Electronic Supplementary Information (ESI)

Self-Assembled Monolayer Protection of Chiral-imprinted Mesoporous Platinum Electrodes for Highly Enantioselective Synthesis

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Experimental section

Asymmetric electrosynthesis of 1-(4-bromophenyl) ethanol (4-Br-PE):
Enantioselective synthesis of 4-Br-PE was performed in the experimental set-up as shown in Fig. S13 by the optimized potentiostatic synthesis via reduction of 4-bromoacetophenone (4-Br-AP) at -0.50 V for 13 h in a stirred solution of 5 mM 4-Br-AP dissolved in 7 mL of a mixture of 10/90 (v/v) isopropyl alcohol with 1 M NH₄Cl as supporting electrolyte with a solution pH of 5.0. The product mixtures were extracted with heptane and analyzed by a high-performance liquid chromatography (HPLC), performed on a Shimadzu LC-2030C3D equipped with a CHIRALPAK IB (250 × 4.6 mm inner diameter) column and a photodiode array (PDA) detector at 220 nm, using a mobile phase containing 5% isopropyl alcohol and 95% heptane (v/v) at a flow rate of 0.5 mL min⁻¹.

Reusability tests: To study the reusability of thiol-coated electrodes, the catalyst surface is regenerated by rinsing several times and immersing it overnight in MQ water. Then, the electrode was directly used for the next catalytic run, following the same protocol of enantioselective synthesis as previously. The product solution was analyzed by HPLC (Shimadzu LC-2030C3D) with a CHIRALPAK IB column (250 × 4.6 mm inner diameter) and a PDA detector at 215 nm. A mixture of 7.5 isopropyl alcohol/92.5 heptane (v/v) was used as mobile phase, flowing at a rate of 0.5 mL min⁻¹. Repeating the µCP modification allows regenerating a protected electrode surface.

Calculation of operational parameters: Parameters which express the performance of the different types of electrodes used in this study are: (i) Conversion, (ii) Enantiomeric excess (%ee), (iii) Standard error of the mean of the enantiomeric excess (s.e.m.) and (iv) Efficiency of the catalyst.

(i) The proportion of overall conversion after electroreduction is obtained from a linear relationship, y = 0.0019x (R² = 0.9969), of the calibration curve based on HPLC measurements of the peak area ratios. Solutions of acetophenone (AP) and 1-phenylethanol (PE) were mixed to prepare the standard solutions, representing 0, 5, 10, 15 and 20% conversion of AP to PE. Then, the standard solutions were analyzed by HPLC, the peak areas of AP and PE were integrated with Lab Solution software, and the obtained results were used to calculate the ratios of peak areas of PE and APE. This calibration curve can be applied to estimate the overall conversion for all the experiments listed in Table S1.

(ii) The enantiomeric excess (%ee) was obtained by using equation (1) in order to evaluate the product selectivity of the catalytic electroreduction:
Enantiomeric excess (%ee) = \frac{[(R)PE - (S)PE]}{(R)PE + (S)PE} \times 100 \quad (1)

where (R)PE and (S)PE are the integrated areas of the (R)PE and (S)PE peaks in the HPLC chromatograms, respectively.

(iii) The standard error of the mean of the enantiomeric excess (s.e.m.) is defined by equation (2):

\[ s.e.m. = \frac{S}{\sqrt{n}} \quad (2) \]

where \( S \) is the standard deviation, and \( n \) is a number of experiments.

(iv) The production rate of chiral compound in the present study is defined in terms of the amount of a selectively produced enantiomer (\( mol_{\text{desired chiral product}} \)) with respect to the electrochemically active surface area (\( ESA \)) and the global reaction time (\( t \)) as shown by equation (3).

\[
\text{The production rate of chiral compound} \left[ \frac{mol}{m^2 \cdot h} \right] = \frac{mol_{\text{desired chiral product}}}{ESA \times t} \quad (3)
\]

The \( ESA \) value can be obtained from the hydrogen adsorption/desorption region in the cyclic voltammograms of the electrodes measured in \( H_2SO_4 \) as illustrated in Fig. S6, and the obtained information is summarized in Table S1.
Fig. S1 Schematic illustration of the synthesis steps of chiral encoded mesoporous Pt; (A) Molecular chiral templates of the present work, (R)- and (S)-Phenylethanol; (B) Self-assembly of a columnar non-ionic surfactant structure with adsorbed chiral templates at the column wall in the presence of Pt salt; (C) Electrodeposited Pt around the templates; (D) Structure of chiral imprinted mesoporous Pt after removal of the templates.

Fig. S2 Electroreduction of acetophenone to either (S)- or (R)-phenylethanol based on the acceptance of two electrons and two protons at the electrode surface.
Fig. S3 Full HPLC chromatogram of the product solution after steady-state electrosynthesis for 13 h using the bare (S)-PE imprinted mesoporous Pt as a working electrode. Retention times of acetophenone, (R)-PE and (S)-PE are 10.50, 13.00 and 13.75 min, respectively. The other additional peaks correspond to impurities, already present in the starting compound acetophenone.

