Synthesis and Biological Evaluation of 8-Carboxy-5-(un)substituted-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines
Chapter 4.

Synthesis and Biological Evaluation of 8-Carbethoxy-5-(un)substituted-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines

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4.1. Introduction

Imidazopyrimidines are novel potentially bioactive molecules. Various isomeric imidazopyrimidines are integral part of the biological system as in DNA, RNA and other nucleic acids. Due to the structural resemblance of various isomeric imidazopyrimidines with nucleic acids, these classes of compounds serve as promising candidate for new drug discovery and in fact this is true. Base-modified nucleosides and nucleotides have demonstrated an important impact in various fields. Modification of nucleotide bases through the incorporation of an "etheno" bridge has provided a number of interesting compounds for biochemical and biological studies.

Different types of isomeric imidazopyrimidines are known to exist depending on the way the pyrimidine ring is annelated with imidazole as shown below (246a-e). This type of annulations drastically affects the overall electron density of the imidazopyrimidine ring system.

4.1.1. Biological activity of imidazopyrimidines

Imidazopyrimidines are reported to exhibit variety of activities including anticancer, antiviral, antimicrobial, antifungal, antihypertensive, antiinflammatory, analgesic, antipyretic, bronchodilator. This chemical nucleus has been described as hypnoselective and anxioselective pharmacophore with substantial affinity for benzodiazepine and gamma amino butyric acid (GABA) receptors.

Certain imidazo[1,2-a]pyrimidines were patented for their use in the chemoprevention and treatment of both precancerous lesions and cancers. A number of structurally related purine and pyrimidine derivatives are known to be effective as antitumor agents. Through the simultaneous inclusion of thiol and the nitrogen mustard radical, the antitumor action of 4-[bis-(2-chloroethyl)amino]-1,2-pyrimidinethiol has been demonstrated on an implanted RC mammary adenocarcinoma.
Imidazopyrimidines have been patented as potent inhibitors of the transforming growth factor (TGF)-β signaling pathway. The compounds were useful in the treatment of TGF-β related disease states including cancer and fibrotic diseases. TGF-β activates both antiproliferative and tumor-promoting signaling cascades. TGF-β production promotes tumor progression while its blockade enhances antitumor immune responses and inhibits metastasis.

The antiviral activity of several imidazopyrimidines has been reported. Bicyclic pyrimidine nucleosides, like imidazopyrimidine nucleosides have shown considerable potential as antiviral agents. For example, a series of ribofuranosyl imidazo[1,2-c]pyrimidine base modified nucleosides (247d) with both hydrophobic and hydrophilic functional groups were prepared and screened for their antiviral activity.

The imidazopyrimidines 248 and 249 have been synthesized and tested for their antimicrobial and antifungal activity. Few of the synthesized compounds have shown significant activity against various Gram-positive and Gram-negative bacteria including M. tuberculosis H37Rv.
Imidazopyrimidines have been described as inhibitors of a number of inflammatory cytokines particularly TNF-α and IL-1β. A patent discloses the selective COX-2 inhibitory actions of similar type of compounds (250) and their use in the treatment of inflammation and cancer. The mitogen-activated protein (MAP) kinase p38 is implicated in the release of the pro-inflammatory cytokines TNF-α and IL-1β. Inhibition of cytokine release may be a useful treatment for inflammatory conditions such as rheumatoid arthritis and Crohn's disease. A novel series of imidazopyrimidines have been discovered that significantly inhibit p38 and suppress the production of TNF-α in vivo.

\[
\text{R}_1, \text{R}_2, \text{R}_3 = \text{R, OR, halogen, SR, SOR, SO}_2\text{R}
\]

A positive inotropic property along with vasodilatation activity with minimal effects on blood pressure and heart rate have been documented for some imidazol[1,2-a]pyrimidines (251a). Ueda et al. reported several imidazopyrimidine compounds (251b) useful as agents acting on cardiovascular organs, particularly as a preventing and treating agent for cardiac insufficiency, diseases of coronary arteries and cardiac arrhythmia or as anti-inflammatory, analgesic and hypotensive agent.

\[
\text{R} = \text{H, halogen, Het, OR, SR, NH}_2, \text{NHR, NHAr Etc.}
\]

\[
\text{R}_1 = \text{NH}_2, \text{NHR, NR}_2, \text{OH, OR, NHCOR, NHCH}_2\text{Ar, NHCOAr}
\]

\[
\text{R}_2 = \text{halogen, CF}_3, \text{R, OR, NHCH}_2\text{Ar}
\]

Effects of cannabinoid intake include alterations in memory and cognition, euphony and sedation. Cannabinoids also increase heart rate and vary systemic arterial pressure. Peripheral effects related to bronchial constriction, immunomodulation, and inflammation have also been observed. A patent describes the use of imidazol[1,2-a]pyrimidines (252) as cannabinoid receptor ligands.
Few other imidazo[1,2-a]pyrimidin-2-carboxylic esters, acids and amides (253a, b) were tested in vivo for antiinflammatory and analgesic activities as well as their ulcerogenic potential, and exhibited good potential for such use. Vidal et al. have studied the effects of some hexahydroimidazo[1,2-c]pyrimidine derivatives 254 on leukocyte functions in vitro and screened for antiinflammatory activity in two models of inflammation. Antiinflammatory, analgesic and antipyretic actions were also described for several imidazopyrimidines. A number of imidazopyrimidines 255 have been reported to have anxiolytic, antiseizure and GABA<sub>A</sub> brain receptor ligand characteristics. The GABA<sub>A</sub> brain receptor ligands were highly selective inverse agonists and reported to enhance alertness. The compounds were shown to potentiate the effects of other CNS agents and working as probes for the localization of GABA<sub>A</sub> receptors in tissue sections. Few patents have documented the use of these imidazopyrimidines in dementing illness such as Alzheimer's disease characterized by a progressive deterioration in cognition.

To date, a large number of imidazopyrimidines have been synthesized and studied using behavioral test models. This has made possible investigations focused on the relationships between the structure and efficacy of the ligand. A series of imidazopyrimidines has been reported as benzodiazepine receptor ligands. These data are consistent with these imidazopyrimidines being partial agonists at the benzodiazepine receptor.
Imidazo[1,2-c]pyrimidines – Synthesis and Biological Activity

benzodiazepine receptor Another report describes new fluorescent probes for the visualization and localization of activated microglia and function of the peripheral benzodiazepine receptors (PBRs). Although some intrinsically fluorescent imidazopyrimidine compounds possessed good binding affinity in this report, they cannot be used for visualizing PBRs due to their unfavorable fluorescence characteristics.

Several 5-amino-7-chloro-imidazo[1,2-c]pyrimidines and 7-chloro-8-methylthioimidazo[1,2-c]pyrimidines were synthesized for identifying the role of the purine ring in SAR studies of cytokinin. It was observed that compounds with the imidazopyrimidine ring were generally less active than those with the purine ring, with the exception of the pentenylamino derivatives, which showed an activity comparable with that of the control, kinetin.

There have been reports describing preparation of fluorescent etheno-bridged modifications of various nucleosides and nucleotides (256 and 257) for their use in the tertiary structure determination of proteins by incorporating these fluorescent coenzymes in nucleic acids and studying their spectroscopic profiles. Variations in fluorescence with respect to changes in the polarity, temperature and viscosity of the solvent as well as fluorescence excitation and fluorescence polarization spectra were also examined. Imidazopyrimidines of following type are reported for their herbicidal activity at a concentration of 10 g/arc.
Novel aryl substituted imidazopyrazines, imidazopyrimidines, and imidazopyridines (261) were patented as selective modulators of corticotrophin releasing factor (CRF) receptors and probes for the localization of CRF receptors and as standards in assays for CRF receptor binding. These CRF antagonists were reported for their use in treating psychiatric disorders and neurological diseases, anxiety-related disorders, post-traumatic stress disorder, supranuclear palsy and feeding disorders as well as treatment of immunological, cardiovascular or heart-related diseases and colonic hypersensitivity associated with psychopathological disturbance and stress in mammals. Several other imidazopyrimidines have been reported as potential antipsychotic agents 262

A competition assay for the screening of potential endothelin ETA ligands was established and a series of new disubstituted imidazo[1,2-c]pyrimidines was investigated. Moderate ETA affinity was detected for several derivatives [30-40% inhibition of [3H]BQ-123 binding (3 nmol/L) at a concentration of 10 μmol/L]. Several imidazo[1,2-c]pyrimidines were patented as bronchodilators. Another patent mentions the antiasthmatic, antiallergic actions of certain imidazopyrimidines with antagonistic activity against platelet activation factor and chemical eosinotaxis inhibitory action. Similarly, the pharmacological data established in a study represented new support for the protecting effect of bamifylline against respiratory damage induced by well known anaphylaxis mediators. At the same time, few other imidazo[1,2-c]pyrimidines have been patented for their excellent Syk tyrosine kinase inhibiting activity.

Certain imidazo[1,2-a]pyrimidines have been patented for their gonadotropin-releasing hormone (GnRH) antagonizing activity, and usefulness as a prophylactic or therapeutic agent for sex hormone-dependent diseases.
4.1.2. Methods of synthesis of imidazo[1,2-c]pyrimidines

A survey of the literature uncovered a number of tactics which have been applied to the synthesis of imidazo[1,2-c]pyrimidines. Almost all the methods used to prepare imidazo[1,2-c]pyrimidines utilize either 4-chloro or 4-amino pyrimidines which are cyclocondensed with β-substituted aminoethanes (β-halo or β-hydroxy) or α-halocarbonyl compounds, respectively. The desired imidazo[1,2-c]pyrimidines can be synthesized by various routes.

4.1.2.1. Closure of five membered ring

The classical method for the preparation of imidazo[1,2-c]pyrimidines was described for the first time by Ochiai and Jamai in 1939, who synthesized 7-methyl-2-phenylimidazo[1,2-a]pyrimidine and imidazo[1,2-c]pyrimidine (264) by heating 2/4-amino-6-methylpyrimidine (263) with phenacyl bromide. Subsequently, the method was applied to the synthesis of a whole series of unsubstituted and C- or N-substituted 2- and 4-aminopyrimidines 265.

The method proved to be very promising as it allows use of a wide range of alkylating agents (266) and appreciable variation in the experimental conditions. The alkylating agents employed are α-bromo(chloro) ketones and α-bromo(chloro) aldehydes or their acetals. The alkylation process is usually carried out by heating equimolar amounts of the reactants to 60-100°C in an organic solvent (pure alcohols, dioxane, toluene or DMF) or in water. In order to prevent salts by the aminopyrimidines, which hinders the reaction, basic reagents like sodium hydroxide, sodium bicarbonate or trialkylamines are used. A better way of alkylation is also reported which uses...
carbonyl substrate 269 along with molecular halogen and excludes the preparation and purification of the halogenocarbonyl component 681.

The most common and also the most versatile synthetic method for imidazo[1,2-c]pyrimidines is the condensation of 4-aminopyrimidine with α-halocarbonyl compounds. For example, reaction of chloroacetaldehyde or bromoacetaldehyde with various nucleosides 657-659,662-685 or substituted 4-aminopyrimidines 630-646,648-685.

Bromocarbonyl compounds can also be used instead of chlorocarbonyl compounds owing to the higher reactivity and less mutagenic nature of the former 630,682. The interaction of aminopyrimidines 268 with α-halocarbonyl compounds 271 can proceed in theory via an initial stage involving the quaternization of the pyrimidine N atom or via the formation of Schiff bases 272a. Studies have shown that aminopyrimidines are quaternized, forming extremely labile salts, which are readily converted into imidazopyrimidines 272 689.

As a matter of record, one finds that the reaction of 4-aminopyrimidine with α-halocarbonyl compounds (chloroacetaldehyde) is not a perfectly general synthesis of imidazo[1,2-c]pyrimidine, since there are reports of this reaction giving exclusively...
different unexpected cyclized products, for example leading to formation of pyrrolo[2,3-c]pyrimidines (273a)\textsuperscript{686,688,693} or pyrrolo[1,2-c]pyrimidines or pyrrolo[1,2-a]pyrimidines \textsuperscript{691} This is the product derived from bridging the N\textsuperscript{4} and the 5-position when C-5 of the pyrimidine is unsubstituted

Cyclization of 4-aminopyrimidine with aqueous chloroacetaldehyde had been deeply studied by Kluge\textsuperscript{688} and Kochetkov et al\textsuperscript{684} It was observed that the rate of formation of etheno-bridge at 4-aminopyrimidines with aqueous chloroacetaldehyde was a pH susceptible reaction and exhibited a bell shaped dependence on pH Furthermore, they found that the reaction proceeded most smoothly with very good yields by quenching the \textit{in situ} formed hydrochloric acid by carrying out the reaction between pH 6 to 6.5 in sodium acetate buffered reaction medium

\[ 274 \rightarrow 275 \rightarrow 276 \]

Imidazo[1,2-c]pyrimidines were prepared in a regiospecific fashion by the reaction of 1,2-bis-electrophiles, like 1,2-bis(benzotriazoyl)-1,2-(dialkylamino)ethanes (275) with 4-aminopyrimidine (274, as 1,3-bis-nucleophiles) in one-pot reactions\textsuperscript{694} It was proposed that the reaction proceeds through the attack of 1,3-bis-nucleophile on both the carbon atoms of 1,2-bis(benzotriazoyl)-1,2-(dialkylamino)ethane to give an intermediate which ultimately with the elimination of both good leaving benzotriazole moieties result into regiospecific formation of imidazo[1,2-c]pyrimidines
Thermal cyclocondensation of imines 278, formed by the interaction of certain cyclic amidines with aldehydes, and isocyanides was described using Lewis acids like InCl₃ to shorten the reaction time. The bicyclic products in this case were proposed to form via thermal [4+1]-cycloaddition reaction. Unfortunately, this novel approach was only successful for very electron-deficient carboxaldehydes.

The nucleophilic amination of halogeno, alkylthio-, and aryloxy- (or alkyloxy) derivatives of pyrimidines constitutes a method of preparation of imidazo[1,2-c]pyrimidines which is no less important on preparative scale. In most cases, the method is more laborious than the previous one, but it has nevertheless found applications in the synthesis of imidazo[1,2-c]pyrimidine systems and their hydrogenated analogues. It is better to use β-halogenoalkylamines instead of β-aminoalcohols in these reactions as the step involving conversion of the β-hydroxyalkylaminopyrimidine intermediate into corresponding cyclizing β-chloro derivative can be omitted. Cyclization of 4-chloroacetylaminopyrimidine has been reported with aluminium chloride to give corresponding imidazo[1,2-c]pyrimidine. Several dihydroimidazo[1,2-c]pyrimidines 282 have been prepared through the...
cyclization of 4-β,β-diethoxyethylaminopyrimidine (281b)\(^{666,700}\) and 4-β-chloroethylaminopyrimidine (281a)\(^{699}\) with phosphorus oxychloride

![Chemical structure](attachment:image)

The reactions of N-pyrimidinyl-α-aminocarboxylic acids/esters (283a) under the conditions of cyclization by glacial acetic acid or the acetic acid-acetic anhydride (10.1) mixture have been thoroughly investigated by Ueda and Fox who showed that the only product was 3-alkyl-1,2,3,5-tetrahydroimidazo[1,2-c]pyrimidin-2,5-dione (284)\(^{705,706}\)

![Chemical structure](attachment:image)

4-Chloropyrimidines (285) can be directly converted to imidazo[1,2-c]pyrimidines (287) by cyclocondensation with aminoacetaldehyde diethylacetal in a sealed vessel at 150°C with ethanol as a solvent\(^{688,703}\) Armarego and other workers modified the method slightly and included the nucleophilic displacement of 4-chloro with aminoacetal in the presence of potassium iodide\(^{699,707,708}\) The conversion of the initial chloropyrimidines into the more reactive iodopyrimidines made it possible to achieve quantitative yields of α-pyrimidinylaminoacetals Depending on the type of cyclizing agent used, the latter can be converted into the corresponding imidazo-, 3-hydroxyimidazolino-, and 3-alkoxyimidazolino pyrimidines. Similarly, imidazo[1,2-c]pyrimidines from chloropyrimidine were described by Bakavoli et al using propargylamine\(^{709}\) The nucleophilic replacement of 4-chloro group by propargylamine and subsequent cyclization with sulfuric acid resulted into substituted imidazo[1,2-c]pyrimidines
Imidazo[1,2-c]pyrimidines have been prepared by the condensation of 4-chloropyrimidine with electron poor ω-allylic amines via a sequential intermolecular nucleophilic displacement and intramolecular "conjugate" addition. It was proposed that the condensation reaction of a chloropyrimidine (288) with a secondary amine (289) proceed in high yield only when the amino component did not carry an α-substituent. Similarly, 4-(alkenylamino)pyrimidin-5-carboxaldehydes were proposed to yield corresponding imidazopyrimidines by cyclization of the nucleophilic pyrimidine N atom onto the pendant electrophilic alkene via an intramolecular Michael addition due to a high density of functionality of the aldehyde.

Recently, synthesis of imidazo[1,2-c]pyrimidines has been reported in an unprecedented reaction by Sepúlveda-Arques and González-Rosende who...
attempted to synthesize polyfunctional imidazo[1,2-c]pyrimidines with an amino group at C-2. The reaction of the 2-p-tosylaminopyrimidine (292) with bromoacetamide in the presence of Hunig's base (diisopropylethylamine, DIPEA) in DMF resulted into imidazo[1,2-c]pyrimidines 293a. By heating at reflux with trifluoroacetic anhydride in dichloromethane and p-tolylsulfonic acid as catalyst, these imidazo[1,2-c]pyrimidines were readily isomerized into imidazo[1,2-a]pyrimidines 294. It was proposed that the formation of the imidazo[1,2-c]pyrimidines is the result of a Michael addition of the nucleophilic carboxamide group to the electron deficient α,β-unsaturated imine system. The trans disposition of the H₂ and H₈α hydrogens confirmed that the addition of the amide to the unsaturated imine is diastereoselective with the nucleophilic attack occurring preferentially on the opposite face to the aryl group present on the amide substituent.

4.1.2.2. Closure of six membered ring
Ethyl imidazolone-2-acetate (295) can be reacted with cyanates in benzene to yield derivative of hexahydroidimidazo[1,2-c]pyrimidine-5,5-dione (296). This process proceeds via formation of an intermediate which can be cyclized to imidazo[1,2-c]pyrimidine on boiling in ethanol.

4.1.2.3. Closure of both the rings
In this type of cyclocondensation reactions, the synthesis of imidazo[1,2-c]pyrimidines is accomplished via a double annulation of two reactants. Following are some of the reported methods for the preparation of imidazo[1,2-c]pyrimidines through the closure of both the rings simultaneously. Twofold ring closure of 1-methylthio-2-azabuta-1,3-diene-4,4-dicarbonitrile with ethylenediamine were described to yield imidazo[1,2-c]pyrimidines in good yields. A simple and efficient cyclocondensation reaction of N-acylimidates with imidazolidine ketene aminals to 2,3-dihydroimidazo[1,2-c]pyrimidines under focused microwave irradiation is also described.
Imidazo[1,2-c]pyrimidines — Synthesis and Biological Activity

Reaction of o-aminonitriles (297) with ethyl iso(thio)cyanatoacetate (298b) gave double annelated products, fused pyrimidines 299, in one-pot reactions in 60-70% yield. The cyclization was thought to proceed via a thiourea intermediate. Similarly, these o-aminonitriles 297 can be double cyclized in one-pot annelation with ethyl N-[bis(methylthio)methylene]amino acetate (BMMA, 298a) to imidazo[1,2-c]pyrimidines 299 in fairly good yields.

Michael addition of the thioureaacetamide 303 to the benzylidene intermediate 302, generated by the interaction of benzaldehyde (300) and ethyl cyanoacetate (301), produces intermediates which can undergo [1,6,7]-rearrangement and cyclization by [1,2,(3)5']-elimination to give imidazo[1,2-c]pyrimidines 305.
4.2. Aim of Present work

TB is a leading killer of young adults worldwide and the global scourge of MDR-TB is reaching epidemic proportions. It is endemic in most developing countries and resurgent in developed and developing countries with high rates of HIV infection. XDR-TB has further worsened the situation. Drug regimens have been designed and optimized along with the implementation of the DOTS initiative. However, these regimens are not sufficiently short or convenient to facilitate effective treatment in resource-poor countries. Therefore, drug-resistant strains have emerged to threaten TB control in various areas of the world, including India, China, Russia and the former Soviet Union.

The TB research has achieved great attention today. The search for novel anti-TB agents having completely new mechanisms of action and targets with improved pharmacokinetic properties that can shorten the duration of therapy and replace agents lost to resistance is of major concern. Other special considerations include identifying optimal therapy for patients with AIDS, particularly noting the problems of drug/drug interactions for those receiving antiretroviral treatment.

In recent years a number of compounds, either of synthetic or natural origin, have been synthesized and tested against mycobacteria. Many of these have shown good potential to be further developed as novel anti-TB agents and in fact, few are under clinical investigations, like linezolid, TMC 207, PA-824, OPC-67683, BM 212, SQ-109, several quinolones and macrolide antibiotics.

A large number of imidazopyrimidines and imidazoquinolines have been synthesized and studied using behavioral test models. Imidazo[1,2-c]pyrimidines have also been widely investigated for their antiviral effects due to their structural similarity with the nucleic acids.

PA-824, an imidazooxazinone derivative has generated considerable excitement with its antitubercular potency and presently is undergoing clinical trials. It was thought of interest to replace the oxazine ring of PA-824 with its bioisoster pyrimidine ring and study its influence on anti-TB activity. Further, the 3D structural similarity between PA-824 and the designed imidazopyrimidines was checked by ligand based molecular modeling studies. Low rmsd (root mean square distance) value suggested good 3D structural similarity between the designed molecule and PA-824.
This prompted us to synthesize a series of 8-carbethoxy-5-(substituted)-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines and check its antimycobacterial potential.

Pyrimidines are very important precursors for the biologically active molecules. Various 4-(substituted amino)pyrimidine derivatives are exhibiting promising biological activities including antibacterial, antimalarial, anticancer, diuretic, antihistaminic and β-adrenoceptor blocking activity. Thus, it was thought of interest to explore also the biological activity of 4-(substituted amino)pyrimidines, the intermediates of 2,3-dihydroimidazo[1,2-c]pyrimidines.

