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KINETIC SWITCHING OF ACHIRALITY/CHIRALITY MEMORIZATION OF *META*-ETHYNYLPYRIDINE POLYMER BY COORDINATION OF Cu(II) OUTSIDE THE POLYMER

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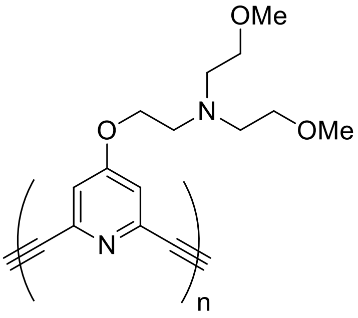
Abstract – Memorization of achirality and chirality of *meta*-ethynylpyridine polymer with amino side chains was actualized by cross-linking with $Cu(OTf)_2$ as a precursor. When β-D-glucopyranoside and $Cu(OTf)_2$ were added to the coordinative polymer in this order, a CD band was induced around 340 nm and enhanced by Cu(II)-coordination. On the other hand, in the case $Cu(OTf)_2$ and β-D-glucopyranoside were added to the polymer in this order, only a weak CD band was induced because achirality was memorized before the addition of the glucoside. For the chiral helical complex with enhanced CD, a chiral memorization effect was assured by the addition of β-L-glucopyranoside causing very slow decay of the CD band.

Dedicated to Professor Masakatsu Shibasaki on the occasion of his 70th birthday

Poly- and oligo(arylene ethynylene)s are one class of molecular devices consisted of sp^2- and sp-atoms.[1,2] Among them, several kinds of curved derivatives such as *meta*- and *ortho*-poly(arylene ethynylene)s have been known to fold into helices, being called as helical foldamers.[2,3] From a viewpoint of host-guest chemistry, helical foldamers possessing heterocyclic coordination sites inside the helix are attractive as host devices for incorporating guest molecules. Occasionally the sense of helices can be biased by the chiral guests and detected by circular dichroism (CD) spectroscopy.[4]

Our group has investigated poly- and oligo(2,6-pyridylene ethynylene), *meta-ethynylpyridine polymers and oligomers*, in which pyridine rings are linked at their 2,6-positions with acetylene bonds.[5] These molecules can associate with saccharides[6] by multipoint hydrogen bonding between pyridine-N and saccharide-OH groups to form a helical complex. Then the chirality of the guest was translated into the chirality of the helix, showing a Cotton effect. So far, we have developed these helical gadgets to improve their functionality, and one strategy is stabilization of the helical structure by cross-linking at the side chains.[7–10] Several types of cross-linking methods have been investigated, for example, covalent bond by alkene metathesis,[7] mechanical bond by rotaxane and pseudorotaxane,[8] and metal-coordination.[9,10] Among these, this article deals with a polymer **1** possessing Cu(II)-coordination sites at each pyridine unit.[9] This polymer associated with alkyl glucoside guests and formed a biased helical complex to show characteristic induced CD. And this induced CD could be enhanced by the addition of $Cu(OTf)_2$ to the mixture of **1** and glucoside, suggesting stabilization of the helical structure (Figure 1).[9]



