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

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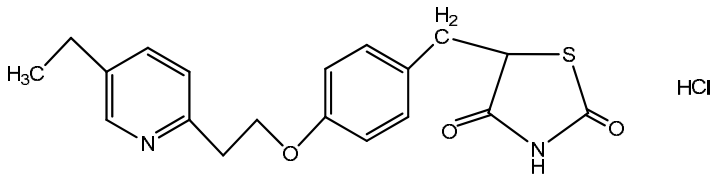
Abstract

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, ^{1}H NMR and ^{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.[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 Grampositive 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.[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.[8-19] The presence of a reactive α,β-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,[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.

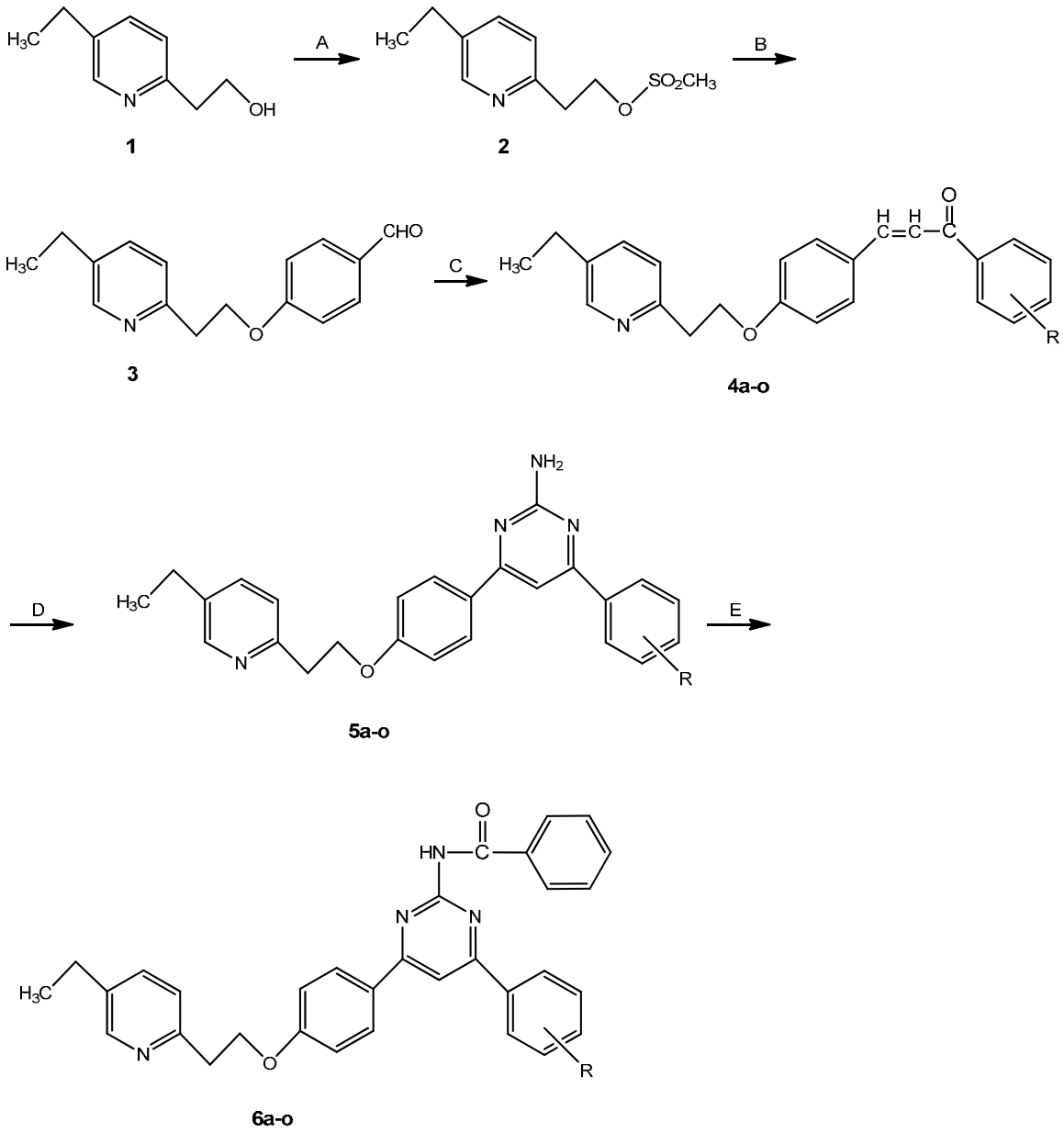
Results and Discussion

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 ν_{max} 2950 cm^{-1} and 2835 cm^{-1} characteristic of the -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 δ 7.11 attributed to the =CH-CO- protons and two protons as a triplet at δ 4.32 confirmed that –CH_2-O- group is present. In the ^{13}C NMR of the chalcones, the -CH=CH- carbon signals appeared at the δ 144.2 and 119.7 ppm respectively. The high-field resonance at δ 190.0 ppm was attributed to the carbonyl group present in chalcone. The structures of compounds **5a-o** and **6a-o** were also confimred using IR and NMR spectroscopy. In the IR spectra of the pyrimidines there was no –C=O band at 1662 cm^{-1} but there were new asymmetric and symmetric broad bands at 3355 cm^{-1} and 3220 cm^{-1} for –NH_2. Signals at δ 5.15 and δ 7.85 for the -NH_2 and –CH of the pyrimidine ring were observed in ^{1}H NMR spectrum and the pyrimidine -CH carbon resonance appeared at δ 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 δ_H 9.25 ppm due to -NHCO together with the δ_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. benzoyl 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.[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

