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A NEW MANEUVER ETIQUETTE FOR SYNTHESIS OF TETRAHYDROPYRIMIDINE DERIVATIVES

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ABSTRACT

Synthesis of a series of *4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(substitutedphenyl)-2-oxopyrimidine-5-carboxamide*. *(4a-j)* was achieved from different N-(substitutedphenyl)-4-methyl-3-oxopentanamide and 2-chloro-6-fluorobenzaldehyde using few drops of conc. hydrochloric acid added and refluxed with methanol so to the fine yield. The structures of the products were supported by FTIR, NMR and mass spectral data.

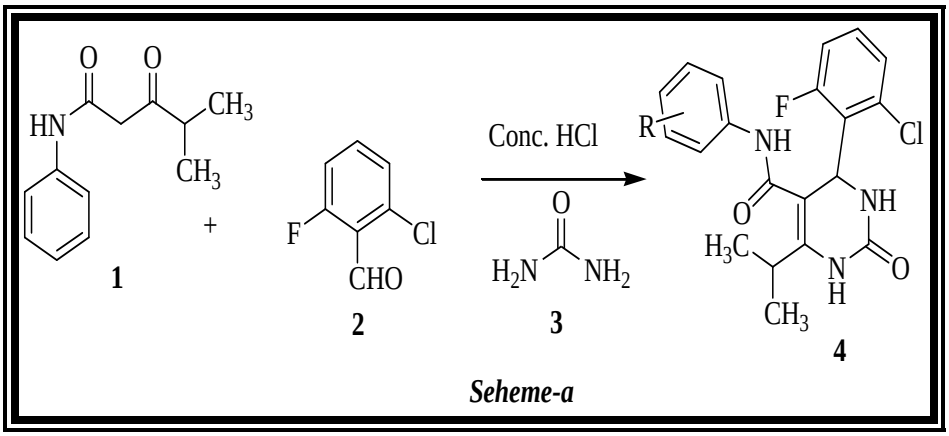
KEYWORDS: 2-chloro-6-fluorobenzaldehyde; hydrochloric acid, methanol only refluxed.

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], inhibitors of bacterial DNA gyrase B [10] and antitumor and cytotoxic activities. Chemicals possessing pyrimidine and dihydro-pyrimidinone (DHPMs) entities showed a wide range of pharmacological properties including antiviral, antitumor, antibacterial, anti-inflammatory

activities [11,12], calcium channel blocking [13], and neuropeptide Y (NPY) antagonistic activity [14]. DHPMs are used as therapeutics agents in the clinical treatment of cardiovascular diseases [15] such as hypertension [16], cardiac arrhythmias and orangina pectoris [17].

We have developed a new decorum for the synthesis 4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(substitutedphenyl)-2-oxopyrimidine-5-carboxamide ***(4a-j)*** with the advantage of fine yield and environmentally easiness (**Scheme-1**).



Seheme-a

EXPERIMENTAL

Typical experimental procedure for the synthesis of fluoro containing pyrimidine derivativess.

To the mixture of N-(substituted phenyl)-4-methyl-3-oxopentanamide, 2-chloro-6-fluorobenzaldehyde and urea in 10 ml ethanol was added one/two drops of Conc. HCl with stirring for 20 hrs. at ambient temperature. After 20 hrs total reaction mass pour in water, Insoluble solid was generated, then filter and crystallization by ethanol.

4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(2-methoxyphenyl)-2-oxo -pyrimidine-5-carboxamide (4a)

Yield: 61%; mp 185ºC; Anal. Calcd. for $C_{21}H_{21}ClFN_3O_3$: C, 60.36; H, 5.07; Cl, 8.48; F, 4.55; N, 10.06; O, 11.49; Found: C, 60.31; H, 5.02; Cl, 8.41; F, 4.51; N, 10.01; O, 11.42%; IR (cm^{-1}): 3450 (N-H stretching of amide), 3110 (C-H stretching of aromatic ring), 2955 (C-H asymmetrical stretching of CH_3 group), 2886 (C-H symmetrical stretching of CH_3 group), 1653 (C=O stretching of amide), 1595 (C=O stretching of cyclic) 1595 (N-H deformation of pyrimidine ring), 1528 (C=C stretching of aromatic ring), 1477 (C-H asymmetrical deformation of CH_3 group), 1413 (C-H symmetrical deformation of CH_3 group), 1345 (C-N-C stretching vibration of pyrimidine ring), 1274 (C-O-C stretching), 1106 (C-F stretching),

