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Conformation of S-shaped aromatic imide foldamers and their induced circular dichroism

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Abstract

Conformation of aromatic foldamers possessing three aromatic rings in a sequence of anthracene–phenylene–anthracene linked with iminodicarbonyl was examined. Their folding structures were confirmed by single crystal X-ray analysis. Two conformations, straight-zigzag and helically-zigzag conformations, were found depending on the substituents at the imide nitrogen atom. Induced circular dichroism originated in the interaction of the upper and bottom anthracene moieties was observed both in solution and in the solid state.

Folding structures are commonly observed in biomolecules and numerous studies have been carried out on proteins related to this. As artificial folding structures[1] we are interested in aromatic foldamers since an array of linearly combined aromatic moieties can be created. In this columnar array, aromatic moieties are forced to face each other in a π–π stacking mode, which results in a unique optical property. Aromatic foldamers with dynamic behaviors, such as photoswitchable[2] and solvocontrollable[3] ones, have been developed recently. Aromatic foldamers can be categorized into two types depending on their shapes, namely, helical and zigzag types. Most of them belong to a helical type as a mimic of peptides with mainly amide[4] or urea linkers.[5] An ethynyl linker is also used for helical type foldamers.[6] For zigzag type foldamers, several functionalities, amide,[7] sulfonamide,[8] urea,[9] guanidine,[10] and methylene,[11] are utilized as linkers. In some cases, zigzag type foldamers were formed in charge transfer duplex.[12] Concerning the way of zigzag folding, there are two types of folding, straight-zigzag and helically-zigzag types. In a straight-zigzag type, aromatic moieties are oriented toward the same direction and each aromatic moiety is stacked right above or below the neighboring one. On the contrary, folding occurs helically in a way that aromatic moieties are rotationally oriented in a helically-zigzag type. Recently, we have shown that iminodicarbonyl is also a potential linker for the construction of aromatic zigzag type foldamers.[13] Due to the intrinsic nature of the iminodicarbonyl linker, electrostatic dipole repulsion of the two carbonyl moieties, two substituents have a tendency to locate parallel to each other. In our work the straight-zigzag type folding structure was found in the foldamer where aromatic moieties were aligned in a sequence of a naphthalene–anthracene–naphthalene[13b] while the helically-zigzag folding structure was observed in a naphthalene–naphthalene–naphthalene system.[13a] They were confirmed by single crystal X-ray analysis. To induce CD, it is essential to have a helically folded structure. An advantage of an iminodicarbonyl linker is an easy introduction of a chiral group on the imide nitrogen atom, which could result in the formation of folded and helically chiral structure. In this letter, we report on our latest findings on the folding conformation of the S-shaped aromatic imide foldamers and their induced CD spectra.

Three S-shaped aromatic imide foldamers **1**, **2**, and **3** possessing *i*-propyl, (*S*)-1-phenylethyl, and (*S*)-1-(1-naphthyl)ethyl as substituents at the imide nitrogen atom,

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respectively, were prepared (Fig. 1). Synthetic procedures of them are cited in Supplementary data. All of them gave crystals suitable for single crystal X-ray analysis. A straight-zigzag type folded conformation was found in **1** (Fig. 2). The distance between the anthracene and the phenylene rings is 3.61 Å and that between the two anthracene rings is 7.21 Å. There is a center of symmetry in this molecule. Therefore, the two anthracene rings are perfectly parallel to each other. Three aromatic rings are well stacked.

In contrast to **1**, a helically-zigzag folding conformation was observed in the crystal structure of **2** (Fig. 3). Although the compound has a chiral auxiliary, a pair of helically-zigzag diastereomeric conformers exists in a unit cell of the crystal. They are stacked in an alternative way to form a columnar structure in which an array of aromatic rings are created.[14] There are two ways of helicities to be designated in respect to the short and long axes of the two anthracene rings. So the molecule has two helicities depending on this designation. The distances between the anthracene and the phenylene rings in the conformers are slightly different. They are in the range 3.35–3.65 Å. The intermolecular distance between the two anthracene rings

