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PAPER

Formation of higher-order structures of chiral poly(ethynylpyridine)s depending on size, temperature, and saccharide recognition†

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Amphiphilic 2,6-pyridylene ethynylene "*meta*-ethynylpyridine" polymers having chiral oligo (oxyethylene) side chains were developed as hosts for saccharide recognition. The polymers were prepared *via* a Sonogashira reaction and fractionated by gel permeation chromatography (GPC). They showed circular dichroism (CD) activity due to their higher-order chiral helical structures, and their CD and UV-vis spectra changed depending on not only saccharide recognition but also molecular size, temperature, and metal cation recognition.

Introduction

A variety of biopolymers such as nucleic acids, proteins, and polysaccharides performs molecular recognition based on their higher-order structure. In the field of supramolecular chemistry, many kinds of synthetic polymers have been studied for the molecular recognition abilities based on their architecture.[1,2]

Recently, our group has been interested in the development of synthetic hosts responsive to saccharide recognition,[3] especially under aqueous conditions.[4–7] During the course of our study on 2,6-pyridylene ethynylene "*meta*-ethynylpyridine" polymers and oligomers,[7,8] we have developed polymer **1** having octaethylene glycol chains (Fig. 1). This water-soluble polymer spontaneously forms a helix in polar solvents and could associate with monosaccharides in aqueous MeOH by accommodating the guests within the cavity of the helix.[7]

As the next step, we designed chiral polymers **2R** and **2S**, which have a chiral side chain at the 4-positions of their pyridine rings (Fig. 1). We expected that repeating chiral centers would stabilize the higher-order chiral helical structure,[9–11] improving recognition ability. Herein we would like to report the preparation of the chiral polymers **2R** and **2S**, which showed CD-response to saccharide recognition in an aqueous solution. Furthermore, CD-response was also observed depending on molecular size, temperature, and association with metal ions.

For recognizing oligosaccharide guests, oligomeric architectures have been applied to the design of host molecules.[5] In reverse, polysaccharides which spontaneously form helical structures have been reported to play a role as a host molecule to form an inclusion complex with synthetic polymer as a guest.[12]

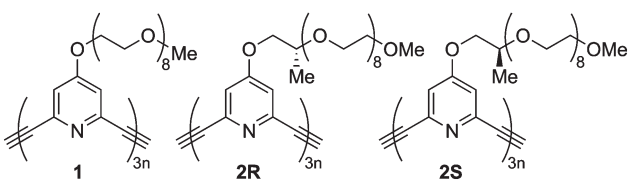

Fig. 1 Water-soluble ethynylpyridine polymers **1**, **2R**, and **2S**.

Results and discussion

Chiral polymer **2R** was prepared as shown in Scheme 1. Ring-opening reductive condensation of (*R*)-propylene oxide (**3R**) with benzaldehyde yielded (*R*)-2-benzyloxy-1-methylethanol (**4R**).[13] This alcohol was coupled with tosylated octaethylene glycol monomethyl ether to **5R**, and the benzyl group was removed to give elongated chiral alcohol **6R**. The alcohol **6R** was condensed with 2,6-diiodo-4-pyridinol (**7**)[7b] to afford **8R**, which was diethynylated to yield **10R** by the Sonogashira reaction with *tert*-butyldimethylsilylacetylene followed by protiodesilylation. The diacetylene **10R** was subjected to reaction with an excess of the diiodide **8R**, and the resulting trimeric diiodide **11R** was diethynylated to **13R**. Finally, co-polymerization of **11R** and **13R** by the Sonogashira reaction under aqueous conditions yielded *R*-polymer **2R**. As well as **1**,[7] **2R** was soluble in various apolar and polar solvents including water. The product of the co-polymerization was separated into four fractions **2R(1)–2R(4)** by gel permeation chromatography (GPC). The average molecular weights M_n for **2R(1)–2R(4)** were estimated as 18 100, 23 300, 29 000, and 36 500 g mol^{-1} *versus* polystyrene standards, respectively. The M_n value for **2R(4)** corresponds to an approximately 67-mer of pyridylene ethynylene

