value of the order parameter. Our experiments also show that both the *N–I* and *N–N* transitions occur at fixed values of the order parameters which are independent of pressure.

The HP studies on liquid crystals in Bangalore were initiated by S. Ramaseshan when he was in the National Aeronautical (now Aerospace) Laboratories[18]. It is indeed a pleasure to contribute this article to the special issue of *Current Science* which is being brought out in honour of his 80th birthday.

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Twist grain boundary smectic A phase in compounds derived from cholesterol*

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The synthesis and characterization of four compounds of a homologous series of cholesteryl-2-fluoro-4-*n*-alkoxybenzoates is reported. The twist grain boundary smectic A phase was observed in three compounds which contain only one phenyl ring. All the compounds exhibiting this phase, also show blue phase, cholesteric, smectic A and smectic C* phases. The mesophases were identified using polarizing optical microscopy, differential scanning calorimetry and helical pitch measurements.

SINCE the discovery[1] of the liquid crystalline state in cholesteryl benzoate, chirality and optical activity have become an important topic for research in orientationally ordered fluids. Based on simple, but very clever symmetry arguments, Meyer *et al*.[2] discovered ferroelectricity in chiral compounds exhibiting the smectic C phase. This was followed by the demonstration of an electro-optical effect[3] that utilized this ferroelectric property exhibited by the chiral smectic C (SmC*) phase. The SmC* phase is the most fluid phase to offer such a property and hence has shown great potential for electro-optical device applications. During the centenary year of the discovery of the liquid crystalline state, two other significant discoveries were made. One is the antiferroelectric smectic C* phase[4], which shows electric-field-induced tristable switching characteristics and the other is the twist grain boundary smectic A (TGB_A) phase[5], which was discovered serendipitously. In the TGB_A phase, small blocks of molecules which have a local smectic A structure, are rotated with respect to one another by screw dislocations, which results in the formation of a helical structure. In this helical macro structure, the smectic A blocks rotate such that the helical axis is parallel to the layer planes and the screw dislocations are periodic.

Though a theoretical model for the existence of TGB_A phase was developed by Renn and Lubensky[6], the first experimental confirmation for its occurrence was made by Goodby *et al*.[5] in a series of 1-methylheptyl-4′-(4″-*n*-alkoxyphenylpropioloyloxy)biphenyl-4-carboxylates. These materials had high optical purities with their chiral centers located adjacent to the rigid molecular cores containing three phenyl rings. Since then, a fairly large number of compounds exhibiting the TGB_A phase have been synthesized[8–10]. It was believed for some time that a relatively

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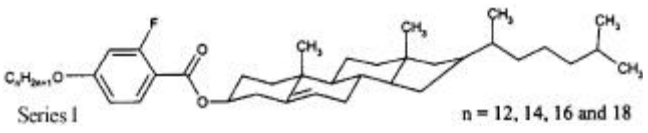
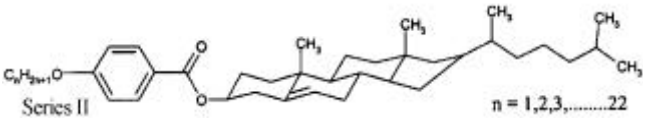
long molecular core comprising a minimum of three aromatic rings is a prerequisite for the formation of TGB_A phase. However, Nguyen *et al.*[11] disproved this by reporting the occurrence of this phase in a homologous series of compounds composed of two phenyl rings. Lateral substituents play an important role in the design and synthesis of useful liquid crystalline materials. A fluorine substituent, with its small van der Waals radius and fairly high polarity, has been found to be very useful in liquid crystal chemistry.

Although a large number of cholesterol derivatives are known to be mesomorphic, there are only very few compounds derived from cholesterol and exhibiting the TGB_A phase, which include dimesogenic systems, polymers and binary mixtures having derivatives of cholesterol as one of the components[12]. Compounds exhibiting the TGB_A phase have generally at least three phenyl rings in the core. In this paper, we report the mesomorphic properties of four compounds of a homologous series which contain only one phenyl ring with cholesterol as the chiral moiety. The influence of a lateral fluorine substituent on the mesomorphic properties, particularly the TGB_A phase, has also been examined.

