Liquid Crystals

Supramolecular Chirality of Thermotropic Liquid-Crystalline Folic Acid Derivatives**

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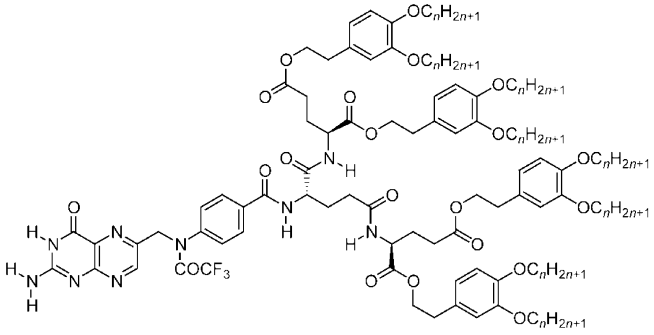
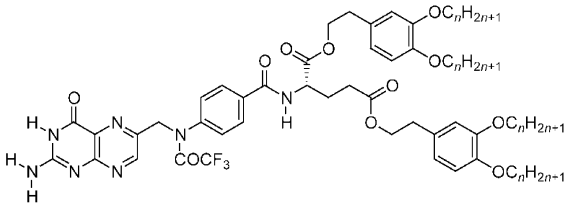
Supramolecular self-assembly of thermotropic columnar and cubic liquid crystals has recently attracted a great deal of attention because their structures in nanometer length scale can be used for new dynamically functional materials.[1–6] The aim of the present study is to introduce supramolecular chirality into columnar and cubic liquid crystals for further functionalization of these materials. The incorporation of chirality into thermotropic columnar[5] and cubic[6] phases is a relatively new and growing area, while a numerous number of chiral materials have been prepared for nematic and smectic materials.[7] Moreover, to the best of our knowledge, supramolecular chiral assemblies of thermotropic cubic materials have not yet been reported except for rod aromatic chiral molecules[6] although supramolecular chirality has been developed for self-assembled molecules in solution.[8] It is of interest that supramolecular chirality may occur for self-assembled columnar and cubic materials in neat states. Our design strategy here is to use hydrogen-bonded chiral molecules derived from biomolecules to induce a supramolecular chiral assembly. Recently, we have shown that a thermotropic liquid-crystalline (LC) folic acid derivative exhibits a change from a smectic to a columnar phase in the presence of alkali metal salts or a lipophilic solvent.[2,3] These results suggest that molecules that have several interacting parts are able to show new self-assembly behavior that is responsive to stimuli by tuning their molecular structures and interactions.

Herein we report that folic acid derivatives **1a–c** that have oligo(glutamic acid) moieties and lipophilic alkyl chains (Scheme 1) exhibit new chiral mesomorphic behavior. Supramolecular chirality is induced for these materials in the hexagonal columnar and *P*m3n cubic LC phases in the presence of sodium triflate ($NaOSO_2CF_3$). Furthermore, the transitions from the chiral columnar to the chiral cubic phases are observed for the first time.



1a (*n* = 6), **1b** (*n* = 11), **1c** (*n* = 18)



2a (*n* = 6), **2b** (*n* = 11), **2c** (*n* = 18)

Scheme 1. Molecular structures of folic acid derivatives.

Compounds **1a–c** and their complexes with $NaOSO_2CF_3$ exhibit stable thermotropic LC phases over a wide temperature ranges as presented in Table 1. Compound **1a** shows only a hexagonal columnar phase, while **1b** and **1c**, which both have longer alkyl chains, both exhibit columnar and cubic phases (see Supporting Information). In our previous papers, we reported that folic acid derivatives **2a–c** (Scheme 1), which have one glutamic-acid moiety, exhibit smectic and columnar phases owing to the formation of ribbonlike and disklike hydrogen bonds, respectively.[3] For the columnar phases of compounds **1a–c**, disklike hydrogen bonds (Scheme 2) should be formed. The infrared spectra of **1a** in the columnar phase are very similar to the spectra of **2c**,

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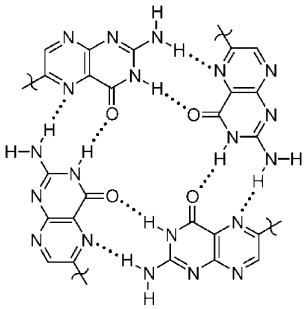
Table 1: Thermal properties of **1** and the complexes of **1**/$NaOSO_2CF_3$.

