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Aromatic Foldamers with Iminodicarbonyl Linkers: Their Structures and Optical Properties

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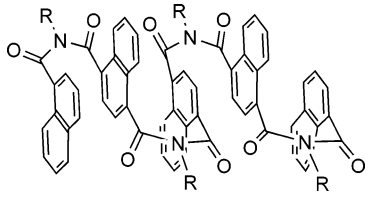

Carboxamides possessing naphthalene rings connected by multiple iminodicarbonyl linkers were synthesized. These molecules forced the naphthalene rings to be placed in the positions facing each other, and they form helical foldamers both in solution and in the crystalline state. Their folding structures were investigated by single-crystal X-ray analysis and ^{1}H NMR spectroscopy. Their absorption and fluorescence spectra showed a red shift as the number of naphthalene moieties increased. This remarkable change is based on the intramolecular interaction between naphthalene moieties. Helicity of the foldamer can be controlled by the introduction of chiral auxiliaries at imide nitrogen atoms, which results in an observation of induced circular dichroism.

Introduction

Oligomers and polymers which adopt specific compact conformations by folding are named foldamers.[1] In solution, folding structures are very common in biopolymers,[2] mostly proteins. The well-defined three-dimensional structures produced by folding, which furnish the appropriate location of active sites in the molecules, are responsible for their sophisticated chemical functions.[3] In the past decade, attempts have been made extensively to prepare synthetic foldamers for the exploration of behavior analogous to that of biopolymers. Hydrogen bonding, electrostatic forces, and hydrophobic forces are utilized for their construction. Hydrogen bonding is the major force for foldamers derived from β-peptides.[4] It is also utilized for the construction of folding structures in the crystalline state.[5] Metal or nonmetal complexes are frequently used to prepare helical structures.[6] Aromatic $\pi-\pi$ stacking is efficient for the creation of aromatic foldamers.[7]

We have been interested in aromatic foldamers because the construction of multilayered aromatic structures can be possible using folding patterns. Unique optical properties can be expected from these multilayered structures

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(1) (a) Gellman, H. S. *Acc. Chem. Res.* **1998**, *31*, 173−180. (b) Li, A. D. Q.; Wang, W.; Wang, L.-Q. *Chem.−Eur. J.* **2003**, *9*, 4594−4601. (c) Schmuck, C. *Angew. Chem., Int. Ed. Engl.* **2003**, *42*, 2448−2452.

(2) (a) Eaton, W. A.; Muñoz, V.; Thompson, P. A.; Henry, E. R.; Hofrichter, J. *Acc. Chem. Res.* **1998**, *31*, 745−753. (b) Hill, R. B.; Raleigh, D. P.; Lombardi, A.; Degrado, W. F. *Acc. Chem. Res.* **2000**, *33*, 745−754. (c) Brooks, C. L., III. *Acc. Chem. Res.* **2002**, *35*, 447−454. (d) Straub, J. E.; Guevara, J.; Huo, S.; Lee, J. P. *Acc. Chem. Res.* **2002**, *35*, 473−481. (e) Wang, W.; Wan, W.; Zhou, H.-H.; Niu, S.; Li, A. D. Q. *J. Am. Chem. Soc.* **2003**, *125*, 5248−5249.

(3) (a) Nakano, T.; Okamoto, Y. *Chem. Rev.* **2001**, *101*, 4013−4038. (b) Lan, T.; McLaughlin, L. W. *Biochemistry* **2001**, *40*, 968−976.

(4) (a) Cubberley, M. S.; Iverson, B. L. *Curr. Opin. Chem. Biol.* **2001**, *5*, 650−653. (b) Corbin, P. S.; Zimmerman, S. C.; Thiessen, P. A.; Hawryluk, N. A.; Murray, T. J. *J. Am. Chem. Soc.* **2001**, *123*, 10475−10488. (c) Patch, J. A.; Barron, A. E. *Curr. Opin. Chem. Biol.* **2002**, *6*, 872−877. (d) Huck, B. R.; Fisk, J. D.; Guzei, I. A.; Carlson, H. A.; Gellman, S. H. *J. Am. Chem. Soc.* **2003**, *125*, 9035−9037. (e) Jiang, H.; Léger, J.; Dolain, C.; Guionneau, P.; Huc, I. *Tetrahedron* **2003**, *59*, 8365−8374.

(5) (a) Moriuchi, T.; Nishiyama, M.; Yoshida, K.; Ishikawa, T.; Hirao, T. *Org. Lett.* **2001**, *3*, 1459−1461. (b) Garric, J.; Léger, J.; Grelard, A.; Ohkita, M.; Huc, I. *Tetrahedron Lett.* **2003**, *44*, 1421−1424.

(6) (a) Piguet, C.; Bernardinelli, G.; Hopfgartner, G. *Chem. Rev.* **1997**, *97*, 2005−2062. (b) Albrecht, M. *Chem. Rev.* **2001**, *101*, 3457−3497. (c) Thünemann, A. F.; Kubowicz, S.; Burger, C.; Watson, M. D.; Tchebotareva, N.; Müllen, K. *J. Am. Chem. Soc.* **2003**, *125*, 352−356.

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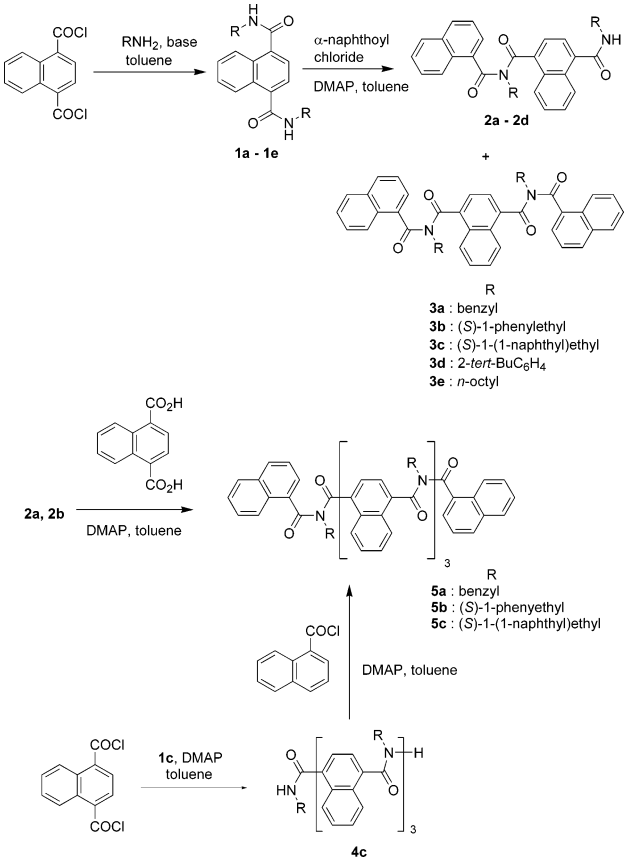
due to aromatic interactions in a vertical direction.[8] A choice of linker to connect arene moieties might be important to regulate folding. Several aromatic foldamers were constructed by connecting arenes with urea,[9] guanidine,[10] or amide[11] linkers. These linkers prefer to have a cis conformation, which promotes the settling of the molecule in a folding conformation.[12] Even methylene could be a linker to afford π-stacked polyfluorene foldamers.[13] Folded aromatic hetero duplexes were reported recently[14] in which a donor−acceptor interaction played an important role. Solvophobically-driven generation of helical foldamers from phenylene ethynyl oligomers has been extensively studied by Moore et al.[15] A folding, crowded aromatic was applied for the construction of a folded columnar superstructure.[16]

