Synthesis and Characterization of New Heterocyclic Compounds Derived from 2-Aminopyrimidine

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Summary

In this study Schiff basses(1) have been prepared by the reaction of 2-aminopyrimidine with benzaldehyde derivatives then Thiazolidene-4-none (2) , imidazolidine-4-ones (3) , and oxazepine-4,7-diones (4) have been prepared from Schiff bases (1) by reaction with 2-mercaptoacetic acid ,glycine and malic anhydride respectively .1-phenyl-3-pyrimidin-2-yl urea(5) and thiourea(6) have been prepared from reaction of 2-aminopyrimidine with naphthylisocyanate and phenylisothiocyanate respectively.1,3-oxazolidine -4-one (7) ,3-phenyl-2,3-dihydrothiazol-2-yl pyrimidine amines (8) have been prepared from the reaction of urea or thiourea derivatives (5,6) with ethylchloroacetate ,p-phenylphenacyl bromide respectively. 2-chloro N-(pyrimidin-2-yl)acetamide (10) have been prepared from reaction of 2-aminopyrimidine with α-chloroacetyl chloride .thenoxazole-2,5-diamines(11) Thiazole-2,5-diamine (12) have been prepared by the reaction of the reaction of (10) with urea and thiourea respectively. All prepared compounds are elucidated by some spectroscopic methods (FTIR, H NMR ,C^{13} NMR).The biological and enzymatic activity of some prepared compounds are evaluated

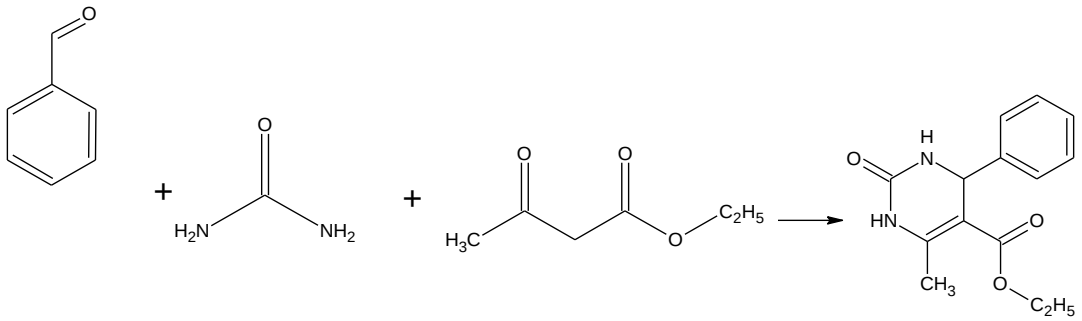
Introduction

1-1 Pyrimidines[1]

Pyrimidines also known as m-daizine, is the parent substance of large group of pyrimidincyclic 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 chemis try , 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.

Folkers and johanson(2) have been have prepare dihydropyrimidines from urea, aldehyde and acetoacetic ester



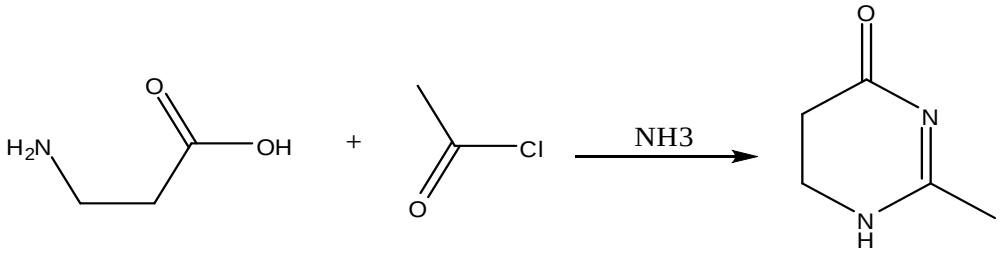
Mitchell et al [3] have shown that the synthesis of oriotic acid (uracil –4-carboxylic acid) from urea and oxaloacetic ester her the initial product is hydenton which rearranged to the pyrimidine only when treated with alkali

Substituted of O-alkyl urea or phenylsimecarbazide lead to 2-alkoxy or 1-anilino pyrimidine respectively [4],[5]

Mohamed.et,al [6]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 [7]have prepare two pyrimidine analogues of the herbicide atrazine test there herbicidal activity they found that they have specific activity.