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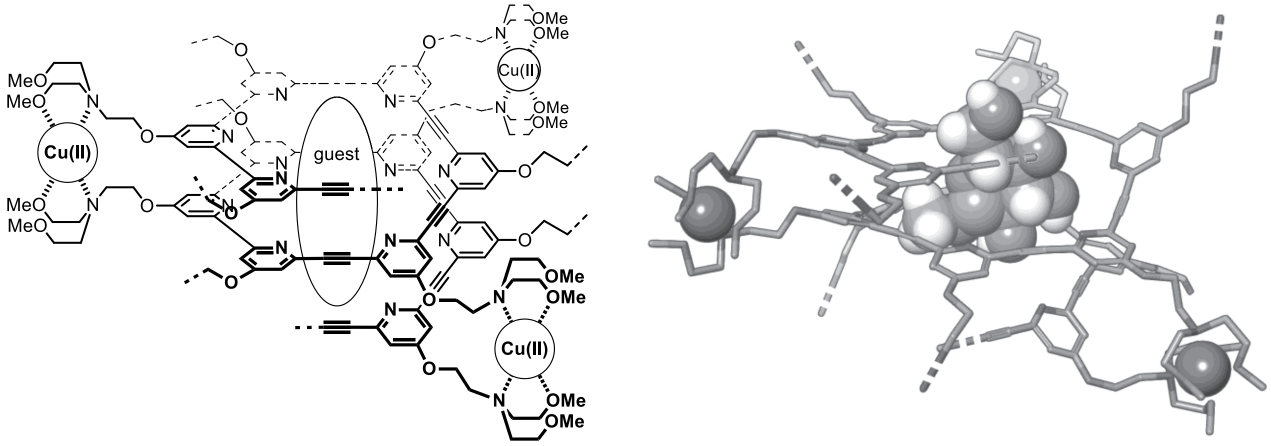
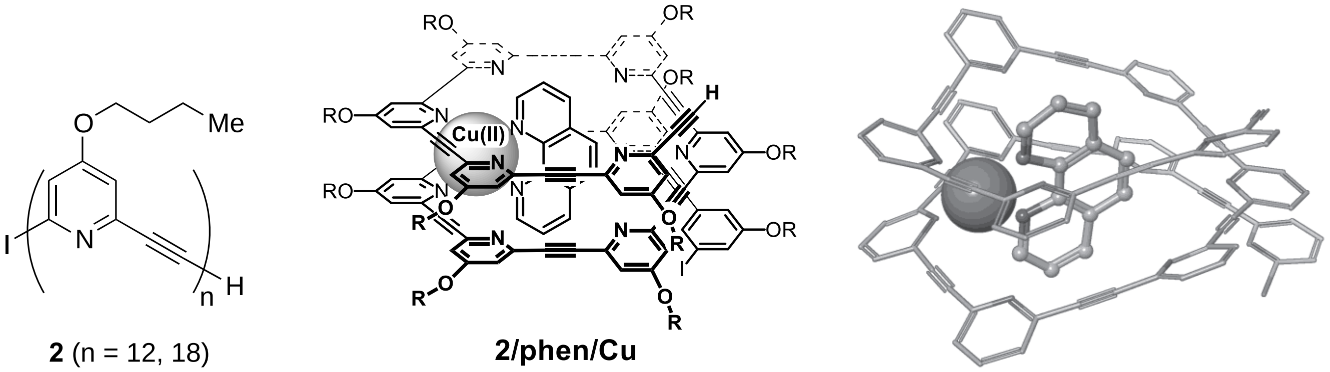


Figure 1. (upper) *meta*-Ethynylpyridine polymer **1** possessing coordination sites at each pyridine unit. (lower) Schematic illustrations for stabilized helix of **1** cross-linked by Cu(II) from outside the helix. Three cross-links are drawn here and one glucose guest is incorporated within the helix.

Not only thermodynamic helix stabilization, but also kinetic helix stabilization can be expected. In general, kinetic stabilization of chirality have been actualized as a chiral memory effect.[11,12] Also in the chemistry of helical compounds, chiral memory effects have been reported by several groups.[13,14]

During the course of our *meta*-ethynylpyridine compounds, a chiral memory effect has been observed. Treatment of oligomer **2** (Figure 2) with octyl β-D-glucopyranoside (**β-D-Glc**, Figure 3) induced a CD band around 340 nm and the subsequent addition of $Cu(OTf)_2$ enhanced the CD band. Interestingly, when *o*-phenanthroline was added to the resulting helical complex **2/β-D-Glc/Cu** to replace **β-D-Glc** with the achiral bidentate ligand, the chirality of the helix was preserved, and even after *β*-L-glucopyranoside (***β*-L-Glc**, Figure 3) was added to that mixture **2/phen/Cu**, CD could be observed for up to 18 days. This chiral memory effects was considered to be caused by Cu(II)-coordination inside the helix (Figure 2).[15]

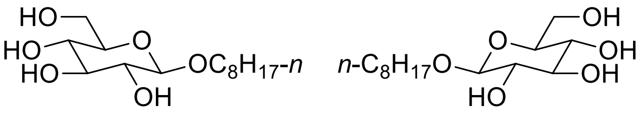
These results about **2** encouraged us to revisit the chemistry of **1**, and herein we report a chiral memory effect observed on **1**, and the effect could be kinetically on/off-switched by the addition of Cu(OTf)$_2$.



