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DOWEX 50W IN AQUEOUS MEDIUM: HIGHLY EFFICIENT BIGINELLI CONDENSATION PROCEDURE FOR THE SYNTHESIS OF 4-ARYL-3,4-DIHYDROPYRIMIDONES

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Abstract – We report here Dowex 50W-mediated efficient synthesis of 4-aryl 3,4-dihydropyrimidones in water for the first time in a one-pot operation.

INTRODUCTION

In recent years, 4-aryl dihydropyrimidones have shown immense interest as calcium channel blockers, antihypertensive agents, alpha-1a-antagonists[1] and neuropeptide Y (NPY) antagonists.[2] Dihydropyrimidone-5-carboxylate moiety is also present in biologically active marine alkaloids.[3] In this series the most important examples are batzelladine alkaloids which are potent HIV group-120-CD4 inhibitors.[4] As a result of their biological properties, synthesis of the dihydropyrimidone nucleus has received much attention. The initial synthesis of dihydropyrimidone following Biginelli condensation has proved to be inefficient with 20-50% yield.[5] Better methods have been discovered, but through multiple sequences and hazardous conditions.[5b,6,7] A few other attractive methods are known, but most of them employ anhydrous reaction conditions and Lewis acids.[1b,8] Therefore, an efficient and operationally simple method is necessary for the synthesis of this type of multifunctionalized rings.

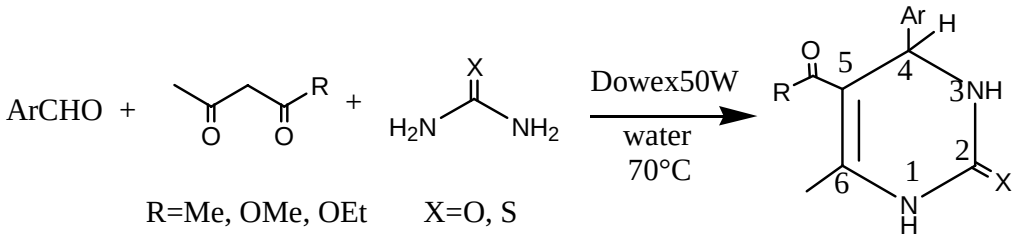
RESULTS AND DISCUSSION

We report here Dowex 50W-mediated synthesis of dihydropyrimidone in water for the first time in a one-pot operation. This method has been successfully applied with a number of substrates and results in excellent yield of the products.

The experimental procedure of our reaction is very simple. In this procedure the reactants and Dowex 50W in water are mixed and heated (70 °C) for the specified time period (Table). After pouring in crushed ice, an extraction of the reaction mixture with organic solvent is then followed to isolate the pure product in excellent yield. Since Dowex 50W is a cationic ion exchange resin, maintenance of dry reaction

conditions is not necessary. In addition, the additional acidic reagent is not required as Dowex 50W acts both as a catalyst and a proton source. Very recently, dihydropyrimidones have been synthesized using solvent free conditions.[9] Our conditions employ temperature of 70 °C, yields excellent, with no side products and very simple operational procedure. Thus Dowex 50W in water is a "**green catalyst**" for the Biginelli condensation as the aqueous medium is non-hazardous and non-toxic to the environment. No reaction takes place without the addition of Dowex 50W.

Scheme1



R=Me, OMe, OEt X=O, S

We have investigated our reactions in water-THF (1:1), water-MeOH (1:1) or water-EtOH (1:1), but no improvement of yield has been observed. In addition to the simplicity, our method has other benefits. For example, this method has become successful with β-keto esters and β-diketones and a variety of substituted aryl aldehydes. Nitro, chloro, hydroxy, methoxy, *N*,*N*-dimethylamino groups on the aryl nucleus have remained unaffected under this reaction condition. Urea and thiourea are equally effective and produce products with excellent yields. It has been found that 20 mg of Dowex 50W per mmol of the aldehyde is sufficient to complete the reaction. Higher amount of Dowex 50W could not improve the yield of the reaction. Dowex 50W can be reused three times without loss of activity. Under the same conditions, the aliphatic aldehydes produced the dihydropyrimidones (crude by IR), but the yields being very poor, could not be isolated in substantial amounts.

