Enantioselective hydrogenation of ethyl pyruvate in biphasic liquid–liquid media by reusable surfactant-stabilized aqueous suspensions of platinum nanoparticles

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Abstract

Aqueous suspensions of modified cinchonidine platinum nanoparticles produced from H_2PtCl_6 reduction in the presence of the surfactant N,N-dimethyl-N-cetyl-N-(2-hydroxyethyl)ammonium chloride salt have shown efficient activity for the asymmetric hydrogenation of ethyl pyruvate in biphasic media under hydrogen pressure. The aqueous phase containing the Pt(0) nanocatalysts can be used for further runs with a total conservation of activity and enantioselectivity for (R)-(+)-ethyl lactate up to 55%. Characterization of the reusable catalytic system by transmission electron microscopy revealed the formation of a "colloidal superstructure."

1. Introduction

Asymmetric hydrogenation of α-ketoesters over cinchona alkaloid-modified platinum catalysts originally reported by Orito and co-workers [1–4] is still a very important research area [5–7]. Excellent results in terms of enantiomeric excesses (up to 97%) have been obtained in the reduction of ethyl pyruvate under optimum reaction conditions with these Pt/cinchona systems [8–10]. In particular, recent studies have been performed with colloidal catalysts [11] and their development continues to attract interest for two reasons: (i) supports such as Al_2O_3, SiO_2, TiO_2, and zeolites and their influence can be eliminated, and (ii) size and shape of the nanoparticles can be controlled. Several investigations on the hydrogenation of pyruvate derivatives were conducted with platinum and other nanoclusters [9,12–15]. In most cases, polyvinylpyrrolidone (PVP)

was largely used as stabilizer of nanoparticles to prevent aggregation [13–15]. Bönnemann et al. also described the use of protonated dihydrocinchonidine as a stabilizer of platinum nanoparticles. In an acetic acid/MeOH mixture and under hydrogen pressures up to 100 bar, (R)-ethyl lactate was obtained with an enantiomeric excess (e.e.) of 80% [16,17]. In our laboratory, we have developed efficient stabilization of various nanoparticles in water by highly water-soluble protective agents such as ammonium surfactant. These colloidal catalysts give satisfactory results for arene derivative hydrogenation in aqueous media [18,19]. In this article, we show that platinum nanoparticles protected by N,N-dimethyl-N-cetyl-N-(2-hydroxyethyl)ammonium chloride salt (HEA16Cl) and modified with (−)-cinchonidine **1** efficiently catalyze the asymmetric hydrogenation of ethyl pyruvate in pure biphasic liquid–liquid (water/substrate) media at room temperature (Scheme 1). We demonstrate that surfactant-protected nanoparticles can be reused for successive hydrogenations with a total conservation of e.e. values up to 55%.

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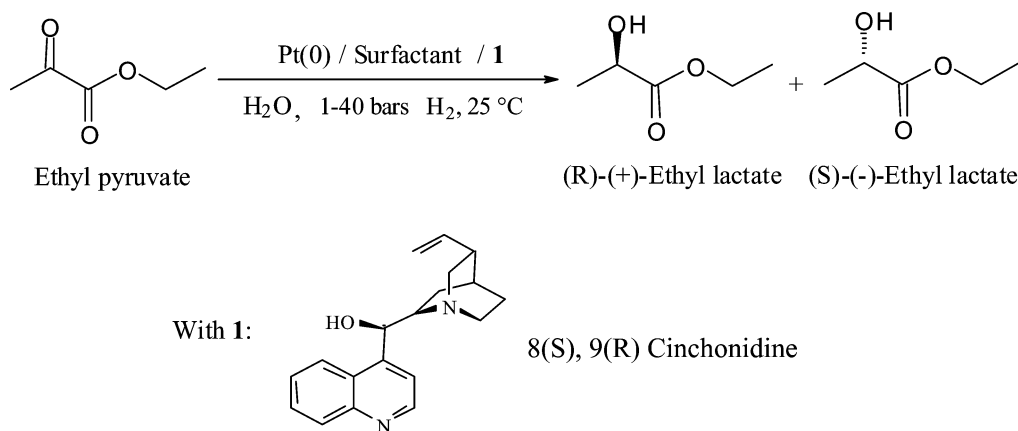
Scheme 1. Asymmetric hydrogenation of ethyl pyruvate in water.

