ejpmr, 2020,7(11), 484-493

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

PHARMACEUTICAL SYNTHESIS OF PYRIMIDINE DERIVATIVES PROJECTING NEW PHARMACEUTICAL DRUG DESIGN, ALONG WITH ITS ANTIFUNGAL ACTIVITY INCLUDING TOXICITY STUDIES

S. Singh*, Dr. Shamim Ahmad and Dr. Shamsher Alam

PHD (Research Scholar), Department of Pharmaceutical Technology; Translam Institute of Pharmaceutical Education and Research Meerut.

***Corresponding Author: Dr. S. Singh**

PHD (Research Scholar), Department of Pharmaceutical Technology; Translam Institute of Pharmaceutical Education and Research Meerut.

Article Received on 01/09/2020 **Article Revised on 21/09/2020** **Article Accepted on 11/10/2020**

ABSTRACT

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. Numerous reports have appeared in the literature that highlights chemistry and uses of pyrimidines, and their derivatives like Sulfadiazine, Sulfamerazine, and Sulfamethazine. A series of Pyrimidine derivatives were synthesized to evaluate their antimicrobial activity, their structure were characterized by UV, NMR, IR and Mass spectrometer. Among the tested Pyrimidine derivatives **P-1** shows good activity against *Penicillium chrysogenum* and lesser toxicity.

KEYWORDS: Antifungal activity, antibacterial activity, analgesic activity, Pyrimidine.

INTRODUCTION

Pyrimidines are present among the three isomeric diazines. Several pyrimidines mainly cytosine (I), uracil (II) and thymine (III) have been isolated from the nucleic acid hydrolysis as shown in Fig 1.1. The nucleic acid are essential constituent of all cell and thus of all living matter cytosine is found to be present in both types of nucleic acids i.e. ribonucleic acid (RNA) and deoxyribonucleic acid (DNA).[1]

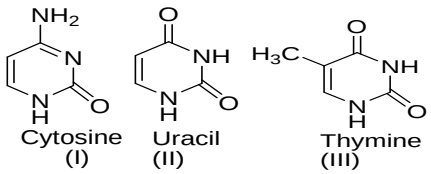


Fig.1.1

In addition to this, Pyrimidines ring is also found in Vitamin B_1, Barbituric acid (IV) and its several derivatives e.g. Veranal (V) which are used as Hypnotics (fig.1.2).[2]

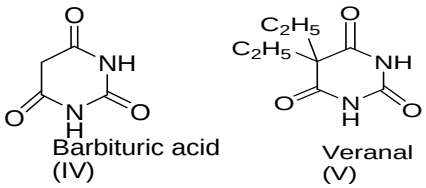


Fig.1.2

Numerous reports have appeared in the literature, that highlight chemistry and uses of pyrimidines, and their derivatives like Sulfadiazines, Sulfamerazines, and Sulfamethazines.[3] 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 pyridines include the nicotinamides, a component of the vitamin B group. Pyridines are precursors to various pharmaceuticals, adhesives, agrichemicals, and synthetic pigments.[4] 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.[5]

2. METHODOLOGY

2.1. Material and Methods

The purified pyrimidine derivatives were obtained, and its yields was around 45-95%. The synthetic route is illustrated in scheme 1 (fig.3.1.) Thin layer chromatography was used to reach completion of reaction and purity of compounds synthesized, using silica gel as stationary phase and Toulene:ethylacetate:formic acid as solvent system (4:2:1) and visualized by U.V. visualizing cabinet.

All solvents used were of 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. 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/$CDCl_3$ as solvent and using tetramethylsilane as internal standard. Mass were recorded on API 2000 triple quadrapole mass spectrophotometer.

2.1.1. Synthetic reaction

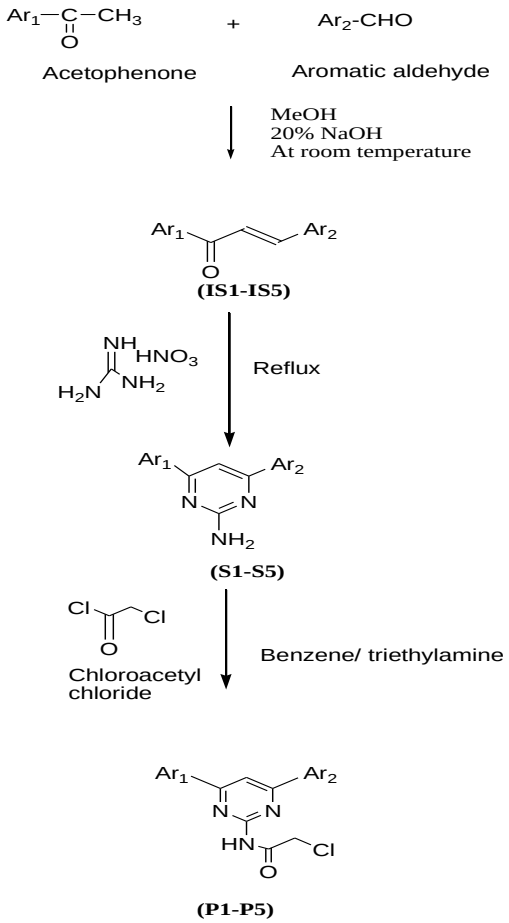


Fig. 2.1

3.2.1.Synthesis of Intermediate Subtstitute derivatives
Aldolic condensation (clasien-schmidt condensation reaction) of equimolar quantities of substituted acetophenone with appropriate quantities of substituted aromatic aldehyde in presence of aqueous alcoholic alkali was used for the 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 ºC. 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 4-6 hrs. 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.

