Synthesis of Novel 3,4-Dihydropyrimidinones on Water Soluble Solid Support Catalyzed by Indium Triflate

P. Shanmugam, G. Annie and P. T. Perumal*

Organic Chemistry Division, Central Leather Research Institute,
Adyar, Chennai-600 020, INDIA
Fax No. 91-044-2491 1589 E-mail: ptperumal@hotmail.com

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Syntheses of several new 3,4-dihydropyrimidinones (DHPMs) on sodium sulfate solid support have been reported. The microwave enhanced rapid synthesis of the title compounds yielded a good percentage of the DHPMs. The catalytic activity of indium triflate enables to prepare a wide range of DHPMs. Syntheses of 2-hydroxyphenyl, 2-hydroxy-4-methoxyphenyl pendant groups on DHPMs scaffold are advantages of the present method, which are rather prone towards cyclization and the presence of free hydroxyl groups on the phenyl ring is confirmed *via* D_2O exchange study. The mechanism of the reaction is expected to proceed *via* absorption of substrates on the solid support followed by promotion of the reaction by $In(OTf)_3$ coupled with microwave irradiation.

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Introduction.

The growing need for novel methods in organic synthesis is unmitigated. Eco-benign versions of organic reactions are potential candidates for the synthesis of biologically active compounds [1,2]. In contemporary research, methods such as microwave assisted synthesis [3a], sonication [3b], and solid-phase reaction [3c,d] are proliferating in all frontiers of organic syntheses. Among the aforesaid methods, microwave assisted rapid syntheses of organic compounds on solid supports are found to meet the increasing needs of organic chemists [4].

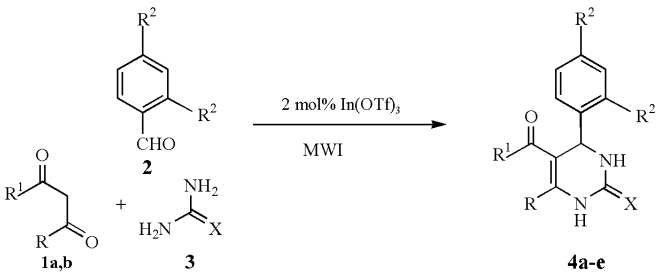
3,4-Dihydropyrimidinones (DHPMs) [5a,b], also called Biginelli compounds possess interesting biological applications [5c-e]. The apparent structural similarities of DHPMs to the well-known Hantzsch type dihydropyridines, calcium channel modulators suggest a good scope for this class of compounds in the field of medicinal chemistry [6a,b]. The classical one-pot condensation [7] of ethyl acetoacetate, benzaldehyde and urea for the preparation of DHPMs had been subjected to several improvements [8]. Different Lewis acid and metal ion catalysts were exploited for the enhancement of the yields [9a-e]. However, it is observed that the scope for syntheses of DHPMs containing sensitive, bulky and interesting heterocyclic groups at C-4 position have not been explored so far.

Results and Discussion.

Recently sodium sulfate supported reaction [10] has been utilized for the synthesis of cyclophanes, which encouraged us to probe into the application of the same to synthesize DHPMs. In the present work, sodium sulfate is used as the solid support along with 2 mol % of $In(OTf)_3$ to prepare DHPMs. The advantage of the method is that the inert solid support can be easily removed by washing with water and the crude reaction mixture can be purified either by recrystallization or column chromatography, leading to the desired products. The reaction is promoted by Lewis acid catalyst $In(OTf)_3$ and accelerated manifolds by microwave rapid heating. Various water-soluble solid supports like sodium chloride, magnesium sulfate and sodium sulfate were screened in the preliminary experiments using $In(OTf)_3$ as the catalyst. Sodium sulfate was found to be the optimum solid support over the rest. Microwave irradiation of different aldehydes with **1** and **3** using $In(OTf)_3$ as the catalyst on sodium sulfate solid support provided the best results. The catalytic activities of various Lewis acids on this reaction were evaluated by considering $InCl_3$, $FeCl_3$, and $ZnCl_2$ and $In(OTf)_3$, individually in the above-mentioned procedure on sodium sulfate solid support. Indium triflate was found to be better over other catalysts based on the yields obtained for different DHPMs.

