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Enantioselective Hydrogenation of (E)-α-phenylcinnamic Acid over Cinchonidine-modified Pd Catalysts Supported on TiO_2 and CeO_2

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Abstract The effects of the catalyst support, reaction temperature, and concentration of the modifier were examined to optimize supported Pd-catalysts and reaction conditions for the achievement of higher enantiomeric excess in the hydrogenation of (E)-α-phenylcinnamic acid. Over 90% of enantioselectivity was achieved using a cinchonidine-modified 40 wt% Pd/TiO_2 catalyst at 288 K.

Keywords Enantioselective hydrogenation · Supported Pd catalyst

1 Introduction

Enantioselective hydrogenation of unsaturated organic compounds using heterogeneous solid catalysts has attracted much attention over the years as a useful reaction for the synthesis of enantiomers used as the raw materials of medicine, agricultural chemicals, and perfume compounds, etc. [1–3]. The enantioselective hydrogenation of unsaturated C=C bonds has been carried out industrially by using homogeneous chiral catalysts [4, 5]. However, heterogeneous catalysts with enough enantioselectivity have not been developed yet to put into practical use [1–3], although enantioselective hydrogenations of C=C bonds have been reported for the hydrogenations of (E)-2,3-diphenyl-2-propenoic acid [(E)-α-phenylcinnamic acid] over Pd/TiO_2 and Pd/Al_2O_3 catalysts [6], (E)-2-methyl-2-pentenoic acid over a Pd/Al_2O_3 catalyst [7], and ethyl-2-oxopropanate (ethyl pyruvate) over Pt/Al_2O_3 catalysts [8], all the catalysts being modified with cinchonidine (CND). The influence of many factors in the catalyst preparation and reaction conditions remains to be clarified, in contrast to the hydrogenations of the C=O double bonds in α- and β-keto esters with modified Pt and Ni catalysts, respectively [2, 3, 9]. Little has been known about a suitable surface state of Pd metal, although the metal-particle morphology is thought to be of greater importance for these reactions. To develop heterogeneous enantioselective catalysts, it is important to find the optimum preparation of the catalysts and the reaction conditions. Concerning the modifier structure, it has been shown that the most stable conformation of CND depends on the solvent polarity [3, 9, 10]. Therefore, it is considered that the modifier–substrate interaction, and hence the adsorption mode of the adducts on Pd surface, may be influenced by the morphology and surface state of Pd particles.

In the present study, enantioselective hydrogenation of (E)-α-phenylcinnamic acid (PCA) [11–17] was examined using CND-modified supported Pd catalysts prepared by an impregnation method. The effects of the catalyst support, reaction temperature, and concentration of the modifier were examined to find optimum catalysts and reaction conditions which yield higher enantiomeric excess (e.e.) of S enantiomer.

2 Experimental

Supported Pd catalysts were prepared by an impregnation method. Pd[$(NH_3)_4Cl_2$] H_2O, Pd$(NO_3)_2$, and Pd$(CH_3COO)_2$

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were used as a precursor, and TiO_2 (JRC-TIO-3, rutile, surface area: 40 m^2 g^{-1}) and CeO_2 (JRC-CEO-3, surface area: 81 m^2 g^{-1}) were used as a support. The catalysts prepared were dried at 373 K for 1 day, and then calcined at 673 K for 4 h. The catalysts were reduced in an H_2/He flow (5% H_2, 133 cm^3 min^{-1}) at 473 K for 1 h before the reaction. The modifier (CND) dissolved in a solvent (2.5% H_2O-1,4-dioxane) was added to the reduced catalyst, and then the catalyst suspension was stirred in an atmospheric pressure of H_2 as a pretreatment. The reactant (PCA) and additive (benzyl amine: BA), when used, in the solvent was added to the catalyst suspension at the reaction temperature (288–318 K) to start the reaction. PCA and BA were commercially supplied (Kanto Kagaku) and used as received. A batch reaction system was used for the hydrogenation reaction. The reaction rate was evaluated from the hydrogen consumption rate at 20% of PCA conversion. The reaction temperature was set at 318 K, when otherwise noted. The reaction products were analyzed using HPLC after esterification with methyl alcohol.

