

Synthesis of 4-Aryl-3,4-dihydropyrimidinones Using Microwave-assisted Solventless Biginelli Reaction

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4-Aryl-3,4-dihydropyrimidinones were synthesized using microwave-assisted, solvent-free protocol of the Biginelli reaction. The simple method provides the title compounds in 78%—95% yields by the reaction of aromatic aldehydes with ethyl acetoacetate and urea/thiourea in the presence of a catalytic amount of conc. HCl. Lewis acids, such as ZnCl₂, SnCl₂, FeCl₃·6H₂O, and CuCl₂·2H₂O, were also found to be efficient catalysts for the synthesis of dihydropyrimidinones.

Keywords dihydropyrimidinones, microwave irradiation, Biginelli reaction

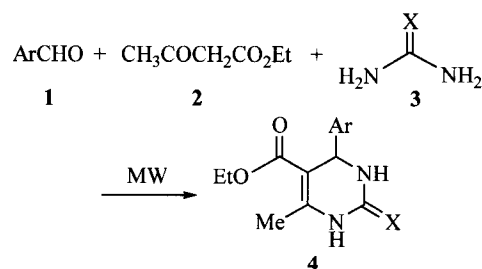
Introduction

4-Aryl-3,4-dihydropyrimidinones (**4**) as a core were observed in some biologically important compounds.¹ More recently, dihydropyrimidinones are shown to be a useful tool for studying dynamic cellular process and can be considered as a new lead for the development of anti-cancer drugs.² Appropriately functionalized dihydropyrimidinones have been used as potent calcium channel blockers³ and antihypertensive agents.⁴ The classical synthesis of dihydropyrimidinones involves the one-pot condensation of ethyl acetoacetate, aromatic aldehyde and urea or thiourea under refluxing conditions. This protocol often provides the products in moderate yields, in particular when substituted aromatic aldehydes or thioureas are employed. Several improved procedures⁵⁻⁷ were reported within the past decade.

Application of microwave irradiation in organic syn-

thesis is becoming an increasingly popular technology⁸ because of its rapid reaction rates, cleaner reaction conditions and ease of manipulation. The microwave promoting Biginelli reaction has also been reported with better yields using ethanol solvent as energy transfer medium⁹ or polyphosphate ester as a reaction mediator.¹⁰ Here a microwave assisted, solvent-free Biginelli condensation in the presence of catalytic amount of conc. HCl or Lewis acids was reported (Scheme 1).

Scheme 1



Results and discussion

Lewis acid ZnCl₂, SnCl₂, FeCl₃, and CuCl₂ are often used as catalysts in organic reactions. In 2000, Qian *et al.* reported that ytterbium triflate was an effective catalyst in the Biginelli condensation under solvent-free condition.^{11,12} More recently, Stefani reported that 4-phenyl-3,4-dihydropyrimidinone was obtained with 30% yield under microwave irradiation without any additive.¹³ We

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found that 4-phenyl-3, 4-dihydropyrimidinone could be prepared (Scheme 1) using various Lewis acids (10%) under solvent-free, microwave irradiation conditions. This procedure affords the product with the yields of 89%—95% (Table 1). The results show that Lewis acid as catalyst accelerates the condensation reaction. We also found that one or two drops of conc. HCl gave comparable high yield under solvent-free, microwave irradiation conditions (Entries 1 and 12 in Table 2).

Table 1 Solvent-free syntheses of 4-phenyl-3, 4-dihydropyrimidinones under microwave irradiation^a

Entry	Ar	X	Lewis-acid	Yield (%) ^b
1	C ₆ H ₅	O	SnCl ₂	89
2	C ₆ H ₅	S	SnCl ₂	92
3	C ₆ H ₅	O	FeCl ₃ ·6H ₂ O	91
4	C ₆ H ₅	S	FeCl ₃ ·6H ₂ O	93
5	C ₆ H ₅	O	ZnCl ₂	92
6	C ₆ H ₅	S	ZnCl ₂	95
7	C ₆ H ₅	O	CuCl ₂ ·2H ₂ O	92
8	C ₆ H ₅	S	CuCl ₂ ·2H ₂ O	92

^a All experiments were irradiated with microwave for 90 s.

^b All isolated yields.