During the course of our study on the photochemical cycloaddition reaction of aromatic carboxamides in the solid state,[17] we have found that an iminodicarbonyl group was a nice linker to place two aromatic moieties in the positions facing each other. Considering this fact, we planned to use an iminodicarbonyl group as a linker to prepare aromatic oligomers, and we examined the folding conformations and optical properties of these oligomers in both solution and in the crystalline state. Folding might be operated in a helical way. Therefore, an introduction of chiral groups could possibly generate chiral helical foldamers. Efficient induction of chirality in helical polymers is a current topic.[18] It is interesting to survey chirality amplification effected by multilayered aromatic structures.[19]

SCHEME 1. Synthesis of Naphthalene-Based Foldamers



Results and Discussion

Aromatic imides possessing one, two, three, and five naphthalene rings connected at their α-position with iminodicarbonyl linkers were prepared by sequential standard amidation reactions as presented in Scheme 1. To examine the steric effects of substituents on foldamer generation, chiral ((*S*)-1-phenylethyl and (*S*)-1-(1-naphthyl)ethyl), bulky (2-*tert*-butylphenyl), and long (*N*-octyl) substituents were introduced at the nitrogen atoms. Pentamers **5a** and **5b** were prepared from the corresponding dimers and naphthalene 1,4-dicarbonyldichloride. However, a similar procedure was not applicable for **5c**. Pentamer **5c** was obtained from the reaction of **4c** with 1-naphthoyl chloride. Single crystals were obtained for **3a**−**3e**; however, **5a**−**5c** were obtained as a powder.

Conformation in the Crystalline State. Single-crystal X-ray analysis was carried out for monoclinic or orthorhombic crystals of **3a**−**3e**. General crystallographic data are shown in Table 1. The X-ray structure of **3a** is presented in Figure 1. The single crystal of **3a** contains a chloroform molecule (the solvent used for recrystalli-

(7) (a) Marsella, M. J.; Kim, I. T.; Tham, F. *J. Am. Chem. Soc.* **2000**, *122*, 974−975. (b) Nakamura, K.; Okubo, H.; Yamaguchi, M. *Org. Lett.* **2001**, *3*, 1097−1099. (c) Adams, H.; Hunter, C. A.; Lawson, K. R.; Perkins, J.; Spey, S. E.; Urch, C. J.; Sanderson, J. M. *Chem.−Eur. J.* **2001**, *7*, 4863−4878. (d) Cubberley, M. S.; Iverson, B. L. *J. Am. Chem. Soc.* **2001**, *123*, 7560−7563. (e) Zhao, D.; Moore, J. S. *J. Org. Chem.* **2002**, *67*, 3548−3554. (f) Huc, I. *Eur. J. Org. Chem.* **2004**, 17−29.

(8) (a) Oda, M.; Nothofer, H.-G.; Lieser, G.; Scherf, U.; Meskers, S. C. J.; Neher, D. *Adv. Mater.* **2000**, *12*, 362−365. (b) Oda, M.; Nothofer, H.-G.; Scherf, U.; Šunjić, V.; Richter, D.; Regenstein, W.; Neher, D. *Macromolecules* **2002**, *35*, 6792−6798.

(9) (a)Yamaguchi, K.; Matsumura, G.; Kagechika, H.; Azumaya, I.; Ito, Y.; Itai, A.; Shudo, K. *J. Am. Chem. Soc.* **1991**, *113*, 5475−5476. (b) Jørgensen, M.; Krebs, F. C. *J. Org. Chem.* **2002**, *67*, 7511−7518. (c) Lewis, F. D.; Kurth, T. L.; Hattan, C. M.; Reiter, R. C.; Stevenson, C. D. *Org. Lett.* **2004**, *6*, 1605−1608.

(10) (a) Tanatani, A.; Kagechika, H.; Azumaya, I.; Fukutomi, R.; Ito, Y.; Yamaguchi, K.; Shudo, K. *Tetrahedron Lett.* **1997**, *38*, 4425−4428. (b) Tanatani, A.; Yamaguchi, K.; Azumaya, I.; Fukutomi, R.; Shudo, K.; Kagechika, H. *J. Am. Chem. Soc.* **1998**, *120*, 6433−6442.

(11) (a) Winkler, J. D.; Piatnitski, E. L.; Mehlman, J.; Kasparec, J.; Axelsen, P. H. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 743−745. (b) Huc, I.; Maurizot, V.; Gornitzka, H.; Léger, J.-M. *Chem. Commun.* **2002**, 578−579.

(12) Itai, A.; Toriumi, Y.; Saito, S.; Kagechika, H.; Shudo, K. *J. Am. Chem. Soc.* **1992**, *114*, 10649−10650.

(13) Rathore, R.; Abdelwahed, S. H.; Guzei, I. A. *J. Am. Chem. Soc.* **2003**, *125*, 8712−8713.

(14) (a) Gabriel, G. J.; Iverson, B. L. *J. Am. Chem. Soc.* **2002**, *124*, 15174−15175. (b) Yanq, X.; Martinovic, S.; Smith, R. D.; Gonq, B. *J. Am. Chem. Soc.* **2003**, *125*, 9932−9933. (c) Zhou, Q.-Z.; Jiang, X.-K.; Shao, X.-B.; Chen, G.-J.; Jia, M.-X.; Li, Z.-T. *Org. Lett.* **2003**, *5*, 1955−1958. (d) Fedorova, A.; Chaudhari, A.; Ogawa, M. Y. *J. Am. Chem. Soc.* **2003**, *125*, 357−362. (e) Zhao, X.; Jia, M.-X.; Jiang, X.-K.; Wu, L.-Z.; Li, Z.-T.; Chen, G.-J. *J. Org. Chem.* **2004**, *69*, 270−279.

(15) (a) Nelson, J. C.; Saven, J. G.; Moore, J. S.; Wolynes, P. G. *Science* **1997**, *277*, 1793. (b) Cubberley, M.; Iverson, B. *J. Am. Chem. Soc.* **2001**, *123*, 7560−7563. (c) Tanatani, A.; Hughes, T. S.; Moore, J. S. *Angew. Chem., Int. Ed. Engl.* **2002**, *41*, 325−328. (d) Goto, H.; Heemstra, J. M.; Hill, D. J.; Moore, J. S. *Org. Lett.* **2004**, *6*, 889−892.

(16) Zhang, W.; Horoszewski, D.; Decatur, J.; Nuckolls, C. *J. Am. Chem. Soc.* **2003**, *125*, 4870−4873.

(17) Kohmoto, S.; Ono, Y.; Masu, H.; Yamaguchi, K.; Kishikawa, K.; Yamamoto, M. *Org. Lett.* **2001**, *3*, 4153−4155.

