Silica–$ZnCl_2$: An Efficient and Reusable Solid Catalyst for One Pot Synthesis of 5-Methyl Mercaptothiocarbonyl-4-aryl-3-dihydropyrimidin-2(1*H*)-ones Under Solvent-Free Conditions

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Synthetic application of Silica–$ZnCl_2$, as an efficient and eco-friendly catalyst for the synthesis of a small library of dihydropyrimidinones is described in this report. The reaction involves a one pot, multicomponent reaction of β-oxodithiocarboxylates, aldehydes, and urea under solvent-free conditions. The experimental procedure is simple, environmental benign, tolerated with many functional groups, and results in good to excellent yield of the products.

Keywords: Dihydropyrimidinones, β-Oxodithiocarbonates, Solvent-free, Silica–$ZnCl_2$

Introduction

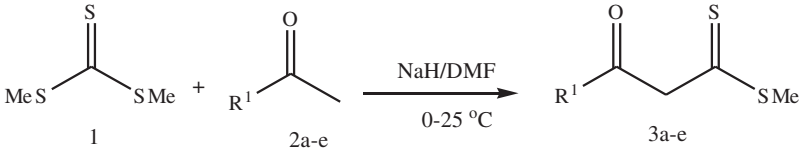
Heterogeneous catalysts are advantageous over homogeneous catalysts as they can be easily recovered from the reaction mixture by simple filtration and reusable after activation, thereby making the process economically viable. Granite, quartz, and silica catalysts were reported also as efficient heterogeneous catalysts for Biginelli reaction.[1] Among of heterogeneous catalysts, silica gel is one of the more extensively used surface material supports for different chemical transformations in organic synthesis.[2] Among the heterogeneous catalysts, solid-based catalyst, silica–$ZnCl_2$, attracted much attention in recent years as catalyst for organic synthesis due to economic and environmental friendly considerations.[3–6] It's surface is both thermally and chemically stable during the reaction process, and it is also an abundant and inexpensive material. We are using this catalytic system for the first time in the synthesis of dihydropyrimidines from a multicomponent reaction of β-oxodithiocarboxylates, aldehydes, and urea (Schemes 1 and 2).

Dihydropyrimidinones (DHPMs) are well-known bioactive heterocycles exhibiting a wide spectrum of biological activities. They show remarkable pharmacological properties such as calcium channel blockers, mitotic kinesin Eg5 motor protein inhibitors, as well as potent HIV gp-120-CD_4 inhibitors.[7–14] They are also reported as potential antifungal, antiviral, antitumor, antibacterial, and anti-inflammatory agents.[15–18] Synthesis of polyfunctionalized dihydropyrimidine was first reported by Biginelli in 1893, involving a one-pot condensation of an aldehyde, β-ketoester, and urea under strongly acidic conditions.[1,2,19,20] Since then, many improved protocols have been reported from time-to-time,[21–28] some of them still suffer from drawbacks such as unsatisfactory yields, cumbersome product isolation procedures, and environmental pollution.[29–37] We are reporting herein the application of silica–$ZnCl_2$ as an effective catalyst in multicomponent reactions under solvent-free conditions for the synthesis of a small library of 5-methylmercaptothiocarbonyl-4-aryl-3-dihydropyrimidin-2(1H)-ones in good to excellent yields.

