Hydrogen-Bonded Lyotropic Liquid Crystals of Folic Acids: Responses to Environment by Exhibiting Different Complex Patterns

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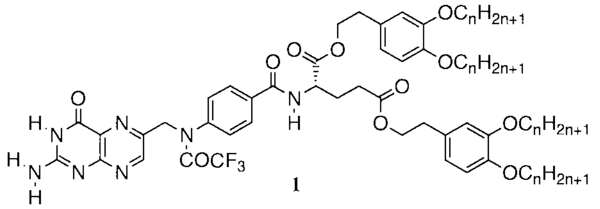
Lipophilic folic acid derivatives exhibit lyotropic liquid-crystalline states in organic solvents. The change of the mesophases from lamellar to columnar is induced by the change of specific hydrogen bonding patterns from ribbon to disk with the increase of hydrophobic environment.

Hydrogen bonding is one of the most important interactions in nature.[1] Hydrogen-bonded molecular self-assemblies are expected to show dynamic behavior such as mass or charge transport, information storage, and molecular sensoring due to reversible nature and dynamic molecular recognition.[2] Generally, biological molecules have functional groups capable of hydrogen bonding, which play key roles for the dynamic functions.[1] For hydrogen-bonded liquid crystals, the combination of molecular anisotropy and dynamics may lead to versatile approaches to a variety of functional materials.[2a,3] One of our approaches is to introduce biomolecular components into the design of supramolecular hydrogen-bonded liquid crystals.[4] Recently, we have developed thermotropic liquid-crystalline (LC) folic acid derivatives **1a**–**c**. These compounds show smectic or discotic LC phases in wide temperature ranges, and the mesophase structures depend on the length of the alkyloxy side-chains. The formation of the different phase structures is attributed to the self-assembling nature of the pterin rings of **1** to show ribbon- and disk-like aggregations.[5,6] Furthermore, we have found that the molecular aggregation style changes from ribbon to disk with the increase of the fraction of sodium triflate. The dynamic control of molecular aggregates would lead to developing stimuli-responsive functional materials.



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1a: n = 6, T_i = 238 °C
1b: n = 11, T_i = 240 °C
1c: n = 18, T_i = 223 °C
T_i: Isotropization temperatures

Here we report lyotropic LC behavior of folic acid compounds **1a**–**c** and the change of the mesophase of **1a** and **1b** from lamellar (L) to discotic hexagonal columnar (D_h) by changing of the specific hydrogen bonding patterns due to the response to environment.

The lyotropic LC properties of **1b** have been examined with a variety of organic solvents.[7] Compound **1b** shows lyotropic LC behavior in CH_2Cl_2, $CHCl_3$, $ClCH_2CH_2Cl$, THF, hexane, and benzene, while in ethanol, DMSO, and DMF, the phase separation of **1b** and the solvents is observed. Compound **1a** exhibits similar lyotropic behavior. For compound **1c**, a lyotropic D_h phase is also observed even in DMSO. Although the lyotropic liquid crystallinity of alkaline metal folate was reported, the behavior has been only limited in aqueous solution.[6a]

To examine the effects of hydrophobic environment, we mixed **1b** with dodecane ($C_{12}H_{26}$).[8] Figure 1 shows a phase diagram of the lyotropic LC behavior for the mixtures of $C_{12}H_{26}$ and **1b**. These mixtures exhibit lyotropic liquid crystallinity over wide ranges of temperatures without phase separation.[9] The addition of $C_{12}H_{26}$ results in the change of the LC phases from L to D_h. The change is clearly seen when more than 7 mol of $C_{12}H_{26}$ is added to 1 mol of **1b**. The addition of $C_{12}H_{26}$ more than 20 mol to 1 mol of **1b** results in the phase separation of those components. The X-ray diffraction measurement supports the phase transition behavior. For example, the pattern for the mixture of $C_{12}H_{26}$/**1b** (12/1, mol/mol) at room temperature is 47.7, 27.5, and 23.7 Å, which is attributable to $d_{(100)}$, $d_{(110)}$, and $d_{(200)}$ lattice.[10] This pattern is characteristic of a disordered D_h (D_{hd}) phase. At 110 °C, a weak diffraction at 43.2 Å and a diffused halo at 4.6 Å are observed for the mixture. This pattern is arising from a nematic columnar (N_C) order.[11] Schlieren texture with low viscosity for the mixture also indicates the formation of the N_C phase (Figure 2).

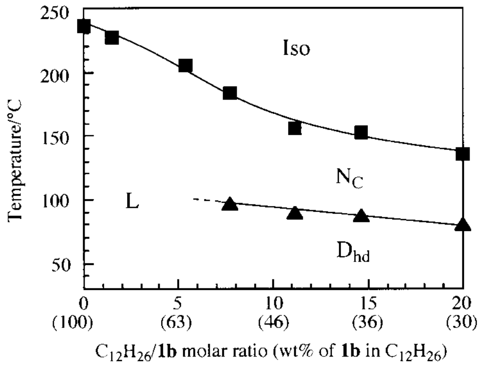

Figure 1. Phase transition behavior of the mixtures of $C_{12}H_{26}$/**1b**. L: lamellar, N_C: nematic columnar, D_{hd}: disordered discotic hexagonal columnar, Iso: isotropic.