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 .[8]



Pyrimidines and their derivatives are well known for their potential biological activity such as Anitifolate [9] Anti -leukemia [10] Herbicidal [11]

Procedure

2-1-Preparation of Schiff base (1)

A mixture of 2-aminopyrimidine (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

2- 2 -Preparation of 2-aryl-3-(pyrimidin-2-yl)thiazolidin-4-one (2)[12]

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 .

2-3-Preparation of 2-aryl-3-(pyrimidin-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 recrystallized from ethanol and THF 25/75.

2-4-Preparation of 2-aryl-3-pyrimidin-2-yl-2,3-dihydro-1,3-oxazepine-4,7-dione (4)[13]

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.

2-5-Preparation of N-phenyl-N'-pyrimidin-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

2-6-Preparation of N-phenyl-N'-pyrimidin-2-ylthiolurea (6)

A (0,001) mole of appropriate pyrimidincyclic 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.

2-7- Preparation of 3-phenyl-2-(pyrimidin-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.

2-8- N-(4-(naphthalen-2-yl)-3-phenyl-2,3-dihydrothiazol-2-yl)pyrimidin-2-amine(9)[14]

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.

2-9-Preparation of 2-chloro-N-(pyrimidin-2-yl)acetamide (10)

A (0.01)mol of appropriate pyrimidincyclic 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).

2-10- Preparation of N5-(pyrimidin-2-yl)oxazole-2,5-diamine (11)[15]

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.

2-11-Preparation of N5-(pyrimidin-2-yl)thiazole-2,5-diamine(12)[15]

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 .

Results and discussion

3-1- Schiff bases preparation

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} .

3-2- Aryl-3-(pyrimidin-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.

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

Imidazolidine derivatives prepared by the heating of Schiff basesderivatives 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.

3-4- Preparation of 2-aryl-3-pyrimidin-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 $^{-1}$

3-5- Preparation 1-phenyl-3-(pyrimidin-2-yl)urea(5).

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}.

3-6- Preparation of 1-phenyl-3-(pyrimidin-2-yl)thiourea(6).

Thiourea derivatives prepared by the reaction of phenylisothiocyanate with 2-aminopyrimidine 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 out of plane bending band of p-substituted benzene.

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

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}.

3-8-N-(4-(naphthalen-2-yl)-3-phenyl-2,3-dihydrothiazol-2-yl)pyrimidin-2-amine(8)

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 .

3-9- Preparation of 2-chloro-N-(pyrimidin-2-yl)acetamide (9)

This compound was 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}.

3-10- Preparation of N5-(pyrimidin-2-yl)oxazole-2,5-diamine(10).

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}.

3-11- Preparation of N5-(pyrimidin-2-yl)thiazole-2,5-diamine(11)

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 (3-1) physical properties of the prepared compounds

Compound No	Yield %	solvent	Melting point
1A	95	THF-Ethanol	230-232
1B	98	THF-Ethanol	360
2	36	Benzene-ethylacetate	145-147
3A	31	THF-Ethanol	205-207
3B	36	THF-Ethanol	116-118
4	22	Benzene-Ethanol	209-211