In the present work DHPMs containing significant pendant groups, unlike usual substituted aryl groups, are considered. However the method is suitable for synthesizing DHPMs with usual aryl groups at C-4 position such as 2-nitrophenyl, 4-chlorophenyl- 4-anisyl-, *etc*. as well. Sensitive aldehydes such as salicylaldehyde, *o*-vanillin and cyanobenzaldehyde were chosen to show the tolerability of this method (Scheme 1, Table 1).

Scheme 1



1a: R = Me, $R^1 = OC_2H_5$
1b: R = Ph, R^1 = Me
X = O, S

Table 1

Synthesis of DHPM Containing Sensitive and o-substituted Pendant Groups

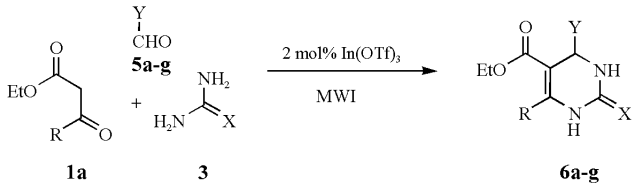
Product	R	R^1	R^2	R^3	X	Irradiation Time (min)	Yield (%) [a,b]
4a	Me	OEt	OH	H	O	11	91
4b	Me	OEt	OH	OMe	O	13	87
4c	Me	OEt	H	CN	O	15	93
4d	Me	OEt	Cl	H	S	8	86
4e	Ph	Me	Cl	Cl	O	11	89

[a] yield of the product obtained by crystallization; [b] all the products were characterized by IR, ^{1}H NMR, ^{13}C NMR and elemental analysis.

Interestingly, the products **4a,b** (Table 1) were obtained without cyclization as confirmed by IR and NMR spectra. It is noteworthy to mention that **4a,b** can not be prepared by any of the previously reported one-pot condensation methods due to tandem cyclization reaction (**4f**) [5a,11]. Atwal modification [12] a multi-step strategy to synthesize DHPMs, also does not afford the expected product **4a,b** as it needs the Knoevenagel condensation product of aldehyde and ethyl acetoacetate as the starting material. But the Knoevenagel condensation does not stop with enone product, which undergoes progressive cyclization to form acylcoumarins (**4g**) [13].

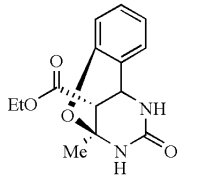
Deuterium exchange study was carried out to confirm that **4a,b** synthesized through the present method are uncyclized. ^{1}H NMR spectra of the deuterium exchanged samples **4a,b** do not contain three signals corresponding to the two NH protons of DHPM skeleton and OH proton of the phenyl ring. Deuterium exchange study authenticates

Scheme 2

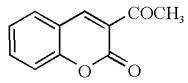


that **4a,b** have not undergone cyclization. The salient feature of this method is that the mild and environmentally friendly reaction conditions employed by us enable the preparation of DHPMs containing very sensitive aromatic pendant groups. Synthesis of DHPM bearing benzonitrile group, **4c** lends additional support to the tolerability of reaction conditions. IR (ν = 2229 cm^{-1}) and ^{13}C NMR (δ = 116 ppm) spectra confirm the presence of cyano group in **4c** (Table 1). The current procedure also yields good percentage of product when *ortho*-substituted aldehydes are employed (**4d** and **4e**).

Attempts to synthesize **6c** by any of the conventional literature reports result in poor yields, while the sodium sulfate supported synthesis afforded **6c** in moderate yield.



4f



4g

Figure 1

However, this reaction requires excess of ethyl acetoacetate (3 moles) that enables acyliminium ion to intercept with **1** to give product **6c**. The heterocyclic aldehydes **5d,f** were prepared in the laboratory by following the reported literature procedures through the Vilsmeier- Haack reaction as they are not commercially available [14]. The aldehydes **5a-g** when subjected to Biginelli reaction under microwave irradiation yielded the required DHPMs **6a-g** in good percentage (Scheme 2, Table 2).

