Research Article

An Efficient One-Pot Multi-Component Synthesis of 3,4-Dihydropyrimidin-2-(1H)-Ones/Thiones Catalyzed by Bismuth (III) Sulfate Trihydrate under Solvent-Free Conditions

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A convenient and efficient protocol for the one-pot synthesis of 3,4-dihydropyrimidin-2-(1H)-one/thione derivatives of aldehydes, and 1,3-dicarbonyl compounds with Bismuth (III) sulfate trihydrate as the catalyst was described. We had the advantages of good performance, simplicity, and short time reaction under solvent-free conditions. The catalyst can be repeatedly reused without loss of its activity.

1. Introduction

Multi-component reactions play an important role in pharmaceutical industries. Pharmacies are trying to develop green chemistry reactions. Solvent-free synthesis of complex organic structures as drugs is the dream of every pharmacy. Multi-component reaction as a powerful tool for the rapid introduction of molecular diversity is evident and developed for the generation of heterocycles which receive growing interest [1–3]. Biginelli reaction is one of the most important multi-component reactions for the synthesis of dihydropyrimidinones/thiones. 3,4-Dihydropyrimidin-2(1H)-ones/thiones (DHPMs) reported the activity of many drugs as having antiviral, antibacterial, and antihypertensive effects, as calcium channel modulators [4–7], and as multidrug resistance reversal [8, 9]. Biological activity of some alkaloids isolated recently to 3,4 dihydropyrimidin-2(1H)-ones/thiones moiety [10, 11]. It was first synthesized by Biginelli in 1893 DHPMs as a pot condensation of an aldehyde, diketone, and urea under acidic conditions. These method has low yields, especially in the cases of some substituted aldehydes. To increase the efficiency of the reaction, Biginelli, various catalysts have been used [12].

Biginelli reaction suffers from low yields (20–50%) of products. Thus, in recent years, several methods to improve the use of $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ [13], ZrCl_4 [14], zeolites [15], silica sulfuric acid [16], $\text{BF}_3 \cdot \text{OEt}_2$ [17], $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ [18], SbCl_3 [19], RuCl_3 [20], natural catalyst [21], and glutamic acid [22] have been reported in the literature. However, some of these methods are expensive and harmful to the environment; stoichiometrically, the amount of catalyst, low yields, and incompatibility with other functional groups including product isolation methods is difficult. Therefore, there is still a need for a simple and efficient method for the synthesis of a pot dihydropyrimidinone and thiones under mild conditions. In recent years, eco-friendly industrial application, using green and reusable catalyst, has been studied.

Thus, green chemistry has been defined as a set of principles that reduces or eliminates the use or generation of hazardous chemical materials. It is as part of our current studies on the development of new routes in heterocyclic synthesis [22].

Herein, we want to use the Bismuth (III) sulfate trihydrate as a catalyst in a pot, three-component Biginelli reaction in solvent-free conditions between benzaldehyde, ethyl acetate, and urea for synthesis of DHPMs. This approach

SCHEME 1: Synthesis of 3,4-dihydropyrimidinones/thiones derivatives.

(Scheme 1) for simple pot Biginelli was a remarkable performance (>86) of dihydropyrimidinones/thiones in a shorter reaction time (60–360 min) versus the reaction time required for other catalysts (Scheme 1).

2. Experimental

All chemicals were obtained from Merck or Fluka. Melting points were measured on an Electrothermal 9100 apparatus. Silica gel SILG/UV 254 plates were used for TLC. IR spectra were measured on a Shimadzu IR-470 Spectrophotometer. ^1H NMR and ^{13}C NMR spectra were determined on Bruker 500 DRX AVANCE instrument at 500 and 125 MHz, respectively. The element analyses (C, H, N) were obtained from a Carlo ERBA Model EA 1108 analyzer carried out on Perkin Elmer 240c analyzer.

