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Enantioselective hydrogenation of ethyl pyruvate catalyzed by TS-1 supported rhodium nanoclusters

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Abstract

The enantioselective hydrogenation of ethyl pyruvate in the presence of TS-1 supported rhodium nanoclusters and chiral modifier cinchonidine, cinchonine and quinine was investigated. The results showed that cinchonidine was the best modifier and THF was an excellent solvent for the reaction. Cinchonidine and quinine not only induced the enantioselectivity, but also accelerated the reaction. The interaction between the support and rhodium nanoclusters, as well as the adsorption of modifier on the support surface played an important role in promoting the increase of the catalytic activity and enantioselectivity. Under the optimum conditions, 268 K, 7 MPa of hydrogen pressure and 4.0×10^{-3} mol/l of cinchonidine in THF, the mole conversion of ethyl pyruvate and enantiomeric excess of *R*-ethyl lactate reached up to 100 and 63.1%, respectively.

Keywords: Supported rhodium nanoclusters; Enantioselective hydrogenation; Ethyl pyruvate; Cinchonidine; Quinine

1. Introduction

The optically pure compounds used as building blocks in the production of pharmaceuticals, agrochemicals, flavors and fragrances have become a basic requirement. Many metal complexes bearing chiral ligands are available as catalysts in the synthesis of chiral compounds and exhibit very high enantioselectivity. However, the separation of chiral catalysts from the products in homogeneous asymmetric catalysis is difficult and thus their application is limited. Due to the multiple advantages of heterogeneous catalytic system such as ease of handling, separation, and the most important, reuse of the catalyst, the extensive efforts have been made for development of chiral solid catalysts in asymmetric synthesis in the recent years [1–4]. Up to date only few heterogeneous catalytic systems have been found to be assymetrically efficient. One of them is the cinchonidine modified and Al_2O_3 supported platinum catalyst, which exhibits excellent enantioselectivity in the asymmetric hydrogenation of α-ketoesters [5–11].

We know that many rhodium complexes containing chiral ligands are very active and highly enantioselective catalysts in the asymmetric homogeneous hydrogenation of unsaturated and carbonyl compounds. However, the supported rhodium catalyst modified by cinchonidine is demonstrated to give lower enantioselectivity than the supported platinum catalyst. The value of e.e. is only 20–30% in the asymmetric hydrogenation of ethyl pyruvate. In order to improve the catalytic performance, the new method preparing

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rhodium nanoclusters and the supported catalysts were studied. As reported in the previous literature [12–14], when the rhodium nanoclusters were supported on the Al_2O_3 or TiO_2, and modified with cinchona by means of the new procedure, their catalytic activities, especially the enantioselectivities, were obviously enhanced. In this paper the TS-1 supported Rh nanocluster catalysts, which were stabilized by PVP, cinchonidine or quinine and further modified by cinchonidine, quinine or cinchonine, were investigated. The effect of the modification and the reaction conditions on the enantioselective hydrogenation of ethyl pyruvate was discussed in detail.

2. Experimental

2.1. Materials

Ethyl pyruvate, cinchonidine (CD), cinchonine (CN), quinine (QN) and polyvinylpyrrolidone (PVP) (MWav. = 10,000) were used as received from Acros without further purification. THF was treated by sodium metal. Other solvents and $RhCl_3{\cdot}3H_2O$ are the reagents of analytical grade. The purity of hydrogen is 99.99%. The specific area of TS-1 is 375 m^2/g.

2.2. Preparation of catalyst

2.2.1. Preparation of rhodium nanoclusters stabilized by PVP (Rh/PVP)

$RhCl_3{\cdot}3H_2O$ (5×10^{-2} mmol) and PVP (0.5 mmol, accounting by pyrrolidone monomer) were dissolved in a mixed solution (50 ml) consisting of distilled water, ethanol, and *i*-propanol (water:ethanol:*i*-propanol = 1:3:6, volume ratio) in a flask. A rose-pink solution was formed. The solution was refluxed for 4 h to give a dark brown solution. When the solution was evaporated to dryness by a Rotavap, the black powder of rhodium nanoclusters was obtained. They were redispersed in ethanol (25 ml) and then TS-1 (1 g) was added, and the solution was stirred for 15 h at room temperature. The supported rhodium nanoclusters were filtrated and washed with distilled water. The filtrate, which was uncolored, indicated that all rhodium nanoclusters were adsorbed on TS-1. The catalyst was dried under vacuum at 50 °C, its rhodium content was 0.5 wt.%. The catalyst was abbreviated as 0.5% Rh/PVP-TS-1. Other Rh/PVP-TS-1 catalysts, which contained different rhodium contents, were prepared using the same method.

