Foldamer for novel peptide derivatives with pyrene units incorporated into the main chain

Shin-ichi Kawamura, Tomoyuki Morita, Shunsaku Kimura*

Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Kyoto-Daigaku-Katsura, Nishikyo-ku, Kyoto 615-8510, Japan

Received 12 January 2006; received in revised form 27 February 2006; accepted 27 February 2006
Available online 26 September 2006

Abstract

A novel foldamer with pyrene units incorporated into a peptide main chain was synthesized and its conformation in solution was investigated by spectroscopic measurements and computational calculations. The foldamer designed here contains 1-aminopyrene-8-carboxylic acid in the sequence, which residue is expected to change the peptide chain direction by 120°. A decapeptide, Boc–Ala–Pyr–Aib–Ala–Aib–Ala–Pyr–Aib–Ala–Aib–OMe, where Boc, Ala, Aib, Pyr, and OMe stand for $t$-butyloxy carbonyl group, L-alanine, $\alpha$-aminoisobutyric acid, 1-aminopyrene-8-carboxylic acid, and methyl ester, respectively, was synthesized. Absorption spectroscopy in acetonitrile showed that the two pyrene units in the decapeptide do not interact with each other in the ground state. On the other hand, the fluorescence spectroscopy suggested that the two pyrene units are fixed at a certain distance that allows interaction in the excited state. The circular dichroism spectra showed distinct exciton coupling peaks around the pyrene absorption, further supporting that the two pyrene units have a specific spatial relationship. According to $^1$H NMR measurements, it was found that the decapeptide has two intramolecular hydrogen bondings and the amide protons of the two 1-aminopyrene-8-carboxylic acid residues are close to each other. The dihedral angles of C–N–C$\alpha$–C in the alanine residues were also determined. Taking all these findings into account, molecular mechanics and semiempirical computational calculations were carried out to give two conformations, left-handed and right-handed helices, in which the two pyrene units partially overlap with each other. Theoretical circular dichroism spectra were calculated from these two conformations and compared to the experimental spectrum. It was shown that the left-handed helix conformation is the plausible conformation. The pyrene units incorporated into the main chain are considered to stack with each other by an aromatic interaction, resulting in the formation of a helical structure as a whole.

Keywords: Foldamer; Peptide; Pyrene; Helix; Hydrogen bonding; Aromatic stacking

1. Introduction

Foldamers are defined as “oligomers that fold into a conformationally ordered state in solution, whose structures are stabilized by a collection of noncovalent interactions between adjacent monomer units” [1–3]. Foldamer research has been motivated by highly-ordered structures of natural proteins and nucleic acids and the fact that the folding into a specific regular structure is the key to their functions such as molecular recognition, catalysis, and information storage. The research objectives are not only to uncover the principles of operations in biological molecular systems but also to design and create novel functional materials based on molecules. Foldamers are roughly classified into three categories with regard to their monomer types: peptidomimetic foldamers [1,2,4–18], nucleotidomimetic foldamers [19–22], and abiotic foldamers [23–28]. The former two are inspired by the structures of proteins and nucleic acids, and are mainly based on the modification of the chemical structure of the monomer (amino acids and nucleotides), while the latter one utilizes aromatic interactions, charge-transfer interactions, and others, that are not general in the nature. Among them, inspired by sophisticated structures and functions of proteins, the peptidomimetic foldamers have been most actively investigated so far. They have a wide variety of structures from peptoids [4] and oligoureas [5] that are
The designed molecule is a decapeptide with two pyrene acid which changes the peptide chain direction by 120° about the present foldamer is 1-aminopyrene-8-carboxylic acid, 1-aminopyrene-8-carboxylic acid, and methyl ester, respectively. Its synthetically intermediate pentamer, Boc–Ala–Pyr–Aib–OMe. Boc–Aib–OH (2.61 g, 12.8 mmol) and HCl in dioxane by the common procedures to afford HCl·H–Aib–OMe. HCl·H–Aib–OMe (3.54 g, 15.7 mmol) were dissolved in dimethylformamide (DMF) and the solution was stirred at 0° C for 15 min, and Na,N-dicyclohexylcarbodiimide (DCC) (3.25 g, 15.7 mmol), 1-hydroxybenzotriazole (HOBt) (2.66 g, 19.2 mmol), and triethylamine (2.2 ml) were added to the solution, and then the solution was stirred at 0° C for 30 min, and thereafter at room temperature for 48 h. After solvent evaporation, the residue was dissolved in ethyl acetate and the solution was stirred at 0° C for 30 min. The precipitate formed was removed by a glass filter and the supernatant was washed with a 4 wt% NaHCO3, saturated NaCl, 4 wt% KHSO4, and saturated NaCl aqueous solutions in this order. The organic layer was dried over anhydrous MgSO4 and the solvent was evaporated. The residue was purified by a silica gel column with ethyl acetate/hexane (3/1 v/v) as eluent to afford the solid (3.20 g, 66.9%). TLC: Rf = 0.87 (chloroform/methanol = 5/1 v/v), Rf = 0.44 (ethyl acetate/hexane = 1/1 v/v). 1H NMR (400 MHz, CDCl3): δ (ppm) 1.36 (3H, d, NHCH(CH3)), 1.42 (9H, s, (CH3)3C), 1.42–1.51 (12H, m, NH(CH3)2), 3.68 (3H, s, OCH3), 4.39 (1H, m, NHCH(CH3)), 4.85 (1H, s, NHCH(CH3)), 6.54 (1H, d, (CH3)3OCONH), 7.11 (1H, s, NH(CH3)2).

