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An eco-safe and solvent-free approach for clean and one-pot synthesis of 3,4-dihydropyrimidin-2-(1*H*)-one/thione derivatives using $Zn(OAc)_2.2H_2O$ as an environmental friendly, readily and efficient catalyst

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An environmental friendly, economical and clean Biginelli approach in presence of readily available zinc acetate dihydrate ($Zn(OAc)_2.2H_2O$) to access biologically active 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives *via* one-pot, three-component reaction of β-keto esters (methyl or ethyl acetoacetate), aromatic aldehyde (benzaldehye derivatives) and urea or thiourea in high to excellent yields has been studied. This solvent-free procedure is sustainable and advantageous compared to conventional methods due to short reaction times, one-pot procedure, easy handling, efficient, environmentally benign nature, low-cost and non-toxic catalyst, eco-friendly, ready availability of starting materials and no requirement of chromatographic purification. The products have been characterized by melting points and ^{1}H NMR spectroscopy.

Keywords: 3,4-Dihydropyrimidin-2-(1*H*)-ones/thiones derivatives, zinc acetate dihydrate ($Zn(OAc)_2.2H_2O$), Biginelli condensation reaction, solvent-free conditions, environment friendly, economical synthesis

In recent years, the design and development of bioactive heterocyclic compounds synthesis performed through multi-component reactions (MCRs)[1-6], involving three or more reactants in one-pot, have attracted considerable interest since such processes improve atom economy, efficiency and convergence.

Pyrimidinone derivatives are a common structural motif in variety of natural and non-natural products. Their derivatives have been known to exhibit a wide range of pharmacological and biological properties (Figure 1). For example these heterocyclic compounds have been used as calcium channel blockers, α-1a-antagonists[7], mitotic kinesin Eg5 inhibition[8], anti cancer (Mal3-101)[9], anti HIV agent[10], antibacterial and antifungal[11], antiviral[12], antioxidative[13]. The representatives such as batzelladines, ptilomycalines and crambescidines exhibit many biological activities such as anticancer, antifungal, anti HIV, *etc*.[14]

Typically, processes involved in the synthesis of these compounds are catalyzed by different catalysts[15-26]. Some of the limitations of these methodologies are low yields, toxic organic solvents and catalyst, harsh reaction conditions and expensive materials.

Based on the above considerations and our interest in the design of efficient and environmental benign methodologies, attempts were directed to synthesize one of Biginelli-type reactions[27]. Finally, herein, we report a simple, clean and mild procedure for synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives *via* reaction of β-keto esters, aldehyde derivatives and urea/thiourea by using of $Zn(OAc)_2.2H_2O$ as a catalyst under thermal and solvent-free conditions with excellent yields and short reaction times (Scheme I). During the past decades, the use of zinc compounds as environmental safe catalysts in organic synthesis have attracted great interest due to their notable advantages such as non-toxic, environmentally-friendly, easy to handle, highly efficient and low-cost[28,29]. Also $Zn(OAc)_2.2H_2O$ can be successfully used in the type of carbon-carbon bonds as an available, eco-friendly and environmental friendly catalyst[30-32] in organic synthesis. Short reaction times, high to excellent yields, eco-friendly, one-pot and efficient, readily, low-cost and non- toxic catalyst that makes our protocol alternative in comparison to some of the earlier reported methods.

Furthermore, one of the source of environmental pollutions is the usage of organic solvents under reflux conditions and the need for column chromatography to purity the products. In this present work, the products were obtained through simple

