

Asymmetric hydrogenation of α -diketones over polymer-stabilized and supported platinum clusters

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Abstract

The asymmetric hydrogenation of α -diketones was investigated over finely dispersed polymer-stabilized and supported platinum clusters. It was shown that the rate-accelerating effect of cinchonidine in this reaction was much less pronounced than the case of Pt/cinchona/ α -ketoester system. The activity and enantiomeric excess (e.e.) for 3-hydroxy-2-butanone reached maximum when the molar ratio of the modifier to reactant was about 1:650. There was no close correlation between the catalytic performance of the platinum clusters and the polarity of the solvents, whereas good enantioselectivity (> 40%) as well as activity could be obtained in a mixture of dichloromethane and ethanol. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: α -Diketone; Cinchonidine; Platinum cluster; Hydrogenation; Enantioselectivity

1. Introduction

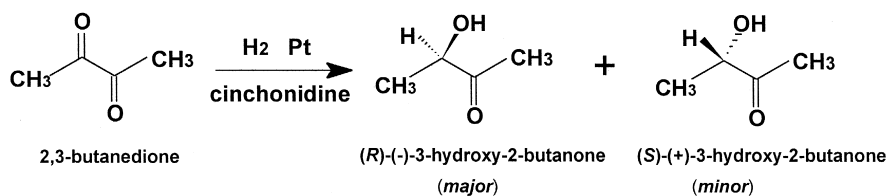
Asymmetric catalysis has become a most challenging subject in the field of organic synthesis and catalysis over the past two decades, both from the theoretical and practical point of view. Among the numerous enantioselective heterogeneous reactions, the Pt/cinchona-catalyzed hydrogenation of α -ketoesters is one of the few successful examples with more than 95% enantiomeric excess (e.e.) under favorable reaction conditions [1–3]. However, this system was shown to be almost enzymic in the earlier

work [4], i.e. considerable enantioselectivity and activity could only be achieved with the special combination of the active metal (Pt), modifier (cinchona alkaloid) and reactant (α -ketoester). It was not until recently that these restrictions were lifted with a series of development in diversification of the reaction [5,6], particularly in the scope of exploring the prochiral compounds that might be hydrogenated effectively in enantiodifferentiation [7–13]. A typical new reaction is the hydrogenation of α -diketones, which was first reported by Vermeer et al. in 1993 [14]. Owing to the conjugated keto groups in the reactant, the hydrogenation consists of two consecutive steps. Take 2,3-butanedione, e.g. the first-step reaction yields 3-hydroxy-2-butanone, similar to the case of α -ketoester. The best e.e., as described in the works of

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Scheme 1.

Studer et al. [10] and Slipszenko et al. [11], was ca. 45% in toluene or dichloromethane over conventional supported Pt catalysts. Interestingly, 3-hydroxy-2-butanone could be obtained with much higher e.e. (ca. 90%) in the course of the second-step hydrogenation due to the kinetic resolution caused by the modifier [10,11]. Nevertheless, its chemical yield was extremely low (< 10%) since most of it was converted to 2,3-butanediol.

As the bridge between metal atoms and bulk metals, ligand or polymer-stabilized metal colloids or clusters have received more and more attention in catalysis because of their unique physical and chemical behaviors [15,16]. Apart from the quantum size effect and high surface area, the catalytic performance can also be modified by the stabilizer, e.g. functional polymers. A large number of reactions have been carried out on this new type of catalysts [17], especially since the successful preparation of polymer-stabilized metal clusters by Hirai et al. with alcohol–water reduction method [18–20]. In the previous papers, we investigated the enantioselective hydrogenation of α -ketoesters over polyvinylpyrrolidone (PVP)-stabilized Pt and Ir nanoclusters [2,21,22]. It was shown that the catalysts not only afforded superior enantioselectivity (e.g. 97.6% e.e. for the hydrogenation of methyl pyruvate on a 1.4-nm Pt cluster), but also exhibited novel catalytic properties, e.g. structure insensitivity, which differs completely from their conventional heterogeneous counterparts. As the extension of such work, this paper deals mainly with the performance of polymer-stabilized and the corresponding supported Pt clusters in the asymmetric hydrogenation of α -

