electrodes.[28i] It has been determined that the photoactive material is the titanium dioxide. The authors have suggested that this photoelectrochromic effect may find application in an erasable optical signal recording system.

Bocarsly et al. have recently reported that semiconductors such as cadmium sulfide are dramatically stabilized against corrosion in the presence of ferrocyanides due to the formation of insoluble cadmium cyanoferrates at the surface.[57] Kaneko et al. have used a dispersion of Prussian blue and a ruthenium complex to carry out photolysis of water.[58] It is interesting to note also that PB films have recently been used as a standard for ellipsometry and Fourier transform photoacoustic spectroscopy.[38d,60,61]

Concluding Comments

We have attempted to describe some new electrochemical perspectives in relation to some very old materials. It has been emphasized that the electrochemical behavior of the prototype compound itself is not fully understood. The structure, stoichiometry, ionic permeability, and electrochemical reactions of PB films deserve further consideration.

We have also attempted to describe the electrochemistry of a few of the cyano analogues of PB. This is a huge class of compounds and they are not all cubic. There are insoluble planar sheet-like structures (e.g., nickel) and linear structures (e.g., silver).[10] We anticipate that a large number of new modified electrode polynuclear cyano complexes will be studied in the near future.

Finally, we have noted a few recent applications of these materials. Here we believe there is great potential for future development. The chemical stability, ease of preparation, and low cost of many metal cyano films are important factors which may lead to a variety of new applications in electrochemistry, electrooptics, and electronics.

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Carbohydrate Liquid Crystals

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Lyotropic liquid crystal behavior is of interest to molecular biologists because of the amphiphilic chemical constitution of membrane components. As the name implies, this is a dissolution property. The implication that liquid crystal phase transitions play an important role in the organization and functioning of cells and tissues is long-standing.[1-3] *Thermotropic* liquid crystal behavior is a solid-state phenomenon caused by the application of heat. It is of particular interest to physicists,[4] since it forms the basis of electrooptical devices. Recently the liquid crystalline state has become important in polymer physics because of its role in the manufacture of high-performance fibres.[5]

Because carbohydrate chemists are neither molecular biologists nor solid-state physicists, they have been slow to exploit their potential for synthesizing a very large number of carbohydrates which have liquid crystal properties. A few *n*-alkyl 1-*O*-glycosides are available from commercial sources because they are used as detergents for cell wall membranes.[6-8] Some *n*-alkyl 1-*S*-glycosides have been synthesized because of their potential for selectively affecting cell surfaces and for use as enzyme substrates.[9-11]

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Emil Fischer in 1911 noted the *double melting point* of some long-chain *n*-alkyl pyranosides,[12] and, in 1938, this was recognized as evidence for the formation of thermotropic liquid crystals,[13] but until recently there has been no sustained interest.

No carbohydrates were included in a compendium of 7000 thermotropic liquid crystals, published in 1973.[14] Of the more than 5000 references under the liquid crystal descriptor in the *Chemical Abstracts* Indices from 1976 to 1981, there is only one to the alkyl glucopyranosides.[15]

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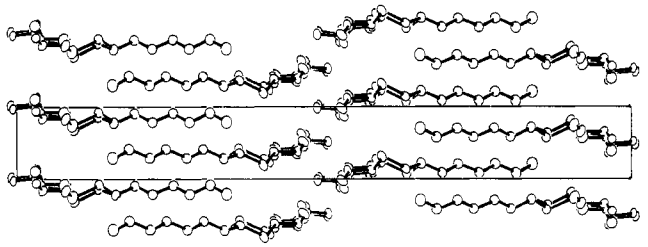

Figure 1. Head-to-head bilayer molecular packing in the crystal structure of heptyl 1-*S*-α-D-mannopyranoside.[16]

X-ray crystallographers are most at ease with experiments where the observation-to-parameter ratios exceed ten to one. For this reason, the study of liquid crystals by diffraction methods is not popular. Of the 3600 abstracts for the 13th International Congress of Crystallography in 1984, only three referred to liquid crystals.

