# Supporting Information

# Power struggles between and among cyclodextrin vesicles and oligopeptides

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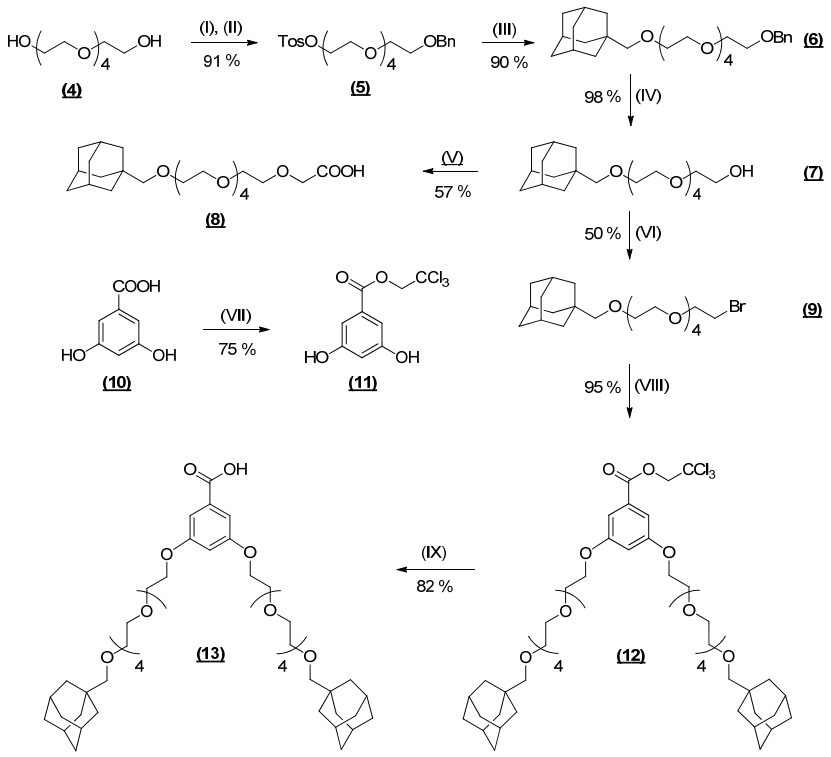
## Synthesis of the adamantane modified peptides




**Scheme S1:** Reaction pathway to the adamantane anchors **(8)** and **(13)**. **(I)** BnBr, NaOH, THF, 24 h, 100 °C, **(II)** TosCl, $NEt_3$, DMAP, $CH_2Cl_2$, rt, 2h, **(III)** Adamantanemethanol, NaH, DMF, 24 h, rt, **(IV)** Pd/C, MeOH, $H_2$, 20 h, rt, **(V)** Bromoacetic acid, *t*-BuOK, DMF, 130°C rt, **(VI)** $PBr_3$, toluene, 24h, rt, **(VII)** Trichloroethanol, $H_2SO_4$, 70 °C, 5 d, **(VIII)** $K_2CO_3$, **(11)**, $CH_3CN$, 70°C, 3d, **(IX)** Zinc dust, acetic acid, THF, 2 h, rt.

## Experimental Part:

All reactions were carried out under an argon atmosphere (Argon 4.8 from *Fa. Messer-Griesheim*) using flasks which were flame-dried under vacuum. Dry septa, disposable syringes and needles were used for the transfer of solvents and chemicals. The air- and water-free solvents were obtained by refluxing with suitable reagents and distillation under an argon atmosphere. Preparative flash column chromatography was performed under 1 bar argon pressure using silica gel grade 40–63 µm purchased from MERCK, Darmstadt. Solvents for column chromatography were distilled prior to us. Thin layer chromatography was done using

commercially available aluminium silica gel cards 60 F 254 purchase from MERCK, Darmstadt. The detection of the products was done under UV light at 254 nm Exact mass spectral measurements were carried out on Micro Tof (Bruer Daltronics, Bremen). Calibrations were done directly before the measurements of samples with sodium formate-clusters.

The $^{1}H$ and $^{13}C$ NMR spectra were recorded at ARX 300 and AMX 400 spectrometer (from BRUKER ANALYTISCHE MESSECHNIK, Karlsruhe). All measurements were carried out in $CDCl_3$ [δ $^{1}H$ ($CHCl_3$) = 7.24;$^{13}C$ ($CDCl_3$) = 77.0 (1:1:1 t)]. TMS [δ $^{1}H$ (TMS) = 0.0;$^{13}C$ (TMS) = 0.0] was used as internal standard for calibrating the NMR spectra. The signals are descripted as s: singlet, dd: doublet of doublet, m: multiplet. The assignment of the resonances were proved by two dimensional homonuclear and heteronuclear correlation experiments like $^{1}H$-$^{1}H$-COSY (GCOSY), $^{13}C$-$^{1}H$-GHSQC, or $^{13}C$-$^{1}H$-GHMBC experiments. With respect to a better comparison of the spectroscopic data the numbering does not follow IUPAC nomenclature.

