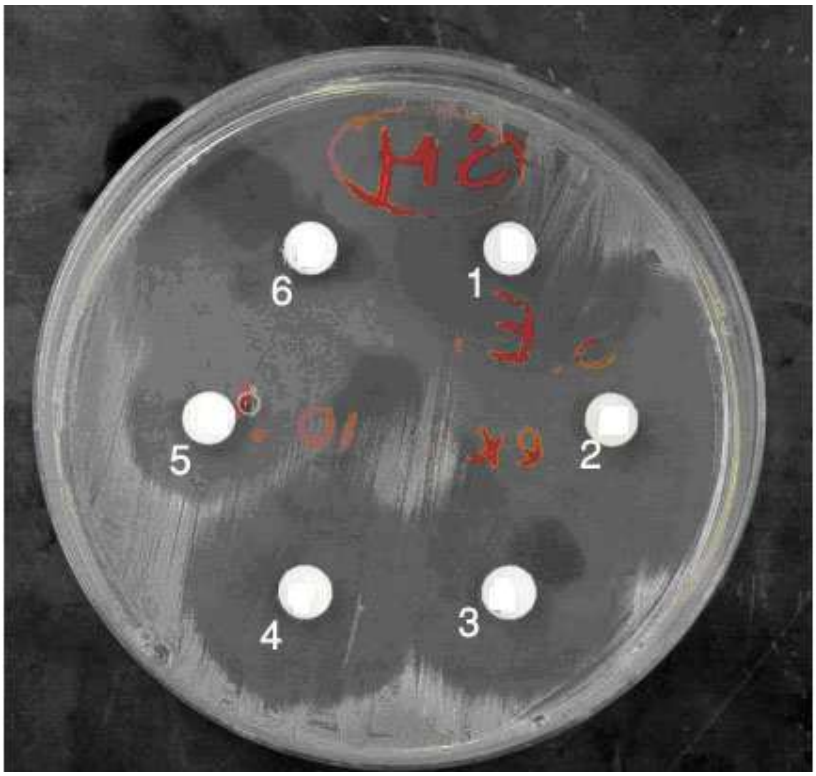
Streptococcus is a genus gram positive bacteria belong to the phylum firmicutes and lactic acid bacteria group occurs along a single axis they

In this work, the antibacterial test was performed according to the disc diffusion method. Compounds (11A,11B,12C,12D,7A,8B) were assayed for their antimicrobial activity *in vitro* against four strains of Gram negative and positive bacteria listed as follow

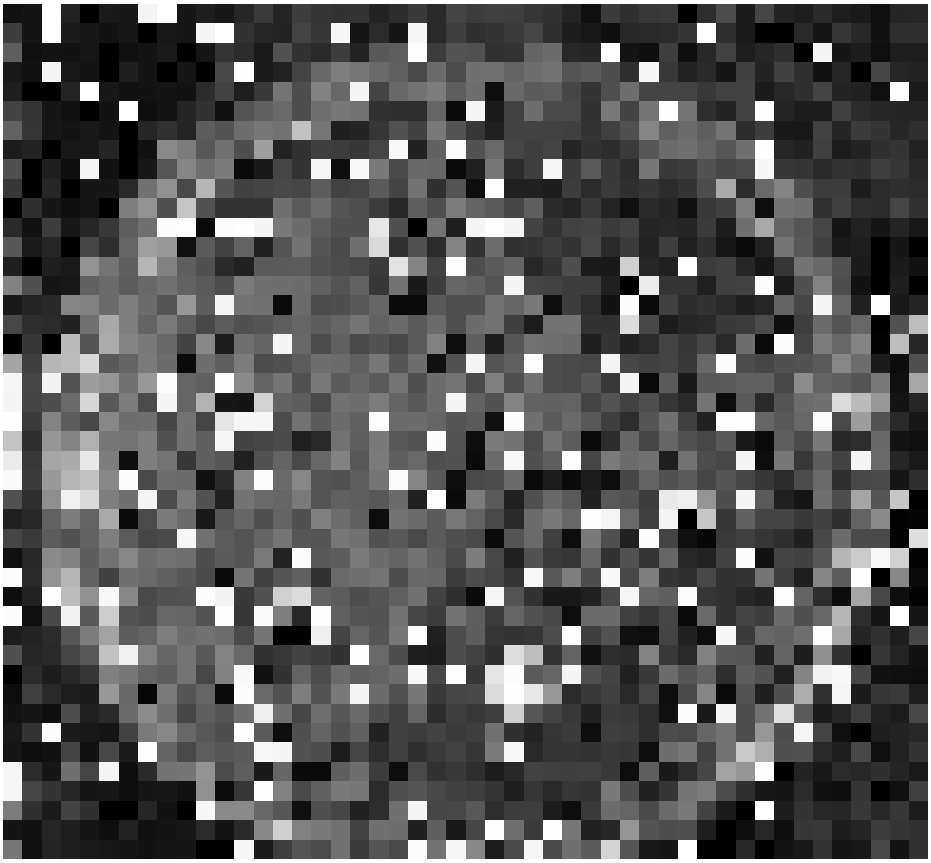


E.colai

Staphylococcus



Pseudomonas



Streptococcus.

Table (4-1) the biological activity of some prepared compounds

Compound No	In figure	Streptococcus	Staphylococcus	E.coli	Pseudomonas
12A	1	+++	+++	+	+
12B	2	+++	+++	-	-
11C	3	+++	+++	+	-
11D	4	+	+++	++	+
7A	5	++	++	++	+
8B	6	+	+	+	+

Note :

- = No inhibition = inactive
+ = (5-10) mm = slightly active
++ = (11-20) mm = moderately active
+++ = more than 20mm = highly active

From the structure the compounds 12A,12Bshow high activity against Strepto and Staphylococcus because hey contain free NH2 group while little effect on E.colic and Pseudomonas
9A has high activity on staphylococcus
12C has little effect on all of the bacteria

4-2 The enzymatic activity

In this work we evaluate the effect of some prepared compounds on the ureas enzyme because of it's cheapness and some prepared compound have amidic bond .
Ureas
Ureas is nickel dependant enzyme which hydrolysis the urea to ammonium carbonate which converted to ammonia and carbonic acid then the carbonic acid convert to CO_2 and H_2O. as shown in the below figure .

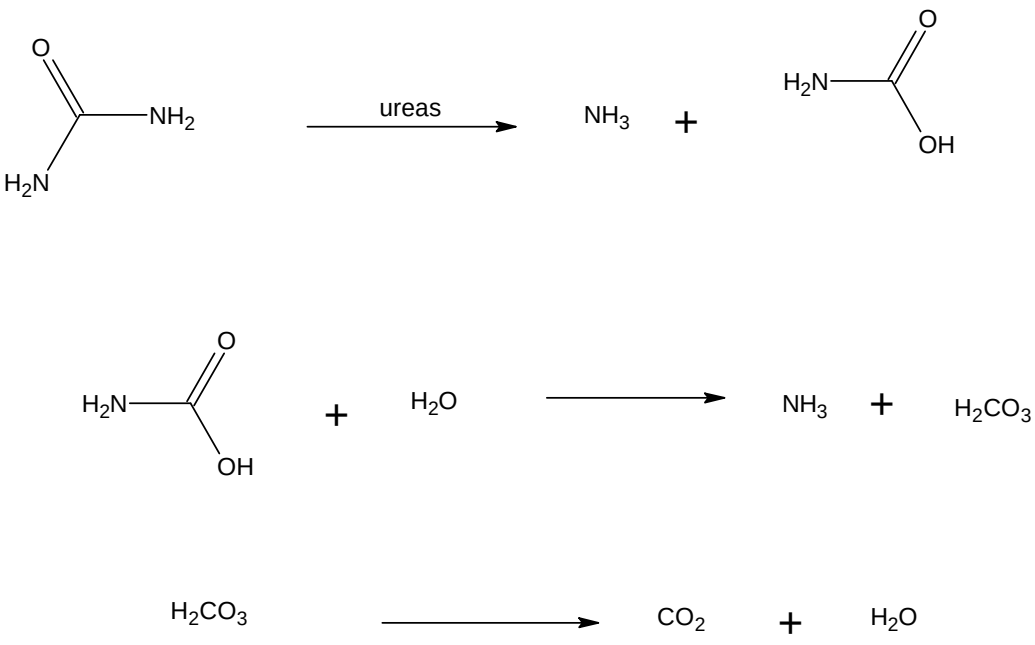


Figure (4-1) the effect of ureas on urea

4-2-1 The procedure [205]

In this work a comparison between the blank and the prepared sample have been taken which depend on randox kit as shown in the below table

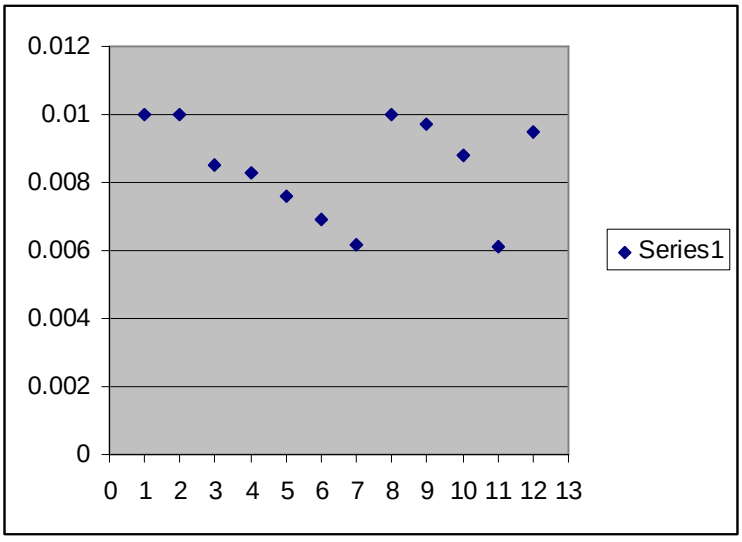
	Bank	Standard	Sample
Sample			10 µl
Standard		10µl	
Working Reagent R1	1ml	1ml	1ml

Shaken for 3 min at 37° C or 5min at 20-25 ° C

Working reagent R2	200 µl	200 µl	200 µl

Then shaken for 3 min then continue the volume to 5 ml then measure the absorption at 600nm then relationship between urea concentration and absorption.

Some of the prepared compound don't have any effect on urease while some of the have little effect .



A	Comp.	
0.01	2A1	1
0.01	2B1	2
0.0085	2C1	3
0.0083	3C1	4
0.0076	3D1	5
0.0069	3B1	6
0.0062	3C1	7
0.01	3A1	8
0.0097	4A	9
0.0088	4B	10
0.0061	4C	11
0.0095	4D	12

figure (4-2) show relationship between absorbance and compounds

Contains

Chapter one

Chapter two Experimental part

Chapter three results and discussion

Chapter two

Experimental part

2.1 Chemicals

Table (2-1) shows all the utilized chemicals in the experimental course of the thesis. Table (2-1) Chemicals and their manufacturer

Chemicals	purity	Supplied from
2-Aminopyrimidine	99%	Merck
4-Aminoantipyrine	99%	Readel-dehean
2-Aminopyrazine	99%	Merck
Benzene	Analar	BDH
Carbon disulfide	Analar	BDH
Chloroacetylchloride	Analar	Fluka
Diethyl ether	Analar	BDH
N,N-diethylaminobenzaldehyde	99%	Merck
Ethyl chloroacetate	99%	BDH
Ethanol absolute	99.9%	Readel-dehean
Ethyl acetate	Analar	BDH
Formaldehyde	65%	BDH
Formic acid	99%	BDH
Hydrazine hydrate	99%	BDH
o-Hydroxybenzaldehyde	99%	Fluka
Isoneazide	99%	Merck
Mercapto acetic aced	99%	BDH
p-Methyl benzaldehyde	99%	Readel-dehean
Maleic anhydride	99%	BDH
p-Ntirobenzaldehyde	99%	Merck
p-Phenylphenacylbromide	99%	Fluka

Chemicals	Purity	Supplied from
Potassium hydroxide	99%	BDH
Phenyl isothiocyanate	99%	Fluka
Phenyl isocyanate	99%	Fluka
Propargyl bromide	99%	Aldrich
Sodium azide	99%	BDH
Terahydrofurane	Analar	Readel-dehean
Thiourea	99%	BDH
Thiosemicarbazide	99%	BDH
Triethylamine	99%	BDH
Urea	99%	BDH

2-2 Apparatus

1-Melting points were recorded on a hot stage electorthermal digital melting point apparatus and were uncorrected.

2. Infrared spectra were recorded on Shimadzu FTIR-8300 spectrometer as potassium bromide disc. al-Nahrine university

3 . Infrared spectra were recorded on Shimadzu FTIR-8400 spectrometer as potassium bromide disc. Kufa university

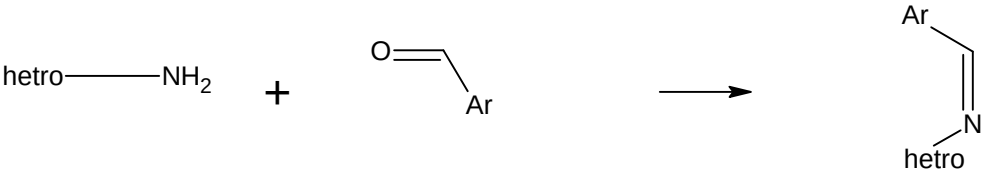
4-. ^{1}H-NMR spectra were recorded on a Fourier transform Bruker spectrometer operating at 300 MHz in deuterrated DMSO with tetramethylsilane as internal standard in DMSO- d^{6}. Measurements were made at the AL-ALbayt university

5- ^{13}C-NMR spectra were recorded on a Fourier transform Bruker spectrometer operating at 75MHz in detoured chloroform. Measurements were made at the AL-ALbayt university.

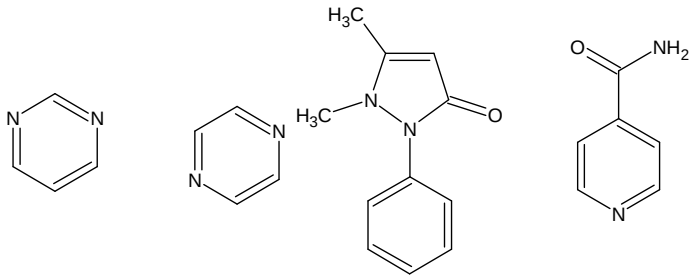
6. Thin layer chromatography (TLC) was carried out using Fertigfollen precoated sheets type Polygram SilG, and the plates were developed with iodine vapor.

2-3 Synthesis of compounds

2-3-1 Preparation of Schiff base for heterocyclic amines(1)



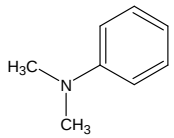
Hetero



A mixture of heterocyclic amine (0.01mole) with aromatic aldehyde (0.01mole) in 15 ml of absolute ethanol were refluxed for appropriate time then cooled to the room temperature the produced precipitates were filtrated and washed with ethanol The end of reaction is detected by TLC by using appropriate mixtures of solvent physical properties of the prepared compounds are shown in table 2-1

Hetero= 2-aminopyrimidine, 2- aminopyrazine , isoiazide , 4-aminoantipyrine

Ar=



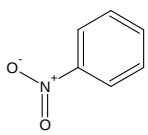
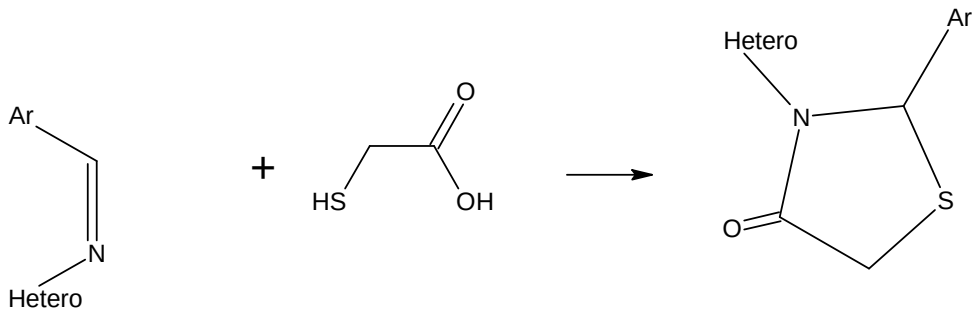


Table 2-1 some physical properties of Schiff bases (A_1-D_2)

Comp No.	Yield%	Solvents	M.P^{0}c
$1A_1$	95	THF-Ethanol	230-232
$1A_2$	98	THF-Ethanol	360
$1B_1$	75	Benzene-Ethanol	180-182
$1B_2$	72	Benzene-Ethanol	205-207
$1C_1$	77	Benzene-Ethanol	200-202
$1C_2$	75	Benzene-Ethanol	199-201
$1D_1$	88	Benzene-Ethanol	222-224
$1D_2$	38	Benzene-Ethanol	144-146

2-3-2 -Preparation of 2-aryl-3-(hetero-2-yl)thiazolidin-4-one (2)[196]

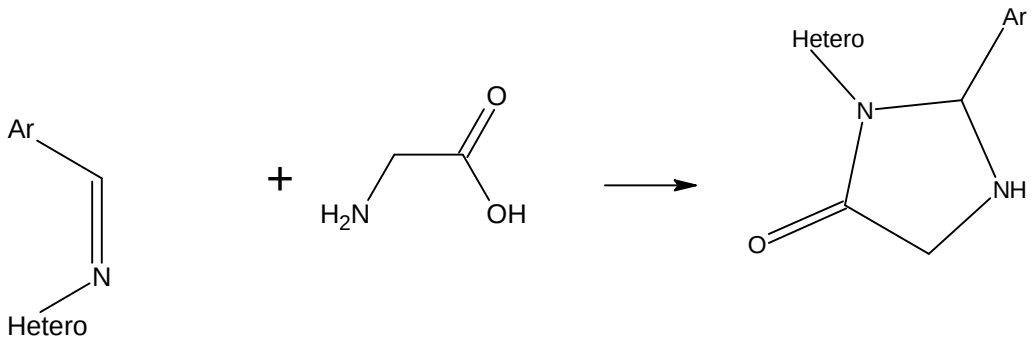


A (0.001)mole of 2-mercptoacetic acid was added dropwise to (0.001) mole of Schiff base in 20 ml of dry benzene , the mixture was refluxed for 24 h then the solvent was evaporated and the precipitate was recrystallized from ethyl acetate and benzene .

Table 2-2 Some physical properties of compound thiazolidinone(2A-2D)

Comp No.	Yield%	Solvent	M.P ^{0}c
2A	49	Benzene-ethylacetate	128-130
2B	36	Benzene-ethylacetate	145-147
2C	28	Benzene-ethylacetate	165-167
2D	41	Benzene-ethylacetate	129-131

2-3-3 Preparation of 2-aryl-3-(hetero-2-yl)imidazolidin-4-one (3)

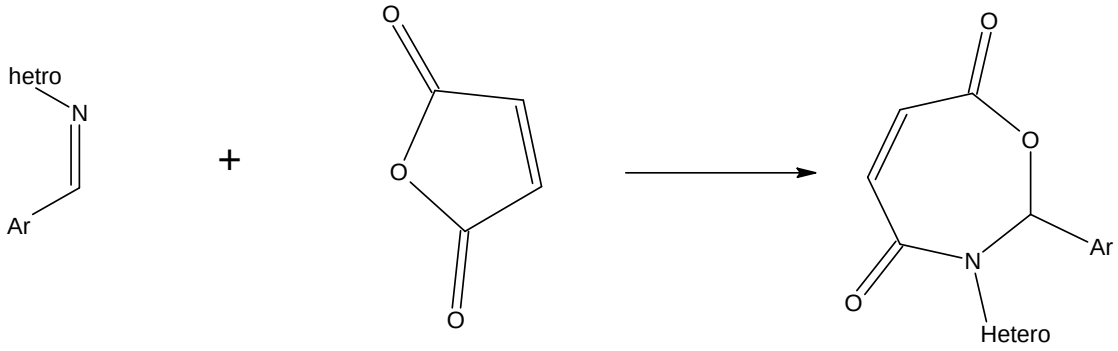


a mixture of Schiff base (0.001)mol and glycine (0.001)mole in 20 ml THF was refluxed for 24 h then it cold to room temperature then the precipitate was filtrated and recrystallizedfrom ethanol and THF 25/75.

Table 2-3 Some physical properties of Imidazolidinone ($3A_1$-$3D_2$)

Comp No.	Yield%	Solvent	M.P^{0}c
$3A_1$	44	THF-Ethanol	188-190
$3A_2$	40	THF-Ethanol	147-149
$3B_1$	31	THF-Ethanol	205-207
$3B_2$	36	THF-Ethanol	116-118
$3C_1$	25	THF-Ethanol	200-202
$3C_2$	33	THF-Ethanol	131-133
$3D_1$	39	THF-Ethanol	226-228
$3D_2$	36	THF-Ethanol	212-214

2-3-4 Preparation of 2-aryl-3-hetero-2-yl-2,3-dihydro-1,3-oxazepine-4,7-dione (4)[197]

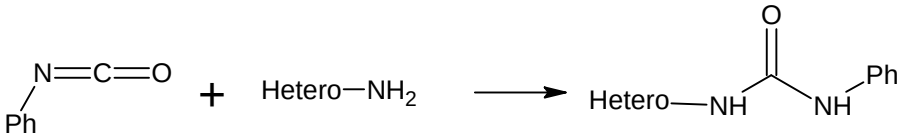


A mixture of (0.001) mole of Schiff base and (0.001) mole of malic anhydride in 20 ml of THF was refluxed for 24 h then the solvent evaporated and then the formed precipitate was recrystallized from appropriate solvents

Table 2-4show the physical properties of oxazipene(4A-4D)

Comp No.	Yield%	Solvents	M.P ^{0}c
4A	39	Benzene-Ethanol	208-210
4B	22	Benzene-Ethanol	209-211
4C	25	Benzene-Ethanol	158-160
4D	34	Benzene-Ethanol	203-205

2-3-5 Preparation of N-phenyl-N'-hetero-2-ylurea (5)



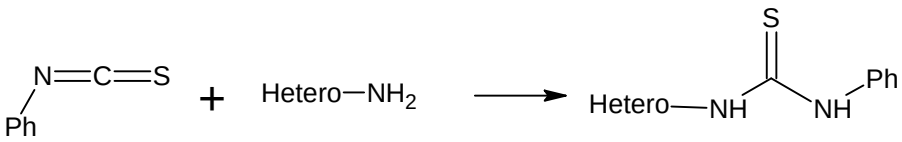
A (0,001) mole of the aromatic amine was dissolved in 20 ml of absolute ethanol then added (0.001) mole of phenylisocynate then the mixture was refluxed for 3h then the formed precipitate was filtrated and washed with ethanol and recrystallized from ethanol and benzene the yield percents and physical properties are shown in the flowing table (2-5)

Table 2-5 some physical properties of urea derivative (5A-5D)

hetero	2-aminopyrimidine	4-aminoantipyrine	Isoniazide	2-aminopyrazine
MW	214	322	256	214
Yield %	77	88	85	80
m.p^{0}c	250-252	207-209	188-186	200-202

`

2-3-6 Preparation of N-phenyl-N'-hetero-2-ylthiolurea (6)

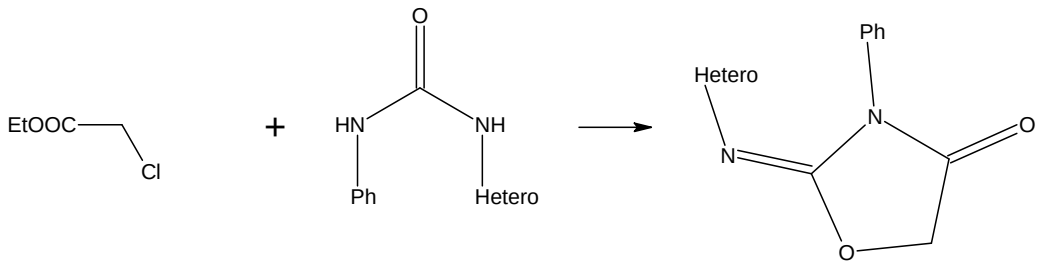


A (0,001) mole of appropriate heterocyclic amine was dissolved in 20 ml of absolute ethanol then added (0.001) mole of phenylisothiocynate then the mixture was refluxed for 2 h then the formed precipitate was filtrated and washed with ethanol and recrystallized the yield percents and physical properties are shown in the flowing table (2-6)

Table 2-6 some physical properties of thiourea(6A-6D)

hetero	2-aminopyrimidine	4-aminoantipyrine	Isoniazide	2-aminopyrazine
MW	230	348	272	230
Yield %	68	90	74	53
m.p^{0}c	99-101	266-268	125-127	114-116

2-3-7 preparation of 3-phenyl-2-(hetero-2-ylamino)-1,3-oxazolidin-4-one(7)

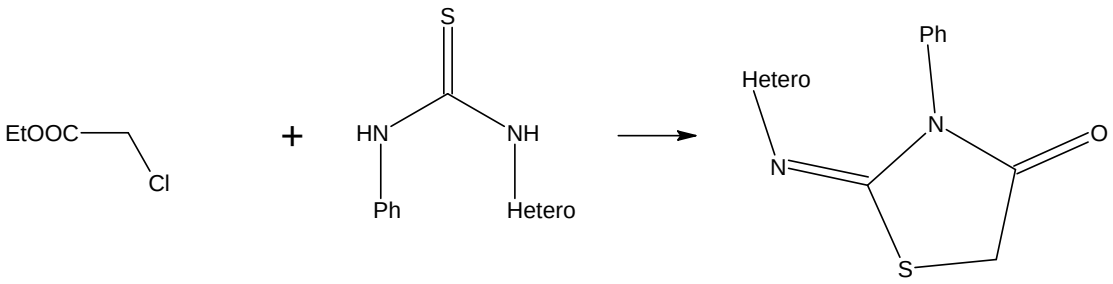


A mixture of (0.001)mole of urea derivatives dissolved in 20ml of ethanol then added (0.001)mole of Ethylchloroacetate drop wise with stirring then refluxed for 4h then the product precipitate filtrated and recrystallized from ethanol the physical properties are shown in the table(2-7)

Table 2-7 Some physical properties of oxazolidinone(7A-7D)

Hetero	2-aminopyrimidine	4-aminoantipyrine	Isoniazide	2-aminopyrazine
MW	271	379	312	271
Yield %	30	44	37	47
m.p^{0}c	188-190	300	237-239	310-312

2-3-8 Preparation of 3-phenyl-2-(hetero-2-ylamino)-1,3-oxazolidin-4-one(8)

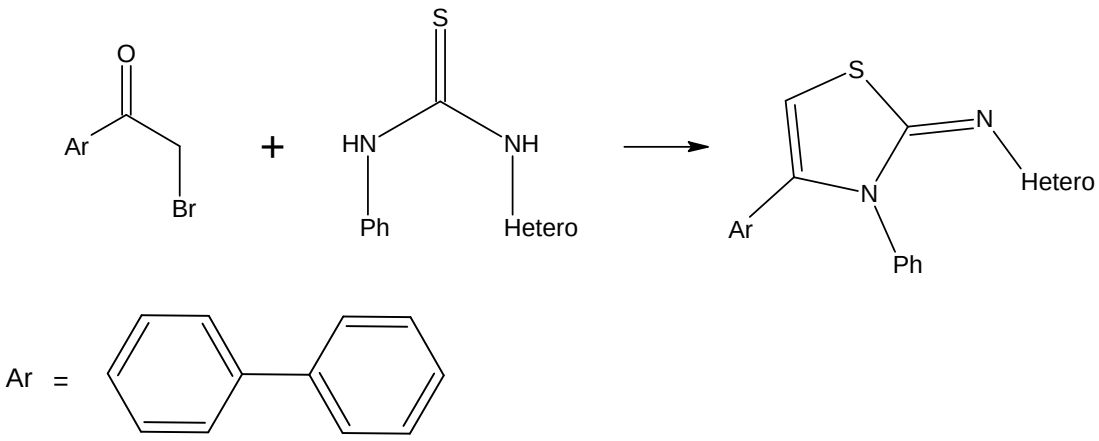


A mixture of(0.001) of thiourea derivatives dissolving in 20ml of ethanol then added (0.001)mole of ethylchloroacetate drop wise with string then refluxeded for 4h then the product precipitate filtrated and recrystallized from ethanol the physical properties are shown in the table

Table 2-8 some physical properties of thiazolidinone (8A-8D)

Hetero	2-aminopyrimidine	4-aminoantipyrine	Isoniazide	2-aminopyrazine
MW	287	395	328	287
Yield %	29	45	41	32
m.p^{0}c	290 decomp	230-232	167-169	288-290

2-3-9 N-(4-(naphthalen-2-yl)-3-phenyl-2,3-dihydrothiazol-2-yl)hetero-2-amine(9)[198]

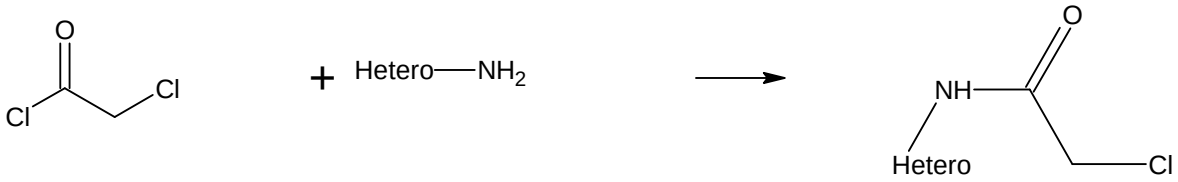


A mixture of thiourea derivatives (0.01)mole and p-phenyl phenacyl bromide (0.01)mole in 20ml of ethanol was refluxed for 3h the produce precipitate filtrated and recrystallized from ethanol the physical properties are shown I the table (2-9)

Table 2-9 some physical properties of thiazoline derivatives(9A-9D)

Hetero	2-aminopyrimidine	4-aminoantipyrine	Isoniazide	2-aminopyrazine
MW	350	463	392	350
Yield %	37	45	42	33
m.p	290 decomp	350-352	284-286	174-146

2-3- 10 Preparation of 2-chloro-N-(hetero-2-yl)acetamide (10)

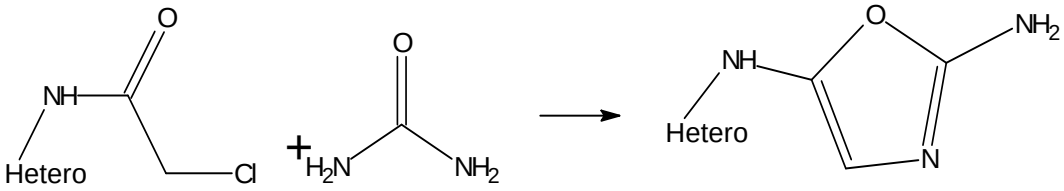


A(0.01)mol of appropriate heterocyclic amine in dry benzene with stirring in ice bath then cholroacetylchloride (0.01) mole was added deropwise then string at room temperature for appropriate time the produced precipitate was filtrated and washed with benzene and recrystallized from benzene and methanol (60:40) the physical properties are shown in table(2-10)

Table 2-10 some physical properties of acetamide derivatives (10A-10D)

Hetero	2-aminopyrimidine	4-aminoantipyrine	Isoniazide	2-aminopyrazine
MW	172	280	214	172
Yield %	88	92	95	72
m.p^{0}c	146-148	149-151	268-270	206-208

2-3-11 Preparation of N5-(hetero-2-yl)oxazole-2,5-diamine (11)[199]

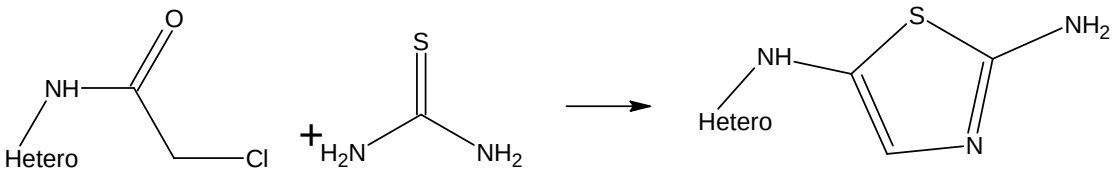


A mixture of (0.001) mole of urea and (0.001) of compound 7 was refluxed for 4h in absolute ethanol then the mixture was cooled to room temperature then the produced precipitate was filtrated and recrystallized from ethanol and benzene the physical properties are shown in the following table (2-11)

Table 2-11 some physical properties of oxazole (11A-11D)

Hetero	2-aminopyrimidine	4-aminoantipyrine	Isoniazide	2-aminopyrazine
MW	197	305	238	197
Yield %	80	85	66	78
m.p^{0}c	205-207	126-128	169-171	160-162 decompos

2-12-preparation of N5-(hetero-2-yl)thiazole-2,5-diamine(12)[199]

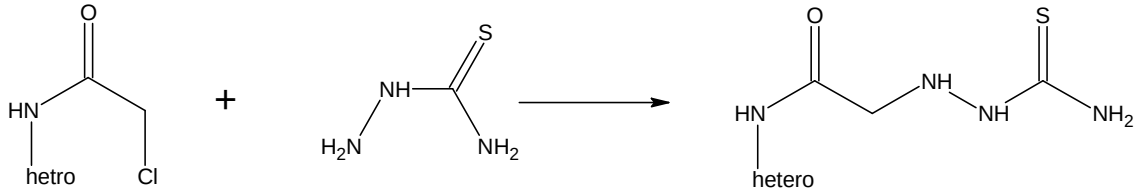


A mixture of (0.001) of thiourea and (0.001) of compound 7 was refluxed for 4h in absolute ethanol then the mixture was cooled at room temperature then the precipitate was filtrated and recrystallized from ethanol and benzene the physical properties are

Table 2-12 some physical properties of Thiazole derivatives (12A-12D)

Hetero	2-aminopyrimidine	4-aminoantipyrine	Isoniazide	2-aminopyrazine
MW	٢١٢	320	253	212
Yield %	78	87	69	76
m.p	300-302	146-148	157-159	360

2-13 preparation of 1-(2-oxo-2-(pyrimidin-2-ylamino) ethyl) thiosemicarbazide (13)

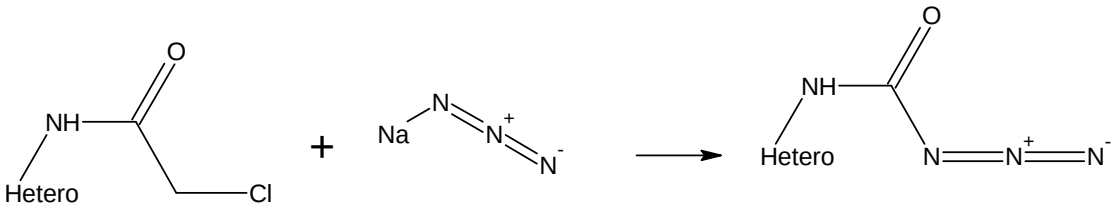


A mixture of (0.001)mole of thiosemicarbazide and (0.001)mole of compound 7 was refluxed for 4h in absolute ethanol then the mixture was cooled to room temperature then the precipitate was filtrated and recrystallized from ethanol the physical properties are shown in the table

Table 2-13 show the physical properties of thiosemicarbazide derivatives (13A-13D)

Hetero	2-aminopyrimidine	4-aminoantipyrine	Isoiazide	2-aminopyrazine
MW	226	334	267	226
Yield %	50	71	66	53
m.p^{0}c	188-190	201-203	194-196	150-152

2-14 - preparation of preparation of 2-azido-N-(hetero-2-yl)acetamide (14)

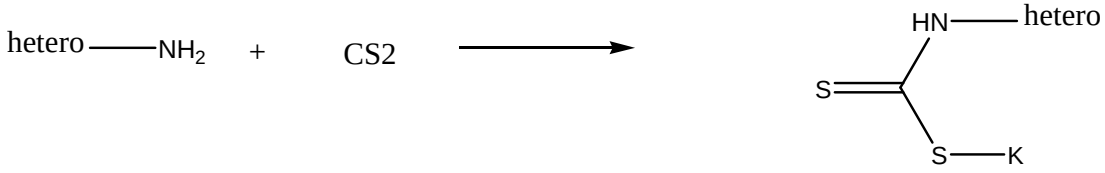


A mixture of(0.001) mole sodium azide and (0.001)mole of compound 7 in 20 ml of absolute ethanol was refluxed for 3 h then the produced precipitate filtrated and recrystallized from ethanol.

Table 2-14 some physical properties of azide derivatives (14A-14D)

Hetero	2-aminopyrimidine	4-aminoantipyrine	Isoniazide	2-aminopyrazine
MW	215	323	257	215
Yield %	65	82	71	68
m.p^{0}c	88-90	144-146	195-197	200-202

2-15 Preparation of potassium hetero-2-ylcarbamodithioate(15)[200]

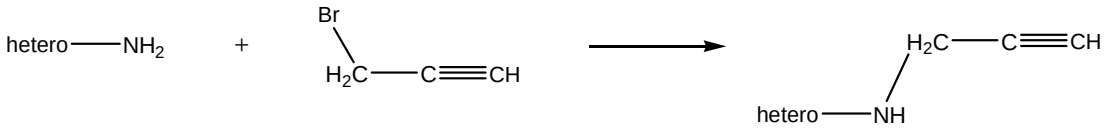


A mixture of suitable heterocyclic amine 0.01 mole , carbons disulfide 0.01 mole and 0.01mole of sodium metal was refluxed for 5h then cooled to room temperature then the formed precipitate was filtrated

Table 2-15 some physical properties of dithiocarbamate derivatives (15A-14C)

Hetero	2-aminopyrimidine	4-aminoantipyrine	2-aminopyrazine
MW	170	277	170
Yield %	53	76	55
m.p^{0}c	82-84	160-162	98-100

2-16 Preparation of N-prop-2-ynylhetero-2-amine(16) [201]

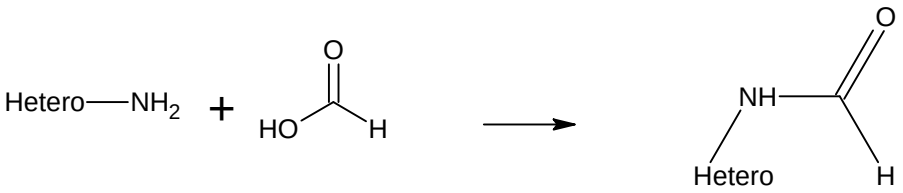


To a mixture of (0.001)mole of hetero amine and (0,001) mole of KOH in absolute ethanol (0,001)mole of propargyl bromide was added dropwise and then refluxed for 3h then cooled to room temperature then filtrated and the filtrate poured into cold water the precipitate was filtrated and recrystallized from ethanol and benzene .

Table 2-16 some physical properties of acetylenic compounds (16A-16C)

Hetero	2-aminopyrimidine	Isoneazide	2-aminopyrazine
MW	133	175	133
Yield %	33	28	30
m.p	350- decomp	360decomp	300-302

2-17 - Preparation of hetero formamide derivatives (17)[202]

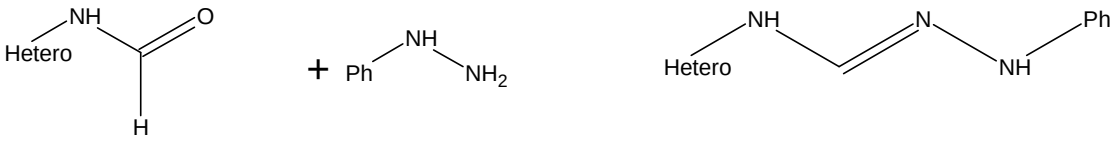


A mixture of heterocyclic amine (0.01) mole and formic acid (0.01) mole was refluxed for 2h then the excess of formic acid was evaporated and the product was recrystallized from appropriate solvent.

Table 2-17 some physical properties of formamide (17A-17D)

Hetero	2-aminopyrimidine	4-aminoantipyrine	Isoneazide	2-aminopyrazine
MW	138	246	179	138
Yield %	66	80	72	60
m.p^{0}c	168-170	145- 147	162-164	241-243

2-18 N'-phenyl-N-hetero-2-ylhydrazonoformamide(18)[200]

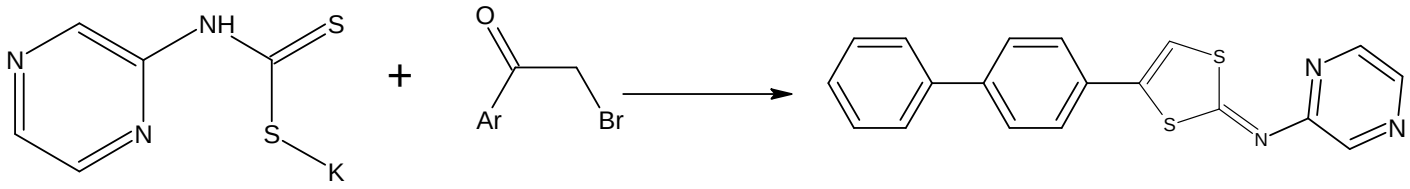


A mixture of (0.001) mole of compound 18 and phenyl hydrazine (0.001) mole in 20ml ethanol was refluxed for 5h then cooled to room temperature the formed precipitate was filtrated and recrystallized from ethanol and benzene .

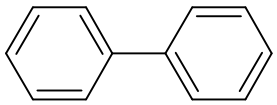
Table 2-18 some physical properties of Schiff bases of phenyl hydrazine (18A-18D)

Hetero	2-aminopyrimidine	4-aminoantipyrine	Isoneazide	2-aminopyrazine
MW	213	321	255	213
Yield %	44	74	58	51
m.p^{0}c	222-224	255-257	210-212	171-173

2-19 Preparation of N-(4-biphenyl-4-yl-1,3-dithiol-2-yl)pyrimidin-2-amine [203]



Ar =



A mixture of (0.001) mole of dithiocarbamate salt (xanthate) and (0.001)mole p-phenylphenacyl bromide in 20ml ethanol was refluxed for 3 h then cooled at room temperature then the precipitate filtrated and recrystallized from appropriate solvents .

m.p 132

yield % 43

M.W 347

Chapter one

Introduction

1-1 Pyrimidines[1]

Pyrimidines also known as m-daizine, is the parent substance of large group of heterocyclic compounds which has attracted much attention for a longtime. these compounds which belong to this group where known as breakdown products of uric acid at a very early date of the history of organic chemistry , but systematic study of this ring system began with work pinner. who first applied the name pyrmidine to the unsubstantiated parent body.

Pyrimidine derivatives play an important role in many biological processes the ring being present in nucleic acid, several vitamin coenzymes, uric acid and other purine.

Many drugs (barbituric acid derivatives) and chemotherapeutic agents (Sulfadiazine) contain pyrimidine ring.

Pyrimidine can be regarded as cyclic amidine and the chemical behavior of its derivatives is dominated by this fact.

According to X-ray diffraction studies pyrimidine exist as distorted hexagon.

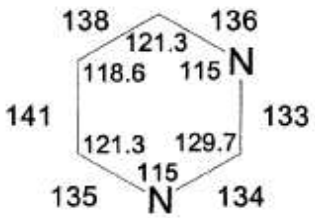
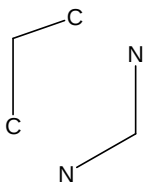


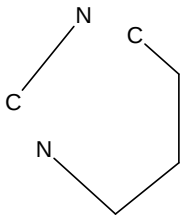
Fig. 1-1 Bond parameters of Pyrimidines(bond lengths in pm, bond angles in degrees)

1-1-1 Synthesis of pyrimidines[1]

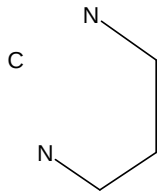
Pyrimidine is a colorless liquid with characteristic pyridine like odor it has been have prepare by the reduction of di or tri chloropyrimidines.
It dose not normally serve as starting point for the prepareation of substituted pyrimidines.
There are three methods for the prepareation of pyrimidine according to the fundamental nature of the fragments which combine together to form pyrimidine nucleus.



Type 1



Type 2



Type 3

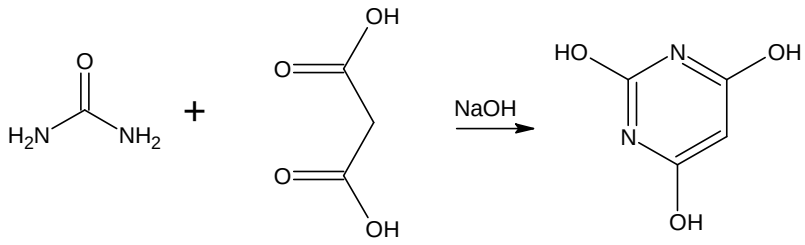
The three basic types of the synthesis are:-

Type 1[2].

The commonest pyrimidine syntheses are belonging to type 1. the stylization usually involves a double condensation with elimination of water, alcohol or hydrogen halide between amino and carbonyl, carboxyl ester and acyl chloride or enol ether. or condensation by addition of amino group to cyano groups or to polarized double bonds with out an elimination reaction .

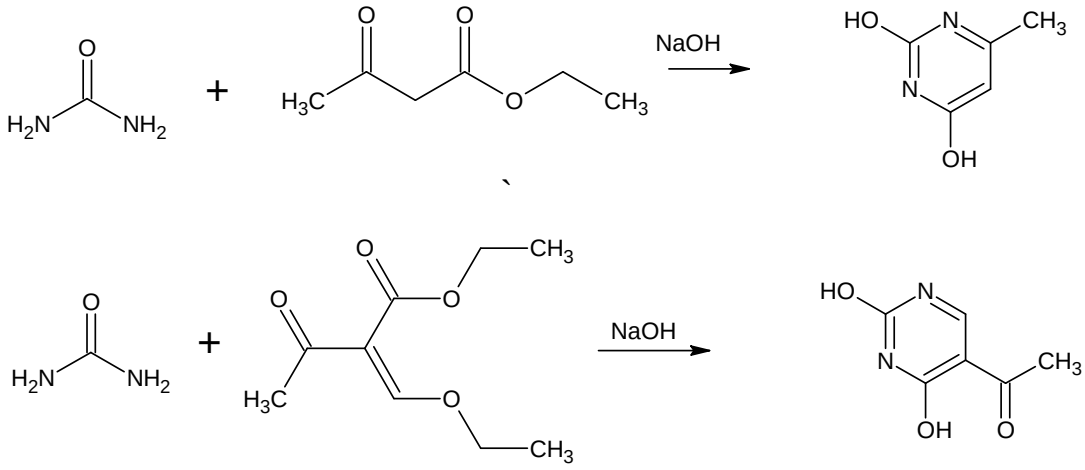
Urea condensed with malonic acid in the presence of phosphoryl chloride and obtain barbituric acid [3]

Then malonic ester is used instead of malonic acid in the presence of sodium alkaloid as catalyst.

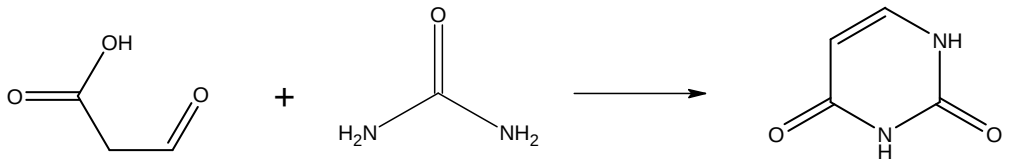


The applications of this process especially with ester of dialkyl malonate are the prepareation of barbiturate drugs[4]

β-ketoesters [5] and there enol [6] form are suitable for condensation with urea to form 4-methyluracil(pyrimidine derivatives).

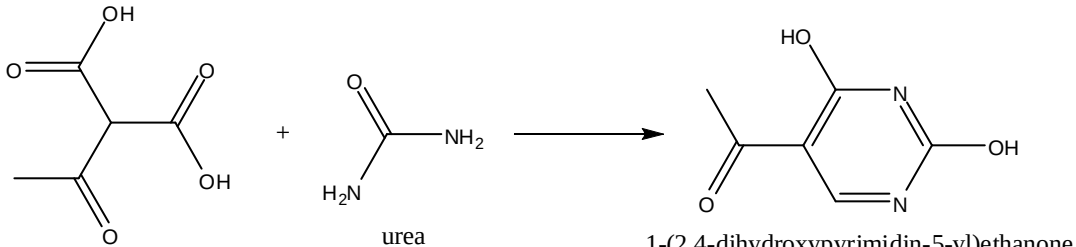


An important example is the prepareation of uracil from urea and formylacetic acid (have prepare in situ by the action of sulfuric acid on malonic acid [7].



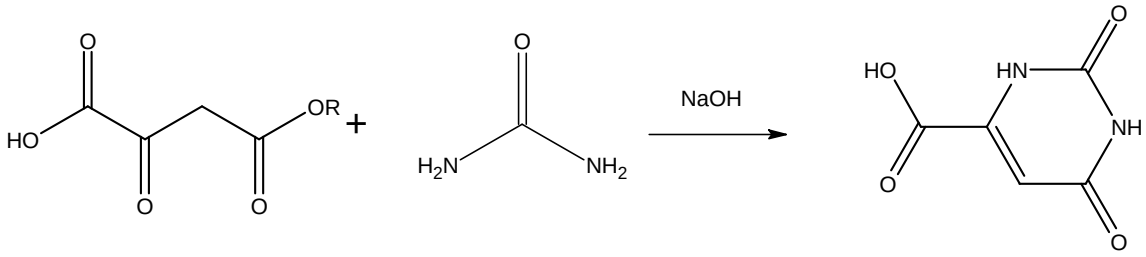
uracil

Acetonedicarboxylic acid (have prepare from citric acid) reacts with urea similarly.[8]



Acetonedicarboxylic acid urea 1-(2,4-dihydroxypyrimidin-5-yl)ethanone

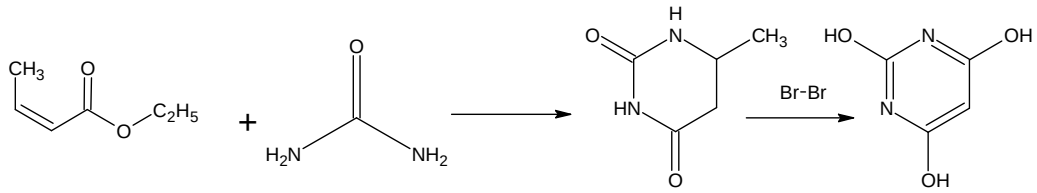
Mitchell et al [9] have shown that the synthesis of oriotic acid (uracil – 4- carboxylic acid) from urea and oxaloacetic ester her the initial product is hydenton which rearranged to the pyrimidine only when treated with alkali



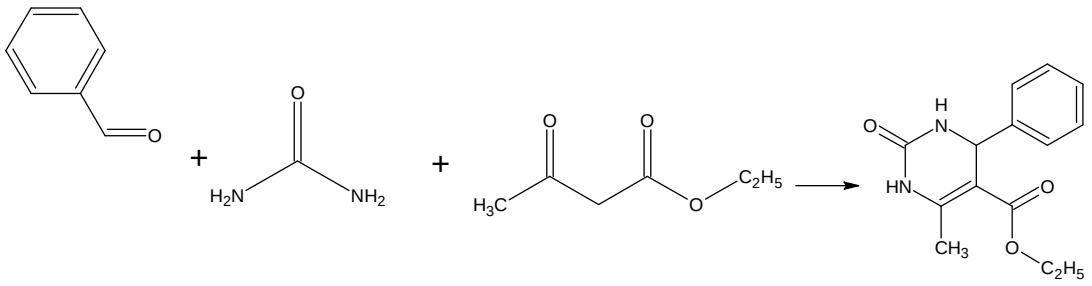
The condensation of β-diketone with urea is analogous to these of keto ester [10]

The alkali catalyzed addition of amino to cyano group is convenient cyclization Process for example the prepareation of 4-amino-2, 6-dihydroxypyrimidine from cyanoacetylurea. [11]

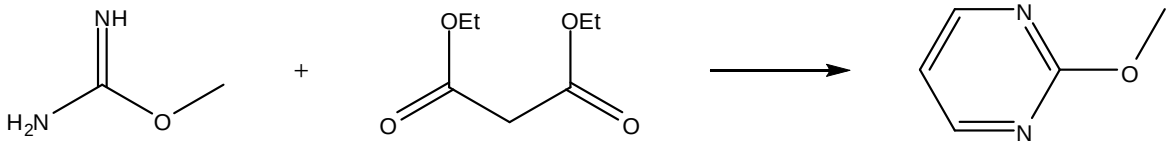
Another method of cylization is the additions of the amino group to the polarized double bond for example the production of dihydro uracil from urea and unsaturated acid and their ester[12]



Folkers and johanson[13] have been have prepare dihydropyrimidines from urea, aldehyde and acetoacetic ester

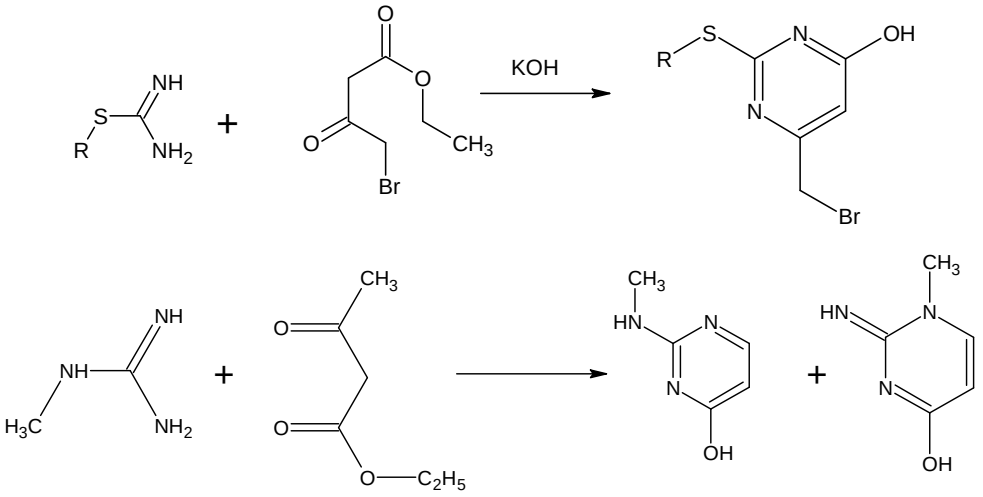


Substituted of O-alkyl urea or phenylsimecarbazide lead to 2-alkoxy or 1-anilino pyrimidine respectively [14],[15]

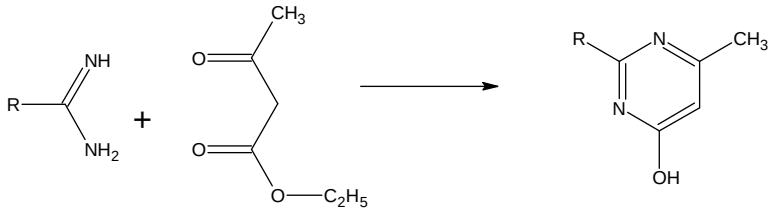


O-methylurea methoxypyrimidine

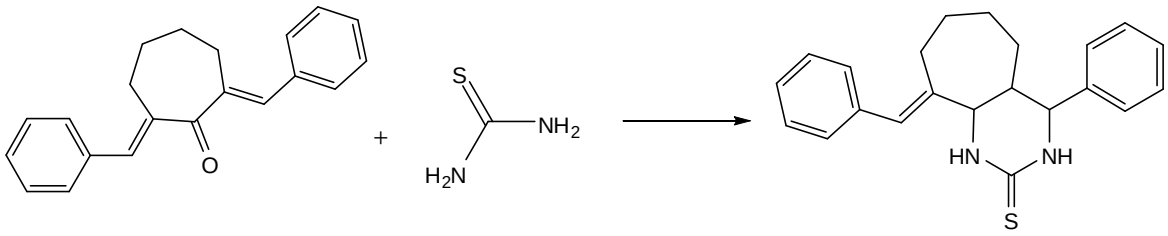
Thiourea and guanidine undergo all cyclization reaction of urea but with great easer. For example methylthiourea reacts with ethyl γ- bromoacetoacetate to yield pyrimidine derivatives in the presence of alkali. [16]



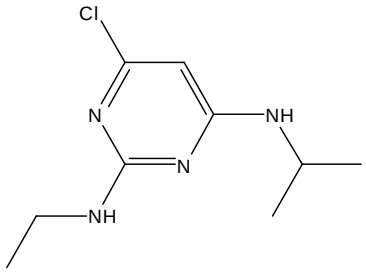
Pyrimidine can be have prepare from amidines because it is consider as cyclic amidine [17]



Mohamed.et,al [18]have prepare Cyclohepteno[1,2-d]pyrimidine-2-thiones by heating 2,7-bis(arylmethylene)cycloheptanones with thiourea in ethanoilc potassium hydroxide .



