C. R. Chimie 16 (2013) 183–188

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Bis[(L)prolinato-N,O]Zn–water: A green catalytic system for the synthesis of 3,4-dihydropyrimidin-2 (*1H*)-ones via the Biginelli reaction

Zeba N. Siddiqui

Department of Chemistry, Aligarh Muslim University, 202002, Aligarh, India

ARTICLE INFO

Article history:
Received 13 September 2012
Accepted after revision 17 October 2012
Available online 30 November 2012

Keywords:
Biginelli reaction
3,4-Dihydropyrimidin-2 (*1H*)-ones
$Zn(L\text{-proline})_2$
Water
Green chemistry

ABSTRACT

A novel, greener approach was adopted for the synthesis of 3,4-dihydropyrimidin-2(*1H*)-one derivatives (**4a**–**i**) using bis[(L)prolinato-N,O]Zn as an inexpensive, efficient and mild Lewis acid catalyst in water. The methodology offers several advantages such as short reaction time, high yields, clean process, low loading of catalyst and simple operational procedure. The catalyst was active up to five cycles and was identified by SEM-EDX analysis.

1. Introduction

The Biginelli reaction, one of the important and useful multicomponent reactions, offers an efficient way to get multifunctionalized 3,4-dihydropyrimidin-2(*1H*)-ones (DHPMs) and related heterocyclic compounds [1]. The Biginelli compounds, viz DHPMs are potent calcium channel blockers [2]. One of the important strategies for synthesis of this valuable class of compound is the one-pot condensation of an aldehyde, β-ketoester, and urea under acidic conditions, first reported by Biginelli. However, this reaction suffered from harsh condition, long reaction times and frequent low yield [3]. Over the past decades, several new methods for synthesis of DHPMs have been reported in the literature including microwave irradiation, ionic liquids, and by using Lewis acids as well as protic acids [4]. Despite the plethora of different catalysts published so far and also proved to be efficient in Biginelli reaction, the synthetic chemists may encounter the problem in finding the right one if the reaction is performed on larger scale as most of the reactions are associated with the high reaction temperature, prolonged reaction time, strong Lewis acidity of the catalyst and laborious work up procedures. Therefore, the discovery of new and inexpensive catalysts for the preparation of 3,4-dihydropyrimidin-2(*1H*)-ones under mild conditions is of prime importance.

Bis[(L)prolinato-N,O]Zn {[Zn(L-proline)2]} is an efficient, stable, inexpensive, recyclable, non-toxic Lewis acid catalyst which is soluble in water but insoluble in organic solvents, which allows simple and quantitative recovery of the catalyst. It has been extensively applied to various catalytic reactions including Aldol condensation [5], direct nitroaldol condensation [6], Hantzsch reaction [7], Knoevenagel condensation [8], Mannich reaction [9], Friedlander condensation [10] etc. It has also been used for the synthesis of 1,5-benzodiazepines [11], 1,2-disubstituted benzimidazoles [12], quinoxalines [13], pyrano[2,3-d]pyrimidines [12], pyrazoles [14], triazoles [15], dicoumarols [16], chromonyl chalcones [17], xanthenediones [18] and chromanones [19] etc. Further, there is much scope for exploration of this catalyst in the synthesis of various privileged medicinal scaffolds. In continuation of our research for developing economically viable and environmentally benign methodologies for organic synthesis [20–23] and to reveal the efficient utility of [Zn(L-proline]2 [8,10,16,17,19], we report herein, for the first time, a green, sequential, three-component protocol for the synthesis

Email address: siddiquizeba@yahoo.co.in.

1631-0748/$ – see front matter © 2012 Published by Elsevier Masson SAS on behalf of Académie des sciences.
http://dx.doi.org/10.1016/j.crci.2012.10.008

3,4-dihydropyrimidin-2(*1H*)-ones by the reaction of active methylene compounds, urea and various aldehydes using [Zn(L-proline)2] in water. The catalyst was recyclable up to five cycles and identified first time by SEM-EDX analysis.

