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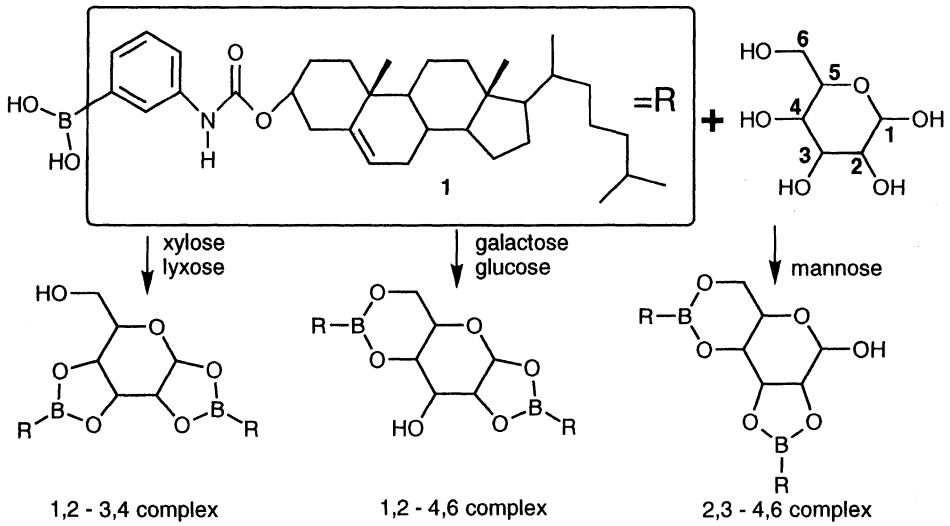
Chiral Discrimination of Monosaccharides through Gel Formation

Tony D. JAMES, Kazutaka MURATA, Takaaki HARADA, Keiko UEDA,
and Seiji SHINKAI*
CHEMIRECOGNICS Project, ERATO, Research Development Corporation of Japan, 2432-3,
Aikawa-cho, Kurume, Fukuoka 830

The cholesterylphenylboronic acid (**1**) and its complexes with mono saccharides (2:1; **1**/monosaccharide) were prepared. Many of the isolated complexes form gels in a variety of solvents, some of which display D *vs* L chiral discrimination. This is the first example of chiral discrimination in a saccharide based gel system.

The cholesterol moiety provides an excellent platform on which it is possible to build or design systems for molecular recognition.[1-4] Since the cholesterol unit itself possesses inherent intermolecular cohesion, "readable" outputs can be generated from functional appendages introduced to modify the natural intermolecular packing; that is to say the bulk amplifies individual "molecular recognition" events.

Recently a new class of cholesterol-based gels, held together by weak hydrogen bonding or van-der-Waals interactions were reported.[5-7] Our interest was sparked, since we have previously nurtured cholesterol derivatives bearing crown ether, azobenzene or boronic acid moieties.[8-14] Our continuing theme is the development of signal-responsive chemistry; employing molecular transducers capable of translating host-guest interactions into readable outputs. Gelation has provided us with a new medium in which to explore such interactions, we met with an early success, the sol-gel phase transition temperature (T_{gel}) can be controlled by both metal cations and photo isomerization of the azobenzene moiety.[12]



1,2 - 3,4 complex　　1,2 - 4,6 complex　　2,3 - 4,6 complex

As we previously reported [14] cholesterol-bound saccharides have a dramatic influence on the pitch length in mixed cholesteric liquid crystals. Addition of 2 or 3 mol% of the 2:1 saccharide complex to a composite liquid crystal membrane alters the pitch in a direction relative to the absolute configuration of the complexed saccharide. This change could be read-out by eye as a color change in the liquid crystal. In this paper we present a novel cross link between the liquid crystal system and the gelation abillity of this type of complex.