Experimental

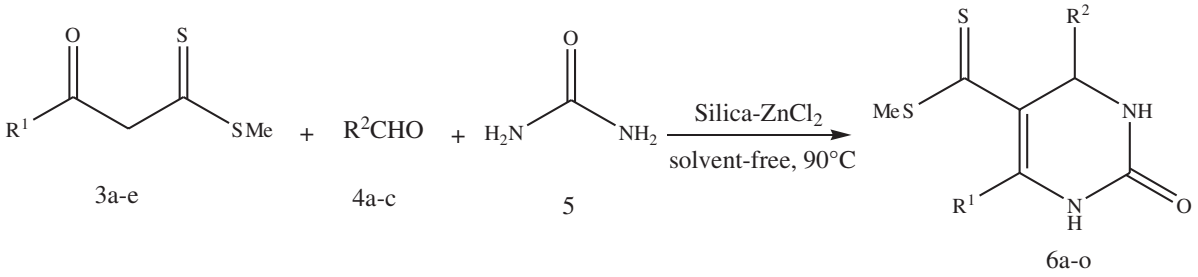
^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on FT-NMR spectrometer using $CDCl_3$. Chemical shifts δ are measured in parts per million (ppm) with either $CDCl_3$ as solvent and are relative to tetramethylsilane (TMS) as the internal reference. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad) and coupling constants (*J*) in Hertz. The FT-IR spectra were recorded on a **Perkin-Elmer FT-IR spectrometer (KBr). Elemental analyses were recorded using Perkin-Elmer 2400 analytical instrument. Mass spectra (ESI-MS) were recorded at **Waters, Q-TOF LC-MS spectrometer. Melting points were determined on a "*Veego*" capillary melting point apparatus and are uncorrected. Silica gel 60 was used for column separations. Chemical yields refer to the pure isolated substances.

Preparation of SiO_2–$ZnCl_2$. A mixture of activated SiO_2 (10 g) and anhydrous $ZnCl_2$ (3 g) was refluxed in



1 2a-e 3a-e

Scheme 1. Synthesis of β-oxodithiocarbonates.



3a-e 4a-c 5 6a-o

R_1 = C_6H_5, 4-$MeOC_6H_5$, 4-ClC_6H_5, 4-MeC_6H_5, CH_3

R_2 = C_6H_5, 4-ClC_6H_4, 4-$MeOC_6H_4$

Yield= 70-82%

Scheme 2. Synthesis of dihydropyrimidines.

dichloromethane (30 mL) for 10 h. SiO_2-$ZnCl_2$ was obtained as a free-flowing powder after filtration under reduced pressure and dried over P_2O_5.

Preparation of β-Oxodithioester 3a-e. β-Oxodithioesters **3a–e** were prepared according to our earlier reported methods.[38–40]

General Procedure for Synthesis of 5-Methylmercaptothiocarbonyl-4-aryl-3-dihydropyrimidin-2(1*H*)-ones (6a–o). A mixture of β-oxodithioester 3 (5 mmol), aldehyde 4 (5 mmol), urea 5 (5 mmol), and silica–$ZnCl_2$ (100 mg) was heated in a preheated oil bath at 90 °C with stirring for 1 h. The progress of the reaction was monitored by TLC (hexane/EtOAc, 8:2). After cooling, EtOAc (30 mL) was added and silica–$ZnCl_2$ was filtered. The organic phase was washed with H_2O (2 × 50 mL) and extracted with EtOAc (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the resulting crude residue was subjected to column chromatography on SiO_2 (gradient elution using EtOAc/hexanes as the eluent). All the compounds were characterized by spectroscopy, mass spectrometry, and elemental analysis.

5-Methylmercaptothiocarbonyl-4,6-diphenyl-3,4-dihydropyrimidin-2(1*H*)-one (6a): Bright yellow powder. mp 198–200 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3H), 5.87 (d, *J* = 2.7 Hz, 1H), 6.32 (s, 1H, NH), 7.28–7.44 (m, 10H), 7.61 (s, 1H, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.5, 60.9, 119.4, 127.2, 128.1, 128.2, 128.7, 128.8, 129.9, 134.6, 136.5, 141.7, 152.6, 227.0; IR (KBr) (ν_{max}, cm^{-1}) 1226, 1629, 1700, 3084, 3198; MS (ESI): *m/z* = 340 $(M)^+$. Anal. Calcd for $C_{18}H_{16}N_2OS_2$: C, 63.50; H, 4.74; N, 8.23. Found: C, 63.58; H, 4.79; N, 8.30.

5-Methylmercaptothiocarbonyl-4-(4-methoxyphenyl)-6-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (6b): Bright yellow powder. mp 182–183 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.79 (s, 3H), 5.83 (d, *J* = 2.1 Hz, 1H), 6.17 (s, 1H, NH), 6.83 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.37–7.46 (m, 5H), 8.07 (s, 1H, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.4, 55.2, 60.4, 113.9, 119.6, 128.2, 128.4, 128.8, 129.8, 134.1, 134.6, 136.2, 152.7, 159.3, 227.2; IR (KBr) (ν_{max}, cm^{-1}) 1244, 1610, 1691, 3095, 3213; MS (ESI): *m/z* = 370 $(M)^+$. Anal. Calcd for $C_{19}H_{18}N_2O_2S_2$: C, 61.60; H, 4.90; N, 7.56. Found: C, 61.50; H, 4.84; N, 7.53.