Compd.	R	Minimal bactericidal concentration μg/ml				Minimal fungicidal concentration μg/ml		
		Gram negative		Gram positive				
		E. coli	*P. aeruginosa*	*S. aureus*	*S. pyogenus*	*C. albicans*	*A. niger*	*A. clavatus*
4a	2,4-Cl,5-F	200	250	1000	1000	1000	500	500
4b	4-OCH_3	100	150	250	250	1000	1000	1000
4c	2,4-Cl	150	500	500	500	500	500	1000
4d	4-OH	150	200	250	250	500	500	1000
4e	2,6-Cl,5-F	500	250	500	1000	1000	500	500
4f	4-CH_3	100	150	100	250	1000	1000	1000
4g	-H	500	1000	1000	1000	200	500	500
4h	4-F	62.5	100	150	150	250	>1000	>1000
4i	2,4-F	250	250	500	500	1000	1000	1000
4j	4-Br	500	500	500	250	1000	>1000	>1000
4k	3,4-Cl	500	500	1000	1000	1000	>1000	>1000
4l	4-Cl	500	250	500	250	1000	500	500
4m	3-OCH_3	500	500	1000	1000	500	500	500
4n	3-F	250	500	250	500	500	1000	1000
4o	3,4-F	125	250	500	500	1000	1000	1000
5a	2,4-Cl,5-F	150	250	500	500	500	500	1000
5b	4-OCH_3	62.5	150	250	250	500	>1000	>1000
5c	2,4-Cl	500	500	250	500	500	>1000	>1000
5d	4-OH	250	200	500	500	500	500	1000
5e	2,6-Cl,5-F	250	150	1000	1000	500	500	500
5f	4-CH_3	200	200	250	250	500	500	500
5g	-H	250	250	500	500	500	500	500

Table 1. Continued

5h	4-F	250	250	100	100	500	250	250
5i	2,4-F	62.5	150	150	200	500	1000	1000
5j	4-Br	250	250	200	200	1000	1000	1000
5k	3,4-Cl	250	250	250	250	1000	500	500
5l	4-Cl	250	100	150	250	500	500	500
5m	3-OCH3	250	250	500	500	1000	500	500
5n	3-F	500	500	250	250	500	1000	1000
5o	3,4-F	250	500	500	250	200	200	200
6a	2,4-Cl,5-F	200	250	250	250	1000	1000	1000
6b	4-OCH3	150	200	200	250	500	1000	1000
6c	2,4-Cl	500	250	1000	1000	500	1000	1000
6d	4-OH	150	100	150	150	1000	1000	1000
6e	2,6-Cl,5-F	500	1000	1000	1000	1000	1000	1000
6f	4-CH_3	250	500	500	200	500	>1000	>1000
6g	-H	200	250	500	500	500	1000	1000
6h	4-F	500	500	250	250	1000	500	500
6i	2,4-F	500	500	500	500	250	>1000	>1000
6j	4-Br	150	100	200	200	200	200	200
6k	3,4-Cl	62.5	100	200	200	1000	500	500
6l	4-Cl	500	500	250	500	500	1000	>1000
6m	3-OCH_3	1000	1000	1000	1000	500	500	500
6n	3-F	1000	1000	100	100	1000	500	500
6o	3,4-F	500	500	125	200	500	500	500
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-OCH_3)** 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. pyogeneus,* 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. pyogeneus*, 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.[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.

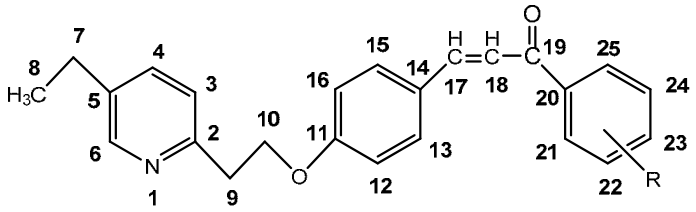


Figure 1. Chalcones **4a-o**.

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}) ν: 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) δ (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, $CDCl_3$) δ (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 $C_{24}H_{20}NO_2Cl_2F$: C 64.88, H 4.54, N 3.15; found C 64.84, H 4.50, N 3.10.

