

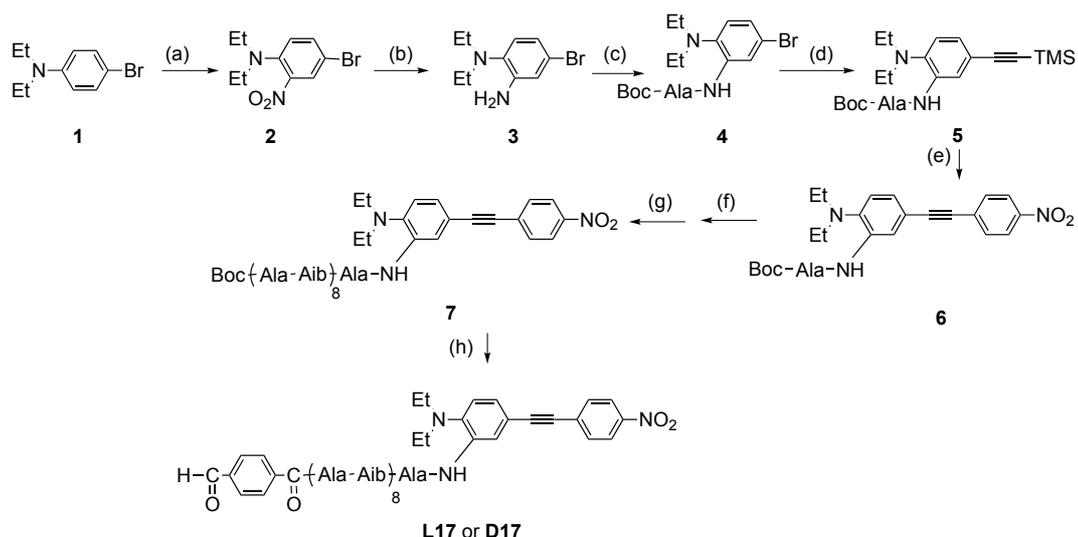
Supporting Information for

**Vertical Orientation with a Narrow Distribution of Helical Peptides
Immobilized on Quartz Substrate by Stereocomplex Formation**

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Scheme S1. Synthetic scheme of **D17** and **L17**: (a) acetic acid, sodium nitrite, water, overnight, (b) tin dichloride, hydrochloric acid, (c) Boc-Ala-OH, 2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU), diisopropylethylamine (DIEA), *N,N*-dimethylformamide (DMF), (d) trimethylsilylacetylene, bis(benzonitrile)palladium(II) dichloride, diisopropylamine, copper(I) iodide, tri(*tert*-butyl)phosphine, 1,4-dioxane, (e) potassium carbonate in methanol and dichloromethane, then 4-nitroiodobenzene, bis(triphenylphosphine)palladium(II) dichloride, DIEA, copper(I) iodide, tetrahydrofuran (f) 4 N hydrochloric acid/dioxane, (g) Boc-(Ala-Aib)₄-OH, HATU, DIEA, DMF, (h) trifluoroacetic acid/anisole with dichloromethane, then 4-formylbenzoic acid, HATU, DIEA, DMF.

Synthesis

D17 and **L17** were both synthesized according to Scheme S1. The following descriptions are synthesis method for **D17**. **L17** were synthesized similarly using L-Ala instead of D-Ala.

4-bromo-2-amino-*N,N*-diethylaniline (2): To a 500 mL round-bottomed flask were added 4-bromo-*N,N*-diethylaniline (**1**, 1.53 g, 6.71 mmol), deionized water (210 mL), and acetic acid (21 mL). To the mixture 20 mL of aqueous solution of sodium nitrite (601 mg, 8.72 mmol) were added dropwise. The mixture was stirred overnight and extracted with dichloromethane (3×) and the organic solution was dried over MgSO₄. The product was purified with column chromatography (silica gel, chloroform/hexane = 1/3). 1.0 g (4.11 mmol, 61% yield) of the desired product was obtained. ¹H NMR (CDCl₃ 400 MHz): δ (ppm) 0.96 (6H, t, (CH₃CH₂)₂N), 2.90 (4H, q, (CH₃CH₂)₂N), 7.01 (1H, d, aromatic), 7.48 (1H, dd, aromatic), 7.79 (1H, d, aromatic). EI-MS: *m/z* = 271.99 (calcd for C₁₀H₁₃O₂N₂Br M⁺, 272.0).