Molecular modeling

Three dimensional structural similarity between the designed series of imidazo[1,2-c]pyrimidines and PA-824 was checked by ligand based molecular modeling studies. All the structures were generated, energy minimized and superimposed using PC based ChemDraw Ultra software (Version 11.0, CambridgeSoft Corporation). All geometries were fully optimized by minimizing the energy with respect to geometrical variables without symmetry constraints, using a 0.01 kcal/mol gradient. The r.m.s.d observed was 0.244. The low r.m.s.d value suggests good 3D similarity between PA-824 and imidazo[1,2-c]pyrimidines.
Figure 4.1 3D Structures of PA-824 and a compound of designed series (IF 04)

IF 04 (Designed compound)
PA-824

Figure 4.2 3D Overlay of IF 04 with PA-824
4.3. Results and Discussion
4.3.1. Synthetic approach
4.3.1.1. Synthesis of vinyl amidines

Vinyl amidines, the difficultly isolable open chain intermediates in the pyrimidine synthesis, have been serendipitously isolated by the condensation of S,N-acetals with various amidines like formamidine, acetamidine, benzamidine and morpholine carboxamidine, under controlled reaction conditions in our laboratory. Various reaction conditions include stirring the reactants at room temperature in ethanol with concomitant use of stoichiometric amount of base needed for the in situ liberation of the amidine from its salt.

Cyanoketene S,N-acetals 306 are obtained by nucleophilic displacement of one methyl mercapto group of the S,S-acetal 305b by alkyl or aryl amines. One of the general methods for the preparation of ketene S,S-acetals with an alkyl substituent on the sulfur atom is through the alkylation of dithiolate anion obtained by the base catalyzed condensation of an active methylene compound with carbon disulfide.

In the present work we have used ethyl cyanoacetate (301) as an active methylene compound.

Thus, α-cyanoketene S,N-acetals (306), when treated with amidines, liberated from their salts by treatment with an equivalent amount of sodium hydroxide in ethanol, at room temperature, afforded colorless N-cyanovinylamidines in 70-80% yield.

Alternatively, the α-cyanoketene S,N-acetals can also be obtained through the base catalyzed condensation of the active methylene nitrile with an appropriate aryl.
isothiocyanate followed by alkylation of the resultant enethiolate salts (307) with one mole of DMS.612,721

$$\text{EtO}_2\text{C} = \text{CN} \quad \text{KOH} \quad \begin{bmatrix} \text{EtO}_2\text{C} = \text{CN} \\ \text{HN} \quad \text{K}^+ \text{S} \quad \text{R} \end{bmatrix} \quad \text{DMS} \quad \text{EtO}_2\text{C} = \text{CN}$$

DMS = Dimethyl sulfate

Due to presence of three isomerizable hydrogen atoms, the vinylamidmes exist in variety of tautomeric and stereoisomeric forms. Based on the IR and $^1$H NMR spectra it was suggested that the vinylamidmes exist preferentially in E-form, from their various potential tautomeric and stereoisomeric forms, which is stabilized by the formation of the hydrogen bonding between hydrogen of secondary amino group at C-2 and oxygen of the carbonyl group of ester.612

![Diagram of vinylamidine](image)

4.3.1.2. Synthesis of 4-chloropyrimidines

Earlier, cyclization of N-cyanovinylamide (242) under different catalytical conditions has been reported from our laboratory.502,609-612

![Diagram of 4-chloropyrimidine synthesis](image)
Cyclization of vinylamidine in the presence of strong base such as sodium ethoxide in ethanol yielded 4-hydroxypyrimidine (243). On the other hand, when heated in the presence of strong acid like p-tolylsulfonic acid (p-TSA), vinyl amidine is cyclized to 4-aminopyrimidine (244). Similarly, vinylamidine is reported to give 4-chloropyrimidine (245) when treated with dioxane saturated with dry HCl gas. All these reactions could be very easily used to explain the reactivity of vinylamidines in various catalytic conditions.

Hydrogen chloride is known to enhance the reactivity of nitriles in a variety of reactions undergone by nitriles and this fact has been utilized in the hydrogen chloride catalyzed reactions of nitriles with o-aminocarbonyl compounds for the synthesis of condensed pyrimidines. The acid catalyzed pyrimidine cyclization presumably proceeds via o-aminocarbonyl intermediate. Thus, vinylamidine was stirred with 30 mL of saturated solution of dry hydrogen chloride gas in dioxane (6M) for three hours and allowed to stand at room temperature for 12 h. The work-up of the reaction yielded 4-chloropyrimidines as pale yellow colored crystalline solid.

\[
\begin{align*}
\text{EtO}_2\text{C}-\text{CN} & \xrightarrow{\text{Dry HCl gas/Dioxane}} \text{EtO}_2\text{C}-\text{Cl} \\
\text{HN} & \text{N} \quad \text{HN} \\
\text{R} & \quad \text{R}_1
\end{align*}
\]

\( R = \text{alkyl, aryl} \)
\( R_1 = \text{H, alkyl, aryl} \)

The IR spectrum of the product was devoid of \( \text{C}\equiv\text{N} \) stretching absorption around 2200 cm\(^{-1}\), indicating the participation of the nitrile function in the cyclization. The IR and \(^1\text{H} \) NMR spectra of the product indicated the absence of a primary amino group. Also, the product was tested positive for chlorine atom (Beilstein test). All cyanovinylamidines (242) are found to cyclize to the corresponding 4-chloropyrimidines (245) in good yields.
A plausible mechanism for this interesting novel transformation can be expressed as follow.\(^{613}\)

\[
\begin{align*}
\text{EtO}_2\text{C} & \xrightarrow{\text{Dioxane}} \text{HN}^+ \\
\text{C} = \text{N} & \xrightarrow{\text{HCl}} \text{Cl} \\
\text{HN} & \xrightarrow{\text{R} \text{R} \text{HCl}} \text{Cl} \\
\text{EtO}_2\text{C} & \xrightarrow{\text{HN}} \text{R} \\
\end{align*}
\]

Though the precise stage at which the chlorine atom gets incorporated is not certain, it is however, reasonable to assume a concerted mechanism for the formation of 4-chloropyrimidines. The protonated amidine 309 may undergo attack by chloride ion on the nitrile group and concomitant cyclization with the elimination of ammonia to yield the pyrimidine (path a) In view of the known tendency of the nitriles to form imidoyl chlorides, the formation of amidino-imidoyl intermediate 310 cannot also be ruled out. The amidino-imidoyl chloride can undergo cyclization with the elimination of ammonia to yield the 4-chloropyrimidine (path b).

\[
\begin{align*}
\text{EtO}_2\text{C} & \xrightarrow{\text{Dioxane}} \text{HN}^+ \\
\text{C} = \text{N} & \xrightarrow{\text{HCl}} \text{Cl} \\
\text{HN} & \xrightarrow{\text{R} \text{R} \text{HCl}} \text{Cl} \\
\text{EtO}_2\text{C} & \xrightarrow{\text{HN}} \text{R} \\
\end{align*}
\]

The formation of a cyanovinylimidoyl chloride 311b, through protonation of the cyanovinylamidine, and the displacement of ammonia by chloride ion, followed by
cyclization can also be conceived as an alternate reaction pathway for the formation of 4-chloropyrimidine. However, the intermediate, cyanovinylimidoyl chloride seems unlikely due to the absence of any reports on the conversion of amidines into imidoyl chlorides under the influence of hydrogen chloride. Moreover, there does not seem to be any report on the synthesis of such imidoyl chlorides.

### 4.3.1.3. Synthesis of 4-(substituted amino)pyrimidines

The 4-chloropyrimidines can be looked upon as useful starting materials for the synthesis of various condensed pyrimidines. The nucleophilic displacement of the 4-chloro group with appropriate bisnucleophiles followed by the cyclization reaction can be viewed as possible method for the construction of another heterocyclic ring system on the pyrimidine framework. The 4-chloro group was easily replaced by strong nucleophilic reagents like aminoalkanols or hydrazine hydrate yielding corresponding 4-(substituted amino)pyrimidines. The synthesis of 4-(substituted amino)pyrimidine was attempted by refluxing corresponding 4-chloropyrimidine with excess ethanolamine or hydrazine hydrate (85%) in ethanol. The product was characterized as 4-(substituted amino)pyrimidines based on their IR, 1H NMR and mass spectral data. Moreover, the compounds were not showing positive Beilstein test on copper foil when heated on direct flame and thus suggesting the nucleophilic displacement of chlorine atom by the amino group.

![Chemical Structure](image)

### 4.3.1.4. Synthesis of 2,3-dihydroimidazo[1,2-c]pyrimidines

The displacement of the chlorine atom with appropriate nucleophilic reagents followed by cyclization reaction can be viewed as possible method for the construction of another heterocyclic ring system on the pyrimidine framework. We have synthesized certain novel 2,3-dihydroimidazo[1,2-c]pyrimidines by the method reported by Turner with some modifications. Various 2,3-dihydroimidazo[1,2-c]pyrimidines have been prepared by the cyclocondensation of 5-carboxethoxy-4-ethanolamino-2-substituted-6-(substituted amino)pyrimidines with the dehydrating agents like orthophosphoric acid, thionyl chloride or phosphoryl chloride. The reaction catalyzed by orthophosphoric acid is a convenient route but it may promote...
soluble salt formation. The use of organic nonpolar solvents facilitates isolation of the 2,3-dihydroimidazo[1,2-c]pyrimidines with high purity.

\[
\begin{array}{c}
\text{EtO}_2\text{C} \quad \text{Cl} \\
\text{HM} \quad \text{N} \\
\text{R} \quad \text{R}_1 \quad \text{NH}_2\text{CH}_2\text{CH}_2\text{OH} \\
\text{EtO}_2\text{C} \quad \underline{\text{EtOH}} \\
\text{NHCH}_2\text{CH}_2\text{OH} & \text{POCl}_3 & \text{EtO}_2\text{C} \\
\text{HN} & \text{C}_6\text{H}_6 & \text{N} \\
\text{R} & \text{R}_1 \\
\end{array}
\]

It has been observed that the use of β-halogenoalkylamines is better instead of β-aminoalcohols in these reactions as the step involving conversion of the β-hydroxyalkylaminopyrimidine intermediate 313 into corresponding cyclizing β-chloro derivative 315 can be omitted. However, no such increase of reactivity was required in our reaction and the product could be isolated by a smooth reaction. As C-5 position is occupied by carbethoxy group the possible side reaction of alternative cyclization could also be eliminated. Moreover, as the hydroxyl group of aminoethanol is not sufficiently nucleophilic in nature to attack the carbethoxy group, the cyclization with the later cannot be expected (formation of 314). Therefore, 2,3-dihydropyrimido[1,2-c]pyrimidine 316 was the only isolated products in the cyclocondensation reaction with phosphorus oxychloride.

\[
\begin{array}{c}
\text{O} \quad \text{Cl} \\
\text{HN} \quad \text{N} \\
\text{R} \quad \text{R}_1 \quad \underline{\text{NH}_2\text{CH}_2\text{CH}_2\text{OH}} \\
\text{EtO}_2\text{C} \quad \underline{\text{POCl}_3} \\
\text{HN} \quad \text{Cl} \\
\text{R} \quad \text{R}_1 \\
\end{array}
\]

Thus, various 4-chloropyrimidines 245 were refluxed with ethanolalmine in ethanol for 30 minutes to 2 h to obtain 4-ethanolaminopyrimidines (313), which on cyclization by refluxing with phosphorous oxychloride or thionyl chloride in anhydrous benzene gave 2,3-dihydropyrimido[1,2-c]pyrimidines (316) in good yields. The structures of the
synthesized compounds were confirmed on the basis of their spectral data like IR, mass and \(^1\)H NMR and elemental analysis

**4.3.2. Physical and spectral characteristics**

**4.3.2.1. 4-(Substituted amino)pyrimidines**
The 5-carbethoxy-2-(un)substituted-4-(substituted amino)-6-(substituted amino)pyrimidines are colorless to white crystalline compounds. A sharp decrease in the melting point was observed in the conversion of cyanovinylamidines to the 4-chloropyrimidines, while a slight increase in the melting point during the transformation of 4-chloropyrimidines into 5-carbethoxy-2-(un)substituted-4-(substituted amino)-6-(substituted amino)pyrimidines. Various 4-chloropyrimidines were freely soluble in most of the organic solvents and moderately soluble in n-hexane from which they were crystallized. The 5-carbethoxy-2-(un)substituted-4-(substituted amino)-6-(substituted amino)pyrimidines are soluble in most of the organic solvents and insoluble in nonpolar solvents like n-hexane. These 4-(substituted amino)pyrimidines were crystallized from ethanol or benzene or benzene-n-hexane mixture.

**UV Spectra**
The UV spectra of 4-(substituted amino)pyrimidines were measured in methanol. 4-Ethanolaminopyrimidines exhibit absorption around 240 nm and 295 nm, while the 4-hydrazinopyrimidines exhibit maximum absorption around 237 nm and 312 nm. Thus, the cyclization of vinlylamidines to 4-aminopyrimidines results in an increase in the intensity of absorption at around 231 nm and a decrease in the intensity of the absorption at 305 nm for 4-ethanolaminopyrimidines but increase in case of 4-hydrazinopyrimidines.

**IR Spectra**
The IR spectra of 5-carbethoxy-2-(un)substituted-4-(substituted amino)-6-(substituted amino)pyrimidines had shown peaks at 3400-3200 cm\(^{-1}\) due to amino stretching vibrations. Additionally various 4-ethanolaminopyrimidines have shown broad band at 3600-3400 cm\(^{-1}\) due to the OH stretching vibrations. The ester C=O absorption appears at a lower wave number around 1680-1650 cm\(^{-1}\) indicating the presence of intramolecular hydrogen bonding involving the carbonyl group. Various other stretching and bending vibrations were observed in the fingerprint region.
**1H NMR Spectra**

The $^1$H NMR spectra of 4-hydrazinopyrimidines exhibited a sharp singlet in the region of $\delta$ 10.3-10.5 due to aryl substituted amino proton at C-6. The aromatic protons at C-6 amino group and/or C-2 showed multiplets in the region of $\delta$ 6.99-7.65. A triplet around $\delta$ 1.4 and quartet around $\delta$ 4.3 confirms the presence ethyl moiety of the carbethoxy group. The presence of a broad band in the region of $\delta$ 5.0-5.7 indicated the presence of hydrazino group. The hydrazine NH proton has shown a triplet around $\delta$ 6.7-7.0. Additionally, 4-hydrazinopyrimidines unsubstituted at C-5 showed an intense peak at $\delta$ 8.3 corresponding to the presence of one proton at this place.

Similar pattern was observed in the $^1$H NMR spectra of 4-ethanolaminopyrimidines. A triplet around $\delta$ 1.3 and quartet around $\delta$ 4.7 confirms the presence ethyl moiety of the carbethoxy group. The aromatic protons at C-6 amino group and/or C-2 showed multiplets in the region of $\delta$ 7.0-7.5. Two additional triplets due to the ethylene moiety were observed around $\delta$ 3.9 and $\delta$ 4.5. The NH proton of 4-ethanolamino group has shown a triplet around $\delta$ 5.4 and a triplet at $\delta$ 8.2 indicated the hydroxyl proton. The proton at C-2 in unsubstituted 4-ethanolaminopyrimidines exhibited a peak at $\delta$ 8.4.

**Mass Spectra**

4-(Substituted amino)pyrimidines exhibited intense ion peaks corresponding to the ion peak at (M+1). The compounds possessing chloro or bromo atom in the aromatic ring at C-6 show (M+2) peaks, about 25-30% as intense as the (M+1) peak due to the isotopic abundance McLafferty rearrangement and loss of ethanol from molecular ion of 4-(substituted amino)pyrimidines lead second intense mass peak. The (M+1) ion peak in the 4-(substituted amino)pyrimidines were about 80-90% intense. The ion peak at 332 and 287 can be attributed to the fragmentation of ethanolamine radical. The loss of benzonitrile as neutral molecule (m/z 103) yields molecular ions m/z 229 and m/z 184 (Scheme 4.1). Similar loss of neutral molecule HCN from 5-carbethoxy-4-ethanolamino-6-phenylaminopyrimidine leads to the ion peak at m/z 170. The Formation of daughter ions may explain various other ion peaks (Scheme 4.2).

Loss of ethanol and McLafferty rearrangement was also observed in the fragmentation of 4-hydrazinopyrimidines (Scheme 4.3) resulting into the ion peaks at m/z 228. The loss of different neutral molecules ammonia, HCN and CO from cation
m/z 228 may explain various other ion peaks at m/z 212, m/z 185 and m/z 157 respectively.

**Scheme 4.1** Mass fragmentation pattern of 5-carbethoxy-4-ethanolamino-6-[(4-methylphenyl)amino]-2-phenylpyrimidine

**Scheme 4.2** Mass fragmentation pattern of 5-carbethoxy-4-ethanolamino-6-phenylaminopyrimidine
4.3.2.2. 2,3-Dihydroimidazo[1,2-c]pyrimidines

All the 2,3-dihydroimidazo[1,2-c]pyrimidines were fluorescent yellow crystalline compounds having melting points below 200°C. In most of the cases, the compounds substituted with phenyl ring at C-5 were melting at higher temperatures as compared to corresponding unsubstituted congeners. All the 2,3-dihydroimidazo[1,2-c]pyrimidines were freely soluble in methanol, chloroform, toluene, DMF, and DMSO and insoluble in nonpolar solvents like n-hexane. All the compounds were recrystallized from dichloromethane-n-hexane mixture.

UV Spectra

The UV spectra of 2,3-dihydroimidazo[1,2-c]pyrimidines were measured in methanol. In the UV spectra, the 2,3-dihydroimidazo[1,2-c]pyrimidines exhibit absorption around 260 nm. Compounds in the IB series have shown additional UV absorption around
320 nm Thus the cyclization of 4-ethanolaminopyrimidines resulted in slight increase in the UV absorption wavelength

**IR spectra**
The IR spectra of 2,3-dihydroimidazo[1,2-c]pyrimidines showed weak to moderate peaks in the region of 3400-3200 cm\(^{-1}\) due to -NH- stretching vibrations. The absence of -OH stretching vibration peaks around 3600-3400 cm\(^{-1}\) indicated the participation of -OH group in the cyclization reaction resulting in the formation of 8-carbethoxy-5-substituted-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines. An intense sharp peak was observed around 1690-1645 cm\(^{-1}\) due to the carbonyl group of ester. The downward shift of carbonyl peak is due to the intramolecular hydrogen bonding with secondary amino group. Various other stretching and bending vibrations due to the aromatic rings were also observed.

**\(^1\)H NMR Spectra**
The \(^1\)H NMR spectra of 2,3-dihydroimidazo[1,2-c]pyrimidines were measured in CDCl\(_3\), DMSO-d\(_6\) or in the CDCl\(_3\)/DMSO-d\(_6\) mixture. The \(^1\)H NMR spectra exhibited a sharp singlet in the region of \(\delta\) 11.1-11.7 due to aryl substituted amino proton. The aromatic protons at C-7 and/or C-5 showed multiplets in the region of \(\delta\) 7.2-7.8. A triplet around \(\delta\) 1.3 and quartet around \(\delta\) 4.6 confirms the presence ethyl moiety of the carboxy group. The presence of two consecutive triplets in the region of \(\delta\) 4.0-4.6 indicated the presence of ethylene bridge between two nitrogen atoms at 1\(^{st}\) and 4\(^{th}\) place. Additionally, 2,3-dihydroimidazo[1,2-c]pyrimidines unsubstituted at C-5 showed an intense peak at \(\delta\) 8.4 corresponding to the presence of one proton at this place.

**Mass Spectra**
All the 2,3-dihydroimidazo[1,2-c]pyrimidines exhibited intense ion peaks corresponding to the ion peak at (M+1). The compounds possessing chloro or bromo atom in the aromatic ring show (M+2) peaks, about 25-30% as intense as the (M+1) peak due to the isotopic abundance. The (M+1) ion peaks in the 8-carbethoxy-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines was about 80-90% intense. The loss of ethanol from molecular ion of 2,3-dihydroimidazo[1,2-c]pyrimidines due to the McLafferty rearrangement may explain second intense mass peak. The loss of HCN further characterizes formation of molecular ions. The schematic mass
fragmentation pattern of 8-carbethoxy-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines is shown in Scheme 4.4

\[ \text{Scheme 4.4 Mass fragmentation pattern of 8-carbethoxy-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines} \]

Mass fragmentation pattern observed for 8-carbethoxy-7-(4-methoxyphenylamino)-2,3-dihydroimidazo[1,2-c]pyrimidine is presented in Scheme 4.5. An intense ion peak was observed at m/z 315 due to the (M+1) molecular ion. A daughter ion peak of 40% intensity at m/z 299 is resulted by the loss of methyl radical from the molecular ion. Moderately intense ion peaks at m/z 287, 269, 253 are due to the loss of HCN and ethanol respectively.

Similar fragmentation pattern was observed for 8-carbethoxy-7-(substituted amino)-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidines with additional molecular ion peaks due to fragmentation of the pyrimidine ring (Scheme 4.6). The molecular ion peak at m/z 102 appear common to all the 8-carbethoxy-7-(substituted amino)-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidines which is formulated as following fragment.

\[ \text{Scheme 4.4 Mass fragmentation pattern of 8-carbethoxy-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines} \]
Scheme 4.5 Mass fragmentation of 8-carbethoxy-7-(4-methoxyphenylamino)-2,3-dihydroimidazo[1,2-c]pyrimidine
Scheme 4.6 Mass fragmentation pattern of 8-carbethoxy-5-phenyl-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines
4.4. Biological activity

All the synthesized compounds were screened for their antibacterial activity against two different strains of Gram-negative (Escherichia coli and Pseudomonas aeruginosa) and Gram-positive (Bacillus pumilis and Staphylococcus aureus) bacteria. The antifungal activity was measured against Aspergillus niger. Various microbial and fungal strains were maintained on Mueller-Hinton agar (E.coli, P. aeruginosa, B. pumilis and S. aureus), Sabouraud agar with glucose (A. niger) or Lowenstein-Jensen (L-J) medium (M. tuberculosis H37Rv). The MIC was determined by serial dilution technique.

