Facile Room-Temperature Synthesis of Cerium Carbonate and Cerium Oxide Nano- and Microparticles Using 1,1′-Carbonyldiimidazole and Imidazole in a Nonaqueous Solvent

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ABSTRACT: Ceria nanoparticles (CeONPs) are versatile materials due to their unique catalytic properties, and cerium carbonate particles (CeCbPs) have been widely used as precursors for cerium oxide due to their ease of production. Urea is a widely used precipitant and a source of carbonate ions for the synthesis of CeONPs and CeCbPs, and the reaction temperature is important for controlling the rate of urea decomposition. However, the precise control of the temperature is often difficult, especially in large-scale reactions. Herein, we propose a homogeneous precipitation method that uses 1,1′-carbonyldiimidazole (CDI) and imidazole in acetone without heating. The decomposition rate of CDI can be controlled by the amount of water in the reaction mixture. In the synthesis of CeCbPs, unique particle morphologies of plate-, flying-saucer-, and macaron-like shapes and a wide range of sizes from 180 nm to 13 μm can be achieved by adjusting the amount of CDI, imidazole, and water in the reaction. These CeCbPs are transformed into ceria particles by calcination while maintaining their characteristic morphology. Moreover, the direct synthesis of 130 nm spherical CeONPs was possible by decreasing the amount of CDI in the reaction and the mixing time. These nanoparticles exhibited higher production efficiency and superior reactive oxygen species (ROS) scavenging properties compared to the other CeONPs obtained from calcination. These results demonstrate a novel method using CDI and imidazole in the synthesis of CeONPs and CeCbPs without the aid of a heating process, which may be useful in the large-scale synthesis and application of CeO nanomaterials.

1. INTRODUCTION

Ceria oxide (ceria, CeO₂), one of the most versatile rare-earth materials, has received significant attention, owing to its unique physicochemical and catalytic properties in a variety of applications, including industrial catalysis,¹ polishing agents,² photocatalysis,³ oxygen storage materials,⁴ and electrolytes for solid oxide fuel cells.⁵ In particular, its catalytic properties can be greatly improved by reducing the size to a nanoscale, which can generate more oxygen vacancies on the surface of nanoparticles, owing to the coexistence of Ce³⁺ and Ce⁴⁺ oxidation states.⁶⁻⁸ Due to their highly efficient catalytic properties that mimic those of catalase (CAT) and superoxide dismutase (SOD),⁹,¹⁰ cerium oxide nanoparticles (CeONPs) have recently expanded their application to the biomedical area, including the theragnostics of systemic inflammatory diseases,¹¹⁻¹³ hepatic diseases,¹⁴,¹⁵ brain diseases,¹⁶⁻¹⁸ and eye diseases.¹⁹,²⁰

Cerium carbonates (CeCb), including cerium hydroxycarbonate (Ce(OH)CO₃), cerium oxycarbonate hydrate (Ce₂O(CO₃)₂·H₂O), and cerium carbonate octahydrate (Ce₂(CO₃)₃·8H₂O), have been widely investigated as precursors of cerium oxide, owing to their facile synthesis and ease of scalable production.²¹⁻²³ In addition, distinctive morphologies of nano- and microparticles composed of cerium oxides, such as shuttle-, butterfly-, flower-, and globin-like particles,²⁴⁻²⁶ can be achieved through their synthesis using CeCb as a precursor, making them powerful synthetic alternatives that enhance desirable and controllable physicochemical and catalytic properties.²²,²⁷

Urea is a widely used chemical component as a precipitating agent and a source of carbonate ions in various synthetic methods for cerium carbonate, such as the urea homogeneous precipitation method,²¹,²⁸ hydrothermal synthesis,²⁹,³⁰ sonochemical synthesis,³¹ and microwave-hydrothermal method.³² Urea can be decomposed into ammonium and carbonate ions by hydrolysis and the rate of urea decomposition is governed by the reaction temperature.²¹,³³ Compared to other synthetic
routes, the urea homogeneous precipitation method does not require a special instrument, such as an autoclave, microwave device, or ultrasonic probe, which is beneficial for the facile and inexpensive preparation of CeCb particles. However, it usually requires additional heating and long reaction times to achieve appropriate urea decomposition rates. Urea is also commonly used in various synthetic methods for preparing CeONPs. As in the case of CeCb, urea can act as a precipitating agent in the synthesis of CeONP via thermal decomposition. In the hydrothermal synthesis of CeONPs, urea can act as either a reducing agent or a supporting substance for crystal growth. In addition, urea can act as a fuel for exothermic reactions in a microwave-assisted combustion method. Although urea is commonly used for the synthesis of CeCb and CeONPs, a heating process to induce the decomposition of urea is necessary. Therefore, a synthetic method that does not need heat can be an option to shorten the reaction time and increase the preparation efficiency of CeCb and CeONPs.