3.2.1.1. Synthesis of *(E)*-1-(2,4-dichloro)-3-(3,4,5-trimethoxyphenyl)lprop-2-en-1-one (IS1)

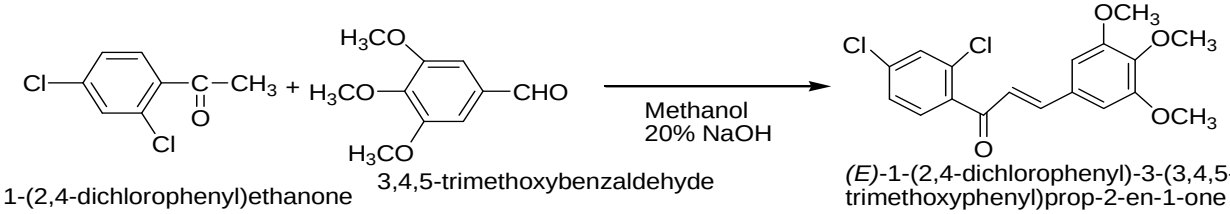
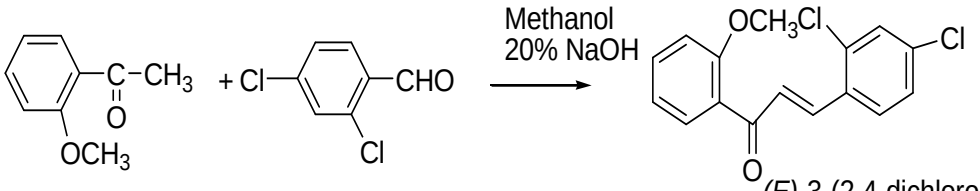


Fig.3.2.1

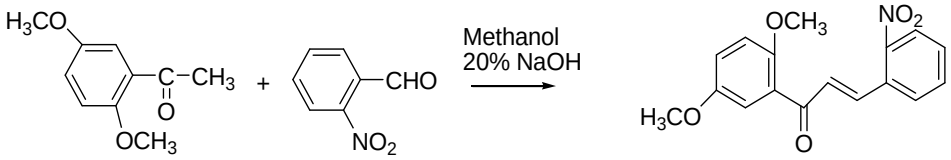
3.2.1.2. Synthesis of *(E)*-1-(2,4-dichlorophenyl)-1-(2-methoxyphenyl)lprop-2-en-1-one(IS2):



1-(2-methoxyphenyl)ethanone 2,4-dichlorobenzaldehyde *(E)*-3-(2,4-dichlorophenyl)-1-(2-methoxyphenyl)prop-2-en-1-one

Fig.3.2.2

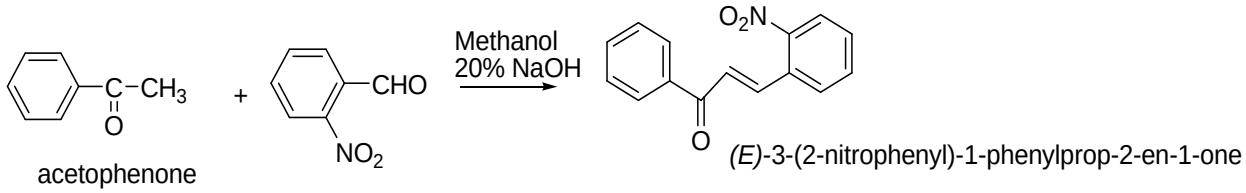
3.2.1.3. Synthesis of *(E)*-1-(2,5-dimethoxyphenyl)-3-(2-nitrophenyl)prop-2-en-1-one (IS3):



1-(2,5-dimethoxyphenyl)ethanone 2-nitrobenzaldehyde *(E)*-1-(2,5-dimethoxyphenyl)-3-(2-nitrophenyl)prop-2-en-1-one

Fig.3.2.3

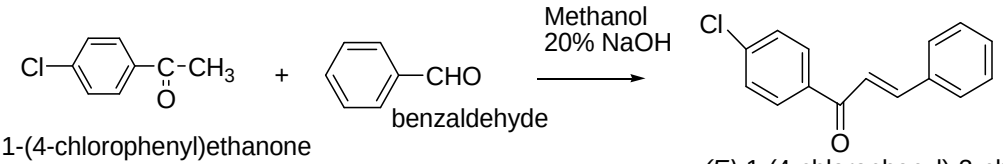
3.2.1.4. Synthesis of *(E)*-3-(2-nitrophenyl)-1-phenylprop-2-en-1-one (IS4):



acetophenone 2-nitrobenzaldehyde *(E)*-3-(2-nitrophenyl)-1-phenylprop-2-en-1-one

Fig.3.2.4

3.2.1.5.Synthesis of*(E)*-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one(IS5):



