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Synthesis, Characterization of substituted 4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl)benzamide Derivatives and Evaluation of their Anti-microbial activity.

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ABSTRACT

The substituted 4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl) benzamide derivatives **6a-k** has been synthesis from reaction in between substituted 4-ethyl-6-methylpyrimidin-2-amine and 4-(bromomethyl)benzoyl bromide **5** in presence of KOH. Type of aldol condensation reaction in between aldehydes and ketones to form α,β-Unsaturated carbonyl compounds**3** this compound has been reacted with guanidine in presence of dry alcohol to convert 4-ethyl-6-methylpyrimidin-2-amine**4.**Chemical structures of all the new compounds were established by IR, 1H, 13C NMR, MS and elemental data. The compounds **6a-k** were evaluated for their antibacterial activity against Gram-positive bacteria *viz*. *Bacillus subtilis*, *Bacillus sphaericus* and *Staphylococcus aureus*, and three Gram-negative bacteria *viz*. *Pseudomonas aeruginosa*, *Klebsiella aerogenes* and *Chromobacterium violaceum* and also evaluate their antifungal activity against *Candida albicans* (*C.albicans*)(ATCC 10231), *Aspergillus fumigates(A.fumigatus)* (HIC 6094), *Trichophyton rubrum(T. rubrum)* (IFO 9185), and *Trichophyton mentagrophytes(T. mentagrophytes)* (IFO 40996) Amongst them, compounds containing [3-hydrophenyl] moiety **6d**, [3-chlorophenyl] moiety **6f** and [4-nitrophenyl] moiety **6h** showed significant antibacterial and antifungal activity, almost equal/more than the activity of the standard drugs Streptomycin and Amphotericin-B. Further, the compounds **6a-k** were also screened for Most of these new compounds showed appreciable activity against test bacteria and fungi and emerged as potential molecules for further development.

Keywords: Synthesis,4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl) Benzamide, antibacterial activity, antifungal activity.

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INTRODUCTION

Heterocyclic compounds corresponding to one of the most active classes of compounds possessing a wide range of biological activities, including antibacterial, antifungal, and other biological activities[1-10] Further, the treatment of infectious diseases still remains an important and challenging problem because of a combination of factors including emerging infectious diseases and the increasing number of multi-drug resistant microbial pathogens. In spite of a large number of antibiotics and chemotherapeutics available for medical use, at the same time the emergence of old and new antibiotic resistance created in the last decades revealed a substantial medical need for new classes of antimicrobial agents. There is a real perceived need for the discovery of new compounds endowed with antimicrobial activity. Similarly in recent decades, an increased incidence of fungal infections has been observed as a consequence of the growing number of immune compromised patients and the frequent use of antibacterial and cytotoxic drugs. For many fungal infections, polyenes, such as amphotericin B, represent the standard therapy. *Mycobacterium tuberculosis*[11]. Benzamie derivatives are also known to exhibit diverse bioactivities such as anti-convulsant[12], antidiarrheal[13], antihistaminic[14], anti-diabetic[15], cyclooxy genase (COX) inhibitory[16], Ca2+-channel blocker[17], cardioprotective[18], anti-ischemic[19], anti-cancer[20].The synthesis of heterocycles containing multi structure in a molecule has received much attention in recent years[21]. However, literature survey revealed that linked heterocycles containing Benzamide have been reported. Based on the wide range spectrum of biological profile of Benzamide and their increasing importance in pharmaceutical, and biological field, and in continuation of our on going research on biologically active heterocycles[22-24] it was thought of interest to accommodate benzamide moieties in a single molecular frame work to synthesize some new heterocyclic compounds with potential biological activity.

