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Nano-$BBr_3.SiO_2$: a novel highly efficient heterogeneous catalyst for the one-pot synthesis of 3,4-dihydropyrimidin-2-(1H)-one derivatives

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This article describes a simple protocol for the efficient synthesis of 3,4-dihydropyrimidin-2(1H)-one derivatives using aromatic aldehydes, ethyl acetoacetate and urea in the presence of nano-$BBr_3.SiO_2$ as a catalyst. The structural features of the synthesized compounds were characterized by m.p., IR, MS, ^{1}H NMR, ^{13}C NMR, and CHN elemental analysis. We synthesized nano-$BBr_3.SiO_2$ for the first time as a nanocatalyst and characterized it by XRD, SEM and TEM techniques. High yields, mild conditions, easy availability, reusability, and green chemistry were some advantages of using this catalyst.

Keywords: Dihydropyrimidin-2(1H)-ones, Nano-$BBr_3.SiO_2$, One-pot, Mild conditions.

INTRODUCTION

It has been reported that 3,4-dihydropyrimidin-2(1H)-ones (DHPMs) possess many pharmacological qualities, such as antiviral, antibacterial, and antihypertensive activity, and are efficacious as calcium channel modulators and for multi drug resistance reversal [1-2]. The biological activity of some recently isolated alkaloids has also been attributed to the 3,4-dihydropyrimidin-2(1H)-ones moiety [3].

Biginelli (1893) reported that the first stage in the synthesis of DHPMs was the one-pot condensation of aldehyde, diketone and urea under acidic conditions. This method produces low yields, particularly in the case of some substituted aldehydes [4]. Various catalysts have been used to increase the efficiency of the Biginelli reaction. As is known, the Biginelli reaction has low product yields.

Recently, several improved methodologies have been developed such as microwave irradiation [5], ultrasound irradiation [6,7], use of ionic liquids [8], lanthanide triflate [9], silicasulfuric acid [10], HCOOH [11], copper (II) sulfamate [12], potassium tert-butoxide (t-BuOK) [13], ammonium dihydrogen phosphate [14], silica-gel [15], cyanuric chloride [16], TiO_2 [17], $KHSO_4$ [18,19], silica triflate [20], Li(glycine)(CF_3SO_3) [21], Brønsted acidic ionic liquid [Btto][*p*-TSA] [22], glutamic acid [23], use of solvent-free conditions [24], bismuth(III) sulfate trihydrate [25] and others. Some of these methods are expensive, environmentally unfriendly, produce low yields, and are incompatible with other functional groups, involving labor-intensive product isolation procedures. Therefore, a simple, efficient, and reusable procedure for one-pot dihydropyrimidinone synthesis under mild conditions is required.

In recent years, the use of eco-friendly, industrially applicable, and reusable green catalysts has been a matter of concern and interest. We define green chemistry as a set of principles that reduce or eliminate the use or generation of dangerous chemicals. This is part of our recent set of studies relating to the development of new methods in the synthesis of heterocyclic compounds [23-25].

Recently, nanoparticles have emerged as nanocatalysts alternative to conventional materials in various fields of chemistry. Nanoparticles are known to be promising heterogeneous catalysts in various organic reactions. Nanoparticles have a larger volume ratio for improved productivity, selectivity and performance of catalytic processes. The suitable choice of nanoparticles to the reaction produces less waste and less impurities, which leads to a more secure way and reduces environmental effect.

As an example, PbO nanoparticles have been studied as catalysts in organic reactions, including reactions such as paal-knorr [26], oxidative coupling of methane [27], synthesis of tetrahydrobenzopyrans and benzylidene malononitriles [28]. The catalyst's properties include: high yields, short reaction time, one-pot procedure, experimental simplicity. This prompted us to use nano-$BBr_3.SiO_2$ nanoparticles as a catalyst.

