Double helix formation of poly(m-phenylene)s bearing achiral oligo(ethylene oxide) pendants and transformation into an excess one-handed single helix through cholate binding in water

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1. Instruments

The solution pH was measured with a B-211 pH meter (Horiba, Japan) or a GST-5428S pH meter (DKK-TOA, Tokyo, Japan). The NMR spectra were taken on a Varian UNITY INOVA-500S spectrometer operating at 500 MHz for $^1$H and 125 MHz for $^{13}$C. Chemical shifts are reported in parts per million ($\delta$) downfield from tetramethylsilane (TMS) as the internal standard in CDCl$_3$, and from acetone dissolved in D$_2$O. The DOSY experiments were carried out by using pulsed field gradient with the BPPSTE pulse sequence. The electron spray ionization mass spectra (ESI-MS) were recorded on a JEOL JMS-T100CS spectrometer (Akishima, Japan). The matrix-assisted laser desorption-ionization time-of-flight mass spectra (MALDI-TOF-MS) were measured using a Shimadzu AXIMA-CFR Plus spectrometer (Kyoto, Japan). The elemental analyses were performed by the laboratory of elemental analyses in the Department of Agriculture, Nagoya University. The IR spectra were recorded using a JASCO Fourier Transform IR-680 spectrophotometer (Hachioji, Japan). The absorption and CD spectra were measured in a 1 mm quartz cell on a JASCO V-570 spectrophotometer and a JASCO J-820 spectropolarimeter, respectively. The temperature was controlled by a JASCO PTC-423L apparatus (–10 to 90 °C). The dynamic light scattering (DLS) measurements were performed using an Otsuka Photol DLS-7070YN spectrometer equipped with a 10mW He-Ne laser (632.8 nm).

References

2. Molecular Modeling and Calculations

The molecular modeling and molecular mechanics calculations were performed using the Compass Force Field as implemented in the Materials Studio software (version 4.0; Accerlys Software Inc.). The single-stranded helical structure of 5-methoxy-$m$-phenylene 30-mer (PMP$_{30}$) as a model of P1$_{11}$ and the inclusion complex of PMP$_{30}$ and sodium cholate (2) were constructed using Materials Visualizer in the Materials Studio. The parameter, “relative electric” was set to 4 which is the recommended value for the calculations in water. The energy minimization of PMP$_{30}$ and the inclusion complex of PMP$_{30}$ with 2 was performed using the Smart Minimizer of the Discover module until the root-mean-square value became less than 0.1 kcal·mol$^{-1}$.

3. Materials
All starting materials and dehydrated solvents were purchased from Aldrich, Wako Pure Chemical Industries (Osaka, Japan), and Tokyo Kasei Kogyo (TCI) (Tokyo, Japan) unless otherwise noted. Triethylamine (NEt₃) was distilled over CaH₂ under Ar after being stirred with KOH pellets overnight under Ar. The distilled water and D₂O (99.9 atom %D) purchased from Wako and Cambridge Isotope Laboratories (Andover, MA, USA), respectively, were degassed with Ar and used throughout all the experiments. Silica gel (SiO₂) and aminopropyl-modified silica gel (NH-SiO₂) for the flash chromatography were purchased from Merck and Fuji Silysia Chemical Ltd. (Kasugai, Japan), respectively.

4. Synthesis of Poly(m-phenylene)s

3,5-Dibromo-(2-(2-(2-(2-methoxyethoxy)ethoxy)ethoxy)ethoxy)benzene (1): To a solution of 3,5-dibromophenol (5.49 g, 21.8 mmol), tetraethylene glycol monomethyl ether (5.00 g, 24.0 mmol), and PPh₃ (6.25 g, 23.8 mmol) in dehydrated THF (200 mL) was added dropwise a solution of diisopropyl azodicarboxylate (4.81 g, 23.8 mmol) in THF (125 mL) over 30 min with a water bath (ca. 20 °C), and the mixture was stirred at ambient temperature for 1 day. After evaporation, EtOAc was added to the dried residue, and then the EtOAc-insoluble fraction was removed by Celite® filtration. After the filtrate was concentrated in vacuo, the residue was purified by SiO₂ chromatography (n-hexane/EtOAc (1/1, v/v)) to afford 1 as a slightly yellow oil (6.83 g, 15.4 mmol, 70.6% yield). IR (neat, cm⁻¹): 2873, 1584, 1557, 1437, 1419, 1257, 1108, 1056, 955, 832, 742, 669. 