(18) (a) Applequist, J.; Bode, K. A.; Appella, D. H.; Christianson, L. A.; Gellman, S. H. *J. Am. Chem. Soc.* **1998**, *120*, 4891−4892. (b) Yashima, E.; Maeda, K.; Okamoto, Y. *Nature* **1999**, *399*, 449−451. (c) Feringa, B. L.; Delden, R. A.; Koumura, N.; Geertsema, E. M. *Chem. Rev.* **2000**, *100*, 1789−1816. (d) Yu, Z.; Wan, X.; Zhang, H.; Chen, X.; Zhou, Q. *Chem. Commun.* **2003**, 974−975. (e) Goto, H.; Zhang, H. Q.; Yashima, E. *J. Am. Chem. Soc.* **2003**, *125*, 2516−2523.

(19) Yashima, E.; Maeda, K.; Nishimura, T. *Chem.−Eur. J.* **2004**, *10*, 42−51.

TABLE 1. Crystallographic Data for Compounds 3a, 3b, 3c, 3d, and 3e

	3a[a]	**3b**[b]	**3c**[c]	**3d**	**3e**
formula	$C_{48}H_{34}N_2O_4 \cdot CHCl_3$	$C_{50}H_{38}N_2O_4 \cdot {}^1/_2C_4H_8O$	$C_{58}H_{42}N_2O_4 \cdot C_4H_8O_2$	$C_{54}H_{46}N_2O_4$	$C_{50}H_{54}N_2O_4$
crystal system	monoclinic	monoclinic	orthorhombic	monoclinic	monoclinic
space group	*C*2/c	*C*2	$P2_12_12_1$	$P2_1/n$	$P2_1/c$
a (Å)	18.836 (3)	19.550(3)	11.2677(19)	22.015(5)	21.571(4)
b (Å)	14.828 (3)	14.449 (2)	16.808(3)	13.7857(8)	10.548(2)
c (Å)	14.441 (3)	14.925 (2)	25.638(4)	14.917(2)	19.756(3)
β (deg)	99.516 (3)	96.767 (3)	90.000	108.93(2)	107.503(3)
V (Å^3)	3978.1 (12)	4186.7 (11)	4855.5(14)	4282(1)	4286(1)
T (K)	150	150	90	298	273
R (F)	0.0777	0.0908	0.0818	0.0534	0.0685

[a] Crystal contains chloroform molecules. [b] Crystal contains THF molecules. [c] Crystal contains ethyl acetate molecules.

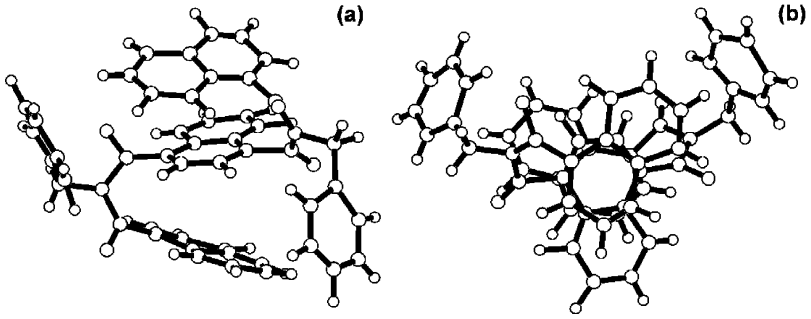


FIGURE 1. Ball-and-stick presentations for **3a** (a) along and (b) perpendicular to the helix axis.

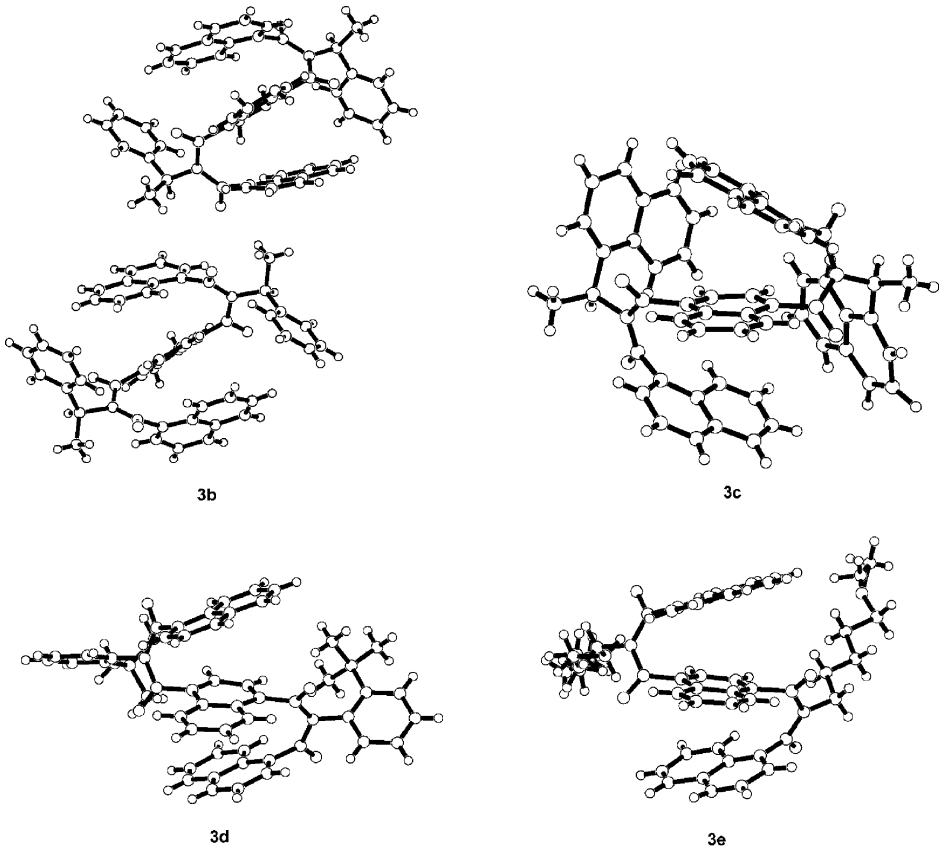
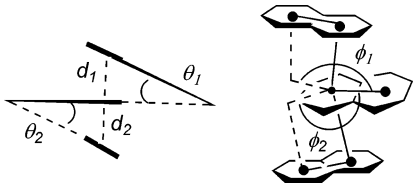


FIGURE 2. Ball-and-stick presentations for **3b**, **3c**, **3d**, and **3e**.

zation), which is omitted in Figure 1. The main chain has a zigzag type structure (Figure 1a). Three naphthalene rings in a main chain are stacked on each other with a neighboring naphthalene ring and spread out radially (Figure 1b). The molecule is folded in a helical way. The X-ray structures of four other trimers, **3b**−**3e** (Figure 2), show that they have similar folding structures independent of substituents at the nitrogen atoms. Because of the disorders originated in the substituents at the nitrogen atom, the *R*-factors for **3b**, **3c**, and **3e** could not

TABLE 2. Folding Parameters for 3a, 3b, 3c, 3d, and 3e Obtained from Their Single Crystal X-ray Structures



	3a	3b	3c	3d	3e
d_1 (Å)	3.5	3.7	3.8	3.5	3.5
d_2 (Å)	3.5	3.7	3.9	3.6	3.6
θ_1 (deg)	25	31	31	21	23
θ_2 (deg)	25	31	37	23	26
ϕ_1 (deg)	137	134	129	138	144
ϕ_2 (deg)	137	134	134	139	135

be reduced sufficiently in their X-ray analyses even at low temperature (150 K for **3a** and **3b** and 90 K for **3c**).