1-Nitropyrene-8-carbonyl–Aib–Ala–Aib–OMe. The Boc group was removed by 4 N HCl in dioxane by the common procedure to afford HCl·H–Aib–Ala–Aib–OMe. HCl·H–Aib–Ala–Aib–OMe (3.54 g, 15.7 mmol) were dissolved in dimethylformamide (DMF) and the solution was stirred at 0° C for 15 min, and Na,N-dicyclohexylcarbodiimide (DCC) (3.25 g, 15.7 mmol), 1-hydroxybenzotriazole (HOBt) (2.66 g, 19.2 mmol), and triethylamine (2.2 ml) were added to the solution, and then the solution was stirred at 0° C for 30 min, and thereafter at room temperature for 48 h. After solvent evaporation, the residue was dissolved in ethyl acetate and the solution was stirred at 0° C for 30 min. The precipitate formed was removed by a glass filter and the supernatant was washed with a 4 wt% NaHCO3, saturated NaCl, 4 wt% KHSO4, and saturated NaCl aqueous solutions in this order. The organic layer was dried over anhydrous MgSO4 and the solvent was evaporated. The residue was purified by a silica gel column with ethyl acetate/hexane (3/1 v/v) as eluent to afford the solid (3.20 g, 66.9%). TLC: Rf = 0.87 (chloroform/methanol = 5/1 v/v), Rf = 0.44 (ethyl acetate/hexane = 1/1 v/v). 1H NMR (400 MHz, CDCl3): δ (ppm) 1.36 (3H, d, NHCH(CH3)), 1.42 (9H, s, (CH3)3C), 1.42–1.51 (12H, m, NH(CH3)2), 3.68 (3H, s, OCH3), 4.39 (1H, m, NHCH(CH3)), 4.85 (1H, s, NHCH(CH3)), 6.54 (1H, d, (CH3)3OCONH), 7.11 (1H, s, NH(CH3)2).