**Synthesis of toluene-4-sulfonic acid 2-{2-[2-(2-benzyloxy-ethoxy)-ethoxy]-ethoxy}-ethyl ester (5):**:

(I) A solution of NaOH (1.00 g, 25 mmol) in DMF (15 ml) was added to a mixture of tetraethylene glycol **1** (20 g, 100 mmol) and benzyl bromide (2.34 g, 25 mmol). The reaction mixture was stirred at 100°C for 24 h. The reaction mixture was cooled, extracted with $CH_2Cl_2$ (3 x 50 ml) and the organic extracts were combined. Drying of the organic layer with $MgSO_4$, and evaporation of the solvent under reduced pressure afforded (6.74 g, 95% yield) product **2**. $^{1}H$ NMR (400 MHz, $CDCl_3$, 25°C, TMS): $\delta$=7.30 (s, 5H; $=CH^{Bn}$), 4.48 (s, 2H; $OCH_2^{Bn}$), 3.65–3.31 (m, 16H; $OCH_2CH_2O$) ppm; $^{13}C$ NMR (100 MHz, $CDCl_3$, 25°C, TMS): $\delta$=138.3 ($C_q$, *ipso*-$C^{Bn}$), 128.4, 128.1, 127.6 (CH, $=CH^{Bn}$), 72.5 ($CH_2$, $OCH_2^{Bn}$), 70.6, 70.5, 69.9, 69.4 ($CH_2$, $OCH_2CH_2O$ [without assignment]), 61.5 ($CH_2$, $CH_2OH$) ppm; IR: $\tilde{\nu}$=3390,

3290, 2870, 1103 $cm^{-1}$; Exact mass for $C_{15}H_{24}O_5Na$: *m/z* calcd: 307.1516; found: 307.1520 $[M + Na]^+$.

(II) $NEt_3$ (3.20 g, 32 mmol) was added dropwise to a solution of **2** (6.00 g, 20 mmol) and DMAP (0.08 g) in $CH_2Cl_2$ (5 mL) at 0°C and stirred at 0°C for 5 minutes. Subsequently, *p*-toluenesulfonyl chloride (4.00 g, 20 mmol) was added slowly and the reaction mixture was stirred for 3 h at room temperature. Then the reaction mixture was extracted with $Et_2O$ (3 × 20 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (petroleum ether : EtOAc = 2:1, $R_f$ = 0.37) to give **3** (8.90 g, 96% yield). $^1$H NMR (400 MHz, $CDCl_3$, 25°C, TMS): $\delta$=7.5 (dd, $^3J$(H,H)=8.3Hz, $^3J$(H,H)=3.7Hz, 4H; $=CH^{Tos}$), 7.26 (s, 5H; $=CH^{Bn}$), 4.0 (dd, $^2J$(H,H)=5.9Hz, $^2J$(H,H)=4.8Hz, 2H; $OCH_2^{Bn}$), 3.61–3.48 (m, 16H; $OCH_2CH_2O$), 2.36 (s, 3H; $CH_3$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$, 25°C, TMS): $\delta$=144.7 ($C_q$, *ipso*-$C^{Tos}$), 138.2 ($C_q$, *ipso*-$C^{Bn}$), 133.0 ($C_q$, *ipso*-$C^{Tos}$), 129.8, 128.3 (CH, $=CH^{Tos}$), 127.9, 127.6, 127.4, (CH, $=CH^{Bn}$), 73.2 ($CH_2$, $OCH_2^{Bn}$), 70.7, 70.6, 70.5, 69.4 ($CH_2$, $OCH_2CH_2O$), 21.6 ($CH_3$, $CH_3$) ppm; IR: $\tilde{\nu}$=2868, 1598, 1496 $cm^{-1}$; Exact mass for $C_{22}H_{30}O_7SNa$: *m/z* calcd: 461.1634; found: 461.1611 $[M + Na]^+$.

**Synthesis of 1-(2-{2-[2-(2-Benzyloxy-ethoxy)-ethoxy]-ethoxy}-ethoxymethyl)-adamantane (6):**

A suspension of sodium hydride (1.00 g, 40 mmol) in DMF (2 ml) was added slowly to a solution of 1-adamantanmethanol (**4**) (3.32 g, 20 mmol) in DMF (15 ml) at 0°C, under argon atmosphere. The reaction mixture was stirred at room temperature for 90 min. The solution of **3** (8.80 g, 20 mmol) in DMF (5ml) was added to the reaction mixture. Subsequently, the reaction mixture was stirred at room temperature for 24 h. Then reaction mixture was extracted with $CH_2Cl_2$ (3 x 50 ml) and the organic extracts were combined. Drying of the organic layer with $MgSO_4$, evaporation of the solvent under reduced pressure and purification

by flash column chromatography on silica gel (petroleum ether : EtOAc = 3:1, $R_f$ = 0.65) afforded (7.76 g, 90% yield) product **5**. $^1$H NMR (400 MHz, $CDCl_3$, 25°C, TMS): $\delta$=7.26 (s, 5H; $=CH^{Bn}$), 4.49 (s, 2H; $OCH_2^{Bn}$), 3.58–3.46 (m, 16H; $OCH_2CH_2O$), 2.94 (s, 2H; $OCH_2^{Ad}$), 1.87 (m, 3H; 3-$CH^{Ad}$), 1.65 (m, 6H; 4-$CH_2^{Ad}$), 1.55 (m, 6H; 2-$CH_2^{Ad}$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$, 25°C, TMS): $\delta$=137.2 ($C_q$, *ipso*-$C^{Bn}$), 127.3, 127.1, 126.7 (CH, $=CH^{Bn}$), 108.7 ($CH_2$, $OCH_2^{Ad}$), 81.4 ($CH_2$, $OCH_2^{Bn}$), 75.2 ($CH_2$, $OCH_2^{Bn}$), 72.8, 72.2, 69.6, 69.6 ($CH_2$, $OCH_2CH_2O$), 38.6 ($CH_2$, 2-$CH_2^{Ad}$), 37.4 ($CH_2$, 4-$CH_2^{Ad}$), 33.4 ($C_q$, 1-$C^{Ad}$), 27.1 (CH, 3-$CH^{Ad}$) ppm; IR: $\tilde{\nu}$=2848, 1674, 1503, 1387 cm$^{-1}$; Exact mass for $C_{26}H_{40}O_5Na$: *m/z* calcd: 455.2768; found: 455.2766 $[M + Na]^+$.