The phase transition behavior of the mixtures of **1a**–**c** with $C_{12}H_{26}$ is summarized in Table 1. The isotropization temperatures for all mixtures of **1** decrease with the increase of the fraction of $C_{12}H_{26}$. For compound **1a**, the L phase is changed to the D_{hd} and N_C phases by the increase of $C_{12}H_{26}$. The behavior is similar to **1b**. The D_{hd}–N_C and N_C–Isotropic (Iso) transition temperatures for the mixtures of **1a** are higher than **1b** at similar concentration. On the other hand, **1c** shows lyotropic ordered D_h (D_{ho}) and D_{hd} phases in $C_{12}H_{26}$. No N_C phases are observed for **1c**.

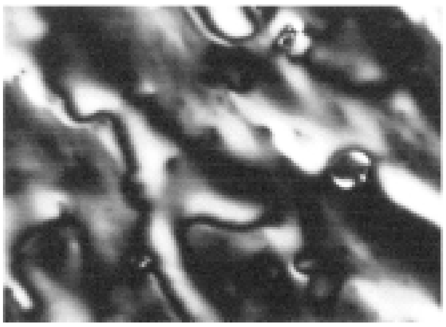

Figure 2. A polarized micrograph of $C_{12}H_{26}$/**1b** = 15/1 (molar ratio) at 99 °C (N_C Phase).

Table 1. Phase transition temperatures of complexes of **1** with $C_{12}H_{26}$[a]

Mixture	Ratio[b]	wt% of **1**	Phase transition temp./°C				
$C_{12}H_{26}$/**1a**	7	49	D_{hd}	130	N_C	204	Iso
	16	29	D_{hd}	124	N_C	183	Iso
$C_{12}H_{26}$/**1b**	8	51	D_{hd}	97	N_C	184	Iso
	14	37	D_{hd}	85	N_C	149	Iso
$C_{12}H_{26}$/**1c**	4	73	D_{ho}	52	D_{hd}	214	Iso
	9	54	D_{ho}	48	D_{hd}	158	Iso
	16	40	D_{ho}	46	D_{hd}	135	Iso

D_{ho}: discotic ordered hexagonal columner; D_{hd}: discotic disordered hexagonal columner; N_C: nematic columnar; Iso: isotropic.
[a]Determined with a polarizing microscope on heating. [b]Molar ratio of $C_{12}H_{26}$ to compound **1**.

The infrared measurements of the mixtures of **1a**–**1c** with $C_{12}H_{26}$ have been carried out to examine the hydrogen-bonded self-organized structures.[12] In a previous paper,[4] we described that **1a** and **1b** forming the thermotropic smectic phases showed the peaks due to N–H stretching at 3351 and 3341 cm^{-1}, respectively. The peaks could be attributed to the ribbon-like aggregation of pterin rings (Figure 3, A). On the other hand, the N–H stretching peak of **1c** forming the disk-like aggregated structure (Figure 3, B) is split into 3304 and 3251 cm^{-1}. Therefore, the peak patterns are dependent on the LC phase structures.[4] For the mixtures of $C_{12}H_{26}$/**1a** and $C_{12}H_{26}$/**1b** with lyotropic discotic liquid crystallinity, the peaks appear at 3298 and 3252 cm^{-1}, and 3291 and 3256 cm^{-1}, respectively. These peak patterns are similar to those of **1c** showing the disk-like aggregation (Figure 3, B). Therefore, for compounds **1a** and **1b**, we conclude that two hydrogen-bonded patterns, which lead to the different LC phases, have been successfully controlled for the phase change from L to D_h with the increase of the volume fraction of the hydrocarbon solvent inducing hydrophobic environment. To the best of our knowledge, none of phase changes based on the selection of the specific hydrogen bonding patterns is reported, although the transition from L to D_h in lyotropic media is studied.[13]

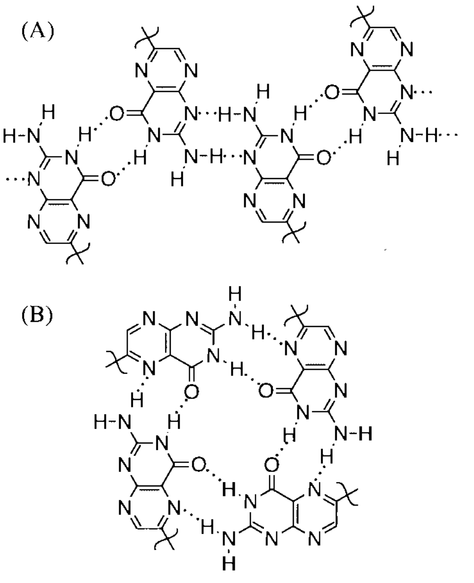

Figure 3. Hydrogen-bonded ribbon-like (A) and disk-like (B) aggregations of pterin ring of folic acid.

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7 A polarizing microscope (Olympus BH2) equipped with a Mettler FP82HT hot stage was used for characterization of the materials.

8 The mixtures of **1** with $C_{12}H_{26}$ were prepared as follows: A requisite amount of $C_{12}H_{26}$ was added to a $CHCl_3$ solution of **1**. The solvent in the resulting mixture was removed using a rotary evaporator (< 30 °C).

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12 Characterization of the hydrogen-bonded patterns was carried out using a JASCO FT/IR-8900μ equipped with a MICRO-20 microsapmling FTIR spectrometer. The samples for the measurements were prepared as follows: the mixtures of **1** with $C_{12}H_{26}$ were sandwiched between two thin pellets of KBr at 140 °C, and the resulting samples were heated to 250 °C followed by cooling to room temperature. Formation of the smectic or the discotic phases was checked by using a polarizing microscope.

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