1-Nitropyrene-8-carbonyl–Aib–Ala–Aib–OMe. The Boc group of Boc–Aib–Ala–Aib–OMe was removed by 4 N HCl in dioxane by the common procedure to afford HCl·H–Aib–Ala–Aib–OMe. HCl·H–Aib–Ala–Aib–OMe (3.54 g, 15.7 mmol) were dissolved in dimethylformamide (DMF) and the solution was stirred at 0° C for 15 min, and Na,N-dicyclohexylcarbodiimide (DCC) (3.25 g, 15.7 mmol), 1-hydroxybenzotriazole (HOBt) (2.66 g, 19.2 mmol), and triethylamine (2.2 ml) were added to the solution, and then the solution was stirred at 0° C for 30 min, and thereafter at room temperature for 48 h. After solvent evaporation, the residue was dissolved in ethyl acetate and the solution was stirred at 0° C for 30 min. The precipitate formed was removed by a glass filter and the supernatant was washed with a 4 wt% NaHCO3, saturated NaCl, 4 wt% KHSO4, and saturated NaCl aqueous solutions in this order. The organic layer was dried over anhydrous MgSO4 and the solvent was evaporated. The residue was purified by a silica gel column with ethyl acetate/hexane (3/1 v/v) as eluent to afford the solid (3.20 g, 66.9%). TLC: Rf = 0.87 (chloroform/methanol = 5/1 v/v), Rf = 0.44 (ethyl acetate/hexane = 1/1 v/v). 1H NMR (400 MHz, CDCl3): δ (ppm) 1.36 (3H, d, NHCH(CH3)), 1.42 (9H, s, (CH3)3C), 1.42–1.51 (12H, m, NH(CH3)2), 3.68 (3H, s, OCH3), 4.39 (1H, m, NHCH(CH3)), 4.85 (1H, s, NHCH(CH3)), 6.54 (1H, d, (CH3)3OCONH), 7.11 (1H, s, NH(CH3)2).
order. The organic layer was dried over anhydrous MgSO₄ and the solvent was evaporated. The residue was purified by a silica gel column with chloroform/methanol (10/1 v/v) as eluent to afford the solid (80 mg, 86%). TLC: \( R_f = 0.47 \) (chloroform/methanol = 10/1 v/v), \( R_f = 0.06 \) (chloroform).

\(^{1}H\) NMR (400 MHz, CDCl₃): \( \delta \) (ppm) 1.54 (9H, m, NHCH(CH₃)₂), 1.80 (6H, d, NHC(CH₃)₂), 3.72 (3H, s, OCH₃), 4.56 (1H, m, NHCH(CH₃)), 6.79 (1H, d, NHCH(CH₃)), 6.84 (1H, s, NHC(CH₃)₂), 7.07 (1H, s, NHC(CH₃)₂), 8.08–8.88 (8H, Pyrene-H).

Boc–Ala–Pyr–Ala–Ala–OMe (P5). 1-Nitropyrene-8-carbonyl–Ala–Ala–Ala–OMe (80 mg, 0.15 mmol) was dissolved in dichloromethane and reduced under a hydrogen atmosphere in the presence of 10 wt% palladium carbon (80 mg) for 5 h. The solvent was removed by evaporation and the product (H–Pyr–Ala–Ala–Ala–OMe) was obtained. Boc–Ala–OH (81 mg, 0.43 mmol) and H–Pyr–Ala–Ala–Ala–OMe (74 mg, 0.14 mmol) were dissolved in DMF (3 ml) and the solution was stirred at 0 °C for 15 min, and HATU (196 mg, 0.52 mmol) and DIEA (135 μl, 0.77 mmol) were added to the solution and then the solution was stirred at 0 °C for 3 h and thereafter at room temperature for 24 h. After that, Boc–Ala–OH (81 mg, 0.43 mmol), HATU (196 mg, 0.52 mmol), and DIEA (135 μl, 0.77 mmol) were further added to the solution, and the solution was stirred at room temperature for 24 h. After solvent evaporation, the residue was dissolved in chloroform and the solution was washed with a 4 wt% KHSO₄, and saturated NaCl aqueous solutions in this order. The organic layer was dried over anhydrous MgSO₄ and the solvent was evaporated. The residue was washed with dichloromethane and reduced under a hydrogen atmosphere in the presence of 10 wt% palladium carbon (80 mg) for 5 h. The solvent was removed by evaporation and the residue was dried under vacuum. The residue was purified by a Sephadex LH-20 column with methanol as eluent and then further purified by a silica gel column with chloroform/methanol (10/1 v/v) as eluent to afford the solid (25 mg, 46%). TLC: \( R_f = 0.63 \) (chloroform/methanol = 5/1 v/v), \( R_f = 0.38 \) (chloroform/methanol = 10/1 v/v). \(^{1}H\) NMR (400 MHz, CDCl₃): \( \delta \) (ppm) 1.39–1.70 (45H, m, (CH₃)₃C, NHCH(CH₃)₂), 1.75 (6H, d, NHC(CH₃)₂), 3.65 (3H, s, OCH₃), 4.62 (1H, m, NHCH(CH₃)), 5.52 (1H, s, (CH₃)₂OCONHCH₂), 6.98 (2H, m, NHC(CH₃)₂), 7.28 (1H, s, NHCH(CH₃)), 7.63–8.31 (8H, m, pyrenyl-H), 9.37 (1H, s, pyrenyl-NH). MS (FAB, matrix; nitrobenzylalcohol): \( m/z \) 1243 (calcd for C₆₈H₇₉N₁₀O₁₃ [(M + H)⁺] m/z 1243.5).

