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COMMUNICATION

Entrapment of alkaloid within silver: from enantioselective hydrogenation to chiral recognition

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Alkaloid@Ag composite was prepared for the first time and used as cathode for the enantioselective hydrogenation. Excellent yield and remarkable enantiomeric excess value were obtained under mild conditions. Moreover, alkaloid@Ag after extraction was demonstrated to retain some chirality by linear sweep voltammetry.

Synthesis of chiral intermediates occupies a crucial position in pharmaceutical and agrochemical industry¹, which requires the preparation of appropriate catalysts, such as heterogeneous chiral catalysts. This kind of catalyst could be obtained by adsorption of chiral molecules on metal surface,²⁻⁴ electrodeposition of epitaxial films on single crystal metal⁵⁻⁷ and slicing of metal crystal for high-Miller-index faces.^{8,9} One of the most successful and well-documented heterogeneous chiral catalysts is Pt/Al₂O₃ (or Pd) modified with alkaloids, which are used for the enantioselective hydrogenation of α -ketoesters.¹⁰⁻¹² However, more abundant and relatively cheap metallic Ag is rarely reported for this application, because the Ag-H bond strength is too low and hydrogen is not soluble in silver.^{13,14}

In our recent work, alkaloid@Ag composite, which belongs to a new series of metallo-organics hybrid materials named organically doped metals,¹⁵⁻²⁰ was synthesised by the entrapment of alkaloids within silver particles for the first time. It was pressed into coin and used as cathode for the enantioselective electrohydrogenation of methyl benzoylformate (MB), avoiding the use of high pressure or high temperature hydrogen which is required in typical enantioselective hydrogenation processes.¹⁰⁻¹² Both the synthesis of catalyst and electrohydrogenation procedure were performed under mild conditions. Moreover, the chiral alkaloid inducers, such as cinchonine (CN), cinchonidine (CD), quinine (QN) or quinidine (QD), were entrapped within aggregated Ag crystallites, which is essentially different from the adsorbed

alkaloids in Pt (Pd)/Al₂O₃ system,^{20,21} and could not be washed away by water or acetonitrile (MeCN).

The synthesis of alkaloid@Ag composite involved reduction of AgNO₃ by NaH₂PO₂ in an alkaloid aqueous solution and alkaloid molecules were entrapped within Ag nanograins during this procedure. Powder with metallic luster was achieved after filtration and drying. Little amount of alkaloid was detected by high performance liquid chromatography (HPLC) in filtrate, revealing that most of the alkaloid molecules were entrapped, which is fundamentally different from physical adsorption (Table S2, Fig. S5). In contrast, pure Ag was prepared in the same way except for the absence of alkaloids in reducing solution. Alkaloids could be extracted from alkaloid@Ag by DMSO. All of the three materials, pure Ag, alkaloid@Ag and alkaloid@Ag after extraction, would be characterized by multiple methods in following research.

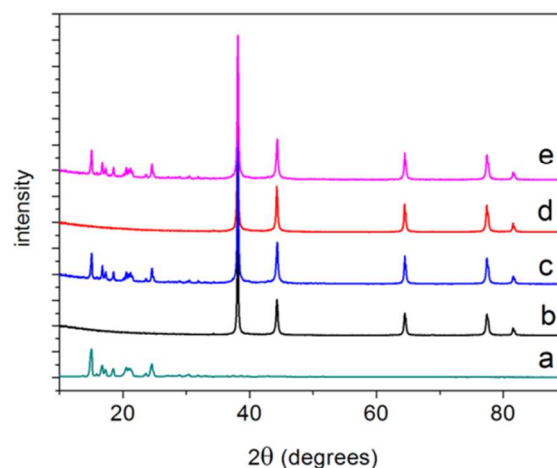


Fig. 1 X-ray diffraction (XRD) patterns of pure CN (a), pure Ag (b), CN@Ag (c), CN@Ag after extraction (d), CN@Ag used for 10 times (e).

Fig. 1 displays the powder XRD patterns of pure CN (a), pure Ag (b), CN@Ag (c), CN@Ag after extraction with DMSO (d). Typical diffraction peaks of Ag are contained in (b), (c), (d). CN@Ag (c) feature the extra diffraction peaks (2 θ =15-25), which is almost identical to pure CN (a). These are additional evidence that CN was indeed entrapped within Ag. According to XRD patterns, there is no trace of other substance except for Ag and CN, such as Ag oxide.

