Electronic Supplementary Material (ESI) for ChemComm.


**Supporting Information**

# Light-responsive vesicles for enantioselective release of chiral drugs prepared by supra-amphiphilic *M*-helix

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## 1. General information

Triethylamine (TEA) and dichloromethane ($CH_2Cl_2$) were dried by distillation with $CaH_2$ for one week. Distilled water was polished by ion exchange and filtration. α-CD, β-CD, hydrazine hydrate, (1*S*)-(-)-camphanic chloride and other organic reagents were purchased from commercial vendors and used without further purification. All reactions were monitored by thin layer chromatography (TLC) visualizing with UV light, and column chromatography purifications were performed by using silica gel ($SiO_2$, 200-300 mesh). Characterization instruments: proton nuclear magnetic resonance ($^1$H NMR) spectra and carbon nuclear magnetic resonance ($^{13}$C NMR) spectra were recorded on Bruker AVANCEIII 500. Chemical shifts were reported in ppm relative to the residual solvent peak ($CHCl_3$ = δ 7.26 ppm, DMSO = δ 2.50 ppm for $^1$H NMR spectrum; $CDCl_3$ = δ 77.16 ppm, DMSO-$d_6$ = δ 39.52 ppm for $^{13}$C NMR spectrum). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad singlet). Circular Dichroism (CD) PMS450 from Biologic Company, Ultraviolet-Visible (UV-vis) Absorption Spectrometry UV-2450 from Shimadzu Company, SEM FESEM 6700F from JEOL, TEM JEM-2100F from JEOL, UV (UV-2450) and Fluorescence (5301PC) Spectrometers were from Shimadzu Company, DLS Zetasizer Nano Series equipped with a He–Ne laser (633 nm, 4 mW) and an avalanche photodiode detector is from Malvern Company.