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Here, Biginelli's reaction between benzaldehyde, ethylacetoacetate and urea to produce 3,4-dihydropyrimidin-2-(1H)-one derivatives using nano-$BBr_3.SiO_2$ as a nanocatalyst, is reported. The solid catalyst was synthesized by the reaction of nano-SiO_2 with BBr_3 by a hydrothermal method and was characterized by XRD, SEM and TEM techniques (Scheme 1).

EXPERIMENTAL

General Remarks

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 using a Shimadzu IR-470 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were determined on a Bruker 300 DRX AVANCE instrument at 300 and 75 MHz, respectively. The elemental analyses (C, H, and N) were performed on a Carlo ERBA Model EA 1108 analyzer. Mass spectra were recorded on a Varian-Saturn 2000 gas chromatograph–mass spectrometer (MS). Scanning electron microscopy (SEM) of the nano-particles was performed on a VEGA/TESCAN scanning electron microscope. Transmission electron microscopy (TEM) was performed by Philips CM10-HT100KV. The X-ray diffraction (XRD) patterns of the materials were recorded by employing a Philips Xpert MPD diffractometer equipped with a Cu Kα anode (λ = 1.54 Å) in the 2θ range from 5 to 80°.

Preparation of nano-$BBr_3.SiO_2$

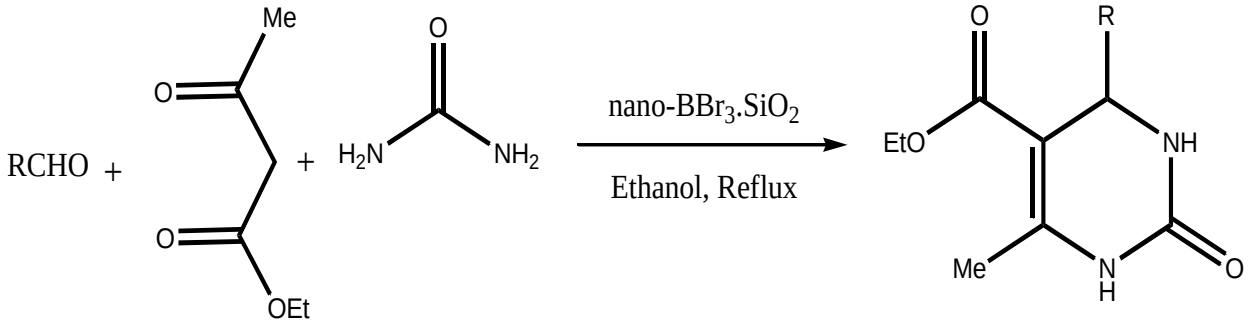
The catalyst was prepared by stirring a mixture of BBr_3 (1 ml) and nano silica gel (20 nm, 1 g) in 5 ml of chloroform for 1 h at room temperature. The slurry was filtered and washed with chloroform. The obtained solid (nano-$BBr_3.SiO_2$) was dried at ambient temperature for 2 h and then stored in a dry container.

Typical procedure for the synthesis of 3,4-dihydropyrimidinones(5a-j)

A mixture of aromaticaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1.2 mmol), nano-$BBr_3.SiO_2$ (0.05 g) and 10 ml of ethanol was refluxed for 1 h. The progress of reaction was monitored by TLC. After finishing, the reaction mixture was poured into crushed ice while stirring. The crude product was filtered, washed with cold water, dried, and recrystallized from ethanol 95% to give the pure products (5a-j) (91%–97%). All compounds were characterized by m.p., IR, CHN, MS, ^{1}H NMR, and ^{13}C NMR spectroscopy. The structures of all synthesized compounds (5a-j) are depicted in Table 2.