2.1. General Procedure for the Preparation of 3,4-Dihydropyrimidinones/Thiones (5a–m). A mixture of aldehyde (2 mmol), ethyl acetoacetate (2.5 mmol), urea/thiourea (2.5 mmol), and Bismuth (III) sulfate trihydrate (10 mol%) was heated with stirring for 60 min in 90°C . After cooling, the reaction mixture was poured into crushed ice with stirring. The crude product was filtered, washed with cold water, dried, and recrystallized from 95 ethanol or ethyl acetate to give pure products (5a–m) (80–95). All compounds were fully characterized by elemental analysis, M.P., IR, CHN, and ^1H NMR and ^{13}C NMR spectroscopy. The structures of all synthesized compounds (5a–m) have been depicted in Scheme 1.

2.2. Selected Spectra

5-(Ethoxycarbonyl)-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one (5a). White crystals, m.p. $206\text{--}208^\circ\text{C}$. IR (KBr, cm^{-1}): 3245, 1725, 1635. ^1H NMR (CDCl_3 , δ ppm): 1.10 (t, 3H, $J = 7.2$ Hz, OCH_2CH_3), 2.24 (s, 3H, CH_3), 3.95 (q, 2H, $J = 7.2$ Hz, OCH_2), 5.10 (d, 1H, $J = 2.2$ –CH), 7.28 (m, 5H, Ar–H), 7.77 (s, 1H, NH), 9.0 (s, 1H, NH). ^{13}C NMR (CDCl_3 , δ ppm): 15.15, 19.00, 55.22, 59.95, 101.02, 112.22, 114.15, 126.33, 126.98, 128.45, 132.12, 149.16, 156.77, 164.11.

Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_3$ (%): C, 64.62; H, 6.15; N, 10.72. Found: C, 64.58; H, 6.13; N, 10.72.

5-(Ethoxycarbonyl)-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (5b). White crystals, m.p. $201\text{--}202^\circ\text{C}$. IR (KBr, cm^{-1}): 3240, 1730, 1635. ^1H NMR (CDCl_3 , δ ppm): 1.18 (t, 3H, $J = 7.15$ Hz, OCH_2CH_3), 2.43 (s, 3H, CH_3), 3.91 (s, 3H, $-\text{OCH}_3$), 4.12 (q, 2H, $J = 7.15$ Hz, OCH_2CH_3), 5.54 (d, 1H, $J = 2.50$ –CH), 6.98 (d, 2H, $J = 9.10$, Ar–H), 7.24 (d, 2H, $J = 9.10$, Ar–H), 7.75 (s, 1H, NH), 9.33 (s, 1H, NH). ^{13}C NMR (CDCl_3 , δ ppm): 14.55, 18.22, 56.11, 56.40, 61.10, 100.23, 116.83, 129.38, 138.54, 147.98, 158.09, 159.55, 165.43. Anal. Calcd for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_4$ (%): C, 62.06; H, 6.25; N, 9.65. Found: C, 62.04; H, 6.28; N, 9.67.

5-(Ethoxycarbonyl)-4-(4-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (5c). White crystals m.p. $211\text{--}213^\circ\text{C}$. IR (KBr, cm^{-1}): 3240, 1735, 1625. ^1H NMR (CDCl_3 , δ ppm): 1.14 (t, 3H, $J = 7.02$ Hz, OCH_2CH_3), 2.35 (s, 3H, CH_3), 4.14 (q, 2H, $J = 7.02$ Hz, OCH_2CH_3), 6.09 (d, 1H, $J = 2.33$, –CH), 7.78 (d, 2H, $J = 8.88$, Ar–H), 7.89 (s, 1H, NH), 8.25 (d, 2H, $J = 8.88$, Ar–H), 9.12 (s, 1H, NH). ^{13}C NMR (CDCl_3 , δ ppm): 15.02, 19.11, 56.31, 60.75, 100.90, 120.18, 130.77, 139.55, 154.76, 155.79, 158.95, 166.44. Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{N}_3\text{O}_5$ (%): C, 55.06; H, 4.92; N, 13.74. Found: C, 55.12; H, 4.95; N, 13.68.

