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Synthesis of new derivatives of 5-((Dimethylcarbamoyl)methyl)-2-butyl-N-alkyl / aryl-4-methyl-6-oxopyrimidine-1(6H)-carboxamides and their biological evaluation of antimicrobial and anticancer activity

P. Krishna Kumari, Prof B Syama Sunder*
Acharya Nagarjuna University, Guntur, Andhra Pradesh-522510

Abstract: *Ten new derivatives of 5-((dimethylcabamoyl)methyl)-2-butyl-N-alkyl / aryl-4-methyl-6-oxopyrimidine-1(6H)-carboxamide (**3a-l**) have been synthesized, and most of the derivatives were promisingly active towards antibacterial and antifungal strains as compared with Ampicilin and flconazole as positive controls due to the presence of pyrimidine heterocyclic ring system. All the new derivatives were prepared from 2-(2-butyl-1,6-dihydro-4-methyl-6-oxopyrimidin-5-yl)-N,N-dimethylacetamide (**1**) When reacted with alkyl / arylisocyanate (**2a-l**) in dichloromethane at room temperature. The structures of newly synthesized derivatives were confirmed by IR, 1H NMR, MS spectral data and elemental analysis.*

Key words: *2-(2-butyl-1,6-dihydro-4-methyl-6-oxopyrimidin-5-yl)-N,N-dimethylacetamide; alkyl / arylisocyanate; 5-((dimethylcabamoyl)methyl)-2-butyl-N-alkyl / aryl-4-methyl-6-oxopyrimidine-1(6H)-carboxamide; antibacterial activity; antifungal activity.*

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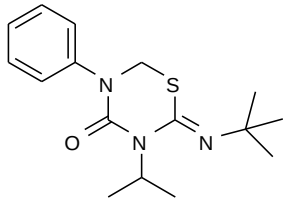
I. Introduction:

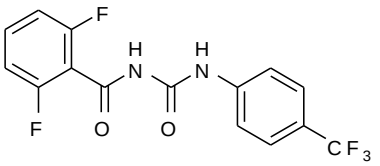
Pyrimidine is a six membered heterocyclic ring with two nitrogen (N) atoms in their ring. Pyrimidine is a weaker base than pyridine, imidazole or amidines as addition of a proton does not increase the resonance energy like imidazole and amidines. Understanding the metabolism of pyrimidine is important for drug metabolism of pyrimidine derivatives[1]. Pyrimidine derivatives form a component in a number of useful drugs and are associated with many biological and therapeutically activities[2]. Condensed pyrimidine derivatives have been reported as anti-microbial[3], analgesic, anti-viral, anti-inflammatory[4], anti-HIV[5], anti-tubercular[6], anti-tumour [7], anti-neoplastic[8], anti-malarial[9], diuretic[10], cardiovascular[11] agents. Pyrimidine compounds are also used as hypnotic drugs for the nervous system [12], calcium-sensing receptor antagonists[13] and also for antagonists of the human A2A adenosine receptor[14].

Urea derivatives represent an extensively used tremendous class of compounds with multi-focal applications in several fields[15]. A number of these compounds are reported to exhibit a wide spectrum of biological and pharmacological activities. In the last decade, much attention has of been paid to the synthesis and application of such substituted urea derivatives.[16-17]

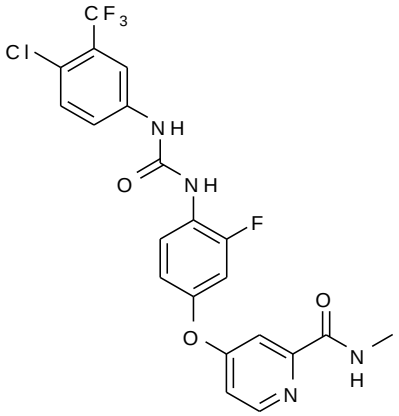
P-heterocyclic pyridine urea derivatives showed significant anti-inflammatory activities both *in vivo* and *vitro*[18] and also acts as antiviral especially piperazine doped with febuxostat urea and thiourea derivatives found to be promising antiviral agents against Tobacco Mosaic Virus [19]. The compounds penfluzuron[20] and buprofezin.[21]