Characteristic folding parameters in the crystalline state are presented in Table 2. The distances between the naphthalene rings (d_1 and d_2) are prescribed as the lengths of centroid to centroid of the benzene rings of naphthalene moieties directly connected to iminodicarbonyl linkers. Angles of plane (θ_1 and θ_2) are defined as the degree of inclination between the two naphthalene π planes. Twisting angles between the naphthalene rings are designated as ϕ_1 and ϕ_2. They are defined as the intersected angles created by the two lines joined between the two centroids of benzene rings of naphthalene moieties. In all five crystal structures, d_1 and d_2 are in the range of 3.5−3.9 Å, which is the typical distance for $\pi-\pi$ stacking.[20] The average values of 134−139° for ϕ_1 and ϕ_2 mean that roughly three naphthalene rings are expected to exist per pitch in longer oligomers.

The X-ray structures of foldamers with chiral substituents at the nitrogen atoms, **3b** and **3c**, showed distinct differences in their crystal structures. Chiral space groups $C2$ and $P2_12_12_1$ were observed for **3b** and **3c**, respectively. In the crystal structure of **3b**, two diastereomeric forms with *P*- and *M*-helicity existed in a ratio of 1:1. In contrast, **3c** showed a single helicity in its crystal structure. It was determined that **3c** possessed *M*-helicity based on the configuration of the chiral substituent, (*S*)-1-(1-naphthyl)ethyl.

Conformation in Solution. To elucidate the conformations of the foldamers in solution, their ^{1}H NMR spectra were examined. The protons H_a (protons at the 2- and 3-positions of the naphthalene moiety) of **1a** were observed at 7.53 ppm in $CDCl_3$. The corresponding H_a signals of **2a** and **3a** were shifted upfield (Figure 3). The assignment of the proton signals was carried out in the following way. For **1a** and **2a**, their signals were assigned from their coupling patterns. The assignment for **3a** was based on HH−COSY and NOE difference spectroscopic measurements. Compound **5a** showed proton signals that were too complicated and broad to be assigned. We tentatively assigned that the signal that appeared in the highest upfield position might be the proton H_a, which should be shielded strongly in the folded conformation. The results suggested that they had folding conformations in solution.[21] As the number of naphthalene moieties increases, shielding caused by them should increase in the folding conformation and the increasing upfield shifts of the protons at the central naphthalene moiety were observed. The folded conformation was also confirmed from NOE in **3a**. The NOEs were observed between the protons H_a-H_d and H_a-H_j, which attested its folded conformation in solution. These NOE relations are shown as arrows in the structure of **3** presented in Table 3. In addition to these ^{1}H NMR data, assignment of all the naphthalene ring protons is also useful to examine their conformation. Table 3 shows the chemical shifts of the naphthalene ring protons for **3a**, **3b**, **3d**, and

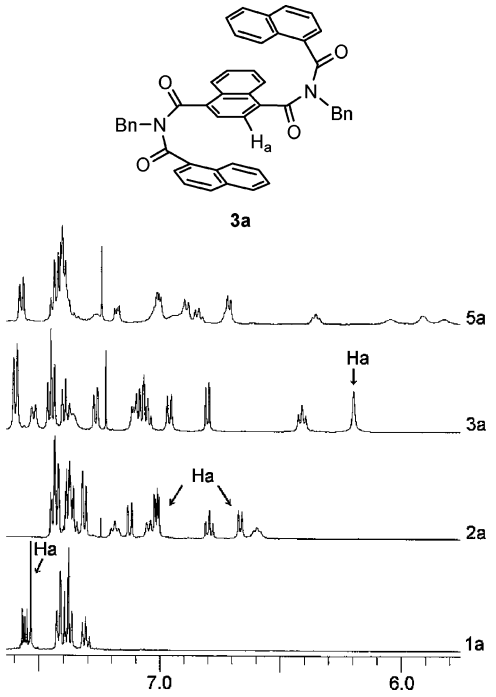
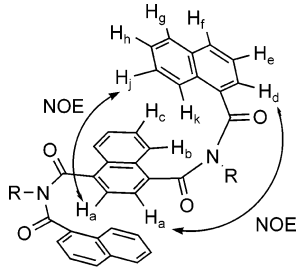


FIGURE 3. Proton chemical shifts of H_a (the protons at the central naphthalene rings of **1a**, **2a**, **3a**, and **5a**) in $CDCl_3$.

TABLE 3. Chemical Shifts of the Naphthalene Protons of 3a, 3b, 3d, and 3e



3

	3a	3b	3d	3e		3a	3b	3d	3e
H_a	6.20	6.41	6.37	6.44	H_f	6.97	6.94	7.02	7.10
H_b	7.37	7.22	7.73	7.46	H_g	7.28	7.38	7.35	7.40
H_c	7.13	7.07	7.39	7.20	H_h	7.06	*a*	7.23	7.25
H_d	6.82	6.94	7.27	6.96	H_i	7.09	*a*	*a*	7.30
H_e	6.43	6.49	6.37	6.54	H_j	7.52	7.68	7.88	7.67

[a] Due to the overlapping of several peaks, the assignment was difficult.

(20) (a) Blatchly, R. A.; Tew, G. N. *J. Org. Chem.* **2003**, *68*, 8780−8785. (b) Aravinda, S.; Shamala, N.; Das, C.; Sriranjini, A.; Karle, I. L.; Balaram, P. *J. Am. Chem. Soc.* **2003**, *125*, 5308−5315.

(21) Krebs, F. C.; Jørgensen, M. *J. Org. Chem.* **2002**, *67*, 7511−7518.

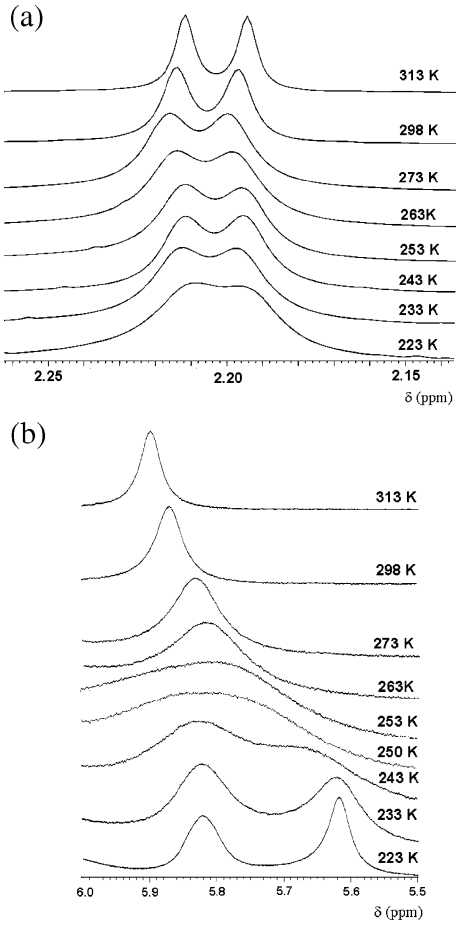


FIGURE 4. Variable temperature ^{1}H NMR spectra of (a) the methyl protons and (b) the proton H_a of **3c** in $CDCl_3$.