The products 4-quinolinyl-3,4-dihydropyrimidinone **6d** and 4-chromonyl-3,4-dihydropyrimidinone **6f** are new in the DHPM series reported as of now. The formation of **6d** is confirmed by proton resonance peaks at δ = 5.7 ppm (for CH (4)) and NH protons resonating at δ = 9.39 ppm and δ = 8.29 ppm. Similarly proton resonance peaks at δ = 5.22 ppm and NH protons resonating at δ = 9.39 ppm and δ = 8.1 ppm confirm the formation of **6g** (Table 2). To synthesize **6d**, conventionally, the necessary ingredients in acidified ethanolic solution were mixed and refluxed over oil bath. However, the reaction yielded less than 30 % of product after prolonged heating (>24 h) and excess of **1** (2.5 equiv).

It is presumed that the mechanism of the reaction proceeds *via* acyliminium ion as predicted by Kappe [15a]. The rate enhancement under microwave irradiation may be attributed to the effective absorption of microwave by polar sodium sulfate solid support thereby triggering the reaction rate. In addition, the improved surface area and

Table 2

Synthesis of DHPM Containing Different Aryl and Heterocyclic Pendant Groups

Entry	Y	Product	Irradiation Time (min)	Yield (%) [a]
1	Phenyl-	6a	8	91 [b]
2	1-Naphthyl-	6b	15	84 [b]
3	9-Anthryl-	6c	30	63 [c,d]
4	2-Chloro-3-quinolyl	6d	15	76 [d]
5	Thienyl-	6e	9	85 [b]
6	6-Methoxy-3-chromonyl-	6f	21	81 [d]
7	2-pyridyl-	6g	13	83 [b]

[a] All products were characterized by IR, NMR and MS techniques; [b] products obtained by recrystallization of crude product; [c] 1:3:1.5 equivalents of anthraldehyde, ethyl acetoacetate, and urea were taken; [d] products obtained by column chromatography.

bringing the reagents in close proximity due to the presence of pores may be the reason for the rate enhancement of the organic reactions by employing inorganic solid supported catalysts [15b].

Conclusion.

We have presented an environmentally friendly method to synthesize DHPMs. The present study, in addition to focus on usual aromatic aldehydes as building blocks to prepare DHPMs, is also aimed at the aldehydes of sensitive type (such as salicylaldehyde, *o*-vanillin and cyano benzaldehyde), with bulky pendant groups (1-naphthaldehyde and 9-anthraldehyde) and interesting heterocycles (chromon-3-carboxaldehyde and quinolin-3-carboxaldehyde) to synthesize DHPMs. The fact that the DHPMs with sensitive functional groups such as phenolics **4a,b** could be prepared by this method stands testimony to the milder reaction conditions. An additional advantage of the method is the solubility of sodium sulfate in water, making the work-up methodology a convenient one. Sodium sulfate supported reaction would find enough scope in synthetic organic chemistry as an eco-benign choice to organic chemists.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. IR measurements were obtained as KBr pellets using Perkin Elmer Spectrum RXI FT-IR. The ^{1}H NMR and ^{13}C NMR were recorded in $CDCl_3$ + DMSO-d_6 with JEOL 400 MHz (model GSX 400) high resolution NMR spectrometer with TMS as an internal standard. Mass spectra were obtained using JEOL DX- 303 in EI ionization mode at 70 eV. The reaction was carried out in commercial BPL-SANYO microwave oven operating at 2.45 GHz. TLC was performed on precoated polygram SIL G/ UV_{254} sheets.

Optimization and General Method of Preparation of 4-Aryl-3,4-dihydropyrimidinone.