5–(Ethoxycarbonyl)–6–methyl–4–phenyl–3,4–dihydropyrimidin–2(1H)–one **(5a).** White solid; yield 95%; mp 203–205 °C; IR (KBr, *v*max, cm^{-1}): 3255, 3110, 3005, 1720, 1688, 1636; ^{1}H NMR (300.13 MHz, DMSO-d_6, δ/ppm): 1.10(t, *J*=7.10 Hz, 3H, CH_3); 2.26(s, 3H, CH_3); 3.88(q, *J*= 7.10 Hz, 2H, CH_2); 5.42(s, H, CH); 7.32-7.54(m, 5H, Ar-H); 7.72(s, H, NH); 9.24(s, H, NH); ^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm): 18.30, 19.00, 53.42, 58.63, 103.32, 111.27, 115.15, 124.54, 130.41, 148.24, 158.34, 166.71; MS(ESI): *m/z* 261 $(M+H)^+$; Anal. Calc. for $C_{14}H_{16}N_2O_3$: C, 64.62; H, 6.15; N, 10.72; found: C, 64.50; H, 6.14; N, 10.68.

5–(Ethoxycarbonyl)–4–(4-chlorophenyl)–6–methyl–3,4–dihydropyrimidin–2(1H)–one **(5b).** White solid; yield 95%; mp 213–215°C; IR (KBr, *v*max, cm^{-1}): 3253, 3125, 3000, 1708, 1648, 1611; ^{1}H NMR (300.13 MHz, DMSO- d_6, δ/ppm): 1.18(t, *J*=7.20 Hz, 3H, CH_3); 2.21(s, 3H, CH_3); 3.63(q, *J*=7.20 Hz, 2H, CH_2); 5.27(s, H, CH); 7.14-7.28(m, 4H, Ar–H); 7.77(S, H, NH); 9.23(s, H, NH); ^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm): 16.47, 19.34, 57.06, 60.77, 101.02, 120.12, 133.42, 144.23, 153.64, 156.80, 158.66, 165.48; MS(ESI): *m/z* 295 $(M+H)^+$; Anal. Calc. for $C_{14}H_{15}ClN_2O_3$: C, 57.12; H, 5.08; N, 9.55; found: C, 57.02; H, 5.03; N, 9.56.



Scheme 1. Nano-$BBr_3.SiO_2$-catalyzed Biginelli reaction.

5–(Ethoxycarbonyl)–4–(4-hydroxyphenyl)–6–methyl–3,4–dihydropyrimidin–2(1H)–one (**5c).** White solid; yield 91%; mp 231-233°C; IR (KBr, ν_{max}, cm^{-1}): 3442, 3345, 3107, 1710, 1680, 1629; ^1H NMR (300.13 MHz, DMSO-d_6, δ/ppm): 1.22 (t, 3H, *J*=7.50 Hz, CH_3), 2.45 (s, 3H, CH_3), 4.23 (q, 2H, *J*=7.50 Hz, CH_2), 6.10 (s, H, CH), 6.77 (s, 1H, OH), 7.15-7.80 (m, 4H, Ar–H), 7.89 (s, 1H, NH), 8.26 (d, 2H, *J*=8.2, Ar-H), 9.14 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm): 15.2, 19.15, 54.31, 59.75, 101.90, 122.5, 132.23, 140.5, 155.66, 155.88, 158.5, 167.75; MS(ESI): *m/z* 277 $(M+H)^+$; Anal. Calc. for $C_{14}H_{15}N_3O_5$: C, 55.06; H, 4.92; N, 13.74; found: C, 55.15; H, 4.90; N, 13.70.

5–(Ethoxycarbonyl)–4–(4–methoxyphenyl)–6–methyl–3,4–dihydropyrimidin–2(1H)–one **(5d).** White solid; yield 94%; mp 202–203°C; IR (KBr, ν_{max}, cm^{-1}): 3241, 3122, 3010, 1703, 1647, 1517; ^1H NMR (300.13 MHz, DMSO-d_6, δ/ppm): 1.07(t, *J*=7.08 Hz, 3H, CH_3); 2.23(s, 3H, CH_3); 3.89(s, 3H, CH_3); 3.97(q, *J*=7.08 Hz, 2H, CH_2); 5.09(s, H, CH); 7.14-7.64(m, 4H, Ar–H); 7.66(s, H, NH); 9.15(s, H, NH); ^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm): 14.11, 20.45, 57.73, 58.40, 60.90, 101.37, 114.03, 125.38, 136.76, 148.22, 158.25, 159.75, 164.27; MS(ESI): *m/z* 291 $(M+H)^+$; Anal. Calc. for $C_{15}H_{18}N_2O_4$: C, 62.06; H, 6.25; N, 9.65; found: C, 61.98; H, 6.20; N, 9.59.

