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Design, synthesis, characterization and biological evaluation, of novel *N*-substituted 1,2,3,4-tetrahydropyrimidines-5-carboxamide derivatives

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Pyrimidine and its derivatives play a significant role in bioactive heterocyclic compounds especially for antibacterial and as well as antifungal activities. By keeping these as central facts, some newly designed pyrimidine derivatives of 5-[*N*-(substitutedphenyl)]-carboxamido-1,2,3,6-tetrahydro-1,4-dimethyl-2-oxo-6-(*m*-phenoxyphenyl)-pyrimidines **4a-j** have been synthesized by the condensation of *m*-phenoxybenzaldehyade, *N*-(4-substitutedphenyl)-oxobutanamides and *N*-methyl urea in presence of catalytic amount of acid. The structure of these synthesized novel compounds have been confirmed by methods like IR, NMR and mass spectroscopy, and screened for their antibacterial activities.

Keywords: *m*-Phenoxybenzaldehyde, Biginelli reaction, Pyrimidines, Spectral studies, Antibacterial activity

Pyrimidine is a six membered heterocyclic compound consisting of two nitrogen atoms at one and three positions of heterocyclic ring. Generally pyrimidine derivatives such as 2-hydroxy-substituted-pyrimidine, 2-mercapto-substituted-pyrimidine and 2-amino-substituted pyrimidine are studied. Pyrimidines have been isolated from the nucleic acid hydrolysates. In prior art search of wide range spectrum of pyrimidines and biodynamic activities[1-14]. In recent scenario need to have potent therapeutic agents, such as 5-[*N*-(substitutedphenyl)]-carboxamido-1,2,3,4-tetrahydro-6-isopropyl-2-oxo-4-(*m*-phenoxyphenyl)-pyrimidines **4a-j** have been synthesized.

Pyrimidines are among those molecules that make life possible, have been some of the building blocks of DNA and RNA. Several analogues of pyrimidines have been used as compounds that interfere with the synthesis and functioning of nucleic acids *e.g.* fluorouracil, which has been used in cancer treatment. Also there are some thiouracil derivatives, which produce adverse reduction in susceptible patients and found more potent and less likely to produce side effects and is being widely used[7]. There are several other important groups of pyrimidines with medicinal uses.

Pyrimidine ring carrying various substituents may be built up from two or three aliphatic fragments by the principle synthesis and by a variety of other syntheses, which are complimentary rather than alternative to it. An alternative method of synthesis is the isomerisation alternatively break down of another heterocyclic such as hydration of purine, but such methods are rarely used.

Pyrimidine is best considered as a resonance hybrid to which the uncharged equivalent Kekule structures **1** and **1a** and charged structures 1b and 1e contribute (Fig. 1). The self consistent π (pi) electron densities required for the ground state of pyrimidine are 0.776, 0.825 and 1.103 for positions 2, 4 and 5 respectively[12]. Despite considerable localization of π (pi) electrons at nitrogen atoms of pyrimidines the ring system is still sufficiently aromatic to possess substantial stability. This has a great advantage in the primary synthesis of pyrimidines.