1,1′-Carbonyldiimidazole (CDI) is a useful coupling agent for the formation of amide bonds and carbamate bonds. CDI decomposes into imidazole and carbon dioxide very quickly by hydrolysis at room temperature. Imidazole resulting from the decomposition of CDI is a key component in the synthesis of various imidazole-coordinated metal complexes, including imidazolate-bridged copper(II) complex, imidazole-coordinated cadmium(II) complex, imidazole-coordinated cobalt(II) complex, and zeolitic imidazolate frameworks (ZIFs). Recently, a coprecipitation method for the synthesis of a CeONP-decorated cerium(III)–imidazole network at room temperature with CDI has been reported. Although this report shows the potential of using cerium compounds and imidazole derivatives to synthesize CeONPs, CeONPs can only be obtained in a mixed form with a cerium–imidazole network. Moreover, most reports focus on the reaction of metal ions with imidazoles derived from CDI decomposition. The role of carbon dioxide, the other chemical component derived from CDI decomposition, as a source of carbonate ions in various chemical reactions has not received scientific attention.

In the present study, we propose a facile and rapid method for synthesizing CeCb nano- and microparticles and CeONPs at room temperature without heating, using CDI and imidazole in acetone (Figure 1). CDI acts as a carbonate source (via carbon dioxide) as well as a precipitating agent (via imidazole) after its decomposition. Due to the fast and controllable decomposition of CDI depending on the amount of water in the acetone solution, CeCb particles of diverse sizes ranging from around 180 nm to 13 μm could be prepared without a heating process within a relatively short mixing time (∼3 h). The morphology of CeCbNPs could be varied from a nanoplate to a flying-saucer shape (nanosaucer) by adding imidazole and adjusting the amount of CDI. The CeCbNPs could be converted into CeONPs via calcination while maintaining their morphology. In addition, we have demonstrated the direct synthesis of uniform CeONPs with high ROS-scavenging properties in the presence of CDI and additional imidazole. This method may provide a useful methodological tool for designing nanoparticles and microparticles composed of cerium carbonate and cerium oxide with an efficient synthetic process and numerous applications.

2. RESULTS AND DISCUSSION

To investigate the effect of CDI on the formation of particles, cerium nitrate hexahydrate was reacted with various concentrations of CDI and the speed of precipitation was observed. A relatively small amount of CDI (0.5 and 1 mmol) led to slow precipitation, while higher CDI amounts (2 and 4 mmol) clearly showed rapid precipitation (Video S1, Supporting Information). The actual time scale for the occurrence of precipitation ranged from a few seconds to tens of minutes...
Scanning electron microscopy (SEM) images revealed that microsized aggregation occurred with small amounts of CDI (Figure S2, Supporting Information), but the shape of the particles changed dramatically into nanoplates 350 nm in diameter and 35 nm in thickness as the amount of CDI increased (Figure 2a). The magnified SEM images show that the nanoplates are composed of an assembly of smaller rod-shaped 67 × 33 nm nanoparticles, and it is confirmed from the transmission electron microscopy (TEM) images that these smaller rod-shaped nanoparticles are made up of about 4-nm-sized nanoparticles (Figure 2b). X-ray diffraction (XRD) analysis shows that the nanoplates are composed of mixed phases of cerium oxycarbonate (Ce2(CO3)2·H2O, PDF #44-0617) and cerium carbonate hydrate (Ce2(CO3)3·8H2O, PDF #38-0377) (Figure 2c). As the amount of CDI increases, the peak intensity of cerium carbonate hydrate increases compared to that of cerium oxycarbonate, indicating that the formation of cerium carbonate hydrate is dominant over cerium oxycarbonate in conditions with higher CDI concentrations (Figure S3, Supporting Information). In particular, the peak corresponding to the (020) facet at 10.5° was highly intensified as the amount of CDI increased. To determine whether the amount of generated CO2 (the carbonate source) correlates with the amount of CDI, the amounts of dissolved CO2 in acetone were measured by a titration kit (Figure S4, Supporting Information). Although this kit was optimized for measuring dissolved CO2 in aqueous solutions, it was able to measure the relative amount of CO2 contained in acetone indirectly. As the amount of CDI increased, the amount of dissolved CO2 in acetone increased, which means that CO2 dissolved in acetone, which can serve as a carbonate source, is derived from the decomposed CDI.

