

Redox Properties of CeO₂ at Low Temperature: The Direct Synthesis of Imines from Alcohol and Amine

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Abstract: We disclosed the redox properties of CeO₂ in organic reactions at low temperature of 303 K. CeO₂ works as the most effective heterogeneous catalyst for imine formation from benzyl alcohol and aniline at 303 K among various metal oxides and showed more than 38-fold higher activity than other simple metal oxides. CeO₂ is applicable to the reaction of various alcohols and amines and gives high yields (80–98 %) and high selectivities (89–>99 %). Kinetic measurements, MS, and FTIR analyses demonstrated that the high activity of CeO₂ is a result of reactive oxygen species at the redox sites on CeO₂. This discovery can help to create a new field in metal oxide catalysis.

Metal oxides are used in various fields of chemistry due to both their acid–base and redox properties and constitute the largest family of catalysts in heterogeneous catalysis. If metal oxides could be used to catalyze organic reactions at low temperature by making use of their redox properties, they might substitute transition metal complexes and supported metal catalysts. Among metal oxides, CeO₂ is particularly promising, because of its redox and acid–base bifunctional properties and therefore attracts much attention in the fields of catalyst and biological chemistry.^[1] However, these properties of CeO₂ are generally utilized at high temperature (>473 K) in catalysis such as the conversion of exhaust gases. Recently, it was reported that the unique acid–base bifunctionality of CeO₂ at low temperature (≤373 K) is related to high catalytic activity in liquid-phase organic reactions,^[2] but the redox property of CeO₂ at low temperature (≤373 K) in organic reactions has never been reported. On the other hand, direct observation of the oxygen vacancies on CeO₂ has been investigated. Noncontact atomic force microscopy (NC-AFM) studies demonstrated that oxygen vacancies on CeO₂ are mobile at 303 K,^[3] which is related to the presence of the surface site with redox ability at low temperature. In contrast, the combination of scanning tunneling microscopy (STM) analysis and DFT calculations suggested that the oxygen vacancies on CeO₂ are immobile at room temperature.^[4] Therefore, clarification of the redox property of CeO₂ at low temperature (≤373 K) is of great importance to understand the unique properties of CeO₂. New findings regarding organic reactions catalyzed at low temperature by the redox

property of CeO₂ will lead to new applications of metal oxide catalysis.

Imines are very important intermediates in the synthesis of various biological, agricultural, and pharmaceutical compounds, because they can undergo versatile transformations (reductions, additions, condensations, and multicomponent reactions).^[5] Traditionally, imines are synthesized by the condensation reaction of aldehydes or ketones with amines in the presence of an acid catalyst. Recently, versatile alternative methods have been reported such as the oxidation or dehydrogenation of secondary amines,^[6] the dimerization of primary amines,^[7] the direct coupling of alcohol and amine,^[8] and the hydroamination of alkynes with amines.^[9] Among these methods, the direct coupling of alcohol and amine is one of the most promising approaches, because alcohols are readily available and inexpensive, and only hydrogen and/or water is produced as a by-product. Various effective homogeneous^[8a–g] and heterogeneous^[8h–i] catalysts have been reported. However, most reaction systems require a strong inorganic or organic base such as KOH, NaOH, and DABCO as a catalyst or co-additive, which is undesirable, because a large amount of salts is produced. Unlike these reaction systems, the groups of Milstein^[8g] and Schomaker^[8c] reported effective homogeneous Ru complex catalysts without using base under N₂ atmosphere, which, however, had the drawbacks of high required temperature (>373 K) and low activity. With regard to reusability and durability, heterogeneous catalysts are desirable and some catalysts working without additives were reported such as Au,^[8l,s] Ru,^[8q] Pd,^[8r] and Pt^[8o] catalysts. However, these catalysts are based on noble metals and require the use of pure O₂. Therefore, the development of an inexpensive and effective heterogeneous catalyst that does not require additives and works under mild reaction conditions such as air and low temperature is desirable.

