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Enantioselective hydrogenation of α-phenylcinnamic acids over cinchonidine-modified Pd/C commercial catalysts

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Abstract Enantioselective hydrogenation of α-phenylcinnamic acid (PCA) and *p*,*p*′-dimethoxyphenylcinnamic acid (DMPCA) was studied over a variety of commercial 5 % Pd/C catalysts to reveal catalyst properties suitable for obtaining high enantioselectivity. The catalysts were characterized by CO adsorption, X-ray photoelectron spectroscopy (XPS), and transmission electron microscopy (TEM). It is confirmed that pretreatment at 353 K under atmospheric pressure of H_2 before modification with cinchonidine is very effective for all the Pd/C catalysts used here to improve the selectivity and reaction rate. It is suggested that the distribution of Pd metal particles is crucial to attain high selectivity (ee% = 79 ± 1 for PCA, 89 ± 2 for DMPCA): a uniform or eggshell-type distribution of Pd is more suitable than an egg-white or egg-yolk-type distribution. It is also suggested that the dispersion of Pd metal particles controls the enantioselectivity over cinchonidine (CD)-modified Pd/C catalysts. XPS techniques are proposed to provide a convenient method to find

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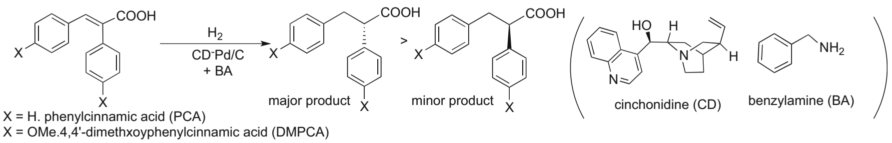
desirable catalysts. The choice of such Pd/C catalysts could facilitate high-throughput guided study on highly enantioselective hydrogenation of α,β-unsaturated carboxylic acids.

Keywords Enantioselective hydrogenation · Heterogeneous catalysis · Pd/C · Cinchonidine · α,β-Unsaturated carboxylic acid

Introduction

Enantiodifferentiating hydrogenation of prochiral ketones and olefins over heterogeneous metal catalysts modified with adsorbed chiral molecules has attracted much attention because of the prominent advantages of industrial application of solid catalysts, which enable easier separation of reactants and catalysts and easier handling and rejuvenation of catalysts, compared with corresponding homogeneous catalyst systems [1–9]. Nevertheless, heterogeneous enantioselective hydrogenation presents great opportunities for better understandings of two-dimensional molecular recognition chemistry on metal surface and thereby sufficient improvements of the selectivity and reaction rate of hydrogenation to meet industrial requirements. One prospective heterogeneous catalyst system is represented by cinchonidine (CD)-modified palladium catalysts for asymmetric hydrogenation of C=C double bonds of α,β-unsaturated carboxylic acids, such as α-phenylcinnamic acid (PCA) and *p*,*p*′-dimethoxyphenylcinnamic acid (DMPCA) (Scheme 1) [1–3, 10–13]. Addition of auxiliary achiral amine, for example, benzyl amine (BA), significantly improves the enantioselectivity as well as the hydrogenation rate [14], although the roles of the added amine are still under debate [10, 11, 15–20].

A variety of supported Pd catalysts have been used for enantiodifferentiating hydrogenation of PCA. Perez et al. [21] showed for the first time that PCA was enantioselectively hydrogenated over CD-modified 5 % Pd/C to produce (2*S*)-2,3-diphenylpropionic acid with moderate enantioselectivity of 30.5 % enantiomeric excess (ee). Later, Nitta and coworkers [10, 11, 22–24] extensively studied catalyst preparation to improve the enantioselectivity of the reaction. They found that a CD-modified 5 % Pd/TiO_2 catalyst prepared by a precipitation–deposition method was more active and selective (62 % ee) for hydrogenation of PCA (298 K) than SiO_2−, Al_2O_3−, or ZrO_2− supported Pd catalysts, when $PdCl_2$ was precipitated at 348 K by using Na_2CO_3 on nonporous TiO_2 and then the catalyst was reduced in H_2 flow at



Scheme 1 Enantioselective hydrogenation of α,β-unsaturated carboxylic acids over cinchonidine-modified Pd catalysts

473 K. More recently, Nitta and Kobiro [25] attained 72 % ee over homemade Pd/TiO_2 catalysts by optimizing PCA reaction conditions. Subsequently, Nitta [14] made prominent findings that, for PCA hydrogenation over 5 % Pd/TiO_2, the enantioselectivity could be greatly increased from 59 to 71 % ee by addition of BA under standard reaction conditions. Using Pd/TiO_2 prepared by an impregnation method, Kubota et al. [26] showed that CD-modified 38 % Pd/TiO_2 exhibited the record highest ee of 91 % for enantioselective hydrogenation of PCA at 288 K at a high CD/substrate ratio and in the presence of BA. CD-modified 5 % Pd/Al_2O_3 and Pd/CeO_2 were less selective and less active than TiO_2-supported Pd catalysts under the same reaction conditions, suggesting that strong Pd metal–support interactions are unfavorable for enantioselective hydrogenation.