1-(4-Mehtoxyphenyl)-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}) ν: 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) δ (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, 3H, Pyridine-H), 7.05-8.11 (m, 8H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 189.5 (C_{19}), 143.5 (C_{17}), 124.0-160.0 (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_{26}), 37.0 (C_9), 25.5 (C_7), 15.3 (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}) ν: 3066 (Ar-H), 2953, 2835 (-CH_2-), 1660 (-C=O), 1592 (-CH=CH-), 1218, 1030 (C-O-C), 740 (C-Cl). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.18 (t, 3H, -CH_3), 2.56 (q, 2H, -CH_2-), 3.18 (t, 2H, -CH_2-), 4.35 (t, 2H, -CH_2-O), 7.03-7.69 (m, 7H, Ar-H), 7.13 (d, 1H, =CH-CO), 7.17 (d, 1H, -CH), 7.39-8.29 (m, 3H, Pyridine-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 190.8 (C_{19}), 144.0 (C_{17}), 127.3-141.5 (C_{20}-C_{25}), 122.0-159.5 (C_2-C_6), 119.5 (C_{18}), 114.5-156.5 (C_{11}-C_{16}), 67.3 (C_{10}), 38.5 (C_9), 25.8 (C_7), 15.4 (C_8). Anal. calcd for $C_{24}H_{21}NO_2Cl_2$: C 67.61, H 4.96, N 3.29; found C 67.60, 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. R_f: 0.59. IR (KBr, cm^{-1}) ν: 3057 (Ar-H), 2945, 2832 (-CH_2-), 1660 (-C=O), 1595 (-CH=CH-), 1216, 1033 (C-O-C), 3375 (-OH). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH_3), 2.58 (q, 2H, -CH_2-), 3.15 (t, 2H, -CH_2-), 4.36 (t, 2H, -CH_2-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). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 190.5 (C_{19}), 144.5 (C_{17}), 122.4-160.5 (C_2-C_6), 119.2 (C_{18}), 116.3-132.0 (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 $C_{24}H_{23}NO_3$: 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. R_f: 0.53. IR (KBr, cm^{-1}) ν: 3065 (Ar-H), 2955, 2837 (-CH_2-), 1657 (-C=O), 1589 (-CH=CH-), 1225, 1036 (C-O-C), 976 (C-F), 747 (C-Cl).^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.16 (t, 3H, -CH_3), 2.55 (q, 2H, -CH_2-), 3.17 (t, 2H, -CH_2-), 4.33 (t, 2H, -CH_2-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). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 190.3 (C_{19}), 144.2 (C_{17}), 122.0-160.0 (C_2-C_6), 119.5 (C_{18}), 117.5-162.0 (C_{20}-C_{25}), 115.5-156.5 (C_{11}-C_{16}), 67.3 (C_{10}), 38.0 (C_9), 25.4 (C_7), 15.2 (C_8). Anal. calcd for $C_{24}H_{20}NO_2Cl_2F$: C 64.88, H 4.54, N 3.15; found C 64.86, 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. R_f: 0.55. IR (KBr, cm^{-1}) ν: 3060 (Ar-H), 2950, 2835 (-CH_2-), 1662 (-C=O), 1599 (-CH=CH-), 1223, 1033 (C-O-C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.16 (t, 3H, -CH_3), 2.34 (s, 3H, -CH_3), 2.55 (q, 2H, -CH_2-), 3.18 (t, 2H, -CH_2), 4.32 (t, 2H, -CH_2-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). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 190.0 (C_{19}), 144.2 (C_{17}), 127.5-142.4 (C_{20}-C_{25}), 123.4-160.9 (C_2-C_6), 119.7 (C_{18}), 115.0-155.3 (C_{11}-C_{16}), 67.4 (C_{10}), 37.4 (C_9), 25.8 (C_7), 21.7 (C_{26}) 15.4 (C_8). Anal. calcd for $C_{25}H_{25}NO_2$: 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. R_f: 0.53. IR (KBr, cm^{-1}) ν: 3055 (Ar-H), 2947, 2832 (-CH_2-), 1657 (-C=O), 1596 (-CH=CH-), 1217, 1029 (C-O-C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.18 (t, 3H, -CH_3), 2.56 (q, 2H, -CH_2-) , 3.17 (t, 2H, -CH_2-), 4.30 (t, 2H, -CH_2-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). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 190.2 (C_{19}), 144.5 (C_{17}), 127.8-138.0 (C_{20}-C_{25}) 122.4-160.5 (C_2-C_6), 119.5 (C_{18}), 115.5-156.2 (C_{11}-C_{16}), 67.3 (C_{10}), 38.2 (C_9), 25.5 (C_7), 15.5 (C_8). Anal. calcd for $C_{24}H_{23}NO_2$: 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. R_f: 0.54. IR (KBr, cm^{-1}) ν: 3062 (Ar-H), 2953, 2838 (-CH_2-), 1661 (-C=O), 1594 (-CH=CH-), 1222, 1037 (C-O-C), 970 (C-F). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.18 (t, 3H, -CH_3), 2.56 (q, 2H, -CH_2-), 3.16 (t, 2H, -CH_2-), 4.33 (t, 2H, -CH_2-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. calcd for $C_{24}H_{22}NO_2F$: 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-[2-(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}) ν: 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. calcd for $C_{24}H_{21}NO_2F_2$: C 73.27, H 5.38, N 3.56; found C 73.25, H 5.34, N 3.49.

1-(4-Bromophenyl)-3-{4-[2-(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}) ν: 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. calcd for $C_{24}H_{22}NO_2Br$: 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-[2-(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}) ν: 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. calcd for $C_{24}H_{21}NO_2Cl_2$: C 67.61, H 4.96, N 3.29; found C 67.58, H 4.90, N 3.23.

1-(4-Chlorophenyl)-3-{4-[2-(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}) ν: 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. calcd for $C_{24}H_{22}NO_2Cl$: C 73.56, H 5.66, N 3.57; found C 73.52, H 5.61, N 3.55.

