Electronic Supplementary Information

Pickering interfacial catalysts for asymmetric organocatalysis

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1. Materials and instruments

All chemicals that were obtained from commercial suppliers, Sigma-Aldrich and VWR Chemicals, were used without further purification. All the solvents were dried by 4 Å molecular sieves if not mentioned otherwise. Tris[2-(dimethylamino) ethyl]amine (Me6TREN) was purchased from ABCR.

The Fourier-transform infrared spectroscopy (FT-IR) was recorded on a Perkin Elmer spectrum 65 FT-IR spectrometer, with a spectral resolution of 0.25 cm^{-1}, in the range from 400 to 4000 cm^{-1}. The pellet was prepared by mixing 10 mg of sample and 300 mg of KBr.

Dynamic light scattering (DLS) measurements were performed at Beckman Coulter DelsaMax Pro (10 scans 12 seconds). The particles were dispersed in MilliQ water. Measurements were performed at room temperature.

^{1}H NMR spectra were recorded at 25 ^{o}C using Bruker AVANCE III 400Hz equipped with tunable multinuclear probes and auto-sampler.

Chiral-phase high performance liquid chromatography (HPLC) was performed on the Agilent instrument installed with chiral column (Chiral Pak IB) 25 $^{\circ}C$, flowrate = 1 mL min^{-1}. n-hexnane/isopropanol = 95/5, flowrate = 1 mL min^{-1}, UV = 265 nm.

Scanning electron microscopy (SEM) images were recorded with a S-4800 II microscope (Hitachi) operated at an accelerating voltage of 1 kV.

High-angle annular dark-field scanning transmission electron microscopy (HAADF-STEM) imaging and spectrum imaging based on energy-dispersive X-ray spectroscopy (EDXS) were performed at 200 kV with a Talos F200X microscope equipped with an X-FEG electron source and a Super-X EDXS detector system (FEI). Prior to STEM analysis, the specimen mounted in a high-visibility low-background holder was placed for 2 s into a Model 1020 Plasma Cleaner (Fischione) to remove contamination.

Thermogravimetric analysis (TGA) was carried out with a TG 50 modular unit and a TC 15 TA controller (Mettler-Toledo, Giessen, Germany) by heating samples from 35 to 800 ^{o}C under a dynamic nitrogen atmosphere with a heating rate of 10 ^{o}C min^{-1}.

2. Synthesis

2.1 Synthesis of initiator (N-2-bromo-2-methylpropanoyl-β-alanine N′-oxysuccinimide ester).

N-2-bromo-2-methylpropionyl-β-alanine N′-oxysuccinimide ester was synthesized as the published method.[1] A mixture of dichloromethane (50 mL) and 2-bromo-2-methylpropionyl bromide (12.4 mL, 100 mmol) was slowly added into a solution of β-alanine (8.9 g, 100 mmol) and sodium hydrogen carbonate (21 g, 250 mmol) in deionized water (200 mL) at 0 °C. Then the mixture was stirred at room temperature for 2 h. After that, the water phase was washed with dichloromethane (100 mL × 3) and adjusted to pH 2.0 with 1.0 N HCl aq. at 0 °C. The product was extracted with ethyl acetate (150 mL × 4). The organic phase was dried with $MgSO_4$, filtered, and evaporated. N-2-bromomethylpropionyl-β-alanine was obtained as colorless solid and used directly for subsequent steps. N, N'-diisopropylcarbodiimide (DIC) (2.8 g, 22 mmol) was slowly added to the solution of N-2-bromo-2-methylpropionyl-β-alanine (4.8 g, 20 mmol) and N-hydroxysuccinimide (2.5 g, 22 mmol) in dichloromethane (200 mL) at 0 °C. The mixture was stirred at room temperature for 4 h. After filtration, the solvent was removed under vacuum. N-2-bromo-2-methylpropionyl-β-alanine N'-oxysuccinimide ester was purified by recrystallization from 2-propanol with a yield of 5.7 g (85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.96 (s, 6 H), 2.87–2.89 (m, 6 H), 3.69 (t, 2 H, J = 6.3 Hz), 7.20 (s, 1 H) ppm.

