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ARTICLE

Highly Efficient Stabilisation of *meta*-Ethynepyridine Polymers with Amide Side Chains in Water by Coordination of Rare-Earth Metals

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An amphiphilic *meta*-ethynepyridine polymer with chiral amide side chains was developed. The polymer was prepared by sequential Sonogashira reaction, and the product was soluble in polar and apolar solvents. The additive effects of metal salts on the polymer were examined in water and aqueous EtOH on the basis of UV-vis and CD spectra. The enhancement of the positive Cotton effect and hypochromism around 360 nm occurred by the addition of various metal salts, indicating the coordination of the cations to the amide side chains of the polymer to stabilise the helical structure. Among them, rare-earth metal salts, especially Sc(OTf)₃ showed much efficient additive effect probably because of its strong coordination ability even in water. Positive cooperativity was observed for the coordination of Sc(OTf)₃ to the polymer in an aqueous EtOH.

Introduction

Chiral helical structures are seen in many kind of biomacromolecules such as proteins, nucleic acids, and polysaccharides. To mimic such chiral helical structures, a variety of artificial helical polymers and oligomers, also called as foldamers, have been developed.¹ Since Moore and coworkers reported the sophisticated example of *meta*-phenylene ethynyls in 1997, solvophobic interactions have been widely used as a driving force for the construction of helical structures of artificial foldamers.^{2–4}

We have developed *meta*-ethynepyridine polymers and oligomers, in which a number of pyridine rings are linked with acetylene bonds at their 2 and 6 positions.^{5,6} These polymers and oligomers prefer to form transoid conformation in apolar conditions to suppress the repulsion caused by dipole moments at pyridine rings. On the other hand, spontaneous formation of higher-order helical structure has been achieved in aqueous conditions by using amphiphilic *meta*-ethynepyridine polymers with oligoethylene glycol side chains.⁶ Indeed, amphiphilic (*R*)- and (*S*)-**1** with chiral centres could form circular dichroism (CD)-active biased helices (Fig. 1). Those helix formations were driven by solvophobic interaction, and the CD activity was found to be enhanced by the addition of a large excess amount of metal salts such as NaClO₄ and Ca(ClO₄)₂.

Herein, we report a new type of amphiphilic *meta*-ethynepyridine polymer **2**, poly(4-(((*S*)-1-methyl-3,6,9,12-tetraoxatridecyl)aminocarbonyl)-2,6-pyridyl) ethynylene 4-(1,4,7,19,13,16,19,22-octaotricosanyl)-2,6-pyridyl) ethynylene), in which chiral amide side chains were introduced

as a coordination site for metal cations (Fig. 1). The polymer formed chiral helical structures in not only polar solvents such as H₂O, MeOH, THF, and MeCN, but also in CH₂Cl₂. The chiral helical structure of the polymer can be stabilised by the addition of various kinds of metal salts, and in particular rare-earth metal salts were so efficient that only an equimolar amount of the salts was needed even in H₂O. The data of IR and ¹H NMR analyses indicated that the coordination of the rare-earth cations to the amide carbonyl groups of **2** led the efficient stabilisation of the helix.

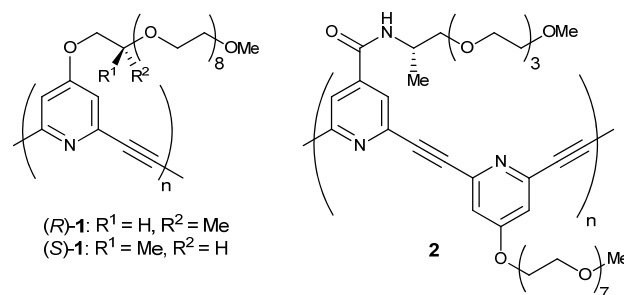
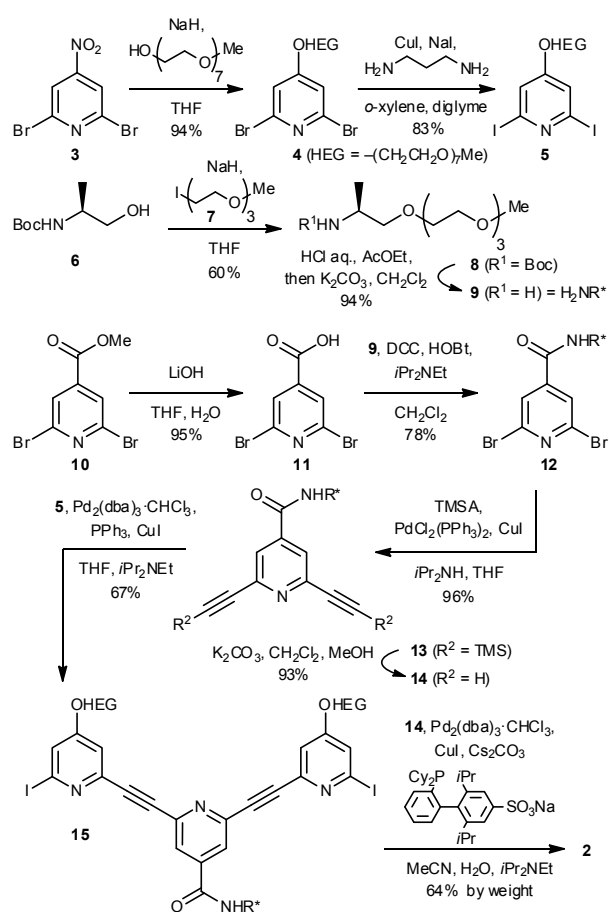