**Synthesis of 2-(2-{2-[2-(Adamantan-1-ylmethoxy)-ethoxy]-ethoxy}-ethoxy)-ethanol (7):**

A suspension of catalytic amount of Pd/C (0.20 mg) and **5** (7.20 g, 16 mmol) in EtOH (40 ml) was stirred at room temperature under 2 bar $H_2$ atmosphere for 20 h. The suspension was filtrated and solvent was evaporated. Product **6** was used without further purification (5.60 g, 98% yield). $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=3.65–3.48 (m, 16H; $OCH_2CH_2O$), 2.94 (s, 2H; $OCH_2^{Ad}$), 1.88 (m, 3H; 3-$CH^{Ad}$), 1.62 (m, 6H; 4-$CH_2^{Ad}$), 1.45 (m, 6H; 2-$CH_2^{Ad}$) ppm; $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=82.9 ($CH_2$, $OCH_2^{Ad}$), 73.1, 71.1, 71.0, 70.8, ($CH_2$, $OCH_2CH_2O$), 62.1 ($CH_2$, $CH_2OH$), 40.1 ($CH_2$, 2-$CH_2^{Ad}$), 37.4($CH_2$, 4-$CH_2^{Ad}$), 34.6 ($C_q$, 1-$C^{Ad}$), 28.7 (CH, 3-$CH^{Ad}$) ppm; IR: $\tilde{\nu}$=2844, 1642 cm$^{-1}$; Exact mass for $C_{19}H_{34}O_5Na$: *m/z* calcd: 365.2298; found: 365.2302 $[M + Na]^+$.

**Synthesis of [2-(2-{2-[2-(Adamantan-1-ylmethoxy)-ethoxy]-ethoxy}-ethoxy)-ethoxy]-acetic acid (8):**

A suspension of *t*BuOK (1.47 g, 12.90 mmol) in DMF (2 ml) was added slowly to a solution of **6** (1.50 g, 4.38 mmol) in DMF (15 ml) at 0°C, under argon atmosphere and the mixture was stirred at room temperature for 30 min. To this reaction mixture the solution of bromoacetic acid (1.20 g, 8.76 mmol) in DMF (1 ml) was added. The reaction mixture was stirred at 130°C

for 15 h. Subsequently, the reaction mixture was extracted with $CH_2Cl_2$ (3 x 30 ml) and 2 M HCl. The organic extracts were combined, the organic layer was dried with $MgSO_4$. Evaporation of the solvent under reduced pressure and purification by flash column chromatography on silica gel ($CH_2Cl_2$ : MeOH = 5:1, $R_f$ = 0.3) afforded (1.00 g, 58% yield) product **7**. $^1$H NMR (400 MHz, $CDCl_3$, 25°C, TMS): $\delta$=3.98 (s, 2H; $OCH_2C{=}O$), 3.63–3.45 (m, 16H; $OCH_2CH_2O$), 2.96 (s, 2H; $OCH_2^{Ad}$), 1.85 (m, 3H; 3-$CH^{Ad}$), 1.64 (m, 6H; 4-$CH_2^{Ad}$), 1.44 (m, 6H; 2-$CH_2^{Ad}$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$, 25°C, TMS): $\delta$=175.0 ($C_q$, C=O), 82.4 ($CH_2$, $OCH_2^{Ad}$), 71.1, 70.9, 70.6, 69.7, ($CH_2$, $OCH_2CH_2O$), 69.0 ($CH_2$, $OCH_2C{=}O$), 39.6 ($CH_2$, 2-$CH_2^{Ad}$), 37.2 ($CH_2$, 4-$CH_2^{Ad}$), 34.1 ($C_q$, 1-CAd), 28.2 (CH, 3-$CH^{Ad}$) ppm; IR: $\tilde{\nu}$=2856, 1594, 1448 cm$^{-1}$; Exact mass for $C_{21}H_{36}O_7Na$: *m/z* calcd: 423.2353; found: 423.2355 $[M + Na]^+$.

**Synthesis of 1-(2-{2-[2-(2-Bromo-ethoxy)-ethoxy]-ethoxy}-ethoxymethyl)-adamantane (9):**

$PBr_3$ (1.56 g, 5.84 mmol) was added dropwise to a solution of 7 (4.00 g, 12.00 mmol) in toluene (25 mL) at 0°C and reaction mixture was stirred at 0°C for 30 minutes. Then reaction mixture was stirred for 15 h at room temperature. Subsequently, the mixture was extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel ($CH_2Cl_2$ : MeOH = 99:1, $R_f$ = 0.8) to give 9 (2.36 g, 50% yield). $^1$H NMR (400 MHz, $CDCl_3$, 25°C, TMS): $\delta$=3.66–3.42 (m, 16H; $OCH_2CH_2O$), 2.86 (s, 2H; $OCH_2^{Ad}$), 1.83 (m, 3H; 3-$CH^{Ad}$), 1.54 (m, 6H; 4-$CH_2^{Ad}$), 1.32 (m, 6H; 2-$CH_2^{Ad}$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$, 25°C, TMS): $\delta$=82.4 ($CH_2$, $OCH_2^{Ad}$), 71.2, 70.7, 70.6, 70.5, ($CH_2$, $OCH_2CH_2O$), 39.6 ($CH_2$, 2-$CH_2^{Ad}$), 37.3 ($CH_2$, 4-$CH_2^{Ad}$), 33.8 ($C_q$, 1-$C^{Ad}$), 28.2 (CH, 3-$CH^{Ad}$) ppm; IR: $\tilde{\nu}$=2957, 1633, 1450 cm$^{-1}$; Exact mass for $C_{19}H_{33}O_4BrNa$: *m/z* calcd: 427.1436; found: 427.1460 $[M + Na]^+$.