The molecular structures of the compounds investigated in the present study (series I) and that of the analogous parent compounds (series II) are shown in Schemes 1 and 2 respectively.



Scheme 1.



Scheme 2.

The four compounds belonging to series I were prepared following a method shown schematically in Figure 1. Cholesterol was obtained commercially and used without further purification. The 2-fluoro-4-*n*-alkoxybenzoic acids were synthesized following a procedure already described[13]. The procedure for the synthesis of compound **4** and its characterization is given below.

A mixture of 2-fluoro-4-*n*-octadecyloxybenzoic acid (0.2 g, 0.5 mmol), cholesterol (0.21 g, 0.54 mmol), 4-*N*,*N*-dicyclohexylcarbodiimide (0.11 g, 0.54 mmol), 4-*N*,*N*-(dimethylamino) pyridine (0.06 g, 0.05 mmol) and dry dichloromethane (10 ml) was stirred overnight at room temperature. The precipitated *N*,*N′*-dicyclohexylurea was filtered off and the filtrate diluted with dichloromethane (20 ml). The resultant solution was washed with 5% aqueous acetic acid (2 × 10 ml), water (2 × 25 ml) and dried over anhydrous sodium sulphate. The residue obtained on removal of solvent was chromatographed on silica gel using a mixture of chloroform and petroleum ether as eluant. Removal of solvent from the eluate afforded the required material as a white product. This was purified further by crystallization from 2-methoxyethanol; yield 0.3 g, m.p. 94°C; $[a]\ D^{25} = 0.8°$ (9.9 mg/ml in $CHCl_3$); IR n_{max} (nujol), 2900, 1700, 1610, 1450, 1370, 1250 and 1130 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) d (ppm): 1.08–2.16 (*m*, 58H, 26 × CH_2, 6 × CH), 0.68 (*s*, 3H, tertiary CH_3), 1.055 (*s*, 3H, tertiary CH_3), 0.853–0.875 (*d*, 3H, [R CH $(CH_3)_2$]), 0.89–0.92 (*m*, 6H, 2 × CH_3), 2.44–2.46 (*m*, 2H, allylic H), 5.41 (*m*, 1H, olefinic H), 3.95–3.98 (*t*, 2H, $ArOCH_2$–), 4.8–4.9 (*m*, 1H, –CHOCOAr), 6.57–7.87 (*m*, 3H, ArH).

In general, the purity of all the compounds was checked by thin layer chromatography (Merck Kieselgel $60F_{254}$ pre-coated plates). The chemical structure of the compounds was confirmed by using a combination of ^1H NMR spectroscopy (Bruker AMX 400 spectrometer) with 1% tetramethylsilane in deuteriochloroform as an internal standard and infrared spectroscopy (Shimadzu FTIR-8400 spectrophotometer). Specific optical rotations were measured using chloroform as a solvent (optical activity AA1000 polarimeter).

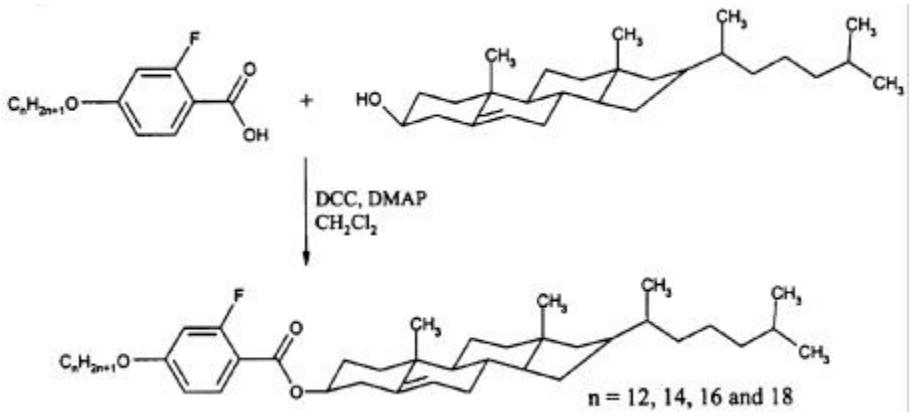


Figure 1. The method used to prepare cholesteryl 2-fluoro 4-*n*-alkoxybenzoates.