1065 (C-H in plane deformation of aromatic ring), 835 (para-substituted), 785 (C-H in out plane deformation of aromatic ring), 671 (C-Cl stretching); ^{1}H NMR (DMSO-*d6*) δ ppm: 1.18 (s, 3H, H), 1.17 (s, 3H, H), 3.52-3.54 (m, 1H, H), 3.98 (s, 3H, H), 6.51 (s, 1H, H), 6.83-6.89 (m, 3H, H), 7.19-7.23 (m, 2H, H), 7.54-7.57 (m, 2H, H), 8.53 (s, 1H, H), 10.05 (s, 1H, H), 10.08 (s, 1H, H); MS: *m/z* 417.

4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(3-methoxyphenyl)-2-oxo - pyrimidine-5-carboxamide (4b)

Yield: 61%; mp 194ºC; Anal. Calcd. for $C_{21}H_{21}ClFN_3O_3$: C, 60.36; H, 5.07; Cl, 8.48; F, 4.55; N, 10.06; O, 11.49; Found: C, 60.32; H, 5.01; Cl, 8.48; F, 4.53; N, 10.06; O, 11.41%; IR (cm^{-1}): 3411 (N-H stretching of amide), 3101 (C-H stretching of aromatic ring), 2951 (C-H asymmetrical stretching of CH_3 group), 2880 (C-H symmetrical stretching of CH_3 group), 1650 (C=O stretching of amide), 1593 (C=O stretching of cyclic) 1593 (N-H deformation of pyrimidine ring), 1528 (C=C stretching of aromatic ring), 1477 (C-H asymmetrical deformation of CH_3 group), 1411 (C-H symmetrical deformation of CH_3 group), 1343 (C-N-C stretching vibration of pyrimidine ring), 1250 (C-O-C stretching), 1106 (C-F stretching), 1065 (C-H in plane deformation of aromatic ring), 830 (para-substituted), 781 (C-H in out plane deformation of aromatic ring), 671 (C-Cl stretching); ^{1}H NMR (DMSO-*d6*) δ ppm: 1.17 (s, 3H, H), 1.18 (s, 3H, H), 3.52-3.56 (m, 1H, H), 3.88 (s, 3H, H), 6.54 (s, 1H, H), 6.87-6.89 (m, 2H, H), 7.14-7.18 (m, 2H, H), 7.27 (s, 1H, H), 7.54-7.58 (m, 2H, H), 8.50 (s, 1H, H), 10.01 (s, 1H, H), 10.07 (s, 1H, H); MS: *m/z* 417.

4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(4-methoxyphenyl)-2-oxo - pyrimidine-5-carboxamide (4c)

Yield: 60%; mp 194ºC; Anal. Calcd. for $C_{21}H_{21}ClFN_3O_3$: C, 60.36; H, 5.07; Cl, 8.48; F, 4.55; N, 10.06; O, 11.49; Found: C, 60.30; H, 5.13; Cl, 8.50; F, 4.53; N, 10.02; O, 11.53%; IR (cm^{-1}): 3413 (N-H stretching of amide), 3058 (C-H stretching of aromatic ring), 2985 (C-H asymmetrical stretching of CH_3 group), 2874 (C-H symmetrical stretching of CH_3 group), 1645 (C=O stretching of amide), 1590 (C=O stretching of cyclic) 1590 (N-H deformation of pyrimidine ring), 1521 (C=C stretching of aromatic ring), 1477 (C-H asymmetrical deformation of CH_3 group), 1413 (C-H symmetrical deformation of CH_3 group), 1341 (C-N-C stretching vibration of pyrimidine ring), 1243 (C-O-C stretching), 1101 (C-F stretching), 1063 (C-H in plane deformation of aromatic ring), 828 (para-substituted), 775 (C-H in out plane deformation of aromatic ring), 679 (C-Cl stretching); ^{1}H NMR (DMSO-*d6*) δ ppm:

1.19 (s, 3H, H), 1.20 (s, 3H, H), 3.50-3.54 (m, 1H, H), 3.90 (s, 3H, H), 6.51 (s, 1H, H), 6.82-6.85 (d, 2H, H), 7.13-7.17 (d, 2H, H), 7.54-7.58 (m, 1H, H), 7.67 (m, 1H, H), 7.82-7.85 (m, 1H, H), 8.53 (s, 1H, H), 10.12 (s, 1H, H), 10.20 (s, 1H, H); MS: *m/z* 417.

4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(2-chlorophenyl)-2-oxo-pyrimidine-5-carboxamide (4d)

Yield: 57%; mp 192ºC; Anal. Calcd. for $C_{20}H_{18}Cl_2FN_3O_2$: C, 56.88; H, 4.30; Cl, 16.79; F, 4.50; N, 9.95; O, 7.58; Found: C, 56.80; H, 4.34; Cl, 16.74; F, 4.55; N, 9.92; O, 7.54%; IR (cm^{-1}): 3480 (N-H stretching of amide), 3100 (C-H stretching of aromatic ring), 2950 (C-H asymmetrical stretching of CH_3 group), 2882 (C-H symmetrical stretching of CH_3 group), 1653 (C=O stretching of amide), 1590 (C=O stretching of cyclic) 1590 (N-H deformation of pyrimidine ring), 1529 (C=C stretching of aromatic ring), 1479 (C-H asymmetrical deformation of CH_3 group), 1412 (C-H symmetrical deformation of CH_3 group), 1346 (C-N-C stretching vibration of pyrimidine ring), 1270 (C-N stretching), 1100 (C-F stretching), 1054 (C-H in plane deformation of aromatic ring), 845 (para-substituted), 765 (C-H in out plane deformation of aromatic ring), 659 (C-Cl stretching); ^{1}H NMR (DMSO-*d6*) δ ppm: 1.12 (s, 3H, H), 1.14 (s, 3H, H), 3.53-3.58 (m, 1H, H), 6.45 (s, 1H, H), 6.80-6.82 (m, 3H, H), 7.23-7.27 (m, 2H, H), 7.47-7.51 (m, 2H, H), 8.56 (s, 1H, H), 10.08 (s, 1H, H), 10.12 (s, 1H, H); MS: *m/z* 422.

4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(3-chlorophenyl)-2-oxo-pyrimidine-5-carboxamide (4e)

Yield: 59%; mp 200ºC; Anal. Calcd. for $C_{20}H_{18}Cl_2FN_3O_2$: C, 56.88; H, 4.30; Cl, 16.79; F, 4.50; N, 9.95; O, 7.58; Found: C, 56.81; H, 4.35; Cl, 16.74; F, 4.57; N, 9.91; O, 7.63%; IR (cm^{-1}): 3474 (N-H stretching of amide), 3102 (C-H stretching of aromatic ring), 2976 (C-H asymmetrical stretching of CH_3 group), 2875 (C-H symmetrical stretching of CH_3 group), 1653 (C=O stretching of amide), 1592 (C=O stretching of cyclic) 1592 (N-H deformation of pyrimidine ring), 1524 (C=C stretching of aromatic ring), 1471 (C-H asymmetrical deformation of CH_3 group), 1410 (C-H symmetrical deformation of CH_3 group), 1346 (C-N-C stretching vibration of pyrimidine ring), 1270 (C-N stretching), 1111 (C-F stretching), 1050 (C-H in plane deformation of aromatic ring), 840 (para-substituted), 760 (C-H in out plane deformation of aromatic ring), 652 (C-Cl stretching); ^{1}H NMR (DMSO-*d6*) δ ppm: 1.14 (s, 3H, H), 1.16 (s, 3H, H), 3.52-3.56 (m, 1H, H), 6.43 (s, 1H, H), 6.82-6.85 (m, 2H, H),

7.14-7.18 (m, 2H, H), 7.28 (s, 1H, H), 7.46-7.50 (m, 2H, H), 8.57 (s, 1H, H), 10.08 (s, 1H, H), 10.10 (s, 1H, H); MS: *m/z* 422.