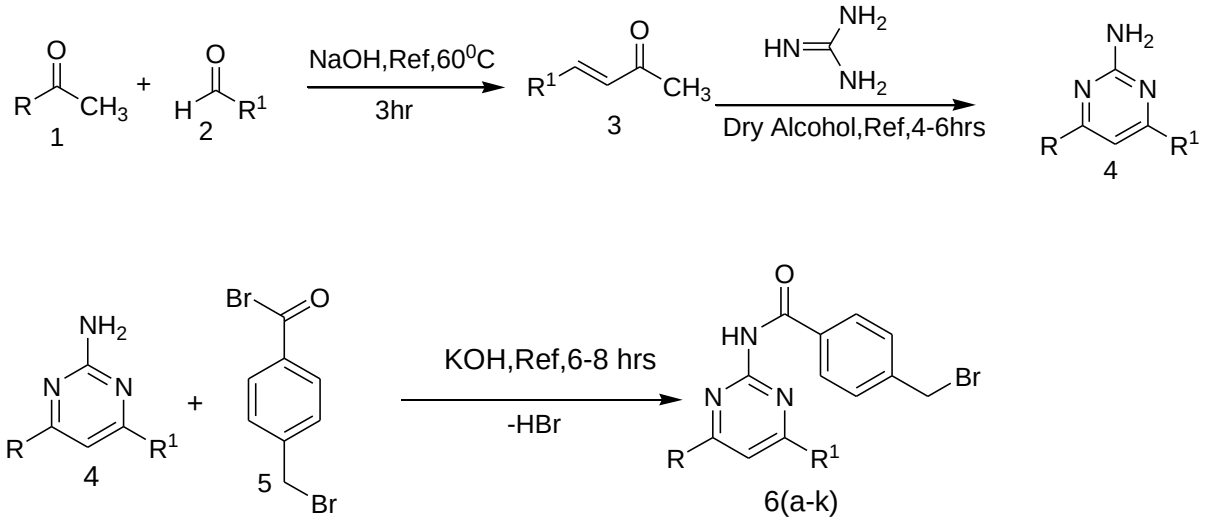
The present investigation deals with the synthesis of some new 4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl) benzamide derivatives **6a-k** in good yields, from substituted 4-ethyl-6-methylpyrimidin-2-amine **5** and 4-(bromomethyl)benzoyl bromide **4.**The antibacterial and antifungal activities of the compounds **6a-k** have also been evaluated.

RESULTS AND DISCUSSION

The present investigation deals with the synthesis of some new preparation of substituted 4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl)benzamide**(I-6a-k)** in (60-78%) good yields,

from starting material carbonyl compounds **(I-1&2).**The antibacterial and antifungal activities of the compounds **I-6(a-k)** have also been evaluated.

Synthesis of the α,β-Unsaturated carbonyl compounds**(I-3)** commenced from condensation in presence of basic condition (NaOH) under reflux condition at 60-80^{0}C for 3-4 hrs in between ketone and substituted aldehydes**(I-1&2)(Scheme-1).**The key intermediate has been prepared in excellent yields(86%). The cyclization of compound **3** with Guanidine in presence of dry alcohol at reflux for 4-6 hrs, furnished the 4-ethyl-6-methylpyrimidin-2-amine in 84%, yield (**Scheme-2**) **M.P**: 128-130^{0}C. The IR spectrum of compound **4** showed absorption bands at 3468,3445(d) cm^{-1} assignable to primary amine functional group(NH_2), The IR spectrum of compound **27** showed absorption bands 3350(s)cm^{-1} assignable 2^0-amine provide a strong evidence that 1^0-amine undergoes to cyclization reaction.



Scheme 1. Synthetic pathways for compounds 6a-k

Compound 6:

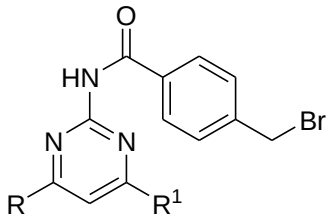


Table 1:

Compound No	R	R^1	Molecular Formula	Molecular Weight	Yield(%)	M.P(^{0}C)
6a	CH_3	C_2H_5	$C_{15}H_{16}N_3OBr$	333	78	144-146
6b	CH_3	C_3H_7	$C_{16}H_{18}N_3OBr$	347	76	158-160
6c	CH_3	C_6H_5	$C_{19}H_{16}N_3OBr$	381	68	152-154
6d	CH_3	3-OH-Ph	$C_{19}H_{16}N_3O_2Br$	397	64	160-162

6e	CH_3	4-OH-Ph	$C_{19}H_{16}N_3O_2Br$	397	65	172-174
6f	CH_3	3-Cl-Ph	$C_{19}H_{15}N_3OClBr$	413.5	74	174-176
6g	CH_3	4-Cl-Ph	$C_{19}H_{15}N_3OClBr$	413.5	72	172-174
6h	CH_3	4-NO_2-Ph	$C_{19}H_{15}N_4O_3Br$	426	68	162-164
6i	CH_3	4-CH_3-Ph	$C_{20}H_{18}N_3OBr$	395	62	170-172
6j	CH_3	4-F-Ph	$C_{19}H_{15}N_3OBrF$	398	64	168-170
6k	CH_3	4-Br-Ph	$C_{19}H_{15}N_3OBr_2$	459	60	184-186

Antimicrobial Activity:

Antibacterial Activity:

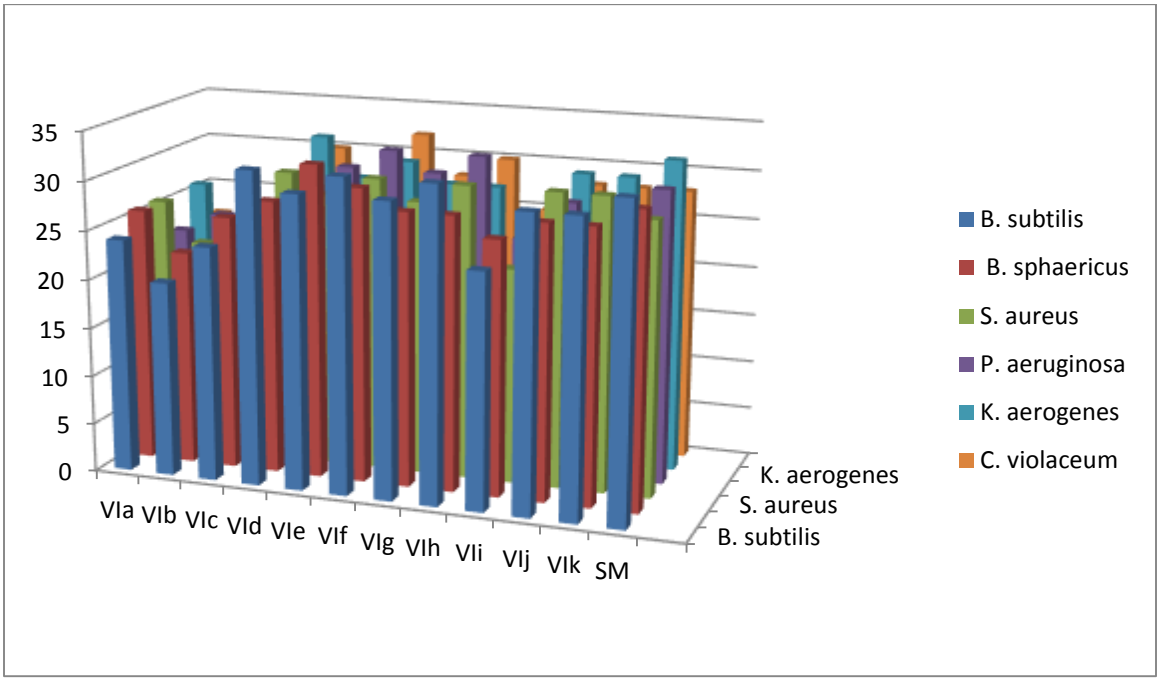
The *in vitro* antibacterial activity 4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl)benzamide **6(a-k)** was assessed against three representative Gram-positive bacteria *viz. Bacillus subtilis*, *Bacillus sphaericus* and *Staphylococcus aureus*, and three Gram-negative bacteria *viz*. *Pseudomonas aeruginosa*, *Klebsiella aerogenes* and *Chromobacterium violaceum* by the disc diffusion method in DMSO[25].In the series of **6(a-k)**, the compounds **6d,6f** and **6h** are found to be the most active against Gram-positive bacteria and the Gram-negative bacteria [Table 1]. The remaining compounds showed moderate to good activity against all the Gram-positive bacteria and the Gram-negative bacteria.

Table 1: Antibacterial activity of compounds 6(a-k).

Compd.	**Minimum Inhibitory Concentration (MIC) in *µ*g/mL**					
	B. subtilis	***B. sphaericus***	***S. aureus***	***P. aeruginosa***	***K. aerogenes***	***C. violaceum***
6a	24	26	26	22	26	22
6b	20	22	22	24	22	20
6c	24	26	22	22	24	26
6d	32	28	30	28	32	30
6e	30	32	28	30	28	26
6f	32	30	30	32	30	32
6g	30	28	28	30	28	28
6h	32	28	30	32	28	30
6i	24	26	22	24	22	25
6j	30	28	30	28	30	28
6k	30	28	30	28	30	28
SM	32	30	28	30	32	28

SM = Streptomycin.

