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Enantioselective hydrogenation of methyl benzoylformate on Ag electrode electrosorbed with cinchonine

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Cinchonine was demonstrated to be adsorbed on electrodeposited Ag for enantioselective hydrogenation. Moderate ee and excellent selectivity was obtained under mild conditions. The adsorption amount of cinchonine on electrode was proved to be related with ee by HPLC.

Chirality is very common in biomolecules and chiral compounds are widely used in agrochemical and pharmaceutical industry[1]. Therefore, proper chiral catalysts are required for large-scale industrial production, such as heterogeneous chiral catalysts[2]. Very limited heterogeneous catalytic systems were proved to be useful and well studied, such as Pt (Pd)/Al$_2$O$_3$ modified with alkaloids for the enantioselective hydrogenation of α-ketoesters, which were performed under rigorous conditions as high pressure and high temperature, with complicated pretreatment procedure for catalyst[3-6]. However, electrocatalysis, another kind of enantioselective hydrogenation method, could be performed under mild conditions without the utilization of high pressure and temperature hydrogen.

In our previous research, more abundant and relatively cheap metallic silver, which is rarely reported for enantioselective hydrogenation, was used as working electrode for the enantioselective electrohydrogenation of acetophenone in the presence of alkaloids to produce optically active phenethanol with a 21.6% ee and a 3.6% yield [7]. What's more, carbon supported Pd[8] and mercury pool electrodes[9, 10] modified with certain alkaloids have been reported for enantioselective electrocatalytic hydrogenation to yield optically active compounds with 13%-15% ee value.

In the continuity of our previous works, we reported herein the enantioselective electrohydrogenation of methyl benzoylformate (MB) in the presence of cinchonine (CN) on electrodeposited Ag (ED Ag) cathode, which has relatively large specific surface area, to synthesis optically active methyl mandelate (MM). Fig. 1 displays the procedure of enantioselective electrocatalysis. CN was demonstrated to be electrosorbed on ED Ag cathode during this procedure, which is similar to former studies on metallic Pt or Pd[11, 12]. Moreover, the adsorption amount of CN was investigated to deeply understand the effect of reaction conditions on ee value in the following research.
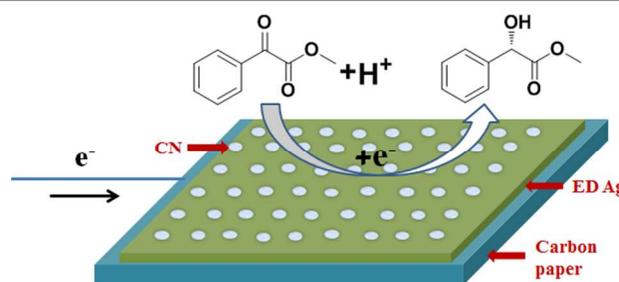

Fig. 1 Procedure of enantioselective electrohydrogenation on ED Ag cathode.

The ED Ag cathode was prepared by potentiostatic reduction of 20 mM AgNO$_3$ and 0.1 M polyethylene glycol (400) aqueous solution on carbon paper (CP) at -1.6 V (vs saturated calomel electrode) for 300 s. The electrosorption of CN on an ED Ag cathode was conducted in a mixture of 0.1 M tetraethylammonium iodide TEAI, certain concentration CN in 20 mL solvent in an undivided glass cell under N$_2$ atmosphere for 30 mins. Adsorbed Ag (AD Ag) cathode was obtained after electrosorption. The adsorption amount of CN was calculated from CN concentration differences before and after the electrosorption in the electrolyte, which was detected by HPLC[13].

High-resolution SEM characterized the structure of ED Ag (Fig. 2). According to SEM partterns, ED Ag presents dendritic morphology in the ~100 nm size range. Moreover, Nitrogen adsorption-desorption isotherms show that ED Ag has an

average specific surface area of 7.6 m^2 g^{-1}. About 0.05 g Ag was electrodeposited on CP (4 cm^2), so the surface area of ED Ag is 0.38 m^2, which is far more than that of Ag flake (4 cm^2).
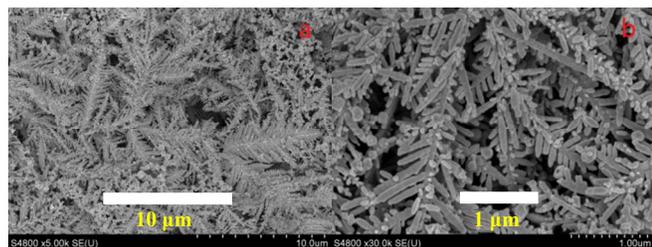

Fig. 2 FE-SEM patterns of ED Ag at four different magnifications (original magnifications: a, 5K; b, 30k.

A typical galvanostatic electrohydrogenation was carried out in a mixture of 50 mM MB, 0.1 M tetraethylammonium iodide (TEAI), 1.0 mM CN in 20 mL co-solvent in an undivided glass cell under a N$_2$ atmosphere, with an ED Ag work electrode and sacrificial magnesium (Mg) anode. Table 1 summarizes the results of conversion, selectivity and ee value for the enantioselective electrohydrogenation of MB in the presence of CN to investigate the influence of reaction conditions, such as cathode, co-solvent, CN concentration (C_{CN}) and charge.