٥	77		250-252
٦	68		99-101
٧	30		188-190
٨	29		290 decomp
١٠	37		290 decomp

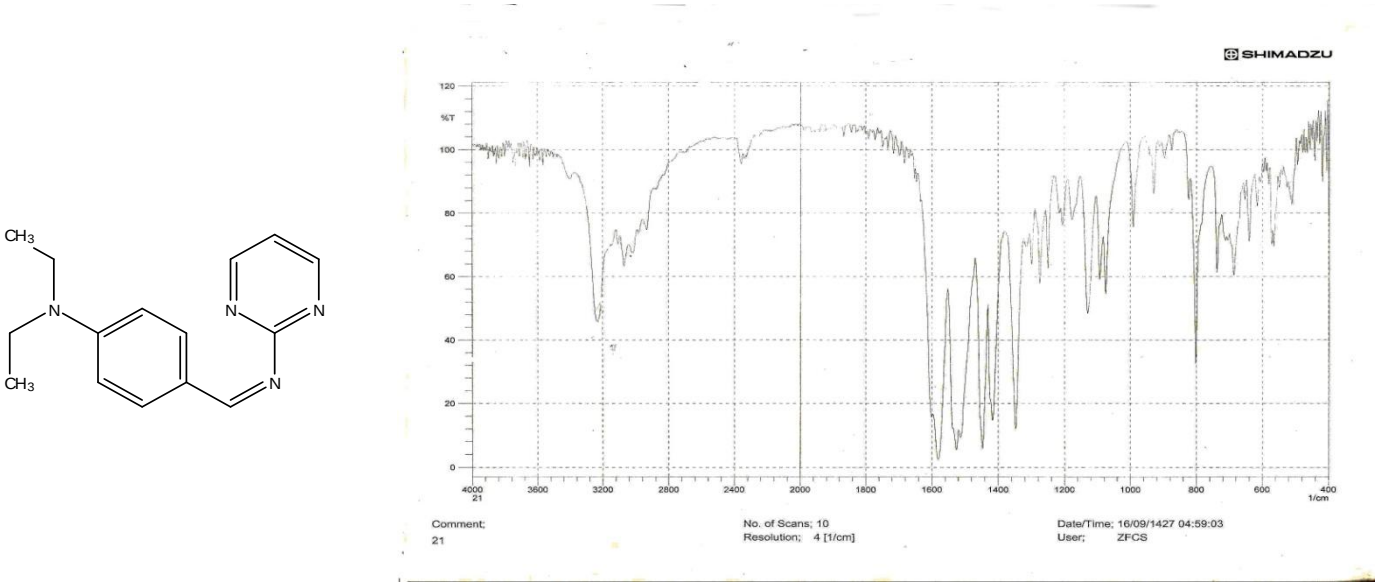


Figure (3-1) FTIR spectrum of compound (1A) (Z)-N-(4-(diethylamino)benzylidene)pyrimidin-2-amine

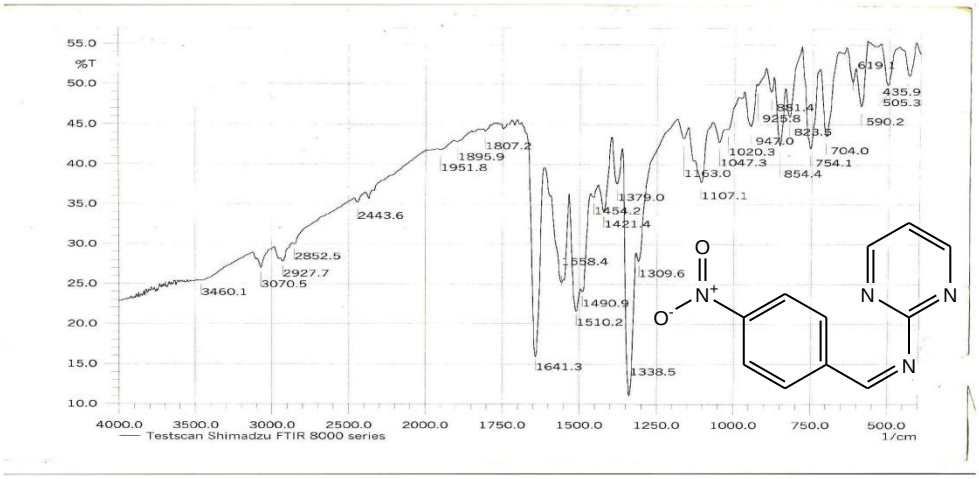


Figure (3-2) FTIR spectrum of compound (1B) (Z)-N-(4-nitrobenzylidene)pyrimidin-2-amine

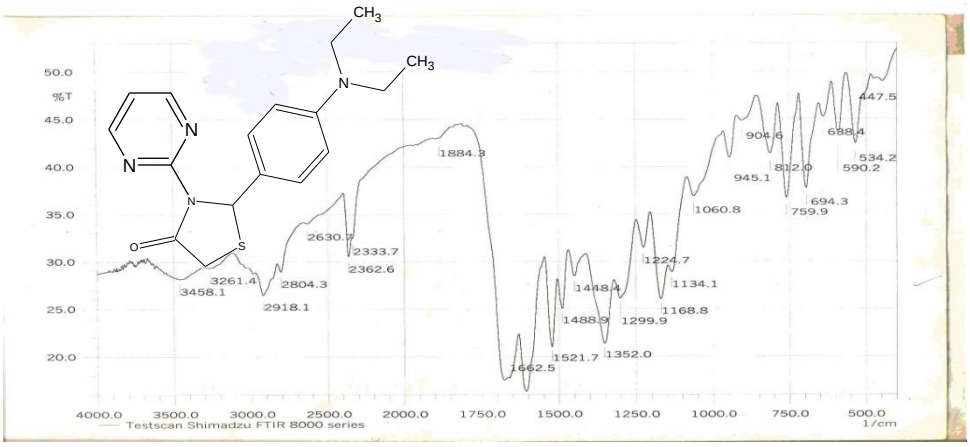


Figure (3-3) FTIR spectrum of compound (2) 2-[4-(diethylamino) phenyl]-3-pyrimidin-2-yl-1,3-thiazolidin-4-one