Since it is known that imidazole is a byproduct from the hydrolysis of CDI and participates in the precipitation, we hypothesize that the presence of imidazole prior to CDI decomposition may affect the formation of CeCnb particles. To investigate the effect of imidazole, additional imidazole (6 mmol) was added to the reaction mixture of cerium nitrate hexahydrate and CDI in acetone and the precipitation was characterized. As extra imidazole was added, the morphology and particle size changed significantly. The resulting nanoparticles show a morphology of flaying saucers (nanosaucers) composed of assembled smaller particles and the size of the nanosaucers is 176 ± 42 nm (Figures 2d,e and S5, Supporting Information). When larger amounts of extra imidazole (4 and 6 mmol) are added, the size of the nanosaucers decreases without any significant morphological differences compared to the reaction to which a smaller amount of extra imidazole (2 mmol) was added. However, there was no significant difference in size between the reaction products to which 4 or 6 mmol of imidazole was added, indicating that adding more than a certain amount of imidazole no longer affects the size reduction of the particles (Figure S6, Supporting Information). XRD patterns exhibiting representative peaks corresponding to the (110), (111), (102), (131), and (221) facets at 20.6, 23.9, 30.3, 38.4, and 43.7°, respectively, show that the nanosaucers can be assigned to Ce2(CO3)2·H2O (PDF #44-0617) (Figure 2c).

Figure 2. Morphological and structural characteristics of CeCnb particles. SEM (a, d, g), TEM (b, e, h), and XRD (c, f, i) results of (a–c) CeCnb nanoplates, (d–f) CeCnb nanosaucers, and (g–i) macaron-shaped CeCnb microparticles obtained from addition of 1000 μL of deionized water. Scale bars of the inset: 100 nm for (a) and (d) and 1 μm for (g).
revealing that these nanosaucers consist of cerium oxycarbonate regardless of the amount of imidazole added (Figure S7, Supporting Information). Imidazole can be formed through the slow hydrolysis of CDI and act as a weak base in the case of the reaction of cerium nitrate hexahydrate and CDI,\textsuperscript{51,52} which can induce the slow formation of Ce\textsubscript{2}(CO\textsubscript{3})\textsubscript{3} from a weak basic condition.\textsuperscript{53} However, the addition of extra imidazole may increase the pH of the reaction mixture more quickly, and formation of Ce\textsubscript{2}(CO\textsubscript{3})\textsubscript{2}O\textsubscript{·}H\textsubscript{2}O can be more favored through the reaction of 2Ce\textsuperscript{3+} + 2OH\textsuperscript{−} + 2CO\textsubscript{3}\textsuperscript{2−} → Ce\textsubscript{2}(CO\textsubscript{3})\textsubscript{2}O\textsubscript{·}H\textsubscript{2}O.\textsuperscript{54,55} Taken together, these results show that the addition of extra imidazole not only transforms the morphology of CeCb nanoparticles from nanoplates (Figure 2a,b) to nanosaucers (Figure 2d,e) but also changes their phase composition from cerium carbonate hydrate (Ce\textsubscript{2}(CO\textsubscript{3})\textsubscript{3}·8H\textsubscript{2}O) (Figure 2c) to cerium oxycarbonate (Ce\textsubscript{2}(CO\textsubscript{3})\textsubscript{2}O·H\textsubscript{2}O) (Figure 2f).

In the urea homogeneous precipitation method, it is known that reaction temperature can control the decomposition rate of urea into NH\textsubscript{4}\textsuperscript{+}, OH\textsuperscript{−}, and CO\textsubscript{3}\textsuperscript{2−} ions by hydrolysis and subsequently control the precipitation process owing to an increase in alkalinity.\textsuperscript{21} Therefore, it has been reported that the shape and size of nanoparticles can be changed by controlling the reaction temperature in the urea homogeneous precipitation method.\textsuperscript{56,57} In a similar vein to the case of urea, we wanted to know whether controlling the decomposition rate of CDI affects the structure of the nanoparticles in the present study. Based on this, we further investigated whether controlling the decomposition rate of CDI can affect the formation of CeCb particles. To control the decomposition rate of CDI without using heat, we used the extra addition of small amounts of water in the reaction mixture, as CDI can decompose rapidly into imidazole and carbon dioxide in the presence of water.\textsuperscript{41} Although acetone was used as a solvent in the present study, the reaction mixture contained a small amount of water derived from cerium nitrate hexahydrate and 99.5% acetone and this water is capable of decomposing the CDI. This led us to investigate the effect of the addition of extra water on nanoparticle formation.