2-amino-4-bromo-*N,N*-diethylaniline (3): To a 100 mL round-bottomed flask were added **2** (1.13 g, 4.1 mmol) and tin(II) chloride dihydrate (3.15 g, 16.55 mmol) in 8 mL of concentrated hydrochloric acid. The mixture was stirred for 30 min and 5 N sodium hydroxide aqueous solution was added until the mixture turned to pH = 10. The mixture was extracted with dichloromethane (3×) and the combined organic layers were washed with brine. The organic layers was then dried over MgSO₄ and concentrated in reduced atmosphere. The residue was purified by column chromatography (silica gel, chloroform/hexane = 1/3 then 1/2). 800 mg (3.31 mmol, 80%) of the desired product was obtained. ¹H NMR (CDCl₃ 400 MHz): δ (ppm) 0.96 (6H, t, (CH₃CH₂)₂N), 2.90 (4H, q, (CH₃CH₂)₂N), 4.14 (2H, s, (NH₂)), 6.78–6.88 (3H, m, aromatic). EI-MS: *m/z* = 242.1 (calcd for C₁₀H₁₅N₂Br M⁺, 242.0).

4: To a 100 mL two-neck round-bottomed flask were added **3** (1.16 g, 4.85 mmol),

Boc-D-Ala-OH (918.25 mg, 4.85 mmol), 2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU) (2.40 g, 6.31 mmol), diisopropylethylamine (DIEA) (1.72 mL, 9.71 mmol) and *N,N*-dimethylformamide (DMF) (7 mL) at 0 °C. The mixture was stirred for 14 hr at room temperature and concentrated in reduced atmosphere. The residue was taken up with ethyl acetate and washed successively with water (1×), 4 wt % aqueous sodium hydrogen carbonate (3×), brine (1×), 4 wt % aqueous potassium hydrogen sulfate, (3×), and brine (1×). The organic layer was dried over anhydrous magnesium sulfate and concentrated in reduced atmosphere. The residue was further purified by column chromatography (silica gel, ethyl acetate/hexane = 1/4). 1.04 g (2.51 mmol, 52%) of the desired product was obtained. ¹H NMR (CDCl₃ 400 MHz): δ (ppm) 0.94 (6H, t, (CH₃CH₂)₂N), 1.44–1.47 (12H, (CH₃)₃C, AlaC^β), 2.90 (4H, q, (CH₃CH₂)₂N), 4.45 (1H, s, AlaC^α), 5.10 (1H, s, Boc-NH), 7.02 (1H, d, aromatic) 7.18 (1H, dd, aromatic), 8.64 (1H, d, aromatic). FAB-MS: *m/z* = 413.13 (calcd for C₁₈H₂₈BrN₃O₃ [M + H]⁺, 414.2).

5: To an oven dried 50 mL two-neck round-bottomed flask were added **4** (1.00 g, 2.41 mmol), bis(benzonitrile)palladium(II) dichloride (37.0 mg, 96.54 μmol), trimethylsilylacetylene (467 μL, 3.38 mmol) copper (I) iodide (13.8 mg, 72 μmol), tri(*tert*-butyl)phosphate (48.8 mg, 241 μmol), diisopropylamine (847 μL, 6.03 mmol) and dry dioxane (1.5 mL). The mixture was stirred under argon atmosphere at 40–45 °C for 1 d. The mixture was concentrated under reduced atmosphere and the residue was purified by column chromatography (silica gel, chloroform) 941 mg (2.35 mmol, 97%) of the desired product was obtained. ¹H NMR (CDCl₃ 400 MHz): δ (ppm) 0.22 (9H, s, (CH₃)₃Si), 0.92 (6H, t, (CH₃CH₂)₂N), 1.44–1.47 (12H, (CH₃)₃C, AlaC^β), 2.90 (4H, q, (CH₃CH₂)₂N), 4.35 (1H, s, AlaC^α), 5.06 (1H, s, Boc-NH-), 7.06 (1H, d, aromatic), 7.17 (1H, d, aromatic), 8.56 (1H, s, aromatic) 9.30 (Ala-NH-Ar). FAB-MS: *m/z* = 432.4 (calcd for C₂₃H₃₈N₃O₃Si [M + H]⁺, 431.3).