5–(Ethoxycarbonyl)–4–(3-bromophenyl)–6–methyl–3,4–dihydropyrimidin–2(1H)–one **(5e).** White solid; yield 95%; mp 183–185°C; IR (KBr, ν_{max}, cm^{-1}): 3319, 3211, 3015, 1695, 1634, 1544; ^1H NMR (300.13 MHz, DMSO- d_6, δ/ppm): 1.08 (t, *J*=7.11 Hz, 3H, CH_3), 2.18 (s, 3H, CH_3), 3.77 (q, *J*=7.11 Hz, 2H, CH_2), 5.67 (s, H, CH), 7.14-7.25 (m, 4H, Ar-H), 7.66 (s, 1H, NH), 9.31 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm): 15.11, 18.94, 56.56, 61.35, 100.68, 122.44, 127.56, 128.50, 129.07, 135.22, 142.55, 154.34, 160.77, 165.55; MS(ESI): *m/z* 340 $(M+H)^+$; Anal. Calc. for $C_{14}H_{15}ClN_2O_3$: C, 57.14; H, 5.10; N, 9.50; found: C, 57.09; H, 5.05; N, 9.45.

5-Ethoxycarbonyl-4-(2-hydroxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one (**5f).** White solid; yield 91%; mp 209–211 °C; IR (KBr, ν_{max}, cm^{-1}): 3456, 3232, 2883, 1712, 1641, 1594 cm^{-1}: ^1H NMR (300.13 MHz, DMSO- d_6, δ/ppm): 1.15 (t, *J*=7.5 Hz , 3H, CH_3), 2.21 (s, 3H, CH_3), 3.82 (q, *J*=7.5, Hz, 2H, CH_2), 5.21 (s, H, CH), 6.10 (S, 1H, Ar-OH), 6.8-7.40 (m, 4H, Ar-H), 8.33 (s,1H, NH), 9.25 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm): 17.22, 19.38, 55.46, 62.42, 102.33, 121.32, 125.23, 126.92, 127.28, 130.63, 139.71, 148.55, 161.85, 163.36; MS(ESI): *m/z* 277 $(M+H)^+$; Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.80; N, 10.14; Found: C, 60.80; H, 5.72; N, 10.12.

5-Ethoxycarbonyl-4-(2-chlorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one **(5g).** White solid; yield 93%; mp 204–206 °C; IR (KBr, ν_{max}, cm^{-1}): 3433, 3211, 2890, 1715, 1625, 1587 cm^{-1}: ^1H NMR (300.13 MHz, DMSO- d_6, δ/ppm): 1.07 (t, *J*=7.18 Hz , 3H, CH_3), 2.24 (s, 3H, CH_3), 3.75 (q, *J*=7.2, Hz, 2H, CH_2), 6.02 (s, H, CH), 6.9-7.42 (m, 4H, Ar-H), 7.98 (s, 1H, NH), 8.88 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm): 16.56, 17.34, 56.43, 60.65, 103.38, 123.43, 126.66, 127.70, 128.67, 132.77, 143.36, 150.14, 160.65, 166.72; MS(ESI): *m/z* 295 $(M+H)^+$; Anal. Calcd for $C_{14}H_{15}ClN_2O_3$: C, 57.14; H, 5.10; N, 9.52; Found: C, 56.88; H, 5.00; N, 9.46.