2 (n = 12, 18)

2/phen/Cu

Figure 2. (left) *meta*-Ethynylpyridine oligomer **2**. (center and right) Schematic illustrations of helical complex **2/phen/Cu**, cross-linked from inside the helix by Cu(II) and phenanthroline, showing a chiral memory effect (ref 15).



***β*-D-Glc**

***β*-L-Glc**

Figure 3. Structure of octyl *β*-D-glucopyranoside (***β*-D-Glc**) and octyl *β*-L-glucopyranoside (***β*-L-Glc**)

The synthetic route to the polymer **1** was previously reported[9] and the GPC fractions of $M_n = 1.3 \times 10^4$, 2.1×10^4, and 2.7×10^4 g/mol were used in this study. When ***β*-D-Glc** (up to 4.0×10^{-3} M) was added to a solution of **1** (1.0×10^{-3} M, unit concentration) in CH_2Cl_2, an induced CD band appeared around 339 nm (Figure 4A). The shape of this band was typical one to indicate the formation of chiral helical complexes of *meta*-ethynylpyridine polymers with saccharides.[5,7–10] Therefore, here it was indicated that **1** associated with ***β*-D-Glc** to form a chiral helical structure as well. The CD titration experiment with ***β*-D-Glc** to **1** was performed and gradual increase of the CD was observed.[16] The titration curve from CD at 339 nm could be fitted with a 1:1 binding isotherm (Figure 4B). By a curve-fitting analysis, the formal association constant K_a' was estimated as $(1.2 \pm 0.2) \times 10^3$ M^{-1}.

As reported in our previous report[9] the addition of Cu(OTf)$_2$ to the mixture of **1** and ***β*-D-Glc** caused Cotton effect around 340 nm (Figures 4C, broken line). Here we changed the order of the addition Cu(OTf)$_2$ and ***β*-D-Glc**. Unexpectedly, the resulting CD spectra was much different to the previous case.

A CD band appeared around 341 nm but it was very small (Figure 4C, solid line) compared to that observed in the previous case. It is obvious that this differences came from a kinetic reason, and likely because the polymer **1** was fixed by Cu(II)-coordination at an achiral structure other than helix or a racemate of a helical structure.