Herein, we report that CeO₂, a simple metal oxide, is the most effective heterogeneous catalyst among various metal oxides for imine synthesis from alcohol and amine even at low temperature of 303 K under air. This is the first report that CeO₂ exhibits the redox property at 303 K in organic reactions. Kinetic measurements, MS, and FTIR analyses confirmed that the high activity is derived from the reactive oxygen species at the redox sites of CeO₂.

Initially, the catalytic activity of various metal oxides for imine synthesis from benzyl alcohol and aniline was investigated at 303 K under air (Table 1). CeO₂ showed activity in this reaction, but other simple metal oxides are nearly inactive. The activity of CeO₂ was more than 38-fold higher than those of other simple metal oxides in terms of both the catalyst amount and surface area, and the yield of benzylidene

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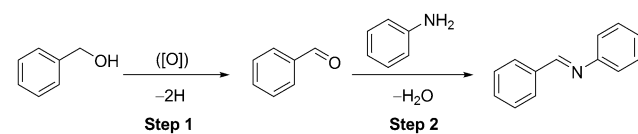
Table 1: Imine synthesis from benzyl alcohol and aniline over various metal oxides.^[a]

Metal oxide	$S^{[b]}$ [m ² g ⁻¹]	t [h]	Yield [%]	$V^{[c]}$ [mmol h ⁻¹ g ⁻¹]	$V \times 10^{3[d]}$ [mmol h ⁻¹ m ⁻²]
CeO ₂	84	5	12	0.46	5.3
CeO ₂	84	48	75	—	—
CeO ₂ ^[e]	84	24	96	—	—
MnO ₂	64	48	2.1	0.0088	0.14
Al ₂ O ₃	182	48	1.1	0.0046	0.025
Y ₂ O ₃	62	48	0.6	0.003	0.04
Pr ₆ O ₁₁	33	48	0.5	0.002	0.06
La ₂ O ₃	8.0	48	0.2	0.001	0.08
Nb ₂ O ₅	47	48	0.2	0.001	0.02
ZrO ₂	91	48	0.2	0.001	0.01
MgO	37	48	0.1	< 0.001	0.01
TiO ₂	48	48	0.1	< 0.001	0.01
Dy ₂ O ₃	2.5	48	0.0	< 0.001	< 0.01
Ta ₂ O ₅	3.2	48	0.0	< 0.001	< 0.01
Fe ₂ O ₃	3.3	48	0.0	< 0.001	< 0.01
CaO	12	48	0.0	< 0.001	< 0.01
ZnO	50	48	0.0	< 0.001	< 0.01
SiO ₂	530	48	0.0	< 0.001	< 0.01
SiO ₂ -Al ₂ O ₃	560	48	0.0	< 0.001	< 0.01
CeO ₂ -ZrO ₂ (Ce/Zr = 4) ^[f]	54	24	4.1	0.034	0.59
CeO ₂ -ZrO ₂ (Ce/Zr = 1) ^[f]	55	24	2.4	0.020	0.36
CeO ₂ -ZrO ₂ (Ce/Zr = 0.25) ^[f]	57	24	1.2	0.010	0.18

[a] Conditions: benzyl alcohol 1.0 mmol, aniline 2.0 mmol, mesitylene 1.5 g, metal oxide 50 mg, 303 K, air. [b] Specific surface area determined by the Brunauer—Emmett—Teller (BET) method. [c] Formation rate per catalyst amount. [d] Formation rate per surface area. [c,d] Formation rates were measured under the conditions at which the conversion was below 20%. [e] 333 K. [f] Molar ratio of Ce to Zr.

aniline reached 75% in 48 h. When the temperature was 333 K, CeO₂ provided the highest yield of 96% in 24 h. In addition, mixed metal oxides of CeO₂-ZrO₂ were also tested in the reaction. The formation rate drastically decreased upon the introduction of Zr. These results indicate that pure CeO₂ is the most effective catalyst for the imine synthesis among the tested metal oxides.