2. Results and discussion

As expected, the catalytic system is influenced by various reaction parameters, such as amount of the catalyst employed, effect of catalyst and solvent system. Therefore, in our initial investigation to established the optimum reaction conditions benzaldehyde (**3a**), ethyl acetoacetate (**1a**) and urea (**2**) in water were taken as a model substrate to study the generality of our methodology towards synthesis of 3,4-dihydropyrimidin-2(*1H*)-ones (**4a–i**).

2.1. Effect of catalysts

Various catalysts were employed to evaluate the capability and efficiency of the catalyst (Table 1). Initially, the model reaction was performed in the absence of any catalyst and no reaction occurred (entry 14). When the model reaction was examined with, $FeCl_3$. $6H_2O$, $Fe(NO_3)_2$. $9H_2O$, $AlCl_3$, PTS the reaction took longer time period for completion with lower yield of the product (entry 2–5). With Zn compounds such as $Zn(CH_3COO)_2$, $Zn(NO_3)_2$, $ZnCl_2$, and ZnO again lower yields of the product were obtained after prolong heating (entry 6–9). With other catalysts $NiCl_2$, L-proline, $SnCl_2$. $2H_2O$ either reactions were unsuccessful or products were obtained in traces (entry 10–12). When, model reaction was performed with Zn(L-histidine)$_2$, the reaction was accelerated but a mixture of products was obtained in poor yield (entry 13). Thus, [Zn(L-proline)$_2$] exhibited highest catalytic activity (entry 1) as compared to other catalysts.

In order to prove the efficiency of [Zn(L-proline)$_2$] for the synthesis of **4a**, a comparison with other reported Zn catalysts was also made (Table 2). It is thus, clear from the table that [Zn(L-proline)$_2$] is superior to other Zn compounds in terms of time, yield and reaction condition.

Table 1
Effect of various catalysts for model reactions in water.

Entry[a]	Catalyst	Time[b]	Yield[c] (%)
1	Zn(L-proline)$_2$	5 min	92
2	$FeCl_3.6H_2O$	12 h	35
3	$Fe(NO_3)_2.9\ H_2O$	12 h	25
4	$AlCl_3$	8 h	45
5	PTS	8 h	68
6	$Zn(CH_3COO)_2$	4.5 h	45
7	$Zn(NO_3)_2$	6 h	42
8	$ZnCl_2$	6 h	39
9	ZnO	6 h	52
10	L-proline	8 h	Trace
11	$SnCl_2.\ 2H_2O$	48 h	Trace
12	$NiCl_2$	48 h	No reaction
13	Zn(L-histidine)$_2$	2 h	35
14	No catalyst	No reaction	No reaction

[a] Reaction of ethylacetoacetate (**1a**), urea (**2**) and benzaldehyde (**3a**) in the presence of [Zn(L-proline)$_2$] (10 mol %) catalyst in water.
[b] Reaction progress monitored by TLC.
[c] Isolated yield.

Table 2
Comparison of the results obtained using [Zn(L-proline)$_2$] with other reported Zn catalysts for synthesis of 4a.

Entry	Catalysts	Solvents	Time	Yield (%)
1	ZnO	Solvent-free	19 min	97 [24]
2	$Zn(BF_4)_2$	Water	3 h	73 [25]
3	$Zn(ClO_4)_2$	Solvent-free	15 min	95 [26]
4	$ZnBr_2$	Solvent-free	0.7 h	94 [27]
5	$ZnCl_2$/natural phosphate	Toluene	48 h	98 [28]
6	$Zn(HSO_4)_2$	Solvent-free	2.5 h	74 [29]
7	$Zn(NH_2SO_3)_2$	Ethanol	3 h	96 [30]
8	$Zn(OTf)_2$	Solvent-free	20 h	94 [31]
9	$Zn(OAc)_2$	Ethanol	4.5 h	85 [32]
10	Zn[(L-proline)$_2$]	Water	5 min	92

2.2. Loading of the catalyst

The effect of catalyst loading on the synthesis of **4a** was investigated by varying the catalyst amount from 0 to 15 mol % (Table 3). It was observed that increase in catalyst amount from 0 to 10 mol % increased the yield of the product from 74 to 92%. Further increases in the amount of catalyst had no significant change in the product formation. Thus, optimum catalyst loading was found to be 10 mol % for the formation of 3,4-dihydropyrimidin-2(*1H*)-ones.

