

Enantioselective hydrogenation of trifluoroacetophenone over polymer-stabilized platinum nanoclusters

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Abstract

The enantioselective hydrogenation of 2,2,2-trifluoroacetophenone to (*R*)-1-phenyl-2,2,2-trifluoroethanol was investigated over finely dispersed polyvinylpyrrolidone-stabilized platinum nanoclusters modified with cinchonidine. It was shown that the modifier, apart from inducing enantioselectivity, has a considerable rate-promoting effect on this reaction. Different from what had been reported for the conventional supported platinum catalyst, polyvinylpyrrolidone-stabilized platinum nanoclusters were demonstrated to be associated with structure insensitivity for this reaction. The favorable reaction pressure was 2.0 MPa with a mixture of *o*-dichlorobenzene and ethanol (*v/v* = 20/1) as solvent. Moderate cinchonidine concentration was also advantageous for enantiodifferentiation. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Trifluoroacetophenone; Cinchonidine; Platinum nanocluster; Enantioselective hydrogenation

1. Introduction

Asymmetric catalysis is, without doubt, one of the most promising methods for the synthesis of chiral compound [1]. In response to industrial and economic needs, researchers have paid much attention to heterogeneous asymmetric catalysis for many years [2–5]. Within this domain, the Orito reaction [6,7] is one of the most frequently studied reactions.

Orito reaction was first observed in the late 1970s. However, this reaction was regarded as enzymic in the earlier work, i.e. considerable enantioselectivity and activity could only be achieved with the special combination of active metal (platinum), modifier

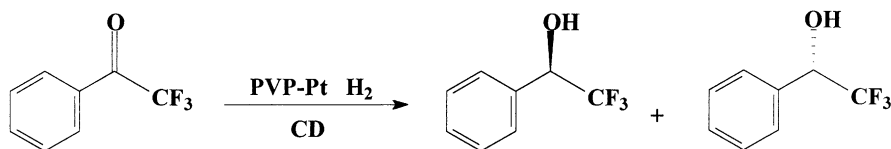
(cinchona alkaloid) and reactant (α -ketoester). Over the past 2 decades, continuing efforts have been directed towards optimizing reaction conditions [8–11], developing novel modifiers [12], obtaining information about the exact structure of modifier–substrate intermediate complex [13] and expanding substrate scopes [4,14–22]. The asymmetric hydrogenation of 2,2,2-trifluoroacetophenone (TFAP) over conventional supported platinum catalysts modified with cinchona alkaloids, which was reported by Baiker and co-workers in 1997 [15], is one of the few successful examples of the above efforts.

Polymer stabilized metal colloids or clusters are of interest in catalysis, both from a theoretical and practical point of view [23–25]. Recently, we investigated the enantioselective hydrogenation of α -ketoesters [10,26,27] and α -diketones [28] over polyvinylpyrrolidone-stabilized platinum or iridium

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Scheme 1.

nanoclusters. It was shown that the catalyst not only afforded superior enantioselectivity but also exhibited novel catalytic properties that differ completely from their conventional heterogeneous counterparts. Interested by the unusual performances of this type of catalyst, we initiated a study of the asymmetric hydrogenation of TFAP over polyvinylpyrrolidone-stabilized platinum nanocluster catalysts (PVP-Pt) with cinchonidine (CD) as the modifier (Scheme 1). In this paper, we report the results of this investigation.

2. Experimental

2.1. Materials and instruments

Firstly, 2,2,2-trifluoroacetophenone (TFAP, Acros) and cinchonidine (CD, Acros) were used as received. Hydrogen (H_2) with a purity of 99.999% was supplied by Beijing Gases Factory. Other reagents were purchased from Beijing Chemicals and had a level of analytical grade. Polyvinylpyrrolidone-stabilized platinum nanoclusters (PVP-Pt) in the form of dark-brown homogeneous dispersions were prepared and characterized according to our published procedures [26,28].

The enantioselectivity and activity were determined by a Bei-Fen SQ-204 gas chromatograph with a Chirasil-DEX CB (Chrompack) capillary column. The enantioselectivity is expressed as $ee (\%) = 100 \times ([R] - [S]) / ([R] + [S])$.