The author's interest in the field was therefore serendipic. A crystal structure analysis of heptyl 1-*S*-α-mannopyranoside,[16] for reasons concerned with the exo-anomeric effect, revealed the molecular packing shown in Figure 1. A visit to a colleague's office showed a match to the structure of cholesterol myristate,[17] a well-known liquid crystal mesogen which also has a bilayer structure with interdigitizing alkyl chains. Similar analogies are to be found with the molecular packing of other mesogens, such as the alkyl benzoic acids[18] and salt alkyl ammoniates.[19]

Optical and X-ray diffraction quickly confirmed that the crystalline heptyl thiomannoside transformed to a liquid crystal phase at 60 °C. This was just prior to a Carbohydrate Gordon Conference where an announcement of this result led to a supply of some long-chain alkylated glycosides, which had been synthesized for reasons quite apart from their liquid crystal properties.[9,10]

On the basis of X-ray diffraction and optical examinations of these compounds, we concluded that the chemical constitution necessary for a *mesogenic* mono-, di-, or oligosaccharide is that the sugar moiety is linked to an *n*-alkyl chain containing more than six carbon atoms. The sugar moieties can be cyclic or acyclic, and must have some unblocked hydroxyl groups. Full acetylation of the carbohydrate component or the substitution of polar function groups, such as –OH, –Cl, –C≡N at the terminus of the alkyl chains prevented liquid crystal formation.[20] Even with these limitations, there can be great constitutional variety, not only in the sugar and the alkyl chain length, but also in the type of linkage and its position of attachment to the sugar molecule. Clearly, O–, C–, N–, or S–glycosyl, acyl, ester, amide, and glyceryl are all possible linkages. The permutations of the *n*-alkyl chains and linkages with the variety of sugar moieties gives an estimate of several million potential carbohydrate liquid crystals. Hitherto, few have been synthesized, or, if synthesized, recognized as mesogens. Others may be hidden in the literature, as, for example, the report of a "double melting point" for 1-*O*-hexadecanoyl-α-D-glucopyranose.[21]

Table I
Crystal Transition Temperatures, Melting Points, and Clearing Points of Known Carbohydrate Mesogens

compd	transition, °C	MP, °C	CP, °C	ref
1-*O*-β-D-glucopyranoside:				
heptyl	56	59	69	*a*
octyl	57–60	67–69	106–110	*a, b, c*
nonyl	51–66	68–71	113	*a*
decyl	65–68	70–75	133–137	*a, d*
dodecyl	55, 63	80	142	*d*
1-*O*-α-D-glucopyranoside:				
heptyl		53	99	*d*
octyl	52	55–72	116	*b, c*
nonyl		57–65	113–130	*d*
decyl[j]		73–76	130–138	*d*
dodecyl		70–77	137–151	*d*
hexadodecyl		108	170–175	*e*
decyl 2-*N*-acetylglucosamide	60–67, 82	93	186	*f*
3-*O*-glucoses:				
nonanoic		105–107	130–132	*g*
decanoic		103–106	138–140	*g*
dodecanoic		105–108	152–154	*g*
heptyl 1-*S*-α-D-mannopyranoside[j]		60	151	*h*
1-*S*-β-xylopyranoside:				
heptyl	72	97	105	*a*
octyl[j]	57	100	114	*a*
D-gluconamide:				
heptyl	79, 96	150	156[k]	*c*
octyl[j]	72, 87	158	159[k]	*c*
nonyl	84, 99	159	175[k]	*c*
decyl	75, 91	157	182[k]	*c*
undecyl	77, 99	157	190[k]	*c*
dodecyl	81, 94	155	189[k]	*c*
dodecyl 1-*O*-β-maltoside		102	>245[k]	*c*
octadecyl maltobionamide	56	110	>207[k]	*c*
hexadecyl ascorbate	47, 76	112	160	*i*

[a] Reference 20. [b] Dorset, D. L.; Rosenbusch, J. P. *Chem. Phys. Lipids* **1981**, *29*, 299–307. [c] Reference 36. [d] Reference 15. [e] *Reference* 21. [f] *Reference* 31. [g] Köll, P., private communication, 1985. [h] *Reference* 16. [i] Goodby, J. W., private communication, 1985. [j] Includes crystal structure determination. [k] Onset of decomposition.