2.3. Effect of solvents

Since [Zn(L-proline)$_2$] is homogeneous in water, therefore, to further explore the scope of this protocol, the investigation was carried out using model reaction in different solvents with varying polarity and protic nature. It was observed that in THF, n-hexane no reaction was observed and starting materials were recovered (Table 4, entry 10, 11), whereas in CH_2Cl_2 and CH_3CN lower yield of the product (**4a**) was obtained after longer time period (Table 4, entry 2, 3). In acetic acid, methanol, isopropanol and ethanol relatively high yield of the product was obtained (Table 4, entry 4–7), but the reaction was completed in longer time period. When the model reaction was carried out in [Zn(L-proline)$_2$]-water catalytic system at reflux temperature, a significant improvement was observed and the product was obtained in 92%. Further in a comparative study using other green solvents, the model reaction was also performed in PEG-400 and glycerol and it was observed that the reaction completed relatively in shorter time but with mixture of products (entries 8, 9). These results revealed that water is the best solvent in

Table 3
Effect of catalyst loading on the synthesis of 4a[a].

Entry	Catalyst (mol %)	Time[b]	Yield[c] (%)
1	0	–	–
2	2.5	1 h	74
3	5	8 min	89
4	10	5 min	92
5	15	5 min	92

[a] Reaction of ethylacetoacetate (1a), urea (2) and benzaldehyde (3a) in the presence of [Zn(L-proline)$_2$] (10 mol%) catalyst in water.
[b] Reaction progress monitored by TLC.
[c] Isolated yield.

Table 4
Effect of various solvents on model reaction[a].

Entry	Solvent	Time[b]	Yield[c] (%)
1	Water	5 min	92
2	CH_2Cl_2	48 h	35
3	CH_3CN	48 h	38
4	Acetic acid	7 h	76
5	EtOH	6 h	68
6	MeOH	6 h	64
7	Isopropanol	8 h	58
8	PEG-400	5 h	56 (mixture)
9	Glycerol	3.5 h	68 (mixture)
10	n-Hexane	No reaction	No reaction
11	THF	No reaction	No reaction

[a] Reaction of ethylacetoacetate (**1a**), urea (**2**) and benzaldehyde (**3a**) in the presence of [Zn(L-proline)$_2$] (10 mol%) catalyst.
[b] Reaction progress monitored by TLC.
[c] Isolated yield.

terms of reduced reaction time and maximum yield of the products. Thus, H_2O was chosen as the reaction medium for all other reactions.

Encouraged by the remarkable results obtained with the above reaction conditions and in order to show the generality and scope of this new protocol, we performed the reaction with a variety of aromatic aldehydes (**3a**–**e**) and active methylene compounds (**1a**–**b**) and the results obtained are summarized in Table 5. All the reactions proceeded smoothly and the reaction was completed within 5 to 10 min to afford the products (**4a**–**i**) in excellent yields (81–92%) (Table 5) (Scheme 1). All the products were characterized by ^{1}H NMR, ^{13}C NMR, IR, and mass spectra and compared with authentic samples.

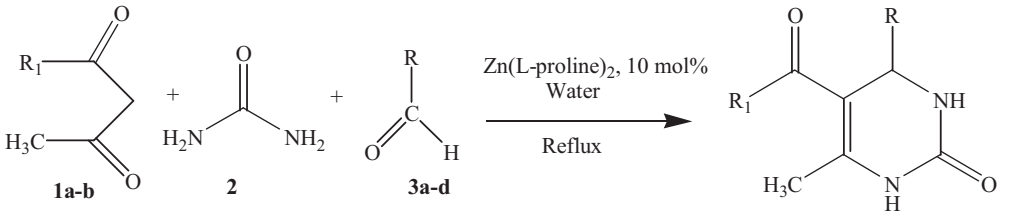
Table 5
[Zn(L-proline)$_2$] catalyzed synthesis of 3,4-dihydropyrimidin-2(*1H*)-ones (**4a**–**i**).