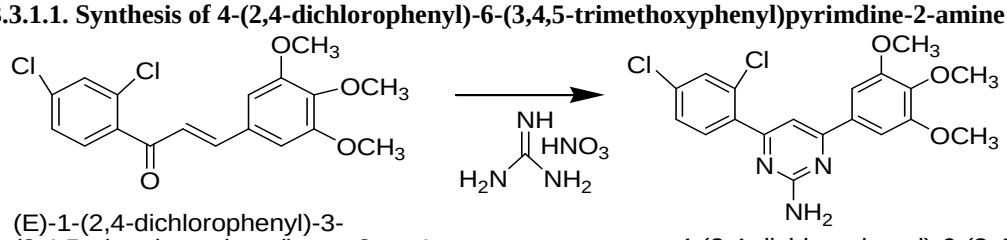
1-(4-chlorophenyl)ethanone benzaldehyde *(E)*-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one

Fig.3.2.5

3.3.1.Synthesis of Intermediate Substituted Derivatives (Step 2):

From step 1, the chalcone 10 mmol was obtained, guanidine nitrate was added and for two hours the reflux was given. The newly formed precipitate was washed with cold water till it comes back to the neutral pH point. The process of filtration and recrystallization was applied from ethyl alcohol to produce various derivatives. **(S1-S5)**.

3.3.1.1. Synthesis of 4-(2,4-dichlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimdine-2-amine (S1):

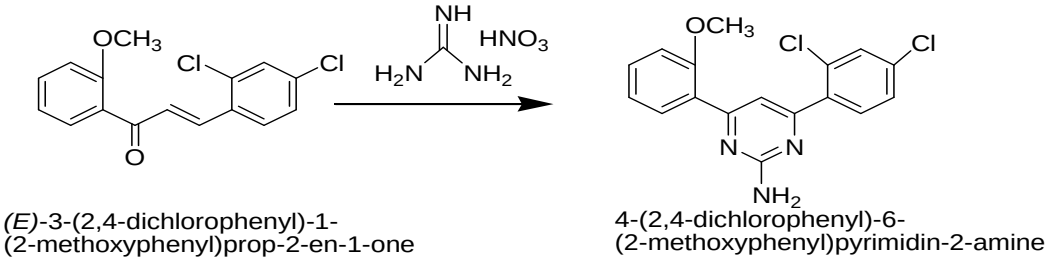


(E)-1-(2,4-dichlorophenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one

4-(2,4-dichlorophenyl)-6-(3,4,5-trimethoxyphenyl) pyrimidin-2-amine

Fig.3.3.1

3.3.1.2. Synthesis of 4-(2,4-dichlorophenyl)-6-(2-methoxyphenyl)pyrimdine-2-amine (S2):

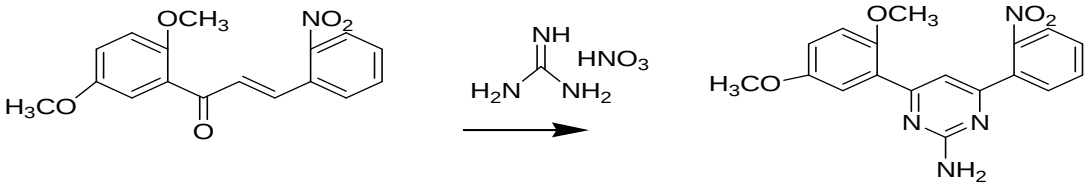


(E)-3-(2,4-dichlorophenyl)-1-(2-methoxyphenyl)prop-2-en-1-one

4-(2,4-dichlorophenyl)-6-(2-methoxyphenyl)pyrimidin-2-amine

Fig.3.3.2

3.3.1.3. Synthesis of 4-(2,5-dimethoxyphenyl)-6-(2,nitrophenyl)pyrimdine-2-amine (S3):

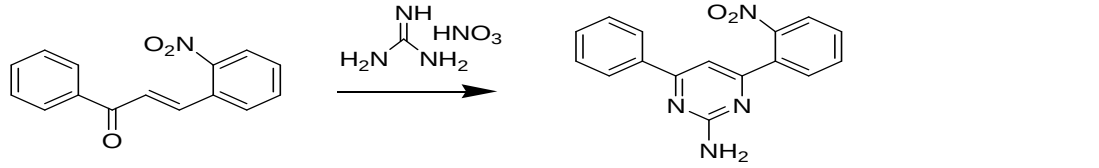


(E)-1-(2,5-dimethoxyphenyl)-3-(2-nitrophenyl)prop-2-en-1-one

4-(2,5-dimethoxyphenyl)-6-(2-nitrophenyl)pyrimidin-2-amine

Fig.3.3.3

3.3.1.4.Synthesis of 4-(2-nitrophenyl)-6-phenylpyrimdine-2-amine (S4):