2.2. Hydrogenation reaction

The hydrogenation reaction was carried out in a 100 ml stainless steel autoclave. Typically, the reaction mixture contained 0.52 g (2.99×10^{-3} mol) TFAP, 5.0×10^{-3} g (1.70×10^{-5} mol) CD and 10 ml PVP-Pt dispersion (containing 6.4×10^{-6} mol Pt and 10 ml solvent). Hydrogen was charged several times to replace air. The reaction mixture was stirred vigor-

ously at 298 K for 3.5 h under a hydrogen pressure of 1.0–5.0 MPa. The reaction was then stopped for the gas chromatography analysis.

3. Results and discussion

3.1. Influence of solvents

Solvent is an essential factor in asymmetric hydrogenation [4,29,30]. We investigated the influence of solvent on the title reaction extensively. Considering that PVP-Pt can only be dissolved in polar solvents like alcohol, we utilized mixed solvents (consist of ethanol and another solvent) in most cases. Under the reaction conditions employed in this work, all the solvents were stable towards hydrogenation as indicated by GC analysis. The influence of solvent on the conversion and enantioselectivity is listed in Table 1. Fig. 1 shows the dependence of enantioselectivity and conversion on the *o*-dichlorobenzene/ethanol volume ratio. It is interesting to note that solvents with similar molecular structure to TFAP, such as *o*-dichlorobenzene, toluene, etc. are generally ad-

Table 1

The influence of solvents on the conversion and enantioselectivity of the asymmetric hydrogenation of TFAP over PVP-Pt catalyst^a

Entry	EtOH/solvent ^b	Conversion (%)	ee (%) ^c
1	EtOH/acetone	50.9	8.5
2	EtOH/dichloromethane	7.3	2.8
3	EtOH/tetrahydrofuran	18.2	19.5
4	EtOH/toluene	94.8	17.0
5	EtOH/ <i>o</i> -dichlorobenzene	88.8	20.4
6	EtOH/ <i>o</i> -chlorotoluene	23.4	15.5

^a Reaction conditions: 298 K, 4.0 MPa, 2.99×10^{-3} mol TFAP, 6.4×10^{-6} mol Pt (particle diameter: 1.5 nm, $\sigma = 0.38$ nm), 1.70×10^{-5} mol CD, 10 ml mixed solvent, 3.5 h.

^b $v/v = 1/20$.

^c (*R*)-1-phenyl-2,2,2-trifluoroethanol in excess.

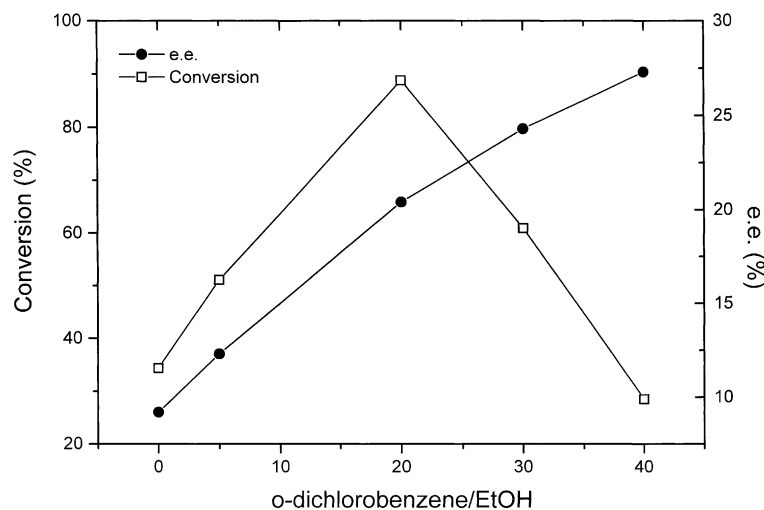


Fig. 1. The dependence of enantioselectivity and conversion on the *o*-dichlorobenzene/ethanol volume ratio (reaction conditions: 298 K, 4.0 MPa, 2.99×10^{-3} mol TFAP, 6.4×10^{-6} mol Pt (particle diameter: 1.5 nm, $\sigma = 0.38$ nm), 1.70×10^{-5} mol CD, 10 ml mixed solvent, 3.5 h).

vantageous for conversion and enantiodifferentiation. With the increase of *o*-dichlorobenzene content in the mixed solvent, ee increases regularly (see Fig. 1). However, the conversion culminates to its maximum with an *o*-dichlorobenzene/ethanol ratio of 20. Above this optimum point the conversion drops rapidly. This is caused by the insolubility of PVP-Pt in the mixed solvent that contains more *o*-dichlorobenzene.