4.4.1. Methods

4.4.1.1. Antimicrobial Activity

The compounds were tested for their antimicrobial activity against Gram-negative and Gram-positive bacteria using Mueller-Hinton agar. The bacterial strains were obtained from Microbiology Department, University School of Sciences, Gujarat University, Ahmedabad, Gujarat. The antibacterial MIC values of test compounds were compared with reference antibiotics tetracycline, ciprofloxacin and gentamicin.

Preparation of inoculums

Various microbial strains were maintained on Mueller-Hinton agar. The inoculum was prepared from master culture (not less than 48 h old) by transferring several spadesful of growth to a sterilized test tube containing nutrient broth. The suspension was adjusted to the 0.5 McFarland turbidity standard (incubation at 37°C for 24 h) and the number of colony forming units per mL (CFU/mL) of the final inoculum was confirmed by plating serial dilutions on nutrient agar (1.5x10^8 CFU/mL).

Preparation of test compound solutions

The test compounds were dissolved in DMSO to prepare a stock solution of 10 mg/mL solution. From the stock solution various serial dilutions were made in DMSO to achieve a concentration range of 1 to 50 µg/mL, with one unit increment and used for the MIC determination.

Method

A preliminary pilot antibacterial screening was performed at three different concentrations (5, 50 and 500 µg/mL) and in the second stage, MIC values were determined using serial dilution in the concentration range between 1 – 50 µg/mL.
concentration. Test compounds were added to culture medium in sterilized borosilicate test tubes and different bacterial strains were inoculated (0.1 mL). The tubes were incubated at 37°C for 24 h and then examined for the presence or absence of growth of the test organisms (Tables 4.1 – 4.6). The MIC values were obtained from the lowest concentration where tubes remained clear indicating complete inhibition of the bacterial growth at that concentration. All the experiments were performed in triplicate.

4.4.1.2. Antimycobacterial activity

The antimycobacterial activity of the synthesized compounds was measured against *M. tuberculosis* H37Rv strain by 1% proportion method. The antimycobacterial activity was performed using L-J medium enriched with oleic acid-albumin-dextrose-catalase (OADC) and added with Grufi mycobacterial supplement. Rifabutin and amikacin were used as standard drugs.

**Preparation of inoculums**

*M. tuberculosis* H37Rv strain was obtained from New Delhi TB Centre, New Delhi and was maintained on L-J medium at 37°C. The inoculum was prepared from master culture by transferring several spadesful of growth to a sterilized screw cap bottle containing 6-8 glass beads and 3 mL of Tween-albumin liquid medium (Middlebrook 7H9) and the content of the bottle was homogenized. Large particles were allowed to settle and the supernatant suspension was withdrawn. The suspension was adjusted to the 0.5 McFarland turbidity standard (incubation at 37°C for 7 days) and the number of CFU/mL of the final inoculum was confirmed by plating serial dilutions on L-J medium (1.5x10⁵ CFU/mL). A 0.1 mL inoculum was used in the sensitivity testing experiment.

**Preparation of test compound solutions**

The compounds were dissolved in DMSO to prepare a solution of 3 mg/mL. Further, 1 mL of this stock solution is diluted to 15 mL to get final concentration of 200 µg/mL in the culture medium. From this, a series of consecutive double fold dilutions (100, 50, 20, 10, 5 and 2 µg/mL) were prepared for all the compounds and tested against *M. tuberculosis* H37Rv strain.
Method

Aseptically, 10 mL of L-J medium was transferred to sterile vials. The specified volume of the test compound solutions were added aseptically to the vial and mixed well while the medium is in liquid state so that the required concentration of the compounds could be achieved (200, 100, 50, 20, 10, 5 and 2 µg/mL) The slants were prepared by allowing the medium to cool in an inclined position *M. tuberculosis* H37Rv culture inoculum (0.1 mL) was added in L-J medium slants (15 mL) previously containing a specified concentration of the test compounds Rifabutin and amikacin were used as standard drugs The inoculated L-J medium slants were incubated at 37°C for 30 days and results were observed at 14th, 21st and 30th day for the growth of mycobacteria (Tables 4.7 and 4.8) MIC values were determined for H37Rv strain of *M. tuberculosis* as the concentration of test compound in the L-J slant without any visible growth All the experiments were performed in triplicate

4.4.1.3. Antifungal Activity

The antifungal activity of the test compounds was also investigated against the fungus *A. niger* using Sabouraud agar Nystatin and griseofulvin were used as reference drugs to compare the antifungal activity of the test compounds. The antifungal activity was determined same as that of antimicrobial activity only with the change of the growth medium by Sabouraud medium The results of the antifungal activity were read after 72 h and are summarized in Table 4.9 and 4.10 All the experiments were performed in triplicate

4.4.2. Results and discussion

4.4.2.1. Antimicrobial Activity

4.4.2.1.1. 4-{Substituted amino)pyrimidines

The results of antimicrobial activity of 4-(substituted amino)pyrimidines are presented in Tables 4.1 – 4.4 which reveal that the synthesized compounds exhibit potent antimicrobial activity. All the synthesized compounds were found more active against Gram-positive bacteria as compared to Gram-negative bacteria The 4-ethanolaminopyrimidines (EF and EB series) have shown compelling antimicrobial activity against the bacterial strains screened, with MIC values in the range of 1 – 40 µg/mL Corresponding hydrazine derivatives (HF and HB series) were comparatively less potent The series of compounds unsubstituted at C-5 were significantly active than a phenyl substitution as indicated by their small MIC values. Compounds EF 10,
EF 11, EF 12, EF 15 and EF 16 exhibited MIC values comparable to the reference antibiotics tetracycline and gentamicin on *P. aeruginosa*, *B. pumilis* and *S. aureus*.

It was observed that the compounds possessing electron-withdrawing groups on the aromatic ring at C-7 are more active with smaller MIC values (EF 8 – 12, EF 15, EF 16, EB 8 – 10, EB 13 and EB 14). However, a methyl substitution in the aromatic ring at C-5 was also significantly active (EF 05 – 07, EB 05 and EB 06). Other substitutions on the aromatic ring at C-5 were also active against the microbial strains screened. Alkyl substitution was found to have detrimental effect on the antimicrobial activity of 4-(substituted amino)pymidines. Additionally, the potency against *E. coli* was comparatively less than other microorganisms tested.

**4.4.2.1.2. 2,3-Dihydroimidazo[1,2-c]pyrimidines**

The MIC values of 2,3-dihydroimidazo[1,2-c]pyrimidines against Gram-negative and Gram-positive bacteria are summarized in Tables 4, 5, and 6. The results revealed that the synthesized compounds exhibited promising inhibitory activity against Gram-negative and Gram-positive bacteria with MIC values in the range of 3 to 40 µg/mL. However, though the test compounds were potent against three of the bacterial strains screened (MIC values 3-20 µg/mL), the MIC values were found higher for *E. coli* (12-35 µg/mL).

In the series unsubstituted at C-5, compounds IF 07 – IF 12 have shown significant inhibitory activity. Though IF 16 has MIC of 3 µg/mL against *P. aeruginosa*, it has failed to show significant activity against other bacterial strains studied. More or less all the compounds tested have exhibited promising activity against various bacterial strains screened with MIC values in the range of 3 – 35 µg/mL. Compounds with phenyl ring at C-5 position (IB 01 – IB 14) were found less potent as compared to unsubstituted compounds. However, five compounds (IB 04 – IB 06, IB 09 and IB 10) of the series showed significant antimicrobial activity.

The results of antibacterial screening suggest that substitution at C-5 have significant influence on the biological activity of the target compounds; the unsubstituted compounds were found more active than phenyl substitution. Moreover, the presence of aromatic ring at C-7, and the substitutions therein, was also critically determining the antibacterial activity of the test compounds.
### Table 4.1 Antimicrobial activity of 5-carbethoxy-4-ethanolamino-6-(substituted amino)pyrimidines

<table>
<thead>
<tr>
<th>Sr No.</th>
<th>Code</th>
<th>MIC (µg/mL)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>P aerogenosa</td>
</tr>
<tr>
<td>1</td>
<td>EF 01</td>
<td>20±0.5</td>
</tr>
<tr>
<td>2</td>
<td>EF 02</td>
<td>20±0.3</td>
</tr>
<tr>
<td>3</td>
<td>EF 03</td>
<td>30±0.8</td>
</tr>
<tr>
<td>4</td>
<td>EF 04</td>
<td>10±0.9</td>
</tr>
<tr>
<td>5</td>
<td>EF 05</td>
<td>8±0.5</td>
</tr>
<tr>
<td>6</td>
<td>EF 06</td>
<td>8±0.5</td>
</tr>
<tr>
<td>7</td>
<td>EF 07</td>
<td>8±0.6</td>
</tr>
<tr>
<td>8</td>
<td>EF 08</td>
<td>8±0.8</td>
</tr>
<tr>
<td>9</td>
<td>EF 09</td>
<td>5±0.3</td>
</tr>
<tr>
<td>10</td>
<td>EF 10</td>
<td>3±0.3</td>
</tr>
<tr>
<td>11</td>
<td>EF 11</td>
<td>3±0.5</td>
</tr>
<tr>
<td>12</td>
<td>EF 12</td>
<td>1±0.1</td>
</tr>
<tr>
<td>13</td>
<td>EF 13</td>
<td>10±0.5</td>
</tr>
<tr>
<td>14</td>
<td>EF 14</td>
<td>10±0.6</td>
</tr>
<tr>
<td>15</td>
<td>EF 15</td>
<td>1±0.1</td>
</tr>
<tr>
<td>16</td>
<td>EF 16</td>
<td>3±0.5</td>
</tr>
<tr>
<td>17</td>
<td>Tetracycline</td>
<td>2±0.1</td>
</tr>
<tr>
<td>18</td>
<td>Ciprofloxacin</td>
<td>0.5±0.01</td>
</tr>
<tr>
<td>19</td>
<td>Gentamicin</td>
<td>1±0.01</td>
</tr>
</tbody>
</table>

*Experiment was carried out in triplicate
Table 4.2 Antimicrobial activity of 5-carbethoxy-4-hydrazino-6-(substituted amino)pyrimidines

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Code</th>
<th>MIC (μg/mL)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>*P aerogenosa</td>
</tr>
<tr>
<td>1</td>
<td>HF 01</td>
<td>62±1.2</td>
</tr>
<tr>
<td>2</td>
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<td>30±1.5</td>
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<td>14</td>
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<td>2±0.1</td>
</tr>
<tr>
<td>16</td>
<td>Ciprofloxacin</td>
<td>0.5±0.01</td>
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<td>1±0.01</td>
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*Experiment was carried out in triplicate
### Table 4.3 Antimicrobial activity of 5-carbethoxy-4-ethanolamino-2-phenyl-6-(substituted amino)pyrimidines

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<td>Ciprofloxacin</td>
<td>0.5±0.01</td>
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*Experiment was carried out in triplicate*
Table 4.4 Antimicrobial activity of 5-carbethoxy-4-hydrazino-2-phenyl-6-(substituted amino)pyrimidmes

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<td>Ciprofloxacin</td>
<td>0.5±0.01</td>
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</table>

*Experiment was carried out in triplicate.
Table 4.5 Antimicrobial activity of 8-carbethoxy-7-(substituted amino)-2,3-dihydrimidazo-[1,2-c]pyrimidines

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<td>IF 04</td>
<td>12±0.2</td>
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<td>IF 05</td>
<td>16±0.6</td>
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<td>IF 06</td>
<td>14±0.8</td>
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<td>IF 07</td>
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<td>IF 08</td>
<td>8±0.6</td>
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<tr>
<td>9</td>
<td>IF 09</td>
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<tr>
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<td>IF 10</td>
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<td>5±0.1</td>
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<td>IF 13</td>
<td>10±0.5</td>
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<td>15</td>
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*Experiment was carried out in triplicate*
### Table 4.6 Antimicrobial activity of 8-carbethoxy-5-phenyl-7-(substituted amino)-2,3-dihydropyrido[1,2-c]pyrimidines

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<td><em>P</em> aeruginosa</td>
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<td>IIB 05</td>
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<td>IIB 06</td>
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<td>7</td>
<td>IIB 07</td>
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<tr>
<td>8</td>
<td>IIB 08</td>
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<td>9</td>
<td>IIB 09</td>
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<td>IIB 13</td>
<td>16±0.5</td>
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<td>IIB 14</td>
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<td>0.5±0.01</td>
</tr>
<tr>
<td>17</td>
<td>Gentamicin</td>
<td>1±0.1</td>
</tr>
</tbody>
</table>

*Experiment was carried out in triplicate*
4.4.2.2. Antimycobacterial activity

The antimycobacterial activity of 2,3-dihydroimidazo[1,2-c]pyrimidines was evaluated against *M. tuberculosis* H37Rv using the L-J medium enriched with oleic acid-albumin-dextrose-catalase (OADC) and added with Gruft mycobacterial supplement. The MIC values were determined by serial dilution, 1% proportional method and the results are summarized in Table 4.7 and 4.8. Rifabutin and amikacin were used as standard drugs.

Some of the test compounds have shown remarkable activity against *M. tuberculosis* H37Rv strain after 21 days as indicated by their MIC values, except compound IF 08 which had MIC of >200 μg/mL (Tables 4.7 and 4.8). Compounds IF 04, IF 07, IF 09 – IF 11 and IF 15 have shown potent antimycobacterial activity after 21 days with MIC values in the range of 2-20 μg/mL. Although compounds IB 04, IB 06 and IB 09 were found to be potent antibacterials against Gram-negative and Gram-positive bacteria, but failed to exhibit sufficient effect on the mycobacteria. On the other hand, in the series containing phenyl ring at C-5 compounds IB 08, IB 10 and IB 13, have shown significant activity against *M. tuberculosis* H37Rv strain after 21 days. Compounds IF 07, IF 10, IF 11, IF 15, IB 08 and IB 10 were found more potent than amikacin with MIC value of 5 μg/mL. Although all these compounds were found less potent as compared to rifabutin, the most potent compound IF 09 has exhibited MIC of 2 μg/mL.

Additionally, it was observed that substitution on the *para*-position of the phenyl ring at C-7 was influencing the antimicrobial activity significantly. The presence of electron-withdrawing halogen atoms (IF 10, IF 11 and IF 15) or methoxy (IF 09) improved potency as indicated by their low MIC values. However, a methyl group (IF 07) was also equally permissible at that position. A similar type of antimycobacterial profile was observed for C-5 phenyl substituted series and compounds IB 08, IB 10 and IB 13 exhibited potent activity with the MIC values 5, 5, 20 μg/mL respectively after 21 days. Other substitution in the aromatic ring at C-7 lead to drastic decrease in the activity but were found significantly active on other microorganisms. Incorporation of small aliphatic alkyl groups like methyl or ethyl groups at C-7 remarkably reduced the potency of the test compounds.
### Table 4.7 Antimycobacterial activity of 8-carbethoxy-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines

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<td>&gt;200</td>
</tr>
<tr>
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<td>IF 03</td>
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<td>5±0 2</td>
</tr>
<tr>
<td>8</td>
<td>IF 08</td>
<td>&gt;200</td>
</tr>
<tr>
<td>9</td>
<td>IF 09</td>
<td>2±0.1</td>
</tr>
<tr>
<td>10</td>
<td>IF 10</td>
<td>5±0.2</td>
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<td>5±0 4</td>
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*Experiment was carried out in triplicate*
Table 4.8 Antimycobacterial activity of 8-carbethoxy-5-phenyl-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines

<table>
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<td>IB 07</td>
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</tbody>
</table>

*Experiment was carried out in triplicate
4.4.2.3. Antifungal Activity

The 4-(substituted amino)pirimidines when screened against the fungus *A. niger*, showed trivial activity and not worth mentioning. An interesting fact observed was that although 4-hydrazinopyrimidines exhibited insignificant antimicrobial activity, their antifungal MIC values were smaller as compared to 4-ethanolaminopyrimidines (Tables 4.9 and 4.10).

Some of the 2,3-dihydroimidazo[1,2-c]pyrimidines were also explored for their antifungal activity against *A. niger* on Sabouraud medium using nystatin and griseofulvin as reference compounds and the result is summarized in Table 4.11. The results of antifungal activity reveal that the synthesized compounds do not exhibit significant potency when compared with reference drugs. The MIC values were in the range of 35-60 μg/mL suggesting trivial potential of the series as antifungal agents. Though IF 04 and IB 06 inhibited the growth of *A. niger* (MIC 35 μg/mL) but the MIC values were quite high as compared to the reference drugs nystatin or griseofulvin (MIC 7 and 15 μg/mL, respectively).
## Table 4.9 Antifungal activity of 5-carbethoxy-4-(substituted amino)-2-(un)substituted-6-(substituted amino)pyrimidines

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<tr>
<td>17</td>
<td>Griseofulvin</td>
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*Experiment was carried out in triplicate.*
### Table 4.10 Antifungal activity of 5-carbethoxy-4-(substituted amino)-2-(un)substituted
-6-(substituted amino)pynmdines

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<td>40±1.8</td>
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<tr>
<td>19</td>
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<tr>
<td>20</td>
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<td>15±0.4</td>
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*Experiment was carried out in triplicate
Table 4.11 Antifungal activity of 8-carbethoxy-5-(un)substituted-7-(substituted amino)-2,3-dihydroimidazo[1,2-c]pyrimidines

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<tr>
<td>2</td>
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<tr>
<td>3</td>
<td>IF 11</td>
<td>40±1.7</td>
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<td>4</td>
<td>IF 12</td>
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<td>IF 16</td>
<td>40±2.5</td>
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<td>6</td>
<td>IB 01</td>
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<tr>
<td>11</td>
<td>Nystatin</td>
<td>7±2</td>
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<td>12</td>
<td>Griseofulvin</td>
<td>15±0.2</td>
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</table>

*Experiment was carried out in triplicate.*
**Imidazo[1,2-c]pyrimidines – Synthesis and Biological Activity**

Table 4.12 Physical data of ethyl 2-cyano-3-(substituted amino)-3-methylthioacrylate

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Code</th>
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<th>Mol Formula</th>
<th>M. P (°C) (Reported)</th>
<th>Yield (%)*</th>
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<tbody>
<tr>
<td>1</td>
<td>SN 01</td>
<td>CH₃</td>
<td>C₈H₁₂N₂O₂S</td>
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<tr>
<td>2</td>
<td>SN 02</td>
<td>C₂H₅</td>
<td>C₉H₁₄N₂O₂S</td>
<td>84-86 (83-84)⁶¹²</td>
<td>72</td>
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<tr>
<td>3</td>
<td>SN 03</td>
<td>C₆H₅CH₂</td>
<td>C₁₄H₁₆N₂O₂S</td>
<td>102-104 (102-104)⁶¹¹</td>
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<tr>
<td>4</td>
<td>SN 04</td>
<td>C₆H₅</td>
<td>C₁₃H₁₄N₂O₂S</td>
<td>82-84 (83-85)⁶¹¹</td>
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</tr>
<tr>
<td>5</td>
<td>SN 05</td>
<td>2-CH₃-C₆H₄</td>
<td>C₁₄H₁₆N₂O₂S</td>
<td>112-115 (114-116)⁶¹¹</td>
<td>86</td>
</tr>
<tr>
<td>6</td>
<td>SN 06</td>
<td>3-CH₃-C₆H₄</td>
<td>C₁₄H₁₆N₂O₂S</td>
<td>115-117 (115-117)⁶¹¹</td>
<td>70</td>
</tr>
<tr>
<td>7</td>
<td>SN 07</td>
<td>4-CH₃-C₆H₄</td>
<td>C₁₄H₁₆N₂O₂S</td>
<td>76-78 (79-81)⁶¹¹</td>
<td>87</td>
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<td>8</td>
<td>SN 08</td>
<td>2-CH₃O-C₆H₄</td>
<td>C₁₄H₁₆N₂O₃S</td>
<td>110-112 (115-117)⁶¹¹</td>
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<tr>
<td>9</td>
<td>SN 09</td>
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<td>C₁₄H₁₆N₂O₃S</td>
<td>116-118 (118-120)⁶¹¹</td>
<td>86</td>
</tr>
<tr>
<td>10</td>
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<td>102-104 (104-106)⁶¹²</td>
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<td>SN 11</td>
<td>4-F-C₆H₄</td>
<td>C₁₃H₁₃F₂N₂O₂S</td>
<td>104-106 (104-106)⁶¹²</td>
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<td>SN 12</td>
<td>3-CF₃-C₆H₄</td>
<td>C₁₃H₁₃F₃N₂O₂S</td>
<td>102-104 (102-104)⁶¹²</td>
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<tr>
<td>13</td>
<td>SN 13</td>
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<td>C₁₃H₁₃Cl₂N₂O₂S</td>
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<td>15</td>
<td>SN 15</td>
<td>4-Cl-C₆H₄</td>
<td>C₁₃H₁₃Cl₂N₂O₂S</td>
<td>112-114 (110-112)⁶¹¹</td>
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<tr>
<td>16</td>
<td>SN 16</td>
<td>4-Br-C₆H₄</td>
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<td>112-114 (117-119)⁶¹¹</td>
<td>89</td>
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* All the compounds were recrystallized from ethanol
### Table 4.13 Physical data of N-[2-carbethoxy-2-cyano-1-(substituted amino)vinyl] formamidines