5-Methylmercaptothiocarbonyl-4-(4-chlorophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (6c): Yellow powder. mp 230–231 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3H), 5.45 (s, 1H, NH), 5.93 (d, *J* = 1.8 Hz, 1H), 6.46 (s, 1H, NH), 7.28–7.41 (m, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.4, 60.8, 119.6, 127.1, 128.2, 128.7, 128.9, 129.7, 132.7, 135.3, 135.8, 141.5, 153.1, 226.8; IR (KBr) (ν_{max}, cm^{-1}): 1256, 1614, 1695, 3086; MS: *m/z* = 374.5 $(M)^+$. Anal. Calcd for $C_{18}H_{15}N_2OS_2Cl$: C, 57.67; H, 4.03; N, 7.47. Found: C, 57.60; H, 4.14; N, 7.43.

5-Methylmercaptothiocarbonyl-4-phenyl-6-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1*H*)-ones (6d): Yellow powder. mp 188–189 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.83 (s, 3H), 5.60 (s, 1H, NH), 5.90 (d, *J* = 2.1 Hz, 1H), 6.72 (s, 1H, NH), 6.87 (d, *J* = 6.6 Hz, 2H), 7.26–7.39 (m, 7H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.5, 55.4, 60.9, 119.1, 127.1, 128.0, 128.1, 128.6, 129.4, 131.6, 136.7, 140.1, 141.7, 152.6, 227.1; IR (KBr) (ν_{max}, cm^{-1}): 1253, 1610, 1695, 3086, 3211; MS (ESI): *m/z* = 370 $(M)^+$. Anal. Calcd for $C_{19}H_{18}N_2O_2S_2$: C, 61.60; H, 4.90; N, 7.56. Found: C, 61.59; H, 4.93; N, 7.53.

5-Methylmercaptothiocarbonyl-4-(4-methoxyphenyl)-6-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1*H*)-ones (6e): Yellow powder. mp 207–208 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.78 (s, 3H), 3.82 (s, 3H) 5.48 (s, 1H,

NH), 5.85 (s, 1H), 6.61(s, 1H, NH), 6.82 (d, J = 6.3 Hz, 2H), 6.85–6.89 (m, 2H), 7.26–7.30 (m, 2H), 7.36 (d, J = 6.3 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.5, 60.9, 60.11, 119.1, 127.1, 128.0, 128.1, 128.6, 129.4, 131.6, 136.7, 140.1, 141.7, 152.6, 227.1; MS (ESI): m/z = 400 $(M)^+$. Anal. Calcd for $C_{20}H_{20}$ $N_2O_3S_2$: C, 59.98; H, 5.03; N, 6.99. Found: C, 59.95; H, 5.07; N, 6.97.

5-Methylmercaptothiocarbonyl-4-(4-chlorophenyl)-6-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1*H*)-ones (6f): Yellow powder. mp 194–195 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.78 (s, 3H), 5.43 (s, 1H, NH), 5.91 (s, 1H), 6.59 (s, 1H, NH), 6.89 (d, J = 6.9 Hz, 2H), 7.22–7.31 (m, 4H), 7.38 (d, J = 6.6 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.8, 55.8, 60.9, 119.1, 127.1, 128.0, 128.1, 128.6, 129.4, 131.6, 136.7, 140.1, 141.7, 153.6, 227.8; MS (ESI): m/z = 404 $(M)^+$. Anal. Calcd for $C_{19}H_{17}$ $N_2O_2S_2Cl$: C, 56.36; H, 4.23; N, 6.92. Found: C, 56.33; H, 4.25; N, 6.95.