Fig. 1 Chemical structures of previously reported (*R*)- and (*S*)-**1**, and newly designed chiral polymer **2**.



Scheme 1 Preparation of chiral polymer **2**. DCC = *N,N'*-dicyclohexylcarbodiimide, HOBT = 1-hydroxybenzotriazole, TMSA = trimethylsilylacetylene, dba = dibenzylideneacetone

Results and discussion

Synthesis of amide-introduced chiral polymer **2**

Chiral polymer **2** was synthesised as shown in Scheme 1. Nucleophilic replacement of the nitro group of 2,6-dibromo-4-nitropyridine (**3**) with sodium monomethyl heptaethylene glycolate gave ether **4**, which was converted to diiodide **5** by copper-catalysed halogen exchange reaction.⁷ The building block **9** for the chiral side chain of **2** was prepared by assembling *N*-Boc-*L*-alaninol (**6**) and 10-iodo-2,5,8-trioxadecane (**7**).⁸ Condensation of **6** and the iodinated ether **7** gave Boc-protected amphiphilic chiral amine **8**, and then the Boc group was removed to yield chiral amine **9**. Hydrolysis of methyl 2,6-dibromoisonicotinate (**10**)⁹ with LiOH gave 2,6-dibromoisonicotinic acid (**11**), which was condensed with **9** to form chiral amide **12**. Two bromine atoms of **12** were converted to ethynyl groups to give **14** via TMS-protected intermediate **13** by Sonogashira reaction with trimethylsilylacetylene (TMSA) followed by protodesilylation. Trimeric block **15** was obtained by Sonogashira reaction using **14** and an excess amount of diiodide **5**. Finally, copolymerisation of **14** and **15** furnished the target polymer **2** by applying Sonogashira reaction in aqueous conditions.¹⁰ The

crude product was purified by centrifugation, and the product was subjected to preparative gel permeation chromatography (GPC) using CHCl₃ as eluent to collect a fraction of relatively longer size. It was found that **2** is soluble in a wide range of solvents, such as CH₂Cl₂, CHCl₃, THF, MeCN, MeOH, EtOH, and H₂O. The number-average molecular weight (*M_n*) and dispersity (*M_w*/*M_n*) of each fraction were determined by analytical GPC using a DMF solution of LiBr (0.1 M) as eluent. In the following studies, fractions from four lots (*M_n* = 1.2 × 10⁴, 1.9 × 10⁴, 5.3 × 10⁴ and 5.6 × 10⁴ g mol⁻¹, see Table S1 in ESI[†]) were applied as a substrate. Among these fractions, no meaningful size-dependence could be noticed.

Solvent effects on the chiral polymer **2**

In advance, the concentration dependence of the polymer **2** was studied in MeCN and in H₂O by UV-vis measurements. The results were summarised in Figs. S1 and S2 in ESI[†], and the intermolecular interaction of **2** was considered to be negligible because the absorbance of **2** in MeCN (unit conc = 7.8 × 10⁻⁶ M to 3.6 × 10⁻³ M) and that in H₂O (unit conc = 7.8 × 10⁻⁶ M to 4.0 × 10⁻³ M) were almost in proportion to the unit concentrations of **2**.

As mentioned above, the polymer **2** was expected to spontaneously form a chiral helical structure in H₂O by hydrophobic interaction stabilising π -stacking as well as the precedent examples.^{3,4,6} Here, solvent effects on the polymer **2** were investigated on the basis of UV-vis and CD spectra to collect information about the higher-order structures without metal salts (Fig. 2). In CH₂Cl₂, THF, MeCN, and MeOH, the first absorption bands were observed around 330 nm, while remarkably red-shifted one at λ_{max} = 340 nm in H₂O (Fig. 2a). In our previous study for amphiphilic ethynylpyridine polymers **1**, a similar type of red shift of the absorption band was seen in H₂O attributed to hydrophobic π -stacking interactions.⁶ Therefore, the red shift for **2** would also be caused by intramolecular π -stacking interaction among pyridine rings at an interval of one pitch in the helical structure.

