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A bilayer to monolayer phase transition in liquid crystal glycolipids†

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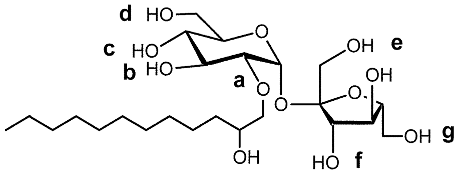
Investigations of the thermotropic liquid-crystalline properties of 6,6′-di-*O*-stearoylsucrose show, for the first time, that glycolipids can exhibit phase transitions within the smectic A phase.

Glycolipids, found in artificial and biological membranes, often have been shown to exhibit lyotropic and thermotropic liquid crystal phases. Conventional wisdom, based on property–structure analyses, indicates that most mesogenic variants would be expected to exhibit smectic A* or columnar phases on heating. Conversely, the addition of water to glycolipids, thereby causing the swelling of the head groups, can result in the formation of lamellar, cubic and/or columnar phases as a function of the induced curvature in the packing arrangements of the molecules. Thus, a higher degree of mesomorphic richness is found in the lyotropic state in comparison to the thermotropic state. Interestingly, although the richness is found in the lyotropic state, more materials have been shown to exhibit thermotropic than lyotropic phases. The number and range of materials that exhibit thermotropic phases in comparison to those exhibiting lyotropic phases suggest that glycolipids are in fact not particularly good amphiphiles. Furthermore, it is very rare that smectic polymorphism is exhibited at all in the thermotropic state, and indeed only one or two examples of such materials exist, and they are bolaphiles with two head groups and a bridging aliphatic chain.

Recently, we examined the effects of the position of substitution of a dodecyl chain in mono-*O*-[2-hydroxydodecyl]-sucroses on mesomorphic behaviour. It was found that as the aliphatic chain was moved from location **a** to **g**, as shown in structure **1**, smectic phases were obtained when the cross-sectional area of the aliphatic chain was comparable to that of the sugar moiety, and columnar and cubic phases where the head group appeared to be much larger than the chain, *i.e.* at positions **a** and **f**.[1] The smectic A* phases exhibited by compounds **b** to **e** and **g** were found to have interdigitated structures. Thus, the results of our studies show that the packing of molecules with wedge-shaped structures induces curvature into the system thereby favouring the formation of columnar and cubic phases, just as swelling of the head group does upon hydration in lyophases.



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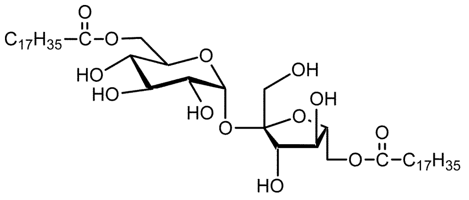
The introduction of two aliphatic chains we rationalised would induce the formation of lamellar phases at the expense of columnar and cubic. Surprisingly one material prepared, 6,6′-di-*O*-stearoylsucrose, **2**, showed polymorphism in the smectic A* phase, providing us with the first example of a glycolipid that exhibits a phase transition within the smectic A* phase.



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The 6,6′-di-*O*-stearoylsucrose was prepared as described in the supplementary information. The material was found to melt at 109.8 °C (T_{onset}) to give a smectic A* phase, and at 164.3 °C, it underwent a second melting to the amorphous liquid. Cooling from the isotropic liquid reproduced the transition back to the smectic A* phase, however, recrystallisation to solid state was suppressed to 70 °C due to supercooling.

Thermal polarising light microscopy (POM) showed that the smectic A* phase exhibited homeotropic and oily streak textures between untreated glass slides. Close examination of the oily streak texture showed that it was mostly composed of floating edge dislocations. However, at the edges of the cover-slip focal-conic defects appeared which were characterised by their elliptical and hyperbolic lines of optical discontinuity. The presence of these defect lines is diagnostic for the formation of a lamellar phase. The absence of tilt domains confirms the phase as smectic A, and as the material is chiral it is defined as SmA*.

Differential scanning calorimetry confirmed the results obtained by POM. The enthalpy ΔH obtained for the smectic to isotropic liquid phase transition was 1.147 J g^{-1}, and the entropy of the transition ΔS was 2.6 mJ $g^{-1}K^{-1}$ (= ΔH/Cp). Thus the results obtained were as expected for a typical glycolipid.

X-ray diffraction experiments were performed using a MAR345 diffractometer equipped with a 2D image plate detector (CuKα radiation, graphite monochromator, λ = 1.54 Å). The samples were heated in the presence of a magnetic field ($B \approx 1$ T) using a home-built capillary furnace. The diffraction patterns show the intensity as a function of the modulus of the scattering wave vector (**q**), where

$$q = |\mathbf{q}| 4\pi\sin\theta/\lambda = 2\pi n/d$$

and θ is the diffraction angle, λ is the wavelength (1.54 Å), n is an integer and d is the lattice distance.

The diffraction intensity (using a logarithmic scale) as a function of the scattering wave vector q and temperature T is shown in Fig. 1. Surprisingly, an intense small angle reflection is observed in the isotropic phase as shown by the blue curves in the figure. This indicates substantial ordering in the liquid state and the possible presence of TGB and/or entangled/disentangled flux phases. When cooling down into the SmA* phase (brown lines) the second order reflection (002) also can be seen. The fundamental (001) reflection is best fitted by a Lorentzian distribution function, indicating *short-range* positional order. At lower temperatures, T = 100 °C, the shape of the reflection changes to a Gaussian distribution function, indicating the presence of long-range positional order, as is usually observed for smectic phases. Also a third order reflection is observed. Further cooling the sample results in crystallisation (green lines).