Graphical Data of Anti-Bacterial Activity:



Antifungal Activity

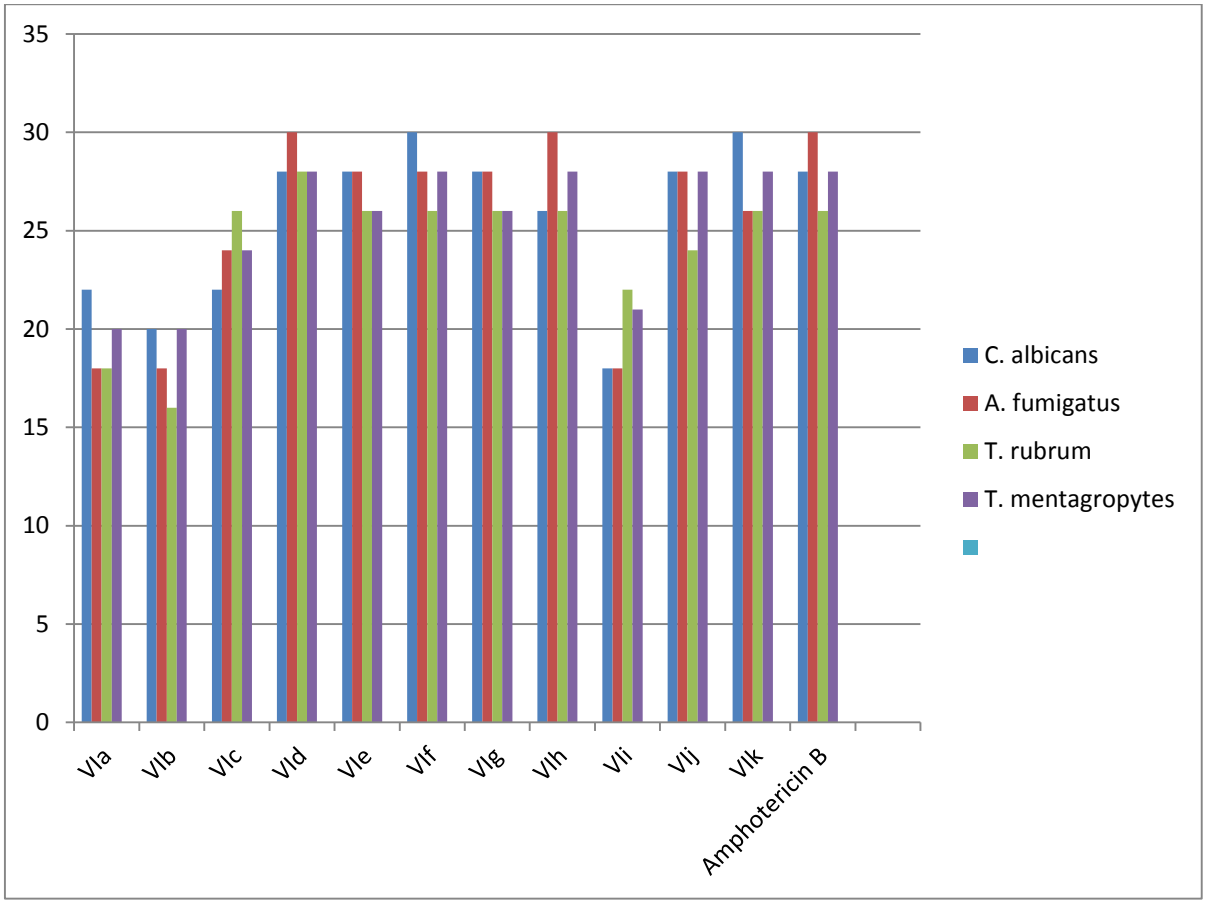
The compounds **6(a-k)** were also screened for their antifungal activity against *Candida albicans* (*C.albicans*)(ATCC 10231), *Aspergillus fumigates(A.fumigatus)* (HIC 6094), *Trichophyton rubrum(T. rubrum)* (IFO 9185), and *Trichophyton mentagrophytes(T. mentagrophytes)* (IFO 40996) in dimethyl sulfoxide (DMSO) by disc difusion method. Amphotericin B was used as a standard drug. The antifungal screening data showed appreciable activity of the test compounds. Among the screened compounds **6d,6f** and **6h** showed good antifungal activity[Table 2].Remaining compounds showed moderate anti fungal activity against test compounds.

Table 2. Antifungal Activity of Compounds 6(a-k)

Compound	**Mean zone inhibition (MZI)[a] in 10 *μ*g/mL**			
	C. albicans	***A. fumigatus***	***T. rubrum***	***T. mentagropytes***
6a	22	18	18	20
6b	20	18	16	20
6c	22	24	26	24
6d	28	30	28	28
6e	28	28	26	26
6f	30	28	26	28
6g	28	28	26	26
6h	26	30	26	28
6i	18	18	22	21
6j	28	28	24	28
6k	30	26	26	28
Amphotericin B	28	30	26	28

[a] Values are mean (n = 3).

