

Supporting information for:

Asymmetric catalysis at the mesoscale: Gold nanoclusters embedded in chiral self-assembled-monolayer as heterogeneous catalyst for asymmetric reactions

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1. Methods:

Catalysts preparation:

Preparation of Boc-proline-OH: 6 gr of (L) Proline were dissolved in 75 mL of saturated NaHCl₃ (aq). The solution was cooled in an ice-bath, 12.5 gr Boc₂O dissolved in 30 mL THF were added drop-wise to the reaction mixture. The reaction mixture was then stirred at RT for 2 hours. The reaction mixture was acidified to pH=1 with 6.5 mL of 1M HCl.

Coupling of proline amino-acids: 646 mg of Boc-Pro-OH were dissolved in 10 mL CH₂Cl₂, the solution was cooled to 0°C. 497 mg H-Pro-OMe-HCl was added following by the addition of 0.42 mL Et₃N and 575 mg EDC. The reaction mixture was then warmed to RT. 530 mg Boc-Pro-Pro-OMe was mixed with 8 mL (5 equivalents) NaOH (1.0M) in 10 mL THF at RT for the formation Boc-Pro-Pro-OH.

Immobilization of amino-acids or peptide on MCF-17: Mesoporous MCF-17 silica was prepared utilizing a conventional method (24). In a typical experiment, 1 gr of MCF was heated to 120°C under high vacuum for 72 hours. Following that step, 20 mL of dry toluene and 3 mmol Br(CH₂)₃Cl₃Si were added to the reaction flask under 1 atm of N₂, the solution was refluxed for 72 hours. The solid was then washed with toluene, dried in oven and stored in a desiccator cabinet. The filtrate was concentrated and the amount of Br(CH₂)₃Cl₃Si that was left in the solution phase was analyzed by H1 NMR, using mesitylene as an internal standard. 1.2 mmol Boc protected amino acid (**1** or **2**) was mixed with 200 mg Br/MCF and 1.8 mmol of K₂CO₃·1.5H₂O in 10 mL of THF at RT for 72 hours. The

amino-acid/MCF solid powder was washed with H₂O and acetone to remove the base and amino acid residues. Deprotection of the Boc group was done by mixing the Boc-Amino-acid/MCF with 10 equivalents of Trifluoroacetic acid in 10 mL of DCM for 24 hours. The solid was then washed with acetone and toluene, dried in oven and stored in a desiccator cabinet.

Immobilization of quinine **3** on MCF-17: 1. Propargylation of quinine: 250 mg of quinine were dissolved in 2.5 mL of DMF. The solution was cooled to 0°C and 64 mg of NaH was added. Following the addition of 0.1 mL propargyl bromide (80 wt % in toluene), after 1 hour, the reaction was heated to RT. The reaction was quenched after 4 hours, by the addition of H₂O (1).

2. 5 mg of Br/MCF was azidated by the addition of 100 mg NaN₃ and 2.5 mg TBAI in 3 mL DMSO at 80°C for 24 hours. Following that step, to 4 mL of degassed MeCN, 0.3 mL DIPEA and 200 mg N₃/MCF and 200 mg propargylquinine were added, following by the addition of 5.5 mg of CuI in 0.5 mL MeCN. The reaction was done at RT for 10 hours. (2)

Supported nanoparticles: 300 mg of SAM/MCF was mixed with 10 mL DI H₂O (pH=7). The solution was mixed for 1 hour under N₂ and then 0.4 w/w % of HAuCl₄ was added. The solid was washed three times in order to remove the residues of Au ions, which were did not form complexes with the SAM. The Au@SAM/MCF was dried and the reduction was completed by exposure to 1 atm of H₂ at 40 °C for 24 hours. The catalyst was then stored in a desiccator cabinet. The loading of Au was determined by ICP-MS.

