Synthesis and pharmacological studies of 5-ethyl pyridin-2-ethanol analogs derivatives

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Abstract
A novel series of chalcones and pyrimidines is described. A series of 1-(substituted phenyl)-3-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-propan-1-ones 4a-o, 4-(substituted phenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-pyrimidinamines 5a-o and 4-(substituted phenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenyl carboxamido pyrimidines 6a-o are prepared. The structures of the synthesized compounds were assigned on the basis of elemental analysis, IR, \textsuperscript{1}H NMR and \textsuperscript{13}C NMR spectral data. All the products were screened against various strains of bacteria and fungi.

Keywords: Pyridine, chalcone, pyrimidine, pharmacological studies

Introduction

Pioglitazone is a well known pharmaceutically active compound used as an insulin sensitizing agent in the treatment of diabetes.\textsuperscript{1} 4-[2-(5-Ethylpyridin-2-yl)ethoxy]benzaldehyde is a main active metabolite, which is one of the key intermediates to pioglitazone. So we thought it useful to use 4-[2-(5-ethylpyridin-2-yl)ethoxy]benzaldehyde as a lead molecule.

The rising prevalence of multi-drug resistant Gram-positive and Gram-negative bacteria continues to provide impetus for the search for and discovery of novel antimicrobial agents active against
these pathogens. During the last two decades, a large number of substituted pyridines have been claimed to have several biological activities.\textsuperscript{2-7}

Chalcones, either natural or synthetic, are known to exhibit various biological activities. They have been reported to possess antimicrobial, antimalarial, anti-inflammatory, antimycobacterial and anticancer.\textsuperscript{8-19} The presence of a reactive $\alpha,\beta$-unsaturated keto function in chalcones is found to be responsible for their antimicrobial activity, which may be altered depending on the type and position of substituents on the aromatic rings.

Pyrimidines are associated with various biological activities,\textsuperscript{20-29} and this ring system is also present in vitamin B$_2$ and folic acid.

This broad spectrum of biological activity of these derivatives prompted us to synthesize and evaluate the antimicrobial activity of novel chalcones, pyrimidine and amide derivatives.

**Results and Discussion**

**Chemistry**
The synthesis of chalcones, pyrimidines and amide derivatives was performed as shown in Scheme 1. In the initial step, chalcones (4a-o) were synthesized by condensing 4-[2-(5-ethylpyridin-2-yl)ethoxy]benzaldehyde with aromatic acetophenones in dilute methanolic sodium hydroxide solution at room temperature. The compounds (5a-o) were synthesized by the reaction of the chalcones (4a-o) with guanidine nitrate using sodium ethoxide in ethanol. Compounds (6a-o) were prepared from the reaction of pyrimidines (5a-o) with benzoyl chloride. The purity of the compounds was determined by TLC and elemental analysis. Spectral data (IR, $^1$H NMR and $^{13}$C NMR) of all the newly synthesized compounds were in full agreement with the proposed structures.

The structure of compounds 4a-o was confirmed with IR and NMR spectra. In the IR the typical sharp absorptions at $\nu_{max}$ 2950 cm$^{-1}$ and 2835 cm$^{-1}$ characteristic of the $-\text{CH}_2$-, a sharp band of a C=O at 1662 cm$^{-1}$, -CH=CH- of chalcone at 1599 cm$^{-1}$, and the asymmetric and symmetric band of C-O-C ether linkage at 1223 cm$^{-1}$ and 1036 cm$^{-1}$ were observed. The $^1$H NMR spectra exhibited one doublet at $\delta$ 7.11 attributed to the $=\text{CH}-\text{CO}$- protons and two protons as a triplet at $\delta$ 4.32 confirmed that $-\text{CH}_2$-O- group is present. In the $^{13}$C NMR of the chalcones, the $-\text{CH}=\text{CH}$- carbon signals appeared at the $\delta$ 144.2 and 119.7 ppm respectively. The high-field resonance at $\delta$ 190.0 ppm was attributed to the carbonyl group present in chalcone. The structures of compounds 5a-o and 6a-o were also confirmed using IR and NMR spectroscopy. In the IR spectra of the pyrimidines there was no $-\text{C}=\text{O}$ band at 1662 cm$^{-1}$ but there were new asymmetric and symmetric broad bands at 3355 cm$^{-1}$ and 3220 cm$^{-1}$ for $-\text{NH}_2$. Signals at $\delta$ 5.15 and $\delta$ 7.85 for the $-\text{NH}_2$ and $-\text{CH}$ of the pyrimidine ring were observed in $^1$H NMR spectrum and the pyrimidine $-\text{CH}$ carbon resonance appeared at $\delta$ 103.2 in the $^{13}$C NMR spectra. The three bands observed at 1674, 1535 and 1249 cm$^{-1}$ in the IR spectrum corresponded to the amide -
C=O, -NH- and -C-N stretching frequencies, respectively. Furthermore, the disappearance of -NH$_2$ and the appearance of a signal at $\delta_H$ 9.25 ppm due to -NHCO together with the $\delta_C$ (C=O) 165.3 ppm in the $^{13}$C NMR provided further evidence for the conversion of compounds 5 into 6. On the basis of the above spectral data the structures of the compounds 4a-o, 5a-o and 6a-o compounds were confirmed.

Reagents and conditions: A. methanesulfonyl chloride, toluene, triethylamine; B. 4-hydroxybenzaldehyde, ethanol, NaOH; C. substituted acetophenone, methanol, 2% NaOH; D. guanidine nitrate, sodium ethoxide, ethanol; E. benzyol chloride, pyridine.

**Scheme 1.** Synthesis of the compounds 4a-o, 5a-o and 6a-o.
Biological activity
Minimum inhibitory concentration (MIC) of all the synthesized compounds was determined against four different strains, viz two Gram positive bacteria (S. aureus & S. pyogenes) and two Gram negative bacteria (E. coli & P. aeruginosa) compared with standard drugs gentamycin, ampicillin, chloramphenicol, ciprofloxacin, & norfloxacin by broth dilution method.\textsuperscript{30} Antifungal activities against C. albicans, A. niger and A. clavatus organisms were compared with standard drugs nystatin and greseofulvin by same method. We have synthesized 4-(phenyl/sub.phenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenylcarboxamidopyrimidines of 4-(phenyl/sub.phenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-pyrimidinamine via 15 chalcones which showed some of them to have excellent activity against Gram positive and Gram negative bacteria.

Table 1. Antimicrobial activity of compounds 4a-o, 5a-o and 6a-o

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<th>Compd.</th>
<th>R</th>
<th>Minimal bactericidal concentration µg/ml</th>
<th>Minimal fungicidal concentration µg/ml</th>
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<td>6o</td>
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Gentamycin | 0.05 | 1 | 0.25 | 0.5 | - | - | - |
Ampicillin | 100 | 100 | 250 | 100 | - | - | - |
Chloramphenicol | 50 | 50 | 50 | 50 | - | - | - |
Ciprofloxacin | 25 | 25 | 50 | 50 | - | - | - |
Norfloxacin | 10 | 10 | 10 | 10 | - | - | - |
Nystatin | - | - | - | - | 100 | 100 | 100 |
Greseofulvin | - | - | - | - | 500 | 100 | 100 |

**Antibacterial activity**

From screening results, substituted chalcones **4h** (-4-F) possesses very good activity against *E. coli*, *S. aureus* & *P. aeruginosa* compared with ampicillin. The remaining chalcones possesses moderate to poor activity against all four bacterial species and the corresponding pyrimidine derivatives, **5b** (-4-OCH3) possessed very good activity against *E. coli*, *S. aureus*, & *P. aeruginosa*. Compound **5i** (-2,4-diF) exhibited excellent activity against *E. coli* and *S. aureus*. The remaining pyrimidines displayed moderate to poor activities against all four bacterial species.
Against *S. aureus*, *P. aeruginosa* & *S. pyogenes*, amide derivative 6k (-3,4-diCl) showed excellent activity compared to ampicillin. Both 6d (-4-OH) and 6j (-4-Br) were very active against *E. coli*, *S. pyogenes*, and *P. aeruginosa* while the remaining amide derivatives possessed moderate to poor activity against all four bacterial species.

**Antifungal activity**

Antifungal screening data showed that chalcones 4g (-H) & 4h (-4-F) show highly promising activity against *C. albicans*. Pyrimidine 5o (-3,4-diF) possessed excellent activity against *C. albicans*. In the amide derivatives, compounds 6j (-4-Br) and 6k (-3,4-diCl) had good activity against *C. albicans*. The remaining compounds of the entire series exhibited only moderate to poor activity.

**Conclusions**

Some of the newly synthesized compounds exhibited promising antibacterial activities against *E. coli*, *S. aureus*, & *P. aeruginosa* and exhibited excellent antifungal activity against *C. albicans*. Compounds 6j (-4-Br) and 6k (-3,4-diCl) possessed excellent activity against both bacterial and fungal species. It seems that the amide linkage is very significant for activity against both bacterial and fungal species. These results make novel chalcone, pyrimidine and amide derivatives interesting lead molecules for further synthetic and biological evaluation.

