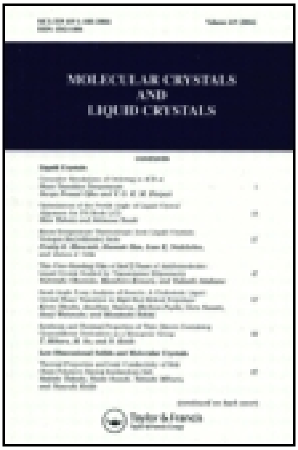

Molecular Crystals and Liquid Crystals

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Carbohydrate Liquid Crystals

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CARBOHYDRATE LIQUID CRYSTALS

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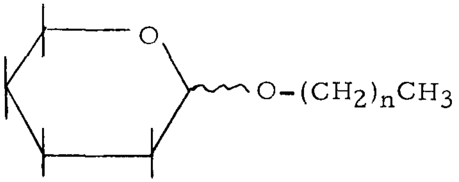
Certain alkyl 1-O and 1-S glycosides with hydrocarbon chain lengths greater than hexyl have been shown to form thermotropic liquid crystals at temperatures between 60 and 100°C. These are believed to be members of a large class of alkyl and acyl carbohydrate mesogens which, apart from their intrinsic value as potentially useful solid-state materials, could provide a variety of structurally accessible model systems for studying the phase transitions in the cell-membrane glycolipids.

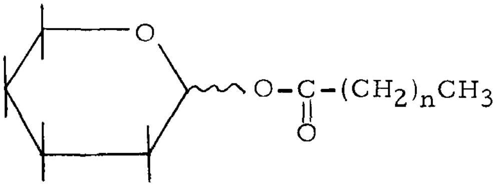
1. INTRODUCTION

It is proposed that the alkyl and acyl glycosides and aldosides of the type I, II, III and IV constitute a large class of thermotropic and possibly lyotropic liquid crystals. In view of their interesting properties, these compounds have hitherto not received the attention that they deserve. A compilation of thermotropic mesogens made in 1973[1] lists over 5000 compounds, none of which are carbohydrates.

(I)

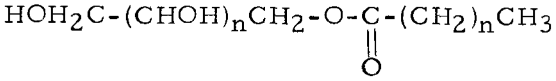


(II)



(III) $HOH_2C\text{-}(CHOH)_nCH_2\text{-}O\text{-}(CH_2)_nCH_3$

(IV)



$HOH_2C\text{-}(CHOH)_nCH_2\text{-}O\text{-}\underset{\underset{O}{\|}}{C}\text{-}(CH_2)_nCH_3$

Only the octyl and decyl β-D-glucopyranosides are well-known chemicals due to their use as non-ionic detergents in the isolation and purification of membrane proteins.[2]

These carbohydrates are relatively simple compounds which are straightforward to synthesize, purify, and study, compared with their complex relatives, the biologically important glycolipids. Since both classes of molecules are amphiphilic with polar carbohydrate and nonpolar hydrocarbon moieties, they might be expected to display similar thermotropic and lyotropic mesophase behavior. The glycolipids are particularly inaccessible to structural studies by diffraction methods due to the difficulty of crystallizing materials which are not easily obtained configurationally homogeneous. The simpler alkyl and acyl glycosides, which can frequently be crystallized, might therefore serve as relevant model systems for the complex structural transitions that occur in the functioning of the glycolipids in cell membranes.[3]

The isomeric variety that occurs in carbohydrate chemistry leads to the prediction that the alkyl and acyl glycosides and aldosides could provide a source of the order of half a million different mesogens (see Table I)

TABLE I Possible carbohydrate liquid crystals.

		D D,L	α β	alkyl acyl
26 Aldoses 30 Alditols 70 Reducing disaccharides	= 126	x 2	x 2	x 2
	1-O 1-S 1-C 1-N	C(7) to C(14)		
	x 4	x 7		≈ 50,000
Deoxy sugars Amino sugars Anhydro sugars Acidic sugars	x 10 ≈ 500,000			

all of which could be relatively easily synthesized and would have liquid crystal phases in the range from room temperatures to about 150°C.

