

**SYNTHESIS OF SUBSTITUTED PYRIMIDINE DERIVATIVES AND ITS
ANTIBACTERIAL ACTIVITY****S. Singh*, Dr. Shamim Ahmad and Dr. Shamsher Alam**

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ABSTRACT

A novel series of substituted Pyrimidine derivatives have been synthesized from substituted acetophenone with appropriate quantity of substituted aromatic aldehyde in presence of aqueous alcoholic alkali was used for formation of α , β – unsaturated ketones (i.e. chalcones). Equimolar portions of the substituted acetophenone (10mmol, 1 equiv) and substituted benzaldehyde (10mmol, 1 equiv) were dissolved in 15ml of ethanol and recrystallized from ethanol to give chalcone derivatives (I). To chalcone (10mmol) obtained from step 1, added guanidine nitrate then reflux for 2 hr The precipitate formed washed with cold water until it turns neutral to pH paper, filtered and recrystallized from ethanol to give derivatives (II). To mixture of derivatives (II) (10mmol), 1,3-dichloroethane (10mmol) and 25% NaOH (0.025 mol, 10 ml) was refluxed in methanol(25 ml) for 8-12 h. The resulting mixture (III) was poured into ice-water and stirred. The crude product Pyrimidine were separated and recrystallized from Acetone.

KEYWORDS: Antibacterial activity, Antifungal activity, Pyrimidine etc.**INTRODUCTION**

Medicinal chemistry is a chemistry-based discipline involving aspects of biological, medical and pharmaceutical sciences. It is concerned with the invention, discovery, design, identification of biologically active compounds, the study of their metabolism, interpretation of their mode of action at the molecular level and the construction of structure activity relationship (SAR), the relationship between chemical structure and pharmacological aspects.^[1]

Although there has been a great deal of success in understanding the relationship between the chemical structure and biological activities in numerous areas, especially for antibacterial drugs, there are still many human afflictions that requires new and improved drugs.^[2]

When a new pharmaceutical lead compound has been discovered, extensive and costly efforts are usually made to prepare a series of analogues so that better activity can be found. The metabolism of drug is an important aspect in medicinal chemistry and considerable efforts are spent on detailed analysis of bioconversion that a new drug series undergoes. Modern analytical methods such as mass spectrophotometry permit the identification of minute amount of metabolites. The intellectual goal of a medicinal chemistry is to know the mode of action of drugs at molecular level. The objective of medicinal chemistry is to design and production of compounds that

can be used in medicine for the prevention, treatment and cure of humans or animal diseases.^[3] Five and six membered heterocyclic nitrogen containing systems such as pyrazole, imidazole, triazoles, thiazolidine, pyrazolidine, piperidine, oxane pyrimidine, pyridine, thiane, pyran etc. as far by the most important in the ongoing research for more efficacious drugs in the fields such as antibacterials, antifungal, antitubercular, anti-inflammatory, diuretics, antirheumatics and antihistaminics. Nitrogen containing heterocyclic compounds have received considerable attention due to their wide range of pharmacological activity. Pyrimidine and their derivatives are considered to be important for medicinal drugs. As pyrimidine is a basic nucleus in DNA & RNA, it has been found to be associated with diverse biological activities. Pyridine, a heterocyclic nucleus, played a pivotal role in the development of different medicinal agents. It is seen from the current literature that pyridine congeners are associated with different biological activities like pesticidal, fungicidal and antibacterial activity. Pyrimidines and pyridines have contributed to the diverse library of compounds demonstrating selective affinity to the 5-HT₇ receptor. Pyrimidines are the most important six member heterocyclic, containing two nitrogen atoms on 1, 3 positions as shown in fig 1.

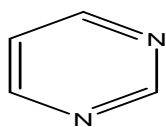


Figure 1.

Pyrimidines are present among the three isomeric diazines. Several pyrimidines mainly cytosine (I), uracil

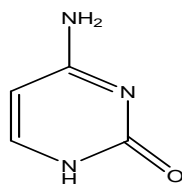
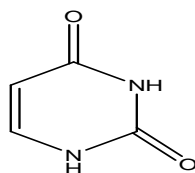
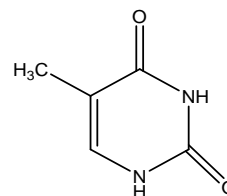
Cytosine
(I)Uracil
(II)Thymine
(III)

Figure 2.

In addition to this, Pyrimidines ring is also found in Vitamin B₁, Barbituric acid (IV) and its several

derivatives e.g. Veranal (V) which are used as hypnotics (fig. 3).^[5]

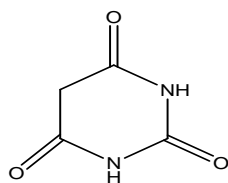
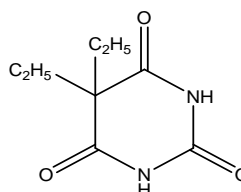
Barbituric acid
(IV)Veranal
(V)

Figure 3.

Numerous reports have appeared in the literature that highlights chemistry and uses of pyrimidines and their derivatives like Sulfadiazine, Sulfamerazine and Sulfamethazine. These agents are inhibitors of folic acid biosynthesis in microorganism. Pyridine is a ubiquitous chemical compound. The aromatic, monocyclic azine is utilized as a reagent or as a polar aprotic solvent. It is salient in a number of biological systems and industrial applications. Naturally occurring pyrimidines include the nicotinamides, a component of the vitamin B group. Pyrimidines are precursors to various pharmaceuticals, adhesives, agrichemicals, and synthetic pigments.

A pyrimidine has many properties in common with pyridine, as the number of nitrogen atoms in the ring increases the ring pi electrons become less energetic and

electrophilic aromatic substitution gets more difficult while nucleophilic aromatic substitution gets easier.^[6]

1. Synthesis of pyrimidine

Several approaches are available for synthesis of pyrimidine as follows.

1.1. Synthesis from enamines, triethyl orthoformate.

A ZnCl₂-catalyzed three-component coupling reaction allows the synthesis of various 4,5-disubstituted pyrimidine derivatives in a single step from functionalized enamines, triethyl orthoformate, and ammonium acetate. The procedure can be successfully applied to the efficient synthesis of mono- and disubstituted pyrimidine derivatives, using methyl ketone derivatives instead of enamines.^[7]

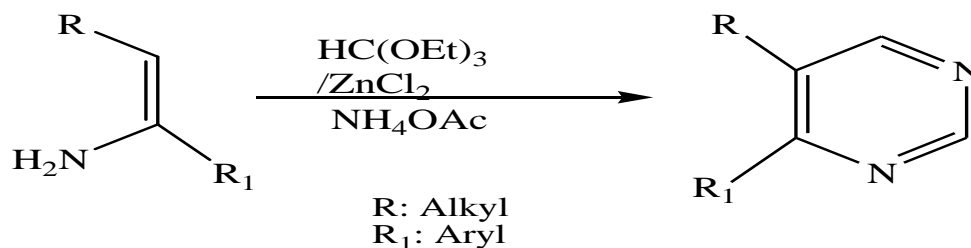


Figure 4.