diketones, which might render us a better understanding of the characteristics of these cluster catalysts. The study will be focused on the first-step hydrogenation (e.g. 2,3-butanedione, Scheme 1) for the convenience of the comparison with that of α -ketoester, in which some important reaction parameters such as modifier concentration, solvent, less studied in the literature, will be investigated in detail to optimize the enantioselectivity as well as the activity.

2. Experimental

2.1. Materials

Poly (*N*-vinyl-2-pyrrolidone) (PVP) ($M_w = 40,000$; Fluka), 2,3-butanedione, 3,4-hexanedione, cinchonidine (all Acros) were used as received. Other reagents were supplied by Beijing Chemicals with a level of analytical grade.

2.2. Preparation of the colloidal clusters (PVP–Pt)

The PVP-stabilized platinum colloidal cluster (designated as PVP–Pt) was prepared by the alcohol–water reduction method in the literature [18–20]. For example, 5.1×10^{-2} mmol chloroplatinic acid ($\text{H}_2\text{PtCl}_6 \cdot 6\text{H}_2\text{O}$) was dissolved in a mixture of *n*-propanol (63 ml) and distilled water (7.0 ml) containing 0.51 mmol PVP and heated under reflux for 3 h. A dark brown sol resulted, which was then evaporated to dryness by a Rotavap and redispersed in ethanol prior to use.

2.3. Preparation of the supported cluster ($\text{Al}_2\text{O}_3\text{-Pt}$)

In a 100-ml beaker, 1.8 g Al_2O_3 (specific surface area $16.8 \text{ m}^2 \text{ g}^{-1}$) was stirred with the required amount of PVP–Pt sol for 22 h at room temperature. After filtration, the supported cluster was washed with ethanol and water and then dried at ambient temperature under vacuum for 18 h. The content of platinum was 0.5% by weight as determined by atomic absorption spectroscopy (AAS). Elemental analysis showed the content of nitrogen to be out of detection level, which indicated that the stabilizing polymer PVP, was thoroughly washed off.

2.4. Hydrogenation of α -diketones

Enantioselective hydrogenation of α -diketones was conducted in a 100-ml stainless autoclave. Typically, 11.3 mmol α -diketone, 5.0 mg cinchonidine and 7.0 ml PVP–Pt (containing 6.4×10^{-3} mmol Pt, 6.4×10^{-2} mmol PVP and 7.0 ml solvent) or 0.1 g $\text{Al}_2\text{O}_3\text{-Pt}$ (containing 2.6×10^{-3} mmol Pt) with 7.0 ml solvent were mixed and stirred vigorously in 4.0 MPa hydrogen at 25°C for a period of time. Then, the reaction was stopped for the gas chromatography analysis.

2.5. Analysis

Transmission electron microscopy (TEM) photographs were taken by using a Hitachi-9000NAR instrument. Specimens were prepared by placing a drop of the colloidal solution upon a copper grid covered with a perforated carbon film and then evaporating the solvent. The particle diameter was determined from the enlarged photographs and the size distribution histogram was obtained on the basis of the measurement of about 250 particles.

The conversion was analyzed on a Bei-Fen SQ-204 gas chromatograph (column: DEGS, 2 m, 110°C). The e.e. (%) = $100 \times ([R] - [S]) / ([R] + [S])$ was measured on a Bei-Fen SP-3700

gas chromatograph (column: bikis (2,6-di-*O*-pentyl-3-*O*-hex-6-enyl)-pentakis(2,6-di-*O*-pentyl-3-*O*-methyl)- β -cyclodextrin-polysiloxane, 20 m, 70°C).

Identification of the by-products was carried out on a Shimadzu QP-5050 gas chromatograph-mass spectrometer (GC-MS).