5-(Ethoxycarbonyl)-4-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (5d). White crystals, m.p. $215\text{--}216^\circ\text{C}$. IR (KBr, cm^{-1}): 3230, 1725, 1615. ^1H NMR (CDCl_3 , δ ppm): 1.16 (t, 3H, $J = 7.09$ Hz, OCH_2CH_3), 2.44 (s, 3H, CH_3), 4.12 (q, 2H, $J = 7.09$ Hz, OCH_2CH_3), 5.79 (d, 1H, $J = 2.27$, –CH), 7.24 (d, 2H, $J = 9.22$, Ar–H), 7.79 (s, 1H, NH), 7.84 (d, 2H, $J = 9.22$, Ar–H), 9.20 (s, 1H, NH). ^{13}C NMR (CDCl_3 , δ ppm): 14.58, 18.72, 56.46, 61.32, 101.92, 119.77, 131.59, 143.57, 154.26, 155.67, 159.98, 165.65. Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{ClN}_2\text{O}_3$ (%): C, 57.12; H, 5.08; N, 9.55. Found: C, 57.08; H, 5.06; N, 9.56.

5-(Ethoxycarbonyl)-4-(3-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (5e). White crystals, m.p. $192\text{--}193^\circ\text{C}$. IR (KBr, cm^{-1}): 3235, 1725, 1630. ^1H NMR (CDCl_3 , δ ppm): 1.11 (t, 3H, $J = 7.16$ Hz, OCH_2CH_3), 2.30 (s, 3H, CH_3), 4.01 (q, 2H, $J = 7.16$ Hz, OCH_2CH_3), 5.96 (d, 1H, $J = 2.30$, –CH), 7.22–7.55 (m, 4H, Ar–H), 7.66 (s, 1H, NH), 9.18 (s, 1H, NH). ^{13}C NMR (CDCl_3 , δ ppm): 14.65, 19.04, 56.33, 60.67, 100.89, 125.31, 128.35, 128.98, 129.83, 136.67, 143.64, 154.78, 159.57.

165.25. Anal. Calcd for $C_{14}H_{15}ClN_2O_3$ (%): C, 57.14; H, 5.10; N, 9.50. Found: C, 57.13; H, 5.08; N, 9.48.

5-(Ethoxycarbonyl)-4-(4-fluorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (5f). White crystals, m.p. 182–184°C. IR (KBr, cm^{-1}): 3255, 1740, 1650. 1H NMR ($CDCl_3$ δ ppm): 1.18 (t, 3H, $J = 7.11$ Hz, OCH_2CH_3), 2.39 (s, 3H, CH_3), 4.10 (q, 2H, $J = 7.11$ Hz, OCH_2CH_3), 6.13 (d, 1H, $J = 2.20$, -CH), 7.55 (s, 1H, NH), 7.78 (d, 2H, $J = 9.1$, Ar-H), 7.95 (d, 2H, $J = 9.1$, Ar-H), 9.21 (s, 1H, NH). ^{13}C NMR ($CDCl_3$ δ ppm): 14.63, 18.98, 56.44, 61.35, 101.89, 122.78, 135.66, 148.08, 155.37, 158.67, 159.65, 165.90. Anal. Calcd for $C_{14}H_{15}FN_2O_3$ (%): C, 60.43; H, 5.39; N, 10.07. Found: C, 60.39; H, 5.36; N, 10.08.

5-(Ethoxycarbonyl)-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-thione (5g). Yellow crystals, m.p. 208–210°C. IR (KBr, cm^{-1}): 3235, 1715, 1645, 1585, 1525. 1H NMR ($CDCl_3$ δ ppm): 1.12 (t, 3H, $J = 7.25$ Hz, OCH_2CH_3), 2.31 (s, 3H, CH_3), 4.18 (q, 2H, $J = 7.25$ Hz, OCH_2CH_3), 5.23 (d, 1H, $J = 2.15$ -CH), 7.38 (m, 5H, Ar-H), 7.75 (s, 1H, NH), 9.11 (s, 1H, NH). ^{13}C NMR ($CDCl_3$ δ ppm): 14.66, 18.67, 56.87, 60.76, 100.25, 112.75, 118.39, 125.08, 128.22, 130.14, 133.61, 153.86, 163.42, 181.48. Anal. Calcd for $C_{14}H_{16}N_2O_2S$ (%): C, 60.85; H, 5.84; N, 10.14; S, 11.60. Found: C, 60.66; H, 5.86; N, 10.14; S, 11.66.