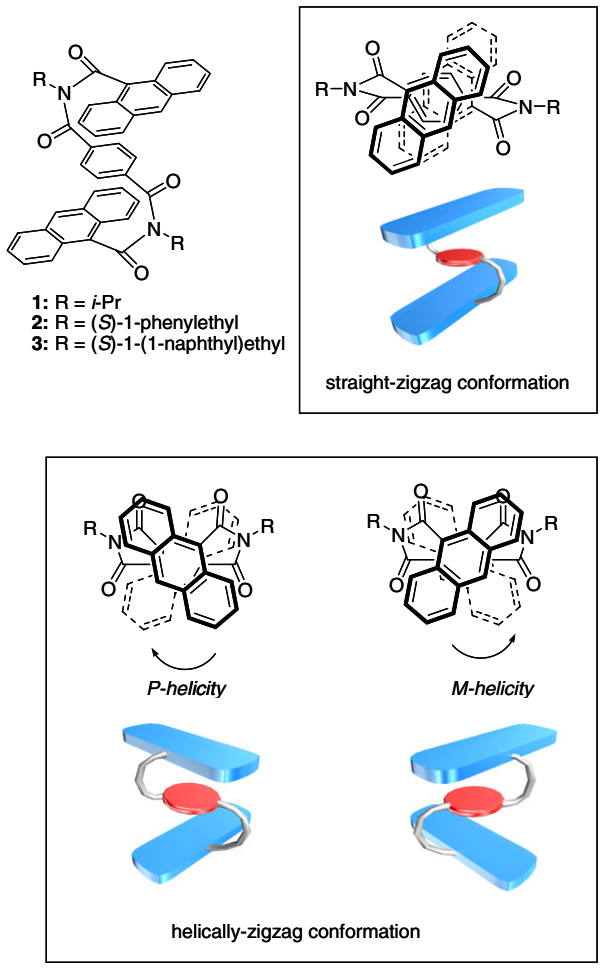


Fig. 1. Three possible conformations of S-shaped aromatic imide foldamers. Helicities presented here are based on the long axes of the two anthracene rings.

is 3.80 Å. The intramolecular distances between the two anthracene rings are 6.76 and 6.85 Å for conformers A and B, respectively. The distances are shorter than that of **1**. The torsion angles between the axes of two anthracene rings are 70° for both conformers. The angles created by the two anthracene ring planes are 12° and 8° for the conformers A and B, respectively.

Different crystal structure was observed for foldamer **3** with bulky substituent at the imide nitrogen atom. It gave a chiral crystal (space group: $P2_1$) with a single helically-zigzag conformer in it as shown in Figure 4. The intramolecular distances between the two anthracene rings (6.79 Å) are similar to that of **2**. The torsion angle between them is 69° which is also similar to that of **2**. Two anthracene rings are not exactly parallel. The angle between their ring planes is 10°.

All the compounds have S-shaped folding structures, but the way of folding is different. A straight-zigzag type folding is not suitable to show induced CD. No exciton coupling is expected for this folding since two anthracene rings are aligned perfectly parallel with the torsion angle of 0°. To confirm that two anthracene rings are the origin of induced CDs and also the chiral auxiliary at the imide nitrogen atom is not the direct source of them, structurally similar concave-shaped molecules **4** and **5** were synthesized. Single crystal X-ray structure of **5** showed that the molecule is structurally equivalent to the half of the molecule of **3** (Fig. 5). The distance between the centroids of the anthracene and phenyl rings is 3.55 Å, which is similar to that of **3**. Figure 6 shows the CD spectra of **2**, **3**, **4**, and **5** in CH_3CN. Only **3** has a relatively large CD signal in the region over 350 nm. The *M*-helicity indicated by the sign of Cotton effect (–) in this region agrees to the helicity in respect to the short axes of the anthracene rings observed in its single crystal X-ray structure. The band at 337 nm might be the intrinsic CD originated in the chiral (*S*)-1-(1-naphthyl)ethyl group. The concave shaped imide **5** with the same chiral group showed the CD signal only in the similar shorter wavelength region due to the intrinsic CD of this chiral group. The lack of induced CD in a longer wavelength region in **5** indicates that the induced CD in **3** could be originated in the exciton coupling of anthracene–anthracene chromophores in their short axes. In contrast to **3**, imide **2** showed a very weak intensity CD signal. We expected no induced CD for **2** since its single crystal X-ray analysis showed that the compound had two helical conformers in an equi-amount in its crystal. Therefore, the cancellation of CD by both helical conformers took place. However, they are not enantiomers. Their geometries are quite similar but not exactly the same. The CD spectrum of **2** exhibited that its spectral shape was almost the mirror image of that of **3** though its intensity was fairly small. The results suggest that the *P*-helical conformer in respect to the short axes of the anthracene moieties might have a slightly larger signal intensity than that of the conformer with *M*-helicity. Almost no CD signal was observed for **4**. There is no significant solvent effect on