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<th>Sr No</th>
<th>Code</th>
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<th>Mol Formula</th>
<th>M. P (°C) (Reported)</th>
<th>Yield (%)*</th>
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<tbody>
<tr>
<td>1</td>
<td>VF 01</td>
<td>CH₃</td>
<td>C₈H₁₂N₄O₂</td>
<td>154-155 (155-157)⁶¹²</td>
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<tr>
<td>2</td>
<td>VF 02</td>
<td>C₂H₅</td>
<td>C₉H₁₄N₄O₂</td>
<td>158-160 (160-162)⁶¹²</td>
<td>62</td>
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<tr>
<td>3</td>
<td>VF 03</td>
<td>CH₃CH₂</td>
<td>C₁₀H₁₆N₄O₂</td>
<td>168-170 (170-171)⁶¹²</td>
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<tr>
<td>4</td>
<td>VF 04</td>
<td>C₆H₅</td>
<td>C₁₃H₁₄N₄O₂</td>
<td>168-170 (166-168)⁶¹²</td>
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<tr>
<td>5</td>
<td>VF 05</td>
<td>2-CH₃C₆H₄</td>
<td>C₁₄H₁₆N₄O₂</td>
<td>172-174 (172-173)⁶¹²</td>
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<tr>
<td>6</td>
<td>VF 06</td>
<td>3-CH₃C₆H₄</td>
<td>C₁₄H₁₆N₄O₂</td>
<td>170-172 (181-183)⁶¹²</td>
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<tr>
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<td>VF 07</td>
<td>4-CH₃C₆H₄</td>
<td>C₁₄H₁₆N₄O₂</td>
<td>180-182 (181-197)⁶¹²</td>
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<tr>
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<td>2-CH₂O-C₆H₄</td>
<td>C₁₄H₁₆N₄O₃</td>
<td>195-197 (197-198)⁶¹²</td>
<td>75</td>
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<tr>
<td>9</td>
<td>VF 09</td>
<td>4-CH₂O-C₆H₄</td>
<td>C₁₄H₁₆N₄O₃</td>
<td>198-200 (200-201)⁶¹²</td>
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<tr>
<td>10</td>
<td>VF 10</td>
<td>2-F-C₆H₄</td>
<td>C₁₃H₁₃F₃N₄O₂</td>
<td>162-164 (172-174)⁶¹²</td>
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<tr>
<td>11</td>
<td>VF 11</td>
<td>4-F-C₆H₄</td>
<td>C₁₃H₁₃F₃N₄O₂</td>
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<td>C₁₄H₁₃F₃N₄O₂</td>
<td>188-190 (195-197)⁶¹²</td>
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<td>202-204 (217-219)⁶¹²</td>
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* All the compounds were recrystallized from dichloromethane-n-hexane
Table 4.14 Physical data of N-[2-carbethoxy-2-cyano-1-(substituted amino)vinyl] benzamidines

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<th>M P (°C) (Reported)</th>
<th>Yield (%)</th>
<th>Recryst *</th>
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<td>VB 02</td>
<td>C₂H₅</td>
<td>C₁₅H₁₈N₄O₂</td>
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<td>DCM-H</td>
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<td>(144-146)</td>
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<td>C₆H₅</td>
<td>C₁₅H₁₈N₄O₂</td>
<td>188-190</td>
<td>79</td>
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<td>188-190</td>
<td>70</td>
<td>B</td>
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<td></td>
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<td></td>
<td></td>
<td>(180-182)</td>
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<td>70</td>
<td>B</td>
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<td>E</td>
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*DCM = Dichloromethane, H = Hexane, E = Ethanol
**Table 4.15** Physical data of 5-carbethoxy-4-chloro-6-(substituted amino)pyrimidines

*All the compounds were recrystallized from n-hexane*
**Table 4.16 Physical data of 5-carbethoxy-4-choro-2-phenyl-6-(substituted amino)pyrimidines**

<table>
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<th>M. P (°C)</th>
<th>Yield (%)*</th>
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<td>C₂H₅</td>
<td>C₁₅H₁₆ClN₃O₂</td>
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<td>C₆H₅CH₂</td>
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<td>C₁₉H₁₀ClN₃O₂</td>
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<td>4-CH₃-C₆H₄</td>
<td>C₂₀H₁₈ClN₃O₂</td>
<td>116-118</td>
<td>55</td>
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<td>115-117</td>
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<td>C₂₀H₁₈ClN₃O₃</td>
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* All the compounds were recrystallized from n-hexane
Table 4.17 Physical data of 5-carbethoxy-4-ethanolamino-6-(substituted amino) pyrimidines

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<th>Sr No</th>
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*DCM = Dichloromethane; H = Hexane, B= Benzene; E = Ethanol
### Physical data of 5-carbethoxy-4-ethanolamino-2-phenyl-6-(substituted amine)pyrimidines

![Structural formula](image)

<table>
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<tr>
<th>Sr No.</th>
<th>Code</th>
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<th>Mol Formula</th>
<th>M. P (°C)</th>
<th>Yield (%)</th>
<th>Recryst</th>
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*DCM = Dichloromethane, H = Hexane; B= Benzene, E = Ethanol
**Imidazo[1,2-c]pyrimidines – Synthesis and Biological Activity**

Table 4.19 Physical Data of 5-carbethoxy-4-hydrazino-6-(substituted amino) pyrimidines

![Chemical Structure](image)

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<th>Yield* (%)</th>
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*All the compounds were recrystallized from ethanol*
Table 4.20 Physical Data of 5-carbethoxy-4-hydrazino-2-phenyl-6-(substituted amino)pyrimidines

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<th>M P. (°C)</th>
<th>Yield (%)</th>
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*T = Toluene, H = Hexane; B = Benzene; E = Ethanol
Table 4.21 Physical Data of 8-carbethoxy-7-(substituted amino)-2,3-dihy roimidazo [1,2-c]pyrimidines

<table>
<thead>
<tr>
<th>Sr No</th>
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<th>Mol. Formula</th>
<th>M P (°C)</th>
<th>Yield (%)</th>
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* All the compounds were recrystallized from dichloromethane-n-hexane.
Table 4.22 Physical Data of 8-carbethoxy-5-phenyl-7-(substituted amino)-2,3-dihydropyrimido[1,2-c]pyrimidines

<table>
<thead>
<tr>
<th>Sr No</th>
<th>Code</th>
<th>R</th>
<th>Mol Formula</th>
<th>M P. (°C)</th>
<th>Yield (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>IB 01</td>
<td>CH₃</td>
<td>C₁₆H₁₈N₄O₂</td>
<td>180-182</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>IB 02</td>
<td>C₂H₅</td>
<td>C₁₇H₂₀N₄O₂</td>
<td>187-190</td>
<td>42</td>
</tr>
<tr>
<td>3</td>
<td>IB 03</td>
<td>C₆H₅CH₂</td>
<td>C₂₂H₂₂N₄O₂</td>
<td>154-156</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>IB 04</td>
<td>C₆H₅</td>
<td>C₂₁H₂₀N₄O₂</td>
<td>192-194</td>
<td>50</td>
</tr>
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<td>5</td>
<td>IB 05</td>
<td>2-CH₃-C₆H₄</td>
<td>C₂₂H₂₂N₄O₂</td>
<td>182-184</td>
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<td>6</td>
<td>IB 06</td>
<td>4-CH₃-C₆H₄</td>
<td>C₂₂H₂₂N₄O₂</td>
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<td>52</td>
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<td>7</td>
<td>IB 07</td>
<td>2-CH₃O-C₆H₄</td>
<td>C₂₂H₂₂N₄O₃</td>
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<td>8</td>
<td>IB 08</td>
<td>4-CH₃O-C₆H₄</td>
<td>C₂₂H₂₂N₄O₃</td>
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<td>9</td>
<td>IB 09</td>
<td>2-F-C₆H₄</td>
<td>C₂₁H₁₉FN₄O₂</td>
<td>160-162</td>
<td>55</td>
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<td>10</td>
<td>IB 10</td>
<td>4-F-C₆H₄</td>
<td>C₂₁H₁₉FN₄O₂</td>
<td>164-166</td>
<td>49</td>
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<td>11</td>
<td>IB 11</td>
<td>2-Cl-C₆H₄</td>
<td>C₂₁H₁₉ClN₄O₂</td>
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<td>12</td>
<td>IB 12</td>
<td>3-Cl-C₆H₄</td>
<td>C₂₁H₁₉ClN₄O₂</td>
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<td>IB 13</td>
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<td>C₂₁H₁₉ClN₄O₂</td>
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<td>IB 14</td>
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<td>51</td>
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</tbody>
</table>

* All the compounds were recrystallized from dichloromethane-n-hexane
4.5. Experimental

General

All the melting points were determined in open capillaries in microprocessor based melting point apparatus model VMP-D (Veego make) and are uncorrected.

UV spectra were recorded on UV-VIS 160A Shimadzu Spectrophotometer

Infrared spectra were recorded in KBr discs on 8400S Shimadzu Fourier Transform Spectrophotometer

Proton Nuclear Magnetic spectra were taken on Bruker Avance 400 Spectrophotometer at 400 MHz and the chemical shifts are given as parts per million (δ ppm), downfield from tetramethylsilane (TMS) as internal standard

Mass spectra were obtained on Perkin-Elmer LC-MS PE Sciex API/ 65

The elemental analysis were done on Elementar Vario EL III Carlo Erba 1108

Thin layer chromatography was performed on microscopic slides (2x7.5cm) coated with silica gel G and spots were visualized by exposure to iodine vapours and UV radiation
Synthesis of ethyl 2,2-di(methylthio)methylenecyanoacetate\textsuperscript{611,612}
Ethyl cyanoacetate 11.3 g (0.1 M) was reacted with 7.6 g (0.1 M) of carbon disulfide in the presence of 13.2 g (0.2 M) of potassium hydroxide (85%) in 30 mL of DMF and 25.2 g (0.2 M) of DMS was added drop-wise with continuous stirring, maintaining the temperature at 20°C. The reaction mixture was allowed to stand at room temperature for 12 h and poured into ice-water mixture. The solid obtained was filtered, washed with water and dried. Recrystallization from n-hexane yielded 18.4 g (85%) of light yellow colored crystalline product M.P. 57-59°C (57-59°C).

General procedure for synthesis of ethyl 2-cyano-3-(alkylamino)-3-methylthioacylates (SN 01 and 02)\textsuperscript{611,612}
Alkylamine (0.01 M) was added, with stirring, to a solution of 2.2 g (0.01 M) of ethyl 2,2-di(methylthio)methylenecyanoacetate, in 20 mL of ethanol. The mixture was allowed to stand at room temperature for 12 h and poured into ice water. Solid obtained was filtered, washed with water and dried. Recrystallization of the crude product from ethanol yielded a colorless crystalline product.

General procedure for synthesis of ethyl 2-cyano-3-(arylamino)-3-methylthioacylates (SN 03-16)\textsuperscript{611,612}
A mixture of 0.01 M arylamine and 2.2 g (0.01 M) of ethyl 3,3-di(methylthio)-2-methylenecyanoacrylate was refluxed in 15 mL ethanol for 3-6 h. The reaction mixture was allowed to stand at room temperature for 12 h and poured into ice water. Crystalline product was filtered, washed with ethanol and dried. Recrystallization of crude product from ethanol yielded colorless crystalline product.

General procedure for synthesis of N-[2-carbethoxy-2-cyano-1-(substituted amino)vinyl]formamidines (VF 01-16)\textsuperscript{611,612}
To a solution of 0.8 g (0.02 M) of sodium hydroxide in 30 mL of ethanol was added, with stirring, 2.4 g (0.02 M) of formamidine acetate. After stirring for 30 minutes, 0.02 M of ethyl 2-cyano-3-(methylthio)-3-(substituted amino)acrylate was added portion wise, with continuous stirring. The reaction mixture was stirred for 3-6 h and allowed to stand at room temperature for 12 h. The reaction mixture was poured into ice cold water. The solid obtained was filtered, washed with water and dried. Recrystallization of the crude product from dichloromethane-n-hexane yielded colorless crystalline product.
General procedure for synthesis of N-[2-carbethoxy-2-cyano-1-(substituted amino)vinyl]benzamidines (VB 01-14)\textsuperscript{611,612}

To a solution of 0.8 g (0.02M) of sodium hydroxide in 30 mL of ethanol was added, with stirring, 3.85 g (0.02M) of benzamidine hydrochloride dihydrate. After stirring for 30 minutes, the precipitated sodium chloride was filtered and 0.02M of ethyl 2-cyano-3-(methylthio)-3-(substituted amino)acrylate was added portion wise, with continuous stirring. The reaction mixture was stirred for 3-6 h and allowed to stand at room temperature for 12 h. The reaction mixture was poured into ice cold water. The solid obtained was filtered, washed with water and dried. Recrystallization of the crude product from dichloromethane-n-hexane yielded colorless crystalline product.

General procedure for synthesis of 5-carbethoxy-4-chloro-6-(substituted amino)-2-(un)substitutedpyrimidines (CF 01-16 and CB 01-14)\textsuperscript{611,612}

To 0.01 M of N-[2-carbethoxy-2-cyano-1-(substituted amino)vinyl]formamidine/benzamidine 30 mL of dioxane, saturated with dry hydrogen chloride gas was added and stirred for 6 h. The reaction mixture was allowed to stand at room temperature for 12 h and poured into ice. The solid obtained was filtered, triturated with saturated sodium bicarbonate solution, filtered, washed with water and dried. Recrystallization of the crude product from n-hexane yielded light yellow to colorless crystalline product.
Experimental

Synthesis of 5-carbethoxy-4-ethanolamino-6-(methylamino)pyrimidine (EF 01)
To a solution of 5-carbethoxy-4-chloro-6-(methylamino)pyrimidine (CF 01) (2.2 g, 0.01M) in ethanol (15 mL), was added ethanolamine 0.61 g (0.01M). The reaction mixture was refluxed for 1 h on water bath, cooled and poured into ice-water mixture. It was kept at 20°C for 12 h. The solid obtained was filtered and dried. Recrystallization from dichloromethane-n-hexane yielded 1.9 g (79%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-(methylamino)pyrimidine (EF 01). M P 96-98°C

ANALYSIS:
Microanalysis C_{10}H_{16}N_{4}O_{3} (240 26)
TLC Benzene Methanol (4.5 0.5), R_f value = 0.44
IR (KBr, cm^{-1}) 3442 (OH), 3309, 3234 (NH), 1662 (C=O)
UV (λ_{max}, nm) 233 (Methanol)
^1H NMR (δ) 1.23-1.30 (t, 3H, OCH_{2}CH_{3}); 2.71-2.77 (d, 3H, NHCH_{3}); 3.45-3.54 (t, 2H, NHCH_{2}CH_{2}); 4.06-4.11 (t, 2H, NHCH_{2}CH_{2}); 4.32-4.40 (q, 2H, OCH_{2}CH_{3}); 4.45-4.52 (b, 1H, NHCH_{3}); 4.89-4.96 (b, 1H, NHCH_{2}CH_{2}); 8.05-8.13 (t, 1H, OH); 8.45 (s, 1H, NCH-N)
Mass (m/z) 241 (M+1), 195, 180, 135

Synthesis of 5-carbethoxy-4-ethanolamino-6-(ethylamino)pyrimidine (EF 02)
A solution of 5-carbethoxy-4-chloro-6-(ethylamino)pyrimidine (CF 02) (2.3 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from dichloromethane-n-hexane yielded 1.8 g (72%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-(ethylamino)pyrimidine (EF 02). M P 106-108°C

ANALYSIS:
Microanalysis C_{11}H_{18}N_{4}O_{3} (254 29)
TLC Benzene Methanol (4.5 0.5), R_f value = 0.45
IR (KBr, cm^{-1}) 3421 (OH), 3309, 3153 (NH), 1670 (C=O)
UV (λ_{max}, nm) 234 (Methanol)
Experimental

Synthesis of 6-(benzylamino)-5-carbethoxy-4-ethanolaminopyrimidine (EF 03)
A solution of 6-(benzylamino)-5-carbethoxy-4-chloropyrimidine (CF 03) (2.9 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from dichloromethane-n-hexane yielded 2.1 g (66%) of white crystalline compound which was characterized as 6-(benzylamino)-5-carbethoxy-4-ethanolamino-pyrimidine (EF 03). M P. 74-76°C.

ANALYSIS:
- Microanalysis : C₁₆H₂₀N₄O₃ (316.35)
- TLC : Benzene Methanol (4:5:0.5); Rf value = 0.41
- IR (KBr, cm⁻¹) : 3421 (OH), 3305, 3261 (NH), 1676 (C=O)
- UV (λₘₚ, nm) : 236 (Methanol)

Synthesis of 5-carbethoxy-4-ethanolamino-6-(phenylamino)pyrimidine (EF 04)
A solution of 5-carbethoxy-4-chloro-6-(phenylamino)pyrimidine (CF 04) (2.8 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from benzene-n-hexane yielded 2.6 g (86%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-(phenylamino)pyrimidine (EF 04). M. P 106-108°C.

ANALYSIS:
- Microanalysis : C₁₅H₁₈N₄O₃ (302.33)
- TLC : Benzene Methanol (4:5:0.5); Rf value = 0.46
- IR (KBr, cm⁻¹) : 3367 (OH), 3313, 3226 (NH), 1680 (C=O)
- UV (λₘₚ, nm) : 239 (Methanol)
- ¹H NMR (DCl₃) : 1.33-1.41 (t, 3H, OCH₂CH₃), 4.28-4.31 (t, 2H, NHCH₂CH₃), 4.65-4.67 (t, 2H, NHCH₂CH₃); 5.35-5.42 (b,1H, NHAr), 7.20-7.36 (m, 5H, NHAr), 8.11-8.23 (t, 1H, OH), 8.46 (s, 1H, NCH₃); 11.38 (s, 1H, NHAr)
- Mass (m/z) : 303 (M+1), 257, 230, 197, 171
Synthesis of 5-carbethoxy-4-ethanolamino-6-[(2-methylphenyl)amino]-pyrimidine (EF 05)

A solution of 5-carbethoxy-4-chloro-6-[(2-methylphenyl)amino]pyrimidine (CF 05) (2.9 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from benzene-n-hexane yielded 2.3 g (72%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(2-methylphenyl)amino]pyrimidine (EF 05). M. P. 110-112°C

ANALYSIS:
Microanalysis: C_{18}H_{20} N_{4}O_{3} (316.35)
TLC: Benzene-Methanol (4:5:0.5), R_f value = 0.45
IR (KBr, cm^{-1}): 3404 (OH), 3382, 3260 (NH), 1672 (C=O)
UV (λ_{max}, nm): 238 (Methanol)

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(3-methylphenyl)amino]-pyrimidine (EF 06)

A solution of 5-carbethoxy-4-chloro-6-(3-methylphenyl)amino]pyrimidine (CF 06) (2.9 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from benzene-n-hexane yielded 1.5 g (47%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-(3-methylphenyl)amino]pyrimidine (EF 06). M. P. 111-113°C

ANALYSIS:
Microanalysis: C_{18}H_{20} N_{4}O_{3} (316.35)
TLC: Benzene-Methanol (4:5:0.5), R_f value = 0.41
IR (KBr, cm^{-1}): 3593 (OH), 3307, 3186 (NH), 1641 (C=O)
UV (λ_{max}, nm): 237 (Methanol)
Experimental

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(4-methylphenyl)amino]-pyrimidine (EF 07)
A solution of 5-carbethoxy-4-chloro-6-[(4-methylphenyl)amino]pyrimidine (CF 07) (2.9 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from ethanol yielded 2.8 g (88%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(4-methylphenyl)amino]pyrimidine (EF 07). M. P 116-118°C

ANALYSIS:
Microanalysis C_{16}H_{20}N_{4}O_{3} (316.35)
TLC Benzene: Methanol (4:5:0.5); R_f value = 0.46
IR (KBr, cm⁻¹) 3375 (OH), 3313, 3234 (NH), 1674 (C=O)
UV (λ_{max}, nm) 238 (Methanol)

^1H NMR (δ) 1.29 (s, 3H, ArCH₃), 1.32-1.41 (t, 3H, OCH₂CH₃), 4.12-4.24 (t, 2H, NHCH₂CH₂), 4.65-4.75 (q, 2H, OCH₂CH₃); 5.66-5.79 (b, 1H, NHCH₂CH₂); 6.89-7.17 (m, 4H, NHArH); 8.10-8.22 (t, 1H, OH), 8.31 (s, 1H, NCH₂N), 11.45 (s, 1H, NHAr)
Mass (m/z) 317 (M+1), 271, 256, 231, 186

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(2-methoxyphenyl)amino]-pyrimidine (EF 08)
A solution of 5-carbethoxy-4-chloro-6-[(2-methoxyphenyl)amino]pyrimidine (CF 08) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from benzene-n-hexane yielded 2.7 g (82%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(2-methoxyphenyl)amino]pyrimidine (EF 08). M. P 104-106°C

ANALYSIS:
Microanalysis C_{16}H_{20}N_{4}O_{3} (332.35)
TLC Benzene: Methanol (4.5:0.5); R_f value = 0.43
IR (KBr, cm⁻¹) 3400 (OH), 3334, 3261 (NH), 1668 (C=O)
UV (λ_{max}, nm) 238 (Methanol)
Experimental

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(4-methoxyphenyl)amino]pyrimidine (EF 09)
A solution of 5-carbethoxy-4-chloro-6-[(4-methoxyphenyl)amino]pyrimidine (CF 09) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from ethanol yielded 3 g (91%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(4-methoxyphenyl)amino]pyrimidine (EF 09). M P 114-116°C

ANALYSIS:
Microanalysis: C_{15}H_{20}N_{4}O_{4} (332.35)
TLC: Benzene-Methanol (4.5:0.5), Rf value = 0.45
IR (KBr, cm^{-1}): 3377 (OH), 3317, 3226 (NH), 1672 (C=O)
UV (λ_{max}, nm): 240 (Methanol)
{^1}H NMR (δ): 1.35-1.47 (t, 3H, OCH_{2}CH_{3}), 3.80 (t, 3H, ArOCH_{3}); 4.28-4.35 (q, 2H, OCH_{2}CH_{3}), 5.37-5.47 (b, 1H, NHArH); 7.08-7.32 (m, 4H, NHArH), 8.15-8.28 (t, 1H, OH), 8.52 (s, 1H, NCH_{3}), 11.45 (s, 1H, NHAr)
Mass (m/z): 333 (M+1), 287, 227, 200

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(2-fluorophenyl)amino]pyrimidine (EF 10)
A solution of 5-carbethoxy-4-chloro-6-[(2-fluorophenyl)amino]pyrimidine (CF 10) (3 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from ethanol yielded 2.7 g (84%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(2-fluorophenyl)amino]pyrimidine (EF 10). M P 102-104°C

ANALYSIS:
Microanalysis: C_{15}H_{17}FN_{4}O_{3} (320.32)
TLC: Benzene-Methanol (4.5:0.5), Rf value = 0.44
IR (KBr, cm^{-1}): 3365 (OH), 3321, 3236 (NH), 1676 (C=O)
UV (λ_{max}, nm): 236 (Methanol)
Synthesis of 5-carbethoxy-4-ethanolamino-6-[(4-fluorophenyl)amino]pyrimidine (EF 11)

A solution of 5-carbethoxy-4-chloro-6-[(4-fluorophenyl)amino]pyrimidine (CF 11) (3 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from ethanol yielded 2.4 g (75%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(4-fluorophenyl)amino]pyrimidine (EF 11) M. P. 125-127°C

ANALYSIS:
Microanalysis: C₁₁H₁₇FN₄O₃ (320.32)
TLC: Benzene-Methanol (4.5:0.5), Rf value = 0.47
IR (KBr, cm⁻¹): 3550 (OH), 3301, 3236 (NH), 1670 (C=O)
UV (λmax, nm): 238 (Methanol)

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(3-trifluorophenyl)amino]pyrimidine (EF 12)

A solution of 5-carbethoxy-4-chloro-6-[(3-trifluorophenyl)amino]pyrimidine (CF 12) (3.5 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from benzene-n-hexane yielded 1.7 g (46%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(3-trifluorophenyl)amino]pyrimidine (EF 12) M. P. 110-112°C

ANALYSIS:
Microanalysis: C₁₆H₁₇F₃N₄O₃ (370.33)
TLC: Benzene-Methanol (4.5:0.5); Rf value = 0.44
IR (KBr, cm⁻¹): 3438 (OH), 3310, 3274 (NH), 1660 (C=O)
UV (λmax, nm): 237 (Methanol)
Synthesis of 5-carbethoxy-6-[[2-chlorophenyl]amino]-4-ethanolamino-pyrimidine (EF 13)

A solution of 5-carbethoxy-4-chloro-6-[[2-chlorophenyl]amino]pyrimidine (CF 13) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from benzene yielded 2.5 g (74%) of white crystalline compound which was characterized as 5-carbethoxy-6-[[2-chlorophenyl]amino]-4-ethanolamino-pyrimidine (EF 13) M P 104-106°C.

