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Chiral Induction in Phenanthroline-Derived Oligoamide Foldamers: An Acid- and Base-Controllable Switch in Helical Molecular Strands

Hai-Yu Hu,[†,‡] Jun-Feng Xiang,[†] Yong Yang,[†] and Chuan-Feng Chen*[,†]

Beijing National Laboratory for Molecular Sciences, Center for Chemical Biology, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, China, and Graduate School, Chinese Academy of Sciences, Beijing 100049, China

cchen@iccas.ac.cn

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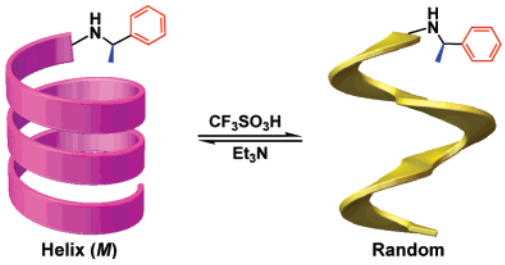
ABSTRACT



A series of phenanthroline-derived oligoamides bearing a chiral (*R*)-phenethylamino end group were synthesized that displayed chiral helical induction and subsequently formed one-hand helical foldamers in solution. Moreover, an acid- and base-controllable switch in the helical molecular strands was observed, which has been demonstrated by NMR, UV–vis, and circular dichroism spectroscopy.

The macromolecular and supramolecular helicities are one of the most important and unique chiralities as exemplified by biological macromolecules, such as proteins, nucleic acids, and their helical assemblies.[1] In recent years, artificial helical foldamers with a predominantly one-hand helix sense have attracted great interest not only for their mimicking biological macromolecules such as DNA and proteins, but also for their possible applications in material sciences including enantioselective adsorbents and catalysts.[2] However, the successful examples of one-hand artificial helical foldamers still remain rare,[3] especially in aromatic oligoamide-based systems.[4,5]

It is known that the folding/unfolding molecular motion between a helical state and a random form is an important natural phenomenon in biology,[6] but related artificial systems

[†] Institute of Chemistry, Chinese Academy of Sciences.
[‡] Graduate School, Chinese Academy of Sciences.

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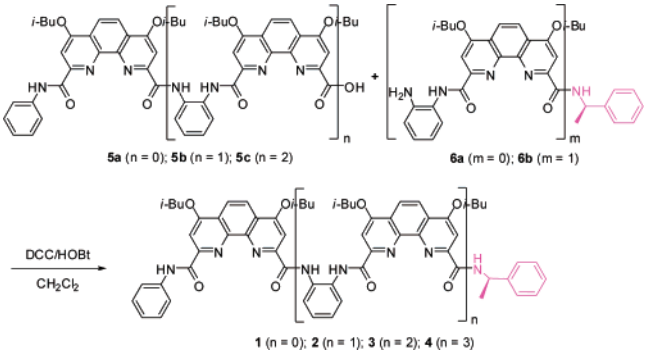
are limited.[7] One particular interest example is the oligopyridine-dicarboxamide system reported by Huc and Lehn's groups, which showed protonation-induced molecular motions from one helical structure to another.[8] Recently, we reported a new class of aromatic oligoamides based on phenanthroline dicarboxamides, which exhibited well-defined helical secondary structures in solution and in the solid state.[9] As part of our continuing work, we herein report a series of new phenanthroline-derived oligoamides bearing a chiral (*R*)-phenethylamino end group, which shows the chiral helical induction and subsequently forms one-hand helical foldamers in solution. Moreover, such helical molecular strands also display an acid and base controlled structural switching process, which is demonstrated by NMR, UV−vis, and CD spectroscopy.

Synthesis of oligoamides **1**−**4** is depicted in Scheme 1.