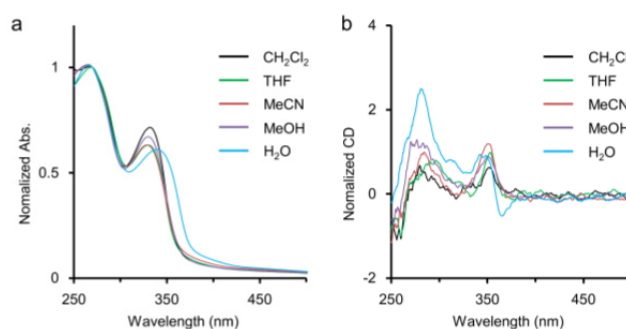


Fig. 2 Solvent effects on (a) UV-vis and (b) CD spectra of **2**. Conditions: **2** (*M_n* = 1.9 × 10⁴ g mol⁻¹, *M_w* = 2.7 × 10⁴ g mol⁻¹), 25 °C, path length = 1 mm. UV spectra were normalised at 270 nm. CD spectra were normalised as that the absorbance at 270 nm is 1.0.

The polymer **2** showed a positive Cotton effect around 350 nm in CH₂Cl₂, THF, MeCN, and MeOH (Fig. 2b). In our previous study about chiral ethynylpyridine polymers and oligomers

such as **1**,^{6a} no meaningful CD activity has been observed in less polar solvents such as CH₂Cl₂ and CHCl₃. It was because that the solvophobic intramolecular interaction was too weak to form a helix in less polar environments. On the other hand, **2** showed weak but clearly perceivable CD activity around 350 nm even in CH₂Cl₂, indicating that some kind of intramolecular interaction other than solvophobic one would work to stabilise the helical structure. The major structural difference of **2** against **1** is the presence of amide groups in the side chains. The hydrogen bonds between the amide groups in the side chains might stabilise the CD-active chiral helical structure. Recently, Sanda reported poly(*meta*-phenylene ethynylene)s containing hydrophobic chiral amino acid side chains,¹¹ and Yashima reported poly(*meta*-phenylene ethynylene)s bearing hydrophilic L- or D-alanine-derived oligo(ethylene glycol) side chains.¹² These polymers were reported to form chiral helical structures in less polar solvents such as CH₂Cl₂ and CHCl₃, driven by intramolecular hydrogen-bonding network between the amide groups of the side chains. In H₂O, the shape of CD spectrum of **2** was rather different from those in other solvents (Fig. 2b). Actually, a bisignate CD signal was observed at a range of about 330 nm to 380 nm, so that the polymer **2** would form a different kind of higher-order structure in H₂O.

Additive effects of main-group metal cations for the polymer **2**

Metal salts such as NaClO₄ and Ca(ClO₄)₂ were found to stabilise the chiral helical structures of our previous (*S*)-**1** and (*R*)-**1** accompanied by displaying strong CD bands in H₂O.^{5a,b,d,f,g,6a} This stabilisation of the helical structure of **1** might be caused by complexation of metal cations at ethylene glycol side chains and/or at the nitrogen atoms of pyridine rings inside the helix. Herein the additive effect of main-group metal salts was also studied for aqueous solutions of the polymer **2** by UV-vis and CD measurements, and the data were compared to those in the cases of **1**. As shown in Fig. 3a, the addition of a large excess amount of metal salts induced hypochromic effects on the first and second absorption bands around 340 nm and 265 nm, respectively. It has been reported that when foldamers form helical structures by hydrophobic interaction, hypochromism is often observed in the absorption spectra. The hypochromic changes in Fig. 3a would indicate that the addition of metal salts improved the hydrophobic π -stacking interaction to stabilise the chiral helical structure of **2**. The coordination manner of the metal cations would be speculated to the following three possible complexation patterns among the functional groups in **2**: (i) for ethylene glycol side chains; (ii) for amide carbonyl groups in the side chains; (iii) for nitrogen of pyridine ring inside the helix. Afterwards, we will discuss these possibilities on the basis of IR and ¹H NMR studies.