5-Methylmercaptothiocarbonyl-4-phenyl-6-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1*H*)-ones (6g): Yellow powder. mp 224–225 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3H), 5.52 (s, 1H, NH), 5.89 (d, J = 1.8 Hz, 1H), 6.79 (s, 1H, NH), 7.26–7.35 (m, 5H), 7.37–7.41 (m, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.4, 60.8, 119.6, 127.1, 128.2, 128.7, 128.9, 129.7, 132.7, 135.3, 135.8, 141.5, 153.1, 226.8; MS: m/z = 374 $(M)^+$. Anal. Calcd for $C_{18}H_{15}N_2O$ S_2Cl: C, 57.67; H, 4.03; N, 7.47. Found: C, 57.65; H, 4.05; N, 7.49.

5-Methylmercaptothiocarbonyl-4-(4-methoxyphenyl)-6-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1*H*)-ones (6h): Yellow powder. mp 195–196 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 3.78 (s, 3H), 5.77 (d, J = 2.1 Hz, 1H), 6.32 (s, 1H, NH), 6.82 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 7.28–7.37 (m, 5H), 8.07 (s, 1H, NH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.5, 21.4, 60.9, 119.1, 127.1, 128.0, 128.1, 128.6, 129.4, 131.6, 136.7, 140.1, 141.7, 152.6, 227.1; IR (KBr) (ν_{max}, cm^{-1}): 1253, 1610, 1695, 3086, 3211; MS (ESI): m/z = 404 $(M)^+$. Anal. Calcd for $C_{19}H_{17}$ $N_2O_2S_2Cl$: C, 56.36; H, 4.23; N, 6.92. Found: C, 56.39; H, 4.21; N, 6.95.

5-Methylmercaptothiocarbonyl-4-(4-chlorophenyl)-6-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1*H*)-ones (6i): Yellow powder. mp 226–227 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 5.5 (s, 1H, NH), 5.96 (d, J = 2.1 Hz, 1H), 6.64 (s, 1H, NH), 7.25–7.34 (m, 4H), 7.37–7.39 (m, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.5, 21.4, 60.9, 119.1, 127.1, 128.0, 128.1, 128.6, 129.4, 131.6, 136.7, 140.1, 141.7, 152.6, 227.1; IR (KBr) (ν_{max}, cm^{-1}): 1256, 1617, 1695, 3086, 3210; MS (ESI): m/z = 407 $(M)^+$. Anal. Calcd for $C_{18}H_{14}N_2OS_2Cl_2$: C, 52.81; H, 3.45; N, 6.84. Found: C, 52.85; H, 3.41; N, 6.85.

5-Methylmercaptothiocarbonyl-4-phenyl-6-(4-methylphenyl)-3,4-dihydropyrimidin-2(1*H*)-ones (6j): Yellow powder. mp 203–205 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3H), 2.37 (s, 3H), 5.43 (s, 1H, NH), 5.92 (d, J = 2.1 Hz, 1H), 6.44 (s, 1H, NH), 7.18 (d, J = 5.8 Hz, 2H), 7.26–7.35 (m, 5H), 7.37 (d, J = 5.8 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.5, 21.4, 60.9, 119.1, 127.1, 128.0, 128.1, 128.6, 129.4, 131.6, 136.7, 140.1, 141.7, 152.6, 227.1; IR (KBr) (ν_{max}, cm^{-1}): 1259, 1619, 1697, 3083, 3210; MS (ESI): m/z = 354 $(M)^+$. Anal. Calcd for $C_{19}H_{18}N_2OS_2$: C, 64.38; H, 5.12 N, 7.90. Found: C, 64.35; H, 5.15; N, 7.95.

5-Methylmercaptothiocarbonyl-4-(4-methoxyphenyl)-6-(4-methylphenyl)-3,4-dihydropyrimidin-2(1*H*)-ones (6k): Yellow powder. mp 228–229 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17 (s, 3H), 2.32 (s, 3H), 3.82 (s, 3H), 5.58 (s, 1H, NH), 5.90 (d, J = 1.8 Hz, 1H), 6.62 (s, 1H, NH), 6.88 (d, J = 6.6 Hz, 2H), 7.25–7.31 (m, 2H), 7.32–7.38 (m, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.6, 21.5, 56.1, 60.9, 119.1, 127.1, 128.0, 128.1, 128.6, 129.4, 131.6, 136.7, 140.1, 141.7, 152.6, 227.1; MS (ESI): m/z = 384 $(M)^+$. Anal. Calcd for $C_{20}H_{20}N_2O_2S_2$: C, 62.47; H, 5.24; N, 7.29. Found: C, 62.45; H, 5.27; N, 7.26.