3e. Assignment for **3c** was not possible because of its complexity. A similar tendency in the order of chemical shifts was observed for these compounds. The proton H_a appeared in the highest upfield position followed by H_e in the second, and the proton H_j appeared in the lowest downfield position in all five compounds. The results indicate that naphthalene moieties are overlapping each other on their benzene rings when connected with iminodicarbonyl linkers in solution as well as in the solid state.

A variable temperature ^{1}H NMR study on **3c** was carried out in $CDCl_3$. As the temperature was lowered, a broadening of most of the signals was observed. Figure 4a shows the measurements for the doublet corresponding to the methyl signal of the (*S*)-1-(1-naphthyl)ethyl moiety. Coalescence could not be observed at the temperature measured (down to 223 K). However, the signal of proton H_a, the most shielded proton in the central naphthalene ring, finally became two singlet peaks (δ 5.61 and 5.89) in a ratio of 1:1 at 223 K (Figure 4b). The assignment was difficult for other naphthalene ring protons. It showed the coalescence temperature at 250 K. The $\Delta G^{\ddagger}$ at this temperature was calculated to be 12.0 kcal/mol. The results suggest the existence of two stable conformations at this temperature. If diastereomerization (equilibration in helical structures) took place to give the mixture of *M*/*P*-helical structures in a ratio of 1:1, no CD signal would be observed due to a cancellation of the CD signal by that of the opposite helicity. The CD signal of **3c** measured at a similar low temperature (218 K, see Figure 11 in the discussion of CD spectra) was slightly more intense than the one at 298 K. Therefore, it is hard to consider that the helical conformational equilibrium is the major cause of this NMR behavior. *E*/*Z* isomerization of the imide groups might also be excluded, since this isomerization would change the shape of the molecule from the folded conformation to the linear one, which would cause disappearance of its CD signal. Moreover, the proton H_a should appear downfield, since the shielding caused by the folding structure might be canceled out. However, the peak of H_a at 223 K appeared in the same chemical shift region as that at room temperature. The possible explanation for this ^{1}H NMR behavior might be the restricted rotation of the (*S*)-1-(1-naphthyl)ethyl moiety along the C−N bond. At low temperature, two stable rotamers may exist. This restricted rotation may cause neither the helical conformational change nor the unfolding (*E*/*Z* isomerization), and the folding conformation of the molecule remains intact.

Absorption and Fluorescence Spectra. UV−vis absorption and fluorescence spectra of imides were measured in solution and in the solid state. The series of compounds with the same substituent at the nitrogen atom were examined for comparison. Figure 5 shows those spectra for the benzyl series (**1a**, **2a**, **3a**, and **5a**). Compound **1a,** with one naphthalene moiety, showed λ_{max} at 300 nm (chloroform) in its absorption spectrum. However, for **2a**, **3a**, and **5a**, new absorptions appeared as shoulders at 331, 344, and 370 nm, respectively. These new bands might be the results of $\pi-\pi$ interaction of naphthalene moieties in the folding conformations. They showed red shifts with increasing number of naphthalene moieties. An increase of molar extinction coefficients was also observed (**1a**: $\lambda_{max} = 295$ nm, $\epsilon_{max} = 7\,800$; **5a**: $\lambda_{max} = 311$ nm, $\epsilon_{max} = 13\,000$). No concentration dependence was observed on their λ_{max} and ϵ_{max} (10^{-5} to 10^{-4} M). A similar red shift was observed in their absorption spectra in the solid state, which were taken in a reflection mode. This tendency was distinct in the solid state. There is a characteristic difference between their solution and solid-state fluorescence spectra. In chloroform, **1a** showed its emission maximum at 402 nm (excitation wavelength: 300 nm). However, **2a**, **3a**, and **5a** exhibited their emission maxima at nearly the same wavelength, 470 nm, as a single band. In contrast, their fluorescence spectra in the solid state showed two emission bands. Compound **1a** showed the band at 384 nm together with a shoulder at 462 nm. Gradual increase of the shoulder occurred according to the increasing number of naphthalene moieties. Finally, this shoulder became the major emission band of **5a,** which was nearly the same as those of **2a**, **3a**, and **5a** in solution. It is conceivable that intramolecularly formed excimers between naphthalene moieties are responsible for those emission bands at 470 nm. Due to their immobility in crystals, an intramolecular excimer formation might be rather ineffective compared to that in solution, since two naphthalene moieties are twisted about 130−140° in their crystals. As the number of naphthalene moieties increases, the probability of excimer formation might be boosted, which results in a gradual increase of the excimer emission

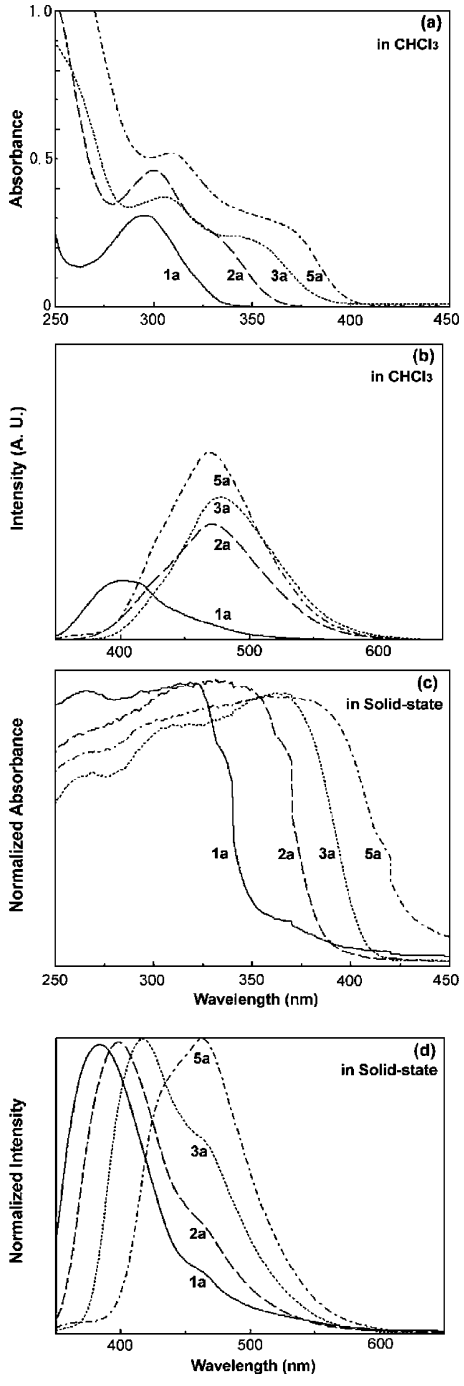


FIGURE 5. Absorption and fluorescence spectra of **1a**, **2a**, **3a**, and **5a**: (a) absorption spectra in $CHCl_3$, 40 μM; (b) fluorescence spectra in $CHCl_3$, 40 μM (excitation wavelength: 300 nm); (c) absorption spectra in the solid state; (d) fluorescence spectra in the solid state (excitation wavelength: 300 nm).

