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RESEARCH ARTICLE

Preparation and Characterization of a Series of Narrative Pyrimidine Derivatives

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ABSTRACT

Synthesis of a series of *1,2,3,4-tetrahydro-4-(substitutedphenyl)-6-methyl-2-oxo-N-(pyridin-3-yl)pyrimidine-5-carboxamide (4a-h)* was achieved from different Aldehydes, N-(pyridin-3-yl)-3-oxo-butanamide and urea using catalytical amount of concentrated hydrochloric acid in ethanol the product obtained was isolated and recrystallized from ethanol. So to the fine yield. The structures of the products were supported by FTIR, ^{1}H NMR and mass spectral data.

KEYWORDS

N-(Pyridin-3-yl)-3-Oxo-Butanamide, Aldehyde, Hydrochloric Acid and Urea Only Refluxed

INTRODUCTION

Heterocyclic nucleus imparts an important role in medicinal chemistry and serves as a key template for the development of various therapeutic agents. Synthetic studies of fused Pyrimidine have been reported extensively because of their structural diversity and association with a wide spectrum of biological activity.

It has been observed over the years that thiazole nucleus possess different biological activities such as antihypertensive[1], anti-inflammatory[2], anti-schizophrenic[3], antibacterial[4], anti-HIV[5], hypnotic[6], anti-allergic[7] and more recently analgesic[8], fibrinogen receptor antagonists with antithrombotic activity[9].

Here few Fluoro Containing Pyrimidine Derivatives[10] synthesis 4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-phenyl)-2-thioxopyrimidine-5- carboxamide and this pyrimidine derivatives[11]

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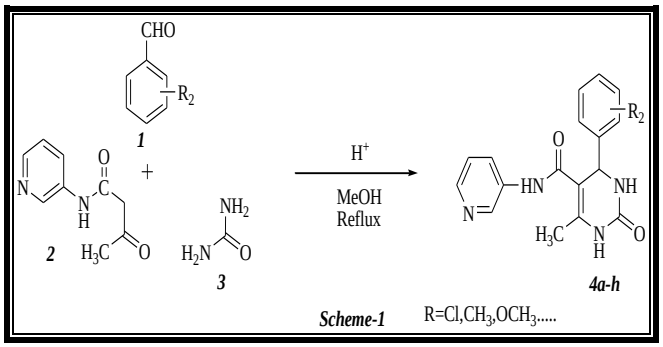
1,2,3,4-Tetrahydropyrimidine (DHPM) calcium channel blockers are important class of drugs which induce relaxation of vascular smooth muscle, preferentially in arteries, and display a negative inotropic effect on isolated cardiac muscle[12].

They exert these effects by binding to a high affinity binding site in L-type voltage dependent Ca^{2+} channels[13]. So, this class of drug is effective in the treatment of hypertension, angina pectoris and other cardiovascular disorder[14].

DHPMs may lead to other beneficial effects such as regression of left ventricular pressure and vascular hypertrophy, renal protection, weak anti-platelet, anti-ischemic and anti- atherogenic activity[15-18].

We have urbanized a new etiquette for the synthesis 1,2,3,4-tetrahydro-4-(substituted-phenyl)-6-methyl-2-oxo-N-(pyridin-3-yl)pyrimi-dine-5-carboxamide ***(4a-h)*** with the advantage of fine yield and environmentally easiness (**Scheme-1**).



Scheme-1

EXPERIMENTAL

Typical Experimental Procedure

A mixture of N-(pyridin-3-yl)-3-oxo-butanamide, appropriate aromatic aldehydes, urea and catalytical amount of concentrated hydrochloric acid in ethanol was heated under reflux condition for 8 to10 hrs. The reaction mixture was kept at room temperature for 24 hrs. The product obtained was isolated and recrystallized from ethanol.

