International Journal for Pharmaceutical Research Scholars (IJPRS)

V-5, I-1, 2016 ISSN No: 2277 - 7873

RESEARCH ARTICLE

Synthesis of Plausible Fluoro Containing Pyrimidine Derivatives

Pooja Kothari*[1], Hemangi Desai[2]

[1]*Research Scholar, Department of Chemistry, Veer Narmad South Gujarat University, Surat, India.*

[2]*Shree Ramkrishna Institute of Computer Education and Applied Sciences, Gujarat, India.*

Manuscript No: IJPRS/V5/I1/00032, Received On: 23/02/2016, Accepted On: 06/03/2016

ABSTRACT

Synthesis of a series of ***4-(4-(4-(trifluoromethyl)-2-nitrophenoxy)phenyl)-N-(substitutedphenyl) -1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4a-j)*** was completed from 4-(4-(trifluoromethyl)-2-nitrophenoxy)benzaldehyde, N-(substituted phenyl)-3-oxobutanamides and using catalytical amount of Conc. hydrochloric acid in methanol the product obtained was isolated. So to the excellent yield. The structures of the products were supported by FTIR, ^{1}H NMR and mass spectral data.

KEYWORDS

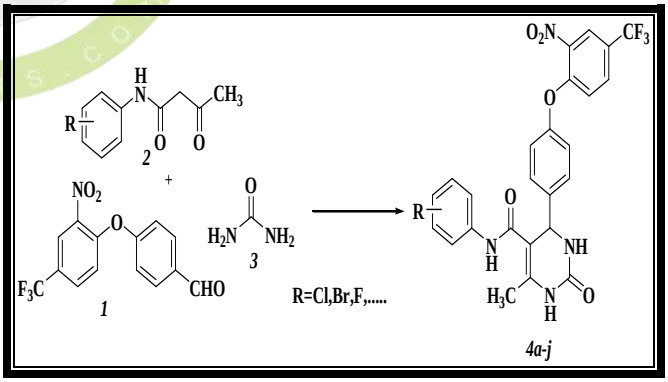
N-(Substituted phenyl)-3-Oxobutanamides, 4-(4-(Trifluoromethyl)-2-Nitrophenoxy) Benzaldehyde, Conc. HCl, Methanol Only Refluxed

INTRODUCTION

Biological activity of the pyrimidine derivatives has led us to the synthesis of substituted pyrimidine. It has been found to be associated with diverse biological activities.[1] The synthesis of substituted pyrimidine and many detailed reviews have been appeared.[2,3]. The nitrogen containing portion may be an amidine, urea, thiourea or guanidine and acetyl acetone serves as an brilliant instructive model in that it eagerly undergoes reaction with formamidine,[4] guanidin,[5] urea,[6] or thiourea[7] to produce the corresponding pyrimidines. The structure of the pyrimidine ring is similar to benzene and pyridine[8]. The key role pyrimidines play in cellular processes has made them valuable leads for drug discovery[9]. Pyrimidine derivatives are known to be biologically active compounds and substituted pyrimidines have shown wide range of biological activities like antitubercular[10-14], antibacterial[15-17], antioxidant, anti-inflammatory[18] activity.

***Address for Correspondence:**
Pooja Kothari,
Research Scholar Department of Chemistry, Veer Narmad South Gujarat University, Surat, India.
E-Mail Id: pooja_kothari201020@yahoo.com

And Synthesis of a series of 1,2,3,4-tetrahydro-4-(substitutedphenyl)-6-methyl-2-oxo-N-(pyridin-3-yl)pyrimidine-5-carboxamide[19] and 1,2,3,4-tetrahydro-4-(substitutedphenyl)-6-methyl-N-(pyridin-3-yl)-2-thioxo pyrimidine-5-carboxamide[20].



EXPERIMENTAL

Typical Untried Procedure

A mixture of *N*-(substituted phenyl)-3-oxobutanamides, 4-(4-(trifluoromethyl)-2-nitrophenoxy) benzaldehyde, urea and catalytic

amount of conc. hydrochloric acid in methanol was heated under reflux condition for 7 to 12 hrs.