Entry	Product	Time (min)[a]	Yield (%)[b]
1	**4a**	5	92
2	**4b**	9	82
3	**4c**	8	85
4	**4d**	7	88
5	**4e**	5	89
6	**4f**	6	78
7	**4g**	7	84
8	**4h**	8	88
9	**4i**	9	81

[a] Reaction progress monitored by TLC.
[b] Isolated yields.

2.4. Reusability of the catalyst

After completion of the model reaction in specified time, (Table 6) the crude product obtained was extracted with dichloromethane, and the catalyst was recovered by



1a= $R_1 = OCH_2CH_3$
1b= $R_1 = CH_3$

R= **3a**= C_6H_5
3b= *m*-NO_2 C_6H_4
3c= *p*-OH C_6H_4
3d= *o*-Cl C_6H_4
3e= *p*-Cl C_6H_4

4a= $R_1 = OCH_2CH_3$, R= C_6H_5
4b= $R_1 = CH_3$, R= C_6H_5
4c= $R_1 = OCH_2CH_3$, R=3-NO_2 C_6H_4
4d= $R_1 = CH_3$, R=3-NO_2 C_6H_4
4e= $R_1 = OCH_2CH_3$, R=4-OH C_6H_4
4f= $R_1 = CH_3$, R=4-OH C_6H_4
4g= $R_1 = OCH_2CH_3$, R=2-Cl C_6H_4
4h= $R_1 = CH_3$, R=2-Cl C_6H_4
4i= $R_1 = OCH_2CH_3$, R=4-Cl C_6H_4

Scheme 1. [Zn(L-proline)$_2$] catalyzed synthesis of 3,4-dihydropyrimidin-2(*1H*)-one derivatives (**4a**–**i**).

Table 6
Recycling study of catalyst for the model reaction[a].

Catalyst recycle	Time (min)[b]	Yield[c] (%)
I	5	92
II	5	92
III	5	92
IV	5	92
V	5	92
VI	10	88

[a] Reaction of ethylacetoacetate (**1a**), urea (**2**) and benzaldehyde (**3a**) in the presence of [Zn(L-proline)$_2$] (10 mol%) catalyst in water.
[b] Reaction progress monitored by TLC.
[c] Isolated yield.

separation of aqueous and organic phases. The catalyst present in the aqueous medium was used for the subsequent cycle. The same procedure was applied to all recycling studies. The results (Table 6) revealed that the catalyst exhibited good catalytic activity up to five cycles.

The identity of the recovered catalyst was checked by SEM-EDX (Fig. 1 b) and it was observed that there was no change in the morphology of the catalyst as compared to fresh catalyst (Fig. 1 a).

3. Experimental

3.1. General

Melting points were taken in Riechert Thermover instrument and are uncorrected. The IR spectra were recorded on Perkin Elmer spectrometer in KBr. ^{1}H NMR, ^{13}C NMR spectra were recorded on a Bruker DRX-300 Spectrometer using tetra methyl silane (TMS) as an internal standard. DART-MS recorded on a JEOL-Accu TOF JMS-T100LC mass spectrometer having a DART source. Chemical shifts are reported in ppm downfield from TMS as internal standard. The micro analytical data were collected on Elementar vario EL III elemental analyzer. Other chemicals were purchased from Sigma-Aldrich chemicals Pvt. Ltd. and Otto chemie Pvt. Ltd. and were used without further purification. The purity of all compounds was checked on silica gel (E-Merck G_{254}) plates using iodine vapors as visualizing agents. The SEM-EDX characterization of the catalyst was performed on a JEOL JSM-6510 scanning electron microscope, equipped with energy dispersive X-ray spectrometer, operating at 20 kV.

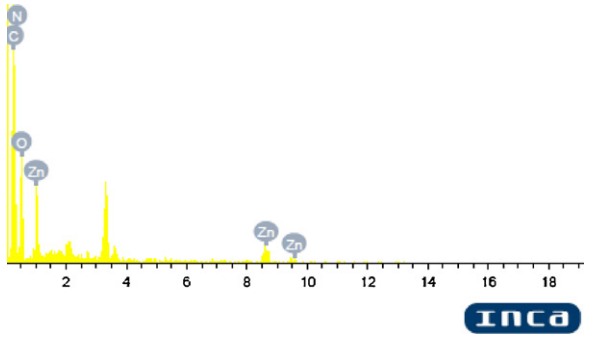


Fig. 2. EDX spectrum of the catalyst.