Buprofezin

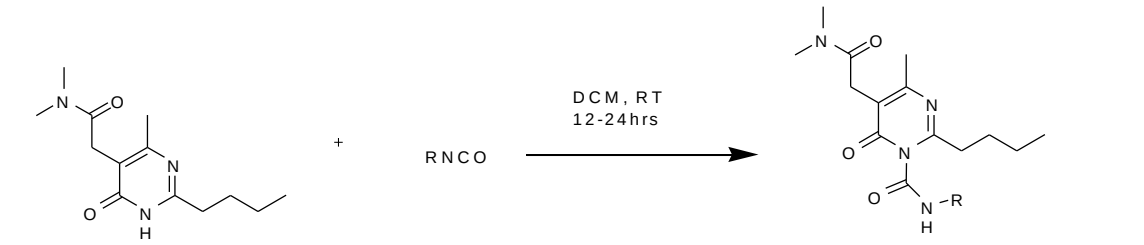


Penfluzuron



Regorafenib

It was envisaged that these two active pharmacophores, if linked together would generate novel molecular templates which are likely to exhibit interesting biological properties. The above-cited applications pyrimidine derivatives and urea derivatives prompted us to synthesize a series of urea containing pyrimidine derivatives. Owing to this importance and in continuation of our work on synthesis of biologically active compounds35–37, now we wish to describe the synthesis of urea containing pyrimidine derivatives in the following cheme. The newly synthesized compounds were screened for their antimicrobial activity.



2-(2-Butyl-1,6-dihydro-4-methyl-6-oxopyrimidin-5-yl)-*N*,*N*-dimethylacetamide(**1**)

Alkyl /Arylisocyanates(**2a-l**)

5-((Dimethylcarbamoyl)methyl)-2-butyl-*N*-alkyl /aryl -4-methyl-6-oxopyrimidine-1(6*H*)-carboxamide (**3a-l**)

Scheme

Table-1

Compound	R
3a	2,5-Dimethoxyphenyl
3b	3-Trifluoromethyl
3c	2-Methoxyphenyl
3d	Trimethylsilyl
3e	3-Fluorophenyl
3f	3-Methylphenyl
3g	Isopropyl
3h	3,4-Dichlorophenyl
3i	Cyclopropyl
3j	4-Trifluomethoxyphenyl
3k	Trichloroacetyl
3l	2-Fluorophenyl

II. Results and Discussion:

Chemistry:

The target compounds were synthesized as shown in the above scheme. The reaction of 2-(2-butyl-1,6-dihydro-4-methyl-6-oxopyrimidin-5-yl)-N,N-dimethylacetamide (**1**) with alkyl / arylisocyanate **(2a-l)** in dichloromethane at room temperature yields new derivatives of 5-((dimethylcabamoyl)methyl)-2-butyl-N-alkyl /

aryl-4-methyl-6-oxopyrimidine-1(6H)-carboxamide (**3a-l**). The target compounds 3a-l have been characterized by 1HNMR, 13CNMR mass spectroscopy and elemental analysis.

Biological Evaluation:

The synthesized new pyrimidine derivatives were tested for their *in vitro* antimicrobial against four bacterial and one fungal species using disk diffusion method. Tetracycline and nystatin were used as standards against bacteria and fungi, respectively. The gram +ve bacteria screened were Staphylococcus aureus (S.A) NCCS 2079 and Bacillus Subtills (B.S) NCCS 2106. The gram _ve bacteria screened were Escherichia coli (E.Coli) NCCS 2065 and Pseudomonas aeruginosa (P.A) NCCS2200.The synthesized compounds were used at the concentration of 250 µg/ml using DMSO as a solvent.. The antibacterial activity data is tabulated in Table 2. The result indicated that among the tested compounds, compounds **3b**, **3e, 3g** and **3i** showed good activity against all selected bacterial strains at concentration of 250 mg/mL as compared to standard drug ciprofloxacin. Compound **3a, 3c, 3d, 3k and 3l** showed comparable activity against all selected bacteria as that of standard. The remaining compounds showed moderate activity against all of the tested bacterial strains.

