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Liquid crystalline derivatives of galactose and galactitol: dependence of thermotropic mesomorphism on carbohydrate form

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An almost complete homologous series of the acyclic, open-chain 6-*O*-*n*-alkyl-D-galactitols has been prepared. Most homologues in this series exhibit an enantiotropic smectic A* phase. The liquid crystal transition temperatures of these open-chain carbohydrates are compared with those of the corresponding homologues in the cyclic form, i.e., with those of the 6-*O*-*n*-alkyl-α-D-galactopyranoses. In general the carbohydrates in the open-chain form exhibit higher clearing points than those of the analogous cyclic pyranoses. However, the melting point of the galactitols is generally significantly lower than that of the corresponding galactopyranoses. This leads to a much wider temperature range of the smectic A* phase for the carbohydrates in the pyranose form. The lowest clearing point was found for related galactoses in the furanose form. Alternation was found for the clearing point of the 6-*O*-*n*-alkyl-α-D-galactopyranoses and the 6-*O*-*n*-alkyl-D-galactitols. Powder X-ray diffraction studies indicate a non-intercalated structure for the crystalline state and an interdigitated arrangement in the smectic A* phase with a degree of chain melting for both series.

1. Introduction

Glycophospholipids, glycoproteins and glycolipids are basic components of biological membranes [1–5]. The oligosaccharide parts of some of these molecules are responsible for intercellular recognition and also act as specific binding sites for viruses, hormones and proteins [3–5]. Many glycophospholipids and glycolipids exhibit thermotropic and lyotropic liquid crystalline behaviour [6–8]. Related, but simpler and synthetically modified, carbohydrates also have significant practical applications as non-ionic, low toxicity, biocompatible and biodegradable surfactants easily prepared in a high overall yield from a diverse, renewable and natural resource. Mixtures of monosaccharides, oligosaccharides and polysaccharides, such as alkyl polyglycosides (APGs), are used in tens of thousands of tons per annum as cost-effective surfactants as components of detergents for laundry and dishwashing applications [9–11]. More expensive, monodisperse monosaccharides, such as alkyl glycosides, are commercially available as mild solvents for proteins in membranes which can be solvated, extracted, separated and reconstituted in a non-denatured form [12, 13]. They are also used as components of liposomes and vesicles in drug release formulations [14, 15] as well as exhibiting antiviral and antibacterial activity themselves [16–18]. Perfluorinated carbohydrate derivatives have also been used as artificial blood [19]. Most of these practical applications of carbohydrates involve aqueous solutions, suspensions, emulsions or gels. Since the solubility, surface tension, critical micelle concentration, lyotropic phase formation, aqueous gel formation, etc., are all dependent on the hydrophilic–lipophilic balance (HLB) [20], i.e. on the chain length of the alkyl/acyl substituent for a given carbohydrate head group, it is important to synthesize homologous series for systematic investigations of their physical and biological properties. Therefore, we report here the synthesis of an almost complete homologous series ($n = 2, 3, 5$–$16, 18$) of 6-*O*-*n*-alkyl-D-galactitols. Although a number of homologous series of substituted carbohydrates has been reported, such as open-chain aldose dialkyl dithioacetals [21, 22], the number of homologues has generally been limited, since it is known that liquid crystalline properties are generally found for carbohydrates after a critical alkyl chain length has been exceeded (≈3–8 methylene units, depending on the form of the sugar), see below.

The first alkyl glycosides with surfactant properties were prepared and reported more than 120 years ago [23–29]. However, it was not until much later that they were recognized and characterized [30–44] as liquid crystal materials exhibiting lamellar smectic A* (SmA*)

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[21, 22, 29–38], discotic (columnar) or cubic [39–41] mesophases. Furthermore, glycolipids often possess amphotropic behaviour [42], as they exhibit liquid crystalline properties both on melting the pure material to generate a thermotropic mesophase and also in the presence of solvents, e.g. with water to produce lyotropic mesophases [43, 44], which are also temperature dependent. In the meantime, and especially in the last ten years, many substituted carbohydrates with liquid crystal properties have been synthesized [45–62]. However, most thermal data for liquid crystalline carbohydrate derivatives to be found in the literature are for glucose as it is a cheap, readily available starting material, which is relatively easy to derivatize regio- and stereo-selectively. However, other carbohydrates, such as galactose [56–60], may well exhibit a more advantageous property spectrum for the above applications. Therefore, we have started a systematic study of substituted derivatives of galactose with alkyl chains attached to the carbohydrate core in various positions by diverse linkages [60].

In the crystalline and liquid crystalline states the carbohydrate cores of amphiphilic substituted carbohydrates tend to separate into discrete layers stabilized by intermolecular hydrogen bonding between the carbohydrate hydroxy groups, whereas the aliphatic terminal chains aggregate to form a complementary layer held together by van der Waals forces. These bilayers may show a degree of interdigitation of either the hydrophilic sugar or the lipophilic chain. It is this microscopic phase separation of the hydrophilic and lipophilic parts of amphiphilic substituted carbohydrates which determines the nature of the thermotropic and lyotropic mesophases exhibited by them as well as the absolute values of their transition temperatures [21, 22, 62]. Therefore, the bilayer structure and its liquid crystallinity should also depend upon the form of the sugar, i.e. on its furanose, pyranose or open-chain forms. Since it has been shown that the smectic A*–isotropic transition temperature (T_{SmA*-I}) is dependent on the number of groups capable of hydrogen bonding [29, 33, 46–48], it may be speculated that carbohydrates in the open chain form would exhibit a higher T_{SmA*-I} than the corresponding carbohydrate in the pyranose and furanose forms, as well as changing the shape and rotation volume of the polar head group. Conversely, cyclic forms could imbue the sugar with a higher degree of conformational stability compared with the open chain form at elevated temperatures, since the relative orientations of the hydroxy groups (primarily equatorial) are maintained, despite the existence of a wide variety of conformations for the ring itself. This is not the case for the acyclic, open-chain analogues. Therefore, we report here a direct comparison of the transition temperatures of alkyl substituted galactose derivatives in the open chain, pyranose and furanose forms in order to investigate these effects further.

Some X-ray diffraction data are available for a number of liquid crystalline carbohydrate derivatives. The limited amount of data is mostly for the crystalline state [34–36, 62–66], although the results of some measurements made on the liquid crystalline state have recently been reported [42, 60, 66]. Therefore, it was hoped that X-ray diffraction studies on these new compounds in the crystalline *and* mesomorphic state would yield information on the molecular ordering in these states. There are two prime models for the molecular organization in the lamellar SmA* phase of liquid crystal carbohydrates [34–38], although they are strongly related. One model suggests that the layers are held together by hydrogen bonding of the carbohydrate moieties along the median of the layers; the non-interdigitated aliphatic chains form the outer regions of the layers [37]. The other model suggests that the aliphatic chains are intercalated in the SmA* phase and located at the centre of the layers, whereas the carbohydrate moieties self-assemble in the outer regions of the bilayers [38]. Although X-ray diffraction studies primarily carried out on such liquid crystalline carbohydrate derivatives in the crystalline state indicate that intercalation of the alkyl chains is indeed present, there is *no* correlation between the ordering in the crystalline state and in the mesomorphic state [34–38, 60].

2. Synthesis

The 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**) were prepared as previously described [60] by alkylation of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose using appropriate bromoalkanes and potassium hydroxide to produce the intermediate 6-*O*-*n*-alkyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoses, followed by deprotection using trifluoroacetic acid [67, 68], see the reaction scheme. The conditions for the deacetalization were chosen to permit α anomer formation. The galactopyranoses were then reduced with $NaBH_4$ [69] to give the desired 6-*O*-*n*-alkyl-D-galactitols (**16**-**30**).