CD or QN stabilized rhodium nanoclusters (Rh/CD or Rh/QN) were prepared using the above-mentioned procedures except that PVP was substituted by CD or QN, and the mole ratio of $RhCl_3$ to CD or QN was 1:2. The preparation method of the catalyst supported on TS-1 was the same as the catalyst Rh/PVP-TS-1. The rhodium content of the two catalysts was 0.5 wt.% and they were abbreviated as 0.5% Rh/CD-TS-1 and 0.5% Rh/QN-TS-1.

The sizes of rhodium nanoclusters of Rh/PVP and 0.5% Rh/PVP-TS-1 were measured by TEM (JEM-100CX). The average diameter was about 2.0 nm and there was no change before and after they were supported.

2.3. Modification of TS-1 supported rhodium nanoclusters

CD, CN and QN were used as the chiral modifier for the TS-1 supported rhodium nanocluster catalysts. The modification of the catalysts was carried out in a 30 ml stainless steel autoclave with the glass liner and magnetic stirrer. The catalysts (20 mg, containing 1×10^{-3} mmol of Rh), CD (4×10^{-3} mol/l), CN (4×10^{-3} mol/l) or QN (4×10^{-3} mol/l) and THF (2.0 ml) were added into the autoclave, then hydrogen was introduced up to 5.0 MPa. The catalysts were modified under stirring state at 298 K for 1 h.

2.4. Catalytic hydrogenation

When the modification of the catalysts was completed, the ethyl pyruvate (1 mmol) was added into the autoclave. Then it was purged with hydrogen for three times. The reaction system was pressurized with hydrogen to the desired pressure and checked for leaks. The hydrogenation reaction was performed at a constant pressure for a desired period of time. After the reactor was cooled to ambient temperature, the solution was filtrated and the products were determined by GC 960 with FID detector and DEX^{TM}120 column (30 m × 0.25 mm) at 80 °C.

Table 1
Effect of different stabilizers and supports

Catalyst	Conversion (mol%)[a]	e.e. (%)[a]	Conversion (mol%)[b]	e.e. (%)[b]
Rh/PVP	32.5	42.2	16.6	27.0
0.5% Rh/PVP-TS-1	99.7	59.8	99.6	58.9
0.5% Rh/CD-TS-1	99.8	59.2	97.6	59.9
0.5% Rh/QN-TS-1	99.8	59.7	97.9	59.5

Reaction conditions: catalyst (Rh/PVP, 2.2 mg or supported catalysts, 20 mg, containing 1×10^{-3} mmol Rh); P_{H_2} (7.0 MPa), 298 K, 1 h.
[a] CD is used as modifier (4×10^{-3} mol/l).
[b] QN is used as modifier (4×10^{-3} mol/l).

3. Results and discussions

3.1. Effect of different stabilizers and supports

The catalytic properties of three TS-1 supported rhodium nanoclusters were studied in the asymmetric hydrogenation of ethyl pyruvate. The data in Table 1 suggested that the activity and enantioselectivity of Rh/PVP were much lower than that of the supported catalyst Rh/PVP-TS-1, although their content of rhodium in the solution was the same. The three catalysts, which were prepared using PVP, CD and QN as stabilizer, had almost the same activities and enantioselectivities; moreover, CD and QN exhibited very similar modification efficiency for promoting the enantioselective hydrogenation. It was possible that the high specific area and the porous structure of TS-1 played an important role. The support could protect rhodium nanoclusters against agglomeration and thereby was favorable for their dispersions and stabilization on the surface. At the same time, the adsorption of the modifier on the surface could form a chiral micro-circumstance, which would enhance its chiral induction effect.

3.2. Effect of modifier and rhodium content

The data in Table 2 showed that the enantioselectivities decreased with the increase of rhodium content in the catalyst owing to the change of metal dispersions. When the catalyst was modified by CN, as showed in Table 3, its activity and enantioselectivity was lower than when it was modified by CD and QN; moreover, the *S*-ethyl lactate is obtained in excess in the hydrogenation product. This suggested that the configuration of the modifier had a key influence on the catalyst properties, although the composition of CN was the same as that of CD.

