SUPPORTING INFORMATION

ZnO Nanoparticles as an Efficient, Heterogeneous, Reusable, and Eco-friendly Catalyst for One-Pot three-Component Synthesis of 3,4-dihydropyrimidin-2(1*H*)-(thio)one Derivatives in Water

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Materials and Instruments:

All the reagent and solvents were obtained from Merck (Germany) and were used without further purification. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 and DMSO at 300, 400 and 500 MHz, on a Varian Gemini 200 MHz spectrometer. The chemical shift values were reported on δ scale in ppm with respect to TMS (δ 0.00 ppm) as internal standard. Melting points were measured on an Electro Thermal 9100 apparatus.

Experimental Section:**Preparation of ZnO nanoparticles**

In a typical procedure, 0.44 g (2.00 mmol) of $\text{Zn}(\text{CH}_3\text{CO}_2)_2 \cdot 2\text{H}_2\text{O}$ was suspended in 220 mL of 2-propanol under vigorous stirring at 50 °C. A sodium hydroxide alcoholic solution was prepared by adding 0.16 g (4.00 mmol) NaOH to 60 mL of 2-propanol under vigorous stirring at 50 °C. The flasks containing $\text{Zn}(\text{CH}_3\text{CO}_2)_2 \cdot 2\text{H}_2\text{O}$ and NaOH alcoholic solution were cooled in an ice-water bath. The sodium hydroxide solution was then added to zinc acetate solution under vigorous stirring to give a total volume of 300 mL. Final solution was heated in a controlled microwave cavity for 5 min. During the microwave irradiation the temperature of the solution reached up 80 °C. After 5 min, the transparent solution was obtained. The centrifugation of transparent solution yields white products, which were washed twice with absolute ethanol and dried at 70 °C for 4 h. Then white powders were calcined at 600 °C for 1 h. The results obtained from XRD pattern and SEM micrograph of the ZnO nanoparticles show that the mean particle size is 30 nm.

General procedure for the preparation of 3,4- dihydropyrimidin-2(1*H*)-(thio)ones 4a-z:

General procedure for one-pot preparation of 3,4- dihydropyrimidin-2(1*H*)-(thio)ones using ZnO nanoparticle as a catalyst is that to a stirred suspension of ZnO nanoparticles (4 mol%) in water (5 ml) were added an aldehyde (1.00 mmol), ethyl acetoacetate (1.10 mmol), urea or thiourea (3.00 mmol), and then heated in water as solvent at 80 °C while being stirred for 20–40 min. The completion of the reaction was monitored by TLC. After completion of the reaction, which resulted in precipitation of the desired 3,4- dihydropyrimidin-2(1*H*)-(thio)ones 4a-w. The precipitated solid was filtered, dried, washed with petroleum ether to remove any residual starting material and then recrystallized from ethanol to afford the pure product. The catalyst could be recovered after evaporation of the aqueous layer, the reused in subsequent reaction without losing any significant activity. Products were characterized by spectral (^1H and ^{13}C

NMR) data and by comparisons with those of authentic samples and also by the mixed melting points with the authentic samples.

Product Characterization:

Ethyl 4-(4-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4c): White solid, mp: 226-228 °C, 93 % yield; ^1H NMR (DMSO- d_6 , 300 MHz) δ (ppm): 1.10 (t, $J = 7.2$ Hz, CH_3CH_2); 2.22 (s, CH_3), 3.97 (q, $J = 6.9$ Hz, CH_3CH_2), 5.03 (d, $J = 3$ Hz, CH), 6.68 (d, $J = 8.4$ Hz, 2H), 7.03 (d, $J = 8.4$ Hz, 2H), 7.59 (t, $J = 2.5$ Hz, 1H), 9.09 (d, NH), 9.31 (s, NH); ^{13}C NMR (DMSO- d_6 , 300 MHz) δ (ppm): 14.1, 17.7, 53.4, 59.1, 99.7, 115.0, 127.4, 135.4, 147.7, 152.2, 156.5, 165.4; Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.83; H, 5.84; N, 10.12.