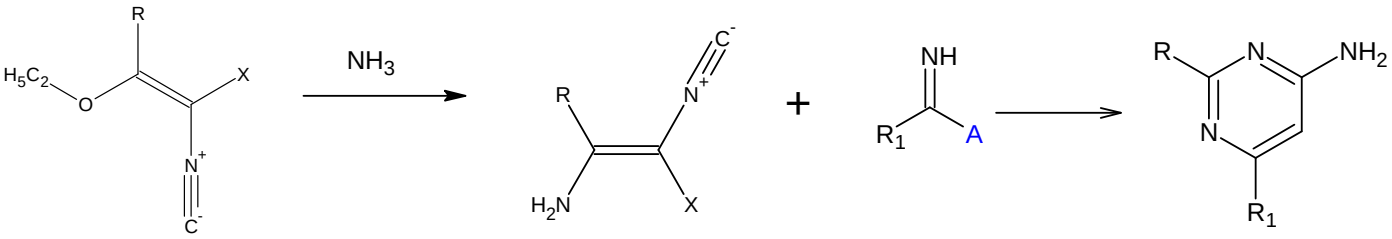
Chia et,al [19]have prepare two pyrimidine analogues of the herbicide atrazine test there herbicidal activity they found that they have specific activity



4-chloro-2-(ethylamino)-6-(2-propylamino)pyrimidin

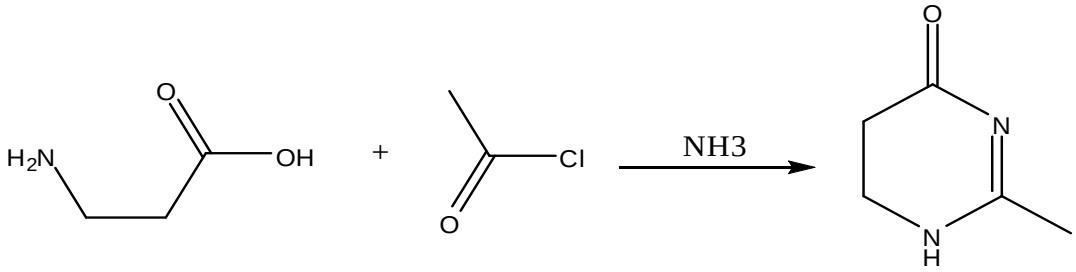
Type 2[20]

This method required amino ethylene intermediate which may be obtained from the corresponding ethoxy methylene compounds with ammonia but it can also result from reaction of imino ether or amidine with reactive methylene compounds .[21] [22]



A=good leaving group

β-Amino acids and β-amino ketones may be employed to obtain dihydropyrimidine closer being effected with acetyl chloride, HCl.acetic anhydride in the presence of ammonia .[23]

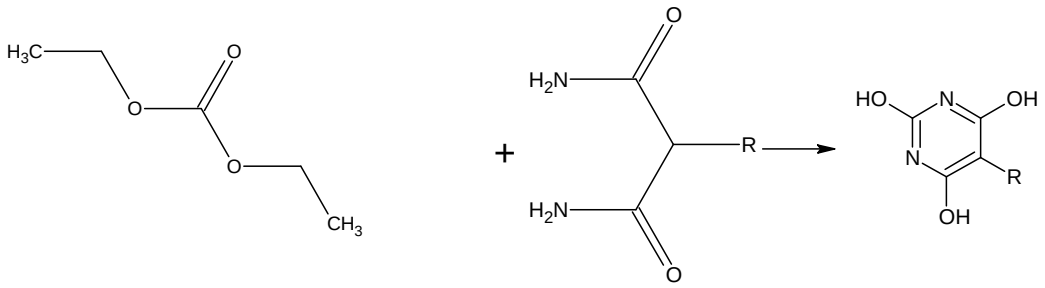


Type 3

The insertion of a single carbon atom between nitrogen of 1,3 diamines to obtain hydrogenated pyrimidine may be achieved by a number of conventional process , for instance treatment with diethyl carbonate[24] , phosgene[25] oraldehyde [26] The amide derived from carboxylic acid also can be cyclized to terahydropyrimidine

The amide of β-amio acid may be converted into 4-hydroxy 5,6-dihydropyrimidine with derivatives of carbonic acid .[27]

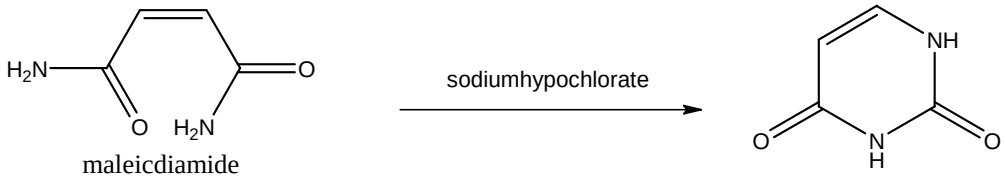
Malonic ester or malonyl chloride with malonamide yield 4,6-dihydroxy-2- methyl pyrimidine [28] remfry, with hypobromate or permanganate, methylene asparagine undergoes an oxidative cyclization followed by dehydrogenation yielding Pyrimidines [29]



Malonamide and its derivatives were used for synthesis of both reduced and unreduced pyrimidine thus babituric acid derivatives are produced from malonamide with dialkyl carbonates.[30]

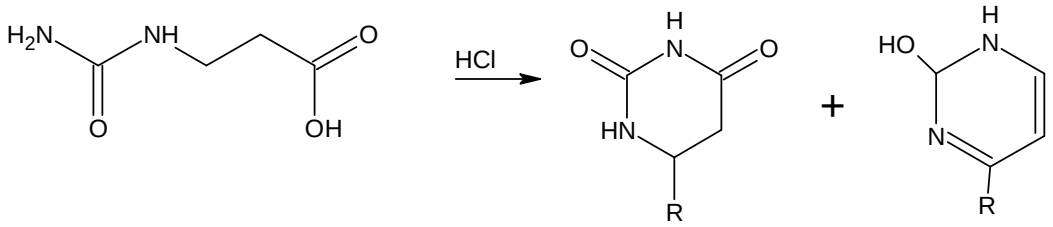
Unclassified methods

A few pyrimidine syntheses which do not fall into any three main types and they are not important , malic diamide is converted by sodiumhypochlorate into uracil [31] [32]

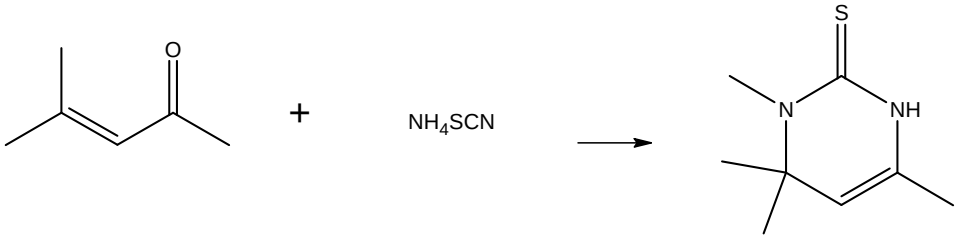


maleicdiamide uracil

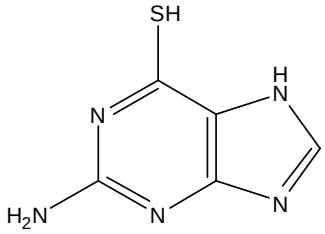
β-urido acid derivatives on heating with HCl give mixture of dihydropyrimidine Pyrimidines [33]



Mathes. and Swedish [34] have prepare Pyrimidine derivatives from mesityloxide ammoniumthiocyanate and primary amine

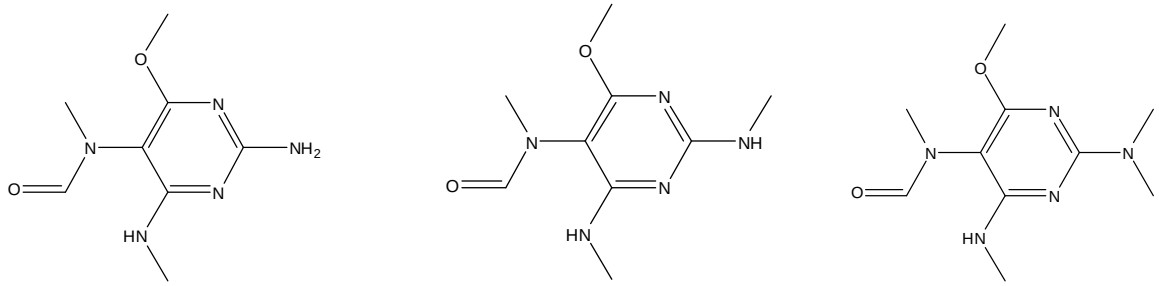


Koppe [35] et,al have prepare 2-amino-6-purinethiol as antitumor compounds

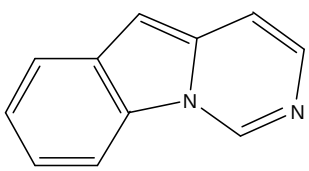


2-amino-6-purinethiol

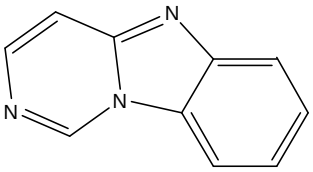
Yueh- [36] isolate three new Pyrimidines from aerial parts of Heterostemma brownie one of them



Alejandro et,al [37]have prepare some azolo pyrimidines , the method involve reaction of N-protected bromomethylazoles and tosylmehylisocyanide derivatives in non hydrous media

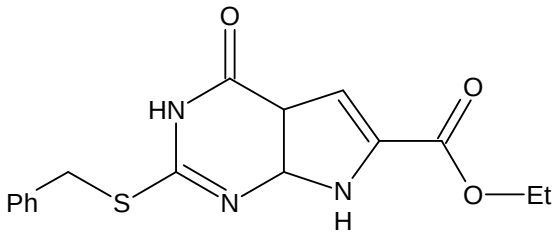


pyrimido[1,6-a]indole

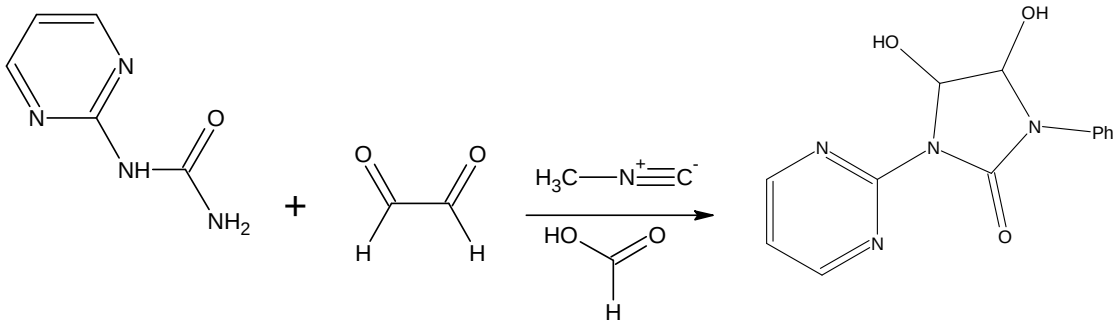


benzo[4,5]imidazo-[1,2-c]pyrimidine

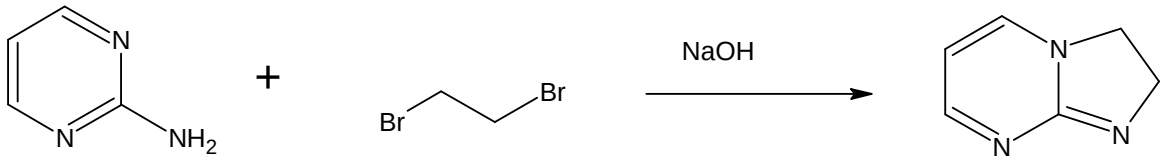
Gibson et,al [38]have prepare pyrimidine derivatives which have inhibition on gunosine triphosphate cyclohydrolase1



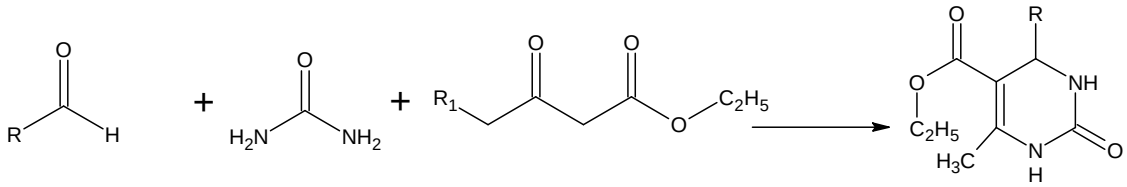
Ghndi et,al [39]have prepare the below compound from urea derivatives and formaldehyde



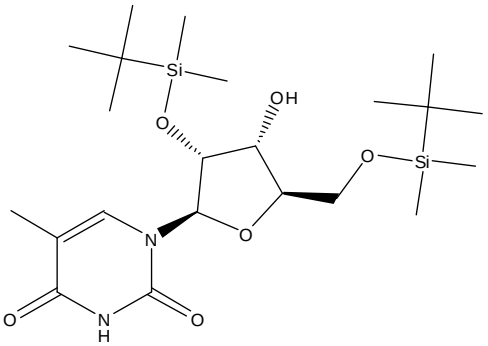
Kochergi [40] . have prepare the below compound from 2-aminopyrimidine and 1,2-dibromoethane



Bose et,al [41] have prepare pyrimidine derivatives by reaction of aldehyde ,urea derivatives and acetoacetic ester in the presence of $CeCl_3$ 7 H_2O as catalyst



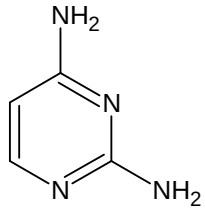
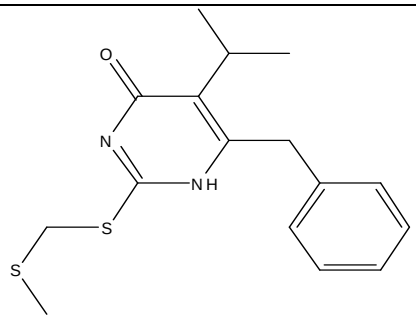
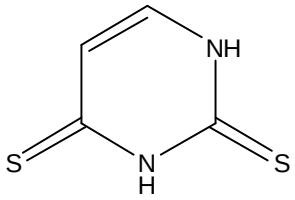
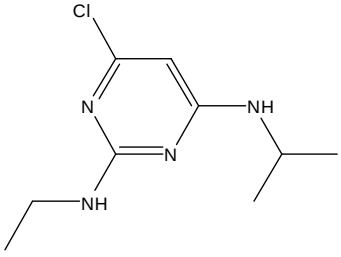
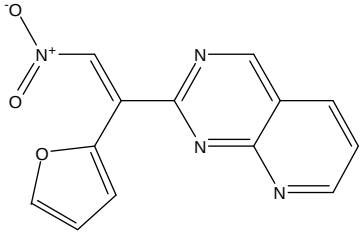
San et,al [42] have prepare some substitutes pyrimidine as anti HIV



[1-[2',5'-bis-O-(tert-butyldimethylsilyl)-beta-D-ribofuranosyl]thymine]

1-1-2 Uses of Pyrimidines

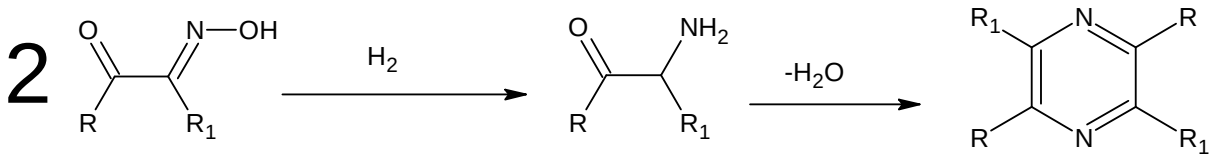
Pyrimidines and their derivatives are well known for their potential biological activity such as fungicide, algaecide and as antibiotic[43]

Compound	Structure	Activity	Ref.
2,4 diaminopyrimidine		Anitifolate	44
5-isopropyl-2-[(methylthiomethyl)thio]-6-(benzyl)-pyrimidin-4-(1H)-one		Anti-Human Immunodeficiency Virus Activity	**45**
Dithiouracil		Anti - leukemia	46
4-chloro-2-(ethylamino)-6-(2-propylamino)pyrimidine		Herbicidal	47
Nitrofurylvinylpyrido [2,3-d] pyrimidine		Antibacterial	48

1-2Pyrazines[49]

Pyrazine is have prepare first by laurant in 1844 but the systematic study of this series of compounds was initiated by victor Meyers who found that the reduction of nitrosated ketons result in the formation of oxygen – free bases instead of α-amino ketons

It is now known that this transformation may be represented as followed.



The formation of Pyrazine from α-amino ketons require loss of hydrogen as well as water it was found that considerably higher yield were obtained when oxidizing agents were added to the reaction mixture after the condensation had been allowed to take place.

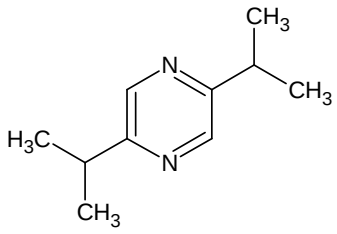
Gabrial demonstrate the intermediate is formation of dihydropyrazine by the isolation of these compounds under anaerobic conditions and subsequent oxidation to the corresponding Pyrazine

1-2-1Occurrence

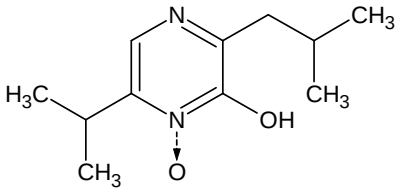
Pyrazine have not been found in any quantity in natural product from various prepareations of fused oil small amount of 2, 5-dimethyl tetramethyl and trimethyl Pyrazine have been isolated [49]

It is probable that these compound result from the cyclization of decomposition products of protein in the fermentation mixture

There are two interest derivatives of Pyrazine product by the mold aspergillus flavus one of these flavocal 3,6-diisobutyl-2-hydroxypyrazine and the other is aspergillic acid which is bactericidal antibiotic .[50]

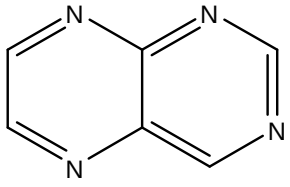


flavocal



aspergillic acid

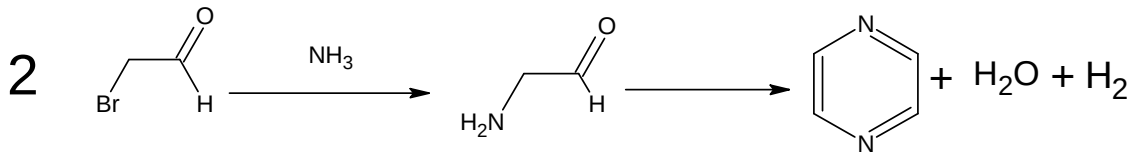
Among the more complex compound containing Pyrazine nucleus are the pteridines based on pyrimido [4, 5-b] pyrazine ring system which are the most widespread and most important of the naturally occurring derivatives of pyrazine. [51]



pteridine

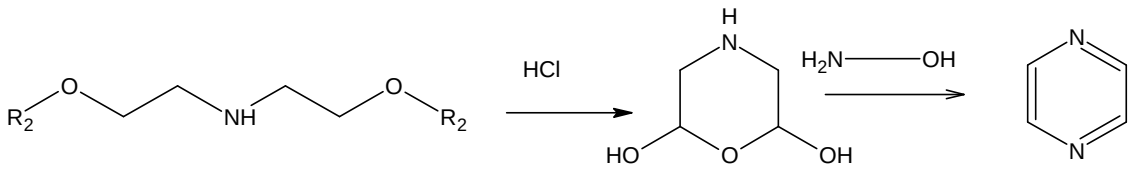
1-2-2 Synthesis of pyrazine

The classical method for prepareation of prazines including the self – condensation of α-amino carbonyl compounds but the product is low for example aminoacetaldehyde which formed from ammonation of bromoacetaldehyde hydrolysis to give pyrazine.



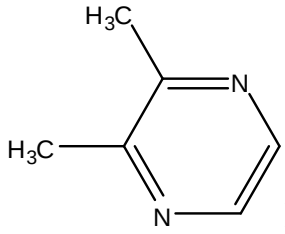
Pyrazine obtained by an indirect method by the decarboxylation of pyrazine carboxylic acid [52],[53]

The most efficient method for the synthesis of pyrazine was that of wolf and Marburg from the acetal of iminodiacetaldehyde when this compound is treated with HCl the acetal linkages are cleavage and 2,6-dihydroxymorpholine is formed which reacts with hydroxylamine to yield pyrazine .



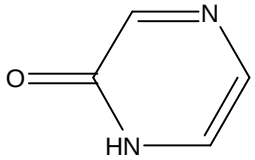
Pyrazine have been have prepare directly in 78% from acetal when the latter is treated with hydroxylamine hydrochloride the disadvantage of this method that starting material are not accessible compounds.

Takuya et,al [54] have prepare some alkyl pyrazine derivatives from diketones and diamines which form dihydropyrazine and reducting the product by metal oxide MnO_2 this method gave 80% of pyrazine



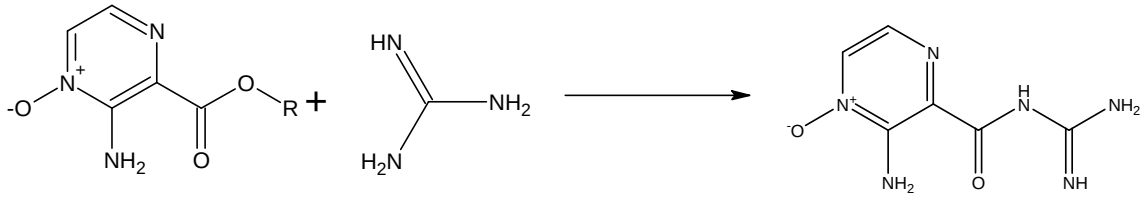
Dimethyl pyrazine

Bobek and Bloch [55] have prepare some pyrazine derivatives which have biological activity and as pyrimidine analogs

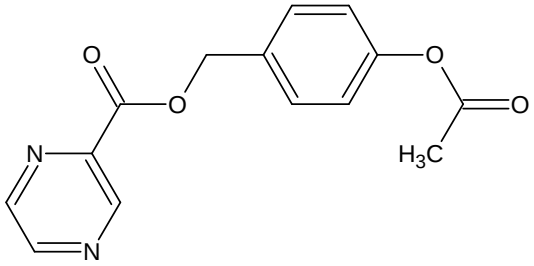


1,2-dihydro-2-oxopyrazine

James and Edward [56] have prepare N-Amidino-3-aminopyrazinecarhoxamide4-Oxides which acts as diuretic these compounds were have prepare by the reaction of the corresponding pyrazine ester with guanidine

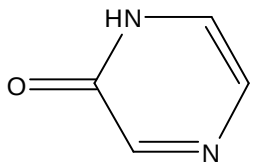


Lainne et,al [57]have prepare some pyrazine derivatives from reaction of pyrazoic acid and 4-acetoxybenzyl alcohol they found that they have excellent activity against Mycobacterium avium.



Chi-Kuen [58]have prepare pyrazine from L-serine and L-threonine the formed pyrazine is indentied by GC\MS It was found that pyrazine, methylpyrazine, ethylpyrazine, 2-ethyl-6-methylpyrazine, and 2,6-diethylpyrazine were formed from serine, whereas 2,5-dimethylpyrazine, 2,6-dimethylpyrazine, trimethylpyrazine, 2-ethyl-3,6-dimethylpyrazine, and 2-ethyl-3,5-dimethylpyrazine were formed from threonine.

Hana et,al [59]have prepare A series of pyrazines by reacting diazo-ketoesters with amino acid amides in the presence of rhodium octanoate as catalyst The pyrazine-6-ones were further derivatized by N-alkylation or by conversion to the arylpyrazines using sequential bromination.

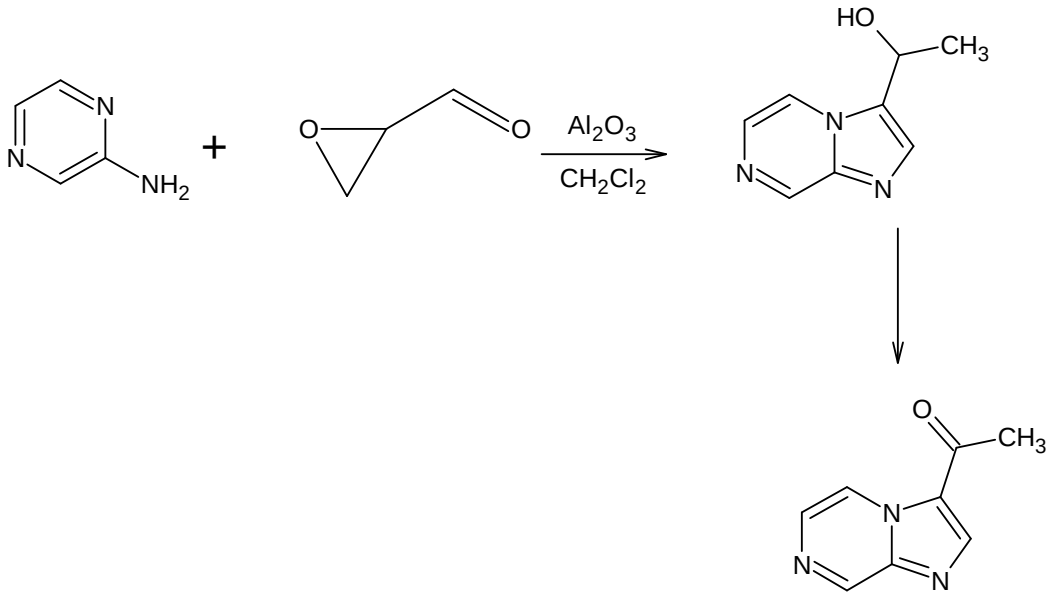


Frédéric et,al [60]preared some pyrazine alkaloids from chloropyrazine

Douglass et,al [(61)]have prepare pyrazines from reaction of epoxides and

1,2 aminoalcohol the product (aminodiols) oxidized then condensed with hydroxyl amine.

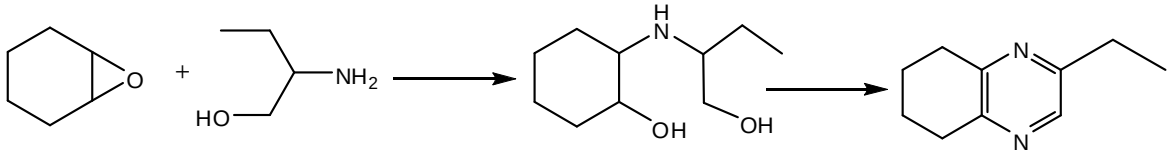
William et al ([(62)]have prepare some pyrazine derivatives by condensation of 2,3- epoxybutanal with 2-aminopyrazine



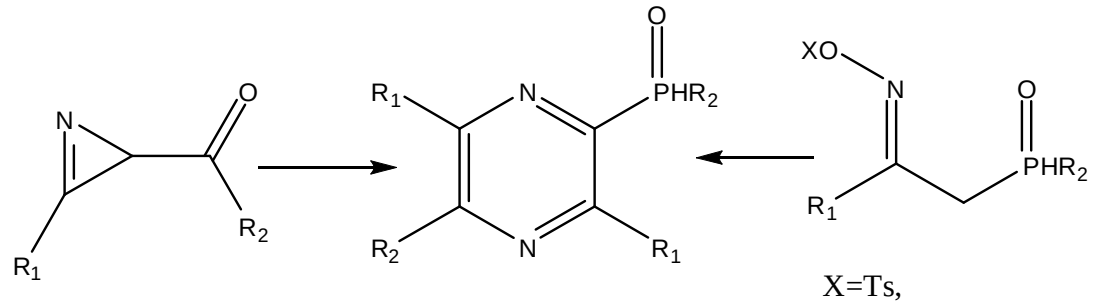
Hideki and Satoru ([63)]have prepare some alkoxy-, (alkylthio)-phenoxy-, and (pheny1thio) Pyrazines derivatives

Mikail et,al [64] have prepare some Pyridines and pyrazines substituted with 1,2,4-oxadiazole-5-ones, 1,2,4-oxadiazole-5-thiones, and 1,3,4-oxathiazoline-2-ones were synthesized and tested against Mycobacterium tuberculosis.

Douglass te,al [65] have prepare pyrazine derivatives by the reaction of epoxides with 1,2-amino alcohols delivered the amino diols. The product amino diols were then oxidized under Swern conditions.



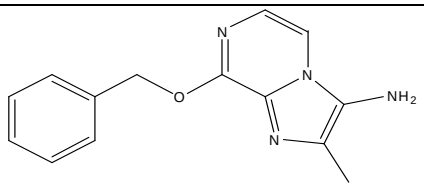
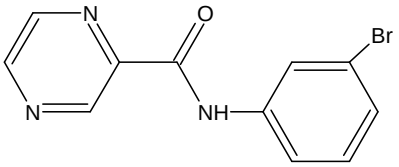
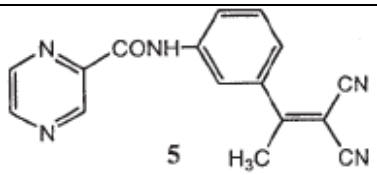
Francisco ,et,al [66] tetrasubstituted pyrazines containing two phosphonate groups in positions 2 and 5 and trisubstituted pyrazines containing a phosphonate or a phosphine oxide group in position 2 are obtained by thermal treatment of 2*H*-azirine-2-phosphonates and -phosphine oxides **6**. These pyrazines can also be have prepare from β-ketoxime tosylates or from oxime derived from phosphine oxide.

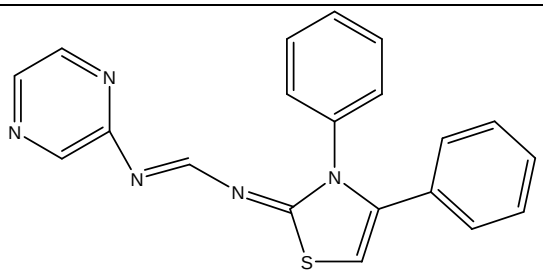
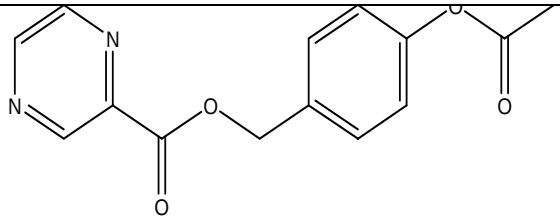


R=OEt,Ph

R_2=$PO(OEt)_2$
R_1=Me,Et,Ph

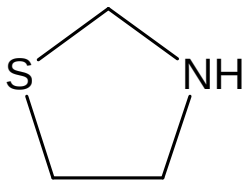
1-2-3 The uses of pyrazine

Name	structure	Use	Ref.
3-amino-2-methyl-8-(phenylmethoxy) imidazo[1,2-a] pyrazine		Antiulcer Agent	67
N-(3-bromophenyl)pyrazine -2-carboxamide		antimycobacterial activity; antifungal	*68*
N-[3-(2,2-dicyano-1-methylethenyl)phenyl] pyrazine-2-carboxamide		Antimicrobial and Leuconostoc mesenteroides growth inhibition activity	*69*

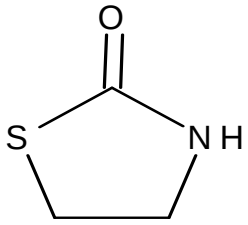
3,4-diphenyl-2-imino-N-(2′-pyrazinyliminomethyl)-4-thiazoline		anticancer, anti-inflammatory and analgesic activity	70
4-acetoxybenzyl pyazoate	 4-acetoxybenzyl pyrazoate	Antimycobacterial Activity	*71*

1- 3 Thiazolidine &thiazolidinone [72]

Thiazolidines and thiozolidinones are five member ring heterocyclic compounds contain sulfur and nitrogen atoms and three carbon atoms these compounds are not aromatic they have the below structure



Thiazolidine

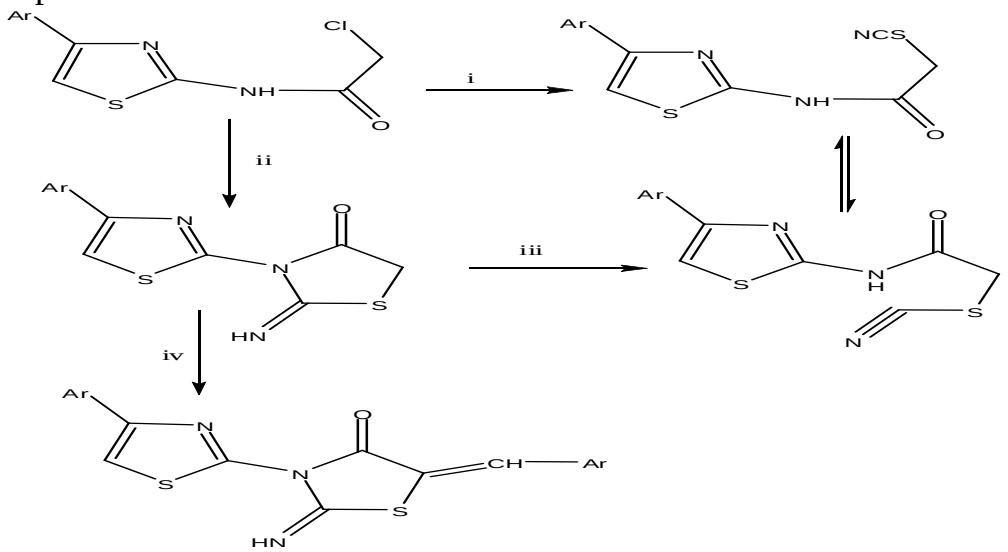


Thiazolidinone

1-3-1Synthesis of thiazolidinone & thiozolidinone

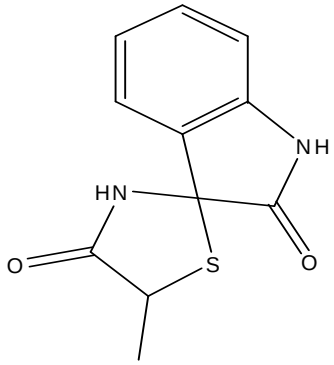
The best method of prepareation of thiazaolidinone by he reaction of mercaptoacetic acid with imines (Schiff bases) [73],[74]

Ram and Singh [75] have prepare some thiazolidinone derivatives by reaction of 2-amino-4-arylthiazole with potassium thiocyanate these compounds show anti fungal activity

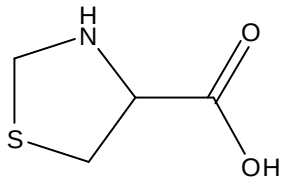


i and ii KSCN,acetone boile 3h (iii) DMF 150-160 (iv) ArCHO pyridine xylene 160-150^{o}c 3h

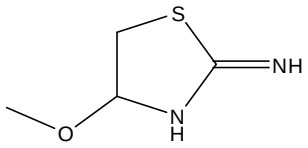
Milind, and Frank[76] have prepare 5'-Methylspiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-diones by the cyclocondensation of thiolactic acid with isatin-3-imines



D Chiarino et,al [77] have prepare Number of-substituted-4-thiazolidin carboxylic acid derivatives by cyclocondensation of L-cysteine or its esters with various aldehydes, with anti- inflammatory properties



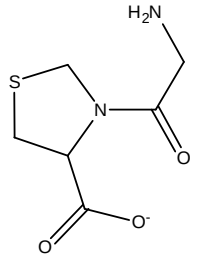
Norbert et,al [78] have prepare 3,4-disubstituted-4-methoxy-2-iminothiazolidines from α-chloromethyl and α-bromomethyl ketimines by condensation with thiourea

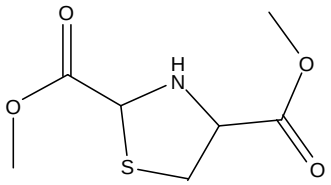


2-Imino-4-methoxythiazolidine

Nuket et,al [79] have prepare alkyl and aryl substituted furothiazolidine derivatives by the reaction of Wittig reagent with benzylidene derivatives of 4-thiazolidinones obtained from aldimines and thioglicolic acid

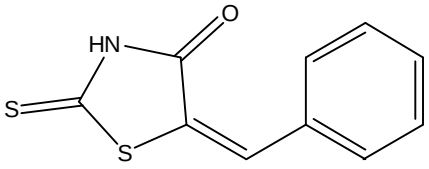
Pellegrini et,al [80] have prepare Dimethyl thiazolidine-2,4-dicarboxylate and 3-aminoacetylthiazolidine-4-carboxylate



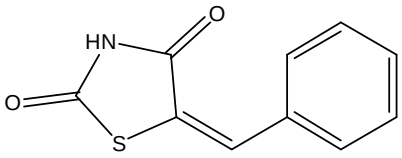


Mateja et,al [81] have prepare some new polysubstituted 3-thiocarbamoylthiazolidines by the reaction between 2-(2-methoxyphenyl)iminothiazolidine and sulfamoylphenyl isothiocyanates

Prashantha et,al [82] have prepare novel microwave induced method for the synthesis of 5-benzylidene-thiazolidine-2,4-dione and benzylidene-2-thioxothiazolidine-4-one under solvent free conditions

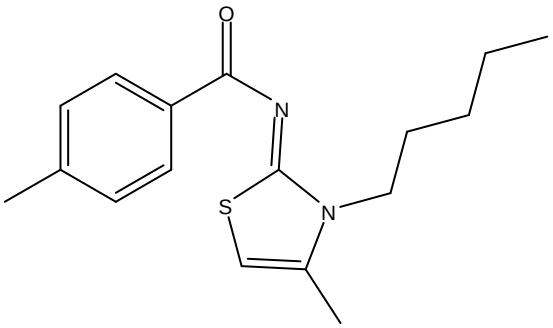


5-benzylidene-2-thioxothiazolidine-4-one



5-benzylidene-thiazolidine-2,4-dione

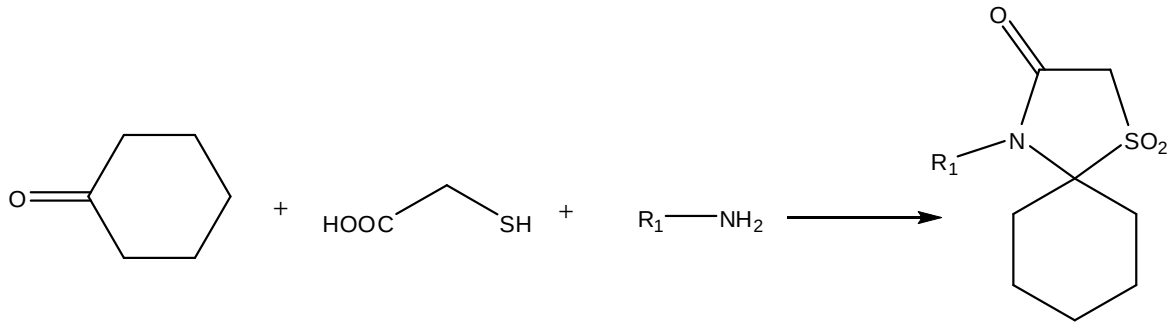
Aamer and Masood [83] have prepare some new 2-(4-methylbenzoylimino)-3-aryl-4-methyl-1,3-thiazolines by the cyclization of 1-(4-methylbenzoyl)-3-arylthioureas with acetone in the presence of bromine and triethylamine



Yoshinobu et,al [84] have prepare thiazoline compounds by the reaction of allylbenzthioamide with chloramines T and iodine

Sayeed , et,al [85] have prepare 2-[2-Carboxymethylthio-2-(4-chlorophenyl)ethyl]-2-(4- chlorophenyl)-4-thiazolidinone p, p'-dichlorochalcone using thioglycollic acid in the presence of ammonium carbonate

Tumul et,al [86] have prepare some thiazolidinone by the reaction of amines with cyclic ketones and mercapto acetic acids

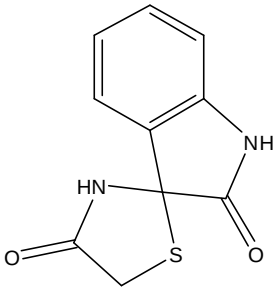


1-3-2 The uses of Thiazolidinone

Over the years, 4-thiazolidinones have enjoyed a prominent place in heterocyclic chemistry largely due to the wide-ranging biological activity demonstrated by this class of compounds [87]

Toshio , et,al have prepare some fluorinated thiazolidinone derivatives which used in prepareation of momofloro β-lactams [88]

Thiazolidinones are used as Cardio protective Drug**s** [89] HIV-1 Integrase Inhibitors [90] antileukemia drugs [91]



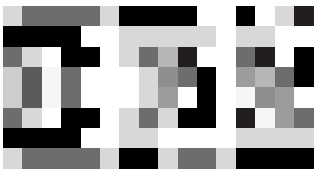
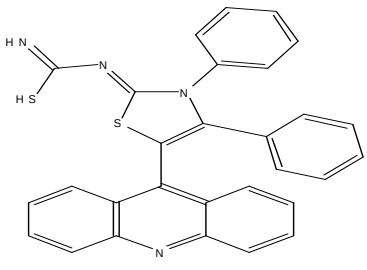
Spiro[indoline-3,2'-thiazolidine]-2,4'-dione

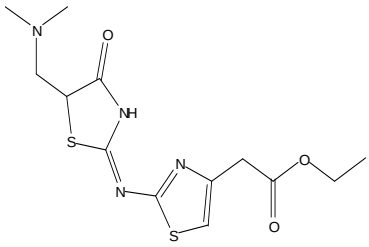
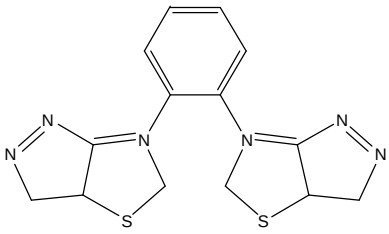
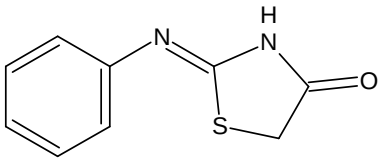
Anti leukemia

Bernard et,al [92] have prepare series of new 2-substituted thiazolidine

-4-carboxamide derivatives which have potentially useful immunological properties, they synthesized in a stereoselective manner by coupling 2-substituted thiazolidine-4-carboxylic acids with amines or amino esters

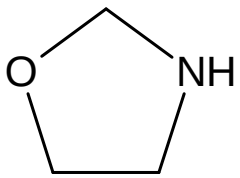
The uses of Thiazoline and Thiazolidine

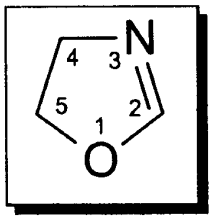
Name	Structure	Use	ref.
5-(benzyloxy)-2-[(2-thioxo-1,3-thiazolidin-3-yl)carbonyl]-4H-pyran-4-one		Antimicrobial agent	93
[(Acridin-9-yl)-3-(3,4-diphenyl)thiazol-2(3H)-ylidene] isothiourea		Anti-inflammatory	94

5-(*N*,N-Dimethylaminomethyl) -2-[(4-carbethoxy-methylthiazol-2-yl)imino]-4-thiazolidinones		antimicrobial	95
p-bis[cis-5H-3,3a-dihydropyrazolo[3,4-d]thiazol-6-yl]phenylene		Anti gram-positive & gram-negative	96
2-(phenylimino)-1,3-thiazolidine-4-one		Antimalareal	97

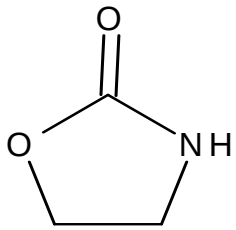
1-4 Oxazolines and oxazolidines [98]

Oxazoline and oxazolidine are class of heterocyclic compound contain oxygen and nitrogen atoms they are not aromatic 4,5-Dihydrooxazole was previously known as A2-oxazoline or 2-oxazoline. It follows from microwave spectra that the ring is planar as in below structure

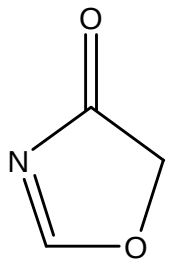




When they contain carbonyl group in the ring they named oxazlinone and oxazolidinone



oxazolidinone

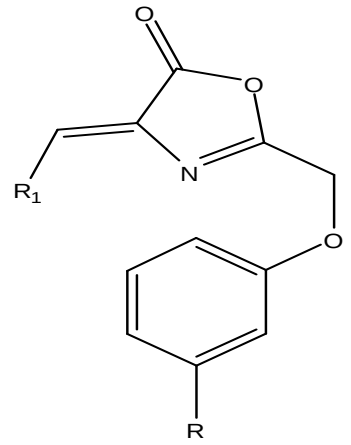


oxazolinone

1-4-1 Synthesis of oxazolidine and Oxazoline and their derivatives

Andrew J. Phillips et,al[(99)] have preparee A mild and highly efficient cyclization of -hydroxy amides to oxazolines using DAST and Deoxo-Fluor reagents. A one-pot protocol for the synthesis of oxazoles from -hydroxy amides is also presented.

M. J. Aaglawe et,al [(100)]have prepare A series of oxazolone derivatives have been synthesized as a potential antibacterial agent by the condensation of aryloxy acetyl-amino-acetic acid with aldehyde in presence of ethanol, acetic anhydride and sodium acetate .

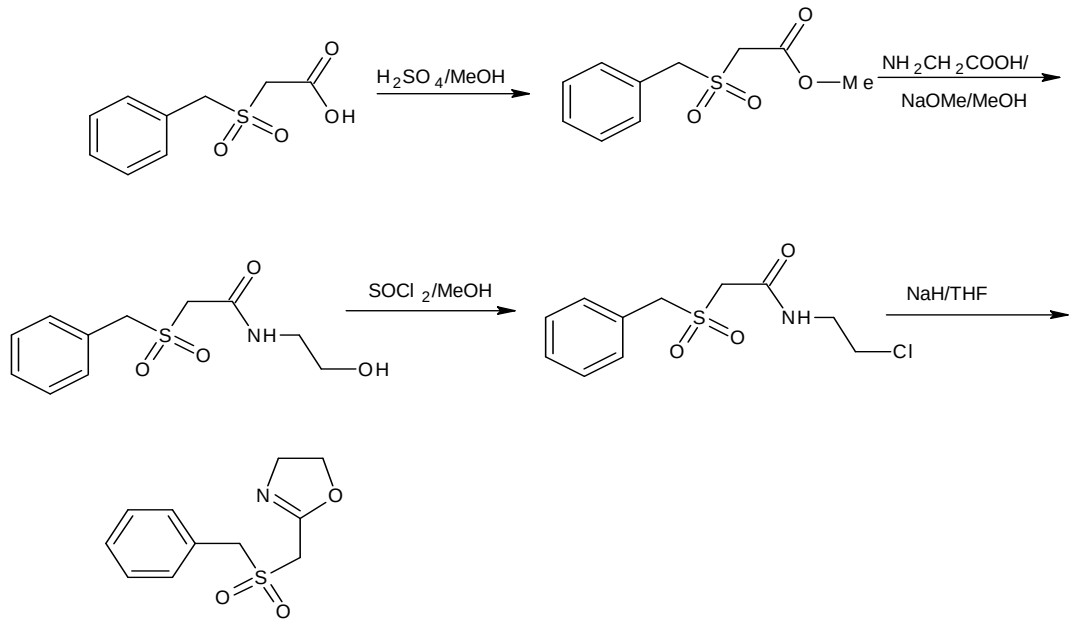


R=H,Me
R1=Aryl

G.Madhusudhan et,al [101] Ethyl -4-substitutedphenyl-2-oxo-1,3-oxazolidine-5- carboxylates have been synthesized stereoselectivelyfrom *N*-Boc-β-amino alcohols by *O*-tosylation followed by S_N2 cyclization.

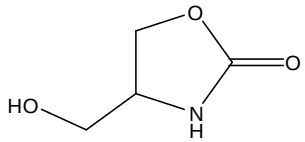
all the compounds have prepare are tested for their anti-bacterialactivity *in vitro* against S. aureus, E.faecalis and E.faecium.

V Padmavathi et,al [102] A new class of 2-oxazolines have been have prepare from N-(2-chloroethyl) sulfonamides by base promoted cyclization with NaH in tetrahydrofurane

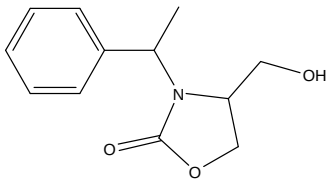


Cicily & Agrawal[103] have prepare new ring system of 1,3-disubstituted-5a-hydropyrrolo[2,3-d]quinazolino [3,2-e]pyrimidin-6(5H)-ones has been from 4-chloropyrrolo[2,3-d] pyrimidines which are have prepare using phase transfer catalysts.

Shigeo et,al [104] have prepare some oxazolidine derivatives from serinol derivatives



4-(hydroxymethyl)oxazolidin-2-one



4-hydroxymethyl-3-(-methylbenzyl)-2-oxazolidinone

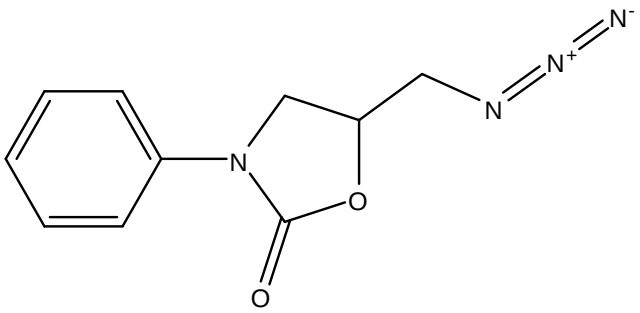
Nobuya et,al [105] have prepare oxazolidine by the Cycloaddition of chiral cyclic ketones such as (−)-menthone, (+)-nopinone, and (+)-camphenilone to nitrosoketene generated by thermolysis of 5-hydroxyimino-2,2-dimethyl-1,3-dioxane-4,6-dione gave the

corresponding chiral spiro 3-oxazolin-5-one 3-oxides (chiral cyclic

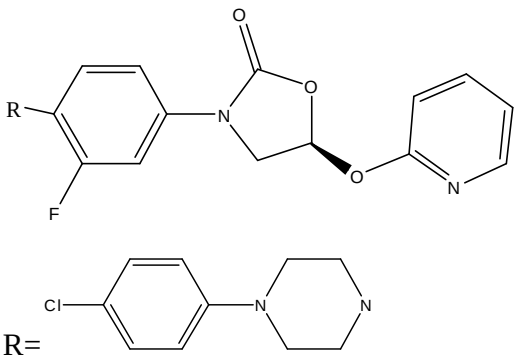
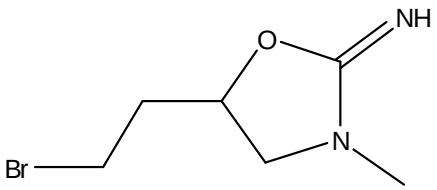
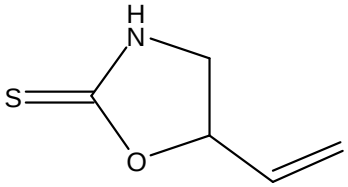
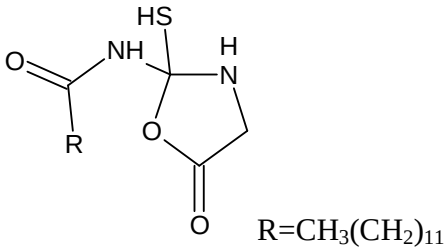
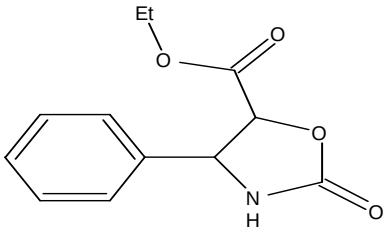
Name Structure Use Ref.

nitrones) .

G Madhusudhan et,al [106] have prepare new convergent and short approach for oxazolidinone class of antibacterial agents by condensing 3-chloro-2-((phenoxycarbonyl)oxy) propyl azide with arylamine followed by reductive acetylation. This one pot approach for N-aryl-5-azidomethyl- 2-oxazolidinone could provide access for rapid prepareation of various oxazolidinone analogues



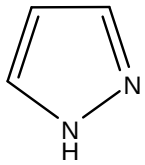
N-phenyl-5-azidomethyl- 2-oxazolidinone

(4-chlorophenyl) piprazine-1-yl-3-florophenyl)-5-(pyridine-2-yloxy)oxazolidine-2-one		antibacterial activity	107
3-methyl-5-(2-bromoethyl)-2-iminooxazolidines		anorectic activity	108
DL-5-vinyloxazolidine-2-thione		Anti thyroid	109
N-(mercapto-5-oxo-1,3-oxazolidin-2-yl)stearamide		antimicrobial and surface active agents	110
ethyl 2-oxo-4-phenyl-1,3-oxazolidine-5-carboxylate		anti-bacterial	111

1-4-2 The use of Oxazoline and oxazolidines

1-5 Pyrazoles [112]

Pyrazoles are 1,2 –diazoles and they considered as azapyrroles the shape of these molecules illustrated below



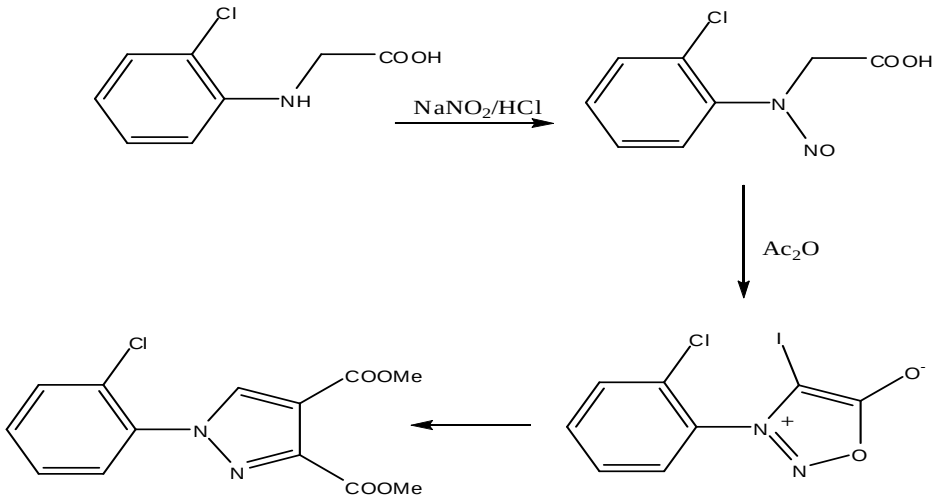
The pyrazole molecule is planar. Bond lengths and bond angles have been calculated from microwave spectra . Consistent with the structural formula, the bond between atoms 3 and 4 is the longest

Pyrazole shows the following UV and NMR

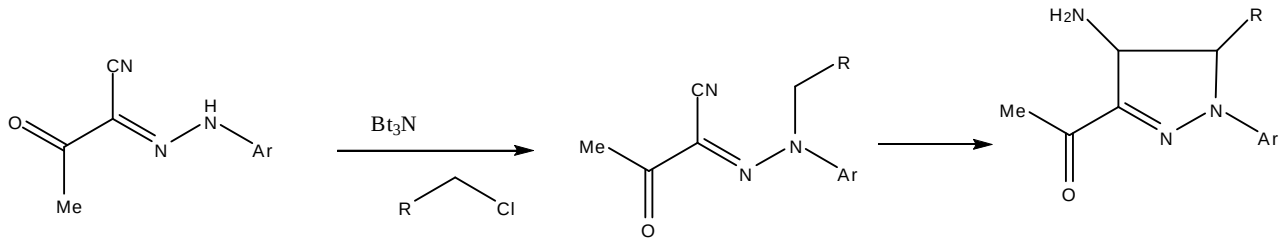
Pyrazoles have an important role in the life they are bioactive compounds and they used as U.V stabilizer [113] in prepareation of ion selective electrode [114] and inhibitor of some enzymes [115],[116]

1-5-1 prepareation of pyrazoles

Dumitraşcu et,al [117] have prepare new halogenated pyrazoles by 1,3-dipolar cycloaddition reaction of several halogenated sydnones with dimethyl acetylenedicarboxylate .



Said et,al [118] have prepare 4-aminopyrazoles by the reaction of 3-Oxo-2-arylhydrazononitriles with chloroacetonitrile, ethyl chloroacetate, and with phenacyl chloride .

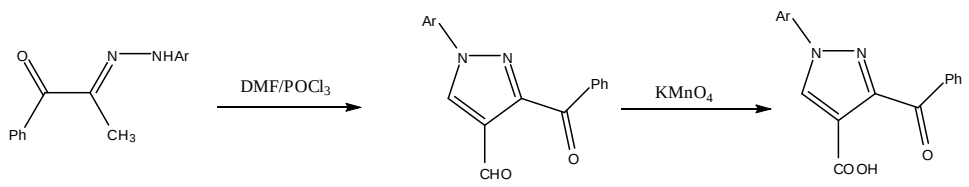


Ar=C_6H_5 R=COOEt

Hadiétou et,al [119] have prepare some pyrazole derivatives by the reaction of acetylenic compounds with diphenylnitrilamine

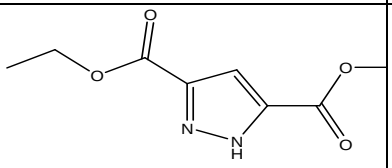
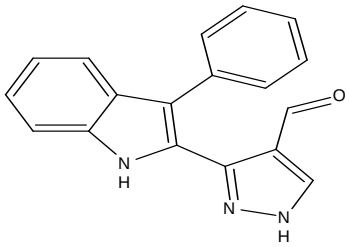
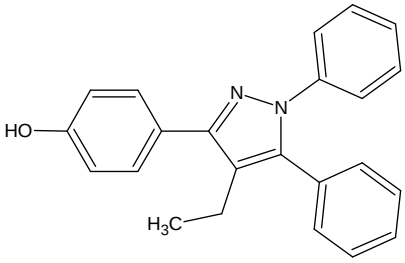
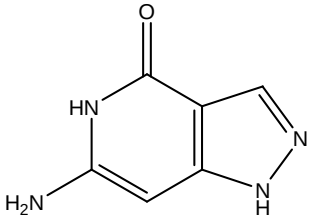
Albert et,al ([120] have prepare new tricyclic fused pyrazolines by the reaction of 3- arylidenechromanones and 3-arylidene-1-thiochromanones with hydrazine in hot acetic acid or propionic acid solution.

Bratenko1, and. Vovk [121] have prepare 1-aryl-3- benzoyl-4-carboxypyrazoles by the cyclization of 1-phenylpropane-1,2-dione monoarylhydrazones under Vilsmeier-Haack conditions gave1-aryl-3-benzoyl-4-formylpyrazoles which were converted by using potassium permanganate in aqueous pyridine medium



Ar=benzene

.1-5-2The use of pyrazoles

name	Structures	Use	Ref
Diethyl pyrazole dicarboxylate		Amphiphilic Receptor for Dopamine and Amphetamines	122
3-(3-phenyl-1H-indol-2-yl)-1H-pyrazole-4-carbaldehyde		antimicrobial	123
4-(4-ethyl-1,5-diphenyl-1H-pyrazol-3-yl)phenol		Potential Estrogen Receptor Ligands	124
6-amino-1H-pyrazolo[4,3-c]pyridin-4(5H)-one		**Analogue of Guanine**	125

1-6 Azides[126]

Azide are compounds contain three adjacent nitrogen atoms the simplest example for the azides are sodium azide and phenyl azide .

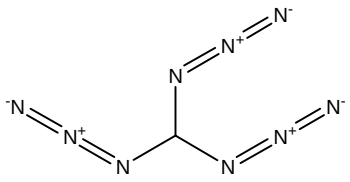
Sodium azide is being well used as an antiseptic (preservative)b in biochemical researches and as a material for synthesis of organic compounds It can be also used as a pesticide (herbicide), disinfectant for soil and antiseptic for lumbers there had been no regulation for its use in spite of its high toxicity

azide can used in the synthesis of primary amines [127] can used used as inhibitor of some enzymes [128]

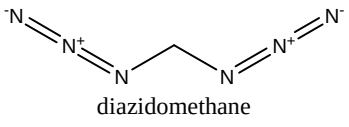
1-6-1 Heterocyclic compound contain azide

Hassner ***et,al**[129] have prepare di-triazidomethane by the methyl iodide was converted into methyl azide, methylene bromide and methylene chloride

into diazido methane, and bromoform into triazido methane.

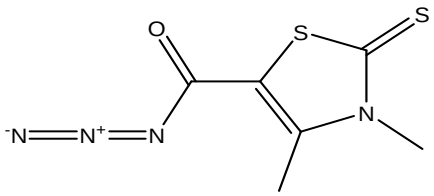


triazidomethane



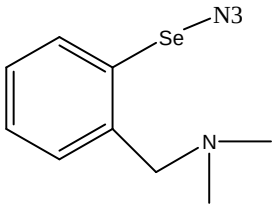
diazidomethane

Dovlatyan et,al [130] have prepare some azide derivatives by the diazotization of the hydrazide derivatives



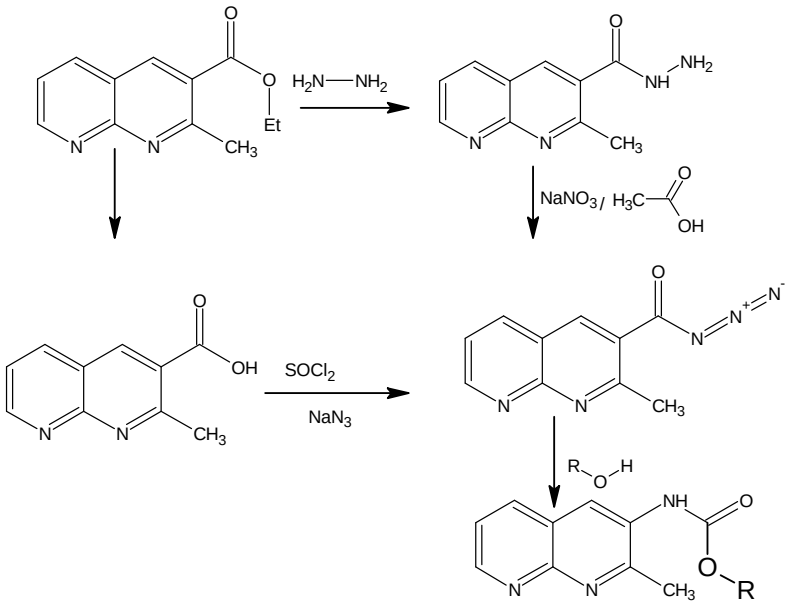
3,4-dimethyl-2-thioxothiazoline-5-carboxylic acid azide

Thomas et,al , [131] have prepare some selenium azide compounds



azido-2-((dimethylamino)methyl)benzeneselenol

Ramesh and Sreenivasulu [132] have prepare 2-Methyl-1,8-naphthyridine-3-carb**azide** from ethyl 2-methyl-1,8-naphthyridine-3-carboxylate by the diazotization of hydrazide derivatives or be the reaction of acid chloride with sodium azide. The **azide** on heating with different alcohols including benzyl alcohols underwent Curtius rearrangement to furnish 2-methyl-1,8-naphthyridine-3-carbamic acid esters



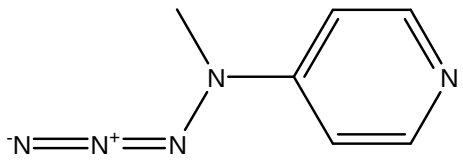
R=alkyl benzyl

Alan et,al [133]have prepare acyl azides from the corresponding *N*-acyl benzotriazoles NO^+ equivalents typically employed to synthesize these compounds from acid chlorides and hydrazides, respectively

Qi and Yitzhak [134]have prepare aromatic azides from the corresponding amines using triflyl azide under mild conditions

Viktor et,al [135]Azidoiodinanes can be have prepare from the appropriate benziodoxoles and trimethylsilyl azide in the form of stable

Philip , et,al [136] have prepare N-azido-N-methylpyridin-4-amine by the reaction of N,N-dimethypyridine and triisopropylsilyl(TIPS) enol ethers



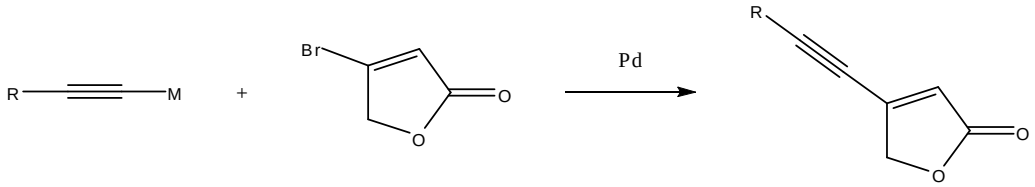
1-7 Acetylenic compounds[137]

Acetylenic compounds are compounds contain triple carbon carbon triple bonds the reactivity of these compounds come from the triple bond and the terminal acetylenic hydrogen

1-7-1 Acetylenic compounds contain heterocyclic rings

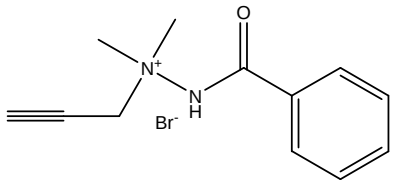
Acetylenic compounds play important intermediate in prepareation of natural product [138]

John , et,al [139] have prepare 4-(1-alkynyl)-2(5H)-furanones coupling of terminal acetylenes with b-tetronic acid bromide



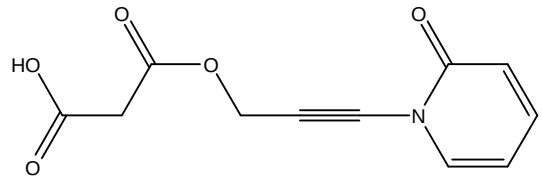
M=$SnBu_3$
M=ZnC_{l2}
M=BF_3K

Nakhmanovich et,al [140] have prepare 1,1-dimethyl-1-(2-propyn-1-yl)-2-benzoylhydrazinium bromide by the reaction of 1-benzoyl-2,2-dimethylhydrazines with propargyl bromide .



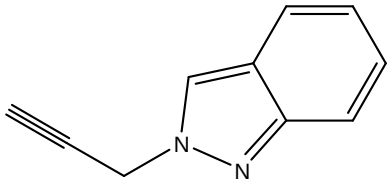
1,1-dimethyl-1-(2-propyn-1-yl)-2-benzoylhydrazinium bromide

Lijian et,al[141] have prepare (Pyridonyl-1)propargyl malonate by the reaction of pyridine with propargyl bromide then the product react with diethyl malonate .

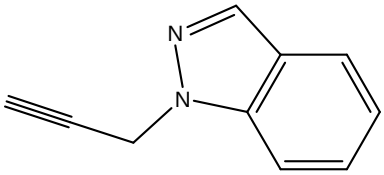


(Pyridonyl-1)propargyl malonate

Tkachenko et,al [142] have prepare 1- and 2-propargyl indazole by the reaction of indazole with propargyl bromide, the ratio of 1-propargyl indazole is increased in the presence of potassium hydroxide

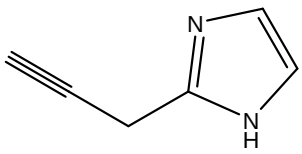


2-propargyl indazole



1-propargyl indazole

Martín- et,al [143]have prepare propargyl imidazole by the prpargylation of imidazole using some magnesium oxides as catalysts under microwave irradiation was carried out with a high activity and without solvent



1-propargyl imidazole

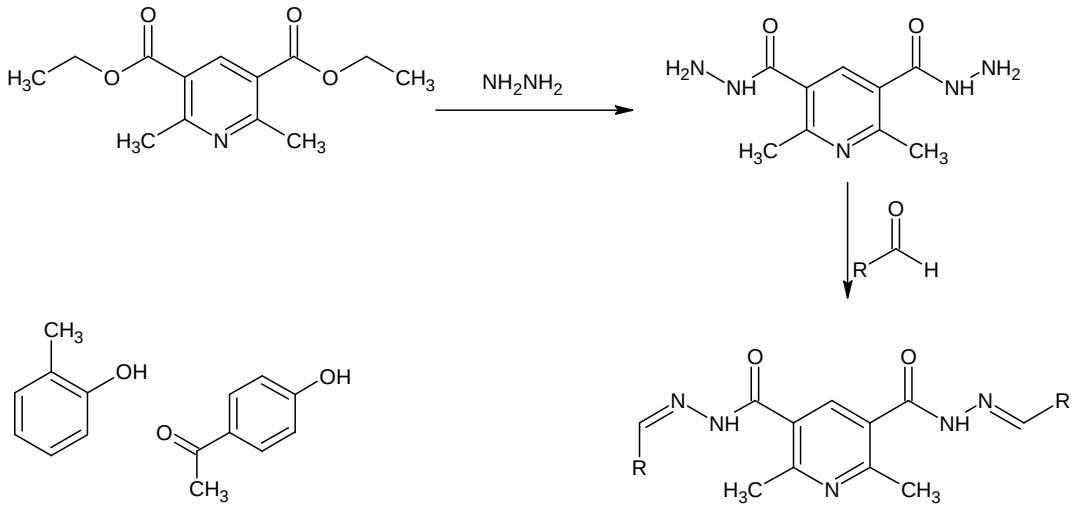
1-8 Schiff bases

Schiff bases are compounds which prepare by the reaction of aldehyde or ketone with primary amines always aromatic amines

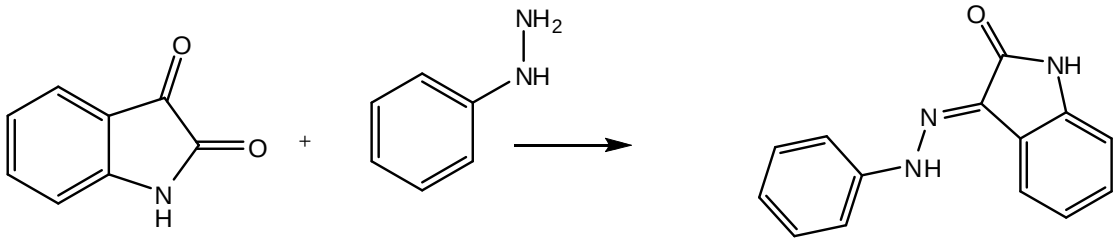
Schiff bases exhibit good antimicrobial activity and pharmacological applications. These compounds show good fungicidal activity[144] and antiviral[145], antimicrobial[146] and anti inflammatory activities and play as antioxidant [147], anticancer. [148] ,antibacterial [149] antifungal [150] and herbicidal [151]

1-8-1 prepareation of Schiff bases

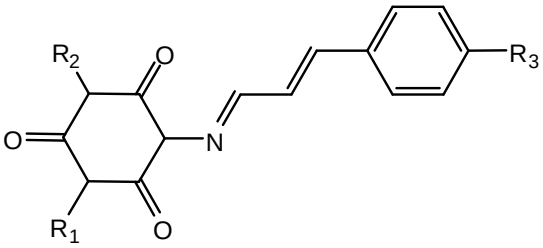
Regina Lozytska[(152)] have prepare series of new Schiff bases containing pyridine skeleton has been synthesized by reaction of an appropriate aldehyde with 2,6-dimethyl-3,5- pyridinedicarboxhydrazide.