1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenyl-N-(pyridin-3-yl)pyrimidine-5-carboxamide (4a)

Yield: 66%; mp 160-162 ºC; IR (cm^{-1}): 3331 (N-H stretching of primary amide), 3294 (N-H stretching of pyrimidine ring), 3059 (C-H symmetrical stretching of CH_3 group), 3024 (C-H stretching of aromatic ring), 2931 (C-H asymmetrical stretching of CH_3 group), 1699 (C=O stretching of amide), 1631 and 1525 (C=C stretching of aromatic ring), 1593 (N-H deformation of pyrimidine ring), 1460 (C-H asymmetrical deformation of CH_3 group), 1342 (C-H symmetrical deformation of CH_3 group), 1323 (C-N-C stretching of pyrimidine ring), 1282 (C-N stretching of pyrimidine ring), 1234 (C-H in plane deformation of aromatic ring), 759 and 713 (C-H out of plane deformation of mono substituted benzene ring); 1H NMR (DMSO-d6) δ ppm: 2.25 (s, 3H, Ha), 5.43 (s, 1H, Hb), 7.21-7.36 (m, 6H, Hcc'-f), 7.67 (s, 1H, Hg), 7.95-7.97 (d, 1H, Hh, J = 8.0 Hz), 8.20-8.21 (d, 1H, Hi, J = 4.0 Hz), 8.69 (s, 1H, Hk), 9.76 (s, 1H, Hl): m/z 308; Anal. Calcd. for $C_{17}H_{16}N_4O_2$: C, 66.22; H, 5.23; N, 18.17; O, 10.38. Found: C, 66.15; H, 5.20; N, 18.11; O, 10.30%.

1,2,3,4-tetrahydro-6-methyl-2-oxo-N-(pyridin-3-yl)-4-p-tolylpyrimidine-5-carboxamide (4b)

Yield: 64%; mp 191-193 ºC; MS: m/z 322; IR (cm^{-1}): 3334 (N-H stretching of primary amide), 3290 (N-H stretching of pyrimidine ring), 3054 (C-H symmetrical stretching of CH_3 group), 3024 (C-H stretching of aromatic ring), 2931 (C-H asymmetrical stretching of CH_3 group), 1654 (C=O stretching of amide), 1630 and 1615 (C=C stretching of aromatic ring), 1590 (N-H deformation of pyrimidine ring), 1430 (C-H asymmetrical deformation of CH_3 group), 1332 (C-H symmetrical deformation of CH_3 group), 1303 (C-N-C stretching of pyrimidine ring), 1252 (C-N stretching of pyrimidine ring), 1235 (C-H in plane deformation of aromatic ring), 755 and 753 (C-H out of plane deformation of mono substituted benzene ring); Anal. Calcd. for $C_{18}H_{18}N_4O_2$: C, 67.07; H, 5.63; N, 17.38; O, 9.93. Found: C, 67.02; H, 5.59; N, 17.31, O, 9.90%.

1,2,3,4-tetrahydro-4-(4-methoxyphenyl)-6-methyl-2-oxo-N-(pyridin-3-yl) pyrimidine-5-carboxamide (4c)

Yield: 63%; mp 221-223 ºC; IR (cm^{-1}): 3498 (N-H stretching of primary amide), 3230 (N-H stretching of pyrimidine ring), 3115 (C-H symmetrical stretching of CH_3 group), 2937 (C-H asymmetrical stretching of CH_3 group), 1712 (C=O stretching of amide), 1641 (N-H deformation of pyrimidine ring), 1525 and 1483 (C=C stretching of aromatic ring), 1435 (C-H asymmetrical deformation of CH_3 group), 1408 (C-N-C stretching of pyrimidine ring), 1340 (C-H symmetrical deformation of CH_3 group), 1276 (C-N stretching of pyrimidine ring), 1240 (Ph-O-C asymmetrical stretching of ether linkage), 1174 (C-H in plane deformation of aromatic ring), 1062 (Ph-O-C symmetrical stretching of ether linkage), 866 (C-H out of plane deformation of 1,4-disubstitution); 1H NMR (DMSO-d6) δ ppm: 2.11 (s, 3H, Ha), 3.73 (s, 3H, Hb), 5.44 (s, 1H, Hc), 6.82-6.84 (d, 2H, Hdd', J = 8.0 Hz), 7.18-7.25 (m, 3H, He-g), 7.49 (s, 1H, Hh), 7.99-8.00 (d, 2H, Hii', J = 4.0 Hz), 8.17-8.18 (d, 1H, Hj, J = 4.0 Hz), 8.70 (s, 2H, Hkj), 9.60 (s, 1H, Hl); MS: m/z 338; Anal. Calcd. for