Ethyl 6-methyl-2-oxo-4-(*p*-tolyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4d): White solid, mp: 215-217 °C, yield 92 %; ^1H NMR (300 MHz, CDCl_3) δ (ppm): 1.08 (t, $J = 6.9$, CH_3CH_2), 2.23 (s, CH_3), 2.24 (s, CH_3), 3.96 (q, $J = 6.9$, CH_3CH_2), 5.10 (d, $J = 2.7$, CH), 7.10 (br s, Ar), 7.67 (s, NH), 9.14 (s, NH); ^{13}C NMR (DMSO- d_6 , 75 MHz) δ (ppm): 14.0, 17.7, 20.6, 53.6, 59.1, 99.5, 126.2, 128.9, 139.4, 141.9, 148.1, 152.2, 165.3. Anal. Calcd for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_3$: C, 65.68; H, 6.61; N, 10.21. Found: C, 65.66; H, 6.62; N, 10.23.

Ethyl 4-(4-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4e) White solid, mp: 210-223 °C, 90 % yield; ^1H NMR (DMSO- d_6 , 300 MHz) δ (ppm): 1.05 (t, $J = 6.9$ Hz, CH_3CH_2); 2.23 (s, CH_3), 3.98 (q, $J = 6.9$ Hz, CH_3CH_2), 5.13 (d, $J = 3.3$ Hz, CH), 7.28 (d, $J = 8.5$ Hz, 2H), 7.39 (d, $J = 8.5$ Hz, 2H), 7.76 (s, NH), 9.23 (s, NH), ^{13}C NMR (DMSO- d_6 , 75 MHz) δ (ppm): 14.0, 17.7, 53.4, 59.2, 98.8, 127.9, 128.1, 128.3, 131.7, 143.7, 148.7, 151.9, 157.6, 165.2. Anal. Calcd for $\text{C}_{13}\text{H}_{13}\text{ClN}_2\text{O}_3$: C, 55.62; H, 4.67; N, 9.98. Found: C, 55.65; H, 4.69; N, 10.00.

Ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4f): Yellow solid, mp: 199-201 °C, 91 % yield; ^1H NMR (DMSO- d_6 , 500 MHz) δ (ppm): 1.07 (t, $J = 7$ Hz, CH_3CH_2); 2.23 (s, CH_3), 3.96 (q, $J = 7.1$ Hz, CH_3CH_2), 5.12 (d, $J = 2.5$ Hz, CH), 7.21-7.23 (m, 4H), 7.28-7.31 (t, $J = 7.5$ Hz, 1H), 7.71 (s, NH), 9.17 (s, NH); ^{13}C NMR (DMSO- d_6 , 125 MHz) δ (ppm): 14.6, 18.3, 54.5, 59.8, 99.9, 126.8, 127.8, 128.9, 145.4, 148.9, 152.7, 165.9. Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.61; H, 6.19; N, 10.75.

Ethyl 6-methyl-2-oxo-4-styryl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4h):

White solid, mp: 234-236 °C, yield 80 %; ¹H NMR (300 MHz, DMSO -d₆) δ (ppm): 1.19 (t, *J* = 6.5 Hz, CH₃CH₂), 2.17 (s, CH₃), 4.10 (q, *J* = 6.7 Hz, CH₃CH₂), 4.73 (d, *J* = 1.8, CH), 6.17-6.21 (m, 1H), 6.36 (d, *J* = 8.7, 1H), 7.21-7.48 (m, 5H), 7.54 (s, NH), 9.14 (s, NH); ¹³C NMR (75 MHz, DMSO-d₆) δ (ppm): 14.2, 17.7, 51.8, 59.2, 97.7, 126.3, 127.5, 128.1, 128.6, 130.0, 136.2, 148.5, 152.5, 165.1. Anal. Calcd for C₁₆H₁₈N₂O₃: C, 67.12; H, 6.34; N, 9.78. Found: C, 67.09; H, 6.36; N, 9.79.