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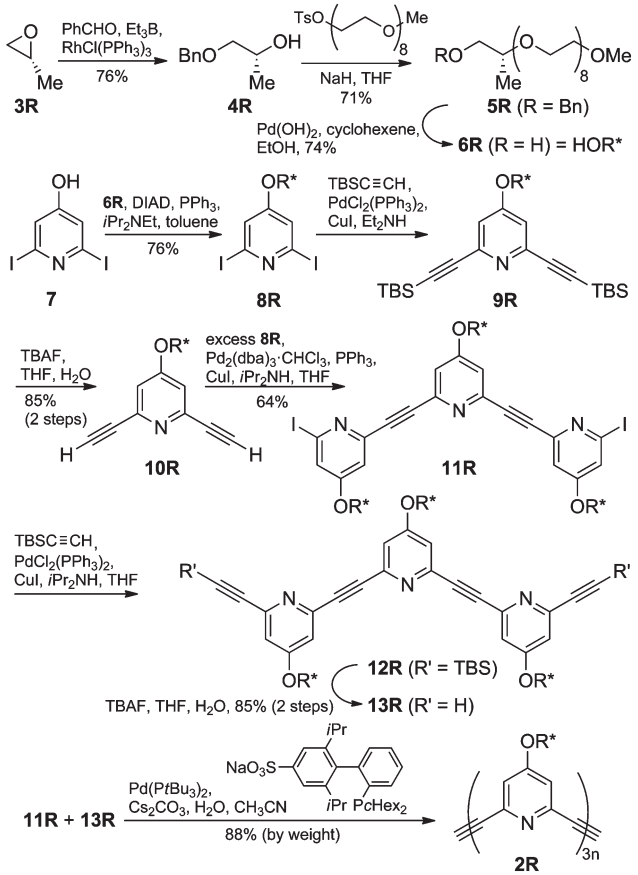
† Electronic supplementary information (ESI) available: The experimental detail of preparation of **2S**, characteristics of new compounds, Fig. S1–S13. See DOI: 10.1039/c2ob25816a



Scheme 1 Preparation of chiral polymer **2R**. DIAD = diisopropyl azodicarboxylate, TBS = *tert*-butyldimethylsilyl, TBAF = tetra-*n*-butylammonium fluoride, dba = dibenzalacetone.

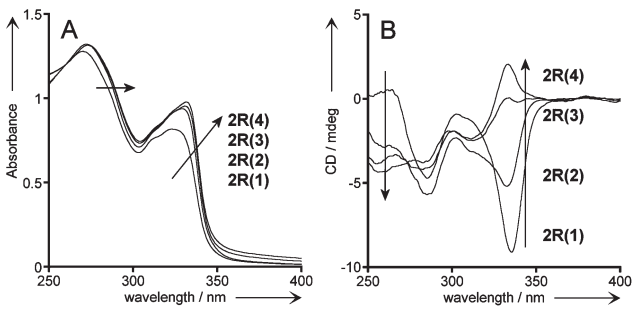


Fig. 2 Molecular size dependence of (A) UV-vis and (B) CD spectra of **2R**. Conditions: **2R** (**2R(4)**: 1.0×10^{-3} M (unit conc.), Abs_{260} = 1.20; **2R(1)**, **2R(2)**, **2R(3)**: *ca.* 1×10^{-3} M (unit conc., normalized as Abs_{260} = 1.20)), H_2O, 25 °C, path length = 1 mm.

units. The antipodal polymer **2S** was similarly prepared from (*S*)-propylene oxide (**3S**) (see the ESI†), and the M_n values of GPC fractions **2S(1)–2S(4)** were 17 100, 23 000, 26 500, and 33 100 g mol^{-1} *versus* polystyrene standards, respectively.

To study the influence of the molecular size, each of the GPC fractions **2R(1)–2R(4)** was subjected to UV-vis and CD analyses. Fig. 2 shows the comparison of the spectra after normalization as Abs_{260} = 1.20. When the first absorptive band for **2R(4)** was compared with that for **2R(1)**, a red-shift of λ_{max} from

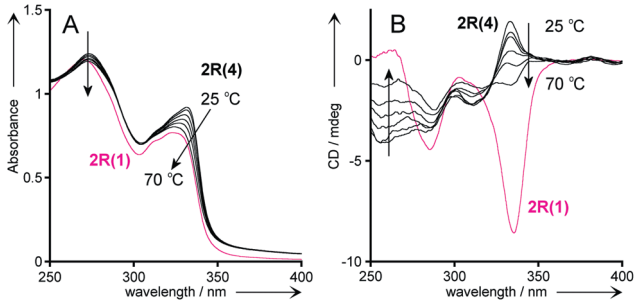


Fig. 3 Temperature dependence of (A) UV-vis and (B) CD spectra of **2R(4)**. Conditions: **2R(4)** (1.0×10^{-3} M, unit conc.), H_2O, 25 to 70 °C, path length = 1 mm. Red lines show spectra for **2R(1)** normalized at 260 nm absorption.

323 to 332 nm was observed with increase of absorption. More remarkable is that the shape of the CD spectrum drastically changed by molecular size, and the characteristic CD band around 333 nm showed inversion of the sign for the heavier fractions. These findings suggested that there was a contribution of a different type of chiral higher-order structure for the case of heavier polymer, in addition to the conventional single-helical higher-order structure that **1** forms.[7] On the other hand, the trimers **11R** and **13R** showed only weak CDs (Fig. S1 in the ESI†) probably because they are too short to form a helical higher-order structure, therefore the CDs shown in Fig. 2B were due to the chiral higher-order structures of the polymer **2R**.