3.2. Synthesis of [Zn(L-proline)$_2$] complex

A mixture of (L)-Proline (10 mmol) and potassium hydroxide (10 mmol) was dissolved in absolute ethanol (25 mL) and magnetically stirred for 15 min in a round-bottomed flask at room temperature. $Zn(NO_3)_2.6H_2O$ (5 mmol) was dissolved in minimum quantity of double distilled water and added in drops to the above solution. The contents were vigorously stirred for 6 h by using a magnetic stirrer. The [Zn(L-proline)$_2$] complex was obtained as a white solid. It was collected by filtration and dried at 70 °C in vacuum for 6 h. Formation of [Zn(L-proline)$_2$] complex was confirmed by the EDX spectrum (Fig. 2) which showed the presence of Zn, C, O and N.

3.3. [Zn(L-proline)$_2$] catalyzed synthesis of 3,4-dihydropyrimidin-2(1H)-ones derivatives (4a–i) in aqueous medium

A mixture of active methylene compounds (**1a**–**b**) (1 mmol), urea (**2**) (1 mmol), aromatic aldehydes (**3a**–**e**) (1 mmol) and [Zn(L-proline)$_2$] (10 mol %) was refluxed in water (12 mL) for the specified time (Table 5). After

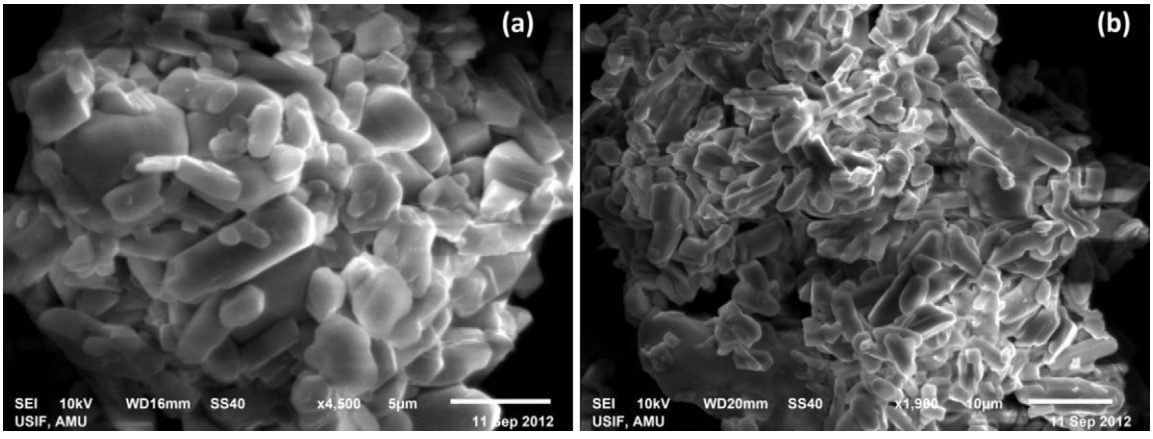


Fig. 1. SEM images of the fresh (a) and recovered catalyst (b).

completion of the reaction, monitored by TLC, the reaction mixture was allowed to cool to room temperature. The crude product was extracted with dichloromethane, dried over anhydrous Na_2SO_4 and concentrated to furnish **4a**–**i**. The recrystallization of crude products (**4a**–**i**) was done with chloroform-methanol mixture (1:4 v/v). The catalyst was recovered by simple separation of aqueous and organic phases. The catalyst present in the aqueous layer was used for the subsequent cycle.

3.4. Spectral data of the products

*3.4.1. 5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (**4a**)*

M.p. 202–204 °C; Anal. calcd. for $C_{14}H_{16}N_2O_3$ (%) C 64.60, H 6.19, N 10.76. Found. C 64.47, H 6.24, N 10.71. IR (KBr, cm^{-1}): 1650 (C = O), 1729 (C = O), 3122 (NH), 3245 (NH). ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.11 (t, *J* = 7.2 Hz, 3H, CH_3), 2.24 (s, 3H, CH_3), 4.01 (q, *J* = 7.2 Hz 2H, OCH_2), 5.17 (s, *1H*, H-4), 7.48-7.22 (m, 5H, Ar-H), 7.74 (br s, *1H*, NH), 9.20 (br s, *1H*, NH). MS-ESI (m/z, %): 261.14 (M^+ +1).

