Synthesis of bioactive heterocycles using reusable heterogeneous catalyst 
HClO$_4$–SiO$_2$ under solvent-free conditions

Leimajam Vartima Chanua$^a$, Thokchom Prasanta Singh$^a$, Laishram Ronibala Devi$^b$ and Okram Mukherjee Singh$^a$

$^a$Chemistry Department, Manipur University, Canchipu, Manipur, India; $^b$Chemistry Department, National Institute of Technology, Lamphel, Manipur, India

ABSTRACT

We are reporting a simple, efficient and green protocol for the synthesis of chromenes and dihydropyrimidines (products of Knoevenagel and Biginelli reaction, respectively) by the use of silica-supported perchloric acid (HClO$_4$–SiO$_2$) as an effective heterogeneous catalyst. Short reaction times, high product yields, simple procedure and reusability of the catalyst are the superior characteristics of this protocol.

ARTICLE HISTORY

Received 27 February 2018
Accepted 2 August 2018

KEYWORDS

Knoevenagel condensation; Biginelli reaction; chromenes; dihydropyrimidine; green catalyst

Introduction

Solid-supported catalysts have been increasingly attracting synthetic chemists as unique acid catalysts in terms of green chemical methodologies over the last two decades (1,2). Low cost, environment friendly, easy to handle, easy catalyst separation and regeneration, thermal stability, and long catalytic life are some of the other important features of the solid-supported catalysts (3). Solid-supported reagents are expected to be performed better than the individual reagent because of the increased effective surface area of the reagent, their activity and selectivity (4). Among the solid-supported catalytic systems, perchloric acid adsorbed on silica gel (HClO$_4$–SiO$_2$) is found in various organic functional group transformations and also in the synthesis of many bioactive heterocycles (5–15). Among the heterocycles, coumarins or chromenes are an important class of benzopyrones being the core unit of different natural products (16). Coumarins comprise a vast array of biologically active compounds with several types of pharmaceutical agents possessing anticancer, anti-HIV, anticoagulant, spasmylytic and antibacterial activity, cytotoxic activity in vitro and in vivo (17,18). Similarly, dihydropyrimidines are well-known bioactive heterocyclic compounds exhibiting a wide range of biological activities such as anticancer, anti-inflammatory, antibacterial, antifungal, anthelmintic activities, as calcium channel blockers, mitotic kinesin Eg5 motor protein inhibitors, as well as potent HIV gp-120-CD$_4$ inhibitors (19,20). Because of their varied biological activities, the preparations of coumarins and dihydropyrimidines have attracted the attention of organic chemists. Knoevenagel condensation reactions have been employed as convenient methods of synthesis of coumarin derivatives (21–23). Since, Pietro Biginelli pioneered the synthesis of dihydropyrimidines by one-pot condensation of an aldehyde, β-ketoester, and urea under strongly acidic conditions (24) much improved protocols have been developed (25,26). However, the main drawback of almost all methodologies is that the recovery or reusability of the catalyst is destroyed in the workup procedure. Therefore, still there is a need for the
development of versatile, simple, and environmentally friendly processes for the synthesis of these compounds. These reports prompted us to study the catalytic role of HClO₄–SiO₂ in our present investigations, particularly in the synthesis of coumarins and dihydropyrimidines.

Our group has long-standing interest on the synthesis of bioactive heterocycles (27-29) using β-oxodithioesters as synthon (30). We are reporting herein the application of silica-supported perchloric acid HClO₄–SiO₂ as an effective catalyst in solvent-free synthesis of chromenes by Knoevenagel condensation and dihydropyrimidinone by Biginelli type reaction using β-oxodithioesters as common starting material (Scheme 1).

Results and discussion
(a) Chromenes 3a–e
Initially, we carried out the Knoevenagel cyclocondensation reaction of salicylaldehyde 1 (1 mmol) and methyl 3-oxo-3-phenylpropanedithioate 2a (1 mmol) using SiO₂–HClO₄ (5 mol %) in refluxing in acetonitrile. After refluxing for two hours and as monitored by TLC, we could isolate 3-benzoyl-2H-chromene-2-thione (3a) having melting point of 170–171°C with 54% yield. The structure was confirmed by IR spectroscopy, NMR and mass spectrometer and elemental analysis data. In order to optimize the reaction conditions, various solvents and different catalytic systems were tested. The yield of the product 3a was found to be moderate using solvents such as THF, methanol and ethanol (Table 1, entries 1–4) when the same catalyst was used. However, when we carried out the same reaction, under solvent-free condition at 80°C with continuous stirring for 2 h, surprisingly, the yield was found to be increased appreciably (entry 5). Thus, solvent-free condition was the best condition for the reaction using silica-supported perchloric acid as catalyst. By increasing the catalyst loading from 5 to 10 (mol %), the yield of the reaction remains constant (entries 5–7). It would be unnecessary to increase the catalytic loading. Thus, we optimized the catalytic loading at 5 (mol %). Next, we