Table 2 Syntheses of 4-aryl-3, 4-dihydropyrimidinones (**4**) catalyzed by conc. HCl (1—2 drops) under microwave irradiation

Entry	Ar	X	Time (s)	Product	Yield ^a (%)
1	C ₆ H ₅	O	90	4a	90
2	3-(OH)-C ₆ H ₄	O	90	4b	93
3	4-(OH)-C ₆ H ₄	O	90	4c	86
4	4(Cl)-C ₆ H ₄	O	120	4d	79
5	4-(NO ₂)-C ₆ H ₄	O	150	4e	78
6	3-(NO ₂)-C ₆ H ₄	O	150	4f	83
7	2-(Cl)-C ₆ H ₄	O	120	4g	93
8	4(OCH ₃)-C ₆ H ₄	O	90	4h	95
9	4-(OH)-3-(OCH ₃)-C ₆ H ₃	O	120	4i	88
10	2,4-(OCH ₃)-C ₆ H ₃	O	90	4j	83
11	3-(OCH ₃)-C ₆ H ₄	O	90	4k	93
12	C ₆ H ₅	S	90	4l	91
13	3-(OH)-C ₆ H ₄	S	90	4m	95
14	4-(OH)-C ₆ H ₄	S	90	4n	88
15	4(Cl)-C ₆ H ₄	S	120	4o	83
16	4-(NO ₂)-C ₆ H ₄	S	150	4p	89
17	3-(NO ₂)-C ₆ H ₄	S	150	4q	79
18	2-(Cl)-C ₆ H ₄	S	120	4r	95
19	4(OCH ₃)-C ₆ H ₄	S	90	4s	92
20	4-(OH)-3-(OCH ₃)-C ₆ H ₃	S	90	4t	90
21	2,4-(OCH ₃)-C ₆ H ₃	S	90	4u	86
22	3-(OCH ₃)-C ₆ H ₄	S	90	4v	96

^a All isolated yields.

Obviously, HCl was preferred to Lewis acid due to its cost and ease of handling. The results in Table 2 showed that good to excellent yields were obtained for variation of aromatic aldehyde. Longer reaction time is necessary for obtaining high yield when electron-withdrawing substitutions are on the aryl group of aldehyde. Similar high yields were also observed when thiourea was employed in the reaction (Entries 12—22 in Table 2). The products were characterized on the basis of their IR spectra, NMR spectroscopic data and the melting points.

We have described a highly efficient microwave-induced solvent-free Biginelli reaction. By using conc. HCl as catalyst, the yields of dihydropyrimidinones can be increased to 78%—95% while the reaction time is shortened to 90—150 s. Lewis acid ZnCl₂, SnCl₂, FeCl₃·6H₂O, and CuCl₂·2H₂O are also found to be efficient catalysts in the Biginelli condensation. In summary, this method not only preserves the simple and fast procedure but also produces excellent yields of the title compounds.

Experimental

General

Melting points were measured on a XT-4 apparatus and uncorrected. IR spectra were recorded on a Perkin-Elmer FT210 spectrophotometer. ¹H NMR spectra were measured with a Bruke DPX500 spectrometer using TMS as an internal standard. High resolution mass spectra were obtained with a Micromass GCT TOF mass spectrometer.

General procedure

A mixture of aromatic aldehyde (2.0 mmol), ethyl acetoacetate (2.4 mmol), urea/thiourea (2.4 mmol) and Lewis acid (0.2 mmol)/conc. HCl (1—2 drops) was placed in a 10 mL-glass tube. After the mixture had been stirred for 10—15 s with spatula, the reaction vessel was inserted into a 250 mL-glass beaker filled with neutral alumina, and irradiated in the microwave oven at 150 W for 30 s. After cooling for 1 min, the mixture was irradiated for another 30 s at the same power level. The irradiation and cooling cycle were repeated with the total irradiation time indicated in Tables 1 and 2. After the addition of H₂O (5 mL), the mixture was stirred for 20—30 s with spatula, then allowed to stand overnight at room tem-

perature. The solid product was filtered, washed with H₂O, dried and recrystallized from hot ethanol.

Ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4a) Yield, 90%; m.p. 204—206 °C (Lit.⁹ 204—205 °C); ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.08 (t, *J* = 7.1 Hz, 3H, CH₃), 2.29 (s, 3H, CH₃), 4.02 (q, *J* = 7.1 Hz, 2H, CH₂), 5.16 (d, *J* = 3.6 Hz, 1H, CH), 7.21—7.36 (m, 5H, arom), 9.64 (brs, 1H, NH), 10.32 (brs, 1H, NH); IR (KBr) ν: 3244, 3115, 1724, 1701, 1648 cm⁻¹.