6: **5** (941 mg, 2.18 mmol) was treated with potassium carbonate (903 mg, 6.54 mmol) in a mixture of methanol (30 mL) and dichloromethane (30 mL) for 2 hr. The mixture was extracted with dichloromethane (3×) and the organic layer was washed with brine, followed by drying in vacuum. The product was then mixed in an oven dried 50 mL two-neck round-bottomed flask with 4-iodonitrobenzene (1.08 g, 4.34 mmol), bis(triphenylphosphine)palladium(II) dichloride (91 mg, 130 μmol), copper(I) iodide (41 mg, 216 μmol), DIEA (1.45 mL, 8.68 mmol) at 0 °C. The mixture was kept 0 °C and stirred for 1 hr. The mixture was then concentrated under reduced atmosphere followed by purification by column chromatography (silica gel, chloroform/ethyl acetate = 45/1 then 40/1). 580 mg (1.21 mmol, 56%) of the desired product was obtained. ¹H NMR (CDCl₃ 400 MHz): δ (ppm) 0.96 (6H, t, (CH₃CH₂)₂N), 1.44–1.47 (12H, (CH₃)₃C, AlaC^β), 2.96 (4H, q, (CH₃CH₂)₂N), 4.37 (1H, s, AlaC^α), 5.02 (1H, s, Boc-NH-), 7.16 (1H, d, aromatic), 7.27 (1H, d, aromatic), 7.64 (2H, d, aromatic), 8.21 (2H, d, aromatic), 8.67 (1H, d, aromatic), 9.34 (Ala-NH-Ar). FAB-MS: *m/z* = 481.3 (calcd for C₂₆H₃₃N₄O₅ [M + H]⁺, 481.2).

7: The Boc group was deprotected by treatment with 4 N hydrochloric acid/dioxane, followed by washing with diisopropylether. The deprotected product was mixed in a 20 mL round-bottomed flask with Boc-(D-Ala-Aib)₄-OH (420 mg, 307 μmol), HATU (186 mg, 491 μmol), DIEA (241 μL, 1.39 mmol) at 0 °C. The mixture was stirred under argon atmosphere at room temperature for 24 hr. The mixture was concentrated under reduced atmosphere and purified with column chromatography (Sephadex LH-20, methanol), giving 400 mg (290 μmol, 73%). ¹H NMR (CDCl₃ 400 MHz): δ (ppm) 0.93 (6H, t, (CH₃CH₂)₂N), 1.3–1.5 (84H, m, (CH₃)₃C, AlaC^β, AibC^β), 2.99 (4H, q, (CH₃CH₂)₂N), 3.90–4.0 (7H, m, AlaC^α), 4.33 (1H, m, AlaC^α), 4.71 (1H, m, AlaC^α), 5.48 (1H, s, Boc-NH), 6.79 (1H, s, NH), 7.06 (1H, s, NH), 7.27–7.80 (17H, m, NH and aromatic), 8.20 (2H, d, aromatic), 8.51 (1H, s, NH), 9.31 (1H, s, NH). FAB-MS: *m/z* = 1730.1 (calc. for C₈₂H₁₂₉N₂₀O₂₁ [M + H]⁺, 1730.0).

D17. 7 (200 mg, 115 μmol) was treated with trifluoroacetic acid/anisole (2 mL/200 μL) in dichloromethane (1 mL) at 0 °C for 4 hr. Then another trifluoroacetic acid/anisole (1 mL/100 μL) was added and further treated at 0 °C for 3 hr. The mixture was concentrated under reduced atmosphere and washed with diisopropylether. The product was dried in vacuum. Then the product was mixed in a 20 mL two-neck round-bottomed flask with 4-formylbenzoic acid (56 mg, 380 μmol), HATU (239 mg, 630 μmol), DIEA (220 μL , 1.26 mmol) and DMF (1 mL) at 0 °C. The mixture was stirred at room temperature for 28 hr and concentrated under reduced atmosphere. The residue was purified by column chromatography (Sephadex LH-20, methanol) 160 mg (90 μmol , 72%) of the desired product was obtained. Further purification was conducted by a reversed phase HPLC (methanol/water = 9/1) before the product was used for measurements. ^1H NMR (CDCl_3 400 MHz): δ (ppm) 0.95 (6H, t, $(\text{CH}_3\text{CH}_2)_2\text{N}$), 1.3–1.5 (75H, m, AlaC^β , AibC^β), 2.98 (4H, q, $(\text{CH}_3\text{CH}_2)_2\text{N}$), 3.96 (6H, br, AlaC^α), 4.23 (2H, br, AlaC^α), 4.46 (1H, br, AlaC^α), 7.04 (1H, m, aromatic), 7.16 (1H, m, aromatic), 7.3–8.2 (26H, m, NH , aromatic), 9.16 (1H, s, NH), 9.94 (1H, s, CHO). FAB-MS: (HR) m/z = 1761.9301 (calc. for $\text{C}_{85}\text{H}_{125}\text{N}_{20}\text{O}_{21}$ $[\text{M} + \text{H}]^+$, 1761.9328).