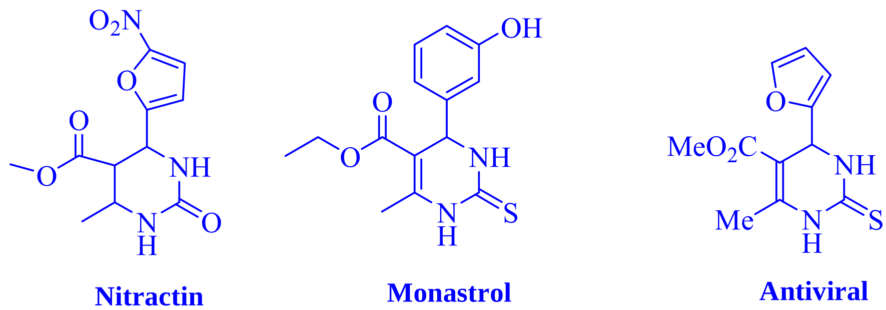
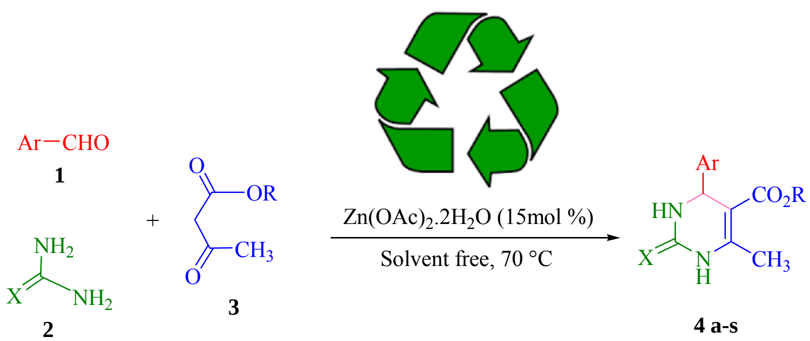


Figure 1 — Biologically active compounds containing the dihydropyrimidine unit



(Ar)**1a**,**1b**=Ph; **1c**= 3-Cl-C_6H_4; **1d**, **1e**= 4-Cl-C_6H_4; **1f**= 4-OH-C_6H_4; **1g**= 4-Me-C_6H_4; **1h**= N,N-di Me-C_6H_3; **1i**, **1j**= 3-MeO- C_6H_4; **1k**= 4-MeO-C_6H_4; **1l**= 4-NO_2-C_6H_4; **1m**= 4-F-C_6H_4; **1n**, **1o**=2-Cl-C_6H_4; **1p**= 4-MeO-C_6H_4; **1q**= 4-F-C_6H_4; **1r**= 4-NO_2-C_6H_4; **1s**= 4-OH-C_6H_4

(X) **2a**= O; **2b**= S

(R) **3a**= Et; **3b**= Me

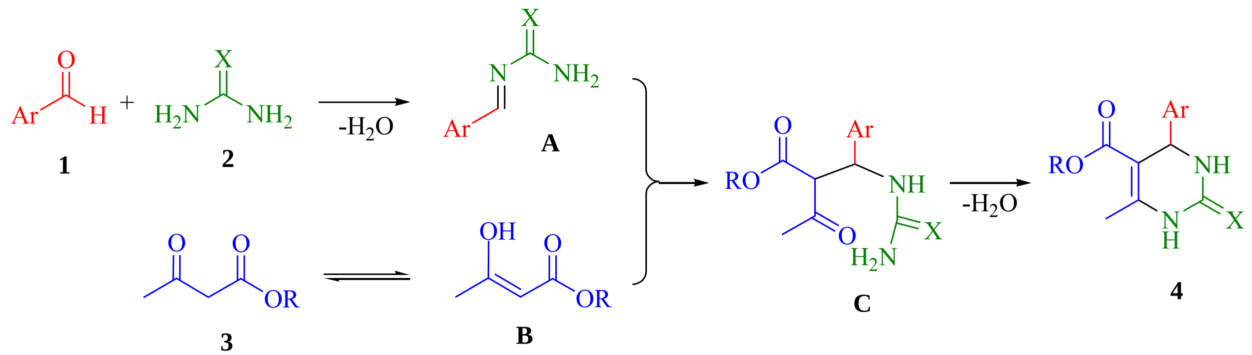
Scheme I — Synthesis of 3,4-dihydropyrimidin-2-(1*H*)-one/thione derivatives

filtering with no need column chromatographic separation.

