Enantioselective Hydrogenation of Pyruvates over Polymer-stabilized and Supported Platinum Nanoclusters

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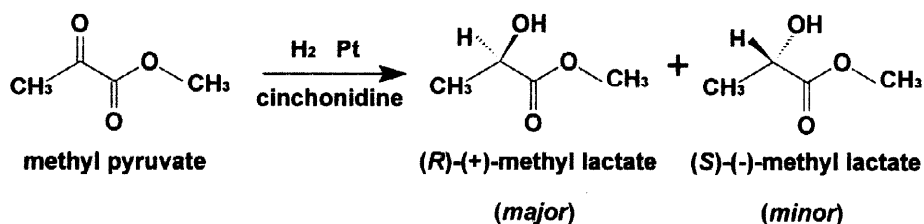
Abstract:

The cinchonidine-modified enantioselective hydrogenation of pyruvates has been studied over polyvinylpyrrolidone-stabilized platinum (PVP-Pt) and the corresponding alumina-supported platinum (Al_2O_3-Pt) clusters. It is shown that the catalysts with particle size less than 2.0 nm demonstrate >90% enantioselectivity in favor of (R)-lactates. The solvent effect is similar to that over the conventional supported platinum catalyst except for tetrahydrofuran. These colloidal and supported clusters are stable with no obvious loss of activity and enantioselectivity even after 18 months standing in air at room temperature. Molecular mechanics calculations of the modifier-reactant interaction on the platinum surface suggest that it is possible to obtain good enantioselectivity on the small clusters. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: enantioselective hydrogenation; pyruvate; platinum nanocluster; molecular mechanics

1. Introduction

The enantioselective hydrogenation of α-ketoesters (e.g. methyl pyruvate, Scheme 1) to the corresponding α-hydroxyesters on cinchona alkaloid (as well as some newly synthesized modifiers) modified platinum, originally reported by Orito and co-workers [1-4], has gained great attention in the past decade with approximately 100 papers published covering various

aspects of this catalytic reaction. An interesting characteristic of this reaction over the conventional supported Pt catalyst is the distinct structure sensitivity, which was shown in Baiker and Blaser's earlier work that good enantioselectivity and activity can only be achieved with Pt particles larger than about 3-4 nm in diameter [5, 6]. So far the reason for this phenomenon remains unclear yet. A possible explanation, as they proposed, is that "the probability of obtaining large ensembles where the modifier and reactant can adsorb in a stereochemically defined arrangement is higher for the larger particles", based on the assumption of the co-adsorption of the modifier and reactant on the Pt surface [5].

methyl pyruvate $\xrightarrow[\text{cinchonidine}]{\text{H}_2 \text{ Pt}}$ (R)-(+)-methyl lactate (major) + (S)-(-)-methyl lactate (minor)

Scheme 1

Nanocluster or colloidal catalysts, especially with the size ranging from 1 to 4 nm, have become a hot topic in recent years and many researches have been focused on investigating their unique catalytic properties as compared to the conventional supported counterparts [7, 8]. However, their application in the title reaction is less studied. Bönnemann et al. synthesized several Pt colloidal clusters stabilized by the protonated modifier dihydrocinchonidine and obtained about 80% e.e. in the hydrogenation of ethyl pyruvate [9]. Employing polyvinylpyrrolidone (PVP) as the stabilizer, we prepared a series of finely dispersed Pt colloidal clusters with different particle diameters which have proved to be very effective with enantioselectivity above 95% in favor of (R)-methyl lactate [10]. Most importantly, it has been found that in both Bönnemann's and our work the reaction is related to structure insensitivity and that an excellent e.e. is observed on a tiny cluster bearing a mean size of ca. 1.5 nm.[1] Thus, the colloidal clusters have indeed shown different features from the conventional heterogeneous catalysts, which deserves an intensive study because it will not only render a deeper understanding of the reaction mechanism, but also provide a

[1] In the course of this study, we received a personal communication from Professor J. Bradley (a report on American Chemical Society Meeting in Orlando) that a colloidal cluster stabilized by PVP with a mean size of about 1.7 nm is very effective in this asymmetric hydrogenation.

possibility of utilizing effectively Pt with more surface atoms for industrial application. This paper deals with these further investigations including the effect of the size of the reactant, the aging of the colloidal clusters and the behavior of the supported ones. Molecular mechanics calculations are also performed in the study of the modifier-reactant interaction on the surface of the Pt clusters.