Ethyl 6-methyl-4-(3-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4i):

White solid, mp: 231-233 °C, 79 % yield; ¹H NMR (300 MHz, DMSO -d₆) δ (ppm): 1.11 (t, *J* = 7.3 Hz, CH₃CH₂), 2.28 (s, CH₃), 4.01 (q, *J* = 7.4, CH₃CH₂), 5.30 (d, *J* = 3.3 Hz, CH), 7.62-7.71 (m, 2H), 7.90 (s, NH), 8.08-8.13 (m, 2H), 9.36 (s, NH). Anal. Calcd for C₁₄H₁₅N₃O₅: C, 55.08; H, 4.95; N, 13.76. Found: C, 55.05; H, 4.97; N, 13.76.

Ethyl 6-methyl-4-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4j):

Yellow solid, mp: 206-208 °C, yield 78 %; IR (KBr) (ν_{max}/cm⁻¹): 3359, 3232, 3121, 2976, 1691, 1629, 1571, 1458, 1367, 1319, 1300, 1252, 1231, 1148, 1092, 1021; ¹H NMR (300 MHz, DMSO-d₆) δ (ppm): 1.08 (t, *J* = 7.2, CH₃CH₂), 2.25 (s, CH₃), 3.97 (q, *J* = 7.2, CH₃CH₂), 5.26 (d, *J* = 3.3, CH), 7.48 (d, *J* = 8.9, 2H), 7.87 (s, NH), 8.19 (d, *J* = 8.9, 2H), 9.32 (s, NH); ¹³C NMR (DMSO-d₆, 75 MHz) δ (ppm): 13.9, 17.8, 53.5, 59.3, 98.1, 123.7, 127.5, 148.5, 149.3, 151.8, 151.9, 164.3. Anal. Calcd for C₁₄H₁₅N₃O₅: C, 55.08; H, 4.95; N, 13.76. Found: C, 55.09; H, 4.96; N, 13.78.

Ethyl 4-(furan-2-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4k):

Yellow solid, mp: 206-208 °C, yield 85 %; ¹H NMR (DMSO-d₆, 300 MHz) δ (ppm): 1.13 (t, *J* = 7.2 Hz, CH₃CH₂), 2.22 (s, CH₃), 4.01 (q, *J* = 7.2 Hz, CH₃CH₂), 5.20 (d, *J* = 3.6 Hz, CH), 6.07 (d, *J* = 3.3 Hz, 1H), 6.33 (m, 1H), 7.51 (m, 1H), 7.71 (s, NH), 9.21 (s, NH); ¹³C NMR (DMSO-d₆, 75 MHz) δ (ppm): 14.6, 18.2, 48.2, 59.7, 97.2, 105.7, 110.8, 142.6, 149.8, 152.8, 165.4, 156.4. Anal. Calcd for C₁₁H₁₂N₂O₄: C, 55.93; H, 5.12; N, 11.86. Found: C, 55.91; H, 5.14; N, 11.89.

Ethyl 4-cyclohexyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4l):

White solid, mp: 237-239 °C, yield 74 %; ¹H NMR (400 MHz, CDCl₃) δ (ppm): 0.97-1.02 (m, 1H), 1.12-1.19 (m, 4H), 1.29 (t, *J* = 6.8 Hz, CH₃CH₂), 1.50-1.75 (m, 6H), 2.33 (s, CH₃), 4.16-4.24 (m, 3H), 8.07 (s, NH), 8.58 (s, NH); ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 14.1, 17.9, 25.8, 26.0,

26.1, 26.5, 28.5, 44.8, 57.0, 60.2, 101.6, 143.8, 165.8, 175.5; Anal. Calcd for C₁₃H₂₀N₂O₃: C, 61.88; H, 7.99; N, 11.10. Found: C, 61.86; H, 8.01; N, 11.12.

Methyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4o): White solid, mp: 221-223 °C, yield 88 %; ¹H NMR (DMSO-*d*₆, 300 MHz) δ (ppm): 2.24 (s, CH₃); 3.51 (s, CH₃), 5.14 (d, *J* = 3.6 Hz, CH), 7.20-7.33 (m, 5H), 7.74 (s, NH), 9.20 (s, NH). ¹³C NMR (DMSO-*d*₆, 75 MHz) δ (ppm): 18.3, 51.3, 54.3, 99.5, 126.6, 127.8, 128.9, 145.1, 149.1, 152.7, 166.3. Anal. Calcd for C₁₃H₁₄N₂O₃: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.41; H, 5.74; N, 11.40.