¹H NMR (CDCl₃): δ 3.37 (s, OCH₃, 3H), 3.83 (m, CH₂, 2H), 3.6–3.8 (m, CH₂, 10H), 3.83 (t, J = 4.8 Hz, CH₂, 2H), 3.83 (t, J = 4.8 Hz, CH₂, 2H), 7.01 (d, J = 1.5 Hz, Ar-H₂ and 6, 2H), 7.24 (t, J = 1.5 Hz, Ar-H₄, 1H). ¹³C NMR (CDCl₃): δ 59.02, 68.10, 69.41, 70.52, 70.62, 70.64, 70.90, 71.94, 117.13, 123.03, 126.57, 160.00. ESI-MS (CH₃OH, positive): Calcd for C₁₅H₂₂Br₂O₅Na [1+Na]⁺: m/z = 464.97. Found: m/z = 464.92. Elemental Anal. Calcd for C₁₅H₂₂Br₂O₅: C, 40.75; H, 5.02. Found: C, 40.75; H, 5.06.

Polymerization of Monomer (1) with Ni(0) Complex: To a solution of bis(1,5-cyclooctadiene)nickel(0) (Ni(cod)₂) (1.20 g, 4.36 mmol) and 2,2’-bipyridyl (680 mg, 4.35 mmol) in dehydrated DMF (2.4 mL) was added 1,5-cyclooctadiene (cod) (0.51 mL, 4.16 mmol), and the mixture was aged at 80 °C for 1 h. To the resultant purple nickel solution was added 1 (530 mg, 1.20 mmol), and the mixture was stirred at 80 °C overnight to obtain a deep purple suspension. After cooling to room temperature, conc. HCl aq. was added to the mixture until it turned to a green clear solution. After neutralization with NEt₃, the volatile components were completely removed in vacuo. THF was added to the dried residue, and then the THF-insoluble fraction was removed by
Celite® filtration. After the filtrate was concentrated in vacuo, the residue was purified by chromatography (NH-SiO₂, MeOH) to obtain P₁ as a slightly brown oil (340 mg, 1.20 mmol, quant.). The P₁ was subjected to recycling SEC to afford a high molecular weight part, P₁_H (76 mg, 0.268 mmol, 22.3% yield; $M_n = 1.51 \times 10^4$, $DP_n = 53$, $M_w/M_n = 1.46$) and a low molecular weight part, P₁_L (255 mg, 0.903 mmol, 75.3% yield; $M_n = 0.32 \times 10^4$, $DP_n = 11$, $M_w/M_n = 1.06$).

P₁_H: IR (neat, cm⁻¹): 2873, 1582, 1455, 1387, 1193, 1105, 849. ¹H NMR (CDCl₃): δ 3.32 (s, OCH₃, 3H), 3.50 (t, $J = 4.5$ Hz, CH₂, 2H), 3.60 (t, $J = 4.5$ Hz, CH₂, 2H), 3.63 (d, $J = 4.5$ Hz, CH₂, 2H), 3.65 (t, $J = 4.5$ Hz, CH₂, 2H), 3.68 (t, $J = 4.5$ Hz, CH₂, 2H), 3.75 (t, $J = 4.5$ Hz, CH₂, 2H), 3.92 (t, $J = 4.5$ Hz, CH₂, 2H), 4.27 (t, $J = 4.5$ Hz, CH₂, 2H), 7.20 (s, Ar-H₄ and 6, 2H), 7.45 (s, Ar-H₃, 1H). ¹³C NMR (CDCl₃): δ 58.97, 67.76, 69.77, 70.47, 70.59, 70.83, 71.88, 112.96, 119.06, 142.99, 159.54. Elemental Anal. Calcd for (C₁₅H₂₂O₅)n: C, 63.81; H, 7.85. Found: C, 63.71; H, 7.85.
**Fig. S1.** SEC profiles of P1s before and after fractionation (A) and $^1$H NMR (B), MALDI-TOF-MS (C), and ESI-MS (D) spectra of P1_H and P1_L.
5. Investigation of Single- and Double-stranded Helix Formation of P1$_H$