2. Results and discussion

2.1. Effect of the size of the reactant

Structure-sensitive and structure-insensitive reactions are generally diagnosed in catalysis experiments by varying the sizes of metal particles [11]. But from another point of view, the effect of the sizes of the reactants can also be studied to give some indirect evidence. Up to now the α-ketoesters studied include methyl and ethyl pyruvate [2, 5, 6, 12-15], methyl and ethyl benzoylformate [1, 3, 4], ethyl 4-phenyl-2-oxobutyrate [14] and ketopantolactone [16, 17]. However, the results associated with the reactant size effect are not systematic due to the inconsistency in reaction conditions and the relatively large difference in the structures of the substituted groups (e.g. methyl and phenyl group) of the α-ketoesters. In this research we changed the size of the reactants by using pyruvates with different alkyl groups in the ester groups. It has been shown in our previous report [10] that a 97.6% e.e. was recorded in the hydrogenation of methyl pyruvate over a PVP-Pt of ca.1.4 nm, which seems to contradict Baiker's study [5, 6] in view of the enantioselective hydrogenation site capable of anchoring the bulky modifier-reactant complex. For further research, we synthesized four sorts of pyruvates, i.e. n-propyl, iso-propyl, n-butyl and iso-butyl pyruvate by transesterification (see the Experimental) and tested their reaction properties in comparison with those of methyl and ethyl pyruvate. As shown in Table 1, the activity and enantioselectivity have a tendency to decrease with the increase of -CH$_2$- in ester groups of the reactants over the 1.4 nm PVP-Pt. This is in agreement with the previous findings that higher e.e. is often accompanied by a higher reaction rate on account of the ligand-accelerated effect exhibited by the Pt/cinchona system [18, 19]. Although a sudden decrease both in e.e. and activity is observed for the case of iso-propyl pyruvate, the reason is still obscure. Nevertheless, the enantioselective reaction

runs well for all of the reactants, thus demonstrating circumstantially its structure insensitivity over the colloidal Pt cluster.

Table 1

Effect of the reactant size on the activity and enantioselectivity for the enantioselective hydrogenation of pyruvates over a 1.4 nm (σ=0.35 nm) PVP-Pt colloidal cluster [a]

Reactant	Conversion (%)	E. e. (%) [b]
methyl pyruvate	100	97.6
ethyl pyruvate	100	93.8
n-propyl pyruvate	100	95.6
iso-propyl pyruvate	58.5	77.1
n-butyl pyruvate	86.7	90.5
iso-butyl pyruvate	95:5	93.1

[a] t=0.5 h, solvent = acetic acid; for other conditions see the Experimental.

[b] (R)-lactate in excess.

2.2. Effect of solvent over the alumina-supported Pt cluster

Solvent plays a crucial role in the enantiodifferentiation ability of the catalysts. So far most of the work is concentrated on the relationship between the activity as well as enantioselectivity and the solvent polarity often expressed as the dielectric constant. Blaser et al. investigated the performance of a PVP-Pt (particle size not mentioned) in toluene, ethanol and iso-propanol and found that better results were realized in polar solvents, e.g. ethanol (45%–e.e.; 0.3 min^{-1}–average turnover frequency) instead of a weakly polar one, e.g. toluene (15%; 0.1) [20]. However, the accuracy of this kind of solvent effect is suspected because of the limited solubility of the stabilizer PVP in apolar and weakly polar solvents such as toluene.[2] To overcome this problem, we studied the solvent effect related to the cluster by using the Al_2O_3-Pt derived from the immobilization of the PVP-Pt. It is shown in Table 2 that similar to the experience over the conventional supported Pt [21], the activity shows a less clear correlation, whereas the enantioselectivity decreases with the increasing dielectric constant of the solvent, accompanied by a maximum for acetic acid. An obvious difference is that tetrahydrofuran, a very good solvent in Blaser's work [21] (total conversion of ethyl

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[2] In accordance with the experimental conditions shown in Ref. 20, we mixed 5 mL ethyl pyruvate, 20 mL toluene and 2.5 mL PVP-Pt (dispersed in the 1:1 mixture of methanol and water) and got two phases in the system with the PVP-Pt concentrated in the water phase.

pyruvate with an e.e. of near 80%), is not suitable under our conditions where both the activity and e.e. are the lowest (Table 2). This is not special for the Al_2O_3-Pt cluster since a similar observation has also been made on the title reaction over the Al_2O_3-Ir cluster prepared in the same way [22]. Solvent can not only interact with the reactant (hemiketal formation, transesterification, etc.) but can also change the conformation of the modifier and consequently affect the enantioselectivity [23]. For example, it is inferred from Baiker's work [24] that in apolar solvents the modifier is apt to adopt a more favorable conformation

Table 2

Effect of solvent on the activity and enantioselectivity for the enantioselective hydrogenation of methyl pyruvate over a 1.2 nm (σ=0.30 nm) Al_2O_3-Pt cluster[a]

Solvent	Dielectric constant	Conversion (%)	E. e. (%)[b]
cyclohexane	2.02	100	73.5
toluene	2.38	86.6	73.8
acetic acid	6.15	99.0	89.5
tetrahydrofuran	7.6	21.2	45.2
dichloromethane	9.08	63.7	70.5
n-butanol	17.1	80.9	63.5
ethanol	24.3	74.2	59.0
methanol	33.6	47.1	57.0
H_2O	80.4	79.9	44.6

[a] t=2.0 h except in acetic acid 1.0 h, for other conditions see the Experimental.