Table 2
Effect of rhodium content in the catalysts

Catalyst	Conversion (mol%)[a]	e.e. (%)[a]	Conversion (mol%)[b]	e.e. (%)[b]
0.5% Rh/PVP-TS-1	99.7	59.8	99.6	58.9
1% Rh/PVP-TS-1	98.6	53.5	96.4	52.5
2% Rh/PVP-TS-1	96.5	47.0	81.7	40.6

The reaction conditions are the same as those listed in Table 1.
[a] CD is used as modifier (4×10^{-3} mol/l).
[b] QN is used as modifier (4×10^{-3} mol/l).

Table 3
Effect of different modifiers

Modifier	Conversion (mol%)	e.e. (%)	Configuration
Cinchonidine (CD)	96.5	47.0	*R*
Quinine (QN)	81.7	40.6	*R*
Cinchonine (CN)	69.9	26.3	*S*

Catalyst: 2% Rh/PVP-TS-1. The reaction conditions are the same as those listed in Table 1.

3.3. Effect of solvents

The properties of the solvent, for example its solubility for the reactants and its interaction with the modifier and metal cluster surface, could influence the catalytic behavior. The effect of different solvents was investigated and the data are listed in Table 4. The results showed that THF was the most suitable

Table 4
Effect of different solvents

Solvent	Conversion (mol%)	e.e. (%)
Toluene	51.4	20.1
Acetic acid	26.5	13.3
Tetrahydrofuran	99.7	59.8
Ethanol	98.5	22.2
Methanol	52.5	18.5
i-Propanol	91.4	31.0
i-Propanol/KOH	97.4	18.1

Catalyst: 0.5% Rh/PVP-TS-1 (20 mg, containing 1×10^{-3} mmol Rh); modifier: cinchonidine (4×10^{-3} mol/l). The reaction conditions are the same as those listed in Table 1.

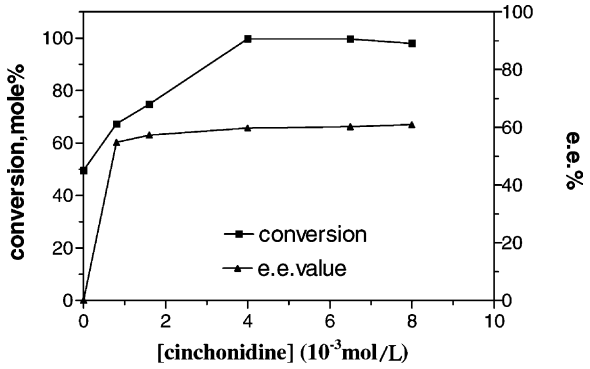

Fig. 1. Effect of the concentration of cinchonidine on the enantioselective hydrogenation of ethyl pyruvate. The reaction conditions are the same as those listed in Table 4.

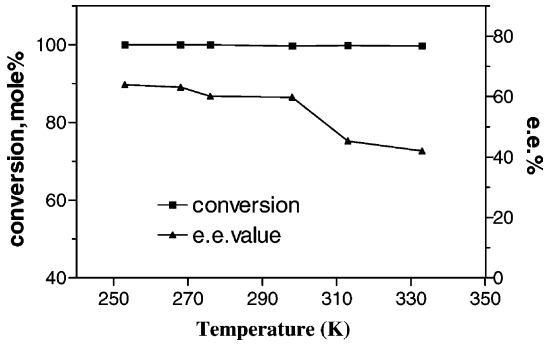

Fig. 2. Effect of the temperature on the enantioselective hydrogenation of ethyl pyruvate. The reaction conditions are the same as those listed in Table 4.

solvent for the reaction, in which the conversion of ethyl pyruvate and e.e. value the highest. This is in agreement with our previous reports [4,12–14], but different from the results obtained using the catalyst system Pt/Al_2O_3-cincohona, which exhibited the best catalytic activity and enantioselectivity in acetic acid. The mechanism of interaction between THF and the catalyst needs further studies.