The time course of the imine synthesis over CeO₂ at 333 K was investigated (Figure 1 a). The reaction proceeds smoothly to afford the corresponding imine in 96% yield with 97% selectivity in 24 h, and the initial reaction rate was 2.2 mmol h⁻¹ g⁻¹. Benzaldehyde was observed at the initial stage and the amount slowly decreased with time, suggesting that benzaldehyde is an intermediate and that the reaction proceeds by two consecutive steps (Scheme 1); 1) the trans-



Scheme 1. Reaction pathway for imine synthesis.

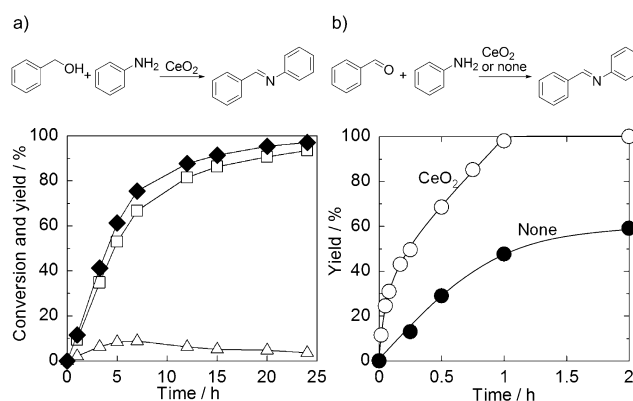


Figure 1. a) Time dependence for imine formation from benzyl alcohol and aniline over CeO₂ (♦: conversion, □: imine yield, △: aldehyde yield). Conditions: benzyl alcohol 1.0 mmol, aniline 2.0 mmol, mesitylene 1.5 g, CeO₂ 50 mg, 333 K, air. b) Time dependence for imine formation from benzaldehyde and aniline with/without CeO₂ (○: imine yield with CeO₂, ●: imine yield without CeO₂). Conditions: benzaldehyde 1.0 mmol, aniline 2.0 mmol, mesitylene 1.5 g, CeO₂ 50 mg, 333 K, air.

formation of benzyl alcohol to benzaldehyde and 2) the imine formation of benzaldehyde with aniline.

Generally, the imine formation readily proceeds upon heating. To estimate the contribution of CeO₂ to imine formation, the reaction was performed in the absence and presence of the CeO₂ catalyst (Figure 1 b). CeO₂ clearly catalyzed the reaction (136 mmol h⁻¹ g⁻¹), resulting in about 10-fold higher activity than that without CeO₂. This indicates that CeO₂ works as an effective catalyst for the imine formation of benzaldehyde with aniline. Therefore, we concluded that CeO₂ catalyzed both the steps of the imine synthesis from benzyl alcohol and aniline. The reaction rate of step 2 (136 mmol h⁻¹ g⁻¹) is more than 60 times higher than that of the overall reaction (2.2 mmol h⁻¹ g⁻¹), indicating that step 1 is the rate-determining step.

To clarify the mechanism of the step 1, the effect of oxygen concentration on the reaction rate was examined (Figure S1). The reaction without O₂ (under Ar) provided no product, suggesting that oxygen is essential for the process. The reaction rate increased linearly below ca. 20% with increasing O₂ concentration and became constant between 20 and 100%. Considering that the reaction is conducted under air (O₂ content is ≈ 21%), molecular O₂ is not involved in the rate-determining step.

If the reaction proceeds by the oxidative dehydrogenation mechanism, H₂O is produced in step 1 as a by-product. The behavior of H₂O production was investigated by mass spectrometry by the addition of 5 μL benzyl alcohol (0.048 mmol) to CeO₂ (0.58 mmol) under He at 373 K, followed by the introduction of 14% O₂ (Figure 2 a). CeO₂ was preheated at 873 K to remove surface H₂O and CO₂. The introduction of benzyl alcohol provided a sharp signal of H₂O under He, but no change of H₂ signal. The amount of detected H₂O is estimated to be 0.014 mmol before O₂ introduction, which corresponds to about 29% of the introduced benzyl alcohol. This indicates that H₂O is formed by CeO₂ under He and that oxygen atoms of CeO₂ are used for the production of