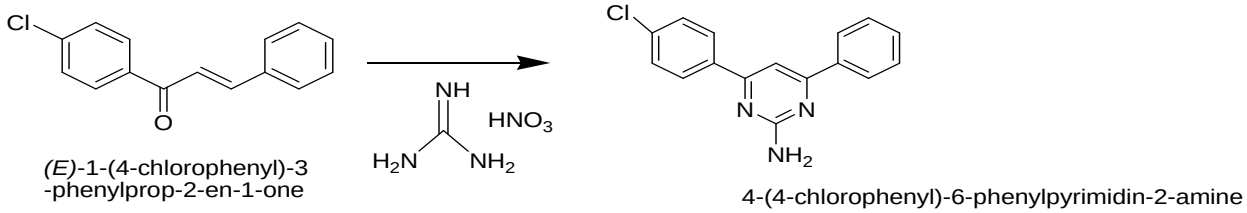


(E)-3-(2-nitrophenyl)-1-phenylprop-2-en-1-one

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

Fig.3.3.4

3.3.1.5.. Synthesis of 4-(4-chlorophenyl)-6-phenylpyrimdine-2-amine (S5):



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

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

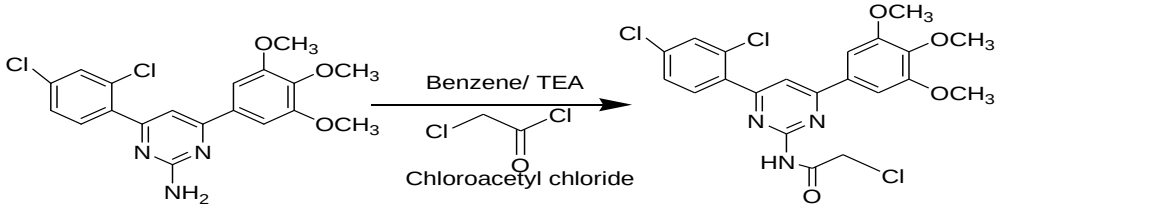
Fig.3.3.5

Step 3:

3.4.2. Synthesis of Pyrimidine Derivatives (Step 3): (P1-P5)

To the resultant mixture of derivatives **(S1-30)** (10mmol) added 2-3 ml of benzene solution, chloro acetyl chloride and 3-4 drops of TEA and reflux for one to two hours, the white precipitate was obtained as a result which was filtered and later washed with the benzene. It was collected and purified by the process of recrystallization from acetone.

3.4.1.1. Synthesis of (4-(2,4-dichlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl)acetamide (P1) :

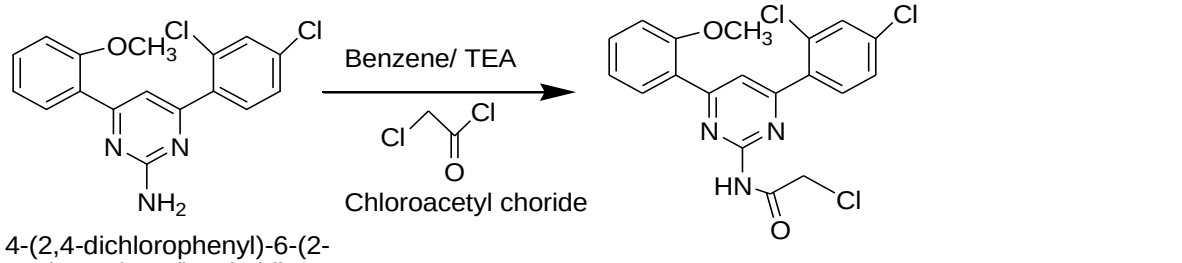


4-(2,4-dichlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-amine

2-chloro-*N*-(4-(2,4-dichlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl)acetamide