3. Phase characterization

3.1. *Phase characterization by thermal optical microscopy*

The thermotropic mesophases observed for the 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**) [60] and the 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**) exhibited similar textures during optical microscopy. For the carbohydrates with an enantiotropic mesophase, the crystals melt on heating at a discrete temperature (T_m) to form a birefringent, fluid texture with an oily streak appearance of webbed focal conic-like defects typical of a SmA* phase, see figure 1. Upon further heating the material became

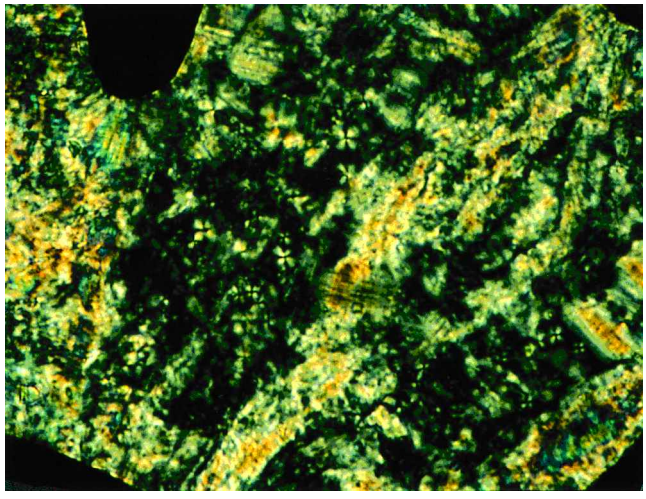


Figure 1. The oily streak texture observed on melting 6-*O*-decyl-D-galactitol (**23**) at 147°C on a glass substrate (×160).

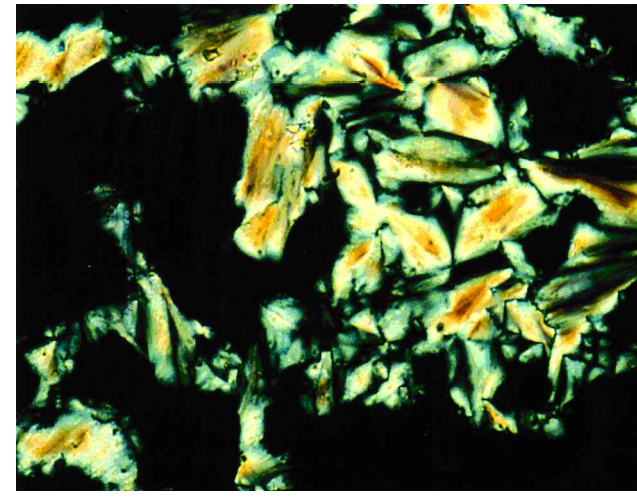


Figure 3. The focal conic defect texture of 6-*O*-decyl-D-galactitol (**23**) formed on cooling from the isotropic liquid down to 150°C on a glass substrate (×160).

optically extinct at the clearing point (T_{SmA*-I}). Several homologues of the 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**) started to decompose just below T_{SmA*-I} to form birefringent strips of focal conic texture with isotropic areas of decomposed material, see figure 2. Upon further heating the birefringent areas eventually disappeared completely. This was taken as the clearing point for these materials. Surprisingly good agreement (≈1–5°C) was found with those values determined by differential scanning calorimetry, see § 3.2. Upon cooling from the isotropic liquid, bâtonnets were observed, which coalesced spontaneously in the bulk to form focal conic domains, see figure 3. As the sample was cooled further, the polar hydrophilic end of the carbohydrate molecules sometimes tended to adhere more strongly to the glass surface *via* hydrogen bonding. Thus, most of the resultant texture became homeotropic and optically extinct viewed between crossed polarizers. This indicates that the phase is optically uniaxial (if the mesophase were biaxial then a residual birefringence for the sample would be observed). However, focal conic defects can still be observed in parts of the area of view and especially around air bubbles and at the edges of the preparation. This optical behaviour, i.e. simultaneous presence of both homeotropic and focal conic textures, indicates that the mesophase observed should be a calamitic smectic A* phase (SmA*). The notation smectic A* is used to describe the smectic A phase exhibited by these compounds which possess reduced symmetry since they are optically active. The elliptical and hyperbolic lines of optical discontinuity characteristic of focal conic defects were observed. The characterization of these defects classifies the mesophase as smectic A* with a layered structure where the long axes of the molecules are on average orthogonal to the layer planes and the in-plane and out-of-plane positional ordering of the molecules is short range.

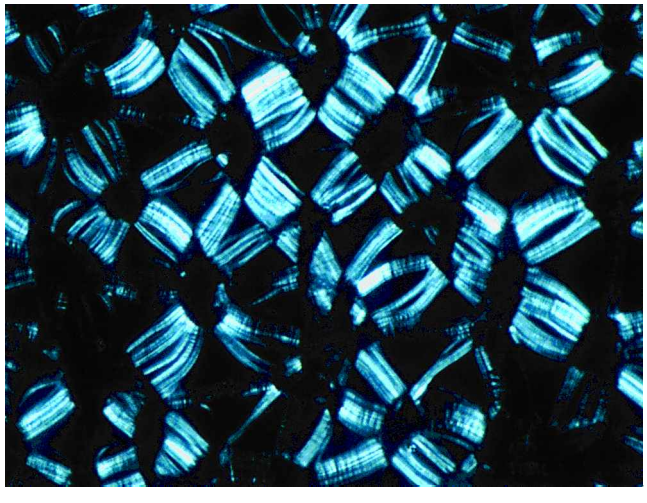
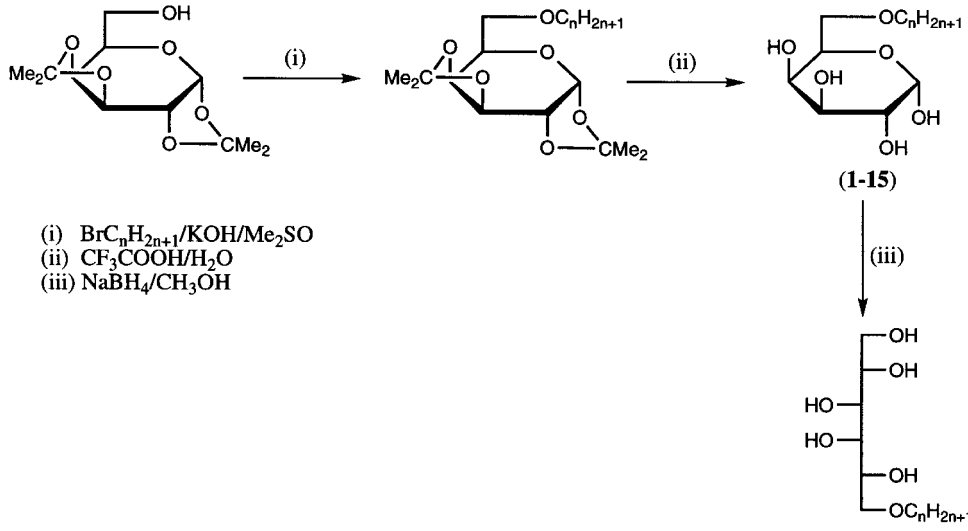


Figure 2. The focal conic defect texture with isotropic areas of decomposed material at 170°C just below the clearing point of 6-*O*-decyl-D-galactitol (**23**) on a glass substrate (×160).