The mechanism of the dihydropyrimidone formation is similar as proposed by Folkers and Johnson.[10] The sulphonic acid group in Dowex 50W may stabilize the acylimine intermediate and this intermediate may then react with the β-diketone or the β-ketoester effectively. Finally, a favorable cyclisation and dehydration path may follow to produce the dihydropyrimidone system. Thus our method has the following advantages:

a) the reactions are investigated in water

b) dry conditions are not needed

c) the conditions of the reactions are mild

d) additional proton sources are not required

e) Dowex 50W can be reused several times

In contrast, most the available procedures require expensive acids (catalytic or stoichiometric), dry reaction conditions and dry solvents.

CONCLUSION

In conclusion we have demonstrated a new, mild, efficient and cost effective highly efficient procedure for the synthesis of 4-aryl-3, 4-dihydropyrimidones in aqueous Dowex 50W. Considering the wide generality of the substrates, this method may find useful application in synthetic organic chemistry and chemistry of drug design.

EXPERIMENTAL

General Procedure for the Synthesis of Dihydropyrimidones: Aromatic aldehyde (4 mmoles), β-diketone (5 mmoles) or β-ketoester (5 mmoles) and urea (6 mmoles) or thiourea (6 mmoles) were mixed with Dowex 50W (80 mg) in water (3 mL) and heated with stirring on a water bath at 70 °C for the specified time period (Table) till the TLC showed the absence of the starting aldehyde. The reaction mixture was then cooled, poured onto crushed ice, stirred for 10 minutes when the solid dihydropyrimidones separated out. It was filtered to remove Dowex 50W, dissolved in hot ethanol and allowed to settle when the pure dihydropyrimidone crystals separated out. The products were characterized (mp, IR, ^{1}H NMR and ^{13}C NMR) with respect to the known compounds (references given in the Table).

Table. Dowex 50W catalysed synthesis of 4-aryl, 3-4 dihydropyrimidones in aqueous medium

Entry	Ar	R	X	Time(h)	Yield (%)	References
1	Ph	Me	O	6	85	8, 11,13
2	Ph	OMe	O	7	80	1b, 8
3	Ph	OEt	O	7	82	1b, 8
4	Ph	Me	S	8	82	8
5	Ph	OEt	S	8	81	9a
6	3-OH-C_6H_4	OEt	O	6	80	8
7	4OMe-C_6H_4	Me	O	7	88	8, 13, 15
8	4OMe-C_6H_4	OMe	O	7	87	13, 15
9	4OMe-C_6H_4	OEt	O	8	85	13, 15
10	4OMe-C_6H_4	OEt	S	9	80	13, 15
11	4NMe_2-C_6H_4	OEt	O	7	78	12

12	4-Cl-C_6H_4	OMe	O	10	77	1b, 8, 13, 15
13	4-Cl-C_6H_4	OEt	O	10	75	1b, 8, 13, 15
14	3-NO_2 C_6H_4	OEt	O	10	77	12, 14, 15
15	3-NO_2-C_6H_4	OMe	O	10	75	15
16	4-OH-C_6H_4	OMe	O	3	82	8, 16
17	4-OH-C_6H_4	OEt	O	3	84	8 ,16
18	4-NO_2-C_6H_4	OMe	O	12	75	13, 15
19	4-NO_2-C_6H_4	OEt	O	11	73	13, 15
20	2-furanyl	Me	O	6	75	8
21	2-furanyl	OEt	O	7	70	16
22	4OH-3OMe-C_6H_3	OEt	O	6	81	12
23	4OH-3OMe-C_6H_3	OMe	S	4	82	
24	4OH-3OMe-C_6H_3	OMe	O	5	75	17