**Synthesis of 3,5-Dihydroxy-benzoic acid 2,2,2-trichloro-ethyl ester (11):**

To a solution of 2,2,2-trichloroethanol (30 ml) was added 3,5-dihydroxybenzoic acid (5.00 g, 32.50 mmol) followed by concentrated sulphuric acid (1 ml), and the mixture was heated at 70°C for 5 days under argon atmosphere. The reaction mixture was extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel ($CH_2Cl_2$ : EtOAc = 1:5) to give **10** (6.60 g, 75% yield). $^1$H NMR (400 MHz, $CDCl_3$, 25°C, TMS): $\delta$=7.08 (s, 2H; =$CH^{Ph}$), 6.57 (s, 1H; =$CH^{Ph}$), 4.83 (s, 2H; $OCH_2CCl_3$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$, 25°C, TMS): $\delta$=163.3, ($C_q$, C=O), 156.9 ($C_q$, $C^{Ph}$), 130.4 ($C_q$, $C^{Ph}$), 109.6 (CH, =$CH^{Ph}$), 108.7 (CH, =$CH^{Ph}$), 99.2 ($C_q$, $CCl_3$), 74.7 ($CH_2$, O*C*$H_2CCl_3$) ppm; Exact mass for $C_9H_7O_4Cl3Na$: *m/z* calcd: 306.9302; found: 306.9290 $[M + Na]^+$.

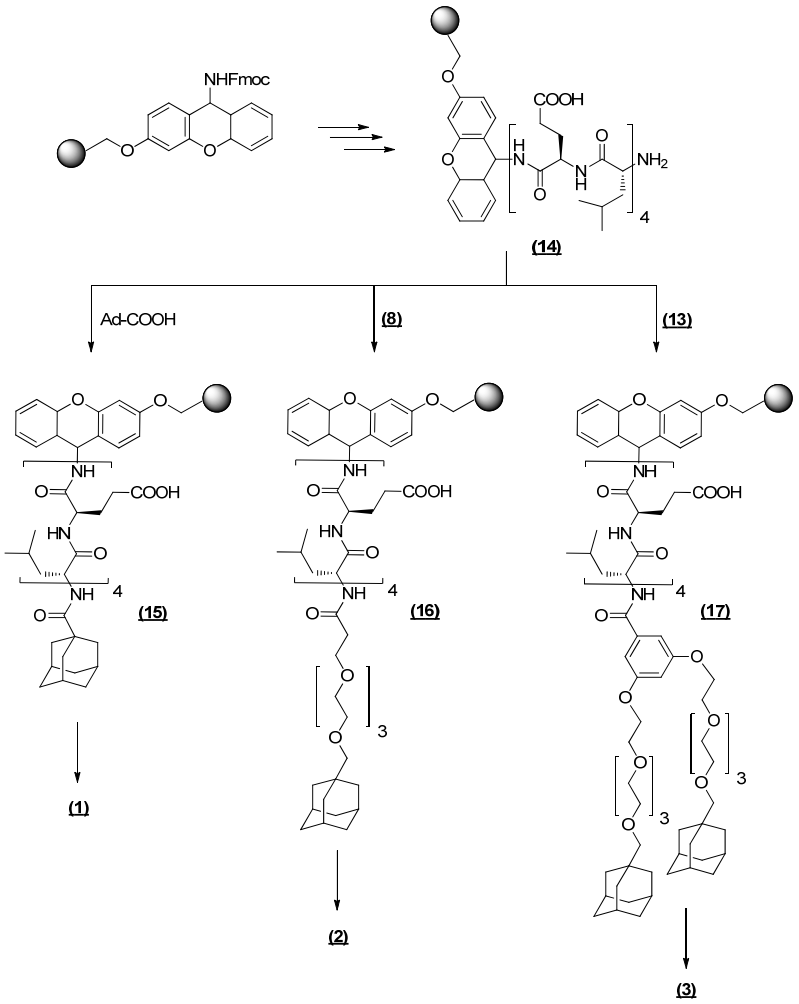
**Synthesis of 3,5-Bis-[2-(2-{2-[2-(adamantan-1-ylmethoxy)-ethoxy]-ethoxy}-ethoxy)-ethoxy]-benzoic acid 2,2,2-trichloro-ethyl ester (12):**

The reaction mixture of **10** (0.67 g, 2.46 mmol) and $K_2CO_3$ in $CH_3CN$ (100 ml) was heated at 70°C. Subsequently, the mixture of KI (0.50 g, 0.71 mmol) and **8** (2.00 g, 4.0 mmol) in $CH_3CN$ (10 ml) was added slowly to the reaction mixture. The final reaction mixture was heated at 80°C for 72 h. Then reaction mixture was extracted with $CH_2Cl_2$ (3 x 30 ml) and 2 M HCl. The organic extracts were combined and the organic layer was dried with $MgSO_4$. Evaporation of the solvent under reduced pressure and purification by flash column chromatography on silica gel ($CH_2Cl_2$ : MeOH = 9:1, $R_f$ = 0.87) afforded **12** (2.20 g, 95% yield). $^1$H NMR (400 MHz, $CDCl_3$, 25°C, TMS): $\delta$=7.25 (s, 2H; =$CH_{ortho}$), 6.73 (s, 1H; =$CH_{meta}$), 4.92 (s, 2H; $OCH_2CCl_3$), 4.13 (m, 2H; $C_{ipso}OCH_2CH_2O$), 3.67–3.43 (m, 14H; $OCH_2CH_2O$), 2.89 (s, 2H; $OCH_2^{Ad}$), 1.89 (m, 3H; 3-$CH^{Ad}$), 1.62 (m, 6H; 4-$CH_2^{Ad}$), 1.49 (m, 6H; 2-$CH_2^{Ad}$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$, 25°C, TMS): $\delta$=164.5 ($C_q$, C=O), 159.8 ($C_q$, $C_{ipso}O$), 130.3 ($C_q$, $C_{ipso}C$=O), 108.5 (CH, =$CH_{ortho}$), 107.3 (CH, =$CH_{meta}$), 94.9 ($C_q$, $CCl_3$),