**Experimental Section**

**General Procedures.** Laboratory Chemicals were supplied by Rankem India Ltd. and Ficher Scientific Ltd. 5-Ethylpyridin-2-ethanol was purchased from a chemical trader (imported from China; Hangzhou Longshan Chemical Co., Ltd.). Melting points were determined by the open tube capillary method and are uncorrected. The purity of the compounds was monitored by thin layer chromatography (TLC) plates (silica gel G) in the solvent system toluene: ethyl acetate (7.5:2.5). The spots were observed by exposure to iodine vapour or by UV light. The IR spectra were obtained on a Perkin-Elmer 1720 FT-IR spectrometer (KBr pellets). The $^1$H-NMR & $^{13}$C-NMR spectra were recorded on a Bruker Avance II 400 spectrometer using TMS as the internal standard in CDCl$_3$. Elemental analysis of the newly synthesized compounds were carried out on Carlo Erba 1108 analyzer.

**Procedure for the synthesis of 4-[2-(5-ethylpyridin-2-yl)ethoxy]benzaldehyde (3).** 4-[2-(5-Ethylpyridin-2-yl)ethoxy]benzaldehyde (3) was synthesized by the method described in the literature.\textsuperscript{31,32}
General preparation of the compounds (4a-o)

To a solution of 3 (0.01 mol) in methanol (50 mL), the aromatic acetophenone (0.01 mol) was added in the presence of 2% NaOH solution (5 mL). The reaction mixture was stirred for 10–12 h at room temperature. The solvent was distilled off and crude product poured into ice water. The compound thus obtained was washed with water and recrystallised from ethanol.

Figure 1. Chalcones 4a-o.

1-(2,4-Dichloro-5-fluorophenyl)-3-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-propane-1-one (4a). Yield, 80%, off white crystalline solid, mp 121-123 °C. R$_f$: 0.58. IR (KBr, cm$^{-1}$) $\nu$: 3062 (Ar-H), 2953, 2836 (-CH$_2$-), 1664 (-C=O), 1598 (-CH=CH-), 1223, 1033 (C-O-C), 975 (C-F), 742 (C-Cl). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ (ppm): 1.17 (t, 3H, -CH$_3$), 2.54 (q, 2H, -CH$_2$-), 3.16 (t, 2H, -CH$_2$-), 4.32 (t, 2H, -CH$_2$-O), 7.00-7.84 (m, 6H, Ar-H), 7.10 (d, 1H, =CH-CO), 7.18 (d, 1H, -CH), 7.36-8.28 (m, 3H, Pyridine-H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm): 190.5 (C$_{19}$), 144.5 (C$_{17}$), 122.4-160.5 (C$_2$-C$_6$), 119.2 (C$_{18}$), 117.3-161.5 (C$_{20}$-C$_{25}$), 115.5-156.0 (C$_{11}$-C$_{16}$), 67.5 (C$_{10}$), 38.0 (C$_9$), 25.1 (C$_7$), 15.5 (C$_8$). Anal. calcd for C$_{24}$H$_{20}$NO$_2$Cl$_2$F: C 64.88, H 4.54, N 3.15; found C 64.84, H 4.50, N 3.10.

1-(4-Methoxyphenyl)-3-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-propane-1-one (4b). Yield, 72%, white solid, mp 84-86 °C. R$_f$: 0.56. IR (KBr, cm$^{-1}$) $\nu$: 3064 (Ar-H), 2947, 2835 (-CH$_2$-), 1663 (-C=O), 1596 (-CH=CH-), 1220, 1028 (C-O-C).

$^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ (ppm): 1.19 (t, 3H, -CH$_3$), 2.57 (q, 2H, -CH$_2$-), 3.19 (t, 2H, -CH$_2$-), 3.84 (s, 3H, -OCH$_3$), 4.33 (t, 2H, -CH$_2$-O), 7.12 (d, 1H, =CH-CO), 7.20 (d, 1H, -CH), 7.38-8.27 (m, 8H, Ar-H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm): 189.5 (C$_{19}$), 143.5 (C$_{17}$), 122.4-160.5 (C$_2$-C$_6$), 119.2 (C$_{18}$), 117.3-161.5 (C$_{20}$-C$_{25}$), 115.5-156.0 (C$_{11}$-C$_{16}$), 67.5 (C$_{10}$), 38.0 (C$_9$), 25.1 (C$_7$), 15.5 (C$_8$). Anal. calcd for C$_{25}$H$_{25}$NO$_3$: C 77.49, H 6.50, N 3.61; found C 77.42, H 6.42, N 3.54.

1-(2,4-Dichlorophenyl)-3-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-propane-1-one (4c). Yield, 82%, off yellow solid, mp 95-97 °C. R$_f$: 0.54. IR (KBr, cm$^{-1}$) $\nu$: 3066 (Ar-H), 2953, 2835 (-CH$_2$-), 1663 (-C=O), 1596 (-CH=CH-), 1220, 1028 (C-O-C). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ (ppm): 1.18 (t, 3H, -CH$_3$), 2.56 (q, 2H, -CH$_2$-), 3.19 (t, 2H, -CH$_2$-), 3.84 (s, 3H, -OCH$_3$), 4.33 (t, 2H, -CH$_2$-O), 7.12 (d, 1H, =CH-CO), 7.20 (d, 1H, -CH), 7.38-8.27 (m, 8H, Ar-H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ (ppm): 189.5 (C$_{19}$), 143.5 (C$_{17}$), 122.4-160.5 (C$_2$-C$_6$), 118.5 (C$_{18}$), 115.0-116.4 (C$_{20}$-C$_{25}$), 115.2-155.5 (C$_{11}$-C$_{16}$), 66.4 (C$_{10}$), 55.5 (C$_9$), 25.0 (C$_7$), 15.3 (C$_8$). Anal. calcd for C$_{24}$H$_{21}$NO$_2$Cl$_2$: C 66.61, H 4.96, N 3.29; found C 66.70, H 4.90, N 3.23.
1-(4-Hydroxyphenyl)-3-[4-(2-(5-ethyl-2-pyridyl)ethoxy)phenyl]-2-propane-1-one (4d). Yield, 78%, greenish solid, mp 178-179 °C. Rf: 0.59. IR (KBr, cm⁻¹): v: 3057 (Ar-H), 2945, 2832 (-CH₂-), 1660 (-C=O), 1595 (-CH=CH-), 1216, 1033 (C-O-C), 3375 (-OH). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH₃), 2.58 (q, 2H, -CH₂-), 3.15 (t, 2H, -CH₂-), 4.36 (t, 2H, -CH₂-O), 5.15 (s, 1H, -OH), 7.01-8.05 (m, 8H, Ar-H), 7.12 (d, 1H, =CH-CO), 7.19 (d, 1H, -CH), 7.37-8.31 (m, 3H, Pyridine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 190.5 (C₁₉), 144.5 (C₁₇), 122.4-160.5 (C₂₋₆), 119.2 (C₁₈), 116.3-132.0 (C₂₀₋₂₅), 115.5-156.0 (C₁₁₋₁₆), 67.3 (C₁₀), 38.0 (C₉), 25.1 (C₇), 15.5 (C₈). Anal. calcd for C₄₄H₳₂NO₅: C 77.19, H 6.21, N 3.75; found C 77.13, H 6.16, N 3.70.

1-(2,6-Dichloro-5-fluorophenyl)-3-[4-(2-(5-ethyl-2-pyridyl)ethoxy)phenyl]-2-propane-1-one (4e). Yield, 85%, off white solid, mp 101-103 °C. Rf: 0.53. IR (KBr, cm⁻¹): v: 3065 (Ar-H), 2955, 2837 (-CH₂-), 1657 (-C=O), 1589 (-CH=CH-), 1225, 1036 (C-O-C), 976 (C-F), 747 (C-Cl).¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.16 (t, 3H, -CH₃), 2.55 (q, 2H, -CH₂-), 3.17 (t, 2H, -CH₂-), 4.33 (t, 2H, -CH₂-O), 7.03-7.32 (m, 6H, Ar-H), 7.11 (d, 1H, =CH-CO), 7.19 (d, 1H, -CH), 7.37-8.29 (m, 3H, Pyridine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 190.3 (C₁₉), 144.2 (C₁₇), 122.0-160.0 (C₂₋₆), 119.5 (C₁₈), 117.5-162.0 (C₂₀₋₂₅), 115.5-156.5 (C₁₁₋₁₆), 67.3 (C₁₀), 38.0 (C₉), 25.4 (C₇), 15.2 (C₈). Anal. calcd for C₂₄H₁₉NO₃Cl₂F: C 68.48, H 4.54, N 3.15; found C 68.46, H 4.50, N 3.07.