Figure 3. Morphological and structural characteristics of Cal-CeO particles. SEM (a–c) and TEM (d–f) images of (a, d) Cal-CeO nanoplates, (b, e) Cal-CeO nanosaucers, and (c, f) Cal-CeO micromacarons obtained from the addition of 1000 μL of deionized water. (g) XRD patterns and (h) calculated crystallite sizes of Cal-CeO particles.
When more water was added in the reaction mixture of cerium nitrate hexahydrate and CDI, the precipitation occurred more rapidly (Video S2, Supporting Information). SEM images of the precipitate obtained with addition of different amounts of water (0.3, 0.6, 1.0, 1.3 mL) in the reaction mixture of CeCb nanosaucers in the presence of 6 mmol imidazole showed that the particle size increases dramatically to a range of 412 nm to 13.6 μm (Figures 2g,h, S8, and S9, Supporting Information). When a relatively small amount of water was added, the overall morphology of particles remained similar to the CeCb nanosaucers prepared without the use of additional deionized water. When a larger volume of deionized water was added, characteristic macaron-like microparticles were observed with a layered structure that was somewhat squashed. The macaron-like microparticles prepared with 1000 μL of deionized water showed the XRD pattern of cerium oxy carbonate Ce₄(CO₃)₂(OH)₄, indicating that there was no phase change regardless of the addition of deionized water during the reaction (Figure 2i). In the absence of extra imidazole to prepare the CeCb nanoplates, the addition of extra water showed a similar tendency of increasing the particle size according to the amount of deionized water added, but the overall plate shape was maintained without a significant change (Figure S10, Supporting Information). To verify the effect of water added into the reaction mixture, the change in the amount of CO₂ generated according to the change in the amount of water was indirectly evaluated by counting the CO₂ bubbles generated during the reaction and titrating the amount of NaOH consumed due to the CO₂ dissolution after the reaction (Figure S11, Supporting Information). As the amount of water added to the cerium salt-free acetone solution increased, the amount of CO₂ generated during the reaction increased. In addition, the generated CO₂ from the reaction can react with NaOH in a different reactor to form NaHCO₃ and the amount of NaOH consumed can be measured by titration with HCl. In the case of adding a large amount of water, the amount of NaOH consumed was plenty compared to the reaction to which a smaller amount of water was added, indicating that the addition of water could be the important factor accelerating the decomposition of CDI. The addition of cerium nitrate hexahydrate to the reaction mixture decreased the amount of CO₂ generated, suggesting that some of the CO₂ generated was consumed to form reaction products in the reaction. Taken together, these results indirectly showed that the addition of water can accelerate the production of CO₂ by faster decomposition of CDI and that this generated CO₂ can participate in the reaction as a reactant. The result of adding water in the CeCb particle formation process is contrary to previous reports that describe faster nucleation by rapid decomposition of urea at high reaction temperature that leads to the formation of smaller size particles in the urea homogenous precipitation method. However, the particle size synthesized at 70 °C by the urea homogenous precipitation method could be smaller due to incomplete urea decomposition. Similarly, incomplete and slow decomposition of CDI in the reaction mixture containing small amounts of water may be one of the reasons for the smaller-size CeCb particles. On the other hand, it has been reported that the particle size increases with longer reaction times due to continuous growth of the particles and a more complete reaction. In our study, since burst precipitation already occurred owing to the presence of extra imidazole early in the synthesis of the CeCb nanosaucers, deionized water added to the reaction mixture may serve to increase the reaction time by rapidly producing reactants at the beginning of the reaction due to the induction of rapid decomposition of the CDI. However, further studies are needed to confirm the possibility that water participates not only in the decomposition of CDI but also in the reaction with other reactants directly. Cerium carbonate is known as a good precursor for conversion into cerium oxide. CeCb nanoplates, CeCb nanosaucers, and macaron-shaped CeCb microparticles were calcined in air (Cal-CeO particles) and the resulting powders were characterized by SEM, TEM, and XRD. Despite the CeO₂ conversion process at high temperature (500 °C), the original morphologies of nanoplates, nanosaucers, and macaron-shaped microparticles were well maintained with the assembly of smaller subunits (Figure 3a–c). The TEM images also showed that the Cal-CeO particles were composed of subunits of nanoparticles, similar to the case of CeCb particles, but the size of nanoparticles increased due to calcination (Figure 3d–f). XRD analysis of all calcined particles showed that the typical CeO₂ phase of a cubic fluorite structure with high crystallinity was obtained after calcination (Figure 3g). The calculated crystallite sizes by the Debye–Scherrer equation using XRD data showed comparable values between Cal-CeO particles (Figure 3h). Then, we further investigated the effect of the calcination temperature and the heating rate on the properties of Cal-CeONPs (Figure S12, Supporting Information). There was no definite morphological change according to the changes in the calcination temperature and the heating rate. However, as the calcination temperatures increased, the XRD peaks with a cubic fluorite structure of cerium oxide became sharper, and the crystallite sizes increased from 4.9 nm at 300 °C to 9.3 nm at 500 °C. In addition, the effect of the heating rate seemed to
be small compared to the calcination temperature, as previously reported for other nanoparticles.64 The plate shape of cerium oxide has recently attracted attention owing to its UV-shielding effect and pearlescence in cosmetic applications, but the synthesis of plate-shaped particles composed of cerium oxide is not as easy, owing to its crystal structure.65 In this regard, the synthesis of ceria nanoplates using CeCb nanoplates as precursors can be further investigated for potential applications in cosmetics.