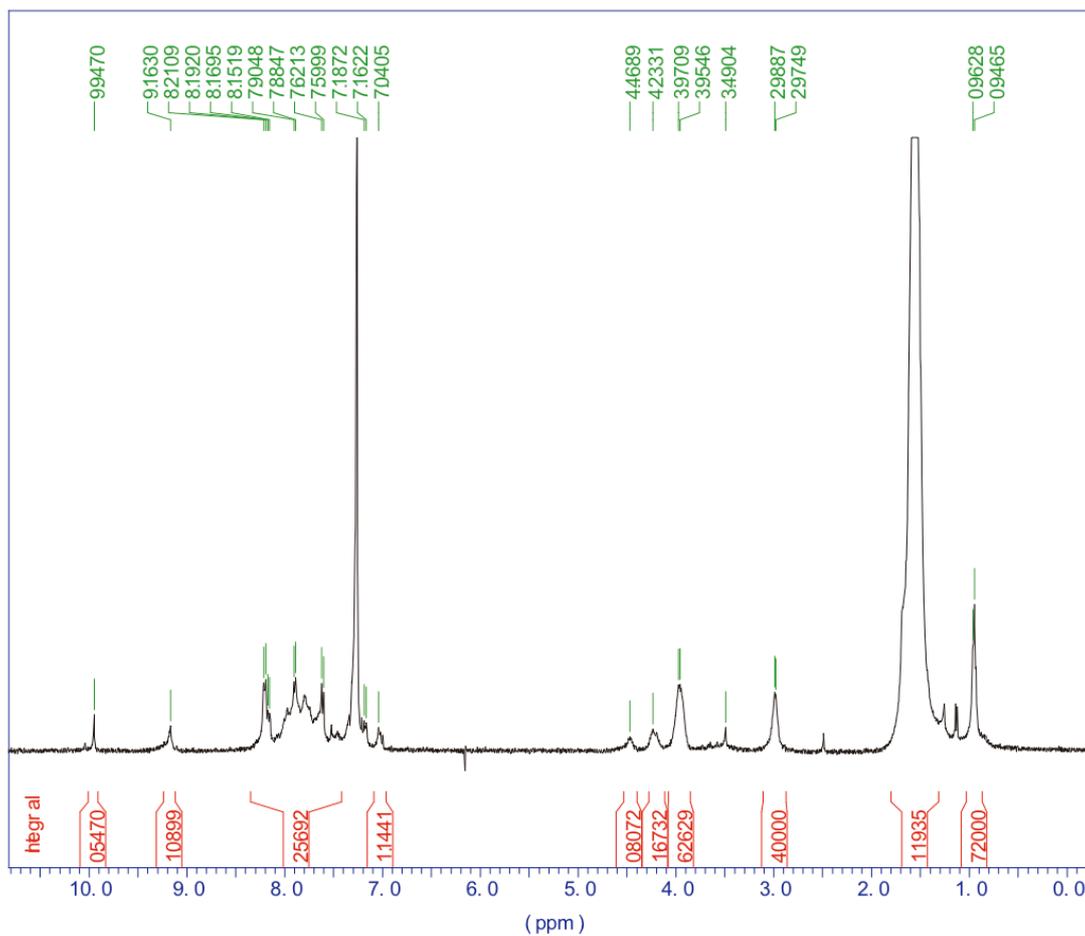


Figure S1. ^1H NMR spectrum of **D17** in chloroform- d_3 .

First principle calculation. DFT calculations on b3lyp/6-31G(d,p) level were performed to reveal how the chirality on the peptide moiety is transferred to the D- π -A moiety. A model geometry **LM** was designed and optimized (Figure S2). In the optimized structure (Figure S2b, c), the two ethyl groups on the nitrogen of the diethylamine group point near to perpendicular way from the benzene ring. This indicates that the wavefunction of the lone pair of the nitrogen does not couple with that of the π -conjugate orbitals of the benzene ring, which results in increase in energy.

The amount of the energy increase induced by the twist was calculated. Another model geometry **D π A** was designed and optimized (Figure S3a, b). In the optimized structure, the two ethyl groups of the diethylamine group point to the parallel way to the plane of the benzene ring, which suggest good coupling between the wavefunction of the lone pair electrons on the diethylamine group and that of π -conjugate electrons on the benzene ring. CD spectrum of the geometry shows little Cotton effect. Change in the energy and Cotton effect when the angle of the diethylamine group respect to the benzene ring was rotated by 30° 60°, and 90° (Figure S3c, d, e) in a right-handed way was estimated (Figure S3f). Decoupling of the two wavefunctions results in the loss of the stabilization energy by ca. 35 kJ mol⁻¹ in maximum. The interference between the diethylamine group and the alanine which is introduced at the *ortho* position of the group must be the reason for the unfavorable conformation of the diethylamine group against the π -conjugate. And, this twist should be the origin of the Cotton effect.

