Molecular Recognition at the Liquid-Liquid Interface of Colloidal Microcapsules

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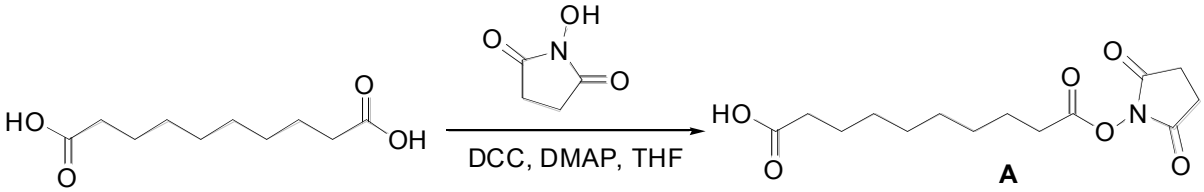
Experimental Section:

SI 1.1: Synthesis of Dopamine-C_8-TEI Ligand:

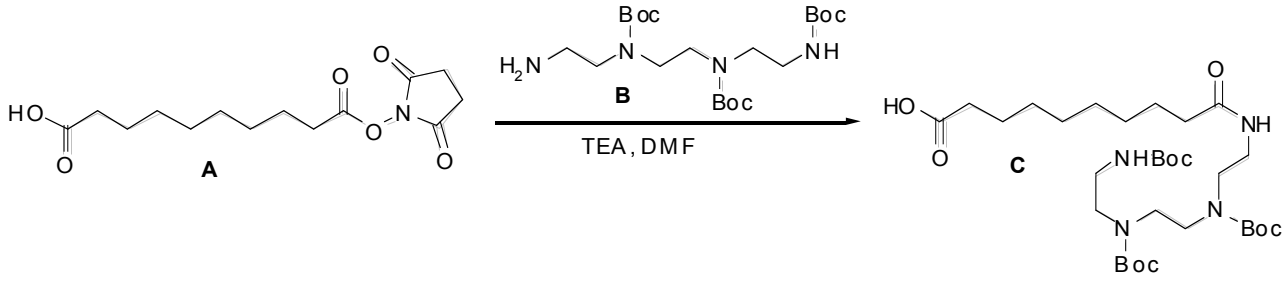
Step 1:



Sebacic acid (2.00 g, 9.89 mmol) was dissolved in dry THF (25 mL). To this solution N-hydroxysuccinimide (1.36 g, 11.87 mmol) was added followed by a solution of DCC (2.02 g, 10.09 mmol) in 5 mL of dry THF at 0°C. The mixture was stirred for 15 min, then DMAP (0.01 g, 0.08 mmol) was added. The reaction mixture was allowed to go to r.t. and stirred for 7 h. The white precipitate was filtered and the solvent was removed from the filtrate to give a residue that was then re-dissolved in CH_2Cl_2 and washed with water. The organic layer was dried over Na_2SO_4, filtered and evaporated and the crude product obtained was purified by flash chromatography with 1/2=EtOAc/CH_2Cl_2 as eluent to give activated acid in 72% yield.

^{1}H NMR _ (400 MHz , $CDCl_3$): 1.20-1.42 (m, 12H, CH_2); 1.55 (quintet, *J*=7.2 Hz, 2H, CH_2); 1.70 (quintet, *J*=7.2 Hz, 2H, CH_2); 2.30 (t, *J*=7.2Hz, 2H, CH_2); 2.30 (t, *J*=7.2Hz, 2H, CH_2); 2.56 (t, *J*=7.2Hz, 2H, CH_2); 2.80 (s, 4H, CH_2).

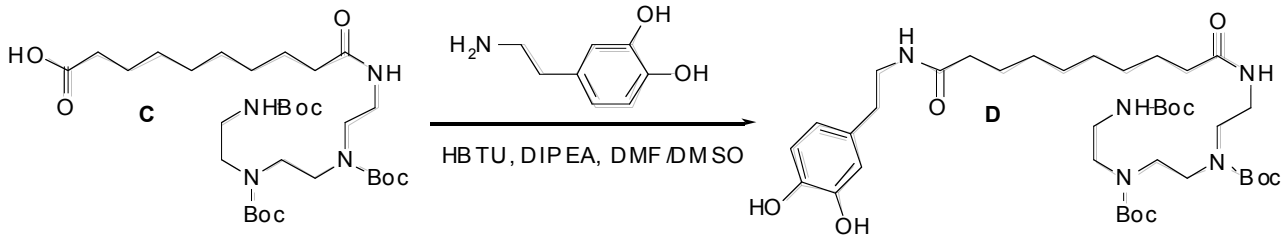
Step 2:



Compound **B** was synthesized according to the literature reported method.[i] In the next step, TEA was added to a solution of **B** (0.20 g, 0.45 mmol) in DMF/H_2O (5 mL/5 mL), until pH 9 is reached. This basic solution was then added to another solution of **A** (0.15 g, 0.45 mmol) in 11 mL of DMF. The reaction mixture was stirred for 18 h under argon, then poured onto water and extracted with EtOAc (6x100 mL). The recollected organic layers were washed with water, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography with 50/1=CH_2Cl_2/MeOH as eluent to yield amide **C** in 99% yield.