In biological applications, nanoparticles of about 100 nm in size are known to have the advantage of exhibiting prolonged circulation time and efficient drug delivery to target sites such as tumors.66 We further controlled and optimized the reaction parameters (CDI, imidazole, water, mixing time) in the synthesis of CeCb nanosaucers to investigate if we could achieve the fabrication of smaller and more uniform nanoparticles suitable for biomedical applications. In the case of further reducing the amount of CDI from 1 to 0.5 mmol in the reaction mixture of acetone and imidazole without adding deionized water, a mixture of plate-shaped microparticles and spherical nanoparticles (130–200 nm size according to the amount of imidazole) were observed after a mixing time of 3 h (Figure S13, Supporting Information). When the mixing time was decreased to 1 h (Ce-CDI-IM CeONPs), uniform spherical nanoparticles that averaged 130 nm in size were observed without microparticles, different from the reaction products with longer mixing times (Figures 4a and S14, Supporting Information). TEM analysis revealed that these 130 nm nanoparticles are composed of an assembly of small nanoparticles with a size of a few nm (Figure 4b). In the SEM image of the product separated 1 min after the start of the reaction of the synthesis of Ce-CDI-IM CeONPs, small subunits of nanoparticles with a size of about 13 nm were observed (Figure S15, Supporting Information). As the size of nanoparticles decreases, the surface energy increases due to an increase in dangling bonds and defects on the surface of the nanoparticles.67,68 Therefore, the reaction may have progressed in the direction of forming 130-nm-sized nanoparticles, which can be called aggregates.69 XRD analysis of the 130 nm nanoparticles obtained from short mixing time (1 h) exhibits representative peaks at 28.4, 33.0, 47.5, and 56.3°, corresponding to the (111), (200), (220), and (311) facets of CeO2 (PDF #43-1002), respectively, and the average crystalline size using the Debye–Scherrer equation is 3.1 nm (Figure 4c). Taken together with the TEM observations, it is clear that the 130 nm CeONPs are an assembled form of 3-nm-sized small nanoparticles. As the mixing time increases, the XRD peaks assigned to the phase of Ce(CO₃)₂O·H₂O appear to be mixed with peaks for CeO₂. Based on SEM and XRD data, the identity of the microparticles in the reaction products at higher mixing times is cerium oxycarbonate. Taken together, these results showed that CeONPs can be directly synthesized from the reaction of cerium nitrate hexahydrate, CDI, and imidazole in acetone at room temperature at short mixing times.

To understand the role of CDI in the Ce-CDI-IM CeONPs, we prepared nanoparticles without addition of CDI in the synthesis of Ce-CDI-IM CeONPs. Interestingly, the resulting precipitate (Ce-IM CeONPs) shows a uniform morphology of 130 nm spherical nanoparticles (Figure S16a, Supporting Information), which are similar to those of Ce-CDI-IM CeONPs. The hydrodynamic size is 296.4 ± 5.0 nm, comparable to that of Ce-CDI-IM CeONPs (297.1 ± 4.6 nm). XRD analysis reveals that the phase of nanoparticles is CeO₂ (PDF #43-1002) and the average size of nanoparticles derived from the Debye–Scherrer equation is 3.0 nm (Figure S16b, Supporting Information). Although similar 130 nm CeONPs were obtained without using CDI, the yield of synthesized Ce-IM CeONPs was much lower than that of Ce-CDI-IM CeONPs. The yield of Ce-CDI-IM CeONPs synthesized from the same amount of cerium salts was 10.6 times higher than that of Ce-IM CeONPs. Although the size and phase of the resulting nanoparticles were similar, the addition of a small amount of CDI in the reaction led to a significantly higher yield.

