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Synthesis and mesomorphic behaviour of new mesogenic compounds possessing a cholesteryl ester moiety connected to a pyrimidine core

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ABSTRACT

New mesogenic compounds containing a cholesteryl ester and a pyrimidine moiety connected through a polymethylene spacer have been prepared. The mode of linkage has been made via –C═C– and –C═N– to understand the structure-property relationship. Only two compounds with a pentamethylene spacer show mesomorphic behaviour. The mesomorphic behaviour has been investigated by polarizing optical microscopy, differential scanning calorimetry and HRXRD studies. Enantiotropic smectic A, twist grain boundary (TGB) and chiral nematic mesophases are exhibited by the newly synthesized compounds.

Chiral liquid crystals (LCs) have occupied one of the fascinating fields of research over the last few decades.[1] Chiral LC phases are formed either by self-assembly or when a chiral material is doped with a host showing a non-chiral LC phase. They are intrinsically characterized by an array of unique properties and structure which are promising from both advanced technology and fundamental points of view.[2] Chiral moieties have a tendency to stabilize frustrated fluid phases such as blue phases (BPs) and twist grain boundary (TGB) phases.[3] They also generate chiral nematic (N^*), chiral smectic C (SmC^*) and chiral smectic A (SmA^*) phases which have been used in thermochromic, electro-optic devices and in light modulation applications.[4] Due to the commercial availability of cholesterol as an inexpensive natural product, its rigid structure with eight chiral centres and the ease with which the structure can be derivatized, it has been incorporated extensively in chiral liquid crystalline material. The ability of cholesterol in inducing a liquid crystalline property in its various derivatives motivated many researchers to synthesize thousands of monomers, oligomers and polymers derived from cholesterol.[5] Among them, dimeric compounds consisting of either two identical (symmetric) or two non-identical (non-symmetric) mesogenic units interlinked through a central spacer are a relatively new class of liquid crystalline compounds, which encouraged not only experimentalists but also theoreticians to study the structure-liquid crystalline property relationship.[6] These dimers offer a unique and practical means of accomplishing a multifunctional system through an appropriate selection of mesogens.[7] In general, cholesterol dimers contain a cholesterol moiety and another mesogen, such as a Schiff's base,[8] and an azobenzene,[9] stilbene[10] or tolane unit.[11] Those containing the Schiff's base mesogen exhibit a very wide variety of mesophases. Since these dimers exhibit novel liquid crystalline phases as well as interesting thermal phase behaviour, they serve as useful models for semiflexible, main chain liquid crystalline polymers. Uracil and barbituric acid are found in various natural products and have numerous applications in organic synthesis.[12] Itahara et al. reported[13] on the liquid crystalline materials formed by connecting adenine or thymine (**1**) to cholesteryl benzoate or related steroid groups through a polymethylene spacer.

The nature of phase variation in different substituted or unsubstituted dimers is strongly influenced by the functional group present in the aromatic moiety, the nature of substituents in the end alkyl chain and by the length of the end alkyl chain. Uracil and barbituric acid do not possess any end alkyl group, but possess a strong dipolar effect. In continuation of our ongoing research on the synthesis of heterocycles containing liquid crystalline materials,[14] and for understanding the structure-liquid crystalline property relationship, we have undertaken a study on the synthesis and characterization of new mesogenic compounds containing uracil and barbituric acid moieties connected to a cholesteryl ester moiety either through a pentamethylene spacer or through a decamethylene spacer.

The methodology for the synthesis of dimeric materials **7a–d** and **8a**,**b** is depicted in Scheme 1. The reaction between cholesterol and *n*-bromohexanoyl chloride in THF at room temperature gave the corresponding ester derivatives **3a**,**b**. The *p*-hydroxybenzaldehydes

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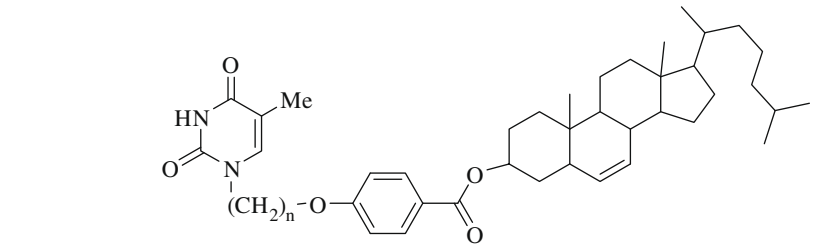