2. Experimental

2.1. Materials

Ethyl pyruvate, (−)-cinchonidine 96%, and hexachloro-platinic acid hexahydrate ($H_2PtCl_6 \cdot 6H_2O$) were used as received from Acros. To remove ionic impurities, water was deionized by a conventional resin method (final resistivity, 15 MΩ). The surfactant HEA16Cl was prepared and fully characterized as previously reported [18,19].

2.2. Preparation of stabilized platinum nanoparticles

The suspensions were prepared in pure water at $20\,°C$ by hydrogen reduction in a stainless-steel autoclave. For example, hexachloroplatinic acid (10 mg, 1.9×10^{-2} mmol) was dissolved in deionized water (10 ml) containing N,N-dimethyl-N-cetyl-N-(2-hydroxyethyl)ammonium chloride salt (3.8×10^{-2} mmol). Then, the autoclave was flushed with hydrogen several times, and reduction was carried out under 40 bar of hydrogen. The mixture was stirred ($1500\ \mathrm{min}^{-1}$) for 2 h to give an aqueous Pt(0) colloidal suspension. The reduction was characterized by a color change from yellow to black. The highly stable aqueous suspension of nanoparticles can be stored in air for a long time without aggregation.

Finally, the appropriate amount of cinchonidine (3.8×10^{-2} mmol for a molar ratio of cinchonidine/Pt of 2) was introduced into the aqueous suspension of platinum nanoparticles. The mixture was stirred for several hours (1–24 h). The aqueous solution obtained was stable and can be used for catalytic hydrogenation.

2.3. Size distribution of nanoparticles

Transmission electronic microscopic studies were conducted using a Philips CM 12 instrument at 120 keV. Samples were prepared by the dropwise addition of the stabilized platinum nanoparticles in water onto a copper sample mesh covered with carbon. The colloidal dispersion was removed after 1 min using cellulose before transferring to the microscope. Histograms of the nanoparticles size distribution were estimated once the original negative had been digitally scanned for more accurate resolution. Measurement of about 250 particles was made with an automatic counting objects program (SCION Image) and was analyzed with Kaleida-Graph program.

2.4. Catalytic hydrogenation of ethyl pyruvate

Enantioselective hydrogenations were conducted in a 150-ml stainless-steel autoclave with a magnetic stirrer at $20\,°C$. Five milliliters of the aqueous suspension (containing 9.5×10^{-3} mmol Pt, 1.9×10^{-2} mmol surfactant, 1.9×10^{-2} mmol cinchonidine), and 441 mg (3.8 mmol, substrate/Pt = 400) of ethyl pyruvate was introduced into the autoclave. The autoclave was flushed with hydrogen several times. Finally, the required hydrogen was added until the desired pressure was reached (40 bar). The hydrogenation reaction was conducted for a desired period (up to 1 h). At the end of the reaction, the two phases were separated by decantation and the aqueous phase could be reused. The conversion of ethyl pyruvate and the e.e. value of the final product were determined on a Fison GC 9000 with a FID equipped with a Chrompack CP-Chirasil-Dex CB column ($25\ \mathrm{m} \times 0.25\ \mathrm{mm}$, 0.25-μm film) at $90\,°C$. The enantioselectivity is expressed as e.e. (%) $= 100 \times ([R] - [S])/([R] + [S])$.