82.5 ($CH_2$, $OCH_2^{Ad}$), 74.4 ($CH_2$, $OCH_2CCl_3$), 71.9, 71.7, 70.6, 70.5, ($CH_2$, $OCH_2CH_2O$), 39.6 ($CH_2$, 2-$CH_2^{Ad}$), 37.1 ($CH_2$, 4-$CH_2^{Ad}$), 34.0 ($C_q$, 1-$C^{Ad}$), 28.2 (CH, 3-$CH^{Ad}$) ppm; IR: $\tilde{\nu}$=2848, 1735, 1592, 1446 $cm^{-1}$; Exact mass for $C_{47}H_{71}Cl_3O_{12}Na$: *m/z* calcd: 955.3887; found: 957.3846 $[M + Na]^+$.

**Synthesis of 3,5-Bis-[2-(2-{2-[2-(adamantan-1-ylmethoxy)-ethoxy]-ethoxy}-ethoxy)-ethoxy]-benzoic acid (13):**

Acetic acid (4.5 ml) was added to a solution of **12** (1.70 g, 1.82 mmol) in THF (40 ml) and the reaction mixture was stirred at room temperature under argon atmosphere. Subsequently, zinc dust (0.78 g) was added, and the mixture was stirred vigorously at room temperature for 1 h. The reaction mixture was filtered, and the filtrate was extracted with $Et_2O$ (3 x 50 ml). The combined extracts were washed with water and dried over $MgSO_4$. The solvent was removed and the crude product was purified by flash column chromatography on silica gel ($CH_2Cl_2$ : MeOH = 7:1, $R_f$ = 0.88) and product **13** (1.20 g, 82% yield) was obtained as an oil. $^1$H NMR (400 MHz, $CDCl_3$, 25°C, TMS): $\delta$=7.20 (s, 2H; $=CH_{ortho}$), 6.69 (s, 1H; $=CH_{meta}$), 4.13 (m, 2H; $C_{ipso}OCH_2CH_2O$), 4.11 (m, 2H; $C_{ipso}OCH_2CH_2O$), 3.69–3.45 (m, 12H; $OCH_2CH_2O$), 2.89 (s, 2H; $OCH_2^{Ad}$), 1.92 (m, 3H; 3-$CH^{Ad}$), 1.69 (m, 6H; 4-$CH_2^{Ad}$), 1.50 (m, 6H; 2-$CH_2^{Ad}$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$, 25°C, TMS): $\delta$=170.2 ($C_q$, C=O), 159.7 ($C_q$, $C_{ipso}O$), 131.7 ($C_q$, $C_{ipso}C$=O), 108.4 (CH, $=CH_{ortho}$), 107.3 (CH, $=CH_{meta}$), 82.5 ($CH_2$, $OCH_2^{Ad}$), 71.3, 71.1, 70.8, 70.6, ($CH_2$, $OCH_2CH_2O$), 39.7 ($CH_2$, 2-$CH_2^{Ad}$), 37.1 ($CH_2$, 4-$CH_2^{Ad}$), 34.0 ($C_q$, 1-$C^{Ad}$), 28.2 (CH, 3-$CH^{Ad}$) ppm; IR: $\tilde{\nu}$=2848, 1716, 1592, 1446 $cm^{-1}$; Exact mass for $C_{45}H_{70}O_{12}Na$: *m/z* calcd: 825.4759; found: 825.4748 $[M + Na]^+$.




**Scheme S2**: Reaction pathway to the adamantane modified peptides **(1)**, **(2)** and **(3)**.

## Fmoc-NH-(leu-glu)$_4$-NH-resin (14)

The octapeptide was synthesized using a conventional Fmoc solid phase peptide synthesis protocol on an Applied Biosystems 431A automated peptide synthesizer. The peptide was synthesized on a Sieber amide resin with a loading of 0.64 mmol/g at a 250 μmol scale. Amino acid couplings were performed in NMP for 1 hour with 4 equivalents of HCTU, 8 equivalents of base and 4 equivalents of the appropriate amino acid. Fmoc deprotection was performed with 20 vol% piperidine in NMP.

**Ad-(leu-glu)$_4$-NH-resin (15)**

The octapeptide (**14**) was conjugated to adamantane by coupling adamantane 1-carboxylic acid to the N-terminus of the peptide. The resin was swollen in NMP for 1 hour. A mixture of 4 eq. adamantane 1-carboxylic acid, 4 eq. of HCTU and 8 eq. of DIPEA in NMP was left to preactivate for 2 minutes after which it was added to the resin and coupled overnight.

**Ad-TEG$_4$-(leu-glu)$_4$-NH-resin (16)**

The octapeptide (**14**) was conjugated to **8** by coupling it to the N-terminus of the peptide. The resin was swollen in NMP for 1 hour. A mixture of 4 eq. of **13**, 4 eq. of HCTU and 8 eq. of DIPEA in NMP was left to preactivate for 2 minutes after which it was added to the resin and coupled overnight.