Ethyl 6-methyl-2-oxo-4-(3-hydroxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4b) Yield, 93%; m.p. 210—212 °C; ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.16 (t, *J* = 7.1 Hz, 3H, CH₃), 2.29 (s, 3H, CH₃), 4.03 (q, *J* = 7.1 Hz, 2H, CH₂), 5.05 (d, *J* = 2.9 Hz, 1H, CH), 6.61—6.67 (m, 3H, arom), 7.07—7.10 (m, 1H, arom), 7.66 (brs, 1H, NH), 9.13 (brs, 1H, NH), 9.34 (brs, 1H, OH); IR (KBr) ν: 3513, 3352, 3243, 3120, 2978, 1723, 1676, 1642, 1600 cm⁻¹; HRMS for C₁₄H₁₆O₄N₂ 276.1110, found 276.1111.

Ethyl 6-methyl-2-oxo-4-(4-hydroxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4c) Yield, 86%; m.p. 223—224 °C (Lit.⁹ 225—226 °C); ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.16 (t, *J* = 7.1 Hz, 3H, CH₃), 2.25 (s, 3H, CH₃), 3.99 (q, *J* = 7.1 Hz, 2H, CH₂), 5.07 (d, *J* = 3.2 Hz, 1H, CH), 6.87 (d, *J* = 8.6 Hz, 2H, arom), 7.15 (d, *J* = 8.6 Hz, 2H, arom), 7.68 (brs, 1H, NH), 9.13 (brs, 1H, NH), 9.33 (brs, 1H, OH); IR (KBr) ν: 3387, 3276, 3173, 1611, 1471, 1414 cm⁻¹.

Ethyl 6-methyl-2-oxo-4-(4-chlorophenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4d) Yield, 79%; m.p. 211—213 °C (Lit.¹¹ 210—212 °C); ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.08 (t, *J* = 7.1 Hz, 3H, CH₃), 2.48 (s, 3H, CH₃), 3.98 (q, *J* = 7.1 Hz, 2H, CH₂), 5.12 (d, *J* = 3.2 Hz, 1H, CH), 7.23 (d, *J* = 8.4 Hz, 2H, arom), 7.37 (d, *J* = 8.4 Hz, 2H, arom), 7.68 (brs, 1H, NH), 9.14 (brs, 1H, NH); IR (KBr) ν: 3242, 3116, 2979, 1703, 1648 cm⁻¹.

Ethyl 6-methyl-2-oxo-4-(4-nitrophenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4e) Yield, 78%; m.p. 206—208 °C (Lit.¹¹ 207—210 °C); ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.09 (t, *J* = 7.1 Hz, 3H, CH₃), 2.49 (s, 3H, CH₃), 3.98 (q, *J* = 7.1

Hz, 2H, CH₂), 5.27 (d, *J* = 3.2 Hz, 1H, CH), 7.50 (d, *J* = 8.6 Hz, 2H, arom), 7.88 (brs, 1H, NH), 8.21 (d, *J* = 8.6 Hz, 2H, arom), 9.34 (brs, 1H, NH); IR (KBr) ν: 3237, 3118, 2975, 1729, 1699, 1645, 1595, 1520 cm⁻¹.

Ethyl 6-methyl-2-oxo-4-(3-nitrophenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4f) Yield, 83%; m.p. 226—227 °C (Lit.⁹ 226—228 °C); ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.07 (t, *J* = 7.1 Hz, 3H, CH₃), 2.49 (s, 3H, CH₃), 3.98 (q, *J* = 7.1 Hz, 2H, CH₂), 5.29 (d, *J* = 3.3 Hz, 1H), 7.61—7.69 (m, 2H, arom), 7.81 (brs, 1H, NH), 8.06—8.11 (m, 2H, arom), 9.27 (brs, 1H, NH); IR (KBr) ν: 3329, 3216, 3104, 2965, 1708, 1629, 1525 cm⁻¹.

Ethyl 6-methyl-2-oxo-4-(2-chlorophenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4g) Yield, 93%; m.p. 216—218 °C (Lit.¹⁰ 215—218 °C); ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.07 (t, *J* = 7.1 Hz, 3H, CH₃), 2.32 (s, 3H, CH₃), 3.91 (q, *J* = 7.1 Hz, 2H, CH₂), 5.67 (d, *J* = 2.7 Hz, 1H, CH), 7.22—7.46 (m, 4H, arom), 7.72 (brs, 1H, NH), 9.30 (brs, 1H, NH); IR (KBr) ν: 3431, 3331, 2978, 1667, 1611, 1524 cm⁻¹.

