

# Enantioselective hydrogenation of ethyl pyruvate catalyzed by polyvinylpyrrolidone-stabilized and supported rhodium nanocluster

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## Abstract

The enantioselective hydrogenation of ethyl pyruvate catalyzed by finely dispersed oxide supported rhodium nanocluster was studied with cinchonidine as chiral modifier. The results indicated that cinchonidine not only exhibited good enantiodifferentiating ability but also could accelerate the reaction by a factor 10. Supports ( $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, SiO<sub>2</sub>, TiO<sub>2</sub>) played an important role in promoting the further increase of catalytic activity and enantioselectivity of polyvinylpyrrolidone-stabilized rhodium nanoclusters (Rh/PVP). Under the optimum reaction conditions (298 K, 7.0 MPa of hydrogen pressure and tetrahydrofuran as solvent), TOF and the enantiomeric excess reached 58.6 min<sup>-1</sup> and 65.4% e.e., respectively.

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## 1. Introduction

Asymmetric catalysis has been the most challenging and interesting subject of applications in the synthesis of drugs, agrochemicals and fragrances/flavors over the past two decades. Homogeneous transition metal complexes with chiral ligands are the most versatile and efficient catalysts [1]. However, the separation of expensive chiral catalysts from products is often complicated by the air and thermal sensitivity of these catalysts [2]. For ease of reuse and environmental considerations, researchers have concentrated

on finding ways to improve homogeneous catalysis. The heterogeneous catalysis plays an important and crucial role in many chemical processes because of its inherent practical advantages connected with the easy separation and handling. Recently, the heterogeneous asymmetric catalysis has become a rapidly growing and interesting field [3,4]. For the enantioselective hydrogenation of  $\alpha$ -ketoesters (Orito reaction [5]), the supported metal catalyst, Pt/cinchonidine, achieved enantiomeric excess (e.e.) values exceeding 95% under optimum reaction conditions [6–8]. The utilization of other transition metals, such as Ru, Rh, Pd, Ir, to replace Pt leads to lower enantioselectivity [9–11]. For example, the enantioselectivity is only 20–30% e.e. in hydrogenation of ethyl pyruvate using Rh catalyst and cinchonidine as a chiral modifier [9].

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Rh nanocluster catalysts, however, exhibited high activity and chemoselectivity in achiral hydrogenation catalysis [12–17]. This is related to the high quantum size effect and high surface area of nanoclusters. Because of its advantages, attention [18–20] has been directed towards nanocluster catalysts stabilized by ligands, polymers and solvents. However except that we have published paper [21], the application of Rh nanocluster and supported Rh nanocluster in enantioselective hydrogenation has not been reported up to now. In this paper, we report the catalytic performance of supported Rh nanoclusters stabilized by polyvinylpyrrolidone (PVP) in the enantioselective hydrogenation of ethyl pyruvate. The effects of some reaction parameters and the support materials on the enantioselectivities and catalytic activities have been studied in detail.

## 2. Experimental

### 2.1. Materials

Ethyl Pyruvate, PVP (MW = 10,000) were used as received from Acros. Hydrogen (99.9%) was purified prior to use.  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  and other reagents of analytical grade were used. The specific surface areas of  $\gamma\text{-Al}_2\text{O}_3$ ,  $\text{SiO}_2$  and  $\text{TiO}_2$  are listed in Table 1.

### 2.2. Preparation of the rhodium nanocluster (Rh/PVP)

The PVP-stabilized rhodium colloidal nanoclusters (designated as Rh/PVP) was prepared by a method as reported in the literature [14–16]. The  $5.0 \times 10^{-2}$  mmol rhodium chloride trihydrate and 0.5 mmol PVP (referring to the monomer units) were dissolved in a mixture

of ethanol and distilled water (70 ml, ethanol:water = 9:1) in a 100 ml round flask. The solution was refluxed at  $79^\circ\text{C}$  for 1 h. A dark brown solution was obtained and then evaporated to dryness by a rotary evaporator.