^{1}H NMR _ (400 MHz , $CDCl_3$): 1.20-1.30 (m, 12H, CH_2); 1.43 (s, 9H, CH_3); 1.47 (s, 18H, CH_3); 1.52-1.61 (m, 1H, NH); 2.13 (at, *J*=7.2 Hz, 2H, CH_2); 2.30 (t, *J*=7.2 Hz, 2H, CH_2); 3.18-3.45 (m, 12H, CH_2).

Step3:

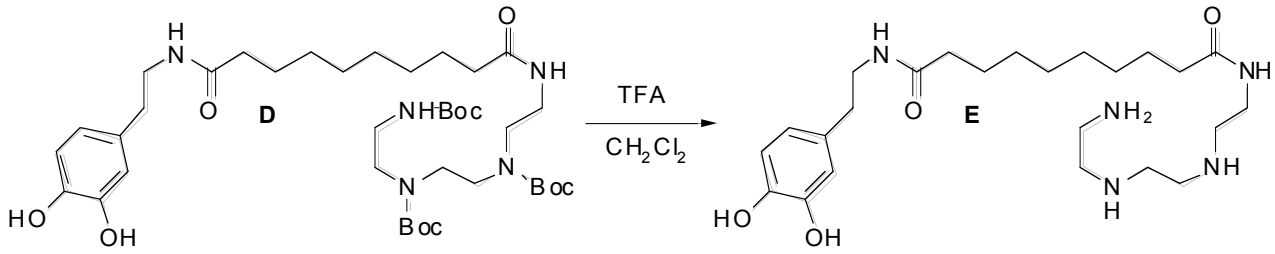


Compound **C** (0.28 g, 0.44 mmol) and dopamine hydrochloride (0.08 g, 0.49 mmol) were dissolved in 8 mL of DMSO. The solution was degassed with argon and cooled to 0 °C before adding HBTU (0.21 g, 0.56 mmol) and DIPEA (0.24 g, 1.79 mmol). The reaction mixture was then stirred at r.t. for 64 h, concentrated and, after the addition of EtOAc, washed with HCl 1M

and water. The resulting solution was dried over Na_2SO_4, filtered and concentrated to give the desired dopamine derivative **D** in 99% yield without further purification.

^{1}H NMR _ (400 MHz , $CDCl_3$): 1.21-1.29 (m, 12H, CH_2); 1.35-1.59 (m, 31H, CH_3 + CH_2); 2.11-2.17 (m, 4H, CH_2); 2.62 (at, *J*=7.2 Hz, 2H, CH_2); 3.19 (bs, 2H, CH_2); 3.27-3.41 (m, 10H, CH_2); 6.51 (d, *J*=8.0 Hz, 1H, H_{arom}); 6.66-6.75 (m, 2H, H_{arom}).

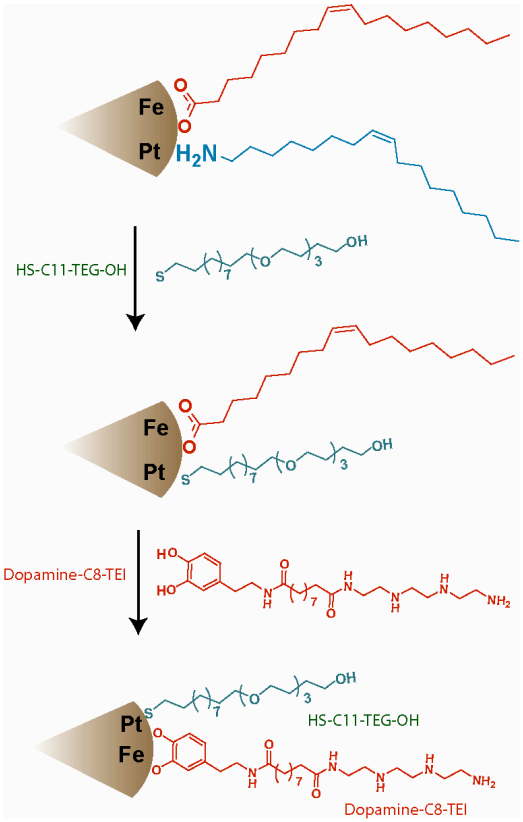
Step 4:



Compound **D** (0.34 g, 0.45 mmol) was dissolved in 15 mL of CH_2Cl_2 and TFA (5.00 mL, 43.17 mmol) was added. The mixture was stirred under argon for 4 h. The solvent was removed under vacuum and the residue was purified by washing with Hexane (3 times) and Et_2O (twice) to obtain amine **E** in 99% yield.