Representative Procedure for Catalytic Reactions: Prior to the addition of all other reaction materials, the catalyst, Au@SAM/MCF (0.4 w/w % Au, 0.002 mmol), added to an oven-dried 10-mL Schlenk tube with a stir bar was placed under 1 atm of H₂. The catalyst was then heated to 40 °C for 24 h, and afterward the H₂ atmosphere was replaced with N₂. The catalyst was mixed with PhICl₂ (1.9 mg, 0.01 mmol) in 1 ml toluene-*d*₈, for 1 hour. For the intermolecular cyclopropane formation a mixture of styrene (40 μL, 0.25 mmol), propargyl pivalate **4** (10 mg, 0.25 mmol), PhICl₂ (1.9 mg, 0.01 mmol), PhMe₆ (2 mg, 0.012 mmol, internal standard) and toluene-*d*₈ (1.5 mL) were added. The reaction was stirred for 12 hours at RT.

For the intramolecular cyclopropane formation a mixture of propargyl ester **7** (0.25 mmol), PhICl₂ (1.9 mg, 0.01 mmol), PhMe₆ (2 mg, 0.012 mmol, internal standard) and toluene-*d*₈ (1.5 mL) were added. The reaction was stirred for 12 hours at RT. Following these reactions, the solid catalyst was filtered through glass microfiber filter (Whatman GF-H). The filtrate was analyzed by ¹H NMR spectroscopy.

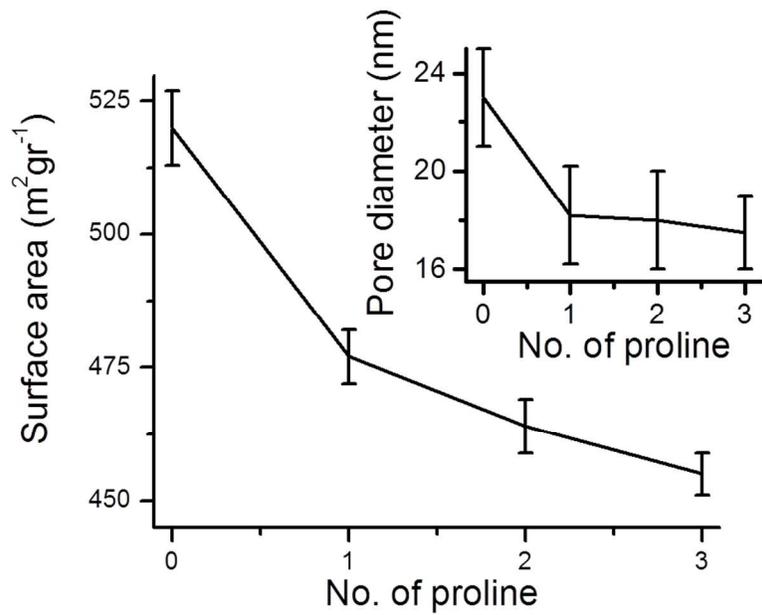
Separation and chirality: The desired product was purified by flash chromatography and the enantioselectivity was measured by chiral HPLC. Intermolecular cyclopropanation product **5** HPLC: Chiralpak IA column, 1 mL/min, 99.5:0.5 hexanes/IPA, T = 4.33, 4.56 min. Intramolecular cyclopropanation product **8** HPLC: Chiralpak IA column, 1 mL/min, 99:1 hexanes/IPA, T = 4.2, 7.3 min.

References:

1. Ishii, Y.; Fujimoto, R.; Mikami, M.; Murakami, S.; Miki, Y.; Furukawa, Y. *Org. Pro. R&D* **2007**, 11, 609.
2. Kacprzak, K. M.; Maier, N. M.; Lindner W. *Tetrahedron Lett.* **2006**, 47, 8721.