2.2 Synthesis of O-(2-methacryloyloxyethylsuccinoyl)-trans-4-hydroxy-L-proline.

O-(2-Methacryloyloxyethylsuccinoyl)-trans-4-hydroxy-L-proline was synthesized according to the previous method.[2] A 500 mL round bottom flask was charged with trans-4-hydroxy-L-proline (8.8 g, 67 mmol), and dissolved by addition of CF_3CO_2H (40.0 mL) to give a clear and colorless solution. The crude methacrylic acid chloride was dropwise added, and the reaction mixture was stirred at room temperature for 5 h. The solution was cooled in an ice/water bath and Et_2O (250 mL) was added slowly under vigorous stirring. A syrupy precipitate forms, and then the precipitate was allowed to settle by gravity for 1 h. The reaction flask was removed from the ice/water bath, the supernatant was decanted and Et_2O (100 mL) was added, swirled and then decanted. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.85 (s, 3 H), 2.20–2.60 (m, 6 H), 3.37–3.67 (m, 2 H), 4.25 (s, 4 H), 4.58 (m, 1 H), 5.35 (br. s, 1 H), 5.51 (s, 1 H), 6.03 (s, 1 H) ppm.

2.3 Synthesis of silica nanoparticles.

Silica nanoparticles were prepared by hydrolysis and condensation of tetraethyl orthosilicate (TEOS) in ethanol using ammonia as the catalyst. First, a solution containing ethanol (147 mL), ammonia (9 mL) and deionized water (3 mL) was stirred for 5 minutes to ensure complete mixing. Then, TEOS (4.5 mL) was added to the above solution, the reaction proceeded at ambient temperature for 1.5 h. Thereafter, the colloidal solution was separated by centrifugation, the silica nanoparticles were washed by absolute ethanol three times to remove the residues, followed by drying in an oven at 70 °C for 12 h.[3, 4]

2.4 Silanization of silica nanoparticles.

For modification, 1 gram of the dry NPs was dispersed in 50 mL anhydrous toluene in a 250 ml flask. The corresponding amount of the organosilicon compounds, (3-aminopropyl)triethoxysilane (APETS) and trimethoxy(octadecyl)silane (TMODS) were added to the solution for the target APTES-to-TMODS ratios. The reactions proceeded for 12 hours at 110 °C under reflux. The product was collected by centrifugation (5000 rpm, 10 min) and washed 3 times with toluene. The particles were dried at 70 °C overnight and stored under dry conditions. [3]

2.5 Preparation of SiO_2-initiator.

To 1 gram particle in the 20 mL anhydrous tetrahydrofuran (THF) and 40 μL trimethylamine, the initiator (200 mg) was added and stirred for 12 hours at room temperature.[5] The particles were collected by centrifugation (5000 rpm, 10 min) and washed 3 times with THF. After drying overnight, the particles were characterized by X-ray Photoelectron Spectroscopy (XPS), where the weak peak at 74 eV confirms the presence of the initiator on the particles.

2.6 Preparation of SiO_2-polymer.

SiO_2-initiator (1g) was dispersed in 40 mL water and assisted with sonication, followed by the adding of the proline monomer (0.2g 0.5 μmol). The pH of the solution was adjusted to 7.5 by