**(Ad-TEG$_4$)$_2$-Phe-(leu-glu)$_4$-NH-resin (17)**

The octapeptide (**14**) was conjugated to **13** by coupling it to the N-terminus of the peptide. The resin was swollen in NMP for 1 hour. A mixture of 4 eq. of **13**, 4 eq. of HCTU and 8 eq. of DIPEA in NMP was left to preactivate for 2 minutes after which it was added to the resin and coupled overnight.

**Cleavage and purification of (15), (16) and (17)**

Products **(1)**, **(2)** and **(3)** were obtained by cleaving the corresponding molecules from the resin by treating them with a solution containing TFA:$H_2O$ (9:1 v/v). The solutions with the products were co-evaporated with toluene 3 times to obtain the dry crude product. Subsequent RP-HPLC was performed on a Shimazu HPLC system with two LC-8A pumps and an SPD-10AVP UV-VIS detector. Two different eluents were used: (A) $H_2O$ (with 0.1% TFA) and (B) $CH_3CN$ (with 0.1% TFA). The flow rate was 20 mL/min. The gradient was set to 10%-90% B over 3 column volumes. Collection of the product peak was determined by UV

absorption at 214 nm. The acetonitril was removed through rotary evaporation and subsequent lyophilization yielded the pure products in powder form. The purity of compounds **(1)**, **(2)** and **(3)** was determined by LCMS, and was estimated to be greater than 95%.

**Preparation of the cyclodextrin-vesicles**

Amphiphilic *β*-cyclodextrin **1** was synthesized as described.[2] To prepare unilamellar bilayer vesicles, **1** was dissolved in CHCl3 and the solvent was evaporated with a rotary evaporator and a vacuum oven for one hour. The obtained thin film of **1** was hydrated with phosphate buffered saline and was vortexed extensively at room temperature (PBS, pH 7.4) to provide a 1 mM turbid aqueous solution of **1**. After sonication under heating for 30 minutes, a clear solution was obtained. The size of the vesicles was set around 100 nm by extrusion through a polycarbonate membrane. The average diameter of the particles was estimated to be 77 nm with dynamic light scattering.

***β*-Sheet formation on the surface of the CD vesicle**

After the appropriate amount of peptide **2** (typically 0.5 mM solution in PBS) was added to vesicles composed of **1** (typically 0.5 mM solution in PBS), the pH of the mixture was set to 5.0 with a minimum amount of a 0.1 M H3PO4 or 1 M HCl.

**Circular dichroism (CD) spectroscopy**

CD spectra were measured with a J-815 Spectropolarimeter (JASCO) at room temperature. A 0.1 cm quartz cuvette was used. The CD spectra were obtained after averaging of six scans and subtraction of the background. The Molar ellipicity, [θ] (deg cm2 dmol-1), was calculated from the observed ellipticity, θ*obs* (mdeg), by applying the following equation: $[\theta] = \theta obs \cdot M/(10 \cdot l \cdot c)$, where $M$ is the mean residue molecular weight, $l$ is the path length of the cuvette and $c$ is the concentration of the peptide.

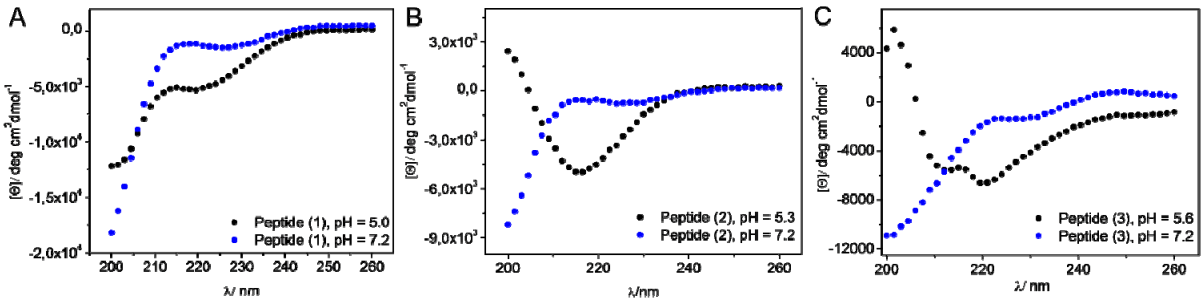



**Fig. S3:** CD spectra of **(1)**, **(2)** and **(3)** at pH = 7.2 (black) and pH = ~5 (blue).

## Dynamic Light Scattering (DLS)

DLS data were obtained using a Zetasizer Nano ZS (Malvern Instruments Ltd). The observed intensity autocorrelation function, $g(2)(t)$, was measured experimentally, which is related to the normalized autocorrelation function, $g(1)(t)$, by the Siegert relation, $g(2)(t) = 1 + \beta \cdot [g(1)(t)]2$, where β is a constant parameter for an optical system. To obtain the average relaxation time (τ), the first cumulant method was employed to analysis of $g(1)(t)$ according to the equation, $g(1)(t) = \exp(-t/\tau)$. The apparent translational diffusion coefficient, $D$, is calculated from $D = \Gamma\_/q2$, where Γ is the relaxation rate, $\Gamma = 1/\tau$, and $q$ represents the magnitude of scattering vector expressed as $q = (4\pi n/\lambda\square)\cdot\sin(\theta/2)$, where θ is the scattering angle, 173°, $n$ is the refractive index of the solution and λ is the wavelength (633 nm). The apparent hydrodynamic radius, $r$, is given by the Einstein-Stokes equation $r = kBT/(6\pi\eta D)$, where $kB$ is the Boltzmann constant, $T$ is the absolute temperature, and η is the solvent viscosity.