Benzaldehyde (1 g, 9.43 mmol), ethylacetoacetate (1.84 g, 14.15 mmol) and urea (0.6792 g, 11.32 mmol) were dissolved in 10 mL of chloroform (a few drops of methanol is added if urea is not dissolved). To this solution $In(OTf)_3$ (0.106 g, 2 mol %) was added followed by 10 g of sodium sulfate and the mixture was made into dry slurry. The slurry was transformed into 30 mL Borosil bottle with tight screw cap, which was kept in an alumina bath and irradiated in a domestic microwave oven for appropriate time with a pulse rate of 40 sec. and 30 % of power. The total consumption of aldehyde as monitored by TLC was an indication of completion of the reaction. After the reaction was over, the mixture was poured into 150 mL of water and heated over water bath for 30 minutes followed by stirring one hour at room temperature. The solid thus obtained in the reaction was collected by filtration and column chromatographed with 1:3 petroleum ether and ethylacetate mixture to give the required 4-phenyl-3,4-dihydropyrimidinone. The same method was repeated for Magnesium sulfate and Sodium chloride. Yields obtained on these solid supports are 90%, 56% and 67% respectively. For the optimization of catalysts, $ZnCl_2$, $InCl_3$, $FeCl_3$ and $In(OTf)_3$ were considered. Optimization of different catalysts on sodium sulfate solid support were performed and yields are 77%, 73%, 84%, and 91% respectively; *i.e.* best with $In(OTf)_3$.

Ethyl 6-Methyl-4-phenyl-3,4-dihydropyrimidin-2(*1H*)-one-5-carboxylate (**6a**).

This compound has mp 198-199 °C; ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 8.93 (s, 1H, NH(1)), 7.40 (s, 1H, NH(3)), 7.30 (m, 5H, Ar-H), 5.28 (s, 1H, CH(4)), 4.03 (q, *J* = 7.5 Hz, 2H, -O*CH*$_2$CH$_3$), 2.30 (s, 3H, 6-Me), 1.12 (t, 3H, *J* = 7.5 Hz, -OCH$_2$*CH*$_3$); ^{13}C NMR: δ 165.53, 152.69, 144.64, 128.03, 127.07, 126.29, 99.83, 59.23, 54. 41, 17.85, 13.83; IR (KBr) 3310, 2950, 1728, 1700 cm^{-1}; MS (EI, m/z): 260 (M^+).

Anal. Calcd. for $C_{14}H_{16}N_2O_3$: C, 64.60; H, 6.15; N, 10.76. Found: C, 64.85; H, 6.32; N, 10.78.

The above-mentioned procedure was followed for the other remaining substituents to obtain DHPMs.

Ethyl 6-Methyl-4-(2-hydroxyphenyl)-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (**4a**).

This compound has mp 224-226 °C; ^{1}H NMR (DMSO-d_6): δ 9.57 (s, 1H, OH), 9.09 (s, 1H, NH (1)), 7.08 (t, 1H, *J* = 8 Hz, Ar-H), 7.04 (d, 1H, *J* = 7.6 Hz, Ar-H), 6.97 (s, 1H, NH (3)), 6.79 (d, 1H, *J* = 8 Hz, Ar-H), 6.70 (t, 1H, *J* = 7.6 Hz, Ar-H), 5.47 (s, 1H, CH (4)), 3.93 (q, 2H, *J* = 6.8 Hz, CH$_3$*CH*$_2$), 2.29 (s, 3H, 6- Me), 1.04 (t, 3H, *J* = 7.2 Hz, *CH*$_3$CH$_2$-); ^{1}H NMR (DMSO-d_6 + D_2O): δ 7.08 (t, 1H, *J* = 8 Hz, Ar-H), 6.99 (d, 1H, *J* = 7.6 Hz, Ar-H)), 6.82 (d, 1H, *J* = 8.0 Hz, Ar-H), 6.74 (q, 1H, *J* = 7.6 Hz, Ar-H),

5.49 (s, 1H, CH (4)), 3.93 (q, 2H, *J* = 6.8 Hz, CH_3CH_2), 2.29 (s, 3H, 6-Me), 1.04 (t, 3H, *J* = 7.2 Hz, CH_3CH_2-); ^{13}C NMR: δ 166.52, 155.09, 153.70, 149.32, 130.01, 118.73, 111.84, 98.79, 60.21, 49.86, 18.29, 14.67; IR (ν, cm^{-1}): 3410, 3343, 3108, 2915, 1660, 1592, 1488. MS (EI, m/z): 275 (M^+- 1).