### 2.2. Methods

The absorption spectra of the peptides in solution were recorded at the pyrene concentration of 4.0 × 10⁻⁵ M on a Shimadzu UV-2450PC spectrometer. The fluorescence spectroscopy was performed at the pyrene concentration of 2.2 × 10⁻⁴ M with 355 nm excitation on a Hitachi F-4010 fluorometer. The CD spectra of the peptides were measured at the pyrene concentration of 2.0 × 10⁻⁴ M on a JASCO J-600 spectropolarimeter with an optical cell of a 0.1 cm optical path length. \(^{1}H\) NMR spectroscopy was carried out by a Bruker Avance DPX400 spectrometer. All the spectroscopic measurements were done at room temperature. For computational calculations, the initial geometries were generated by a Fujitsu CAChe Work-System 6.1.1 software and the geometries were then optimized by a Molecular Mechanics program 2 (MM2) method and a semiempirical Austin Model 1 (AM1) method in the MOPAC 2002 package on the same program. Using these energy-minimized geometries, CD spectra were theoretically calculated by a Mark Thompson and Planaria Software ArgusLab 4.0.1 software. The transition strengths were plotted against the wavelength corresponding to the transition energy with Gaussian broadening of a
15 nm half-width to generate the absorption and CD spectra, respectively. This drawing was carried out on a Wolfram Research Mathematica 5 software. The wavelength scaling was adjusted so that the calculated absorption spectrum agrees with the experimental spectrum.

3. Results and discussion

3.1. Absorption, fluorescence, and CD spectroscopy

In order to examine the interchromophoric interactions between the two pyrene units in P10, the absorption, fluorescence, and CD spectra of P10 in solution were measured. P5 was also examined as a control molecule having one pyrene unit. The absorption spectra in acetonitrile are shown in Fig. 3. The spectra do not show a vibrational structure that is familiar with unmodified pyrene since the pyrenyl framework is directly modified by amino and carbonyl groups. The spectra of P5 and P10 approximately coincide with each other showing that there is no strong interaction such as dimer formation between the two pyrene units of P10 in the ground state. Similar results were obtained in other solvents such as ethanol and chloroform. On the other hand, the fluorescence spectra of P10 were strongly dependent on solvents whereas the spectra of P5 had almost the same pattern independent on solvents (Fig. 4). Excimer emission around 500 nm in addition to monomer emission around 430 nm of P10 appeared slightly in the case of acetonitrile and evidently in the cases of ethanol and chloroform. Moreover, the total emission was significantly reduced probably due to lower emission quantum yield of the excimer compared to the monomer. This excimer observation suggests two possibilities. One is that the two pyrene units are fixed in a certain proximity that allows an interchromophoric interaction in the excited state (static excimer formation). The other is that the spacer connecting the two pyrene units is flexible enough to allow formation of an encounter complex in the singlet lifetime (dynamic excimer formation). The second possibility can be excluded here from the following reason. In the case of DMF as solvent, the spectrum was mainly dominated by monomer emission and was very close to the P5 spectrum in the same solvent. DMF which is well known as a good solvent for peptides generally form hydrogen bonding with the amide groups of a peptide chain and accordingly suppresses intramolecular hydrogen bonding in the peptide chain. Peptide chains are thus flexible in DMF. If there were dynamic excimer formation, more excimer would be observed in DMF compared to the other solvents. Therefore, it is considered that the two pyrene units in P10 are fixed at a certain distance probably by peptide chain folding based on intramolecular hydrogen bonding among the amide groups in acetonitrile, ethanol, and chloroform, while they are separated in DMF due to flexibility of the peptide chain. To investigate the chromophoric interaction in detail, CD measurements were carried out. The CD spectra of P5 and P10 in acetonitrile and DMF are shown in Fig. 5. Distinct exciton coupling around the pyrene absorption was observed in P10 in acetonitrile, while P5 in acetonitrile and both P5 and P10 in DMF did not show significant CD peaks. The CD profile of P10 in acetonitrile was unchanged under various temperatures and a similar CD pattern was observed in ethanol and chloroform (data not shown). These findings also support that the two pyrene units have a specific spatial relationship in P10 in solvents other than DMF, and they are fixed by hydrogen bonding among the amide groups on the peptide chain. The shape of the CD spectra of P10 in acetonitrile will be qualitatively discussed in the later section of computational calculations.

