



Molecular Crystals and Liquid Crystals

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/gmcl20>

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Version of record first published: 31 Aug 2006

To cite this article: Yuko Kamikawa, Masayuki Nishii & Takashi Kato (2005): Supramolecular Chiral Cubic Phases Formed by Folic Acid Derivatives, *Molecular Crystals and Liquid Crystals*, 435:1, 95/[755]-105/[765]

To link to this article: <http://dx.doi.org/10.1080/15421400590954560>

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Supramolecular Chiral Cubic Phases Formed by Folic Acid Derivatives

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We have prepared a series of thermotropic liquid-crystalline folate derivatives which have hierarchical chiral structures at the oligo(glutamic acid) parts. The complexes of the folic acids with sodium salts show hexagonal columnar and Pm3n cubic phases. The addition of the salts induces supramolecular chirality in the columnar and cubic phases. Tuning of molecular chirality at the oligo (glutamic acid) moieties greatly affects their supramolecular chiral structures.

Keywords: chirality; columnar phase; cubic phase; hydrogen bond; self-assembly

INTRODUCTION

Supramolecular liquid crystals are useful candidates for developing functional molecular materials with ordered structures as layers, cylinders, and spheres [1–11]. Here we describe tuning of supramolecular chirality in the columnar and cubic liquid crystals formed by folic acid derivatives having hierarchical chiral structures. Incorporation of chirality to the columnar [12–18] and cubic [19–21] phases will provide new self-assembled materials of chiral liquid-crystals

This work was financially supported by a Grant-in-Aid for Scientific Research on Priority Areas of “Dynamic Control of Strongly Correlated Soft Materials” (No. 413/13031009) and a Grant-in-Aid for The 21st Century COE Program for Frontiers in Fundamental Chemistry from the Ministry of Education, Culture, Sports, Science and Technology.

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with ferroelectric [14,16,22–23], optoelectronic [18,21], and molecular recognition properties [13,15].

In the design of supramolecular materials, biomolecules are useful as molecular building blocks because of their self-assembling characteristics [24–33]. Liquid-crystalline molecules based on glycosides, nucleosides, and amino acids have been prepared. Recently, we have developed [26–28] a series of thermotropic and lyotropic liquid crystals based on the folic acid [34–36], a vitamin molecule, which forms multiple hydrogen bonds. These folic acid derivatives can interact with sodium salts, which leads to the formation of columnar liquid-crystalline phases displayed by its tetramers [25]. Furthermore, it has been shown that chirality of glutamic acid moieties greatly influences their mesomorphic properties. We showed, for the first time, the formation of a chiral cubic phase in which helically assembled cyclic tetramers of the folates are involved [25]. It is of interest that helical chirality is observed in optically isotropic micelles.

In the present paper, we show the effect of molecular chirality to the supramolecular chiral liquid crystals by changing the chiral structures of the oligo(glutamic acid) parts (Fig. 1). A series of folic acid derivatives having different chiral structures incorporating L- and D-glutamic acids are prepared, whereas in our previous work [25] the cubic phase of the folic acid derivatives consisting of only L-glutamic acid were examined. We have examined their liquid-crystalline properties and chiral self-assembled structures.

EXPERIMENTAL

Synthesis

The folic acid derivatives **1a–c** have been synthesized according to the literature procedure [25]. Compound **1a** is prepared using L-glutamic acid while **1b** is synthesized from D-glutamic acid. Compound **1c** is a diastereomer of **1a** having a D-glutamic acid moiety at the inner part, and two L-glutamic acid moieties at the outer part.