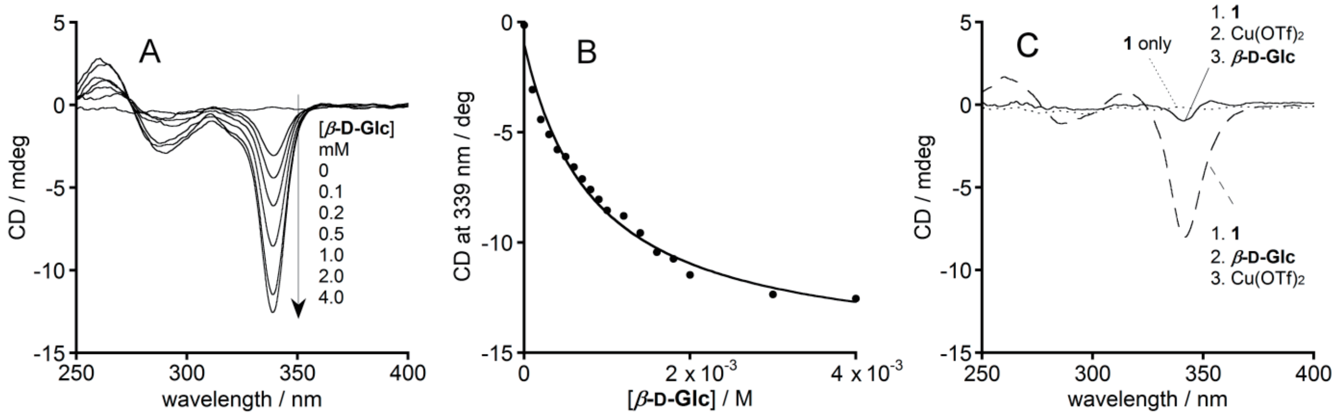


Figure 4. The change of CD spectra of **1** during the addition of ***β*-D-Glc** (A) in the absence of Cu(OTf)$_2$. Conditions: **1** (M_n = 2.7 × 10^4 g/mol, unit conc. = 1.0 × 10^{-3} M), ***β*-D-Glc** (0 to 4.0 × 10^{-3} M), CH_2Cl_2, 25 °C, path length = 1 mm. (B) A titration curve drawn from the changes of CD at 339 nm in the Figure 4A. The line is fitted curve assuming 1:1 binding. (C) The change of CD spectra of **1** after the addition of (solid line) (i) Cu(OTf)$_2$ then (ii) ***β*-D-Glc**, and (broken line) (i) ***β*-D-Glc** then (ii) Cu(OTf)$_2$ as reported in ref 9. Dotted line is CD spectrum of **1**. Conditions: **1** (M_n = 1.3 × 10^4 g/mol, unit conc. = 1.0 × 10^{-3} M), Cu(OTf)$_2$ (5.0 × 10^{-4} M), ***β*-D-Glc** (2.0 × 10^{-3} M), CH_2Cl_2, 25 °C.

Thus, we found one example in which Cu(II) inhibited chiral induction on helical structure, in other word, memorization of achirality. Next we examined the possibility of **1**/guest/Cu(OTf)$_2$ system for memorizing chirality by using a pair of enantiomers, ***β*-D-Glc** and ***β*-L-Glc** (Figure 3).

As mentioned above, when ***β*-D-Glc** (1.2 × 10^{-3} M) was added to a solution of **1** (unit conc. = 1.0 × 10^{-3} M) in CH_2Cl_2, a CD band was induced around 339 nm. To this mixture, ***β*-L-Glc** (equimolar to ***β*-D-Glc**) was added, and as a result it was observed that the CD band induced by ***β*-D-Glc** was cancelled off as soon as the addition of ***β*-L-Glc**, thus chiral memory effect was not observed without Cu(II). Now Cu(OTf)$_2$ (5.0 × 10^{-4} M) was added to a mixture of ***β*-D-Glc** (1.2 × 10^{-3} M) and **1** (1.0 × 10^{-3} M, unit conc.) in CH_2Cl_2, and subsequently ***β*-L-Glc** (equimolar to ***β*-D-Glc**) was added to the CD-active mixture.[17] The time-course change of CD at 344 nm was pursued, and the CD band could be observed still over one week (Figure 5). This is a chiral memory effect similar to the previous results in the case of **2** treated with Cu(OTf)$_2$ (Figure 2).[15] The major different between the cases of **1** and **2** was that the helix from **1** was cross-linked from outside of the helix, and **2** was from inside of the helix.