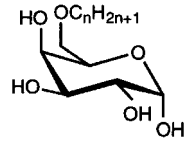
3.2. *Phase characterization by differential scanning calorimetry*

The enthalpy values for the melting (T_m) and clearing (T_{SmA*-I}) points of the 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**) [60] and the corresponding 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**) prepared are listed in brackets in tables 1 and 2, respectively. A typical heating thermogram for the 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**) and for the corresponding 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**), i.e. for 6-*O*-tetradecyl-α-D-galactopyranose (**12**) and 6-*O*-tetradecyl-D-galactitol (**27**), are shown in figures



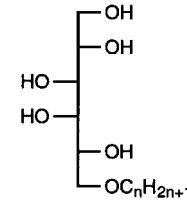
Scheme.

Table 1. Transition temperatures (°C) and enthalpies of transition (J g^{-1} in brackets) for the 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**).



Compound	*n*	Cr		SmA*		I
(**1**)	2	•	−2 (t_g)	—	—	•
(**2**)	3	•	−18 (t_g)	—	—	•
(**3**)	5	•	114 (14·5)	•	123 (4·82)	•
(**4**)	6	•	106 (14·5)	•	145 (8·80)	•
(**5**)	7	•	113 (110·7)	•	168 (7·88)	•
(**6**)	8	•	113 (117·1)	•	169 (7·75)	•
(**7**)	9	•	120 (91·7)	•	176 (2·94)	•
(**8**)	10	•	117 (72·7)	•	172 (1·87)	•
(**9**)	11	•	127 (128·6)	•	176 (4·16)	•
(**10**)	12	•	119 (127·8)	•	171 (3·70)	•
(**11**)	13	•	129 (141·9)	•	174 (2·4)	•
(**12**)	14	•	114 (118·1)	•	169 (6·92)	•
(**13**)	15	•	127 (138·2)	•	170 (2·06)	•
(**14**)	16	•	121 (127·1)	•	167 (1·58)	•
(**15**)	18	•	119 (125·6)	•	164 (1·16)	•

Table 2. Transition temperatures (°C) and enthalpies of transition (J g^{-1} in brackets) for the 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**).



Compound	*n*	Cr		SmA*		I
(**16**)	2	•	>170 (dec)	—		•
(**17**)	3	•	>180 (dec)	—		•
(**18**)	5	•	147	—		•
(**19**)	6	•	149	—		•
(**20**)	7	•	148 (147·3)	•	193	•
(**21**)	8	•	147 (205·7)	•	154 (6·75)	•
(**22**)	9	•	144 (168·9)	•	195	•
(**23**)	10	•	145 (174·1)	•	170 (4·77)	•
(**24**)	11	•	146 (198·3)	•	193 (5·00)	•
(**25**)	12	•	142 (189·5)	•	171 (4·25)	•
(**26**)	13	•	142 (162·6)	•	185	•
(**27**)	14	•	138 (139·3)	•	167 (0·55)	•
(**28**)	15	•	143 (173·3)	•	172 (1·12)	•
(**29**)	16	•	146 (170·4)	•	165 (2·01)	•
(**30**)	18	•	139 (101·5)	•	149 (1·43)	•

4 and 5, respectively. It is clear that the transitions T_m and T_{SmA*-I} are both first order transitions. Whereas the galactoses tend to form a glass, the galactitols generally recrystallize on cooling. All the sugars show a substantial degree of supercooling at T_{SmA*-I} and below T_m.

The galactitols appear to decompose much more readily at elevated temperatures than the corresponding galactopyranoses. A greater tendency of open-chain sugars compared with the corresponding cyclic sugars to decompose (caramelize) on heating has already been observed [42]. The homologues with an odd number of carbon atoms in the terminal chain decompose so strongly in the DSC apparatus that the T_{SmA*-I} values given for them in table 2 represent the temperature at which birefringent material was no longer observable by microscopy. A typical DSC trace showing such decomposition on heating is shown in figure 6 for 6-*O*-heptyl-D-galactitol (**20**).

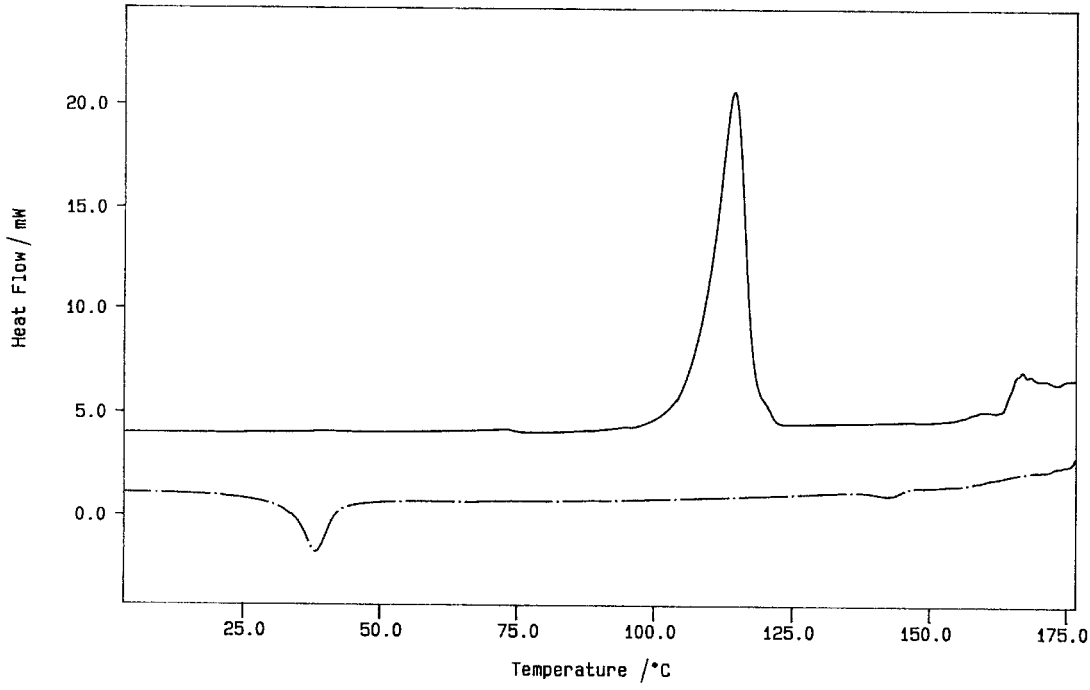


Figure 4. Differential scanning thermogram for the first heating cycle for 6-*O*-tetradecyl-α-D-galactopyranose (**12**), scan rate 10°C min^{-1}.

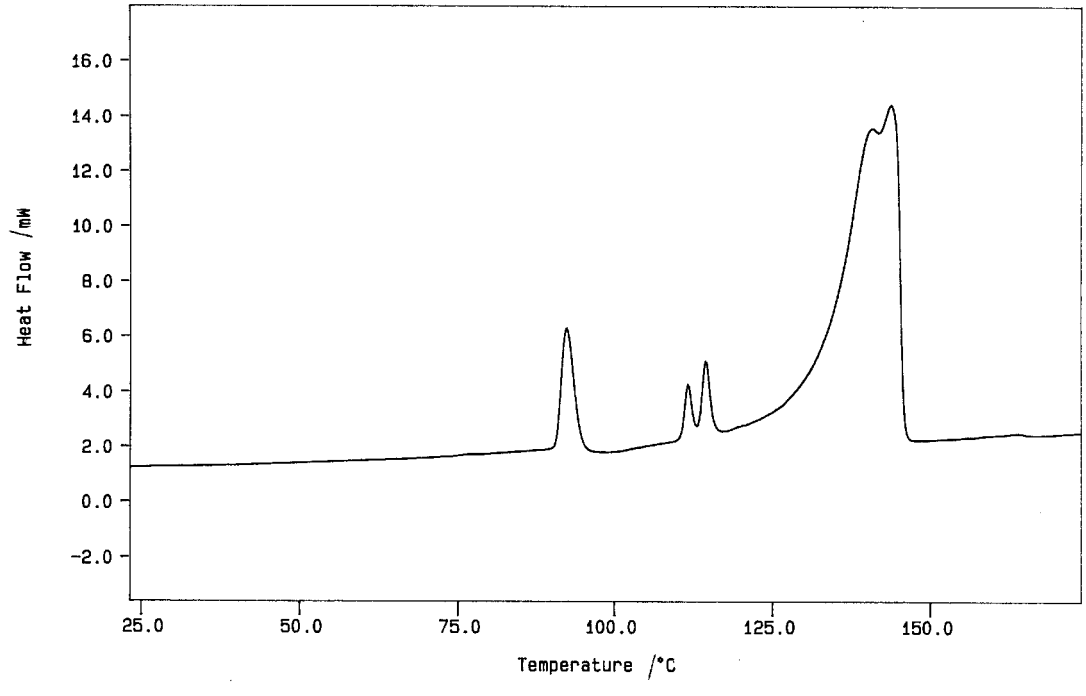


Figure 5. Differential scanning thermogram for the first heating cycle for 6-*O*-tetradecyl-D-galactitol (**27**), scan rate 10°C min^{-1}.