5-Ethoxycarbonyl-4-(3-fluorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one **(5h).** White solid; yield 95%; mp 182–184°C; IR (KBr, ν_{max}, cm^{-1}): 3423, 3242, 2880, 1722, 1656, 1605 cm^{-1}: ^1H NMR (300.13 MHz, DMSO- d_6, δ/ppm): 1.14 (t, *J*=7.4 Hz , 3H, CH_3), 2.15 (s, 3H, CH_3), 3.71 (q, *J*=7.4, Hz, 2H, CH_2), 5.78 (s, H, CH), 6.93-7.72 (m, 4H, Ar-H), 7.92 (s, 1H, NH), 9.10 (s, 1H, NH)); ^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm): 16.33, 18.78, 57.15, 60.24, 102.56, 121.23, 125.54, 126.87, 127.13, 130.48, 140.79, 156.36, 163.62, 165.47; MS(ESI): *m/z* 279 $(M+H)^+$; Anal. Calcd for $C_{14}H_{15}FN_2O_3$: C, 60.43; H, 5.39; N, 10.07; Found: C, 60.30; H, 5.28; N, 10.10.

5-Ethoxycarbonyl-4-(4-fluorophenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one **(5i).** White solid; yield 92%; mp 185–188°C; IR (KBr, ν_{max}, cm^{-1}): 3420, 3217, 2874, 1708, 1635, 1580 cm^{-1}: ^1H NMR (300.13 MHz, DMSO- d_6, δ/ppm): 1.16 (t, *J*=7.12 Hz , 3H, CH_3), 2.34 (s, 3H, CH_3), 3.83 (q, *J*=7.12 Hz, 2H, CH_2), 6.05 (s, H, CH), 6.85-7.40 (m, 4H, Ar-H), 8.10 (s, 1H, NH), 9.03 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm): 18.62, 18.14, 54.46, 64.67, 102.85, 123.75, 128.23, 138.11, 143.91, 154.46, 159.35, 167.42; MS(ESI): *m/z* 279 $(M+H)^+$; Anal. Calcd for $C_{14}H_{15}FN_2O_3$: C, 60.43; H, 5.39; N, 10.07; Found: C, 60.33; H, 5.30; N, 10.04.

5-Ethoxycarbonyl-4-(4-tolyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one **(5j).** White solid; yield 97%; mp 250–252 °C; IR (KBr, ν_{max}, cm^{-1}): 3227, 3220, 2982, 1695, 1666, 1582, cm^{-1}; ^1H NMR (300.13 MHz, DMSO- d_6, δ/ppm): 1.11 (t, *J*=7.25 Hz , 3H, CH_3), 1.92 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 3.65 (q, *J*=7.25 Hz, 2H, CH_2), 6.14 (s, H, CH), 7.05-7.68 (m, 4H, Ar-H), 8.38 (s, 1H, NH), 9.20 (s, 1H, NH);); ^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm): 18.78, 19.37, 23.1, 59.04, 64.91, 105.15, 1

22.37, 125.48, 128.57, 138.44, 152.19, 160.48, 164.38; MS(ESI): *m/z* 275 $(M+H)^+$; Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.61; N, 10.21; Found C, 65.60; H, 6.55; N, 10.15.

RESULTS AND DISCUSSION

The development of new nanocatalysts has emerged as an available field for research and innovation. Nanotechnology enhances catalytic activity and the inexpensive nanocatalysts replace expensive catalysts. The advantage of nano-$BBr_3.SiO_2$ over bulk catalysts may be attributed to the higher surface area of nanocatalysts and the increased catalytic activity. This is assumed to be due to morphological differences, as shown in the SEM and TEM images and the XRD pattern. According to the SEM and TEM images and the XRD pattern, the particle size of nano-$BBr_3.SiO_2$ is 40 nm (Figure 1).