Table 1. Transition temperatures (°C) and enthalpies (kJ mol^{-1}) for compounds of series I

Compound	*n*	Cr		SmC*		SmA		TGB_A		N*		BP		I
1	12	•	118.5 *31.9*	–		–		–		•	194.5 *0.05*	•	195.0 *0.57*	•
2	14	•	105.0 *26.1*	•	113.5 *	•	147.0 *	•	150.5 *	•	185.6 *	•	186.0 *	•
3	16	•	85.0 *23.6*	•	97.0 *	•	152.5 *	•	154.0 *	•	176.9 *	•	177.5 *	•
4	18	•	94.0 *26.5*	(•	82.0) *	•	151.5 *	•	152.5 *	•	169.8 *	•	170.5 *	•

*The enthalpy could not be measured; (): Indicates a monotropic transition.
Cr: Crystalline phase; SmC*: Chiral smectic C phase; SmA: Smectic A phase; TGB_A: Twist grain boundary smectic A phase; BP: Blue phase; I: Isotropic phase; N*: Cholesteric phase; –: Phase does not exist; •: Phase exists.

The optical textures of the mesophases were examined using a polarizing microscope (Leitz Laborlux 12 POL) in conjunction with a heating stage and a controller (Mettler FP52 and FP5 control unit respectively). Differential scanning calorimetry (DSC, Perkin-Elmer, Pyris ID) was used to determine both the transition temperatures and the associated enthalpy values. The heating and cooling rates were 5°C min^{-1}, and the calorimeter was calibrated using pure indium as a standard. The helical pitch was determined by the well-known Grandjean–Cano method as a function of temperature using a graduated eye-piece, which was calibrated using a micrometer provided by Leitz company.

All the four compounds synthesized have been studied using polarizing optical microscopy (POM) and DSC. The transition temperatures and the associated enthalpy values for these compounds (series I) are summarized in Table 1. As can be seen all the compounds are enantiotropic mesomorphic. Compound **1** exhibited blue phase, reflecting blue and green colours, over a short temperature range of 0.5°C and a cholesteric (N*) phase with a characteristic planar texture. However, compounds **2**, **3** and **4** exhibited chiral smectic C (SmC*), smectic A (SmA) and twist grain boundary smectic A (TGB_A) phases in addition to N* and blue phases. On cooling an unaligned sample of compound **2** from the planar texture of the cholesteric phase, a focal-conic texture characteristic of the SmA phase[14] was obtained. When this phase was cooled further, banded focal-conic texture typical of the SmC* phase[14] was formed. To identify the phase between the N* and SmA phases, as observed on a DSC thermogram, the sample was examined in a cell treated for homeotropic alignment. When the sample was heated slowly from the dark regions of the homeotropically aligned SmA phase, fine filaments began to grow and a photomicrograph of this filamentary growth pattern is shown in Figure 2. This is the characteristic feature of the TGB_A phase.

As a conclusive evidence for the existence of the TGB_A phase, the sample was examined in a wedge-shaped cell, the surfaces of which were treated for planar alignment.

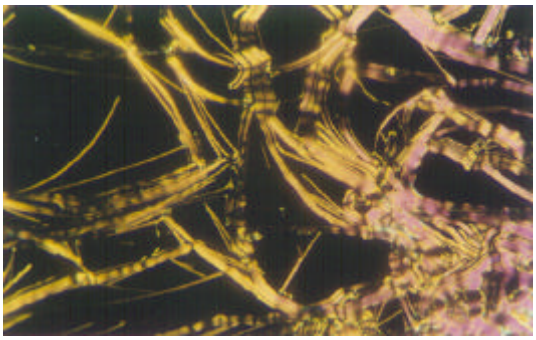


Figure 2. Photomicrograph showing the filamentary texture of TGB_A phase developing from the homeotropic smectic A phase of compound **2**.

Figure 3. Photomicrograph of the Grandjean planar texture of the TGB_A phase of compound **2**.

In such a cell, where the thickness varies continuously from one edge of the cell to the other, an array of equidistant, colourful Grandjean-Cano lines similar to those seen for the N* phase was obtained. This texture shows that the helix direction is perpendicular to the glass plates and a typical photomicrograph of the Grandjean planar texture of the TGB_A phase of compound **2** is shown in Figure 3. Since compound **1** with *n*-decyloxy terminal chain did not exhibit the TGB_A phase, the lower homologues were not prepared. As can be seen in Table 1, the thermal range of the TGB_A phase decreases on increasing the *n*-alkoxy chain length. A plot of the transition temperatures as a function of the number of

carbon atoms in the terminal *n*-alkoxy chain is shown in Figure 4. The plot shows fairly smooth curve relationship for like transitions.