The antifungal activity of pyrimidine derivatives against one fungal species, i.e. *Candida albicans* (CA) is tested at a sample concentration of 250 µg/ml in DMSO using fluconazole as standard. The antifungal activity data are tabulated in Table 2.The result indicated that among the tested compounds, compounds **3b**, **3e, 3g** and **3i** showed good activity against selected fungal strains at concentration of 250 µg/ml as compared to standard drug fluconazole. Compounds **3a, 3c, 3d, 3k** and **3l** showed comparable activity as that of standard, against *C. albicans* (CA). The remaining compounds are inactive against *C. albicans* (CA).

Table-2

	Antibacterial activity zone diameter in mm				**Antifungal activity**
Compound	**B.Subtills**	**S.Aureus**	**E.Coli**	**P.Aurg.**	**Candida Albicans**
3a	10.2	7.5	8.2	7.5	4.3
3b	16.0	8.4	18.0	16.2	8.9
3c	10.3	4.7	8.9	8.0	4.8
3d	10.0	5.0	8.6	7.7	4.9
3e	17.5	8.5	17.0	17.0	8.0
3f	4.8	2.2	5.3	3.8	ND
3g	16.0	8.4	18.3	16.4	9.0
3h	4.0	1.0	3.3	1.8	ND
3i	16.6	8.0	18.7	18.8	8.7
3j	3.5	1.8	4.3	2.9	ND
3k	10.2	4.8	9.2	7.9	5.2
3l	13.0	5.6	12.0	11.0	6.8
Ciprofloxacin	**24.0**	**10.5**	**24.0**	**20.5**	
Fluconazole					**12.0**

Anticancer Activity:

Anticancer activity screening of the newly synthesized compounds was investigated for their activity with respect to HepG-2, MCF-7 and HCT-116 cell lines and such activity behavior has been estimated using MTT assay.

The percentage of the intact cells was determined and compared to the control (table 2). The cytotoxicity of compounds under test towards the previously mentioned carcinoma cells were compared with that of Doxorubicin. The afforded results indicated that the tested compounds exhibited dose-dependent behavior against the three cancer cell lines. From Table 2 we can deduce that, at 100 µg/mL, All the synthesized compounds are not active towards the cancer cell lines as compared to the standard compound Doxorubicin based on IC50 (µg / ml) values.

Compound	**IC50 in (µg / ml)**		
	MCF-7	**HEPG2**	**HCT116**
II-3a	14.02	16.20	16.20
II-3b	10.50	10.80	11.35
II-3c	17.80	16.30	17.15
II-3d	13.60	15.20	13.90
II-3e	9.85	7.52	8.14
II-3f	18.40	16.00	16.75
II-3g	22.50	19.25	20.05

II-3h	10.15	7.75	10.85
II-3i	17.30	15.45	16.0
II-3j	18.60	15.30	17.20
Doxorubicin	8.50	4.62	8.32

III. Conclusion:

A new series of 5-((dimethylcabamoyl)methyl)-2-butyl-N-alkyl / aryl-4-methyl-6-oxopyrimidine-1(6H)-carboxamide derivatives were synthesized and screened for their antimicrobial and anticancer activity. Compounds **3b**, **3e, 3g** and **3i** were found to be active against all selected bacterial strains.Compounds **3a, 3c, 3d, 3k and 3l** showed moderately active against all selected bacterial strains. Compounds **3b**, **3e, 3g** and **3i** showed good activity against selected fungal strains. Compounds **3a, 3c, 3d,** 3k and **3l** showed comparably active against all fungal strain as compared to standard. None of the compounds are active against cancer cell lines compared to standard. ADME prediction revealed that the compounds could be considered as good candidates for antimicribial drug development.

General

All the melting points are uncorrected. The purity was checked by thin layer chromatography with silica gel 60 GF254 E.Merck pre-coated plates (0.25 mm) was visualized using UV. 0.1 for flash chromatography on silica gel (particle size 100-200 mesh). And characterized by spectral studies. The IR spectra were recorded on shimadzu FTIR model 8010 spectrophotometer and are given in cm^{-1} in KBr. The ^{1}H-NMR & ^{13}C-NMR spectra were recorded on Bruker AM-400 NMR spectrometers in deuterated chloroform and deuterated DMSO. The chemical shifts are reported in δ (ppm) relative to tetramethylsilane as internal standard. Mass spectra analyses performed with an Agilent 6400 Series equipped with an electro spray ionization source (capillary voltage at 4000V, nebulizing gas temperature at 300 °C, nebulizing gas flow at 12 L/ min).