Pd/C is widely used as a typical Pd metal catalyst supported on almost inactive support. Nitta et al. [22] showed that commercial and homemade Pd/C catalysts modified with CD were unexpectedly less active and less selective (10–21 % ee with PCA) than Pd catalysts supported on SiO_2, Al_2O_3, or TiO_2. However, more recently, the selectivity was reported to increase up to 49 % ee when an eggshell-type Pd/C catalyst was employed for hydrogenation of PCA [27]. The relatively low enantioselectivity of Pd/C catalysts were overcome by the finding by Nitta et al. [28] that a 5 % Pd/C commercial catalyst exhibited very high selectivity of 79 % ee for hydrogenation of PCA in the presence of BA only when the catalyst was pretreated at elevated temperature (353 K) in solvent under atmospheric pressure of H_2 prior to modification with CD, in contrast to 43 % ee without pretreatment. This pretreatment was found to be applicable to specially prepared homemade Pd/C catalysts having uniform or eggshell-type distribution of Pd, rendering them highly selective as observed with commercial Pd/C catalysts. On the other hand, the pretreatment was not very effective for Pd/TiO_2 or Pd/Al_2O_3. The establishment of the in situ pretreatment method has enabled us to use conventional commercial Pd/C for highly enantioselective hydrogenation of α,β-unsaturated carboxylic acids with high reproducibility without using specially designed and prepared homemade Pd metal catalysts such as Pd/TiO_2 [29, 30]. Kim et al. [31] reported that high enantioselectivity of PCA hydrogenation over CD-modified Pd/C catalysts could also obtained by successive evacuation–solvent injection–evacuation pretreatment before CD modification.

There are a variety of commercially available Pd/C catalysts, each of which is specially designed and prepared for certain reactions under specific reaction conditions. In our previous study [32], we proposed to employ commercial Pd/C catalysts for high-throughput screening research on enantioselective hydrogenation of α,β-unsaturated carboxylic acids. In the present study, we further extend this to provide more information on commercial Pd/C catalysts for enantioselective hydrogenation of PCA and DMPCA as representative substrates. It should be noted that our purpose is not to recommend any specific commercial products but to reveal the catalytic properties suitable for enantioselective hydrogenation from a scientific point of view.

Experimental

Catalysts

The catalysts employed in the present study were wet-form 5 % Pd/C commercial catalysts. Table 1 presents a list of the catalysts, some of which were already used in our previous study [32, 33]. The catalysts were donated by N.E. Chemcat Co. and Evonik Industries AG.

Hydrogenation procedures

The substrate α-phenylcinnamic acid (PCA, Aldrich; 98 %) was purified by recrystallization from acetone solution. *p*,*p*′-Dimethoxyphenylcinnamic acid (DMPCA) was synthesized from *p*-anisaldehyde and *p*-methoxyphenylacetic acid by the Perkin reaction and characterized by nuclear magnetic resonance (NMR), as reported previously [34]. Solvents (Wako Pure Chemicals; special grade), cinchonidine (CD, Wako Pure Chemicals; 99 %), and benzylamine (BA, Wako Pure Chemicals, 98 %) were used as received.

Enantioselective hydrogenation of PCA or DMPCA was conducted as reported in our previous study [28]. Typically, wet 5 % Pd/C (23 mg as dry form, 0.01 mmol of Pd) was pretreated in 5 ml wet dioxane (dioxane containing 2.5 % water) at 353 K under atmospheric pressure of H_2 for 30 min. After the catalyst had cooled to 296 K, CD (0 or 0.02 mmol) in wet dioxane was added to the catalyst. The resulting suspension was then stirred for 30 min, while the H_2 atmosphere was maintained. Next, the substrate (PCA or DMPCA, 0.5 mmol) and then BA (0.3 mmol) was injected into the reactor. Hydrogen uptake was measured, while the reaction solution was maintained under atmospheric pressure of H_2 in order to monitor the progress of the reaction. Hydrogenation rates were determined at 20–25 % conversion of the substrate. In another hydrogenation procedure, the catalyst and CD were prereduced at 296 K by stirring for 30 min in 5 ml of the solvent under H_2

Table 1 Dispersion of Pd in the commercial 5 % Pd/C catalysts used in the present study

Catalyst	Dispersion of Pd (%)
E-1	53
E-2	49
E-3	41
E-4	45
E-5	47
E-6	45
E-7	41
E-8	39
STD	59, 57[a] 76[b] (2.2 nm)[c]
AER	67[b]

[a] Ref. [33]

[b] Nominal dispersion

[c] Particle size from extended X-ray absorption fine-structure (EXAFS) analysis, Ref. [32]

atmosphere prior to substrate injection, followed by BA addition. This latter procedure is called "without the pretreatment" here.