Results and Discussion

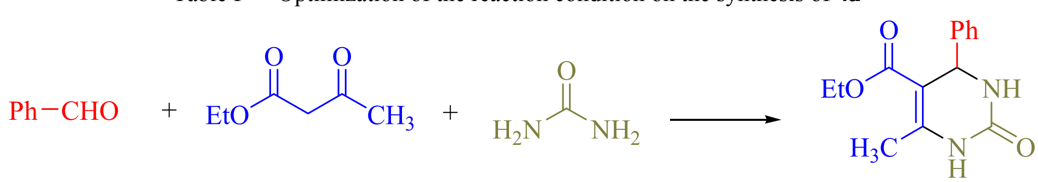
At beginning we performed three-component condensation Biginelli reaction of benzaldehyde (**1**, 1.0 mmol), urea (**3**, 1.5 mmol) and ethyl acetoacetate (**2,** 1.0 mmol) in the present of $Zn(OAc)_2.2H_2O$ (15 mol%) under solvent-free at 70 °C, the product **4a** was found in 89%, which was confirmed by ^{1}H NMR spectroscopy. Encouraged by this result, we chosen this reaction as a model reaction to study the reaction conditions further for the synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives (**4a-s**). The catalyst plays an important role in the success of the reaction in terms of rate of the reaction and yields. In order to optimize the reaction conditions, quantity of the catalyst required was determined. No product could be detected in the absence of the catalyst even after 4h (Table I, entry 1). Then, 5 mol% $Zn(OAc)_2.2H_2O$ was used to perform the reaction. But it requires slightly long reaction time and low yields. Therefore, the loading of catalyst was gradually increased from 5 mol% to 20 mol% (Table I). It was found that 15 mol% of $Zn(OAc)_2.2H_2O$ is optimal to carry out the reactions in a short duration (Table I, entry 4). The use of excess of catalyst did not alter either reaction time or yield of the product. Thus, the use of 15 mol% $Zn(OAc)_2.2H_2O$ is ideal to achieve the desired product in high yields. We also investigated different temperatures for the model reaction Table I). It was observed that fast reaction occurred on raising the temperature from RT to 80 °C and the yield of preferred product increased significantly (Table I). We were satisfied to find that the reaction proceeded smoothly and almost complete conversion of reactants was observed at 70 °C to afford the desired product (**4a**) in 89% yields within 15 min (Table I, entry 4). Further increase in the temperature did not affect the product yield (Table I, entry 8). Having optimized reaction conditions for the synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/tiones derivatives (**4a-s**) using 15 mol% $Zn(OAc)_2.2H_2O$ as the catalyst under solvent-free conditions at 70 °C we subsequently applied for a variety of aldehydes, urea/ thiourea and ethyl/methyl acetoacetate (Table II).

Proposed mechanistic route of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones synthesis in the presence of zinc acetate dihydrate are shown in Scheme II. In this probable mechanism, the zinc acetate dihydrate catalyzed Biginelli condensation *via* acylimin intermediate (**A**) is presented in Scheme II. The reaction of aldehydes (**1**) and urea(**2**) generates an acylimin intermediate (**A**), which further reacts with the activated 1,3-dicarbonyl compound (**B**) producing an open-chain ureide (**C**) undergoing subsequent cyclization and dehydration to give the major product (**4**).



Scheme II — Proposed mechanistic route for the synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones

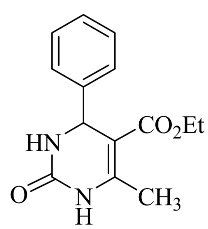
Table I — Optimization of the reaction condition on the synthesis of **4a** [a]



Entry	$Zn(OAc)_2.2H_2O$ (mol %)	Temperature (°C)	Time (min)	Isolated Yields (%)
1	Catalyst free	70	240	Not product
2	5	70	35	53
3	10	70	20	71
4	15	70	15	89
5	15	rt	360	Not product
6	15	40	45	49
7	15	60	25	74
8	15	80	15	89
9	20	70	15	90

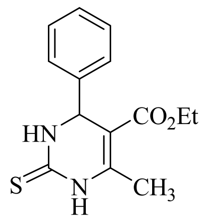
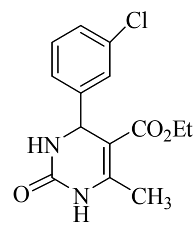
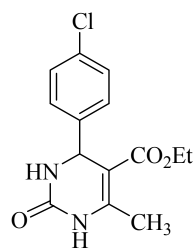
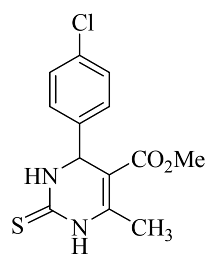
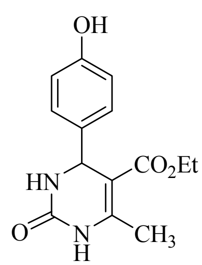
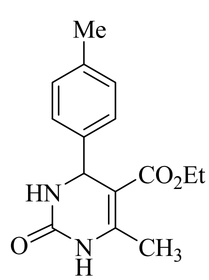
[a] Reaction conditions: benzaldehyde (1.0 mmol), ethyl acetoacetate (1.0 mmol), urea (1.5mmol) and zinc acetate dihydrate was heated under various temperatures for the appropriate time.