Table 1. Results of the Gelation Tests Caried Out with Monosaccharide Complexes [a]

Solvent	Lyxose		Xylose		Mannose		Glucose		Galactose	
	D-Blue[b]	L-Red[b]	D-Red[b]	L-Blue[b]	D-Blue[b]	L-Red[b]	D-Red[b]	L-Blue[b]	D-Blue[b]	L-Red[b]
Hexane	SW	SW	I	I	I	I	I	I	I	I
Benzene	G	G	G	G	S	R	S	I	G	G
Toluene	G	G	G	G	I	G	S	I	G	G
Dichloromethane	G	G	G	I	I	Gc	S	I	G	Gc
Chloroform	G	G	G	G	Gc	G	S	I	S	S
Carbon disulfide	G	G	G	SW	G	G	I	I	S	S
Diethyl ether	I	S	SW	I	R	S	I	I	S	S
Tetrahydrofuran	S	S	S	S	I	S	I	I	S	S
1,4-Dioxane	G	S	S	G	S	S	S	S	S	S
Ethyl acetate	S	S	R	R	S	S	R	I	S	S
Acetone	R	S	R	R	R	R	R	R	I	R
Methanol	R	R	R	I	I	I	I	I	I	I
Ethanol	S	S	S	I	R	R	R	I	R	R

a) [Gelator]=0.1-5 wt%; Gel formed when cooled to 23 °C (G) or cooled in a refrigerator to -7 °C (Gc); Gel not formed because of crystallization (R), soluble (S), or insoluble (I), SW=swollen.
b) Colour induced in composite liquid crystal membrane.

Solvent extraction of saccharides was carried out at 25 °C using solid-liquid ($CDCl_3$) extraction. Characterization of the extracted saccharides could be achieved employing ^1H NMR spectroscopy ($CDCl_3$). The molar ratio of the extracted species could be conveniently estimated by the integral intensities of selected proton resonances of the monosaccharide versus either the phenyl or the alkenyl protons of compound **1**.[14] It was established on the basis of ^1H NMR spectral analysis that all the saccharides form a 1:2 complex with compound **1**. Two main structural classes exist for the extracted monosaccharides, either, two five membered rings are formed (1,2-3,4 complex), or a five and a six membered ring are formed (1,2-4,6 and 2,3-4,6 complexes).

The gelation test was carried out as follows: the complexes (0.1-5 wt%) were mixed with solvent in a septum-capped test tube and the mixture was heated in hot water at 60 °C until the solid was dissolved. (I in Table 1 denotes that at this temperature and 0.1wt% the complex was insoluble) The solution was cooled to room temperature (G in Table 1 denotes that a gel is formed at this stage). In the case that a gel was not formed at room temperature, the solution was cooled in a refrigerator (at -6 °C) for one day

(Gc in Table 1 denotes that a gel was formed at this stage). If no gel formed at 0.1wt% the wt% was gradually increased up to a maximum of 5wt% (S in Table 1 indicates that at 5wt% no gel was formed). The results are summarized in Table 1.

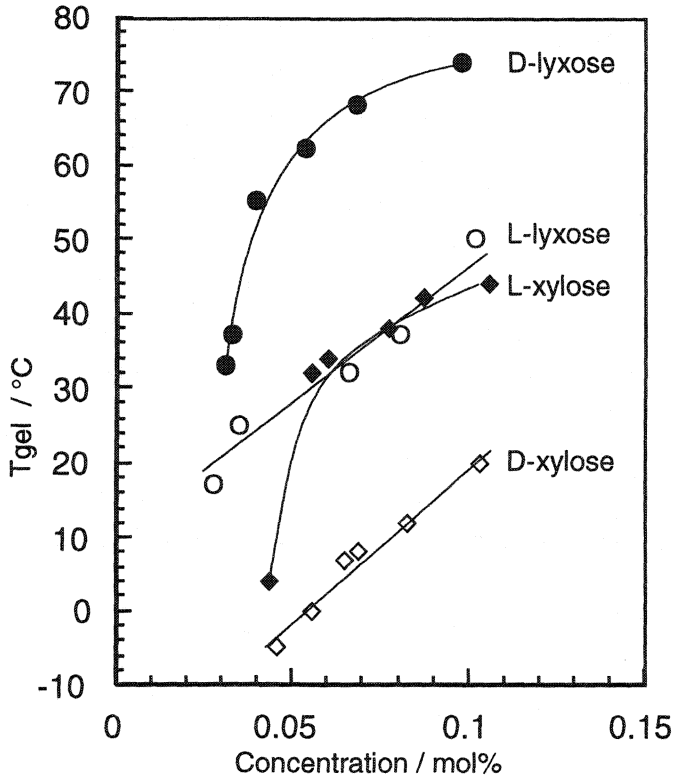


Fig. 1. Gel-solution phase transition temperature (*Tgel*) in chloroform versus the mol% of complex.