1.2. Synthesis from *N*-vinyl/aryl amides

The direct condensation of cyanic acid derivatives with *N*-vinyl/aryl amides affords the corresponding C4-heteroatom substituted pyrimidines (as shown in fig 5).^[8]

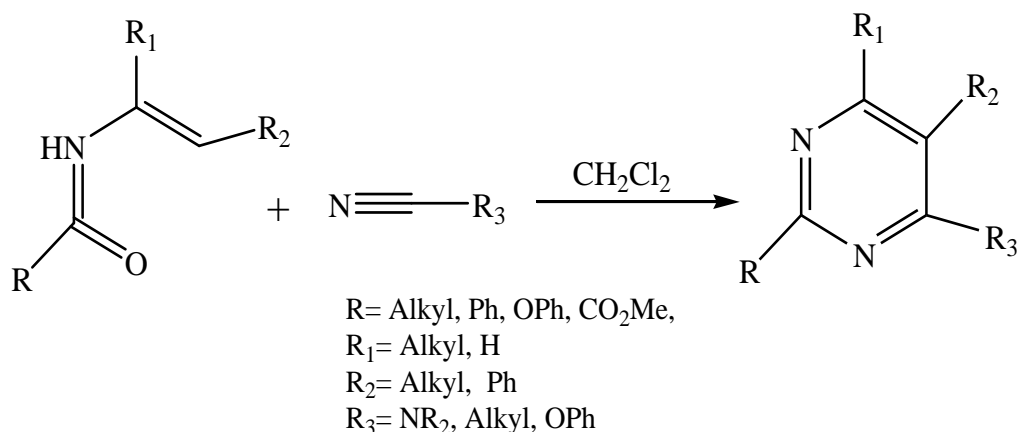


Figure 5.

1.3 Synthesis of pyrimidine from β -formyl enamides.

A novel and efficient synthesis of pyrimidine from β -formyl enamide involves samarium chloride catalyzed

cyclisation of β -formyl enamides using urea as source of ammonia under microwave irradiation (as shown in fig. 6).^[9]

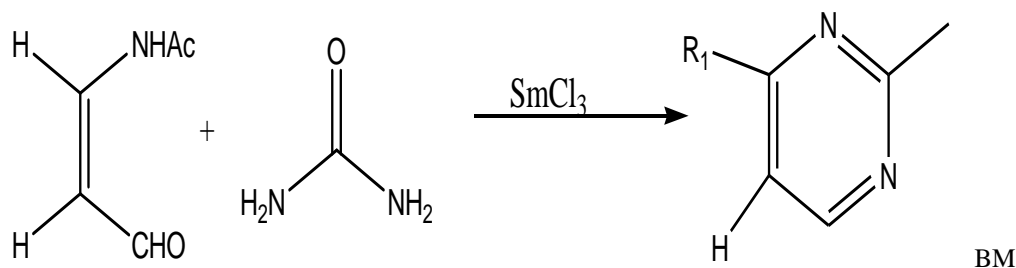


Figure 6.

1.4. Synthesis from activation of amide with 2-chloropyridine

A single-step conversion of various *N*-vinyl and *N*-aryl amides to the corresponding pyrimidine and quinazoline

derivatives involves amide activation with 2-chloropyridine and trifluoromethanesulfonic anhydride followed by nitrile addition into the reactive intermediate and cycloisomerization (as shown in fig.7).^[10]

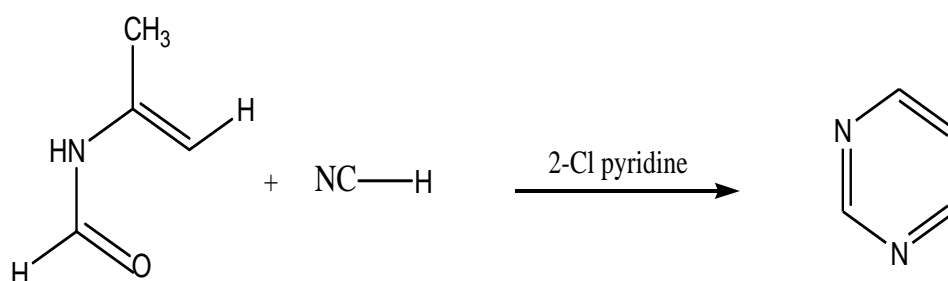
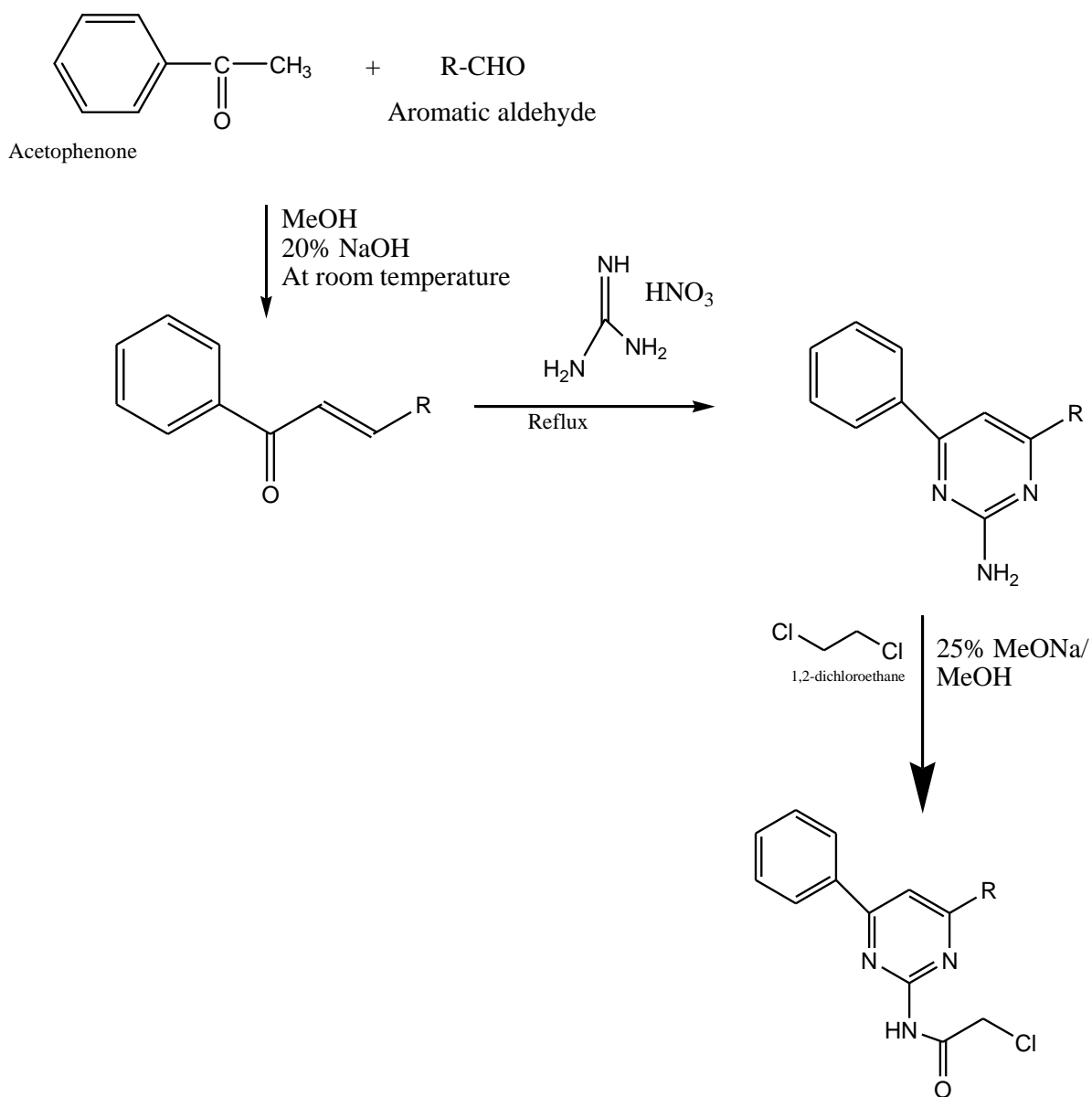


Figure 7.

2. Reaction scheme



3. SYNTHETIC WORK

3.1 Material and Methods

The purified pyrazole derivatives were obtained in yields of 45-95%. The synthetic scheme is illustrated in??. Thin layer chromatography was used to reach completion of reaction and purity of compounds synthesized, using silica gel as stationary phase and Toulene: ethyl acetate: formic acid as solvent system (4:2:1) and visualized by U.V. visualizing cabinet.