General Methods

Differential scanning calorimetry (DSC) measurements were conducted on a Mettler DSC 30 (scanning rate: $10^{\circ}\text{C min}^{-1}$). A polarizing optical microscope Olympus BH-2 equipped with a Mettler FP82HT hot stage was used for visual observation. X-ray diffraction (XRD) measurements were carried out on a Rigaku RINT 2100 diffractometer with a heating stage using Ni-filtered $\text{CuK}\alpha$ radiation. Infrared (IR)

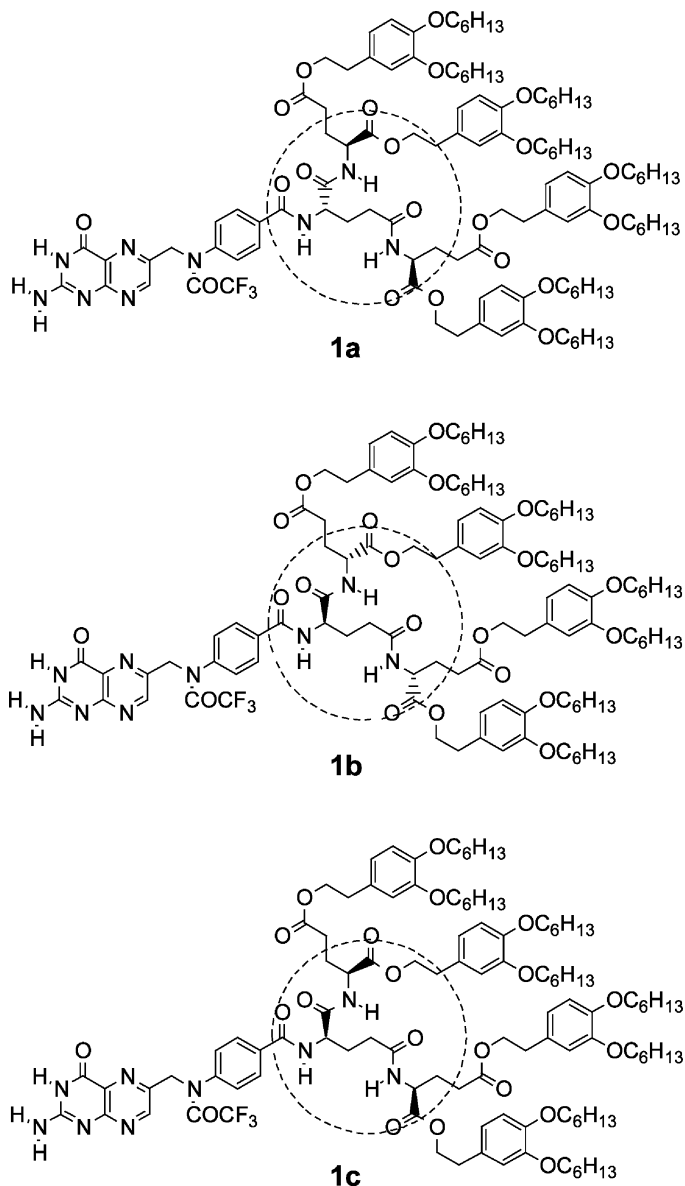


FIGURE 1 Molecular structures of the folate derivatives **1a–c** having hierarchical chiral structures at oligo(glutamic acid) moieties.

measurements were conducted on a JASCO FT/IR-660 Plus in KBr. The ultraviolet-visible light (UV-Vis) absorption spectra were recorded on an Agilent 8453 spectrophotometer equipped with a Mettler FP82HT hot stage. Circular dichroism (CD) spectra were recorded on a Jasco J-820 spectropolarimeter with a Mettler FP82HT hot stage. The samples in the LC states were deposited on 200 μm quartz plates casting from chloroform solution, followed by annealing for 10 min to obtain clear films.

RESULTS AND DISCUSSION

Compounds **1a–c** exhibit hexagonal columnar phases (Table 1). Compound **1b** shows exactly the same thermal properties as **1a**, while the isotropization temperature of **1c** is 10 degrees higher than **1a**. The columnar assemblies of **1c** are thermally more stable than those of **1a,b**. The addition of the sodium triflate ($\text{NaOSO}_2\text{CF}_3$) increases the isotropization temperatures for **1a,b** by 7 degrees though no thermal stabilization is observed for the compound **1c** (Table 1). Furthermore, the complexation of **1** and $\text{NaOSO}_2\text{CF}_3$ induces optically isotropic cubic phases at higher temperature ranges. The columnar to cubic phase transitions are not detected on DSC thermograms [25].