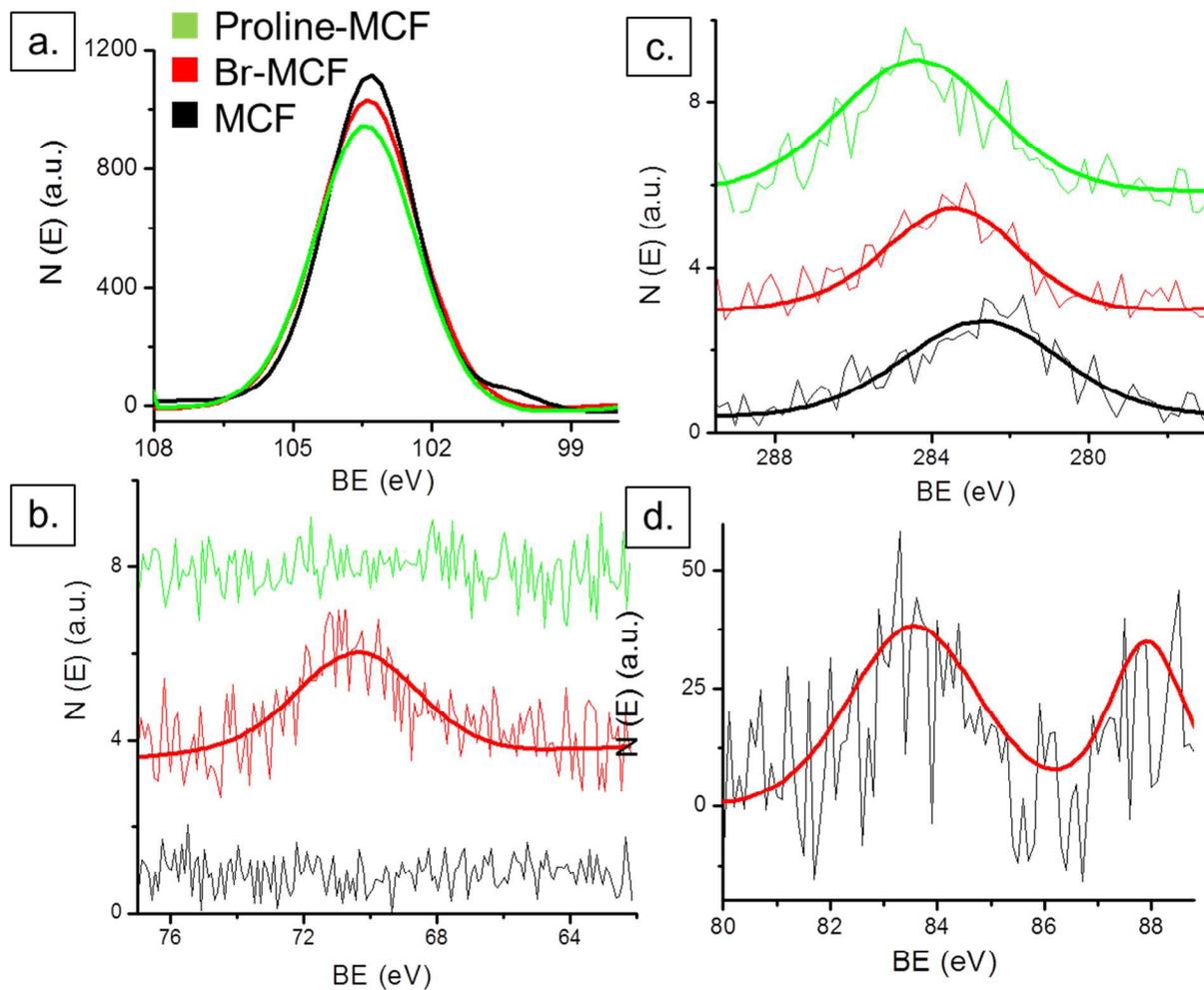
2. Supplementary Figures:

Supp. Fig. S1



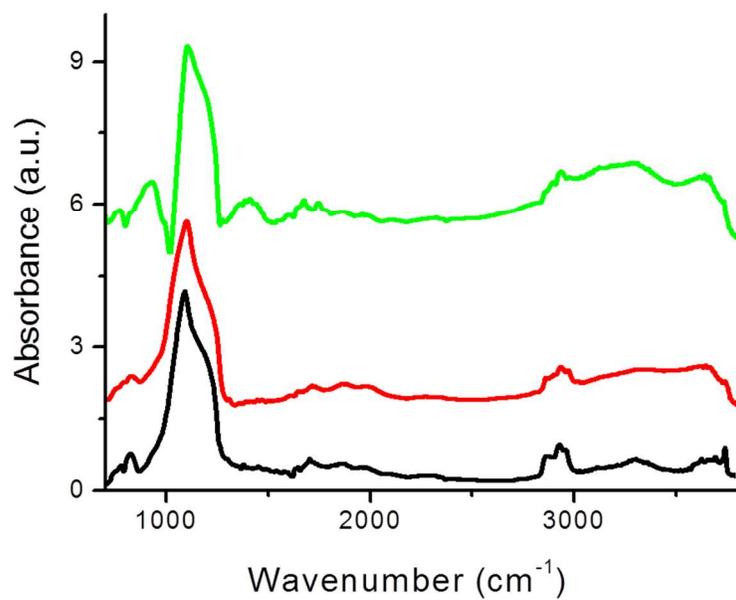
Supp. Fig. S1: N₂ BET analysis of the surface area and pore size diameter (inset) as function of the number of proline units which construct the peptide chain used for the formation of chiral SAM.