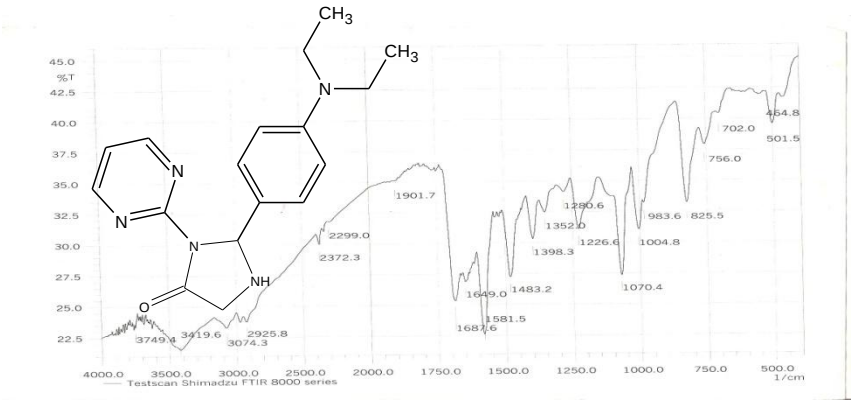


Figure (3-4) FTIR spectra of compound (3A)

2-[4-(nitrobenzyledinl]-3-pyrimidin-2-ylimidazolidin-4-one

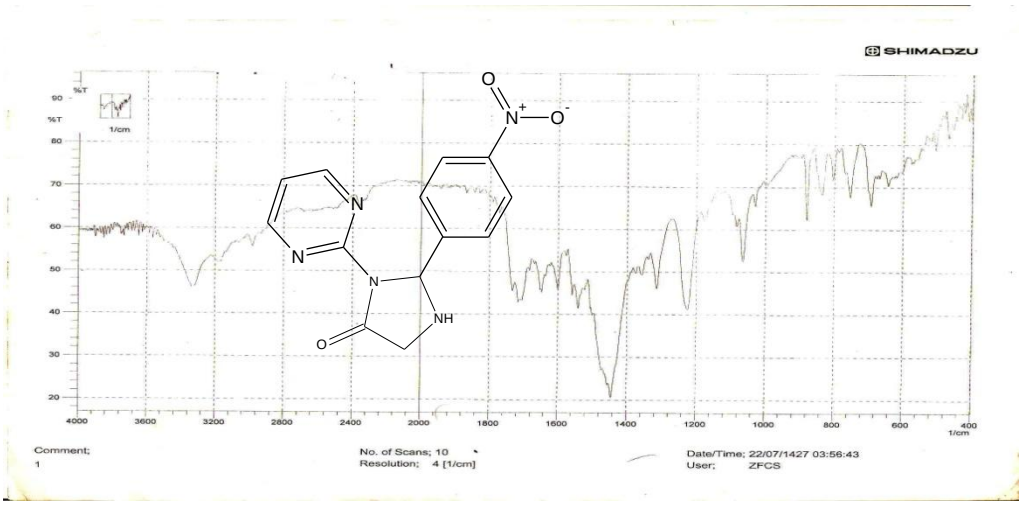


Figure (3-5) FTIR spectra of compound (3B)