Table I gives a list of carbohydrates which have been shown to have thermotropic liquid crystal properties. Hitherto, there are no examples of mesogens with more than one alkyl chain. However, *n*-alkyl substitution at three or more positions around an inositol ring has been shown to give rise to *discostic liquid crystals*.[22] These are based on a different structural principle from the rod-like or *calamitic n*-alkyl glycosides studied by us.

Why Do the Molecules Shown in Table I Form Liquid Crystals?

An amphiphilic molecule is one which contains moieties with differing physical properties. Carbohydrates are characteristically soluble in water and polar solvents; hydrocarbons are insoluble in water and soluble in nonpolar solvents. It is this dichotomy that gives rise to lyotropic liquid crystal formation.

Carbohydrates form relatively hard crystals with high melting points, since their principal cohesive forces are

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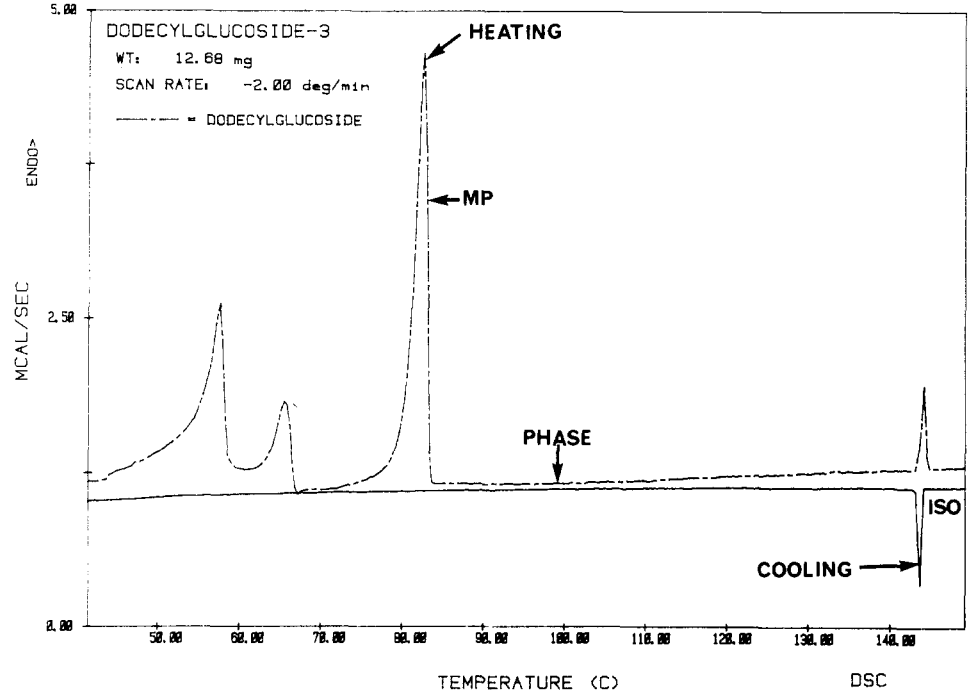

Figure 2. The heating and cooling differential scanning calorimeter curves for dodecyl 1-*O*-β-D-glucopyranoside.[30]

