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Synthesis of Mesoporous Cerium Oxide (CeO₂) Nanoparticles and Effect of Cerium Precursors on Transamidation of Acetamide with *N*-Octylamine Under Solvent-Free Conditions

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Mesoporous cerium oxide (CeO₂) nanoparticles act as an effective heterogeneous catalyst for the transamidation reaction of amides with amines. The mesoporous CeO₂ nanoparticles were prepared by hydrothermal method using different cerium precursor such as: cerium(III) chloride hep-tahydrate [CeCl₃ · 7H₂O], cerium nitrate hexahydrate [Ce(NO₃)₃] · 6H₂O], ceric ammonium nitrate [(NH₄)₂Ce(NO₃)₆], and cerium(III) acetate [Ce(C₂H₃O₂)₃ · 1.5H₂O]. It shows highest catalytic activity for transamidation of acetamide with *N*-octylamine under solvent free conditions. This is the first example of a heterogeneous catalyst for transamidation using aliphatic amines as substrates. The X-ray diffraction, BET surface area analysis, and FT-IR characterizations of CeO₂ suggested its excellent catalytic activity for transamidation reaction.

Keywords: Nanostructures, Transamidation Reaction, Hydrothermal Synthesis, Mesoporous CeO₂, One-Pot Synthesis.

1. INTRODUCTION

The amide bond is a fundamental part of biological and synthetic polymers (i.e., proteins and nylons) and also the most important linkages in industrial and medicinal chemistry nowadays. Synthesis of *N*-alkyl amides have been a great interest of study because they are synthetic intermediates of numerous natural products, pesticides, pharmaceuticals, and polymers.¹ The most common way to make an amide bond by using a stoichiometric amount of a coupling reagent with growing focus on green chemistry is still an expensive and wasteful procedure.² In the view of green chemistry, there has been high interest in developing catalytic methods of amide bond formation, which avoid using these coupling reagents.³

Clearly, there is a lack of an efficient catalytic procedure for selective synthesis of the secondary amide from simple primary amides (acetamide) and amines (*N*-octylamine), as a transamidation reaction. However, most of them suffer from low activity, low selectivity or limited scope. Herein, we report such a procedure utilizing catalytic quantities of lab made mesoporous ceria to activate the primary amide and promote a transamidation reaction. During the course of our on-going effort into developing catalytic synthesis of amide bonds,⁴ we envisioned that a catalytic method of primary amide activation would not only be an exceptionally atom efficient and clean reaction but it also need to be highly synthetically useful due to the primary amide group inertness in presence of many other catalysts and common organic reagents.

Transamidation generally requires harsh conditions (>250 °C), long reaction times and stoichiometric reagents to cleave the chemically robust amide bond. CeO_2 has acid–base and redox properties and has been used as an effective catalyst for various organic reactions^{5,6}

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Scheme 1. Reaction mechanism of transamidation reaction over mesoporous CeO₂ nanoparticles.

such as; dehydration of alcohols,⁷⁻¹⁰ alkylation of aromatic compounds,^{11, 12} dimerization of alcohols, aldehydes, esters¹³ and carboxylic acids^{14, 15} to ketones, cyclazation of diols,¹⁶ and reduction of benzoic acid.¹⁷

In this study we report lab made mesoporous CeO_2 acts as a recyclable heterogeneous catalyst for onepot *N*-alkyl amides (*N*-octyl acetamide) formation from amides (acetamide) and amines (*N*-octylamine) at 160 °C, which provides a new and green catalytic system for *N*-alkyl amides synthesis with high yields (75% to 94%) under solvent-free conditions. Catalytic studies show that our method is particularly effective for the transamidation reaction. The possible reaction mechanism is proposed in Scheme 1, which supports the transamidation of primary amide with amine as rate-limiting step. This reaction mechanism provides a reason why the present catalytic system gives high selectivity.