Table 1 Enantioselective electrohydrogenation of MB under galvanostatic conditions [a].

Entry	Cathode	C_{CN} (mM)	Charge (F mol^{-1})	Conv[b] (%)	Sel[b] (%)	ee[b] (%)
1	Ag flake	1.0	2.0	65	95	13
2	CP	1.0	2.0	22	74	--
3	ED Ag	1.0	2.0	57	95	34
4	ED Ag[c]	1.0	2.0	70	93	15
5	ED Ag[d]	1.0	2.0	45	90	22
6	ED Ag	0.5	2.0	55	94	24
7	ED Ag	1.5	2.0	50	95	33
8	ED Ag	2.0	2.0	48	94	33
9	ED Ag	1.0	0.5	17	92	41
10	ED Ag	1.0	1.0	29	94	37
11	ED Ag	1.0	3.0	76	92	26
12	ED Ag	1.0	4.0	98	90	21
13	ED Ag	--	0.5	17	92	--
14	AD Ag	--	0.5	16	94	8

[a] Electrolyses carried out in an undivided cell, anode: Mg, co-solvent: MeCN/H$_2$O (9/1), supporting electrolyte: 0.1 M TEAI, MB concentration: 50 mM, current density: 3 mA cm^{-2}, temperature: 25 °C. [b] Determined by HPLC with a chiral column. [c] Co-solvent: MeOH/H$_2$O (9/1). [d] Co-solvent: DMF/H$_2$O (9/1).

As expected, a higher ee value was achieved on ED Ag than Ag flake (Table 1 entries 1, 13% ee; 3, 34% ee). Simultaneously, racemic MM was obtained on CP (Table 1 entry 2). These could be interpreted by the different adsorption capacity of diverse electrodes. CN is much more easily adsorbed to ED Ag (Table 2 entry 3) than Ag flake (Table 2 entry 1), while carbon paper has no ability to adsorbing CN (Table 2 entry 2). These could be confirmed by further research using FT-IR.

Table 2 Adsorption of CN under galvanostatic conditions [a].

Entry	Cathode	C_{CN} (mM)	Solvent	Adsorption amount[b] (μg cm^{-2})
1	Ag flake	1.0	MeCN	5±0.2
2	CP	1.0	MeCN	0±0.2
3	ED Ag	1.0	MeCN	21±0.2
4	ED Ag	1.0	MeOH	9±0.2
5	ED Ag	1.0	DMF	13±0.2
6	ED Ag	0.5	MeCN	12±0.2
7	ED Ag	1.5	MeCN	22±0.2
8	ED Ag	2.0	MeCN	22±0.2

[a] Electrosoprtion carried out in an undivided cell, anode: Mg, supporting electrolyte: 0.1 M TEAI, current density: 3 mA cm^{-2}, time: 30 mins, temperature: 25 °C. [b] Determined by HPLC with a chiral column.

FT-IR spectra of CP before and after the electrosorption (Fig. 3 curve b, c) are almost the same, which is consistent with the adsorption amount of Table 2 entry 2. FT-IR spectra of AD Ag electrode (Fig. 3 curve e) is almost identical to the one of pure CN (Fig. 3 curve d), while no significant IR band was detected on ED Ag (Fig. 3 curve a), indicating an adsorption of CN on AD Ag electrode. Moreover, the adsorption amount of CN on ED Ag is 4-fold larger than that on Ag flake (Table 2 entries 1, 5 μg cm^{-2}; 3, 21 μg cm^{-2}). More CN adsorbed on the electrode surface, creating a chiral environment, favors the enantioselective electrohydrogenation, increasing the ee value.
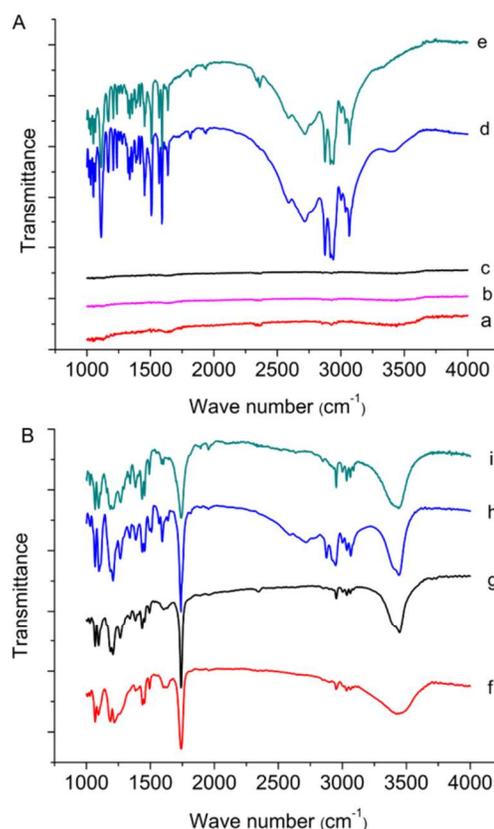

Fig. 3 FT-IR spectra of pure CN (d) and MM (f), CP (b, c) and ED Ag (a, e) before (a, b) and after (c, e) electrosorption, AD Ag after electrohydrogenation of MB in the absence of CN for 0.5 F mol^{-1} (g), ED Ag after electrohydrogenation of MB in the presence of CN for 2.0 (h) and 4.0 (i) F mol^{-1}.