## 2. Figures mentioned in manuscript

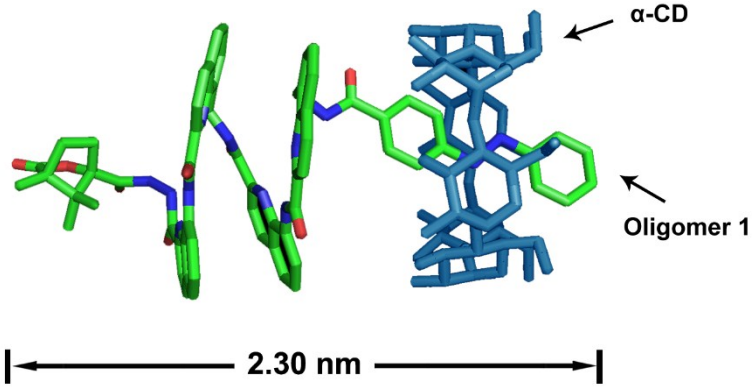



**Figure S1.** Schematic representation of the length of host-guest complex of α-CD⊃**1**.

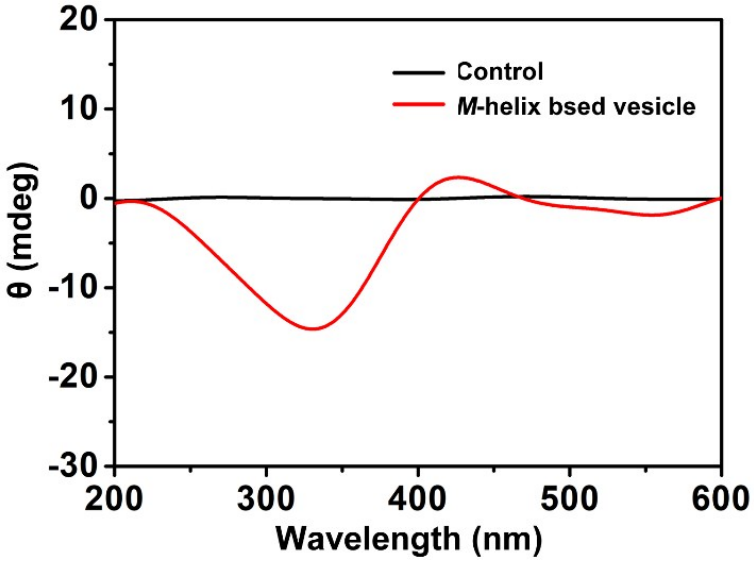



**Figure S2.** CD spectra of the *M*-helix based vesicles in water with obvious negative Cotton effect.

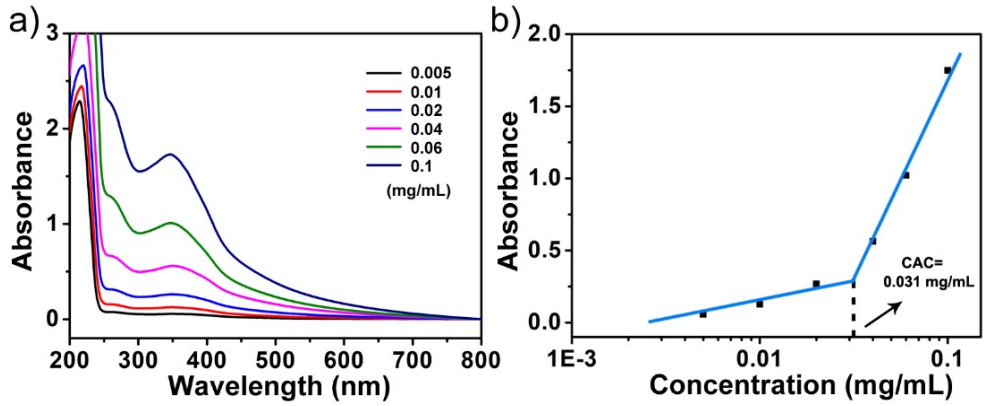



**Figure S3.** a) UV-vis spectra of host-guest complex of α-CD⊃**1** at different concentrations in water. b) The absorbance at 350 nm was adopted to serve as a function of concentration to calculate the CAC of this vesicle.

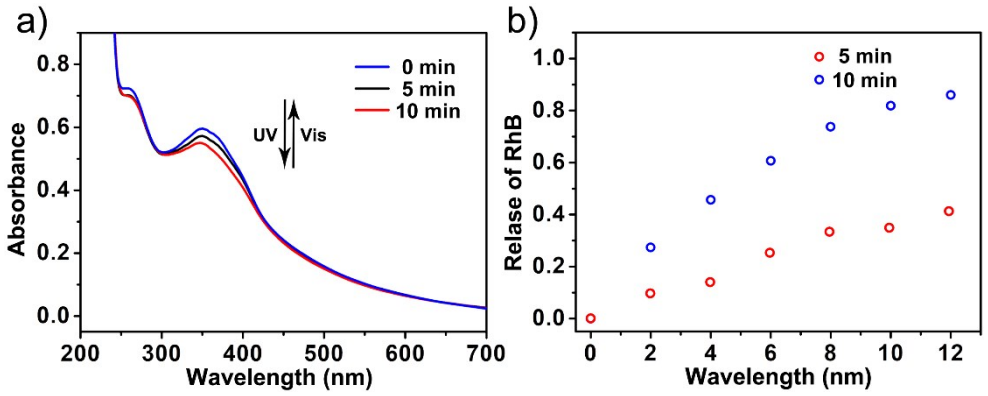



**Figure S4.** a) UV–vis spectra variation of the *M*-helix based vesicles when alternatively exposed to UV and visible light at the concentration of 0.02 mM in water. b) The release behaviors of this *M*-helix based vesicle when irradiated by UV light for 5 and 10 min, respectively.