As prepared high surface area mesoporous ceria can be used in various important applications such as; catalysis, sensors, and fuel cells. Hence, cerium oxide (CeO₂) is an important rare earth oxide and has the potential of becoming a very useful material.^{18–20} The rare earth oxide materials are of interest as designing catalysts since they are less expensive in comparison to precious metal catalysts like platinum and palladium.

In view of organic synthesis and green chemistry, it is important to study CeO_2 -catalyzed organic reactions further at lower temperatures (<200 °C). In this work we reported that mesoporous CeO_2 , synthesized by different precursors of cerium, as a effectively catalyzes transamidation of acetamide with *N*-octylamine to yield corresponding *N*-octyl acetamide in high yields at 160 °C under solvent-free conditions.

2. EXPERIMENTAL DETAILS

2.1. Materials

All the chemicals were used of analytical grade without any further purification. All the cerium precursor viz cerium(III) chloride heptahydrate [CeCl₃ · 7H₂O], cerium nitrate hexahydrate [Ce(NO₃)₃ · 6H₂O], ceric ammonium nitrate [(NH₄)₂Ce(NO₃)₆], cerium(III) acetate $[Ce(C_2H_3O_2)_3 \cdot 1.5H_2O]$, tetraethylorthosilicate (TEOS), cetyl trimethyl ammonium bromide (CTAB), ethanol, were purchased from Sigma-Aldrich and ammonia solution was purchased from Fisher scientific were used in synthesis catalyst. The solutions were made in deionized water.

2.1.1. Synthesis of Mesoporous CeO₂

In a typical synthesis procedure,²¹ 2.0 mmol CeCl₃ · 7H₂O was slowly added to the solution containing 4.1 mmol of *L*-glycine and 10 mL of H₂O under stirring. After that, 10 mL of 0.15 M Na₂(CO₂)₂ solution was added into the above solution to obtain white precipitate of cerium oxalate. Finally, the solution along with precipitate was transferred into an autoclave, which was tightly sealed and hydrothermally treated at 160 °C for 24 h in an oven. The as-synthesized sample was collected through filtration, washed successively 3 times with water and ethanol and then dried at 60 °C for 12 h. The sample was finally calcined at 360 °C in air for 1 h, to yield yellowish ceria powder and named as C1.

In this case as the hydrated acetate $(Ce(C_2H_3O_2)_3 \cdot 1.5H_2O)$ used as cerium precursor.²² 6 g hexadecylamine as a surfactant was added to 35 ml of a 50% aqueous ethanol solution. Inorganic precursor: surfactant molar ratio of 2 was achieved by adding the required quantity of cerium precursor. The mixture was stirred for 1 h at room temperature and placed in an oven at 60 °C for 2 days (ambient atmospheric conditions). The precipitate formed was washed with ethanol–water mixture and harvested by filtration. The solid product was again washed with deionized water and dried in air at 120 °C for 6 h. Subsequently described as the as-synthesized material and then calcined at temperatures from 360 °C in air for 4 h and named as C2.

The high-surface area mesoporous CeO₂ was prepared by using Ce(NO₃)₃ · 6H₂O as cerium precursor¹⁹ with surfactant cetyltrimethyl ammonium bromide (CTAB) as templating agent. A solution of NaOH (2 g) in 300 mL distilled water was added to a stirred solution of Ce(NO₃)₃ · 6H₂O (4.3 g) and CTAB (2.2 g) in 200 mL distilled water. The pH of the resulting mixture is approximately 12. The mixture was then allowed to react at 90 °C, and the precipitate obtained was filtered after aging at 60 °C for 12 h and washed with hot water. The resultant yellow powder was dried at 110 °C for 10 h and then calcined at 360 °C in air for 4 h and named as C3.