The reaction mixture was kept at room temperature for 24 hrs. The crystalline product obtained and recrystallized from ethanol.

4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-N-(4-chlorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4a)

Yield: 62%; mp 200ºC; Anal. Calcd. For $C_{25}H_{18}ClF_3N_4O_5$: CC, 54.91; H, 3.32; Cl, 6.48; F, 10.42; N, 10.24; O, 14.63; Found: C, 54.90; H, 3.30; Cl, 6.49; F, 10.43; N, 10.20; O, 14.68%; IR (cm^{-1}): 3440 (N-H stretching of amide), 3074 (C-H stretching of aromatic ring), 2945 (C-H asymmetrical stretching of CH_3 group), 2845 (C-H symmetrical stretching of CH_3 group), 1694 (C=O stretching of amide), 1694 (C=O stretching of cyclic) 1604 (N-H deformation of pyrimidine ring), 1545 (C=C stretching of aromatic ring), 1545 (C-NO_2 asymmetrical deformation of NO_2 group), 1459 (C-H asymmetrical deformation of CH_3 group), 1354 (C-H symmetrical deformation of CH_3 group), 1354 (C-N-C stretching vibration of pyrimidine ring), 1354 (C-NO_2 symmetrical deformation of NO_2 group), 1275 (C-N stretching), 1245 (C-O-C asymmetrical stretching OCH_3), 1155, 1054 (C-H in plane deformation of aromatic ring), 1035 (C-F stretching) 825 (para-substituted); MS: *m/z* 547; ^{1}H NMR (DMSO-*d6*) δ ppm: 2.03 (s, 3H, H_a), 5.43-5.44 (s, 1H, H_b), 6.95-6.99 (d, 1H, H_c), 7.10 (s, 1H, H_d), 7.14-7.17 (m, 1H, H_e), 7.25-7.28 (d, 3H, H_{fgh}), 7.45-7.54 (m, 3H, H_{ijk}), 7.67 (s, 1H, H_l), 8.20-8.27 (m, 1H, H_m), 8.82 (s, 1H, H_n), 8.86 (s, 1H, H_o), 9.70 (s, 1H, H_p).

4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-N-(4-bromophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4b)

Yield: 63%; mp 210ºC; Anal. Calcd. for $C_{25}H_{18}BrF_3N_4O_5$: C, 50.78; H, 3.07; Br, 13.51; F, 9.64; N, 9.47; O, 13.53; Found: C, 50.80; H, 3.05; Br, 13.58; F, 9.67; N, 9.40; O, 13.50%; MS: *m/z* 591.

4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-N-(4-fluorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4c)

Yield: 57%; mp 197ºC; Anal. Calcd. for $C_{25}H_{18}F_4N_4O_5$: C, 56.61; H, 3.42; F, 14.33; N, 10.56; O, 15.08; Found: C, 56.63; H, 3.44; F, 14.35; N, 10.54; O, 15.04%; IR (cm^{-1}): 3327 (N-H stretching of amide), 3101 (C-H stretching of aromatic ring), 2942 (C-H asymmetrical stretching of CH_3 group), 2828 (C-H symmetrical stretching of CH_3 group), 1702 (C=O stretching of amide), 1681 (C=O stretching of cyclic) 1583 (N-H deformation of pyrimidine ring), 1533 (C=C stretching of aromatic ring), 1514 (C-NO_2 asymmetrical deformation of NO_2 group), 1433 (C-H asymmetrical deformation of CH_3 group), 1393 (C-H symmetrical deformation of CH_3 group), 1342 (C-NO_2 symmetrical deformation of NO_2 group), 1342 (C-N-C stretching vibration of pyrimidine ring), 1243 (C-N stretching), 1143 (C-H in plane deformation of aromatic ring), 1084 (C-F stretching) 829 (para-substituted), 761 (C-H in out plane deformation of aromatic ring), 763 (C-Cl stretching) ; MS: *m/z* 530; ^{1}H NMR (DMSO-*d6*) δ ppm: 2.09 (s, 3H, H_a), 5.40-5.43 (s, 1H, H_b), 7.00-7.10 (m, 3H, H_c), 7.23-7.26 (d, 2H, $H_{dd'}$), 7.40-7.43 (d, 2H, $H_{ee'}$), 7.54-7.57 (m, 2H, H_{fg}), 7.68 (s, 1H, H_h), 8.43-8.46 (s, 1H, H_i), 8.81 (s, 1H, H_j), 8.88 (s, 1H, H_k), 9.69 (s, 1H, H_l).