The clearing point enthalpies are relatively small in comparison with the melting enthalpies, and the values measured are of a similar magnitude to those found for conventional liquid crystal systems which exhibit SmA* to isotropic liquid transitions, although the variations are quite large (0·55–6·75 J g^{-1}) for T_{SmA*-I} and much larger than the percentage change for T_m (101·5–205·7 J g^{-1}). As the solubility of an amphiphile in water is mainly determined [70] by the amount of energy required to overcome the crystal lattice forces, the high values

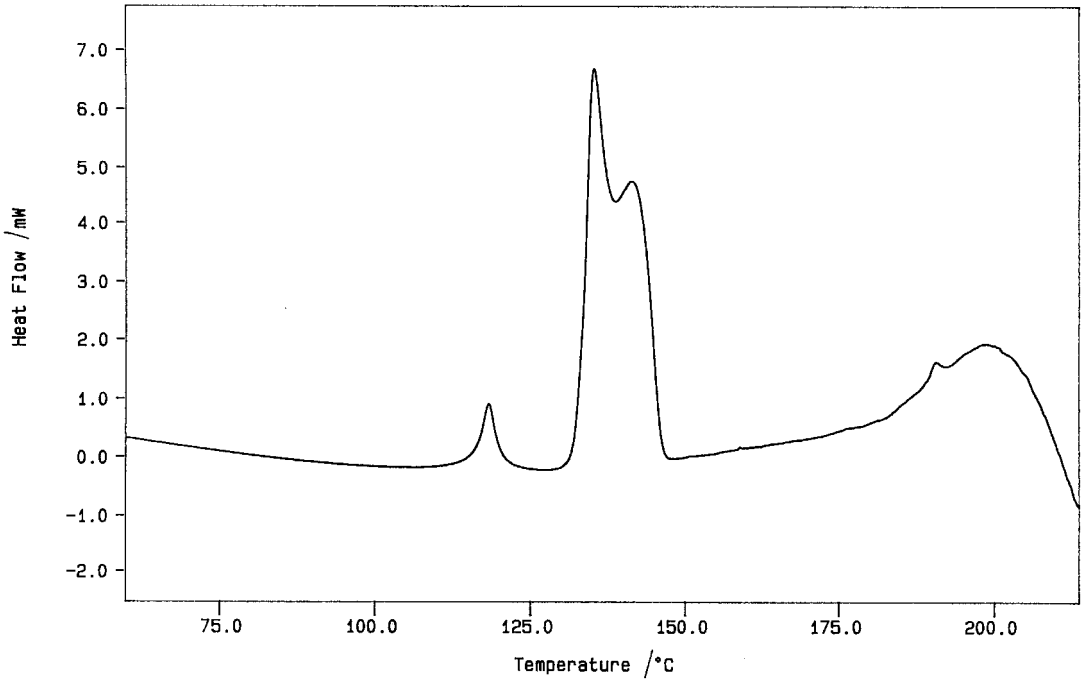


Figure 6. Differential scanning thermogram for the first heating cycle for 6-*O*-heptyl-D-galactitol (**20**), scan rate 10°C min^{-1}.

generally found for the melting process of the galactitols (**16**–**30**) indicate that these materials will be sparingly soluble in water and indeed this was found to be the case. The large enthalpy values determined for T_m compared with those found for T_{SmA*-I} indicate that these values correspond to the breaking of a three-dimensional crystal lattice primarily held together by intermolecular hydrogen bonding between the carbohydrate moieties, which defines the melting point [62]. This is followed by the breaking down at the clearing point of the less-ordered and fluid bilayer structure of the SmA* phase, stabilized by van der Waals forces between the aliphatic chains, to give the isotropic liquid. Some residual hydrogen bonding will no doubt still be present in the liquid crystalline and liquid states.

3.3. *X-ray analysis*

The experimental values for the *d*-spacings are listed in figure 7 for 6-*O*-decyl-D-galactitol (**23**) measured at a scan rate of 2°C min^{-1}. At 140°C reflections relating to lattice parameters of $d_1 = 37{\cdot}9$ Å and $d_2 = 30{\cdot}5$ Å were observable. With increasing temperature reflections relating to d_1 became very weak above 145°C and were not detectable above 147°C. For d_2 a contraction from 30·5 Å in the crystalline state to 29·6 Å in the fully formed SmA* phase was observable. These results are in agreement with those made by optical polarizing microscopy and by DSC measurements.

Upon reaching the liquid crystalline state, the intensities of the powder-type diffraction pattern changed in such

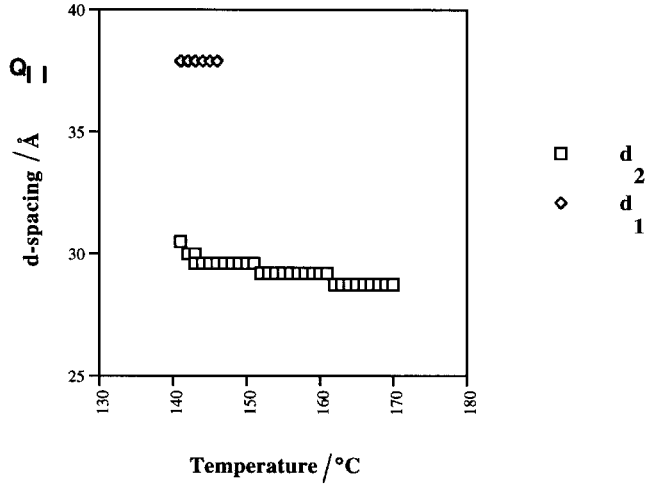


Figure 7. The experimental values for the *d*-spacings for 6-*O*-decyl-D-galactitol (**23**) as a function of temperature; scan rate 2°C min^{-1}.

a manner that a maximum in the meridium was found, indicative of some macroscopic alignment of the material *via* interactions with the walls of the capillary. Elevation of the temperature led to a broadening of the maximum, indicating a loss of macroscopic ordering. Up to 170°C, the *d*-spacing fluctuates between 30·5 to 28·8 Å. Whereas the values for the recorded intensities relating to d_2 remain almost constant up to 160°C, above that temperature the observed diffraction starts to decrease. However, even at 170°C, above the transition temperature observed

by optical polarizing microscopy, small angle scattering occurs, indicative of a biphasic transition to the isotropic liquid. Thermal decomposition at these high temperatures during the X-ray measurements is probable, see § 3.1 and § 3.2, and may also contribute to some extent to the observed variations in the *d*-spacings.