V. Ravichandra et,al[153] have have prepare Schiff base by the reaction of isatine with phenyl hydrazine

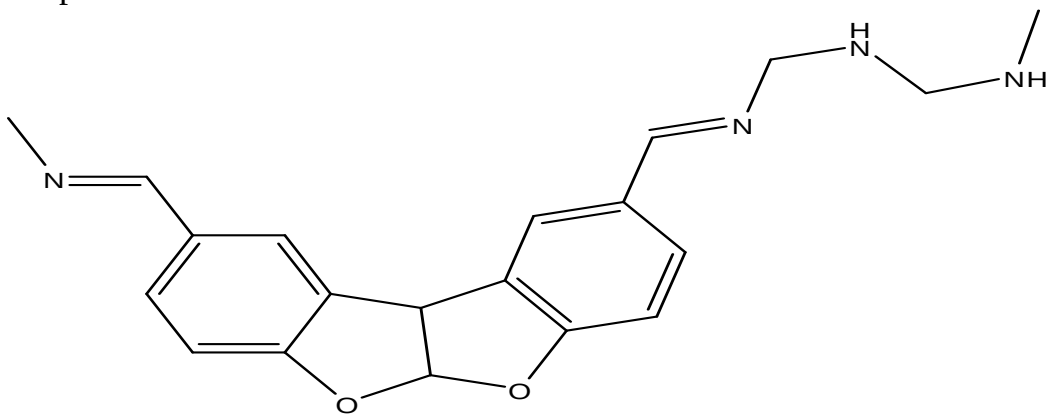


Ina Bolz ,et,al [154] have synthesized and characterized of novel Schiff bases with multiple binding sites for supramolecular assemblies For this purpose 1,3- dimethyl- and 1-butyl-5- aminobarbituric acid are condensed with para-nitro- and para-N,N-dimethylaminocinnamaldehyde respectively.

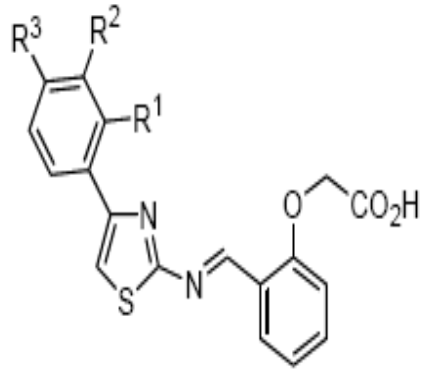


$R^1 = R^2 = H$
$R^1 = R^2 = CH_3$
$R^1 = H, R^2 = n\text{-}C_4H_9$

Mahnaz, and Ali[155] have prepare three new poly Schiff bases by polycondensation of diethylenetriamine, 1,2-diaminopropane and o-diaminobenzene with dihydrobenzofuro [2,3-b] benzofuran-2,9-dicarbaldehyde .

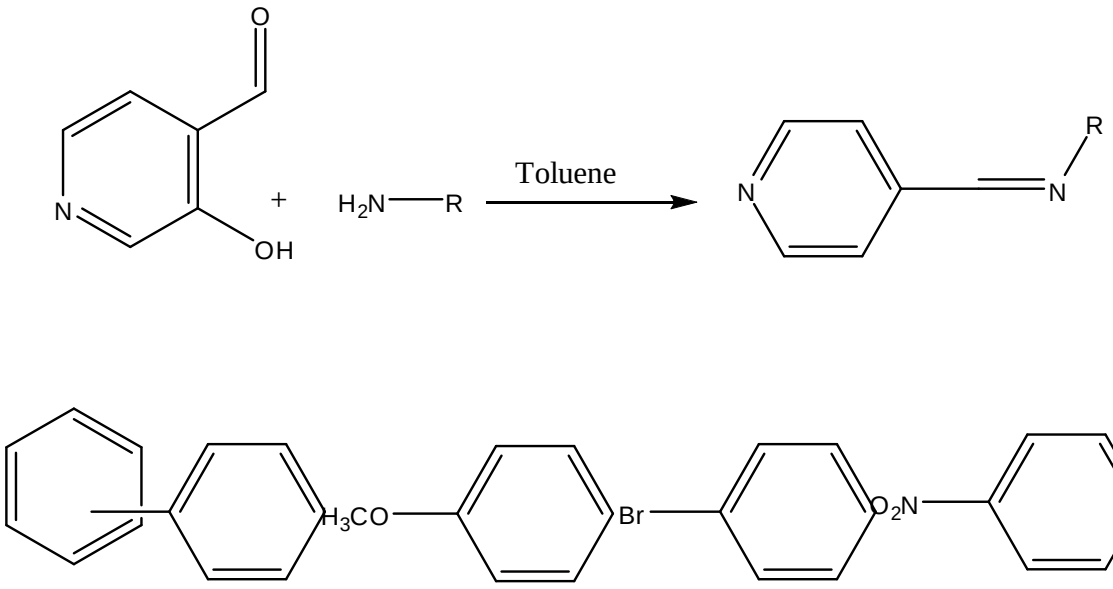


Hamid et,al [(156)] have prepare five novel Schiff bases have been have prepare from *o*-formylphenoxyacetic acid and a series of aminothiazoles to form a number of potentially biologically active compounds

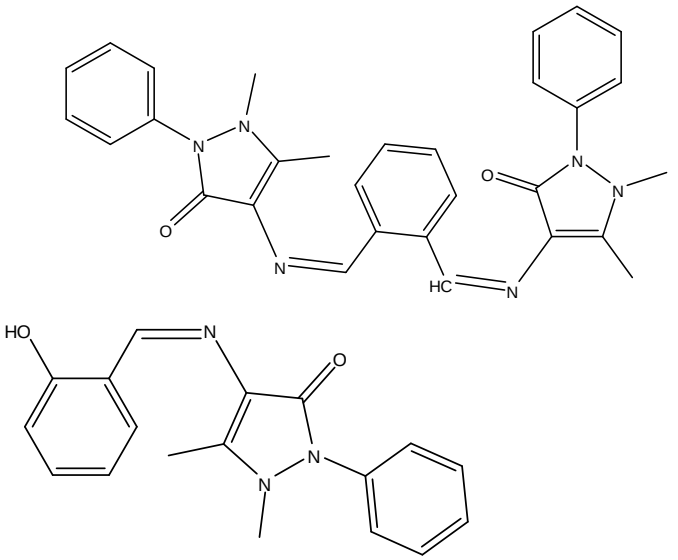


a R^1 = Br, R^2 = H, R^3 = H
b R^1 = H, R^2 = H, R^3 = Br
c R^1 = F, R^2 = H, R^3 = H
d R^1 = H, R^2 = F, R^3 = H
e R^1 = H, R^2 = H, R^3 = F

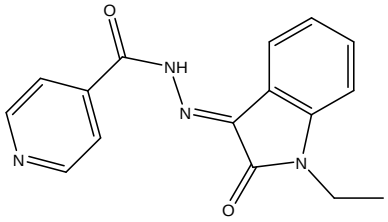
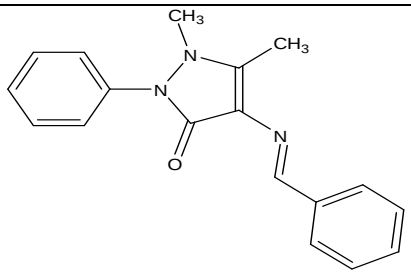
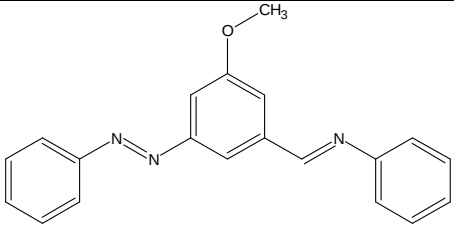
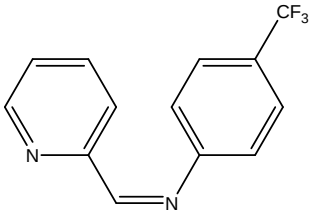
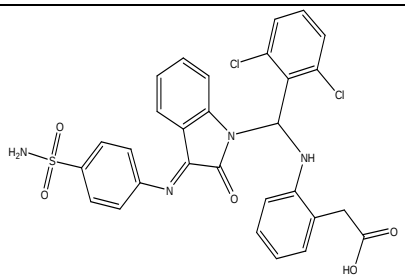
Almudena et,al [(157)] have prepare **,**new Schiff bases by reacting 3-hydroxy-4-pyridinecarboxaldehyde with various amines.



Tudor Rosu [158] have prepare of Cu(II) complexes derived from Schiff base ligands obtained by the condensation of 2-hydroxybenzaldehyde or terephtalic aldehyde with 4-aminoantipyrine



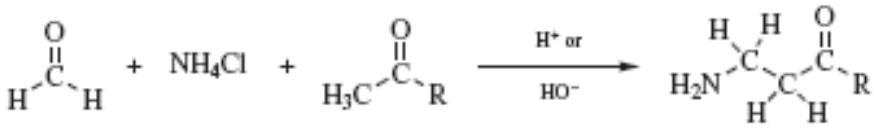
1-8-2 The use of Schiff bases

Name	Structure	Uses	Ref.
N'-(1-ethyl-2,3-dihydro-2-oxo-1H-3-indolyliden)-4-pyridinecarboxylic acid hydrazide		Antitubercular	159
(E)-4-(benzylideneamino)-2,3-dimethyl-1-phenyl-1,2-dihydropyrazol-5-one		Antibacterial	160
N-((1E)-{3-methoxy-5-[(E)-phenyldiazenyl]phenyl}methylene)-N-phenylamine		Antibacterial	161
(Z)-N-(pyridin-2-ylmethylene)-4-(trifluoromethyl)benzenamine		anti-inflammatory	162
(2-{(2,6-Dichlorophenyl)-[2-oxo-3-(4-sulfamoylphenylimino)-2,3-dihydroindol-1-yl-methyl] amino}phenyl)acetic acid.		antifungal	163

1-9 Mannich bases [164]

In the Mannich reaction, formaldehyde (or sometimes another aldehyde) is condensed with ammonia, in the form of its salt, and a compound containing an active hydrogen. this can formally be considered as an addition of ammonia to give H2NCH2OH, followed by a nucleophilic substitution. Instead of ammonia, the reaction can be carried out with salts of primary or secondary amines or with amides,in which cases the product is substituted on the nitrogen with R, R2, and RCO, respectively The imines can be generated in situ, and the reaction of a ketone, formaldehyde, and diethylamine with microwave irradiation gave the Mannich product, a b-amino ketone The product is referred to as a Mannich base

.



The Mannich base can react further in three ways. If it is a primary or secondary amine, it may condense with one or two additional molecules of aldehyde and active compound, for example

,

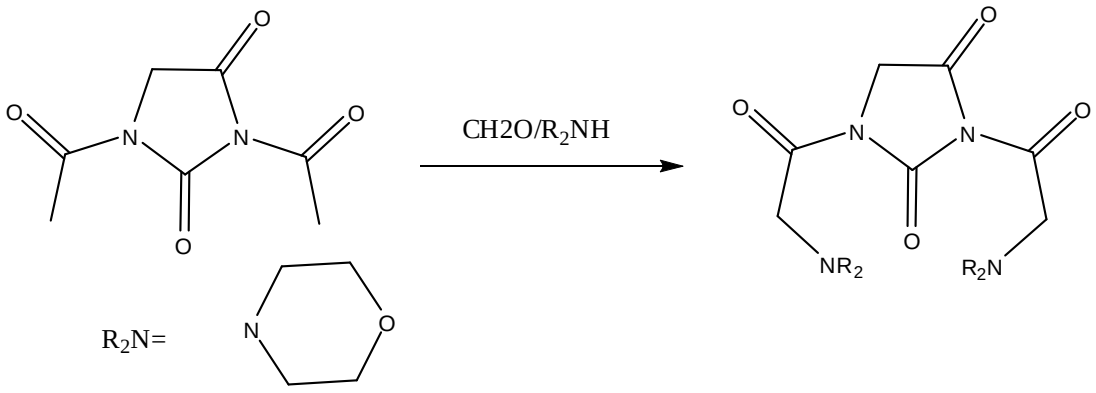
If the active hydrogen compound has two or three active hydrogens, the Mannich base may condense with one or two additional molecules of aldehyde and ammonia or amine, for example

Another further reaction consists of condensation of the Mannich base with excess formaldehyde:

1-9-1 prepareation of Mannich bases derivatives

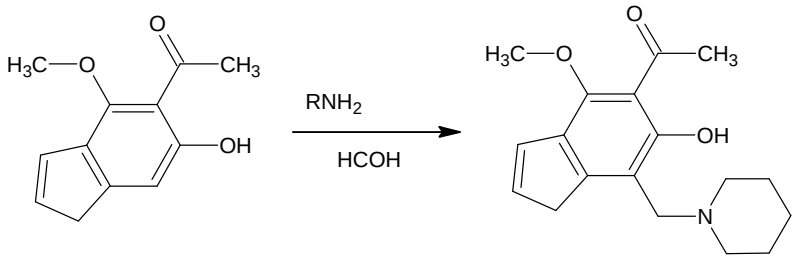
FERNANDEZ and JEANNE M. [165] have prepare Mannich bases of 2-naphthol by reacting 0.01 molar quantities of2-naphthol, formalin, and the secondary amine in 10 ml. of dioxane for 24 hours at room temperature

COKER AND FIELDS [166] have prepare some Mannich bases by treatment of 1,3-Diacetylhydantoin with aqueous formaldehyde and either piperidine or morpholine was found to yield crystalline Mannich bases in excellent yield

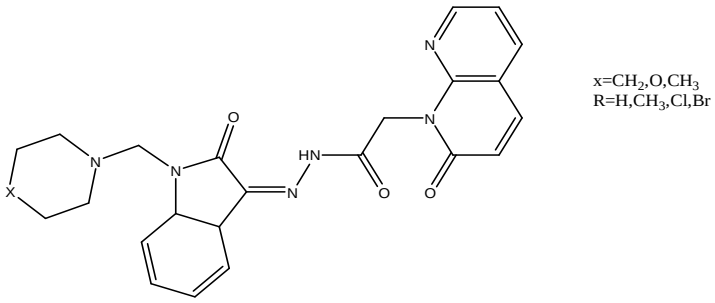


Abdel Hafez et,al [167] have prepare Mannich bases by the reaction of visnaginone 5-acetyl-6-hydroxy-4-methoxybenzo[b]furan with piperidine and benzylamine in the presence of formalin.

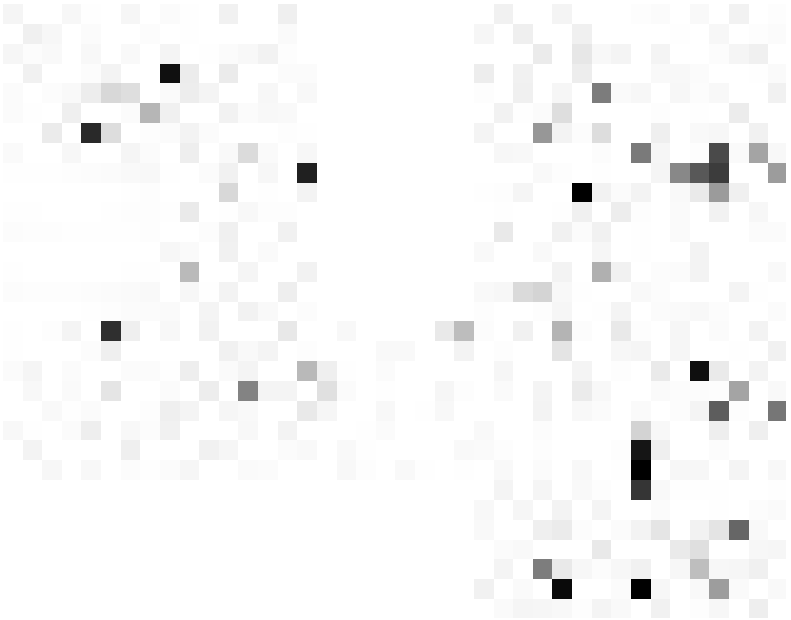
.



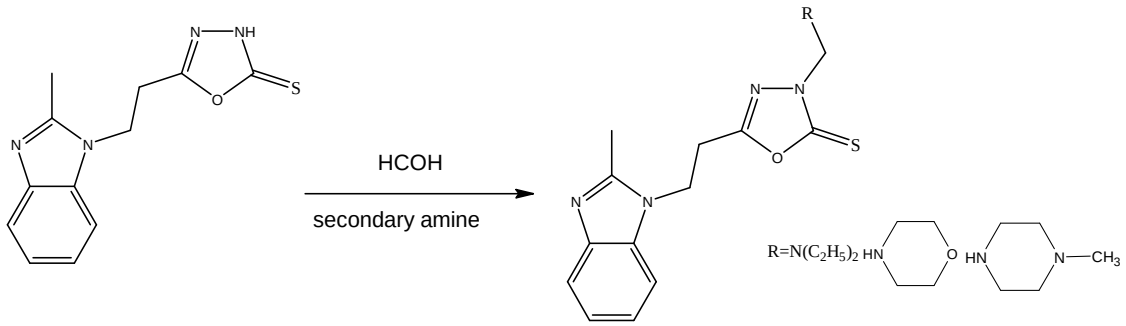
Mogilaiah & Sakram [168] have prepare some Mannich bases be the reaction of Aminomethylationof of with formaldehyde and cyclic secondary amines furnishes(2-oxo-3-phenyl-2*H*-[1,8]naphthyridin-1-yl)acetic acid(1-aminomethyl-2-oxo-1,2-dihydroindol-ylidene)hydrazides



Juliusz and Jarosław [169] have prepare a N-Mannich bases such as benzimidazoles 1a and 1c by chloromethylalkyl ether afforded two products 2 and 3



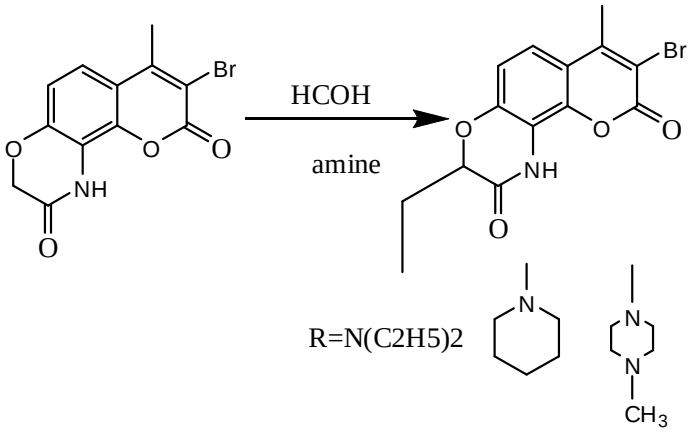
El-masry et,al [170] pepared mnnich bases for 3-(2-methylbenzimidazol-1-yl)propanoic acid hydrazide which react with CS2/KOH to gave oxadiazole which underwent Mannich reaction to give the below compound.

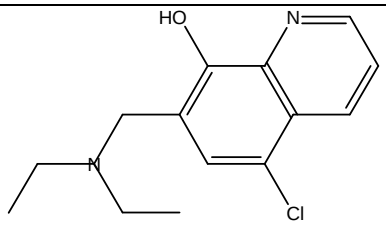
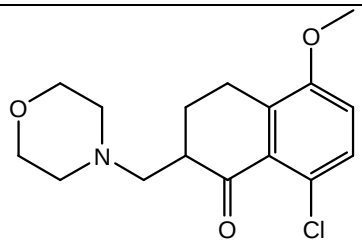
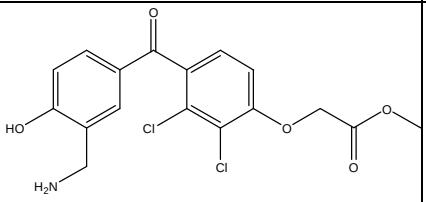
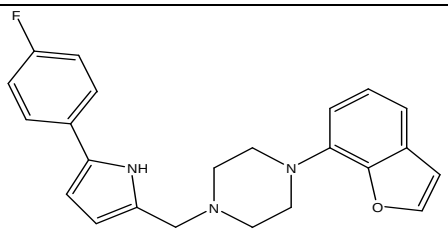
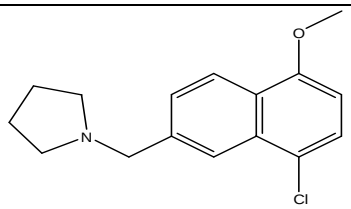


Nofal et,al [171] allowed oxazine derivative **to** undergo a Mannich reaction using different secondary amines, namely diethyl amine, piperidine and/or methylpiprazine in the presence of paraformaldehyde to give the

Name	Structure	Uses	Ref.

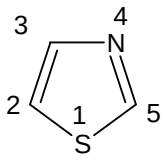
corresponding 8-bromo-7-methyl-3-substituted 9H-pyrano-1,4-oxazine-2,9-dione Mannich bases



5-chloro-7-(2-ethylbutyl)quinolin-8-ol		Antiamebic	172
8-Chloro-5-methoxy-2-morpholinomethyl-tetralone		Analgesic &Tranquilize	173
Ethyl [2,3-dichloro-4- [3-(aminomethyl)-4-hydroxybenzoyl]phenoxy]acetate		Diuretic	174
2- [[4-(7-benzofuranyl)-l-piperazinyl]methyl]-5-(4-fluorophenyl)pyrrole		Antipsychotics	175
8-chloro-3,4-dihydro-5-methoxy-2-pyrrolidinomethyl naphthalene		Analgesic	176

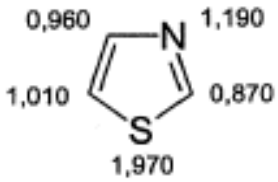
1-9-2 The uses of Mannich bases

1-10 Thiazole [177]

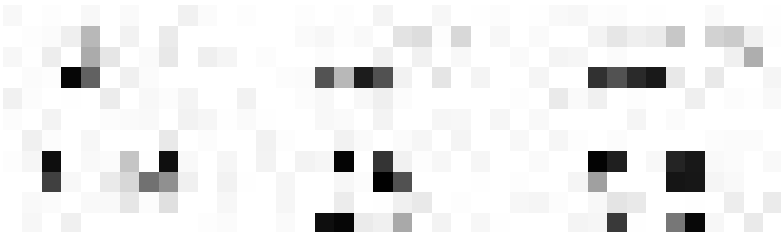


Thiazole (1,3-thiazole) possesses a pyridine-like N-atom and an S-atom as present in thiophene.

The univalent radical is known as thiazolyl. The thiazole molecule is planar and the C-S bond length is 171.3 pm, similar to that in thiophene as below



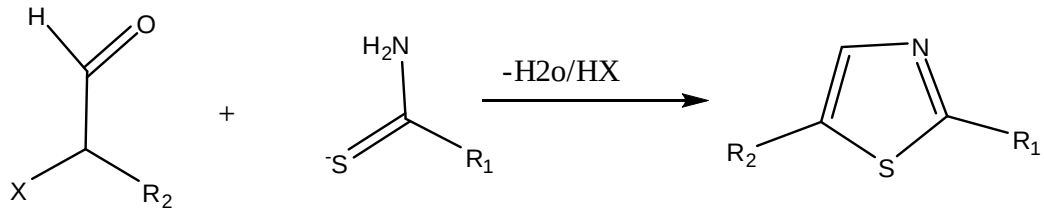
A comparison with the bond lengths of oxazole (see Fig. 5.9, p 123) leads to the conclusion that the delocalization of the ^"-electrons in thiazole is greater. Thus, the aromaticity of thiazole is greater than that of oxazole. The ionization potential is 9.50 eV and its dipole moment 1.61 D. UV and NMR data are listed in the following table:



1-10-1 Synthesis of thiazole

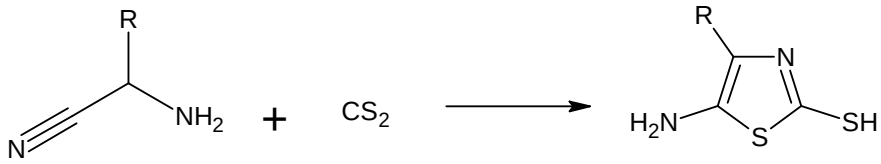
Thiazole have prepare by the some method

The cyclocondensation of or-halocarbonyl compounds with thioamides (Hantzsch synthesis) offers considerable scope

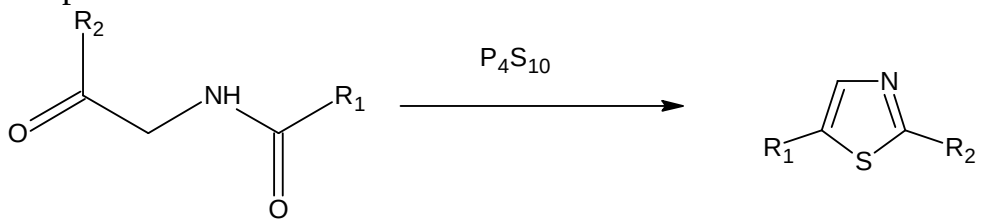


The HANTZSCH synthesis involves three intermediate steps. In the first, the halogen atom of the α-halo aldehyde or a-halo ketone is nucleophilically substituted. The resulting S-alkyliminium salt 2 undergoes
a proton transfer (2 -> 3); cyclization produces a salt of a 4-hydroxy-4,5-dihydrothiazole 4 which is converted into a 2,5-disubstituted thiazole 1 in protic solvents by an acid-catalysed elimination of water.

α-Aminonitriles react with CS_2, COS, salts or esters of dithiocarboxylic acids and with isothiocyanates, under mild conditions, to give 2,4-disubstituted 5-aminothiazoles 8 (Cook-Heilbron synthesis), e.g

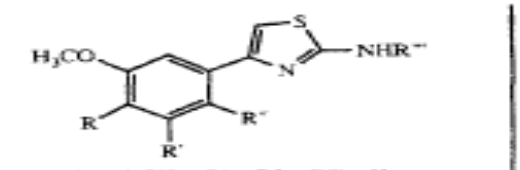


α-(Acylamino)ketones react with P_4S_{10} yielding thiazoles (Gabriel synthesis

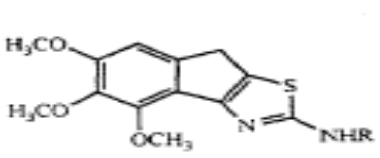


David R et,al [178]have prepare thiazole derivatives by wittig reaction by using phosphoniun salt as intermediate

K. Darrell [179]have prepare series of new 2-amino- or 2-allylamino-4-aryl-substituted thiazoles from the corresponding α-brominated acetophenones via reaction of the latter with thiourea or allylthiourea in HCCl3:C2H5OH(abs) in a one-pot sequence



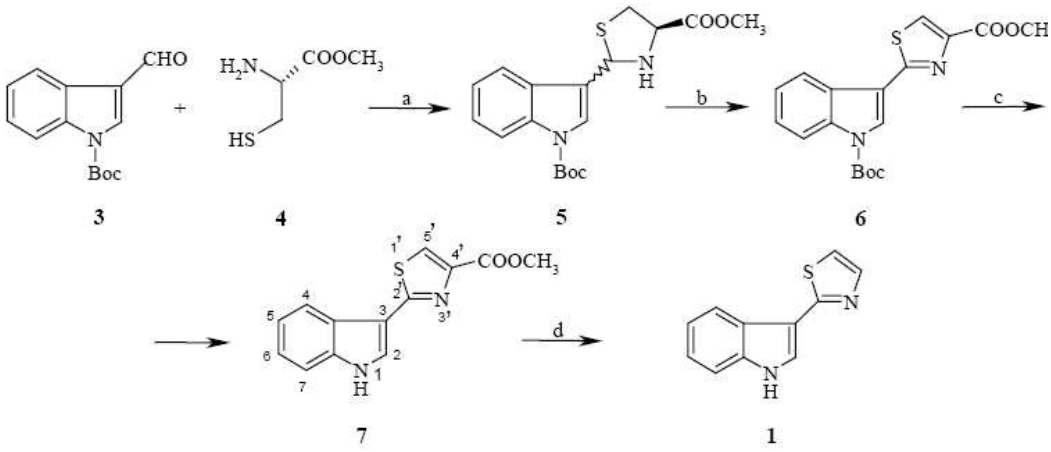
1 a. R = OCH_3, R' = R'' = R''' = H
b. R = OCH_3, R' = R'' = H, R''' = allyl
c. R = OCH_3, R' = R'' = H, R''' = acetyl
d. R = R' = R''' = H, R'' = OCH_3
e. R = R' = H, R'' = OCH_3, R''' = allyl
f. R = R' = H, R'' = OCH_3, R''' = acetyl
g. R = R' = OCH_3, R'' = R''' = H
h. R = R' = OCH_3, R'' = H, R''' = allyl
i. R = R' = OCH_3, R'' = H, R''' = acetyl



2 a. R = H
b. R = allyl
c. R = acetyl

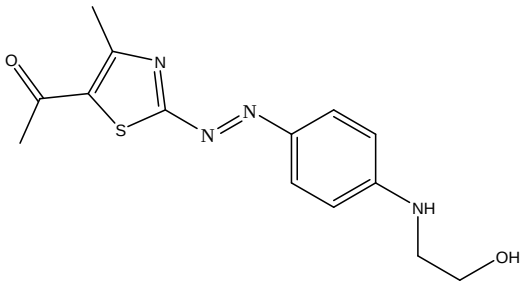
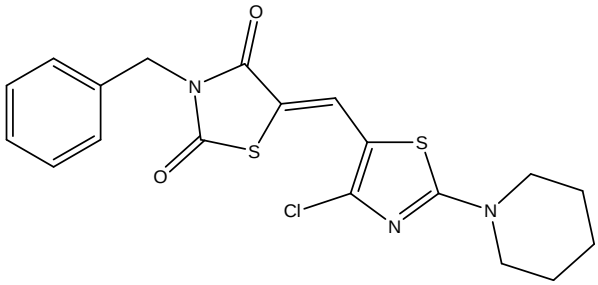
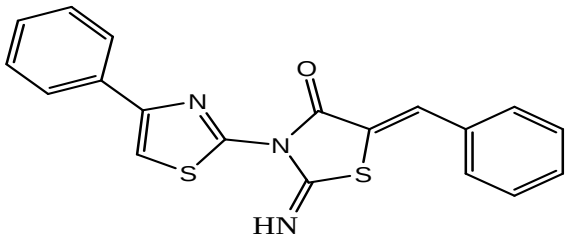
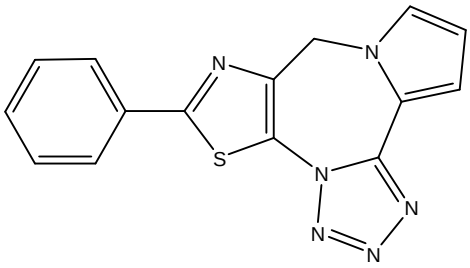
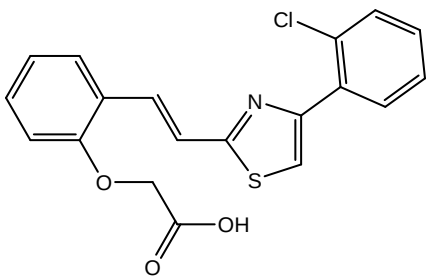
Gregory et ,al [180] used 1,3-Dichloropropene (a mixture of cis and trans isomers) to synthesize thiazole derivatives by starting its reaction with sodium thiocyanate to give 3-chloro-2- Propenylthiocyanate This mixture of cis and trans isomers of isothiocyanate on chlorination gave 2-chloro-5- chloromethylthiazole

.Dzurilla et,al [181] have prepare a new method for the synthesis of camalexin based on the reaction of 1-(tert-butoxycarbonyl)indole-3-carboxaldehyde with methyl Lcysteinate hydrochloride, followed by oxidation and decarboxylation



a) 1:2 methanol/benzene, $(C_2H_5)_3N$, 25° C, 3 h. (85%); b) MnO_2, benzene/pyridine, 55° C, 1.5 h., (44%); c) CH_3ONa, methanol, 25° C, 20 min.(59%); d) NaOH, $NaHCO_3$, 25° C, 2 h., (12%).

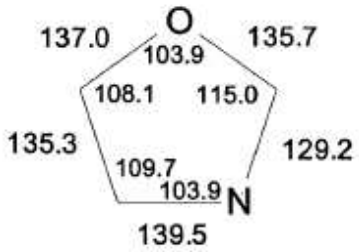
1-10-2 The use of thiazole

Name	Structure	Uses	Ref.
5-acetyl-2-[4-[N-(2-hydroxyethy)amino] phenylazo]- 4-methylthiazole		Azo Disperse Dyes .	182
(Z)-3-benzyl-5-((4-chloro-2-(piperidin-1-yl)thiazol-5-yl)methylene)thiazolidine-2,4-dione		Antimicrobial	183
(Z)-5-benzylidene-2-imino-3-(4-phenylthiazol-2-yl)thiazolidin-4-one		Antifungal	184
7-phenyl-5H-thiazolo[5,4-e][1,2,3,4]tetrazolo[5,1-c]pyrrolo[1,2-a][1,4]diazepine		Anticonvulsant Activities	185
(2-{[4-(2′-chlorophenyl)-thiazole-2-yl imino]methyl}phenoxy)acetic acid		Antimicrobial	186

186

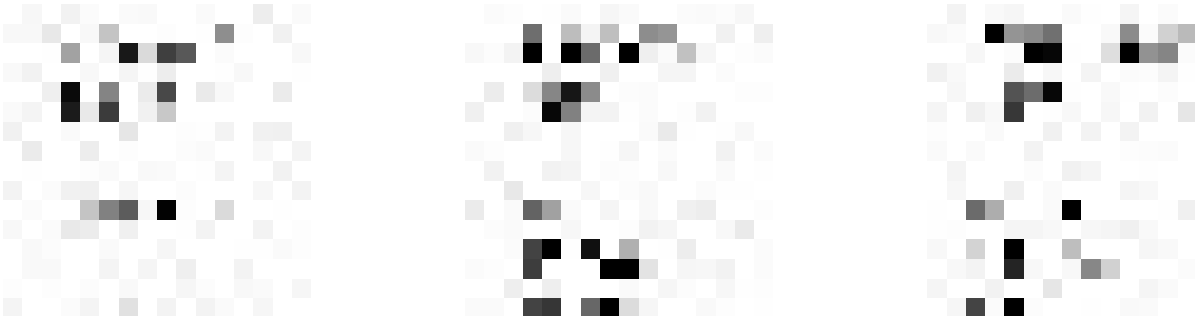
1-11 Oxazole [187]

Oxazole (1,3-Oxazole) contains an O-atom bonded as in furan, and also a pyridine-like N-atom The univalent radical is known as oxazolyl. The oxazole molecule is planar and its structure can be represented by a distorted pentagon



The differences in the bond lengths, especially between the bonds N/C-2 and N/C-4 indicate that the delocalization of the ^-electrons is affected by the heteroatoms. As in the case of furan, the structural formula with two ;π-bonds is a good representation of the electronic structure of the molecule

. The ionization energy of oxazole is 9.83 eV and its dipole moment is 1.5 D. The UV absorption and chemical shifts in the NMR spectra are as follows:



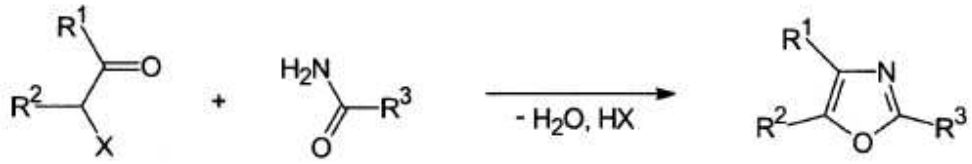
1-11-1 prepareation of oxazole

a-Acylamino ketones, esters or -amides are cyclodehydrated by H2SÜ4 or polyphosphoric acid to give oxazoles *(Robinson-Gabriel synthesis):*

α-Acyloxy ketones **,** obtainable from a-halo ketones and salts of carboxylic acids, form oxazoles on treatment with ammonia

:

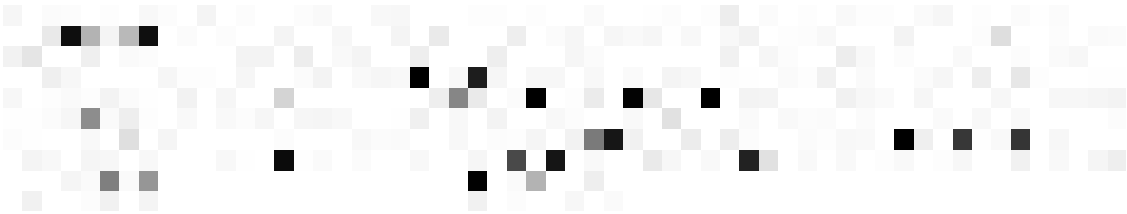
α-Halo and α -hydroxy ketones condense with acid amides via an O-alkylation to give oxazoles*(Blümlein-Lewy synthesis).* Formamide yields oxazoles unsubstituted in the 2-position, urea yields 2- aminooxazoles:



Oxazole syntheses employing isocyanides as starting materials are of considerable prepareative value. In the *van Leusen synthesis*, tosylmethyl isocyanide (TosMIC) reacts with aldehydes under base catalysis, e.g. in the presence of K2CO3. The primary products are 4,5-dihydro-l,3-oxazoles **12,** which are converted into oxazoles by elimination of sulfinic acid

α-Diazocarbonyl compounds undergo addition to nitriles with elimination of N2 in the presence of LEWIS acids or transition metal compounds [Cu(II), Pd(II), especially Rh(n)] as catalysts to give oxazoles This reaction is likely to proceed via intermediate formation of nitrile ylides 15 and their electrocyclic ring closure as 1,5-dipoles yielding the oxazole system

.



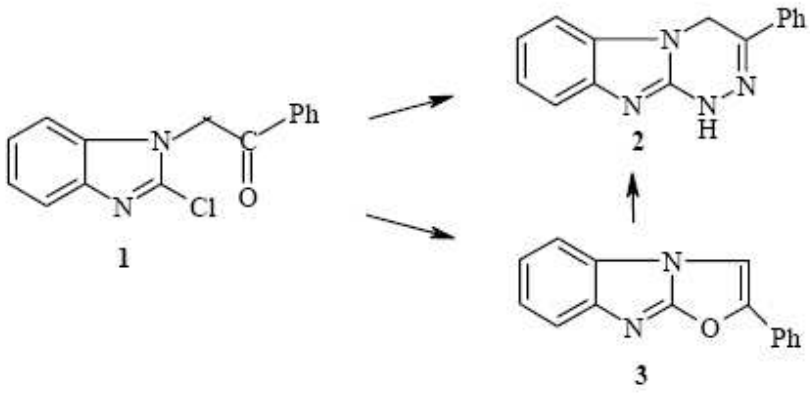
Vyatsheslav et, al[188] have prepare oxazole derivatives by adding Isonicotinoyl chloride to an ice-cooled 2-aminoethanone solution in DMF then the resulting mixture Amidoketone was heated for 15 min to 170-180

Josif et,al [189] have prepare oxazole derivatives by Acylaminoacylation of aromatic hydrocarbons (benzene, toluene, *meta*-xylene, mesitylene) with2-[4-benzenesulfonyl-(4-halophenyl)]-5-oxazolones in the presence of anhydrous aluminum chloride leads to 2-aza-1,4-diones **5** which cyclize under the action of phosphorus oxychloride yielding the corresponding 2-[4-(4-halobenzenesulphonyl)-phenyl]-5-aryloxazoles

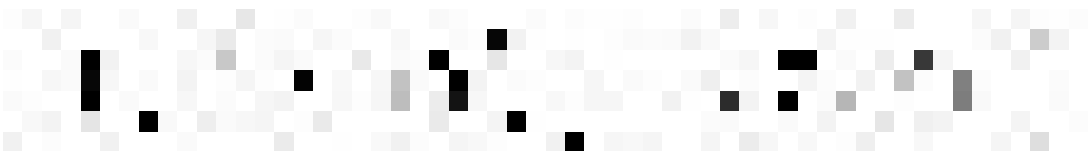
Alexander et,al [190] have prepare oxazole derivatives by dissolveding N-Phenacyl-2-pyridone in concentrated sulfuric acid and kept for 20-25 hours. Then 71% perchloric acid (2.5 mL, 25 mmol) was carefully added to the mixture and after stirring 10-15 min

X= NO_2 CH_3 Cl

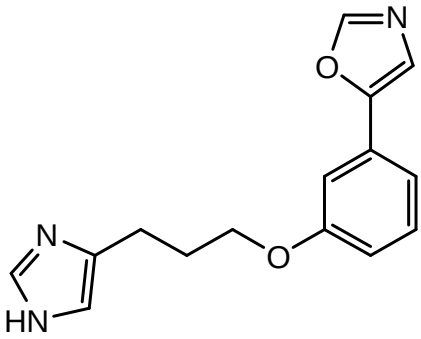
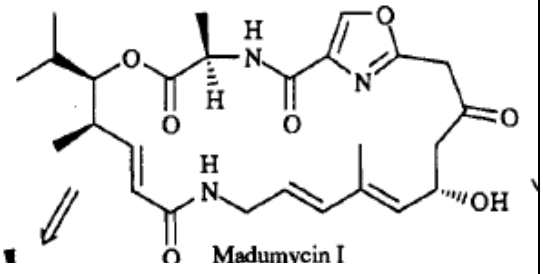
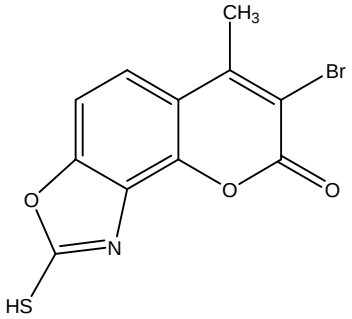
Povstyanoi [191] obtained oxazole derivatives in 76% yield by heating ketone with sodium benzoate in DMF at reflux for 2 h.



Christopher et,al [192] have prepare the below compound by the rhodium(I1) catalysed addition of diazocarbonyl compounds to nitriles,



The uses of oxazole

Name	Structure	Uses	Ref.
4-(3-(3-(oxazol-5-yl)phenoxy)propyl)-1H-imidazole		selective histamine H - receptor antagonists	193
Madumvcin		Antimicrobial	194
7-bromo-2-mercapto-6-methyl-8H-chromeno[8,7-d]oxazol-8-one		antibacterial	195

Republic of Iraq
Ministry of higher education
and scientific research
Al-Nahrine university
College of science
Department of Chemistry

Synthesis and Characterization of New Heterocyclic Compounds Derived from Some Heterocyclic Amines and Evaluating of Biological Activity of Some Compounds

A Thesis submitted to the College of Science Al-Nahrin University
in partial fulfillment of the requirements for the
Degree of Doctor of Philosophy in Chemistry

By
Ahmed Thamer Salem

B. sc. Baghdad university 2000
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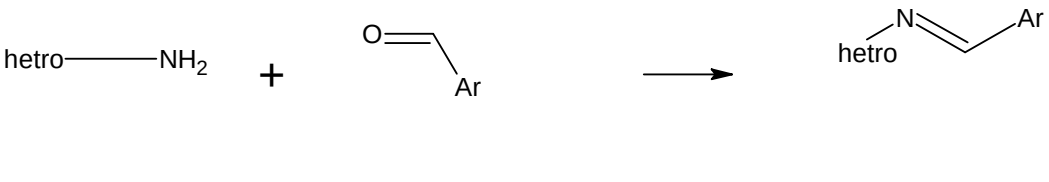
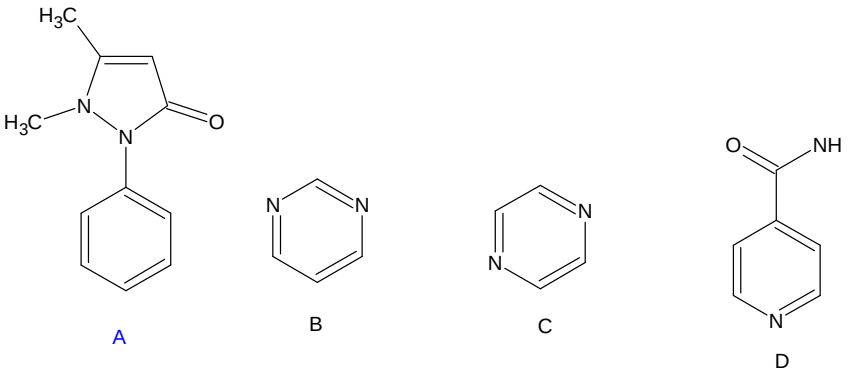
2008 1429

Chapter three

Result & Discussion

3-1 Schiff bases preparation





The Schiff bases are prepared by the reaction of the heterocyclic amines with different aromatic aldehyde in absolute ethanol in the presence of glacial acetic acid as catalyst the products were characterized by the TLC and by the FTIR spectrum which show by the stretching vibration the absorption of the doublet of NH_2 of the amine in the region 3450-and3220 cm^{-1} for symmetric and asymmetric stretching vibration respectively and the disappearance of C=O band of the aldehydes in 1660-1740 cm^{-1} and appearance of the stretching vibration of C=N bond in region 1580-1630 cm^{-1}

The proposed mechanism for this reaction

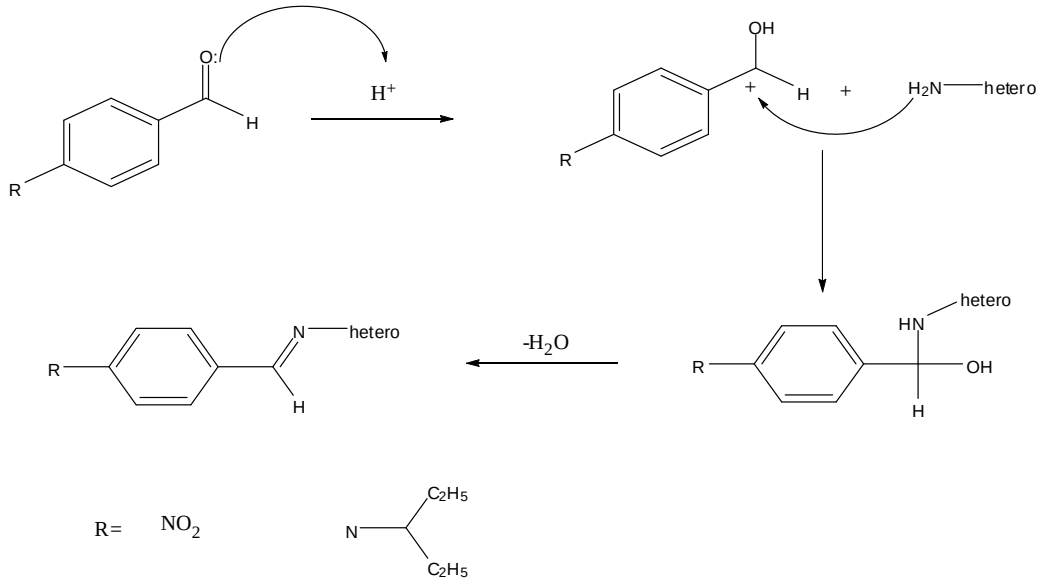


Table (3-1) IR spectrum data for schiff bases

Comp No.	Fig. No.	ν C-H aromatic	ν C=N schiff	υ C=C	NO_2	C=H aromatic OOP
$1A_1$	3-5	3070	1606	1583-1483	1542-1367	821
$1A_2$	3-6	3090	1600	1598-1437		813
$1B_1$	3-7	3100	1599	1570-1490	1558-1330	854
$1B_2$	3-8	3120	1600	1590-1440		800
$1C_1$	3-9	3120	1600	1580-1450	1530-1350	800
$1C_2$	3-10	3120	1620	1580-1480		825
$1D_1$	3-11	3120	1600	1560-1430	1540-1365	810
$1D_2$	3-12	3080	1610	1580-1470		840

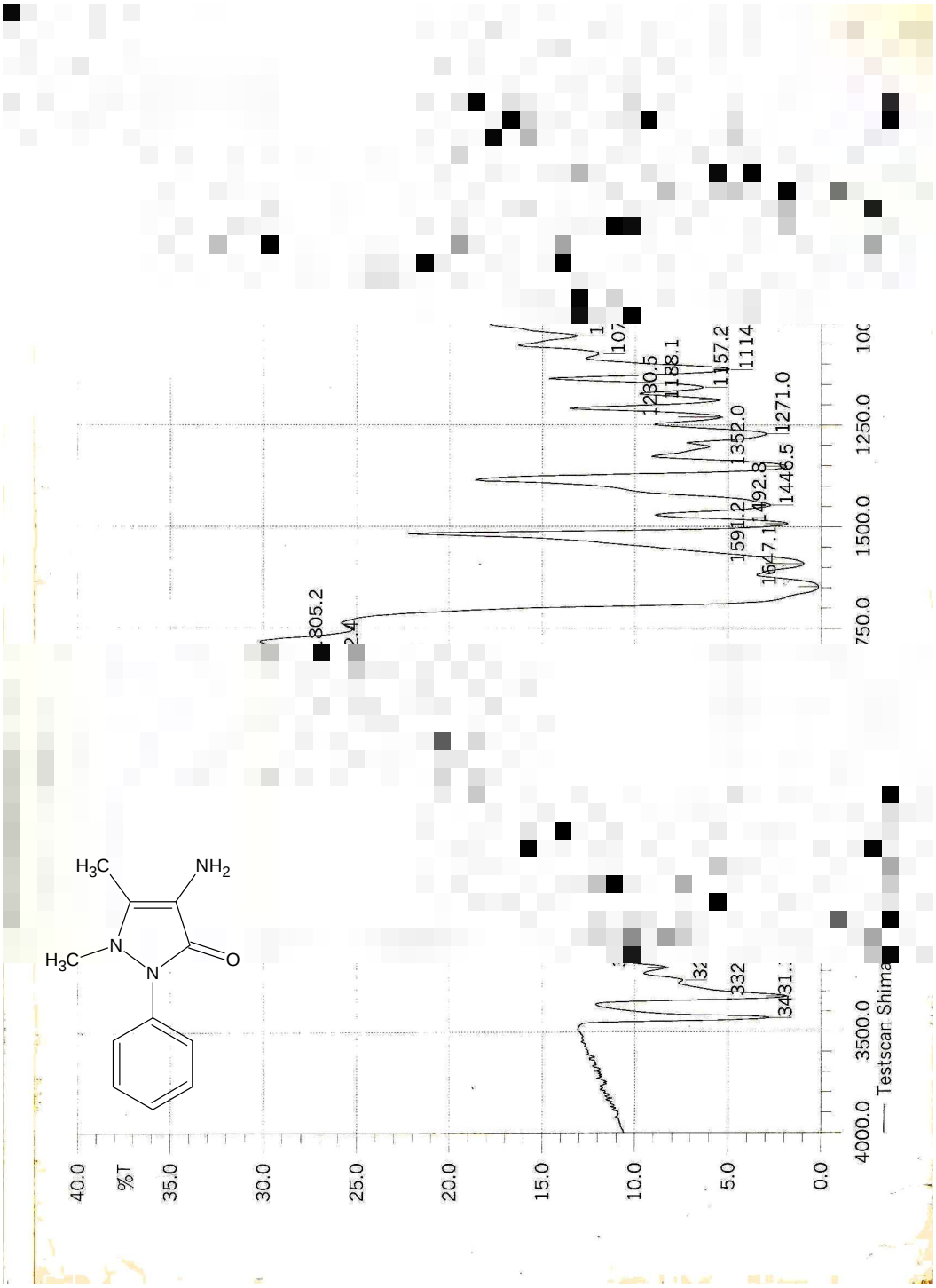
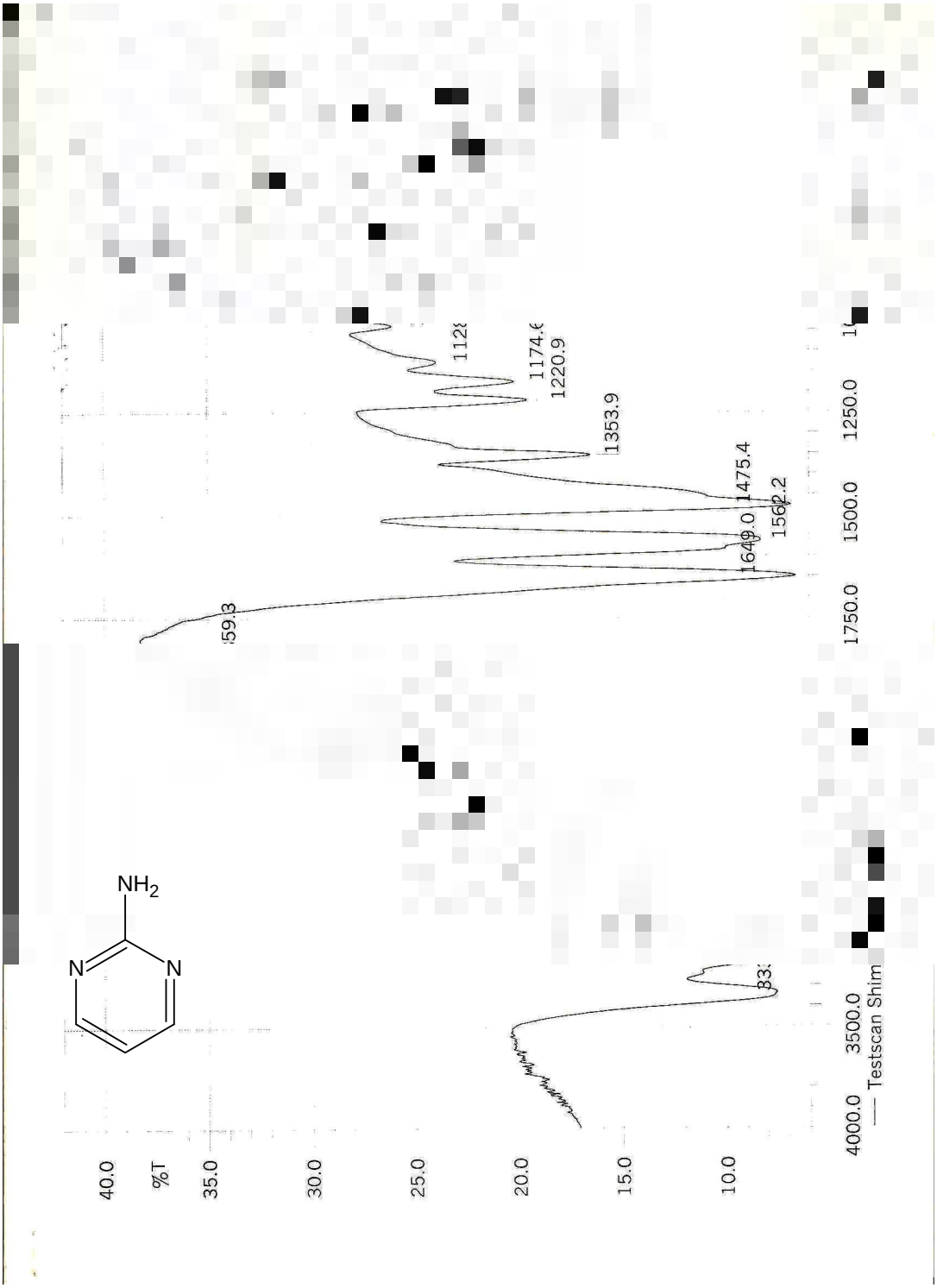


Figure (3-1) FTIR of 4-aminoantipyrine (A 0)



Figure(3-2) FTIR spectrum of 2-aminopyrimidine (B 0)

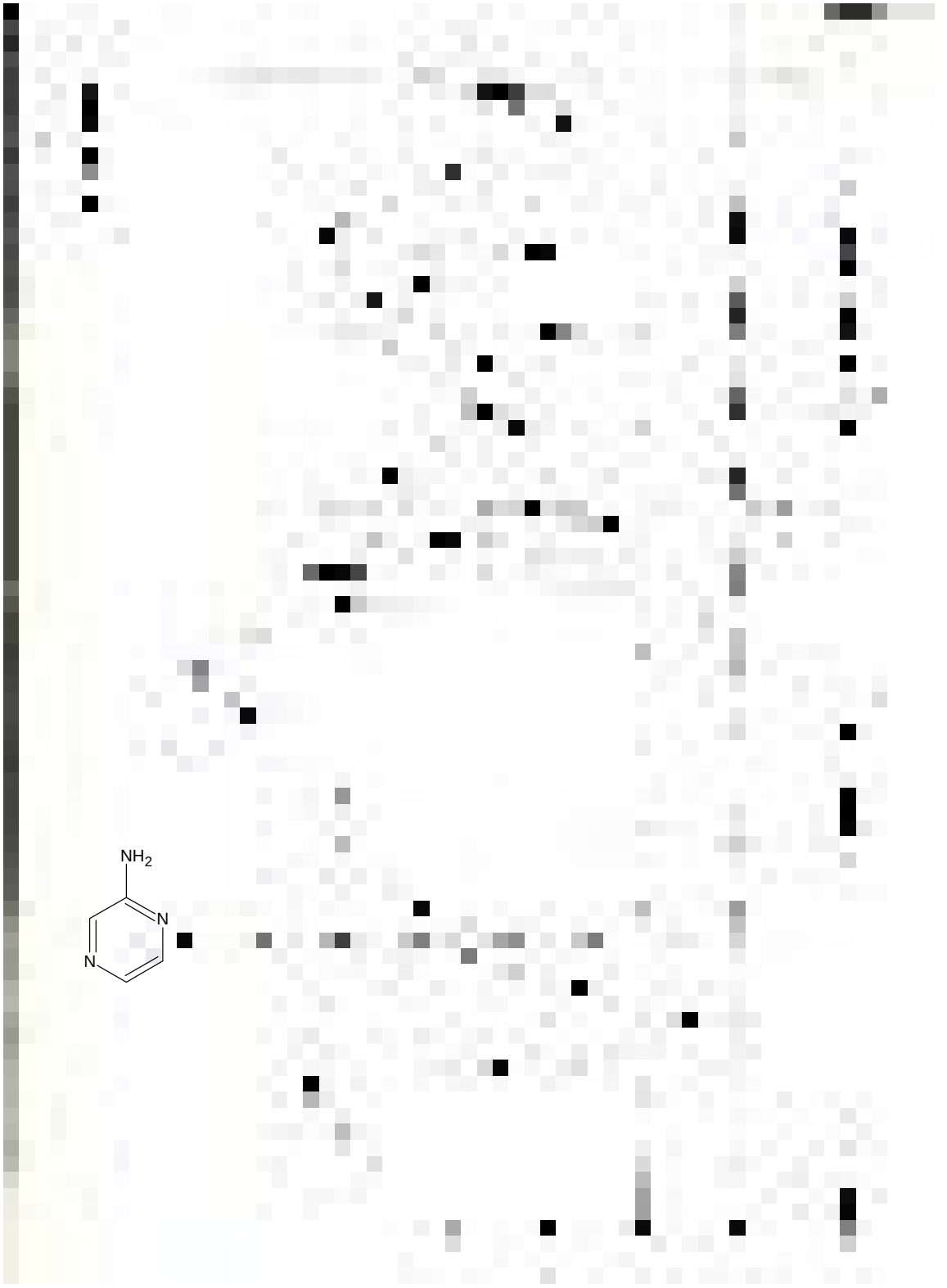
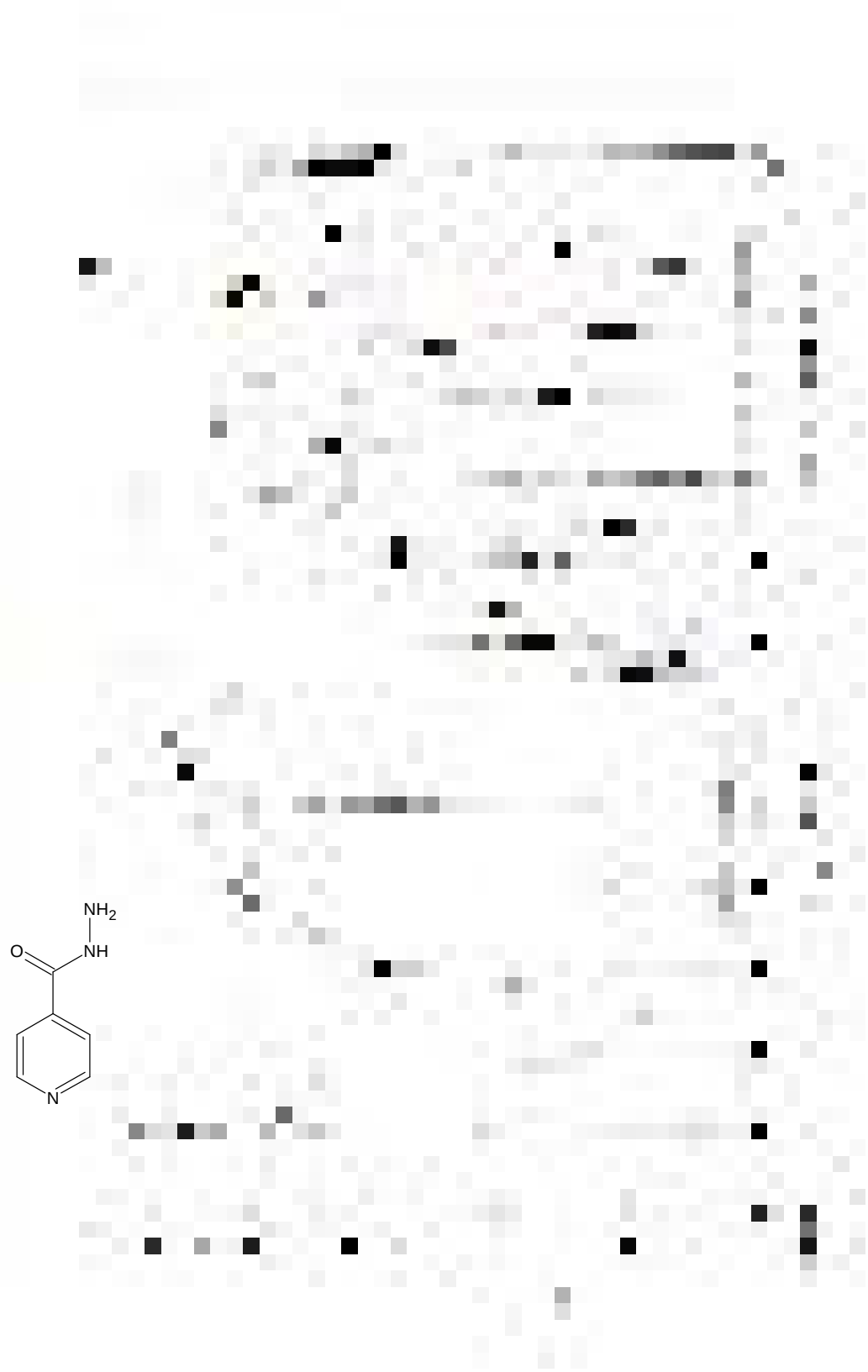


Figure (3-3) FTIR spectrum of 2-aminopyrazine (C 0)



Figur(3-4) FTIR spectrumum of isoneazide (d 0)