$C_{18}H_{18}N_4O_3$: C, 63.89; H, 5.36; N, 16.56; O, 14.19. Found: C, 63.81; H, 5.30; N, 16.50; O, 14.11%.

4-(4-chlorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxo-N-(pyridin-3-yl) pyrimidine-5-carboxamide (4d)

Yield: 76%; mp 199-201 ºC; MS: m/z 342; IR (cm^{-1}): 3344 (N-H stretching of primary amide), 3298 (N-H stretching of pyrimidine ring), 3056 (C-H symmetrical stretching of CH_3 group), 3024 (C-H stretching of aromatic ring), 2934 (C-H asymmetrical stretching of CH_3 group), 1664 (C=O stretching of amide), 1630 and 1616 (C=C stretching of aromatic ring), 1596 (N-H deformation of pyrimidine ring), 1436 (C-H asymmetrical deformation of CH_3 group), 1338 (C-H symmetrical deformation of CH_3 group), 1313 (C-N-C stretching of pyrimidine ring), 1264 (C-N stretching of pyrimidine ring), 1230 (C-H in plane deformation of aromatic ring), 982 (C-Cl stretching), 734 and 713 (C-H out of plane deformation of mono substituted benzene ring); Anal. Calcd. for $C_{17}H_{15}ClN_4O_2$: C, 59.57; H, 4.41; N, 16.34; O, 9.34. Found: C, 59.51; H, 4.35; N, 16.27; O, 9.25%.

4-(4-fluorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxo-N-(pyridin-3-yl)pyrimidine-5-carboxamide (4e)

Yield: 80%; mp 198-200 ºC; MS: *m/z* 326; IR (cm^{-1}): 3338 (N-H stretching of primary amide), 3220 (N-H stretching of pyrimidine ring), 3133 (C-H symmetrical stretching of CH_3 group), 2937 (C-H asymmetrical stretching of CH_3 group), 1735 (C=O stretching of amide), 1637 (N-H deformation of pyrimidine ring), 1483 (C=C stretching of aromatic ring), 1433 (C-H asymmetrical deformation of CH_3 group), 1419 (C-N-C stretching of pyrimidine ring), 1334 (C-H symmetrical deformation of CH_3 group), 1253 (C-N stretching of pyrimidine ring), 1230 (Ph-O-C asymmetrical stretching of ether linkage), 1173 (C-H in plane deformation of aromatic ring), 1064 (Ph-O-C symmetrical stretching of ether linkage), 1003 (C-F stretching), 860 (C-H out of plane deformation of 1,4-disubstitution); Anal. Calcd. for $C_{17}H_{15}FN_4O_2$: C, 62.57; H, 4.63; N, 17.17; O, 9.81. Found: C, 62.50; H, 4.57; N, 17.10; O, 9.75%.

1,2,3,4-tetrahydro-6-methyl-4-(4-nitrophenyl)-2-oxo-N-(pyridin-3-yl) pyrimidine-5-carboxamide (4f)