Anal. Calcd. for $C_{14}H_{16}N_2O_4$: C, 60.85; H, 5.84; N, 10.14. Found: C, 60.74; H, 5.47; N, 10.12.

Ethyl 6-Methyl-4-(4-methoxy-2-hydroxyphenyl)-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (**4b**).

This compound has mp 204-206 °C; ^{1}H NMR (DMSO-d_6): δ 9.08 (s, 1H, OH), 8.72 (s, 1H, NH (1)), 7.05 (s, NH (3)), 6.84 (d, 1H, *J* = 8 Hz, Ar-H), 6.68 (q, 1H, *J* = 7.6 Hz, Ar-H), 6.61 (q, 1H, *J* = 7.6 Hz, Ar-H), 5.52 (s, 1H, CH (4)), 4.17 (q, 2H, *J* = 6.8 Hz, CH_3CH_2-), 3.93 (s, 3H, -OMe), 2.27 (s, 3H, 6-Me), 1.03 (t, 3H, *J* = 7.2 Hz, CH_3CH_2-); ^{1}H NMR (DMSO-d_6 +D_2O): δ 6.84 (d, 1H, *J* = 8 Hz, Ar-H), 6.68 (q, 1H, *J* = 7.6 Hz, Ar-H), 6.61 (q, 1H, *J* = 7.6 Hz, Ar-H), 5.20 (s, 1H, CH (4)), 3.92 (q, 2H, *J* = 6.8 Hz, CH_3CH_2-), 3.73 (s, 3H, -OMe), 2.29 (s, 3H, 6- Me), 1.03 (t, 3H, *J* = 7.2 Hz, CH_3CH_2-): ^{13}C NMR: δ 166.88, 153.70, 149.32, 148.37, 144.04, 130.49, 120.04, 119.73, 111.84, 99.28, 60.64, 56.71, 49.71, 18.45, and 14.82. IR (ν, cm^{-1}): 3380, 3235, 3108, 2937, 1693, 1644, and 1488. MS (m/z): 306 (M^+).

Anal. Calcd. for $C_{15}H_{18}N_2O_5$: C, 58.82; H, 5.92; N 9.15. Found: C, 58.63; H, 5.81; N, 9.12.

Ethyl 4-(4-Cyanophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (**4c**).

This compound has mp 180-182 °C; ^{1}H NMR (DMSO-d_6): δ 9.21 (s, 1H, NH (1)), 7.75 (s, 1H, NH (3)), 7.67 (d, 2H, *J* = 8.3 Hz, Ar-H), 7.45 (d, 2H, *J* = 8.3 Hz, Ar-H), 5.28 (s, 1H, CH(4)), 4.01 (q, 2H, *J* = 7.3 Hz, CH_3CH_2-), 2.29 (s, 3H, 6- Me), 1.12 (t, 3H, *J* = 7.3 Hz, CH_3CH_2-); ^{13}C NMR: δ 163.55, 150.52, 148.37, 147.49, 130.52, 125.80, 116.90, 108.81, 96.85, 57.70, 52.48, 16.39, and 12.45; IR (ν, cm^{-1}): 3233, 3111, 2929, 2229, 1735, 1708, 1648.

Anal. Calcd. for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73; Found: C, 63.12; H, 5.19; N, 14.70.

Ethyl4-(2-Chlorophenyl)-6-methyl-2-thioxo-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (**4d**).

This compound has mp 168-168 °C; IR (KBr) 3235, 3050, 1674, 1636 cm^{-1}; ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 1.02 (t, 3H, *J* = 7.6 Hz, -OCH_2CH_3), 2.45 (s, 3H, 6-Me), 3.98 (q, 2H, *J* = 7.6 Hz, -OCH_2CH_3), 5.90 (d, 1H, *J* = 2.7 Hz, 4 - CH), 7.34 (s, 1H, NH (3)), 7.36 - 7.41 (m, 4H, Ar-H), 8.25 (s, 1H, NH (1)).