[b] (R)-methyl lactate in excess.

which is beneficial for the enantiodifferentiation. In our opinion, however, there is another important factor which might have been neglected in the previous study. Blackmond et al. have recently proved that the solution hydrogen concentration ($[H_2]$) has a positive effect on the formation of the (R) isomer (10,11-dihydrocinchonidine as the modifier) [25, 26]. Keeping the hydrogen pressure constant, they obtained different enantioselectivities upon different $[H_2]$ by varying the agitation speed. As is known, H_2 is an apolar molecule and more ready to dissolve in apolar solvents. The solubility of H_2 under 4.0 MPa and 25°C in cyclohexane, ethanol and H_2O is about 4.0 mL, 2.5 mL and 1.0 mL (normalized to 25°C and 0.1 MPa, per mL solvent), respectively [27]. So the better performance in apolar solvents can be additionally ascribed to the higher $[H_2]$ in the reaction system.

2.3. Effect of the metal particle size of the alumina-supported Pt cluster

As has been reported in our previous work concerning the PVP-Pt [10], the title reaction is structure insensitive with the Pt particle diameter in the range of 1.4 to 3.9 nm. To make a further confirmation about this intriguing feature exhibited by the clusters, we immobilized the PVP-Pt (1.1–3.3 nm) onto the alumina support and then rinsed all the PVP out. It should also be noted that the Pt particle size and the size distribution remain unchanged after the immobilization, as verified by TEM observation in our previous study [28-31]. As shown in Figure 1, the reaction in acetic acid is less structure sensitive over the as-prepared Al_2O_3-Pt clusters with the turnover frequency (TOF) somewhat better and e.e. lower for the larger particles. In addition, toluene, a less polar solvent, was also used to eliminate the possibility that the conclusion drawn might be explained as being solvent specific. As shown in the Figure, a similar trend can also be observed with the e.e. a bit more obviously better for the smaller particles, which is in line with our result over the PVP-Pt that the cluster of 3.9 nm affords a lower enantioselectivity in ethanol [10]. All of these experiments indicate that the cluster catalysts must have a different mode of action because e.e. is considerably higher in general for larger particles (especially>3-4 nm) over the conventional supported Pt catalysts. It has been reported that the metal-support interaction plays a very important role in the heterogeneous catalysis [32, 33]. Combining this and the large difference in the preparative procedure between the conventional supported Pt metal catalysts and our cluster catalysts, we propose that the structure-sensitive reaction property of the former might be related to the stronger metal-support interaction caused by the high temperature treatment process during the preparation (e.g. reduction with thermal decomposition) or that commonly carried out prior to the reaction (400°C pre-reduction in hydrogen). On the other hand, since the cluster catalysts are more narrowly dispersed (σ<0.5 nm) than those prepared in Baiker's work [5, 6] and even than the two commercial ones (3.1± 0.9 nm, 2.6 ± 0.7 nm) often used, our conclusion about the particle size on this reaction should be more convincing.

2.4. Effect of the aging of the Pt cluster

As compared to the conventional supported catalysts prepared by high-temperature treatment, the polymer-stabilized Pt and their supported analogues are synthesized under

much milder conditions and thus may display some unusual properties in the field of catalysis because of their immaturity in metallography. On the other hand, in the course of
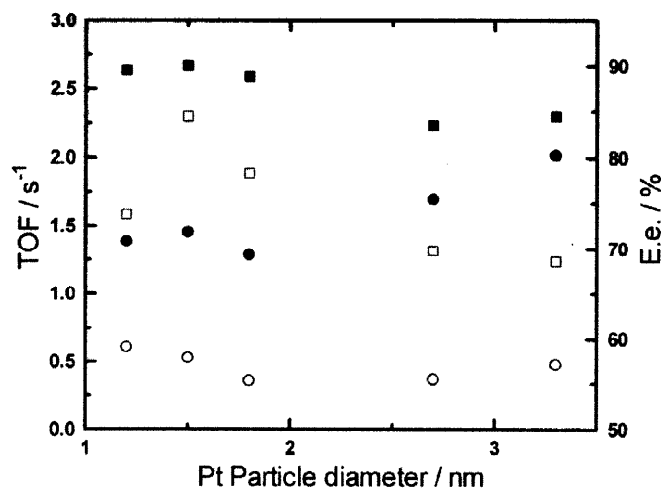