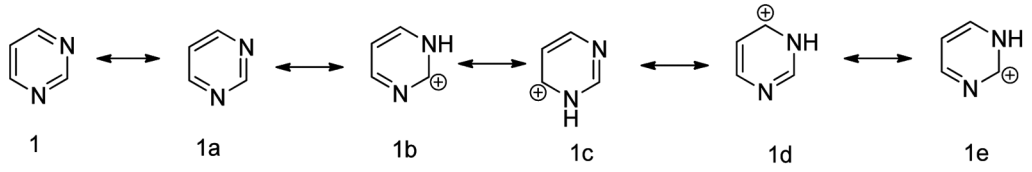


Fig. 1 — Resonating structures of lead pyrimidine molecule

The first primary synthesis from aliphatic fragments was carried out by Frankland et.al. in 1848. Since then a many distinct primary synthetic methods have been devised[15,17-19,23,25,28,29,30,33]. It is also possible to prepare pyrimidines from other heterocyclic compounds such as pyrrole[2], imidazole[34], isoxazole and oxazole[22,24], 1,3,5 triazine[27], oxazine[29], pyridine[32], pyrazine[33], thiazine[21] by different processes. Sathish Kumar *et al*.[35] synthesized a copper nanoparticle (AEEA-Cu(II)-NPs) was used to synthesize novel bioactive 2-thioxo-pyrimidine-5-carboxamides **1a-o** and evaluated the cytotoxicity of cancer cell lines (HepG2, MCF-7, and HeLa). By keeping these all type of activities of Pyrimidine derivatives, in current work it has been synthesized 5-[*N*-(substitutedphenyl)]-carboxamido-1,2,3,6-tetra-hydro-1,4-dimethy-l-2-oxo-6-(*m*-phenoxyphenyl) –pyr-imidines (**4a-j**) by the condensation of *m*-phenoxybenza-ldehyade, *N*-(4-substitutedphenyl)-oxobutanamides and *N*-methyl urea in the presence of catalytic amount of conc. acid.

The constitutions of the products (**4a-j**) have been characterized by elemental analyses, IR, NMR and Mass spectral data.

The products (**4a-j**) were assayed for their *in vitro* biological assay like antibacterial activity towards *S. pyogens MTCC-442*, *S. aureusMTCC-96* and *P. aeruginosa MTCC-124* (Gram positive) and *E. coli MTCC-443* (Gram negative) bacterial strain and antifungal activity towards *Aspergillusniger MTCC-282* and *A. clavatus MTCC-1323* at different concentrations: *i.e*. 0 (control), 5, 25, 50, 100, 250 (μg/mL) for their MIC (Minimum Inhibitory Concentration) values. The biological activities of the synthesized compounds ($\mathbf{2}_{\mathbf{a\text{-}j}}$) were compared with standard drugs *viz*., Ampicillin, Chloramphenicol, Sparfloxacin, Ciprofloxacin, Griseofulvin and Nystatin.

Experimental Section

Thin-layer chromatography was accomplished on 0.2-mm precoated plates of silica gel G60 F254 (Merck). Visualization was made with UV light (254 and 365nm). All the melting points were measured by open capillary method and are uncorrected. The IR absorption spectra (ν max in cm^{-1}) were recorded on a Shimadzu FTIR 8400 Spectrophotometer, ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Bruker Avance II spectrometer in DMSO-d_6 as solvent and TMS as an internal standard. ^{13}C (100 MHz) NMR were recorded on 100 MHz spectrometer using DMSO-d_6 as solvent. Chemical shifts are expressed in δ (ppm) downfield from TMS as an internal standard. LC Mass spectra analysis performed on Agilent Technologies/6120 quadrupole LC/MS. The chemicals used in this work were purchased from Merck and Spectrochem Chemical Companies. All chemicals were reagent grade and used without further purification, and all solvents were freshly distilled before use.

General procedure for the preparation of 5-[*N*-(substituted phenyl)]-carboxamido-1,2,3,6-tetrahydro-1, 4-dimethyl-2-oxo-6-(*m*-phenoxyphenyl)-pyrimidines, 4a-i

(A) Preparation of *N*-substituted-phenyl butanamide-3-ones

For preparation of *N*-substituted-phenyl butanamide-3-ones has been under taken according to literature[36,37].

(B) General procedure for the preparation of Preparation of 5-[*N*-(4-Chlorophenyl)]-carboxamido-1,2,3,6-tetrah-ydro-1,4- dimethyl-2-oxo-6-(*m*-phenoxyphenyl)-pyrimidine, 4a-i

A mixture of *N*-(4-chlorophenyl)-3-oxobutanamide (1) (2.11 g, 0.01M), *m*-phenoxybenzaldehyde (2) (1.98 mL, 0.01M), *N*-methyl urea (3) (1.11 g, 0.015 M) and catalytic amount of conc. acid in ethanol (30 mL) was heated under reflux condition for 8-10 h. The reaction mixture was kept at RT for 24 h. The yellow crystalline product obtained was isolated and recrystallized from ethanol. Yield 58-68%. m.p. 235-240°C. Required for $C_{25}H_{22}ClN_3O_3$: C, 67.04; H, 4.95; N, 9.38. Found: C, 66.99; H, 4.91; N, 9.34%.