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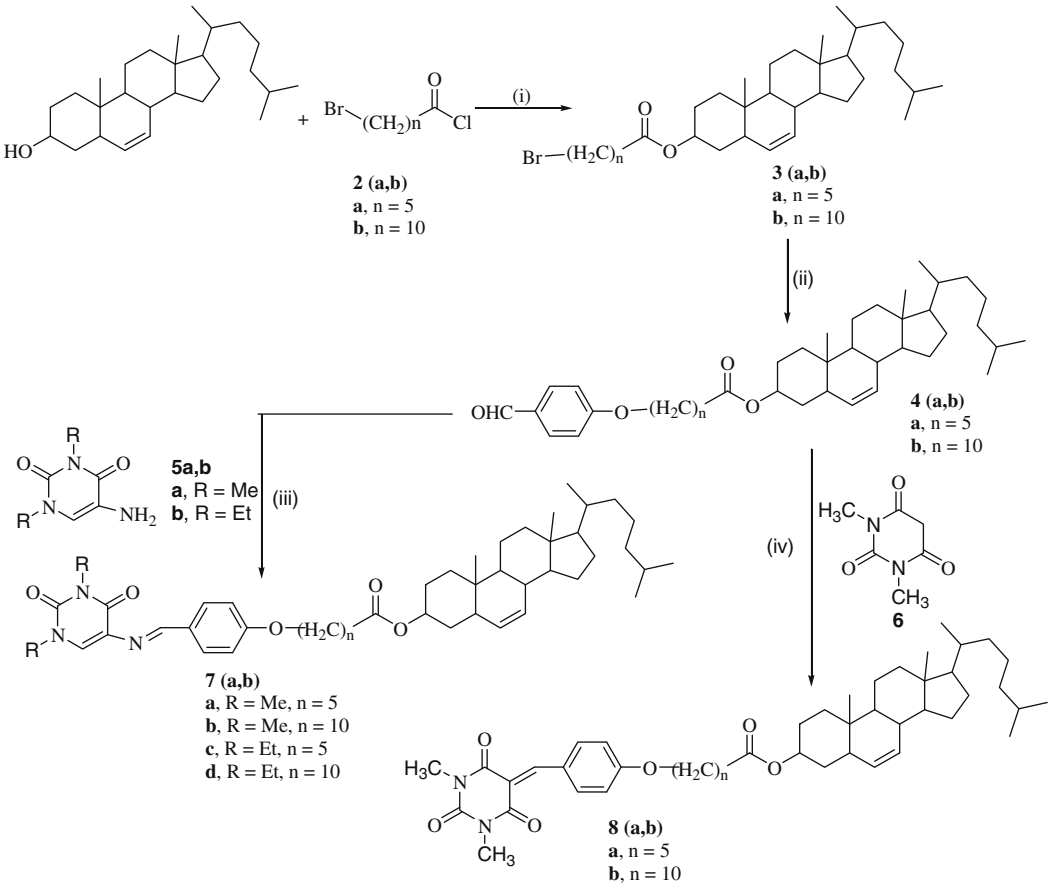

Scheme 1. Reagents and conditions: (i) THF, pyridine, rt, 12 h (ii) *p*-hydroxybenzaldehyde, K_2CO_3, acetone, reflux, 12 h (iii) AcOH, EtOH, reflux, 1–12 h (iv) EtOH, reflux, 1–12 h.

were then subjected to alkylation with cholesteryl ester derivatives in refluxing dry acetone in the presence of anhydrous K_2CO_3 to afford the corresponding aldehyde derivatives **4a,b**.[15] The aldehydes **4a,b** on condensation with different amino uracils and barbituric acid afforded the compounds **7a–d**[16] and **8a,b**[17].