Hydrogen bond formation for the compounds have been examined by IR spectroscopy. The spectrum of **1a** in the LC state shows the N-H stretching bands of the pterin rings at 3054, 3155, and 3320 cm^{-1} ,

TABLE 1 Thermal Properties and X-ray Results of **1** and the Complexes of **1**/ $\text{NaOSO}_2\text{CF}_3$

Compounds ^a	Phase transition behavior ^{b,c}						X-ray results	
							<i>T</i> (°C)	Lattice parameter (Å)
1a		G	−28	Col _h	162	Iso	100	48.2
1b		G	−28	Col _h	162	Iso	100	47.8
1c		G	−19	Col _h	173	Iso	100	48.3
1a / $\text{NaOSO}_2\text{CF}_3$	G	−22	Col _h	143	Cub	169	100	49.2
							150	93.4
1b / $\text{NaOSO}_2\text{CF}_3$	G	−22	Col _h	143	Cub	169	100	51.3
							150	93.8
1c / $\text{NaOSO}_2\text{CF}_3$	G	−16	Col _h	143	Cub	171	100	50.6
							150	95.1

^aMolar ratio of $\text{NaOSO}_2\text{CF}_3$ to **1** is 0.25. ^bTransition temperatures (°C). G: glassy; Col_h: hexagonal columnar; Cub: cubic; Iso: isotropic. ^cTransitions from columnar to cubic phases were not detected on DSC thermograms.

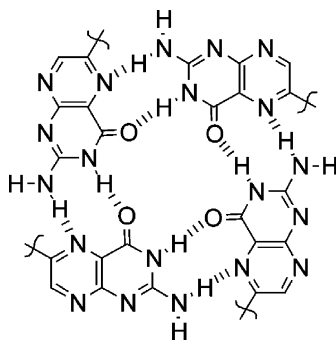


FIGURE 2 Hydrogen-bonded structure of cyclic tetramer of pterin rings.

which indicate that cyclic tetramers are formed (Fig. 2, Fig. 3) [25,28]. The hydrogen-bonded structure of **1a** is the same as that of complex **1a**/NaOSO₂CF₃ (Fig. 3a). The intermolecular hydrogen bonds which direct disk-like association are maintained in the mesophases (Fig. 3a). The folic acid derivatives form columnar and cubic phases based on the hydrogen-bonded disks. The IR spectra of **1b** and **1c** are the same for **1a** both in the presence and absence of sodium salts including columnar and cubic phases.

The XRD measurements of **1a** show that the hexagonal columnar phase with the diameter of 48 Å is formed (Fig. 4a). This value is

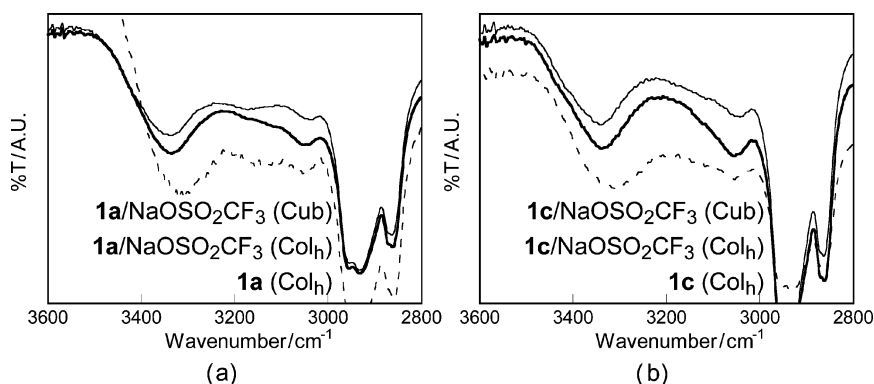


FIGURE 3 IR spectra of (a) **1a** in the Col_h phase at 100°C (broken line), **1a**/NaOSO₂CF₃ in the Col_h phase at 100°C (thick line), **1a**/NaOSO₂CF₃ in the Cub phase at 160°C (solid line), and (b) **1c** in the Col_h phase at 100°C (broken line), **1c**/NaOSO₂CF₃ in the Col_h phase at 100°C (thick line), **1c**/NaOSO₂CF₃ in the Cub phase at 160°C (solid line).

