Supporting Information

Two One-Dimensional Arrays of Naphthyl and Anthryl Groups along Peptide Nanotube

Prepared from Cyclic Peptide Comprising α- and β-Amino Acids

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Materials

Scheme 1 Synthetic schemes for CP6.



S2

Boc-β-Ala₂-OMe (3) Boc-β-Ala-OH (1) (1.00 g, 5.29 mmol) and HCl·H-β-Ala-OMe (2) (885 mg, 6.34 mmol) were dissolved in dry dimethylformamide (DMF) under Ar atmosphere at 0 °C. Then dicyclohexyl carbodiimide (DCC) (1.64 g, 7.93 mmol) and hydroxybenzotriazole (HOBt) (1.07 g, 7.93 mmol) were added to the solution. Triethylamine (TEA) (1.62 mL, 11.6 mmol) was added to the mixture and stirred at room temperature for 20 h. After evaporation, ethyl acetate was added to the residue and filtered. The filtrate was exchanged with CHCl₃ and washed with 4% KHSO₄ aq. and saturated NaHCO₃ aq. for three times each. The organic phase was washed with brine, dried over MgSO₄ for 30 min, and filtered. The residue was dissolved in CHCl₃ and purified by a column chromatography (silica gel, eluent: CHCl₃/CH₃OH = 15/1 v/v) to afford the product 6 (1.32 g, 5.39 mmol, 91%).

¹H-NMR (400 MHz, CDCl₃, δ): 1.42 (s, 9H, Boc), 2.37–2.53 (m, 4H, NHCH₂CH₂CO), 3.39–3.52 (m, 4H, NHCH₂CH₂CO), 3.70 (s, 3H, OMe), 5.17 (s, 1H, urethane), 6.19 (s, 1H, amide).

Boc-Ala(nap)-\beta-Ala₂-OMe (7) The Boc group of Boc- β -Ala₂-OMe (3) (200 mg, 729 µmol) was removed by 4 N HCl/dioxane, the solvent was removed in vacuo. HCl·H- β -Ala₂-OMe (5), Boc-Ala(nap)-OH (4) (275 mg, 875 µmol), 2-(1H-7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyl uronium hexafluorophosphate (HATU) (333 mg, 875 µmol) and 1-hydroxy-7-azabenzotriazole (HOAt) (119 mg, 875 µmol) were dissolved in dry DMF and cooled to 0 °C. Then diisopropylethylamine (DIEA) (394 µL, 2.26 mmol) was added to the mixture and stirred at 0 °C for 10 min and at r.t. overnight under Ar atomosphere. After concentration, the residue was dissolved in ethyl acetate and washed with 4% KHSO₄ ag. (three times), saturated NaHCO₃ ag. (three times) and brine and dried over MgSO₄. The residue was

dissolved in CHCl₃ and purified by column chromatography (silica gel, eluent: CHCl₃/MeOH = 10/1 v/v), then concentrated under reduced pressure to afford the product (312 mg, 662 µmol, 90%).

¹H-NMR (400 MHz, CDCl₃, δ): 1.21 (s, 9H, Boc), 2.10-2.25 (m, 4H, NHCH₂CH₂CO), 3.21-3.44 (m, 6H, NHCH₂CH₂CO and naphtylCH₂), 3.67 (s, 3H, OMe), 4.44 (m, 1H, NHCHCO), 5.15 (s, 1H, urethane), 5.83 and 6.58 (s, 2H, amide), 7.45-7.83 (m, 7H, aromatic).

Boc-Ala(anth)-β-Ala₂-OMe (8) The Boc group of Boc-β-Ala₂-OMe (3) (285 mg, 547 µmol) was removed by 4 N HCl/dioxane, the solvent was removed in vacuo. HCl·H-β-Ala₂-OMe (5), Boc-Ala(anth)-OH (6) (239 mg, 656 µmol), HATU (249 mg, 656 µmol) and HOAt (89.3 mg, 656 µmol) were dissolved in dry DMF and cooled to 0 °C. Then DIEA (295 µL, 1.70 mmol) was added to the mixture and stirred at 0 °C for 10 min and at r.t. overnight under Ar atomosphere. After concentration, the residue was dissolved in ethyl acetate and washed with 4% KHSO₄ aq. (three times), saturated NaHCO₃ aq. (three times) and brine and dried over MgSO₄. The residue was dissolved in CHCl₃ and purified by column chromatography (silica gel, eluent: CHCl₃/MeOH = 10/1 v/v), then concentrated under reduced pressure to afford the product (215 mg, 412 µmol, 75%).

¹H-NMR (400 MHz, CDCl₃, δ): 1.37 (s, 9H, Boc), 2.07-2.36 (m, 4H, NHCH₂CH₂CO), 3.22-3.45, 3.32-3.54 (m, 6H, NHCH₂CH₂CO and anthrylCH₂), 3.65 (s, 3H, OMe), 4.42 (m, 1H, NHCHCO), 5.14 (s, 1H, urethane), 5.84 and 6.60 (s, 2H, amide), 7.46-8.34 (m, 9H, aromatic).