Figure 1 Effect of Pt particle size on the TOF and E.e. for the enantioselective hydrogenation of methyl pyruvate. In acetic acid (t=1.0 h), ●–TOF, ■–E.e.; in toluene (t=2.0 h), O–TOF, □–E.e..

the aging, e.g. standing, there is the chance that the micro-crystals of the clusters tend to be perfect, which may also affect their catalytic behavior, as has been shown in the selective hydrogenation of o-chloronitrobenzene: the activity and the selectivity to o-chloroaniline decrease gradually with lengthening standing time of a 1.2 nm PVP-Pt (PVP/Pt=50) [34]. In the title reaction, we tested the performance of the Pt clusters that are treated by three methods: (I) the PVP-Pt standing at room temperature (r. t.) for a period of time; (II) the PVP-Pt immobilized onto alumina after standing at r. t. for a period of time; (III) the PVP-Pt immobilized onto alumina immediately after preparation and then standing at r. t. for a period of time. However, the results in Table 3 show that in all of the three cases the activity and enantioselectivty changed little even when the clusters have been standing for one year or more. This suggests that the enantioselective hydrogenation of pyruvate is insensitive to the aging process of the clusters. Moreover, it should be reiterated that PVP is such an excellent stabilizer that even for the colloidal cluster with less amount of the polymer (PVP/Pt=10), there is little variation in the particle size after about one and a half years' standing, as shown by TEM (Figure 2). The slight agglomeration may account for the
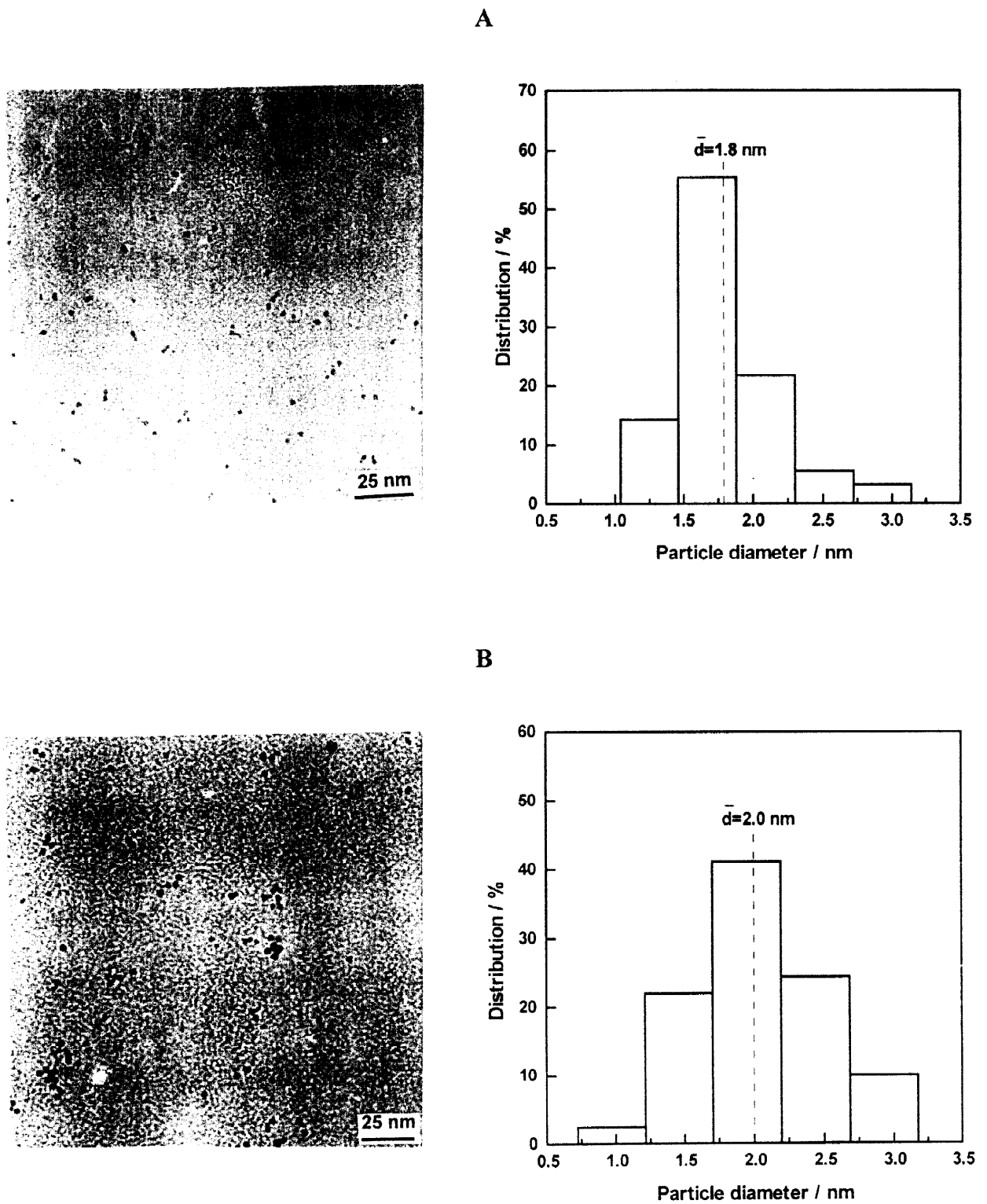
A