The product ee% was determined via high-performance liquid chromatography (HPLC) [Daicel Chiralpak OJ-H; 25 cm × 4.6 mm; Hex/IPA/TFA = 95/5/0.1, retention times: 15.4 min (*R*) and 24.4 min (*S*) at a flow rate of 1 mL/min], and the final reaction conversions were determined via ^{1}H NMR (600 MHz) spectroscopy. After washing each portion with 1 N HCl, the reaction mixture was found to contain only the substrate and the corresponding hydrogenation products. The enantiomeric excess (ee%) was calculated according to the following equation:

$$\mathrm{ee\%} = 100 \times ([S]-[R])/([S]+[R]),$$

where [*S*] and [*R*] represent the concentrations of *S*- and *R*-enantiomers, respectively.

Catalyst characterizations

We used CO adsorption, XPS, and TEM to characterize the 5 % Pd/C catalysts. The dispersion of Pd metal particles on Pd/C was evaluated on the basis of CO adsorption capacity using a pulse technique [33]. Wet Pd/C was dried in air at 373 K for 24 h. A certain amount of dried Pd/C (20–50 mg) was placed in a U-shaped tube and purged with He for 10 min. The sample was then heated to 313 K in flowing He, then the He stream was replaced with a stream of H_2 for 10 min, followed by flushing with He for 10 min. CO pulses (4.1 μmol/pulse) were repeatedly injected at 313 K into the carrier gas (He) until no adsorption was detected (3–6 pulses). The Pd dispersion was estimated from the amounts of chemisorbed CO and Pd, assuming a ratio of 1:2 for chemisorbed CO/surface Pd atoms.

X-ray photoelectron spectra of the Pd/C catalysts as received were measured on a photoelectron spectrometer (CL 150, VSW Ltd.) using Mg K_α radiation (1253.6 eV, 450 W) [33]. The catalyst sample was pressed onto indium foil in air and transferred to a measurement chamber. The background pressure of the spectrometer was better than 2×10^{-7} Pa during the measurements. The binding energies were referenced to the C 1*s* level at 248.6 eV due to the carbon supports. The background of the spectra was removed by assuming a Shirley function.

Transmission electron microscopy (TEM) images were obtained using a Hitachi 8000 [32]. The sample was prepared by mounting the catalyst suspension onto carbon grids, followed by drying in ambient atmosphere. TEM images of the sample were observed at 200 keV to reduce any electron beam-induced damage.

Results and discussion

Table 1 lists the commercial Pd/C catalysts used in the present study. The Pd metal dispersions of the Pd/C catalysts are presented in Table 1, together with previous results for STD and AER [32, 33]. The dispersion of Pd metal in STD (59 %) is consistent with the previous value (57 %) [33], but slightly smaller than the nominal value (76 %). The dispersions of Pd metal in the commercial Pd/C catalysts examined here were considerably high, ranging between 30 and 60 % after H_2 treatment at 313 K.

TEM images of 5 % Pd/C were observed to provide qualitative information on the Pd metal particles supported on carbon. Representative images are presented in Fig. 1. For E-1, one can observe mainly well-dispersed particles with diameter of