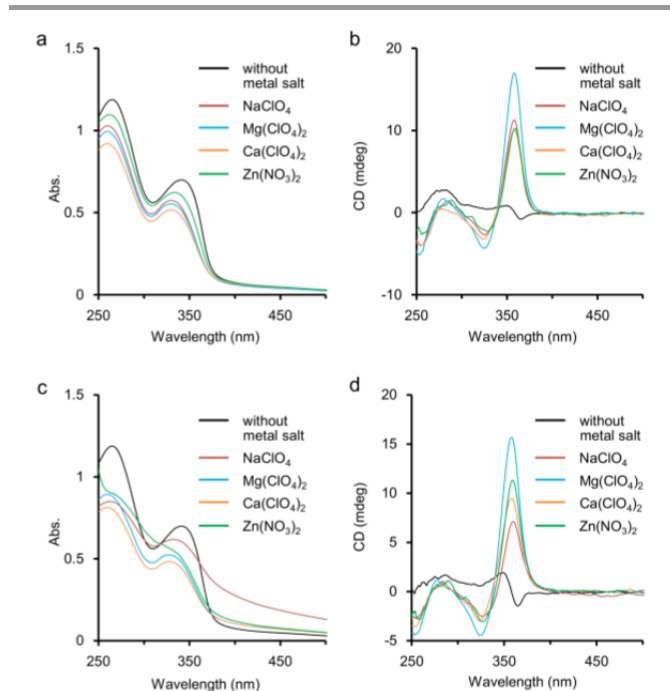


Fig. 3 Additive effects of metal cations on aqueous solutions of **2**. (a) UV-vis spectra at 25 °C (b) CD spectra at 25 °C (c) UV-vis spectra at 85 °C (d) CD spectra at 85 °C. Conditions: [**2**] = 1.0×10^{-3} M ($M_n = 1.2 \times 10^4$ g mol⁻¹, $M_w = 1.4 \times 10^4$ g mol⁻¹, unit conc), [metal salt] = 1.0 M, H₂O, path length = 1 mm.

For CD, an intense positive CD band appeared around 360 nm after the addition of the metal salts, and the shapes of the CD spectra were typical for ethynylpyridine polymers and oligomers of chiral helical conformation (Fig. 3b).^{5,6} The thermal resistance was studied about the chiral helical complexes of **2** and metal cations (Figs. 3c and 3d). When an aqueous solution containing **2** (1.0×10^{-3} M, unit conc) and Mg(ClO₄)₂ or Ca(ClO₄)₂ (1.0 M) was heated to 85 °C, the CD band around 360 nm was weakened only to some extent, and hypochromism was observed in the UV-vis spectrum. These changes suggested that the folded chiral helical structures of **2** were largely preserved even by heating up to subsequently high temperature. Without metal salt, enhancement of the CD band for **2** occurred by heating, accompanied by small hypochromism (see also Fig. S3 in ESI†). For Zn(NO₃)₂ at 85 °C, the first CD band was slightly enhanced than at 25 °C, and the fine structures of absorption bands almost lost. At that temperature the presence of NaClO₄ (1.0 M) brought about remarkable tailing to over 700 nm in Fig. 3c. This tailing would be due to scattering by aggregate of **2** mediated by Na(I) cation. Indeed, under the heating at 85 °C, clouding and precipitation subsequently occurred over time for the solution of **2** and NaClO₄. Aggregation by heating has been reported not only for poly- and oligoethylene glycol¹³ but also for their derivatives,¹⁴ e.g. oligoethylene glycol-introduced shape-persistent macrocycles.

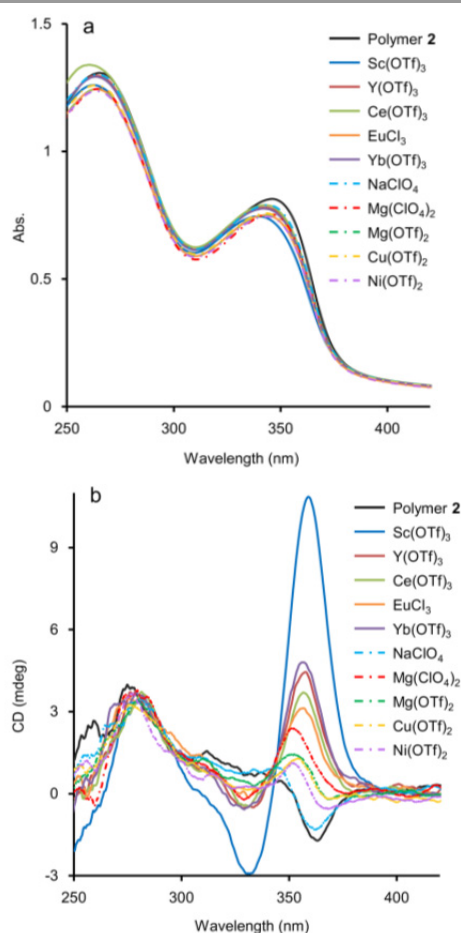


Fig. 4 Additive effects of an equimolar amount of metal salts in aqueous solutions on (a) UV-vis and (b) CD spectra. Conditions: $[2] = 1.0 \times 10^{-3}$ M ($M_n = 5.6 \times 10^4$ g mol $^{-1}$, $M_w = 9.8 \times 10^4$ g mol $^{-1}$, unit conc), [metal salts] = 1.0×10^{-3} M, H₂O, 25 °C, path length = 1 mm. These spectra were uniformly measured after 2 h from the preparation of the sample solutions (see text).