General Experimental Procedure:

2-(2-Butyl-1,6-dihydro-4-methyl-6-oxopyrimidin-5yl)-N,N-dimethylacetamide (0.01mole) was dissolved in 3 ml of dry dichloromethane to which monomer isocyanides (1.0 m.eq) dissolved in 3ml of dry DCM was added drop wise while stirring at room temperature. Once addition was complete the mixture was stirred for 3h at room temperature. After 3h. Reaction mass diluted with diethyl ether solid was precipitated then filtered solid was washed with diethyl ether dried under vacuum to afford desired compound 5-((dimethylcarbamoyl)methyl)-2-butyl-N-alkyl / aryl-4-methyl-6-oxopyrimidin-1(6H)-carbamide. Yield: 55 to 60%).

3a : 2-Butyl-N-(2,5-dimethoxyphenyl)-5-(2-(dimethylamino)-2-oxoethyl)-4-methyl-6-oxopyrimidine-1(6H)-carboxamide.

Yield : 59%, M.P : 150-152^{0}C, ^{1}H-NMR (δ) : 0.95-0.98 (3H, t, $-CH_3$), 1.35-1.39 (2H, m, $-CH_2$), 1.48-1.51 (2H, m, $-CH_2$), 2.24-2.27 (2H, t, $-CH_2$), 2.88 (2H, s, $-CH_2$), 2.95 (6H, s, $-CH_3$), 3.20 (3H, s, $-CH_3$), 3.77 (3H, s, $-OCH_3$), 3.83 (3H, S, $-OCH_3$), 6.78-6.80 (1H, d, -Ar-H), 7.01-7.03 (1H, d, -Ar-H), 7.54 (1H, s, -Ar-H), 8.92 (1H, s, -NH), ^{13}C-NMR (δ) : 13.8, 20.9, 21.5, 22.5, 23.1, 25.2, 38.3, 55.8, 105.7, 110.5, 110.9, 123.5, 125.2, 141.9, 150, 153.1, 153.8, 156.4, 164.6, 166.1, FAB Mass : m/z 431.34 (M+), CHN analysis : Found : C (61.37%), H (7.12%), N (13.04%), Calc. : C (61.38%), H (7.02%), N (13.01%).

3b:2-Butyl-5-(2-(dimethylamino)-2-oxoethyl)-4-methyl-6-oxo-N-(3-(trifluoromethyl)phenyl) pyrimidine-1(6H)-carboxamide.

Yield : 53%, M.P : 161-163^{0}C, ^{1}H-NMR (δ) : 0.95-0.98 (3H, t, $-CH_3$), 1.37-1.41 (2H, m, $-CH_2$), 1.42-1.46(2H, m, $-CH_2$), 2.24-2.27 (2H, t, $-CH_2$), 2.85 (2H, s, $-CH_2$), 2.98 (6H, s, $-CH_3$), 3.26 (3H, s, $-CH_3$), 7.41-7.43 (1H, d, -Ar-H), 7.47-7.56 (2H, m, -Ar-H), 7.95 (1H, s, -Ar-H), 8.93 (1H, s, -NH), ^{13}C-NMR (δ) : 13.8, 20.9, 21.5, 22.5, 23.1, 25.2, 38.3, 120.9, 123.5, 124.1, 124.9, 125.7, 129.2, 131.2, 136.2, 150, 153.8, 156.4, 164.6, 166.1, FAB Mass : m/z 439.22 (M^{+}), CHN analysis : Found : C (57.62%), H (5.77%), N (12.85%), Calc. : C (57.53%), H (5.75%), N (12.78%).

3c:2-Butyl-5-(2-(dimethylamino)-2-oxoethyl)-N-(2-methoxyphenyl)-4-methyl-6-oxopyrimidine-1(6H)-carboxamide.