The physical data for majority of the compounds are given below:

5-Acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (entry 1): mp 232-235°C (lit.,[13] mp 233-236 °C); IR (KBr): 3260, 2924, 2368, 1704, 1603, 1235 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.11 (s, 3H. –$COCH_3$), 2.29 (s, 3H, C_6-CH_3), 5.29 (d, J=3.4Hz, 1H, C_4-H), 7.22-7.36 (m, 5H, phenyl protons), 7.84 (s, 1H, NH), 9.19 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 19.4, 30.8, 54.3, 110.1, 126.9, 127.8, 128.9, 144.7, 148.6, 152.6, 194.8.

5-Methoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (entry 2): mp 210-212 °C (lit.,[1b] mp 209-212 °C); IR (KBr): 3333, 3226, 1697, 1668, 1237, 1092 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.26 (s, 3H, CH_3), 3.54 (s, 3H, -OCH_3), 5.15 (d, J=3.6Hz, 1H, C_4-H), 7.22-7.35 (m, 5H, phenyl protons), 7.75

(brt, 1H, NH), 9.21 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 18.3, 51.2, 54.3, 99.5, 126.6, 127.7, 128.9, 145,1, 149.1, 152.6, 166.3.

5-Acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-thione (entry 4): mp 218-220 °C (lit.,[8] mp 220-222 °C); IR (KBr): 3287, 1610, 1456, 1184 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.16 (s, 3H, $COCH_3$), 2.33 (s, 3H, CH_3), 5.30 (d, J=3.6Hz, 1H, C_4-H), 7.22-7.37 (m, 5H, phenyl protons), 9.73 (d, J=3.3Hz, 1H, NH), 10.26 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 18.7, 30.8, 54.3, 111.0, 127.0, 128.2, 129.1, 143.3, 145.1, 174.5, 195.4.

5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-thione (entry 5): mp 222-224 °C (lit.,[9a] mp 223-224 °C); IR (KBr): 3328, 3174, 1671, 1575, 1465, 1190, 1114 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 1.10 (t, J=7.2Hz, 3H, -$OCH_2\underline{CH_3}$), 2.30 (s, 3H, CH_3), 4.01 (q, J=7.2Hz, 2H, -$O\underline{CH_2}CH_3$), 5.19 (d, J=3.6Hz,1H, C_4-H), 7.21-7.37(m, 5H, phenyl protons), 9.64(s, 1H, NH), 10.32(s, 1H, NH); ^{13}C NMR(DMSO-d_6): δ 14.5, 17.6, 54.5, 60.1, 101.2, 126.8, 128.1, 129.0, 143.9, 145.5, 165.6, 174.7.

5-Ethoxycarbonyl-4-(3-hydroxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (entry 6): mp 163-165 °C (lit.,[8] mp 164-166 °C); IR (KBr): 3244, 1724, 1678, 1639, 1600, 1458, 1224, 1095 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 1.12 (t, J=7.2Hz, 3H, -$OCH_2\underline{CH_3}$), 2.24 (s, 3H, C_6-CH_3), 4.00 (q, J=7.2Hz, 2H, -$O\underline{CH_2}CH_3$), 5.07 (d, J=3.3Hz, 1H, C_4-H), 6.61-6.69 (m, 3H, aromatic C_2-H, C_4-H and C_6-H), 7.09 (t, J=8.1Hz, 1H, aromatic C_5-H), 7.67 (s, 1H, NH), 9.14 (s, 1H, OH), 9.36 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.6, 18.2, 54.3, 59.7, 99.9, 113.6, 114.6, 117.4, 129.7, 146.7, 148.5, 152.7, 157.8, 165.9.