All solvents used were analytical grade. The chemicals used were obtained from sigma –Aldrich (St. Louis Mossuri, USA). The structures of compounds were identified using infrared spectroscopy, Mass spectroscopy and proton nuclear magnetic resonance

studies. Melting points were determined by digital melting point apparatus and were uncorrected. Elemental proportions for ‘C’, ‘N’ and ‘S’ were determined by instrument Elementar vario EL III-C, Elementar vario EL III-N, Elementar vario EL III-S, Respectively. IR Spectra were recorded by KBR pellet technique using FTIR-84005 shimadzu spectrophotometer. ¹HNMR Spectra were obtained on Bruker model DRX (300MHzNMR) Spectrometer in DMSO-d₆/CDCl₃ as solvent and using tetramethylsilane as internal standard. Mass were recorded on API 2000 triple quadrapole mass spectrophotometer. The purity of the synthesized compounds was analyzed by thin-layer chromatography.

3.2 General syntheses of derivatives

3.2.1 General Synthesis of chalcone compounds (Step 1)

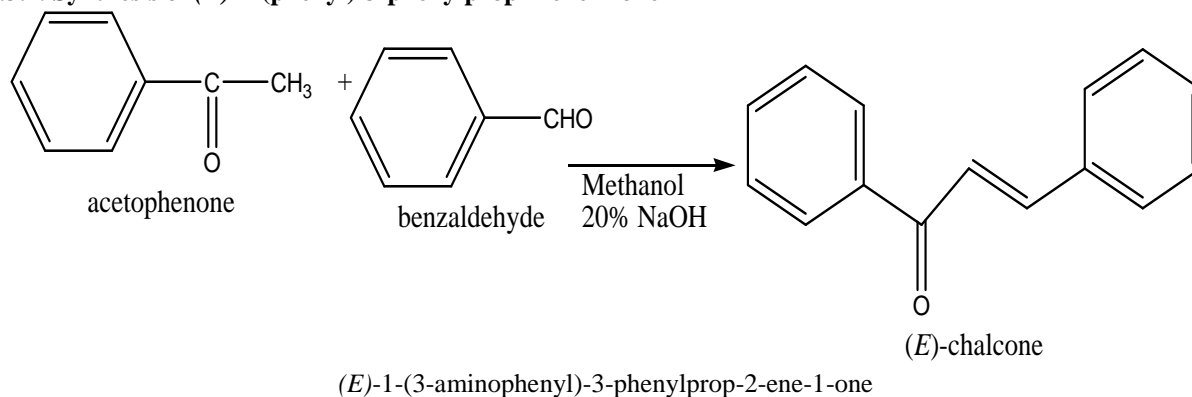
Aldolic condensation (Claisen-Schmidt condensation reaction) of equimolar quantities of substituted acetophenone with appropriate quantity of substituted aromatic aldehyde in presence of aqueous alcoholic alkali was used for formation of α, β – unsaturated ketones (i.e. chalcones). Equimolar portions of the substituted acetophenone (10mmol, 1 equiv) and substituted benzaldehyde (10mmol, 1 equiv) were dissolved in 15ml of ethanol. The mixture was allowed to stir for several minutes at 5-10°C. Aliquot of a 40% aqueous NaOH solution was then slowly added to the reaction flask. The reaction mixture was allowed to stir in ice bath for approximately 4-6hrs. All the crude products were washed first with cold water until washings were neutral to pH paper and precipitate formed was then collected and recrystallized from ethanol to give chalcone derivatives (I).

3.2.2 General synthesis (Step 2)

To chalcone (10mmol) obtained from step 1, added guanidine nitrate then reflux for 2 hr. The precipitate formed was washed with cold water until it turns neutral to pH paper, filtered and recrystallized from ethanol to give derivatives (II).

Synthesis of Intermediate Compound

3.2.3.1. Synthesis of (*E*)-1-(phenyl)-3-phenylprop-2-ene-1-one



Aldolic condensation (Claisen-Schmidt condensation reaction) of equimolar quantities of acetophenone with appropriate quantity of benzaldehyde in presence of aqueous alcoholic alkali was used for formation of α, β – unsaturated ketones (i.e. chalcones). Equimolar portions of the substituted acetophenone (10mmol, 1 equiv) and substituted benzaldehyde (10mmol, 1 equiv) were dissolved in 15ml of ethanol. The mixture was allowed to stir for several minutes at 5-10 °C. Aliquot of a 40% aqueous NaOH solution was then slowly added to the reaction flask. The reaction mixture was allowed to stir in ice bath for approximately 4-6hrs. All the crude products were washed first with cold water until washings were neutral to pH paper and precipitate

3.2.3 General synthetic procedure of pyrimidine compounds (Step 3)

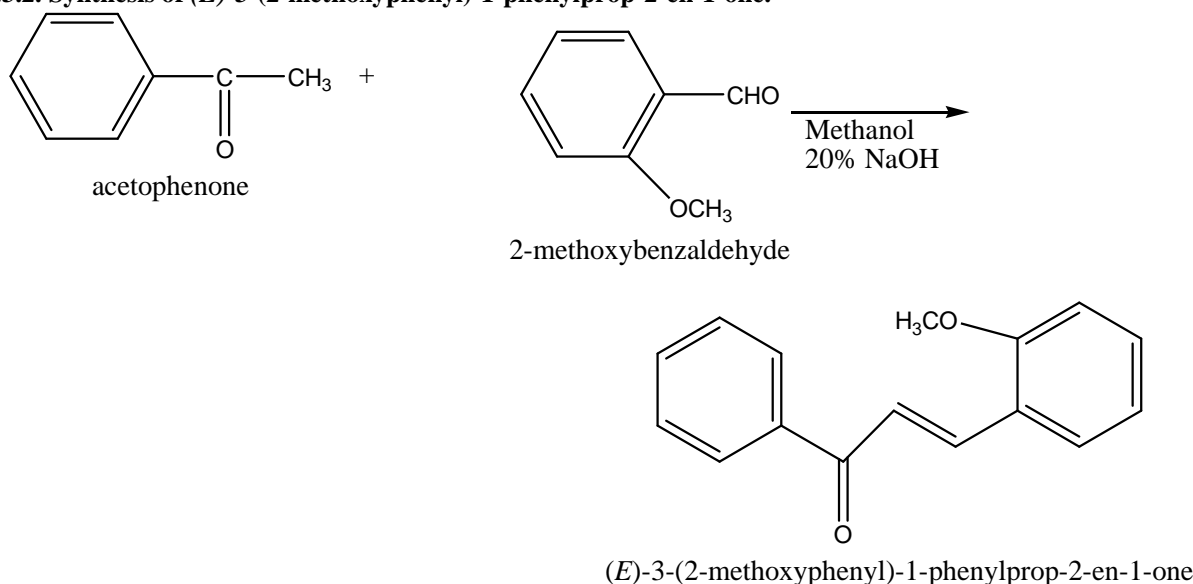
To mixture of derivatives (II) (10mmol), 1,3-dichloroethane (10mmol) and 25% NaOH (0.025 mol, 10 ml) was refluxed in methanol (25 ml) for 8-12 h. The resulting mixture (III) was poured into ice-water and stirred. The crude product (III) were separated and recrystallized from Acetone.

Synthesis of Intermediate Compound

3.3 Physicochemical data of synthesized compounds (Table 1): Synthetic Procedure

The melting point of products were determined by open capillaries method and are uncorrected. IR Spectra (KBr) were recorded on FTIR Spectrophotometer (Shimadzu FTIR 84005, 4000-400 cm^{-1}). The electrospray mass spectra were recorded on a THERMO Finnigan LCQ Advantage max ion trap mass spectrometer. The 10 μl samples (dissolve in solvent such as methanol/ acetonitrile/ water) were introduced into the ESI source through Finnigan survey or autosampler. The mobile phase 90: 10 MeOH/ ACN : H₂O flowed at the rate of 250 $\mu\text{l}/\text{min}$ by MS pump. Ion spray voltage was set at 5.3 KV and capillary voltage 34 V. ¹H NMR were recorded on a Bruker DRX-300 MHz spectrometer in CDCl₃ using TMS as an internal standard, with ¹H resonance frequency of 300 MHz. Chemical shift values are expressed in δ ppm.