Boc-Ala(nap)-β-Ala₂-Ala(anth)-β-Ala₂-OMe (11) Boc-Ala(nap)-β-Ala₂-OMe (7) (233 mg, 495 μmol) was dissolved in methanol (2 ml) and stirred at 0 °C. 1N NaOH aq. (0.5 ml) was added to the solution and stirred at room temperature overnight. After neutralization with 1N HCl aq., the solvent was removed under reduced pressure. The

residue was purified by a Sephadex LH20 column with methanol. The Boc group of Boc-Ala(anth)- β -Ala₂-OMe (8) (215 mg, 412 µmol) was removed by 4 N HCl/dioxane, the solvent was removed in vacuo. Boc-Ala(nap)- β -Ala₂-OH (9), HCl·H-Ala(anth)- β -Ala₂-OMe (10), HATU (235 mg, 619 µmol) and HOAt (67.4 mg, 495 µmol) were dissolved in dry DMF and cooled to 0 °C under Ar atomosphere. Then DIEA (223 µL, 1.28 mmol) was added to the mixture and stirred at 0 °C for 10 min and at r.t. overnight under Ar atomosphere. After concentration, the residue was washed with ethyl acetate to afford the product (142 mg, 164 µmol, 40%).

¹H-NMR (400 MHz, DMSO-*d*₆, δ): 1.21 (s, 9H, Boc), 2.15-3.26 (m, 20H, NHCH₂CH₂CO, COCH₂CH₂CO, naphthylCH₂ and anthrylCH₂), 3.60 (s, 3H, OMe), 4.32 and 4.61 (m, 2H, NHCHCO), 6.5 (s, 1H, urethane), 7.39-8.50 (m, 21H, aromatic and amide).

ESI-MS (*m/z*): [M+H]⁺ calcd for C₄₈H₅₆N₆O₉, 861.4160; found, 861.4182, [M+Na]⁺ calcd, 883.3977; found, 883.4001.

CP6 (12) Boc-Ala(nap)-β-Ala₂-Ala(anth)-β-Ala₂-OMe (11) (100 mg, 116 µmol) was dissolved in methanol (2 ml) and stirred at 0 °C. 1N NaOH aq. (0.5 mL) was added to the solution and stirred at room temperature overnight. After neutralization with 1N HCl aq., the solvent was removed under reduced pressure. The residue was purified by a Sephadex LH20 column with methanol. Then, the Boc group was removed by trifluoroacetic acid (TFA) and anisole, and the solvent was removed under reduced pressure. The residue was washed with diisopropyl ether for two times. TFA·H-ED-SA-β-Ala₂-β-Ala(nap)-OH, HATU (441 mg, 1.16 mmol) and HOAt (237 mg, 1.74 mmol) were dissolved in dry DMF (80 mL) and stirred at 0 °C. DIEA (363 µL, 2.09 mmol) in dry DMF (20 mL) was added dropwise over 1.5 h. Then, the solution was stirred at r.t. for 72 h. After evaporation, the residue was washed with

ethyl acetate (three times), 2,2,2-trifluoroethanol (TFE) (three times), and methanol to afford the product (35 mg, 48.0 μmol, 41%).

¹H-NMR (400 MHz, HFIP-*d*₂/CD₃OD=5/1(v/v) δ): 2.12–2.51 (m, 8H, NH₂CH₂CH₂CO), 3.11–3.69 (m, 10H, NHCH₂CH₂CO, COCH₂CH₂CO, naphthylCH₂ and anthrylCH₂), 4.76, 4.87 (m, 2H, NHCHCO), 7.27–8.39 (m, 16H, aromatic).

ESI-MS (*m/z*): [M+H]⁺ calcd for C₄₂H₄₄N₆O₆, 729.3395; found, 729.3400. [M+Na]⁺ calcd, 751.3215; found, 751.3214.







Figure S2 Configurations of molecular stacking of $L-\alpha-\beta-\beta-D-\alpha-\beta-\beta$ in regard of 6 component amibno-acid types of cyclic hexapeptide. A: parallel stacking, B: flipping the middle cyclic peptide with aligning L- α components and D- α components at the same sides, C: flipping the middle cyclic peptide with alternating alignment of L- α and D- α components, and D: parallel stacking with alternating alignment of L- α and D- α components.



Figure S3 Configurations of molecular stacking of $L-\alpha-\beta-\beta-L-\alpha-\beta-\beta$ in regard of 6 component amibno-acid types of cyclic hexapeptide. A: parallel stacking, B: flipping the middle cyclic peptide with aligning L- α components and the other L- α components at the same sides, C: flipping the middle cyclic peptide with alternating alignment of L- α and the other L- α components, and D: parallel stacking with alternating alignment of L- α and the other L- α components.



Figure S4 Gaussian calculations¹ for the total energy of the dimers in the parallel (blue) and antiparallel (red) staking modes of (a) cyclo(L-Ala $-\beta$ -Ala $-\beta$ -Ala $-\beta$ -Ala $-\beta$ -Ala $-\beta$ -Ala(b) cyclo(Gly $-\beta$ -Ala $-\beta$ -Ala $-\beta$ -Ala-Gly $-\beta$ -Ala $-\beta$ -Ala) and (b) cyclo(Gly $-\beta$ -Ala $-\beta$ -Ala-Gly $-\beta$ -Ala $-\beta$ -Ala). Two cyclic peptides were initially stacked with a full overlap. The top cyclic peptide was rotated from -10 degree to 30 degree by a step of 10 degree.



Figure S5 DLS histogram of CP6 in (a) formic acid and (b) HFIP.



Figure S6 Absorption changes of anthracene (0.01 mM) at 355 nm upon UV-light irradiation in formic acid (red) and HFIP (blue).



Figure S7. Current–voltage (*I-V*) curves of CP6 crystals.



Figure S8 Molecular structures of (a) SL16M and (b) AL16M.

Reference

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