Catalytic performance of CuO@SiO₂ for one-pot synthesis of pyrimidine derivative, ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate

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Abstract. We have prepared a three-component reaction of ethyl acetoacetate, urea and benzaldehyde for synthesis of a pyrimidine derivative, ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate using CuO@SiO₂ nanocatalyst. The catalyst was prepared by using glycerol as green solvent, and then it was characterized by FT-IR, EDAX spectroscopy and TEM analysis. The copper oxide nanoparticles are dispersed as fine and amorphous phase and made nanoclusters with average size of 14 nm. In pyrimidine derivative synthesis, the catalyst shows good activity for one-pot three-component reaction in mild reaction condition with the highest yield of 85%.

1. Introduction
Pyrimidines and their derivatives play a key role in some biological processes, as they are part of nucleic acid DNA and RNA [1,2]. They continue to attract great attention because many pyrimidine derivatives are reported to exhibit numerous bioactivities such as antimicrobial [3], anti-inflammatory [4], anticancer [5], antiviral [6] and antimycobacterial [7]. Thus, facile and applicable methods for the synthesis of pyrimidine derivatives are of considerable research interest.

Supported copper and nickel catalysts are frequently used in a variety of organic transformation and fine chemical production, such as methane reforming, hydrogenolysis, hydrogenation, dehydrogenation and methanol steam reforming [8–14]. Particularly, CuO@SiO₂ has been prepared by several methods such as sol-gel, hydrothermal and precipitation [15–17]. It has been applied in high performance electrochemical sensing and multifunctional coating in building stone [18,19]. However, CuO@SiO₂ has not been reported for pyrimidine synthesis yet. Therefore, in the present work, we will explore catalytic ability of CuO@SiO₂ for the one-pot three-component reaction in pyrimidine derivative synthesis.

2. Materials and methods

2.1. Materials
All chemicals were purchased from Merck in high purity, without further purification. Element composition of the catalyst was determined by EDAX spectroscopy. Size and shape of the CuO@SiO₂ was observed using Tecnai D2350 S-Twin Transmission Electron Microscope (TEM) with the accelerated voltage of 200 kV. FT-IR spectrum of the catalyst was recorded on Shimadzu 8400 spectrophotometer with KBr background. The UV-Vis spectrum of pyrimidine derivative was recorded on Shimadzu UV mini type 1240 spectrophotometer, whereas mass spectrum was obtained from Shimadzu GC-MS QP Mass Spectrometer 2010A.
2.2. Preparation of CuO@SiO$_2$ nanocatalyst
In a 50 mL Beaker glass, Cu(NO$_3$)$_2$.3H$_2$O (1 mol/L), TEOS (10 mL) and glycerol (5 mL) were mixed and pH of solution was adjusted to 1.5 by adding 0.125 mol/L nitric acid. The mixture was stirred at room temperature for 3h. Then, ammonia solution was added dropwise until pH reached 9. Resulting gel was filtered and washed with ethanol:water (1:1), then it was aged for 3 days. Gel was calcined at 500 °C for 5h. the formed catalyst was characterized by FT-IR, EDAX and TEM.

2.3. Synthesis of a pyrimidine derivative
In a 50 mL round-bottom flask equipped with condenser, mixture of benzaldehyde (2 mmol), ethyl acetoacetate (2 mmol), urea (3 mmol) and 5 mL ethanol as solvent was stirred in the presence of certain amount of catalyst in various reaction condition (table 1), for example, 7.5% mol catalyst at 70 °C. After specified time, the obtained solid was filtered and then washed with deionized water. The crude product was recrystallized using hot ethanol. The product was identified by FT-IR, UV-Vis and GC-MS instruments.