Additive effects of rare-earth metal salts for the polymer 2

As mentioned above, although the addition of metal salts to **2** induced strong CD enhancement, a large excess amount of metal salts were needed to observe the phenomena. Next we studied the additive effect of rare-earth metal salts, expecting that the multivalent coordination ability of the metal cations would stabilise the helical structure efficiently. Those salts have been known for their Lewis acidity compatible with aqueous environments and utilised as a potent catalyst for organic syntheses in aqueous media.¹⁵ To study the efficiency of rare-earth metal additives on the formation of higher-order structure of **2**, UV-vis and CD measurements of solutions of **2** (1.0×10^{-3} M, unit concentration) were carried out in the presence of an equimolar amount of rare-earth, main group, and transition metal salts (1.0×10^{-3} M) (Fig. 4). Under the conditions of these experiments, time-dependence was seen, so that the spectra were uniformly measured after 2 h from the preparation of the sample solutions (see below for the time-dependence issue). As shown in Fig. 4b, the addition of an equimolar amount of NaClO₄ brought little CD change, and for Mg(OTf)₂, Mg(ClO₄)₂, Cu(OTf)₂, and Ni(OTf)₂, only small

changes of CD were observed. In the case that Sc(OTf)₃, Y(OTf)₃, Ce(OTf)₃, Yb(OTf)₃, or EuCl₃ was presence, hypochromism occurred for the absorption around 350 nm, compared to that in the absence of metal salt (Fig. 4a). Noteworthy is that the addition of rare-earth metal salts induced stronger positive CD bands around 360 nm than those induced by the addition of main group and transition metal salts (Fig. 4b). The use of a large excess amount of the rare-metal salts over the unit concentration of **2** was not necessary here, probably because of the strong Lewis acidity of the rare-earth metal salts even in H₂O. Judging from the CD spectra in Fig. 4b, the extent of the additive effect to enhance CD varied with the kind of salts. The order of the efficiency of the additives was Sc(OTf)₃ >> Yb(OTf)₃ > Y(OTf)₃ > Ce(OTf)₃ > EuCl₃. Recently, Imamoto and coworkers investigated the relative Lewis acidity of triflates of Sc(III), Y(III), lanthanide(III) (except Pm) by tandem mass spectrometry.¹⁶ Picked up from their reports, the order of Lewis acidity of the rare-earth metals is Sc(III) >> Yb(III) > Y(III) > Eu(III) >> Ce(III). For triflate additives, this order by Imamoto's group agrees well with the order of the CD enhancement efficiency shown in Fig. 4b. Therefore, the Lewis acidity, or coordination ability was actually important to stabilise the chiral helical structure of **2**. The position of EuCl₃ did not match in the two orders because the chloride anions would affect on the coordination. The additive effects of Sc(NO₃)₃ and TfOH were also studied as control experiments. The addition of an equimolar amount of Sc(NO₃)₃ enhanced the CD of **2** similarly to Sc(OTf)₃ (Fig. S4 in ESI[†]), showing the effectiveness of Sc(III) cation. On the other hand, the addition of an equimolar amount of TfOH showed little change in the CD spectrum (Fig. S5 in ESI[†]), and an excess amount of TfOH (1.0×10^{-1} M, 100 equiv to unit conc of **2**) brought strong CD enhancement as well as the cases shown in Fig. 3. Thus, the strong Brønsted acidity could affect on the polymer, however not so much as the cases of the coordination with lanthanide salts.

Time-dependence was observed in these experiments using an equimolar amount of metal salts. After the addition of the salts at 25 °C, the positive CD band in **2** around 360 nm grew up gradually and became static within a few days as shown in Fig. S6 in ESI[†]. In the cases using a large excess amount of additive salts (Fig. 3), time-dependence was negligible and the CD spectra became static within one hour (Fig. S7 in ESI[†]). Instead of waiting for a lot of hours, the equilibrium state could be reached by annealing the mixture of **2** and the metal salts at 50 °C for 10 min. A CD titration experiment was performed for **2** with Sc(OTf)₃ as a titrant with this annealing process to obtain a titration curve (Fig. 5), which could be fitted well with a 1:1 binding isotherm, and the apparent binding constant¹⁷ was calculated as $K_a' = 3.4 \times 10^3$ M $^{-1}$.

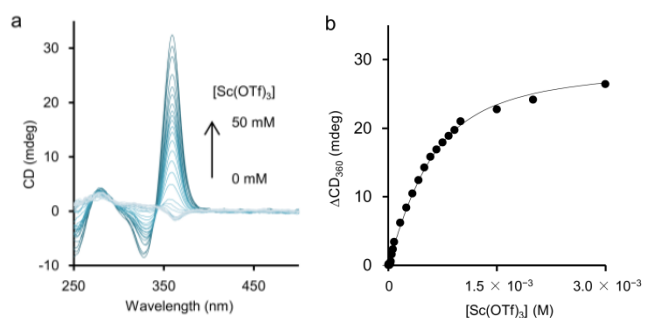


Fig. 5 (a) Changes of the CD spectrum of **2** during the titration with Sc(OTf)₃ in H₂O. (b) Titration curve of the changes of the CD at 360 nm (the range of [Sc(OTf)₃] = 0 to 3.0 × 10⁻³ M was shown). Fitted solid line is drawn according to 1:1 binding isotherm. Conditions: [**2**] = 1.0 × 10⁻³ M (*M_n* = 5.3 × 10⁴ g mol⁻¹, *M_w* = 1.0 × 10⁵ g mol⁻¹, unit conc), [Sc(OTf)₃] = 0 to 5.0 × 10⁻² M, H₂O, 25 °C, path length = 1 mm.