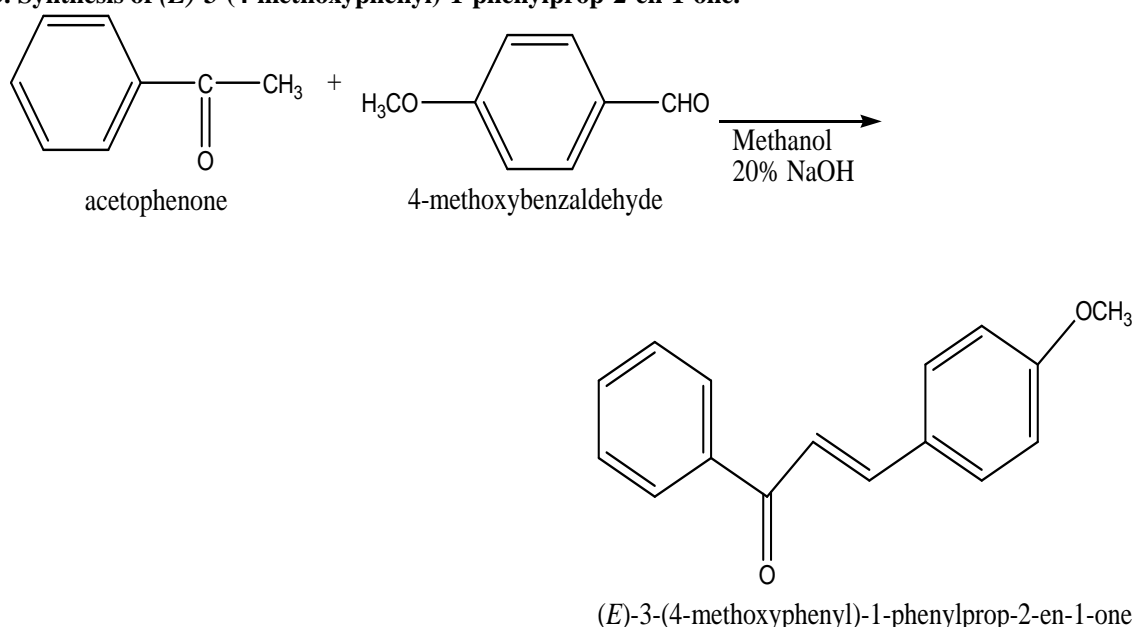
3.2.3.2. Synthesis of (*E*)-3-(2-methoxyphenyl)-1-phenylprop-2-en-1-one.



Aldolic condensation (Claisen-Schmidt condensation reaction) of equimolar quantities of acetophenone with appropriate quantity of 2-methoxy benzaldehyde in presence of aqueous alcoholic alkali was used for formation of α, β – unsaturated ketones (i.e. chalcones). Equimolar portions of the acetophenone (10mmol, 1 equiv) and 2-methoxy benzaldehyde (10mmol, 1 equiv) were dissolved in 15ml of ethanol. The mixture was allowed to stir for several minutes at 5-10 °C. Aliquot of

a 40% aqueous NaOH solution was then slowly added to the reaction flask. The reaction mixture was allowed to stir in ice bath for approximately 4-6hrs. All the crude products were washed first with cold water until washings were neutral to pH paper and precipitate formed was then collected and recrystallized from ethanol to give chalcone derivatives of (*E*)-3-(2-methoxyphenyl)-1-phenylprop-2-en-1-one.

3.2.3.3. Synthesis of (*E*)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one.



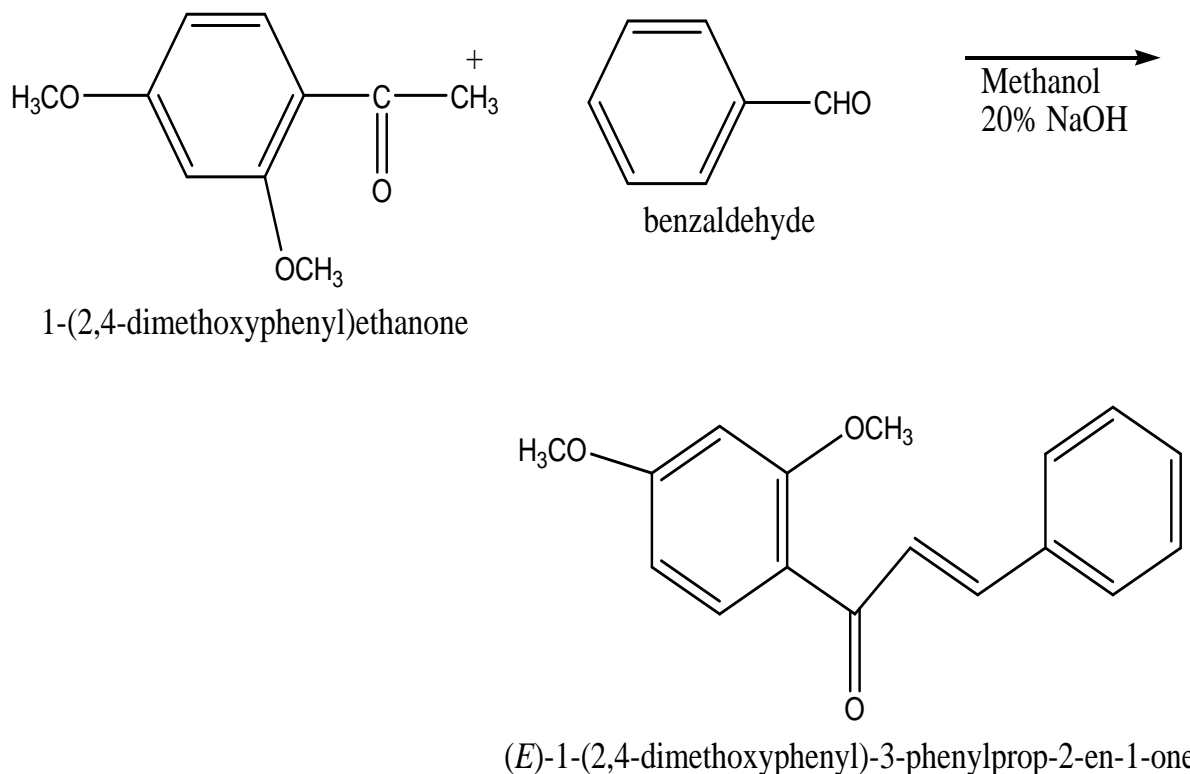
Aldolic condensation (Claisen-Schmidt condensation reaction) of equimolar quantities of acetophenone with appropriate quantity of 4-methoxy benzaldehyde in presence of aqueous alcoholic alkali was used for formation of α, β – unsaturated ketones (i.e. chalcones). Equimolar portions of the acetophenone (10mmol, 1 equivalent) and 4-methoxy benzaldehyde (10mmol, 1

equivalent) were dissolved in 15ml of ethanol. The mixture was allowed to stir for several minutes at 5-10°C. Aliquot of a 40% aqueous NaOH solution was then slowly added to the reaction flask. The reaction mixture was allowed to stir in ice bath for approximately 4-6hrs. All the crude products were washed first with cold water until washings were neutral to pH paper and precipitate

formed was then collected and recrystallized from ethanol to give chalcone derivatives of (*E*)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one.