3. Results and discussion

3.1. Characterization of the catalytic system

The catalytically active aqueous suspension was made of metallic platinum(0) particles prepared by the reduction of hexachloroplatinic acid in dilute aqueous solution of HEA16Cl under hydrogen pressure. The surfactant is easily synthesized by quaternization of N,N-dimethylethanola-
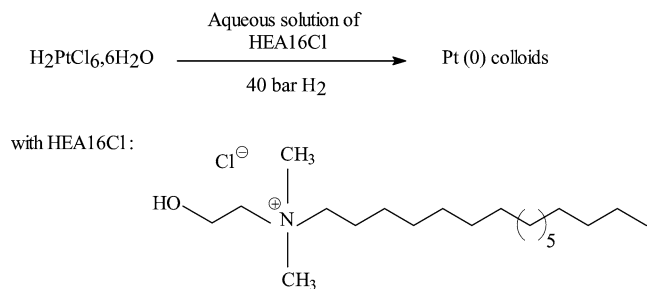
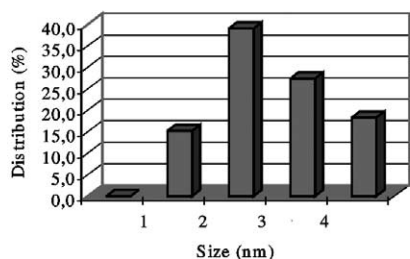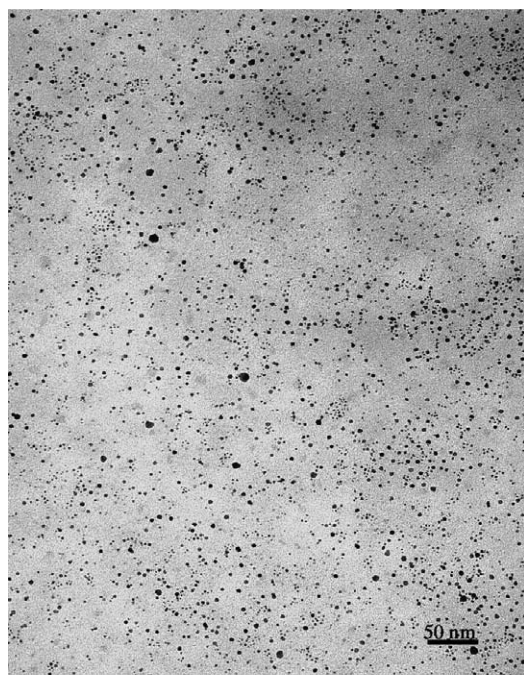Scheme 2. Preparation of aqueous suspension of platinum nanoparticles.

Fig. 1. Transmission electron micrograph and size distribution histogram of Pt–HEA16Cl suspension.

mine with the appropriate 1-chlorohexadecane according the literature [18,19] (Scheme 2).

The molar ratio R = HEA16Cl/Pt has previously been optimized to prevent aggregation and to provide good activity. Based on laboratory studies [18], the best system has been defined as $R = 2$, which gives sufficiently hydrophilic behavior to maintain catalytic species within the aqueous phase. The particle size of the Pt–HEA16Cl system has been determined by transmission electron microscopic observations (Fig. 1). The histogram plot of the particle size distribution was calculated once the original negative had

been digitally scanned. Measurement of about 250 particles showed that the particles size was about 2.5 nm. The aqueous platinum suspension is finely dispersed and can be stored under atmospheric conditions.

3.2. Adsorption of the modifier on surfactant-stabilized platinum catalyst

The cinchona alkaloids used most frequently are cinchonidine and its derivatives. As previously reported [20], these chiral modifiers were characterized by three crucial structural elements:

(i) an extended aromatic moiety, which is assumed to be adsorbed on the platinium surface via the π-bonding system;
(ii) the stereogenic region, which determines the chirality of the product; and
(iii) the tertiary quinuclidine N which is directly involved in the interaction with the carbonyl reactant.