Indeed, the calculated CD spectra well reproduce two important features of the measured spectra. One is large negative Cotton effect at the maximum absorption wavelength of the D- π -A moiety. In the measured spectra, the peak of the negative Cotton effect was at 350 nm, which is the maximum absorption wavelength of the D- π -A moiety. In the calculated spectra, two negative peaks were obtained at around 315 nm and 460 nm, which correspond to the transition from the

HOMO to the LUMO, and that of HOMO – 1 orbital to the LUMO. This inconsistency in the number of peaks is due to large underestimation of energy gap of the HOMO and LUMO in calculations on b3lyp/6-31G(d,p) level. The other feature is a sharp positive Cotton effect at <300 nm. The calculations showed that the absorption bands correspond to the positive Cotton effect are mixture of several transitions. It is thus a right-handed twist between diethylamino group and the π -conjugate backbone is the reason for negative Cotton effect observed from **L17**.

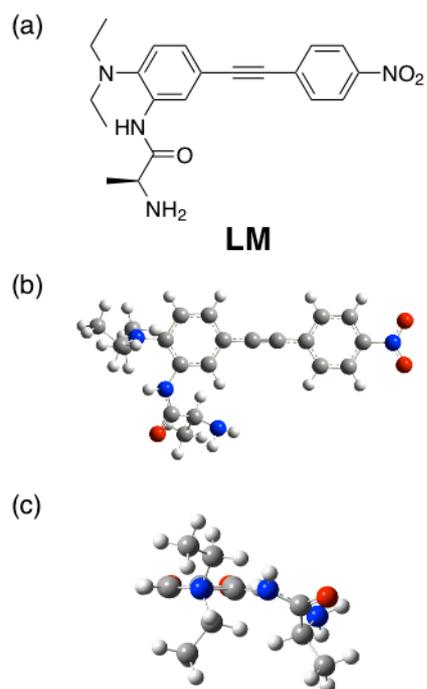


Figure S2. (a) Chemical structure and (b) optimized geometry from top view and (c) from side view of **LM**.

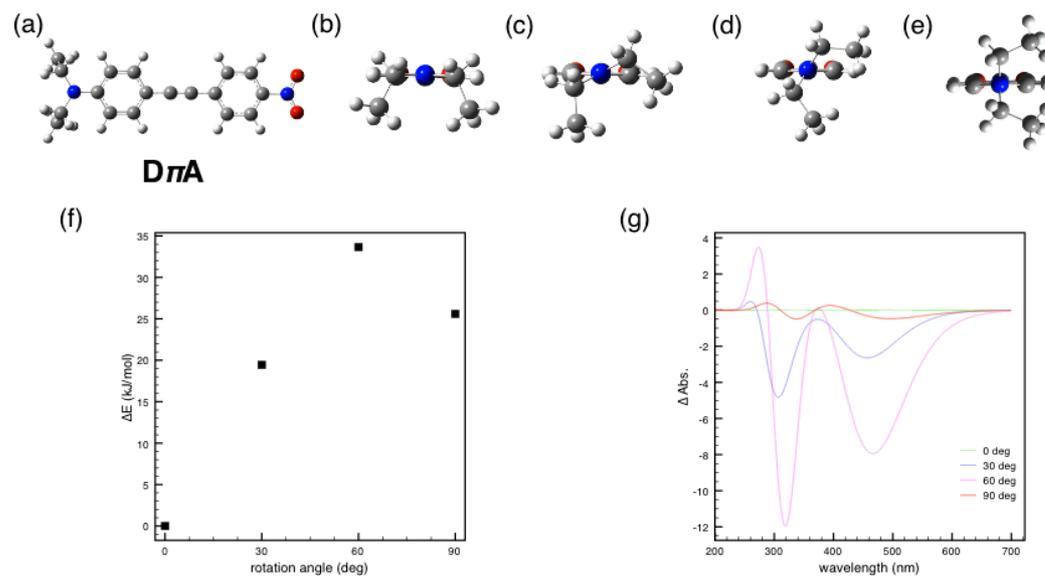


Figure S3. The optimized structure of a geometry **DπA**, (a) top and (b) side view. The diethylamine group was rotated by (c) 30°, (d) 60°, and (e) 90° in right-handed way and TD-DFT calculations were conducted. The relative energy and calculated CD spectrum of the each geometry were shown in panel (f) and (g), respectively.