*3.4.2. 5-Acetyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (**4b**)*

M.p. 232–235 °C. Anal. calcd. for $C_{13}H_{14}N_2O_2$: C 67.81, H 6.12 N 12.16. Found. C 67.73, H 6.22, N 12.11. IR (KBr, cm^{-1}): 1650 (C = O), 1706 (C = O), 3267 (NH); ^{1}H NMR: (300 MHz, DMSO-d_6) δ 2.10 (s, 3H, CH_3), 2.28 (s, 3H, CO-CH_3), 5.25(s, *1H*, H-4), 7.35-7.23 (m, 5H, Ar-H), 7.83 (s, *1H*, NH), 9.19 (s, *1H*, NH). MS-ESI (m/z, %): 231.13 (M^+ +1).

*3.4.3. 5-Ethoxycarbonyl-6-methyl-4-(3-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (**4c**)*

M.p. 227–229 °C. Anal. calcd. for $C_{14}H_{15}N_3O_5$: C 55.08, H 4.94, N 13.76. Found. C 55.16, H 4.97, N 13.70. IR (KBr, cm^{-1}): 1627 (C = O), 1706 (C = O), 3100 (NH), 3223 (NH); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.11 (t, *J* = 7.2 Hz, 3H, CH_3), 2.26 (s, 3H, CH_3), 4.01 (q, *J* = 6.9 Hz, 2H, OCH_2), 5.30 (s, *1H*, H-4), 8.14-7.62 (m, 4H, Ar-H), 7.90 (br s, *1H*, NH), 9.37 (s, *1H*, NH). MS-ESI (m/z, %): 306.13 (M^+ +1).

*3.4.4. 5-Acetyl-6-methyl-4-(3-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (**4d**)*

M.p. 220–225 °C. Anal. calcd. for $C_{13}H_{13}N_3O_4$: C 56.72, H 4.76, N 15.26. Found. C 56.63, H 4.85, N 15.16. IR (KBr, cm^{-1}): 1683 (C = O), 3275 (NH); ^{1}H NMR: (300 MHz, DMSO-d_6) δ 2.05 (s, 3H, CH_3), 2.33 (s, 3H, CO-CH_3), 5.67 (s, *1H*), 7.45-7.27 (m, 4H, Ar-H), 7.72 (s, *1H*, NH), 9.26 (s, *1H*, NH). ^{13}C NMR: (75 MHz, DMSO-d_6): δ 19.55, 21.21, 109.9, 121.58, 122.77, 129.97, 130.64, 133.46, 146.92, 148.36, 152.46, 194.52. MS-ESI (m/z, %): 276.13 (M^+ +1).

*3.4.5. 5-Ethoxycarbonyl-6-methyl-4-(4-hydroxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (**4e**)*

M.p. 227–229 °C. Anal. calcd. for $C_{14}H_{16}N_2O_4$: C 60.86, H 5.83, N 10.13. Found. C 60.72, H 5.89, N 10.16. IR (KBr, cm^{-1}): 1646 (C = O), 1690 (C = O), 3122 (NH), 3246 (NH), 3515 (OH); ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.12 (t, *J* = 7.2 Hz, 3H, CH_3), 2.23 (s, 3H, CH_3), 4.01 (q, *J* = 7.2 Hz, 2H, OCH_2), 5.04 (s, *1H*, H-4), 6.69 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.04 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.60 (br s, *1H*, NH), 9.09 (br s, *1H*, NH), 9.31 (s, *1H*, OH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 14.55, 18.19, 53.92, 59.56, 100.26, 115.45, 127.85, 135.89, 152.65, 157.01, 165.89. MS-ESI (m/z, %): 277.14 (M^+ +1).