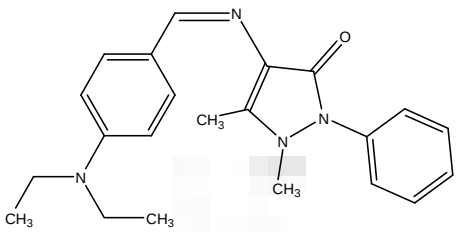


Figure (3-5) FTIR spectrum of compound ($1A_1$)

(Z)-4-(4-(diethylamino)benzylideneamino)-2,3-dimethyl-1-phenyl-1,2-dihydropyrazol-5-one

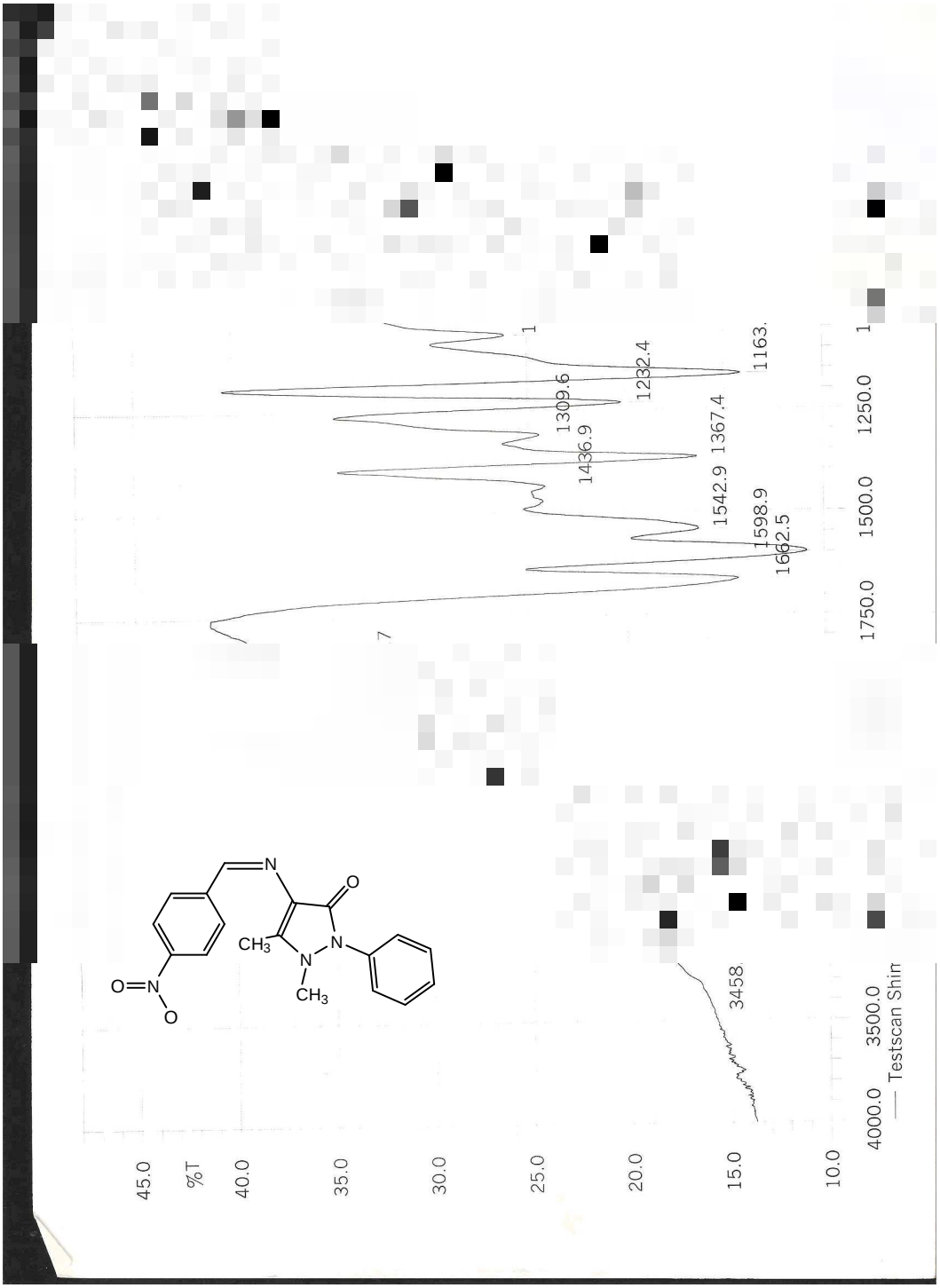


Figure (3-6) FTIR spectrum of compound ($1A_2$)

(Z)-4-(4-nitrobenzylideneamino)-2,3-dimethyl-1-phenyl-1,2-dihydropyrazol-5-one

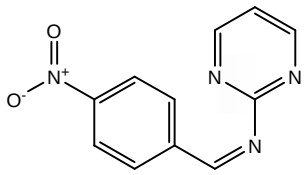


Figure (3-7) FTIR spectrum of compound ($1B_1$)

(Z)-N-(4-nitrobenzylidene)pyrimidin-2-amine

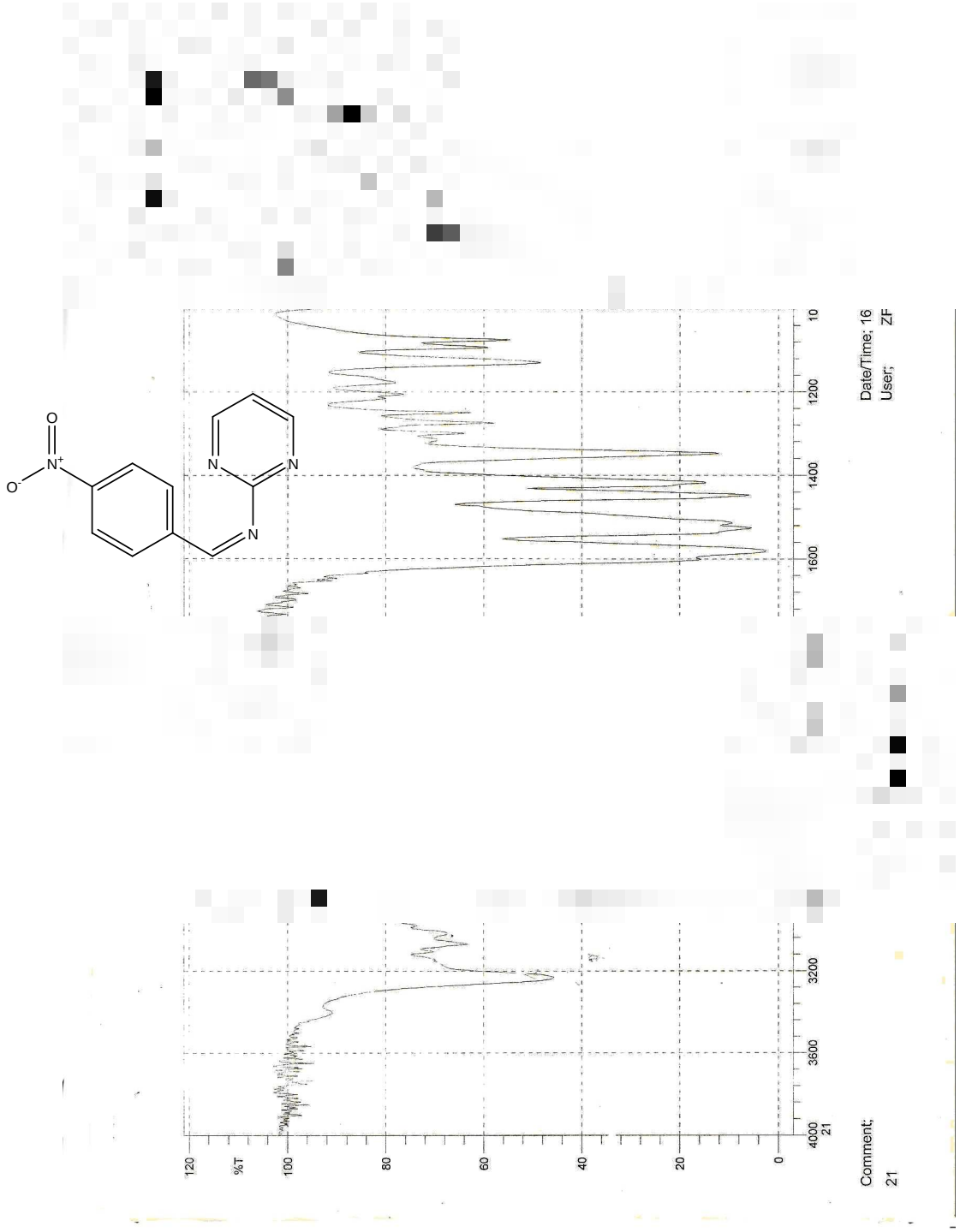


Figure (3-8) FTIR spectrum of compound ($1B_2$)

(Z)-N-(4-nitrobenzylidene)pyrimidin-2-amine

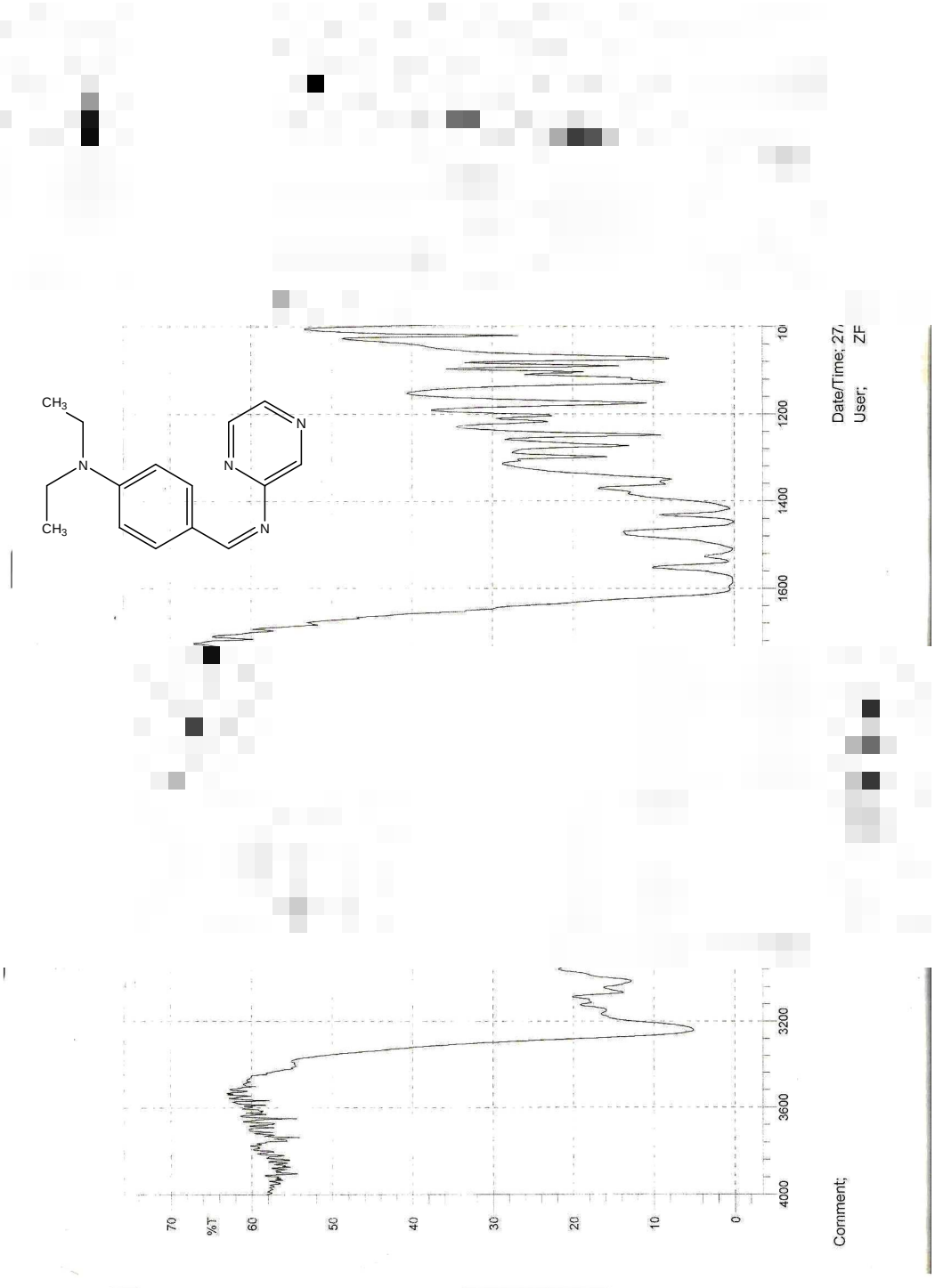


Figure (3-9) FTIR spectrum of compound ($1C_1$)

(Z)-N-(4-(diethylamino)benzylidene)pyrazin-2-amine

Figure (3-10) FTIR spectrum of compound ($1C_2$)

(Z)-N-(4-nitrobenzylidene)pyrazin-2-amine

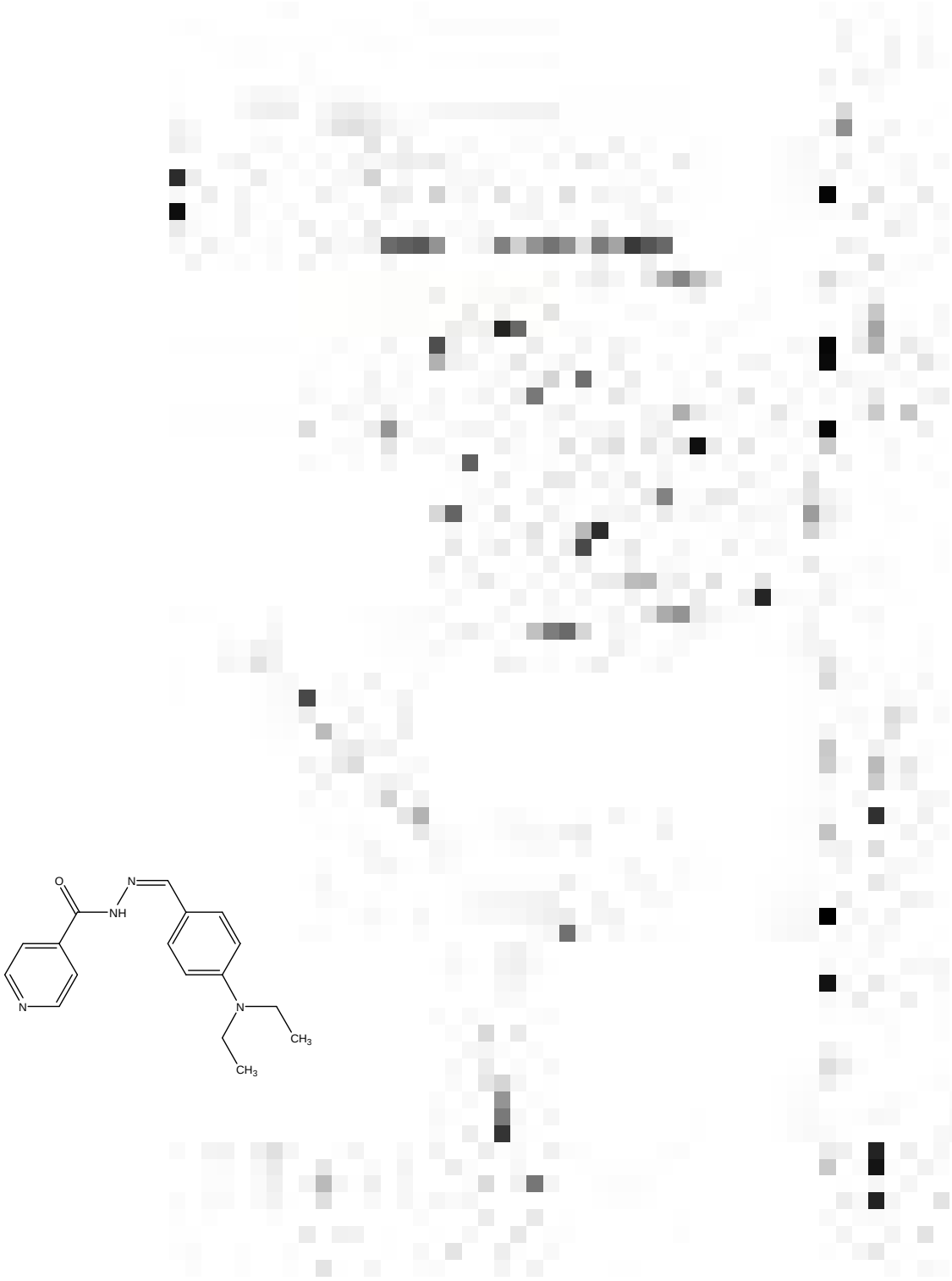


Figure (3-11) FTIR spectrum of compound ($1D_1$)

(Z)-N'-(4-(diethylamino)benzylidene)isonicotinohydrazide

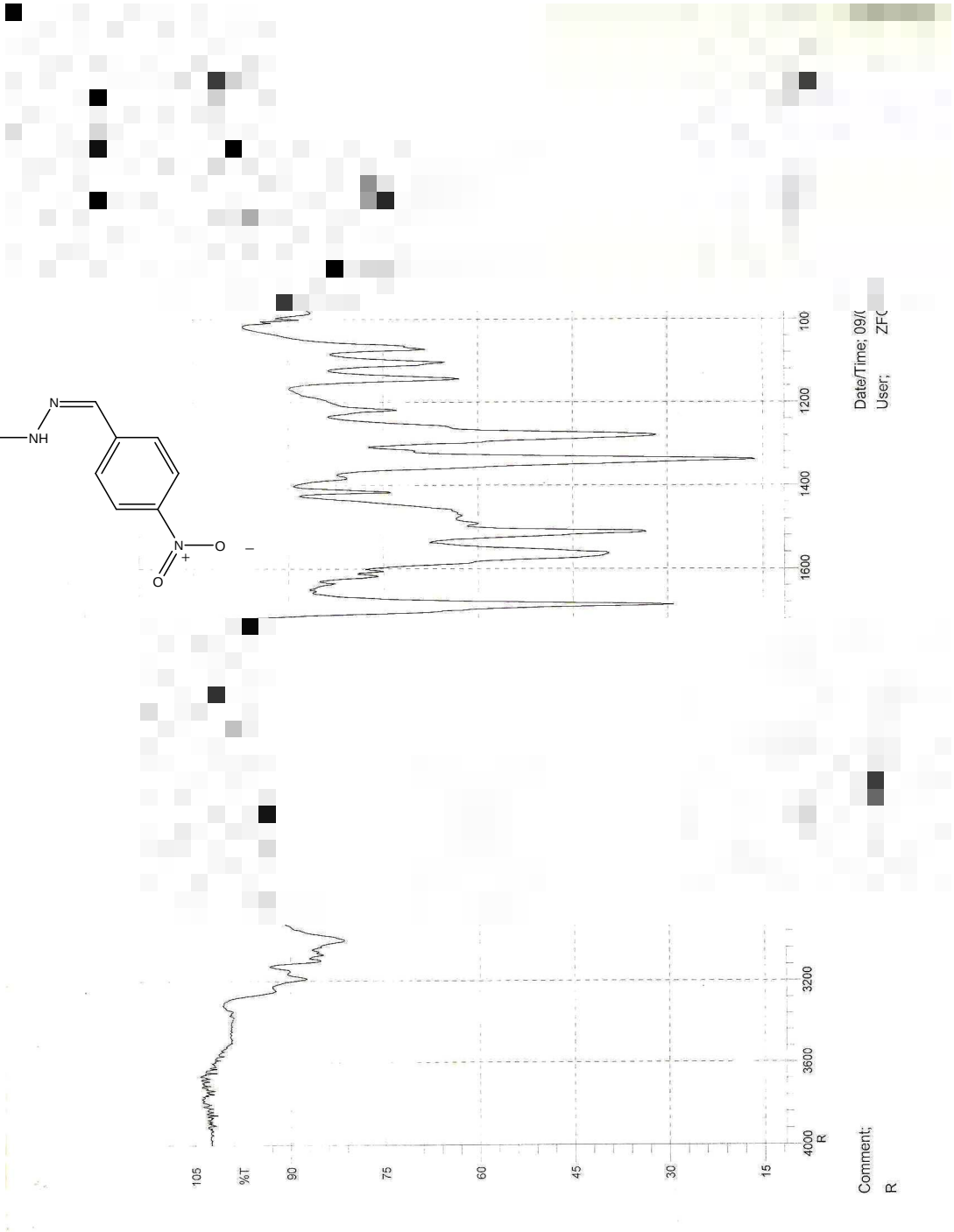
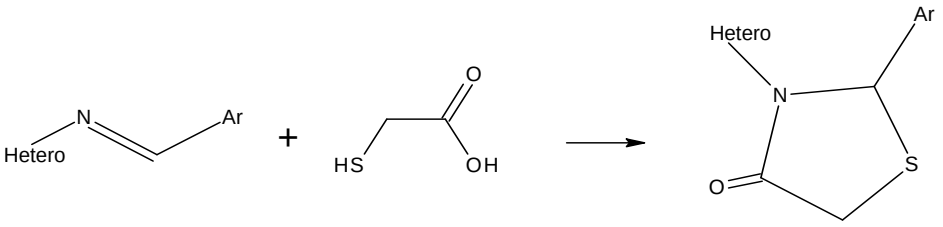


Figure (3-12) FTIR spectrum of compound ($1D_2$)

(Z)-N'-(4-nitrobenzylidene)isonicotinohydrazide

3-2 2-aryl-3-(hetero-2-yl)thiazolidin-4-one



Thazolidinone derivatives prepared by the reaction of Schiff bases and mercaptocetic acid in dry benzene the products were identified by the FTIR spectrum by the appearance of carbonyl group of the thiozolidinone in 1660 cm^{-1} and disappearance of the C=N group in 1600cm-1 and the disappearance of O-H broad band stretching vibration at 3500-3000cm^{-1} of mercaptocetic acid The proposed mechanism of this reaction

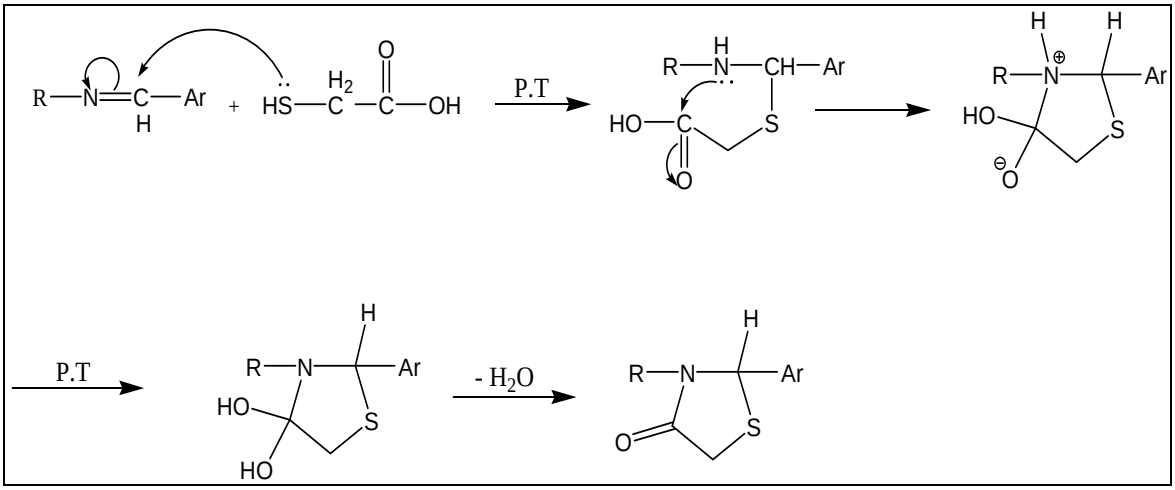


Table (3-2) the stretching vibration of thiazolidinone

Compound No	C=H aromatic	C=O	C=C aromatic	CH_2
3A	3100	1691	1602-1452	2925-2850
3B	3100	1682	1600-1448	2918-2804
3C	3100	1700	1600-1450	2930-2800
3D	3100	1690	1580-1440	2940-2840

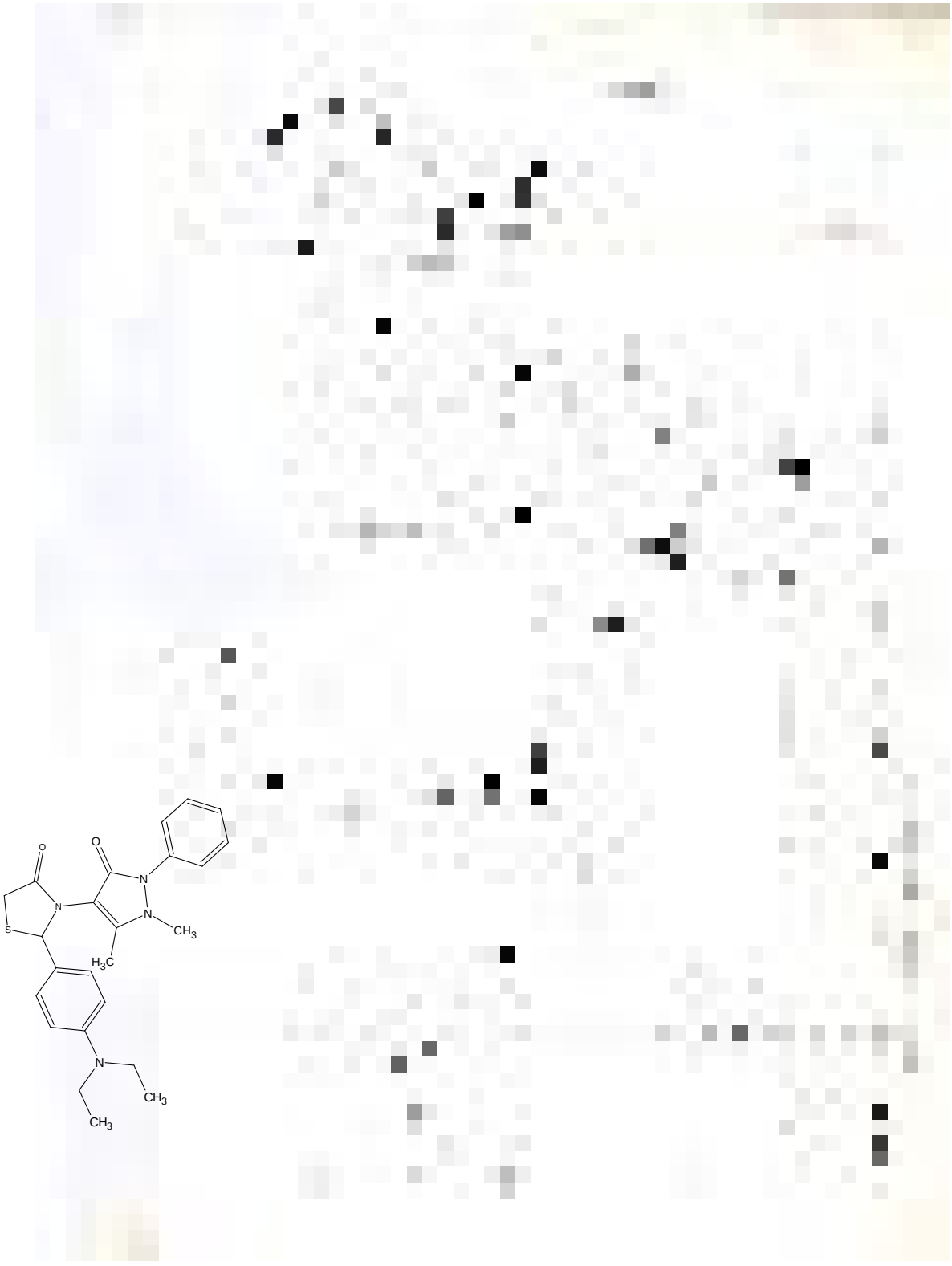
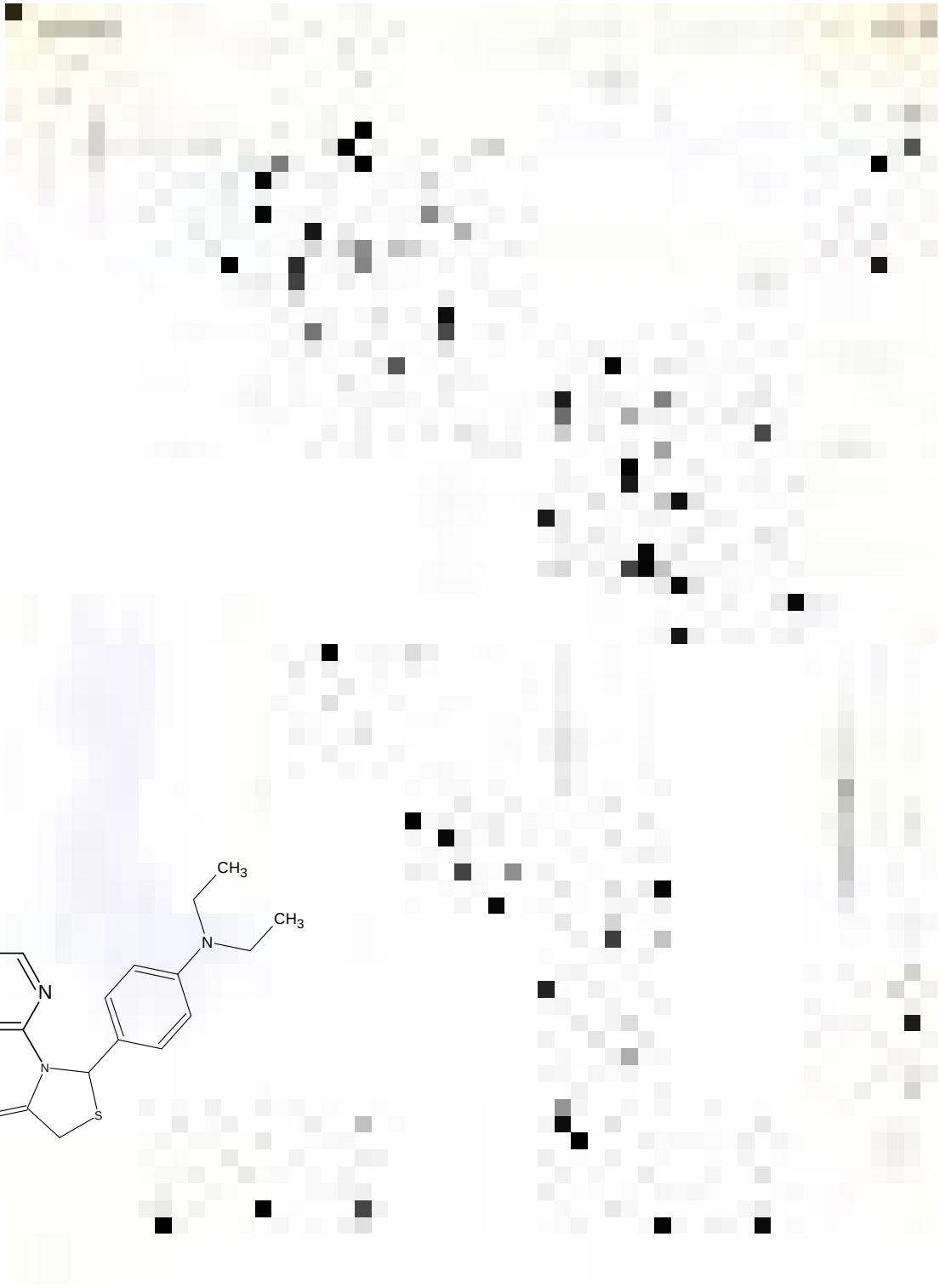


Figure (3-13) FTIR spectrum of compound (2A)

2-[4-(diethylamino)phenyl]-3antipyrin-2-yl-1,3-thiazolidin-4-one



oFigure (3-14) FTIR spectrum of compound (2B)

2-[4-(diethylamino)phenyl]-3-pyrimidin-2-yl-1,3-thiazolidin-4-one

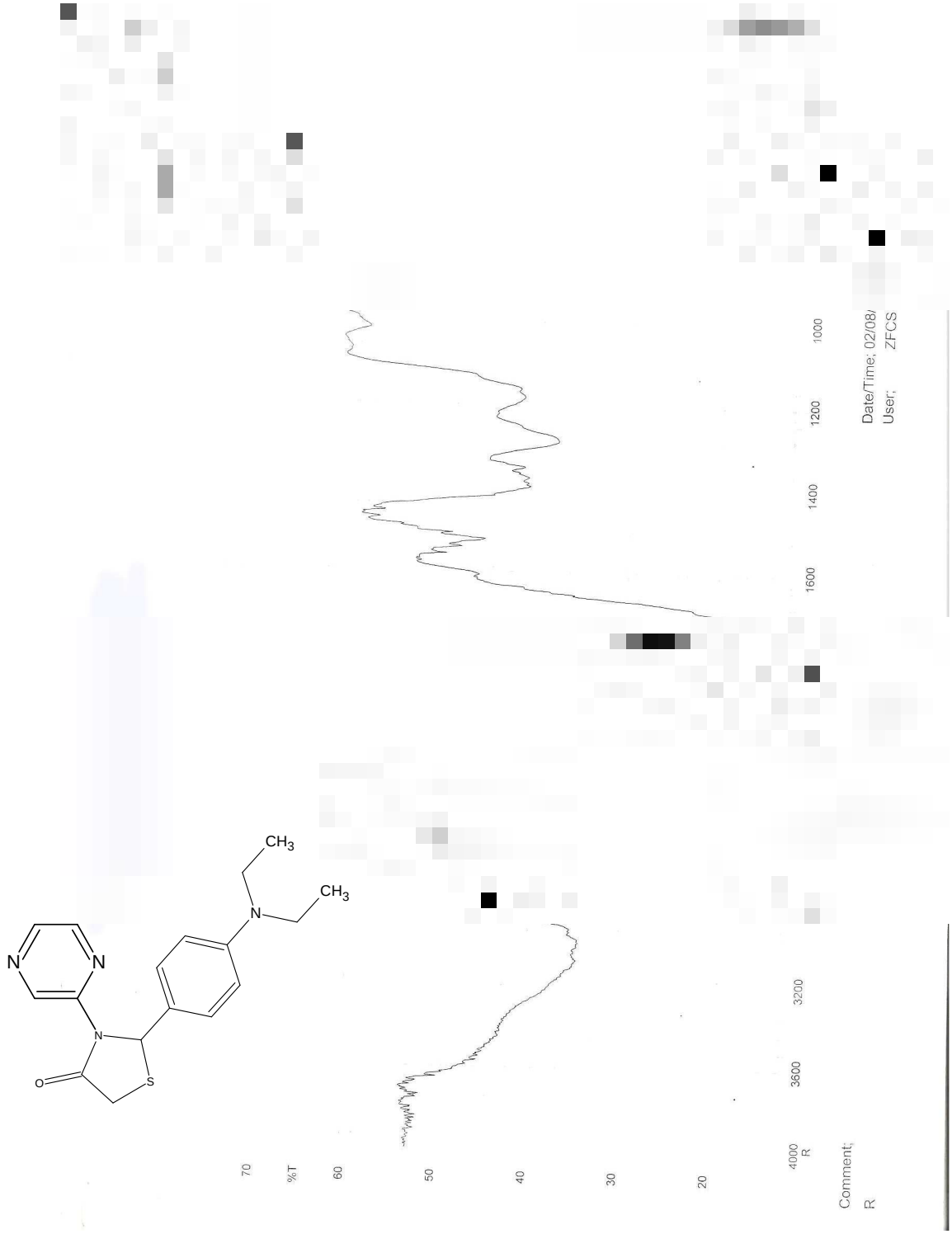


Figure (3-15) FTIR spectrum of compound (2C)

2-[4-(diethylamino)phenyl]-3-pyrazin-2-yl-1,3-thiazolidin-4-one

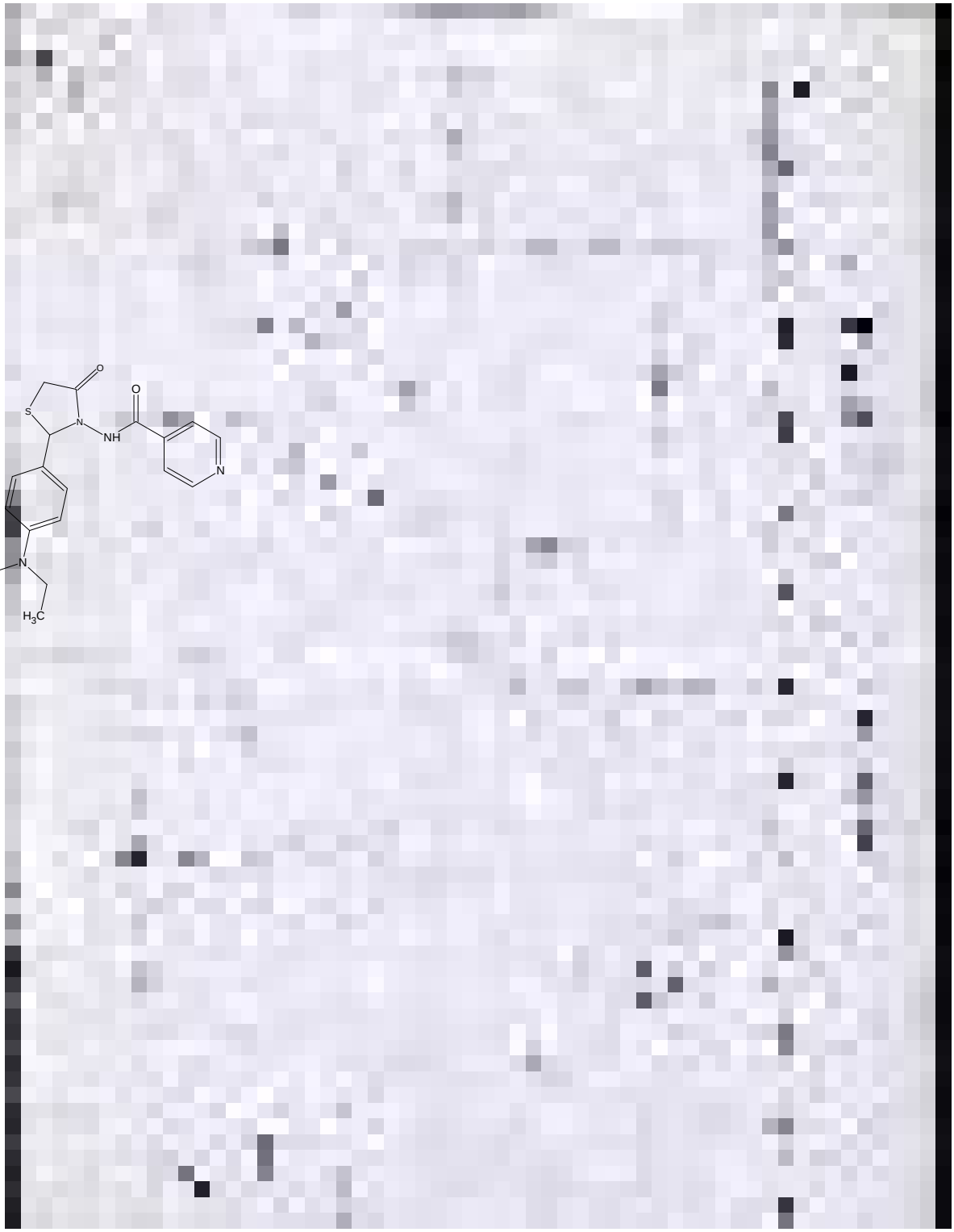
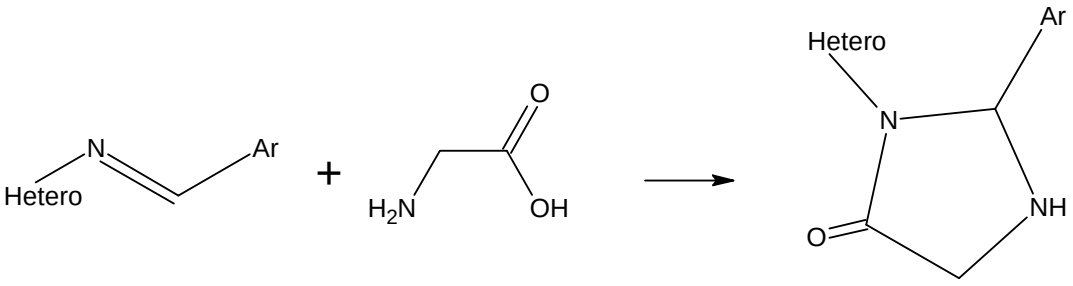


Figure (3-16) FTIR spectrum of compound (2D)

N-{2-[4-(diethylamino)phenyl]-4-oxo-1,3-thiazolidin-3-yl}isonicotinamide

3-3 2-aryl-3-(hetero-2-yl)imidazolidin-4-one



Imidazolidine derivatives prepared by the heating of Schiff bases derivatives with glycine(α-amino acetic acid) in THF the product were identified by the FTIR spectrum which show the appearance of NH vibration in 3320 cm^{-1} and the disappearance of C=N band in 1600cm^{-1}.

The product s are also identified by the HNMR the duplet (7.9)ppm for Ha and Hb protons at appears duplet at 8.8ppm Hc proton appear singlet at 2.45ppm while He,Hd appeared at 6.2,6.5 ppm respectively .

C^{13}NMR show singlate at 167.5 for C=O ,150 and 140 for C=N and at 122.3 (C-H) the aromatic carbon appear at 127 and 133 ppm.

the proposed mechanism of this reaction

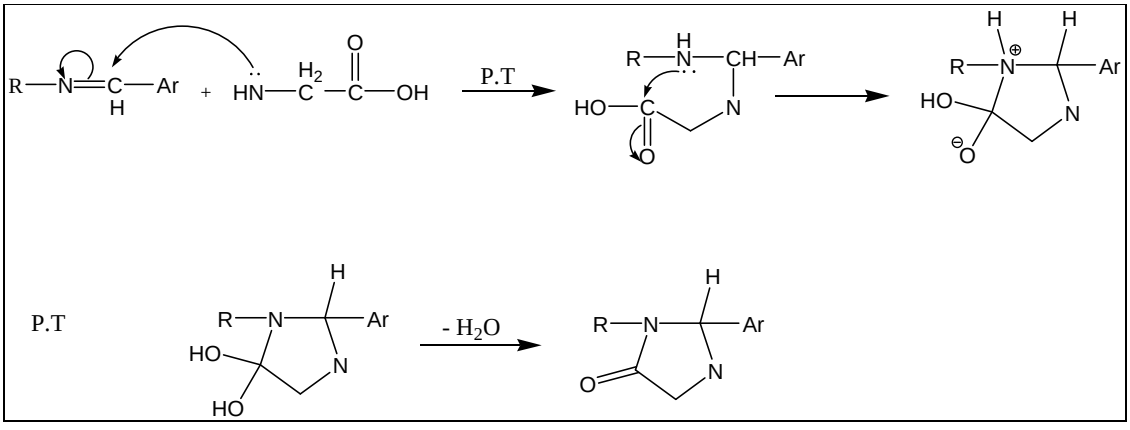


Table (3-3) the IR spectral data of imidazolidine derivatives ($3A_1$-$3D_2$)

Comp No.	CH_2	ν N- H imidazole	ν C=O	C=C aromatic
$3A_1$	2933-2846	3228	1708	1593-1448
$3A_2$	2925-2848	3396	1705	1580-1434
$3B_1$	2925-2830	3419	1687	1581-1398
$3B_2$	29302840	3398	1709	1600-1440
$3C_1$	2940-2850	3280	1680	1580-1440
$3C_2$	2950-2830	3200	1700	1580-1440
$3D_1$	2830-2960	3200	1670	1590-1410
$3D_2$	2940-2860	3280	1700	1580-1400

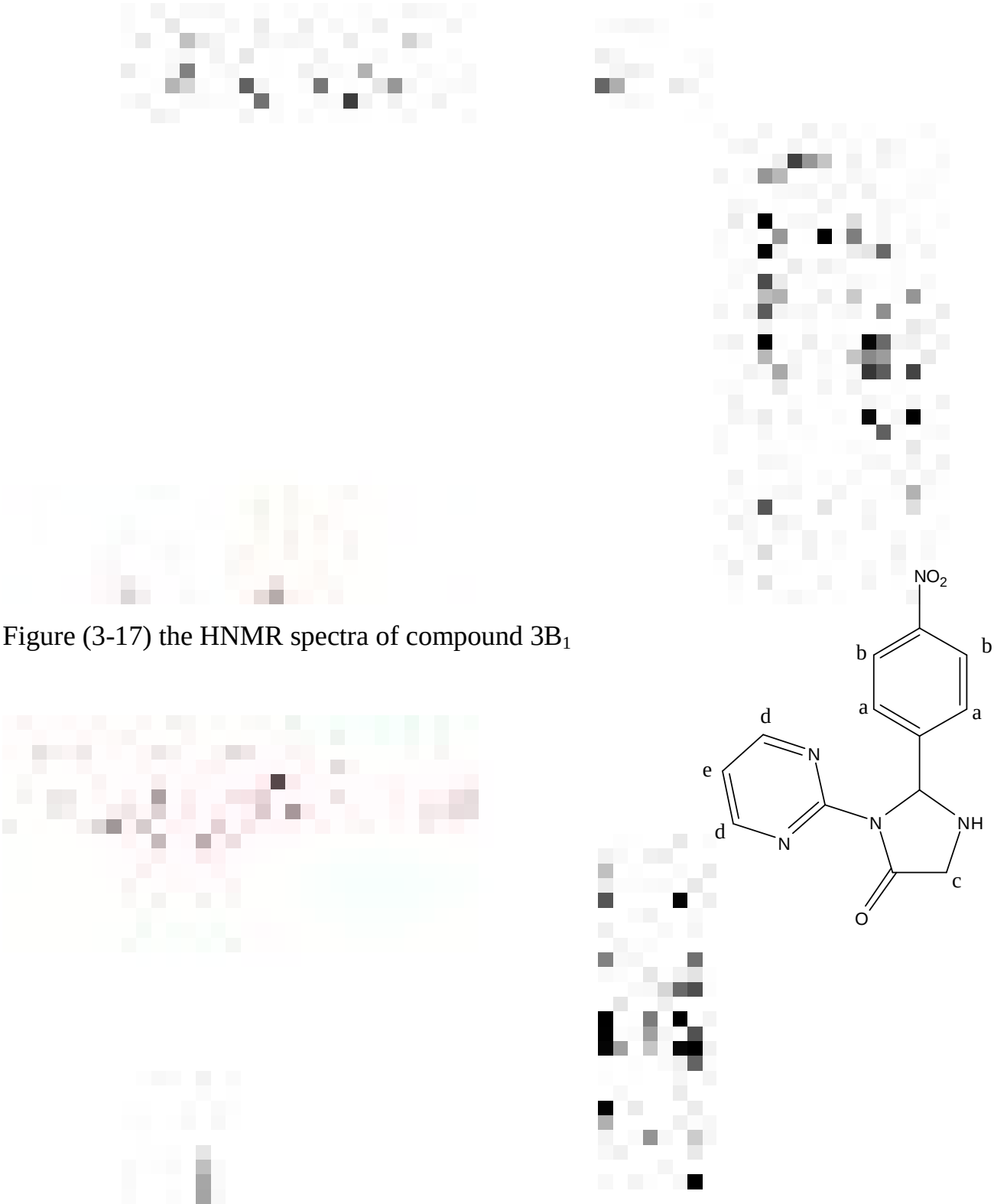


Figure (3-17) the HNMR spectra of compound $3B_1$

Figure (3-18) the C^{13}NMR spectra of compound $3B_1$

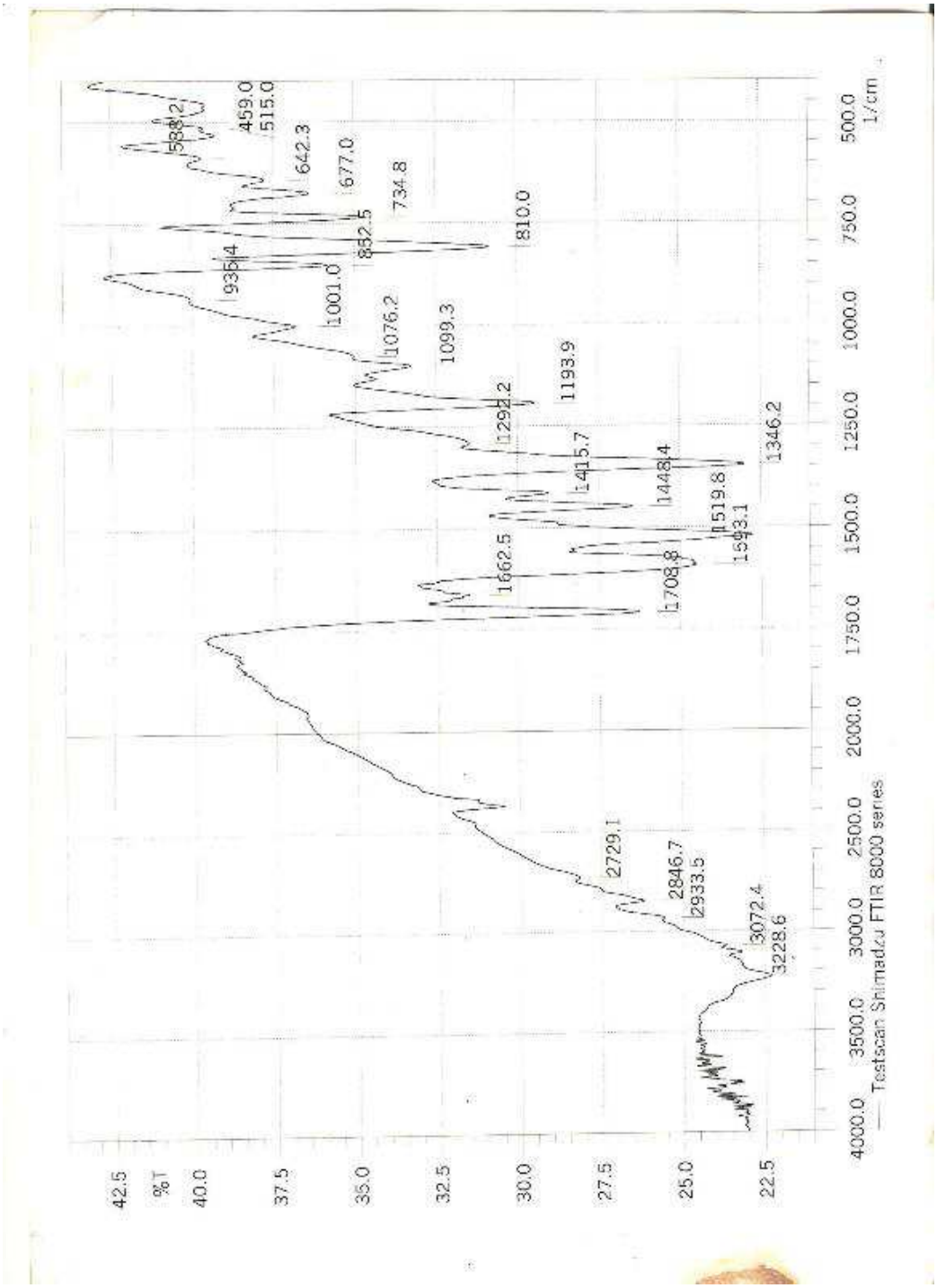


Figure (3-19) FTIR spectrum of compound ($3A_1$)

1,5-dimethyl-4-[2-(diethyl amino)-5-oxoimidazolidin-1-yl]-2-phenyl-1,2-dihydro-3H-pyrazol-3-one

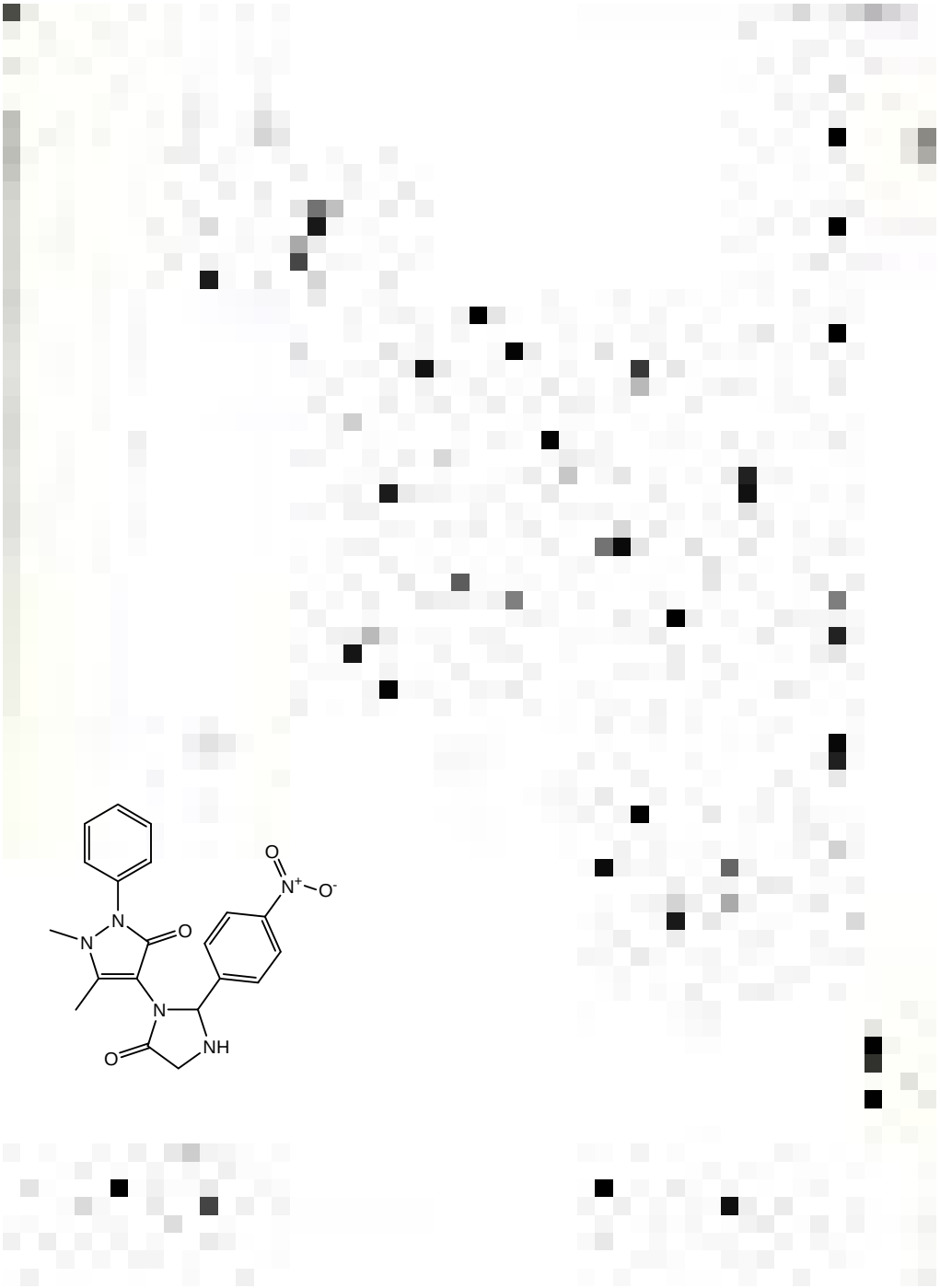


Figure (3-20) FTIR spectrum of compound ($3A_2$)
1,5-dimethyl-4-[2-(4-nitrophenyl)-5-oxoimidazolidin-1-yl]-2-phenyl-1,2-dihydro-3H-pyrazol-3-one .