1-(4-Methylphenyl)-3-[4-(2-(5-ethyl-2-pyridyl)ethoxy)phenyl]-2-propane-1-one (4f). Yield, 80%, white solid, mp 115-120 °C. Rf: 0.55. IR (KBr, cm⁻¹): v: 3060 (Ar-H), 2950, 2835 (-CH₂-), 1662 (-C=O), 1599 (-CH=CH-), 1223, 1033 (C-O-C).¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.16 (t, 3H, -CH₃), 2.34 (s, 3H, -CH₃), 2.55 (q, 2H, -CH₂-), 3.18 (t, 2H, -CH₂-), 4.32 (t, 2H, -CH₂-O), 6.84-7.84 (m, 8H, Ar-H), 7.11 (d, 1H, =CH-CO), 7.19 (d, 1H, -CH), 7.39-8.30 (m, 3H, Pyridine-H).¹³C NMR (100 MHz, CDCl₃) δ (ppm): 190.0 (C₁₉), 144.2 (C₁₇), 127.5-142.4 (C₂₀₋₂₅), 123.4-160.9 (C₂₋₆), 119.7 (C₁₈), 115.0-155.3 (C₁₁₋₁₆), 67.4 (C₁₀), 37.4 (C₉), 25.8 (C₇), 21.7 (C₆), 15.4 (C₈). Anal. calcd for C₂₅H₂₃NO₂: C 80.83, H 6.78, N 3.77; found C 80.81, H 6.74, N 3.71.

1-(1-Phenyl)-3-[4-(2-(5-ethyl-2-pyridyl)ethoxy)phenyl]-2-propane-1-one (4g). Yield, 83%, off yellow solid, mp 90-92 °C. Rf: 0.53. IR (KBr, cm⁻¹): v: 3055 (Ar-H), 2947, 2832 (-CH₂-), 1657 (-C=O), 1596 (-CH=CH-), 1217, 1029 (C-O-C).¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.18 (t, 3H, -CH₃), 2.56 (q, 2H, -CH₂-), 3.17 (t, 2H, -CH₂-), 4.30 (t, 2H, -CH₂-O), 7.01-7.81 (m, 9H, Ar-H), 7.13 (d, 1H, =CH-CO), 7.18 (d, 1H, -CH), 7.38-8.32 (m, 3H, Pyridine-H).¹³C NMR (100 MHz, CDCl₃) δ (ppm): 190.2 (C₁₉), 144.5 (C₁₇), 127.8-138.0 (C₂₀₋₂₅), 122.4-160.5 (C₂₋₆), 119.5 (C₁₈), 115.5-156.2 (C₁₁₋₁₆), 67.3 (C₁₀), 38.2 (C₉), 25.5 (C₇), 15.5 (C₈). Anal. calcd for C₂₄H₂₃NO₂: C 80.64, H 6.49, N 3.93; found C 80.63, H 6.45, N 3.86.

1-(4-Fluorophenyl)-3-[4-(2-(5-ethyl-2-pyridyl)ethoxy)phenyl]-2-propane-1-one (4h). Yield, 79%, white crystalline solid, mp 100-103 °C. Rf: 0.54. IR (KBr, cm⁻¹): v: 3062 (Ar-H), 2953, 2838 (-CH₂-), 1661 (-C=O), 1594 (-CH=CH-), 1222, 1037 (C-O-C), 970 (C-F).¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.18 (t, 3H, -CH₃), 2.56 (q, 2H, -CH₂-), 3.16 (t, 2H, -CH₂-), 4.33 (t, 2H, -CH₂-O), 7.05-7.79 (m, 8H, Ar-H), 7.14 (d, 1H, =CH-CO), 7.19 (d, 1H, -CH), 7.39-8.29 (m,
3H, Pyridine-H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 190.3 (C$_{19}$), 144.2 (C$_{17}$), 122.5-160.3 (C$_2$-C$_6$), 119.5 (C$_{18}$), 116.5-168.0 (C$_{20}$-C$_{25}$), 115.5-156.5 (C$_{11}$-C$_{16}$), 67.0 (C$_{10}$), 38.0 (C$_9$), 25.3 (C$_7$), 15.4 (C$_8$). Anal. calc'd for C$_{24}$H$_{22}$NO$_2$: C 76.78, H 5.91, N 3.73; found C 76.74, H 5.86, N 3.66.

1-(2,4-Difluorophenyl)-3-[4-[(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-propane-1-one (4i). Yield, 81%, pale yellow solid, mp 75-78 °C. R$_f$: 0.57. IR (KBr, cm$^{-1}$): v: 3064 (Ar-H), 2949, 2834 (-CH$_2$-), 1658 (-C=O), 1598 (-CH=CH-), 1217, 1030 (C-O-C), 973 (C-F). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm): 1.16 (t, 3H, -CH$_3$), 2.54 (q, 2H, -CH$_2$-), 3.15 (t, 2H, -CH$_2$-), 4.30 (t, 2H, -CH$_2$-O), 6.87-7.77 (m, 7H, Ar-H), 7.12 (d, 1H, =CH-CO), 7.17 (d, 1H, -CH), 7.38-8.32 (m, 3H, Pyridine-H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 190.1 (C$_{19}$), 144.0 (C$_{17}$), 122.4-160.5 (C$_2$-C$_6$), 119.2 (C$_{18}$), 115.1-156.2 (C$_{11}$-C$_{16}$), 105.5-169.5 (C$_{20}$-C$_{25}$), 67.5 (C$_{10}$), 38.4 (C$_9$), 25.6 (C$_7$), 15.3 (C$_8$). Anal. calc'd for C$_{24}$H$_{22}$NO$_2$: C 73.72, H 5.38, N 3.56; found C 73.25, H 5.34, N 3.49.

1-(4-Bromophenyl)-3-[4-[(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-propane-1-one (4j). Yield, 85%, yellow solid, mp 102-104 °C. R$_f$: 0.56. IR (KBr, cm$^{-1}$): v: 3064 (Ar-H), 2953, 2830 (-CH$_2$-), 1660 (-C=O), 1595 (-CH=CH-), 1225, 1032 (C-O-C), 858 (C-Br). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH$_3$), 2.55 (q, 2H, -CH$_2$-), 3.18 (t, 2H, -CH$_2$-), 4.34 (t, 2H, -CH$_2$-O), 7.00-8.01 (m, 8H, Ar-H), 7.13 (d, 1H, =CH-CO), 7.16 (d, 1H, -CH), 7.37-8.30 (m, 3H, Pyridine-H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 189.5 (C$_{19}$), 144.2 (C$_{17}$), 132.1-136.9 (C$_{20}$-C$_{25}$) 121.4-159.5 (C$_2$-C$_6$), 24.5 (C$_7$), 118.5 (C$_{18}$), 115.5-156.0 (C$_{11}$-C$_{16}$), 67.1 (C$_{10}$), 38.2 (C$_9$), 15.0 (C$_8$). Anal. calc'd for C$_{24}$H$_{22}$NO$_2$Br: C 66.06, H 5.08, N 3.21; found C 66.03, H 5.02, N 3.15.

1-(3,4-Dichlorophenyl)-3-[4-[(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-propane-1-one (4k). Yield, 84%, yellow solid, mp 105-110 °C. R$_f$: 0.55. IR (KBr, cm$^{-1}$): v: 3067 (Ar-H), 2947, 2829 (-CH$_2$-), 1664 (-C=O), 1593 (-CH=CH-), 1220, 1031 (C-O-C), 744 (C-Cl). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm): 1.16 (t, 3H, -CH$_3$), 2.55 (q, 2H, -CH$_2$-), 3.19 (t, 2H, -CH$_2$-), 4.32 (t, 2H, -CH$_2$-O), 7.01-7.76 (m, 7H, Ar-H), 7.11 (d, 1H, =CH-CO), 7.18 (d, 1H, -CH), 7.38-8.32 (m, 3H, Pyridine-H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 188.9 (C$_{19}$), 143.5 (C$_{17}$), 130.4-139.5 (C$_{20}$-C$_{25}$), 122.4-160.5 (C$_2$-C$_6$), 119.8 (C$_{18}$), 114.5-155.2 (C$_{11}$-C$_{16}$), 66.5 (C$_{10}$), 37.2 (C$_9$), 25.1 (C$_7$), 15.5 (C$_8$). Anal. calc'd for C$_{24}$H$_{21}$NO$_2$Cl: C 67.61, H 4.96, N 3.29; found C 67.58, H 4.90, N 3.23.

1-(4-Chlorophenyl)-3-[4-[(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-propane-1-one (4l). Yield, 88%, yellow crystalline solid, mp 138-140 °C. R$_f$: 0.53. IR (KBr, cm$^{-1}$): v: 3028 (Ar-H), 2944, 2827 (-CH$_2$-), 1659 (-C=O), 1596 (-CH=CH-), 1224, 1037 (C-O-C), 746 (C-Cl). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH$_3$), 2.57 (q, 2H, -CH$_2$-), 3.18 (t, 2H, -CH$_2$-), 4.30 (t, 2H, -CH$_2$-O), 7.03-7.86 (m, 8H, Ar-H), 7.10 (d, 1H, =CH-CO), 7.19 (d, 1H, -CH), 7.37-8.32 (m, 3H, Pyridine-H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 190.5 (C$_{19}$), 144.5 (C$_{17}$), 129.5-140.5 (C$_{20}$-C$_{25}$), 121.5-160.8 (C$_2$-C$_6$), 118.2 (C$_{18}$), 114.5-156.0 (C$_{11}$-C$_{16}$), 67.3 (C$_{10}$), 38.3 (C$_9$), 24.8 (C$_7$), 15.4 (C$_8$). Anal. calc'd for C$_{24}$H$_{22}$NO$_2$Cl: C 73.56, H 5.66, N 3.57; found C 73.52, H 5.61, N 3.55.