3. Results and discussion

3.1. TEM characterization of the PVP–Pt cluster

The TEM photograph and particle size distribution of the colloidal cluster are illustrated in Fig. 1. It can be seen from the figure that the PVP–Pt cluster has an average diameter of 1.5 nm and is finely dispersed with the standard deviation (σ) ca. 0.38 nm. Besides, neither the size nor its distribution will be changed after the immobilization of the colloidal cluster onto alumina, as demonstrated in our previous work [23–25].

3.2. Role of cinchonidine in the hydrogenation of α -diketones

As shown in Table 1, the addition of cinchonidine induces modest e.e. in favor of (*R*)-hydroxyketone in the hydrogenation of 2,3-butanedione and 3,4-hexanedione. At the same time, the conversion of the two reactants increases by a factor of 1.5–3 depending on the solvent used (entries 1 and 3; 5 and 7; 9 and 10), indicating that this enantioselective reaction is also ligand-accelerated [26,27]; however, far less notable than that in α -ketoester (methyl pyruvate) reduction [28,29] (entries 12–14). With respect to the racemic reactions, the hydrogenation of 2,3-butanedione proceeds very fast with >90% conversion after 1 h, while that of methyl pyruvate is <10% under the same conditions. This is probably ascribed to the stronger adsorption of α -diketones on the Pt surface [11], which favors the activation of the

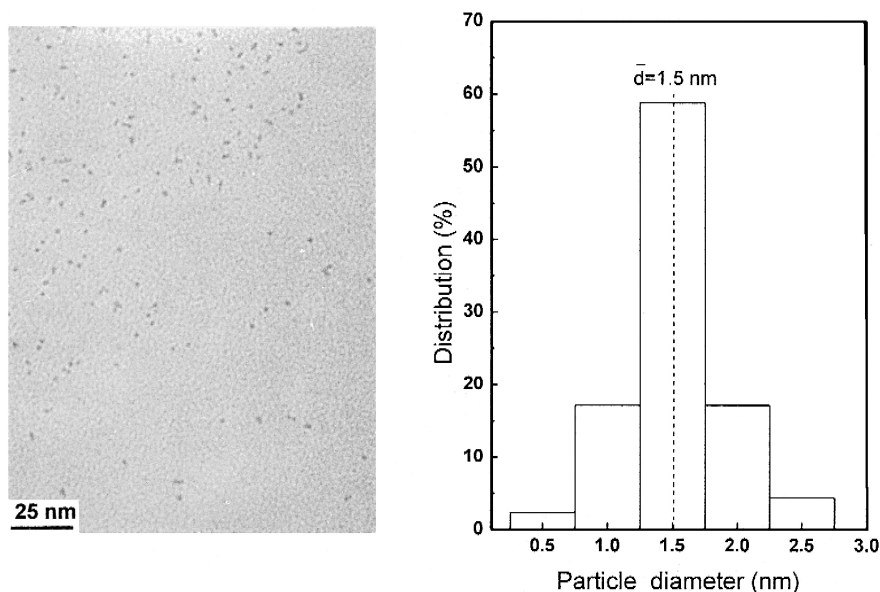


Fig. 1. TEM photograph (left) with the histogram plot of the particle size distribution (right) of the PVP–Pt colloidal cluster.

carbonyl groups and in turn counteracts the rate-promoting effect of the modifier. As reported by Vermeer et al. [14], the e.e. for the hydrogenation of 3,4-hexanedione was substantially higher than that of 2,3-butanedione in

ethanol over the conventional silica-supported Pt catalysts. For comparison, it is found in our experiment that the enantioselectivities are comparable in acetic acid (entries 7 and 11), albeit obviously lower for 4-hydroxy-3-hexanone with

Table 1

The role of cinchonidine in the hydrogenation of α -diketones and methyl pyruvate over the PVP–Pt cluster