Nano-$BBr_3.SiO_2$ can be used as a catalyst in the synthesis of organic compounds. Features of this catalyst that are of interest include: easy separation, environmental friendliness, reusability, cleanness, and economy. The mechanism of formation of dihydropyrimidines using nano-$BBr_3.SiO_2$ as a catalyst is shown in Scheme. 2. Most of the catalysts used for preparation of dihydropyrimidinones are halogen-containing Lewis acids. The present results indicate that the halide present in the catalyst may be playing a crucial role in these transformations and may be the cause of the large number of publications which have appeared recently on the synthesis of dihydropyrimidinones by modified Biginelli reactions using halide catalysts. Nano-$BBr_3.SiO_2$ acts as a Lewis base by interaction with the electrophilic carbon of the aldehyde.

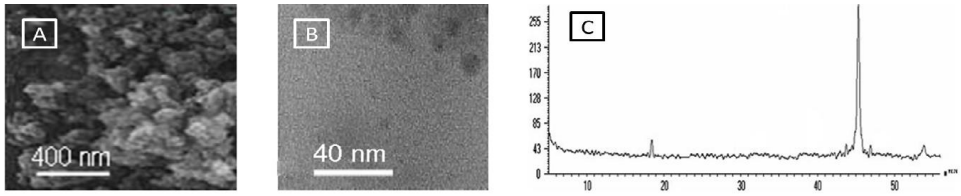
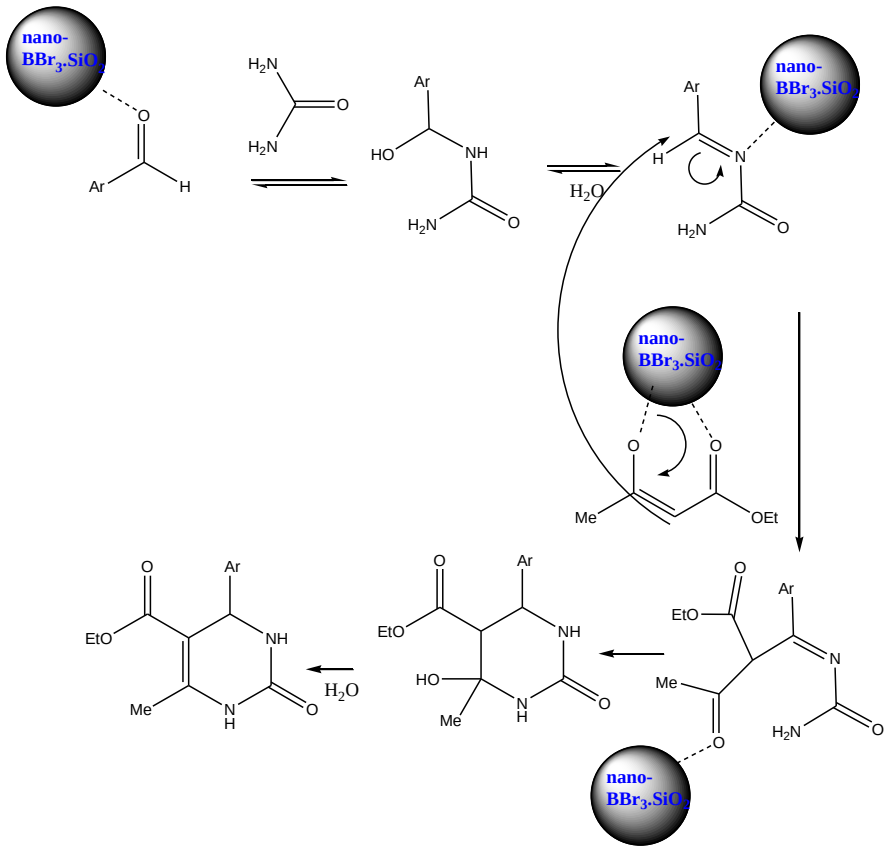


Fig 1. SEM (A) image, TEM (B) image and XRD (C) pattern of nano-$BBr_3.SiO_2$.



Scheme 2. Mechanism of the synthesis of 3,4-dihydropyrimidin-2-(1H)-one catalyzed by nano-$BBr_3.SiO_2$.