3.2.3.4. Synthesis of (*E*)-1-(2,4-dimethoxyphenyl)-3-phenylprop-2-en-1-one: Aldolic condensation (Claisen-Schmidt condensation reaction) of equimolar quantities of 2,4-dimethoxy acetophenone with appropriate quantity of benzaldehyde in presence of aqueous alcoholic alkali was used for formation of α, β - unsaturated ketones (i.e. chalcones). Equimolar portions of the 2,4-dimethoxy acetophenone (10mmol, 1

equivalent) and benzaldehyde (10mmol, 1 equivalent) were dissolved in 15ml of ethanol. The mixture was allowed to stir for several minutes at 5-10°C. Aliquot of a 40% aqueous NaOH solution was then slowly added to the reaction flask. The reaction mixture was allowed to stir in ice bath for approximately 4-6hrs. All the crude products were washed first with cold water until washings were neutral to pH paper and precipitate formed was then collected and recrystallized from ethanol to give chalcone derivatives of (*E*)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one.



Intermediate Series

^a Compounds	R ₁	R ₂	Mol. Formula (Mol.Wt.)	^b R _f value	Yield (%)	m.p. (°C)
IS1	-H	-H	C ₁₅ H ₁₂ O (208.25)	0.85	93.46	58-60
IS2	-H	-2,OCH ₃	C ₁₆ H ₁₄ O ₂ (238.28)	0.87	77.09	64-66
IS3	-H	-4,OCH ₃	C ₁₆ H ₁₄ O ₂ (309.38)	0.91	76.79	38-40
IS4	-2,4,di-OCH ₃	-H	C ₁₇ H ₁₆ O ₃ (268.31)	0.90	71.35	60-62

^a Products were characterized by IR, NMR, MS

^b 1; Toulene : EthylAcetate : Formic Acid (4:2:1), 2; EthylAcetate : n-Hexane (3:7), 3; Pet. Ether: EthylAcetate (2:1)

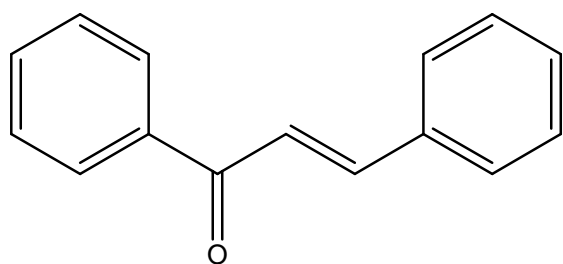
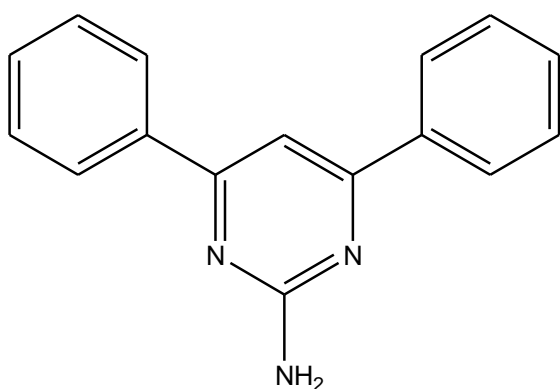
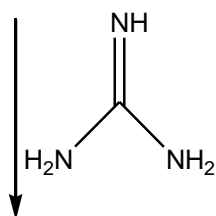
Second step

3.2.4.1. General synthesis (Step 2)

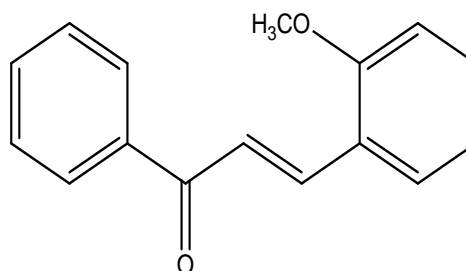
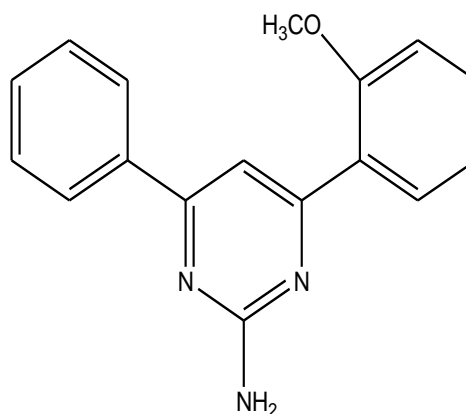
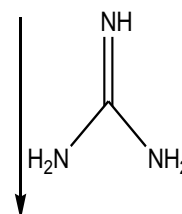
To chalcone (10mmol) obtained from step 1, added guanidine nitrate then reflux for 2 hr The precipitate formed washed with cold water until it turns neutral to pH paper, filtered and recrystallized from ethanol to give derivatives (II).

3.2.4.1.1. Synthesis of 4,6-diphenylpyrimidine-2-amine:

To chalcone (10mmol) obtained from step 1, added guanidine nitrate then reflux for 2 hr The precipitate formed washed with cold water until it turns neutral to pH paper, filtered and recrystallized from ethanol to give 4,6-diphenylpyrimidine-2-amine.

*(E)*-chalcone

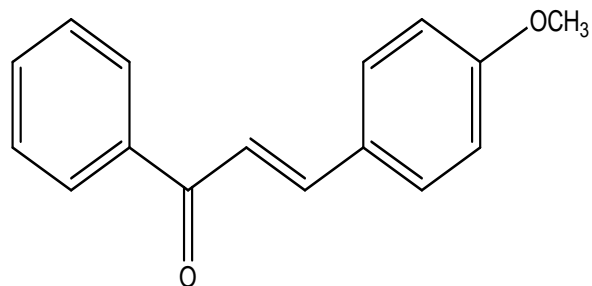
4,6-diphenylpyrimidin-2-amine

*(E)*-3-(2-methoxyphenyl)-1-phenylprop-2-en-1-one

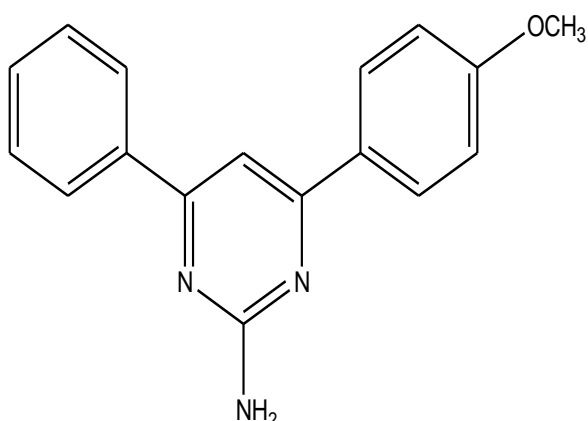
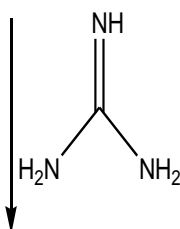
4-(2-methoxyphenyl)-6-phenylpyrimidin-2-amine

3.2.4.1.2. Synthesis of 4-(2-methoxy)-6-phenylpyrimidine-2-amine: To *(E)*-3-(2-methoxyphenyl)-1-phenylprop-2-en-1-one (10mmol) obtained from step 1, added guanidine nitrate then reflux for 2 hr. The precipitate formed washed with cold water until it turns neutral to pH paper, filtered and recrystallized from ethanol to give 4-(2-methoxy)-6-phenylpyrimidine-2-amine.

3.2.4.1.3. Synthesis of 4-(4-methoxy)-6-phenylpyrimidine-2-amine: To *(E)*-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one (10mmol) obtained from step 1, added guanidine nitrate then reflux for 2 hr. The precipitate formed washed with cold water until it turns neutral to pH paper, filtered and recrystallized from ethanol to give 4-(4-methoxy)-6-phenylpyrimidine-2-amine.