Yield: 69%; mp 183-185 ºC; IR (cm^{-1}): 3298 (N-H stretching of primary amide), 3234 (N-H stretching of pyrimidine ring), 3026 (C-H symmetrical stretching of CH_3 group), 2829 (C-H asymmetrical stretching of CH_3 group), 1689 (C=O stretching of amide), 1600 and 1471 (C=C stretching of aromatic ring), 1583 (C-NO_2 symmetrical stretching), 1521 (N-H deformation of pyrimidine ring), 1423 (C-N stretching of pyrimidine ring), 1390 (C-H asymmetrical deformation of CH_3 group), 1348 (C-N-C stretching of pyrimidine ring), 1309 (C-H symmetrical deformation of CH_3 group), 1244 (C-H in plane deformation of aromatic ring), 798 (C-H out of plane deformation of 1,4-disubstitution); 1H NMR (DMSO-d6) δ ppm: 2.19 (s, 3H, Ha), 5.63 (s, 1H, Hb), 7.18-7.22 (m, 1H, Hc), 7.49 (s, 1H, Hd), 7.59-7.61 (d, 2H, Hee', J = 8.0 Hz), 8.01-8.03 (d, 1H, Hf, J = 8.0 Hz), 8.14-8.16 (d, 2H, Hgg', J = 8.0 Hz), 8.23-8.24 (d, 1H, Hh, J = 4.0 Hz), 8.71-8.73 (d, 2H, Hii', J = 8.0 Hz), 9.60 (s, 1H, Hj); MS: m/z 353; Anal. Calcd. for C17H15N5O4: C, 57.79; H, 4.28; N, 19.82; O, 18.11. Found: C, 57.69; H, 4.20; N, 19.76; O, 18.04%.

1,2,3,4-tetrahydro-6-methyl-4-(3-nitrophenyl)-2-oxo-N-(pyridin-3-yl) pyrimidine-5-carboxamide (4g)

Yield: 65%; mp 192-194 ºC; MS: m/z 353; IR (cm^{-1}): 3278 (N-H stretching of primary amide), 3244 (N-H stretching of pyrimidine ring), 3046 (C-H symmetrical stretching of CH_3 group), 2879 (C-H asymmetrical stretching of CH_3 group), 1699 (C=O stretching of amide), 1664 and 1471 (C=C stretching of aromatic ring), 1583 (C-NO_2 symmetrical stretching), 1521 (N-H deformation of pyrimidine ring), 1413 (C-N stretching of pyrimidine ring), 1365 (C-H asymmetrical deformation of CH_3 group), 1346 (C-N-C stretching of pyrimidine ring), 1300 (C-H symmetrical deformation of CH_3 group), 1243 (C-H in plane deformation of aromatic ring), 778

(C-H out of plane deformation of 1,4-disubstitution); Anal. Calcd. for $C_{17}H_{15}N_5O_4$: C, 57.79; H, 4.28; N, 19.82; O, 18.11. Found: C, 57.71; H, 4.22; N, 19.78; O, 18.04%.

1,2,3,4-tetrahydro-6-methyl-4-(2-nitrophenyl)-2-oxo-N-(pyridin-3-yl) pyrimidine-5-carboxamide (4h)

Yield: 79%; mp 226-228 ºC; MS: *m/z* 353; IR (cm^{-1}): 3264 (N-H stretching of primary amide), 3264 (N-H stretching of pyrimidine ring), 3037 (C-H symmetrical stretching of CH_3 group), 2829 (C-H asymmetrical stretching of CH_3 group), 1680 (C=O stretching of amide), 1654 (C=C stretching of aromatic ring), 1581 (C-NO_2 symmetrical stretching), 1520 (N-H deformation of pyrimidine ring), 1420 (C-N stretching of pyrimidine ring), 1343 (C-H asymmetrical deformation of CH_3 group), 1341 (C-N-C stretching of pyrimidine ring), 1311 (C-H symmetrical deformation of CH_3 group), 1241 (C-H in plane deformation of aromatic ring), 791 (C-H out of plane deformation of 1,4-disubstitution); Anal. Calcd. for $C_{17}H_{15}N_5O_4$: C, 57.79; H, 4.28; N, 19.82; O, 18.11. Found: C, 57.70; H, 4.23; N, 19.75; O, 18.00%.

CONCLUSION

In pinnacle, we contain synthesized of inventive pyrimidine derivatives using trouble-free and appropriate method. This method produces these products in first-class yields and trouble-free workup. Product is isolated by easy filtration. The isolated products are very pure and do not need any column purification. This study opens up a new area of beneficial synthesis of potentially biologically active narrative pyrimidine derivatives compounds.

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