The enantiomeric excess (e.e.) of the products was defined as the following equation:

$$\text{e.e.}(\%) = \{[S] - [R]/[S] + [R]\} \times 100$$
$$([S], [R] : \text{amount of } S(R) \text{ enantiomer})$$

In the present study, the e.e. values at a 100% conversion of PCA are reported. By the extraction of CND from the used catalysts, it was found that 98% of CND was adsorbed on the catalyst surface, suggesting that the enantioselective hydrogenation occurs on the catalyst surface modified by CND.

Dispersion of Pd metal particles on supported Pd catalysts was evaluated on the basis of the CO adsorption capacity using a pulse technique. After reduction in the 5% H_2/He stream, the reduced catalysts were flushed with a high purity He stream at room temperature. Then a CO pulse was periodically injected in the carrier gas. The Pd dispersion was estimated from the amount of chemisorbed CO, assuming a CO/Pd ratio of 1:2.

In situ Pd K-edge XAFS spectra for the supported Pd catalysts and reference compounds were measured in a transmission mode at room temperature at BL14B2 in SPring-8 with 8.0 GeV ring energy and 100 mA stored current [18] (proposal No. 2007B1963, 2008A1848). The synchrotron radiation was monochromatized by a Si (111) double-crystal monochromator. The reduced sample was transferred to an EXAFS cell in the presence of the H_2/He. The EXAFS data were analyzed assuming a spherical wave approximation and a single scattering model. The EXAFS data were Fourier-transformed from k-space (30–180 nm^{-1}) to R-space. The empirical backscattering amplitude and phase shift for Pd–Pd pairs was extracted from EXAFS data for Pd foil. The averaged particle size and dispersion of Pd particles were estimated from the Pd–Pd coordination number assuming spherical Pd particles [19].

3 Results and Discussion

3.1 Catalytic Properties of Pd/TiO_2 for Enantioselective Hydrogenation

In the previous studies, we have found that TiO_2 supported Pd catalysts show high enantioselectivity of PCA hydrogenation [11]. So, we first tried detailed optimization of the preparation conditions of TiO_2-supported impregnation catalysts and reaction conditions. Figure 1 shows the dependence of e.e. on the PCA concentration for enantioselective hydrogenation on CND-modified Pd/TiO_2 catalysts with varying Pd loadings. The enantioselectivity, e.e., of Pd/TiO_2 was gradually increased with the increase of Pd loading up to 30–40 wt% of Pd and was decreased by the increase of PCA concentration at a fixed amount of CND (0.15 mol L^{-1}). Figure 1 suggests that the high Pd loading catalysts show a high enantioselectivity in the case of the impregnation catalysts. It should be noted that 73–74% of e.e. was attained for the 30–40 wt% Pd/TiO_2 catalysts at a low PCA concentration.

Figure 2 shows the e.e. and reaction rate as a function of the CND concentration for the enantioselective hydrogenation on a CND-modified 40 wt% Pd/TiO_2 catalyst. It is manifest from Fig. 2 that in a low concentration region of CND, the catalyst showed a low e.e., while the selectivity was drastically increased at a CND concentration of 1 mmol L^{-1} or higher, accompanying a gradual increase of the reaction rate. It is speculated that a modifier arrangement on the surface of the Pd particles depends on the concentration of CND. That is, it is considered that in the high CND concentration region, the selective hydrogenation proceeds

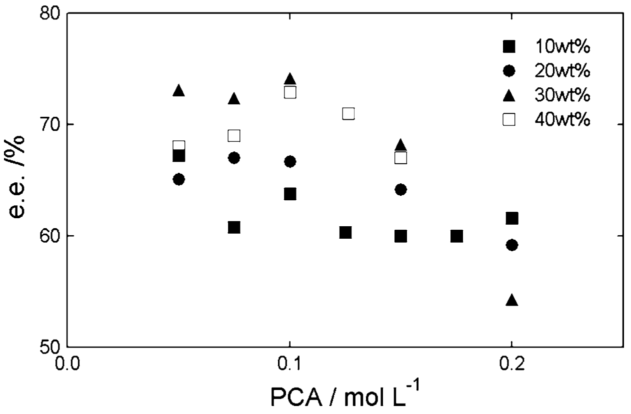

Fig. 1 Dependence of e.e. on the PCA concentration for the enantioselective hydrogenation of PCA on a CND-modified Pd/TiO_2 catalyst (CND 15 mmol L^{-1}, 318 K)