Anal. Calcd. for $C_{14}H_{15}ClN_2O_2S$: C, 54.10; H, 4.86; N, 9.01. Found: C, 54.18; H, 4.88; N, 8.99.

5-Acetyl-4-(2,4-dichlorophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (**4e**).

This compound has mp 220-222 °C; ^{1}H NMR (DMSO-d_6): δ 1.67 (s, 3H), 5.43 (d, 1H, *J* = 3.5Hz), 6.84 (s, 1H, NH(3)), 7.42-7.65 (m, 6H), 7.76 - 8.13 (m, 2H), 9.39 (s, 1H, NH(1)). ^{13}C NMR δ: 19.43, 55.08, 108.32, 121.56, 122.94, 127.95, 128.30, 129.20, 129.33, 130.80, 132.08, 133.63, 142.21, 147.51, 148.04, 148.65, 152.23, 195.06. IR (ν, cm^{-1}): 3315, 3154, 2924, 1716, 1694, 1643.

Anal. Calcd. for $C_{18}H_{14}Cl_2N_2O_2$: C, 59.99; H, 3.92; N, 7.78. Found: C, 59.83; H, 3.95; N, 7.71.

Ethyl 4-(1-Naphthyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (**6b**).

This compound has mp 243-245 °C; ^{1}H NMR (DMSO-d_6): δ 9.05 (s, 1H, NH (1)), 8.21 (m, 1H Ar-H), 7.39 (m, 7H, Ar-H), 6.06 (s, 1H, CH(4)), 3.77 (q, 2H, *J* = 7.2 Hz, CH_3CH_2-), 2.29 (s, 3H, 6- Me), 1.12 (t, 3H, *J* = 7.3, CH_3CH_2-); IR (ν, cm^{-1}): 3336, 3226,3110,1694,1636.

Anal. Calcd. for $C_{18}H_{18}N_2O_3$: C, 69.65; H, 5.85; N, 9.03. Found: C, 69.35; H, 5.91; N, 8.87.

Ethyl 4-(9-Anthryl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (**6c**).

This compound has mp 235-237 °C; ^{1}H NMR (DMSO-d_6): δ 9.41 (s, 1H, NH (1)), 8.58 (d, 2H, *J* = 6.8 Hz), 8.42 (s, 1H, NH(3)), 8.08 (d, 2H, *J* = 6.8 Hz), 7.71 (s, 1H, Ar-H), 7.50 (d, 4H, *J* = 6.8 Hz), 7.01 (s, 1H, CH(4)), 3.35 (q, 2H, *J*= 6.8 Hz, CH_3CH_2-), 2.24 (s, 3H, 6- Me), 0.18 (t, 3H, *J* = 6.8 Hz, CH_3CH_2-); IR (ν, cm^{-1}): 3483, 3387, 3331, 2923, 1693, 1640,1445. MS (EI, m/z): 360 (M^+).

Anal. Calcd. for $C_{22}H_{20}N_2O_3$: C, 73.30; H, 5.60; N, 7.78. Found: C, 72.97; H, 5.63; N, 7.81.

Ethyl 4-(2-Chloro-3-quinolinyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (**6d**).

This compound has mp > 265 °C (decomp); ^{1}H NMR (DMSO-d_6): δ 9.39 (s, 1H, NH (1)), 8.29 (s, 1H, NH (3)), 8.09 (d, 1H, *J* = 8.4 Hz), 7.95 (d, 1H, *J* = 8.4 Hz, Ar-H), 7. 79 (m, 2H, Ar-H), 7.63 (q, 1H, *J* = 7.2 Hz, Ar-H), 5.75 (s, 1H, CH (4)), 3.86 (q, 2H, *J* = 7.2 Hz, CH_3CH_2)), 2.38 (s, 3H, 6-Me), 0.94 (t, 3H, *J* = 7.2 Hz, CH_3CH_2); ^{13}C NMR δ: 165.76, 148.34, 139.86, 133.67, 130.26, 128.60, 128.00, 126.16, 125.62, 125.50, 95.58, 59.37, 50.41, 18.20, 13.88; IR (ν, cm^{-1}): 3490, 3331, 3232, 2915, 1697, 1638, and 1443. MS (EI, m/z): 344 (M^+).