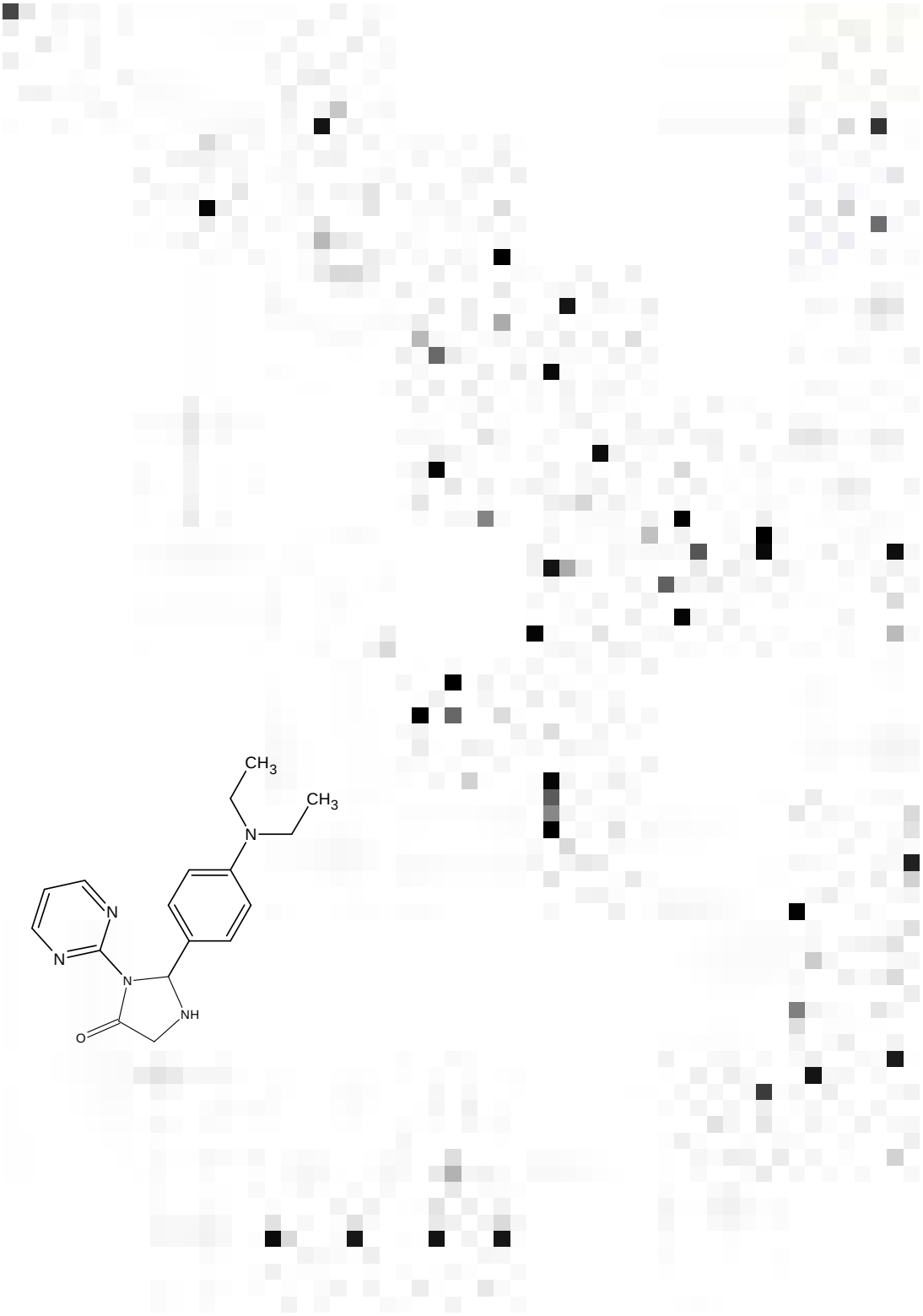


Figure (3-21) FTIR spectrum of compound ($3B_1$)

2-[4-(diethylamino)phenyl]-3-pyrimidin-2-ylimidazolidin-4-one

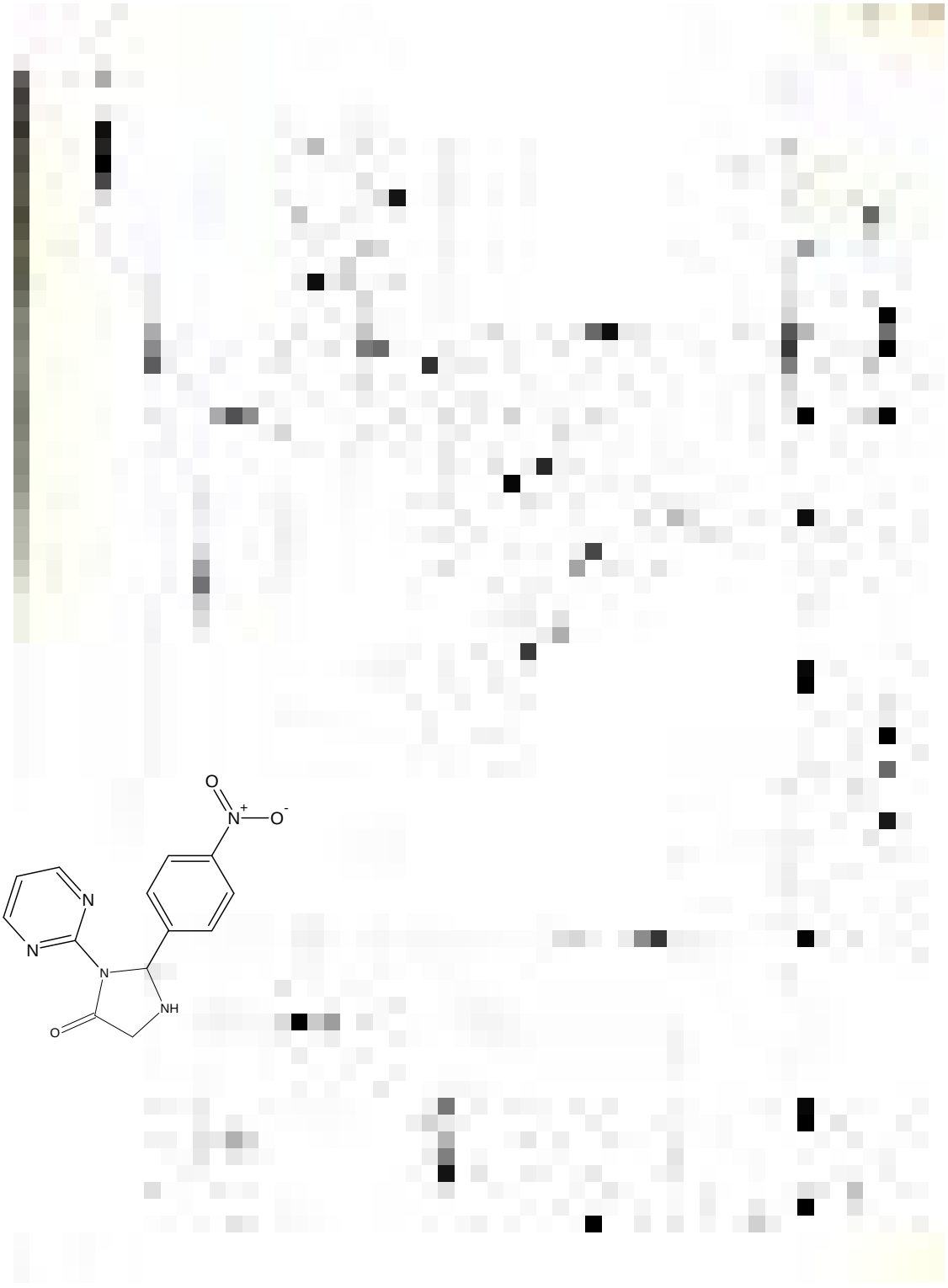


Figure (3-22) FTIR spectrum of compound ($3B_2$)

2-(4-nitrophenyl)-3-pyrimidin-2-ylimidazolidin-4-one

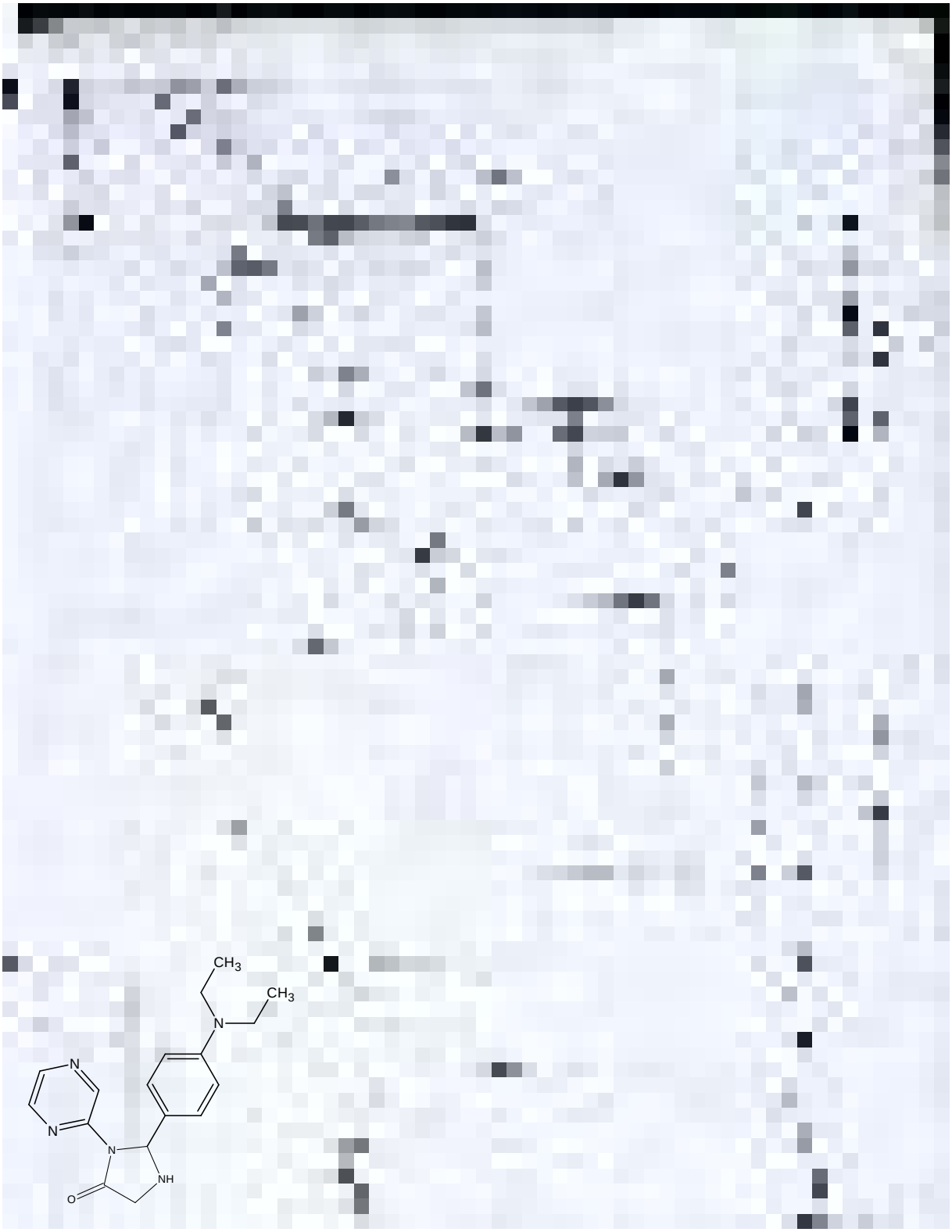


Figure (3-23) FTIR spectrum of compound ($3C_1$)

2-[4-(diethylamino)phenyl]-3-pyrazin-2-ylimidazolidin-4-one

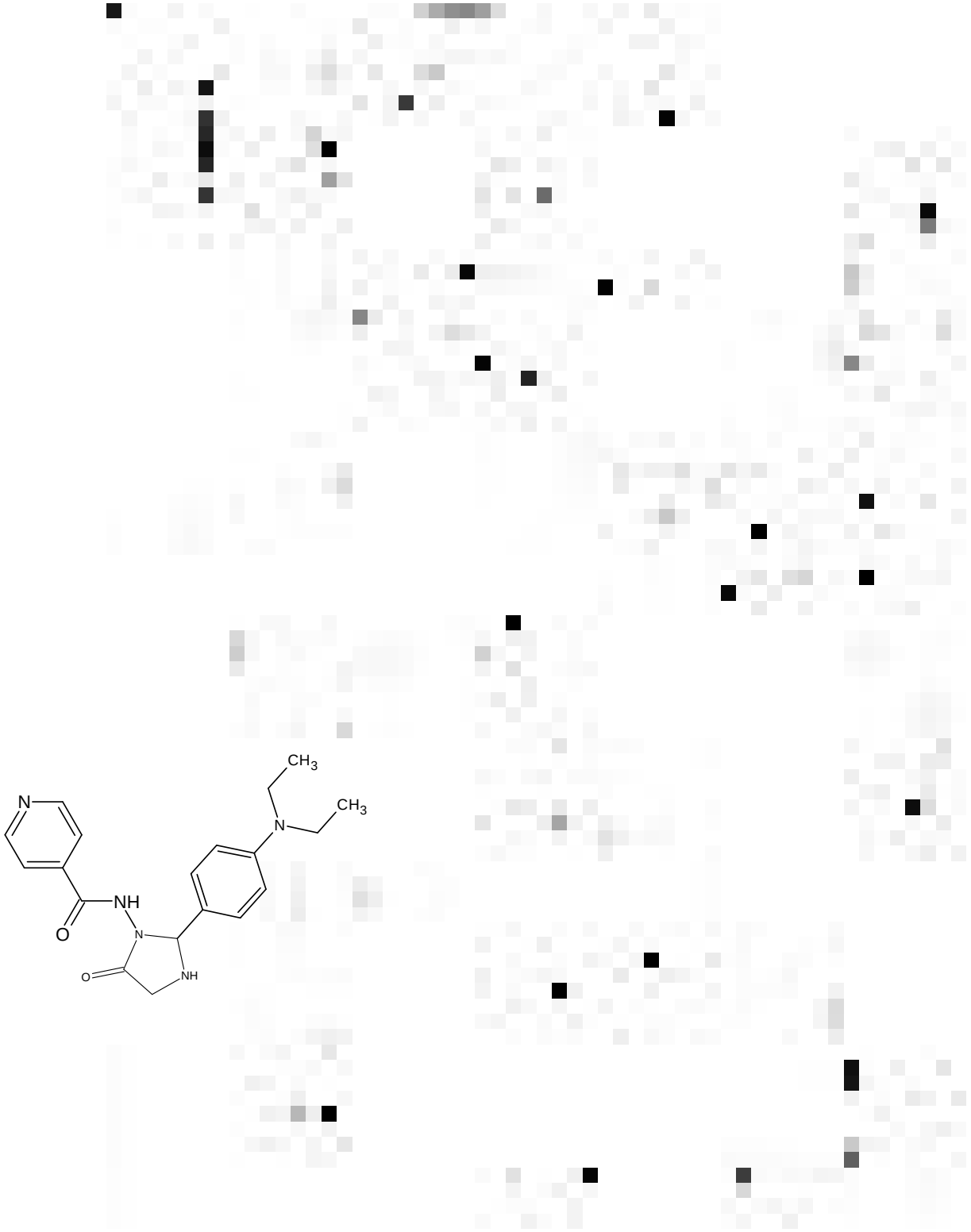


Figure (3-24) FTIR spectrum of compound ($3C_2$)

2-(4-nitrophenyl)-3-pyrazin-2-ylimidazolidin-4-one

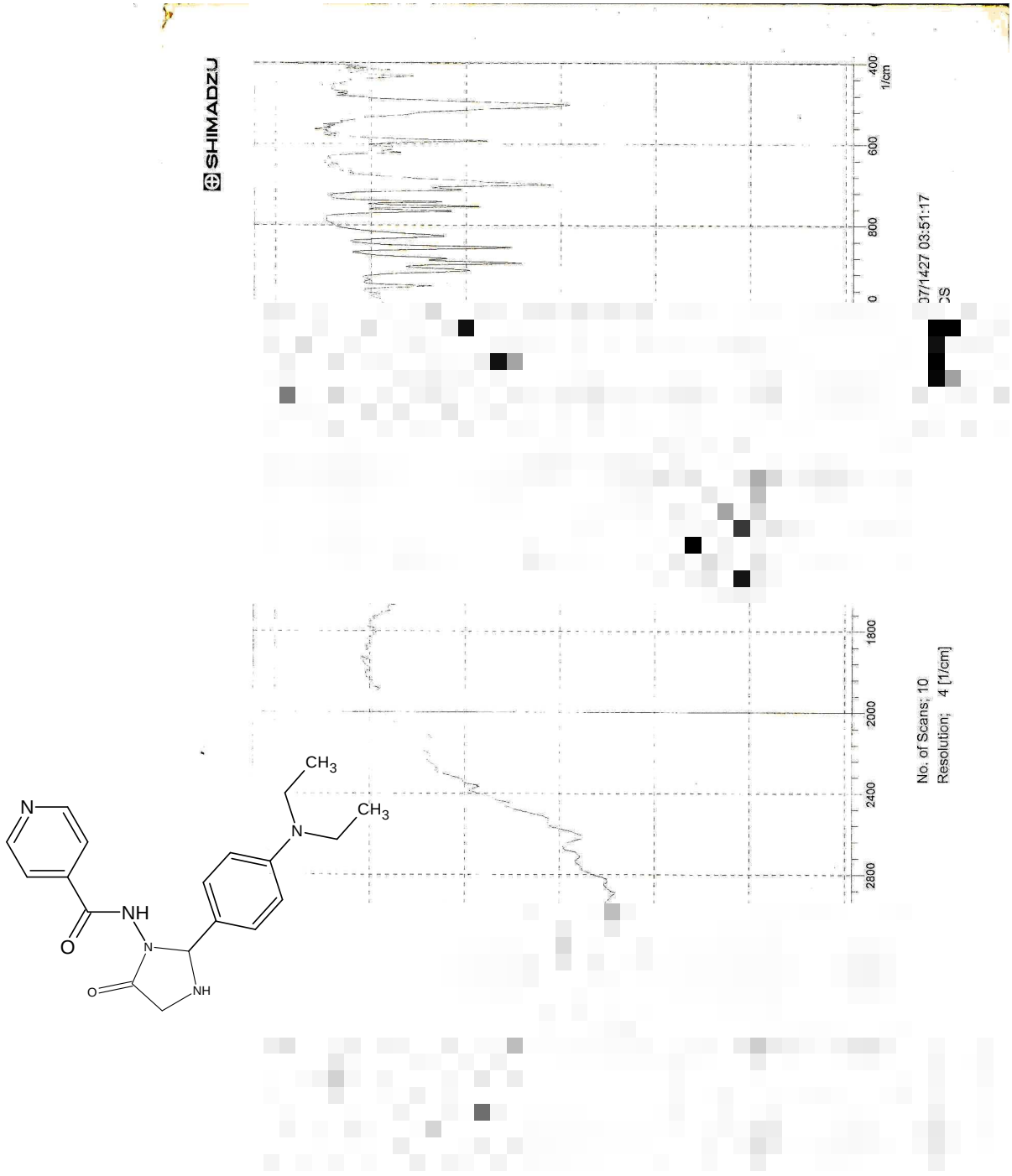


Figure (3-25) FTIR spectrum of compound ($3D_1$)

N-{2-[4-(diethylamino)phenyl]-5-oxoimidazolidin-1-yl}isonicotinamide

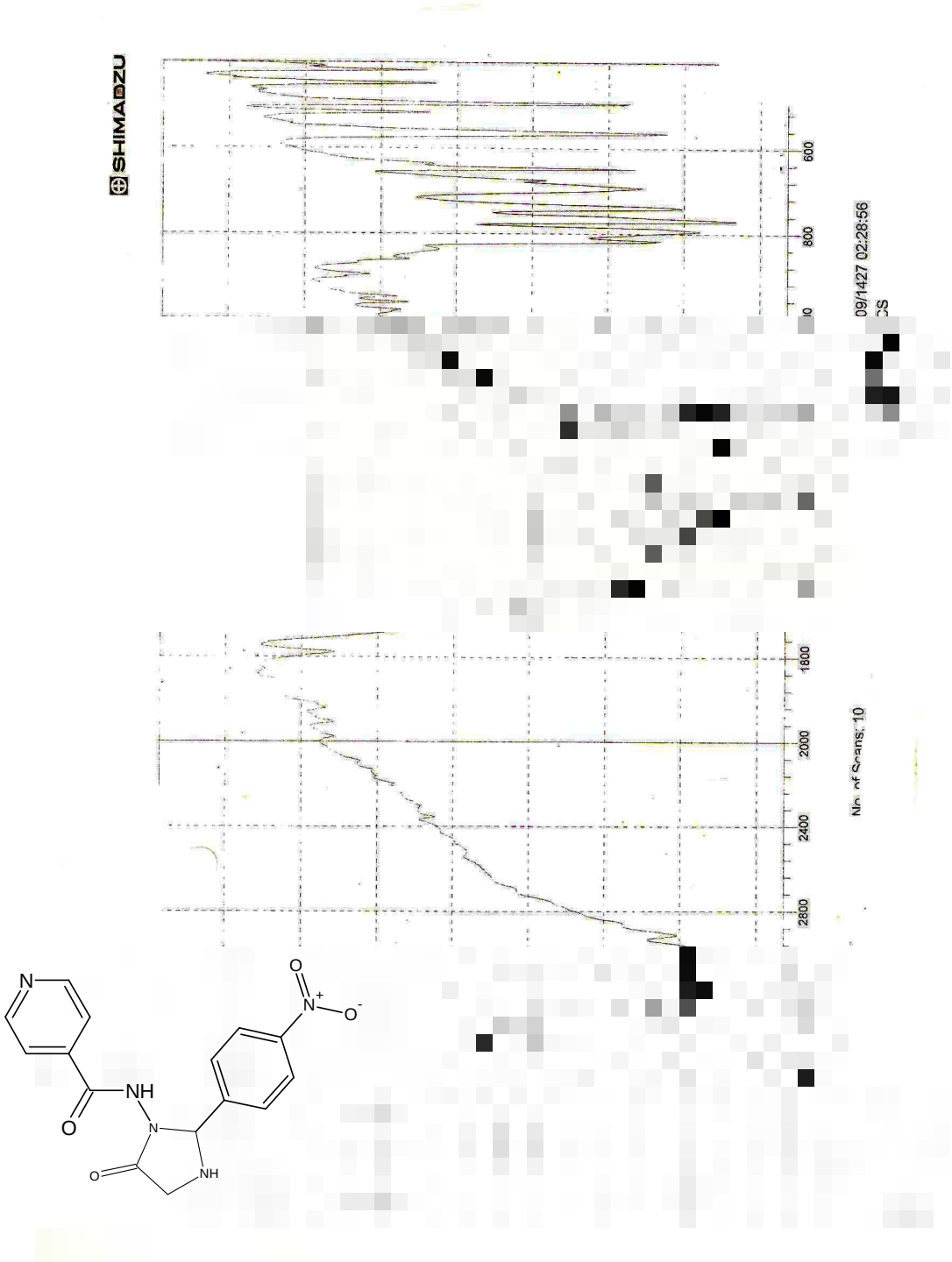
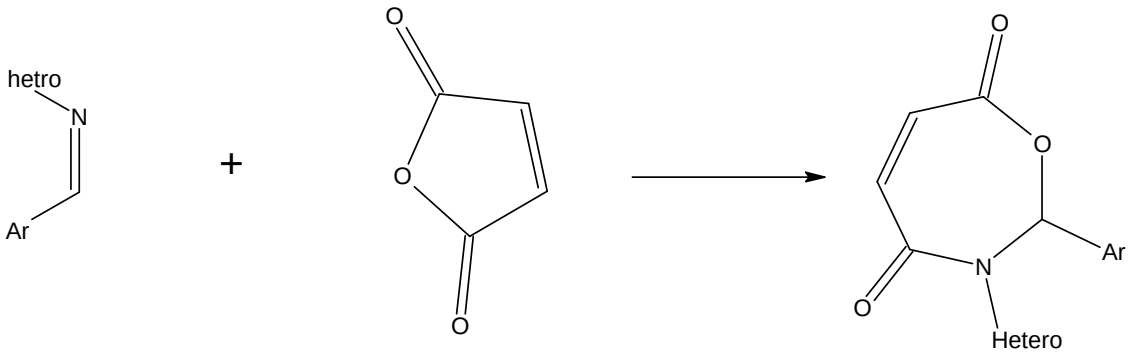


Figure (4-26) FTIR spectrum of compound ($3D_2$)

N-[2-(4-nitrophenyl)-5-oxoimidazolidin-1-yl]isonicotinamide

3-4 preparation of 2-aryl-3-hetero-2-yl-2,3-dihydro-1,3-oxazepine-4,7-dione (4)



Oxazipene derivatives were prepared by the refluxing of Schiff bases with maleic anhydride in dry benzene for 24h the product identified by the FTIR spectrum which show the appearance of C=O stretching vibration of the oxazipene at 1750-1700cm^{-1} and disappearance of C=N stretching vibration band at 1630-1580cm $^{-1}$ the proposed mechanism of this reaction

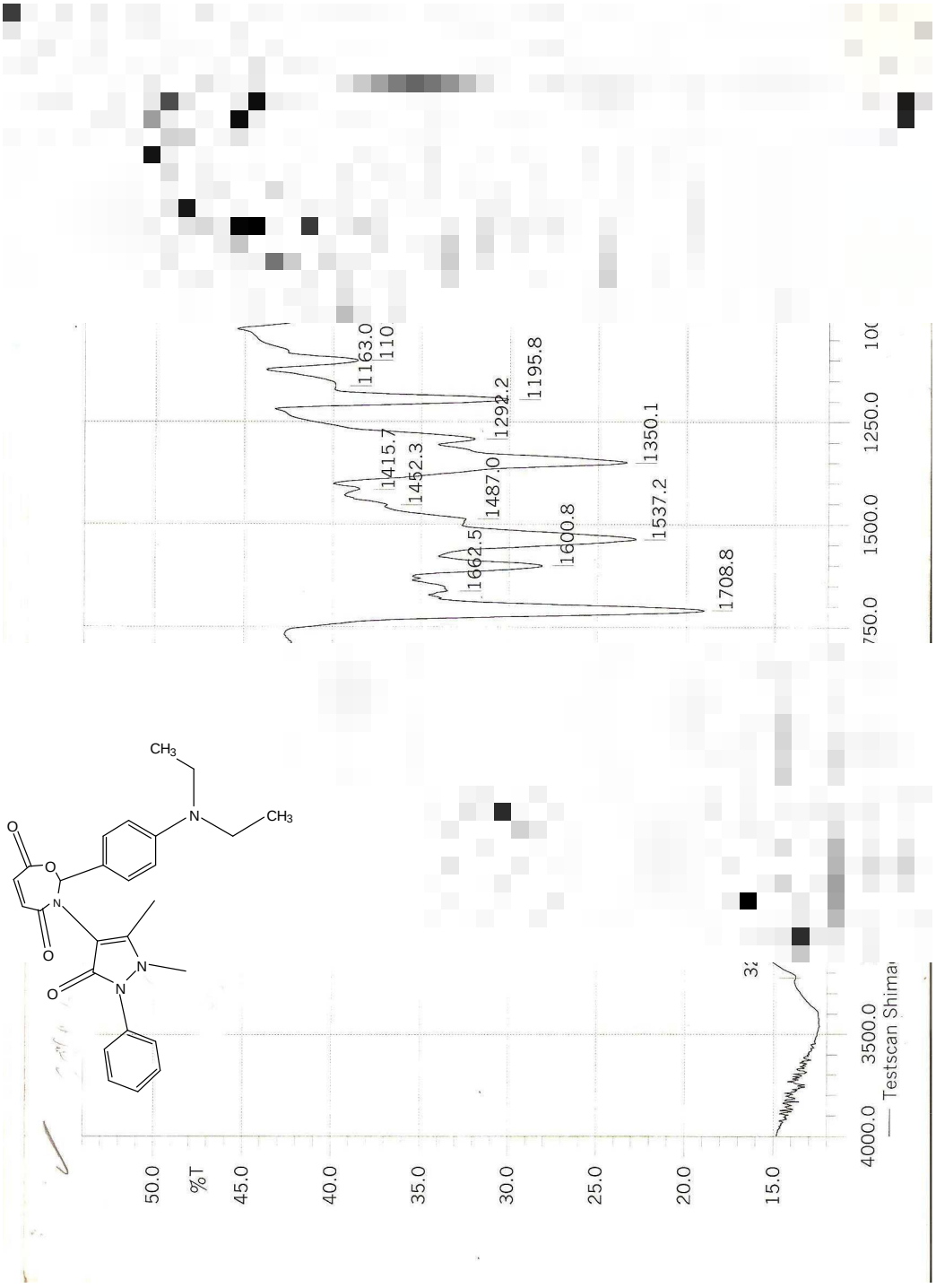


Figure (3-27) the FTIR of compound (4A)
(Z)-2-(4-(diethylamino)phenyl)-3-(2,3-dimethyl-5-oxo-1-phenyl-2,5-dihydro-1H-pyrazol-4-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione

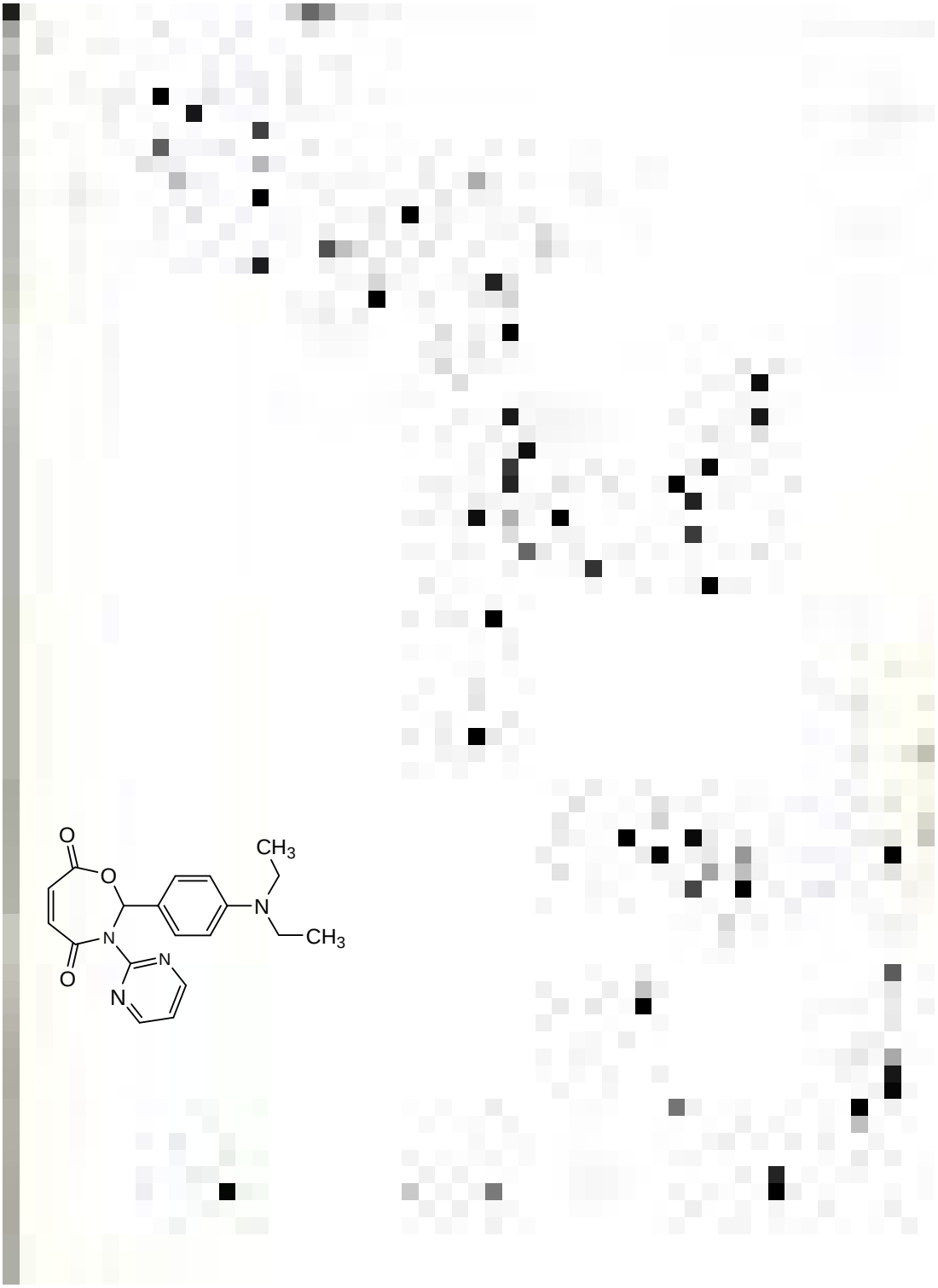


Figure (3-28) the FTIR of compound (4B) (Z)-2-(4-(diethylamino)phenyl)-3-(pyrimidin-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione

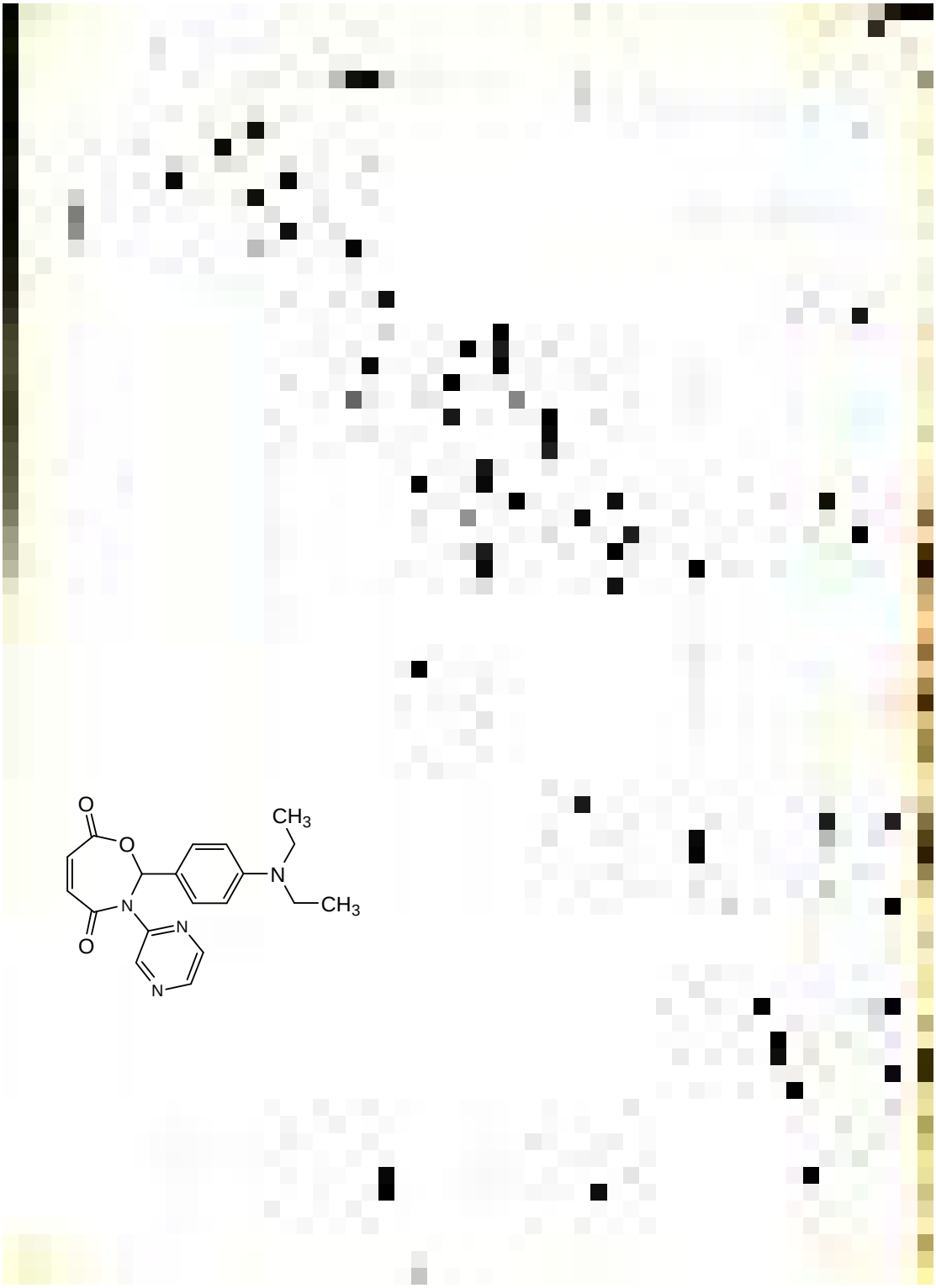


Figure (3-29) the FTIR of compound (4C) (Z)-2-(4-(diethylamino)phenyl)-3-(pyrazin-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione

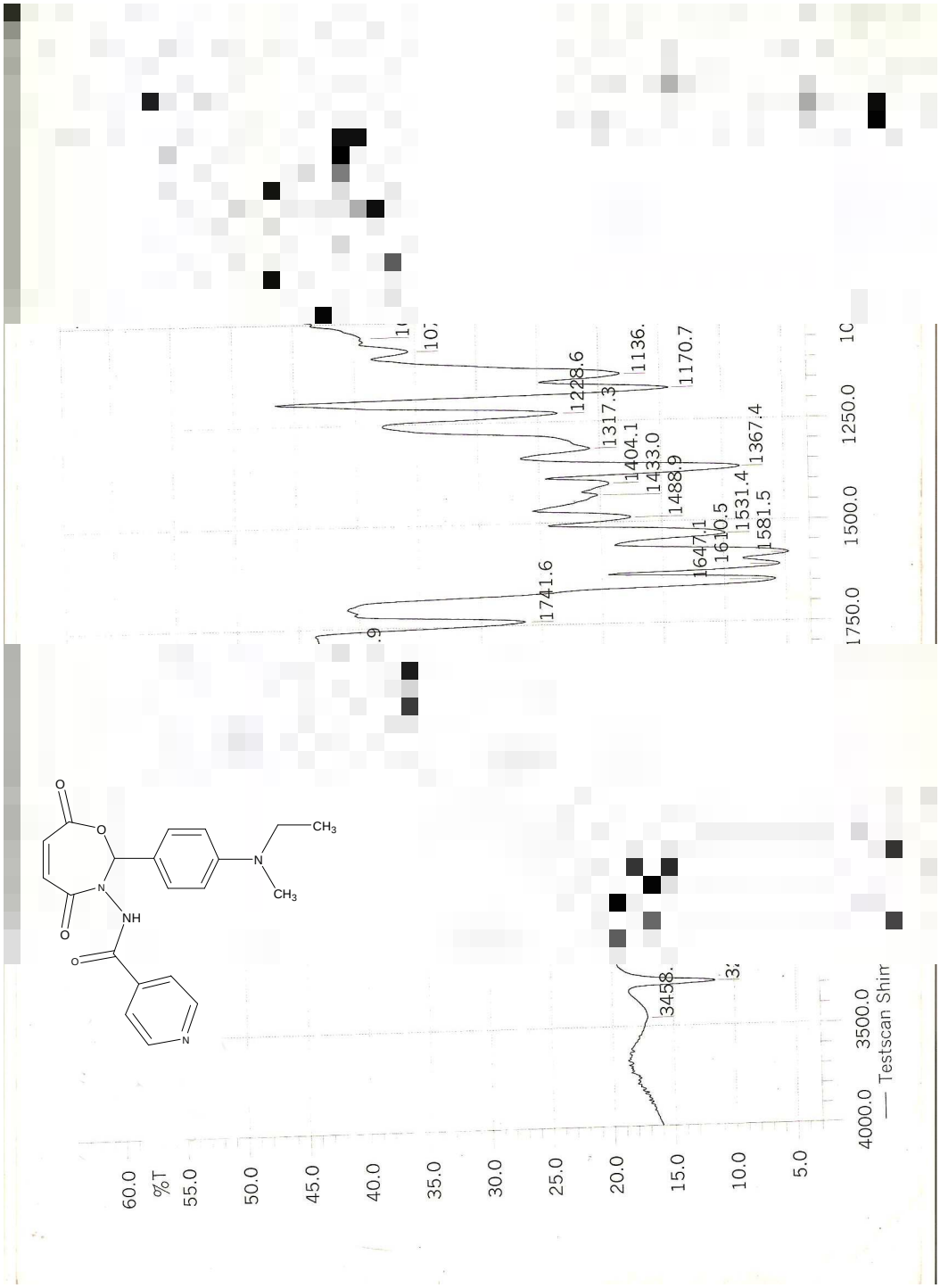
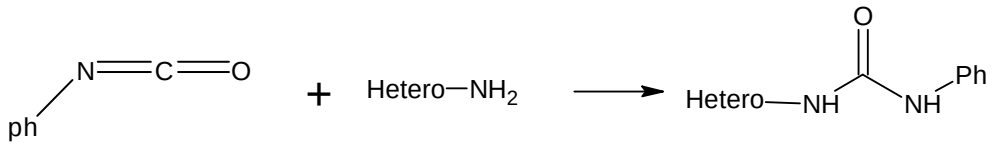
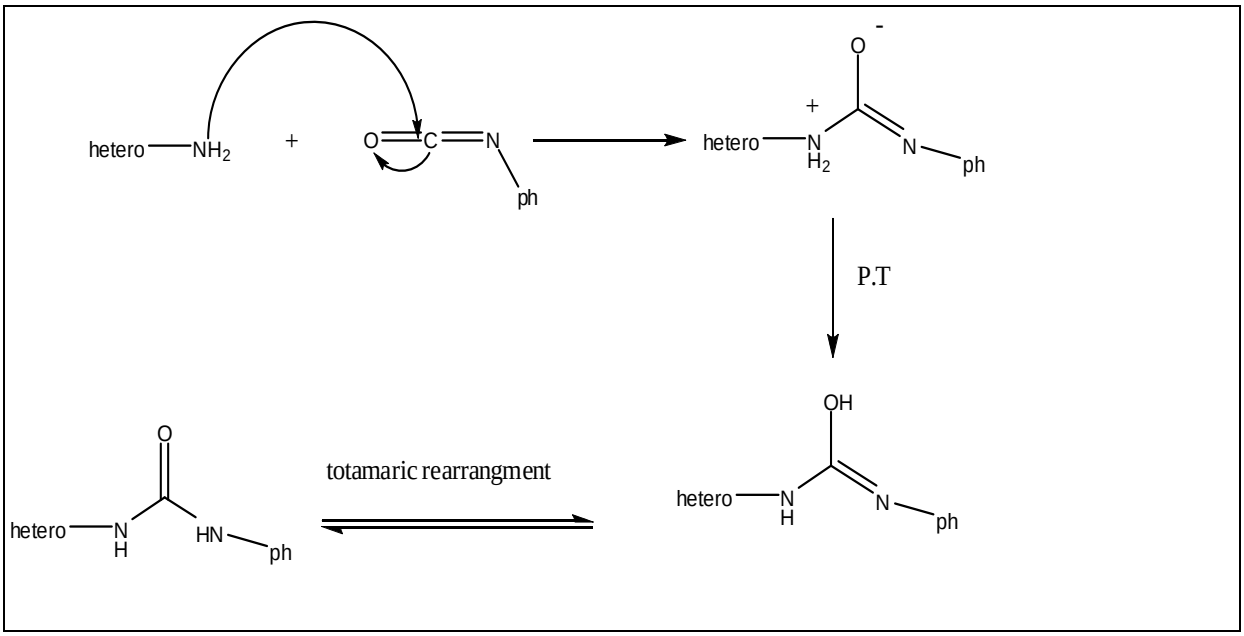


Figure (3-30) the FTIR spectrum of compound (4D) (Z)-N-(2-(4-(ethyl(methyl)amino)phenyl)-4,7-dioxo-1,3-oxazepin-3(2H,4H,7H)-yl)isonicotinamide

3-5 preparation 1-phenyl-3-(hetero-2-yl)urea.



Urea derivatives were prepared by the reaction of hetero amines and phenyl isocyanate the products were identified by the FTIR spectra which show the appearance of the stretching vibration of amidic carbonyl group in 1720-1645 cm^{-1},disappearance of NH_2 stretching vibration in3450-3120cm^{-1} and appearance of CH aromatic in 3010-3080cm^{-1} .the proposed mechanism of this reaction



Keto form enol form

Table (3-5) the IR spectral data of urea derivatives compounds (5A-5D)

Comp No.	O-H enolic	ν N- H	ν C-H aromatic	ν C=O urea	C=C aromatic	C=H aromatic OOP
5A	3200	3180-3139	3120	1700	1556-1448	804
5B	3300	3180-3280	3100	1690	1580-1440	840
5C	3300	320-3140	3000	1701	1590-1410	860
5D	3300	3320-3200	3110	1750	1590-1400	800

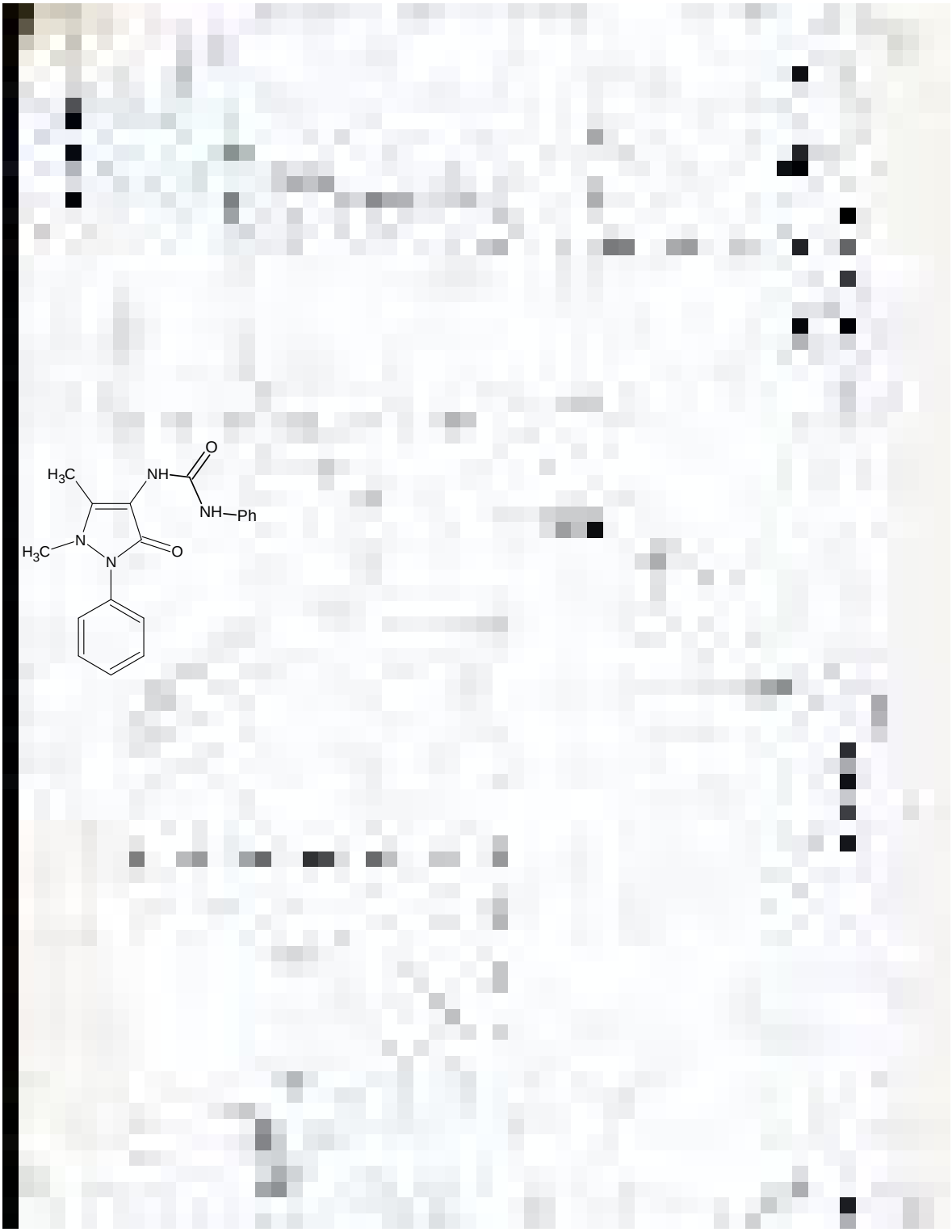


Figure (3-31) FTIR spectrum of compound (5A)

1-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3-phenylurea

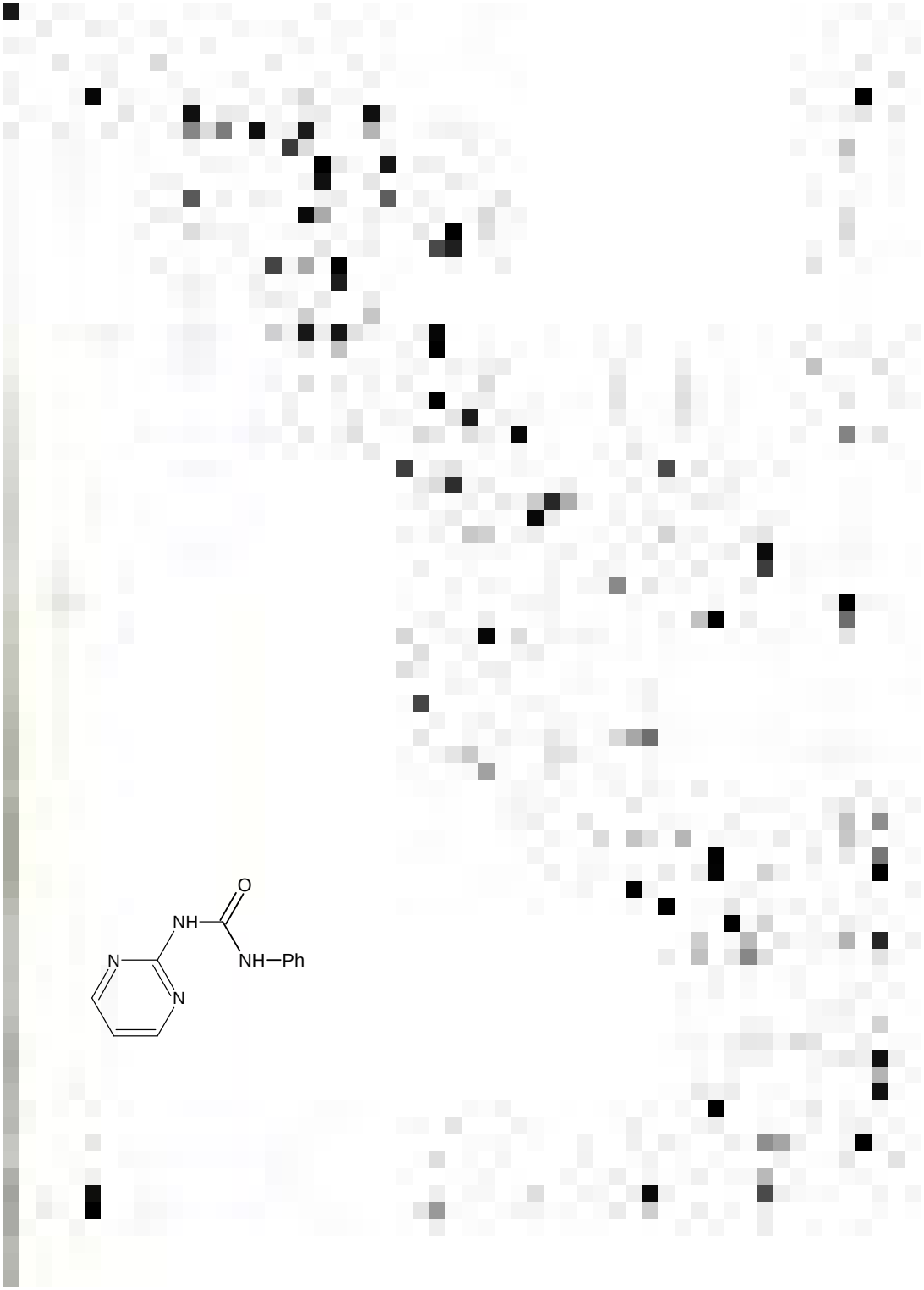


figure (3-32) FTIR spectrum of (5B)

1-phenyl-3-pyrimidin-2-ylurea

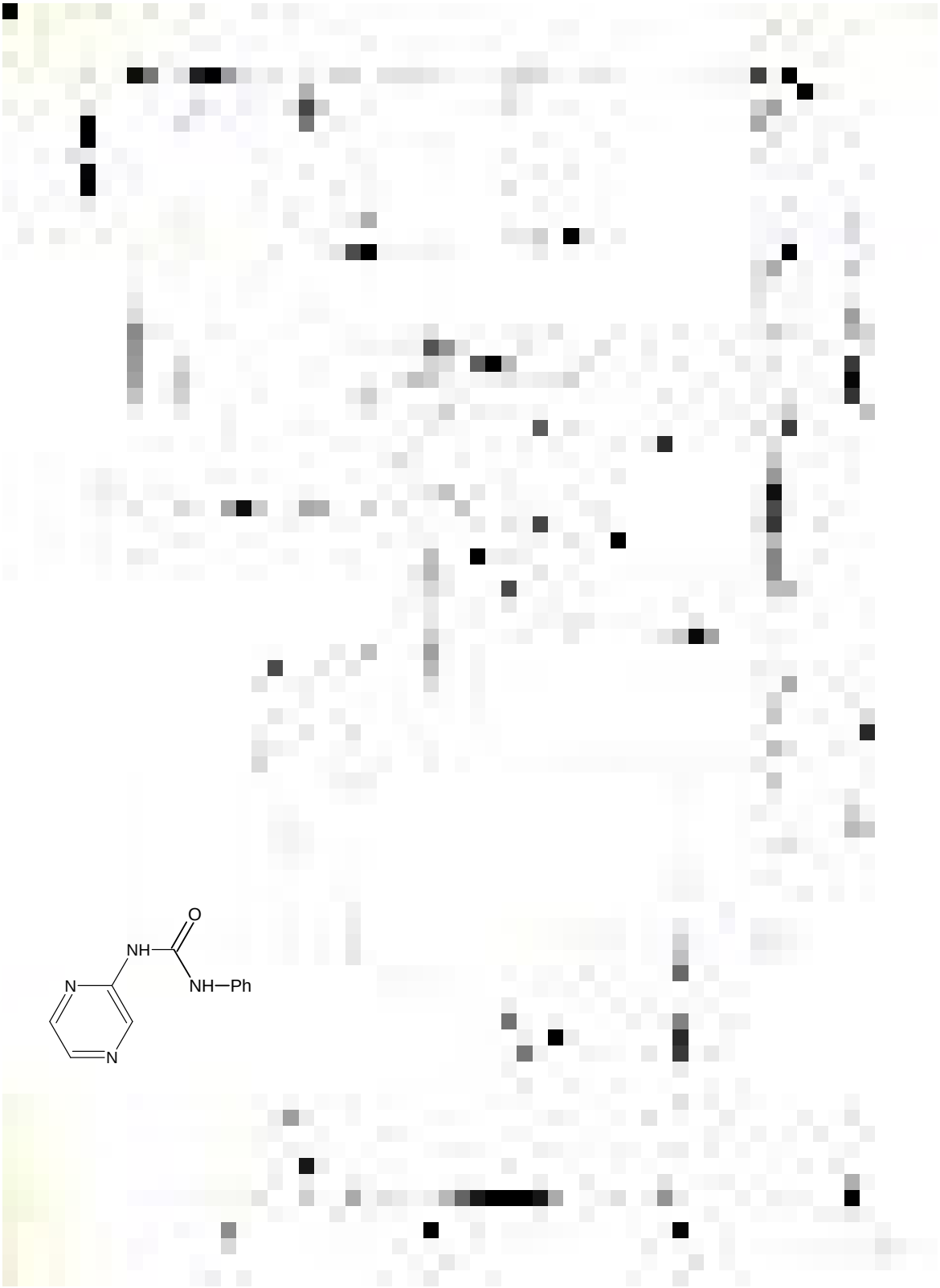


Figure (3-33) FTIR spectrum of (5C)

1-phenyl-3-pyrimidin-2-ylurea

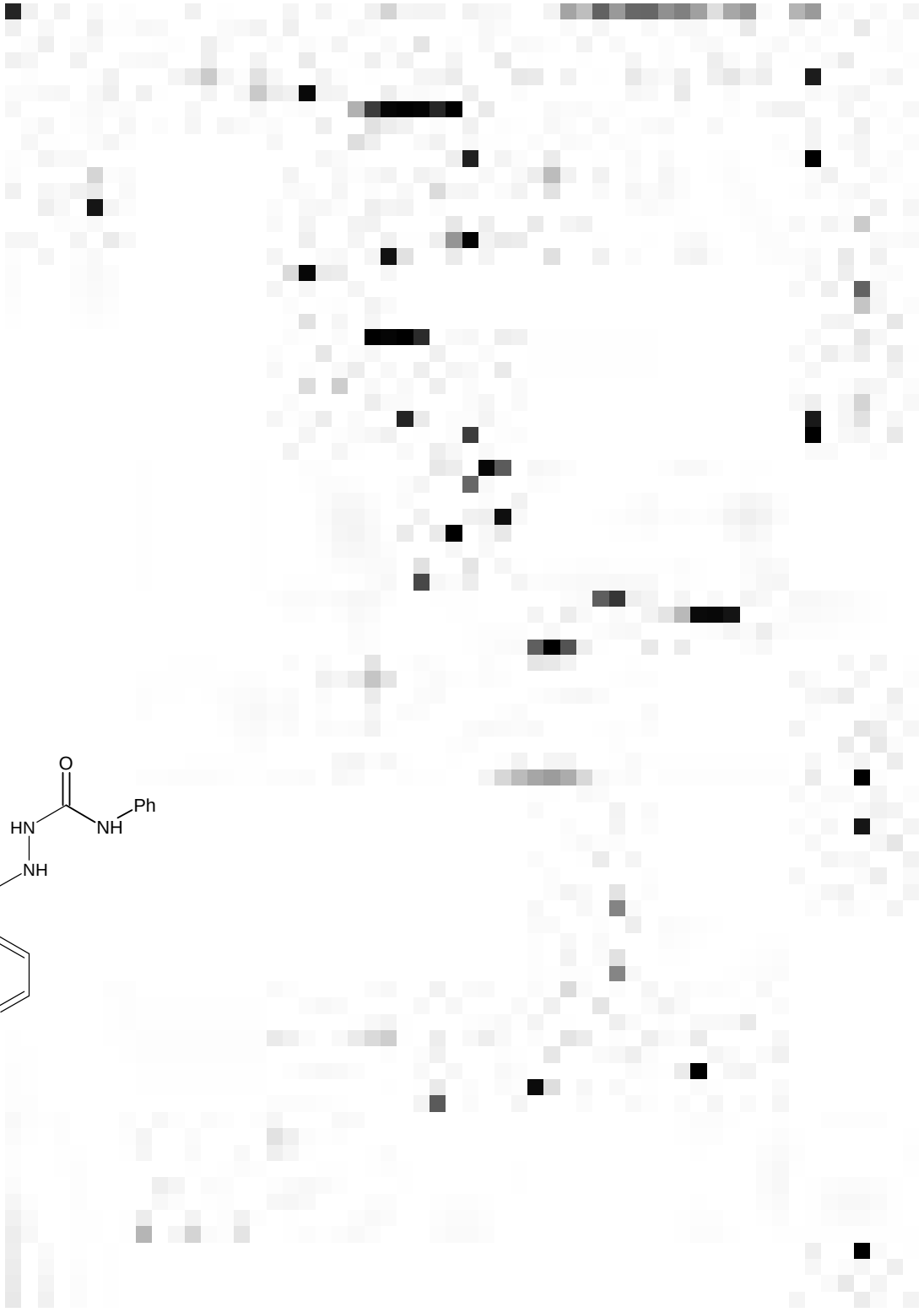
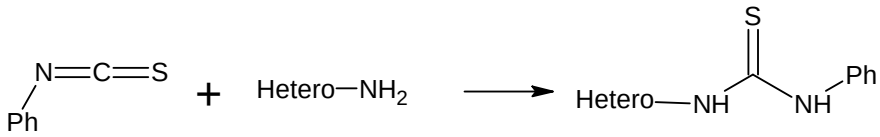


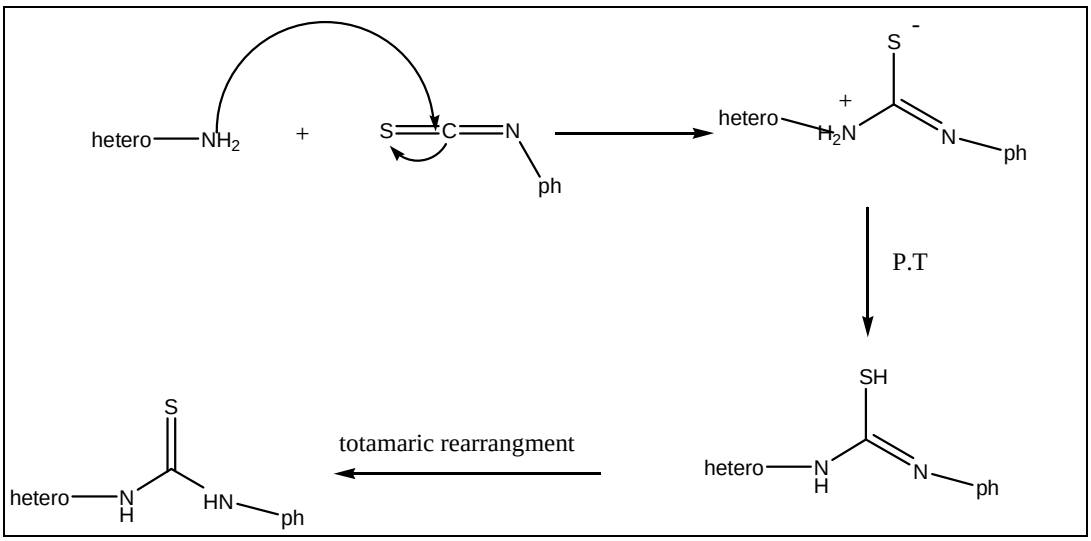
Figure (3-34) FTIR spectrum of (5D) 2-isonicotinoyl-N-phenylhydrazinecarboxamide

3-6 preparation of 1-phenyl-3-(hetero-2-yl)thiourea



Thiourea derivatives prepared by the reaction of phenylisothiocyanate with heteroamines in absolute ethanol the products identified by the FTIR by the disappearance of stretching vibrations NH_2 band in 3450-3320 cm^{-1} and the appearance of new band of C=S stretching vibration band in 1100-1250cm^{-1} moreover other stretching vibration bands were also occurred at (3450-3320) $cm^{-1}$for NH stretching vibration and appearance of CH aromatic in 3010-3080cm^{-1} and appearance of OOP bending band of p-substituted benzene

The proposed mechanism



Keto form enol form

Table (3-6) the IR spectral data of thiourea derivatives (6A-6D)

Comp No.	S-H	ν N- H	ν C-H aromatic	ν C=S	C=H aromatic OOP
6A	2650	3250-3200	3120	1180	800
6B	2670	3240-3180	3100	1160	850
6C	2600	3220-3200	3120	1200	840
6D	2640	3280-3240	3100	1160	820

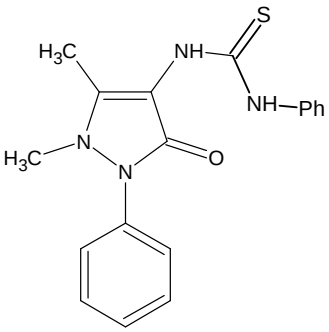


Figure (3-35) FTIR spectrum of (6A) 1-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-3-phenylthiourea

Figure (3-36) FTIR spectrum of compound (6B)

1-phenyl-3-pyrimidin-2-ylthiourea

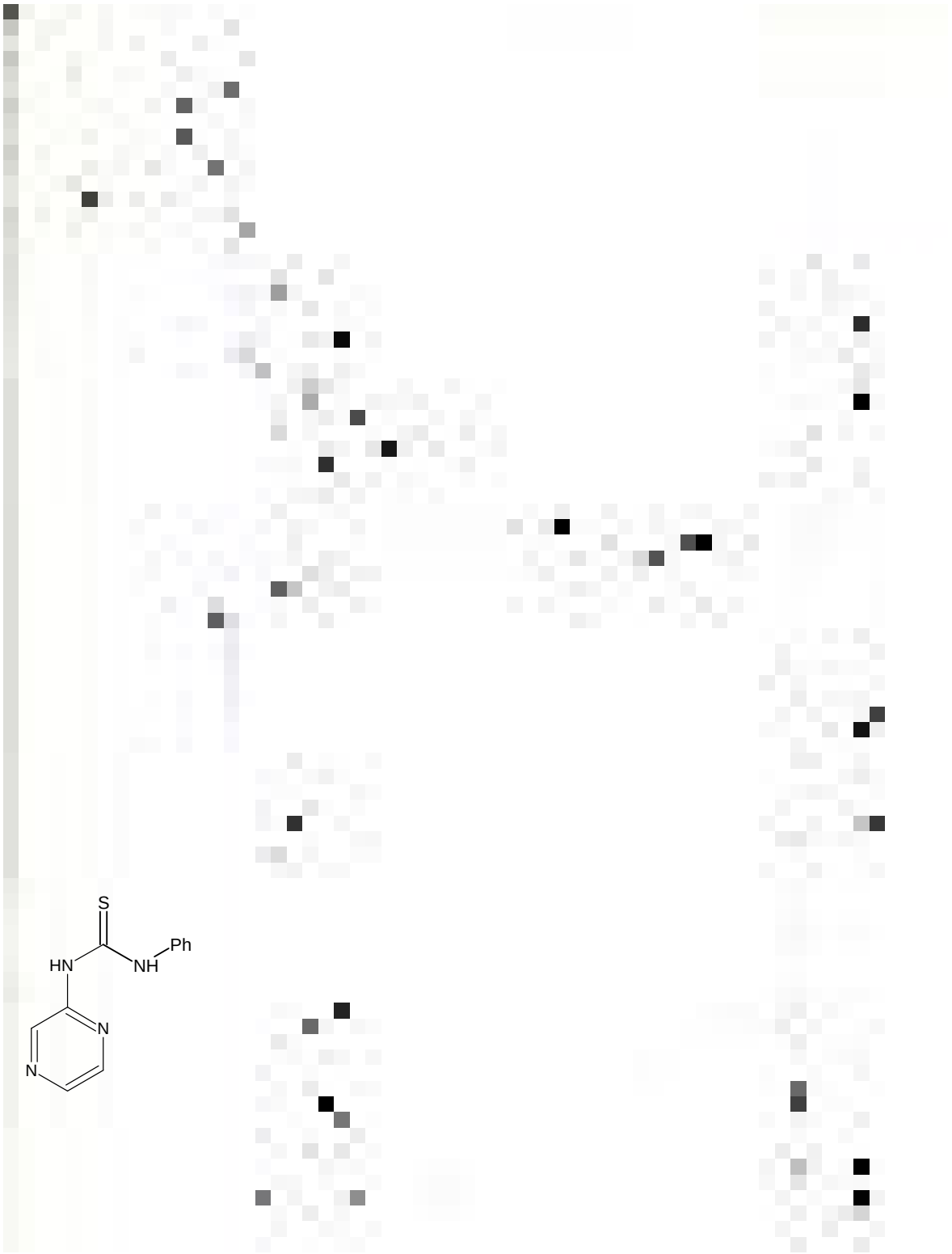


Figure (3-37) FTIR spectrum of (6C)

1-phenyl-3-pyrazin-2-ylthiourea

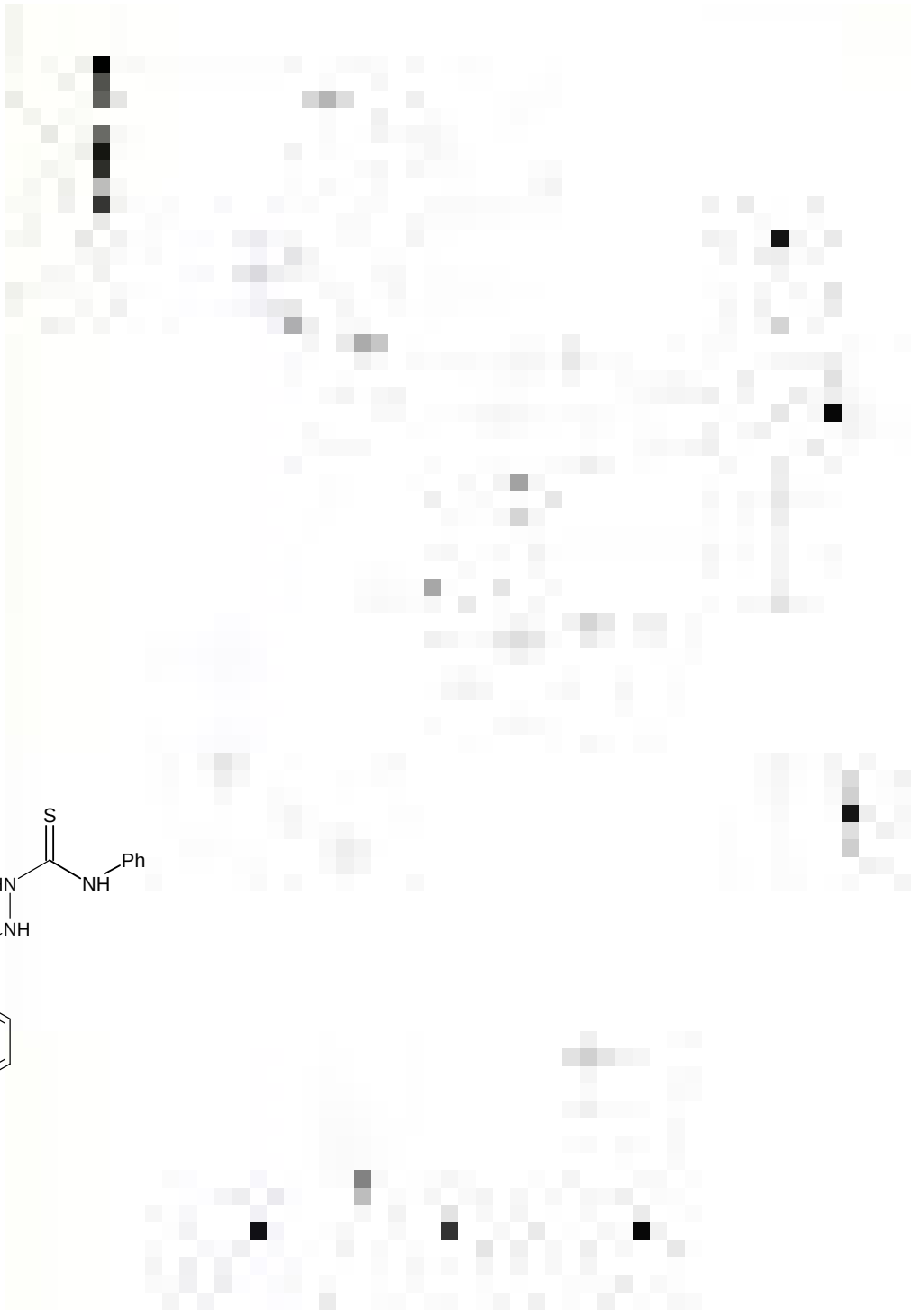
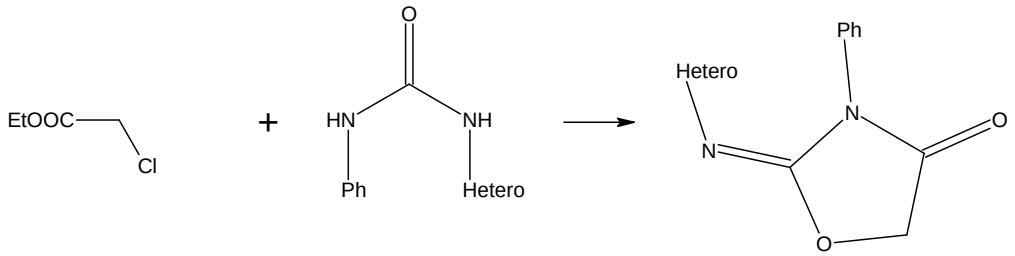