Interestingly, in aqueous EtOH, a positive cooperative effect was observed for the coordination of Sc(III) to **2**. UV-vis and CD measurements were carried out for an aqueous EtOH solution of **2** (1.0 × 10⁻³ M, unit conc, EtOH/H₂O = 9:1) in the absence or presence of an equimolar amount of rare-earth metal salts (1.0 × 10⁻³ M). Unlike in H₂O alone, the time-dependence was not so bothering in aqueous EtOH that an equilibrium state could be reached within 2 h. Rapid molecular motion of **2** in aqueous EtOH might cause the shortening for the equilibrium period. The results were shown in Fig. S8 in ESI†, and the addition of rare-earth metal salts enhanced the positive CD band around 360 nm efficiently. The order of the efficiency of the additives was Sc(OTf)₃ >> Yb(OTf)₃ > Y(OTf)₃ >> EuCl₃ ≈ Ce(OTf)₃, matching with that observed in Fig. 4b except EuCl₃.

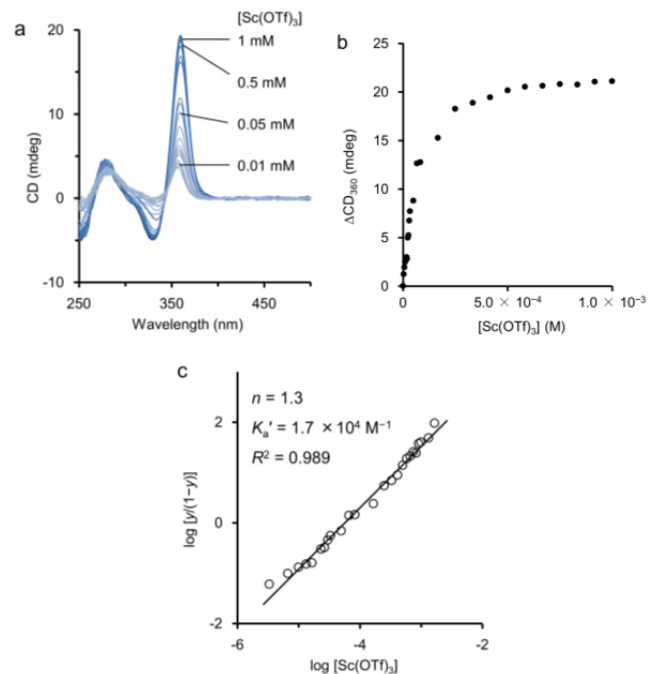


Fig. 6 (a) Changes of CD spectrum of **2** during the titration with Sc(OTf)₃ in aqueous EtOH. (b) Titration curve of the changes of the CD at 360 nm. (c) Hill plot of the data obtained from the titration curve. Fitted solid line is drawn

according to Hill equation (eq 1). Conditions: [**2**] = 1.0 × 10⁻³ M (*M_n* = 5.3 × 10⁴ g mol⁻¹, *M_w* = 1.0 × 10⁵ g mol⁻¹, unit conc), [Sc(OTf)₃] = 0 to 5.0 × 10⁻² M, EtOH/H₂O = 9:1, 25 °C, path length = 1 mm.

When titration experiments were carried out by using Sc(OTf)₃ in an aqueous EtOH solution, the CD intensity at 360 nm was monitored (Fig. 6a). From the titration curve based on the change, we first attempted curve-fitting analyses based on the assumptions of 1:1 and 1:2 models. However, theoretical curves from such models did not fit sufficiently to the experimental titration curve (Fig. 6b). Because the polymer **2** possesses many binding sites in its side chain to coordinate with Sc(III), it is reasonable to assume that the initial complexation between **2** and Sc(III) may assist the further additional complexation by the conformational change of the ethynylpyridine main chain backbone. This interpretation means that the complexation may occur cooperatively among Sc(III) and the binding sites in the side chains of **2**. Based on this hypothesis, we tried to study the binding manner by using the Hill equation (eq 1).¹⁸

$$\log(y/(1-y)) = n \cdot \log[\text{Sc}(\text{OTf})_3] + n \cdot \log K_a' \quad (\text{eq } 1)$$

$y = (\text{CD}^{360} - \text{CD}_0^{360})/(\text{CD}_{\text{max}}^{360} - \text{CD}_0^{360})$: fractional saturation of the CD at 360 nm

K_a' : apparent association binding constant

n : Hill coefficient

The apparent association binding constant K_a' and the Hill coefficient n were estimated to be 1.7 × 10⁴ M⁻¹ and 1.3, respectively, from the least-square fitting shown in Fig. 6c.¹⁷ The estimated n value greater than 1 indicated that the binding was positively cooperative. That is, when one Sc(III) cation binds with **2**, the next Sc(III) cation binds with **2** more strongly. Thus, the positive allosterism operated in the process of the complexation of Sc(III) on **2** in aqueous EtOH.