5-Methylmercaptothiocarbonyl-4-(4-chlorophenyl)-6-(4-methylphenyl)-3,4-dihydropyrimidin-2(1*H*)-ones (6l): Yellow powder. mp 197–198 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17 (s, 3H), 2.30 (s, 3H), 5.43 (s, 1H, NH), 5.90 (d, J = 1.8 Hz,1H), 6.59 (s, 1H, NH), 7.26–7.35 (m, 4H), 7.36–4.41 (m, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.5, 21.4, 60.9, 119.1, 127.1, 128.0, 128.1, 128.6, 129.4, 131.6, 136.7, 140.1, 141.7, 152.6, 227.2; MS (ESI): m/z = 388 $(M)^+$. Anal. Calcd for $C_{19}H_{17}N_2OS_2Cl$: C, 58.67; H, 4.41; N, 7.20. Found: C, 58.65; H, 4.43; N, 7.24.

5-Methylmercaptothiocarbonyl-4-phenyl-6-methyl-3,4-dihydropyrimidin-2(1*H*)-ones (6m): Yellow powder. mp 150–151 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 2.40 (s, 3H), 5.67 (s, 1H, NH), 5.77 (d, J = 2.1 Hz, 1H), 6.32 (s, 1H, NH), 7.29–7.32 (m, 3H), 7.37–7.40 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.4, 24.4, 60.9, 119.6, 126.2, 127.6, 128.5, 143.2, 145.2, 153.1, 226.5; MS (ESI): m/z = 278 $(M)^+$. Anal. Calcd for $C_{13}H_{14}N_2OS_2$: C, 56.09; H, 5.07; N, 10.06. Found: C, 56.07; H, 5.09; N, 10.09.

5-Methylmercaptothiocarbonyl-4-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-ones (6n): Yellow powder. mp 153–155 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.32 (s, 3H), 2.41 (s, 3H), 3.76 (s, 3H), 5.68 (s, 1H, NH), 5.79 (d, J = 2.1 Hz, 1H), 6.33 (s, 1H, NH), 7.29–7.31 (m, 2H), 7.38–7.40 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.4, 24.4, 55.1, 60.9, 119.6, 126.2, 127.6, 128.5, 143.2, 145.2, 153.1, 226.5; MS (ESI): m/z = 308 $(M)^+$. Anal. Calcd for $C_{14}H_{16}N_2O_2S_2$: C, 54.42; H, 5.99; N, 7.68. Found: C, 54.43; H, 5.97; N, 7.70.

Methylmercaptothiocarbonyl-4-(4-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-ones (6o): Yellow powder. mp 147–149 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31 (s, 3H), 2.43 (s, 3H), 5.69 (s, 1H, NH), 5.78 (d, J = 2.1 Hz, 1H), 6.32 (s, 1H, NH), 7.29–7.31 (m, 2H), 7.37–7.40 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 20.7, 24.5, 60.7, 119.5, 126.1, 127.7, 128.5, 143.1, 145.2, 153.3, 226.7; MS (ESI): m/z = 342 $(M)^+$. Anal. Calcd for $C_{13}H_{13}ClN_2OS_2$: C, 49.91; H, 4.19; N, 8.95. Found: C, 49.90; H, 4.17; N, 8.97.