2. IDENTIFICATION OF MESOGENIC PROPERTIES

The thermotropic liquid crystal phases are easily identified by one or all of three methods.

(1) Examination of the birefringence of single crystals, if available, under a polarizing microscope with a heated stage. At the melting point, i.e., the transition from crystalline phase to liquid crystal phase, the crystals lose their morphology and the birefringence disappears, but reappears at a higher temperature when the crystals have a melted appearance. This birefringence of the liquid crystal disappears at the clearing point, i.e., when the liquid crystal transforms to an isotropic liquid. In the carbohydrate liquid crystals, the birefringence is generally accompanied by pleochroism.[4]

(2) Differential scanning-calorimeter thermograms provide the most definite identification of liquid crystal formation. The method does not require single crystals, but is very sensitive to the crystallinity and purity of the compound and to the pre-history of the material. Differential thermograms differ significantly on heating and on cooling the specimens. They show characteristic patterns, a notable feature of which is that the greatest energy transition is from the crystalline to the liquid crystal phase. Hitherto, the majority of the alkyl glycosides examined have shown two crystalline phases between room temperature and the liquid crystal transition.[5]

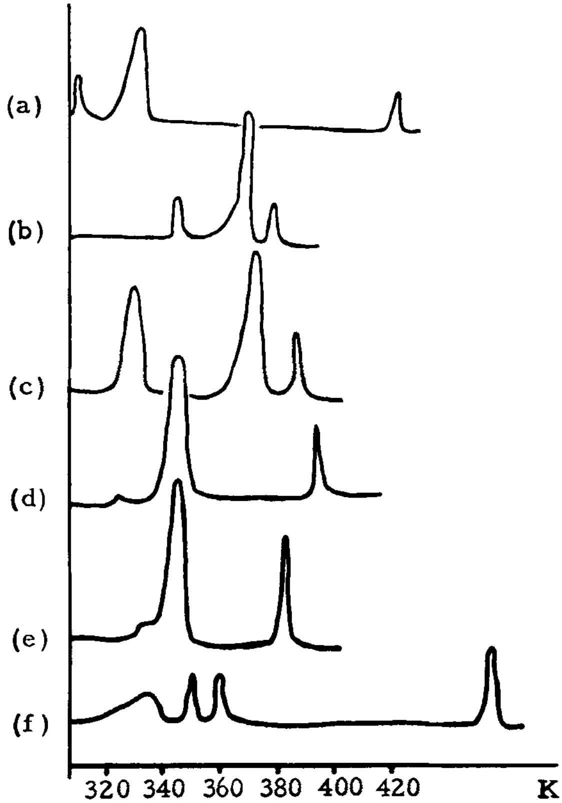


FIGURE 1 Differential scanning thermograms of (a) heptyl 1-S-α-D-mannopyranoside, (b) heptyl 1-S-β-D-xylopyranoside, (c) octyl 1-S-β-D-xylopyranoside (d) octyl 1-O-α-D-glucopyranoside, (e) octyl 1-O-β-D-glucopyranoside, (f) decyl 1-O-N-acetylglucosamine.

Examples of these differential thermograms are shown in Figure 1. An exception is that of decyl 1-O-N-acetylglucosamine, which shows three transitions between room temperature and the clearing point. The compound also showed lyotropic liquid crystal behavior in propanol and acetone solutions, which was characterized by a metastable gel formation which transformed spontaneously to a coagel. Characteristically, the ^{1}H NMR spectrum of the gel in CD_3COCD_3 was almost identical with that of the solution.[6]

(3) The x-ray powder diffraction patterns show a change at the melting point from the characteristic crystalline powder pattern to a pattern having a single intense and relatively sharp diffraction ring corresponding to the periodicity of the liquid crystal molecular cluster, which is of the order of 20 to 50 Å. A much weaker and more diffuse ring at about 4 Å, corresponding to the lateral separation of the hydrogen carbon chains can sometimes be observed.