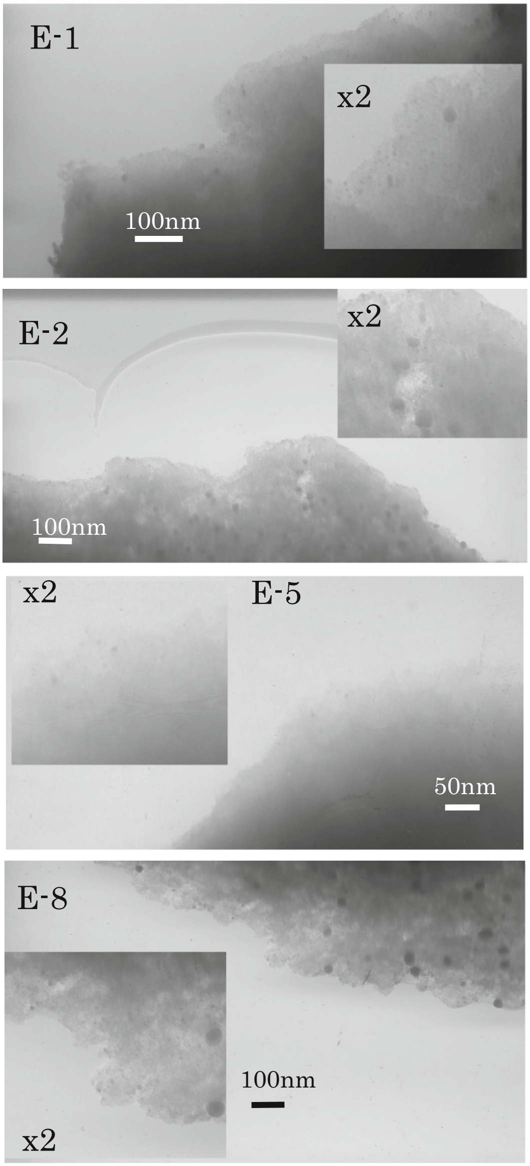


Fig. 1 TEM images of E-1, E-2, E-5, and E-8

3–4 nm, accompanying a small number of larger particles. Unfortunately, we failed to observe smaller particles (<3 nm) using the present TEM settings. Similar TEM images were observed for E-2, E-3, and E-4. As shown in Fig. 1 for E-2, most of the Pd particles in view are present as 20–30 nm particles, with fewer smaller particles of <4 nm. In the images of E-5, Pd metal particles are well dispersed (<3–4 nm) with almost no larger particles being observed. E-6 and E-7 showed TEM images similar to E-5. On the other hand, in the images of E-8 one can observe a homogeneous distribution of relatively large Pd metal particles of 20–30 nm in diameter. It should be noted that Pd metal particles of <3 nm escaped from the present TEM observations due to the limitation of resolution. With STD and AER, we previously reported TEM images showing that Pd metal particles of <2.5 nm were well dispersed on STD and AER, while some larger Pd metal particles were also observed to be present in the latter catalyst [32].

Table 2 Enantioselective hydrogenation of PCA on 5 % Pd/C: reaction rate and selectivity (ee)

Catalyst	Amount of CD added (mmol)	Without the pretreatment		With the pretreatment	
		r (mmol/g-h)	ee (%)	*r* (mmol/g-h)	ee (%)
E-1	0	132	–	82	–
	0.02	55	53	51	70
E-2	0	136	–	120	–
	0.02	64	49	74	75
E-3	0	114	–	102	–
	0.02	62	60	86	79
E-4	0	90	–	82	–
	0.02	40	47	47	72
E-5	0	136	–	128	–
	0.02	72	56	93	78
E-6	0	144	–	102	–
	0.02	64	49	77	78
E-7	0	108	–	111	–
	0.02	66	56	111	80
E-8	0	96	–	93	–
	0.02	53	58	84	80
STD	0	120	–	–	–
	0.02	47, 48[a,b]	58, 43[c], 42[a,b]	93[c,b], 93[a,b]	79[c,b], 81[a,b]
AER	0	–	–	–	–
	0.02	66[a,b]	41[a,b], 59[d]	102[c,b]	81[c,b]

[a] Ref. [33]

[b] Reaction conditions are the same except the amount of BA (0.5 mmol instead of 0.3 mmol in the present study) added to the reaction mixture

[c] Ref. [28]

[d] Ref. [32]

Hydrogenation reactions of PCA and DMPCA were conducted at 296 K over pristine (without CD modification) and CD-modified 5 % Pd/C catalysts with or without the pretreatment at 353 K. The reaction rate (*r*) and the enantioselectivity (ee) are summarized in Tables 2 and 3 for PCA and DMPCA, respectively. First, we compare the activities of pristine 5 % Pd/C (CD = 0 in Table 2) differently pretreated before the PCA hydrogenation to examine the effect of the pretreatment at 353 K under atmospheric H_2 on the reaction rate. It is noted that this reaction forms just racemic products, since this is a simple hydrogenation of the olefin on 5 % Pd/C. It is obvious that the reaction rate is reduced by 5–10 % by the pretreatment at 353 K, except for E-1 which shows a larger decrease and E-7 which exhibits even a 10 % increase. It is considered that the activity decrease can be ascribed to slight sintering of Pd metal particles during the pretreatment at elevated temperature. In fact, Kim et al. [32] noted with STD by use of EXAFS that the pretreatment induced a slight increase in the Pd–Pd coordination number. It is expected that Pd metal particles in E-1 experience more extensive sintering than the other 5 % Pd/C. The increase in the activity of E-7 may be ascribed to removal of a relatively higher level of impurities on the Pd metal surface under atmospheric pressure of H_2 at 353 K to compensate the possible sintering effect. However, further study is required to rationalize the specific behaviors of E-1 and E-7.