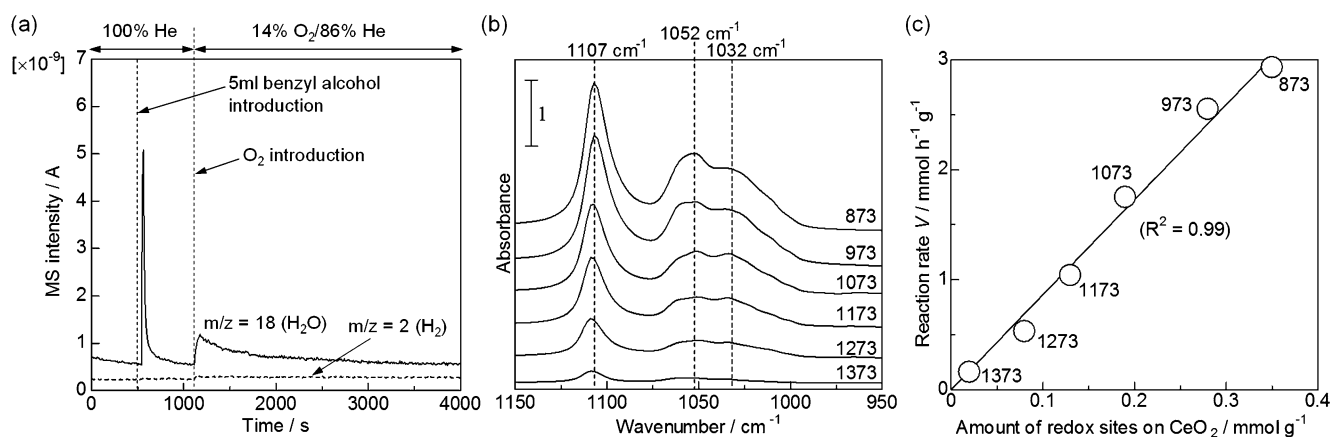
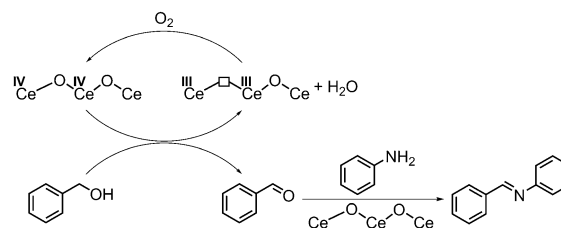


Figure 2. a) MS profiles of H_2O and H_2 for the addition of benzyl alcohol to CeO_2 under He and O_2/He . b) FTIR spectra of methanol adspecies at 323 K on CeO_2 calcined at different temperatures (873–1373 K). c) Reaction rate as a function of the amount of redox sites on CeO_2 . The values in the graph are calcination temperatures in K.

H_2O . Therefore, we conclude that step 1 proceeds by the oxidative dehydrogenation mechanism. After O_2 introduction, the second signal of H_2O was observed and the amount of H_2O was estimated to be 0.027 mmol, corresponding to about 56% of the introduced benzyl alcohol. When O_2 was introduced, the reaction proceeded to reach 85% conversion of benzyl alcohol, which supports the above result that O_2 is necessary for the catalytic reaction progress. In addition, the similar experiment was conducted on time-resolved in situ FTIR (Figure S2). Benzyl alcohol was adsorbed on CeO_2 , and a part of the adsorbed benzyl alcohol reacted on CeO_2 under He to afford benzaldehyde adspecies. Introduction of O_2 resulted in the progress of the reaction, which is in good agreement with the results of MS analyses.