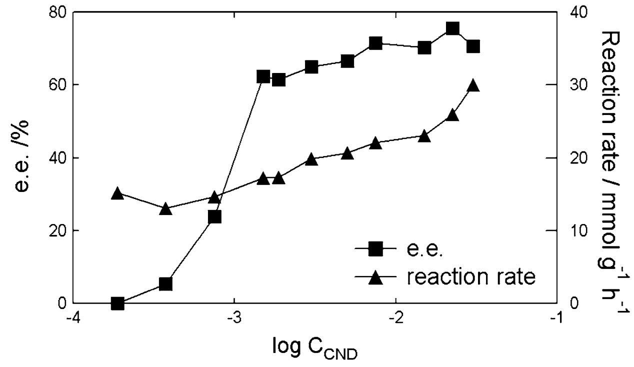

Fig. 2 e.e. and reaction rate as a function of the CND concentration C_{CND} (mol L^{-1}) for the enantioselective hydrogenation of PCA on a CND-modified 40 wt% Pd/TiO_2 catalyst (PCA 75 mmol L^{-1}, 318 K)

at the surface sites of Pd particles in which adsorbed CND molecules are self-assembled to provide an environment suitable for the enantioselective hydrogenation. The increase of the reaction rate with CND concentration indicates the formation of such active sites suitable for the enantioselective hydrogenation. However, in the low CND concentration region, it is suggested that CND adsorbs on the Pd particles in a parallel mode to the surface, leading to a lower enantioselectivity. The dependence of the adsorption mode of the aromatic ring compound (CND) on the surface concentration is supported by the studies using NEXAFS, STM, and ATA-IR [20–23]. About 71–75% of e.e. was obtained at a high CND concentration and the selectivity was comparable or even higher than that reported by far [11].

Figure 3 shows the dependence of e.e. on the Pd loading for the Pd/TiO_2 catalysts prepared by using various precursors of Pd. It is apparent that the catalysts prepared from $[Pd(NH_3)_4]Cl_2$ show higher e.e. than that of the catalysts prepared from other precursors. In particular, in the range of low Pd loading, the e.e. values of the catalysts prepared from $Pd(NO_3)_2$ and $Pd(CH_3COO)_2$ were considerably lower than that from $[Pd(NH_3)_4]Cl_2$.

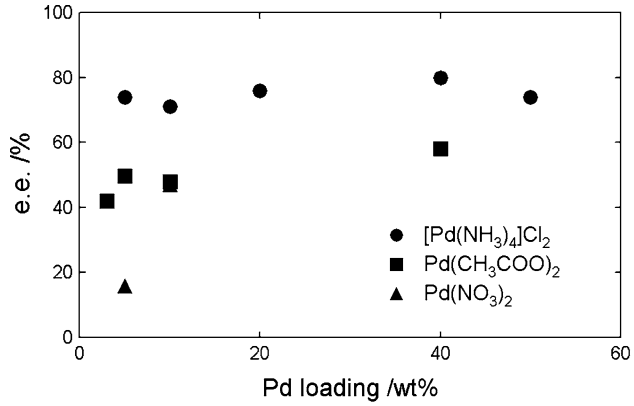

Fig. 3 Dependence of e.e. of the hydrogenation of PCA on the Pd loading for the supported Pd catalysts prepared by using various Pd precursors (PCA: 75 mmol L^{-1}, CND: 15 mmol L^{-1}, 318 K)