3.2. Effect of modifier concentration

Considerable rate-accelerating effect of the modifier on the hydrogenation of α -ketoesters and α -diketones has already been observed [10,26,28,31]. The relationship between enantioselectivity or conversion and CD concentration in the present work is illustrated in Fig. 2. As is shown, the addition of CD in the reaction

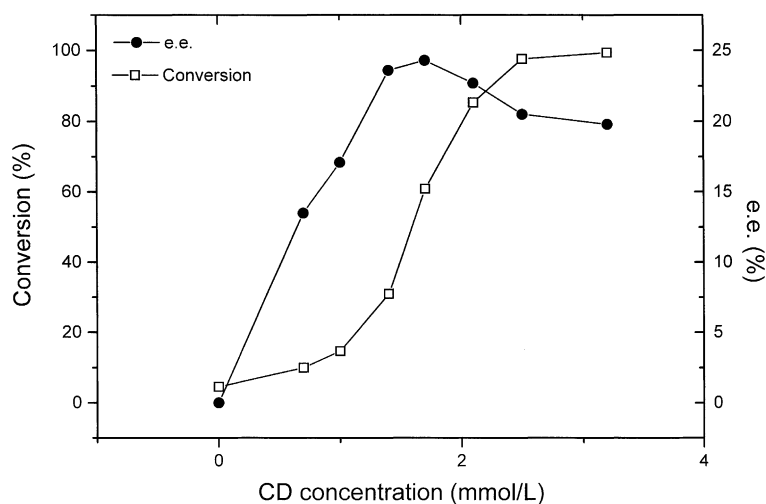


Fig. 2. The relationship between enantioselectivity or conversion and CD concentration (reaction conditions: 298 K, 4.0 MPa, 2.99×10^{-3} mol TFAP, 6.4×10^{-6} mol Pt (particle diameter: 1.5 nm, $\sigma = 0.38$ nm), 10 ml mixed solvent (EtOH/*o*-dichlorobenzene = 1/30), 3.5 h).

system, apart from inducing enantioselectivity, also has a considerable rate-promoting effect on this reaction. Maximum ee is achieved with a CD concentration of 1.7×10^{-3} mol/l. The average rate increases by a factor of 13.5 at this point compared with the average rate of racemic hydrogenation. In the range of low CD concentration (0 to 1.4×10^{-3} mol/l), the activity increases slowly with the increase of CD concentration. This is different from what had been observed in the enantioselective hydrogenation of α -ketoesters [10,26] and α -diketones [28] over the same types of catalyst, in which the rate-promoting effect is remarkable even in the range of low CD concentration. Compared with α -ketoesters or α -diketones, TFAP can be adsorbed more effectively on the platinum surface through the phenyl ring. This strong adsorption is probably responsible for the less remarkable promoting effect observed in the low CD concentration, because a strong substrate–catalyst interaction will hinder the modifier from being adsorbed effectively on the catalyst surface. Under higher CD concentrations (more than 2.5×10^{-3} mol/l), the rate-promoting effect is far more notable. The average rate increases by a factor of 22 compared with racemic hydrogenation and the conversion reaches to 99.4% at the CD concentration of 3.2×10^{-3} mol/l. However, the ee decreases slightly.

3.3. Effect of platinum particle size

The asymmetric hydrogenation of TFAP over conventional supported platinum catalysts is a structure sensitive reaction. Reductive pretreatment of the catalyst in flowing hydrogen improved the ee by a factor of 2, due to the increase of the average particle size of platinum during the pretreatment [15]. Recently, we reported that the asymmetric hydrogenation of α -ketoesters is structure insensitive in the PVP-Pt quasi-homogeneous system [10,26]. This is different from the conclusion obtained in the conventional supported platinum catalyst [32]. Therefore, it is worthwhile to investigate the structure sensitive/insensitive issue of the present reaction. We synthesized a series of PVP-Pt with different platinum particle size (diameter range: 1.4–3.9 nm; standard deviation range: 0.35–0.43 nm) and utilized them in the asymmetric hydrogenation of TFAP. The results indicate that, with a constant molar ratio of PVP to Pt (10:1), the turnover frequencies (calculated on the basis of average rate

and in terms of the fraction of the surface atoms determined according to the $10n^2 + 2$ packing rule for cubic close-packed arrangements of metal atoms with respective particle diameter) and ee change little with the particle diameter of platinum. Therefore, the titled reaction is also associated with structure insensitivity in the polymer-stabilized platinum nanocluster system.