3. Results and discussion
3.1. Catalyst characterization
Functional groups identification of CuO@SiO$_2$ was done using FTIR spectroscopy at 400–4000 cm$^{-1}$ wavenumber range (figure 1). Stretching vibrations of the Cu-O group at 470 cm$^{-1}$ and Si-O-Si groups at 1098 cm$^{-1}$ indicated that CuO@SiO$_2$ were successfully prepared.
Table 1. Different conditions in the synthesis of pyrimidine derivative

| Entry | Catalyst (% wt.) | Time (h) | Temperature (°C) | Yield (%) |
|-------|------------------|----------|------------------|-----------|
| 1     | Free             | 4        | 70               | 31        |
| 2     | 2.5              | 4        | 70               | 52        |
| 3     | 5                | 2        | 50               | 67        |
| 4     | 5                | 3        | 50               | 75        |
| 5     | 5                | 4        | 50               | 80        |
| 6     | 5                | 5        | 50               | 78        |
| 7     | 5                | 6        | 50               | 78        |
| 8     | 5                | 4        | RT               | 36        |
| 9     | 5                | 5        | 70               | 80        |
| 10    | 5                | 4        | 90               | 83        |
| 11    | 7.5              | 4        | 70               | 85        |
| 12    | 10               | 4        | 70               | 82        |

Figure 3. (a) TEM and (b) HRTEM images of CuO@SiO₂.

Composition of CuO@SiO₂ was analysed by using EDAX (figure 2). The material contains several atoms such as Cu (38.05%), Si (33.24%), O (27.16%), and C (1.54%). Metal impurities are not observed in the spectrum indicating the successful of catalyst preparation. Meanwhile, trace of carbon may come from background upon EDAX analysis. Morphology and size of CuO@SiO₂ were characterized by TEM (figure 3). From analysis, CuO@SiO₂ is in spherical shape with size of approximately 14 nm based on HRTEM result.

3.2. Synthesis of pyrimidine derivative

In catalyst-free system, only 31% yield of pyrimidine derivative was isolated. The optimum result of obtained pyrimidine derivative was in 4 hours at 70 °C and 7.5% weight of catalyst. The best yield of pyrimidine derivative was 85% (table 1, Entry 11). Increasing amount of catalyst to 10% will not increase the pyrimidine yield in significant amount. Also, prolonging reaction time up to 6 hours cannot increase the yield of product significantly.

FTIR data in figure 4 shows the presence of secondary N-H vibration at 3325 cm⁻¹, whereas at 2950 cm⁻¹ indicating the presence of a C-H sp³ group. Sharp peak at 1653 cm⁻¹ is corresponds to vibration of C=O ester group. The maximum wavelength of this pyrimidine derivative was 284 nm (figure 5). Mass spectra data showed the molecular weight of pyrimidine derivatives with value of 260 g/mol, suitable with the molecular formula of C₁₄H₁₆N₂O₃ (figure 6).
Figure 4. FTIR spectra of pyrimidine derivatives compound

Figure 5. Uv-Vis spectra of pyrimidine derivatives compound

Figure 6. Mass spectral of pyrimidine derivatives compound

Reaction scheme for the synthesis of 3,4-dihydropyrimidine-2-ones was showed in scheme-1 following below:

\[
\begin{array}{ccc}
\text{CHO} & + & \text{H}_3\text{C} = \text{O} = \text{O} \text{C}_2\text{H}_5 \quad + \quad \text{H}_2\text{N} - \text{O} - \text{NH}_2 \\
& & \quad \xrightarrow{\text{CuO@SiO}_2} \\
& & \text{O} - \text{C} = \text{N} - \text{H} - \text{O} \\
\end{array}
\]

Scheme-1: Reaction scheme for the synthesis of 3,4-dihydropyrimidine-2-ones from benzaldehyde, ethyl acetoacetate and urea using CuO@SiO\(_2\) nanocatalyst.

4. Conclusions
The CuO@SiO\(_2\) nanocatalyst was successfully prepared using glycerol as stabilizer and capping agent with silica from TEOS and characterized by FTIR, EDX, and TEM. Pyrimidine derivative was obtained from the reaction of benzaldehyde, ethyl acetoacetate, and urea using CuO@SiO\(_2\) heterogeneous catalysts. According to mass spectra data, molecular weight of the product was 260 g/mol.

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