Table 3 Enantioselective hydrogenation of DMPCA on 5 % Pd/C: reaction rate and selectivity (ee)

Catalyst	Amount of CD added (mmol)	With the pretreatment	
		r (mmol/g-h)	ee (%)
E-1	0	20	–
	0.02	27	84
E-2	0	26	–
	0.02	28	86
E-3	0	30	–
	0.02	40	87
E-4	0	18	–
	0.02	14	85
E-5	0	37	–
	0.02	33	88
E-6	0	30	–
	0.02	36	88
E-7	0	27	–
	0.02	53	90
E-8	0	23	–
	0.02	41	91
STD	0	–	–
	0.02	32[a], 43[a,b]	89[a], 92[a,b]
AER	0	–	–
	0.02	60[a,b]	92[a,b]

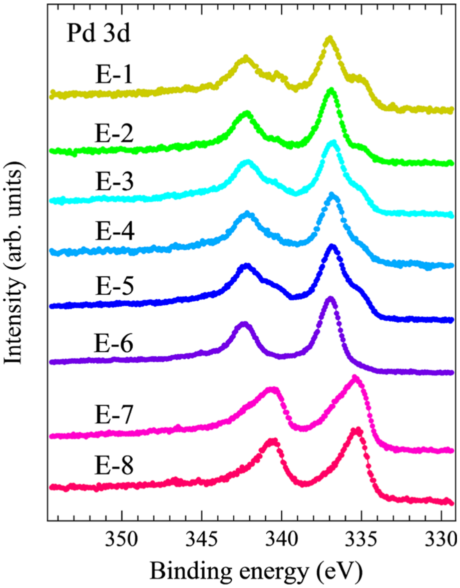
[a] Ref. [28]

[b] Reaction conditions are the same except the amount of BA (0.5 mmol instead of 0.3 mmol in the present study) added to the reaction mixture

As shown in Table 2, the hydrogenation activity of pristine Pd/C is considerably decreased by CD modification (CD = 0.02 mmol), obviously due to poisoning effects of the Pd metal surface by adsorbed CD molecules that suppress adsorption and subsequent hydrogenation of PCA. In contrast to the pristine Pd/C without CD modification, however, the pretreatment at 353 K under atmospheric pressure of H_2 increased the reaction rate of CD-modified Pd/C as well as the enantioselectivity, as reported previously [28]. Taking into account both the slight sintering of Pd metal particles and the great increase in selectivity by the pretreatment, it is considered that the simultaneous increases in the rate and selectivity are correlated to an increase in the number of favorable surface enantioselective ensemble sites created by adsorbed CD molecules, where the substrate (PCA) can be adsorbed through substrate–surface CD interactions and subsequently hydrogenated enantioselectively. It is considered that the H_2 pretreatment at 353 K causes removal of surface impurities and/or exposure of specific Pd metal facets to provide more abundant surface ensembles, allowing increased amounts of CD molecules to be adsorbed and thus an increased number of substrate–surface CD reaction intermediates. These surface changes by the pretreatment may also allow adsorption of more abundant CD molecules in a favorable configuration. It was well envisaged in our previous study [34, 35] that stronger interactions between the surface CD and a substrate induce higher "ligand acceleration" effects, accompanying enhanced hydrogenation rate and enantioselectivity.

Table 3 presents the reaction rate and selectivity of the enantioselective hydrogenation of DMPCA over CD-modified Pd/C pretreated at 353 K under atmospheric pressure of H_2. In contrast to the enantioselective hydrogenation of PCA, the hydrogenation rate is increased by CD modification. As revealed by

Fig. 2 Pd 3*d* XP spectra for a series of 5 % Pd/C commercial catalysts as received



Mameda et al. [34], the substrate DMPCA shows much stronger “ligand acceleration” effects (370 %) than PCA (130 %). It is obvious that the activity increase by CD modification in Table 3 results from the strong interactions between adsorbed CD molecules and DMPCA, thus reaching higher selectivity of up to 91–92 % ee than that of PCA (80–81 % ee). Szöllösi et al. [36, 37] reported as high a selectivity as shown in Tables 2 and 3 for enantioselective hydrogenation of PCA (80 %) and DMPCA (90 %) over CD-modified 5 % Pd/Al_2O_3 at 294 K.