Graphical data of Anti-Fungal activity:



CONCLUSION

In conclusion, a series of activity 4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl)Benzamide derivatives **6(a-k)** were prepared. The antibacterial activity of these compounds was evaluated against various bacteria. The compounds showed variable degree of antimicrobial activity. Among the screened compounds **6d**,**6f** and **6h** were found to be the most active or almost equal active against all the microorganisms employed both for antibacterial and antifungal activity. Further, these compounds showed appreciable activity against the test fungi, and emerged as potential molecules for further development.

EXPERIMENTAL:

In this experiment all reagents are used analytical reagent grade obtained from Sigma-Aldrich, Merck, SD fine and avira chemicals. With using standard procedures we purified Water, methanol, acetone, ether etc 4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl)Benzamide derivatives. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker 400 MHz NMR instrument using tetra methyl silane (TMS) as internal standard compound and coupling constants (*J*) are reported in Hz units.VG AUTOSPEC mass spectrometer. Electronic spectra of all compounds

were recorded on Schimadzu UV–Vis 1601 spectrophotometer. ESI mass spectra were Melting points of the ligands and metal complexes decomposition temperature were determined on Polmon instrument (Model No. MP-102). IR spectra of the compounds were recorded using KBr pellets in the range 4000–600 cm ^{1} on Perkin-Elmer Infrared model 337. The percentage composition of C, H, N of the compounds were determined by using micro analytical techniques on Perkin Elmer 240C (USA) elemental analyzer. All reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel F254 plates from Merck, and compounds visualized either by exposure to UV light. Chromatographic columns 60–120 mesh silica gel for separations were used. Elemental analyses (C, H, N) determined by means of a Perkin–Elmer 240 C,H,N and O elemental analyzer, were within ± 0.4% of Perkin–Elmer theory.

General procedure for the preparation of 4-ethyl-6-methylpyrimidin-2-amine (4):

To a vigorously stirring solution of α,β-unsaturated carbonyl compound; 0.01 mole) in NaOH(20ml, 20 N) solution and guanidine (0.01 mol)in presence of dry alcohol were added to reaction mixture. After complete addition, the solution was stirred for another 30 min at RT(35^0C). Now this reaction reflux at 60-80^0C for 4-6 hrs. The resulting mixture was poured onto crushed ice (100 ml) with stirring. The product was extracted with chloroform (4 x 20 ml), which on evaporation yielded a yellow product. This crude product was used for the next step with purification. Recrystallization with ethyl alcohol.

IR (KBr)(cm^{-1}) ν_{max}**:**3468,3445,3123,2998,2700,2596,1450,1260,875.**^{1}H NMR (DMSO-d$_6$**, 300 MHz**) δ:**1.24(t,3H,-CH_3),2.35(t,3H,CH_3),2.80(q,2H,-CH_2), 4.1(s,2H,NH_2),6.58(s, *J* = 7.8 Hz, 1H,Ar-H,).**^{13}C NMR (DMSO-d$_6$**,75 MHz)**δ:**14.6,29.3,101.9,162.2,167.1,167.9.**Mass (CHCl$_3$)** λ_{max}/nm(cm^{-1})**:** *m/z 1*37 (M^+).***Anal*. Calcd.** for $C_7H_{11}N_3$ C, 78.13; H, 10.11; N, 18.14. Found: C, 75.15; H,9.37; N, 16.90. **Yield:** 84% , **M.P**: 128-130^0C.

General procedure for the preparation of Substituted 4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl)benzamide derivatives(6a-k).

4-ethyl-6-methylpyrimidin-2-amine **(4**;0.01 mole) was dissolved in 10 ml of potassium hydroxide solution (0.01 mol) and add dry alcohol slowly in a drop-wise manner. Reflux at 60-80^0C for 6-8 hrs. This was poured into crushed ice and extracted with chloroform. The chloroform extract was evaporated to get Substituted 4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl)benzamide derivatives**(I-6a-k).**

4-(bromomethyl)-N-(4-ethyl-6-methylpyrimidin-2-yl)benzamide derivatives(6a)

IR(KBr) (cm^{-1}) ν_{max}**:**3350.1,3080.2,2980.5,2650.2,2100.6,1758.2,1450.2,1202,958.**^{1}H NMR (DMSO-d$_6$**, 300 MHz**) δ:**1.20(t,3H,-CH_3),1.98(s,3H,CH_3),3.8(q,2H,-CH_2), 4.6(s,1H,NH),6.6(s, *J*

= 7.8 Hz, 1H,Ar-H),6.8-7.83(m,4H,Ar-H).**^{13}C NMR (DMSO-d$_6$**,75 MHz**)δ:**14.6,25.1,36.7,41.2,101.9,114.2,127.8,120.2,134.4,141.4,156.9,159.4,167.1,167.9.

