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Development of an Environment-Friendly and Solvent-Free Synthetic Route for the Synthesis of 3,4-Dihydropyrimidin-2-(1*H*)-Ones/Thiones Using $La(NO_3)_3.6H_2O$ as an Efficient Catalyst

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Abstract

We present a facile and environmentally friendly procedure for the synthesis of corresponding 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives. The synthesis was achieved using a one-pot three-component Biginelli reaction among β-keto esters (methyl or ethyl acetoacetate), aromatic aldehyde (benzaldehyde derivatives), and urea or thiourea in the presence of lanthanum (III) nitrate hexahydrate ($La(NO_3)_3.6H_2O$), as a highly efficient catalyst under solvent-free conditions. This protocol has numerous advantages: it is an inexpensive, non-toxic, simple reaction work-up catalyst with a high atom-economy, and shows excellent yields with short reaction times.

Abstrak

Pengembangan Jalur Sintesis yang Ramah Lingkungan dan Bebas Pelarut bagi Sintesis 3,4-dihidropirimidin-2-(1H)-on/tion Menggunakan $La(NO_3)_3.6H_2O$ sebagai Katalis yang Efisien. Prosedur sintesis 3,4-dihidropirimidin-2(1H)-on/tion yang mudah dan ramah lingkungan telah dikembangkan. Sintesis berhasil dilakukan dengan menggunakan metoda *Biginelli* satu wadah dan tiga komponen dengan reaksi antara ß-keto ester (metil atau etil asetoasetat), aldehid aromatik (turunan benzaldehid), dan urea atau tiourea dengan adanya lanthanum (III) nitrat heksahidrat ($La(NO_3)_3.6H_2O$), yang berfungsi sebagai katalis yang sangat efisien dengan kondisi bebas pelarut. Protokol ini memiliki berbagai keunggulan: proses yang murah, tidak beracun, reaksi yang sederhana yang bekerja dengan efisiensi atom yang tinggi, sertamenghasilkan presentasi hasil yang tinggi dengan waktu reaksi yang singkat.

Keywords: $La(NO_3)_3.6H_2O$, 3,4-dihydropyrimidin-2-(1H)-ones/thiones derivatives, high atom-economy, environment-friendly procedure, solvent-free conditions

Introduction

The synthesis of pyrimidinone derivatives has attracted great attention recently in synthetic organic chemistry due to their therapeutic and pharmacological features. The preparation of 3,4-dihydropyrimidin-2-(1*H*)-ones /thiones derivatives has drawn wide interest for the various biological properties of these compounds. They have been used as calcium channel blockers, α-1a-antagonists [1], and as antihypertensive [2], anticancer [3], anti-HIV and other antiviral [4-6], antibiotic [5], antifungal [5], antioxidant [7], and anti-inflammatory [8] agents.

Considering the importance of such compounds, many methods for the synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives have been reported. Conventional synthesis involves condensation of β-keto esters, aldehyde derivatives, and urea/thiourea using different catalytic systems such as calcium fluoride [9], copper (II) sulfamate [10], baker's yeast [11], hydrotalcite [12], hexaaquaaluminium (III) tetrafluoroborate [13], tetrabutylammonium bromide (TBAB) [14], copper (II) tetrafluoroborate [15], [Btto] [*p*-TSA] [16], triethyl-ammonium acetate [17], *p*-dodecylbenzenesulfonic acid [18], $SnCl_2.2H_2O$ [19], HPAIL [20], $[Simp]HSO_4$ [21], Dendrimer-PWA [22], 1-Methyl-2-oxopyrrolidinium perchlorate ionic liquid [23], $[pyridineSO_3H]Cl$ [24], and phthalic acid [25]. However, most of these synthetic approaches have drawbacks, including difficult work-ups, toxic or expensive catalysts or reagents, low yields, and prolonged reaction times. We considered it necessary to develop a general rapid, high yielding, cost-effective, environmentally benign, and easy synthetic protocol for