1-(3-Methoxyphenyl)-3-{4-[2-(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}) ν: 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, -CH_3), 2.58 (q, 2H, -CH_2-) , 3.16 (t, 2H, -CH_2-), 3.85 (s, 3H, -OCH_3) 4.34 (t, 2H, -CH_2-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). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 190.1 (C_{19}), 144.1 (C_{17}), 122.6-161.5 (C_2-C_6), 117.3-161.5 (C_{20}-C_{25}), 119.2 (C_{18}), 115.3-156.5 (C_{11}-C_{16}), 68.5 (C_{10}), 55.5 (C_{26}), 38.5 (C_9), 25.5 (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 77.45, 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. R_f: 0.54. IR (KBr, cm^{-1}) ν: 3062 (Ar-H), 2956, 2835 (-CH_2-), 1660 (-C=O), 1597 (-CH=CH-), 1219, 1032 (C-O-C), 976 (C-F). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.11 (t, 3H, -CH_3), 2.53 (q, 2H, -CH_2-), 3.14 (t, 2H, -CH_2-), 4.31 (t, 2H, -CH_2-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). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 189.5 (C_{19}), 144.8 (C_{17}), 122.5-160.5 (C_2-C_6), 119.2 (C_{18}), 115.5-156.1 (C_{11}-C_{16}), 114.5-164.0 (C_{20}-C_{25}), 67.5 (C_{10}), 55.8 (C_{26}), 38.0 (C_9), 25.3 (C_7), 15.8 (C_8). Anal. calcd for $C_{24}H_{22}NO_2F$: 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. R_f: 0.55. IR (KBr, cm^{-1}) ν: 3060 (Ar-H), 2950, 2835 (-CH_2-), 1662 (-C=O), 1599 (-CH=CH), 1223, 1033 (C-O-C), 978 (C-F). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.12 (t, 3H, -CH_3), 2.54 (q, 2H, -CH_2-) , 3.16 (t, 2H, -CH_2-), 4.32 (t, 2H, -CH_2-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). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 190.5 (C_{19}), 144.5 (C_{17}), 122.4-160.2 (C_2-C_6), 119.6 (C_{18}), 116.3-155.5 (C_{20}-C_{25}), 115.5-156.0 (C_{11}-C_{16}), 67.1 (C_{10}), 38.2 (C_9), 25.1 (C_7), 15.5 (C_8). Anal. calcd for $C_{24}H_{21}NO_2F_2$: 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.

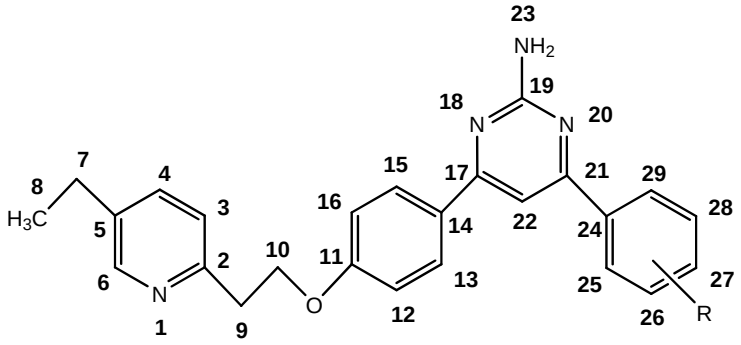


Figure 2. Pyrimidines **5a-o**.

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. R_f: 0.42. IR (KBr, cm^{-1}) ν: 3355, 3222 (-NH_2), 3062 (Ar-H), 2954, 2837 (-CH_2-), 1602 (-C=N), 1225, 1036 (C-O-C), 973 (C-F), 745 (C-Cl). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH_3), 2.54 (q, 2H, -CH_2-) , 3.17 (t, 2H, -CH_2-), 4.33 (t, 2H, -CH_2-O), 5.18 (s, 2H, -NH_2), 6.90-7.82 (m, 8H, Ar-H), 7.39-8.32 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.0 (C_{19}), 163.2 (C_{17}), 160.7 (C_{21}), 123.5-160.5 (C_2-C_6), 118.7-161.4 (C_{24}-C_{29}), 114.0-154.4 (C_{11}-C_{16}), 103.5 (C_{22}), 67.0 (C_{10}), 38.0 (C_9), 25.2 (C_7), 15.3 (C_8). Anal. calcd for $C_{25}H_{21}N_4OCl_2F$: 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. R_f: 0.40. IR (KBr, cm^{-1}) ν: 3352, 3224 (-NH_2), 3065 (Ar-H), 2957, 2834 (-CH_2-), 1609 (-C=N), 1223, 1033 (C-O-C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.14 (t, 3H, -CH_3), 2.53 (q, 2H, -CH_2-) , 3.18 (t, 2H, -CH_2-), 3.83 (s, 3H, -OCH_3) 4.34 (t, 2H, -CH_2-O), 5.12 (s, 2H, -NH_2), 6.89-7.84 (m, 8H, Ar-H), 7.40-8.32 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.1 (C_{19}), 164.5 (C_{17}), 160.5 (C_{21}), 123.8-161.0 (C_2-C_6), 115.3-155.5 (C_{11}-C_{16}), 114.5-160.5 (C_{24}-C_{29}), 103.4 (C_{22}), 67.3 (C_{10}), 55.8 (C_{30}), 37.5 (C_9), 25.0 (C_7), 15.4 (C_8). Anal. calcd for $C_{26}H_{26}N_4O_2$: 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_f: 0.43.R (KBr, cm^{-1}) ν: 3358, 3227 (-NH_2), 3057 (Ar-H), 2953, 2836 (-CH_2-), 1607 (-C=N), 1227, 1037 (C-O-C), 746 (C-Cl). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH_3), 2.52 (q, 2H, -CH_2-) , 3.16 (t, 2H, -CH_2-), 4.32 (t, 2H, -CH_2-O), 5.22 (s, 2H, -NH_2), 6.88-7.81 (m, 8H, Ar-H), 7.39-8.32 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.1 (C_{19}), 163.6 (C_{17}), 160.5 (C_{21}), 127.4-135.5 (C_{24}-C_{29}), 123.6-161.9 (C_2-C_6), 115.1-155.2 (C_{11}-C_{16}), 104.2 (C_{22}), 67.5 (C_{10}), 37.3 (C_9), 26.1 (C_7), 15.2 (C_8). Anal. calcd for $C_{25}H_{25}N_4OCl_2$: 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. R_f: 0.44. IR (KBr, cm^{-1}) ν: 3355, 3224 (-NH_2), 3064