1-(3-Methoxyphenyl)-3-[4-[(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-propane-1-one (4m). Yield, 70%, pale yellow solid, mp 75-80 °C. R$_f$: 0.52. IR (KBr, cm$^{-1}$): v: 3066 (Ar-H), 2952, 2833 (-CH$_2$-), 1664 (-C=O), 1594 (-CH=CH-), 1220, 1032 (C-O-C). $^1$H NMR (CDCl$_3$, 400 MHz) δ
(ppm): 1.14 (t, 3H, -CH₃), 2.58 (q, 2H, -CH₂-), 3.16 (t, 2H, -CH₂-), 3.85 (s, 3H, -OCH₃) 4.34 (t, 2H, -CH₂-O), 6.96-8.11 (m, 8H, Ar-H), 7.11 (d, 1H, =CH-CO), 7.16 (d, 1H, -CH), 7.39-8.30 (m, 3H, Pyridine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 190.1 (C₁₉), 144.1 (C₁₇), 122.6-161.5 (C₂-C₆), 117.3-161.5 (C₂₀-C₂₅), 119.2 (C₁₈), 115.3-156.5 (C₁₁-C₁₆), 68.5 (C₁₀), 55.5 (C₂₆), 38.5 (C₉), 25.5 (C₇), 15.5 (C₈). Anal. calcd for C₂₅H₂₅NO₃: C 77.49, H 6.50, N 3.61; found C 77.45, H 6.48, N 3.52.

1-(3-Fluorophenyl)-3-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-propane-1-one (4n). Yield, 80%, yellow solid, mp 87-90 °C. Rₓ: 0.54. IR (KBr, cm⁻¹) ν: 3062 (Ar-H), 2956, 2835 (-CH₂-), 1660 (-C=O), 1597 (-CH=CH-), 1219, 1032 (C-O-C), 976 (C-F). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.11 (t, 3H, -CH₃), 2.53 (q, 2H, -CH₂-), 3.14 (t, 2H, -CH₂-), 4.31 (t, 2H, -CH₂-O), 7.00-7.58 (m, 8H, Ar-H), 7.13 (d, 1H, =CH-CO), 7.18 (d, 1H, -CH), 7.39-8.30 (m, 3H, Pyridine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 189.5 (C₁₉), 144.8 (C₁₇), 122.5-160.5 (C₂-C₆), 119.2 (C₁₈), 115.5-156.1 (C₁₁-C₁₆), 114.5-164.0 (C₂₀-C₂₅), 67.5 (C₁₀), 55.8 (C₂₆), 38.0 (C₉), 25.3 (C₇), 15.8 (C₈). Anal. calcd for C₂₄H₂₂NO₂F: C 76.78, H 5.91, N 3.73; found C 76.72, H 5.86, N 3.70.

1-(3,4-Difluorophenyl)-3-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-propane-1-one (4o). Yield, 82%, yellow solid, mp limpid. Rₓ: 0.55. IR (KBr, cm⁻¹) ν: 3060 (Ar-H), 2950, 2835 (-CH₂-), 1660 (-C=O), 1599 (-CH=CH-), 1223, 1033 (C-O-C), 978 (C-F). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.12 (t, 3H, -CH₃), 2.54 (q, 2H, -CH₂-), 3.16 (t, 2H, -CH₂-), 4.32 (t, 2H, -CH₂-O), 7.02-7.56 (m, 7H, Ar-H), 7.14 (d, 1H, =CH-CO), 7.19 (d, 1H, -CH), 7.37-8.28 (m, 3H, Pyridine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 190.5 (C₁₉), 144.5 (C₁₇), 122.4-160.2 (C₂-C₆), 119.6 (C₁₈), 116.3-155.5 (C₂₀-C₂₅), 115.5-156.0 (C₁₁-C₁₆), 67.1 (C₁₀), 38.2 (C₉), 25.1 (C₇), 15.5 (C₈). Anal. calcd for C₂₄H₂₁NO₂F₂: C 73.27, H 5.38, N 3.56; found C 73.21, H 5.33, N 3.48.

**General preparation of the compounds 5a-o**

A mixture of freshly prepared solution of sodium ethoxide (0.02 mol Na in 50 mL ethanol), 4a-o (0.01 mol) and guanidine nitrate (0.01 mol) was heated at reflux for 8-12 h, reaction progress was monitored by T.L.C (toluene:ethyl acetate, 7.5:2.5). After completion of the reaction the mixture was concentrated under vaccum and remaining material was poured onto crushed ice. The solid produced was separated and stirred for 1 h to maintain pH neutral with dilute acetic acid. The resulting solid was filtered off and washed with cold ethanol, dried and recrystallized from ethanol.
Figure 2. Pyrimidines 5a-o.

4-(2,4-Dichloro-5-fluorophenyl)-6-[4-{2-(5-ethyl-2-pyridyl)ethoxy}phenyl]-2-pyrimidinamine (5a). Yield, 74%, yellow solid, mp 95-98 °C. Rf: 0.42. IR (KBr, cm⁻¹) v: 3355, 3222 (-NH₂), 3062 (Ar-H), 2954, 2837 (-CH₂-), 1602 (-C=N), 1225, 1036 (C-O-C), 973 (C-F), 745 (C-Cl). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH₃), 2.54 (q, 2H, -CH₂-), 3.17 (t, 2H, -CH₂-), 4.33 (t, 2H, -CH₂-O), 5.18 (s, 2H, -NH₂), 6.90-7.82 (m, 8H, Ar-H), 7.39-8.32 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 165.0 (C₁₀), 163.2 (C₁₇), 160.7 (C₂₁), 123.5-160.5 (C₂-C₆), 118.7-161.4 (C₂₄-C₂₉), 114.0-154.4 (C₁₁-C₁₆), 103.5 (C₂₂), 67.0 (C₁₀), 38.0 (C₉), 25.2 (C₇), 15.3 (C₈). Anal. calcd for C₂₅H₂₁N₄OCl₂F: C 62.12, H 4.38, N 11.59; found C 62.06, H 4.32, N 11.52.

4-(4-Methoxyphenyl)-6-[4-{2-(5-ethyl-2-pyridyl)ethoxy}phenyl]-2-pyrimidinamine (5b).

Yield, 52%, dark brown solid, mp 100-102 °C. Rf: 0.40. IR (KBr, cm⁻¹) v: 3352, 3224 (-NH₂), 3065 (Ar-H), 2957, 2834 (-CH₂-), 1609 (-C=N), 1223, 1033 (C-O-C). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.14 (t, 3H, -CH₃), 2.53 (q, 2H, -CH₂-), 3.18 (t, 2H, -CH₂-), 3.83 (s, 3H, -OCH₃) 4.34 (t, 2H, -CH₂-O), 5.12 (s, 2H, -NH₂), 6.89-7.84 (m, 8H, Ar-H), 7.40-8.32 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 165.1 (C₁₉), 164.5 (C₁₇), 160.5 (C₂₁), 123.8-161.0 (C₂-C₆), 115.3-155.5 (C₁₁-C₁₆), 114.5-160.5 (C₂₄-C₂₉), 103.4 (C₂₂), 67.3 (C₁₀), 55.8 (C₃₀), 37.5 (C₉), 25.0 (C₇), 15.4 (C₈). Anal. calcd for C₂₅H₂₆N₄O₂: C 73.22, H 6.14, N 13.14; found C 73.14, H 6.08, N 13.07.

4-(2,4-Dichlorophenyl)-6-[4-{2-(5-ethyl-2-pyridyl)ethoxy}phenyl]-2-pyrimidinamine (5c).

Yield, 78%, yellow solid, mp 115-118 °C. I R: 0.43.R (KBr, cm⁻¹) v: 3358, 3227 (-NH₂), 3057 (Ar-H), 2953, 2836 (-CH₂-), 1607 (-C=N), 1227, 1037 (C-O-C), 746 (C-Cl). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH₃), 2.52 (q, 2H, -CH₂-), 3.16 (t, 2H, -CH₂-), 4.32 (t, 2H, -CH₂-O), 5.22 (s, 2H, -NH₂), 6.88-7.81 (m, 8H, Ar-H), 7.39-8.32 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 165.1 (C₁₉), 163.6 (C₁₇), 160.5 (C₂₁), 127.4-135.5 (C₂₄-C₂₉), 123.6-161.9 (C₂-C₆), 115.1-155.2 (C₁₁-C₁₆), 104.2 (C₂₂), 67.5 (C₁₀), 37.3 (C₉), 26.1 (C₇), 15.2 (C₈). Anal. calcd for C₂₅H₂₅N₄OCl₂: C 64.52, H 4.76, N 12.04; found C 64.46, H 4.69, N 12.00.

4-(4-Hydroxyphenyl)-6-[4-{2-(5-ethyl-2-pyridyl)ethoxy}phenyl]-2-pyrimidinamine (5d).