a variety of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives. In continuation of our work to develop efficient catalytic [26-31] systems to synthesize organic compounds, we employed $La(NO_3)_3.6H_2O$ (lanthanum [III] nitrate hexahydrate) as a catalyst to promote three-component reactions to obtain 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives. Over the past few decades, the use of lanthanum (III) nitrate hexahydrate as an environmentally safe catalyst [32, 33] in organic synthesis has attracted great interest due to its notable advantages such as its non-toxicity, ease of handling, highly efficiency, low cost, high atom economy, and facile reaction profiles. Also, lanthanum (III) nitrate hexahydrate can be successfully used with these types of organic carbon-carbon bonds as a readily available, mild, and environmentally friendly catalyst in organic synthesis. Finally, we report herein an inexpensive, efficient, lanthanum (III) nitrate hexahydrate-catalyzed procedure for the synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives via a three-component Biginelli [34] reaction under solvent-free conditions. We note that one group of environmental pollutants, organic solvents under reflux conditions, require column chromatography as a purifying agent. In this present work, the organic products were obtained through a simple filter with no need for column chromatographic separation. These notable benefits, together with excellent yields and short reaction times, introduce this catalyst as effective compared with other catalysts presented in previous papers.

Materials and Methods

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

General procedure for preparation of 3,4-dihydropyrimidin-2-(1H)-ones/thiones derivatives (4a-o). A mixture of aldehyde derivatives (**1**, 1.0 mmol), urea/thiourea (**2**, 1.5 mmol), and ethyl/methyl acetoacetate (**3**, 1.0 mmol) was heated under solvent-free conditions at 80 °C for an appropriate time in the presence of lanthanum (III) nitrate hexahydrate (0.06 g). After completion of the reaction by thin layer chromatography, the mixture was cooled to room temperature and cold water was added. The precipitate was separated with filtration and crystallized from ethanol to afford the pure products (**4a-o**). Spectral data of all products are presented below:

***5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4 dihydropyrimidin- 2(1H)-one (4a)*:** Yield: 86%; mp 201–202 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 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, $H_{benzylic}$), 7.26 (3H, d, *J*= .2 Hz, H_{Ar}), 7.33 (2H, t, *J*=7.2 Hz, H_{Ar}), 7.76 and 9.21 (2H, 2s, 2NH).

***5- Ethoxycarbonyl -6-methyl-4-(4-hydroxyphenyl)-3,4-dihydropyrimidin-2(1H)–one (4b)*:** Yield: 77%; mp 232–234 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.11 (3H, t, *J*=9.6 Hz, CH_3CH_2), 2.50 (3H, s, CH_3), 3.98 (2H, q, *J*=9.6 Hz, CH_2O), 5.04 (1H, s, $H_{benzylic}$), 6.68–7.04 (4H, m, H_{Ar}), 7.64 and 9.13 (2H, 2s, 2NH), 9.35 (1H, s, OH).

***5-Ethoxycarbonyl -6-methyl -4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)–one (4c)*:** Yield: 83%; mp 203–205 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.11 (3H, t, *J*= .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, $H_{benzylic}$), 6.89 (2H, d, *J*=8.4Hz, H_{Ar}), 7.15 (2H, d, *J*=8.8Hz, H_{Ar}), 7.70 and 9.18 (2H, 2s, 2NH).

***5-Ethoxycarbonyl-6-methyl-4-(N,N-Dimethylphenyl)-3,4-dihydropyrimidin-2(1H)-one (4e)*:** Yield: 87%; mp 253–255 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 1.12 (3H, t, *J*=9.2 Hz, CH_3CH_2), 2.26 (3H, s, CH_3), 2.85 (6H, s, $2CH_3$), 3.99 (2H, q, *J*=9.2 Hz, CH_2O), 5.04 (1H, s, CHN), 6.66 (2H, d, *J*=11.6 Hz, ArH), 7.42 (2H, d, *J*=11.6Hz, ArH), 7.61 and 9.11 (2H, 2s, 2NH).

***5-Ethoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (4f)*:** Yield: 89%; mp 208–209 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 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, $H_{benzylic}$), 7.50–7.53 (2H, m, H_{Ar}), 7.23 (2H, d, *J*=9.2Hz, H_{Ar}), 7.92and 9.38 (2H, 2s, 2NH).

***5-Methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3,4 -dihydropyrimidin-2(1H)-one (4g)*:** Yield: 91%; mp 216–218 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 2.28 (3H, s, CH_3), 3.55 (3H, s, OCH_3), 5.28 (1H, s, $H_{benzylic}$), 7.52 (2H, d, *J*=8.4Hz, H_{Ar}), 7.22 (2H, d, *J*=8.8Hz, H_{Ar}), 7.93 and 9.40 (2H, 2s, 2NH).