We further characterized the differences between Ce-CIDI-IM CeONPs and Ce-IM CeONPs. In the Fourier transform infrared (FTIR) spectra, peaks corresponding to stretching and bending vibrations of hydroxyl groups on the surface of nanoparticles are observed at 3400 and 1630 cm⁻¹, respectively, for all nanoparticles (Figure 5a).69 In addition, peaks at 500–600 cm⁻¹ for the O–Ce–O stretching vibration,70,71 peaks at ~1380 cm⁻¹ for the vibration mode of Ce–O–Ce,72,73 and small peaks at 1050 cm⁻¹ for physical absorption of water are also found in all nanoparticles. Peaks for a carbonate ion at 1494 cm⁻¹ (νas O–C–O), 1430 cm⁻¹ (νas O–C–O), 840 cm⁻¹ (π–CO₃²⁻), and 720 cm⁻¹ (δ–CO₃²⁻) are found in the spectra of CeCb nanoplates, CeCb nanosaucers, and Ce-CDI-IM CeONPs, but not in Ce-IM CeONPs.5,74 In the spectrum of Ce-IM CeONPs, a sharp peak for the presence of nitrate ions on the surface of https://doi.org/10.1021/acsomega.1c03700
nanoparticles appears at 1382 cm$^{-1}$, suggesting that there is a difference in surface properties between Ce-IM CeONPs and Ce-CDI-IM CeONPs. 70 Thermogravimetric analysis (TGA) analysis shows a similar initial weight loss due to the desorption of water below 200 °C for all particles, and differing weight losses above 200 °C depending on the type of nanoparticles (Figure 5b). For CeCb nanosaucers, a sharp weight loss occurs at 200–300 °C due to the release of carbon dioxide, as previously reported for cerium carbonate. 77 In contrast, smaller weight losses are observed at the same temperature for both CeONPs. Although there is no significant difference in TGA profiles between Ce-CDI-IM CeONPs and Ce-IM CeONPs, a clear weight loss at 200–300 °C is observed for Ce-CDI-IM CeONPs while there is no such weight loss for Ce-IM CeONPs. This is confirmed by the thermogravimetric (DTG) trend (inset of Figure 5b). This means that a small amount of CDI decomposition products are incorporated into Ce-CDI-IM CeONPs.

The catalytic characteristics of CeONPs are attributed to the coexistence of Ce$^{3+}$ and Ce$^{4+}$ oxidation states. In general, the relative percentage of Ce$^{3+}$ oxidation state increases when the size of the nanoparticles decreases, owing to the formation of oxygen deficiencies on the surface of the nanoparticles. As Ce$^{3+}$ and Ce$^{4+}$ ions are ascribed to the superoxide dismutase (SOD) and catalase (CAT) mimetic activity of CeONPs, respectively, 78 the ratio of Ce$^{3+}$/Ce$^{4+}$ oxidation states in Ce-CDI-IM and Ce-IM CeONPs was analyzed through XPS. In the Ce 3d XPS spectrum, Ce-IM CeONPs and Ce-CDI-IM CeONPs show the coexistence of Ce$^{3+}$ and Ce$^{4+}$ oxidation states and these peaks are in good agreement with previous reports (Figure 5c). 78–81 The Ce$^{3+}$ content of Ce-CDI-IM CeONPs is 34.3%, which is higher than 23.7% for Ce-IM CeONPs. In the O 1s spectrum, both CeONPs showed three peaks at 529.5, 531.2, and 532.8 eV, which are attributed to the lattice oxygens of CeO$_2$, oxygens near the oxygen vacancies, and hydroxyl groups on the surface, respectively. 82 However, the relative amount of oxygens in the vicinity of oxygen vacancies of Ce-CDI-IM CeONPs was 41.3%, which was higher than that of Ce-IM CeONPs with 29.6% (Figure S17, Supporting Information). In the N 1s spectrum, there are no peaks at 400 eV corresponding to imidazole for either of the nanoparticles, while a peak at 406.7 eV corresponding to nitrate species is only observed on the surface of Ce-IM CeONPs (Figure S18, Supporting Information). 86–88 This means that the imidazole acts as a precipitating agent but is not a capping agent or an imidazolate linker. These XPS analyses show that the addition of CDI can affect the properties of the nanoparticle surface, especially an increase in the amount of the Ce$^{3+}$ oxidation state, which is known to be an important factor for ROS-scavenging properties. 89

Finally, we investigated the ROS-scavenging properties of the CeONPs. CAT-mimicking activity related to the amount of Ce$^{4+}$ oxidation state was measured by a hydrogen peroxide/peroxidase assay reacting with 20 μM H$_2$O$_2$ for 1 h and SOD-mimetic activity related to the amount of the Ce$^{3+}$ oxidation state was measured by a superoxide radical inhibition assay (Figure 6a,b). Ce-IM CeONPs and Ce-CDI-IM CeONPs show higher ROS-scavenging properties, compared to calcinated nanoparticles, in the results of both assays. In general, crystallite size increases with an increase in calcination temperature, and ceria nanoparticles with a smaller crystallite size exhibit superior catalytic properties due to an increase in oxygen vacancies as an active catalytic site on the surface of the nanoparticles. 84,90–92 The XRD result of calcined Ce-CDI-IM CeONPs exhibits a highly crystalline cubic fluorite structure of cerium oxide with an average 8.5 nm crystalline size calculated from the Debye–Scherrer equation, indicating that this relatively large crystal size may be responsible for the low catalytic activity (Figure S19, Supporting Information). Therefore, it may be advantageous in terms of improving the ROS-scavenging activities of CeONPs to prepare CeONPs without the calcination process. Moreover, the Ce-CDI-IM CeONPs exhibit more powerful CAT- and SOD-mimetic properties compared to other CeONPs. The high amount of the Ce$^{3+}$ oxidation state in Ce-CDI-IM CeONPs confirmed through XPS analysis could be the main reason for its superior SOD scavenging properties, which may be advantageous for biomedical applications. 93 Taken together, these results indicate that the production of CeONP, which exhibits higher production efficiency and superior ROS-scavenging properties compared to the product obtained in the reaction without CDI, can be achieved using a small amount of CDI in the reaction of cerium compounds and imidazole.