B

Figure 2 TEM photograph (left) with the histogram plot of the particle size distribution (right) of the PVP-Pt (PVP/Pt=10:1) colloidal cluster. A: newly prepared; B: standing at r. t. for about one and a half year.

relatively larger decrease of the activity (82.4% to 61.7%) in aging form I (Table 3).

Table 3

Effect of the aging of Pt cluster on the activity and enantioselevtivity for the enantioselective hydrogenation of methyl pyruvate [a]

Catalyst	PVP/Pt [b]	d (σ) [c] (nm)	Aging form [d]	Aging time (d)	Conversion (%)	E. e. [e] (%)
PVP-Pt	10	1.8 (0.37)	I	30	82.4	81.4
				475	61.7	84.6
Al₂O₃-Pt	50	1.2 (0.30)	II	2	99.0	89.5
				55	100	87.8
				105	97.4	86.7
				305	97.8	86.7
Al₂O₃-Pt	50	1.2 (0.30)	III	50	100	91.3
				490	100	89.3
Al₂O₃-Pt	10	1.5 (0.38)	III	10	91.9	90.0
				120	93.5	89.9

[a] Reaction over PVP-Pt and Al₂O₃-Pt carried out in ethanol (t=0.5 h) and acetic acid (t=1.0h), resp., for other conditions see the Experimental.

[b] molar ratio of PVP to Pt in the precursor PVP-Pt for Al₂O₃-Pt preparation.

[c] particle diameter and size distribution (in parenthesis) of the newly prepared PVP-Pt.

[d] as the sequence appeared in the text.

[e] (R)-methyl lactate in excess.

2.5. Molecular modelling

Many efforts have been dedicated to developing a modifier-reactant-metal interaction model to interpret the observed sense of the enantiodifferentiation, since cinchonidine, the most studied modifier and its near enantiomer cinchonine cause the catalyst to produce (R)- and (S)-lactate, respectively. Among them molecular mechanics is a very useful tool, especially with the rapid development of computer science in recent years. Based on the experimental fact that alkylation of the quinuclidine nitrogen almost eliminates the enantiodifferentiation of cinchonidine [35] and theoretical investigations [16, 36-40], Baiker et al. put forward a 1:1 interaction model in which the quinuclidine nitrogen of the modifier acts either as a nucleophile or as an electrophile (upon protonation) to interact with the α-carbonyl group of the reactant. The complex formed in the latter case is more stable due to a favorable electrostatic interaction, thereby offering a good explanation to the experimental observation that the highest e.e. is registered in acetic acid [14]. By means of molecular

mechanics (with Amber or MM2 force field) and AM1 semiempirical methods, two stable complexes between methyl pyruvate and cinchonidine were optimized which upon hydrogenation would yield (R)-methyl lactate and (S)-methyl lactate, respectively. The precursor to (R)-methyl lactate can be located on the ideal Pt (111) "surface" via the quinoline moiety of the modifier and the two carbonyl groups of methyl pyruvate (both adsorbed parallel to the Pt surface), without hindering the interaction between the carbonyl groups and Pt surface; while the one affording (S)-methyl lactate is sterically constrained. An opposite behavior is found when cinchonine is chosen as the modifier. This model has been successful in elucidating the enantiocontrol and from which the explanation for the Pt particle size effect related to the conventional supported catalysts mentioned above seems reasonable since the modifier-reactant complex requires a flat space (Pt surface) large enough (about 20 Pt atoms) to be accommodated on. However, it did not take into account the quantum description of metal-adsorbate interaction, a very important factor in catalytic reactions.

As an extension of Baiker's work, molecular modelling was also used in our present study to explore the possible mechanism of the enantiodifferentiation in the enantioselective hydrogenation of methyl pyruvate (MP). This modelling is aimed at the interactions of molecules in the ground state, and the effect of the existence of the modifier molecule on the enantioface selection of the reactant molecule, which is adsorbed on the same surface. The metal-adsorbate interactions are also considered so that the model may be more close to the real reaction system.