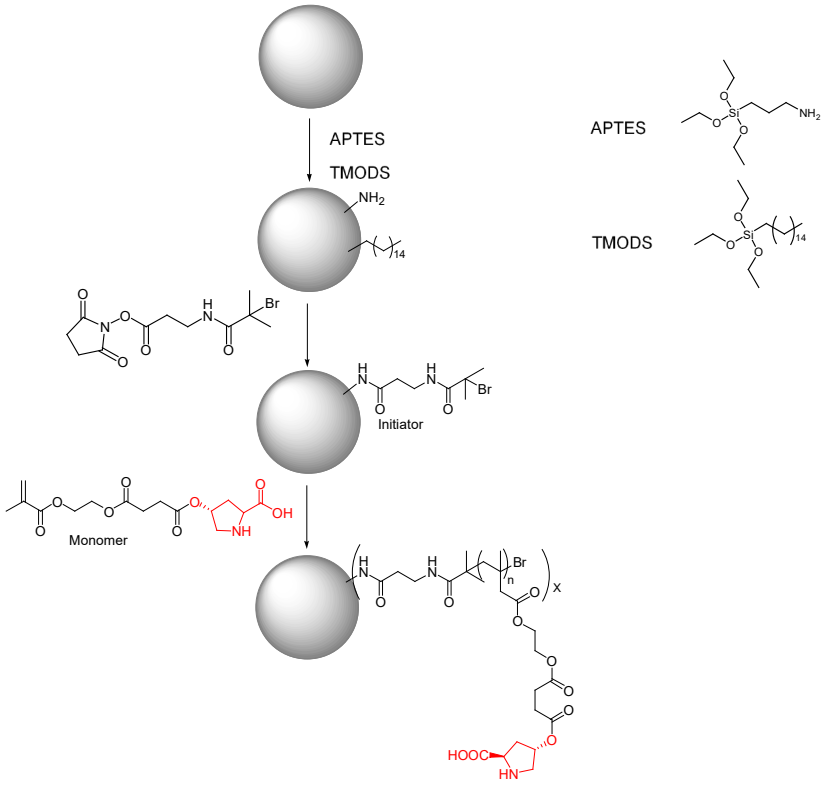
a NaOH solution (0.1 M). The reaction flask was sealed with a rubber stopper and purged with nitrogen for 1 hour. Another reaction flask filled with 10 mL water, 50 mg Cu(I)Br and 7 μL tris(2-dimethylminoethyl)amine (Me_6TREN) was also purged with nitrogen for 1 hour. Afterwards, a copper-containing solution was transferred into a flask of nanoparticles via syringe to initiate the polymerization for 15 hours under an inert atmosphere.[5] After polymerization, the nanoparticles were collected by centrifugation (5000 rpm, 10 min), washed 3 times with ethylenediaminetetraacetic acid (EDTA) solution (0.01M) for removal of the residual copper ions, and 3 times with water, followed by drying in the vacuum oven for overnight.

2.7 Preparation of the Pickering emulsion.

Typically, 20 mg of the SiO_2-polymer particles were dispersed in the mixture of 0.5 mL water and 0.5 mL toluene, followed by mixing via vortex for 30 seconds for emulsification.

2.8 Pickering emulsion for aldol reaction.

To 1 mL emulsion system, 4-Nitrobenzaldehyde (0.1 mmol, 15.1 mg, 1 eq.) and cyclohexanone (0.7 mmol, 72.5 μL, 7 eq.) were added. The catalytic reaction proceeded at ambient temperature without further agitation. After the desired time interval, the reaction mixture was extracted with ethyl acetate and dried with magnesium sulfate. The solvents were removed under vacuum and the product was sent for ^{1}H NMR analysis to determine the diastereoselectivity and conversion. The experiments were carried out in duplicate, and the error bars represent the standard deviations of two parallel measurements. The control experiment with 4-hydroxyproline (1.6% mol/mol) was carried out following the same procedures. To a mixture of 0.5 mL water and 0.5 mL toluene, 4-Nitrobenzaldehyde (0.1 mmol, 15.1 mg, 1 eq.) and cyclohexanone (0.7 mmol, 72.5 μL, 7 eq.) were added. The catalytic reaction proceeded at ambient temperature without further agitation. The experiments were carried out in duplicate, and the error bars represent the standard deviations of two parallel measurements.



Scheme S1. Preparation of the proline-functionalized silica nanoparticles.

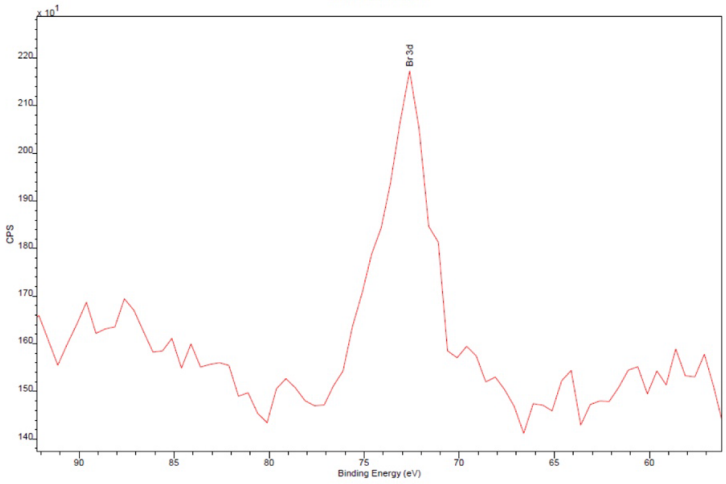


Figure S1. XPS spectrum of SiO_2-initiator, magnification from Figure 1a for better Br signal visualization.