4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-N-(4-nitrophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4d)

Yield: 62%; mp 202ºC; Anal. Calcd. for $C_{25}H_{18}F_3N_5O_7$: C, 53.87; H, 3.25; F, 10.22; N, 12.56; O, 20.09; Found: C, 53.88; H, 3.26; F, 10.26; N, 12.53; O, 20.06%; MS: *m/z* 557.

4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-N-(4-methylphenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4e)

Yield: 70%; mp 200ºC; Anal. Calcd. for $C_{26}H_{21}F_3N_4O_5$: C, 59.32; H, 4.02; F, 10.83; N, 10.64; O, 15.20; Found: C, 59.37; H, 4.00; F, 10.80; N, 10.62; O, 15.22%; MS: *m/z* 526.

4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-N-(3-chlorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4f)

Yield: 60%; mp 199ºC; Anal. Calcd. For $C_{25}H_{18}ClF_3N_4O_5$: CC, 54.91; H, 3.32; Cl, 6.48; F,

10.42; N, 10.24; O, 14.63; Found: C, 54.93; H, 3.34; Cl, 6.42; F, 10.40; N, 10.22; O, 14.69%; MS: *m/z* 547.

4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-N-(3-bromophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4g)

Yield: 63%; mp 210ºC; Anal. Calcd. for $C_{25}H_{18}BrF_3N_4O_5$: C, 50.78; H, 3.07; Br, 13.51; F, 9.64; N, 9.47; O, 13.53; Found: C, 50.79; H, 3.03; Br, 13.57; F, 9.64; N, 9.43; O, 13.53%; MS: *m/z* 591.

4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-N-(3-fluorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4h)

Yield: 59%; mp 198ºC; Anal. Calcd. for $C_{25}H_{18}F_4N_4O_5$: C, 56.61; H, 3.42; F, 14.33; N, 10.56; O, 15.08; Found: C, 56.65; H, 3.46; F, 14.39; N, 10.50; O, 15.00%; MS: *m/z* 530.

4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-N-(2-fluorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4j)

Yield: 57%; mp 195ºC; Anal. Calcd. For $C_{25}H_{18}F_4N_4O_5$: C, 56.61; H, 3.42; F, 14.33; N, 10.56; O, 15.08; Found: C, 56.66; H, 3.49; F, 14.35; N, 10.45; O, 15.05%; MS: *m/z* 530.

4-(4-(4-(trifluoromethyl)-2-nitrophenoxy) phenyl)-N-(2-chlorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxamide (4j)

Yield: 57%; mp 195ºC; Anal. Calcd. For $C_{25}H_{18}ClF_3N_4O_5$: C, 54.91; H, 3.32; Cl, 6.48; F, 10.42; N, 10.24; O, 14.63; Found: C, 54.96; H, 3.30; Cl, 6.50; F, 10.44; N, 10.27; O, 14.77%; MS: *m/z* 547.

CONCLUSION

In construct, we take in synthesized of creative pyrimidine derivatives using without any troubles and suitable method. By method produces these products in good yield and trouble-free workup. Product is isolated by easy filtration. The isolated products are much unpolluted and do not need any another purification.