Table II — Synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives

Entry	R^1	R^2	X	Product [a]	Time (min)	Yield (%) [b]	m.p. (°C)	Lit. m.p. (°C)
1	H	CH_3CH_2	O	 **4a**	15	89	202-204	200-202[16]

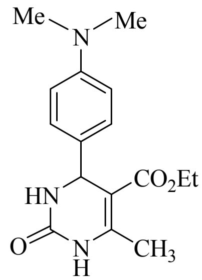
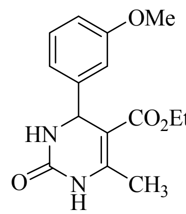
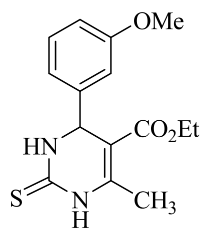
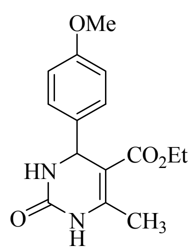
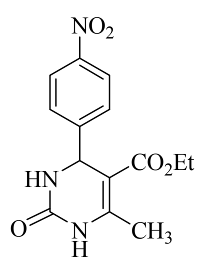
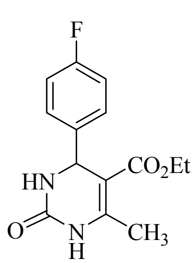
Contd.

Table II — Synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives (Contd.)

Entry	R^1	R^2	X	Product [a]	Time (min)	Yield (%) [b]	m.p. (°C)	Lit. m.p. (°C)
2	H	CH_3CH_2	S	 **4b**	15	86	207-209	208-210[16]
3	3-Cl	CH_3CH_2	O	 **4c**	25	84	191-194	194-196[16]
4	4-Cl	CH_3CH_2	O	 **4d**	25	82	213-215	214-215[18]
5	4-Cl	CH_3	S	 **4e**	30	80	192-194	191-195[15]
6	4-OH	CH_3CH_2	O	 **4f**	35	76	233-236	234-236[22]
7	4-CH_3	CH_3CH_2	O	 **4g**	15	88	204-206	204-205[17]

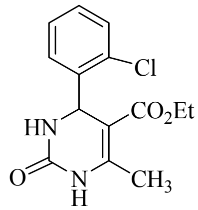
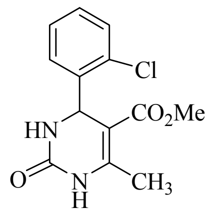
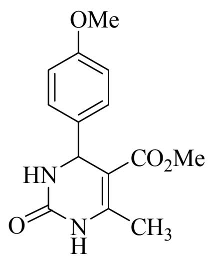
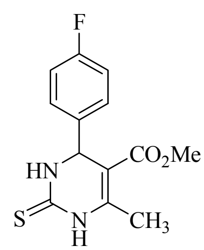
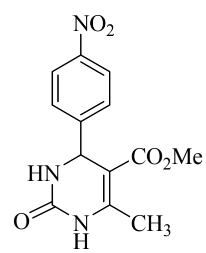
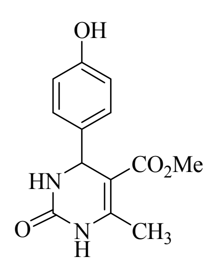
Contd.

Table II — Synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives (Contd.)

Entry	R^1	R^2	X	Product [a]	Time (min)	Yield (%) [b]	m.p. (°C)	Lit. m.p. (°C)
8	4-$N(CH_3)_2$	CH_3CH_2	O	 **4h**	20	89	256-258	254-256[22]
9	3-OCH_3	CH_3CH_2	O	 **4i**	20	84	202-204	205-206[17]
10	3-OCH_3	CH_3CH_2	S	 **4j**	25	81	150-152	150-151[17]
11	4-OCH_3	CH_3CH_2	O	 **4k**	20	82	201-203	203-205[23]
12	4-NO_2	CH_3CH_2	O	 **4l**	15	91	206-208	207-209[16]
13	4-F	CH_3CH_2	O	 **4m**	10	93	172-174	174-176[20]

Contd.

Table II — Synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives (Contd.)