Compounds[a]	Phase transition behavior[b]						
1a			G	−28	Col_h	162	Iso
1b	Cr	−9	Col_h	135	Cub	187	Iso
1c	Cr	55	Col_h	117	Cub	200	Iso
1a/$NaOSO_2CF_3$ (0.25)	G	−22	Col_h	143	Cub	169	Iso
1b/$NaOSO_2CF_3$ (0.25)	Cr	−10	Col_h	137	Cub	195	Iso
1c/$NaOSO_2CF_3$ (0.25)	Cr	54	Col_h	167	Cub	222	Iso
1a/$NaOSO_2CF_3$ (1.00)	G	−29	Col_h	146	Cub	171	Iso
1b/$NaOSO_2CF_3$ (1.00)	Cr	−10	Col_h	169	Cub	211	Iso

[a] The ratio of $NaOSO_2CF_3$ to **1** is in parentheses. [b] Transition temperatures (°C). G: glassy; Cr: crystalline; Col_h: hexagonal columnar; Cub: cubic; Iso: isotropic.



Scheme 2. Hydrogen-bonded tetramer of pterin rings.

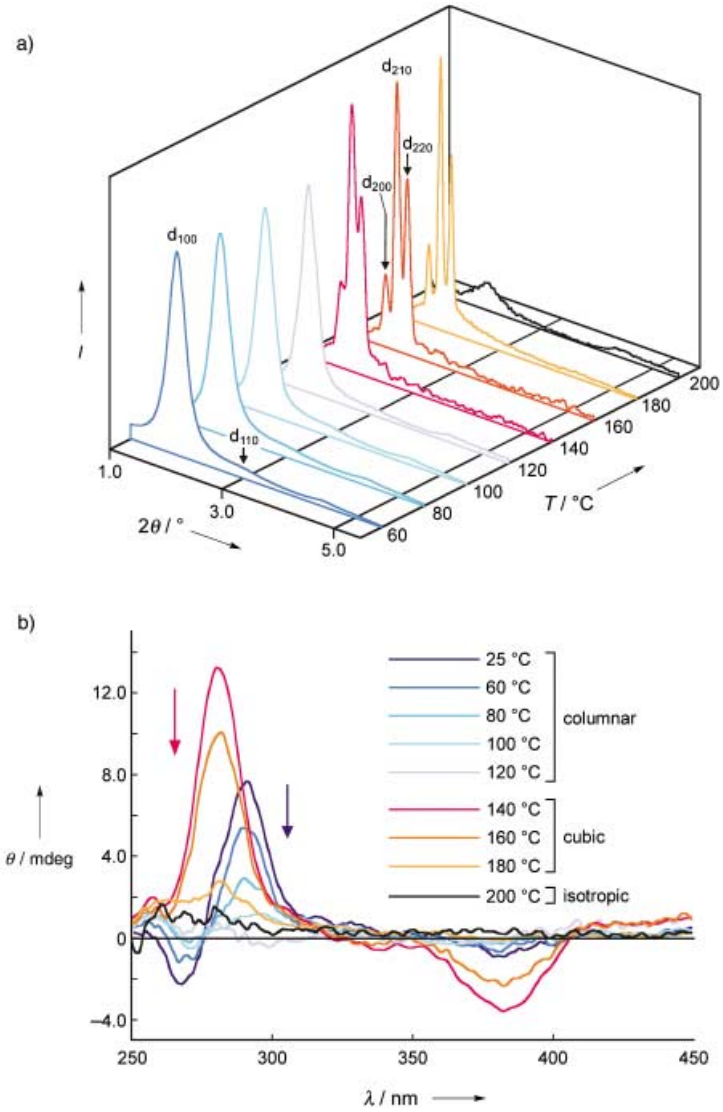


Figure 1. Small angle X-ray diffraction profiles a) and CD spectra b) of the complex of **1b**/$NaOSO_2CF_3$ (1:0.25 molar ratio) on heating.

which forms a tetramer (see Supporting Information). The diameter of the tetramer of **1a** is estimated to be about 50 Å by molecular modeling, which is consistent with the results of X-ray diffraction measurements (intercolumnar spacing = 49.0 Å). The values of enthalpy changes for isotropization of **1a–c** also support the formation of disklike aggregates[3b] (see Supporting Information). Cubic phases, which are optically isotropic under the polarizing optical microscope, are observed for **1b** and **1c**, whereas the less bulky compounds **2a–c** exhibit only smectic and columnar phases.