![Scheme 1. Synthesis of chromenes and dihydropyrimidinones.](image)

| Entry | Catalyst | Solvent | Catalyst loading (%) | Time (h) | Yield (%) |
|-------|----------|---------|----------------------|---------|-----------|
| 1°    | HClO₄–SiO₂ | Acetonitrile | 5 | 2 | 54 |
| 2°    | HClO₄–SiO₂ | THF | 5 | 2 | 58 |
| 3°    | HClO₄–SiO₂ | Methanol | 5 | 2 | 61 |
| 4°    | HClO₄–SiO₂ | Ethanol | 5 | 2 | 57 |
| 5     | HClO₄–SiO₂ | – | 5 | 2 | 80 |
| 6     | HClO₄–SiO₂ | – | 6 | 2 | 80 |
| 7     | HClO₄–SiO₂ | – | 8 | 2 | 80 |
| 8     | AlCl₃ | – | 5 | 4 | 62 |
| 9     | ZnCl₂ | – | 5 | 4 | 70 |
| 10    | CuCl₂ | – | 5 | 4 | 68 |
| 11    | MgCl₂ | – | 5 | 4 | 50 |
| 12    | – | – | 4 | – | – |

*°Reaction conditions: Salicylaldehyde (1 mmol), methyl 3-oxo-3-phenylpropanedithioate (1 mmol) and HClO₄–SiO₂ (5 mol%), 80°C.
*aIsolated yields.
*bRefluxed.
evaluated the feasibility of the same reaction using various metal halides like AlCl₃, ZnCl₂, CuCl₂, MgCl₂ and a comparative result of the yield analyses was evaluated with HClO₄–SiO₂. Even though the reaction goes smoothly with the other metal halides, the yield of the reaction could not be improved (entries 8–11), instead the reaction required longer duration. The reaction was also tested in absence of catalyst but it failed to give the desired product. Thus, we optimized the reaction condition under solvent-free condition at 80°C in presence of 5 mol % of the HClO₄–SiO₂.

**Reaction scope of substrates**

Next, we evaluated the generality and scope of the condensation reaction by using optimized conditions to salicylaldehyde 1 with different β-oxodithioesters 2b–e. Several substituents such as, Cl, Me and OMe on the phenyl ring of β-oxodithioesters were used. However, there was no appreciable effect on the yield of the reaction with the position and the nature of the substituents. All the β-Oxodithioesters give good yields of the chromene-2-thiones 3a–e (Table 2). New paragraph: use this style when you need to begin a new paragraph.

**(b) Dihydropyrimidines 4a–k**

To extend the scope of this catalytic system, we turn our attention to the synthesis of dihydropyrimidines from β-oxodithioesters using Biginelli type multi-component reaction. A mixture of methyl 3-oxo-3-phenylpropanedithioate 1a (1 mmol), benzaldehyde 2b (1 mmol), urea (1 mmol), and HClO₄–SiO₂ (5 mol%) was heated at 80°C with continuous stirring for 2 h. Water (30 mL) was then added followed by chloroform (50 mL) and after filtration the organic portion was extracted with chloroform. The organic layer was dried with anhydrous Na₂SO₄ and evaporated. The crude product was subjected to column chromatography on SiO₂, using increasing amounts of ethyl acetate in petroleum ether as eluent and the compound 4a was obtained. Structure elucidation of this product was confirmed by various spectroscopic and analytical data.

**Scope of substrates of dihydropyrimidines under the same reaction condition**

In order to check the generality of the present methodology of dihydropyrimidine synthesis using HClO₄–SiO₂ as an effective catalytic system, a series of substituted benzaldehydes and β-oxodithioesters have been utilized in this multicomponent reaction. We have used aldehydes with electron donating substituents as the yields are higher in comparison with the electron withdrawing substituents and thus many dithioester functional group attached dihydropyrimidines, 4b–k were synthesized (shown in Table 3). It is clearly observed that all the β-oxodithioesters give good results under this catalytic condition. Thus, in all the reactions HClO₄–SiO₂ was found to be successful giving the desired products in moderate to good yield.