5-(Ethoxycarbonyl)-4-(3-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-thione (5h). Yellow crystals, m.p. 205–207°C. IR (KBr, cm^{-1}): 3260, 1740, 1635, 1580, 1545. 1H NMR ($CDCl_3$ δ ppm): 1.15 (t, 3H, $J = 7.12$ Hz, OCH_2CH_3), 2.33 (s, 3H, CH_3), 4.22 (q, 2H, $J = 7.12$ Hz, OCH_2CH_3), 5.75 (d, 1H, $J = 2.11$, -CH), 7.24–7.46 (m, 4H, Ar-H), 7.88 (s, 1H, NH), 9.45 (s, 1H, NH). ^{13}C NMR ($CDCl_3$ δ ppm): 14.66, 19.12, 58.12, 60.68, 101.71, 127.45, 128.82, 129.55, 132.39, 135.28, 145.83, 161.02, 165.58, 180.29. Anal. Calcd for $C_{14}H_{15}N_3O_4S$ (%): C, 52.33; H, 4.67; N, 13.08; S, 9.97. Found: C, 52.30; H, 4.66; N, 13.09; S, 9.98.

5-(Ethoxycarbonyl)-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-thione (5i). Yellow crystals, m.p. 153–155°C. IR (KBr, cm^{-1}): 3235, 1720, 1630, 1570, 1535. 1H NMR ($CDCl_3$ δ ppm): 1.18 (t, 3H, $J = 7.14$ Hz, OCH_2CH_3), 2.44 (s, 3H, CH_3), 4.23 (s, 3H, -O CH_3), 4.38 (q, 2H, $J = 7.14$ Hz, OCH_2CH_3), 5.84 (d, 1H, $J = 2.22$ -CH), 7.31 (d, 2H, $J = 8.33$, Ar-H), 7.42 (d, 2H, $J = 8.33$, Ar-H), 7.56 (s, 1H, NH), 9.21 (s, 1H, NH). ^{13}C NMR ($CDCl_3$ δ ppm): 14.87, 19.15, 56.25, 56.49, 60.78, 100.32, 115.65, 128.86, 138.28, 145.84, 160.35, 163.47, 181.66. Anal. Calcd for $C_{15}H_{18}N_2O_3S$ (%): C, 58.82; H, 5.88; N, 9.15; S, 10.45. Found: C, 58.78; H, 5.86; N, 9.16; S, 10.44.

5-(Ethoxycarbonyl)-4-(2-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-thione (5j). Yellow crystals, m.p. 218–220°C. IR (KBr, cm^{-1}): 3430, 3340, 1710, 1668, 1358, 1276. 1H NMR ($CDCl_3$ δ ppm): 1.03 (t, $J = 7.0$ Hz, 3H, CH_3), 2.11 (s, 3H, CH_3), 4.20 (q, $J = 7.0$, 4.28 Hz, 2H, CH_2O), 5.20 (s, 1H, CH), 6.90–7.25 (m, 4H, Ar-H), 8.41 (s, 1H, NH), 9.51 (s, 1H, NH). ^{13}C NMR ($CDCl_3$ δ ppm): 14.52, 57.66, 61.05, 103.27, 125.55, 127.34, 128.62, 131.44, 132.53, 144.22, 160.11, 163.26, 177.43. Anal. Calcd for $C_{14}H_{15}ClN_2O_2S$ (%): C, 54.19; H, 4.84; N, 9.03; S, 10.32. Found: C, 54.14; H, 4.77; N, 9.10; S, 10.25.

TABLE 1: Bismuth (III) sulfate trihydrate catalyzed synthesis of 5-(ethoxycarbonyl)-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one (5a) in different solvents conditions.