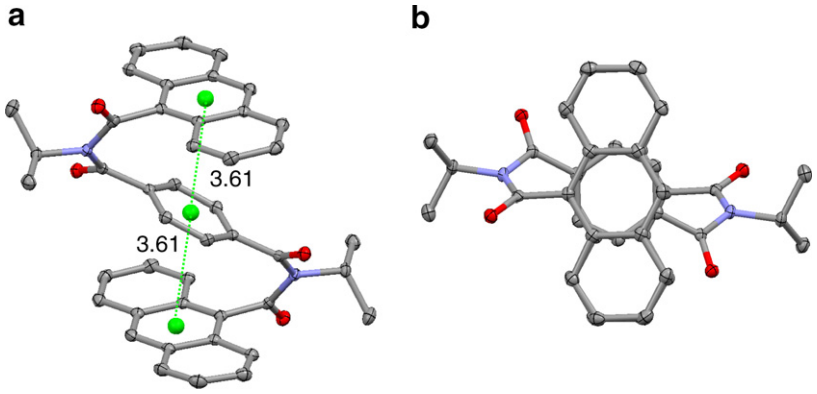


Fig. 2. Single crystal X-ray structure of **1** showing straight-zigzag conformation, a side view (a) and a top view (b). For clarity the hydrogen atoms are omitted. Distances between the centroids of aromatic rings are presented in Å. The distance (centroid–centroid) between the two anthracene rings is 7.21 Å.

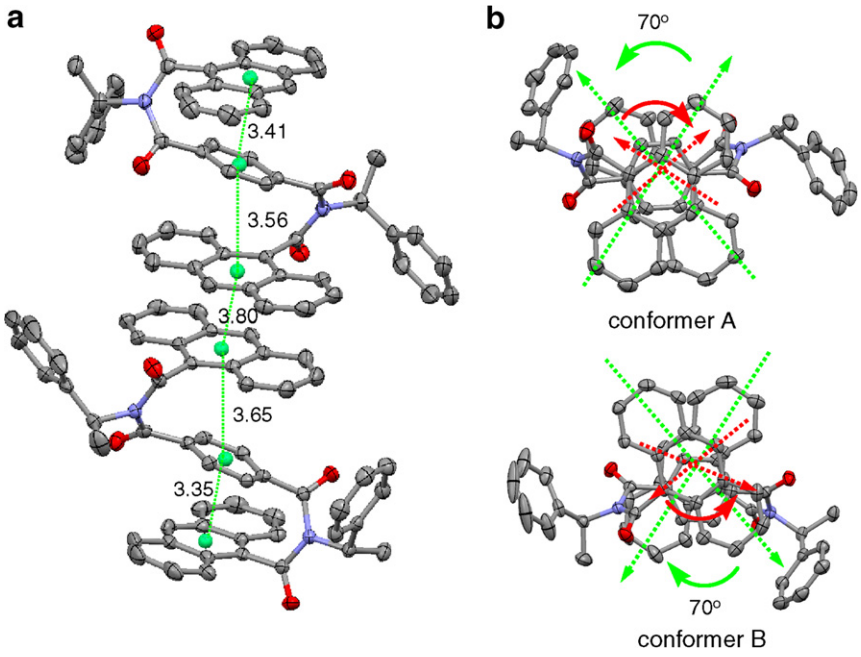


Fig. 3. Single crystal X-ray structure of **2** showing two helically-zigzag folding conformers, a side view (a) and a top view (b). For clarity the hydrogen atoms are omitted. Distances between the centroids of the aromatic rings are presented in Å. Green and red arrows indicate the helicity in respect to the long and short axes of the anthracene rings, respectively.