5-Acetyl-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (entry 7): mp 178-179 °C (lit.,[15] mp177-179 °C); IR (KBr): 3249, 3108, 1717, 1625, 1237 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.08 (s, 3H, -$COCH_3$), 2.28 (s, 3H, C_6-CH_3), 3.72 (s, 3H, aromatic OMe), 5.21(d, J=3.3Hz, 1H, C_4-H), 6.88 (d, J=8.6Hz, 2H, aromatic C_3-H and C_5-H), 7.17 (d, J=8.6 Hz, 2H, aromatic C_2-H and C_6-H), 7.74 (s, 1H, NH), 9.13 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 19.3, 30.6, 53.8, 55.5, 110.1, 114.3, 128.1, 136.8, 148.2, 152.6, 159.0, 194.9.

5-Ethoxycarbonyl-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (entry 9): mp 199-201 °C (lit.,[15] mp 199-201 °C; IR (KBr): 3243, 3113, 2938, 1709, 1649, 1460, 1224, 1090, 781 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 1.10 (t, J=7.2 Hz, 3H, -$OCH_2\underline{CH_3}$), 2.24 (s, 3H, C_6-CH_3), 3.71 (s, 3H, aromatic OCH_3), 3.98 (q, J=7.2Hz, 2H, -$O\underline{CH_2}CH_3$), 5.10 (d, J=3.3 Hz, 1H, C_4-H), 6.87 (d, J=8.7Hz, 2H, aromatic C_3-H and C_5-H), 7.15 (d, J=8,7Hz, 2H, aromatic C_2-H and C_6-H), 7.65 (s, 1H, NH), 9.12 (d, J=1.2 Hz, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.5, 18.2, 53.8, 55.5, 59.7, 100.1, 114.2, 127.9, 137.5, 148.4, 152.7, 158.9, 165.9.

5-Ethoxycarbonyl-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-thione (entry 10): mp 138-139 °C (lit.,[15] mp 138-140 °C); IR (KBr): 3313, 3171, 1668, 1575, 1462, 1184, 1115, 1025 cm^{-1};

^{1}H NMR(DMSO-d_6): δ 1.10 (t, J=7.2Hz, 3H, -OCH$_2$CH$_3$), 2.28 (s, 3H, C_6-CH$_3$), 3.71 (s, 3H, aromatic OMe), 3.99 (q, J=7.2Hz, 2H, -OCH$_2$CH$_3$), 5.12 (d, J=3.6Hz, 1H, C_4-H), 6.89 (d, J=8.4Hz, 2H, aromatic C_3-H and C_5-H), 7.13 (d, J=8.4Hz, 2H, aromatic C_2-H and C_6-H), 9.57 (s, 1H, NH), 10.25 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.5, 17.6, 53.9, 55.6, 60.1, 101.5. 114.3, 128.1, 136.1, 145.2, 159.2, 165.7, 174.5.

5-Ethoxycarbonyl-4-(4-dimethylaminophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (entry 11): mp 256-257 °C(lit.,[12] mp 255-257 °C); IR (KBr): 3242, 3115, 2363, 1707, 1649, 1228, 1091 cm^{-1}; ^{1}H NMR(DMSO-d_6): δ 1.12 (t, J=7.2Hz, 3H, -OCH$_2$CH$_3$), 2.23 (s, 3H, C_6-CH$_3$), 2.85 [s, 6H, N(CH$_3$)$_2$], 3.98 (q, J=7.2Hz, 2H, -OCH$_2$CH$_3$), 5.04 (d, J=3.3Hz, 1H, C_4-H), 6.65 (d, J=8.7Hz, 2H, aromatic protons), 7.04 (d, J=8.7Hz, 2H, aromatic protons), 7.57 (s, 1H, NH), 9.06 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.6, 18.2, 53.8, 59.6, 100.4, 112.7, 127.4, 133.1, 148.0, 150.2, 152.8, 166.0.