In our study, (−)-cinchonidine as the chiral modifier was introduced into the stabilized system Pt–HEA16Cl. During nanoparticle formation, the pH value decreased from 7 for pure water to about 2.1 due to the formation of hydrochloric acid. This acid probably accelerates the solubilization of the modifier in the aqueous phase by protonation of the quinuclidine N atom and formation of ammonium salts. Moreover, spectroscopic studies have shown that this protonation favors interaction between modifier and the carbonyl reactant, which is crucial for the enantiodifferentiation [20,21]. Extensive efforts have been made in the development of a reproducible biphasic catalytic system. The most important parameters in developing an efficient Pt–HEA/(−)-cinchonidine system in water are

(i) modifier concentration,
(ii) solubility time and adsorption time of the cinchonidine on the Pt surface, and
(iii) hydrogen pressure.

The effects of these experimental parameters have been studied in detail, and the results are summarized in Table 1. First, the optimal modifier concentration was investigated. Reduction of ethyl pyruvate was performed with various molar cinchonidine/Pt(0) ratios from 0.5 to 4. These mixtures were stirred for 2 h before their transfer into the autoclave. The results obtained in ethyl pyruvate hydrogenation (S/Pt = 400) after 30 min of reaction and under 20 bar H_2 are summarized in Table 1 (entries 1–4). The enantiomeric excess value (e.e.%) for (R)-ethyl lactate was determined by GLC analysis on a gas–liquid chromatograph equipped with a Chrompack CP-Chirasil-Dex CB column.

In all cases, the conversion rate determined by GLC analysis was complete. An optimal e.e. value of 48% was obtained for a molar ratio of 2 (entry 3). The enantiomeric

Table 1
Effects of experimental parameters on enantiomeric excess of the hydrogenation of ethyl pyruvate

Entry	Amount of CD[a]	Time of adsorption (h)	P_{H_2} (bar)	Substrate/Pt (mol/mol)	T (°C)	Reaction time (min)	e.e. (%)
1	0.5	2	20	400	25	30	42(R)
2	1	2	20	400	25	30	44(R)
3	2	2	20	400	25	30	48(R)
4	4	2	20	400	25	30	36(R)
5	2	0.5	20	400	25	60	30(R)
6	2	1	20	400	25	60	41(R)
7	2	2	20	400	25	60	49(R)
8	2	4	20	400	25	60	47(R)
9	2	24	20	400	25	60	38(R)
10	2	2	1	400	25	60	32(R)
11	2	2	20	400	25	60	49(R)
12	2	2	40	400	25	13	55(R)

[a] Defined as moles of (−)-cinchonidine divided by moles of Pt.

excess decreased when R was greater than 2. In this case, the quantity of cinchonidine was somewhat excessive and therefore not solubilized in water.

The adsorption time for the modifier was also investigated. The hydrogenation was studied after different adsorption times at 20 bar H_2. These results showed that the (−)-cinchonidine is able to adsorb onto the Pt surface and proved that this adsorption process was compatible with an electrical double layer around the nanoparticles, induced by the counterions of the ammonium salts. For a cinchonidine/Pt(0) ratio of 2, the mixture was stirred from 30 min to 24 h (Table 1, entries 5–9). Below $t < 2$ h, the quantity of cinchonidine was not solubilized in water and could not react on the surface of Pt nanoparticles. The better enantiomeric excess (49%) was obtained for $t = 2$ h (Table 1, entry 7). The usual literature on of colloid stabilization [19,22–25] report that nanoparticles can be stabilized by the adsorption of chloride anions to the electron-deficient metal surface (Stern layer); consequently competitive adsorption was possible between the adsorbed N-protonated modifier in its open conformation and the chloride counterion of the ammonium surfactant. Moreover, the N-protonated modifier in its chloride form can be described as a efficient stabilizer of platinum nanoparticles in water in competition with the introduced surfactant, justifying, in opposition to the optimal ratio established in the literature, the large excess of cinchonidine molecules relative to Pt atoms to have the best e.e. (entry 3).