Yield : 65%, M.P : 190-191^{0}C, ^{1}H-NMR (δ) : 0.94-0.97 (3H, t, $-CH_3$), 1.37-1.41 (2H, m, $-CH_2$), 1.43-1.47 (2H, m, $-CH_2$), 2.22-2.25(2H, t, $-CH_2$), 2.86 (2H, s, $-CH_2$), 2.99 (6H, s, $-CH_3$), 3.20 (3H, s, $-CH_3$), 3.81 (3H, s, $-OCH_3$), 7.08-7.17 (3H, m, -Ar-H), 7.80-7.82 (1H, d, -Ar-H), 8.91 (1H, s, -NH), ^{13}C-NMR (δ) : 13.8, 20.9, 21.5, 22.5, 23.1, 25.2, 38.3, 120.7, 123.5, 124.1, 124.9, 125.7, 129.2, 131.2, 136.2, 150, 153.8, 156.4, 164.6, 166.1, FAB Mass : m/z 401.21 (M^{+}), CHN analysis : Found : C (63.14%), H (7.12%), N (13.99%), Calc. : C (62.98%), H (7.05%), N (13.99%).

3d: 2-Butyl-5-(2-(dimethylamino)-2-oxoethyl)-4-methyl-6-oxo-N-(trimethylsilyl)pyrimidine-1(6H)-carboxamide.
Yield : 58%, M.P : 172-175^{0}C, ^{1}H-NMR (δ) : 0.09 (9H, s, -CH_3), 0.94-0.97 (3H, t, -CH_3), 1.35-1.39 (2H, m, -CH_2), 1.44-1.49 (2H, m, -CH_2), 2.22-2.25 (2H, t, -CH_2), 2.83 (2H, s, -CH_2), 2.95 (6H, s, -CH_3), 3.24 (3H, s, -CH_3), 6.2 (1H, s, -NH), ^{13}C-NMR (δ) : 4.1, 13.8, 20.9, 21.5, 22.5, 23.1, 25.2, 38.3, 123.5, 153.8, 154.5, 156.4, 164.6, 166.1, FAB Mass : m/z 367.26 (M^+), CHN analysis : Found : C (55.76%), H (8.14%), N (15.34%), Calc. : C (55.71%), H (8.25%), N (15.29%).

3e:2-Butyl-5-(2-(dimethylamino)-2-oxoethyl)-N-(3-fluorophenyl)-4-methyl-6-oxopyrimidine-1(6H)-carboxamide.
Yield : 60%, M.P : 148-150^{0}C, ^{1}H-NMR (δ) : 0.95-0.98 (3H, t, -CH_3), 1.36-1.41(2H, m, -CH_2), 1.42-1.46 (2H, m, -CH_2), 2.24-2.27 (2H, t, -CH_2), 2.81 (2H, s, -CH_2), 2.97 (6H, s, -CH_3), 3.20 (3H, s, -CH_3), 6.95-6.97 (1H, d, -Ar-H), 7.36-7.41 (2H, m, -Ar-H), 7.78 (1H, s, -Ar-H), 8.93 (1H, s, -NH), ^{13}C-NMR (δ) : 13.8, 20.9, 21.5, 22.5, 23.1, 25.2, 38.3, 116.1, 116.5, 117.2, 123.5, 130.5, 137.5, 150, 153.8, 156.4, 163.1, 164.6, 166.1, FAB Mass : m/z 389.20 (M^+), CHN analysis : Found : C (61.93%), H (6.52%), N (14.45%), Calc. : C (61.84%), H (6.49%), N (14.42%).

3f: 2-Butyl-5-(2-(dimethylamino)-2-oxoethyl)-4-methyl-6-oxo-N-(m-tolyl)pyrimidine-1(6H)-carboxamide.
Yield : 58%, M.P : 175-178^{0}C, ^{1}H-NMR (δ) : 0.94-0.97 (3H, t, -CH_3), 1.38-1.42 (2H, m, -CH_2), 1.43-1.48 (2H, m, -CH_2), 2.26-2.29(5H, m, -CH_2, -CH_3), 2.81 (2H, s, -CH_2), 2.94 (6H, s, -CH_3), 3.22 (3H, s, -CH_3), 6.94-6.96 (1H, d, -Ar-H), 7.05-7.08 (1H, t, -Ar-H), 7.23 (1H, s, -Ar-H), 7.46-7.48 (1H, d, -Ar-H), 8.91 (1H, s, -NH), ^{13}C-NMR (δ) : 13.8, 20.9, 21.3, 21.5, 22.5, 23.1, 25.2, 38.3, 118.6, 123.5, 124.6, 125.4, 128.8, 135.8, 138.6, 150, 153.8, 156.4, 164.6, 166.1, FAB Mass : m/z 385.22 (M^+), CHN analysis : Found : C (65.72%), H (7.39%), N (14.56%), Calc. : C (65.60%), H (7.34%), N (14.57%).