TLC solvent system $R_{f1:}$ Ethyl acetate: Hexane (3.0:7.0) = 0.60

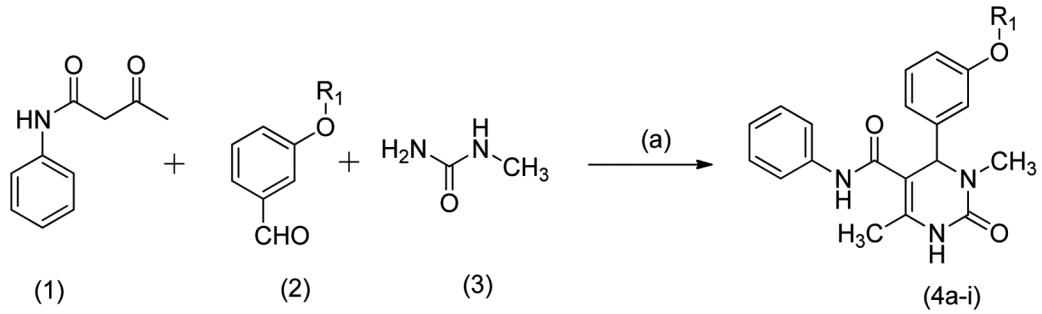
TLC solvent system $R_{f2:}$ Methanol: Chloroform (0.5:9.5) = 0.75

Similarly other compound **4a-i** were synthesized (Scheme 1). The physical data are available in the Supplementary Information.

(C) Antimicrobial activity of 5-[*N*-(substitutedphenyl)]-carboxamido-1,2,3,4-tetrahydro-6-methyl-2-oxo-4-(*m*-phenoxyphenyl)pyrimidine, 4a-i

Antimicrobial activity testing was carried out by using cup-plate method[38], and the result of activity is described in Table 1.

3,6-Dimethyl-2-oxo-*N*-phenyl-4-(3-(p-tolyloxy) phenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxa mide, 4a: Yellow powder. Yield 66%. m.p. 245-247°C. Mol. Wt. 427.50 Anal. Calcd for $C_{26}H_{25}N_3O_3$. Found: C, 73.07; H, 5.82; O, 11.26; N, 9.86. Requires C, 73.10; H, 5.89; O, 11.21; N, 9.82%. IR (KBr): 3149, 2872 (C-H(asym) alkyl), 3410 (N-H), 1676 (C=O), 1510(C=C Aromatic skeletons), 1239 cm^{-1}



Scheme 1 — Synthesis of 5-[*N*-(substitute-dphenyl)]-carboxamido-1,2,3,6-tetrahydro-1,4-dimethyl-2-oxo-6-(*m*-phenoxyphenyl)-pyrimidines **4a-j**

Table 1 — Comparative *in vitro* activity of **4a-j** with known chosen standard drugs

	Standard drug (Zones of inhibition in mm)					Antibacterial activity (Zones of inhibition in mm)				
				IV_f	IVg, IVh, IV_f			IV_f	IVe, IV_f	IVc, IV_f
Amplicilline	11	14	16	18	19	10	13	14	16	18
Chloramphenicol	10	13	19	20	20	12	14	19	20	21
Ciprofloxacin	16	19	21	21	22	17	19	21	22	21
Norfloxacin	18	19	20	21	21	19	22	25	26	28

(C-O-C ether linkage); ^{1}H NMR (400 MHz, DMSO-d_6): δ H 1.78 (singlet, 3H, methyl), H 2.48 of aromatic ring (singlet, 3H, methyl) 2.94 (singlet, 3H, *N*-methyl), 5.99 (singlet, 1H, -NH of Pyrimidine ring), 5.57 (singlet, 1H, -CH- of pyrimidine ring), 6.81-7.63 (multiplet, 13H, Aromatic -H), 8.83 (singlet, 1H, NH-CO); ^{13}C NMR (DMSO-d_6): δ 17.2 21.3, 34.9, 77.4, 108.6, 115.2, 117.1, 121.0, 121.6, 128.0, 128.7, 128.9, 131.5, 137.6 137.8, 146.1, 149.4, 154.0,156.8, 163.1; MS: *m/z* (M+) 427.49.