To investigate the effects of the pretreatment of a Pd/TiO_2 catalyst on the catalytic property, the e.e. and reaction rate are listed in Table 1 for the enantioselective hydrogenation on CND-modified 40 wt% Pd/TiO_2 catalysts reduced at varying temperature. It was found that the reduction of the catalyst at 473 K for 1 h is the best pretreatment condition in agreement with 5% Pd/TiO_2 catalysts prepared by a deposition method [15, 17], suggesting that the severe reduction conditions cause excessive sintering of Pd particles, while the mild conditions cause insufficient reduction of Pd particles and insufficient removal of surface impurities such as Cl^-. From these results, it is considered that the surface states and size of Pd particles are expected to be key properties for the enantioselectivity. Figure 4 shows the dependences of e.e. and dispersion of Pd particles on the Pd loading of

Table 1 The e.e. value and reaction rate for the enantioselective hydrogenation of PCA on a CND-modified 40 wt% Pd/TiO_2 catalyst reduced in a 5% H_2/He stream; PCA 75 mmol L^{-1}, CND 15 mmol L^{-1}

Temperature (K)	Reduction time (*h*)	e.e. (%)	Reaction rate (mmol g^{-1} h^{-1})
473	0.5	68	7
	1	70	23
	2	60	13
573	0.5	58	17
	1	65	14
	2	61	11
673	0.5	52	9
	1	57	9
	2	46	6

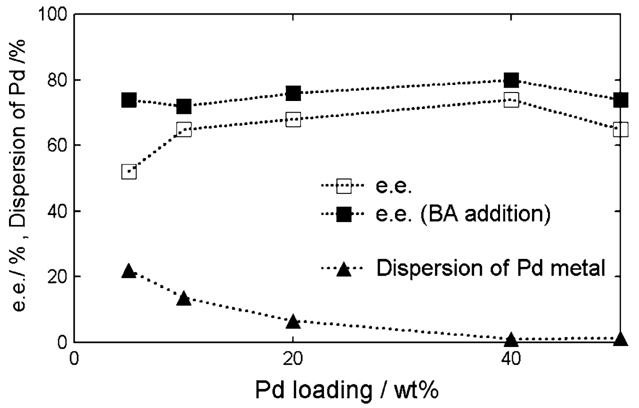

Fig. 4 e.e. of the hydrogenation of PCA with and without BA addition and dispersion of Pd particles against Pd loading for the Pd/TiO_2 catalysts. (PCA 75 mmol L^{-1}, CND 15 mmol L^{-1}, BA: 50 mmol L^{-1}, 318 K)

the Pd/TiO_2 catalysts. The dispersion of Pd particles was monotonically decreased with Pd loading. On the other hand, e.e. was mildly increased with increasing Pd loading irrespective of a BA addition in the range of Pd loading <40 wt%, and decreased at a higher Pd loading. The increase in the e.e. by the BA addition is ascribed to the increased desorption rate of the products, resulting in the increase of the reaction rate on the modified active sites and hence the selectivity [14, 24]. On the basis of these results, we adopted a 38 wt% Pd/TiO_2 supported catalyst for further experiments to achieve higher e.e.

Figure 5 shows the dependence of e.e. and reaction rate on the reaction temperature for enantioselective hydrogenation of PCA on a CND-modified 38 wt% Pd/TiO_2 catalyst. The e.e. value increased with decreasing reaction temperature and reached 91% at 288 K. It is speculated that the increase of e.e. is caused by a decrease of thermal fluctuation of the interactions between the substrate and the modifier on the catalyst surface. It is worth noting that over 90% of enantioselectivity was achieved with excellent reproducibility under the conditions of reaction temperature 288 K and BA addition. The reaction rate of the hydrogenation of PCA without a BA addition was decreased by the decrease of the reaction temperature as expected. However, when BA was added to the reaction system, the reaction rate was not changed by the temperature, suggesting that the absorption and/or diffusion of hydrogen is the rate determining step in this reaction system. On the other hand, the reaction rate was extremely increased by the BA addition, indicating an acceleration of the reaction on the modified active sites as mentioned in Fig. 4 and in agreement with Nitta [13].