^{1}H NMR _ (400 MHz, CD_3OD): 1.21-1.29 (m, 8H, CH_2); 1.51-1.62 (m, 4H, CH_2); 2.13 (t, *J*=7.2 Hz, 2H, CH_2); 2.22 (t, *J*=7.6 Hz, 2H, CH_2); 2.61-2.69 (m, 2H, CH_2); 3.23 (bs, 2H, CH_2); 3.27-3.41 (m, 12H, CH_2); 6.51 (d, *J*=8.0 Hz, 1H, H_{arom}); 6.66-6.75 (m, 2H, H_{arom}).

Functionalization of FePt NPs:



Scheme S1: Schematic representation of ligand exchange reaction of FePt NPs

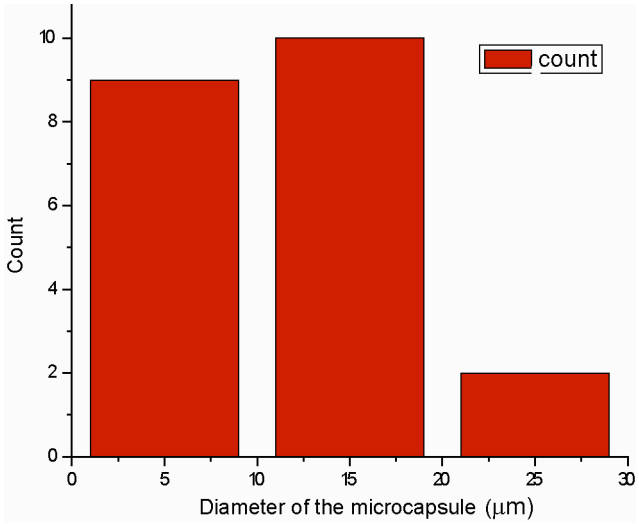
In a typical experiment 10 mg of oleic acid and oleylamine stabilized FePt NPs were mixed with 30 mg of SH-C11-TEG-OH ligand in 5 mL of dichloromethane (DCM). The mixture was stirred at RT for over night under inert atmosphere. Black precipitation was observed after 12 hours. MeOH (5mL) was added to dissolve the resultant NPs. In the next step, 7.5 mg of DOP-PEI (in 5 ml of MeOH) was added and the resulting mixture stirred for 48 hours at 35 °C. After removing solvent, functionalized NPs were dissolved back in MeOH and purified by precipitation using DCM. Finally, the purified FePt NPs were dissolved in 2 mL of water. (Final concentration of the stock solution: 5 mg / mL).

SI 1.2: Fabrication of colloidal microcapsule:

In a typical procedure, 100 _L stock solutions of functionalized FePt NPs were transferred in an eppendorf tube and diluted by adding 200 _L of milliQ water. The pH of the NPs solution was adjusted to ~ 9 by adding 0.1 M NaOH solution. In the next step, 10

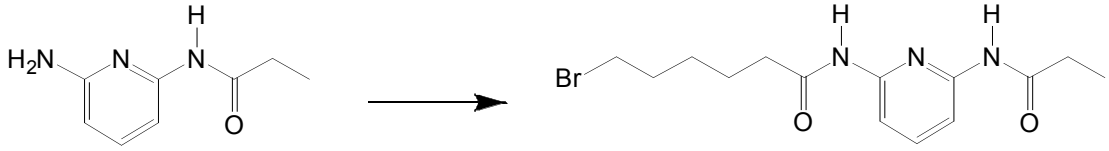
_L of oil (mixture of 0.5 M of CS_2 and flavin polymer in TCB) were added to the aqueous solution of the FePt NPs. The heterogeneous mixture was vigorously shaken by hand for 10-15 seconds. As a result, the solution appeared to be cloudy due to the formation of microemulsions. After 30 minutes, emulsions settled at the bottom of the tube and the supernatant liquid was washed several times by milli Q water prior to characterization.