The temperature dependence of UV-vis and CD spectra was studied for the heaviest fraction **2R(4)**. As mentioned above, this fraction showed a positive CD band around 333 nm. When an aqueous solution of **2R(4)** (1.0×10^{-3} M) was heated from 25 °C, both hypochromism and a blue-shift were observed in the first absorptive band. At 70 °C the shape of the UV-vis spectrum became close to that for the lightest fraction **2R(1)** at 25 °C (Fig. 3A). In the CD experiment, heating the solution of **2R(4)** from 25 °C to 70 °C caused transformation of the spectrum as shown in Fig. 3B. During this process, the positive CD around 333 nm decreased and turned negative, approaching the CD of **2R(1)** at 25 °C as in the case of the UV-vis experiment. Thus, heating **2R(4)** and decreasing molecular size from **2R(4)** to **2R(1)** caused similar changes in optical properties. When the concentration effect was studied for **2R(4)**, the absorbance showed linearity with the concentration of the polymer from 2.2×10^{-6} to 1.0×10^{-3} M (unit conc.) (Fig. S2 in the ESI†). Thus, intermolecular interaction was judged to be negligible for the polymer up to 1.0×10^{-3} M. The size and temperature dependences of UV-vis and CD spectra were also studied for the fractions of the antipodal polymer **2S(1)–2S(4)**. As shown in Fig. 4 and 5, changes were observed for UV-vis spectra in a similar manner to the cases of the **2R** series. In the CD experiments, spectral changes were observed in a mirror-image manner to that for **2R**.

The association abilities of the longer polymers with various saccharides were studied in aqueous solutions of **2R(4)** and **2S(4)**. When D- or L-mannose was added to the solution of **2R(4)**, the CD spectrum changed as shown in Fig. 6. L-Mannose induced a little bigger CD change around 333 nm than D-mannose did. Other kinds of monosaccharides such as glucose

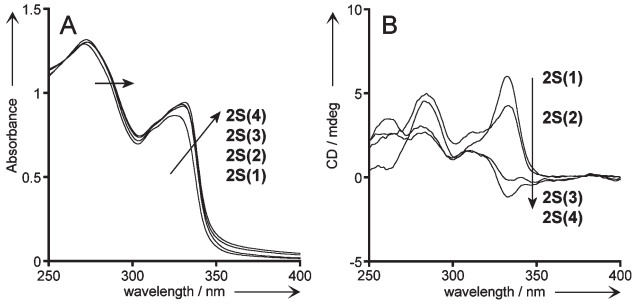


Fig. 4 Molecular size dependence of (A) UV-vis and (B) CD spectra of **2S**. Conditions: **2S** (**2S(4)**: 1.0×10^{-3} M (unit conc.), $Abs_{260} = 1.20$; **2S(1)**, **2S(2)**, **2S(3)**: *ca.* 1×10^{-3} M (unit conc., normalized as $Abs_{260} = 1.20$)), H_2O, 25 °C, path length = 1 mm.

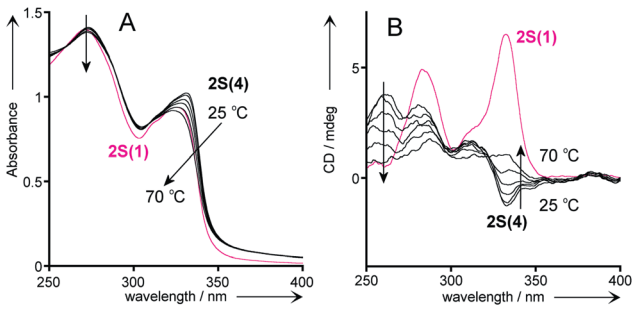


Fig. 5 Temperature dependence of (A) UV-vis and (B) CD spectra of **2S(4)**. Conditions: **2S(4)** (1.0×10^{-3} M, unit conc.), H_2O, 25 to 70 °C, path length = 1 mm. Red lines show spectra for **2S(1)** normalized at 260 nm absorption.

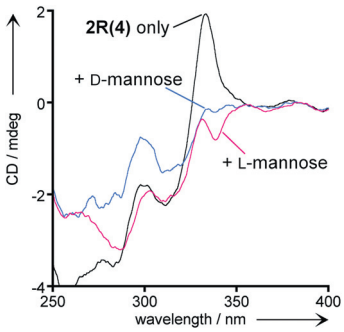


Fig. 6 CD responses of **2R(4)** to the addition of (blue) D-mannose and (red) L-mannose. Conditions: **2R(4)** (1.0×10^{-3} M, unit conc.), mannose (3.0 M), H_2O, 25 °C, path length = 1 mm.

