Solvent Effect on Enantioselective Hydrogenation of (*E*)-α-Phenylcinnamic Acid with Cinchonidine-Modified Palladium Catalysts

Yuriko Nitta* and Kazuya Kobiro
Niihama National College of Technology, Yagumo-cho, Niihama, Ehime 792

(Received October 31, 1994)

The use of a solvent with larger dielectric constant results in higher enantioselectivity in the hydrogenation of (*E*)-α-phenylcinnamic acid with a cinchonidine-modified Pd catalyst. The reaction in *N,N*-dimethylformamide containing 10vol% of water with a 5wt% Pd/TiO_2 catalyst leads to an optical yield of 53% of *S*-(+)-2,3-diphenylpropionic acid.

Enantioselective hydrogenation of prochiral C=C bonds using chiral heterogeneous catalysts has been investigated with a little success and is still a challenging subject.[1-4] Recently, we have shown that (*E*)-α-phenylcinnamic acid (**1**) is enantioselectively hydrogenated to give (*S*)-(+)-2,3-diphenylpropionic acid (**2**) over cinchonidine-modified 5wt% Pd/Al_2O_3 and Pd/TiO_2 catalysts with optical yields (OYs) of 36.9% and 44.4%, respectively.[5] We also found that water content in the solvent has a significant effect on the enantioselectivity in the reaction. Therefore, we examined the effect of solvent polarity in this work.

The hydrogenation reactions were carried out at 298K under an atmospheric pressure of hydrogen mainly with a 5wt% Pd/Al_2O_3 catalyst prepared by an impregnation method.[5] The hydrogenation products were analyzed according to the procedure described before.[5]

Both hydrogenation activity and enantioselectivity were strongly dependent on the solvent used as expected. In most cases, higher enantioselectivity was accompanied by higher activity.[6] As shown in Figure 1, the OY of **2** increased almost linearly with increasing dielectric constant (ε_r) of the solvent. *N,N*-dimethylformamide (DMF) gave the highest OY (19.4%) as a single solvent under our experimental conditions, while dimethyl sulfoxide (DMSO) deactivated the catalyst. Table 1 lists the results of the reactions in mixed solvents containing water. A mixed solvent of DMF and 10vol% water was found to be the best of all the solvents examined here. Addition of water more than 10vol% to DMF, as well as 10vol% water to methanol, was unfavorable for both activity and enantioselectivity. These observations suggest that too high polarity of the solvent is undesirable for this reaction.

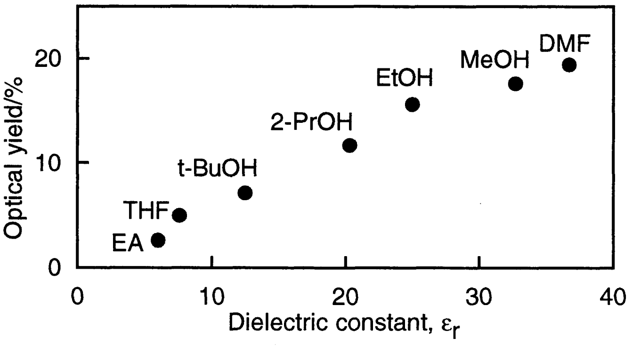

Figure 1. Dependence of optical yield on the polarity of the solvent; EA:ethyl acetate.

Table 1. Hydrogenation of (*E*)-α-Phenylcinnamic Acid with a Cinchonidine-Modified Pd/Al_2O_3 Catalyst in Mixed Solvents[a]

Run	Solvent (volume ratio)	R_0[b]/mmol $g^{-1}h^{-1}$	OY[c]/%
1	ethanol+water (9:1)	8.2	19.5
2	methanol+water (9:1)	9.7	16.5
3	DMF+water (9:1)	10.9	29.0
4	DMF+water (8:2)	8.7	27.4
5	DMF+water (7:3)	7.9	21.8
6	ethyl acetate+ ethanol+water (15:7:3)	7.0[d]	22.1[d]
7	ethyl acetate+DMF+water (15:7:3)	12.6	27.2
8[e]	ethyl acetate+ethanol+water (15:7:3)	23.6[d]	44.4[d]
9[e]	DMF+water (9:1)	24.0	53.0

[a]Reaction conditions; **1**: 5mmol, solvent: 25 cm^3, catalyst: 0.15g, cinchonidine: 0.15 mmol, H_2: 0.1 MPa, Reaction temperature: 298K. [b]Initial reaction rate. [c]Optical yield of **2**. [d]Data from reference 5. [e]Reaction with a 5wt% $Pd/TiO_2(p)$ catalyst.[5]

In order to obtain higher OY, hydrogenation was carried out using the best solvent described above with the most selective catalyst reported in our previous paper.[5] As compared in Table 1, this catalytic system gave the highest OY (53.0%) of **2** in the data reported with heterogeneous catalysts until now.[3,5] Optimization of other reaction conditions as well as preparation variables of Pd catalysts would lead to a more improved enantioselectivity in this reaction.

References and Notes

1 H.-U. Blaser, *Tetrahedron: Asymmetry,* **2**, 843 (1991).

2 Y. Izumi and A. Tai, "Stereo-differentiating Reactions," Kodansha, Tokyo, and Academic Press, New York (1977), Chap. 5.

3 J. R. G. Perez, J. Malthete, and J. Jacques, *C. R. Acad. Sc. Paris,* t.**300,** Serie II, no 5, 169 (1985).

4 M. Bartok, G. Wittmann, G. B. Bartok, and G. Gondos, *J. Organomet. Chem.*, **384**, 385 (1990).

5 Y. Nitta, Y. Ueda, and T. Imanaka, *Chem. Lett.*, **1994**, 1095.

6 Reactions with unmodified catalysts were much faster than those with cinchonidine-modified catalysts both in highly polar and less polar solvents: the initial hydrogenation rates were 98 and 126 mmol $g^{-1}h^{-1}$ in DMF with 10vol% water and in ethyl acetate, respectively. This is completely different from the results reported for the hydrogenation of α-keto acids with cinchonidine-modified Pt catalysts where the modification of catalysts not only causes the enantioselectivity but also accelerates the reaction rate: H.-U. Blaser and H. P. Jalett, *Stud. Surf. Sci. Catal.*, **78**, 139 (1993).