(Ar-H), 2955, 2832 (-CH_2-), 1600 (-C=N), 1220, 1032 (C-O-C), 3357 (-OH). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH_3), 2.54 (q, 2H, -CH_2-), 3.15 (t, 2H, -CH_2-), 4.33 (t, 2H, -CH_2-O), 5.12 (s, 2H, -NH_2), 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). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.2 (C_{19}), 163.8 (C_{17}), 160.3 (C_{21}), 122.9-159.9 (C_2-C_6), 116.3-158.5 (C_{24}-C_{29}) 115.7-155.7 (C_{11}-C_{16}), 103.5 (C_{22}), 67.3 (C_{10}), 37.6 (C_9), 25.5 (C_7), 15.7 (C_8). Anal. calcd for $C_{25}H_{24}N_4O_2$: C 72.80, H 5.86, N 13.58; found C 72.74, H 5.78, N 13.52.

4-(2,6-Dichloro-5-fluorophenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-pyrimidinamine (**5e).** Yield, 76%, yellow solid, mp 105-108 °C. R_f: 0.40. IR (KBr, cm^{-1}) ν: 3348, 3219 (-NH_2), 3062 (Ar-H), 2953, 2830 (-CH_2-), 1606 (-C=N), 1220, 1034 (C-O-C), 975 (C-F), 747 (C-Cl). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.12 (t, 3H, -CH_3), 2.55 (q, 2H, -CH_2-), 3.16 (t, 2H, -CH_2-), 4.31 (t, 2H, -CH_2-O), 5.24 (s, 2H, -NH_2), 6.91-7.83 (m, 8H, Ar-H), 7.38-8.30 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H). ^{13}C NMR (400MHz, $CDCl_3$) δ (ppm): 165.4 (C_{19}), 163.0 (C_{17}), 160.5 (C_{21}), 123.0-160.4 (C_2-C_6), 118.3-161.4 (C_{24}-C_{29}), 113.9-154.1 (C_{11}-C_{16}), 103.2 (C_{22}), 67.2 (C_{10}), 38.2 (C_9), 25.1 (C_7), 15.2 (C_8). Anal. calcd for $C_{25}H_{21}N_4OCl_2F$: 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-pyridyl)ethoxy]phenyl}-2-pyrimidinamine (5f). Yield, 78%, brown solid, mp 133-136 °C. R_f: 0.42. IR (KBr, cm^{-1}) ν: 3355, 3220 (-NH_2), 3057 (Ar-H), 2952, 2834 (-CH_2-), 1610 (-C=N), 1220, 1034 (C-O-C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH_3), 2.33 (s, 3H, -CH_3), 2.53 (q, 2H, -CH_2-), 3.17 (t, 2H, -CH_2-), 4.32 (t, 2H, -CH_2-O), 5.15 (s, 2H, -NH_2), 6.89-7.80 (m, 8H, Ar-H), 7.39-8.30 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.5 (C_{19}), 163.5 (C_{17}), 160.9 (C_{21}), 129.2-144.4 (C_{24}-C_{29}), 123.4-160.9 (C_2-C_6), 115.0-155.4 (C_{11}-C_{16}), 103.2 (C_{22}), 67.5 (C_{10}), 37.5 (C_9), 25.5 (C_7), 21.7 (C_{30}) 15.4 (C_8). Anal. calcd for $C_{26}H_{26}N_4O$: 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-pyridyl)ethoxy]phenyl}-2-pyrimidinamine (5g). Yield, 65%, brown solid, mp 110-115 °C. R_f: 0.44. IR (KBr, cm^{-1}) ν: 3356, 3225 (-NH_2), 3058 (Ar-H), 2952, 2832 (-CH_2-), 1605 (-C=N), 1227, 1038 (C-O-C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH_3), 2.52 (q, 2H, -CH_2-), 3.18 (t, 2H, -CH_2-), 4.30 (t, 2H, -CH_2-O), 5.20 (s, 2H, -NH_2), 6.89-7.82 (m, 8H, Ar-H), 7.38-8.31 (m, 3H, Pyridine-H), 7.87 (s, 1H, Pyrimidine-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 164.9 (C_{19}), 163.2 (C_{17}), 160.5 (C_{21}), 123.6-160.4 (C_2-C_6), 118.7-161.4 (C_{24}-C_{29}), 114.9-154.1 (C_{11}-C_{16}), 103.7 (C_{22}), 67.2 (C_{10}), 38.2 (C_9), 25.1 (C_7), 15.3 (C_8). Anal. calcd for $C_{26}H_{24}N_4O$: 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-pyridyl)ethoxy]phenyl}-2-pyrimidinamine (5h). Yield, 70%, brown solid, mp 244-246 °C. R_f: 0.45. IR (KBr, cm^{-1}) ν: 3356, 3222 (-NH_2), 3064 (Ar-H), 2950, 2835 (-CH_2-), 1602 (-C=N), 1226, 1036 (C-O-C), 975 (C-F). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH_3), 2.53 (q, 2H, -CH_2-) , 3.17 (t, 2H, -CH_2-), 4.31 (t, 2H, -CH_2-O), 5.16 (s, 2H, -NH_2), 6.88-7.80 (m, 8H, Ar-H), 7.39-8.32 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 164.5 (C_{19}), 163.0 (C_{17}), 160.7 (C_{21}), 123.9-160.9 (C_2-C_6), 116.0-163.0 (C_{24}-C_{29}), 114.1-154.3 (C_{11}-C_{16}), 103.9 (C_{22}), 67.4 (C_{10}),