Yield, 50%, pale yellow solid, mp >300 °C. Rf: 0.44. IR (KBr, cm⁻¹) v: 3355, 3224 (-NH₂), 3064
(Ar-H), 2955, 2832 (-CH2-), 1600 (-C=N), 1220, 1032 (C-O-C), 3357 (-OH). 1H NMR (CDCl3, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH3), 2.54 (q, 2H, -CH2-), 3.15 (t, 2H, -CH2-), 4.33 (t, 2H, -CH2-O), 5.12 (s, 2H, -NH2), 9.85 (s, 1H, -OH), 6.84-7.78 (m, 8H, Ar-H), 7.39-8.30 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H). 13C NMR (100 MHz, CDCl3) δ (ppm): 165.2 (C19), 163.8 (C17), 160.3 (C21), 122.9-159.9 (C2-C6), 116.3-158.5 (C24-C29) 115.7-155.7 (C11-C16), 103.5 (C22), 67.3 (C10), 37.6 (C9), 25.5 (C7), 15.7 (C8). Anal. calcd for C25H24N4O2: C 72.80, H 5.86, N 13.58; found C 72.74, H 5.78, N 13.52.

4-(2,6-Dichloro-5-fluorophenylimino)-6-[4-[2-(5-ethyl-2-pyridyldethoxy]phenyl]-2-pyrimidinamine (5e). Yield, 76%, yellow solid, mp 105-108 °C. Rf 0.40. IR (KBr, cm-1) ν: 3348, 3219 (-NH2), 3062 (Ar-H), 2953, 2830 (-CH2-), 1606 (-C=N), 1220, 1034 (C-O-C), 975 (C-F), 747 (C-Cl). 1H NMR (CDCl3, 400 MHz) δ (ppm): 1.12 (t, 3H, -CH3), 2.55 (q, 2H, -CH2-), 3.16 (t, 2H, -CH2-), 4.31 (t, 2H, -CH2-O), 5.24 (s, 2H, -NH2), 6.91-7.83 (m, 8H, Ar-H), 7.38-8.30 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H). 13C NMR (400MHz, CDCl3) δ (ppm): 165.4 (C19), 163.0 (C17), 160.5 (C21), 123.0-160.4 (C2-C6), 118.3-161.4 (C24-C29), 113.9-154.1 (C11-C16), 103.2 (C22), 67.2 (C10), 38.2 (C9), 25.1 (C7), 15.2 (C8). Anal. calcd for C25H21N4OCl2F: C 62.12, H 4.38, N 11.59; found C 62.04, H 4.31, N 11.55.

4-(4-Methylphenyl)-6-[4-[2-(5-ethyl-2-pyridyldethoxy]phenyl]-2-pyrimidinamine (5f). Yield, 78%, brown solid, mp 133-136 °C. Rf 0.42. IR (KBr, cm-1) ν: 3355, 3220 (-NH2), 3057 (Ar-H), 2952, 2834 (-CH2-), 1610 (-C=N), 1220, 1034 (C-O-C). 1H NMR (CDCl3, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH3), 2.33 (s, 3H, -CH3), 2.53 (q, 2H, -CH2-), 3.17 (t, 2H, -CH2-), 4.32 (t, 2H, -CH2-O), 5.15 (s, 2H, -NH2), 6.89-7.80 (m, 8H, Ar-H), 7.39-8.30 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H). 13C NMR (100 MHz, CDCl3) δ (ppm): 165.5 (C19), 163.5 (C17), 160.9 (C21), 129.2-144.4 (C24-C29), 123.4-160.9 (C2-C6), 115.0-155.4 (C11-C16), 103.2 (C22), 67.5 (C10), 37.5 (C9), 25.5 (C7), 21.7 (C30) 15.4 (C8). Anal. calcd for C26H26N4OCl: C 76.07, H 6.38, N 13.65; found C 76.00, H 6.32, N 13.57.

4-(1-Phenyl)-6-[4-[2-(5-ethyl-2-pyridyldethoxy]phenyl]-2-pyrimidinamine (5g). Yield, 65%, brown solid, mp 110-115 °C. Rf 0.44. IR (KBr, cm-1) ν: 3356, 3225 (-NH2), 3058 (Ar-H), 2952, 2832 (-CH2-), 1605 (-C=N), 1227, 1038 (C-O-C). 1H NMR (CDCl3, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH3), 2.52 (q, 2H, -CH2-), 3.18 (t, 2H, -CH2-), 4.30 (t, 2H, -CH2-O), 5.20 (s, 2H, -NH2), 6.89-7.82 (m, 8H, Ar-H), 7.38-8.31 (m, 3H, Pyridine-H), 7.87 (s, 1H, Pyrimidine-H). 13C NMR (100 MHz, CDCl3) δ (ppm): 164.9 (C19), 163.2 (C17), 160.5 (C21), 123.6-160.4 (C2-C6), 118.7-161.4 (C24-C29), 114.9-154.1 (C11-C16), 103.7 (C22), 67.2 (C10), 38.2 (C9), 25.1 (C7), 15.3 (C8). Anal. calcd for C28H24N4O: C 75.73, H 6.10, N 14.13; found C 75.68, H 6.04, N 14.10.

4-(4-Fluorophenyl)-6-[4-[2-(5-ethyl-2-pyridyldethoxy]phenyl]-2-pyrimidinamine (5h). Yield, 70%, brown solid, mp 244-246 °C. Rf 0.45. IR (KBr, cm-1) ν: 3356, 3222 (-NH2), 3064 (Ar-H), 2950, 2835 (-CH2-), 1602 (-C=N), 1226, 1036 (C-O-C), 975 (C-F). 1H NMR (CDCl3, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH3), 2.53 (q, 2H, -CH2-), 3.17 (t, 2H, -CH2-), 4.31 (t, 2H, -CH2-O), 5.16 (s, 2H, -NH2), 6.88-7.80 (m, 8H, Ar-H), 7.39-8.32 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H). 13C NMR (100 MHz, CDCl3) δ (ppm): 164.5 (C19), 163.0 (C17), 160.7 (C21), 123.9-160.9 (C2-C6), 116.0-163.0 (C24-C29), 114.1-154.3 (C11-C16), 103.9 (C22), 67.4 (C10),
38.3 (C_9), 25.4 (C_7), 14.9 (C_8). Anal. calcd for C_{25}H_{23}N_4OF: C 72.45, H 5.59, N 13.52; found C 72.35, H 5.54, N 13.48.

4-(2,4-Difluorophenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-pyrimidinamine (5i). Yield, 72%, yellow solid, mp 135-139 °C. Rf: 0.41. IR (KBr, cm\(^{-1}\)) v: 3347, 3225 (-NH\(_2\)), 3066 (Ar-H), 2945, 2832 (-CH\(_2\)), 1604 (-C=N), 1220, 1034 (C-O-C), 978 (C-F). \(^1\)H NMR (CDCl\(_3\), 400 MHz) δ (ppm): 1.14 (t, 3H, -CH\(_3\)), 2.54 (q, 2H, -CH\(_2\)_2), 3.16 (t, 2H, -CH\(_2\)_2), 4.32 (t, 2H, -CH\(_2\)_O), 5.18 (s, 2H, -NH\(_2\)), 6.90-7.83 (m, 8H, Ar-H), 7.37-8.30 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) δ (ppm): 164.4 (C_19), 163.2 (C_17), 160.5 (C_21), 123.5-160.8 (C_2-C_6), 116.6-164.5 (C_24-C_29), 114.2-153.9 (C_11-C_16), 103.5 (C_22), 67.8 (C_10), 38.1 (C_9), 25.4 (C_7), 15.1 (C_8). Anal. calcd for C_{25}H_{22}N_4OF_2: C 69.43, H 5.13, N 12.96; found C 69.37, H 5.08, N 12.92.

4-(4-Bromophenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-pyrimidinamine (5j). Yield, 77%, brown solid, mp 115-117 °C. Rf: 0.40. IR (KBr, cm\(^{-1}\)) v: 3354, 3225 (-NH\(_2\)), 3057 (Ar-H), 2952, 2837 (-CH\(_2\)), 1608 (-C=N), 1224, 1032 (C-O-C), 860 (C-Br). \(^1\)H NMR (CDCl\(_3\), 400 MHz) δ (ppm): 1.15 (t, 3H, -CH\(_3\)), 2.53 (q, 2H, -CH\(_2\)_2), 3.18 (t, 2H, -CH\(_2\)_2), 4.33 (t, 2H, -CH\(_2\)_O), 5.14 (s, 2H, -NH\(_2\)), 6.86-7.81 (m, 8H, Ar-H), 7.38-8.33 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) δ (ppm): 164.5 (C_19), 163.1 (C_17), 160.7 (C_21), 123.8-160.6 (C_2-C_6), 123.1-132.1 (C_24-C_29), 114.1-154.2 (C_11-C_16), 103.9 (C_22), 67.7 (C_10), 38.8 (C_9), 25.1 (C_7), 15.2 (C_8). Anal. calcd for C_{25}H_{22}N_4OBr: C 63.16, H 4.88, N 11.79; found C 63.11, H 4.82, N 11.73.