Entry	R^1	R^2	X	Product [a]	Time (min)	Yield (%) [b]	m.p. (°C)	Lit. m.p. (°C)
14	2-Cl	CH_3CH_2	O	 **4n**	25	85	221-223	220-223[16]
15	2-Cl	CH_3	O	 **4o**	25	83	250-252	248-252[16]
16	4-OCH_3	CH_3	O	 **4p**	20	86	192-194	190-194[21]
17	4-F	CH_3	S	 **4q**	15	88	208-210	208-210[20]
18	4-NO_2	CH_3	O	 **4r**	15	92	215-217	214-216[16]
19	4-OH	CH_3	O	 **4s**	35	80	243-245	245-246[17]

[a] Isolated yield.
[b] Reaction conditions: benzaldehyde (1.0 mmol), ethyl/methyl acetoacetate (1.0 mmol), urea/thiourea (1.5 mmol) and zinc acetate dihydrate (15 mol %) was heated at 70 °C.

Comparison of catalytic ability some of catalysts reported in the literature for synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives are shown in Table III. Also ^{1}H NMR data of products have been compared with literature (Table IV). This study reveals that zinc acetate dihydrate ($Zn(OAc)_2.2H_2O$) has shown its extraordinary potential to be an alternative readily, environmental friendly, efficient, low-cost and economical catalyst for the Biginelli reaction. In addition, the use of solvent-free conditions with excellent yields and short reaction times in the reaction with both urea and thiourea are the notable advantages this present methodology.

Experimental Section

Melting points of all compounds were determined using an Electro Thermal 9100 apparatus. ^{1}H NMR spectra were recorded on a Bruker DRX-400 Avance instrument with DMSO-d_6 as solvent. All reagents and solvents were purchased from Merck, Fluka and Acros chemical companies and used without further purification.

General procedure for preparation of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives, 4a-s

A mixture of aldehydes derivatives (**1**, 1.0 mmol) and urea/thiourea (**3**, 1.5 mmol), ethyl/methyl acetoacetate (**2**, 1.0 mmol) was heated under solvent-free conditions at 70°C for appropriate time in the presence of $Zn(OAc)_2.2H_2O$ (15 mol %). After completion of the reaction (determined by thin layer chromatography TLC) the mixture was cooled to RT, cold water added, the precipitate separated with filtration and recrystallized from ethanol to afford the pure products **4a-s**. Spectral data of products are represented below.

5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one, 4a: Crystalline solid. Yield 89%. m.p.202-204°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.10 (3H, t, *J*= 7.2 Hz, CH_3CH$_2$), 2.26 (3H, s, CH$_3$), 3.99 (2H, q, *J*=7.2 Hz, CH$_2$O), 5.15 (1H, s, CHN), 7.26 (3H, d, *J*= 7.2 Hz, ArH), 7.33 (2H, t, *J*=7.2 Hz, ArH), 7.76 and 9.21 (2H, 2s, 2NH).

5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-thione, 4b: Crystalline solid. Yield 86%. m.p.207-209°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.11 (3H, t, *J*= 7.2 Hz, CH_3CH$_2$), 2.31 (3H, s, CH$_3$), 4.02 (2H, q, *J*=7.2 Hz, CH$_2$O), 5.19 (1H, s, CHN), 7.23 (2H, d, *J*=7.2 Hz, ArH), 7.28 (1H, t, *J*=7.2 Hz, ArH), 7.36 (2H, t, *J*=7.2 Hz, ArH), 9.68 and 10.36 (2H, 2s, 2NH).

5-Ethoxycarbonyl-6-methyl-4-(4-hydroxyphenyl) -3,4-dihydropyrimidin-2(1*H*)-one, 4f: Crystalline solid. Yield 76%. m.p.233-236°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.11 (3H, t, *J*= 9.6 Hz, CH_3CH$_2$), 2.50 (3H, s, CH$_3$), 3.98 (2H, q, *J*=9.2 Hz, CH$_2$O), 5.04 (1H, s, CHN), 6.68-7.04(4H, m, ArH), 7.64 and 9.13 (2H, 2s, 2NH), 9.35 (1H, s, OH).