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. R_f: 0.41. IR (KBr, cm^{-1}) ν: 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-) , 3.16 (t, 2H, -CH_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. R_f: 0.40. IR (KBr, cm^{-1}) ν: 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-) , 3.18 (t, 2H, -CH_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 $C_{25}H_{23}N_4OBr$: 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. R_f: 0.43. IR (KBr, cm^{-1}) ν: 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-) , 3.15 (t, 2H, -CH_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 $C_{25}H_{25}N_4OCl_2$: 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. R_f: 0.42. IR (KBr, cm^{-1}) ν: 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-) , 3.15 (t, 2H, -CH_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 12.98.

4-(3-Methoxyphenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-pyrimidinamine (5m). Yield, 54%, yellow solid, mp 98-111 °C. R_f: 0.44. IR (KBr, cm^{-1}) ν: 3356, 3225 (-NH_2), 3066 (Ar-H), 2956, 2838 (-CH_2-), 1609 (-C=N), 1220, 1033 (C-O-C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.15 (t, 3H, -CH_3), 2.53 (q, 2H, -CH_2-) 3.17 (t, 2H, -CH_2-), 3.82 (s, 3H, -OCH_3), 4.34 (t, 2H, -CH_2-O), 5.22 (s, 2H, -NH_2), 6.90-7.85 (m, 8H, Ar-H), 7.40-8.33 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 164.3 (C_{19}), 163.2 (C_{17}), 160.1 (C_{21}), 123.1-160.5 (C_2-C_6), 114.9-160.0 (C_{24}-C_{29}), 113.9-154.5 (C_{11}-C_{16}), 103.2 (C_{22}), 67.8 (C_{10}), 55.7 (C_{30}), 38.5 (C_9), 25.6 (C_7), 15.2 (C_8). Anal. calcd for $C_{26}H_{26}N_4O_2$: 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. R_f: 0.43. IR (KBr, cm^{-1}) ν: 3352, 3225 (-NH_2), 3065 (Ar-H), 2957, 2838 (-CH_2-), 1601 (-C=N), 1218, 1029 (C-O-C), 976 (C-F). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.14 (t, 3H, -CH_3), 2.52 (q, 2H, -CH_2-) , 3.18 (t, 2H, -CH_2-), 4.33 (t, 2H, -CH_2-O), 5.14 (s, 2H, -NH_2), 6.88-7.84 (m, 8H, Ar-H), 7.40-8.32 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 3352,3225 (-NH_2), 3065 (Ar-H), 2957, 2838 (-CH_2-), 1597 (-C=N), 1218, 1029 (C-O-C), 976 (C-F). Anal. calcd for $C_{25}H_{23}N_4OF$: 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. R_f: 0.44. IR (KBr, cm^{-1}) ν: 3357, 3218 (-NH_2), 3062 (Ar-H), 2957, 2832 (-CH_2-), 1602 (-C=N), 1225, 1034 (C-O-C), 975 (C-F). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH_3), 2.53 (q, 2H, -CH_2-) , 3.17 (t, 2H, -CH_2-), 4.34 (t, 2H, -CH_2-O), 5.20 (s, 2H, -NH_2), 6.89-7.85 (m, 8H, Ar-H), 7.39-8.33 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 163.5 (C_{19}), 162.9 (C_{17}), 160.6 (C_{21}), 123.6-160.9 (C_2-C_6), 115.0-149.5 (C_{24}-C_{29}), 114.0-154.1 (C_{11}-C_{16}), 102.9 (C_{22}), 68.0 (C_{10}), 37.9 (C_9), 25.9 (C_7), 14.6 (C_8). Anal. calcd for $C_{25}H_{22}N_4OF_2$: 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 reacion 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.

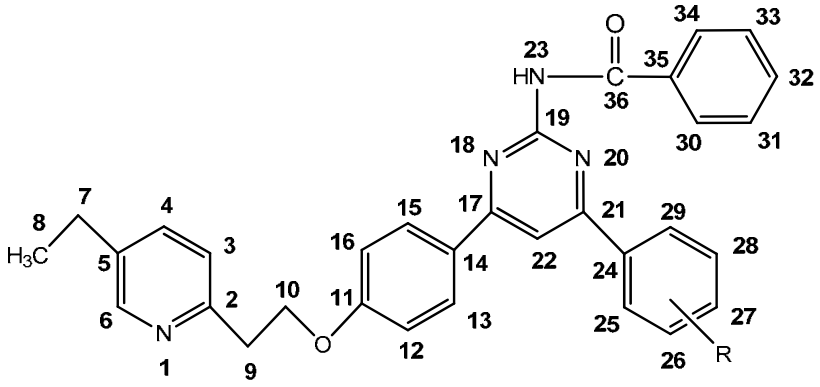


Figure 3. Carboxamido pyrimidines **6a-o**.