SI 1.3: Size distribution of the microcapsules (determined from optical microscopy imgae):



Mean	12.529 _m
SD	5.061 _m

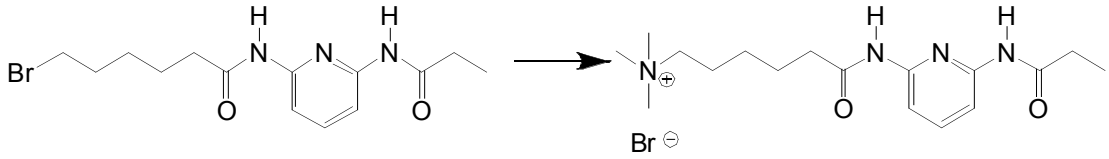
SI 1.4: Synthesis of DAP amphiphile:



The synthesis of ammonium was synthesized from a literature reported procedure. [ii]To a stirred solution of 2-ethylamido-6-aminopyridine (0.4g, 2.4 mmol) in CH_2Cl_2 (200 ml) was added 6-bromohexanoyl chloride (0.57 g. 2.7 mmol) and triethylamine (0.35 ml). The reaction mixture was stirred for 24 h. at room temperature and then water was cautiously added (100 ml). The organic layer was separated and the aqueous layer was further extracted with CH_2Cl_2 (2 x 100 ml). The organic extracts were combined, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude extract was purified using silica gel column chromatography (eluent: CH_2Cl_2/ethyl acetate, 80/20 (v/v)) to afford the product as a white solid (0.5 g, 61 %).

Mpt. 93-95 ^oC.

^{1}H NMR _ (400 MHz, $CDCl_3$): _ 7.90 (2H, t); 7.70 (1H, t); 3.30 (2H, t); 2.30 (4H, m); 1.80 (2H, m); 1.65 (2H, m); 1.40 (2H, m); 1.10 (3H, m). ^{13}C NMR (100 MHz, $CDCl_3$): _ 173.03; 171.98; 149.78; 149.76; 140.41; 109.44; 50.08; 44.78; 36.97; 33.63; 32.28; 30.40; 27.57; 24.44; 9.38. MS (m/z, CI) 342/344 (100%) (M+H). Anal. Calc. for $C_{14}H_{20}N_3O_2Br$ C, 49.13, H, 5.89; N, 12.28; found C, 49.46, H, 5.78, N, 12.11.



To a stirred solution of 2-ethylamido-6-(6-bromohexylamido) pyridine (0.5 g, 1.5 mmol) in methanol (10 ml) was added trimethylamine (2 ml, 30 % solution in methanol). The reaction was heater under reflux for 24 h. The solution was concentrated under reduced pressure and precipitated into a vigorously stirred solution of diethyl ether (100 ml). The precipitate was filtered off and washed with ice-cold diethyl ether. The product was dried under high-vacuum for 24 hrs to afford the product as a white solid (0.5 g. 83%).

Mp. 87-92 ^oC.

^{1}H NMR _ (400 MHz, D_2O): _ 7.70 (1H, t); 7.45 (2H, d); 7.37 (2H, m); 3.20 (2H, m); 3.00 (9H, s); 2.40 (4H, m); 1.75 (2H, m); 1.65 (2H, m); 1.35 (2H, m); 1.10 (3H, t). ^{13}C NMR (100 MHz, D_2O): _ 141.22; 111.17; 111.03; 66.37; 52.80; 52.76; 52.72; 36.30; 30.02; 24.97; 24.39; 22.07; 8.96. MS (m/z, FAB) 322 (40 %) (M+ (-Br)). Anal. Calc. for $C_{17}H_{29}N_4O_2Br$ C, 50.87, H, 7.28; N, 13.96; found C, 50.66, H, 7.20, N, 13.69.

SI 1.5: Fluorescence measurement at a planar interface:

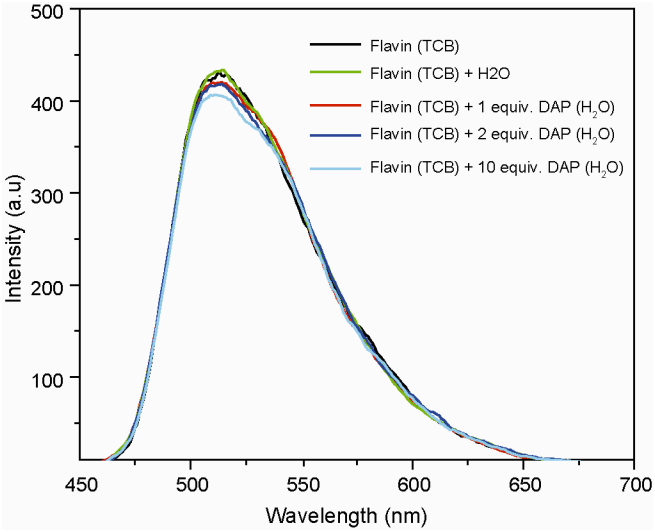


Fig. S1: Fluorescence titration of flavin polymer with variable DAP equivalents at the flat interface.

Notes and References:

[i] S. Srinivasachari, K. M. Fichter, T. M. Reineke, *J. Am. Chem. Soc.*, 2008, **130**, 4618.

[ii] S. C. Hirst, A. D. Hamilton, *Tetrahedron Lett.*, 1990, **31**, 2401.