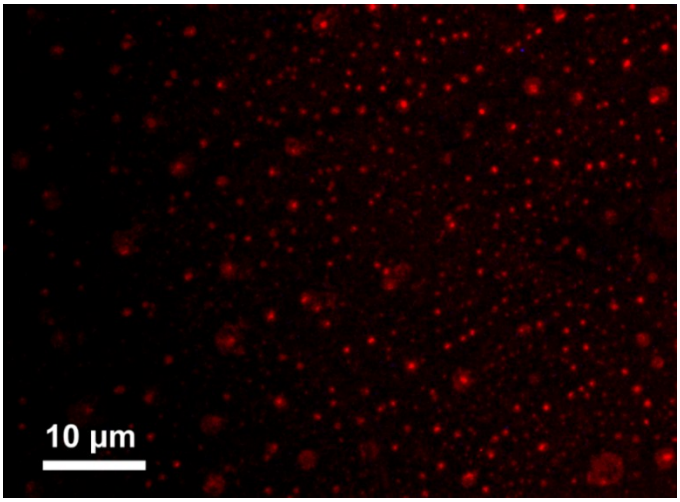



**Figure S5.** Fluorescence image of the RhB-loaded vesicles after sufficient dialysis in water.

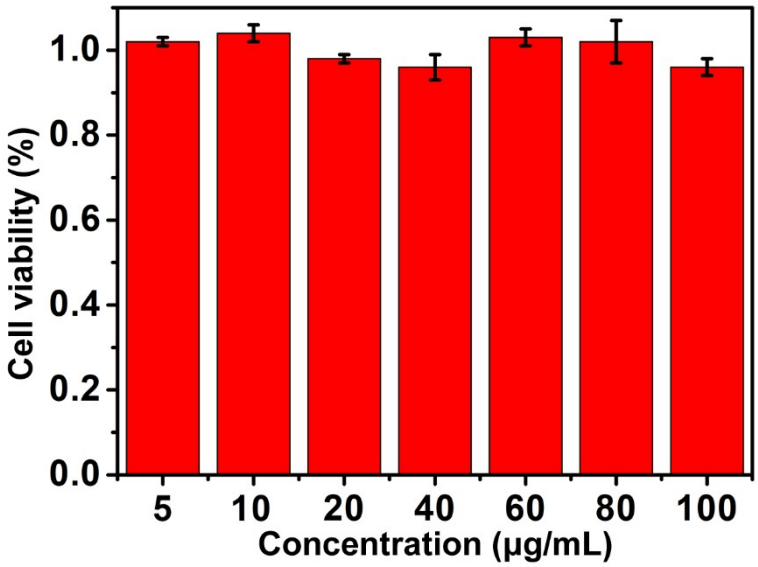



**Figure S6.** MTT assay of 3T3 cell when co-cultured with different concentrations of *M*-helix based vesicles.

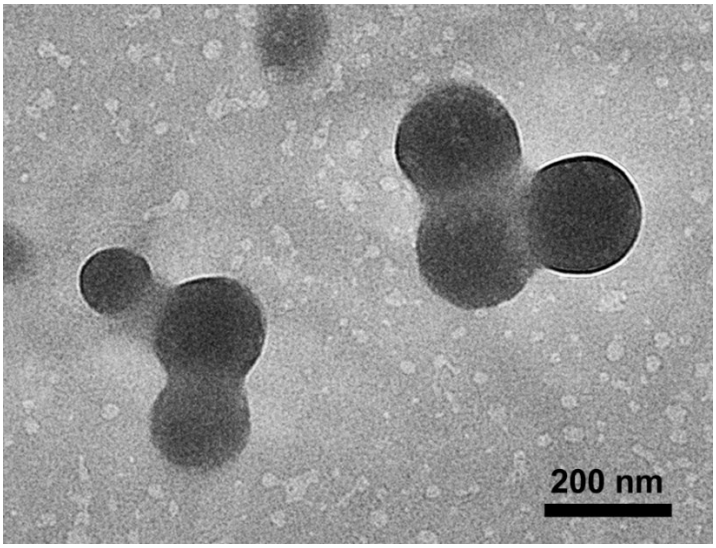



**Figure S7.** TEM image of racemic propranolol loaded vesicles with dark interiors.

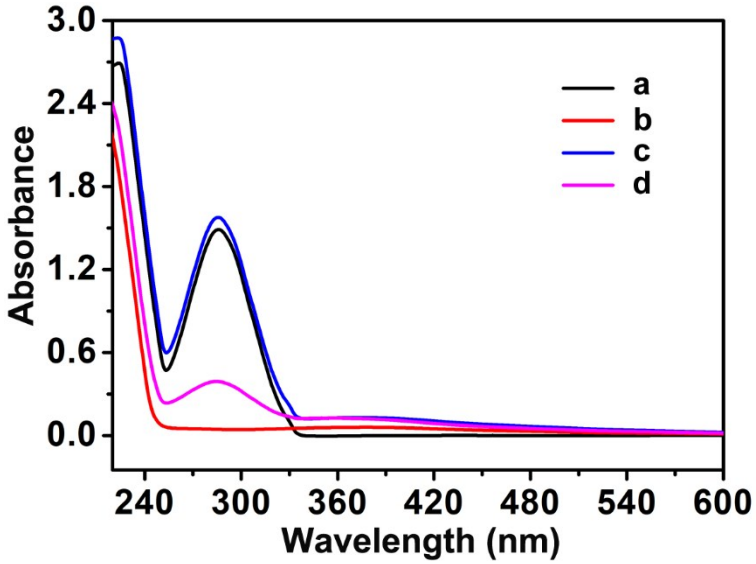



**Figure S8.** UV-vis spectra of free propranolol (**a**), *M*-helix based vesicles (**b**), propranolol-loaded vesicles before (**c**) and after dialysis (**d**) in water.