The particle size of the modified cinchonidine/Pt–HEA-16Cl system was determined by transmission electron microscopy (Fig. 2). The histogram plot of the nanoparticle size distribution was elaborated with a SCION Image program. Measurement of about 200 particles in an arbitrarily chosen area showed that the particle size was about 2.7 nm.

Comparative TEM studies (Figs. 1 and 2) showed that the catalytic suspensions had a similar average diameter and thus confirmed the stability of the catalytic system. Nevertheless, we observed a slight agglomeration without consequences on catalytic activities.
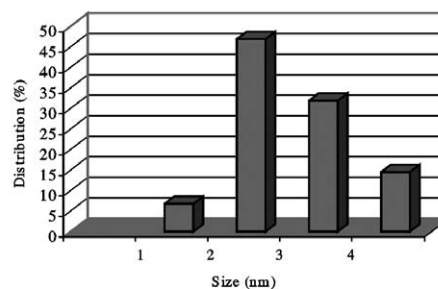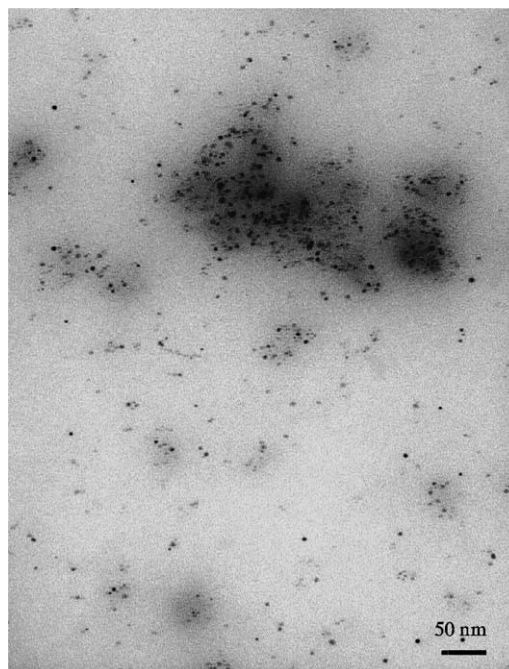

Fig. 2. Transmission electron micrograph and size distribution histogram of the modified cinchonidine/Pt–HEA16Cl system.