### 2.3. Preparation of the supported rhodium nanocluster (0.5% Rh/PVP- $\gamma\text{-Al}_2\text{O}_3$ )

1.0 g  $\gamma\text{-Al}_2\text{O}_3$  was treated with the required amount of Rh/PVP in ethyl alcohol (10 ml) at room temperature while being stirred for 1 day in a round bottom flask. After evaporation, the supported rhodium nanocluster catalyst was washed with water and ethanol for several times, and then dried under vacuum at room temperature for 6 h. The rhodium content in the catalyst was 0.5 wt.% as determined by atomic absorption spectroscopy. Other two catalysts, 0.5% Rh/PVP- $\text{SiO}_2$  and 0.5% Rh/PVP- $\text{TiO}_2$ , were also prepared by the similar methods.

### 2.4. Determination of rhodium particle diameter

The particle diameter of rhodium particles were determined from the enlarged photographs of TEM using a JEM-100CX instrument as described in the literature [21]. The size distribution histogram was established from the data of 200 particles.

### 2.5. Enantioselective hydrogenation of ethyl pyruvate

Enantioselective hydrogenation of ethyl pyruvate (Scheme 1) was performed in a 20 ml stainless autoclave with a glass linear and magnetic stirrer. The catalysts (containing  $2.0 \times 10^{-3}$  mmol rhodium), cinchonidine, solvent (2.0 ml), ethyl pyruvate (2.0 mmol) were introduced into the autoclave. After the autoclave

Table 1  
Enantioselectivity-improving effect of the supports<sup>a</sup>

Catalyst	Support	Specific area (m <sup>2</sup> /g)	TOF (min <sup>-1</sup> )	e.e. (%)	Configuration
Rh/PVP	No	–	15.7	42.2	<i>R</i>
0.5% Rh/PVP- $\gamma\text{-Al}_2\text{O}_3$	$\gamma\text{-Al}_2\text{O}_3$	154	58.6	65.4	<i>R</i>
0.5% Rh/PVP- $\text{SiO}_2$	$\text{SiO}_2$	121	58.6	60.9	<i>R</i>
0.5% Rh/PVP- $\text{TiO}_2$	$\text{TiO}_2$	103	58.6	56.4	<i>R</i>

<sup>a</sup> Reaction conditions: catalyst (containing  $2.0 \times 10^{-3}$  mmol rhodium), cinchonidine ( $4.0 \times 10^{-3}$  mol/l), THF (2.0 ml), ethyl pyruvate (2.0 mmol), 298 K, 7.0 MPa.



Table 2

Solvent effect on enantioselectivity and TOF of the hydrogenation of ethyl pyruvate<sup>a</sup>

Solvent	Dielectric constant	TOF (min <sup>-1</sup> )	e.e. (%)	Configuration
Toluene	2.4	38.9	33.2	<i>R</i>
Ethyl acetate	6.0	8.3	31.6	<i>R</i>
Tetrahydrofuran	7.6	58.6	65.4	<i>R</i>
Dichloromethane	9.1	7.6	45.5	<i>R</i>
Toluene/ethanol (1:1)	13.4	39.8	49.5	<i>R</i>
Ethyl acetate/ethanol (1:1)	15.2	14.3	40.1	<i>R</i>
Ethanol	24.3	39.6	29.8	<i>R</i>
H <sub>2</sub> O	80.4	38.0	6.1	<i>R</i>

<sup>a</sup> Reaction conditions: catalyst is 0.5% Rh/ $\gamma$ -Al<sub>2</sub>O<sub>3</sub>-PVP, the others are the same as in Table 1.

the case of asymmetric hydrogenation of pyruvate catalyzed by Pt/cinchonidine and Ir/cinchonidine systems [26–28,11]. Solvents with dielectric constant ranging from 2 to 80 have been included in this study for the hydrogenation of ethyl pyruvate catalyzed by alumina-supported Rh nanocluster. The enantioselectivity and TOF data in Table 2 indicate that there is no clear correlation between the catalytic performance of 0.5% Rh/PVP- $\gamma$ -Al<sub>2</sub>O<sub>3</sub> and solvent polarity, which is different from the results in the literature [29,30]. Among the solvents investigated, tetrahydrofuran is the best, leading to TOF and e.e. values of 58.6 min<sup>-1</sup> and 65.4%, respectively.