ANALYSIS:

Microanalysis: C_{15}H_{17}ClN_{4}O_{3} (336.77)

TLC: Benzene- Methanol (4.5 0.5), Rf value = 0.42

IR (KBr, cm^{-1}): 3478 (OH), 3307, 3240 (NH), 1675 (C=O)

UV (A_{max}, nm): 238 (Methanol)

Synthesis of 5-carbethoxy-6-[[3-chlorophenyl]amino]-4-ethanolamino-pyrimidine (EF 14)

A solution of 5-carbethoxy-4-chloro-6-[[3-chlorophenyl]amino]pyrimidine (CF 14) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EF 01. Recrystallization from benzene-n-hexane yielded 2 g (59%) of white crystalline compound which was characterized as 5-carbethoxy-6-[[3-chlorophenyl]amino]-4-ethanolamino-pyrimidine (EF 14) M P 108-110°C.

ANALYSIS:

Microanalysis: C_{15}H_{17}ClN_{4}O_{3} (336.77)

TLC: Benzene- Methanol (4.5 0.5), Rf value = 0.43

IR (KBr, cm^{-1}): 3375 (OH), 3323, 3207 (NH), 1670 (C=O)

UV (A_{max}, nm): 237 (Methanol)
**Synthesis of 5-carbethoxy-6-[(4-chlorophenyl)amino]-4-ethanolaminopyrimidine (EF 15)**

A solution of 5-carbethoxy-4-chloro-6-[(4-chlorophenyl)amino]pyrimidine (CF 15) (3.1 g, 0.01 M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01 M) according to the procedure described for EF 01. Recrystallization from benzene-n-hexane yielded 2.8 g (82%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(4-chlorophenyl)amino]-4-ethanolaminopyrimidine (EF 15). M. P. 126-128°C

**ANALYSIS:**
- Microanalysis: C₁₅H₁₇ClN₄O₃ (336.77)
- TLC: Benzene: Methanol (4.5:0.5); Rᵣ value = 0.46
- IR (KBr, cm⁻¹): 3433 (OH), 3301, 3223 (NH), 1666 (C=O)
- UV (λ max, nm): 238 (Methanol)
- ¹H NMR (δ): 1.37-1.45 (t, 3H, OCH₂CH₃); 4.35-4.47 (t, 2H, NHCH₂CH₂), 4.65-4.72 (t, 2H, NHCH₂CH₂), 4.75-4.87 (q, 2H, OCH₂CH₂), 5.34-5.47 (b, 1H, NH₂CH₂CH₂), 7.18-7.42 (m, 4H, NHArH), 8.25-8.37 (t, 1H, OH), 8.49 (s, 1H, NCH₃); 11.42 (s, 1H, NHAr)
- Mass (m/z): 338 (M+2), 337 (M+1)

**Synthesis of 6-[(4-bromophenyl)amino]-5-carbethoxy-4-ethanolaminopyrimidine (EF 16)**

A solution of 6-[(4-bromophenyl)amino]-5-carbethoxy-4-chloro-pyrimidine (CF 16) (3.6 g, 0.01 M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01 M) according to the procedure described for EF 01. Recrystallization from ethanol yielded 3 g (79%) of white crystalline compound which was characterized as 6-[(4-bromophenyl)amino]-5-carbethoxy-4-ethanolaminopyrimidine (EF 16). M. P. 127-130°C

**ANALYSIS:**
- Microanalysis: C₁₅H₁₇BrN₄O₃ (381.22)
- TLC: Benzene: Methanol (4.5:0.5); Rᵣ value = 0.45
- IR (KBr, cm⁻¹): 3367 (OH), 3315, 3207 (NH), 1680 (C=O)
- UV (λ max, nm): 240 (Methanol)
Experimental

Synthesis of 5-carbethoxy-4-ethanolamino-6-(methylamino)-2-phenylpyrimidine (EB 01)

A solution of 5-carbethoxy-4-chloro-6-(methylamino)-2-phenylpyrimidine (CB 01) (2.9 g, 0.01M) in ethanol (15 mL), was added ethanolamine 0.61 g (0.01M) The reaction mixture was refluxed for 1 h on water bath, cooled and poured into ice-water mixture. It was kept at 20°C for 12 h. The solid obtained was filtered and dried. Recrystallization from dichloromethane-n-hexane yielded 2.2 g (69%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-(methylamino)-2-phenylpyrimidine (EB 01) M P 138-140°C

ANALYSIS:

| Microanalysis | C_{16}H_{20}N_{4}O_{3} (316 35) |
| TLC | Benzene. Methanol (4 5 0 5); Rf value = 0.43 |
| IR (KBr, cm^{-1}) | 3446 (OH), 3361, 3265 (NH), 1679 (C=O) |
| UV (λ_{max}, nm) | 290 (Methanol) |
| ^{1}H NMR (δ) | 1.29-1.40 (t, 3H, OCH₂CH₃), 2.76-2.81 (d, 3H, NHCH₃); 3.48-3.55 (t, 2H, NHCH₂CH₂), 3.88-4.01 (t, 2H, NHCH₂CH₂); 4.30-4.38 (q, 2H, OCH₂CH₃), 4.44-4.52 (b, 1H, NHCH₃), 4.82-4.97 (b, 1H, NHCH₂CH₂), 6.99-7.18 (m, 5H, NHArH), 8.01-8.15 (t, 1H, O-H), 8.45 (s, 1H, NHAr) |
| Mass (m/z) | 317 (M+1), 271, 211, 168, 102 |

Synthesis of 5-carbethoxy-4-ethanolamino-6-(ethylamino)-2-phenylpyrimidine (EB 02)

A solution of 5-carbethoxy-4-chloro-6-(ethylamino)-2-phenylpyrimidine (CB 02) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EB 01. Recrystallization from dichloromethane-n-hexane yielded 2.4 g (73%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-(ethylamino)-2-phenylpyrimidine (EB 02) M P 142-144°C

ANALYSIS:

| Microanalysis | C_{17}H_{22}N_{4}O_{3} (330 38) |
| TLC | Benzene. Methanol (4 5 0 5); Rf value = 0.42 |
| IR (KBr, cm^{-1}) | 3433 (OH), 3298 (NH), 1668 (C=O) |
| UV (λ_{max}, nm) | 290 (Methanol) |
Experimental

Synthesis of 6-(benzylamino)-5-carbethoxy-4-ethanolamino-2-phenylpyrimidine (EB 03)

A solution of 6-(benzylamino)-5-carbethoxy-4-chloro-2-phenylpyrimidine (CB 03) (3.7 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EB 01. Recrystallization from dichloromethane-n-hexane yielded 2.2 g (56%) of white crystalline compound which was characterized as 6-(benzylamino)-5-carbethoxy-4-ethanolamino-2-phenylpyrimidine (EB 03) M. P. 110-112°C

ANALYSIS:

Microanalysis C_{22}H_{24}N_{4}O_{3} (392.45)
TLC Benzene: Methanol (4 5 0.5), Rf value = 0.42
IR (KBr, cm⁻¹) 3431 (OH), 3334 (NH), 1645 (C=O)
UV (λ_max, nm) 292 (Methanol)

Synthesis of 5-carbethoxy-4-ethanolamino-2-phenyl-6-(phenylamino)pyrimidine (EB 04)

A solution of 5-carbethoxy-4-chloro-2-phenyl-6-(phenylamino)pyrimidine (CB 04) (3.5 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EB 01. Recrystallization from benzene yielded 3.3 g (87%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-2-phenyl-6-(phenylamino)pyrimidine (EB 04) M. P. 128-130°C

ANALYSIS:

Microanalysis C_{21}H_{22}N_{4}O_{3} (378.42)
TLC Benzene: Methanol (4 5 0.5), Rf value = 0.43
IR (KBr, cm⁻¹) 3373 (OH), 3326, 3234 (NH), 1679 (C=O)
UV (λ_max, nm) 294 (Methanol)

^1H NMR (δ) 1.30-1.42 (t, 3H, OCH₂CH₃), 4.25-4.35 (t, 2H, NHCH₂CH₂),
(CDCl₃) 4.59-4.65 (t, 2H, NHCH₂CH₂), 4.67-4.75 (q, 2H, OCH₂CH₃);
5.38-5.45 (b, 1H, NHCH₂CH₂); 7.25-7.42 (m, 10H, ArH),
8.09-8.20 (t, 1H, OH), 11.42 (s, 1H, NHAr)
Mass (m/z) 378 (M+1), 333, 215, 170, 102
Synthesis of 5-carbethoxy-4-ethanolamino-6-[(2-methylphenyl)amino]-2-phenylpyrimidine (EB 05)

A solution of 5-carbethoxy-4-chloro-6-[(2-methylphenyl)amino]-2-phenylpyrimidine (CB 05) (3.7 g, 0.01 M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01 M) according to the procedure described for EB 01. Recrystallization from benzene-n-hexane yielded 3.1 g (80%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(2-methylphenyl)amino]-2-phenylpyrimidine (EB 05). M. P. 126-128°C

ANALYSIS:
Microanalysis: C_{22}H_{24}N_{4}O_{3} (392.45)
TLC: Benzene-Methanol (4:5:0.5), R_{f} = 0.41
IR (KBr, cm^{-1}): 3425 (OH), 3310, 3240 (NH), 1680 (C=O)
UV (λ_{max}, nm): 294 (Methanol)

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(4-methylphenyl)amino]-2-phenylpyrimidine (EB 06)

A solution of 5-carbethoxy-4-chloro-6-[(4-methylphenyl)amino]-2-phenylpyrimidine (CB 06) (3.7 g, 0.01 M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01 M) according to the procedure described for EB 01. Recrystallization from benzene-n-hexane yielded 3.1 g (80%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(4-methylphenyl)amino]-2-phenylpyrimidine (EB 06). M. P. 129-131°C

ANALYSIS:
Microanalysis: C_{22}H_{24}N_{4}O_{3} (392.45)
TLC: Benzene-Methanol (4:5:0.5), R_{f} = 0.43
IR (KBr, cm^{-1}): 3415 (OH), 3325, 3240 (NH), 1666 (C=O)
UV (λ_{max}, nm): 296 (Methanol)
^1H NMR (δ) (CDCl_{3}): 1.32-1.45 (t, 3H, OCH_{2}CH_{3}); 2.39 (s, 3H, Ar-CH_{3}); 3.62-3.78 (t, 2H, NHCH_{2}CH_{2}); 4.29-4.38 (t, 2H, NHCH_{2}CH_{2}); 4.65-4.78 (q, 2H, OCH_{2}CH_{3}); 5.38-5.45 (b, 1H, NHCH_{2}CH_{2}); 7.25-7.39 (m, 9H, Ar); 8.09-8.20 (t, 1H, OH); 11.42 (s, 1H, NHAr)
Mass (m/z): 393 (M+1), 347, 332, 287, 229, 184, 103
Experimental

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(2-methoxyphenyl)amino]-2-phenylpyrimidine (EB 07)
A solution of 5-carbethoxy-4-chloro-6-[(2-methoxyphenyl)amino]-2-phenylpyrimidine (CB 07) (3.8 g, 0.01 M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01 M) according to the procedure described for EB 01. Recrystallization from benzene yielded 3.1 g (76%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(2-methoxyphenyl)amino]-2-phenylpyrimidine (EB 07) M P 122-124°C.

ANALYSIS:
Microanalysis C_{22}H_{24}N_{4}O_{4} (408.45)
TLC Benzene. Methanol (4:5:0.5); R_f value = 0.41
IR (KBr, cm^{-1}) 3419 (OH), 3369, 3160 (NH), 1668 (C=O)
UV (\lambda_{\text{max}}, \text{nm}) 295 (Methanol)
^1H NMR (\delta) (CDCl_3/DMSO-d_6) 1.30-1.42 (t, 3H, OCH_2CH_3); 3.09 (s, 3H, Ar-OCH_3), 3.78-3.91 (q, 2H, OC\dot{CH}_3); 4.32-4.40 (t, 2H, NHCH_2CH_2); 4.62-4.72 (m, 9H, ArH), 8.11-8.22 (t, 1H, OH), 11.51 (s, 1H, NHAr), 190
Mass (m/z) . 409 (M+1), 363, 303, 200, 102

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(4-methoxyphenyl)amino]-2-phenylpyrimidine (EB 08)
A solution of 5-carbethoxy-4-chloro-6-[(4-methoxyphenyl)amino]-2-phenylpyrimidine (CB 08) (3.8 g, 0.01 M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01 M) according to the procedure described for EB 01. Recrystallization from ethanol yielded 3.7 g (90%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(4-methoxyphenyl)amino]-2-phenylpyrimidine (EB 08) M. P 124-126°C

ANALYSIS:
Microanalysis C_{22}H_{24}N_{4}O_{4} (408.45)
TLC Benzene. Methanol (4:5:0.5); R_f value = 0.44
IR (KBr, cm^{-1}) : 3417 (OH), 3396, 3224 (NH), 1689 (C=O)
UV (\lambda_{\text{max}}, \text{nm}) 297 (Methanol)
Experimental

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(2-fluorophenyl)amino]-2-phenylpyrimidine (EB 9)
A solution of 5-carbethoxy-4-chloro-6-[(2-fluorophenyl)amino]-2-phenylpyrimidine (CB 9) (3.7 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EB 01. Recrystallization from benzene-n-hexane yielded 3.5 g (88%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(2-fluorophenyl)amino]-2-phenylpyrimidine (EB 9) M.P. 126-128°C.

ANALYSIS:
Microanalysis C_{21}H_{21}FN_{4}O_{3} (396.41)
TLC Benzene. Methanol (4:5:0.5), R_{f} value = 0.43
IR (KBr, cm\(^{-1}\)) 3413 (OH), 3317, 3170 (NH), 1670 (C=O)
UV (\lambda_{max}, nm) 294 (Methanol)

Synthesis of 5-carbethoxy-4-ethanolamino-6-[(4-fluorophenyl)amino]-2-phenylpyrimidine (EB 10)
A solution of 5-carbethoxy-4-chloro-6-[(4-fluorophenyl)amino]-2-phenylpyrimidine (CB 10) (3.7 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EB 01. Recrystallization from benzene-n-hexane yielded 3.7 g (93%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(4-fluorophenyl)amino]-2-phenylpyrimidine (EB 10) M.P. 142-144°C.

ANALYSIS:
Microanalysis C_{21}H_{21}FN_{4}O_{3} (396.41)
TLC Benzene. Methanol (4:5:0.5), R_{f} value = 0.45
IR (KBr, cm\(^{-1}\)) 3394 (OH), 3317 (NH), 1666 (C=O)
UV (\lambda_{max}, nm) 296 (Methanol)
\(^1\)H NMR (\delta) 1.35-1.47 (t, 3H, OCH\(_2\)CH\(_3\)); 3.70-3.84 (t, 2H, NHCH\(_2\)CH\(_3\)); 4.40-4.55 (t, 2H, NHCH\(_2\)CH\(_3\)); 4.68-4.79 (q, 2H, OCH\(_2\)CH\(_3\)); 5.40-5.52 (b, 1H, NHCH\(_2\)CH\(_3\)); 7.12-7.29 (m, 9H, ArH); 8.01-8.18 (t, 1H, OH); 10.72 (s, 1H, NHAr)
Mass (m/z) 397 (M+1), 351, 291, 188, 102
Experimental

Synthesis of 5-carbethoxy-6-[(2-chlorophenyl)amino]-4-ethanolamino-2-phenylpyrimidine (EB 11)

A solution of 5-carbethoxy-4-chloro-6-[(2-chlorophenyl)amino]-2-phenylpyrimidine (CB 11) (3.9 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EB 01. Recrystallization from benzene-n-hexane yielded 2.1 g (51%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(2-chlorophenyl)amino]-4-ethanolamino-2-phenylpyrimidine (EB 11). M. P. 108-110°C.

ANALYSIS:

Microanalysis C_{21}H_{21}ClN_{4}O_{3} (412.87)

TLC Benzene: Methanol (4:5:0.5); Rf value = 0.41

IR (KBr, cm^{-1}) 3562 (OH), 3336, 3255 (NH), 1645 (C=O)

UV (λ_{max}, nm) 297 (Methanol)

Synthesis of 5-carbethoxy-6-[(3-chlorophenyl)amino]-4-ethanolamino-2-phenylpyrimidine (EB 12)

A solution of 5-carbethoxy-4-chloro-6-[(3-chlorophenyl)amino]-2-phenylpyrimidine (CB 12) (3.9 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EB 01. Recrystallization from benzene-n-hexane yielded 1.9 g (46%) of white crystalline compound which was characterized as 5-carbethoxy-4-ethanolamino-6-[(3-chlorophenyl)amino]-2-phenylpyrimidine (EB 12). M. P. 98-100°C.

ANALYSIS:

Microanalysis C_{21}H_{21}ClN_{4}O_{3} (412.87)

TLC Benzene: Methanol (4:5:0.5); Rf value = 0.40

IR (KBr, cm^{-1}) 3520 (OH), 3292, 3200 (NH), 1677 (C=O)

UV (λ_{max}, nm) 296 (Methanol)
Experimental

Synthesis of 5-carbethoxy-6-[(4-chlorophenyl)amino]-4-ethanolamino-2-phenylpyrimidine (EB 13)
A solution of 5-carbethoxy-4-chloro-6-[(4-chlorophenyl)amino]-2-phenylpyrimidine (CB 13) (3.9 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EB 01. Recrystallization from benzene yielded 3.2 g (78%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(4-chlorophenyl)amino]-4-ethanolamino-2-phenylpyrimidine (EB 13) M P 142-144°C.

ANALYSIS:
Microanalysis C_{21}H_{21}ClN_{4}O_{3} (412.87)
TLC Benzene Methanol (4:5:0.5); R_f value = 0.44
IR (KBr, cm^{-1}) 3348 (OH), 3317, 3222 (NH), 1658 (C=O)
UV (A_{max}, nm) 298 (Methanol)

Synthesis of 6-[(4-bromophenyl)amino]-5-carbethoxy-4-ethanolamino-2-phenylpyrimidine (EB 14)
A solution of 6-[(4-bromophenyl)amino]-5-carbethoxy-4-chloro-2-phenylpyrimidine (CB 14) (4.3 g, 0.01M) in ethanol (15 mL), was reacted with ethanolamine 0.61 g (0.01M) according to the procedure described for EB 01. Recrystallization from benzene-n-hexane yielded 4.2 g (91%) of white crystalline compound which was characterized as 6-[(4-bromophenyl)amino]-5-carbethoxy-4-ethanolamino-2-phenylpyrimidine (EB 14) M P 165-167°C.