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}) ν: 3063 (Ar-H), 2955, 2830 (-CH_2-), 1608 (-C=N) 1224, 1032 (C-O-C), 1675 (Amide -1), 1534 (Amide-2), 1247 (Amide-3), 976 (C-F), 748 (C-Cl). ^{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), 7.01-7.95 (m, 11H, Ar-H), 7.35-8.27 (m, 3H, Pyridine-H), 7.84 (s, 1H, Pyrimidine-H), 9.23 (s, 1H –NHCO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.4 (C_{36}), 163.2 (C_{17}), 161.7 (C_{19}), 160.9 (C_{21}), 127.3-144.8 (C_{24}-C_{35}) 123.4-160.5 (C_2-C_6), 115.5-155.3 (C_{11}-C_{16}), 103.3 (C_{22}), 67.9 (C_{10}), 37.8 (C_9), 25.7 (C_7), 15.4 (C_8). Anal. calcd for $C_{32}H_{25}Cl_2FN_4O_2$: 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, mp 95-98 °C. R_f: 0.65. IR (KBr, cm^{-1}) ν: 3062 (Ar-H), 2955, 2836 (-CH_2-), 1611 (-C=N), 1674 (Amide-1), 1535 (Amide-2), 1244 (Amide-3) 1226, 1039(C-O-C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.14 (t,3H, -CH_3), 2.53 (q, 2H, -CH_2-) , 3.17 (t, 2H, -CH_2-), 3.84 (s, 3H, -OCH_3), 4.32 (t, 2H, -CH_2-O), 7.02-7.96 (m, 13H, Ar-H), 7.36-8.28 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H), 9.24 (s, 1H –NHCO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.0 (C_{36}), 164.5 (C_{37}), 163.3 (C_{17}), 161.7 (C_{19}), 160.4 (C_{21}), 123.5-161.5 (C_2-C_6), 115.5-155.6 (C_{11}-C_{16}), 114.8-160.5 (C_{24}-C_{35}), 103.6 (C_{22}), 67.3 (C_{10}), 37.8 (C_9), 25.3 (C_7), 15.3 (C_8). Anal. calcd for $C_{33}H_{30}N_4O_3$: 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}) ν: 3062 (Ar-H), 2954, 2832 (-CH_2-), 1678 (Amide -1), 1603 (-C=N), 1536 (Amide-2), 1247 (Amide-3), 1225, 1037 (C-O-C), 745 (C-Cl). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.13 (t, 3H, -CH_3), 2.55 (q, 2H, -CH_2-) , 3.16 (t, 2H, -CH_2-), 4.33 (t, 2H, -CH_2-O), 7.02-7.96 (m, 12H, Ar-H), 7.36-8.29 (m, 3H, Pyridine-H), 7.85 (s, 1H, Pyrimidine-H), 9.25 (s, 1H -NHCO-). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.2 (C_{36}), 163.9 (C_{17}), 161.9 (C_{19}), 161.0 (C_{21}), 127.4-135.7 (C_{24}-C_{35}), 123.7-160.9 (C_2-C_6), 114.9-155.0 (C_{11}-C_{16}), 103.3 (C_{22}), 67.8 (C_{10}), 37.5 (C_9), 25.5 (C_7), 15.1 (C_8). Anal. calcd for $C_{32}H_{26}Cl_2N_4O_2$: 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 125-127 °C. R_f: 0.63. IR (KBr, cm^{-1}) ν: 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) δ (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 –NHCO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (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}-C_{35}), 115.0-154.9 (C_{11}-C_{16}), 103.0 (C_{22}), 67.5 (C_{10}), 37.3 (C_9), 15.4 (C_8). Anal. calcd for $C_{32}H_{28}N_4O_3$: 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-phenyl carboxamido pyrimidine (6e). Yield, 72%, brown solid, mp 118-120 °C. R_f: 0.65. IR (KBr, cm^{-1}) ν: 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) δ (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 –NHCO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.1 (C_{36}), 163.2 (C_{17}), 161.5 (C_{19}), 161.0 (C_{21}), 123.0-160.8 (C_2-C_6), 116.1-161.4 (C_{24}-C_{35}), 116.0-155.3 (C_{11}-C_{16}), 102.9 (C_{22}), 67.1(C_{10}), 37.3 (C_9), 25.1 (C_7), 15.7 (C_8). Anal. calcd for $C_{32}H_{25}Cl_2FN_4O_2$: 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. R_f: 0.66. IR (KBr, cm^{-1}) ν: 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) δ (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 –NHCO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.3 (C_{36}), 163.5 (C_{17}), 161.5 (C_{19}), 161.0 (C_{21}), 127.5-144.4 (C_{24}-C_{35}), 123.3-160.8 (C_2-C_6), 115.0-155.4 (C_{11}-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. calcd for $C_{33}H_{30}N_4O_2$: 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. R_f: 0.63. IR (KBr, cm^{-1}) ν: 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) δ (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 –NHCO).^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.7 (C_{36}), 163.2 (C_{17}), 161.7 (C_{19}), 160.9 (C_{21}), 127.5-134.0 (C_{24}-C_{35}) 123.4-160.9 (C_2-C_6), 115.1-155.6 (C_{11}-C_{16}), 103.8 (C_{22}), 67.5 (C_{10}), 37.8 (C_9), 25.7 (C_7), 15.3 (C_8). Anal. calcd for $C_{32}H_{28}N_4O_2$: 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. R_f: 0.66. IR (KBr, cm^{-1}) ν: 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 $C_{32}H_{27}N_4O_2F$: 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-phenylcarboxamido pyrimidine (6i). Yield, 70%, brown solid, mp 175-180 °C. R_f: 0.64. IR (KBr, cm^{-1}) ν: 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 $C_{32}H_{26}F_2N_4O_2$: 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-phenylcarboxamido pyrimidine (6j). Yield, 68%, brown solid, mp 90-92 °C. R_f: 0.65. IR (KBr, cm^{-1}) ν: 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 $C_{32}H_{27}N_4O_2Br$: C 66.32, H 4.70, N 9.67; found C 66.27, H 4.69, N 9.63.