The e.e. values of products are higher when mixtures of ethanol and toluene are used instead of pure solvent, toluene or ethanol, as shown in Fig. 1. The e.e. value reaches 49.5% when the volume ratio of ethyl

alcohol to toluene is 1:1. No obvious change, however, is observed for TOF, indicating no loss of activity in the mixed solvent. Enhancement of enantioselectivity is also observed in mixtures of ethanol and ethyl acetate, but in this system, TOF in the mixed solvent is lower than that in pure ethanol and higher than that in ethyl acetate (Table 2).

### 3.4. Effect of reaction temperature and hydrogen pressure

The results given in Fig. 2 for the 0.5% Rh/PVP- $\gamma$ -Al<sub>2</sub>O<sub>3</sub> catalyst suggest that a lower temperature is more favorable for enantioselectivity. At 298 K, the e.e. is 65.4% and it drops slowly with increasing temperature to 55% at 353 K. However, the activity (TOF) keeps rising from 58.6 min<sup>-1</sup> at 273 K

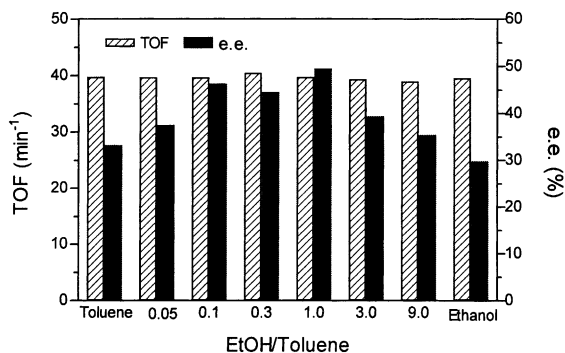


Fig. 1. The effect of mixed solvent on the enantioselective hydrogenation of ethyl pyruvate catalyzed by 0.5% Rh/PVP- $\gamma$ -Al<sub>2</sub>O<sub>3</sub>. The reaction conditions are the same as in Table 2 except solvent used.

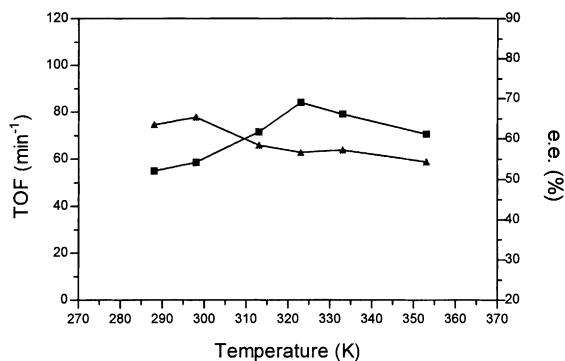


Fig. 2. The effect of temperature on TOF and enantioselectivity catalyzed by 0.5% Rh/PVP- $\gamma$ -Al<sub>2</sub>O<sub>3</sub>. (■: TOF; ▲: e.e.). The reaction conditions are the same as in Table 1 except reaction temperature and catalyst.

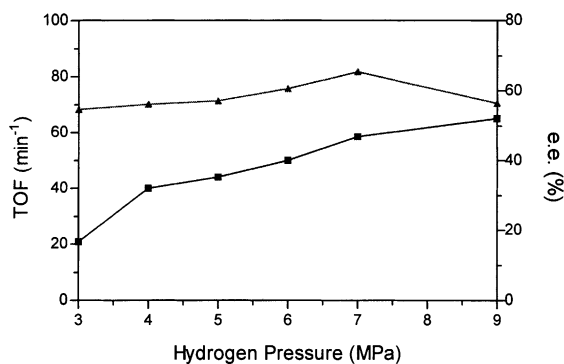


Fig. 3. The effect of hydrogen pressure on TOF and enantioselectivity. (■: TOF; ▲: e.e.). The reaction conditions are the same as in Table 1 except catalyst and hydrogen pressure.

to  $84.0 \text{ min}^{-1}$  at 323 K, and then decreases gradually with further increase in temperature. This drop in activity was also observed for conventional supported Pt and Ir catalysts when the temperature is higher than 318 K [6,31,32]. The effect of temperature on enantioselectivity and TOF could be attributed to the thermal desorption of cinchonidine or the change of its adsorption mode on Rh nanocluster surface.