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

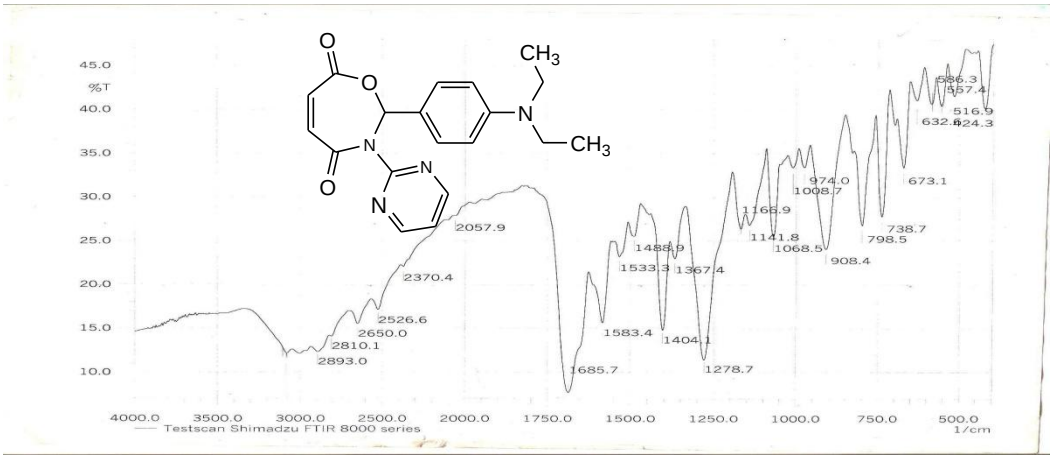


Figure (3-6) the FTIR of compound (4) (Z)-2-(4-(diethylamino)phenyl)-3-(pyrimidin-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione

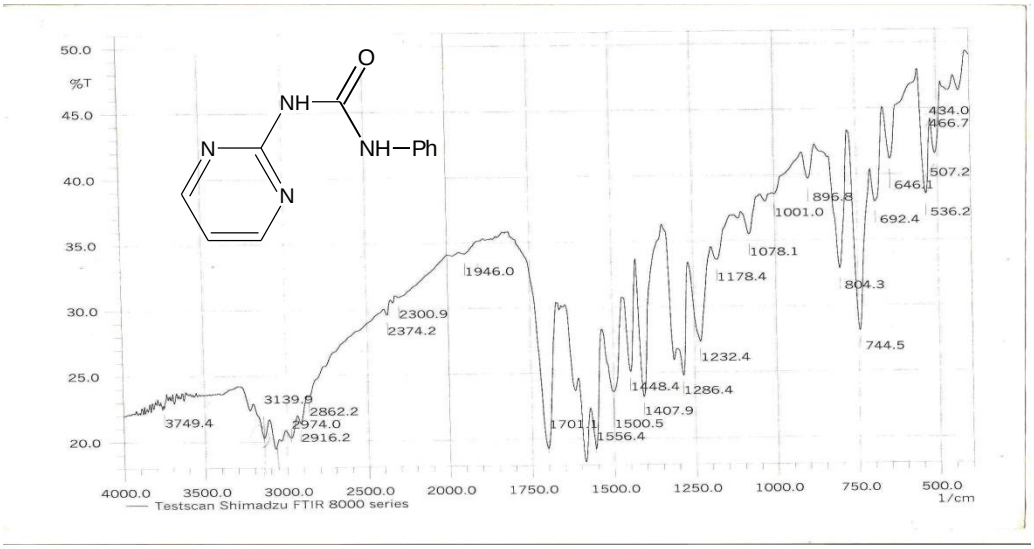


Figure (3-7) FTIR spectra of compound (5)1-phenyl-3-pyrimidin-2-ylurea

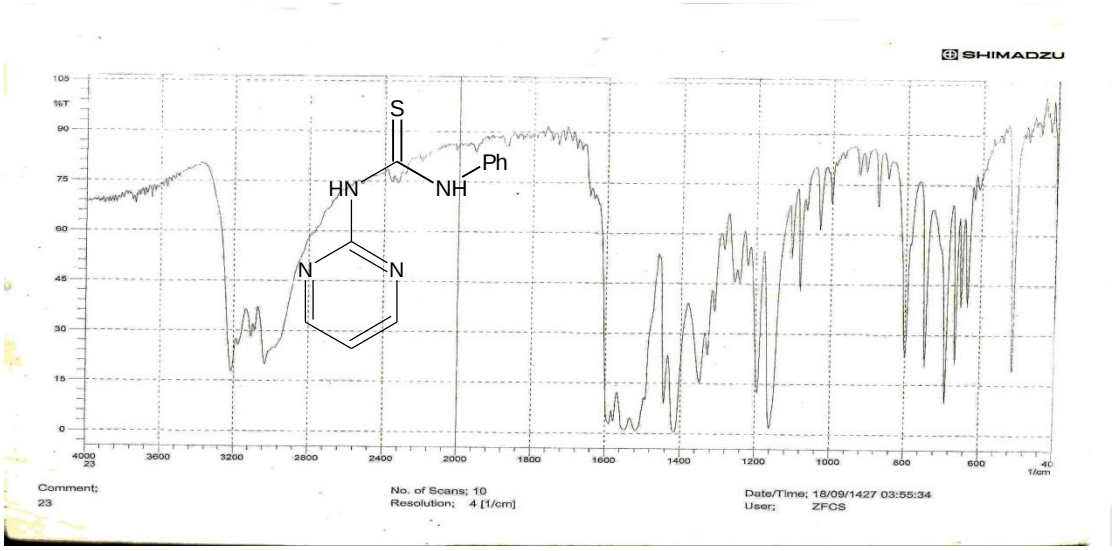


Figure (3-8) FTIR spectra of compound (6)1-phenyl-3-pyrimidin-2-ylthiourea

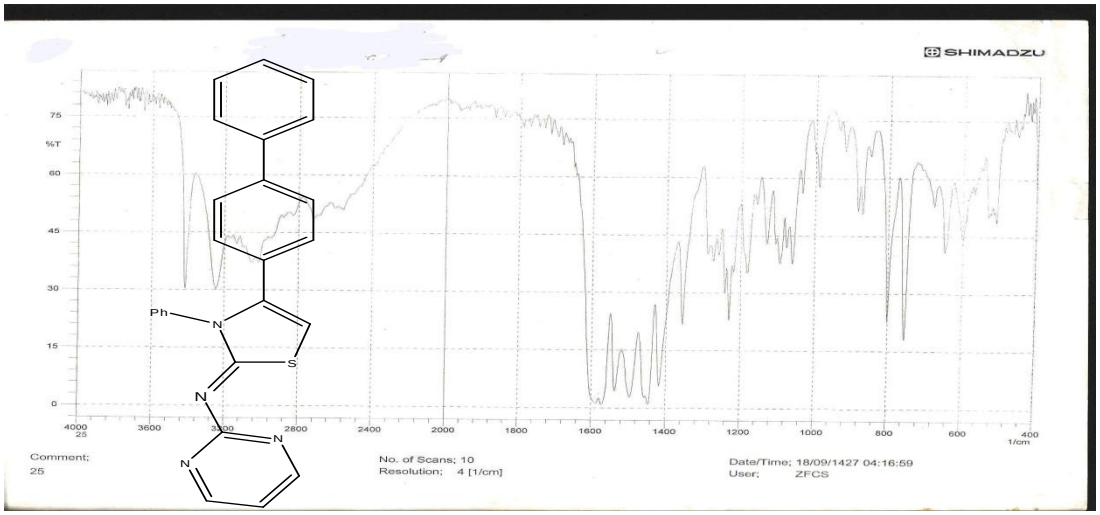
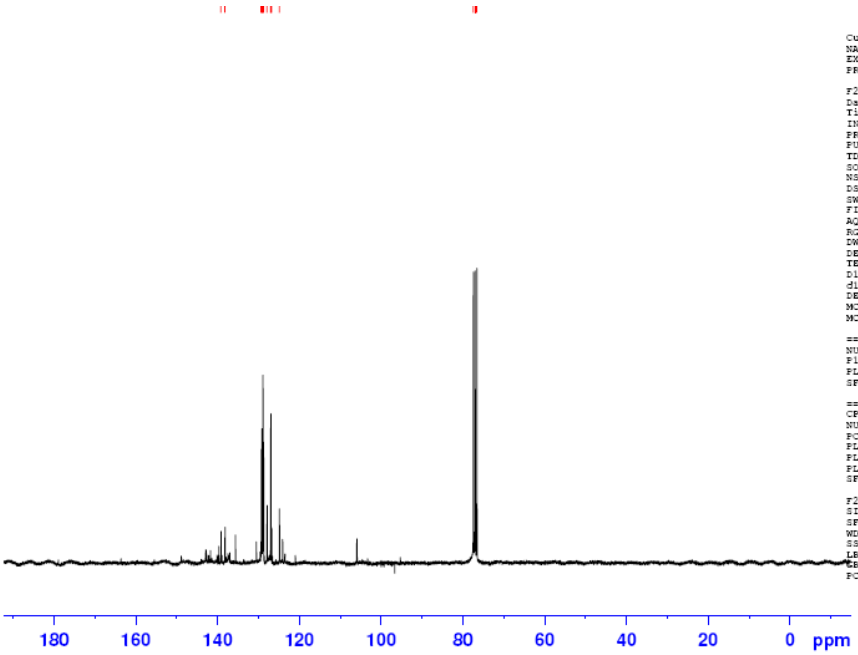