Scheme 1. Synthesis of Oligoamides **1**−**4**



By the reaction of the appropriate monoacid **5**[9] with (*R*)-1-phenylethanamine (**6a**) in dichloromethane in the presence of dicyclohexylcarbodiimide (DDC) and 1-hydroxybenzotriazole (HOBt), oligoamides **1**−**3** were synthesized in excellent yields. Following the similar method, oligoamide **4** was synthesized by the condensation reaction of monoacid **5c** and monoamine **6b**. The structures of new compounds were confirmed by the ^{1}H NMR, ^{13}C NMR, MS spectra, and elemental analysis.[10]

Similar to the oligo(phenanthroline dicarboxamide)s we previously reported,[9] the ^{1}H NMR and 2D NOESY studies clearly supported formation of helical secondary structures of oligoamides **2**−**4** in solution.[10] The UV/vis absorption spectra further confirmed the intramolecular interactions of the helical foldamers. As expected, a hypochromic effect with an increased number of phenanthroline rings was observed, indicating that helical ordering and $\pi-\pi^*$ stacking of the phenanthroline units in **2**−**4** might exist.[10,11]

It is noteworthy that the ^{1}H NMR spectra of the oligoamides **2**−**4** showed only one set of signals in $CDCl_3$ at ambient temperature, which implied that they could exist in one-hand helical conformation in solution. These results are different from those of the chiral induction in quinoline-derived oligoamide foldamers, in which an equilibrium between *R*-P and *R*-M distereomers existed.[4]

The chirality induction in the oligoamide foldamers was further studied by circular dichroism (CD) spectroscopy.[12] Consequently, the CD spectra of **1**−**4** were recorded in CH_3CN and shown in Figure 1. In contrast with the silent CD

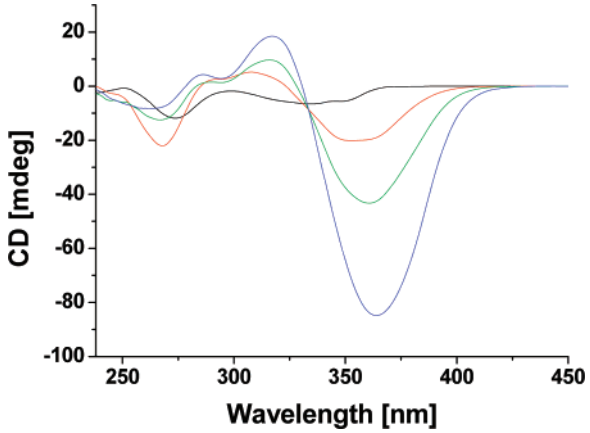


Figure 1. CD spectra of the molecular strands **1** (black), **2** (red), **3** (green), and **4** (blue) in CH_3CN ($c = 2 \times 10^{-5}$ M).

spectra of helical oligomers bearing no chiral groups and the CD spectrum of **1** with no chirality induction, the helical foldamers **2**−**4** show a positive and then a negative CD band between 300 and 420 nm due to the $\pi-\pi^*$ electronic transition of the phenanthroline moiety, which indicates that the oligoamides may have a predominant one-handed (*R*-M) helical structure.[13] Furthermore, the increase in the molar CD ($\Delta\epsilon$) from **2** to **4** (factor of 3.8) is much larger than the increase in UV/vis absorption coefficient ϵ (factor of 1.8), which displays a marked amplification of the optical activity in **3** and **4**.

Oligoamides **2**−**4** fold into stable helical structures arising from the strongly preferred conformation of phenanthroline dicarboxamide units, which is stabilized by intramolecular hydrogen bonds as shown in the X-ray crystal structure of phenanthroline dicarboxamide (Figure 2a). We speculated

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(10) See the Supporting Information.

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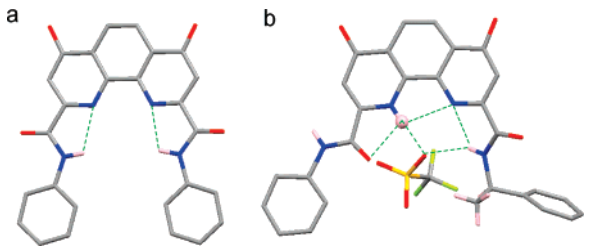

Figure 2. Crystal structures of (a) phenanthroline dicarboxamide and (b) **1**−TfOH, green lines denote the intra- and intermolecular hydrogen bonds. Isobutyl chains and hydrogen atoms not involved in the hydrogen bonds are omitted for clarity.

that protonation of the phenanthroline might be expected to cause a conformational inversion, so as to allow formation of new hydrogen bonds between the carbonyl groups and the phenanthrolinium protons. As a result, when a suspension of oligoamides **1**−**4** in acetonitrile was treated with triflic acid separately, the corresponding protonated species of **1**−**4** formed immediately. The subsequent compounds became soluble, and the color of the solutions changed from colorless to light yellow.