Dihydropyrimidines exhibit a wide range of biological activities. We are interested in studying the mechanism of the Biginelli reaction in order to develop a simple method for the synthesis of DHPMs. Urea is not sufficiently nucleophilic to react directly with aldehydes. However, nano-$BBr_3.SiO_2$ as a Lewis acid causes the reaction to occur by coordination at the carbonyl oxygen, activating the carbonyl group to nucleophilic attack.

We started our study of one-pot, three-component Biginelli condensation using nano-$BBr_3.SiO_2$ as a catalyst (Scheme 2) and carrying out reactions using benzaldehyde, ethyl acetoacetate, and urea to create corresponding DHPM products. As the model reaction the synthesis of compound 5a was selected to determine suitable reaction conditions in the presence of nano-$BBr_3.SiO_2$ with various amounts of catalyst (Table 1). We found that yield was strongly affected by the amount of catalyst and the temperature. Best results were obtained (Entry 8) in the presence of 0.05 g catalyst under reflux conditions for 1 h (Table 1).

We have successfully synthesized many 3,4-dihydropyrimidin-2(1H)-one derivatives from aldehydes, ethyl acetoacetate and urea using nano-$BBr_3.SiO_2$. Several aromatic aldehydes were condensed with ethyl acetoacetate and urea as shown in Scheme. 1. These results are shown in Table 2. Nano-$BBr_3.SiO_2$ as a catalyst significantly increases the reaction rate and is easily separated and reused (Table 2). All reactions were monitored by TLC and carried forward to maximum atom utilization. All compounds were characterized using melting point, IR, ^{1}H NMR, ^{13}C NMR, and CHN techniques. All of our results were in agreement with the cited literature. It was noted that aldehydes that had electron donating/withdrawing substituents reacted within the reaction time to give DHPMs with very good to excellent isolated yields.

The structures of products 5a–5j were characterized based on their ^{1}H and ^{13}C NMR, IR and CHN data. The ^{1}H NMR spectrum of compound **5a** in DMSO-d6 shows a singlet at 5.42 ppm, which is related to H-4, whereas the two separated methyl groups resonate at 1.10 (t, *J*=7.10 Hz, 3H, CH_3) and 2.26 (s, 3H, CH_3) ppm. In the ^{13}C NMR spectrum of compound **5a**, the peak at 58.63 ppm is related to C-4 (sp3), which confirms the formation of a product. The two different carbonyl groups resonate at 158.3 and 166.7 ppm. In the ^{1}H NMR spectra of **5a** and **5b**, H-4 resonates at 5.42 and 5.27 ppm, respectively.

Finally, the reusability of the nano-$BBr_3.SiO_2$ catalyst was investigated in subsequent reactions, using benzaldehyde, ethyl acetoacetate, and urea to afford the corresponding DHPM product **5a** as a model reaction. Comparison of reaction conditions and product yield (**5a**) between previously reported methods and the present method is shown in Table 3. The catalyst was easily recovered by simple filtration after dilution of the reaction mixture with ethyl acetate and was reused after being vacuum dried. Nano-$BBr_3.SiO_2$ was reused for four runs without significant loss of activity (run 1: 87%; run 2: 84%; run 3: 80%; run 4: 75%).

Table 1. Nano-$BBr_3.SiO_2$ catalyzed synthesis of 5–(ethoxycarbonyl)–6–methyl–4–phenyl–3,4–dihydropyrimidin–2(1H)–one (1) at various temperatures and various amounts of the catalyst [a]

Entry	Catalyst (mol%)	Temp. (°C)	Yield (%)[b]
1	0.03	70	66
2	0.03	80	76
3	0.03	90	78
4	0.04	70	80
5	0.04	80	84
6	0.04	90	85
7	0.05	70	87
8	0.05	80	95
9	0.05	90	94
10	0.06	70	78
11	0.06	80	84
12	0.06	90	85
13	-	70	30
14	-	80	32
15	-	90	35
16	0.05	-	18

[a] Reaction conditions: benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1.2 mmol) and nano-$BBr_3.SiO_2$ as a catalyst for 1 h under reflux conditions;

[b] Isolated yield.