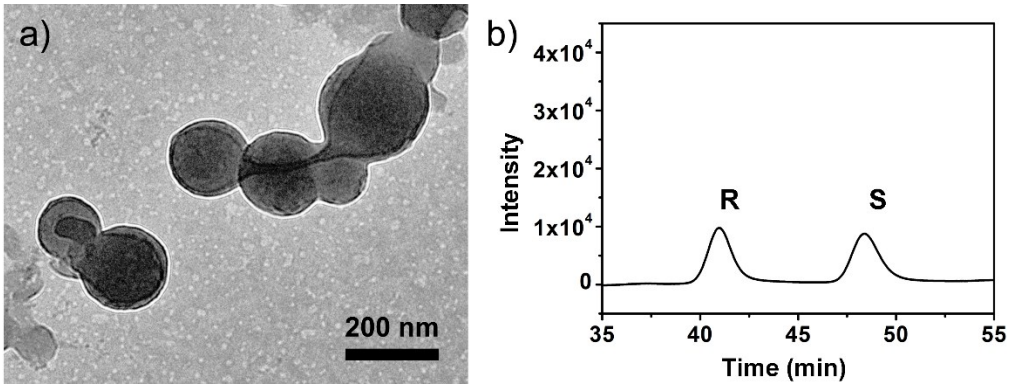



**Figure S9.** a) TEM image of vesicles self-assembled by **2** and α-CD in water. b) Chiral HPLC chromatograms of the released propranolol after 12 hours, which served as a control experiment.

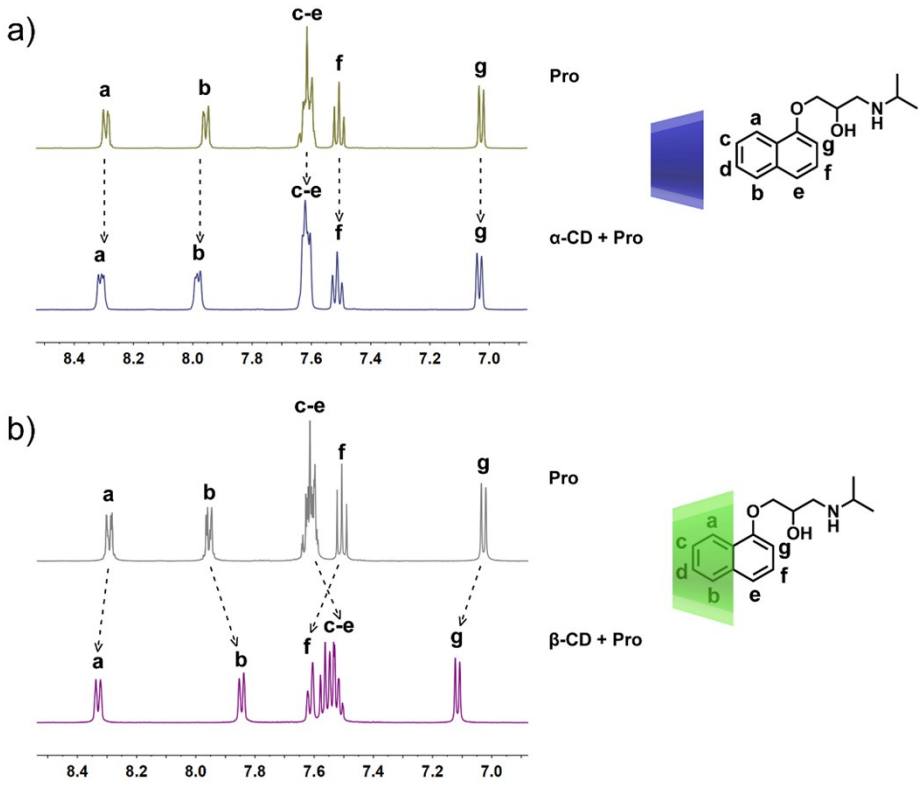
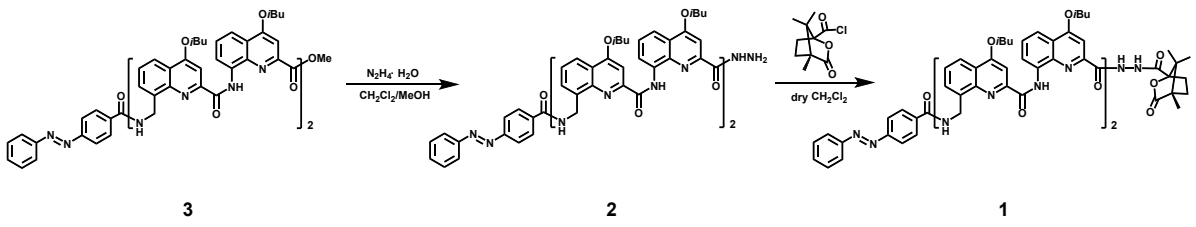



**Figure S10.** a) Partial $^1$H NMR spectra of propranolol (top) and the mixture of α-CD and propranolol in $D_2O$ (down). b) Partial $^1$H NMR spectra of propranolol (top) and host-guest complex of β-CD⊃propranolol in $D_2O$ with obvious shifting of resonance peaks (down).