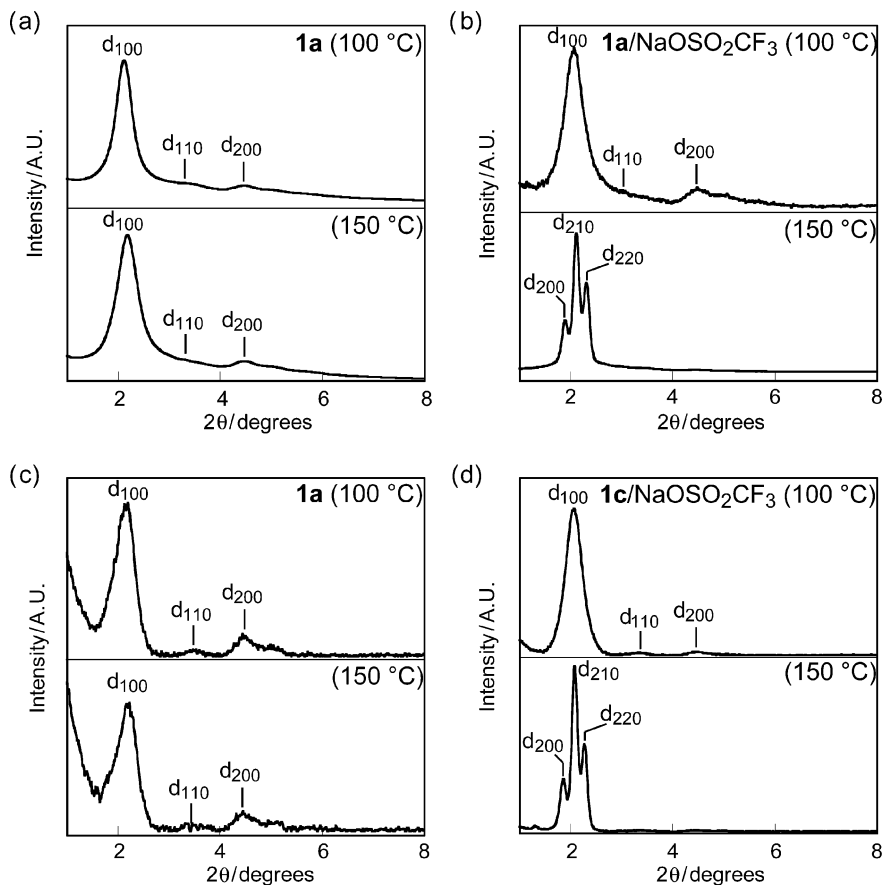


FIGURE 4 XRD profiles of **1a** (a); **1a**/NaOSO₂CF₃ (b); **1c** (c); **1c**/NaOSO₂CF₃ (d).

appropriate for the formation of disk-like tetramers taking into account the results of MM2 calculations [25]. In the wide angle region, compounds **1a–c** exhibit only broad halos (data not shown), which are indicative of the formation of disordered columnar phases.

In the addition of sodium triflates, the diameter of the column slightly increases (Fig. 4b). Upon heating to over 140°C, three sharp peaks which can be attributed to d_{200} , d_{210} , and d_{220} reflections of Pm3n cubic lattice are observed (Fig. 4b). Heat activates the molecular motion of the peripheral alkyl chains, which results in the segmentation of the columns and the formation of inversed micelles[25,37]. Average number of molecules per sphere is calculated