3.2 Catalytic Properties of Pd/CeO_2 for Enantioselective Hydrogenation

Although it has been reported that supported Pd catalysts show high enantioselectivity [1, 14], the effects of supports have not been extensively studied on the enantioselective hydrogenation reaction [25]. In the present study, we investigated Pd catalysts supported on CeO_2 to get more detailed insights into the support effects on the enantioselective hydrogenation. Figure 6 shows the dependence of e.e. with and without BA addition and the dispersion of Pd particles on the Pd loading for the Pd/CeO_2 catalysts. Comparing with Pd/TiO_2 (Fig. 4), Pd/CeO_2 catalysts show a higher dispersion of Pd particles even at the same surface density of Pd, indicating a stronger metal-support interaction between Pd metal particles and CeO_2 surface. However, the e.e. value of Pd/CeO_2 was much lower than that of Pd/TiO_2. It is considered that the lower e.e. of Pd/CeO_2 may be attributed to the strong metal-support interaction, modifying the electronic state/morphology of Pd metal particles.

To clarify the difference between Pd/TiO_2 and Pd/CeO_2, the dependence of e.e. and reaction rate on the CND concentration is shown in Fig. 7 for 20 wt% Pd/CeO_2 with and without BA addition. It was found that there is an optimum amount of CND. Furthermore, the effect of BA addition on e.e. was smaller in a low CND concentration region (see also Fig. 6). In a high CND concentration region, however, the effect of BA addition on e.e. was increased, suggesting the acceleration of the reaction on the modified active sites by the acceleration of the desorption of the products [13].

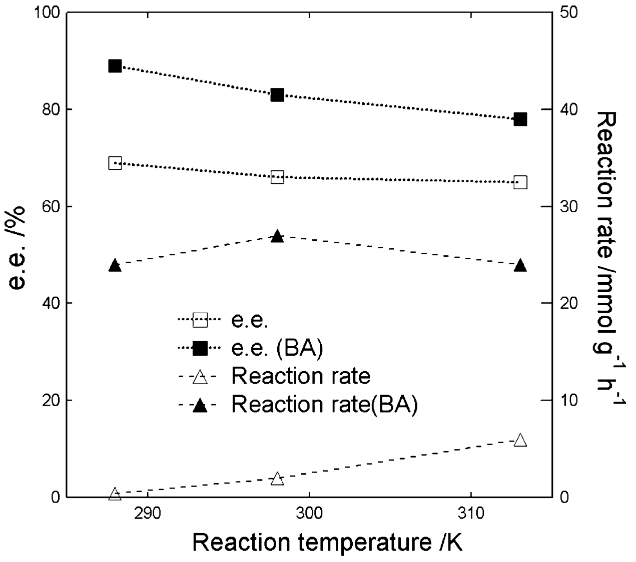

Fig. 5 Dependence of the e.e. and reaction rate on the reaction temperature for the enantioselective hydrogenation of PCA on a CND-modified 38 wt% Pd/TiO_2 catalyst. (PCA: 75 mmol L^{-1}, CND: 15 mmol L^{-1}, BA: 50 mmol L^{-1})

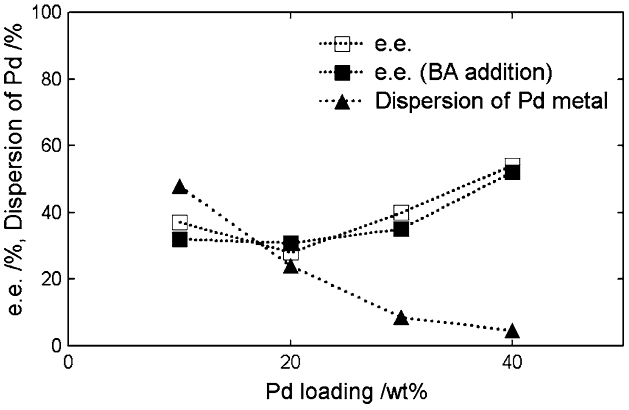

Fig. 6 e.e. of the hydrogenation of PCA with and without BA addition and the dispersion of Pd particles as a function of the Pd loading for the Pd/CeO_2 catalyst (PCA 75 mmol L^{-1}, CND 15 mmol L^{-1}, BA 50 mmol L^{-1}, 318 K)