In comparison with ED Ag electrode (Table 1 entry 13, 0% ee), using pre-adsorbed AD Ag as cathode in the absence of CN, gave a 8% ee value with similar conversion and selectivity (Table 1 entry 14). It again demonstrate the electrosorption of CN on the ED Ag surface and its effect on asymmetric induction, in agreement with the former results on other materials[9, 14, 15].

Although optically active MM could be synthesized on AD Ag electrode, much higher ee value was achieved on ED Ag in the presence of CN during the electrolysis without pre-adsorption (Table 1 entry 9, 41% ee). Therefore, the following electrolysis was carried out on ED Ag in the presence of CN as in-situ electrosorption.

The co-solvents were found to have great effect on the ee value (Table 1 entries 3-5), in the order MeCN > DMF > MeOH, identically with the adsorption amount of CN on ED Ag in these solvents (Table 2 entries 3-5). Since the adsorption amount plays an important role in this enantioselective electrohydrogenation, the effect of CN concentration was investigated (Table 1 entries 3, 6-8; Table 2 entries 3, 6-8). As CN concentration increases, the adsorption amount and ee value both increase, reaching a maximum at 1.0 mM. Increasing CN concentration beyond 1.0 mM leads to a platform for both adsorption amount and ee value. According to the relationship between ee value of MM and adsorption amount of CN (Fig. S2), we can infer that higher ee value could be achieved by increasing the adsorption amount of CN on electrode surface.

Another issue we are concerned is the stability of the electrosorpted CN. With increasing the electric quantity from 0.5 to 4.0 F mol^{-1}, selectivity remains almost unchanged, while conversion increases from 17% to 98% and ee value decreases from 41% to 21% (Table 1 entries 3, 9-12). The adsorption and desorption are dynamic procedure[8, 16]. During the electrolysis, the substrate MB and target product MM could also be adsorbed on electrode surface. After electrohydrogenation of MB for 0.5 F mol^{-1} in the absence of CN (Table 1, entry 14), no trace of CN could be detected on AD Ag electrode by FT-IR (Fig. 3 curve g), instead, which is the same as the one of pure MM (Fig. 3 curve f). It indicates that CN could desorb from AD Ag electrode in electrohydrogenation process and MM may be much easier to be adsorbed than CN. Therefore, during the in-situ electrosorption and electrohydrogenation process, the competitive adsorption between CN and MM may occur. FT-IR spectra of ED Ag after the electrohydrogenation of MB for 2.0 and 4.0 F mol^{-1} in the presence of 1 mM CN (Table 1 entry 3, 12) are contained in Fig. 3 curve h, i. In both cases (Fig. 3 curve h, i), a single, sharp band at 1750 cm^{-1} due to carbonyl group and a broad, strong band at 3450 cm^{-1} due to hydroxyl group are consistent with the presence of MM. In addition, the features around 3000 cm^{-1} of curve h, which are in agreement with the presence of CN, are much more significant than those of curve i. Moreover, when certain concentration of MM was added into electrolyte, both the adsorption amount of CN and ee values would decrease (Table S1). To sum up, along with the electrohydrogenation of MB, MM was synthesized and adsorbed on the ED Ag surface, which would occupy the site of CN on ED Ag and then decrease the ee value.

In summary, CN could be in-situ electrosorbed on ED Ag surface, creating a chiral atmosphere for the enantioselective electrohydrogenation of MB. The adsorption amount of CN on electrode is linearly related to ee value of MM. Optically active MM with a 34% ee, a 57% conversion and a 95% selectivity was achieved in 50 mM MB dissolved in 20 mL co-solvent (MeCN/H$_2$O=9/1) using ED Ag cathode in the presence of 1 mM CN.

Notes and references

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† Electronic Supplementary Information (ESI) available: materials, instruments, structure of inducer, general methods and graph of ee value of MM versus CN adsorption amount. See DOI: 10.1039/c000000x/

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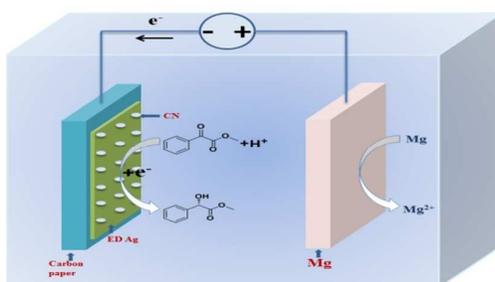
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Graphical abstract

Cinchonine was demonstrated to be adsorbed on electrodeposited Ag for enantioselective hydrogenation with moderate ee and excellent selectivity.