5-Ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl) -3,4-dihydropyrimidin-2(1*H*)-one, 4k: Crystalline solid. Yield 82%. m.p.201-203°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.11 (3H, t, *J*= 9.6 Hz, CH_3CH$_2$), 2.24(3H, s, CH$_3$), 3.73 (3H, s, OCH$_3$), 3.99 (2H, q, *J*=9.6 Hz, CH$_2$O), 5.09 (1H, s, CHN), 6.89 (2H, d, *J*= 8.4Hz, ArH), 7.15 (2H, d, *J*= 8.8Hz, ArH), 7.70 and 9.18 (2H, 2s, 2NH).

5-Ethoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1*H*)-one, 4l: Crystalline solid. Yield 91%. m.p.206-208°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.10 (3H, t, *J*= 9.6 Hz, CH_3CH$_2$), 2.28(3H, s, CH$_3$), 3.99 (2H, q, *J*=9.2 Hz, CH$_2$O), 5.27 (1H, s, CHN), 7.50-7.53 (2H, m, ArH), 7.23 (2H, d, *J*= 9.2Hz, ArH), 7.92 and 9.38 (2H, 2s, 2NH).

Table III — Comparison of catalytic ability some of catalysts reported in the literature for synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives [a]

Entry	Catalyst	Conditions	Time/Yield (%)	Ref. No.
1	Bakers' yeast	RT	24h/84	17
2	Hydrotalcite	Solvent-free, 80 °C	35 min/84	18
3	$[Al(H_2O)_6](BF_4)_3$	MeCN, Reflux	20 h/81	19
4	$Cu(BF_4)_2.xH_2O$	RT	30 min/90	21
5	[Btto][*p*-TSA]	Solvent-free, 90 °C	30 min/96	23
6	Triethylammonium acetate	Solvent-free, 70 °C	45min/90	24
7	*p*-Dodecylbenzenesulfonic acid	Solvent-free, 80 °C	3 h/94	25
8	TMSPTPOSA	EtOH/Reflux	3 h/95	26
9	$Zn(OAc)_2.2H_2O$	Solvent-free, 70 °C	15 min/89	This work

[a] Based on the three-component reaction of benzaldehyde, ethyl acetoacetate and urea.

Table IV — Comparison of ^{1}H NMR data

Entry	Product	H Shift (Found)	H Shift (Lit.)	Ref.
1	**4a**	1.10 (3H, t, *J*= 7.2 Hz, CH_3CH_2) 2.26 (3H, s, CH_3) 3.99 (2H, q, *J*=7.2 Hz, CH_2O) 5.15 (1H, s, CHN) 7.76 and 9.21 (2H, 2s, 2NH)	1.15 (3H, t, *J*= 6.5 Hz, CH_3CH_2) 2.30 (3H, s, CH_3) 4.00 (2H, q, *J*=6.5 Hz, CH_2O) 5.20 (1H, s, CHN) 7.74 and 9.20 (2H, 2s, 2NH)	21
2	**4b**	1.11 (3H, t, *J*= 7.2 Hz, CH_3CH_2) 2.31 (3H, s, CH_3) 4.02 (2H, q, *J*=7.2 Hz, CH_2O) 5.19 (1H, s, CHN) 9.68 and 10.36 (2H, 2s, 2NH)	1.09 (3H, t, *J*= 7.00 Hz, CH_3CH_2) 2.28 (3H, s, CH_3) 4.00 (2H, q, *J*=7.00 Hz, CH_2O) 5.16 (1H, s, CHN) 9.64 and 10.33 (2H, 2s, 2NH)	21
3	**4f**	1.11 (3H, t, *J*= 9.6 Hz, CH_3CH_2) 2.50 (3H, s, CH_3) 3.98 (2H, q, *J*=9.2 Hz, CH_2O) 5.04 (1H, s, CHN) 7.64 and 9.13(2H, 2s, 2NH) 9.35 (1H, s, OH)	1.08 (3H, t, *J*= 7.00 Hz, CH_3CH_2) 2.21 (3H, s, CH_3) 3.96 (2H, q, *J*=7.00 Hz, CH_2O) 5.02 (1H, s, CHN) 7.64 and 9.10(2H, 2s, 2NH) 9.34 (1H, s, OH)	21
4	**4k**	1.11 (3H, t, *J*= 9.6 Hz, CH_3CH_2) 2.24(3H, s, CH_3) 3.73 (3H, s, OCH_3) 3.99 (2H, q, *J*=9.6 Hz, CH_2O) 5.09 (1H, s, CHN) 7.70 and 9.18 (2H, 2s, 2NH)	1.00 (3H, t, *J*= 6.78 Hz, CH_3CH_2) 2.20 (3H, s, CH_3) 3.70 (3H, s, OCH_3) 3.96 (2H, q, *J*=6.80 Hz, CH_2O) 5.07 (1H, s, CHN) 7.64 and 9.14 (2H, 2s, 2NH)	21
5	**4l**	1.10 (3H, t, *J*= 9.6 Hz, CH_3CH_2) 2.28(3H, s, CH_3) 3.99 (2H, q, *J*=9.2 Hz, CH_2O) 5.27 (1H, s, CHN) 7.92and 9.38 (2H, 2s, 2NH)	1.08 (3H, t, *J*= 7.00 Hz, CH_3CH_2) 2.25 (3H, s, CH_3) 3.97 (2H, q, *J*=7.00 Hz, CH_2O) 5.26 (1H, s, CHN) 7.89and 9.35 (2H, 2s, 2NH)	21
6	**4n**	1.00 (3H, t, *J*= 9.2 Hz, CH_3CH_2) 2.31 (3H, s, CH_3) 4.02 (2H, q, *J*=9.2 Hz, CH_2O) 5.63 (1H, s, CHN) 7.73 and 9.29(2H, 2s, 2NH)	0.97 (3H, t, *J*= 6.9 Hz, CH_3CH_2) 2.28 (3H, s, CH_3) 3.87 (2H, q, *J*=6.9 Hz, CH_2O) 5.61 (1H, s, CHN) 7.70 and 9.25(2H, 2s, 2NH)	21
7	**4o**	2.31 (3H, s, CH_3) 3.46 (3H, s, OCH_3) 5.62 (1H, s, CHN) 7.72 and 9.36(2H, 2s, 2NH)	2.33 (3H, s, CH_3) 3.48 (3H, s, OCH_3) 5.64 (1H, s, CHN) 7.70 and 9.32(2H, 2s, 2NH)	21
8	**4r**	2.28(3H, s, CH_3) 3.55 (3H, s, OCH_3) 5.28 (1H, s, CHN) 7.93 and 9.40 (2H, 2s, 2NH)	2.25(3H, s, CH_3) 3.52 (3H, s, OCH_3) 5.26 (1H, s, CHN) 7.91 and 9.38 (2H, 2s, 2NH)	21