Entry	Reactant ^a	CD addition	Solvent	Reaction time (min)	Conversion (%)	E.e. ^b (%)
1	2,3-B	No	Ethanol	20	45.7 ^c	0
2	2,3-B	No	Ethanol	60	91.3 ^d	0
3	2,3-B	Yes	Ethanol	20	90.7	23.5
4	2,3-B	Yes	Ethanol	60	95.5	27.9
5	2,3-B	No	Acetic acid	20	32.5	0
6	2,3-B	No	Acetic acid	60	57.5	0
7	2,3-B	Yes	Acetic acid	20	92.9	22.6
8 ^e	2,3-B	Yes	Acetic acid	60	80.5	20.4
9	3,4-H	No	Ethanol	60	60.8	0
10	3,4-H	Yes	Ethanol	60	94.9	18.0
11	3,4-H	Yes	Acetic acid	60	87.8	20.6
12	MP	No	Ethanol	60	6.2	0
13	MP	Yes	Ethanol	60	79.0	81.8
14	MP	Yes	Acetic acid	30	100	93.8

^a2,3-B: 2,3-butanedione; 3,4-H: 3,4-hexanedione; MP: methyl pyruvate.

^b(*R*)-hydroxyketone or (*R*)-methyl lactate in excess.

^c10% by-product.

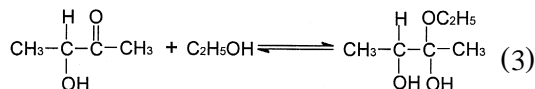
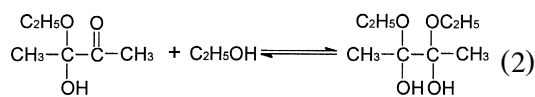
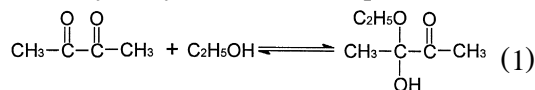
^d20% by-product.

^ePVP–Ir as catalyst.

ethanol as the solvent (entries 4 and 10). In addition, it is noteworthy that a 1.4-nm PVP–Ir cluster, synthesized by a similar method [22], is also suitable for 2,3-butanedione hydrogenation with the enantioselectivity approximate to the case of the PVP–Pt (entries 7 and 8); whereas the use of Ir catalyst in this reaction was not reported in the previous study.

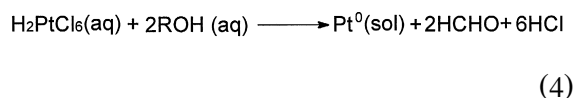
Acetic acid is a very efficient solvent for Pt/cinchona/ α -ketoester and Ir/cinchona/ α -ketoester systems, in which both the highest e.e. and activity can be registered. According to the molecular mechanics and quantum chemical calculations [30,31], the protonation of the quinuclidine nitrogen in the modifier favors its interaction with the α -carbonyl group in the reactant. However, this advantage is not exhibited in the hydrogenation of α -diketones since the PVP–Pt behaves somewhat better in ethanol (entries 3 and 7; 10 and 11). Therefore, it seems that in acetic acid, the favorable modifier–reactant interaction varies with the kind of the reactant, which might exert a large influence on the performance of the catalysts.

It is interesting to note that in the absence of cinchonidine, 10–20% of by-products arises during the reaction, which does not occur upon the addition of the modifier (entries 1–4). GC-MS analyses show that they are the hemiketals formed between ethanol and 2,3-butanedione as well as 3-hydroxy-2-butanone (Eqs. (1)–(3)).



As is known, hemiketals are liable to form in an acidic medium. In our experiment, the hydro-

chloric acid (HCl), generated during the preparation of the Pt cluster (Eq. 4), is hard to be removed completely, even after the rotary evaporation process [32] (see Section 2). Thus, the residual trace of HCl, introduced to the reaction solution by ethanol, catalyzes the hemiketal formation. On the basis of this fact, we propose that the addition of cinchonidine — an alkaloid, neutralizes the HCl in the system and inhibits the yield of the by-products. So the modifier in the PVP–Pt-catalyzed reaction is beneficial for not only the enantioselection, but also for the chemical yield of the target product.



