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Research Note

Activation-temperature dependence in enantioselective hydrogenation of unsaturated carboxylic acids over cinchonidine-modified Pd/C catalysts

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Abstract

The enantioselective hydrogenation of α,β-unsaturated acids catalyzed by cinchonidine-modified Pd/C was found to be highly dependent on the pretreatment temperature of the catalyst. An asymmetric yield as high as 92% was achieved in the hydrogenation of (*E*)-2,3-di(4-methoxyphenyl)propenoic acid using a conventional 5%Pd/C catalyst activated in situ at elevated temperatures before modification with cinchonidine.

Keywords: Enantioselectivity; Hydrogenation; Unsaturated carboxylic acid; Palladium catalyst; Cinchonidine; Activation temperature

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1. Introduction

The enantioselective hydrogenation of prochiral compounds with heterogeneous catalysts remains a challenging subject. So far, two types of catalysts—cinchona-modified platinum and tartaric acid-modified nickel—have been developed to convert ketones to the corresponding chiral alcohols at 97–98% enantiomeric excess (ee) [1]. Concerning the hydrogenation of prochiral olefins, cinchona-modified palladium (CM-Pd) catalysts have been shown to be effective [2–9], although their enantioselectivities are still moderate. At present, the highest ee measured was 94% in the hydrogenation of a pyrone derivative, which was achieved only under the condition of a very low (2/1) substrate/modifier ratio [10].

As for the hydrogenation of α,β-unsaturated carboxylic acids, (*E*)-2,3-diphenylpropenoic acid [α-phenylcinnamic acid (**1**)], one of the well-studied substrates, gives the highest enantioselectivity (71–72% ee) with a 5%Pd/TiO_2 catalyst prepared by a precipitation–deposition method with a non-porous titania [4,11,12]. Recently, we showed that the best ee improved to 82% in the hydrogenation of (*E*)-2,3-di(4-methoxyphenyl)propenoic acid (**2**) as a result of an approach designing the substrate structure to enhance the substrate–modifier interaction [13]. We also found that even a commercially available Pd/C catalyst could bring about a relatively high ee, up to 71%, when used under optimized conditions, although we previously reported that catalysts prepared with porous support materials were unfavorable for this kind of reaction [14]. Further improved ee of the hydrogenation of α,β-unsaturated carboxylic acids using conventional catalysts would be very useful, because it is handy and economical and also can avoid the difficulties in reproducibility expected in the reaction with the precipitated Pd/TiO_2 catalysts. In the present study we investigated the effect of the activation process of a commercially available Pd/C on the catalytic performance in enantioselective hydrogenations of **1** and **2** (Scheme 1).

2. Experimental

A carbon-supported Pd catalyst (5%Pd/C, STD type; N.E. CHEMCAT Co.) was mainly used in this study, with some other Pd/C catalysts used for comparison. Substrate **1** (Aldrich; 98%) was purified by recrystallization from an acetone solution, and substrate **2** was synthesized from *p*-anisaldehyde and *p*-methoxyphenylacetic acid by the Perkin reaction [15] and characterized by NMR. Solvents (Wako Pure Chemical; special grade), cinchonidine (CD) (Wako Pure Chemical; 99%),

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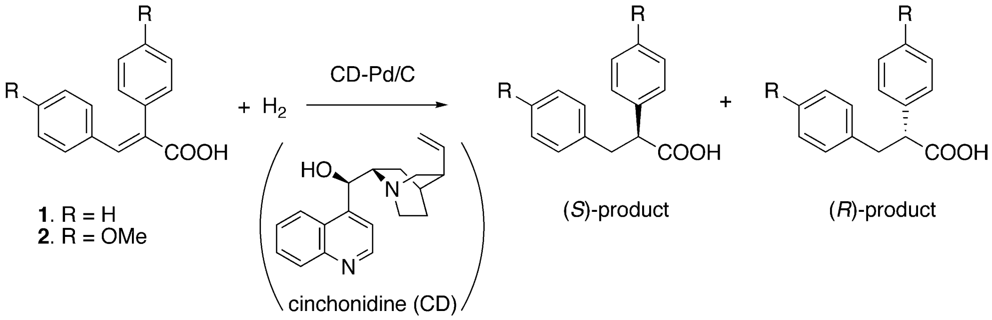

Scheme 1.

and benzylamine (BA) (Wako Pure Chemical; 98%) were used as received.