Table 2. Nano-$BBr_3.SiO_2$ catalyzed synthesis of 3,4-dihydropyrimidinone derivatives[a]

Entry	Product	RCHO	Yield (%)[b]	MP (^OC)	
				Found	Reported (Ref.)
1	5a	C_6H_5CHO	95	203–205	201–203[11]
2	5b	4-ClC_6H_4CHO	95	213–215	212-214[11]
3	5c	4-HOC_6H_4CHO	91	231-233	231-233[12]
4	5d	4-$CH_3OC6H4CHO$	94	202–203	203-204[11]
5	5e	3-BrC_6H_4CHO	95	183–185	182–184[12]
6	5f	2-HOC_6H_4CHO	91	209–211	210–212[30]
7	5g	2-ClC_6H_4CHO	93	204–206	206–208[29]
8	5h	3-FC_6H_4CHO	95	182–184	180-182[30]
9	5i	4-FC_6H_4CHO	92	185–188	186–188[30]
10	5j	4-$CH_3C_6H_4CHO$	97	250-252	49–251[31]

[a]Reaction conditions: aldehyde (1 mmol), *β*-ketoester (1 mmol), urea (1.2 mmol), nano-$BBr_3.SiO_2$ (0.05 g) under reflux conditions;

[b]Isolated yield.

Table 3. Comparison of reaction conditions and yield of product (1) of reported methods [32-35] *versus* the present method.

Entry	Catalyst	Condition	Time	Yield (%)
1	Methanesulfonic acid	Ethanol, reflux	60 min	95
2	P_2O_5	Ethanol, reflux	240 min	91
3	Chlorosulfonic acid	Solvent free, 60°C	30 min	93
4	P_2O_5/SiO_2	Solvent free, 85°C	120 min	95
5	$ZnCl_2$	Solvent free, 80°C	20 min	90
6	I_2	Solvent free, 90°C	15 min	86
7	CF_3COONH_4	Solvent free, 80°C	10 min	98
8	1:10 $P_2O_5/MeSO_3H$	Solvent free, r.t.	5 min	94
Present method	Nano-$BBr_3.SiO_2$	Ethanol, reflux	60 min	95

CONCLUSION

In conclusion, we have demonstrated a novel catalyst nano-$BBr_3.SiO_2$ for the synthesis of substituted dihydropyrimidinones. The advantages of this method using nano-$BBr_3.SiO_2$ include: high yields, reasonable time, one-pot procedure, experimental simplicity, environmental friendliness and easy separation with reuse of this catalyst.

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НАНО-$BBr_3.SiO_2$: НОВ ВИСОКОЕФЕКТИВЕН КАТАЛИЗАТОР ЗА ЕДНОСТАДИЙНА ХЕТЕРОГЕННА СИНТЕЗА НА ПРОИЗВОДНИ НА 3,4-ДИХИДРОПИРИМИДИН-2-(1H)-ОН

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(Резюме)

В тази статия се описва прост протокол за ефективна синтеза производни на 3,4-дихидропиримидин-2(1H)-он, използвайки ароматни алдехиди, етил ацет-ацетат и карбамид в присътствие на нано-$BBr_3.SiO_2$ като катализатор**.** Структурата на синтезираните съединения е охарактеризирана чрез точката на топене, ИЧ, МС, ^{1}H ЯМР, ^{13}C ЯМР and CHN-елементен анализ. Ние синтезирахме за първи път нано-$BBr_3.SiO_2$ като нано-катализатор и охарактеризирахме чрез XRD, SEM и TEM-техниките. Високи добиви, меки условия, лесна достъпност, повторна употреба и „зелени“ условия са някои от предимствата на използвания катализатор.