Fig.3.4.1

3.4.1.2. Synthesis of (4-(2,4-dichlorophenyl)-6-(2-methoxyphenyl)pyrimidin-2-yl)carbamic chloride(P2):

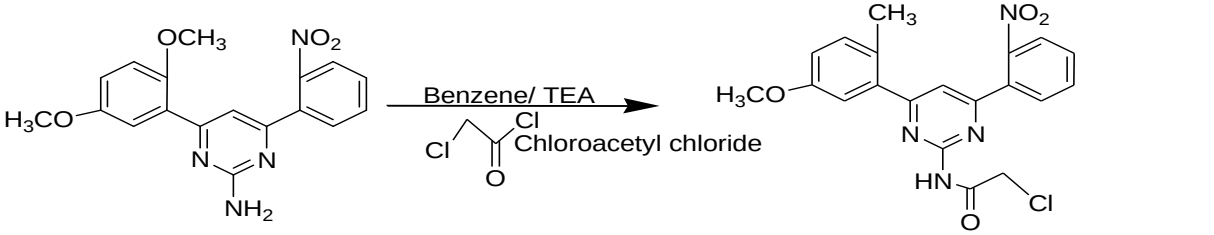


4-(2,4-dichlorophenyl)-6-(2-methoxyphenyl)pyrimidin-2-amine

2-chloro-*N*-(4-(2,4-dichlorophenyl)-6-(2-methoxyphenyl)pyrimidin-2-yl)acetamide

Fig.3.4.2

3.4.1.3. Synthesis of 2-chloro-*N*-(4-(5-methoxy-2-methylphenyl)-6-(2-nitrophenyl)pyrimidin-2-yl)acetamide (P3):

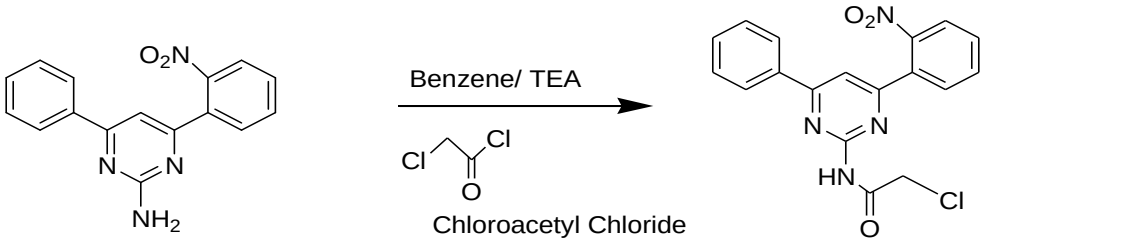


4-(2,5-dimethoxyphenyl)-6-(2-nitrophenyl)pyrimidin-2-amine

2-chloro-N-(4-(5-methoxy-2-methylphenyl) -6-(2-nitrophenyl)pyrimidin-2-yl)acetamide

Fig.3.4.3

3.4.1.4. Synthesis of (4-(2-nitrophenyl)-6-phenylpyrimidin-2-yl)carbamic chloride (P4):

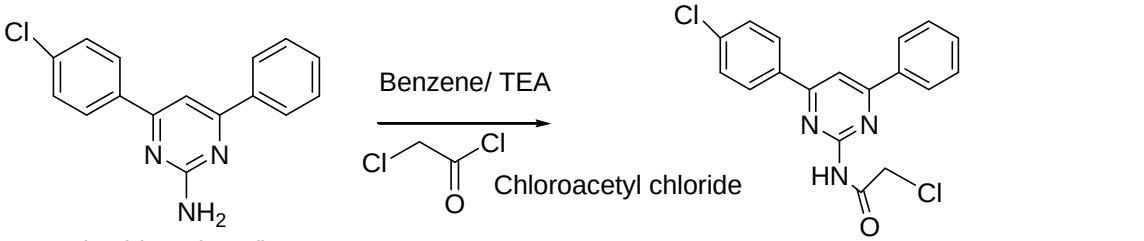


4-(2-nitrophenyl)-6-phenylpyrimidin-2-amine

2-chloro-N-(4-(2-nitrophenyl)-6-phenylpyrimidin-2-yl)acetamide

Fig.3.4.4

3.4.1.10. Synthesis of 2-chloro-*N*-(4-(4-chlorophenyl)-6-phenylpyrimidine-2-yl)acetamide (P5):

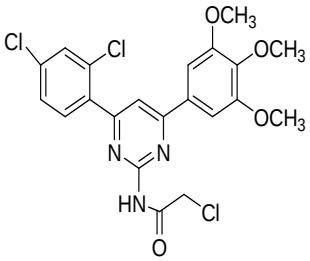
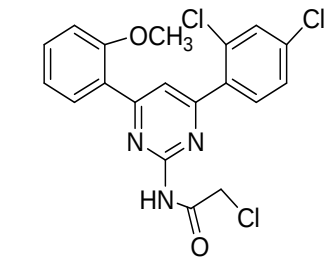
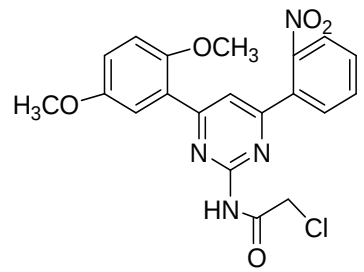
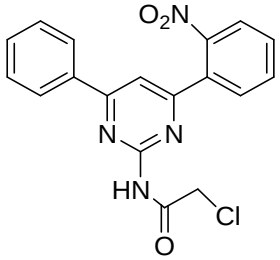


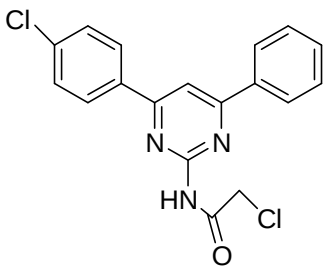
4-(4-chlorophenyl)-6-phenylpyrimidin-2-amine

2-chloro-N-(4-(4-chlorophenyl)-6-phenylpyrimidin-2-yl)acetamide

Fig.3.4.5

4.1.Spectral characterization:

1.	**2-chloro-*N*-(4-(2,4-dichlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl)acetamide (P6):**  2-chloro-*N*-(4-(2,4-dichlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl)acetamide	**IR (KBr, cm^{-1})**: 3665 (NH str), 3052 (C-H str), 1608 (Ar C=C),1683 (C=O str), 1578 (C=C Ar str), 1544 (C=N str), 1188 (-OCH_3str),767 cm-1 (C-Cl str.). **^{1}H NMR**: **($CDCl_3$, δ, ppm):** 7.9 (s, 1H, CH of pyrimidine), 8.2 (m, 5H, Ar-H), 8.0 (s, 1H, NH), 2.5 (d, 2H, CH_2), 3.32 (s,9H, OCH_3) **MS (m/z)** : **(**M^+= 482), 430, 366.
2.	**2-chloro-*N*-(4-(2,4-dichlorophenyl)-6-(2-methoxyphenyl)pyrimidin-2-yl)acetamide (P7):**  2-chloro-*N*-(4-(2,4-dichlorophenyl)-6-(2-methoxyphenyl)pyrimidin-2-yl)acetamide	**IR (KBr, cm^{-1})**: 3660 (NH str), 3052(C-H str), 1598 (C=N str), 1108 (-OCH_3 str), 767(C-Cl str.), 1608 (C=C). **^{1}H NMR**:**($CDCl_3$, δ, ppm):** 7.3 (s, 1H, CH of pyrimidine), 7.5 (m, 7H, Ar-H), 7.8 (s, 1H, NH), 3.34 (s, 3H,-OCH_3), 2.5 (d, 2H, CH_2). **MS (m/z)** : **(**M^+= 421), 400, 380.
3.	**2-chloro-*N*-(4-(2,5-dimethoxyphenyl)-6-(2-nitrophenyl)pyimidin-2-yl)acetmide (P8) :**  2-chloro-*N*-(4-(2,5-dimethoxyphenyl)-6-(2-nitrophenyl)pyrimidin-2-yl)acetamide	**IR (KBr, cm^{-1})**: 3608 (NH str), 3452 (C-H str), 1647 (C=O of α,β unsaturated ketone) , 1628.00 (C=N str), 1608 (Ar C=C), 1234 (-OCH_3), 767 (C-Cl str.), 682 (*o*- nitro Ar substitution) **^{1}H NMR**: **($CDCl_3$, δ, ppm):** 7.6 (s, 1H, CH of pyrimidine), 7.9-8.4 (m, 7H, Ar-H), 8.5 (s, 1H, NH), 3.34 (s, 6H,-OCH_3), 2.5 (d, 2H, CH_2). **MS (m/z)** : **(**M^+= 428), 400, 396.
4.	**2-chloro-*N*-(4-(2-nitrophenyl)-6-phenylpyrimidin-2-yl)acetamide(P9):**  2-chloro-*N*-(4-(2-nitrophenyl)-6-phenylpyrimidin-2-yl)acetamide	**IR (KBr, cm^{-1})**: 3770 (NH str), 3452 (C-H str), 1698 (C=N str), 1600 (Ar C=C) and 1706(C=O str), 767 (C-Cl str.), 700 *o*- nitro Ar substitution). **^{1}H NMR**: **($CDCl_3$, δ, ppm):** 7.4 (m, 1H, CH of pyrimidine), 8.1 (m, 4H, Ar-H), 2.5 (d, 2H, CH_2) **MS (m/z)** :(M^+= 368), 312, 316.

5.	**2-chloro-*N*-(4-(4-chlorophenyl)-6-phenylpyrimidin-2-yl)acetamide (P10):**  2-chloro-*N*-(4-(4-chlorophenyl)-6-phenylpyrimidin-2-yl)acetamide	**IR (KBr, cm^{-1})**: 1553 (C=C str), 1565 (C=N), 3355 (-NH, 2° amine), 3208 (C-H, aromatic), 1553 (C=O), 767 (C-Cl str.). **^{1}H NMR**: **($CDCl_3$, δ, ppm):** 7.5 (m, 1H, CH of pyrimidine), 8.0 (m, 4H, Ar-H), 8.3 (s, 1H, NH), 3.3 (d, 2H, CH_2). **MS (m/z)** : **(**M^+= 358), 302, 313.

4.2.Antifungal activity

Table .4.3.2.Antifungal activity of some synthesized Pyrimidine derivative sagainst *Penicillium chyrsogenum*.