Supp. Fig. S2



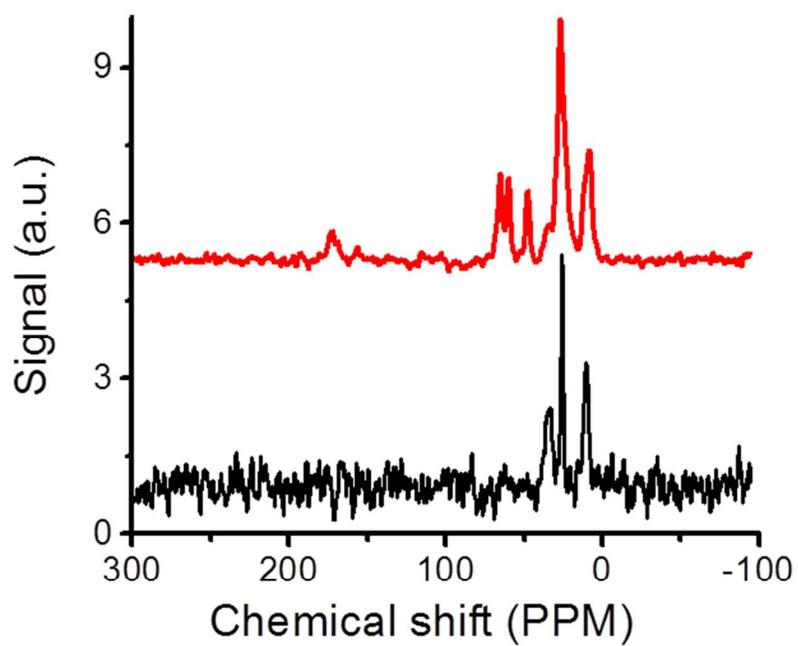
Supp. Fig. S2: XPS spectra of Si2P (a.) Br3d (b.) C1S (c.) of the MCF mesoporous silica substrate (black), Br/MCF (red) and proline/MCF (green). Au4f XPS spectra of 1 mol % Au@proline/MCF is shown in d.

Supp. Fig. S3



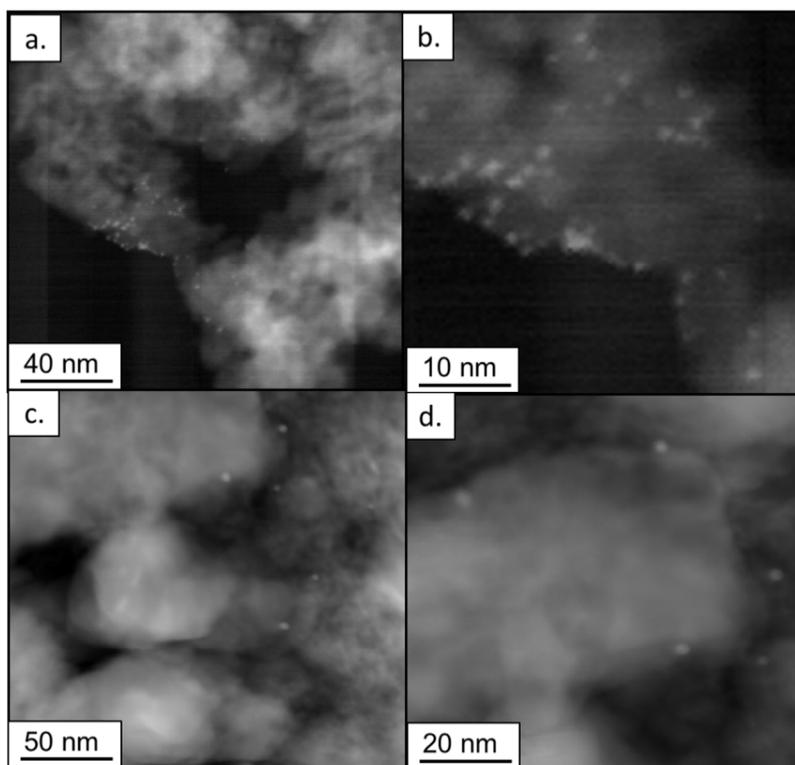
Supp. Fig. S3: DRIFT spectra of MCF (black), Br/MCF (red) and proline/MCF (green).