*3.4.6. 5-Acetyl-6-methyl-4-(4-hydroxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (**4f**)*

M.p. 231–234 °C. Anal. calcd. for $C_{13}H_{14}N_2O_3$: C 63.40, H 5.73, N 11.37. Found. C 63.48, H 5.82, N 11.33. IR (KBr, cm^{-1}): 1647 (C = O), 1687 (C = O), 3120 (NH), 3283 (NH), 3516 (OH). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.10 (s, 3H, CH_3), 2.22 (s, 3H, CO-CH_3), 5.04 (s, *1H*), 6.69 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.04 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.60 (s, 1H, NH), 9.09 (s, 1H, NH), 9.31 (s, *1H*, OH). ESI-MS (%): 247.08 (M^+ +1).

*3.4.7. 5-Ethoxycarbonyl-6-methyl-4-(2-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (**4g**)*

M.p. 214–216 °C. Anal. calcd. for $C_{14}H_{15}N_2O_3Cl$: C 57.05, H 5.12, N 9.50. Found. C 57.12, H 5.29, N 9.46. IR (KBr, cm^{-1}): 1650 (C = O), 1700 (C = O), 3115 (NH), 3230 (NH); ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.01 (t, *J* = 6.9 Hz, 3H, CH_3), 2.30 (s, *J* = 6.9 Hz, 3H, CH_3), 3.92 (q, 2H, OCH_2), 5.63 (s, *1H*), 7.25–7.41 (m, 4H, Ar-H), 7.68 (br s, *1H*, NH), 9.25 (br s, *1H*, NH). ESI-MS (m/z, %): 295.11(M^+ +1).

*3.4.8. 5-Acetyl-6-methyl-4-(2-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (**4h**)*

M.p. 303–305 °C. Anal. calcd. for $C_{13}H_{13}N_2O_2Cl$: C 58.98, H 4.95, N 10.58. Found. C 58.92, H 4.97, N 10.63. IR (KBr, cm^{-1}): 1625 (C = O), 1708 (C = O), 3092 (NH), 3246 (NH). ^{1}H NMR: (300 MHz, DMSO-d_6) δ 2.05 (s, 3H, CH_3), 2.33 (s, 3H, CO-CH_3), 5.67 (s, *1H*), 7.45-7.27 (m, 4H, Ar-H), 7.72 (s, 1H, NH), 9.26 (s, *1H*, NH). ESI-MS (m/z, %): 265.09 (M^+ +1).

*3.4.9. 5-Ethoxycarbonyl-6-methyl-4-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (**4i**)*

M.p. 213–215 °C. Anal. calcd. for $C_{14}H_{15}N_2O_3Cl$: C 58.98, H 4.95, N 10.58. Found. C 58.94, H 5.02, N 10.56. IR (KBr, cm^{-1}): 1651 (C = O), 1718 (C = O), 3120 (NH), 3243 (NH). ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.10 (t, *J* = 7.2 Hz, 3H, CH_3), 2.24 (s, 3H, CH_3), 4.01 (q, *J* = 6.9 Hz, 2H, OCH_2), 5.14 (s, *1H*, H-4), 7.25-7.23 (d, 2H, *J* = 8.4 Hz), 7.40-7.37 (d, 2H, *J* = 8.1 Hz), 7.78 (br s, *1H*, NH), 9.26 (s, *1H*, NH). ESI-MS (m/z, %): 295.10 (M^+ +1).

4. Conclusion

In conclusion, a practical, efficient, ecofriendly and convenient method for the synthesis of a series of biologically relevant 3,4-dihydropyrimidin-2(*1H*)-ones is described using [Zn(L-proline)$_2$]-water catalytic system. Short reaction time, high yields, clean process, simple methodology, easy workup, and green sustainable conditions are the key features involved in the present protocol. These features will enable this protocol to find widespread applications in the field of organic synthesis.

Acknowledgments

Financial assistance in the form of major research project [F.No. 37-15/2009 (SR)] from University Grants

commission, New Delhi, is gratefully acknowledged. The author would also like to thank Prof. R.C. Kamboj, department of Chemistry, Kurukshetra University, India for spectral data and University Sophisticated Instrument Facility (USIF), AMU, Aligarh for providing SEM-EDX facilities.

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