4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(4-chlorophenyl)-2-oxo-pyrimidine-5-carboxamide (4f)

Yield: 60%; mp 190ºC; Anal. Calcd. for $C_{20}H_{18}Cl_2FN_3O_2$: C, 56.88; H, 4.30; Cl, 16.79; F, 4.50; N, 9.95; O, 7.58; Found: C, 56.79; H, 4.40; Cl, 16.50; F, 4.61; N, 9.90; O, 7.67%; IR (cm^{-1}): 3487 (N-H stretching of amide), 3107 (C-H stretching of aromatic ring), 2951 (C-H asymmetrical stretching of CH_3 group), 2886 (C-H symmetrical stretching of CH_3 group), 1653 (C=O stretching of amide), 1596 (C=O stretching of cyclic) 1596 (N-H deformation of pyrimidine ring), 1529 (C=C stretching of aromatic ring), 1479 (C-H asymmetrical deformation of CH_3 group), 1417 (C-H symmetrical deformation of CH_3 group), 1346 (C-N-C stretching vibration of pyrimidine ring), 1278 (C-N stretching), 1108 (C-F stretching), 1068 (C-H in plane deformation of aromatic ring), 837 (para-substituted), 786 (C-H in out plane deformation of aromatic ring), 671 (C-Cl stretching); ^{1}H NMR (DMSO-*d6*) δ ppm: 1.16 (s, 3H, H), 1.17 (s, 3H, H), 3.54-3.58 (s, 1H, H), 6.50 (s, 1H, H), 6.84-6.87 (d, 2H, H), 7.13-7.15 (d, 2H, H), 7.54-7.58 (m, 1H, H), 7.65 (m, 1H, H), 7.85-7.89 (m, 1H, H), 8.54 (s, 1H, H), 10.03 (s, 1H, H), 10.04 (s, 1H, H); MS: *m/z* 422.

4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(2-fluorophenyl)-2-oxo-pyrimidine-5-carboxamide (4g)

Yield: 70%; mp 178ºC; Anal. Calcd. for $C_{20}H_{18}ClF_2N_3O_2$: C, 59.19; H, 4.47; Cl, 8.74; F, 9.36; N, 10.35; O, 7.88; Found: C, 59.15; H, 4.47; Cl, 8.78; F, 9.33; N, 10.38; O, 7.85%; IR (cm^{-1}): 3413 (N-H stretching of amide), 3081 (C-H stretching of aromatic ring), 2956 (C-H asymmetrical stretching of CH_3 group), 2878 (C-H symmetrical stretching of CH_3 group), 1652 (C=O stretching of amide), 1587 (C=O stretching of cyclic) 1587 (N-H deformation of pyrimidine ring), 1520 (C=C stretching of aromatic ring), 1477 (C-H asymmetrical deformation of CH_3 group), 1403 (C-H symmetrical deformation of CH_3 group), 1342 (C-N-C stretching vibration of pyrimidine ring), 1278 (C-N stretching), 1104 (C-F stretching), 1068 (C-H in plane deformation of aromatic ring), 673 (C-Cl stretching); ^{1}H NMR (DMSO-*d6*) δ ppm: 1.13 (s, 3H, H), 1.15 (s, 3H, H), 3.45-3.50 (m, 1H, H), 6.61 (s, 1H, H), 6.84-6.87 (m, 3H, H), 7.27-7.29 (m, 2H, H), 7.54-7.58 (m, 2H, H), 8.53 (s, 1H, H), 10.05 (s, 1H, H), 10.14 (s, 1H, H); MS: *m/z* 405.