Supp. Fig. S4



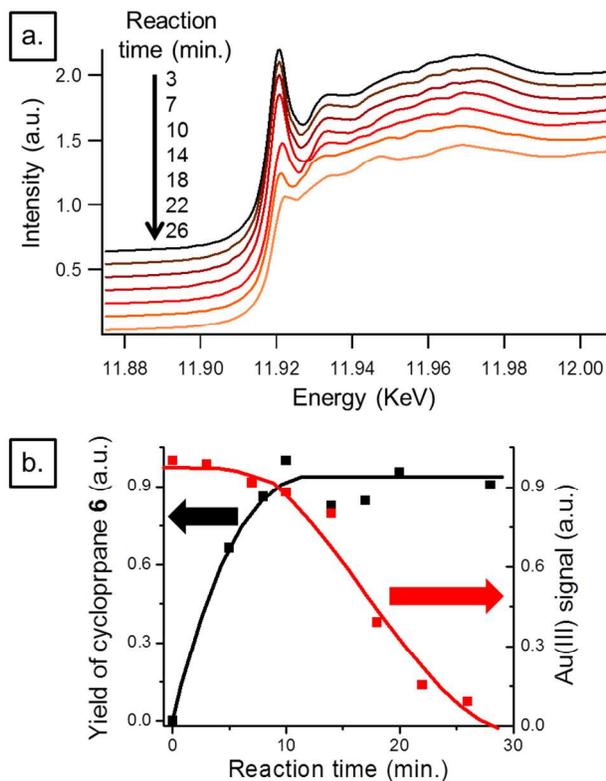
Supp. Fig. S4: CP-MAS NMR spectra of Br/MCF-17 (black) and diproline/MCF-17 (red).

Supp. Fig. S5



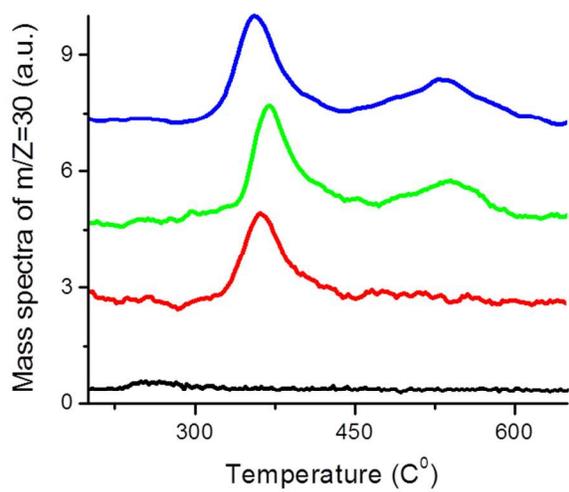
Supp. Fig. S5: HR-STEM of 2 (a. and b.) and 0.4 (c. and d.) w/w % Au encapsulated in proline/MCF.

Supp. Fig. S6



Supp. Fig. S6: In-situ NEXAFS (a.) and reactivity (b.) of 1 w/w % Au@dipriline/MCF-17 measured under reaction conditions. Products formation (as analyzed by GC) and amount of highly oxidized Au(III) ions (analyzed from NEXAFS spectra) indicate the correlation between the concentration of highly oxidized Au ions and the catalytic reactivity (b.).

Supp. Fig. S7



Supp. Fig. S7: TGA-MS spectra of 30 m/Z detected from MCF (black), Br/MCF (red), proline/MCF (green) and diproline/MCF (blue).