Supporting Information (SI)

Thermotropic chirality enhancement of nanoparticles constructed from foldamer/bis(amide acid) complexes

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Experimental section

Materials

L-Homocystine and L-cystine were purchased from Energy Chemical Technology Co., Ltd. Chloroform and acetonitrile were available from Sinopharm Chemical Reagent Co., Ltd.

Characterization

Circular dichroism (CD) and ultraviolet-visible (UV–Vis) absorption spectra were taken on a JASCO J-810 spectropolarimeter. The fluorescence spectra were measured on a JASCO FP-6500 spectrofluorescence. Transmission electron microscopy (TEM) images were recorded using a FEI Talos F200X with an acceleration voltage of 200 kV. The samples for TEM observation were prepared by dropping the solution onto a carbon-coated copper grid and dried under vacuum at room temperature for 6 h.

Synthesis of L-Hcy

L-Homocystine (5.0 g, 18.6 mmol) was added to methanol (100 mL) at 0 °C. After stirring for 10 min, a 70% water solution of perchloric acid (5.35 g, 37.3 mmol) was then added to the solution. The resultant mixture was stirred at room temperature overnight and the solvent was concentrated under reduced pressure. The residue was purified by recrystallization from acetonitrile/chloroform (1/19, v/v) to afford L-Hcy as a colorless crystalline solid (3.19 g, 37%). 1H NMR (400 MHz, DMSO-d6, TMS, ppm): δ = 8.27 (s, -CH-NH$_3^+$, 3H), 4.01 (q, J = 5.2 Hz, -CH-NH$_3^+$, 1H), 2.88–2.76 (m, -S-CH$_2$-, 2H), 2.24–2.07 (m, -CH$_2$-CH-, 2H). 13C NMR (100 MHz, DMSO-d6, TMS, ppm): δ = 171.1 (-COOH), 51.3 (-CH-NH$_3^+$), 32.8 (-CH$_2$-CH-), 30.0 (-S-CH$_2$-).
Synthesis of \(\text{L-Cys}\)

The synthesis of \(\text{L-Cys}\) was conducted in the same way as that of \(\text{L-Hcy}\). Yield: 42%. Spectroscopic data of \(\text{L-Cys}\). \(^1\)H NMR (400 MHz, DMSO-\(d_6\), TMS, ppm): \(\delta = 8.75\) (s, -CH-\(\text{NH}_3^+\), 3H), 4.21 (t, \(J = 8.0\) Hz, -CH-\(\text{NH}_3^+\), 1H), 3.39–3.29 (m, -S-\(\text{CH}_2^-\), 2H). \(^{13}\)C NMR (100 MHz, DMSO-\(d_6\), TMS, ppm): \(\delta = 169.7\) (-COOH), 51.7 (-CH-\(\text{NH}_3^+\)), 37.8 (-S-\(\text{CH}_2^-\)).

CD, UV–Vis absorption and fluorescence measurements

In the CD, UV–Vis absorption and fluorescence titrations of Poly-1 with \(\text{L-Hcy}\) and \(\text{L-Cys}\), stock solutions of Poly-1 (2.4 mM) in chloroform and \(\text{L-Hcy}\) and \(\text{L-Cys}\) (48 mM) in acetonitrile were prepared. To 5 mL vessels equipped with a screwcap were added the stock solutions of \(\text{L-Hcy}\) or \(\text{L-Cys}\) (12.5, 25, 50, 62.5, 75, 87.5, 100, 150, 200, 250, 300, 350, 400, and 450 \(\mu\)L), respectively. A 50 \(\mu\)L of the stock solution of Poly-1 was transferred to the vessels, and the resulting solutions were diluted with acetonitrile to keep the Poly-1 concentration at 240 \(\mu\)M. CD, UV–Vis absorption and fluorescence spectra were then measured in the 1 mm quartz cell. The concentration of Poly-1 was calculated on basis of the monomer units.
Supporting data

Fig. S1. (a) Fluorescence ($\lambda_{ex} = 310$ nm), (b) CD (top) and UV–Vis absorption (bottom) spectra of Poly-1 in CHCl$_3$/CH$_3$CN (1/9, v/v) at room temperature. [Poly-1] = 240 μM.

Fig. S2. Peak-differentiation-imitating analysis of fluorescence spectrum for pure Poly-1.

Fig. S3. $^1$H (a) and $^{13}$C NMR (b) spectra of l-Hcy in DMSO-$d_6$ at room temperature.
**Fig. S4.** Plot of absorbance at 342 nm for **Poly-1** versus the concentration ratio of l.-Hcy to Poly-1.

**Fig. S5.** $^1$H NMR spectra of **Poly-1** (a), l.-Hcy (b), and **Poly-1** with 10 equiv l.-Hcy (c) in CDCl$_3$/CD$_3$CN (1/9, v/v) at room temperature. [**Poly-1**] = 240 μM; [L-Leu] = 2.4 mM.