5-Methoxycarbonyl-4-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (entry 12): mp 203-205 °C (lit.,[15] mp 204-206 °C); IR (KBr): 3364, 3106, 2953, 1706, 1636, 1228, 1090 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.25 (s, 3H, C_6-CH$_3$), 3.53 (s, 3H, -COOMe), 5.15 (d, J=3.3Hz, 1H, C_4-H), 7.25 (d, J=8.4Hz, 2H, aromatic protons), 7.39 (d, J=8.4Hz, 2H, aromatic protons), 7.78 (s, 1H, NH), 9.25 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 18.3, 51.3, 53.7, 99.2, 128.6, 128.9, 132.3, 144.0, 149.4, 152.5, 166.2.

5-Ethoxycarbonyl-6-methyl-4-(3-nitrophenyl)-3,4-dihydropyrimidin-2(1*H*)-one (entry 14): mp 226-228 °C (lit.,[15] mp 225-227 °C); IR (KBr): 3332, 2960, 1703, 1626, 1526, 1338, 1221, 1088 cm^{-1}; ^{1}H NMR(DMSO-d_6): δ 1.10(t, J=7.2Hz, 3H, -OCH$_2$CH$_3$), 2.28 (s, 3H, C_6-CH$_3$), 4.00 (q, J=7.2Hz, 2H, -OCH$_2$CH$_3$), 5.31 (d, J=3.3Hz, 1H, C_4-H), 7.63-7.72 (m, 2H, aromatic C_5-H and C_6-H), 7.90 (s, 1H, NH), 8.09-8.15 (m, 2H, aromatic C_2-H and C_4-H), 9.36 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.4, 18.3, 54.0, 59.9, 98.9, 121.5, 122.8, 130.7, 133.4, 147.5, 148.2, 149.9, 152.3, 165.5.

5-Ethoxycarbonyl-4-(4-hydroxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (entry 17): mp 228-230 °C (lit.,[16] mp 227-229 °C); IR (KBr): 3512, 3119, 1687, 1645, 1463, 1232, 1090 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 1.09 (t, J=7.2Hz, 3H, -OCH$_2$CH$_3$), 2.23 (s, 3H, C_6-CH$_3$), 3.97 (q, J=7.2Hz, 2H, -OCH$_2$CH$_3$), 5.05 (d, J=3.0 Hz, 1H, C_4-H), 6.69 (d, J=8.4Hz, 2H, aromatic protons), 7.03 (d, J=8.4Hz, 2H, aromatic protons), 7.59(s,1H, NH), 9.07 (s, 1H, NH), 9.40 (brs, 1H, OH); ^{13}C NMR (DMSO-d_6): δ 14.5, 18.2, 53.9, 59.6, 100.3, 115.5, 127.9, 135.9, 148.2, 152.7, 157.0, 166.0.

5-Ethoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1*H*)-one (entry 19): mp 205-207 °C(lit.,[15] mp 205-207 °C); IR (KBr): 3235, 3119, 2363, 1706, 1642, 1521, 1216, 1092, 779 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 1.09 (t, J=7.2Hz, 3H, -OCH$_2$CH$_3$), 2.26 (s, 3H, C_6-CH$_3$), 3.98 (q, J=7.2Hz, 2H, -OCH$_2$CH$_3$), 5.28 (d, J=3.3 Hz, 1H, C_4-H), 7.51 (d, J=8.7Hz, 2H, aromatic C_2-H and C_6-H), 7.87 (s, 1H, NH), 8.21 (d, J=8.7Hz, 2H, aromatic C_3-H and C_5-H), 9.32 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.5, 18.3, 54.1, 59.9, 98.7, 124.3, 128.1, 147.2, 149.8, 152.2, 152.4, 165.6.

5-Ethoxycarbonyl-4-(2-furanyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (entry 21): mp 202-204 °C (lit.,[16] mp 204-205 °C); IR (KBr): 3354, 3116, 2363, 1697, 1643, 1306, 1227, 1097 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.13 (t, J=6.9Hz, 3H, -$OCH_2\underline{CH_3}$), 2.23 (s, 3H, C_6-CH_3), 4.03 (q, J=6.9 Hz, 2H, -$O\underline{CH_2}CH_3$), 5.21 (d, J=3.3 Hz, 1H, C_4-H), 6.09 (d, J=3Hz, 1H, furanyl proton), 6.35 (t, J=2.4 Hz, 1H, furanyl proton), 7.54 (t, J=1.2Hz, 1H, furanyl C_5-H), 7.74 (s, 1H, NH), 9.21(s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.6, 18.2, 48.2, 59.7, 97.3, 105.8, 110.8, 142.6, 149.8, 152.9, 156.3, 165.5.