4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(3-fluorophenyl)-2-oxo - pyrimidine-5-carboxamide (4h)

Yield: 52%; mp 183ºC; Anal. Calcd. for $C_{20}H_{18}ClF_2N_3O_2$: C, 59.19; H, 4.47; Cl, 8.74; F, 9.36; N, 10.35; O, 7.88; Found: C, 59.10; H, 4.49; Cl, 8.78; F, 9.37; N, 10.33; O, 7.85%; IR (cm^{-1}): 3389 (N-H stretching of amide), 3082 (C-H stretching of aromatic ring), 2950 (C-H asymmetrical stretching of CH_3 group), 2871 (C-H symmetrical stretching of CH_3 group), 1652 (C=O stretching of amide), 1583 (C=O stretching of cyclic) 1587 (N-H deformation of pyrimidine ring), 1520 (C=C stretching of aromatic ring), 1458 (C-H asymmetrical deformation of CH_3 group), 1411 (C-H symmetrical deformation of CH_3 group), 1349 (C-N-C stretching vibration of pyrimidine ring), 1278 (C-N stretching), 1095 (C-F stretching), 1059 (C-H in plane deformation of aromatic ring), 677 (C-Cl stretching); ^{1}H NMR (DMSO-*d6*) δ ppm: 1.20 (s, 3H, H), 1.22 (s, 3H, H), 3.45-3.48 (m, 1H, H), 6.57 (s, 1H, H), 6.84-6.88 (m, 2H, H), 7.12-7.14 (m, 2H, H), 7.31 (s, 1H, H), 7.52-7.54 (m, 2H, H), 8.67 (s, 1H, H), 10.07 (s, 1H, H), 10.13 (s, 1H, H); MS: *m/z* 405.

4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(4-fluorophenyl)-2-oxo - pyrimidine-5-carboxamide (4i)

Yield: 64%; mp 186ºC; Anal. Calcd. for $C_{20}H_{18}ClF_2N_3O_2$: C, 59.19; H, 4.47; Cl, 8.74; F, 9.36; N, 10.35; O, 7.88; Found: C, 59.11; H, 4.49; Cl, 8.78; F, 9.33; N, 10.38; O, 7.87%; IR (cm^{-1}): 3405 (N-H stretching of amide), 3074 (C-H stretching of aromatic ring), 2942 (C-H asymmetrical stretching of CH_3 group), 2854 (C-H symmetrical stretching of CH_3 group), 1643 (C=O stretching of amide), 1578 (C=O stretching of cyclic) 1578 (N-H deformation of pyrimidine ring), 1520 (C=C stretching of aromatic ring), 1450 (C-H asymmetrical deformation of CH_3 group), 1411 (C-H symmetrical deformation of CH_3 group), 1341 (C-N-C stretching vibration of pyrimidine ring), 1271 (C-N stretching), 1095 (C-F stretching), 1051 (C-H in plane deformation of aromatic ring), 671 (C-Cl stretching); ^{1}H NMR (DMSO-*d6*) δ ppm: 1.11 (s, 3H, H), 1.13 (s, 3H, H), 3.42-3.47 (m, 1H, H), 6.52 (s, 1H, H), 6.87-6.89 (d, 2H, H), 7.13-7.17 (d, 2H, H), 7.52-7.55 (m, 1H, H), 7.64 m, 1H, H), 7.80-7.85 (m, 1H, H), 8.64 (s, 1H, H), 10.04 (s, 1H, H), 10.09 (s, 1H, H); MS: *m/z* 405.

4-(2-chloro-6-fluorophenyl)-1,2,3,4-tetrahydro-6-isopropyl-N-(2-bromophenyl)-2-oxo - pyrimidine-5-carboxamide (4j)

Yield: 49%; mp 171ºC; Anal. Calcd. for $C_{20}H_{18}ClBrFN_3O_2$: C, 51.47; H, 3.89; Br, 17.12; Cl, 7.60; F, 4.07; N, 9.00; O, 6.86; Found: C, 51.45; H, 3.87; Br, 17.16; Cl, 7.64; F, 4.03; N,