The chemical state and dispersion/distribution of Pd species of the Pd/C catalysts were estimated using XPS. The X-ray photoelectron (XP) spectra of the Pd 3*d* level are presented in Fig. 2 for the series of as-received 5 % Pd/C catalysts listed in Table 1. The XP spectra for STD and AER have already been reported elsewhere [33]. It is noted that all the XP spectra were measured under ex situ conditions. The wide-scan spectra of the Pd/C catalysts showed no detectable impurities on the catalysts except oxygen. The Pd 3*d* spectra apparently show the presence of more than one Pd species. We found that the spectral envelopes were best fit by assuming two Pd components whose Pd $3d_{5/2}$ binding energies (BEs) are summarized in Table 4. The Pd species with Pd $3d_{5/2}$ BE of 335.3 eV is assigned to Pd metal, while the one at 336.9 eV is assigned to Pd^{2+} species, possibly PdO-like species [38], indicating that part of the Pd in the commercial 5 % Pd/C catalysts is oxidized as received or during storage. The fraction of Pd metal estimated by deconvolution is summarized in Table 4. Palladium is heavily oxidized in E-1 through E-6, while Pd metal prevails in E-7 and E-8. It is considered that the chemical states of Pd in the catalyst depend on the preparation procedures and history of sample handling and storage. We could not, however, find any correlation between the catalytic activity of 5 % Pd/C in Table 2 or 3 and the oxidation state of Pd in Table 4, indicating that the initial states of Pd are not very important in the present hydrogenations. Our

Table 4 XPS analysis of 5 % Pd/C commercial catalysts as received

Catalyst	BE of Pd $3d_{5/2}$ level (eV)		Fraction of Pd metal (%)	Pd 3*d*/C 1*s* XPS intensity ratio
	Metal	Oxides		
E-1	335.3	337.0	32	0.47
E-2	335.2	336.9	17	0.45
E-3	335.2	336.9	29	1.25
E-4	335.2	336.8	25	0.33
E-5	335.2	336.9	35	1.22
E-6	335.2	336.9	5	1.76
E-7	335.3	336.9	77	0.68
E-8	335.3	336.9	85	0.65
STD[a]	335.3	336.9	40	0.92
AER[a]	335.3	336.9	40	1.42

[a] Ref. [33]. The XPS intensity Pd $3d_{5/2}$/C 1*s* ratio in the reference is converted to the Pd 3*d*/C 1*s* ratio by multiplying the value by 10/6

previous EXAFS results showed that oxidized Pd species were readily reduced during the pretreatment at 353 K or even during the CD modification at the reaction temperature [32]. The TEM images of as-received Pd/C in Fig. 1 were discussed above by assuming the formation of "Pd metal particles" instead of the presence of PdO-like species; It is rational to assume that PdO-like particles in the Pd/C catalysts are readily reduced to Pd metal particles under electron beam flooding during TEM observation.

Together with the information on the chemical states of Pd, XPS can provide clear information on the dispersion and/or distribution of Pd in the supported catalysts by analyzing signal intensities, given that the supported amount of Pd is the same [39, 40]. With 5 % Pd catalysts supported on carbon, the XPS intensity ratio of the Pd 3*d* level due to the active species to that of the C 1*s* level due to the support, that is, the Pd 3*d*/C 1*s* XPS intensity ratio, reflects both the dispersion of Pd on the surface (particle size) and the distribution of Pd inside the catalyst particles (depth profile). Table 4 summarizes the Pd 3*d*/C 1*s* intensity ratio for the 5 % Pd/C catalysts used here together with those for STD and AER. It is noted that STD is a commercial catalyst with a uniform distribution of Pd, while AER has an eggshell-type distribution of Pd [33]. In agreement with the Pd distribution, AER shows a considerably higher Pd 3*d*/C 1*s* ratio than STD. Figure 3 shows a correlation of the Pd 3*d*/C 1*s* XPS intensity ratio and the dispersion of Pd in Table 1. The dotted line in Fig. 3 shows a correlation estimated for a uniform dispersion [39, 40], assuming that Pd is uniformly distributed in STD. The intensity ratios for E-7 and E-8 lie on the line, indicating that Pd metal particles are uniformly distributed in the catalyst particles in these catalysts, although the particle size of Pd metal is smaller in STD than in E-7 or E-8 (Table 1).