The spacing of 37·9 Å at 140°C indicates that, compared with the overall length of one molecule, of 21·8 Å, as obtained *via* molecular modelling of one molecule in the gas phase at zero Kelvin using the CERIUS 2.0 (MSI) software (see figure 8), a bilayer structure may be present in the crystalline state (see figure 9). The experimentally observed values would agree with the structure shown in figure 9 where the carbohydrate groups and the alkyl chains are not intercalated, a structural feature which has been observed earlier for the analogous 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**) [60]. However, it should be stressed that these are powder X-ray diffraction studies and not single crystal measurements. Investigations of samples ordered in a very strong magnetic field are in progress. It is not possible to clarify whether the intensities relating to d_2 are due to crystalline polymorphism, with the lattice having a smaller *d*-spacing more stable at higher temperatures, or an increase of liquid crystal lattice defects preceding the onset of the liquid crystalline phase, due to the absence of wide angle scattering data.

The observed values of d_2 vary between 30·5 and 28·8 Å, a variation which remains nearly constant up to the disappearance of the maximum, indicating a contraction of the layering with respect to the crystalline modification by roughly 8 Å, a value slightly larger than that of the length of the polar head group which has a length of about 6.5 Å. This result corresponds to an arrangement in the type of an intercalated bipolar structure of the SmA* phase primarily involving intercalation of the carbohydrate cores and observed earlier for the crystalline phases of several liquid crystalline carbohydrates [34–36, 62–66]. However, the data are also consistent with some degree of intercalation of the isotropic, melted ends of the aliphatic chains. Therefore the X-ray data are inconclusive and an intermediate arrangement with some interdigitation of the polar head groups within the bilayer and of the chains between layers, as depicted schematically in figure 10, may be closer to the real situation. Thus, the structures of the crystalline and liquid crystalline states are similar, at least as indicated by X-ray studies of the previously reported 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**) [60] and the 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**) prepared in this work [60].

4. Discussion of the transition temperatures

The liquid crystal transition temperatures of the 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**) and the 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**) are collated in tables 1 and

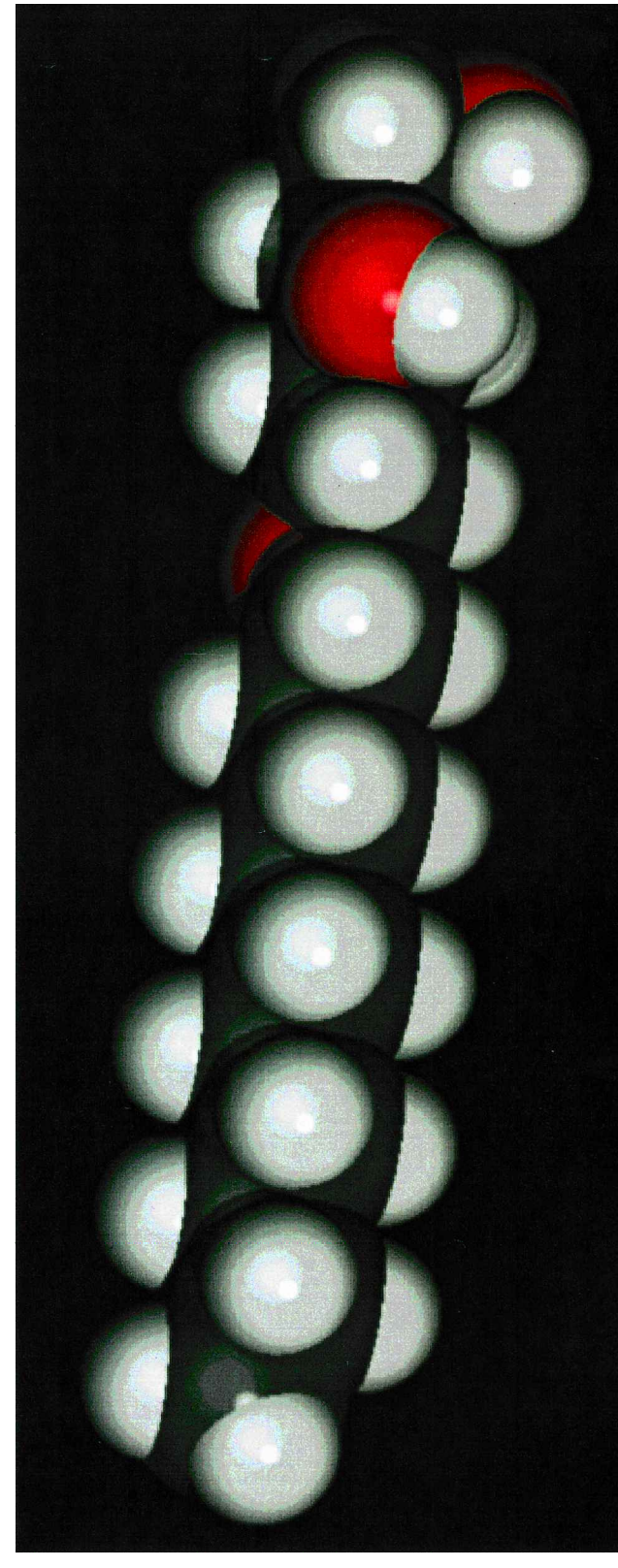


Figure 8. A model of 6-*O*-decyl-D-galactitol (**23**) as obtained by CERIUS 2.0.

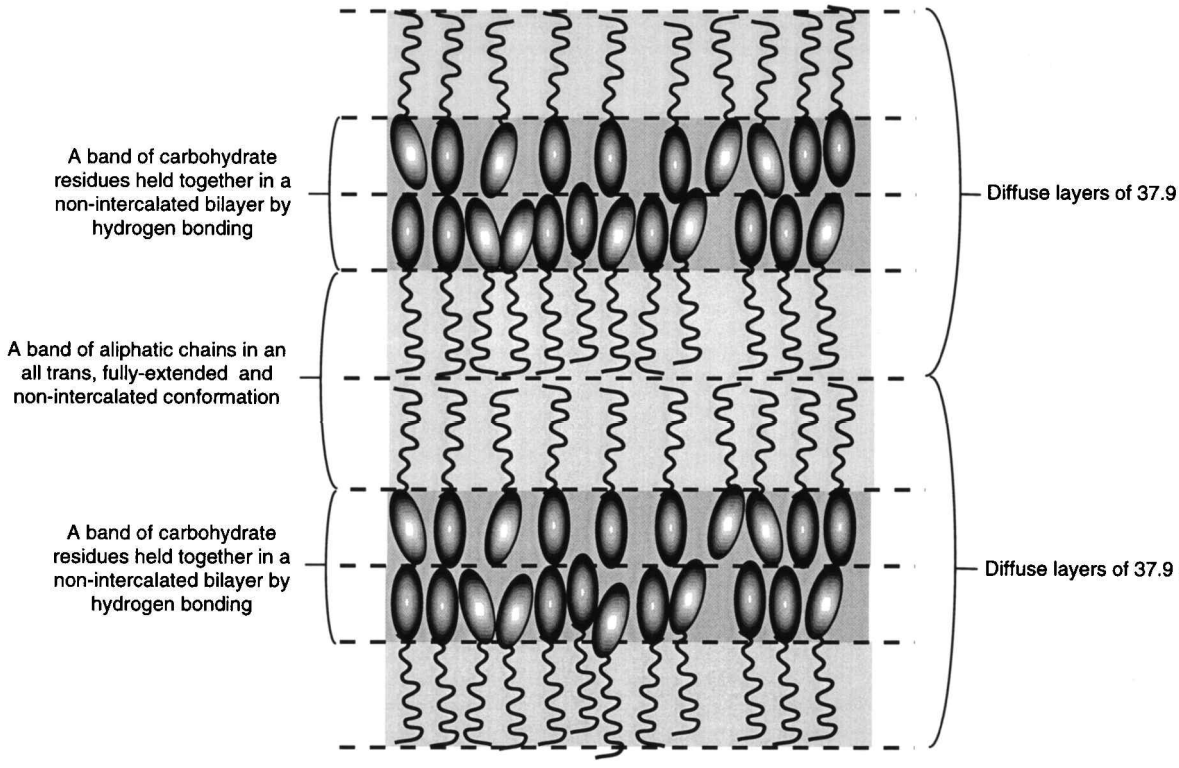


Figure 9. A schematic representation of the crystalline phase of 6-*O*-decyl-D-galactitol (**23**).