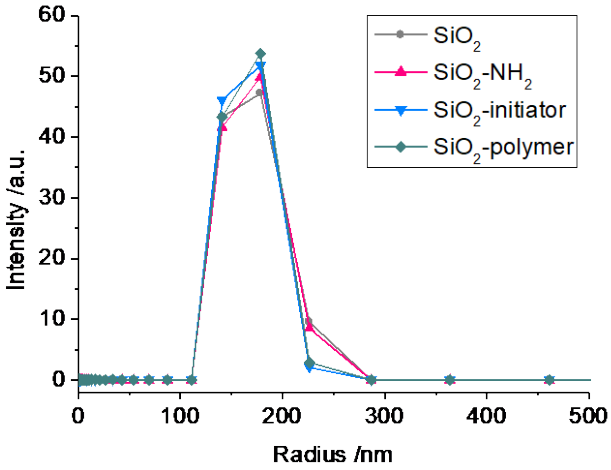


Figure S2. DLS spectra of the nanoparticles

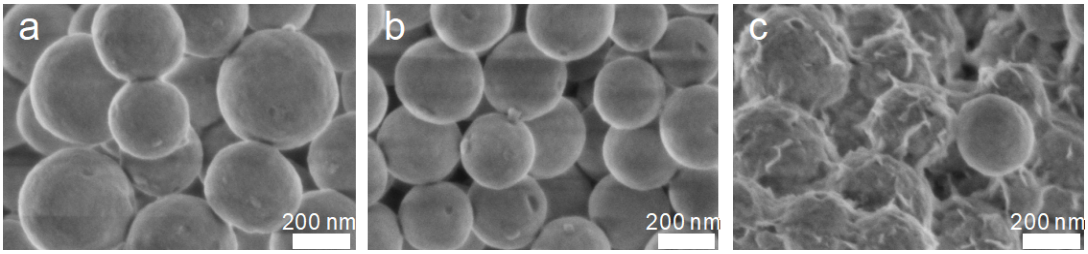


Figure S3. SEM images of a) SiO_2, b) SiO_2-initiator, and c) SiO_2-polymer.

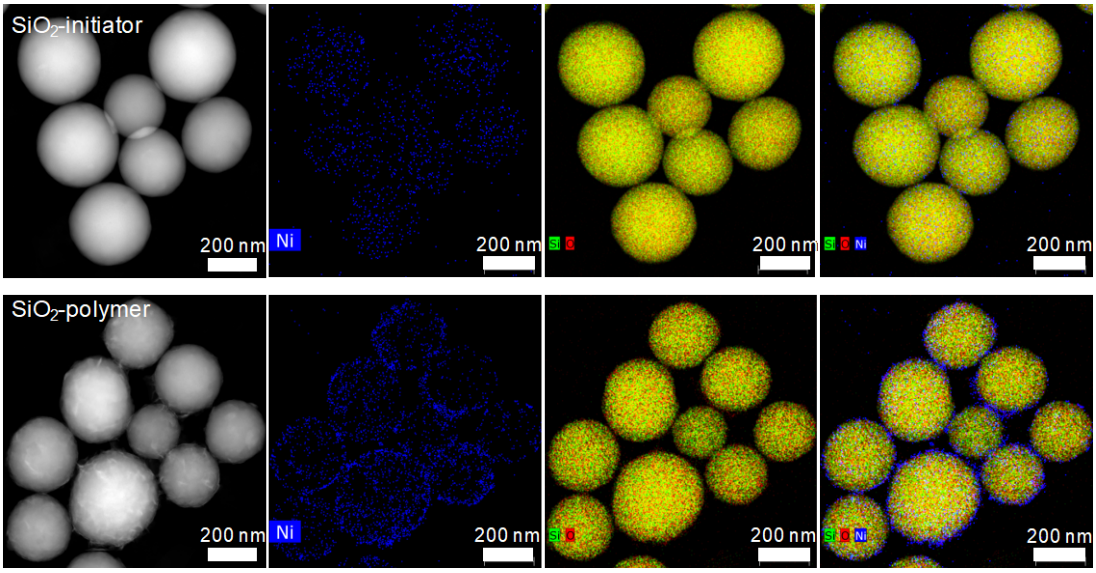


Figure S4. STEM-EDXS analysis of the SiO_2-initiator (top) and SiO_2-polymer (bottom).