The hydrogenation was carried out in a magnetically stirred (1200 rpm) 50-ml glass reactor at room temperature (296 K) in 1,4-dioxane containing 2.5% (v/v) of water under an atmospheric pressure of hydrogen. Two types of in situ procedures for the catalyst activation were used. Procedure A is similar to that used in our previous study [13,14]; the catalyst (0.02 g) and CD (0.02 mmol) were prereduced by stirring for 30 min in 5 ml of solvent under an H_2 atmosphere. In procedure B, the catalyst was pretreated without the modifier for 30 min with stirring in 5 ml of solvent in an H_2 atmosphere before the modification with CD (0.02 mmol in 1 ml of solvent added) for an additional 30 min. Then 0.5 mmol of a substrate in 5 ml (4 ml in procedure B) of the solvent and BA (0.3 mmol unless otherwise noted) as an effective additive [8,11] were injected successively to the mixture, and the stirring was started. After the hydrogen uptake finished, the reaction mixture was neutralized with a diluted HCl solution, extracted with ethyl acetate, and analyzed by HPLC on a chiral column (Daicel Chiralcel OJ-H and Chiralpak AD, for the products from **1** and **2**, respectively). The enantiomeric excess (ee, %) of the S isomers was calculated according to ee $(\%) = 100 \times (S - R)/(S + R)$. The catalytic activities are expressed by the initial reaction rates (r_0) estimated from the hydrogen uptake at 20% conversion.

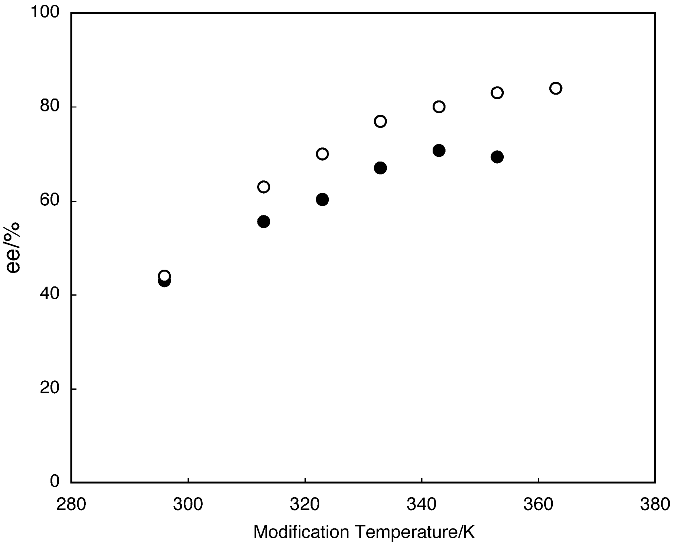

Fig. 1. Modification temperature dependence of the enantioselectivity in the hydrogenations of **1** (●) and **2** (○) with 5%Pd/C (STD) activated by procedure A. Reaction temperature, 296 K.

3. Results and discussion

Preliminary experiments, using 5%Pd/C (STD) as received, showed that the product ee in the reaction of **2** increased significantly with increasing temperature of modification and subsequent hydrogenation reaction, although higher reaction temperatures were reported to be unfavorable in the reactions of **1** with Pd/TiO_2 [4] and of an aliphatic acid with Pd/Al_2O_3 [5]. Therefore, to determine whether or not the temperature effect observed earlier comes from the modification process, a series of experiments with the Pd/C (STD) activated by procedure A were carried out by changing only the modification temperature while keeping the reaction temperature constant at 296 K. As shown in Fig. 1, the product ee for the reactions of both **1** and **2** increased markedly with increasing modification temperature, although the ee values obtained with the catalyst modified at room temperature were only 43% for the reaction of **1** and 44% for the reaction of **2**, both of which are much lower than those reported previously with an eggshell-type catalyst, Pd/C (AER) (59 and 71%), and with Pd/TiO_2 (68 and 82%) under the same reaction conditions. At the same time, the effect of the substrate structure [13] became clear under elevated modification temperatures. The ee values obtained here with the conventional Pd/C (STD) catalysts modified at 343–363 K were already on the same level as those reported with the best catalysts (Pd/TiO_2) reported so far [11–13]; the highest ee values attained were 71% in the reaction of **1** and 84% in the reaction of **2**. The reaction rate also increased to some extent with increasing modification temperature even though the reaction temperature was kept constant (296 K). When the modification procedures were carried out under N_2 atmosphere at 353 K (30 min) and then under H_2 at 296 K (30 min), increased ee was not obtained (43 and 45% ee), whereas the reaction rates decreased considerably. These observations suggest that the improvement in ee induced by the increased modification temperature is attributable to a preferable change in Pd surface in the presence of hydrogen. It seems reasonable to expect such a change in the Pd surface (e.g., the removal of surface contaminations) during the modification process under an H_2 atmosphere, especially at elevated temperatures. The temperature effect observed here is consistent with the fact that the solubility of hydrogen increases moderately with increasing temperature