4-(3,4-Dichlorophenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenylcarboxamido pyrimidine (6k). Yield, 66%, brown solid, mp 92-96 °C. R_f: 0.62. IR (KBr, cm^{-1}) ν: 3056 (Ar-H), 2955, 2838 (-CH_2-), 1678 (Amide -1), 1607 (-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 $C_{32}H_{26}Cl_2N_4O_2$: 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-phenylcarboxamido pyrimidine (6l). Yield, 65%, brown solid, mp 80-82 °C. R_f: 0.64. IR (KBr, cm^{-1}) ν: 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-

C_6), 115.5-155.0 (C_{11}-C_{16}), 103.6 (C_{22}), 67.6 (C_{10}), 37.6 (C_9), 25.7 (C_7), 15.4 (C_8). Anal. calcd for $C_{32}H_{27}N_4O_2Cl$: C 71.83, H 5.09, N 10.47; found C 71.78, H 5.03, N 10.43.

4-(3-Methoxyphenyl)-6-{4-[2-(5-ethyl-2-pyridyl)ethoxy]phenyl}-2-phenylcarboxamido pyrimidine (6m). Yield, 64%, brown solid, mp 117-120 °C. R_f: 0.66. IR (KBr, cm^{-1}) ν: 3065 (Ar-H), 2955, 2837 (-CH_2-), 1674 (Amide -1), 1603 (-C=N), 1535 (Amide-2), 1246 (Amide-3) 1220, 1032 (C-O-C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.15 (t,3H, -CH_3), 2.52 (q, 2H, -CH_2-) , 3.16 (t, 2H, -CH_2-), 3.84 (s, 3H, -OCH_3), 4.32 (t, 2H, -CH_2-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). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.5 (C_{36}), 163.4 (C_{17}), 161.5 (C_{19}), 160.5 (C_{21}), 123.6-160.5 (C_2-C_6), 115.2-155.2 (C_{11}-C_{16}), 114.8-160.5 (C_{24}-C_{35}), 103.5 (C_{22}), 67.4 (C_{10}), 55.7 (C_{37}), 37.2 (C_9), 25.2 (C_7), 15.4 (C_8). Anal. calcd for $C_{33}H_{30}N_4O_3$: 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. R_f: 0.62. IR (KBr, cm^{-1}) ν: 3065 (Ar-H), 2956, 2837 (-CH_2-), 1675 (Amide -1), 1605 (-C=N), 1537 (Amide-2), 1247 (Amide-3), 1223, 1037 (C-O-C), 976 (C-F). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.14 (t, 3H, -CH_3), 2.54 (q, 2H, -CH_2-) , 3.15 (t, 2H, -CH_2-), 4.34 (t, 2H, -CH_2-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). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.0 (C_{36}), 163.5 (C_{17}), 161.4 (C_{19}), 160.2 (C_{21}), 122.9-159.8 (C_2-C_6), 115.9-155.8 (C_{11}-C_{16}), 114.8-160.5 (C_{24}-C_{35}), 103.7 (C_{22}), 67.0 (C_{10}), 37.0 (C_9), 24.8 (C_7), 15.3 (C_8). Anal. calcd for $C_{32}H_{27}N_4O_2F$: 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. R_f: 0.64. IR (KBr, cm^{-1}) ν: 3065 (Ar-H), 2952, 2836 (-CH_2-), 1675 (Amide -1), 1609 (-C=N), 1532 (Amide-2), 1247 (Amide-3), 1220, 1033 (C-O-C), 975 (C-F). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.16 (t, 3H, -CH_3), 2.56 (q, 2H, -CH_2-), 3.17 (t, 2H, -CH_2-), 4.36 (t, 2H, -CH_2-O), 7.03-7.95 (m, 12H, Ar-H), 7.37-8.31 (m, 3H, Pyridine-H), 7.86 (s, 1H, Pyrimidine-H), 9.24 (s, 1H –NHCO). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 165.1 (C_{36}), 163.7 (C_{17}), 161.7 (C_{19}), 160.9 (C_{21}), 123.0-160.1 (C_2-C_6), 115.6-155.6 (C_{11}-C_{16}), 115.5-163.4 (C_{24}-C_{35}), 103.6 (C_{22}), 67.5 (C_{10}), 37.2 (C_9), 25.1 (C_7), 15.4 (C_8). Anal. calcd for $C_{32}H_{26}F_2N_4O_2$: C 71.63, H 4.88, N 10.44; found C 71.57, H 4.83, N 10.42.

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