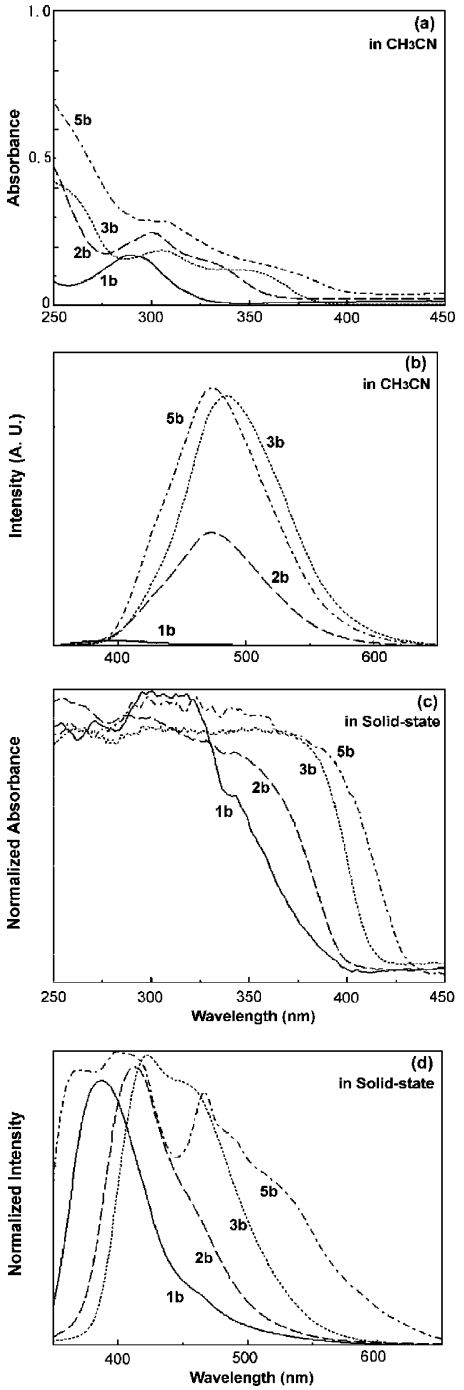


FIGURE 6. Absorption and fluorescence spectra of **1b**, **2b**, **3b**, and **5b**: (a) absorption spectra in CH_3CN, 20 μM; (b) fluorescence spectra in CH_3CN, 20 μM (excitation wavelength: 260 nm); (c) absorption spectra in the solid state; (d) fluorescence spectra in the solid state (excitation wavelength: 300 nm).

intensity. Therefore, the emission corresponding to the excimer becomes almost the sole emission band in **5a**. A similar tendency was observed in acetonitrile and benzene. No solvent effect was observed. Similar results were obtained for the (*S*)-1-phenylethyl series (**1b**, **2b**, **3b**, and **5b**) and the (*S*)-1-(1-naphthyl)ethyl series (**1c**, **2c**, **3c**, and **5c**), as shown in Figures 6 and 7.

To demonstrate that the red shifts observed in the absorption and fluorescence spectra are irrelevant to the aromatic substituents at the imide nitrogen atom, the absorption and fluorescence spectra of the *N*-octyl derivative (**3e**) were investigated (Figure 8). The absorption and fluorescence spectra of **3e** both in solution and in the solid state were similar to those for **3a**, **3b**, and **3c**. The results clearly show that the red shifts observed in a series of foldamers were the result of the stacking of naphthalene moieties in the folding conformation and not because of

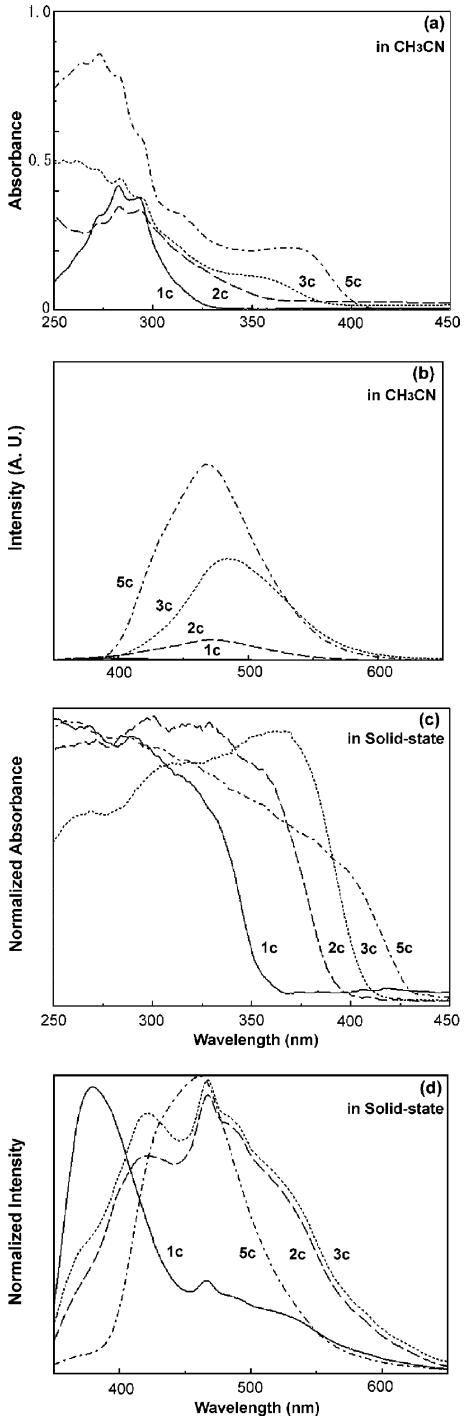


FIGURE 7. Absorption and fluorescence spectra of **1c**, **2c**, **3c**, and **5c**: (a) absorption spectra in CH_3CN, 20 μM; (b) fluorescence spectra in CH_3CN, 20 μM (excitation wavelength: 260 nm); (c) absorption spectra in the solid state; (d) fluorescence spectra in the solid state (excitation wavelength: 260 nm).