hydrogen bonds. Hydrocarbons form soft crystals with low melting points, since their cohesive forces are van der Waals. Thermotropic liquid crystal formation can therefore be thought of as a two-stage melting process, as, in fact, described by Emil Fischer.[12] The hydrocarbon chains disengage from the three-dimensional crystal lattice first, at the so-called *melting point*. The hydrogen-bonded carbohydrate moieties "melt" at a higher temperature because their cohesive forces are the stronger bonds. In consequence, the clusters of ordered molecules necessary for the liquid-crystalline state are retained past the melting point, even though the three-dimensional order of the crystal structure is lost. At a higher temperature, the *clearing point*, these hydrogen-bonded clusters melt to form an isotropic homogeneous liquid. A similar principle applies to the *n*-alkyl benzoic acid mesophases, in which the benzoic acid moieties form hydrogen-bonded dimers, cohering by means of their stacking forces, more strongly than do the alkyl chains.[18,23] Just as the difference in the hydrogen-bonding and van der Waals cohesive forces acting on the two parts of these molecules gives rise to *thermo-mesophases*, so the difference in solubilities of the two parts of the molecules gives rise to *lyo-mesophases*. Many of the compounds given in Table I are surfactants and are expected to form lyotropic liquid crystals in appropriate solvents at appropriate temperatures and concentrations. A study of the smectic A phase of *n*-decyl β-D-glucopyranoside, which persists with up to 20 percent water, indicates that it is thermodynamically identical with the well-known *lyotropic lamellar* phase of Aerosol OT [sodium bis(2-ethylhexyl) sulfosuccinate].[24]

The Recognition of Mesophases

Lyotropic liquid crystal formation occurs in a polar solvent when the nonpolar tails of the amphiphilic molecules aggregate so as to expose only the polar head groups to the solvent molecules. In a nonpolar solvent, the reverse takes place. These molecular clusters arrange in particular patterns which are described as *laminar* (*neat*), *hexagonal* (*middle*), or *cubic* liquid crystals.[5] The macroscopic observation of lyotropic liquid crystal formation is an increase in the opacity of the solution, abnormally high viscosity, and changes in thermodynamic properties.[25] In some compounds, this is accompanied by a gel formation from a dilute solution that may surprise the carbohydrate chemist. In the *n*-alkyl gluconamides, the gels have been shown by electron microscopy to have a substructure consisting of chiral fibrillar ropes with diameters of 70 to 550 Å.[26]

As discovered by Friedel in 1922,[27] the most interesting way to observe thermotropic liquid crystal formation is with a polarizing microscope equipped with a heating stage.[28] The crystal-to-crystal transitions, which commonly precede the mesophase transition, can be recognized by changes in the birefringence with no melting of the crystals. At the melting point, which is the transition to the liquid crystal, the crystals change their morphology, but retain their birefringence. With thin crystals, pleochrism is observed. At the transition to the liquid phase, the clearing point, the birefringence disappears. Experts with the polarizing microscope can identify the liquid crystal phase by inspection of its morphology and by the miscibility properties with a reference liquid crystal of known phase.[29]

The temperatures and enthalpies of the phase transitions are best measured with a differential scanning calorimeter, which gives a *thermogram* such as that of

(23) Bunning, J. D.; Lydon, J. E. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1621.
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dodecyl 1-*O*-β-D-glucopyranoside,[30] shown in Figure 2. These show the temperatures of the crystal-to-crystal phase transitions as well as the large enthalpy change at the melting point. Hysteresis always occurs and, except for the clearing point temperature, the transition temperatures differ on the heating and cooling D.S.C. thermograms. When the liquid crystal phase is observed on both heating and cooling, it is said to be *enantiotropic*. When observed only on supercooling, it is *monotropic*. With carbohydrates, these transition temperatures are sensitive to the rates of heating and cooling, to the history of the sample, and to the impurities by decomposition products, for example. For these reasons, they may not be exactly reproducible between samples and investigators. The clearing point is generally more definitive than the melting point, both of which should be reported from the first heating cycle, since the heating and cooling curves always show considerable hysteresis.