**Probable reaction mechanism of chromenes and dihydropyrimidine synthesis**

On the basis of the results obtained by the control experiments, tentative mechanisms of the chromenes and dihydropyrimidine synthesis have been shown below (Scheme 2). Initially, the condensation product of β-oxodithioesters 3a–e was obtained. Structure elucidation of this product was confirmed by various spectroscopic and analytical data.

**Table 3. HClO₄–SiO₂ catalyzed synthesis of dihydropyrimidines from β-oxodithioesters**

| Entry | R₁ | R₂ | Products | Yields (%) | m.p. (°C) |
|-------|----|----|----------|------------|----------|
| 1     | C₆H₅ | H  | 4a       | 75         | 198–200  |
| 2     | C₆H₅ | CH₃O| 4b       | 71         | 182–183  |
| 3     | C₆H₅ | Cl  | 4c       | 70         | 230–231  |
| 4     | p-Ch₂C₆H₅| H  | 4d       | 73         | 203–205  |
| 5     | p-Ch₂C₆H₅| Cl | 4e       | 70         | 196–197  |
| 6     | p-Ch₂C₆H₅| H  | 4f       | 71         | 188–189  |
| 7     | p-Ch₂C₆H₅| CH₂O| 4j      | 73         | 204–205  |
| 8     | p-Ch₂C₆H₅| CH₃O| 4k      | 73         | 226–227  |

*Reaction conditions: Salicylaldehyde (1 mmol), β-Oxodithioesters (1 mmol) and HClO₄–SiO₂ (5 mol%), 80°C, 2 h.

*Isolated yields.

**Table 2. HClO₄–SiO₂ catalyzed Knoevenagel condensation for Chromenes synthesis from β-oxodithioesters**

| Entry | R₁ | Products | Yield (%) | m.p. (°C) |
|-------|----|----------|-----------|----------|
| 1     | C₆H₅ | 3a       | 80        | 170–171  |
| 2     | 4-CH₂OC₆H₅| 3b | 72        | 187–189  |
| 3     | 4-CIC₆H₅| 3c       | 70        | 185–186  |
| 4     | 4-CH₂C₆H₅| 3d       | 80        | 170–171  |
| 5     | CH₃   | 3e       | 72        | 105–106  |

*Reaction conditions: Salicylaldehyde (1 mmol), β-Oxodithioesters (1 mmol) and HClO₄–SiO₂ (5 mol%), 80°C, 2 h.

*Isolated yields.
oxodithioester 1a and o-hydroxybenzaldehyde 2a, activated by HClO₄–SiO₂, generates an enolate A, which facilitates in subsequent intramolecular aldol condensation to give phenyl(2-thioxo-2H-chromen-3-yl)methanone 3a. The mechanism of Biginelli reaction has been discussed in various experimental and theoretical reports, and has been a topic of much debate. A plausible mechanism for the synthesis of 5-methylmercaptothiocarbonyl-4-aryl-3,4-dihydropyrimidin-2(1H)-ones 4a is presented in (Scheme 2). For dihydropyrimidines, the first step in this reaction, the acid-catalyzed formation of an acyl imine intermediate A formed by reaction of the aldehyde with urea, is the key rate-limiting step. Interception of the iminium ion by β-oxodithioester 1a produces an open-chain ureide B that subsequently cyclizes to the dihydropyrimidinone 4a.

**Reusability of HClO₄–SiO₂ catalyst in the reaction**

In order to accomplish this work, we scrutinized the reusability of the HClO₄–SiO₂. In fact, a heterogeneous catalyst is considered interesting in organic synthesis only when it can be easily recovered and reused. In our process, when the catalytic reaction was completed, HClO₄–SiO₂ could be recovered conveniently from the reaction mixture by simple filtration, washing with CH₂Cl₂, and drying in a vacuum oven at 60°C for 5 h prior to reuse in subsequent reactions.
of the catalyst for a particular reaction i.e. synthesis of 3a from 1a and 2a was evaluated as a representative example. The recovered catalyst could be reused at least three additional times in subsequent reactions without significant loss in product yield as shown in the following graph (Table 4). Similar observation was found in the case of dihydropyrimidine synthesis.