Inspection of Table 1 reveals an interesting general trend: optical pairs of saccharides lie at different points along a path of increasing molecular interaction; the path from solution to crystallinity. From our previous work with composite liquid crystal membranes red shift complexes increase the pitch and blue shift complexes decrease the pitch of the liquid crystal membrane. Obviously factors that work to increase the pitch act to reduce molecular interaction, likewise a decrease in pitch can be correlated with an increase in molecular cohesion. With carbon tetrachloride as solvent: L-lyxose (gel), D-lyxose (insoluble); D-xylose (gel), L-xylose (insoluble); L-mannose (gel), D-mannose (insoluble); D-glucose (solution) and L-glucose (recystalizes). For the chiral pairs of complexes the former are predicted to have weak cohesion from the liquid crystal work (red shift), and the latter strong intermolecular cohesion (blue shift). This prediction clearly holds under this set of conditions, and from further inspection of Table 1 it can be seen that this is a general trend for all solvents.

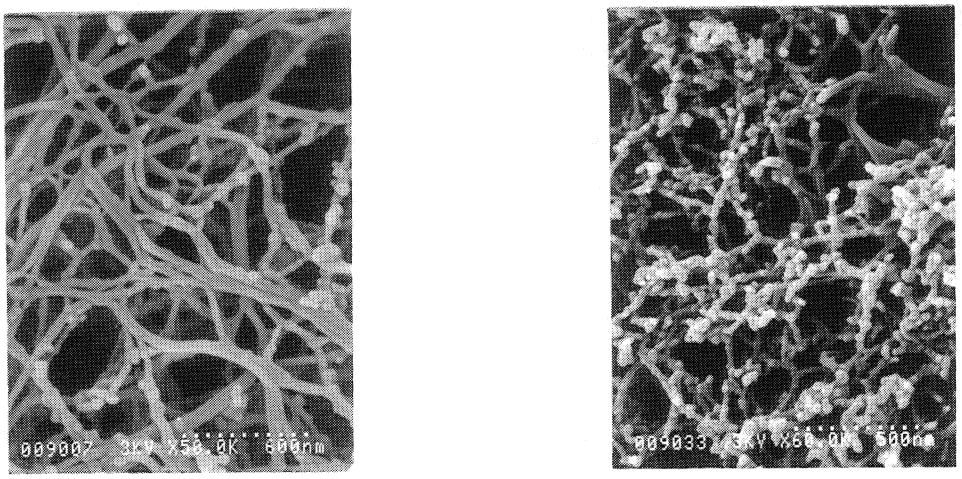


Fig. 2. SEM pictures for the gels formed in benzene from D-lyxose (right) and L-lyxose (left).

With the monosaccharides lyxose and xylose in certain solvents both isomers form gels, but the relative stability of the gel is not the same. The stability of the gel can be conveniently ascertained by plotting the sol-gel phase transition temperature versus mol% of the complex (Fig. 1). From Fig 1 it is clear that L-xylose and D-lyxose have strong intermolecular interactions (blue shift) whereas D-xylose and L-lyxose posses weak intermolecular interactions (red shift). For further evaluation of the gel phase both SEM (Fig. 2) and CD spectroscopy were preformed on the gels produced by the D- and L-xylose complexes. The the CD spectra of the optical pairs are inverted, implying a different chirality exists in the two gels. (D-xylose: λ_{min} 290nm, $[\vartheta]_{max}$ -8000 deg cm^2 $dmol^{-1}$ and L-xylose: λ_{max} 302nm, $[\vartheta]_{max}$ +4000 deg cm^2 $dmol^{-1}$) However, it is unclear if the band observed is a simple single Cotton or an exciton band, the absolute chirality of the gels is therefore not assigned. The SEM pictures (Fig. 2) show that open fiberous gels are formed by these complexes; twists are also clearly visible but these strucures are too large for individual fibrils and so must be the result of multiple copies intertwining (super helixes). Both, the CD and SEM results confirm that the cholesterol moiety is preforming a similar task in the gel and liquid crystal system; holding together a chiral helix.

In corollary, this work represents a rare example of monosaccharide gelation. Also, the gelation ability of the complexes is controlled in a predictable manner by the chirality of the monosaccharide. This description of saccharide chirality is general since it is confirmed by the predictions made in the liquid crystal system.[14]

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