ANALYSIS:
Microanalysis C_{21}H_{21}BrN_{4}O_{3} (457.32)
TLC Benzene Methanol (4:5:0.5); R_f value = 0.45
IR (KBr, cm^{-1}) 3438 (OH), 3357, 3274 (NH), 1716 (C=O)
UV (A_{max}, nm) 297 (Methanol)
^{1}H NMR (δ): 1.30-1.42 (t, 3H, OCH_{2}CH_{3}); 3.78-3.91 (t, 2H, NHCH_{2}CH_{3});
(CDCl_{3}/DMSO-d_{6}) 4.32-4.40 (t, 2H, NHCH_{2}CH_{3}); 4.62-4.72 (q, 2H, OCH_{2}CH_{3}), 5.38-5.45 (b, 1H, NHCH_{2}CH_{3}), 6.88-7.02 (m, 9H, ArH), 8.11-8.22 (t, 1H, OH), 11.51 (s, 1H, NHAr)
Mass (m/z) 459 (M+2), 458 (M+1), 411, 351, 247, 102
Experimental

Synthesis of 5-carbethoxy-4-hydrazino-6-(methylamino)pyrimidine (HF 01)
To a solution of 5-carbethoxy-4-chloro-6-(methylamino)pyrimidine (CF 01) (2.2 g, 0.01M) in ethanol (15 mL), was added hydrazine hydrate (85%) 0.5 g (0.01M). The reaction mixture was refluxed for 1 h on water bath, cooled and poured into ice-water mixture. It was kept at 20°C for 12 h. The solid obtained was filtered and dried. Recrystallization from ethanol yielded 0.9 g (43%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-(methylamino)pyrimidine (HF 01). M.P. 190-192°C

ANALYSIS:
Microanalysis \( \text{C}_8\text{H}_{13}\text{N}_5\text{O}_2 \) (211 22)
TLC Benzene Methanol (4 5 0.5), \( R_f \) value = 0.38
IR (KBr, cm\(^{-1}\)) 3370, 3230 (NH), 1680 (C=O)
UV (\( \lambda_{\text{max}} \), nm) 237 (Methanol)

Synthesis of 5-carbethoxy-6-(ethylamino)-4-hydrazinopyrimidine (HF 02)
A solution of 5-carbethoxy-4-chloro-6-(ethylamino)pyrimidine (CF 02) (2.3 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 0.9 g (39%) of white crystalline compound which was characterized as 5-carbethoxy-6-(ethylamino)-4-hydrazinopyrimidine (HF 02). M.P. 198-200°C

ANALYSIS:
Microanalysis \( \text{C}_9\text{H}_{15}\text{N}_5\text{O}_2 \) (225 25)
TLC Benzene Methanol (4 5 0.5); \( R_f \) value = 0 34
IR (KBr, cm\(^{-1}\)) 3375, 3224 (NH), 1680 (C=O)
UV (\( \lambda_{\text{max}} \), nm) 236 (Methanol)

Synthesis of 6-(benzylamino)-5-carbethoxy-4-hydrazinopyrimidine (HF 03)
A solution of 6-(benzylamino)-5-carbethoxy-4-chloropyrimidine (CF 03) (2.9 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 1.2 g (41%) of white crystalline compound which was characterized as 6-(benzylamino)-5-carbethoxy-4-hydrazinopyrimidine (HF 03). M.P. 202-204°C
Analysis:

Microanalysis \( \text{C}_{13}\text{H}_{13}\text{N}_{5}\text{O}_{2} \) (273 29)

TLC Benzene-Methanol (4 5 0 5), \( R_f \) value = 0.39

IR (KBr, cm\(^{-1}\)) 3380, 3238 (NH), 1675 (C=O)

UV (\( \lambda_{\text{max, nm}} \)) 299 (Methanol)

\( ^1\text{H} \) NMR (\( \delta \))

\( \begin{align*}
4.15 & \text{ (t, 3H, OCH}_2\text{CH}_3) \\
3.95 & \text{ (d, 2H, NHCH}_2\text{Ar) }
\end{align*} \)

Synthesis of 5-carbethoxy-4-hydrazino-6-(phenylamino)pyrimidine (HF 04)

A solution of 5-carbethoxy-4-chloro-6-(phenylamino)pyrimidine (CF 04) (2.8 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 1.8 g (67%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-(phenylamino)pyrimidine (HF 04). M. P. 200-202\(^{\circ}\)C

Analysis:

Microanalysis \( \text{C}_{13}\text{H}_{13}\text{N}_{5}\text{O}_{2} \) (273 29)

TLC Benzene-Methanol (4 5 0 5), \( R_f \) value = 0.39

IR (KBr, cm\(^{-1}\)) 3380, 3238 (NH), 1675 (C=O)

UV (\( \lambda_{\text{max, nm}} \)) 299 (Methanol)

Mass = 374 (M+1), 228, 212, 185, 187

Synthesis of 5-carbethoxy-4-hydrazino-6-[(2-methylphenyl)amino]pyrimidine (HF 05)

A solution of 5-carbethoxy-4-chloro-6-[(2-methylphenyl)amino]pyrimidine (CF 05) (2.9 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 1.8 g (62%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-[(2-methylphenyl)amino]pyrimidine (HF 05). M. P. 152-154\(^{\circ}\)C
ANALYSIS:

Microanalysis C_{14}H_{17}N_{5}O_{2} (287 32)

TLC Benzene Methanol (4.5 0.5), R_{f} value = 0.37

IR (KBr, cm^{-1}) 3360, 3240 (NH), 1680 (C=O)

UV (λ_{max}, nm) 309 (Methanol)

{^1}H NMR (δ) 1.37-1.41 (t, 3H, OCH\_2CH\_3); 2.34 (s, 3H, ArCH\_3); 4.31-4.37 (CDC\_5DMSO-d_6) (q, 2H, OCH\_2CH\_3); 5.13-5.69 (b, 2H, NHNH\_2); 7.12-7.18 (m, 4H, ArH), 8.21 (s, 1H, NCH\_2), 10.35 (s, 1H, NHAr)

Mass (m/z) 288 (M+1), 242, 226, 199, 171

Synthesis of 5-carbethoxy-4-hydrazino-6-[4-methylphenylamino]pyrimidine (HF 06)

A solution of 5-carbethoxy-4-chloro-6-[4-methylphenylamino]pyrimidine (CF 06) (2.9 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 1.3 g (45%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-[4-methylphenylamino]pyrimidine (HF 06). M. P 208-210°C

ANALYSIS:

Microanalysis C_{14}H_{17}N_{5}O_{2} (287 32)

TLC Benzene Methanol (4.5 0.5), R_{f} value = 0.38

IR (KBr, cm^{-1}) 3374, 3231 (NH), 1680 (C=O)

UV (λ_{max}, nm) 310 (Methanol)

Synthesis of 5-carbethoxy-4-hydrazino-6-[2-methoxyphenylamino]pyrimidine (HF 07)

A solution of 5-carbethoxy-4-chloro-6-[2-methoxyphenylamino]pyrimidine (CF 07) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 1.4 g (47%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-[2-methoxyphenylamino]pyrimidine (HF 07). M. P 155-157°C.
Experimental

ANALYSIS:

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<td>Benzene: Methanol (4 5 0 5), R_{f} value = 0 35</td>
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<tr>
<td>IR (KBr, cm^{-1})</td>
<td>3350, 3225 (NH), 1678 (C=O)</td>
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<tr>
<td>UV (\lambda_{\text{max}}, nm)</td>
<td>308 (Methanol)</td>
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Synthesis of 5-carbethoxy-4-hydrazino-6-[(4-methoxyphenyl)amino]pyrimidine (HF 08)

A solution of 5-carbethoxy-4-chloro-6-[(4-methoxyphenyl)amino]pyrimidine (CF 08) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 1.6 g (53%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-[(4-methoxyphenyl)amino]pyrimidine (HF 08). M P 202-204°C.

ANALYSIS:

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<tr>
<td>TLC</td>
<td>Benzene: Methanol (4 5 0 5), R_{f} value = 0 36</td>
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<tr>
<td>IR (KBr, cm^{-1})</td>
<td>3366, 3240 (NH), 1680 (C=O)</td>
</tr>
<tr>
<td>UV (\lambda_{\text{max}}, nm)</td>
<td>312 (Methanol)</td>
</tr>
<tr>
<td>H NMR (δ) (CDCl)</td>
<td>1.32-1.41 (t, 3H, OCH_{2}CH_{3}), 3.35 (s, 3H, ArOCH_{3}), 4.28-4.35 (q, 2H, OCH_{2}CH_{3}), 5.20-5.65 (b, 2H, NHNH_{2}), 6.92-7.03 (b, 1H, NHNH_{2}), 7.18-7.28 (m, 4H, ArH), 8.25 (s, 1H, NCH_{2}N), 10.35 (s, 1H, NHAr)</td>
</tr>
<tr>
<td>Mass (m/z)</td>
<td>304 (M+1), 258, 242, 215</td>
</tr>
</tbody>
</table>

Synthesis of 5-carbethoxy-6-[(2-fluorophenyl)amino]-4-hydrazinopyrimidine (HF 09)

A solution of 5-carbethoxy-4-chloro-6-[(2-fluorophenyl)amino]pyrimidine (CF 09) (3.0 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 1.6 g (55%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(2-fluorophenyl)amino]-4-hydrazinopyrimidine (HF 09). M P 142-144°C.
ANALYSIS:

Microanalysis . C$_{13}$H$_{14}$FN$_{5}$O$_{2}$ (291.28)

TLC . Benzene: Methanol (4:5:0.5); R$_{f}$ value = 0.38

IR (KBr, cm$^{-1}$) . 3372, 3228 (NH), 1670 (C=O)

UV (λ$_{max}$, nm) . 302 (Methanol)

Synthesis of 5-carbethoxy-6-[(4-fluorophenyl)amino]-4-hydrazinopyrimidine (HF 10)

A solution of 5-carbethoxy-4-chloro-6-[(4-fluorophenyl)amino]pyrimidine (CF 10) (3.0 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 2.3 g (79%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(4-fluorophenyl)amino]-4-hydrazinopyrimidine (HF 10). M. P. 190-192°C

ANALYSIS:

Microanalysis . C$_{13}$H$_{14}$FN$_{5}$O$_{2}$ (291.28)

TLC . Benzene: Methanol (4:5:0.5); R$_{f}$ value = 0.39

IR (KBr, cm$^{-1}$) . 3370, 3235 (NH), 1672 (C=O)

UV (λ$_{max}$, nm) . 308 (Methanol)

$^1$H NMR (δ) 1.44-1.48 (t, 3H, OCH$_2$CH$_3$), 4.35-4.38 (b, 2H, NH$_2$N); 4.43-4.48 (q, 2H, OCH$_2$CH$_3$), 7.01-7.06 (b, 1H, NH$_2$N); 7.50-7.55 (m, 4H, ArH), 8.71 (s, 1H, NCHN), 10.35 (s, 1H, NHAr)

Mass (m/z) . 292 (M+1), 246, 230, 203, 175

Synthesis of 5-carbethoxy-6-[(2-chlorophenyl)amino]-4-hydrazinopyrimidine (HF 11)

A solution of 5-carbethoxy-4-chloro-6-[(2-chlorophenyl)amino]pyrimidine (CF 11) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 1.7 g (55%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(2-chlorophenyl)amino]-4-hydrazinopyrimidine (HF 11). M. P. 150-152°C
Experimental

ANALYSIS:
Microanalysis  \( \text{C}_{13}\text{H}_{14}\text{ClN}_5\text{O}_2 \) (307.74)
TLC  Benzene Methanol (4.5:0.5), \( R_f \) value = 0.38
IR (KBr, cm\(^{-1}\))  3370, 3224 (NH), 1680 (C=O)
UV (\( \lambda_{\text{max}}, \text{nm} \)) 310 (Methanol)

Synthesis of 5-carbethoxy-6-[(3-chlorophenyl)amino]-4-hydrazinopyrimidine (HF 12)
A solution of 5-carbethoxy-4-chloro-6-[(3-chlorophenyl)amino]pyrimidine (CF 12) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 1.5 g (48%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(3-chlorophenyl)amino]-4-hydrazino-pyrimidine (HF 12) M P. 170-172°C

ANALYSIS:
Microanalysis  \( \text{C}_{13}\text{H}_{14}\text{ClN}_5\text{O}_2 \) (307.74)
TLC  Benzene Methanol (4.5:0.5); \( R_f \) value = 0.38
IR (KBr, cm\(^{-1}\))  3345, 3210 (NH), 1678 (C=O)
UV (\( \lambda_{\text{max}}, \text{nm} \)) 308 (Methanol)

Synthesis of 5-carbethoxy-6-[(4-chlorophenyl)amino]-4-hydrazinopyrimidine (HF 13)
A solution of 5-carbethoxy-4-chloro-6-[(4-chlorophenyl)amino]pyrimidine (CF 13) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 2.4 g (77%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(4-chlorophenyl)amino]-4-hydrazino-pyrimidine (HF 13) M P. 175-177°C

ANALYSIS:
Microanalysis  \( \text{C}_{13}\text{H}_{14}\text{ClN}_5\text{O}_2 \) (307.74)
TLC  Benzene. Methanol (4.5:0.5), \( R_f \) value = 0.38
IR (KBr, cm\(^{-1}\))  3345, 3210 (NH), 1680 (C=O)
UV (\( \lambda_{\text{max}}, \text{nm} \)) 308 (Methanol)
Experimental

Synthesis of 6-[(4-bromophenyl)amino]-5-carbethoxy-4-hydrazinopyrimidine (HF 14)
A solution of 6-[(4-bromophenyl)amino]-5-carbethoxy-4-chloropyrimidine (CF 14) (3.6 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HF 01. Recrystallization from ethanol yielded 2.4 g (69%) of white crystalline compound which was characterized as 6-[(4-bromophenyl)amino]-5-carbethoxy-4-hydrazinopyrimidine (HF 14). M. P 210-212°C

ANALYSIS:
- Microanalysis C_{13}H_{14}BrN_{2}O_{2} (352.19)
- TLC Benzene Methanol (4:5:0.5); Rf value = 0.37
- IR (KBr, cm^{-1}) 3360, 3220 (NH), 1678 (C=O)
- UV (A_{max}, nm) 310 (Methanol)

Synthesis of 5-carbethoxy-4-hydrazino-6-(methylamino)-2-phenylpyrimidine (HB 01)
To a solution of 5-carbethoxy-4-chloro-6-(methylamino)-2-phenylpyrimidine (CB 01) (2.9 g, 0.01M) in ethanol (15 mL), was added hydrazine hydrate (85%) 0.5 g (0.01M). The reaction mixture was refluxed for 1 h on water bath, cooled and poured into ice-water mixture. It was kept at 20°C for 12 h. The solid obtained was filtered and dried. Recrystallization from toluene yielded 1.0 g (35%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-(methylamino)-2-phenylpyrimidine (HB 01). M. P. 186-188°C

ANALYSIS:
- Microanalysis C_{14}H_{17}N_{5}O_{2} (287.32)
- TLC Benzene. Methanol (4:5:0.5); Rf value = 0.35
- IR (KBr, cm^{-1}) 3384, 3240 (NH), 1678 (C=O)
- UV (A_{max}, nm) 306 (Methanol)
Experimental

Synthesis 5-carbethoxy-6-(ethylamino)-4-hydrazino-2-phenylpyrimidine (HB 02)
A solution of 5-carbethoxy-4-chloro-6-(ethylamino)-2-phenylpyrimidine (CB 02) (3.1 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HB 01. Recrystallization from toluene yielded 1.2 g (40%) of white crystalline compound which was characterized as 5-carbethoxy-6-(ethylamino)-4-hydrazino-2-phenylpyrimidine (HB 02). M. P. 192-194°C.

ANALYSIS:
Microanalysis: $C_{15}H_{19}N_{5}O_{2}$ (301.34)
TLC: Benzene: Methanol (4.5: 0.5); Rf value = 0.34
IR (KBr, cm$^{-1}$): 3382, 3232 (NH), 1680 (C=O)
UV ($\lambda_{max}$, nm): 306 (Methanol)

Synthesis of 6-(benzylamino)-5-carbethoxy-4-hydrazino-2-phenylpyrimidine (HB 03)
A solution of 6-(benzylamino)-5-carbethoxy-4-chloro-2-phenylpyrimidine (CB 03) (3.7 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HB 01. Recrystallization from toluene yielded 1.6 g (44%) of white crystalline compound which was characterized as 6-(benzylamino)-5-carbethoxy-4-hydrazino-2-phenylpyrimidine (HB 03). M. P. 155-157°C.

ANALYSIS:
Microanalysis: $C_{20}H_{21}N_{5}O_{2}$ (363.41)
TLC: Benzene: Methanol (4.5: 0.5); Rf value = 0.36
IR (KBr, cm$^{-1}$): 3362, 3212 (NH), 1678 (C=O)
UV ($\lambda_{max}$, nm): 305 (Methanol)
Experimental

Synthesis of 5-carbethoxy-4-hydrazino-2-phenyl-6-(phenylamino)pyrimidine (HB 04)

A solution of 5-carbethoxy-4-chloro-2-phenyl-6-(phenylamino)pyrimidine (CB 04) (3.5 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HB 01. Recrystallization from ethanol yielded 1.7 g (49%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-2-phenyl-6-(phenylamino)pyrimidine (HB 04) M.P. 140-142°C.

ANALYSIS:

Microanalysis . C_{19}H_{19}N_{5}O_{2} (349 39)
TLC Benzene Methanol (4:5:0.5), R_f value = 0.36
IR (KBr, cm^{-1}) 3380, 3235 (NH), 1680 (C=O)
UV (\lambda_{\text{max}}, \text{nm}) 312 (Methanol)
^1H NMR (δ) 1.32-1.43 (t, 3H, OCH_{2}CH_{3}), 4.25-4.47 (b, 2H, NH_{2}), 4.51-4.65 (q, 2H, OCH_{2}CH_{3}), 7.12-7.39 (m, 10H, NHAr), 8.31-8.47 (b, 1H, NH_{2}), 8.72 (s, 1H, NHAr)
Mass (m/z) 350 (M+1), 304, 273, 246, 201, 102

Synthesis of 5-carbethoxy-4-hydrazino-6-[(2-methylphenyl)amino]-2-phenylpyrimidine (HB 05)

A solution of 5-carbethoxy-4-chloro-6-[(2-methylphenyl)amino]-2-phenylpyrimidine (CB 05) (3.7 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HB 01. Recrystallization from toluene-n-hexane yielded 1.7 g (47%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-[(2-methylphenyl)amino]-2-phenylpyrimidine (HB 05) M.P. 136-138°C.

ANALYSIS:

Microanalysis . C_{20}H_{21}N_{5}O_{2} (363 41)
TLC Benzene Methanol (4:5:0.5), R_f value = 0.34
IR (KBr, cm^{-1}) 3365, 3230 (NH), 1676 (C=O)
UV (\lambda_{\text{max}}, \text{nm}) 308 (Methanol)
Synthesis of 5-carbethoxy-4-hydrazino-6-[(4-methylphenyl)amino]-2-phenylpyrimidine (HB 06)

A solution of 5-carbethoxy-4-chloro-6-[(4-methylphenyl)amino]-2-phenylpyrimidine (CB 06) (3.7 g, 0.01 M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01 M) according to the procedure described for HB 01. Recrystallization from benzene yielded 1.6 g (44%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-[(4-methylphenyl)amino]-2-phenylpyrimidine (HB 06). M P. 140-142°C

ANALYSIS:

Microanalysis C_{20}H_{21}N_{5}O_{2} (363.41)
TLC Benzene Methanol (4.5 0 5), Rf value = 0 36
IR (KBr, cm\(^{-1}\)) 3372, 3212 (NH), 1675 (C=O)
UV (\(\lambda_{max}\), nm) 310 (Methanol)

Synthesis of 5-carbethoxy-4-hydrazino-6-[(2-methoxyphenyl)amino]-2-phenylpyrimidine (HB 07)

A solution of 5-carbethoxy-4-chloro-6-[(2-methoxyphenyl)amino]-2-phenylpyrimidine (CB 07) (3.8 g, 0.01 M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01 M) according to the procedure described for HB 01. Recrystallization from benzene yielded 1.6 g (42%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-[(2-methoxyphenyl)amino]-2-phenylpyrimidine (HB 07). M P 134-136°C

ANALYSIS:

Microanalysis C_{20}H_{21}N_{5}O_{3} (379.41)
TLC Benzene Methanol (4 5 0 5), Rf value = 0 35
IR (KBr, cm\(^{-1}\)) 3365, 3215 (NH), 1678 (C=O)
UV (\(\lambda_{max}\), nm) 310 (Methanol)

\(^1\)H NMR (5) 1.42-1.50 (t, 3H, OCH\(_2\)CH\(_3\)); 2.23 (s, 3H, ArOCH\(_3\)); 4.25-4.47 (CDCl\(_3\)/DMSO-d\(_6\)) (b, 2H, NH\(_2\)NHz); 4.51-4.65 (q, 2H, OCH\(_2\)CH\(_3\)); 6.99-7.25 (m, 5H, ArH); 7.45-7.51 (m, 4H, NHAr\(_H\)); 8.25-8.45 (b, 1H, NH\(_2\)NHz); 8.95 (s, 1H, NHAr)

Mass (m/z) 380 (M+1), 334, 318, 215, 102
Experimental

Synthesis of 5-carbethoxy-4-hydrazino-6-[(4-methoxyphenyl)amino]-2-phenylpyrimidine (HB 08)
A solution of 5-carbethoxy-4-chloro-6-[(4-methoxyphenyl)amino]-2-phenylpyrimidine (CB 08) (3.8 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HB 01 Recrystallization from benzene yielded 1.9 g (50%) of white crystalline compound which was characterized as 5-carbethoxy-4-hydrazino-6-[(4-methoxyphenyl)amino]-2-phenylpyrimidine (HB 08) M P 136-138°C

ANALYSIS:
Microanalysis : C20H21N5O3 (379 41)
TLC : Benzene· Methanol (4 5 0 5), Rf value = 0.36
IR (KBr, cm⁻¹) : 3375, 3230 (NH), 1680 (C=O)
UV (λmax, nm) : 312 (Methanol)

Synthesis of 5-carbethoxy-6-[(2-fluorophenyl)amino]-4-hydrazino-2-phenylpyrimidine (HB 9)
A solution of 5-carbethoxy-4-chloro-6-[(2-fluorophenyl)amino]-2-phenylpyrimidine (CB 9) (3.7 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HB 01 Recrystallization from toluene-n-hexane yielded 2.2 g (60%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(2-fluorophenyl)amino]-4-hydrazino-2-phenylpyrimidine (HB 9) M P 130-132°C.

ANALYSIS:
Microanalysis : C19H18FN5O2 (367.38)
TLC : Benzene· Methanol (4 5 0 5), Rf value = 0.36
IR (KBr, cm⁻¹) : 3380, 3240 (NH), 1678 (C=O)
UV (λmax, nm) : 310 (Methanol)
¹H NMR (δ) : 1.47-1.50 (t, 3H, OCH₂CH₃), 4.21-4.41 (b, 2H, NH₂NH₂); 4.45- (CDCl₃/DMSO-δ₆) 4.50 (q, 2H, OCH₂CH₂), 7.12-7.26 (m, 5H, ArH), 7.45-7.51 (m, 4H, ArH), 8.61-8.65 (b, 1H, NH₂NH₂), 8.99 (s, 1H, NHAr)
Mass (m/z) : 368 (M+1), 322, 306, 203, 175, 102
Synthesis of 4-hydrazino-5-carbethoxy-6-[(4-fluorophenyl)amino]-2-phenylpyrimidine (HB 10)
A solution of 5-carbethoxy-4-chloro-6-[(4-fluorophenyl)amino]-2-phenylpyrimidine (CB 10) (3.7 g, 0.01 M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01 M) according to the procedure described for HB 01. Recrystallization from ethanol yielded 2 g (54%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(4-fluorophenyl)amino]-4-hydrazino-2-phenylpyrimidine (HB 10). M. P. 141-143°C.

ANALYSIS:
- Microanalysis: C_{19}H_{16}F_{1}N_{3}O_{2} (367.38)
- TLC: Benzene-Methanol (4:5:0.5), R_f value = 0.40
- IR (KBr, cm^{-1}): 3372, 3240 (NH), 1680 (C=O)
- UV (λ_{max}, nm): 312 (Methanol)

Synthesis of 5-carbethoxy-6-[(2-chlorophenyl)amino]-4-hydrazino-2-phenylpyrimidine (HB 11)
A solution of 5-carbethoxy-4-chloro-6-[(2-chlorophenyl)amino]-2-phenylpyrimidine (CB 11) (3.9 g, 0.01 M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01 M) according to the procedure described for HB 01. Recrystallization from toluene yielded 1.2 g (32%) of white crystalline compound which was characterized as 4-hydrazino-5-carbethoxy-6-[(2-chlorophenyl)amino]-2-phenylpyrimidine (HB 11). M. P. 128-130°C.