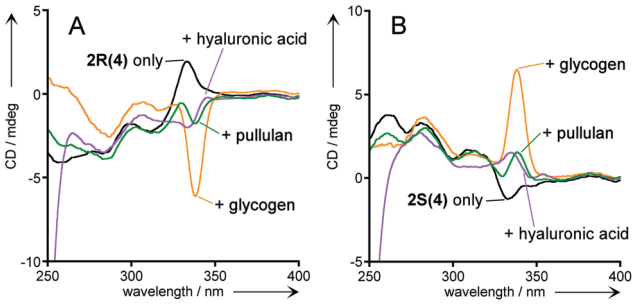


Fig. 7 CD responses of (A) **2R(4)** and (B) **2S(4)** to the addition of polysaccharides. Conditions: **2R(4)** or **2S(4)** (1.0×10^{-3} M, unit conc.), saccharide (4.9 w/v%), H_2O, 25 °C, path length = 1 mm. (black) Only **2R(4)** or **2S(4)**, (orange) with glycogen, (green) with pullulan, (purple) with hyaluronic acid.

and galactose induced only little CD changes. Next we studied the treatment of poly- and cyclooligosaccharides with **2R(4)** and **2S(4)**. The polysaccharides examined were glycogen, pullulan, and hyaluronic acid. Upon addition of these polysaccharides to the polymer solutions, we observed remarkable CD responses as shown in Fig. 7. The CD band around 333 nm showed sign inversion, when the polysaccharide guests were added. Among two kinds of cyclodextrins (α- and γ-CyD), γ-CyD induced much bigger CD responses (Fig. 8).

The additive effects of pullulan and hyaluronic acid also produced a hypochromic effect in the absorption spectra as shown in Fig. S3 in ESI.† In the case of mannose, a similar hypochromic effect was observed for the shorter oligomer (see below).

Titration experiments were performed by using glycogen with **2R(4)** and **2S(4)**. When glycogen was added into aqueous solutions of **2R(4)** and **2S(4)**, the CD spectra gradually changed (Fig. S5 and S6 in the ESI†). The titration curves outwardly fitted well with 1 : 1 binding isotherms. The changes of CD spectra during these titrations resembled those observed in the heating experiments (Fig. 3 and 5) and in the experiment decreasing the molecular size of the polymers (Fig. 2 and 4) as mentioned above. In every case the characteristic CD band around 335 nm decreased and finally its sign was inverted.

Generally, when a guest saccharide is treated with an achiral ethynylpyridine polymer, the sign of induced CD is determined by the chirality of the guest.[7,8] On the other hand, in the cases of chiral polymers **2R** and **2S**, the direction of the CD changes was determined by the chirality of the host. When a guest saccharide was treated with a pair of solutions of **2R(4)** and **2S(4)**, the CD changes were induced roughly in a mirror image manner to each other corresponding to the chirality of the host polymers (Fig. 6–8). Therefore, the helical sense of the resulting polymer–saccharide complexes was determined by the chirality of the host polymers, not by that of the guest, in other words, independent of the chirality of the guest. These findings indicate the possibility that an achiral guest may affect the chiral higher-order structure of **2R** and **2S**. So we studied the influence of inorganic salts as an additive. When $NaClO_4$ or $Ca(ClO_4)_2$ was added to an aqueous solution of **2R(4)**, the inversion of the CD band was clearly observed (Fig. 9A). In experiments using **2S(4)**, similar CD inversion was also observed in a mirror image manner (Fig. 9B). $Ca(ClO_4)_2$ gave much more improvement than $NaClO_4$ did, in both cases.

In our recent reports, it was found that the helical structure of ethynylpyridine oligomers with (or without) coordinating side chains could be stabilized by the addition of a Cu^{2+} cation, which works as a center of the complex outside (or inside) the helix.[8a,c,e] The additive effects of $NaClO_4$ and $Ca(ClO_4)_2$ would be also due to the complexation at the side oligo(oxyethylene) chains and/or the bridging between the pyridine nitrogen atoms and the saccharide hydroxy groups. The stronger Lewis acid Ca^{2+} gave bigger CD bands by stronger chelation.