**3. Preparation procedure of this *M*-helix based vesicle**

First, dissolve 9.7 mg α-CD and 14.2 mg **1** into 1 mL DMF to obtain the supra-amphiphilic building block (α-CD⊃**1**) solution (c = 10 mM). Then, inject the supra-amphiphilic building block solution (10 μL) into 1 mL pure water. After ultrasonic shaking for 15 min and placing at room temperature for 4 hours, the self-assembly solution was sufficiently dialyzed by a dialysis bag (MW 3000 Da) to remove the residual DMF. Finally, we acquired the *M*-helix based vesicles as turbid colloidal solution.

**4. Synthetic procedure and characterization of target molecules**




**Scheme S1**. The synthetic route of oligomer **1**.

Synthesis of oligomer **3**

Oligomer **3** was acquired by previously reported methods and carefully characterized.[1]

Synthesis of oligomer **2**

To a solution of oligomer **3** (200 mg, 0.16 mmol) in 20 mL THF solution was injected 3 mL TEA. Then, a mixed solution of hydrazine hydrate, MeOH, THF (2 mL/2 mL/5 mL) was dropwise added into this reaction medium by a dropping funnel. The reaction of mixture was allowed to proceed for 12 hours at room temperature. After rotary evaporating the solvent, the residue mixture was washed by MeOH to obtain oligomer **2** as yellowish solid (190 mg, 95.0% yield). $^{1}$H NMR (500 MHz, $CDCl_3$, 293K): δ 11.32 (s, 1H), 10.87 (s, 1H), 10.11 (s, 1H), 8.53 (s, 1H), 8.50 (s, 1H), 7.83 (d, *J*(H, H) = 6.6 Hz, 2H), 7.70 (d, *J*(H, H) = 7.9 Hz, 1H), 7.54-7.51 (m, 2H), 7.44-7.40 (m, 2H), 7.34-7.29 (m, 3H), 7.18 (t, *J*(H, H) = 7.2 Hz, 2H), 7.11 (t, *J*(H, H) = 7.4 Hz, 3H), 7.04-7.00 (m, 2H), 6.89 (s, 1H), 6.76 (t, *J*(H, H) = 7.2 Hz, 1H), 6.67 (d, *J*(H, H) = 7.5 Hz, 2H), 6.49 (d, *J*(H, H) = 8.6 Hz, 2H), 6.40 (s, 1H), 5.95 (s, 1H), 5.62 (s, 1H), 5.24 (s, 2H), 4.24 (s, 1H), 4.10 (d, *J*(H, H) = 5.6 Hz, 2H), 3.98 (d, *J*(H, H) = 3.8 Hz, 2H), 3.81 (d, *J*(H, H) = 5.4 Hz, 3H), 3.26 (br, 2H), 2.27-2.05 (m, 4H), 1.76 (br, 1H), 1.19-1.10 (m, 24H). $^{13}$C NMR (500 MHz, $CDCl_3$, 293K): δ 166.51, 165.43, 164.18, 162.17, 161.98, 161.82, 161.18, 152.43, 151.45, 150.55, 150.15, 150.00, 149.73, 148.33, 147.09, 146.17, 144.10, 137.30, 136.63, 133.39, 133.29, 132.70, 132.24, 131.32, 131.02, 130.08, 129.72, 129.24, 129.01, 128.47, 127.60, 126.45, 125.99, 125.31, 123.20, 122.95, 122.71, 122.46, 121.95, 121.47, 121.19, 120.46, 119.91, 118.88, 118.04, 116.30, 116.12, 114.34, 114.07, 112.23, 111.02, 100.08, 99.95, 98.69, 98.30, 97.45, 74.92, 74.70, 44.58, 28.40, 28.09, 19.43, 19.30, 19.23, 19.18. HR-MS (MALDI-TOF): *m/z* calcd for $C_{71}H_{73}N_{12}O_9$ $[M+H]^+$: 1237.5623, Found: 1237.5603.