**Experimental**

All reagents and solvents were purchased from commercial sources such as Merck and Aldrich and were used as received. $^1$H NMR (400 MHz) and $^{13}$C NMR (75 MHz) spectra were recorded on FT-NMR spectrometer using CDCl$_3$ and d$_6$-DMSO. Chemical shifts $\delta$ are measured in parts per million (ppm) 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 ($K\text{Br}$). Melting points were determined on a ‘Veego’ capillary melting point apparatus and are uncorrected. Silica gel 60-120 was used for column separations. Chemical yields refer to the pure isolated substances. X-ray diffractograms (XRD) of the catalyst were recorded in the 2$\theta$ range in a Bruker D8 series XRD. The Scanning Electron Microscope/Energy-Dispersive X-ray spectroscopy (SEM-EDX) characterization of the catalyst was performed on an FEI Quanta FEG 200-High Resolution Scanning Electron Microscope. TGA data were obtained with STA-6000 Perkin–Elmer.

**Materials**

**Characterization of the catalyst: silica-supported perchloric acid**

The silica-supported perchloric acid was prepared by adding 70% aqueous perchloric acid (1.3 g, 9.4 mmol) to stirred suspension of SiO$_2$ (230–400 mesh, 11.6 g) in diethyl ether (40 mL). Then, the mixture was kept for overnight and the residue was heated at 100°C for 72 h. The mixture was concentrated and the residue was dried under vacuum at 100°C for 72 h to afford HClO$_4$–SiO$_2$ as a free-flowing powder. The freshly prepared Silica-supported perchloric acid (HClO$_4$–SiO$_2$) was characterized by using EDX, TGA, SEM images and Powder XRD as shown in Figure 1. From the EDX spectrum it indicates that elements Si, O and Cl are present in the catalyst. The Thermogravimetric analysis of HClO$_4$–SiO$_2$ indicated the loss of the water molecules trapped in the silica framework near 200°C and did not show any other significant weight loss up to 700°C which showed the stability of the catalyst. SEM images of HClO$_4$–SiO$_2$ at different magnification (10 and 50 ml), clearly show that the surface of the catalyst is wavy in nature. The powder XRD pattern of the catalyst confirmed the amorphous nature of the catalyst. The comparison between freshly prepared catalyst and recovered catalyst after four cycles clearly showed that the efficiency of the catalyst did not decrease much even after consecutively used for four different reactions. A broad peak at 2$\theta$ ~23°C corresponds to silica. Paragraph: use this for the first paragraph in a section, or to continue after an extract.

**Preparation of chromenes, 3a–e**

In a 25 mL round bottom flask, a mixture of $\beta$-oxodithioester (1 mmol), salicyldehyde (1 mmol) and HClO$_4$–SiO$_2$ (5 mol %) was heated at 80°C with constant stirring for 2 h. As indicated by TLC, then water was added, and the product was extracted with ethyl acetate. The organic layer was dried (Na$_2$SO$_4$) and evaporated, the residue was recrystallized from ethanol to give good yields of 3. In cases where further purification was required, the crude products were subjected to column chromatography on SiO$_2$ using increasing amounts of ethyl acetate in hexane as eluent.

**3-Benzoyl-2H-chromene-2-thione (3a).** Yellow solid, m.p.170–171°C.$^1$H NMR (300 MHz, CDCl$_3$, $\delta$ ppm): 7.37–7.42(m, 1H), 7.45–7.56(m, 3H),7.59–7.66(m, 3H), 7.68–7.71(m, 1H),7.94–7.96(m, 2H); $^{13}$C NMR (75.5 MHz, CDCl$_3$, $\delta$ ppm): 116.7, 119.9, 125.9, 128.6, 128.7, 129.6, 133.2, 133.6, 133.9, 135.6, 136.3, 157.3, 192.6; IR (KBr) (v max, cm$^{-1}$): 1246, 1604, 1662, 3032, 3052 cm$^{-1}$; MS: m/z = 266 (M$^+$). Anal. Calcd For C$_{16}$H$_{10}$O$_2$S: C, 72.16; H, 3.78; S, 12.04. Found: C, 72.10; H, 3.72; S, 11.84.