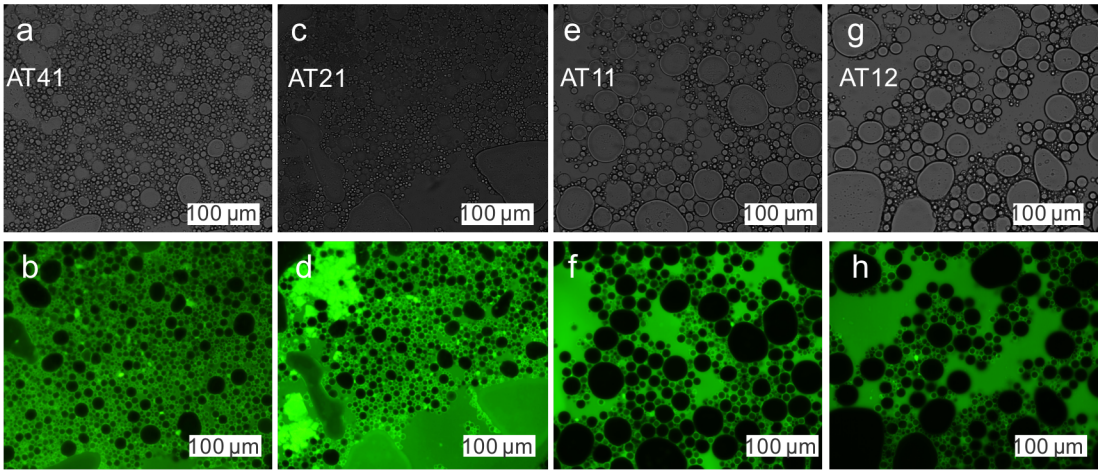


Figure S5. Optical and fluorescent microscopy images used for calculating surface area.

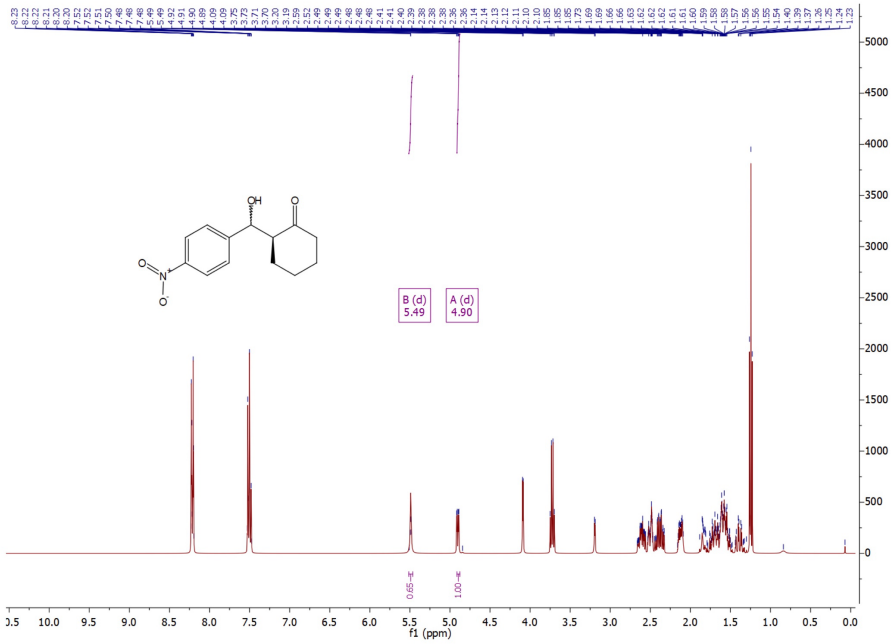


Figure S6. The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 2-[hydroxy-(4-nitrophenyl)methyl]cyclohexan-1-one in AT41 emulsion, δsyn = 5.49, (d) δanti = 4.90 (d).