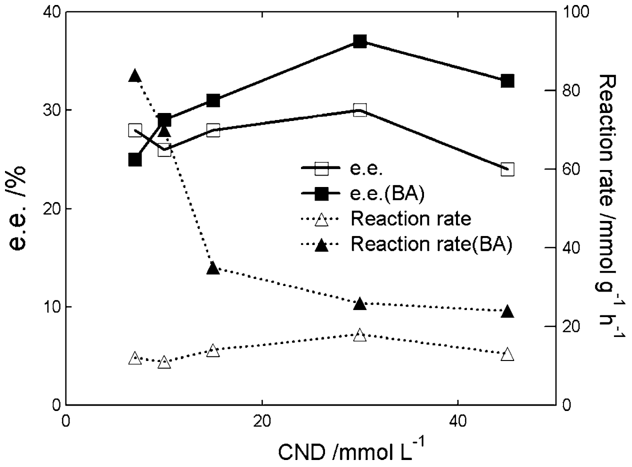

Fig. 7 Dependence of e.e. of the hydrogenation of PCA with and without BA addition and the reaction rate on the CND concentration for 20 wt% Pd/CeO_2. (PCA: 75 mmol L^{-1}, CND: 15 mmol L^{-1}, BA: 50 mmol L^{-1}, 318 K)

A similar trend was observed for TiO_2 supported catalysts as shown in Fig. 2.

At a low CND concentration (<15 mmol L^{-1}), the reaction rate was greatly increased by the BA addition. This effect cannot be explained simply in terms of the acceleration of the desorption of the products from the modified active sites by the addition of BA [13]. It is considered that BA addition causes not only the acceleration of the desorption of the products, but also the formation of the self-assembled arrangement of adsorbed CND molecules, favorable active site structure for the enantioselective hydrogenation of PCA, on the surface of Pd particles, as discussed above. It is speculated that the self-assembled arrangement of CND formed by the addition of BA may increase the fraction of unmodified active sites and then the reaction rate there, resulting in a decrease of e.e. by BA addition. On the other hand, the BA addition promotes the formation of the self-assembled arrangement of CND and increases the reaction rate on the modified sites, leading to the greatly enhanced reaction rate in Fig. 7. Both effects of BA are competitive at a low CND concentration.

3.3 Support and Structural Effects of Pd Particles on Catalytic Properties

In our previous study on the enantioselective hydrogenation of PCA on Pd/TiO_2, the Pd dispersion dependence was examined for both polar and non-polar solvent [11]. From the results of Figs. 4 and 6, it is suggested that there is a correlation between the e.e. values and the dispersion of Pd particles. Figure 8 shows the relationships between the e.e. values with and without BA addition and the dispersion of Pd particles for the TiO_2- and CeO_2- supported Pd catalysts. It is manifest that there is a tendency of e.e. to increase with increasing particle size of Pd metal. We reported that the e.e. value in the hydrogenation of PCA shows a maximum at the dispersion of about 0.2 and that e.e. was significantly decreased below 0.2 [11]. The

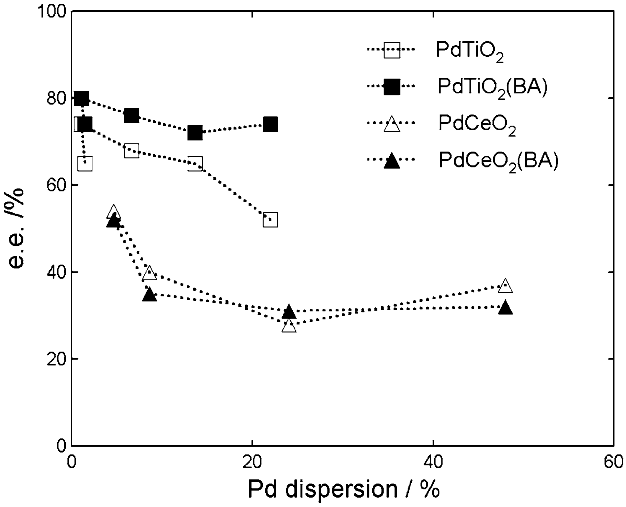

Fig. 8 Relationship between e.e. and the dispersion of Pd particles of the Pd catalysts for the hydrogenation of PCA with and without BA addition (PCA 75 mmol L^{-1}, CND 15 mmol L^{-1}, BA 50 mmol L^{-1}, 318 K)