The addition of $NaOSO_2CF_3$ to **1a** induces a cubic phase, while no cubic phase is seen for **1a** alone. For compounds of **1b** and **1c**, thermally stabilized columnar and cubic phases are observed in the presence of the salts. The small-angle X-ray diffraction (SAXD) patterns of the complex of **1b**/$NaOSO_2CF_3$ (1:0.25 molar ratio) indicate that on heating, the complex forms hexagonal columnar and subsequent *P*m3n cubic phases (Figure 1a). The SAXD spectrum at 60 °C shows that intercolumnar spacing of the columnar structure is 55.2 Å,[9] which decreases to 53.4 Å at 120 °C. The SAXD profile for the cubic phases at 160 °C exhibits reflections of 50.0 (200), 44.6 (210) and 40.9 Å (211).[10] The lattice parameter of the cubic phase is 100.0 Å.

We have found that supramolecular chirality is induced for both of the columnar and *P*m3n cubic LC phases of **1a–c** by the addition of $NaOSO_2CF_3$. Circular dichroism (CD) spectra for the complex of **1b**/$NaOSO_2CF_3$ (1:0.25 molar ratio) from 25 to 200 °C in thin film states (Figure 1b) show the formation of chiral assemblies. For the columnar phases of the complex, we observe coupled CD bands centered at 280 nm (a positive extreme at 290 nm and a negative extreme at 268 nm) and a weaker negative CD band around 380 nm, while no Cotton effect is seen for the columnar phases of **1b** alone. The Cotton effects become weaker as the temperatures increase for the columnar phases. The UV absorption of the pterin rings of **1b** appears at 280 and 358 nm.[11] We observe that the transition from chiral columnar to chiral cubic occurs on further heating. After the transition to the cubic phase at 137 °C, a positive Cotton effect at 280 nm and a negative CD band around 380 nm are induced. The intensities of the CD bands for the complex in the cubic phases decrease as the temperatures increase from 140 to 180 °C (Figure 1b). In contrast, for the cubic phases of **1b** alone, no induced CD spectrum is observed. In the isotropic phase at 200 °C, no Cotton effect is observed. These results indicate that supramolecular chiral order exists in the *P*m3n cubic phases for the complex of **1b**/$NaOSO_2CF_3$.

Figure 2a shows the *P*m3n cubic lattice, which is divided into two interstitial sites (black) and three pairs of columnar sites (gray).[1e,12,13] The columnar sites lie on the faces of unit cells and may form mutually perpendicular and interlocking columns (Figure 2b).[1e,12,13] Up to now, only a few examples for thermotropic liquid crystals that display only nonchiral *P*m3n cubic phases were reported.[1e–g] These *P*m3n cubic phases were considered to be micellar cubic phases based on TEM[1g] and conductivity measurements.[1e] Tschierske and co-workers suggested that at the columnar *P*m3n cubic transition the columns are segregated into micelles.[1e] For the folic-acid materials reported here, segmented columns formed by increasing the motion of the alkyl chain on heating can also form micelles in the cubic phases,[14] which should induce supramolecular chirality. Based on the lattice parameter and density, each micelle is estimated to have eight disks on average (see Supporting Information). A molecular model of a micelle that consists of eight stacked disks of **1b** is shown in Figure 2c. The size of the micelle is consistent with a model of the *P*m3n cubic phase in Figure 2b.