3.2. $^1$H NMR analysis

In order to investigate the intramolecular interactions on the chain of P10 in solution, various $^1$H NMR measurements were carried out. In these measurements, deuterated acetonitrile was chosen as solvent because NMR peaks were not well resolved in the other solvents such as deuterated ethanol and chloroform. All the NH protons of the amide and urethane groups were identified by standard 1D $^1$H NMR and 2D $^1$H COSY NMR measurements. To gain the information on hydrogen bonding, the changes of the NH chemical shifts with addition of deuterated dimethylsulfoxide ((CD$_3$)$_2$SO) were examined. It is well known that an NH proton free from intramolecular hydrogen bonding forms hydrogen bonding with (CD$_3$)$_2$SO which is a hydrogen-bond acceptor, resulting displacement of its chemical shift toward the lower magnetic field, whereas the chemical shift of an NH proton involved in intramolecular hydrogen bonding remains unaltered.
Fig. 4. Fluorescence spectra of P5 and P10 in acetonitrile, ethanol, chloroform, and DMF. The excitation wavelength was 355 nm. The spectra were recorded at the pyrene concentration of $2.2 \times 10^{-6}$ M.

Fig. 5. CD spectra of P5 and P10 in acetonitrile and DMF recorded at the pyrene concentration of $2.0 \times 10^{-4}$ M. The molar ellipticity was calculated on the basis of the concentration of the pyrene unit.
unchanged [30]. The results for P5 and P10 are shown in Fig. 6. Some of data points are missing because the NMR peaks corresponding to these points could not be assigned due to overlapping with other peaks and broadening. The chemical shifts of all the NH protons more or less moved toward the lower magnetic field with the addition of (CD$_3$)$_2$SO. That may be due to perturbation of the folded structure with the addition of (CD$_3$)$_2$SO. However, it is obvious that the displacement in the chemical shifts of the urethane NH of the Ala$^1$ residue and the amide NH of the Pyr$^2$ residue in P10 are remarkably small compared to the urethane NH of P5 and the Pyr$^1$ amide NH of P10, respectively. The suffix numbers are shown in the bottom of Fig. 6. These protons are thus considered to form hydrogen bonding with carbonyl groups somewhere on the peptide chain. Furthermore, a cross peak between the amide NHs of the Pyr$^1$ and Pyr$^2$ residues was observed in the $^1$H NOESY measurement (data not shown), indicating that these protons are close to each other at a distance less than 0.5 nm. Considering these results together with the previous findings on the interchromophoric interactions, the two pyrene units are considered to stack in a parallel orientation with respect to their functional groups (amide and carbonyl groups). The peptide chain linking the two pyrene units makes a loop accordingly, and this loop chain and the N-terminal chain of the Pyr$^2$ residue are linked by hydrogen bond, generating a helical conformation as a whole. In addition to that, the dihedral angles of C–N–C$^\alpha$–C in the Ala$^2$, Ala$^3$, and Ala$^4$ residues were determined to be $-73^\circ$, $-76^\circ$, and $-82^\circ$, respectively, from the spin coupling constants between amide NH and C$^\alpha$H on the basis of the Karplus equation [31]. A similar estimation for the urethane NH of the Ala$^1$ residue failed because of its broadened NMR peak.