As shown in Fig. 3, the e.e. value increases with hydrogen pressure and reaches a maximum 65.4% at 7.0 MPa for the catalyst 0.5% Rh/PVP- $\gamma$ -Al<sub>2</sub>O<sub>3</sub>. Further increase in hydrogen pressure leads to e.e. decrease. This observation is agreement with the results observed in Pt/cinchonidine [32] and Ir/cinchonidine systems [11]. The increase in (*R*)-ethyl lactate can be rationalized from the rise of hydrogen concentration in the reaction system as reported by Blackmond and co-workers [33,34]. The increase in hydrogen pressure is beneficial to the activity of catalyst over the whole pressure range under investigation, as indicated by the TOF results in Fig. 3.

### 3.5. Rate-accelerating effect of cinchonidine

In enantioselective hydrogenation of ethyl pyruvate catalyzed by colloidal rhodium nanocluster (Rh/PVP) and  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> supported Rh nanocluster, the addition of cinchonidine not only can induce the preferential formation of (*R*)-ethyl lactates but also can accelerate the reaction rate, as shown in Fig. 4. For the

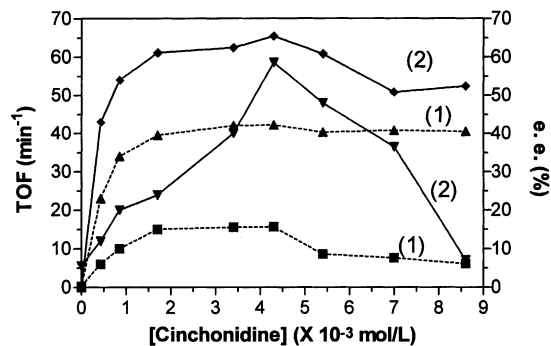


Fig. 4. Effect of cinchonidine concentration on TOF and enantioselectivity. (1) Rh/PVP as catalyst; (2) 0.5% Rh/PVP- $\gamma$ -Al<sub>2</sub>O<sub>3</sub> as catalyst. (■, ▼: TOF; ▲, ◆: e.e.). The reaction conditions are the same as in Table 1 except catalysts and cinchonidine concentration.

latter catalyst (0.5% Rh/PVP- $\gamma$ -Al<sub>2</sub>O<sub>3</sub>), at the concentration of cinchonidine of  $4.3 \times 10^{-3} \text{ mol/l}$  the TOF reaches  $58.6 \text{ min}^{-1}$ , which is much higher than that in the absence of cinchonidine ( $5.6 \text{ min}^{-1}$ ). The accelerating effect was observed in enantioselective hydrogenation of pyruvates catalyzed by heterogeneous Pt/cinchonidine and Ir/cinchonidine systems [7,10,11,24,25,35–39]. When the concentration of cinchonidine is too high, the reaction rate decreases. It is possible that the high concentration of cinchonidine will block some active sites on the surface of the 0.5% Rh/PVP- $\gamma$ -Al<sub>2</sub>O<sub>3</sub> catalyst. Comparing the two catalyst systems, the hydrogenation rate of ethyl pyruvate is always higher on the supported catalyst 0.5% Rh/PVP- $\gamma$ -Al<sub>2</sub>O<sub>3</sub> than that on the Rh/PVP catalyst with a TOF ratio of 3.7:1 under the optimum reaction conditions. The results show firstly that there is a synergistic effect of cinchonidine and  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> in acceleration of the enantioselective hydrogenation of ethyl pyruvate.

## 4. Conclusion

Rh/PVP supported over  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> (0.5% Rh/ $\gamma$ -Al<sub>2</sub>O<sub>3</sub>-PVP) exhibits better catalytic properties than rhodium colloidal nanocluster (Rh/PVP) and conventional heterogeneous Rh catalysts in the enantioselective hydrogenation of ethyl pyruvate using cinchonidine as chiral modifier.  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> plays an essential role in the enhancement of catalytic activity

and enantioselectivity of Rh/PVP nanoclusters adsorbed on its surface.

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