In the urea homogeneous precipitation method, which is widely used as a synthetic route for inorganic nanoparticles including cerium-containing materials, 94,95 a heating process is essential to achieve proper decomposition of the urea during the reaction. However, it is often difficult to control the temperature precisely for a long time and this could be an obstacle for the control of industrial-scale production of
nanoparticles due to a thermal gradient inside the reactor that can lead to adverse consequences such as reduced particle uniformity. Therefore, the concept of sustainability has recently emerged as an important factor in considering the design of a synthesis process for nanoparticles. Therefore, developing a synthetic process that does not require heating is not only a good alternative for reducing energy consumption but also can increase its applicability to the industry. Synthesis processes conducted at room temperature are known as a way to reduce energy consumption, and, from this point of view, the synthetic method developed here, which reacts CDI and imidazole in acetone at room temperature for the synthesis of CeCbPs and CeONPs, could be an attractive route for the homogeneous precipitation method. However, although the mixing process is thought to be faster than the heating process, which can be relatively slow because it is transferred through the reactor walls and the part of the solution, inadequate or slow mixing can cause problems that degrade the quality of the nanoparticles and lead to poor batch-to-batch reproducibility. Therefore, further studies will be needed to clarify the influence of parameters related to the mixing process in the synthetic method presented here.

3. CONCLUSIONS

Nanoparticles composed of CeCb with distinctive morphologies were successfully synthesized by a facile method, which used CDI and imidazole with cerium nitrate hexahydrate in an acetone environment without any heating process. The particle morphology could be transformed in various ways and the size could be controlled from a nanoscale to microscale by adjusting the amount of CDI, imidazole, and deionized water, or by controlling the mixing time. These CeCbPs were transformed into particles composed of cerium oxide while maintaining their characteristic morphologies in air at 500 °C for 2 h. Moreover, CeONPs could be obtained simply by reducing the amount of CDI, and incorporating a small amount of CDI into CeONPs could increase their ROS-scavenging properties and improve production efficiency. These findings suggest that the proposed method of using CDI and imidazole in an acetone solvent may be a new alternative method for the synthesis of versatile particles composed of CeCb or cerium oxide, and it can contribute to promoting sustainability by reducing the amount of energy consumed in the heating process.

4. EXPERIMENTAL SECTION

4.1. Materials. Cerium(III) nitrate hexahydrate (Aldrich), CDI (Aldrich), imidazole (Sigma-Aldrich), acetone (Sigma-Aldrich), hydrogen peroxide (Samchun), Amplex Red hydrogen peroxide/peroxidase assay kit (Invitrogen), and SOD assay kit (Dojindo Molecular Technologies, Inc.) were purchased and used without further purification.

4.2. Synthesis of CeCb Nanoplates and Nanosaucers. Synthetic conditions for each particle are summarized in Table 1. To synthesize CeCb nanoparticles, a cerium nitrate hexahydrate precursor solution, prepared by dissolving 1 mmol cerium nitrate hexahydrate in 25 mL of acetone, and a CDI precursor solution, prepared by dissolving 4 mmol CDI in 25 mL of acetone, were mixed with vigorous stirring at room temperature. For the fabrication of CeCb nanoparticles, 2, 4, or 6 mmol imidazole were added into a reaction mixture containing 1 mmol cerium nitrate hexahydrate and 1 mmol CDI. Macaron-shaped CeCb microparticles were synthesized using the same as the abovementioned method for CeCb nanoplates, except 1000 µL of deionized water was added. After mixing for 3 h at room temperature, the resulting precipitate was centrifuged, washed four times with deionized water, and dried at 60 °C for 12 h in air.

4.3. Conversion of CeCb Nanoparticles into CeONPs. To convert CeCb particles (nanoplates, nanosaucers, and macaron-shaped microparticles) into ceria particles, dried powdered CeCb particles were calcined in air for 2 h at 500 °C, as previously described. The resulting ceria nanoparticles were designated as Cal-CeO nanoparticles, Cal-CeO nanosaucers, or Cal-CeO micromacarons.