Results and Discussion

We initiated our investigation by heating equimolar amounts of aldehyde **1a**, β-oxodithiocarbonate **2a**, and urea **3** in the presence of 100 mg of silica–$ZnCl_2$, using various solvent such as EtOH, MeOH, acetonitrile, and THF. The desired dihydropytrimidines product **4a** was obtained with 40–56% yields as shown in Table 1. Then we attempted the reaction without any solvent by heating at 90 °C, but no satisfactory yield was obtained after 1 h as we have done with other solvents. The heating was kept longer (7 h) and slight improvement in the yield (60%) was observed under solvent-free condition. In order to get the optimum condition, we increased the catalytic amount from 100 to 150 mg under solvent-free condition, we get satisfactory yield of 76% after 1 h (Table 1, entry 6). Increasing the catalytic amount to 200 mg or the prolong heating could not bring any changes in the yield. Thus, we optimized the reaction condition at 90 °C for 1 h under solvent-free condition using 150 mg of silica–$ZnCl_2$.

After optimizing the reaction conditions, we evaluated the generality and scope of the condensation reaction by using different aromatic aldehydes **2b–c** and β-oxodithiocarbonates **3b–e**. Several substituents such as *p*-OMe, *p*-Me, *p*-Cl, *p*-Br, and *p*-F on the phenyl were tolerated. Thus, using the optimized reaction conditions, a library of compounds **3a–m** was synthesized in good yields (Table 2). The structures of the products were confirmed based on their analytical and spectral data (Table 2).

An advantage of the solid-supported catalyst is its recyclability. In view of development of eco-friendly methodologies, recovery and reuse of the catalyst are highly preferable. Silica-supported $ZnCl_2$ was easily separated from the reaction medium by adding EtOAc (5 mL), washed with dry and warm ethanol, and reused in the subsequent reactions. The recovered catalyst can be reused in subsequent reactions without significant loss in its efficiency (Table 3).

Conclusion

In summary, we have developed an efficient and mild method for synthesis of 5-methylmercaptothiocarbonyl-4-aryl-3dihydropyrimidin-2(1*H*)-ones by the reaction of β-oxodithiocarboxylates, aldehyde, and urea in the presence of silica-supported $ZnCl_2$ under solvent-free conditions. The use of an inexpensive reagent under mild reaction conditions,

Table 1. Optimization of the reaction conditions using silica–$ZnCl_2$.[a]

Entry	Amount of silica–$ZnCl_2$ (mg)	Solvents	Temperature (°C)	Time (h)	Yield (%)[b]
1	100	EtOH	Reflux	7	40
2	100	MeOH	Reflux	7	45
3	100	Acetonitrile	Reflux	7	47
4	100	THF	Reflux	7	56
5	100	—	90	7	60
6	150	—	90	1	76
7	200	—	90	1	70

[a] Reaction conditions: **3** (2 mmol), **4** (2 mmol), **5** (2 mmol), solvent (5 mL), and silica–$ZnCl_2$.
[b] Isolated yields.

Table 2. Silica–$ZnCl_2$ catalyzed preparation of dihydropyrimidines.[a]

Entry	R^1	R^2	Yield (%)[b]	Product
1	Ph	Ph	76	**6a**
2	Ph	4-$CH_3OC_6H_4$	75	**6b**
3	Ph	4-ClC_6H_4	71	**6c**
4	4-$CH_3OC_6H_5$	Ph	74	**6d**
5	4-$CH_3OC_6H_5$	4-$CH_3OC_6H_4$	73	**6e**
6	4-$CH_3OC_6H_5$	4-ClC_6H_4	80	**6f**
7	4-ClC_6H_4	Ph	75	**6g**
8	4-ClC_6H_4	4-$CH_3OC_6H_4$	82	**6h**
9	4-ClC_6H_4	4-ClC_6H_4	76	**6i**
10	4-$CH_3C_6H_4$	Ph	70	**6j**
11	4-$CH_3C_6H_4$	4-$CH_3OC_6H_4$	70	**6k**
12	4-$CH_3C_6H_4$	4-ClC_6H_4	73	**6l**
13	CH_3	Ph	72	**6m**

[a] Reaction conditions: **3** (2.0 mmol), **4** (2.0 mmol), **5** (2.0 mmol), silica–$ZnCl_2$ (150 mg), 90 °C, 1.0 h.
[b] Isolated yields.

Table 3. Reusability of silica–$ZnCl_2$ catalyst on the reaction.

Run	Cycle	Yield (%)
1	0	88
2	1	86
3	2	84
4	3	83

and with short reaction times and good yields makes this an attractive addition to existing procedures.

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