**Fig. S6.** FT-IR spectra of **Poly-1** (top), l.-Hcy (middle), and **Poly-1** with 10 equiv l.-Hcy (bottom) measured at room temperature (KBr tablet).
Fig. S7. Plot of helix content for Poly-1 versus the concentration ratio of \( \text{L-Hcy} \) to Poly-1.

Fig. S8. (a) TEM image and (b) the corresponding histogram of particle size distribution of pure Poly-1 in CHCl\(_3\)/CH\(_3\)CN (1/9, v/v) at room temperature. [Poly-1] = 240 \( \mu \)M.

Fig. S9. TEM images of the mixtures between Poly-1 and \( \text{L-Hcy} \) at a \([\text{L-Hcy}]/[\text{Poly-1}]\) ratio of 40/1 (a) and 60/1 (b) in CHCl\(_3\)/CH\(_3\)CN (1/9, v/v) at room temperature. [Poly-1] = 240 \( \mu \)M.
**Fig. S10.** Plot of average particle size of chiral Poly-1/L-Hcy nanoparticles versus the concentration ratio of L-Hcy to Poly-1.

**Fig. S11.** CD spectrum of Poly-1 complexed with 20 equiv L-Hcy before and after the addition of K⁺ in CHCl₃/CH₃CN (1/9, v/v) at room temperature. [Poly-1] = 240 μM.

**Scheme S1.** Chemical structure of L-Cys.

**Fig. S12.** ¹H (a) and ¹³C NMR (b) spectra of L-Cys in DMSO-d₆ at room temperature.
Fig. S13. Photographs (a) and UV–Vis absorption spectra (b) of Poly-1 in the presence of l-Cys in CHCl₃/CH₃CN (1/9, v/v) at room temperature. [Poly-1] = 240 μM. (c) Plot of absorbance at 342 nm for Poly-1 versus the concentration ratio of l-Cys to Poly-1.

Fig. S14. TEM images and the corresponding histograms of particle size distribution of the mixtures between Poly-1 and l-Cys at a [l-Cys]/[Poly-1] ratio of 35/1 (a, c) and 180/1 (b, d) in CHCl₃/CH₃CN (1/9, v/v) at room temperature. [Poly-1] = 240 μM.
Fig. S15. (a) Fluorescence spectra of Poly-1 in the presence of L-Cys in CHCl₃/CH₂CN (1/9, v/v) at room temperature. [Poly-1] = 240 μM; λₑₓ = 310 nm. (b) Plot of helix content for Poly-1 versus the concentration ratio of L-Cys to Poly-1.

Fig. S16. CD spectra of pure L-Cys (a) and Poly-1 in the presence of L-Cys (b, c) in CHCl₃/CH₂CN (1/9, v/v) at room temperature. [Poly-1] = 240 μM. (d) Plot of CD intensity of the 1st Cotton effect for Poly-1 versus the concentration ratio of L-Cys to Poly-1.
Scheme S2. Illustrative formation mechanism of chiral Poly-1/L-Cys complexes.

Fig. S17. Photographs of Poly-1 in the presence of 40 equiv L-Hcy in CHCl₃/CH₃CN (1/9, v/v) when heated from 20 to 50 °C and then cooled to 20 °C. [Poly-1] = 240 µM.

Fig. S18. CD (top) and UV–Vis absorption (bottom) spectra of Poly-1 complexed with L-Hcy at a [L-Hcy]/[Poly-1] ratio of 5/1 (a), 10/1 (b) and 20/1 (c) in CHCl₃/CH₃CN (1/9, v/v) at different temperature. [Poly-1] = 240 µM.
Fig. S19. Fluorescence spectra of Poly-1 complexed with l-Hcy at a [l-Hcy]/[Poly-1] ratio of 5/1 (a), 10/1 (b), 20/1 (c), 25/1 (d), 30/1 (e) and 35/1 (f) in CHCl$_3$/CH$_3$CN (1/9, v/v) at different temperature. [Poly-1] = 240 µM; $\lambda_{ex} = 310$ nm.
Fig. S20. Plots of helix content for Poly-1 complexed with l-Hcy at a [l-Hcy]/[Poly-1] ratio of 20/1 (a) 25/1 (b), 30/1 (c) and 35/1 (d) versus temperature.
Fig. S21. CD spectral changes of Poly-1 complexed with l-Hcy at a [l-Hcy]/[Poly-1] ratio of 25/1 (a), 30/1 (b) and 35/1 (c) in CHCl₃/CH₃CN (1/9, v/v) during the cooling process. [Poly-1] = 240 μM. (d) Plots of CD intensity of the 1st Cotton effect for Poly-1 with different content of l-Hcy versus the temperature.

Scheme S3. Illustrative mechanism of thermotropic chirality decrease of Poly-1/l-Hcy nanoparticles at the [l-Hcy]/[Poly-1] ratios of 5/1 and 10/1.