Mass(CHCl$_3$) λ_{max}/nm(cm^{-1}): *m/z 333* (M$^+$),335(M+2).***Anal*. Calcd.** for $C_{15}H_{16}N_3OBr$ C, 67.72; H, 8.32; N, 12.11;O,6.89. Found: C, 65.72; H, 7.42; N, 11.01; O,5.14 **Yield: 7**8% , **M.P**: 144-146^{0}C.

preparation of 4-(bromomethyl)-N-(4-methyl-6-propylpyrimidin-2-yl)benzamide (6b)

IR(KBr) (cm^{-1}) ν_{max}**:**3330,3075,2970,2640,2080,1708,1440,1190,942.**^{1}H NMR (DMSO-d$_6$**, 300 MHz**) δ:**1.19(t,3H,-CH_3),2.25(s,3H,CH_3),2.32(m,2H,-CH_2),2.52(t,2H,-CH_2), 4.26(s,2H,CH_2),4.56(s,1H,NH),6.18(s, *J* = 7.8 Hz,1H,Ar-H),6.8-7.83(m,4H,Ar-H).**^{13}C NMR (DMSO-d$_6$**,75MHz**)δ:**13.2,22.1,26.5,30.0,33.6,106.9,125.8,126.2,132.4,136.8,139.4,152.9, 160.8,163.1,166.9.**Mass(CHCl$_3$)** λ_{max}/nm(cm^{-1}): *m/z 347* (M$^+$),*349(M+2).**Anal*. Calcd.** for $C_{16}H_{18}N_3OBr$ C, 68.21; H, 9.16; N, 10.08.Found: C, 69.83; H, 8.82; N, 08.72. **Yield: 7**6% , **M.P**: 158-160^{0}C.

Preparation of 4-(bromomethyl)-N-(4-methyl-6-phenylpyrimidin-2-yl)benzamide(6c)

IR (KBr) (cm^{-1}) ν_{max}**:** 3372,3092,2985,2632,2130,1758,1458,1210,736.**^{1}H NMR (DMSO-d$_6$**, 300 MHz**) δ:**1.45(s,3H,-CH_3),3.65(s,2H,CH_2),4.4(s,1H,NH),6.5(s, *J* = 7.8 Hz, 1H,Ar-H),6.8-7.8(m,9H,Ar-H).**^{13}C NMR (DMSO-d$_6$**,75 MHz**) δ:**16.6,29.1, 110.2,121.8,122.3,125.3, 130.2,132.4,134.1,137.8,140.5,141.4,144.3,148.9,152.3,155.9,163.8,165.1,166.2.**Mass(CHCl$_3$)** λ_{max}/nm(cm^{-1}): *m/z 381* (M$^+$),*383(M+2).**Anal*. Calcd.** for $C_{19}H_{16}N_3OBr$ C, 70.38; H, 10.15; N, 13.13. Found: C, 69.12; H,9.42; N, 10.01. **Yield: 6**8% , **M.P**: 152-154^{0}C.

Preparation of 4-(bromomethyl)-N-(4-(3-hydroxyphenyl)-6-methylpyrimidin-2-yl)benzamide (6d)

IR(KBr)(cm^{-1}) ν_{max}**:**3315,3020,2950,2621,2008,1685,1402,1132,940.**^{1}H NMR (DMSO-d$_6$**,300 MHz**) δ:**1.18(s,3H,-CH_3),2.20(s,2H,CH_2),4.36(s,1H,NH),6.56(s, *J* = 7.8 Hz, 1H,Ar-H),6.8-7.8(m,8H,Ar-H),8.1(s,1H,OH).**^{13}C NMR (DMSO-d$_6$**,75 MHz**) δ:**12.6,22.1,112.9, 122.8,128.8,130.4,137.8,138.8,140.2,141.4,145.8,146.9,150.4,154.3,158.9,160.8,163.1,164.9,170 .4.**Mass(CHCl$_3$)** λ_{max}/nm(cm^{-1}): *m/z 397* (M$^+$),*399(M+2).**Anal*. Calcd.** for $C_{19}H_{16}N_3O_2Br$ C,70.18;H,11.52;N,10.12. Found:C,69.42;H,8.02;N,10.01, **Yield: 64**% , **M.P**: 160-162^{0}C.