3. STRUCTURAL CRITERIA FOR ALKYL GLYCOSIDIC LIQUID CRYSTAL FORMATION

The carbohydrates shown in Table II have been identified by at least one of the aforementioned methods as having thermotropic liquid crystal phases. In an examination of the series methyl to octyl 1-S β-D-xylopyranosides,[7] it was observed that liquid crystal phase transformation did not occur for the hexyl and shorter alkyl chains. There is a corresponding discontinuity in the melting points, which

TABLE II Transition temperatures (°C) for some alkyl glycopyranosides.

	Crystalline phases I $\rightleftharpoons$ II	$\rightleftharpoons$ Mesophase	$\rightleftharpoons$ Liquid	Ref.
β-D-glucopyranosides				
heptyl 1-O	56	69	~100	5
octyl 1-O	57-60	69	110	5, 12
nonyl	66	71	113	5
decyl	67	75	137	5
α-D-glucopyranosides				
octyl 1-O	52	68	125	12
decyl 1-O	?	76	138	9
heptyl 1-S-α-D-mannopyranoside	39	60	151	10
β-xylopyranosides				
heptyl 1-S	72	100	110	5
octyl 1-S	59	104	118	5, 11
decyl 1-O-N-acetylglucosamine	60-67 82	93	186	6

are 107°C propyl, 110°C butyl, 115°C pentyl, 160°C hexyl, 100°C heptyl, 104°C octyl derivative. A similar examination of derivatives related to the mesogenic heptyl 1-S-mannopyranoside,[8] showed that the mesogenic property did not occur if the alkyl chain had a terminal polar group, such as $-C{\equiv}N$, $-OH$, $-Cl$. Neither was there any mesophase with fully acetylated carbohydrate derivatives. From these observations, it is provisionally concluded that:

(1) An alkyl chain of at least seven carbon atoms is necessary for liquid crystal formation,

(2) Blocking the hydrogen-bonding functional groups of the carbohydrate moiety inhibits liquid crystal formation,

(3) The presence of a polar or functional group at the terminus of the alkyl chain inhibits liquid crystal formation.

4. THE MESOGENIC CRYSTAL STRUCTURES

Three room temperature alkyl glycosidic crystal structures have been determined by x-ray single crystal analysis; decyl 1-O-α-D-glucopyranoside,[9] heptyl 1-S-α-D-mannopyranoside,[10] and octyl 1-S-β-D-xylopyranoside.[11] The molecular packing in these crystal structures is similar, as shown in Figure 2. In all three structures, the carbohydrate molecules are hydrogen-bonded to form polar bi-layers of tightly associated residues. Similar structures were proposed for the octyl 1-O-α- and β-D-glucopyranosides, which showed the same type of differential thermograms, from electron diffraction of small crystals.[12] The hydrogen-bonding scheme between the carbohydrate moieties in the crystal structure of heptyl 1-S-α-D-mannopyranoside is shown in Figure 3. In this structure, all the carbohydrate hydroxyl groups and the ring oxygen O(5) are hydrogen-bonded in a bonding pattern which is characteristic of carbohydrate crystal structures.[13] The alkyl chains are intercalated to form the amphiphilic sandwich-type molecular packing shown in Figure 4.