Hydrogen pressure is also an important factor in enantioselective hydrogenation [26–29]. The results obtained in ethyl pyruvate after 60 min of reaction time under 1, 20, and 30 bar are summarized in Table 1 (entries 10–12). In all cases, the catalytic aqueous suspension of Pt nanoparticles gives a total conversion. The e.e. values increase with increasing H_2 pressure. A significant difference in e.e. is observed when the pressure increases from 1 bar (e.e. = 32%) to 20 bar (e.e. = 49%). The highest e.e. (55%, entry 12) was obtained at 40 bar, but the increase was not significant and e.e. values reached a plateau. This phenomenon can be explained by the competitive adsorption of substrate and hydrogen on the modified metal surface in the presence of the chiral modifier and the nonchelating Cl^- stabilizer [19]. The effect of time on the enantioselectivity and conversion of ethyl pyruvate has also investigated. The results described in Fig. 3 show a very similar enantiomeric excess value during the reaction process. The e.e. value rises from 51 to 55% and conversion rate increases from 44% after 5 min to 100% after 13 min. Then, no modification of e.e. (%) is observed. The turnover
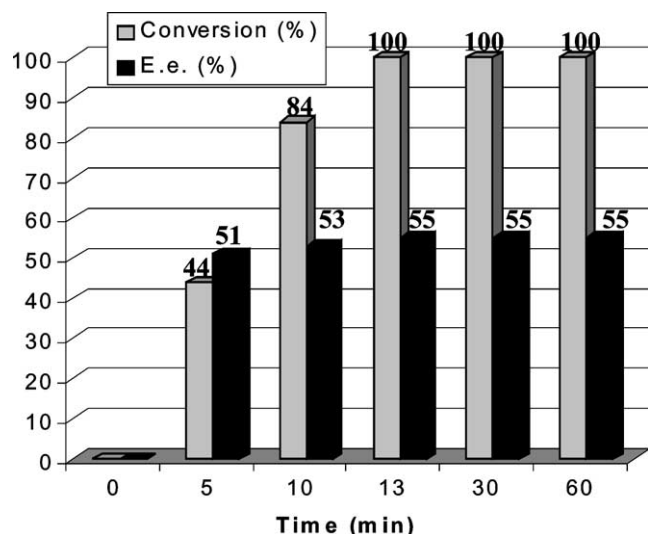
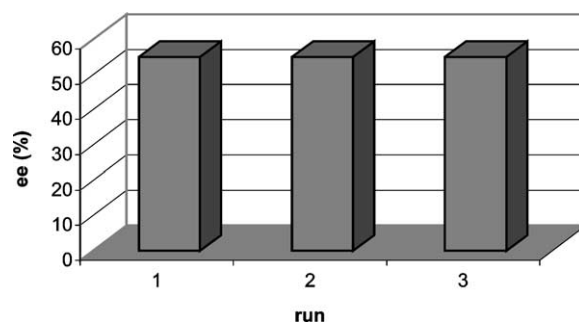Fig. 3. Effect of ethyl pyruvate conversion on enantiomeric excess values.

Fig. 4. Effect of recycling on the enantiomeric excess for the asymmetric hydrogenation of ethyl pyruvate by the modified cinchonidine/Pt–HEA16Cl system.

frequency (TOF), defined as moles ethyl lactate/moles Pt introduced/min was 31 min^{-1}.

Finally, the best result observed in this work (e.e. = 55%) appears to be competitive with that obtained using a supported Pt catalyst for ethyl pyruvate hydrogenation performed in water solvent under similar conditions [30]. Significant results using platinum catalysts are described in Table 2.

In short, the optimized catalytic system prepared with a cinchonidine/Pt–HEA16Cl ratio of 2 and an adsorption time of about 2 h gives a significant enantiomeric excess value when the hydrogenation of ethyl pyruvate is performed under 40 atm hydrogen. Our original approach is to use colloidal metallic particles finely dispersed and stabilized in water by a highly water-soluble surfactant; consequently the aqueous phase can be reused. In this context, the durability of the catalytic system was investigated by employing it in several successive hydrogenations. After the first cycle, the aqueous phase containing the colloidal suspension of platinum was separated from the (R)-ethyl lactate after extraction with hexane and slow decantation and then reused in a second run. In the same way, the catalytic suspension was recovered for a third cycle. The enantiomeric

excesses were calculated for all runs by GLC analysis. Fig. 4 shows the comparable enantioselectivity of 55% for all runs without intermediate addition of cinchonidine. In all cases, we observed complete conversion after a reaction time of 1 h.

After hydrogenation, the aqueous suspension of nanoparticles was studied by transmission electron microscopy (Fig. 5). We observed that nanoparticles essentially have an average diameter of about 3.25 nm, with 73% of the nanoparticles between 2.22 and 3.97 nm. TEM investigation reveals a particular organization of metal particles, suggesting that nanoparticles aggregate to form a superstructure. Apparently, aqueous colloidal dispersions of Pt nanoparticles form higher-order superstructures larger than 100 nm. These aggregated structures or clusters are slightly branched and very slightly dense, justifying the absence of sedimentation. This superstructure has previously been described with Rh metal nanoclusters stabilized by PVP [38] and palladium stabilized by surfactants [39]. Finally, as shown in Fig. 4, the results suggest that the enantioselective hydrogenation of ethyl pyruvate is insensitive to the spatial agglomeration of platinum nanoparticles, and the catalytic activities are conserved during the recycling process. To our knowledge, this is the first example allowing total conversion and conservation of the enantioselectivity with recycling by a modified platinum catalytic system stabilized in water.