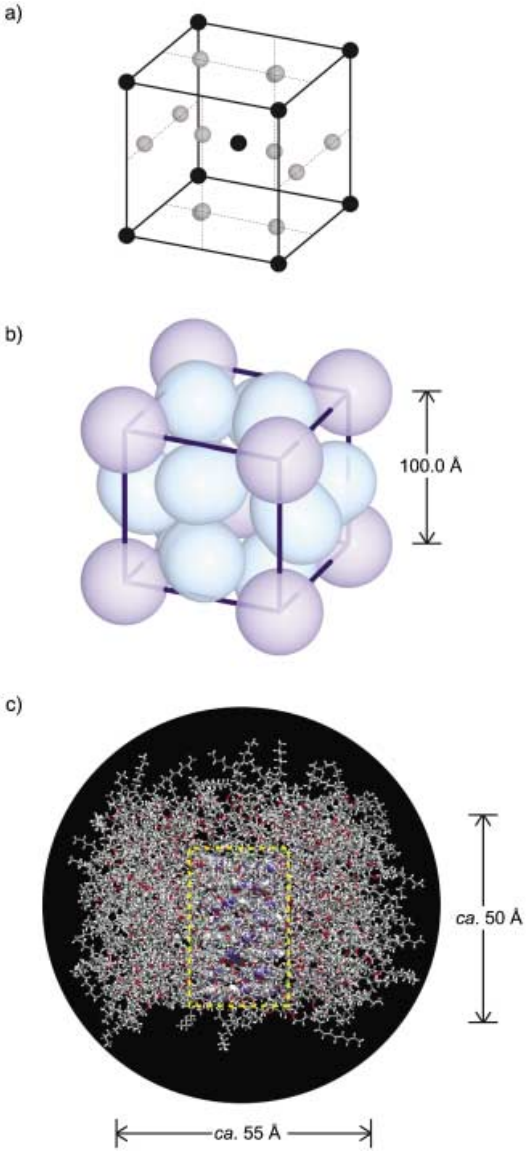


Figure 2. a) The lattice structure of the *P*m3n cubic phase. b) Arrangement of the micelles in the *P*m3n cubic phase. c) Molecular model of a self-assembled micelle of **1b**. Yellow broken line denotes the stacked disks consisting of the pterin rings.

Infrared measurements of the complexes of **1b** in the cubic phase also suggest that the disks are stacked. We previously reported that the columnar LC structures formed by the complex of **2b** and $NaOSO_2CF_3$ comprise hydrogen bonded disklike tetramers of the pterin rings as shown in Scheme 2.[3] For the complex of **1b**/$NaOSO_2CF_3$ in the columnar phases, the IR spectrum (3000–3500 cm^{-1}) is very similar to that of **2b**/$NaOSO_2CF_3$, which forms disklike tetramers (see Supporting Information).[15] For the cubic phases, the IR spectra of **1b**/$NaOSO_2CF_3$ suggest that the disklike tetramer is also formed (see Supporting Information).[15] For guanosine derivatives, Gottarelli, Davis, and co-workers reported the single-crystal structures that form the same hydrogen-bonded tetramer pattern in the presence of alkali metal ions.[16] In this case, the alkali metal ion is sandwiched by the disks of the tetramer. These observations suggest that the supramolecular chirality is induced for the complex of **1b**/$NaOSO_2CF_3$ by helicity locked through the interaction between the ion and the disks along the axis of the column. The molecular chirality of the oligo(glutamic acid) part of compound **1b** should induce chiral stacking of the tetramers in the columnar and cubic phases.

The results presented here are the first example of the cubic phase exhibiting supramolecular chirality. It should also be noted that the supramolecular chirality is induced in the presence of nonchiral ions.