Some of the *n*-alkyl glycoside liquid crystal phases have been studied by X-ray powder diffraction.[31] They give characteristic patterns having a single intense line with a d-spacing greater than the overall length of a single molecule. Despite their obvious potential as model compounds for their more complex biological cousins, these compounds have not been studied by the powerful combination of thermal analysis, X-ray diffraction, and IR and NMR spectroscopy, as was applied to the lecithins, for example.[32] The new methods of ^{13}C CP-MAS solid-state NMR spectroscopy combined with conventional solution methods would now seem to be a promising tool for studying these phase changes in these carbohydrate systems.[33-35]

Phase Behavior of Carbohydrate Liquid Crystals

Both lyo- and thermo-mesophase formation are accompanied by sequences of phase transitions that may be crystal-to-crystal, crystal-to-mesophase, or mesophase-to-mesophase. With lyotropic liquid crystals, these occur with changes in concentration or temperature from a solution through a sequence of liquid crystal phases to a gel. This gel may be metastable and convert to microscopic or macroscopic crystals.

With thermotropic liquid crystals, a sequence of crystal-to-crystal phase transitions precedes the liquid crystal phase or a sequence of liquid crystal phases. In the carbohydrates, two or more crystal-to-crystal phase changes are observed prior to the melting point, but hitherto only one liquid crystal phase has been observed between the melting and clearing points.[30,31,36] The acyclic derivative, 1-*O*-*n*-tetradecyl-D-mannitol,[37] has three crystal-to-crystal phase transitions at 63, 77, and 97 °C prior to melting to a liquid crystal at 115 °C and an isotropic liquid at 185 °C.

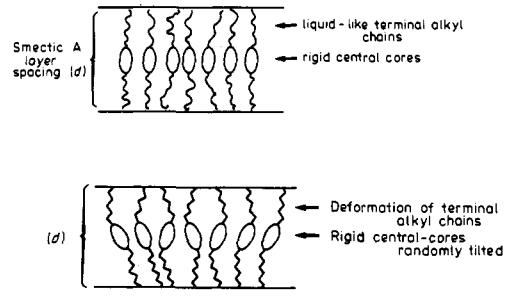

Figure 3. Models for the molecular structure of the smectic A liquid crystal phases.[29]

As yet we have no direct structural information about the conformational or reorientational changes that take place in these pre-liquid-crystal transitions. It is tempting to predict that these transitions are associated with the formation of kinks or the onset of conformational disorder in the alkyl chains similar to that studied by X-ray diffraction in the $ZnCl_4$ *n*-alkyl ammoniates[38] and by ^{13}C NMR spin-lattice relaxation times in alkanes[39] and biological membranes.[40]

The Structure of the Liquid Crystalline Phases

The three-dimensional molecular structure of a crystal can be uniquely determined with considerable precision by X-ray and neutron diffraction. It is described in terms of the space group symmetry, unit cell dimensions, and the positional and thermal parameters of the atoms. In a liquid, this is replaced by the one-dimensional probability distribution function. From the informational point of view, liquid crystals are much closer to liquids than to crystals. For example, the thermotropic carbohydrate liquid crystals of heptyl α-D-mannopyranoside[16] and octyl 1-*S*-β-D-xylopyranoside[41] show only one "powder diffraction" spectrum, indicating that periodicities of 22 and 30 Å respectively persist in the liquid crystal state. These periodicities are greater than 1 but less than 2 times the respective molecular lengths. From this it is deduced that the clusters contain molecular bilayers in which the rod-like molecules are inclined at an angle, as they are in the crystal structures. As with liquids, the interpretation of this, and any other type of experimental measurement on liquid crystals, is, more or less, model-dependent and is never unique.

From the physicist's point of view, the conventional models in which molecules, or clusters of molecules, are represented as rods, are adequate. The chemist or the crystallographer, who is more conscious of the actual shape of molecules, needs a more detailed picture, such as that shown in Figure 3 for a smectic A liquid crystal.