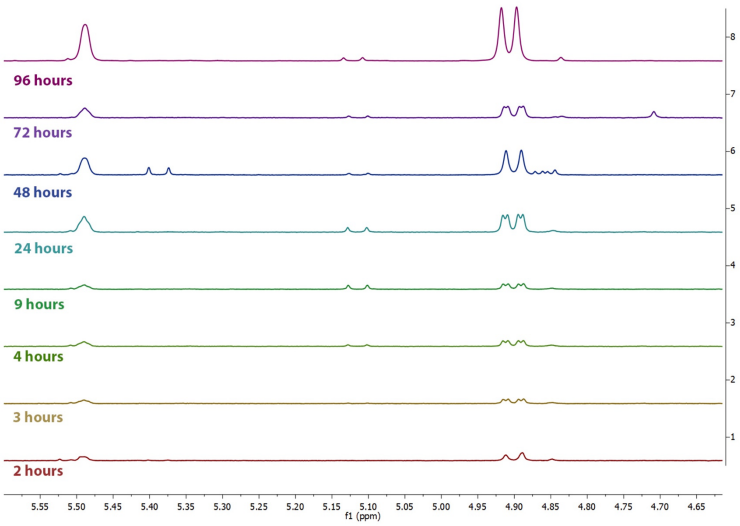


Figure S7. The ^{1}H NMR (400 MHz, $CDCl_3$) spectra of 2-[hydroxy-(4-nitrophenyl)methyl]cyclohexan-1-one monitored over 96 hours, selected region for δsyn = 5.49, (d) δanti = 4.90 (d).

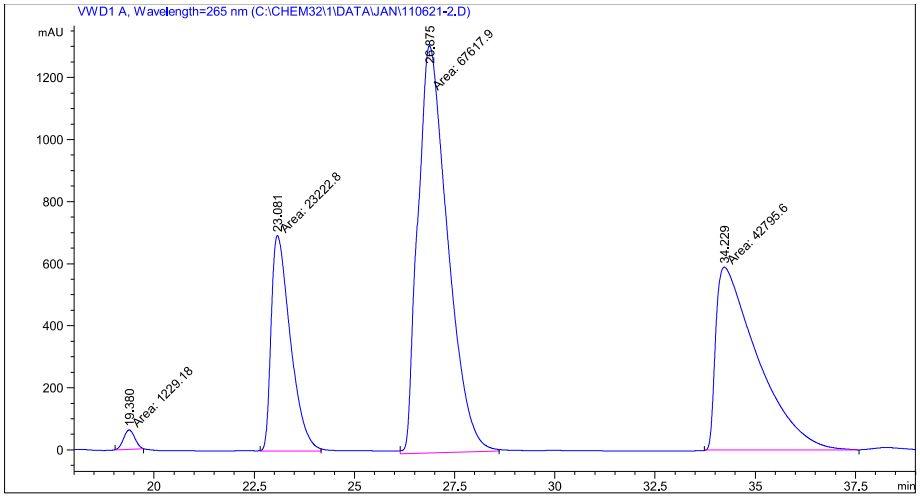


Figure S8. HPLC spectra of 2-[hydroxy-(4-nitrophenyl)methyl]cyclohexan-1-one produced in AT21 emulsion. (R.T. syn = 19.38 min, R.T. syn = 23.08 min, R.T. anti (2S, 1,R)= 26.37 min, R.T. anti (2R, 1,S) = 34.22 min).

3. Reference

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3. Z. Sun, M. Cai, R. Hubner, M. B. Ansorge-Schumacher and C. Wu, *ChemSusChem*, 2020, **13**, 6523-6527.
4. Q. Zhang, T. Zhang, J. Ge and Y. Yin, *Nano Letters*, 2008, **8**, 2867-2871.
5. Z. Sun, U. Glebe, H. Charan, A. Böker and C. Wu, *Angew. Chem. Int. Ed.*, 2018, **57**, 13810-13814.