Figure (3-9) FTIR spectrum of compound (7) (Z)-N-(4-(biphenyl-4-yl)-3-phenylthiazol-2(3H)-ylidene)pyrimidin-2-amine



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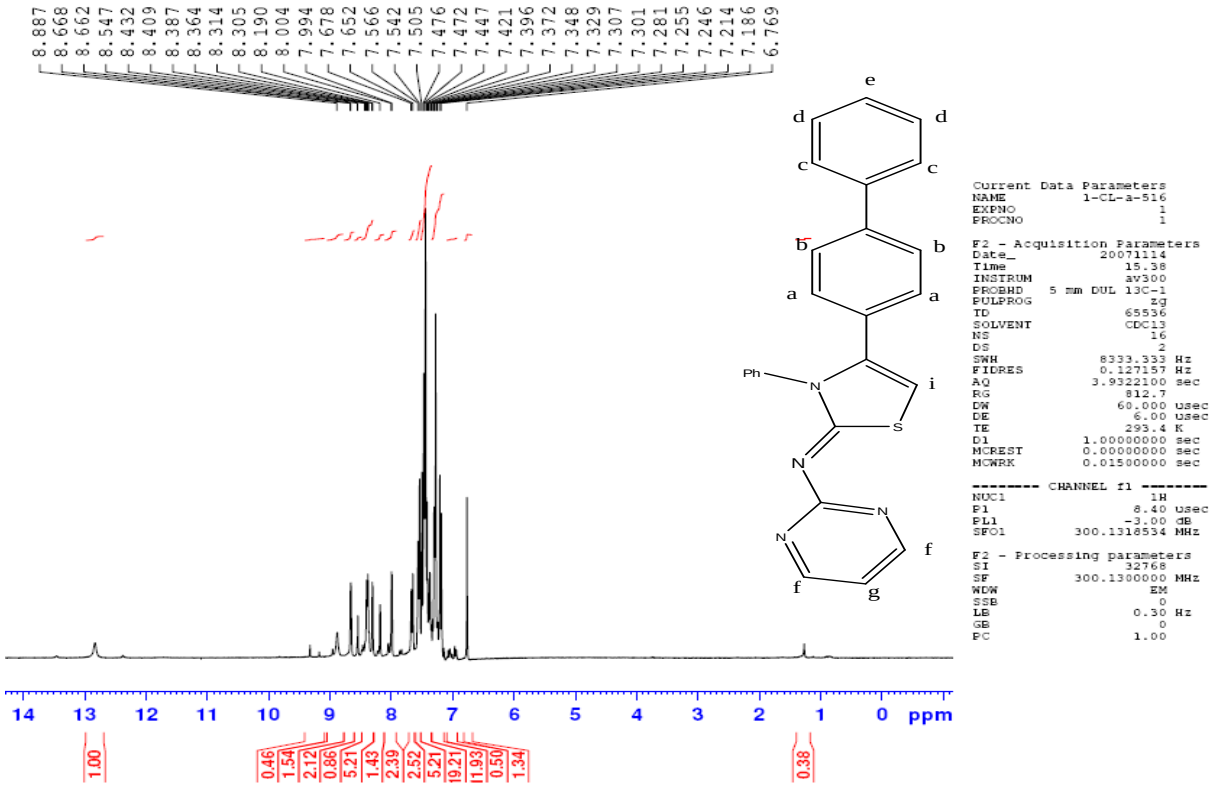

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- Figure (3-8)NMR spectrums of compound(7)