4-(3-(2,3-Dimethylphenoxy)phenyl)-3,6-dimethyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydro pyrimidine-5-carboxamide, 4b: Yellow powder. Yield 59%. m.p. 236-238°C. Mol. Wt. 441.52. Anal. Calcd for $C_{27}H_{27}N_3O_3$. Found: C, 73.46; H, 6.12; O, 10.80; N, 9.55. Requires C, 73.45; H, 6.14; O, 10.84; N, 9.52%. IR (KBr): 3149, 2872 (C-H), 3412 (N-H), 1676 (C=O), 1514(Aromatic skeletons), 1236 cm^{-1} (C-O-C); ^{1}H NMR (400 MHz, DMSO-d_6): δ H 1.78 (singlet, 3H, methyl), 2.40 (singlet, 6H, aromatic methyl), 2.99 (singlet, 3H, -N-methyl), 6.00 (singlet, ^{1}H, -CH- of pyrimidine ring), 5.97 (singlet, 1H, -NH- of pyrimidine ring), 6.81-7.63 (multiplet, 12H, Aromatic -H), 8.82 (singlet, 1H, NH-CO); ^{13}C NMR ($CDCl_3$): δ 17.2 19.1, 34.9,108.6, 112.9, 121.0, 115.2, 121.0, 121.6, 123.4, 125.3, 126.1, 128.0, 128.2, 128.9, 137.6, 137.8,138.0, 146.1, 149.4 151.7,156.8, 163.1, MS: *m/z* 441.47

4-(3-(2,5-Dimethylphenoxy)phenyl)-3,6-dimethyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydro pyrimidine-5-carboxamide, 4c: Yellow powder. Yield 66%. m.p. 247-249°C. Mol. Wt. 441.52. Anal. Calcd for $C_{27}H_{27}N_3O_3$. Found: C, 73.46; H, 6.12; O, 10.83; N, 9.54. Requires C, 73.47; H, 6.13; O, 10.86; N, 9.53%. IR (KBr): 3149, 2872 (C-H), 3412 (N-H), 1676 (C=O), 1514(Aromatic skeletons), 1236 (C-O-C),773 cm^{-1} (C-Cl); ^{1}H NMR (400 MHz, DMSO-d_6): δ H 1.78 (singlet, 3H, methyl), 2.40 (singlet, 6H, aromatic methyl), 2.99 (singlet, 3H, -N-methyl), 6.00 (singlet, 1H, -CH- of pyrimidine ring), 5.97 (singlet, 1H, -NH- of pyrimidine ring), 6.81-7.63 (multiplet, 12H, Aromatic -H), 8.82 (singlet, 1H, NH-CO); ^{13}C NMR (DMSO-d_6): δ 17.2,21.6, 34.9, 77.4, 108.6, 115.2,116.2, 117.2, 121.0, 122.0, 127.4, 128.2, 128.6, 135.1, 137.8, 146.1,149.4,151.7, 156.8, 163.1 MS: *m/z* 441.49

3,6-Dimethyl-4-(3-(3-nitrophenoxy)phenyl)-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide, 4d: Yellow powder. Yield 60%. m.p. 222-244°C. Mol. Wt. 458.46. Anal. Calcd for $C_{25}H_{22}N_4O_5$. Found: C, 65.60; H, 4.82; O, 17.56; N, 12.25. Requires C, 65.35; H, 4.80; O 17.46; N, 12.22%.