Anal. Calcd. for $C_{17}H_{16}N_3O_3Cl$: C, 59.12; H, 4.67; N, 12.17. Found: C, 59.02; H, 4.74; N, 12.29.

Ethyl 4-(2-Thienyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (**6e**).

This compound has mp 215-217 °C; ^{1}H NMR (DMSO-d_6): δ 9.33 (s, NH (1)), 7.92 (s, NH (3)), 7.35 (d, 1H, *J* = 4.9 Hz, Ar-H), 6.94 (d, 1H, *J* = 3.54 Hz, Ar-H), 6.89 (d, 1H, *J* = 10.2 Hz, Ar-H), 5.41 (d, 1H, *J* = 3.54 Hz, CH(4)), 4.01 (q, 2H, *J* = 7.1 Hz, CH_3CH_2-), 2.22 (s, 3H, 6- Me), 1.15 (t, 3H, *J* = 7.1 Hz, CH_3CH_2-); IR (ν, cm^{-1}): 3344, 3250, 2922, 1696, 1646 , 1484. MS (EI, m/z): 266 (M^+).

Anal. Calcd. for $C_{12}H_{14}N_2O_3S$: C, 54.12; H, 5.30; N, 10.52. Found: C, 54.08; H, 5.26; N, 10.39.

Ethyl 4-(6-Methoxy-3-chromonyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (**6f**).

This compound has mp > 250 °C (decomp); ^{1}H NMR (DMSO-d_6): δ 9.23 (s, 1H, NH (1)), 8.15 (s, 1H, NH (3)), 7.61 (d, 1H, *J* = 9.2 Hz, Ar-H), 7.46 (d, 1H, *J* = 3.2 Hz, Ar-H), 7.38 (q, 2H, *J* = 3.2 Hz & 9.2 Hz, Ar-H), 7.21 (s, 1H, pyran-H), 5.23 (s, 1H, CH(4)), 3.97 (q, 2H, *J* = 6.8 Hz, CH_3CH_2-), 3.86 (s, 3H, Ar-OMe), 2.25 (s, 3H, 6- Me), 1.07 (t, 3H, *J* = 6.8 Hz, CH_3CH_2-); ^{13}C NMR: δ 161.58, 158.09, 155.02, 151.16, 150.11, 147.98, 138.94, 137.12, 124.13, 119.26, 117.32, 109.58, 97.85, 60.12, 57.82, 53.48, 17.49, 13.92; IR (ν, cm^{-1}): 3435, 3233, 3069, 2922, 1720, 1672, 1624. MS (EI, m/z): 358.

Anal. Calcd. for $C_{18}H_{18}N_2O_6$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.19; H, 5.21; N, 7.73.

Ethyl 4-(2-Pyridyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one-5-carboxylate (**6g**).

This compound has mp 212 - 214 °C; ^{1}H NMR (DMSO-d_6): δ 9.51 (m, 2H), 9.17 (s, 1H, NH (1)), 8.06 (s, 1H, NH (3)), 7.38 (m, 2H), 5.41 (s, 1H, CH(4)), 3.96 (q, 2H, *J* = 6.84 Hz, CH_3CH_2-), 2.24 (s, 3H, 6- Me), 1.11 (t, 3H, *J* = 6.84 Hz, CH_3CH_2-); ^{13}C NMR: δ 165.02, 159.54, 151.20, 148.62, 126.11, 123.06, 122.50, 121.42, 94.69, 58.38, 45.92, 17.66, 13.97; IR (ν, cm^{-1}): 3422, 3210, 3072, 2932, 1718, 1675, 1625.

Anal. Calcd. for $C_{13}H_{15}N_3O_3$: C, 59.76; H, 5.79; N, 16.08. Found: C, 59.70; H, 5.83; N, 15.99.

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