Figure (3-38) FTIR spectrum of (6D) 2-isonicotinoyl-N-phenylhydrazinecarbothioamide

3-7 preparation of 3-phenyl-2-(hetero-2-ylamino)-1,3-oxazolidin-4-one



Oxazolidinone derivatives were prepared by heating mixture of urea derivatives with ethylchloroacetate in absolute ethanol the product identified by the FTIR which show the disappearance of carbonyl stretching vibration band of the ester at 1740 cm^{-1} and the disappearance of one NH of urea at 3400-3200cm^{-1} and appearance of C=N band of the ring at 1600cm^{-1}

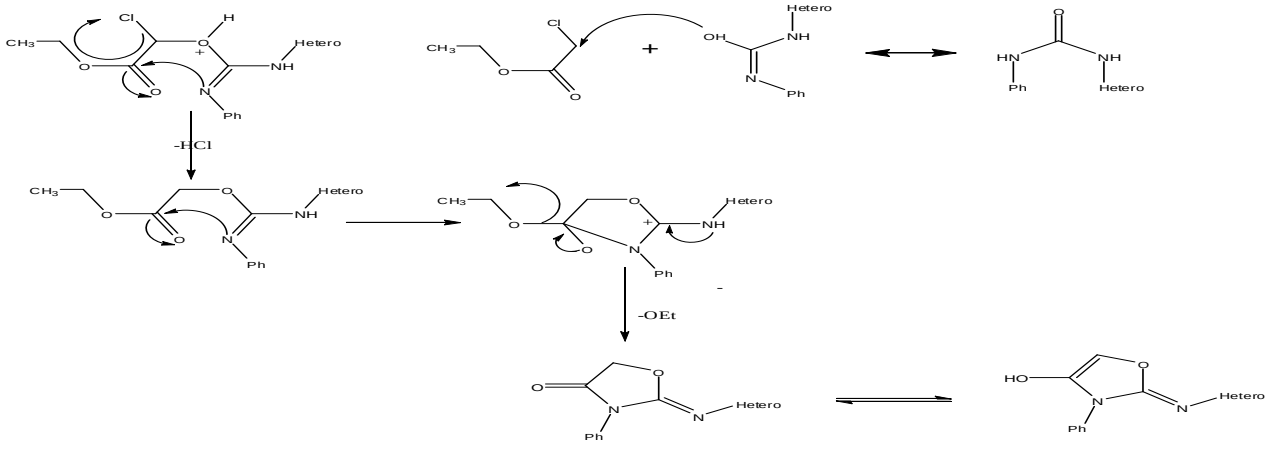


Table (3-7) IR spectral data of thiazolidinones (7A-7C)

Compound No.	O-H	CH_2	υ C=O		υ C=N
7A	3200	2920-2860	1680		1600
7B	3200	2940-2860	1720		1600
7C	3400-3200	2930-2850	1740		1580

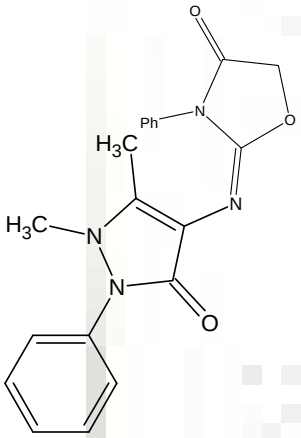


Figure (3-39) FTIR spectrum of compound (7D)

2-[(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino]-3-phenyl-1,3-oxazolidin-4-one (7A)

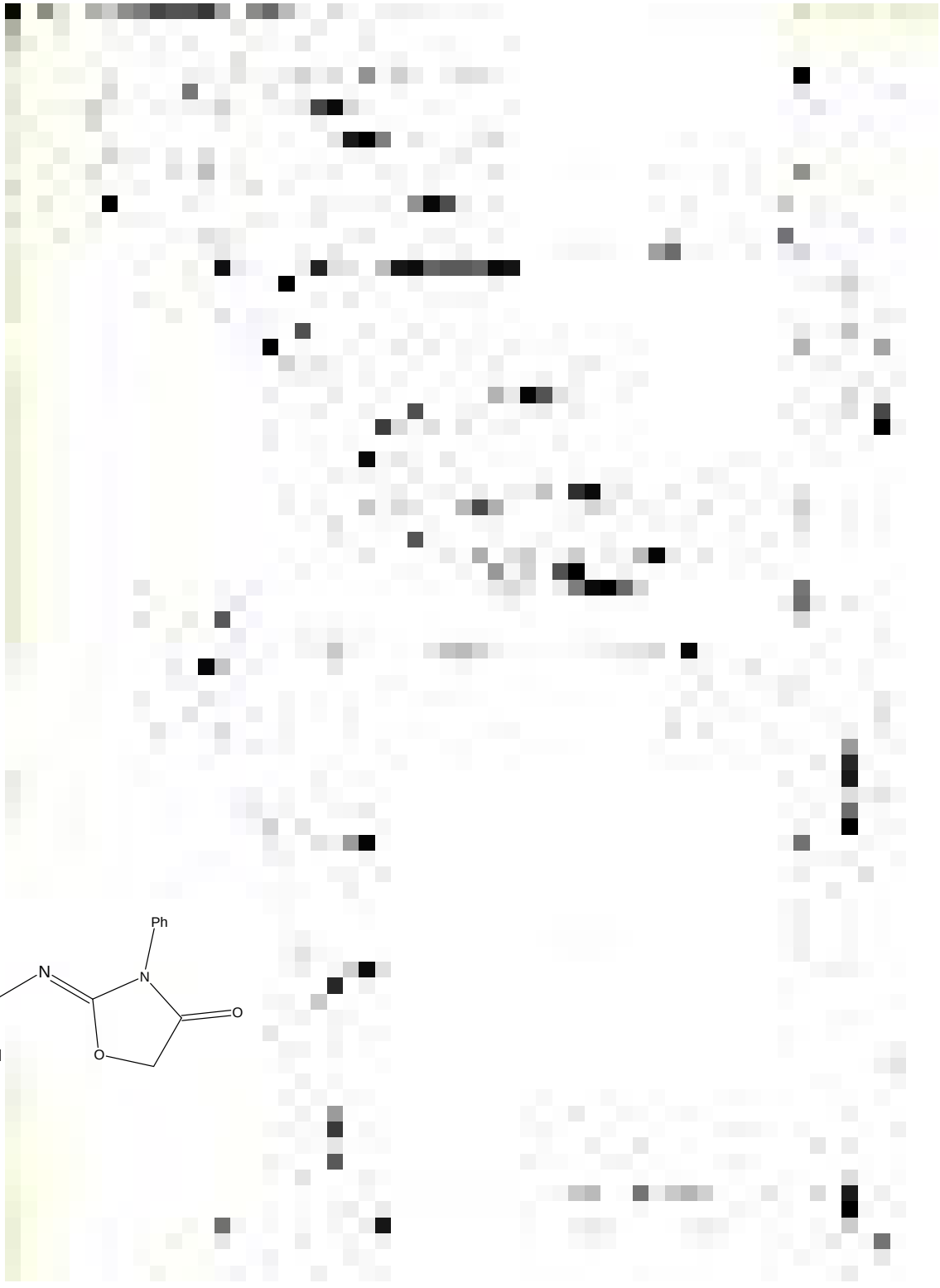


Figure (3-40) FTIR spectrum of 3-phenyl-2-(pyrimidin-2-ylamino)-1,3-oxazolidin-4-one (7B)

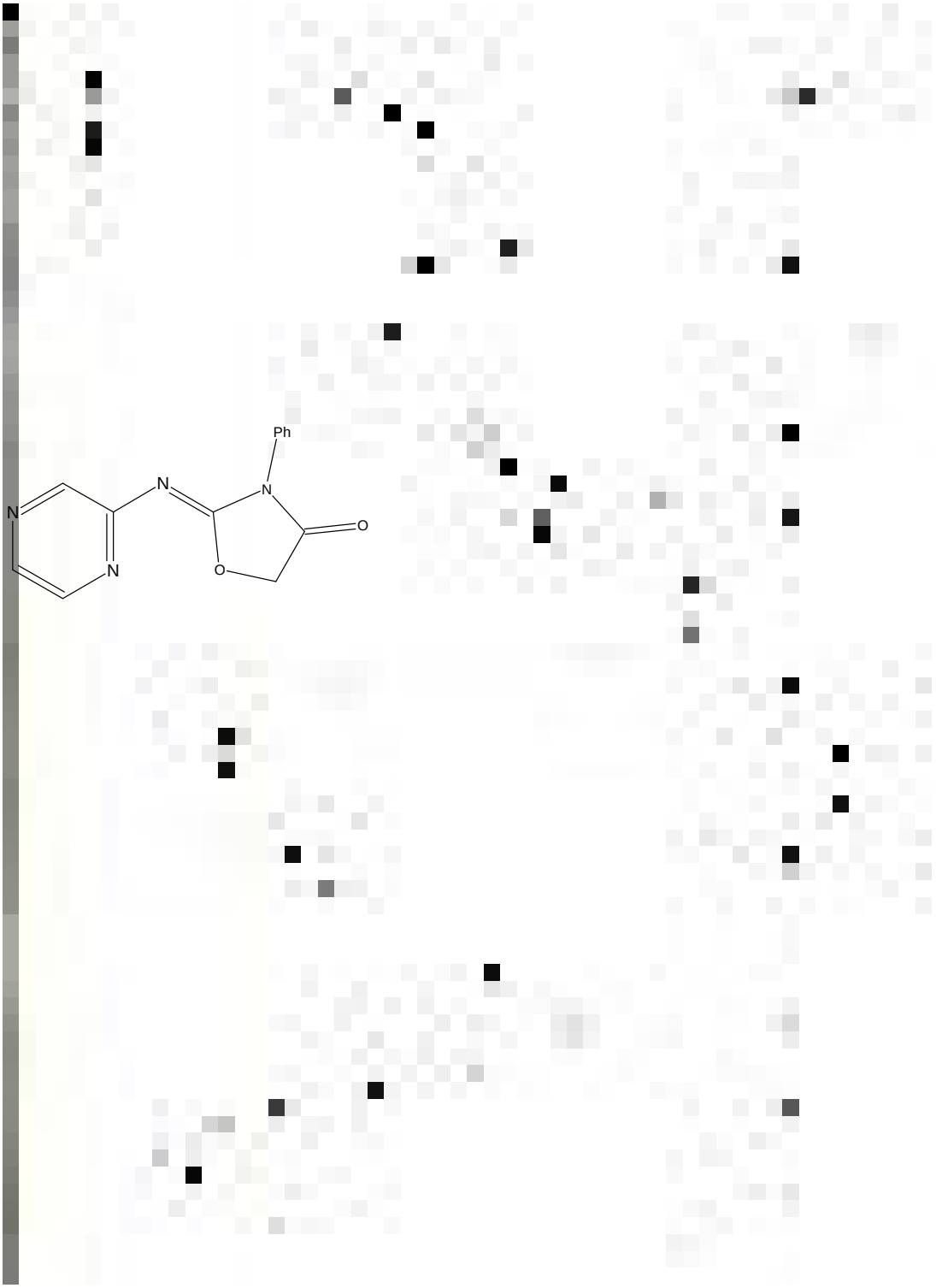
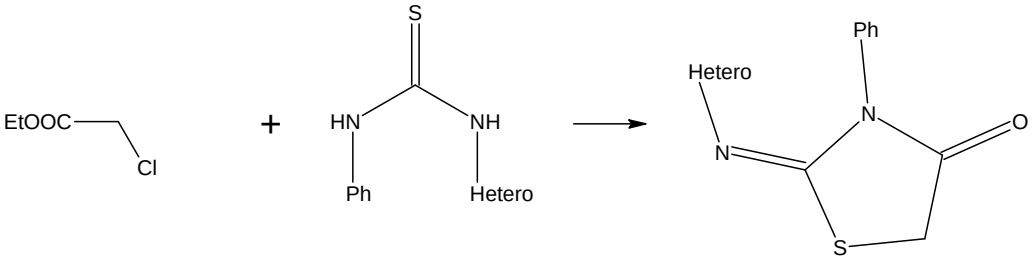


Figure (3-41) FTIR spectrum of phenyl-2-(pyrazin-2-ylamino)-1,3-oxazolidin-4-one (7C)

3-8-Peparation 3-phenyl-2-(hetero-2-ylamino)-1,3-oxazolidin-4-one(8)



Oxazolidinone derivatives prepared by the reaction of thiourea derivatives and ethylchloroacetate in absolute ethanol the product identified by FTIR by the disappearance of C=O of the ester in 1740 cm^{-1} and the appearance of amidic C=O band at 1640cm-1

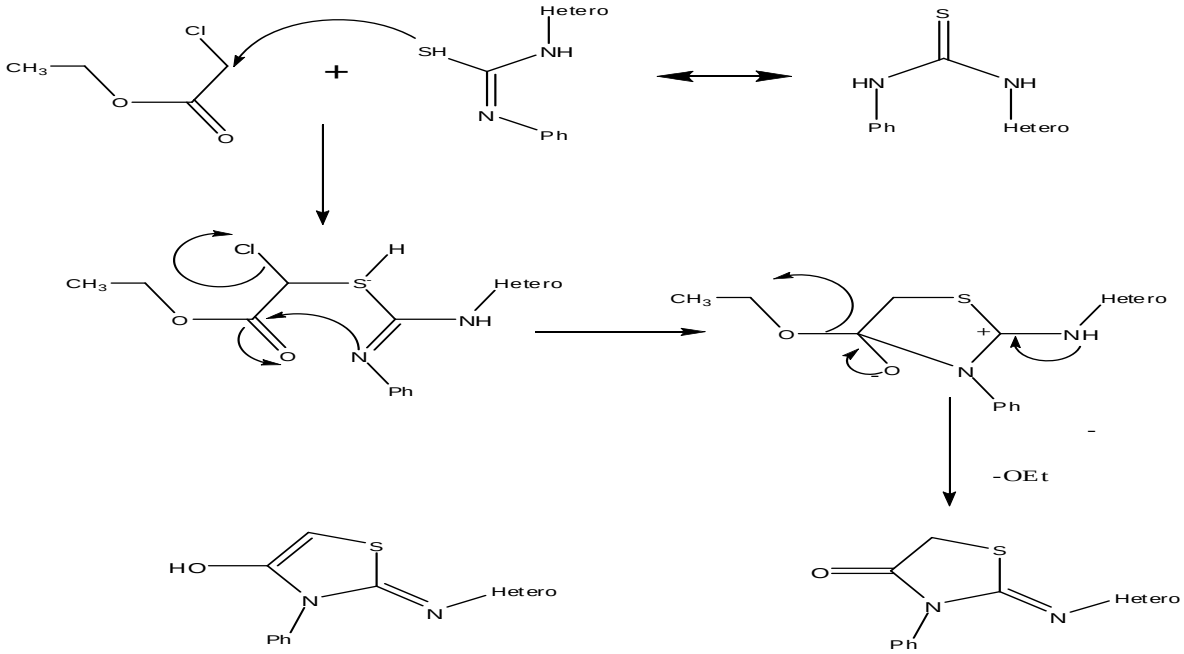


Table (3-9) the IR spectral data of oxazolidinone (9B-9C)

Compound No	SH	C=O	C=N
9B	2700	1700	1600
9C	2680	1690	1580

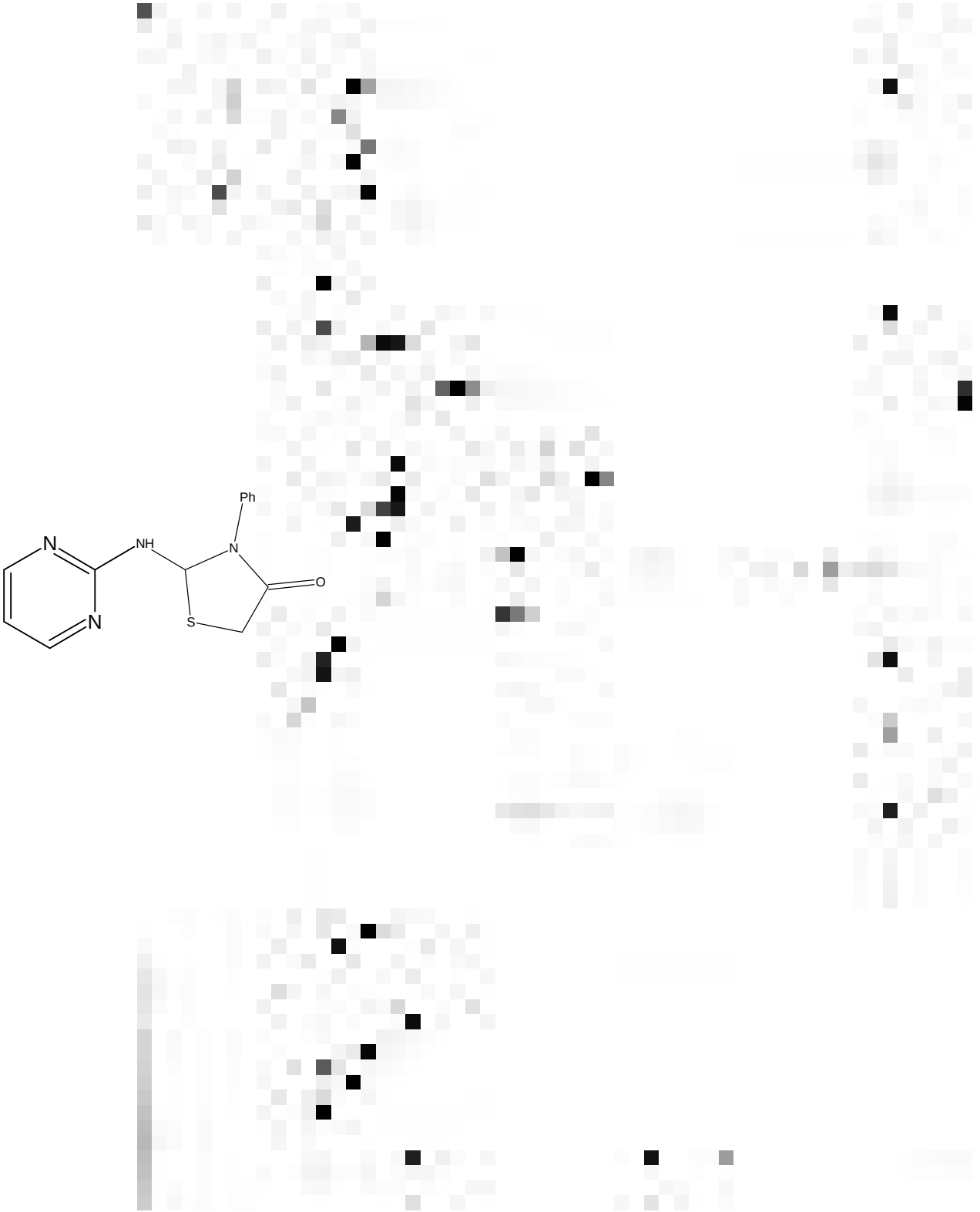


Figure (3-40) FTIR spectrum of compound 9B

3-phenyl-2-(pyrimidin-2-ylamino)-1,3-thiazolidin-4-one

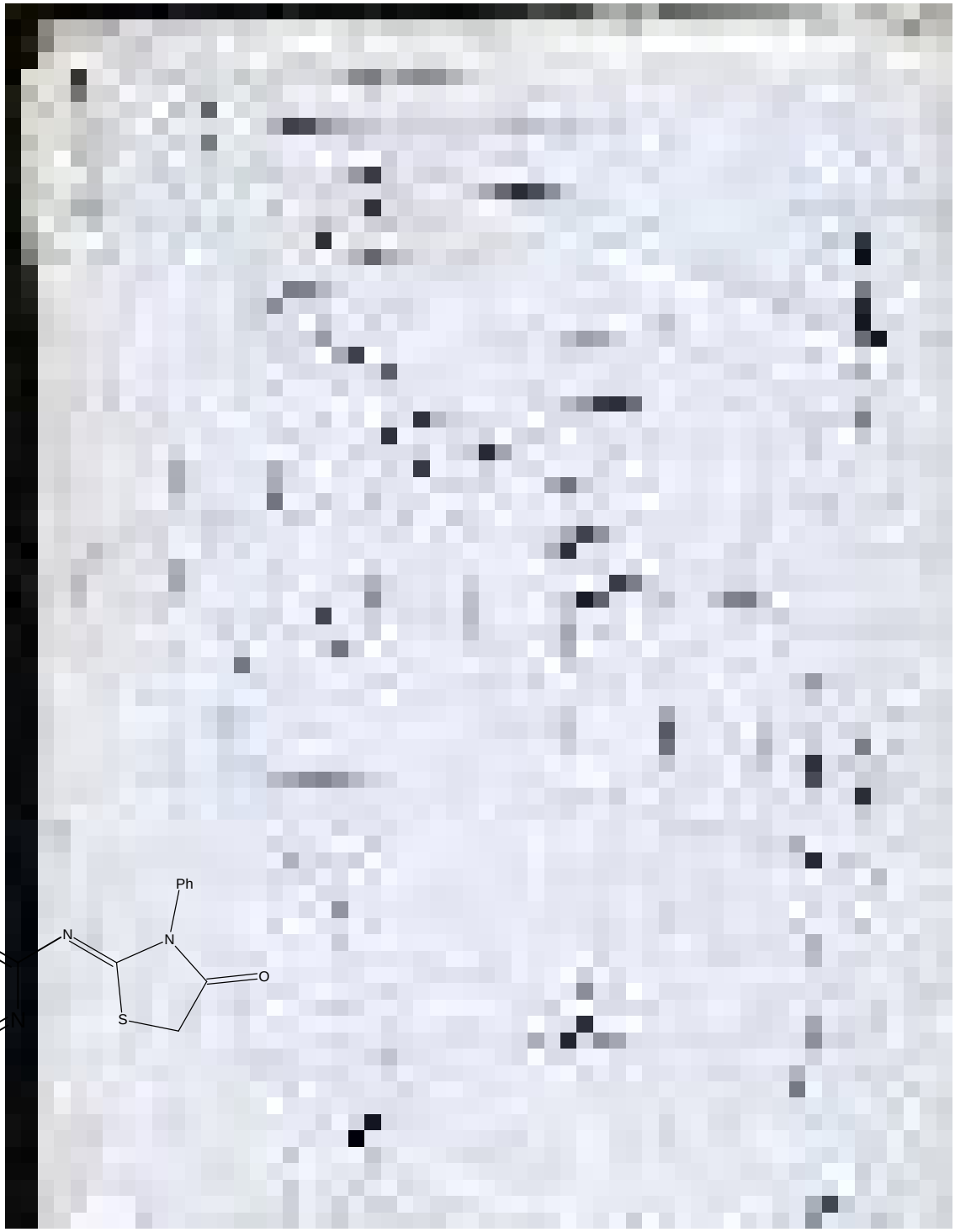
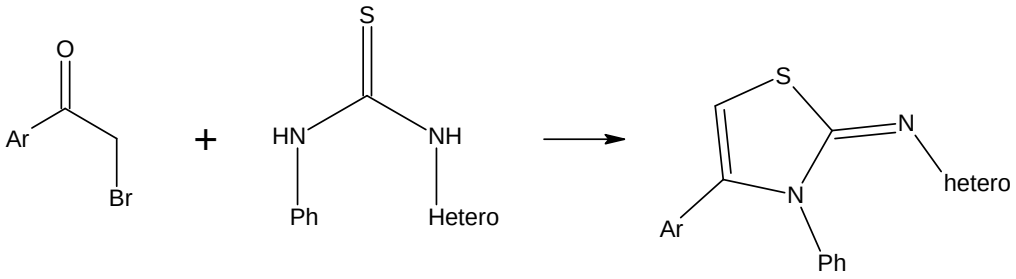


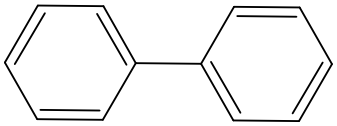
Figure (3-41) FTIR spectrum of compound 9C

3-phenyl-2-(pyrazin-2-ylamino)-1,3-thiazolidin-4-one

3-9- N-(4-(naphthalen-2-yl)-3-phenyl-2,3-dihydrothiazol-2-yl)hetero-2-amine



Ar =

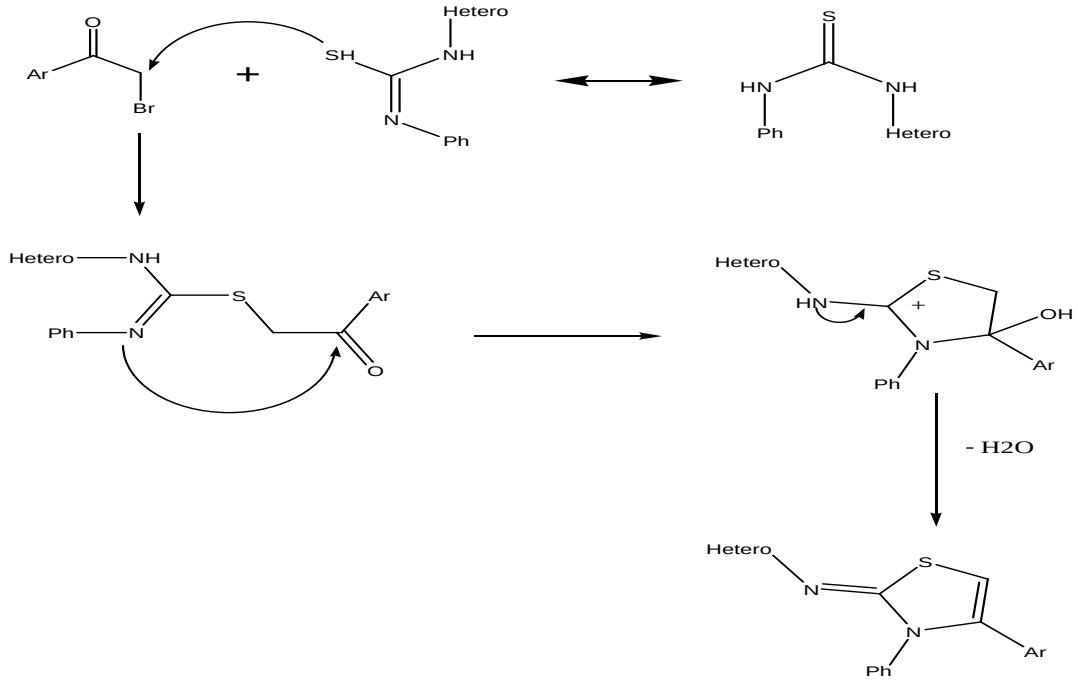


Thiazoline derivatives prepared by the reaction of thiourea derivatives with p-phenylphenacy bromide in absolute ethanol the products identified by FTIR by the disappearance of C=O and C=S bands of the haloketone and thiourea in 1740cm^{-1} and 1200cm^{-1} respectively and the appearance of CH olifenic in 3010 cm^{-1}

H NMR singlate at (8-8.9) for f,g,h,i and j protons and singlet at 6.5 ppm for olifenic proton (i)

Aromatic proton appear at (7.2-7.7)ppm

CNMR show singlate at 134 for C=N and singlate at 127,128.128.9 ppm are attribute to aromatic carbon



Compound No	Fig.	C=N
8A	3-36	1640
8B	3-37	1640
8C	3-38	1640
8D	3-39	1640

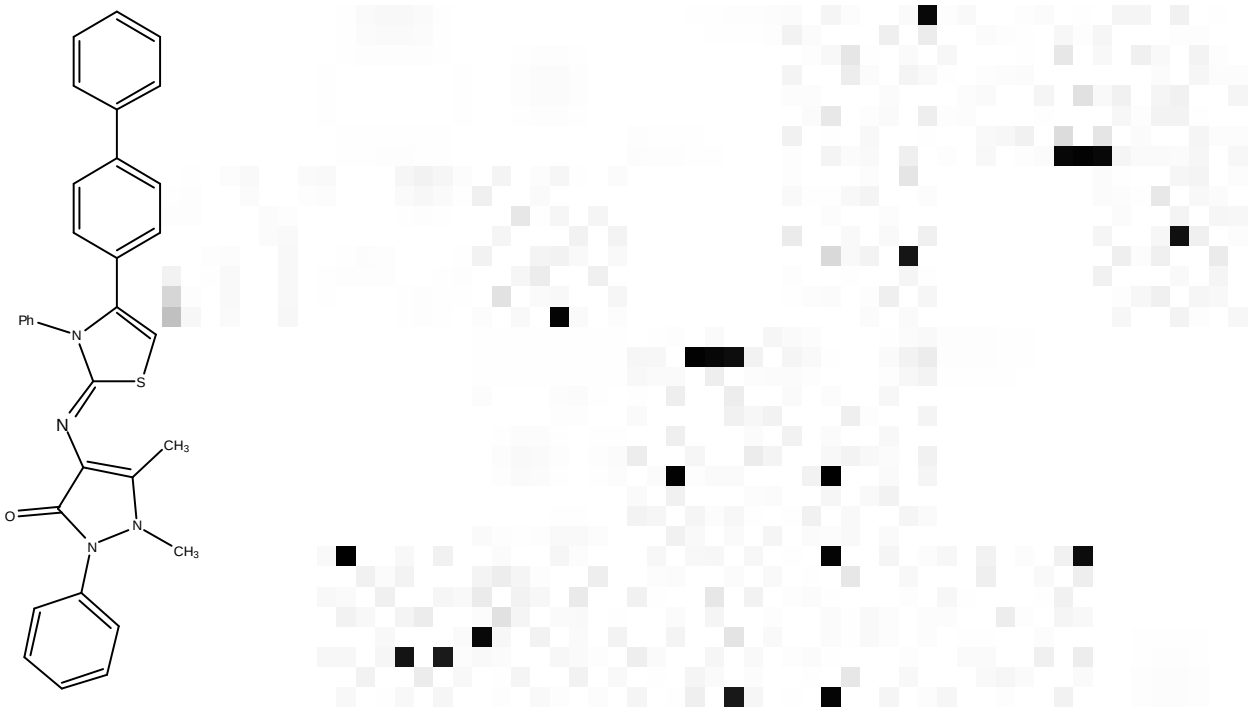


Figure (3-36) FTIR spectrum of compound (8A) 4-(4-(biphenyl-4-yl)-3-phenyl-2,3-dihydrothiazol-2-ylamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one

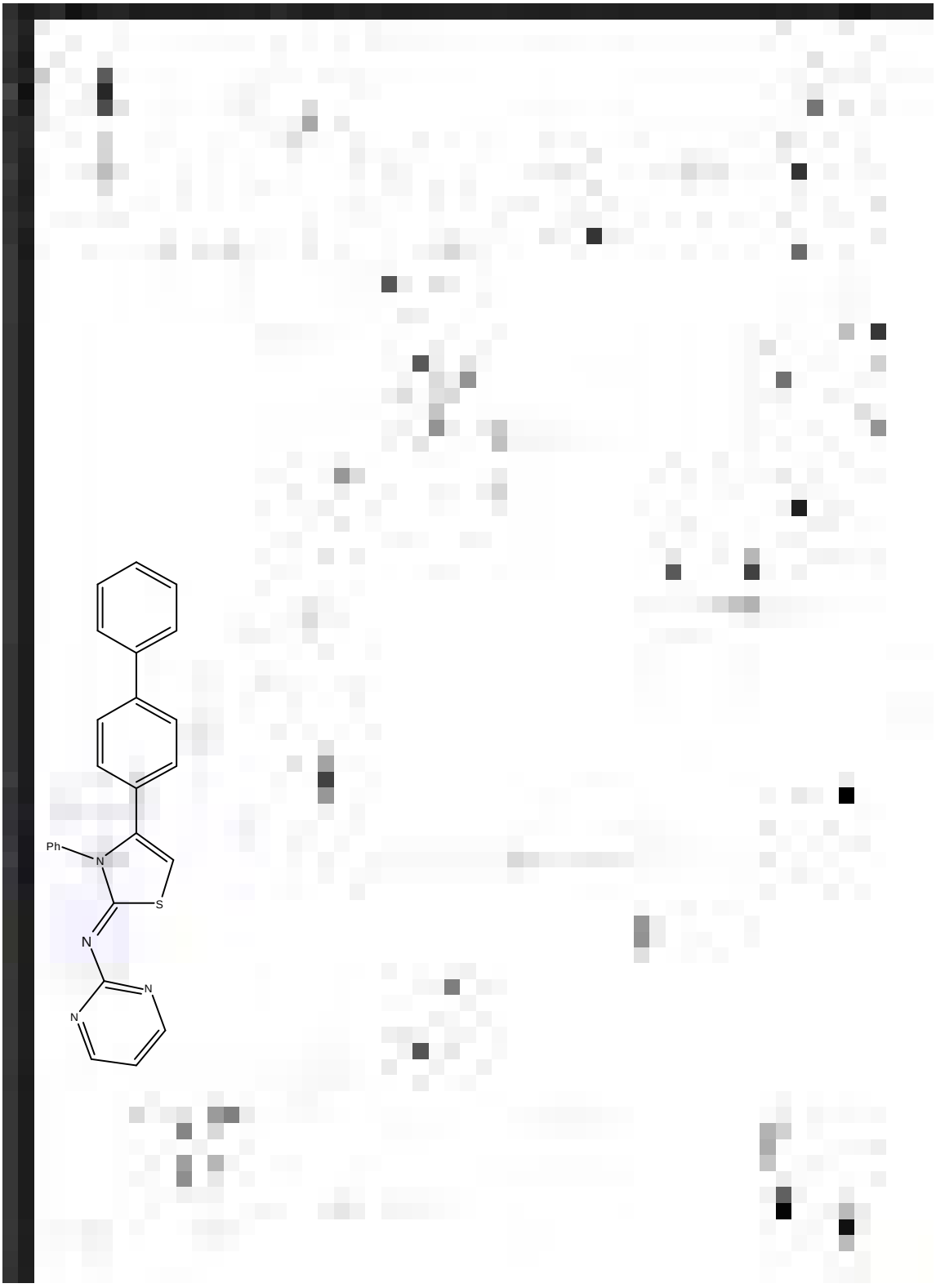


Figure (3-37) FTIR spectrum of compound (8B) (Z)-N-(4-(biphenyl-4-yl)-3-phenylthiazol-2(3H)-ylidene)pyrimidin-2-amine

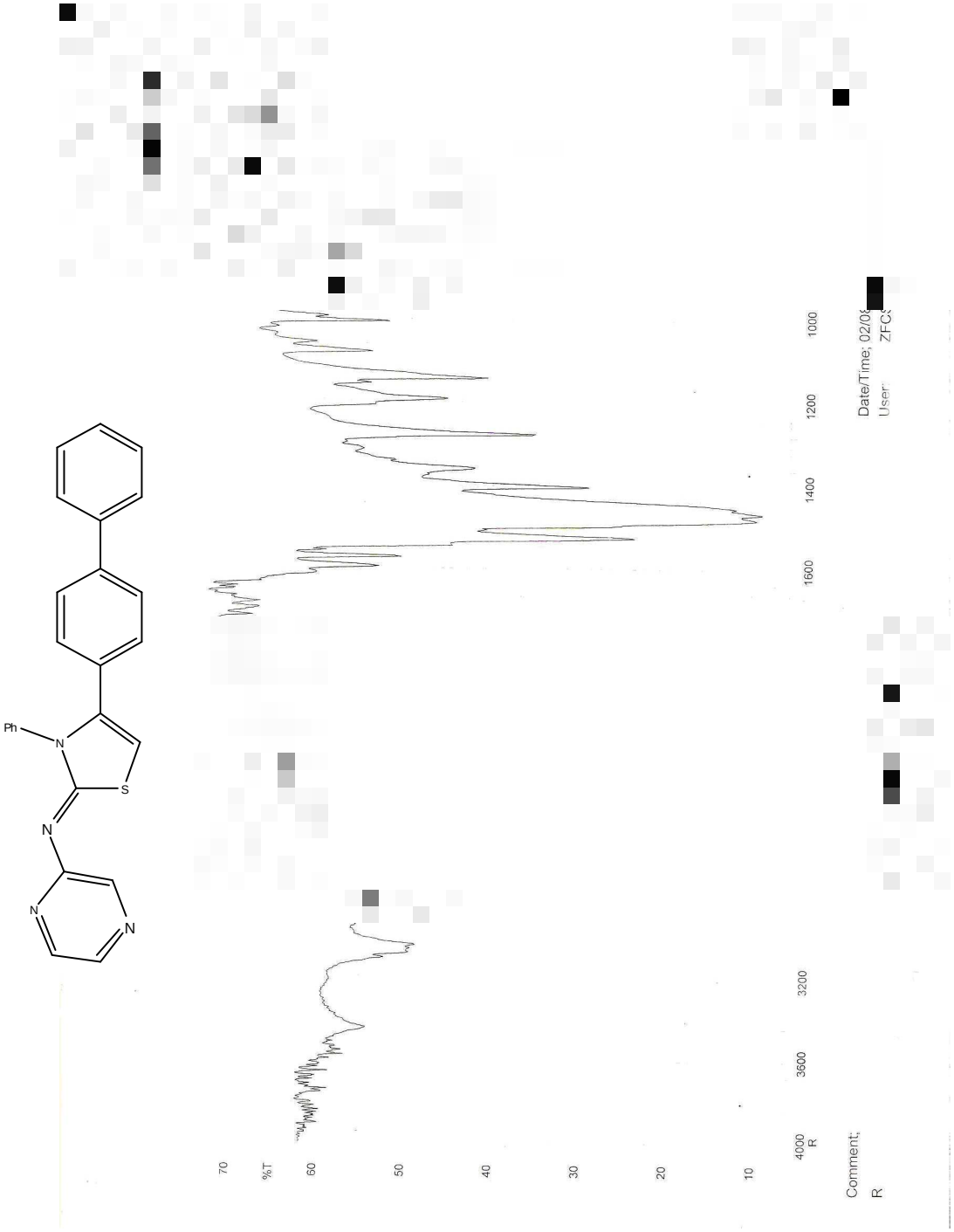
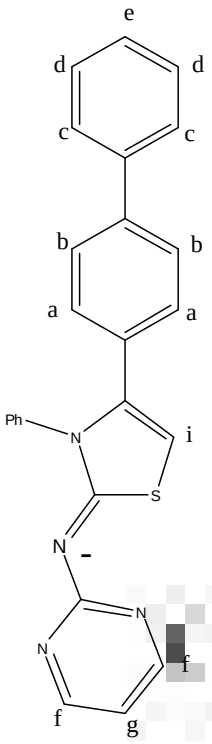
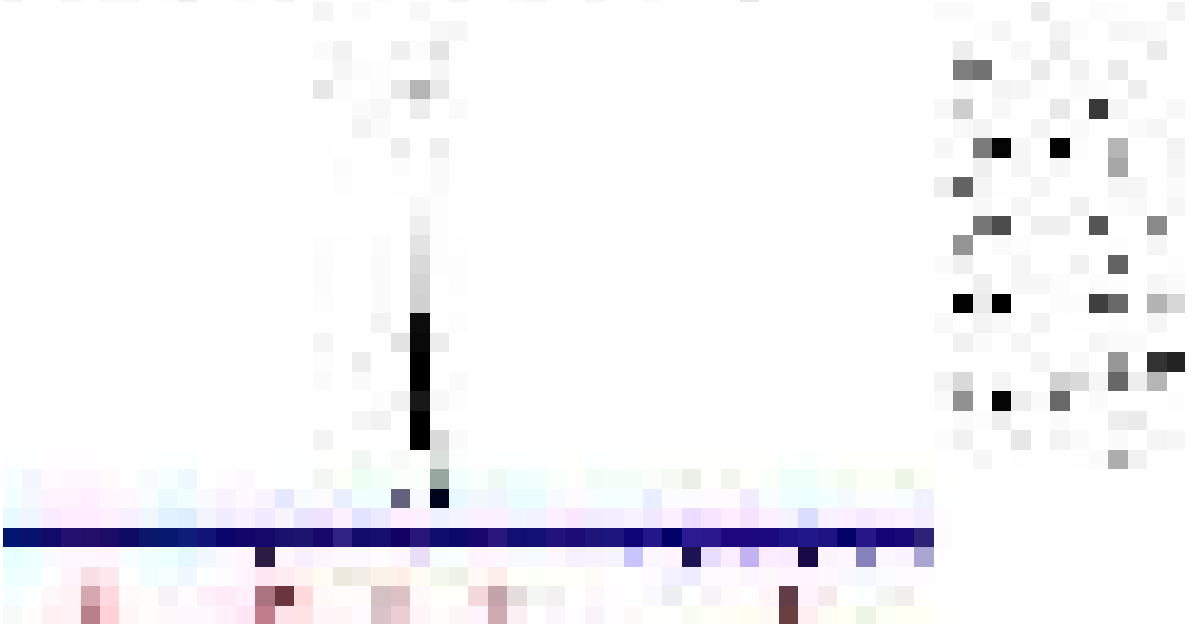


Figure (3-38) FTIR spectrum of compound (8C) **(Z)-N-(4-(biphenyl-4-yl)-3-phenylthiazol-2(3H)-ylidene)pyrimidin-2 amine**





- The NMR spectrums of compound 8C

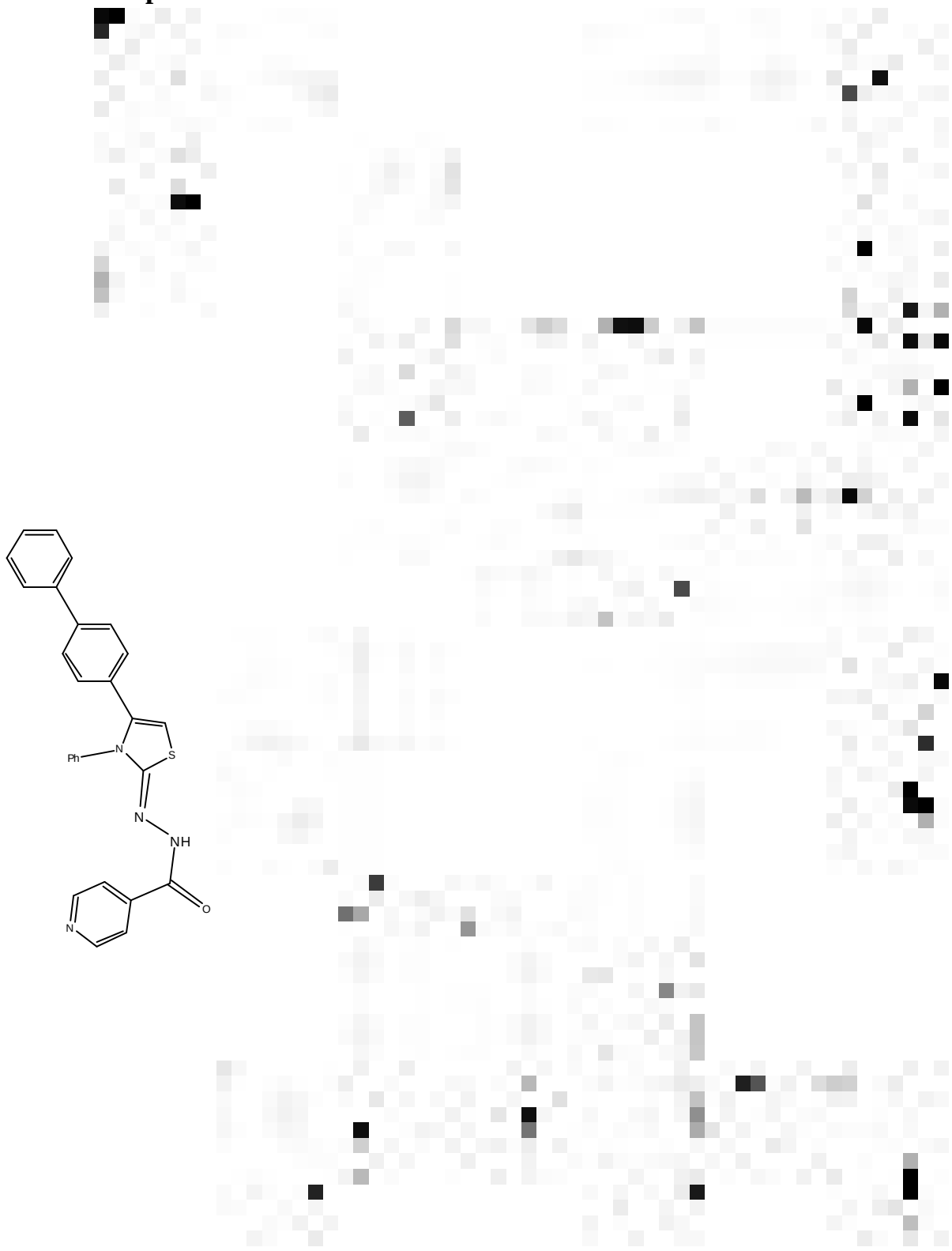
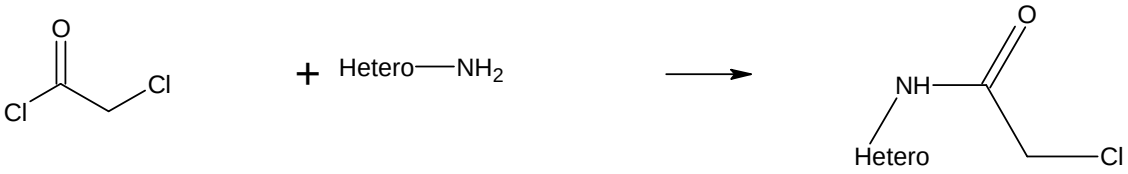


Figure (3-39) the FTIR of compound (8D)

3-10 preparation of 2-chloro-N-(hetero-2-yl)acetamide(10)



These compounds were prepared by the reaction of approparate heterocyclic amine with chloroacetylchloride in dry benzene the products identified by FTIR which show the disappearance of the starching NH_2 double band at 3450-3320cm^{-1} , appearance of C=O band of the amide at 1680 cm^{-1} , appearance of CH_2 band at 2980-and 2870 cm^{-1} , the formation of CH_2 straching vibration at 2980-2870$cm^{-1}$and the appearance of C-Cl bond at 740cm^{-1} the mechanism of this reaction is tetrahedral formation intermediate

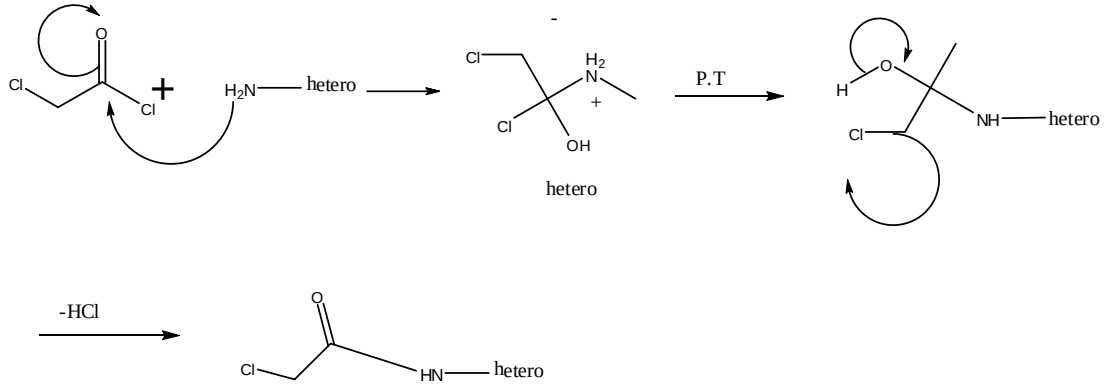


Table 3-10 the IR specteral data of acetamide derivatives

Compound No	Fig No.	C=O	N-H
10A	3-42	1693	3143
10B	3-43	1700	3280
10C	3-44	1700	3400
10D	3-45	1720	3300

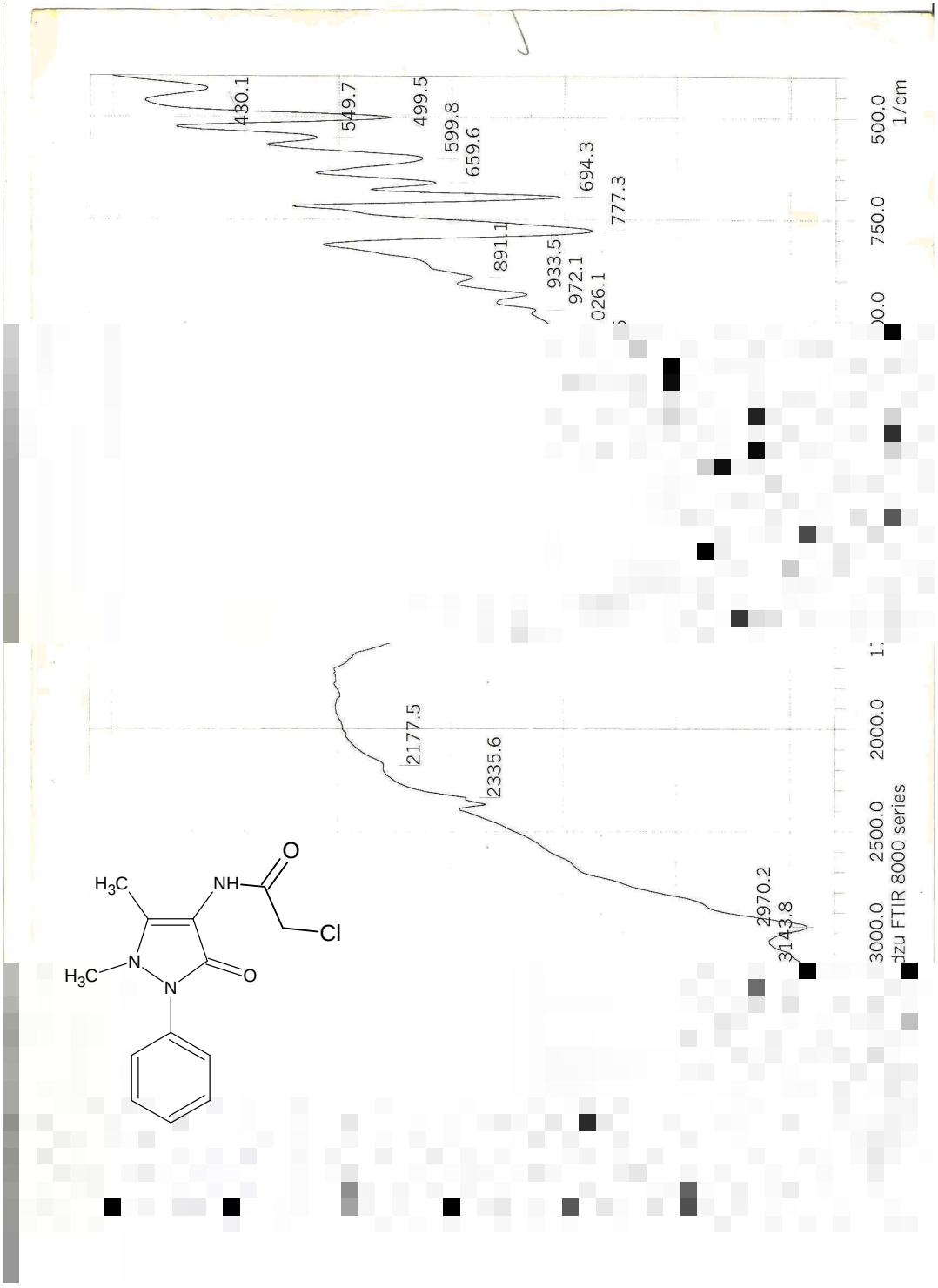


Figure (3-42) FTIR spectrum of compound (10A)

2-chloro-N-(2,3-dimethyl-5-oxo-1-phenyl-2,5-dihydro-1H-pyrazol-4-yl)acetamide

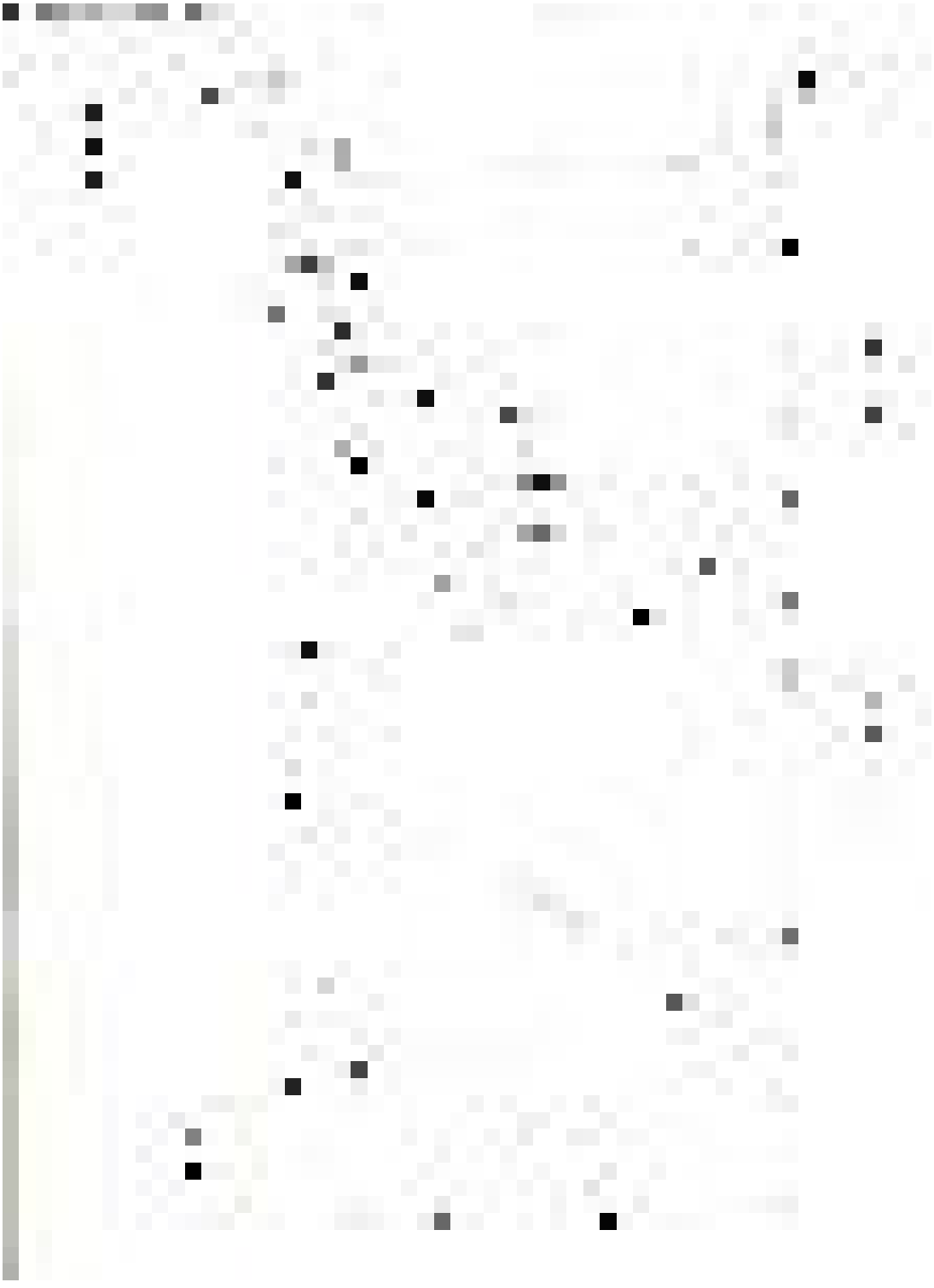


Figure (3-44) FTIR spectrum of compound (10C)

2-chloro-N-pyrazin-2-ylacetamide

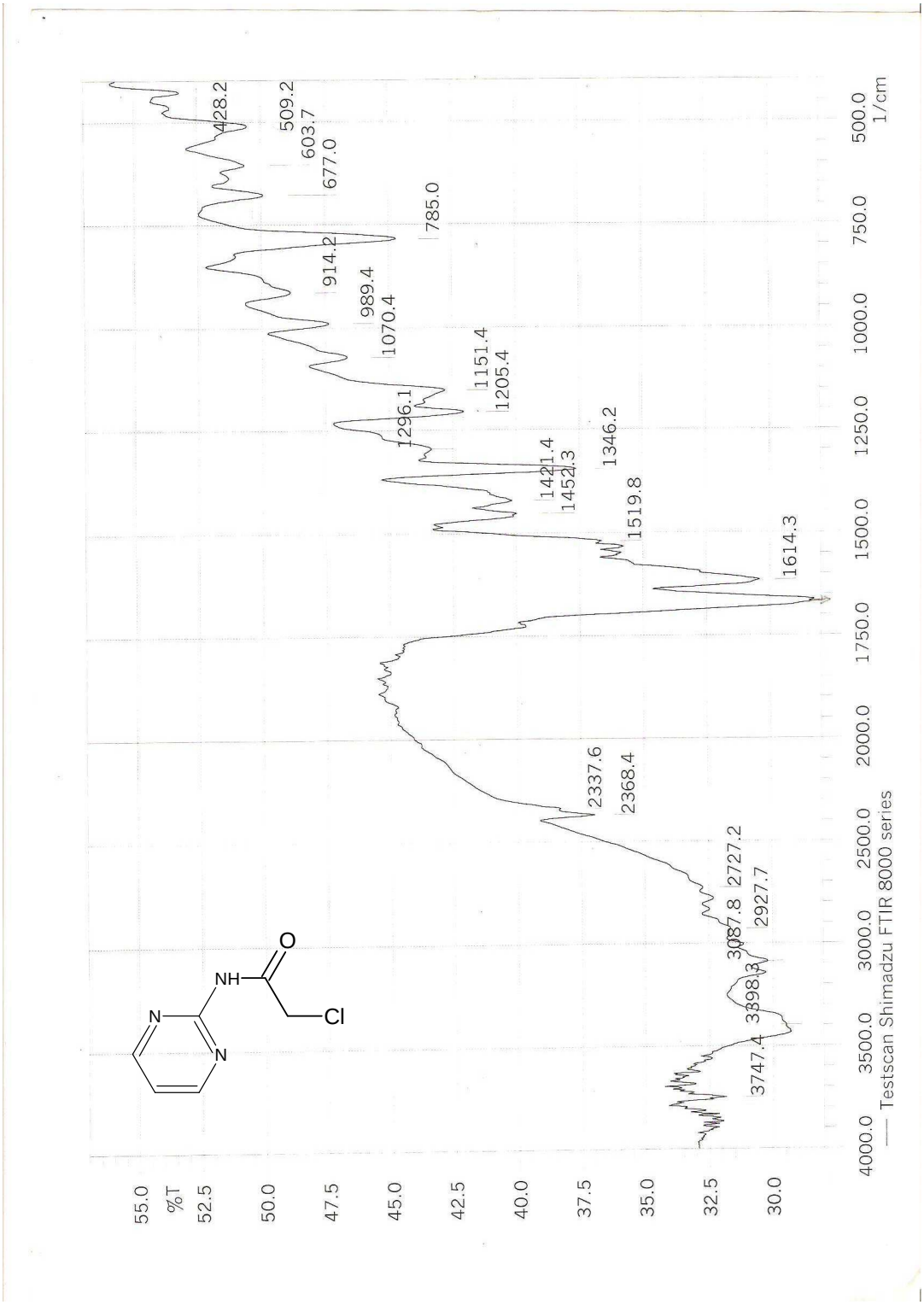


Figure (3-43) FTIR spectrum of compound (10B 2-chloro-N-pyrimidin-2-ylacetamide

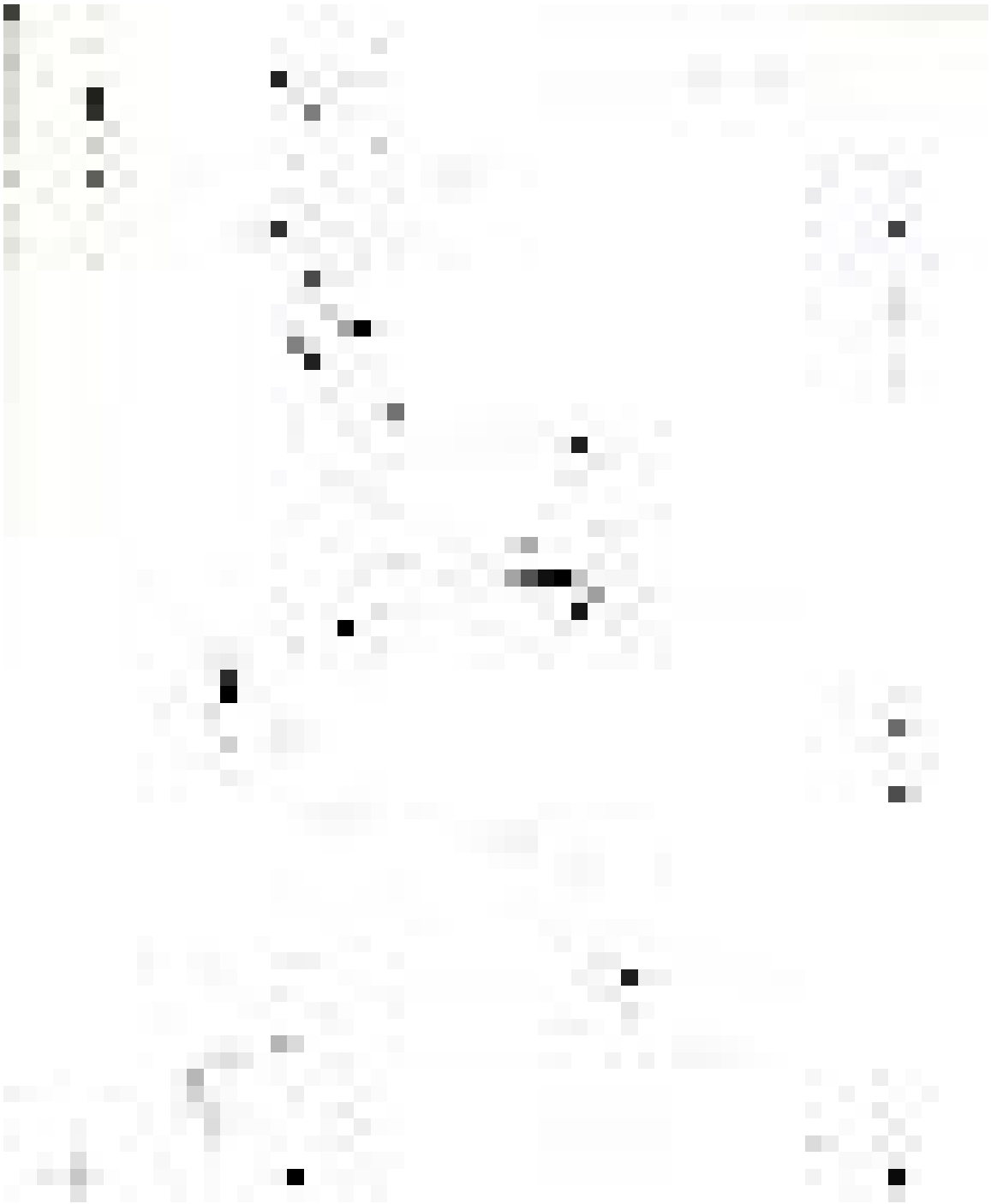
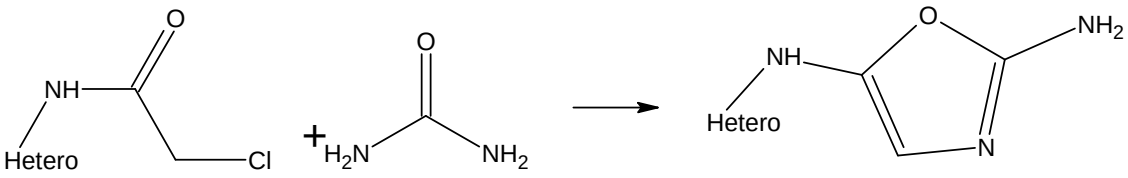