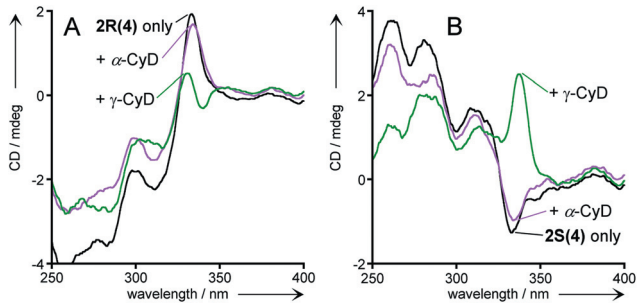


Fig. 8 CD responses of (A) **2R(4)** and (B) **2S(4)** to the addition of cyclodextrins (CyDs). Conditions: **2R(4)** (1.0×10^{-3} M, unit conc.) or **2S(4)** (1.0×10^{-3} M, unit conc.), cyclodextrin (0.1 M), H_2O, 25 °C, path length = 1 mm. (black) Only **2R(4)** or **2S(4)**, (purple) with α-cyclodextrin, (green) with γ-cyclodextrin.

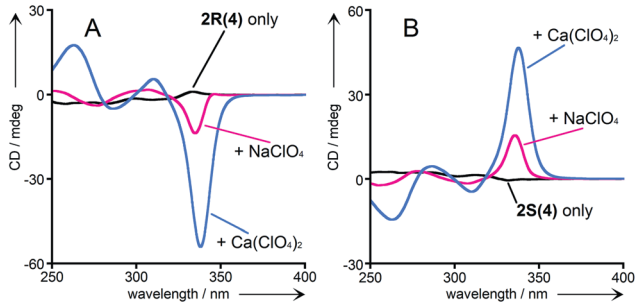
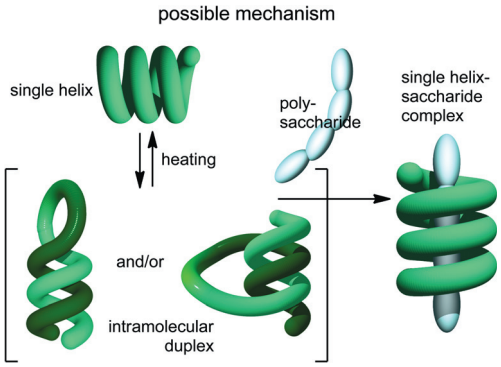


Fig. 9 CD responses of (A) **2R(4)** and (B) **2S(4)** to the addition of (red) $NaClO_4$ or (blue) $Ca(ClO_4)_2$. Conditions: **2R(4)** or **2S(4)** (1.0×10^{-3} M, unit conc.), $NaClO_4$ or $Ca(ClO_4)_2$ (1.0×10^{-1} M), H_2O, 25 °C, path length = 1 mm.

Several additional titration experiments were carried out by using the fraction of **2R** of smaller molecular weight (M_n = 8800 g mol^{-1}). As shown in Fig. S8–S10 in ESI,† the titrations with D-mannose and D-glucose to **2R** caused a hypochromic effect around 330 nm in UV-vis spectra. The binding constants were estimated as K_a = 3.7 M^{-1} *vs.* D-mannose and 1.9 M^{-1} *vs.* D-glucose on the assumption of 1 : 1 binding. During these titrations, no meaningful change of the CD spectrum was observed. On the other hand, the titration with $NaClO_4$ to **2R** caused changes both of CD and UV-vis spectra as shown in Fig. S11 in ESI.† The absence of an isoabsorptive point and an isodichroic point suggests the involvement of several kinds of complexes of different molar ratios of the oligomer and metal.

The solvent effect was studied for H_2O, CH_3CN, MeOH, and CH_2Cl_2 solutions of **2S** as shown in Fig. S12 in ESI.† In polar solvents CH_3CN and MeOH, weak CD was still found, while in apolar CH_2Cl_2 CD activity was not observed probably due to the lack of a solvophobic effect.

As shown in Fig. 2–8, the similarity of the optical responses to size, temperature, and recognition would correspond to the similarity of structural changes, however, it is not clear how the polymers in the heaviest fractions **2R(4)** and **2S(4)** change their structure. The temperature dependence of UV-vis and CD properties observed in Fig. 3 and 5 would suggest the contribution of some entropic factors. A possible explanation is: at lower temperature the longer polymers in **2R(4)** and **2S(4)** may form



Scheme 2 A possible transformation mechanism of higher-order structures of polymers **2R** and **2S** of bigger size which were heated or associated with a guest on the assumption of contribution of an intramolecular duplex. For molecular models depicted for these single and double helices by using Monte-Carlo MM analyses, see Fig. S13 in ESI.†

more-ordered structures such as an intramolecular double helix[11a,15] and transform into a less-ordered simple single helix at higher temperature (Scheme 2).[11a] The single helix can be also stabilized by host–guest association with a saccharide as shown in our previous work,[7,8] thus the addition of saccharide guests induced the changes of CD spectra as mentioned above.