Ethyl 6-methyl-2-oxo-4-(4-methoxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4h) Yield, 95%; m.p. 198—200 °C (Lit.¹¹ 199—201 °C); ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.10 (t, *J* = 7.1 Hz, 3H, CH₃), 2.24 (s, 3H, CH₃), 3.71 (s, 3H, OCH₃), 3.98 (q, *J* = 7.1 Hz, 2H, CH₂), 5.08 (d, *J* = 3.1 Hz, 1H, CH), 6.87 (d, *J* = 8.6 Hz, 2H, arom), 7.14 (d, *J* = 8.6 Hz, 2H, arom), 7.65 (brs, 1H, NH), 9.13 (brs, 1H, NH); IR (KBr) ν: 3313, 3171, 2982, 1667, 1575, 1509, 1462 cm⁻¹.

Ethyl 6-methyl-2-oxo-4-(4-hydroxy-3-methoxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4i) Yield, 88%; m.p. 229—231 °C (Lit.⁹ 233—234 °C); ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.20 (t, *J* = 7.1 Hz, 3H, CH₃), 2.27 (s, 3H, CH₃), 3.18 (s, 3H, OCH₃), 4.01 (q, *J* = 7.1 Hz, 2H, CH₂), 5.08 (d, *J* = 3.5 Hz, 1H, CH), 6.57—6.59 (m, 1H, arom), 6.71—6.79 (m, 2H, arom), 8.99 (brs, 1H, OH), 9.55 (brs, 1H, NH), 10.25 (brs, 1H, NH); IR (KBr) ν: 3415, 3175, 2997, 1687, 1586, 1517, 1197 cm⁻¹.

Ethyl 6-methyl-2-oxo-4-(2,4-dimethoxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4j) Yield, 83%; m.p. 192—193 °C; ¹H NMR (DMSO-

d_6 , 500 MHz) δ : 1.04 (t, $J = 7.1$ Hz, 3H, CH₃), 2.26 (s, 3H, CH₃), 3.72 (s, 3H, OCH₃), 3.77 (s, 3H, OCH₃), 3.89 (q, $J = 7.1$ Hz, 2H, CH₂), 5.40 (d, $J = 2.8$ Hz, 1H, CH), 6.42–6.45 (m, 2H, arom), 6.91–6.93 (m, 1H, arom), 7.18 (brs, 1H, NH), 9.05 (brs, 1H, NH); IR (KBr) ν : 3273, 3113, 2935, 1721, 1699, 1643, 1613, 1588, 1306, 1221 cm^{-1} ; HRMS for C₁₆H₂₀O₅N₂ 320.1372, found 320.1385.

Ethyl 6-methyl-2-oxo-4-(3-methoxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4k) Yield, 93%; m.p. 180–182 °C; ¹H NMR (DMSO- d_6 , 500 MHz) δ : 1.09 (t, $J = 7.1$ Hz, 3H, CH₃), 2.30 (s, 3H, CH₃), 3.72 (s, 3H, OCH₃), 3.98 (q, $J = 7.1$ Hz, 2H, CH₂), 5.18 (d, $J = 3.3$ Hz, 1H, CH), 6.76–6.81 (m, 3H, arom), 7.20–7.23 (m, 1H, arom), 7.63 (brs, 1H, NH), 9.08 (brs, 1H, NH); IR (KBr) ν : 3241, 3118, 2934, 1702, 1649, 1598, 1226 cm^{-1} ; HRMS for C₁₅H₁₈O₄N₂ 290.1267, found 290.1258.

Ethyl 6-methyl-2-thioxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4l) Yield, 91%; m.p. 206–208 °C (Lit.⁹ 205–206 °C); ¹H NMR (DMSO- d_6 , 500 MHz) δ : 1.06 (t, $J = 7.1$ Hz, 3H, CH₃), 2.29 (s, 3H, CH₃), 4.01 (q, $J = 7.1$ Hz, 2H, CH₂), 5.18 (d, $J = 3.2$ Hz, 1H, CH), 7.21–7.36 (m, 4H, arom), 9.60 (brs, 1H, NH), 10.28 (brs, 1H, NH); IR (KBr) ν : 3244, 3114, 2977, 1724, 1700, 1648, 1220, 1090 cm^{-1} .