## Cryo-TEM

Glow-discharged carbon-coated lacey Formvar grids (300 mesh, Ted Pella) or Quantifoil R2/2 grids (Quantifoil, Jena Germany) were loaded with 3 μL sample. Grids were blotted and plunged into liquid ethane using a fully automated home-built vitrification device operating at 100 % humidity and 22 ºC. Electron microscopy images were recorded on a FEI Tecnai 12

electron microscope at an accelerating voltage of 120 keV and equipped with a 4k x 4k Eagle camera (FEI, Eindhoven, The Netherlands). Images were recorded at liquid nitrogen temperature using a Gatan 626 cryo-holder (Gatan Inc., Pleasanton, U.S.A.) under low-dose conditions. As we observed absorptions of the material onto the Quantifoil grids (Figure 2a), we used lacey Formvar grids (Figure 2b and 2c).

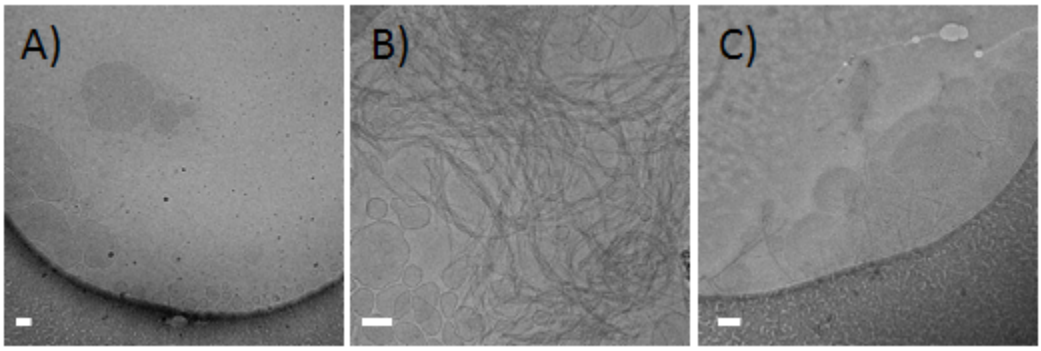



**Fig. S4. A)** Cryo-TEM images acquired of the assembly CDV + peptide **(2)** at pH = 7.4, B) Cryo-TEM images acquired of the assembly CDV + peptide **(2)** at pH = 5.3, C) Cryo-TEM images acquired of the assembly CDV + peptide **(2)** back to pH = 7.4.

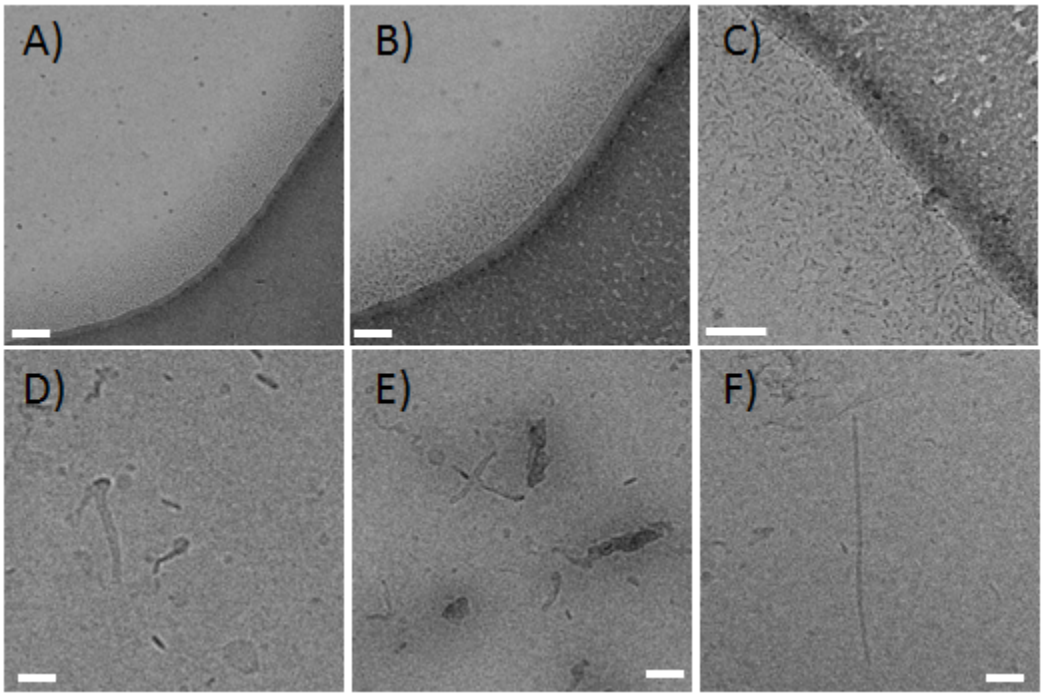



**Fig. S5. A)-C)** Cryo-TEM images acquired of the assembly CDV + peptide **(3)**. The images show assemblies with 50 mol% peptide **(3)** at pH 7.2. **D)-F)** Cryo-TEM images acquired of the assembly CDV + peptide **3**. The images show assemblies with 50 mol% peptide **(3)** at pH 5.6.

## Fluorescence Spectroscopy

Fluorescence measurements were performed using a FS920 fluorometer (Edinburgh Instruments Ltd.) with a DTMS-300X excitation monochrometer and a peltier-controlled thermostatic cell. All spectra were obtained at 25 °C using a quartz cuvette with a 1 cm path length. Each spectrum was measured with the step size of 1.0 nm, and a sampling time of 0.1 s, and single scan. Excitation and emission slits were 1 nm. The excitation wavelength was 282 nm. For the fluorescence experiment we used 10 μM of tetrasodium 1,3,6,8-pyrenetetrasulfonate and 100 mM of NaI. To destroy the assembly, we used a minimum amount of 20 wt% Triton X-100 solution. The experiment was performed as follows: tetrasodium 1,3,6,8-pyrenetetrasulfonate (Py) was added during the preparation of the vesicular system composed of **1** and **2**. Next, NaI was added to quench all non-encapsulated dyes, the observed signal was due only to encapsulated dyes. The pH was then lowered to 5.0

with 1 M HCl and the fluorescence intensity was measured for 1 hour. Triton X-100 was then added and the fluorescence intensity was measured again.