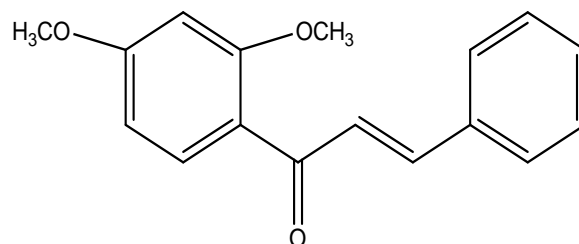


(E)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one

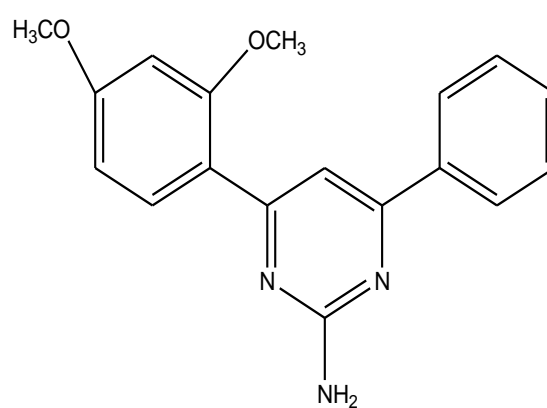
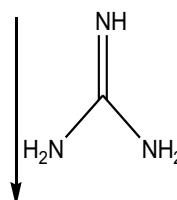


4-(4-methoxyphenyl)-6-phenylpyrimidin-2-amine

until it turns neutral to pH paper, filtered and recrystallized from ethanol to give 4-(2,4-dimethoxy)-6-phenylpyrimidine-2-amine.



(E)-1-(2,4-dimethoxyphenyl)-3-phenylprop-2-en-1-one



4-(2,4-dimethoxyphenyl)-6-phenylpyrimidin-2-amine

3.2.4.1.4. Synthesis of 4-(2,4-dimethoxy)-6-phenylpyrimidine-2-amine: To (E)-1-(2,4-dimethoxyphenyl)-3-phenylprop-2-en-1-one (10mmol) obtained from step 1, added guanidine nitrate then reflux for 2 hr The precipitate formed washed with cold water

Table 2: Second step mderivaive series.

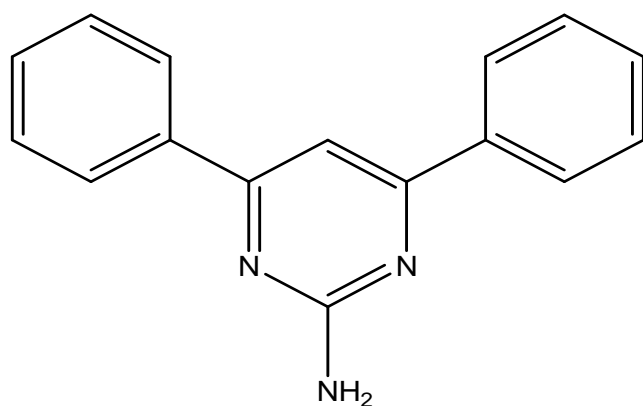
^a Compounds	R ₁	R ₂	Mol. Formula (Mol.Wt.)	^b R _f value	Yield (%)	m.p. (°C)
S1	-H	-H	C ₁₇ H ₁₂ ClN ₃ O (309)	0.90	68	66-68
S2	-H	-2,OCH ₃	C ₁₈ H ₁₄ ClN ₃ O ₂ (339.08)	0.83 ¹	84.15	123-125
S3	-H	-4,OCH ₃	C ₁₈ H ₁₄ ClN ₃ O ₂ (339.08)	0.68 ¹	41.66	146-148
S4	-2,4,di-OCH ₃	-H	C ₁₉ H ₁₆ ClN ₃ O ₃ (369.09)	0.84 ¹	47.34	144-146

^a Products were characterized by IR, NMR, MS.

^b 1; Toulene : EthylAcetate : Formic Acid (4:2:1), 2; EthylAcetate : n-Hexane (3:7), 3; Pet. Ether: EthylAcetate (2:1).

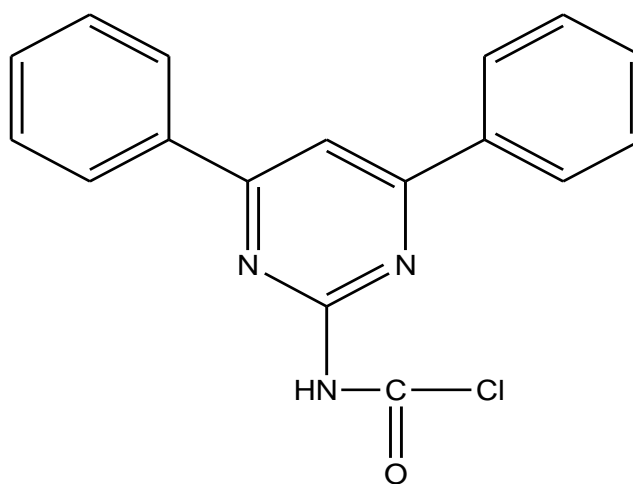
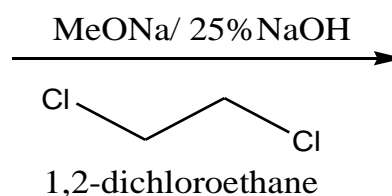
Step 3.**3.2.5.1. Synthesis of pyrimidine derivatives.**

To mixture of derivatives (II) (10mmol), 1,3-dichloroethane (10mmol) and 25% NaOH (0.025 mol, 10 ml) was refluxed in methanol(25 ml) for 8-12 h. The resulting mixture (III) was poured into ice-water and stirred. The crude product (III) were separated and recrystallized from Acetone.



4,6-diphenylpyrimidin-2-amine

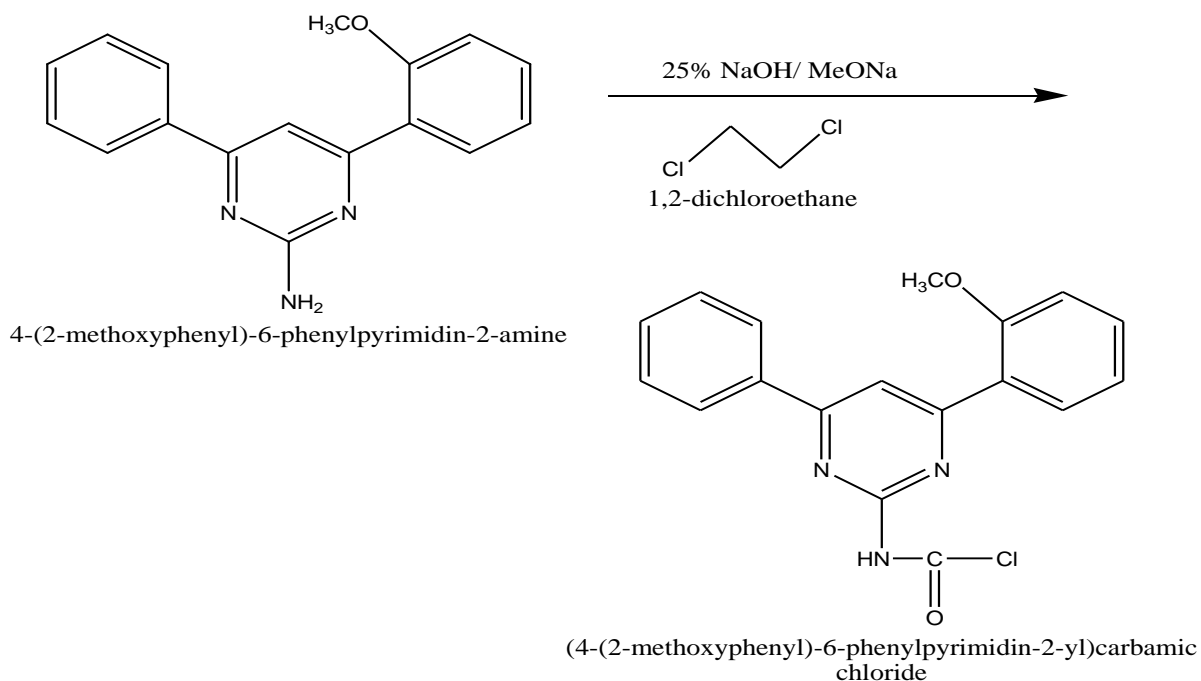
3.2.5.1.1. Synthesis of (4,6-diphenylpyrimidine-2-yl)carbamic acid: To mixture of derivatives 4,6-diphenylpyrimidin-2-amine (10mmol), 1,3-dichloroethane (10mmol) and 25% NaOH (0.025 mol, 10 ml) was refluxed in methanol(25 ml) for 8-12 h. The resulting mixture (4,6-diphenylpyrimidine-2-yl)carbamic acid (III) was poured into ice-water and stirred. The crude product (III) (4,6-diphenylpyrimidine-2-yl)carbamic acid were separated and recrystallized from Acetone.