**3-(4-Methoxybenzoyl)-2H-chromene-2-thione (3b).** Yellow crystals, m.p.187–189°C. $^1$H NMR (300 MHz, CDCl$_3$, $\delta$ ppm): 3.85(d, J = 8.7 Hz, 2H),7.36–7.43(m, 1H), 7.53–7.71(m, 4H), 7.89(d, J = 8.7 Hz, 2H); $^{13}$C NMR (75.5 MHz, CDCl$_3$, $\delta$ ppm): 55.5, 114.0, 116.7,
120.0, 125.9, 128.4, 128.6, 132.2, 133.0, 133.2, 139.5, 157.0, 164.3, 190.8, 193.8; IR (KBr) (ν max, cm⁻¹): 1242, 1597, 1654, 3018, 3055 cm⁻¹; MS: m/z = 296 (M⁺). Anal. Calcd for C₁₇H₁₂O₃S: C, 68.90; H, 4.08; S, 10.82. Found: C, 68.88; H, 3.98; S, 10.79.

3-(4-Chlorobenzoyl)-2H-chromene-2-thione (3c).
Light yellow solid, m.p. 185–186°C. ¹H NMR (300 MHz, CDCl₃, δ ppm): 7.37–7.39 (m, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.51–7.54 (m, 1H), 7.60–7.72 (m, 3H), 7.85 (d, J = 8.7 Hz, 2H); ¹³C NMR (75.5 MHz, CDCl₃, δ ppm): 116.7, 119.8.

Figure 1. Characterization of silica-supported perchloric acid using EDX, TGA, SEM and powder XRD.
126.0, 128.7, 129.1, 130.9, 133.4, 134.1, 138.7, 140.3, 157.1, 191.1, 193.4; IR (KBr) (ν max, cm⁻¹): 1326, 1629, 1700, 3084, 3198 cm⁻¹; MS: m/z = 370 (M⁺). Anal. Calcd for C₁₉H₁₈N₂O₂S: C, 57.67; H, 4.03; N, 7.43; S, 17.34. Found: C, 57.60; H, 4.14; N, 7.43; S, 18.06.

5-Methylmercaptothiocarbonyl-4-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-ones (4e). Yellow crystals, m.p. 187–188°C. ¹H NMR (300 MHz, CDCl₃, δ ppm): 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); ¹³C NMR (75.5 MHz, CDCl₃, δ ppm): 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 cm⁻¹; MS: m/z = 388 (M⁺). Anal. Calcd for C₁₉H₁₈N₂O₂S: C, 58.67; H, 4.41; N, 7.20; S, 16.49. Found: C, 58.65; H, 4.43; N, 7.24; S, 16.47.

5-Methylmercaptothiocarbonyl-4-phenyl-6-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-ones (4f). Yellow crystals, m.p. 187–188°C. ¹H NMR (300 MHz, CDCl₃, δ ppm): 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), 7.37 (d, J = 8.4 Hz, 2H), 7.38–7.46 (m, 5H), 8.07 (s, 1H, NH); ¹³C NMR (75.5 MHz, CDCl₃, δ ppm): 20.4, 55.0, 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 cm⁻¹; MS: m/z = 388 (M⁺). Anal. Calcd for C₁₉H₁₈N₂O₂S: C, 58.67; H, 4.41; N, 7.20; S, 16.49. Found: C, 58.65; H, 4.43; N, 7.24; S, 16.47.
5-Methylmercaptocarbonyl-4-(4-methoxyphenyl)-6-(4-methylphenyl)-3,4-dihydropyrimidin-2(1H)-ones (4g). Yellow powder. m.p. 204–205°C. ¹H NMR (300 MHz, CDCl₃, δ ppm): 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); ¹³C NMR (75.5 MHz, CDCl₃, δ ppm): 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; IR (KBr) (v max, cm⁻¹): 1272, 1634, 1673, 3087, 3210 cm⁻¹; MS: m/z = 400 (M⁺). Anal. Calcd for C₁₉H₁₈N₂O₂S₂Cl: C, 56.36; H, 4.23; N, 6.95; S, 15.84. Found: C, 56.39; H, 4.21; N, 6.95; S, 15.81.

5-Methylmercaptocarbonyl-4-(4-chlorophenyl)-6-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-ones (4h). Yellow crystals, m.p. 224–225°C. ¹H NMR (300 MHz, CDCl₃, δ ppm): 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); ¹³C NMR (75.5 MHz, CDCl₃, δ ppm): 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) (v max, cm⁻¹): 1267, 1621, 1699, 3089, 3215 cm⁻¹; MS: m/z = 374 (M⁺). Anal. Calcd for C₁₈H₁₇N₂O₂S₂Cl: C, 57.67; H, 4.03; N, 7.47; S, 17.11. Found: C, 57.65; H, 4.05; N, 7.49; S, 17.09.