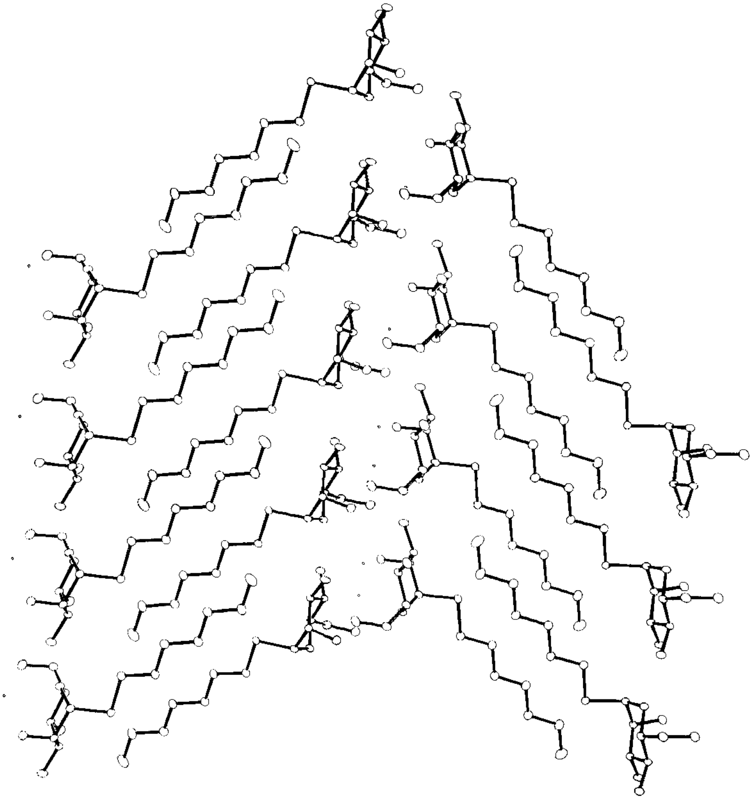


FIGURE 2a Molecular packing in heptyl 1-S-α-D-mannopyranoside.[10]

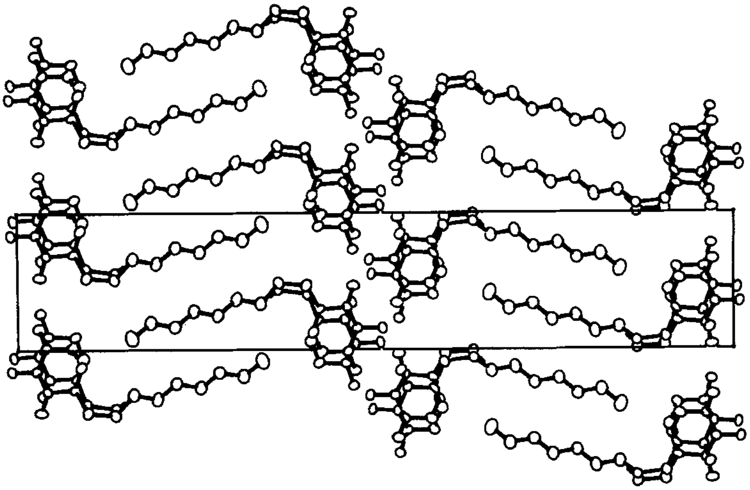


FIGURE 2b Molecular packing in octyl 1-S-β-D-xylopyranoside. The xylopyranoside moieties are disordered over two orientations.[11]

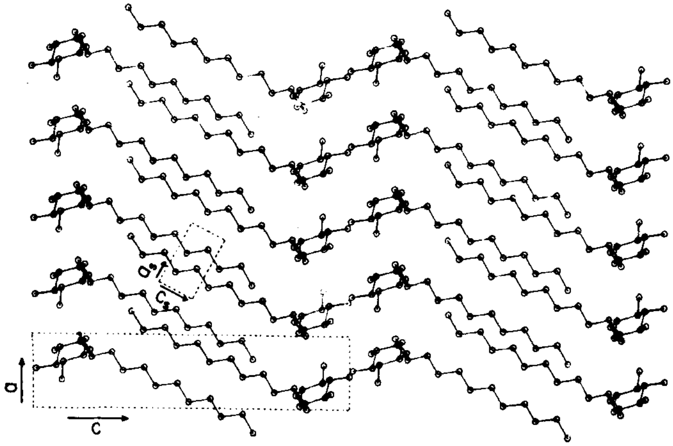


FIGURE 2c Molecular packing in decyl 1-O-α-D-glucopyranoside.[9]