5-1. Solvent Effect

Fig. S2. $^1$H NMR (A) and absorption (B) spectra of P1$_H$ in CDCl$_3$, CD$_3$OD, and D$_2$O at 25 °C; [P1$_H$] = 1 mM unit$^{-1}$. Plots of the chemical shifts of Ar-H$_2$ (blue circles), Ar-H$_{4,6}$ (green circles), and the pendant methyl group (red circles) (C) and the molar absorptivities ($\epsilon_{\text{max}}$, black full circles) and the wavelengths ($\lambda_{\text{max}}$, black open circles) at ca. 300 nm (D) of P1$_H$ in various solvent mixtures.
5-2. DLS Measurements

Fig. S3. Histogram analysis of DLS measurement of \( \text{P1}_{\scriptscriptstyle \text{II}} \) in \( \text{H}_2\text{O} \) (2.9 mM / unit\(^{-1}\)) at ca. 25 °C.
6. Inclusion Complexation of $\text{P1}_{\text{H}}$ with 2

6-1. Titration Experiment of 2 to $\text{P1}_{\text{H}}$

**Fig. S4.** Plots of the molar absorptivities at 300 nm ($\varepsilon_{300}$) of $\text{P1}_{\text{H}}$ upon the addition of 2 in H$_2$O (pH = 6.1–6.5) at 25 °C. $[\text{P1}_{\text{H}}] = 0.2$ mM (5 unit$^{-1}$) and [2] = 0–69 mM. The solid line in the UV titration curve represents the nonlinear curve fitting result.

\[ K_a = 75 \pm 8 \text{ M}^{-1} \text{ (/5 units)} \]
\[ R = 0.998 \]
6-2. Temperature Effect of 2-P1H Complex

**Fig. S5.** (A) Changes in the CD and absorption spectra of P1H with 2 in H2O (pH = 6.1) at various temperatures (5–75 °C). [P1H] = 1 mM unit⁻¹ and [2] = 69 mM. (B) Plots of the molar circular dichroisms at 264 nm (Δε₂₆₄) and the molar absorptivities at 300 nm (ε₃₀₀) against temperature.
**6-3. 2D NMR Analyses**

**Fig. S6.** Full (A) and partial (B) NOESY spectra of \( \text{P1}_H \) with 2 in D\(_2\)O (pD = 6.5) at 25 °C. [\( \text{P1}_H \)] = 60 mM unit\(^{-1}\), [2] = 1 mM, and mixing time = 0.3 s.
Table S1. Diffusion Coefficients ($D$) of $\text{P1}_\text{H}$, $2$, and Their Complexes in D$_2$O at 25 °C.

<table>
<thead>
<tr>
<th>system</th>
<th>concentration (mM)</th>
<th>$D$ ($10^{-10}$ m$^2$ s$^{-1}$)</th>
<th>$\text{P1}_\text{H}$</th>
<th>Guest</th>
<th>water</th>
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</thead>
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<tr>
<td>$\text{P1}_\text{H}$</td>
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<td>–</td>
<td>18.8</td>
<td></td>
</tr>
<tr>
<td>$2$</td>
<td>1</td>
<td>–</td>
<td>4.29</td>
<td>20.4</td>
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<tr>
<td>$\text{P1}_\text{H}/2$</td>
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<td>1.68</td>
<td>18.2</td>
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</table>

$^a \eta$(H$_2$O) = 0.895 mPa·s.