Control of Stereoselectivity in 4-*tert*-Butylphenol Hydrogenation over a Carbon-supported Rhodium Catalyst by Carbon Dioxide Solvent

Norihito Hiyoshi,[1] Eiichi Mine,[1] Chandrashekhar V. Rode,[2] Osamu Sato,[1]
Takeo Ebina,[1] and Masayuki Shirai*[1]
[1]*Research Center for Compact Chemical Process, National Institute of Advanced Industrial Science and Technology (AIST), 4-2-1 Nigatake, Miyagino, Sendai 983-8551*
[2]*Homogeneous Catalysis Division, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411008, India*

(Received June 30, 2006; CL-060737; E-mail: m.shirai@aist.go.jp)

cis-4-*tert*-Butylcyclohexanol was obtained with a high cis ratio (cis/(cis + trans) = 0.9) in the hydrogenation of 4-*tert*-butylphenol over a carbon-supported rhodium catalyst along with hydrochloric acid in supercritical carbon dioxide solvent.

Highly stereoselective hydrogenation to cis forms is a significant reaction in organic synthesis. *cis*-4-*tert*-Butylcyclohexanol, an important intermediate in the production of fragrance,[1] is usually synthesized by the hydrogenation of 4-*tert*-butylphenol over metal catalysts in organic solvents;[1,2] however, low selectivity to cis form is critical. Hydrogenation reactions of solid substrates in organic solvents have wide range application in pharmaceutical and fine chemical processes; however, an energy intensive one or more distillations are mandatory for separation of products from solvents. Also, due to the toxic and hazardous nature of organic solvents, their elimination in the organic transformation is highly desirable. On the other hand, higher reaction rate and easy separation of products can be obtained in gas-phase hydrogenation; however, the control of selectivity is very difficult. Kalantar et al. reported low cis selectivity (cis/(cis + trans) = 0.47), low yield (high byproducts formation) and poor stability of catalysts for the vapor-phase hydrogenation of 4-*tert*-butylphenol over silica-supported platinum catalysts (above 400 K).[3]

Hydrogenations over solid catalysts in supercritical carbon dioxide solvent have several advantages: 1) higher miscibility of hydrogen in supercritical carbon dioxide, leading to higher reaction rates and controlling the product selectivity, 2) easy separation of products and catalysts, and 3) maintaining clean active sites of solid surfaces by washing with supercritical carbon dioxide solvent.[4] We have reported that carbon dioxide solvent is very effective for the stereoselective hydrogenation of naphthalene and tetralin to *cis*-decalin.[5] In this paper, we report the control of stereoselectivity to *cis*-4-*tert*-butylcyclohexanol in hydrogenation of 4-*tert*-butylphenol over a carbon-supported rhodium catalyst with hydrochloric acid and carbon dioxide solvent.

A carbon-supported rhodium catalyst with metal loading of 5 wt % from Wako Pure Chemical Ind., Ltd., Japan was used without further treatment. The dispersion values of metal particles on charcoal, determined by a hydrogen adsorption method,[6] was 12%. The hydrogenation of 4-*tert*-butylphenol (2.0 mmol) was carried out in high-pressure stainless-steel reactors (50-mL capacity). After the required temperature (313 K) was attained with an oil bath, first hydrogen and then carbon dioxide were introduced into the reactor containing 4-*tert*-butylphenol and catalyst to the desired pressure levels and then the content was magnetically stirred. After the reaction was over, the unreacted 4-*tert*-butylphenol and products were recovered with acetone, which showed a material balance of more than 95%. The quantitative analysis was conducted using GC-FID (HP-6890) equipped with DB-WAX capillary column.

Figure 1a shows the reaction profile for the hydrogenation of 4-*tert*-butylphenol over Rh/C under 2 MPa of hydrogen in 15 MPa of carbon dioxide at 313 K. From the beginning of reaction, *cis*-, *trans*-4-*tert*-butylcyclohexanol and 4-*tert*-butylcyclohexanone were formed in a constant proportion along with a small amount of by-products (*tert*-butylcyclohexane and unidentified with 0.4 and 5.0% of selectivity, respectively). After most of 4-*tert*-butylphenol was hydrogenated in 60 min, further hydrogenation of 4-*tert*-butylcyclohexanone to *cis*- and *trans*-4-*tert*-butylcyclohexanol was also observed. The cis ratio was almost constant at 0.77 from the beginning of reaction up to 150 min (Figure 1c). The cis ratio was found to be almost the same at 0.76 in the case of hydrogenation of 4-*tert*-butylcyclohexanone carried out separately. Further, cis to trans isomeriza-