***5-Ethoxycarbonyl -6-methyl -4-(3-methoxyphenyl) -3,4-dihydropyrimidin-2(1H)–one (4h)*:** Yield: 86%; mp 205–207 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.13 (3H, t, *J*=9.6 Hz, CH_3CH_2), 2.26 (3H, s, CH_3), 3.74 (3H, s, OCH_3), 4.01 (2H, q, *J*=9.6 Hz, CH_2O), 5.13 (1H, s, $H_{benzylic}$), 6.78–6.86 (3H, m, H_{Ar}), 7.26 (1H, t, *J*= 10.4Hz, H_{Ar}), 7.76 and 9.20 (2H, 2s, 2NH).

***5- Ethoxycarbonyl -6-methyl -4-(2-chlorophenyl)-3,4-dihydropyrimidin-2(1H)–one (4i)*:** Yield: 78%; mp 219–221 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 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, $H_{benzylic}$), 7.25–7.34 (3H, m, H_{Ar}), 7.41 (1H, d, *J*=8.8 Hz, H_{Ar}), 7.73 and 9.29 (2H, 2s, 2NH).

***5-Methoxycarbonyl-6-methyl-4-(2-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (4j)*:** Yield: 81%; mp 248–250 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 2.31 (3H, s, CH_3), 3.46 (3H, s, OCH_3), 5.62 (1H, s, $H_{benzylic}$), 7.28–

7.34 (3H, m, H_{Ar}), 7.42 (1H, d, *J*=7.2 Hz, H_{Ar}), 7.72 and 9.36 (2H, 2s, 2NH).

***5-Ethoxycarbonyl-6-methyl-4-(4-fluorophenyl)-3,4-dihydropyrimidin-2(1H)–one (4k)*:** Yield: 92%; mp 173–175 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 1.11 (3H, t, *J*=9.6 Hz, CH_3CH_2), 2.25 (3H, s, CH_3), 3.99 (2H, q, *J*=9.6 Hz, CH_2O), 5.14 (1H, s, CHN), 7.13–7.20 (2H, m, ArH), 7.24–7.29 (2H, m, ArH), 7.78 and 9.25 (2H, 2s, 2NH).

***5-Ethoxycarbonyl-6-methyl-4-(4-methylphenyl) -3,4-dihydropyrimidin-2(1H)-one (4l)*:** Yield: 90%; mp 202–204 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.11 (3H, t, *J*=7.2 Hz, CH_3CH_2), 2.25 (3H, s, CH_3), 2.27 (3H, s, CH_3), 3.99 (2H, q, *J*=7.2 Hz, CH_2O), 5.11 (1H, s, CHN), 7.13 (4H, s, ArH), 7.70 and 9.17 (2H, 2s, 2NH).

***5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4 dihydropyrimidin-2(1H)-thione (4 m)*:** Yield: 85%; mp 210–212 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.11 (3H, t, *J*=7.2 Hz, $\underline{CH_3}CH_2$), 2.31 (3H, s, CH_3), 4.02 (2H, q, *J*=7.2 Hz, CH_2O), 5.19 (1H, s, $H_{benzylic}$), 7.23 (2H, d, *J*=7.2 Hz, H_{Ar}), 7.28 (1H, t, *J*=7.2 Hz, H_{Ar}), 7.36 (2H, t, *J*=7.2 Hz, H_{Ar}), 9.68 and 10.36 (2H, 2s, 2NH).

***5-Ethoxycarbonyl-6-methyl-4-(4–methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-thione (4n)*:** Yield: 81%; mp 152–154 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 1.13 (3H, t, *J*=9.6 Hz, CH_3CH_2), 2.29 (3H, s, CH_3), 3.74 (3H, s, OCH_3), 4.03 (2H, q, *J*=9.6 Hz, CH_2O), 5.15 (1H, s, CHN), 6.77 (2H, m, ArH), 6.87 (1H, m, ArH), 7.28 (1H, t, *J*=9.6 Hz, ArH), 9.66 and 10.37 (2H, 2s, 2NH).

***5-Methoxycarbonyl-6-methyl-4-(4-fluorophenyl)-3,4-dihydropyrimidin-2(1H)-thione (4o)*:** Yield: 87%; mp 207–209 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 2.31 (3H, s, CH_3), 3.57 (3H, s, OCH_3), 5.19 (1H, s, $H_{benzylic}$), 7.17–7.44 (4H, m, H_{Ar}), 9.70 and 10.41 (2H, 2s, 2NH).