First, molecular mechanics (MM) calculations with universal 1.02 force field (UFF) were performed to determine the conformation of cinchonidine (CD). It is known that the two dihedral angles of T_1 and T_2, shown in Scheme 2, are significant for the stable conformation of CD [41, 42]. The calculated results on the individual CD indicate that the values of T_1 and T_2 obtained here are more close to the experimental ones [43] than those from MM2 force field [16] (Table 4). Therefore, UFF adopted in this calculation is appropriate for the CD system.

Since UFF includes many metal elements, e.g. Pt, the adsorption of CD on the Pt surface can be feasibly described with the force field. The results show that the quinoline ring of CD

is the main moiety adsorbed on the Pt (100) surface and it adopts a parallel adsorption. This
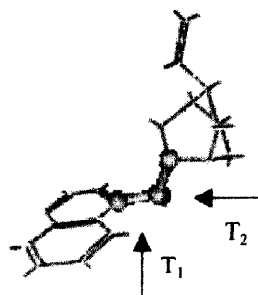
Scheme 2

Table 4

Values of T_1 and T_2

Method	T_1	T_2
X-ray structure	101.4°	158.1° [43]
Ab initio	100.5°	156.2° [16]
MM2	93.2°	156.4° [16]
UFF (this work)	100.2°	154.7°

obtained geometry corresponds well with the hydrogen isotope (H/D) exchange study made by Wells [44], meanwhile, it is in agreement with the assumption in the earlier study where the quinoline ring is considered as the reference plane in place of the Pt surface for the sake of simplicity [36]. In the adsorbed system, the CD structure changes little on the two torsion angles, T_1 and T_2, which appear as 100.8° and 154.1°, respectively. When placing MP on the Pt surface, the same performance shows that the carbonyl groups of MP are adsorbed parallel to the Pt surface, also in line with the assumption of the previous space-filling model [40]. The adsorption energy for individual MP was found to be 33~42 kJ/mol higher than that in the case of the existence of CD on the Pt surface.

The model proposed in the present study consists of CD, MP and Pt surface. Using the optimized geometry of CD on the Pt, we examined the stable enantioface selections when MP is involved in turn with two kinds of them shown in Figure 3. These two selections have been recognized in the literature [38-40] as the precursors that lead to (R)-methyl lactate (Figure 3A) and (S)-methyl lactate (Figure 3B) upon hydrogenation. The examination shows that the energy difference (ΔE) between them is 6.4 kJ/mol in favor of (R)-methyl lactate. This is comparable to the 5.9 kJ/mol calculated with the AM1 method in Baiker's model [39]. However, the difference from the earlier work is on the distance D_{N-O} which is between the quinuclidine nitrogen atom in CD and the oxygen atom of the α-carbonyl group in MP. The values of D_{N-O} for the two selections calculated here are 8.7 and 8.2 Å, respectively.

The above modelling shows that the molecules in the ground state do recognize each other with specific selections. It is through non-bonding interactions that CD allows most of MP which results in (R)-methyl lactate to adsorb around in certain distance. Observed results
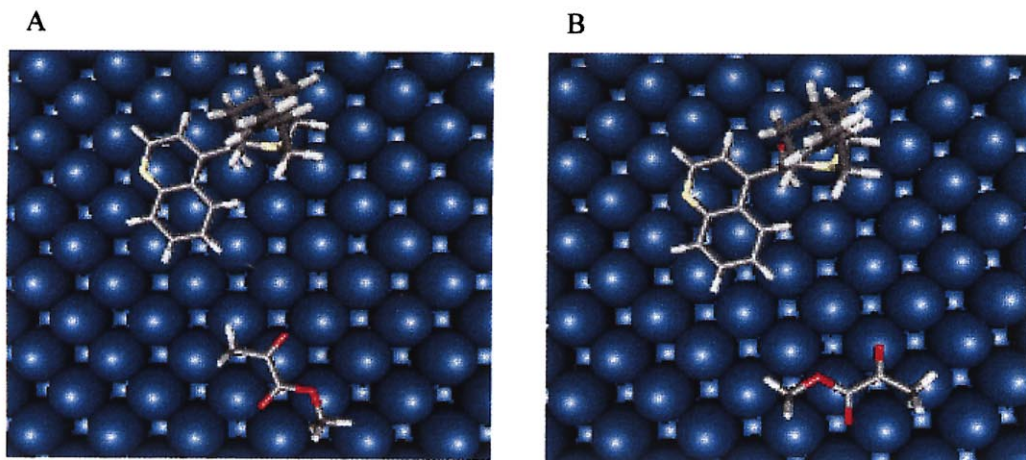
Figure 3 The precursors formed between CD and MP. A: yielding (*R*)- and, B: yielding (*S*)-methyl lactate. C is grey, O is red, H is white, N is yellow.
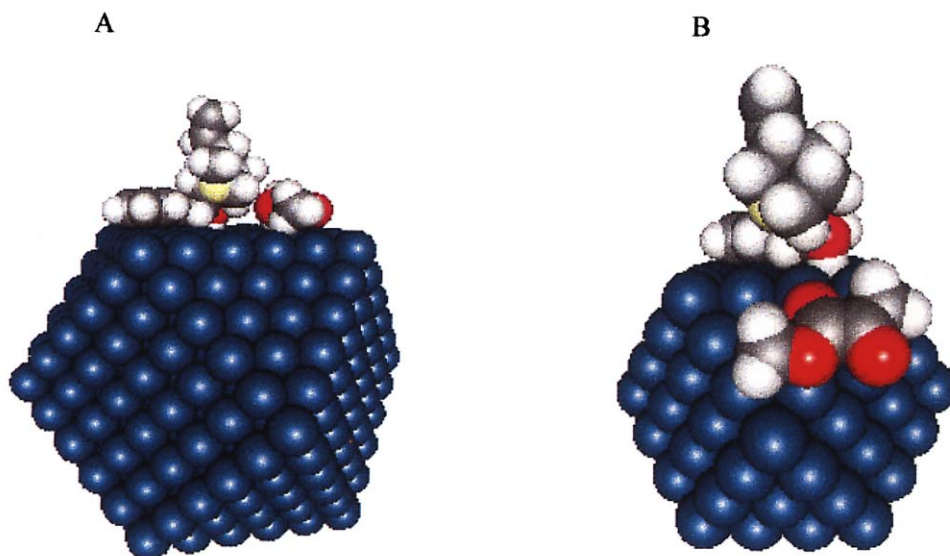