Table 2
Comparison of platinum systems in asymmetric hydrogenation of pyruvate derivatives

| Entry	Catalyst	Substrate	Solvent	T (°C)	P_{H_2} (bar)	e.e. (%) (conf.)	Ref.
1	Pt–PVP	Methyl pyruvate	EtOH/AcOH	25	40	98(R)	[12]
2	Pt–PVP	Methyl pyruvate	EtOH	25	40	81(R)	[12]
3	Pt/Al$_2$O$_3$	Methyl pyruvate	H$_2$O	25	40	44(R)	[12]
4	Pt/C	Methyl pyruvate	EtOH	40	10	35(R)	[31]
5	Pt/Al$_2$O$_3$, Pt/SiO$_2$	Methyl pyruvate	EtOH	20	10	64–77(R)	[32]
6	Pt/Al$_2$O$_3$, Pt/SiO$_2$	Ethyl pyruvate	EtOH	20	70–100	76(R)	[33]
7	Pt/Al$_2$O$_3$	Ethyl pyruvate	MeOH/AcOH	25	10	97	[34]
8	Pt/graphite	Methyl pyruvate	CH$_2$Cl$_2$	20	30	48(R)	[35]
9	Pt/HNaY	Ethyl pyruvate	AcOH	25	70	88(R)	[36]
10	Pt/K10	Ethyl pyruvate	Toluene	25	20	75(R)	[37]
11	Pt–HEA16Cl	Ethyl pyruvate	Water	25	40	55(R)	This work
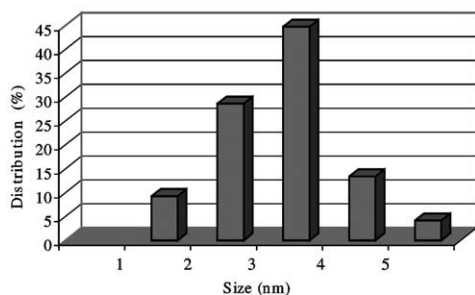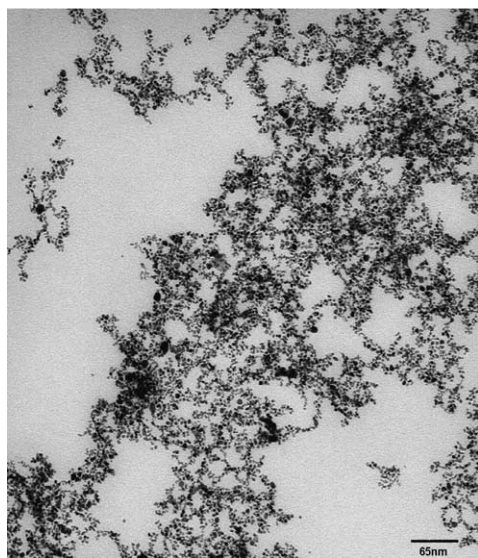
Fig. 5. Spatial organization of the stabilized aqueous suspension of Pt nanoparticles.

4. Conclusion

These results show that our modified cinchonidine platinum nanoparticle system protected by N,N-dimethyl-N-cetyl-N-(2-hydroxyethyl) ammonium chloride salt leading to electrosteric stabilization can be used for quantitative and enantioselective reduction of ethyl pyruvate. The enantioselective hydrogenation was carried out under pure biphasic conditions (water/substrate) at room temperature and under 40 bar H_2. Enantiomeric excesses up to 55% was obtained without loss of e.e. during the recycling process. TEM investigations reveal that the catalytic system slowly leads to a higher-order superstructure without consequences on enantioselectivity.

Acknowledgment

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