Preparation of 4-(bromomethyl)-N-(4-(4-hydroxyphenyl)-6-methylpyrimidin-2-yl)benzamide (6e)

IR (KBr) (cm^{-1}) ν_{max}**:**3320,3010,2960,2631,2098,1635,1412,1132,940.**^{1}H NMR (DMSO-d$_6$**,300 MHz**) δ:**1.20(s,3H,-CH_3),2.25(s,2H,CH_2),4.40(s,1H,NH),6.36(s, *J* = 7.8 Hz, 1H,Ar-H),6.8-

7.8(m,8H,Ar-H),8.1(s,1H,OH).**^{13}C NMR (DMSO-d$_6$**,75 MHz**) δ:**12.6,22.1,112.9, 122.8,128.8,130.4,137.8,138.8,140.2,141.4,145.8,146.9,150.4,154.3,158.9,160.8,163.1,164.9,170 .4.**Mass(CHCl$_3$)** λ_{max}/nm(cm^{-1}): *m/z 397* (M$^+$),*399(M+2).**Anal.*** **Calcd.** for $C_{19}H_{16}N_3O_2Br$ C, 69.72; H,11.32; N,09.11. Found: C, 68.83; H,10.97; N, 10.01. **Yield: 65**% , **M.P**: 172-174^{0}C.

Preparation of 4-(bromomethyl)-N-(4-(3-chlorophenyl)-6-methylpyrimidin-2-yl)benzamide (6f).

IR (KBr)(cm^{-1}) ν_{max}**:** 3421,3105,2982,2612,2120,1762,1320,1210,940.**^{1}H NMR (DMSO-d$_6$**, 300 MHz**) δ:**1.10(s,3H,-CH_3),2.40(s,3H,CH_3),4.30(s,1H,NH),6.28(s, *J* = 7.8 Hz, 1H,Ar-H),6.8-7.82(m,10H,Ar-H).**^{13}C NMR (DMSO-d$_6$**,75 MHz**) δ:**16.6,28.1,112.9,120.8, 130.2,131.4,134.4,136.9,140.4,142.6,144.8,151.8,154.6,155.8,156.6,162.8,164.6,168.0.**Mass(C HCl$_3$)** λ_{max}/nm(cm^{-1}): *m/z 413.5* (M$^+$),*415.5(M+2).**Anal.*** **Calcd.** for $C_{19}H_{15}N_3OClBr$ C, 70.32; H,9.52; N, 11.12.Found: C, 69.32; H, 8.32; N, 10.32. **Yield: 7**4% , **M.P**: 174-176^{0}C.

Preparation of 4-(bromomethyl)-N-(4-(4-chlorophenyl)-6-methylpyrimidin-2-yl)benzamide (6g).

IR (KBr) (cm^{-1}) ν_{max}**:** 3410,3135,2986,2583,2112,1765,1435,1090,968,695.**^{1}H NMR (DMSO-d$_6$**, 300 MHz**) δ:**1.18(s,3H,-CH_3),2.50(s,2H,CH_2),4.02(s,1H,NH),6.28(s, *J* = 7.8 Hz, 1H,Ar-H),6.8-7.83(m,10H,Ar-H).**^{13}C NMR (DMSO-d$_6$**,75 MHz**) δ:**14.6,25.1,114.9,121.6, 125.8,126.6,127.8,129.2,134.4,137.8,141.4,143.6,144.8,152.8,156.9,164.8,168.1,170.1.**Mass(C HCl$_3$)** λ_{max}/nm(cm^{-1}): *m/z 413.5 (M$^+$),415.5(M+2).**Anal.*** **Calcd.** for $C_{19}H_{15}N_3OClBr$ C, 71.02; H, 9.45; N, 10.20. Found: C,69.43; H,8.32; N, 10.01. **Yield: 7**2% , **M.P**: 172-174^{0}C.

Preparation of 4-(bromomethyl)-N-(4-methyl-6-(4-nitrophenyl)pyrimidin-2-yl)benzamide (6h).