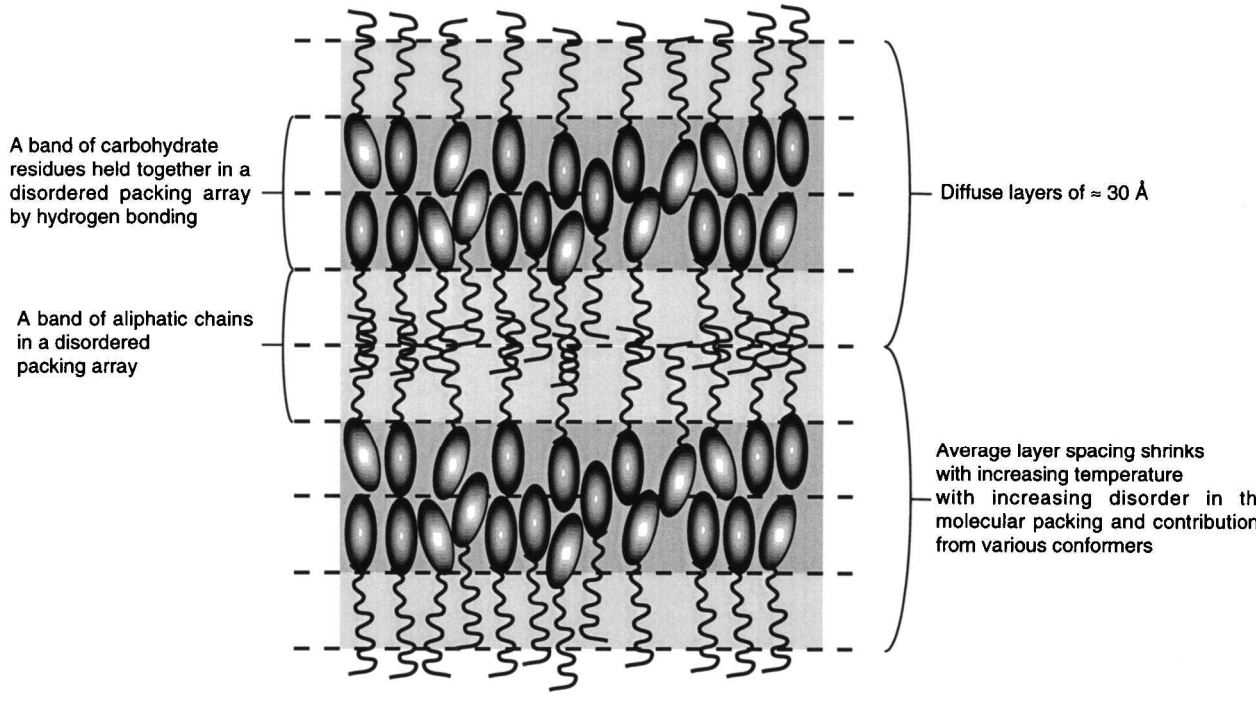


Figure 10. A schematic representation of the SmA* phase of 6-*O*-decyl-D-galactitol (**23**).

2, respectively, and plotted against the number (n) of methylene units in the terminal chain in figures 11 and 12, respectively. T_{SmA*I} increases from very low values for short alkyl chain lengths of the 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**), but then reaches a maximum before decreasing gradually as the chain becomes longer

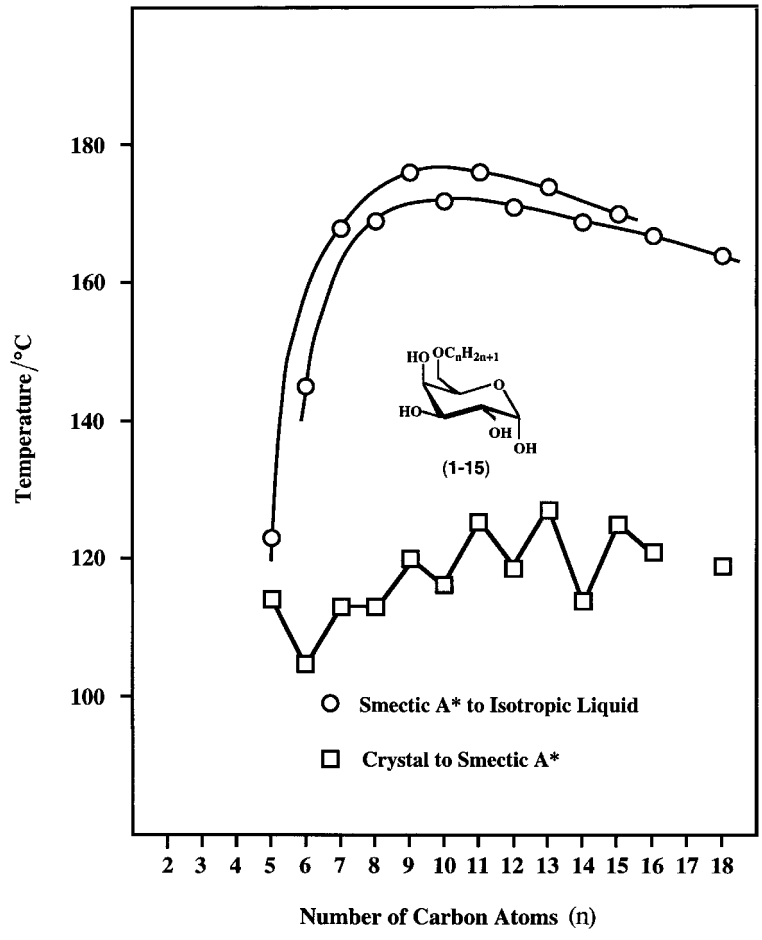


Figure 11. Plot of the transition temperatures of the 6-*O*-alkyl-α-D-galactopyranoses (**1**–**15**) against the number of the carbon atoms (*n*) in the alkyl part of the alkyl terminal chain.

(see table 1 and figure 11). For short alkyl chains (**1** and **2**; $n = 1$ and 2) only a glass transition temperature could be observed and these two homologues are liquids at room temperature ($T_g < 25$°C). D-(+)-Galactose itself is a high melting solid ($T_m = 165$–168°C). T_m shows a certain degree of alternation and a general tendency to increase with increasing chain length, although the differences for the absolute values of T_m are generally small. Therefore, a broad SmA* phase is observed for most homologues of the 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**) after a critical length of the alkyl chain ($n = 5$) has been attained, although most homologues exhibit high T_m and T_{SmA*I}. In contrast the first two homologues (**16** and **17**; $n = 2$ and 3) of the corresponding 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**) exhibit a very high T_m (170 and 180°C, respectively), see table 2 and figure 12. The other homologues prepared (**18**–**30**) with longer alkyl chains ($n = 5$–16, 18) possess a T_m which is almost independent of chain length. This trend for T_m for both series is consistent with the assumption that T_m is determined primarily by the dissociation of a three-dimensional lattice held together by intermolecular hydrogen bonding between the hydroxy groups of the carbohydrate part of the molecule, rather than due to van der Waals forces mainly attributable to the alkyl chain. Apart from a dilution effect due to the alkyl chain, these forces will be independent of the length of the carbon chain, thus giving rise to a relatively stable value for T_m [71–75].