4-(3,4-Dichlorophenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-pyrimidinamine (5k). Yield, 73%, brown solid, mp 125-130 °C. Rf: 0.43. IR (KBr, cm\(^{-1}\)) v: 3356, 3227 (-NH\(_2\)), 3066 (Ar-H), 2955, 2838 (-CH\(_2\)), 1605 (-C=N), 1225, 1037 (C-O-C), 748 (C-Cl). \(^1\)H NMR (CDCl\(_3\), 400 MHz) δ (ppm): 1.13 (t, 3H, -CH\(_3\)), 2.55 (q, 2H, -CH\(_2\)_2), 3.15 (t, 2H, -CH\(_2\)_2), 4.35 (t, 2H, -CH\(_2\)_O), 5.17 (s, 2H, -NH\(_2\)), 6.92-7.83 (m, 8H, Ar-H), 7.41-8.30 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) δ (ppm): 164.5 (C_19), 163.1 (C_17), 160.5 (C_21), 127.0-133.5 (C_24-C_29), 123.6-160.8 (C_2-C_6), 114.1-154.3 (C_11-C_16), 103.8 (C_22), 67.5 (C_10), 38.3 (C_9), 25.4 (C_7), 15.8 (C_8). Anal. calcd for C_{25}H_{25}N_4OCl: C 64.52, H 4.76, N 12.04; found C 64.48, H 4.71, N 12.00.

4-(4-Chlorophenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-pyrimidinamine (5l). Yield, 74%, dark brown solid, mp 92-95 °C. Rf: 0.42. IR (KBr, cm\(^{-1}\)) v: 3356, 3227 (-NH\(_2\)), 3066 (Ar-H), 2955, 2838 (-CH\(_2\)), 1611 (-C=N), 1225, 1037 (C-O-C), 748 (C-Cl). \(^1\)H NMR (CDCl\(_3\), 400 MHz) δ (ppm): 1.13 (t, 3H, -CH\(_3\)), 2.55 (q, 2H, -CH\(_2\)_2), 3.15 (t, 2H, -CH\(_2\)_2), 4.35 (t, 2H, -CH\(_2\)_O), 5.10 (s, 2H, -NH\(_2\)), 6.92-7.83 (m, 8H, Ar-H), 7.41-8.30 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) δ (ppm): 164.5 (C_19), 163.1 (C_17), 160.5 (C_21), 127.0-133.5 (C_24-C_29), 123.6-160.8 (C_2-C_6), 114.1-154.3 (C_11-C_16), 103.8 (C_22), 67.5 (C_10), 38.3 (C_9), 25.4 (C_7), 15.8 (C_8). Anal. calcd for C_{25}H_{23}N_4OCl: C 69.68, H 5.38, N 13.00; found C 69.63, H 5.34, N 13.48.
4-(3-Methoxyphenyl)-6-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-pyrimidinamine (5m). Yield, 54%, yellow solid, mp 98-111 °C. Rf: 0.44. IR (KBr, cm⁻¹) v: 3356, 3225 (-NH₂), 3066 (Ar-H), 2956, 2838 (-CH₂-), 1609 (-C=N), 1220, 1033 (C-O-C). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH₃), 2.53 (q, 2H, -CH₂-), 3.17 (t, 2H, -CH₂-O), 3.82 (s, 3H, -OCH₃), 4.34 (t, 2H, -CH₂-O), 5.22 (s, 2H, -NH₂), 6.90-7.85 (m, 8H, Ar-H), 7.40-8.33 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 164.3 (C₁₉), 163.2 (C₁₇), 160.1 (C₂₁), 123.1-160.5 (C₂-C₆), 114.9-160.0 (C₂₄-C₂₉), 113.9-154.5 (C₁₁-C₁₆), 103.2 (C₂₂), 67.8 (C₁₀), 55.7 (C₃₀), 38.5 (C₉), 25.6 (C₇), 15.2 (C₈). Anal. calcd for C₂₆H₂₆N₄O₂: C 73.22, H 6.14, N 13.14; found C 73.18, H 6.10, N 13.10.

4-(3-Fluorophenyl)-6-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-pyrimidinamine (5n). Yield, 72%, brown solid, mp 95-100 °C. Rf: 0.43. IR (KBr, cm⁻¹) v: 3352, 3225 (-NH₂), 3065 (Ar-H), 2957, 2838 (-CH₂-), 1601 (-C=N), 1218, 1029 (C-O-C), 976 (C-F). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.14 (t, 3H, -CH₃), 2.52 (q, 2H, -CH₂-), 3.18 (t, 2H, -CH₂-O), 4.33 (t, 2H, -CH₂-O), 5.14 (s, 2H, -NH₂), 6.88-7.84 (m, 8H, Ar-H), 7.40-8.32 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 3352, 3225 (-NH₂), 3065 (Ar-H), 2957, 2838 (-CH₂-), 1597 (-C=N), 1218, 1029 (C-O-C), 976 (C-F). Anal. calcd for C₂₅H₂₃N₄OF: C 72.45, H 5.59, N 13.52; found C 72.40, H 5.54, N 13.49.

4-(3,4-Difluorophenyl)-6-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-pyrimidinamine (5o). Yield, 74%, brown solid, mp 115-118 °C. Rf: 0.44. IR (KBr, cm⁻¹) v: 3357, 3218 (-NH₂), 3062 (Ar-H), 2957, 2832 (-CH₂-), 1602 (-C=N), 1225, 1034 (C-O-C), 975 (C-F). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH₃), 2.53 (q, 2H, -CH₂-), 3.17 (t, 2H, -CH₂-O), 4.34 (t, 2H, -CH₂-O), 5.20 (s, 2H, -NH₂), 6.89-7.85 (m, 8H, Ar-H), 7.39-8.33 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 163.5 (C₁₉), 162.9 (C₁₇), 160.6 (C₂₁), 123.6-160.9 (C₂-C₆), 115.0-149.5 (C₂₄-C₂₉), 114.0-154.1 (C₁₁-C₁₆), 102.9 (C₂₂), 68.0 (C₁₀), 37.9 (C₉), 25.9 (C₇), 14.6 (C₈). Anal. calcd for C₂₅H₂₂N₄OF₂: C 69.43, H 5.13, N 12.96; found C 69.38, H 5.06, N 12.92.

General preparation of the compounds 6a-o

A solution of 5a-o (0.01 mol) and the appropriate benzoyl chloride (0.02 mol) in pyridine (10 mL) was heated under reflux for 6-8 h and heating continued until the reaction was complete. The progress of reaction was monitored by T.L.C (toluene:ethyl acetate, 7.5:2.5). The reaction mixture was added to ice cold water, the solid obtained was filtered off, washed it with cold water until netural pH, dried and recrystallised from ethanol.
Figure 3. Carboxamido pyrimidines 6a-o.

4-(2,4-Dichloro-5-fluorophenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenyl carboxamido pyrimidine (6a). Yield, 70%, brown solid, mp 105-107 °C. R_f: 0.63. IR (KBr, cm⁻¹) v: 3063 (Ar-H), 2955, 2830 (-CH₂-), 1608 (-C=N) 1224, 1032 (C-O-C), 1675 (Amide -1), 1534 (Amide-2), 1247 (Amide-3), 976 (C-F), 748 (C-Cl). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH₃), 2.55 (q, 2H, -CH₂-), 3.18 (t, 2H, -CH₂-), 4.34 (t, 2H, -CH₂-O), 7.01-7.95 (m, 11H, Ar-H), 7.35-8.27 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H), 9.23 (s, 1H –NHCO). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 165.4 (C₃₆), 163.2 (C₁₇), 161.7 (C₁₉), 160.9 (C₂₁), 127.3-144.8 (C₂₄-C₃₅) 123.4-160.5 (C₂-C₆), 115.5-155.3 (C₁₁-C₁₆), 103.3 (C₂₂), 67.9 (C₁₀), 37.8 (C₉), 25.7 (C₇), 15.4 (C₈). Anal. calcd for C₃₂H₂₅Cl₂FN₄O₂: C 65.42, H 4.29, N 9.54; found C 65.36, H 4.22, N 9.50.

4-(4-Methoxyphenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenylcarboxamido pyrimidine (6b). Yield, 65%, brown solid, m p 95-98 °C. R_f: 0.65. IR (KBr, cm⁻¹) ν: 3062 (Ar-H), 2955, 2836 (-CH₂-), 1611 (-C=N), 1674 (Amide-1), 1535 (Amide-2), 1244 (Amide-3) 123.4-160.5 (C₂-C₆), 115.5-155.3 (C₁₁-C₁₆), 103.3 (C₂₂), 67.9 (C₁₀), 37.8 (C₉), 25.7 (C₇), 15.4 (C₈). Anal. calcd for C₃₃H₃₀N₄O₃: C 74.70, H 5.70, N 10.56; found C 74.64, H 5.63, N 10.51.