IR (KBr) (cm^{-1}) ν_{max}**:** 3425,3145,2915,2510,2123,1765,1430,1230,922,667.**^{1}H NMR (DMSO-d$_6$**, 300 MHz**) δ:**1.23(s,3H,-CH_3),2.50(s,2H,CH_2), 4.01(s,1H,NH),6.28(s, *J* = 7.8 Hz, 1H,Ar-H),6.8-7.8(m,10H,Ar-H).**^{13}C NMR (DMSO-d$_6$**,75 MHz**) δ:**12.6,23.1,110.9,112.8, 121.8,122.2,126.8,128.5,130.3,132.6,134.4,136.7,137.8,141.4,144.5,150.8,156.9,164.8,167.9.**Ma ss(CHCl$_3$)** λ_{max}/nm(cm^{-1}): *m/z 426* (M$^+$),428(M+2).***Anal.*** **Calcd.** for $C_{19}H_{15}N_3O_3Br$ C, 68.72; H, 9.32; N, 10.11. Found: C, 67.72; H, 8.42; N, 10.01. **Yield: 6**8% , **M.P**: 162-164^{0}C.

Preparation of 4-(bromomethyl)-N-(4-methyl-6-p-tolylpyrimidin-2-yl)benzamide (6i).

IR(KBr)(cm^{-1})ν_{max}**:**3320,3165,2960,2530,2010,1756,1440,1190,942.**^{1}H NMR (DMSO-d$_6$**, 300 MHz**) δ:**1.1(s,3H,-CH_3),1.86(s,3H,CH_3),2.01(s,2H,-CH_2),3.98(s,1H,NH),6.28(s, *J* = 7.8 Hz,1H,Ar-H),7.24-7.83(m,10H,Ar-H).**^{13}C NMR (DMSO-d$_6$**,75 MHz**) δ:** 11.6,22.1,110.9, 112.8,121.8,122.2,126.8,128.5,129.3,131.6,134.4,136.7,137.8,141.4,143.5,150.8,156.9,163.8,168

.9.**Mass(CHCl$_3$)** λ_{max}/nm(cm^{-1}): *m/z 395* (M$^+$),397(M+2).***Anal.* Calcd.** for $C_{20}H_{18}N_3OBr$ C, 72.72; H, 10.32; N, 9.11. Found: C, 71.70; H, 9.42; N, 10.01. **Yield: 62**% , **M.P**: 170-172^{0}C.

Preparation of 4-(bromomethyl)-N-(4-(4-fluorophenyl)-6-methylpyrimidin-2-yl)benzamide (6j).

IR (KBr) (cm^{-1}) ν_{max}**:** 3330,3075,2970,2640,2080,1708,1440,1190,942.**^{1}H NMR (DMSO-d$_6$**, 300 MHz**) δ:**1.20(t,3H,-CH_3),2.35(s,3H,CH_3),2.58(q,2H,-CH_2), 4.56(s,2H,CH_2),6.28(s, *J* = 7.8 Hz, 1H,Ar-H),7.24-7.83(m,10H,Ar-H).**^{13}C NMR (DMSO-d$_6$**,75 MHz**) δ:** 12.6,20.1, 115.9,116.8,118.8,120.2,122.8,128.5,129.3,131.6,134.4,136.7,137.8,141.4,143.5,150.8,158.9,165 .8,169.9.**Mass(CHCl$_3$)** λ_{max}/nm(cm^{-1}): *m/z 398* (M$^+$),400(M+2).***Anal.* Calcd.** for $C_{19}H_{15}N_3OBrF$ C,62.72; H, 11.32; N, 08.11. Found: C, 61.72; H, 10.42; N, 7.01. **Yield: 64**%, **M.P**: 168-170^{0}C.

Preparation of 4-(bromomethyl)-N-(4-(4-bromophenyl)-6-methylpyrimidin-2-yl) benzamide (6k).

IR (KBr) (cm^{-1}) ν_{max}**:** 3330,3115,2910,2480,2110,1798,1340,1090,941,720,663.**^{1}H NMR (DMSO-d$_6$**, 300 MHz**) δ:**1.24(s,3H,-CH_3),2.32(s,2H,CH_2),4.52(s,1H,NH),6.58(s, *J* = 7.8 Hz,1H,Ar-H),6.8-7.8(m,10H,Ar-H).**^{13}C NMR (DMSO-d$_6$**,75 MHz**)δ:** 12.6,20.1,115.9, 116.8,118.8,120.2,122.8,128.5,129.3,131.6,134.4,136.7,137.8,141.4,146.5,149.8,152.9,162.8,170 .9.**Mass (CHCl$_3$)** λ_{max}/nm(cm^{-1}): *m/z 459* (M$^+$),463(M+2).***Anal.* Calcd.** for $C_{19}H_{15}N_3OBr_2$ C, 70.72; H, 9.32; N, 11.11. Found: C, 65.72; H, 7.42; N, 11.01.**Yield: 60**% , **M.P**: 184-186^{0}C.

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