3.3. Computational analysis on conformation

To determine the plausible conformation of P10 in acetonitrile, possible conformations were generated and examined on computers as follows. Conveniently, the peptide chain at the N-terminal of the Pyr$^1$ residue, the chain linking the two pyrene units, and the chain at the C-terminal of the Pyr$^2$ residue, are labeled as the N-terminal chain, the middle chain, and the C-terminal chain, respectively. First, two pyrene units were located with a parallel orientation with full overlapping, and the peptide chains were set to take a $\beta$-sheet like structure in which the amide groups orient perpendicular to the pyrene plane so that the N-terminal chain and the middle chain can form hydrogen bonding. The separation of the pyrene units was set to be a little less than 0.5 nm considering the result of the NOESY measurement. Under these conditions, there are two ways to arrange the peptide chains, left-handed and right-handed helices. It was considered that the hydrogen bonding that are formed between the N-terminal chain and the middle chain are Ala$^1$ NH to Aib$^2$ C═O and Pyr$^2$ NH to Ala$^1$ C═O (Fig. 7). At these sites, the distance between the amino nitrogen and carbonyl oxygen was fixed to be 0.3 nm to hold a geometry suitable for hydrogen bonding. The dihedral angles of C–N–C$^\alpha$–C in the three Ala residues other than the Ala$^1$ residue were also fixed to be the respective values estimated by the NMR measurements. Under the location of atoms in the pyrene units also being locked, the first optimization was carried out by the MM2 and AM1 methods in this order. After that, the conformations were further optimized by the AM1 method with the pyrene atoms unlocked to afford the final conformations. In this last procedure, the pyrene units were somewhat misaligned from the initial
full overlapping. The obtained two conformations are shown in Fig. 7 together with their schematic illustrations for ease of understanding. The heats of formation are $-375.1$ and $-362.7 \text{ kcal/mol}$ for the left-handed and right-handed helices, respectively. The former left-handed helix is much more stable compared to the right-handed helix. Moreover, the left-handed helix held a helical conformation throughout the molecule after the geometry optimization and the two pyrene units partially stack with a nearly face to face orientation. On the other hand, in the right-handed helix, the C-terminal chain rewound during the geometry optimization and the pyrene units have a considerable angle with each other rather than stacking. The separation of the amide NHs of the Pyr1 and Pyr2 residues is 0.47 nm in both conformations, that is in an agreement with the NOESY result. In order to determine which conformation is more plausible, CD spectra were theoretically calculated on the basis of these optimized conformations, and were compared to the experimental spectrum. One hundred excited states were generated from 40 highest occupied molecular orbitals and 40 lowest unoccupied molecular orbitals and the oscillation strength at each excitation was calculated by the ZINDO–RPA method, and then the theoretical CD spectra were drawn with Gaussian broadening. The calculated spectra of the two helical conformations are shown in Fig. 8 as well as the experimental spectrum recorded in acetonitrile. The molar ellipticity is based on the concentration of the pyrene unit.

![Fig. 7. Optimized geometries of left-handed and right-handed helices in a ball and stick presentation (top) and their schematic illustrations (bottom). Hydrogen atoms are omitted for simplicity in the top graphics.](image)

![Fig. 8. The calculated CD spectra of P10 assuming left-handed and right-handed helices together with the experimental spectrum recorded in acetonitrile. The molar ellipticity is based on the concentration of the pyrene unit.](image)
geometry. The diameter of the helix is about 1.6 nm. In this conformation, the pyrene units are considered to act as planar joints that partially overlap each other by an aromatic stacking interaction to make a helical structure with the help of the intramolecular hydrogen bonding on the peptide chain.

4. Conclusion

A novel foldamer with two pyrene units incorporated into the peptide main chain was synthesised and its conformation in solution was investigated by spectroscopic measurements and computational calculations. Absorption spectroscopy showed that the two pyrene units in the foldamer do not interact with each other in the ground state, while the fluorescence and circular dichroism spectroscopy suggested that the two pyrene units are fixed in a certain spatial relationship that allows interaction in the excited state. 1H NMR measurements revealed that the foldamer has at least two intramolecular hydrogen bonds and the two amide protons from the pyrene units are close to each other. Taking all the experimental findings into account, a left-handed helix conformation of a 1.6 nm diameter was generated by computational calculations. The theoretical circular dichroism spectrum calculated using this conformation, agreed well with the experimental spectrum, showing that the left-handed helix conformation is the plausible conformation of the foldamer in solution. It is considered that the pyrene units incorporated into the main chain act as planar joints that stack each other to make a helical structure as a whole. This research demonstrates that a unique combination of α-amino acids and aromatic derivatives having amino and carboxyl groups is one of the effective ways to design and construct a new peptide conformation, that will also lead to creation of novel functional materials based on molecules.

Acknowledgements

This work was partly supported by Grant-in-Aids for Young Scientists B (16750098) and for Scientific Research B (15350068), and 21st century COE program, COE for a United Approach to New Materials Science, from the Ministry of Education, Culture, Sports, Science, and Technology, Japan. The authors are grateful to Dr. Yoshihito Inai at Nagoya Institute of Technology for his kind and valuable instructions on the theoretical calculations of CD spectra.