As shown in Fig. 3, the intensity ratios for E-3, E-5, and E-6 are far above the line, while the ratios for E-1, E-2, and E-4 are apparently below the line. It is concluded that E-3, E-5, and E-6 have an eggshell-type distribution of Pd, whereas

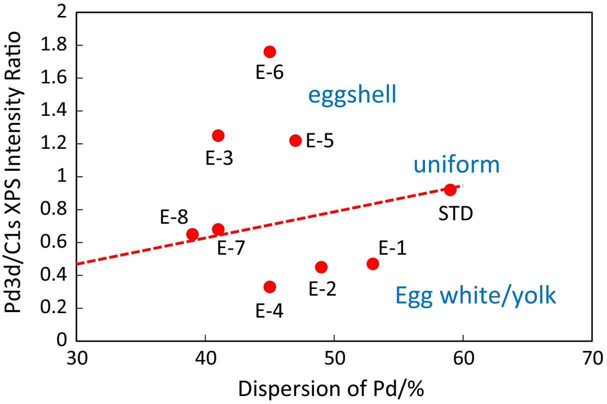


Fig. 3 Correlation between Pd 3*d*/C 1*s* XPS intensity ratio and Pd dispersion for 5 % Pd/C catalysts. The *dotted line* shows a correlation estimated for a uniform distribution of Pd, assuming a uniform distribution of Pd in STD

E-1, E-2, and E-4 have an egg-white- or egg-yolk-type distribution inside these catalyst particles. Considering that the catalyst particles are provided in fine powder form for the present catalysts, it is estimated that the Pd metal particles in E-1, E-2, and E-4 are embedded relatively deep in the pores of the support.

We now discuss the catalyst properties of 5 % Pd/C suitable for enantioselective hydrogenation of PCA or DMPCA. As presented in Tables 2 and 3, the enantioselectivity or ee% considerably depends on the catalyst and the pretreatment before the reaction. We confirmed in the present study the importance of the pretreatment of Pd/C at 353 K under atmospheric pressure of H_2 before modification with CD to obtain high selectivity as well as enhanced reaction rate [28]. Thus, we focus here on the enantioselectivity of the catalysts pretreated at 353 K.

It has been revealed that the selectivity of the enantiodifferentiating hydrogenation of PCA over CD-modified Pd catalysts depends on a variety of catalyst properties as well as the reaction conditions and pretreatments. Regarding catalyst properties, it is suggested that the selectivity and reaction rate are affected by the size and distribution of Pd metal particles [10, 11, 23, 41], the pore size of the support where Pd metal particles are embedded [27], and the support material, which may modify the Pd metal particle–support interactions and thereby adsorption properties of the substrate and modifier molecules involved [10, 11, 23, 24, 42, 43]. Nitta et al. [23, 41] revealed that, with CD-modified Pd/TiO_2, the highest selectivity for PCA hydrogenation was attained at moderate Pd dispersion of 20–25 %, with the selectivity gradually decreasing for higher or lower dispersion. However, as presented in Table 2, STD shows a very high ee at Pd dispersion of 59 %. Thus, the dependence of ee on the dispersion of Pd or the particle size of Pd metal is different between TiO_2- and carbon-supported Pd catalysts, as previously suggested by Kubota and coworkers [33]. A comparison between the selectivity (ee%) on CD-modified Pd/C pretreated at 353 K (Table 2 or 3) and the dispersion of

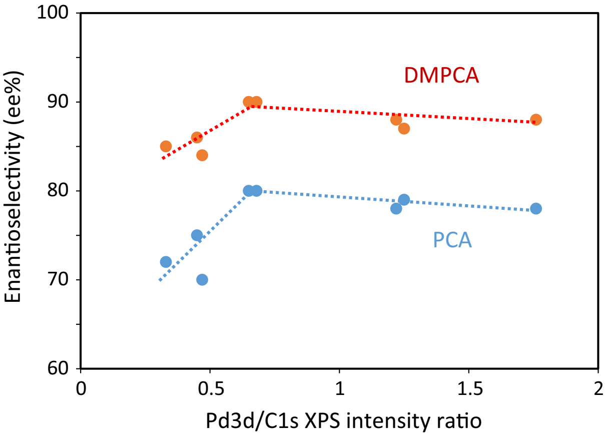


Fig. 4 Correlation between enantioselectivity of hydrogenation of PCA or DMPCA over CD-modified 5 % Pd/C and Pd 3*d*/C 1*s* XPS intensity ratio

Pd in Table 1 showed no simple correlation between the dispersions of 30 and 60 %, as presented in Fig. S1 (supplementary material) for PCA, suggesting that other factors may also be important in controlling the selectivity of the Pd/C catalysts in the enantioselective hydrogenation of PCA and DMPCA.