The cooperativity observed here could be rationalised as follow: Since rare-earth metal cations have multivalent coordination ability, they can favourably coordinate with two or more side chains of the polymer **2**. So the cations are able to be a bridge between the side chains. It could be meaningless if such the bridge was thrown between the side chains of adjacent two pyridine units because the distance between the units was kept by the rigidity of acetylene bonds. Therefore, the coordination bridge would be thrown between the side chains of the pyridine units with a separation of one helix pitch, stabilising the helical conformation. After one bridge was built, subsequent bridging would become favourable, because other pyridine units also get nearer one another to show the positive allosterism. In the one side chain of **2**, there is a chiral centre nearby the amide group. In the case the bridging by the rare-earth metal cations is influenced by chiral environment, the selective stabilisation to recognise either right- or left-handed helical structure to induce strong CDs.

IR and ¹H NMR studies for the complexation

The spectral change of IR absorption caused by the addition of $\text{Sc}(\text{OTf})_3$ was studied to explore which functional group of **2** works as a coordination site. The samples for IR measurements were prepared by drop-casting CHCl_3 solutions of the polymer **2** with or without $\text{Sc}(\text{OTf})_3$ on an NaCl plate. In the absence of $\text{Sc}(\text{OTf})_3$, the polymer **2** showed IR absorption bands at 1654 cm^{-1} for the amide carbonyl group and at 1541 cm^{-1} for the pyridine rings (Fig. 7, blue). The presence of $\text{Sc}(\text{OTf})_3$ made the band for the amide carbonyl group shifted to 1635 cm^{-1} , whereas the band for the pyridine rings was observed at 1541 cm^{-1} without meaningful shift (Fig. 7, red). This finding suggests that Sc(III) cation prefers to coordinate to the amide group in the polymer **2**.

The chemoselectivity of the coordination of Sc(III) on **2** was further studied by $^1\text{H NMR}$ measurements using diacetylenic **14** (Fig. 8) as a model compound, showing a signal for the amide *N-H* proton at 7.35 ppm in $\text{CDCl}_3/\text{DMSO-}d_6 = 300:1$. In the presence of 0.5×10^{-3} and 1.0×10^{-3} M of $\text{Sc}(\text{OTf})_3$, the chemical shift of the signal was observed at 7.36 and 7.38 ppm, respectively, with a small downfield shift (Fig. 8). On the other hand, the chemical shifts for the *C-H* protons at ethynyl groups, pyridine ring, and ethylene glycol side chain kept constant by the addition of $\text{Sc}(\text{OTf})_3$. These IR and $^1\text{H NMR}$ experiments indicate that Sc(III) cation tends to interact with the amide groups, probably carbonyl oxygen atoms, of the polymer **2** preferably.

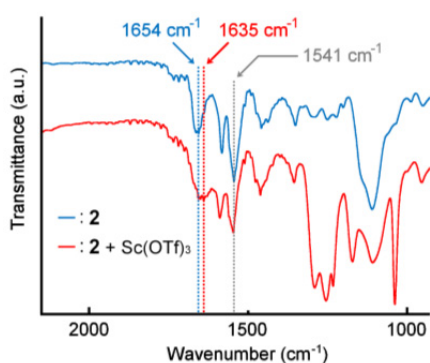


Fig. 7 IR spectra of polymer **2** (blue) without $\text{Sc}(\text{OTf})_3$ and (red) with $\text{Sc}(\text{OTf})_3$ (0.5 eq to unit conc of **2**) casted on an NaCl plate. **2** ($M_n = 5.3 \times 10^4\text{ g mol}^{-1}$, $M_w = 1.0 \times 10^5\text{ g mol}^{-1}$), NaCl.

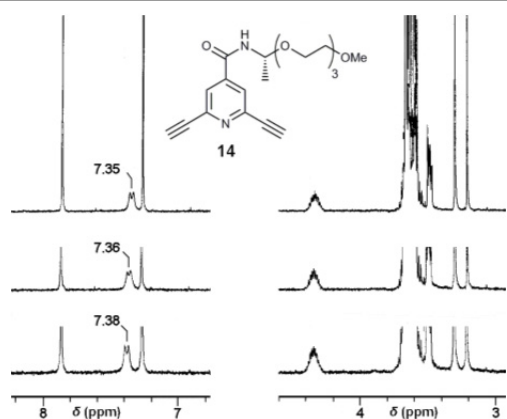


Fig. 8 The additive effect of $\text{Sc}(\text{OTf})_3$ on $^1\text{H NMR}$ (300 MHz) spectrum of diacetylene **14**. The chemical shifts for the amide proton shifted downfield by the addition of $\text{Sc}(\text{OTf})_3$. (a) **14** (1.0×10^{-2} M); (b) **14** (1.0×10^{-2} M) + $\text{Sc}(\text{OTf})_3$ (5.0×10^{-4} M); (c) **14** (1.0×10^{-2} M) + $\text{Sc}(\text{OTf})_3$ (1.0×10^{-3} M). Conditions: 300 MHz, $\text{CDCl}_3/\text{DMSO-}d_6 = 300:1$, $23\text{ }^\circ\text{C}$.