Ethyl 6-methyl-2-thioxo-4-(3-hydroxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4m) Yield, 95%; m.p. 191–193 °C; ¹H NMR (DMSO- d_6 , 500 MHz) δ : 1.12 (t, $J = 7.1$ Hz, 3H, CH₃), 2.28 (s, 3H, CH₃), 4.02 (q, $J = 7.1$ Hz, 2H, CH₂), 5.09 (d, $J = 3.6$ Hz, 1H), 6.38–6.57 (m, 3H, arom), 7.08–7.11 (m, 1H, arom), 9.35 (brs, 1H, OH), 9.52 (brs, 1H, NH), 10.21 (brs, 1H, NH); IR (KBr) ν : 3500, 3183, 3014, 1685, 1647, 1580, 1203, 1099 cm^{-1} ; HRMS for C₁₄H₁₆O₃N₂S 292.0882, found 292.0882.

Ethyl 6-methyl-2-thioxo-4-(4-hydroxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4n) Yield, 88%; m.p. 170–173 °C; ¹H NMR (DMSO- d_6 , 500 MHz) δ : 1.09 (t, $J = 7.1$ Hz, 3H, CH₃), 2.27 (s, 3H, CH₃), 4.00 (q, $J = 7.1$ Hz, 2H, CH₂), 5.05 (d, $J = 3.6$ Hz, 1H, CH), 6.70 (d, $J = 8.4$ Hz, 2H, arom), 6.99 (d, $J = 8.4$ Hz, 2H,

arom), 9.41 (brs, 1H, OH), 9.55 (brs, 1H, NH), 10.23 (brs, 1H, NH); IR (KBr) ν : 3513, 3354, 3243, 3122, 1724, 1676, 1643, 1600, 1222 cm^{-1} ; HRMS for C₁₄H₁₆O₃N₂S 292.0882, found 292.0889.

Ethyl 6-methyl-2-thioxo-4-(4-chlorophenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4o) Yield, 83%; m.p. 180–182 °C; ¹H NMR (DMSO- d_6 , 500 MHz) δ : 1.10 (t, $J = 7.1$ Hz, 3H, CH₃), 2.29 (s, 3H, CH₃), 4.01 (q, $J = 7.1$ Hz, 2H, CH₂), 5.17 (d, $J = 3.4$ Hz, 1H, CH), 7.22 (d, $J = 8.4$ Hz, 2H, arom), 7.43 (d, $J = 8.4$ Hz, 2H, arom), 9.66 (brs, 1H, NH), 10.38 (brs, 1H, NH); IR (KBr) ν : 3327, 3172, 2982, 1671, 1573, 1464 cm^{-1} ; HRMS for C₁₄H₁₅O₂N₂SCl 310.0543, found 310.0511.

Ethyl 6-methyl-2-thioxo-4-(4-nitrophenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4p) Yield, 89%; m.p. 210–213 °C; ¹H NMR (DMSO- d_6 , 500 MHz) δ : 1.10 (t, $J = 7.1$ Hz, 3H, CH₃), 2.31 (s, 3H, CH₃), 4.01 (q, $J = 7.1$ Hz, 2H, CH₂), 5.30 (d, $J = 3.5$ Hz, 1H, CH), 7.48 (d, $J = 8.6$ Hz, 2H, arom), 8.24 (d, $J = 8.6$ Hz, 2H, arom), 9.76 (brs, 1H, NH), 10.49 (brs, 1H, NH); IR (KBr) ν : 3323, 3170, 3102, 2985, 1678, 1575, 1521, 1467, 1200 cm^{-1} ; HRMS for C₁₄H₁₅O₄N₃S 321.0783, found 331.0796.

Ethyl 6-methyl-2-thioxo-4-(3-nitrophenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4q) Yield, 79%; m.p. 208–209 °C (Lit.¹⁰ 208–209 °C); ¹H NMR (DMSO- d_6 , 500 MHz) δ : 1.09 (t, $J = 7.1$ Hz, 3H, CH₃), 2.35 (s, 3H, CH₃), 4.01 (q, $J = 7.1$ Hz, 2H, CH₂), 5.32 (d, $J = 3.6$ Hz, 1H, CH), 7.64–7.68 (m, 2H, arom), 8.05–8.15 (m, 2H, arom), 9.69 (brs, 1H, NH), 10.42 (brs, 1H, NH); IR (KBr) ν : 3177, 2988, 1714, 1660, 1594, 1531, 1475, 1189 cm^{-1} .