IR (KBr): 3149, 2872 (C-H), 3412 (N-H), 1676 (C=O), 1514(Aromatic skeletons), 1236 (C-O-C),773 cm^{-1} (C-Cl); ^1H NMR (400 MHz, DMSO-d_6): δ H1.72 (singlet, 3H, methyl), 2.87 (singlet, 3H, N-methyl), 5.61 (singlet, 1H, CH- of pyrimidine ring), 6.71-7.65 (multiplet, 13H, Aromatic -H), 8.83 (singlet, 1H, NH-CO), 6.22 (singlet, 1H, -NH- Aromatic-NH); ^{13}C NMR (DMSO-d_6): δ 17.2, 34.9, 77.4, 108.6, 115.2,117., 117.2, 121.0, 122.0, 125.0, 127.4, 128.2, 128.6, 129.3 135.1, 137.8, 146.1, 147.6,149.4,151.7, 156.8, 157.9, 163.1. MS: *m/z* 458.45

3,6-Dimethyl-4-(3-(4-nitrophenoxy)phenyl)-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide, 4e: Yellow powder. Yield 67%. m.p. 262-264°C. Reaction time: 5.0 h. R_f value: 0.47. Mol. Wt. 458.46. Anal. Calcd for $C_{25}H_{22}N_4O_5$. Found: C, 65.60; H, 4.82; O, 17.56; N, 12.25. Requires C, 65.35; H, 4.80; O 17.46; N, 12.22%. IR (KBr): 3149, 2872 (C-H), 3412 (N-H), 1676 (C=O), 1514(Aromatic skeletons), 1236 (C-O-C),773 cm^{-1} (C-Cl); ^1H NMR (400 MHz, DMSO-d_6): δ 1.72 (singlet, 3H, methyl), 2.87 (singlet, 3H, N-methyl), 5.61 (singlet, 1H, -CH- of pyrimidine ring), 6.71-7.65 (multiplet, 13H, Aromatic -H), 8.83 (singlet, 1H, NH-CO), 6.22 (singlet, 1H, -NH- Aromatic-NH); ^{13}C NMR (DMSO-d_6): δ 17.2, 34.9, 77.4, 108.6, 115.2,117., 117.2, 121.0, 122.0, 125.0, 127.4, 128.2, 128.6, 129.3 135.1, 137.8, 146.1, 147.6,149.4,151.7, 156.8, 157.9, 163.1. MS: *m/z* 458.43

4-(3-(4-Chlorophenoxy)phenyl)-3,6-dimethyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide, 4f: Yellow powder. Yield 61%. m.p. 228-230°C. Reaction time: 5.0 h. R_f value: 0.49. Mol. Wt. 447.91. Anal. Calcd for $C_{25}H_{22}ClN_3O_3$: Anal. Found: C, 66.92; H, 4.9; Cl, 7.06; O,10.71%; N, 13.95. Requires C, 66.95; H, 4.88; Cl, 7.01; O,10.71%;N, 9.38%. IR (KBr): 3149, 2872 (C-H), 3412 (N-H), 1676 (C=O), 1514(Aromatic skeletons), 1236 (C-O-C),773 cm^{-1} (C-Cl); ^1H NMR (400 MHz, DMSO-d_6): δ H 1.78 (singlet, 3H, methyl), 3.0 (singlet, 3H, N-methyl of pyridine ring), 5.59 (singlet, 1H, CH- of pyrimidine ring), 6.47 (singlet, 1H, -NH- of pyrimidine ring), 6.81-7.63 (multiplet, 13H, Aromatic -H),8.83 (singlet, 1H, NH-CO); ^{13}C NMR (DMSO-d_6): δ 17.2, 34.9, 77.4, 108.6, 115.2, 117.2, 118.9, 121.0, 121.6, 127.4, 128.0, 128.2, 129.6, 128.9, 137.6, 137.8, 146.1, 149.4, 155.1, 156.8, 163.1. MS: *m/z* 447.89