(4,6-diphenylpyrimidin-2-yl)carbamic chloride

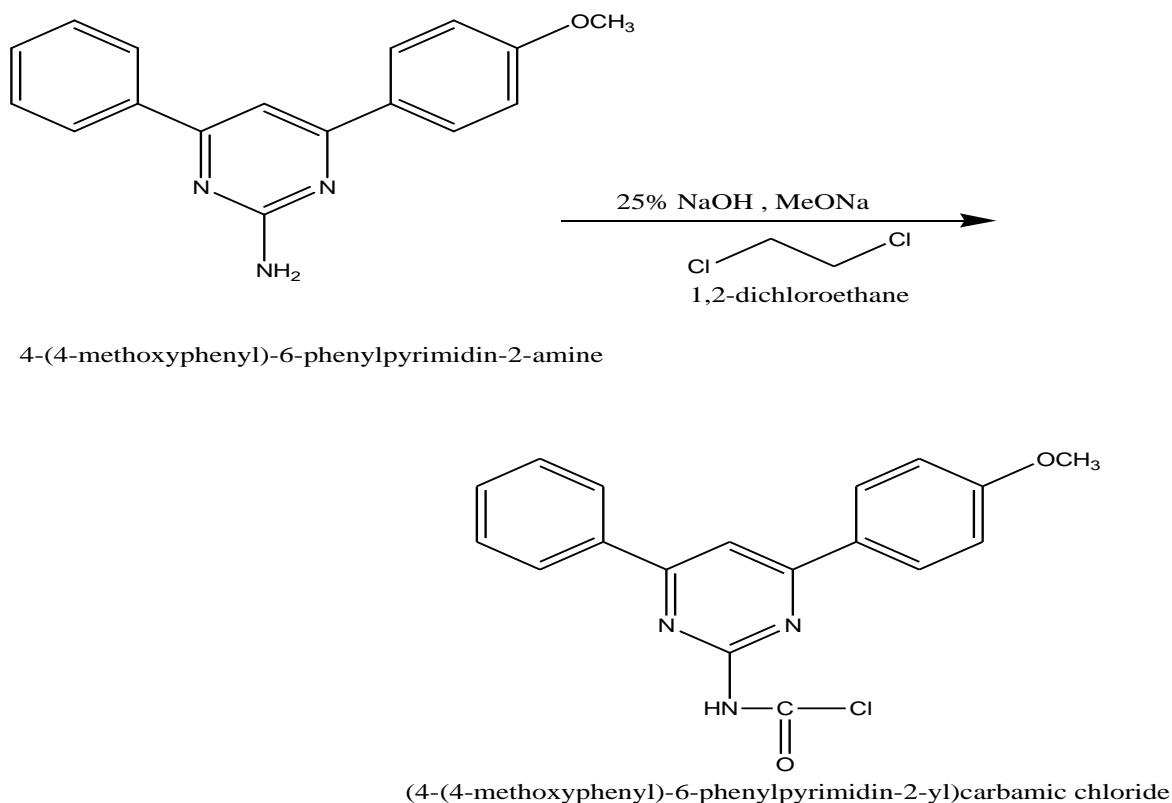
3.2.5.1.2 Synthesis of (4,2-methoxyphenyl)-6-phenylpyrimidine-2-yl carbamic chloride: To mixture of derivatives (4,2-methoxyphenyl)-6-phenylpyrimidine-2-amine (10mmol), 1,3-dichloroethane (10mmol) and 25% NaOH (0.025 mol, 10 ml) was refluxed in methanol(25 ml) for 8-12 h. The resulting mixture (4,2-

methoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride (III) was poured into ice-water and stirred. The crude product (III) (4,2-methoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride were separated and recrystallized from Acetone.



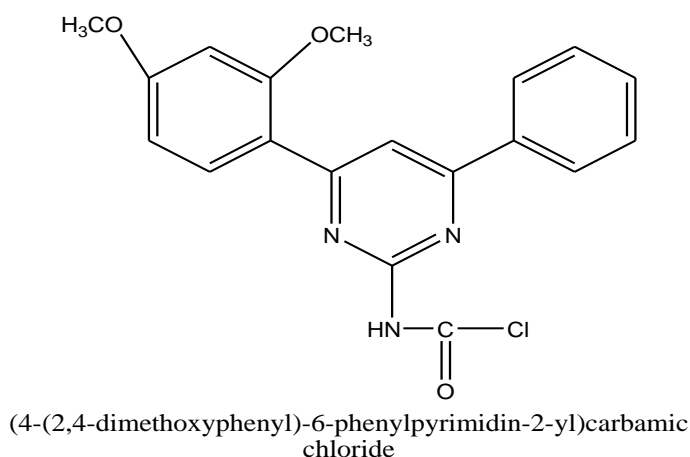
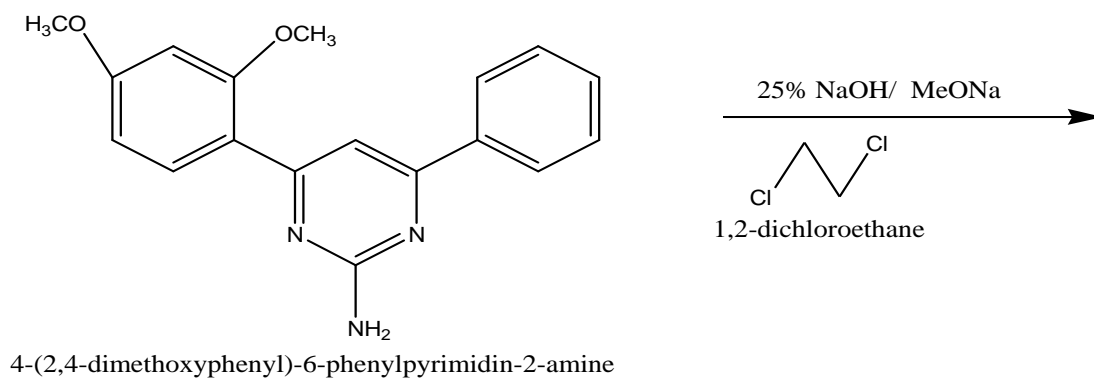
3.2.5.1.3. Synthesis of (4,4-methoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride: To mixture of derivatives (4,4-methoxyphenyl)-6-phenylpyrimidine-2-amine (10mmol), 1,3-dichloroethane (10mmol) and 25% NaOH (0.025 mol, 10 ml) was refluxed in methanol(25 ml) for 8-12 h. The resulting mixture (4,4-

methoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride (III) was poured into ice-water and stirred. The crude product (III) (4,2-methoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride were separated and recrystallized Acetone.