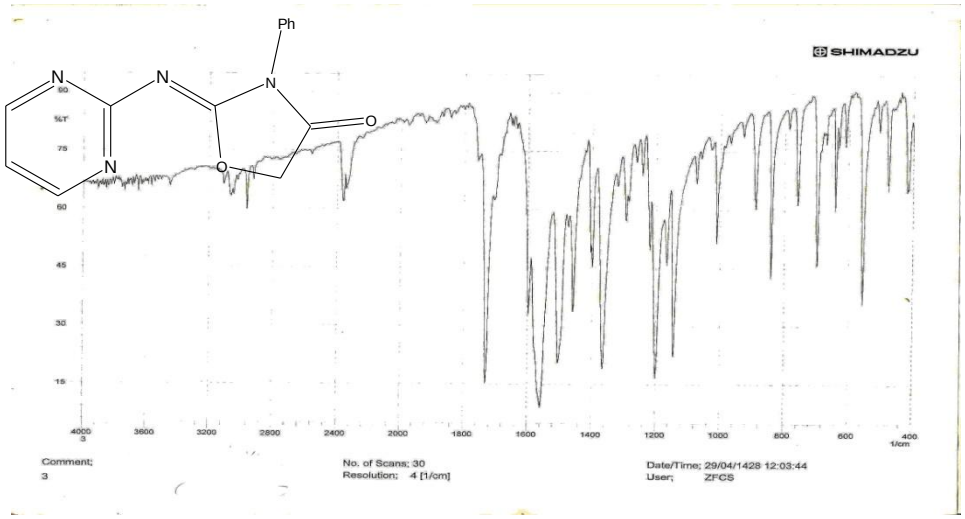

Figure (3-9) FTIR spectrum of compound (8) 3-phenyl-2-(pyrimidin-2-ylamino)-1,3-oxazolidin-4-one

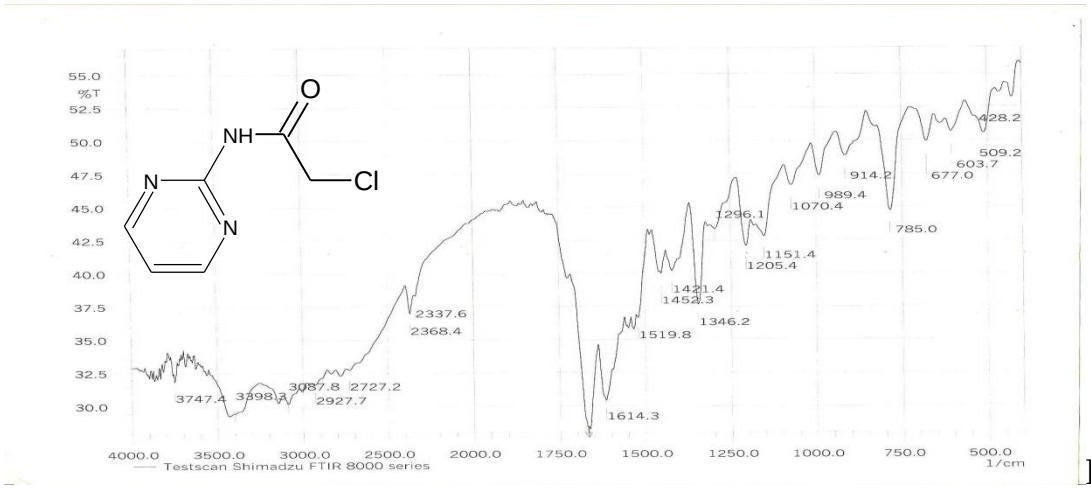

Figure (3-10) FTIR spectrum of compound (9) 2-chloro-N-pyrimidin-2-ylacetamide

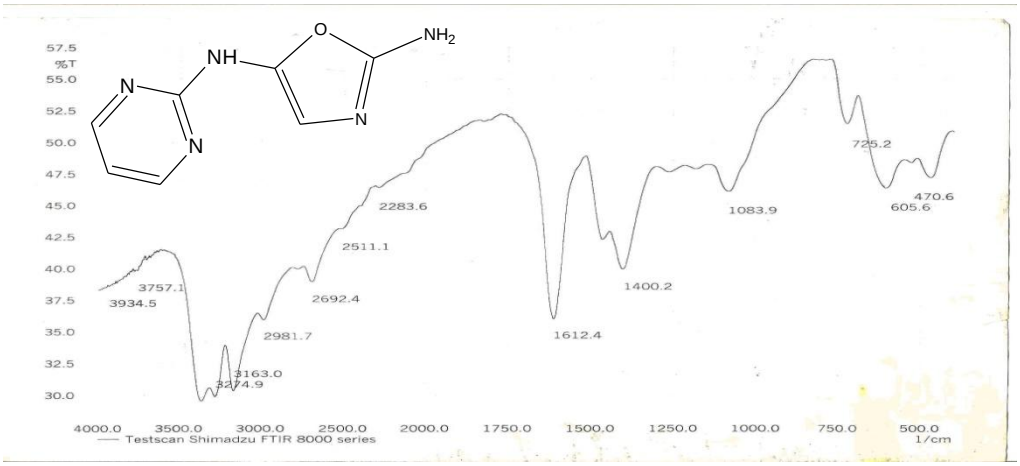

Figure (3-11) FTIR spectrum of compound (10) N5-pyrimidin-2-yl-1,3-oxazole-2,5-diamine

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