4-(3-(3-Chlorophenoxy)phenyl)-3,6-dimethyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide, 4g: Yellow powder. Yield 58%. m.p. 246-248°C. Reaction time: 4.5 h. R_f value: 0.46. Mol. Wt. 447.91. Anal. Found: C, 66.92; H, 4.9; Cl, 7.06; O,10.71%; N, 13.95. $C_{25}H_{22}ClN_3O_3$. Requires C, 66.95; H, 4.88; Cl, 7.01; O,10.71%;N, 9.38%. IR (KBr): 3149, 2872 (C-H), 3412 (N-H), 1676 (C=O), 1514(Aromatic skeletons), 1236 (C-O-C),773 cm^{-1} (C-Cl); ^1H NMR (400 MHz, DMSO-d_6): δ H 1.78 (singlet, 3H, methyl), 3.0 (singlet, 3H, N-methyl of pyridine ring), 5.59 (singlet, 1H, CH- of pyrimidine ring), 6.47 (singlet, 1H, -NH- of pyrimidine ring), 6.81-7.63 (multiplet, 13H, Aromatic -H),8.83 (singlet, 1H, NH-CO); ^{13}C NMR (DMSO-d_6): δ 17.2, 34.9, 77.4, 108.6, 115.2, 117.2, 118.9, 121.0, 121.6, 127.4, 128.0, 128.2, 129.6, 128.9, 135.2, 137.6, 137.8, 146.1, 149.4, 155.1, 156.8, 163.1. MS: *m/z* 447.87

4-(3-(4-Fluorophenoxy)phenyl)-3,6-dimethyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamide, 4h: Yellow powder. Yield 60%. m.p. 235-237°C. Reaction time: 4.5 h. R_f value: 0.45. Mol. Wt. 431.45. Anal. Found: C, 69.63; H, 5.12; F, 4.46; O, 11.16%N, 9.75. $C_{25}H_{22}FN_3O_3$. Requires C, 69.61; H, 5.10; F, 4.41; O, 11.13%;N, 9.74%. IR (KBr): 3149, 2872 (C-H), 3412 (N-H), 1676 (C=O), 1514(Aromatic skeletons), 1236 (C-O-C),773 cm^{-1} (C-Cl); ^1H NMR (400 MHz, DMSO-d_6): δ H2.48 (singlet, 3H, methyl), 3.64 (singlet, 3H, methoxy), 4.99 (singlet, 2H, -CH2-O), 6.47 (singlet, 1H, -CH- of pyrimidine ring), 6.81-7.63 (multiplet, 13H, Aromatic -H),9.83 (singlet, 1H, NH-CO), 10.22 (singlet, 1H, -NH- Aromatic-NH); MS: *m/z* 431. ^{13}C NMR ($CDCl_3$): δ 13.15,63.50, 73.20, 110.58, 115.28, 116.80, 113.15, 122.26, 127.14, 127.45, 128.31, 128.73,130.25,131.55, 132.38, 133.67, 138.76,148.52, 154.50, 160.12, 167.35, 188.86, MS: *m/z* 433.30(M^{+2}), (M^+) 431.32.

4-(3-(3,4-Dichlorophenoxy)phenyl)-3,6-dimethyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydro pyrimidine-5-carboxamide, 4i: Yellow powder. Yield 61%. m.p. 271-274°C. Reaction time: 5 h. R_f value: 0.49. Mol. Wt. 481.51. Anal. Found: C, 62.20; H, 4.39; Cl, 14.76; O,10.00%; N, 8.79. $C_{25}H_{21}Cl_2N_3O_3$. Requires C, 62.24; H, 4.35; Cl, 14.73; O, 9.96%; N, 8.70%. IR (KBr): 3149, 2872 (C-H), 3412 (N-H), 1676 (C=O), 1514(Aromatic skeletons), 1236 (C-O-C),773 cm^{-1} (C-Cl); ^1H NMR (400 MHz, DMSO-d_6): δ H 1.78 (singlet, 3H, methyl), 3.0 (singlet, 3H, *N*-methyl of pyridine ring), 5.59 (singlet, 1H, CH- of pyrimidine ring), 6.47 (singlet, 1H, -NH- of pyrimidine ring), 6.81-7.63 (multiplet, 12H, Aromatic -H),8.83 (singlet, 1H, NH-CO); ^{13}C NMR ($CDCl_3$): δ 13.15,63.50, 73.20, 110.58, 115.28, 116.80, 113.15, 126.26, 127.14, 127.45, 128.31, 128.73,130.25,131.55, 132.38, 133.67, 138.76,148.52, 154.50, 160.12, 167.35, 188.86, MS: *m/z* 481.49