Ethyl 6-methyl-2-thioxo-4-(2-chlorophenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4r) Yield, 95%; m.p. 203–205 °C; ¹H NMR (DMSO- d_6 , 500 MHz) δ : 1.10 (t, $J = 7.1$ Hz, 3H, CH₃), 2.32 (s, 3H, CH₃), 3.91 (q, $J = 7.1$ Hz, 2H, CH₂), 5.63 (d, $J = 3.0$ Hz, 1H, CH), 7.28–7.35 (m, 3H, arom), 7.41–7.43 (m, 1H, arom), 9.59 (brs, 1H, NH), 10.35 (brs, 1H, NH); IR (KBr) ν : 3381, 3275, 3173, 1614, 1474, 1414, 1084 cm^{-1} ; HRMS for C₁₄H₁₅O₂N₂SCl 310.0543, found 310.0534.

Ethyl 6-methyl-2-thioxo-4-(4-methoxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4s)

Yield, 92%; m.p. 136—138 °C (Lit.⁹ 134—135 °C); ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.09 (t, *J* = 7.1 Hz, 3H, CH₃), 2.28 (s, 3H, CH₃), 3.72 (s, 3H, CH₃), 3.92 (q, *J* = 7.1 Hz, 2H, CH₂), 5.11 (d, *J* = 3.6 Hz, 1H, CH), 6.88—6.91 (d, *J* = 8.6 Hz, 2H, arom), 7.11—7.13 (d, *J* = 8.6 Hz, 2H, arom), 9.55 (brs, 1H, NH), 10.24 (brs, 1H, NH); IR (KBr) ν: 3306, 3180, 3103, 2962, 2936, 2832, 1705, 1652, 1614, 1568, 1504, 1449 cm⁻¹.

Ethyl 6-methyl-2-thioxo-4-(4-hydroxy-3-methoxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4t) Yield, 90%; m.p. 191—193 °C; ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.05 (t, *J* = 7.1 Hz, 3H, CH₃), 2.54 (s, 3H, CH₃), 3.81 (q, *J* = 7.1 Hz, 2H, CH₂), 4.03 (s, 3H, OCH₃), 5.07 (d, *J* = 3.6 Hz, 1H, CH), 6.56—6.58 (m, 1H, arom), 6.69—6.79 (m, 2H, arom), 8.89 (brs, 1H, OH), 9.47 (brs, 1H, NH), 10.16 (brs, 1H, NH); IR (KBr) ν: 3415, 3175, 2997, 1687, 1586, 1517, 1197 cm⁻¹; HRMS for C₁₅H₁₈O₄N₂S 322.0987, found 322.0987.

Ethyl 6-methyl-2-thioxo-4-(2,4-dimethoxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4u) Yield, 86%; m.p. 143—145 °C; ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.06 (t, *J* = 7.1 Hz, 3H, CH₃), 2.27 (s, 3H, CH₃), 3.74 (s, 3H, OCH₃), 3.77 (s, 3H, OCH₃), 3.98 (q, *J* = 7.1 Hz, 2H, CH₂), 5.40 (d, *J* = 3.4 Hz, 1H, CH), 6.44—6.47 (m, 2H, arom), 6.54—6.55 (m, 1H, arom), 9.17 (brs, 1H, NH), 10.17 (brs, 1H, NH); IR (KBr) ν: 3306, 3179, 2962, 2935, 1705, 1652, 1615, 1568, 1183 cm⁻¹; HRMS for C₁₆H₂₀O₄N₂S 336.1144, found 336.1151.

Ethyl 6-methyl-2-thioxo-4-(3-methoxyphenyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4v) Yield, 96%; m.p. 158—161 °C; ¹H NMR (DMSO-*d*₆, 500 MHz) δ: 1.07 (t, *J* = 7.1 Hz, 3H, CH₃), 2.28 (s, 3H, CH₃), 3.73 (s, 3H, OCH₃), 4.02 (q, *J* = 7.1 Hz, 2H, CH₂), 5.16 (d, *J* = 3.2 Hz, 1H, CH), 6.76—6.86 (m, 3H, arom), 7.24—7.28 (m, 1H, arom), 9.59 (brs, 1H, NH), 10.29 (brs, 1H, NH); IR (KBr) ν: 3241, 3118, 2934, 1702, 1649,

1598, 1226 cm⁻¹; HRMS for C₁₅H₁₈O₂N₂S 306.1038, found 306.1029.

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