REFERENCES

1. Ghoneim, K. M., and Youssef, R. (1986). *Journal of Indian Chemical Society*, 53, 914.
2. Kenner, G. W. and Todd, A. (1957). Heterocyclic Compounds, Ed. R C Elderfield, Wiley, New York, 6.
3. Brown, D. J. (2009). *The Chemistry of Heterocyclic Compounds, The Pyrimidines* (Vol. 52). John Wiley & Sons., 16.
4. Hunt, R. R., McOmie, J. F. M., and Sayer, E. R. (1959). *Journal of the Chemical Society*, 525.
5. Haley, C. A. C., & Maitland, P. (1951). 697. Organic reactions in aqueous solution at room temperature. Part I. The influence of pH on condensations involving the linking of carbon to nitrogen and of carbon to carbon. *Journal of the Chemical Society (Resumed)*, 3155-3174.
6. Hale, W. J. (1914). *J Am Chem Soc*, 36,104.
7. Hunt, R. R., McOmie, J. F. M., and Sayer, E. R. (1959). *Journal of the Chemical Society*, 527.
8. Bano, T., Kumar, N., & Dudhe, R. (2012). Free radical scavenging properties of pyrimidine derivatives. *Organic and Medicinal Chemistry Letters*, *2*(1), 1-6.
9. Kotaiah, Y., Krishna, N. H., Raju, K. N., Rao, C. V., Jonnalagadda, S. B., & Maddila, S. (2012). Synthesis and biological evaluation of novel isopropyl 2-thiazolopyrimidine-6-carboxylate derivatives. *Journal of the Korean Chemical Society*, *56*(1), 68-73.
10. Elumalai, K., Ali, M. A., Elumalai, M., Eluri, K., & Srinivasan, S. (2013). Novel isoniazid cyclocondensed 1, 2, 3, 4-tetrahydropyrimidine derivatives for treating infectious disease: a synthesis and in vitro biological evaluation. *Journal of Acute Disease*, *2*(4), 316-321.
11. Trivedi, A. R., Dodiya, D. K., Ravat, N. R., & Shah, V. H. (2008). Synthesis and

biological evaluation of some new pyrimidines via a novel chalcone series. *Arkivoc*, *11*, 131-141.

12. Khoje, A. D., Kulendrn, A., Charnock, C., Wan, B., Franzblau, S., & Gundersen, L. L. (2010). Synthesis of non-purine analogs of 6-aryl-9-benzylpurines, and their antimycobacterial activities. Compounds modified in the imidazole ring. *Bioorganic & Medicinal Chemistry*, *18*(20), 7274-7282.
13. Chaudhari, P. K., Pandey, A., & Shah, V. H. (2010). Synthesis and biological studies of 1, 2, 3, 4-tetrahydro pyrimidine derivatives. *Oriental Journal of Chemistry*, *26*(4), 1377.
14. Shmalenyuk, E. R., Kochetkov, S. N., & Alexandrova, L. A. (2013). Novel inhibitors of Mycobacterium tuberculosis growth based on modified pyrimidine nucleosides and their analogues. *Russian Chemical Reviews*, *82*(9), 896.
15. Doan, T. N., & Tran, D. T. (2011). Synthesis, antioxidant and antimicrobial activities of a novel series of chalcones, pyrazolic chalcones, and allylic chalcones. *Pharmacology & Pharmacy*, *2*(04), 282.
16. Jyothi, M. V., Prasad, Y. R., Venkatesh, P., & Sureshreddy, M. (2012). Synthesis and Antimicrobial Activity of Some Novel Chalcones of 3-Acetyl Pyridine and their Pyrimidine Derivatives. *Chemical Science Transactions*, *1*(3), 716-722.
17. Rao, N. S., Kistareddy, C., Balram, B., & Ram, B. (2012). Synthesis and antibacterial activity of novel imidazo [1, 2-a] pyrimidine and imidazo [1, 2-a] pyridine chalcones derivatives. *Der Pharma Chemica*, *4*(6), 2408-2415.
18. Bhalgat, C. M., Ali, M. I., Ramesh, B., Ramu, G. (2011). *Arabian Journal of Chemistry*, 1-8.
19. Vakhariya, C., Ram, H., Shah, V., (2015). *International Journal for Pharmaceutical Research Scholars*, *4*(4), 141-145.
20. Vakhariya, C., Ram, H., Shah, V. (2016). *European Journal of Biomedical and Pharmaceutical sciences*, *3*(1), 247-250.