3.4. Effect of hydrogen pressure

Pressure is also an important factor in enantioselective hydrogenation. For the conventional supported platinum catalyst, a higher hydrogen pressure is usually advantageous for activity while a moderate one is generally good for enantioselectivity. We examined the effect of hydrogen pressure from 1.0 MPa to 5.0 MPa. It can be seen from Fig. 3 that hydrogen pressure has little influence on the enantioselectivity of the present reaction. This is different from the enantioselective hydrogenation of α -ketoesters over PVP-Pt [10,26,27] in which a moderate hydrogen pressure (4.0 MPa) is advantageous for enantioselectivity. In our opinion, this difference is also due to the different adsorption ability of the two types of substrate on the platinum surface. The increase or decrease of enantioselectivity caused by the alteration of hydrogen pressure can be ascribed to the competitive adsorption of substrate and hydrogen on the metal surface [27,33,34], which is closely associated with solution concentration of the two types of material. The higher the hydrogen pressure, the higher the solution hydrogen concentration. However, the adsorption of TFAP on the platinum surface is probably too strong to be influenced by the solution hydrogen concentration. Thus, the alteration of hydrogen pressure fails to influence the enantioselectivity. It should be noted that the conversion collapses sharply under higher hydrogen pressure rather than increases regularly as it does over the conventional supported catalyst. This may be attributed to the diminution of the surface atoms of the platinum particle caused by partial agglomeration of the PVP-Pt colloid under higher-pressure as we previously observed on the PVP-Ir colloid [27].

In summary, we have made some researches on the asymmetric hydrogenation of 2,2,2-trifluoroacetophenone by using polyvinylpyrrolidone-stabilized platinum nanocluster catalyst. It is revealed that this reaction exhibits different properties from the well

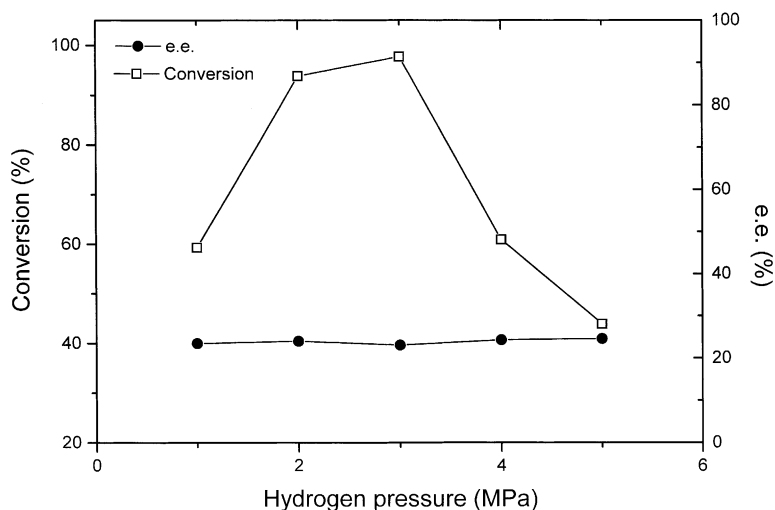


Fig. 3. Effect of hydrogen pressure on conversion and enantioselectivity (reaction conditions: 298 K, 2.99×10^{-3} mol TFAP, 6.4×10^{-6} mol Pt (particle diameter: 1.5 nm, $\sigma = 0.38$ nm), 10 ml mixed solvent (EtOH/*o*-dichlorobenzene = 1/30), 3.5 h).

studied hydrogenation of α -ketoesters or α -diketones, e.g. rate-accelerating effect of the modifier, influence of hydrogen pressure, etc. The difference can be rationalized in terms of the different interaction between substrate and catalyst. Most important of all, the reaction proved to be associated with structure insensitivity. This is different from the conclusion drawn from the conventional supported Pt catalyst.

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