High-resolution SEM further characterized the structures of pure Ag and CN@Ag (Fig. 2). In all cases, porous solid were observed, which were aggregated from silver nanograins in the ~80 nm size range for pure Ag (Fig. 2a, b), and ~100 nm for CN@Ag (Fig. 2c, d). Note that the particle size would not change after being pressed. Nitrogen adsorption-desorption isotherms show that pure Ag has an average specific surface area of 3.5 m²/g and pore size of 6.5 nm, which was decreased to 1.2 m²/g and 3.5 nm for CN@Ag, and increased to 3.3 m²/g and 4.8 nm for CN@Ag after extraction, respectively. A feasible explanation is that abundant entrapped CN occupy the pores and surface of Ag crystallites.

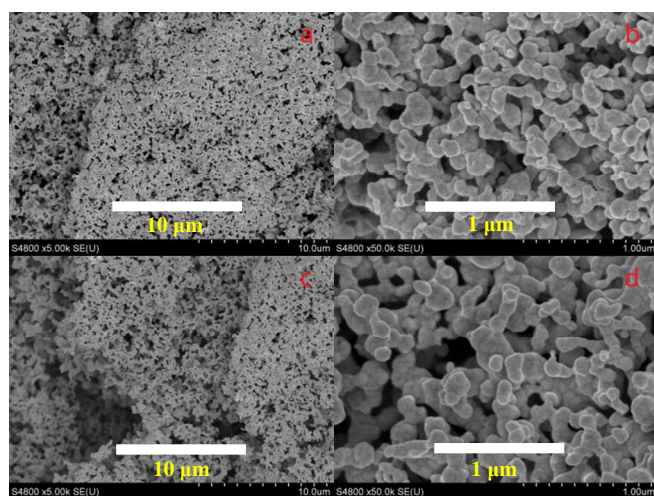


Fig. 2 FE-SEM patterns of pure Ag (a, b), and CN@Ag (c, d).

Powder of alkaloid@Ag was pressed into coin and used as cathode for the enantioselective electrohydrogenation of MB (Scheme 1). A typical galvanostatic electrohydrogenation was carried out in a mixture of 50 mM MB, 0.1 M tetraethylammonium iodide (TEAI) in an undivided glass cell, with a CN@Ag composite cathode and sacrificial magnesium (Mg) anode. Optically active S-methyl mandelate was obtained with a 60% ee and a 93% yield (Table 1 entry 1). Certain ee value and yield could also be achieved with other substrates (Table S1). CN@Ag cathode could be easily cleaned and reused for at least 10 times, and almost the same results were obtained (Fig. 3). CN@Ag was characterized by X-ray diffraction before (Fig. 1c) and after (Fig. 1e) the electrohydrogenation for 10 times. According to XRD patterns, CN@Ag is stable and CN did not leach from Ag crystallites during electrohydrogenation procedure, so CN@Ag electrode is reusable. R-methyl mandelate with 58% ee and a 91% yield was achieved on

CD@Ag under the same conditions (Table 1 entry 2). Only 23% ee on QN@Ag (Table 1 entry 3) and 27% ee on QD@Ag (Table 1 entry 4) were obtained. In contrast, we used pure Ag for cathode with 1mM CN in electrolyte as chiral inducer, 25% ee and 89% yield were obtained (Table 1, entry 5). In our previous research, alkaloids could be electroadsorbed to Ag flake electrode and create chiral atmosphere for the chiral induction, but this kind of adsorption is reversible and unstable, and alkaloids must be added to electrolyte every time.²² Similar results were achieved on Hg²³ or Pd²⁴ electrode. Furthermore, compared to former work, which got a highest 17.1% ee and 70% yield in enantioselective hydrogenation using alkaloid@Pd as catalyst,¹⁹ our work are more effective and avoided the utilization of high pressure hydrogen.

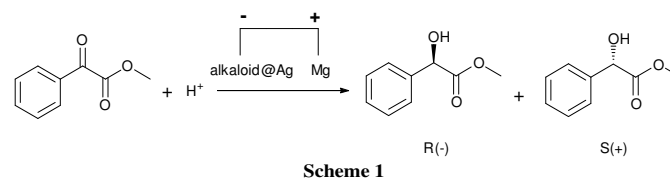


Table 1 Enantioselective electrohydrogenation of MB^{a†}.

Entry	Alkaloid	Yield ^b (%)	ee ^b (%)	Charge efficiency ^b (%)
1	CN	93	60(S)	60
2	CD	91	58(R)	59
3	QN	88	23(S)	57
4	QD	86	27(R)	55
5	CN ^c	89	25(S)	57
6	CN ^d	92	--	59

^a Cathode: alkaloid@Ag, anode: Mg, 20 mL co-solvent (MeCN/H₂O=9/1), 50 mM MB, 0.1 M TEAI, current density: 3 mA cm⁻², electric quantity: 300 C. ^b Determined by HPLC with a chiral column. ^c Cathode: pure Ag, 1mM CN dissolving in electrolyte. ^d Cathode: CN@Ag after extraction.