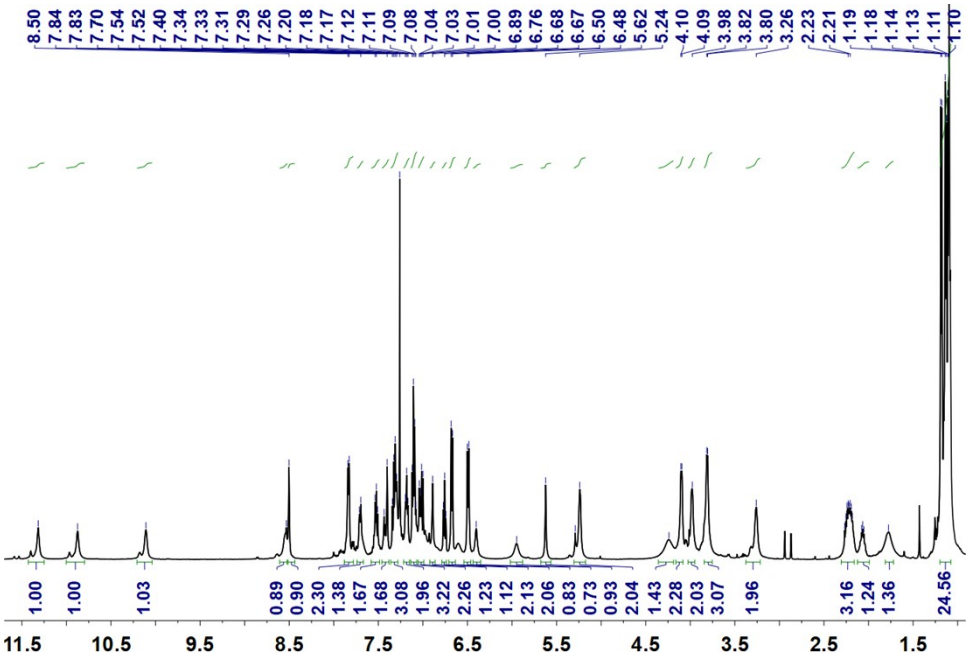



**Figure S11.** $^{1}$H NMR spectrum of oligomer **2** in $CDCl_3$.

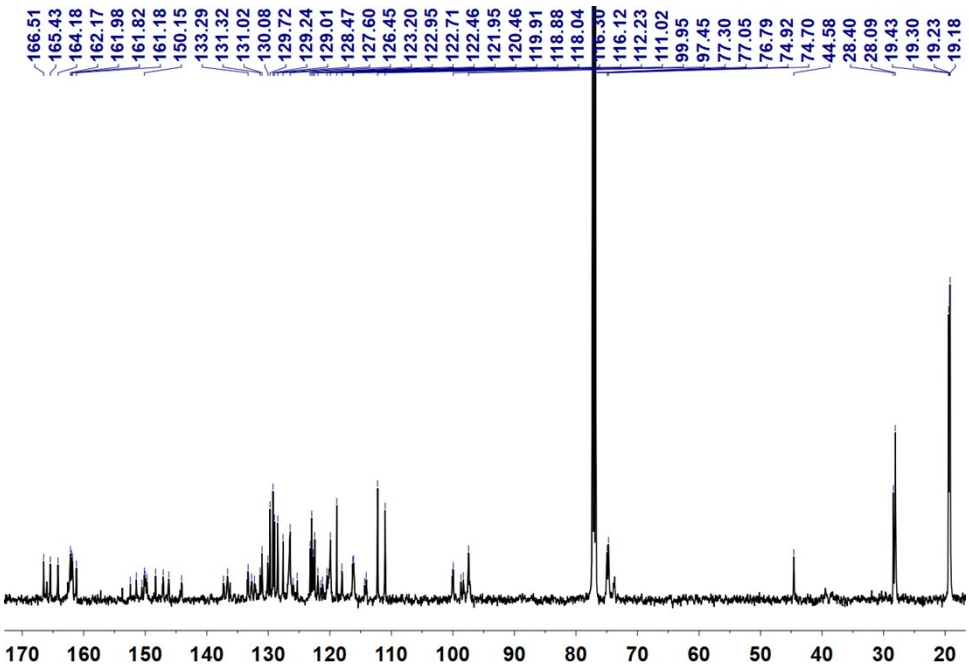



**Figure S12.** $^{13}C$ NMR spectrum of oligomer **2** in $CDCl_3$.

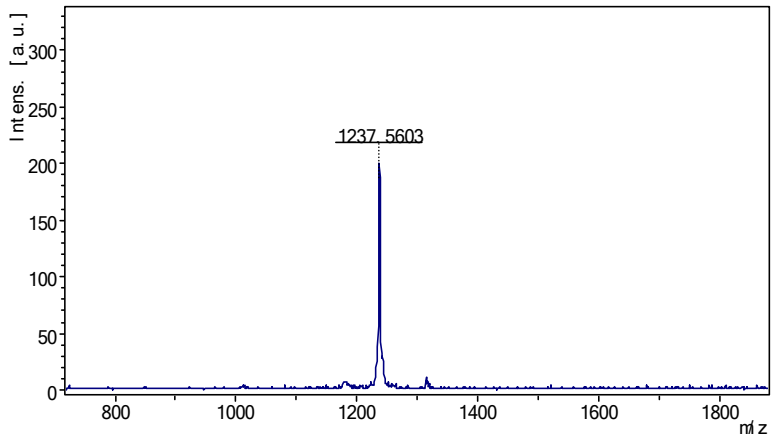



**Figure S13.** HR-MS (MALDI-TOF) spectrum of oligomer **2** in $CH_2Cl_2$.

Synthesis of oligomer **1**

To a mixed solution of oligomer **2** (100 mg, 0.08 mmol) and (1*S*)-(-)-camphanic chloride (34.9 mg, 0.16 mmol) in 10 mL $CH_2Cl_2$ was added 1 mL dry TEA to serve as acid-binding agent by a syringe. The reaction was allowed to proceed for 6 hours at room temperature. Rotary evaporating the solvent and the residues were purified by $SiO_2$ column using $CH_2Cl_2$/MeOH=100:1 as flowing phase. After drying at reduced pressure, we obtained oligomer **1** as yellowish solid (93 mg, 79.2% yield). $^1H$ NMR (500 MHz, $CDCl_3$, 293K): δ 11.46 (s, 1H), 11.06 (s, 1H), 10.48 (s, 1H), 9.15 (s, 1H), 9.00 (s, 1H), 8,95 (d, *J*(H, H) = 7.5 Hz, 1H), 8.03-9.76 (m, 2H), 7.95 (d, *J*(H, H) = 6.8 Hz, 1H), 7.88 (d, *J*(H, H) = 8.3 Hz, 1H), 7.80 (d, *J*(H, H) = 8.2 Hz, 2H), 7.62-7.59 (m, 2H), 7.56 (d, *J*(H, H) = 8.5 Hz, 2H), 7.52-7.49 (m, 4H), 7.34-7.31 (m, 1H), 7.18 (d, *J*(H, H) = 8.2 Hz, 1H), 7.12 (d, *J*(H,

H) = 6.9 Hz, 1H), 7.01 (s, 2H), 6.89 (t, *J*(H, H) = 7.5 Hz, 1H), 6.78 (s, 1H), 4.13-4.11 (m, 4H), 3.84 (d, *J*(H, H) = 5.5 Hz, 2H), 3.58 (d, *J*(H, H) = 6.2 Hz, 2H), 2.31-2.19 (m, 4H), 2.07-2.00 (m, 2H), 1.78 (br, 3H), 1.20-1.26 (m, 37H). $^{13}$C NMR (500 MHz, $CDCl_3$, 293K): δ 177.98, 166.29, 166.04, 165.96, 162.85, 162.78, 162.43, 162.34, 162.12, 162.00, 161.54, 153.74, 152.45, 150.86, 150.68, 149.74, 146.61, 146.47, 144.57, 137.53, 137.15, 136.23, 135.43, 133.43, 133.13, 132.58, 131.34, 131.14, 130.00, 129.03, 127.73, 127.57, 126.72, 126.62, 122.95, 122.48, 122.36, 121.74, 121.03, 120.63, 120.49, 120.37, 118.60, 116.63, 114.60, 100.37, 99.08, 98.11, 97.99, 91.96, 75.27, 75.19, 74.90, 74.31, 55.18, 54.24, 44.51, 39.97, 31.92, 31.53, 30.46, 29.70, 29.38, 28.95, 28.38, 28.30, 28.17, 28.08, 19.43, 19.34, 19.22, 16.65, 16.48, 9.86. HR-MS (MALDI-TOF): *m/z* calcd for $C_{81}H_{85}N_{12}O_{12}$ $[M+H]^+$: 1417.6410, Found: 1417.6406.