**Isothermal Titration Calorimetry (ITC)**

ITC titrations were performed with a Nano-ITC III (Calorimetry Sciences Corporation, USA). The reference cell was filled with Milli-Q grade. water. All solutions were degassed for 10 min before use. The guest molecules (5.00 mM for **(2)**, and 2.50 mM for **(3)**) were dissolved in water with addition of 1 equivalent of NaOMe to increase the water solubility. 20 injections with a volume of 10μL were titrated into a solution of β-CD (0.5 mM) in milli-Q water. Injection intervals were set to 300 seconds with a stirring rate of 300 rpm and a temperature of 23°C.

**Lipid mixing assay**

To check whether in the transition from vesicles to fibers several or just a single vesicle were incorporated into a single fiber, a lipid mixing assay was performed. For this purpose, the amphiphilic cyclodextrin was fluorescently labeled with rhodamine B according to a literature procedure. The amount of fluorescent lable was determined to be 4.6% by a Lamert Beer plot. These labelled cyclodextrins are also able to form vesicles in aqueous media. Due to the close proximity of the rhodamine B units at the vesicle surface a significant quenching is observed. These fluorescent vesicles were mixed with non fluorescent vesicles in a ratio of 1:5 in the presence of either guest **(1)** or **(2)**. If during the pH dependent transformation between vesicles and fibers several vesicles take part, a significant increase in the rhodamine B distance should be the consequence of mixing of labelled and non labelled vesicles. With this a relief of self quenching and an increase of rhodamine B fluorescence should be observed. However, our assay revealed that in every morphological change a single vesicle is involved and not an interaction of different vesicles. It is obvious that no lipid mixing takes place

during the interaction between CDVs and the guest molecules. From figure S6 and S7 it is clearly visible that the addition of the guest molecules **(1)** and **(2)** to the CDVs and changing the pH does not lead to an increase in the emission intensity at 590 nm. This leads to the assumption that no lipid mixing occurs. Disruption of the CDVs by adding Triton X leads to a full loss of self quenching due to complete rhodamine B dilution.

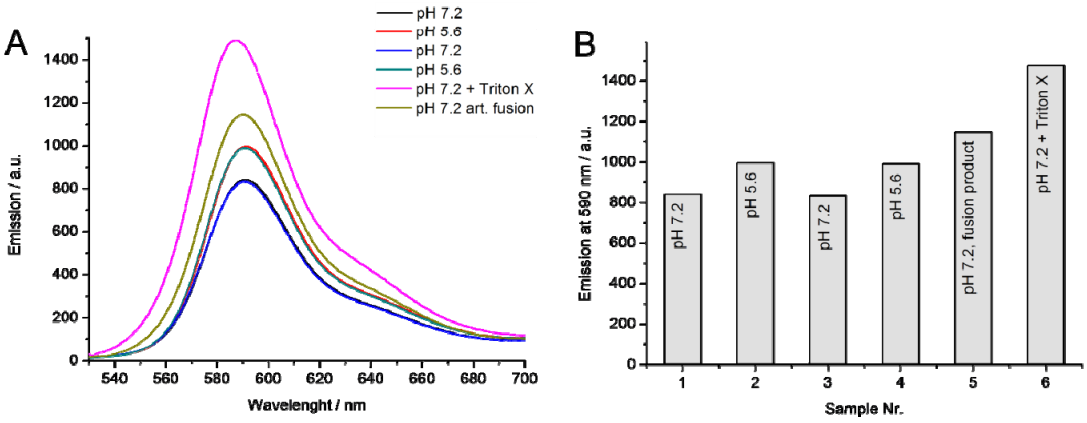



**Fig. S6** Lipid mixing assay of **(1)** with β-CD vesicles. Emission spectra (left) and max. emission at 590 nm (right).

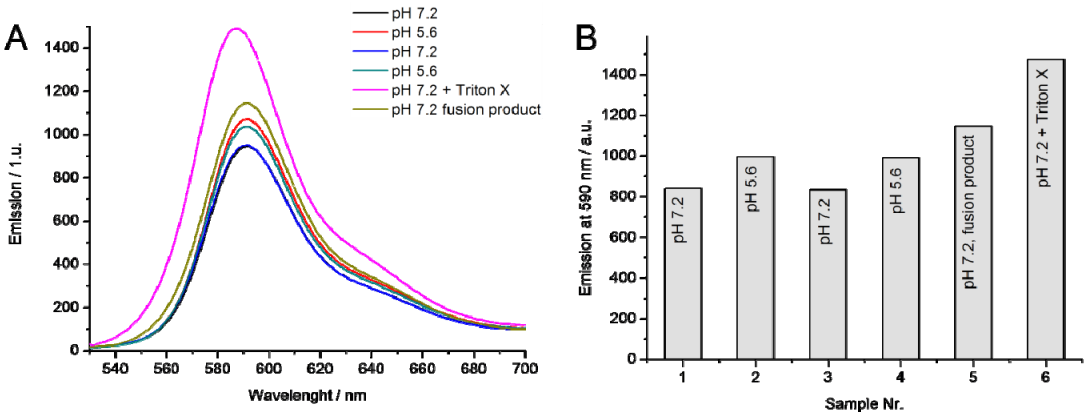



**Fig. S7**; Lipid mixing assay of **(2)** with β-CD vesicles. Emisson spectra (left) and max. emissions at 590 nm (right).