4.4. Direct Synthesis of CeONPs. Spherical CeONPs 130 nm in size were directly synthesized by reacting cerium nitrate hexahydrate, CDI, and imidazole in acetone. Typically, 1 mmol cerium nitrate hexahydrate, CDI, and imidazole were added to a reaction mixture containing 1 mmol cerium nitrate hexahydrate and 1 mmol CDI. Macaron-shaped CeCb microparticles were synthesized using the same as the abovementioned method for CeCb nanoparticles, except 1000 µL of deionized water was added. After mixing for 3 h at room temperature, the resulting precipitate was centrifuged, washed four times with deionized water, and dried at 60 °C for 12 h in air.
cerium nitrate hexahydrate, 0.5 mmol CDI, and 4 mmol imidazole were dissolved in 25, 12.5, and 12.5 mL of acetone, respectively. The solutions of CDI and imidazole were sequentially added to a solution of cerium nitrate hexahydrate with vigorous stirring at room temperature. After mixing for 1 h, the precipitate was centrifuged, washed four times with deionized water, and dried at 60 °C in air for 12 h (designated as Ce-CDI-IM CeONPs). Spherical CeONPs 130 nm in size were also synthesized by mixing cerium nitrate hexahydrate and imidazole in acetone for 3 h without the addition of CDI in the aforementioned synthetic procedure. The resulting nanoparticles were designated as Ce-IM CeONPs.

4.5. Characterization. The morphology of the particles was evaluated using a JSM-6510 scanning electron microscope (SEM, JEOL) and a JEM-2100F transmission electron microscope (TEM) operating at 200 kV. The particle sizes were measured manually by ImageJ software (NIH) using 500 or more particles in SEM images. The hydromorphic size and ζ-potential of the nanoparticles were analyzed using a Zetasizer Nano ZS90 (Malvern Panalytical). X-ray photoelectron spectroscopy (XPS) analysis was performed using an ESCALAB 250 (Thermo Scientific) and deconvolution of the XPS peaks was conducted using CasaXPS software (version 2.3.23PR1.0, Casa Software Ltd.) with a Shirley background and a Gaussian/Lorentzian (GL) line shape. X-ray powder diffraction (XRD) patterns of the samples were obtained using a diffractometer (D8 ADVANCE, Bruker Corporation). Fourier transform infrared (FTIR) spectra of the nanoparticles were obtained using an FTIR spectrometer (IFS-66/S, TENSOR27, Bruker). Thermogravimetric analysis (TGA) was conducted using a TG/DTA7300 (SEIKO Instruments) under a N2 atmosphere at a heating rate of 10 °C/min.

4.6. Measurement of ROS-Scavenging Catalytic Properties. Catalase-mimicking activities of Ce-CDI-IM CeONPs, Ce-IM CeONPs, and Cal-CeONPs were measured using an Amplex Red hydrogen peroxide/peroxidase assay kit. Typically, various CeONPs were added in 1 mL of a 20 μM hydrogen peroxide solution using 24-well plates (final concentration: 100 μg/mL). The microplates were incubated for 1 h with gentle stirring and then 50 μL of samples from each well was transferred to 96-well plates. Then, 50 μL of a working solution containing the Amplex Red reagent (100 μM) and horseradish peroxidase (HRP, 0.2 U/mL) was added to each well. After incubation for another 30 min at room temperature to trigger the reaction between the Amplex Red reagent and hydrogen peroxide, the fluorescence of resorufin, the reaction product, was measured using wavelengths of 545 nm for excitation and 590 nm for emission by a Varioskan (Labsystems) microplate reader at 450 nm to determine the SOD activity as an inhibition activity.

**ASSOCIATED CONTENT**

**Supporting Information**

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c03700. Additional data of SEM, XRD, particle sizes, and XPS about the reaction products (PDF)

Comparison of time points at which precipitation occurred during the reaction according to the amount of CDI (Video S1) (MP4)

Comparison of time points at which precipitation occurred during the reaction according to the amount of deionized water (Video S2) (MP4)

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Notes
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**ABBREVIATIONS**

ROS, reactive oxygen species; SOD, superoxide dismutase; CAT, catalase; CeONPs, cerium oxide nanoparticles; CeCBPs, cerium carbonate particles; CDI, 1,1'-carbonyldiimidazole; XPS, X-ray photoelectron spectroscopy; XRD, X-ray powder diffraction; SEM, scanning electron microscopy; TEM, transmission electron microscopy; FTIR, Fourier transform infrared; TGA, thermogravimetric analysis; DTG, derivative thermogravimetric

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