Ethyl 4-(4-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4t): White solid, mp: 199-201 °C, yield 91 %; ¹H NMR (DMSO-*d*₆, 400 MHz) δ (ppm): 1.08 (t, *J* = 5.6 Hz, CH₃CH₂), 2.25 (s, CH₃), 3.98 (q, *J* = 5.6 Hz, CH₃CH₂), 5.03 (d, *J* = 2.8 Hz, CH), 6.69 (d, *J* = 6.8 Hz, 2H), 6.98 (d, *J* = 6.8 Hz, 2H), 9.52 (s, NH), 9.40 (s, NH), 10.21 (s, OH). ¹³C NMR (DMSO-*d*₆, 100 MHz) δ (ppm): 14.5, 17.6, 54.0, 59.9, 101.6, 115.6, 128.1, 134.6, 144.9, 157.3, 165.6, 174.3. Anal. Calcd for C₁₃H₁₄N₂O₄S: C, 56.10; H, 5.07; N, 10.06. Found: C, 56.12; H, 5.08; N, 10.02.

Ethyl 6-methyl-4-(3-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4x): White solid, mp: 203-205 °C, yield 77 %; ¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm): 1.12 (t, *J* = 6.4 Hz, CH₃CH₂), 2.33 (s, CH₃), 3.99-4.08 (m, CH₃CH₂), 5.36 (d, *J* = 3.6 Hz, CH), 7.65-7.72 (m, 2H), 8.09 (s, 1H), 8.15-8.18 (m, 1H), 9.77 (s, 1H), 10.51 (s, NH); ¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm): 14.4, 17.6, 53.9, 60.2, 100.3, 121.6, 123.1, 130.8, 133.4, 145.9, 146.4, 148.3, 165.3, 175.0; Anal. Calcd for C₁₃H₁₃N₃O₄S: C, 50.81; H, 4.26; N, 13.67. Found: C, 50.81; H, 4.25; N, 13.69.

Ethyl 6-methyl-4-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4y): White solid, mp: 108-110 °C, yield 75%; ¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm) 1.11 (t, *J* = 7.2 Hz, CH₃CH₂), 2.33 (s, CH₃), 4.03 (q, *J* = 7.1 Hz, CH₃CH₂), 5.33 (d, *J* = 3.6 Hz, 1H), 7.50 (d, *J* = 9.2 Hz, 2H), 8.24 (d, *J* = 8.8 Hz, 2H), 9.76 (s, NH), 10.48 (s, NH); ¹³C NMR (100 MHz, DMSO-*d*₆) δ (ppm) 14.4, 17.7, 54.1, 60.2, 100.1, 124.4, 128.2, 146.4, 147.4, 150.8, 165.3, 174.9. Anal. Calcd for C₁₃H₁₃N₃O₄S: C, 50.81; H, 4.26; N, 13.67. Found: C, 50.83; H, 4.27; N, 13.66.

Ethyl 4-(furan-2-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4z): Yellow solid, mp: 183 °C (dec.), yield 80%; ¹H NMR (DMSO-*d*₆, 400 MHz) δ (ppm): 1.11 (t, *J* = 6.0 Hz, CH₃CH₂), 2.25 (s, CH₃), 4.01 (q, *J* = 6.0 Hz, CH₃CH₂), 5.20 (d, *J* = 3.2 Hz, CH), 6.11

(d, $J = 2.4$ Hz, 1H), 6.35 (d, $J = 1.6$ Hz, 1H), 7.56 (s, 1H), 9.61 (s, NH), 10.25 (s, NH). ^{13}C NMR (DMSO- d_6 , 100 MHz) δ (ppm): 14.7, 17.7, 60.2, 98.8, 106.9, 111.1, 143.2, 146.6, 155.2, 165.4, 175.5. Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_3\text{S}$: C, 52.37; H, 4.79; N, 11.10. Found: C, 52.35; H, 4.78; N, 4.76.