Mesoporous ceria with high specific surface area has been prepared using ceric ammonium nitrate as cerium precursor²³ and non-surfactants organic compounds glucose, acryl amide via hydrothermal method. In a typical experiment, glucose (0.005 mol), acryl amide (0.0075 mol) and ceric ammonium nitrate (2.5 mmol) were dissolved into deionized water (40 mL) one by one with magnetic stirring. Then ammonia solution (25 wt%) was added dropwise to the solution until the pH value was about 10. After

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stirring for 5 h, the mixture was transferred into a teflonlined autoclave and kept at 150 °C for 48 h, then the autoclave was allowed to cool to room temperature. After that the solution was filtered and the precipitate was washed with deionized water and alcohol three times. Finally, the obtained sample was dried at 80 °C overnight and calcined at 360 °C for 4 h in air and named as C4.

2.2. Catalyst Characterizations

X-ray diffraction (XRD) patterns of the catalysts were recorded on a Rigaku Miniflex (M/s. Rigaku Corporation, Japan) using Ni filtered Cu-K α radiation ($\lambda =$ 0.15406 nm). The crystallite size of gold was calculated by using Debye-Scherrer equation and the phase identification was done with the help of the JCPDS files. Fourier transform infrared (FT-IR) spectra of the catalysts were taken on the IR (Model: GC-FT-IR Nicolet 670) spectrometer by KBr disc method under ambient condition. Scanning electron microscopy (SEM) analysis was observed in Hitachi S-520 SEM unit. The BET surface area were obtained from N2 adsorption-desorption isotherm (Autosorb I/Quantachrome instruments, USA at -196 °C), where the samples were first out gassed at 300 °C to ensure a clean surface prior to the construction of adsorption isotherms. The Barrett-Joyner-Halenda (BJH) method was used to calculate the pore-size distribution from the desorption branch of the isotherm (Autosorb I/Quantachrome, USA).

2.3. Catalytic Experiments

A typical procedure for transamidation of acetamide with *N*-octylamine is as follows: mesoporous CeO_2 (25 mg, 5.8 mol% Ce with respect to acetamide) was added to the mixture of acetamide (2.5 mmol) and N-octylamine (5.0 mmol) in a reaction vessel equipped with a condenser under N2 atmosphere. The resulting mixture was vigorously stirred at 160 °C. The reaction mixture was analyzed by GC. Conversion and yield of the products were determined based on acetamide and N-octyl acetamide using pentadecane as an internal standard. Once the reaction was completed, the CeO₂ catalyst was separated by centrifugation. In the catalyst recycling experiments, the separated catalyst was washed with acetone three times and calcined in air at 300 °C for 1 h. For measurement of the isolated yields, the reaction of amine (2.6 mmol) and primary amide (2.5 mmol) was carried out. After full conversion of the primary amide was confirmed by GC, the catalyst was separated by filtration. The crude product was purified by evaporating the filtrate at 70 °C to remove the unreacted amine. The resulting products were identified by GC, GC-MS.

The GC (Shimadzu GC-2014) and GC-MS (HP-5973 quadruple) analysis were carried out with a DB-wax 123-7033 (Agilent) capillary column (0.32 mm i.d., 30 m long) using nitrogen as the carrier gas. All chemicals used

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for the organic reactions were of analytical grades and purchased commercially and were used without further purification.

3. RESULTS AND DISCUSSION

3.1. Characterization of Catalysts

3.1.1. X-ray Diffraction (XRD)

It can be seen from Figure 1, the XRD patterns of the calcined mesoporous CeO₂ samples as-prepared by hydrothermal methods using different cerium precursor. The presence of several narrow and intensive diffraction peaks indicates that the precursor is well crystallized. All diffraction peaks can be indexed to a face-centered cubic phase ceria (JCPDS 34-0394) and no signals of impurities are detected. XRD shows main peaks at 2θ values of 28.4° , 32.9°, 47.3°, and 56.2° corresponding to planes of (111), (200), (220) and (311) with interplanar spacing of 3.12, 2.72, 1.91 and 1.63 Å, respectively. The intensities and positions of the diffraction peaks are in good agreement with the literature data. Extremely broad reflections for the as-prepared sample indicating that the crystallite sizes are very small. On the basis of the width of the (111) diffraction peak, the mean crystallite size of the mesoporous ceria samples were calculated by the Scherrer equation to be about 4-10 nm and shown in Table I.