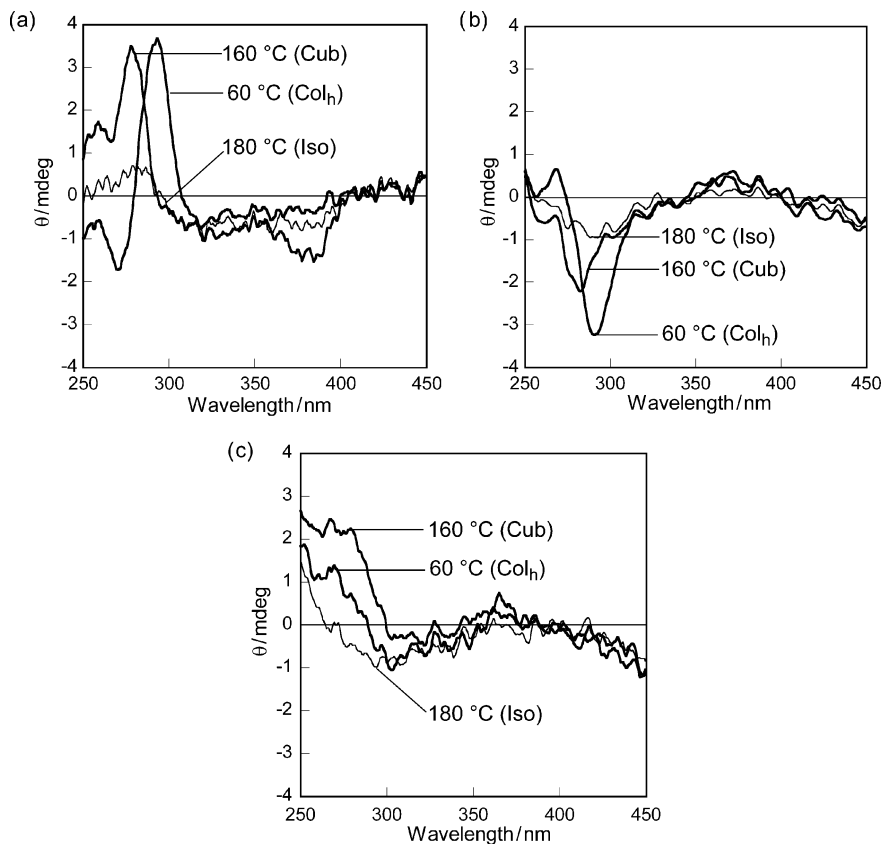


FIGURE 5 Variable-temperature CD spectra of **1a**/NaOSO₂CF₃ (a); **1b**/NaOSO₂CF₃ (b); **1c**/NaOSO₂CF₃ (c).

to be about 32. Therefore, each micelle consists of 8 stacked tetramers [25]. The columnar-cubic transitions are observed for all of compounds **1a–c** at almost the same temperatures both in the presence and absence of the sodium salts.

CD spectroscopy measurements have been carried out for the thin films of compounds **1a–c** and their complexes with sodium salts. No induced CD band is observed for **1a–c** from 60 to 180°C. In contrast, complex **1a**/NaOSO₂CF₃ in the columnar phase exhibits a positive bisignate CD band at 293 nm, and a broad signal around 360 nm (Fig. 5a, thick black line). This spectrum feature indicates that the helicity is induced for the stacked tetramers [25]. At elevated temperatures, the intensity of the induced CD decreases to almost none around

phase-transition temperature, showing that columnar assemblies lose their chiral arrangement between disks. In the cubic phase of **1a**/NaOSO₂CF₃, another Cotton effect is induced with the positive extreme of 280 nm (Fig. 5a, gray line). Thus supramolecular chirality is involved in these optically isotropic micelles. The CD spectrum of **1b**/NaOSO₂CF₃ is similar to that of **1a**/NaOSO₂CF₃ with an opposite helical sense (Fig. 5b). A negative Cotton effect is induced in the cubic phase of **1b**/NaOSO₂CF₃. Supramolecular chirality of the folic acid derivatives in the cubic phases is also tunable by the molecular chirality of the oligo(glutamic acid) moieties.

The CD spectrum of **1c**/NaOSO₂CF₃ is silent in its whole meso-phase range (Fig. 5c). This complex has the same hydrogen-bonded tetramer structures of the pterin rings as complex **1a**/NaOSO₂CF₃,