The situation is quite different for T_{SmA*I}, which increases from very low values for short alkyl chain lengths for both homologous series, reaches a maximum and then decreases gradually as the chain becomes longer. However, the values of T_{SmA*I} are considerably higher for chains of intermediate chain length, although significant thermal decomposition renders measurement of an accurate and reproducible T_{SmA*I} problematical for the 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**). As the homologous series are ascended, there will be increased van der Waals forces of attraction leading to a higher value of T_{SmA*I}. This will reach a maximum for intermediate chain lengths, before decreasing due to back-folding of long alkyl chains leading to non-linear conformations and, thus, a lower T_{SmA*I} [71–75]. These plots of the clearing point are typical for many varied series of non-amphiphilic liquid crystals materials. The plots of

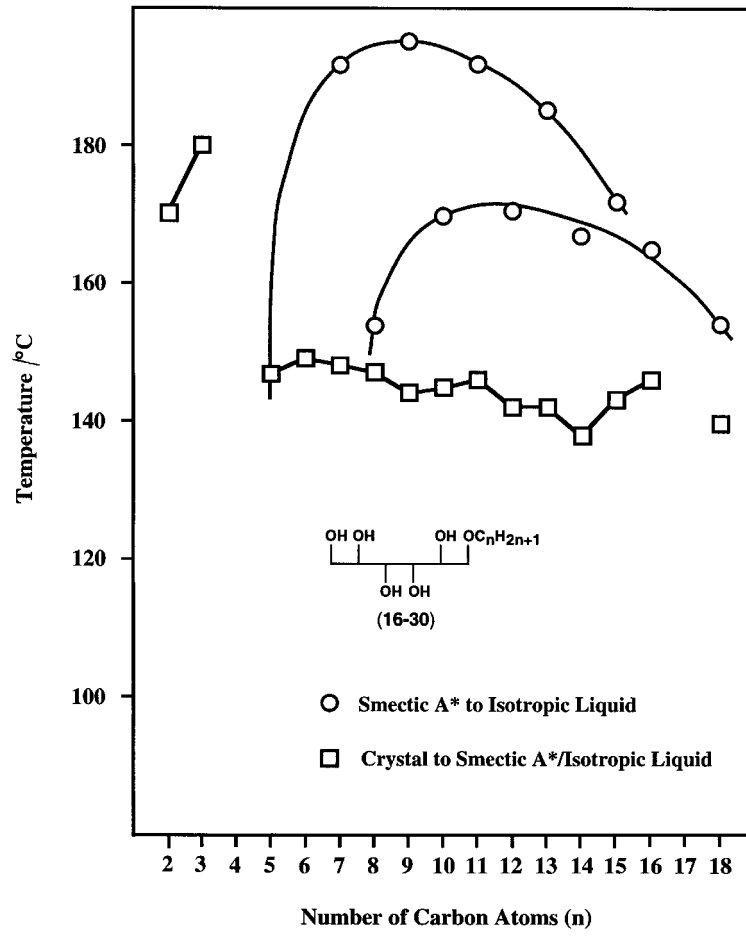


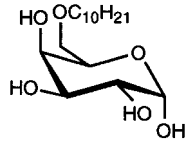
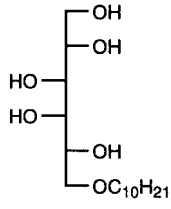
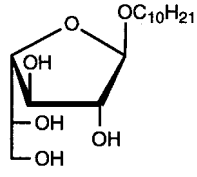
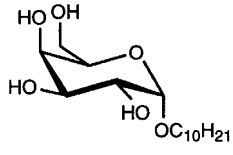
Figure 12. Plot of the transition temperatures of the 6-*O*-alkyl-D-galactitols (**16**–**30**) against the number of the carbon atoms (*n*) in the alkyl part of the alkyl terminal chain.

T_{SmA*-I} for the 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**) and the 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**) can be regarded as similar in shape, although the absolute values differ.

T_{SmA*-I} is generally lower for a cyclic carbohydrate (**1**–**15**) than for the corresponding open-chain homologue (**16**–**30**). This is especially valid for the members of both series with an odd number of carbon atoms in the chain. At long chain lengths, the difference is substantially lower than that observed for shorter chain lengths. This may be a dilution effect. However, as T_m is considerably lower for the galactopyranoses (**1**–**15**) than for the corresponding homologues of the galactitols (**16**–**30**), a wider temperature range for the SmA* phase is generally observed for the galactopyranoses. The plots of T_{SmA*-I} for the homologues with an even or an odd number of carbon atoms (*n*) in the terminal alkyl chain of the galactopyranoses (**1**–**15**) and galactitols (**16**–**30**), shown in figures 11 and 12, show pronounced alternation. This is unusual for homologous series of liquid crystalline carbohydrates only in that either short series have been prepared or the liquid crystalline transition temperatures of longer homologous series, e.g. of alkyl glycosides, have not been plotted against the number of methylene units in the alkyl substituent [45–62]. This is probably a general phenomenon, as observed for non-amphiphilic liquid crystals.

The thermal data collected in table 3 for the 6-*O*-decyl-α-D-galactopyranose (**8**) [60], the 6-*O*-decyl-D-galactitol (**23**), the decyl-β-D-galactofuranoside (**31**) [45] and the decyl-β-D-galactopyranoside (**32**) [56–60] indicate that cyclic forms of sugars increase the liquid crystalline temperature range by depressing T_m compared with T_m of the corresponding open-chain sugar. The T_{SmA*-I} of the furanoside (**31**) is not much lower (12°C) than that of the open chain sugar (**23**), although the latter has five hydroxy groups capable of hydrogen bonding compared with four for the furanose form. It has been shown that T_{SmA*-I} normally increases strongly with the number of groups capable of hydrogen bonding [29, 33, 46–48]. The 6-*O*-decyl-α-D-galactopyranose (**8**) in the pyranose form exhibits a higher T_{SmA*-I} (+14°C and +2°C, respectively) than that of the furanose isomer (**31**) or the open chain sugar (**23**). The decyl-β-D-galactopyranoside (**32**) also exhibits a low T_m as well as a similar value for T_{SmA*-I}. This suggests that the lower conformational mobility associated with the heterocyclic

Table 3. Transition temperatures (°C) for 6-*O*-decyl-α-D-galactopyranose (**8**), 6-*O*-decyl-D-galactitol (**23**), decyl-β-D-galactofuranoside (**31**) and decyl-α-D-galactopyranoside (**32**).

Compound	Structure	Cr		SmA*		I	Reference
(**8**)		•	117	•	172	•	[60]
(**23**)		•	145	•	167	•	
(**31**)		•	98	•	155	•	[45]
(**32**)		•	123	•	169	•	[56–60]

rings, as manifested in a tendency for the hydroxy groups to be maintained in a primarily equatorial conformation, leads to a stabilization of the liquid crystalline state. This is consistent with the behaviour found for related non-amphiphilic carbohydrate derivatives, whose clearing point has been shown to decrease as the proportion of non-linear conformers increases with temperature.

The direct dependence of T_{SmA*-I} on the number of groups capable of hydrogen bonding, in this case hydroxy groups, on carbohydrates is demonstrated clearly by reference to the thermal data collated in table 4 for the open-chain carbohydrates (**23**, **33**–**36**). The T_{SmA*-I} of the 6-*O*-decyl-D-galactitol (**23**) with five hydroxy groups is much higher (+57°C) than that of the 5-*O*-decyl-D-xylitol (**33**) [46, 47] with only four hydroxy groups, and the same alkyl substituent in a terminal position of the open chain sugar; T_m is also much higher (+89°C). The number of hydroxy groups appears to be a much greater factor in determining T_{SmA*-I} than the absolute configuration of the hydroxy groups. This is demonstrated by comparison of the thermal data for the 6-*O*-decyl-D-galactitol (**23**), 5-*O*-decyl-D-xylitol (**33**), 6-*O*-decyl-D-glucitol (**34**) [72, 73], 1-*O*-decyl-D-glucitol (**35**) [71] and 1-*O*-decyl-D-mannitol (**36**) [74]. Some differences in T_{SmA*-I} are still observed which may be due to the configuration of the hydroxy groups [46, 47].