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[1] a) D. Guillon, *Struct. Bonding (Berlin)* **1999**, *95*, 41; b) C. F. van Nostrum, R. J. M. Nolte, *Chem. Commun.* **1996**, 2385; c) T. Kato, *Struct. Bonding (Berlin)* **2000**, *96*, 95; d) M. Sawamura, K. Kawai, Y. Matsuo, K. Kanie, T. Kato, E. Nakamura, *Nature* **2002**, *419*, 702; e) K. Borisch, S. Diele, P. Göring, H. Kresse, C. Tschierske, *Angew. Chem.* **1997**, *109*, 2188; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2087; f) V. S. K. Balagurusamy, G. Ungar, V. Percec, G. Johansson, *J. Am. Chem. Soc.* **1997**, *119*, 1539; g) S. D. Hudson, H.-T. Jung, V. Percec, W.-D. Cho, G. Johansson, G. Ungar, V. S. K. Balagurusamy, *Science* **1997**, *278*, 449; h) A. R. A. Palmans, J. A. J. M. Vekemans, H. Fischer, R. A. Hikmet, E. W. Meijer, *Chem. Eur. J.* **1997**, *3*, 300; i) S. T. Trzaska, H. Zheng, T. M. Swager, *Chem. Mater.* **1999**, *11*, 130; j) R. Auzély-Velty, T. Benvegnu, D. Plusquellec, G. Mackenzie, J. A. Haley, J. W. Goodby, *Angew. Chem.* **1998**, *110*, 2665; *Angew. Chem. Int. Ed.* **1998**, *37*, 2511; k) M. Suárez, J.-M. Lehn, S. C. Zimmerman, A. Skoulios, B. Heinrich, *J. Am. Chem. Soc.* **1998**, *120*, 9526; l) B. Donnio, B. Heinrich, T. Gulik-Krzywicki, H. Delacriox, D. Guillon, D. W. Bruce, *Chem. Mater.* **1997**, *9*, 2951; m) M. Lee, D.-W. Lee, B.-K. Cho, J.-Y. Yoon, W.-C. Zin, *J. Am. Chem. Soc.* **1998**, *120*, 13258; n) S. Ito, M. Wehmeier, J. D. Brand, C. Kübel, R. Epsch, J. P. Rabe, K. Müllen, *Chem. Eur. J.* **2000**, *6*, 4327; o) O. Y. Mindyuk, M. R. Stetzer, P. A. Heiney, J. C.

Nelson, J. S. Moore, *Adv. Mater.* **1998**, *10*, 1363; p) B. A. Pindzola, J. Jin, D. L. Gin, *J. Am. Chem. Soc.* **2003**, *125*, 2940; q) A. Kraft, A. Reichert, R. Kleppinger, *Chem. Commun.* **2000**, 1015; r) N. Mizoshita, H. Monobe, M. Inoue, M. Ukon, T. Watanabe, Y. Shimizu, K. Hanabusa, T. Kato, *Chem. Commun.* **2002**, 428; s) Y. Queneau, J. Gagnaire, J. J West, G. Mackenzie, J. W. Goodby, *J. Mater. Chem.* **2001**, *11*, 2839.

[2] a) T. Kato, *Science* **2002**, *295*, 2414; b) T. Kato, N. Mizoshita, K. Kanie, *Macromol. Rapid Commun.* **2001**, *22*, 797.

[3] a) K. Kanie, T. Yasuda, S. Ujiie, T. Kato, *Chem. Commun.* **2000**, 1899; b) K. Kanie, M. Nishii, T. Yasuda, T. Taki, S. Ujiie, T. Kato, *J. Mater. Chem.* **2001**, *11*, 2875; c) K. Kanie, T. Yasuda, M. Nishii, S. Ujiie, T. Kato, *Chem. Lett.* **2001**, 480.

[4] a) C. Tschierske, *J. Mater. Chem.* **2001**, *11*, 2647; b) C. Tschierske, *Curr. Opin. Colloid Interface Sci.* **2002**, *7*, 355.

[5] a) M. M. Green, H. Ringsdorf, J. Wagner, R. Wüstefeld, *Angew. Chem.* **1990**, *102*, 1525; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1478; b) C. Fouquey, J.-M. Lehn, A.-M. Levelut, *Adv. Mater.* **1990**, *2*, 254; c) S. T. Trzaska, H.-F. Hsu, T. M. Swager, *J. Am. Chem. Soc.* **1999**, *121*, 4518; d) K. Kishikawa, S. Furusawa, T. Yamaki, S. Kohmoto, M. Yamamoto, K. Yamaguchi, *J. Am. Chem. Soc.* **2002**, *124*, 1597; e) M. L. Bushey, A. Hwang, P. W. Stephens, C. Nuckolls, *Angew. Chem.* **2002**, *114*, 2952; *Angew. Chem. Int. Ed.* **2002**, *41*, 2828; f) J. Barberá, E. Cavero, M. Lehmann, J. L. Serrano, T. Sierra, J. T. Vázquez, *J. Am. Chem. Soc.* **2003**, *125*, 4527; g) J. L. Serrano, T. Sierra, *Chem. Eur. J.* **2000**, *6*, 759; h) G. Scherowsky, X. H. Chen, *Liq. Cryst.* **1994**, *17*, 803; i) H. Bock, W. Helfrich, *Liq. Cryst.* **1995**, *18*, 387.