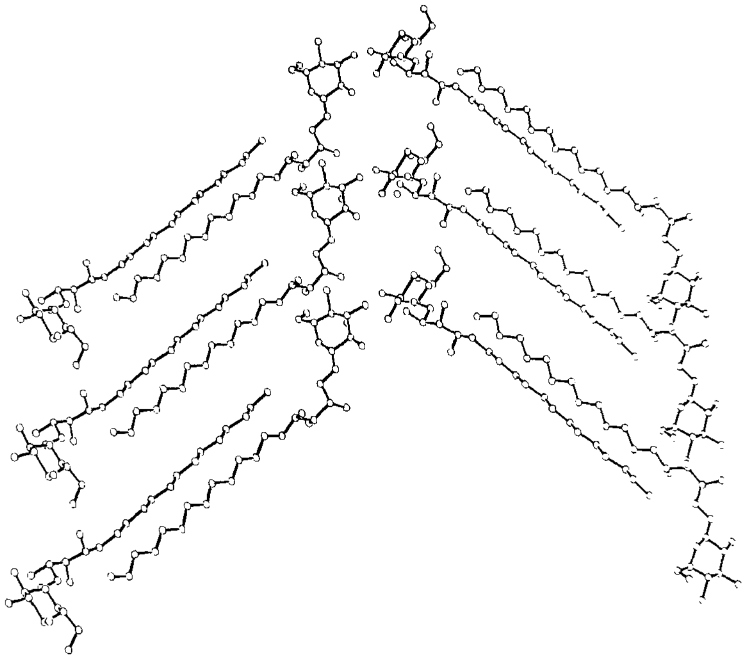


FIGURE 2d Molecular packing in glycosylphytosphingosine hydrochloride.[15]

The intercalation of the hydrocarbon chains is also observed in the molecular packing in the crystal structures of cholesteryl esters[14] and in triacetylsphingosines,[15] as shown in Figures 4a and 4b. The alternate non-intercalated packing for amphiphilic molecules generally postulated for membrane structures is found in the crystal structures of the cerebrosides,[16] shown in Figure 4c.

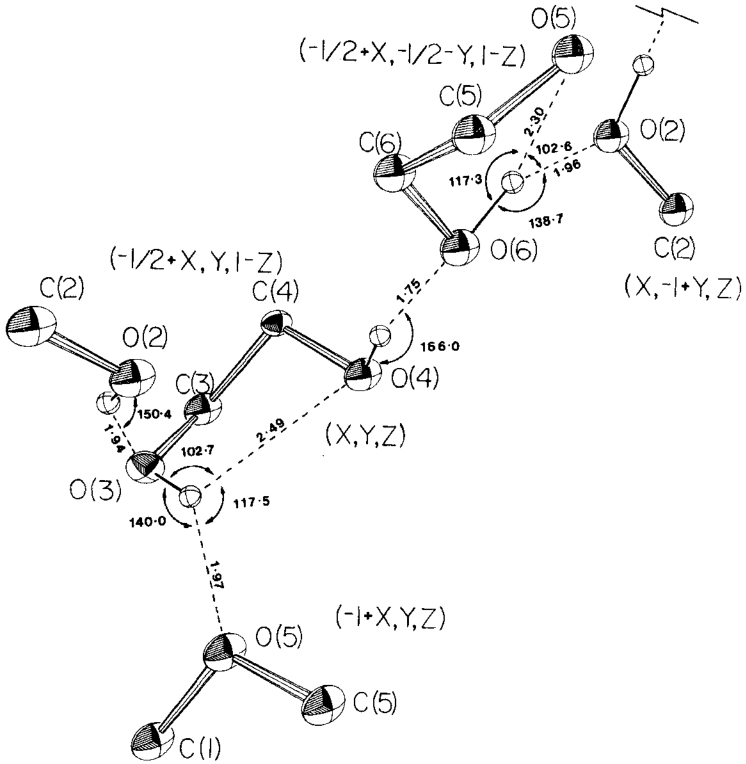


FIGURE 3 Hydrogen-bonding in the crystal structure of heptyl 1-S-α-D-mannopyranoside.[10]

The structures of the intermediate crystalline phases and of the liquid crystal phases are not known in detail. It is presumed, but remains to be proved, that the intermediate phases correspond to the onset of rotational disorder in the alkyl chains, leading to a disengagement of the intercalation at the transition to the liquid crystal.