3.1.2. Fourier Transform Infrared (FT-IR)

The FT-IR spectra of the as-synthesized calcined sample are displayed in Figure 2. The one near 3410 cm⁻¹ is due to the physically adsorbed water (-OH features at 3400 cm⁻¹) and carbonate (adsorbed bidentate carbonate signals at 1500 and 1280 cm⁻¹) features are observed. There appears a broad adsorption peak at around 400 cm⁻¹, which can be attributed to the Ce–O stretching band, according to the literature.²⁴



Figure 1. XRD patterns of mesoporous CeO₂ samples as-prepared by hydrothermal method using different cerium precursor.

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 Table I. BET surface area and pore size distribution data of mesoporous ceria samples prepared by hydrothermal method using different cerium precursor.

CeO ₂ samples	BET surface area (m ² /g)	Total pore volume (cc/g)	Pore diameter (nm)	Crystallite size (nm) ^a
C1	235	0.35	4.4	4.60
C2	205	0.41	4.1	9.37
C3	195	0.46	3.3	9.36
C4	162	0.48	3.2	10.21

Note: ^aCrystallite size determined from XRD.

3.1.3. Scanning Electron Microscopy (SEM)

The morphologies and architectures of mesoporous CeO₂ samples as-prepared by hydrothermal methods using different cerium precursor were investigated by SEM (Fig. 3).

3.1.4. BET Surface Area and Pore Size Distribution Measurements

To characterize the porosity of the mesoporous CeO₂ samples (Table I), N₂ adsorption analysis was carried out. Figure 4(a) displays the N₂ adsorption–desorption isotherms and the corresponding pore size distribution curve (Fig. 4(b)) calculated from the adsorption branch by the BJH method. The obtained ceria sample exhibits the isotherm of type IV, and the adsorption branch shows an uptake of adsorbed volume at low relative pressure (P/P_0) of 0.1–0.4, which indicates the existence of mesopores. The BJH pore size distribution curve displays a wide pore diameter distribution from 3 to 5 nm. The pore volume and the specific surface area of the obtained ceria for sample C1 are 0.35 cm³/g, and 235 m²/g, respectively.

3.2. Catalytic Properties for Transamidation Reaction

Transamidation hardly proceeded without a catalyst. Using different cerium precursor of metal oxides, conversion and yield for transamidation reaction were reported in Table II.



Figure 2. FT-IR spectra for mesoporous CeO_2 samples as-prepared by hydrothermal method using different cerium precursor.



Figure 3. SEM images of mesoporous CeO₂ samples as-prepared by hydrothermal method using different cerium precursor.

The results show that mesoporous CeO_2 (C1) has the highest conversion and yield of *N*-octyl acetamide, indicating that mesoporous CeO_2 is the most effective catalyst for transamidation compared to other CeO_2 .



Figure 4. (a) N_2 adsorption–desorption isotherms and (b) BJH pore size distribution for mesoporous CeO₂ (C1) sample.

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by GC.

O acetamide	+ NH ₂ N-octylamine			Mesoporous CeO ₂ -NH ₃ N-octylacetamide		
Catalyst (Mesoporous CeO ₂)	Time (h)	Conversion (%)	Selectivity (%)	Yield (%)	Synthesis methods	
C1	1	98	96	94	160 °C, Hydrothermal, [CeCl ₃ · 7H ₂ O]	
C2	1	95	92	87	60 °C, Hydrothermal, $[Ce(C_2H_3O_2)_3 \cdot 1.5H_2O]$	
C3	1	85	96	82	90 °C, Hydrothermal, $[Ce(NO_3)_3 \cdot 6H_2O]$	
C4	1	83	90	75	160 °C, Hydrothermal, [(NH ₄) ₂ Ce(NO ₃) ₆]	

Table II. Transamidation of acetamide with N-octylamine to N-octyl acetamide catalyzed by mesoporous CeO₂ with different cerium precursor.