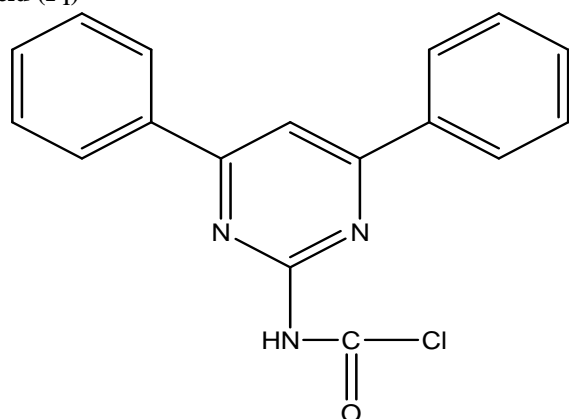
3.2.5.1.4. Synthesis of 4-(2,4-dimethoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride: To mixture of derivatives 4-(2,4-dimethoxyphenyl)-6-phenylpyrimidine-2-amine (10mmol), 1,2-dichloroethane (10mmol) and 25% NaOH (0.025 mol, 10 ml) was refluxed in methanol(25 ml) for 8-12 h. The resulting

mixture 4-(2,4-methoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride (III) was poured into ice-water and stirred. The crude product 4-(2,4-dimethoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride were separated and recrystallized from Acetone.



RESULT AND DISCUSSION

Spectral characterizations of synthesized compounds
Synthesis of (4,6-diphenylpyrimidine-2-yl)carbamic acid (P₁)

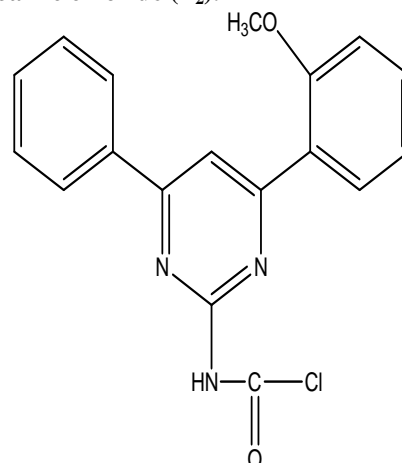


(4,6-diphenylpyrimidin-2-yl)carbamic chloride

IR (KBr, cm⁻¹): 3540.60 (N-H secondary amine), 3346.21 (C-H Ar str), 1647.10 (C=O str), 1598 (C=C str), 1597.13, (Ar C=C) and 750.69 (C-Cl str.). **¹H NMR:** (CDCl₃, δ, ppm): 7.4(s, 1H, CH of pyrimidine), 7.3-7.5

(m, 5H, CH), 8.0 (m, 1H, NH). **MS (m/z):** (M⁺= 311); 290, 300, 280.

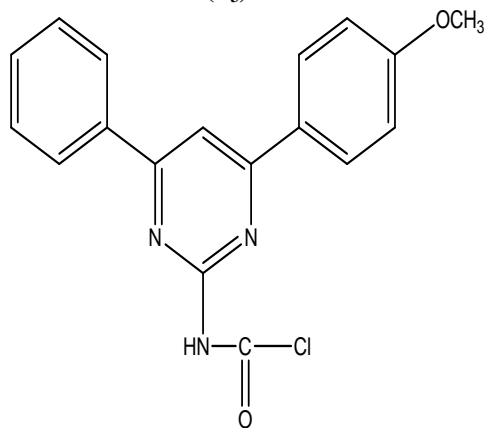
Synthesis of (4,2-methoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride (P₂).



(4-(2-methoxyphenyl)-6-phenylpyrimidin-2-yl)carbamic chloride

IR (KBr, cm^{-1}): 3570 (NH str), 3152 (C-H str), 1606 (C=O str), 1545 (C=N str), 1578.02 (C=C Ar str), 1188.20 cm^{-1} [C-O-C(-OCH₃)] **$^1\text{H NMR}$:** (CDCl_3 , δ , ppm): 7.72 (m, 1H, CH of pyrimidine), 7.5-8.2 (m, 4H, Ar-H), 8.9 (m, 1H, CH). MS (m/z): (M^+ = 398), 340, 329.

Synthesis of (4,4-methoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride (P_3).



(4-(4-methoxyphenyl)-6-phenylpyrimidin-2-yl)carbamic chloride

IR (KBr, cm^{-1}): 3570 (NH str), 3152 (C-H str), 1606(C=O str), 1545 (C=N str), 1578.02 (C=C Ar str), 1188.20 cm^{-1} [C-O-C(-OCH₃)] **$^1\text{H NMR}$:** (CDCl_3 , δ , ppm): 7.72 (m, 1H, CH of pyrimidine), 7.5-8.4 (m, 4H, Ar-H), 8.8 (m, 1H, CH). MS (m/z): (M^+ = 398), 340, 329.

5 Pharmacological Screening

Antibacterial activity

Table 3: Zone of inhibition and % Inhibition of some synthesized compounds.

Gram-positive bacteria <i>Staphylococcus aureus</i> zone of inhibition & % inhibition									
S.NO	Compounds Code	Concentration ($\mu\text{g/ml}$)							
		ZI	% I	ZI	%I	ZI	% I	ZI	% I
1	Std (Ampicillin)	12	13.33	11	12.22	14	15.56	16	17.78
2	P-2	10	11.11	12	13.33	14	15.56	15	16.67
3	P-3	13	14.44	12	13.33	13	14.44	13	14.44
4	P-4	12	13.33	13	14.44	14	15.56	14	15.56

Table 4: Zone of inhibition (mm) % Inhibition of some synthesized compounds.

Gram-negative bacteria <i>Pseudomonas aeruginosa</i> zone of inhibition (mm)									
S.NO	Compounds code	Concentration ($\mu\text{g/ml}$)							
		ZI	% I	ZI	%I	ZI	% I	ZI	% I
1	Std (Ampicillin)	9	11.11	11	12.22	13	14.44	14	15.55
2	P-2	12	13.33	12	13.33	14	15.56	12	13.33
3	P-3	13	14.44	13	14.44	15	16.67	15	16.67
4	P-4	9	10.00	12	12.22	13	11.11	14	13.33

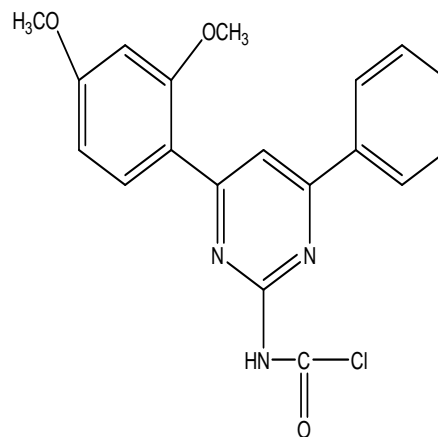
6. CONCLUSION

All the newly synthesized substituted Pyrimidine derivatives were evaluate for their pharmacological activity. Agar well diffusion method were used for evaluation of antibacterial activity.

The antibacterial activity evaluated against gram-positive bacteria *Staphylococcus aureus*, gram-negative bacteria *Pseudomonas aeruginosa* agar well diffusion

Synthesis of 4-(2,4-dimethoxyphenyl)-6-phenylpyrimidine-2-yl)carbamic chloride (P_4).

IR (KBr, cm^{-1}): 1672.36 (C=O of α,β unsaturated ketone), 1688.00 (C=N str), 1606.77 (Ar C=C) and 1160.23, 3570 (NH str), 3152 (C-H str), 1606 (C=O str), 1545 (C=N str), 1578.02 (C=C Ar str), 1188.20 [C-O-C(-OCH₃)], **$^1\text{H NMR}$:** (CDCl_3 , δ , ppm): 7.72 (m, 1H, CH of pyrimidine), 7.5-8.0 (m, 4H, Ar-H), 8.8 (m, 1H, CH). MS (m/z): (M^+ = 370), 320, 329.



(4-(2,4-dimethoxyphenyl)-6-phenylpyrimidin-2-yl)carbamic chloride

method. All the synthesized compounds and standard drugs were dissolved in DMSO and the concentrations of test compounds were adjusted to 25, 50, 100, and 200 $\mu\text{g/ml}$ and of standard drug Ampicillin were used. As indicated in Table 3 & 4. The compounds ompounds P-3 (having methoxy group) active against *Pseudomonas aeruginosa*.

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