Liquid crystals are classified into *nematic*, *cholesteric*, and a bewildering variety of *smectic* structures (from A to I) which are identified by their X-ray diffraction and optical properties.[27,28] The carbohydrate liquid crystals hitherto examined are the smectic A type.[30,36] Although the potential for chirality is present

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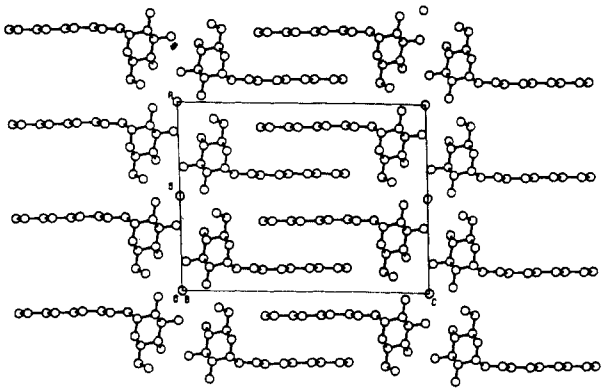


Figure 4. Head-to-head bilayer molecular packing in the crystal structure of octyl 1-*O*-α-D-glucopyranoside.[42]

in the sugar moiety, no cholesteric phases have yet been found.

The Mesogenic Crystal Structures

Crystal structure determinations have been carried out for six of the carbohydrate thermotropic mesogens given in Table I. Heptyl 1-*S*-α-mannopyranoside,[16] octyl 1-*S*-β-xylopyranoside,[41] octyl 1-*O*-α-glucopyranoside and its hemihydrate,[42] and decyl 1-*O*-α-glucopyranoside[43] have similar crystal structures. As illustrated in Figures 1 and 4, the carbohydrate moieties are hydrogen-bonded to form *head-to-head* bilayers which extend throughout the crystal in two dimensions. The alkyl groups pack tail-to-tail, with interdigitated chains. This is the common type of packing observed in the crystal structures of other mesogens, such as the zinc chloride alkyl ammoniates,[19] cholesteryl myristate,[17] triacetylspringosine,[44] glycosylphytospringosine hydrochloride,[45] and 1-octadecyl-2-methylglycerophosphocholine monohydrate.[46]

Quite different molecular packing is observed in the acyclic carbohydrate structure, *n*-octyl glucamide,[47] shown in Figure 5. In this crystal structure, the sugar moieties are hydrogen-bonded to form monolayers and the alkyl chains do not interdigitate. The packing is *head-to-tail.* Noninterdigitated packing of alkyl chains is observed in the cerebrosides, β-D-galactopyranosyl-*N*-(2-D-hydroxyoctadecanoyl)-D-dihydrospringosine,[45] and *N*-tetracosananoylphytospringosine and its hemihydrate,[48] but these are bilayer structures, with head-to-head packing.

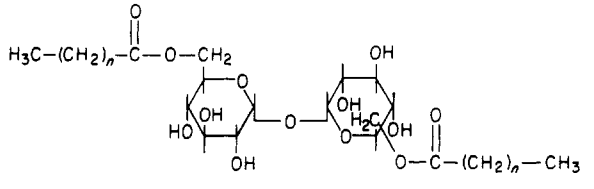
What Role Does Hydrogen-Bonding Play in the Formation of Liquid Crystal Phases?

When the author asked a colleague more familiar with liquid crystals why this vast reservoir of liquid crystal compounds had not been explored previously with any enthusiasm, the response was that it is well-known that carbohydrates form hydrogen-bonded structures and hydrogen-bonded structures do not form liquid crystals. In fact, hydrogen-bonding appears to play a critical role in the liquid crystal formation. In contrast to the alkyl glycosides, some long-chain alkyl purine derivatives, which have the same interdigitated bilayer molecular packing in the crystal, have no liquid crystal phases.[49] Presumably, the hydrophilic purine "*cores*" are not bound strongly enough by the weaker noncooperative NH——N bonds that the molecular clusters, necessary for the liquid crystal phase, survive the thermal motion between the highest temperature crystal phase and the liquid.