Conclusion

meta-Ethynylpyridine polymers **2R** and **2S** having chiral centers at the side chains were prepared and separated into fractions by GPC. The CD spectra of the polymers changed their shape, depending on the molecular size of the polymer and the temperature of the sample solution examined. In addition, the heaviest fractions **2R(4)** and **2S(4)** showed CD responses to the addition of mannose, cyclodextrins, and polysaccharides such as glycogen even in water. These saccharide-induced CD responses resembled those according to heating of the sample solution and decreasing of the molecular size, suggesting that a similar tendency of structural change of the higher-order chiral structure took place. In host–guest chemistry, synthetic host molecules recognizing polysaccharide guests have been relatively unexplored. The use of chiral polymeric hosts will promote this objective.

Experimental section

General

^{1}H NMR spectra were recorded on a 300 MHz NMR spectrometer using tetramethylsilane (TMS) as an internal reference. ^{13}C NMR spectra were recorded on a 75 MHz NMR spectrometer. THF was freshly distilled before use from sodium benzophenone ketyl. (*R*)- and (*S*)-1-Benzyloxypropan-2-ol (**4R**, **4S**) were prepared from (*R*)- and (*S*)-propylene oxide (**3R**, **3S**), respectively, and benzaldehyde by reductive condensation catalyzed by Wilkinson catalyst.[13] Tosylate ester of octaethylene glycol monomethyl ether was prepared from octaethylene glycol monomethyl ether.[16,17] All reactions were carried out under an

argon atmosphere. Glycogen, pullulan, and hyaluronic acid were purchased from TCI.

Preparation of chiral polymer 2R

(*R*)-27-Methyl-28-benzyloxy-2,5,8,11,14,17,20,23,26-nonaoxaoctacosane (5R). A suspension of NaH (0.33 g of 60% oil suspension was washed with hexane before use, 8.4 mmol) in THF (22 mL) was added to (*R*)-1-benzyloxypropan-2-ol (**4R**, 0.93 g, 5.6 mmol), and the mixture was stirred for 6 h at room temperature. Then, tosylated octaethylene glycol monomethyl ether (3.0 g, 5.6 mmol) was added to the reaction mixture. After stirring for 2 days at room temperature, the reaction mixture was filtered with rinsing by AcOEt. The combined filtrate was evaporated, and the resulting residue was purified by silica gel column chromatography (eluent: AcOEt–hexane = 1 : 1 to AcOEt) to afford **5R** (2.1 g, 71%) as a yellow oil. IR (neat) ν 2870, 1107 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.17 (d, J = 6.3 Hz, 3 H), 3.38–3.71 (m, 38 H), 4.55 (s, 2 H), 7.26–7.34 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.3, 59.0, 68.6, 70.5, 70.6, 70.8, 71.9, 73.3, 74.1, 75.1, 127.5, 127.6, 128.3, 138.4; ESI-HRMS m/z calcd for $C_{27}H_{48}NaO_{10}$ ($M + Na^+$): 555.3145; found: 555.3165.

(*R*)-2-Methyl-3,6,9,12,15,18,21,24,27-nonaoxaoctacosan-1-ol (6R). A mixture of **5R** (3.2 g, 6.1 mmol), $Pd(OH)_2$ 20% on carbon (0.43 g), and cyclohexene (47 mL) in EtOH (79 mL) was refluxed for 24 h. The reaction mixture was filtered through a Celite bed. The filtrate was evaporated, and the residue was purified by silica gel column chromatography (eluent: CH_2Cl_2 → AcOEt → AcOEt–acetone = 1 : 1 → acetone) to afford **6R** (2.0 g, 74%) as a yellow oil. $[\alpha]_D^{28} = -6.0$ (c = 3.0, $CHCl_3$); IR (neat) ν 3483, 2872, 1106 cm^{-1}; ^1H NMR δ 1.12 (d, J = 6.3 Hz, 3 H), 3.38 (s, 3 H), 3.53–3.82 (m, 35 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.3, 59.0, 61.8, 66.3, 68.2, 70.4, 70.5, 70.6, 70.8, 71.9, 72.5; ESI-HRMS m/z calcd for $C_{20}H_{42}NaO_{10}$ ($M + Na^+$): 465.2676; found: 465.2694.