5-Methylmercaptocarbonyl-4-(4-chlorophenyl)-6-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-ones (4i). Brown powder. m.p.194–195°C. ¹H NMR (300 MHz, CDCl₃, δ ppm): 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); ¹³C NMR (75.5 MHz, CDCl₃, δ ppm): 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) (v max, cm⁻¹): 1253, 1610, 1695, 3086, 3211 cm⁻¹; MS: m/z = 404 (M⁺). Anal. Calcd for C₁₇H₁₇N₂O₂S₂Cl: C, 56.36; H, 4.23; N, 6.92; S, 15.84. Found: C, 56.39; H, 4.21; N, 6.95; S, 15.81.

Conclusions

We have described convenient synthetic methods of chromenes and dihydropyrimidines using silica-supported perchloric acid (HClO₄·SiO₂) as heterogeneous and recyclable catalyst under solvent-free conditions. The remarkable catalytic activity that HClO₄·SiO₂ exhibited is convincingly superior to other recently reported catalytic methods with respect to high conversions, operational simplicity, enhanced reaction rates, cleaner reaction profiles, and ease of isolation of products. Inexpensive and ready availability of the catalyst makes the procedure an attractive alternative to the existing methods for the synthesis of these bioactive heterocycles.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

L. V. Chanu is thankful to Department of Science and Technology (DST), New Delhi, for giving financial assistance in the form of Inspire Fellowship. OMS is grateful to CSIR and DST, for financial assistance (CSIR project No. 02 (0251)/ 15/ EMR-II) and [DST project No.EMR/2014/00033] respectively.

Notes on contributors

Leimajam Vartima Chanu is studying as a Ph.D candidate in Chemistry Department, Manipur University. Her research has focused on the uses of silica-supported perchloric acid in organic synthesis.

Dr Thokchom Prasanta Singh was born in 1983. He obtained his Ph.D. degree in 2015. He is working as post doctoral
fellow under Prof. O.M. Singh and his research has focused on the synthesis of heterocyclic compounds.

Dr Laishram Ronibala Devi is working in National Institute of Technology (Manipur) as teaching Assistant. She did her Ph.D. under Prof. O.M. Singh.

Prof. Okram Mukherjee Singh is working in Chemistry Department, Manipur University, Manipur, India. His research interest is mainly on the synthesis of heterocyclic chemistry.

References

[1] Munnik, P.; de Jongh, P.E.; de Jong, K.P. Chem. Rev. 2015, 115, 6687–6718.

[2] Smith, K.; Horwood, E. Solid Supports and Catalysts in Organic Synthesis; PTR Prentice Hall: New York, 1992.

[3] Jung, N.; Grassle, S.; Lutjohann, D.S.; Brase, S. Org. Lett. 2014, 16, 1036–1039.

[4] Devi, L.R.; Singh, O.M. In Application of Silica-based Heterogeneous Catalysis for the Synthesis of Bioactive Heterocycles; Ameta, K.L., Penoni, A., Eds.; CRC Press: Florida, 2014; Chapter 6.

[5] Chakraborti, A.K.; Gulhane, R. Chem. Commun. 2003, 1896–1897.

[6] Kantevery, S.; Vuppalapati, S.V.N.; Biradar, D.O.; Nagarapu, L. J. Mol. Cat. A Chem. 2007, 266, 109–113.

[7] Shaterian, H.R.; Yarahmadi, H.; Ghashang, M. Tetrahedron 2008, 1263–1269.

[8] Medina, F.G.; Marrero, J.G.; Macías-Alonso, M.; González, M.C.; Córdova-Guerrero, I.; García, A.G.T.; Oseguerra-Robles, S. Nat. Prod. Rep. 2015, 32, 1472–1507.

[9] Vekariya, R.H.; Patel, H.D. Syn. Commun. 2014, 44, 2756–2788.

[10] Singh, T.P.; Singh, O.M. In Bioactive Heterocycles: Synthesis and Biological Evaluation; Ameta, K.L., Pawar, R.P., Domb, A.J., Eds.; Nova Science Publishers: New York, 2012; Chapter 6.

[11] Matos, L.H.S.; Masson, F.T.; Simeoni, L.A.; Homem-de-Mello, M. Eur. J. Med. Chem. 2018, 143, 1779–1789.

[12] Singh, T.P.; Ghosh, S.; Singh, O.M. In Targets in Heterocyclic Systems; Attanasi, O.A., Domenico Spinelli, D., Eds.; Società Chimica Italiana: Roma, 2012; Chapter 11.