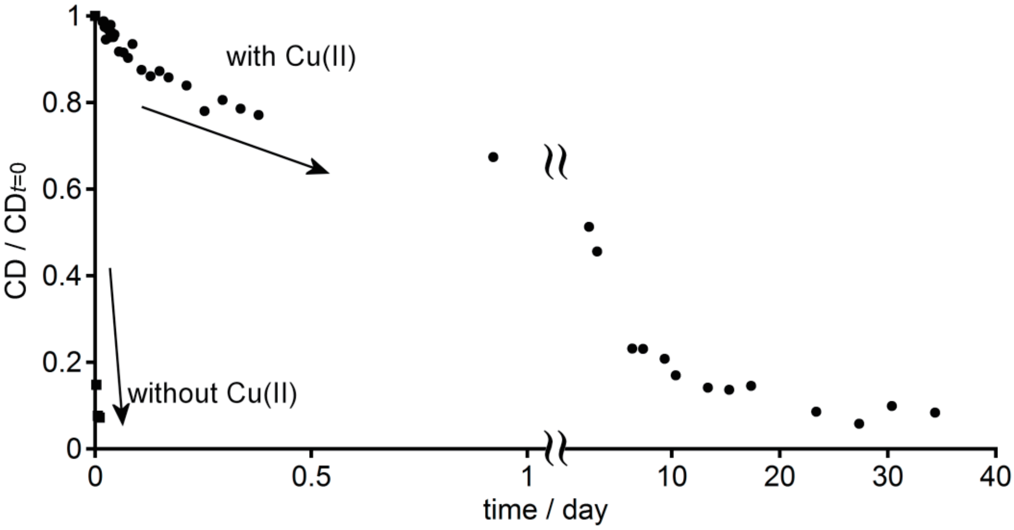


Figure 5. Time-course changes of CD after the addition of ***β*-L-Glc** to the mixture of **1** and ***β*-D-Glc** with or without Cu(OTf)$_2$. (circle) With Cu(OTf)$_2$. CD at 344 nm was observed. (square) Without Cu(OTf)$_2$. CD at 338 nm was observed. Conditions: **1** (M_n = 2.1 × 10^4 g/mol, unit conc. = 1.0 × 10^{-3} M), ***β*-D-Glc** (1.2 × 10^{-3} M), Cu(OTf)$_2$ (5.0 × 10^{-4} M), CH$_2$Cl$_2$, 25 °C, path length = 1 mm. ***β*-L-Glc** (1.2 × 10^{-3} M) was added to this mixture (t = 0) and pursued the CD.

In summary, chiral memory effects for *meta*-ethynylpyridine polymer **1** possessing coordinative amino side chains were studied by cross-linking with Cu(OTf)$_2$ as a coordination precursor. A mixture of **1** and Cu(OTf)$_2$ hardly received chiral induction by the addition of ***β*-D-Glc** because that an achiral or a racemic state would be fixed by Cu(II)-coordination beforehand. This is much different result by the corresponding experiment in which the addition order of Cu(OTf)$_2$ and ***β*-D-Glc** was exchanged to observe enhancement of the CD band. When ***β*-L-Glc** was added to a mixture of **1** and ***β*-D-Glc**, CD was immediately cancelled. On the other hand, after treatment with Cu(OTf)$_2$ for a mixture of **1** and ***β*-D-Glc**, CD cancellation by the addition of ***β*-L-Glc** became very slow in a manner of chiral memory, thus kinetic switching of memorization by Cu(II) was actualized here.

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16. Procedure of the CD titration experiment to evaluate the formal association constant of **1** with ***β*-D-Glc** in the absence of Cu(II): To a solution of **1** ($M_n = 1.3 \times 10^4$ g/mol, unit conc. = 1.0×10^{-3} M) in CH_2Cl_2 (anhydrous grade) was titrated ***β*-D-Glc** (0 to 4.0×10^{-3} M) at 25 °C. The plot of ellipticity at 339 nm against [***β*-D-Glc**] was subjected to a curve-fitting analysis assuming 1:1 binding to give formal association constant $K_a' = (1.2 \pm 0.2) \times 10^3$ M^{-1} ($R = 0.99208$). The applied equation was as follows:
$$\theta_{obs} = \frac{\theta_{11}}{2K_a'[\mathbf{1}]_0}\left[1 + K_a'[\mathbf{1}]_0 + K_a'[\boldsymbol{\beta}\textbf{-D-Glc}]_0 - \left\{(1 + K_a'[\mathbf{1}]_0 + K_a'[\boldsymbol{\beta}\textbf{-D-Glc}]_0)^2 - 4{K_a'}^2[\mathbf{1}]_0[\boldsymbol{\beta}\textbf{-D-Glc}]_0\right\}^{\frac{1}{2}}\right]$$
17. Experimental procedure to study the chiral memory effect of **1** with Cu(II): A mixture of **1** ($M_n = 2.1 \times 10^4$ g/mol, unit conc. = 1.0×10^{-3} M), ***β*-D-Glc** (1.2×10^{-3} M) and $Cu(OTf)_2$ (5.0×10^{-4} M) in CH_2Cl_2 (anhydrous grade) was set in a quartz cell (path = 1 mm) and stood overnight at 25 °C. To this mixture ***β*-L-Glc** (1.2×10^{-3} M) was added and the change of CD spectrum was monitored at 25 °C.