Table 2 — *In vitro* antibacterial screening results for 5-[*N*-(3-chloro-4-fluorophenyl)]-carbaoxamido-1,2,3,6-tetrahydro-1,4-dimethyl-2-oxo-6-(*m*-phenoxyphenyl)-pyrimidines **4a-j**

Compd	R^1	Antibactrial activity (Zones of inhibition in mm)									
		S. pyogens MTCC-442					*S. aureus* MTCC-96				
		5	25	50	100	250	5	25	50	100	250
4a	4-CH_3-C_6H_4	–	10	15	16	17	–	12	13	15	16
4b	2,3-$(CH_3)_2$-C_6H_3	–	12	14	15	18	–	9	13	14	16
4c	2,5-$(CH_3)_2$-C_6H_3	–	12	13	15	17	–	10	13	15	18
4d	3-NO_2-C_6H_4	–	12	15	17	18	–	10	12	14	15
4e	4-NO_2-C_6H_4	–	11	13	15	18	–	10	11	16	17
4f	3-Cl-C_6H_4	–	10	14	18	20	–	12	16	17	18
4g	4-Cl-C_6H_4	–	11	14	15	19	–	10	13	15	16
4h	3, 4-$(Cl)_2$-C_6H_3	–	10	14	17	20	–	9	11	14	17
4i	4-F-C_6H_4	–	12	13	14	17	–	11	13	15	16
4j	3-Cl-4-F-C_6H_3	–	10	12	13	18	–	10	12	15	16

Where value for "–" = no inhibition. CIP = Ciprofloxacin as antibacterial standard.

4-(3-(3-Chloro-4-fluorophenoxy)phenyl)-3,6-dimethyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydro pyrimidine-5-carboxamide, 4j: Yellow powder. Yield 57%. m.p. 263-265°C. Reaction time: 5 h. R_f value: 0.47. Mol. Wt. 465.81. Anal. Found: C, 64.56; H, 4.52; Cl, 7.60; F,4.10; O, 10.30; N, 9.05.$C_{25}H_{21}ClFN_3O_3$. Requires C, 64.61; H, 4.50; Cl, 7.63; F, 4.08; O,10.32; N, 9.02%. IR (KBr): 3149, 2872 (C-H), 3412 (N-H), 1676 (C=O), 1514(Aromatic skeletons), 1236 (C-O-C),773 cm^{-1} (C-Cl); ^{1}H NMR (400 MHz, DMSO-d_6): δ H2.48 (singlet, 3H, methyl), 3.64 (singlet, 3H, methoxy), 4.99 (singlet, 2H, -CH_2-O), 6.47 (singlet, 1H, -CH- of pyrimidine ring), 6.81-7.63 (multiplet, 13H, Aromatic -H),9.83 (singlet, 1H, NH-CO), 10.22 (singlet, 1H, -NH- Aromatic-NH); ^{13}C NMR ($CDCl_3$): δ 13.15,63.50, 73.20, 110.58, 115.28, 116.80,120.5, 113.15, 122.26, 127.14, 127.45, 128.31, 128.73, 130.25, 131.55, 132.38, 133.67, 138.76,147.25,148.52, 152.1 154.50, 160.12, 167.35, 188.86, MS: *m/z* 465.79

Results and Discussion

In summary, we have developed a simple but powerful synthetic strategy that permits the assembly of novel 5-[*N*-(sub-stitutedphenyl)]-carboxamido-1,2,3,4-tetrahydro-6-methyl-2-oxo-4-(mphenoxyphenyl) pyrimidine **4a-j** by using con. HCl as acid catalyst. serving as antimicrobial activities against S.*aureus MTCC 96, S.Pyogenus MTCC 443, EColi, MTCC442, P.aeruginosa MTCC441, C.albicans MTCC 227*. Compound **4i** showed good activity against the tested organism A.niger. Compounds **4c**, **4e** showed moderate activity against both the bacterial strains (Table 2). These compounds were characterized by FT-IR, ^{1}H and ^{13}C NMR, and MS techniques.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

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