5-Ethoxycarbonyl-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (entry 22): mp 230-232 °C (lit.,[12] mp 230-232 °C); IR (KBr): 3244, 3116, 1701, 1645, 1516, 1223 cm^{-1}; ^1H NMR(DMSO-d_6): δ 1.12 (t, J=7.2Hz, 3H, -$OCH_2\underline{CH_3}$), 2.24 (s, 3H, C_6-CH_3), 3.73 (s, 3H, aromatic OMe), 3.99(q, J=7.2Hz, 2H, -$O\underline{CH_2}CH_3$), 5.06 (d, J=3.0 Hz, 1H, C_4-H), 6.62 (brd, J=8.1Hz, 1H, aromatic C_6-H), 6.71 (dd, J=8.1Hz and 0.6 Hz, 1H, aromatic C_5-H), 6.80 (brs, 1H, aromatic C_2-H), 7.62 (s,1H, NH), 8.89 (s, 1H, OH), 9.10 (s,1H, NH); ^{13}C NMR (DMSO-d_6): δ 14.6, 18.2, 54.0, 56.1, 59.6, 100.1, 111.4, 115.8, 118.8, 136.4, 146.3, 147.7, 148.3, 152.7, 165.9.

5-Methoxycarbonyl-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-thione (entry 23): mp 258-260 °C; IR (KBr): 3471, 3334, 3179, 1678, 1571, 1516, 1449, 1274, 1186, 752 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.28 (s, 3H, C_6-CH_3), 3.56 (s, 3H, -COOMe), 3.73 (s, 3H, aromatic OMe), 5.09 (d, J=3.3 Hz, 1H, C_4-H), 6.60 (dd, J=8.1Hz and 1.9Hz, 1H, aromatic C_6-H), 6.72 (d, J=8.1Hz, 1H, aromatic C_5-H), 6.80 (d, J=1.9 Hz, 1H, aromatic C_2-H), 9.04 (s, 1H, OH), 9.55 (d, J=3.0Hz, 1H, NH), 10.25 (s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 17.6, 51.5, 54.0, 56.1, 101.2, 111.4, 115.9, 118.9, 134.8, 145.3, 146.6, 147.9, 166.2, 174.5. Anal. Calcd for $C_{14}H_{16}N_2O_4S$: C, 54.53; H, 5.23; N, 9.08. Found: C, 54.41; H, 5.30; N, 9.11.

5-Methoxycarbonyl-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (entry 24): mp 251-253 °C (lit., [17] mp 253-254 °C); IR (KBr): 3393, 3257, 1680, 1435, 1235, 1094 cm^{-1}; ^1H NMR(DMSO-d_6): δ 2.25 (s, 3H, C_6-CH_3), 3.54 (s, 3H, -COOMe), 3.73 (s, 3H, aromatic OMe), 5.07 (J=3.3 Hz, 1H, C_4-H), 6.60 (dd, J=8.1Hz and 1.9Hz, 1H, aromatic C_6-H), 6.71 (d, J=8.1Hz, 1H, aromatic C_5-H), 6.81 (d, J=1.9Hz, 1H, aromatic C_2-H), 7.64 (s, 1H, NH), 8.91 (s, 1H, OH), 9.14 (s, 1H, NH); ^{13}C NMR(DMSO-d_6): δ 18.2, 51.2, 53.9, 56.1, 99.7, 111.3, 115.7, 118.6, 136.2, 146.3, 147.8, 148.7, 152.7, 166.4.

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