Figure 4 The modelling of CD and MP on Pt cluster with various size. A: 5-layer, 561 atoms, 2.7 nm; B: 3-layer, 147 atom, 1.6 nm. C is grey, O is red, H is white, N is yellow.

indicate that there may exist an efficient potential around the adsorbed CD that selects the specific enantioface of MP and determines the enantiodifferentiation in this system.

We simulated the above behavior of CD and MP on a much larger Pt surface on the one hand. On the other hand, we modelled the modifier and reactant on the surface of Pt clusters. This attempt is focused on the possibility that, in the limited area the modifier and reactant adsorbed on the surface of cluster, could have the same recognition behavior. The Pt clusters are built in fcc structure regularly arranged according to the $10n^2+2$ (n is the layer number) packing rule. The $10n^2+2$ cluster model is a regular icosahedron and possesses two kinds of faces, the smaller one in a triangle shape with $(n+1)(n+2)/2$ atoms and the larger one in a square shape with $(n+1)^2$ atoms.

The energies of CD adsorbed on the larger or on the smaller faces of the 3-layer to 6-layer clusters were examined. It shows that CD is generally more stable on the larger face except for n=5 (a bit more stable on the smaller face). So the following simulations are focused on fixing CD on the larger face and then investigating MP adsorption.

The examination was performed through a series of clusters in the various smaller sizes. Obtained results show that even for the smaller sizes the recognition works, however, with relatively lower efficiency (compared to the results on the much larger Pt surface above), and that the effective recognition can be put into two cases. In one case, CD can be in the same face with MP; in the other, CD and MP are in the adjacent faces. It shows that only when the layer of the cluster increases to 5, i.e. 561 Pt atoms (2.7 nm in particle size) can both of the molecules be fully anchored on the same face, such as the corresponding 36-atom-face (Figure 4A). The energy difference ΔE is 3.1 kJ/mol and favorable for the precursor to (R)-methyl lactate. When the two molecules are located in the adjacent faces, the recognition works until the size of the cluster decreases to 3-layer one (147 atoms, 1.6 nm in particle size). Figure 4B shows that CD and MP are adsorbed parallel to the adjacent faces of a 3-layer Pt particle. In this case, the formation of the (R)-product is energetically more favorable than that of the (S)-product (ΔE=4.2 kJ/mol).

This preliminary study indicates that the interaction of molecules in the ground state is able to control the enantiodifferentiation in the system of CD, MP and Pt. The existence of CD lowers the adsorption energy of MP on the Pt surface, furthermore, it makes the

adsorption of the precursor of the (R)-product more stable than that of the (S)-product. This recognition behavior works generally for larger Pt surface. The possibility of the recognition even working for the limited surface of the smaller Pt cluster, such as 1.6 nm in particle size has also been validated. It thus supports the experiments that the enantiodifferentiation is well performed for the smaller clusters.

3. Conclusion

In the enantioselective hydrogenation of pyruvates modified by cinchonidine, the alumina-supported Pt clusters as well as their finely dispersed colloidal precursors exhibit different functions from the conventional heterogeneous Pt catalysts, i.e. the reaction is less structure sensitive with better enantioselectivity achieved over small clusters. The reaction is also insensitive to the aging of the clusters which are stable after a long period of standing. The molecular mechanics calculations involve the modelling of the non-bonding interaction between the modifier and the reactant on the surface of Pt clusters which to some extent in support of the experimental observations and the possibility of the existence of a chiral potential in the reaction system, thereby may act as a supplement to the 1:1 interaction model in the previous study.