Figure 4 presents the enantioselectivities of the hydrogenation of PCA and DMPCA on CD-modified 5 % Pd/C as a function of the Pd 3*d*/C 1*s* XPS intensity ratio. It is highly significant that the selectivity is nicely correlated to the Pd 3*d*/C 1*s* ratio. The selectivity of PCA hydrogenation is high and remained almost constant at ee% = 79 ± 1 at Pd 3*d*/C 1*s* ratio >0.65, above which ratio Pd metal particles are uniformly distributed over the catalyst particles or have an eggshell-type distribution inside the catalyst particles, as presented in Fig. 3. On the other hand, the selectivity decreases to a moderate value at Pd 3*d*/C 1*s* ratio <0.65, where Pd metal particles are estimated to have an egg-white/yolk-type distribution inside the catalyst particles. For DMPCA hydrogenation, an identical correlation is obtained between the enantioselectivity and the Pd 3*d*/C 1*s* ratio, although the ee values are higher (ee% = 89 ± 2 at Pd 3*d*/C 1*s* ratio >0.65) than those for PCA hydrogenation. The high selectivities of the PCA and DMPCA hydrogenations on CD-modified STD and AER can also be ascribed to preferable distributions of Pd metal particles, that is, uniform and eggshell-type distributions, respectively. Thus, it can be concluded that the distribution of Pd metal in the catalyst particles is one of major catalyst properties determining the selectivity in the enantioselective hydrogenation over CD-modified Pd/C. Nitta et al. [23, 24] found that Pd/TiO_2 prepared using a nonporous TiO_2 support showed excellent selectivity, suggesting the effects of Pd location and/or distribution of Pd inside catalyst particles on the selectivity. In fact, Nitta and Okamoto [27] showed that Pd metal particles embedded into the mesopores of MCM-41 (pore diameter 2.2 nm) or KIT-1 (2.8 nm) exhibited considerably low selectivity in the hydrogenation of PCA, possibly due to strong steric hindrance to CD modification and/or to effective formation of surface intermediates involving CD and PCA. These findings are correlated to a moderate selectivity over the catalysts E-1, E-2, and E-4 with egg-white/yolk-type distribution of Pd metal particles, where these metal particles are expected to be located relatively deep in the small pores of the supports.

Scrutinizing the correlations in Fig. 4, however, it is likely that the ee values attained around Pd 3*d*/C 1*s* = 0.65 very slightly decrease as the intensity ratio increases, suggesting that, with uniform distribution catalysts, Pd metal particles with dispersion of 40 % (E-7, E-8) are more favorable for the hydrogenations than those with 59 % dispersion (STD). It is concluded that the enantioselectivity of CD-modified 5 % Pd/C depends on the particle size of Pd metal, but differently from the dependence for Pd/TiO_2 [23, 41]. Consequently, we propose that 5 % Pd/C catalysts with uniform or eggshell-type distribution of Pd metal particles, possibly with Pd dispersion of 40 %, can be selected for highly selective enantiodifferentiating hydrogenation of α,β-unsaturated carboxylic acids. These Pd/C catalysts could be used for high-throughput directed study in the development of enantioselective hydrogenation. In addition, the uniform correlations in Fig. 4 suggest that XPS techniques provide a very convenient method to select Pd/C catalysts suitable for enantioselective hydrogenation of α,β-unsaturated carboxylic acids.

Conclusions

We conducted enantioselective hydrogenation of α-phenylcinnamic acid (PCA) and *p*,*p*′-dimethoxyphenylcinnamic acid (DMPCA) over a variety of commercial 5 % Pd/C catalysts to find catalyst properties suitable for obtaining high enantioselectivity. It was confirmed that the pretreatment of as-received Pd/C at 353 K under atmospheric pressure of H_2 before modification with cinchonidine (CD) was very effective for all the Pd/C catalysts used here to improve the selectivity and reaction rate. On the basis of a correlation between the selectivity and the Pd 3*d*/C 1*s* XPS intensity ratio, we suggest that the distribution of Pd metal particles is a crucial catalyst property to attain high selectivity (ee% = 79 ± 1 for PCA, 89 ± 2 for DMPCA): a uniform or eggshell-type distribution of Pd is more desirable than an egg-white- or egg-yolk-type distribution. It is also suggested that the enantioselectivity of CD-modified 5 % Pd/C depends on the dispersion of Pd. We suggest that 5 % Pd/C catalysts with uniform or eggshell-type distribution and Pd dispersion of around 40 % could be used to facilitate high-throughput guided study on enantioselective hydrogenation of α,β-unsaturated carboxylic acids. We propose that XPS techniques provide a very convenient method to select Pd/C catalysts suitable for enantioselective hydrogenation of α,β-unsaturated carboxylic acids.

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