The phase transitions of the new mesogenic compounds **7a** and **8a** were measured using differential scanning calorimetry (DSC) at a heating rate of 5 °C min^{-1}. The transition temperatures and associated enthalpies obtained are shown in Table 1. Textural analysis was done with the help of a polarizing optical microscope (POM). Compound **7a** shows the enantiotropic phase sequence of crystal → smectic A_1 → TGB → cholesteric → isotropic, while the compounds of the same series **7b**, **c** and **d** containing a decamethylene spacer do not show any mesomorphic behaviour when

Table 1
Phase transition temperatures and enthalpies of the new mesogenic compounds

Compound	Heating	Cooling
Phase transition temperature/°C (ΔH/kJ mol^{-1})		
7a	Cr 151.6(32.6) SmA_1 154.3(4.4) Ch 158.3(2.9) I	I 157.4(3.2) Ch 151.9(0.8) SmA_1 141.1(37.3) Cr
8a	Cr 84.2(0.1) SmA_d 133.3(11.7) TGB 135.4(0.9) Ch 140.5(0.3) I	I 138.8(0.4) Ch 132.9(0.9) SmA_d 119.6(0.3) Cr

Ch = cholesteric and I = isotropic.

placed in a thin cell with a cell gap of $d = 5 \pm 0.2$ μm with homogeneous planar boundary conditions. Compound **8a** also exhibits the same phase sequence as **7a,** while **8b** is a non-mesomorphic compound. The difference in the Smectic A phase of **7a** and **8a** is that the former shows a monolayer smectic A_1 (SmA_1), while the latter exhibits a partial bilayer smectic A_d (SmA_d) which is described later. On cooling the isotropic phase of compound **7a**, an oily streak texture appeared which changed instantly to a fan-like texture, a characteristic texture of the N^* phase (Fig. 1, a and b). On further cooling the sample, hometropic texture of the SmA phase (Fig. 1c) appeared. However, if the transition is maintained over a length of time, either on slow cooling or on repeated heating and cooling cycles, a filament texture appears, very similar to the so-called fingerprint texture of the characteristic TGB phase. Compound **8a** also shows similar phase transitions. The difference in the textural appearance of SmA of **8a** is that it is not fan-shaped, but is like a stripe of bâttons arranged in layers (Fig. 1, a–c). The replacement of the *N*-methyl group with an *N*-ethyl group resulted in non-mesophase behaviour. On the other hand, when the central spacer is changed from $n = 5$ to $n = 10$, surprisingly, no mesomorphic behaviour is observed.

The powder X-ray diffraction pattern of **7a** and **8a** was performed at 143 °C and 125 °C, respectively. The pretty similar appearance of a sharp signal in the small angle region signifies the layered structure for the smectic phase; the other two sharp signals at $2\theta = 5.8996°$ and 8.8223° with a *d* spacing of 14.98 Å and 10.023 Å, respectively, for **7a** may be due to the fluctuation of crystal in smectic layers whose temperature is very close to smectic in crystal transition. The Debye–Scherrer pattern of **7a** shows a layer thickness of 29.44 Å with a Cu Kα radiation of wavelength $\lambda = 1.5418$ Å, corresponding to $2\theta = 3.001°$, and a fairly sharp diffuse scattering at wide angle $2\theta \sim 17.5°$. The latter corresponds to an in-layer short-range liquid-like order. The small angle reflection of **8a** is at $2\theta = 2.361°$ with a layer thickness $d = 37.41$ Å. The molecular lengths (*L*) calculated from chem3D software are 29.87 Å and 27.73 Å for **7a** and **8a**, respectively.[18] The *d* value of **7a** (29.44 Å) at 143 °C is approximately equal to molecular length *L*. For **8a**, the *d* value 37.41 Å is greater than *L*, but is less than 2*L* ($d/L \sim 1.34$). It is well known that when the reflection within the SmA layer corresponds to $d \sim L$, the smectic A layer is called the monolayer (A_1), and when the layer-spacing is intermediate between *L* and *2L* then it is called a partial bilayer (Ad) phase.[19,20] Therefore, we can designate the SmA phase of compound **7a** as SmA_1 (A_1) and that of compound **8a** as SmA_d (A_d).