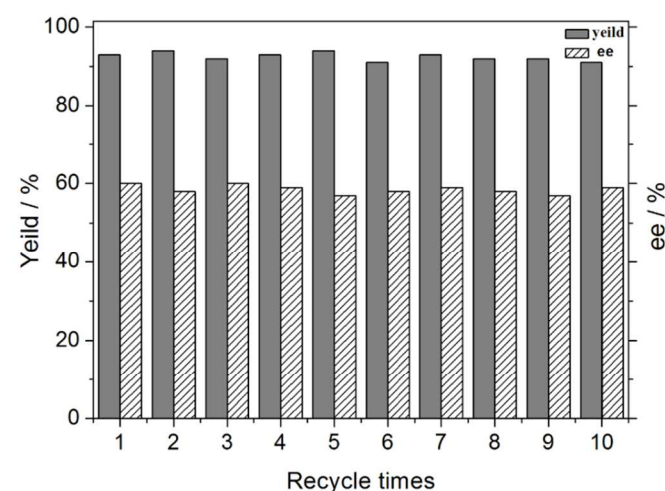


Fig. 3 Reuse of CN@Ag cathode. Reaction conditions as Table 1, entry 1.

Under the same conditions as CN@Ag, no ee value was achieved on CN@Ag after extraction with DMSO (Table 1 entry 6), indicating that substrate-alkaloid intermediate was crucial in this chiral induction process.²⁵ According to former research, metal could retain some chiral character even after

extraction of the dopant.^{19, 26} In our work, linear sweep voltammetry (LSV) was carried out to explore this chirality.⁵ No obvious current was detected at all three electrodes without the addition of any substrate (Fig. 4a, d, g), while the current increased significantly after the addition of tartrate (Fig. 4b, c, e, f, h, i), corresponding to the oxidation of tartrate. LSV recorded at pure Ag electrode are shown in Fig. 4A as comparative experiments. Pure Ag could not distinguish the oxidation of (S, S)-tartrate and (R, R)-tartrate (Fig. 4b, c). However, CN@Ag after extraction shows more electrochemical activity for the oxidation of (S, S)-tartrate than (R, R)-tartrate (Fig. 4e, f), indicating that CN@Ag after extraction could distinguish two enantiomers, which demonstrate the indeed existence of chirality in CN@Ag after extraction. Opposite results were obtained at CD@Ag after extraction, which is more active for the oxidation of (R, R)-tartrate than (S, S)-tartrate (Fig. 4h, i) because CD and CN are pseudo-enantiomers. Similar results were obtained on QN@Ag and QD@Ag after extraction (Fig. S4). Hence, this kind of composites could be used as electrochemical sensors for chiral recognition. On account of the extraction of chiral molecules, this chirality originated from the chiral morphology of metallic Ag. This chiral morphology formed during the entrapped procedure. Chiral molecules dispersed in reducing solution, and the metal crystallites generating around the chiral molecule were chirally imprinted, giving the metal surface a chiral morphology.

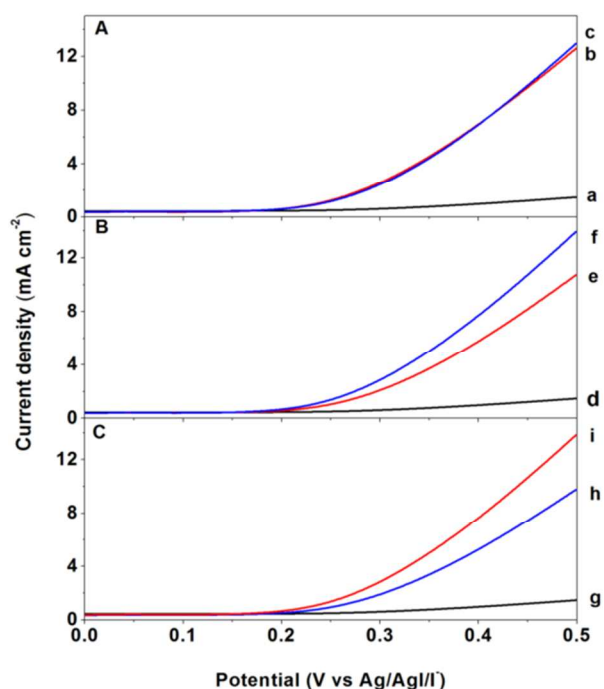


Fig. 4 Linear sweep voltammograms recorded at a sweep rate of 10 mV⁻¹ in 0.1 M TEAI dissolved in 20 mL MeCN at pure Ag electrode (A), CN@Ag after extraction electrode (B) and CD@Ag after extraction electrode (C). Blank solution: a, d, g; 20 mM (S, S)-tartrate: c, f, h; 20 mM (R, R)-tartrate: b, e, i.