8.98; O, 6.84%; IR (cm^{-1}): 3413 (N-H stretching of amide), 3042 (C-H stretching of aromatic ring), 2928 (C-H asymmetrical stretching of CH_3 group), 2874 (C-H symmetrical stretching of CH_3 group), 1643 (C=O stretching of amide), 1570 (C=O stretching of cyclic) 1570 (N-H deformation of pyrimidine ring), 1521 (C=C stretching of aromatic ring), 1450 (C-H asymmetrical deformation of CH_3 group), 1412 (C-H symmetrical deformation of CH_3 group), 1342 (C-N-C stretching vibration of pyrimidine ring), 1273 (C-N stretching), 1095 (C-F stretching), 1053 (C-H in plane deformation of aromatic ring), 742 (C-Br stretching), 673 (C-Cl stretching); ^{1}H NMR (DMSO-*d6*) δ ppm: 1.17 (s, 3H, H), 1.19 (s, 3H, H), 3.38-3.41 (m, 1H, H), 6.57 (s, 1H, H), 6.83-6.85 (m, 3H, H), 7.27-7.30 (m, 2H, H), 7.52-7.57 (m, 2H, H), 8.65 (s, 1H, H), 10.05 (s, 1H, H), 10.11 (s, 1H, H); MS: *m/z* 466.

CONCLUSION

In finale, we have synthesized of new pyrimidine derivatives using simple and opportune method. This method produces these products in first-class yields and trouble-free workup. Product is isolated by simple 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 novel pyrimidine derivatives compounds.

REFERENCES

1. Patt WC, Hamilton HW, Taylor MD, Ryan M. *J. Med. Chem.*, 1992; 35: 2562-72.
2. Sharma RN, Xavier FP, Vasu KK, Chaturvedi SC, Pancholi SS., *J. Enz. Inhib. Med. Chem.*, 2009; 24: 890 – 897.
3. Jaen JC, Wise LD, Caprathe BW, Tecle H, Bergmeier S, Humblet CC., *J. Med. Chem*, 1990; 33: 311-317.
4. Tsuji K, Ishikawa H., *Bioorg. Med Chem. Lett.*, 1994; 4: 1601-1606.
5. Bell FW, Cantrell AS, Hogberg M, Jaskunas SR., *J. Med. Chem.*, 1995; 38: 4929-4936.
6. Ergenc N, Capan G, Gunay NS, Ozkirimli S, Gungor M, Ozbey S, Kendi E., *Arch. Pharm Pharm. Med. Chem.*, 1999; 332: 343-347.
7. Hargrave KD, Hess FK, Oliver JT., *J. Med. Chem.*, 1983; 26: 1158-1163.
8. Carter JS, Kramer S, Talley JJ, Penning T, Collins P, *Bioorg. Med. Chem. Lett.*, 1999; 9: 1171-1174.
9. Badorc A, Bordes MF, Cointet P, Savi P., *J. Med. Chem.*, 1997; 40: 3393-3401.
10. Rudolph J, Theis H, Hanke R, Endermann R, Johannsen L, Geschke FU., *J. Med. Chem.*, 2001; 44: 619-626.

11. Kappe CO, *Tetrahedron,* 1993; 49: 6937-6963.
12. Russowsky D, Canto RFS, Sanches SAA, D'Oca MGM, de Fátima Â, Pilli RA., *Bioorganic Chemistry*, 2006; 34: 173–182.
13. Cho H, Ueda M, Shima K, Mizuno A, Hayashimatsu M, Ohnaka Y., *Journal of Medicinal Chemistry,* 1989; 32: 2399-2406.
14. Hu EH, Sidler DR, Dolling UH, *Journal of Organic Chemistry*, 1998; 63: 3454-3457.
15. Chauhan N, Nimavat K, Vyas K, *Der Pharmacia Sinica*, 2012; 3(4): 394-399.
16. Rovnyak GC, Atwal KS, Hedberg A, Kimball SD, Moreland S, Gougoutas JZ, *Journal of Medicinal Chemistry,* 1992; 35: 3254-3263.
17. Jauk B, Belaj B, Kappe CO, *Journal of the Chemical Society - Perkin Transactions*, 1999; 1: 307-311.