4. Experimental

4.1. Materials and instruments

Poly (N-vinyl-2-pyrrolidone) (PVP) (Mw=40,000 Fluka), methyl pyruvate, ethyl pyruvate, cinchonidine (Acros) were used as received. Pyruvates with n-propyl, iso-propyl, n-butyl and iso-butyl ester groups were synthesized by the transesterification of methyl pyruvate [45]. For example, the mixture of 10.0 mL methyl pyruvate, 30.0 mL n-propanol and 3.0 mL water was refluxed for 40 h and then distilled to obtain the target ester. Other reagents were supplied by Beijing Chemicals with a level of analytical grade.

Transmission electron microscopy (TEM) photographs were taken by using a Hitachi-9000NAR instrument. Specimens were prepared by placing a drop of the colloidal dispersion

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.

4.2. Preparation of the colloidal clusters (PVP-Pt)

The polyvinylpyrrolidone-stabilized Pt colloidal clusters (designated as PVP-Pt) with different particle diameters were prepared by the alcohol/water reduction method in the literature [46] and characterized by TEM. The PVP-Pt sols were evaporated to dryness under reduced pressure by a rotary evaporator and redispersed in a proper solvent prior to use.

4.3. Preparation of the supported clusters (Al$_2$O$_3$-Pt)

In a 100-mL beaker, 1.0 g Al$_2$O$_3$ (specific surface area 16.8 m^{2}g^{-1}) was stirred with the required amount of PVP-Pt sol for a definite time at room temperature. After filtration, the supported cluster was washed with ethanol and water and then dried at ambient temperature under vacuum. The content of platinum was about 0.5% by weight as determined by atomic absorption spectroscopy (AAS). Elemental analysis showed the content of nitrogen to be out of the detection level, which indicated that the stabilizing polymer PVP, was thoroughly washed off.

4.4. Hydrogenation of pyruvates

Enantioselective hydrogenation of pyruvates was conducted in a 100-mL stainless autoclave under the following standard conditions.

a. For hydrogenation over PVP-Pt: 10.5 mmol pyruvate; 1.0 mL n-butanol (as the internal standard); 6.0 mL PVP-Pt (containing 6.4×10^{-3} mmol Pt, 6.4×10^{-2} mmol PVP and 6.0 mL solvent); 2.0 mg cinchonidine; temperature 298K; hydrogen pressure 4.0 MPa.

b. For hydrogenation over Al$_2$O$_3$-Pt: 10.5 mmoL methyl pyruvate; 7.0 mL solvent; 0.1g Al$_2$O$_3$-Pt (containing 2.6×10^{-3} mmol Pt) ; 2.0 mg cinchonidine; temperature 298K; hydrogen pressure 4.0MPa.

Conversion was analyzed by gas chromatography (PEG 20M, 2 m, 120°C). Turnover frequency (TOF) was 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. Enantiomeric excess–e.e.(%)=$100\times([R]-[S])/([R]+[S])$ was determined by gas chromatography [47] (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). The analytical data for the products were as follows:

Methyl lactate: N_2 linear velocity=14.8 cm · s^{-1}; oven temp.=70°C; t_R=7.76 min (*R*) and 8.22 min (*S*).

Ethyl lactate: N_2 linear velocity=14.8 cm · s^{-1}; oven temp.=70°C; t_R=10.39 min (*R*) and 10.90 min (*S*).

n-Propyl lactate: N_2 linear velocity=14.8 cm · s^{-1}; oven temp.=60°C; t_R=32.57 min (*R*) and 33.53 min (*S*).

iso-Propyl lactate: N_2 linear velocity=14.8 cm · s^{-1}; oven temp.=70°C; t_R=11.39 min (*S*) and 11.98 min (*R*).

n-Butyl lactate: N_2 linear velocity=14.8 cm · s^{-1}; oven temp.=60°C; t_R=69.39 min (*R*) and 72.02 min (*S*).

iso-Butyl lactate: Analyzed after transformed into ethyl lactate by transesterification at room temperature. N_2 linear velocity=14.8 cm · s^{-1}; oven temp.=70°C; t_R=10.39 min (*R*) and 10.90 min (*S*).

4.5. Molecular modelling

Molecular mechanics calculations were performed using the universal 1.02 force field [48-50]. In these calculations, all the geometrical parameters were optimized without any constraint. All the calculations, structures and 3D models were performed and visualized on a Silicon Graphics O2 workstation using the program Cerius² version 3.5 developed by Molecular Simulations Incorporated (MSI).

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