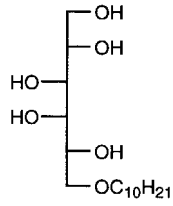
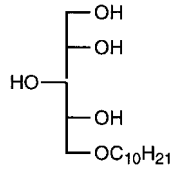
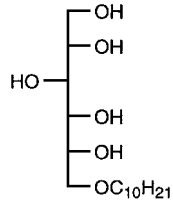
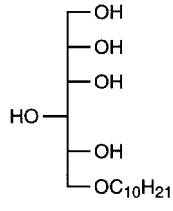
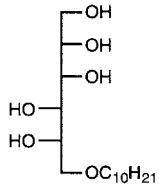
5. Experimental

5.1. *Characterization*

NMR spectra were recorded using a Bruker WB-300 and the solvents $CDCl_3$, Me_2SO or C_5D_5N (internal Me_4Si). Reactions were monitored by either HPLC (Waters 721), using either of the reverse phase columns RP-18 (Merck) or PN 27-196 (Waters) or CPG (Girdel) with columns of either OV 17 or SE 30. The structures of all the compounds were determined by ^1H and ^{13}C NMR spectroscopy.

The purity of the compounds (>99·5%) was determined by thin layer chromatography (TLC), high performance liquid chromatography (HPLC), elemental analysis (CHN) and differential scanning calorimetry (DSC); 4×8 cm precoated TLC plates, SiO_2 SIL G/UV_{254}, layer thickness 0·25 mm (Machery-Nagel, Düren, Germany) were utilized. Melting points were determined with a Büchi apparatus and are uncorrected. Optical rotations were recorded at room temperature using $CHCl_3$ solutions with a Perkin-Elmer 241 polarimeter having a 1 dm cell.

Table 4. Transition temperatures (°C) for 6-*O*-decyl-D-galactitol (**23**), 5-*O*-decyl-D-xyltitol (**33**), 6-*O*-decyl-D-glucitol (**34**), 1-*O*-decyl-D-glucitol (**35**) and 1-*O*-decyl-D-mannitol (**36**)

Compound	Structure	Cr		SmA*		I	Reference
(**23**)		•	145	•	170	•	
(**33**)		•	56	•	113	•	[46, 47]
(**34**)		•	79	•	148	•	[72, 73]
(**35**)		•	82	•	161	•	[71]
(**36**)		•	108	•	162	•	[74]

Column chromatography was performed on silica gel (60 mesh, Matrex) by gradient elution with hexane–acetone (in each case the ratio of silica gel to product mixture to be purified was 30:1). Reaction solvents and liquid reagents were purified by distillation or drying shortly before use. Reactions were carried out under nitrogen unless water was present as a reagent or a solvent. All temperatures were measured externally unless otherwise stated.

Mesophase identification and the determination of the transition temperatures of the carbohydrates prepared were effected by optical microscopy using either a Zeiss Universal or a Olympus BH-2 polarizing light microscope in conjunction with a Mettler FP 52 microfurnace and FP 5 central processor.

Differential scanning calorimetry was used to determine the enthalpies of transition and to confirm the phase transition temperatures determined by optical microscopy. Differential scanning thermograms (scan rate 10°C min^{-1}) were obtained using a Perkin Elmer DSC 7 operating on 7 series/UNIX software. The results obtained were standardized with respect to indium (measured onset 156·68°C, ΔH 28·47 J g^{-1}, literature value 156·60°C, ΔH 28·45 J g^{-1}), nitrotoluene (measured onset 51·17°C, ΔH 118·49 J g^{-1}, literature value 51·63°C, ΔH 122·58 J g^{-1}) and benzil (measured onset 94·42°C, ΔH 108·52 J g^{-1}, literature value 94·87°C, ΔH 92·68 J g^{-1}).

Comparisons of the transition temperatures determined by optical microscopy and differential scanning calorimetry show some discrepancies of about 1–5°C.

These are probably due to decomposition at elevated temperatures at a rate which depends on the rate of heating, the time spent at an elevated temperature and the nature of the supporting substrate, e.g. the materials decomposed more quickly in aluminium DSC pans than on glass microscope slides. As each material was heated, a typical webbing pattern of focal conic-like defects surrounded by isotropic areas of decomposed material was observed [42]. The proportion of birefringent material to optically extinct areas decreased on heating until no more birefringence could be observed. This was taken as the clearing point. This complex transition to the liquid corresponds to multiple small peaks in the DSC traces, see figure 6.

In order to characterize the solid state of these materials further, 6-*O*-decyl-D-galactitol (**23**) was investigated using X-ray diffraction. The tendency of carbohydrates to decompose at high temperatures required an experimental set-up allowing for the recording of sufficient data before degradation of the sample set in. Thus high flux synchrotron radiation was employed, using the experimental set-up of station 8.2 at Daresbury Laboratories, described elsewhere [76–78]. Samples were prepared as polycrystalline powders in Lindemann tubes and maintained at a controlled temperature allowing for the recording of diffraction data whilst performing a temperature scan of 2°C min^{-1} in the temperature range of 120 to 180°C. The selected experimental set-up was limited to the recording of data relating to lattice parameters greater than 17·8 Å. The use of wet rat tail collagen as calibration standard leads to a systematic error of 3% in the observed *d*-spacings [79].

5.2. *General synthetic procedures*

For the synthesis of the 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**), the appropriate homologue of the previously reported 6-*O*-*n*-alkyl-α-D-galactopyranoses (**1**–**15**) [60] (see the reaction scheme) was dissolved in methanol (50 g L^{-1}) and treated with sodium borohydride (6 equiv.) at room temperature for 24 h. The excess of borohydride was destroyed by treatment with formic acid for 5 h at room temperature. The solvent was removed and the crude product obtained was recrystallized from methanol to give the pure 6-*O*-*n*-alkyl-D-galactitol. The ^{13}C and ^{1}H NMR data are collated in table 5.

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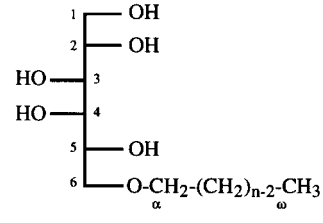
Table 5. NMR data for the 6-*O*-*n*-alkyl-D-galactitols (**16**–**30**) in C_5D_5N at 330 K.



Galactitol moiety						Alkyl chain		
^{13}C NMR chemical shifts, δ/ppm								
C1	C2	C3	C4	C5	C6	α-CH_2	(*n*-2)-CH_2	ω-CH_3
65·7	72·6	72·6	72·4	70·4	74·4	72·0	23·2–32·4	14·5
^{1}H NMR chemical shifts, δ/ppm (J/Hz)								
2 × H1	H2	H3	H4	H5	2 × H6	α-CH_2	(*n*-2)-CH_2	ω-CH_3
4·28 d	4·74 dt ($J_{1,2}$ 5·8)	4·3 dd ($J_{2,3}$ 1·9)	4·52 dd ($J_{3,4}$ 8·5)	4·81 dt ($J_{4,5}$ 1·4)	3·99 m ($J_{6a,6b}$ 14·7)	3·53 t ($J_{\alpha,\beta}$ 6·6)	1·20 m —	0·80 t ($J_{\omega,\omega-1}$ 6·4)

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