Most likely, oxygen species at the redox sites of CeO_2 are the reactive oxygen species. It is known that the concentration of redox sites on CeO_2 can be estimated by FTIR spectroscopy with CH_3OH as a probe molecule.^[10] According to a previous report by Lavalley and co-workers, methanol is dissociated into methoxy species and H^+ on CeO_2 and the band of methoxy species around 970–1085 cm^{-1} is assigned to the potential redox sites on CeO_2 . To examine the correlation between the reaction rates and the amount of redox sites, we performed catalytic tests and FTIR experiments with CeO_2 samples (Table S1 and Figure S3) calcined at different temperatures (Figure 2b). The bands at 1107, 1052, and 1032 cm^{-1} were observed on all CeO_2 samples and assigned to $\nu(\text{C}-\text{O})$ at on-top, doubly bridged, and triply bridged sites, respectively. The redox site amount (mmol g^{-1}) on CeO_2 was calculated from the band around 970–1085 cm^{-1} and the absorption coefficient of the methoxy species (6.9 $\text{cm}^2 \text{mmol}^{-1}$).^[10] A good linearity between the reaction rates and redox site amount was obtained (Figure 2c). This indicates that oxygen species at the redox sites of CeO_2 are active species for the oxidative dehydrogenation of benzyl alcohol, and that this step is the rate-determining step. Above all, we demonstrated for the first time that the redox property of CeO_2 can function in the liquid-phase organic reaction at low temperature.

A plausible reaction mechanism of imine formation from benzyl alcohol and aniline on CeO_2 is proposed (Scheme 2): oxidative dehydrogenation of benzyl alcohol with oxygen species occurs on the redox sites of CeO_2 and Ce will be reduced from tetravalent (+4) to trivalent (+3). The produced benzaldehyde reacts with aniline over CeO_2 to afford the corresponding imine. CeO_2 is regenerated by oxidation of the reduced CeO_2 with O_2 .



Scheme 2. Proposed reaction mechanism over CeO_2 .

Finally, the scope of alcohols and amines in the CeO_2 -catalyzed imine synthesis was examined (Table 2). Benzyl alcohol and substituted benzyl alcohols bearing an electron-donating or -withdrawing group (entries 1 and 6–9) reacted with aniline to afford the corresponding imines in high yields. *o*-Methyl benzyl alcohol (entry 9) required a longer reaction time, which could be due to the steric hindrance of the methyl group at the *o*-position. Moreover, the imine formation from benzyl alcohol and aniline could be performed under the stoichiometric condition of amine/alcohol = 1 (entry 2) or under nonsolvent conditions (entry 3). Aniline derivatives bearing an electron-donating or -withdrawing group also reacted to afford the corresponding imines in high yields (entries 10–13). Furthermore, CeO_2 can be reused without remarkable loss of yield and selectivity at least three times (entries 1, 4, and 5). By inductively coupled plasma atomic emission spectroscopy (ICP-AES) no Ce species was detected in the solution after the reaction (< 0.1 %). Therefore, CeO_2 is an intrinsically reusable heterogeneous catalyst.

Table 2: Scope of alcohols and amines for the imine synthesis.^[a]

$\text{R-OH} + \text{Ph-NH}_2 \xrightarrow[333 \text{ K, air}]{\text{CeO}_2} \text{R=N-Ph} + \text{H}_2\text{O}$				
Entry	Alcohol	Amine	Yield [%]	Selc. [%]
1			96 (93 ^[g])	97
2 ^[b]			80	89
3 ^[c]			99	> 99
4 ^[d]			90	97
5 ^[e]			92	98
6			98	98
7			91	95
8			95	95
9 ^[f]			83	92
10			96	98
11			90	91
12			98	99
13 ^[f]			92	96

[a] Conditions: alcohol 1.0 mmol, amine 2.0 mmol, mesitylene 1.5 g, CeO₂ 50 mg, 333 K, 24 h, air. [b] Amine/alcohol = 1. [c] No solvent. [d] 1st reuse. [e] 2nd reuse. [f] 48 h. [g] Isolated yield.

In summary, we have demonstrated that CeO₂ acts as a reusable and efficient heterogeneous catalyst for the imine formation from benzyl alcohol and aniline even at 303 K and the activity is more than 38-fold higher than those of other simple metal oxides. Based on kinetic measurements as well as MS and FTIR spectroscopy, the high activity can be attributed to the redox properties of CeO₂ at low temperature. This is the first report of the redox property of CeO₂ functioning in organic reactions at low temperature of 303 K. These results could lead to new applications of CeO₂ in organic syntheses and bring about new design strategy of metal oxide catalysts.

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