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Heterogeneous enantioselective hydrogenation of isophorone over proline modified Pd catalysts

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Abstract

Enantioselective hydrogenation of isophorone (3,5,5-trimethyl-2-cyclohexenone) over (*S*)-proline modified Pd catalysts has been studied. Both the Pd particle size and the acid–base properties of the support influenced the hydrogenation reaction of isophorone and the subsequent kinetic resolution of 3,3,5-trimethylcyclohexanone (TMCH). This was explained by assuming the reaction pathway as a consequential process. The rapid hydrogenation of isophorone initially yielded racemic TMCH, and then the slow kinetic resolution consumed the (*R*)-TMCH, leaving (*S*)-TMCH in excess. Most promisingly, the Pd/MgO catalyst with enhanced adsorption of proline and moderate Pd particle sizes resulted in high enantioselectivity (ee of 95%) and 43% yield of TMCH.

Keywords: Enantioselective hydrogenation; Isophorone; Pd catalysts; Proline; Kinetic resolution

1. Introduction

Enantioselective hydrogenation over supported metal catalysts modified by chiral chemicals has been regarded as one of the most promising methods for the synthesis of pure optical compounds. Heterogeneous enantioselective hydrogenations of α and β-ketone esters over Pt/Cinchona [1] and Raney Ni/Tartaric acid-NaBr [2], respectively, were the well-established reactions, and the enantioselectivity was originated from the chiral modifier involved in the enantio-differentiation step which occurred on the surface of the metal catalysts [3–5].

However, the heterogeneous enantioselective hydrogenation of C=C bond compounds has received relatively little attention [6,7]. Hydrogenation of isophorone over proline modified Pd catalysts has been studied in recent years, and the nature of the support which influences the adsorption of proline was observed to significantly affect the reaction performance [8–10]. A promising ee value of 55% was obtained over a Pd/C catalyst [8], and a relatively higher ee value of 85% was recently achieved over a Pd/Al_2O_3 catalyst by ultrasound pretreatment to promote the adsorption of proline [9]. More recently, Pd catalysts supported by $BaCO_3$, $SrCO_3$ and $CaCO_3$ base materials gave very high enantioselectivities (ee up to 99%) due to the enhanced proline adsorption [10]. However, it was also noted that these higher ee values were accompanied by the lower yields of TMCH (about 50%) due to the formation of byproducts. The proposed reaction pathway was that proline and isophorone were initially condensed into an iminium salt, and the further hydrogenation of this intermediate over the Pd catalysts led to the formation of (*S*)-TMCH (3,3,5-trimethylcyclohexanone) and other undesired byproducts [9,10]. Quite recently, Mclntosh et al. [11] reported that the enantioselectivity is merely the result of kinetic resolution process that occurs homogeneously in solution and the metal surface is not involved in the enantio-differentiation step. Hence, it seems that the nature of chirality in the hydrogenation of isophorone over proline-modified Pd catalysts is still under debate.

In this study, we investigated enantioselective hydrogenation of isophorone in the presence of (*S*)-proline over

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Pd catalysts supported by Al_2O_3, TiO_2, MgO and C with respect to the acid–base features of the supporting materials and the particle sizes of Pd. It was found that the enantioselectivity and the (*S*)-TMCH yield can be actually improved by the kinetic resolution of racemic TMCH, which is closely related to the Pd particle size and the nature of the support.

2. Experimental

2.1. Catalyst preparation

Commercially available TiO_2 (P-25, Degussa, 50 m^2/g), Al_2O_3 (SINOPEC, 298 m^2/g), MgO (Shanghai Dunhuang Chemical Co., 40 m^2/g), active carbon (Aldrich, Darco KB, 1500 m^2/g) were used as supports. The activated carbon was pretreated with 15% H_2O_2 at 303 K for 2 h. Typically, 1.90 g of support was added into a solution of 0.210 g $Pd(OAc)_2$ (with the nominal Pd content of 5% in weight) in 40 ml toluene, the suspension was stirred for 5 h at room temperature. After evaporation, the samples were dried at 373 K for 10 h and followed by calcination at 673 K (except for Pd/C) for 4 h. The PdO were reduced to Pd by refluxing in 150 ml ethanol for 3 h and dried under vacuum at 323 K.