In conclusion, alkaloid@Ag was successfully synthesised by the entrapment of alkaloid within Ag. It was pressed into coin

and used as cathode for enantioselective hydrogenation. Excellent yield and ee value were obtained under mild conditions. Ag is nontoxic, relatively cheap, and rarely reported for heterogeneous hydrogenation, unlike Pd or Pt. Metallic Ag was demonstrated to retain some chirality even after the extraction of alkaloid by DMSO. We not only expand the application of metallic Ag in heterogeneous hydrogenation, but also develop a new method for the preparation of chiral modified electrode.

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Notes and references

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†Electronic supplementary information (ESI) available: materials, instruments, structure of alkaloids, general methods and characterization of CD@Ag, QN@Ag and QD@Ag. See DOI: 10.1039/b000000x/

- S. C. Stinson, *Chem. Eng. News.*, 2001, **79**, 34-35.
- K. Chrysanthi, E. Karl-Heinz, *Chem. Comm.*, 2014, **50**, 1814-1816.
- H. U. Blaser, H. P. Jallet, W. Lottenback, M. Studer, *J. Am. Chem. Soc.*, 2000, **122**, 12675-12682.
- M. O.Lorenzo, C. J. Baddeley, C. Muryn, R. Raval, *Nature*, 2000, **404**, 376-379.
- J. A. Switzer, H. M. Kothari, P. Poizot, S. Nakanishi, E. W. Bohannon, *Nature*, 2003, **425**, 490-493.
- E. W. Bohannon, H. M. Kothari, I. M. Nacic, J. A. Switzer, *J. Am. Chem. Soc.*, 2004, **126**, 488-489.
- H. M. Kothari, E. A. Kulp, S. Boonsalee, M. P. Nikiforov, E. W. Bohannon, P. Poizot, S. Nakanishi, J. A. Switzer, *Chem. Mater.*, 2004, **16**, 4232-4244.
- J. D. Horvath, A. J. Gellman, *J. Am. Chem. Soc.*, 2001, **123**, 7953-7954.
- A. Ahmadi, G. Attard, J. Feliu, A. Rodes, *Langmuir*, 1999, **15**, 2420-2424.
- M. Garland, H. U. Blaser, *J. Am. Chem. Soc.* 1990, **112**, 7048-7050.
- A. I. McIntosh, D. J. Watson, J. W. Burton, R. M. Lambert, *J. Am. Chem. Soc.*, 2006, **128**, 7329-7334.
- B. Thomas, B. Alfons, *Acc. Chem. Res.*, 2004, **37**, 909-917
- O. M. Lovvik., R. A. Olsen, *J. Alloys Compd.*, 2002, 330-332, 332-337.
- I. Yosef, R. Abu-Reziq, D. Avnir, *J. Am. Chem. Soc.*, 2008, **130**, 11880-11882.
- H. Behar-Levy, D. Avnir, *Chem. Mater.*, 2002, **14**, 1736-1741.
- H. Behar-Levy, G. E. Shter, G. S. Grader, D. Avnir, *Chem. Mater.*, 2004, **16**, 3197-3202.
- H. Behar-Levy, D. Avnir, *Adv. Funct. Mater.*, 2005, **15**, 1141-1146.
- I. Yosef, D. Avnir, *Chem. Mater.*, 2006, **18**, 5890-5896.
- L. D. Pachon, I. Yosef, T. Z. Markus, R. Naaman, D. Avnir, G. Rothenberg, *Nat. Chem.*, 2009, **1**, 160-164.
- D. Avnir, *Acc. Chem. Res.*, 2013, **47**, 579-592.
- C. LeBlond, J. Wang, J. Liu, A. T. Andrews, Y. K. Sun, *J. Am. Chem. Soc.*, 1999, **121**, 4920-4921.
- B.L. Chen, Y. Xiao., X.M. Xu, H.P. Yang, *Electrochim. Acta.*, 2013, **107**, 320-326.
- E. Kariv, H. A. Terni, E. Gileadi, *Electrochim. Acta.*, 1973, **18**, 433-441.
- M. Vago, F. J. Williams, E. J. Calvo, *Electrochem. Commun.*, 2007, **9**, 2725.
- S. Tan, C. T. Williams, *J. Phys. Chem. C*, 2013, **117**, 18043-18052.
- H. Behar-Levy, O. Neumann, R. Naaman, D. Avnir, *Adv. Mater.*, 2007, **19**, 1207-1211.