[6] a) A. Yoshizawa, J. Umezawa, N. Ise, R. Sato, Y. Soeda, T. Kusumoto, K. Sato, T. Hiyama, Y. Takanishi, H. Takezoe, *Jpn. J. Appl. Phys.* **1998**, *37*, L942; b) Y. Takanishi, T. Ogasawara, A. Yoshizawa, J. Umezawa, T. Kusumoto, T. Hiyama, K. Ishikawa, H. Takezoe, *J. Mater. Chem.* **2002**, *12*, 1325.

[7] a) *Handbook of Liquid Crystals* (Eds.: D. Demus, J. W. Goodby, G. W. Gray, H.-W. Spiess, V. Vill), Wiley-VCH, Weinheim, **1998**. b) For supramolecular chiral smectic and nematic materials, see for example: U. Kumar, J. M. J. Fréchet, T. Kato, S. Ujiie, K. Iimura, *Angew. Chem.* **1992**, *104*, 1545; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1531; T. Kato, H. Kihara, T. Uryu, S. Ujiie, K. Iimura, J. M. J. Fréchet, U. Kumar, *Ferroelectrics* **1993**, *148*, 161; H. Kihara, T. Kato, T. Uryu, J. M. J. Fréchet, *Liq. Cryst.* **1998**, *24*, 413.

[8] a) A. R. A. Palmans, J. A. J. M. Vekemans, E. E. Havinga, E. W. Meijer, *Angew. Chem.* **1997**, *109*, 2763; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2648; b) L. Brunsveld, B. G. G. Lohmeijer, J. A. J. M. Vekemans, E. W. Meijer, *Chem. Commun.* **2000**, 2305; c) H. Engelkamp, S. Middelbeek, R. J. M. Nolte, *Science* **1999**, *284*, 785; d) L. J. Prins, J. Huskens, F. de Jong, P. Timmerman, D. N. Reinhoudt, *Nature* **1999**, *398*, 498.

[9] A sharp reflection of 48.0 Å (100), and a smaller peak of 27.5 Å (110) for the LC phase of **1b**/$NaOSO_2CF_3$ at 60 °C are observed (Figure 1 a). These correspond to the reflections of a hexagonal columnar structure.

[10] The reciprocal *d*-spacing of $2:5^{1/2}:6^{1/2}$ is characteristic of the *P*m3n space group of cubic structures; J. M. Seddon, J. Robins, T. Gulik-Krzywicki, H. Delacroix, *Phys. Chem. Chem. Phys.* **2000**, *2*, 4485.

[11] The comparison of UV/Vis spectra of **1b** and a compound consisting of only aminobenzoic acid with oligo(glutamic acid) moieties shows that the absorptions of 280 and 358 nm can be ascribed to those of the pterin ring. No CD active spectra are observed for the compound that has no pterin ring (see Supporting Information).

[12] K. Fontell, *Colloid Polym. Sci.* **1990**, *268*, 264.

[13] P. Ziherl, R. D. Kamien, *J. Phys. Chem. B* **2001**, *105*, 10147.

[14] Recently, Kamien and Ziherl have suggested that in the columnar sites nonclose-packed lattices can coexist[13] (see Supporting Information). Presently, it is quite difficult to directly determine the phase structures of such soft states.

[15] For the IR spectra of the disklike tetramer, N–H stretchings are observed at about 3320, 3160, and 3060 cm^{-1}. In particular, two bands at 3320 and 3160 cm^{-1} are characteristic of the tetramer.[3] The complexes of **1b** with $NaOSO_2CF_3$ also show the same trend (see Supporting Information).

[16] S. L. Forman, J. C. Fettinger, S. Pieraccini, G. Gottarelli, J. T. Davis, *J. Am. Chem. Soc.* **2000**, *122*, 4060.