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† Electronic supplementary information (ESI) available: synthesis of compound **3**. See http://www.rsc.org/suppdata/cc/b3/b308880d/

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The change in shape of the diffraction patterns, the fundamental reflections at T = 105 °C (Lorentzian) and T = 95 °C (Gaussian), are illustrated in Fig. 2. Note the difference in the shape of the curves, particularly at the "wings" of the reflections.

A strong temperature dependence of the layer spacing is observed in the SmA* phase with the d-values ranging from 35 to 50 Å, see Fig. 3. Remarkably, the d-values change continuously in the smectic phase and also into the isotropic liquid. Crystallisation is observed between 70 and 75 °C, where d_{001} and ζ_{001} become virtually temperature independent. Where the peak shape changes from Gaussian to Lorentzian (T = 100 °C), a local minimum in the correlation length (half-width of the reflection) is observed. This marks a transition from one form of the SmA* phase to another, and demonstrates that the material exhibits polymorphism. (It should be noted that this transition could not be observed by either POM or DSC). Table 1 shows a "snap-shot" of the d spacings taken at two temperatures, above and below the SmA*. The fourth order reflection at 80 °C demonstrates how well ordered the lower temperature phase is.

At low temperatures the layer spacing approaches 48 Å, molecular modelling using ChemDraw 3D Ultra gives the length of the minimised extended molecular conformation of 54.8 Å, and Dreiding Molecular Models give a value of 56 Å. At high temperatures the layer spacing approaches 36 Å, whereas modelling of the folded molecular conformation gives a value of 31.6 Å, and Dreiding Models a value of 29.7 Å.

One explanation for the transition in the smectic A*phase is that there is a transformation from an intercalated to a non-intercalated structuring of the layers. However, this simple model would not necessarily explain the discontinuous change in correlation length. An alternative explanation is that there is a change in molecular conformation at the phase transition from a linear (unfolded) to a folded structure, as shown in Fig. 4. Thus for the folded structure, the molecules would be expected to be organised with their polar groups in non-interrupted sublayers, and their aliphatic chains intercalated. In this arrangement the correlation length would be increased, and thus the model would explain the local minimum in the correlation length at the phase transition between the two smectic A* phases where the incompatibility of the two phase structures would lead to some disorder at the phase transition.

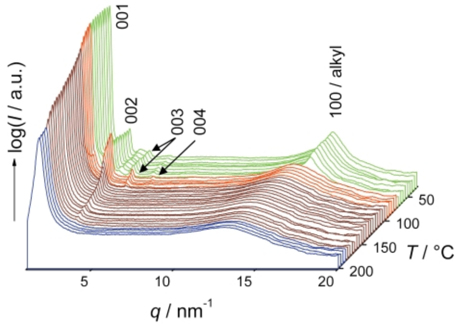


Fig. 1 Radially integrated diffraction patterns of 6,6′-di-*O*-stearoylsucrose as a function of temperature (°C).

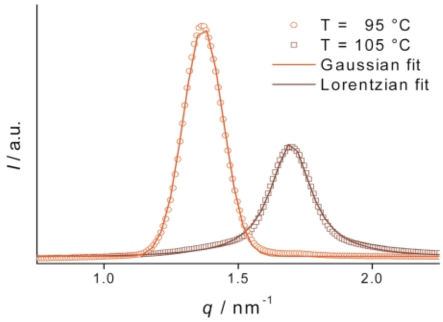


Fig. 2 Lorentzian and Gaussian fits to the diffraction data at temperatures of 105 and 95 °C respectively.

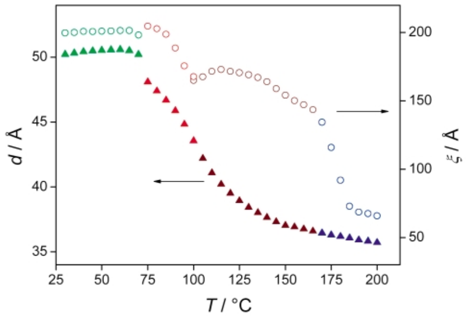


Fig. 3 The lamellar spacing (d) (▲) and correlation length (ζ) (○) as a function of temperature (°C).

Table 1 X-ray data taken at two different temperatures in the smectic A* phase of 6,6′-di-*O*-stearoylsucrose

Temp./°C	Miller indices	q/nm^{-1}	d/Å
80	001	1.32	47.4
	002	2.64	23.8
	003	3.98	15.8
	004	5.27	11.9
110	001	1.53	41.1
	002	3.04	20.7

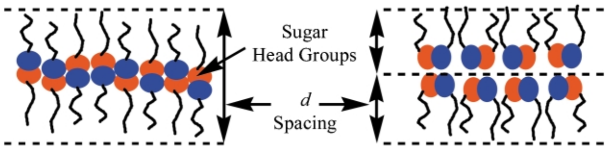
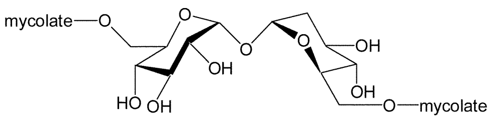


Fig. 4 The SmA* phases of 6,6′-di-*O*-stearoylsucrose.

Interestingly, Bottle and Jenkins[2] showed that the homologous material 6,6′-di-*O*-palmitoylsucrose possesses immunostimulant properties and antitumour activity, and thus one might expect that the distearoyl material will also be bioactive. Furthermore these materials are similar in structure to Cord Factor, **3**, which is associated with virulent strains of *tubercle bacilli*. Cord Factor has been shown to be responsible for the bacteria forming cords in aqueous media,[3] and to exhibit antitumour activity. Thus it is interesting to speculate that Cord Factor will also be mesomorphic and the liquid crystal properties of all three compounds are important in relation to their biological function.



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Notes and references

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