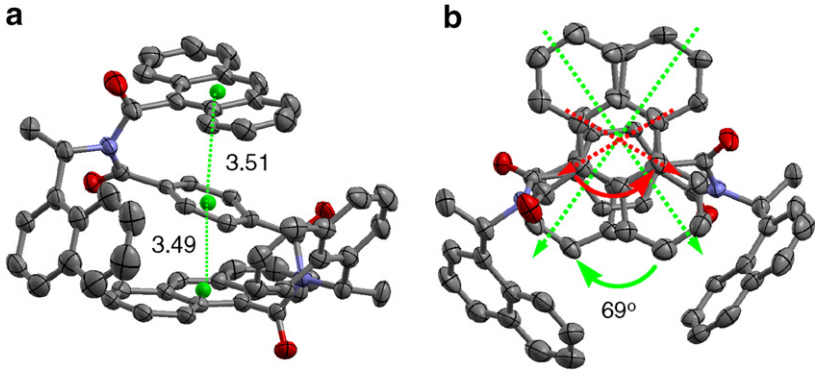


Fig. 4. Single crystal X-ray structure of **3** showing a helically-zigzag conformation, the side view (a) and the top view (b). For clarity hydrogen atoms are omitted. Distances between the centroids of aromatic rings are presented in Å. The distance (centroid–centroid) between two anthracene rings is 6.74 Å. Green and red arrows indicate the helicity in respect to the long and short axes of the anthracene rings, respectively.

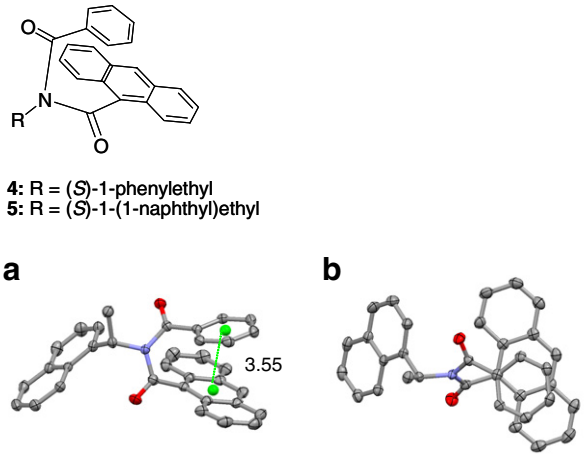


Fig. 5. Single crystal X-ray structure of **5** showing a concave-shaped folding conformation, the side view (a) and the top view (b). For clarity the hydrogen atoms are omitted and the distance between the centroids of aromatic rings are presented in Å.

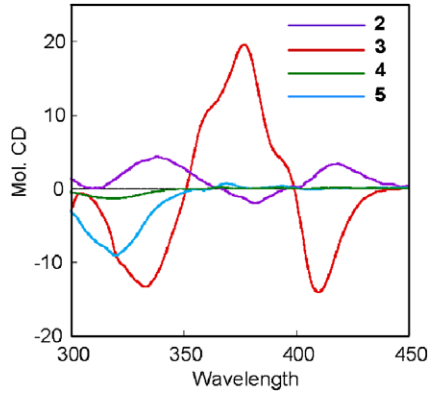


Fig. 6. CD spectra of **2**, **3**, **4**, and **5** in CH_3CN.

CD. Figure 7a shows the CD spectrum of **3** in four different solvents, EtOH, CH_3CN, $CHCl_3$, and toluene. Similar tendency was reported on naphthalene-based foldamers.[13a]

To verify our interpretation of the induced CD in solution, we examined the CD spectra of **2** and **3** in the solid

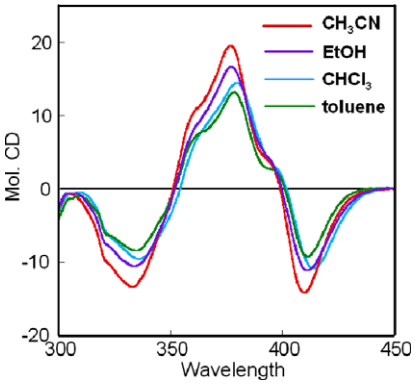


Fig. 7a. CD spectra of **3** in four different solvents showing almost no significant solvent effects.