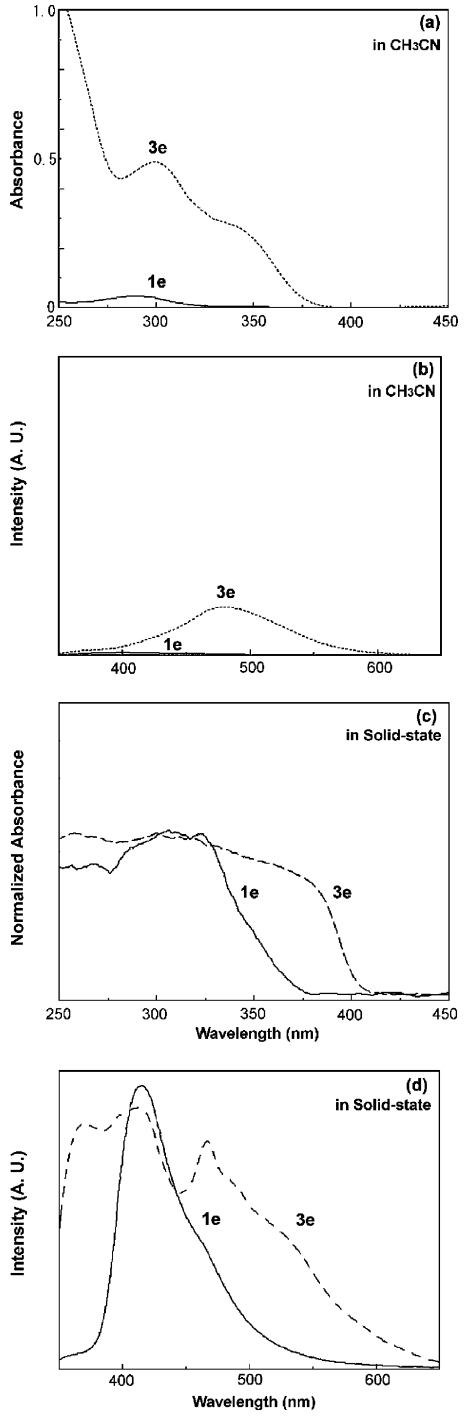


FIGURE 8. Absorption and fluorescence spectra of **1e** and **3e**: (a) absorption spectra in CH_3CN, 20 μM; (b) fluorescence spectra in CH_3CN, 20 μM (excitation wavelength: 260 nm); (c) absorption spectra in the solid state; (d) fluorescence spectra in the solid state (excitation wavelength: 260 nm).

the aromatic substituents, (*S*)-1-phenylethyl or (*S*)-1-(1-naphthyl)ethyl moiety, at the imide nitrogen atom.

CD Spectra. Our major interest is chirality amplification in foldamers.[22] The CD spectra were measured in solution and in the solid state for **1b**, **2b**, **3b**, **5b**, **1c**, **2c**, **3c**, and **5c**. In the (*S*)-1-phenylethyl series (**1b**, **2b**, **3b**, and **5b**), almost no CD signal was observed in acetonitrile (Figure 9a) and marginal spectra were observed in chloroform (Figure 9b) in the region corresponding to the absorption band caused by $\pi-\pi$ interactions between naphthalene moieties. Recently, switching of chiral induction using solid-state−solution-state equilibrium was

(22) (a) Fenniri, H.; Deng, B.-L.; Ribbe, A. E. *J. Am. Chem. Soc.* **2002**, *124*, 11064−11072. (b) Inai, Y.; Ishida, Y.; Tagawa, K.; Takasu, A.; Hirabayashi, T. *J. Am. Chem. Soc.* **2002**, *124*, 2466−2473.

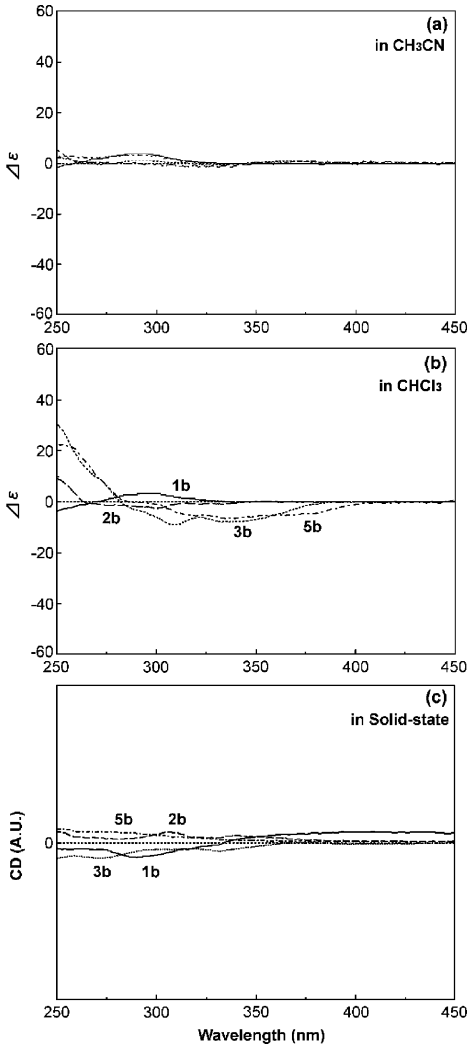


FIGURE 9. CD spectra of **1b**, **2b**, **3b**, and **5b**: (a) in CH_3CN, 20 μM; (b) in CH_3Cl, 20 μM; (c) in the solid state.

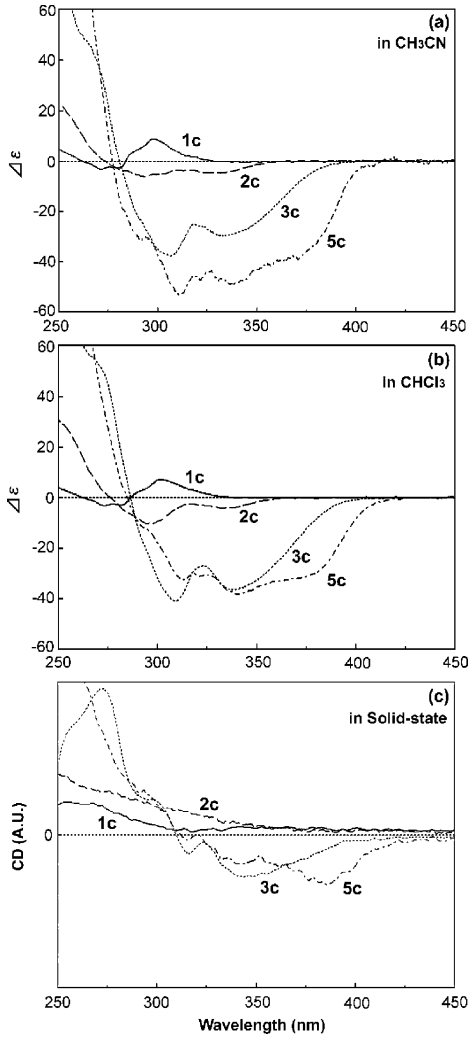


FIGURE 10. CD spectra of **1c**, **2c**, **3c**, and **5c**: (a) in CH_3CN, 20 μM; (b) in CH_3Cl, 20 μM; (c) in the solid state.

reported in helical aromatic oligoamides.[23] The equilibrium inclined to a stable diastereomer in solution when crystals composed of two diastereomers of helical oligoamides were dissolved. In this case, induction of handedness was observed. Probably the *N*-substituent, the (*S*)-1-phenylethyl group, is not bulky enough to incline the equilibrium to one of the diastereomers to induce handedness. After dissolving, their two helical diastereomeric forms might exist nearly in an equivalent amount, which results in the cancellation of the CD signal. The observation of weak CD signals in chloroform suggests that a slight solvent effect on this equilibrium might exist.