(*R*)-Amphiphilic chain-derived 2,6-diiodopyridine 8R. Mitsunobu reaction with 2,6-diiodo-4-pyridinol (7). To a mixture of 2,6-diiodo-4-pyridinol (**7**, 1.6 g, 4.5 mmol), PPh_3 (1.2 g, 4.5 mmol), and iPr$_2$NEt (5.0 mL) in toluene (97 mL) was added diisopropyl azodicarboxylate (DIAD, 0.91 g, 4.5 mmol), and the mixture was stirred for 1 h at room temperature. Then, to the reaction mixture was added **6R** (2.0 g, 4.5 mmol), and the mixture was stirred for 14 h at room temperature and evaporated. The residue was subjected to silica gel column chromatography (eluent: AcOEt–hexane = 1 : 1 → AcOEt → AcOEt–acetone = 4 : 1) to afford **8R** (2.6 g, 76%) as a yellow oil. IR (neat) ν 2871, 1560, 1522, 1107 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25 (d, J = 6.3 Hz, 3 H), 3.38 (s, 3 H), 3.53–4.01 (m, 35 H), 7.25 (s, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.9, 59.0, 69.0, 70.5, 70.6, 70.7, 70.8, 71.0, 71.9, 72.1, 73.9, 114.2, 115.7, 121.3, 164.7; ESI-HRMS m/z calcd for $C_{25}H_{43}I_2NNaO_{10}$ ($M + Na^+$): 794.0874; found: 794.0876.

(*R*)-Amphiphilic chain-derived 2,6-bis(TBS-ethynyl)pyridine 9R. A mixture of **8R** (0.71 g, 0.92 mmol), $PdCl_2(PPh_3)_2$ (26 mg, 0.037 mmol), CuI (3.5 mg, 0.018 mmol), and *tert*-butyldimethylsilylacetylene (0.64 g, 4.6 mmol) in Et_2NH (32 mL) was stirred for 3 h at room temperature. The resulting mixture was filtered and the filtrate was concentrated with a rotary evaporator. The resulting residue was subjected to silica gel column chromatography (eluent: AcOEt–hexane = 1 : 1 to AcOEt) to afford **9R** (0.62 g, 85%) as a yellow oil. IR (neat) ν 2929, 2859, 2162, 1578, 1551, 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.18 (s, 12 H), 0.99 (s, 18 H), 1.27 (d, J = 6.3 Hz, 3 H), 3.38 (s, 3 H), 3.53–4.19 (m, 35 H), 6.93 (s, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.8, 16.7, 17.1, 26.1, 59.0, 68.9, 70.5, 70.6, 70.8, 71.6, 71.9, 73.9, 93.4, 104.0, 113.9, 144.4, 164.8; ESI-HRMS m/z calcd for $C_{41}H_{73}NNaO_{10}Si_2$ ($M + Na^+$): 818.4671; found: 818.4669.

(*R*)-Amphiphilic chain-derived 2,6-diethynylpyridine 10R. To a THF (8.8 mL) solution of **9R** (0.62 g, 0.78 mmol) were added two drops of water and nBu$_4$NF (1.7 mL of 1 M THF solution, 1.7 mmol) dropwise. The mixture was stirred for 3 h at room temperature, evaporated, and instantly subjected to silica gel column chromatography (eluent: AcOEt to AcOEt–acetone = 4 : 1) to afford **10R** (0.47 g, 100%) as a brown oil. IR (neat) ν 3229, 2873, 2110, 1581, 1556, 1107; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.27 (d, J = 6.3 Hz, 3 H), 3.12 (s, 2 H), 3.38 (s, 3 H), 3.53–4.20 (m, 35 H), 7.01 (s, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.9, 59.0, 69.0, 70.46, 70.52, 70.6, 70.8, 71.8, 71.9, 73.9, 77.3, 82.1, 114.1, 143.6, 165.1; ESI-HRMS m/z calcd for $C_{29}H_{45}NNaO_{10}$ ($M + Na^+$): 590.2941; found: 590.2959.

(*R*)-Amphiphilic chain-derived diiodo-trimer 11R. To a mixture of **8R** (5.5 g, 7.1 mmol) and **10R** (0.78 g, 1.4 mmol) in iPr$_2$NH (58 mL) and THF (29 mL) were added $Pd_2(dba)_3{\cdot}CHCl_3$ (28 mg, 0.027 mmol), PPh_3 (29 mg, 0.11 mmol), and CuI (5 mg, 0.027 mmol). The reaction mixture was stirred for 18 h at room temperature and filtered. The filtrate was evaporated with a rotary evaporator, and the residue was subjected to silica gel column chromatography (eluent: AcOEt–hexane = 1 : 1 → AcOEt → AcOEt–acetone = 1 : 1 → acetone) to afford **11R** (1.6 g, 64%) as a brown oil. $[\alpha]_D^{28} = +4.2$ (c = 1.0, $CHCl_3$); IR (neat) ν 2872, 1577, 1532, 1108 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.26–1.30 (m, 9 H), 3.38 (s, 9 H), 3.53–4.20 (m, 105 H), 7.12 (d, J = 2.1 Hz, 2 H), 7.16 (s, 2 H), 7.29 (d, J = 2.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.91, 16.94, 59.0, 68.1, 69.00, 69.05, 69.1, 70.5, 70.6, 70.8, 70.9, 71.9, 72.1, 73.9, 86.6, 88.1, 114.7, 117.7, 121.5, 143.5, 143.8, 164.8, 165.2; ESI-HRMS m/z calcd for $C_{79}H_{129}I_2N_3Na_2O_{30}$ ($M + 2Na^+$): 949.8273; found: 949.8275.