Entry	Solvent	Catalyst (mol%)	Time (min)	Yield (%)
1	Ethanol	10	120	25
2	Methanol	10	120	25
3	Acetonitrile	10	120	40
4	Dichloromethane	10	120	33
5	Chloroform	10	120	35
6	Ethyl acetate	10	120	45
7	THF	10	120	20
8	Solvent-free	5	120	65
9	Solvent-free	10	60	89
10	Solvent-free	15	120	78
11	Solvent-free	20	120	55
12	Solvent-free	0	360	10

Reaction conditions: 2 mmol benzaldehyde, 2.5 mmol ethyl acetoacetate, 2.5 mmol urea/thiourea, and Bismuth (III) sulfate trihydrate (10 mol%) were refluxed with stirring for 60 min.

TABLE 2: Bismuth (III) sulfate trihydrate catalyzed synthesis of 3,4-dihydropyrimidinones/thiones derivatives.

Entry	Compound	Substitution	X	M.p. (°C)	Yield (%)
1	5a	H	O	203–204	89
2	5b	4-Methoxy	O	202–203	92
3	5c	4-Nitro	O	212–214	95
4	5d	4-Chloro	O	215–216	93
5	5e	3-Chloro	O	192–193	93
6	5f	4-Fluro	O	182–184	90
7	5g	H	S	208–210	88
8	5h	3-Nitro	S	206–208	86
9	5i	4-Methoxy	S	156–158	86
10	5j	2-Chloro	S	218–220	80
11	5k	2-Nitro	S	190–192	81
12	5m	3-Methoxy	S	160–162	85

Reaction conditions: 2 mmol aldehyde, 2.5 mmol ethyl acetoacetate, 2.5 mmol urea/thiourea, and Bismuth (III) sulfate trihydrate (10 mol%) were refluxed with stirring for 60 min.

5-(Ethoxycarbonyl)-4-(2-nitrophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-thione (5k). Yellow crystals, m.p. 190–192°C. IR (KBr, cm^{-1}): 3338, 3289, 2996, 1685, 1572, 1355, 1310. 1H NMR ($CDCl_3$ δ ppm): 1.14 (t, $J = 7.4$ Hz, 3H, CH_3), 1.98 (s, 3H, CH_3), 4.15 (q, $J = 7.4$, 4.55 Hz, 2H, CH_2O), 5.15 (s, 1H, CH), 6.8–7.38 (m, 4H, Ar-H): 7.22 (s, 1H, NH), 9.35 (s, 1H, NH). ^{13}C NMR ($CDCl_3$ δ ppm): 18.37, 56.36, 60.44, 101.48, 123.21, 125.72, 126.52, 130.26, 130.83, 142.77, 159.61, 161.12, 175.87. Anal. Calcd for $C_{14}H_{15}N_3O_4S$ (%): C, 52.33; H, 4.67; N, 13.08; S, 9.97. Found: C, 52.26; H, 4.65; N, 13.12; S, 9.96.

5-(Ethoxycarbonyl)-4-(3-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-thione (5m). Yellow crystals, m.p. 160–162°C. IR (KBr, cm^{-1}): 3427, 3287, 2967, 1709, 1613, 1300, 1291. 1H NMR ($CDCl_3$ δ ppm): 1.22 (t, $J = 7.6$ Hz, 3H, CH_3), 2.30 (s, 3H, CH_3), 3.86 (s, 3H, Ar- OCH_3), 4.14 (q, $J = 7.6$, 4.1 Hz,

TABLE 3: Biginelli synthesis of 5-ethoxycarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one: Bismuth (III) sulfate trihydrate in comparison with some recent reports.

Entry	Conditions	Time (h:min)	Yield (%)	Reference
1	Al(NO ₃) ₃ ·9H ₂ O/SF, 80°C	0:15	98	[13]
2	Sulfated tungstate/SF, 80°C	1:00	92	[13]
3	PPA-SiO ₂ /CH ₃ CN, reflux	1:00	88	[13]
4	FeCl ₃ immobilized in Al-MCM 41/CH ₃ CN, reflux	4:00	85	[13]
5	[Hmim] HSO ₄ /solvent-free, 110°C	0:20	92	[13]
6	Alpha-zirconium sulfophenylphosphonate/SF, 80°C	18:0	89	[13]
7	1, 3-Dichloro-5, 5-dimethylhydantoin/CH ₃ CN, reflux Bi(NO ₃) ₃	4:00 1:30	89 92	[13] [23]
8	Bismuth (III) sulfate trihydrate/SF, 90°C	1:00	89	In this research