Conclusions

We prepared a new type of *meta*-ethynylpyridine polymer **2** with amphiphilic amide side chains having chiral centres. The polymer **2** was soluble in a variety of solvents and showed weak CD by itself. When the additive effects of metal salts on **2** were examined in water, several kinds of salts were found to enhance the positive CD band around 360 nm with hypochromism in UV-vis spectra. The additive effects of rare-earth metal salts, especially $\text{Sc}(\text{OTf})_3$ were noticeable, so that only an equimolar amount of $\text{Sc}(\text{OTf})_3$ was almost enough to bring about the maximum enhancement. These strong CD enhancement and UV-vis hypochromism would be due to the stabilisation of the helical structure of **2** by the coordination of Sc(III) to the amide carbonyl groups of the side chains in the polymer. The titration experiment and Hill analyses of an aqueous EtOH solution of **2** with $\text{Sc}(\text{OTf})_3$ revealed that the cation coordinates with **2** and enhance its CD in a cooperative manner.

Experimental

Preparation of chiral amide-introduced polymer **2** (Typical procedure for synthesis of the polymer **2**)

To a solution of **14** (11 mg, 30 μmol) and **15** (35 mg, 24 μmol) in MeCN (1.2 mL) and H_2O (0.6 mL) was added a mixture of $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (3.1 mg, 3.0 μmol), sodium 2'-(dicyclohexylphosphino)-2,6-diisopropylbiphenyl-4-sulphonate¹⁹ (6.4 mg, 12 μmol), CuI (0.58 mg, 3.0 μmol), and Cs_2CO_3 (47 mg, 0.14 mmol) in MeCN (0.1 mL), H_2O (0.1 mL), and *i*Pr₂NEt (0.2 mL). This reaction mixture was stirred for 3 days at $30\text{ }^\circ\text{C}$ and treated with 3-aminopropyl-functionalised silica gel (9.0 mg). The resulting suspension was filtered, and the filtrate was concentrated by a rotary evaporator. The residue was treated with a Sephadex LH-20 column by using CHCl_3 as eluent. The resulting CHCl_3 solution of crude **2** was diluted with CHCl_3 up to 40 mL, washed with distilled H_2O (20 mL \times 2), and concentrated by a rotary evaporator. The resulting residue was dissolved in distilled H_2O (12 mL), and the aqueous solution was washed with hexane (15 mL), Et_2O (15 mL), and hexane/AcOEt = 3:1 (24 mL) successively. The combined organic layer was concentrated by a rotary evaporator to give a brown viscous oil. This viscous oil was again dissolved in CHCl_3 (1.8 mL), and the solution was poured dropwise into ice-cold Et_2O (18 mL) to give a turbid emulsion, from which **2** was taken up by centrifugation. The obtained product was a brown viscous oil and subjected to preparative GPC (Shodex K-2002 and K-2002.5, eluent; CHCl_3) to divide it into several fractions. The weight yield of **2** was 30 mg (64% by weight, the total amount of the fractions (1), (2), and (3) in

Fig. S9 in ESI†). The fraction eluted at earlier retention time (the fraction (2) in Fig. S9, $M_n = 5.3 \times 10^4 \text{ g mol}^{-1}$, 9.8 mg, 21% yield by weight) was brought to the following analyses. ^1H NMR (CDCl_3 , 300 MHz) δ 1.32 (br d, 3n H), 3.29 (br s, 3n H), 3.36 (br s, 3n H), 3.48–3.90 (br m, 40n H), 4.18–4.26 (br m, 2n H), 4.30–4.42 (br m, n H), 7.20 (br s, 2n H), 8.03 (br s, 2n H); IR (neat) ν 3346, 2918, 2872, 1662, 1654, 1579, 1541 cm^{-1} . The molecular weights of the fractions of the polymer **2** were evaluated by analytical GPC using TOSOH TSKgel G2000HHR and TSKgel G3000HHR columns with a DMF solution of 0.1 M LiBr as eluent. In this report, four fractions from four lots (Table S1 in ESI†) were applied as a substrate.

Notes and references

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† Electronic Supplementary Information (ESI) available: Figs. S1–S9, Table S1, experimental details of the synthetic route to **2**, and ^1H and ^{13}C NMR spectra for compounds **4**, **5**, **8**, **12–15**, and **2**. See DOI: 10.1039/b000000x/

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