3g:2-Butyl-5-(2-(dimethylamino)-2-oxoethyl)-N-isopropyl-4-methyl-6-oxopyrimidine-1(6H)-carboxamide.
Yield : 52%, M.P : 137-139^{0}C, ^{1}H-NMR (δ) : 0.93-0.96 (3H, t, -CH_3), 1.14 (6H, s, -CH_3), 1.38-1.43 (2H, m, -CH_2), 1.41-1.46 (2H, m, -CH_2), 2.21-2.26 (2H, m, -CH_2), 2.85 (2H, s, -CH_2), 2.97 (6H, s, -CH_3), 3.20 (3H, s, -CH_3), 4.16 (1H, m, -CH), 6.41 (1H, s, -NH), ^{13}C-NMR (δ) : 13.8, 20.9, 21.5, 22.5, 22.7, 23.1, 25.2, 38.3, 45.2, 123.5, 153.8, 156.4, 157.4, 164.6, 166.1, FAB Mass : m/z 337.12(M^+), CHN analysis : Found : C (60.73%), H (8.45%), N (16.72%), Calc. : C (60.69%), H (8.39%), N (16.65%).

3h:2-Butyl-N-(3,4-dichlorophenyl)-5-(2-(dimethylamino)-2-oxoethyl)-4-methyl-6-oxopyrimidine-1(6H)-carboxamide.
Yield : 49%, M.P : 168-170^{0}C, ^{1}H-NMR (δ) : 0.94-0.97 (3H, t, -CH_3), 1.38-1.43 (2H, m, -CH_2), 1.52-1.57 (2H, m, -CH_2), 2.25-2.28(2H, t, -CH_2), 2.84(2H, s, -CH_2), 2.96 (6H, s, -CH_3), 3.24 (3H, s, -CH_3), 7.36-7.38 (1H, d, -Ar-H), 7.50 (1H, d, -Ar-H), 7.91 (1H, s, -Ar-H), 8.92 (1H, s, -NH), ^{13}C-NMR (δ) : 13.8, 20.9, 21.5, 22.5, 23.1, 25.2, 38.3, 121, 123.5, 124.3, 129.0, 130.5, 131.2, 136.5, 150, 153.8, 156.4, 164.6, 166.1, FAB Mass : m/z 439.14(M^+), CHN analysis : Found : C (54.67%), H (5.54%), N (12.88%), Calc. : C (54.68%), H (5.51%), N (12.75%)

3i:2-Butyl-N-cyclopropyl-5-(2-(dimethylamino)-2-oxoethyl)-4-methyl-6-oxopyrimidine-1(6H)-carboxamide.
Yield : 53%, M.P : 121-123^{0}C, ^{1}H-NMR (δ) : 0.37-0.82 (4H, m, -CH_2), 0.93-0.96 (3H, t, -CH_3), 1.32-1.37 (2H, m, -CH_2), 1.54-1.59 (2H, m, -CH_2), 2.25-2.28(2H, t, -CH_2), 2.74 (2H, s, -CH), 2.82 (2H, s, -CH_2), 2.97 (6H, s, -CH_3), 3.21 (3H, s, -CH_3), 6.48 (1H, s, -NH), ^{13}C-NMR (δ) : 6.1, 13.8, 20.9, 21.5, 22.5, 23.1, 25.2, 28, 38.3, 123.5, 153.8, 156.4, 157.4, 164.6, 166.1, FAB Mass : m/z 335.23 (M^+), CHN analysis : Found : C (61%), H (7.69%), N (16.84%), Calc. : C (61.06%), H (7.84%), N (16.75%).