ANALYSIS:
- Microanalysis: C_{19}H_{18}ClN_{3}O_{2} (383.83)
- TLC: Benzene-Methanol (4:5:0.5), R_f value = 0.37
- IR (KBr, cm^{-1}): 3358, 3225 (NH), 1674 (C=O)
- UV (λ_{max}, nm): 310 (Methanol)
Experimental

Synthesis of 5-carbethoxy-6-[(3-chlorophenyl)amino]-4-hydrazino-2-phenylpyrimidine (HB 12)
A solution of 5-carbethoxy-4-chloro-6-[(3-chlorophenyl)amino]-2-phenylpyrimidine (CB 12) (3.9 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HB 01. Recrystallization from toluene yielded 1.4 g (37%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(3-chlorophenyl)amino]-4-hydrazino-2-phenylpyrimidine (HB 12)
M. P 123-125°C

ANALYSIS:
Microanalysis C_{19}H_{18}ClN_{5}O_{2} (383.83)
TLC . Benzene Methanol (4:5:0.5), R_{f} value = 0.35
IR (KBr, cm^{-1}) 3370, 3232 (NH), 1675 (C=O)
UV (λ_{max}, nm) 311 (Methanol)

Synthesis of 5-carbethoxy-6-[(4-chlorophenyl)amino]-4-hydrazino-2-phenylpyrimidine (HB 13)
A solution of 5-carbethoxy-4-chloro-6-[(4-chlorophenyl)amino]-2-phenylpyrimidine (CB 13) (3.9 g, 0.01M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01M) according to the procedure described for HB 01. Recrystallization from ethanol yielded 2.0 g (53%) of white crystalline compound which was characterized as 5-carbethoxy-6-[(4-chlorophenyl)amino]-4-hydrazino-2-phenylpyrimidine (HB 13)
M. P 139-141°C

ANALYSIS:
Microanalysis C_{19}H_{18}ClN_{5}O_{2} (383.83)
TLC . Benzene Methanol (4:5:0.5), R_{f} value = 0.39
IR (KBr, cm^{-1}) 3375, 3245 (NH), 1680 (C=O)
UV (λ_{max}, nm) 312 (Methanol)
Experimental

Synthesis of 6-[(4-bromophenyl)amino]-5-carbethoxy-4-hydrazino-2-phenyl pyrimidine (HB 14)

A solution of 6-[(4-bromophenyl)amino]-5-carbethoxy-4-chloro-2-phenylpyrimidine (CB 14) (4.3 g, 0.01 M) in ethanol (15 mL), was reacted with hydrazine hydrate (85%) 0.5 g (0.01 M) according to the procedure described for HB 01. Recrystallization from ethanol yielded 2.8 g (65%) of white crystalline compound which was characterized as 6-[(4-bromophenyl)amino]-5-carbethoxy-4-hydrazino-2-phenylpyrimidine (HB 14) M. P. 140-142°C

ANALYSIS:

| Microanalysis | C_{19}H_{18}BrN_{5}O_{2} (428.28) |
| TLC | Benzene Methanol (4:5 0:5), Rf value = 0.39 |
| IR (KBr, cm\(^{-1}\)) | 3380, 3238 (NH), 1675 (C=O) |
| UV (λ_{max}, nm) | 312 (Methanol) |
| \(^{1}\)H NMR (δ) | 1.46-1.49 (t, 3H, OCH2CH3), 4.45-4.48 (q, 2H, OCH2CH3); |
| (CDCl\(_3\)DMSO-d6) | 6.79-6.83 (b, 1H, NH-NH2), 7.44-7.53 (m, 5H, ArH), 7.61-7.65 (m, 4H, ArH), 8.39-8.41 (b, 2H, NH-NH2); 10.58 (s, 1H, NHAr) |
| Mass (m/z) | 430 (M+2), 429 (M+1), 382, 366, 262, 234, 102 |
Synthesis of 8-carbethoxy-7-(methylamino)-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 01)

To a solution of 5-carbethoxy-4-ethanolamino-6-(methylamino)pyrimidine (EF 01) 2.4 g (0.01M) in anhydrous toluene (20 mL), was added phosphoryl chloride 1.68 g (0.01M) The reaction mixture was refluxed for 1 h Excess of toluene was removed under vacuum. The residue obtained was poured into 250 mL of ice-water mixture and neutralized with 10% ammonium hydroxide solution The solid obtained was filtered, washed with water and dried. Recrystallization from dichloromethane-n-hexane yielded 1.0 g (48%) of crystalline product. The product was characterized as 8-carbethoxy-7-(methylamino)-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 01) M. P 178-180° C

ANALYSIS:

Microanalysis \( \cdot C_{10}H_{14}N_{4}O_{2} \) %Required \( \cdot C \) (54.04), H (6.35), N (25.21)
(222 24) % Found \( \cdot C \) (53.73), H (6.49), N (25.07)

TLC Benzene Methanol (4 5 0 5), Rf value = 0.29

IR (KBr, cm\(^{-1}\)) 3375 (NH), 1676 (C=O)

UV (\( \lambda_{\text{max}} \), nm) 246 (Methanol)

\(^1\)H NMR (\( \delta \)) 1.30-1.34 (t, 3H, OCH\(_2\)CH\(_3\)), 2.23-2.27 (d, 3H, NHCH\(_3\)), 3.49 (CDC\(_3\)/DMSO-d\(_6\)) 3.59 (b, 1H, NHCH\(_3\)), 3.90-3.95 (t, 2H, =NCH\(_2\)CH\(_3\)), 4.06-4.11 (t, 2H, =NCH\(_2\)CH\(_3\)), 4.34-4.40 (q, 2H, OCH\(_2\)CH\(_3\)); 7.87 (s, 1H, NCHN)

Mass (m/z) 223 (M+1), 207, 195, 177, 136

Synthesis of 8-carbethoxy-7-(ethylamino)-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 02)

A solution of 5-carbethoxy-4-ethanolamino-6-(ethylamino)pyrimidine (EF 02) 2.5 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 1.3 g (52%) of crystalline product The product was characterized as 8-carbethoxy-7-(ethylamino)-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 02) M. P 186-188° C
Experimental

ANALYSIS:

Microanalysis: C_{17}H_{18}N_{4}O_{2}  %Required: C (55.92), H (6.83), N (23.71)
(236.27)  %Found: C (55.78), H (6.98), N (23.75)

TLC: Benzene Methanol (4505); Rf value = 0.30

IR (KBr, cm^{-1}): 3360 (NH), 1680 (C=O)

UV (\lambda_{max}, nm): 247 (Methanol)

^1H NMR (CDCl_3/DMSO-d_6): 1.21-1.26 (t, 3H, NHCH_2CH_3); 1.32-1.40 (t, 3H, OCH_2CH_3);
2.23-2.37 (m, 2H, NHCH_2CH_3), 3.49-3.59 (b, 1H, NHCH_2H_3),
3.90-3.95 (t, 2H, -NCH_2CH_2); 4.06-4.11 (t, 2H, =NCH_2CH_2),
4.34-4.40 (q, 2H, OC_2H_5CH_3), 7.87 (s, 1H, NCHN)

Mass (m/z): 237 (M+1), 209, 207, 191, 150

Synthesis of 7-(benzylamino)-8-carbethoxy-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 03)

A solution of 6-(benzylamino)-5-carbethoxy-4-ethanolaminopyrimidine (EF 03) 3.2 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01 Recrystallization from dichloromethane-n-hexane yielded 1.6 g (54%) of crystalline product The product was characterized as 7-(benzylamino)-8-carbethoxy-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 03) M. P. 128-130°C

ANALYSIS:

Microanalysis: C_{16}H_{18}N_{4}O_{2}  %Required: C (64.41), H (6.08), N (18.78)
(298.34)  %Found: C (64.31), H (6.02), N (18.24)

TLC: Benzene Methanol (4505); Rf value = 0.31

IR (KBr, cm^{-1}): 3361 (NH), 1680 (C=O)

UV (\lambda_{max}, nm): 256 (Methanol)

^1H NMR (CDCl_3/DMSO-d_6): 1.36-1.40 (t, 3H, OCH_2CH_3), 3.90-3.95 (t, 2H, =NCH_2CH_2),
4.06-4.11 (t, 2H, =NCH_2CH_2), 4.34-4.40 (q, 2H, OCH_2CH_3);
4.73-4.75 (d, 2H, NHCH_2Ar), 7.24-7.35 (m, 5H, CH_2ArH); 7.73
(s, 1H, NCHN), 10.09 (b, 1H, NHCH_2Ar)

Mass (m/z): 299 (M+1), 271, 253, 212, 162, 145, 108

209
Experimental

Synthesis of 8-carbethoxy-7-(phenylamino)-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 04)
A solution of 5-carbethoxy-4-ethanolamino-6-(phenylamino)pyrimidine (EF 04) 3.0 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 1.8 g (62%) of crystalline product. The product was characterized as 8-carbethoxy-7-(phenylamino)-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 04) M P 182-184 °C

ANALYSIS:
Microanalysis. C_{16}H_{16}N_{4}O_{2} %Required C (63.37), H (5.67), N (19.71) (284.31) %Found C (63.78), H (5.15), N (19.55)

TLC. Benzene Methanol (4:5:0.5), Rf value = 0.32
IR (KBr, cm\(^{-1}\)) 3305 (NH), 1676 (C=O)
UV (\(\lambda_{\text{max}}\), nm) 259 (Methanol)

\(^1\)H NMR (\(\delta\)) 1.47-1.51 (t, 3H, OCH\(_2\)CH\(_3\)), 4.28-4.31 (t, 2H, =NCH\(_2\)CH\(_2\));
\((\text{CDCl}_3)\) 4.65-4.67 (t, 2H, =NCH\(_2\)CH\(_2\)), 4.68-4.72 (q, 2H, OCH\(_3\)CH\(_3\)), 7.20-7.36 (m, 5H, NHArH), 8.46 (s, 1H, NCHN), 11.38 (s, 1H, NHAr)

Mass (m/z) 285 (M+1), 257, 239, 198, 148

Synthesis of 8-carbethoxy-7-[(2-methylphenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 05)
A solution of 5-carbethoxy-4-ethanolamino-6-[(2-methylphenyl)amino]pyrimidine (EF 05) 3.2 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 1.7 g (58%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(2-methylphenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 05) M P 140-142 °C
Experimental

**ANALYSIS:**

Microanalysis: C₁₆H₁₈N₄O₂  
%Required: C (64.41), H (6.08), N (18.78)  
(298.34)  
%Found: C (64.38), H (5.89), N (18.62)  

TLC: Benzene. Methanol (4.5:0.5), Rᵢ value = 0.31  

IR (KBr, cm⁻¹): 3307 (NH), 1641 (C=O)  

UV (λ_max, nm): 262 (Methanol)  

¹H NMR (5) (CDCl₃/dMSO-d₆): 1.41-1.50 (t, 3H, OCH₂CH₃); 2.43 (s, 3H, ArCH₃), 4.28-4.31  

Mass (m/z): 299 (M+1), 271, 212, 108

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**Synthesis of 8-carbethoxy-7-[(3-methylphenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 06)**

A solution of 5-carbethoxy-4-ethanoIamino-6-[(3-methylphenyl)amino]pyrimidine (EF 06) 3.2 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 1.5 g (51%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(3-methylphenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 06) M P 138-140°C.

**ANALYSIS:**

Microanalysis: C₁₆H₁₈N₄O₂  
%Required: C (64.41), H (6.08), N (18.78)  
(298.34)  
%Found: C (63.99), H (5.22), N (18.35)  

TLC: Benzene Methanol (4.5:0.5), Rᵢ value = 0.32  

IR (KBr, cm⁻¹): 3394 (NH), 1668 (C=O)  

UV (λ_max, nm): 264 (Methanol)  

Mass (m/z): 299 (M+1), 271, 253, 212, 135, 102
Experimental

Synthesis of 8-carbethoxy-7-[(4-methylphenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 07)
A solution of 5-carbethoxy-4-ethanolamino-6-[(4-methylphenyl)amino]pyrimidine (EF 07) 3.2 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 1.8 g (61%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(4-methylphenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 07). M P. 149-150° C

ANALYSIS:
Microanalysis C₁₆H₁₈N₄O₂ %Required C (64.41), H (6.08), N (18.78) (298 34) %Found C (64.18), H (5.76), N (18.70)
TLC Benzene Methanol (4.5 0.5), Rf value = 0.34
IR (KBr, cm⁻¹) 3300 (NH), 1680 (C=O)
UV (λmax, nm) 262 (Methanol)
¹H NMR (5) 1.47-1.51 (t, 3H, OCH₂CH₃), 2.37 (s, 3H, ArCH₃), 4.28-4.31 (t, (CDCl₃/DMSO-d₆) 2H, =NCH₂CH₂), 4.65-4.67 (t, 2H, =NCH₂CH₂), 4.68-4.72 (q, 2H, OCH₂CH₂), 7.20-7.36 (m, 4H, NHArH), 8.46 (s, 1H, NCHN); 11.38 (s, 1H, NHAr)
Mass (m/z) . 299 (M+1), 271, 253, 212, 135, 102

Synthesis of 8-carbethoxy-7-[(2-methoxyphenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 08)
A solution of 5-carbethoxy-4-ethanolamino-6-[(2-methoxyphenyl)amino]pyrimidine (EF 08) 3.3 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 1.9 g (60%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(2-methoxyphenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 08). M P. 152-154° C
Experimental

ANALYSIS:

Microanalysis $C_{16}H_{18}N_4O_3$  
%Required C (61.13), H (5.77), N (17.82)  
(314.34)  
%Found C (61.55), H (5.18), N (17.81)

TLC Benzene Methanol (4 5 0 5), $R_f$ value = 0.28

IR (KBr, cm$^{-1}$) : 3300 (NH), 1680 (C=O)

UV ($\lambda_{\text{max}}$, nm) 264 (Methanol)

$^1$H NMR (δ) 1 35-1 4 (t, 3H, $\text{OCH}_2\text{CH}_3$), 2 13 (s, 3H, ArOCH$_3$), 3 92-3 98

(cDCl$_3$/DMSO-d$_6$) t, 2H, =NCH$_2$CH$_2$, 4 04-4 12 (t, 2H, =NCH$_2$CH$_2$), 4 41-4 47 (q, 2H, OCH$_2$CH$_3$), 7 12-7 29 (m, 4H, NHAH$^\text{H}$); 7 72(s, 1H, NCHN), 11 35-11 42 (s, 1H, NHAr).

Mass (m/z) 315 (M+1), 287, 269, 239, 147

Synthesis of 8-carbethoxy-7-[(4-methoxyphenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 09)

A solution of 5-carbethoxy-4-ethanolamino-6-[(4-methoxyphenyl)amino]pyrimidine (EF 09) 3 3 g (0 01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1 68 g (0 01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 2 1 g (68%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(4-methoxyphenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 09) M P. 178-180°C

ANALYSIS:

Microanalysis $C_{16}H_{18}N_4O_3$  
%Required C (61.13), H (5.77), N (17.82)  
(314.34)  
%Found C (60.82), H (5.81), N (17.59)

TLC Benzene Methanol (4 5 0 5); $R_f$ value = 0.31

IR (KBr, cm$^{-1}$) 3336 (NH), 1645 (C=O)

UV ($\lambda_{\text{max}}$, nm) 264 (Methanol)

$^1$H NMR (δ) 1 41-1 47 (t, 3H, $\text{OCH}_2\text{CH}_3$); 3.82 (s, 3H, ArOCH$_3$); 3 92-3 98

(cDCl$_3$/DMSO-d$_6$) t, 2H, =NCH$_2$CH$_2$, 4 08-4 12 (t, 2H, =NCH$_2$CH$_2$), 4 40-4 45 (q, 2H, OCH$_2$CH$_3$), 7 27-7 32 (m, 4H, NHAH$^\text{H}$); 7 73(s, 1H, NCHN), 11 35-11 42(s, 1H, NHAr)

Mass (m/z) 315 (M+1), 299, 287, 269, 253, 227
Experimental

Synthesis of 8-carbethoxy-7-[(2-fluorophenyl)amino]-2,3-dihydroimidazo[1,2-c] pyrimidine (IF 10)
A solution of 5-carbethoxy-4-ethanolamino-6-[(2-fluorophenyl)amino]-pyrimidine (EF 10) 3.2 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 2.0 g (68%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(2-fluorophenyl)amino]-2,3-dihydroimidazo[1,2-c] pyrimidine (IF 10). M.P. 135-137°C

ANALYSIS:
Microanalysis C_{15}H_{15}FN_4O_2 %Required C (59.60), H (5.00), N (18.53)
(302.30) %Found C (59.52), H (4.95), N (18.27)
TLC Benzene Methanol (4:5:0.5); Rf value = 0.33
IR (KBr, cm⁻¹) 3252 (NH), 1647 (C=O)
UV (λ_{max}, nm) 256 (Methanol)
Mass (m/z) . 303 (M+1), 275, 257, 216, 202

Synthesis of 8-carbethoxy-7-[(4-fluorophenyl)amino]-2,3-dihydroimidazo[1,2-c] pyrimidine (IF 11)
A solution of 5-carbethoxy-4-ethanolamino-6-[(4-fluorophenyl)amino]-pyrimidine (EF 11) 3.2 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 1.9 g (62%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(4-fluorophenyl)amino]-2,3-dihydroimidazo[1,2-c] pyrimidine (IF 11). M.P. 162-164°C
Experimental

ANALYSIS:

Microanalysis C_{15}H_{15}FN_{4}O_{2} %Required . C (59 60), H (5 00), N (18 53)
(302.30) %Found C (59 67), H (5.01), N (18.45)
TLC Benzene. Methanol (4 5 0 5), R_f value = 0 35
IR (KBr, cm^{-1}) : 3292 (NH), 1678 (C=O)
UV (λ_{max}, nm) 260 (Methanol)
^1H NMR (δ) 1 29-1 37 (t, 3H, OCH_{2}CH_{3}), 3 85-3 92 (t, 2H, =NCH_{2}CH_{2}),
(CDCl_{3}/DMSO-d_{6}) 3 99-4 10 (t, 2H, =NCH_{2}CH_{3}), 4 35-4 47(q, 2H, OCH_{2}CH_{3}),
7 59-7 76 (m, 4H, NHArH), 8 21 (s, 1H, NCHN), 11 21 (s, 1H, NHAr)
Mass (m/z) 303 (M+1), 288, 275, 257, 215, 148

Synthesis of 8-carbethoxy-7-[(3-trifluorophenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 12)
A solution of 5-carbethoxy-4-ethanolamino-6-[(3-trifluorophenyl)amino]pyrimidine (EF 12) 3 7 g (0.01 M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1 68 g (0.01 M) as described for IF 01 Recrystallization from dichloromethane-n-hexane yielded 1 2 g (35%) of crystalline product The product was characterized as 8-carbethoxy-7-[(3-trifluorophenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 12) M. P. 178-180°C

ANALYSIS:

Microanalysis C_{15}H_{15}F_{3}N_{4}O_{2} %Required . C (54 55), H (4 29), N (15 90)
(352 31) %Found C (54 11), H (3 99), N (15 52)
TLC Benzene. Methanol (4 5 0.5), R_f value = 0 35
IR (KBr, cm^{-1}) : 3361 (NH), 1689 (C=O)
UV (λ_{max}, nm) : 262 (Methanol)
Mass (m/z) 353 (M+1), 325, 307, 266, 160, 148
Experimental

Synthesis of 8-carbethoxy-7-[(2-chlorophenyl)amino]-2,3-dihydroimidazo[1,2-c] pyrimidine (IF 13)
A solution of 5-carbethoxy-6-[(2-chlorophenyl)amino]-4-ethanolaminopyrimidine (EF 13) 3.4 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01 Recrystallization from dichloromethane-n-hexane yielded 1.4 g (45%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(2-chlorophenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 13) M. P 132-135°C.