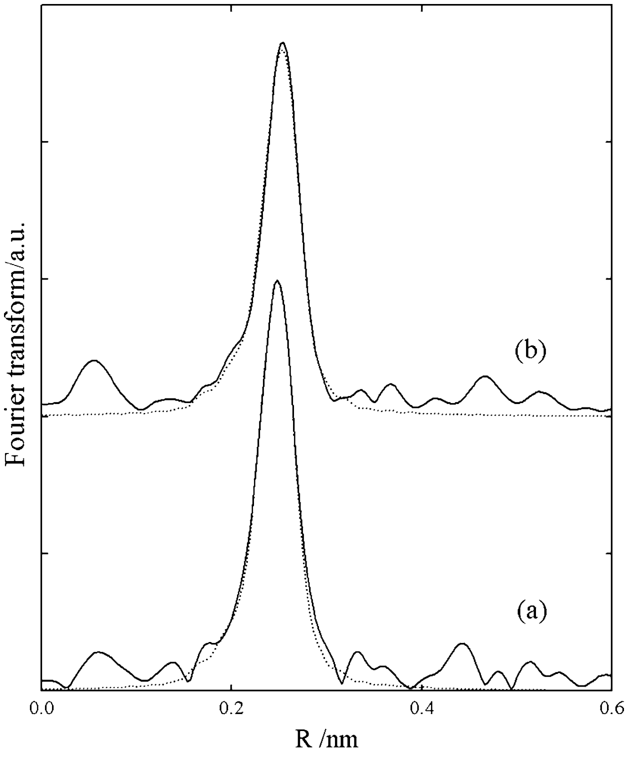

Fig. 9 Fourier transforms of k^3-weighted Pd K-edge EXAFS oscillations of 38 wt% Pd/TiO_2 a and 20 wt% Pd/CeO_2 b. *Dotted lines* present the best fitting result in the analysis

Table 2 Structural parameters obtained by the Pd K-edge EXAFS curve fitting analysis for supported Pd catalysts

Sample	Shell	N	R (nm)	σ (10^{-3} nm)	ΔE (eV)	R_f (%)	R^a (nm)	D^b (%)
38 wt% Pd/TiO_2	Pd–Pd	9.6	0.2795	7.8	−1.5	0.9	26	54
20 wt% Pd/CeO_2	Pd–Pd	8.6	0.2837	7.6	0.07	0.2	20	63
Pd foil	Pd–Pd	12	0.2770	6.0	–	–	–	–

FT range 30–180 nm^{-1}, Inv. FT range 0.10–0.32 nm

N coordination number, R inter-atomic distance, σ Debye–Waller factor, ΔE_0 inner potential, and R_f R-factor

[a] Averaged particle size of Pd particles estimated from the Pd–Pd coordination number assuming spherical Pd particles [18]

[b] Dispersions of Pd particles estimated from the Pd–Pd coordination number assuming spherical Pd particles [18]

structure sensitivity of e.e. in Fig. 8 is, however, smaller even in the dispersion range below 0.2 compared with the previous study, although a similar trend was observed. It is considered that the difference in the preparation method (precipitation–deposition method [11] vs. impregnation method) may change the structure sensitivity of the reaction selectivity. It is worth noting in Fig. 8 that the metal-support interaction between Pd metal and CeO_2 surface has a strong detrimental effects on the enantioselective hydrogenation of PCA.