The Biological Connection

Amphiphilic molecules involving sugar moieties and alkyl chains are widespread in plants and bacteria. In a general class of natural products, known as glycolipids, the mono- and disaccharides, arabinose, glucose, galactose, mannose, rhamnose, fucose, various amino sugars, cellobiose, sophorose, and trehalose are combined with long-chain fatty acids, hydroxy acids, polyols, and ceramides through glycosidic, ester, and amide linkages. Because neither the macromolecules nor their amphiphilic subunits can be readily crystallized, there is very little information concerning their secondary or tertiary structures. Molecules of this type are implicated in the mechanisms of membrane transport. The model generally adopted for the membrane structure is a bilayer with nonintercalacting chains similar to that observed in the cerebrosides. There is much speculation concerning the role of the liquid crystal state in membrane processes, but the structural information at atomic resolution is as sparse for membranes as it is for the simpler liquid crystal systems.

Two carbohydrate systems of particular interest are the "cord factors" and the lipid A components. The descriptor "cord factor" was originated by Koch[50] in 1884 to describe the microscopic appearance of material extracted from tubercle bacteria. Tuberculosis was an endemic disease at that time, and Koch sought a connection between infection and these exotic macroscopic structures, which were probably the strings of microcrystals often formed from metastable lyotropic gels. His paper is worth reading for the Audabon quality of the illustrations. Cord factor is now applied to the mycollic esters of α,α′-D-trehalose, I.[51,52] The synthesis



(I)

of these and related compounds has recently been stimulated by reports of their immunostimulant and antitumor properties.[53,54]

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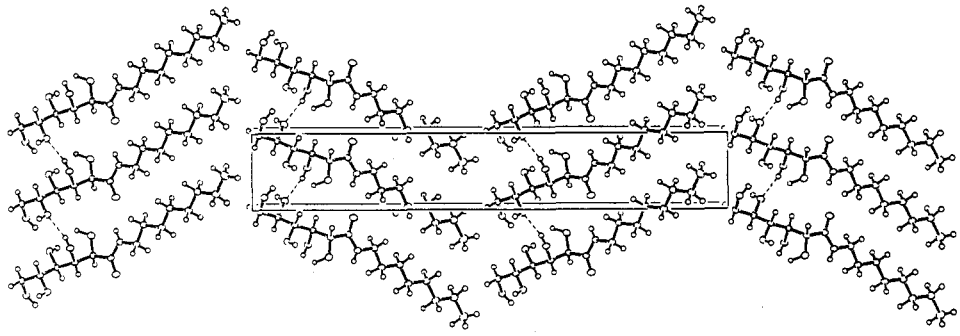

Figure 5. Head-to-tail monolayer molecular packing in the crystal structure of octyl glucamide.[47]

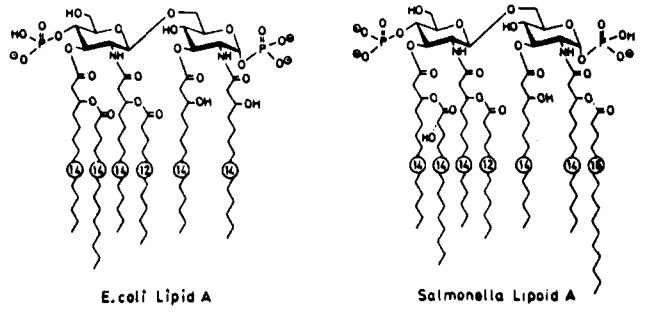

Figure 6. Proposed configurations for *E. coli* Lipid A and *Salmonella* Lipid A.

Related configurations are proposed for the lipid-A moieties, shown in Figure 6, which form the terminus of the endotoxic polysaccharides from salmonella *E. coli* and other bacteria.[55,56] These compounds are also difficult to isolate, purify, and crystallize, and nothing is reported concerning their lyotropic or thermotropic properties.

Concluding Remarks

As in all aspects of biological structure, major advances in this field will occur when there is sufficient homogeneous natural or synthetic material available to permit the growth of the diffraction quality crystals necessary for unambiguous molecular structure determinations. However, direct structural studies on the liquid crystal phases will always be difficult and ambiguous due to the limited degree of molecular order. The simple carbohydrates which we have been describing appear to offer useful structural and thermodynamic model systems by means of which both the connections between the crystal-to-crystal phase transitions and the thermotropic and lyotropic phases can be explored.

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