2H, CH₂O), 5.18 (s, 1H, CH), 6.8 (s, 1H, NH), 6.82–7.84 (m, 4H, Ar–H), 9.42 (s, 1H, NH). ¹³C NMR (CDCl₃ δ ppm): 15.43, 19.62, 56.35, 56.78, 61.44, 100.02, 112.73, 126.11, 135.56, 147.67, 161.48, 164.29, 179.37. Anal. Calcd for C₁₅H₁₈N₂O₃S (%): C, 58.82; H, 5.88; N, 9.15; S, 10.45. Found: C, 58.77; H, 5.84; N, 9.16; S, 10.42.

3. Results and Discussion

Bismuth (III) sulfate trihydrate and other salts of Bismuth can be used as a catalyst in the synthesis of organic compounds considered [23–28]. The features of this catalyst could be of high interest because easily separated, environmentally friendly, reusable, clean and affordable. Dihydropyrimidines show a wide range of biological activities. We are interested to develop a simple method for the synthesis of Biginelli reaction DHPMs. Our own study of one-pot three-component Biginelli condensation using Bismuth (III) sulfate trihydrate as a catalyst (Scheme 1) and the reaction with benzaldehyde, ethyl acetoacetate, and urea to afford the product DHPMs as a model reaction (**5a**) has begun. Synthesis reaction mixture as a model (**5a**) to determine the appropriate response in the presence of various amounts of Bismuth (III) sulfate trihydrate catalyst under solvent-free conditions (Table 1) was selected. It was found that the yield of compound **5a** was strongly affected by the catalyst amount. The best results under solvent-free conditions (entry 9) in the presence of 10 mol% catalyst (Table 1) were obtained. In various solvents such as ethanol, methanol, acetonitrile, dichloromethane and chloroform, ethyl acetate, THF, and under solvent-free conditions in the presence of 10 mol% the catalyst (Table 1) was examined. The best results were obtained in solvent-free conditions at the top and the shortest reaction time (entry 9).

We were successful; 4-dihydropyrimidin-2(1H)-one/thione derivatives of aldehydes and 1,3-dicarbonyl compounds with Bismuth (III) sulfate trihydrate have been synthesized. MCR of benzaldehyde, ethyl acetoacetate, and urea as a model reaction was chosen for optimization. Results are shown in Table 2. With Bismuth (III) sulfate trihydrate as the catalyst, the reaction rate increases dramatically and is easily removed and reused (Table 2). As shown in

Table 1, there is no decrease in catalytic efficiency (entry 12). All reactions were monitored by TLC and forwarded to maximize atom utilization. All compounds with melting points, IR, ¹H NMR, ¹³C NMR, and CHN techniques were identified. Different aldehydes donating/electron withdrawing for synthesis of DHPMs reacted with excellent yield in available time.

The catalyst was easily recovered by simple filtration after dilution of the reaction mixture with ethyl acetate and was reused after being vacuum dried. Bi₂(SO₄)₃ was reused for four runs without significant loss of activity (Run 1: 91%; Run 2: 89%; Run 3: 87%; Run 4: 85%).

In order to standardize the reaction conditions for the condensation reaction, it was decided to synthesize 3,4-dihydropyrimidin-2(1H)-one (**5a**) from benzaldehyde, urea, and ethyl acetoacetate using Bismuth (III) sulfate trihydrate, and we found that the reaction is fast when compared to other reported methods. The results are compared with the reported methods, and it is clear from Table 3 that the present method is more efficient.

4. Conclusion

In conclusion, our Bismuth (III) sulfate trihydrate as a catalyst for the synthesis of dihydropyrimidinones/thiones replaced under solvent-free conditions is displayed. Moderate to good yields of the corresponding DHPMs were obtained. Good yields, One-pot, reused, available time and simple separation experiments under solvent-free conditions with reused catalyst are advantages of this method.

Conflict of Interests

The author declares no financial conflict of interests.

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