***Penicilliumchyrsogenum*Zone of inhibition & % inhibition**									
S.NO	**Compounds code**	**Concentration (µg/ml)**							
		25 ZI	**25 % I**	**50 ZI**	**50 %I**	**100 ZI**	**100 % I**	**200 ZI**	**200 % I**
1	Std (Ketoconazole)	11	12.22	12	13.33	13	14.44	15	16.67
2	P-1	13	14.44	12	13.33	11	12.22	14	15.56
3	P-2	11	12.22	12	13.33	12	12.22	13	13.33
4	P-3	10	11	11	12.22	11	12.22	12	12.22
5	P-4	9	10	13	14.44	15	16.67	15	14.56
6	P-5	9	10	9	10	11	12.22	9	10

5.1. Toxicity screening of newly designed molecules (P1 to P5)

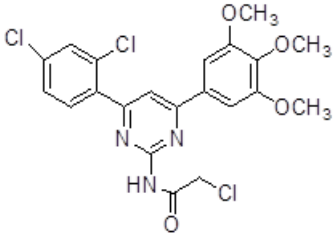
Toxicity screening was performed for: Drug Induced Toxicity, Genomic Toxicity, Aquatic & Terrestrial Toxicity, Reproductive Toxicity, Environmental Factor. These toxicity values were adapted from literature support. Cheng F *et al* 2012 (PubMed ID: 23092397).

The new design molecules also tested for their possible toxicity against following parameters:

- **Human Ether-a-go-go-Related Gene Inhibition:** The Human Ether-a-go-go-related Gene (hERG) Potassium Channel represents an Unusual Target for Protease-mediated Damage. This is responsible for cardiac arrhythmias and sudden death (PubMed ID: 16787254).
- **AMES toxicity:** The Ames test (Salmonella typhimurium reverse mutation assay) is a bacterial short-term test for identification of carcinogens using mutagenicity in bacteria as an endpoint (J.G. Hengstler, F. Oesch, in Encyclopedia of Genetics, 2001).
- Carcinogenesis: Test for causing cancer due to the molecule
- Fish toxicity
- Tetrahymena toxicity
- Honey Bee toxicity
- Biodegradation
- Acute oral toxicity
- Rat acute toxicity

The complete table about toxicity screening of (P1-P5) is available as following. The Pyrimidine derivaritive scan be further estimated for their utility for further study.

5.1.12-chloro-*N*-(4-(2,4-dichlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl)acetamide (P1):

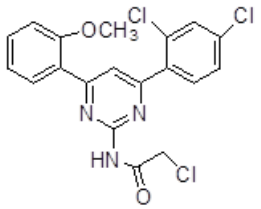


2-chloro-*N*-(4-(2,4-dichlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl)acetamide

P6: Toxicity (Qualitative Prediction & Probability)		
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor	0.9716
	Non-inhibitor	0.8427
AMES Toxicity	Non AMES toxic	0.7140
Carcinogens	Non-carcinogens	0.8418
Fish Toxicity	High FHMT	0.8786
TetrahymenaPyriformis Toxicity	High TPT	0.9897
Honey Bee Toxicity	Low HBT	0.8225
Biodegradation	Not ready biodegradable	1.0000
Acute Oral Toxicity	III	0.5998
Carcinogenicity (Three-class)	Danger	0.4365

Toxicity (Predicted Activity through model)		
Rat Acute Toxicity	2.2266	LD_{50}, mol/kg
Fish Toxicity	1.0378	pLC_{50}, mg/L
TetrahymenaPyriformis Toxicity	1.0469	$pIGC_{50}$, ug/L

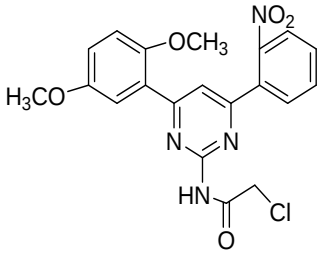
5.1.2.2-chloro-*N*-(4-(2,4-dichlorophenyl)-6-(2-methoxyphenyl)pyrimidin-2-yl)acetamide (P2):



2-chloro-*N*-(4-(2,4-dichlorophenyl)-6-(2-methoxyphenyl)pyrimidin-2-yl)acetamide

P7: Toxicity (Qualitative Prediction & Probability)		
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor	0.8941
	Non-inhibitor	0.7908
AMES Toxicity	Non AMES toxic	0.6281
Carcinogens	Non-carcinogens	0.9083
Fish Toxicity	High FHMT	0.8058
TetrahymenaPyriformis Toxicity	High TPT	0.9819
Honey Bee Toxicity	Low HBT	0.8531
Biodegradation	Not ready biodegradable	1.0000
Acute Oral Toxicity	III	0.7393
Carcinogenicity (Three-class)	Non-required	0.4500
Toxicity (Predicted Activity through model)		
Rat Acute Toxicity	1.9796	LD_{50}, mol/kg
Fish Toxicity	1.2976	pLC_{50}, mg/L
TetrahymenaPyriformis Toxicity	0.8990	$pIGC_{50}$, ug/L

5.1.3. 2-chloro-*N*-(4-(2,5-dimethoxyphenyl)-6-(2-nitrophenyl)pyimidin-2-yl)acetmide (P3):