We have examined the effect of the lateral fluoro substituent by comparing the mesomorphic properties of the analogous unsubstituted parent compounds (series II) which were reported by Vill and Thiem[15]. The transition temperatures and the phase sequence for the analogous four derivatives are summarized in Table 2. It can be seen that all these four compounds show enantiotropic N* and SmA phases and a monotropic SmC* phase. Thus, the occurrence of the TGB_A phase has been attributed to the lateral fluoro substituent. This substituent increases the transverse polarity of the system and stabilizes tilted smectic phases. It should be pointed out that the occurrence of the TGB_A phase also depends on the length of the terminal alkoxy chain. Hence, it can be said that in a single phenyl ring system having cholesterol as the chiral moiety, subtle change in the substitution pattern has an influence on the occurrence of the TGB_A phase.

The helical pitch measurements were performed on the TGB_A phase following the well-known Grandjean–Cano wedge method[8,16]. A sample of compound **3** was taken in a wedge-shaped cell treated for homogeneous alignment. The two glass plates formed a small angle at the wedge. The sample was cooled slowly (0.2°C min^{-1}) from the isotropic phase to the cholesteric phase, which induced an array of equidistant Grandjean–Cano lines. The pitch of the cholesteric phase was determined by measuring the distance between the GC lines as a function of temperature. As the temperature was lowered from the N* phase to the TGB_A phase, the spacing between the lines increased, indicating that the pitch in this phase was increasing. A plot of the evolution of pitch versus temperature in the N* and TGB_A phases for compound **2** is shown in Figure 5. It is evident from this plot that the variation of pitch at the N* phase to the TGB_A phase transition is smooth and continuous. A gradual but small increase in the pitch value from 0.17 to 0.19 μm was observed upon cooling the sample through the N* phase. However, within the TGB_A phase, the value of the pitch increased steeply and reached a maximum of 1 μm at the TGB_A to SmA transition.

In conclusion, four compounds of a homologous series of compounds containing only one phenyl ring with a lateral fluoro substituent and cholesteryl moiety have been synthesized and their mesomorphic properties examined. The influence of the lateral fluoro substituent on the occurrence and stability of the TGB_A phase has been examined. It is concluded that systems containing a

Table 2. Transition temperatures (°C) for compounds of series II (ref. 15)

Compound	*n*	Cr		SmC*	SmA	N*		I
5	12	•	126.4	(+ 84.5)	•	178.4	• 198.3	•
6	14	•	117.0	(+ 75.7)	•	176.4	• 188.9	•
7	16	•	97.8	(+ 62.8)	•	172.8	• 182.1	•
8	18	•	105.5	(+ 56.5)	•	168.3	• 174.5	•

(): Indicates a monotropic transition.
Cr: Crystalline phase; SmC: Chiral smectic C phase; SmA: Smectic A phase; N*: Cholesteric phase; •: Phase exists.

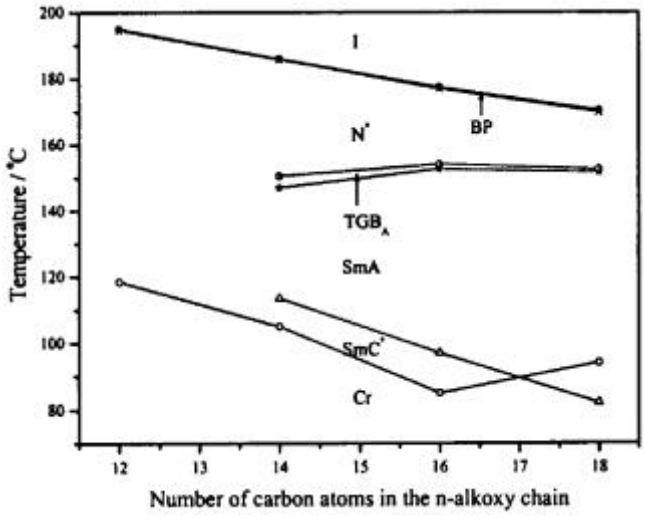


Figure 4. A plot of transition temperatures versus the number of carbon atoms in the *n*-alkoxy chain for compounds of series I.