(*R*)-Amphiphilic chain-derived bis(TBS-ethynyl)trimer 12R. A solution of **11R** (1.1 g, 0.57 mmol) in iPr$_2$NH (87 mL) and THF (55 mL) was added to a mixture of $PdCl_2(PPh_3)_2$ (16 mg, 0.023 mmol), CuI (4 mg, 0.023 mmol), and *tert*-butyldimethylsilylacetylene (0.40 g, 2.9 mmol). The reaction mixture was stirred for 13 h at room temperature. The resulting mixture was filtered, and the filtrate was evaporated with a rotary evaporator. The residue was subjected to silica gel column chromatography (eluent: AcOEt–hexane = 2 : 1 → AcOEt → AcOEt–acetone = 1 : 1 → acetone) to afford **12R** (0.94 g, 87%) as a brown oil. IR (neat) ν 2871, 1581, 1550, 1109 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.20 (s, 12 H), 1.00 (s, 18 H), 1.27–1.29 (m, 9 H), 3.38 (s, 9 H), 3.53–4.20 (m, 105 H), 6.99 (d, J =

2.4 Hz, 2 H), 7.11 (d, J = 2.4 Hz, 2 H), 7.15 (s, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.8, 16.7, 16.96, 17.02, 19.1, 26.2, 59.0, 68.99, 69.03, 70.5, 70.6, 70.8, 71.9, 73.88, 73.94, 87.2, 87.6, 93.7, 103.8, 114.0, 114.6, 143.7, 144.0, 144.6, 165.0; ESI-HRMS m/z calcd for $C_{95}H_{159}N_3Na_2O_{30}Si_2$ (M + 2Na$^+$): 962.0171; found: 962.0161.

(*R*)-Amphiphilic chain-derived diethynyl-trimer 13R. To a THF (29 mL) solution of **12R** (0.89 g, 0.47 mmol) were subsequently added ten drops of water and nBu$_4$NF (1.0 mL of 1 M THF solution, 1.0 mmol) dropwise. The mixture was stirred for 3 h at room temperature, evaporated, and instantly subjected to silica gel column chromatography (eluent: AcOEt–acetone = 1 : 1 → acetone → acetone–MeOH = 10 : 1) to afford **13R** (0.76 g, 98%) as a brown oil. IR (neat) ν 2872, 2110, 1582, 1551, 1107 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.27–1.29 (m, 9 H), 3.15 (s, 2 H), 3.38 (s, 9 H), 3.53–4.19 (m, 105 H), 7.03 (d, J = 2.3 Hz, 2 H), 7.14 (d, J = 2.3 Hz, 2 H), 7.16 (s, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.9, 59.0, 69.0, 70.5, 70.6, 70.8, 71.9, 73.9, 82.1, 87.2, 87.3, 114.2, 114.5, 114.6, 143.7, 143.78, 143.83, 165.1. ESI-HRMS m/z calcd for $C_{83}H_{131}N_3Na_2O_{30}$ (M + 2Na$^+$): 847.9306; found: 847.9275.

(*R*)-Amphiphilic ethynylpyridine polymer 2R. A mixture of **11R** (54 mg, 0.029 mmol), **13R** (59 mg, 0.036 mmol), Pd(PtBu$_3$)$_2$ (9.1 mg, 0.018 mmol), sodium 2′-(dicyclohexylphosphanyl)-2,6-diisopropylbiphenyl-4-sulfonate[14] (14 mg, 0.027 mmol), and Cs_2CO_3 (38 mg, 0.11 mmol) was dispersed with a mixed solvent of CH_3CN (1.25 mL) and H_2O (1.25 mL) which were bubbled with argon before use. The mixture was stirred for 3 days at room temperature with a water bath. The resulting mixture was evaporated, and the residue was dissolved in $CHCl_3$ and purified by using a Sephadex LH-20 column to afford **2R** (99 mg, 88% yield by weight) as a brown oil. The crude product was further purified and fractionated by preparative GPC (Shodex K-2003, K-2002.5, eluent: $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.27–1.33 (m, 3n H), 3.37 (s, 3n H), 3.5–4.2 (m, 35n H), 7.16–7.20 (m, 2n H).

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