3.4. Effect of cinchonidine concentration

The effect of CD concentration in the asymmetric reaction was shown in Fig. 1. If there was no addition of modifier CD in the reaction, the conversion of ethyl pyruvate and e.e. value of the product was very low. When CD concentration increased from 1.2×10^{-3} to 4.0×10^{-3} mol/l, the conversion and e.e. value rose from 50 and 0% to 99 and 60%, respectively. The further increase of CD concentration did not obviously influence the conversion and enantioselectivity. This suggested that after the adsorption amount of CD on the catalyst surface reached an equilibrium concentration, the activity and enantioselectivity of the catalyst could keep a stable level if CD concentration is in a range of the suitable excess.

3.5. Effect of temperature

The effect of the temperature on the asymmetric hydrogenation of ethyl pyruvate was drawn in Fig. 2. The e.e. values decreased gradually from 63.1 to 41.0% with increasing temperature in the range of 253–335 K, but the conversion of ethyl pyruvate did not change. Even at 253 K the conversion of the substrate could still reach 99%. The phenomena could probably be attributed to the transformation of cinchonidine to dihydrocinchonidine (DHCD) and its further hydrogenation products with increasing temperature. The hydrogenation products of DHCD are poor chiral modifications for rhodium nanoclusters, and the desorption of the modifiers easily occur at high temperature as reported in the literature [15,16]. The increase of the temperature could also decrease the difference of energy barrier in the transition state between *R*-ethyl lactate and *S*-ethyl lactate. Therefore the low temperature was favorable for the formation of *R*-ethyl lactate.

3.6. Effect of hydrogen pressure and reaction time

The effect of the hydrogen pressure was shown in Fig. 3. The increase of hydrogen pressure did not obviously influence the conversion, but e.e. values increased initially with increasing hydrogen pressure. When the pressure rose from 2 to 7 MPa, the conversion and e.e. value increased about 2 and 12%, respectively. This indicated that the high adsorption concentration of hydrogen on the catalyst surface would be favorable for the construction of chiral reaction micro-circumstance.

The data listed in Fig. 4 suggested that the optimum reaction time was 1 h, while the ethyl pyru-

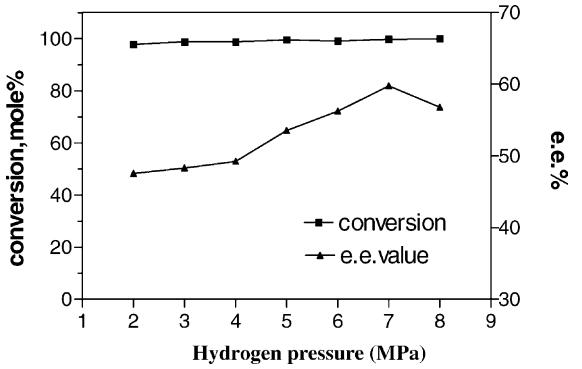

Fig. 3. Effect of the hydrogen pressure on the enantioselective hydrogenation of ethyl pyruvate. The reaction conditions are the same as those listed in Table 4.

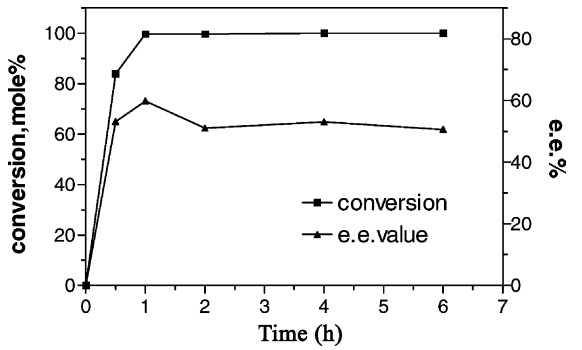

Fig. 4. Effect of the time on the enantioselective hydrogenation of ethyl pyruvate. The reaction conditions are the same as those listed in Table 4.

vate was almost completely converted to ethyl lactate and the enantioselectivity reached to 60% e.e. at 298 K. According to the curve of the conversion versus time, the initial reaction rate was 1675 mol/mol h. The extension of reaction time could also cause the hydrogenation of DHCD [17,18]; this would reduce its modification ability and thereby the enantioselectivity decreased.

4. Conclusion

This study shows that TS-1 supported rhodium nanoclusters is a very active catalyst; CD and QN are excellent chiral modifiers in the asymmetric hydrogenation of ethyl pyruvate. They not only induces the enantioselectivity, but also could greatly accelerate the reaction. The interaction between the support and rhodium nanoclusters as well as the adsorption of modifier on the support surface play an important role in increasing of the catalytic activity and enantioselectivity.

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