4-(2,4-Dichlorophenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenylcarboxamido pyrimidine (6c). Yield, 68%, brown solid, mp 103-106 °C. R_f: 0.64. IR (KBr, cm⁻¹) v: 3062 (Ar-H), 2954, 2832 (-CH₂-), 1678 (Amide -1), 1603 (-C=N), 1536 (Amide-2), 1247 (Amide-3), 1225, 1037 (C-O-C), 745 (C-Cl). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH₃), 2.53 (q, 2H, -CH₂-) , 3.17 (t, 2H, -CH₂-), 3.84 (s, 3H, -OCH₃), 4.32 (t, 2H, -CH₂-O), 7.02-7.96 (m, 13H, Ar-H), 7.36-8.29 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H), 9.24 (s, 1H –NHCO). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 165.0 (C₃₆), 164.5 (C₃₇), 163.3 (C₁₇), 161.7 (C₁₉), 160.4 (C₂₁), 123.5-161.5 (C₂-C₆), 115.5-155.6 (C₁₁-C₁₆), 114.8-160.5 (C₂₄-C₃₅), 103.6 (C₂₂), 67.3 (C₁₀), 37.8 (C₉), 25.3 (C₇), 15.3 (C₈). Anal. calcd for C₃₂H₂₆Cl₂FN₄O₂: C 67.49, H 4.60, N 9.84; found C 67.42, H 4.54, N 9.82.
4-(4-Hydroxyphenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenylcarboxamido pyrimidine (6d). Yield, 64%, brown solid, mp 125-177 °C. Rf: 0.63. IR (KBr, cm\(^{-1}\)) v: 3368 (-OH), 3058 (Ar-H), 2952, 2836 (-CH\(_2\)_), 1670 (Amide -1), 1605 (-C=N), 1535 (Amide-2), 1244 (Amide-3), 1222, 1035 (C=O-C) \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm): 1.16 (t, 3H, -CH\(_3\)), 2.54 (q, 2H, -CH\(_2\)-), 3.19 (t, 2H, -CH\(_2\)-), 4.33 (t, 2H, -CH\(_2\)-O), 5.10 (s,1H, -OH), 7.01-7.95 (m, 13H, Ar-H), 7.35-8.28 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H), 9.23 (s, 1H –NHC0). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm): 164.8 (C\(_{36}\)), 163.0 (C\(_{17}\)), 161.9 (C\(_{19}\)), 160.6 (C\(_{21}\)), 122.9-161.2 (C\(_2\)-C\(_6\)), 25.4 (C\(_7\)), 116.4-158.5 (C\(_{24\text{-C}_{35}\}), 115.0-154.9 (C\(_{11\text{-C}_{16}\}), 103.0 (C\(_{22}\)), 67.5 (C\(_{10}\)), 37.3 (C\(_9\)), 15.4 (C\(_8\)). Anal. calc. for C\(_{32\text{H}_{28\text{N}_{4}\text{O}_{3}}}: C 74.40, H 5.46, N 10.85; found C 74.34, H 5.40, N 10.80.

4-(2,6-Dichloro-5-fluorophenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenylcarboxamido pyrimidine (6e). Yield, 72%, brown solid, mp 118-120 °C. Rf: 0.65. IR (KBr, cm\(^{-1}\)) v: 3062 (Ar-H), 2954, 2835 (-CH\(_2\)-),1675 (Amide -1), 1609 (-C=N), 1532 (Amide-2), 1246 (Amide-3), 1218, 1037 (C=O-C). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm): 1.14 (t, 3H, -CH\(_3\)), 2.55 (q, 2H, -CH\(_2\)-), 3.19 (t, 2H, -CH\(_2\)-), 4.33 (t, 2H, -CH\(_2\)-O), 7.00-7.93 (m, 11H, Ar-H), 7.35-8.26 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H), 9.23 (s, 1H –NHC0). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm): 165.1 (C\(_{36}\)), 163.2 (C\(_{17}\)), 161.5 (C\(_{19}\)), 161.0 (C\(_{21}\)), 123.0-160.8 (C\(_{24\text{-C}_{26}\}), 116.1-161.4 (C\(_{24\text{-C}_{35}\}), 116.0-155.3 (C\(_{11\text{-C}_{16}\}), 102.9 (C\(_{22}\)), 67.1(C\(_{10}\)), 37.3 (C\(_9\)), 25.1 (C\(_7\)), 15.7 (C\(_8\)). Anal. calc. for C\(_{32\text{H}_{25\text{Cl}_{2}NF}_{3}\text{O}_{2}}: C 65.42, H 4.29, N 9.54; found C 65.46, H 4.22, N 9.51.

4-(4-Methylphenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenylcarboxamido pyrimidine (6f). Yield, 74%, brown solid, mp 120-124 °C. Rf: 0.66. IR (KBr, cm\(^{-1}\)) v: 3065 (Ar-H), 2957, 2833 (-CH\(_2\)-), 1674 (Amide -1), 1612 (-C=N), 1535 (Amide-2), 1249 (Amide-3), 1225, 1034 (C=O-C). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm): 1.14 (t, 3H, -CH\(_3\)), 2.33 (s, 3H, -CH\(_3\)), 2.54 (q, 2H, -CH\(_2\)-), 3.17 (t, 2H, -CH\(_2\)-), 4.33 (t, 2H, -CH\(_2\)-O), 7.01-7.96 (m, 13H, Ar-H), 7.36-8.28 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H), 9.25 (s, 1H –NHC0). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm): 165.3 (C\(_{36}\)), 163.5 (C\(_{17}\)), 161.5 (C\(_{19}\)), 161.0 (C\(_{21}\)), 127.5-144.4 (C\(_{24\text{-C}_{35}\}), 123.3-160.8 (C\(_{26}\), 115.0-155.4 (C\(_{11\text{-C}_{16}\}), 103.5 (C\(_{22}\)), 67.6 (C\(_{10}\)), 37.5 (C\(_9\)), 25.6 (C\(_7\)), 21.7 (C\(_{37}\)), 15.5 (C\(_8\)). Anal. calc. for C\(_{33\text{H}_{30\text{N}_{4}\text{O}_{2}}}: C 77.02, H 5.88, N 10.89; found C 76.98, H 5.81, N 10.83.

4-(1-Phenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenylcarboxamido pyrimidine (6g). Yield, 67%, brown solid, mp 85-87 °C. Rf: 0.63. IR (KBr, cm\(^{-1}\)) v: 3063 (Ar-H), 2954, 2835 (-CH\(_2\)-), 1677 (Amide -1), 1606 (-C=N), 1534 (Amide-2), 1245 (Amide-3), 1223, 1033 (C=O-C). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm): 1.12 (t, 3H, -CH\(_3\)), 2.53 (q, 2H, -CH\(_2\)-), 3.16 (t, 2H, -CH\(_2\)-), 4.36 (t, 2H, -CH\(_2\)-O), 7.01-7.94 (m, 14H, Ar-H), 7.33-8.25 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H), 9.24 (s, 1H –NHC0). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (ppm): 165.7 (C\(_{36}\)), 163.2 (C\(_{17}\)), 161.7 (C\(_{19}\)), 160.9 (C\(_{21}\)), 127.5-134.0 (C\(_{24\text{-C}_{35}\}), 123.4-160.9 (C\(_{26}\), 115.1-155.6 (C\(_{11\text{-C}_{16}\}), 103.8 (C\(_{22}\)), 67.5 (C\(_{10}\)), 37.8 (C\(_9\)), 25.7 (C\(_7\)), 15.3 (C\(_8\)). Anal. calc. for C\(_{32\text{H}_{28\text{N}_{4}\text{O}_{2}}}: C 76.78, H 5.64, N 11.19; found C 76.73, H 5.58, N 11.14.

4-(4-Fluorophenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenylcarboxamido pyrimidine (6h). Yield, 69%, brown solid, mp 230-233 °C. Rf: 0.66. IR (KBr, cm\(^{-1}\)) v: 3065 (Ar-H), 2955, 2838 (-CH\(_2\)-),1678 (Amide -1), 1609 (-C=N), 1532 (Amide-2), 1249 (Amide-3), 1217,
1035 (C-O-C), 972 (C-F). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH$_3$), 2.56 (q, 2H, -CH$_2$), 3.15 (t, 2H, -CH$_2$), 4.33 (t, 2H, -CH$_2$O), 7.01-7.93 (m, 13H, Ar-H), 7.36-8.29 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H), 9.24 (s, 1H -NHCO). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 165.4 (C$_{36}$), 163.5 (C$_{17}$), 161.3 (C$_{19}$), 160.5 (C$_{21}$), 123.5-160.7 (C$_{2-C_6}$), 116.0-162.9 (C$_{24-C_35}$), 114.8-155.0 (C$_{11-C_16}$), 103.3 (C$_{22}$), 67.9 (C$_{10}$), 37.7 (C$_9$), 25.3 (C$_7$), 15.4 (C$_8$). Anal. calcd for C$_{32}$H$_{27}$N$_4$O$_2$F: C 74.11, H 5.25, N 10.80; found C 74.05, H 5.19, N 10.78.