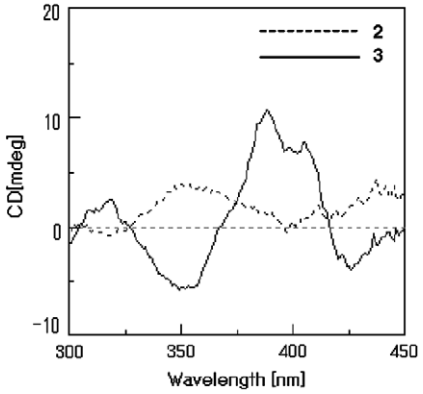
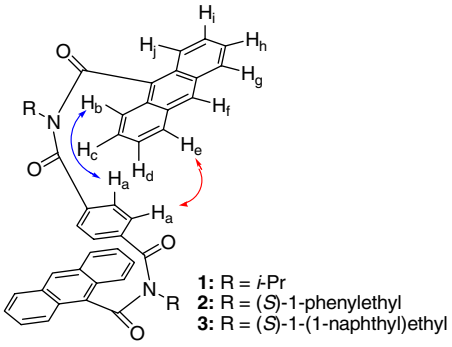


Fig. 7b. CD spectra of **2** and **3** in the solid state.

state (Fig. 7b). The solid-state CD spectra were recorded on their KBr pellets. The pellets were prepared by grinding ca. 1 mg of imide and ca. 10 mg of dry KBr powder followed by pressing under vacuum. Their signs are the same as those in solution. The results indicated that the helical chirality of **3** in the crystalline state was retained even in solution after dissolving it. The CD signal of **2** was weak with the same sign as in solution opposite to that of **3**.

The S-shaped conformations of **1**–**3** in solution were confirmed from their ^1H NMR spectra and NOE experiments. The assignments of the protons in ^1H NMR spectra were carried out based on their HH–COSY spectra. Table 1 shows the chemical shifts of the protons H_a–H_f of the main chain aromatic rings. Strong shielding was observed

Table 1
^1H NMR chemical shifts (δ) of the main chain aromatic ring protons of the S-shaped foldamers in $CDCl_3$



^1H	1	2	3
a	5.46 (s)	5.23 (s)	4.40 (br s)
b	7.71 (d, $J = 8.5$)	7.61 (d, $J = 8.5$)	8.18 (d, $J = 8.0$)
c	7.38 (t, $J = 7.0$)	7.30–7.36[a]	7.83 (t, $J = 7.4$)
d	7.25 (t, $J = 7.0$)	7.20 (t, $J = 7.3$)	7.64–7.74[a]
e	7.58 (d, $J = 8.0$)	7.30–7.36[a]	8.39 (d, $J = 8.5$)
f	7.92 (s)	7.82 (s)	7.64–7.74[a]
g	e	7.43–7.54[a]	6.99–7.04[a]
h	d	7.06 (t, $J = 7.3$)	6.33 (t, $J = 7.6$)
i	c	7.14 (t, $J = 7.5$)	6.47 (t, $J = 7.7$)
j	b	7.30–7.36[a]	7.30 (d, $J = 8.4$)

[a] Overlapped with other peaks. Blue and red arrows show NOEs observed in **1** and **2**, and **3**, respectively.

for the phenylene ring proton H_a, which could have originated in the sandwich structure of the S-shaped foldamers. The shielding was most efficient in **3**. Probably, the H_a is shielded by the naphthyl moiety of the naphthylethyl group as well. The NOE experiments attested the S-shaped conformation of **1**–**3** in solution. Positive NOEs were observed between the protons H_a and H_b (the blue arrow in Table 1), and the protons H_a and H_e (the red arrow in Table 1) for **1** and **2**, and **3**, respectively. The distances between the protons H_a and H_b in the crystal structures obtained by their single crystal X-ray analysis are 2.95 and 2.97 Å for **1** and **2**, respectively. The distance between the protons H_a and H_e in **3** in its crystal structure is 4.16 Å.

We have shown that the two types of zigzag folding, straight-zigzag and helically-zigzag type folding, exist in the same aromatic folding system depending on the substituents at the imide nitrogen atom. Middle-range induced CD was observed efficiently between the upper and bottom anthracene rings.

Crystallographic data of the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 663006 for **1**, No. 663007 for **2**, No. 663008 for **3**, and No. 663009 for **5**. Copies of this information can be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB21EZ, UK (fax: +44 1223 336033; e-mail deposit@ccdc.cam.ac.uk or web: http://www.ccdc.cam.ac.jk).

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Supplementary data

Supplementary data (preparation of materials, copies of NMR spectra, and ORTEP of **1**, **2**, **3**, and **5**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.12.034.

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