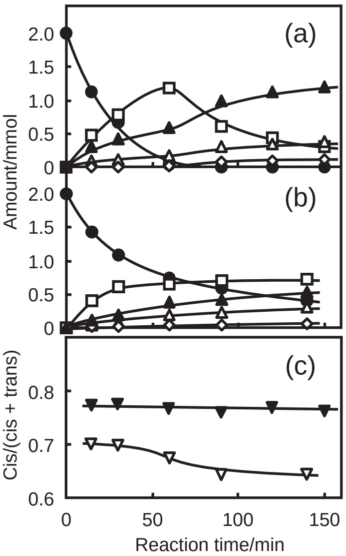

Figure 1. Hydrogenation of 4-*tert*-butylphenol over Rh/C in (a) 15 MPa of carbon dioxide, (b) 10 mL of 2-propanol and (c) cis ratio of 4-*tert*-butylcyclohexanol formed. Amounts of (●) 4-*tert*-butylphenol, (□) 4-*tert*-butylcyclohexanone, (▲) *cis*-4-*tert*-butylcyclohexanol, (△) *trans*-4-*tert*-butylcyclohexanol, and (◇) others. Cis ratio in (▼) 15 MPa of carbon dioxide and (▽) 10 mL of 2-propanol. Catalyst weight, 0.005 g; hydrogen pressure, 2 MPa; reaction temperature, 313 K.

tion of 4-*tert*-butylcyclohexanol did not occur under 2 MPa of hydrogen in 15 MPa of carbon dioxide solvent at 313 K. The hydrogenation of 4-*tert*-butylphenol also proceeded smoothly in 2-propanol solvent (Figure 1b) with much higher selectivity to 4-*tert*-butylcyclohexanone than 4-*tert*-butylcyclohexanols at the beginning of reaction. The yield of 4-*tert*-butylcyclohexanol became larger after 30 min of reaction; however, the cis ratio was low at 0.65 in 2-propanol. This low cis selectivity is comparable to that reported by Konuspaev et al. in the hydrogenation of 4-*tert*-butylphenol over a carbon-supported rhodium catalyst in 2-propanol.[2a]

It is established that phenol compounds adsorbed on active sites are partially hydrogenated to the corresponding tetrahydrophenols, which are tautomerized to ketones on the active sites in an organic solvent. For 4-*tert*-butylphenol hydrogenation, *cis*-4-*tert*-butylcyclohexanol is formed by the direct hydrogenation of 4-*tert*-butylphenol and 4-*tert*-butylcyclohexanone adsorbed on active sites, and *trans*-4-*tert*-butylcyclohexanol is formed via the flipping of 4-*tert*-butyltetrahydrophenol, which can be formed by the partial hydrogenation of 4-*tert*-butylphenol. We have reported that carbon dioxide solvent is very effective for stereoselective hydrogenation of naphthalene and tetralin to *cis*-decalin because of arresting the flipping of 2,3,4,5,6,7,8,10-octahydronaphthalene ($\Delta^{1,9}$-octalin) intermediate adsorbed on active sites by carbon dioxide solvent.[5] The higher cis ratio in carbon dioxide solvent than in 2-propanol could be explained by the inhibition of the flipping of 4-*tert*-butyltetrahydrophenol adsorbed on active sites in carbon dioxide solvent.

Figure 2 shows the effect of carbon dioxide pressure on the hydrogenation of 4-*tert*-butylphenol at 2 MPa of hydrogen pressure. The conversion of 4-*tert*-butylphenol increased with increase in carbon dioxide pressure from 0.1 to 25 MPa. In another experiment using a view cell, it was observed that 4-*tert*-butylphenol did not dissolve in 0.1 MPa of carbon dioxide solvent and the solubility of solid 4-*tert*-butylphenol in carbon dioxide phase increased as carbon dioxide pressure increased particularly over 10 MPa at 313 K under 2 MPa of hydrogen, and 4-*tert*-butylphenol was almost dissolved over 25 MPa of carbon dioxide pressure. The increase in the conversion would be due to the increase in the solubility of 4-*tert*-butylphenol in carbon dioxide.[7] Interestingly, the cis ratio was varied by the variation of carbon dioxide pressure from 0.1 to 25 MPa. The ratio increased from 0.69 to 0.79 with increase in carbon dioxide pressure from 0.1 to 10 MPa, then it decreased with further increasing of carbon dioxide pressure at 313 K under 2 MPa of hydrogen. We have observed in naphthalene and tetralin hydrogenation that higher *trans*-decalin selectivity was obtained over 15 MPa of carbon dioxide solvent, in which higher solubility of $\Delta^{1,9}$-octalin intermediate adsorbed on active site caused the probability of flipping of $\Delta^{1,9}$-octalin species. Over 10 MPa of carbon dioxide, the solubility of 4-*tert*-butyltetrahydrophenol increased with increasing carbon dioxide pressure, then the cis ratio would decrease.