4-(2,4-Difluorophenyl)-6-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-phenylcarbamoido pyrimidine (6i). Yield, 70%, brown solid, mp 175-180 °C. R$_f$: 0.64. IR (KBr, cm$^{-1}$) v: 3060 (Ar-H), 2950, 2835 (-CH$_2$), 1677 (Amide -1), 1611 (-C=N), 1537 (Amide-2), 1248 (Amide-3), 1223, 1033 (C-O-C), 978 (C-F). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH$_3$), 2.54 (q, 2H, -CH$_2$), 3.17 (t, 2H, -CH$_2$), 4.34 (t, 2H, -CH$_2$O), 7.02-7.95 (m, 12H, Ar-H), 7.35-8.28 (m, 3H, Pyridine-H), 7.83 (s, 1H, Pyrimidine-H), 9.22 (s, 1H -NHCO). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 165.4 (C$_{36}$), 163.2 (C$_{17}$), 160.9 (C$_{21}$), 123.4-160.6 (C$_{2-C_6}$), 115.5-155.3 (C$_{11-C_16}$), 105.3-164.8 (C$_{24-C_35}$), 103.3 (C$_{22}$), 67.7 (C$_{10}$), 37.8 (C$_9$), 24.9 (C$_7$), 15.1 (C$_8$). Anal. calcd for C$_{32}$H$_{28}$F$_2$N$_2$O$_2$: C 71.63, H 4.88, N 10.44; found C 71.58, H 4.81, N 10.39.

4-(4-Bromophenyl)-6-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-phenylcarbamoido pyrimidine (6j). Yield, 68%, brown solid, mp 90-92 °C. R$_f$: 0.65. IR (KBr, cm$^{-1}$) v: 3066 (Ar-H), 2955, 2837 (-CH$_2$), 1672 (Amide -1), 1602 (-C=N), 1538 (Amide-2), 1245 (Amide-3), 1220, 1038 (C-O-C), 857 (C-Br). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm): 1.14 (t, 3H, -CH$_3$), 2.55 (q, 2H, -CH$_2$), 3.13 (t, 2H, -CH$_2$), 4.35 (t, 2H, -CH$_2$O), 7.01-7.92 (m, 13H, Ar-H), 7.37-8.30 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H), 9.26 (s, 1H -NHCO). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 165.3 (C$_{36}$), 163.4 (C$_{17}$), 161.4 (C$_{19}$), 160.3 (C$_{21}$), 127.3-134.8 (C$_{24-C_35}$) 123.7-160.5 (C$_{2-C_6}$), 115.5-155.4 (C$_{11-C_16}$), 103.4 (C$_{22}$), 67.4 (C$_{10}$), 37.4 (C$_9$), 25.2 (C$_7$), 15.2 (C$_8$). Anal. calcd for C$_{32}$H$_{28}$BrN$_2$O$_2$: C 62.92, H 3.87, Br 19.48, N 7.46; found C 62.87, H 3.94, Br 19.58, N 7.43.

4-(3,4-Dichlorophenyl)-6-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-phenylcarbamoido pyrimidine (6k). Yield, 66%, brown solid, mp 92-96 °C. R$_f$: 0.62. IR (KBr, cm$^{-1}$) v: 3056 (Ar-H), 2955, 2838 (-CH$_2$), 1678 (Amide -1), 1602 (-C=N), 1534 (Amide-2), 1245 (Amide-3), 1228, 1033 (C-O-C), 749 (C-Cl). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH$_3$), 2.53 (q, 2H, -CH$_2$), 3.15 (t, 2H, -CH$_2$), 4.33 (t, 2H, -CH$_2$O), 7.03-7.96 (m, 12H, Ar-H), 7.34-8.27 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H), 9.23 (s, 1H -NHCO). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 165.6 (C$_{36}$), 163.0 (C$_{17}$), 161.9 (C$_{19}$), 160.3 (C$_{21}$), 127.7-134.8 (C$_{24-C_35}$) 123.4-161.0 (C$_{2-C_6}$) 115.0-155.0 (C$_{11-C_16}$), 103.0 (C$_{22}$), 67.5 (C$_{10}$), 37.1 (C$_9$), 25.0 (C$_7$), 15.3 (C$_8$). Anal. calcd for C$_{32}$H$_{28}$Cl$_2$N$_2$O$_2$: C 67.49, H 4.60, N 9.84; found C 67.44, H 4.52, N 9.81.

4-(4-Chlorophenyl)-6-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-phenylcarbamoido pyrimidine (6l). Yield, 65%, brown solid, mp 80-82 °C. R$_f$: 0.64. IR (KBr, cm$^{-1}$) v: 3062 (Ar-H), 2955, 2832 (-CH$_2$), 1670 (Amide -1), 1610 (-C=N), 1534 (Amide-2), 1244 (Amide-3), 1225, 1036 (C-O-C), 746 (C-Cl). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm): 1.14 (t, 3H, -CH$_3$), 2.57 (q, 2H, -CH$_2$), 3.17 (t, 2H, -CH$_2$), 4.35 (t, 2H, -CH$_2$O), 7.03-7.95 (m, 13H, Ar-H), 7.37-8.31 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H), 9.26 (s, 1H -NHCO). $^{13}$C NMR (100 MHz, CDCl$_3$) δ (ppm): 165.8 (C$_{36}$), 163.7 (C$_{17}$), 161.0 (C$_{19}$), 160.6 (C$_{21}$), 127.5-134.2 (C$_{24-C_35}$), 123.1-160.9 (C$_{2-}$
4-(3-Methoxyphenyl)-6-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-phenylcarboxamido pyrimidine (6m). Yield, 64%, brown solid, mp 117-120 °C. Rf: 0.66. IR (KBr, cm⁻¹) ν: 3065 (Ar-H), 2955, 2837 (-CH₂-), 1674 (Amide -1), 1603 (-C=N), 1535 (Amide-2), 1246 (Amide-3) 1220, 1032 (C-O-C). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH₃), 2.52 (q, 2H, -CH₂-), 3.16 (t, 2H, -CH₂-), 3.84 (s, 3H, -OCH₃), 4.32 (t, 2H, -CH₂-O), 7.02-7.93 (m, 13H, Ar-H), 7.36-8.29 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H), 9.25 (s, 1H –NHCO). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 165.5 (C₃₆), 163.4 (C₁₇), 161.5 (C₁₉), 160.5 (C₂₁), 123.6-160.5 (C₂-C₆), 115.2-155.2 (C₁₁-C₁₆), 114.8-160.5 (C₂₄-C₃₅), 103.5 (C₁₀), 67.4 (C₁₀), 37.2 (C₉), 25.2 (C₇), 15.4 (C₈). Anal. calcd for C₃₃H₃₀N₄O₃: C 74.70, H 5.70, N 10.56; found C 74.66, H 5.64, N 10.51.

4-(3-Fluorophenyl)-6-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-phenylcarboxamido pyrimidine (6n). Yield, 68%, brown solid, mp 110-115 °C. Rf: 0.62. IR (KBr, cm⁻¹) ν: 3065 (Ar-H), 2956, 2837 (-CH₂-), 1675 (Amide -1), 1605 (-C=N), 1537 (Amide-2), 1247 (Amide-3), 1223, 1037 (C-O-C), 976 (C-F). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.14 (t, 3H, -CH₃), 2.54 (q, 2H, -CH₂-), 3.15 (t, 2H, -CH₂-), 4.34 (t, 2H, -CH₂-O), 7.03-7.94 (m, 13H, Ar-H), 7.37-8.32 (m, 3H, Pyridine-H), 7.87 (s, 1H, Pyrimidine-H), 9.27 (s, 1H –NHCO). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 165.0 (C₃₆), 163.5 (C₁₇), 161.4 (C₁₉), 160.2 (C₂₁), 122.9-159.8 (C₂-C₆), 115.9-155.8 (C₁₁-C₁₆), 114.8-160.5 (C₂₄-C₃₅), 103.7 (C₁₀), 67.0 (C₁₀), 37.0 (C₉), 24.8 (C₇), 15.3 (C₈). Anal. calcd for C₃₂H₂₇N₄O₃F: C 74.11, H 5.25, N 10.80; found C 74.11, H 5.18, N 10.79.

4-(3,4-Difluorophenyl)-6-[4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl]-2-phenylcarboxamido pyrimidine (6o). Yield, 69%, brown solid, mp 200-205 °C. Rf: 0.64. IR (KBr, cm⁻¹) ν: 3065 (Ar-H), 2952, 2836 (-CH₂-), 1675 (Amide -1), 1605 (-C=N), 1537 (Amide-2), 1247 (Amide-3), 1223, 1037 (C-O-C), 976 (C-F). ¹H NMR (CDCl₃, 400 MHz) δ (ppm): 1.16 (t, 3H, -CH₃), 2.56 (q, 2H, -CH₂-), 3.17 (t, 2H, -CH₂-), 4.36 (t, 2H, -CH₂-O), 7.03-7.95 (m, 13H, Ar-H), 7.37-8.32 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H), 9.24 (s, 1H –NHCO). ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 165.1 (C₃₆), 163.7 (C₁₇), 161.7 (C₁₉), 160.9 (C₂₁), 123.0-160.1 (C₂-C₆), 115.6-155.6 (C₁₁-C₁₆), 115.5-163.4 (C₂₄-C₃₅), 103.6 (C₂₂), 67.5 (C₁₀), 37.2 (C₉), 25.1 (C₇), 15.4 (C₈). Anal. calcd for C₃₂H₂₆F₂N₄O₂: C 71.63, H 4.88, N 10.44; found C 71.57, H 4.83, N 10.42.

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