Figure (3-45) FTIR spectrum of compound (10D) N'-(2-chloroacetyl)isonicotinohydrazide

3-11 Preparation of N5-(hetero-2-yl)oxazole-2,5-diamine(11)

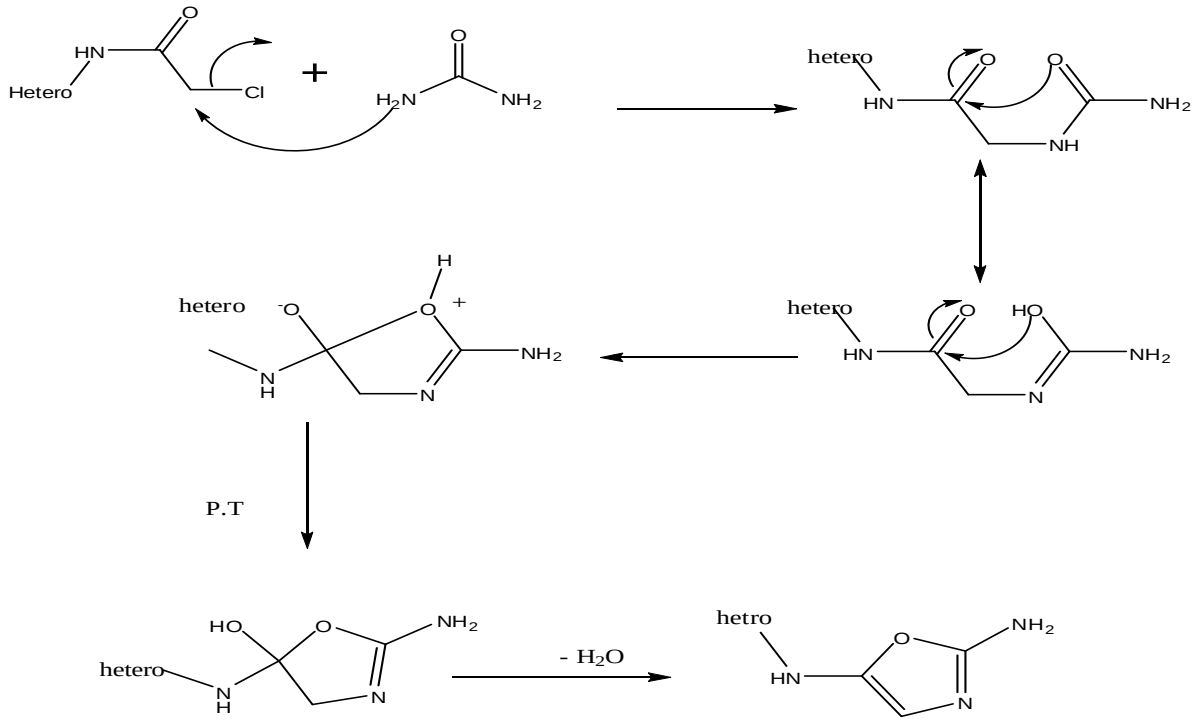


Oxazole derivatives were prepared by the reaction of chloroacetamide with urea in absolute ethanol the product identified by FTIR by the disappearance of amidic carbonyl band of urea at 1640cm-1 and the C=O band of the amide at 1690 cm-1 and appearance of C=N band of the ring at 1600 cm-1 and appearance of C-O band at 1100 cm-1

Table (3-11) the IR spectruml data of oxazole derivatives (11A-11C)

Compound No.	Y NH_2	υ NH	υ C=N oxazol	υ C-O
11A	3280-3320	3180	1610	1100
11B	3274-3300	3160	1612	1083
11C	3300-3400	3100	1620	1000

The proposed mechanism of this reaction



-

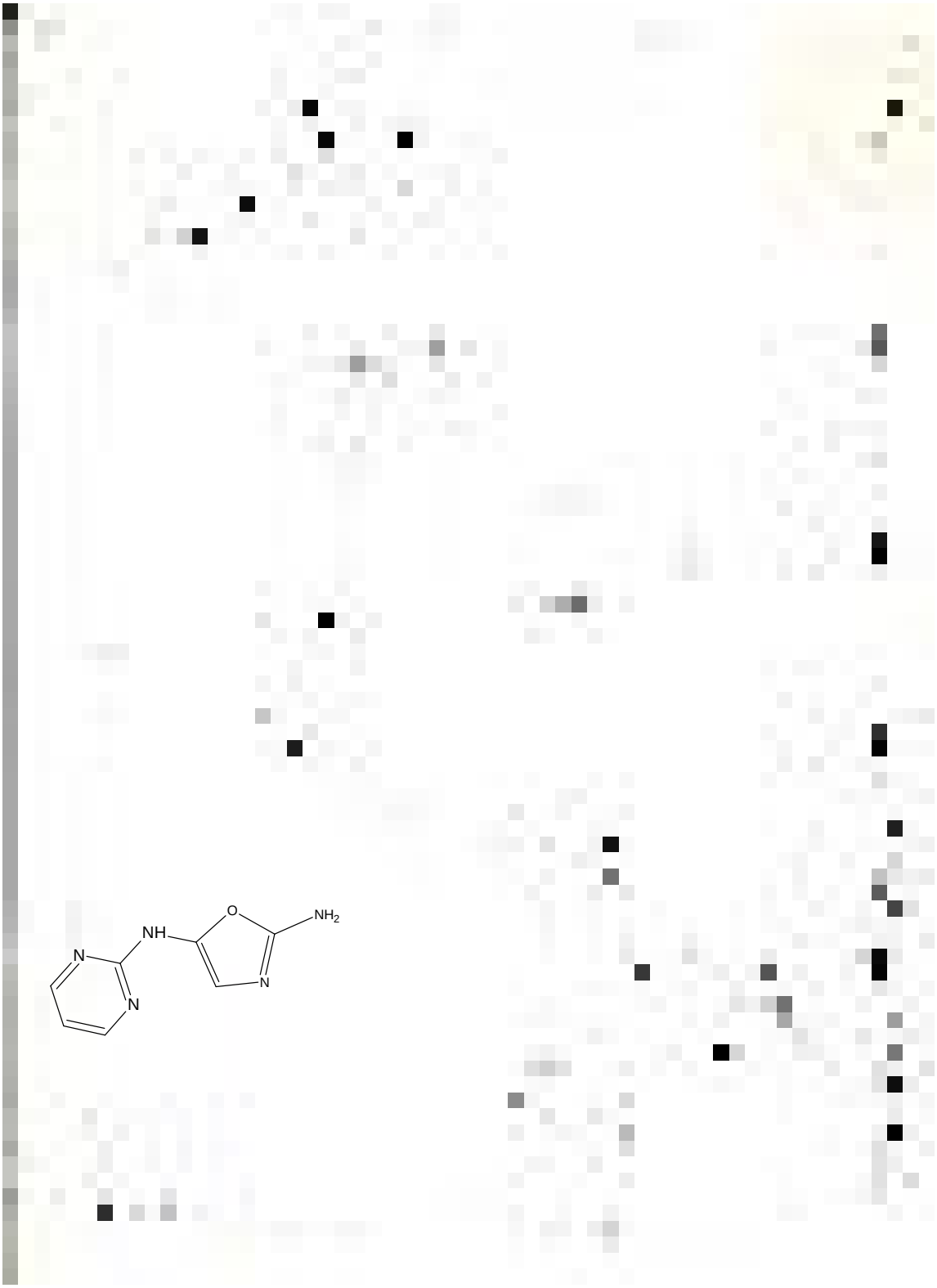


Figure (3-46) FTIR spectrum of compound 11B

N5-pyrimidin-2-yl-1,3-oxazole-2,5-diamine

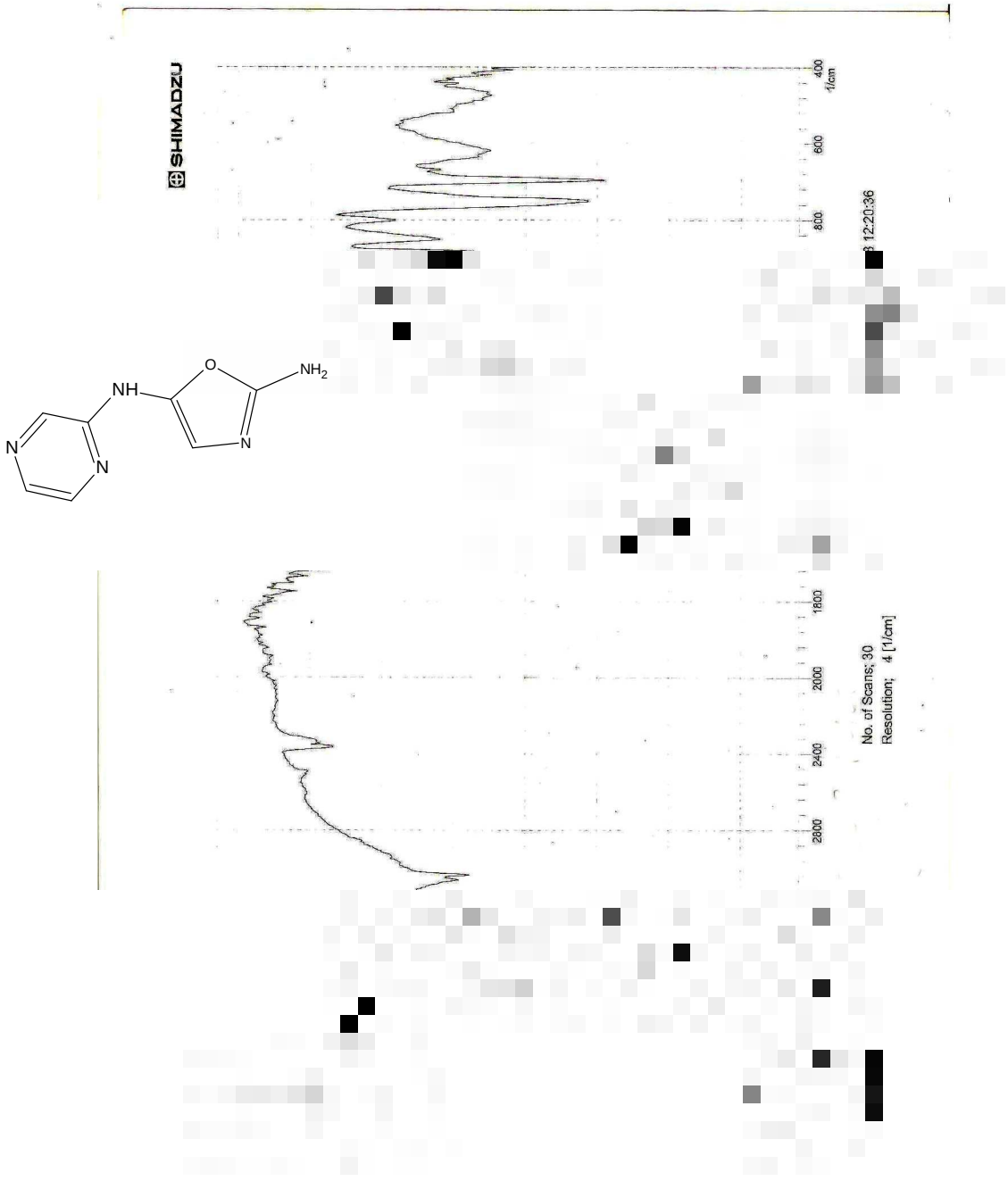


Figure (3-47) FTIR spectrum of compound (11C)

N5-pyrazin-2-yl-1,3-oxazole-2,5-diamine

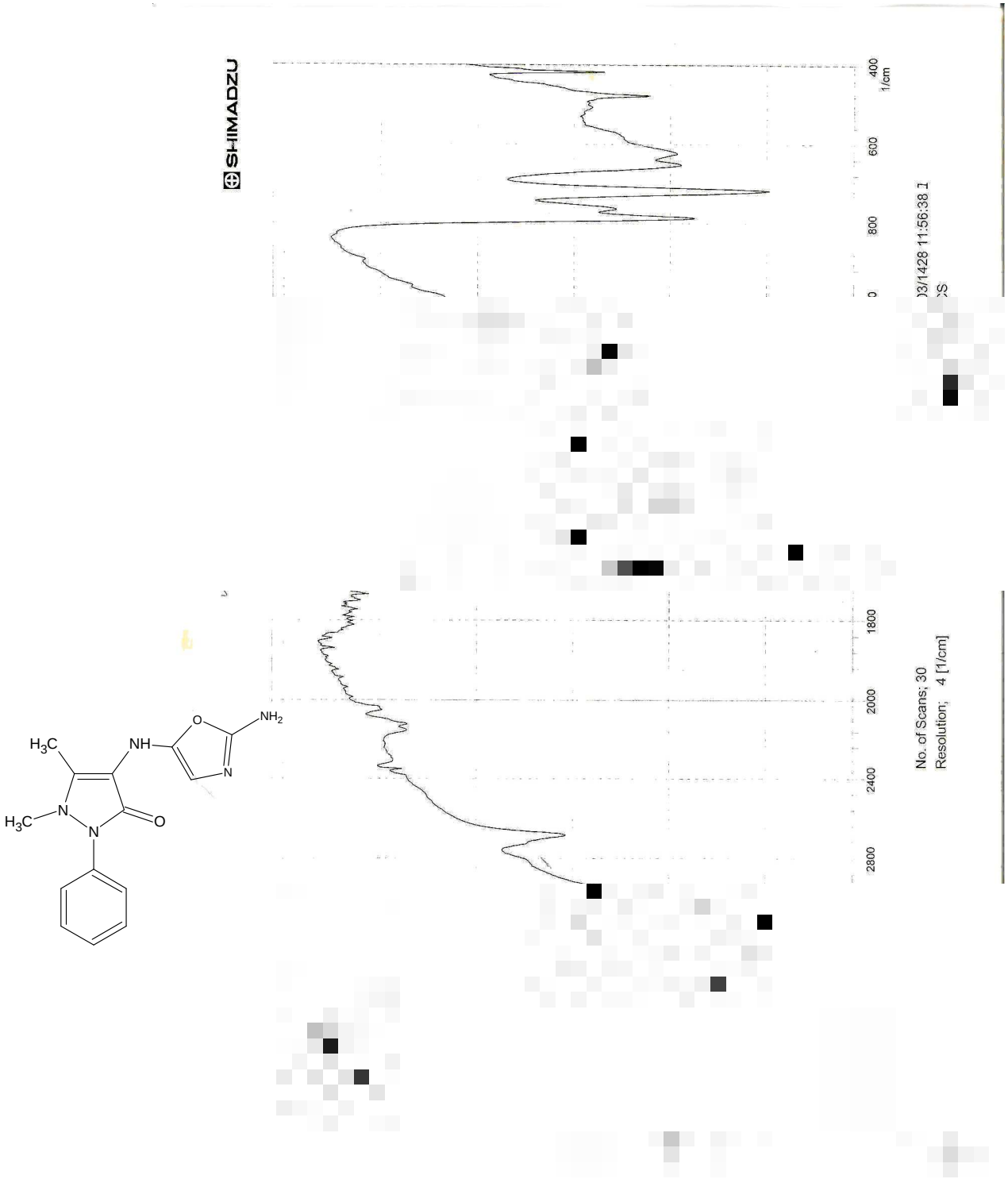
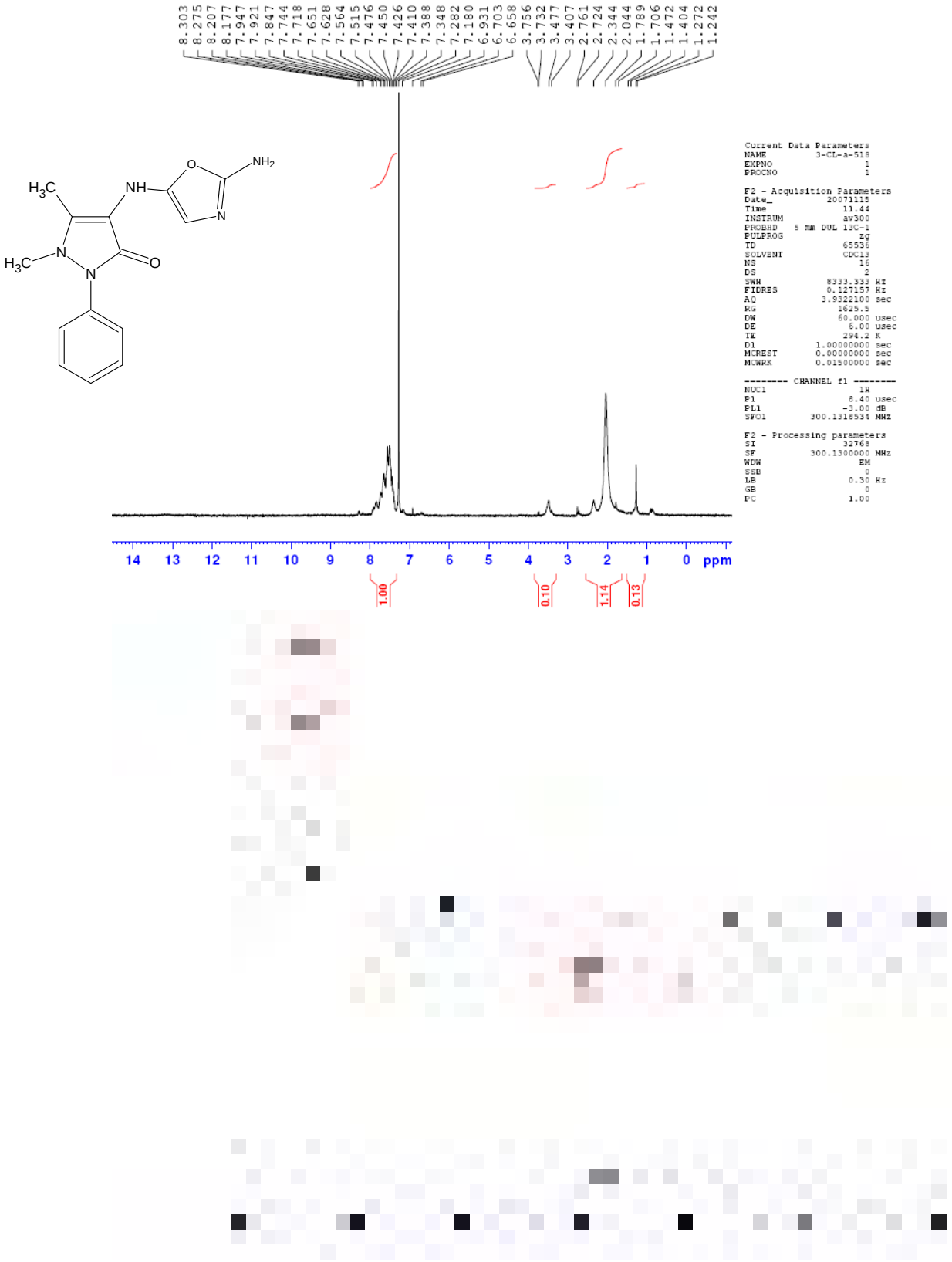


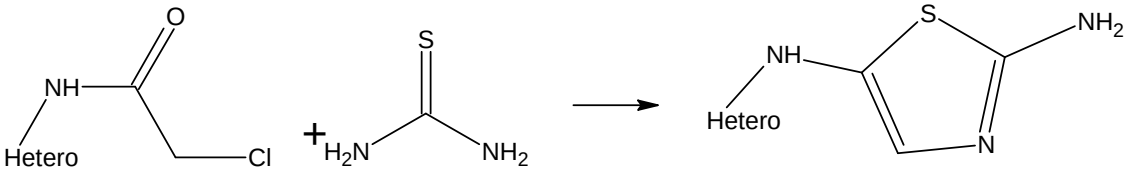
Figure (3-45) FTIR spectrum of compound 11A

4-[(2-amino-1,3-oxazol-5-yl)amino]-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one



The NMR spectrums of compound 11A

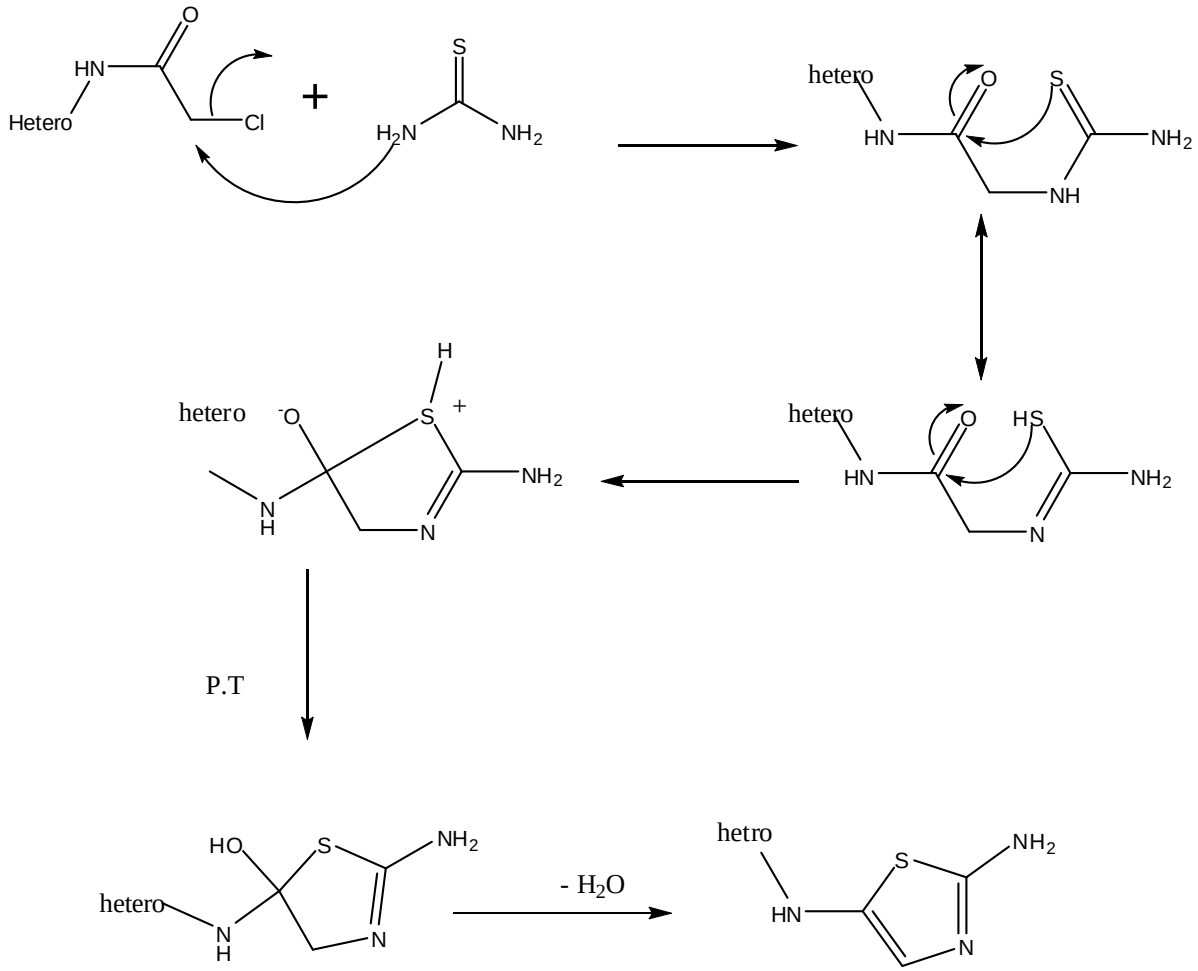
3-12 preparation of N5-(hetero-2-yl)thiazole-2,5-diamine(12)



Thiazole derivatives were prepared by the reaction of chloroacetamide derivatives with thiourea in absolute ethanol the product identified by FTIR which show the disappearance of C=O band of the acetamide at 1690cm^{-1} and appearance of C=N band at 1620 cm^{-1}

Table (3-12) the IR specteral data os thiazole derivatives (12A-12C)

Compound No.	υ NH_2	υ NH	υ C=N thiazol	C-H olifene
12A	3379-3274	3127	1612	3103
12B	3320-3240	3180	1610	3100
12C	3400-3280	3180	1630	3100


O
HN
Hetero
Cl
+
S
H2N
NH2
hetero
O
S
HN
NH2
NH
H
hetero
-O
S
+
NH2
N
H
N
hetero
O
HS
HN
NH2
N
P.T
HO
S
NH2
hetero
N
H
N
- H2O
hetro
S
NH2
HN
N

-

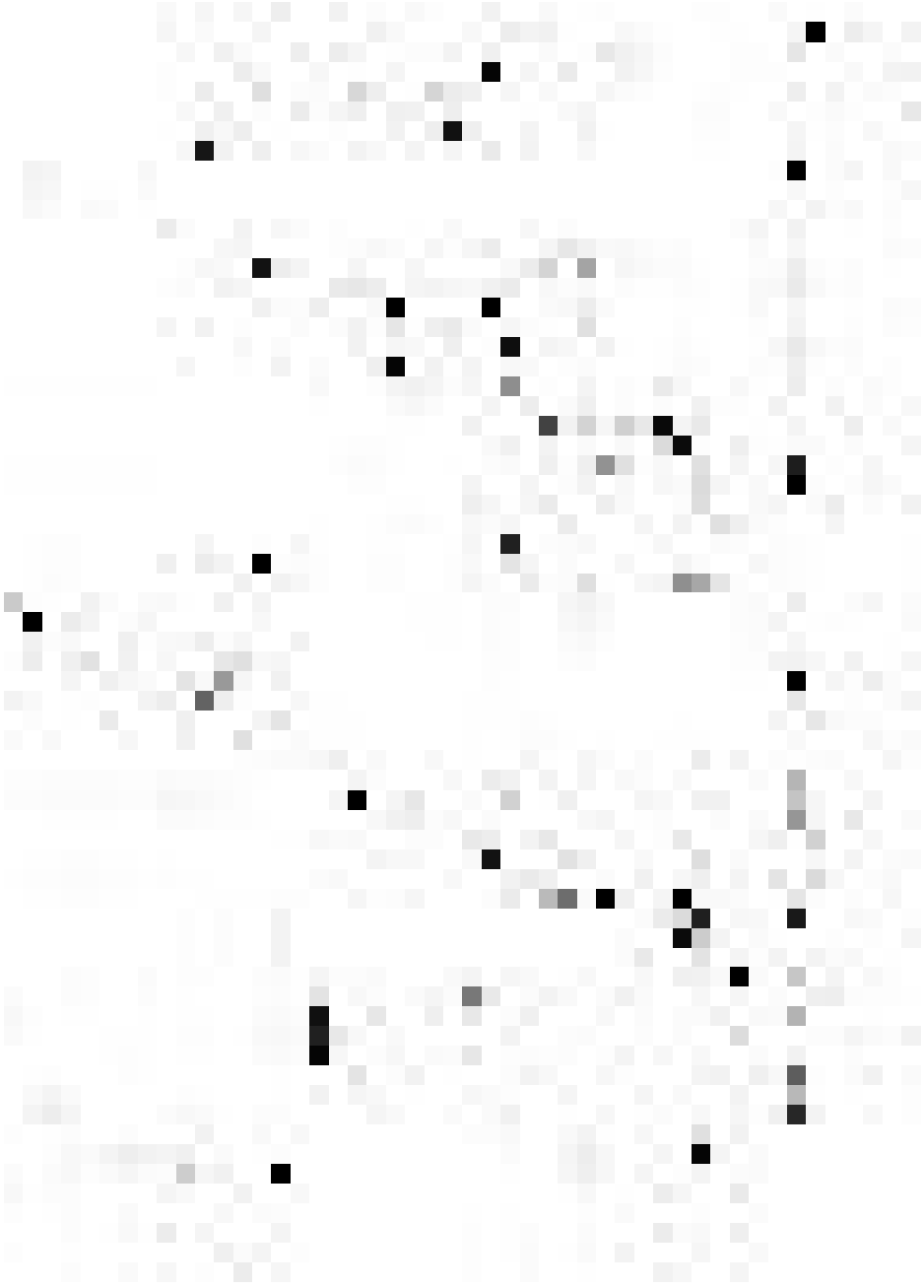


Figure (3-46) FTIR spectrum of compound (12A) 4-[(2-amino-1,3-thiazol-5-yl)amino]-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one

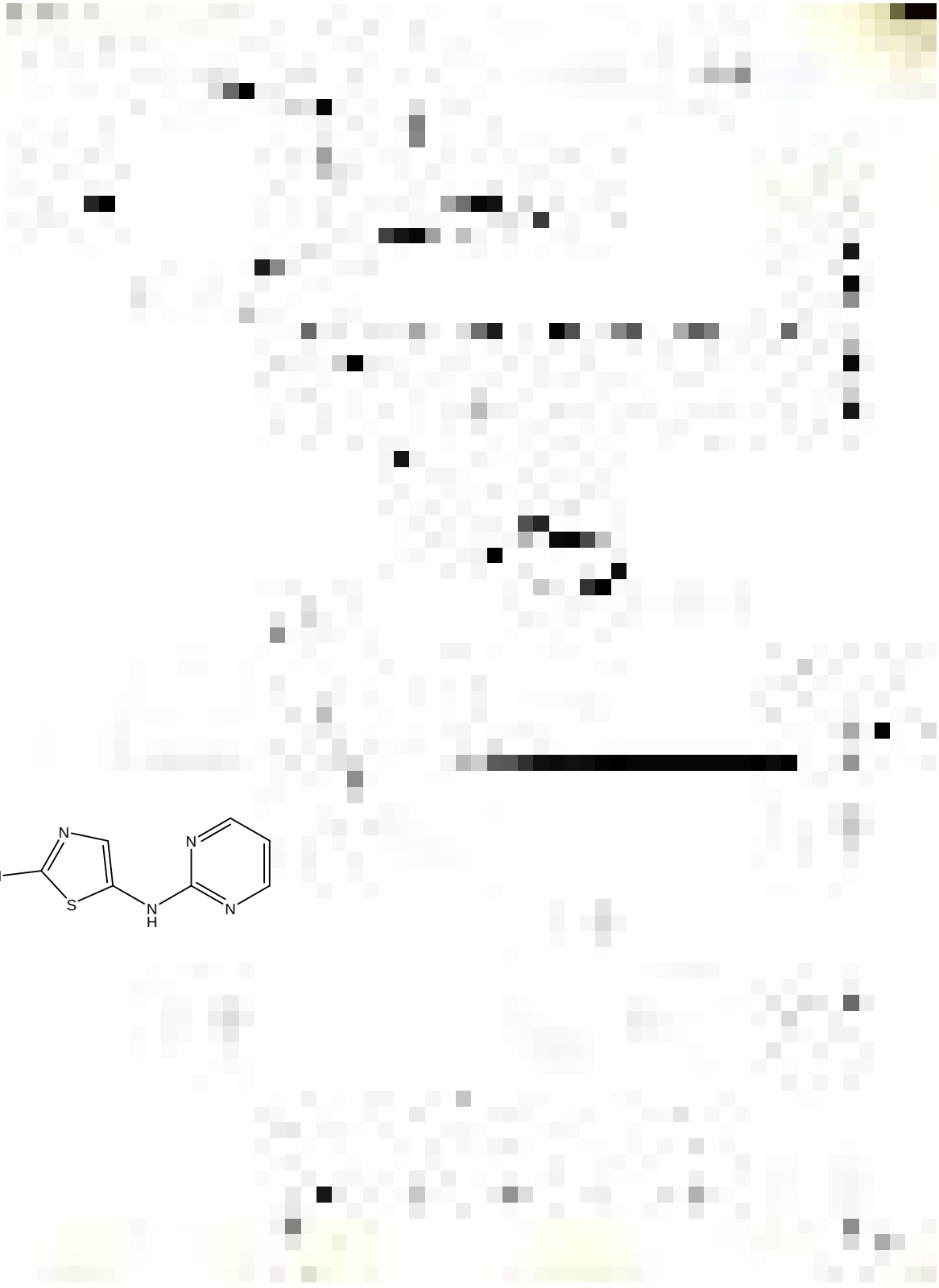
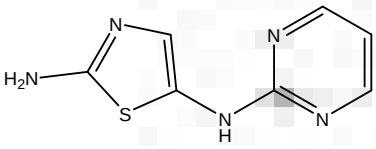


Figure (3-47) the FTIR of compound (12C)

N5-(pyrimidin-2-yl)thiazole-2,5-diamine


N
H2N
S
N
H
N
N

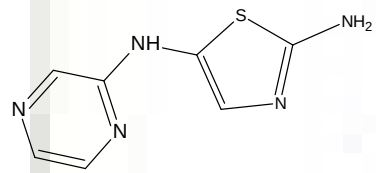
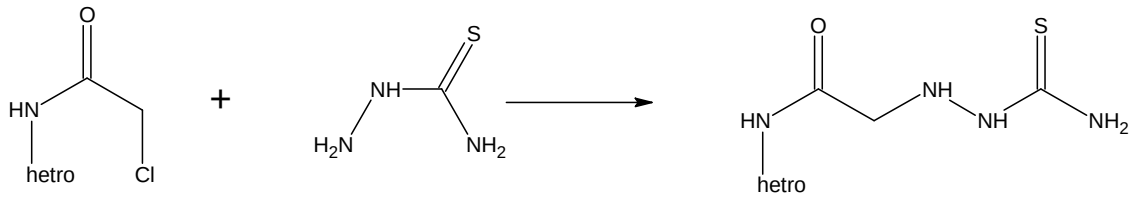


Figure (3-48) FTIR spectrum of compound (12B)

N5-(pyrazin-2-yl)thiazole-2,5-diamine

3-13 preparation of thiosemicarbazide derivatives (13)



Thiosemicarbazide derivatives prepared by reaction of thiosemicarbazide with chloroacetamide derivatives the product identified by FTIR by the appearance of NH_2 band symmetric & asymmetric at 3450-3320cm^{-1} and appearance of C=S band at 1200cm-1 and the tutamaric SH stretching band at 2600-2500cm^{-1}

The proposed mechanism of this this reaction is neucluphelic reaction.

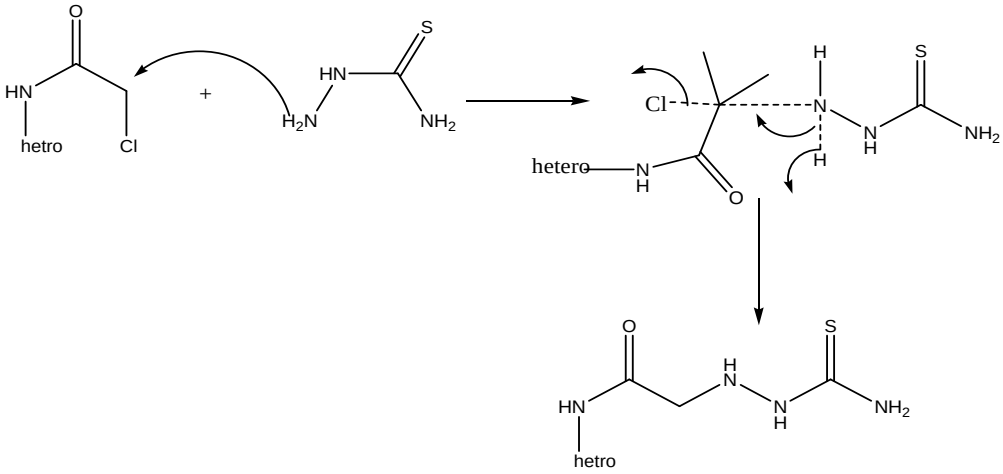


Table (3-13) the IR specteral data of thiosemicarbazide derivatives (13A-13D)

Compound No.	υ NH_2	υ C=O simecarbazide	υ C=S	υ S-H
13A	3380-3213	1682	1205	2650
13B	3400-3320	1660	1180	2600
13C	3400-3300	1660	1180	2600
13D	3400-3320	1650	1220	2650

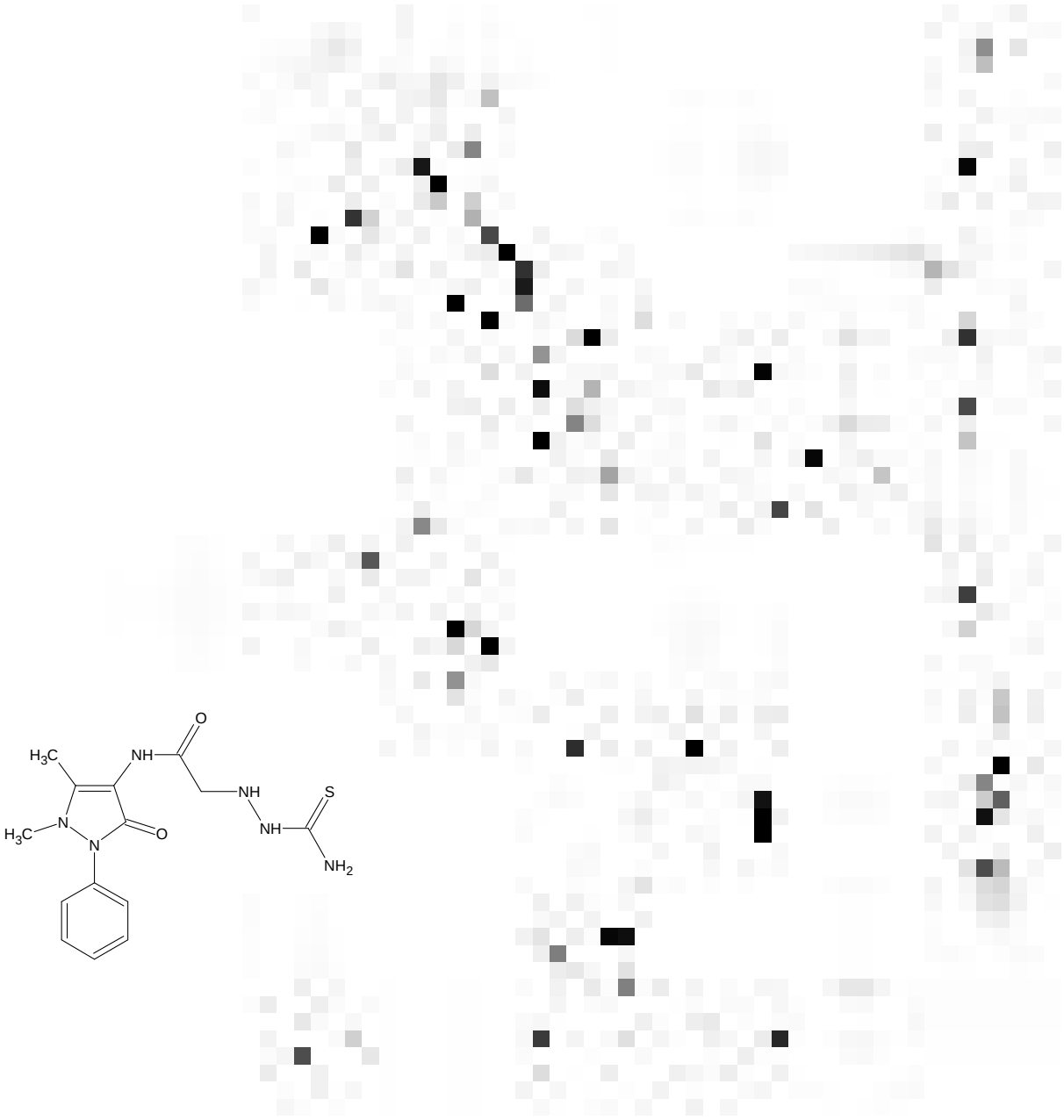


Figure (3-49) FTIR spectrum of compound (13A)

2-[2-(aminocarbonothioyl)hydrazino]-N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)acetamide

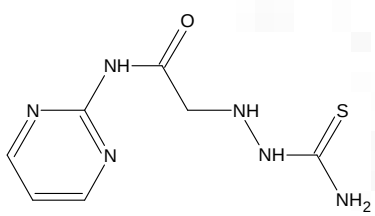


Figure (3-50) FTIR spectrum of compound (13B)

2-[2-(aminocarbonothioyl)hydrazino]-N-pyrimidin-2-ylacetamide

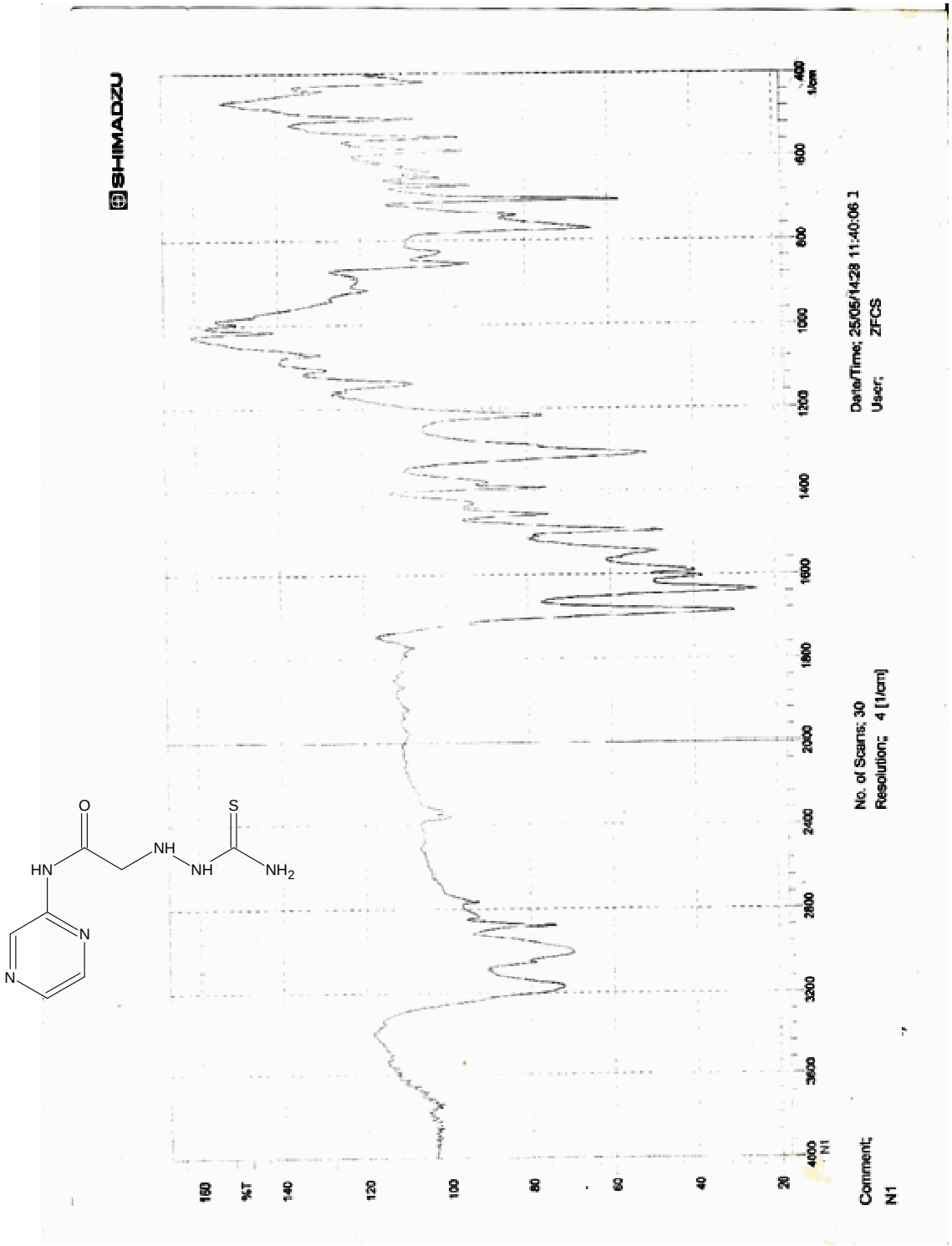


Figure (3-51) the FTIR spectrum of compound (13C)

2-[2-(aminocarbonothioyl)hydrazino]-N-pyrazin-2-ylacetamide

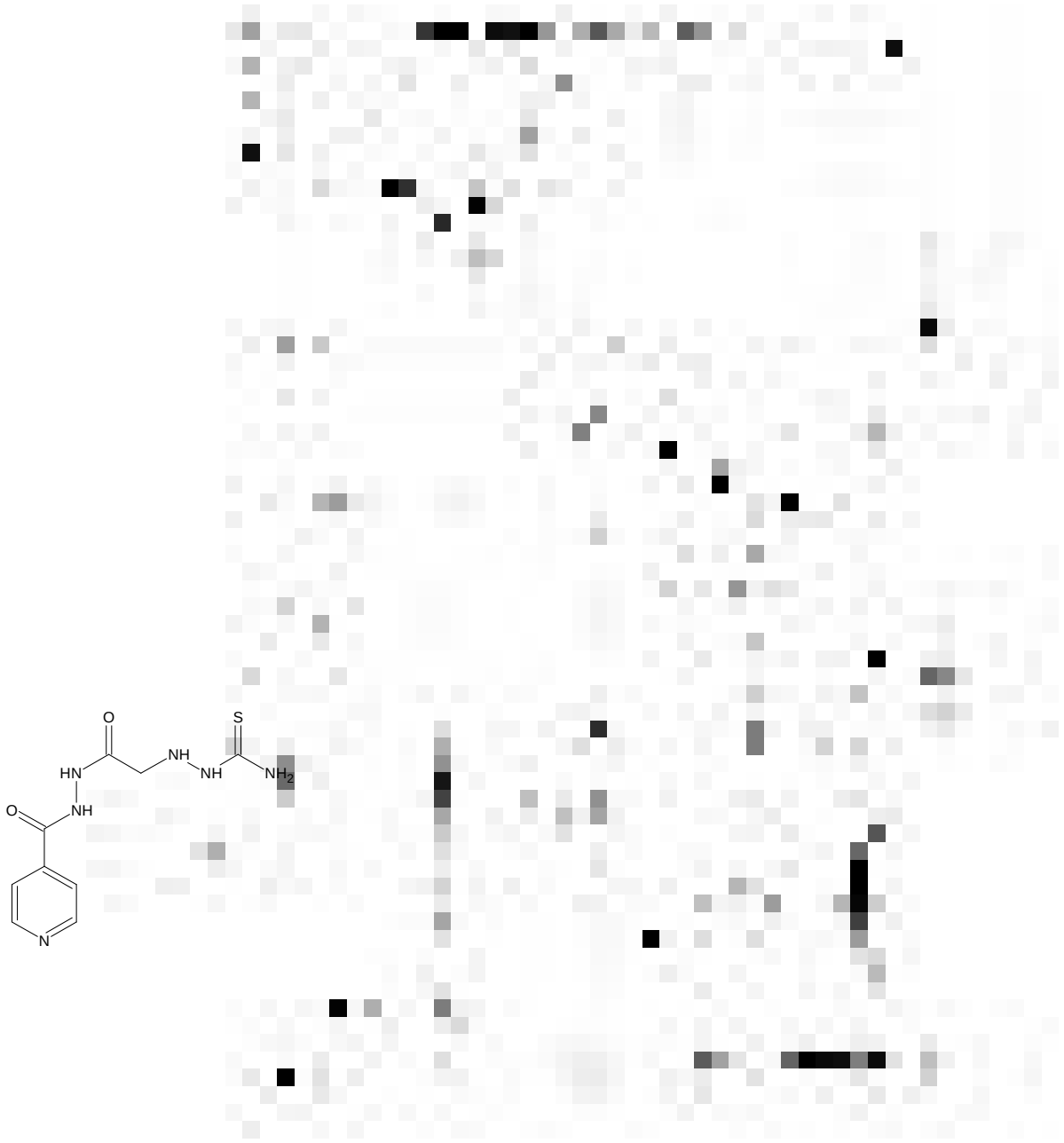
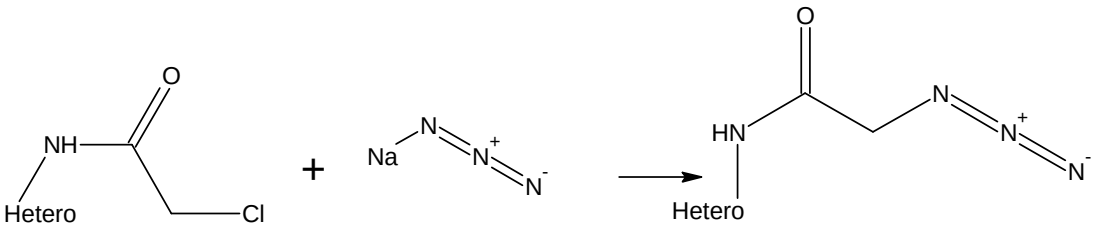


Figure (3-52) FTIR spectrum of compound (13D)

2-[2-(2-isonicotinoylhydrazino)-2-oxoethyl]hydrazinecarbothioamide

3-14 preparation of 2-azido-N-(hetero-2-yl)acetamide(14)



Azide compounds were prepared by the reaction of chloroacetamide with sodium azide in absolute ethanol the product identified by FTIR which show the appearance of azide stretching band at 2130-2200 cm^{-1}

The proposed mechanism of this reaction is

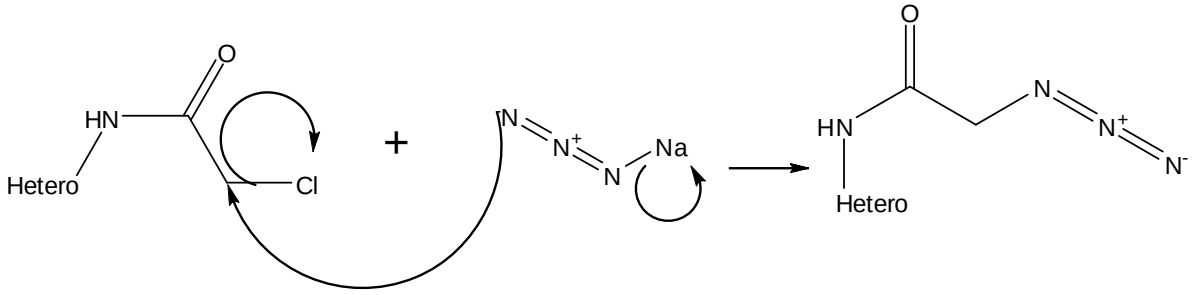


Table (3-14) IR spectruml data of azide derivatives(14A-14D)

Compound No	υ N_3 strch.	υ C=C aromatic	υ NH	υ C=O
14A	2098	1533-1431	3205	1697
14B	2114	1515-1439	3382	1681
14C	2108	1537-1458	3408	1660
14D	2090	1520-1440	3200	1650

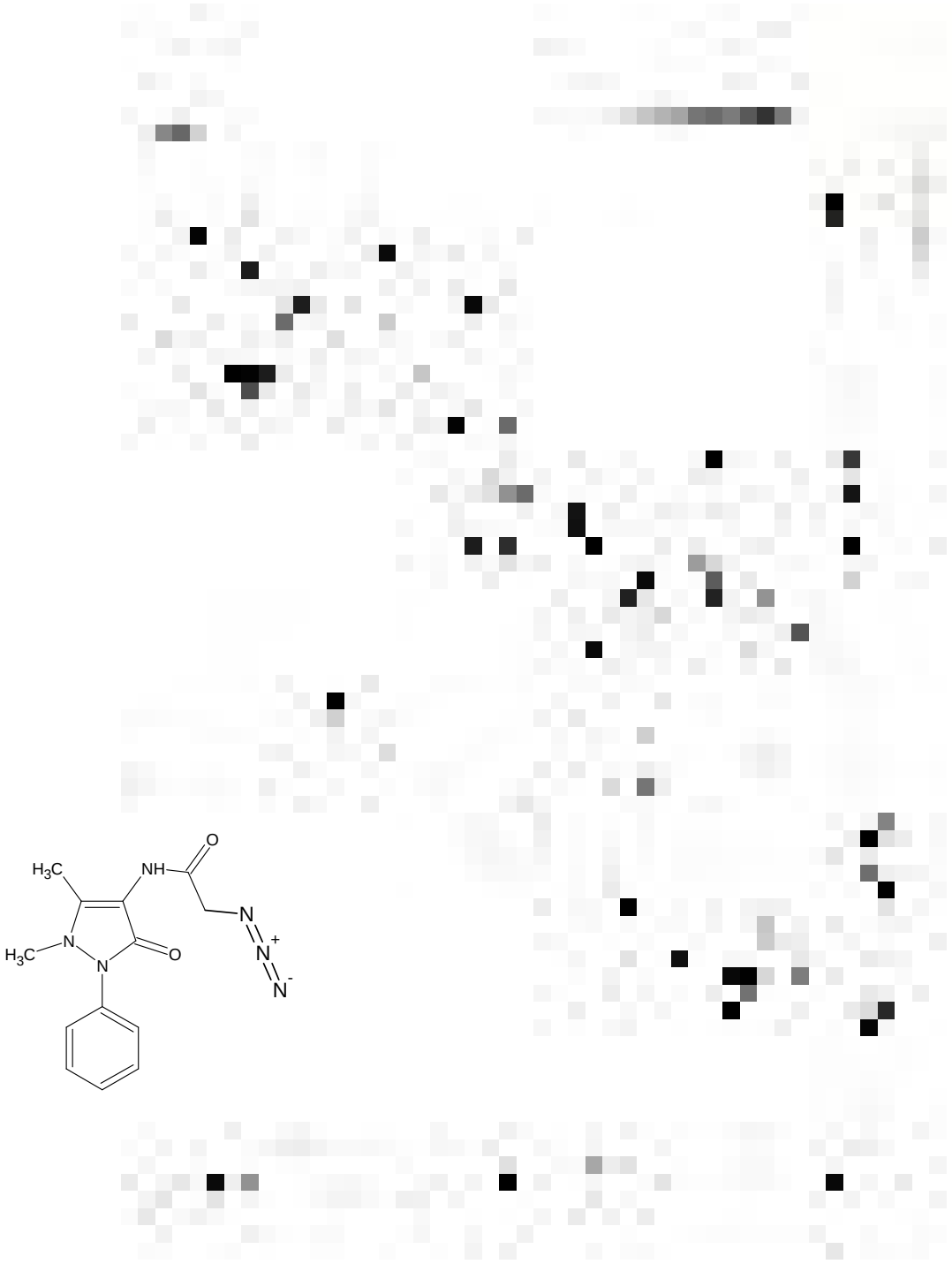


Figure (3-53) FTIR spectrum of compound (14A) 2-azido-N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)acetamide

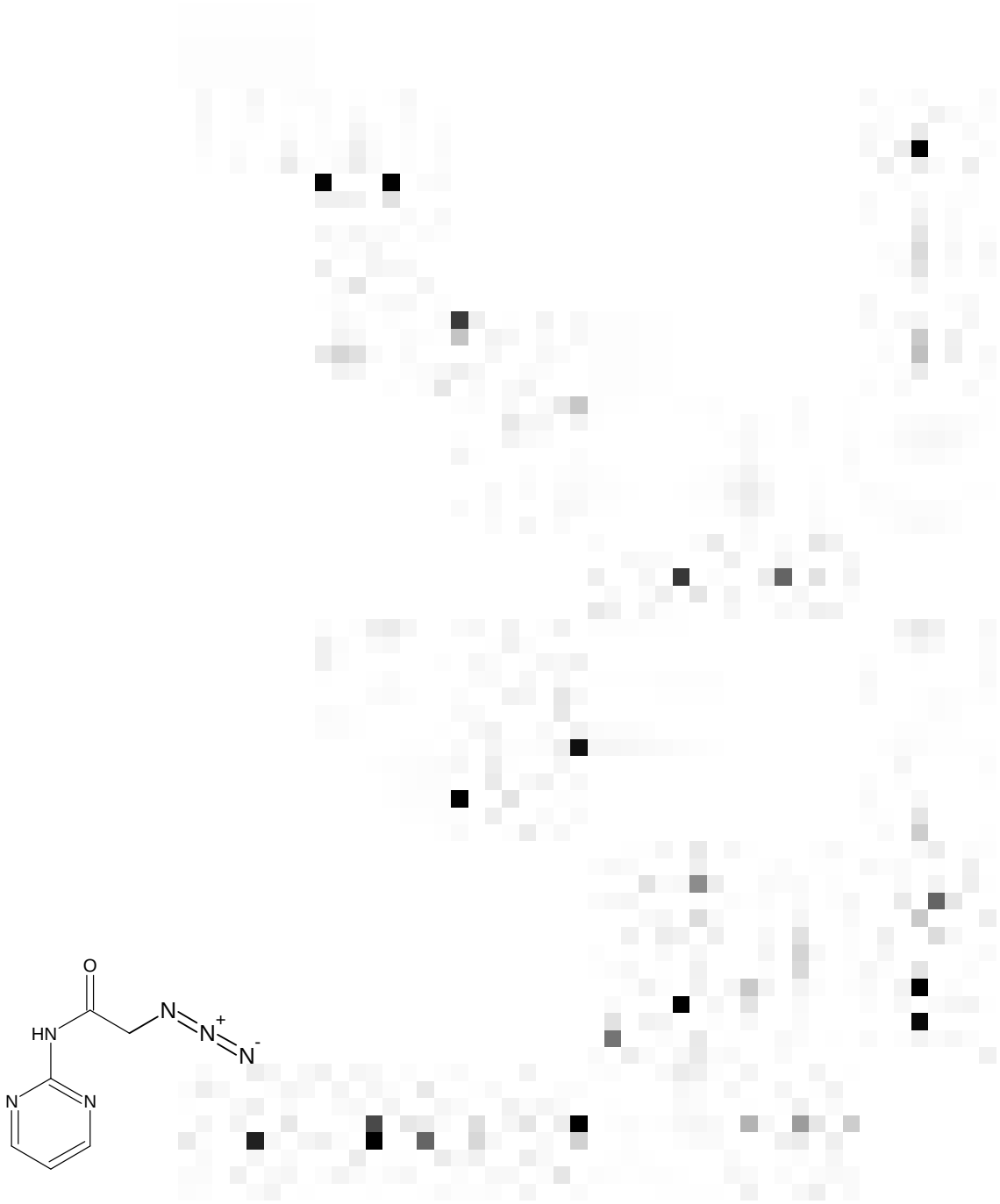


Figure (3-54) FTIR spectrum of compound (14B)

2-azido-N-pyrimidin-2-ylacetamide

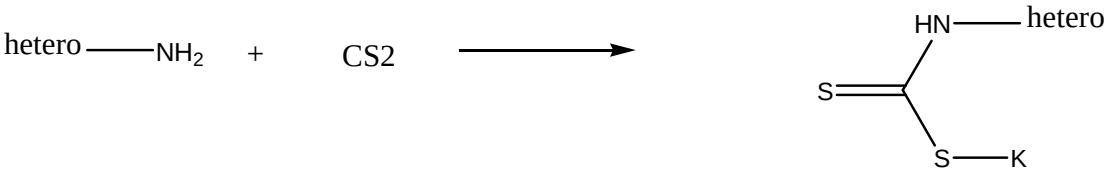
Figure (3-55) FTIR spectrum of compound (14C)

2-azido-N-pyrazin-2-ylacetamide

Figure (3-56) FTIR spectrum of compound (14D)

N'-(2-azidoacetyl)isonicotinohydrazide

3-15 preparation of potassium hetero-2-ylcarbamodithioate(15)



Carbodithionate compounds prepared by the reaction of the heteroamines with carbon disulfide in presence of alkali the product identified bydisappearance of NH_2 scratching at 3450-3320cm-1 and appearance of C=S band at 1200cm^{-1} . The proposed mechanism of this reaction is

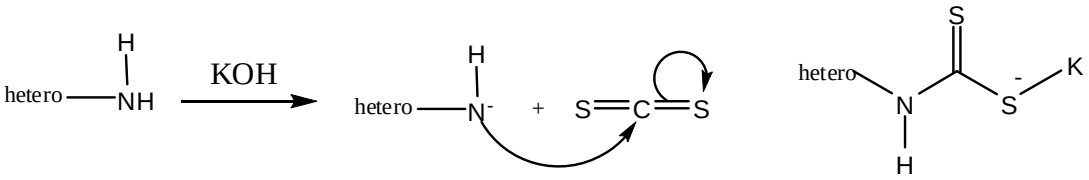


Table (3-15) the IR specteral data of dithiocarbamate (15A-15)

Compound No	υN-H	υC=N ring	υC=C aromatic	υC=S
15A	3220	1610	1560-1420	1220
15B	3240	1600	1570-1450	1220
15C	3280	1600	1520-1473	1220

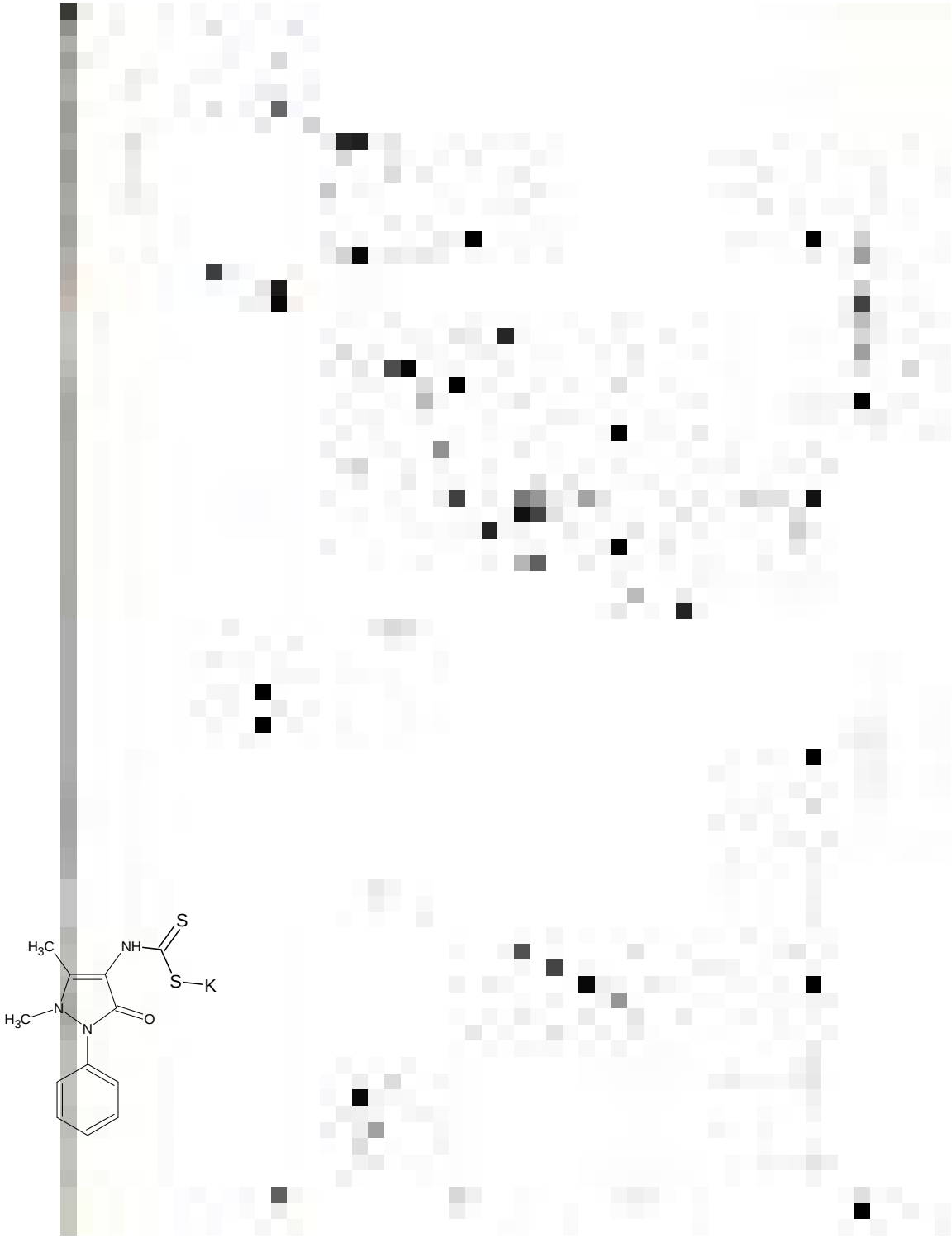


Figure (3-57) FTIR spectrum of compound (15A) potassium (1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)dithiocarbamate

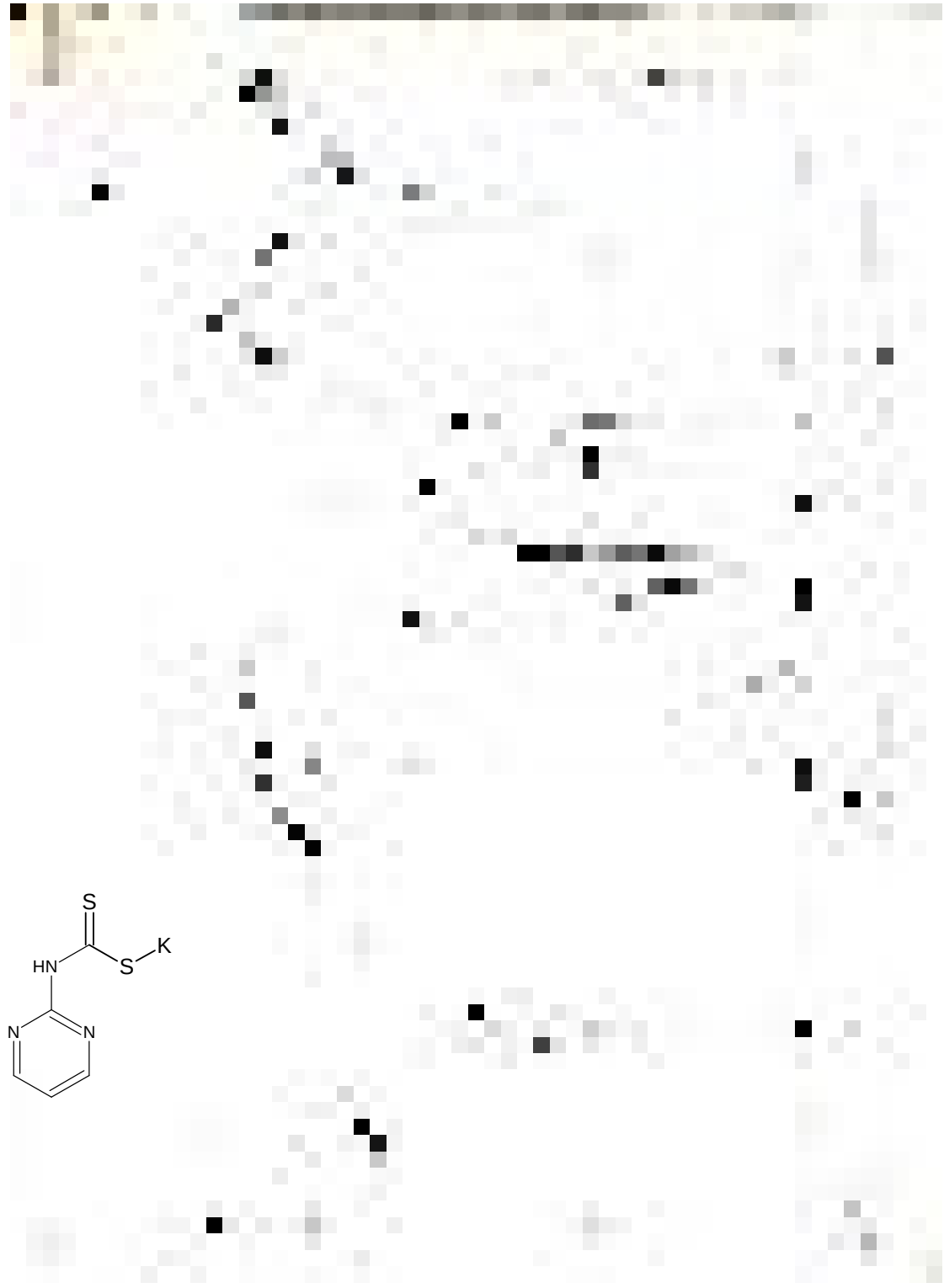


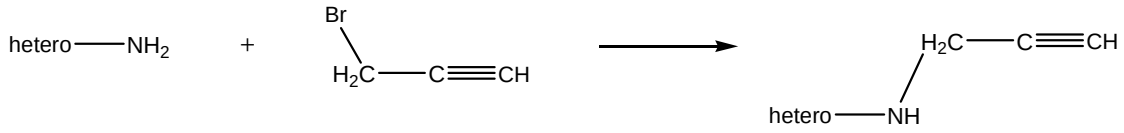
Figure (3-58) FTIR spectrum of compound (16B)

potassium pyrimidin-2-yldithiocarbamate

Figur (3-59) the FTIR of compound (15C)

potassium isoniazid-2-yldithiocarbamate

3-16 Preparation of N-prop-2-ynylhetero-2-amine(16)



Actylenic compounds prepare red by the reaction of propargyl bromide with hetero amines in presence of alkali (trimethyl amine or KOH) the products identified by FTIR by the appearance of actylenic(C-C) stretching band at 2200-2100cm^{-1} and disappearance of NH_2 stretching band at 3450-3320 cm-1 and appearance of C-H acetylenic at 3330-3310cm^{-1} .