We further obtained single crystals of protonated species of **1** from the mixture solution of **1** in CH_3CN in the presence of excess triflic acid by a slow evaporation at room temperature, and the X-ray crystal structure provided a direct evidence for the formation of the phenanthrolinium salt. As shown in Figure 2b, it was interestingly found that the protonation occurred only on one of the nitrogen atoms of the phenanthroline group, which resulted in a 180° rotation about the adjacent arylamide linkage due to the intramolecular $NH^+\cdots OC$ hydrogen bond.

The acid and base controllable switch in oligoamide **2** with a helix extending to one complete turn was first studied by the ^1H NMR method. As shown in Figure 3, when 1 equiv

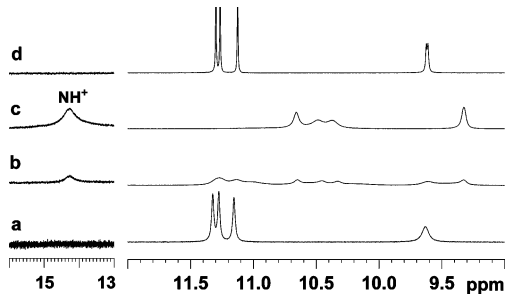

Figure 3. Partial ^1H NMR spectra (10 mM, 600 MHz, $CDCl_3$, 283 K) of (a) free **2**, (b) protonated species **2**-(H^+), and (c) **2**-(H^+)$_2$ upon the addition of triflic acid and (d) deprotonated species **2** upon the addition of Et_3N.

of triflic acid was added into the solution of **2** in $CDCl_3$, a very unshielded signal at 14.2 ppm for the phenanthrolinium proton was observed, while each of the amide protons showed two sets of broadening signals (Figure 3b). The results suggested that the partial protonation occurred on one of the two phenanthroline groups in **2**. Furthermore, it was found that the amide protons in **2** only showed a set of signals while the signal for NH^+ protons became stronger upon the addition 2 equiv of triflic acid (Figure 3c), which implied the formation of the protonated species **2**-(H^+)$_2$ as a random structure. The addition of another equivalent triflic acid into the above solution did not cause any new amide proton signals,[10] indicating no further protonation occurred on the species **2**-(H^+)$_2$. When the above mixture was treated with 3 equiv of Et_3N, it was interestingly found that the proton signals[14] went back to the original positions of **2** (Figure 3d), indicating the helical structure of **2** restored.

The reversibility of the protonation process was also corroborated by absorption spectra experiments. The UV−vis spectrum of oligomer **2** in CH_3CN displays absorption maxima at 321 nm due to the $\pi-\pi^*$ electronic transition of the phenanthroline moiety. Treating oligomer **2** with 1 equiv of triflic acid, the UV spectrum showed a new band at the longer wavelength, which indicated the formation of the protonated species **2**-H^+. Addition of another 1 equiv of triflic acid resulted in an increase of the new band, which suggested the formation of the protonated species **2**-(H^+)$_2$. Addition of more triflic acid did not cause further obvious spectral changes.[10] However, neutralization of the above solution with Et_3N could result in the restored absorption spectra (Figure 4). Correspondingly, the color of the solution was changed