2.2. Chemisorption

Hydrogen chemisorption was measured on Auto Chem 2910 instrument (Micromeritics, USA) at ambient temperature. Prior to adsorption measurements, the sample was reduced in a flow of hydrogen at 573 K for 3 h and flushed with pure helium flow for 1 h at the same temperature.

2.3. TEM observation

TEM images of the catalysts were recorded over a JEOL JEM-2011 operated at 100 kV. Specimens were prepared by ultrasonically suspending the sample in ethanol, and a drop of the suspension was then applied onto clean holy copper grids and dried in air.

2.4. Hydrogenation of isophorone and kinetic resolution of TMCH

The hydrogenation of isophorone was conducted at room temperature in a 100 ml stainless steel autoclave with quartz inner. Isophorone 3.2 mmol, 56 ml of ethanol, 4 ml of *n*-octane (internal standard), 80 mg of catalyst and 3.2 mmol of (*S*)-proline were added. Then the autoclave was flushed with hydrogenation several times and finally filled to the pressure of 3.0 MPa. Samples were withdrawn periodically and analyzed by using an off-line GC (Agilent 6890N) equipped with β-cyclodextrin capillary column (CP-Chirasil-Dex CB) at a temperature of 110 °C and FID detector for monitoring the effluents. Kinetic resolution of TMCH was operated with the same procedure as hydrogenation of isophorone except that TMCH was added instead of isophorone. Enantiomeric excess is expressed as $ee\% = ([S] - [R])/([S] + [R]) \times 100\%$.

3. Results and discussion

3.1. Chemical hydrogenation of isophorone

Fig. 1 shows the TEM images of the Pd catalysts. Obviously, the dispersion of Pd was strongly dependent on the nature of the support. The Pd/C catalyst exhibited well-uniformed Pd particles of about 2–4 nm. Similarly, Pd particles were mainly dispersed over Al_2O_3 with the particle size of about 2–5 nm in the Pd/Al_2O_3 catalyst. The Pd/MgO catalyst showed the coexistence of small particles of about 5 nm and relatively large particles of 20–30 nm, while the Pd/TiO_2 catalyst presented large Pd particles of 20–60 nm. Thus, it seems true that the acid-base features of the supporting materials determined the particle size of Pd.

Without the presence of (*S*)-proline, isophorone was fully hydrogenated to TMCH over the Pd catalysts, which was also strongly dependent on the particle sizes of Pd in the catalysts. Total conversion of isophorone was obtained within 10 min over the Pd/C catalyst with Pd particle size of 2–4 nm, and the Pd/Al_2O_3 catalyst with most of the par-

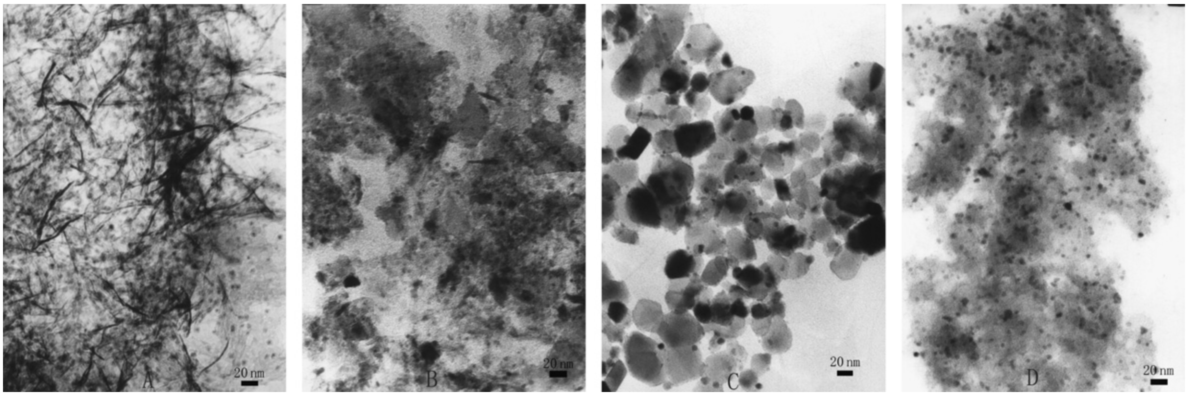

Fig. 1. TEM images of the Pd catalysts. (A): Pd/Al_2O_3, (B): Pd/MgO, (C): Pd/TiO_2, and (D): Pd/C.