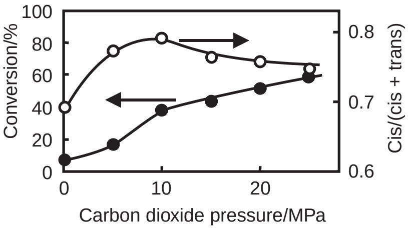

Figure 2. Effect of carbon dioxide pressure on (●) conversion of 4-*tert*-butylphenol with 0.005 g of Rh/C at 15 min of reaction time and (○) cis ratio of 4-*tert*-butylcyclohexanol formed with 0.020 g of Rh/C at 60 min of reaction time. Hydrogen pressure, 2 MPa; initial 4-*tert*-butylphenol, 2.00 mmol; reaction temperature, 313 K.

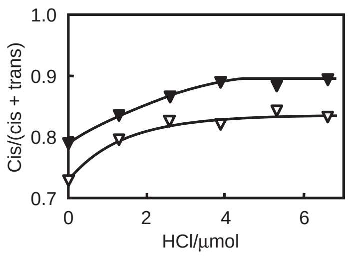

Figure 3. Effect of hydrochloric acid added to Rh/C on cis ratio of 4-*tert*-butylcyclohexanol formed in (▼) 10 MPa of carbon dioxide and (▽) 10 mL of 2-propanol. Catalyst weight, 0.020 g; reaction time, 60 min, hydrogen pressure, 2 MPa; initial 4-*tert*-butylphenol, 2.00 mmol; reaction temperature, 313 K.

Addition of protonic acid to hydrogenation systems is known to be effective to improve the cis ratio for the hydrogenation of 4-*tert*-butylphenol.[1,2d,2e] We also tried to enhance the cis selectivity by addition of hydrochloric acid (36%) along with Rh/C for the hydrogenation of 4-*tert*-butylphenol and results are shown in Figure 3. The cis ratio increased with increase in the amount of hydrochloric acid and remained constant beyond 4 μmol of hydrochloric acid per 0.020 g of Rh/C. The cis ratio reached as high as 0.89 in supercritical carbon dioxide over Rh/C–HCl system. The addition of hydrochloric acid to Rh/C was also effective in 2-propanol solvent; however, higher cis ratio was obtained in supercritical carbon dioxide than in 2-propanol. The interaction between proton and oxygen atom of 4-*tert*-butylcyclohexanone adsorbed on active sites would facilitate the hydrogenation path to *cis*-4-*tert*-butylcyclohexanol.

References

1 M. Sekiguchi, S. Tanaka, Jpn. Patent 3528519, **2004**.
2 a) S. R. Konuspaev, K. N. Zhanbekov, T. S. Imankulov, R. K. Nurbaeva, *Kinet. Katal.* **1993**, *34*, 89. b) D. Y. Murzin, A. I. Allakhverdiev, N. V. Kul'kova, *Kinet. Katal.* **1993**, *34*, 442. c) J. Tobičíf, L. Červeny, *J. Mol. Catal. A: Chem.* **2003**, *194*, 249. d) D. J. Yadav, P. K. Goel, *J. Mol. Catal. A: Chem.* **2002**, *184*, 281. e) H. Takizawa, Jpn. Patent 1310858, **1986**.
3 A. Kalantar, H. Backman, J. H. Carucci, T. Salmi, D. Y. Murzin, *J. Catal.* **2004**, *227*, 60.
4 a) *Chemical Synthesis Using Supercritical Fluids*, ed. by P. G. Jessop, W. Leitner, Wiley, New York, **1999**. b) M. G. Hitzler, F. R. Smail, S. K. Ross, M. Poliakoff, *Org. Process Res. Dev.* **1998**, *2*, 137. c) A. Baiker, *Chem. Rev.* **1999**, *99*, 453. d) C. V. Rode, U. D. Joshi, O. Sato, M. Shirai, *Chem. Commun.* **2003**, 1960.
5 a) N. Hiyoshi, T. Inoue, C. V. Rode, O. Sato, M. Shirai, *Catal. Lett.* **2006**, *106*, 133. b) N. Hiyoshi, E. Mine, C. V. Rode, O. Sato, M. Shirai, *Chem. Lett.* **2006**, *35*, 188.
6 T. Sato, C. V. Rode, O. Sato, M. Shirai, *Appl. Catal., B* **2004**, *49*, 181.
7 N. Hiyoshi, C. V. Rode, O. Sato, M. Shirai, *Appl. Catal., A* **2005**, *288*, 43.