Notes: Reaction conditions: acetamide (2.5 mmol), N-octylamine (5.0 mmol), mesoporous CeO₂ (25 mg), T = 160 °C in N₂. Yield of N-octyl acetamide was determined



Figure 5. Plots of conversion/selectivity/yield versus mesoporous CeO_2 catalysts for transamidation of acetamide. *Reaction conditions*: acetamide (2.5 mmol), *N*-octylamine (5.0 mmol), mesoporous CeO_2 (25 mg), $T = 160 \text{ °C in N}_2$.

3.2.1. Comparison of Different Cerium Precursors Over Transamidation Reaction

First, one-pot synthesis of N-octyl acetamide from acetamide with N-octylamine at 160 °C under solvent free condition was chosen as a test reaction to compare the catalytic activity of different cerium precursors of mesoporous CeO₂ (Table II). The reaction by mesoporous CeO₂ (C1) for 1 h resulted in 98% conversion and the yields of *N*-octyl acetamide was 94% with 96% selectivity compared to other CeO₂ catalysts. Among all the catalysts, mesoporous CeO₂ (C1) showed the highest catalytic reactivity for the direct amidation of acetamide with *N*-octylamine to *N*-octyl acetamide, hence; found to be the best catalyst for this reaction in terms of activity and selectivity.

As shown in Figure 5, it is suggested that CeO_2 catalyzed reaction proceeds via route 1 (Scheme 1) and the secondary amide formation from primary amide, where amine (transamidation) is the rate-limiting step. Note that this reaction mechanism is different from that of the homogenous catalysts reported by Murahashi et al.²⁵ and Williams et al.,^{3,26} in which they have proposed that onepot alkylamidation of nitrile. In contrast, the reaction by CeO_2 proceeds by route 1 (Scheme 1) avails high selectivity to *N*-octyl acetamide.

3.2.2. Reaction Mechanism

The effect of reaction time on the mesoporous CeO_2 catalyzed one-pot secondary amidation of acetamide with *N*-octylamine was investigated as shown in Figure 6. At the initial stage, acetamide was immediately



Figure 6. Plots of conversion and yield versus reaction time for transamidation of acetamide. *Reaction conditions*: acetamide (2.5 mmol), *N*-octylamine (5.0 mmol), mesoporous CeO₂ (25 mg), T = 160 °C in N₂.

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consumed to produce the corresponding *N*-octyl acetamide (94% yield at t = 1 h). Then, the yield of *N*-octyl acetamide decreased with time. After 5 h, the yield of *N*-octyl acetamide reached >88%, and any by-products were detected by GC. These results indicate the one-pot secondary amide formation proceeds by following consecutive steps (in Scheme 1); the secondary amide formation from primary amide and amine. Note there are no other products formed for transamidation reaction catalysed by mesoporous CeO₂.

4. CONCLUSIONS

We have demonstrated that mesoporous CeO_2 acts as an effective heterogeneous catalyst for the transamidation reaction of amides with amines. This novel catalysis provides a clean, convenient and practical route for the direct *N*-octyl acetamide synthesis in view of the following advantages:

(1) The reaction proceeds smoothly and effectively under solvent free conditions,

(2) The catalyst is readily available, cheap, stable, reusable and a non-polluting solid that offers easy handling and ready work-up, and

(3) The present method is applicable in the synthesis of *N*-octyl acetamide, in high yields.

From spectroscopic and kinetic studies, it can be concluded that the cooperation of weak Lewis acid sites and adjacent strong base sites play important roles in the transamidation reaction. This bifunctional catalysis of CeO_2 may be applied to develop new catalytic systems for green organic synthesis.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this.

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