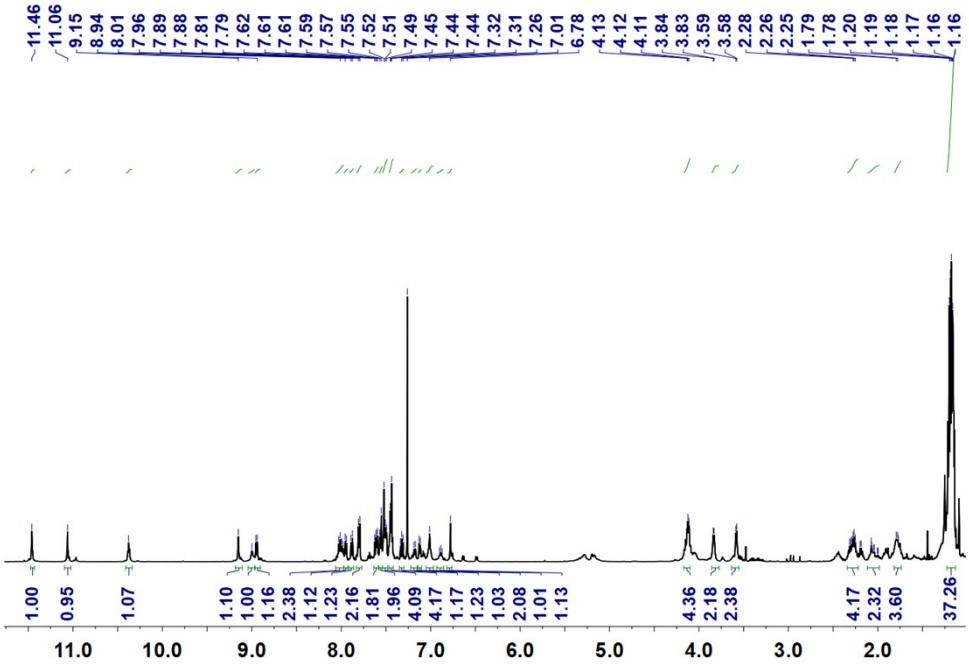



**Figure S14.** $^1$H NMR spectrum of oligomer **1** in $CDCl_3$.

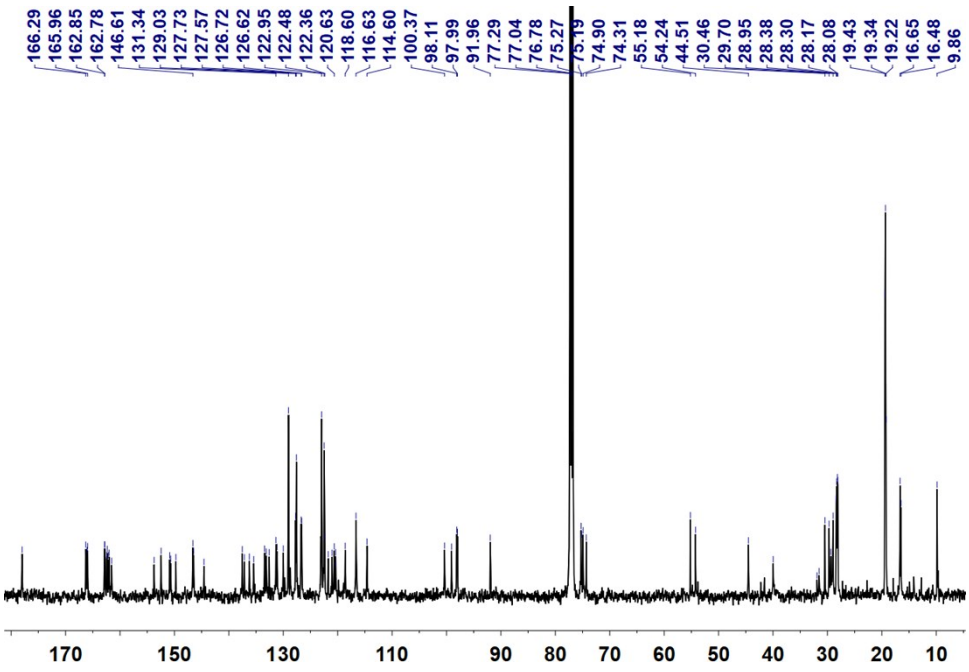



**Figure S15.** $^{13}C$ NMR spectrum of oligomer **1** in $CDCl_3$.

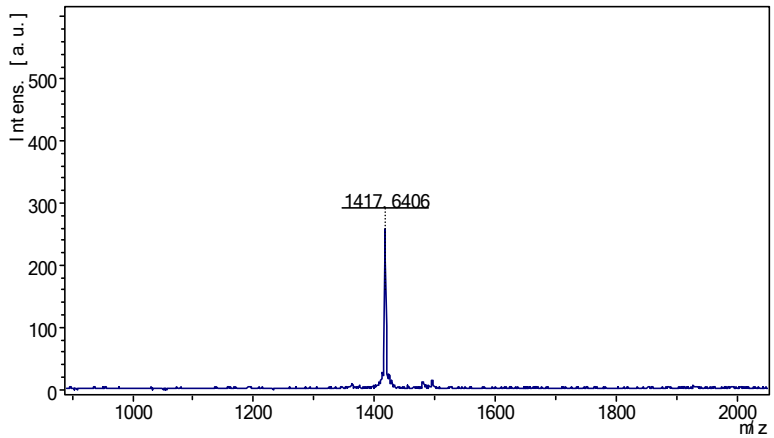



**Figure S16.** HR-MS (MALDI-TOF) spectrum of oligomer **1** in $CH_2Cl_2$.

## 5. References

1. T. Yan, F. Li, J. Tian, L. Wang, Q. Luo, C. Hou, Z. Dong, J. Xu and J. Liu, *ACS Appl. Mater. Interfaces*, 2019, **11**, 30566.