The situation is completely different in the (*S*)-1-(1-naphthyl)ethyl series (**1c**, **2c**, **3c**, and **5c**). Parts a and b of Figure 10 show their CD spectra in acetonitrile and chloroform, respectively. Similar spectra were observed for each compound in both solvents. Compound **1c,** with one naphthalene moiety, showed the weak Cotton effect at 298 nm, presumably due to a chiral (*S*)-1-(1-naphthyl)-ethyl group. A marginal CD was observed for **2c**. In contrast to these, rather intense negative Cotton effects were observed for **3c** and **5c** which corresponded to the band caused by $\pi-\pi$ interactions between naphthalene moieties in the UV−vis absorption spectra.[24] They showed a similar spectral pattern. However, **5c** showed an extra negative Cotton effect in a longer wavelength region than that of **3c**. The results were consistent with the UV−vis spectral behavior of **5c**, whose absorption band shifted ~25 nm compared with that of **3c** at a longer wavelength. The induced CD signals originate in the handedness of a folding conformation and not in the preferred conformation of the (*S*)-1-(1-naphthyl)ethyl chromophore based on the following three reasons: (1) Even though **1c** and **2c** have the (*S*)-1-(1-naphthyl)ethyl moiety, they did not show significant CD signals in a region over 350 nm. Obviously, this signal was not derived simply from the (*S*)-1-(1-naphthyl)ethyl moiety itself. (2) From the X-ray structure of **3c**, it is hard to understand that this (*S*)-1-(1-naphthyl)ethyl moiety can have any interaction with other chromophores. Rather, it is natural to consider that the CD signals originate in the stacked folding naphthalene moieties, as can be seen in its X-ray structure. (3) The CD signals in the longer wavelength region correlate

(23) Jiang, H.; Dolain, C.; Léger, J.-M.; Gornitzka, H.; Huc, I. *J. Am. Chem. Soc.* **2004**, *126*, 1034−1035.

(24) Snatzke, G. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 363−377.

to the red shift in the absorption spectra with the increasing number of naphthalene moieties. This does not require the (*S*)-1-(1-naphthyl)ethyl moiety, since a similar phenomenon was observed with the *N*-benzyl moiety in **3a** and **5a**.

Intensities of the Cotton effects become larger with the increasing number of naphthalene moieties in acetonitrile. The amplification of CD intensities might be due to the increasing number of folding units, which increases the number of exciton couplings. Even though both the (*S*)-1-phenylethyl and the (*S*)-1-(1-naphthyl)ethyl series showed similar absorption bands in their UV−vis spectra, only the (*S*)-1-(1-naphthyl)ethyl series were CD-active for these absorption bands. This difference might originate in the difference in bulkiness of these chiral substituents.

For comparison to the CD signals in solution, the CD spectra of both series were investigated in the solid state (Figures 9c and 10c). The crystalline compound was grounded minutely and mixed with Nujol. The measurement was carried out using NaCl plates. In the (*S*)-1-(1-naphthyl)ethyl series, **3c** and **5c** showed the same sign and relatively similar shapes of CD signals in their solid state as in solution. To examine the effect of annealing, an acetonitrile solution of **3c** was refluxed for 4 h. Since no spectral change in its CD spectrum was observed before (immediately after dissolving) and after reflux, the equilibrium between the two helices might incline to one of them completely. Therefore, the conformation for **3c** (*M*-helicity) observed in the X-ray structure is plausible to be the stable conformation in solution as well.[25] From these results, we can conclude that the helicities that exist in the crystalline state for the (*S*)-1-(1-naphthyl)-ethyl series might be maintained in solution. Since the same sign of Cotton effect was observed for **5c** as for **3c**, **5c** may possibly have the same helicity (*M*-helicity) as that of **3c**. However, it is not always ambiguous to determine the secondary structure by comparing the similarity of CD signals.[26] In the (*S*)-1-phenylethyl series, no CD signals were observed for **3b** and **5b** in a longer wavelength region, which might be the result of the existence of two diastereomeric helices in their crystalline state, as can be seen in the single-crystal X-ray structure of **3b**. This stability is attributed to the multiple $\pi-\pi$ stacking of naphthalene moieties enhanced by iminodicarbonyl linkers and to the bulkiness of the (*S*)-1-(1-naphthyl)ethyl substituent.

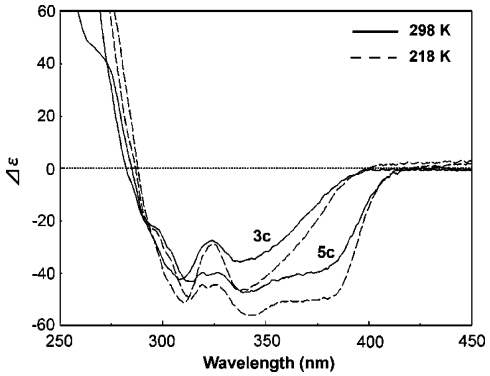


FIGURE 11. Temperature effect on CD spectra of **3c** and **5c**.

To study the effect of temperature on the folding conformation, CD spectral measurements of **3c** and **5c** were carried out at 218 K and compared with those at 298 K (Figure 11). At 218 K, a slight increase in their intensities was observed. This may be caused partly by a volumetric change of the solvent at low temperature. The results indicate that the helical folding conformation was preserved at room temperature and that almost no diastereomerization occurred.

Conclusion

Carboxamides which possess naphthalene chromophores connected by multiple iminodicarbonyl linkers formed the helical foldamer both in solution and in the solid state. Their absorption and fluorescence spectra showed a red shift as the number of naphthalene rings increased by the multiple interactions between intramolecular naphthalene rings. Helicity of the foldamer could be controlled by the introduction of a chiral auxiliary at the imide nitrogen atom. The (*S*)-1-(1-naphthyl)ethyl substituent on the nitrogen atom was sufficiently bulky to regulate the conformational change in equilibration of two helices, which resulted in the predominance of one helix leading to induction of a CD signal. The present study contributes to the designing of chiral foldamers, which is one of the current topics in the construction of artificial high-order structures.

Supporting Information Available: Preparation information, spectral data, and ORTEP diagrams of the compounds (PDF and CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(25) (a) Azumaya, I.; Yamaguchi, K.; Okamoto, I.; Kagechika, H.; Shudo, K. *J. Am. Chem. Soc.* **1995**, *117*, 9083−9084. (b) Kohmoto, S.; Masu, H.; Tatsuno, C.; Kishikawa, K.; Yamamoto, M.; Yamaguchi, K. *J. Chem. Soc., Perkin Trans. 1*, **2000**, 4464−4468. (c) Tabei, J.; Nomura, R.; Masuda, T. *Macromolecules* **2003**, *36*, 573−577. (d) Sakamoto, M.; Iwamoto, T.; Nono, N.; Ando, M.; Arai, W.; Mino, T.; Fujita, T. *J. Org. Chem.* **2003**, *68*, 942−946.

(26) Glättli, A.; Daura, X.; Seebach, D.; van Gunstern, W. F. *J. Am. Chem. Soc.* **2002**, *124*, 12972−12978.