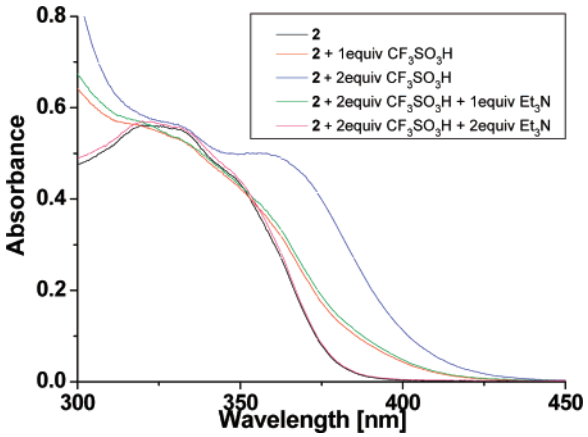

Figure 4. UV−vis spectra of **2** (2×10^{-5} M) in CH_3CN (black), protonated species **2**-(H^+) (red), **2**-(H^+)$_2$ (blue) upon the addition of triflic acid and deprotonated species **2**-(H^+) (green) and **2** (pink) upon the addition of Et_3N.

from light yellow back to its original colorless. The results provided another evidence for the acid and base controlled structural switch in the helical molecular strand.

(14) The sharper signals of the NH protons may be ascribed to the formation of more stable helical structure of **2** in the polar and/or protonic solvent. Similar phenomena see reference 9.

The structural switch in the helical molecular strand was further demonstrated by the CD spectroscopy. As shown in Figure 5, the solution of **2** in CH_3CN showed a strong

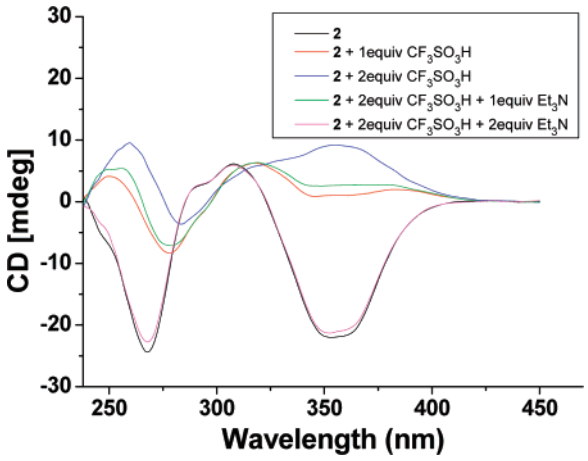

Figure 5. CD spectra of **2** (2×10^{-5} M) in CH_3CN (black), protonated species **2**-(H^+) (red) and **2**-$(H^+)_2$ (blue) upon the addition of triflic acid and deprotonated species **2**-(H^+) (green) and **2** (pink) upon the addition of Et_3N.

negative Cotton effect at 353 nm, which was almost disappeared upon the addition of 1 equiv of triflic acid. The results implied a transition from the helical conformation of **2** to the unfolded, undulating ribbon of protonated species **2**-(H^+). However, when another equivalent triflic acid was added into the above solution, a weak positive CD signal was observed, which might be attributed to the protonation-induced molecular motion resulting in an unregular right-hand helical structure of species **2**-$(H^+)_2$. Furthermore, neutralization of the above solution with Et_3N showed the restoration of the CD signal of oligoamide **2**, which is in agreement with the acid and base controllable switch. Similar to **2**, the longer helical molecular strands **3** and **4** also displayed the acid and base controllable structural switching, which was demonstrated by the UV−vis and CD spectroscopy.[10]

In conclusion, we have synthesized a series of new phenanthroline-derived oligoamides bearing a chiral (*R*)-phenethylamino end group, and found that they could show chiral helical induction and subsequently form one-hand helical foldamers in solution. Moreover, we have also found that the protonation of phenanthroline group could occur on one of the two nitrogen atoms, and a subsequent acid and base controllable switch in the phenanthroline dicarboxamide-based helical molecular strands could be obtained, which has been demonstrated by NMR, UV−vis and circular dichroism spectroscopy. The results presented here will be helpful to develop new one-hand synthetic helical foldamers, and also find potential applications in the artificial molecular machines.

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Supporting Information Available: Synthesis and characterization data of the new compounds. Copies of ^1H and ^{13}C NMR spectra. TOCSY and NOESY spectra of **2** and UV−vis and CD spectra of oligoamides **1**−**4** in the presence of acid and base. X-ray crystallographic files (CIF) for phenanthroline dicarboxamide and **1**−TfOH. This material is available free of charge via the Internet at http://pubs.acs.org.

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