Itahara et. al.[13] explained the thermotropic behaviour of their mesogenic compounds containing adenine and thymine by considering Watson–Crick base pairing (H-bonding). However, in the present instance, the compounds cannot form Watson–Crick base pairing or similar hydrogen bonds. The liquid crystalline behaviour in this case is a consequence of the supramolecular interaction of the dipoles inherent in the molecular structure. The direction of the dipoles of **7a** and **8a** was calculated by Density Functional Theory (DFT), which may determine the presence of dipolar interaction within the molecules. All calculations have been performed by the Chem3D (version 10) with GAUSSIAN 03 Interface.[21] We have computed the DFT (B3LYP) level of theory using the basis set 6-31G to obtain the dipole moment and dipolar orientation of **7a** and **8a** molecules. The dipole moments of **7a** and **8a** have been calculated as 6.62 D and 7.82 D, respectively. The direction of the dipole moment of **7a** is supposed to be axial, having a value of 3.7109, −5.465 and −0.3931 in the *X*, *Y* and *Z directions,* respectively. The maxima of the dipole must be in between the negative direction of *Y* and *X*. The net dipole of the **8a** molecule is supposed to be along the *X* direction (*X*, *Y*, *Z*: −7.4585, −2.2411, −0.7065). However, if the molecules have a strong longitudinal dipole moment, near-neighbour antiparallel correlations will exist which can result in subtle changes in the structure that can exhibit more than one form of the SmA phase. Usually, the dipoles of the monolayer A_1 phase can point up or down with equal probability within each layer.[22] The appearance of the SmA_d phase of compound **8a** at sufficiently high temperature (125 °C) may be due to the overlap of two neighbouring rod-shaped molecules in antiparallel orientation as in the case of highly polar rod-shaped molecules[23,24].

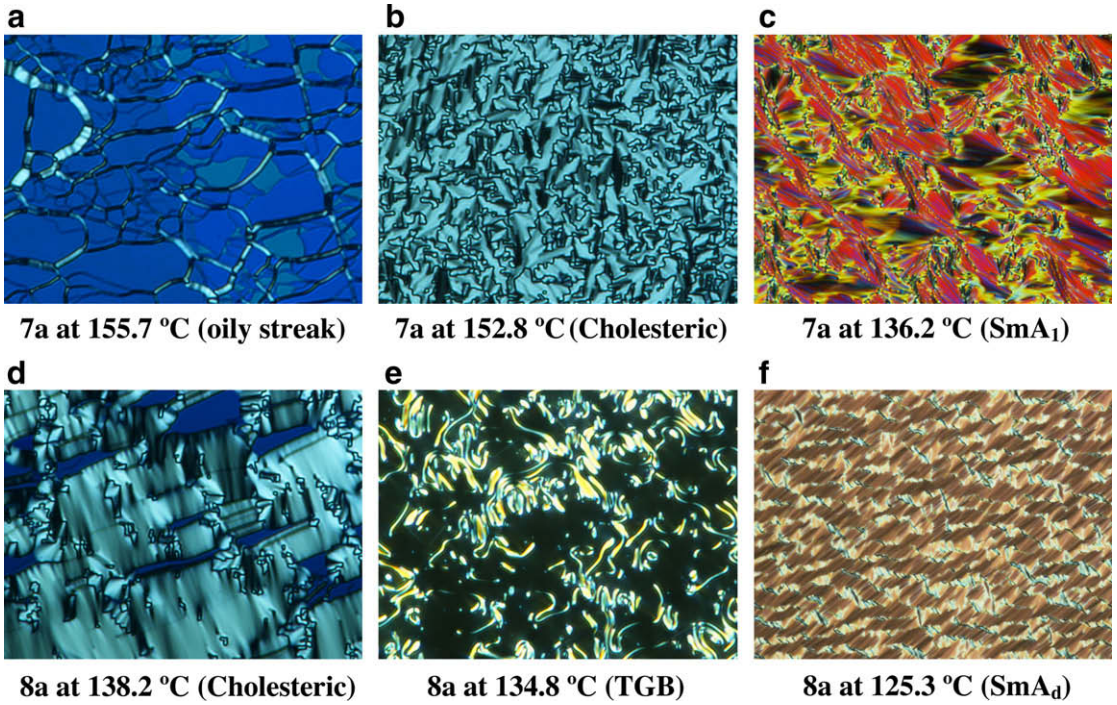

Figure 1.