Results and Discussion

We have developed a clean, eco-friendly, and simple methodology for one-pot three-component synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives by means of arylaldehyde derivatives (**1**, 1.0 mmol), urea/thiourea (**2**, 1.5 mmol), and ethyl/methyl acetoacetate (**3**, 1.0 mmol) in the presence of a catalytic amount of lanthanum (III) nitrate hexahydrate as a mild and efficient catalyst. This synthesis was achieved under thermal and solvent-free conditions with excellent yields and short reaction times.

To optimize the reaction conditions, the synthesis of compound **4a** was used as a model reaction. We studied the effects of differing amounts of catalyst on the reaction in this protocol. No product could be detected in the absence of the catalyst at 80 °C even after 360 min, indicating the need for a catalyst for this transformation (Table 1, entry 1). Optimized conditions for the reaction were determined by changing determinative parameters such as amount of catalyst and temperature. Thereafter, for determining the optimum quantity of catalyst, the model reaction was performed in the presence of different amounts of lanthanum (III) nitrate hexahydrate. Various loadings of catalyst, including 5%, 10%, 15%, and 20% by mass, were screened in our model reaction. By lowering the catalyst loading to 5% by mass, the corresponding product was obtained at a lower yield (Table 1, entry 2). By increasing the amount of catalyst from 5% to 10% and 15% by mass, the reaction time was reduced and the yield of the product increased (Table 1, entries 2–4). So, of the different amounts of catalyst, 15% by mass of lanthanum (III) nitrate hexahydrate proved to be the most efficient quantity for this reaction (Table 1, entry 4). Larger amounts of catalyst did not improve the yields (Table 1, entry 10). With catalyst increased to 20% by mass, there was no significant increase in reaction yield and no change in reaction time (Table 1, entry 10). The results of these comparative experiments are summarized in Table 1. We also examined the influence of temperature on the reaction yield. No product could be detected under room temperature conditions after 360 min (Table 1, entry 5). The reaction was investigated for temperatures running from 40° to 80 °C. Results indicated that when the reaction proceeded using lanthanum (III) nitrate hexahydrate 15% by mass at 40 °C for 75 min, the yield of corresponding product was low (42 %) (Table 1, entry 6). The reaction time was decreased from 75 min to 20 min when the reaction temperature was increased from 40 ° to 80 °C. The high yield of product was obtained at an 80 °C temperature (Table 1, entry 4); yields of product at different temperature are reported in Table 1. The reaction was also carried out at a temperature of 90 °C, but there was no significant change in yield or reaction time (Table 1, entry 9).

We therefore employed the optimized conditions of 15% by mass lanthanum (III) nitrate hexahydrate as a catalyst at 80 °C for the condensation reaction of aryl aldehyde derivatives (**1**, 1.0 mmol), urea/thiourea (**2**, 1.5 mmol), and ethyl/methyl acetoacetate (**3**, 1.0 mmol) into their corresponding 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives. Encouraged by the results obtained from the above conditions, and to demonstrate the wide applicability and scope of this protocol, we used various aromatic aldehydes, bearing either electron-withdrawing functional groups or electron-donating groups such as Cl, Me, NO_2, and OMe-substituted banzaldehydes, for the synthesis of corresponding 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives. The effects of substituents on the aromatic rings were estimated to be strong in terms of yield under these reaction conditions. Both classes of aromatic aldehydes, those with electron-releasing and those with electron-

withdrawing substituents in their aromatic rings, synthesized the appropriate products with high reaction yields and short reaction times. We also applied urea/thiourea and ethyl/methyl acetoacetate. In each of these substitutions, there was no significant difference in the reaction rate or product yields. The results are summarized in Table 2. The desirable features of this catalyst are its ease of handling, mild and environmentally benign properties, operational simplicity, high reaction yields, and short reaction times.

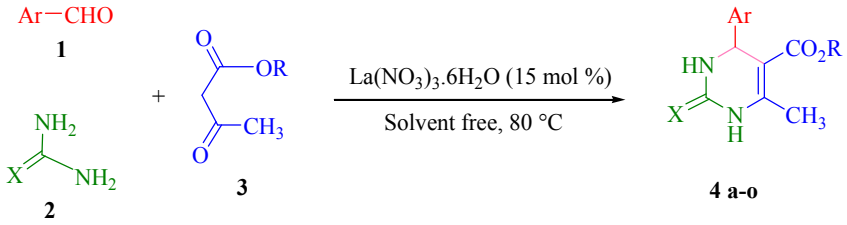
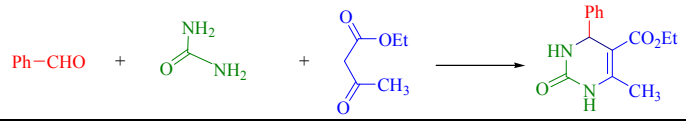