Pd K-edge EXAFS of supported Pd catalysts was analyzed to investigate the local structure of Pd atoms for 38 wt% Pd/TiO_2 and 20 wt% Pd/CeO_2. The results of analysis are presented in Fig. 9 and Table 2. With both catalysts, Pd atoms form metal particles as suggested by the FT peak assigned to a Pd–Pd shell (ca. 0.280 nm, phase shift uncorrected). The inter atomic distance between Pd–Pd of the catalysts was longer than that of Pd metal foil (0.277 nm). This increase in the bond length is attributed to the absorption of hydrogen into the Pd particles [26]. The averaged Pd particle size of the Pd/TiO_2 catalyst was larger than that of Pd/CeO_2 in agreement with the results of CO adsorption capacity. However, the ratio of the dispersion (D_{TiO2}/D_{CeO2}) shows a very large difference between the CO adsorption experiment and EXAFS analysis (0.04 and 0.86, respectively). This difference may suggest an agglomeration of Pd metal crystals (26 nm) in 40 wt% Pd/TiO_2 to form larger metal particles on the support surface, resulting in a lower amount of surface sites for the adsorption of CO molecules.

4 Conclusions

1. Over 90% of enantioselectivity was achieved under the conditions of reaction temperature 288 K and BA addition.
2. It was found that Pd/CeO_2 catalysts show a lower enantioselectivity than Pd/TiO_2. It is considered that strong metal-support interaction is not favorable for the enantioselective hydrogenation.
3. The e.e. value increased with the loading of Pd and hence the size of Pd metal particles increased, suggesting that the selective hydrogenation takes place at a low index plane [like (111)] of Pd particles modified by self-assembled cinchonidine ad-layer.

These observations suggest that the improvement of e.e. can be achieved by a further optimization of the reaction conditions

References

1. Nitta Y (2006) J Synthetic Org Chem Jpn 64:827
2. Blaser HU, Studer M (2007) Acc Chem Res 40(1):348
3. Mallat T, Orglmeister E, Baiker A (2007) Chem Rev 107:4863
4. Shimizu H, Nagasaki I, Matsumura K, Sayo N, Saito T (2007) Acc Chem Res 40:1385
5. Johnson NB, Lennon IC, Moran PH, Ramsden JA (2007) Acc Chem Res 40:1291
6. Szöllösi G, Hermán B, Felföldi K, Balazsik K, Fülöp F, Bartók M (2008) J Mol Catal A 290:54
7. Kun I, Torok B, Felfordi K, Bartók M (2000) Appl Catal A 203:71
8. Margitfalvi JL, Talás E, Zsilab F, Kristyán S (2007) Tetrahedron Asymmetry 18:750
9. Osawa T, Harada T, Takayasu O (2000) Top Catal 13:155
10. Bürgi T, Baiker A (1998) J Am Chem Soc 120:12920
11. Nitta Y, Kubota T, Okamoto Y (2004) J Mol Catal A 212:155
12. Nitta Y, Kobiro K (1996) Chem Lett 28:897
13. Nitta Y (1999) Chem Lett 28:635
14. Nitta Y (2000) Top Catal 13:179
15. Nitta Y, Kubota T, Okamoto Y (2000) Bull Chem Soc Jpn 73:2635
16. Nitta Y, Kubota T, Okamoto Y (2001) Bull Chem Soc Jpn 74:2161
17. Nitta Y, Watanabe J, Sugimura T, Okuyama T (2005) J Catal 236:164
18. Kubota T, Okamoto Y (2001) J Synchrotron Rad 8:645
19. de Graaf J, van Dillen AJ, de Jong KP, Koningsberger DC (2001) J Catal 203:307
20. Bonello JM, Lindsay R, Santra AK, Lambert RM (2002) J Phys Chem B 106:2672

21. Wahl M, von Arx M, Jung TA, Baiker A (2006) J Phys Chem B 110:21777
22. Schmidt E, Ferri D, Baiker A (2007) Langmuir 23:8087
23. Bürgi T, Baiker A (2002) J Catal 210:160
24. Szöllösi G, Hanaoka T, Niwa S, Mizukami F, Bartók M (2005) J Catal 231:480
25. Nitta Y, Kobiro K, Okamoto Y (1997) Stud Surf Sci Catal 108:191
26. Kubota T, Kitajima Y, Asakura K, Iwasawa Y (1999) Bull Chem Soc Jpn 72:673