In conclusion, we have developed nucleobase derivatives by connecting pyrimidine moieties with cholesterol for new liquid crystalline materials. There are several reports of the formation of lyotropic liquid crystals by DNA and nucleotides.[25,26] However, unsuccessful attempts[27,28] were made to prepare thermotropic liquid crystals of nucleobase derivatives, and there is only one report by Itahara et al. who succeeded in the preparation of thermotropic liquid crystals adjoining adenine and thymine with cholesterol and observed only the cholesteric phase.[13] We have synthesized new mesogenic compounds derived from cholesterol with uracil and barbituric acid linked with an alkyl chain spacer giving rise to monolayer SmA_1 and partial bilayer SmA_d associated with the TGB and cholesteric phases. The presence of two sharp signals in the XRD profile besides the small angle peak and diffuse peak implies that the smectic layer is fluid with a long range order in both the compounds (**7a** and **8a**). The remaining compounds of both the series do not exhibit any mesomorphic behaviour. The stacking of bâttonets in the SmA_d phase suggests attractive interaction between the adjoining bâttons. The variation of the smectic A phase is observed when cholesterol is linked with uracil in place of barbituric acid.

Acknowledgements

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16. *Typical procedure for the synthesis of compound* **7a**: A mixture of compound **5a** (128 mg, 0.827 mmol) and cholesteryl benzoate **4a** (500 mg, 0.827 mmol) was refluxed in absolute ethanol in the presence of a catalytic amount of glacial acetic acid for 2 h. The schiff base **7a** was obtained as a precipitate from the hot reaction mixture. It was repeatedly washed with hot ethanol and dried in vacuum.
Compound **7a**: Yield 96%; IR (KBr): 2945, 1733, 1693, 1655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H = 0.66–2.32 (m, 51H), 3.40 (s, 3H), 3.46 (s, 3H), 3.99 (t, J = 6.4 Hz, 2H), 4.59–4.62 (m, 1H), 5.35 (d, J = 4.0 Hz, 1H), 6.91 (d, J = 8.7 Hz, 2H), 7.43 (s, 1H), 7.74 (d, J = 8.7 Hz, 2H), 9.50 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C = 12.2, 19.1, 19.7, 23, 23.2, 24.2, 25.2, 26, 28.4, 28.5, 28.6, 29.3, 32.2, 32.3, 35, 36.2, 37, 37.5, 38.6, 39.9, 40.1, 42.7, 50.4, 56.5, 57, 68.1, 74.2, 115, 123, 123.3, 130.3, 139.9, 140, 160.5, 161.1, 161.9, 173.4. HRMS: *m/z* calcd for $C_{46}H_{67}N_3O_5$ $[M+H]^+$: 742.5153; found: 742.5156; $[\alpha]_D$ −17.8 (*c* 0.16, $CHCl_3$). Anal. Calcd for $C_{46}H_{67}N_3O_5$: C, 74.46; H, 9.10, N, 5.66. Found: C, 73.89; H, 8.93; N, 5.79.
17. *Typical procedure for the synthesis of compound* **8a**: A mixture of compound **6** (106 mg, 0.827 mmol) and cholesteryl benzoate **4a** (500 mg, 0.827 mmol) was refluxed in absolute ethanol for 2 h. The product **8a** was obtained as a precipitate from the hot reaction mixture. It was repeatedly washed with hot ethanol and dried in vacuum.
Compound **8a**: Yield 98%; IR (KBr): 2943, 1730, 1669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H = 0.66–2.33 (m, 51H), 3.38 (s, 3H), 3.40 (s, 3H), 4.05 (t, J = 6.4 Hz, 2H), 4.59–4.61 (m, 1H), 5.36 (d, J = 4.0 Hz, 1H), 6.94 (d, J = 8.9 Hz, 2H), 8.31 (d, J = 9.0 Hz, 2H), 8.50 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C = 19.3, 21, 22.5, 22.8, 23.8, 24.3, 24.7, 25.5, 27.8, 28, 28.2, 28.3, 28.7, 29, 31.8, 31.9, 34.5, 35.8, 36.2, 36.6, 37, 38.1, 39.5, 39.7, 42.3, 50, 56.1, 56.7, 68, 73.8, 114.1, 114.4, 122.6, 125.4, 138.1, 139.6, 151.4, 158.9, 161, 163.2, 163.9, 172.9. HRMS: *m/z* calcd for $C_{46}H_{66}N_2O_6$ $[M+Na]^+$: 765.4813; found: 765.4819; $[\alpha]_D$ −16.3 (*c* 0.16, $CHCl_3$). Anal. Calcd for $C_{46}H_{66}N_2O_6$: C, 74.36; H, 8.95, N, 3.77. Found: C, 74.04; H, 8.86; N, 3.72.
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