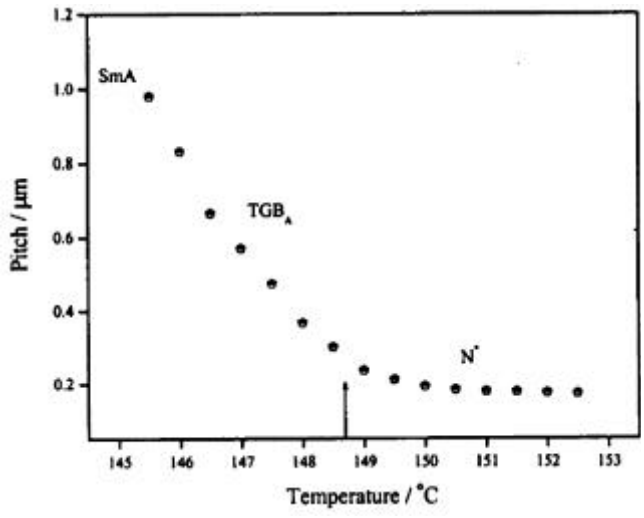


Figure 5. A plot of the variation of helical pitch as a function of temperature in the N* and TGB_A phases of compound **2**.

single phenyl ring with fairly long terminal *n*-alkoxy chain and having cholesterol as the chiral moiety exhibits TGB_A phase when there is a lateral fluoro substituent *ortho* to the carboxylate group close to the chiral moiety.

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Approaches to relieve the burden of cataract blindness through natural antioxidants: use of *Ashwagandha* (*Withania somnifera*)*

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Cataract is the major cause of blindness the world over. Efforts to ease the cataract burden will be of great social and health economic benefit. Oxidative stress is known to be a major factor in age-related cataract of the eye lens. Regular systemic intake of antioxidant vitamins appears to retard the progression of cataract. These are beyond the reach of people in developing countries, who could, however, be encouraged to use antioxidant plant products that form part of their diet and traditional health practices. *Ashwagandha* (extract of the plant *Withania somnifera*) is one such product used in traditional medicine. We have studied the antioxidant, cytoprotective and related properties of *Ashwagandha* here, and find it to be excellent in these respects. It is also able to retard the formation of 'cold cataract' *in vitro*, suggesting that *Ashwagandha* could well act as a cataracto-static agent.

AGE-related cataract is the leading cause of blindness and visual impairment worldwide. Effective surgical procedures are available for treatment, but besides the requirement of highly trained personnel, the problem of post-operative complications, cost of surgery and high number of people requiring surgery pose a substantial economic burden. In India alone, there are about 9.5 million people who are cataract-blind, and at least twice as many suffering from various stages of development of this sight-threatening condition[1].

Oxidative stress, either as the primary event or secondary to risk factors like ageing and smoking, is one of the predominant factors that leads to cataract. A major mode of damage to lens proteins involves oxidative reactions[1–3]. For this reason, the possible role of antioxidants in delaying the onset or progression of age-related cataract has gained considerable interest. Endogenous defence mechanisms which protect the lens against oxidative damage include compounds like glutathione, ascorbate and antioxidant enzymes like catalase, superoxide dismutase, glutathione reductase, glutathione peroxidase and related ones[4–6]. But with increasing age, the levels of these protective enzymes are known to decline in the human eye[7,8]. Supplementation with antioxidants thus appears to be an attractive possibility to delay the onset of age-related cataract. It has been estimated that a delay in cataract formation of approximately 10 years would reduce the cataract surgical burden[9] by perhaps 45%.

Most research on nutrition and cataract has been regarding vitamins (vitamins A, C and E) and several studies have found their intake to be associated with a reduced risk of cataract[10–15]. Supplementation of antioxidants on a regular basis is beyond the economic reach of people in the developing world, who form the major fraction of cataract-afflicted across the globe. However, they include a range of plant material, rich in antioxidants and micronutrients, in their diet and health practices. Hence, we have studied the role of certain plant extracts that are

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