5-Ethoxycarbonyl-6-methyl-4-(2-chlorophenyl)-3,4-dihydropyrimidin-2(1*H*)-one, 4n: Crystalline solid. Yield 85%. m.p.221-223°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.00 (3H, t, *J*= 9.2 Hz, CH_3CH_2), 2.31 (3H, s, CH_3), 4.02 (2H, q, *J*=9.2 Hz, CH_2O), 5.63 (1H, s, CHN), 7.25-7.34 (3H, m, ArH), 7.41 (1H, d, *J*=8.8 Hz, ArH), 7.73 and 9.29 (2H, 2s, 2NH).

5-Methoxycarbonyl-6-methyl-4-(2-chlorophenyl)-3,4-dihydropyrimidin-2(1*H*)-one, 4o: Crystalline solid. Yield 83%. m.p.250-252°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.31 (3H, s, CH_3), 3.46 (3H, s, OCH_3), 5.62 (1H, s, CHN), 7.28-7.34 (3H, m, ArH), 7.42 (1H, d, *J*=7.2 Hz, ArH), 7.72 and 9.36 (2H, 2s, 2NH).

5-Methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1*H*)-one, 4r: Crystalline solid. Yield 92%. m.p.215-217°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.28(3H, s, CH_3), 3.55 (3H, s,

OCH_3), 5.28 (1H, s, CHN), 7.52 (2H, d, *J*= 8.4Hz, ArH), 7.22 (2H, d, *J*= 8.8Hz, ArH), 7.93 and 9.40 (2H, 2s, 2NH).

Conclusion

In summary, a facile and clean procedure for Biginelli synthesis of biologically active 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives *via* one-pot three-component reaction of aldehydes, urea/thiourea and ethyl/methyl acetoacetate in the present of an efficient and readily zinc acetate dihydrate ($Zn(OAc)_2.2H_2O$) as catalyst under thermal and solvent-free conditions have described. The notable advantages of the synthetic routes are including efficient, eco-friendly, readily, inexpensive and non-toxic catalyst, solvent-free conditions, high to excellent yields, one-pot procedure and environmentally benign nature synthesis.

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