The mechanism of this reaction is SN^2

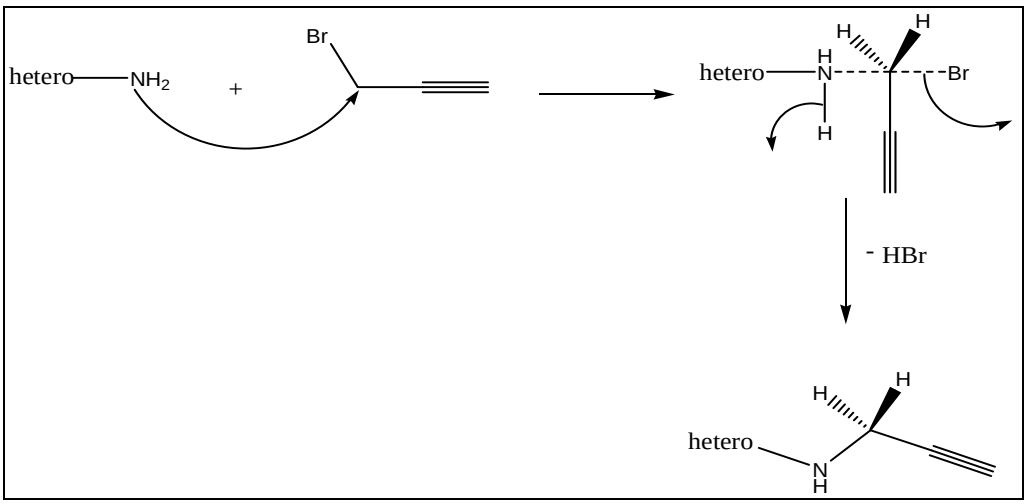


Table (3-16) the IR specteral dataof acetylinic compound(16B-16D)

Compound No	C-H acetylenic	C-C acetylenic	N-H
16B	3300	2100	3190
16C	3320	2080	3180
16D	3280	2120	3200

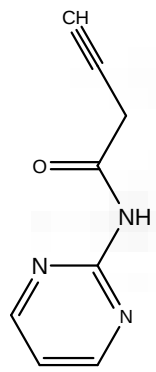


Figure (3-59) FTIR spectrum of compound (16B)

N-pyrimidin-2-ylbut-3-ynamide

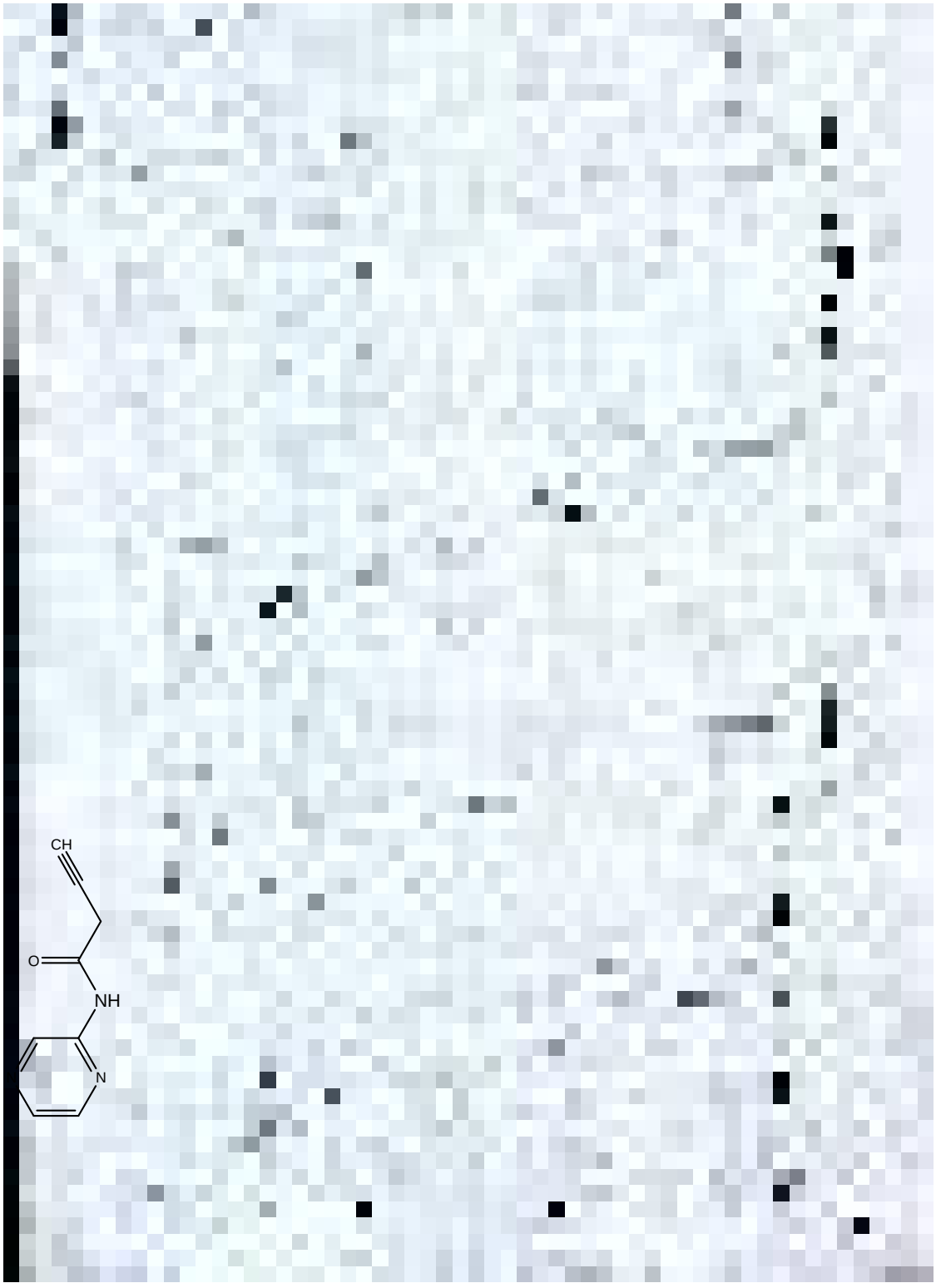


Figure (3-60) FTIR spectrum of compound (16C)

N-pyrazin-2-ylbut-3-ynamide

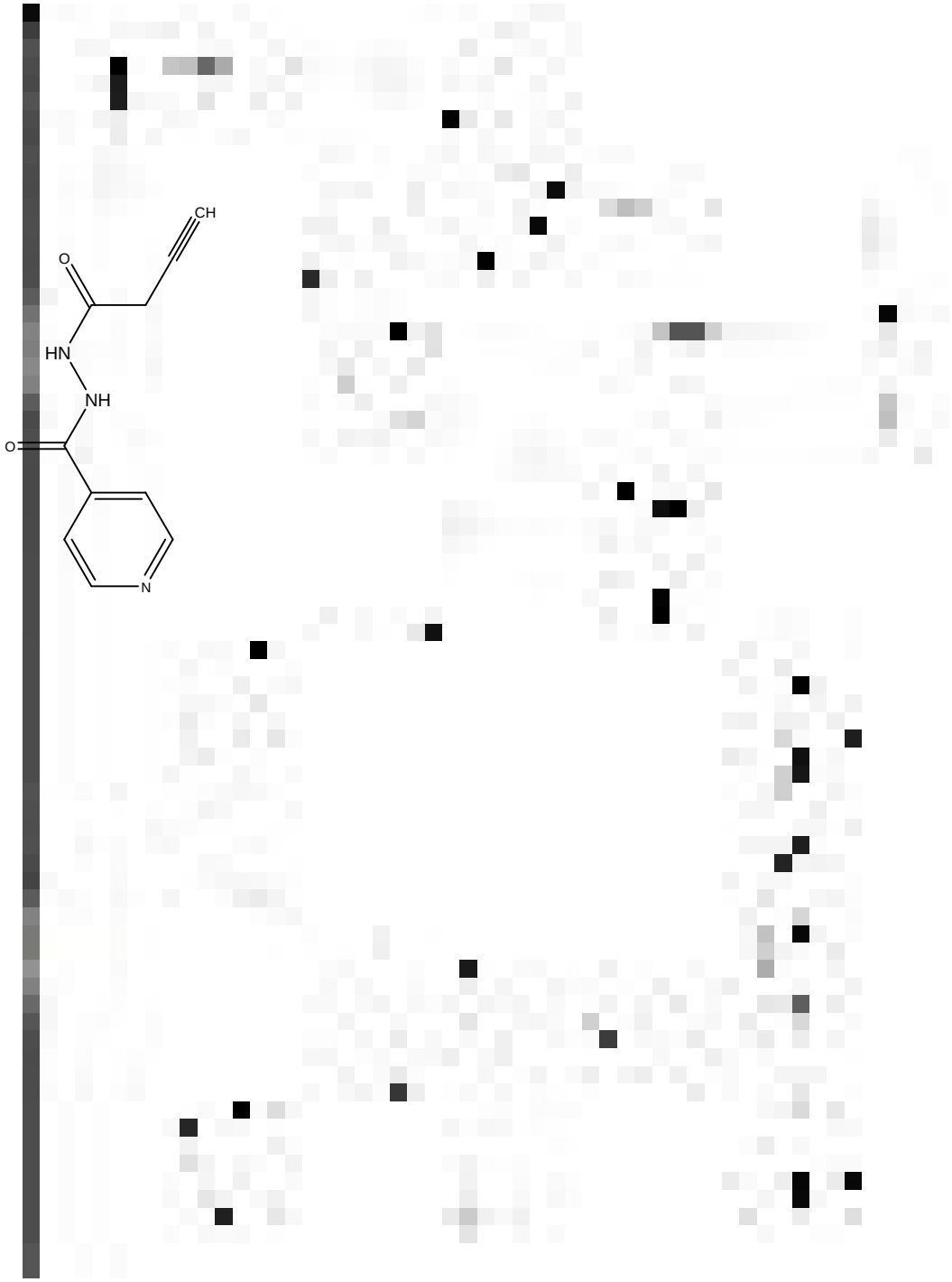
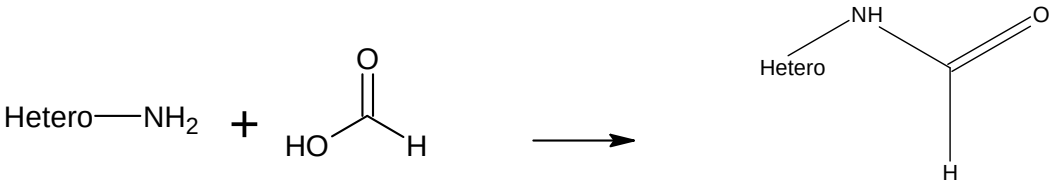


Figure (3-61) FTIR spectrum of compound (16D)

N'-but-3-ynoylisonicotinohydrazide

3-17 preparation of hetero-2-yl formamide(17)



formamide derivatives prepared by the reaction of hetero amine with formic acid the product identified by the TLC and FTIR spectrum by the appearance of the amidic carbonyl at 1675-1790 cm^{-1} and disappearance of NH_2 double band at 3450- 3320 cm^{-1} and the disappearance of O- H stretching vibration at 3500-3200 as broad band of the formic acid .the proposed mechanism for this reaction is

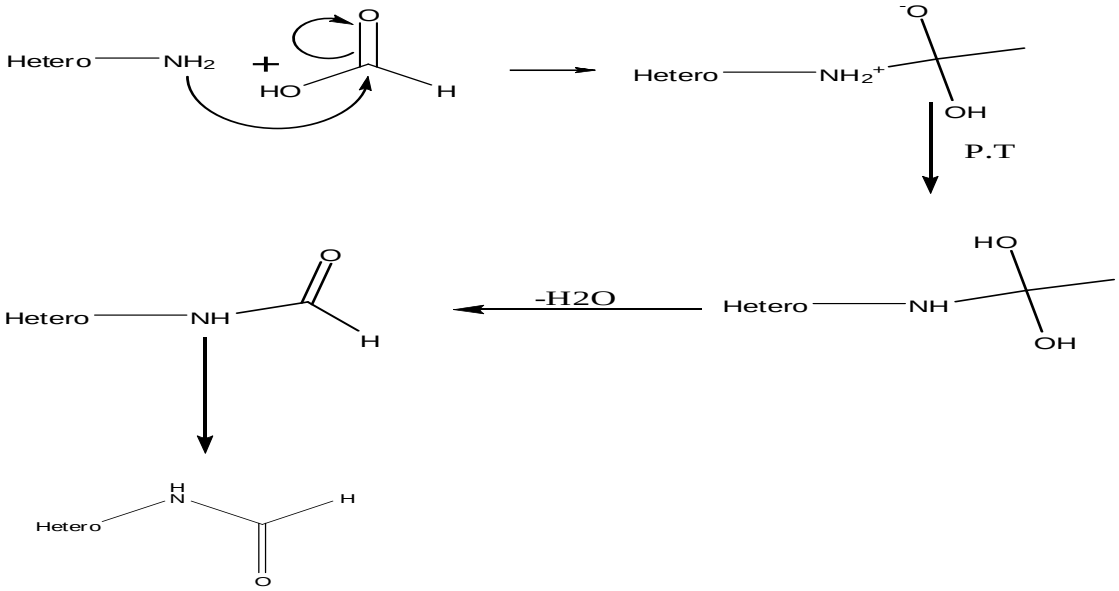


Table (3-17) IR spectruml data of formamide derivatives (17A-17D)

Compound No.	υ C=O str.cm^{-1}	υC=C aromatic	υ NH	υ CH formic
17 A	1680	1500-1400	3190	2780-2840
17 B	1690	1541-1408	3200	2800-2820
17 C	1680	1560-1420	3180	2780-2840
17D	1675	1520-1410	3200	2780-2820

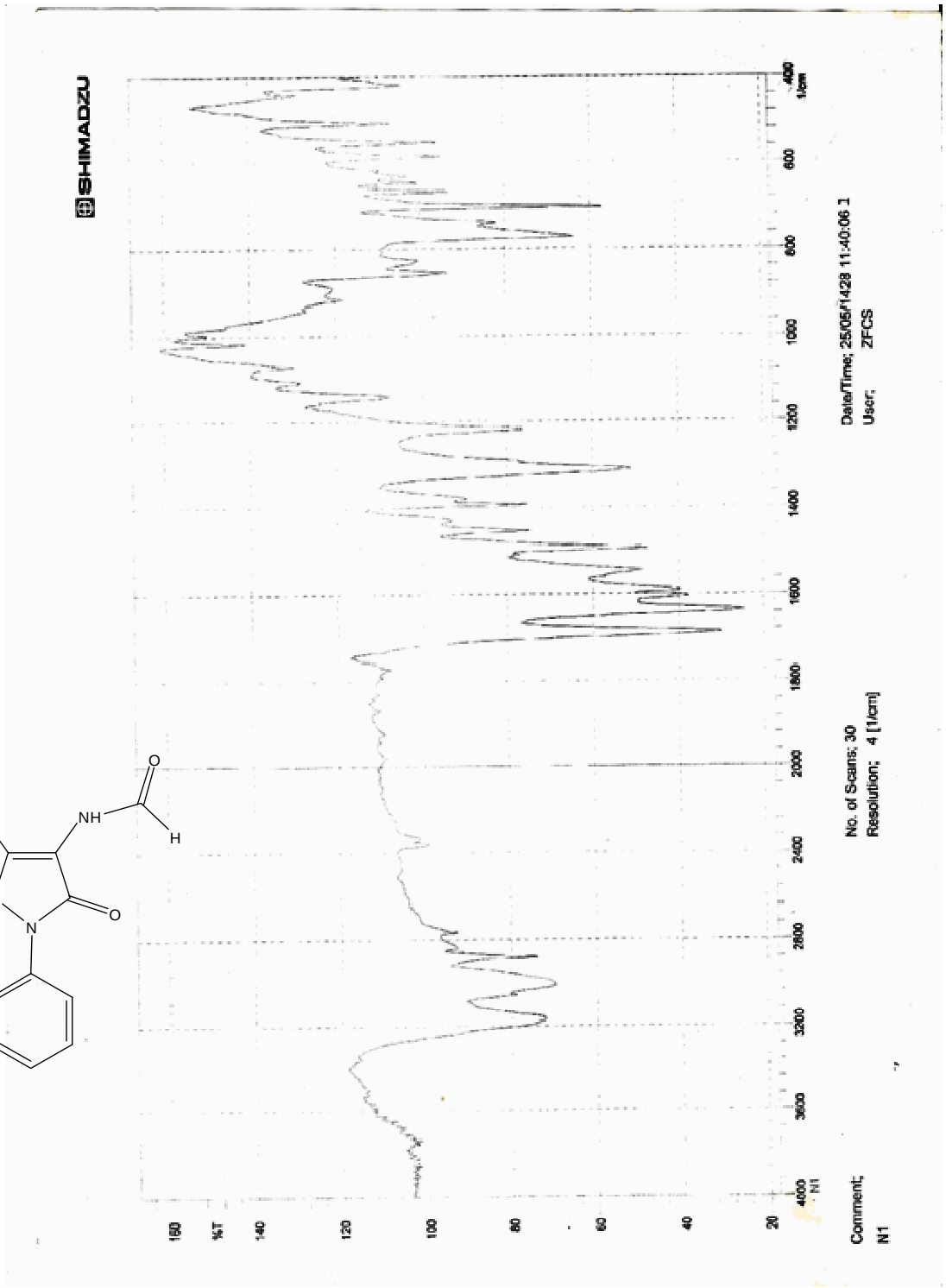


Figure (3-62) FTIR spectrum of (17A)

N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)formamide

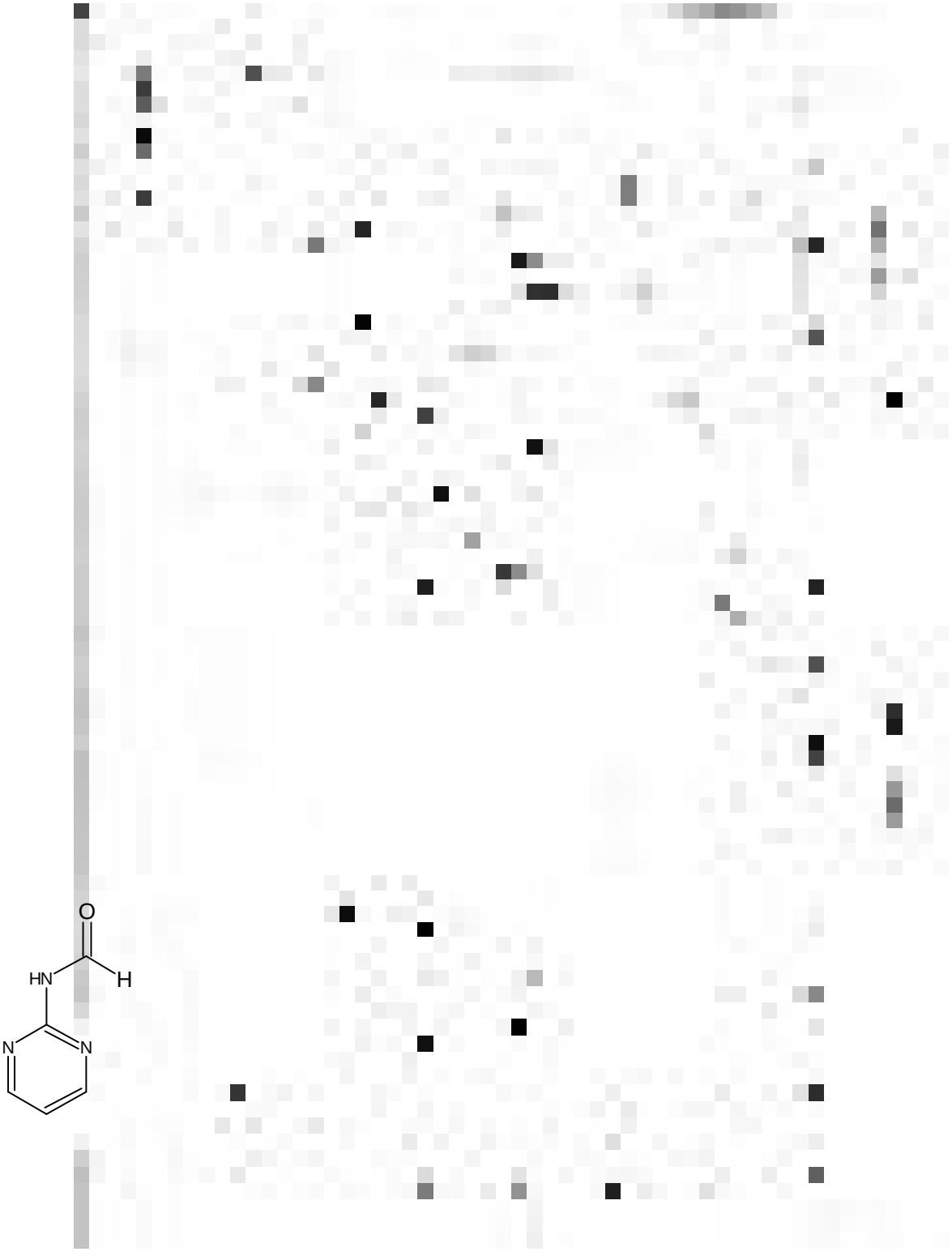


Figure (3-63) FTIR spectrum of 17B

N-pyrimidin-2-ylforamide

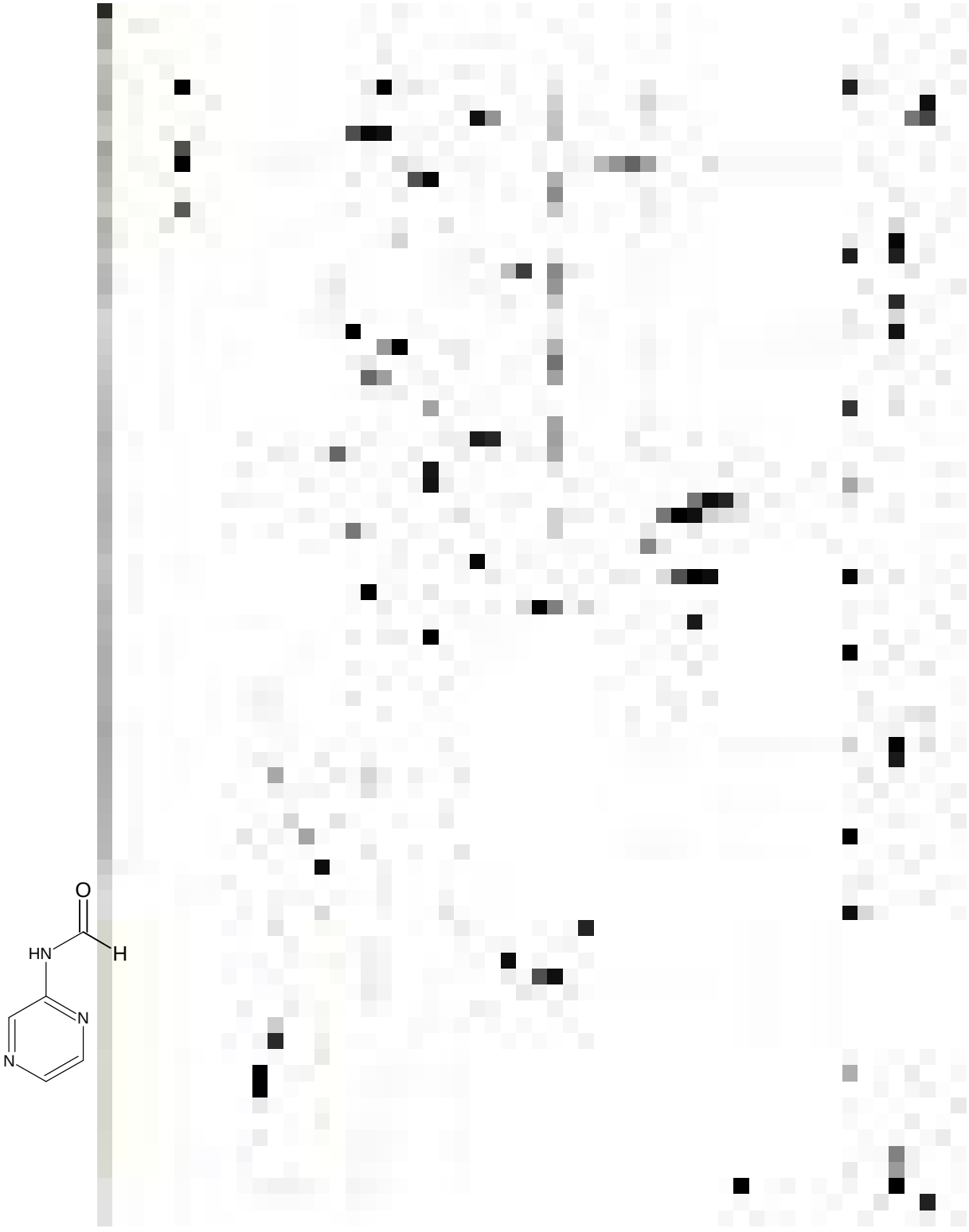


Figure (3-64) FTIR spectrum of 17C N-pyrazin-2-ylfroamide

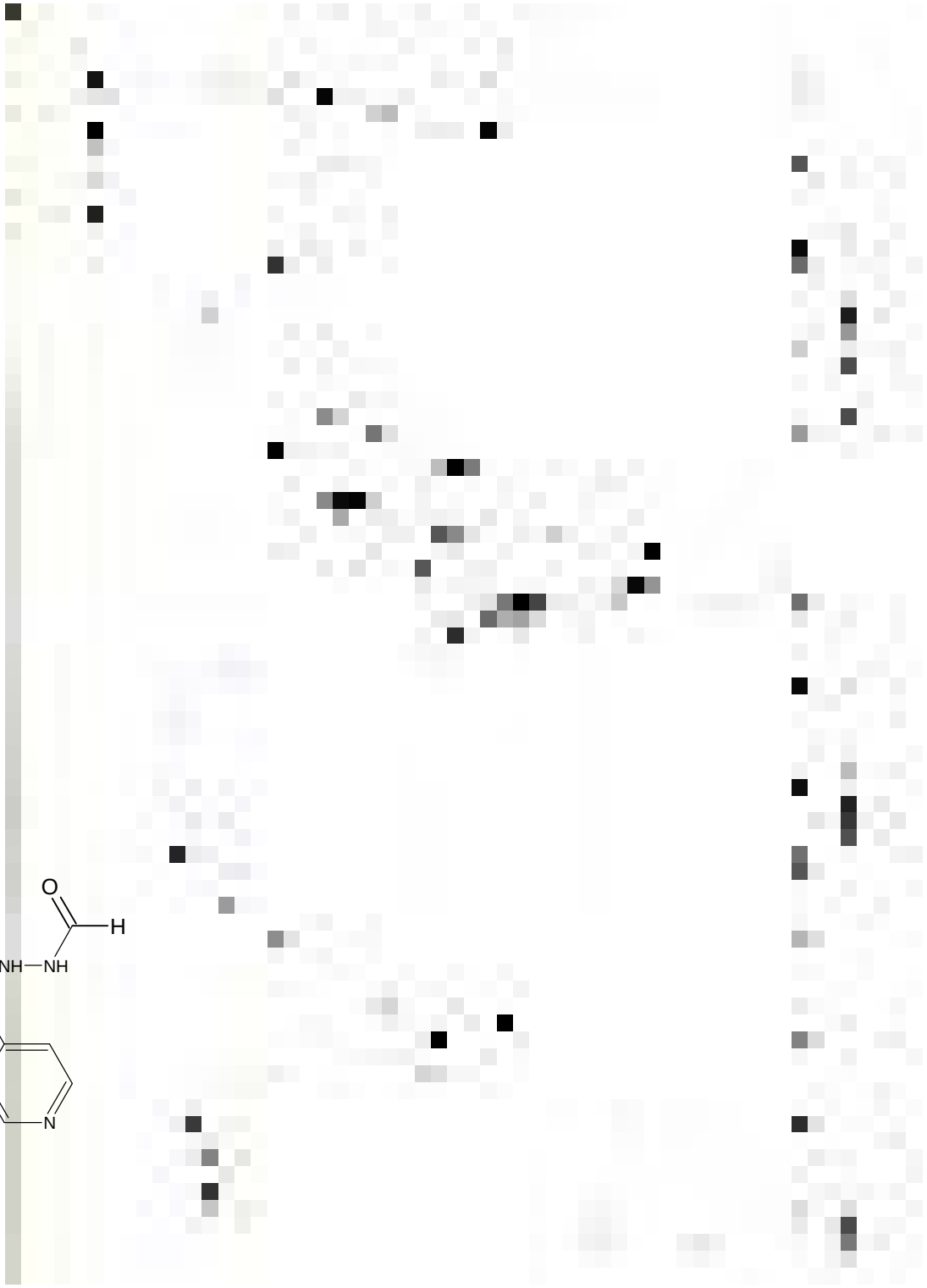
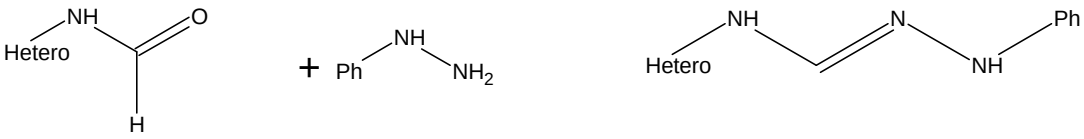


Figure (3-65) FTIR spectrum of compound (17 D)

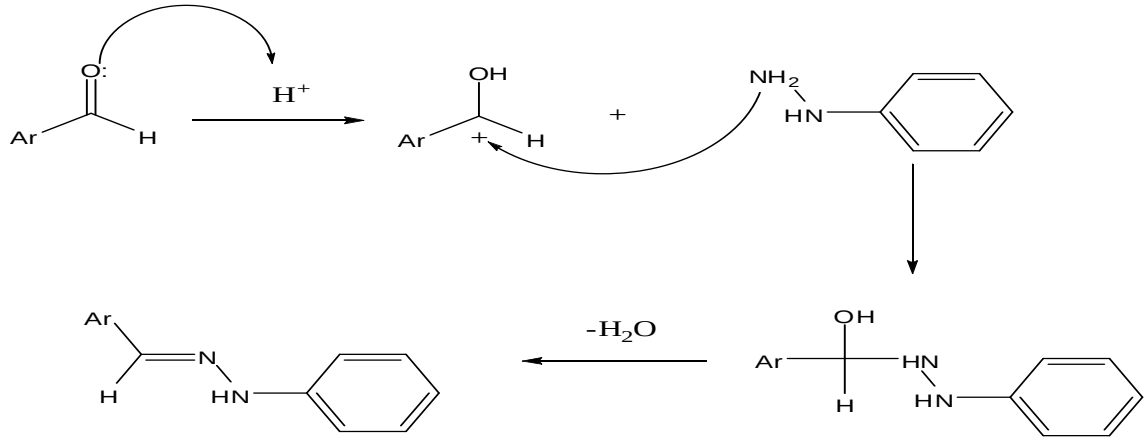
N'-formylisonicotinohydrazides

3-18 N'-phenyl-N-hetero-2-ylhydrazonoformamide(18)



Hydrazine formamide derivatives are prepared by the reaction of phenyl hydrazine with formamide derivatives in absolute ethanol the product identified by the FTIR spectrum by the disappearance of the C=O of the formic at 1700cm^{-1} and the appearance of C=N stretching band at 1600cm^{-1}

The proposed mechanism for this reaction



Ar= hetero—NH

Table (3-18) the IR spectruml data of hydrazine formamides(18A-18D)

Compound No.	υ C=N str.cm^{-1}	υ NH starching	υ CH hydazide
18 A	1600	3300	2780
18 B	1643	3200	2800
18 C	1639	3180	2780
18D	1604	3200	2780

Figure (3-66) the FTIR of compound (18A)

(E)-N-(2,3-dimethyl-5-oxo-1-phenyl-2,5-dihydro-1H-pyrazol-4-yl)-N'-(phenylamino)formamidine

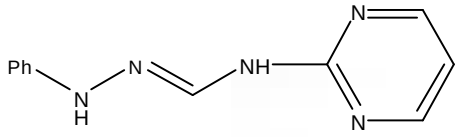


Figure (3-67) IR spectrum of compound (18B)

(E)-N'-phenyl-N-(pyrimidin-2-yl)formohydrazonamide

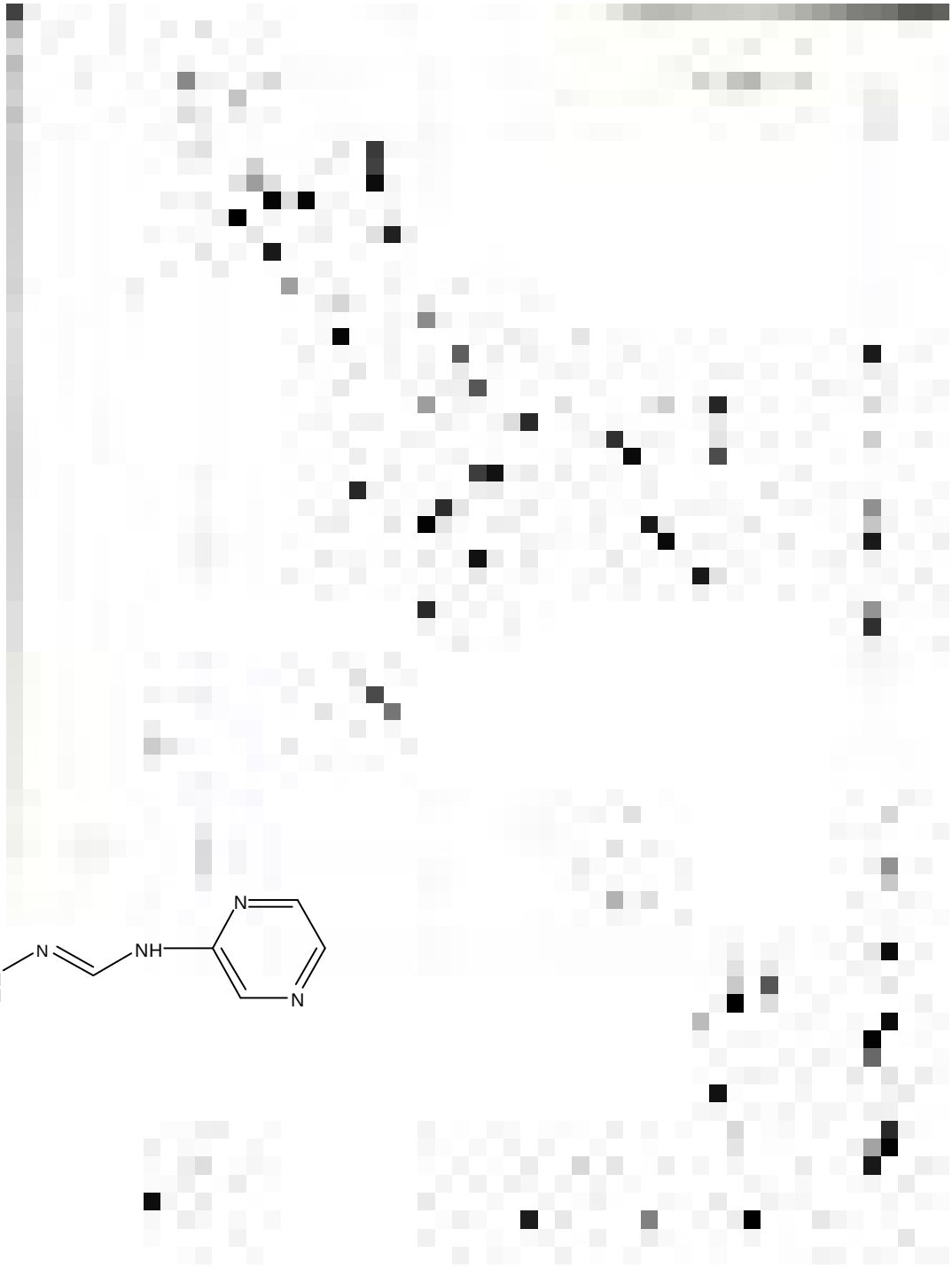


Figure (3-68) IR spectrum of compound (18C)
(E)-N'-phenyl-N-(pyrazin-2-yl)formohydrazonamide

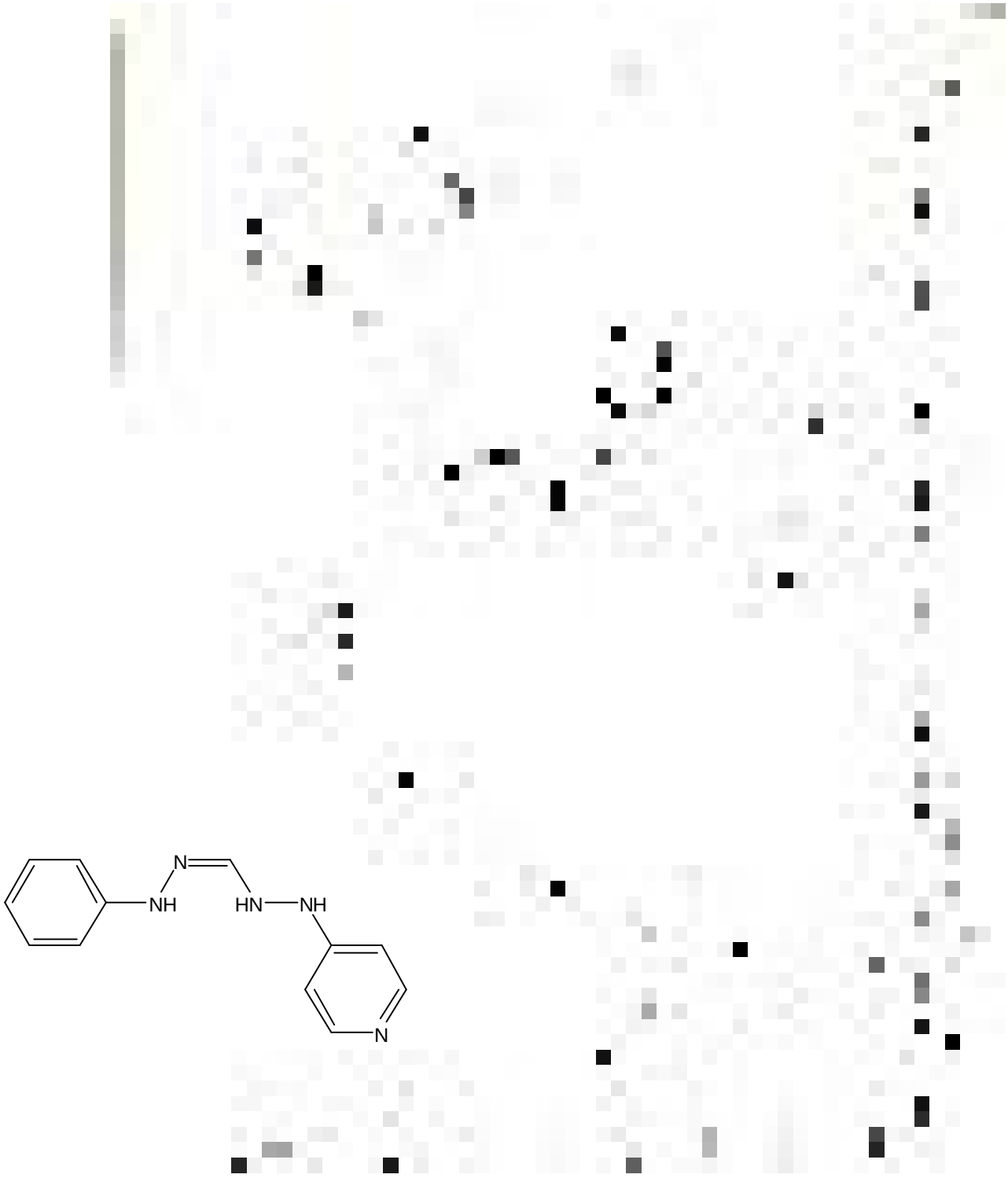
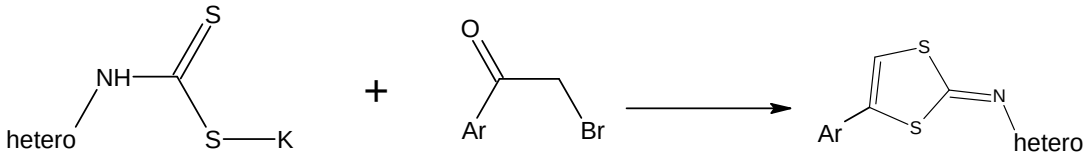


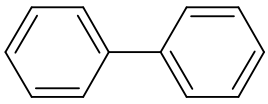
Figure (3-69) IR spectrum of compound (18D)

(E)-N'-phenyl-N-(isoneazid-2-yl)formohydrazonamide

3-19 Preparation of N-(4-biphenyl-4-yl-1,3-dithiol-2-yl)pyrazin-2-amine



Ar =



1,3 Dithiolane derivatives were prepared by the reaction of the dithiocarbamate (xanthate) derivatives with α-halo carbonyl compounds the product was identified by TLC and the FTIR HNMR and C^{13}NMR spectrum by the disappearance carbonyl band and the disappearance of C=S band at 1200-1100 cm^{-1} and disappearance of carbonyl band of halo carbonyl at 1680cm^{-1}

The proposed mechanism for this reaction is

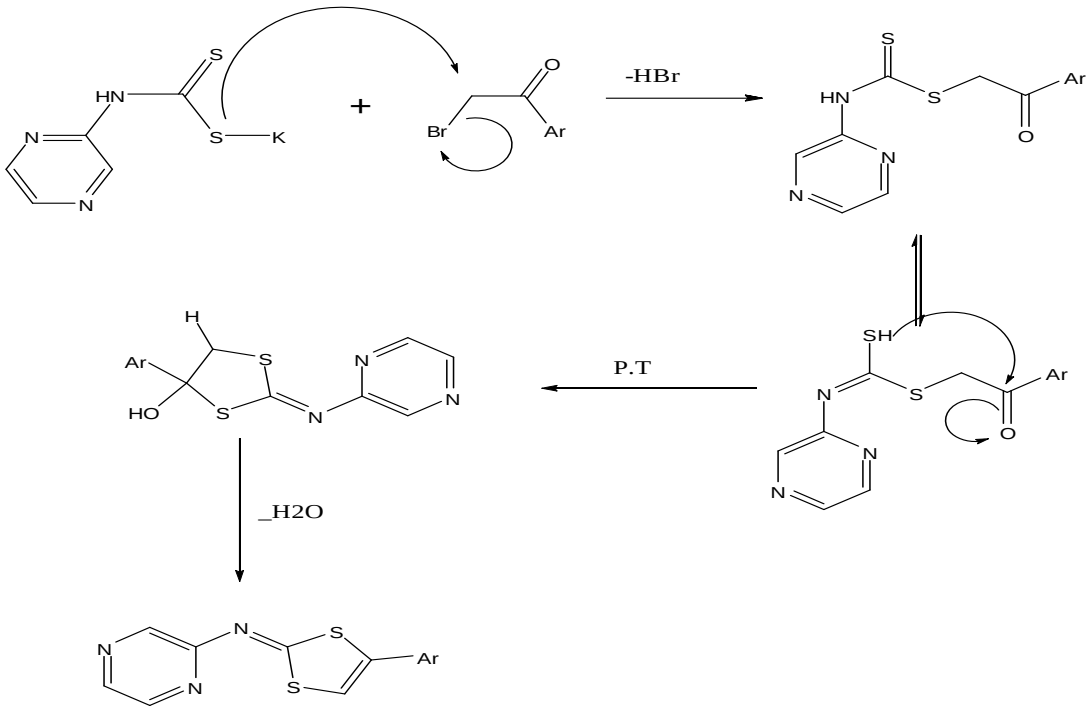


Figure (3-70)The C13 NMR of compound 19C N-(4-biphenyl-4-yl-1,3-dithiol-2-yl)pyrazin-2-amine

Figure (3-71)The H NMR spectrum of compound 19C N-(4-biphenyl-4-yl-1,3-dithiol-2-yl)pyrazin-2-amine

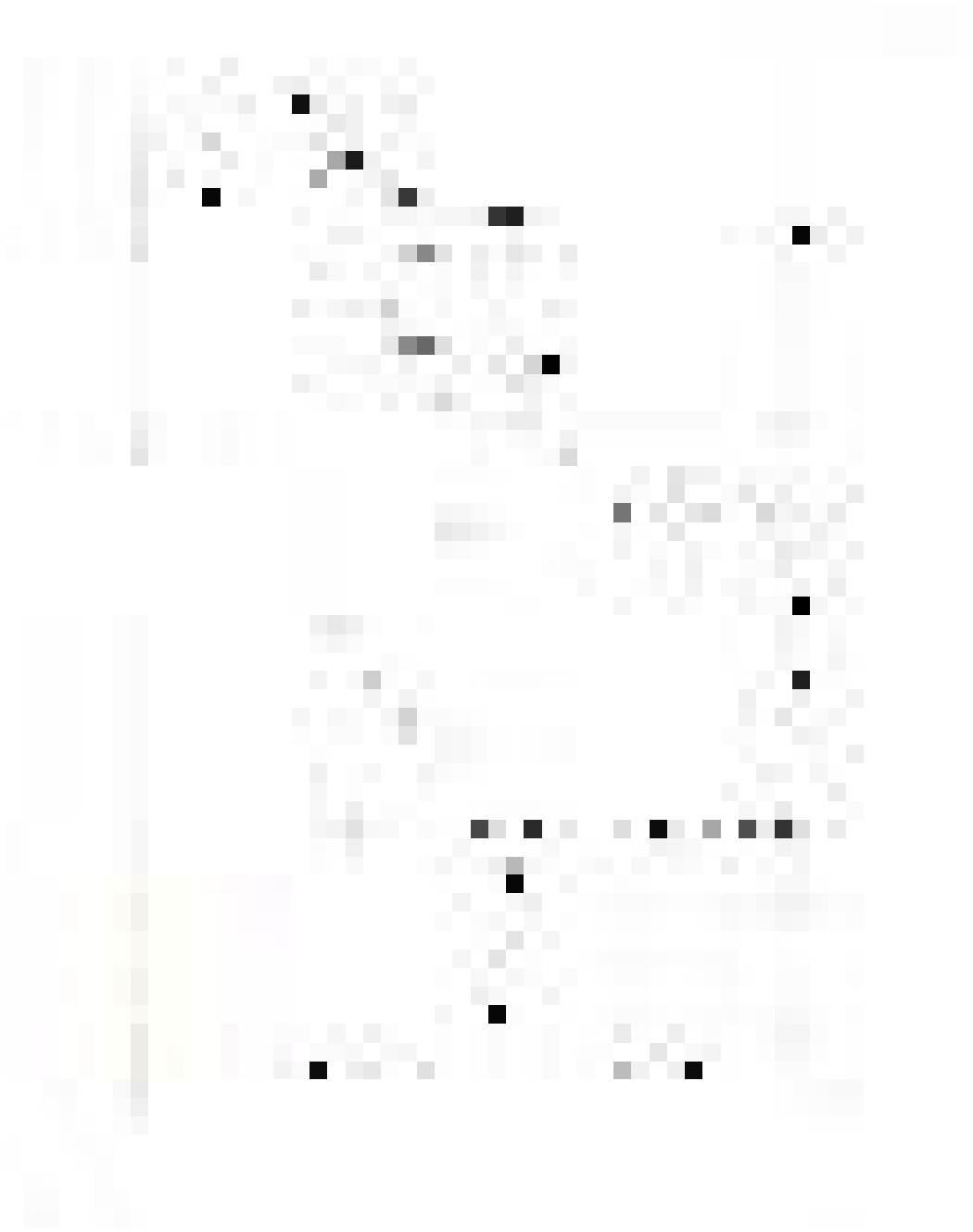
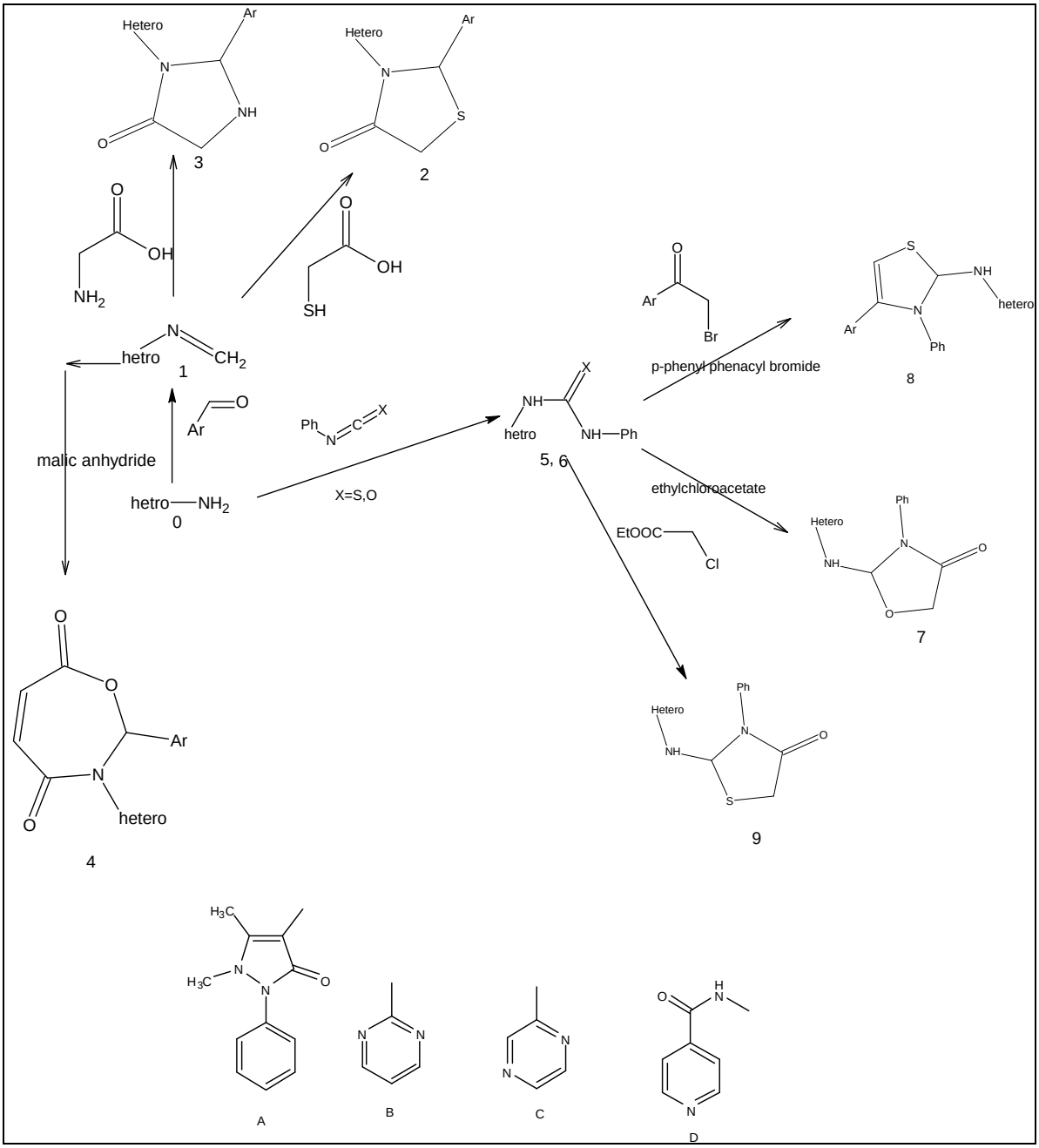


Figure (3-72) the IR spectrum of N-(4-biphenyl-4-yl-1,3-dithiol-2-yl)pyrazin-2-amine

Summary

1- preparation of thiazolidene-4-none (2) , imidazolidine-4-ones (3) , and oxazepine-4,7-diones (4) from schiff bases (1) by reaction with 2-mercaptoacetic acid ,glycine and malic anhydride respectively .
2- preparation of 1-phenyl-3-hetero-2-yl urea and thiourea from reaction of hetero amines with phenylisocyanate and phenylisothiocyanate respectively .
3- preparation of 1,3-oxazolidine -4-one (7) ,3-phenyl-2,3-dihydrothiazol-2-yl hetero amines (8) and 1,3 –oxazolidine-4-one (9) from the reaction of urea or thiourea derivatives (5,6) with ethylchloroacetate ,p-phenylphenacyl bromide respectively.
4- Preparation of 2-chloro N-(hetero-2-yl)acetamide (10) from reaction of heterocyclic amines with α-chloroacetyl chloride .
5- Preparation of oxazole-2,5- diamines(11) Thiazole-2,5-diamine (12) , thiosemicarbazide (13) ,and acetazide derivatives (14) from the reaction of compound (10) with urea ,thiourea ,thiosemicarbazide and sodium azide respectively.
6- Preparation of carbamadithionate (15) ,hetero-2-aminoacetylene derivatives , and formide derivatives from the reaction of hetero amines with CS_2 ,propargyl bromide and formic acid respectively .
7- Preparation of hydrazinoformamide (18) from reaction of heteroformamide (17) with phenyl hydrazine .
8- Preparation of dithiolene (19) by the reaction of carbamadithionate (15) with p-phenyl phenacyl bromide .
9- All prepared compounds are elucidated by some spectroscopic methods (FTIR,H NMR ,C^{13} NMR).
10- The biological activity of some prepared compounds are evaluated

All reactions are shown in the following schemes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3
Hetero
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2
OH
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CH2
1
malic anhydride
Ar
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hetro
NH2
0
Ph
N
C
X
X=S,O
NH
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hetro
NH
Ph
5, 6
Ar
O
Br
p-phenyl phenacyl bromide
S
NH
hetero
Ar
N
Ph
8
ethylchloroacetate
EtOOC
Cl
Hetero
Ph
N
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O
7
O
O
Ar
N
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hetero
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Hetero
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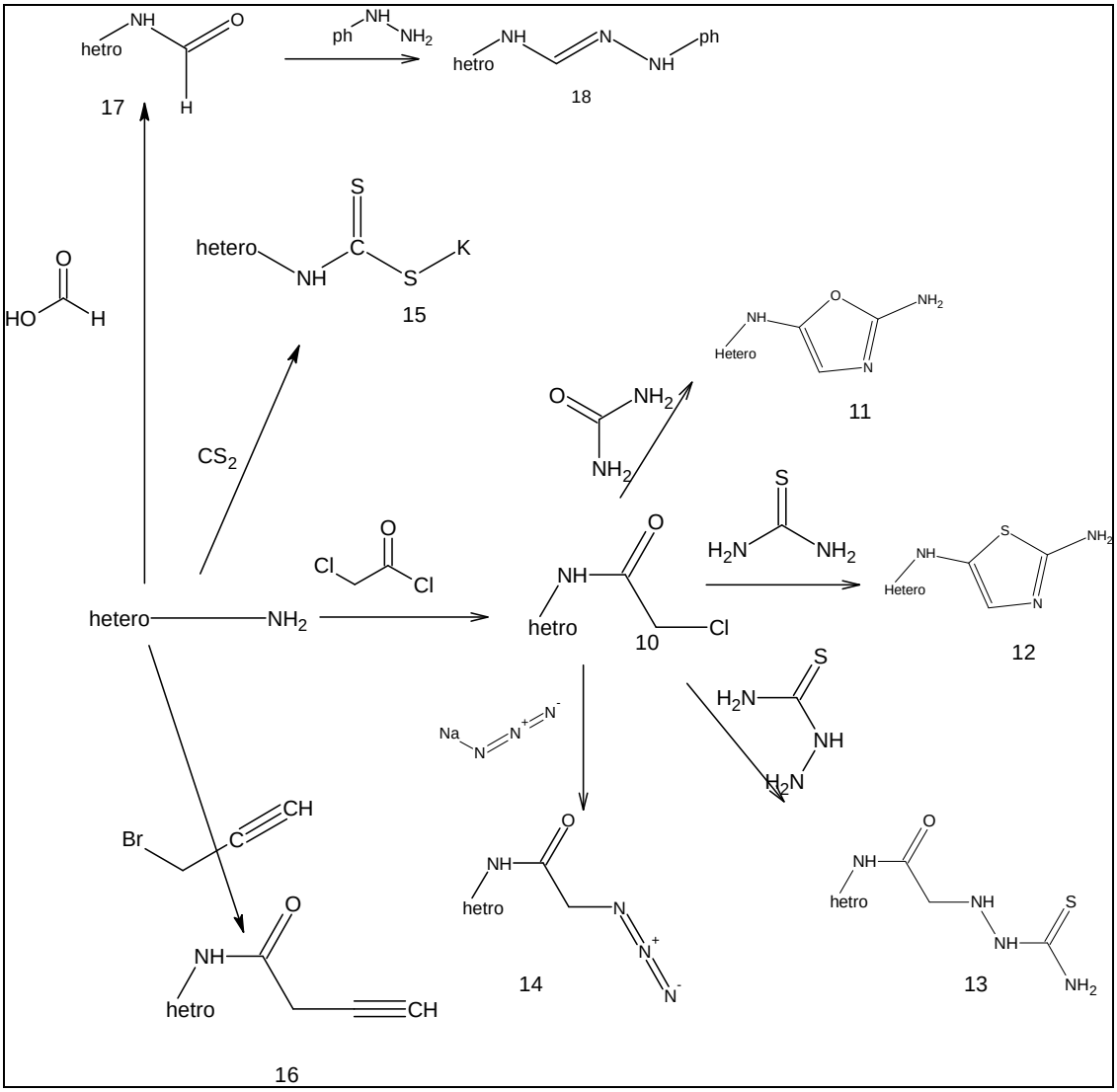
Scheme one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NH2
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Hetero
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NH2
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Hetero
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N+
N-
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H2N
NH
H2N
Br
C
CH
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CH
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hetro
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N+
N-
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hetro
NH
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NH
NH
S
NH2
13

Scheme two