Figure 1. Synthesis of 3, 4-Dihydropyrimidin-2-(1*H*)-Ones/Tiones Derivatives

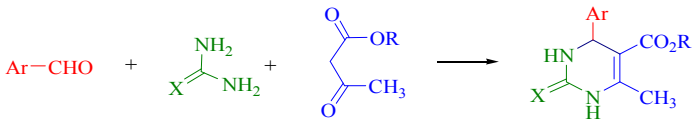
Table 1. Optimization of the Reaction Condition on the Synthesis of 4a [a]



Entry	Lanthanum (III) nitrate hexahydrate % by mass [mol %]	Temperature (°C)	Time (min)	Isolated Yields (%)
1	Catalyst free	80	360	No product
2	5	80	65	47
3	10	80	35	63
4	**15**	**80**	**20**	**86**
5	15	rt	360	No product
6	15	40	75	42
7	15	60	50	56
8	15	70	30	73
9	15	90	20	86
10	20	80	20	87

[a] Reaction conditions: benzaldehyde (1.0 mmol), ethyl acetoacetate (1.0 mmol), urea (1.5 mmol) and lanthanum (III) nitrate hexahydrate were heated under various temperatures for the appropriate times.

Table 2. Lanthanum (III) Nitrate Hexahydrate Catalyzed Synthesis of 3,4-Dihydropyrimidin-2-(1*H*)-Ones/Thiones Derivatives



Entry	Ar	R	X	Product	Time (min)	Yield %[a]	mp (°C)	Lit. mp (°C)
1	C_6H_5	C_2H_5	O	**4a**	20	86	201–202	200–202[13]
2	4-HO-C_6H_4	C_2H_5	O	**4b**	30	77	232–234	230–232[14]
3	4-MeO-C_6H_4	C_2H_5	O	**4c**	25	83	203–205	202–203[12]
4	3-HO-C_6H_4	C_2H_5	O	**4d**	30	79	165–167	163–166[15]
5	4-$(Me)_2$N-C_6H_4	C_2H_5	O	**4e**	25	87	253–255	255–257[12]
6	4-O_2N-C_6H_4	C_2H_5	O	**4f**	20	89	208–209	207–209[13]
7	4-O_2N-C_6H_4	CH_3	O	**4g**	15	91	216–218	214–216[13]
8	3-MeO-C_6H_4	C_2H_5	O	**4h**	25	86	205–207	205–206 [11]
9	2-Cl-C_6H_4	C_2H_5	O	**4i**	30	78	219–221	220–223[10]
10	2-Cl-C_6H_4	CH_3	O	**4j**	25	81	248–250	248–252[10]
11	4-F-C_6H_4	C_2H_5	O	**4k**	15	92	173–175	174–176[14]
12	4-Me-C_6H_4	C_2H_5	O	**4l**	15	90	202–204	204–205[11]
13	C_6H_5	C_2H_5	S	**4m**	20	85	210–212	208–210[13]
14	4-MeO-C_6H_4	C_2H_5	S	**4n**	25	81	152–154	150–152[13]
15	4-F-C_6H_4	CH_3	S	**4o**	15	87	207–209	208–210[14]

[a] Isolated yield.

Although different mechanistic pathways have been previously proposed [12, 15, 19], we believe that the reaction may proceed through an initial *N*-acylimine B formed from aldehyde 3 and urea 2 (Figure 2). The coordination of the lone-pair of the nitrogen atom in the *N*-acylimine B with the lanthanum (III) nitrate hexahydrate could lead to the *in-situ* formation of an *N*-carbamoyliminium ion C, which is sufficiently electrophilic to react with the enol form of ethyl acetoacetate A affording the open chain intermediate D.

Further intramolecular cyclization, with loss of H_2O, produced the 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives 4.

A comparison of catalytic ability of some of catalysts reported in the literature for synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/thiones derivatives is shown in Table 3. Our study revealed that lanthanum (III) nitrate hexahydrate has demonstrated potential to be an alternative eco-friendly and cost-effective catalyst for the Biginelli reaction. In addition, the use of solvent-free conditions with excellent yields and short times in the reactions with both urea and thiourea were the notable advantages of this present methodology.