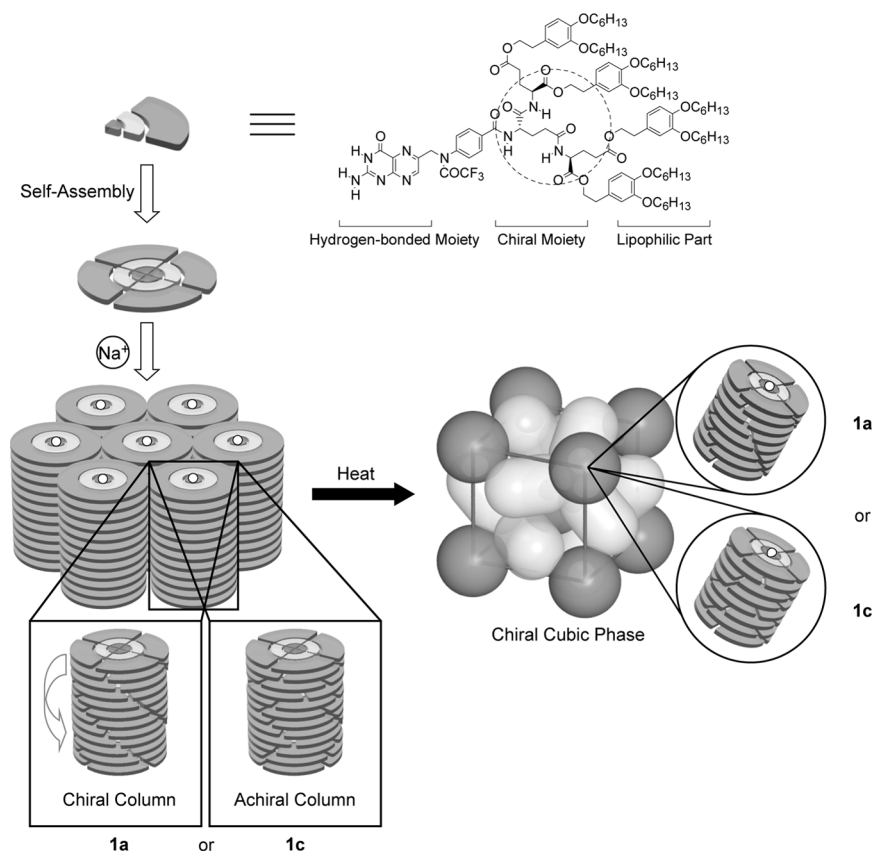


FIGURE 6 Schematic illustration of the induction of a chiral cubic phase.

while supramolecular chirality is absent in the both columnar and cubic structures. It should be noted that slight structural differences in the oligo(glutamic acid) parts induce drastic changes in CD properties of the folic acid derivatives.

In the columnar phase of **1a**/NaOSO₂CF₃, the ions are incorporated between tetramers to induce the chiral arrangement of pterin rings [38]. It is known that supramolecular chirality is induced to the self-assembled guanosine G-quartets by the addition of potassium ions [39]. Concentrated aqueous solution of folic acid also induced a cholesteric phase exhibiting supramolecular chirality in the presence of sodium salts [34]. Moreover, the CD behavior of compounds **1a–c** is only activated by the sodium ions [25].

The induction of the cubic phase in **1**/NaOSO₂CF₃ suggests that the columnar-cubic phase transitions are promoted by the presence of ions while compounds **1a–c** without ions in the columnar phase directly become the isotropic liquid states. In this cubic phase, supramolecular chirality is induced due to interactions between the cyclic tetramers. This chiral structure also consists of the helical assemblies of tetramers as in the columnar states, as is considered based on the results of DSC and IR measurements (Fig. 6). In contrast, in the columnar assemblies of **1c**, the conformational differences of oligo(glutamate) moieties may induce more stabilized structures than **1a**, which is suggested by the higher clearing point of **1c** than **1a**. Nevertheless, no thermal stabilization is observed for the diastereomer by the addition of the salts. In the case of **1c**, assembled structure is determined by the packing mode of the peripheral glutamic acid moiety and lipophilic part, and interactions between ions are not dominant. The ions incorporated between tetramers induce the columnar-cubic phase transition though **1c** induces little CD behavior due to the different stacking mode from **1a**.

CONCLUSION

In summary, supramolecular chirality is induced in the cubic phases of **1a–c**. These chiral structures can be tuned by the change of molecular chirality of oligo(glutamate) moieties. One structural difference greatly affects the chiral behavior of self-assembled liquid crystals.

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