3.3. Effect of modifier concentration

Asymmetric catalysis is distinguished from stoichiometrical asymmetric synthesis by the feature that a great quantity of chiral product can be induced by only a catalytic amount of the modifier. This is also clearly reflected in the hydrogenation of 2,3-butanedione in acetic acid. As shown in Fig. 2, the induction of enantioselectivity as well as the rate-accelerating effect

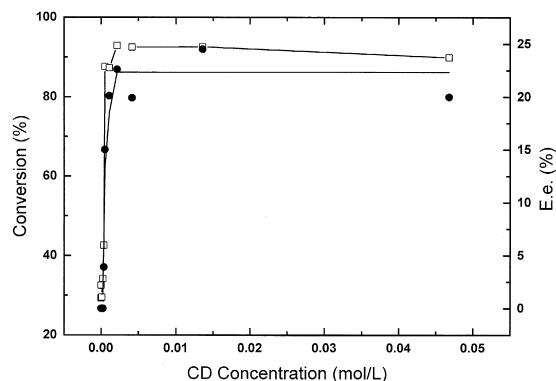


Fig. 2. Effect of modifier concentration on the activity and enantioselectivity for the hydrogenation of 2,3-butanedione over the PVP–Pt cluster (solvent: acetic acid, $t = 20$ min; □ conversion, ● e.e.).

commences at a 3.8×10^{-4} mol/l of cinchonidine. Subsequently, both the e.e. and activity reach maximum when the concentration is increased to ca. 2.2×10^{-3} mol/l, corresponding to the modifier/reactant ratio as low as 1:650. However, this value is still remarkably higher than that achieved in the hydrogenation of methyl pyruvate, i.e. less than 1/13 000 [33]. In our opinion, the reason for this tremendous difference can also be rationalized by assuming that α -diketone is more strongly adsorbed than α -ketoester on the Pt surface, as is mentioned above. On the other hand, since the reactant competed effectively for the surface with the modifier [4], larger amount of cinchonidine should be added to realize the maximum e.e. and activity in α -diketone hydrogenation.

3.4. Effect of solvent

Solvent is an essential factor for Pt/cinchona/ α -ketoester system, which modulates the modifier conformation [34], modifier–reactant interaction [5], solution hydrogen concentration [35] etc. and ultimately affect the enantioselectivity. As far as we know, dichloromethane, toluene, acetone and ethanol were chosen by Vermeer et al. [14] as the solvents in the hydrogenation of 2,3-butanedione to 3-hydroxy-2-butanone. The preliminary investigation re-

corded that the enantioselectivity tended to be better in weakly polar solvent, e.g. dichloromethane; while the activity was higher in polar solvent, e.g. ethanol. To make a more comprehensive understanding, we studied the solvents with a wider range of polarity commonly measured as dielectric constant, i.e. from 2 to 50 (Table 2).

Considering the limited solubility of the PVP–Pt cluster in weakly polar solvents, we immobilize it onto alumina for the investigation. Table 2 illustrates the solvent effect over the as-prepared Al_2O_3 –Pt cluster. As is shown, the activity and e.e. change irregularly with advantage for the enantioselectivity, whereas alcohol and its mixture with water good for the activity. This is consistent with the result over the conventional supported Pt catalyst [14]. Combining the respective merit displayed by the two kinds of solvents, we examined the catalytic performance of the Al_2O_3 –Pt cluster in the mixed solution of dichloromethane and ethanol. To our surprise, the conversion of 2,3-butanedione is elevated from 24.7% to 66.4% (Table 2) upon introducing only 0.1 ml ethanol to dichloromethane ($\text{C}_2\text{H}_5\text{OH}:\text{CH}_2\text{Cl}_2 = 1:70$); when the amount of ethanol is 1.0 ml, the conversion rises to 82.2%, i.e. the same as in the pure ethanol. Furthermore, It should be noted that the addition of ethanol causes no decrease in e.e., as compared to that in the pure dichloromethane.