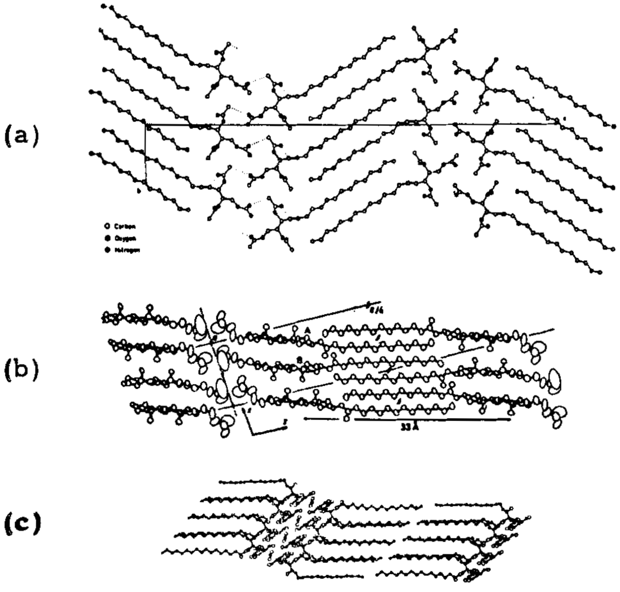


FIGURE 4 The intercalated alkyl chain packing in (a) triacetylsphingosine,[16] (b) cholesteryl myristate.[14] (c) The non-intercalated alkyl chain packing in the cerebroside, β-D-galactosyl-N-(2-D-hydroxyoctadecanoyl)-D-dihydrosphingosine.[16]

The liquid crystal molecular clusters would then consist of double layers of hydrogen-bonded carbohydrate moieties of variable extension in two dimensions, with a well-defined thickness corresponding to the width of the hydrogen-bonded carbohydrate layer plus the width of two thermally disordered alkyl chains. The correspondence between the major liquid crystal diffraction periodicities and the double layer distances in the mesogenic crystal structure supports this hypothesis.

5. SYNTHESIS OF ALKYL GLYCOSIDES

The preparation of alkyl glycosides involves relatively simple procedures which have been described by a number of investigators: n-alkyl-β-D-xylopyranosides,[17] n-alkyl-1-thio-β-D-xylopyranosides,[18,19] n-alkyl-α-D-gluco- and mannopyranosides,[20] and n-alkyl-β-D-glycosides.[21]

6. RELATIONSHIP TO THE GLYCOLIPIDS

Apart from their intrinsic interest as potentially useful and relatively benign mesogens, some of which may have transitions near body temperatures, the alkyl and acyl glycosides can be used as "membrane mimics"[3] i.e., structurally accessible models for simulating the phase behavior of the more complex biological glycolipids, of which there is a wide variety (Table III), very few of which have been obtained pure and crystallized.

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TABLE III Naturally occurring carbohydrate-lipids.

Carbohydrate moiety	Lipid moiety	Linkage	Distribution
glucose, galactose, mannose, uronic acids	diglycerides	glycosides	bacteria, plants, animals
glucose, sophorose, cellobiose, rhamnose	hydroxy acids	glycosides	fungi, plants, bacteria
glucose, galactose, sailic acids, amino sugars	ceramides	glycosides	animals
α,α-trehalose	lauric, palmitic, myristic, mycollic acids	ether	cord factors, mycobacteria
myo-inositol	phytoceramides		plants, fungi
N-acetyl glucosamine	hydroxy acids	amide	lipid A in gram negative bacteria

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