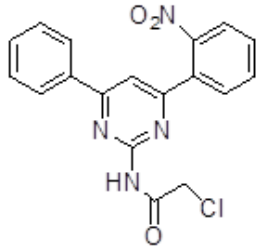


2-chloro-*N*-(4-(2,5-dimethoxyphenyl)-6-(2-nitrophenyl)pyrimidin-2-yl)acetamide

P8: Toxicity (Qualitative Prediction & Probability)		
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor	0.8696
	Non-inhibitor	0.7384
AMES Toxicity	AMES toxic	0.6865
Carcinogens	Non-carcinogens	0.6656
Fish Toxicity	High FHMT	0.9648
TetrahymenaPyriformis Toxicity	High TPT	0.9905
Honey Bee Toxicity	Low HBT	0.8344
Biodegradation	Not ready biodegradable	1.0000
Acute Oral Toxicity	III	0.5847
Carcinogenicity (Three-class)	Non-required	0.4210

Toxicity (Predicted Activity through model)		
Rat Acute Toxicity	2.5414	LD_{50}, mol/kg
Fish Toxicity	0.9284	pLC_{50}, mg/L
TetrahymenaPyriformis Toxicity	1.2757	$pIGC_{50}$, ug/L

5.1.4. 2-chloro-*N*-(4-(2-nitrophenyl)-6-phenylpyrimidin-2-yl)acetamide(P4):

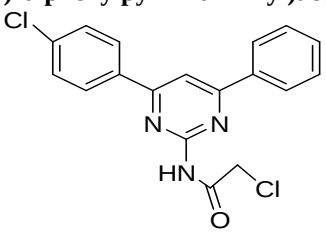


2-chloro-*N*-(4-(2-nitrophenyl)-6-phenylpyrimidin-2-yl)acetamide

P9: Toxicity (Qualitative Prediction & Probability)		
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor	0.9128
	Non-inhibitor	0.8573
AMES Toxicity	AMES toxic	0.7221
Carcinogens	Non-carcinogens	0.6831
Fish Toxicity	High FHMT	0.9102
TetrahymenaPyriformis Toxicity	High TPT	0.9529
Honey Bee Toxicity	Low HBT	0.9078
Biodegradation	Not ready biodegradable	0.9970
Acute Oral Toxicity	III	0.6275
Carcinogenicity (Three-class)	Non-required	0.4810

Toxicity (Predicted Activity through model)		
Rat Acute Toxicity	2.6118	LD_{50}, mol/kg
Fish Toxicity	1.0809	pLC_{50}, mg/L
TetrahymenaPyriformis Toxicity	1.0539	$pIGC_{50}$, ug/L

5.1.5. 2-chloro-*N*-(4-(4-chlorophenyl)-6-phenylpyrimidin-2-yl)acetamide (P5):



2-chloro-*N*-(4-(4-chlorophenyl)-6-phenylpyrimidin-2-yl)acetamide

P10: Toxicity (Qualitative Prediction & Probability)		
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor	0.9449
	Non-inhibitor	0.8505
AMES Toxicity	Non AMES toxic	0.8224
Carcinogens	Non-carcinogens	0.8784
Fish Toxicity	High FHMT	0.7836
TetrahymenaPyriformis Toxicity	High TPT	0.9851
Honey Bee Toxicity	Low HBT	0.9011
Biodegradation	Not ready biodegradable	1.0000
Acute Oral Toxicity	III	0.7366
Carcinogenicity (Three-class)	Non-required	0.6170

Toxicity (Predicted Activity through model)		
Rat Acute Toxicity	1.8875	LD_{50}, mol/kg
Fish Toxicity	1.3267	pLC_{50}, mg/L
TetrahymenaPyriformis Toxicity	1.0385	$pIGC_{50}$, ug/L

RESULT AND DISCUSSION

A novel series of compounds (**P1**-**P5**) were synthesized and characterized.The Infrared spectra of compounds (**P1**-**P5**) revealed absorption bands within 3770–3357 cm^{-1} for (NH str), 1608- 1585 cm^{-1} for C=N.1H NMR spectrum which showed a singlet signal at *d* (7.2-7.8) ppm.

All the newly synthesized Pyrimidine derivatives were evaluatedfor their biological activity by using Agar well diffusion method.

The antifungal activity evalauated against *Penicilliumchyrsogenum* by agar well diffusion method. All the synthesized Pyrimidine derivatives and standard drugs were dissolved in DMSO and the concentrations of test compounds were adjusted to 25, 50, 100, and 200 µg/ml and Ketoconazole were used as an standard drug.

Based on the structure activity relationships, it can be concluded that presence of bulky group OCH_3, at 3,4,5 position shows good activity.

CONCLUSION

Among all the synthesized Pyrimidine derivatives, **P1** shows good activity against *Penicillium chrysogenum* and lesser toxicity.

REFERENCES

1. Singh, H. and Kapoor, V. K. Medicinal and pharmaceutical chemistry, 2003; pp. 29.
2. Agarwal, O.P., Organic chemistry, Reaction and Reagent, 2002; pp. 735.
3. Jain, M. K., andSharnevas, S.C. Organic chemistry, 2006; pp. 997-999.
4. David, A. Williams, and Thomas, L. Foye's principles of medicinal chemistry. Fifth edition, 2002; pp. 12-13.
5. Remington, the science and practice of pharmacy Fifth edition, pp. 458.