ANALYSIS:
Microanalysis C_{12}H_{15}ClN_{5}O_{2}\% Required C (56.52), H (4.74), N (17.58)
(318 76) % Found C (56.24), H (4.51), N (17.50)
TLC Benzene-Methanol (4:5:0.5), Rf value = 0.33
IR (KBr, cm\(^{-1}\)) 3394 (NH), 1668 (C=O)
UV (λ_{max}, nm) 262 (Methanol)
\(^1\)H NMR (δ) 1.21-1.34 (t, 3H, OCH\(_2\)CH\(_3\)); 3.67-3.85 (t, 2H, =NCH\(_2\)CH\(_2\)),
(CDCl\(_3\)/DMSO-d\(_6\)) 3.93-4.00 (t, 2H, =NCH\(_2\)CH\(_2\)); 4.26-4.32 (q, 2H, OCH\(_2\)CH\(_3\)),
7.39-7.51 (m, 4H, NHArH), 8.13 (s, 1H, NCH\(_3\)), 11.19 (s, 1H, NHAr)
Mass (m/z) 320 (M+2), 319 (M+1), 291, 273, 232, 148

Synthesis of 8-carbethoxy-7-[(3-chlorophenyl)amino]-2,3-dihydroimidazo[1,2-c] pyrimidine (IF 14)
A solution of 5-carbethoxy-6-[(3-chlorophenyl)amino]-4-ethanolaminopyrimidine (EF 14) 3.4 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01 Recrystallization from dichloromethane-n-hexane yielded 1.5 g (51%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(3-chlorophenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 14) M. P 135-137°C.
Synthesis of 8-carbethoxy-7-[(4-chlorophenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 15)

A solution of 5-carbethoxy-6-[(4-chlorophenyl)amino]-4-ethanolaminopyrimidine (EF 15) 3.4 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 2.0 g (63%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(4-chlorophenyl)amino]-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 15). M P 146-148°C.
Experimental

Synthesis of 7-[(4-bromophenyl)amino]-8-carbethoxy-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 16)

A solution of 6-[(4-bromophenyl)amino]-5-carbethoxy-4-ethanoIamino-pyrimidine (EF 01) 3.8 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IF 01. Recrystallization from dichloromethane-n-hexane yielded 2.6 g (70%) of crystalline product. The product was characterized as 7-[(4-bromophenyl)amino]-8-carbethoxy-2,3-dihydroimidazo[1,2-c]pyrimidine (IF 16) M. P. 168-171°C

ANALYSIS:

Microanalysis: C_{15}H_{15}BrN_{4}O_{2} % Required C (49.60), H (4.16), N (15.43) (363 21) % Found C (49.36), H (3.78), N (14.98)

TLC: Benzene Methanol (4:5, 0.5), Rf value = 0.34

IR (KBr, cm\(^{-1}\)) 3400 (NH), 1680 (C=O)

UV (\(\lambda_{\text{max}}, \text{nm}\)) 3400 (NH), 1680 (C=O)

\(^1\)H NMR (\(\delta\)): 1.21-1.34 (t, 3H, OCH\(_2\)CH\(_3\)); 3.77-3.84 (t, 2H, =NCH\(_2\)CH\(_2\)), 3.93-4.00 (t, 2H, =NCH\(_2\)CH\(_2\)), 4.16-4.27 (q, 2H, OCH\(_2\)CH\(_3\)), 7.39-7.51 (m, 4H, NHArH), 8.09 (s, 1H, NCH\(_2\)N), 11.17 (s, 1H, NHAr)

Mass (m/z) 364 (M+2), 363 (M+1), 335, 317, 290, 169, 148

Synthesis of 8-carbethoxy-7-(methylamino)-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 01)

To a solution of 5-carbethoxy-4-ethanolamino-5-(methylamino)-2-phenylpyrimidine (EB 01) 3.2 g (0.01M) in anhydrous toluene (20 mL), was added phosphoryl chloride 1.68 g (0.01M). The reaction mixture was refluxed for 1 h. Excess of toluene was removed under vacuum. The residue obtained was poured into 250 mL of ice-water mixture and neutralized with 10% ammonium hydroxide solution. The solid obtained was filtered, washed with water and dried. Recrystallization from dichloromethane-n-hexane yielded 1.2 g (40%) of crystalline product. The product was characterized as 8-carbethoxy-7-(methylamino)-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 01) M. P. 180-182°C
Experimental

ANALYSIS:

Microanalysis  \( \text{C}_{16}\text{H}_{18}\text{N}_{4}\text{O}_{2} \) %Required  C (64.1), H (6.08), N (18.78)

(298.34) %Found: C (64.22), H (6.02), N (18.51)

TLC Benzene Methanol (4:5.0), \( R_f \) value = 0.34

IR (KBr, cm\(^{-1}\)) 3228 (NH), 1672 (C=O)

UV (\( \lambda_{\text{max}}, \text{nm} \)) 262, 315 (Methanol)

\(^1\)H NMR (\( \delta \)) 1.23-1.28 (t, 3H, OCH\(_2\)CH\(_3\)), 1.49-1.54 (d, 3H, NHCH\(_3\)), 3.40-

\( \text{(CDCl}_3\text{)}\text{DMSO-d}_6 \) 3.48 (q, 1H, NHCH\(_3\)), 3.51-3.55 (q, 2H, OCH\(_2\)CH\(_3\)); 3.97-4.02

(t, 2H, =NCH\(_2\)CH\(_3\)), 4.22-4.29 (t, 2H, =NCH\(_2\)CH\(_3\)), 7.40-7.48

\( \text{(m, 5H, ArH)} \)

Mass (m/z) 299 (M+1), 271, 253, 153, 145, 102

Synthesis of 8-carbethoxy-7-(ethylamino)-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 02)

A solution of 5-carbethoxy-4-ethanolamino-6-(ethylamino)-2-phenylpyrimidine (EB 02) 3.3 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 1.3 g (42%) of crystalline product. The product was characterized as 8-carbethoxy-7-(ethylamino)-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 02). M P 187-190°C

ANALYSIS:

Microanalysis  \( \text{C}_{17}\text{H}_{20}\text{N}_{4}\text{O}_{2} \) %Required. C (65.37), H (6.45), N (17.94)

(312.37) %Found: C (65.04), H (6.25), N (17.83)

TLC Benzene. Methanol (4.5:0.5), \( R_f \) value = 0.32

IR (KBr, cm\(^{-1}\)) 3340 (NH), 1695 (C=O)

UV (\( \lambda_{\text{max}}, \text{nm} \)) 262, 318 (Methanol)

\(^1\)H NMR (\( \delta \)) 1.11-1.15 (t, 3H, NHCH\(_2\)CH\(_3\)); 1.29-1.31 (t, 3H, OCH\(_2\)CH\(_3\)),

\( \text{(CDCl}_3\text{)}\text{DMSO-d}_6 \) 3.21-3.26 (m, 2H, NHCH\(_2\)CH\(_3\)), 3.31-3.36 (t, 1H, NHCH\(_2\)CH\(_3\)),

3.97-4.02 (t, 2H, =NCH\(_2\)CH\(_3\)), 4.22-4.29 (t, 2H, =NCH\(_2\)CH\(_3\)),

4.51-4.55 (q, 2H, OCH\(_2\)CH\(_3\)), 7.49-7.59 (m, 5H, ArH)

Mass (m/z) 313 (M+1), 285, 267, 164, 159, 102
Synthesis of 7-(benzylamino)-8-carbethoxy-5-phenyl-2,3-dihydroimidazo[1,2-c]
pyrimidine (IB 03)
A solution of 6-(benzylamino)-5-carbethoxy-4-ethanolamino-2-phenylpyrimidine (EB
03) 3.9 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl
chloride 1.68 g (0.01M) as described for IB 01 Recrystallization from
dichloromethane-n-hexane yielded 1.9 g (52%) of crystalline product The product
was characterized as 7-(benzylamino)-8-carbethoxy-5-phenyl-2,3-
dihydroimidazo[1,2-c]pyrimidine (IB 03) M P 154-156°C

ANALYSIS:

Microanalysis C_{22}H_{22}N_{4}O_{2} %Required C (70.57), H (5.92), N (14.96)
(374.44) %Found C (70.27), H (5.63), N (15.23)
TLC Benzene Methanol (4.5:0.5), Rf value = 0.34
IR (KBr, cm^{-1}) 3240 (NH), 1680 (C=O)
UV (λ_{max}, nm) ■ 264, 316 (Methanol)
{^1}H NMR (δ) 1.19-1.22 (t, 3H, OCH_{2}CH_{3}), 3.22-3.29 (b, 1H, NHCH_{2}Ar),
(CDCl_{3}/DMSO-d_{6}) 4.17-4.22 (t, 2H, =NCH_{2}CH_{2}), 4.55-4.60 (t, 2H, =NCH_{2}CH_{2}),
4.63-4.68 (q, 2H, OCH_{2}CH_{3}), 4.72-4.77 (d, 2H, NHCH_{2}Ar),
7.23-7.41 (m, 5H, CH_{2}ArH), 7.56-7.79 (m, 5H, ArH)
Mass (m/z) 375 (M+1), 347, 329, 226, 221, 153, 102

Synthesis of 8-carbethoxy-5-phenyl-7-(phenylamino)-2,3-dihydroimidazo[1,2-c]
pyrimidine (IB 04)
A solution of 5-carbethoxy-4-ethanolamino-2-phenyl-6-(phenylamino)pyrimidine (EB
04) 3.8 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl
chloride 1.68 g (0.01M) as described for IB 01 Recrystallization from
dichloromethane-n-hexane yielded 1.8 g (50%) of crystalline product The product
was characterized as 8-carbethoxy-5-phenyl-7-(phenylamino)-2,3-
dihydroimidazo[1,2-c]pyrimidine (IB 04) M P 192-194°C
Experimental

ANALYSIS:

Microanalysis . C_{21}H_{20}N_{4}O_{2} %Required C (69.98), H (5.59), N (15.55) (360.41) %Found C (69.71), H (5.48), N (15.02)

TLC · Benzene Methanol (4.5:0.5), R_f value = 0.32

IR (KBr, cm^{-1}) 3215 (NH), 1677 (C=O)

UV (\lambda_{max}, nm) 262, 315 (Methanol)

^1H NMR (d) 1.49-1.52 (t, 3H, OCH_2CH_3), 4.17-4.22 (t, 2H, =NCH_2CH_2), 4.58-4.62 (t, 2H, =NCH_2CH_2), 4.63-4.68 (q, 2H, OCH_2CH_3), 7.23-7.41 (m, 5H, ArH); 7.55-7.79 (m, 5H, NHArH), 11.42 (s, 1H, NHAr)

Mass (m/z) 361 (M+1), 333, 315, 212, 207, 153, 102

Synthesis of 8-carbethoxy-7-[(2-methylphenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 05)

A solution of 5-carbethoxy-4-ethanolamino-6-[(2-methylphenyl)amino]-2-phenylpyrimidine (EB 05) 3.9 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 1.8 g (50%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(2-methylphenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 05) M P 182-184°C.

ANALYSIS:

Microanalysis . C_{22}H_{22}N_{4}O_{2} %Required C (70.57), H (5.92), N (14.96) (374.44) %Found C (70.35), H (5.57), N (14.73)

TLC · Benzene Methanol (4.5:0.5), R_f value = 0.30

IR (KBr, cm^{-1}) 3302 (NH), 1676 (C=O)

UV (\lambda_{max}, nm) 262, 315 (Methanol)

^1H NMR (d) 1.42-1.46 (t, 3H, OCH_2CH_3); 1.88 (s, 3H, ArCH_3), 3.95-3.99 (CDCl_3/DMSO-d_6) (t, 2H, =NCH_2CH_2); 4.05-4.08 (t, 2H, =NCH_2CH_2), 4.45-4.51 (q, 2H, OCH_2CH_3), 6.86-7.01 (m, 4H, NHArH), 7.49-7.67 (m, 5H, ArH), 11.81 (s, 1H, NHAr)

Mass (m/z) 375 (M+1), 347, 329, 226, 153, 102
Synthesis of 8-carbethoxy-7-[(4-methylphenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 06)

A solution of 5-carbethoxy-4-ethanolamino-6-[(4-methylphenyl)amino]-2-phenylpyrimidine (EB 06) 3.9 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 2.0 g (52%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(4-methylphenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 06) M. P. 184-186°C

ANALYSIS:

Microanalysis C_{22}H_{22}N_{4}O_{2} %Required C (70.57), H (5.92), N (14.96) (374 44) %Found C (70.55), H (5.97), N (14.75)

TLC • Benzene Methanol (4 5 0 5); Rf value = 0.30

IR (KBr, cm⁻¹) : 3334 (NH), 1645 (C=O)

UV (λ max, nm) 264, 320 (Methanol)

¹H NMR (δ) 1.50-1.54 (t, 3H, OCH₂CH₃); 2.35 (s, 3H, ArCH₃); 4.28-4.33 (CDCl₃) (t, 2H, =NCH₂CH₃); 4.53-4.58 (t, 2H, =NCH₂CH₂); 4.70-4.75 (q, 2H, OCH₂CH₃), 7.16-7.43 (m, 4H, NHArH), 7.55-7.75 (m, 5H, ArH); 11.50 (s, 1H, NHAr)

Mass (m/z) . 375 (M+1), 347, 329, 221, 153, 102

Synthesis of 8-carbethoxy-7-[(2-methoxyphenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 07)

A solution of 5-carbethoxy-4-ethanolamino-6-[(2-methoxyphenyl)amino]-2-phenylpyrimidine (EB 07) 4.1 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 1.8 g (42%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(2-methoxyphenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 07) M. P 162-164°C
ANALYSIS:

Microanalysis • $C_{22}H_{22}N_4O_3$ %Required C (67.68), H (5.68), N (14.35)

(390 44) %Found C (67.65), H (5.52), N (13.98)

TLC Benzene Methanol (4 5 0.5), Rf value = 0.31

IR (KBr, cm$^{-1}$) 3352 (NH), 1668 (C=O)

UV ($\lambda_{max}$, nm) 264, 321 (Methanol)

$^1$H NMR (δ) 1 48-1.52 (t, 3H, OCH$_2$CH$_3$), 3.80 (s, 3H, ArOCH$_3$), 4.27-4.32 (t, 2H, =NCH$_2$CH$_2$), 4.49-4.54 (t, 2H, =NCH$_2$CH$_2$), 4.65-4.71 (q, 2H, OCH$_2$CH$_3$), 7.41-7.44 (m, 4H, NHArH), 7.54-7.72 (m, 5H, ArH), 11.42 (s, 1H, NHAr)

Mass (m/z) 391 (M+1), 363, 345, 242, 153, 102

Synthesis of 8-carbethoxy-7-[(4-methoxyphenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 08)

A solution of 5-carbethoxy-4-ethanolamino-6-[(4-methoxyphenyl)amino]-2-phenylpyrimidine (EB 08) 4.1 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 1.6 g (45%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(4-methoxyphenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 08) M P 192-194°C.

ANALYSIS:

Microanalysis • $C_{22}H_{22}N_4O_3$ %Required C (67.68), H (5.68), N (14.35)

(390 44) %Found C (67.39), H (5.25), N (14.21)

TLC Benzene Methanol (4 5 0.5), Rf value = 0.31

IR (KBr, cm$^{-1}$) 3315 (NH), 1676 (C=O)

UV ($\lambda_{max}$, nm) 266, 320 (Methanol)

$^1$H NMR (δ) 1.45-1.52 (t, 3H, OCH$_2$CH$_3$), 3.08 (s, 3H, ArOCH$_3$), 3.97-4.02 (t, 2H, =NCH$_2$CH$_2$), 4.39-4.45 (t, 2H, =NCH$_2$CH$_2$), 4.61-4.67 (q, 2H, OCH$_2$CH$_3$), 7.35-7.49 (m, 4H, NHArH), 7.55-7.67 (m, 5H, ArH), 11.55 (s, 1H, NHAr)

Mass (m/z) 391 (M+1), 363, 345, 242, 160, 153, 102
Experimental

Synthesis of 8-carbethoxy-7-[(2-fluorophenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 09)
A solution of 5-carbethoxy-4-ethanolamino-6-[(2-fluorophenyl)amino]-2-phenylpyrimidine (EB 09) 4.0 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 2.1 g (55%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(2-fluorophenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 09). M. P 160-162°C

ANALYSIS:

Microanalysis C_{21}H_{19}FN_{40} %Required. C (66 66), H (5 06), N (14 81)
(378 40) %Found: C (66 62), H (4 86), N (14 54)

TLC Benzene-Methanol (4 5. 0 5); R_f value = 0.33
IR (KBr, cm^{-1}) 3226 (NH), 1647 (C=O)
UV (λ_{max}, nm) 264, 318 (Methanol)

^1H NMR (5) 1.42-1.46 (t, 3H, OCH=CH), 3.94-4.00 (t, 2H, =NCH=CH),
(CDCl_{3}/DMSO-d_6) 4.06-4.11 (t, 2H, =NCH=CH), 4.45-4.51 (q, 2H, OCH=CH),
7.01-7.10 (m, 5H, ArH), 7.47-7.66 (m, 3H, NHArH); 11.68 (s, 1H, NHAr)

Mass (m/z) 379 (M+1), 351, 333, 230, 153, 102

Synthesis of 8-carbethoxy-7-[(4-fluorophenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 10)
A solution of 5-carbethoxy-4-ethanolamino-6-[(4-fluorophenyl)amino]-2-phenylpyrimidine (EB 10) 4.0 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 1.8 g (49%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(4-fluorophenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 10). M. P 164-166°C
Experimental

ANALYSIS:

Microanalysis C_{21}H_{19}FN_{4}O_{2} %Required C (66.66), H (5.06), N (14.81)
(378 40) %Found C (66.75), H (5.14), N (14.88)
TLC Benzene Methanol (4.5:0.5); R_f value = 0.34
IR (KBr, cm^{-1}) 3348 (NH), 1658 (C=O)
UV (λ_{max}, nm) 262, 321 (Methanol)
{^1}H NMR (δ) 1.41-1.50 (t, 3H, OCH_{2}CH_{3}), 4.01-4.11 (t, 2H, =NCH_{2}CH_{2}),
(CDCl_{3}/DMSO-d_{6}) 4.15-4.22 (t, 2H, =NCH_{2}CH_{2}), 4.42-4.52 (q, 2H, OCH_{2}CH_{3}),
7.21-7.41 (m, 5H, ArH), 7.48-7.55 (m, 4H, NHArH); 11.72 (s, 1H, NHAr)
Mass (m/z) 379 (M+1), 351, 333, 256, 153, 123, 102

Synthesis of 8-carbethoxy-7-[(2-chlorophenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 11)

A solution of 5-carbethoxy-6-[(2-chlorophenyl)amino]-4-ethanolamino-2-phenylpyrimidine (EB 11) 4.1 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 1.8 g (45%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(2-chlorophenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 11) M P 130-132°C

ANALYSIS:

Microanalysis C_{21}H_{19}ClN_{4}O_{2} %Required C (63.88), H (4.85), N (14.19)
(394 85) %Found C (62.97), H (4.32), N (13.83)
TLC Benzene Methanol (4.5:0.5); R_f value = 0.29
IR (KBr, cm^{-1}) 3375 (NH), 1678 (C=O)
UV (λ_{max}, nm) 264, 318 (Methanol)
{^1}H NMR (δ) 1.32-1.37 (t, 3H, OCH_{2}CH_{3}), 4.17-4.22 (t, 2H, =NCH_{2}CH_{2});
(CDCl_{3}/DMSO-d_{6}) 4.58-4.62 (t, 2H, =NCH_{2}CH_{2}), 4.63-4.68 (q, 2H, OCH_{2}CH_{3}),
7.23-7.41 (m, 5H, ArH), 7.55-7.79 (m, 4H, NHArH); 11.37 (s, 1H, NHAr)
Mass (m/z) 397 (M+2), 396 (M+1), 367, 349, 246, 164, 153, 102

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**Experimental**

Synthesis of 8-carbethoxy-7-[(3-chlorophenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 12)

A solution of 5-carbethoxy-6-[(3-chlorophenyl)amino]-4-ethanolamino-2-phenylpyrimidine (EB 12) 4.1 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 1.5 g (37%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(3-chlorophenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 12). M. P 135-137°C.

**ANALYSIS:**

- Microanalysis: C_{21}H_{19}ClN_{4}O_{2} % Required. C (63.88), H (4.85), N (14.19) (394.85) % Found. C (63.58), H (4.56), N (14.01)
- TLC: Benzene Methanol (4:5:0.5), Rf value = 0.31
- IR (KBr, cm⁻¹): 3274 (NH), 1660 (C=O)
- UV (λ_max, nm): 264, 315 (Methanol)
- Mass (m/z): 397 (M+2), 396 (M+1), 367, 349, 246, 164, 153, 102

Synthesis of 8-carbethoxy-7-[(4-chlorophenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 13)

A solution of 5-carbethoxy-6-[(4-chlorophenyl)amino]-4-ethanolamino-2-phenylpyrimidine (EB 13) 4.1 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 1.9 g (48%) of crystalline product. The product was characterized as 8-carbethoxy-7-[(4-chlorophenyl)amino]-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 13). M. P 170-171°C.
ANALYSIS:

Microanalysis  
\[ \text{C}_{21}\text{H}_{19}\text{BrN}_{4}\text{O} \]  
%Required  C (57.41), H (4.36), N (12.75)  
(439 31)  
%Found  C (57.49), H (4.41), N (12.86)  

TLC  
Benzene. Methanol (4:5:0.5), \( R_f \) value = 0.34  

IR (KBr, cm\(^{-1}\))  
3380 (NH), 1666 (C=O)  

UV (\( \lambda_{\text{max}} \), nm)  
264, 320 (Methanol)  

\(^1\text{H} \) NMR (5)  
1.39-1.42 (t, 3H, OCH\(_2\)CH\(_3\)), 4.28-4.31 (t, 2H, \( =\text{NCH}_2\text{CH}_2 \)),  
(\( \text{CDCl}_3/\text{DMSO-d}_6 \))  
4.58-4.62 (t, 2H, \( =\text{NCH}_2\text{CH}_2 \)), 4.68-4.72 (q, 2H, OCH\(_2\)CH\(_3\)),  
7.35-7.48 (m, 5H, ArH), 7.55-7.79 (m, 4H, NHArH), 11.45 (s, 1H, NHAr)  

Mass (m/z)  
441 (M+2), 440 (M+1), 411.393, 290, 285, 153, 102

**Synthesis of 7-[(4-bromophenyl)amino]-8-carbethoxy-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 14)**

A solution of 6-[(4-bromophenyl)amino]-5-carbethoxy-4-ethanolamino-2-phenylpyrimidine (EB 14) 4.6 g (0.01M) in anhydrous toluene (20 mL), was reacted with phosphoryl chloride 1.68 g (0.01M) as described for IB 01. Recrystallization from dichloromethane-n-hexane yielded 2.3 g (51%) of crystalline product. The product was characterized as 7-[(4-bromophenyl)amino]-8-carbethoxy-5-phenyl-2,3-dihydroimidazo[1,2-c]pyrimidine (IB 14). M. P 178-180°C

ANALYSIS:

Microanalysis  
\[ \text{C}_{21}\text{H}_{19}\text{BrN}_{4}\text{O}_{2} \]  
%Required  C (57.41), H (4.36), N (12.75)  
(439 31)  
%Found  C (57.49), H (4.41), N (12.86)  

TLC  
Benzene. Methanol (4:5:0.5), \( R_f \) value = 0.34  

IR (KBr, cm\(^{-1}\))  
3380 (NH), 1666 (C=O)  

UV (\( \lambda_{\text{max}} \), nm)  
264, 320 (Methanol)  

\(^1\text{H} \) NMR (5)  
1.39-1.42 (t, 3H, OCH\(_2\)CH\(_3\)), 4.28-4.31 (t, 2H, \( =\text{NCH}_2\text{CH}_2 \)),  
(\( \text{CDCl}_3/\text{DMSO-d}_6 \))  
4.58-4.62 (t, 2H, \( =\text{NCH}_2\text{CH}_2 \)), 4.68-4.72 (q, 2H, OCH\(_2\)CH\(_3\)),  
7.35-7.48 (m, 5H, ArH), 7.55-7.79 (m, 4H, NHArH), 11.45 (s, 1H, NHAr)  

Mass (m/z)  
441 (M+2), 440 (M+1), 411. 393, 290, 285, 153, 102