3j:2-Butyl-5-(2-(dimethylamino)-2-oxoethyl)-4-methyl-6-oxo-N-(4-(trifluoromethoxy)phenyl)pyrimidine-1(6H)-carboxamide.
Yield : 52%, M.P : 144-146^{0}C, ^{1}H-NMR (δ) : 0.94-0.97 (3H, t, -CH_3), 1.38-1.43 (2H, m, -CH_2), 1.52-1.57 (2H, m, -CH_2), 2.26-2.29 (2H, t, -CH_2), 2.84 (2H, s, -CH_2), 3.1 (6H, s, -CH_3), 3.26 (3H, s, -CH_3), 6.93-6.97 (2H, dd, -Ar-H), 7.27-7.31 (2H, dd, -Ar-H), 8.93 (1H, s, -NH), ^{13}C-NMR (δ) : 13.8, 20.9, 21.5, 22.5, 23.1, 25.2, 38.3, 114.5, 119.8, 123.5, 129.7, 131.7, 146.2, 150.0, 153.8, 156.4, 164.6, 166.1, FAB Mass : m/z 455.18 (M^+), CHN analysis : Found : C (55.52%), H (5.60%), N (12.39%), Calc. : C (55.50%), H (5.55%), N (12.33%).

3k:2-Butyl-5-(2-(dimethylamino)-2-oxoethyl)-4-methyl-6-oxo-N-(2,2,2-trichloroacetyl)pyrimidine-1(6H)-carboxamide.
Yield : 66%, M.P : 115-117^{0}C, ^{1}H-NMR (δ) : 0.92-0.95 (3H, t, -CH_3), 1.32-1.37 (2H, m, -CH_2), 1.54-1.59 (2H, m, -CH_2), 2.26-2.29(2H, t, -CH_2), 2.83 (2H, s, -CH_2), 2.95 (6H, s, -CH_3), 3.20 (3H, s, -CH_3), 10.92 (1H, s, -NH), ^{13}C-NMR (δ) : 13.8, 20.9, 21.5, 22.5, 23.1, 25.2, 38.3, 91.3, 123.5, 139.4, 152.5, 153.8, 156.4, 164.6, 166.1, FAB Mass : m/z 439.06 (M^+), CHN analysis : Found : C (43.66%), H (4.83%), N (12.69%), Calc. : C (43.70%), H (4.81%), N (12.74%).

3l:2-Butyl-5-(2-(dimethylamino)-2-oxoethyl)-N-(2-fluorophenyl)-4-methyl-6-oxo-N-(2,2,2-trichloroacetyl)pyrimidine-1(6H)-carboxamide.

Yield : 52%, M.P : 134-137^{0}C, ^{1}H-NMR (δ) : 0.92-0.95 (3H, t, -CH_3), 1.35-1.40 (2H, m, -CH_2), 1.54-1.59 (2H, m, -CH_2), 2.26-2.28(2H, t, -CH_2), 2.97 (6H, s, -CH_3), 3.21 (3H, s, -CH_3), 7.03-7.06 (1H, t, -Ar-H), 7.11-7.19 (2H, m, -Ar-H), 7.95-7.98 (1H, d, -Ar-H), 8.90 (1H, s, -NH), ^{13}C-NMR (δ) : 13.8, 20.9, 21.5, 22.5, 23.1, 25.2, 38.3, 115.7, 119.1, 123.2, 123.5, 129.0, 129.9, 150.0, 153.8, 156.4, 158.3, 164.6, 166.1, FAB Mass : m/z 389.21 (M^+), CHN analysis : Found : C (61.75%), H (6.51%), N (14.46%), Calc. : C (61.84%), H (6.49%), N (14.42%).