Fig. S4 Enantioselective synthesis with (S)-PE imprinted mesoporous Pt electrodes after coating with a thiol layer self-assembled from solution; (A) HPLC chromatograms and (B) Histogram showing the variation of enantiomeric excess as a function of different thiol coating times 30 min (black), 1 h (red), 2 h (green) and 4 h (blue). The s.e.m value is around 3.0.
Fig. S5 Enantioselective synthesis with (S)-PE imprinted mesoporous Pt electrodes after coating with a thiol layer by using microcontact printing (μCP); (A) HPLC chromatograms and (B) Histogram showing the variation of enantiomeric excess as a function of the number of μCP cycles, once (black), three (red) and five times (green). The s.e.m value is around 1.0.

Fig. S6 Cyclic voltammograms in 0.5 M H₂SO₄ at a scan rate of 100 mV s⁻¹ of non-coated mesoporous Pt (black), in comparison with the thiol-coated electrodes obtained via microcontact printing for five times (blue) or classic solution coating for 4 h (red). All mesoporous Pt electrodes were synthesized with a charge density of 4 C cm⁻². The electrochemically active surface areas (ESA) of the three electrodes are approximately 44, 39 and 25 cm⁻², respectively.
Fig. S7 HPLC chromatograms of the product solution after electrosynthesis with non-imprinted mesoporous Pt (orange), or with (S)-PE imprinted mesoporous Pt electrodes obtained for different weight ratios of (S)-PE/PtCl$_6^-$, 0.0375 (green), 0.0750 (blue), after functionalization with thiol ligands by the µCP strategy for one cycle.

Fig. S8 Electroreduction of 4-bromoacetophenone to 1-(4-bromophenyl) ethanol via the acceptance of two electrons and two protons at the electrode surface.
Fig. S9 Asymmetric electrosynthesis using a µCP thiol SAM on (S)-4-Br-PE and (R)-4-Br-PE encoded mesoporous Pt electrodes, labeled in black and red, respectively; (A) HPLC chromatograms of the product mixtures showing the enantiomers of (S)-4-Br-PE (14.35 min) and (R)-4-Br-PE (14.85 min) and (B) Histogram illustrating enantiomeric excess values for the different working electrodes. The s.e.m value is around 2.4.

Fig. S10 Original HPLC chromatograms of the product solutions demonstrating comparative product selectivity and conversion of the solution after electrosynthesis with (S)-PE imprinted mesoporous Pt electrodes without further thiol functionalization (black) and with thiol coating using the solution (red) or the microcontact printing (blue) strategy. Retention time of the enantiomers (R)-PE and (S)-PE at 13.00 and 13.75 min, respectively.
Fig. S11 Reusability test of the thiol-coated Pt electrodes; (A) HPLC chromatograms of the products, obtained with (S)-PE imprinted mesoporous Pt modified with a single µCP step only at the beginning, for two sequential electrocatalytic runs; (B) HPLC chromatograms of the products, obtained with (R)-PE imprinted mesoporous Pt for two electrocatalytic runs, but with a renewal of the µCP step after the first run; (C) Histogram representing the enantiomeric excess for the two µCP strategies used in (A) and (B). Retention time of the enantiomers for (R)-PE and (S)-PE are 11.15 and 11.80 min, respectively. The s.e.m value is around 1.0.
**Fig. S12** Proposed reaction mechanism for the electroreduction of acetophenone.

**Fig. S13** Experimental set-up for the asymmetric electrosynthesis via chronoamperometry using a potentiostat equipped with a three-electrode system in a stirred solution of the reactant.
Table S1 Summary of efficiency for the bare mesoporous Pt and the different thiol-coated mesoporous Pt electrodes for both continuous and pulsed electrosynthesis.

| No. | Reaction conditions                                                                 | ESA (cm²) | Total reaction time (h) | %ee | %conversion | Production rate of a given enantiomer [µmol/m² h] |
|-----|------------------------------------------------------------------------------------|-----------|------------------------|-----|-------------|--------------------------------------------------|
| 1   | Non-coated mesoporous Pt with continuous electrosynthesis                           | 44        | 13                     | 26.0| 4.1         | 6.4                                              |
| 2.1 | Thiol-coated mesoporous Pt via solution coating for 30 min with continuous electrosynthesis | 42        | 13                     | 93.3| 1.5         | 8.8                                              |
| 2.2 | Thiol-coated mesoporous Pt via solution coating for 1 h with continuous electrosynthesis | 36        | 13                     | 89.0| 0.7         | 4.7                                              |
| 2.3 | Thiol-coated mesoporous Pt via solution coating for 4 h with continuous electrosynthesis | 25        | 13                     | 78.6| 0.4         | 3.6                                              |
| 3.1 | Thiol-coated mesoporous Pt via one time microcontact printing with continuous electrosynthesis | 42        | 13                     | 91.2| 0.9         | 5.1                                              |
| 3.2 | Thiol-coated mesoporous Pt via three times microcontact printing with continuous electrosynthesis | 40        | 13                     | 90.4| 0.8         | 5.1                                              |
| 3.3 | Thiol-coated mesoporous Pt via five times microcontact printing with continuous electrosynthesis | 39        | 13                     | 88.7| 0.7         | 4.3                                              |
| 4   | Non-coated mesoporous Pt with pulse electrosynthesis (60s pulse time-120s relaxation time) | 44        | 39                     | 38.3| 0.4         | 0.3                                              |