Table 2
Effect of solvent on the activity and enantioselectivity for the hydrogenation of 2,3-butanedione over the Al_2O_3 –Pt cluster^a

Solvent	Dielectric constant	Conversion (%)	E.e. (%) ^b
Cyclohexane	2.02	55.6	18.3
Toluene	2.38	43.3	18.2
Acetic acid	6.15	79.4	31.0
Tetrahydrofuran	7.6	24.9	21.4
Dichloromethane	9.08	24.7	24.0
Dichloromethane/ethanol (70:1)	–	66.4	24.9
Dichloromethane/ethanol (7:1)	–	82.2	24.1
Acetone	20.7	38.3	15.6
Ethanol	24.3	82.8	18.3
Methanol	33.6	75.0	17.2
Ethanol/ H_2O (1:1)	ca. 50	91.5	16.0

^a $t = 60$ min.

^b (*R*)-hydroxyketone in excess.

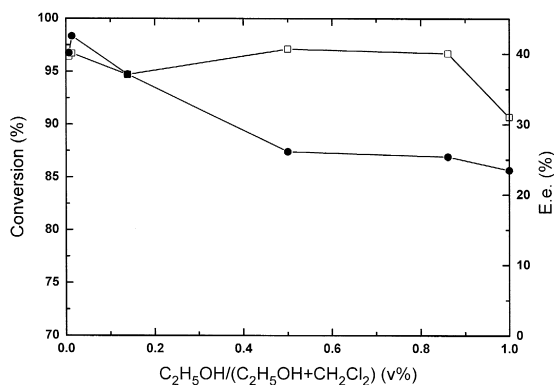


Fig. 3. Effect of the ratio of the mixed solution (as the solvent) on the activity and enantioselectivity for the hydrogenation of 2,3-butanedione over the PVP–Pt cluster ($t = 20$ min; □ conversion, ● e.e.).

Likewise, we carried out the reaction over the PVP–Pt cluster, which is readily to dissolve in the mixture of dichloromethane and ethanol, even if merely 0.05 ml ethanol is added. As shown in Fig. 3, the catalyst is quite effective at low volume ratio of ethanol (< 0.14), showing the enantioselectivity up to 42.4%, which almost equals the best result achieved over the conventional supported Pt catalysts [10,11]. Simultaneously, more than 95% of the reactant is hydrogenated, indicating no loss of activity in the mixed solution with dichloromethane in absolute excess.

The above results provide us the possibility of optimizing the catalytic performance by means of employing the mixture of weakly and strongly polar solvents, in which good enantioselectivity can be obtained, accompanied by high activity in this enantioselective hydrogenation.

In summary, we have made some researches on the asymmetric hydrogenation of α -diketones by using PVP–Pt and Al_2O_3 –Pt cluster as the catalysts. It is revealed that this reaction exhibits different properties from the well-studied α -ketoester hydrogenation, e.g. rate-accelerating effect of the modifier, solvent effect etc. Most important of all, the best e.e. for α -hydroxyketone on both the Pt cluster and conventional heterogeneous Pt catalysts is much

lower than that obtained for α -hydroxyester. On one hand, the faster racemic α -diketone hydrogenation weakens the enantiodifferentiation ability of the modifier. On the other, the electronic character of the carbon adjacent to the α -carbonyl group has a marked effect on the enantioselectivity. It seems to be deduced from the work of Mallat et al. [7] that excellent e.e. correlates with the carbonyl compound bearing a strong electron-withdrawing group in α position. For comparison, $-COOR$ has a stronger electron-withdrawing ability than $-COR$, which partly accounts for the better e.e. in the hydrogenation of α -ketoesters. Further investigations over the cluster including those on the search for new reactants are being undertaken in our laboratory.

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