References:

[1]. Adrien A, Advances in Heterocyclic Chemistry, United Kingdom Ed., 32, Academic Press, London, 1982, 30.
[2]. Patel, R.; Desai, K.; Chikhalia, K. *J. Ind. Chem. Soc.* **80**, 138(2003).
[3]. Desai, K.; Patel, R.; Chikhalia, K. *J. Ind. Chem.* **45 (B)**, 773(2006).
[4]. Amr, A.E., Nermien, M.S., Abdulla, M.M. (2007) *Monatsh. Chem.* **138**, 699.
[5]. Fujiwara, N., Nakajima, T., Ueda, Y., Fujita, H., Kawakami, H. (2008) *Bioorg. Med. Chem.* **16**, 9804.
[6]. Ballell, L., Field, R.A., Chung, G.A.C., Young, R.J. (2007) *Bioorg. Med. Chem. Lett*. **17**, 1736.
[7]. Wagner, E., Al-Kadasi, K., Zimecki, M., Sawka-Dobrowolska, W. (2008) *Eur. J. Med. Chem.* **43**, 2498.
[8]. Cordeu, L., Cubedo, E., Bandres, E., Rebollo, A., Saenz, X., Chozas, H., Victoria Dominguez, M., Echeverria,M., Mendivil, B., Sanmartin, C. (2007) *Bioorg. Med. Chem.* **15**, 1659.
[9]. Gorlitzer, K., Herbig, S., Walter, R.D. (1997) *Pharmazie* **52**, 670.
[10]. Ukrainets, I.V.; Tugaibei, I.A.; Bereznykova, N.L.; Karvechenko, V.N.; Turov, A.V. *Chemistry of Heterocyclic Compounds* **5**, p565(2008).
[11]. Kurono, M.; Hayashi, M.; Miura, K.; Isogawa, Y.; Sawai, K. Sanwa Kagaku Kenkyusho Co., *Japan*, *Kokai Tokkyo Koho* JP 62, 267, 272, 1987; Chem. Abstr. 1988, 109, 37832t.
[12]. Wang, S.Q.; Fang, L.; Liu, X.J.; Zhao, K. *Chinese Chem. Lett.* **15**, p885(2004).
[13]. Yang, W.; Ruan, Z.; Wang, Y.; Van Kirk, K.; Ma, Z.; Arey, B. J.; Cooper, C.B.; Seethala, R.; Feyen, J.H.M.; Dickson, J.K. *J. Med. Chem.* **52**,p 1204(2009).
[14]. Gillespie, R.J.; Bamford, S.J.; Botting, R.; Comer, M.; Denny, S.; Gaur, S.; Griffin, M.; Jordan, A.M.; Knight,A.R.; Lerpiniere, J.; Leonardi, S.; Lightowler, S.; McAteer, S.; Merrett, A.; Misra, A.; Padfield, A.; Reece,M.; Saadi, M.; Selwood, D.L.; Stratton, G.C.; Surry, D.; Todd, R.; Tong, X.; Ruston, V. *J. Med. Chem.* **52**,p33(2009).
[15]. I. L. Finar, Organic Chemistry, Vol. 1, 6th ed., Pearson Education Asia Ltd., Hong Kong, 2003, p. 460.
[16]. P. Y. S. Lam, P. K. Jadhav, C. J. Eyermann, C. N. Hodge, Y. Ru, L. T. Bacheler, J. L. Meek, M. J. Otto, M. M. Rayner, Y. N. Wong, C. H. Chang, P. C. Weber, D. A. Jackson, T. R. Sharpe, S. Erickson-Viitanen, Science 263 (1994) 380.
[17]. J. L. Castro, R. G. Ball, H. B. Broughton, M. G. N. Russell, D. Rathbone, A. P. Watt, R. Baker, K. L. Chapman, A. E. Fletcher, S. Patel, A. J. Smith, G. R. Marshall, W. Ryecroft, V. G. Matassa, J. Med. Chem. 39 (1996) 842
[18]. H. Pluempe, W. Pulls, Chemical Abstracts. **1971**, 74, 12511544n.
[19]. D. Subba Rao, G. Madhava, C. Naga Raju, M. Balaji, S. Madhusudhana, A. Usha Rani, *Med Chem. Res*., **2016**, 25, 751-768.
[20]. R. Chenna Krishna Reddy, S. Rasheed, D. SubbaRao, S. Adam, Y. Venkataramireddy, C. Naga Raju, *The Scientific World Journal*. **2013**.
[21]. F. Fournet, C. Sannier, N. Monteny, *J. Amer Mosq. Control Assoc*., **1993**, 9(4), 420-430.

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