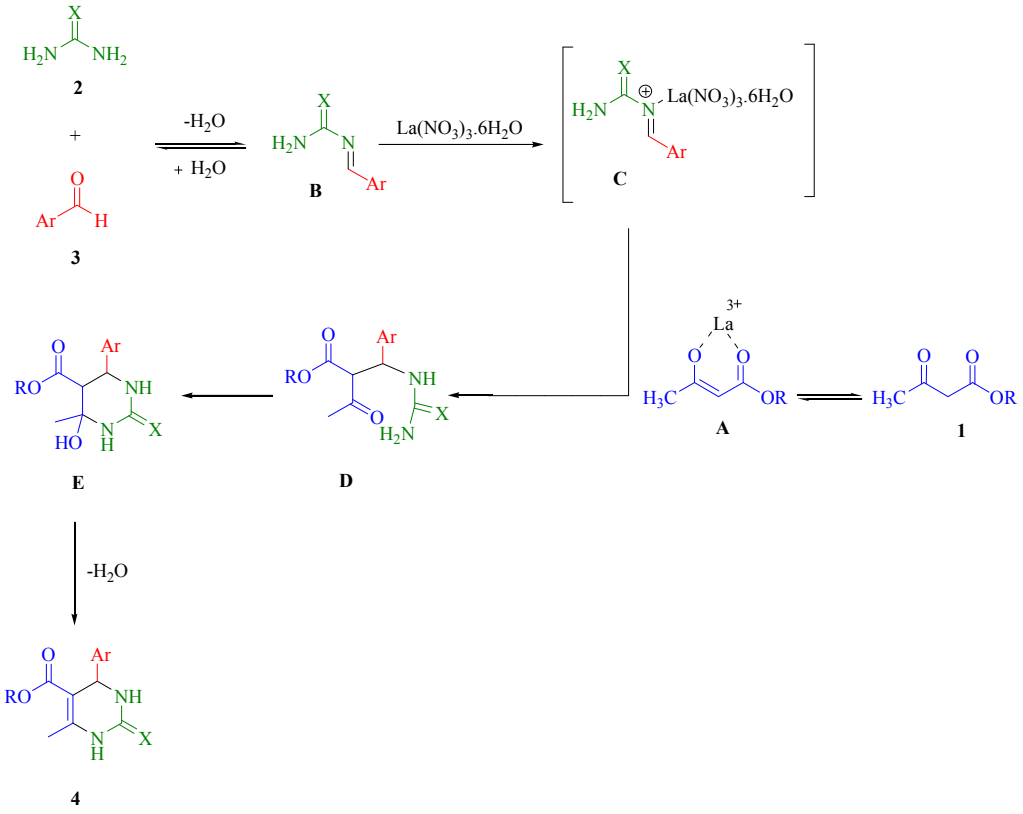


Figure 2. Proposed Mechanistic Route for the Synthesis of 3,4-Dihydropyrimidin-2-(1*H*)-Ones/Tiones

Table 3. Comparison of Catalytic Ability of Some Catalysts Reported in the Literature for Synthesis of 4a[a]

Entry	Catalyst	Conditions	Time/Yield (%)	References
1	Bakers' yeast	Room temperature	24 h/84	[11]
2	Hydrotalcite	Solvent-free, 80 °C	35 min/84	[12]
3	$[Al(H_2O)_6](BF_4)_3$	MeCN, Reflux	20 h/81	[13]
4	$Cu(BF_4)_2.xH_2O$	Room temperature	30 min/90	[15]
5	[Btto][*p*-TSA]	Solvent-free, 90 °C	30 min/96	[16]
6	Triethylammonium acetate	Solvent-free,70 °C	45 min/90	[17]
7	*p*-dodecylbenzenesulfonic acid	Solvent-free, 80 °C	3 h/94	[18]
8	Lanthanum (III) nitrate hexahydrate	Solvent-free, 80 °C	20 min/86	This work

[a]Based on reaction of benzaldehyde, ethyl acetoacetate and urea.

Conclusions

We have introduced lanthanum (III) nitrate hexahydrate as an economical and highly efficient catalyst for facile one-pot synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones/ thiones via three-component reactions of aryl aldehydes, urea/thiourea and ethyl/methyl acetoacetate under solvent-free conditions. The promising features that have distinguished this approach from other reported methods of this synthesis include its high catalytic ability, low cost, ready availability, and simple reaction work-up, making this methodology more economical and industrially relevant. Additional advantages of this protocol include excellent yields and short reaction times under solvent-free conditions.

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